Organocatalytic Asymmetric Electrophilic Amination of Allylic Boronates

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GENERAL

All the NMR spectra were recorded on Inova 300 MHz, Gemini 400 MHz or 600 MHz Varian or Bruker spectrometers for ^{1}H, 101 MHz and 151 MHz for ^{13}C, 192 MHz or 193 MHz for ^{11}B. The chemical shifts (δ) for ^{1}H, ^{13}C are given in ppm relative to internal standard TMS (0.0 ppm) or residual signals of $CHCl_3$ (7.26 ppm). The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. Purification of reaction products was carried out by flash chromatography (FC) on silica gel (230-400 mesh). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. High Resolution Mass Spectra (HMRS) were obtained from the Mass Facility unit on a Waters Xevo Q Tof spectrometer. Optical rotations were measured on a Perkin Elmer 241 Polarimeter provided with a sodium lamp and are reported as follows: $[\alpha]_{\mathrm{D}}^{\mathrm{rt}}$ (*c* in g/100 mL, solvent). Unless otherwise noted all reactions were set up in the air and using undistilled solvent, without any precautions to exclude moisture.

Materials

Commercial grade reagents and solvents were used without further purification; otherwise, where necessary, they were purified as recommended.[1] (*E*)-2-(but-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **1aa**, azodicarboxylates **2a**, **2b** and **2c**, catalysts **A**, **B**, **D**, **E**, **F**, **G** and ***ent*-G** were purchased from suppliers. Boronic esters **1ba-1ea**, **1cb-1cw** and **N-1c** were prepared according to the literature procedure with some modifications.[2] Catalysts **C**, **H**, **I**, **L**, **M**, **N** were prepared according to the literature procedures.[3, 4, 5, 6]

Determination of Enantiomeric/Diasteromeric Purity

The enantiomeric ratio (e.r.) was determined by HPLC analysis on chiral stationary phase on an Agilent 1100- and 1200-series instrumentation using mixtures of i-PrOH/hexane as the eluent or by GC analysis on an Agilent 6890 equipped with a Rt-BetaDex-sm (30 m length x 0.32 mm ID x 0.25 μ m film thickness) with hydrogen as carrier gas (2.0 mL, spilt ratio 50:1) and using the following conditions: 120 °C, 2 min then 2 °C/min up to 230 °C, 5 min; injector : 230 °C, FID detector: 230 °C. HPLC and GC traces of enantioenriched products were compared to racemic ones obtained from the reaction using catalyst ***rac*-G**. Only for compounds **3u** and **3u'** the diasteromeric ratio was measured by ^{1}H NMR analysis at 100°C.

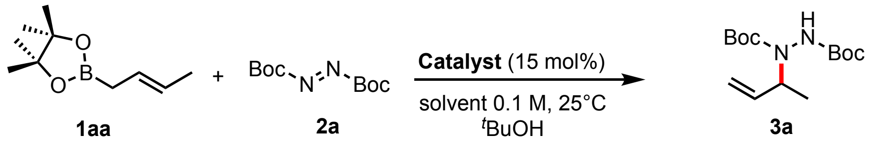
Calculations

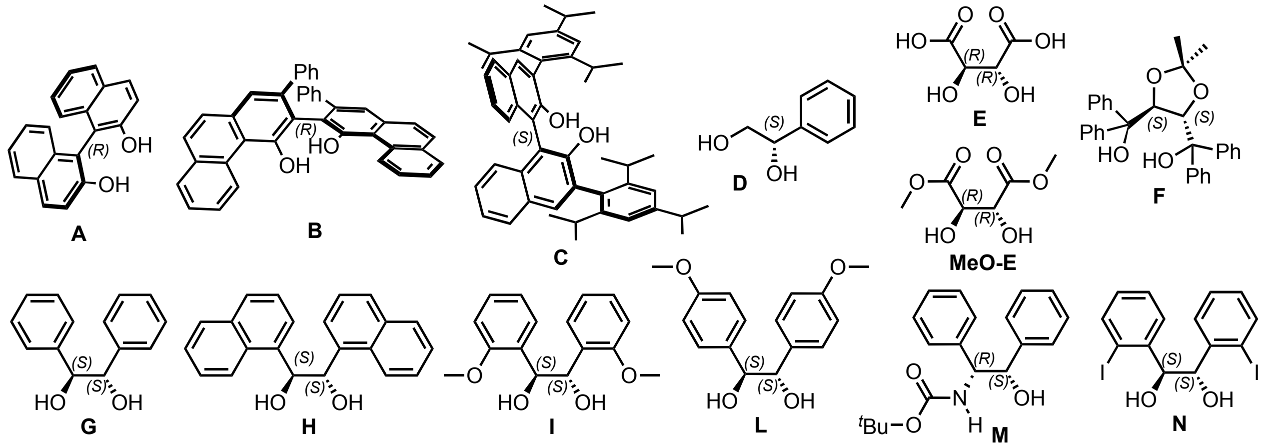
Each structure has undergone a process of conformational research and subsequent refinement. The conformational search has been performed using CREST (version 2.12)[7] with the iMTD-GC algorithm using as an implicit solvent the wet octanol with the ALPB model.[8] To reduce the number of conformers, a statistical clustering of the conformers has been performed using the PCA analysis on the dihedral angles of the molecules. These ensembles have been further refined using ORCA (version 5.0.4),[9] ordered, and eventually sorted out with two different single-point energy calculations with different theories: B97-3c/def2-SVP,[10] and B3LYP[11]-D4/def2-SVP. Both analyses have been carried out in gas phase. The best conformer resulting from this protocol has been optimized to the r^{2}scan-3c d4/def2-mTZVPP[12] level; in this case, to better simulate the reaction condition the relative dielectric constant (ε_r) of the implicit CPCM solvation model has been set to

12 (which is the molar average of the two solvents $\varepsilon_{r,\ AcOH} = 6.15$, $\varepsilon_{r,\ iPrOH} = 19.92$). To choose the functional that best fits the experimental data, a preliminary analysis has been conducted. To reduce the complexity and the various degrees of freedom of the system, **2a** was modified to a methyl ester, instead of the *tert*-butyl group. So, the two Zimmerman-Traxler[13] like TS's are designed, and the reaction have been simulated following the two diasteromeric faces of the crotyl. Seven different functionals were tested, keeping the basis set constant to def2-SVP: B3LYP-D4, MN15, PBE, r^{2}scan-3c D4, REVPBE98-D4, TPSSH-D4, and ωB97x-D4. All functionals indicated the same stereoselectivity of the reaction and substantially the enantiomeric ratio was consistent, it was chosen to operate with the fastest functional to converge: **r^{2}scan-3c D4**. Considering the few atoms in the system, the basis set of choice was enlarged to the modified triple-ζ **def2-mTZVPP**. Furthermore, a single-point energy correction with the **def2-QZVP** basis-set was performed to better simulate the iodine atoms. The default basis set for the effective core potential (ECP) of the iodine atom is used – def2-ECP. Following up, to analyze and to rationalize the energy gaps, the Non-Covalent interaction (NCI) index was calculated with NCIPlot (version 4.0)[14] using FINE integration grid. For visualizing the geometries, frequencies and surfaces ChimeraX software have been used.[15]

OPTIMIZATION OF THE ASYMMETRIC AMINATION

Table S1: Catalysts screening

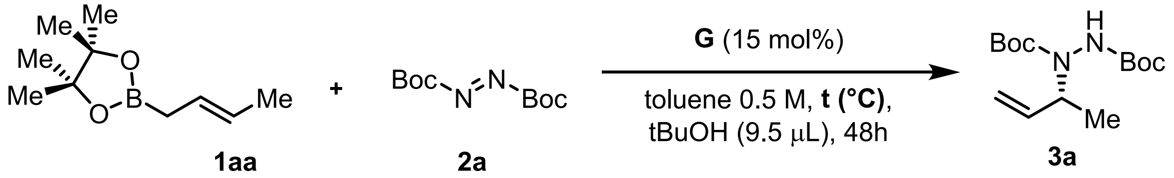




Catalyst	^{t}-BuOH (equiv.)	Time (h)	Conversion (%)	e.r.
/	/	48	17	/
A	/	40	17	50:50
A	1.0	48	21	50:50
B	/	48	17	50:50
B	1.0	48	23	50:50
C	1.0	48	22	50:50
D	1.0	24	19	53.5:46.5
E	1.0	24	27	52:48
MeO-E	1.0	24	13	53:47
F	1.0	24	30	50:50
G[a]	1.0	48	60	80:20
H[b]	1.0	48	60	77:23
I[b]	1.0	48	40	80:20
L[a]	1.0	48	53	77:23
M[a]	1.0	48	26	50:50
N[a]	1.0	48	68	80:20

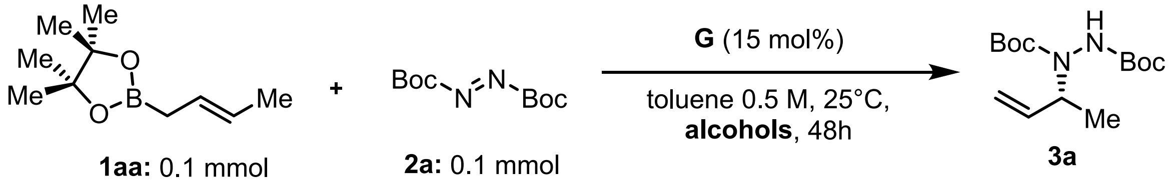
[a] 0.5 M in toluene instead of 0.1 M. [b] 0.5 M in $PhCF_3$ instead of toluene.

Table S2: Screening of temperature and equivalents of reaction partners



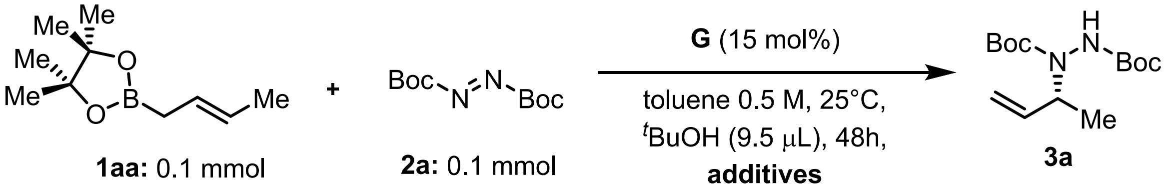
1a (mmol)	2a (mmol)	T (°C)	Conversion (%)	e.r.
0.15	0.1	25	72%	50:50
0.1	**0.15**	25	68%	50:50
0.1	0.1	**50**	82%	63:37
0.1	0.1	**0**	37%	82.5:16.5

Table S3: Screening of alcohols



Additive	Equivalents	Conversion (%)	e.r.
/	/	60	69.5:31.5
MeOH	1.0	58	70:30
EtOH	1.0	55	70:30
^{i}PrOH	1.0	55	81:19
^{t}BuOH	0.5	55	73:27
^{t}BuOH	1.0	60	80:20
^{t}BuOH	1.5	55	77:23
^{t}BuOH	2.0	30	50:50
1-adamantanol	1.0	44	77:23
methanesulfonamide	1.0	54	68:32
(tetrahydropyranyl)methanol	1.0	53	61.5:39.5
(S)-2-butanol	1.0	57	81:19
Ethylene glycole	1.0	34	74:26
2,3-butandiol	1.0	36	74:26

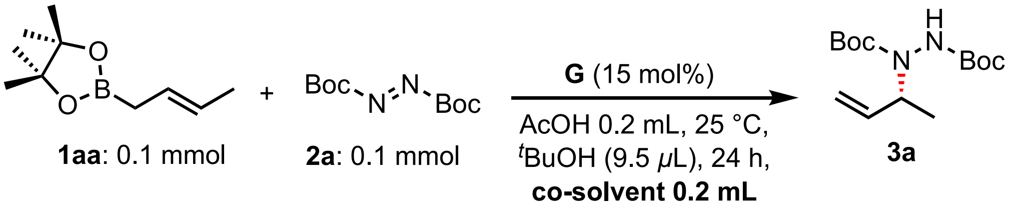
Table S4: Screening of additives in the presence of ^{t}BuOH



Additive	Equivalents	Time (h)	Conversion (%)	e.r.
Sc(OTf)$_3$	0.15	48	35	70:30
La(OTf)$_3$	0.15	48	32	57:43
^{t}BuOK	0.15	48	41	63:37
AcOK	1.0	22	43	76:52
AcOH	1.0	24	50	83:17
AcOH[a]	1.0	24	50	82:18
AcOH	2.0	24	55	85:15
AcOH[b]	16	22	60	85:15

[a] No ^{t}BuOH added. [b] AcOH employed as cosolvent (0.1 M in AcOH).

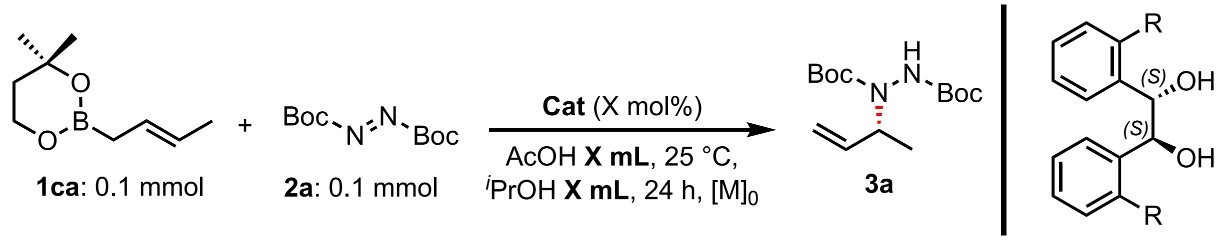
Table S5: Screening of co-solvents



Co-solvent	Conversion (%)	e.r.
DMSO	46	83:17
DMF	46	85:15
THF	47	85:15
Pyridine	48	79:21
Dioxane	51	75:25
ACN	52	86:14
Diethyl ether	61	85:15
Ethyl acetate	65	85:15
DCM	70	85:15
CHCl$_3$	68	88:12
MTBE	66	85:15
MeOH[a]	71	83:17
EtOH[a]	70	86:14
^{i}PrOH[a]	75	88:12
^{t}BuOH	71	83:17

[a] Reaction performed without ^{t}BuOH.

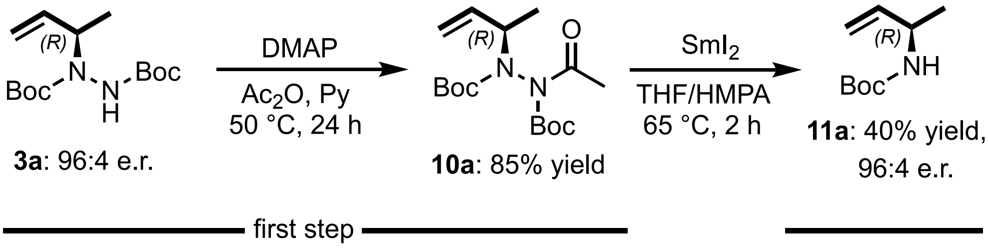
Table S6: Optimization of conditions with (*E*)-2-(but-2-en-1-yl)-4,4-dimethyl-1,3,2-dioxaborinane **1ca**



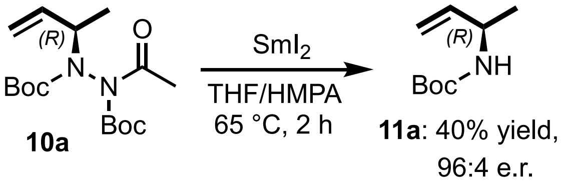
Catalyst	R	X (mol%)	AcOH (mL)	^{i}PrOH (mL)	[M]$_0$	time (h)	Conversion (%)	e.r.
G	**H**	15	0.2	0.2	0.25	16	80	96:4
G	**H**	10	0.2	0.2	0.25	16	70	95:5
G	**H**	10	0.2	0.2	0.25	24	82	95:5
G	**H**	10	0.2	0.2	0.25	48	89	94:6
G	**H**	5	0.2	0.2	0.25	16	60	94:6
N	**I**	15	0.2	0.2	0.25	24	98	97:3
N	**I**	15	0.1	0.1	0.5	19	94	96:4
N	**I**	10	0.1	0.1	0.5	24	93	96:4
N	**I**	5	0.1	0.1	0.5	20	82	96:4

DETERMINATION OF THE ABSOLUTE CONFIGURATION OF 3A

The absolute configuration of **3a** obtained employing (*S*,*S*)-**N** was determined through the optical rotatory power of **11a** and compared with that reported in literature.[16] **11a** is accessible via 2 steps starting from **3a**:

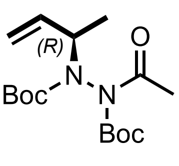


First step:



Allylic hydrazide **3a** (143 mg, 0.5 mmol, 1 eq.) was added to a capped vial and dissolved with 1 mL of acetic anhydride and 0.5 mL of pyridine. Afterward DMAP (30 mg, 0.33 mmol, 0.6 eq.) was added and the vial was placed in an oil bath at 50°C. The reaction mixture was vigorously stirred for 24 hours. Then, the vessel was cooled to room temperature and quenched with distilled water. The layers were separated and the aqueous phase was extracted three times with Et_2O. The organic phases were collected, washed two times with sat $NaHCO_3$, twice with sat NH_4Cl and two times with brine. The organic layer was separated, dried with $MgSO_4$ and concentrated at reduced pressure. The residue was purified by flash chromatography (from 1:6 to 1:4 Et_2O/Hex) to afford **10a** (140 mg, 0.425 mmol, 85% yield).

Di-*tert*-butyl (*R*)-1-acetyl-2-(but-3-en-2-yl)hydrazine-1,2-dicarboxylate (10a)

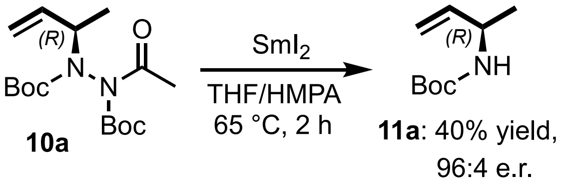


^{1}H NMR (600 MHz, $CDCl_3$) δ 6.24 – 5.70 (m, 1H), 5.26 – 5.00 (m, 2H), 4.87 – 4.37 (m, 1H), 2.54 – 2.40 (m, 3H), 1.56 – 1.38 (m, 18H), 1.32 – 1.22 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.29, 171.14, 171.02, 153.18, 153.01, 152.99, 152.62, 152.48, 138.54, 138.31, 137.78, 137.53, 116.03, 115.97, 115.44, 115.41, 83.90, 83.87, 83.84, 81.70, 80.93, 80.91, 58.55, 58.23, 56.56, 56.38, 28.32, 28.26, 28.17, 28.14, 27.92, 27.88, 25.58, 25.53, 25.49, 25.42, 17.92, 17.60, 17.23, 17.04.

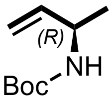
HRMS (ESI$^+$): m/z for $C_{16}H_{28}N_2O_5Na$ [M+Na]$^+$ calcd. 351.1890, found 351.1896.

Second step:



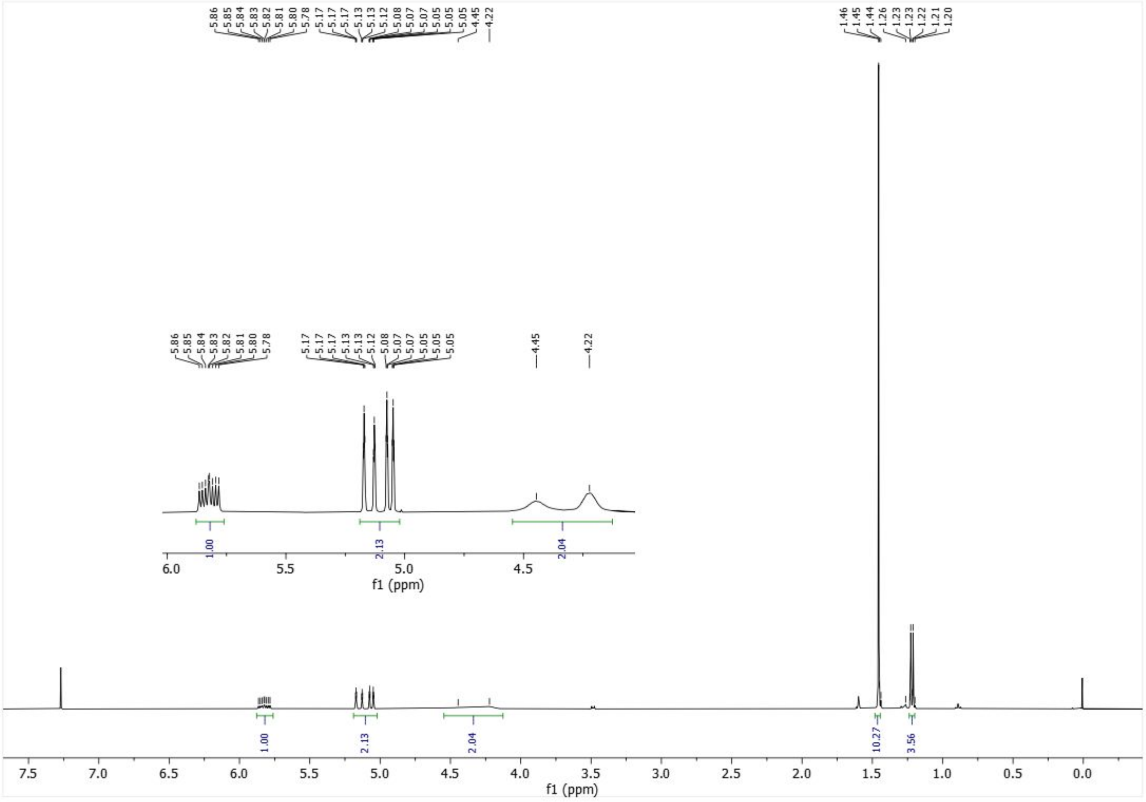
Compound **10a** (82 mg, 0.25 mmol, 1 eq.) was added to an oven dried two necks round bottom flask under nitrogen flow containing 3 mL of degassed THF and 0.45 mL of degassed HPMA. The flask was placed in an oil bath at 65°C and 15 mL of SmI_2 0.1 M in THF (1.5 mmol, 15 eq.uiv.) were added dropwise while the solution was under stirring. After two hours the flask was removed from the bath and the reaction was quenched with sat $NaHCO_3$ and extracted three times with Et_2O. Eventually the organic phases were collected, dried with $MgSO_4$ and concentrated at reduced pressure. The residue was purified by flash chromatography (from 1:5 to 1:3 Et_2O/Hex) to afford **11a** (20 mg, 0.12 mmol, 40% yield).

***tert*-butyl (*R*)-but-3-en-2-ylcarbamate (11a)**



^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 17.3, 10.4, 5.1 Hz, 1H), 5.19 – 5.02 (m, 2H), 4.57-4.10 (m, 2H), 1.46 (s, 9H), 1.22 (d, *J* = 6.8 Hz, 3H).

$[\alpha]_{589}^{20}$ = +4.6 (*c* = 1.0, in $CHCl_3$)



PREPARATIONS OF STARTING ALLYLIC ALCOHOLS

Allylic boronic esters were prepared starting from either commercially available (Figure S1) or synthetic allylic alcohols, accessible through three diverse strategies.

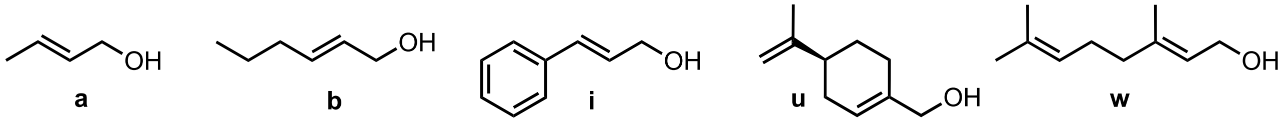
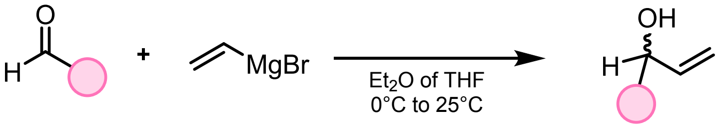


Figure S1: Alcohols commercially available

- **Strategy A**: Addition of vinylmagnesium bromide to aldehydes.
- **Strategy B**: Reduction of unsatured aldehydes.
- **Strategy C**: Wittig reaction followed by reduction.

Strategy A



7 mmol of the aldehyde were added to a flame dried two necks round bottom flask under nitrogen flow and dissolved with 7 mL of either THF or Et_2O. The flask was cooled to 0°C and the 7 mL of vinyl magnesium bromide (1.0 M in THF) was added dropwise. The mixture was allowed to warm to room temperature and the reaction continued for 2-3 hours. After the consumption of the starting aldehyde checked by TLC, a saturated solution of NH_4Cl was added and was extracted three times with Et_2O. The organic phases were collected and washed two times with brine, then dried under $MgSO_4$ and concentrated at reduced pressure. The crudes were considered to be used for the next step without further purifications. The spectra of the alcohols reported in figure S2 matched with those reported in literature [17,18,19,20,21].

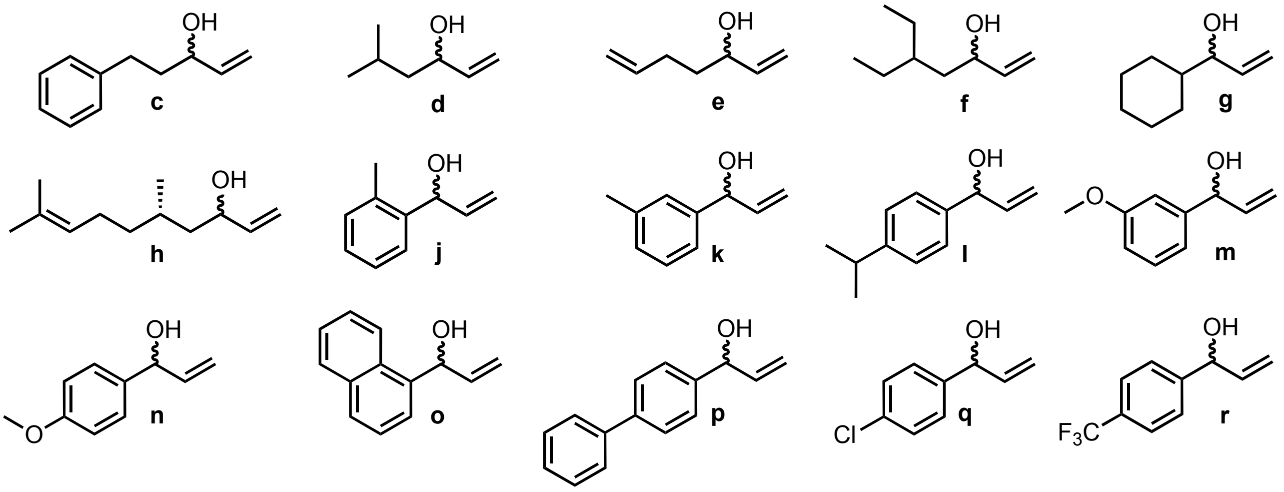
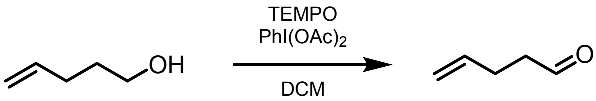


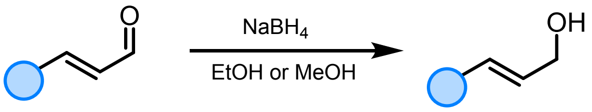
Figure S2: Alcohols from vinylation of aldehydes (Strategy A)

All the aldehyde used for this strategy are commercially available; only the aldehyde used for **e** was synthesized starting from the corresponding alcohol:



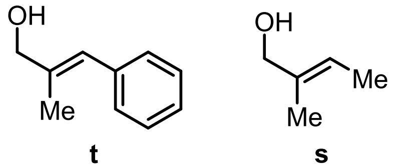
Following a reported procedure[22], 20 mmol of a pent-4-en-1-ol were added to a solution of 20 mL of DCM, TEMPO (1.4 mmol) and of $PhI(OAc)_2$ (21 mmol) and the mixture was stirred for one hour at room temperature. The solvent was removed and the product was distilled under reduced pressure and collected in a separate flask. Although this fraction was contaminated with 50% of acetic acid, the product was not purified further. The ^{1}H NMR agrees with those reported in literature. Before the addition of vinylmagnesium bromide the flask was cooled to -78°C and 1 eq. of NaH was added to remove the acetic acid. The mixture was stirred for 30 min in an ice-water bath, then the vinyl magnesium bromide was introduced dropwise to the reaction mixture. The work up is the same of Strategy A.

Strategy B



5 mmol of the allylic aldehyde (1 eq.) was introduced into a round bottom flask and dissolved with either 5 mL of ethanol or methanol. 5 mmol of $NaBH_4$ were added in small portions and then the reaction was stirred for 2-3 hours. After the consumption of the starting material monitored by TLC, the reaction was quenched with a saturated solution of NH_4Cl and extracted three times with Et_2O. The organic phases were collected and washed two times with brine, then dried under $MgSO_4$ and concentrated at reduced pressure. The crudes were sufficiently clean to be used without further

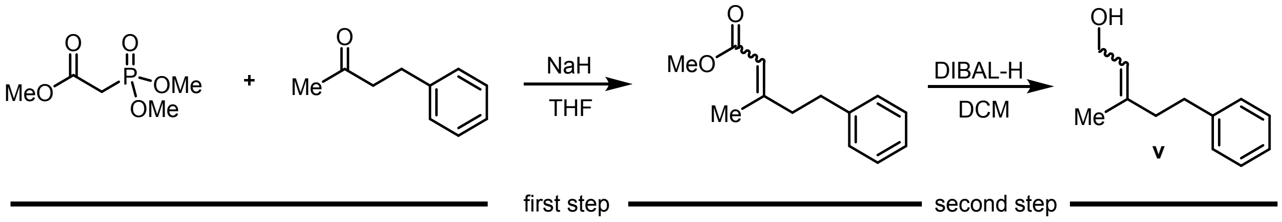
purifications. Alcohols **t** and **s** (Figure S4) have been prepared with this procedure and the NMR data were consistent with those reported in literature.[23,24]



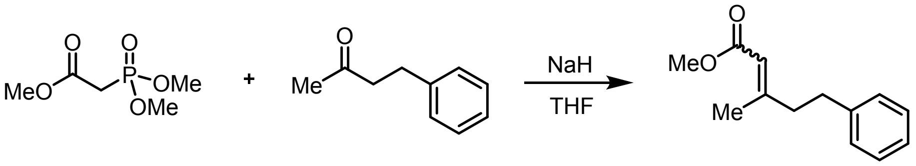
t **s**

Figure S3: Alcohols from vinylation of aldehydes (Strategy A)

Strategy C

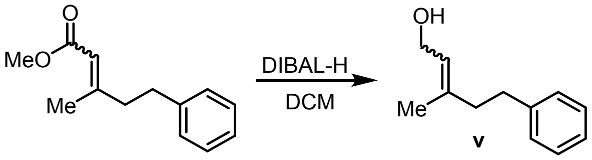


First step:



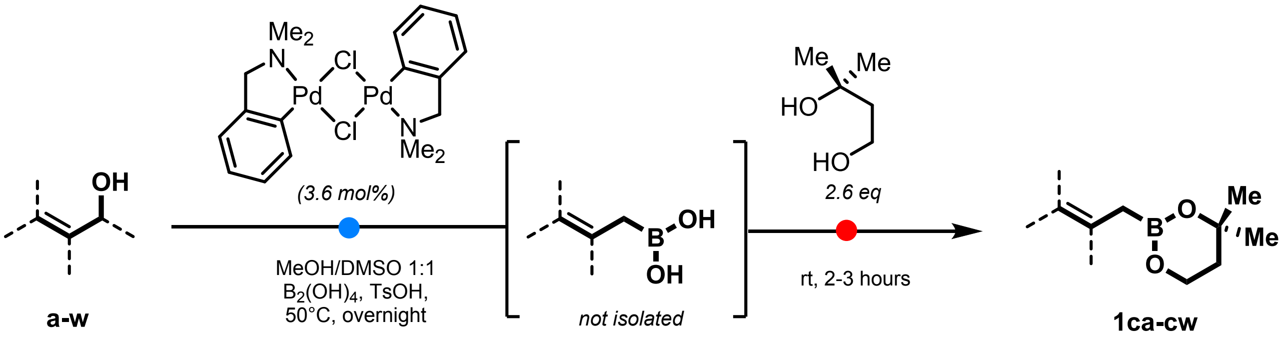
To an ice-cooled flask containing a solution of 3.0 g of 4-phenylbutan-2-one (20 mmol) and 4.0 g of methyl 2-(dimethoxyphosphoryl)acetate (1.1 eq., 22 mmol) in 30 mL of dry THF, 0.96 g of NaH (60% dispersion in mineral oil, 1.2 eq., 24 mmol) were added stepwise. Then the flask was removed from the bath and the reaction was allowed to stir overnight. The mixture was quenched with a saturated solution of NH_4Cl, the layers were separated and the aqueous phase was washed three times with Et_2O. The organic phases were collected, washed two times with brine, dried under $MgSO_4$ and concentrated at reduced pressure. Flash chromatography of the crude (1:5 Et_2O /hexane) afforded 3.17 grams of methyl 3-methyl-5-phenylpent-2-enoate in 78% yield. NMR data were consistent with those reported in literature.[25]

Second step:



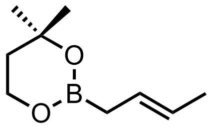
Following a reported procedure,[26] methyl 3-methyl-5-phenylpent-2-enoate (10.4 mmol, 2.27 g) was dissolved in 30 mL of dry DCM and transferred into a flame dried two necks round bottom flask under nitrogen flow. A solution of [1.0 M] DIBAL-H 1.0 M in hexane (2.7 eq., 28 mmol, 28 mL) was added dropwise at -78 °C. The reaction was allowed to stir at the same temperature for two hours, when the total conversion of the starting material was observed by TLC. The reaction was quenched with 50 mL of saturated solution of NH_4Cl, and the mixture was allowed to reach room temperature. Afterward, the layers were separated and the aqueous phase was extracted three times with DCM. The organic phases were collected, washed two times with brine, dried under $MgSO_4$ and concentrated at reduced pressure. The residue was purified with flash chromatography (1:2 diethyl ether/hexane) to give compound 3-methyl-5-phenylpent-2-en-1-ol (**v**) in 67% yield (1.2 g, 7 mmol). NMR data were consistent with those reported in literature.[26]

GENERAL PROCEDURE FOR THE SYNTHESIS OF ALLYLIC BORONIC ESTERS



Following a reported procedure[2] with some modification, to an oven-dried two necks round bottom flask provided of a magnetic stir bar and under nitrogen flow, 1 equivalent of allylic alcohol, dry DMSO and distilled MeOH (1:1 mixture, 0.25 M), 0.036 eq. of di-µ-chlorobis[2-[(dimethylamino)methyl]phenyl-C,N]dipalladium(II), 0.054 equivalents of anhydrous TsOH and 3 equivalents of $B_2(OH)_4$ were added. The reaction was stirred at 50°C overnight, then the flask was cooled to room temperature and 2.6 equivalents of 3-methylbutane-1,3-diol were added. After the consumption of the boronic acid monitored with TLC, the entire solution was transferred into a packed column and a flash chromatography was performed to isolate the product. High vacuum is not recommended because some of the boronic esters proved to be volatile. Unless otherwise reported, all allylic boronic esters have been obtained with (E)-configuration at the double bond.

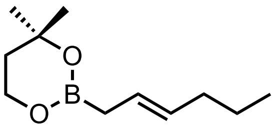
(E)-2-(but-2-en-1-yl)-4,4-dimethyl-1,3,2-dioxaborinane (1ca)



The titled compound was obtained from alcohol **a** in 70% yield (353 mg) after column chromatography (1:4.5 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.48 (m, 1H), 5.39 – 5.29 (m, 1H), 4.04 – 3.98 (m, 2H), 1.83 – 1.76 (m, 2H), 1.64 (dq, 3H), 1.53 (d, 2H), 1.30 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 127.56, 124.13, 70.03, 59.06, 38.01, 29.24, 18.08. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 29.48. **HRMS (ESI$^+$)**: m/z for $C_9H_{18}BO_2$ $[M+H]^+$ calcd. 169.1400, found 169.1403.

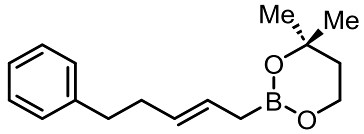
(*E*)-2-(hex-2-en-1-yl)-4,4-dimethyl-1,3,2-dioxaborinane (1cb)



The titled compound was obtained from alcohol **b** in 41% yield (117 mg) after column chromatography (1:4.5 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.50 – 5.38 (m, 1H), 5.38 – 5.25 (m, 1H), 4.03 – 3.95 (m, 2H), 2.00 – 1.89 (m, 2H), 1.80 – 1.73 (m, 2H), 1.51 (d, 1H), 1.47 – 1.29 (m, 2H), 1.28 (s, 6H), 0.87 (t, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 129.64, 126.53, 69.98, 59.03, 38.03, 34.88, 29.23, 22.83, 13.62. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 29.56. **HRMS (ESI$^+$)**: m/z for $C_{11}H_{22}BO_2$ $[M+H]^+$ calcd. 197.1713, found 197.1716.

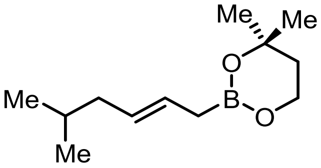
(*E*)-4,4-dimethyl-2-(5-phenylpent-2-en-1-yl)-1,3,2-dioxaborinane (1cc)



The titled compound was obtained from alcohol **c** in 65% yield (251 mg) after after flash chromatography (1:5 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 2H), 7.22 – 7.13 (m, 3H), 5.51 (m, 1H), 5.43 – 5.32 (m, 1H), 4.02 – 3.96 (m, 2H), 2.70 – 2.62 (m, 2H), 2.36 – 2.23 (m, 2H), 1.81–1.74 (m, 2H), 1.56 – 1.49 (d, 2H), 1.28 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.45, 128.89, 128.46, 128.15, 127.16, 125.55, 70.05, 59.06, 38.03, 36.26, 34.61, 29.25. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 28.19. **HRMS (ESI$^+$)**: m/z for $C_{16}H_{24}BO_2$ $[M+H]^+$ calcd 259.1869, found 259.1872.

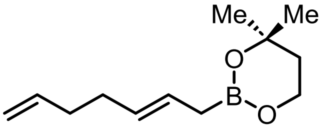
(*E*)-4,4-dimethyl-2-(5-methylhex-2-en-1-yl)-1,3,2-dioxaborinane (1cd)



The titled compound was obtained from alcohol **d** in 47% yield (148 mg) after after flash chromatography (1:9 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.48 – 5.39 (m, 1H), 5.32 (dtt, *J* = 15.4, 7.1, 1.4 Hz, 1H), 4.03 – 3.98 (m, 2H), 1.86 (tq, *J* = 6.9, 1.1 Hz, 2H), 1.82 – 1.76 (m, 2H), 1.62 – 1.51 (d, 2H), 1.29 (s, 6H), 0.97 – 0.86 (m, 7H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 128.46, 127.53, 69.99, 59.04, 42.19, 38.04, 29.25, 28.55, 22.24. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 28.25. **HRMS (ESI$^+$)**: m/z for $C_{12}H_{24}BO_2$ $[M+H]^+$ calcd. 211.1869, found 211.1872.

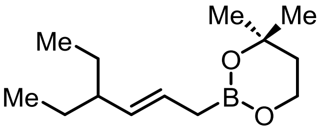
(*E*)-2-(hepta-2,6-dien-1-yl)-4,4-dimethyl-1,3,2-dioxaborinane (1ce)



The titled compound was obtained from alcohol **e** in 30% yield (94 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 – 5.77 (m, 1H), 5.49 (dtt, *J* = 16.3, 7.2, 1.2 Hz, 1H), 5.40 – 5.29 (m, 1H), 5.05 – 4.89 (m, 2H), 4.03 – 3.97 (m, 2H), 2.09 (dtdd, *J* = 5.7, 4.7, 2.2, 1.2 Hz, 4H), 1.81 – 1.75 (m, 2H), 1.56 – 1.49 (m, 2H), 1.29 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.81, 128.91, 127.01, 114.23, 70.05, 59.07, 38.05, 34.01, 32.23, 29.27. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 29.53. **HRMS (ESI$^+$)**: m/z for $C_{12}H_{22}BO_2$ $[M+H]^+$ calcd. 209.1713, found 209.1715.

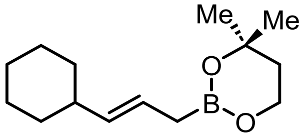
(*E*)-2-(4-ethylhex-2-en-1-yl)-4,4-dimethyl-1,3,2-dioxaborinane (1cf)



The titled compound was obtained from alcohol **f** in 74% yield (248.8 mg) after after flash chromatography (1:6 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.38 (dt, *J* = 15.1, 7.5 Hz, 1H), 5.01 (dd, *J* = 15.3, 8.7 Hz, 1H), 3.99 (t, *J* = 5.7 Hz, 2H), 1.77 (m, 2H), 1.68 (dq, *J* = 9.4, 4.3 Hz, 1H), 1.53 (d, *J* = 7.5 Hz, 2H), 1.41 – 1.29 (m, 2H), 1.28 (s, 6H), 1.23 – 1.13 (m, 2H), 0.83 (t, *J* = 7.5 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 133.75, 126.45, 69.95, 59.02, 46.44, 38.07, 29.25, 27.90, 11.75.**^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.43. **HRMS (ESI$^+$)**: m/z for $C_{13}H_{26}BO_2$ $[M+H]^+$ calcd. 225.2026, found 225.2028.

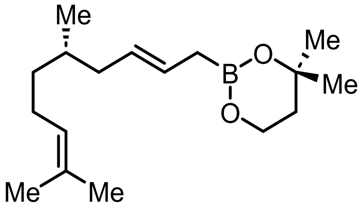
(*E*)-2-(3-cyclohexylallyl)-4,4-dimethyl-1,3,2-dioxaborinane (1cg)



The titled compound was obtained from alcohol **g** in 56% (198 mg) after flash chromatography (1:9 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 (dtd, *J* = 15.4, 7.2, 1.1 Hz, 1H), 5.27 (ddt, *J* = 15.4, 6.7, 1.4 Hz, 1H), 4.02 – 3.95 (m, 2H), 1.92-1.85 (m,1H), 1.77 (dd, *J* = 6.2, 5.3 Hz, 2H), 1.73 – 1.64 (m, 4H), 1.64 – 1.57 (m, 1H), 1.50 (d, *J* = 7.1 Hz, 2H), 1.28 (s, 6H), 1.27 – 0.95 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.99, 123.79, 69.97, 59.03, 40.83, 38.03, 33.38, 29.25, 26.28, 26.18. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 28.32. **HRMS (ESI$^+$)**: m/z for $C_{14}H_{26}BO_2$ $[M+H]^+$ calcd. 237.2026, found 237.2029.

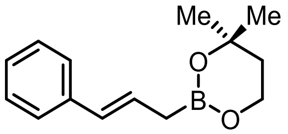
(*S*,*E*)-2-(5,9-dimethyldeca-2,8-dien-1-yl)-4,4-dimethyl-1,3,2-dioxaborinane (1ch)



The titled compound was obtained from alcohol **h** in 74% yield (308.8 mg) after flash chromatography (1:6 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.44 (dtt, *J* = 14.8, 7.3, 1.3 Hz, 1H), 5.30 (dtt, *J* = 15.5, 7.2, 1.5 Hz, 1H), 5.10 (tp, *J* = 7.1, 1.4 Hz, 1H), 4.02 – 3.98 (m, 2H), 2.03 – 1.92 (m, 3H), 1.85 – 1.79 (m, 1H), 1.79 – 1.76 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.54 (d, *J* = 7.4 Hz, 2H), 1.47 – 1.41 (m, 1H), 1.29 (s, 6H), 1.11 (dddd, *J* = 13.5, 9.7, 7.7, 5.9 Hz, 1H), 0.91 – 0.84 (m, 5H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 130.83, 128.13, 127.68, 125.10, 69.98, 59.02, 40.17, 38.02, 36.58, 32.88, 29.22, 25.69, 25.60, 19.34, 17.59. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 28.17. **HRMS (ESI$^+$)**: m/z for $C_{17}H_{32}BO_2$ $[M+H]^+$ calcd. 279.2495, found 279.2498.

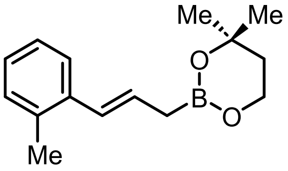
2-cinnamyl-4,4-dimethyl-1,3,2-dioxaborinane (1ci)



The titled compound was obtained from alcohol **I** in 50% yield (173 mg) after flash chromatography (1:9 AcOEt/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2H), 7.34 – 7.22 (m, 2H), 7.19 – 7.10 (m, 1H), 6.31 (s, 1H), 6.37 – 6.24 (m, 1H), 4.05 – 3.97 (m, 2H), 1.83 – 1.70 (m, 4H), 1.30 (s, 5H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.51, 129.18, 128.34, 128.25, 126.23, 125.71, 70.28, 59.14, 38.04, 29.27. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 29.34. **HRMS (ESI$^+$)**: m/z for $C_{14}H_{20}BO_2$ $[M+H]^+$ calcd. 231.1556, found 231.1559.

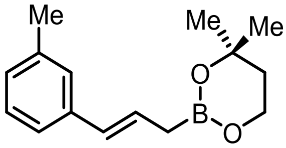
(*E*)-4,4-dimethyl-2-(3-(o-tolyl)allyl)-1,3,2-dioxaborinane (1cj)



The titled compound was obtained from alcohol **j** in 75% yield (174 mg) after flash chromatography (1:9 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.3 Hz, 1H), 7.19 – 7.04 (m, 3H), 6.51 (dt, *J* = 15.7, 1.7 Hz, 1H), 6.20 (dt, *J* = 15.5, 7.6 Hz, 1H), 4.06 – 3.99 (m, 2H), 2.33 (s, 3H), 1.85 – 1.76 (m, 4H), 1.32 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.56, 134.60, 130.05, 129.42, 126.95, 126.25, 125.88, 125.28, 70.26, 59.15, 38.07, 29.29, 19.90. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.40. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{21}BO_2K$ $[M+K]^+$ calcd. 283.1266, found 283.1272.

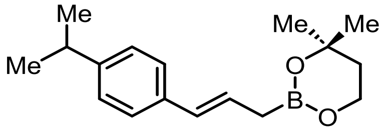
(*E*)-4,4-dimethyl-2-(3-(m-tolyl)allyl)-1,3,2-dioxaborinane (1ck)



The titled compound was obtained from alcohol **k** in 60% yield (217.7 mg) after flash chromatography (1:6 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 – 7.10 (m, 3H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.31 – 6.24 (m, 2H), 4.03 – 3.98 (m, 2H), 2.32 (s, 3H), 1.81 – 1.73 (m, 4H), 1.30 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.46, 137.80, 129.23, 128.25, 128.02, 127.04, 126.43, 122.89, 70.27, 59.14, 38.05, 29.28, 21.42. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 29.27. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{22}BO_2$ $[M+H]^+$ calcd. 245.1713, found 245.1716.

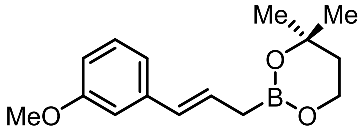
(*E*)-2-(3-(4-isopropylphenyl)allyl)-4,4-dimethyl-1,3,2-dioxaborinane (1cl)



The titled compound was obtained from alcohol **l** in 71% yield (290 mg) after flash chromatography (1:9 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.31 – 6.20 (m, 2H), 3.99 (t, *J* = 5.7 Hz, 2H), 2.86 (p, *J* = 6.9 Hz, 1H), 1.80 – 1.70 (m, 4H), 1.29 (d, *J* = 3.5 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.94, 136.19, 128.96, 127.29, 126.39, 125.65, 70.24, 59.12, 38.04, 33.77, 29.27, 24.00. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.42. **HRMS (ESI$^+$)**: m/z for $C_{17}H_{25}BO_2K$ $[M+K]^+$ calcd. 311.1579, found 311.1585.

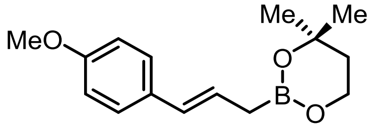
(*E*)-2-(3-(3-methoxyphenyl)allyl)-4,4-dimethyl-1,3,2-dioxaborinane (1cm)



The titled compound was obtained from alcohol **m** in 30% yield (117 mg) after flash chromatography (1:6 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.9 Hz, 1H), 6.94 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.89 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.72 (ddd, *J* = 8.1, 2.6, 0.9 Hz, 1H), 6.39 – 6.24 (m, 2H), 4.06 – 3.98 (m, 2H), 3.81 (s, 3H), 1.79 (dt, *J* = 11.6, 5.8 Hz, 4H), 1.31 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.68, 139.98, 129.25, 129.03, 128.64, 118.45, 111.89, 111.01, 70.28, 59.12, 55.14, 38.01, 29.24. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.42. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{21}BO_3K$ $[M+K]^+$ calcd. 299.1215, found 299.1221.

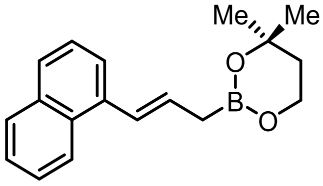
(*E*)-2-(3-(4-methoxyphenyl)allyl)-4,4-dimethyl-1,3,2-dioxaborinane (1cn)



The titled compound was obtained from alcohol **n** in 50% yield (195 mg) after flash chromatography (1:6 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 2H), 6.87 – 6.77 (m, 2H), 6.30 – 6.21 (m, 1H), 6.16 (m, 1H), 4.05 – 3.93 (m, 2H), 3.79 (s, 3H), 1.82-1.77 (m, 2H), 1.75– 1.70 (d, 2H), 1.30 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.23, 131.43, 128.52, 126.73, 125.96, 113.78, 70.23, 59.12, 55.26, 38.03, 29.26. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 28.12. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{22}BO_3$ $[M+H]^+$ calcd. 261.1662, found 261.1665.

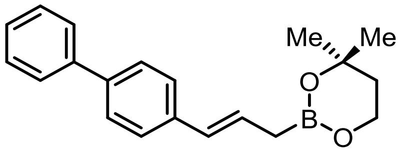
(*E*)-4,4-dimethyl-2-(3-(naphthalen-1-yl)allyl)-1,3,2-dioxaborinane (1co)



The titled compound was obtained from alcohol **o** in 64% yield (269 mg) after flash chromatography (1:5 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.21 (m, 1H), 7.91 – 7.84 (m, 1H), 7.76 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.62 (dt, *J* = 7.2, 1.1 Hz, 1H), 7.57 – 7.43 (m, 3H), 7.11 (dt, *J* = 15.5, 1.8 Hz, 1H), 6.40 (dt, *J* = 15.5, 7.7 Hz, 1H), 4.10 – 4.04 (m, 2H), 1.96 (dd, *J* = 7.7, 1.6 Hz, 2H), 1.87 – 1.82 (m, 2H), 1.37 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.32, 133.68, 131.53, 131.14, 128.37, 126.74, 126.23, 125.70, 125.57, 125.48, 124.22, 123.30, 70.34, 59.18, 38.06, 29.31. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 29.42. **HRMS (ESI$^+$)**: m/z for $C_{18}H_{22}BO_2$ $[M+H]^+$ calcd. 281.1713, found 281.1716.

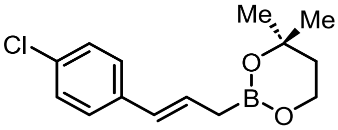
(*E*)-2-(3-([1,1'-biphenyl]-4-yl)allyl)-4,4-dimethyl-1,3,2-dioxaborinane (1cp)



The titled compound was obtained from alcohol **p** in 23% yield (106 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.54 (m, 2H), 7.57 – 7.44 (m, 2H), 7.44 – 7.34 (m, 4H), 7.34 – 7.25 (m, 1H), 6.38 – 6.28 (m, 2H), 4.04 – 3.97 (m, 2H), 1.82 – 1.74 (m, 4H), 1.29 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.04, 138.98, 137.63, 128.73, 128.71, 128.56, 127.08, 127.00, 126.86, 126.11, 70.33, 59.18, 38.07, 29.29. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.52. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{23}BO_2K$ $[M+K]^+$ calcd. 345.1423, found 345.1428.

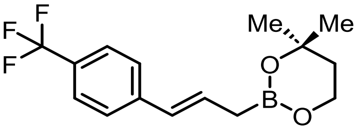
(*E*)-2-(3-(4-chlorophenyl)allyl)-4,4-dimethyl-1,3,2-dioxaborinane (1cq)



The titled compound was obtained from alcohol **q** in 55% yield (218.3 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.19 (m, 4H), 6.32 – 6.22 (m, 2H), 4.01 (m, 2H), 1.81 – 1.77 (m, 2H), 1.75 (d, 2H), 1.30 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.01, 131.69, 129.10, 128.44, 128.02, 126.91, 70.35, 59.18, 38.04, 29.27. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 29.32. **HRMS (ESI$^+$)**: m/z for $C_{14}H_{19}BClO_2$ $[M+H]^+$ calcd. 265.1167, found 265.1169.

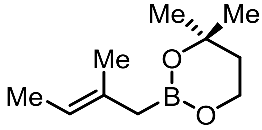
(*E*)-4,4-dimethyl-2-(3-(4-(trifluoromethyl)phenyl)allyl)-1,3,2-dioxaborinane (1cr)



The titled compound was obtained from alcohol **r** in 43% yield (192 mg) after flash chromatography (1:6 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 6.44 (dt, *J* = 15.5, 7.7 Hz, 1H), 6.37 – 6.30 (m, 1H), 4.02 (dd, *J* = 7.3, 4.3 Hz, 2H), 1.83 – 1.77 (m, 4H), 1.32 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.98, 131.41, 128.15, 128.03, 127.94, 125.77, 125.35, 125.32, 125.29, 125.27, 70.43, 59.21, 38.04, 29.26. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.34. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.31. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{19}BF_3O_2$ $[M+H]^+$ calcd. 299.1430, found 299.1433.

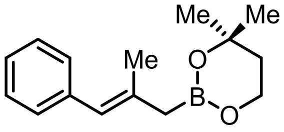
(*E*)-4,4-dimethyl-2-(2-methylbut-2-en-1-yl)-1,3,2-dioxaborinane (1cs)



The titled compound was obtained from alcohol **s** in 50% yield (136 mg) after flash chromatography (1:5 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) 5.15 – 5.11 (m, 1H), 4.03 – 4.00 (m, 2H), 1.79 – 1.75 (m, 2H), 1.63 (s, 3H), 1.59-1.53 (m, 5H), 1.32 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 134.04, 117.27, 70.03, 59.05, 38.06, 29.28, 17.55, 13.63. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.70. **HRMS (ESI$^+$)**: m/z for $C_{16}H_{24}BO_2$ $[M+H]^+$ calcd. 259.1869, found 259.1872.

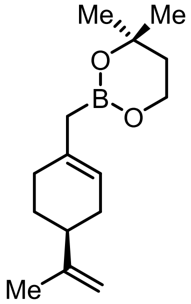
(*E*)-4,4-dimethyl-2-(2-methyl-3-phenylallyl)-1,3,2-dioxaborinane (1ct)



The titled compound was obtained from alcohol **t** in 56% (205 mg) after flash chromatography (1:8 Et_2O/Hex). Mixture of 1:9 *Z*/*E* isomers.

^{1}H NMR (*E* isomer) (600 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.26 – 7.23 (m, 2H), 7.18 – 7.13 (m, 1H), 6.23 (1H), 4.05 – 4.01 (m, 2H), 1.93 – 1.88 (m, 3H), 1.83 – 1.79 (m, 2H), 1.76 (s, 2H), 1.32 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.28, 139.13, 138.04, 137.97, 128.81, 128.61, 127.90, 127.89, 125.44, 125.33, 123.91, 123.46, 70.28, 70.21, 59.18, 59.11, 38.07, 29.29, 29.26, 19.74. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.27. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{22}BO_2$ $[M+H]^+$ calcd. 245.1713, found 245.1716.

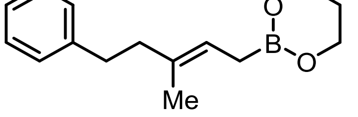
(*S*)-4,4-dimethyl-2-((4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methyl)-1,3,2-dioxaborinane (1cu)



The titled compound was obtained from alcohol **u** in 87% yield (648 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.35 (ddd, *J* = 5.4, 2.6, 1.4 Hz, 1H), 4.70 (dh, *J* = 3.4, 1.4 Hz, 2H), 4.03 – 3.99 (m, 2H), 2.16 – 2.04 (m, 3H), 2.04 – 1.88 (m, 2H), 1.80 – 1.76 (m, 3H), 1.74 (t, *J* = 1.1 Hz, 3H), 1.55 – 1.45 (m, 3H), 1.30 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.63, 135.73, 119.39, 108.18, 70.06, 59.05, 41.15, 38.06, 31.06, 30.89, 29.30, 28.16, 20.83. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.39. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{26}BO_2$ $[M+H]^+$ calcd. 249.2026, found 249.2029.

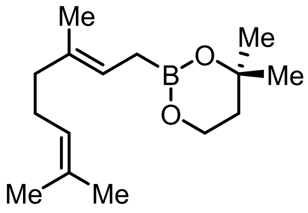
(*E*)-4,4-dimethyl-2-(3-methyl-5-phenylpent-2-en-1-yl)-1,3,2-dioxaborinane (1cv)



The titled compound was obtained from alcohol **v** in 45% (184 mg) after flash chromatography (1:6 Et_2O/Hex). Mixture of 1:1.92 *Z*/*E* isomers.

^{1}H NMR (*E* isomer) 600 MHz, $CDCl_3$) δ 7.29 – 7.10 (m, 5H), 5.33 – 5.21 (m, 1H), 3.99 (t, *J* = 5.7 Hz, 2H), 2.68 (m, 2H), 2.29 (q, *J* = 9.0 Hz, 2H), 1.78-1.73 (m, 2H), 1.72 (s, 1H) 1.63 (s, 2H), 1.52-1.44 (m, 2H), 1.28 (d, *J* = 1.9 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.83, 133.66, 133.61, 128.42, 128.21, 128.17, 125.60, 125.52, 121.25, 120.57, 70.05, 70.02, 59.08, 59.06, 41.79, 38.05, 34.96, 34.36, 34.01, 29.29, 22.67, 16.10. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.71. **HRMS (ESI$^+$)**: m/z for $C_{16}H_{26}BO_2Na$ $[M+Na]^+$ calcd. 295.1845, found 295.1848.

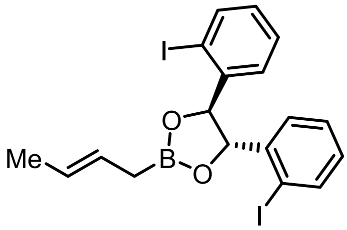
(*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4,4-dimethyl-1,3,2-dioxaborinane (1cw)



The titled compound was obtained from alcohol **w** in 98% yield (735 mg) after flash chromatography (1:10 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.26 (ddq, *J* = 7.6, 6.0, 1.3 Hz, 1H), 5.12 (tp, *J* = 7.0, 1.4 Hz, 1H), 4.03 – 3.97 (m, 2H), 2.10 – 1.96 (m, 4H), 1.80 – 1.74 (m, 2H), 1.63 – 1.57 (m, 6H), 1.50 (d, *J* = 7.6 Hz, 2H), 1.29 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 134.03, 131.03, 124.66, 120.07, 69.97, 59.05, 39.88, 38.07, 29.29, 26.92, 25.72, 17.69, 15.91. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 29.54. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{28}BO_2$ $[M+H]^+$ calcd. 251.2182, found 251.2185.

(4*S*,5*S*)-2-((*E*)-but-2-en-1-yl)-4,5-bis(2-iodophenyl)-1,3,2-dioxaborolane (N-1c)



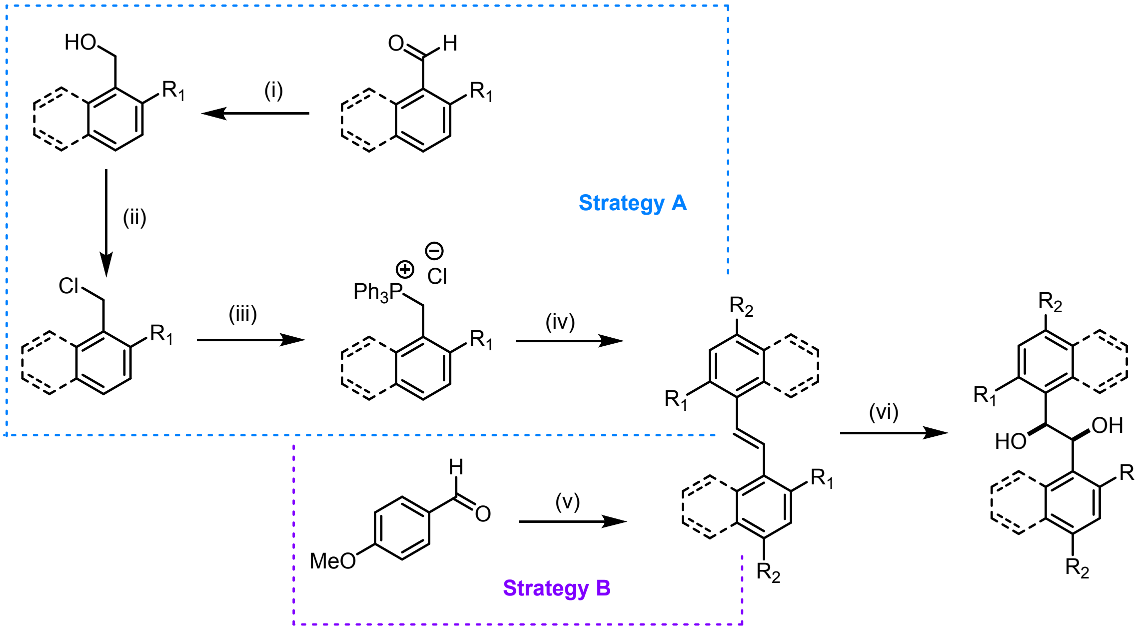
Following the general procedure, but using **N** instead of 3-methylbutane-1,3-diol.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.0, 1.1 Hz, 2H), 7.40 – 7.32 (m, 4H), 6.95 (ddd, *J* = 7.9, 6.7, 2.3 Hz, 2H), 5.59 – 5.42 (m, 2H), 5.38 (s, 2H), 1.87 (dt, *J* = 7.0, 1.4 Hz, 2H), 1.64 – 1.59 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 141.10, 138.71, 129.10, 127.82, 126.59, 125.13, 124.19, 96.93, 87.88, 17.09. **^{11}B NMR** (193 MHz, $CDCl_3$) δ 34.55. **HRMS (ESI$^+$)**: m/z for for $C_{18}H_{17}BO_2I_2Na$ $[M+Na]^+$ calcd. 552.9303, found 552.9306.

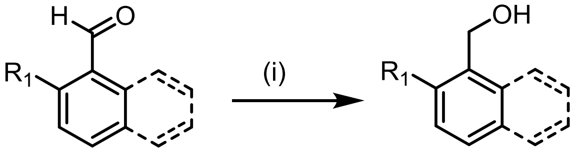
PREPARATIONS OF CHIRAL HYDROBENZOINS

All chiral hydrobenzoins except **N** were prepared via Sharpless asymmetric dihydroxylation. The starting *E*-olefines were synthetized through two different strategies depicted in the Scheme S1.



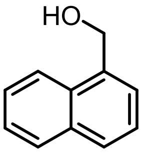
Scheme S1: strategy to access the final chiral hydrobenzoins

Strategy A



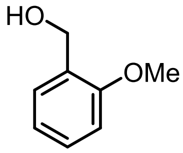
In a round bottom flask containing 20 mmol of the alcohol in 40 mL THF were added 20 mmol of $NaBH_4$. The reaction was monitored by TLC until the total consumption of the starting aldehyde. The reaction mixture was quenched with water and extracted 3 times with Et_2O. The organic phases were collected, dried under $MgSO_4$ and concentrated at reduced pressure. No further purification was needed.

Naphthalen-1-ylmethanol

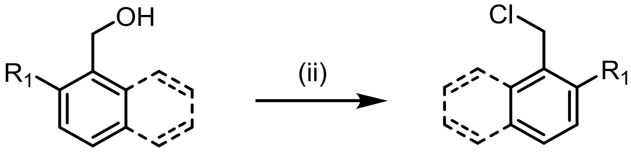


Quantitative yield, white solid. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm): δ 8.09-8.02 (m, 1H); 7.96-7.88 (m, 1H); 7.88-7.80 (dd, 1H); 7.61-7.50 (m, 2H); 7.50-7.40 (m, 2H); 5 (s, 2H); 3.55 (bs, OH). Data consistent with the literature.[27]

(2-methoxyphenyl)methanol

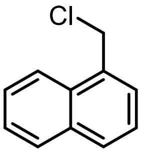


Quantitative yield, white solid. ^{1}**H NMR** (300 MHz, $CDCl_3$, ppm): δ 7.33-7.27 (m, 2H); 6.99-6.94 (m, 1H); 6,92-6,89 (m, 1H); 4.7 (s, 2H); 3,89 (s, 3H); 2.3 (bs, OH). Data consistent with the literature.[28]



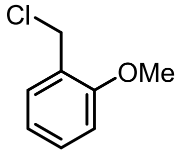
In a round bottom flask 20 mmol of the previous alcohol were introduced with 20 mL of HCl 37% and the stirring was turned on. The reaction proceeded as heterogeneous mixture overnight, then the solution was transferred into a separating funnel and extracted three times with DCM. The organic phases were collected, dried under $MgSO_4$ and concentrated at reduced pressure. No further purification was needed.

1-(chloromethyl)naphthalene

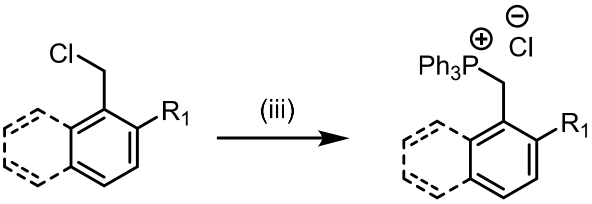


Quantitative yield, pale yellow oil. ^{1}**H NMR** (300 MHz, $CDCl_3$, ppm): δ 8.28-8.21 (m, 1H); 8- 7.89 (m, 2H); 7.73-7.54 (m, 3H); 7.47-7.41 (m, 1H); 5.07 (s, 1H). Data consistent with the literature.[29]

1-(chloromethyl)-2-methoxybenzene

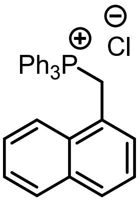


Quantitative yield, Pale yellow oil. ^{1}**H NMR** (300 MHz, $CDCl_3$, ppm): δ 7.43-7.31 (m, 2H); 7.01-6.89 (m, 2H); 4.69 (s, 2H); 3.9 (s, 3H). Data consistent with the literature.[30]



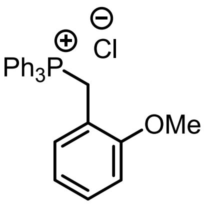
20 mmol of the chloride were dissolved in 40 mL of toluene and 1 equivalent of PPh_3 was added to the flask. The reaction was stirred and refluxed overnight. Afterward the flask was cooled to room temperature and the precipitate was filtrated and washed with cold ethyl acetate. No further purification was needed.

(naphthalen-1-ylmethyl)triphenylphosphonium

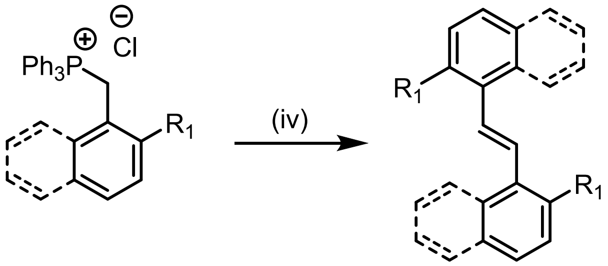


Quantitative yield, white solid.^{1}**H NMR** (300 MHz, $CDCl_3$, ppm): δ 7.67-7.50 (m, 11H); 7.48- 7.35 (m, 7H); 7.27 (d, 1H); 7.20-7.09 (m, 2H); 6.97-6.88 (m, 1H); 5.68 (d, 2H).

(2-methoxybenzyl)triphenylphosphonium

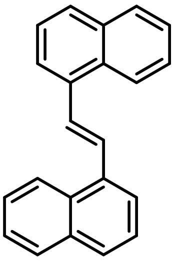


Quantitative yield, white solid. **H NMR** (300 MHz, $CDCl_3$, ppm): δ 7.80 (m, 3H,); 7.66 (m, 6H); 7.61 (m, 6H); 7.30 (m, 1H); 7.25 (m, 1H); 6.80 (m, 1H), 6.62 (d, 1H), 5.05 (d, 2H), 3.20 (s, 3H). Data consistent with the literature.[31]



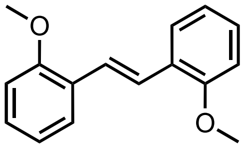
To a suspension of 20 mmol of the phosphonium salt in 100 mL ethanol, 2 equivalents of sodium were added in small portions. The reaction was stirred for one hour, then 1 eq. of the corresponding aldehyde was added to the mixture. After 24 hours the reaction was quenched by the addition of water and extracted three times with toluene. The organic phases were collected, dried under $MgSO_4$ and concentrated at reduced pressure. The residue was purified by flash chromatography followed by recrystallization in hot methanol. If the alkene was obtained as a mixture of *E/Z* it was converted into the *E* isomer in the presence of traces of iodine in refluxing toluene.

(*E*)-1,2-di(naphthalen-1-yl)ethene



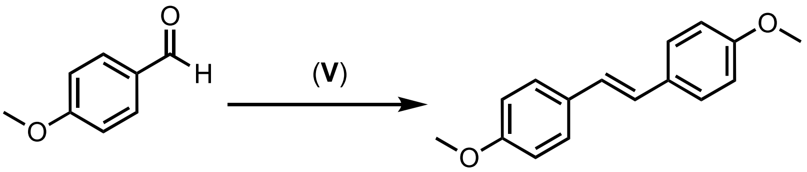
Pale yellow solid. 30% yield, isolated after flashchromatography (9:1 Hex/Et_2O) as a mixture of 1:1 Z/E. Converted into the *trans* isomer with traces of iodine in refluxing toluene. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm): δ 8.30-8.24 (m, 2H); 7.95-7.84 (m, 8H); 7.59-7.50 (m, 6H). Data consistent with the literature.[32]

(*E*)-1,2-bis(2-methoxyphenyl)ethene



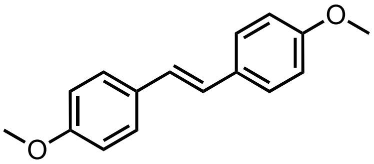
White solid. 40% yield, isolated after flashchromatography 8:2 Hex/Et2O (Rf= 0,77). Resa 40%. Only *trans* isomer present. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm): δ 7.66 (dd, 2H); 7.48 (s, 2H); 7.27-7.20 (m, 2H); 6.68 (td 2H); 6.90 (dd, 2H); 3,89 (s, 6H). Data consistent with the literature.[33]

Strategy B



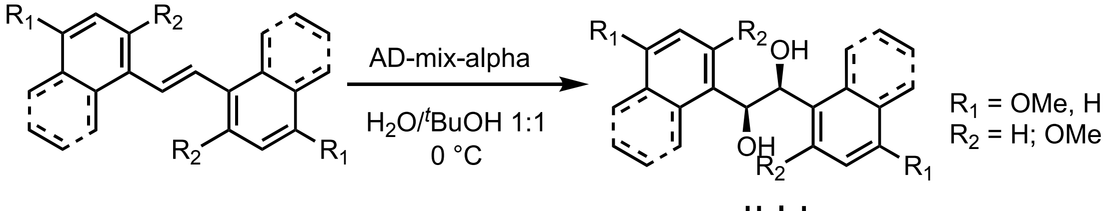
To a suspension of 1.176 g of zinc (18 mmol, 3 eq.) in 60 mL of freshly distilled THF, 9 mL of a solution of $TiCl_4$ (1.0 M in DCM, 1.5 eq.) were added dropwise. The reaction was stirred and refluxed for one hour, then 0.73 mL of the aldehyde (6 mmol, 1 eq.) were added. The reaction proceeded at reflux temperature for three hours, then the flask was allowed to cool to room temperature and 60 mL of cold HCl 1N were added. The biphasic mixture was filtrated under celite, then the water layer was separated and extracted three times with DCM. The organic phases were collected, dried under $MgSO_4$ and concentrated at reduced pressure. Recrystallization with acetone allowed the isolation of the pure alkene in 20% yield.

(*E*)-1,2-bis(4-methoxyphenyl)ethene



White solid, 20% of pure *E* isomer after recrystallization in acetone. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm): 7.47-7.41 (m, 4H); 6.94 (s, 2H); 6.93-6.87 (m, 4H); 3.84 (s, 6H).[34]

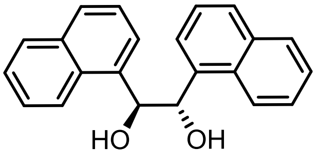
Asymmetric dihydroxylation



H, I, L

To a heterogeneous mixture of water/terbutanol (1:1, 0.1 M) the AD-mix-alpha (1.4 g per mmol of alkene) was added. When the solid was fully dissolved, the flask was cooled to 0°C and the alkene from the previous step (1 eq.) was added to the mixture. The reaction proceeded for 5-6 days under vigorously stirring at the same temperature. Then, a saturated solution of Na_2SO_3 (2.0 g per mmol of alkene) was added to the flask and the reaction was further stirred at room temperature for 1h. The mixture was filtrated, washed with EtOAc and the organic layers were separated from the aqueous one, which was extracted three times with DCM. Afterward, the organic phases were collected, dry over Na_2SO_4 and concentrated at reduced pressure. The final product was obtained after the flash chromatography.

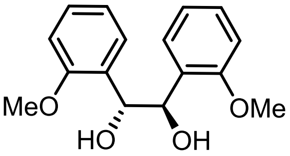
(1*S*,2*S*)-1,2-di(naphthalen-1-yl)ethane-1,2-diol (H)



White solid, 60% yield after flash chromatography 8:2 Hex:AcOEt.

^{1}H NMR (300 MHz, $CDCl_3$, ppm): 7.88 (d, 2H); 7.78-7.68 (m, 6H); 7.43-7.25 (m, 6H); 5.80 (s, 2H); 2,99 (bs, 2H). Data consistent with the literature.[3]

The e.r. was determined by **HPLC** analysis on Lux-amylose 2 column: hexane/*i*-PrOH 80/20 flow rate 1 mL/min, 25 °C, λ = 210 nm: t_1= 13.1 min, t_2= 22.8 min; e.r.= 56:44. The enantiomers were separated by preparative HPLC on Lux-amylose 2 column, hexane/*i*-PrOH 70:30 flow rate 5 mL/min, 25°C.

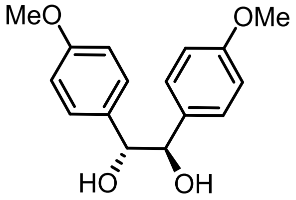


(1*R*,2*R*)-1,2-bis(2-methoxyphenyl)ethane-1,2-diol (I)

White solid. 90% yield after flash chromatography 7:3 Hex/Et_2O. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm): δ 7.21-7.16 (m, 4H); 6.88-6.82 (m, 2H); 6.77-6.74 (m, 2H); 5.07-5.02 (m, 2H); 3.66 (s, 6H); 3.5-3.44 (m, 2H). Data consistent with the literature.[3]

The e.r. was determined by **HPLC** analysis on Lux-amylose 2 column: hexane/*i*-PrOH 80/20 flow rate 1 mL/min, 25 °C, λ = 210 nm: t_1= 13.1 min, t_2= 22.8 min; e.r.= 26%. The enantiomers were separated by preparative HPLC on Lux-amylose 2 column, hexane/*i*-PrOH 70:30 flow rate 5 mL/min, 25°C.

(1*R*,2*R*)-1,2-bis(4-methoxyphenyl)ethane-1,2-diol (L)

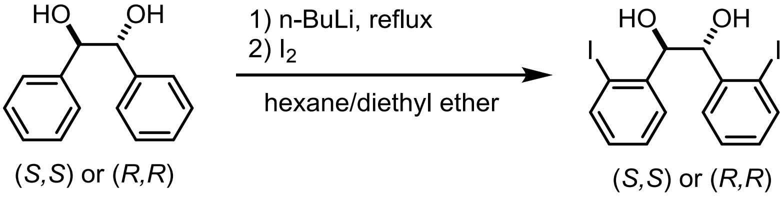


White solid. 50% yield after flash chromatography 6:4 Hex/AcOEt. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm): 7.07-7.02 (m, 4H); 6.79-6.74 (m, 4H); 4.64 (s, 2H); 3.78 (s, 6H); 2.8 (bs, 2H). Data consistent with the literature.[3]

The e.r. was determined by **HPLC** analysis on Lux-amylose 2 column: hexane/*i*-PrOH 80/20 flow rate 1 mL/min, 25 °C, λ = 210 nm, only one peak at 33.4 min; e.r.> 99.05:0.5%.

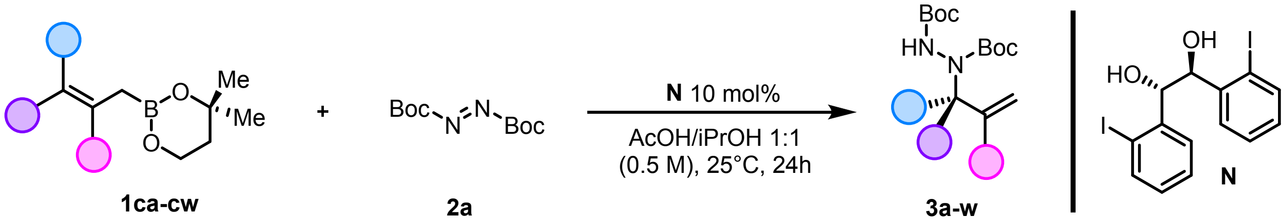
Synthesis of catalyst N

The compound **N** was readily prepared following a reported procedure:[6]



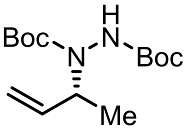
To an oven dried three necks round bottom flask under nitrogen flow 1 gram of (*S,S*)- or (*R,R*)-hydrobenzoin (1.0 eq., 4.7 mmol), 18.5 mL of hexane an 18 mL of Et_2O were added. To this suspension, 17.5 mL of n-BuLi in hexane (6.0 eq., 28 mmol, 1.6 M) were added dropwise and the reaction was refluxed overnight. Afterward the flask was allowed to reach room temperature, then it was cooled to -78°C and 8.23 gram of iodine (7.0 eq., 32.69 mmol) dissolved into a minimal volume of Et_2O were added to the mixture. The flask was removed from the cooling bath and the stirring continued for 5 hours at room temperature. The reaction was quenched with 100 mL of saturated $Na_2S_2O_3$, then the layers were separated and the aqueous phase was extracted four times with 120 mL of AcOEt. The organic phases were collected, dried under $MgSO_4$ and concentrated at reduced pressure. Flash chromatography (3.5:1 hexane/ethyl acetate) followed by recrystallization with DCM/hexane allowed the isolation of **N** in 30% of yield.

GENERAL PROCEDURE FOR THE ASYMMETRIC SYNTHESIS OF ALLYLIC HYDRAZIDES



To a screw cap vial 0.3 mmol of boronic ester, 0.3 mL of ^{i}PrOH, 0.3 mL of AcOH, 0.03 mmol of **N** (14 mg) were added. The solution was stirred for 10 minutes, afterward 0.3 mmol of di-tertbutyl-azodicarboxylate (69 mg) were introduced to the vessel and the reaction was stirred for 24 hours at rt. Then the mixture was diluted with hexane and poured into a packed column to perform the flash chromatography.

Di-tert-butyl (*R*)-1-(but-3-en-2-yl)hydrazine-1,2-dicarboxylate (3a)

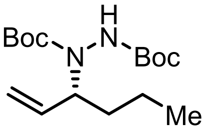


White solid. The titled compound was obtained from **1ca** in 92% yield (79 mg on 0.3 mmol) or 90% yield (386 mg on 1.5 mmol) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (s, 1H), 5.85 (m, 1H), 5.15-5.08 (m, 2H), 4.77 (m, 1H), 1.47 (s, 18H), 1.25 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.62, 154.75, 139.59, 138.01, 115.26, 87.93, 81.19, 80.84, 28.25, 28.16, 16.52. **HRMS (ESI$^+$)**: m/z for $C_{14}H_{26}N_2O_4Na$ $[M+Na]^+$ calcd. 309.1785, found 309.1791.

The enantiomeric ratio (e.r.) was determined by **GC-FID** analysis on a Rt-βDEXsm column, temperature ramp starting from 120°C, increment of 2°C/min. Two couple of peaks with the same e.r. were observed due to the deprotection of the Boc group promoted by high temperature. First couple of enantiomers t_1= 6.4 min; t_2= 6.5 min; second couple of enantiomers t_3= 9.5 min; t_4= 9.9 min. e.r.= 96:4.

Di-tert-butyl (*R*)-1-(hex-1-en-3-yl)hydrazine-1,2-dicarboxylate (3b)

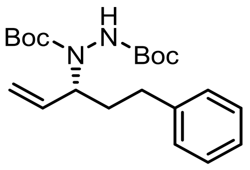


White solid. The titled compound was obtained from **1cb** in 93% yield (88 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.23-5.67 (m, 2H), 5.21 – 5.02 (m, 2H), 4.55 (s, 1H), 1.82-1.22 (m, 22H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.04, 141.90, 139.75, 137.38, 131.24, 130.17, 129.28, 128.82, 127.79, 124.97, 115.79, 81.12, 80.82, 79.86, 56.72, 38.14, 37.22, 28.25, 28.17, 25.69, 25.35, 19.68, 17.66. **HRMS (ESI$^+$)**: m/z for $C_{16}H_{30}N_2O_4Na$ $[M+Na]^+$ calcd. 337.2098, found 337.2103.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 97.5/2.5 flow rate 1 mL/min, 25 °C, λ = 210 nm: t_1= 5.2 min, t_2= 6.2 min. e.r.= 97:3

Di-tert-butyl (*R*)-1-(5-phenylpent-1-en-3-yl)hydrazine-1,2-dicarboxylate (3c)

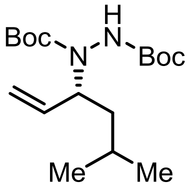


White solid. The titled compound was obtained from **1cc** in 86% yield (97 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.14 (m, 5H), 6.22 – 5.53 (m, 2H), 5.26-5.05 (m, 2H), 4.82-4.25 (m, 1H), 3.00 – 2.46 (m, 2H), 2.00 (s, 1H), 1.82 (s, 1H), 1.57-1.39 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.52, 155.01, 142.02, 136.55, 135.78, 128.53, 128.31, 125.76, 125.52, 116.69, 81.30, 80.91, 58.99, 33.20, 32.50, 30.33, 29.70, 28.24, 28.18. **HRMS (ESI$^+$)**: m/z for $C_{21}H_{32}N_2O_4Na$ $[M+Na]^+$ calcd. 399.2254, found 399.2260.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 97.5/2.5 flow rate 1 mL/min, 25 °C, λ = 210 nm: t_1= 6.6 min, t_2= 8.5 min; e.r.= 95.5:4.5.

Di-tert-butyl (*R*)-1-(5-methylhex-1-en-3-yl)hydrazine-1,2-dicarboxylate (3d)

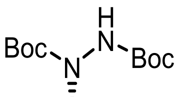


White solid. The titled compound was obtained from **1cd** in 75% (74 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.14-5.63 (m, 2H), 5.24-5.04- (m, 2H), 4.80-4.36 (m, 1H), 1.78 – 1.52 (m, 2H), 1.47 (s, 18H), 1.38 – 1.22 (m, 1H), 0.92 (dd, *J* = 14.4, 6.5 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.16, 155.18, 154.73, 141.05, 140.09, 139.95, 139.02, 138.75, 137.83, 137.22, 137.12, 135.08, 134.75, 134.22, 133.36, 132.69, 130.84, 130.18, 130.10, 129.75, 129.64, 129.50, 128.96, 128.81, 128.76, 128.71, 128.66, 128.59, 128.44, 128.20, 128.10, 128.02, 127.88, 127.71, 127.66, 124.01, 119.07, 118.68, 118.33, 115.60, 81.84, 81.12, 79.83, 74.80, 74.68, 60.40, 58.56, 56.74, 29.70, 28.19, 28.10, 21.05, 14.20. **HRMS (ESI$^+$)**: m/z for $C_{17}H_{33}N_2O_4$ $[M+H]^+$ calcd. 329.2435, found 329.2440.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 98/2 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 9.50 min, t_2= 12.3 min; e.r. = 94:6.

Di-tert-butyl (*R*)-1-(hepta-1,6-dien-3-yl)hydrazine-1,2-dicarboxylate (3e)

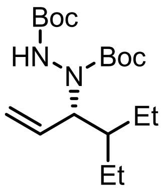


White solid. The titled compound was obtained from **1ce** in 83% yield (81 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.14 – 5.68 (m, 3H), 5.21 – 5.08 (m, 2H), 5.07 – 4.93 (m, 2H), 4.71-4.29 (m, 1H), 2.25 – 1.93 (m, 2H), 1.88-1.70 (m, 1H), 1.66-1.54 (m, 1H), 1.46 (s, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.53, 154.91, 138.13, 136.52, 125.52, 116.59, 114.93, 81.23, 80.89, 58.72, 30.48, 30.33, 30.29, 29.70, 28.25, 28.17. **HRMS (ESI$^+$)**: m/z for $C_{17}H_{31}N_2O_4$ $[M+H]^+$ calcd. 327.2278, found 327.2284.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 95/5 flow rate 0.5 mL/min, 23 °C, λ = 210 nm: t_1= 8.4 min, t_2= 9.7 min; e.r.= 96:4.

Di-tert-butyl (*S*)-1-(4-ethylhex-1-en-3-yl)hydrazine-1,2-dicarboxylate (3f)

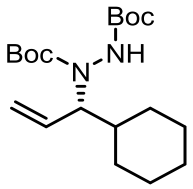


White solid. The titled compound was obtained from **1cf** in 75% (77 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.13 – 5.67 (m, 2H), 5.27-4.96 (m, 2H), 4.50-4.16 (m, 1H), 1.62 – 1.13 (m, 22H), 0.91 – 0.77 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.40, 155.28, 139.74, 135.50, 133.76, 130.10, 128.83, 127.50, 126.45, 117.60, 88.83, 81.15, 80.85, 69.96, 59.84, 59.03, 46.44, 40.73, 38.08, 30.33, 29.25, 29.02, 28.27, 28.16, 27.90, 20.89, 20.43, 11.83, 11.75, 10.24, 9.96. **HRMS (ESI$^+$)**: m/z for $C_{18}H_{34}N_2O_4Na$ $[M+Na]^+$ calcd. 365.2411, found 365.2416.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 95/5 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 7.4 min, t_2= 8.4 min; e.r.= 95:5.

Di-tert-butyl (*S*)-1-(1-cyclohexylallyl)hydrazine-1,2-dicarboxylate (3g)

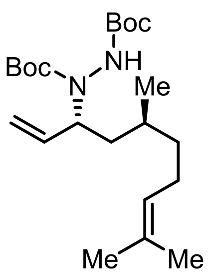


White solid. The titled compound was obtained from **1cg** in 75% (80 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 – 5.61 (m, 2H), 5.24-5.08 (m, 2H), 4.33-3.91 (m, 1H), 1.79 – 1.61 (m, 5H), 1.50-1.42 (m, 19H), 1.30 – 1.10 (m, 3H), 0.92 (dd, *J* = 47.5, 12.0 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.70, 155.26, 139.76, 135.18, 117.85, 88.84, 81.05, 65.86, 59.83, 38.39, 33.31, 30.20, 30.05, 29.02, 28.47, 28.28, 28.16, 27.75, 26.42, 25.98, 25.36, 20.54, 15.27. **HRMS (ESI$^+$)**: m/z for $C_{19}H_{34}N_2O_4Na$ $[M+Na]^+$ calcd. 377.2411, found 377.2416.

The e.r. was determined by **HPLC** analysis on a Chiralcel OD-H column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 7.7 min, t_2= 8.4 min; e.r.= 94:6.

Di-tert-butyl 1-((3*R*,5*S*)-5,9-dimethyldeca-1,8-dien-3-yl)hydrazine-1,2-dicarboxylate (3h)

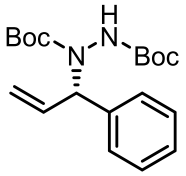


White solid. The titled compound was obtained from **3ch** in 70% yield (83 mg) after flash chromatography (1:9 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.07-5.68 (m, 2H), 5.23-5.02 (m, 3H), 4.85-4.46 (m, 1H), 1.98 (dp, *J* = 41.4, 7.7 Hz, 2H), 1.75-1.65 (m, 4H), 1.58 (s, 3H), 1.46 (s, 18H), 1.37 – 1.12 (m, 4H), 0.92 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.99, 139.63, 136.80, 129.92, 129.87, 128.42, 116.30, 81.14, 80.83, 79.83, 59.03, 33.35, 29.71, 28.72, 28.26, 28.17, 25.69, 25.35, 19.35, 17.67, 13.89. **HRMS (ESI$^+$)**: m/z for $C_{22}H_{40}N_2O_4Na$ $[M+Na]^+$ calcd. 419.2880, found 419.2886.

The d.r. was determined by **HPLC** analysis on a Chiralpak AD-H column: hexane/*i*-PrOH 95/5 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 13.7 min, t_2= 15.4 min; e.r. > 99.5:0.5; d.r.= 65:1.

Di-tert-butyl (*S*)-1-(1-phenylallyl)hydrazine-1,2-dicarboxylate (3i)

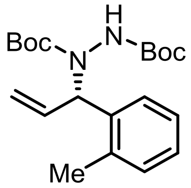


Pale yellow solid. The titled compound was obtained from **1ci** in 61% yield (64 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.09 (m, 5H), 6.22 – 5.50 (m, 3H), 5.30-4.98 (m, 2H), 1.57 – 0.89 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.25, 155.22, 142.01, 141.92, 139.70, 139.55, 139.05, 135.16, 130.14, 129.99, 129.81, 128.81, 128.36, 127.89, 127.82, 126.41, 117.83, 115.44, 99.14, 97.87, 88.90, 87.97, 81.05, 80.83, 67.52, 65.36, 63.96, 58.78, 43.50, 40.30, 38.40, 33.38, 32.79, 30.19, 30.06, 29.70, 28.28, 28.16, 26.42, 26.16, 26.09, 26.01, 25.99, 25.96, 25.78. **HRMS (ESI$^+$)**: m/z for $C_{19}H_{28}N_2O_4Na$ $[M+Na]^+$ calcd. 371.1941, found 371.1947.

The e.r. was determined by **HPLC** analysis on a Chiralcel OD-H column: hexane/*i*-PrOH 95/5 flow rate 1 mL/min, 25 °C, λ = 210 nm: t_1= 4.2 min, t_2= 4.7 min; e.r.= 95:5.

Di-tert-butyl (*S*)-1-(1-(o-tolyl)allyl)hydrazine-1,2-dicarboxylate (3j)

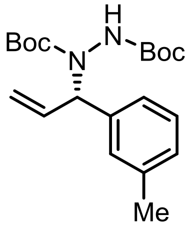


Colourless oil. The titled compound was obtained from **1cj** in 69% yield (75 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34-7.06 (m, 4H), 6.31 – 5.72 (m, 3H), 5.33 – 5.03 (m, 2H), 2.48 – 2.25 (m, 3H), 1.67 – 0.92 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.24, 154.79, 142.27, 139.76, 139.55, 139.50, 138.32, 137.89, 136.00, 135.50, 131.13, 130.68, 130.48, 130.30, 130.09, 129.73, 129.14, 128.84, 127.82, 127.54, 127.40, 126.78, 126.55, 126.43, 126.28, 126.18, 125.97, 125.88, 125.77, 125.58, 118.11, 115.41, 115.10, 97.98, 88.78, 81.41, 80.75, 79.92, 75.05, 71.98, 60.22, 52.73, 35.94, 29.71, 28.17, 28.07, 27.48, 24.64, 20.01, 19.65, 19.40, 19.11. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{30}N_2O_4Na$ $[M+Na]^+$ calcd. 381.2098, found 385.2103.

The e.r. was determined by **HPLC** analysis on a Lux cellulose-1 column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 10.7 min, t_2= 12.3 min; e.r.= 95:5.

Di-tert-butyl (*S*)-1-(1-(m-tolyl)allyl)hydrazine-1,2-dicarboxylate (3k)

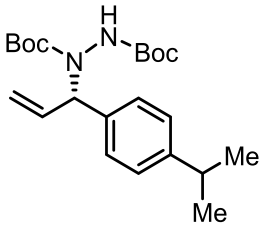


Pale yellow solid. The titled compound was obtained from **1ck** in 55% yield (60 mg) after flash chromatography (1:6 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.04 (m, 4H), 6.28 – 6.01 (m, 2H), 5.96-5.65 (m, 1H), 5.34 – 5.13 (m, 2H), 2.35 (s, 3H), 1.65-1.09 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.87, 135.17, 128.27, 127.14, 125.00, 123.59, 123.39, 118.08, 114.98, 81.56, 80.88, 75.04, 28.23, 28.13, 21.46, 21.37. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{30}N_2O_4Na$ $[M+Na]^+$ calcd. 381.2098, found 385.2103.

The e.r. was determined by **HPLC** analysis on a Chiralcel OD-H column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 9.0 min, t_2= 9.9 min; e.r.= 94.5:5.5.

Di-tert-butyl (*S*)-1-(1-(4-isopropylphenyl)allyl)hydrazine-1,2-dicarboxylate (3l)

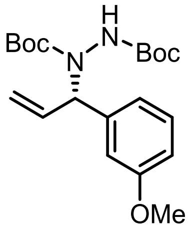


Pale yellow solid. The titled compound was obtained from **1cl** in 60% yield (69 mg) after flash chromatography (1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 6.98 (m, 4H), 6.57-6.02 (m, 2H), 5.96-5.6 (m, 1H), 5.50-5.08 (m, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.65 – 0.97 (m, 24H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.01, 154.41, 154.13, 147.43, 146.42, 142.61, 140.92, 140.69, 139.29, 138.86, 138.28, 136.63, 135.44, 134.51, 130.07, 129.83, 129.78, 129.64, 129.59, 129.27, 129.03, 128.40, 128.14, 127.87, 127.72, 127.66, 127.49, 127.29, 126.08, 126.02, 126.00, 125.99, 125.91, 125.85, 125.71, 123.51, 116.23, 116.14, 115.82, 98.58, 87.38, 80.40, 79.65, 79.61, 74.83, 74.32, 33.44, 27.59, 23.47, 10.35, 7.72. **HRMS (ESI$^+$)**: m/z for $C_{22}H_{34}N_2O_4Na$ $[M+Na]^+$ calcd. 413.2411, found 413.2416.

The e.r. was determined by **HPLC** analysis on a Chiralcel OD-H column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 20 °C, λ = 230 nm: t_1= 9.0 min, t_2= 9.6 min; e.r.= 96:4.

Di-tert-butyl (*S*)-1-(1-(3-methoxyphenyl)allyl)hydrazine-1,2-dicarboxylate (3m)

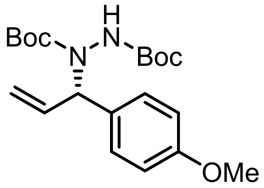


White solid. The titled compound was obtained from alcohol **1cm** in 47% yield (53 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (t, *J* = 7.9 Hz, 1H), 6.91 – 6.69 (m, 3H), 6.09 – 5.51 (m, 3H), 5.20 (m, 2H), 3.74 – 3.69 (m, 3H), 1.54 – 0.96 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.82, 158.78, 158.61, 154.14, 153.83, 143.30, 140.84, 139.89, 139.13, 138.58, 133.88, 128.87, 128.56, 128.51, 128.33, 127.38, 119.20, 118.08, 117.58, 117.24, 114.15, 112.67, 112.28, 111.81, 110.68, 98.09, 80.61, 79.89, 78.82, 74.23, 54.21, 29.30, 28.68, 27.19, 27.11, 26.92. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{30}N_2O_5Na$ $[M+Na]^+$ calcd. 401.2047, found 401.2052.

The e.r. was determined by **HPLC** analysis on a Chiralcel OD-H column: hexane/*i*-PrOH 95/5 flow rate 0.5 mL/min, 25 °C, λ = 254 nm: t_1= 9.3 min, t_2= 10.7 min; e.r.= 96:4.

Di-tert-butyl (*S*)-1-(1-(4-methoxyphenyl)allyl)hydrazine-1,2-dicarboxylate (3n)

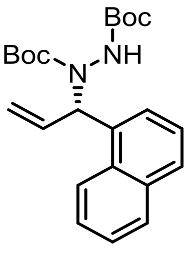


Pale yellow solid. The titled compound was obtained from **1cn** in 40% yield (45 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34-7.20 (m, 2H), 6.90 – 6.83 (m, 2H), 6.27 – 5.92 (m, 2H), 5.76 (m, 1H), 5.24 (m, 2H), 3.80 (s, 3H), 1.58 – 1.03 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.02, 154.86, 141.82, 139.63, 135.48, 130.95, 130.10, 129.92, 129.87, 129.38, 128.42, 127.96, 127.67, 127.61, 126.29, 120.68, 117.67, 114.05, 114.02, 113.97, 113.71, 113.69, 81.53, 80.86, 79.82, 63.93, 55.28, 31.93, 30.33, 29.70, 28.24, 28.13, 22.70, 14.13. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{30}N_2O_5Na$ $[M+Na]^+$ calcd. 401.2047, found 401.2052.

The e.r. was determined by **HPLC** analysis on a Chiralcel OD-H column: hexane/*i*-PrOH 98/2 flow rate 1 mL/min, 25 °C, λ = 228 nm: t_1= 11.3 min, t_2= 12.1 min; e.r.= 94:6.

Di-tert-butyl (*S*)-1-(1-(naphthalen-1-yl)allyl)hydrazine-1,2-dicarboxylate (3o)

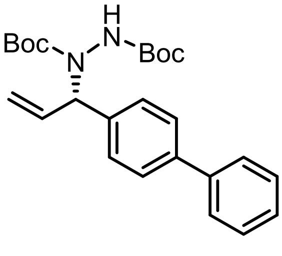


Colourless oil. The titled compound was obtained from **1co** in 58% yield (69 mg) after flash chromatography (1:7 Et_2O/Hex). 69 mg, 58% yield.

^{1}H NMR (25°C) (400 MHz, $C_2D_2Cl_4$) δ 8.44-7.97 (m, 1H), 7.94 – 7.82 (m, 2H), 7.63 – 7.41 (m, 4H), 6.92-6.11 (m, 2H), 5.55-5.09 (m, 2H), 1.79 – 1.09 (m, 16H), 0.53 (bs, 2H). **^{1}H NMR (105°C)** (400 MHz, $C_2D_2Cl_4$) δ 8.26 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.62 – 7.44 (m, 4H), 6.63 (d, *J* = 5.9 Hz, 1H), 6.43-6.30 (m, *J* = 8.7 Hz, 1H), 5.87 (s, 1H), 5.42 – 5.28 (m, 2H), 1.52 (s, 10H), 1.21 (bs, 8H). **^{13}C NMR** (151 MHz, $C_2D_2Cl_4$) δ 135.59, 133.76, 128.83, 126.75, 125.92, 125.38, 124.36, 81.81, 74.31, 74.23, 74.05, 73.87, 28.37, 27.89, 27.05, 20.48. **HRMS (ESI$^+$)**: m/z for $C_{23}H_{30}N_2O_4Na$ $[M+Na]^+$ calcd. 421.2098, found 421.2104.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 95/5 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 10.4 min, t_2= 12 min; e.r.= 94.5:5.5.

Di-tert-butyl (*S*)-1-(1-([1,1'-biphenyl]-4-yl)allyl)hydrazine-1,2-dicarboxylate (3p)

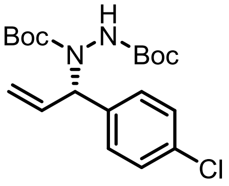


Colourless oil. The titled compound was obtained from **1cp** in 57% yield (72 mg) after flash chromatography (from 1:8 Et_2O/Hex to 1:5 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 – 7.30 (m, 9H), 6.45 – 6.03 (m, 2H), 6.06 – 5.68 (m, 1H), 5.44 – 5.15 (m, 2H), 1.72 – 1.00 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.21, 154.92, 154.59, 141.70, 140.84, 140.71, 140.44, 140.25, 139.76, 138.29, 137.75, 135.83, 135.07, 130.71, 129.91, 128.88, 128.79, 128.73, 128.51, 128.40, 128.15, 127.42, 127.34, 127.32, 127.25, 127.23, 127.16, 127.13, 127.10, 127.04, 127.01, 126.98, 126.94, 126.88, 126.79, 126.68, 118.59, 118.32, 118.09, 115.22, 81.74, 81.01, 75.12, 58.71, 57.22, 31.61, 29.72, 28.45, 28.25, 28.21, 28.15, 22.67, 20.74, 14.15. **HRMS (ESI$^+$)**: m/z for $C_{25}H_{32}N_2O_4Na$ $[M+Na]^+$ calcd. 447.2254, found 447.2260.

The e.r. was determined by **HPLC** analysis on a Lux 5u cellulose-1 column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 23 °C, λ = 210 nm: t_1= 16.9 min, t_2= 19.1 min; e.r.= 96:4.

Di-tert-butyl (*S*)-1-(1-(4-chlorophenyl)allyl)hydrazine-1,2-dicarboxylate (3q)

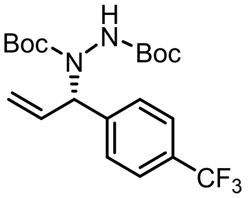


White solid. The titled compound was obtained from **1cq** in 60% yield (69 mg) after flash chromatography (1:7 Et_2O/Hex). 69 mg, 60% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.17 (m, 4H), 6.34-5.59 (m, 3H), 5.35-5.10 (m, 2H), 1.54-0.99 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.16, 155.18, 154.73, 141.05, 140.09, 139.95, 139.02, 138.75, 137.83, 137.22, 137.12, 135.08, 134.75, 134.22, 133.36, 132.69, 130.84, 130.18, 130.10, 129.75, 129.64, 129.50, 128.96, 128.81, 128.76, 128.71, 128.66, 128.59, 128.44, 128.20, 128.10, 128.02, 127.88, 127.71, 127.66, 124.01, 119.07, 118.68, 118.33, 115.60, 81.84, 81.12, 79.83, 74.80, 74.68, 60.40, 58.56, 56.74, 29.70, 28.19, 28.10, 21.05, 14.20. **HRMS (ESI$^+$)**: m/z for $C_{19}H_{27}N_2O_4ClNa$ $[M+Na]^+$ calcd. 405.1552, found 405.1557.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 95/5 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1=11.7 min, t_2= 14 min; e.r.= 96:4.

Di-tert-butyl (*S*)-1-(1-(4-(trifluoromethyl)phenyl)allyl)hydrazine-1,2-dicarboxylate (3r)

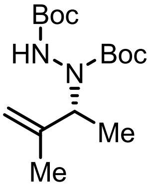


White solid. The titled compound was obtained from **1cr** in 34% yield (43 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 – 7.41 (m, 4H), 6.23 – 5.62 (m, 3H), 5.35 (d, *J* = 10.3 Hz, 1H), 5.23 (d, *J* = 17.4 Hz, 1H), 1.56 – 1.00 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.70, 139.66, 134.40, 131.29, 129.83, 128.39, 126.83, 126.59, 125.23, 123.24, 82.01, 81.25, 79.80, 65.86, 63.35, 28.17, 28.08, 15.28. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.59. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{28}N_2O_4F_3$ $[M+H]^+$ calcd. 417.1996, found 417.2001.

The e.r. was determined by **HPLC** analysis on a Lux cellulose-1 column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 10.0 min, t_2= 10.7 min; e.r.= 97:3.

Di-tert-butyl (*R*)-1-(3-methylbut-3-en-2-yl)hydrazine-1,2-dicarboxylate (3s)

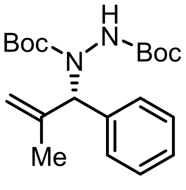


White solid. The titled compound was obtained from **1cs** in 86% yield (78 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.15-5.52 (m, 1H), 4.98-4.33 (m, 3H), 1.92-1.62 (m, 3H), 1.57-1.42 (m, 18H), 1.28 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.04, 144.65, 111.79, 81.14, 80.75, 28.25, 28.17, 20.76, 15.37. **HRMS (ESI$^+$)**: m/z for $C_{15}H_{28}N_2O_4Na$ $[M+Na]^+$ calcd. 323.1941, found 323.1947.

The e.r. was determined by **HPLC** analysis on a Chiralcel OD-H column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 8 min, t_2= 9.2 min; e.r.> 99.5:0.5.

Di-tert-butyl (*S*)-1-(2-methyl-1-phenylallyl)hydrazine-1,2-dicarboxylate (3t)

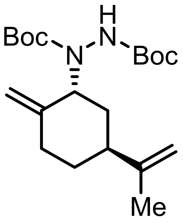


White solid. The titled compound was obtained from **1ct** in 89% yield (97 mg) after flash chromatography (from 100% Hex to 1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 5H), 6.24-5.95 (m, 1H), 5.82-5.52 (m, 1H), 5.11-4.66 (m, 2H), 1.87 – 1.01 (m, 21H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.19, 154.72, 154.37, 143.02, 141.92, 139.74, 139.58, 137.60, 136.19, 130.67, 130.17, 130.08, 129.94, 129.86, 129.54, 129.05, 128.88, 128.83, 128.68, 128.38, 128.33, 128.19, 128.17, 128.13, 128.02, 127.80, 127.53, 126.59, 126.45, 126.41, 124.96, 111.14, 99.12, 97.84, 87.94, 81.51, 81.34, 80.79, 80.56, 79.88, 68.93, 67.15, 65.85, 62.26, 30.33, 29.70, 28.37, 28.16, 28.04, 27.94, 27.57, 21.79, 21.08, 18.23, 15.27, 14.12. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{30}N_2O_4Na$ $[M+Na]^+$ calcd. 385.2098, found 385.2103.

The e.r. was determined by **HPLC** analysis on a Chiralpak AS-H column: hexane/*i*-PrOH 97/3 flow rate 0.5 mL/min, 25 °C, λ = 220 nm: t_1= 17 min, t_2= 20.2 min; e.r.= 99.5:0.5.

Di-tert-butyl 1-((1*R*,5*S*)-2-methylene-5-(prop-1-en-2-yl)cyclohexyl)hydrazine-1,2-dicarboxylate (3u)

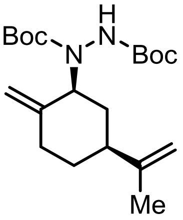


White solid. The titled compound was obtained from **1cu** in 55% yield (61 mg) after flash chromatography (1:9 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.33-5.85 (m, 1H), 5.00 – 4.48 (m, 5H), 2.58 – 1.33 (m, 28H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.60, 155.33, 154.91, 150.61, 148.81, 147.43, 146.83, 139.75, 135.73, 130.11, 128.85, 127.54, 125.52, 122.39, 119.38, 114.07, 110.16, 109.77, 108.99, 108.78, 108.66, 108.19, 88.91, 81.35, 81.20, 80.86, 67.23, 65.85, 60.96, 59.05, 56.97, 41.16, 41.01, 39.33, 38.06, 36.79, 34.32, 33.50, 32.81, 32.21, 31.72, 31.43, 31.06, 30.89, 30.41, 30.33, 29.70, 29.30, 29.05, 28.35, 28.23, 28.18, 27.48, 26.12, 21.59, 21.19, 21.00, 20.92, 20.83, 20.80. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{35}N_2O_4$ $[M+H]^+$ calcd. 367.2591, found 367.2597.

The d.r was determined by **^{1}H NMR** analysis at 100°C. dr> 20:1.

Di-tert-butyl 1-((1*S*,5*S*)-2-methylene-5-(prop-1-en-2-yl)cyclohexyl)hydrazine-1,2-dicarboxylate (3u')

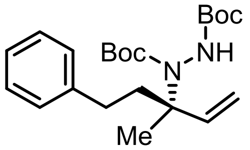


Pale yellow oil. The titled compound was obtained from **1cu** with ***ent*-N** in 44% yield (49 mg) after flash chromatography (1:9 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.32-5.98 (m, 1H), 4.88-4.63 (m, 4H), 4.54 – 4.29 (m, 1H), 2.50-2.40 (m, 1H), 2.33 – 2.02 (m, 4H), 1.87-1.75 (m, 1H), 1.58-1.38 (m, 18H), 1.36 – 1.15 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.79, 154.15, 153.89, 147.80, 138.73, 129.09, 127.83, 126.52, 118.37, 108.09, 107.96, 107.42, 107.16, 104.12, 103.75, 87.89, 80.41, 80.21, 79.79, 64.84, 58.03, 57.84, 43.37, 43.16, 40.13, 38.31, 37.04, 34.01, 33.60, 33.29, 30.89, 30.64, 30.03, 29.99, 28.28, 28.01, 27.17, 19.90, 14.25. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{35}N_2O_4$ $[M+H]^+$ calcd. 367.2591, found 367.2597.

The d.r. was determined by **^{1}H NMR** analysis at 100°C. dr: 89:11.

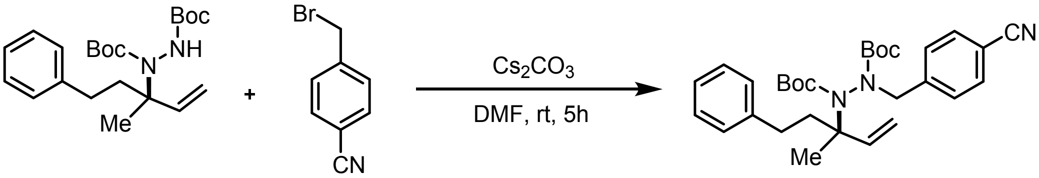
Di-tert-butyl (*R*)-1-(3-methyl-5-phenylpent-1-en-3-yl)hydrazine-1,2-dicarboxylate (3v)



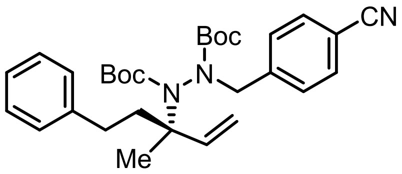
Pale yellow solid. The titled compound was obtained from **1cv** in 50% yield (59 mg) after flash chromatography (1:7 Et_2O/Hex).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.09 (m, 5H), 6.29-5.89 (m, 2H), 5.17 – 5.03 (m, 2H), 2.80 – 2.20 (m, 3H), 2.14-1.60 (m, 2H), 1.53-1.40 (m, 20H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.50, 127.35, 124.76, 110.31, 84.60, 80.25, 63.70, 39.62, 29.84, 27.25, 27.24, 27.21, 22.69. **HRMS (ESI$^+$)**: m/z for $C_{22}H_{34}N_2O_4Na$ $[M+Na]^+$ calcd. 413.2411, found 413.2416.

To determine the *e.r.*, 50 mg of the compound (0.1 mmol) were converted into the N-benzylated analogue in 0.2 mL of dry DMF with 49 mg of Cs_2CO_3 (0.15 mmol) and 19 mg of 4-(bromomethyl)benzonitrile (0.096 mmol, 0.96 eq.), under vigorously stirring at room temperature for 5 hours. The reaction was quenched with water and extracted one time with Et_2O. The organic layer was directly poured into a packed column to perform the purification (1:5 Et_2O/Hex).



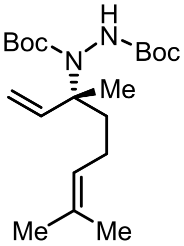
Di-tert-butyl (*R*)-1-(4-cyanobenzyl)-2-(3-methyl-5-phenylpent-1-en-3-yl)hydrazine-1,2-dicarboxylate (3vb)



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 – 7.40 (m, 2H), 7.32 – 6.99 (m, 7H), 6.30 – 5.92 (m, 1H), 5.42 – 4.94 (m, 2H), 4.52 (d, *J* = 136.2 Hz, 1H), 2.77 – 2.57 (m, 1H), 2.59 – 2.19 (m, 2H), 1.95 (m, 1H), 1.52 – 1.25 (m, 18H), 1.23 – 1.19 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.54, 132.03, 130.56, 128.43, 128.41, 128.35, 128.27, 125.86, 125.78, 118.82, 111.71, 111.34, 82.07, 81.91, 80.89, 65.86, 64.45, 57.29, 55.91, 44.07, 41.33, 41.06, 40.64, 31.34, 30.86, 30.33, 28.38, 28.27, 28.24, 28.12, 28.05, 25.38, 23.71, 15.29. **HRMS (ESI$^+$)**: m/z for $C_{30}H_{39}N_3O_4Na$ $[M+H]^+$ calcd. 528.2833, found 528.2838.

The d.r and e.r. were determined by **HPLC** analysis on a Chiralpak ID-3 column: hexane/*i*-PrOH 98/2 flow rate 0.5 mL/min, 25 °C, λ = 254 nm: t_1= 21 min, t_2= 21.5 min; t_3=26.1 min; t_4=29 min. d.r. (peak 1 and peak 3 one diastereoisomer; peak 2 and peak 4 one diastereoisomer) =1:1. The e.r. of the starting trisubstituted hydrazide is 70:30.

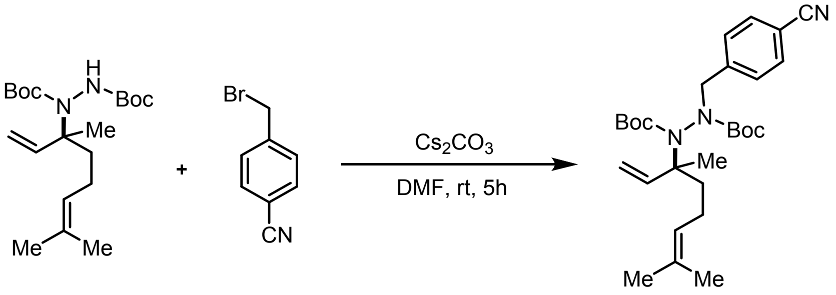
Di-tert-butyl (*R*)-1-(3,7-dimethylocta-1,6-dien-3-yl)hydrazine-1,2-dicarboxylate (3w)



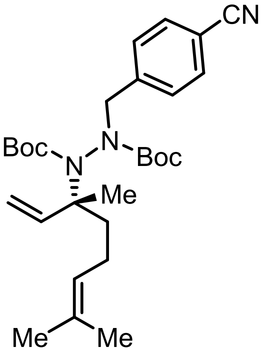
Colourless oil. The titled compound was obtained from **1cw** in 80% yield (88 mg) after flash chromatography (from 100% Hex to 1:8 Et_2O/Hex).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.23 – 5.80 (m, 2H), 5.25 – 4.90 (m, 3H), 2.11 – 1.87 (m, 3H), 1.86 – 1.69 (m, 1H), 1.70-1.64 (m, 3H), 165-1.53 (m, 4H), 1.53 – 1.40 (m, 18H), 1.40-1.29 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.99, 144.93, 142.61, 131.47, 124.28, 111.55, 110.89, 81.02, 80.89, 80.68, 64.46, 38.82, 38.05, 37.74, 28.40, 28.21, 28.19, 28.18, 25.64, 23.72, 23.05, 22.99, 22.76, 17.58, 15.22. **HRMS (ESI$^+$)**: m/z for $C_{20}H_{36}N_2O_4Na$ $[M+Na]^+$ calcd. 391.2567, found 391.2573.

To determine the e.r., 37 mg of the compound (0.1 mmol) were converted into the N-benzylated analogue in 0.2 mL of dry DMF with 49 mg of Cs_2CO_3 (0.15 mmol) and 19 mg of 4-(bromomethyl)benzonitrile, (0.096 mmol, 0.96 eq.) under vigorously stirring at room temperature for 5 hours. The reaction was quenched with water and extracted one time with Et_2O. The organic layer was directly poured into a packed column to perform the purification (1:4 Et_2O/Hex).



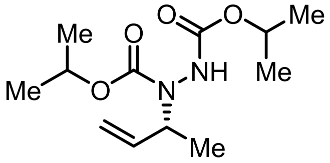
Di-tert-butyl (*R*)-1-(4-cyanobenzyl)-2-(3,7-dimethylocta-1,6-dien-3-yl)hydrazine-1,2-dicarboxylate (3wb)



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 2H), 7.49 – 7.43 (m, 2H), 6.19 – 5.95 (m, 1H), 5.15 – 4.99 (m, 3H), 4.55 – 4.30 (m, 2H), 2.10 –1.10 (m, 31H). **HRMS (ESI$^+$)**: m/z for $C_{28}H_{41}N_3O_4Na$ $[M+Na]^+$ calcd. 506.2989, found 506.2995.

The d.r and e.r. were determined by **HPLC** analysis on a Chiralpak ID-3 column: hexane/*i*-PrOH 98/2 flow rate 0.5 mL/min, 25 °C, $\lambda = 210$ nm: t_1= 13.5 min, t_2= 14 min; t_3=16 min; t_4=17.3 min. d.r. (peak 1 and peak 3 one diasterisomer; peak 2 and peak 4 one diastereoisomer) =1.15:1, e.r. (major diastereoisomer)= 94.5:5.5, e.r. (minor diastereoisomer)= 95:5. Enantiomeric ratio of the starting trisubstitued hydrazide= 90%.

Diisopropyl (*R*)-1-(but-3-en-2-yl)hydrazine-1,2-dicarboxylate (3x)

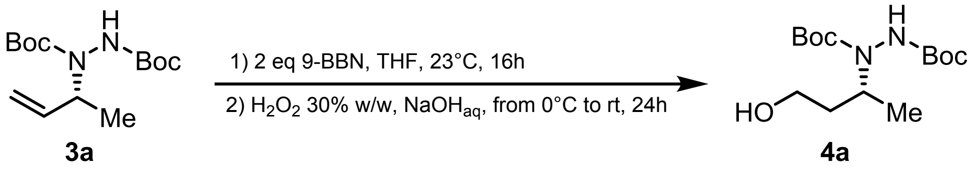


^{1}H NMR (400 MHz, CDCl$_3$) δ 6.01 (m, 2H), 5.21 – 5.04 (m, 2H), 4.92 (hept, *J* = 6.2 Hz, 2H), 4.78 (m, 1H), 1.22 (m, 15H). **HRMS (ESI$^+$)**: m/z for $C_{12}H_{22}N_2O_4Na$ [M+Na]$^+$ calcd. 281.1472, found 281.1478.

The e.r. was determined by **HPLC** analysis on a Chiralcel IC column: hexane/*i*-PrOH 97/3 flow rate 1 mL/min, 25 °C, λ = 210 nm: t_1= 31.10 min, t_2= 33,3 min; e.r.=99.5:0.5.

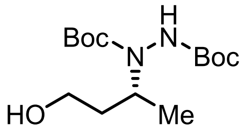
DERIVATIZATIONS REACTIONS

Synthesis of 4a



In a 50 mL two necks round bottom flask under nitrogen flow were added 6.3 mL of freshly distilled THF, 85.8 mg of x (0.3 mmol, 1 eq.) and 1.2 mL of 9-BBN (0.5M in THF, 0.6 mmol, 2 eq.). The solution was stirred overnight at room temperature. When the starting material was fully consumed (monitored by TLC), the reaction was quenched with 2 mL of distilled water and 0.6 mL of 1.0 M NaOH. Then the flask was cooled to 0°C and 0.22 mL of H_2O_2 (30% w/w) were added dropwise. The stirring continued for 24 hours at room temperature; afterward the layers were separated and the aqueous phase was washed three times with Et_2O. The organic phases were collected, washed with brine, dried with $MgSO_4$ and concentrated at reduced pressure. The residue was purified by flash chromatography (2:1 Et_2O/Hex) to obtain 64 mg of the desired product (0.21 mmol, 70% yield).

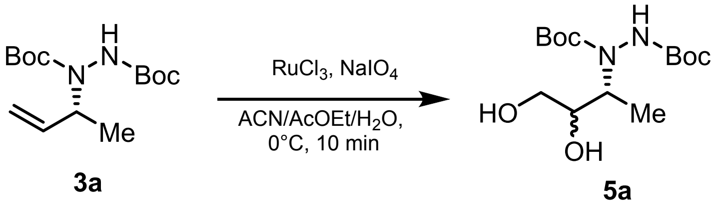
Di-tert-butyl (*R*)-1-(4-hydroxybutan-2-yl)hydrazine-1,2-dicarboxylate (4a)



^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20-6.5.71 (m, 1H), 4.51-4.22 (m, 1H), 3.80-3.49 (m, 1H), 1.61-1.50 (m, 3H), 1.44 (bs, 18H), 1.15-1.13 (d, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.00, 155.76, 135.81, 125.52, 81.59, 81.32, 81.07, 59.42, 49.24, 36.98, 36.40, 34.24, 31.93, 30.33, 29.70, 28.20, 22.70, 20.61, 18.41, 17.89, 14.12. **HRMS (ESI$^+$)**: m/z for $C_{21}H_{31}N_3O_5Na$ $[M+Na]^+$ calcd. 327.1890, found 327.1896.

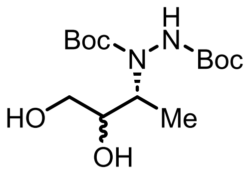
The e.r. was determined by **HPLC** analysis on a Chiralpak IA-3 column: hexane/*i*-PrOH 90/10 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1= 19.8 min, t_2= 26.2 min; e.r.= 96:4.

Synthesis of 5a



In a 25 mL round bottom containing 286 mg of **3a** (1 mmol, 1 eq.) 6 mL of AcOEt and 6 mL of ACN were added. The resulting solution was cooled to 0°C and 14.5 mg of $RuCl_3$ x $3H_2O$ (0.05 mmol, 0.05 eq.), 321 mg of $NaIO_4$ (1.5 mmol, 1.5 eq.) and 2 mL of distilled water were added. The dark mixture was stirred for 10 minutes in the ice bath. Afterward, 15 mL of water were added to the solution and extracted three times with AcOEt. The organic phases were collected, dry under Na_2SO_4 and concentrated at reduced pressure. The residue was purified with flash chromatography (1.5:1 AcOEt/Hex) to afford 266 mg of **5a** as a mixture of diastereosiomers (0.83 mmol, 83% yield).

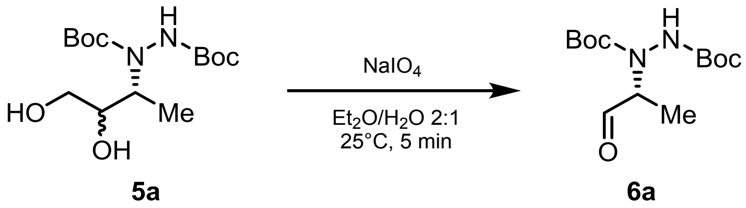
Di-tert-butyl 1-((2R)-3,4-dihydroxybutan-2-yl)hydrazine-1,2-dicarboxylate (5a)



^{1}H NMR (600 MHz, $CDCl_3$) δ 6.80-6.09 (m, 1H), 5.40-4.70 (m, 1H), 4.49-4.06 (m, 1H), 3.94 – 3.23 (m, 3H), 3.16-2.39 (m, 1H), 1.62 – 1.27 (m, 18H), 1.22 – 0.97 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.17, 155.20, 88.30, 82.71, 81.95, 72.69, 63.44, 60.41, 53.58, 30.94, 28.25, 28.19, 28.17, 28.14, 21.06, 14.29, 14.21. **HRMS (ESI$^+$)**: m/z for $C_{14}H_{28}N_2O_6Na$ $[M+Na]^+$ calcd. 343.1845, found 343.1840.

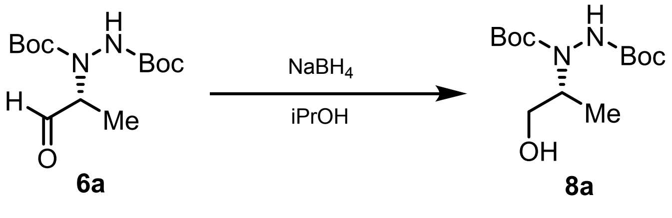
The d.r and e.r. were determined by **HPLC** analysis on a Chiralpak IA column: hexane/*i*-PrOH 90/10 flow rate 0.5 mL/min, 25 °C, λ = 210 nm: t_1 = 11 min, t_2 = 11.6 min; t_3 = 17.2 min; t_4 = 19.4 min. dr = 2.2:1, e.r. (major diastereoisomer) = e.r.= 96:4.

Synthesis of 6a



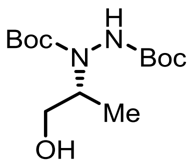
128 mg of the previous diol **5a** (0.4 mmol, 1 eq.) were added to a screw cap vial containing an heterogeneous mixture of 4.2 mL of Et_2O/H_2O (2:1). Then, 214 mg of $NaIO_4$ (0.4 mmol, 1.0 eq.) were added and was vigorously stirred for 5 minutes. The mixture was diluted with Et_2O and extracted with water. The layers were separated, dried under Na_2SO_4 and concentrated at the rotary evaporator without heating. The crude was immediately dissolved in 4 mL of Et_2O, split in two parts to proceed with the next derivatizations.

Synthesis of 8a



Half of the crude was concentrated at reduced pressure, redissolved in 4 mL of iPrOH and subjected to the reduction with 7.55 mg of $NaBH_4$ (0.2 mmol, 1 eq.). After 2 hours the reaction was quenched with a saturated solution of NH_4Cl and extracted three times with AcOEt. The organic phases were collected, washed with brine, dried with $MgSO_4$ and concentrated at reduced pressure. The crude did not require further purifications.

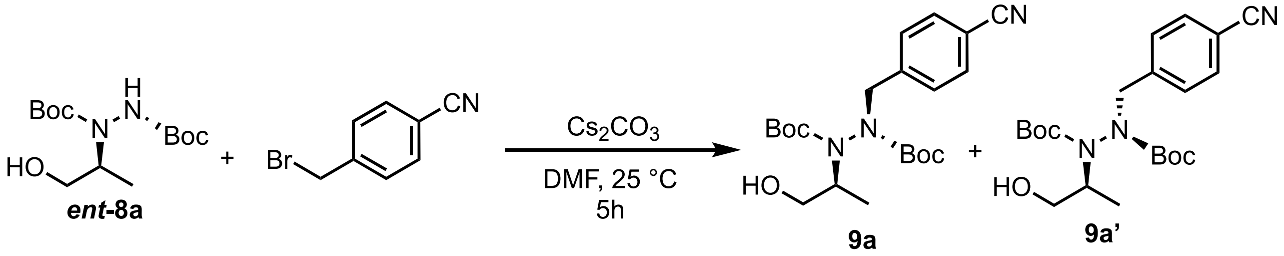
Di-tert-butyl (*R*)-1-(1-hydroxypropan-2-yl)hydrazine-1,2-dicarboxylate (8a)



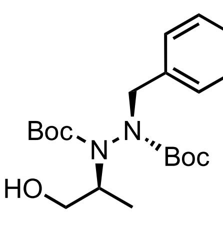
White solid, 48 mg, 83% yield after 2 steps (from **5a**).

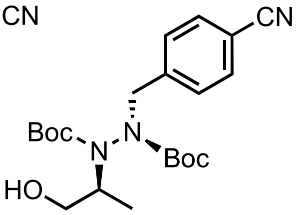
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.36 – 5.86 (m, 1H), 4.66 – 4.16 (m, 2H), 3.65 – 3.21 (m, 2H), 1.48 (d, *J* = 11.7 Hz, 19H), 1.13 – 0.93 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.55, 157.95, 155.71, 154.84, 82.30, 81.98, 81.40, 78.56, 67.75, 67.29, 63.36, 56.01, 53.73, 38.71, 29.70, 28.21, 28.11, 27.95, 26.98, 13.71, 10.61, 9.97, 9.42. **HRMS (ESI$^+$)**: m/z for $C_{13}H_{27}N_2O_5$ $[M+H]^+$ calcd. 291.1914, found 291.1920.

Compound ***ent*-8a** (29 mg, 0.1 mmol), prepared from ***ent*-3a** following the so far reported procedures of derivatization, was directly converted into the N-benzylated analogue **9** in 0.2 mL of dry DMF with 49 mg of Cs_2CO_3 (0.15 mmol) and 19 mg of 4-(bromomethyl)benzonitrile (0.096 mmol, 0.96 eq.), under vigorously stirring at room temperature for 5 hours. The reaction was quenched with water and extracted one time with Et_2O. The organic layer was directly poured into a packed column to perform the purification (100% Et_2O).



Di-tert-butyl -1-(4-cyanobenzyl)-2-(1-hydroxypropan-2-yl)hydrazine-1,2-dicarboxylate (9)


9a

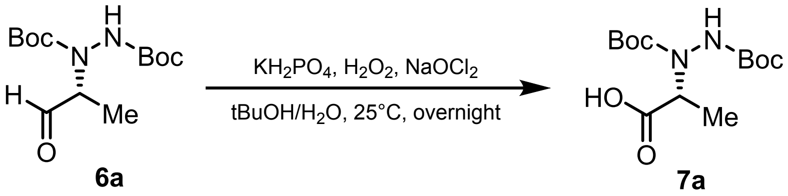

9a'

The product was obtained as a mixture of diastereoisomers **9a** and **9a'**. Viscous oil. 30 mg, 75% yield after two steps (from **5a**).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 – 7.50 (m, 2H), 7.45 – 7.36 (m, 2H), 5.46 – 4.08 (m, 3H), 3.70 –3.39 (m, 2H), 1.53 – 0.76 (m, 21H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.36, 157.64, 154.65, 154.41, 146.21, 143.71, 143.09, 132.33, 132.22, 132.18, 129.21, 128.00, 127.60, 127.02, 118.85, 118.73, 118.58, 111.24, 110.96, 83.66, 83.57, 82.32, 81.72, 64.59, 64.25, 63.64, 63.62, 60.40, 58.64, 58.37, 58.30, 56.69, 55.13, 31.59, 30.33, 29.70, 28.26, 28.21, 28.18, 28.11, 27.99, 27.88, 22.66, 21.06, 15.25, 15.02, 14.21, 14.12. **HRMS (ESI$^+$)**: m/z for $C_{21}H_{31}N_3O_5Na$ $[M+Na]^+$ calcd. 428.2156, found 428.2162.

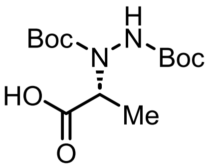
The d.r and e.r. were determined by **HPLC** analysis on a Lux cellulose-2 column: hexane/*i*-PrOH 90/10 flow rate 1 mL/min, 25 °C, λ = 254 nm: t_1= 14.1 min, t_2= 14.9 min; t_3=20.6 min; t_4=23.6 min. d.r.=1:12 (peak 1 and peak 2 one diasterisomer; peak 3 and peak 4 one diasteroisomer). The e.r. of **9a** and **9a'** is 90:10. The e.r. of starting trisubstitued hydrazide ***ent*-8a** is 90:10.

Synthesis of 7a



Half of the crude from **6a** was concentrated at reduced pressure and redissolved in 2.5 mL of *t*BuOH to be subjected to the Pinnick oxidation. To the solution were added 0.5 mL distilled water, 46 mg of KH_2PO_4 (0.34 mmol, 1.7 eq.), 0.1 mL of H_2O_2 30% w/w (9.6 mmol, 4.8 eq.) and 62 mg of $NaOCl_2$ (0.69 mmol, 3.45 eq.) and the stirring was continued overnight. Then the reaction was quenched with distilled water and extracted three times with AcOEt. The organic phases were collected, washed with brine, dried under $MgSO_4$ and concentrated at reduced pressure. The crude did not require further purifications.

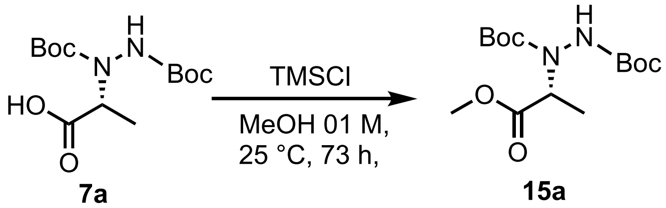
N-(tert-butoxycarbonyl)-N-((tert-butoxycarbonyl)amino)-D-alanine (7a)



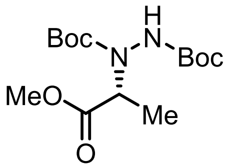
Viscous oil. 47 mg, 78% yield after 2 steps (from **5a**).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96-6.32 (m, 1H), 5.20-4.12 (m, 1H), 1.55-1.41 (m, 21H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.31, 153.00, 83.12, 64.84, 59.11, 55.83, 30.91, 30.56, 30.42, 30.12, 28.68, 28.34, 27.14, 27.05, 27.00, 21.67, 14.20, 14.04, 13.50, 13.10. **HRMS (ESI$^+$)**: m/z for $C_{13}H_{24}N_2O_6Na$ $[M+Na]^+$ calcd. 327.1527, found 327.1532.

To determine the e.r., 30 mg of the compound **8a** (0.1 mmol, 1 eq.) was converted into the corresponding methyl-ester in MeOH (0.1 M) with 25 µL of TMSCl (0.2 mmol, 2 eq.), stirring at 25°C for three days. Afterward, the solvent was removed under reduced pressure to afford the desired product.

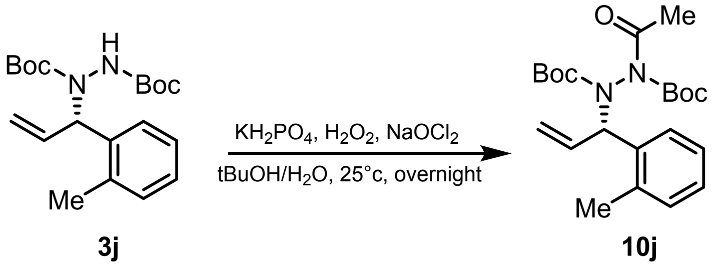


Di-tert-butyl (*R*)-1-(1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate (15a)



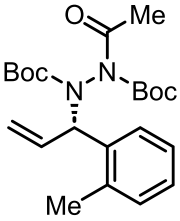
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.27 (d, *J* = 165.1 Hz, 1H), 4.83 (d, *J* = 171.9 Hz, 1H), 3.73 (s, 3H), 1.47 (d, *J* = 6.1 Hz, 22H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.04, 154.09, 80.79, 51.26, 28.68, 27.15, 27.11, 13.32. **HRMS (ESI$^+$)**: m/z for $C_{14}H_{25}N_2O_6Na$ $[M+Na]^+$ calcd. 341.1683, found 341.1689.

Synthesis of 10j



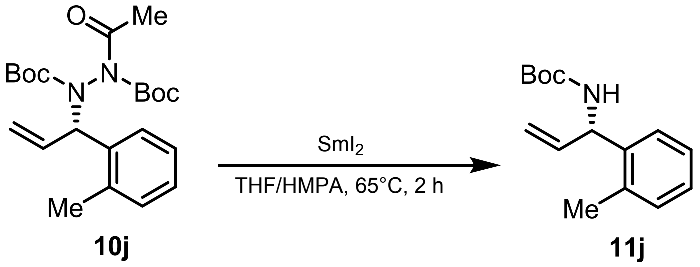
51 mg of **3j** (0.14 mmol, 1 eq.) were added to a capped vial and dissolved with 0.3 mL of acetic anhydride and 0.14 mL of pyridine. Afterward, 8.5 mg of DMAP (0.07 mmol, 0.5 eq.) were added to the solution and the vial was placed in an oil bath at 50°C and the mixture was vigorously stirred for 24 hours. Then, the reaction was cooled to room temperature and quenched with distilled water. The layers were separated and the aqueous phase was extracted three times with Et_2O. The organic phases were collected, washed two times with sat $NaHCO_3$, twice with sat NH_4Cl and eventually two times with brine. The organic layer was separated, dried with $MgSO_4$ and concentrated at reduced pressure. The residue was purified by flash chromatography (from 1:5 to 1:3 Et_2O/Hex) to afford 45 mg **10j** (0.11 mmol, 80% yield).

Di-tert-butyl (S)-1-acetyl-2-(1-(o-tolyl)allyl)hydrazine-1,2-dicarboxylate (10n)



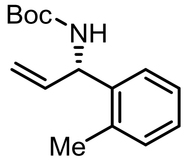
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 – 7.05 (m, 4H), 5.96 – 4.93 (m, 4H), 2.53 – 2.21 (m, 6H), 1.64-1.00 (m, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 134.46, 130.54, 130.18, 126.68, 126.27, 125.82, 117.73, 84.39, 81.83, 30.94, 28.04, 28.01, 27.85, 27.72, 27.61, 25.77, 19.32. **HRMS (ESI$^+$)**: m/z for $C_{22}H_{32}N_2O_5Na$ $[M+Na]^+$ calcd. 427.2203, found 427.2209.

Synthesis of 11j



45 mg of **10j** (0.11 mmol, 1 eq.) were added to an oven dried two necks round bottom flask under nitrogen flow containing 1.5 mL of degassed THF and 0.2 mL of degassed HPMA. Then the flask was placed in an oil bath at 65°C and 8 mL of SmI_2 (0.1 M in THF) were added dropwise while the solution is under stirring. After two hours the flask was removed from the bath and the reaction was quenched with sat $NaHCO_3$ and extracted three times with Et_2O. The organic phases were collected, dried with $MgSO_4$ and concentrated at reduced pressure. The residue was purified by flash chromatography (from 1:5 to 1:3 Et_2O/Hex) to afford 21 mg of **11j** (0.08 mmol, 76% yield).

Tert-butyl (S)-(1-(o-tolyl)allyl)carbamate (11j)



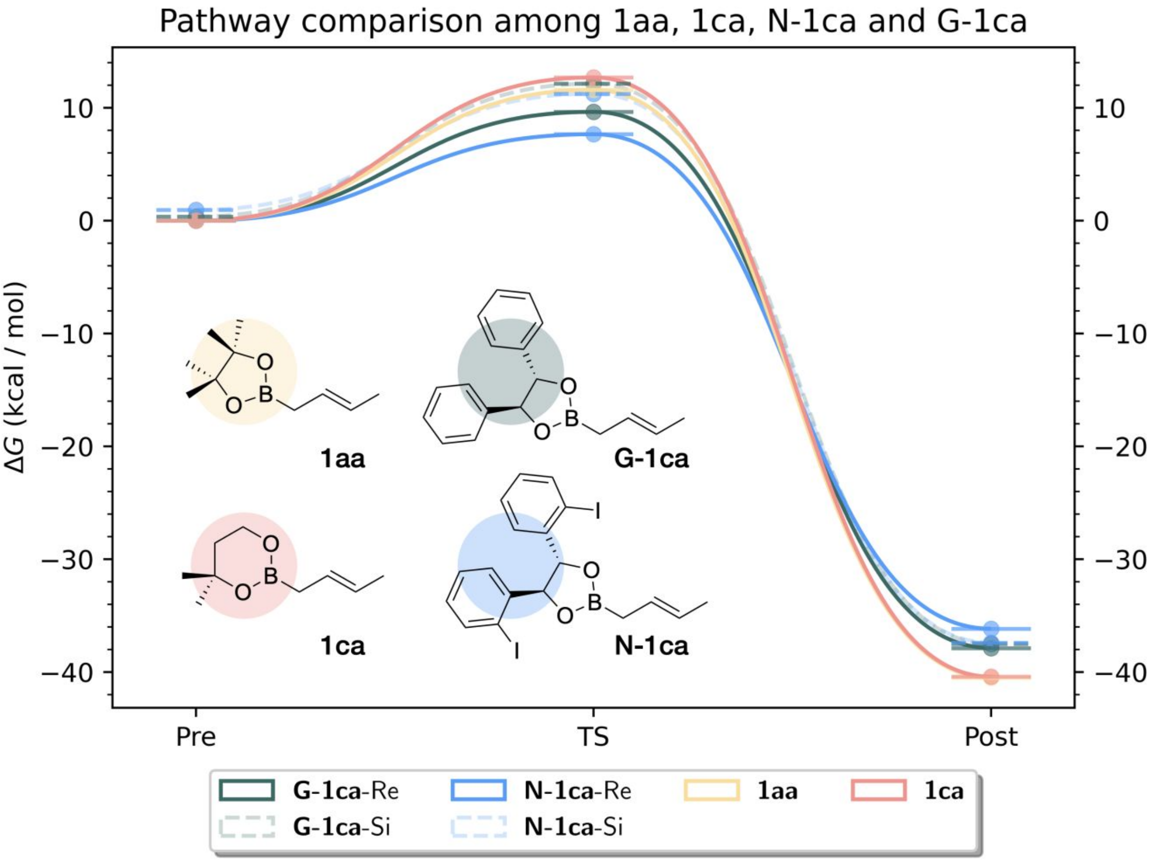
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 4H), 6.06 – 5.96 (m, 1H), 5.48 (bs, 1H), 5.22 (d, 1H) 5.18 (d, 1H), 2.38 (s, 3H), 1.43 (bs, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.98, 138.96, 137.65, 130.71, 127.51, 126.36, 126.19, 115.24, 115.23, 53.07, 28.38, 19.19. **HRMS (ESI$^+$)**: m/z for $C_{22}H_{32}N_2O_5Na$ $[M+Na]^+$ calcd. 427.2203, found 427.2209.

COMPUTATIONAL STUDY

Reaction pathways

The electrophilic amination reaction has been studied with four different crotyl boronates (**1aa**, **1ca**, **G**, and **N**) and **2a**. The results are shown in Table S7 and visualized in Figure S4.

Table S7: Comparison between reaction pathways.



	1aa	**1ca**	**N**		**G**	
			Re face	*Si* face	*Re* face	*Si* face
Pre	0.0	0.0	0.0	1.0	0.0	0.4
TS	11.6	12.7	7.7	11.3	9.7	12.1
Post	-40.5	-40.4	-36.1	-37.4	-37.9	-37.5

Comparison between reaction pathways. Energies are in kcal/mol. Theory level: r2scan-3c d4/def2-mTZVPP-CPCM[e =12]//r2scan-3c d4/def2-QZVP-CPCM[e=12] calculated at standard condition.

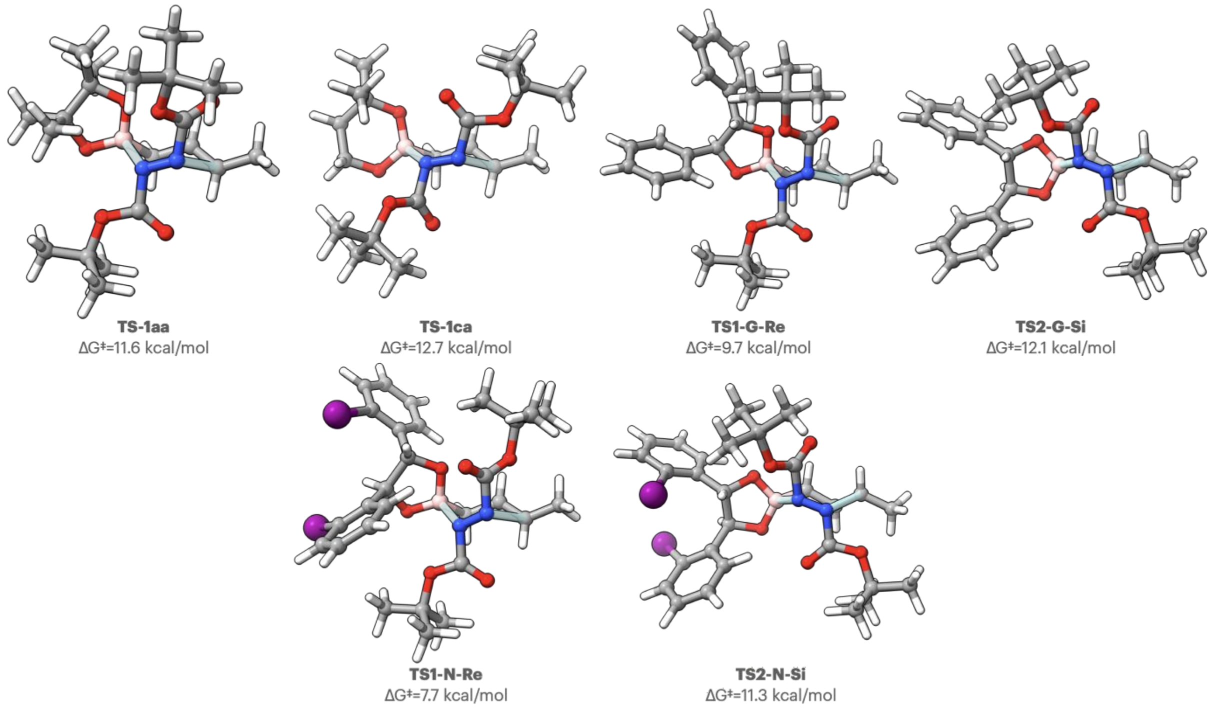


Figure S4. 3D Geometries of the various Transition States (TSs) with their relative energies. Level of theory: r2scan-3c d4/def2-mTZVPP-CPCM[e=12]//r2scan-3c d4/def2-QZVP-CPCM[e=12] calculated at standard condition.

The reactions with achiral boronates **1aa** and **1ca** show a higher ΔG‡ than those with the chiral boronates **G-1ca** and **N-1ca**, this result is in accordance with the experimental observation that the background racemic reaction is slow compared with the catalytic ones. In perfect accord with the experimental results, DFT calculations predict the formation of the product with (*R*) stereochemical configuration when using boronates **G-1ca** and **N-1ca** with the (*S,S*) configuration of the catalyst. In both cases the enantiomeric ratio (e.r.) of the reaction is slightly overestimated: calculations predict an e.r. of 97.8:2.2 for **G** (ΔΔG = 2.4 kcal/mol) and of 99.8:0.2 for **N** (ΔΔG = 3.6 kcal/mol) while the experimental values is 96:4. for both **G** and **N**.

Relative position of iodine atoms in TS1-N-Re

In addition to the standard conformational analysis of the TS, an additional analysis of the possible arrangements of the iodine atom was conducted for the TS of **N**, as shown in Figure S5. The structures differ in the relative positions of the iodine atoms and have been simply named according to their position, where “in” refers to a position “inside” the aromatic pocket, and “out” outside of it.

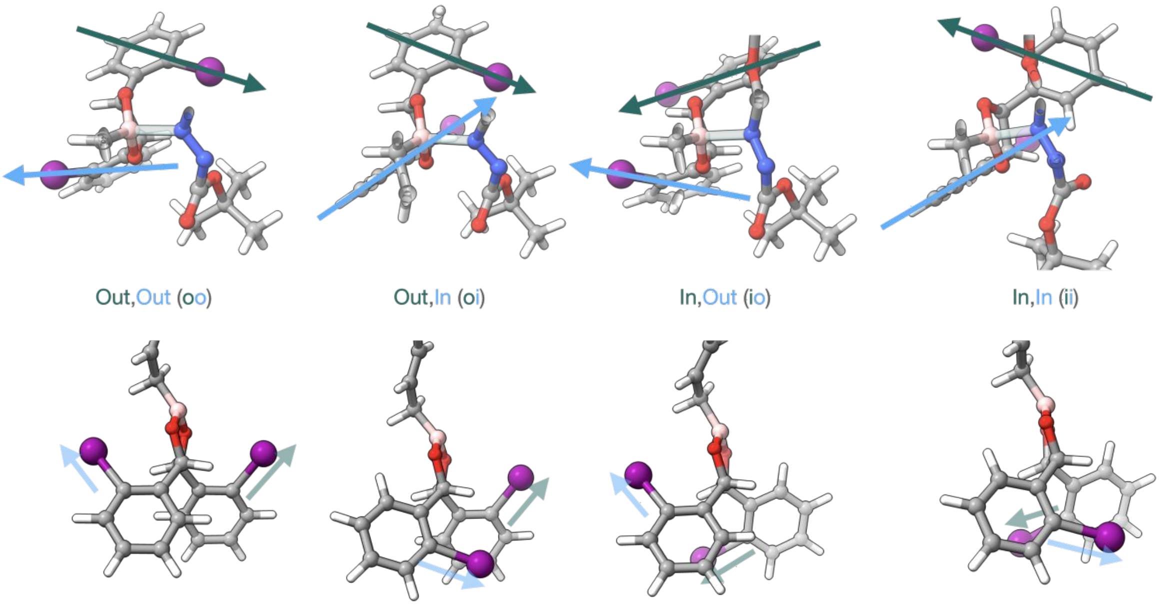


Figure S5. Possible disposition of the iodine atoms and relative denomination. Representation of the same geometries but with different prospective view of the **TS1-N-*Re*** geometry: upper line frontal view centred on the boron atom; bottom line perpendicular view emphasising the aromatic pocket (**2a** has been omitted for clarity).

All geometries of the possible conformations were optimized towards the TS. The results are compiled in Table S8.

Table S8. Relative energy of the four possible conformations of the iodine atoms for both the possible faces of **N**.

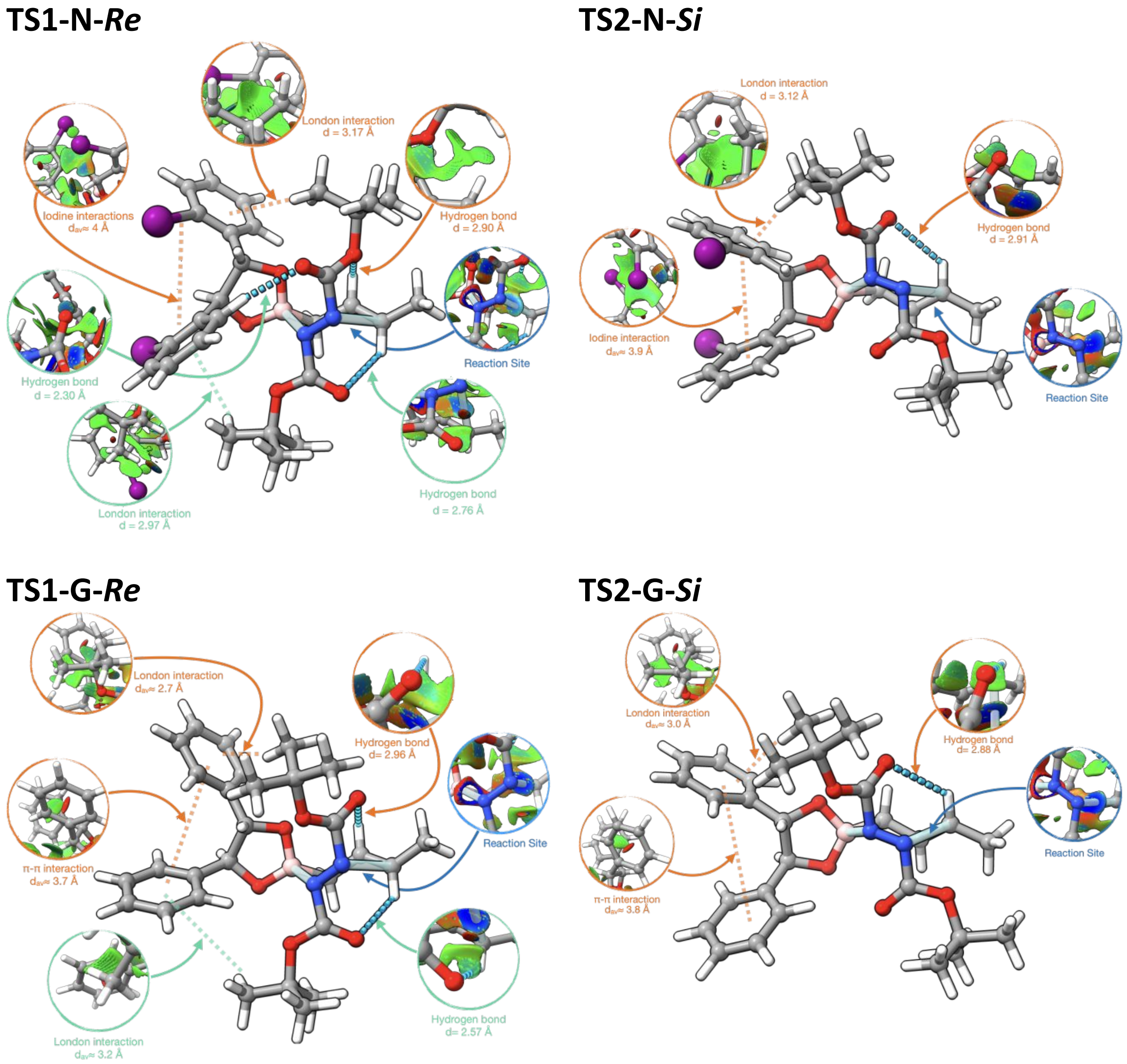
ΔΔG‡ [kcal/mol]	*Re* face	*Si* face
oo	*(142)*	*(166)*
oi	*(141)*	*N.C.*
io	4.72	4.08
ii	0.00	3.58

Theory level: r2scan-3c d4/def2-mTZVPP-CPCM[e=12] at standard condition. N.C.: not converged.

The results for the “oo” and “oi” geometries are extremely high due to steric clashes between the iodine atoms and the reaction zone; therefore, they were not further refined. The favourite one is that with both the iodine atoms inside the aromatic pocket (“ii”) for both the Re and Si approaches, and the further conformational search have been conducted one these geometries.

Analysis of TSs of catalyst N and G.

For the geometries of the catalytic reactions, the NCI surfaces have been plotted and are shown in Figure S6.


TS1-N-*Re*

TS2-N-*Si*

TS1-G-*Re*

TS2-G-*Si*

Figure S6. NCI analysis of the four catalytic TSs. Dashed blue lines represent a hydrogen bond and semi-transparent bonds represent the TS bond. Surface color scheme: blue attractive; green London; and red repulsive interaction. Circle color scheme: orange interactions present in both the diasteromeric TSs; blue for the reaction site; and green interactions present only in one TS.

Main common interactions that can be spotted are: i) the hydrogen bond (HB) between the oxygen of the carbonyl and the β-vinylic proton of the crotyl, ii) the London interaction of the methyl moiety of the BOCs pointing toward the aryl part of the catalyst, and iii) iodine-iodine interaction inside the aryl pocket. Comparing **TS1-N-*Re*** and **TS2-N-*Si***, there are three interactions which are present in both (shown in orange in the figure) and three additional interactions that are unique to the preferred **TS1-N-*Re*** (shown in green in the figure). These unique interactions include two hydrogen bonds and one London dispersion interaction between the remaining BOC group and the nearby aromatic ring. The hydrogen bond between the carbonyl oxygen and the ortho proton of the aryl group on the catalyst is particularly strong (d=2.30 Å). These interactions can explain the enantioselective preference for this TS and therefore for the formation of the *(R)* centre, as observed experimentally. The same analysis performed on **TS1-G-*Re*** and **TS2-G-*Si*** shows that, once again, the number of interactions is greater in the favoured TS, thus favouring the approach on the *Re* face of the crotyl. Finally, the comparison between the two preferred transition states (**TS1-N-*Re*** and **TS1-G-*Re***) reveals that **TS1-N-*Re*** has an extra hydrogen bond, which is also the shortest present in the structures. This may explain why the $\Delta G^{\ddagger}$ of the reaction with the iodine-containing catalyst is lower by 2 kcal/mol. In Table S9 are reported the selected geometrical parameters relevant to compare the TSs in Figure S6.

Table S9. Selected geometrical parameter of the 4 asymmetrical reactions

	γ Ar-Ar	NBC	C-N [Å]	B-N [Å]	Pyramidalization B	Boc-Ph [Å]	
TS1-N-*Re*	133°	93°	2.95	1.98	21.9°	**2.97**	**3.17**
TS2-N-*Si*	91°	95°	2.80	1.94	26.0°	**> 4**	**3.12**
TS1-G-*Re*	90°	92°	2.76	1.98	21.4°	**3.20**	**2.68**
TS2-G-*Si*	86°	95°	2.77	1.91	26.7°	**> 4**	**2.99**

Ar-Ar is the dihedral angle between the two aryl groups; NBC is the bite angle between the nitrogen, boron and allylic carbon atoms; C-N is the distance between the two reacting atoms; pyramidalization B represents the dihedral angle between O-O-C-B and helps understanding how much the boron atom is outside of the plane described from the two ester oxygens and the allylic carbon; Boc-Ph is the minimum distance between the hydrogens of the methyls of the Bocs and the nearest carbon atom of the phenyl ring.

From these parameters and from the distances highlighted in Figure S6, the favorable **TS1-N-*Re*** shows three hydrogen bonds, one of these is a highly stabilizing interaction between the oxygen of the carbonyl moiety and the hydrogen of the C6 of the iodophenyl ring of the catalyst. This interaction produces the highly distorted γ Ar-Ar dihedral angle without disrupting the constructive interaction inside the aromatic pocket, with the aromatic ring oriented towards the methyl group thus reinforcing this London interaction between them. This kind of interaction was possible also in the **TS1-G-*Re***, but the absence of the iodine atoms does not allow the aromatic rings to move towards the *tert*-butyl group and the BOC's carbonyl group; in addition, the carbonyl oxygen is pointing towards the vinylic β-proton, so the so HB between them can't be present.

Orbitals analysis

From the steric data above described, the focus of this study shifted toward the understanding of the orbital's contribution and interactions. To do so, the projection of the molecular orbitals (MOs) of both the **TSs** for catalyst **G** (here labelled Ξ_{i}) on the two different fragments: borocrotyl (**G-1ca**) ϕ_i and **2a** θ_i. This analysis was performed assuming that ϕ_i and θ_i are orthonormalized.

$$\Xi_i = \sum_{j}^{N} a_{ij}\,\phi_j \;+\; \sum_{j}^{N} b_{ij}\theta_j \qquad \text{(Eq. S1)}$$

$$a_{ij} = \int \Xi_i^*\,\phi_j d\boldsymbol{r} \qquad \text{(Eq. S2)}$$

$$b_{ij} = \int \Xi_i^*\,\theta_i d\boldsymbol{r} \qquad \text{(Eq. S3)}$$

$$\sum_{j}^{N} a_{ij}^2 \;+\; \sum_{j}^{N} b_{ij}^2 \coloneqq 1 \qquad \text{(Eq. S4)}$$

Where *i* is the number of the orbitals selected to describe the TSs geometry (HOMO-1, HOMO, LUMO, LUMO+1), *j* is related to the orbital's number of the selected fragments, and *a* and *b* represent the coefficients to weight the fragments' orbitals and are required to be normalized for each TS's orbital. The orbitals of the two fragments are represented in Figure S7.

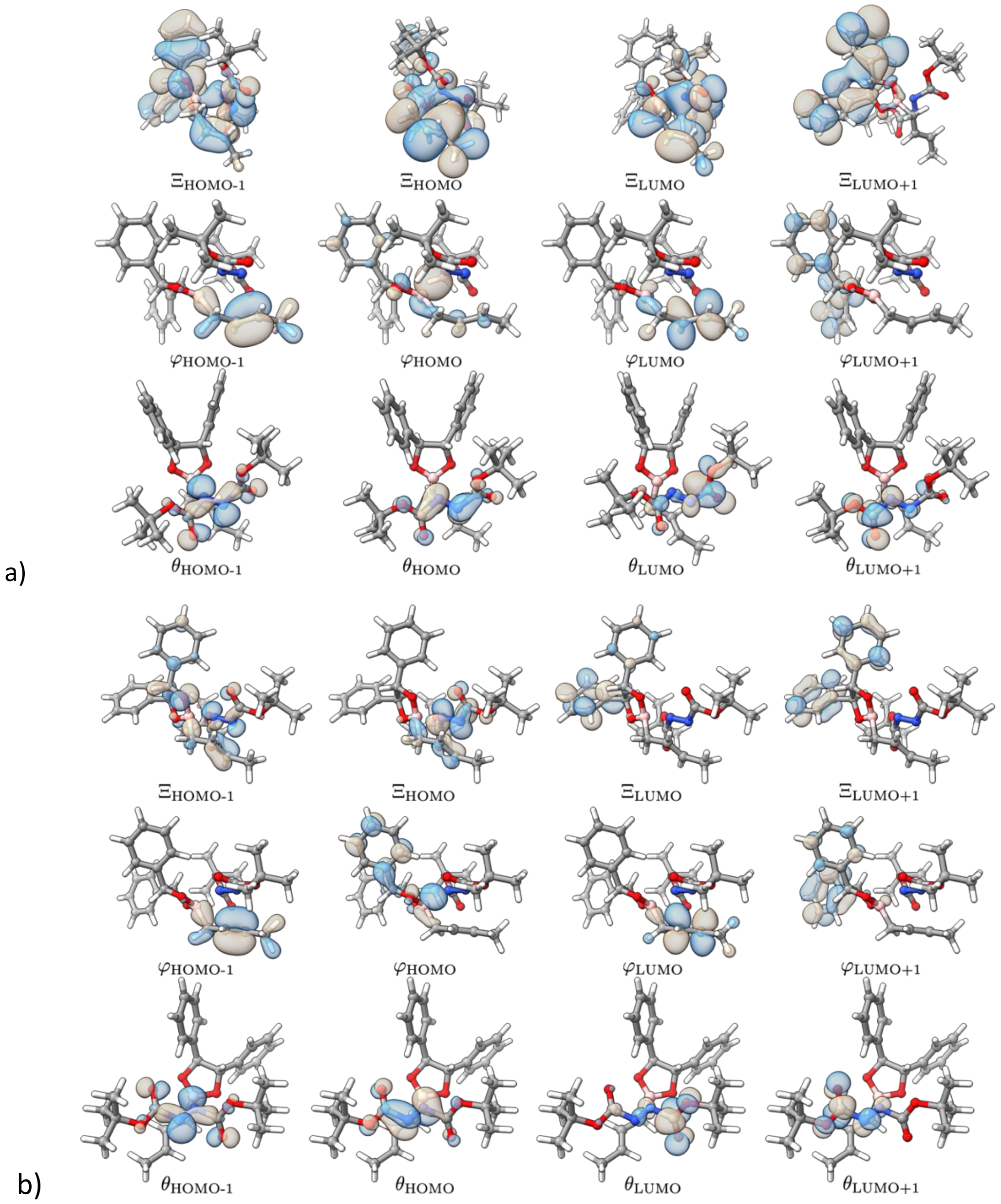


Figure S7. Orbital chosen for the projection analysis. a) Orbitals for the **Ts1-G-*Re***. b) Orbitals for the **Ts2-G-*Si***. List of the orbitals selected: Borocrotyl **G-1ca**: HOMO-1: p of C=C; HOMO: p_z of B; LUMO: p* of C=C and s* of C-B; LUMO+1: p* of G. Azodicarboxylate **2a**: HOMO-1: lone pair of N-atoms in **2a**; HOMO: p* of N=N; LUMO p* of C=O; LUMO+1 p* of C=O.

From the results of this analysis, it is evident that the composition of the MOs of the two TSs is substantially different (Figure S8). For the attack on the *Re* face, the two occupied orbitals of the TS (HOMO-1 and HOMO) are predominantly described by the HOMO and HOMO-1 of the **G-1ca** and by the HOMO-1, HOMO, and LUMO of the **2a**. On the other hand, the orbitals involved for the attack on the Si face are more mixed, making a clear separation difficult.

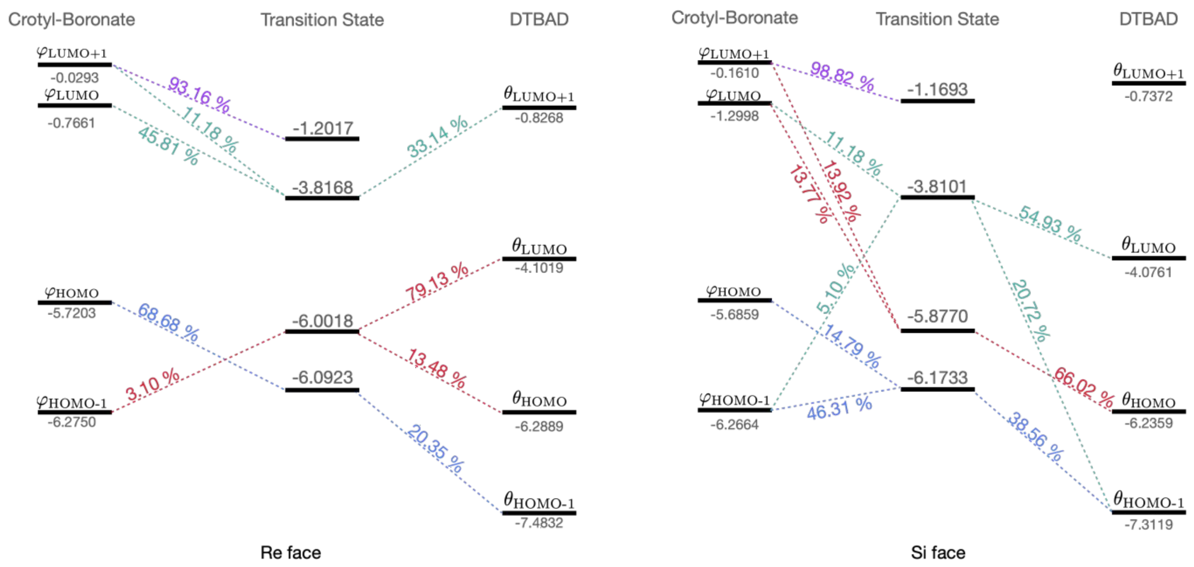


Figure S8. Projection diagram of the TS's MOs on the two different fragments with main characters highlighted.

Moreover, a second orbital analysis was conducted to find a reason that could rationalize the energy difference and thus the enantioselection of the catalyst. To do so, the overlap of the orbitals of the fragments as basis function was employed.

$$S_{ij} = \int \phi_i^* \theta_j dr \qquad \text{(Eq. S5)}$$

$$s_{ij} = \left(\frac{S_{ij}}{\max(S)}\right)^2 \times 100 \qquad \text{(Eq. S6)}$$

The results (Table S10) show a crucial difference in relative overlap: the maximum overlap is between θ_{HOMO-1} (so the lone pair of the nitrogen atoms) with the ϕ_{HOMO} (so the p_z of the boron atom).

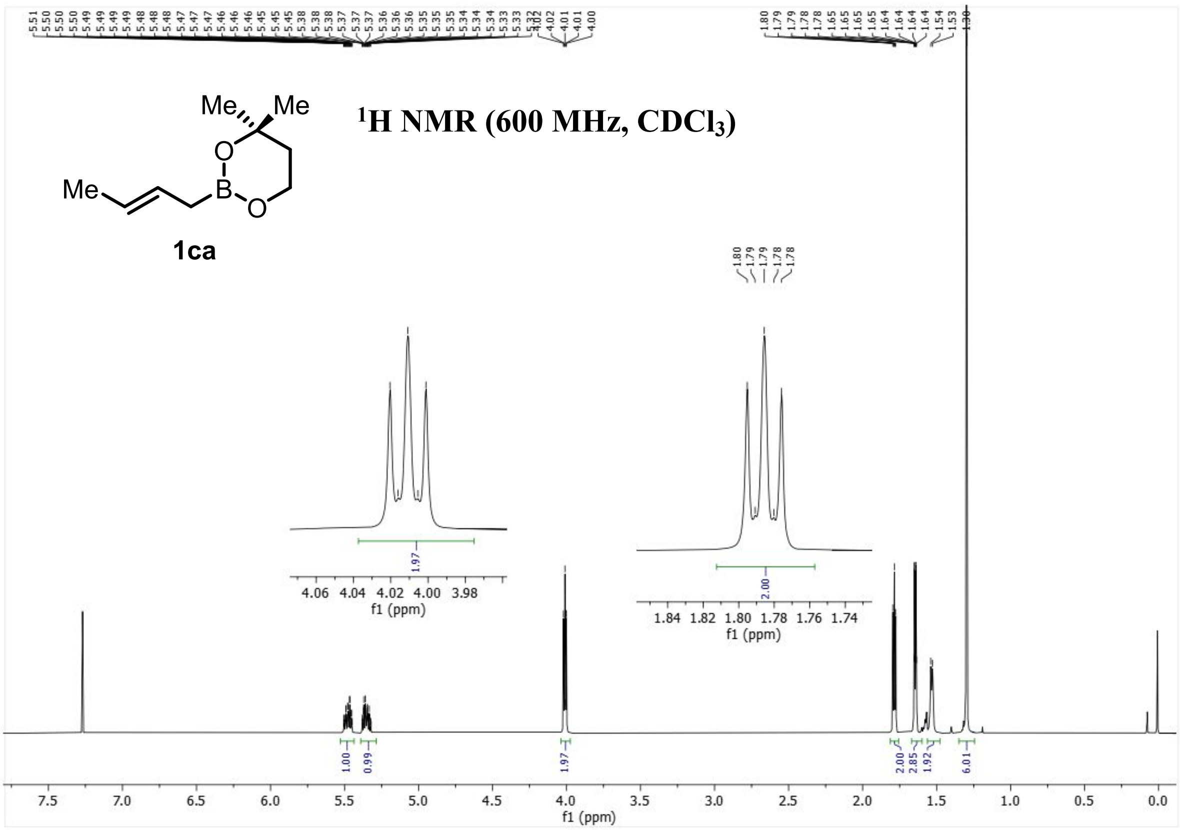
Table S10. Relative overlap coefficient of the two diasteromeric TSs of **G** resulting from Eq. S6.

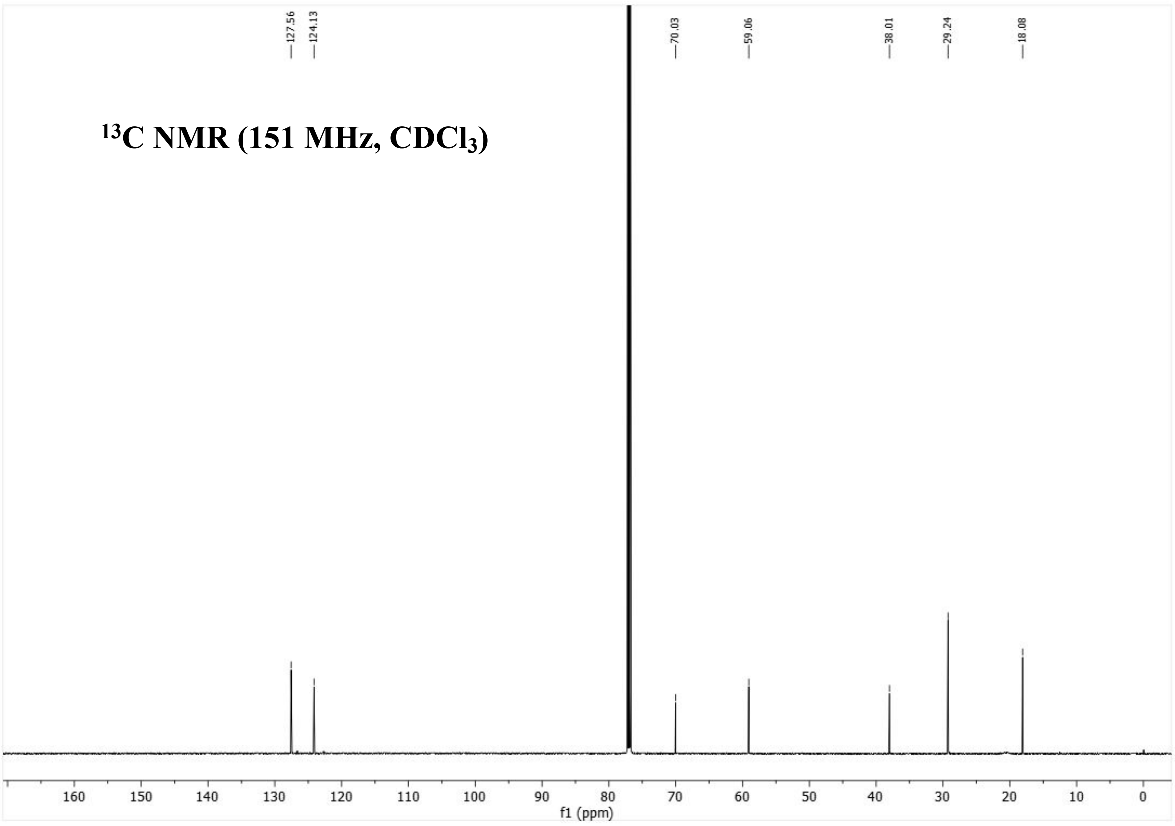
TS1-G-*Re*	**HOMO-1**	**HOMO**	**LUMO**	**LUMO+1**
HOMO-1	1.1%	26.0%	0.0%	2.7%
HOMO	100.0%	3.9%	7.2%	8.9%
LUMO	0.8%	1.1%	2.4%	5.2%
LUMO+1	4.6%	0.1%	1.0%	0.7%

TS1-G-Si	**HOMO-1**	**HOMO**	**LUMO**	**LUMO+1**
HOMO-1	0.27%	30.99%	0.78%	0.93%
HOMO	57.71%	1.42%	3.93%	3.21%
LUMO	2.16%	0.31%	1.48%	14.02%
LUMO+1	8.66%	0.59%	0.51%	0.71%

This interaction is maximum in the **TS1-G-*Re*** and only the 58% of that in **TS1-G-*Si***. Another important interaction is the ϕ_{HOMO-1} (so the p system of the crotyl) with the θ_{HOMO} (so the π* of **2a**) but the difference of this overlap is not so predominant as the one of before (26% in the **TS1-G-*Re*** against 31% of **TS2-G-*Si***).

NMRs TRACES OF BORONIC ESTERS

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124.13
70.03
59.06
38.01
29.24
18.08
¹³C NMR (151 MHz, CDCl₃)
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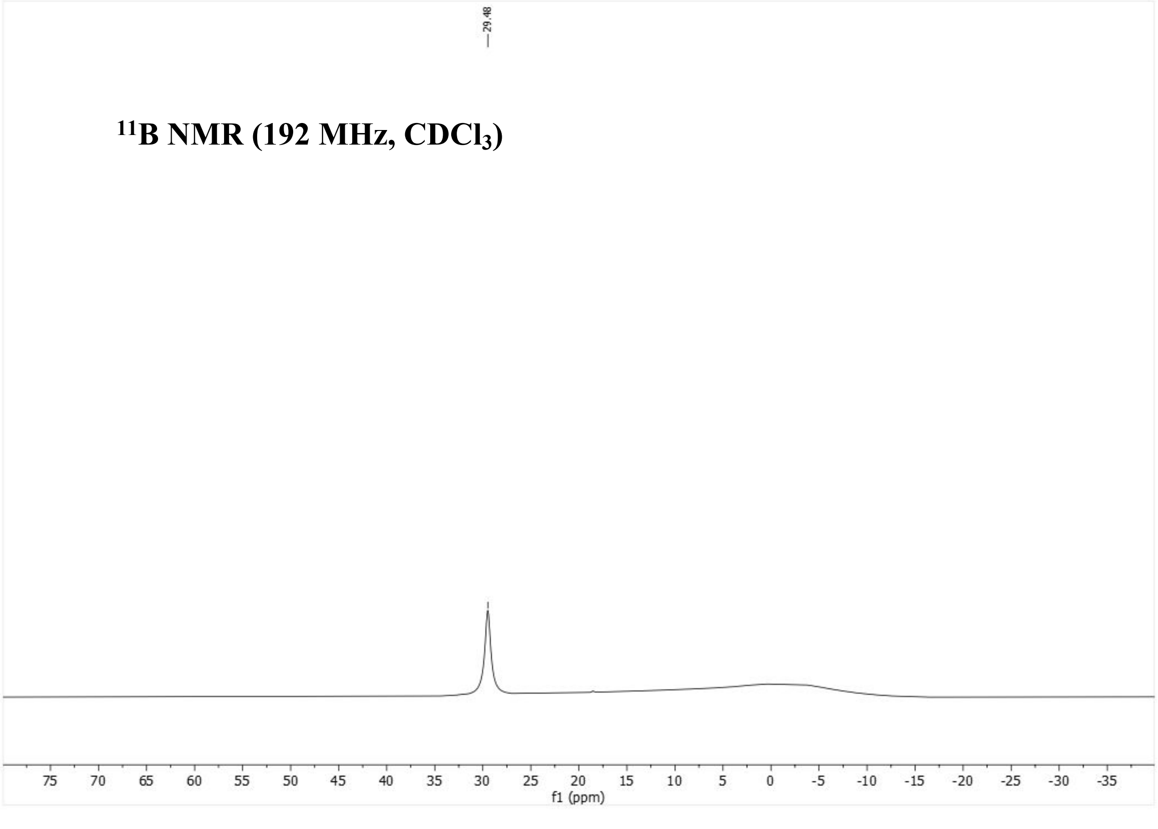
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
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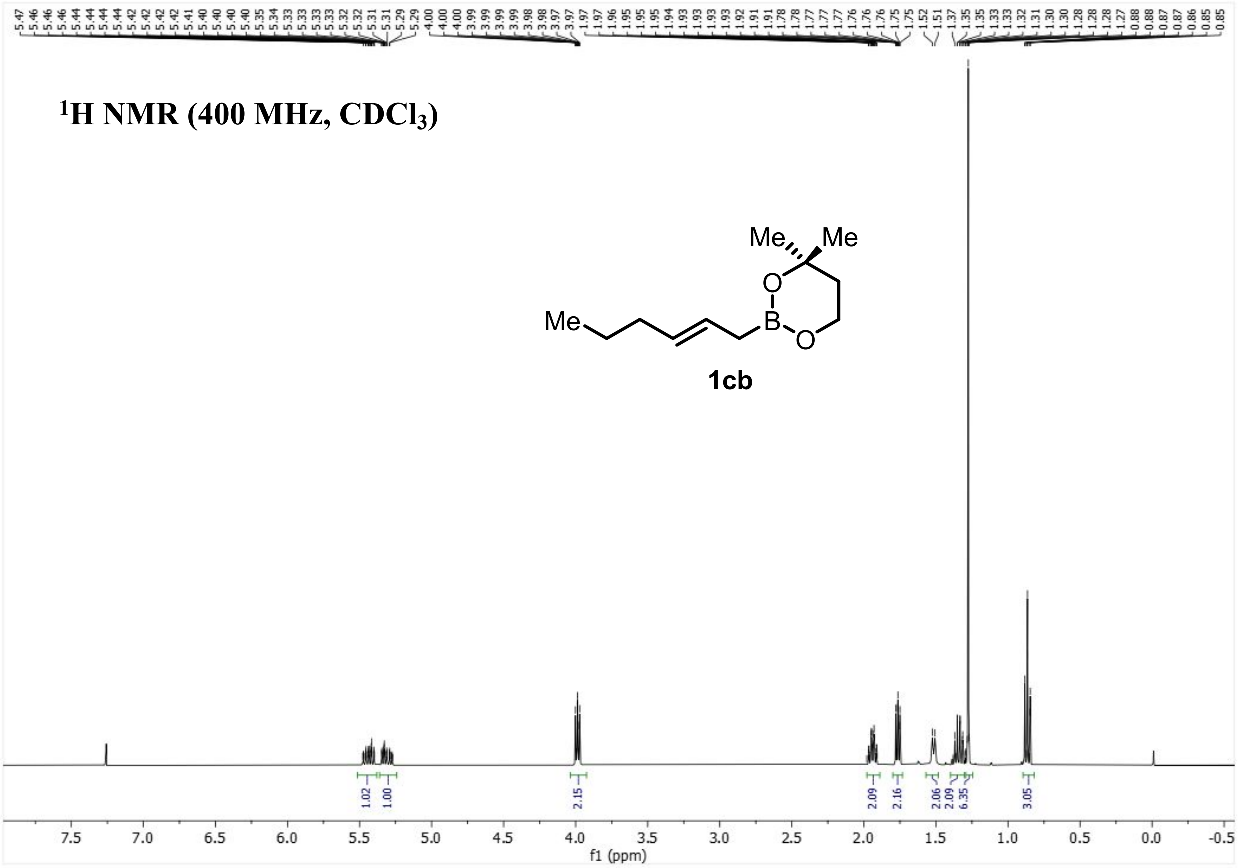
-10
-15
-20
-25
-30
-35
f1 (ppm)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5.46
5.46
5.44
5.44
5.44
5.42
5.42
5.42
5.41
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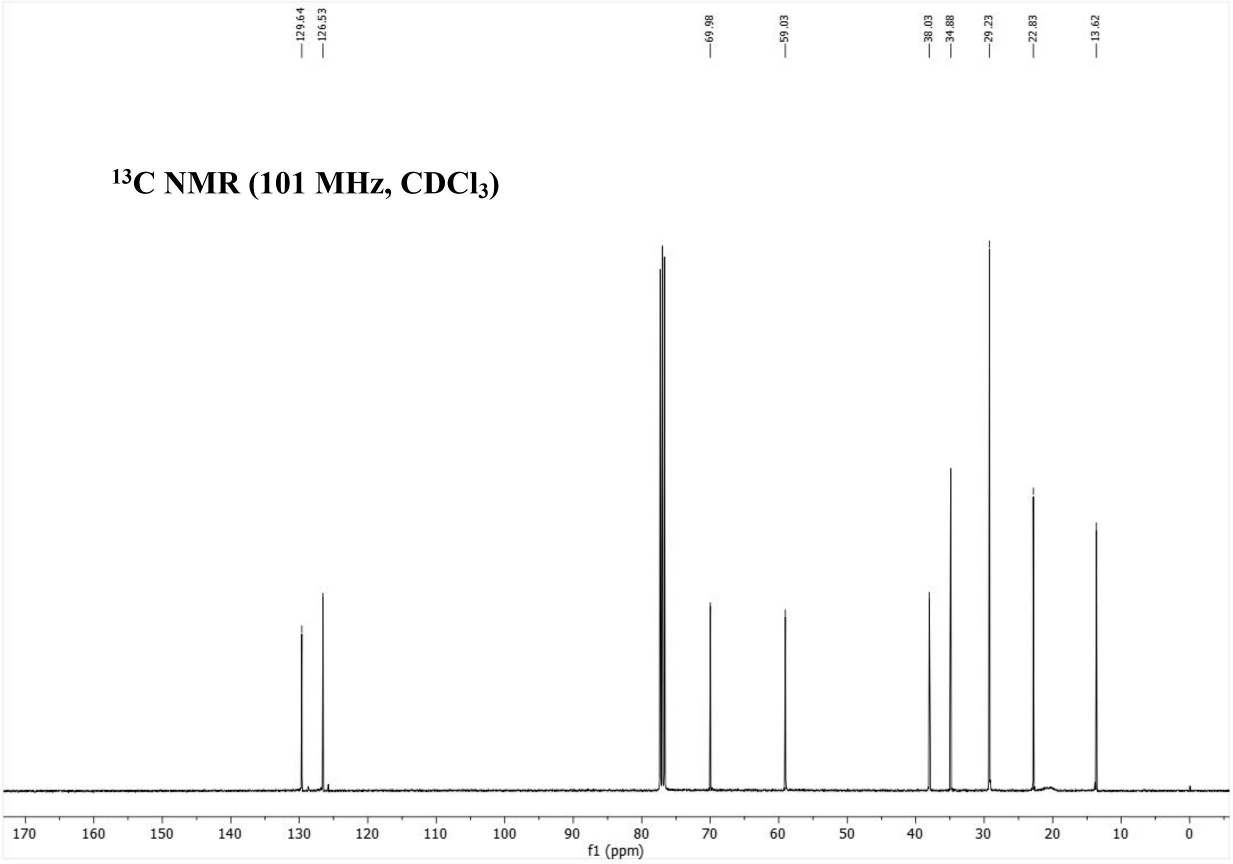
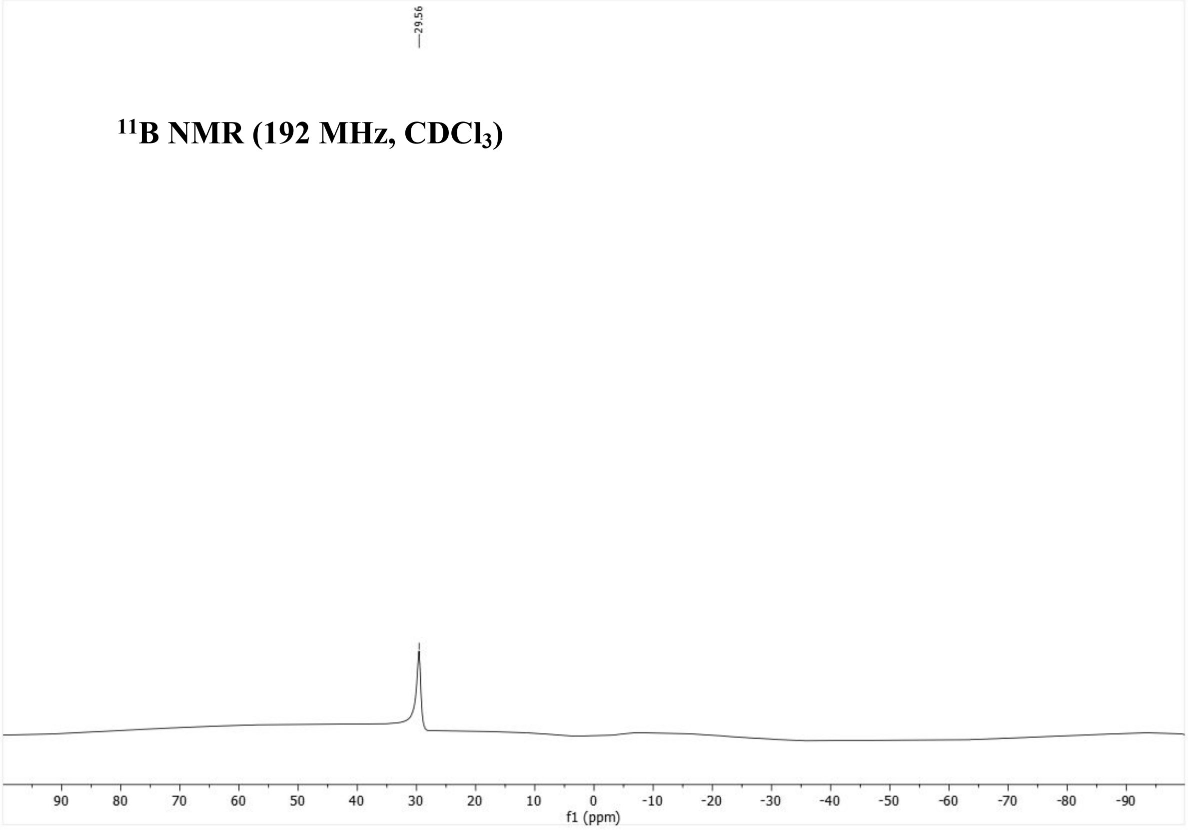
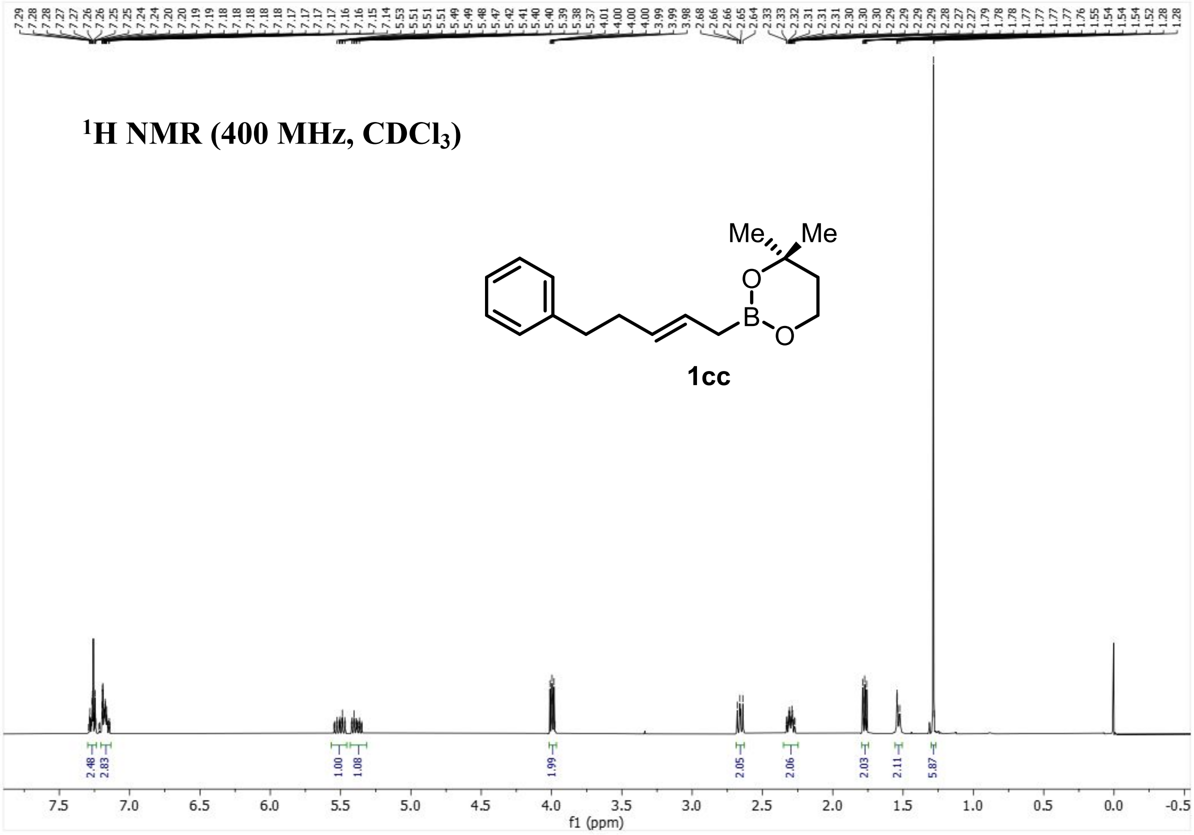
5.40
5.35
5.34
5.33
5.33
5.33
5.33
5.32
5.32
5.31
5.31
5.29
5.29
4.00
4.00
3.99
3.99
3.99
3.99
3.98
3.97
3.97
1.97
1.97
1.96
1.95
1.95
1.95
1.94
1.93
1.93
1.93
1.93
1.92
1.91
1.91
1.78
1.78
1.77
1.77
1.77
1.76
1.76
1.76
1.75
1.75
1.52
1.51
1.37
1.35
1.35
1.35
1.33
1.33
1.32
1.31
1.30
1.30
1.28
1.28
1.28
1.27
0.88
0.88
0.87
0.87
0.86
0.85
0.85
¹H NMR (400 MHz, CDCl₃)
Me
Me
O
B
O
Me
1cb
1.02
1.00
2.15
2.09
2.16
2.06
2.09
6.35
3.05
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)


129.64
126.53
69.98
59.03
38.03
34.88
29.23
22.83
13.62
¹³C NMR (101 MHz, CDCl₃)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



29.56
¹¹B NMR (192 MHz, CDCl₃)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)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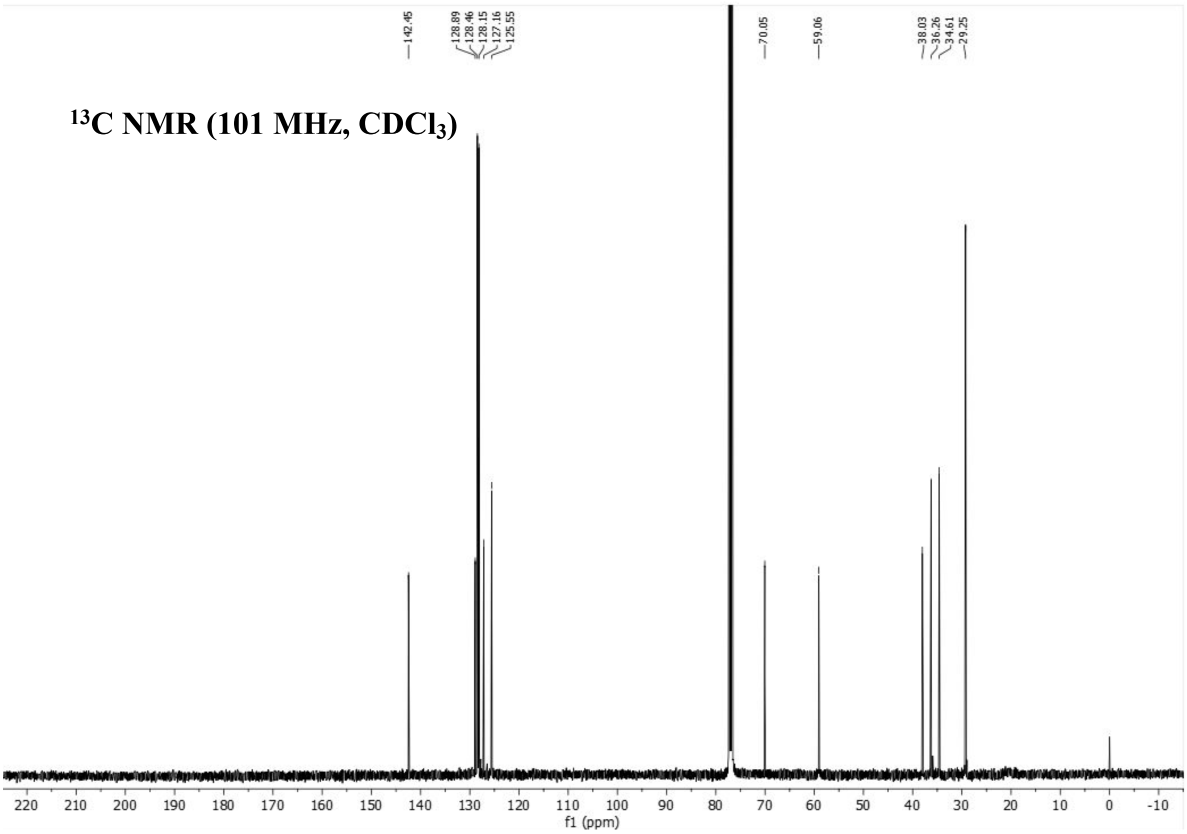
^{1}H NMR (400 MHz, CDCl$_3$)
Me
Me
O
B
O
1cc
2.48
2.83
1.00
1.08
1.99
2.05
2.06
2.03
2.11
5.87
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


142.45
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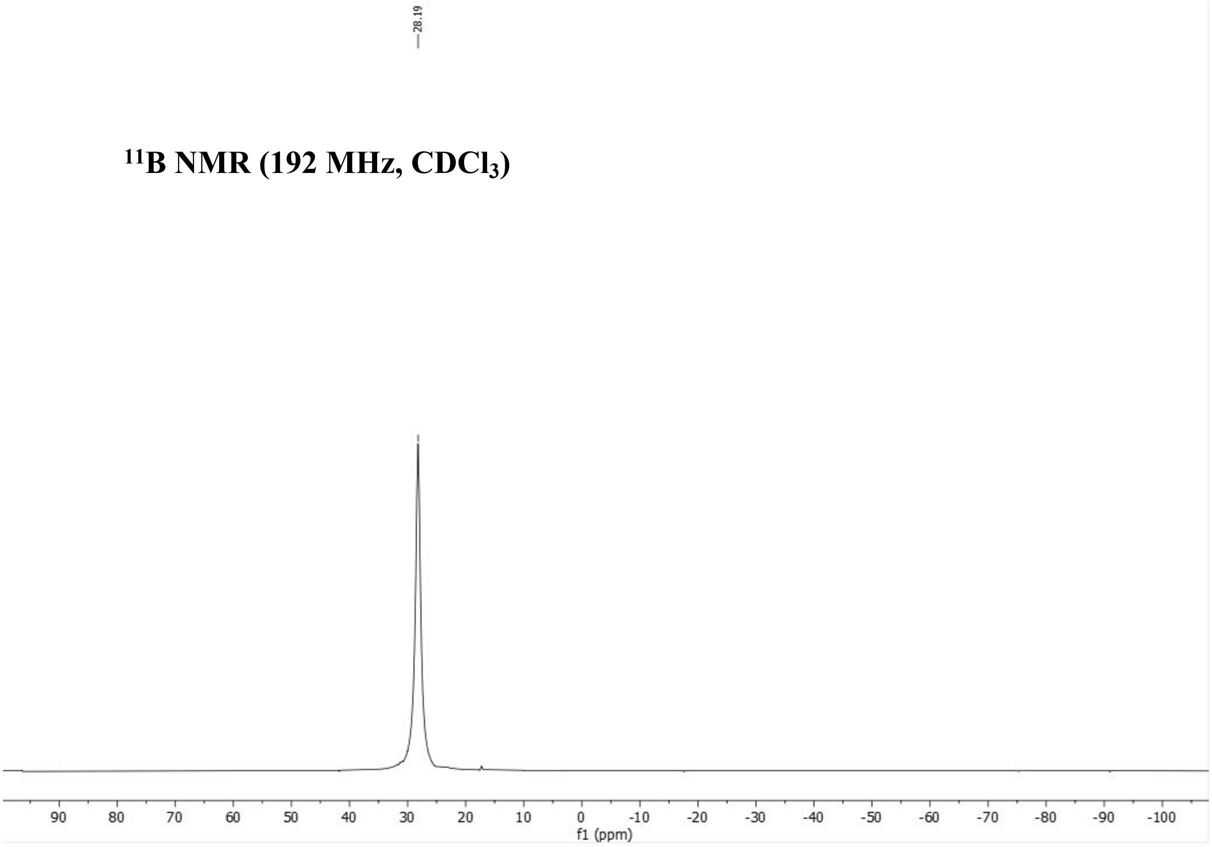
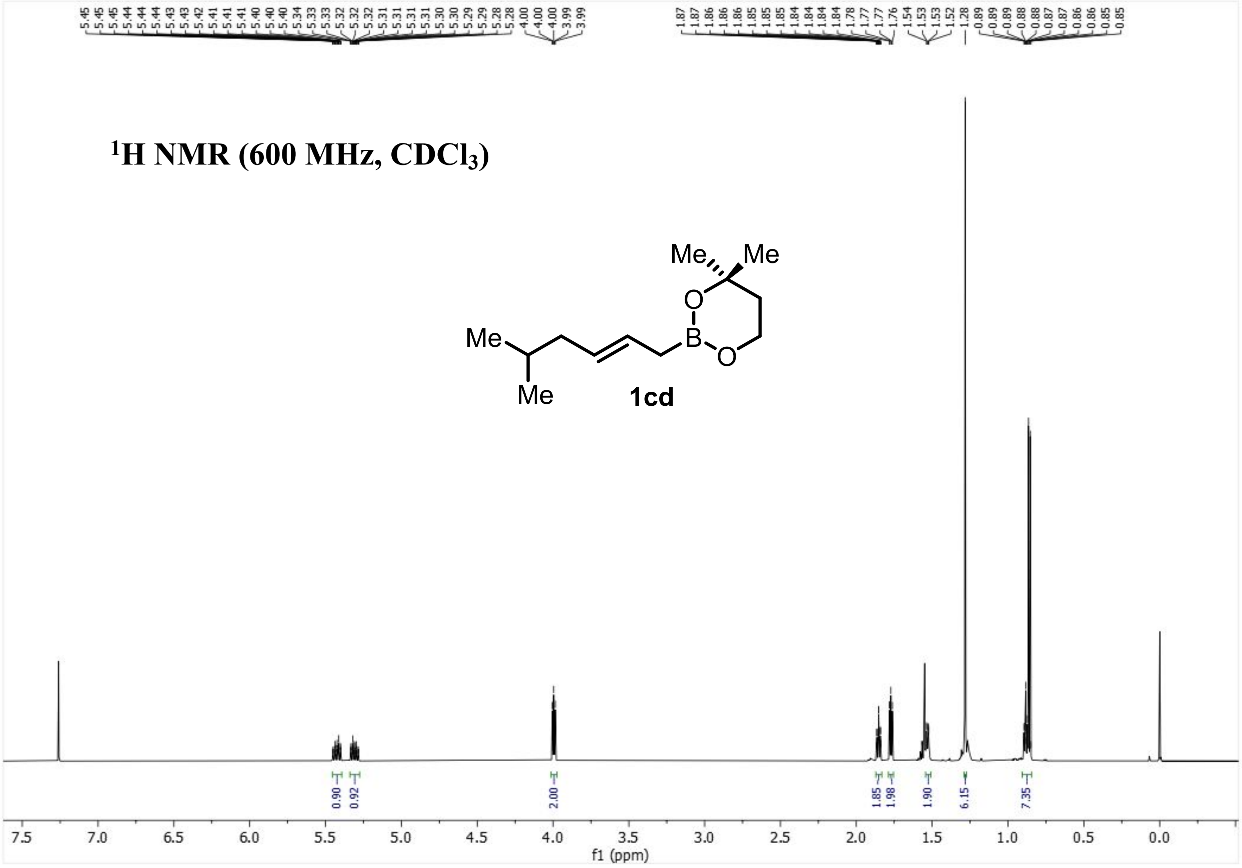
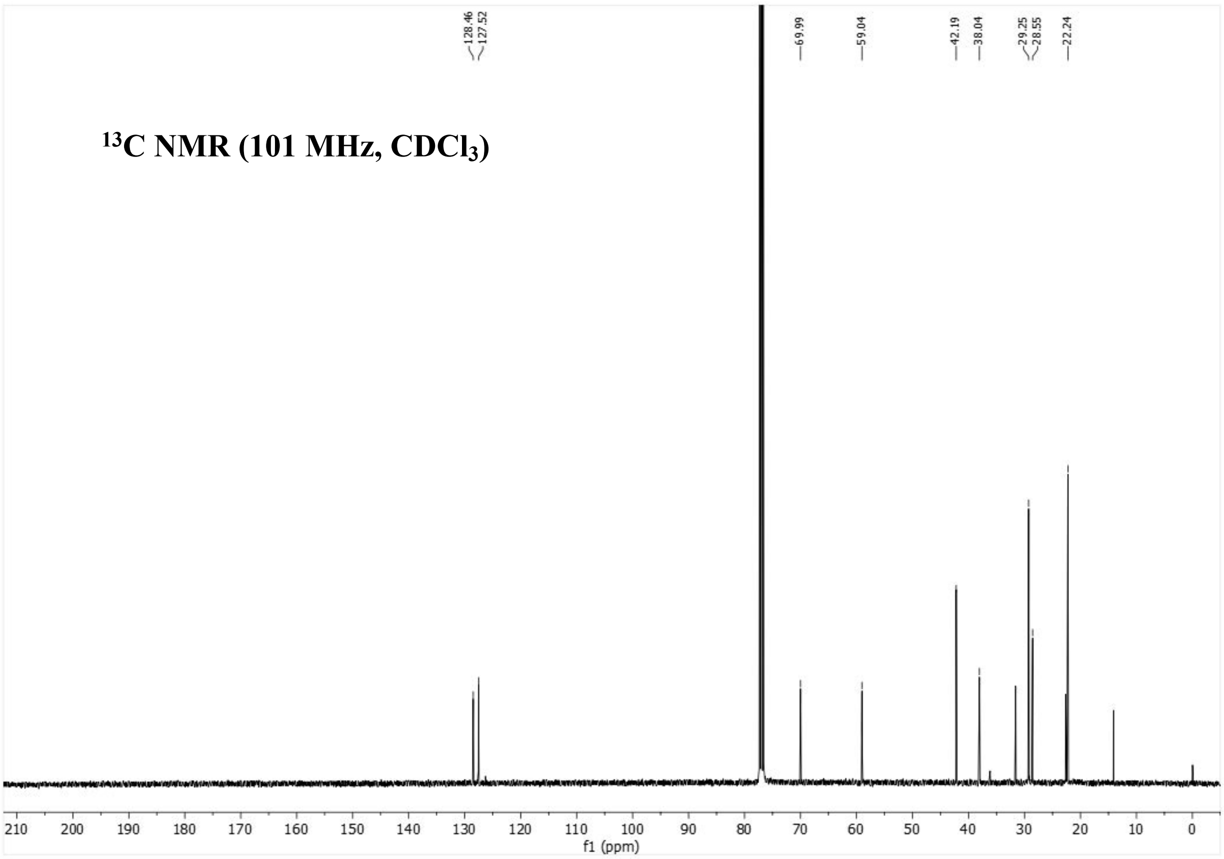
128.46
128.15
127.16
125.55
70.05
59.06
38.03
36.26
34.61
29.25
^{13}C NMR (101 MHz, CDCl$_3$)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{11}B NMR (192 MHz, CDCl$_3$)

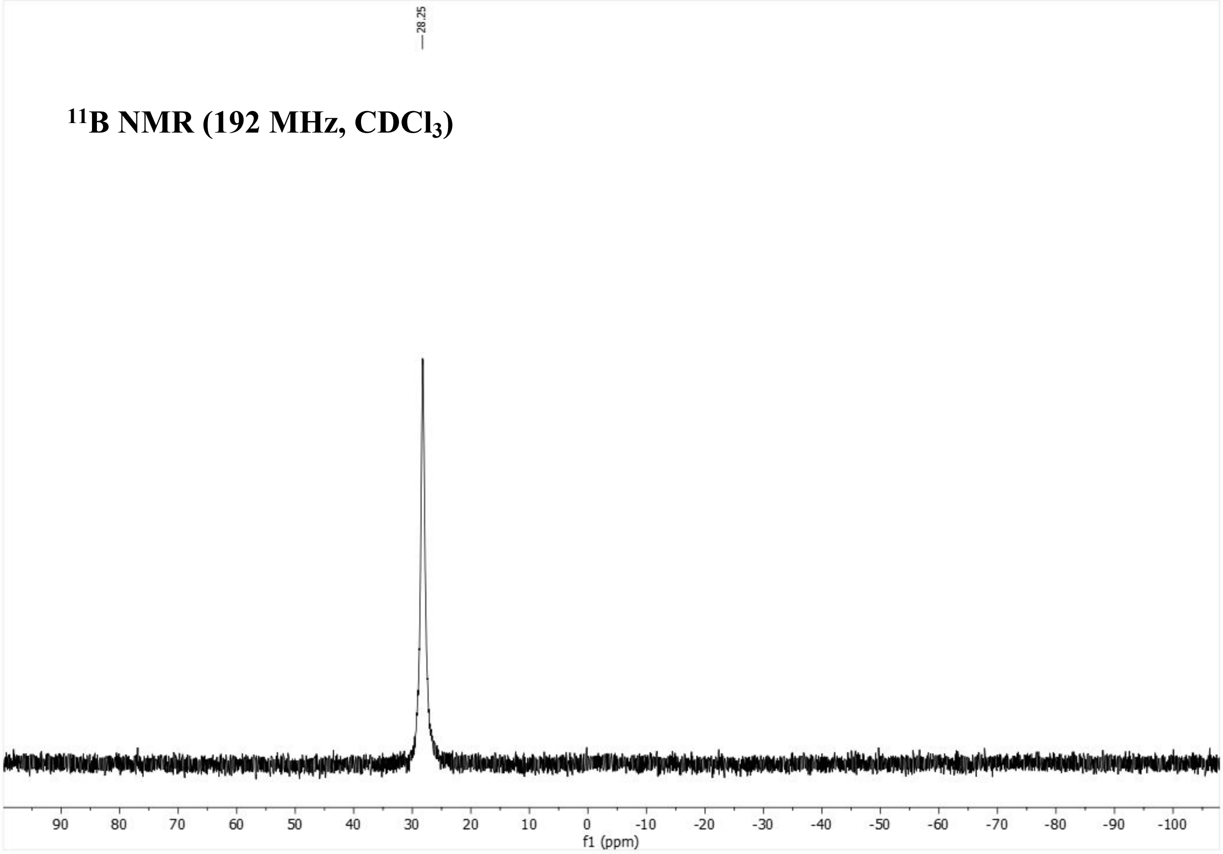




5.45 5.45 5.45 5.44 5.44 5.43 5.43 5.42 5.41 5.41 5.41 5.40 5.40 5.40 5.34 5.33 5.33 5.32 5.32 5.32 5.31 5.31 5.31 5.30 5.30 5.29 5.29 5.28 5.28 4.00 4.00 4.00 3.99 3.99
1.87 1.87 1.86 1.86 1.86 1.85 1.85 1.85 1.84 1.84 1.84 1.84 1.78 1.77 1.77 1.76 1.54 1.53 1.53 1.52 1.28 0.89 0.89 0.89 0.88 0.88 0.87 0.87 0.86 0.86 0.85 0.85
¹H NMR (600 MHz, CDCl₃)
Me
Me
O
B
O
Me
Me
1cd
0.90
0.92
2.00
1.85
1.98
1.90
6.15
7.35
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
f1 (ppm)



128.46
127.52
69.99
59.04
42.19
38.04
29.25
28.55
22.24
¹³C NMR (101 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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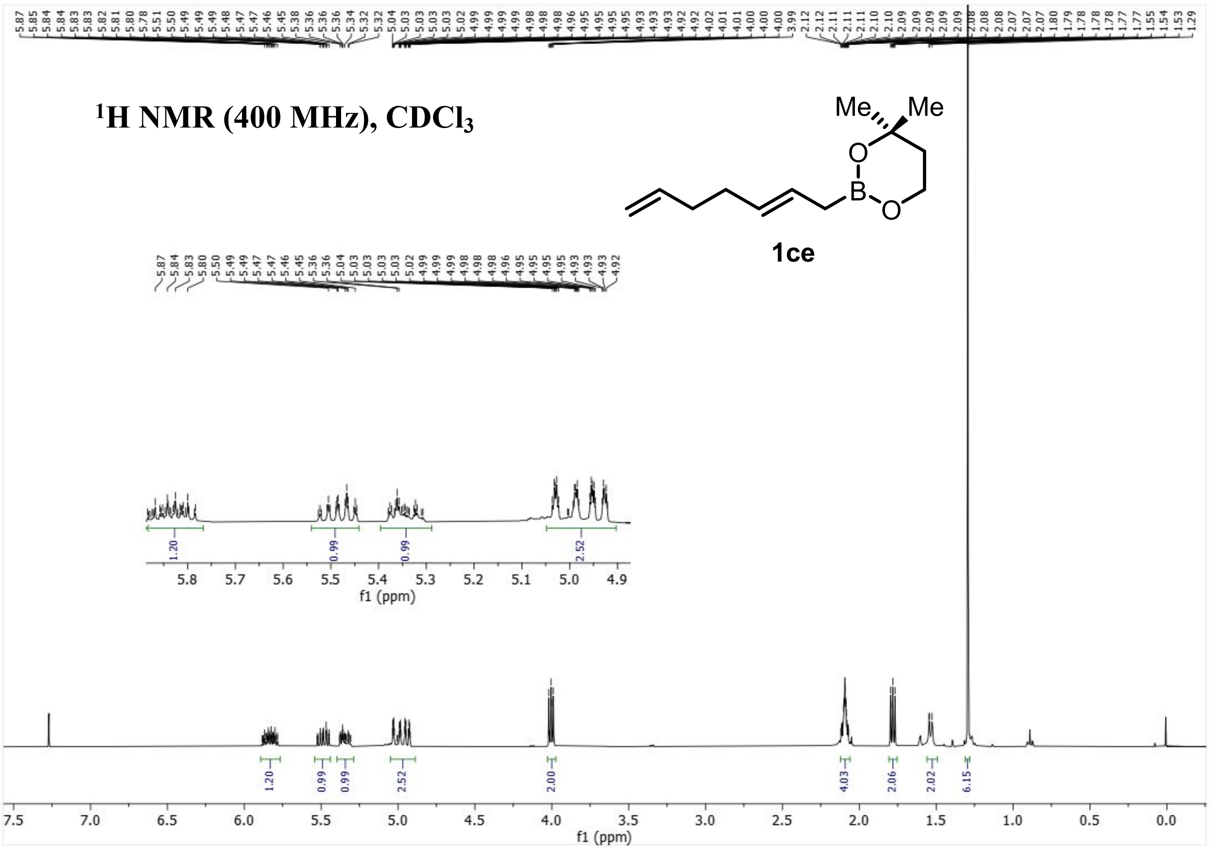
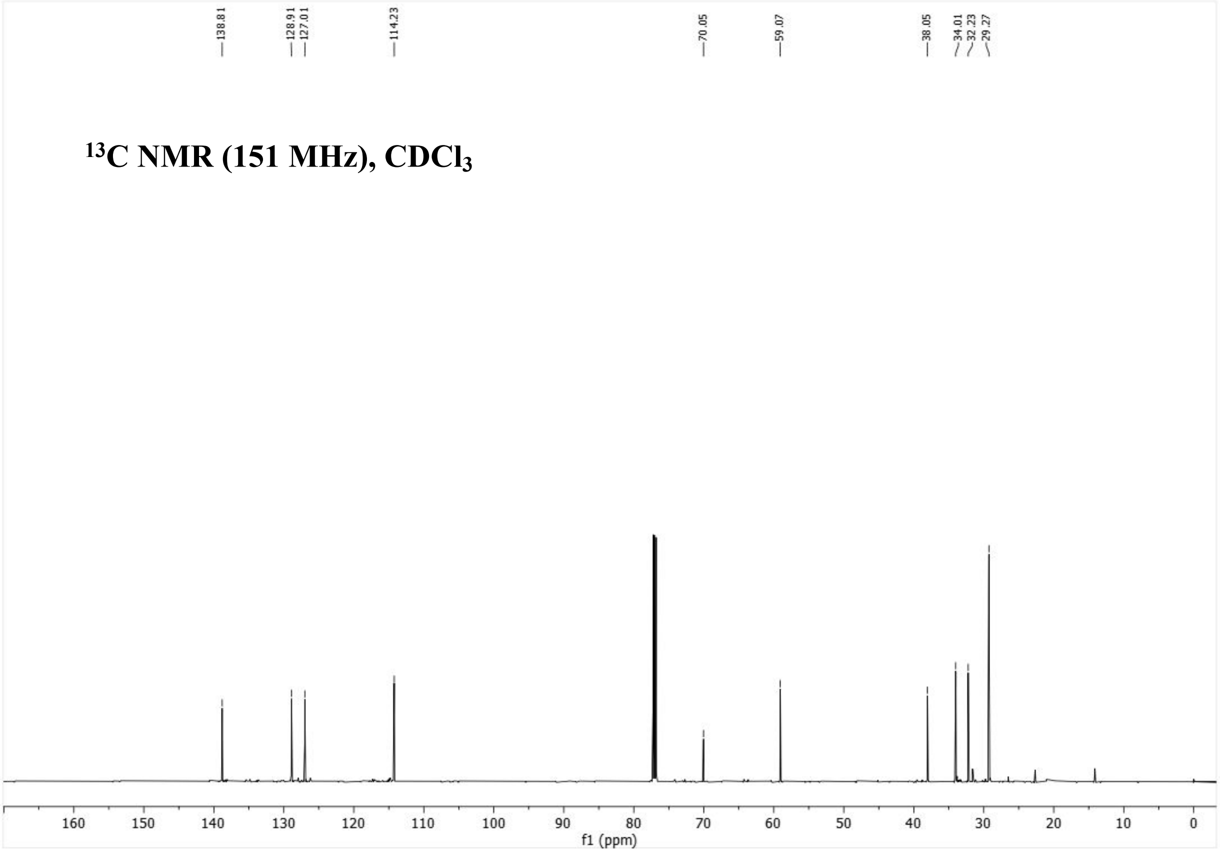


^{1}H NMR (400 MHz), CDCl$_3$

1ce



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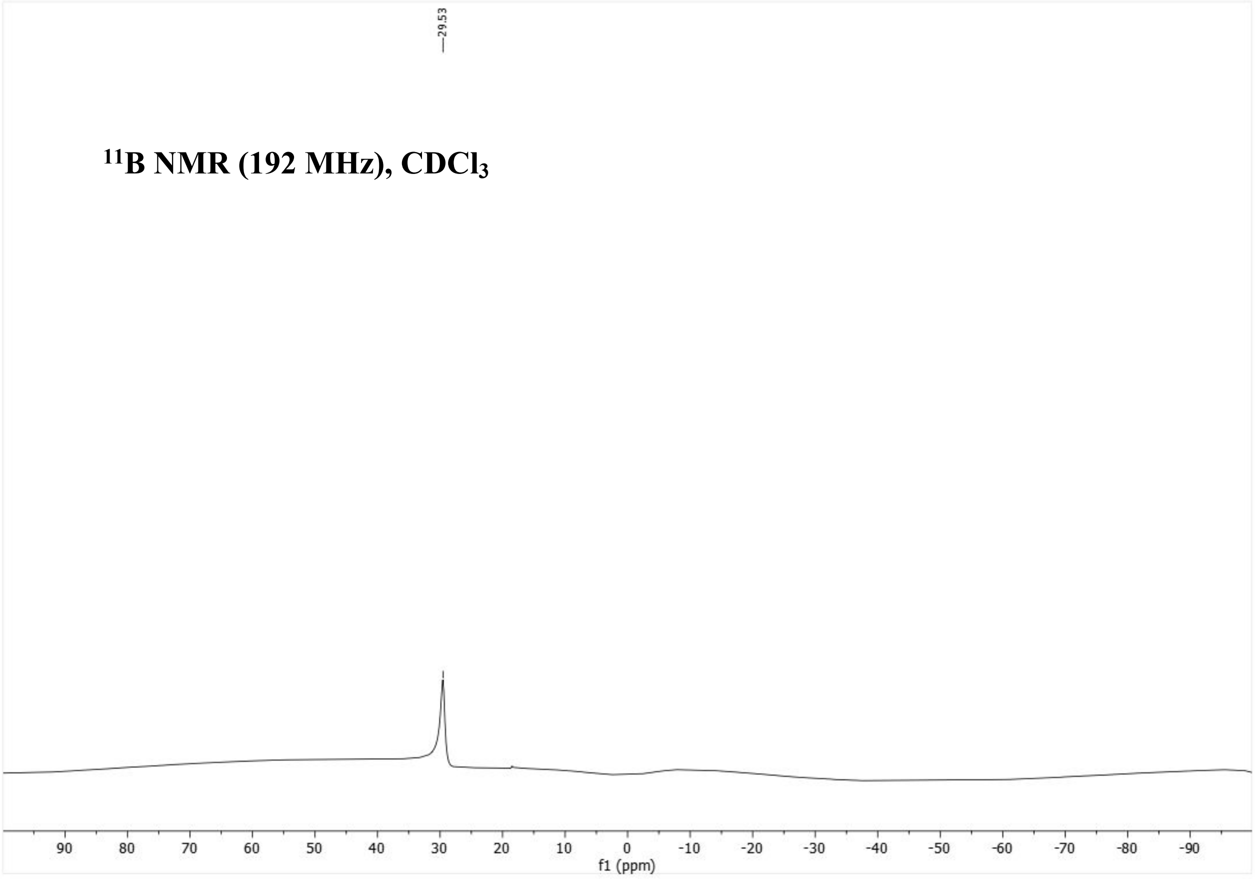
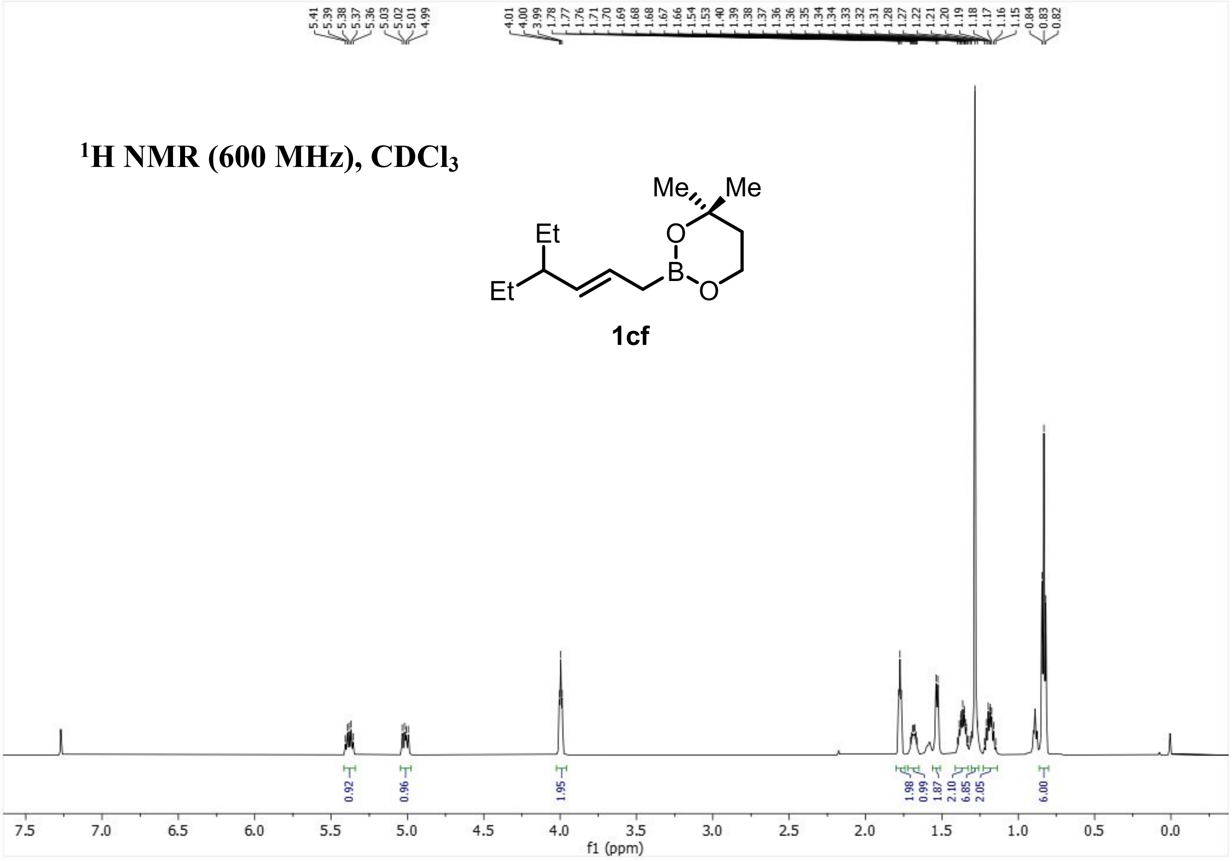
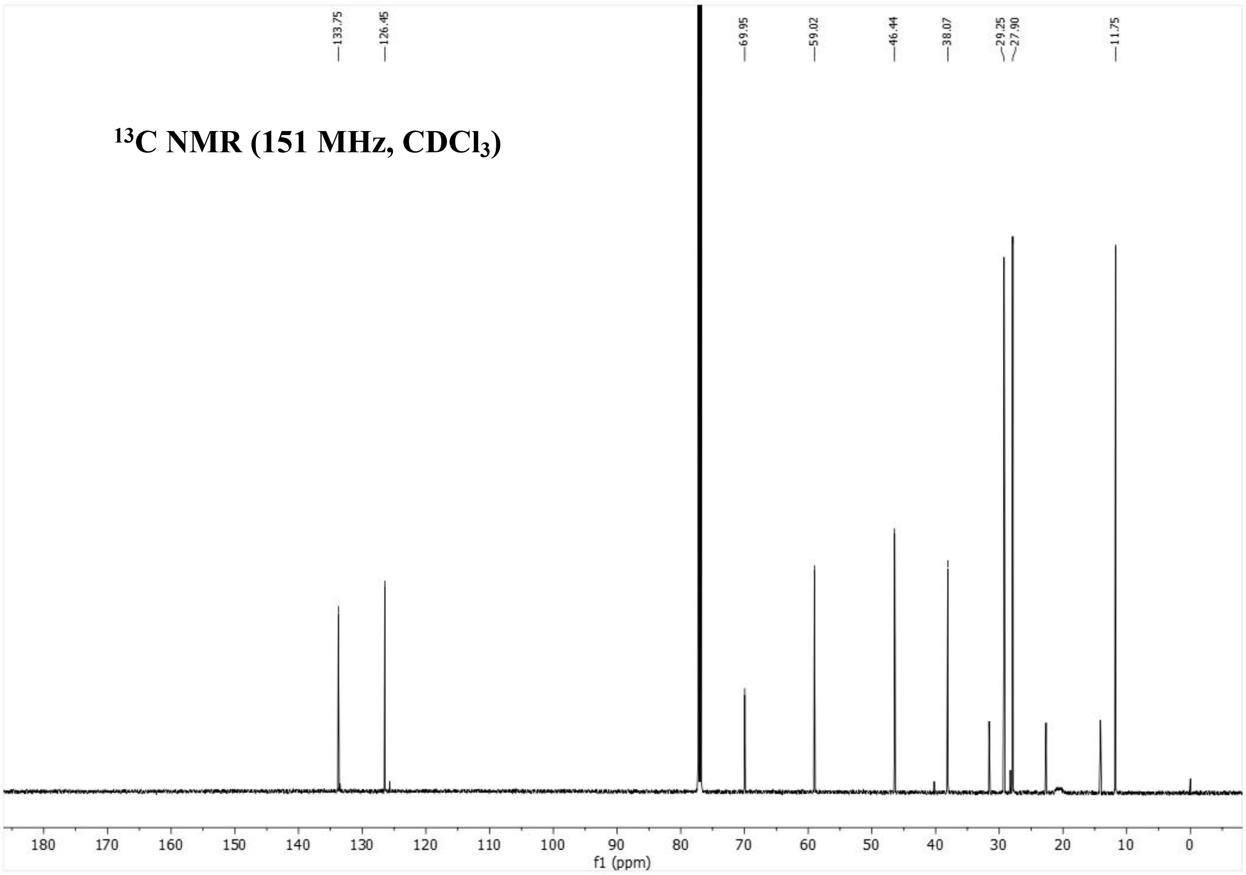


^{11}B NMR (192 MHz), CDCl$_3$

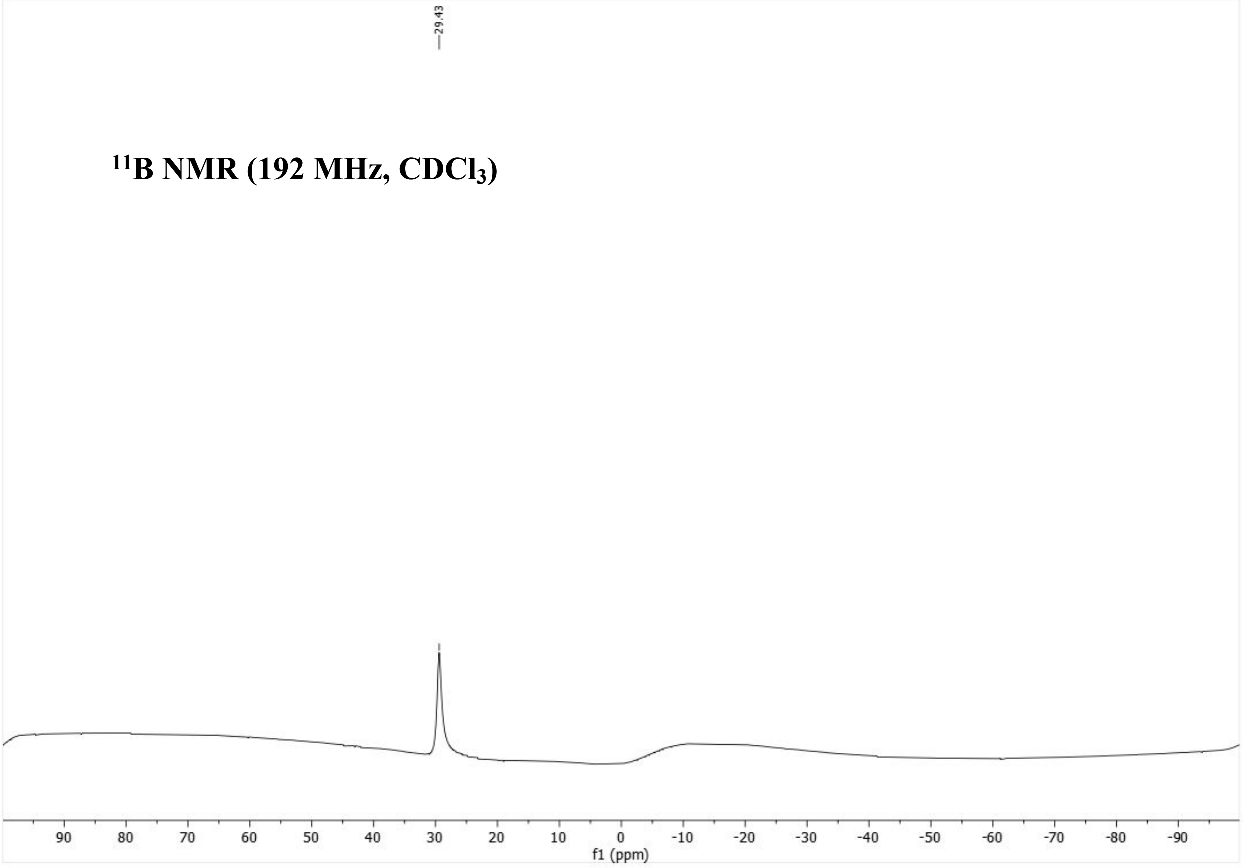


^{1}H NMR (600 MHz), CDCl$_3$

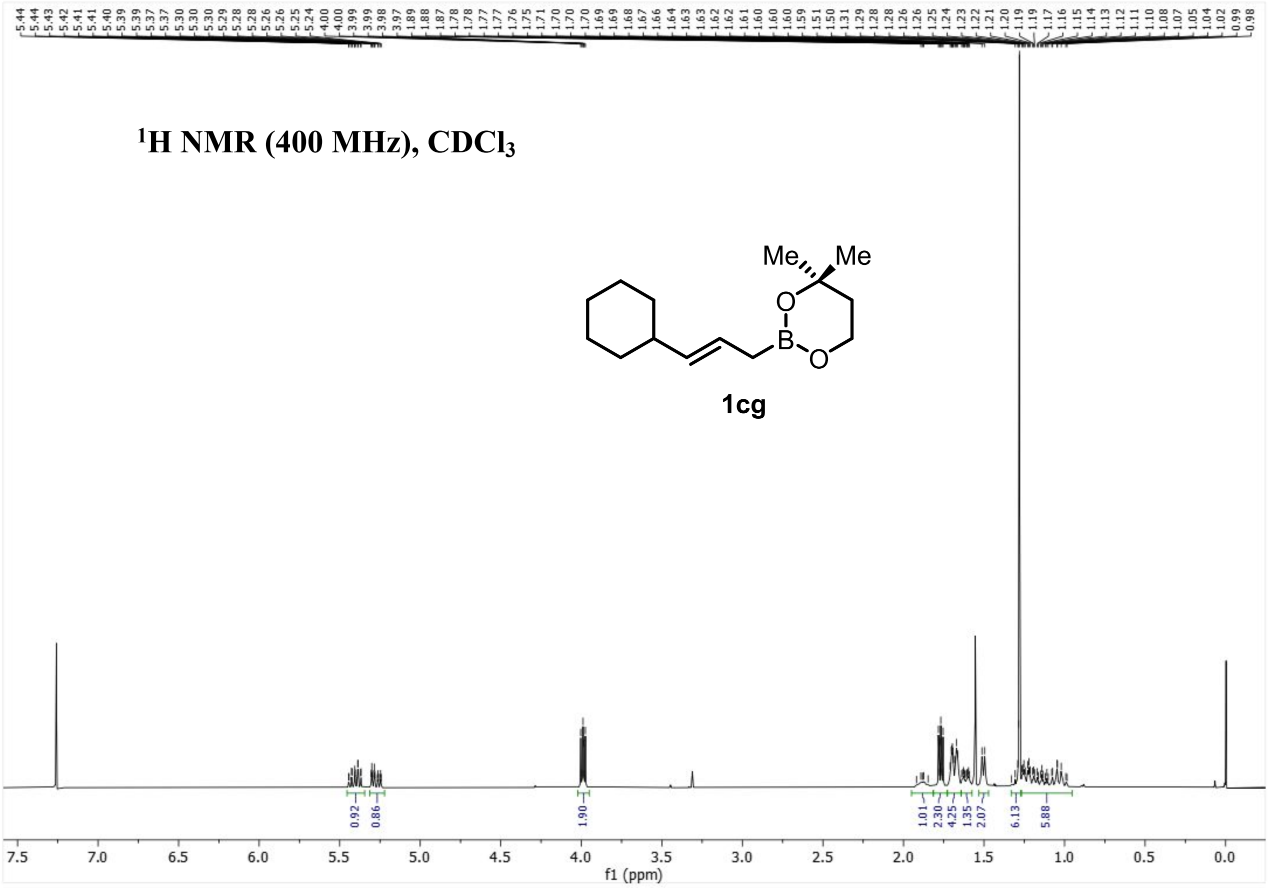
1cf



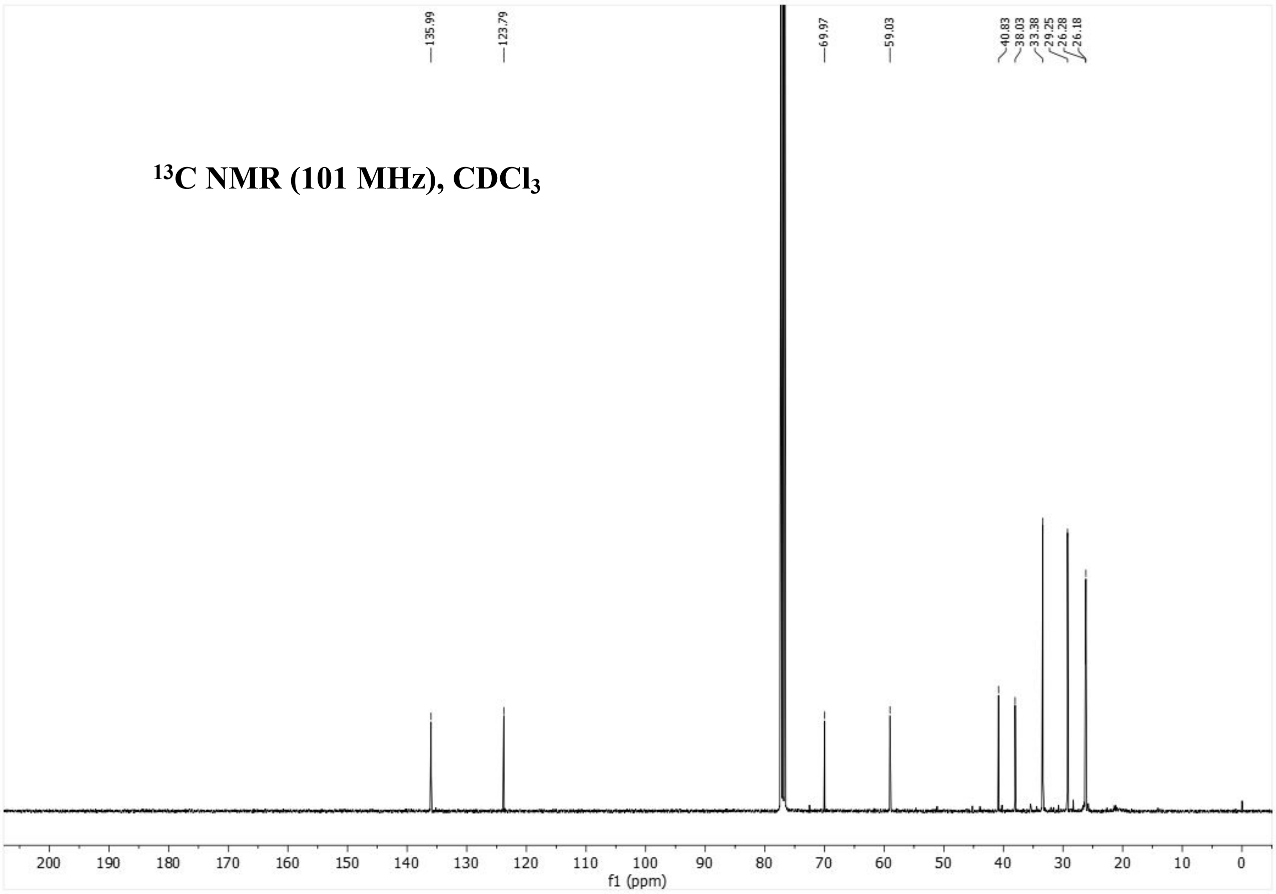
^{13}C NMR (151 MHz, CDCl$_3$)

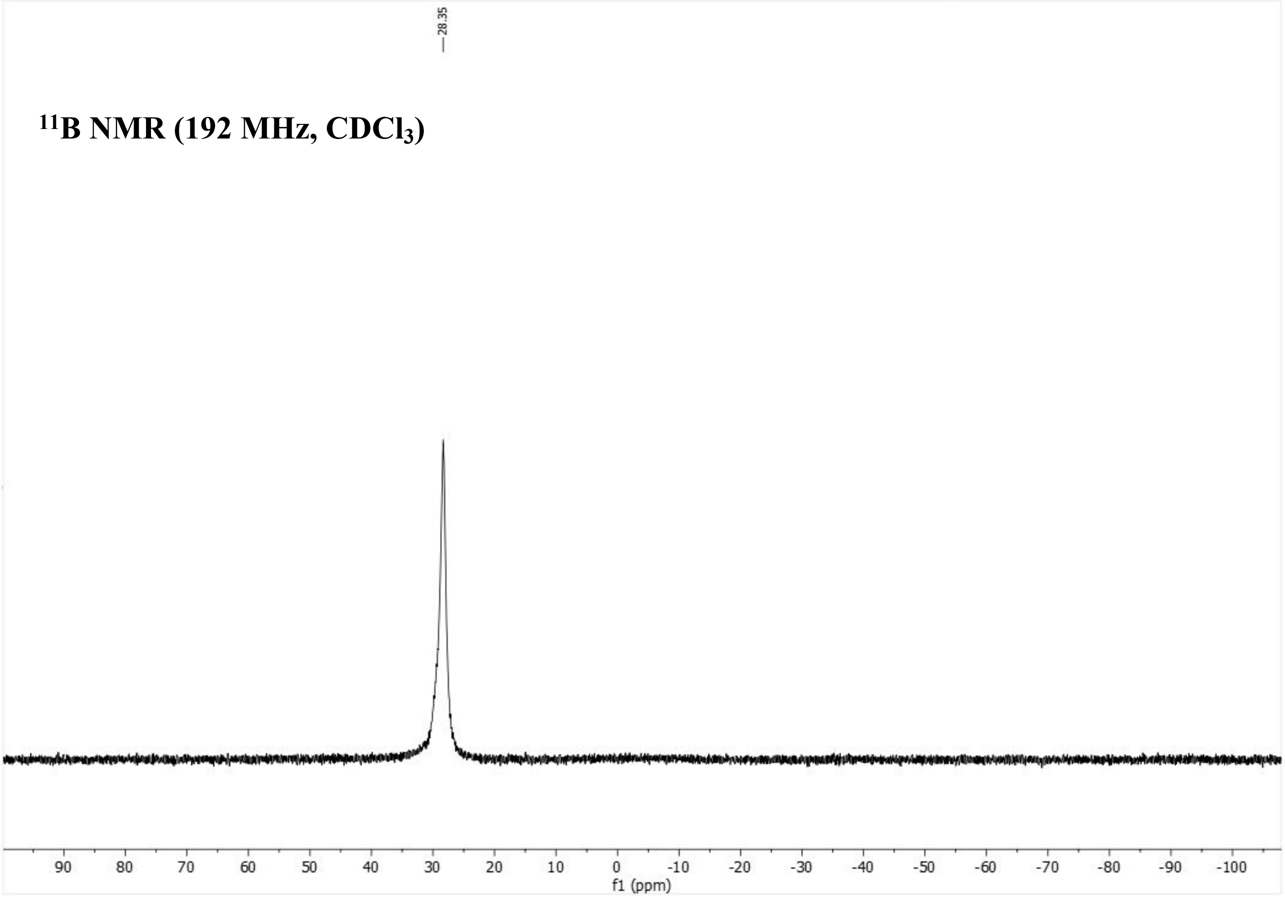


29.43
^{11}B NMR (192 MHz, CDCl$_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

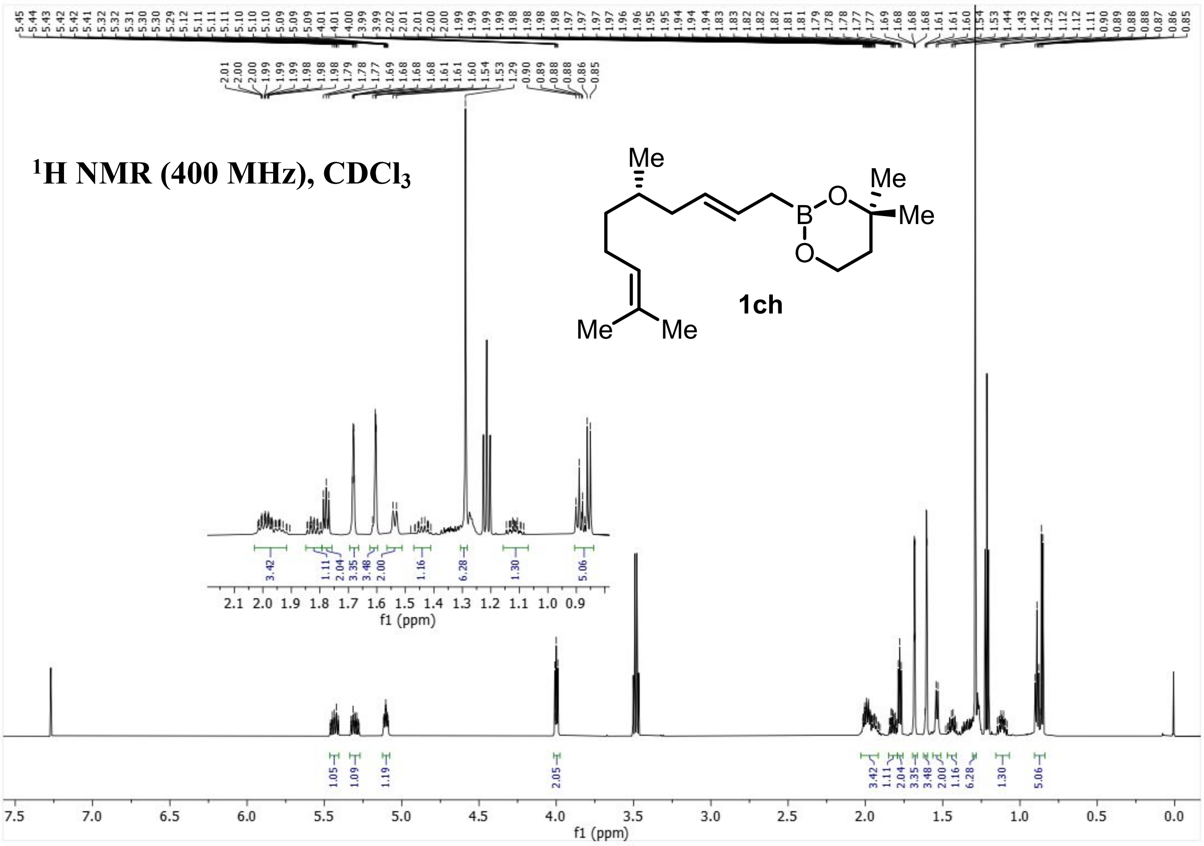

¹H NMR (400 MHz), CDCl$_3$

1cg


¹³C NMR (101 MHz), CDCl$_3$

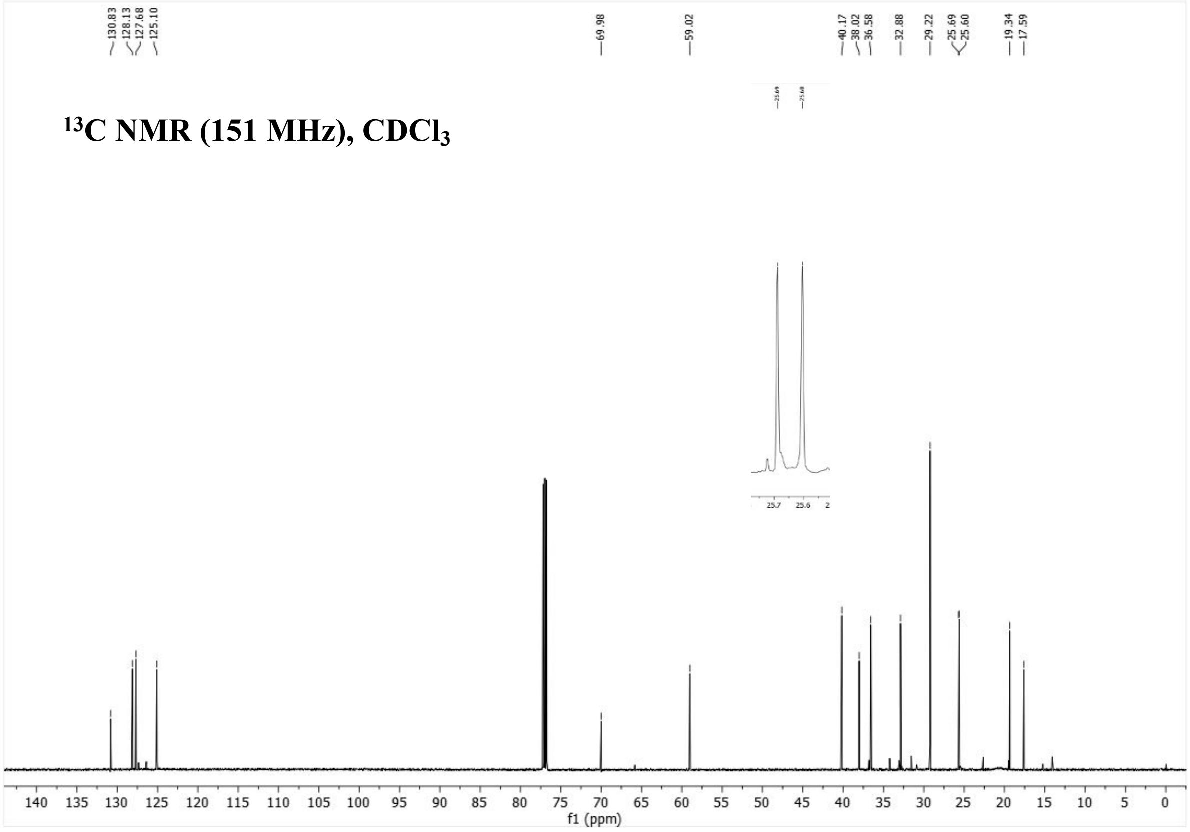

28.35
^{11}B NMR (192 MHz, CDCl$_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
f1 (ppm)

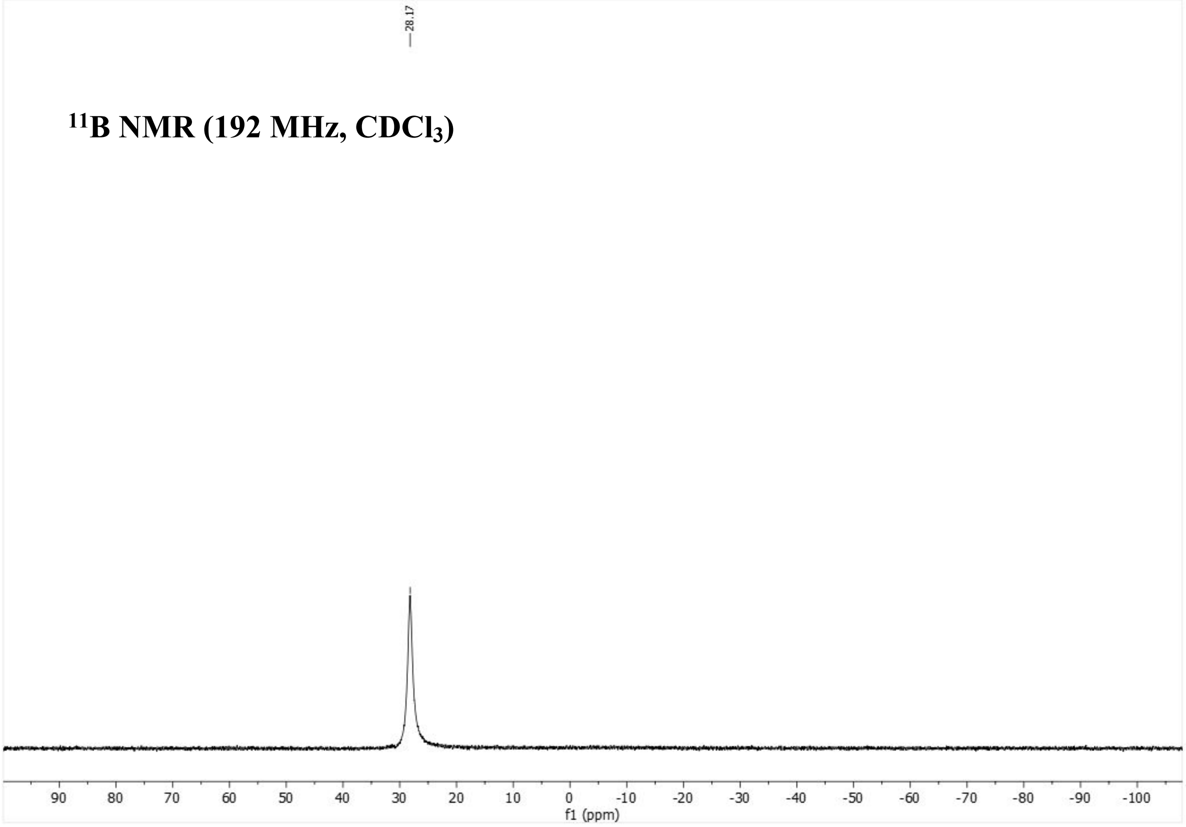
^{1}H NMR (400 MHz), CDCl$_3$

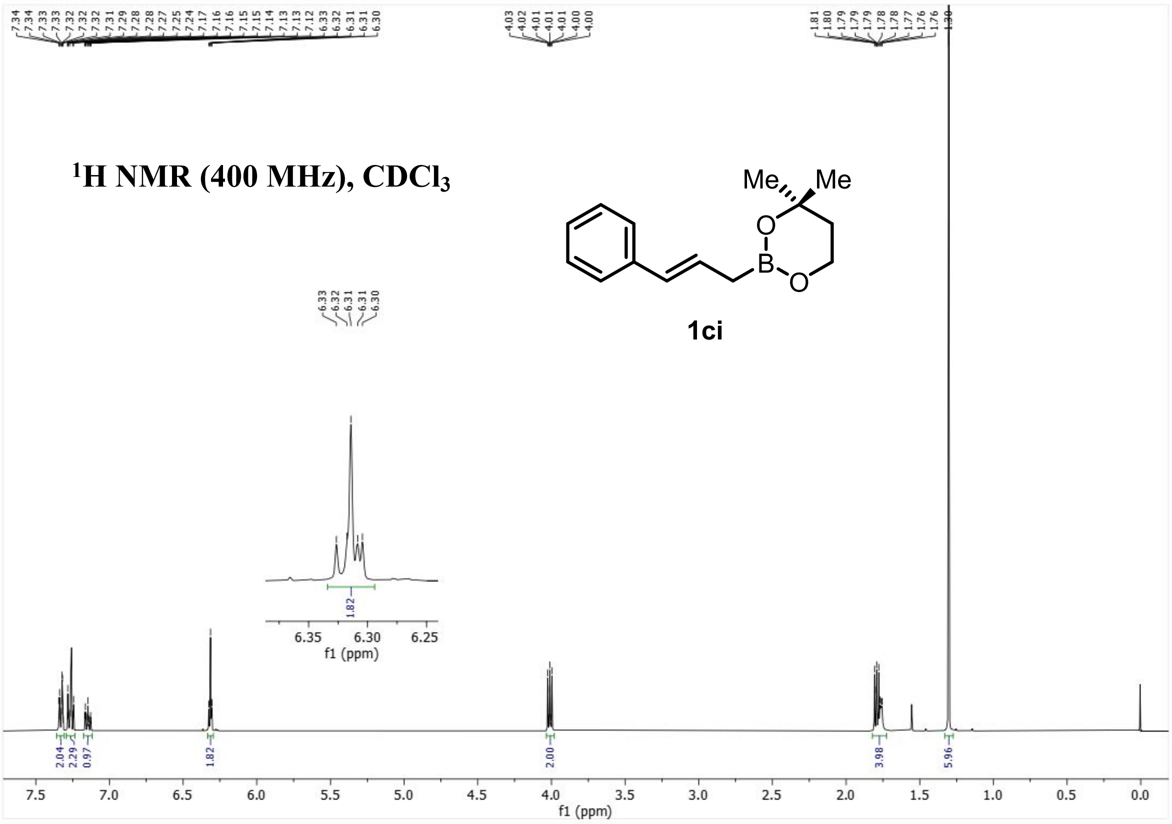


1ch

^{13}C NMR (151 MHz), CDCl$_3$

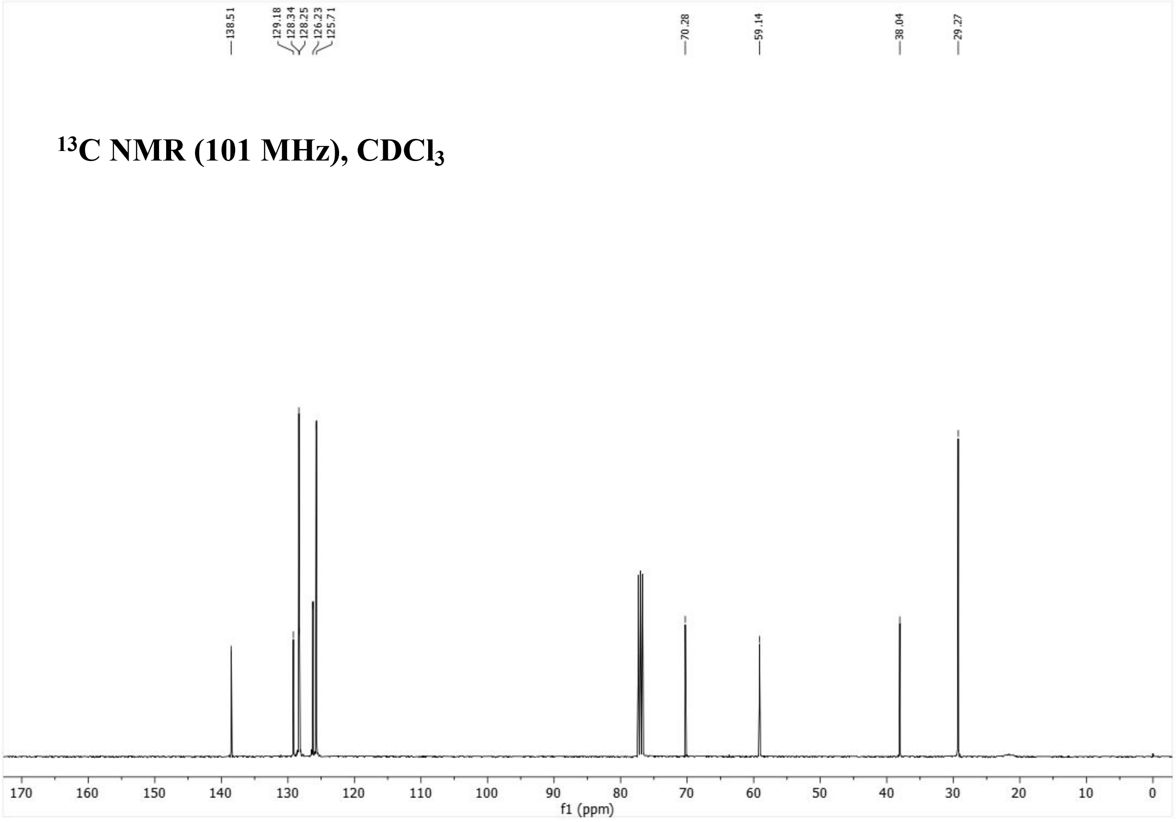



28.17
^{11}B NMR (192 MHz, CDCl$_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
f1 (ppm)



^{1}H NMR (400 MHz), CDCl$_3$

1ci



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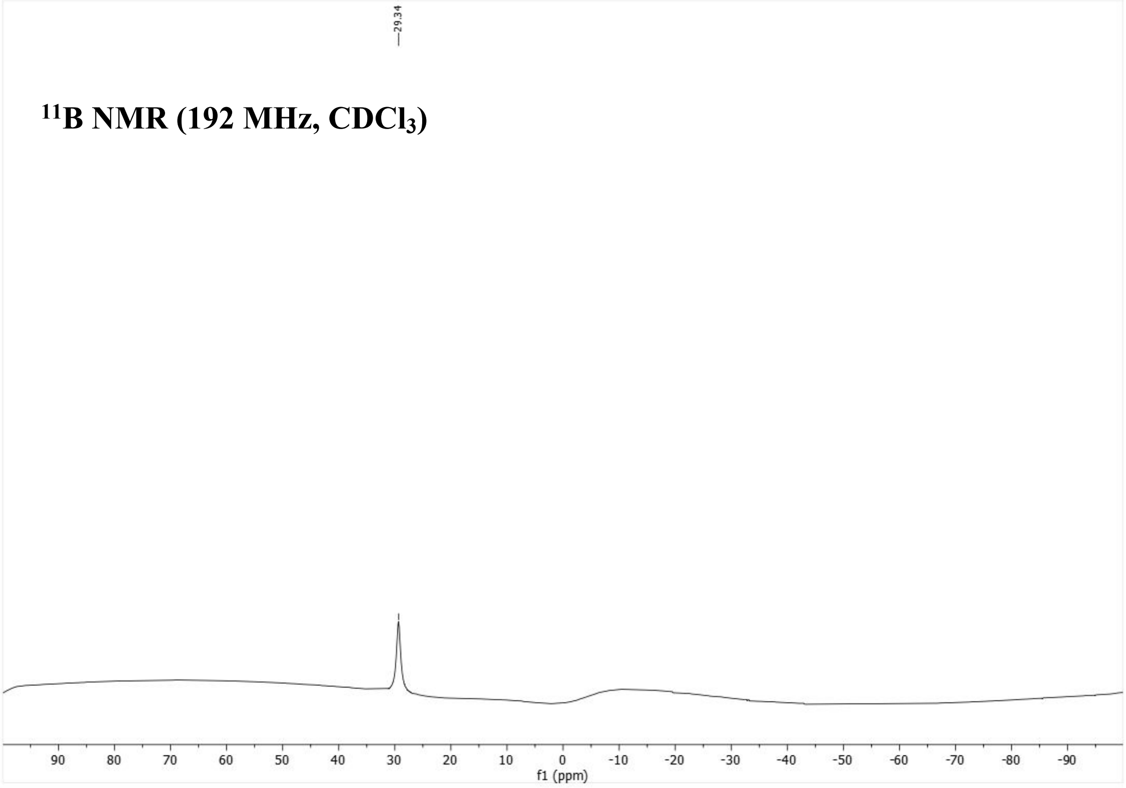
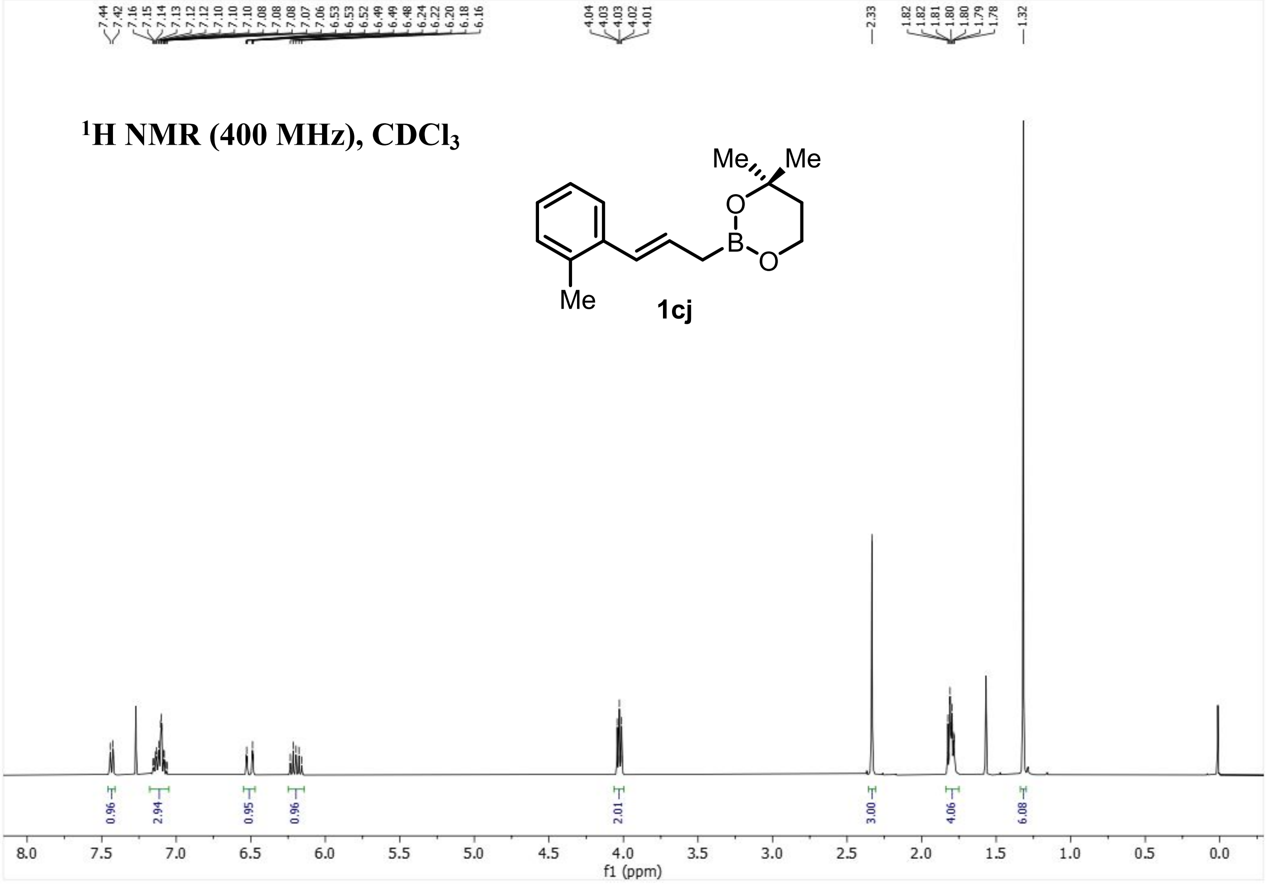
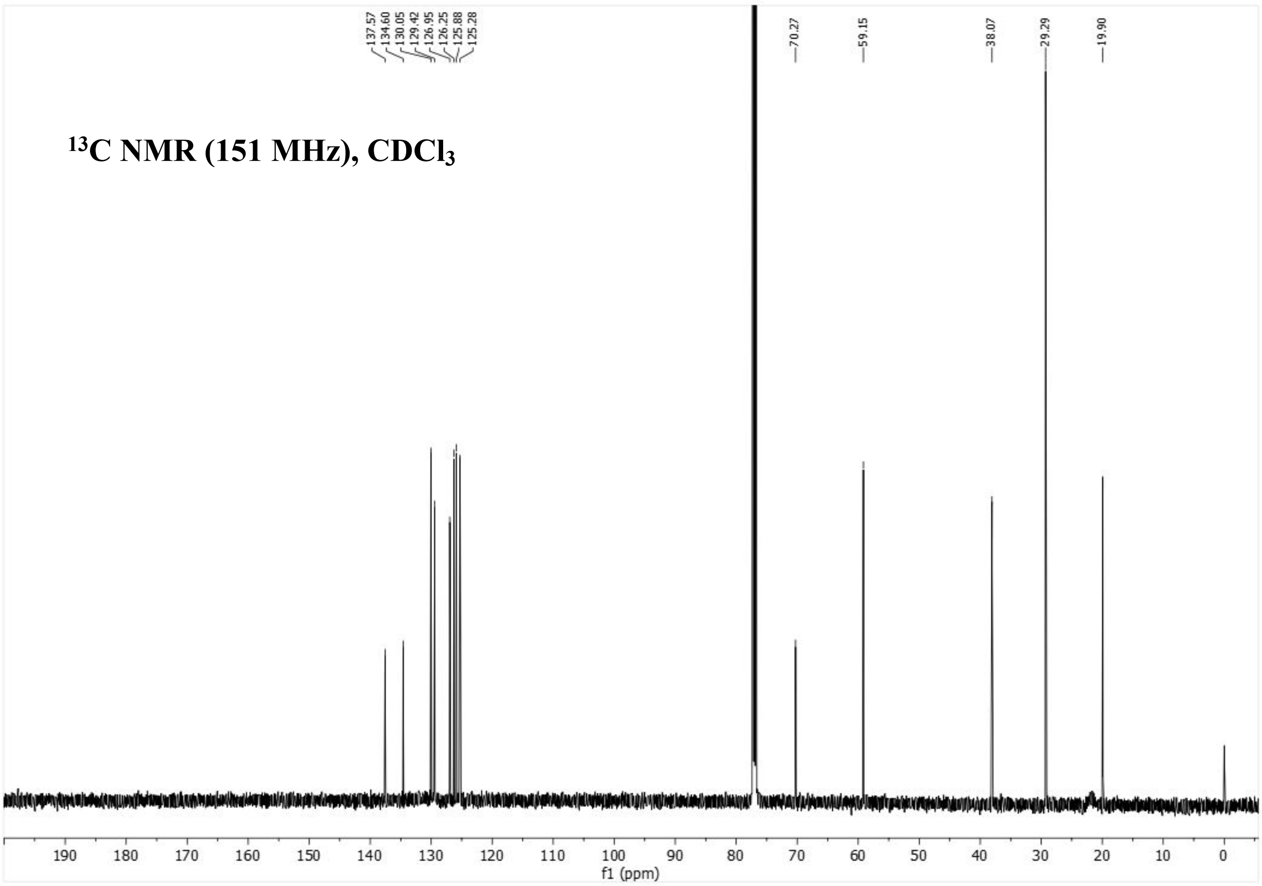

29.34
11B NMR (192 MHz, CDCl3)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

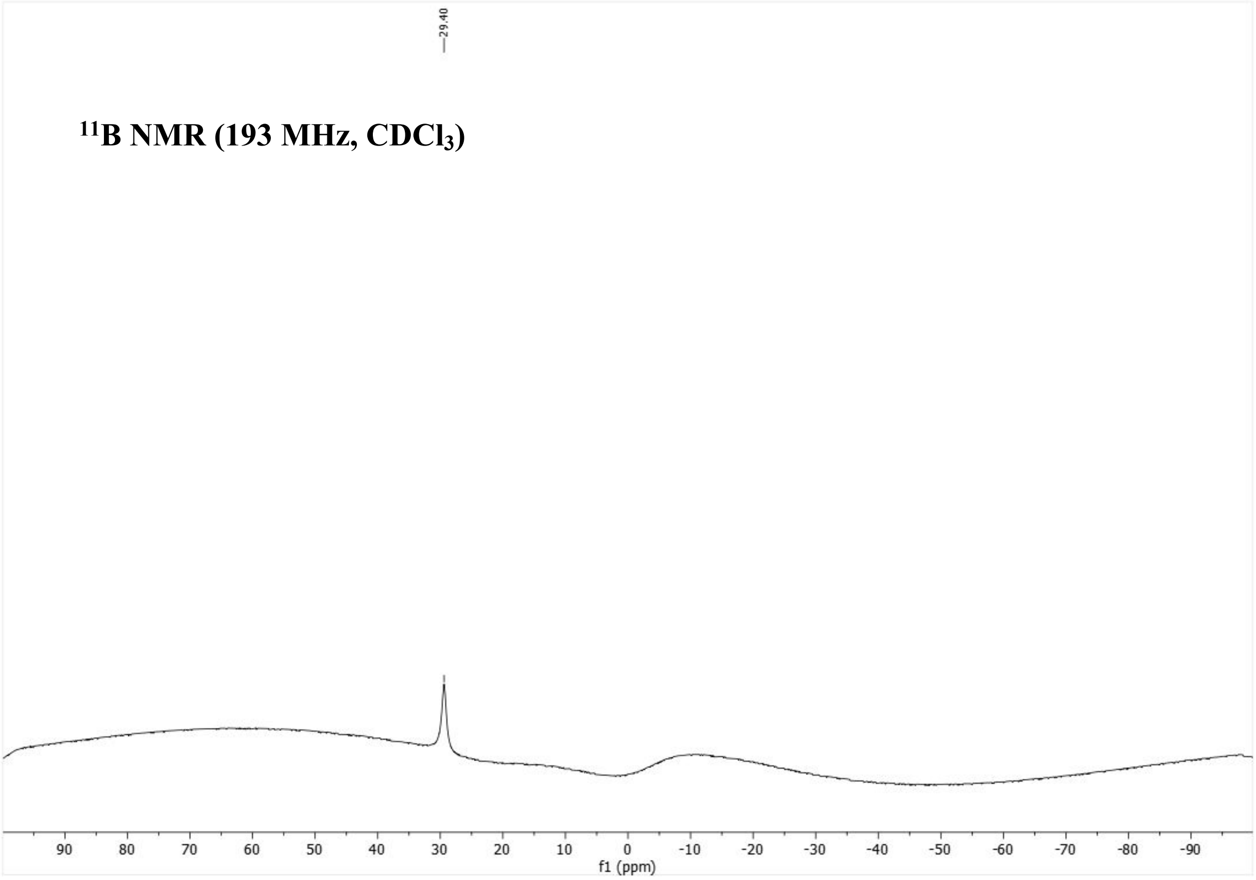


^{1}H NMR (400 MHz), CDCl$_3$

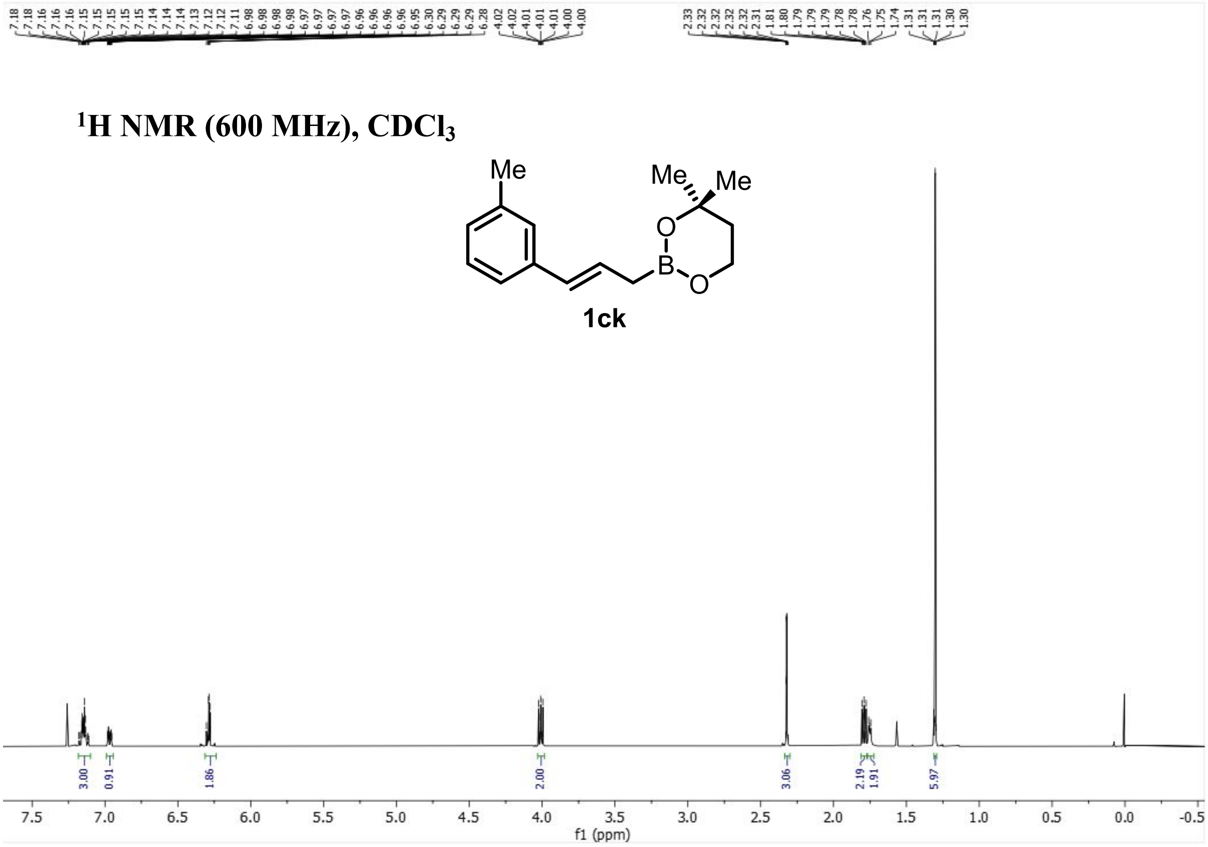
1cj



^{13}C NMR (151 MHz), CDCl$_3$

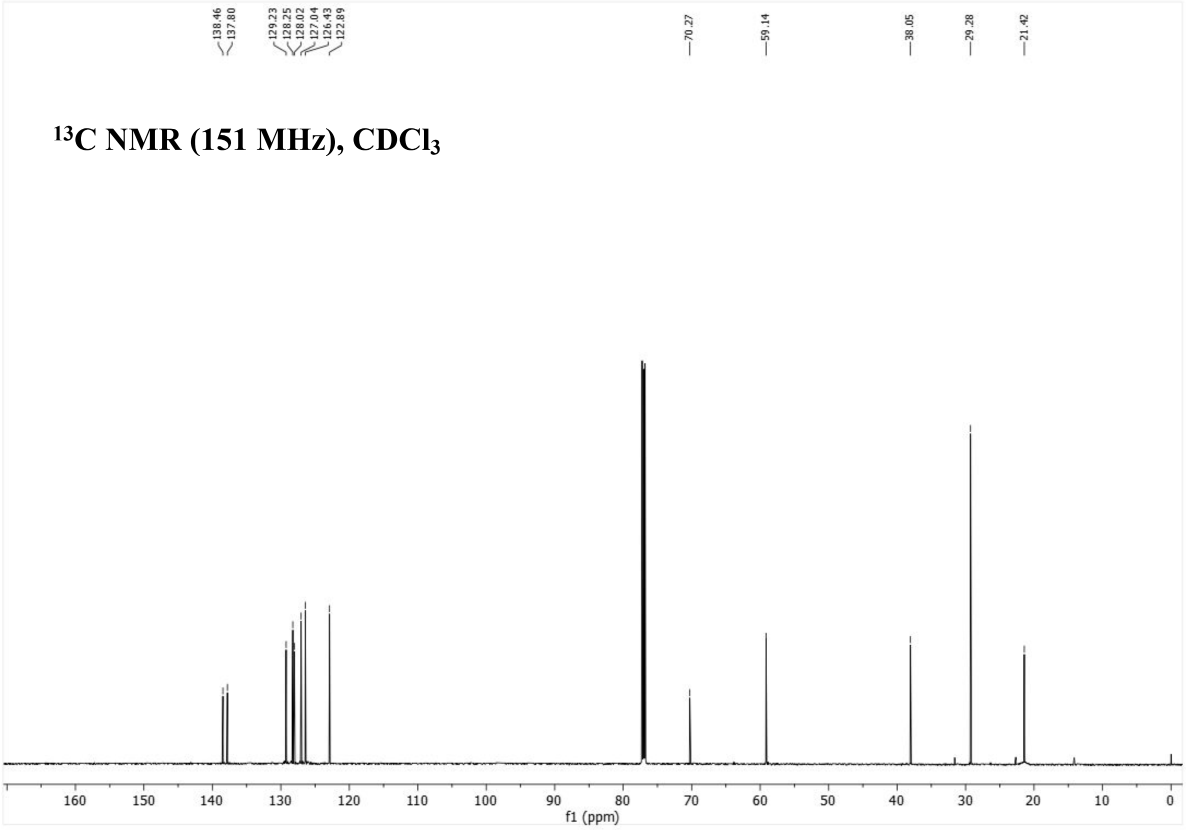


^{11}B NMR (193 MHz, $CDCl_3$)

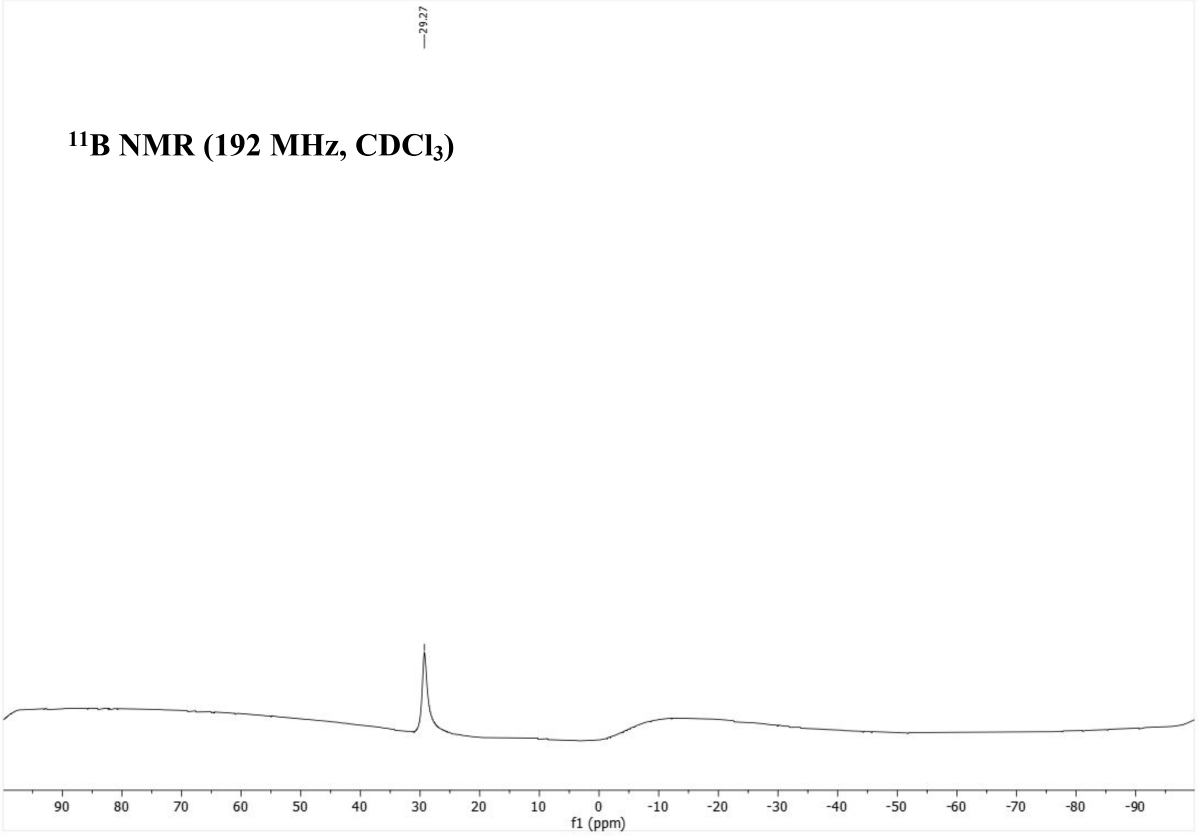


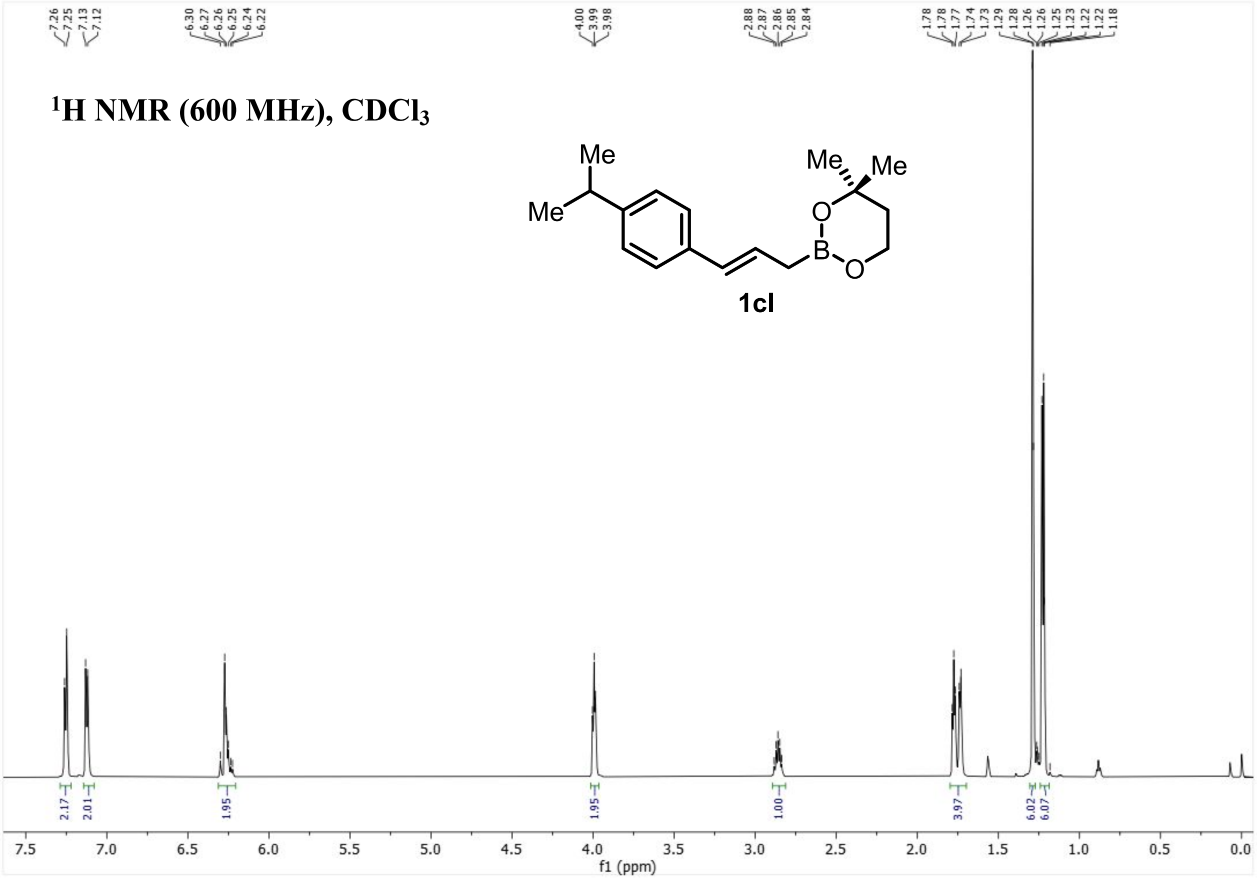
^{1}H NMR (600 MHz), CDCl$_3$

1ck



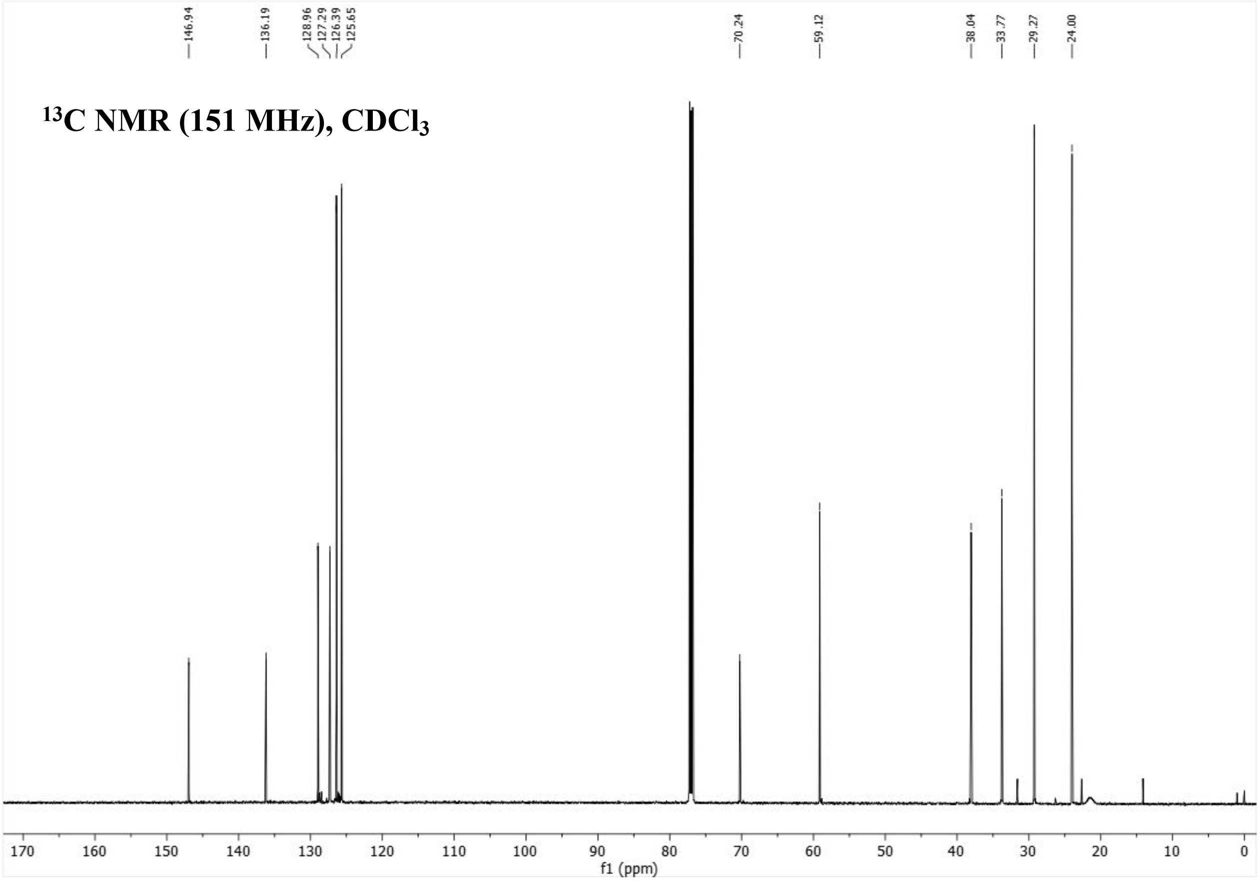
^{13}C NMR (151 MHz), CDCl$_3$


29.27
11B NMR (192 MHz, CDCl3)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

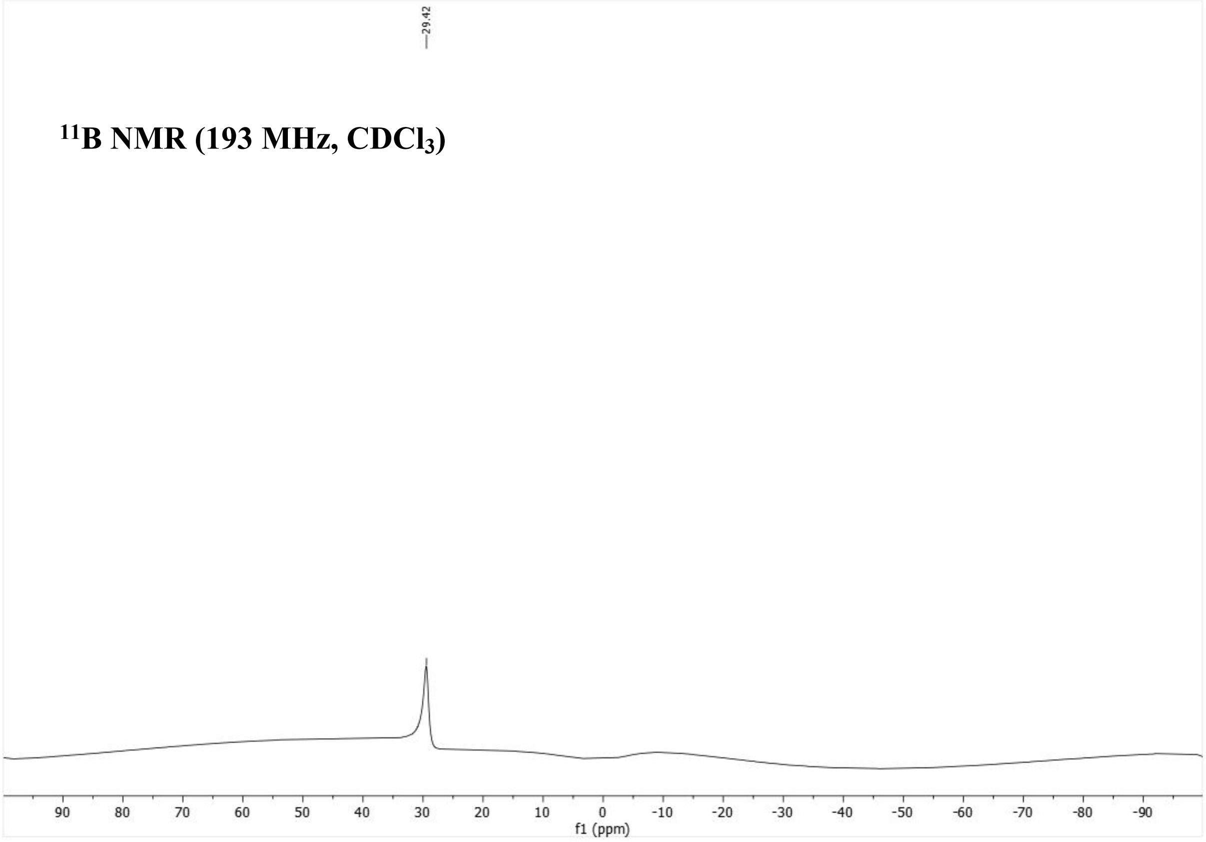


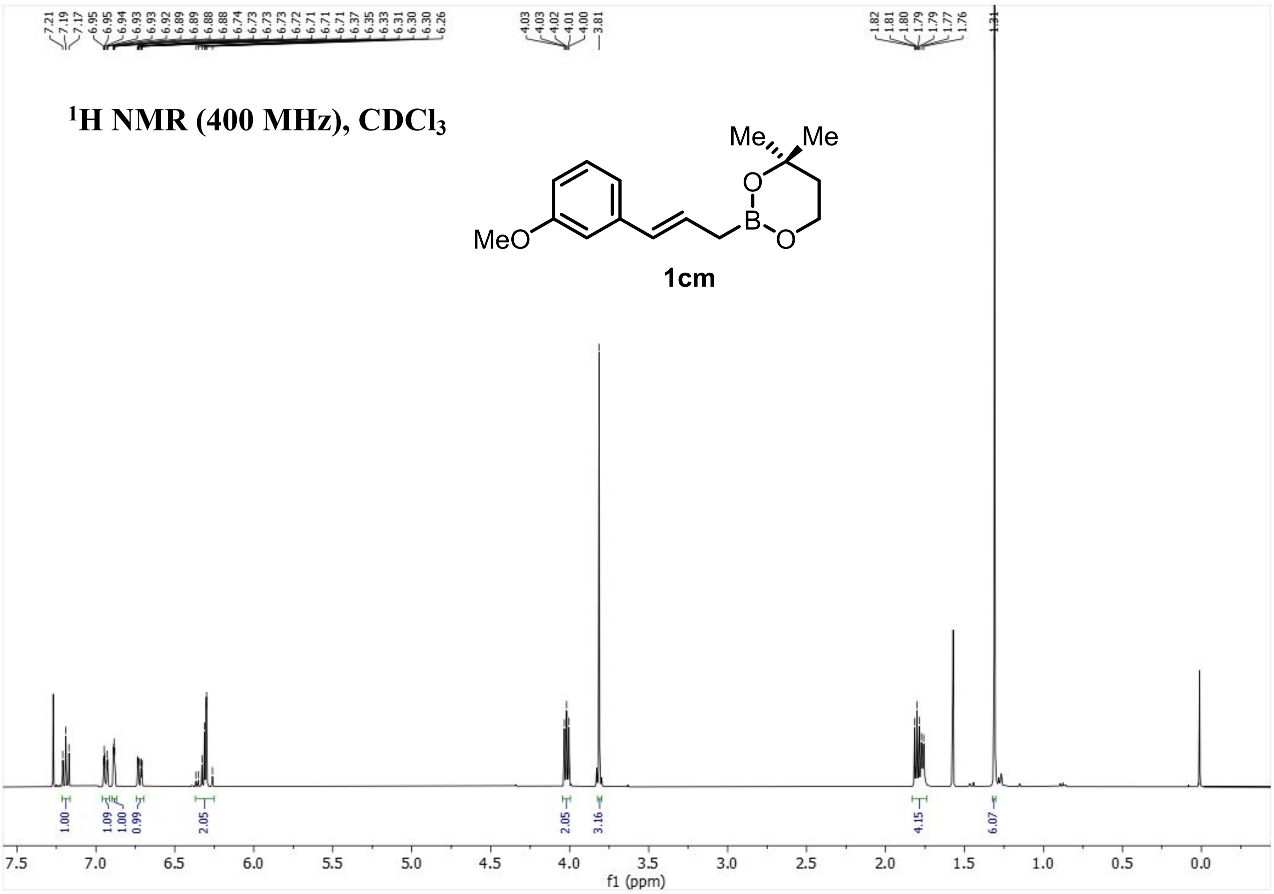
^{1}H NMR (600 MHz), CDCl$_3$

1cl

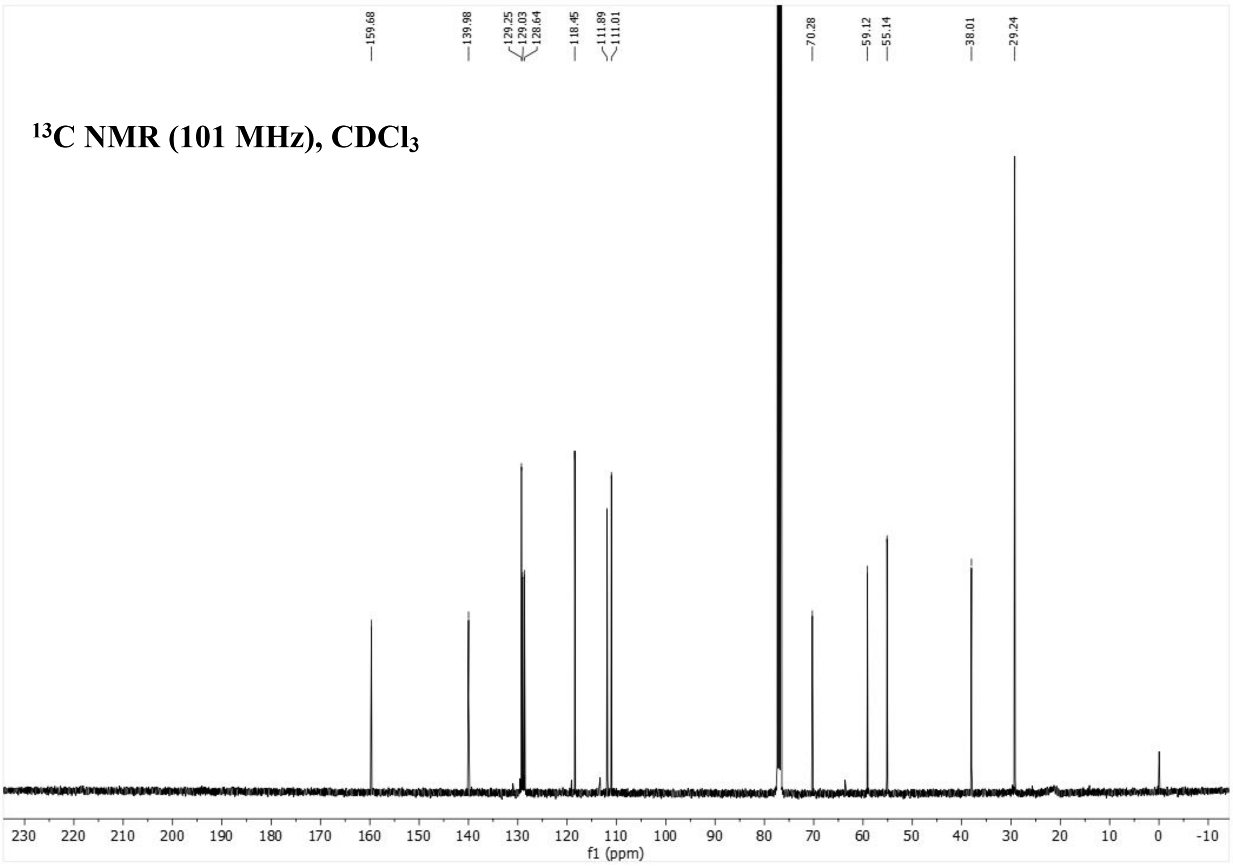


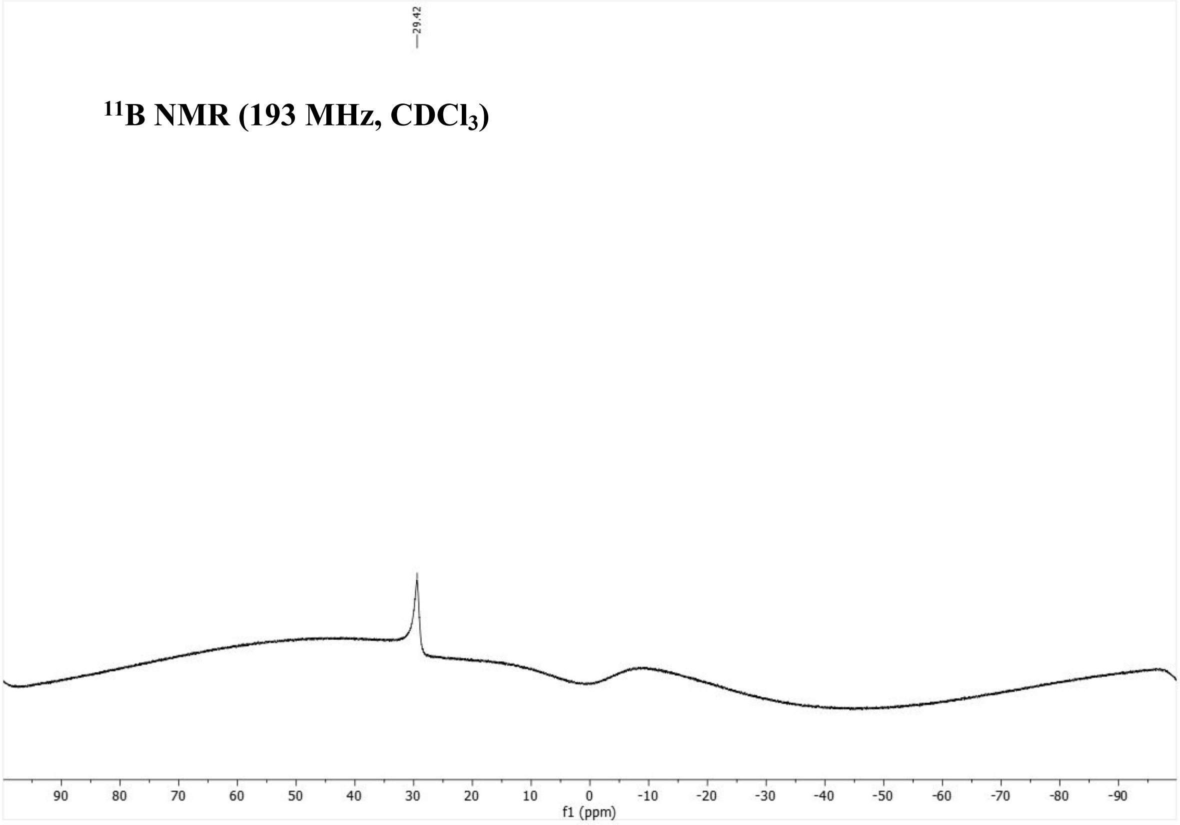
^{13}C NMR (151 MHz), CDCl$_3$

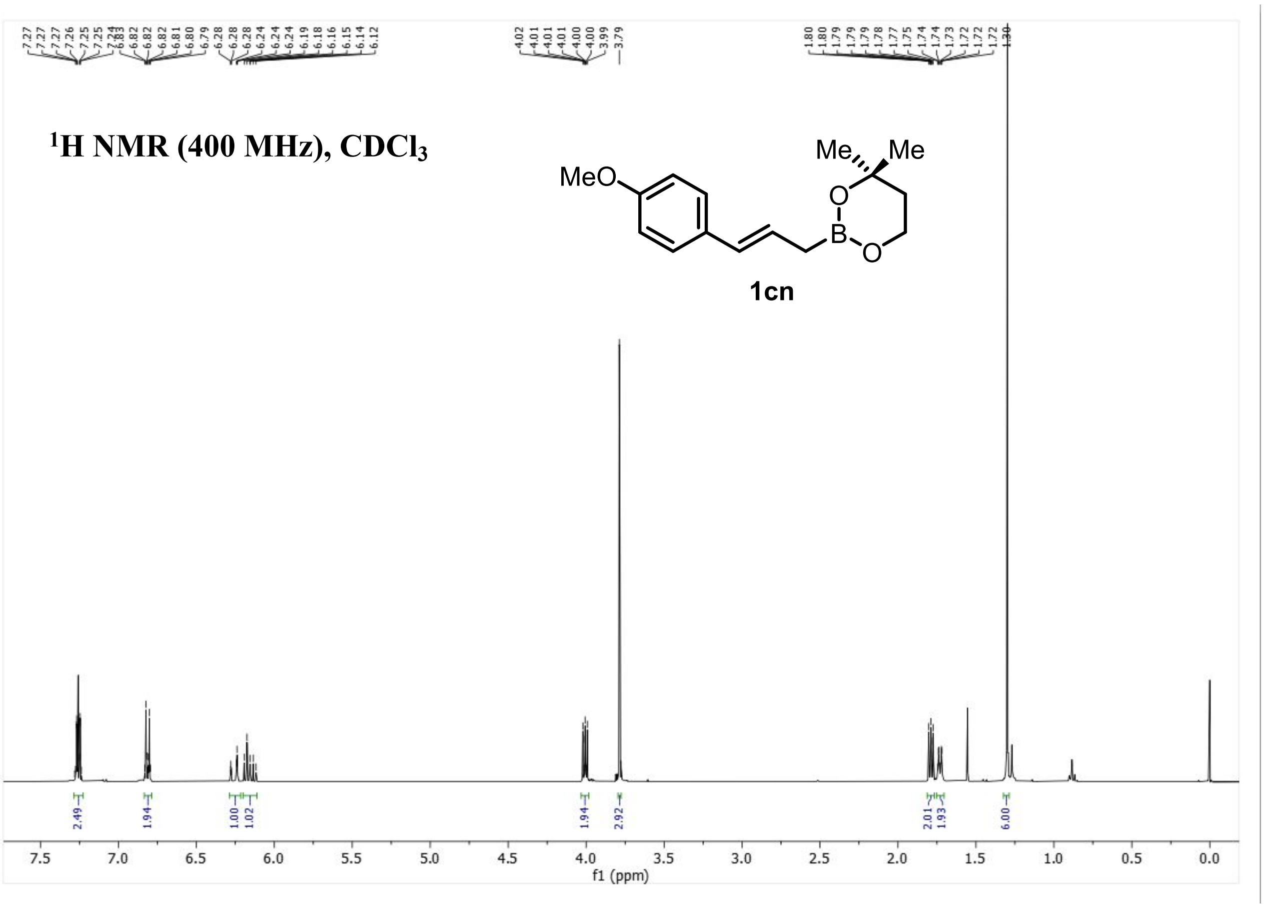

29.42
^{11}B NMR (193 MHz, CDCl$_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

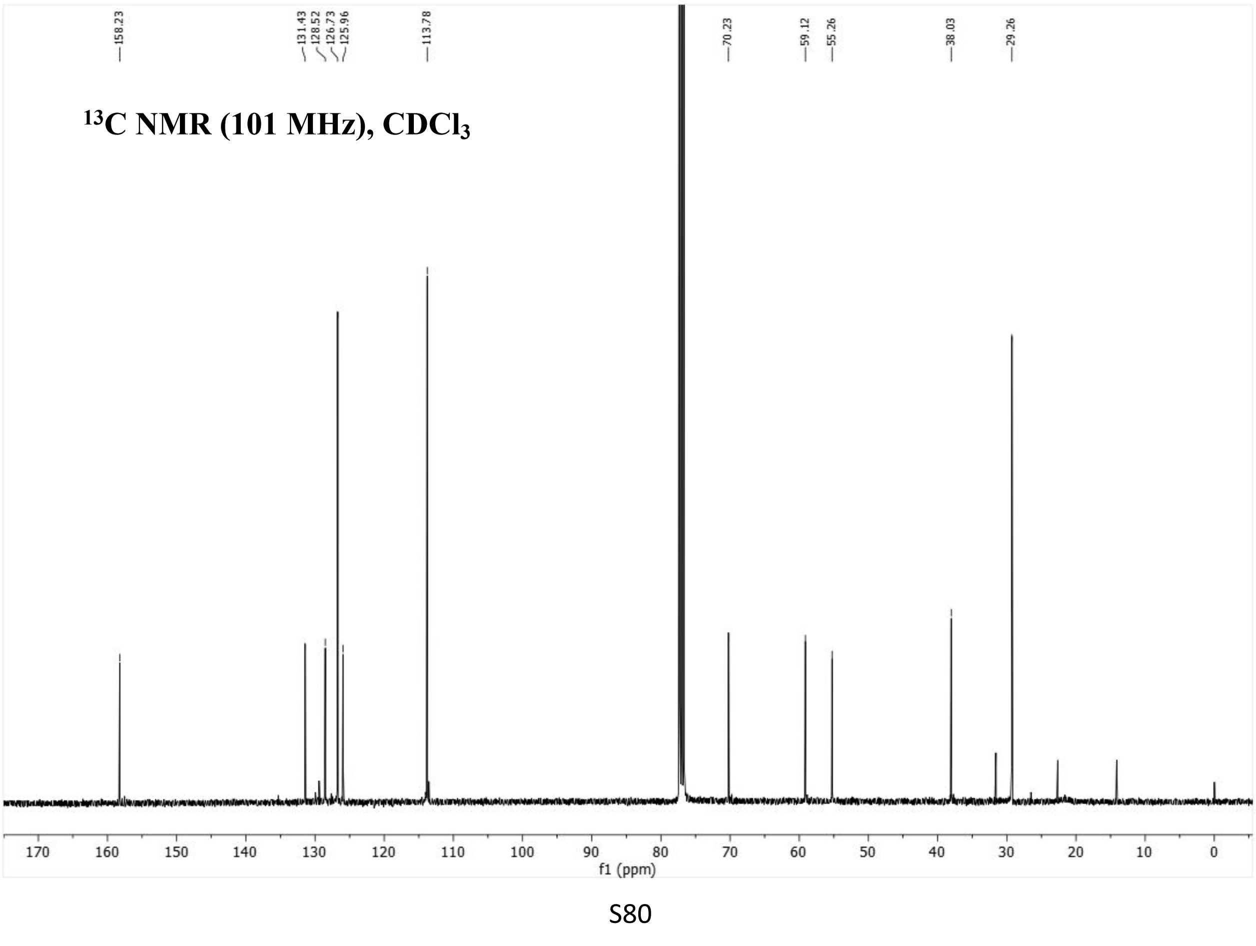

^{1}H NMR (400 MHz), $CDCl_3$

1cm

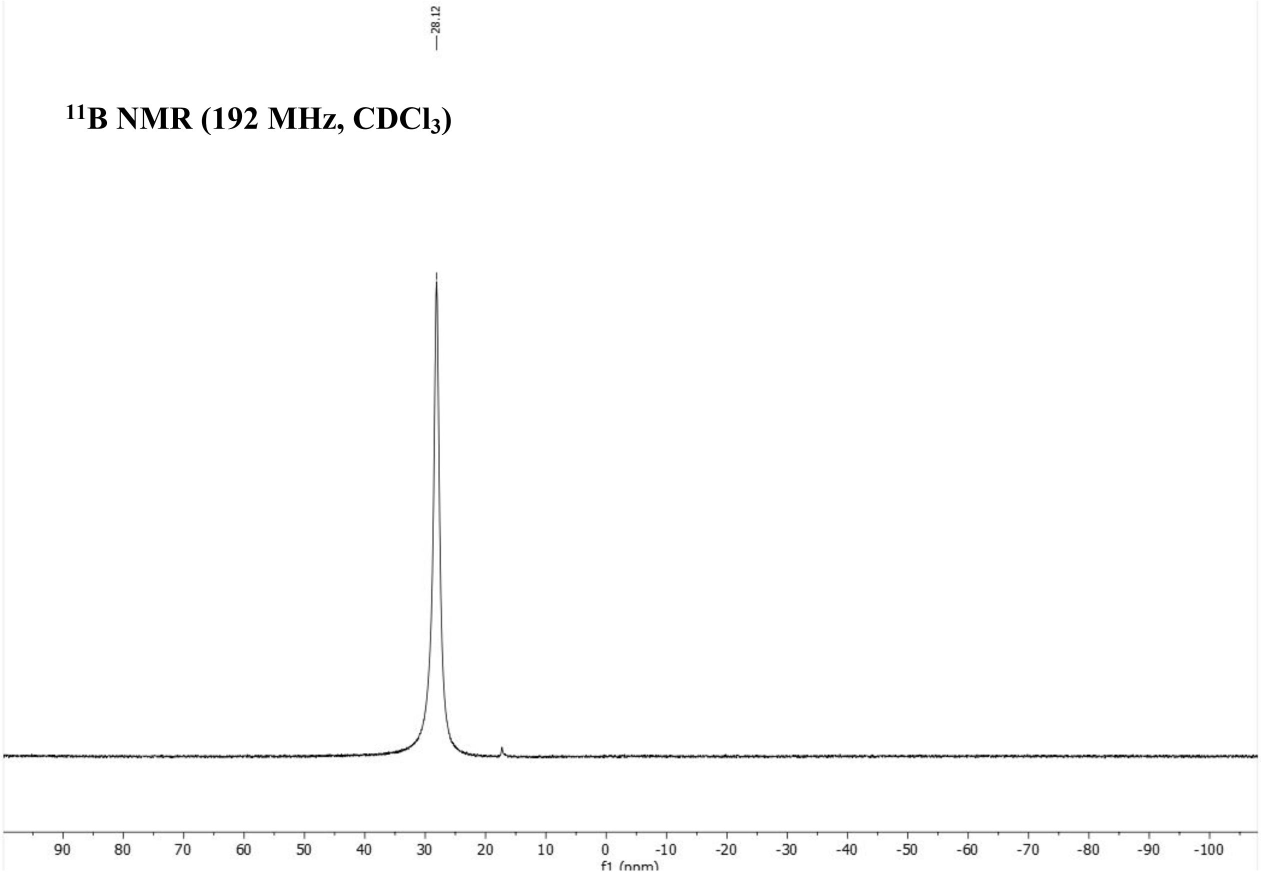

^{13}C NMR (101 MHz), $CDCl_3$

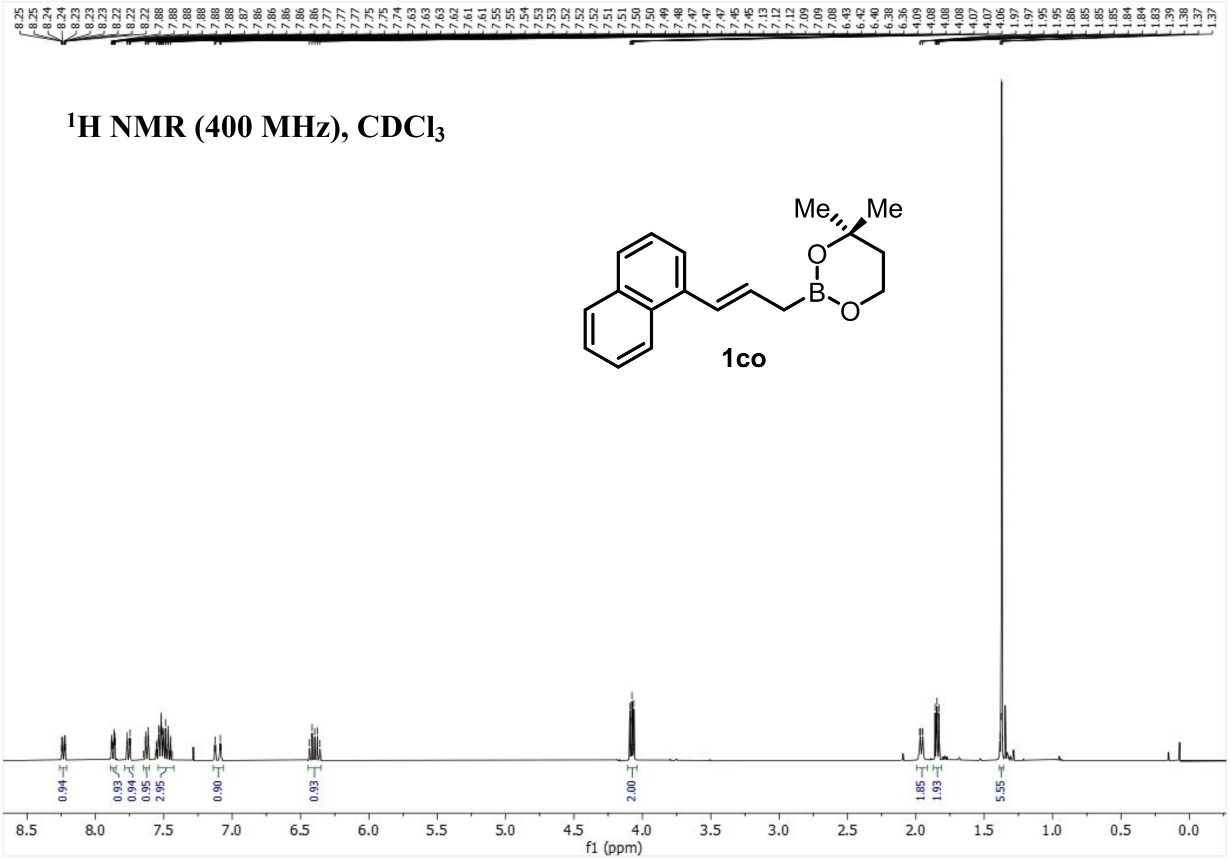

29.42
^{11}B NMR (193 MHz, CDCl$_3$)
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)


7.27
7.27
7.27
7.26
7.25
7.25
7.24
6.83
6.82
6.82
6.82
6.81
6.80
6.79
6.28
6.28
6.28
6.24
6.24
6.24
6.19
6.18
6.16
6.15
6.14
6.12
4.02
4.01
4.01
4.01
4.00
3.99
3.79
1.80
1.80
1.79
1.79
1.78
1.77
1.75
1.74
1.74
1.73
1.72
1.72
1.72
1.30
^{1}H NMR (400 MHz), CDCl$_3$
MeO
Me
Me
O
B
O
1cn
2.49
1.94
1.00
1.02
1.94
2.92
2.01
1.93
6.00
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
f1 (ppm)


158.23
131.43
128.52
126.73
125.96
113.78
70.23
59.12
55.26
38.03
29.26
^{13}C NMR (101 MHz), CDCl$_3$
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

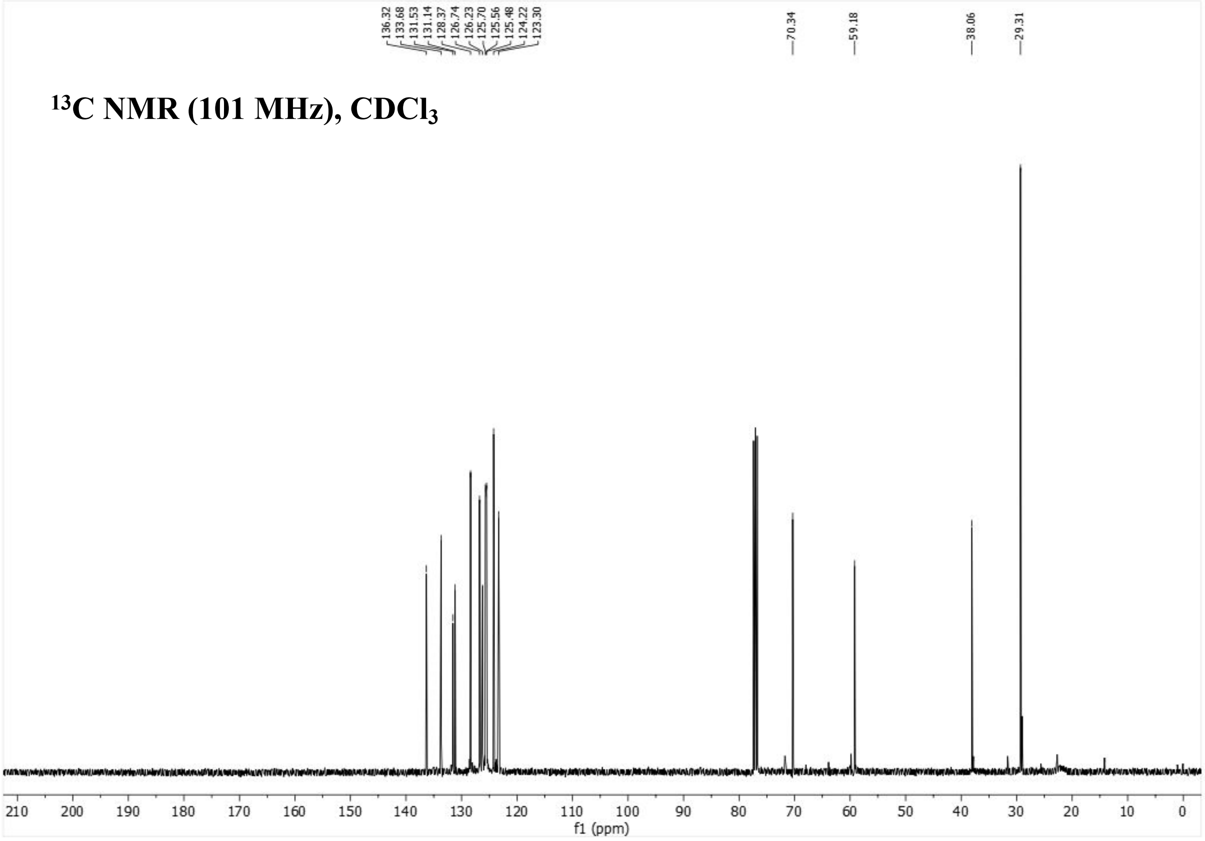
^{11}B NMR (192 MHz, CDCl$_3$)



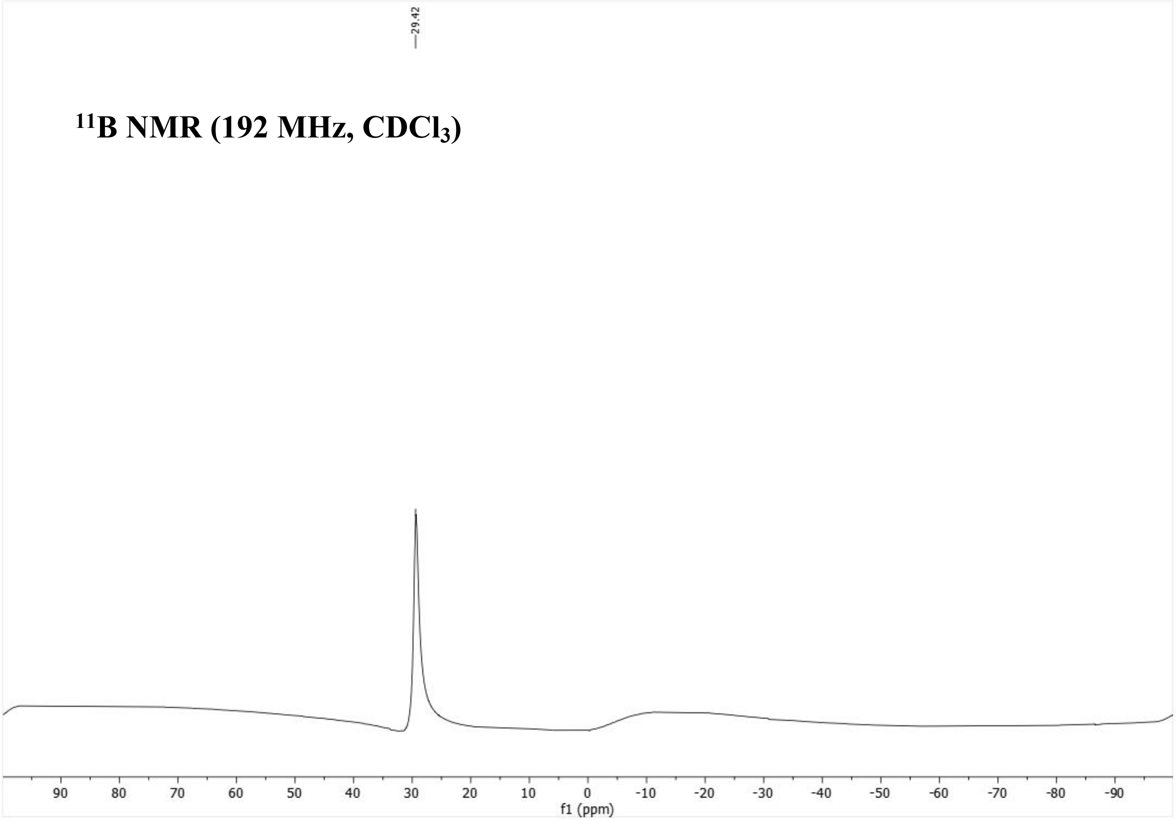


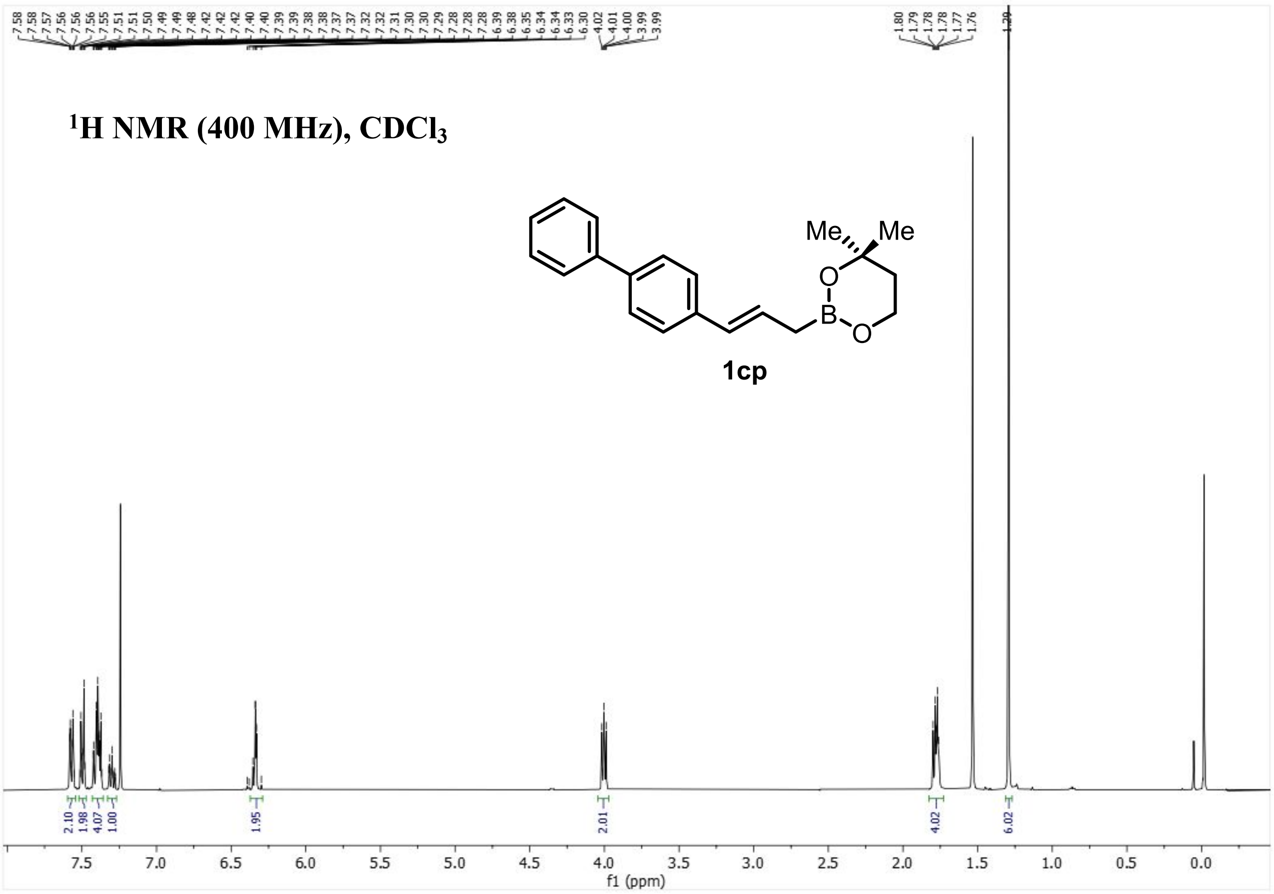
^{1}H NMR (400 MHz), CDCl$_3$

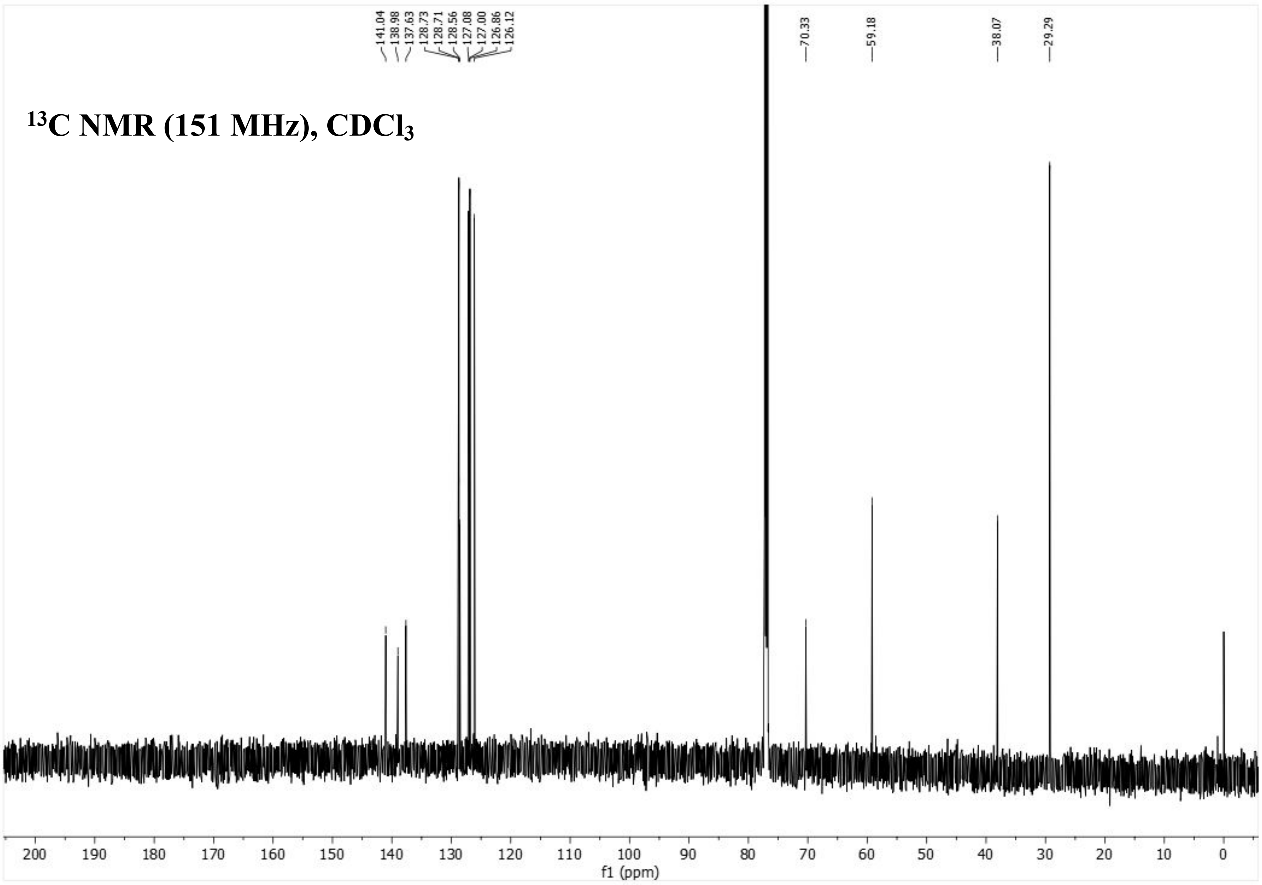
1co

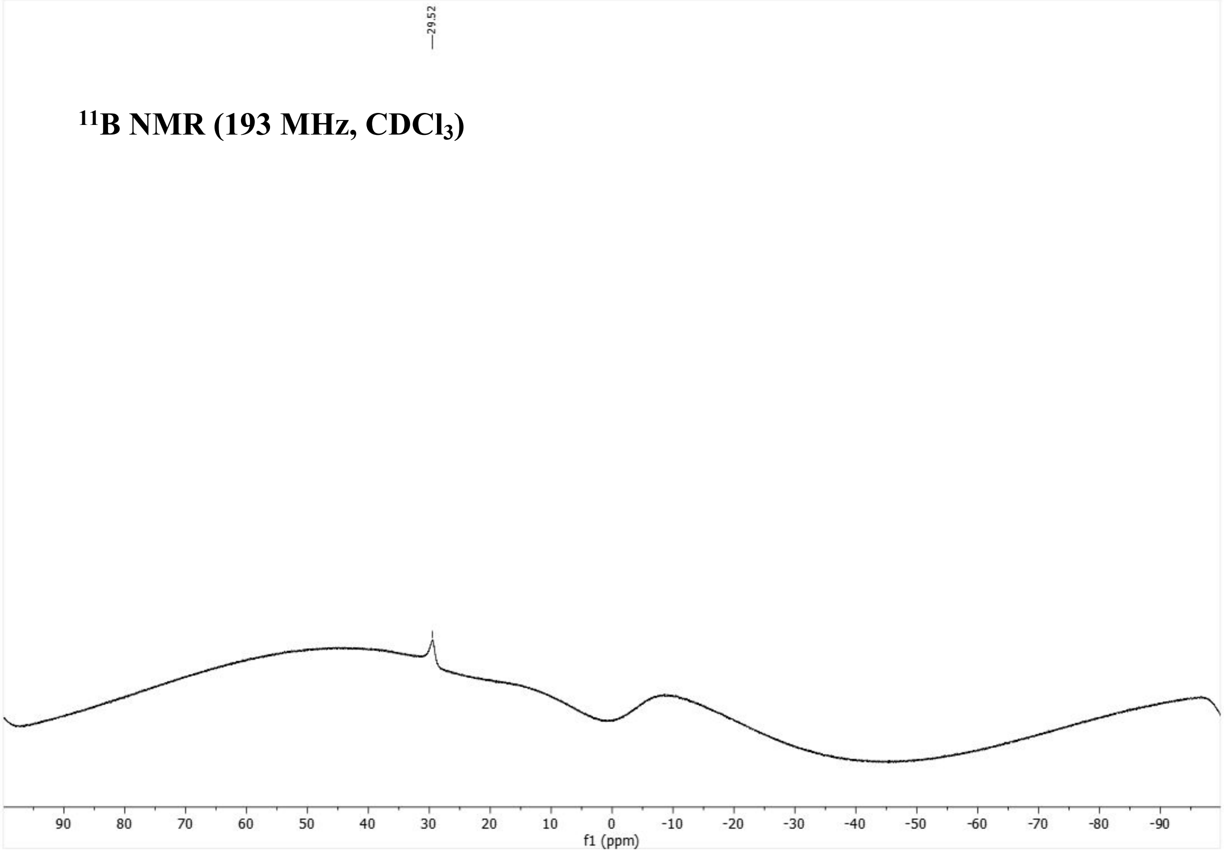


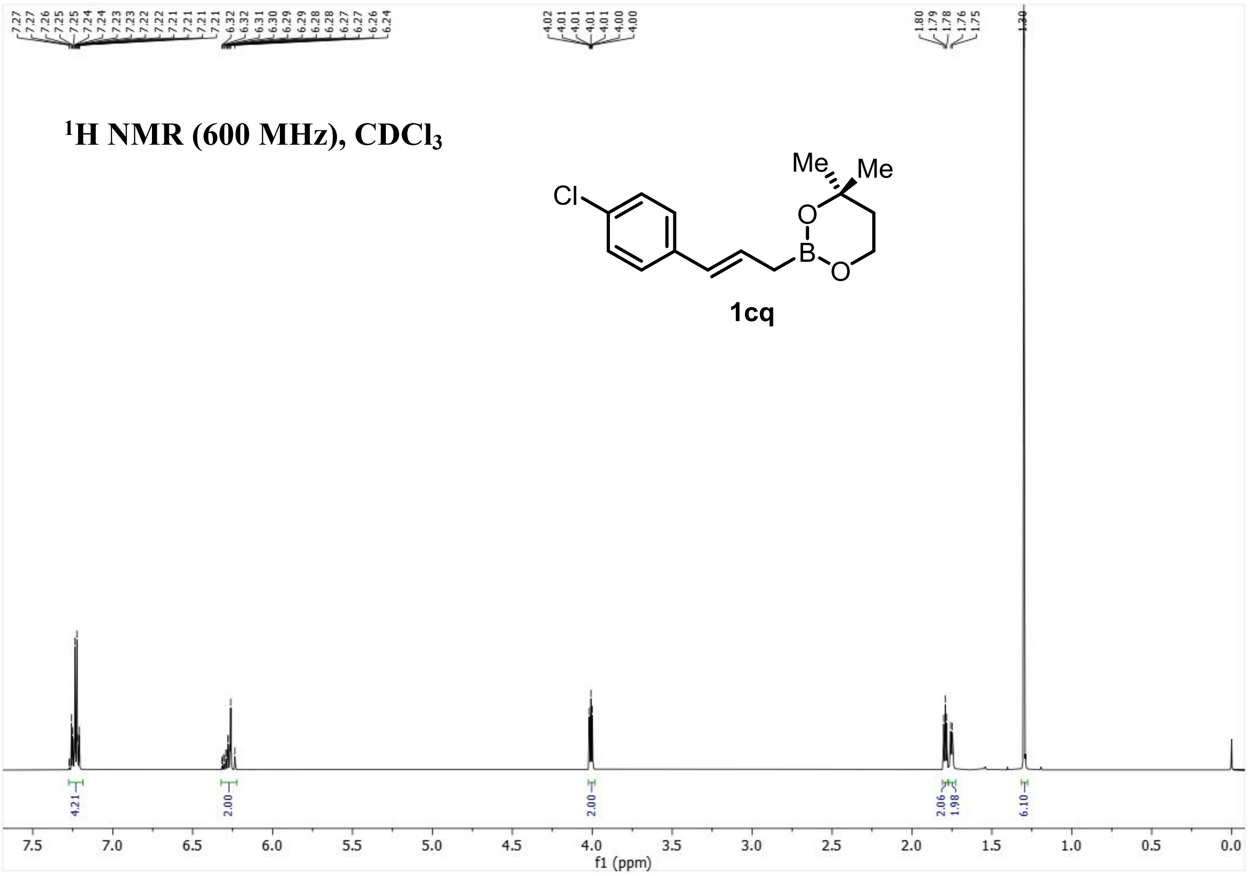
^{13}C NMR (101 MHz), CDCl$_3$


29.42
^{11}B NMR (192 MHz, CDCl$_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)


7.58 7.58 7.57 7.56 7.56 7.56 7.55 7.51 7.50 7.49 7.49 7.48 7.42 7.42 7.42 7.40 7.40 7.39 7.39 7.38 7.38 7.37 7.37 7.32 7.32 7.31 7.30 7.30 7.29 7.28 7.28 7.28 6.39 6.39 6.38 6.35 6.34 6.34 6.33 6.30 4.02 4.01 4.00 3.99 3.99
1.80 1.79 1.78 1.78 1.77 1.76
1.29
^{1}H NMR (400 MHz), CDCl$_3$
Me
Me
O
B
O
1cp
2.10 1.98 4.07 1.00
1.95
2.01
4.02
6.02
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
f1 (ppm)

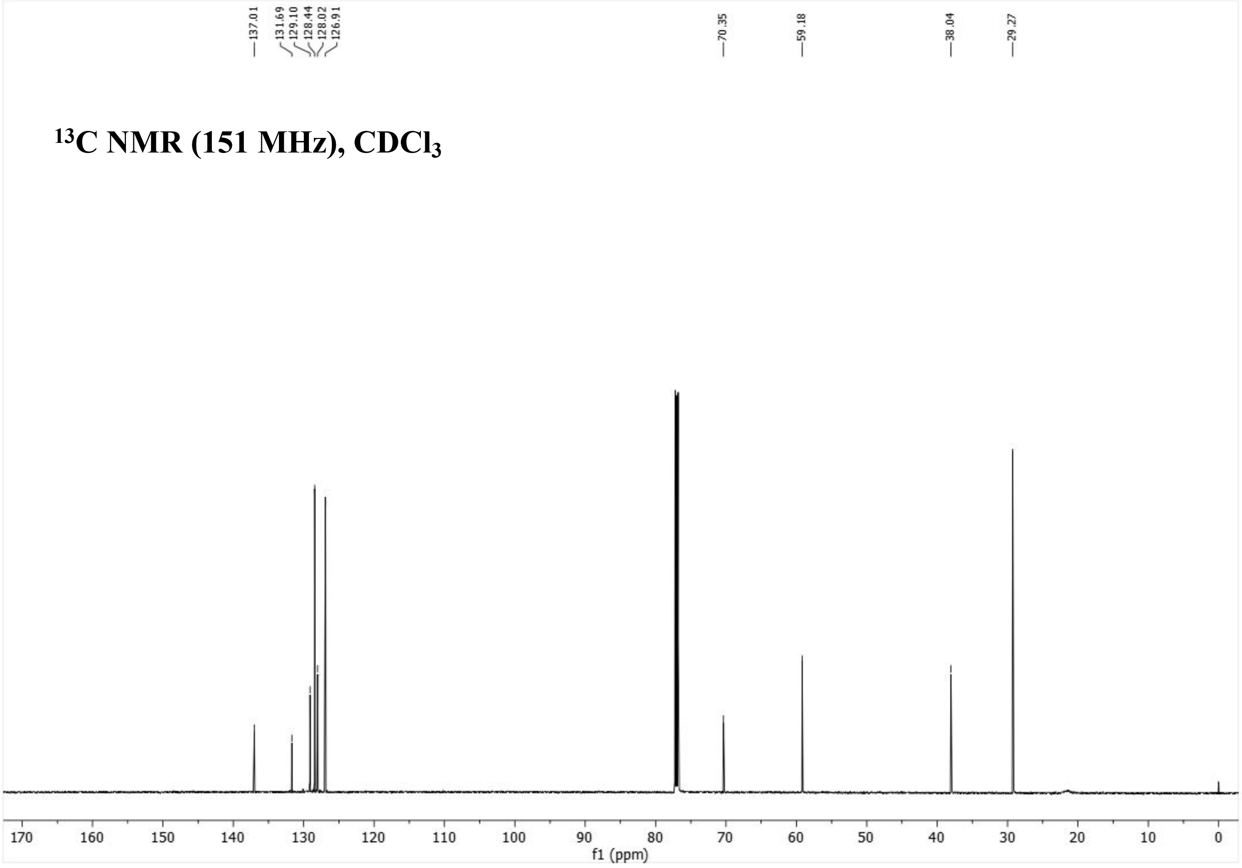

141.04 138.98 137.63 128.73 128.71 128.56 127.08 127.00 126.86 126.12
70.33
59.18
38.07
29.29
^{13}C NMR (151 MHz), CDCl$_3$
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


29.52
^{11}B NMR (193 MHz, CDCl$_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

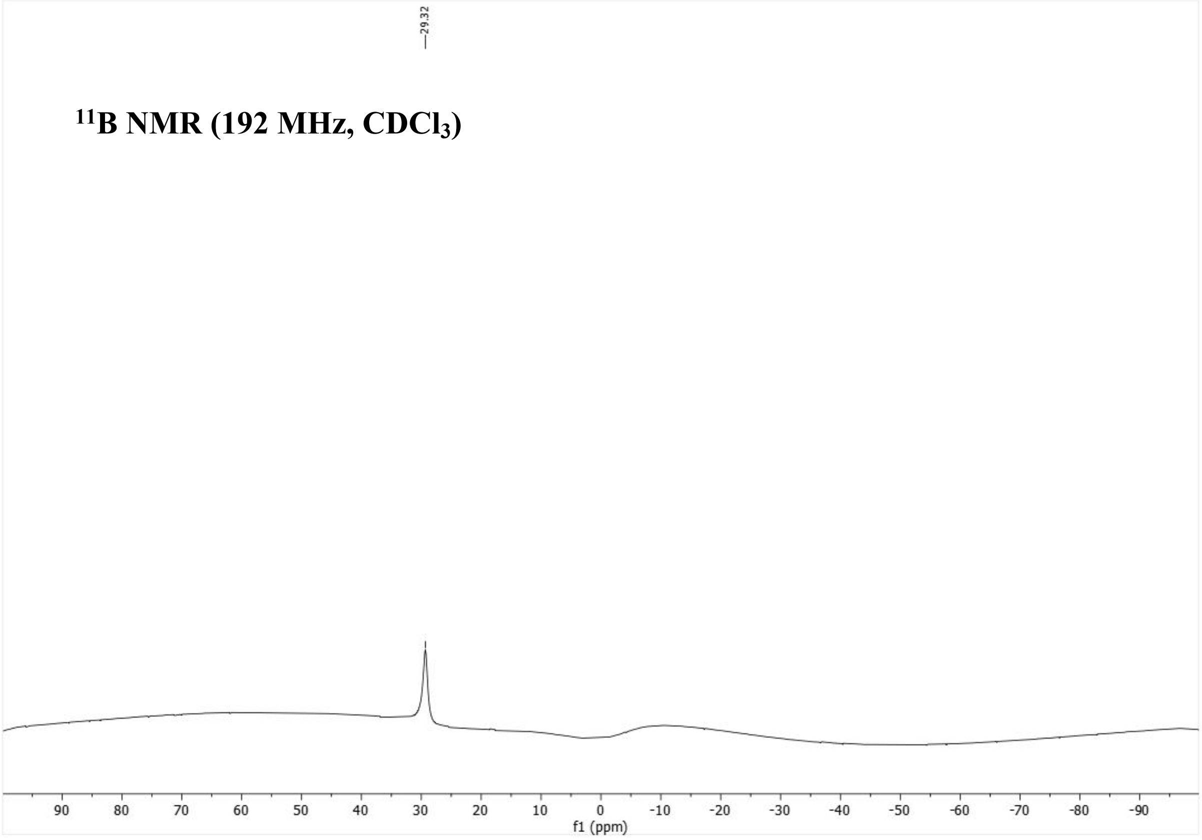


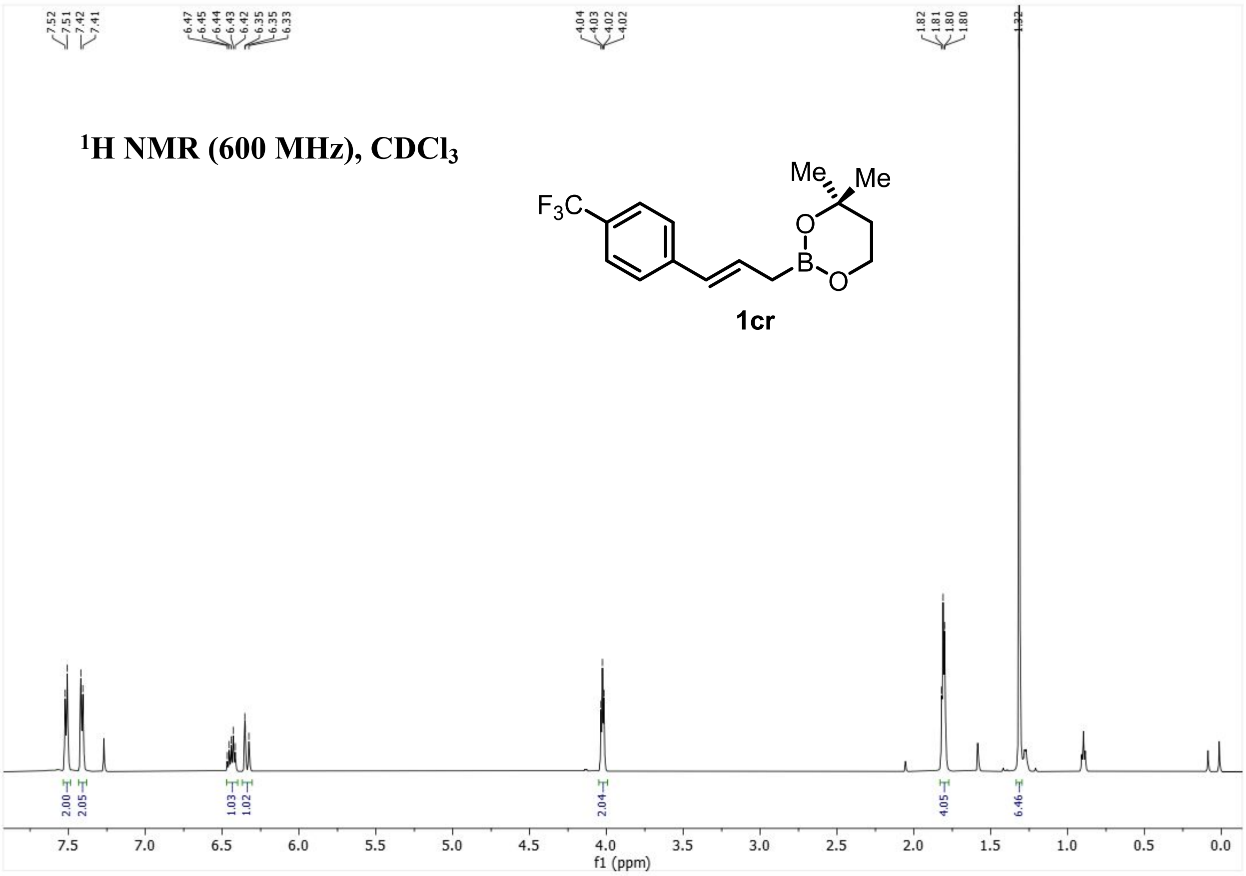
^{1}H NMR (600 MHz), CDCl$_3$

1cq

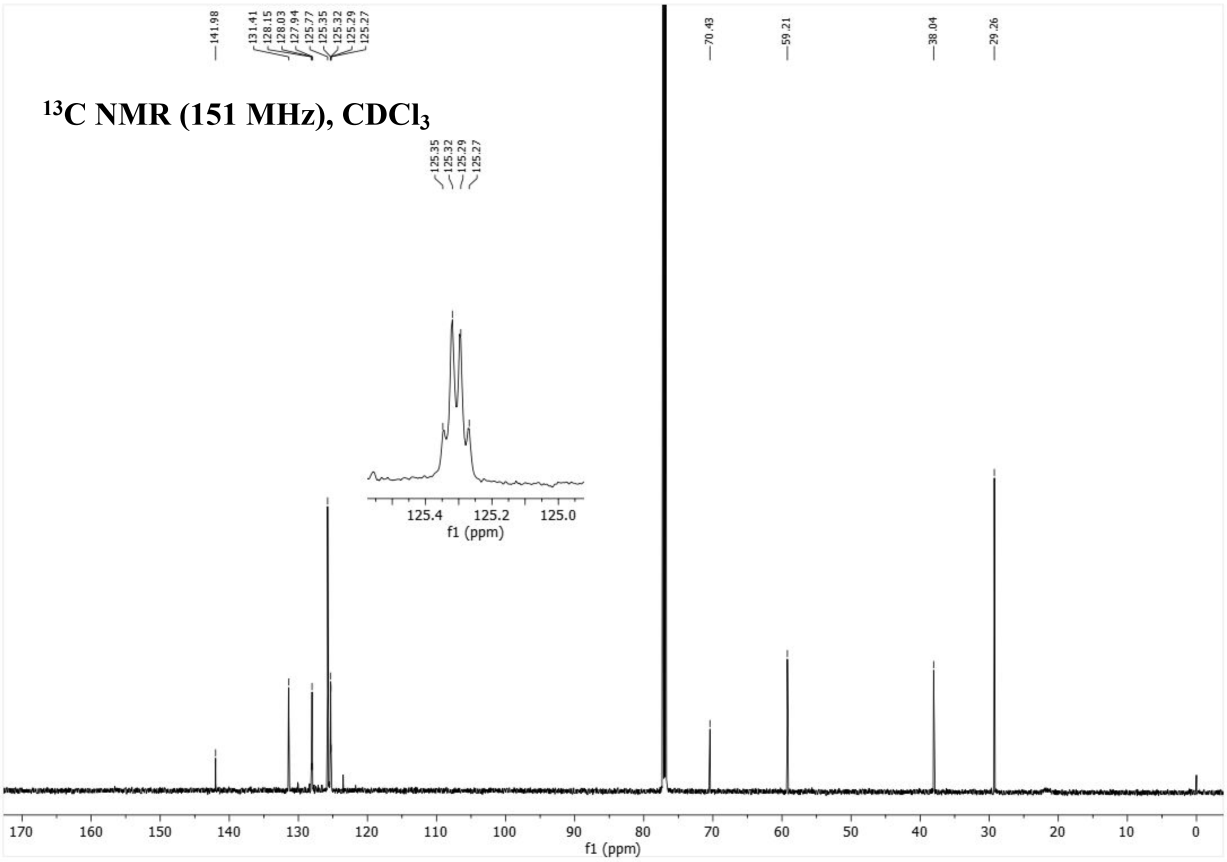


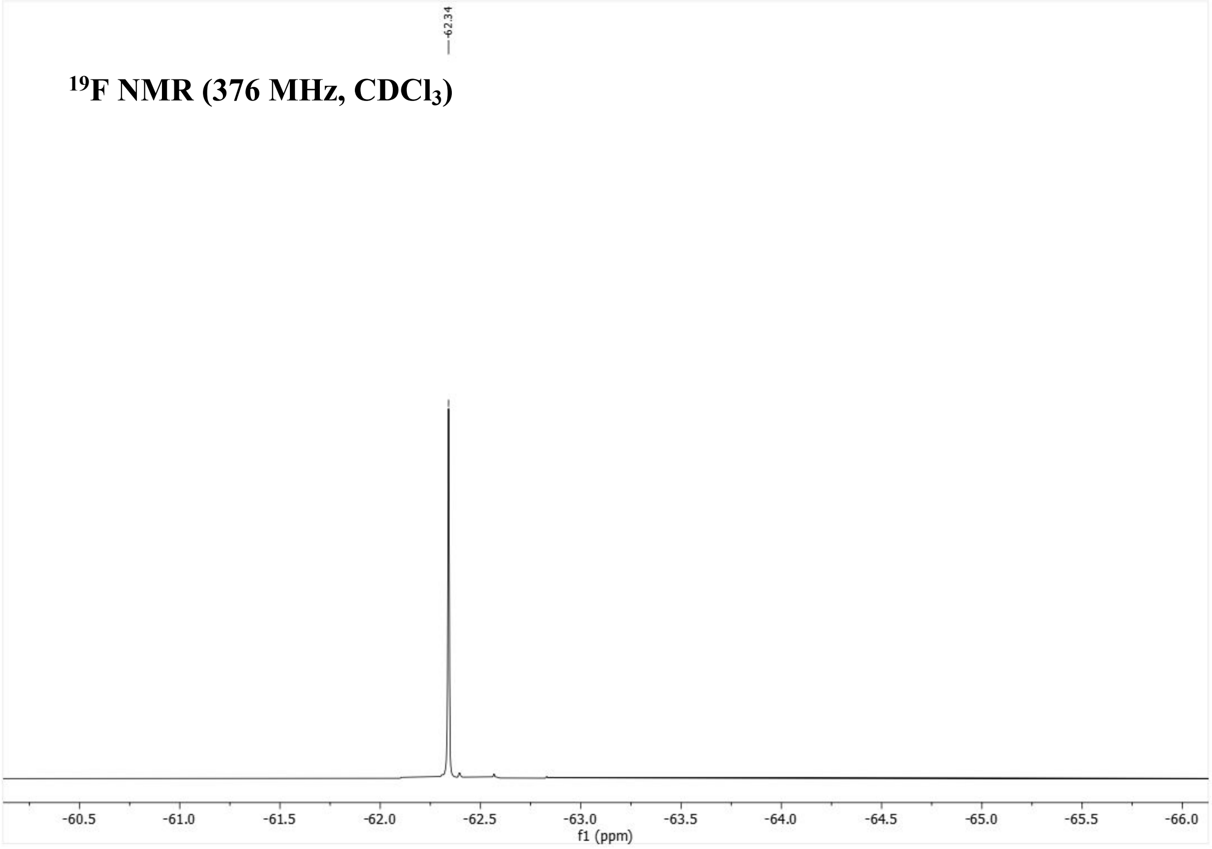
^{13}C NMR (151 MHz), CDCl$_3$

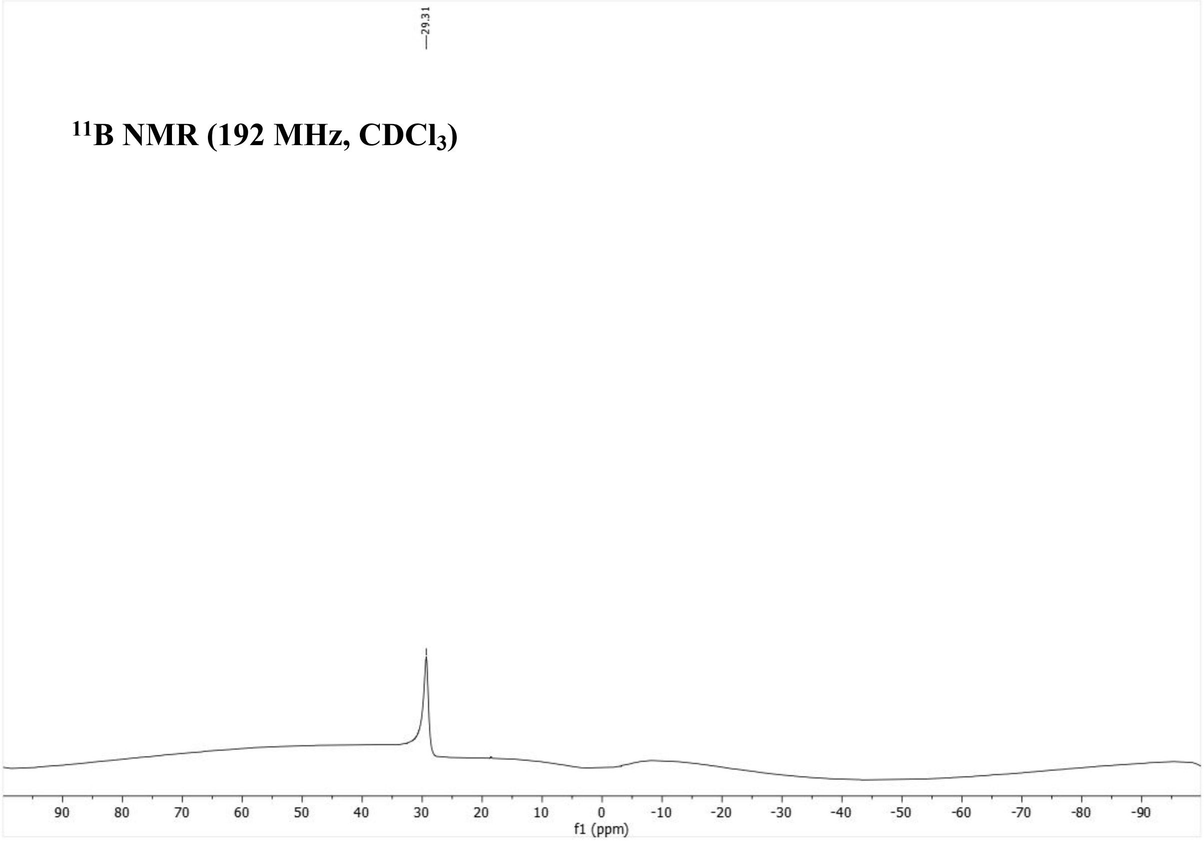

29.32
¹¹B NMR (192 MHz, CDCl₃)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

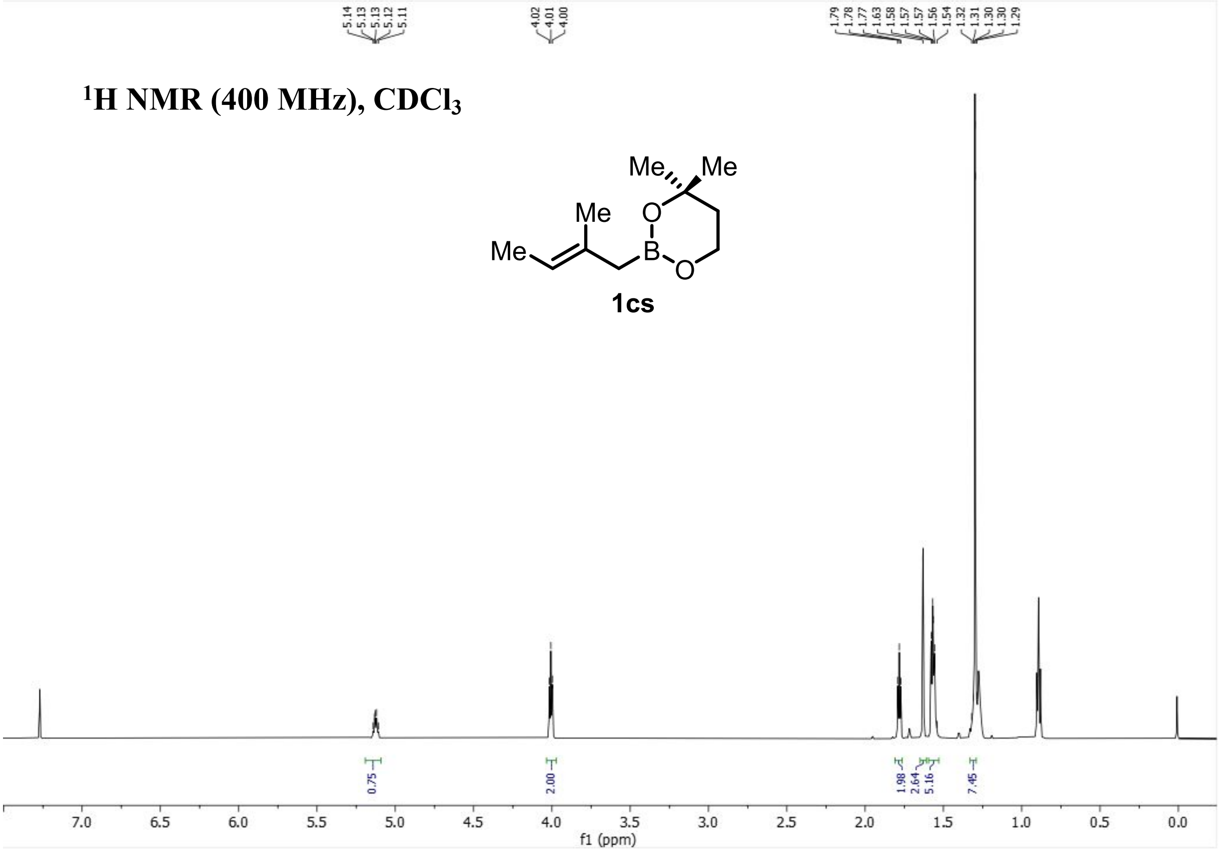

7.52
7.51
7.42
7.41
6.47
6.45
6.44
6.43
6.42
6.35
6.35
6.33
4.04
4.03
4.02
4.02
1.82
1.81
1.80
1.80
1.32
^{1}H NMR (600 MHz), CDCl$_3$
F$_3$C
Me
Me
O
B
O
2.00
2.05
1.03
1.02
2.04
4.05
6.46
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

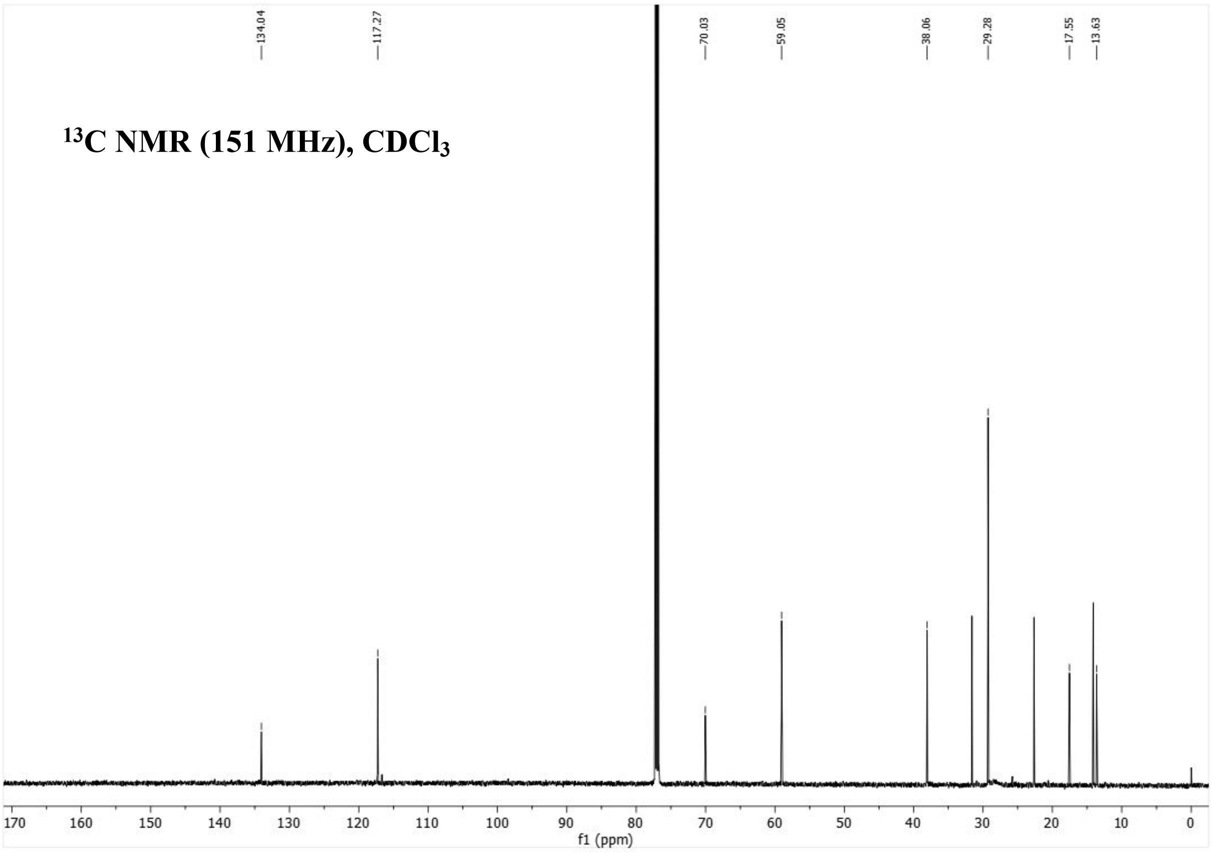
1cr

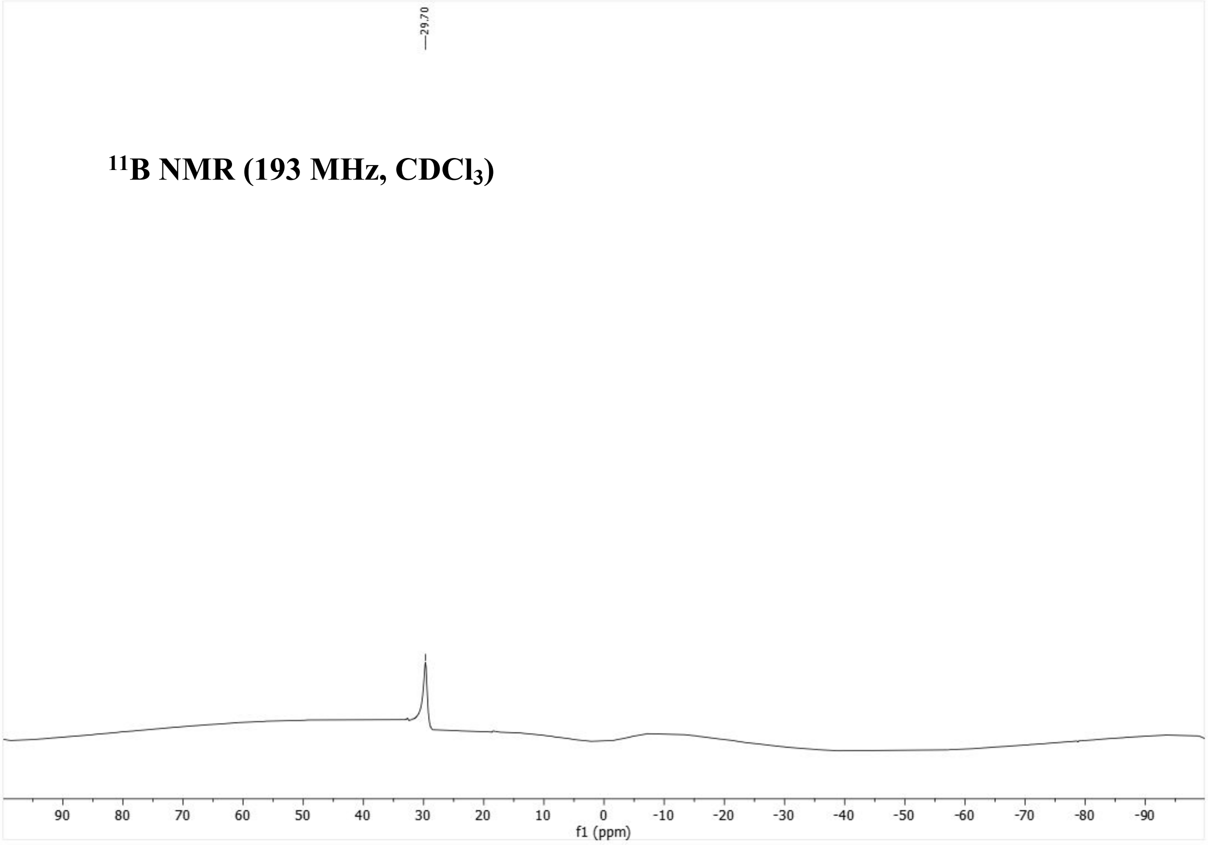

141.98
131.41
128.15
128.03
127.94
125.77
125.35
125.32
125.29
125.27
70.43
59.21
38.04
29.26
^{13}C NMR (151 MHz), CDCl$_3$
125.35
125.32
125.29
125.27
125.4
125.2
125.0
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

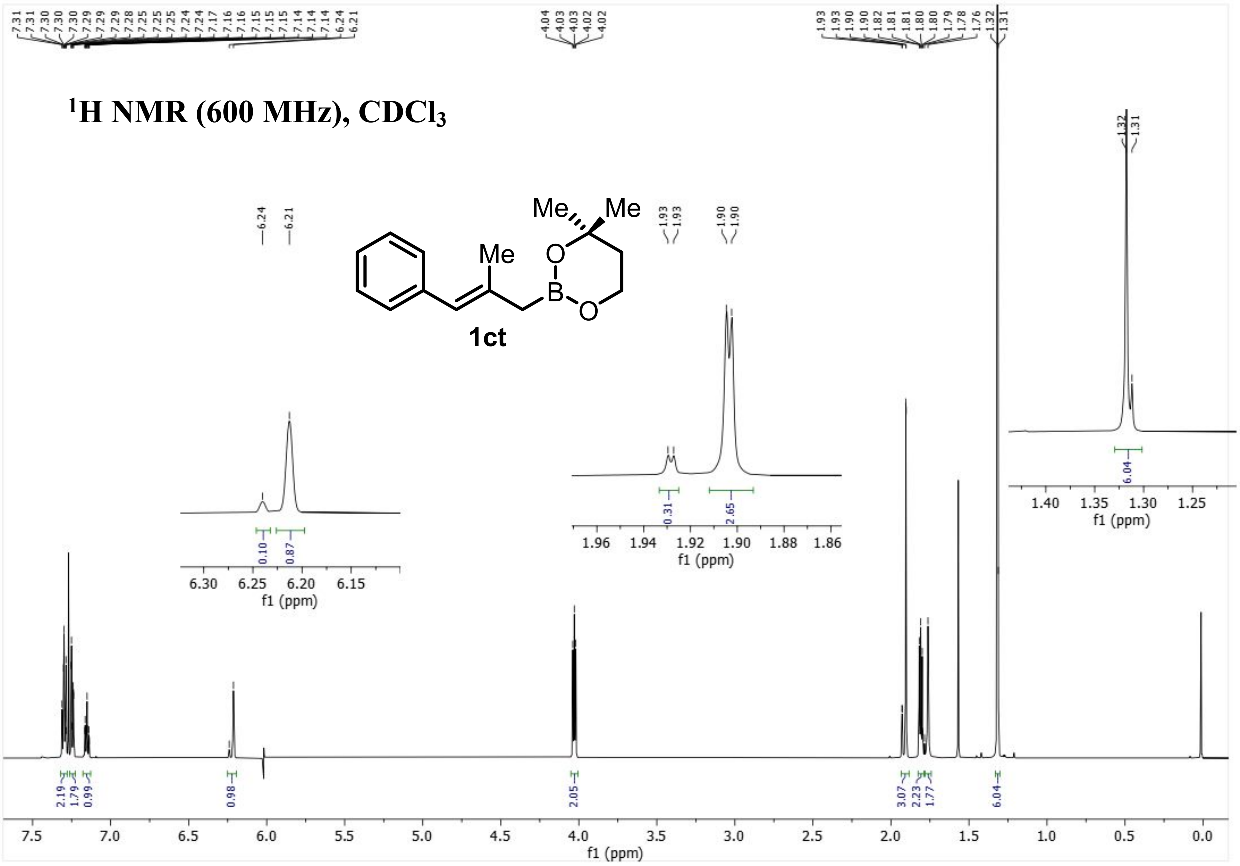

-62.34
^{19}F NMR (376 MHz, $CDCl_3$)
-60.5
-61.0
-61.5
-62.0
-62.5
-63.0
-63.5
-64.0
-64.5
-65.0
-65.5
-66.0
f1 (ppm)


29.31
^{11}B NMR (192 MHz, $CDCl_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

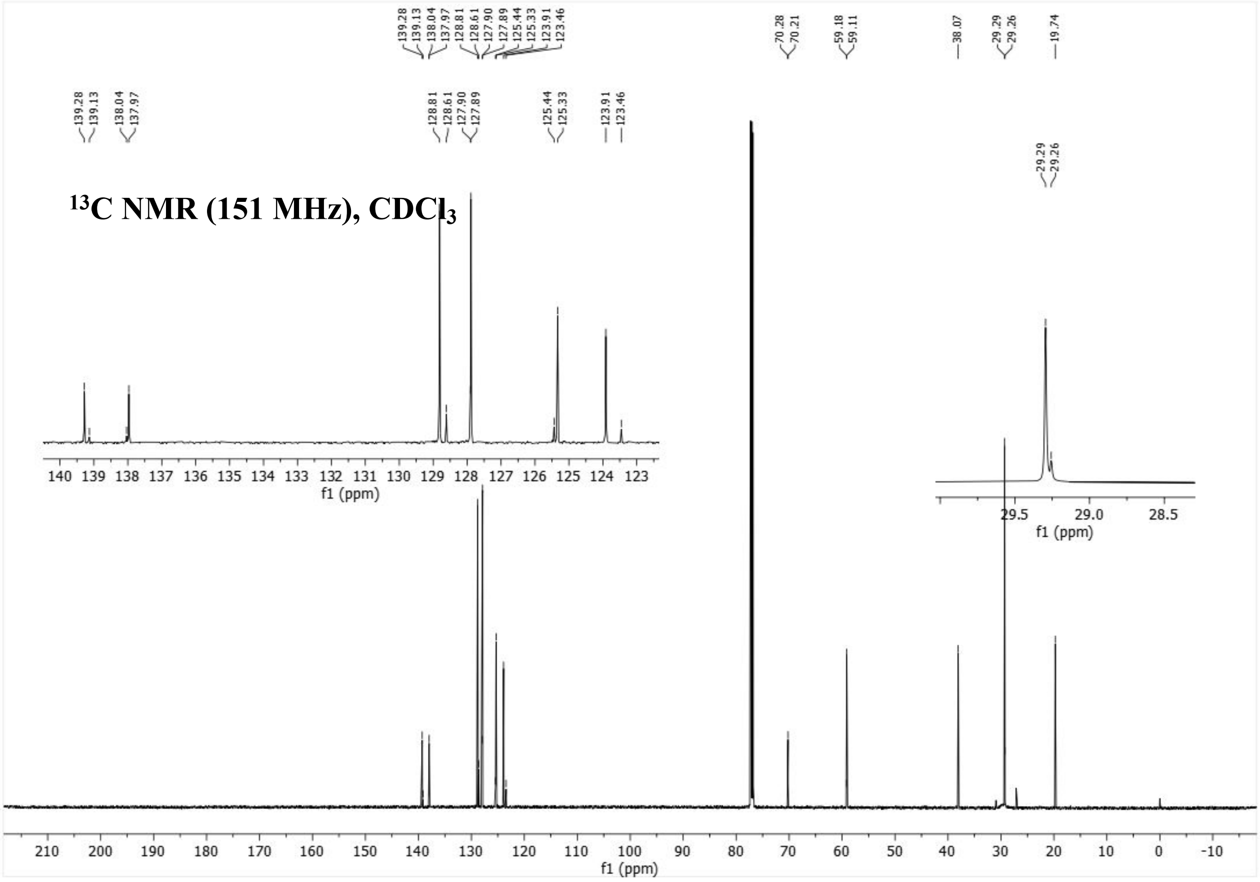

5.14
5.13
5.13
5.12
5.11
4.02
4.01
4.00
1.79
1.78
1.77
1.63
1.58
1.57
1.57
1.56
1.54
1.32
1.31
1.30
1.30
1.29
^{1}H NMR (400 MHz), CDCl$_3$
Me
Me
Me
Me
O
B
O
1cs
0.75
2.00
1.98
2.64
5.16
7.45
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

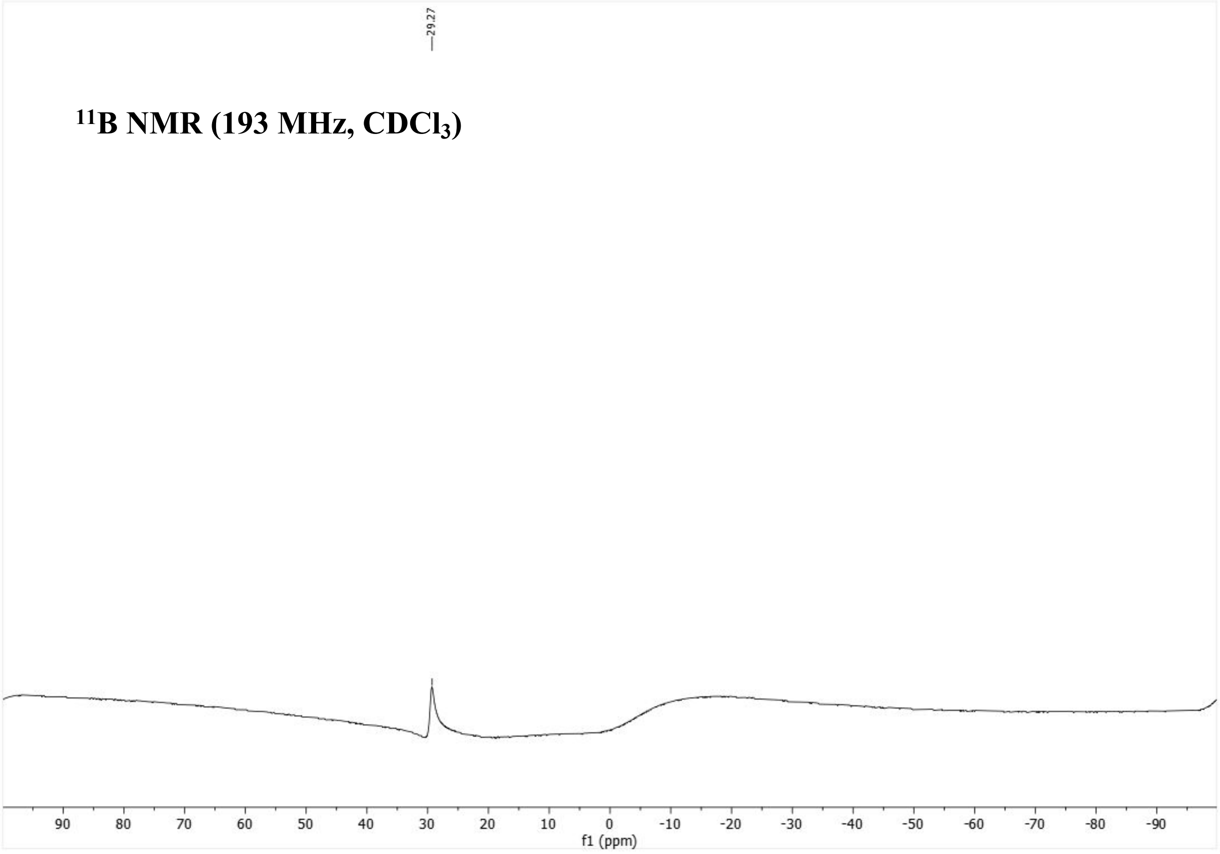

134.04
117.27
70.03
59.05
38.06
29.28
17.55
13.63
^{13}C NMR (151 MHz), CDCl$_3$
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


29.70
¹¹B NMR (193 MHz, CDCl₃)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

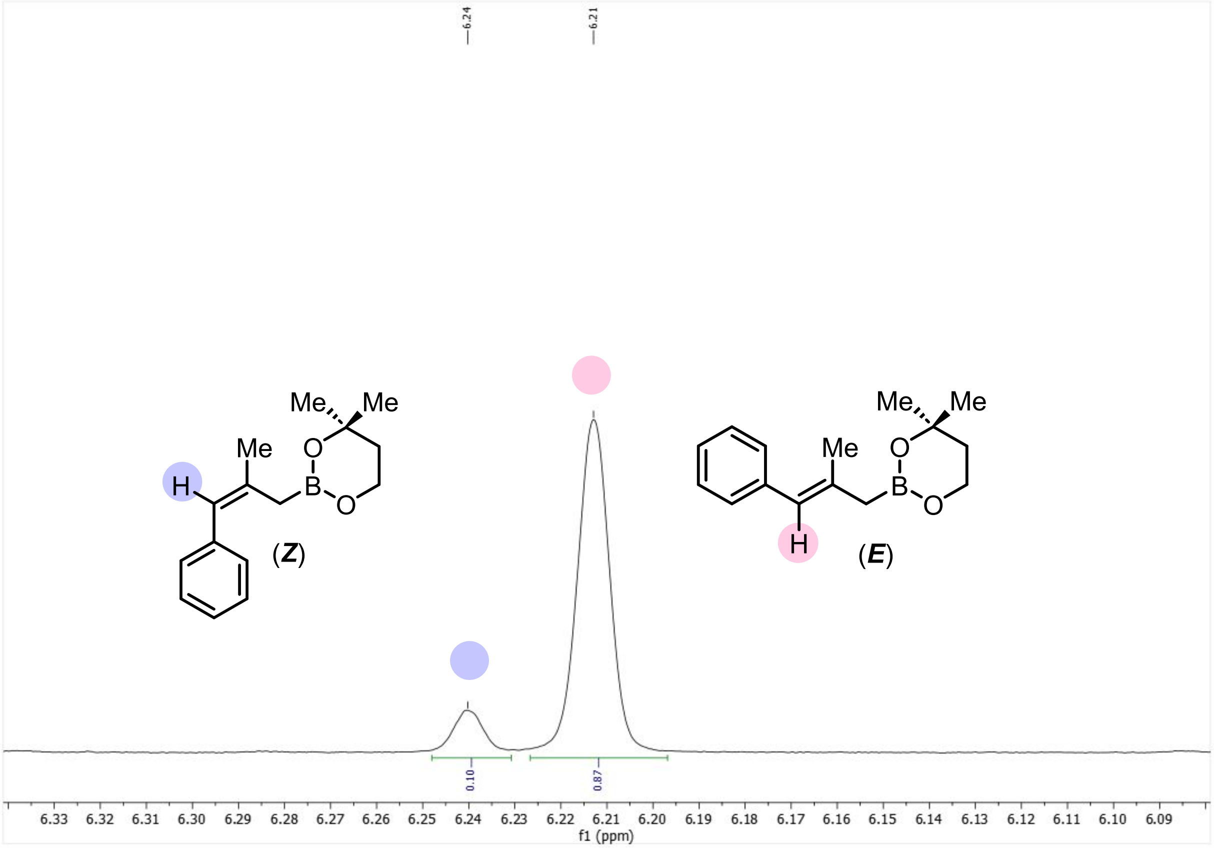

^{1}H NMR (600 MHz), CDCl$_3$

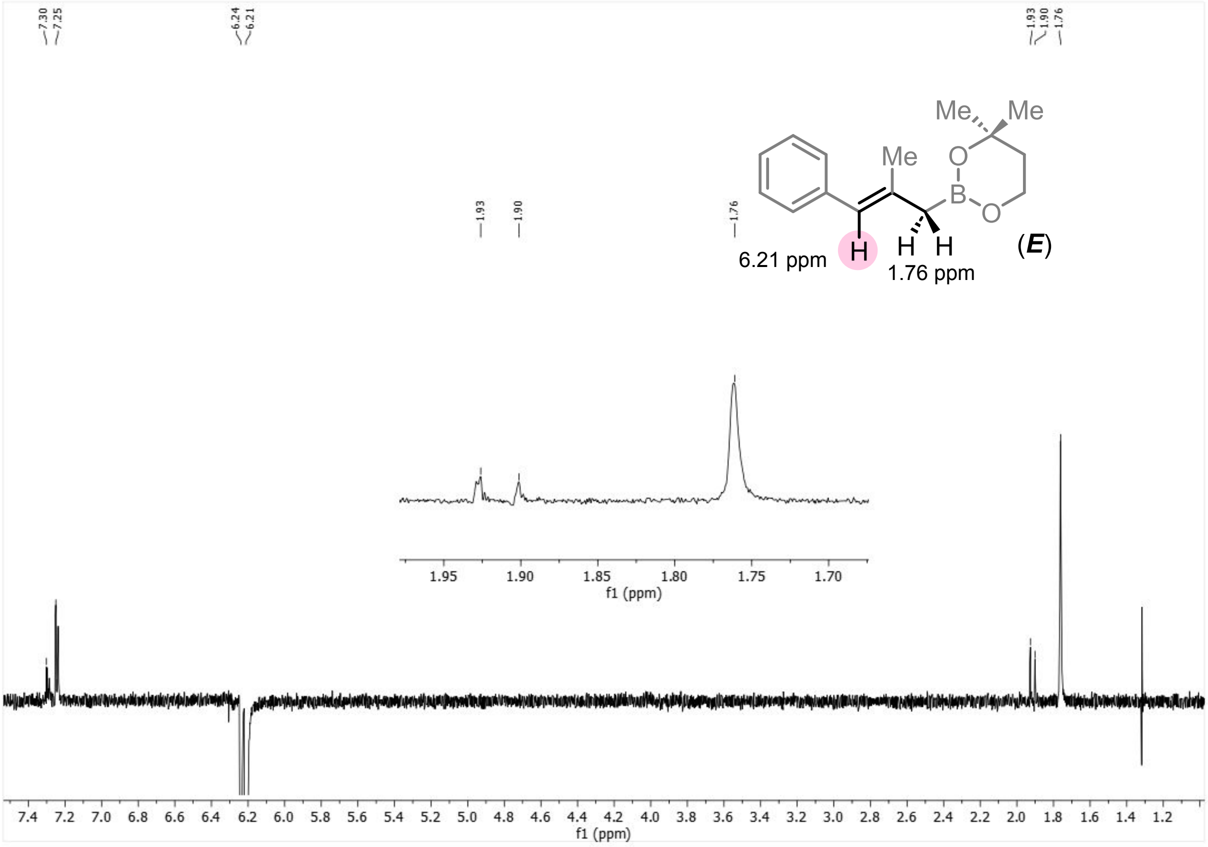
1ct

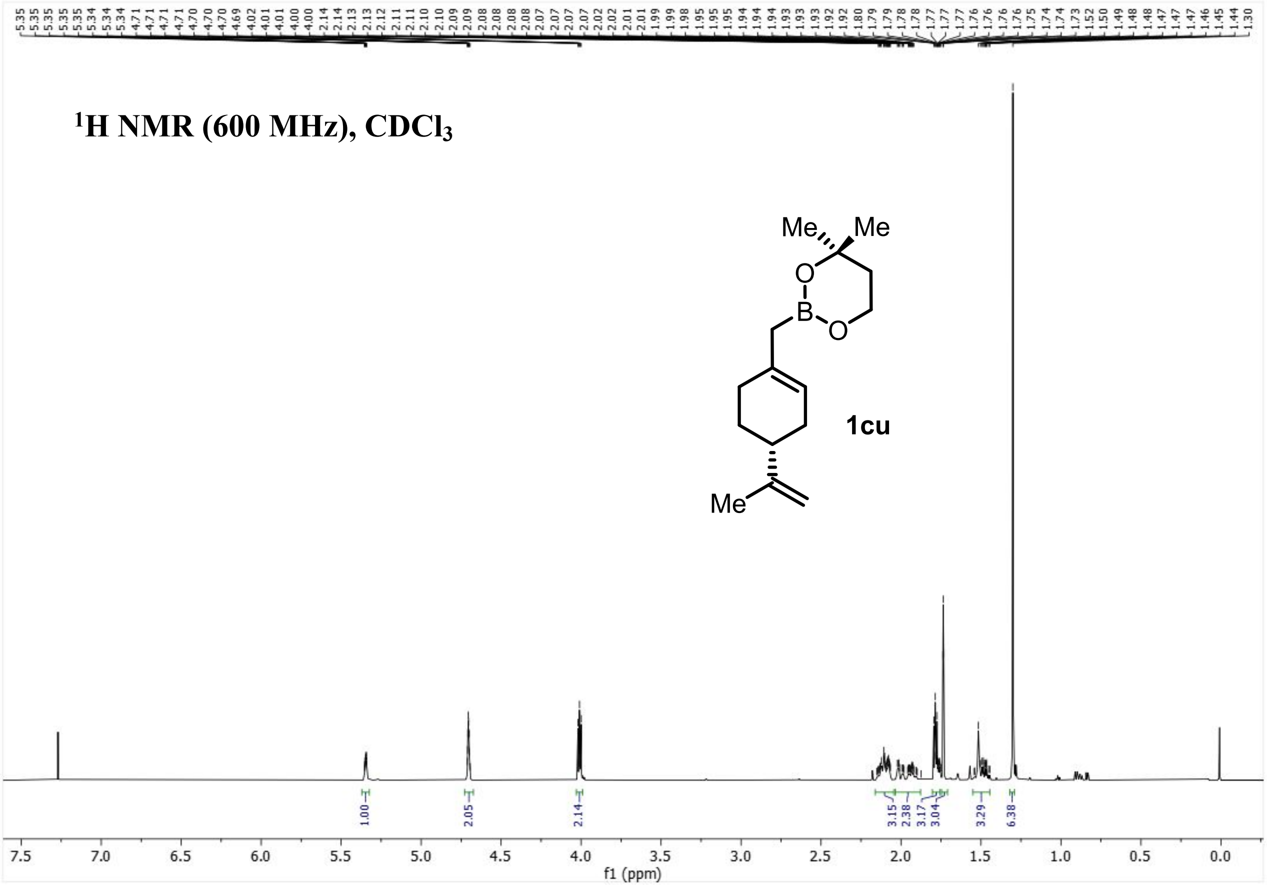

^{13}C NMR (151 MHz), CDCl$_3$

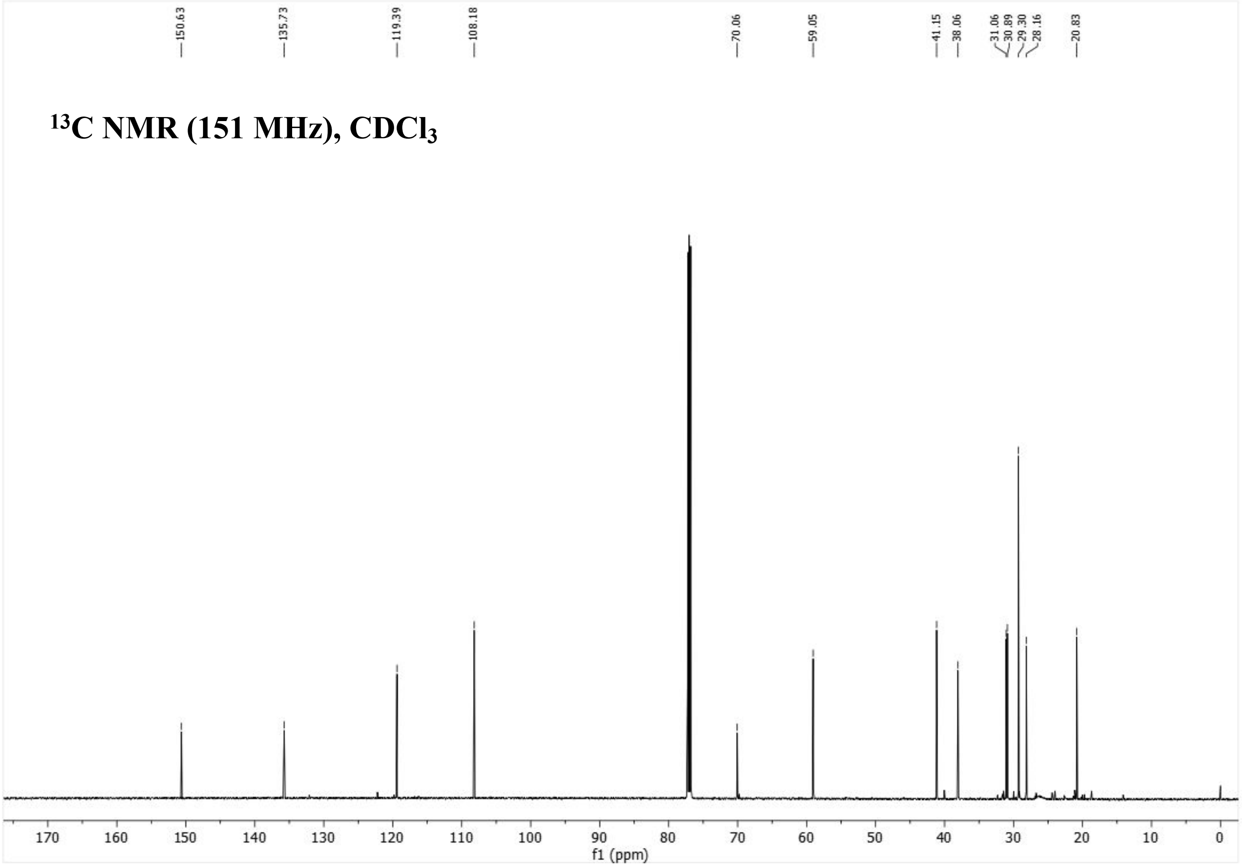

29.27
^{11}B NMR (193 MHz, CDCl$_3$)
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

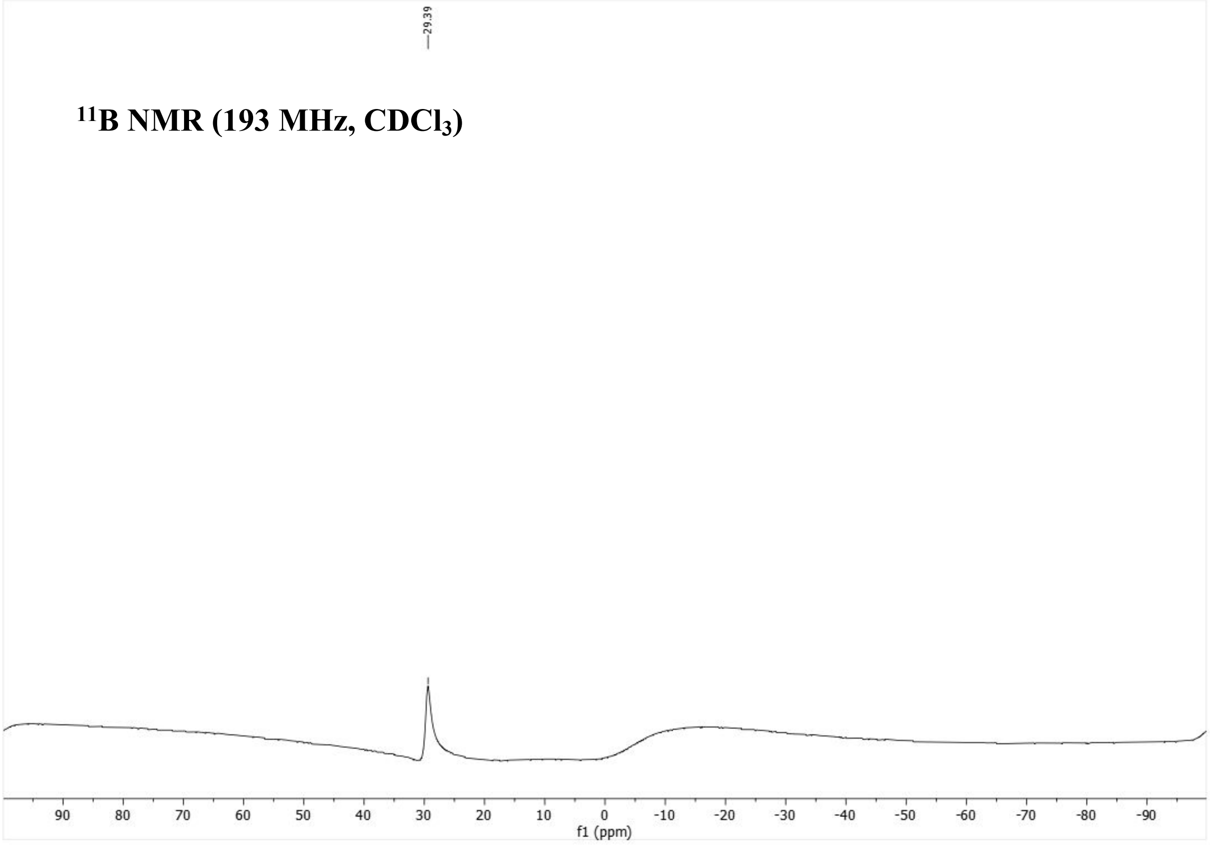
NOE

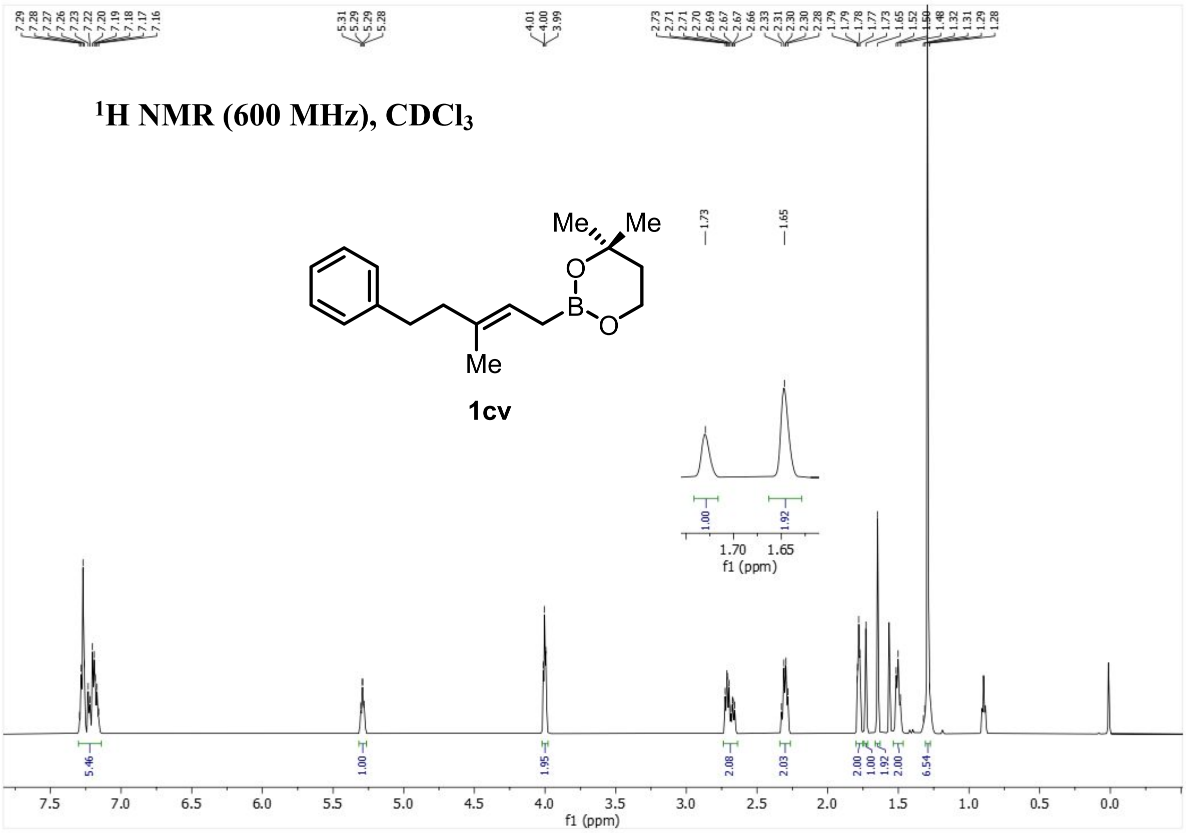

6.24
6.21
Me
Me
Me
O
B
O
H
(Z)
Me
Me
Me
O
B
O
H
(E)
0.10
0.87
6.33 6.32 6.31 6.30 6.29 6.28 6.27 6.26 6.25 6.24 6.23 6.22 6.21 6.20 6.19 6.18 6.17 6.16 6.15 6.14 6.13 6.12 6.11 6.10 6.09
f1 (ppm)


7.30
7.25
6.24
6.21
1.93
1.90
1.76
Me
Me
Me
O
B
O
6.21 ppm
H
H
H
1.76 ppm
(E)
1.95
1.90
1.85
1.80
1.75
1.70
f1 (ppm)
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
f1 (ppm)


5.35
5.35
5.35
5.35
5.35
5.34
5.34
5.34
4.71
4.71
4.71
4.71
4.70
4.70
4.70
4.69
4.02
4.01
4.01
4.00
4.00
2.14
2.14
2.13
2.13
2.12
2.11
2.11
2.10
2.10
2.09
2.09
2.08
2.08
2.08
2.08
2.07
2.07
2.07
2.07
2.02
2.02
2.01
2.01
1.99
1.99
1.98
1.95
1.95
1.95
1.94
1.94
1.94
1.93
1.93
1.93
1.92
1.92
1.80
1.79
1.79
1.78
1.78
1.77
1.77
1.77
1.76
1.76
1.76
1.76
1.75
1.74
1.74
1.73
1.52
1.50
1.49
1.48
1.48
1.47
1.47
1.47
1.46
1.45
1.44
1.30
^{1}H NMR (600 MHz), CDCl$_3$
Me
Me
O
B
O
1cu
Me
1.00
2.05
2.14
3.15
2.38
3.17
3.04
3.29
6.38
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
f1 (ppm)

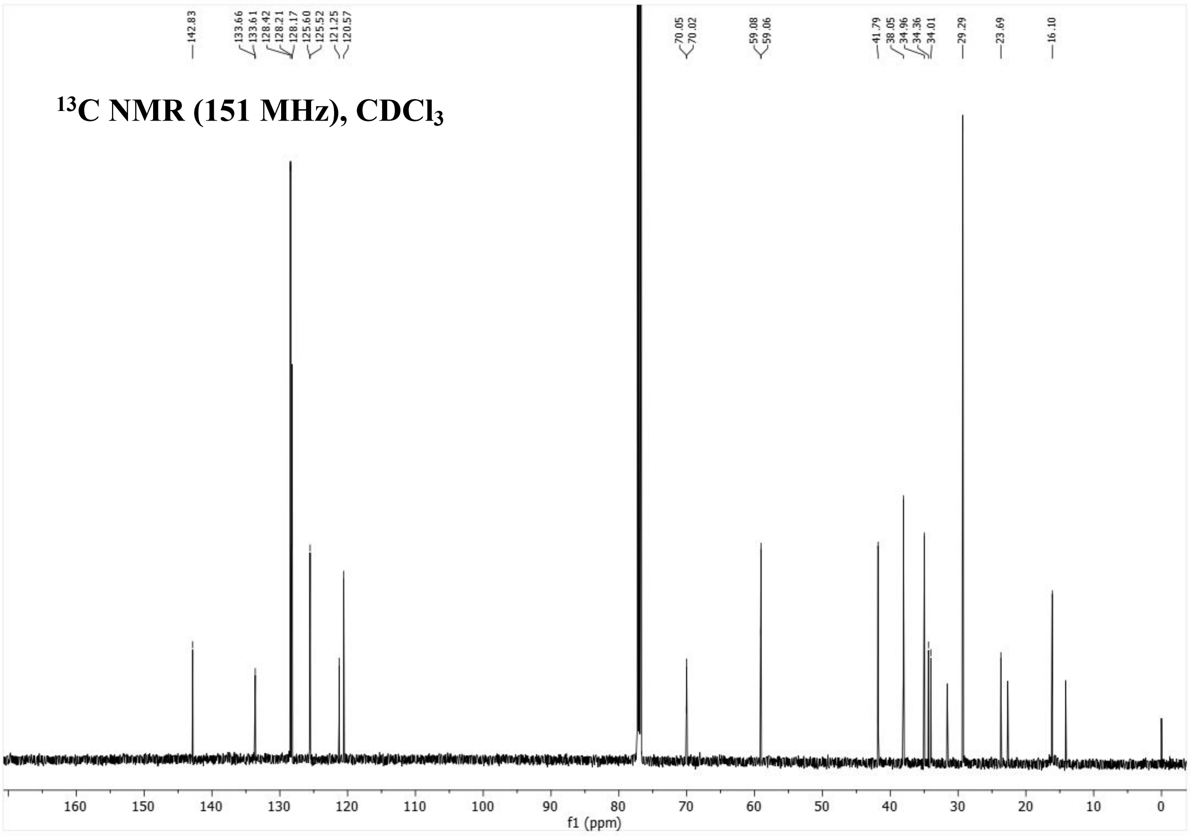

150.63
135.73
119.39
108.18
70.06
59.05
41.15
38.06
31.06
30.89
29.30
28.16
20.83
^{13}C NMR (151 MHz), CDCl$_3$
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


29.39
^{11}B NMR (193 MHz, CDCl$_3$)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

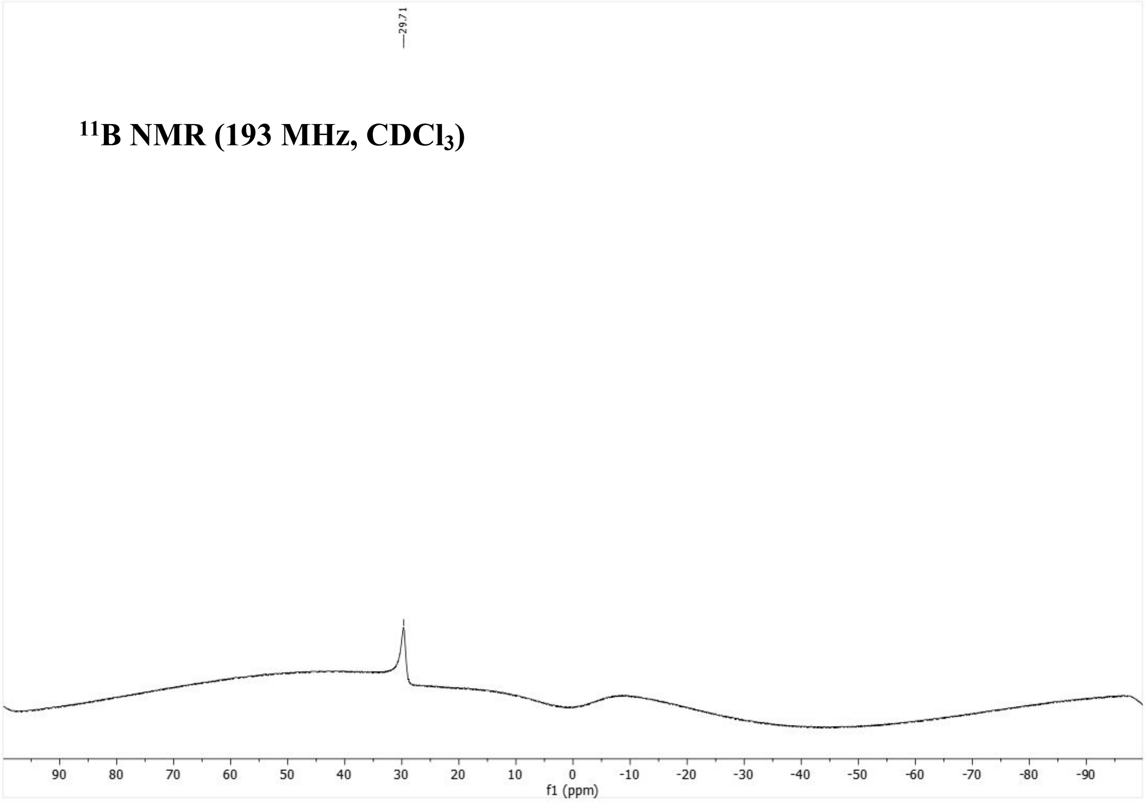


1cv

7.29
7.28
7.27
7.26
7.23
7.22
7.20
7.19
7.18
7.17
7.16
5.31
5.29
5.29
5.28
4.01
4.00
3.99
2.73
2.71
2.71
2.70
2.69
2.67
2.67
2.66
2.33
2.31
2.30
2.30
2.28
1.79
1.79
1.78
1.77
1.73
1.73
1.65
1.52
1.50
1.48
1.32
1.31
1.29
1.28
^{1}H NMR (600 MHz), CDCl$_3$
Me
Me
O
B
O
Me
1.73
1.65
1.00
1.92
1.70
1.65
f1 (ppm)
5.46
1.00
1.95
2.08
2.03
2.00
1.00
1.92
2.00
6.54
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
f1 (ppm)

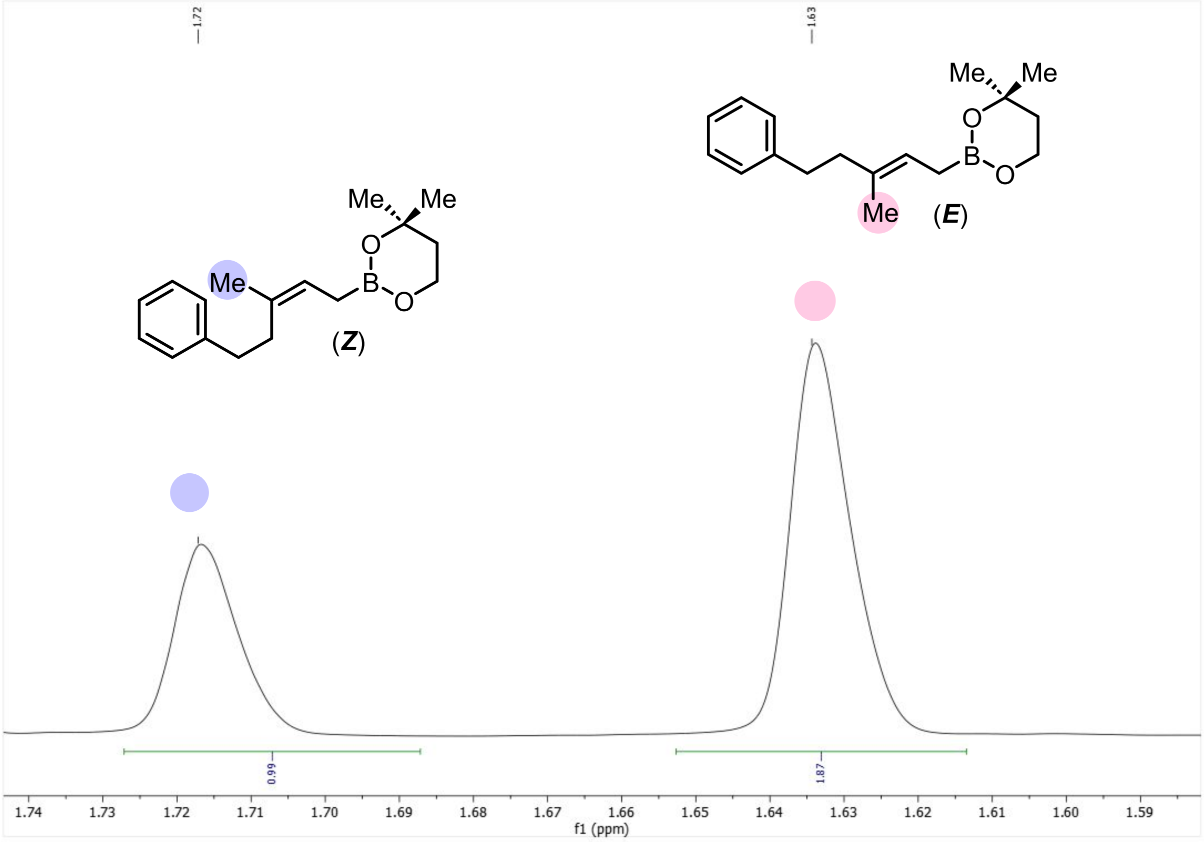


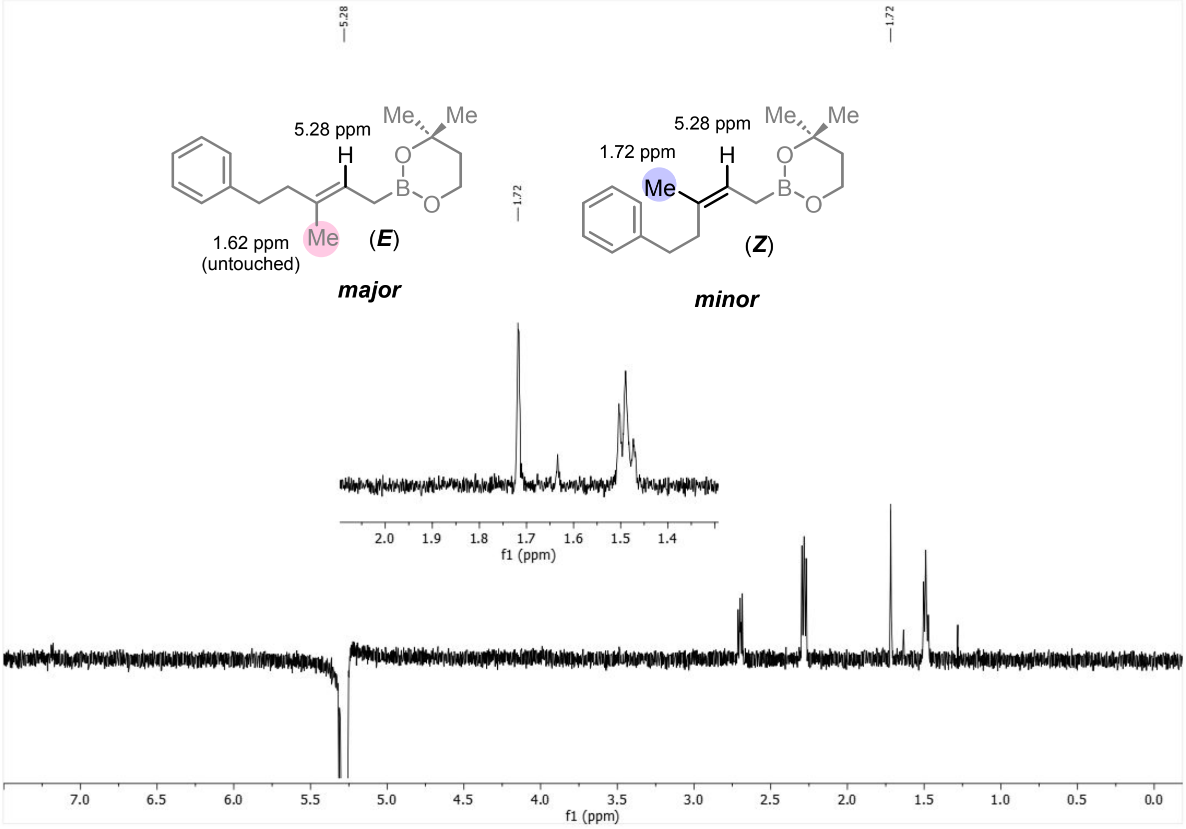
142.83
133.66
133.61
128.42
128.21
128.17
125.60
125.52
121.25
120.57
70.05
70.02
59.08
59.06
41.79
38.05
34.96
34.36
34.01
29.29
23.69
16.10
^{13}C NMR (151 MHz), CDCl$_3$
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



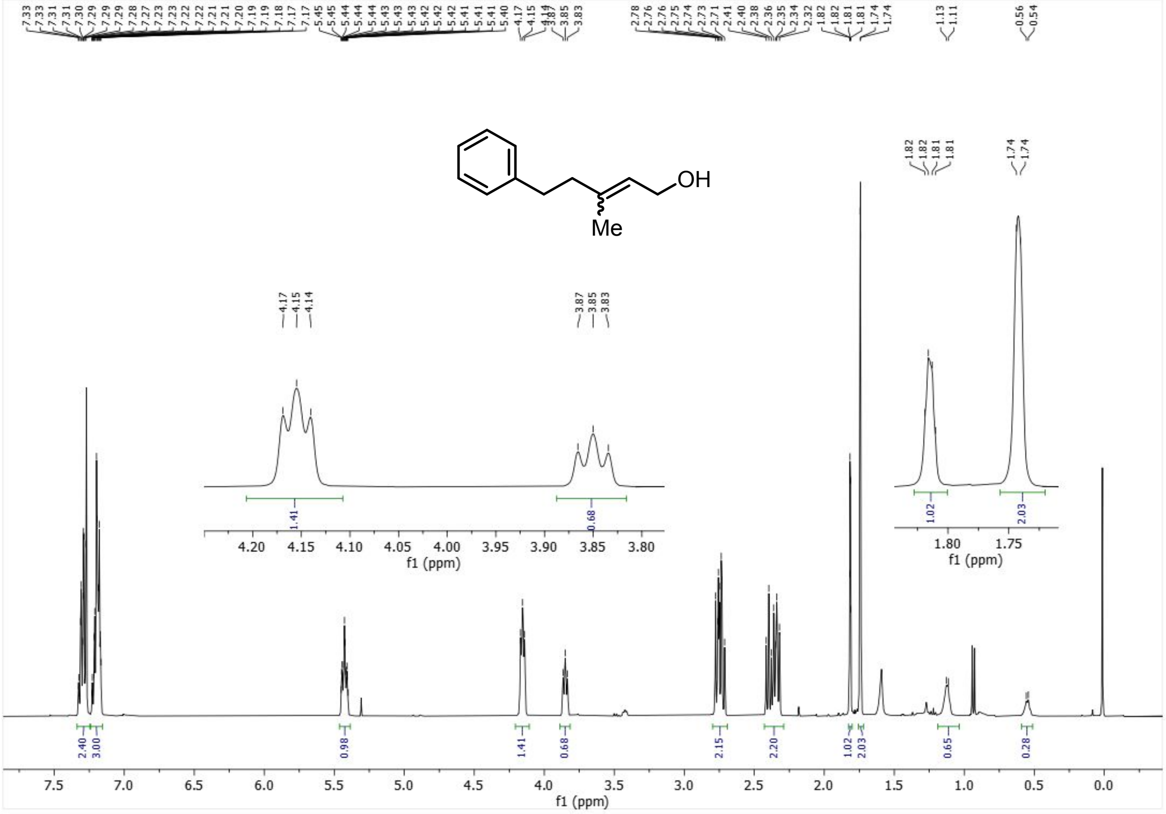
^{11}B NMR (193 MHz, $CDCl_3$)

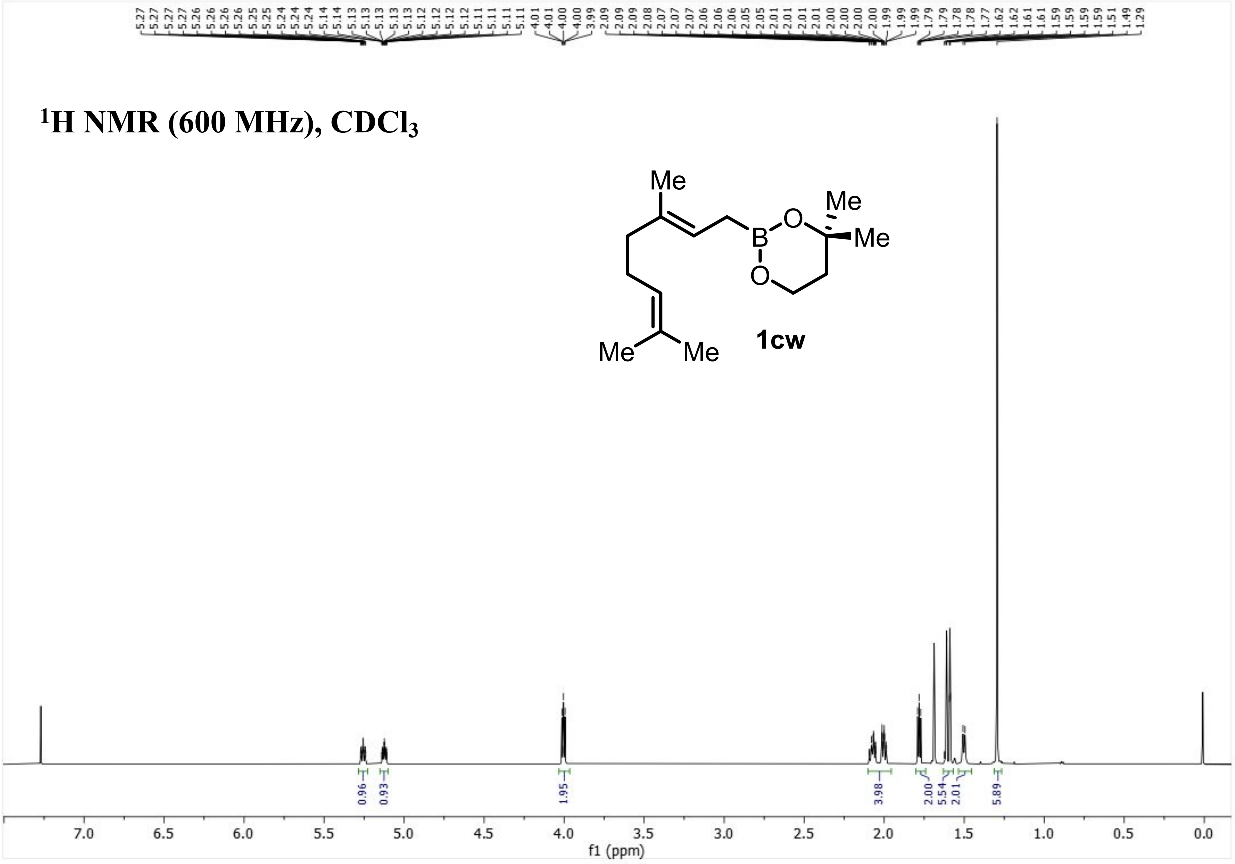
NOE



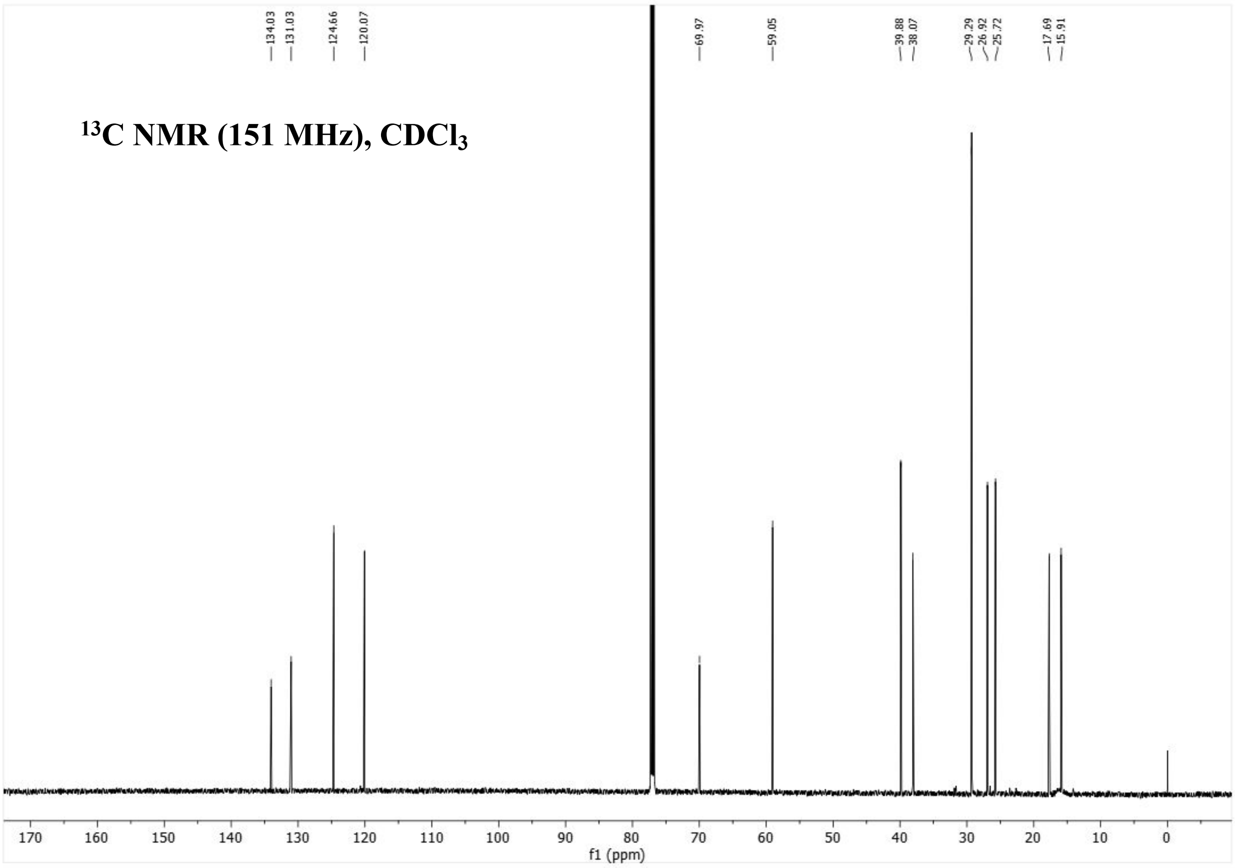


Similar ratio of the starting alcohol (1 : 2.07)

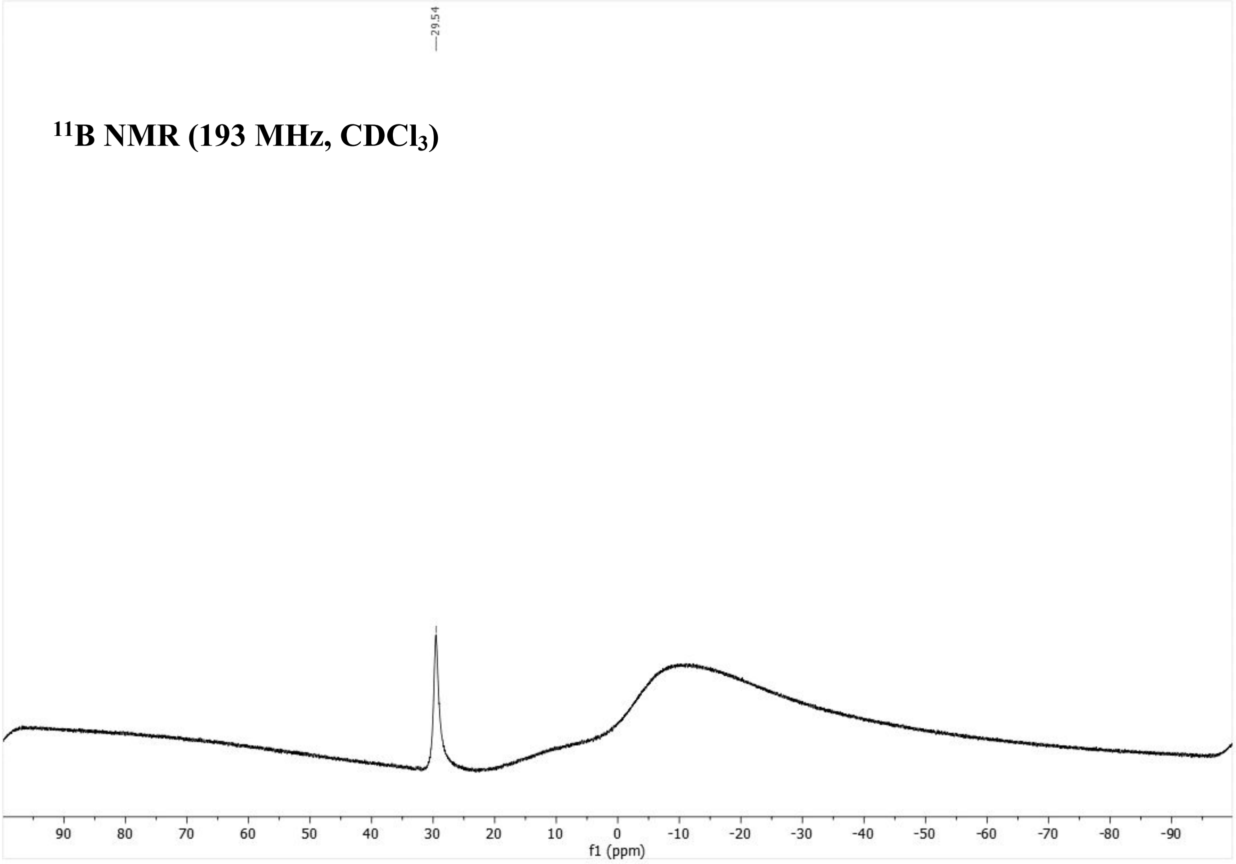




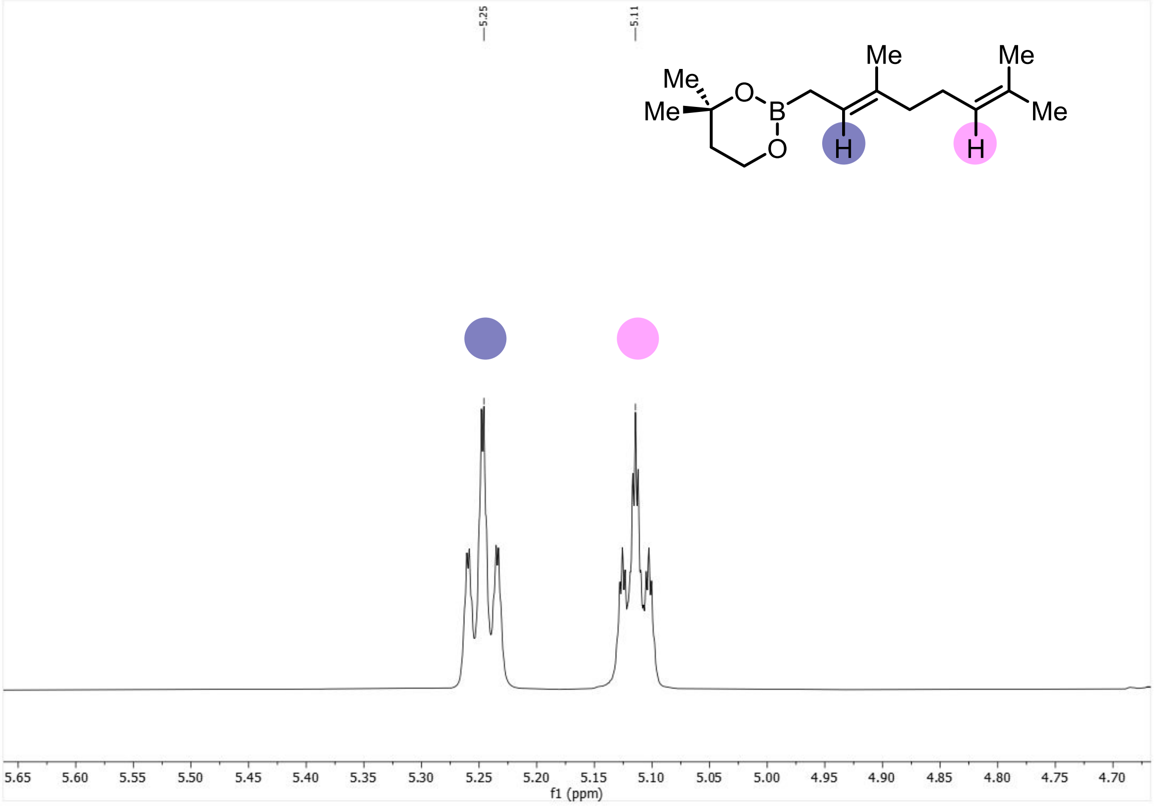
^{1}H NMR (600 MHz), CDCl$_3$

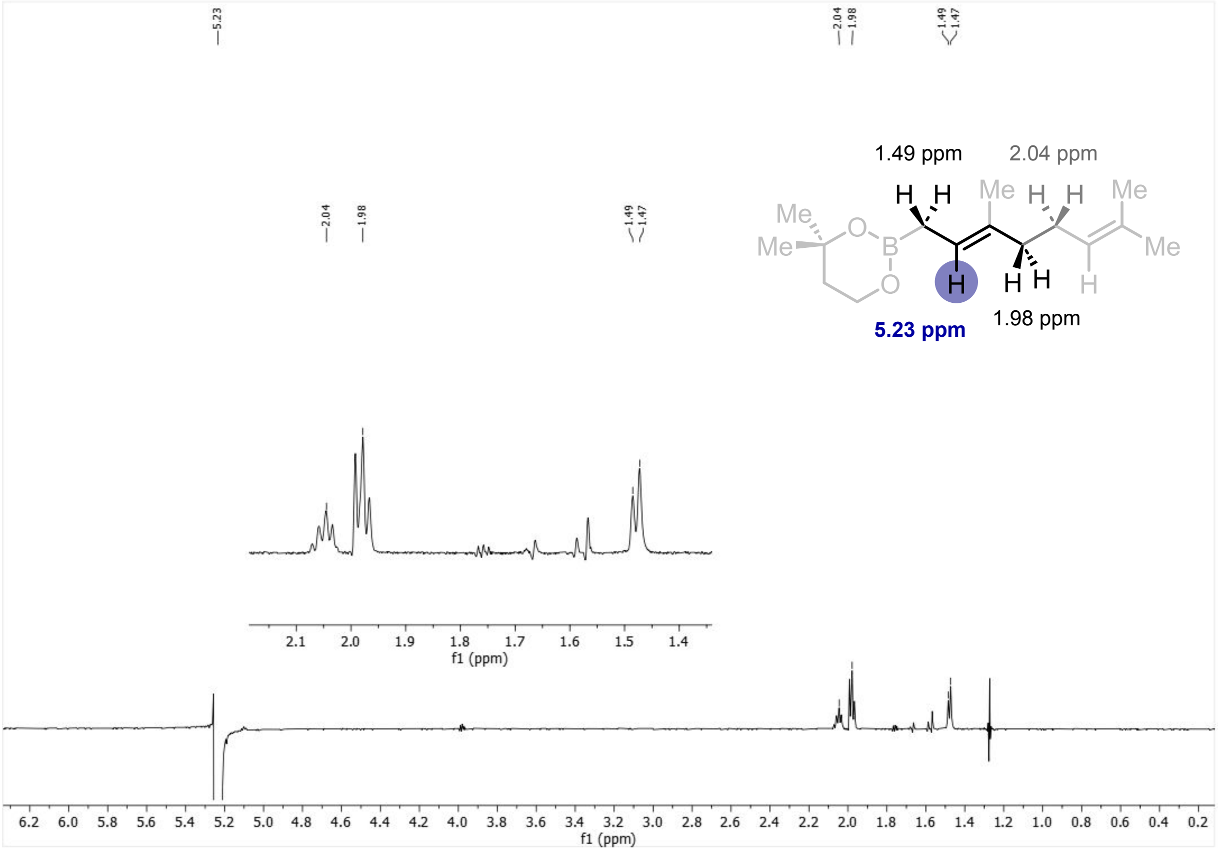


^{13}C NMR (151 MHz), CDCl$_3$

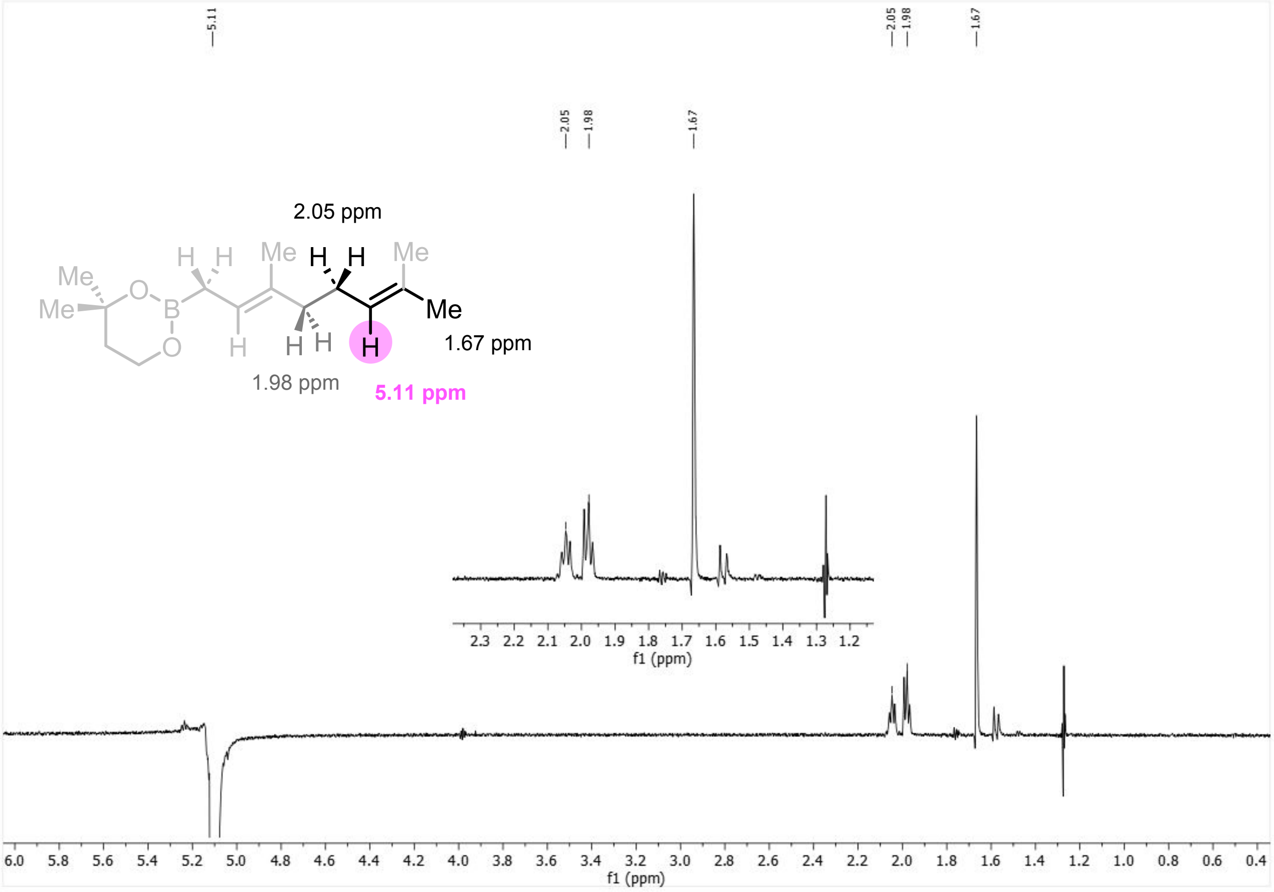

^{11}B NMR (193 MHz, $CDCl_3$)

NOE

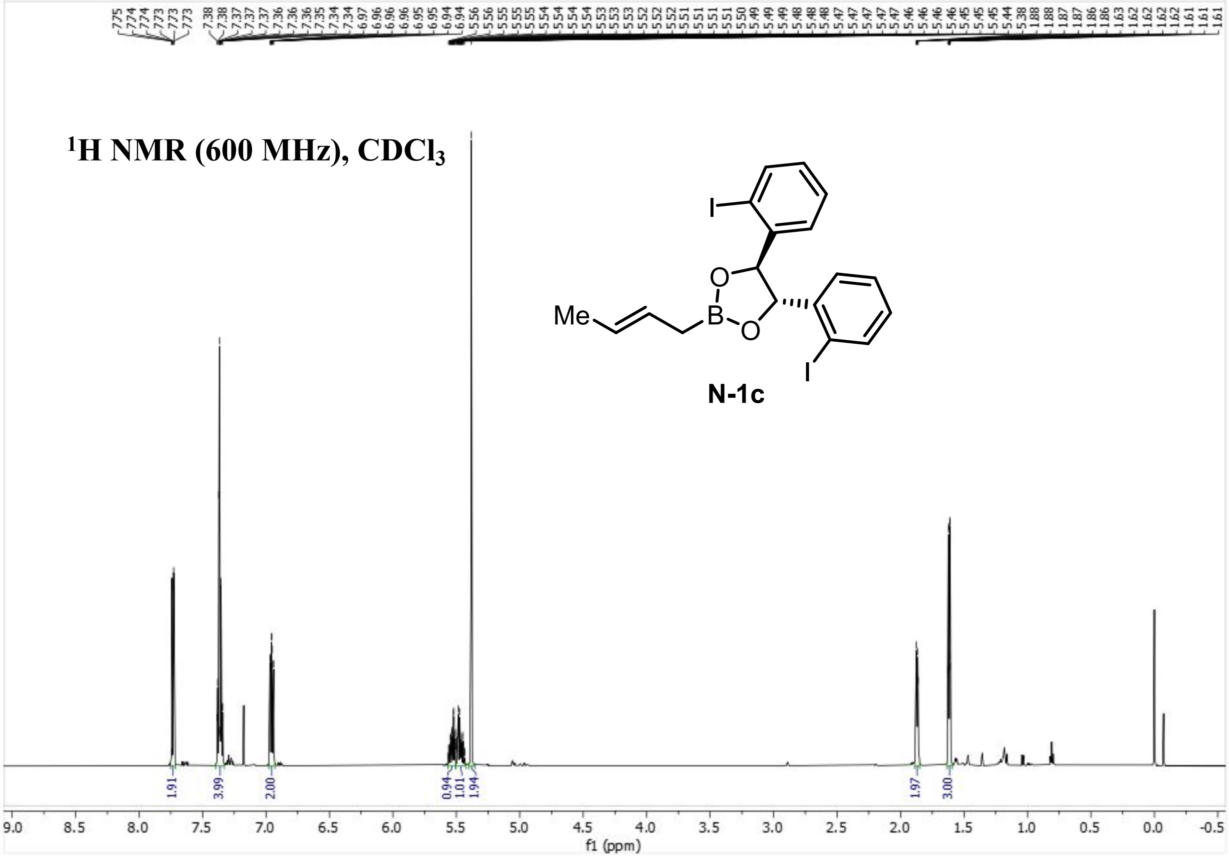


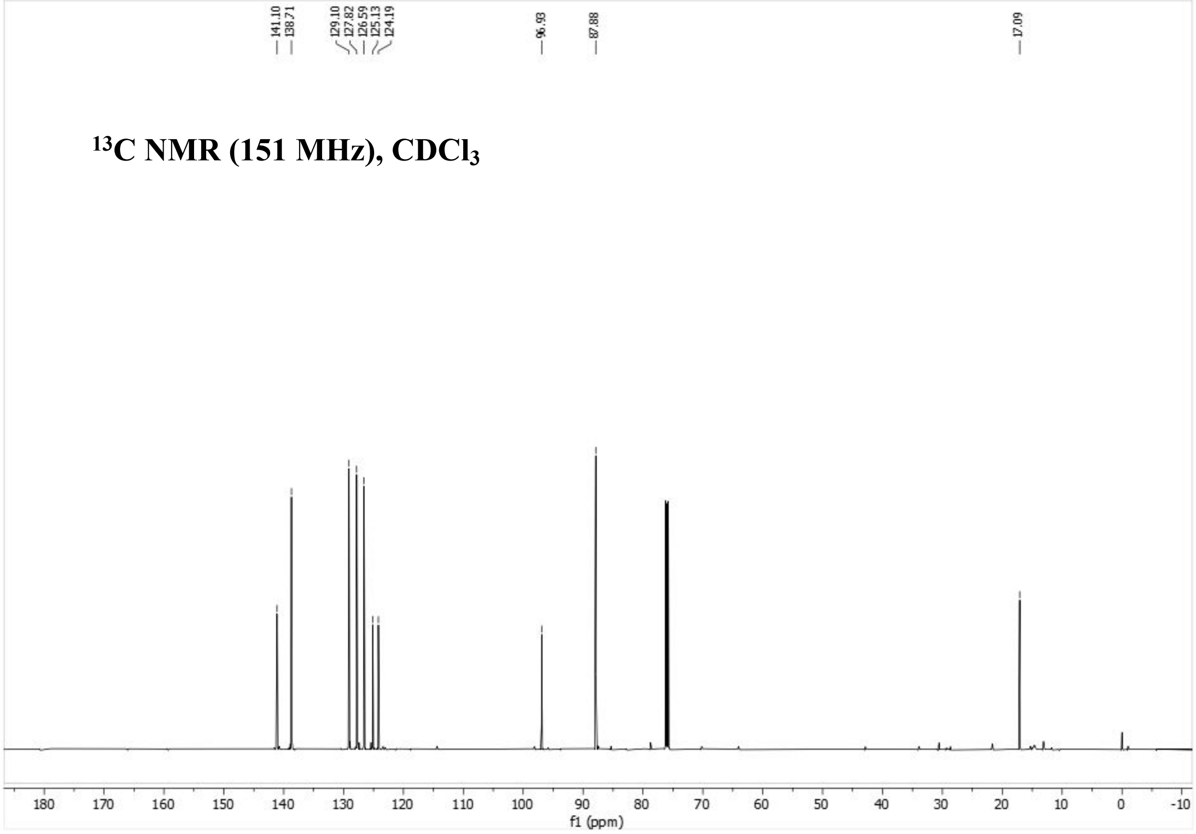


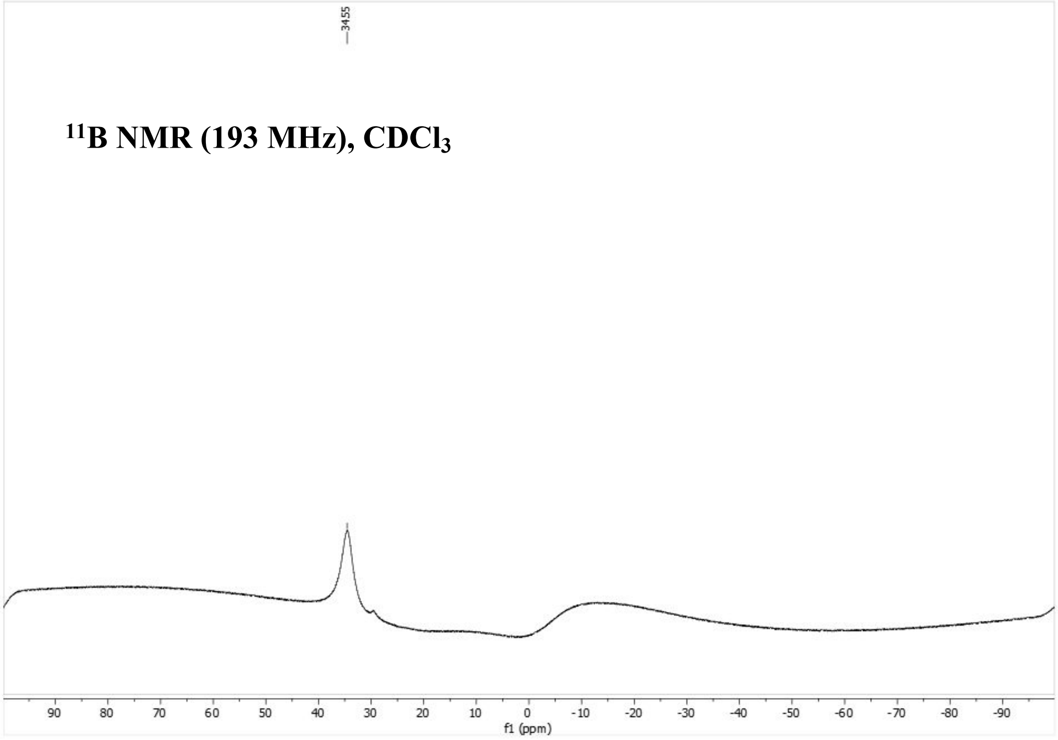
5.23
2.04
1.98
1.49
1.47
1.49 ppm
2.04 ppm
5.23 ppm
1.98 ppm
Me
O
B
H
2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4
f1 (ppm)
6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2
f1 (ppm)



5.11
2.05
1.98
1.67
2.05 ppm
1.67 ppm
1.98 ppm
5.11 ppm
Me
O
B
H
2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2
f1 (ppm)
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4
f1 (ppm)


7.75
7.74
7.74
7.73
7.73
7.73
7.38
7.38
7.37
7.37
7.37
7.36
7.36
7.36
7.35
7.34
7.34
6.97
6.96
6.96
6.96
6.95
6.95
6.94
6.94
5.56
5.56
5.55
5.55
5.55
5.54
5.54
5.54
5.54
5.53
5.53
5.53
5.52
5.52
5.52
5.51
5.51
5.51
5.50
5.49
5.49
5.49
5.48
5.48
5.47
5.47
5.47
5.47
5.47
5.46
5.46
5.46
5.45
5.45
5.45
5.44
5.38
1.88
1.88
1.87
1.87
1.86
1.86
1.63
1.62
1.62
1.62
1.61
1.61
1.61
¹H NMR (600 MHz), CDCl₃
I
O
Me
B
O
I
N-1c
1.91
3.99
2.00
0.94
1.01
1.94
1.97
3.00
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)

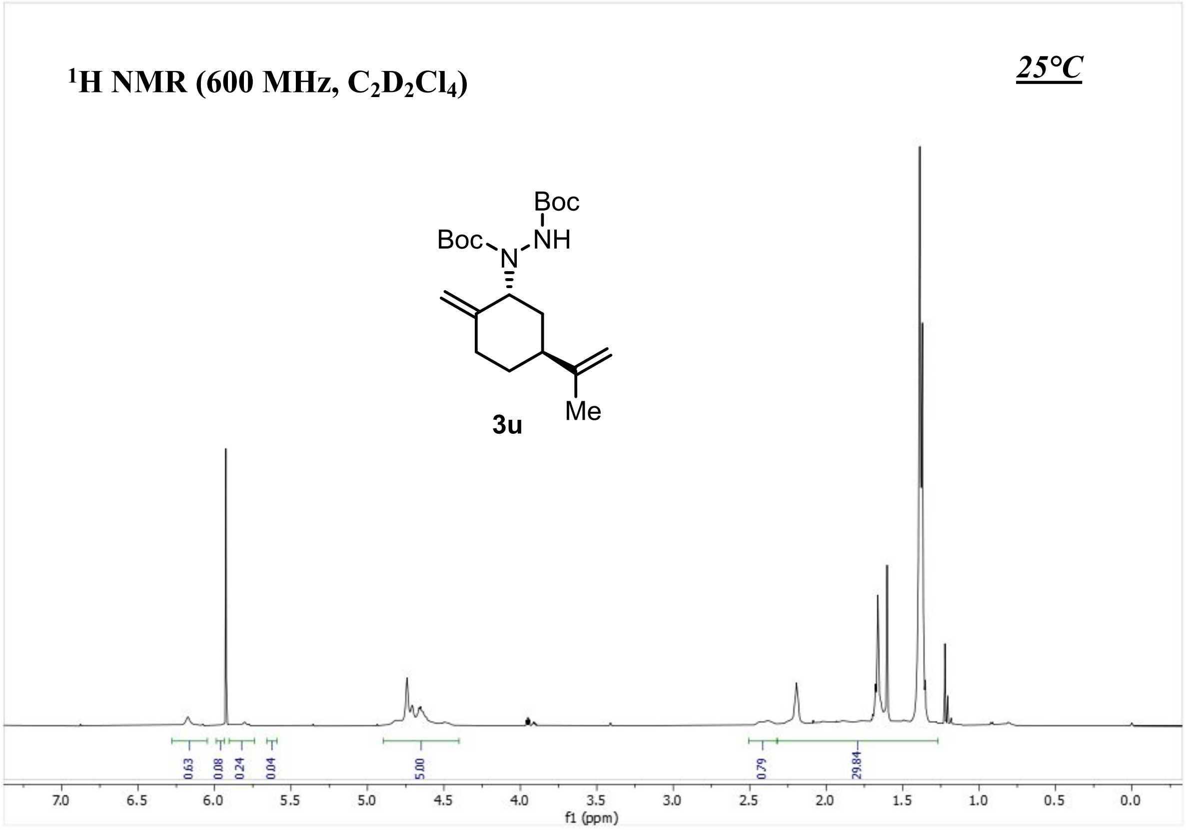

141.10
138.71
129.10
127.82
126.59
125.13
124.19
96.93
87.88
17.09
¹³C NMR (151 MHz), CDCl₃
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

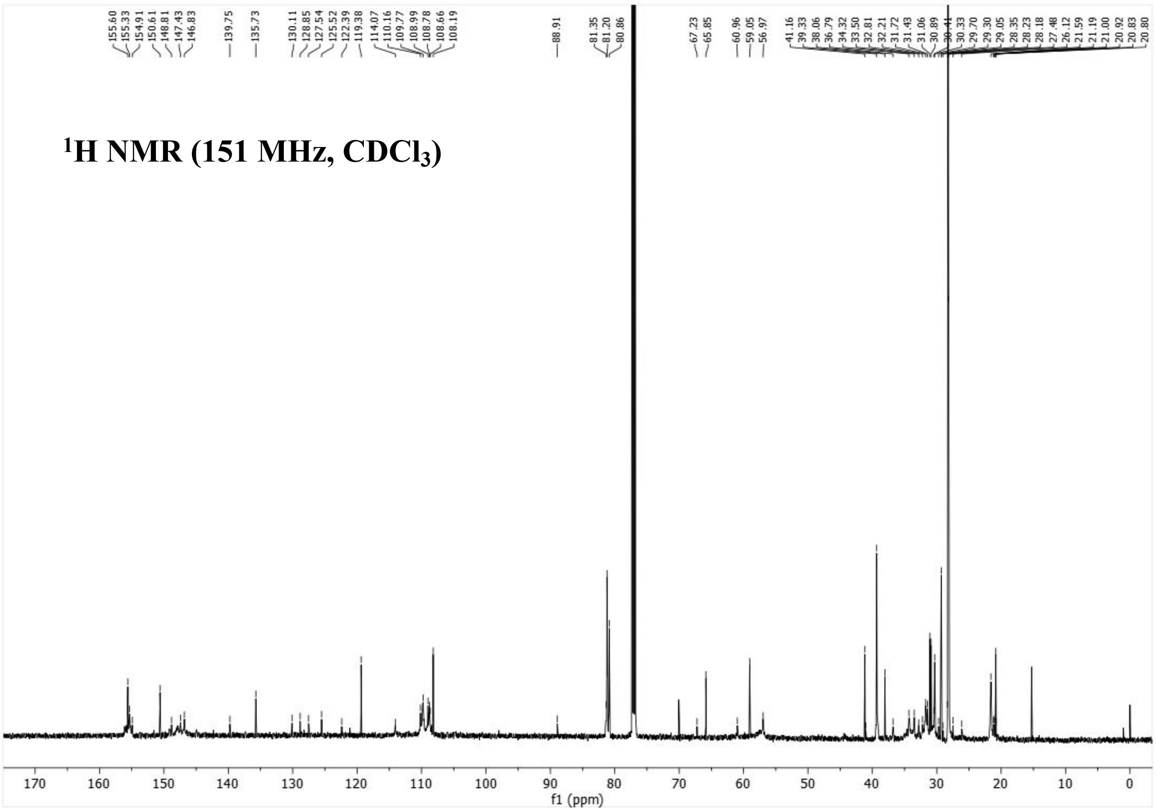


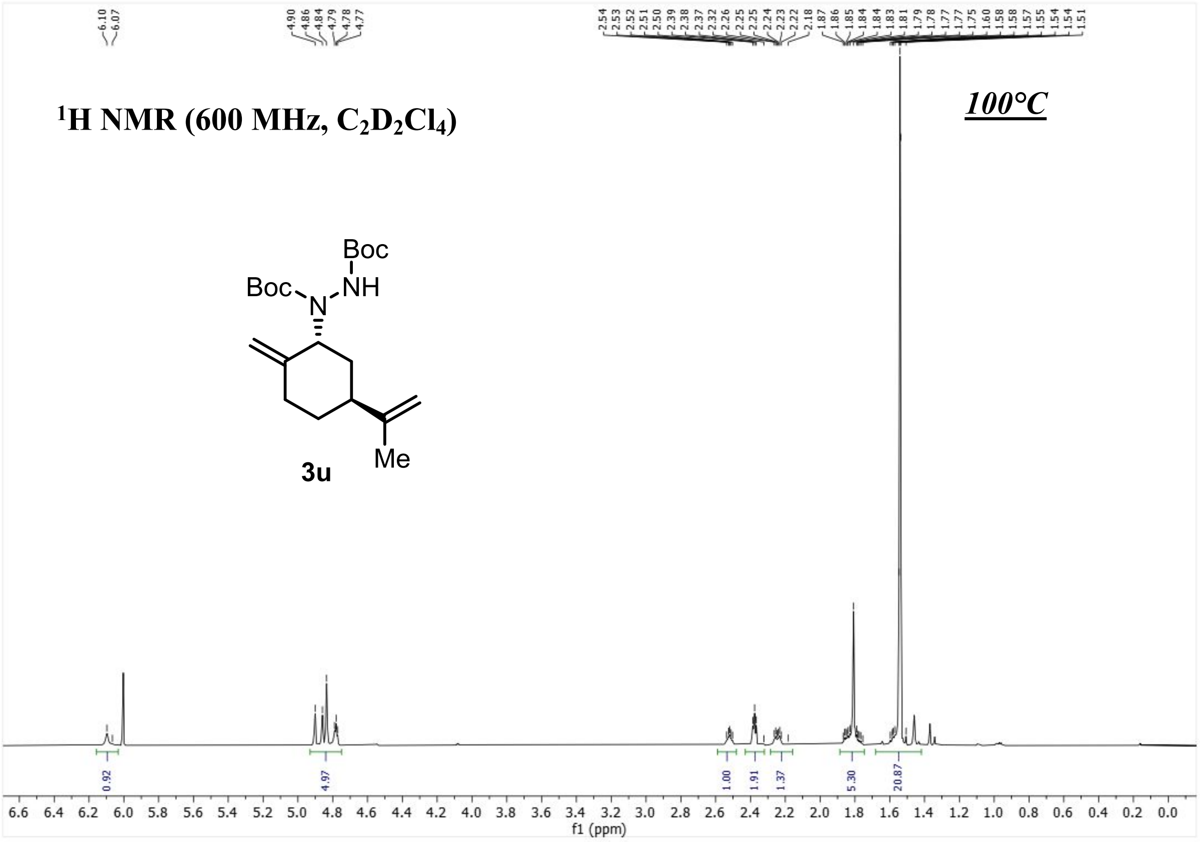
^{11}B NMR (193 MHz), CDCl$_3$

NMRs TRACES OF ALLYLIC HYDRAZIDES

All the ^{1}H NMR spectra display very broad signals due to the rotamers of the Boc groups. To further prove this well-known feature, one aliphatic and one aromatic compound were selected to be analysed by NMR at 23°C and at higher temperature. As you can see, at higher temperature the peaks are sharper and more resolved. A similar trend is also observed by ^{13}C NMR where the signals rarely correspond to the number of the carbons of the compound, appearing broad and not intense although the high concentration of the sample.

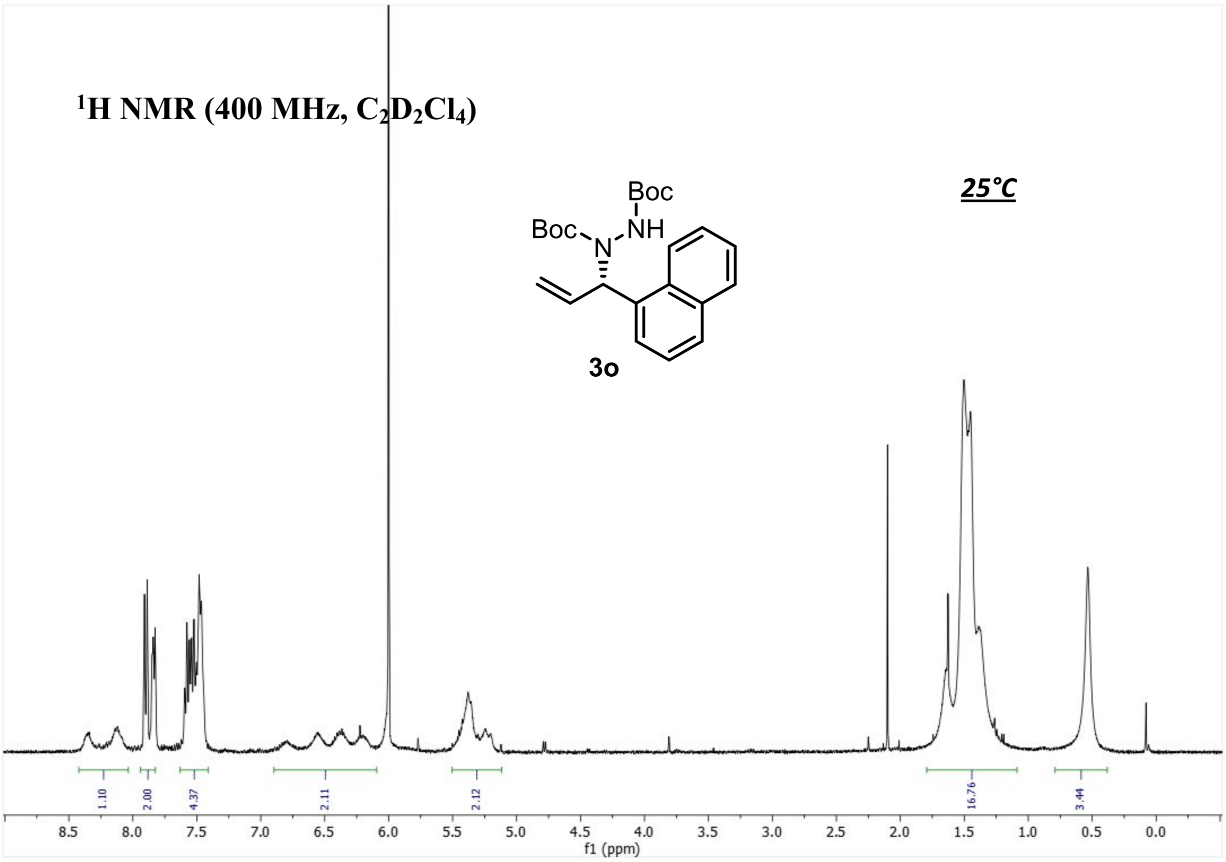


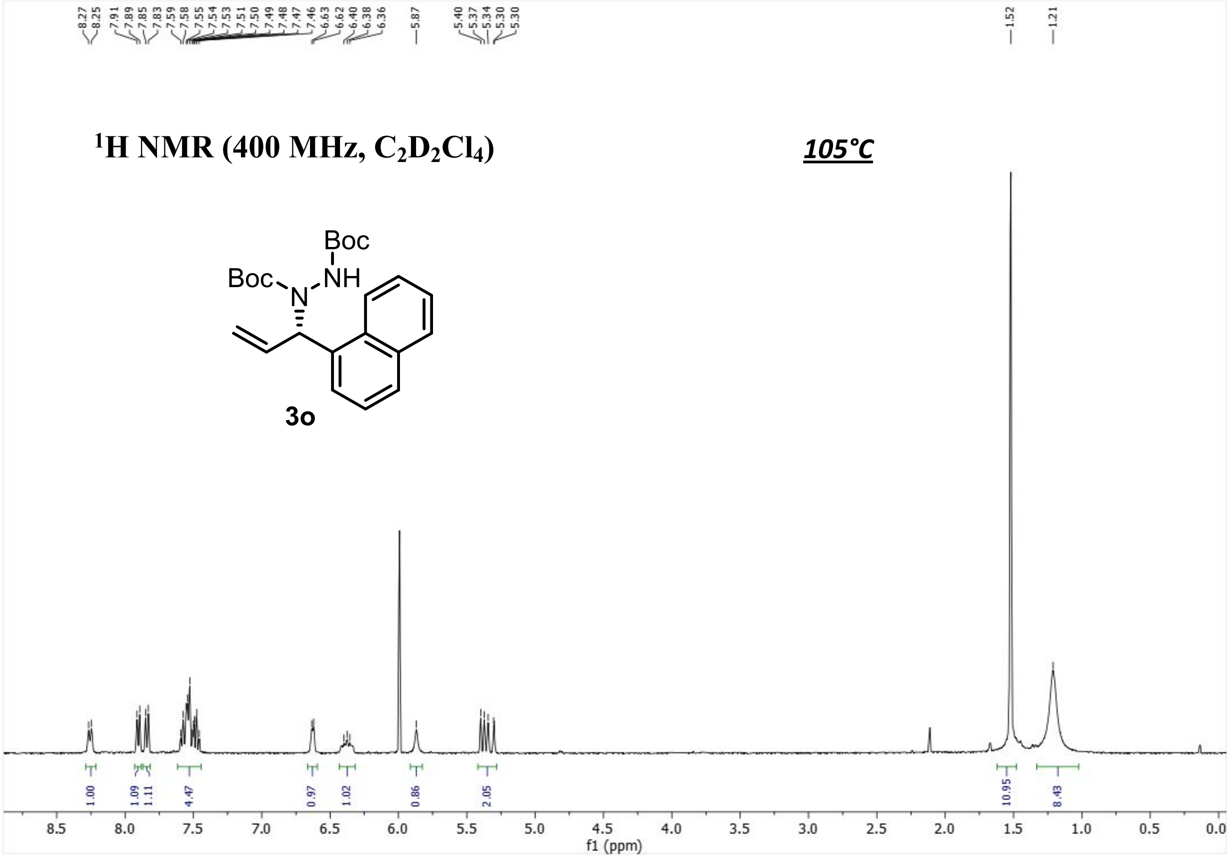

^{1}H NMR (151 MHz, $CDCl_3$)


^{1}H NMR (600 MHz, $C_2D_2Cl_4$)

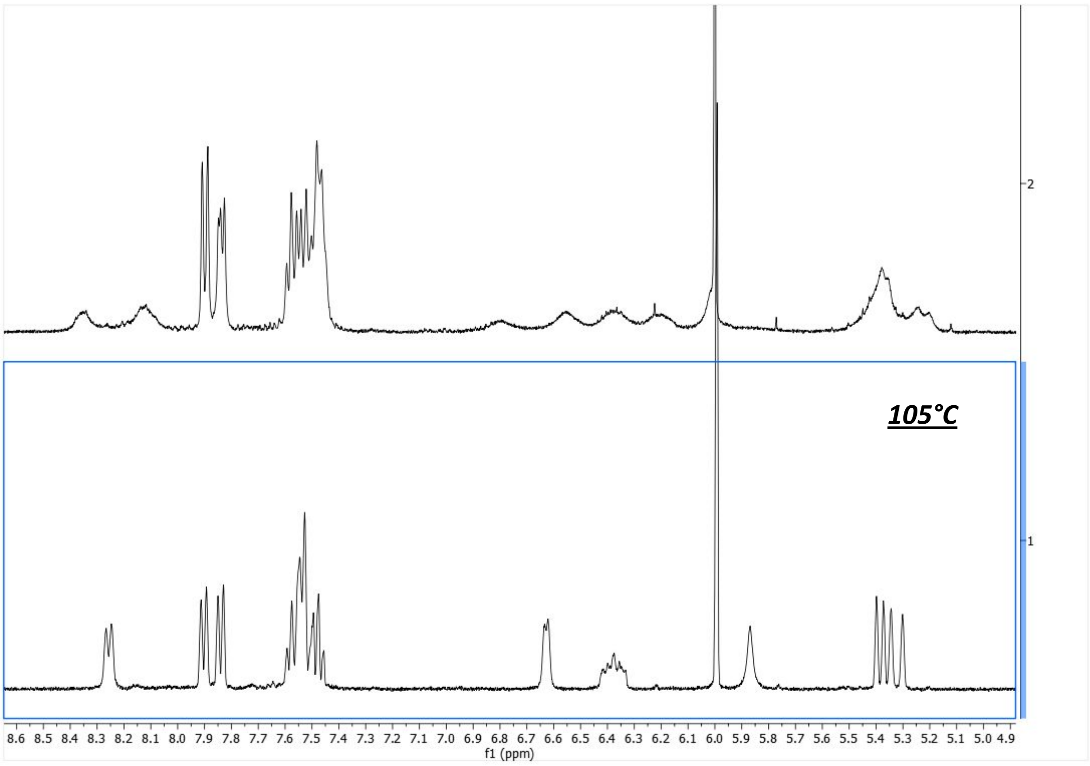
100°C

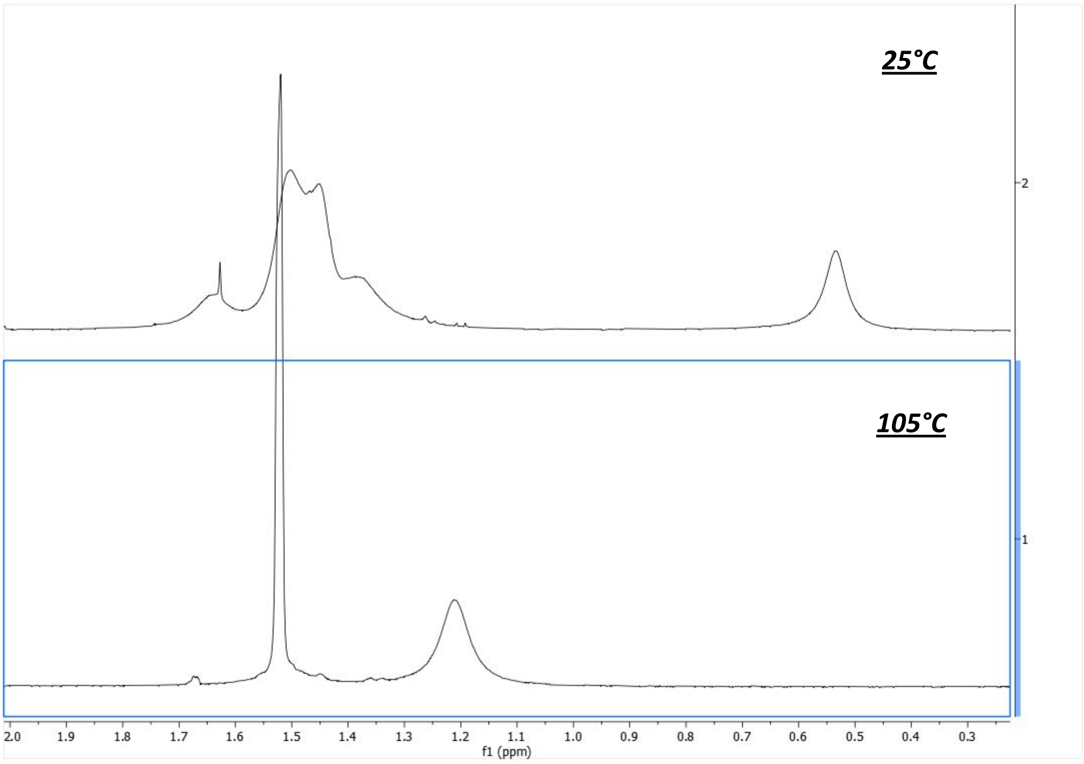
3u

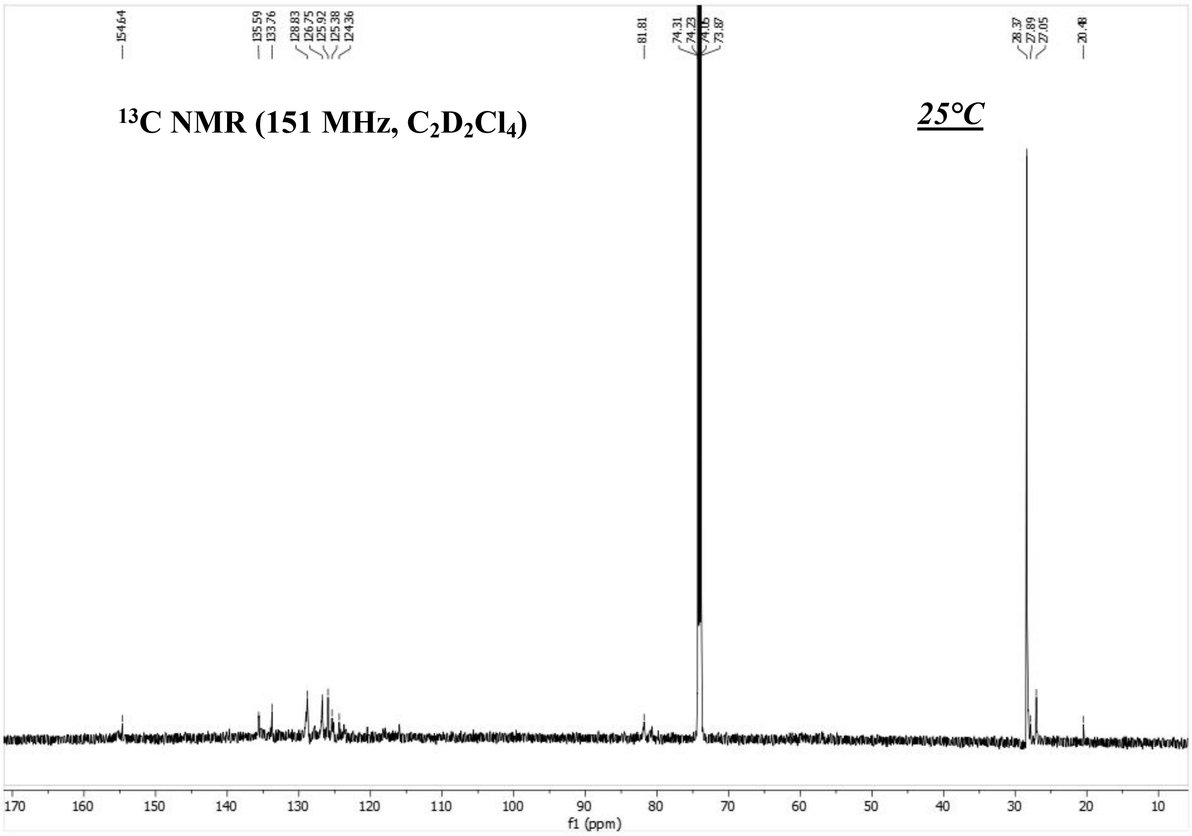

^{1}H NMR (400 MHz, $C_2D_2Cl_4$)
25°C
Boc
Boc
NH
N
3o
1.10
2.00
4.37
2.11
2.12
16.76
3.44
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


8.27
8.25
7.91
7.89
7.85
7.83
7.59
7.58
7.55
7.54
7.53
7.51
7.50
7.49
7.48
7.47
7.46
6.63
6.62
6.40
6.38
6.36
5.87
5.40
5.37
5.34
5.30
5.30
1.52
1.21
^{1}H NMR (400 MHz, $C_2D_2Cl_4$)
105°C
Boc
Boc
NH
N
3o
1.00
1.09
1.11
4.47
0.97
1.02
0.86
2.05
10.95
8.43
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
f1 (ppm)

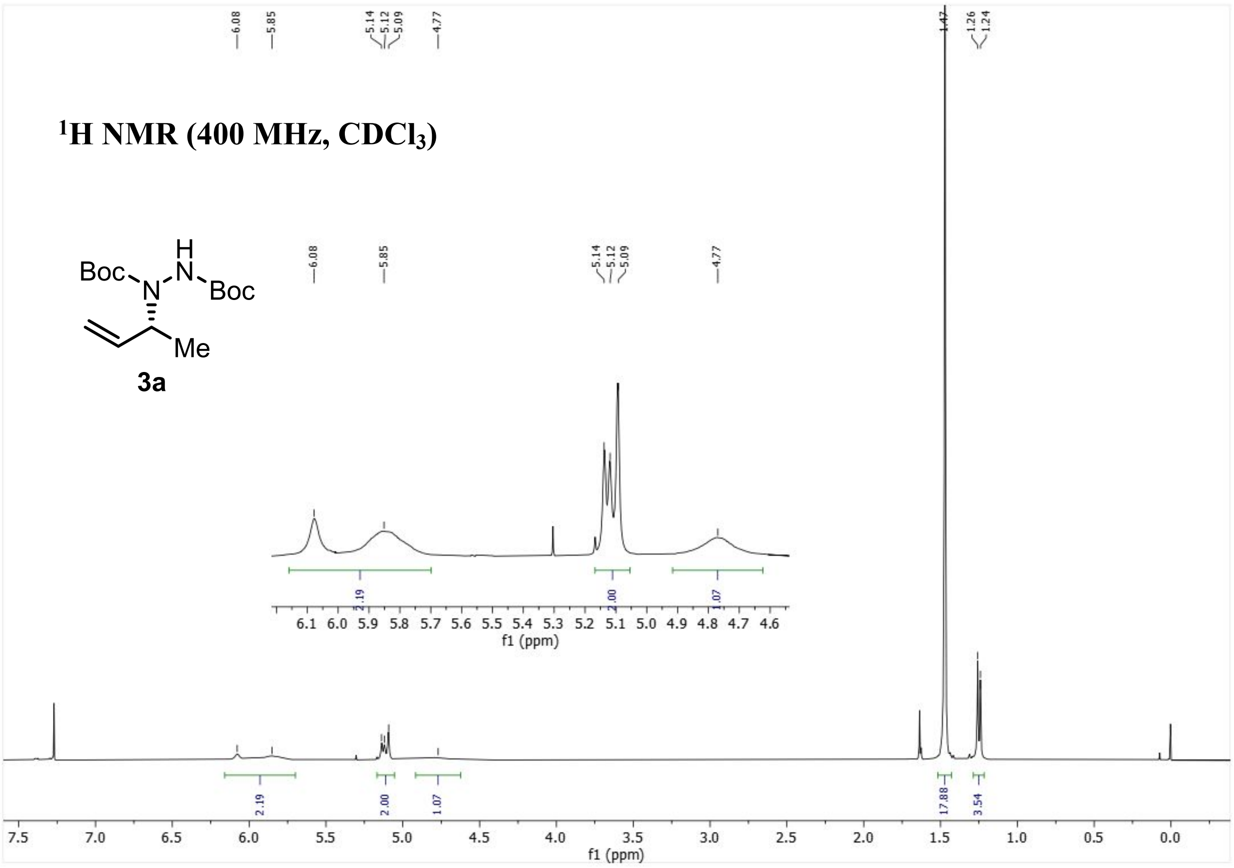
Comparison of NMRs





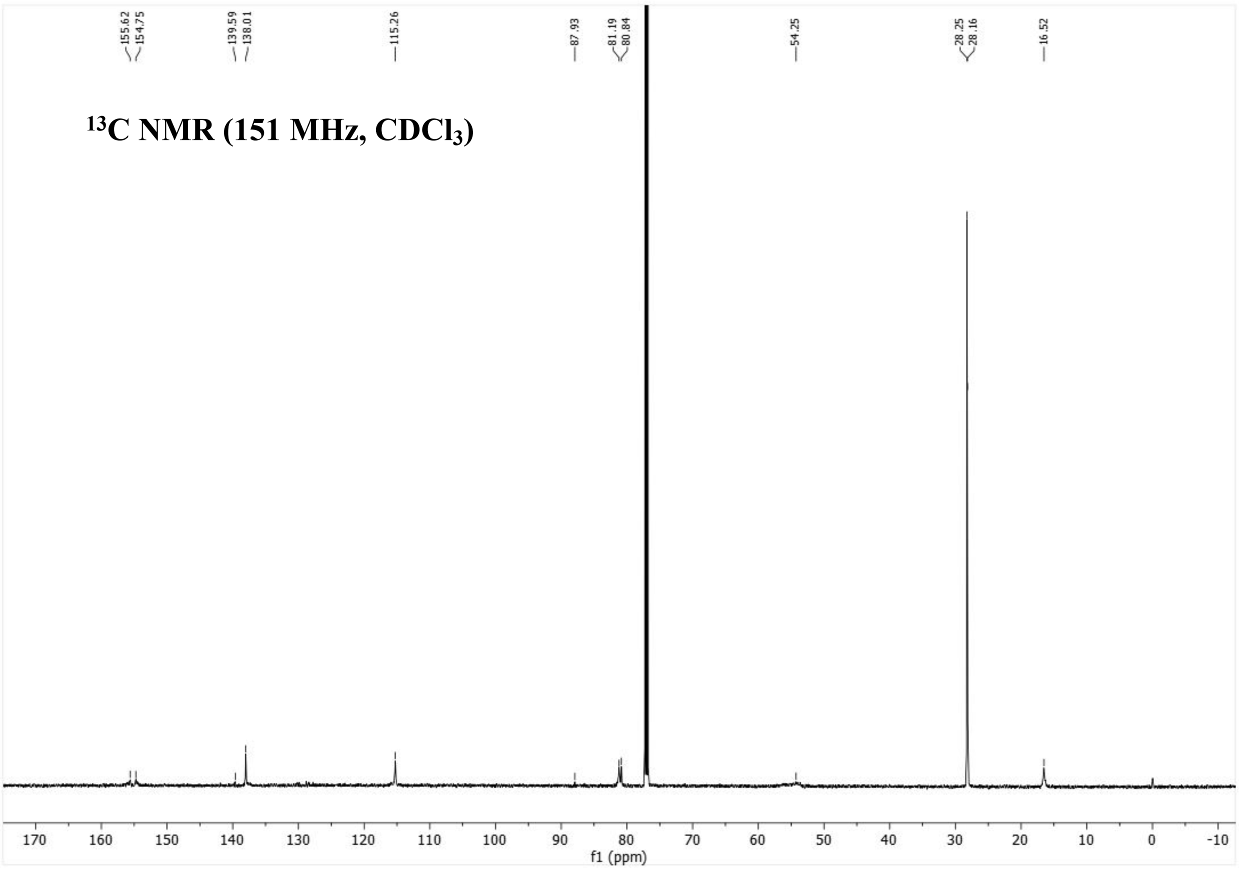


154.64
135.59
133.76
128.83
126.75
125.92
125.38
124.36
81.81
74.31
74.23
74.05
73.87
28.37
27.89
27.05
20.48
^{13}C NMR (151 MHz, $C_2D_2Cl_4$)
25°C
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

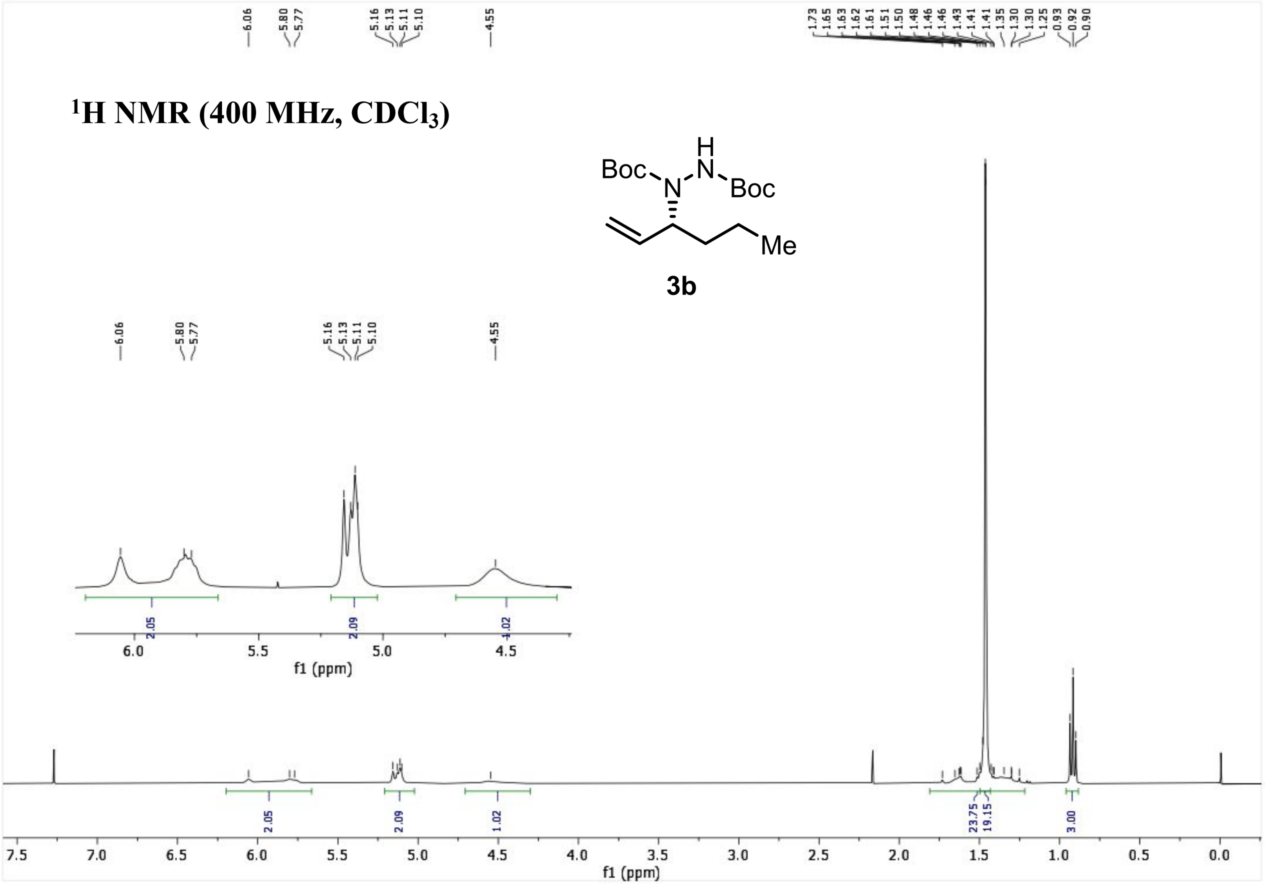


^{1}H NMR (400 MHz, $CDCl_3$)

3a

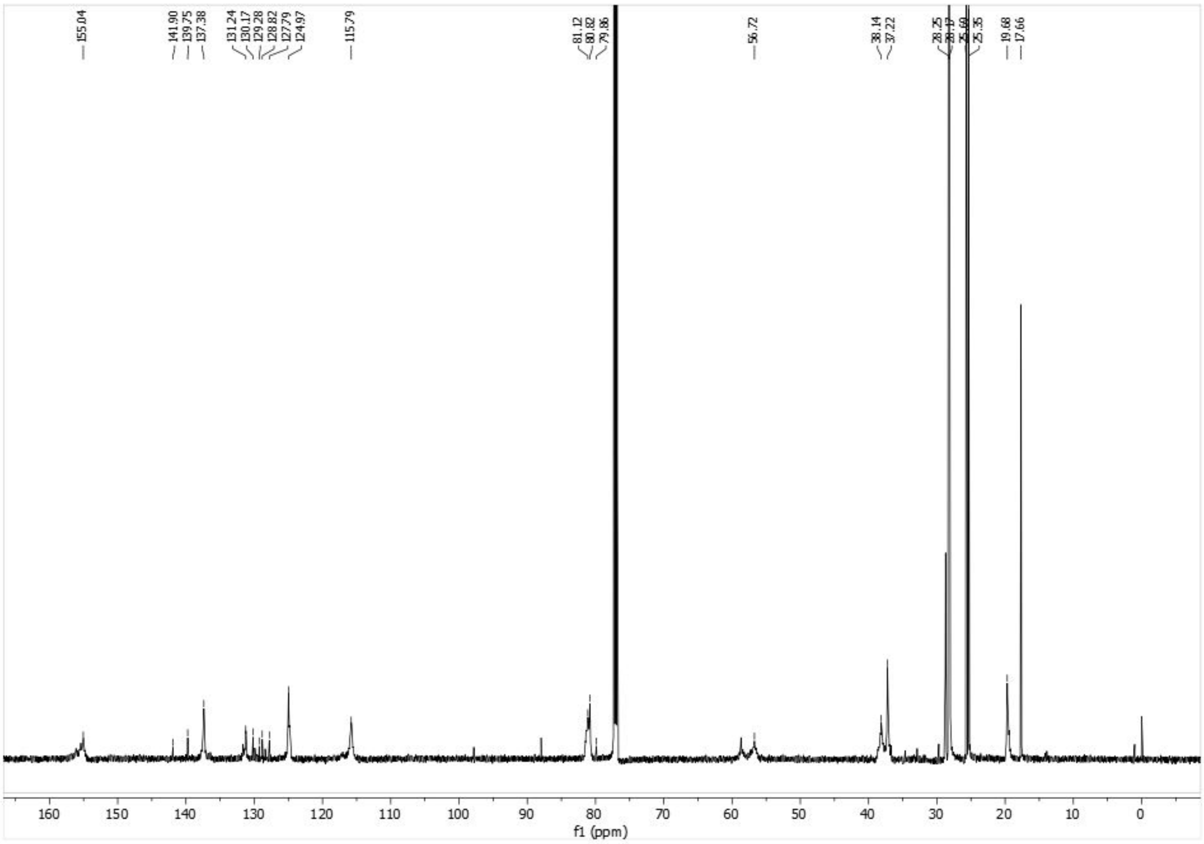


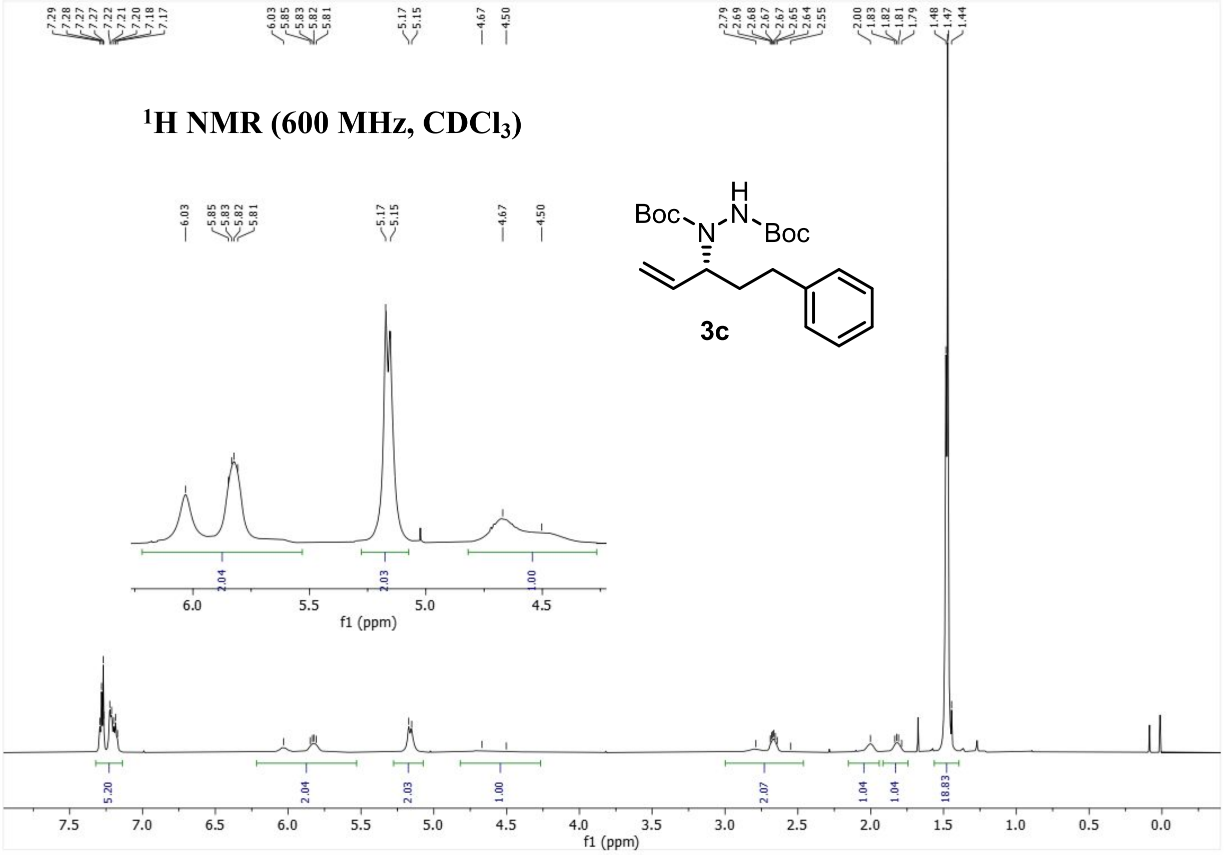
^{13}C NMR (151 MHz, $CDCl_3$)



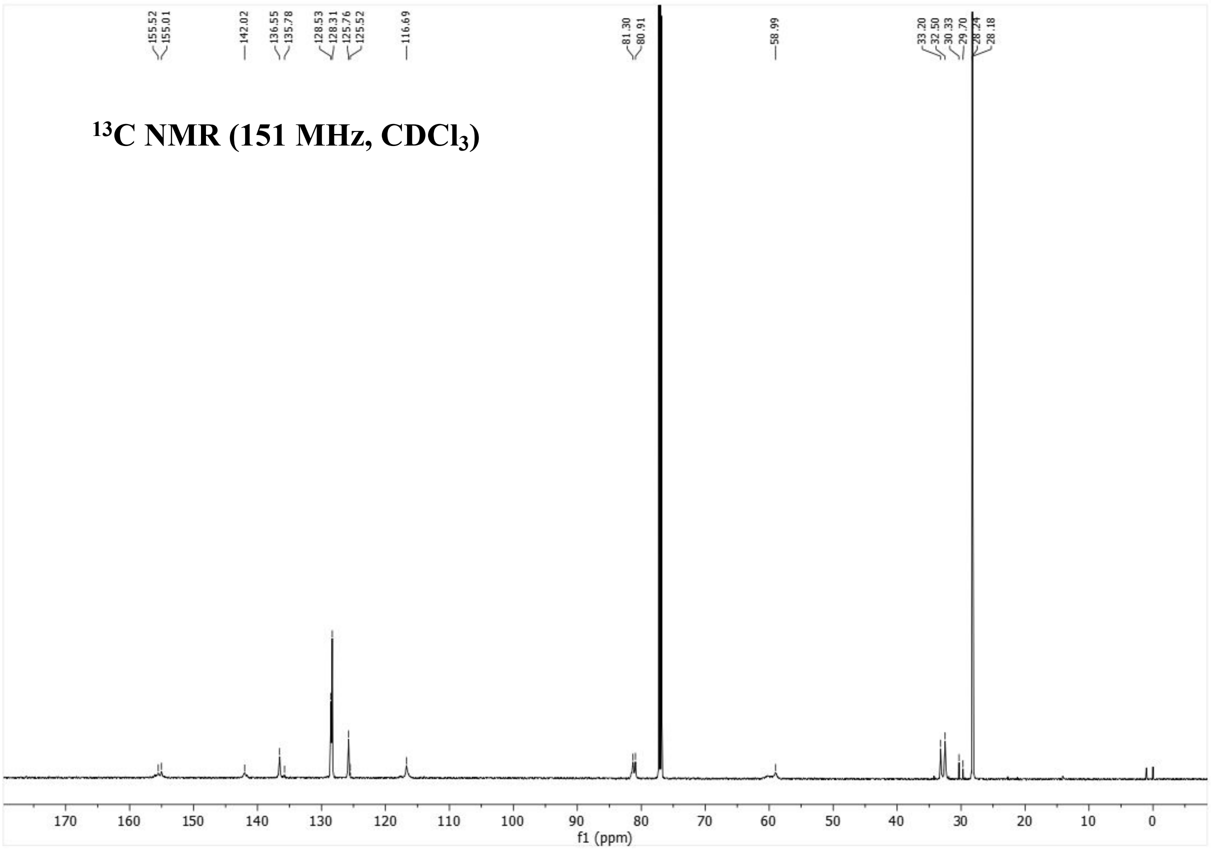
^{1}H NMR (400 MHz, CDCl$_3$)

3b

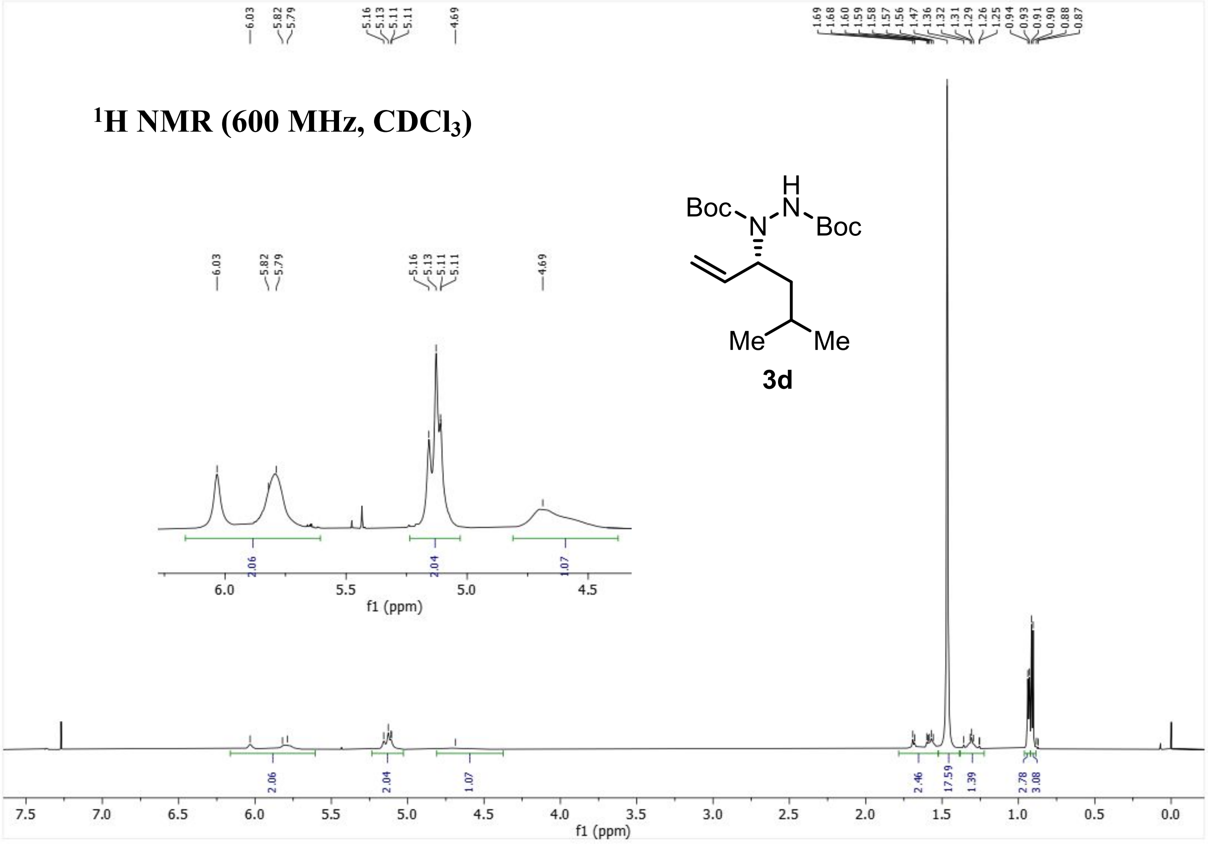


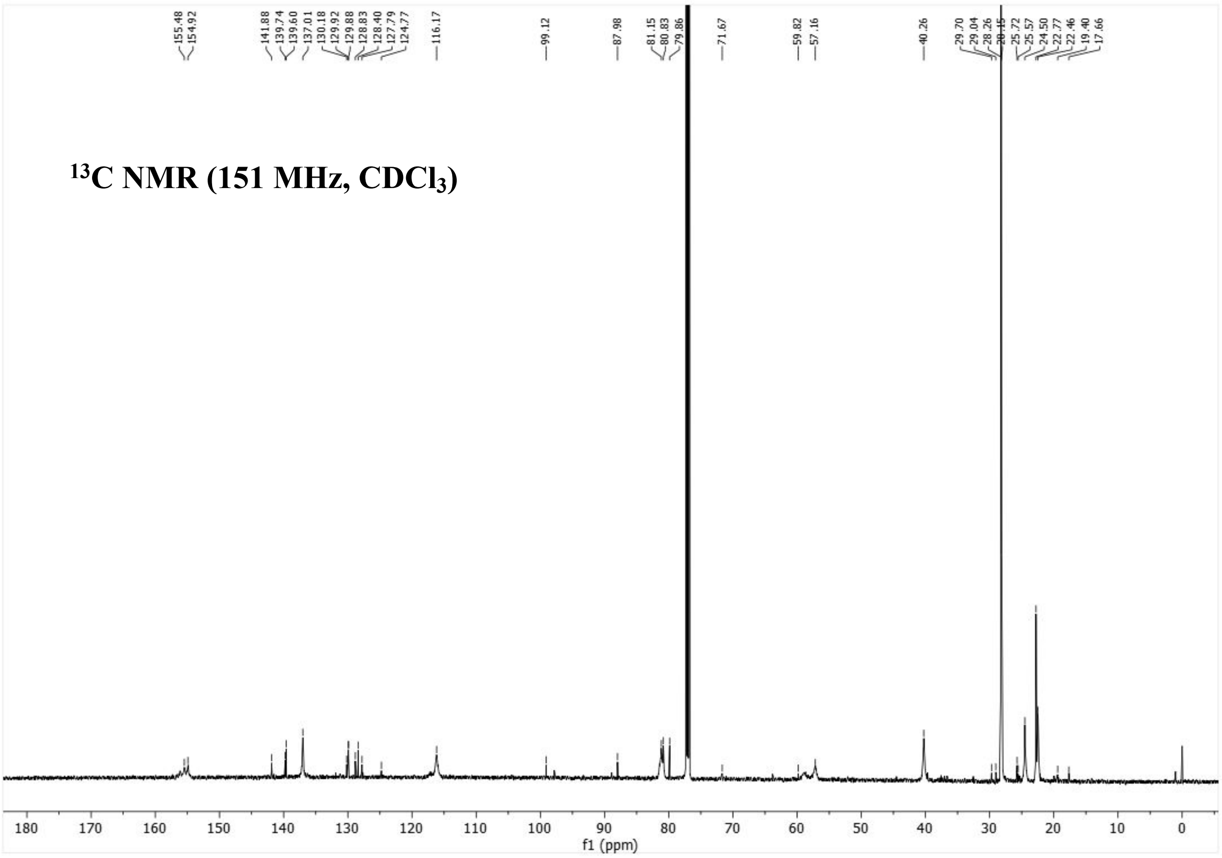


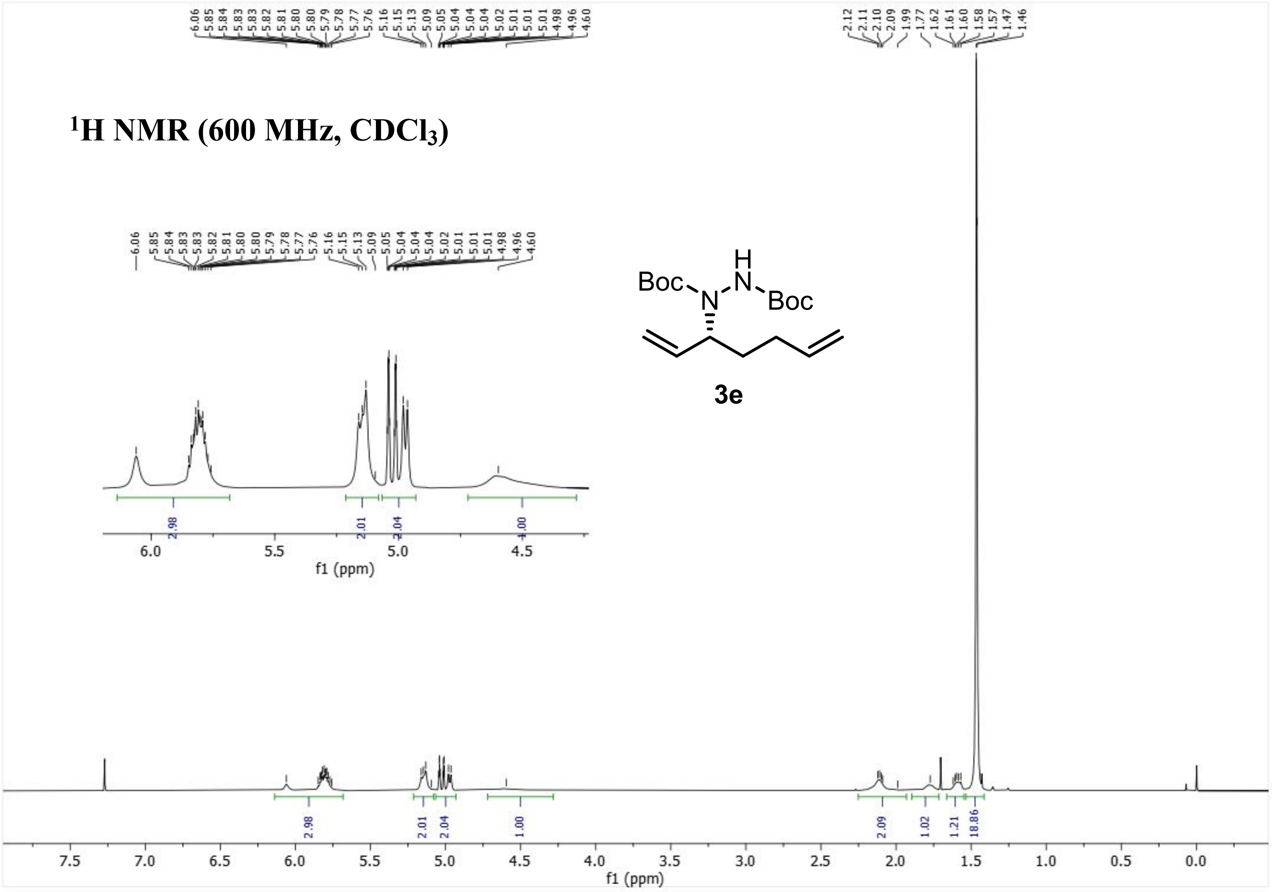
^{1}H NMR (600 MHz, CDCl$_3$)



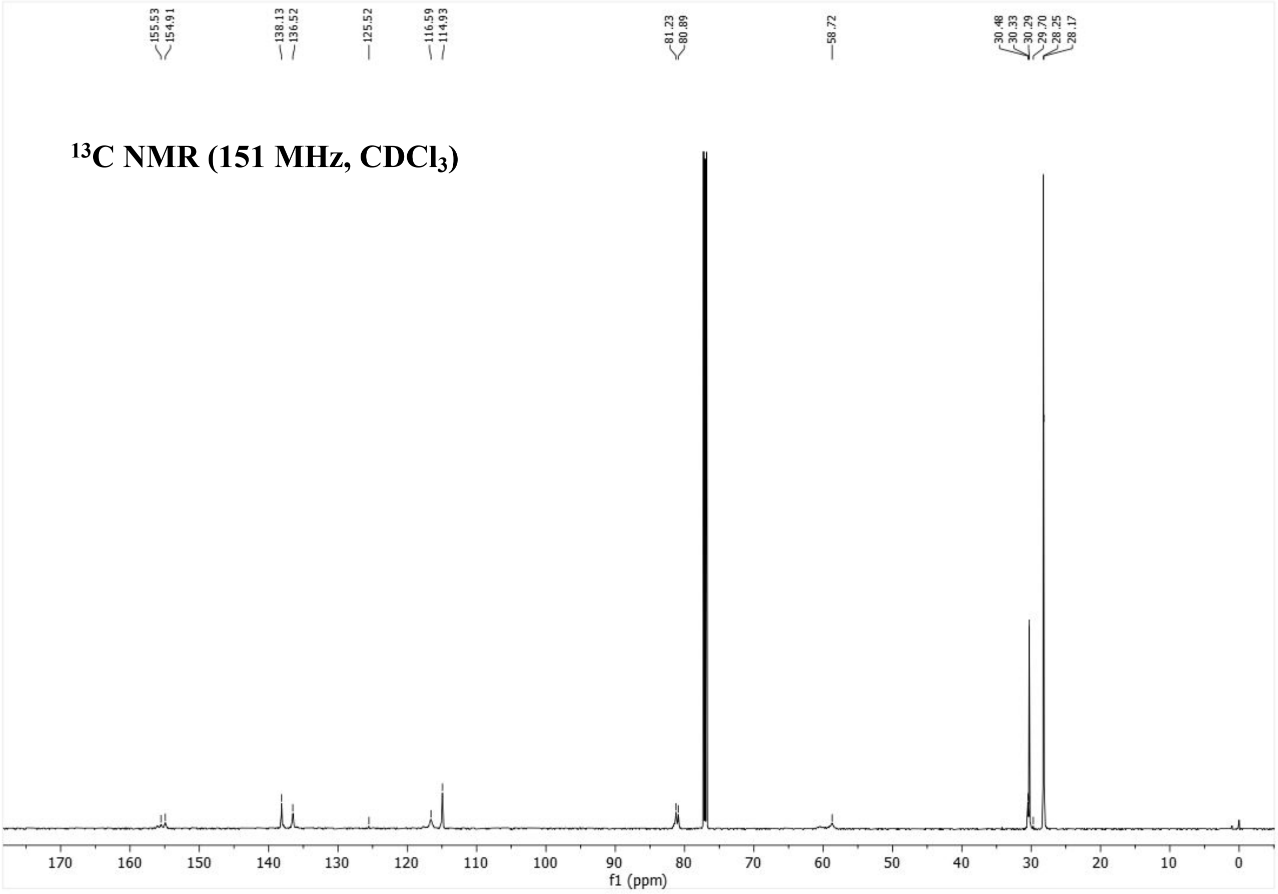
^{13}C NMR (151 MHz, CDCl$_3$)


^{1}H NMR (600 MHz, CDCl$_3$)
6.03
5.82
5.79
5.16
5.13
5.11
5.11
4.69
1.69
1.68
1.60
1.59
1.58
1.57
1.56
1.47
1.36
1.32
1.31
1.29
1.26
1.25
0.94
0.93
0.91
0.90
0.88
0.87
Boc
H
N
N
Boc
Me
Me
3d
2.06
2.04
1.07
2.46
17.59
1.39
2.78
3.08
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
f1 (ppm)

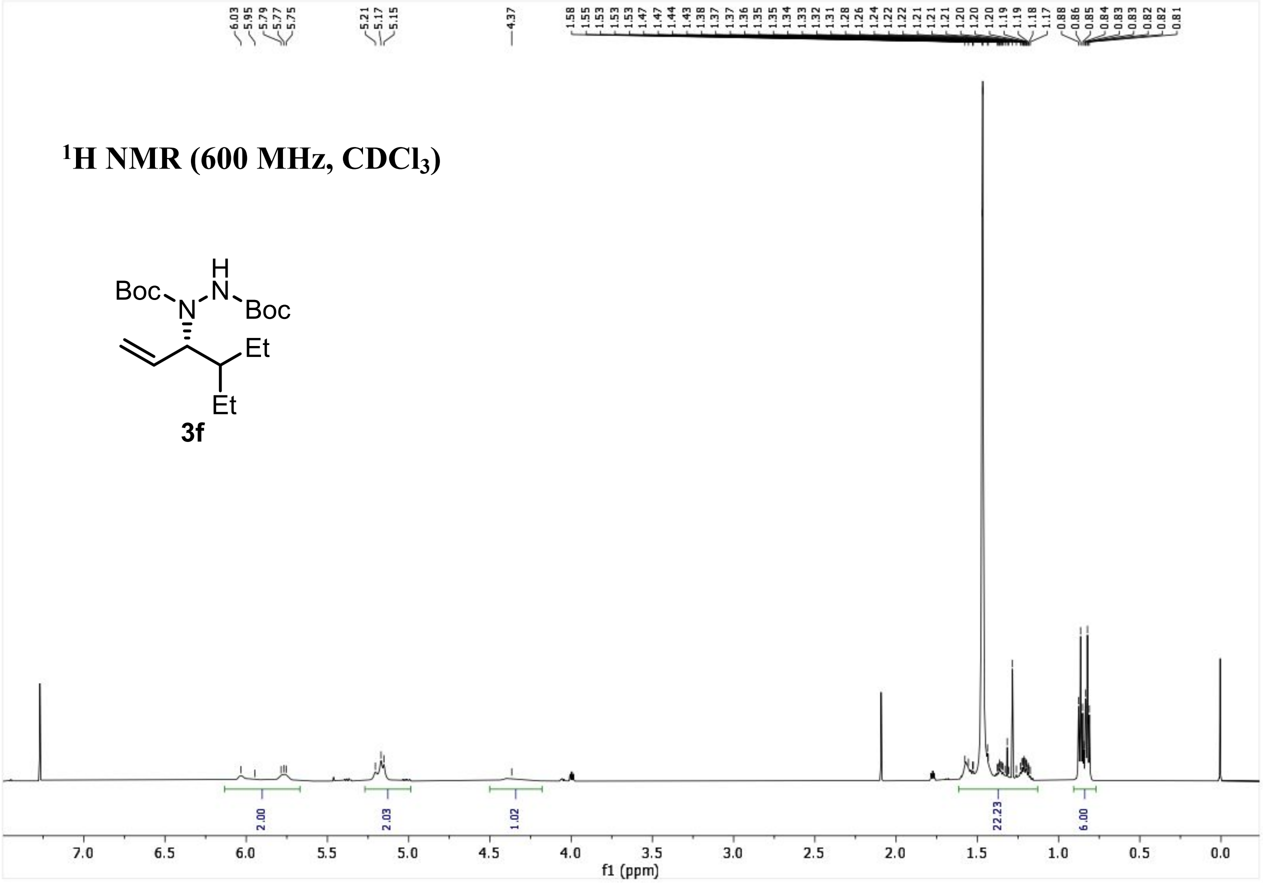

^{13}C NMR (151 MHz, CDCl$_3$)
155.48
154.92
141.88
139.74
139.60
137.01
130.18
129.92
129.88
128.83
128.40
127.79
124.77
116.17
99.12
87.98
81.15
80.83
79.86
71.67
59.82
57.16
40.26
29.70
29.04
28.26
28.15
25.72
25.57
24.50
22.77
22.46
19.40
17.66
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



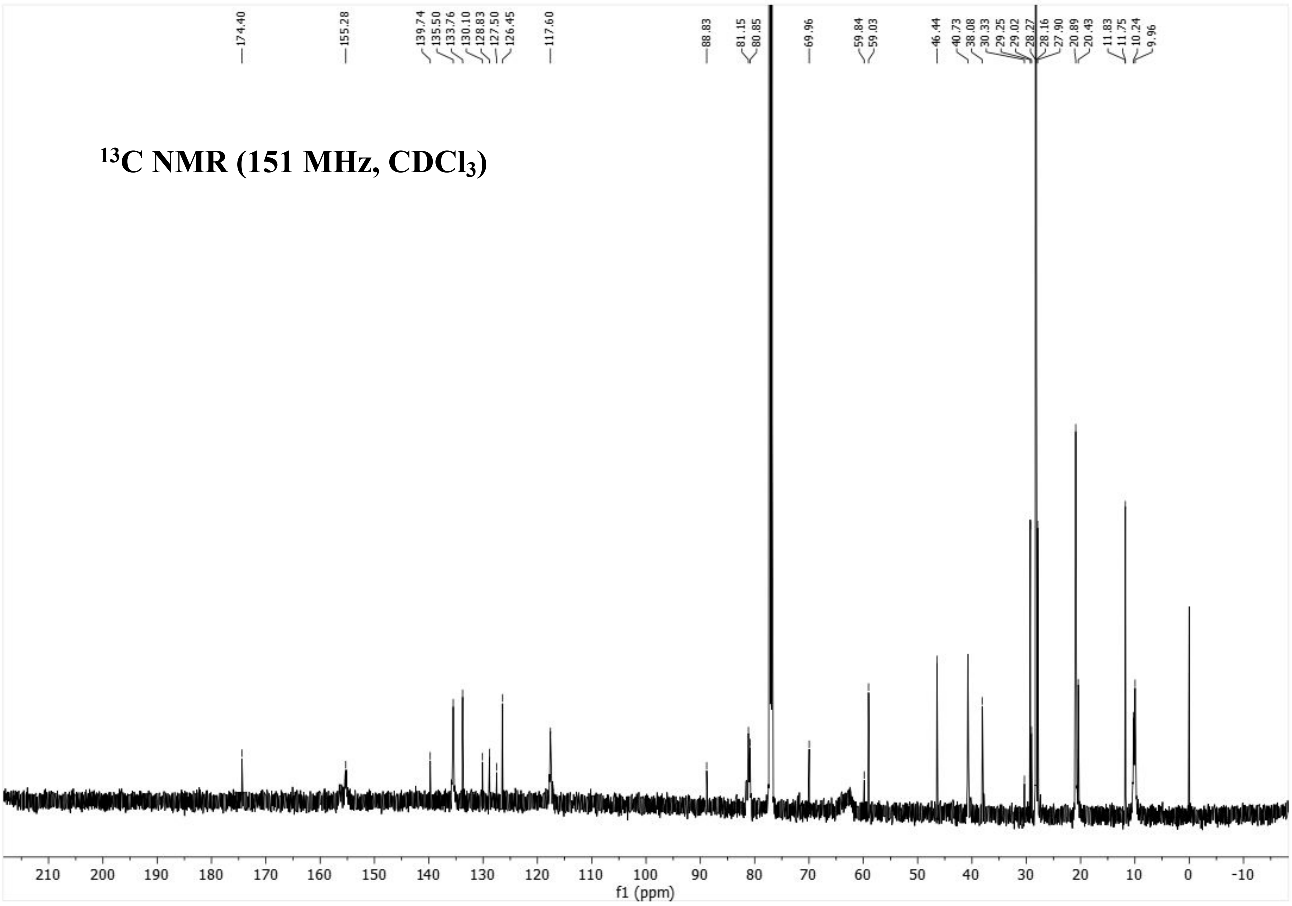
^{1}H NMR (600 MHz, CDCl$_3$)

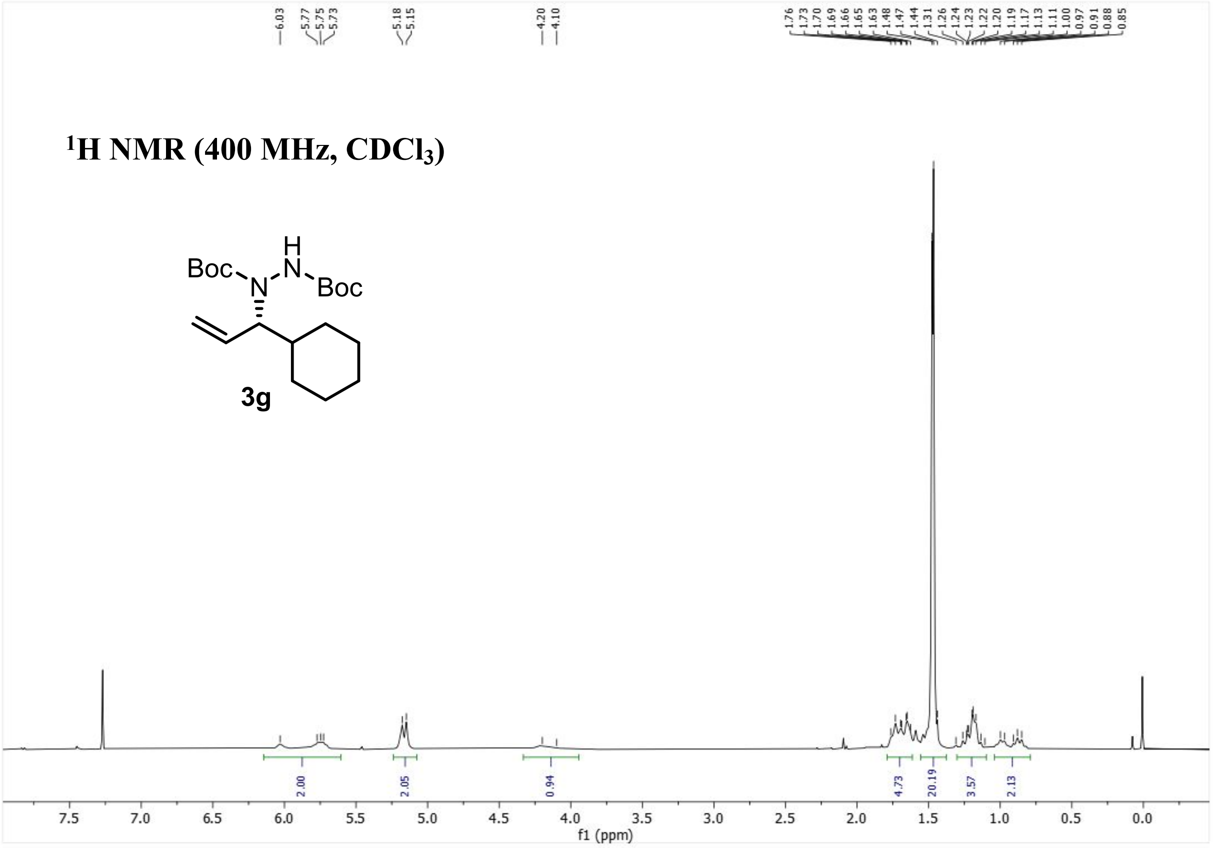


^{13}C NMR (151 MHz, CDCl$_3$)


^{1}H NMR (600 MHz, $CDCl_3$)

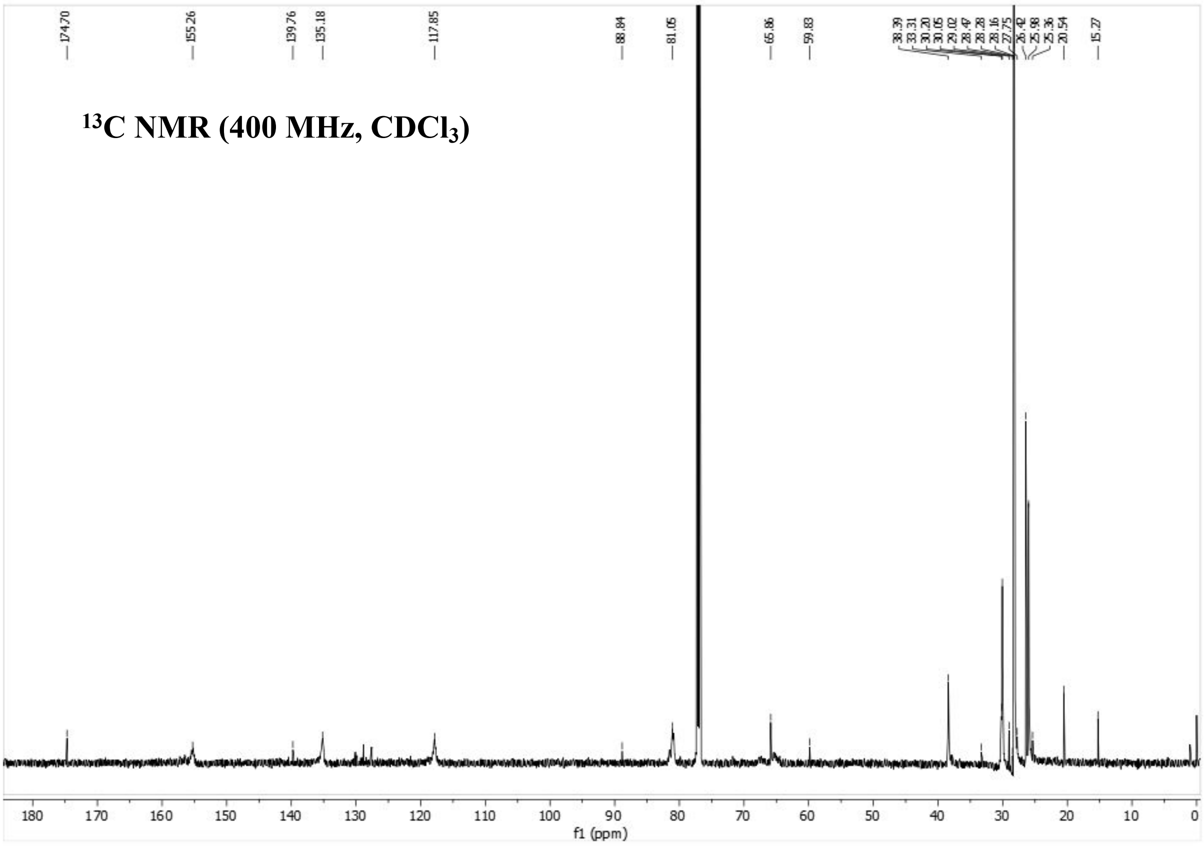
3f


^{13}C NMR (151 MHz, $CDCl_3$)

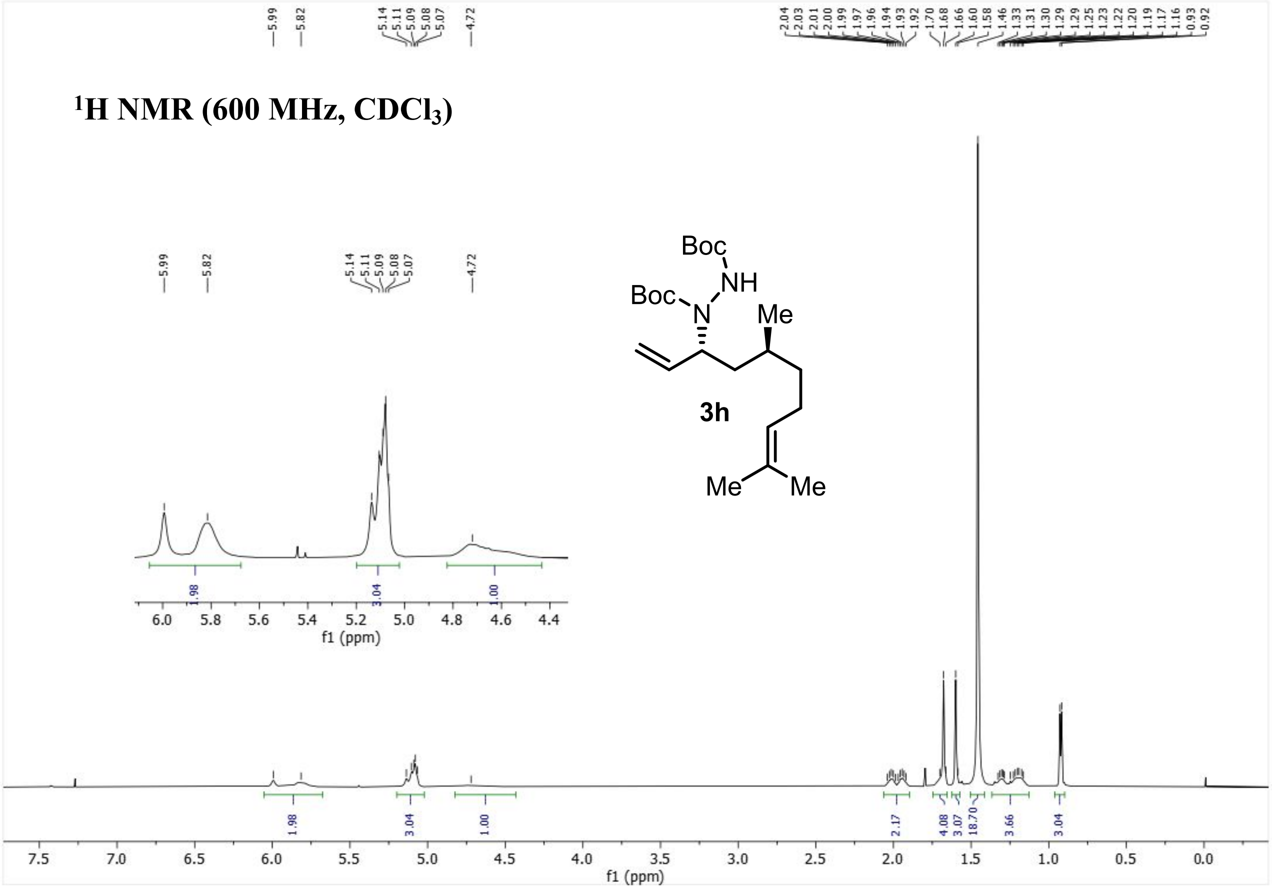


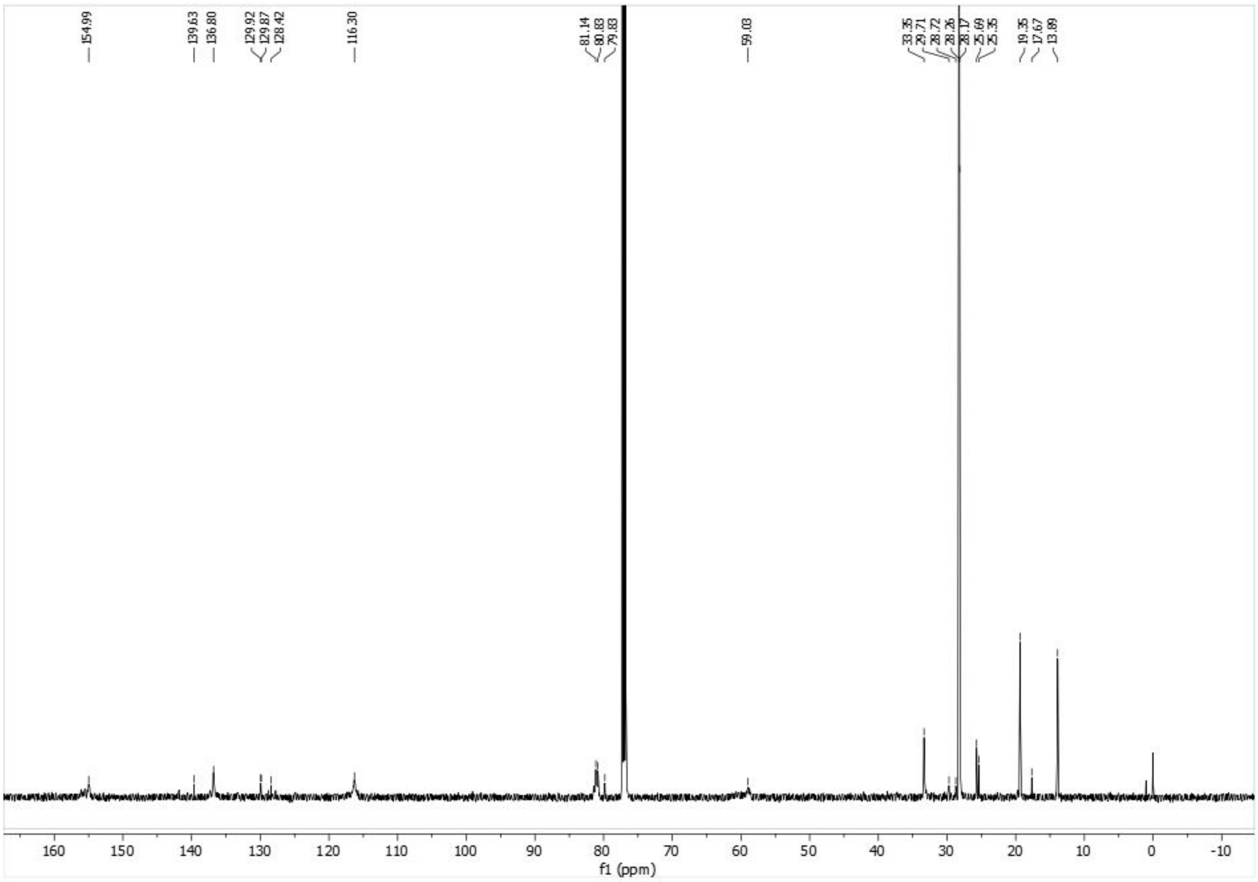
^{1}H NMR (400 MHz, CDCl$_3$)

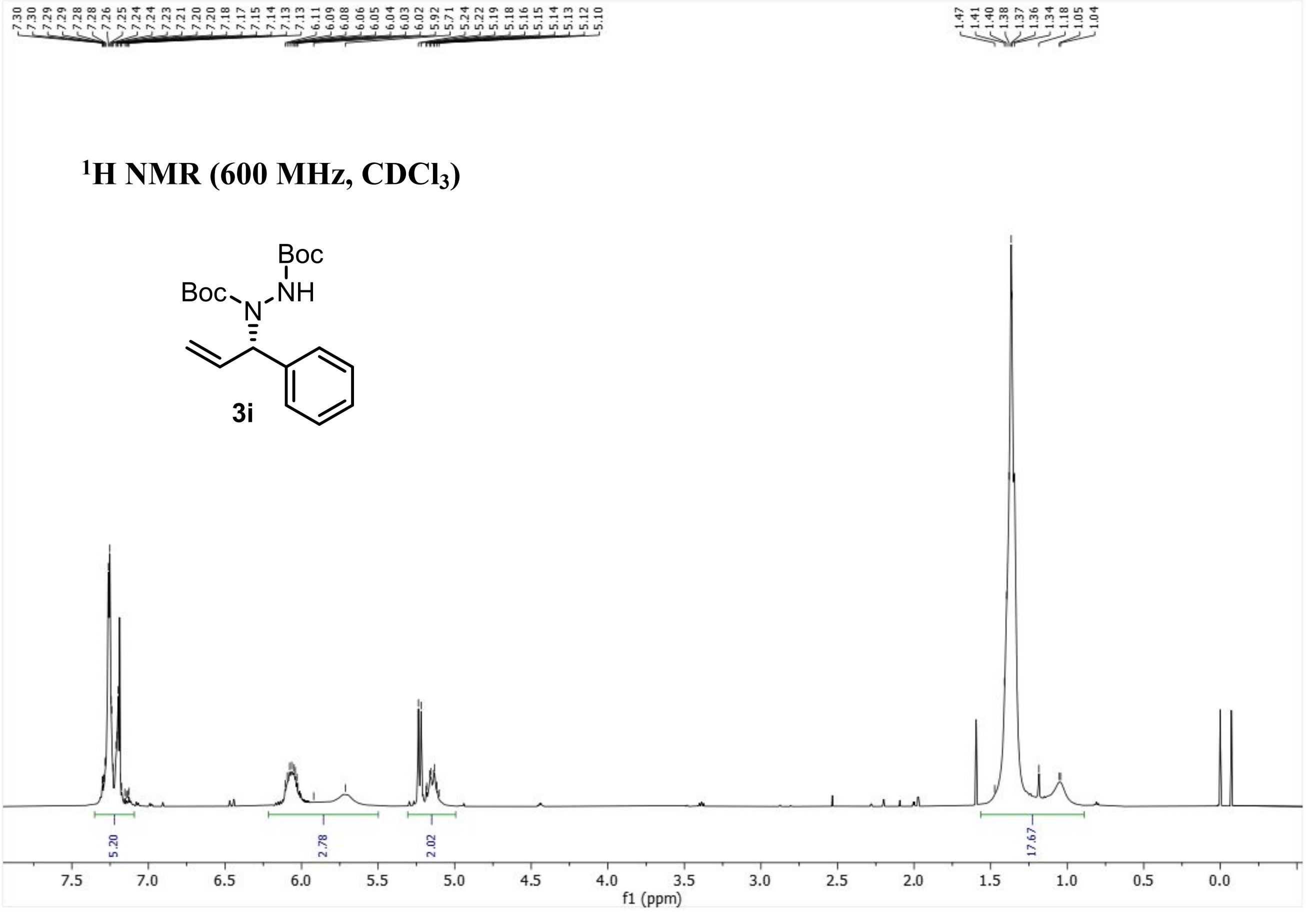
3g



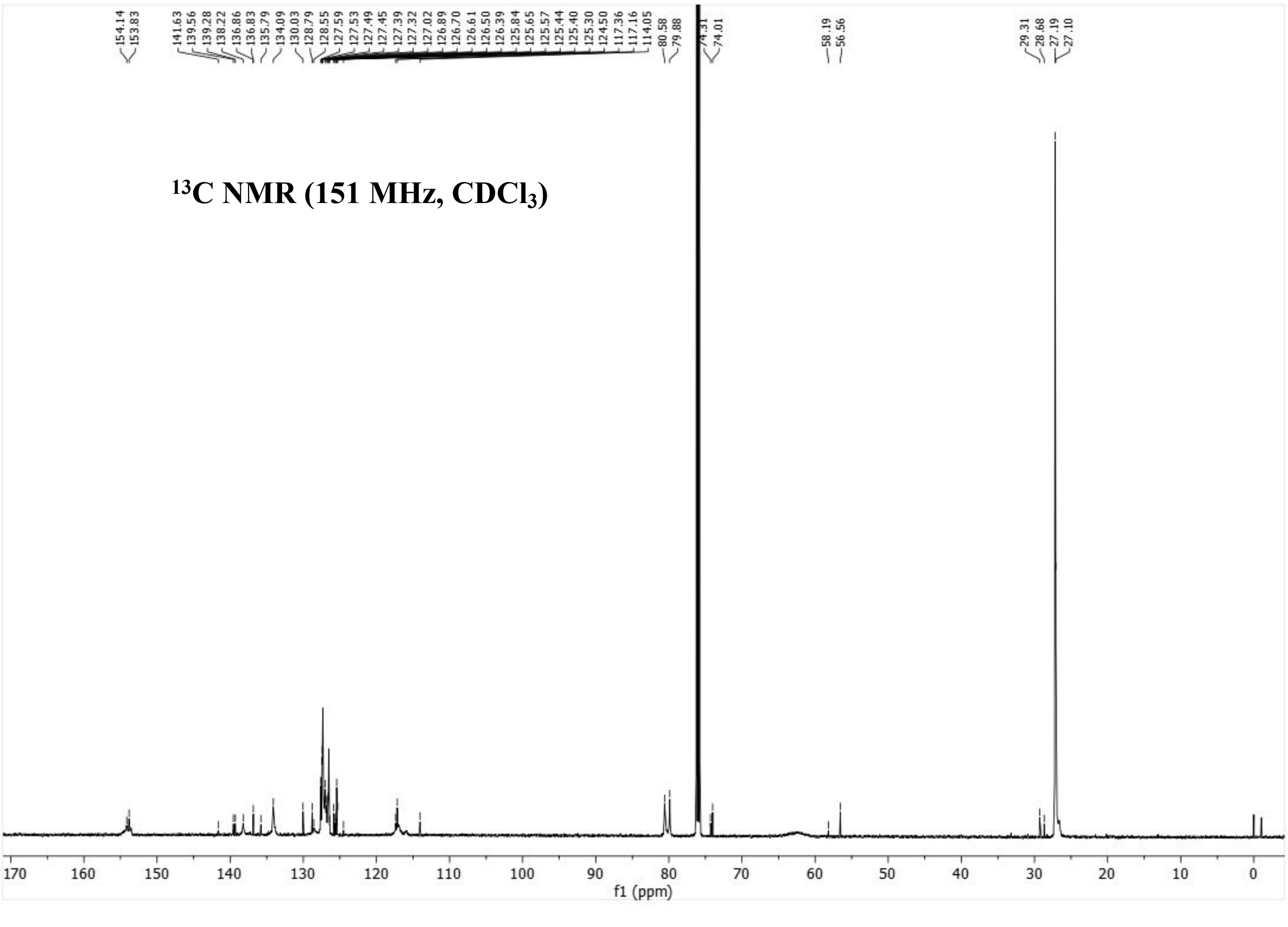
^{13}C NMR (400 MHz, CDCl$_3$)

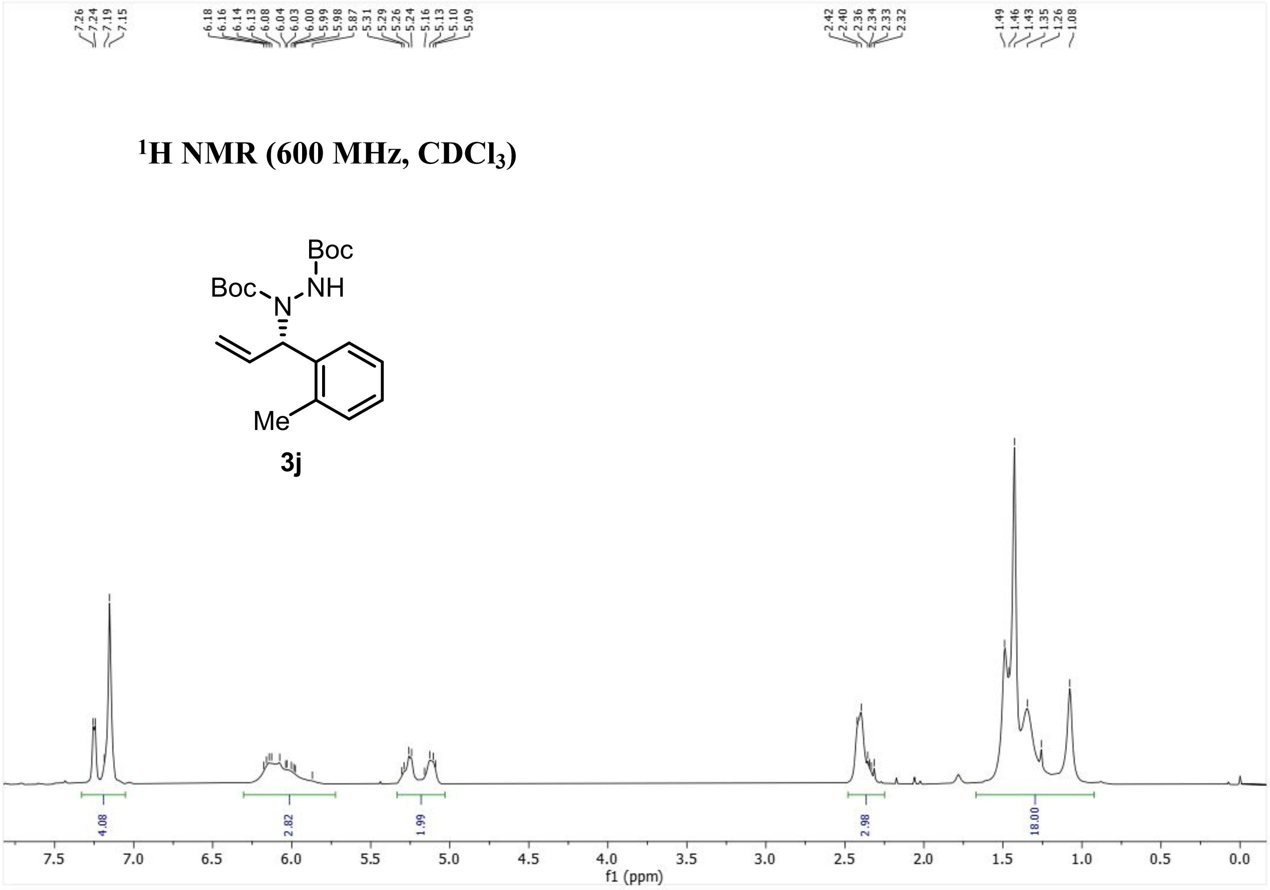

¹H NMR (600 MHz, CDCl₃)
Boc
NH
Boc
N
Me
3h
Me
Me
5.99
5.82
5.14
5.11
5.09
5.08
5.07
4.72
2.04
2.03
2.01
2.00
1.99
1.97
1.96
1.94
1.93
1.92
1.70
1.68
1.66
1.60
1.58
1.46
1.33
1.31
1.30
1.29
1.29
1.25
1.23
1.22
1.20
1.19
1.17
1.16
0.93
0.92
1.98
3.04
1.00
2.17
4.08
3.07
18.70
3.66
3.04
f1 (ppm)

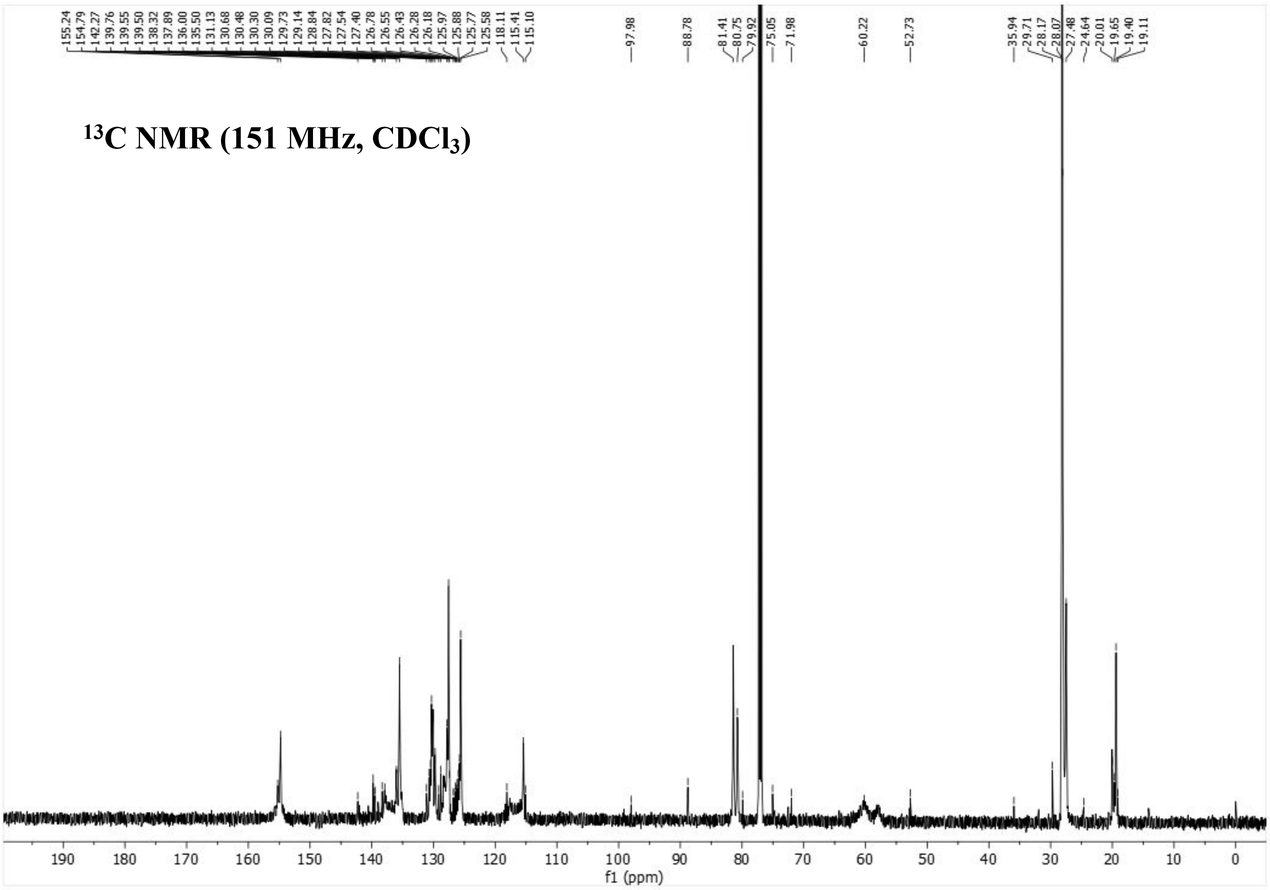

154.99
139.63
136.80
129.92
129.87
128.42
116.30
81.14
80.83
79.83
59.03
33.35
29.71
28.72
28.26
28.17
25.69
25.35
19.35
17.67
13.89
f1 (ppm)


^{1}H NMR (600 MHz, CDCl$_3$)

3i


^{13}C NMR (151 MHz, CDCl$_3$)


7.26
7.24
7.19
7.15
6.18
6.16
6.14
6.13
6.08
6.04
6.03
6.00
5.99
5.98
5.87
5.31
5.29
5.26
5.24
5.16
5.13
5.10
5.09
2.42
2.40
2.36
2.34
2.33
2.32
1.49
1.46
1.43
1.35
1.26
1.08
¹H NMR (600 MHz, CDCl₃)
Boc
Boc
N
NH
Me
3j
4.08
2.82
1.99
2.98
18.00
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
f1 (ppm)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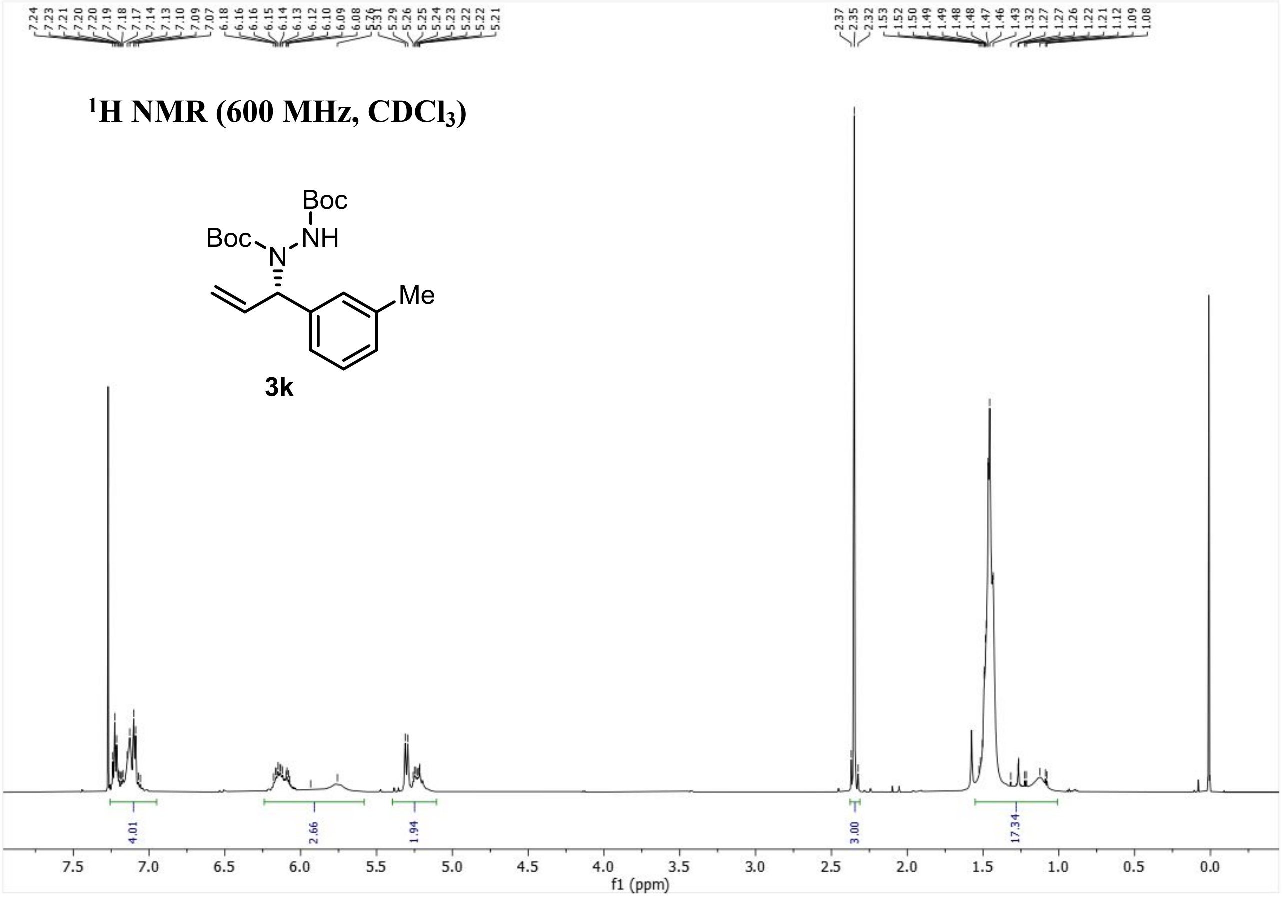
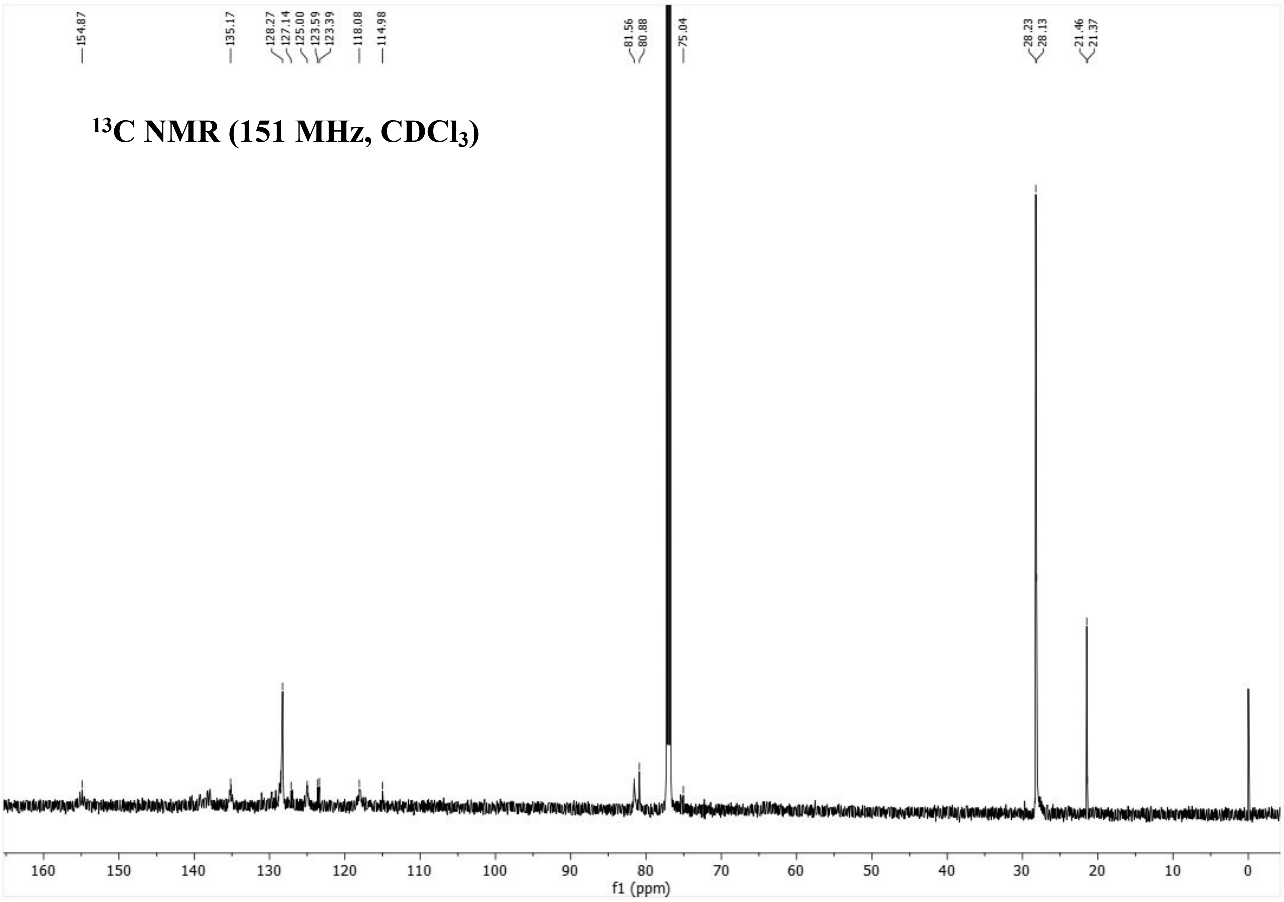
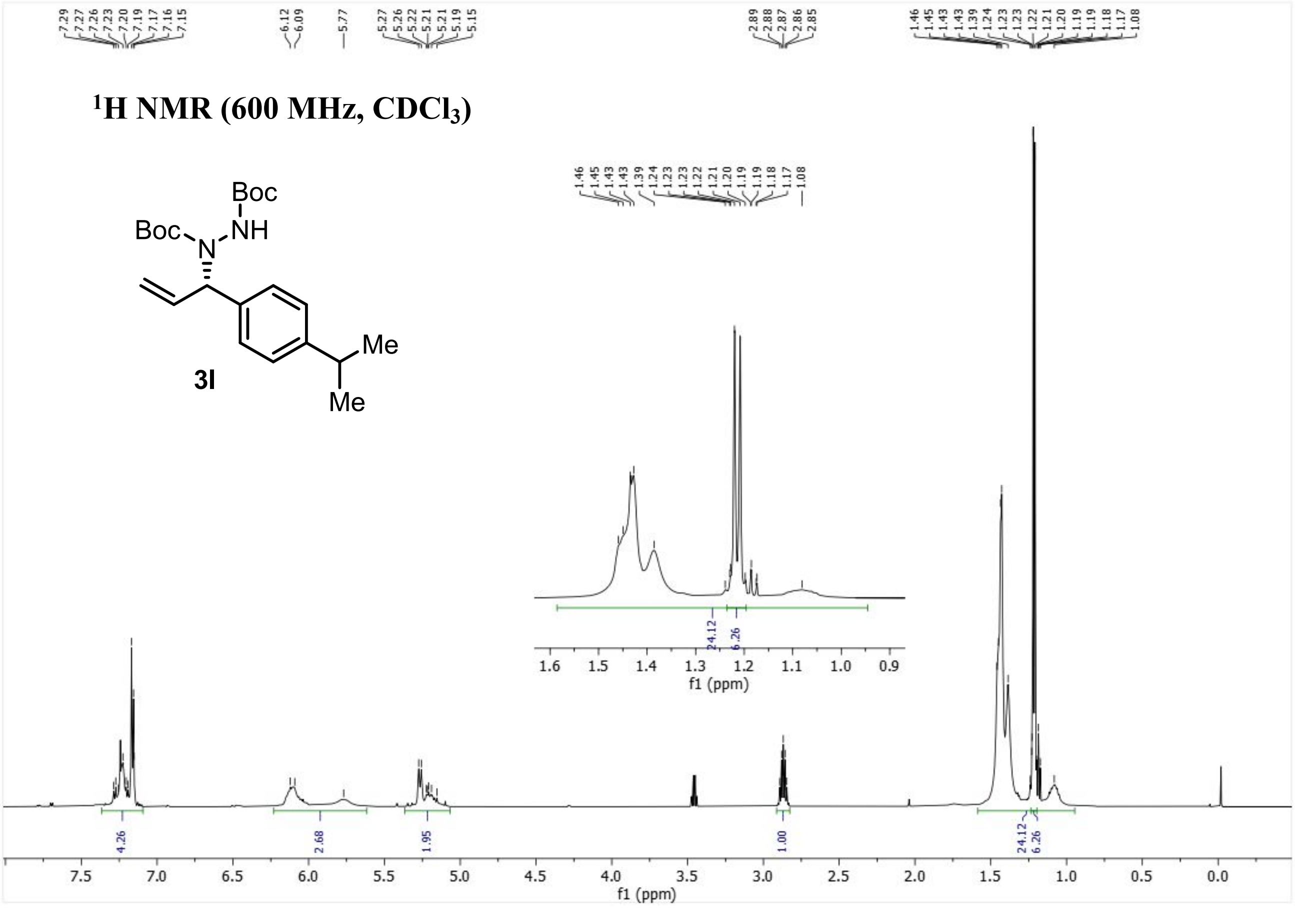
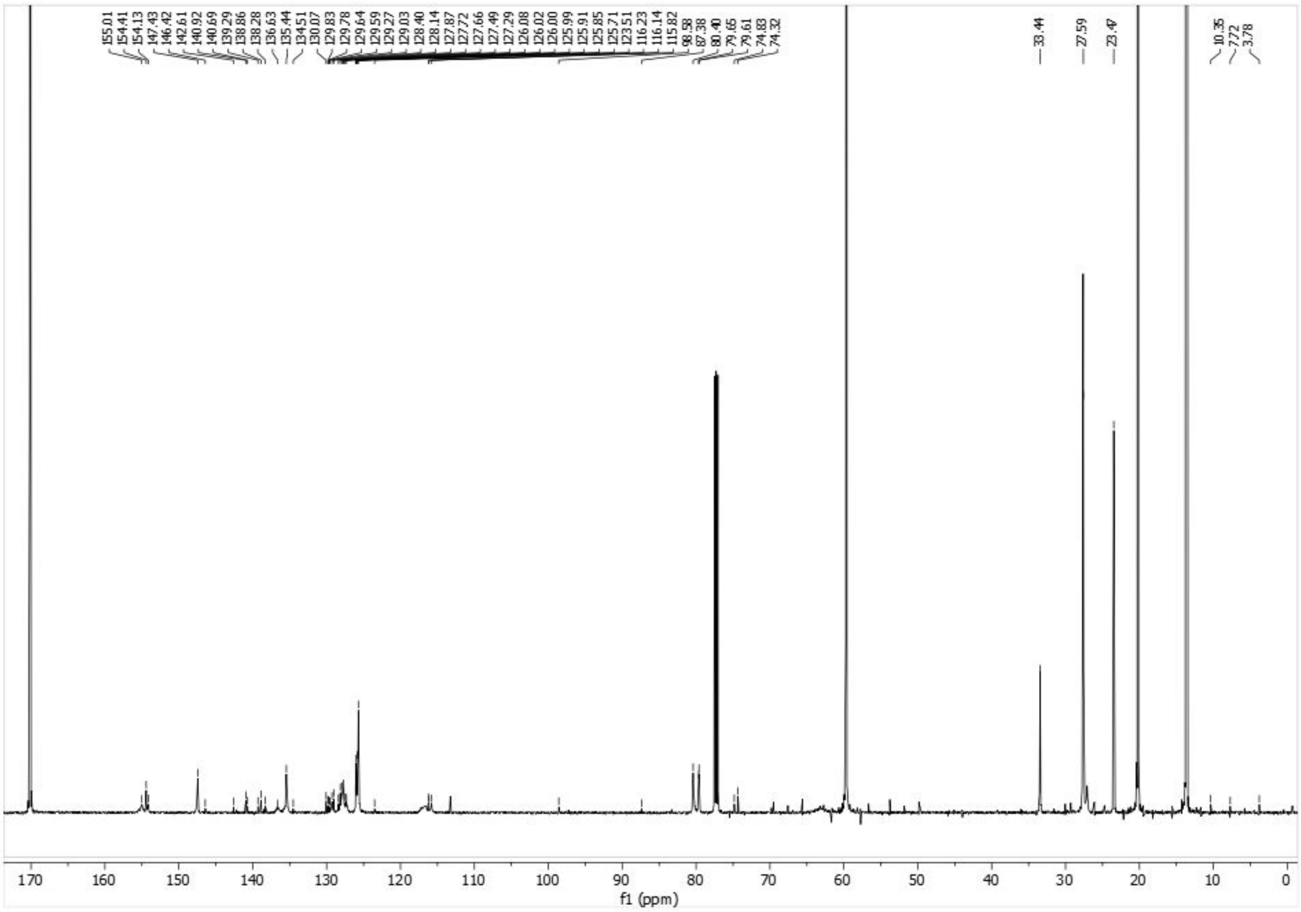
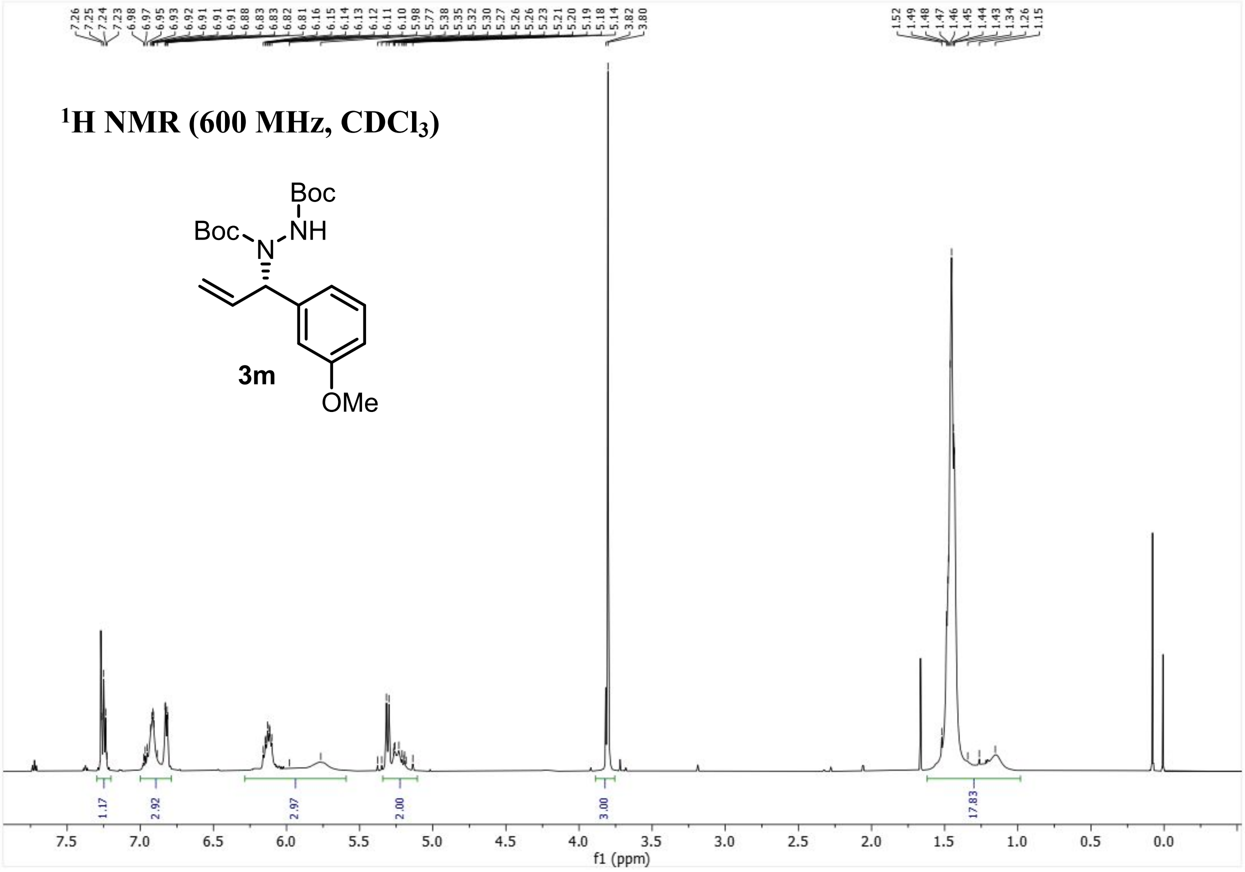
154.79
142.27
139.76
139.55
139.50
138.32
137.89
136.00
135.50
131.13
130.68
130.48
130.30
130.09
129.73
129.14
128.84
127.82
127.54
127.40
126.78
126.55
126.43
126.28
126.18
125.97
125.88
125.77
125.58
118.11
115.41
115.10
97.98
88.78
81.41
80.75
79.92
75.05
71.98
60.22
52.73
35.94
29.71
28.17
28.07
27.48
24.64
20.01
19.65
19.40
19.11
¹³C NMR (151 MHz, CDCl₃)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.24
7.23
7.21
7.20
7.20
7.19
7.18
7.17
7.14
7.13
7.10
7.09
7.07
6.18
6.16
6.16
6.15
6.14
6.13
6.12
6.10
6.09
6.08
5.76
5.31
5.29
5.26
5.25
5.24
5.23
5.22
5.21
2.37
2.35
2.32
1.53
1.52
1.50
1.49
1.48
1.48
1.47
1.46
1.43
1.32
1.27
1.27
1.26
1.22
1.21
1.12
1.09
1.08
¹H NMR (600 MHz, CDCl₃)
Boc
NH
Boc
N
Me
3k
4.01
2.66
1.94
3.00
17.34
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
f1 (ppm)


154.87
135.17
128.27
127.14
125.00
123.59
123.39
118.08
114.98
81.56
80.88
75.04
28.23
28.13
21.46
21.37
¹³C NMR (151 MHz, CDCl₃)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

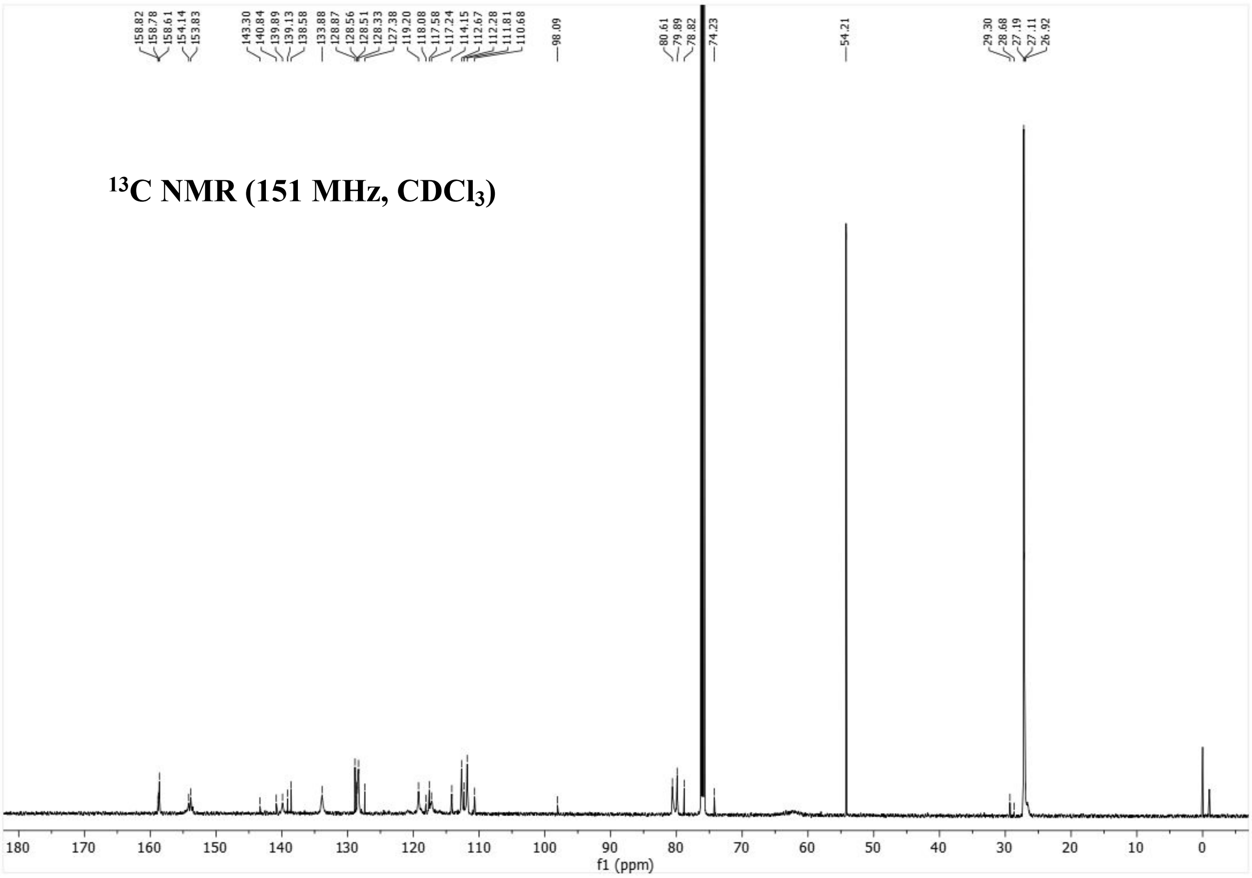

7.29
7.27
7.26
7.23
7.20
7.19
7.17
7.16
7.15
6.12
6.09
5.77
5.27
5.26
5.22
5.21
5.21
5.19
5.15
2.89
2.88
2.87
2.86
2.85
1.46
1.45
1.43
1.43
1.39
1.24
1.23
1.23
1.22
1.21
1.20
1.19
1.19
1.18
1.17
1.08
^{1}H NMR (600 MHz, CDCl$_3$)
Boc
Boc
NH
N
Me
Me
3l
24.12
6.26
1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9
f1 (ppm)
4.26
2.68
1.95
1.00
24.12
6.26
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
f1 (ppm)


155.01
154.41
154.13
147.43
146.42
142.61
140.92
140.69
139.29
138.86
138.28
136.63
135.44
134.51
130.07
129.83
129.78
129.64
129.59
129.27
129.03
128.40
128.14
127.87
127.72
127.66
127.49
127.29
126.08
126.02
126.00
125.99
125.91
125.85
125.71
123.51
116.23
116.14
115.82
98.58
87.38
80.40
79.65
79.61
74.83
74.32
33.44
27.59
23.47
10.35
7.72
3.78
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

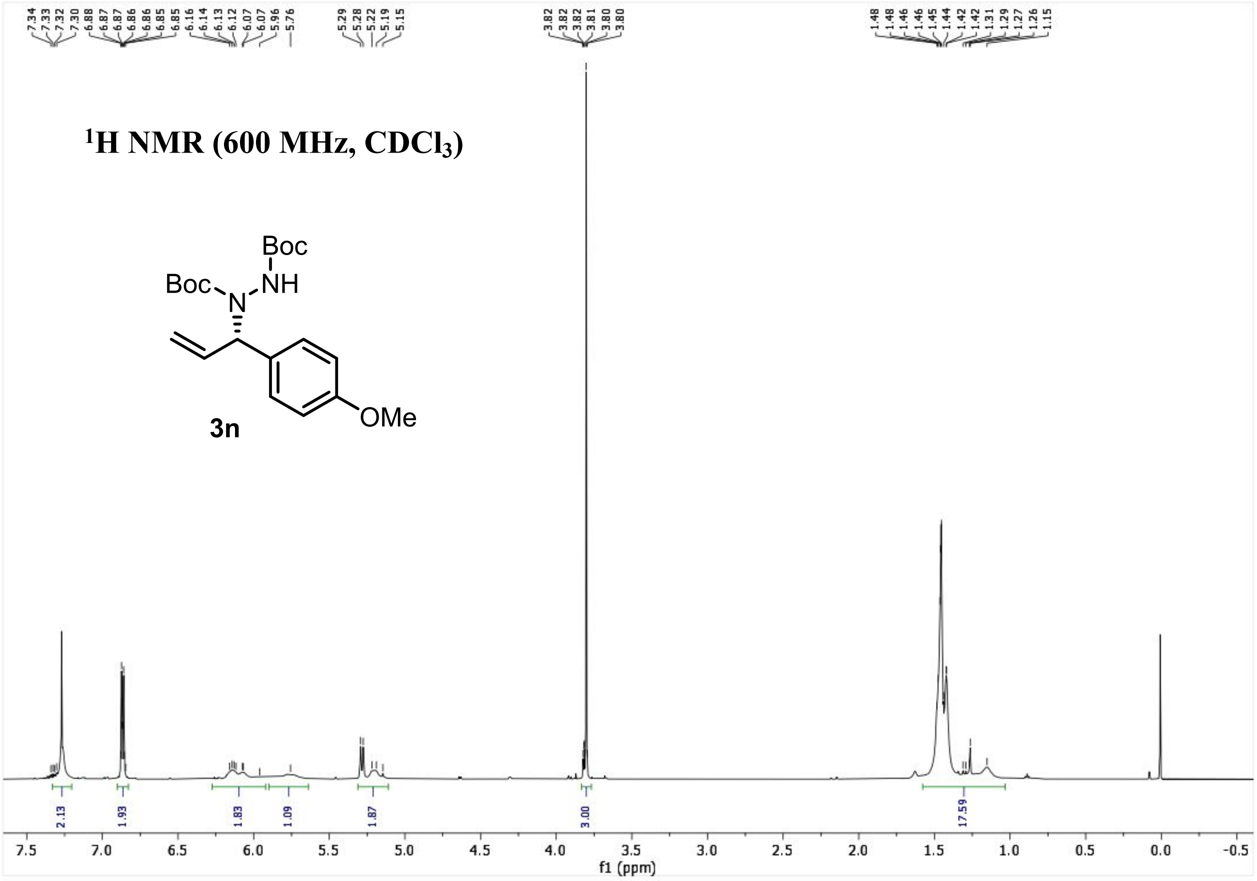


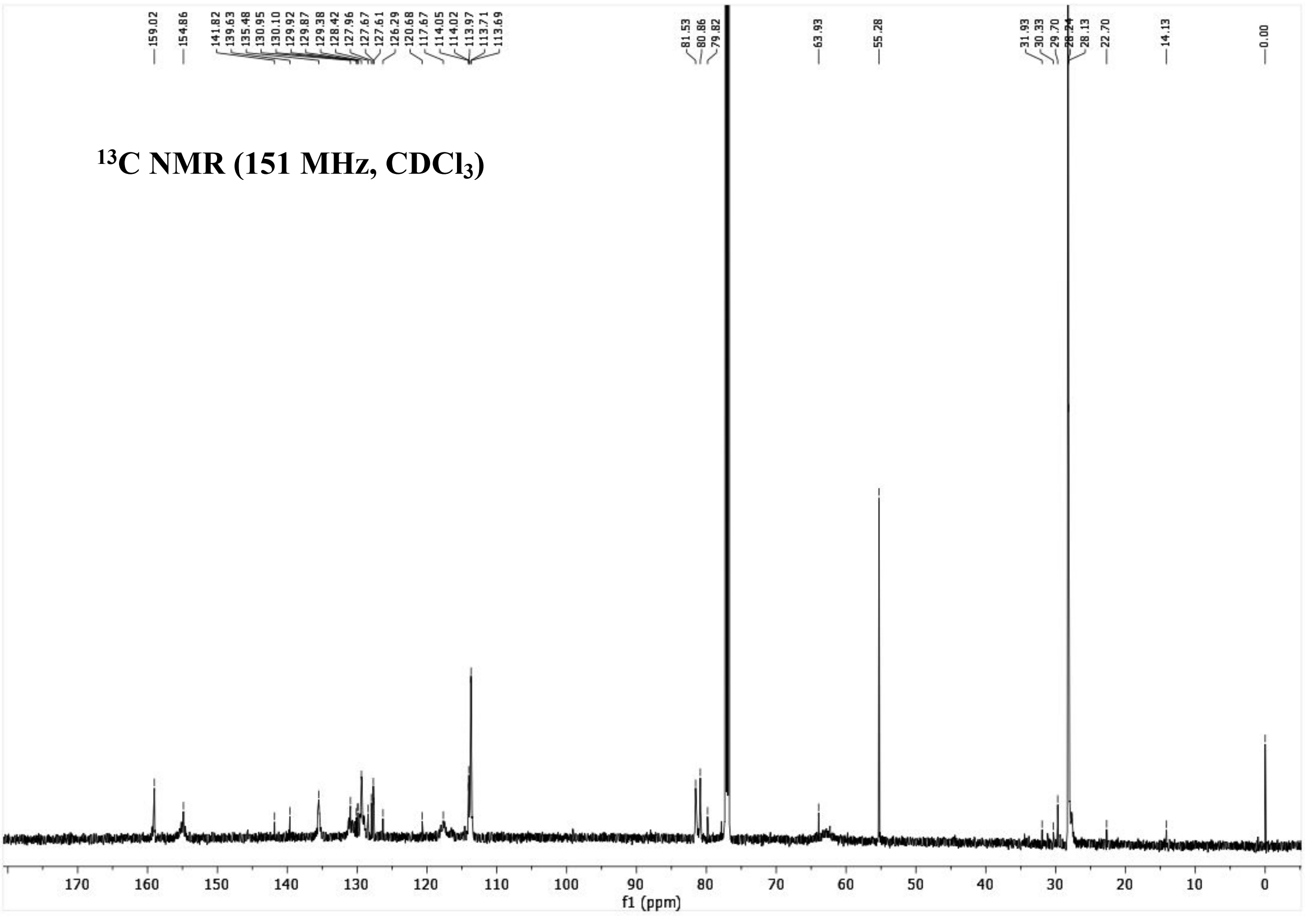
^{1}H NMR (600 MHz, CDCl$_3$)

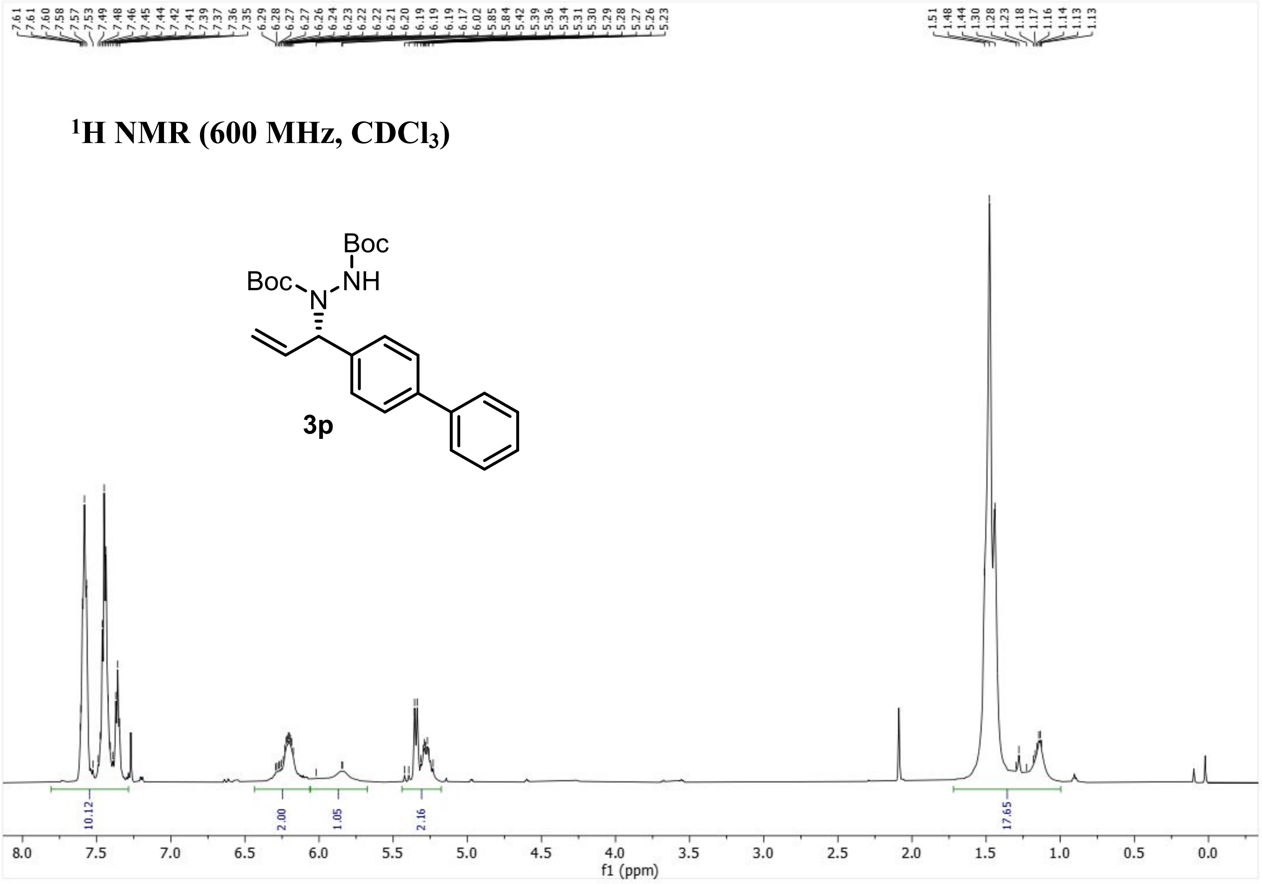
3m



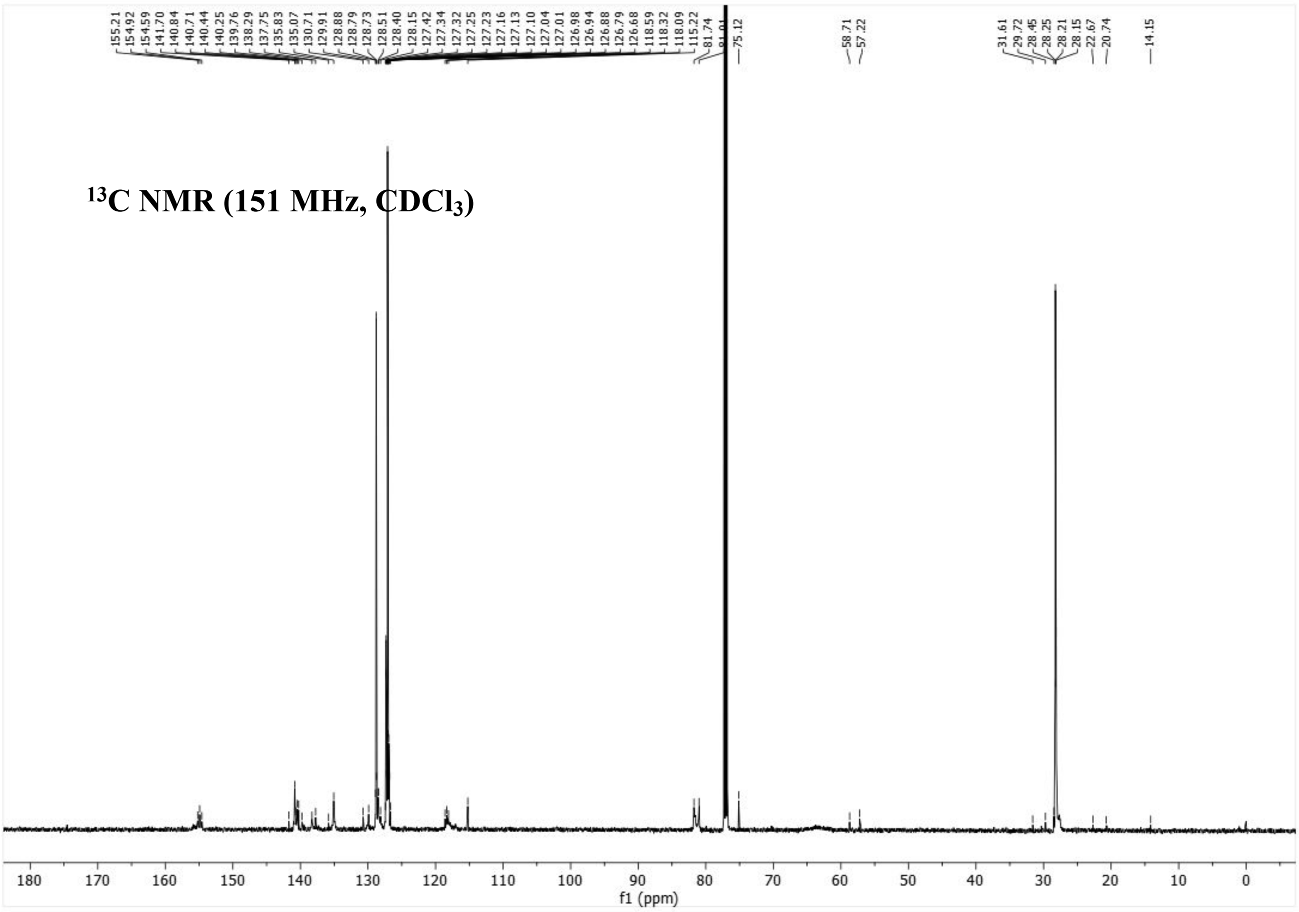
^{13}C NMR (151 MHz, CDCl$_3$)


7.34
7.33
7.32
7.30
6.88
6.87
6.87
6.86
6.86
6.85
6.85
6.16
6.14
6.13
6.12
6.07
6.07
5.96
5.76
5.29
5.28
5.22
5.19
5.15
3.82
3.82
3.82
3.81
3.80
3.80
1.48
1.48
1.46
1.46
1.45
1.44
1.42
1.42
1.31
1.29
1.27
1.26
1.15
¹H NMR (600 MHz, CDCl₃)
Boc
NH
Boc
N
OMe
3n
2.13
1.93
1.83
1.09
1.87
3.00
17.59
f1 (ppm)

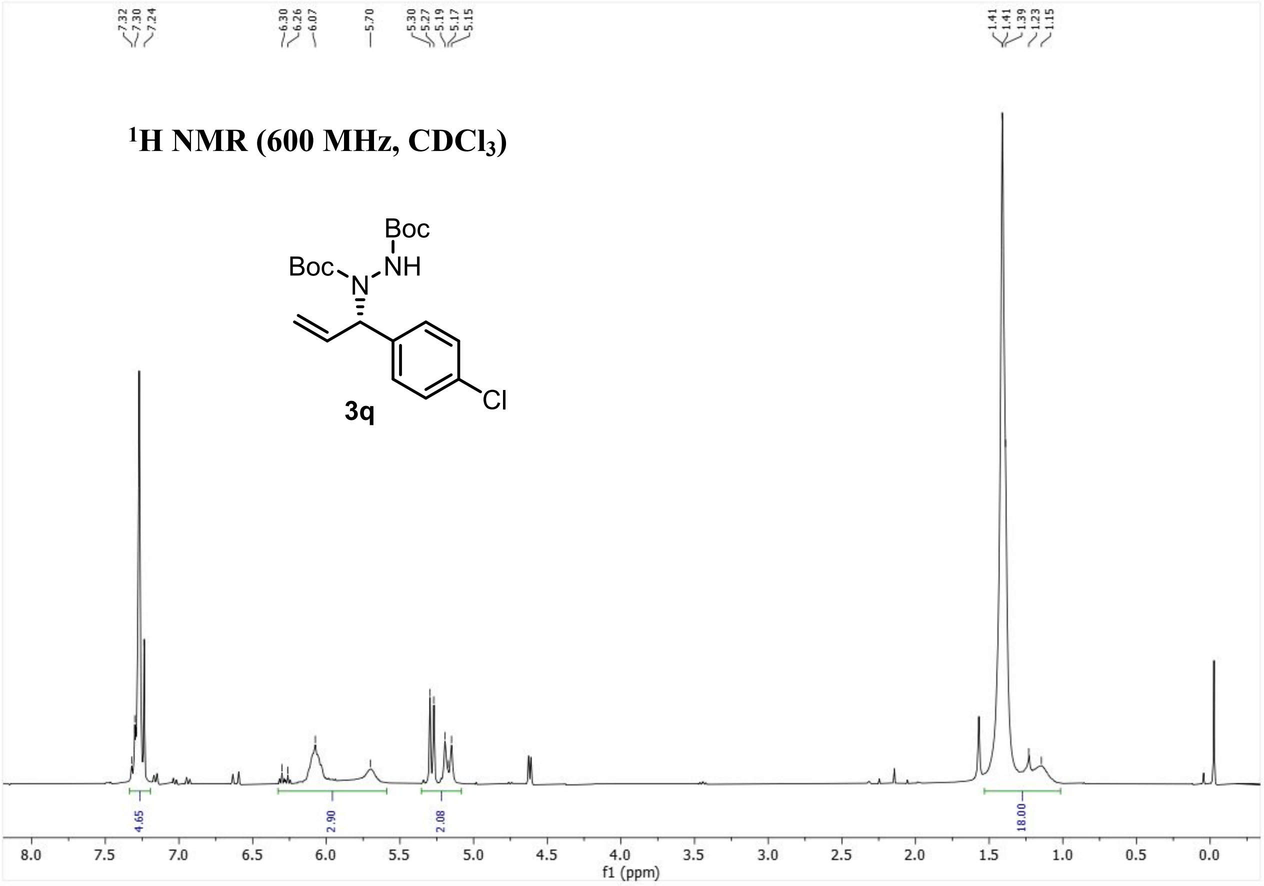

159.02
154.86
141.82
139.63
135.48
130.95
130.10
129.92
129.87
129.38
128.42
127.96
127.67
127.61
126.29
120.68
117.67
114.05
114.02
113.97
113.71
113.69
81.53
80.86
79.82
63.93
55.28
31.93
30.33
29.70
28.24
28.13
22.70
14.13
0.00
¹³C NMR (151 MHz, CDCl₃)
f1 (ppm)

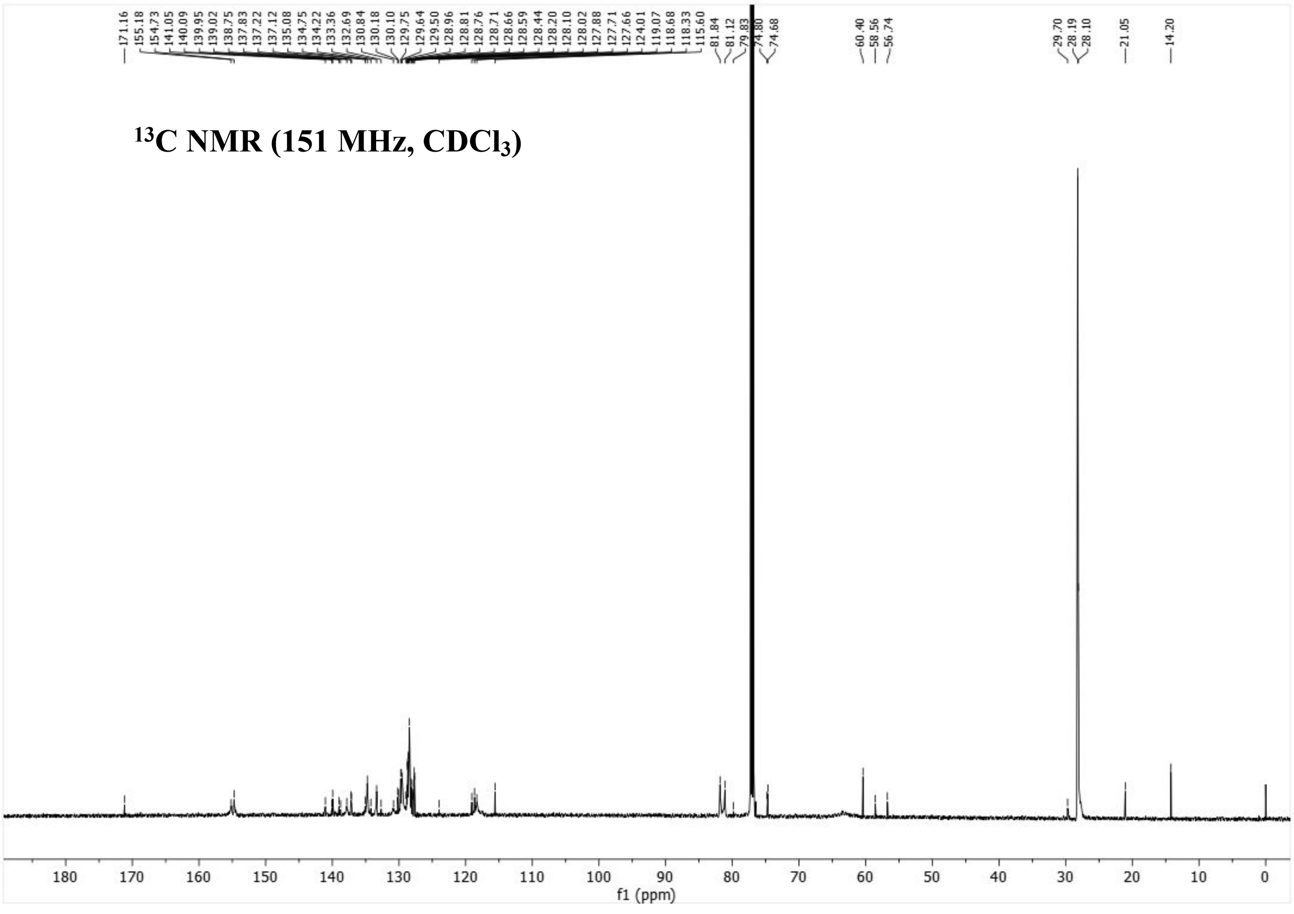


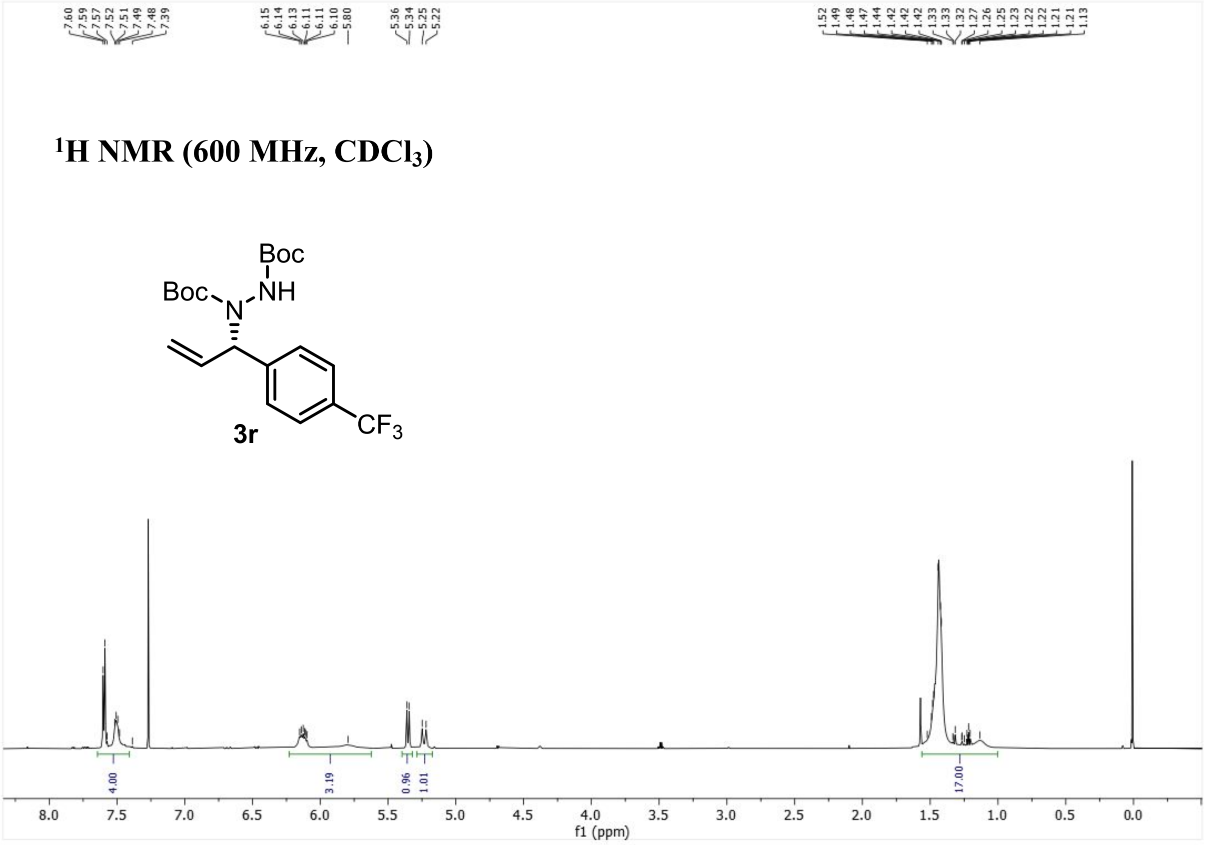
^{1}H NMR (600 MHz, $CDCl_3$)

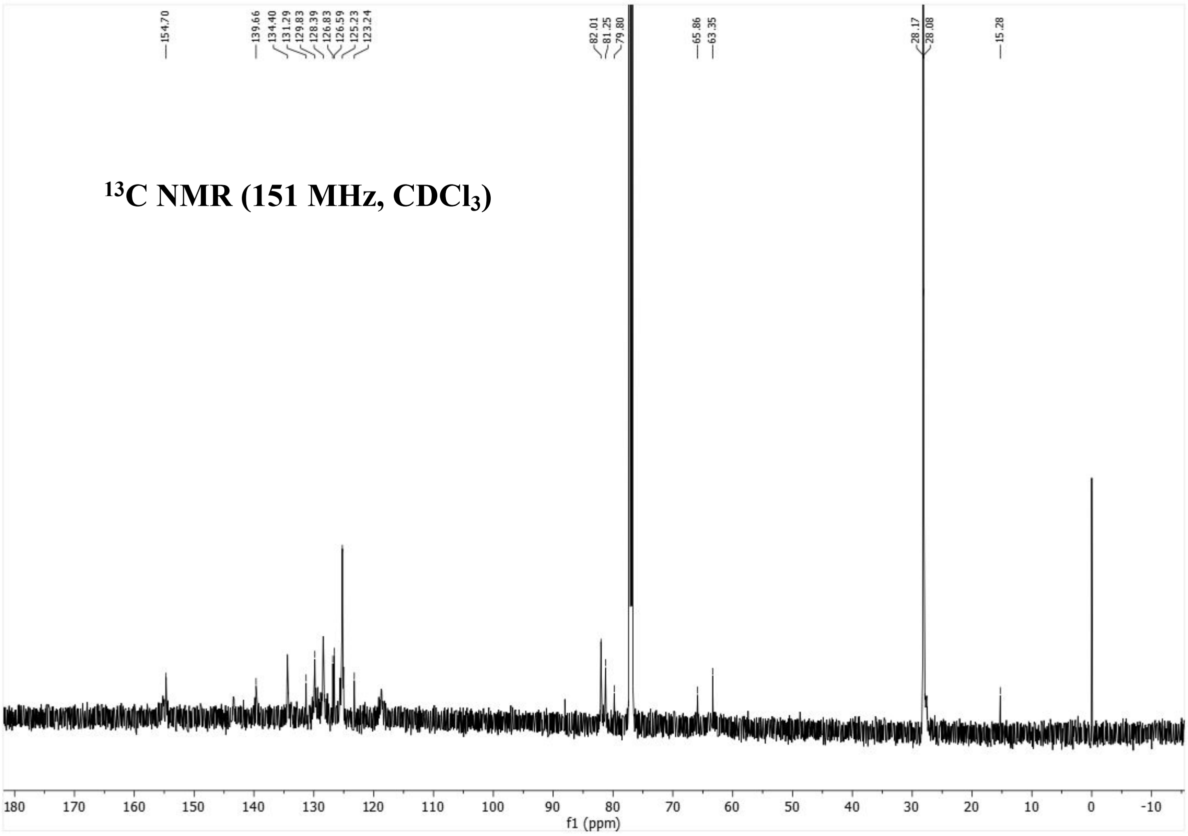


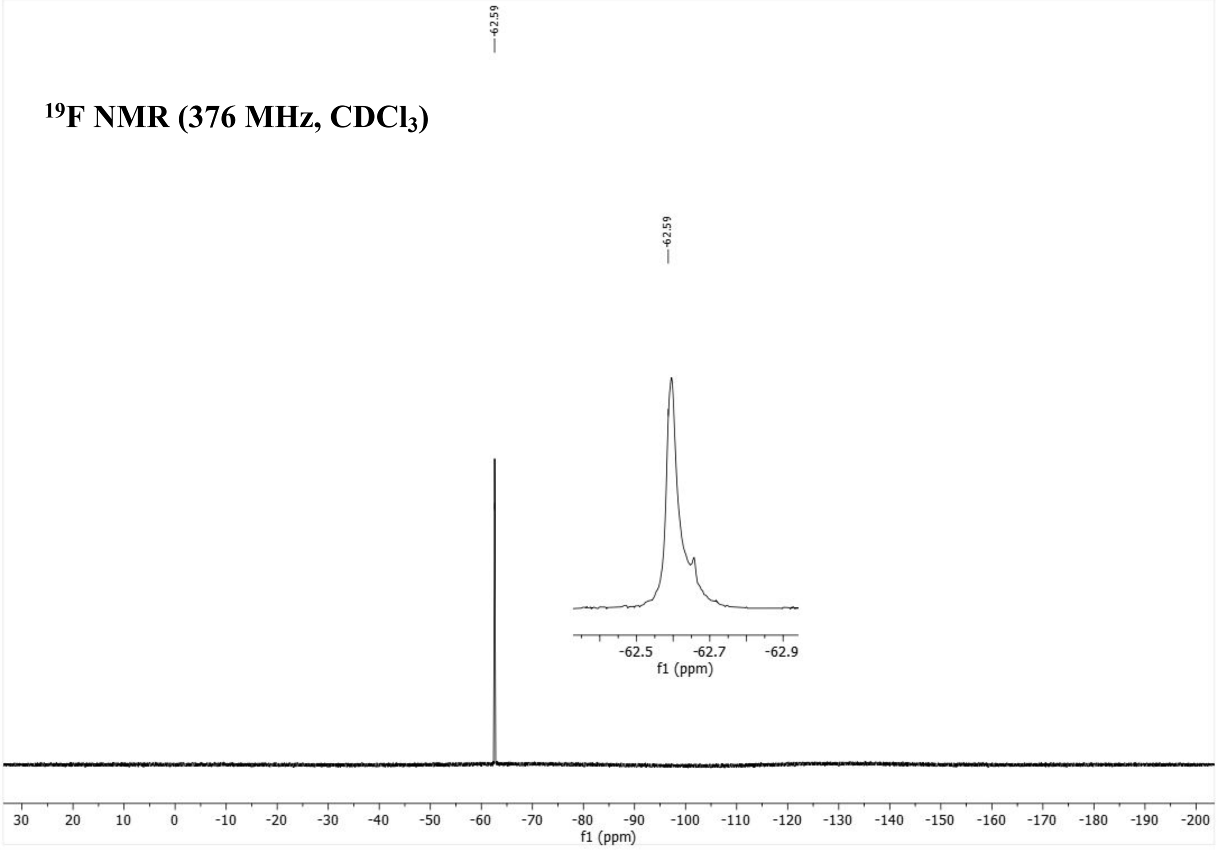
^{13}C NMR (151 MHz, $CDCl_3$)

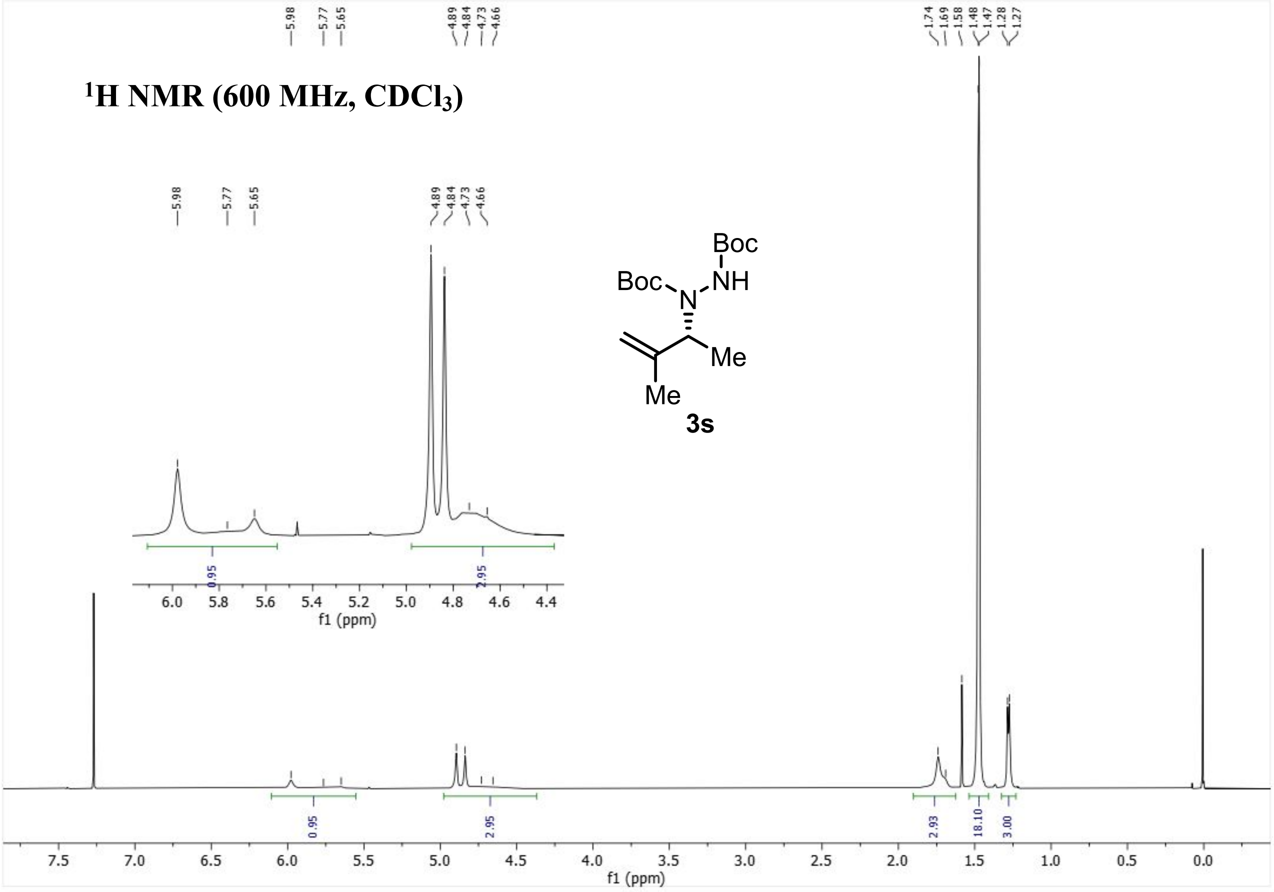

7.32
7.30
7.24
6.30
6.26
6.07
5.70
5.30
5.27
5.19
5.17
5.15
1.41
1.41
1.39
1.23
1.15
^{1}H NMR (600 MHz, CDCl$_3$)
Boc
NH
Boc
N
Cl
3q
4.65
2.90
2.08
18.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

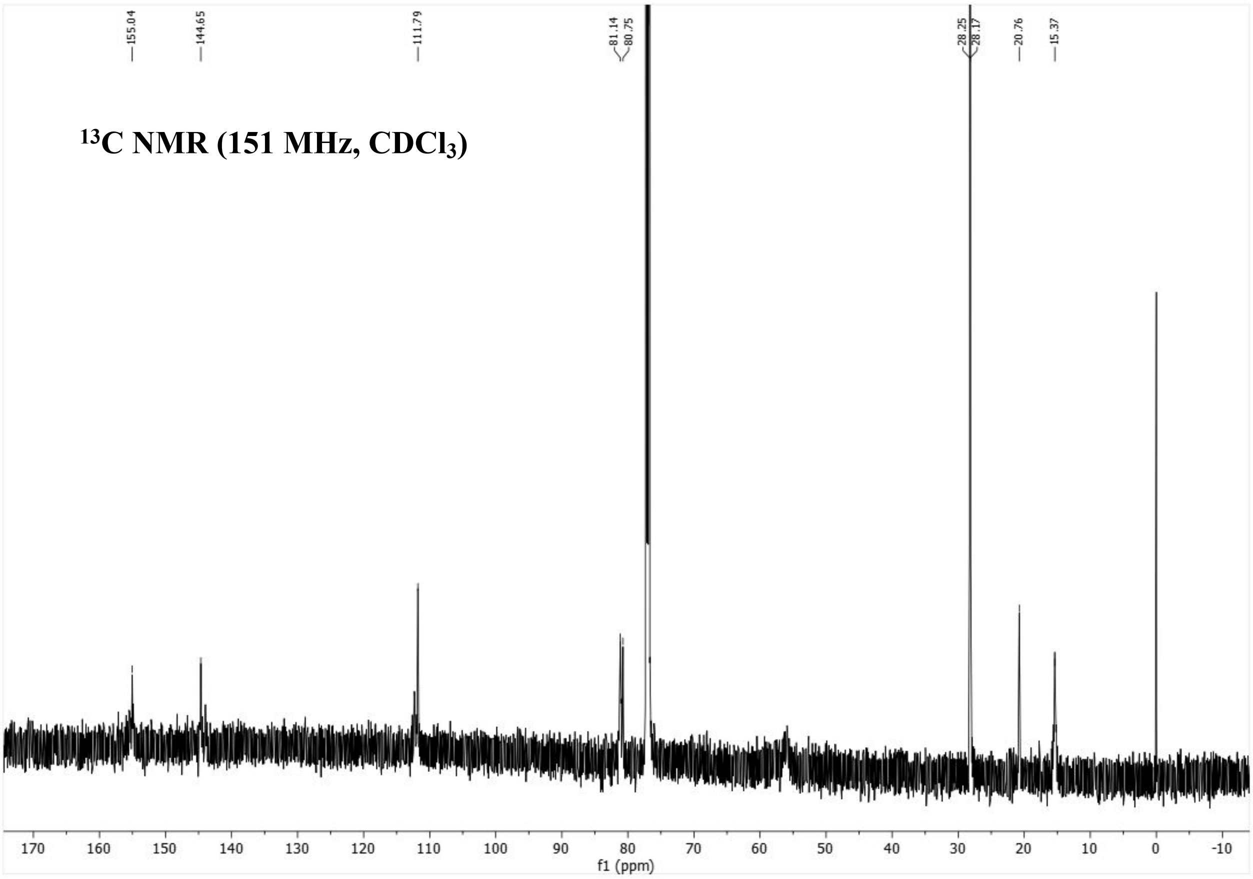

171.16
155.18
154.73
141.05
140.09
139.95
139.02
138.75
137.83
137.22
137.12
135.08
134.75
134.22
133.36
132.69
130.84
130.18
130.10
129.75
129.64
129.50
128.96
128.81
128.76
128.71
128.66
128.59
128.44
128.20
128.10
128.02
127.88
127.71
127.66
124.01
119.07
118.68
118.33
115.60
81.84
81.12
79.83
74.80
74.68
60.40
58.56
56.74
29.70
28.19
28.10
21.05
14.20
^{13}C NMR (151 MHz, CDCl$_3$)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

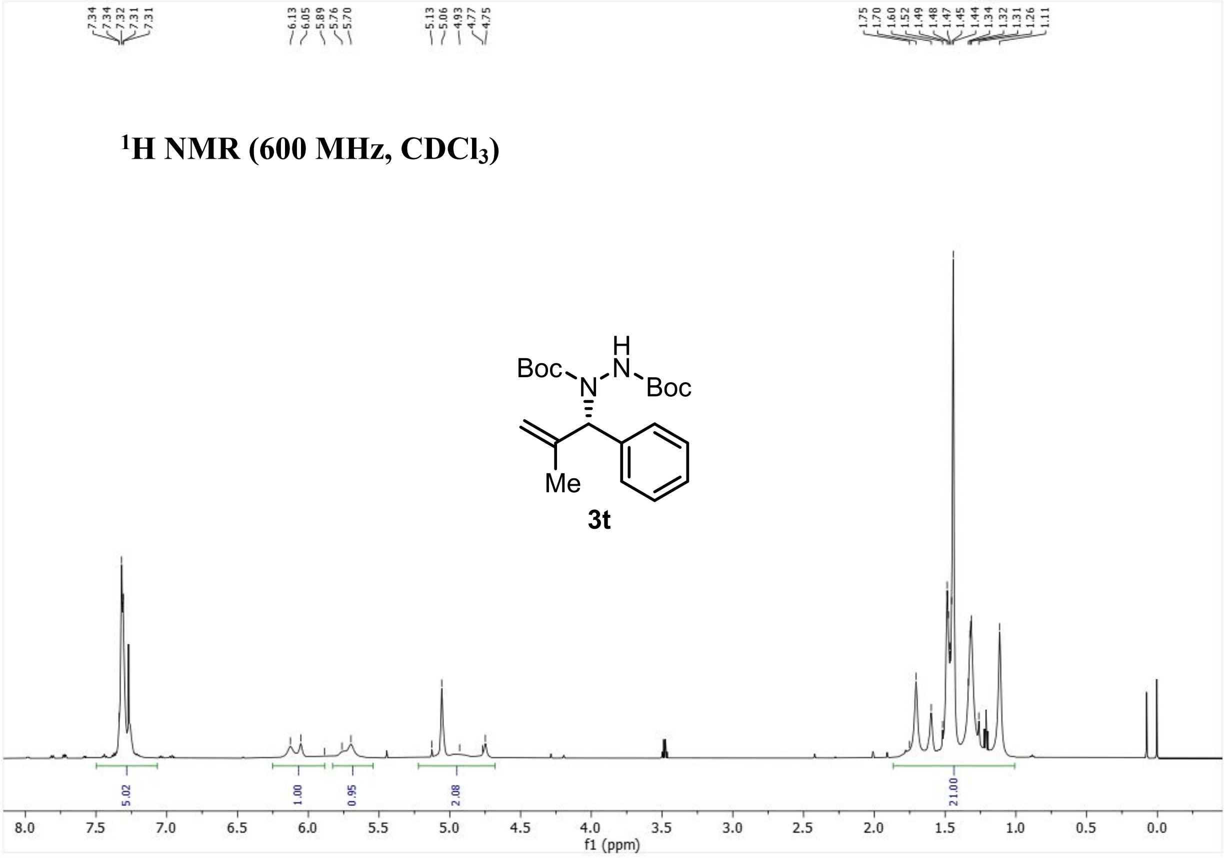

7.60
7.59
7.57
7.52
7.51
7.49
7.48
7.39
6.15
6.14
6.13
6.11
6.11
6.11
6.10
5.80
5.36
5.34
5.25
5.22
1.52
1.49
1.48
1.47
1.44
1.42
1.42
1.42
1.33
1.33
1.32
1.27
1.26
1.25
1.23
1.22
1.22
1.21
1.21
1.13
^{1}H NMR (600 MHz, CDCl$_3$)
Boc
Boc
N
NH
CF$_3$
3r
4.00
3.19
0.96
1.01
17.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

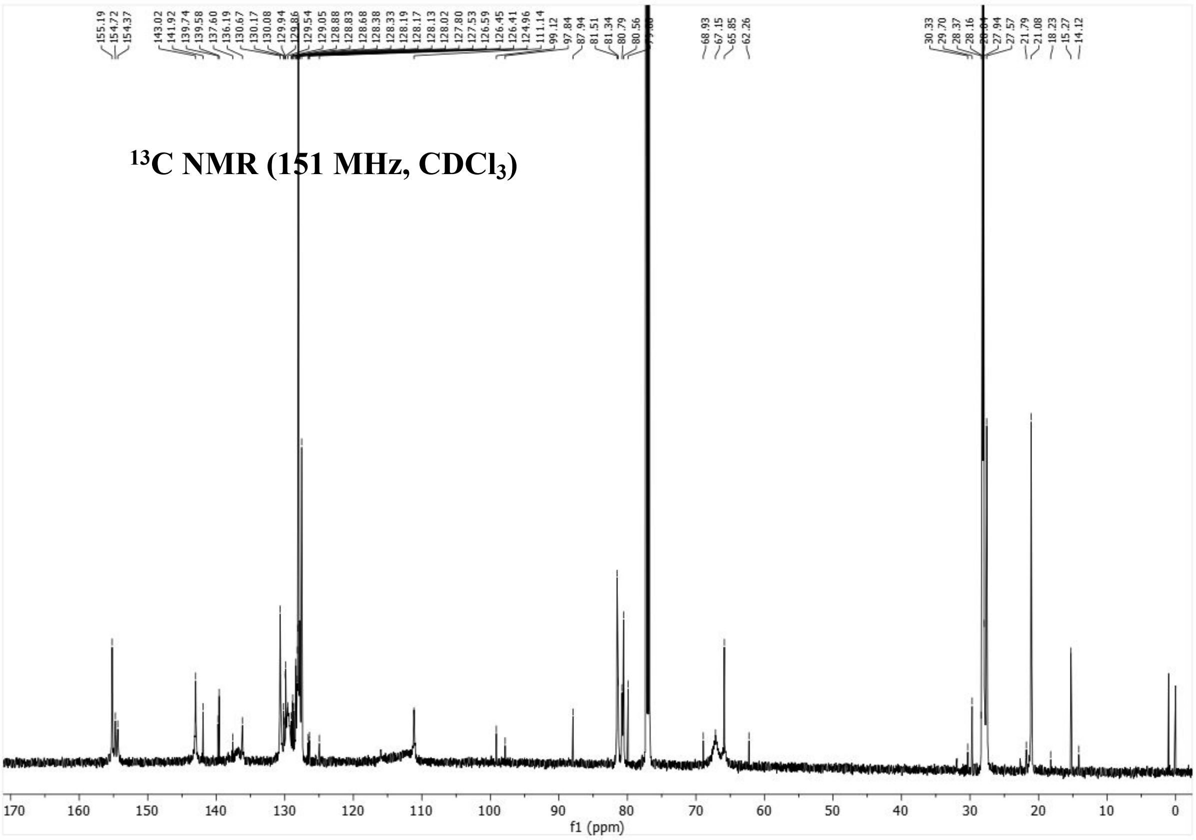

154.70
139.66
134.40
131.29
129.83
128.39
126.83
126.59
125.23
123.24
82.01
81.25
79.80
65.86
63.35
28.17
28.08
15.28
^{13}C NMR (151 MHz, CDCl$_3$)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

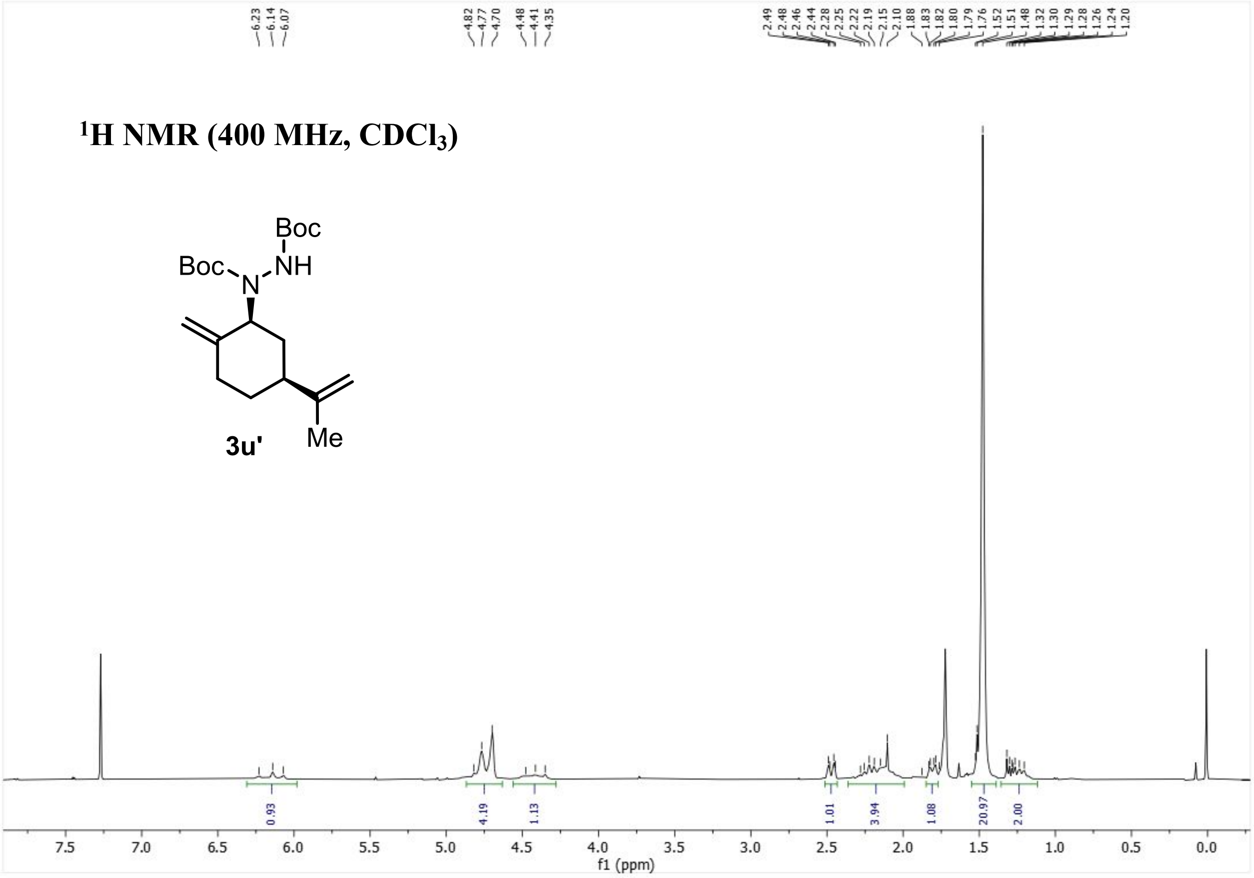

-62.59
^{19}F NMR (376 MHz, CDCl$_3$)
-62.59
-62.5
-62.7
-62.9
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

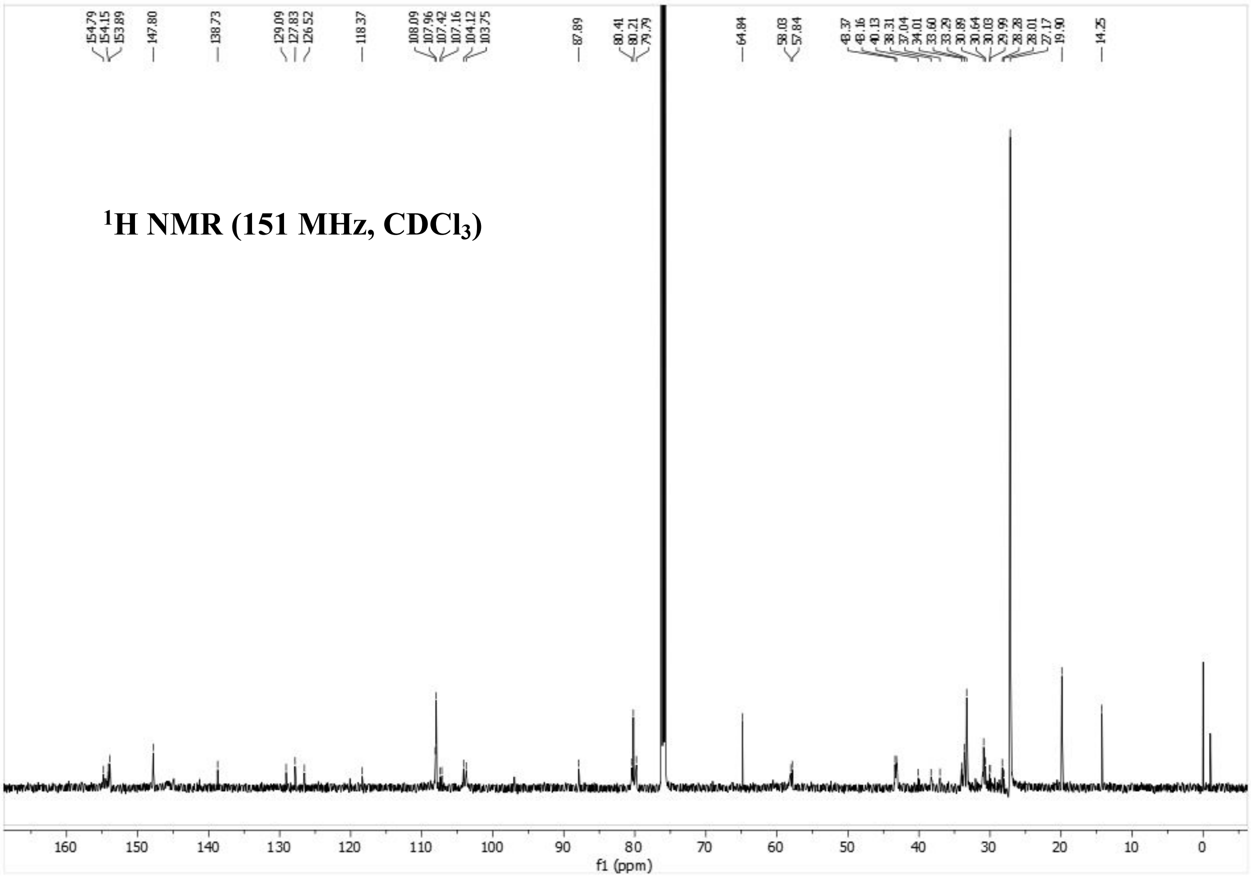

1H NMR (600 MHz, CDCl3)
5.98
5.77
5.65
4.89
4.84
4.73
4.66
1.74
1.69
1.58
1.48
1.47
1.28
1.27
Boc
Boc
NH
N
Me
Me
3s
0.95
2.95
2.93
18.10
3.00
f1 (ppm)

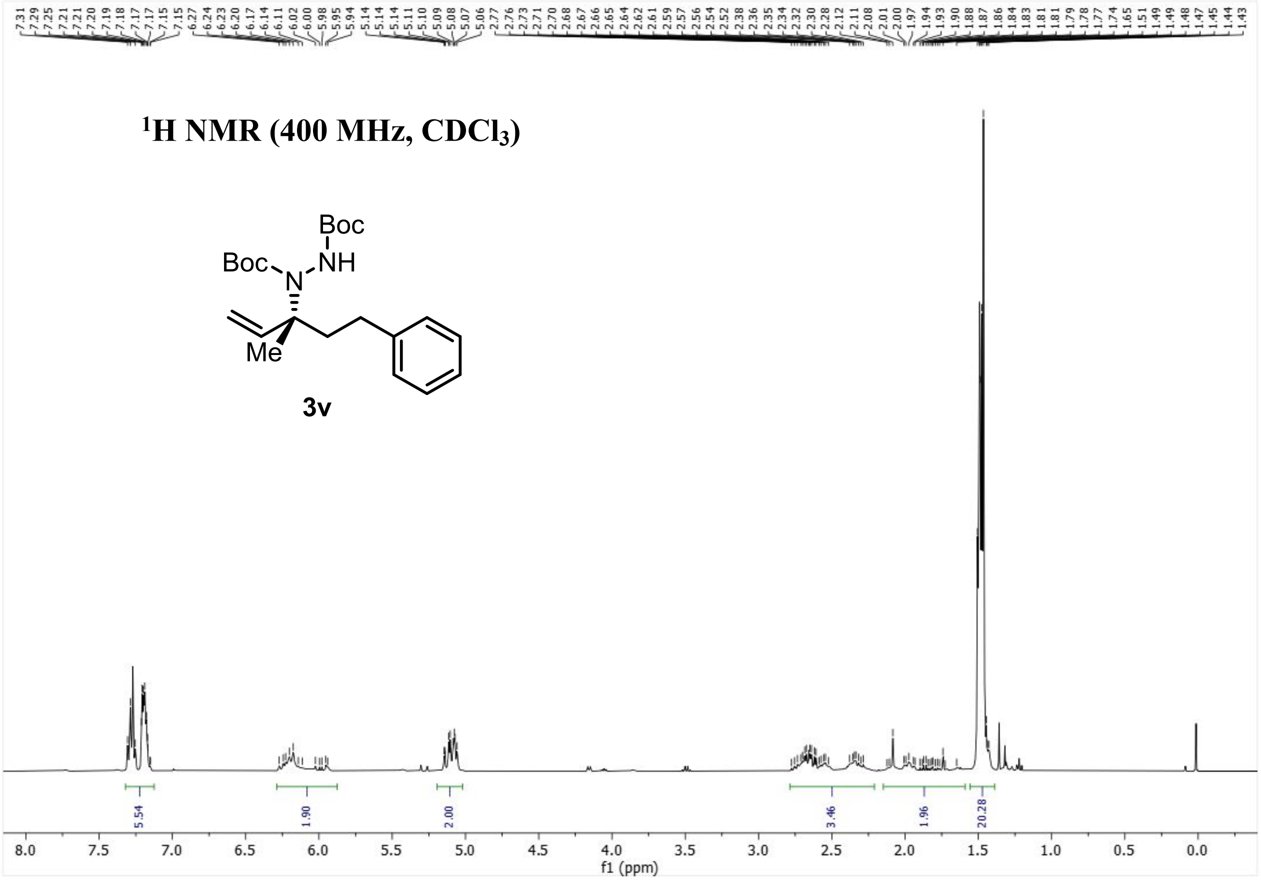

13C NMR (151 MHz, CDCl3)
155.04
144.65
111.79
81.14
80.75
28.25
28.17
20.76
15.37
f1 (ppm)

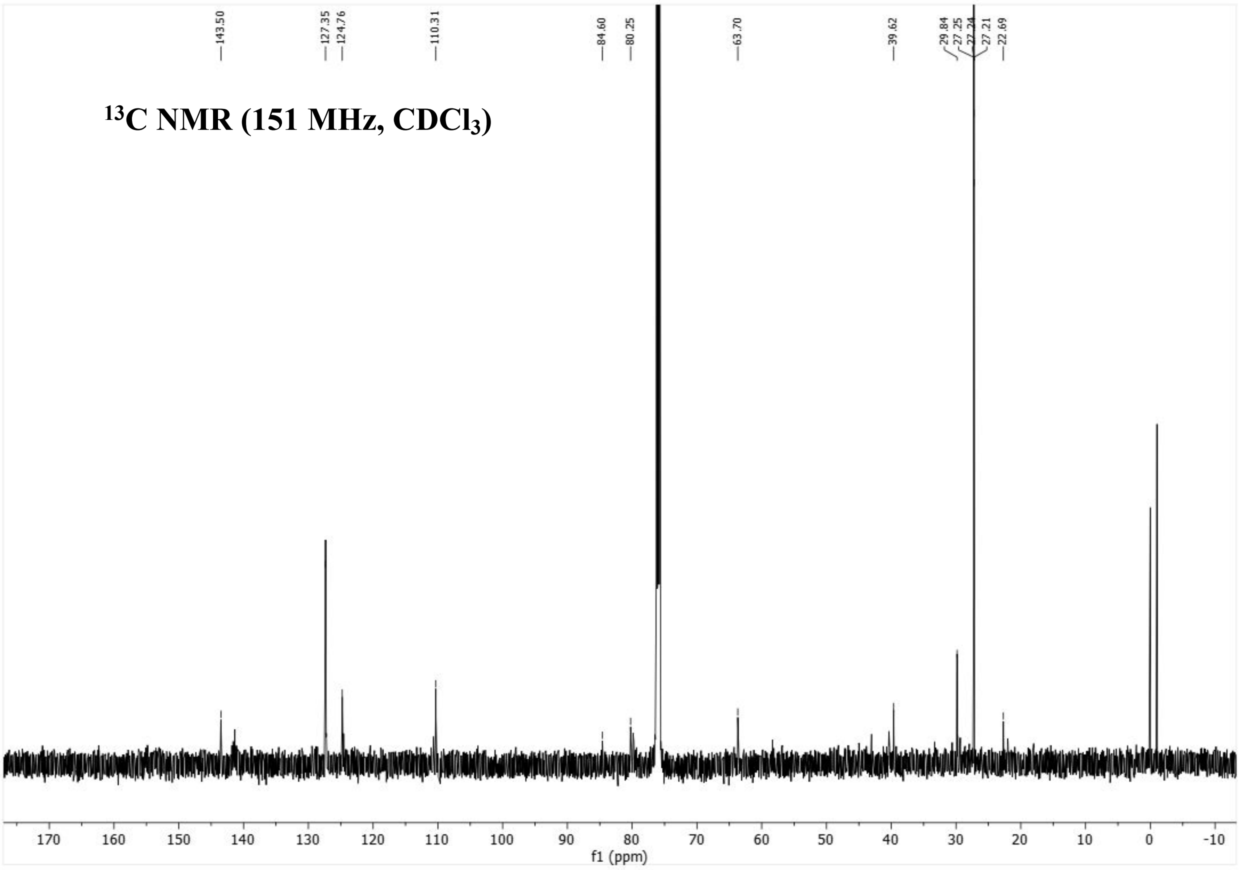

7.34
7.34
7.32
7.31
7.31
6.13
6.05
5.89
5.76
5.70
5.13
5.06
4.93
4.77
4.75
1.75
1.70
1.60
1.52
1.49
1.48
1.47
1.45
1.44
1.34
1.32
1.31
1.26
1.11
^{1}H NMR (600 MHz, CDCl$_3$)
Boc
H
N
N
Boc
Me
3t
5.02
1.00
0.95
2.08
21.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

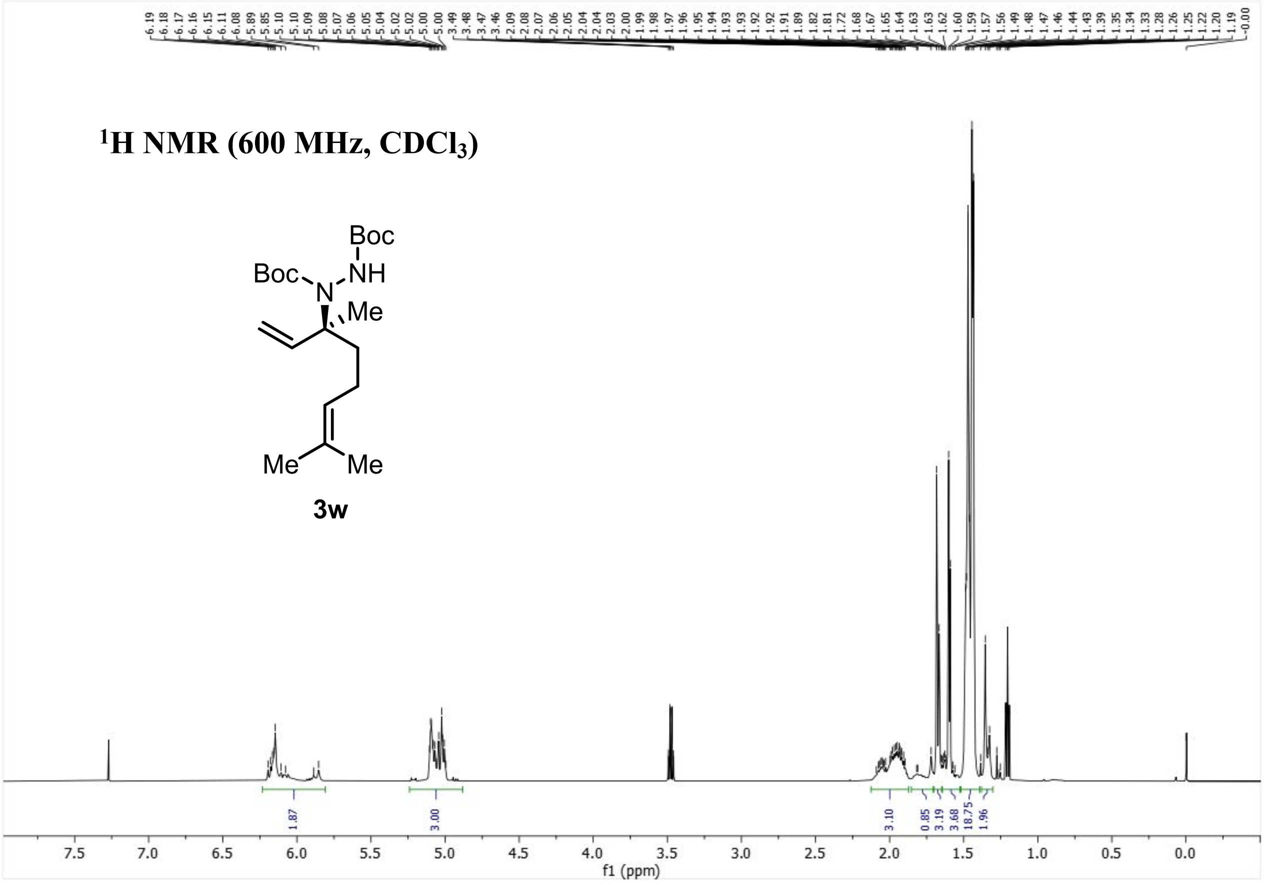

155.19
154.72
154.37
143.02
141.92
139.74
139.58
137.60
136.19
130.67
130.17
130.08
129.94
129.86
129.54
129.05
128.88
128.83
128.68
128.38
128.33
128.19
128.17
128.13
128.02
127.80
127.53
126.59
126.45
126.41
124.96
111.14
99.12
97.84
87.94
81.51
81.34
80.79
80.56
68.93
67.15
65.85
62.26
30.33
29.70
28.37
28.16
27.94
27.57
21.79
21.08
18.23
15.27
14.12
^{13}C NMR (151 MHz, CDCl$_3$)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


6.23
6.14
6.07
4.82
4.77
4.70
4.48
4.41
4.35
2.49
2.48
2.46
2.44
2.28
2.25
2.22
2.19
2.15
2.10
1.88
1.83
1.82
1.80
1.79
1.76
1.52
1.51
1.48
1.32
1.30
1.29
1.28
1.26
1.24
1.20
^{1}H NMR (400 MHz, CDCl$_3$)
Boc
Boc
N
NH
Me
3u'
0.93
4.19
1.13
1.01
3.94
1.08
20.97
2.00
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
f1 (ppm)


154.79
154.15
153.89
147.80
138.73
129.09
127.83
126.52
118.37
108.09
107.96
107.42
107.16
104.12
103.75
87.89
80.41
80.21
79.79
64.84
58.03
57.84
43.37
43.16
40.13
38.31
37.04
34.01
33.60
33.29
30.89
30.64
30.03
29.99
28.28
28.01
27.17
19.90
14.25
^{1}H NMR (151 MHz, CDCl$_3$)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

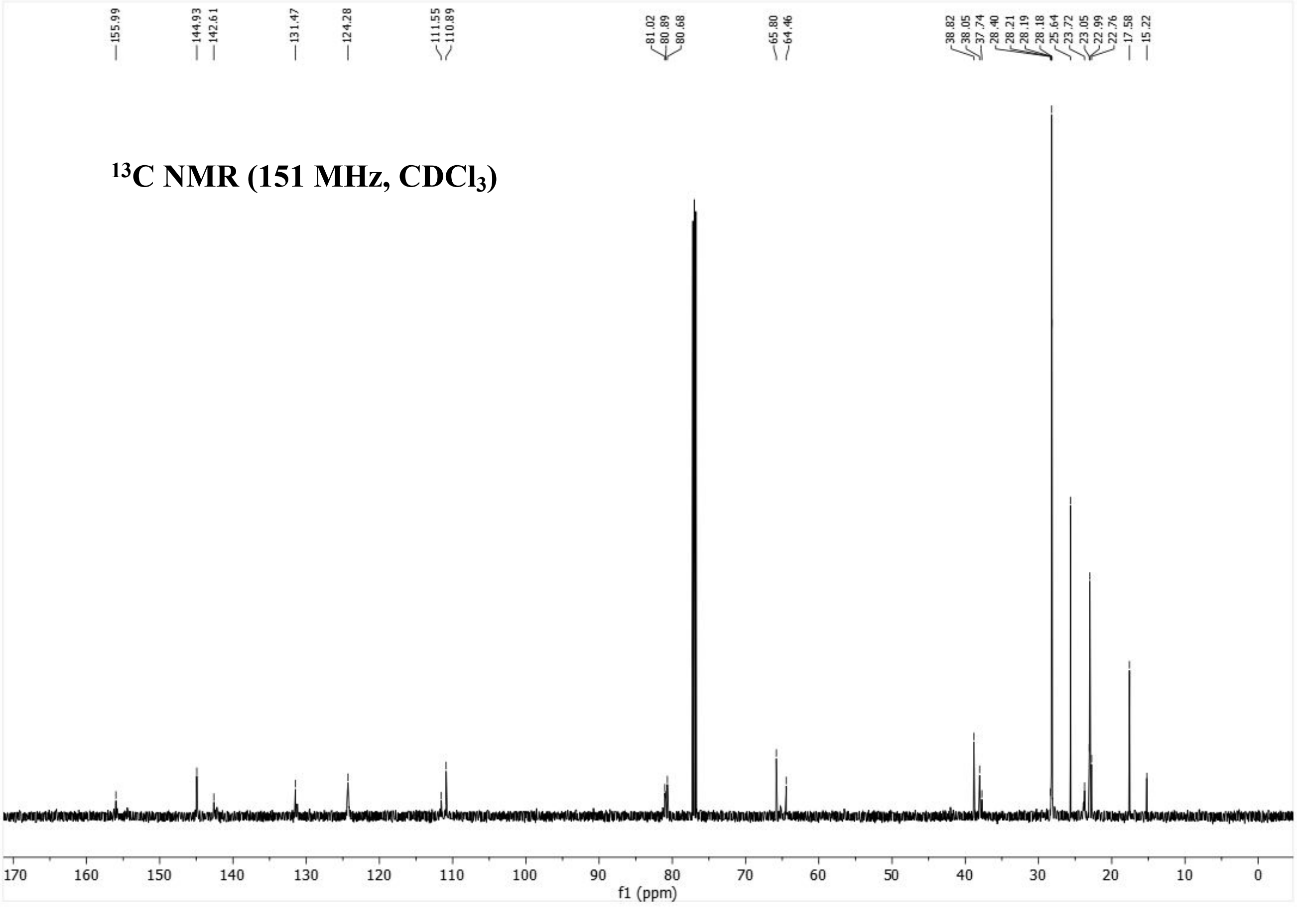

7.31
7.29
7.25
7.21
7.21
7.20
7.19
7.18
7.17
7.17
7.15
6.27
6.24
6.23
6.20
6.17
6.14
6.11
6.02
6.00
5.98
5.95
5.94
5.14
5.14
5.11
5.10
5.09
5.08
5.07
5.06
2.77
2.76
2.73
2.71
2.70
2.68
2.67
2.66
2.65
2.64
2.62
2.61
2.59
2.57
2.56
2.54
2.52
2.38
2.36
2.35
2.34
2.32
2.30
2.28
2.12
2.11
2.08
2.01
2.00
1.97
1.94
1.93
1.90
1.88
1.87
1.86
1.84
1.83
1.81
1.81
1.79
1.78
1.77
1.74
1.65
1.51
1.49
1.49
1.48
1.47
1.45
1.44
1.43
^{1}H NMR (400 MHz, CDCl$_3$)
Boc
NH
Boc
N
Me
3v
5.54
1.90
2.00
3.46
1.96
20.28
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
f1 (ppm)


143.50
127.35
124.76
110.31
84.60
80.25
63.70
39.62
29.84
27.25
27.24
27.21
22.69
^{13}C NMR (151 MHz, CDCl$_3$)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

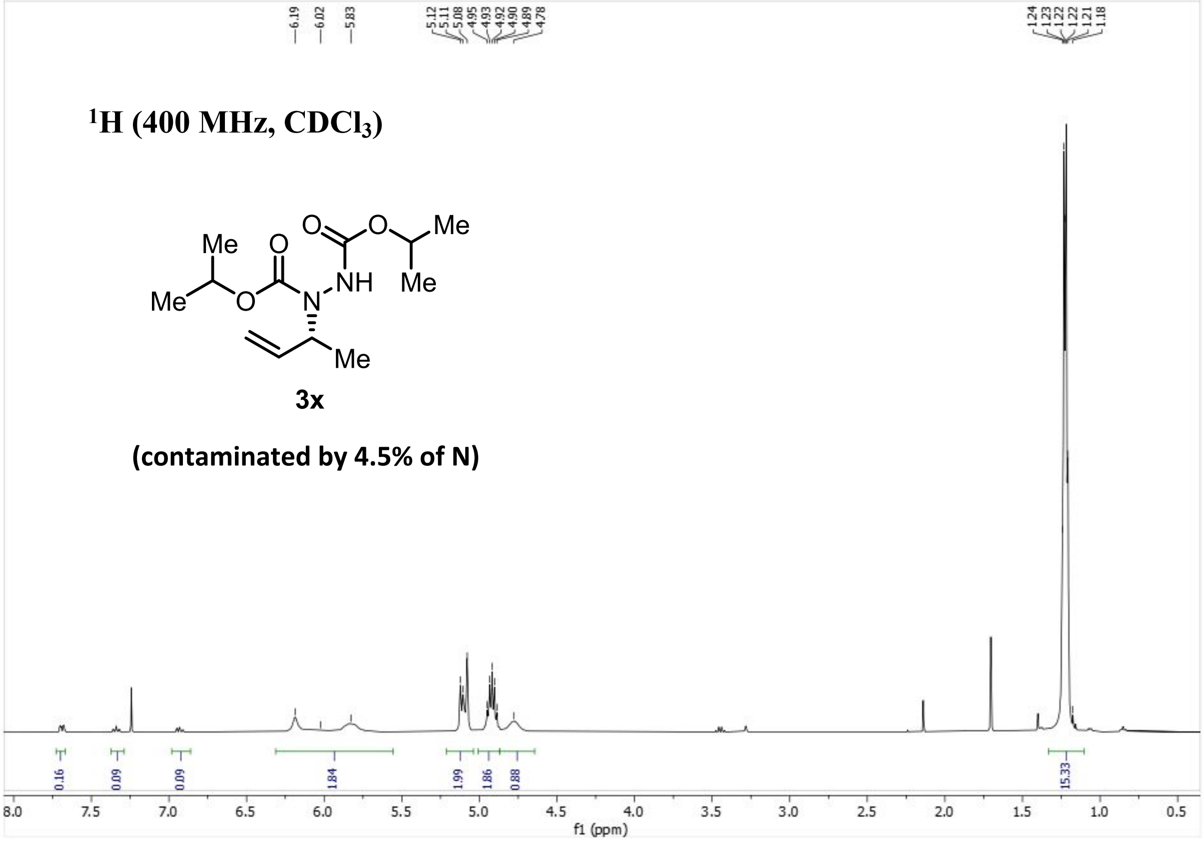


^{1}H NMR (600 MHz, CDCl$_3$)

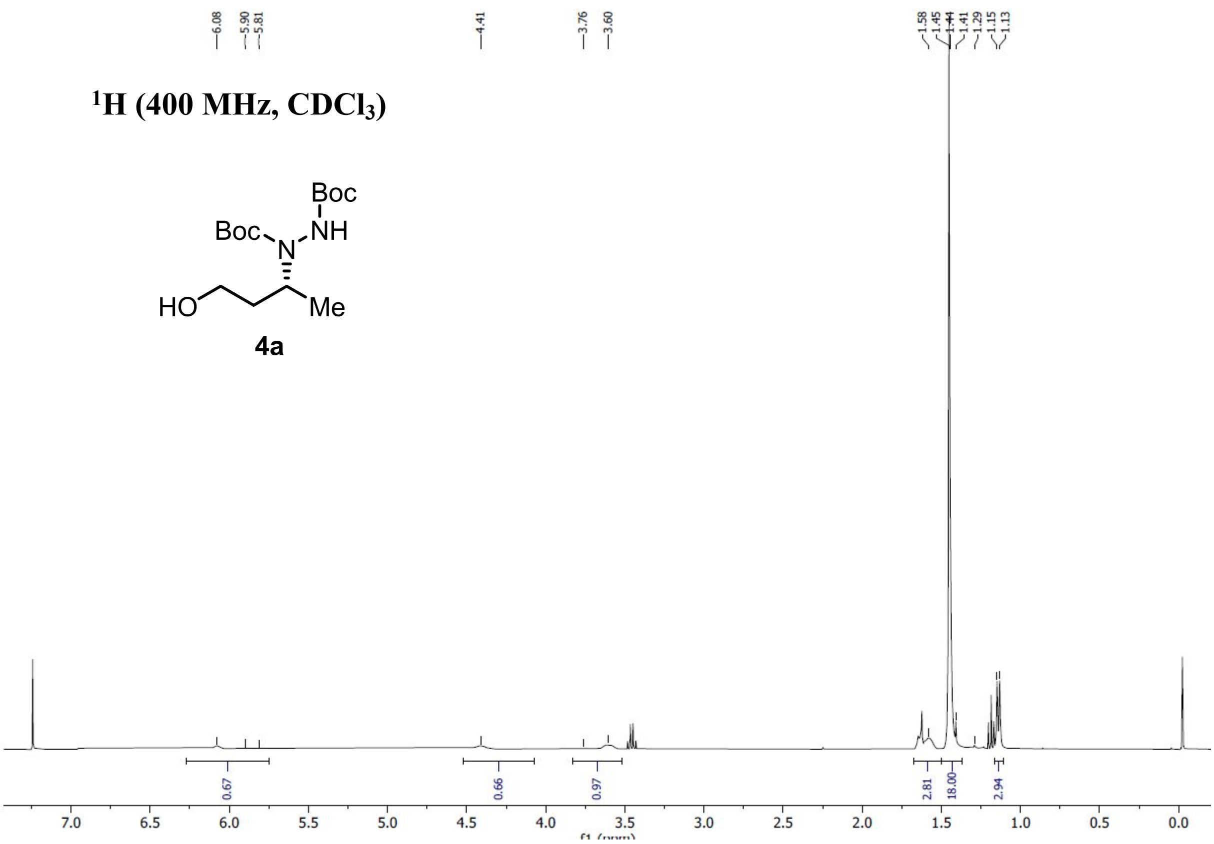
3w

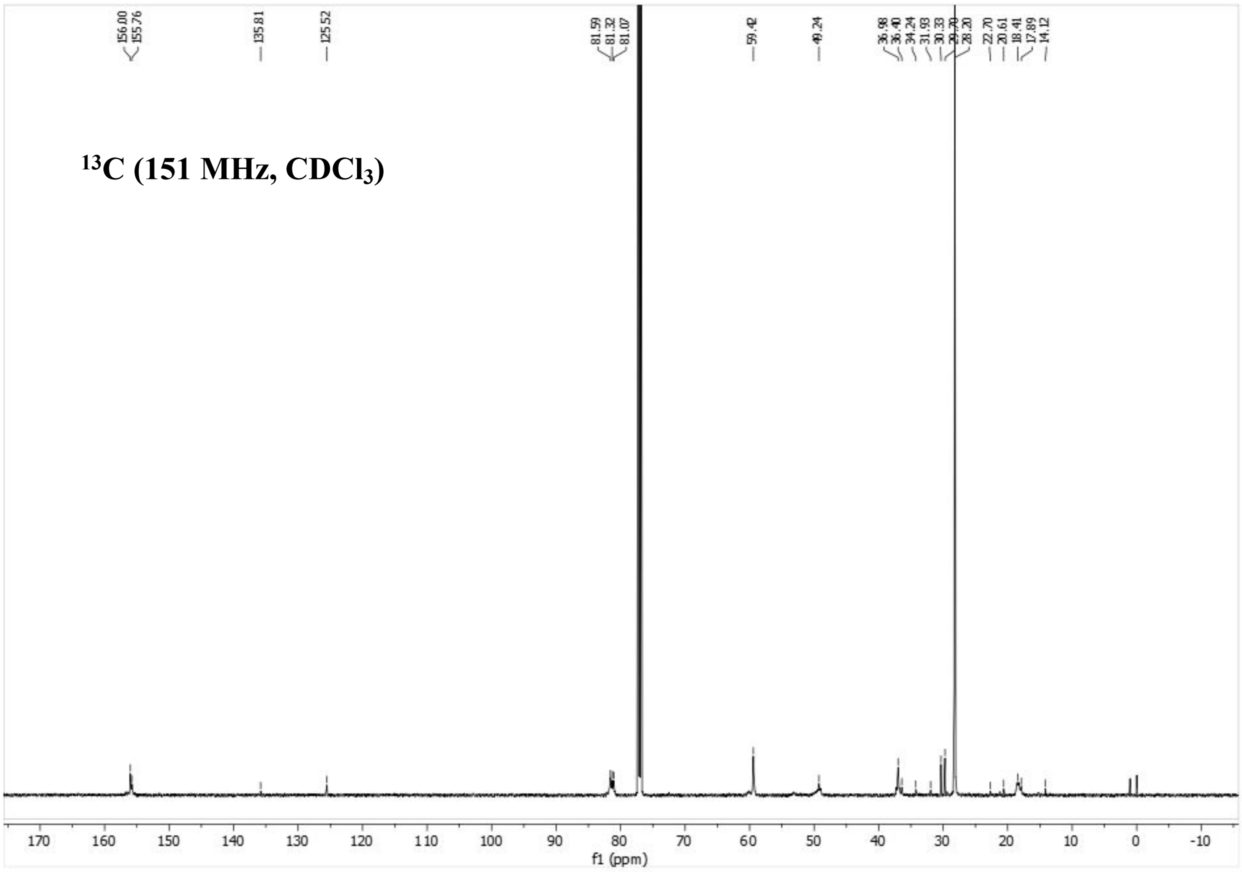


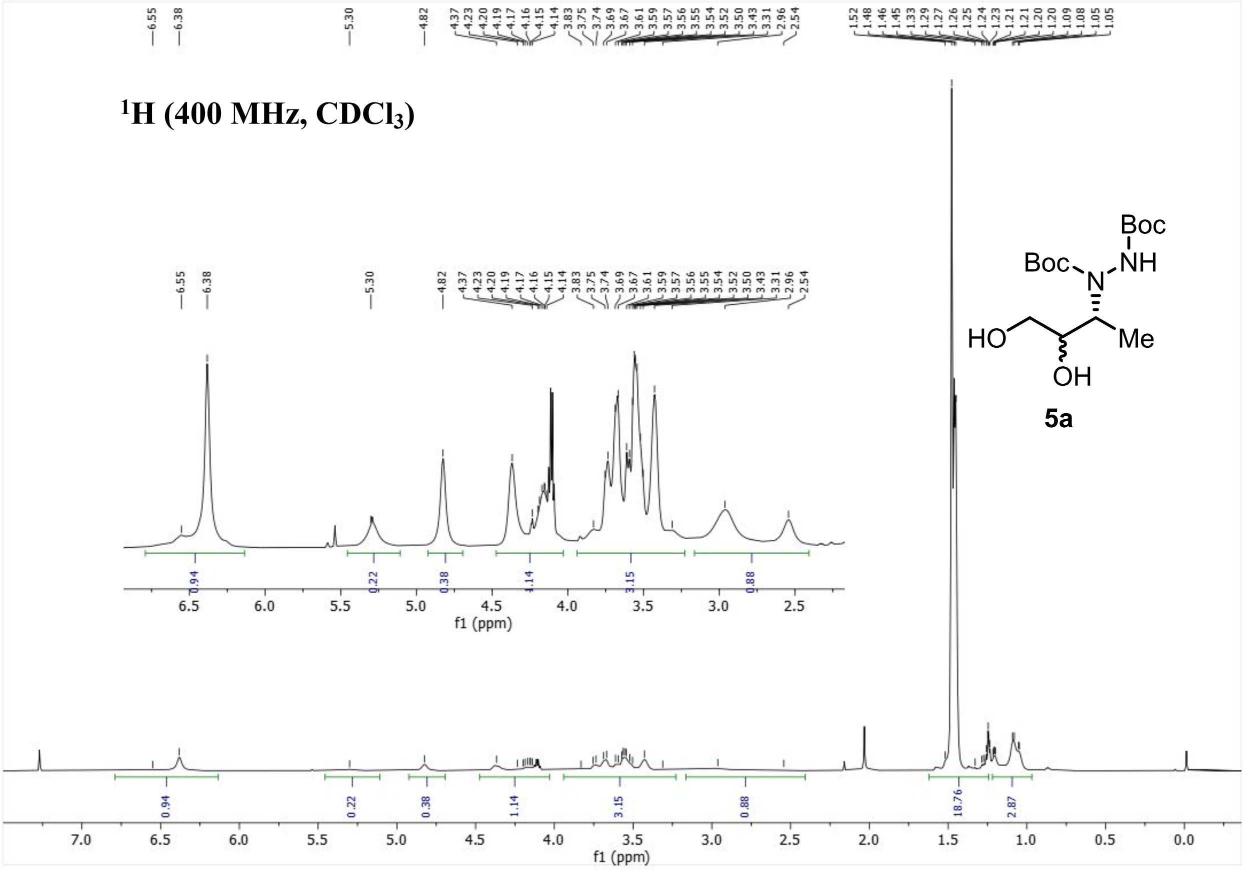
^{13}C NMR (151 MHz, CDCl$_3$)

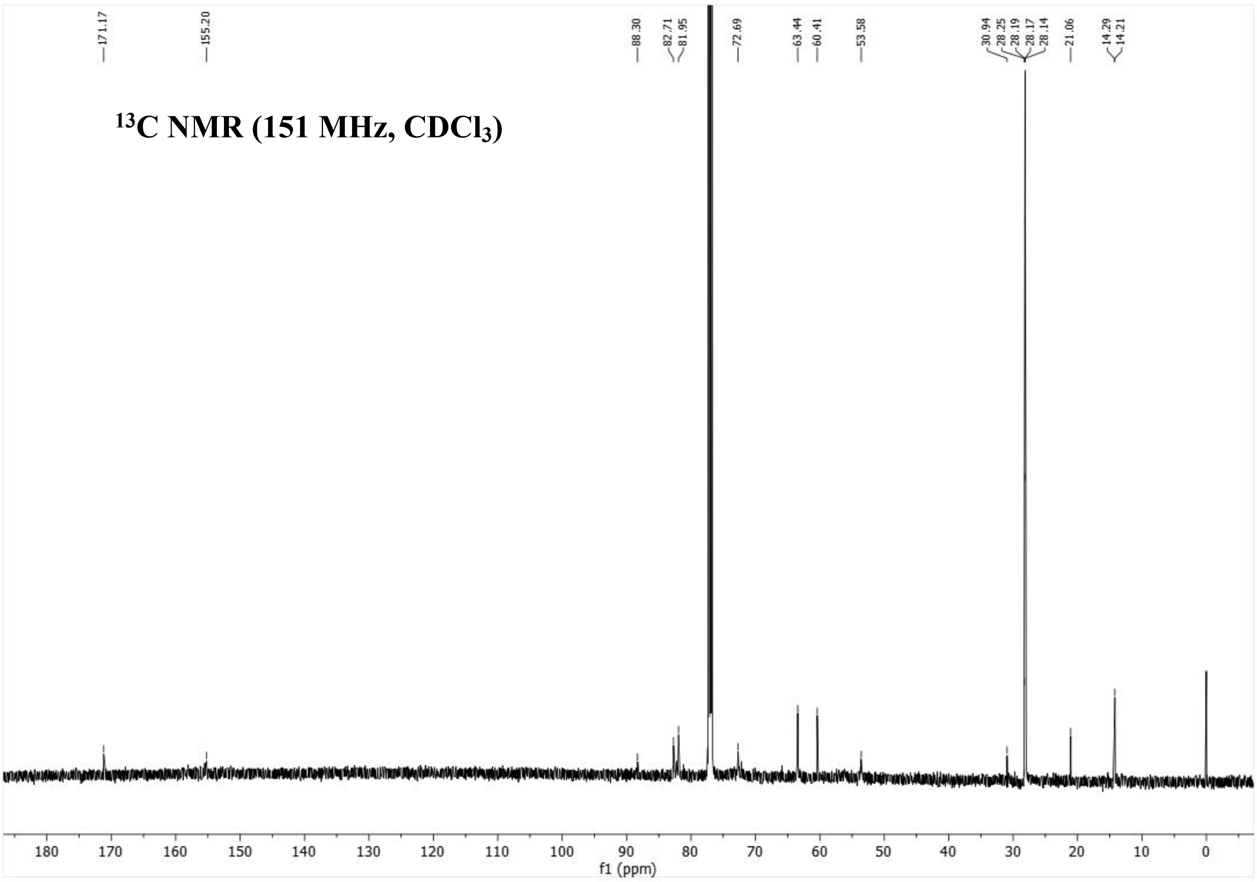


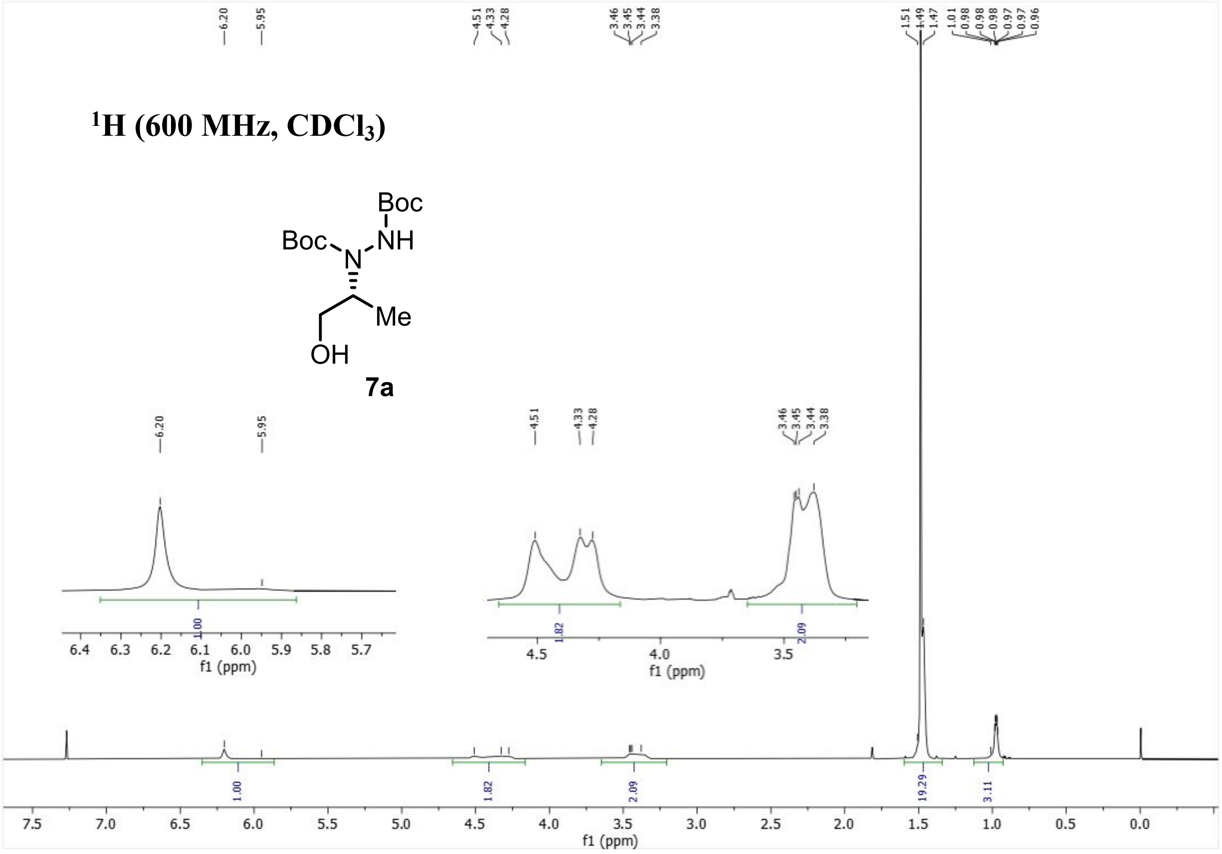
¹H (400 MHz, CDCl₃)
Me
O
O
O
Me
Me
O
N
NH
Me
Me
Me
3x
(contaminated by 4.5% of N)
6.19
6.02
5.83
5.12
5.11
5.08
4.95
4.93
4.92
4.90
4.89
4.78
1.24
1.23
1.22
1.22
1.22
1.21
1.18
0.16
0.09
0.09
1.84
1.99
1.86
0.88
15.33
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


6.08
5.90
5.81
4.41
3.76
3.60
1.58
1.45
1.44
1.41
1.29
1.15
1.13
^{1}H (400 MHz, CDCl$_3$)
Boc
Boc
NH
N
HO
Me
4a
0.67
0.66
0.97
2.81
18.00
2.94
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
f1 (ppm)


156.00
155.76
135.81
125.52
81.59
81.32
81.07
59.42
49.24
36.98
36.40
34.24
31.93
30.33
29.70
28.20
22.70
20.61
18.41
17.89
14.12
^{13}C (151 MHz, CDCl$_3$)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

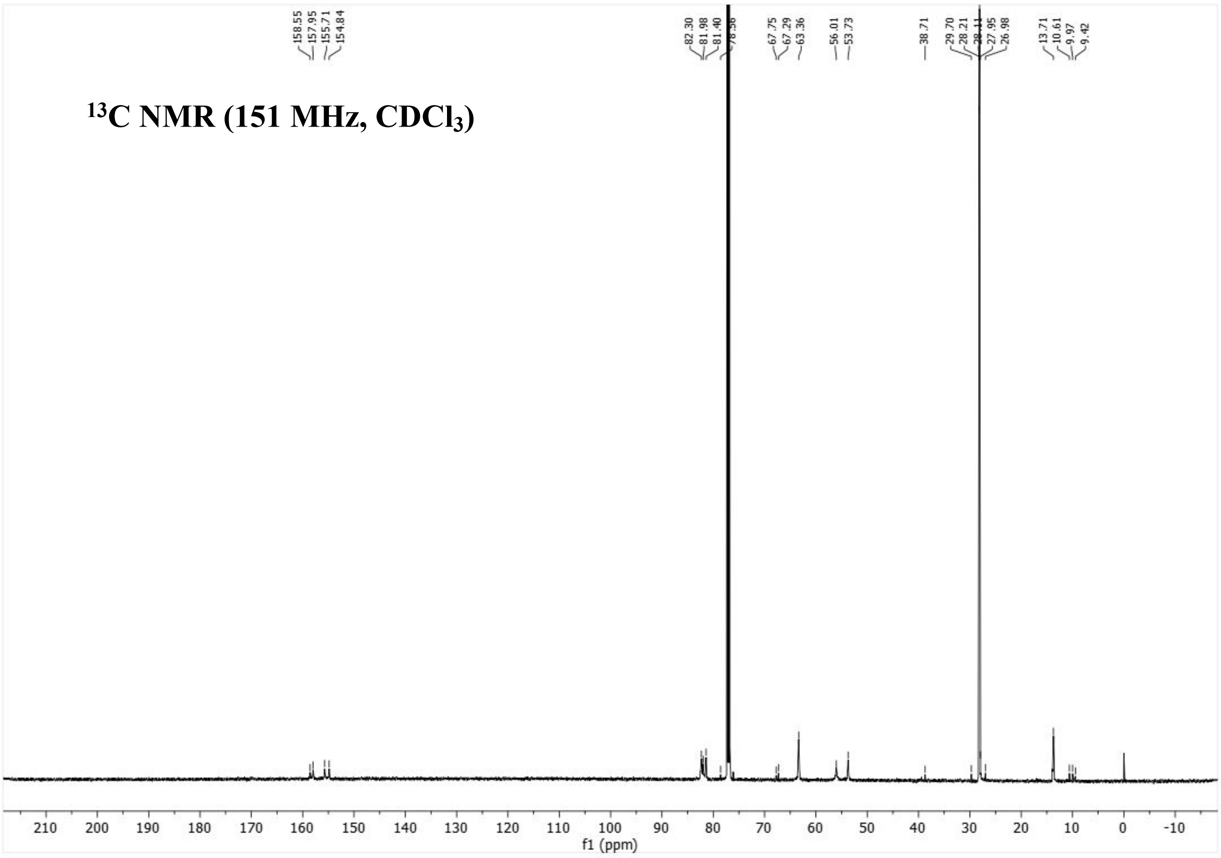

1H (400 MHz, CDCl3)
6.55
6.38
5.30
4.82
4.37
4.23
4.20
4.19
4.17
4.16
4.15
4.14
3.83
3.75
3.74
3.69
3.67
3.61
3.59
3.57
3.56
3.55
3.54
3.52
3.50
3.43
3.31
2.96
2.54
1.52
1.48
1.46
1.45
1.33
1.29
1.27
1.26
1.25
1.24
1.23
1.21
1.21
1.20
1.20
1.09
1.08
1.05
1.05
Boc
NH
Boc
N
HO
Me
OH
5a
0.94
0.22
0.38
1.14
3.15
0.88
18.76
2.87
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
f1 (ppm)


13C NMR (151 MHz, CDCl3)
171.17
155.20
88.30
82.71
81.95
72.69
63.44
60.41
53.58
30.94
28.25
28.19
28.17
28.14
21.06
14.29
14.21
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

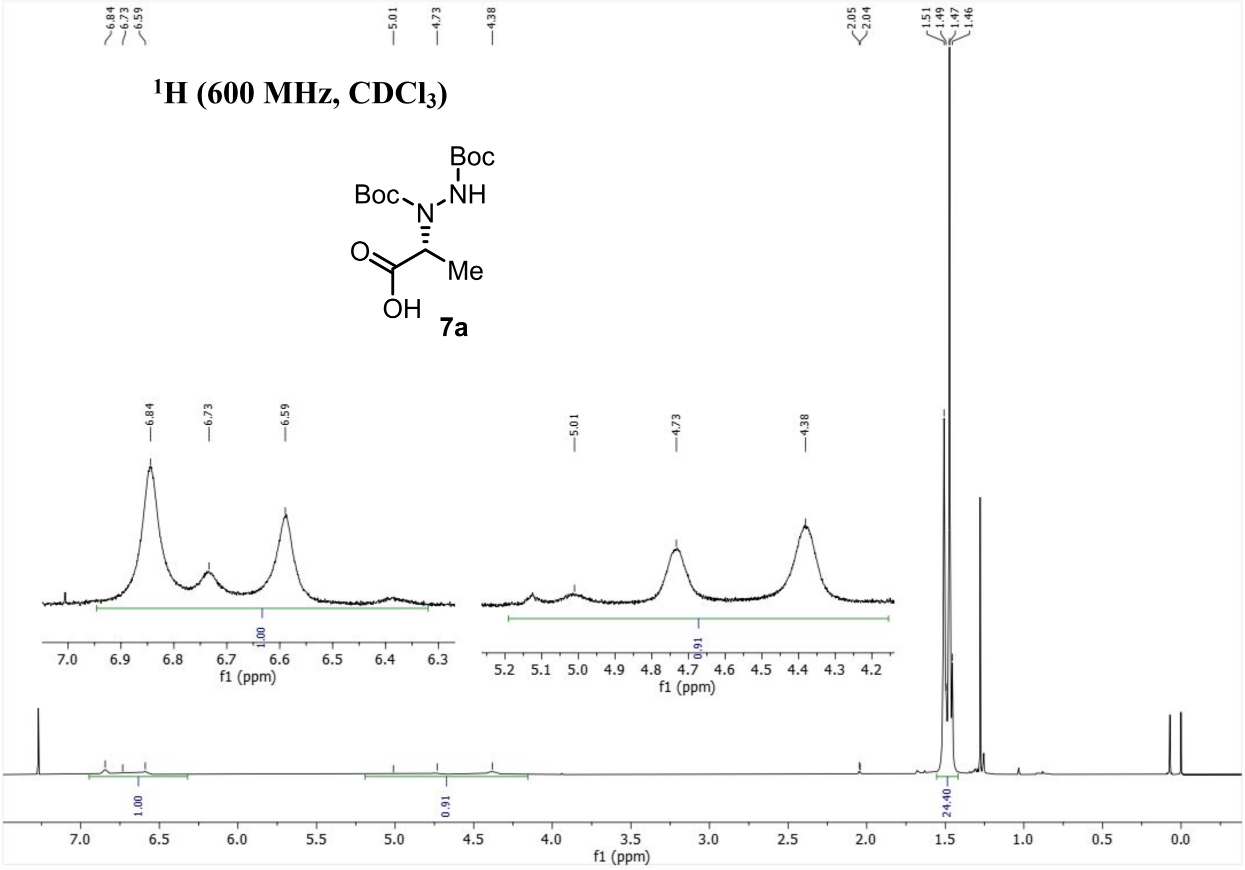


^{1}H (600 MHz, CDCl$_3$)

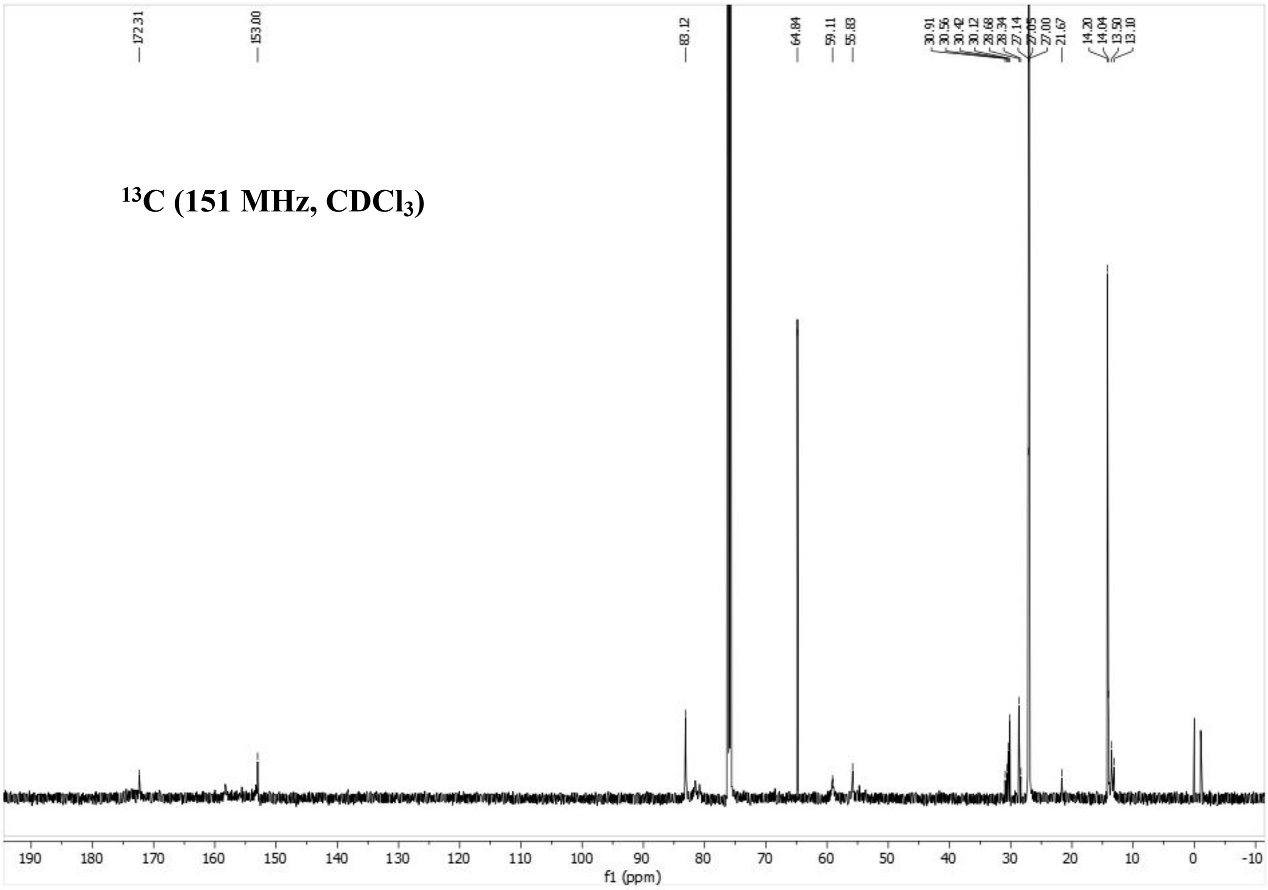
7a



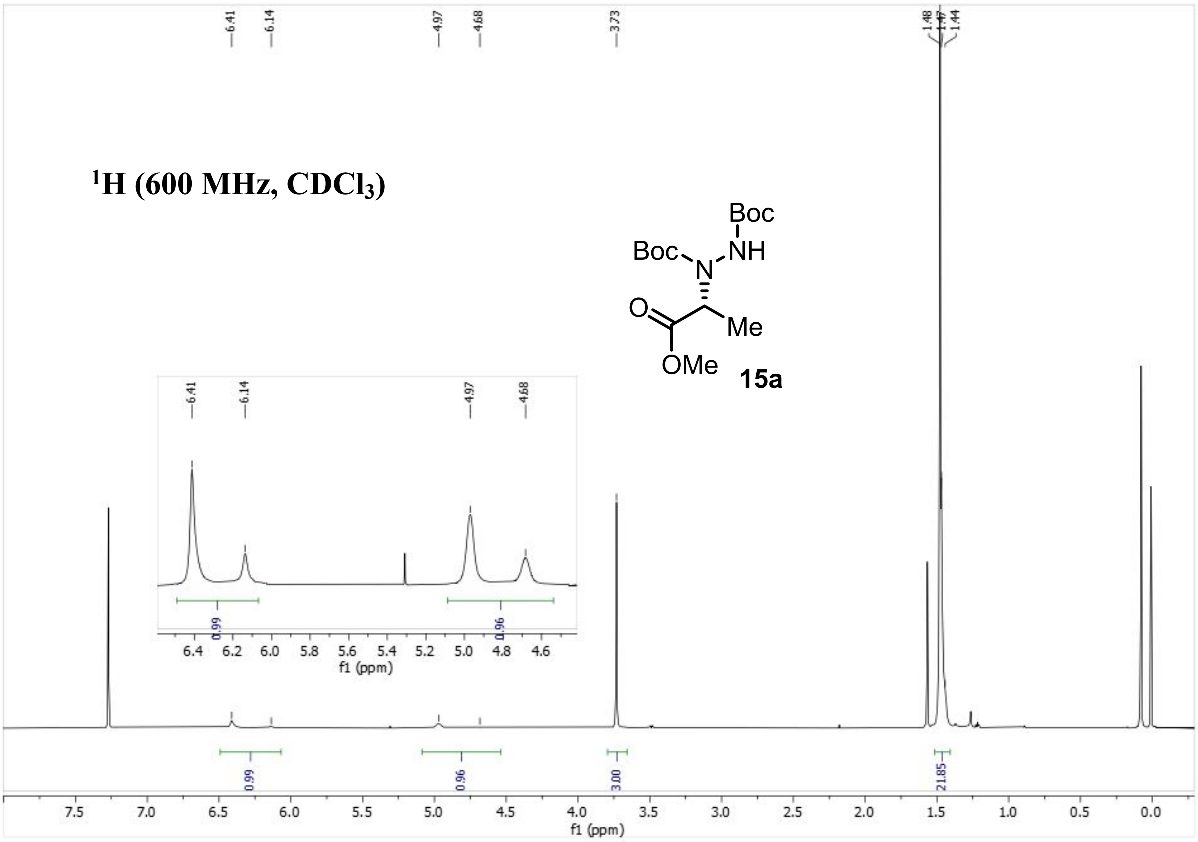
^{13}C NMR (151 MHz, CDCl$_3$)



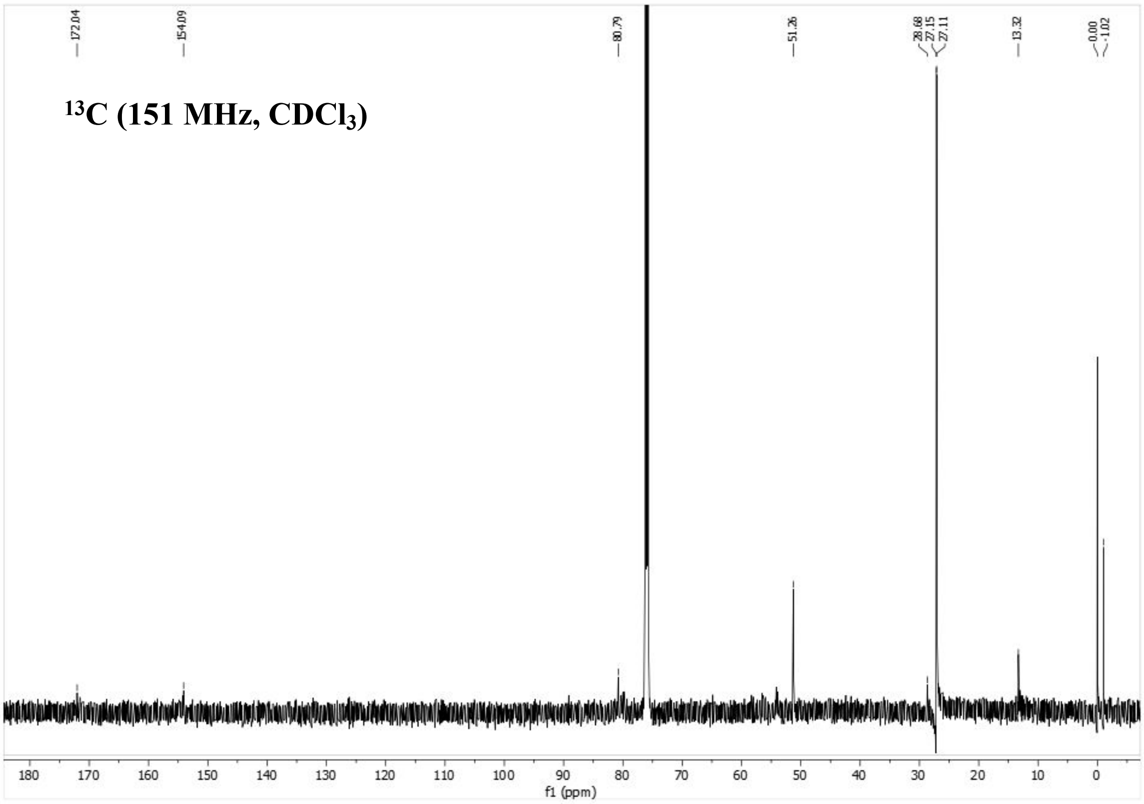
^{1}H (600 MHz, CDCl$_3$)
Boc
NH
Boc
N
O
Me
OH
7a
6.84
6.73
6.59
5.01
4.73
4.38
2.05
2.04
1.51
1.49
1.47
1.46
1.00
0.91
24.40
f1 (ppm)



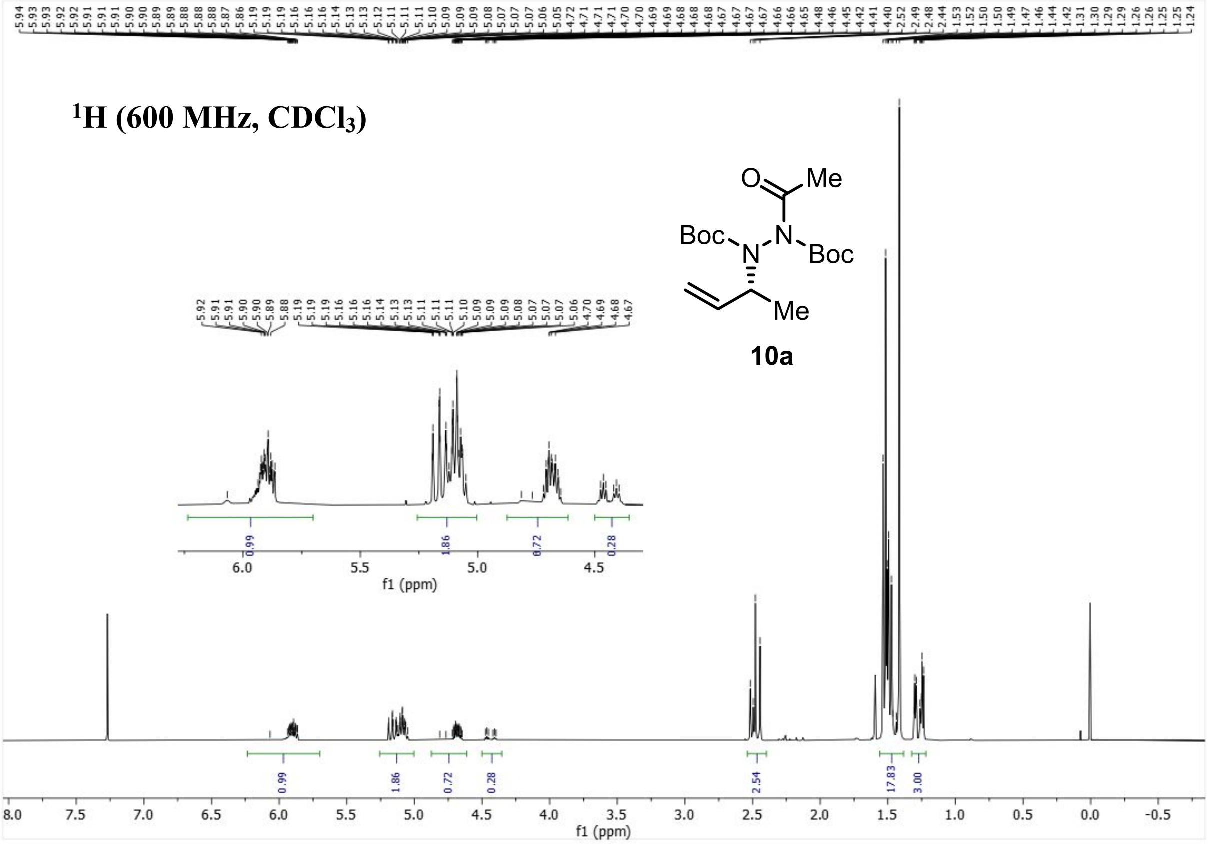
^{13}C (151 MHz, CDCl$_3$)
172.31
153.00
83.12
64.84
59.11
55.83
30.91
30.56
30.42
30.12
28.68
28.34
27.14
27.05
27.00
21.67
14.20
14.04
13.50
13.10
f1 (ppm)



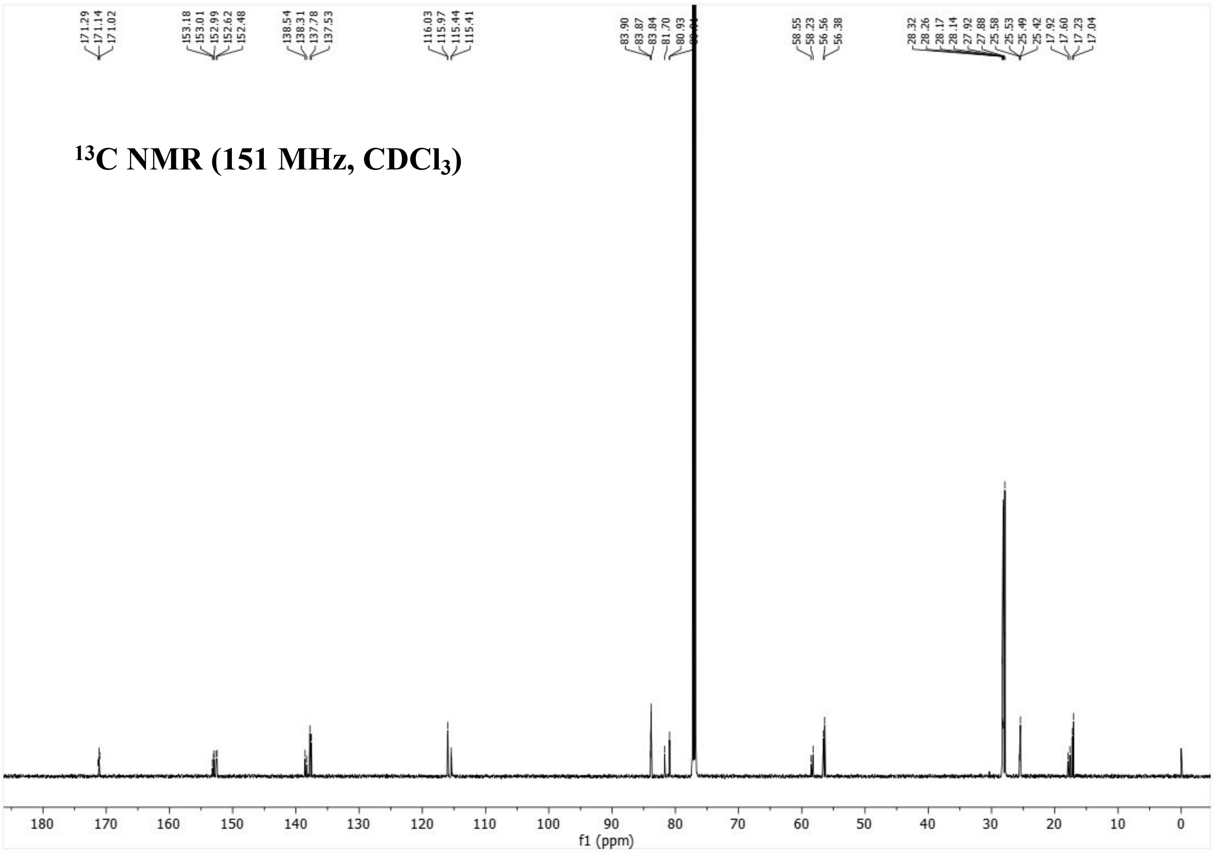
¹H (600 MHz, CDCl₃)
6.41
6.14
4.97
4.68
3.73
1.48
1.47
1.44
Boc
Boc
N
NH
O
OMe
Me
15a
0.99
0.96
3.00
21.85
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



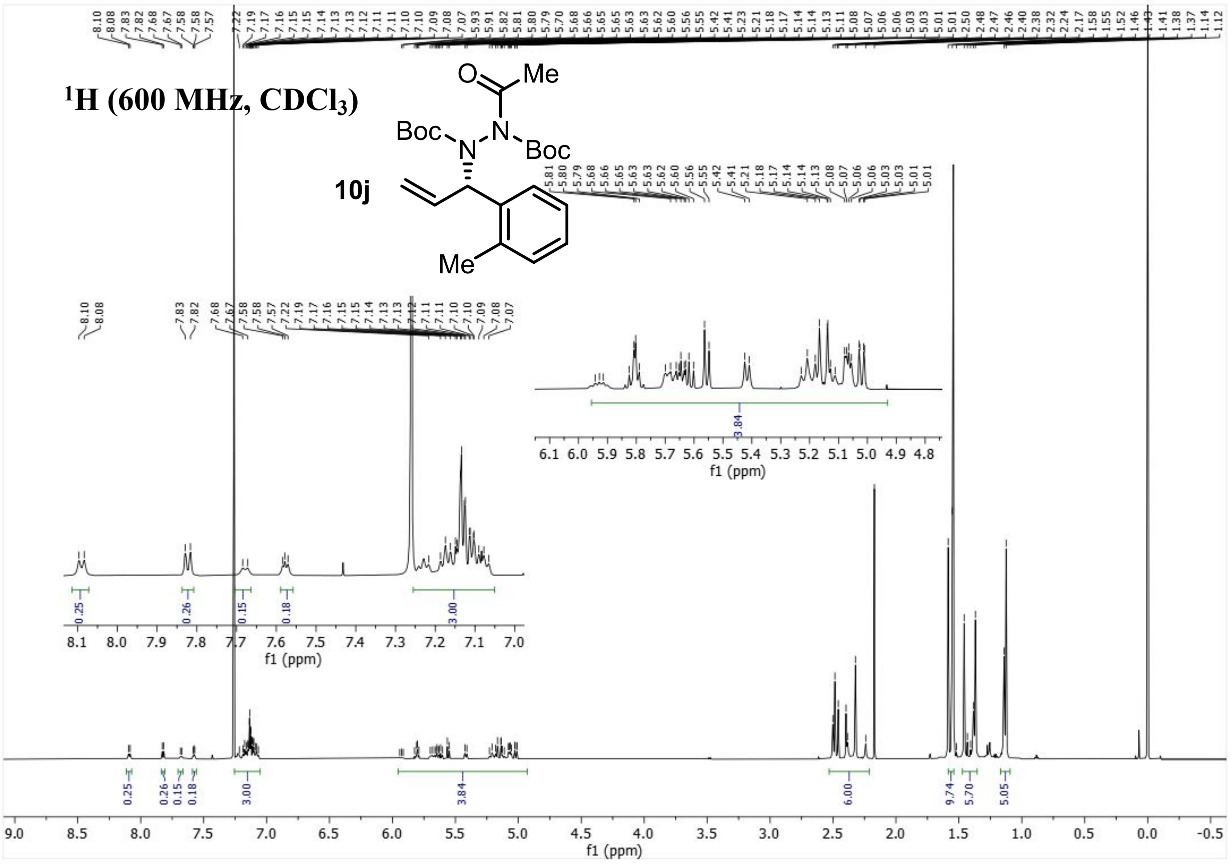
¹³C (151 MHz, CDCl₃)
172.04
154.09
80.79
51.26
28.68
27.15
27.11
13.32
0.00
-1.02
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

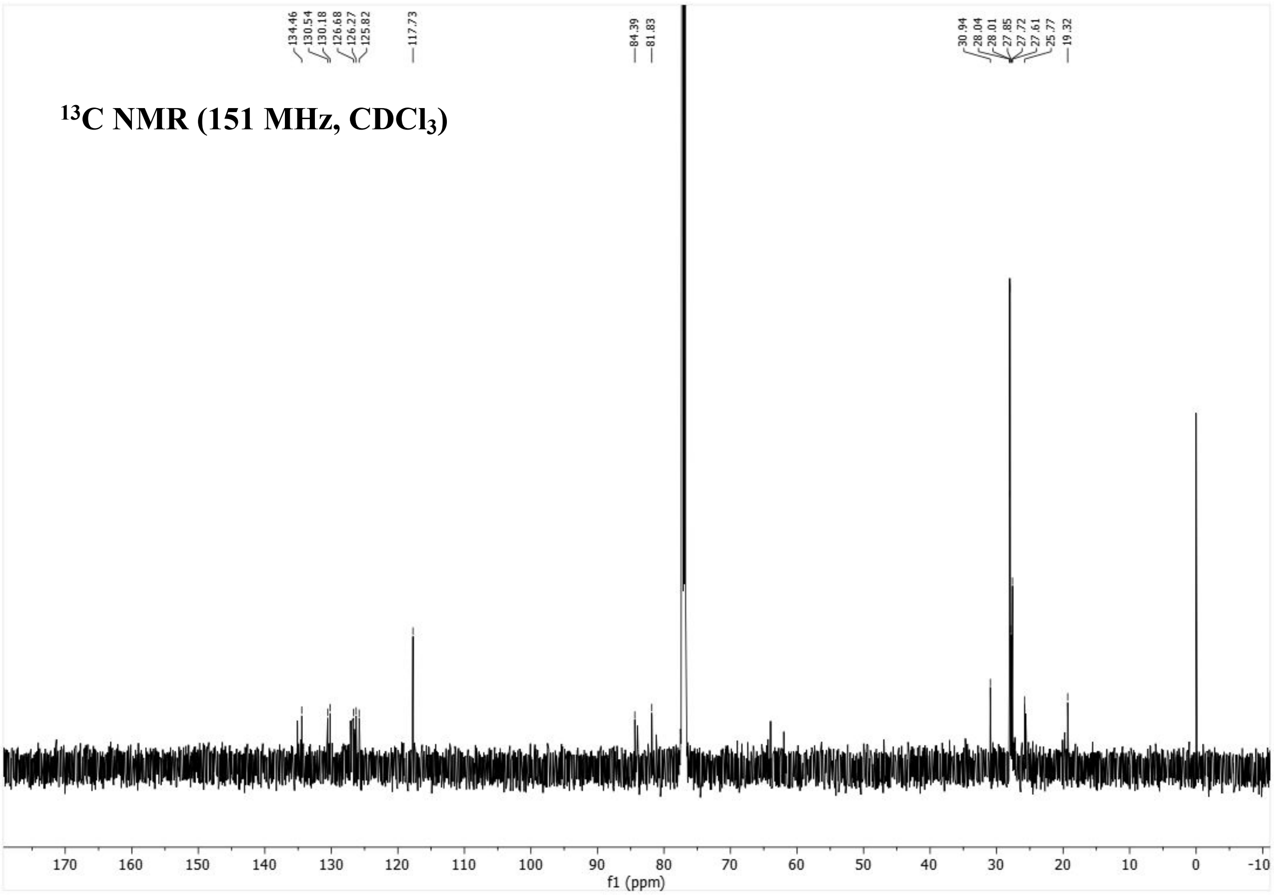


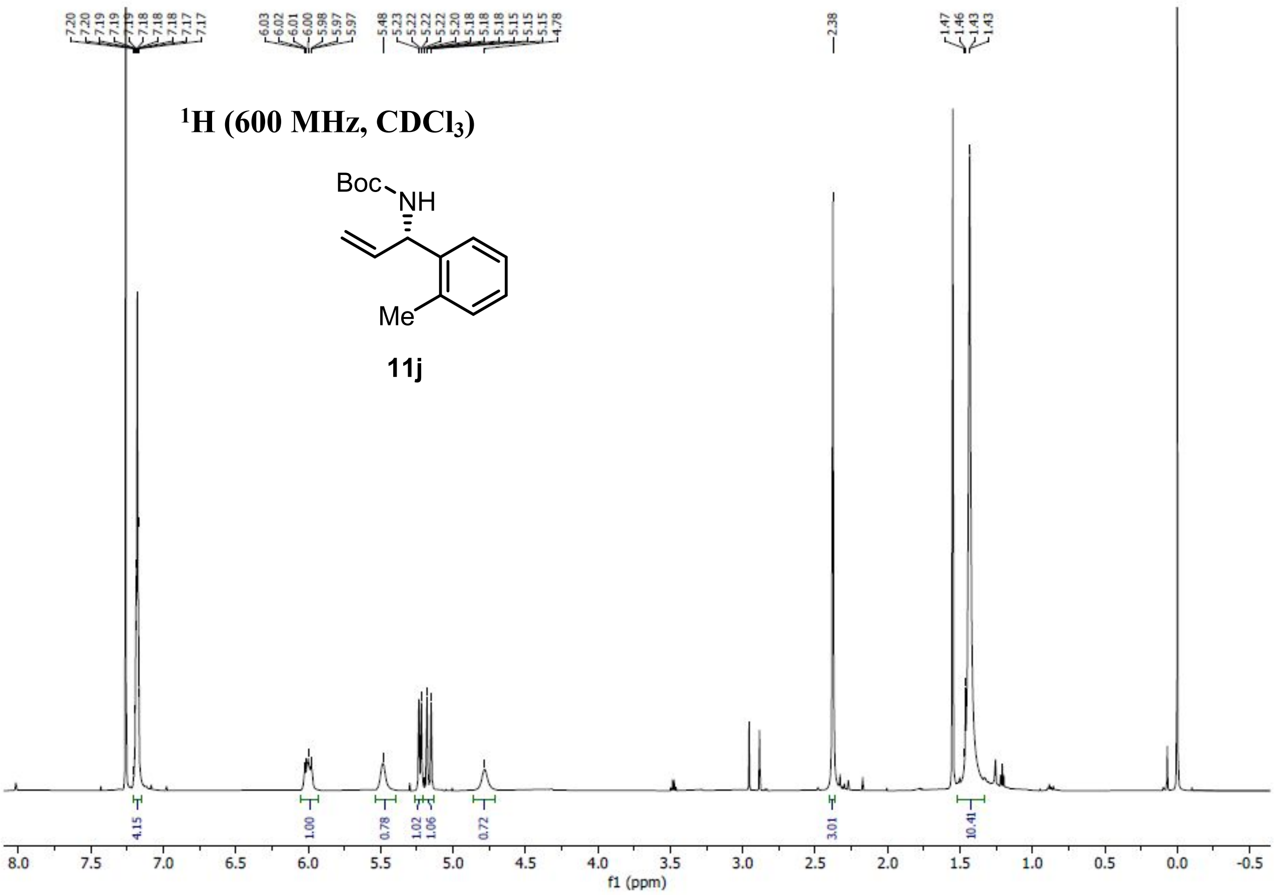
^1H (600 MHz, $CDCl_3$)

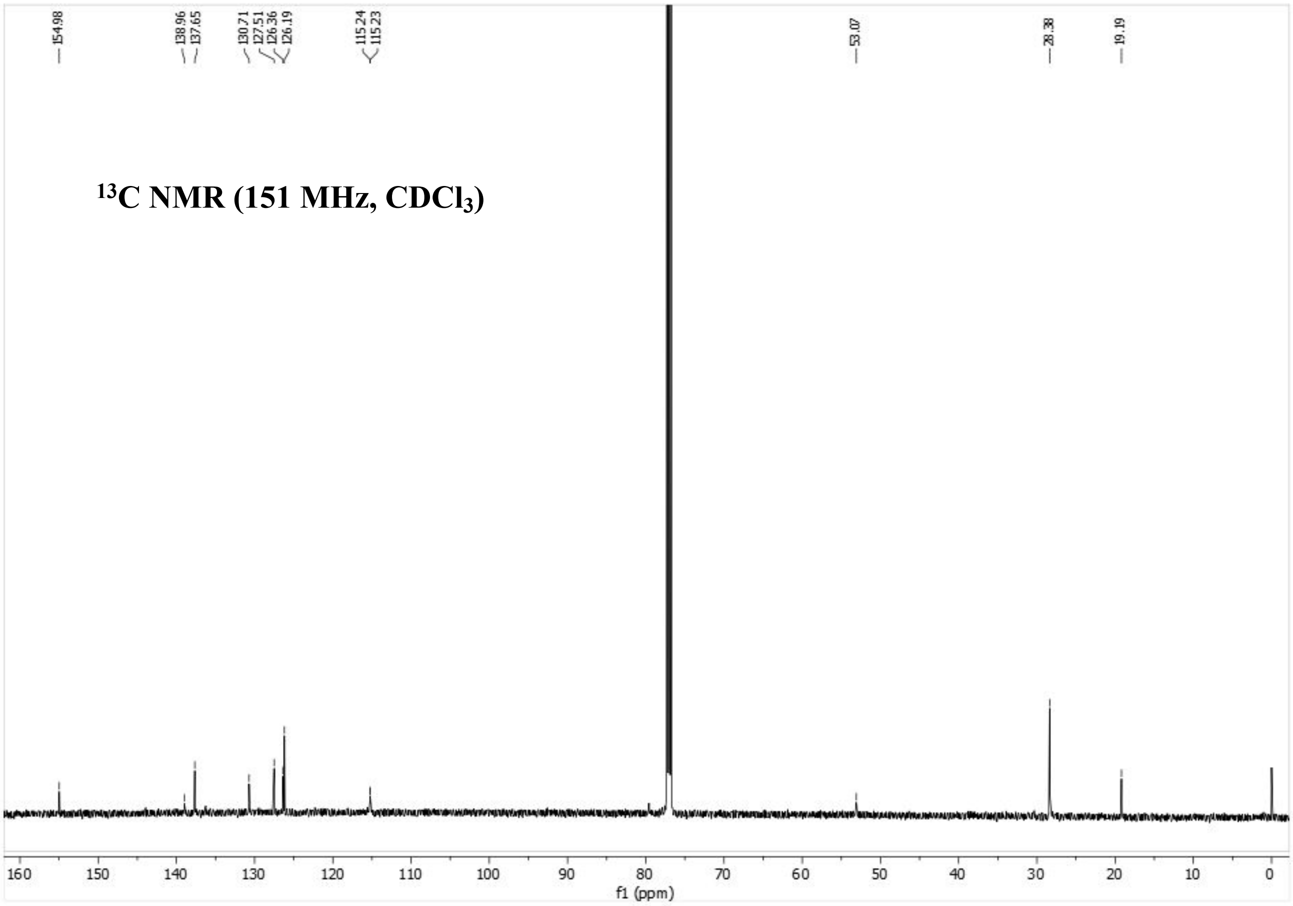


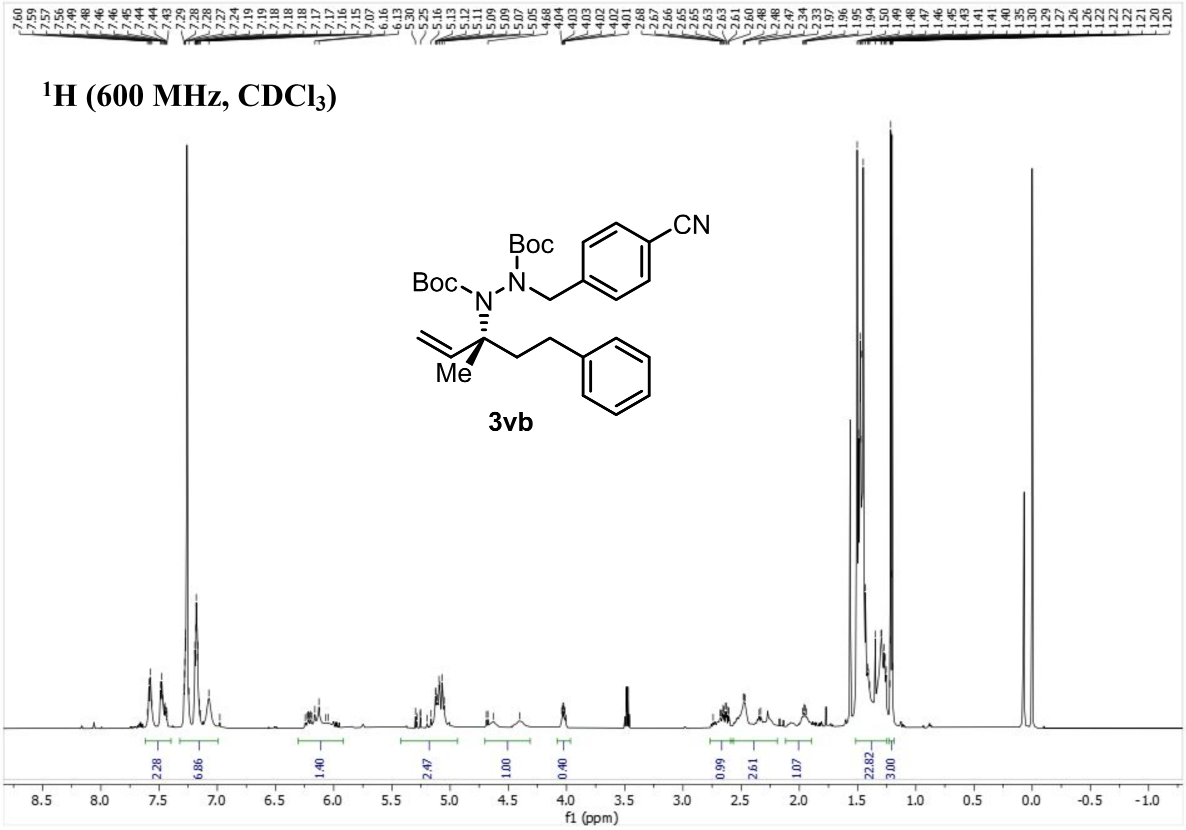
^{13}C NMR (151 MHz, $CDCl_3$)


1H (600 MHz, CDCl3)
10j
O
Me
Boc
N
N
Boc
Me
8.10 8.08 7.83 7.82 7.68 7.67 7.58 7.58 7.57 7.22 7.19 7.17 7.16 7.15 7.15 7.14 7.13 7.13 7.12 7.11 7.11 7.10 7.10 7.09 7.08 7.07 5.93 5.91 5.82 5.81 5.80 5.79 5.70 5.68 5.66 5.65 5.65 5.63 5.63 5.62 5.60 5.56 5.55 5.42 5.41 5.23 5.21 5.18 5.17 5.14 5.14 5.13 5.11 5.08 5.07 5.06 5.06 5.03 5.03 5.01 5.01 2.50 2.48 2.47 2.46 2.40 2.38 2.32 2.24 2.17 1.58 1.55 1.52 1.46 1.43 1.41 1.38 1.37 1.14 1.12
0.25 0.26 0.15 0.18 3.00 3.84 6.00 9.74 5.70 5.05
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)


13C NMR (151 MHz, CDCl3)
134.46 130.54 130.18 126.68 126.27 125.82 117.73 84.39 81.83 30.94 28.04 28.01 27.85 27.72 27.61 25.77 19.32
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

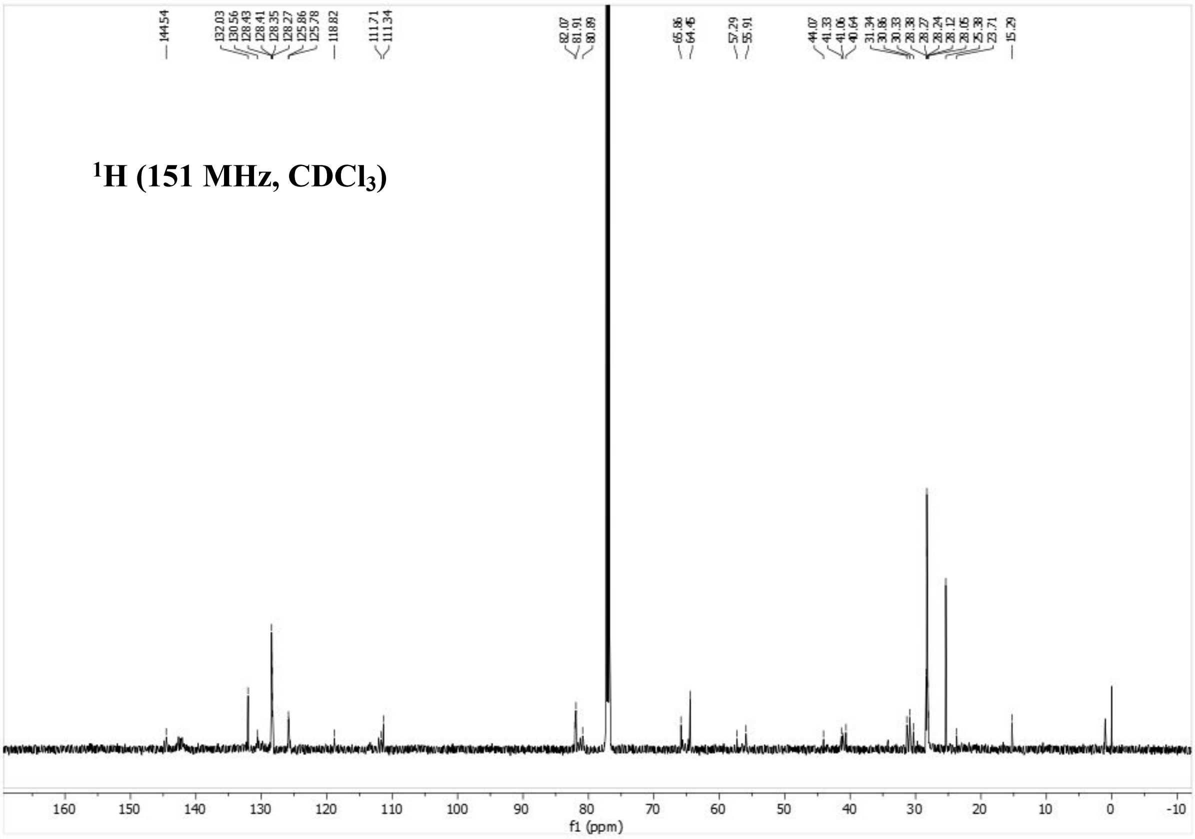

7.20
7.20
7.19
7.19
7.19
7.18
7.18
7.18
7.17
7.17
6.03
6.02
6.01
6.00
5.98
5.97
5.97
5.48
5.23
5.22
5.22
5.22
5.20
5.18
5.18
5.18
5.15
5.15
5.15
4.78
2.38
1.47
1.46
1.43
1.43
^{1}H (600 MHz, CDCl$_3$)
Boc
NH
Me
11j
4.15
1.00
0.78
1.02
1.06
0.72
3.01
10.41
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


154.98
138.96
137.65
130.71
127.51
126.36
126.19
115.24
115.23
53.07
28.38
19.19
^{13}C NMR (151 MHz, CDCl$_3$)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

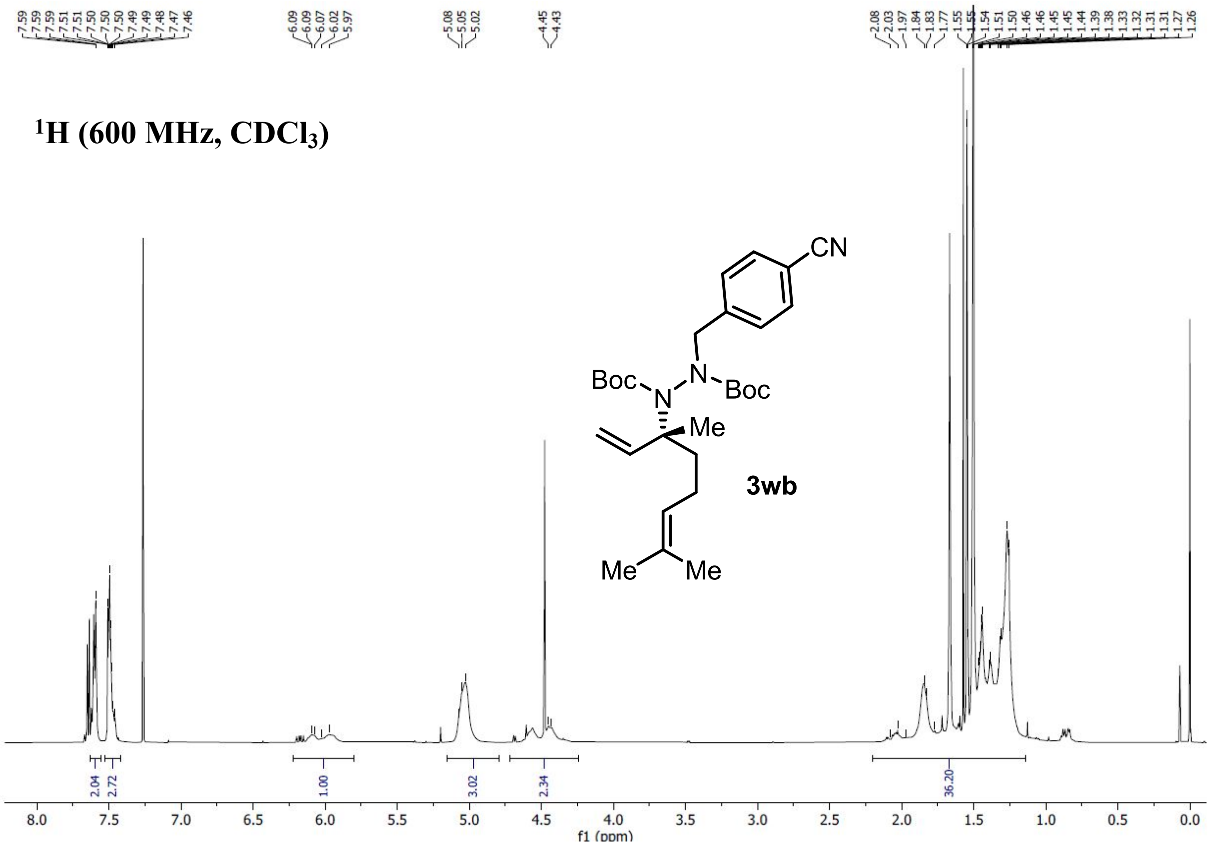


^{1}H (600 MHz, CDCl$_3$)

3vb

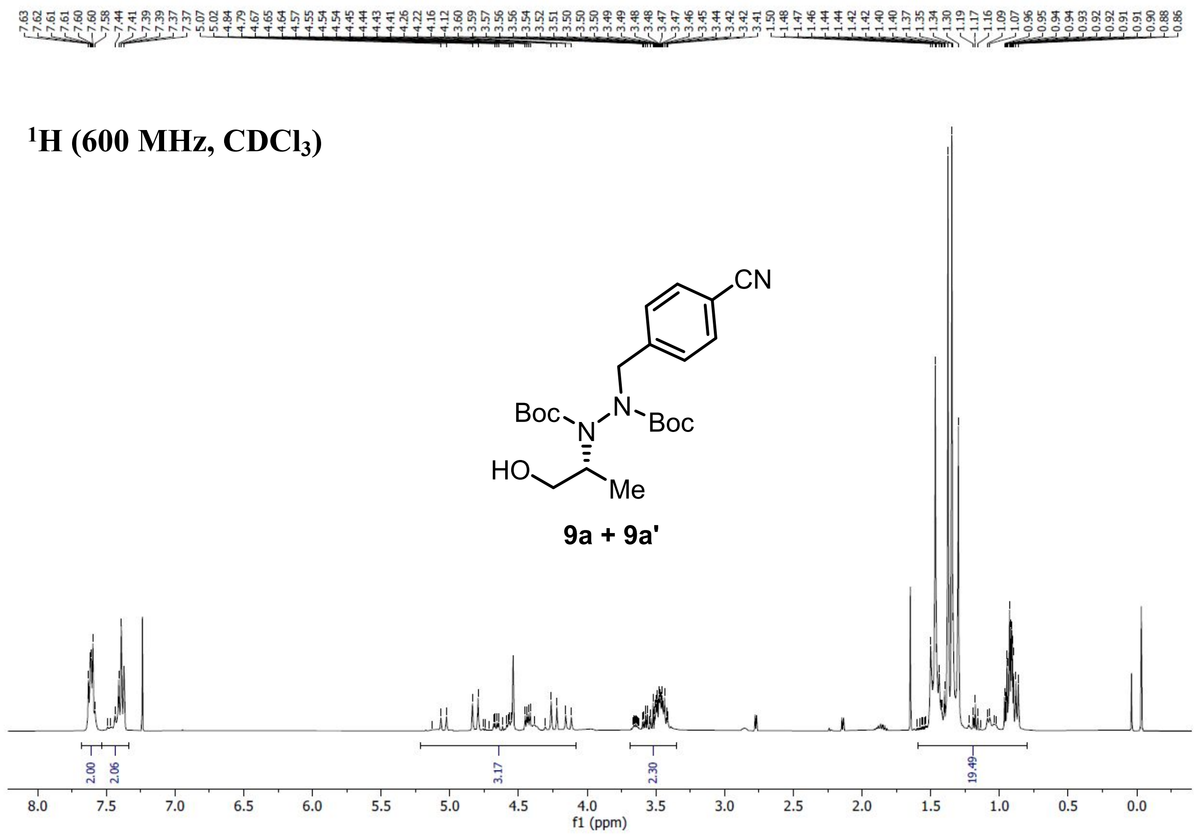


^{1}H (151 MHz, CDCl$_3$)

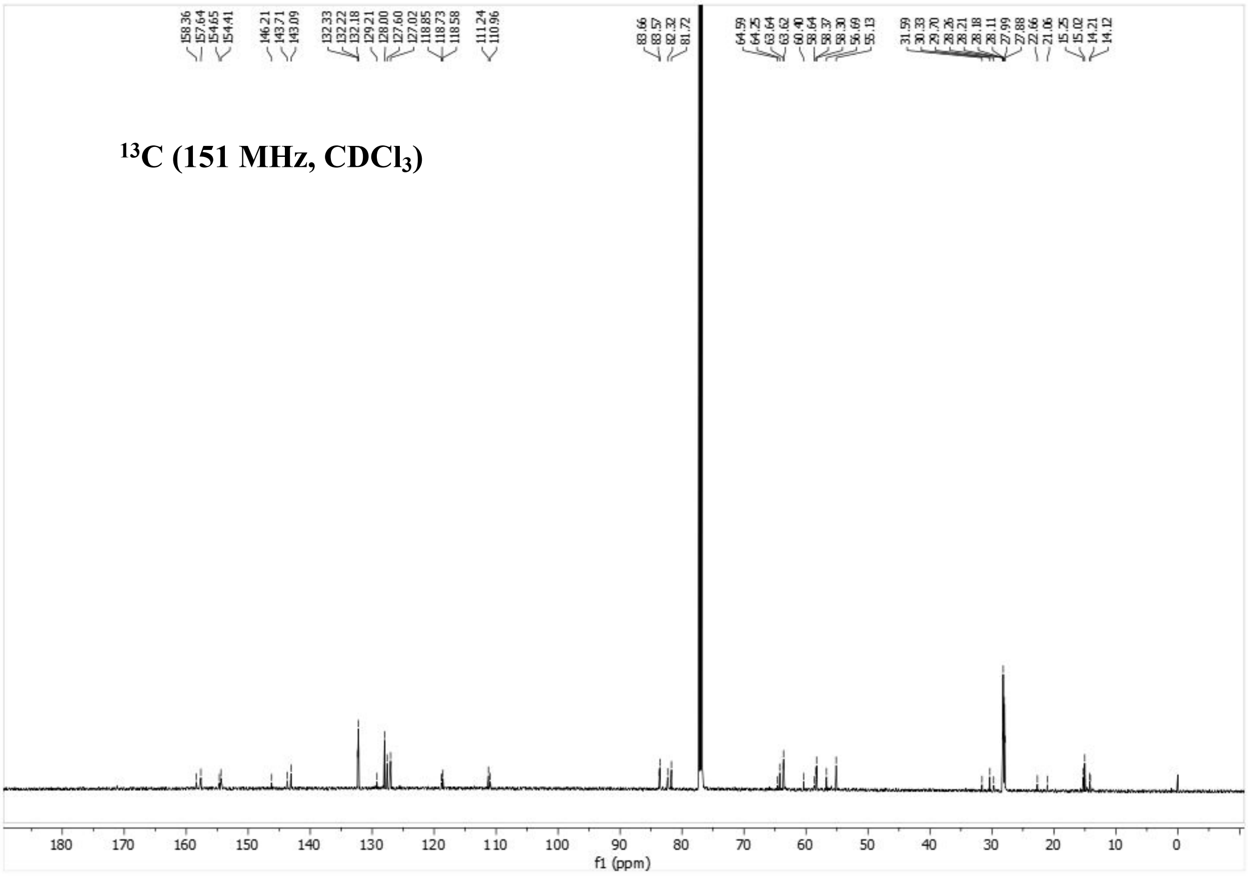


^{1}H (600 MHz, CDCl$_3$)

3wb


7.63
7.62
7.61
7.61
7.60
7.58
7.44
7.41
7.39
7.39
7.37
7.37
5.07
5.02
4.84
4.79
4.67
4.65
4.64
4.57
4.55
4.54
4.54
4.45
4.44
4.43
4.41
4.26
4.22
4.16
4.12
3.60
3.59
3.57
3.56
3.56
3.54
3.52
3.51
3.50
3.50
3.49
3.48
3.48
3.47
3.46
3.45
3.44
3.42
3.41
1.50
1.48
1.47
1.46
1.44
1.44
1.42
1.42
1.40
1.37
1.35
1.34
1.30
1.19
1.17
1.16
1.09
1.07
0.96
0.95
0.94
0.94
0.93
0.92
0.92
0.91
0.90
0.88
0.86
^{1}H (600 MHz, CDCl$_3$)
CN
Boc
N
N
Boc
HO
Me
2.00
2.06
3.17
2.30
19.49
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
f1 (ppm)

9a + 9a'

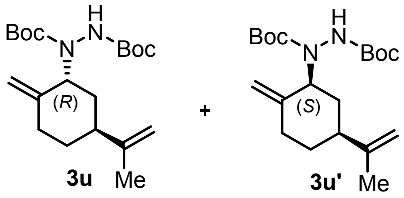

158.36
157.64
154.65
154.41
146.21
143.71
143.09
132.33
132.22
132.18
129.21
128.00
127.60
127.02
118.85
118.73
118.58
111.24
110.96
83.66
83.57
82.32
81.72
64.59
64.25
63.64
63.62
60.40
58.64
58.37
58.30
56.69
55.13
31.59
30.33
29.70
28.26
28.21
28.18
28.11
27.99
27.88
22.66
21.06
15.25
15.02
14.21
14.12
^{13}C (151 MHz, CDCl$_3$)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

DETERMINATION OF STEREOSELECTIVITY

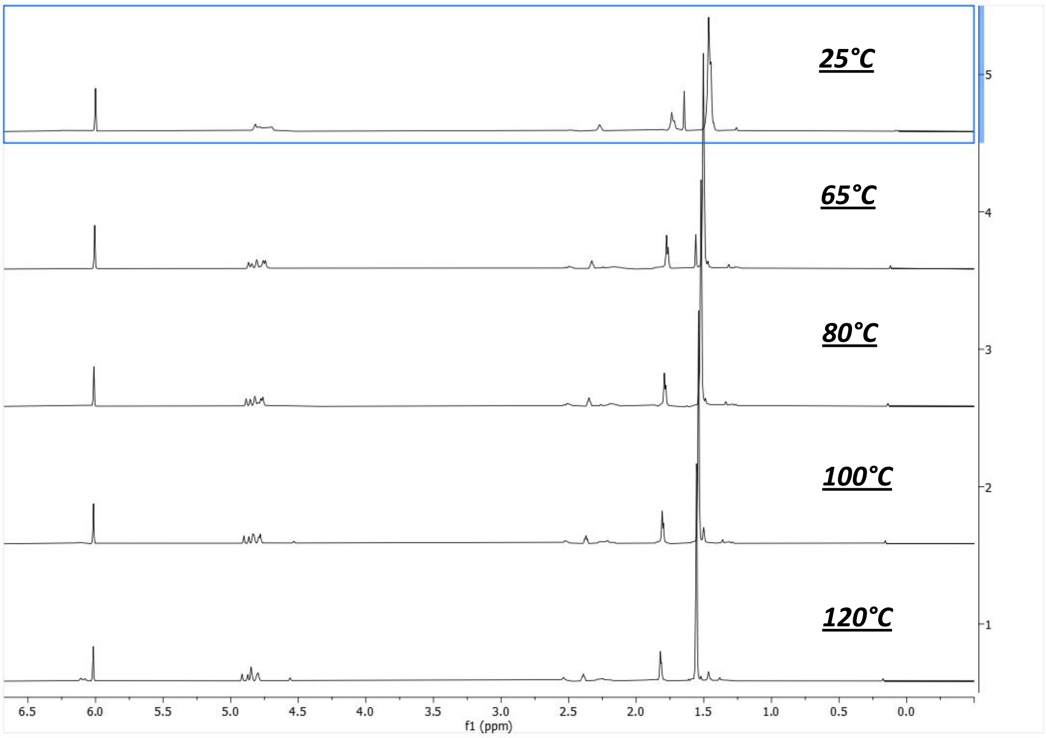
Determination of d.r. of 3u and 3u’ through ^{1}H NMR

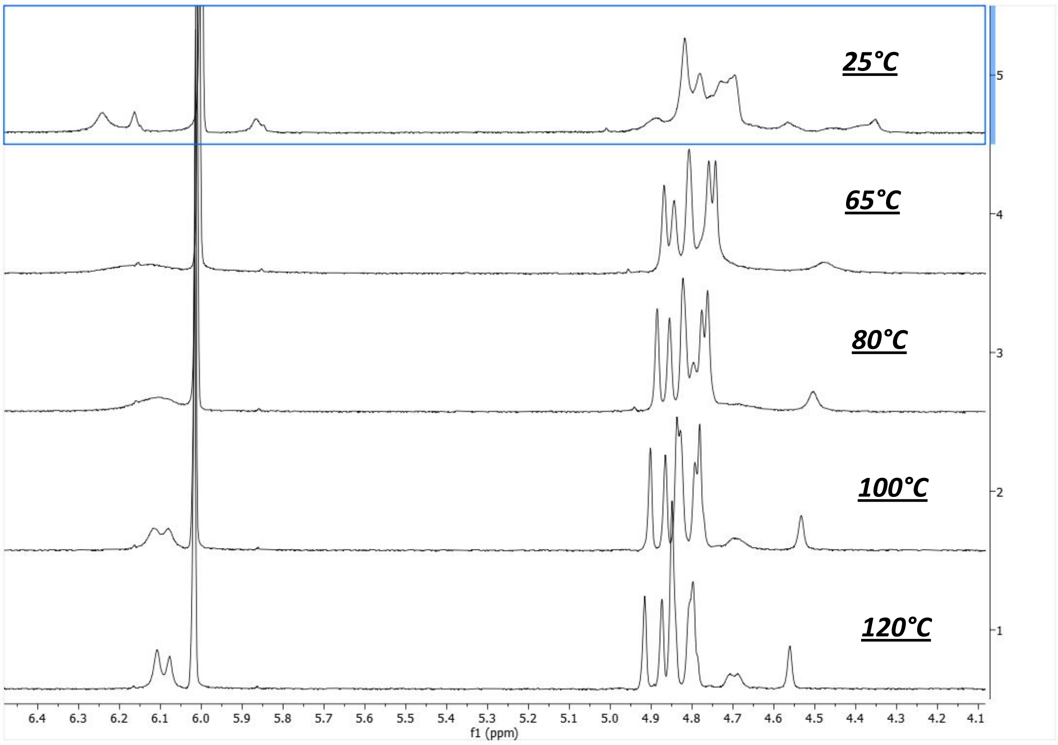
3u and **3u’** were poorly separated by HPLC technique, therefore we opted to determine their diasteromeric excess through NMR analysis. Due to a complex combination of rotamers, we recorded the ^{1}H NMR spectra of **3u**, **3u’** and their mixture at 100°C in $C_2D_2Cl_4$ after a screening of temperature conducted on the mixture (**Figure S9**). The comparison of those spectra revealed the d.r. of each compound (for **3u** d.r.> 20:1; for **3u’** d.r.= 89:11).

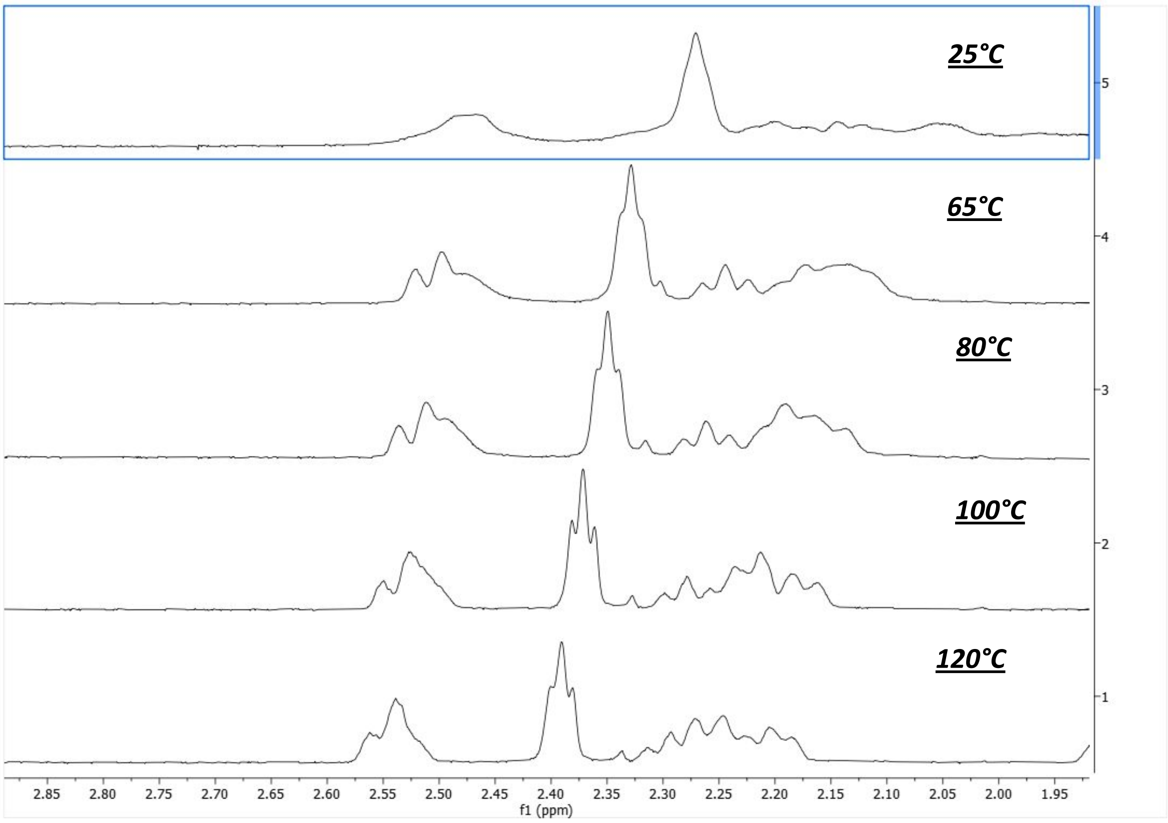
Figure S9: screening of temperature for the mixture

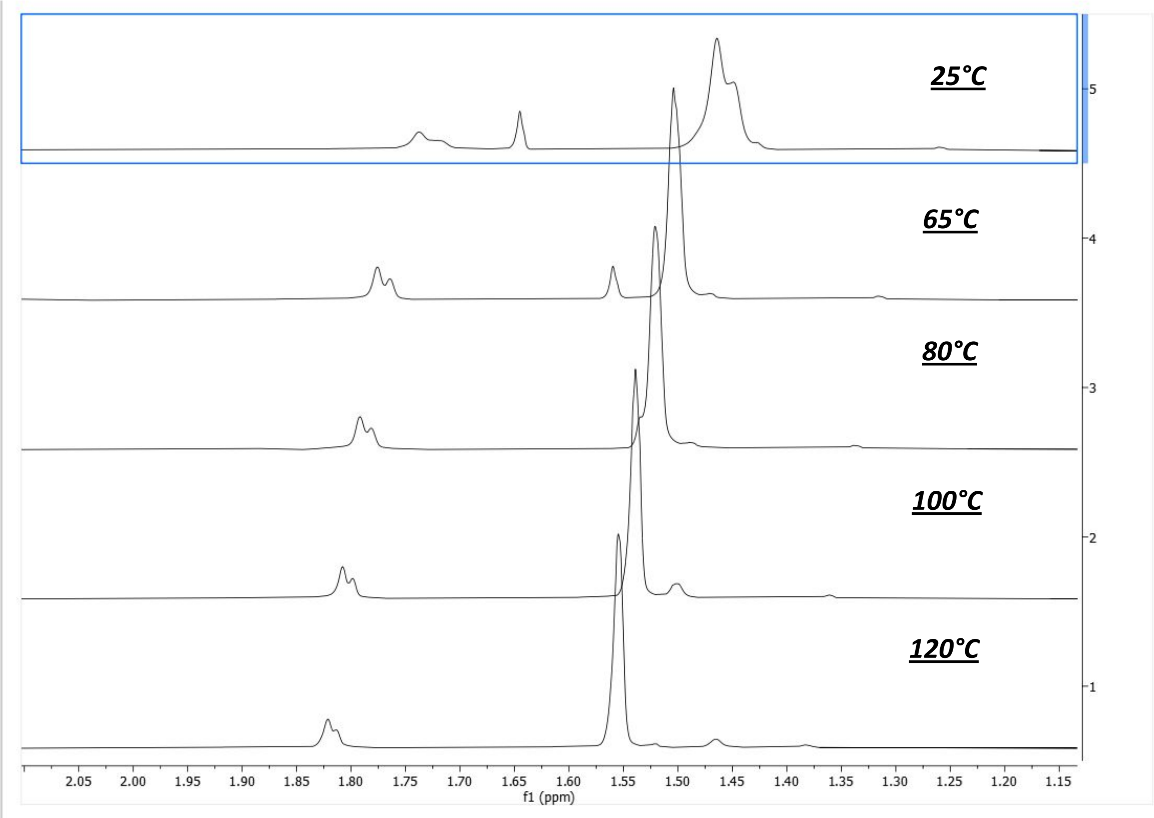


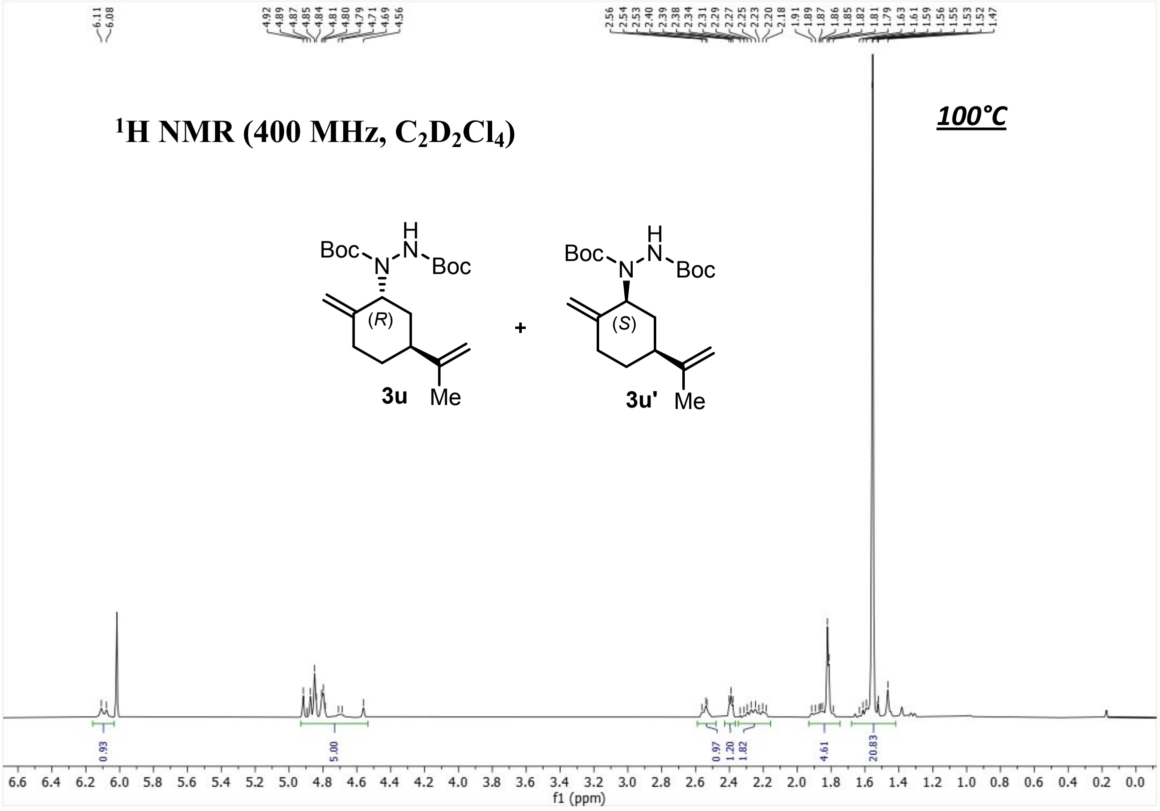
3u **3u'**

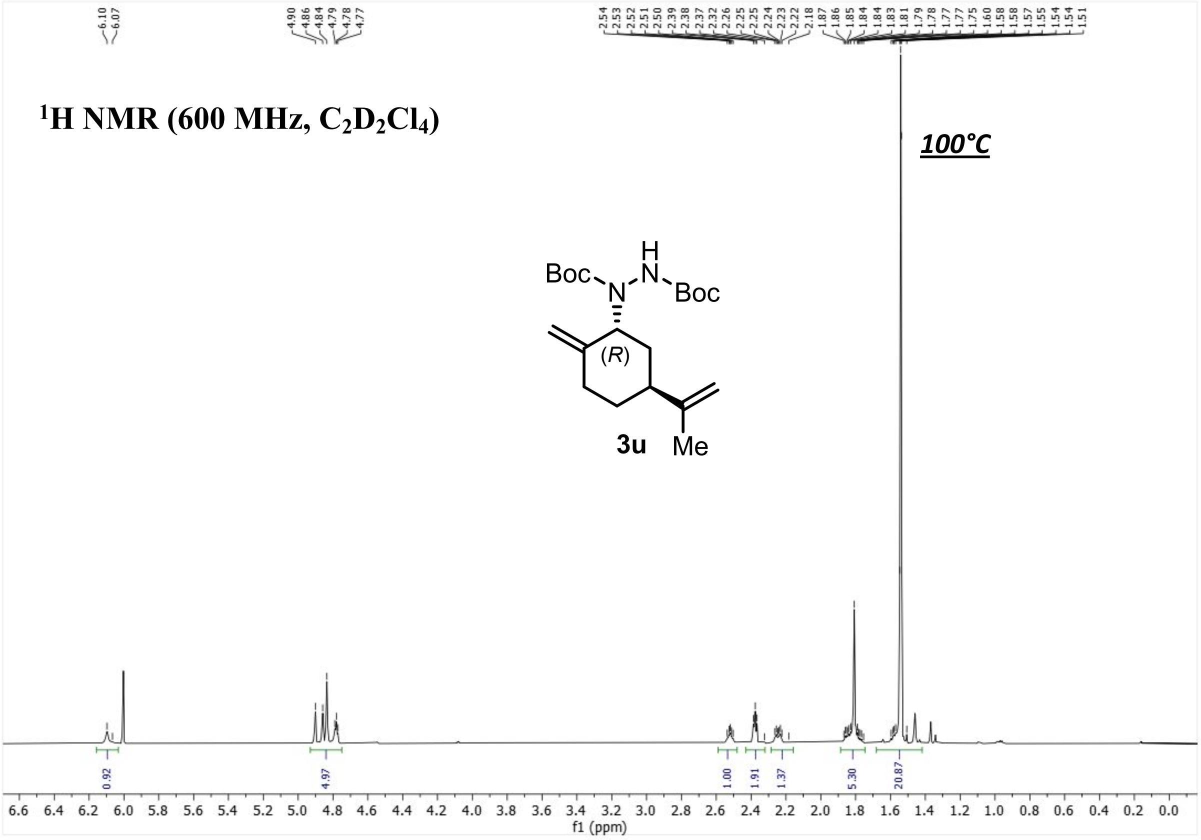


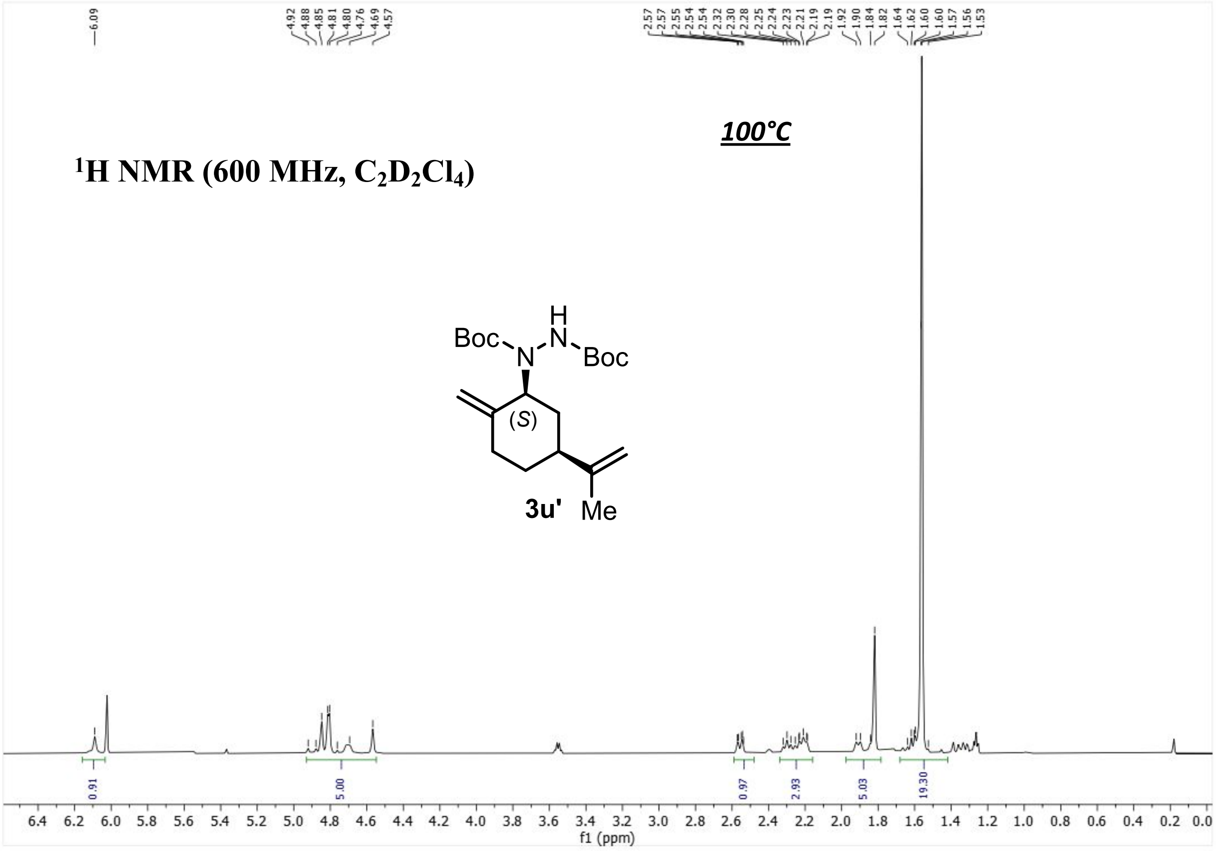

25°C
65°C
80°C
100°C
120°C
5
4
3
2
1
6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1
f1 (ppm)

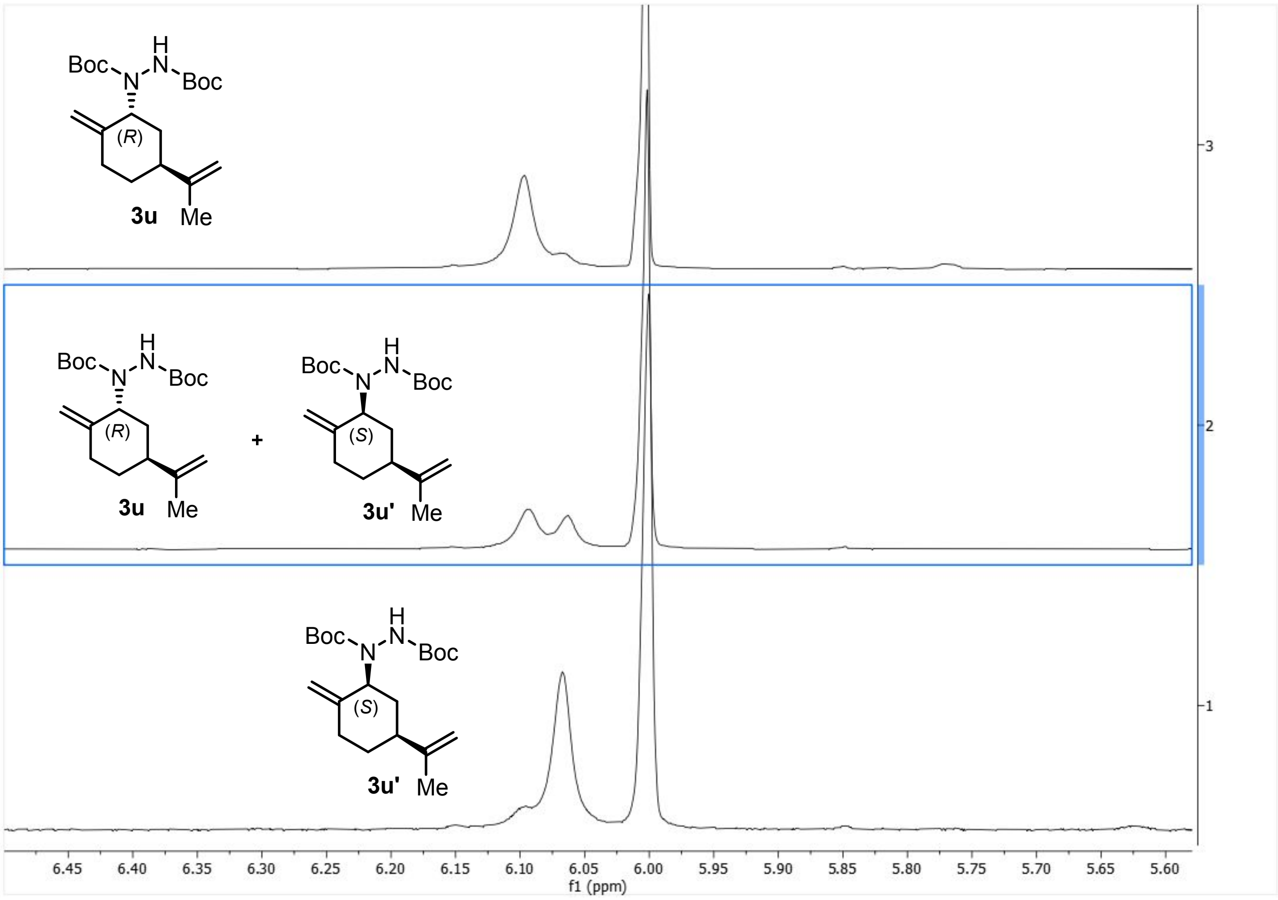

25°C
65°C
80°C
100°C
120°C
5
4
3
2
1
2.85 2.80 2.75 2.70 2.65 2.60 2.55 2.50 2.45 2.40 2.35 2.30 2.25 2.20 2.15 2.10 2.05 2.00 1.95
f1 (ppm)

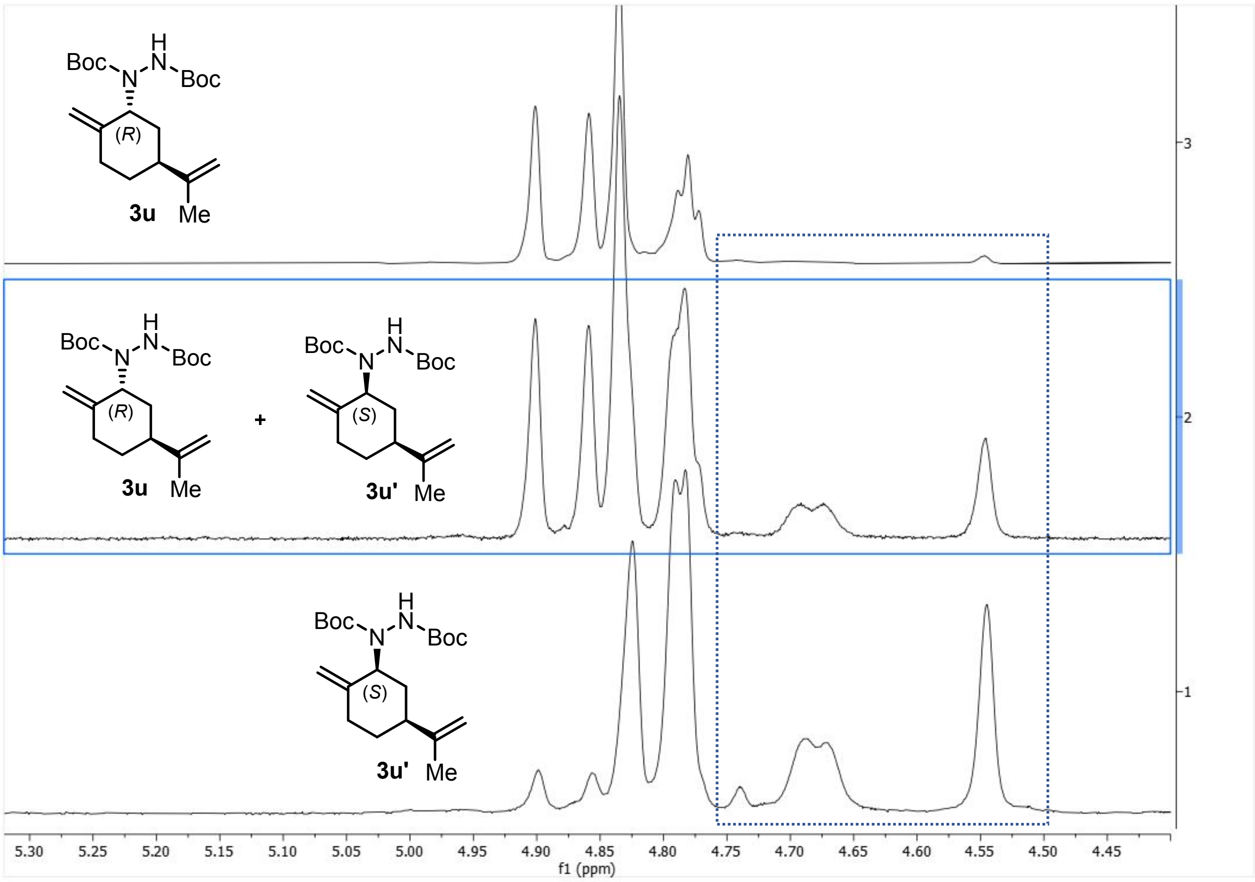

25°C
65°C
80°C
100°C
120°C
5
4
3
2
1
2.05 2.00 1.95 1.90 1.85 1.80 1.75 1.70 1.65 1.60 1.55 1.50 1.45 1.40 1.35 1.30 1.25 1.20 1.15
f1 (ppm)

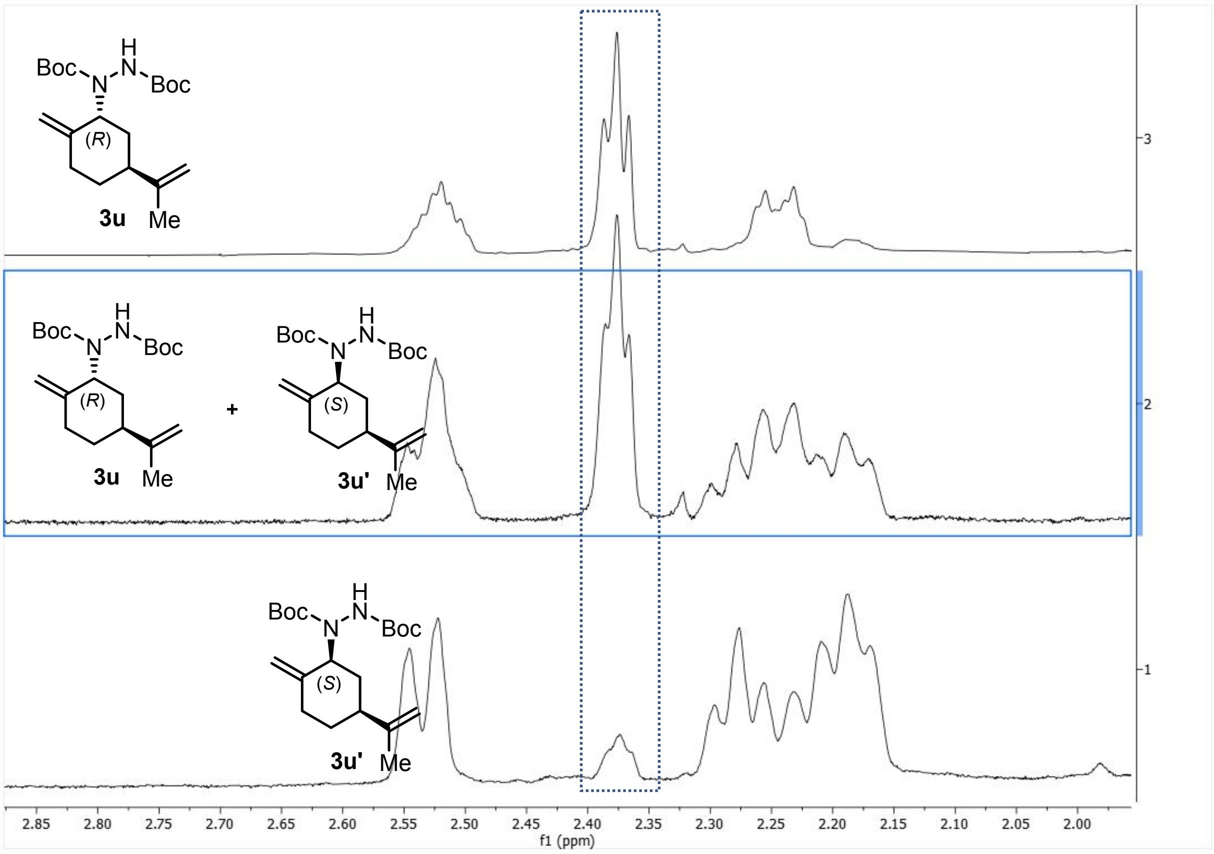

6.11
6.08
4.92
4.89
4.87
4.85
4.84
4.81
4.80
4.79
4.71
4.69
4.56
2.56
2.54
2.53
2.40
2.39
2.38
2.34
2.31
2.29
2.27
2.25
2.23
2.20
2.18
1.91
1.89
1.87
1.86
1.85
1.82
1.81
1.79
1.63
1.61
1.59
1.56
1.55
1.53
1.52
1.47
¹H NMR (400 MHz, C₂D₂Cl₄)
100°C
Boc
H
N
N
Boc
(R)
+
(S)
3u
Me
3u'
0.93
5.00
0.97
1.20
1.82
4.61
20.83
6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0.0
f1 (ppm)

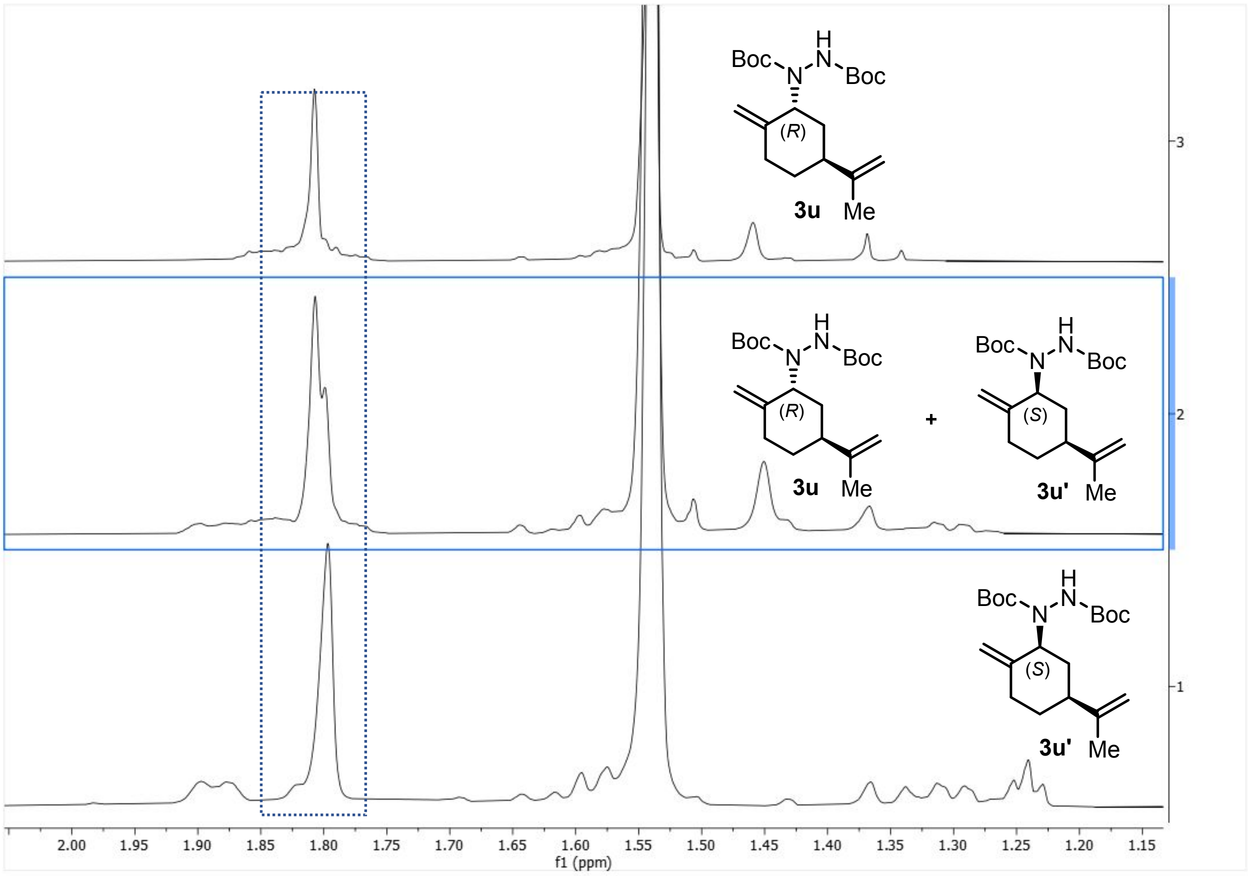

6.10
6.07
4.90
4.86
4.84
4.79
4.78
4.77
2.54
2.53
2.52
2.51
2.50
2.39
2.38
2.37
2.32
2.26
2.25
2.25
2.24
2.23
2.22
2.18
1.87
1.86
1.85
1.84
1.83
1.81
1.79
1.78
1.77
1.77
1.75
1.60
1.58
1.58
1.57
1.55
1.54
1.54
1.51
1H NMR (600 MHz, C2D2Cl4)
100°C
Boc
H
N
N
Boc
(R)
3u
Me
0.92
4.97
1.00
1.91
1.37
5.30
20.87
6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0.0
f1 (ppm)

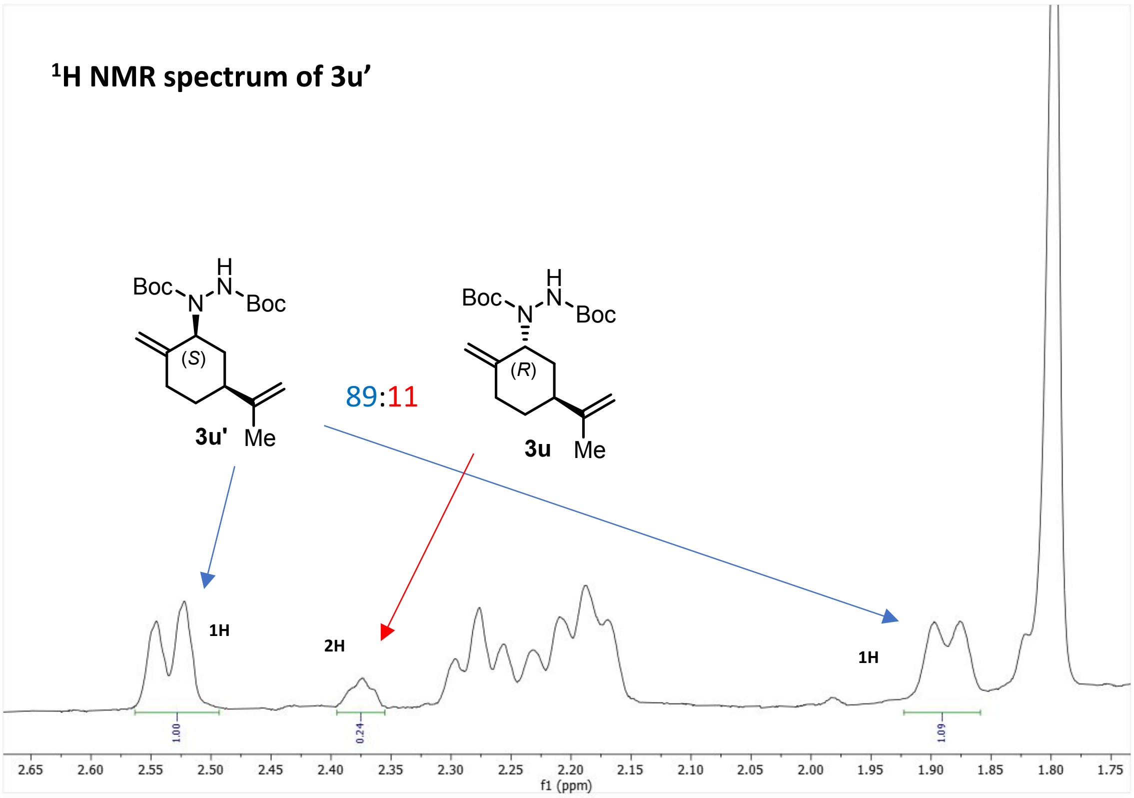

6.09
4.92
4.88
4.85
4.81
4.80
4.76
4.69
4.57
2.57
2.57
2.55
2.54
2.34
2.32
2.30
2.28
2.25
2.24
2.23
2.21
2.19
1.92
1.90
1.84
1.82
1.64
1.62
1.60
1.60
1.57
1.56
1.53
100°C
1H NMR (600 MHz, C2D2Cl4)
Boc
H
N
N
Boc
(S)
3u'
Me
0.91
5.00
0.97
2.93
5.03
19.30
6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0.0
f1 (ppm)


Boc
H
N
N
Boc
(R)
3u
Me
Boc
H
N
N
Boc
(R)
3u
Me
+
Boc
H
N
N
Boc
(S)
3u'
Me
Boc
H
N
N
Boc
(S)
3u'
Me
3
2
1
6.45
6.40
6.35
6.30
6.25
6.20
6.15
6.10
6.05
6.00
5.95
5.90
5.85
5.80
5.75
5.70
5.65
5.60
f1 (ppm)


Boc
H
N
N
Boc
(R)
3u
Me
Boc
H
N
N
Boc
(R)
3u
Me
+
Boc
H
N
N
Boc
(S)
3u'
Me
Boc
H
N
N
Boc
(S)
3u'
Me
3
2
1
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
4.75
4.70
4.65
4.60
4.55
4.50
4.45
f1 (ppm)

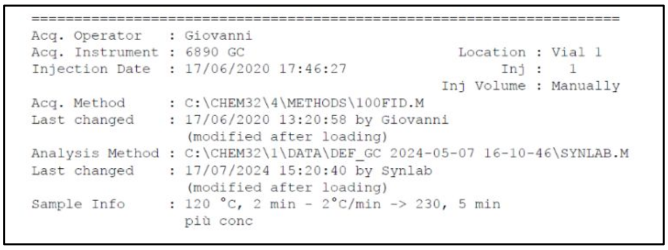

3u
3u
3u'
3u'
Boc
N
H
Boc
(R)
(S)
Me
+
3
2
1
2.85
2.80
2.75
2.70
2.65
2.60
2.55
2.50
2.45
2.40
2.35
2.30
2.25
2.20
2.15
2.10
2.05
2.00
f1 (ppm)


3u
3u
3u'
3u'
Boc
N
H
Boc
(R)
(S)
Me
+
3
2
1
2.00
1.95
1.90
1.85
1.80
1.75
1.70
1.65
1.60
1.55
1.50
1.45
1.40
1.35
1.30
1.25
1.20
1.15
f1 (ppm)

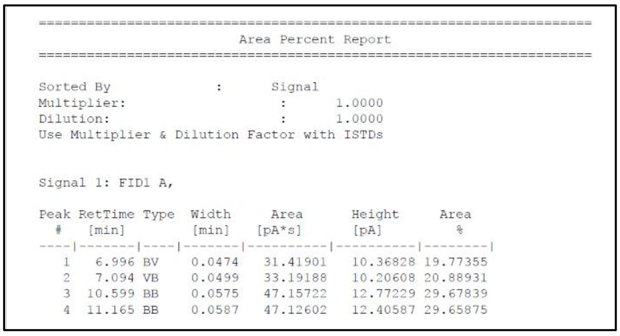


^{1}H NMR spectrum of 3u’

Determination of e.r. and d.r. by GC-FID and HPLC



```
=====================================================================
Acq. Operator   : Giovanni
Acq. Instrument : 6890 GC                          Location : Vial 1
Injection Date  : 17/06/2020 17:46:27                   Inj :    1
                                                 Inj Volume : Manually
Acq. Method     : C:\CHEM32\4\METHODS\100FID.M
Last changed    : 17/06/2020 13:20:58 by Giovanni
                  (modified after loading)
Analysis Method : C:\CHEM32\1\DATA\DEF_GC 2024-05-07 16-10-46\SYNLAB.M
Last changed    : 17/07/2024 15:20:40 by Synlab
                  (modified after loading)
Sample Info     : 120 °C, 2 min - 2°C/min -> 230, 5 min
                  più conc
```

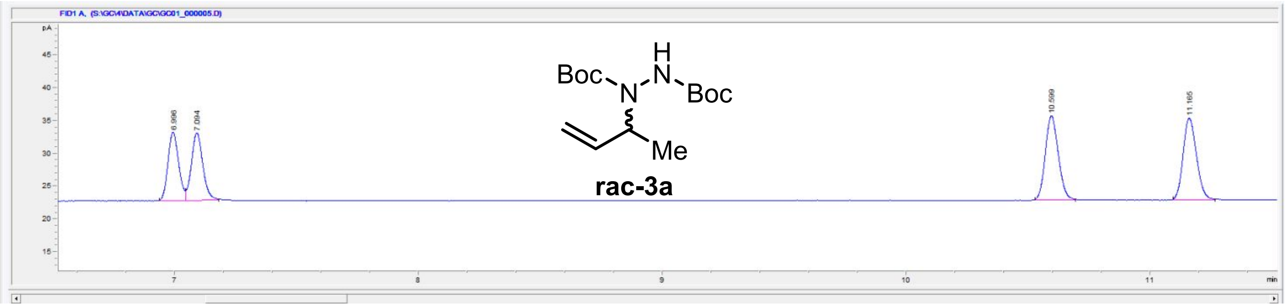


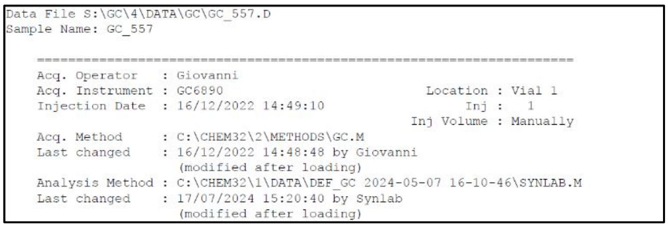
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A,

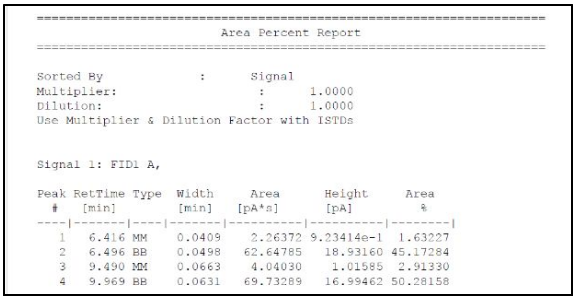
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1   6.996 BV    0.0474   31.41901   10.36828 19.77355
   2   7.094 VB    0.0499   33.19188   10.20608 20.88931
   3  10.599 BB    0.0575   47.15722   12.77229 29.67839
   4  11.165 BB    0.0587   47.12602   12.40587 29.65875
```





```
Data File S:\GC\4\DATA\GC\GC_557.D
Sample Name: GC_557

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : GC6890                         Location : Vial 1
    Injection Date  : 16/12/2022 14:49:10                 Inj :    1
                                                   Inj Volume : Manually
    Acq. Method     : C:\CHEM32\2\METHODS\GC.M
    Last changed    : 16/12/2022 14:48:48 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\DATA\DEF_GC 2024-05-07 16-10-46\SYNLAB.M
    Last changed    : 17/07/2024 15:20:40 by Synlab
                      (modified after loading)
```

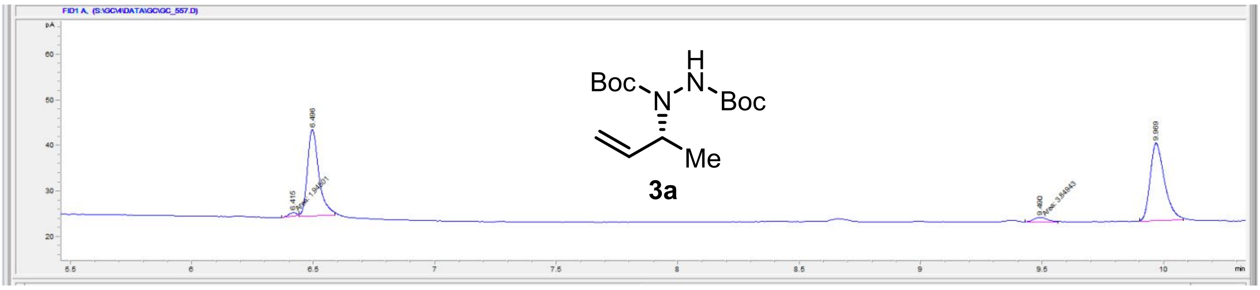


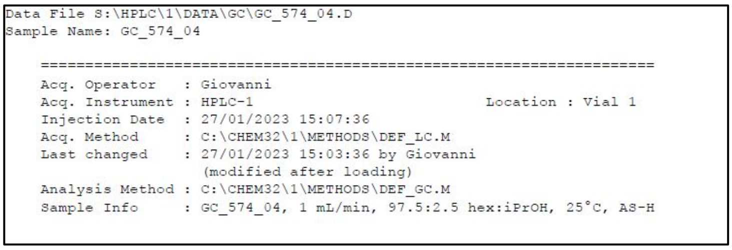
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A,

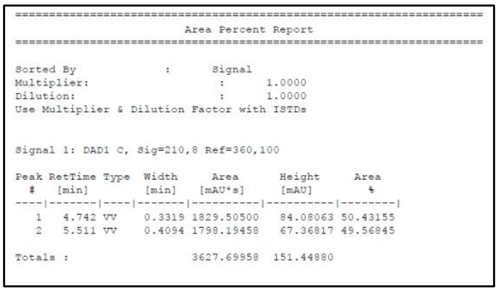
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1   6.416 MM    0.0409    2.26372 9.23414e-1  1.63227
   2   6.496 BB    0.0498   62.64785   18.93160 45.17284
   3   9.490 MM    0.0663    4.04030    1.01585  2.91330
   4   9.969 BB    0.0631   69.73289   16.99462 50.28158
```





```
Data File S:\HPLC\1\DATA\GC\GC_574_04.D
Sample Name: GC_574_04

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 27/01/2023 15:07:36
    Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
    Last changed    : 27/01/2023 15:03:36 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_574_04, 1 mL/min, 97.5:2.5 hex:iPrOH, 25°C, AS-H
```



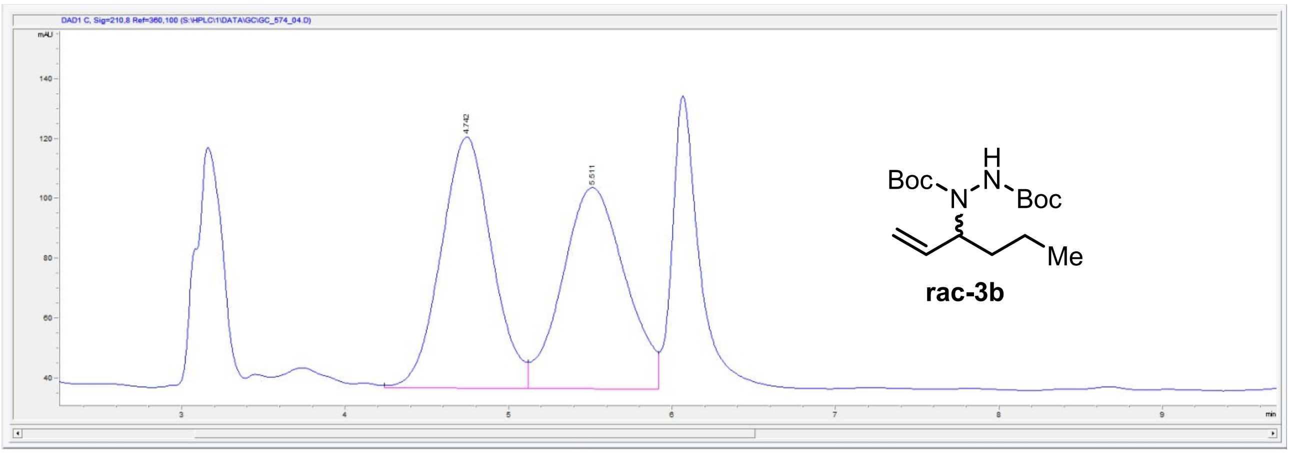
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

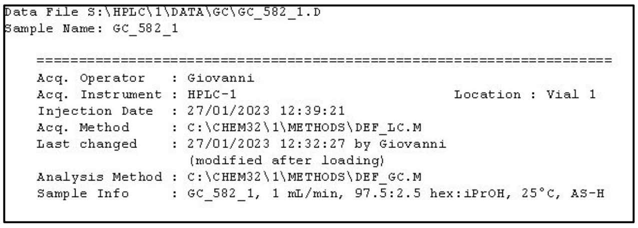

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.742 VV    0.3319 1829.50500   84.08063 50.43155
   2   5.511 VV    0.4094 1798.19458   67.36817 49.56845

Totals :                  3627.69958  151.44880
```

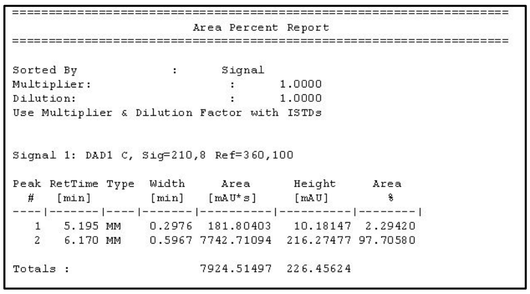


rac-3b



```
Data File S:\HPLC\1\DATA\GC\GC_582_1.D
Sample Name: GC_582_1

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 27/01/2023 12:39:21
    Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
    Last changed    : 27/01/2023 12:32:27 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_582_1, 1 mL/min, 97.5:2.5 hex:iPrOH, 25°C, AS-H
```



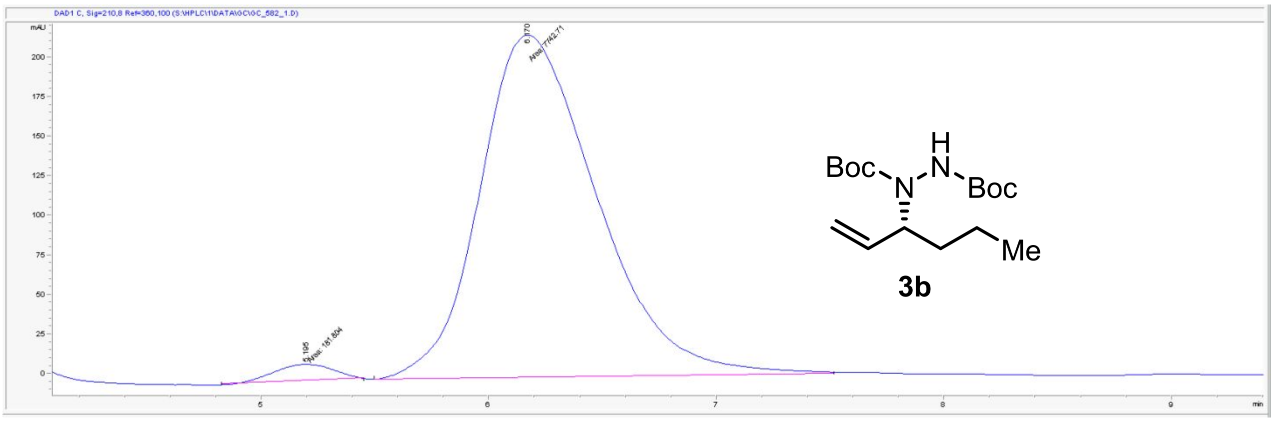
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

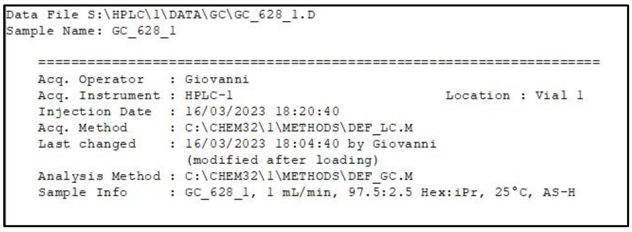

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   5.195 MM    0.2976  181.80403   10.18147  2.29420
   2   6.170 MM    0.5967 7742.71094  216.27477 97.70580

Totals :                  7924.51497  226.45624
```

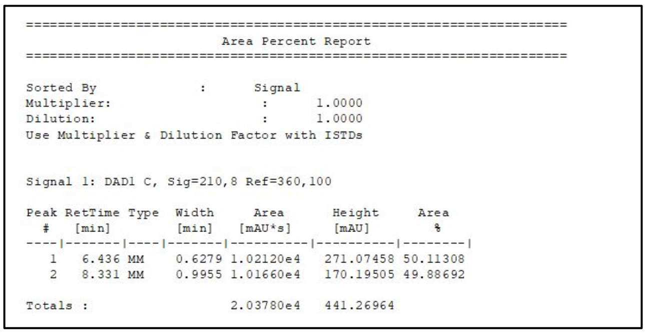


3b



```
Data File S:\HPLC\1\DATA\GC\GC_628_1.D
Sample Name: GC_628_1

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 16/03/2023 18:20:40
    Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
    Last changed    : 16/03/2023 18:04:40 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_628_1, 1 mL/min, 97.5:2.5 Hex:iPr, 25°C, AS-H
```



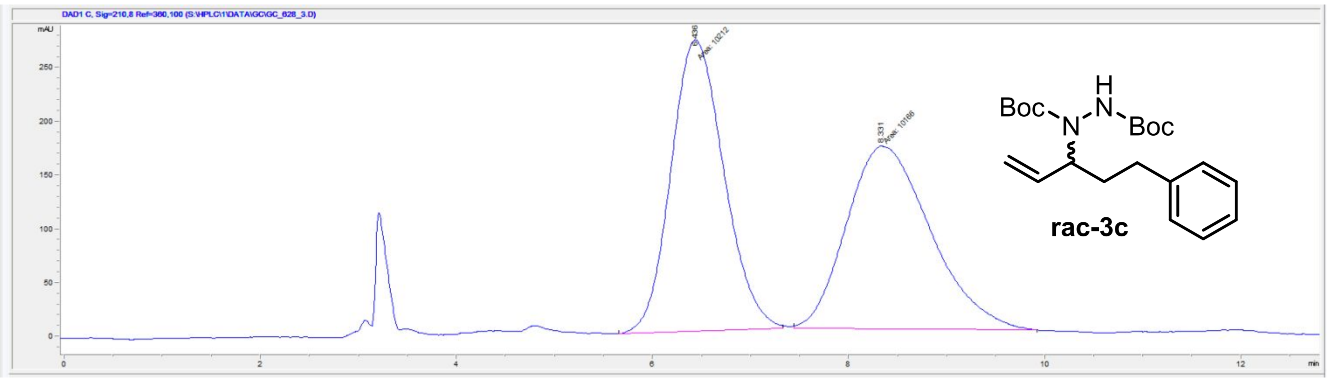
```
=====================================================================
                         Area Percent Report
=====================================================================

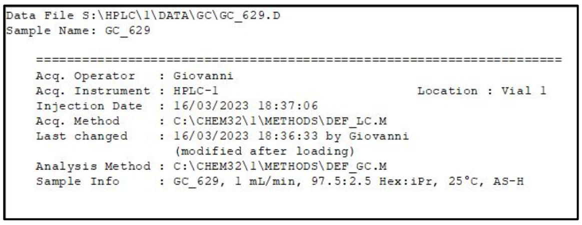
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.436 MM    0.6279 1.02120e4  271.07458 50.11308
   2   8.331 MM    0.9955 1.01660e4  170.19505 49.88692

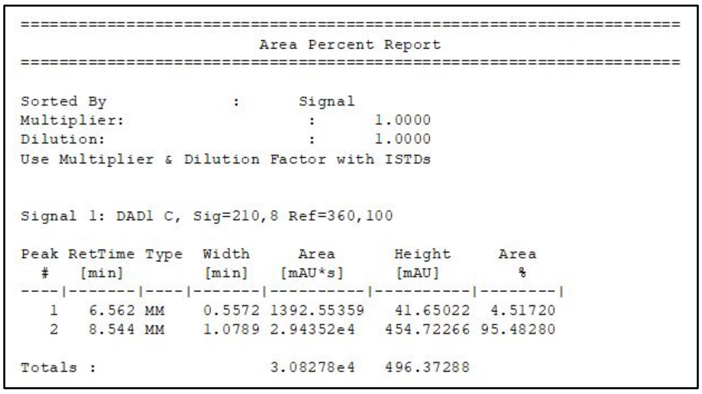
Totals :                  2.03780e4  441.26964
```





```
Data File S:\HPLC\1\DATA\GC\GC_629.D
Sample Name: GC_629

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 16/03/2023 18:37:06
    Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
    Last changed    : 16/03/2023 18:36:33 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_629, 1 mL/min, 97.5:2.5 Hex:iPr, 25°C, AS-H
```



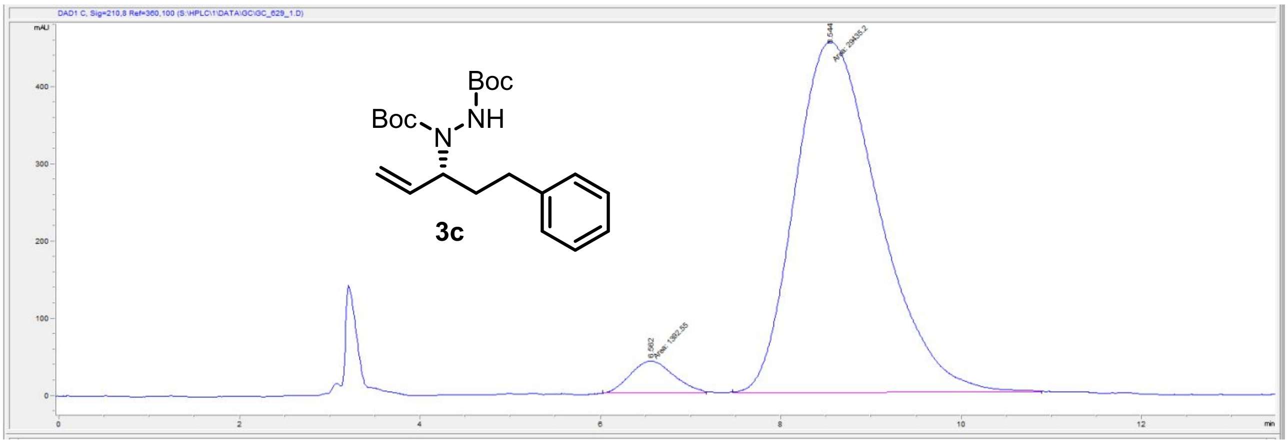
```
=====================================================================
                         Area Percent Report
=====================================================================

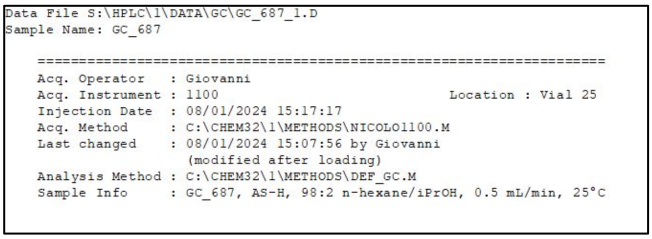
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.562 MM    0.5572 1392.55359  41.65022  4.51720
   2   8.544 MM    1.0789 2.94352e4  454.72266 95.48280

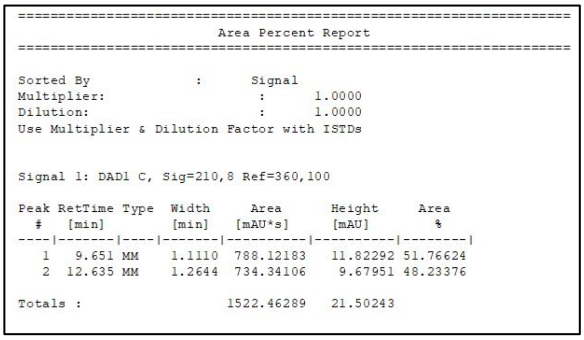
Totals :                  3.08278e4  496.37288
```





```
Data File S:\HPLC\1\DATA\GC\GC_687_1.D
Sample Name: GC_687

    ===================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1100                           Location : Vial 25
    Injection Date  : 08/01/2024 15:17:17
    Acq. Method     : C:\CHEM32\1\METHODS\NICOLO1100.M
    Last changed    : 08/01/2024 15:07:56 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_687, AS-H, 98:2 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



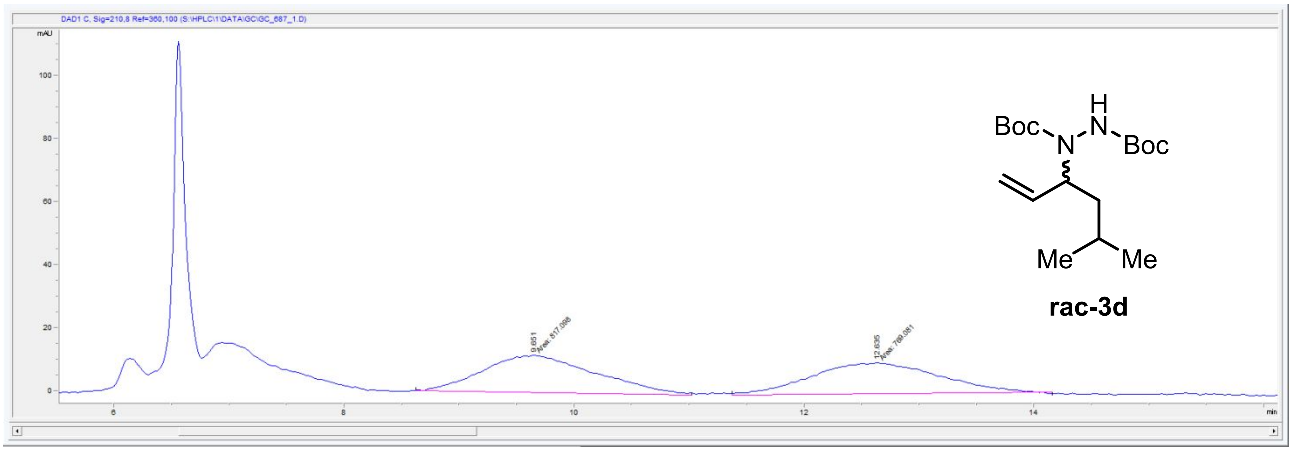
```
=====================================================================
                         Area Percent Report
=====================================================================

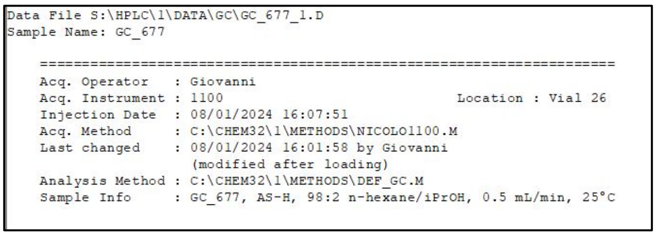
Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.651 MM    1.1110  788.12183   11.82292 51.76624
   2  12.635 MM    1.2644  734.34106    9.67951 48.23376

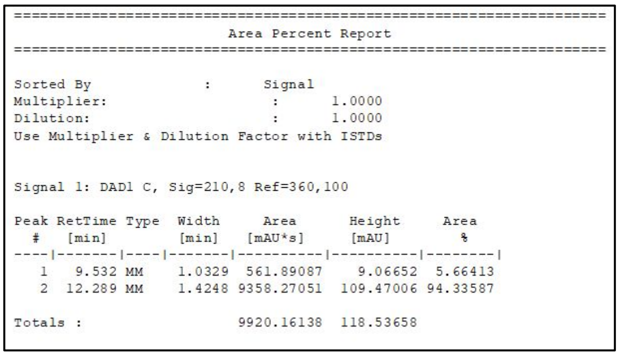
Totals :                  1522.46289   21.50243
```





```
Data File S:\HPLC\1\DATA\GC\GC_677_1.D
Sample Name: GC_677

    ===================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1100                           Location : Vial 26
    Injection Date  : 08/01/2024 16:07:51
    Acq. Method     : C:\CHEM32\1\METHODS\NICOLO1100.M
    Last changed    : 08/01/2024 16:01:58 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_677, AS-H, 98:2 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



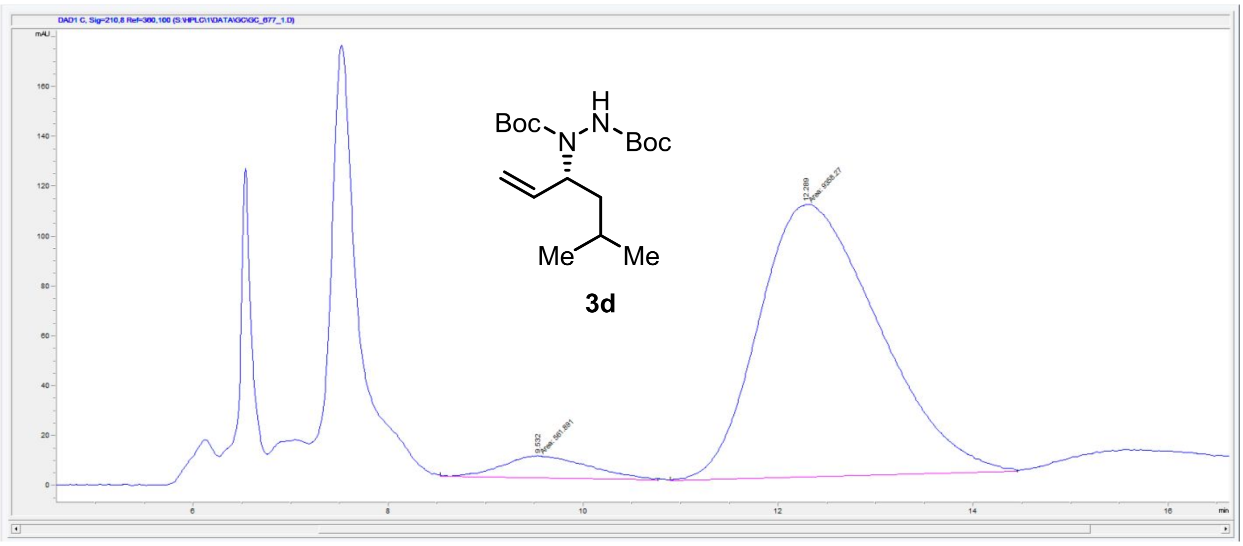
```
=====================================================================
                         Area Percent Report
=====================================================================

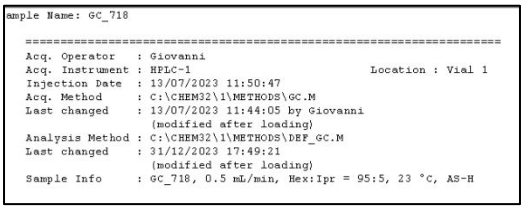
Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.532 MM    1.0329  561.89087    9.06652  5.66413
   2  12.289 MM    1.4248 9358.27051  109.47006 94.33587

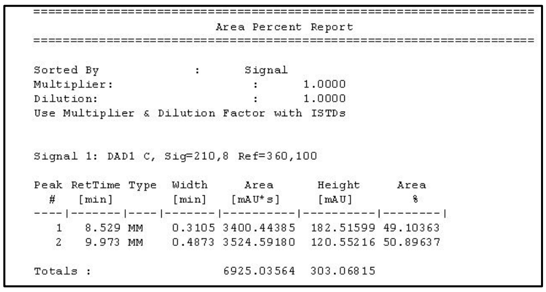
Totals :                  9920.16138  118.53658
```





```
ample Name: GC_718

  =====================================================================
  Acq. Operator   : Giovanni
  Acq. Instrument : HPLC-1                          Location : Vial 1
  Injection Date  : 13/07/2023 11:50:47
  Acq. Method     : C:\CHEM32\1\METHODS\GC.M
  Last changed    : 13/07/2023 11:44:05 by Giovanni
                    (modified after loading)
  Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
  Last changed    : 31/12/2023 17:49:21
                    (modified after loading)
  Sample Info     : GC_718, 0.5 mL/min, Hex:Ipr = 95:5, 23 °C, AS-H
```



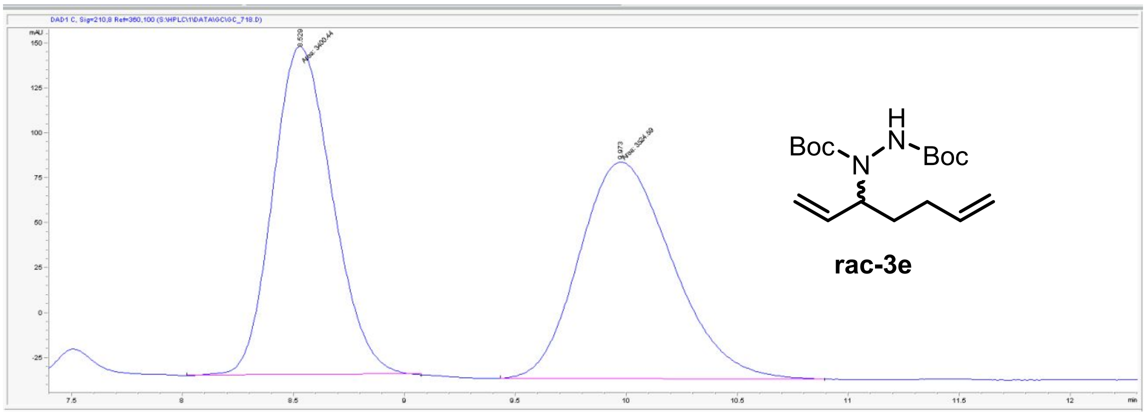
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

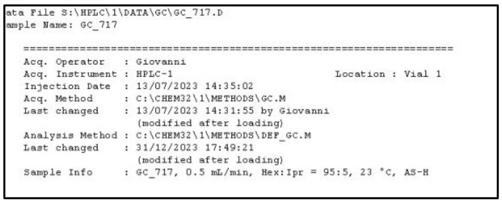

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   8.529 MM    0.3105 3400.44385  182.51599 49.10363
   2   9.973 MM    0.4873 3524.59180  120.55216 50.89637

Totals :                  6925.03564  303.06815
```

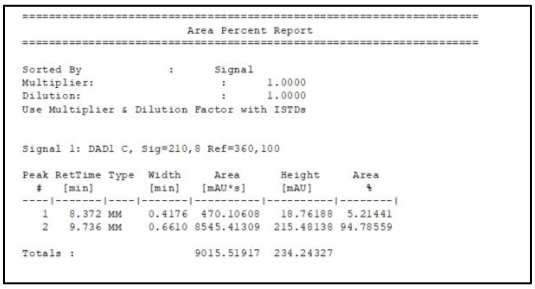


rac-3e



```
ata File S:\HPLC\1\DATA\GC\GC_717.D
ample Name: GC_717

  =====================================================================
  Acq. Operator   : Giovanni
  Acq. Instrument : HPLC-1                          Location : Vial 1
  Injection Date  : 13/07/2023 14:35:02
  Acq. Method     : C:\CHEM32\1\METHODS\GC.M
  Last changed    : 13/07/2023 14:31:55 by Giovanni
                    (modified after loading)
  Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
  Last changed    : 31/12/2023 17:49:21
                    (modified after loading)
  Sample Info     : GC_717, 0.5 mL/min, Hex:Ipr = 95:5, 23 °C, AS-H
```



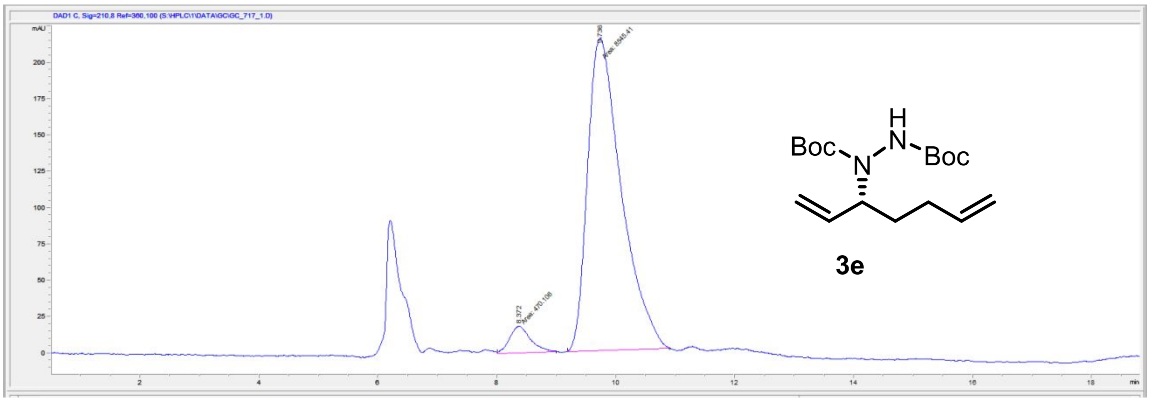
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

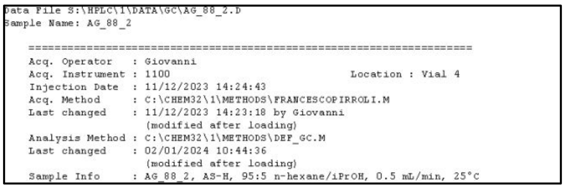

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   8.372 MM    0.4176  470.10608   18.76188  5.21441
   2   9.736 MM    0.6610 8545.41309  215.48138 94.78559

Totals :                  9015.51917  234.24327
```

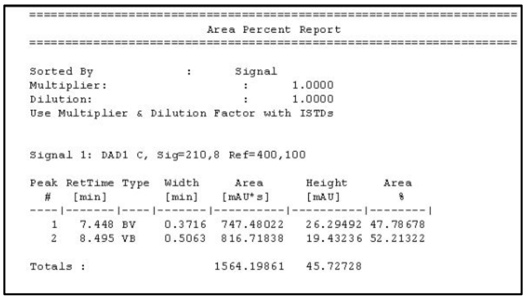


3e



```
Data File S:\HPLC\1\DATA\GC\AG_88_2.D
Sample Name: AG_88_2

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                            Location : Vial 4
   Injection Date  : 11/12/2023 14:24:43
   Acq. Method     : C:\CHEM32\1\METHODS\FRANCESCOPIRROLI.M
   Last changed    : 11/12/2023 14:23:18 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : AG_88_2, AS-H, 95:5 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



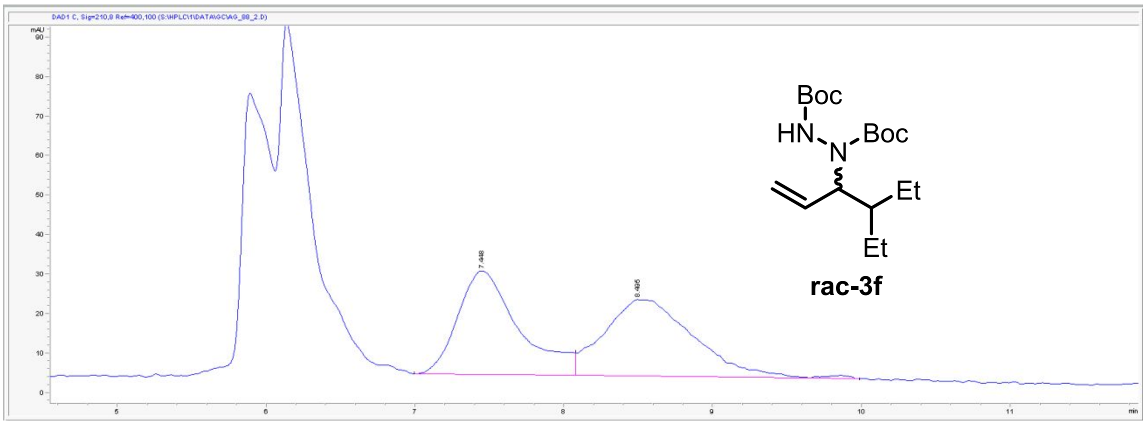
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

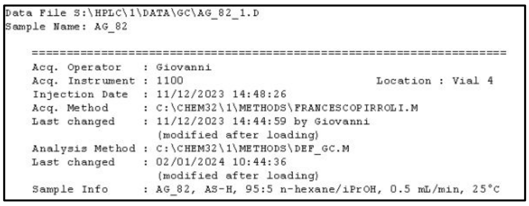

Signal 1: DAD1 C, Sig=210,8 Ref=400,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.448 BV    0.3716  747.48022   26.29492 47.78678
   2   8.495 VB    0.5063  816.71838   19.43236 52.21322

Totals :                   1564.19861   45.72728
```

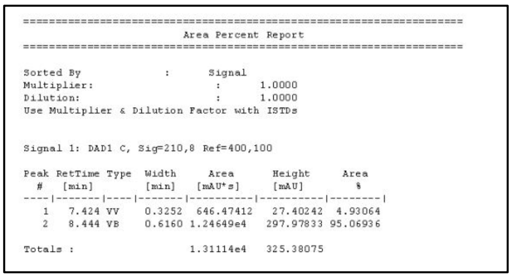


rac-3f



```
Data File S:\HPLC\1\DATA\GC\AG_82_1.D
Sample Name: AG_82

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                            Location : Vial 4
   Injection Date  : 11/12/2023 14:48:26
   Acq. Method     : C:\CHEM32\1\METHODS\FRANCESCOPIRROLI.M
   Last changed    : 11/12/2023 14:44:59 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : AG_82, AS-H, 95:5 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



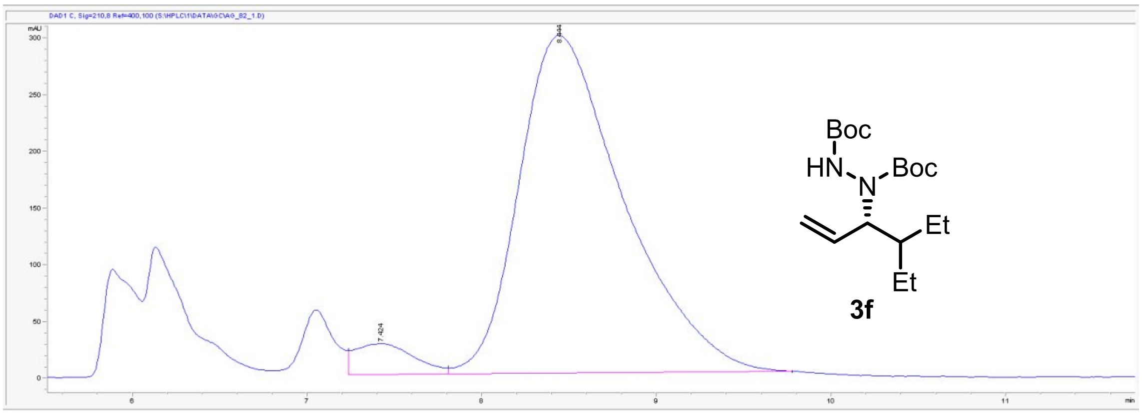
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

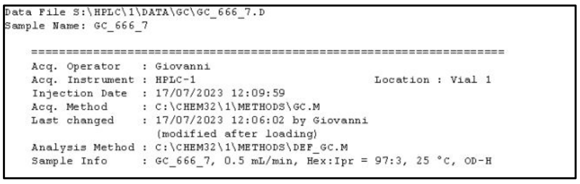

Signal 1: DAD1 C, Sig=210,8 Ref=400,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.424 VV    0.3252  646.47412   27.40242  4.93064
   2   8.444 VB    0.6160 1.24649e4   297.97833 95.06936

Totals :                   1.31114e4   325.38075
```

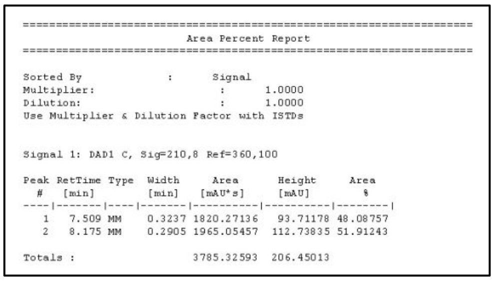


3f



```
Data File S:\HPLC\1\DATA\GC\GC_666_7.D
Sample Name: GC_666_7

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 17/07/2023 12:09:59
    Acq. Method     : C:\CHEM32\1\METHODS\GC.M
    Last changed    : 17/07/2023 12:06:02 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_666_7, 0.5 mL/min, Hex:Ipr = 97:3, 25 °C, OD-H
```



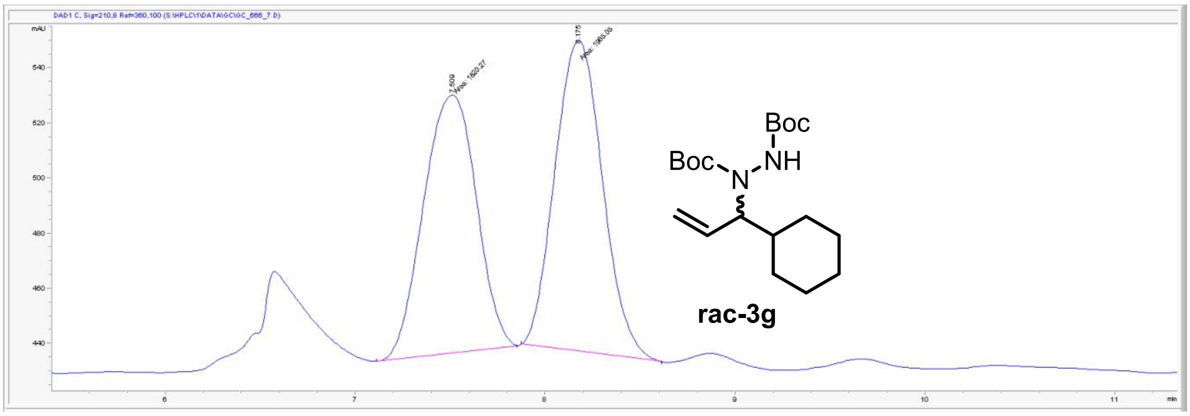
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

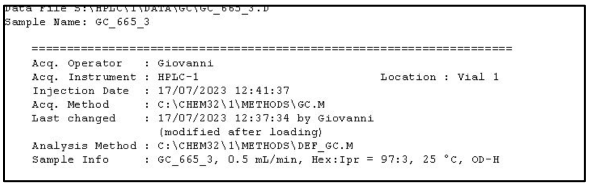

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.509 MM    0.3237 1820.27136   93.71178 48.08757
   2   8.175 MM    0.2905 1965.05457  112.73835 51.91243

Totals :                  3785.32593  206.45013
```

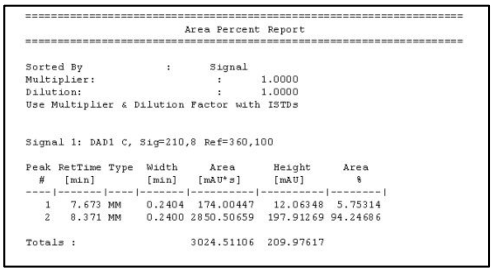


rac-3g



```
Data File S:\HPLC\1\DATA\GC\GC_665_3.D
Sample Name: GC_665_3

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 17/07/2023 12:41:37
    Acq. Method     : C:\CHEM32\1\METHODS\GC.M
    Last changed    : 17/07/2023 12:37:34 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_665_3, 0.5 mL/min, Hex:Ipr = 97:3, 25 °C, OD-H
```



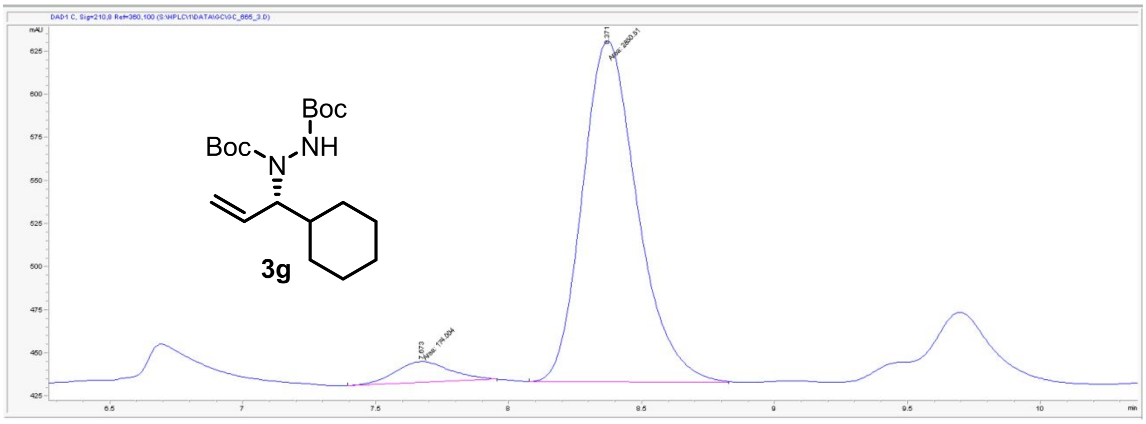
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

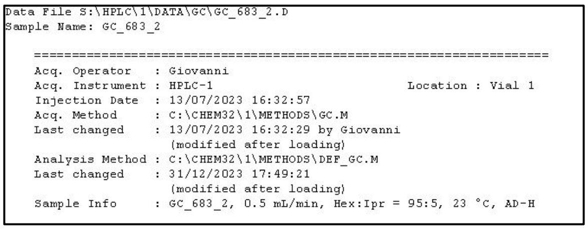

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.673 MM    0.2404  174.00447   12.06348  5.75314
   2   8.371 MM    0.2400 2850.50659  197.91269 94.24686

Totals :                  3024.51106  209.97617
```

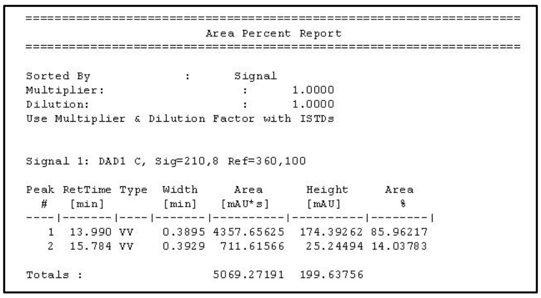


3g



```
Data File S:\HPLC\1\DATA\GC\GC_683_2.D
Sample Name: GC_683_2

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : HPLC-1                        Location : Vial 1
   Injection Date  : 13/07/2023 16:32:57
   Acq. Method     : C:\CHEM32\1\METHODS\GC.M
   Last changed    : 13/07/2023 16:32:29 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 31/12/2023 17:49:21
                     (modified after loading)
   Sample Info     : GC_683_2, 0.5 mL/min, Hex:Ipr = 95:5, 23 °C, AD-H
```



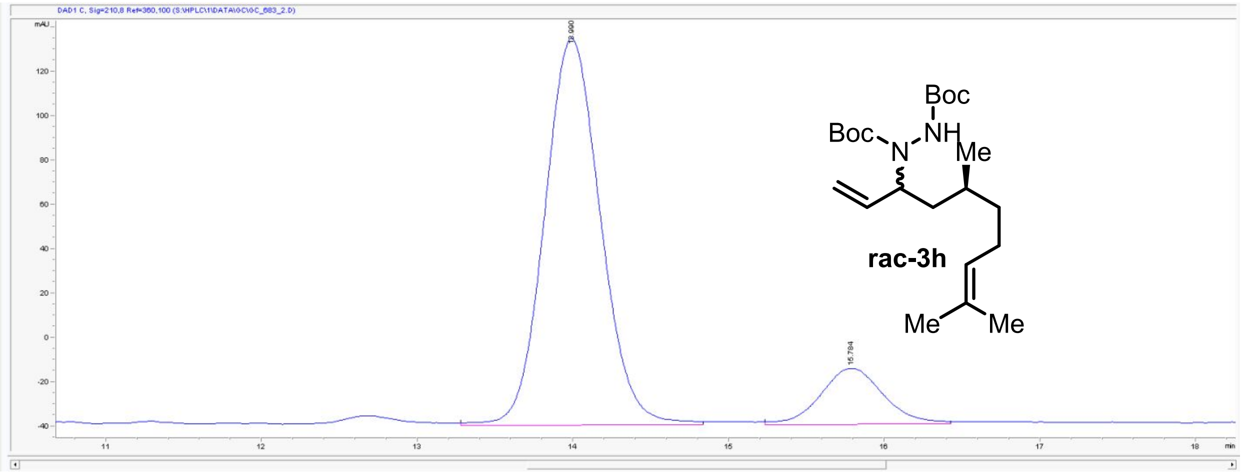
```
=====================================================================
                         Area Percent Report
=====================================================================

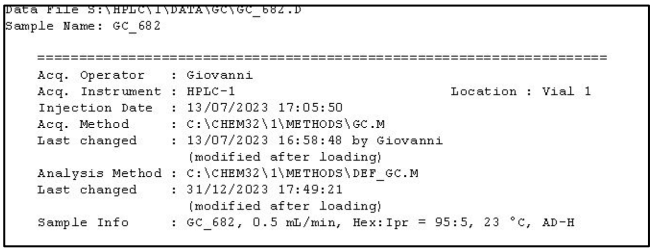
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  13.990 VV    0.3895 4357.65625  174.39262 85.96217
   2  15.784 VV    0.3929  711.61566   25.24494 14.03783

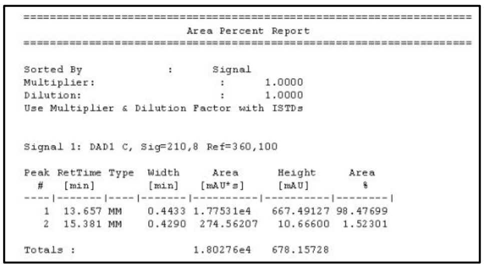
Totals :                  5069.27191  199.63756
```





```
Data File S:\HPLC\1\DATA\GC\GC_682.D
Sample Name: GC_682

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : HPLC-1                        Location : Vial 1
   Injection Date  : 13/07/2023 17:05:50
   Acq. Method     : C:\CHEM32\1\METHODS\GC.M
   Last changed    : 13/07/2023 16:58:48 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 31/12/2023 17:49:21
                     (modified after loading)
   Sample Info     : GC_682, 0.5 mL/min, Hex:Ipr = 95:5, 23 °C, AD-H
```



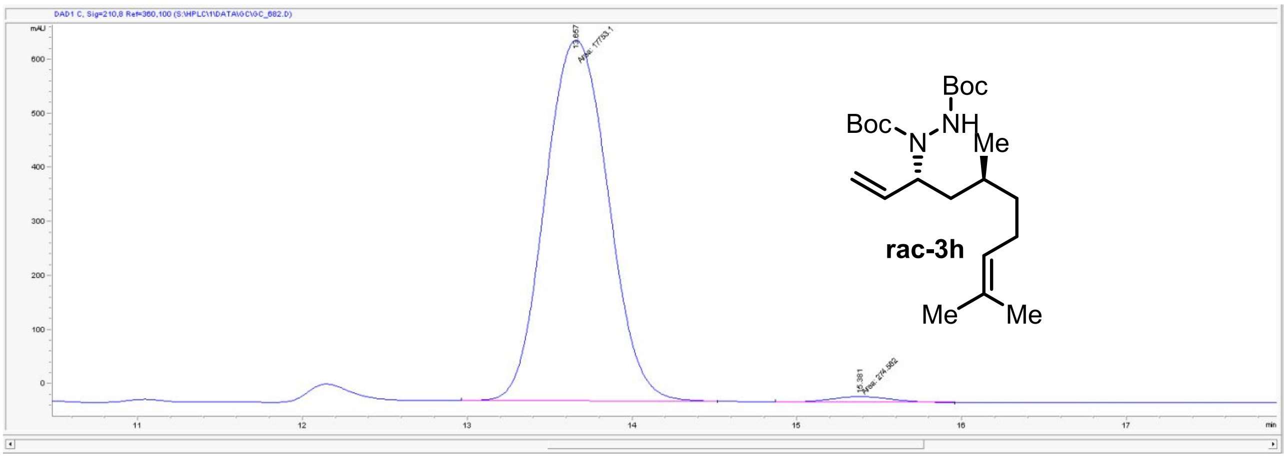
```
=====================================================================
                         Area Percent Report
=====================================================================

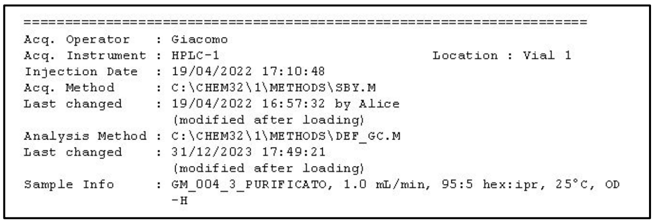
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

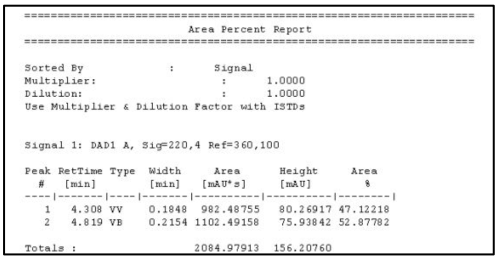
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  13.657 MM    0.4433 1.77531e4  667.49127 98.47699
   2  15.381 MM    0.4290  274.56207  10.66600  1.52301

Totals :                  1.80276e4   678.15728
```





```
=====================================================================
Acq. Operator   : Giacomo
Acq. Instrument : HPLC-1                         Location : Vial 1
Injection Date  : 19/04/2022 17:10:48
Acq. Method     : C:\CHEM32\1\METHODS\SBY.M
Last changed    : 19/04/2022 16:57:32 by Alice
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
Last changed    : 31/12/2023 17:49:21
                  (modified after loading)
Sample Info     : GM_004_3_PURIFICATO, 1.0 mL/min, 95:5 hex:ipr, 25°C, OD
                  -H
```



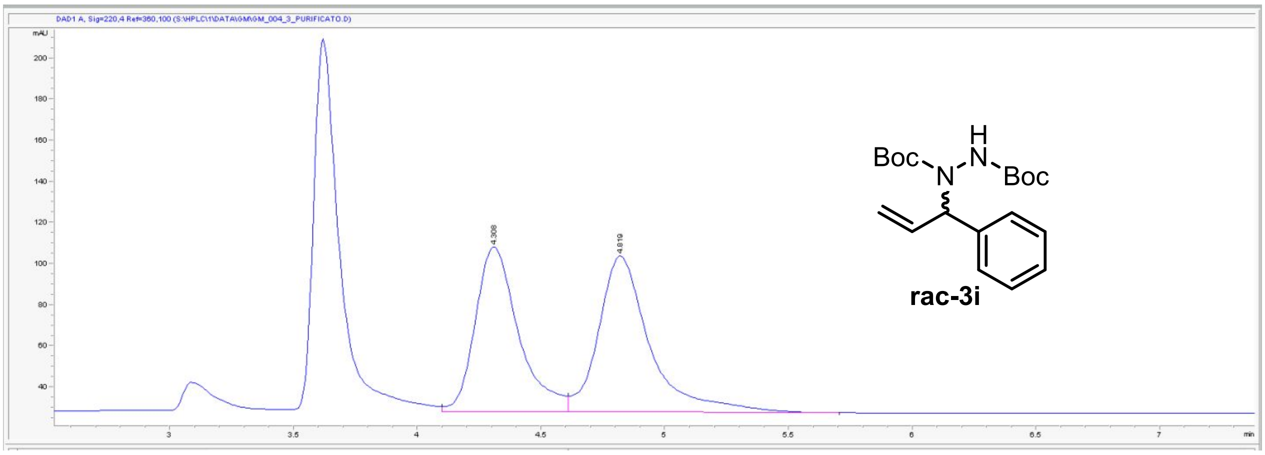
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

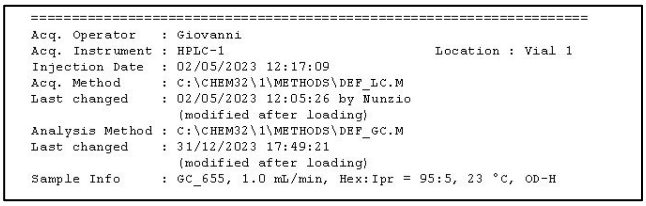

Signal 1: DAD1 A, Sig=220,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.308 VV    0.1848  982.48755   80.26917 47.12218
   2   4.819 VB    0.2154 1102.49158   75.93842 52.87782

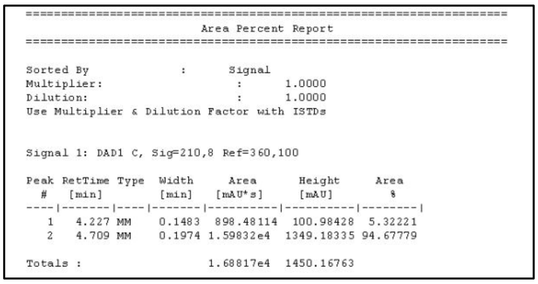
Totals :                  2084.97913  156.20760
```



rac-3i



```
=====================================================================
Acq. Operator   : Giovanni
Acq. Instrument : HPLC-1                         Location : Vial 1
Injection Date  : 02/05/2023 12:17:09
Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 02/05/2023 12:05:26 by Nunzio
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
Last changed    : 31/12/2023 17:49:21
                  (modified after loading)
Sample Info     : GC_655, 1.0 mL/min, Hex:Ipr = 95:5, 23 °C, OD-H
```



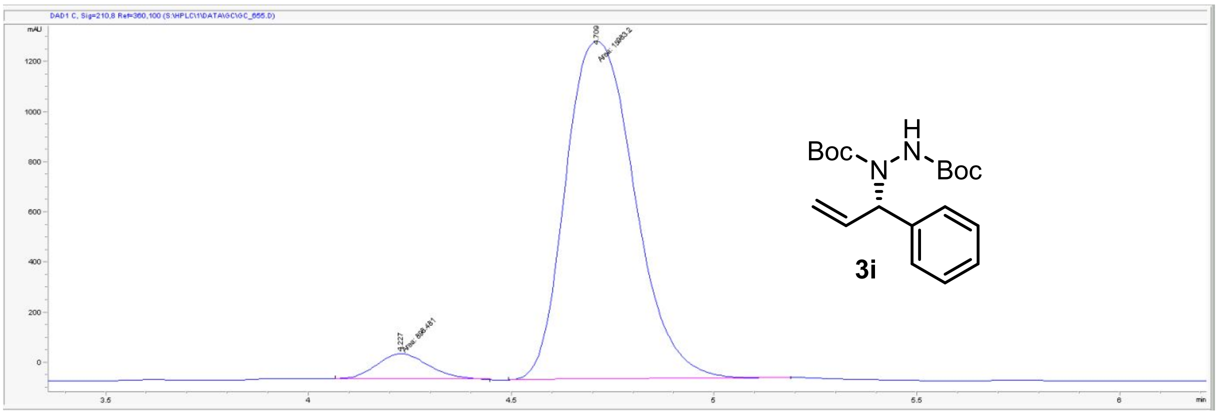
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

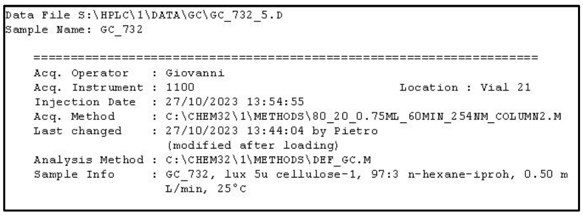

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.227 MM    0.1483  898.48114  100.98428  5.32221
   2   4.709 MM    0.1974 1.59832e4  1349.18335 94.67779

Totals :                  1.68817e4  1450.16763
```

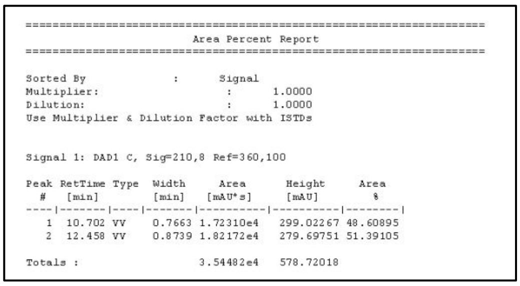


3i



```
Data File S:\HPLC\1\DATA\GC\GC_732_5.D
Sample Name: GC_732

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1100                          Location : Vial 21
    Injection Date  : 27/10/2023 13:54:55
    Acq. Method     : C:\CHEM32\1\METHODS\80_20_0.75ML_60MIN_254NM_COLUMN2.M
    Last changed    : 27/10/2023 13:44:04 by Pietro
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_732, lux 5u cellulose-1, 97:3 n-hexane-iproh, 0.50 m
                      L/min, 25°C
```



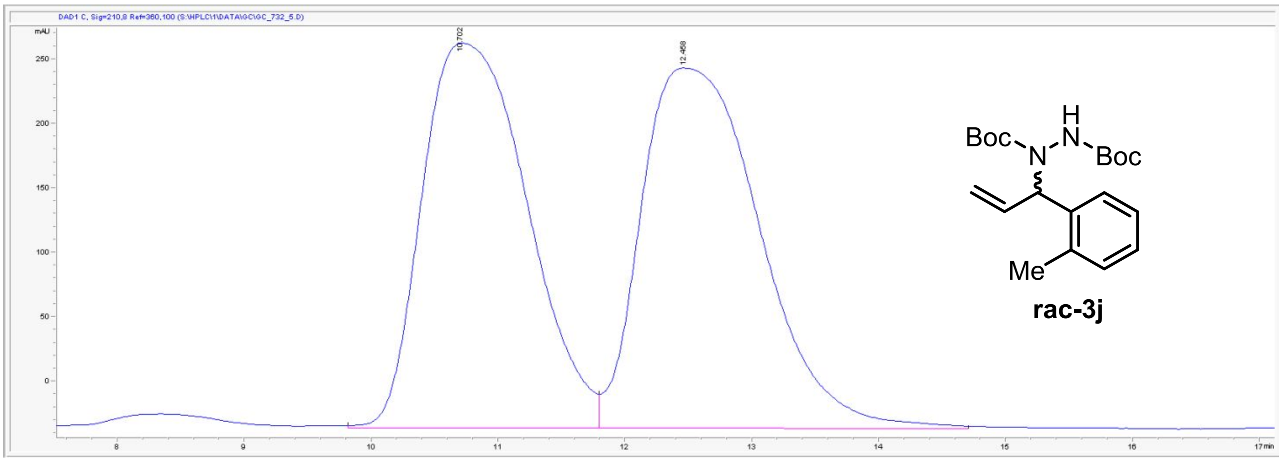
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

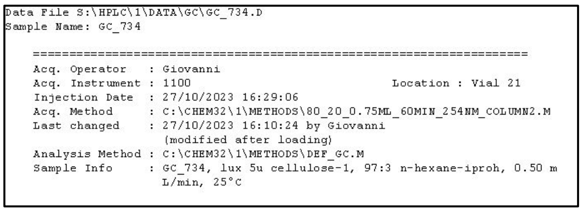

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.702 VV    0.7663 1.72310e4  299.02267 48.60895
   2  12.458 VV    0.8739 1.82172e4  279.69751 51.39105

Totals :                  3.54482e4  578.72018
```

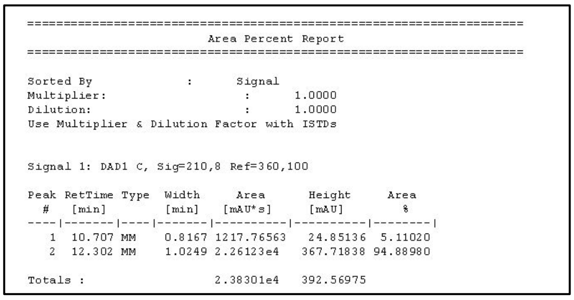


rac-3j



```
Data File S:\HPLC\1\DATA\GC\GC_734.D
Sample Name: GC_734

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1100                          Location : Vial 21
    Injection Date  : 27/10/2023 16:29:06
    Acq. Method     : C:\CHEM32\1\METHODS\80_20_0.75ML_60MIN_254NM_COLUMN2.M
    Last changed    : 27/10/2023 16:10:24 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_734, lux 5u cellulose-1, 97:3 n-hexane-iproh, 0.50 m
                      L/min, 25°C
```



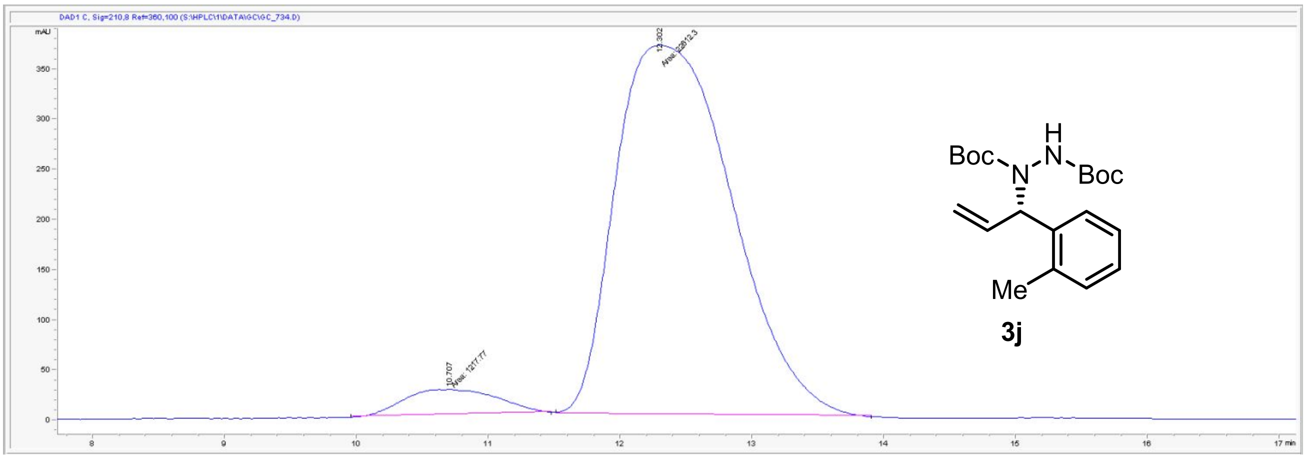
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

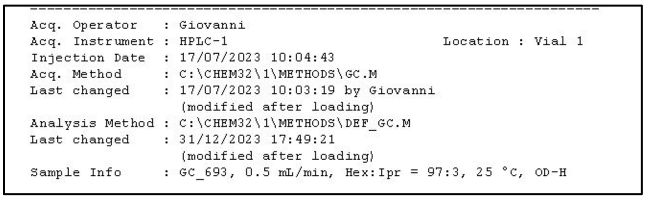

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.707 MM    0.8167 1217.76563   24.85136  5.11020
   2  12.302 MM    1.0249 2.26123e4  367.71838 94.88980

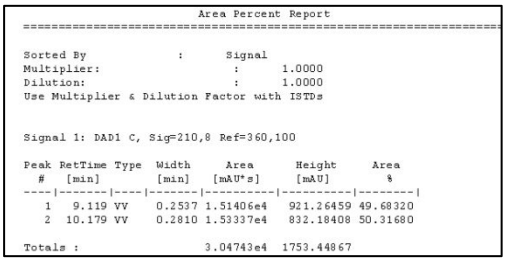
Totals :                  2.38301e4  392.56975
```



3j



```
  ========================================================================
  Acq. Operator   : Giovanni
  Acq. Instrument : HPLC-1                          Location : Vial 1
  Injection Date  : 17/07/2023 10:04:43
  Acq. Method     : C:\CHEM32\1\METHODS\GC.M
  Last changed    : 17/07/2023 10:03:19 by Giovanni
                    (modified after loading)
  Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
  Last changed    : 31/12/2023 17:49:21
                    (modified after loading)
  Sample Info     : GC_693, 0.5 mL/min, Hex:Ipr = 97:3, 25 °C, OD-H
```



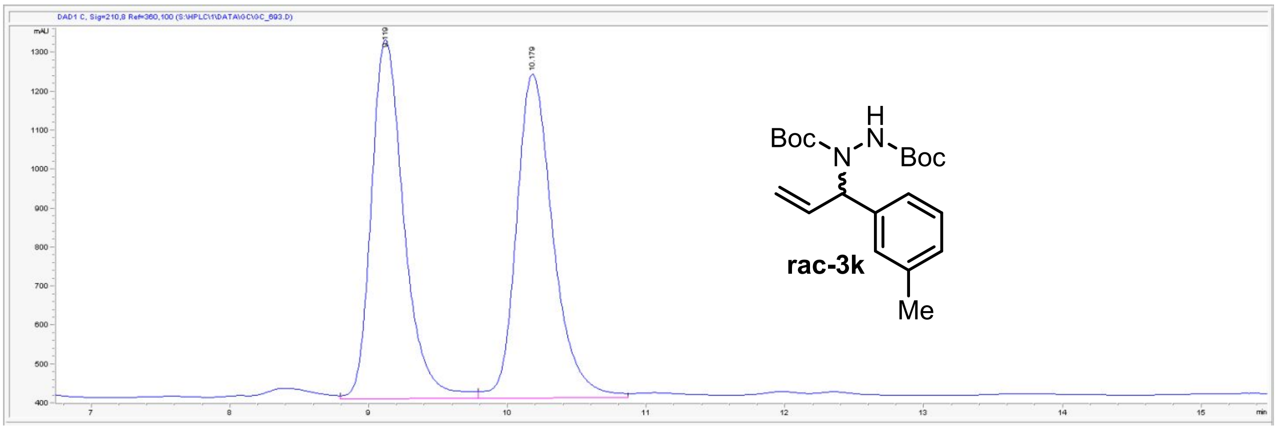
```
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

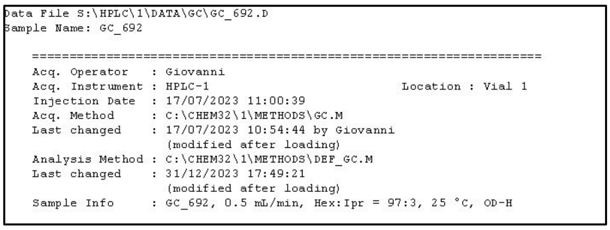

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.119 VV    0.2537 1.51406e4  921.26459 49.68320
   2  10.179 VV    0.2810 1.53337e4  832.18408 50.31680

Totals :                  3.04743e4  1753.44867
```

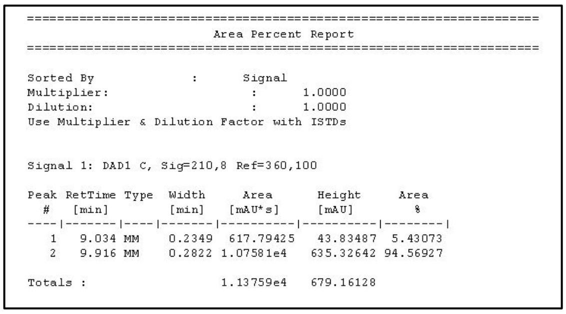


+



```
Data File S:\HPLC\1\DATA\GC\GC_692.D
Sample Name: GC_692

    ====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                        Location : Vial 1
    Injection Date  : 17/07/2023 11:00:39
    Acq. Method     : C:\CHEM32\1\METHODS\GC.M
    Last changed    : 17/07/2023 10:54:44 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Last changed    : 31/12/2023 17:49:21
                      (modified after loading)
    Sample Info     : GC_692, 0.5 mL/min, Hex:Ipr = 97:3, 25 °C, OD-H
```



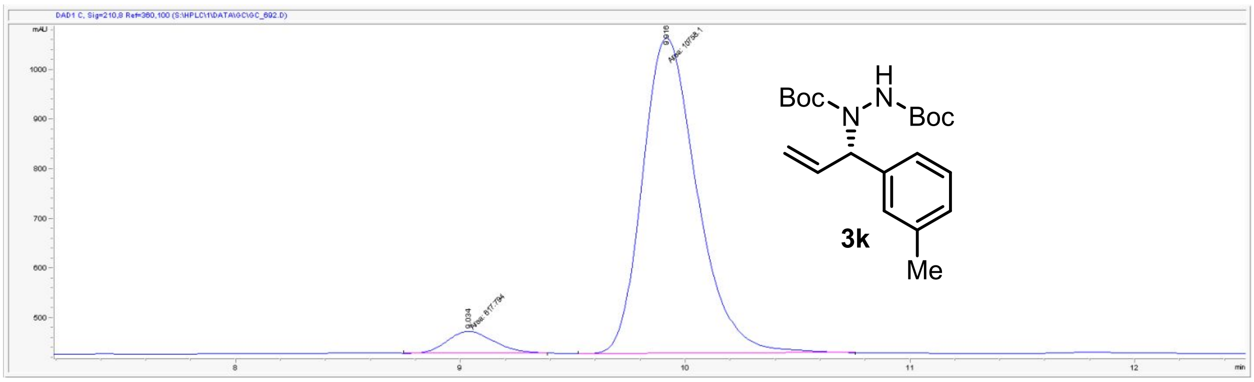
```
==================================================================
                        Area Percent Report
==================================================================

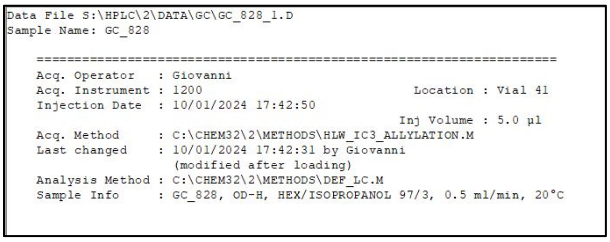
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.034 MM    0.2349  617.79425   43.83487  5.43073
   2   9.916 MM    0.2822 1.07581e4  635.32642 94.56927

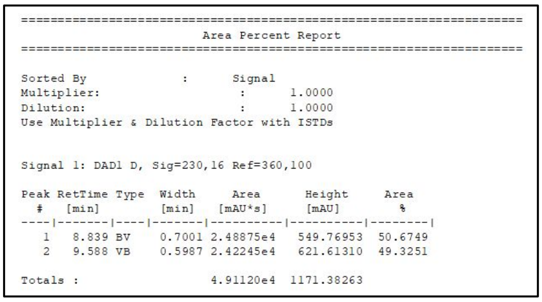
Totals :                  1.13759e4   679.16128
```





```
Data File S:\HPLC\2\DATA\GC\GC_828_1.D
Sample Name: GC_828

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1200                           Location : Vial 41
    Injection Date  : 10/01/2024 17:42:50
                                                 Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\2\METHODS\HLW_IC3_ALLYLATION.M
    Last changed    : 10/01/2024 17:42:31 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\2\METHODS\DEF_LC.M
    Sample Info     : GC_828, OD-H, HEX/ISOPROPANOL 97/3, 0.5 ml/min, 20°C
```



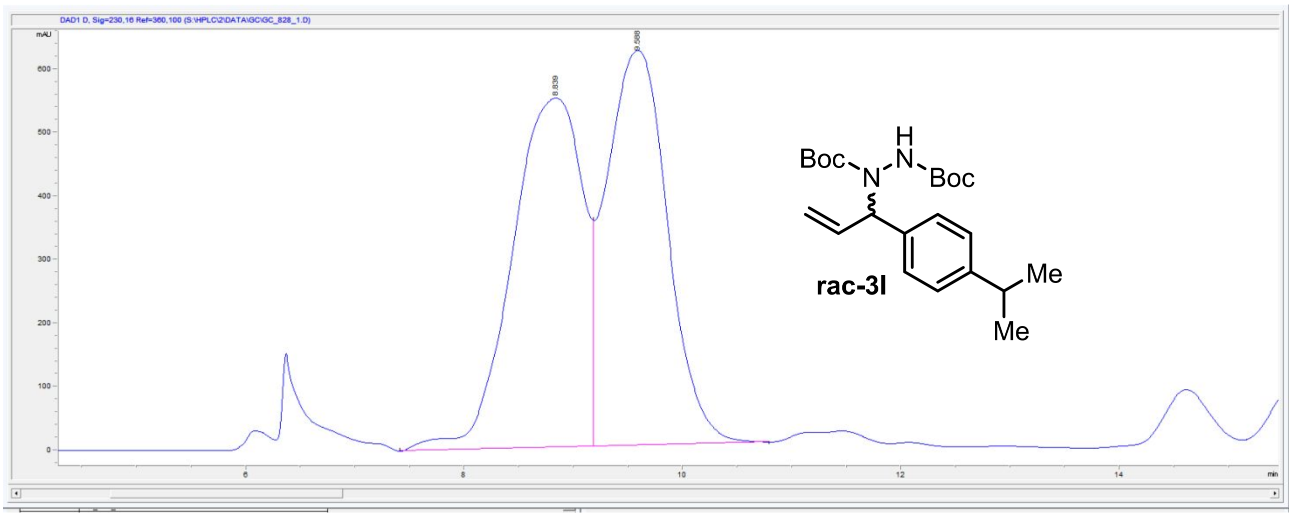
```
=====================================================================
                         Area Percent Report
=====================================================================

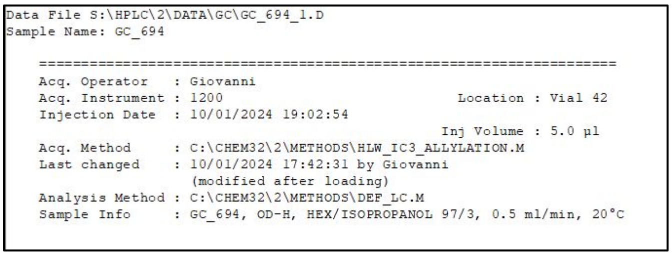
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.839 BV    0.7001 2.48875e4  549.76953 50.6749
   2   9.588 VB    0.5987 2.42245e4  621.61310 49.3251

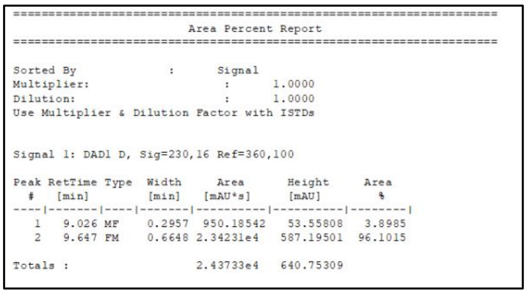
Totals :                  4.91120e4  1171.38263
```





```
Data File S:\HPLC\2\DATA\GC\GC_694_1.D
Sample Name: GC_694

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1200                           Location : Vial 42
    Injection Date  : 10/01/2024 19:02:54
                                                 Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\2\METHODS\HLW_IC3_ALLYLATION.M
    Last changed    : 10/01/2024 17:42:31 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\2\METHODS\DEF_LC.M
    Sample Info     : GC_694, OD-H, HEX/ISOPROPANOL 97/3, 0.5 ml/min, 20°C
```



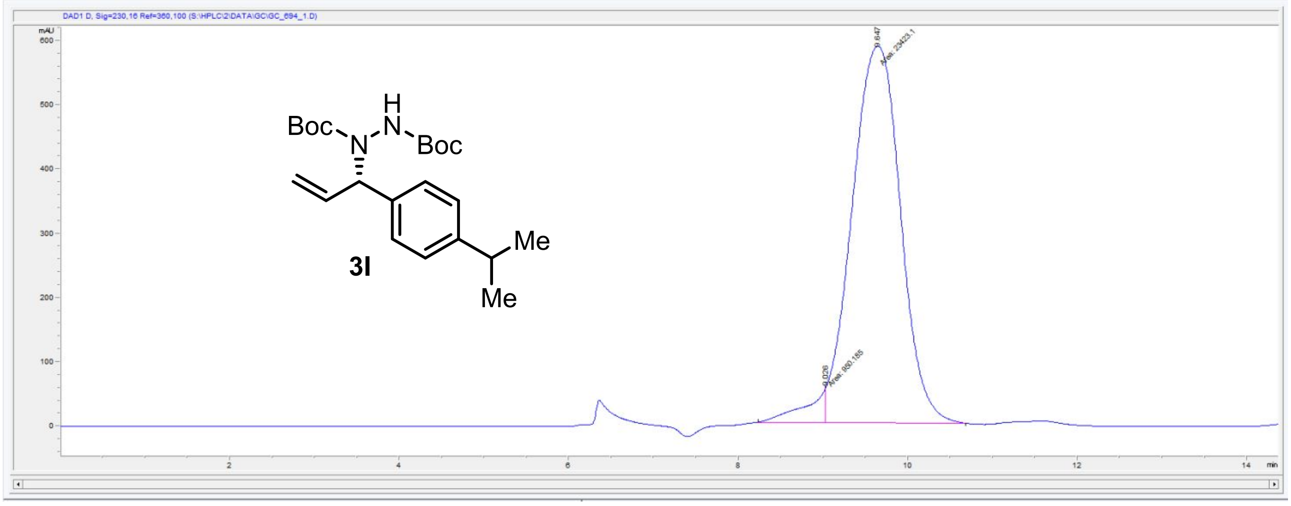
```
=====================================================================
                         Area Percent Report
=====================================================================

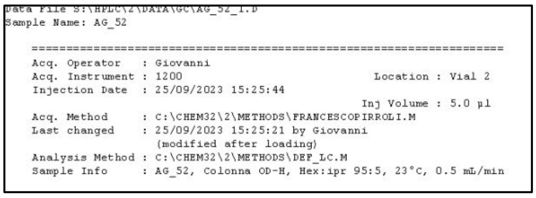
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.026 MF    0.2957  950.18542   53.55808   3.8985
   2   9.647 FM    0.6648 2.34231e4  587.19501  96.1015

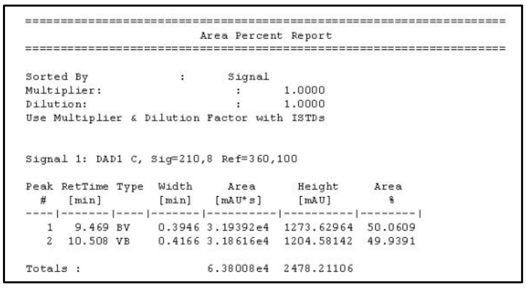
Totals :                  2.43733e4  640.75309
```





```
Data File S:\HPLC\2\DATA\GC\AG_52_1.D
Sample Name: AG_52

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1200                          Location : Vial 2
    Injection Date  : 25/09/2023 15:25:44
                                                 Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\2\METHODS\FRANCESCOPIRROLI.M
    Last changed    : 25/09/2023 15:25:21 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\2\METHODS\DEF_LC.M
    Sample Info     : AG_52, Colonna OD-H, Hex:ipr 95:5, 23°C, 0.5 mL/min
```



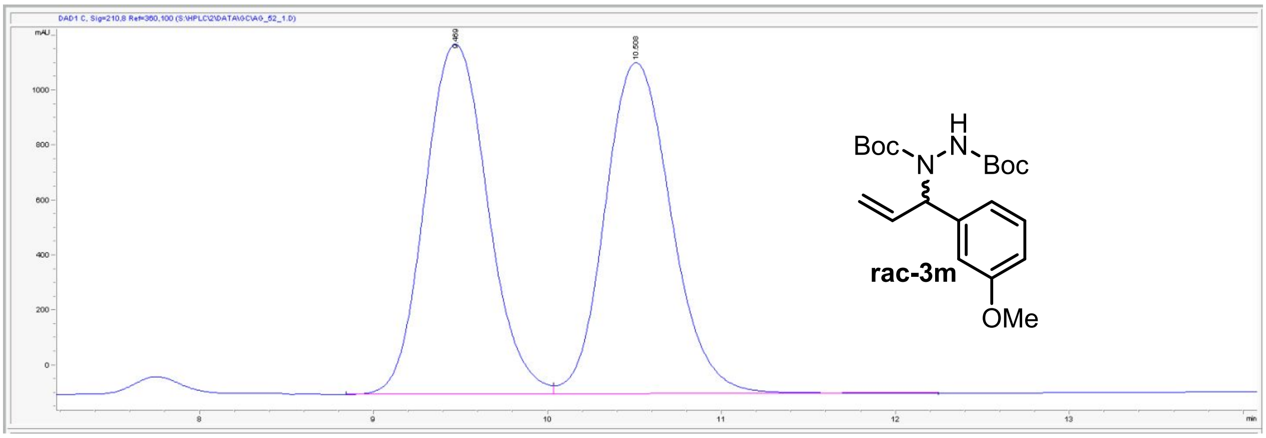
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

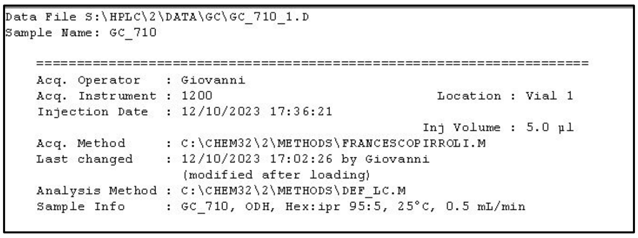

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.469 BV    0.3946 3.19392e4 1273.62964 50.0609
   2  10.508 VB    0.4166 3.18616e4 1204.58142 49.9391

Totals :                  6.38008e4  2478.21106
```

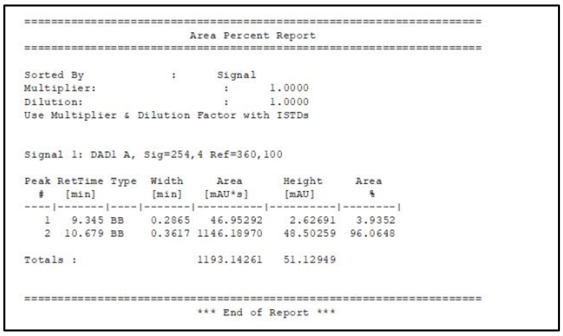


rac-3m



```
Data File S:\HPLC\2\DATA\GC\GC_710_1.D
Sample Name: GC_710

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1200                          Location : Vial 1
    Injection Date  : 12/10/2023 17:36:21
                                                 Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\2\METHODS\FRANCESCOPIRROLI.M
    Last changed    : 12/10/2023 17:02:26 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\2\METHODS\DEF_LC.M
    Sample Info     : GC_710, ODH, Hex:ipr 95:5, 25°C, 0.5 mL/min
```



```
=====================================================================
                         Area Percent Report
=====================================================================

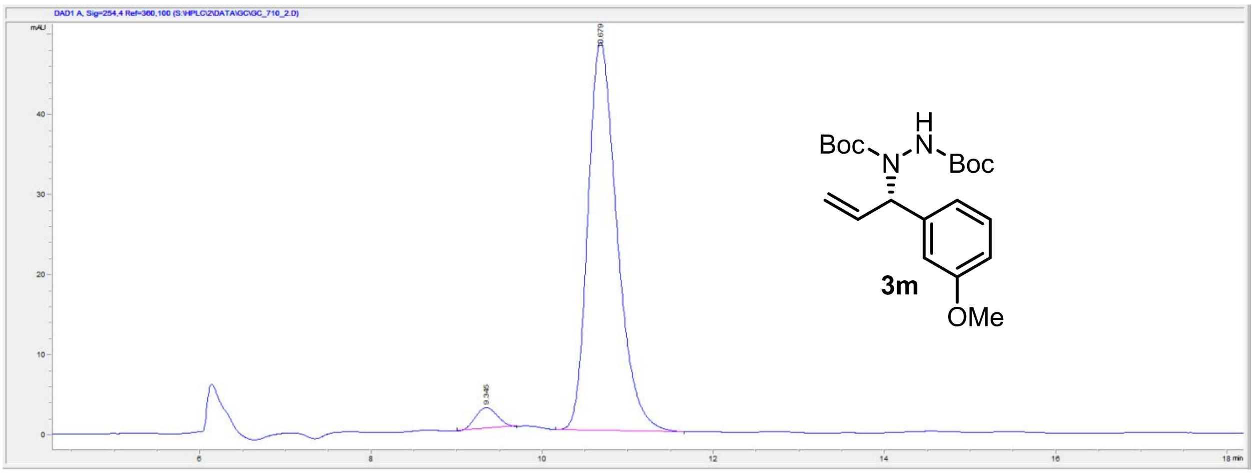
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

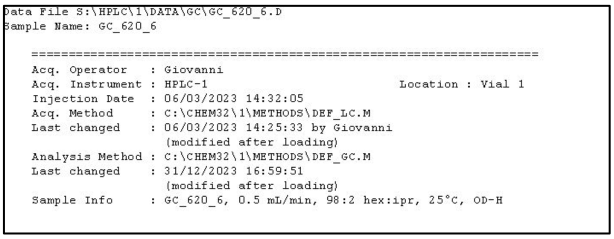
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.345 BB    0.2865   46.95292    2.62691   3.9352
   2  10.679 BB    0.3617 1146.18970   48.50259  96.0648

Totals :                  1193.14261   51.12949

=====================================================================
                          *** End of Report ***
```

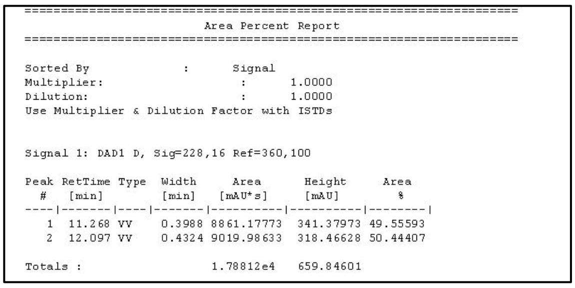


3m



```
Data File S:\HPLC\1\DATA\GC\GC_620_6.D
Sample Name: GC_620_6

    ====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 06/03/2023 14:32:05
    Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
    Last changed    : 06/03/2023 14:25:33 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Last changed    : 31/12/2023 16:59:51
                      (modified after loading)
    Sample Info     : GC_620_6, 0.5 mL/min, 98:2 hex:ipr, 25°C, OD-H
```



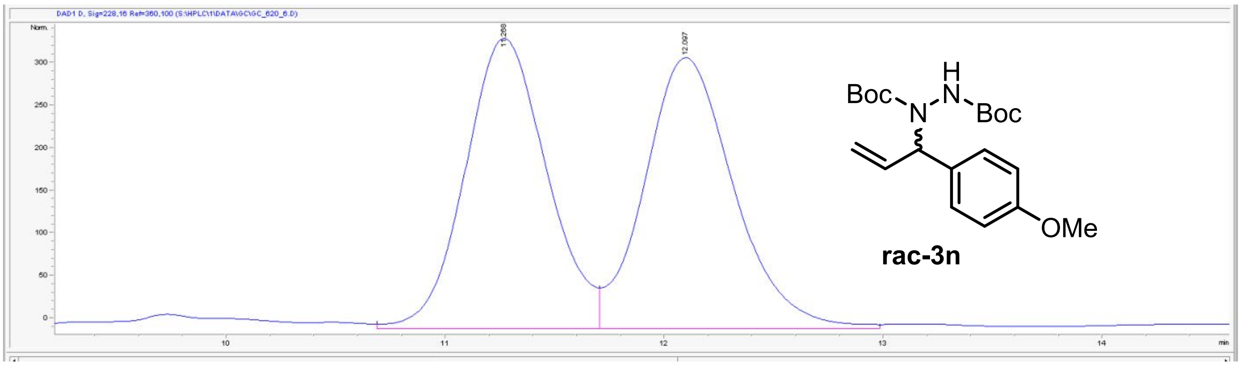
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

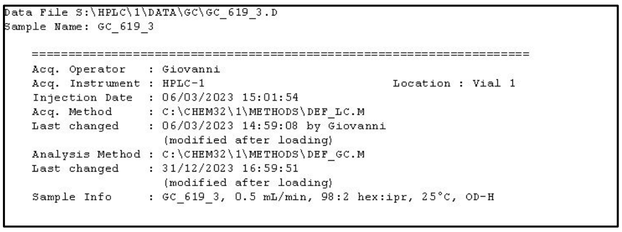

Signal 1: DAD1 D, Sig=228,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.268 VV     0.3988 8861.17773  341.37973 49.55593
   2  12.097 VV     0.4324 9019.98633  318.46628 50.44407

Totals :                   1.78812e4   659.84601
```

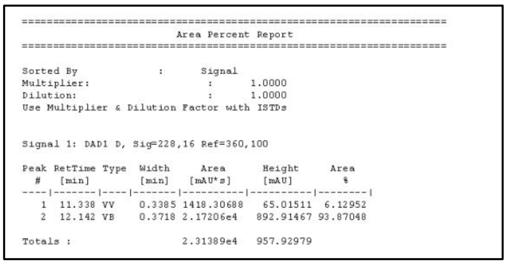


rac-3n



```
Data File S:\HPLC\1\DATA\GC\GC_619_3.D
Sample Name: GC_619_3

    ====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                          Location : Vial 1
    Injection Date  : 06/03/2023 15:01:54
    Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
    Last changed    : 06/03/2023 14:59:08 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Last changed    : 31/12/2023 16:59:51
                      (modified after loading)
    Sample Info     : GC_619_3, 0.5 mL/min, 98:2 hex:ipr, 25°C, OD-H
```



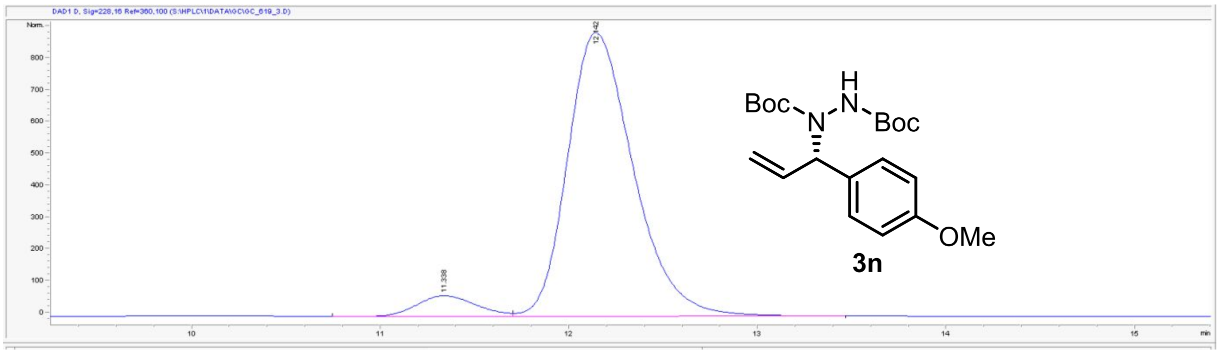
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

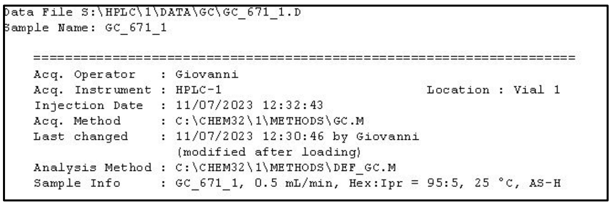

Signal 1: DAD1 D, Sig=228,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.338 VV     0.3385 1418.30688   65.01511  6.12952
   2  12.142 VB     0.3718 2.17206e4   892.91467 93.87048

Totals :                   2.31389e4   957.92979
```

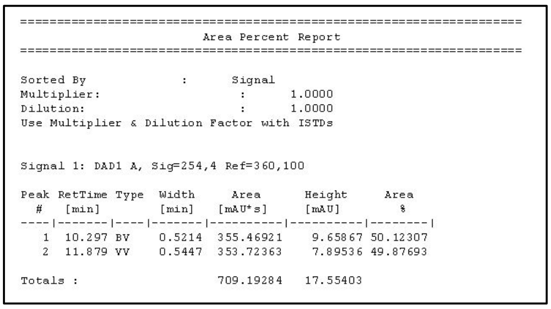


3n



```
Data File S:\HPLC\1\DATA\GC\GC_671_1.D
Sample Name: GC_671_1

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                        Location : Vial 1
    Injection Date  : 11/07/2023 12:32:43
    Acq. Method     : C:\CHEM32\1\METHODS\GC.M
    Last changed    : 11/07/2023 12:30:46 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_671_1, 0.5 mL/min, Hex:Ipr = 95:5, 25 °C, AS-H
```



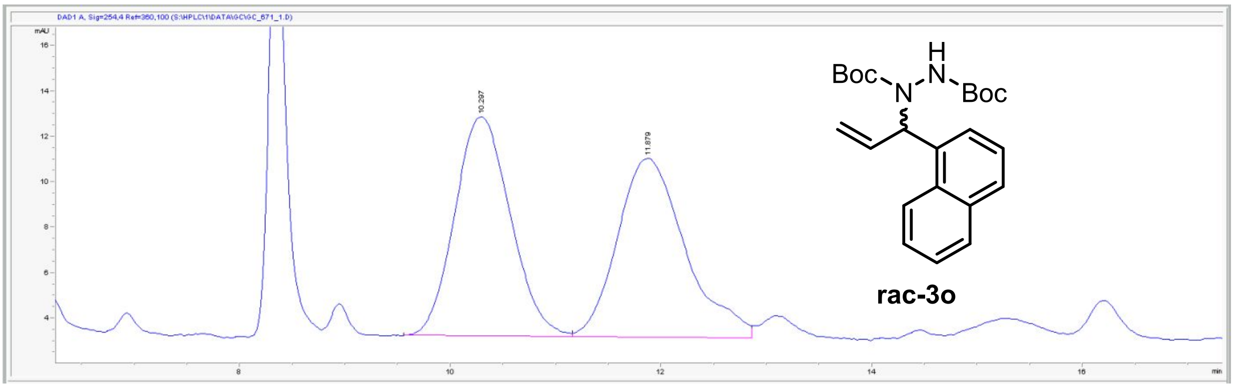
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :       1.0000
Dilution:                    :       1.0000
Use Multiplier & Dilution Factor with ISTDs

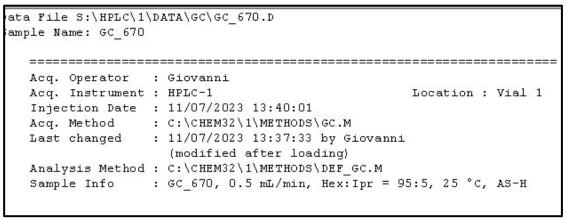

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.297 BV    0.5214  355.46921    9.65867 50.12307
   2  11.879 VV    0.5447  353.72363    7.89536 49.87693

Totals :                   709.19284   17.55403
```

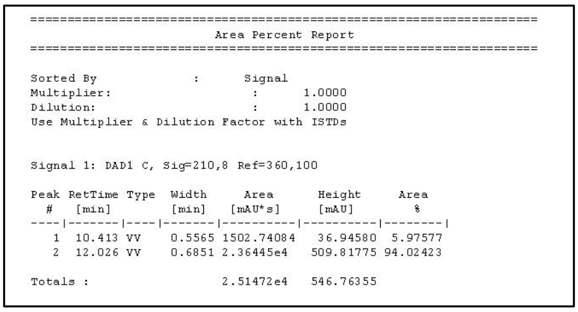


rac-3o



```
ata File S:\HPLC\1\DATA\GC\GC_670.D
ample Name: GC_670

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                        Location : Vial 1
    Injection Date  : 11/07/2023 13:40:01
    Acq. Method     : C:\CHEM32\1\METHODS\GC.M
    Last changed    : 11/07/2023 13:37:33 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_670, 0.5 mL/min, Hex:Ipr = 95:5, 25 °C, AS-H
```



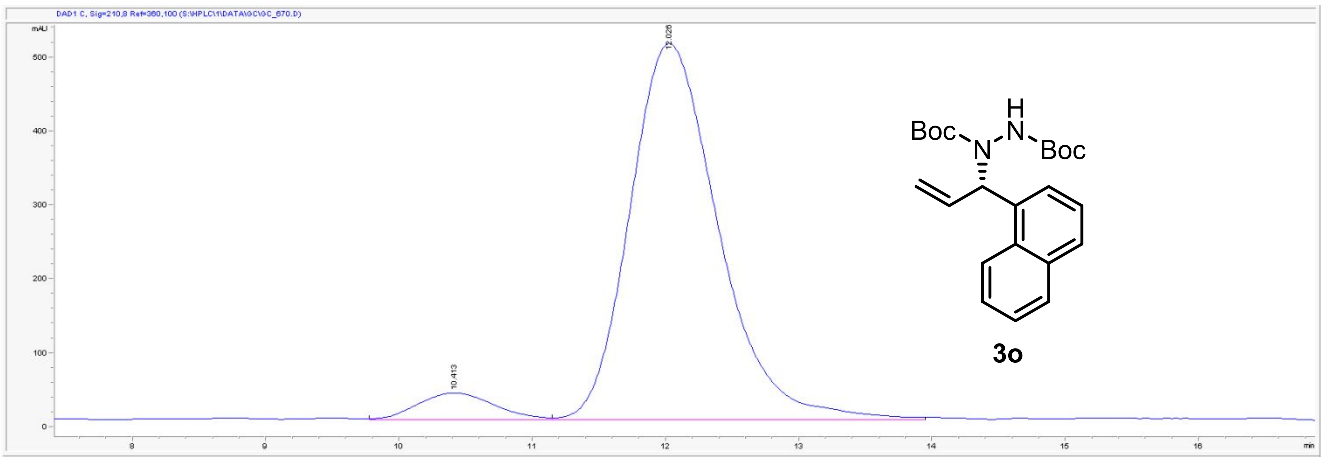
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :       1.0000
Dilution:                    :       1.0000
Use Multiplier & Dilution Factor with ISTDs

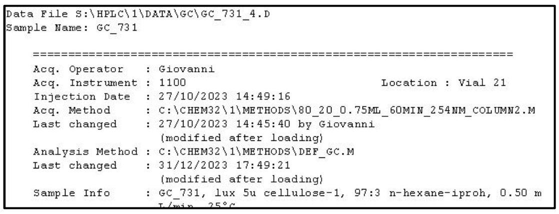

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.413 VV    0.5565 1502.74084   36.94580  5.97577
   2  12.026 VV    0.6851 2.36445e4   509.81775 94.02423

Totals :                   2.51472e4  546.76355
```

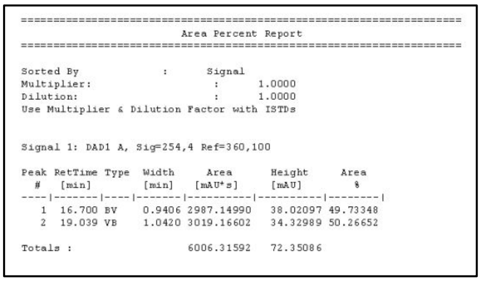


3o



```
Data File S:\HPLC\1\DATA\GC\GC_731_4.D
Sample Name: GC_731

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1100                            Location : Vial 21
    Injection Date  : 27/10/2023 14:49:16
    Acq. Method     : C:\CHEM32\1\METHODS\80_20_0.75ML_60MIN_254NM_COLUMN2.M
    Last changed    : 27/10/2023 14:45:40 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Last changed    : 31/12/2023 17:49:21
                      (modified after loading)
    Sample Info     : GC_731, lux 5u cellulose-1, 97:3 n-hexane-iproh, 0.50 m
                      L/min, 25°C
```



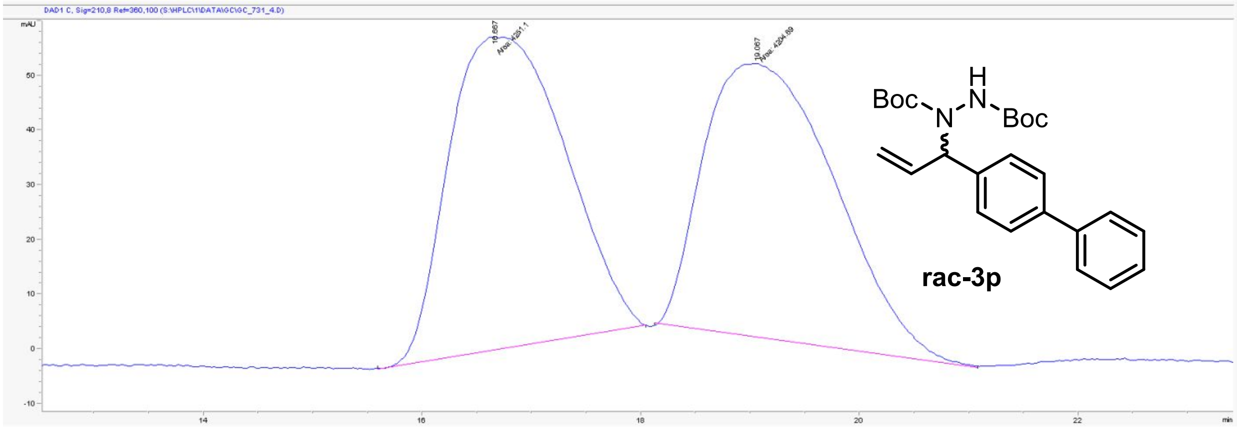
```
=====================================================================
                         Area Percent Report
=====================================================================

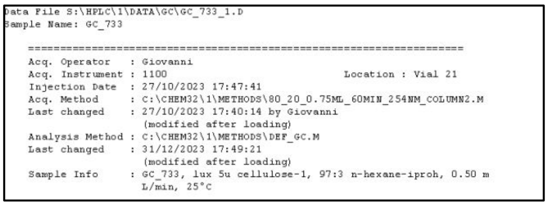
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  16.700 BV    0.9406 2987.14990   38.02097 49.73348
   2  19.039 VB    1.0420 3019.16602   34.32989 50.26652

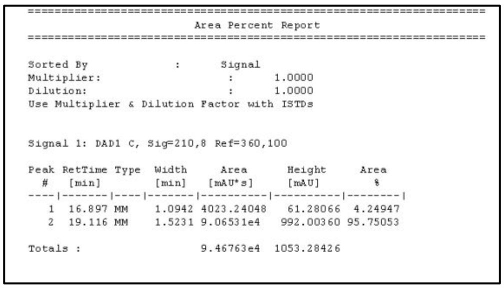
Totals :                  6006.31592   72.35086
```





```
Data File S:\HPLC\1\DATA\GC\GC_733_1.D
Sample Name: GC_733

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : 1100                            Location : Vial 21
    Injection Date  : 27/10/2023 17:47:41
    Acq. Method     : C:\CHEM32\1\METHODS\80_20_0.75ML_60MIN_254NM_COLUMN2.M
    Last changed    : 27/10/2023 17:40:14 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Last changed    : 31/12/2023 17:49:21
                      (modified after loading)
    Sample Info     : GC_733, lux 5u cellulose-1, 97:3 n-hexane-iproh, 0.50 m
                      L/min, 25°C
```



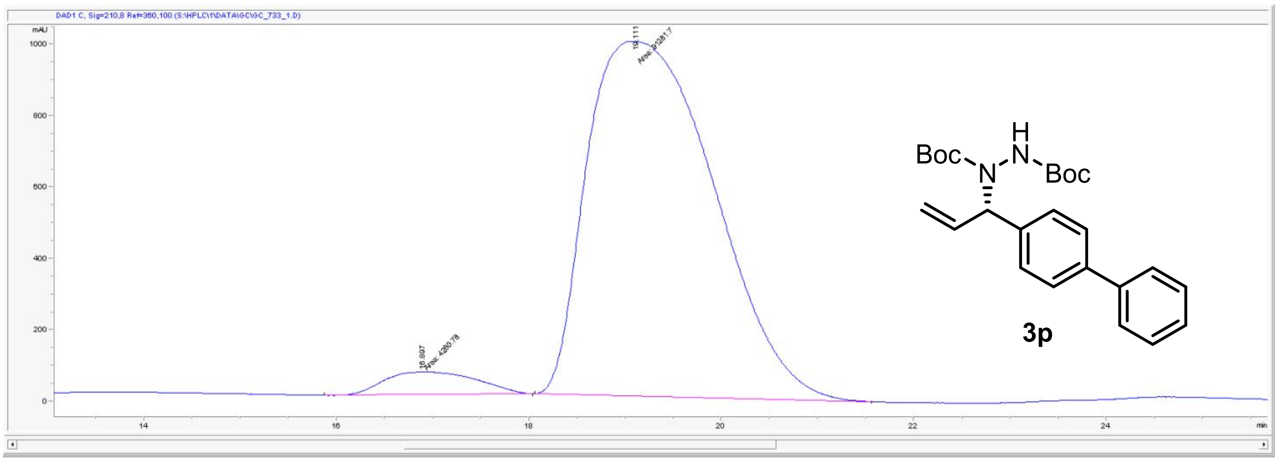
```
=====================================================================
                         Area Percent Report
=====================================================================

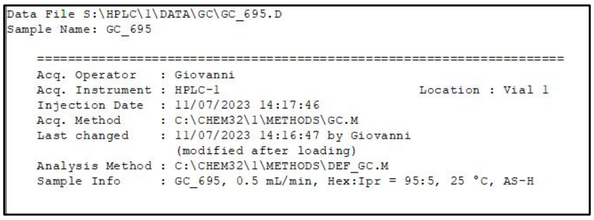
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  16.897 MM    1.0942 4023.24048   61.28066  4.24947
   2  19.116 MM    1.5231 9.06531e4   992.00360 95.75053

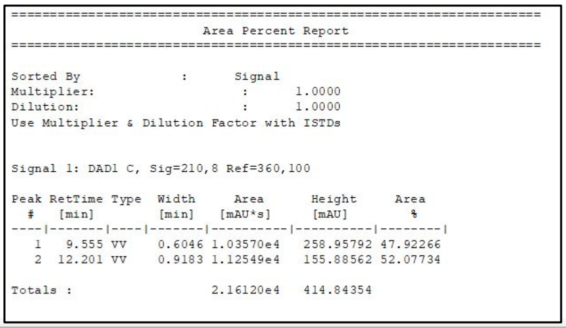
Totals :                  9.46763e4  1053.28426
```





```
Data File S:\HPLC\1\DATA\GC\GC_695.D
Sample Name: GC_695

    =====================================================================
    Acq. Operator   : Giovanni
    Acq. Instrument : HPLC-1                      Location : Vial 1
    Injection Date  : 11/07/2023 14:17:46
    Acq. Method     : C:\CHEM32\1\METHODS\GC.M
    Last changed    : 11/07/2023 14:16:47 by Giovanni
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_695, 0.5 mL/min, Hex:Ipr = 95:5, 25 °C, AS-H
```



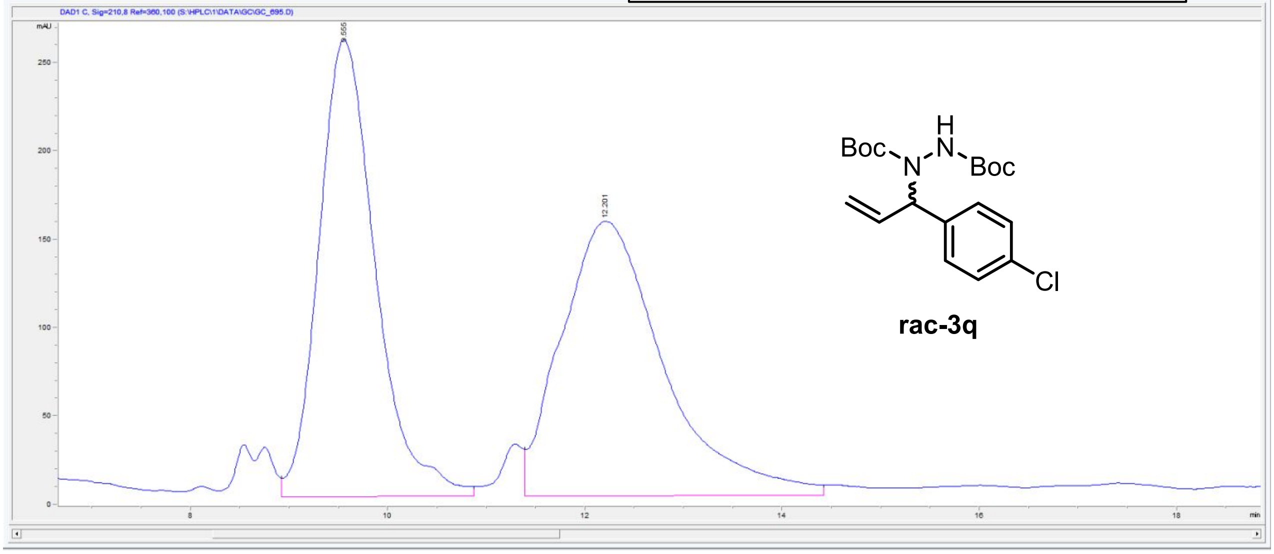
```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

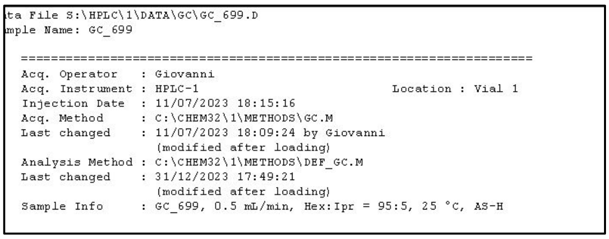

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.555 VV    0.6046 1.03570e4   258.95792 47.92266
   2  12.201 VV    0.9183 1.12549e4   155.88562 52.07734

Totals :                  2.16120e4   414.84354
```

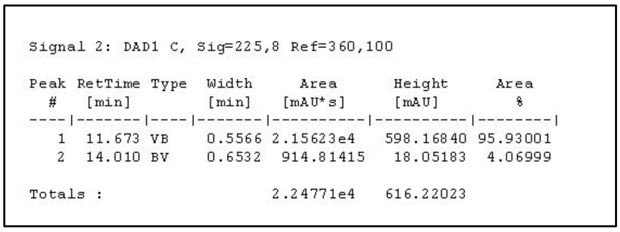


rac-3q



```
ta File S:\HPLC\1\DATA\GC\GC_699.D
mple Name: GC_699

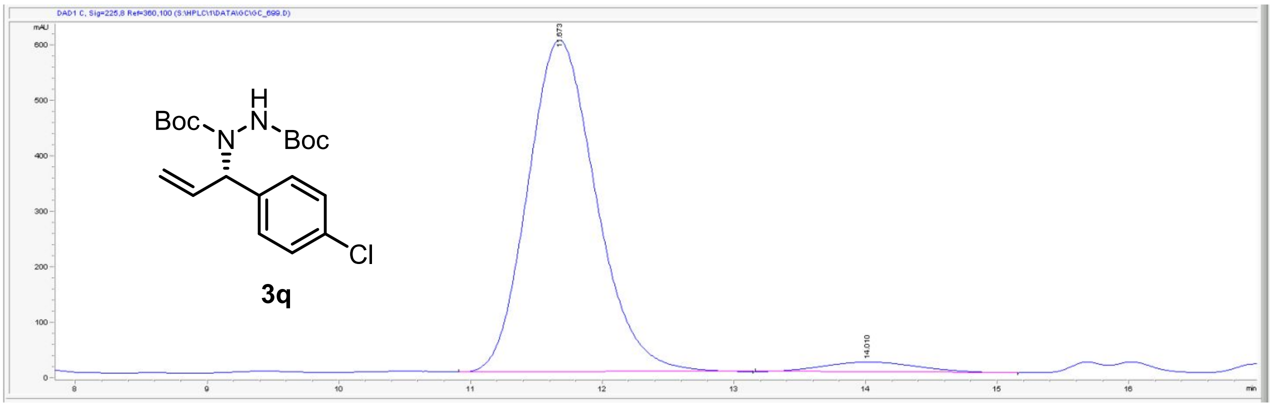
  =====================================================================
  Acq. Operator   : Giovanni
  Acq. Instrument : HPLC-1                      Location : Vial 1
  Injection Date  : 11/07/2023 18:15:16
  Acq. Method     : C:\CHEM32\1\METHODS\GC.M
  Last changed    : 11/07/2023 18:09:24 by Giovanni
                    (modified after loading)
  Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
  Last changed    : 31/12/2023 17:49:21
                    (modified after loading)
  Sample Info     : GC_699, 0.5 mL/min, Hex:Ipr = 95:5, 25 °C, AS-H
```



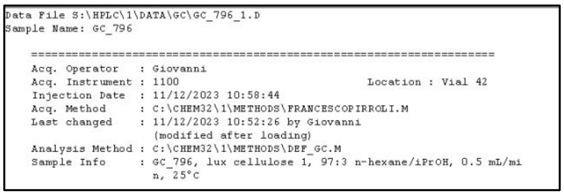
```
Signal 2: DAD1 C, Sig=225,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.673 VB    0.5566 2.15623e4   598.16840 95.93001
   2  14.010 BV    0.6532  914.81415   18.05183  4.06999

Totals :                  2.24771e4   616.22023
```

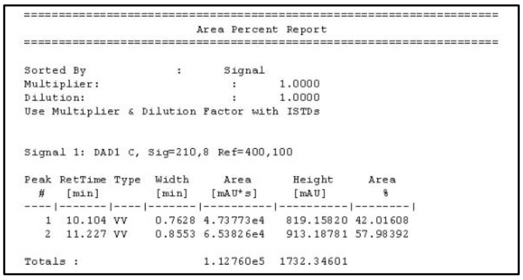


3q



```
Data File S:\HPLC\1\DATA\GC\GC_796_1.D
Sample Name: GC_796

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                          Location : Vial 42
   Injection Date  : 11/12/2023 10:58:44
   Acq. Method     : C:\CHEM32\1\METHODS\FRANCESCOPIRROLI.M
   Last changed    : 11/12/2023 10:52:26 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Sample Info     : GC_796, lux cellulose 1, 97:3 n-hexane/iPrOH, 0.5 mL/mi
                     n, 25°C
```



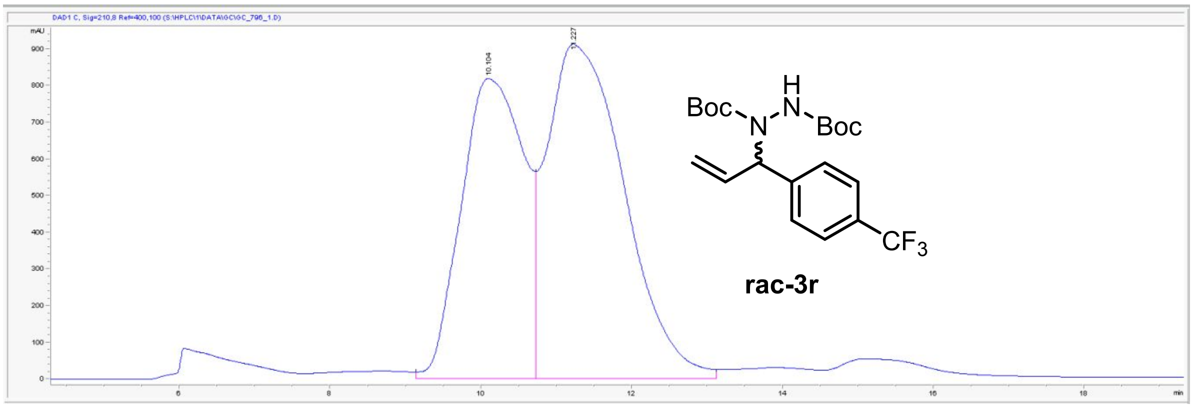
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

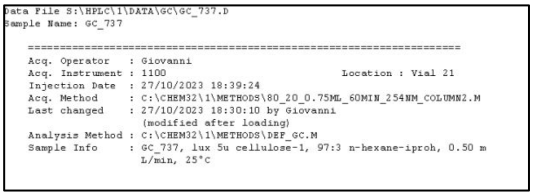

Signal 1: DAD1 C, Sig=210,8 Ref=400,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.104 VV    0.7628 4.73773e4  819.15820 42.01608
   2  11.227 VV    0.8553 6.53826e4  913.18781 57.98392

Totals :                  1.12760e5  1732.34601
```

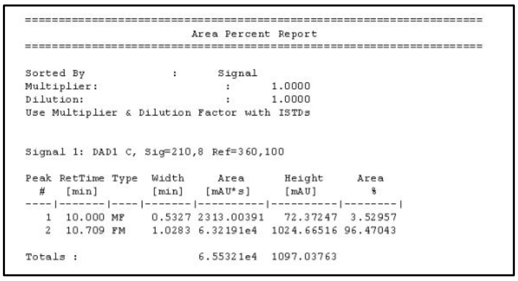


rac-3r



```
Data File S:\HPLC\1\DATA\GC\GC_737.D
Sample Name: GC_737

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                          Location : Vial 21
   Injection Date  : 27/10/2023 18:39:24
   Acq. Method     : C:\CHEM32\1\METHODS\80_20_0.75ML_60MIN_254NM_COLUMN2.M
   Last changed    : 27/10/2023 18:30:10 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Sample Info     : GC_737, lux 5u cellulose-1, 97:3 n-hexane-iproh, 0.50 m
                     L/min, 25°C
```



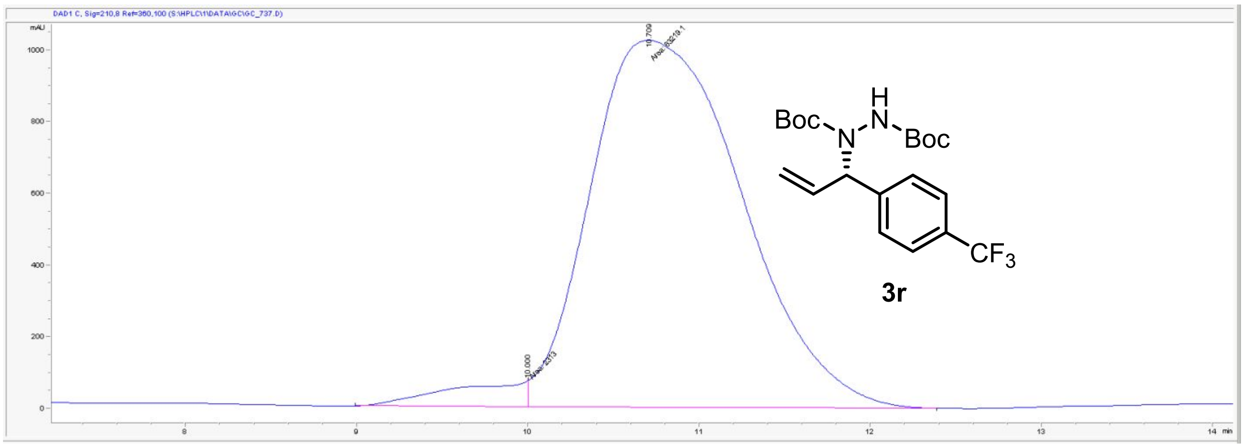
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

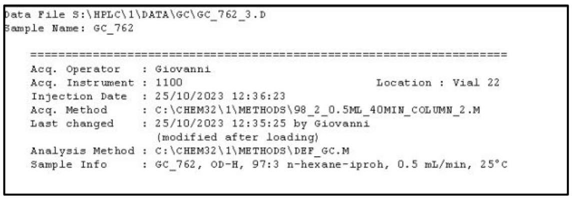

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.000 MF    0.5327 2313.00391   72.37247  3.52957
   2  10.709 FM    1.0283 6.32191e4 1024.66516 96.47043

Totals :                  6.55321e4  1097.03763
```

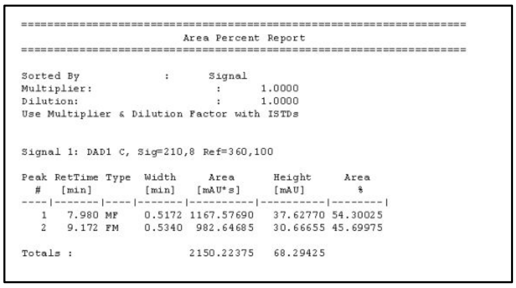


3r



```
Data File S:\HPLC\1\DATA\GC\GC_762_3.D
Sample Name: GC_762

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                         Location : Vial 22
   Injection Date  : 25/10/2023 12:36:23
   Acq. Method     : C:\CHEM32\1\METHODS\98_2_0.5ML_40MIN_COLUMN_2.M
   Last changed    : 25/10/2023 12:35:25 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Sample Info     : GC_762, OD-H, 97:3 n-hexane-iproh, 0.5 mL/min, 25°C
```



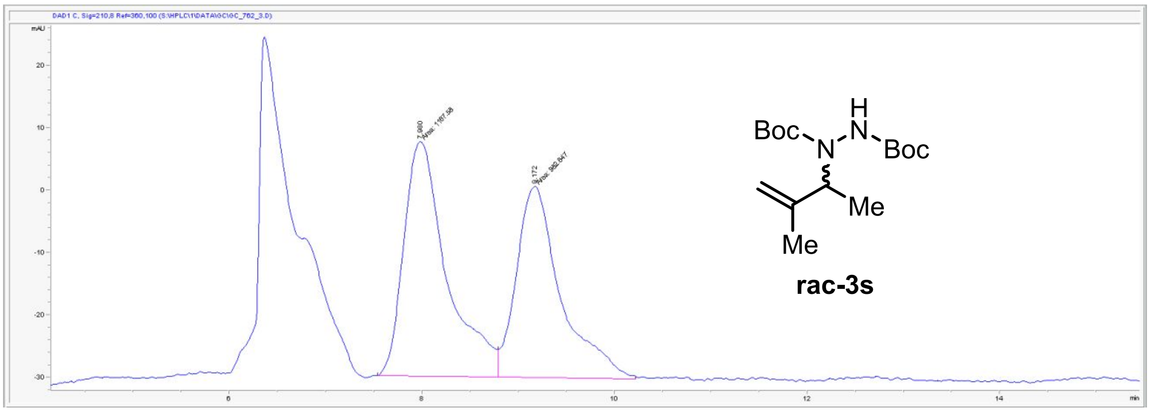
```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

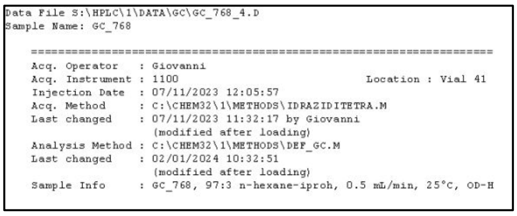

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.980 MF    0.5172 1167.57690   37.62770 54.30025
   2   9.172 FM    0.5340  982.64685   30.66655 45.69975

Totals :                  2150.22375   68.29425
```

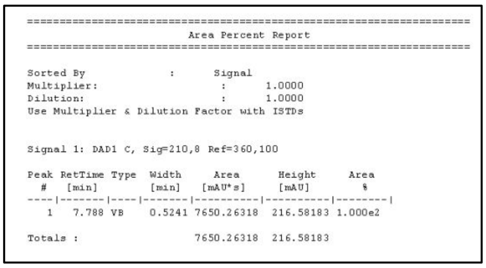


rac-3s



```
Data File S:\HPLC\1\DATA\GC\GC_768_4.D
Sample Name: GC_768

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                         Location : Vial 41
   Injection Date  : 07/11/2023 12:05:57
   Acq. Method     : C:\CHEM32\1\METHODS\IDRAZIDITETRA.M
   Last changed    : 07/11/2023 11:32:17 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:32:51
                     (modified after loading)
   Sample Info     : GC_768, 97:3 n-hexane-iproh, 0.5 mL/min, 25°C, OD-H
```



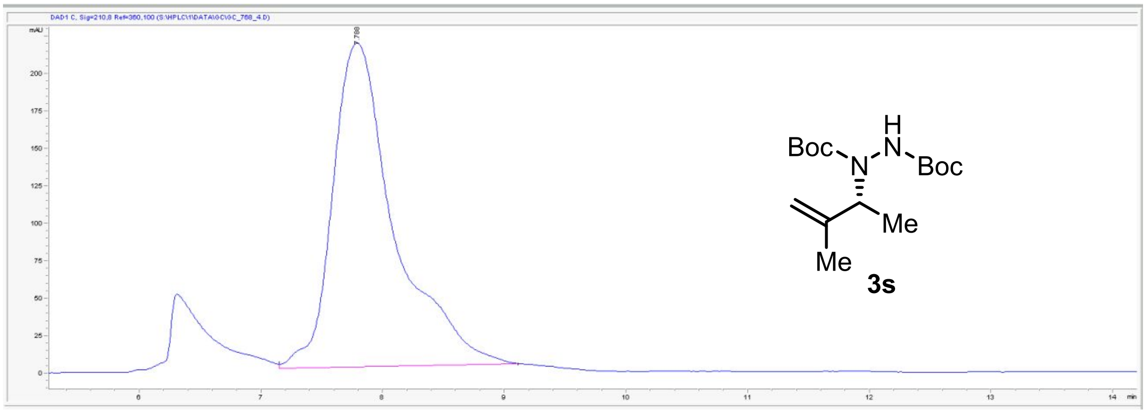
```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs

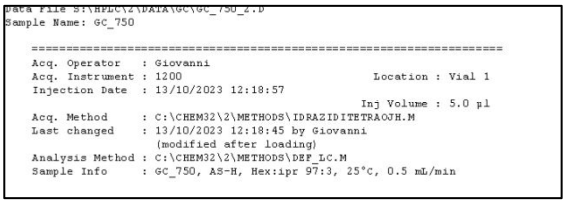

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.788 VB    0.5241 7650.26318  216.58183 1.000e2

Totals :                  7650.26318  216.58183
```

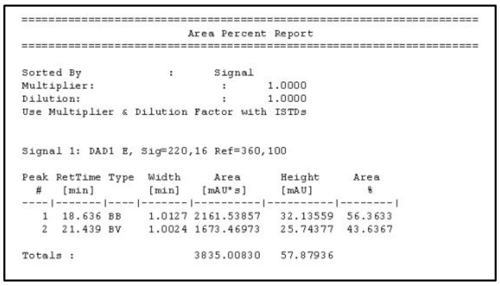


3s



```
Data File S:\HPLC\2\DATA\GC\GC_750_2.D
Sample Name: GC_750

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1200                            Location : Vial 1
   Injection Date  : 13/10/2023 12:18:57
                                                  Inj Volume : 5.0 µl
   Acq. Method     : C:\CHEM32\2\METHODS\IDRAZIDITETRAOJH.M
   Last changed    : 13/10/2023 12:18:45 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\2\METHODS\DEF_LC.M
   Sample Info     : GC_750, AS-H, Hex:ipr 97:3, 25°C, 0.5 mL/min
```



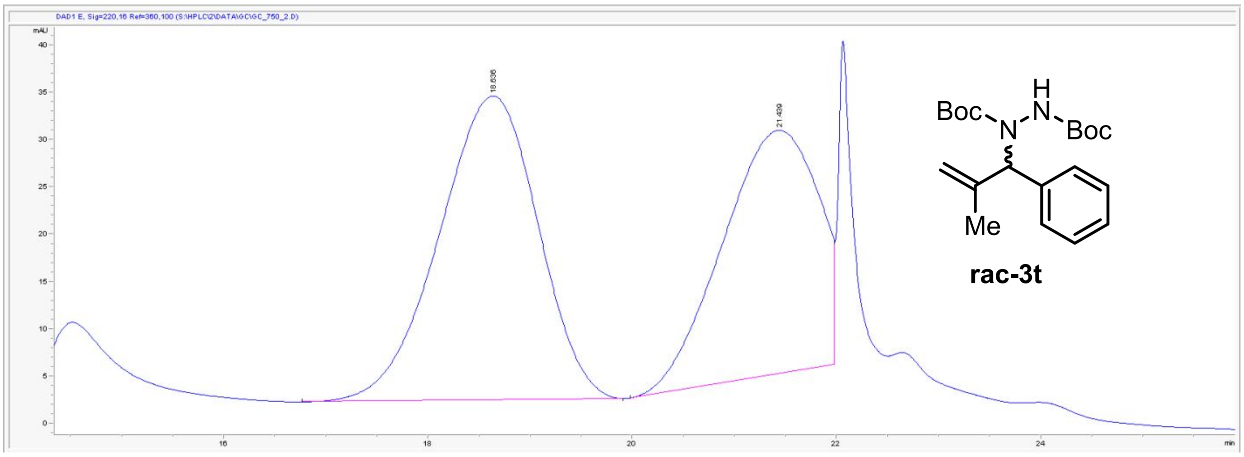
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

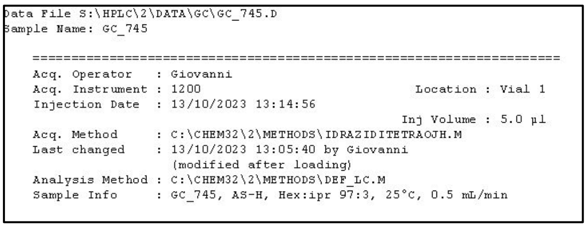

Signal 1: DAD1 E, Sig=220,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  18.636 BB    1.0127 2161.53857   32.13559  56.3633
   2  21.439 BV    1.0024 1673.46973   25.74377  43.6367

Totals :                  3835.00830   57.87936
```

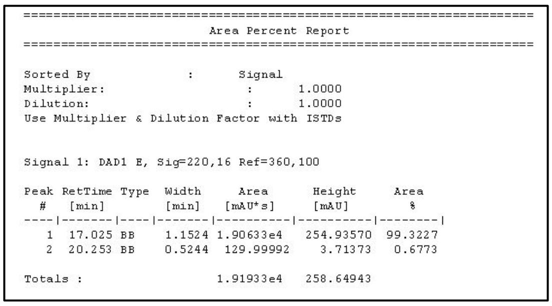


rac-3t



```
Data File S:\HPLC\2\DATA\GC\GC_745.D
Sample Name: GC_745

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1200                            Location : Vial 1
   Injection Date  : 13/10/2023 13:14:56
                                                  Inj Volume : 5.0 µl
   Acq. Method     : C:\CHEM32\2\METHODS\IDRAZIDITETRAOJH.M
   Last changed    : 13/10/2023 13:05:40 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\2\METHODS\DEF_LC.M
   Sample Info     : GC_745, AS-H, Hex:ipr 97:3, 25°C, 0.5 mL/min
```



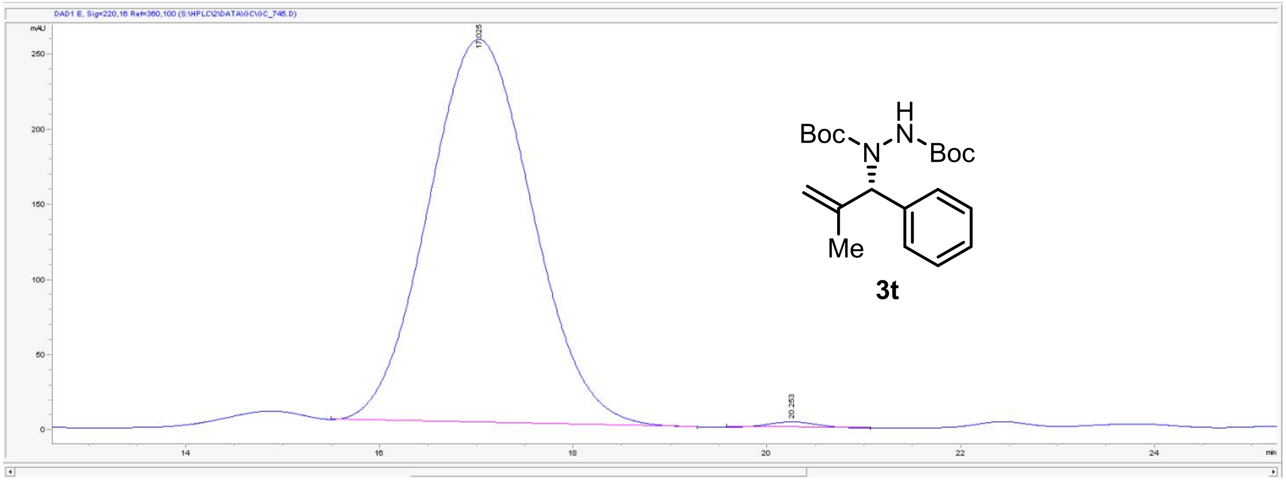
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

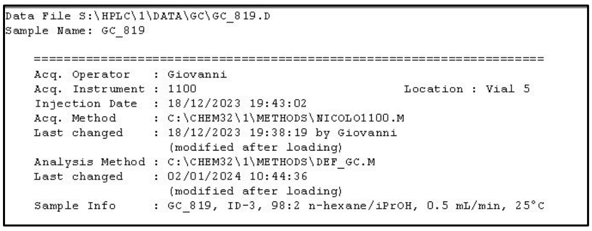

Signal 1: DAD1 E, Sig=220,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  17.025 BB    1.1524 1.90633e4   254.93570  99.3227
   2  20.253 BB    0.5244  129.99992    3.71373   0.6773

Totals :                  1.91933e4   258.64943
```

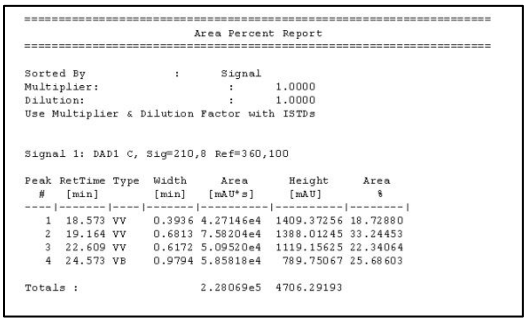


3t



```
Data File S:\HPLC\1\DATA\GC\GC_819.D
Sample Name: GC_819

   ====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                          Location : Vial 5
   Injection Date  : 18/12/2023 19:43:02
   Acq. Method     : C:\CHEM32\1\METHODS\NICOLO1100.M
   Last changed    : 18/12/2023 19:38:19 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : GC_819, ID-3, 98:2 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



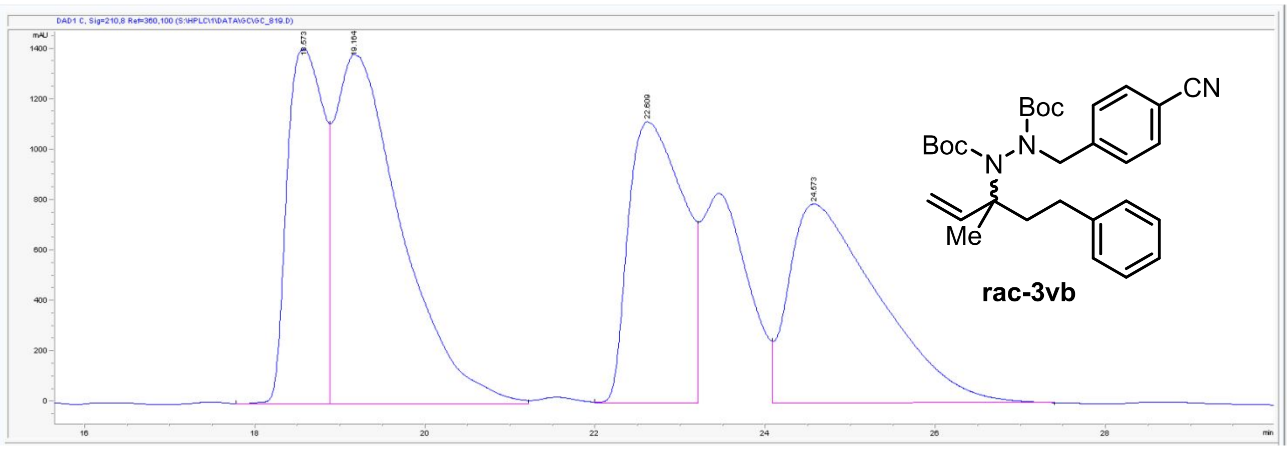
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

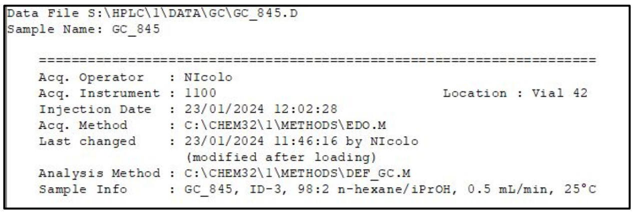

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  18.573 VV    0.3936 4.27146e4 1409.37256 18.72880
   2  19.164 VV    0.6813 7.58204e4 1388.01245 33.24453
   3  22.609 VV    0.6172 5.09520e4 1119.15625 22.34064
   4  24.573 VB    0.9794 5.85818e4  789.75067 25.68603

Totals :                  2.28069e5  4706.29193
```

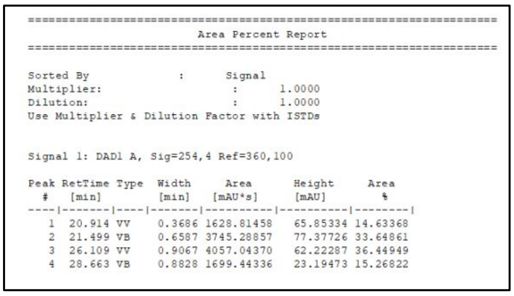


rac-3vb



```
Data File S:\HPLC\1\DATA\GC\GC_845.D
Sample Name: GC_845

    ====================================================================
    Acq. Operator   : NIcolo
    Acq. Instrument : 1100                         Location : Vial 42
    Injection Date  : 23/01/2024 12:02:28
    Acq. Method     : C:\CHEM32\1\METHODS\EDO.M
    Last changed    : 23/01/2024 11:46:16 by NIcolo
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Sample Info     : GC_845, ID-3, 98:2 n-hexane/iPrOH, 0.5 mL/min, 25°C
```

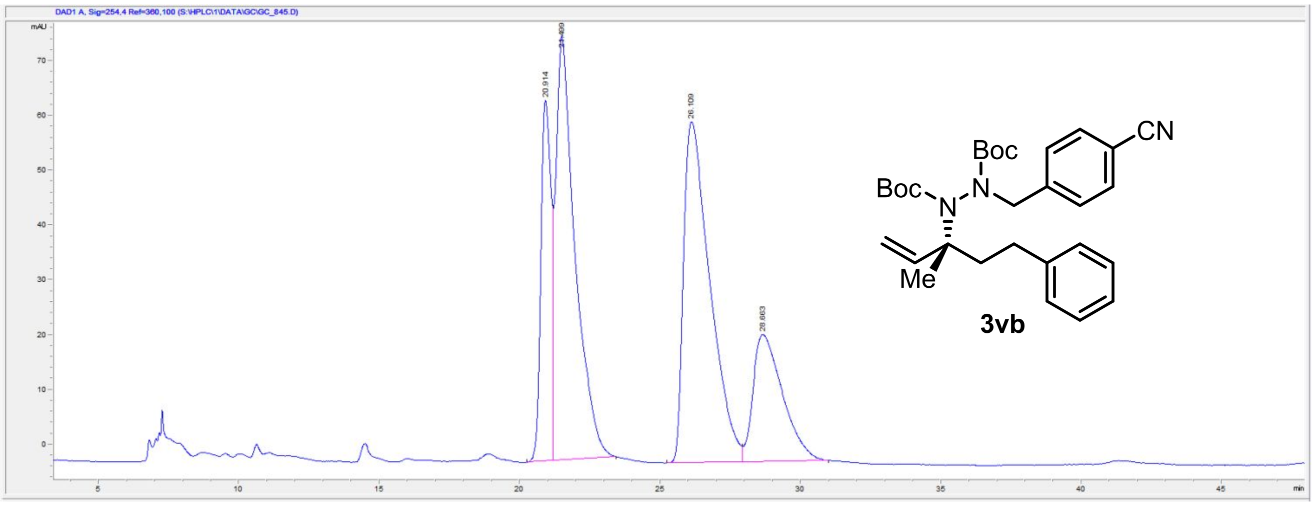


```
=====================================================================
                         Area Percent Report
=====================================================================

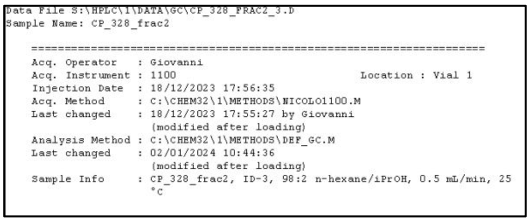
Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  20.914 VV    0.3686 1628.81458   65.85334 14.63368
   2  21.499 VB    0.6587 3745.28857   77.37726 33.64861
   3  26.109 VV    0.9067 4057.04370   62.22287 36.44949
   4  28.663 VB    0.8828 1699.44336   23.19473 15.26822
```

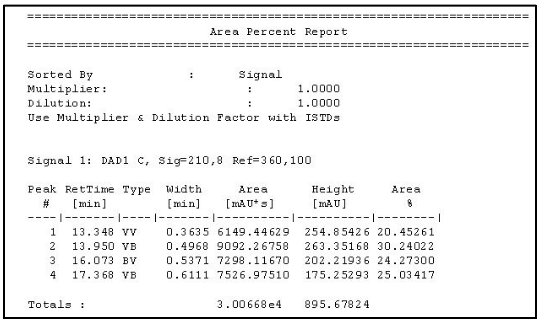


3vb



```
Data File S:\HPLC\1\DATA\GC\CP_328_FRAC2_3.D
Sample Name: CP_328_frac2

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                            Location : Vial 1
   Injection Date  : 18/12/2023 17:56:35
   Acq. Method     : C:\CHEM32\1\METHODS\NICOLO1100.M
   Last changed    : 18/12/2023 17:55:27 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : CP_328_frac2, ID-3, 98:2 n-hexane/iPrOH, 0.5 mL/min, 25
                     °C
```



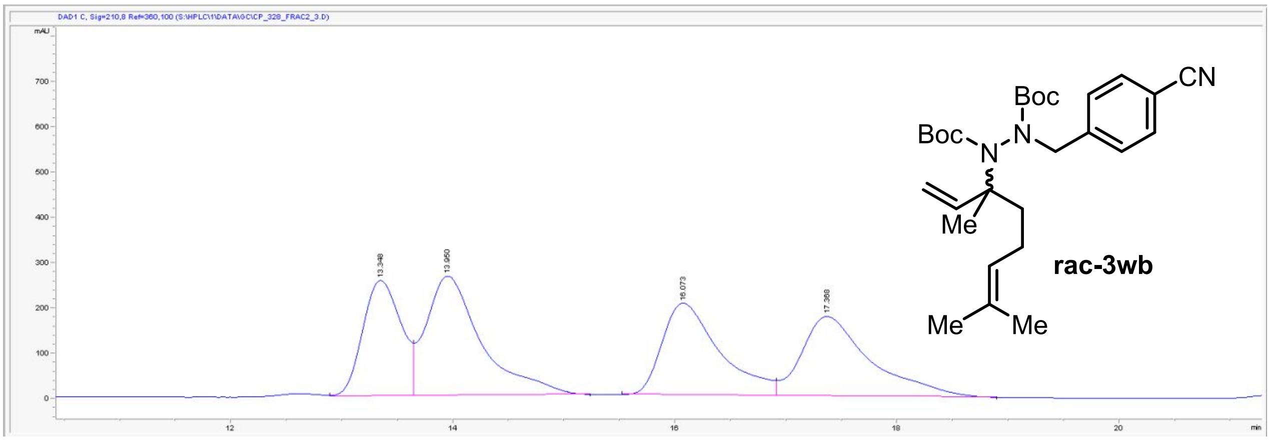
```
=====================================================================
                         Area Percent Report
=====================================================================

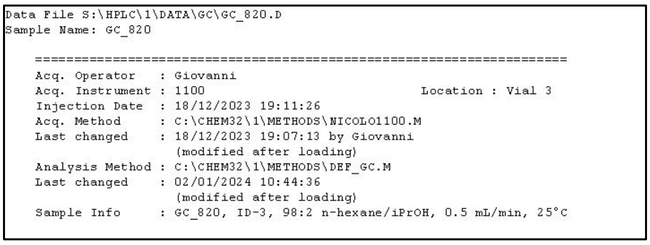
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  13.348 VV    0.3635 6149.44629  254.85426 20.45261
   2  13.950 VB    0.4968 9092.26758  263.35168 30.24022
   3  16.073 BV    0.5371 7298.11670  202.21936 24.27300
   4  17.368 VB    0.6111 7526.97510  175.25293 25.03417

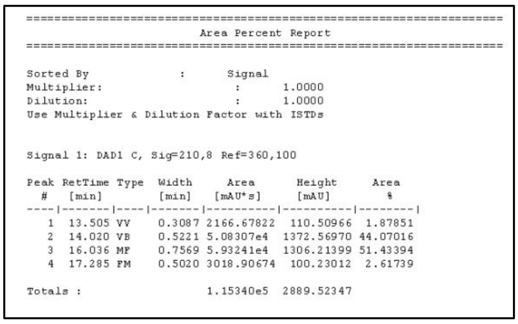
Totals :                  3.00668e4   895.67824
```





```
Data File S:\HPLC\1\DATA\GC\GC_820.D
Sample Name: GC_820

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                            Location : Vial 3
   Injection Date  : 18/12/2023 19:11:26
   Acq. Method     : C:\CHEM32\1\METHODS\NICOLO1100.M
   Last changed    : 18/12/2023 19:07:13 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : GC_820, ID-3, 98:2 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



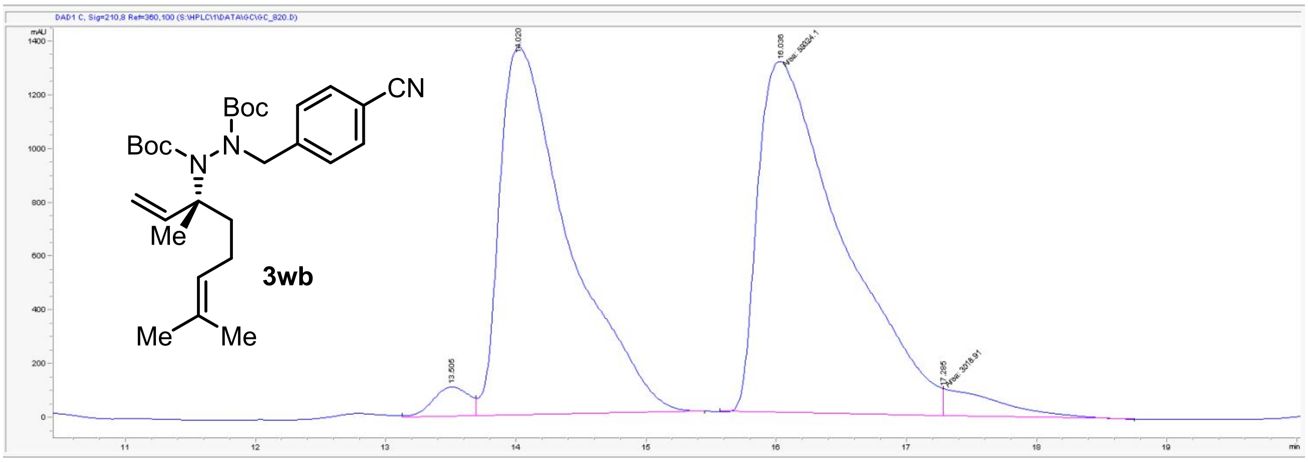
```
=====================================================================
                         Area Percent Report
=====================================================================

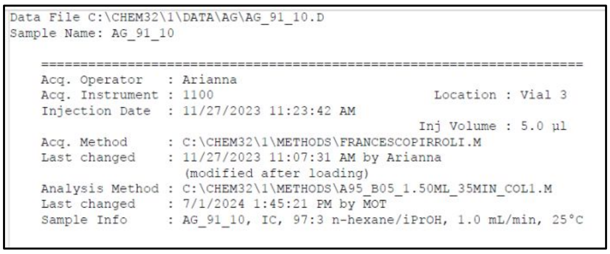
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  13.505 VV    0.3087 2166.67822  110.50966  1.87851
   2  14.020 VB    0.5221 5.08307e4  1372.56970 44.07016
   3  16.036 MF    0.7569 5.93241e4  1306.21399 51.43394
   4  17.285 FM    0.5020 3018.90674  100.23012  2.61739

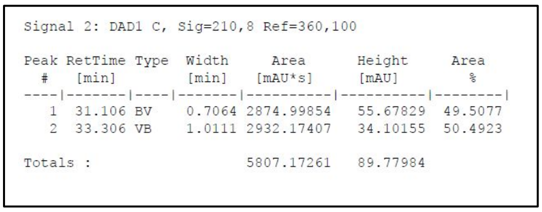
Totals :                  1.15340e5  2889.52347
```





```
Data File C:\CHEM32\1\DATA\AG\AG_91_10.D
Sample Name: AG_91_10

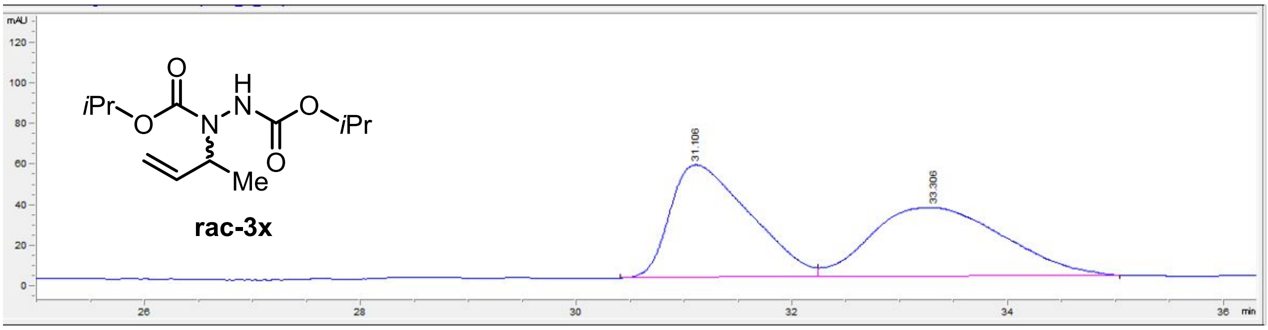
    =====================================================================
    Acq. Operator   : Arianna
    Acq. Instrument : 1100                            Location : Vial 3
    Injection Date  : 11/27/2023 11:23:42 AM
                                                   Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\1\METHODS\FRANCESCOPIRROLI.M
    Last changed    : 11/27/2023 11:07:31 AM by Arianna
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\A95_B05_1.50ML_35MIN_COL1.M
    Last changed    : 7/1/2024 1:45:21 PM by MOT
    Sample Info     : AG_91_10, IC, 97:3 n-hexane/iPrOH, 1.0 mL/min, 25°C
```



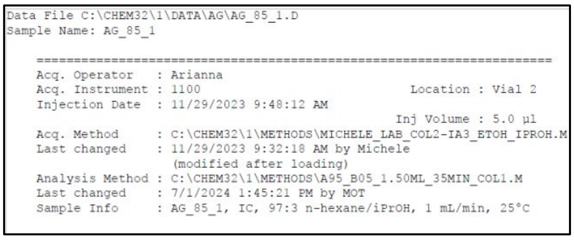
```
Signal 2: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  31.106 BV    0.7064 2874.99854   55.67829 49.5077
   2  33.306 VB    1.0111 2932.17407   34.10155 50.4923

Totals :                  5807.17261   89.77984
```

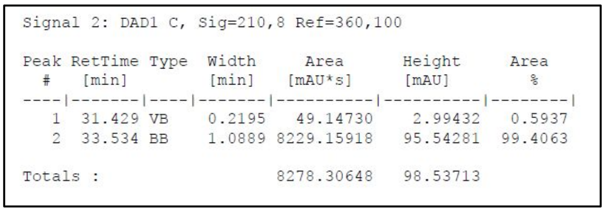


rac-3x



```
Data File C:\CHEM32\1\DATA\AG\AG_85_1.D
Sample Name: AG_85_1

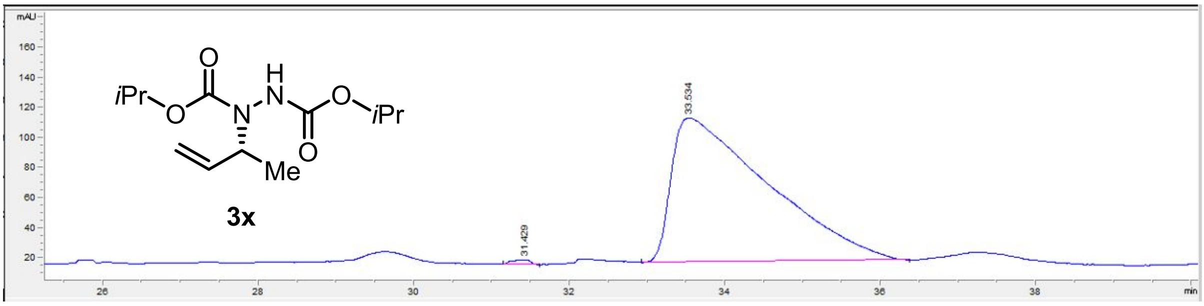
    =====================================================================
    Acq. Operator   : Arianna
    Acq. Instrument : 1100                            Location : Vial 2
    Injection Date  : 11/29/2023 9:48:12 AM
                                                   Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\1\METHODS\MICHELE_LAB_COL2-IA3_ETOH_IPROH.M
    Last changed    : 11/29/2023 9:32:18 AM by Michele
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\A95_B05_1.50ML_35MIN_COL1.M
    Last changed    : 7/1/2024 1:45:21 PM by MOT
    Sample Info     : AG_85_1, IC, 97:3 n-hexane/iPrOH, 1 mL/min, 25°C
```



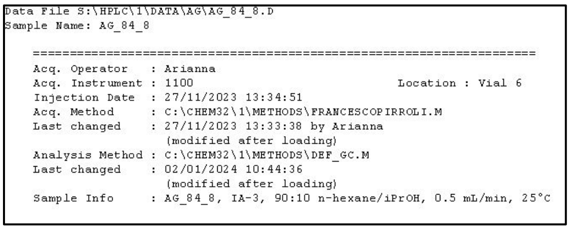
```
Signal 2: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  31.429 VB    0.2195   49.14730    2.99432   0.5937
   2  33.534 BB    1.0889 8229.15918   95.54281  99.4063

Totals :                  8278.30648   98.53713
```

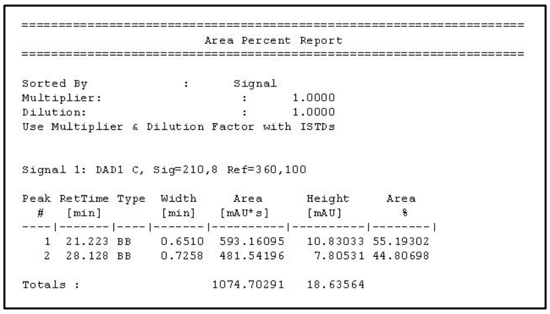


3x



```
Data File S:\HPLC\1\DATA\AG\AG_84_8.D
Sample Name: AG_84_8

   =====================================================================
   Acq. Operator   : Arianna
   Acq. Instrument : 1100                            Location : Vial 6
   Injection Date  : 27/11/2023 13:34:51
   Acq. Method     : C:\CHEM32\1\METHODS\FRANCESCOPIRROLI.M
   Last changed    : 27/11/2023 13:33:38 by Arianna
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : AG_84_8, IA-3, 90:10 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



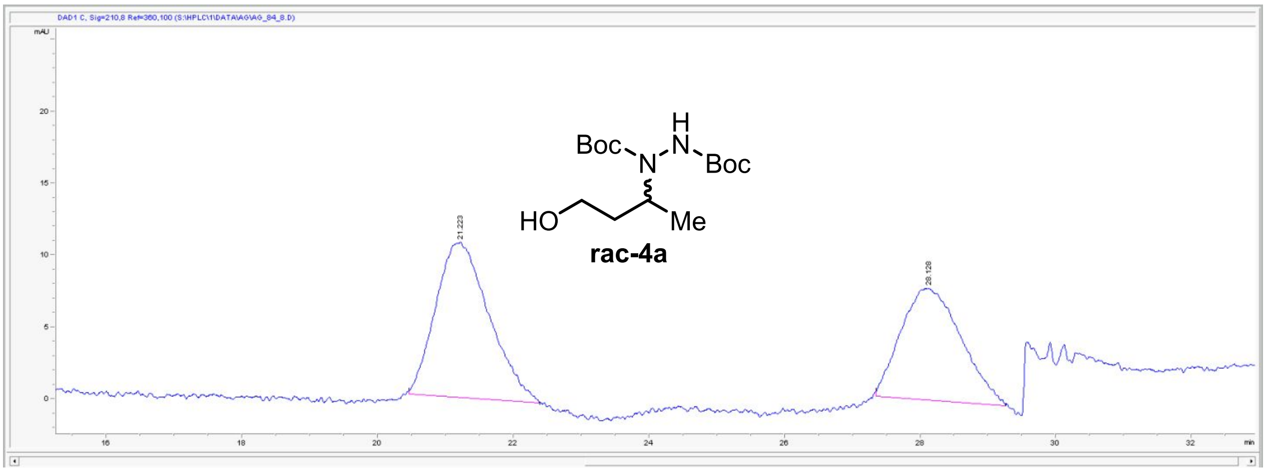
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

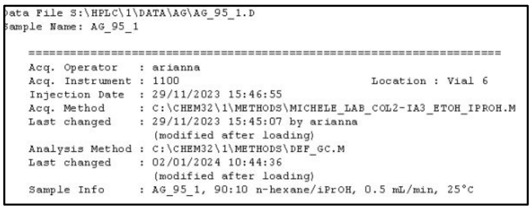

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  21.223 BB    0.6510  593.16095   10.83033 55.19302
   2  28.128 BB    0.7258  481.54196    7.80531 44.80698

Totals :                  1074.70291   18.63564
```

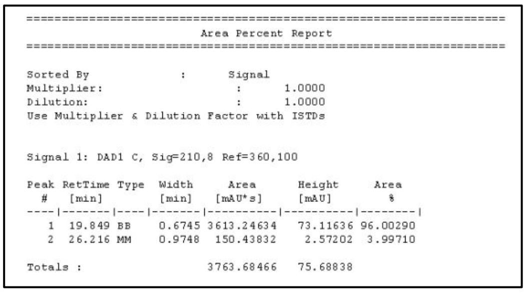


rac-4a



```
ata File S:\HPLC\1\DATA\AG\AG_95_1.D
ample Name: AG_95_1

   =====================================================================
   Acq. Operator   : arianna
   Acq. Instrument : 1100                            Location : Vial 6
   Injection Date  : 29/11/2023 15:46:55
   Acq. Method     : C:\CHEM32\1\METHODS\MICHELE_LAB_COL2-IA3_ETOH_IPROH.M
   Last changed    : 29/11/2023 15:45:07 by arianna
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : AG_95_1, 90:10 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



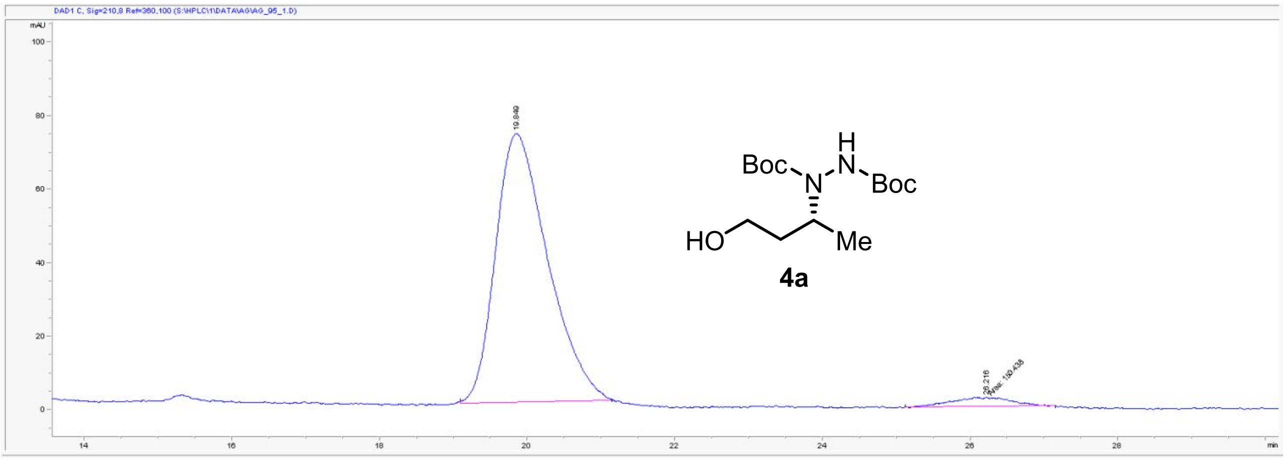
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

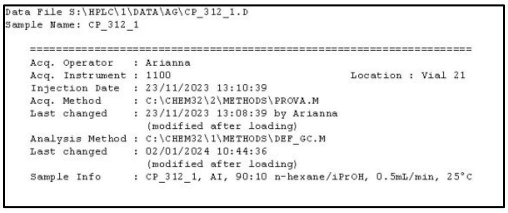

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  19.849 BB    0.6745 3613.24634   73.11636 96.00290
   2  26.216 MM    0.9748  150.43832    2.57202  3.99710

Totals :                  3763.68466   75.68838
```

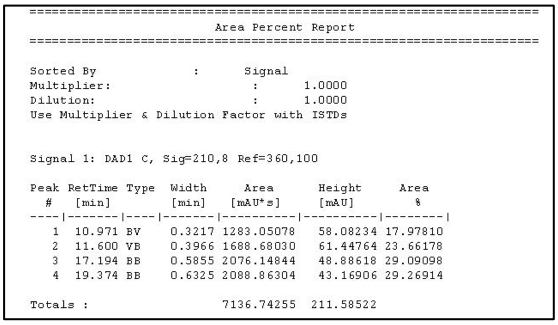


4a



```
Data File S:\HPLC\1\DATA\AG\CP_312_1.D
Sample Name: CP_312_1

    ====================================================================
    Acq. Operator   : Arianna
    Acq. Instrument : 1100                            Location : Vial 21
    Injection Date  : 23/11/2023 13:10:39
    Acq. Method     : C:\CHEM32\2\METHODS\PROVA.M
    Last changed    : 23/11/2023 13:08:39 by Arianna
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Last changed    : 02/01/2024 10:44:36
                      (modified after loading)
    Sample Info     : CP_312_1, AI, 90:10 n-hexane/iPrOH, 0.5mL/min, 25°C
```



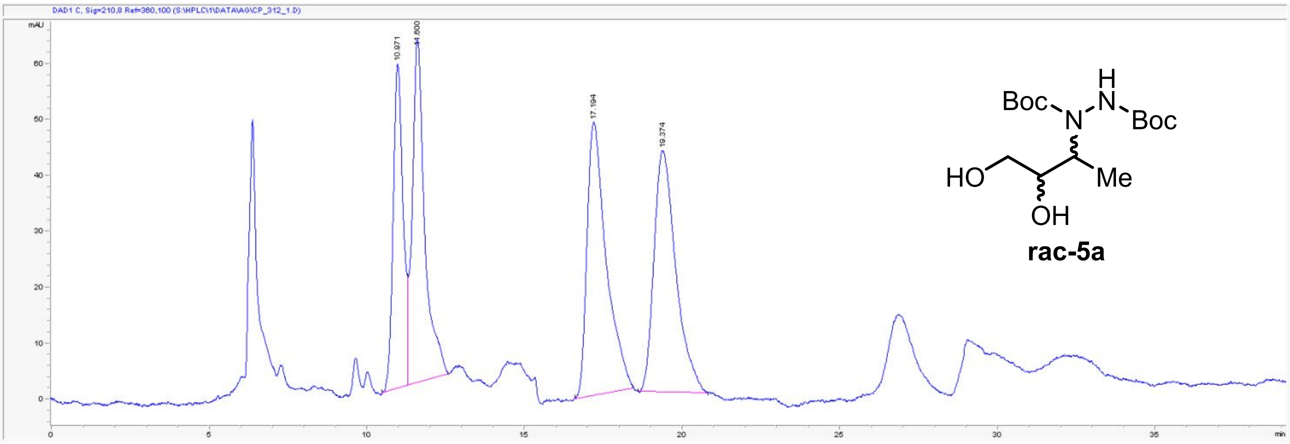
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

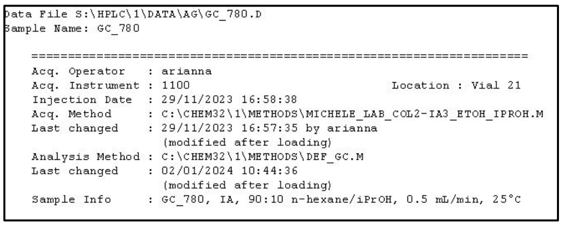

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.971 BV    0.3217 1283.05078   58.08234 17.97810
   2  11.600 VB    0.3966 1688.68030   61.44764 23.66178
   3  17.194 BB    0.5855 2076.14844   48.88618 29.09098
   4  19.374 BB    0.6325 2088.86304   43.16906 29.26914

Totals :                  7136.74255  211.58522
```

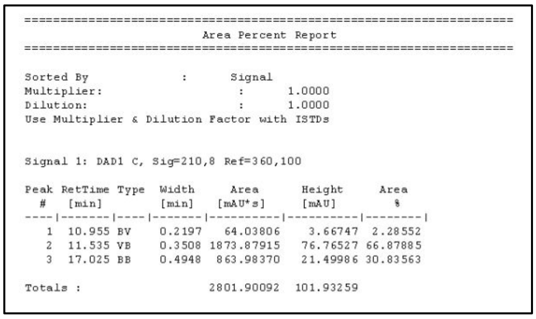


rac-5a



```
Data File S:\HPLC\1\DATA\AG\GC_780.D
Sample Name: GC_780

    ====================================================================
    Acq. Operator   : arianna
    Acq. Instrument : 1100                            Location : Vial 21
    Injection Date  : 29/11/2023 16:58:38
    Acq. Method     : C:\CHEM32\1\METHODS\MICHELE_LAB_COL2-IA3_ETOH_IPROH.M
    Last changed    : 29/11/2023 16:57:35 by arianna
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
    Last changed    : 02/01/2024 10:44:36
                      (modified after loading)
    Sample Info     : GC_780, IA, 90:10 n-hexane/iPrOH, 0.5 mL/min, 25°C
```



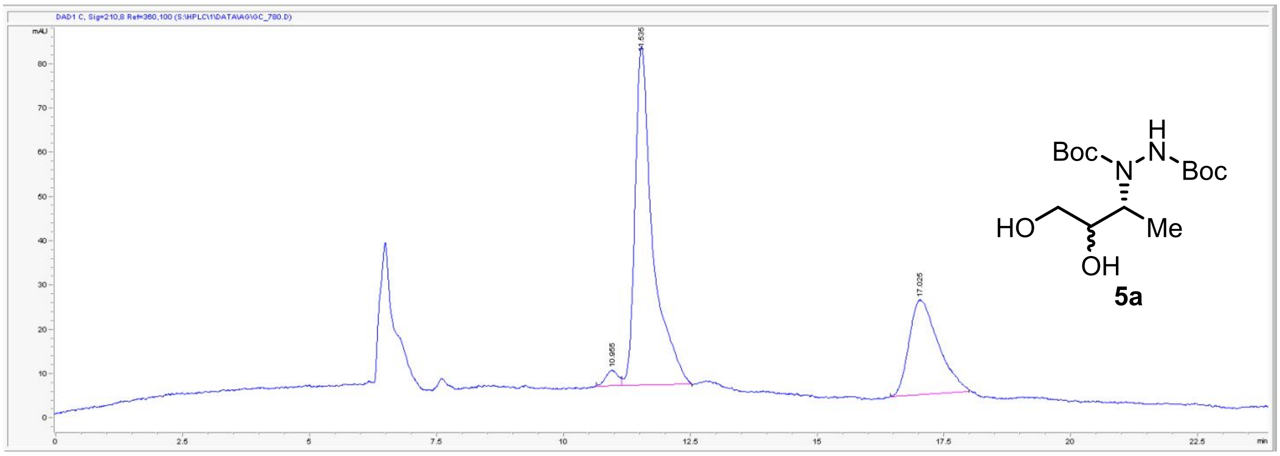
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs

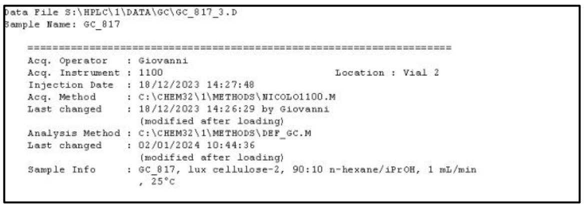

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.955 BV    0.2197   64.03806    3.66747  2.28552
   2  11.535 VB    0.3508 1873.87915   76.76527 66.87885
   3  17.025 BB    0.4948  863.98370   21.49986 30.83563

Totals :                  2801.90092  101.93259
```

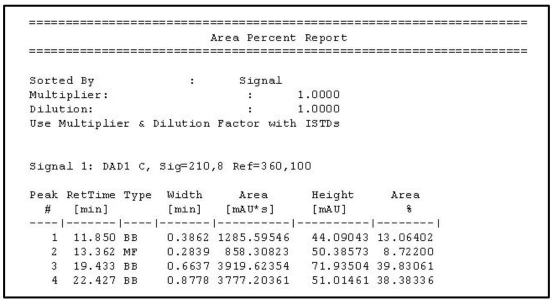


5a



```
Data File S:\HPLC\1\DATA\GC\GC_817_3.D
Sample Name: GC_817

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                           Location : Vial 2
   Injection Date  : 18/12/2023 14:27:48
   Acq. Method     : C:\CHEM32\1\METHODS\NICOLO1100.M
   Last changed    : 18/12/2023 14:26:29 by Giovanni
                     (modified after loading)
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Last changed    : 02/01/2024 10:44:36
                     (modified after loading)
   Sample Info     : GC_817, lux cellulose-2, 90:10 n-hexane/iPrOH, 1 mL/min
                     , 25°C
```

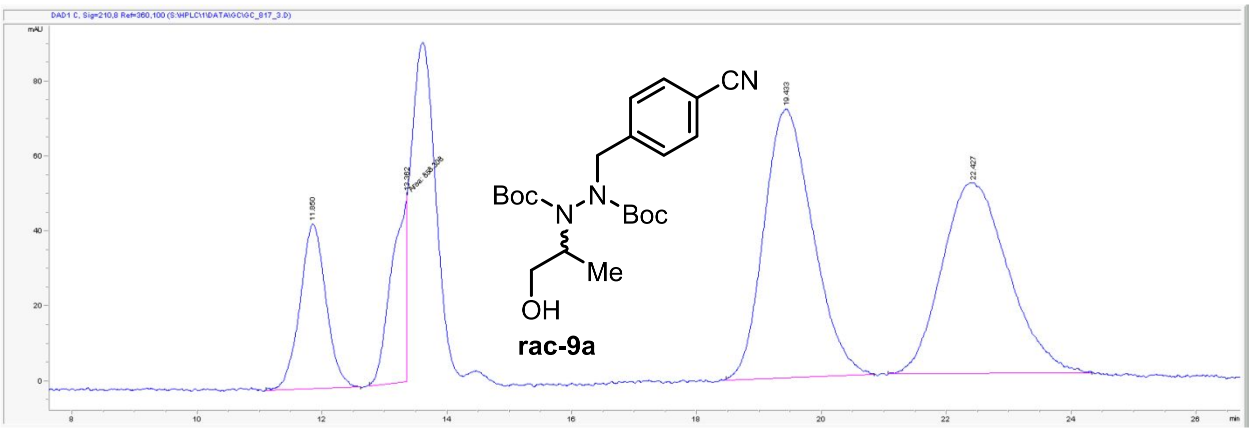


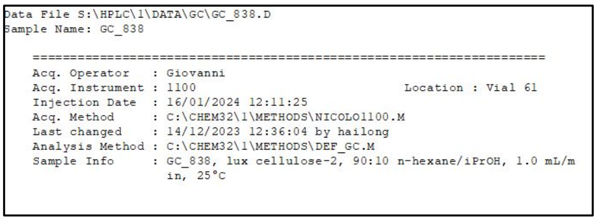
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.850 BB    0.3862 1285.59546   44.09043 13.06402
   2  13.362 MF    0.2839  858.30823   50.38573  8.72200
   3  19.433 BB    0.6637 3919.62354   71.93504 39.83061
   4  22.427 BB    0.8778 3777.20361   51.01461 38.38336
```





```
Data File S:\HPLC\1\DATA\GC\GC_838.D
Sample Name: GC_838

   =====================================================================
   Acq. Operator   : Giovanni
   Acq. Instrument : 1100                           Location : Vial 61
   Injection Date  : 16/01/2024 12:11:25
   Acq. Method     : C:\CHEM32\1\METHODS\NICOLO1100.M
   Last changed    : 14/12/2023 12:36:04 by hailong
   Analysis Method : C:\CHEM32\1\METHODS\DEF_GC.M
   Sample Info     : GC_838, lux cellulose-2, 90:10 n-hexane/iPrOH, 1.0 mL/m
                     in, 25°C
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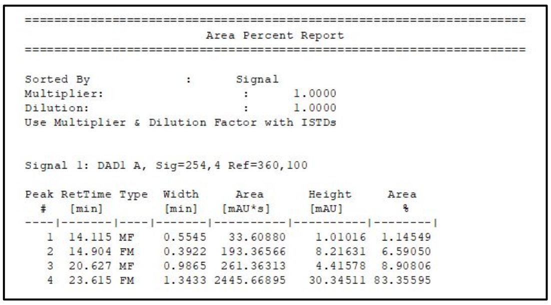

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=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  14.115 MF    0.5545   33.60880    1.01016  1.14549
   2  14.904 FM    0.3922  193.36566    8.21631  6.59050
   3  20.627 MF    0.9865  261.36313    4.41578  8.90806
   4  23.615 FM    1.3433 2445.66895   30.34511 83.35595
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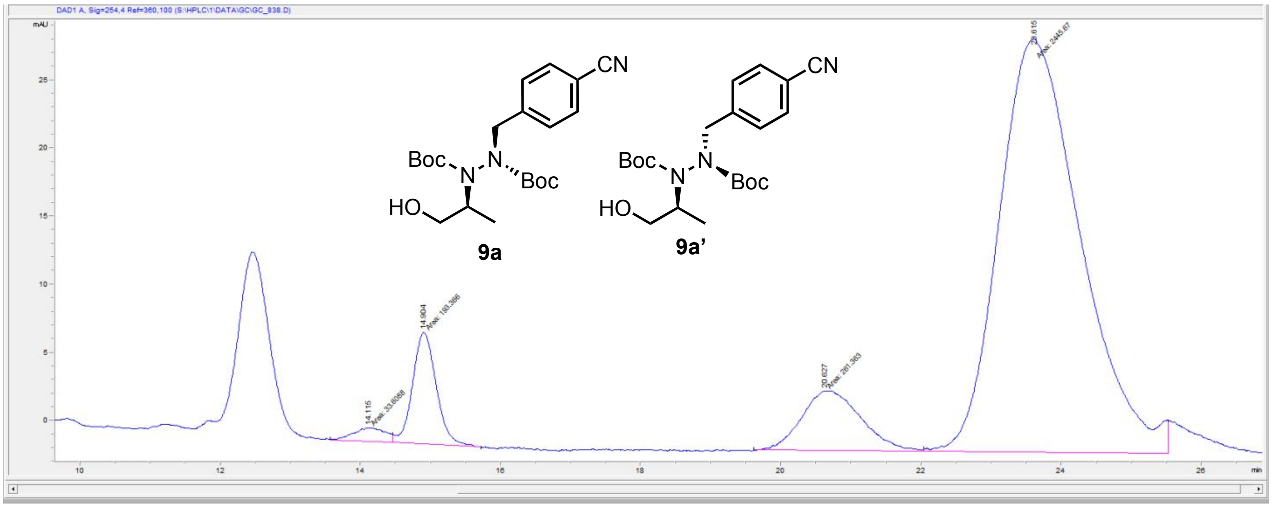
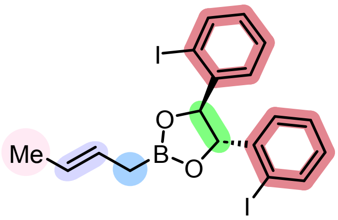
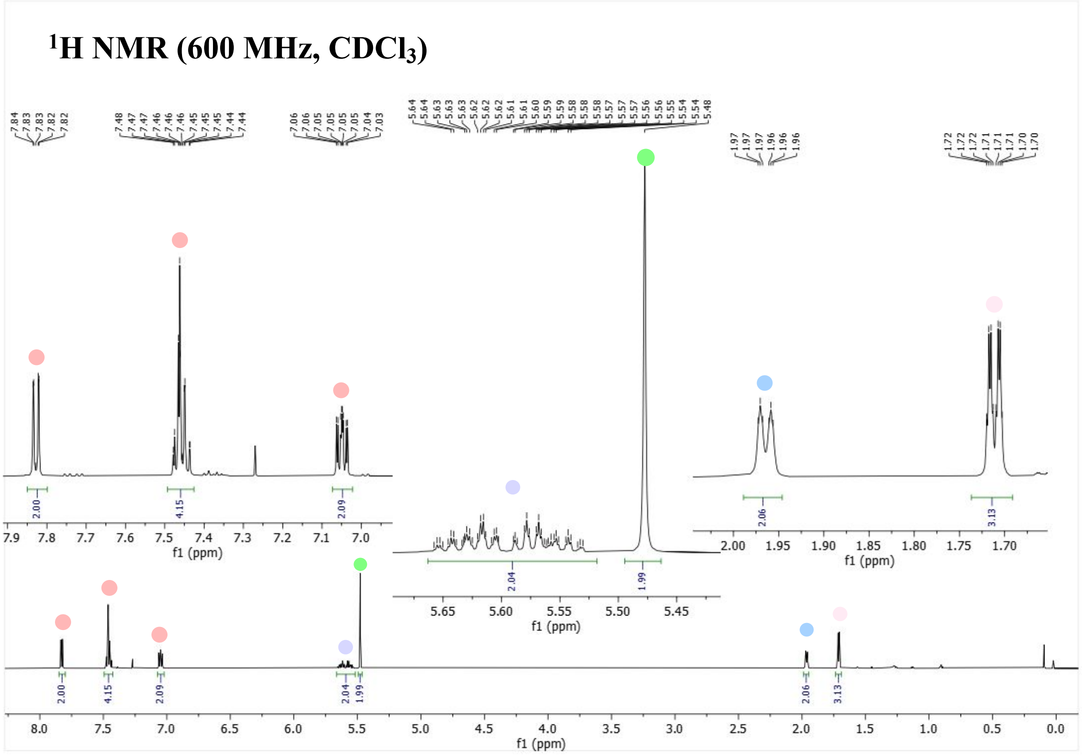


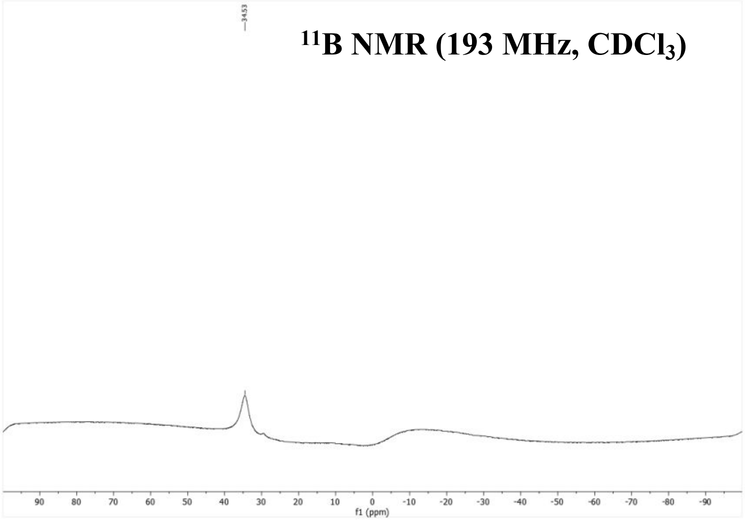
MECHANISM INVESTIGATION

To investigate the role of isopropanol and acetic acid and to gain a better insight into the mechanism, different experiments were conducted in $CDCl_3$ and checked by ^{1}H NMR and ^{11}B NMR. The NMRs of the main compounds involved are reported below before further discussions.

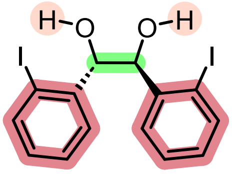
Compound N-1ca



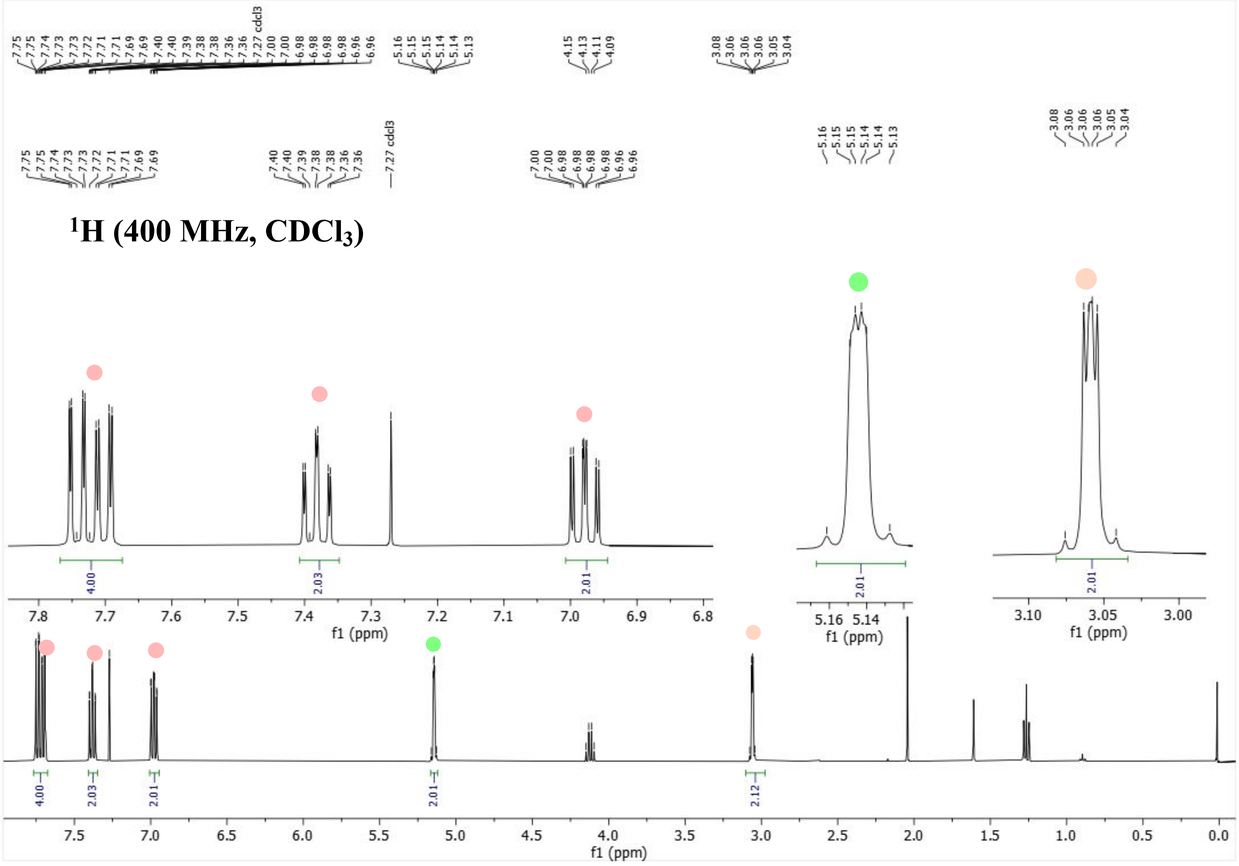




Compound N

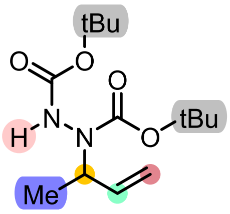


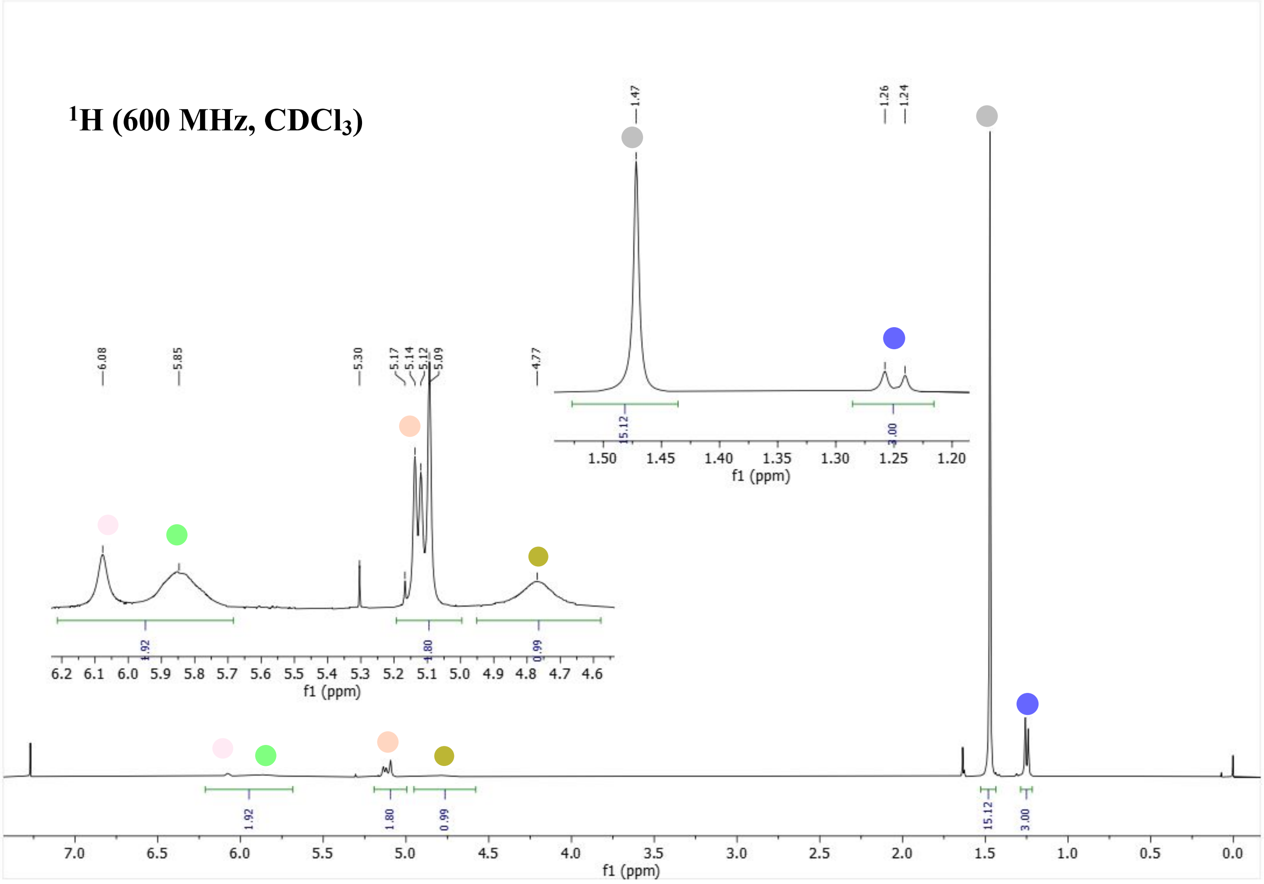
H
O
O
H
I
I



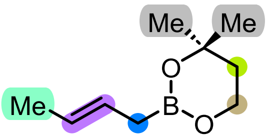
7.75 7.75 7.74 7.73 7.73 7.72 7.71 7.71 7.69 7.69 7.40 7.40 7.39 7.38 7.38 7.36 7.36 7.27 cdcl3 7.00 7.00 6.98 6.98 6.98 6.98 6.96 6.96
5.16 5.15 5.15 5.14 5.14 5.13
4.15 4.13 4.11 4.09
3.08 3.06 3.06 3.06 3.05 3.04
^{1}H (400 MHz, CDCl$_3$)
4.00
2.03
2.01
2.01
2.01
2.12
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
5.16 5.14
3.10 3.05 3.00
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

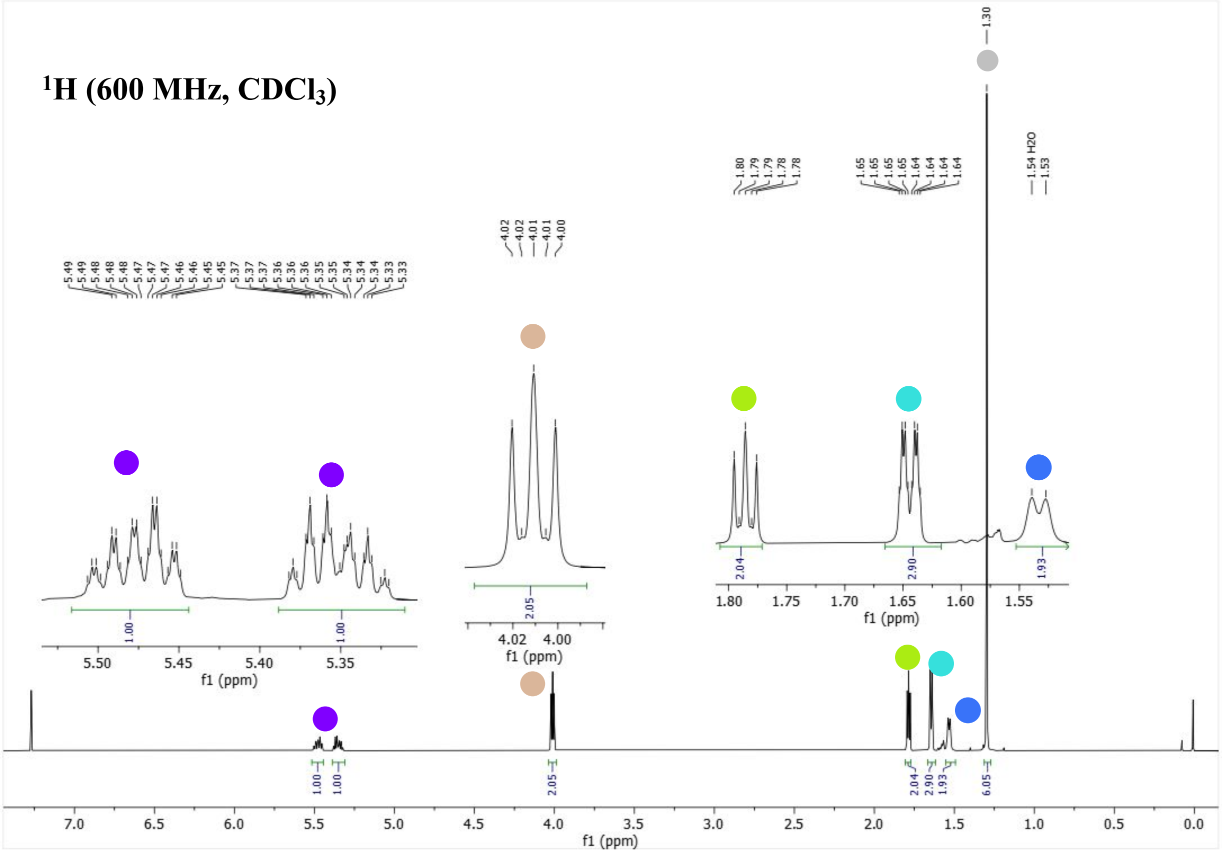
Compound 3a

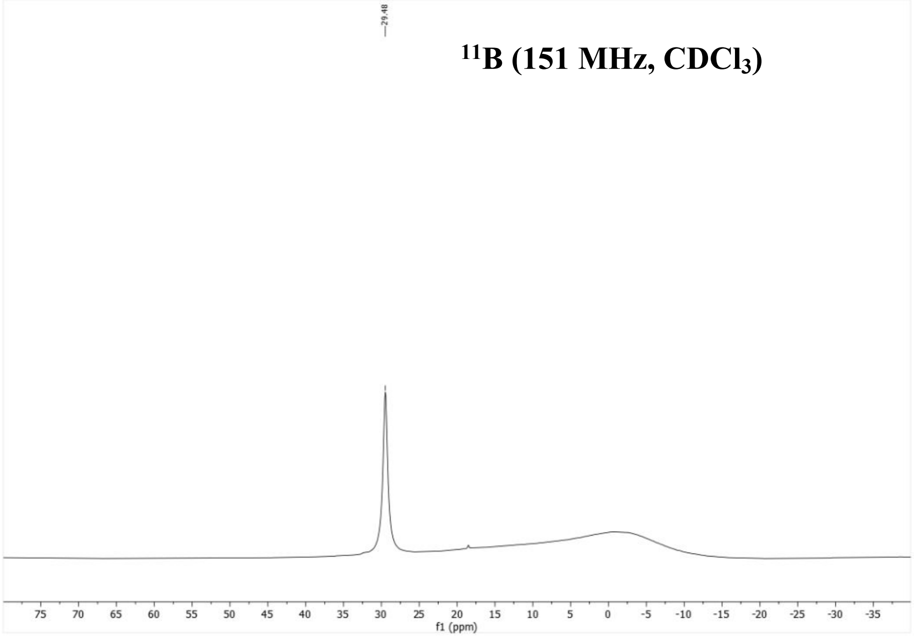

tBu
O
O
O
H
N
N
O
tBu
Me


^{1}H (600 MHz, CDCl$_3$)
6.08
5.85
5.30
5.17
5.14
5.12
5.09
4.77
1.92
1.80
0.99
6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6
f1 (ppm)
1.47
1.26
1.24
15.12
3.00
1.50 1.45 1.40 1.35 1.30 1.25 1.20
f1 (ppm)
1.92
1.80
0.99
15.12
3.00
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
f1 (ppm)

Compound 1ca



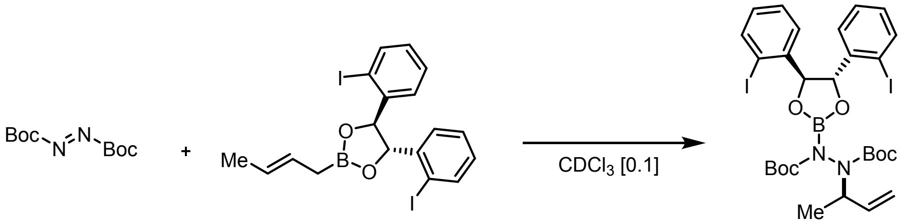




NMRs EXPERIMENT n1

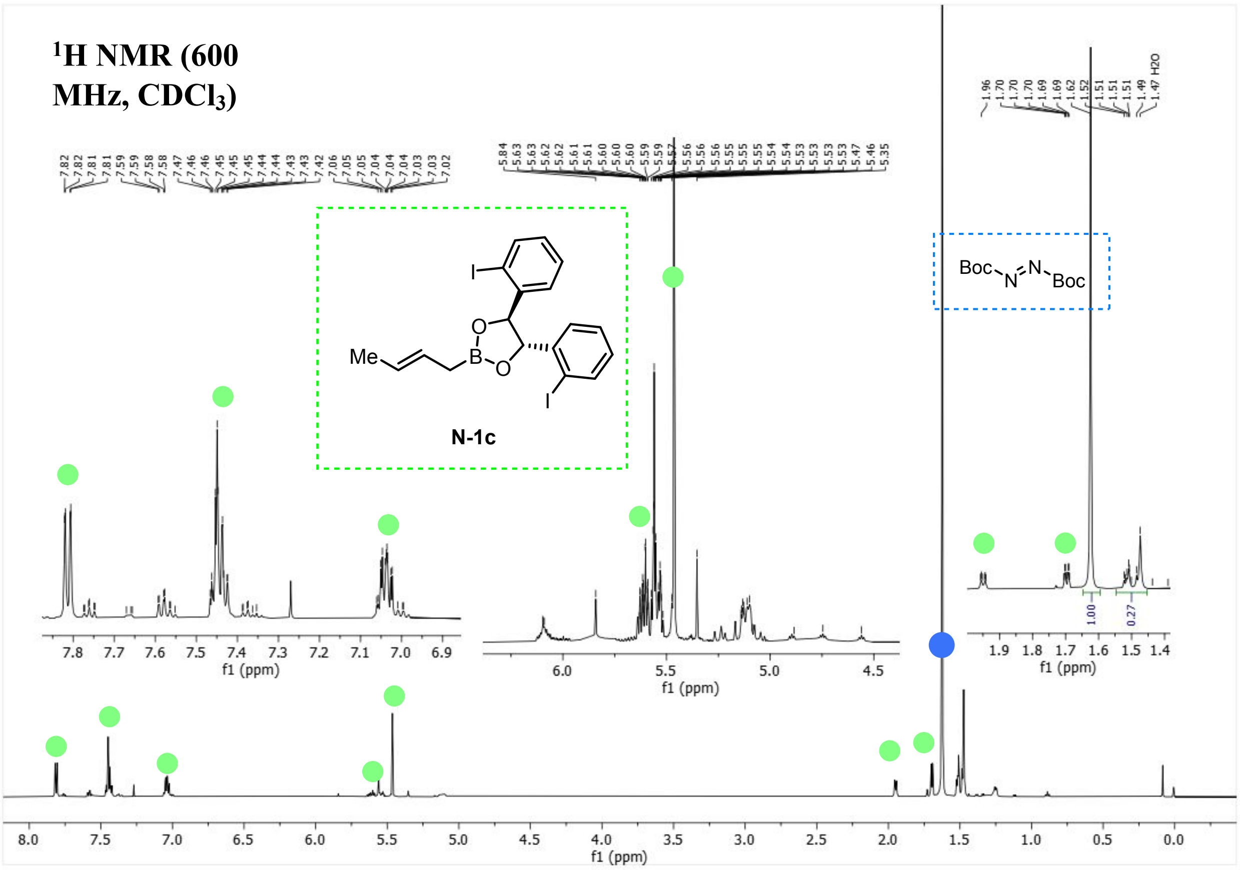
This experiment has been designed to study the reaction between the catalytically active species **N-1ca** and the azodicarboxylate **2a**.

<u>Conditions</u>: 40 mg of **N-1ca** (0.07 mmol), 0.65 mL of $CDCl_3$ and 34.5 mg (0.15 mmol) of di-tertbutyl-azodicarboxylate were added to a screw cap vial provided of a magnetic stir bar. The reaction was stirred at 25°C and occasionally transferred into an NMR tube to be monitored.

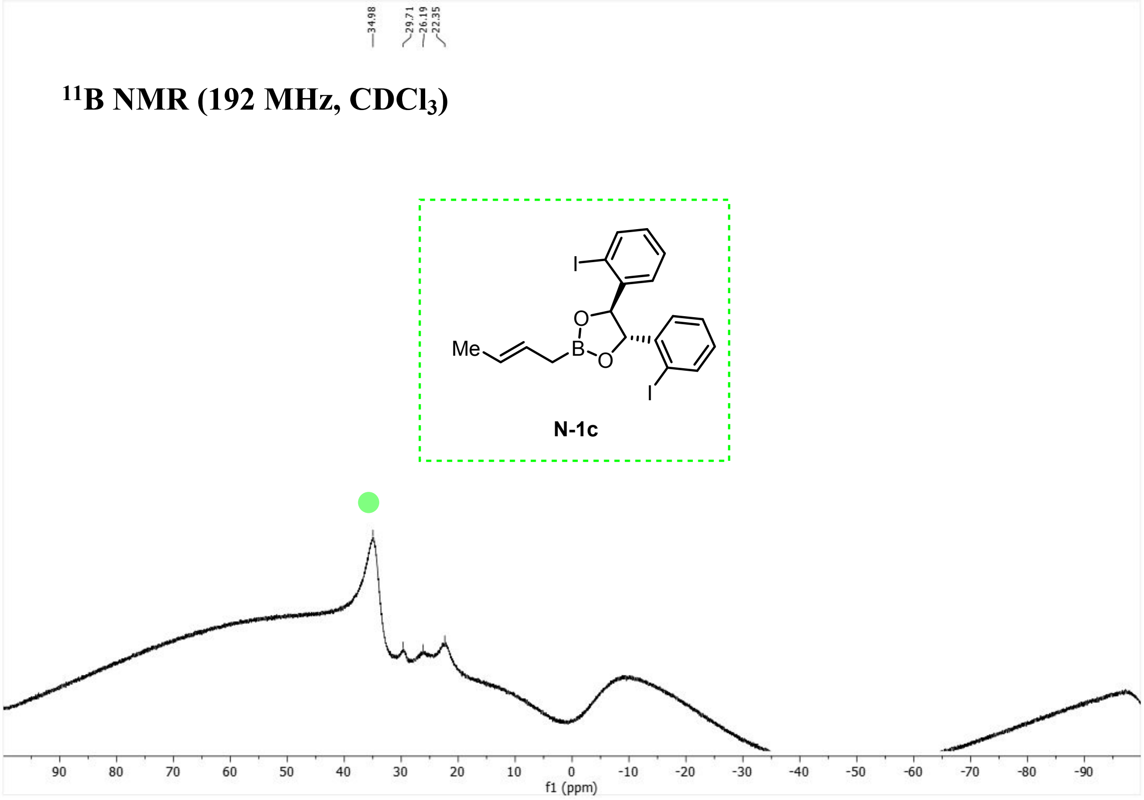


2a **N-1c** **N-3a**

30 minutes:



This spectrum recorded after 30 minutes evidence the formation of a new compound which does not correspond to the expected product. To help in visualizing the new signals, those of the starting (**N-1ca** and **2a**) have been marked with coloured dots. We speculated that the new compound corresponds to the adduct **N-3a**, being the reasonable product of the allylation occurring through the Zimmerman-Traxler transition state. Interestingly, the multitude of the peaks may be ascribable to a restricted rotation around the N-N bond. This feature is also observable by ^{11}B NMR spectrum:

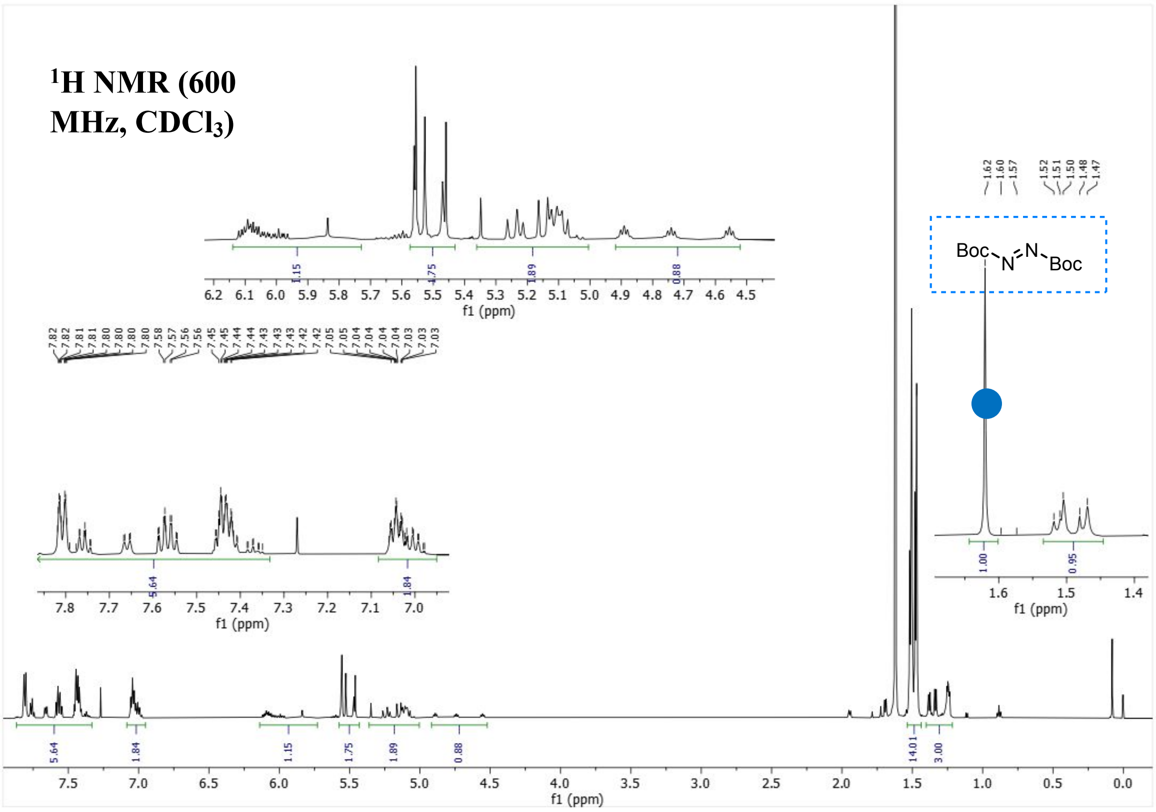


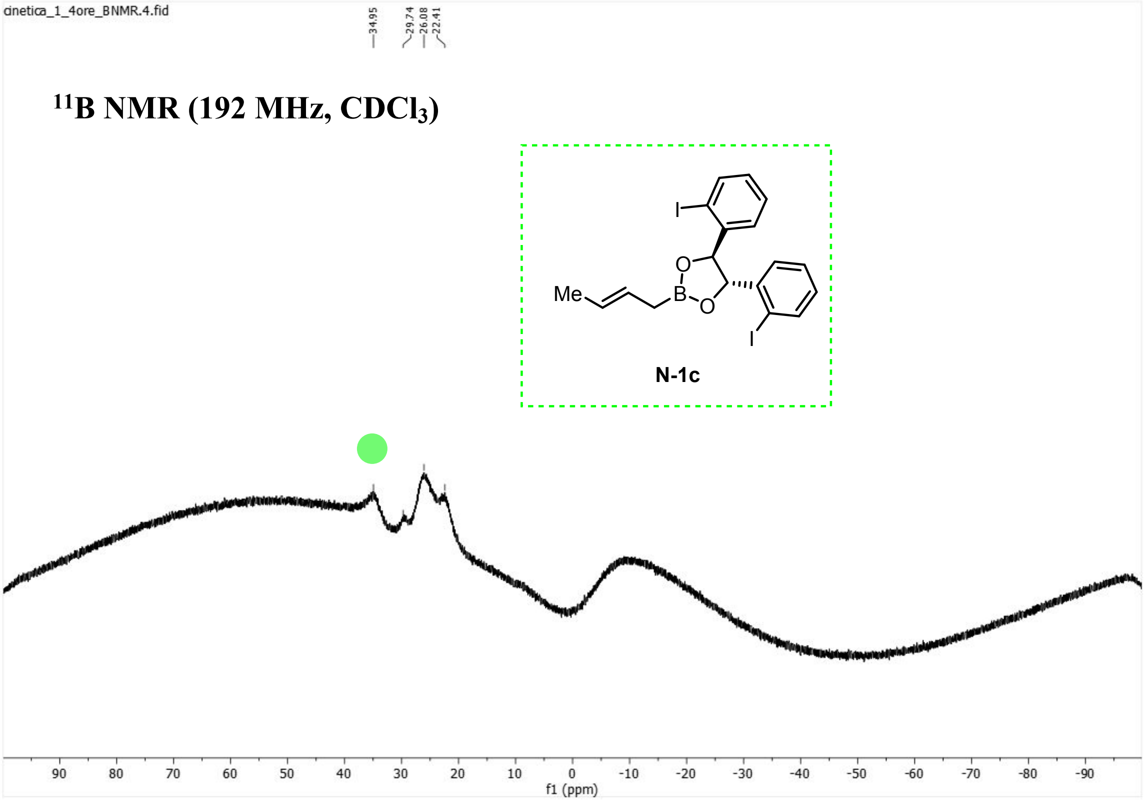
^{11}B NMR (192 MHz, CDCl$_3$)

N-1c

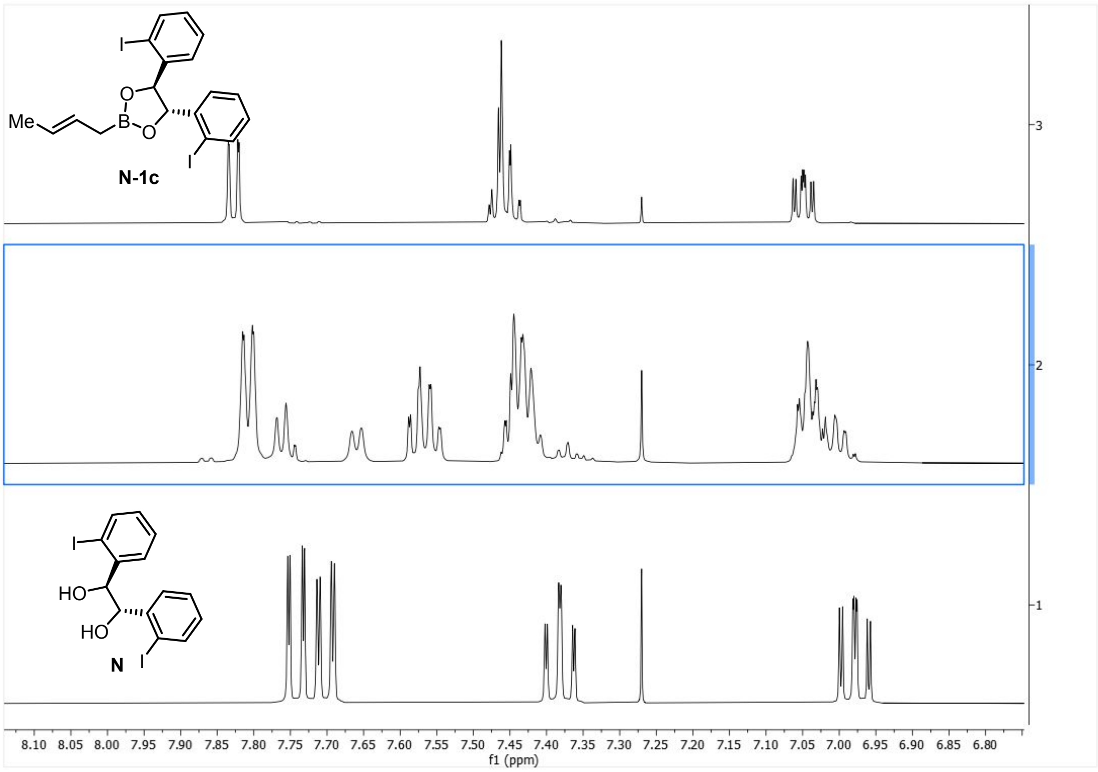
4 hours:

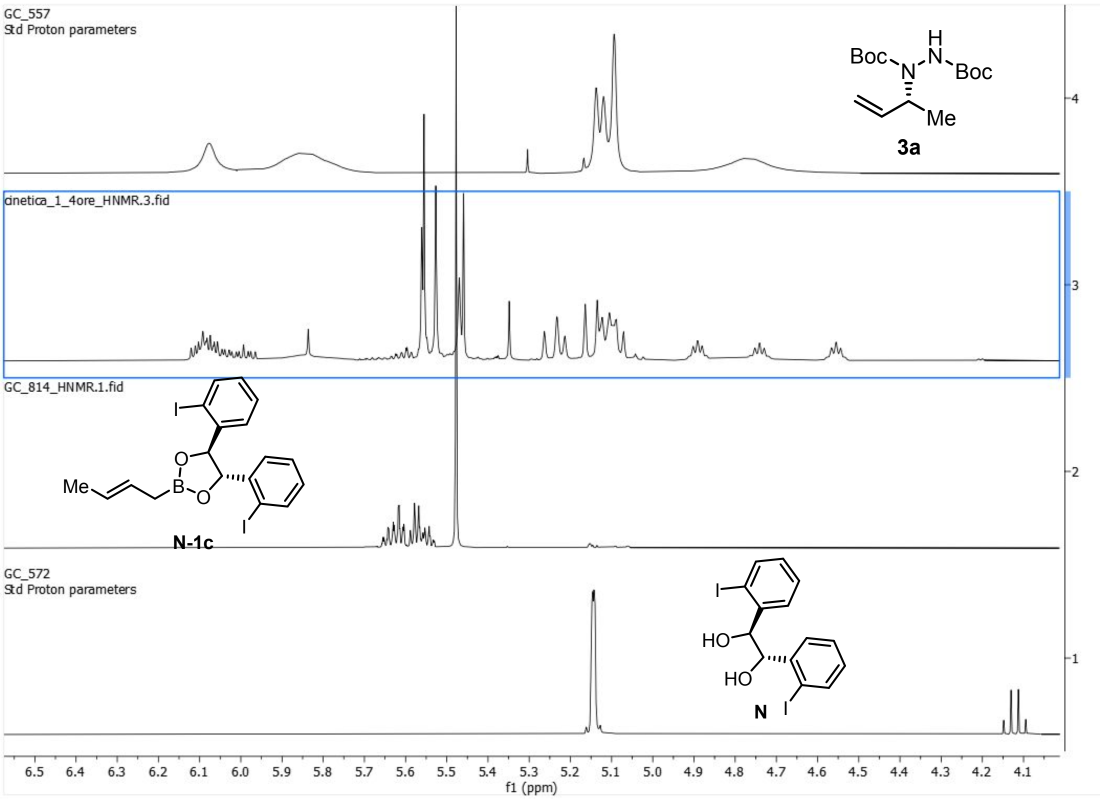
After 4 hours the catalytically active specie is almost fully consumed. A rough integration of the peaks corresponding to the signals of the intermediate is shown.

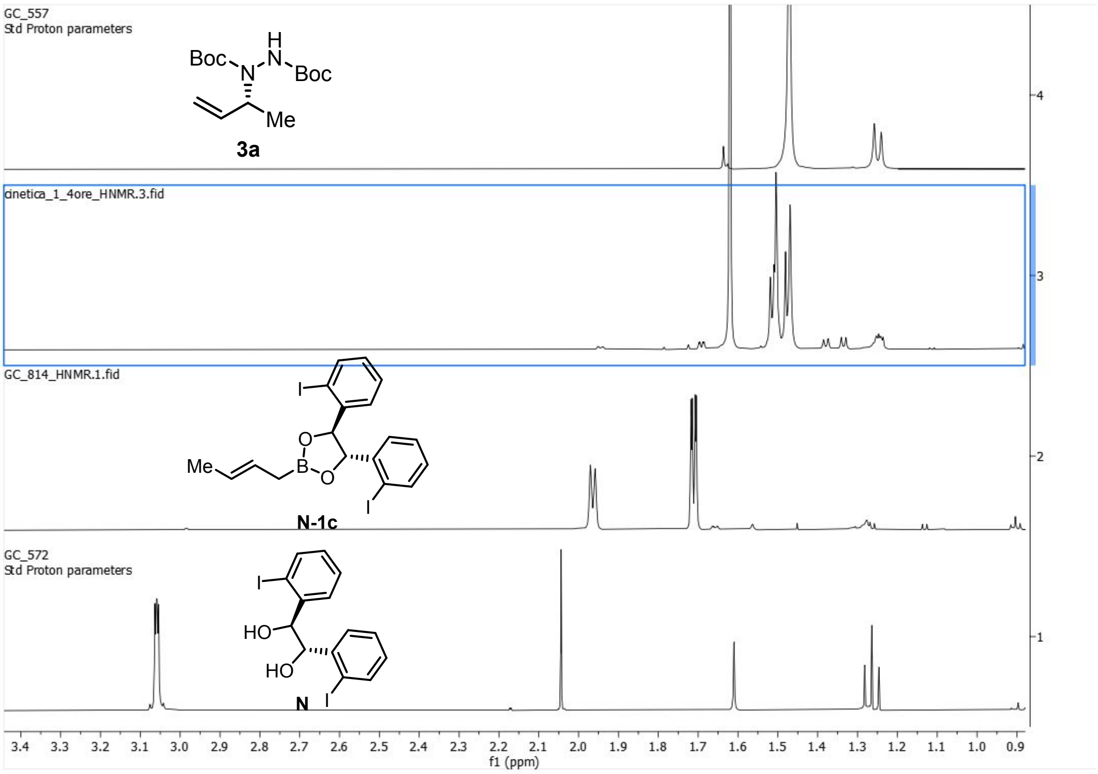




Because of the formation of such adduct **N-3a**, the catalyst **N** as well the product **3a** cannot be detected in the reaction mixture:

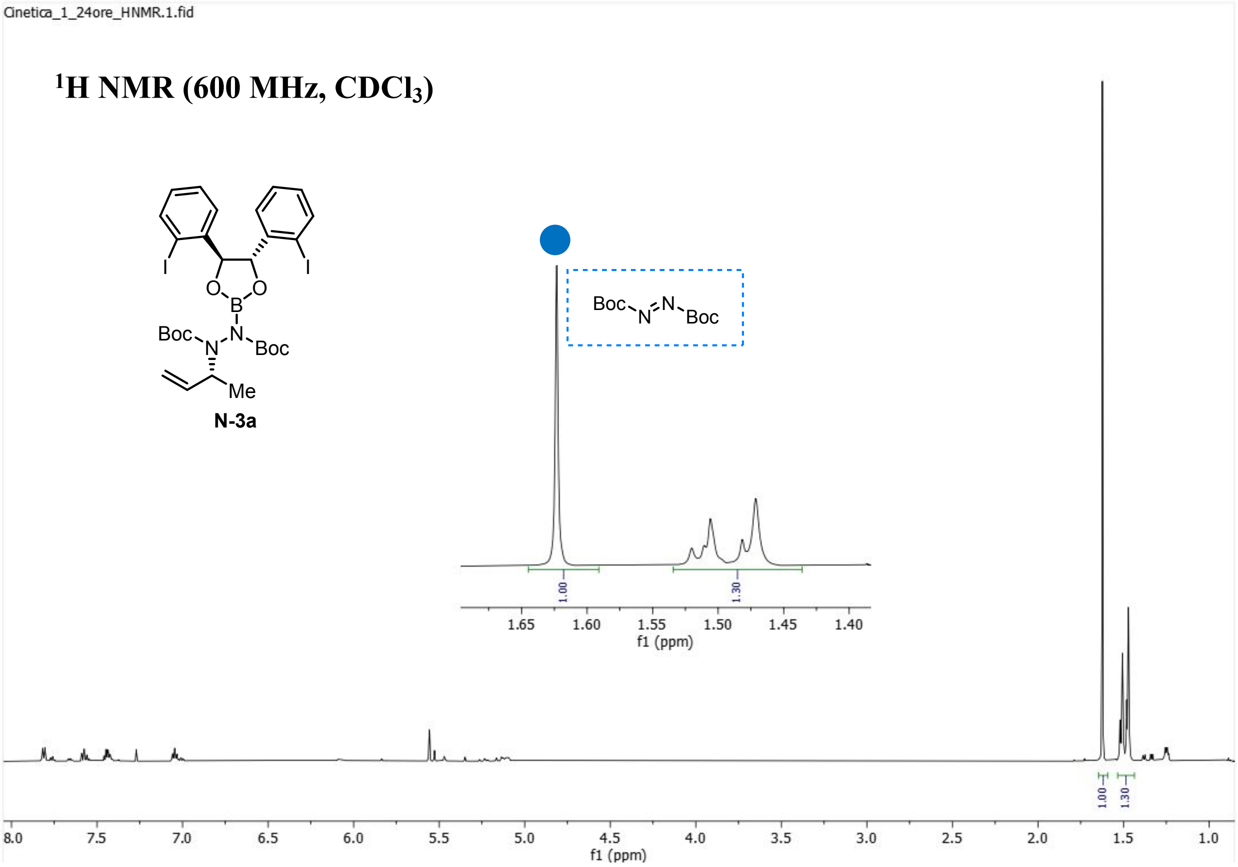


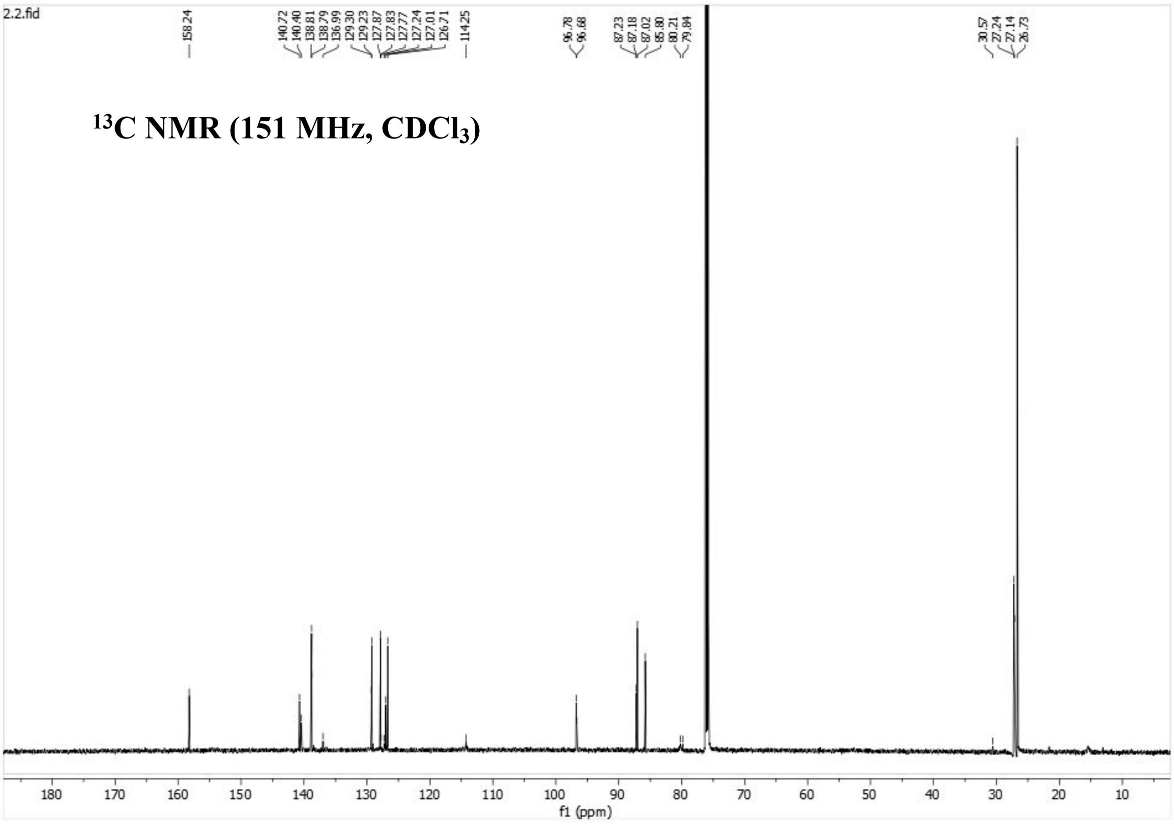


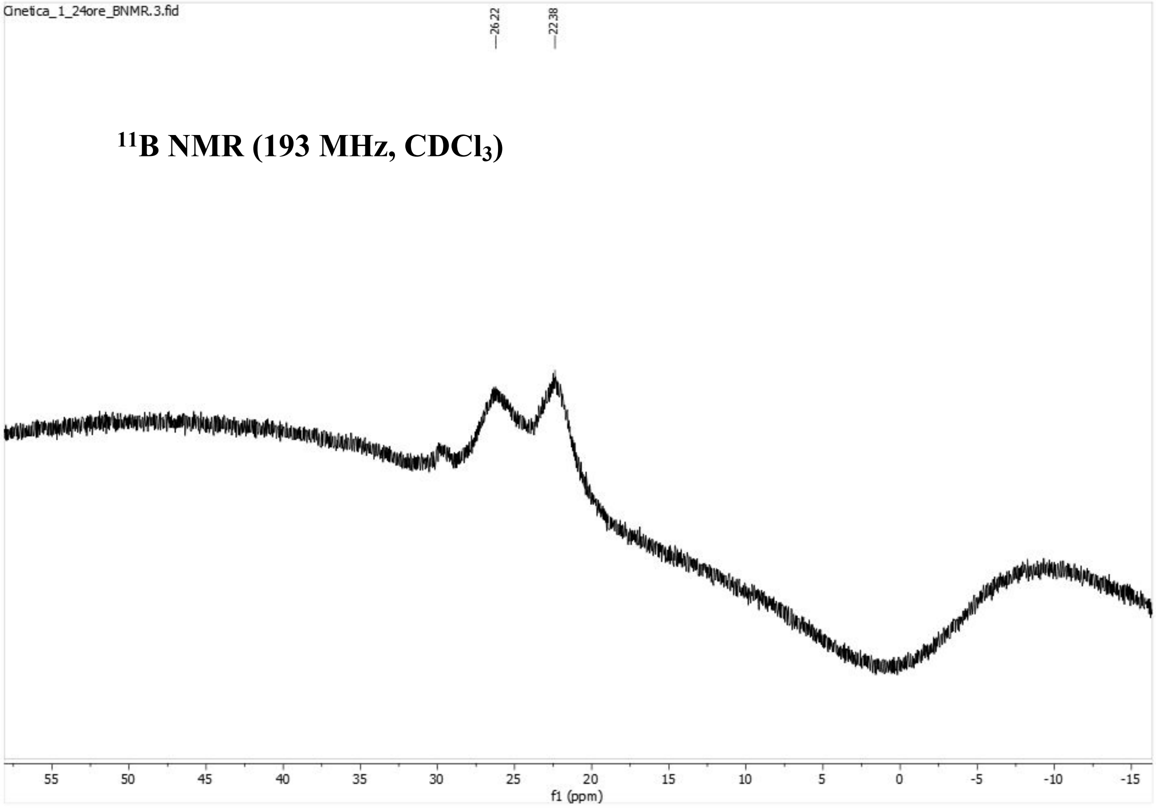


24 hours:

After 24 hours **N-1ca** is no longer present and only the clean intermediate **N-3a** with the remaining excess of the **2a** can be detected.



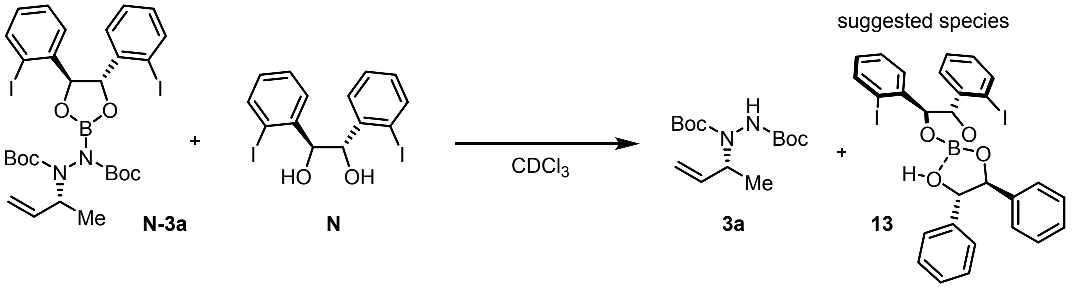




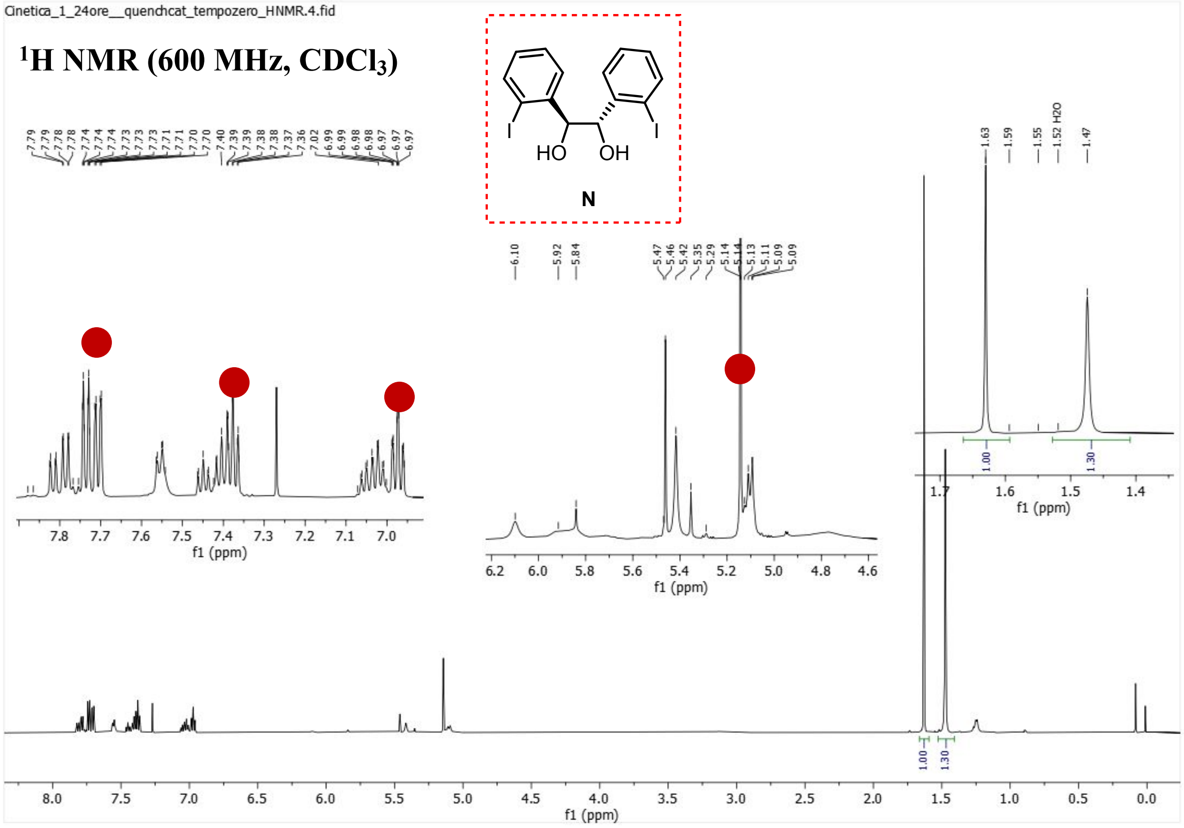
The reaction mixture was split into two parts of equal volume which were diluted with 0.3 mL of $CDCl_3$ each. 24 mg (0.05 mmol, 1.57 eq.) of **N** were added to the first portion (**NMRs experiment**

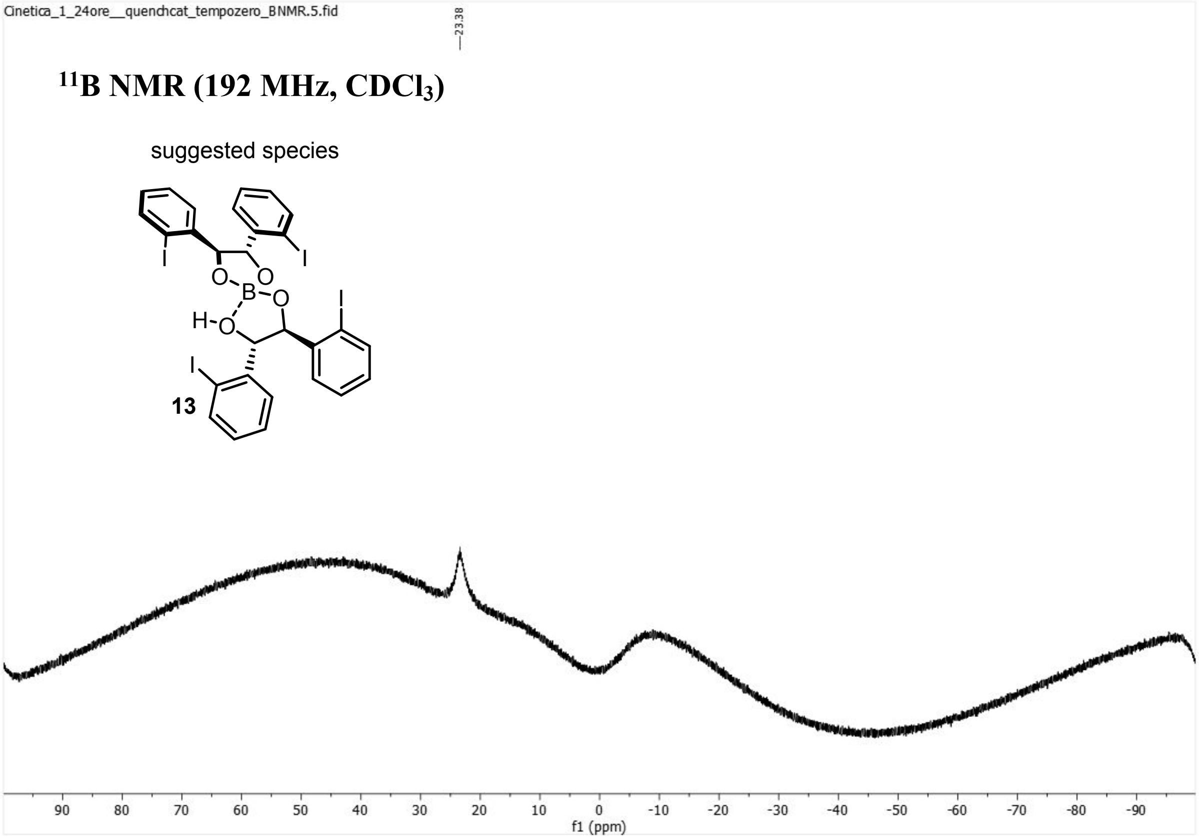
1.1), while 7 µL of isopropanol and 7 µL of acetic acid were added to the second solution (**NMRs experiment 1.2**).

NMRs EXPERIMENT n1.1

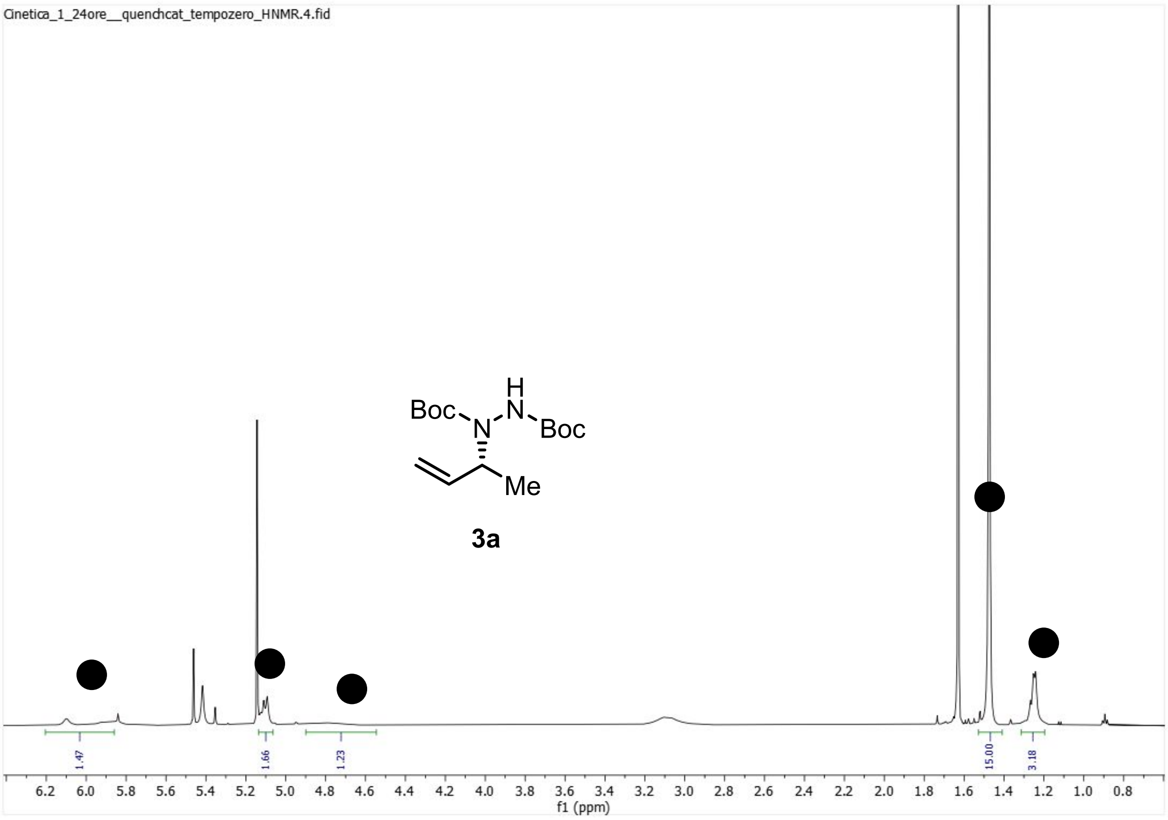


The NMRs show the signals of **3a** due to the hydrolysis of the B-N bond of the adduct **N-3a**, but not those belonging to **N**. This means that the B-N is particularly sensitive and in the regular reaction conditions even the free catalyst may provoke its hydrolysis, while the B-O bond appears to be more robust.

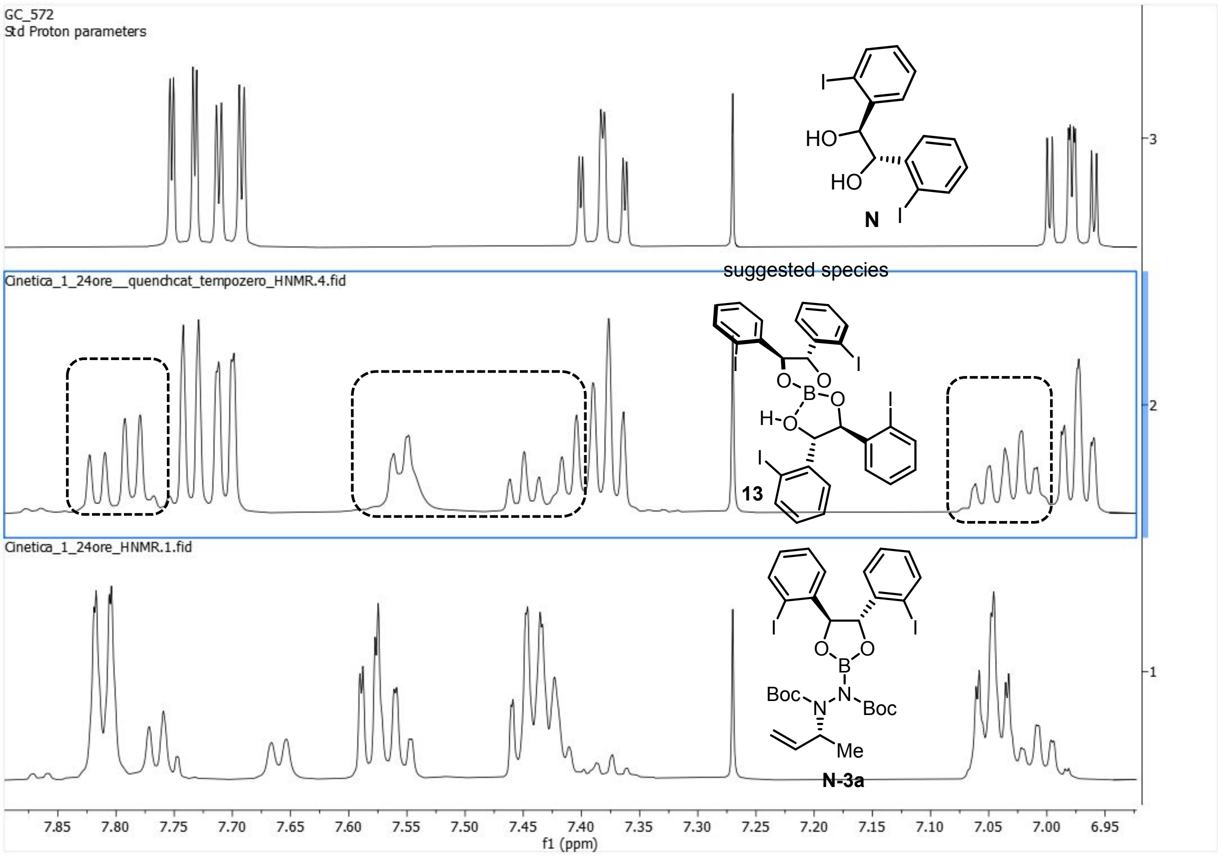


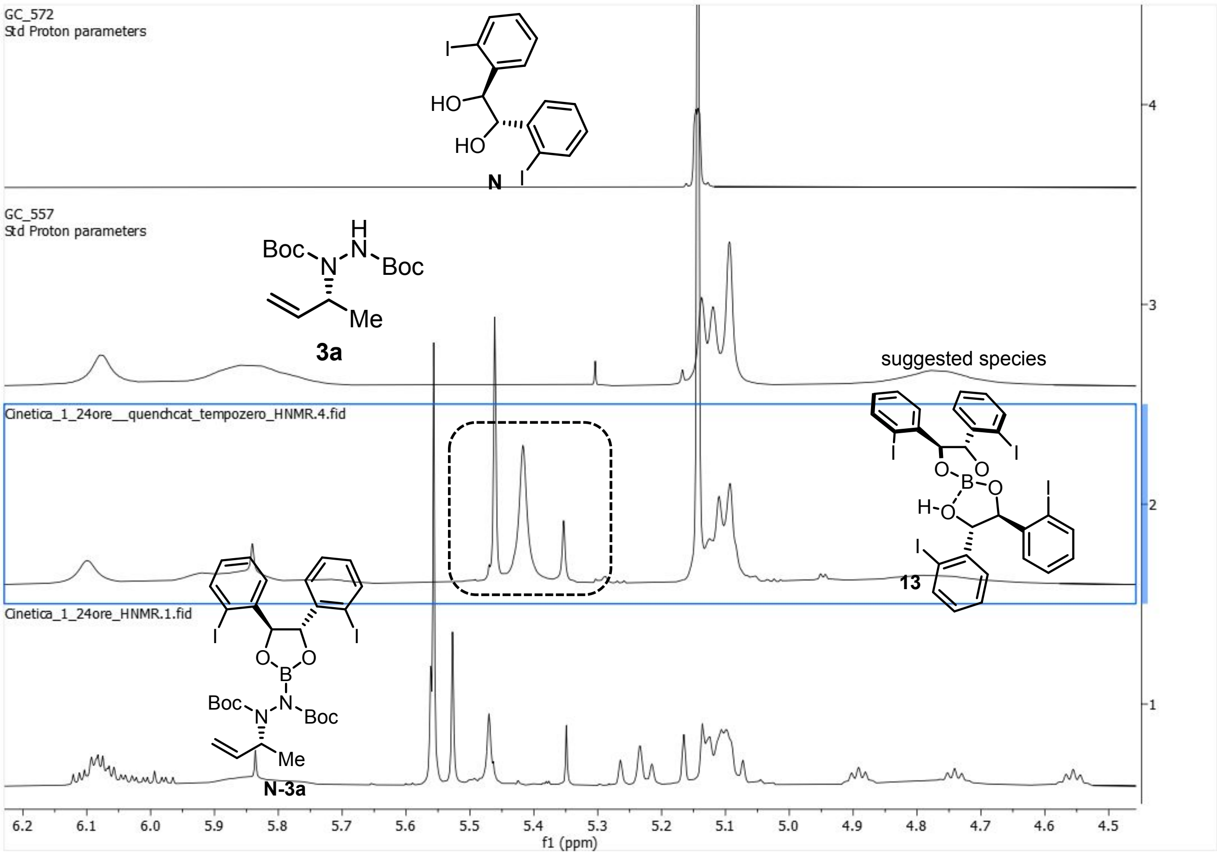


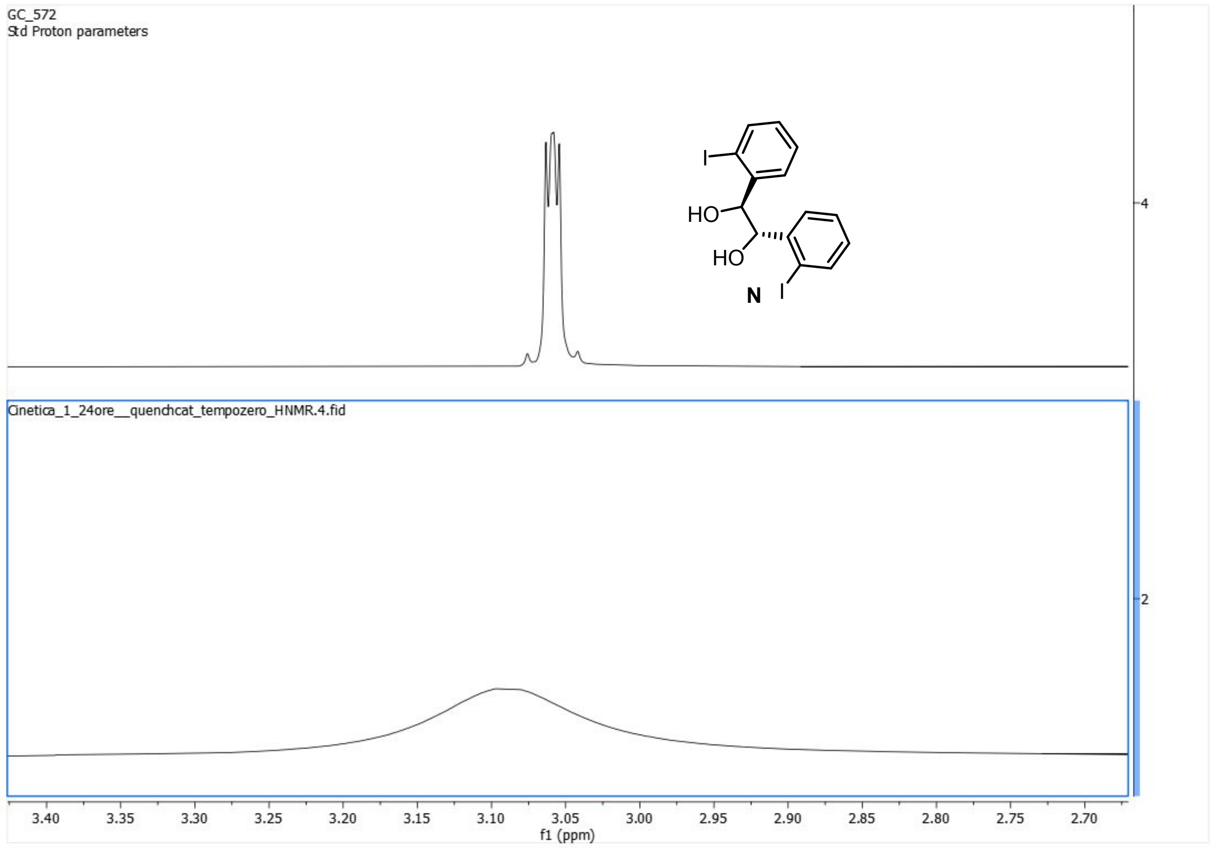
The integration of the signals belonging to **3a** is shown below:

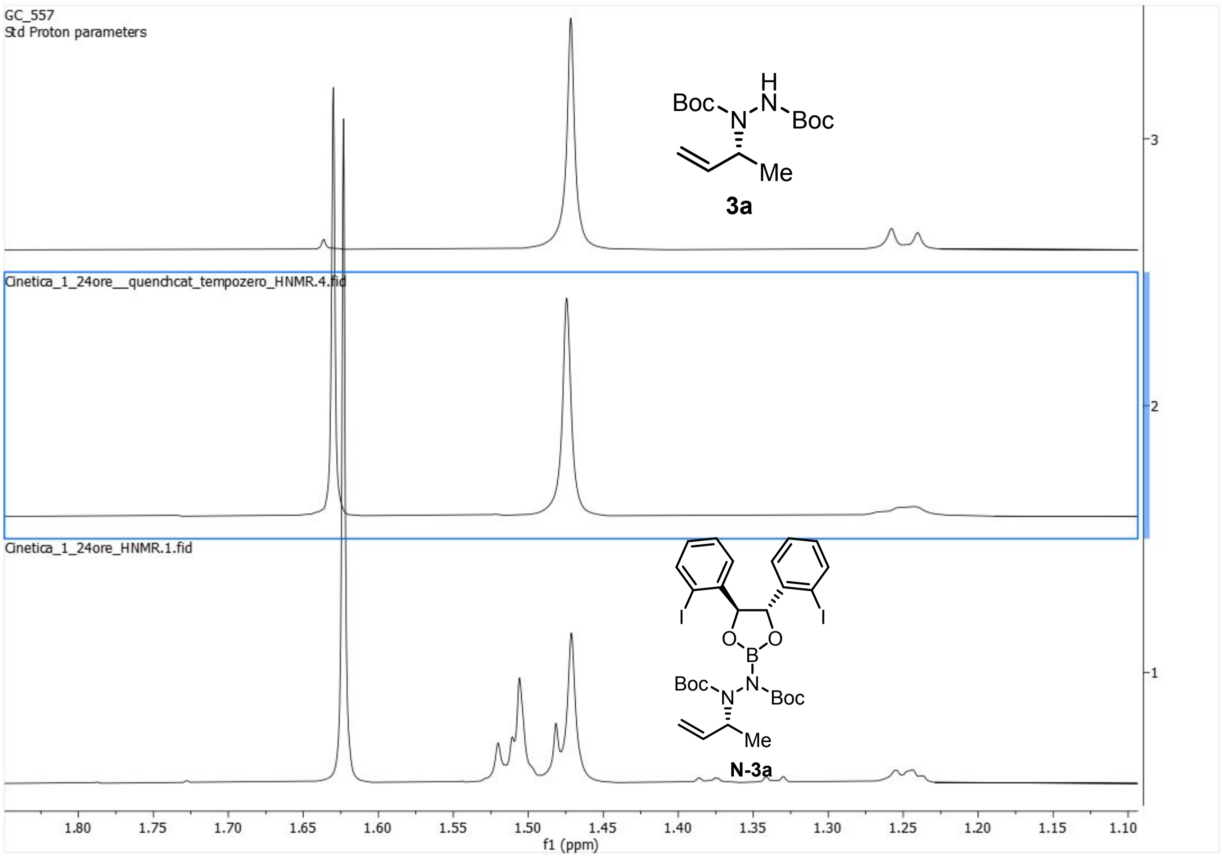


Beside the formation of the product, another compound is detected which is believed to be something similar to **13**.



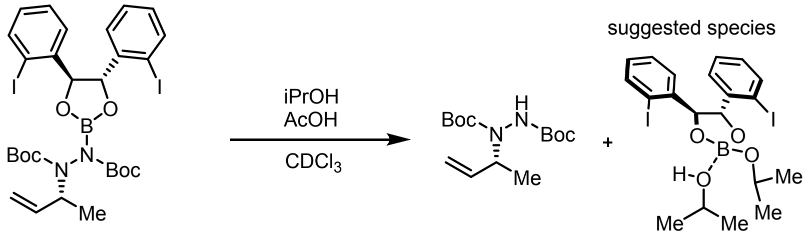



GC_572
Std Proton parameters
I
HO
HO
I
N
Cinetica_1_24ore__quenchcat_tempozero_HNMR.4.fid
4
2
3.40
3.35
3.30
3.25
3.20
3.15
3.10
3.05
3.00
2.95
2.90
2.85
2.80
2.75
2.70
f1 (ppm)

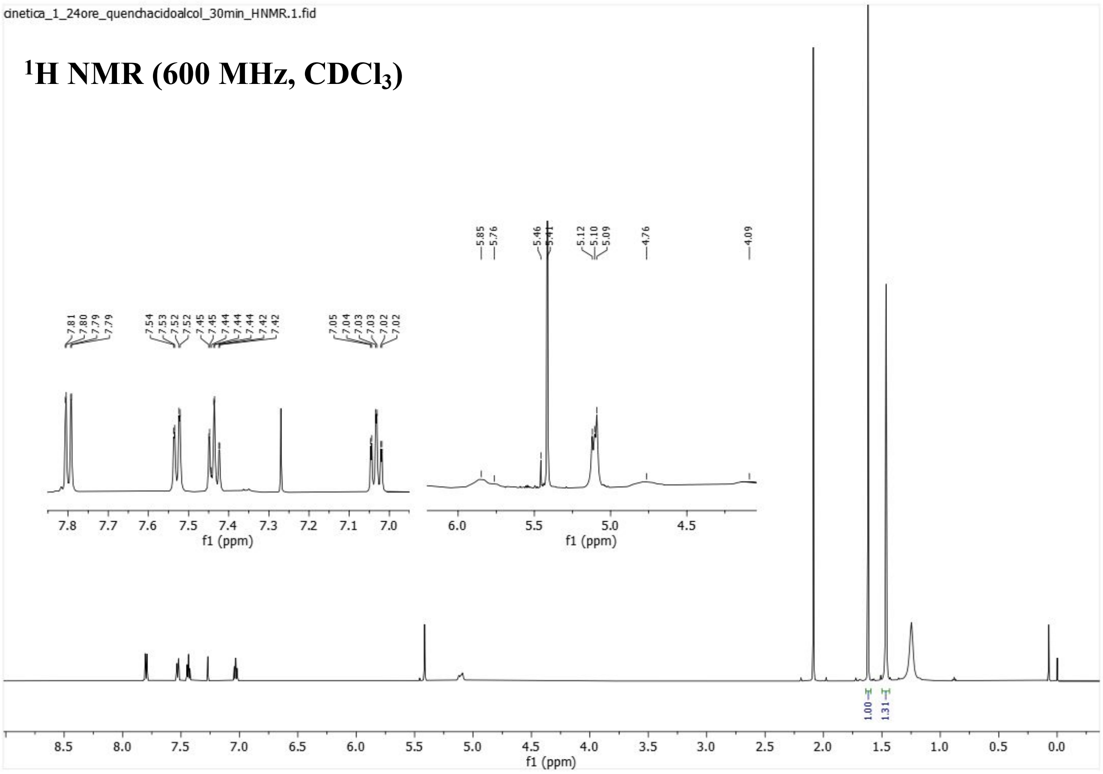

GC_557
Std Proton parameters
H
Boc
N
N
Boc
Me
3a
Cinetica_1_24ore__quenchcat_tempozero_HNMR.4.fid
Cinetica_1_24ore_HNMR.1.fid
I
I
O
B
O
Boc
N
N
Boc
Me
N-3a
3
2
1
1.80
1.75
1.70
1.65
1.60
1.55
1.50
1.45
1.40
1.35
1.30
1.25
1.20
1.15
1.10
f1 (ppm)

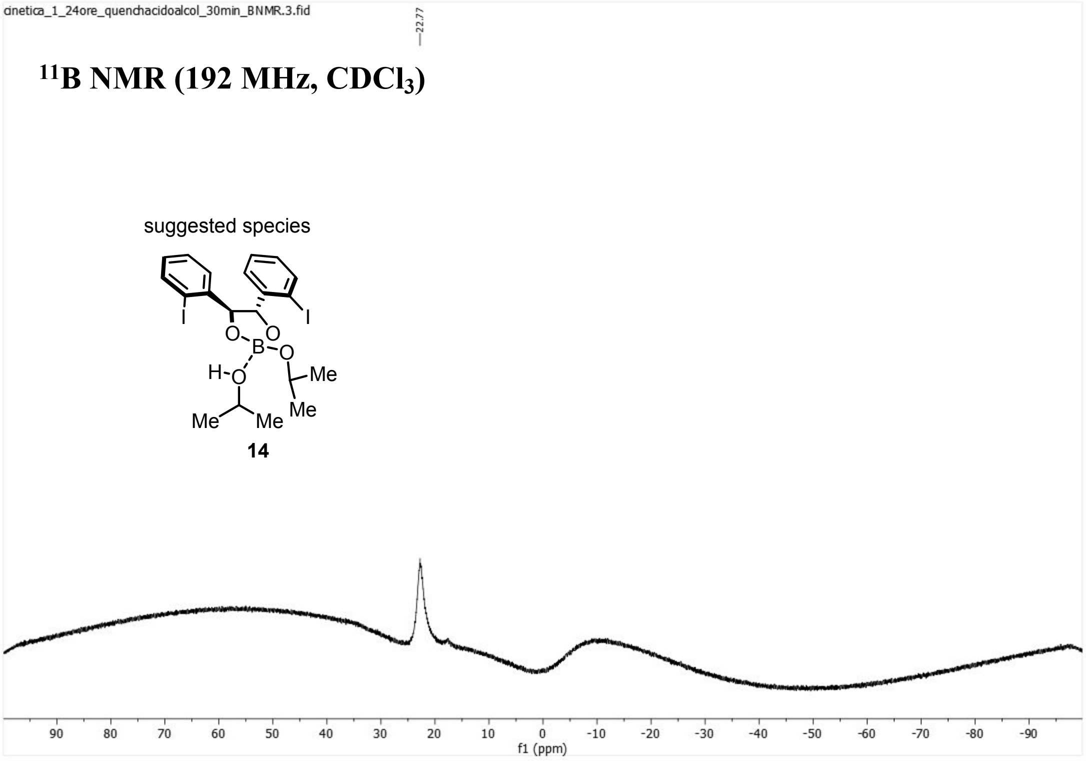
NMRs EXPERIMENT n1.2

The addition of iPrOH and AcOH cause the hydrolysis of the B-N bond and the formation of **3a**. Even in this case **N** seems to be still involved with the boron atom.

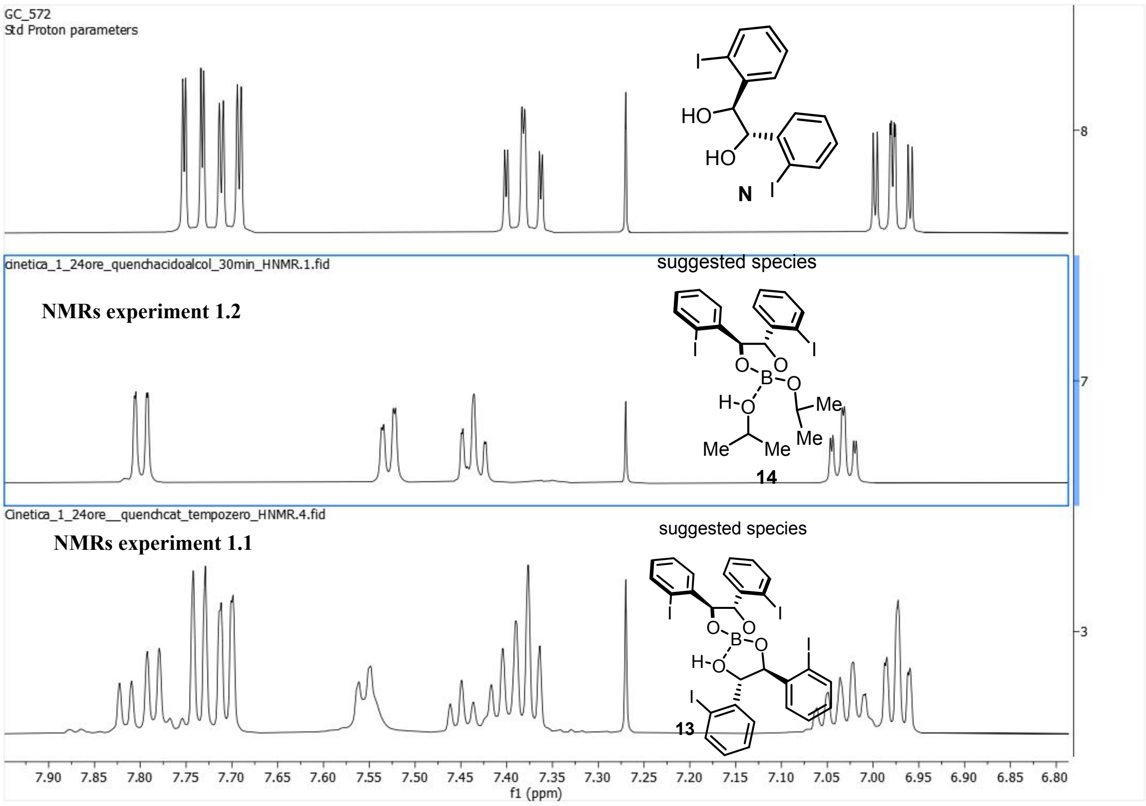


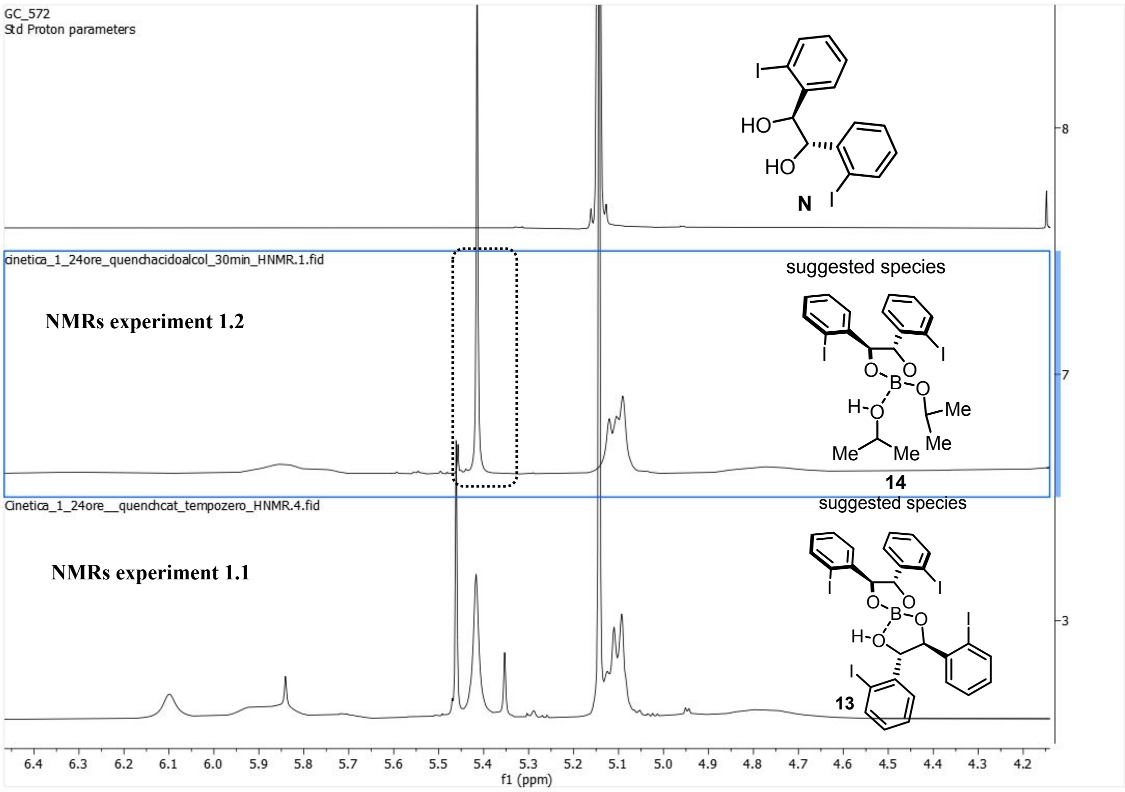
N-3a **3a** **14**

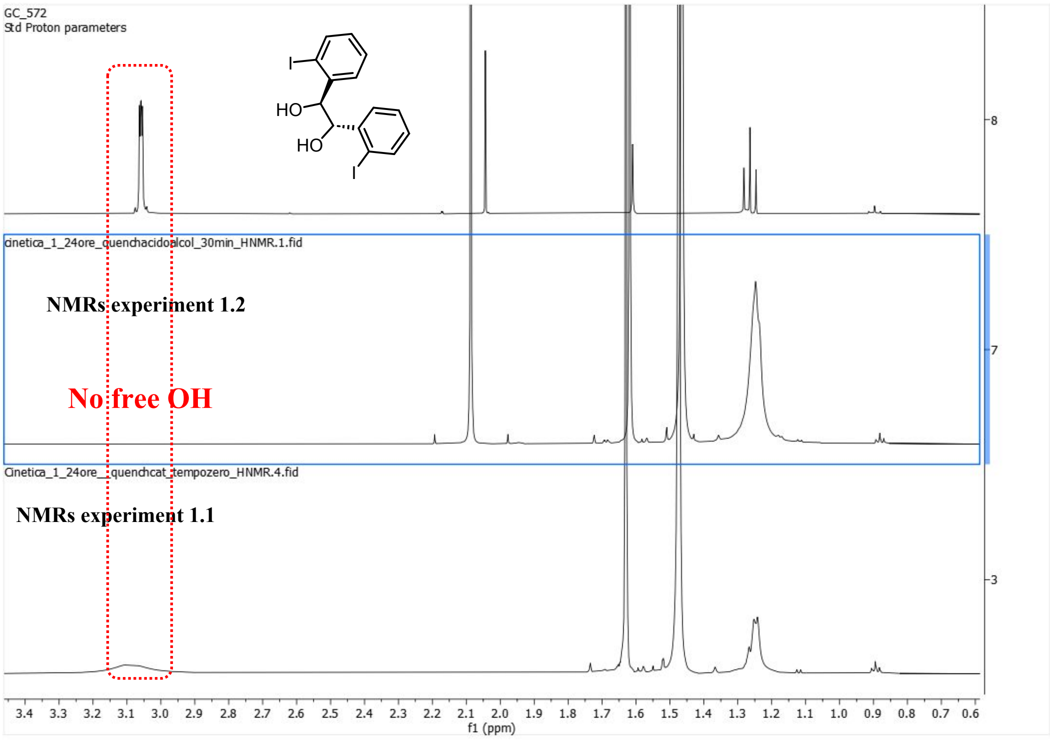




The side-product of the hydrolysis involving the catalyst seems to be different from the adduct **13** detected in the **NMRs experiment 1.1**.





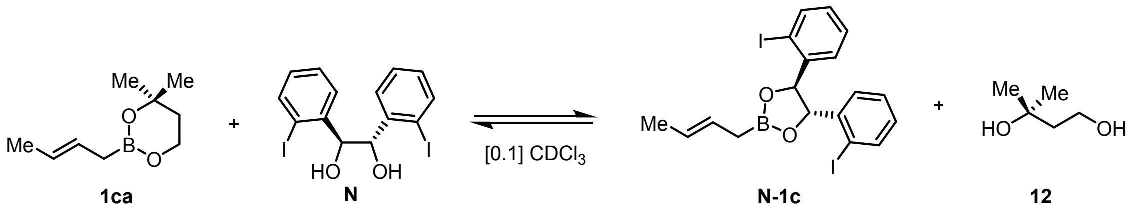


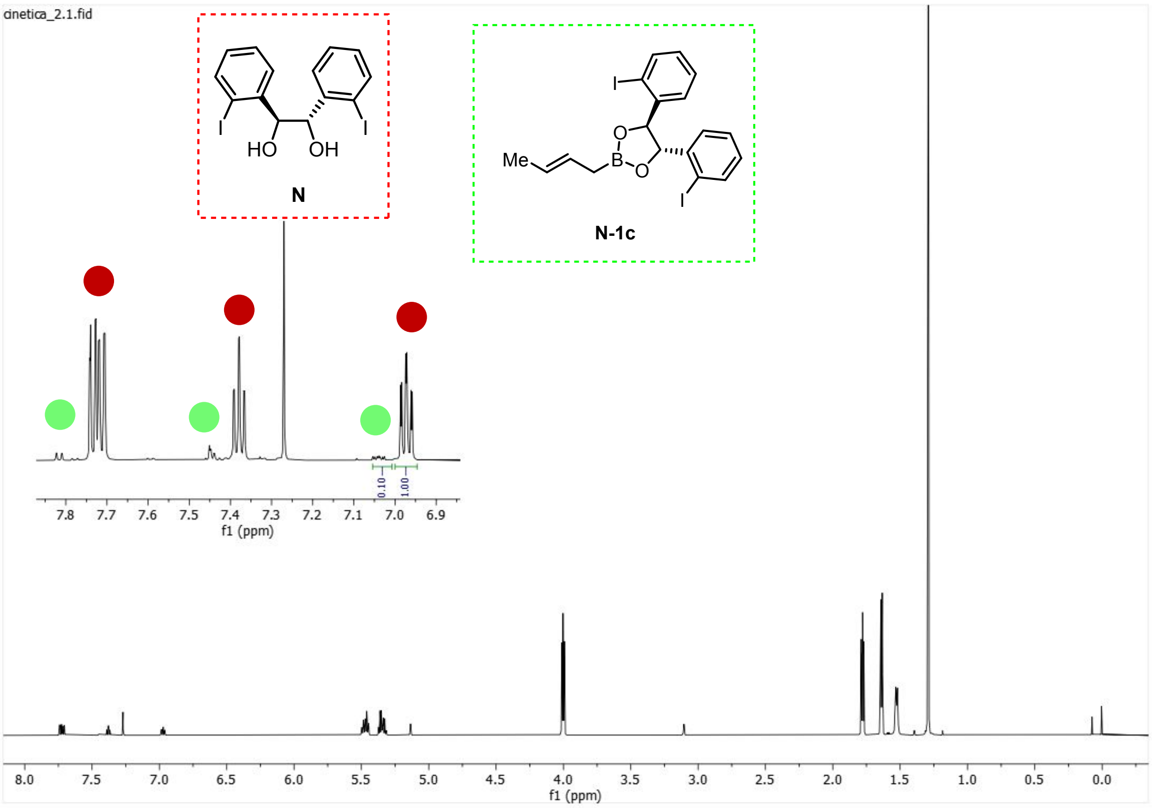
In conclusion, these two experiments evidence the easiness toward the hydrolysis of the intermediate **N-3a** detected in experiment 1 and may further provide an explanation on why this specie has never been detected during the regular reaction conditions. The e.r. of the isolated product: 96:4.

NMRs EXPERIMENT n2

This experiment aims to reproduce the reaction between the starting materials **1ca** and **2a** in the presence of **N** but without iPrOH and AcOH.

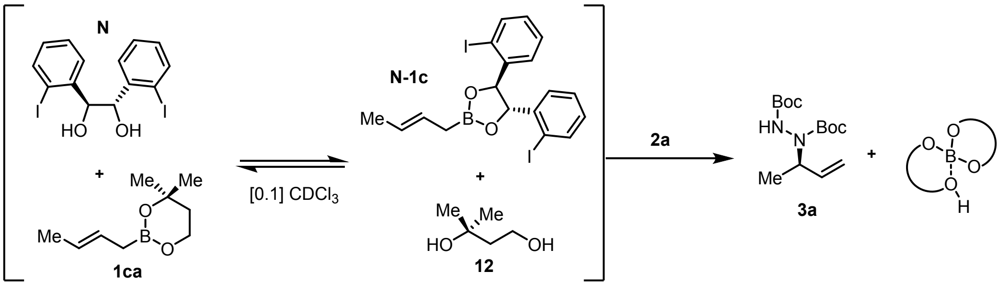
Conditions: In a screw cap vial provided of a magnetic stir bar 25.5 mg of **1ca** (0.15 mmol), 0.65 mL of $CDCl_3$ and 7 mg of **N** (0.015 mmol) were added. The reaction was stirred for 10 minutes, then a ^1H NMR of the mixture was recorded.



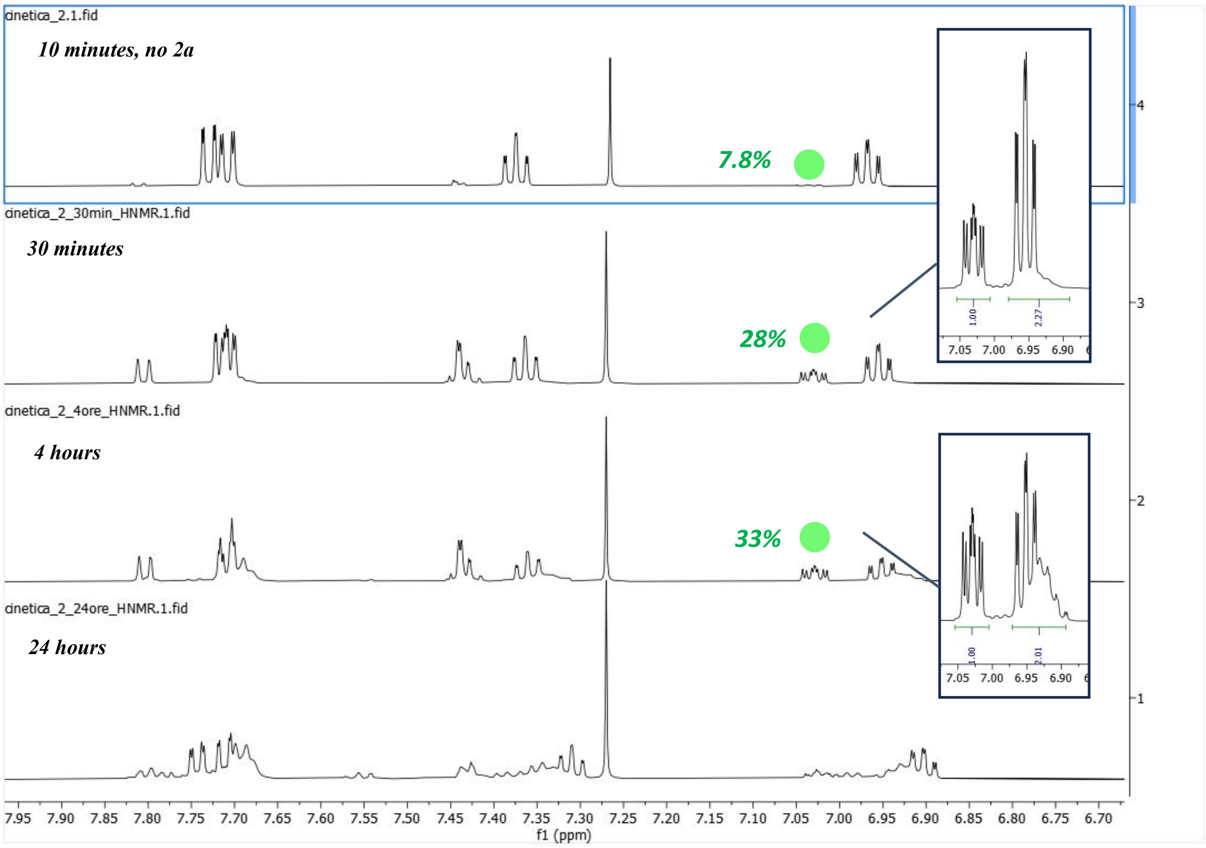


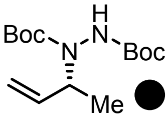
After 10 minutes 7.8% of the starting amount of **N** is converted into **N-1c**.

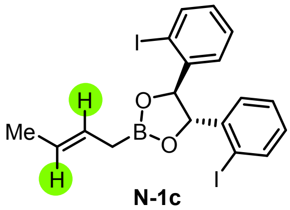
Afterward, the solution was transferred into a screw cap vial and 34.5 mg (0.15 mmol) of **2a** were added and the mixture was stirred at room temperature.

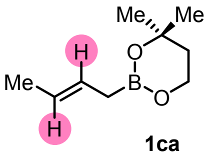


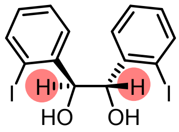
NMRs were recorded after 30 minutes, 4 hours and 24 hours. The concentration of the **N-1c** gradually increases over 4 hours, but the ^{1}H NMR at this time also shows new aromatic signals. Interestingly, after 24 hours a complexity of signals are visible in the aromatic region and there is no clear evidence of the presence either of **N** or **N-1c**. Moreover, these signals do not match with the suggested compounds **13**-**14** detected in **NMR experiments 1.1** and **1.2**. The percentages refer to the initial amount of **N**.

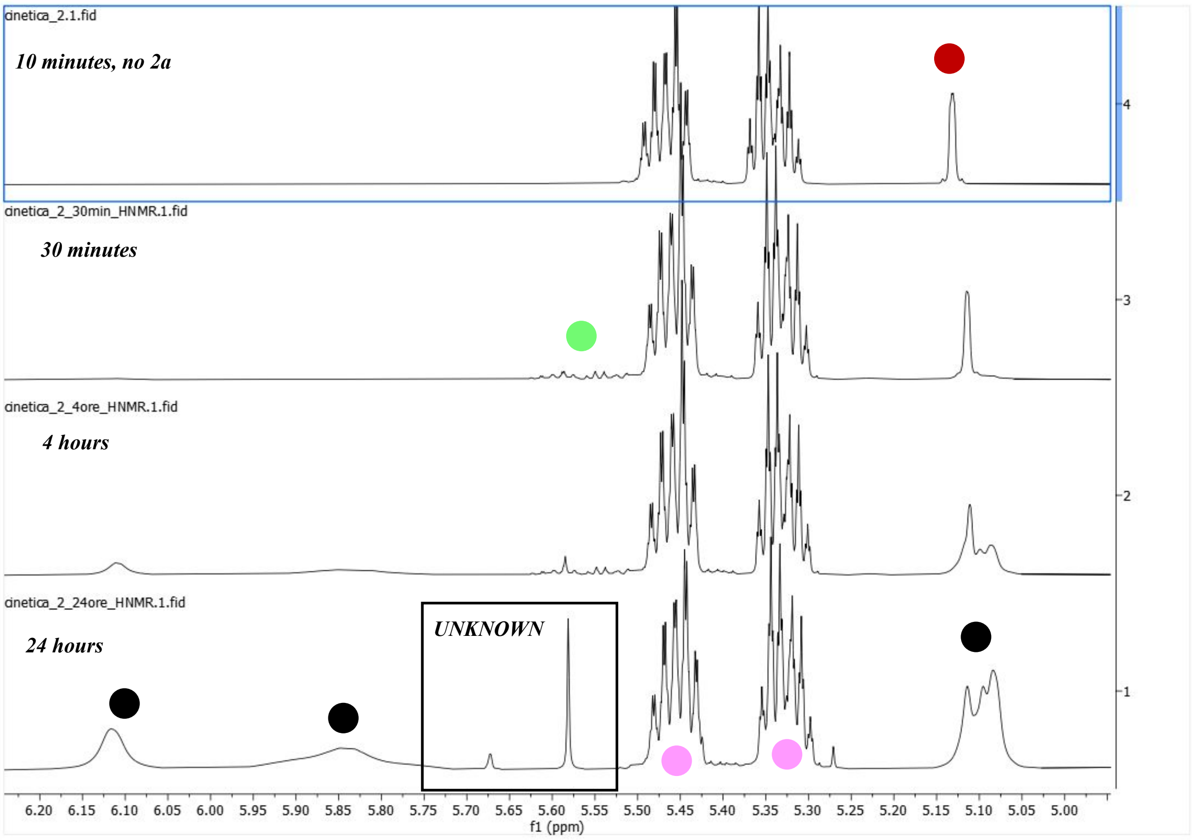


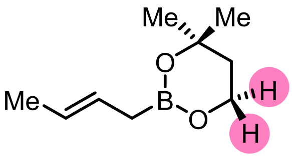

3a


N-1c

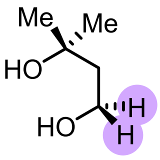

1ca


N

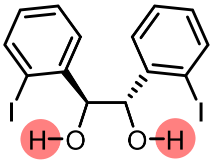

cinetica_2.1.fid
10 minutes, no 2a
cinetica_2_30min_HNMR.1.fid
30 minutes
cinetica_2_4ore_HNMR.1.fid
4 hours
cinetica_2_24ore_HNMR.1.fid
24 hours
UNKNOWN
6.20 6.15 6.10 6.05 6.00 5.95 5.90 5.85 5.80 5.75 5.70 5.65 5.60 5.55 5.50 5.45 5.40 5.35 5.30 5.25 5.20 5.15 5.10 5.05 5.00
f1 (ppm)
4
3
2
1


Me
Me
O
B
O
Me
H
H

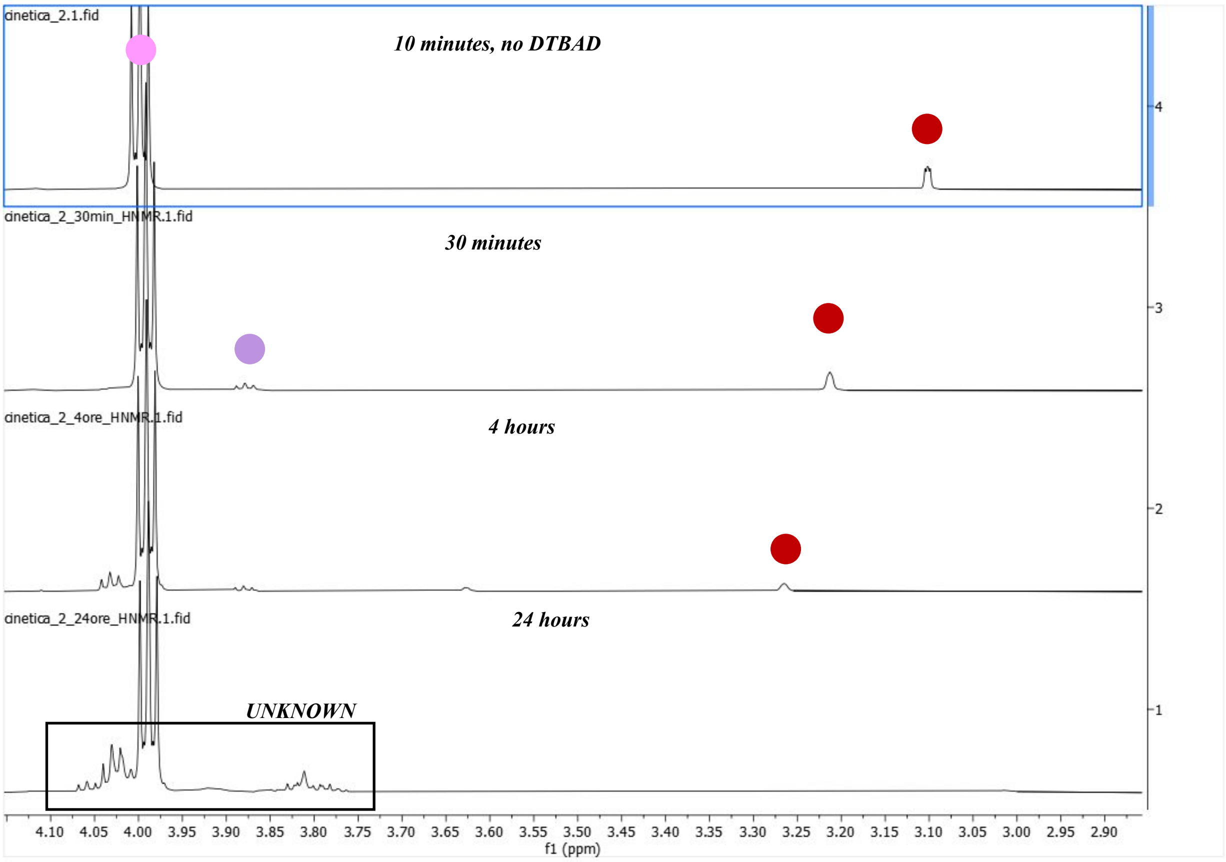
1ca

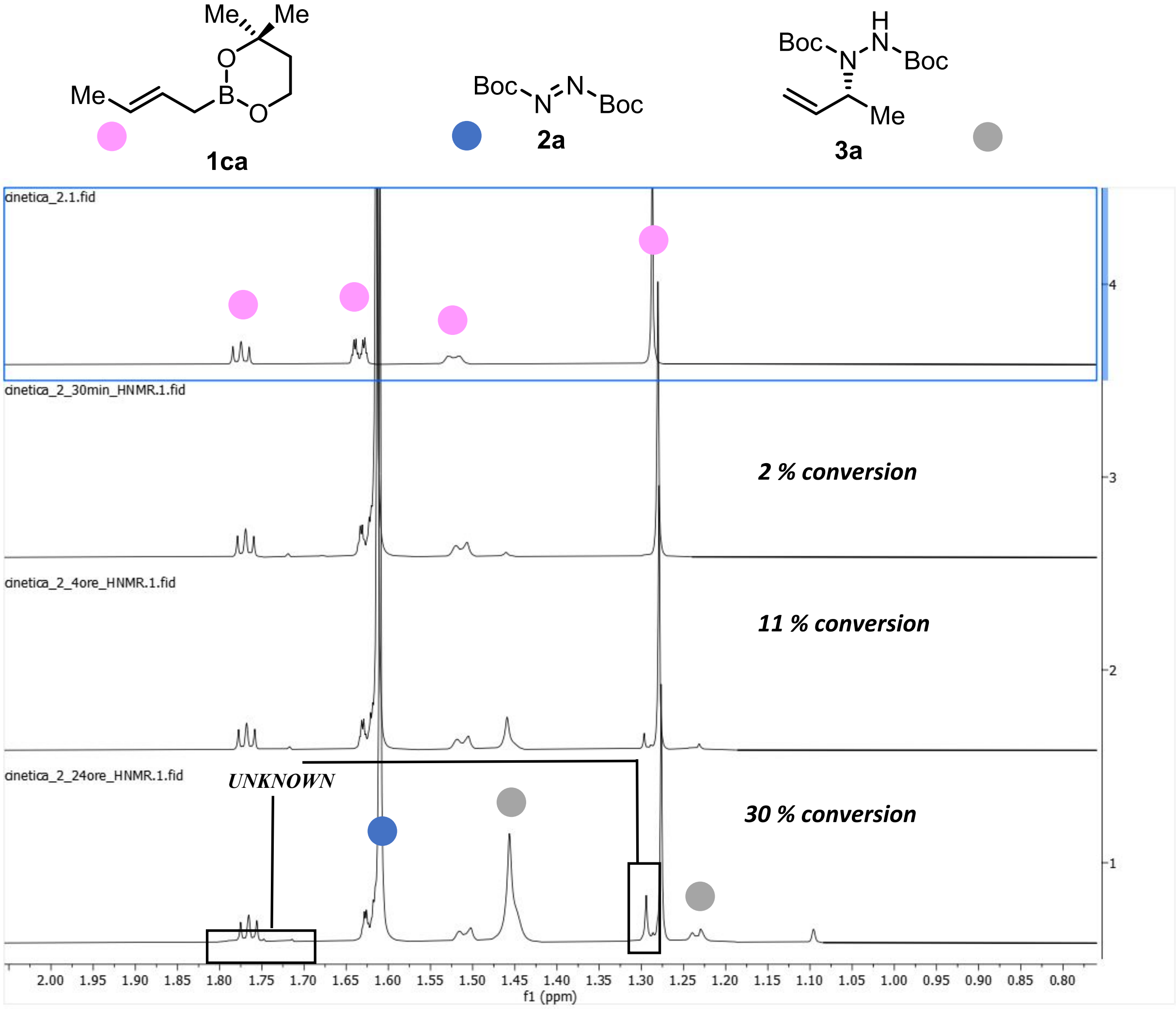

Me
Me
HO
HO
H
H

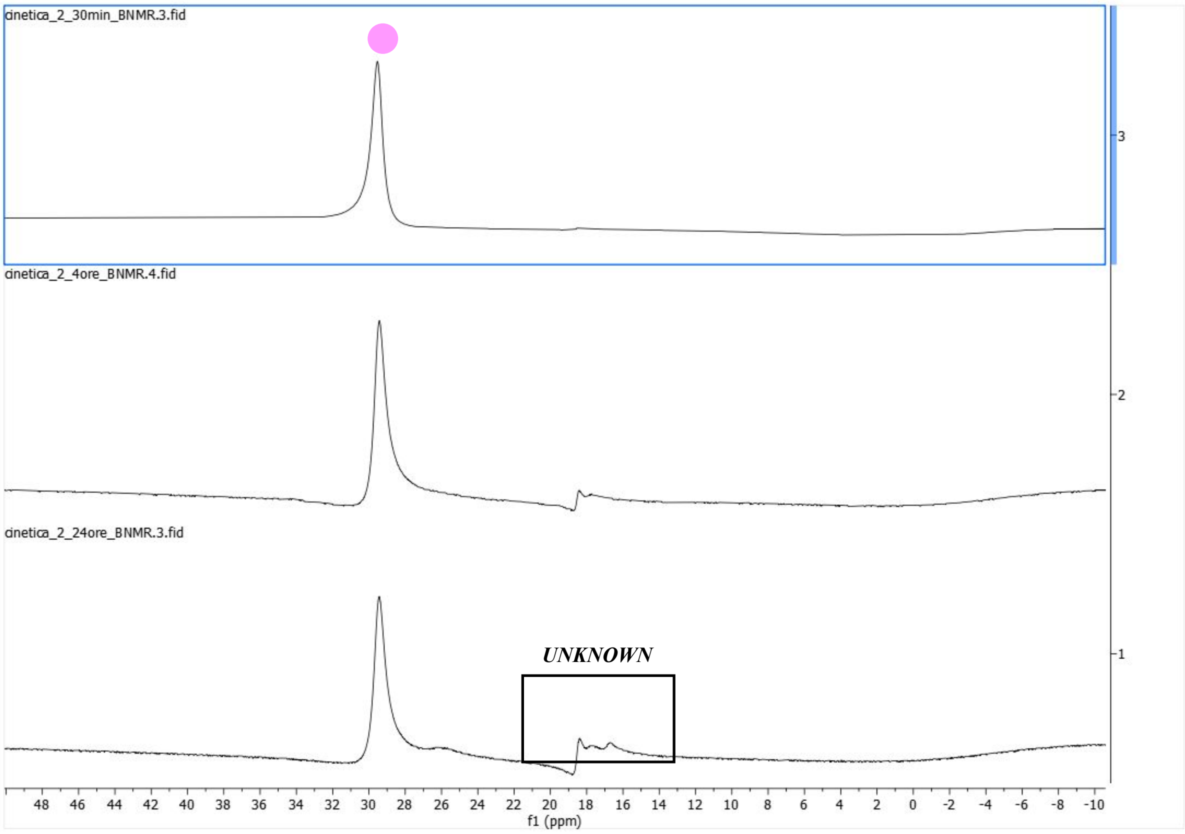
12


I
I
H–O
O–H

N

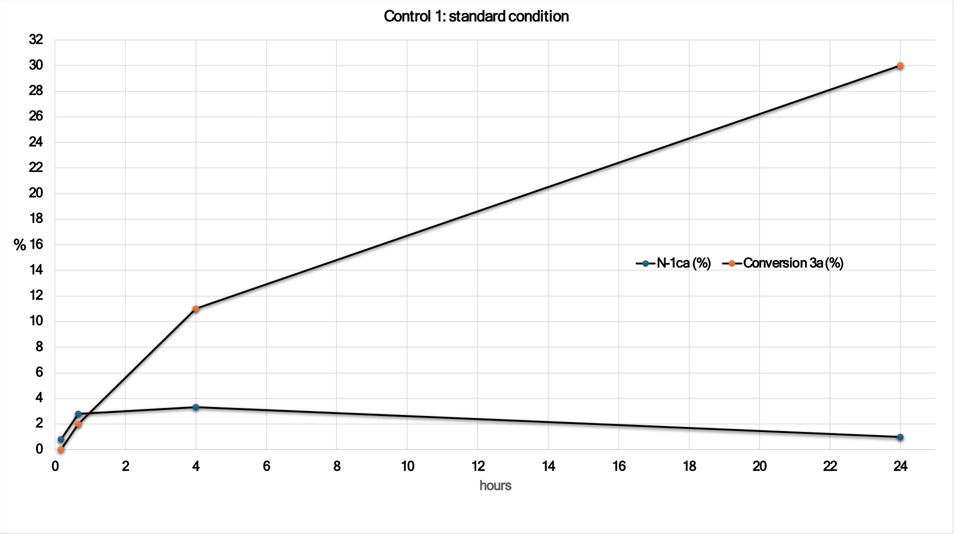

cinetica_2.1.fid
10 minutes, no DTBAD
cinetica_2_30min_HNMR.1.fid
30 minutes
cinetica_2_4ore_HNMR.1.fid
4 hours
cinetica_2_24ore_HNMR.1.fid
24 hours
UNKNOWN
4
3
2
1
4.10
4.05
4.00
3.95
3.90
3.85
3.80
3.75
3.70
3.65
3.60
3.55
3.50
3.45
3.40
3.35
3.30
3.25
3.20
3.15
3.10
3.05
3.00
2.95
2.90
f1 (ppm)


Me
Me
O
B
O
Me
1ca
Boc
N
N
Boc
2a
H
N
Boc
Boc
N
Me
3a
cinetica_2.1.fid
cinetica_2_30min_HNMR.1.fid
2 % conversion
cinetica_2_4ore_HNMR.1.fid
11 % conversion
cinetica_2_24ore_HNMR.1.fid
UNKNOWN
30 % conversion
4
3
2
1
2.00 1.95 1.90 1.85 1.80 1.75 1.70 1.65 1.60 1.55 1.50 1.45 1.40 1.35 1.30 1.25 1.20 1.15 1.10 1.05 1.00 0.95 0.90 0.85 0.80
f1 (ppm)



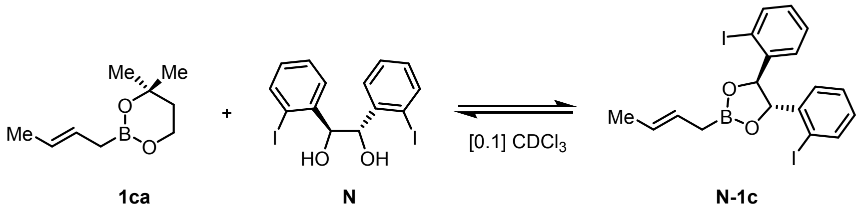
Since the unknown signals detected by ^{1}H NMR are close to the signals of **N** and those of **12** and according to ^{11}B NMR where multiple peaks between 19 and 15 ppm are present, we speculated that **N** and **12** are somehow bonded to the boron atom. It seems that within these conditions there is no efficient way to release the catalyst. Thus, as confirmed by the e.r of the isolated product after 24 hours (83:17), also the background reaction could have a relevant contribution on the overall conversion. The percentage of **N-1ca** refers to the initial amount of **N**.

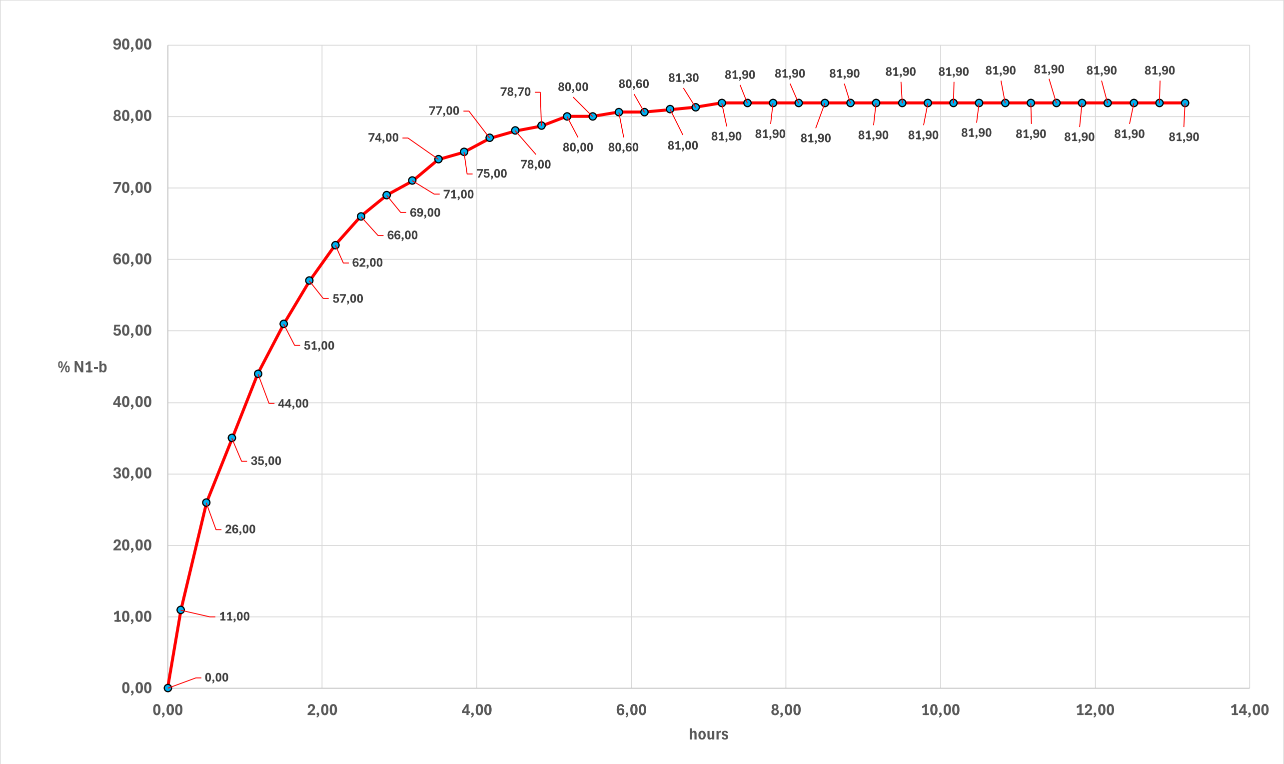
Time (h)	N-1ca	3a
0.17	8	/
0.67	28	2
4	33	11
24	10	30



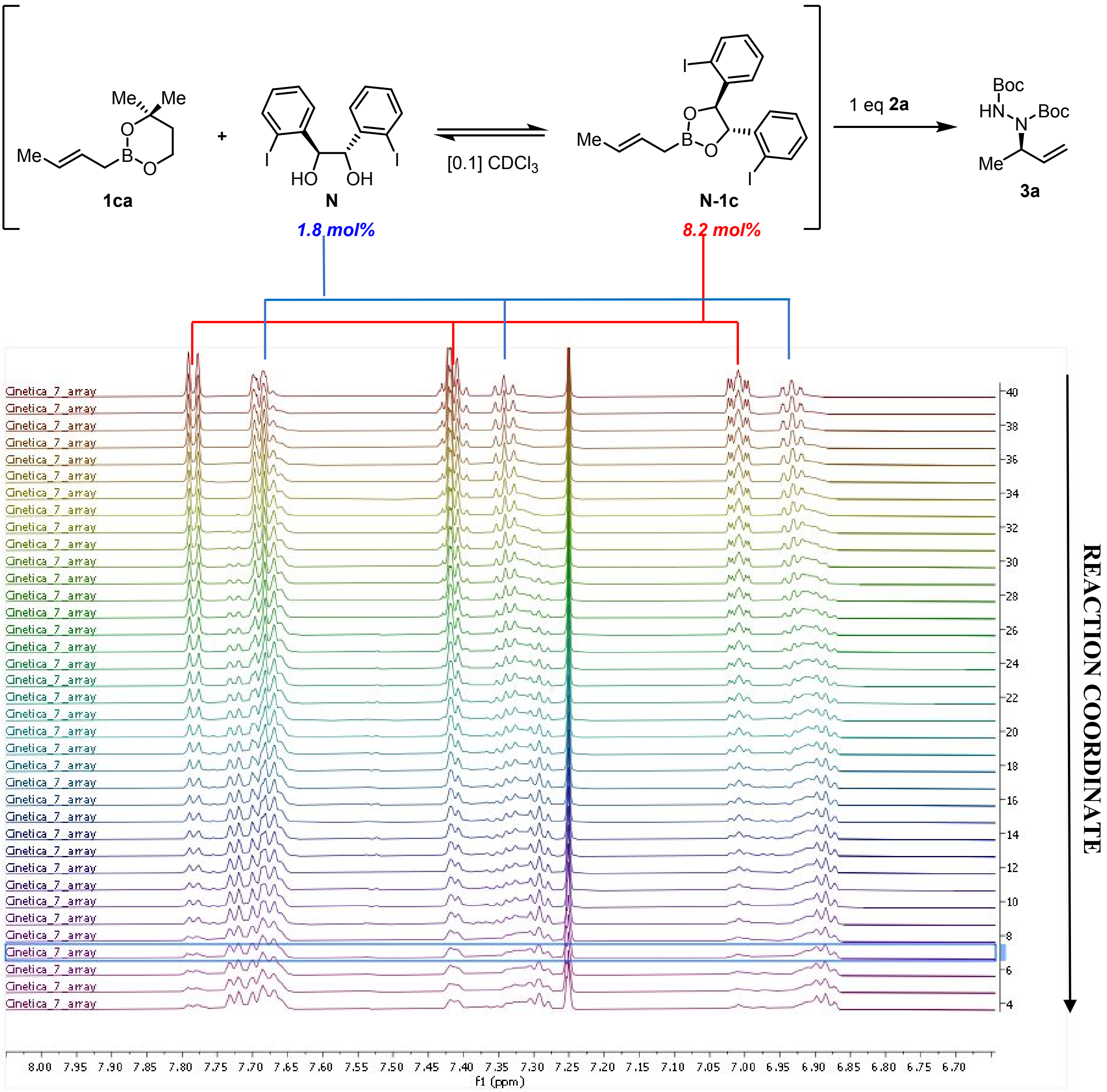
NMRs EXPERIMENT n2.1

To better study the disappearance of **N** along with **N-1ca** during the reaction we run the following experiment. 25.5 mg of **1ca** (0.15 mmol) were dissolved into a solution of 0.65 mL of $CDCl_3$ containing 7 mg of **N** (0.015 mmol). The mixture was transferred into an NMR tube and an ^1H NMR spectrum was recorded every 20 minutes:





After 13h we observed a well-established equilibrium, so we added 34.5 mg (1.0 eq.) of **2a** and we recorded an ^{1}H NMR every 20 minutes:

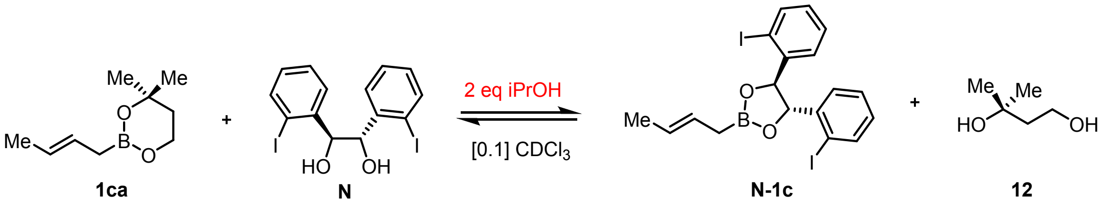


The gradual loss of the catalytically active species **N-1ca** during the reaction coordinate would be accountable for the inefficient regeneration the free catalyst **N**.

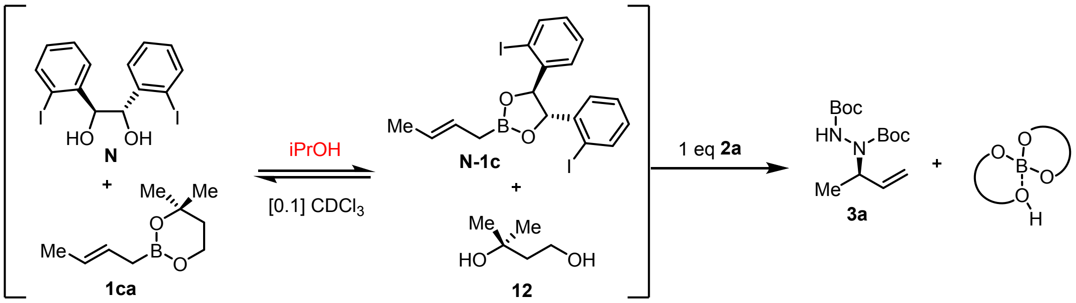
NMRs EXPERIMENT n3

This experiment aims to understand the role of the isopropanol.

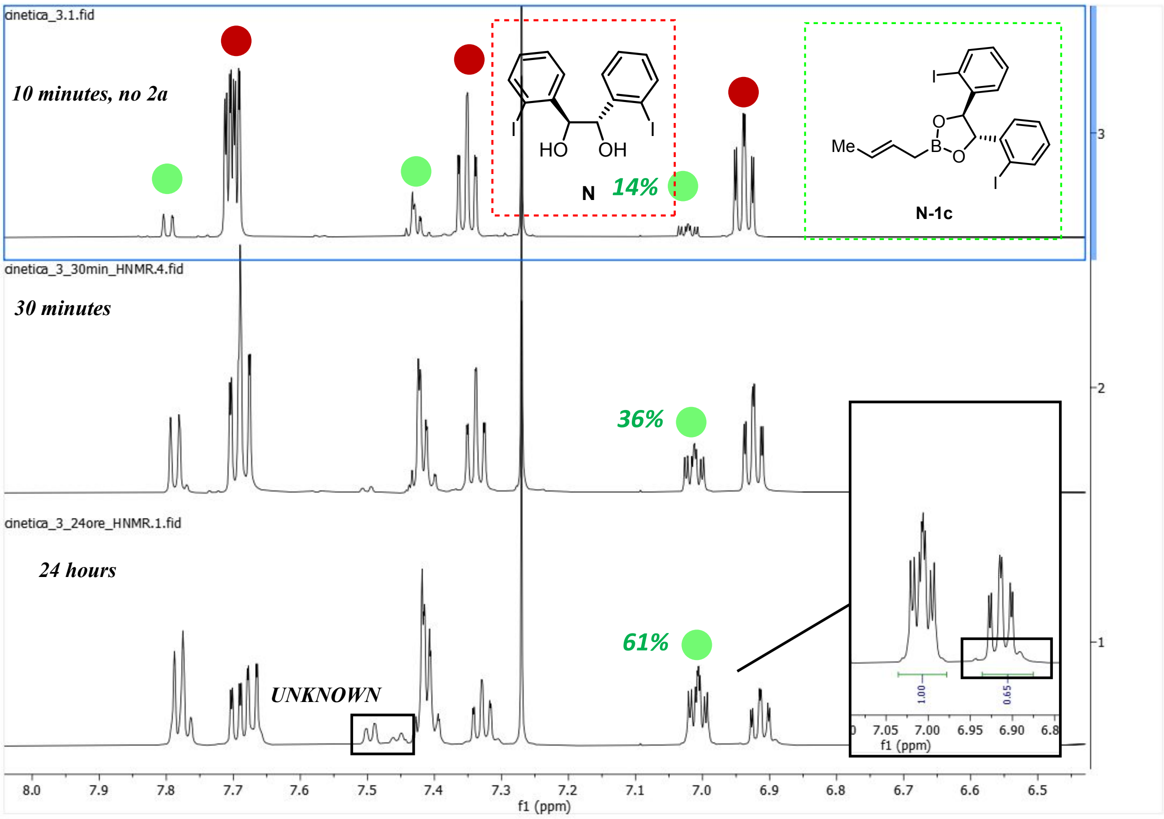
__Conditions__: In a screw cap vial provided of a magnetic stir bar 25.5 mg of **1ca** (0.15 mmol), 0.65 mL of $CDCl_3$,7 mg of **N** (0.015 mmol) and 23 µL of isopropanol (0.3 mmol, 2 eq.) were added. The reaction was stirred for 10 minutes, then the ^{1}H NMR of the mixture was recorded.

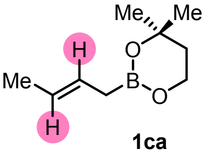


Then, 34.5 mg (0.15 mmol) of **2a** were added to the reaction mixture and the stirring was continued at rt.

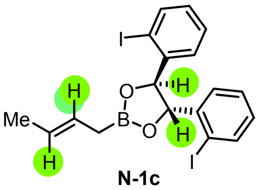


The equilibrium toward the formation of **N-1ca** seems to occur quicker compared to the experiment n2 and **N-1ca** accumulates over time. After 24 hours only few new peaks are observed in the aromatic region and both the catalytically active species **N-1ca** and the catalyst **N** are clearly visible.

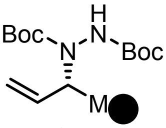

cinetica_3.1.fid
10 minutes, no 2a
HO
OH
N
14%
Me
O
B
O
I
N-1c
cinetica_3_30min_HNMR.4.fid
30 minutes
36%
cinetica_3_24ore_HNMR.1.fid
24 hours
61%
UNKNOWN
1.00
0.65
7.05
7.00
6.95
6.90
6.8
f1 (ppm)
3
2
1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
f1 (ppm)


Me
Me
Me
H
H
O
B
O

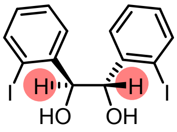
1ca


I
H
H
H
H
O
B
O
Me
I

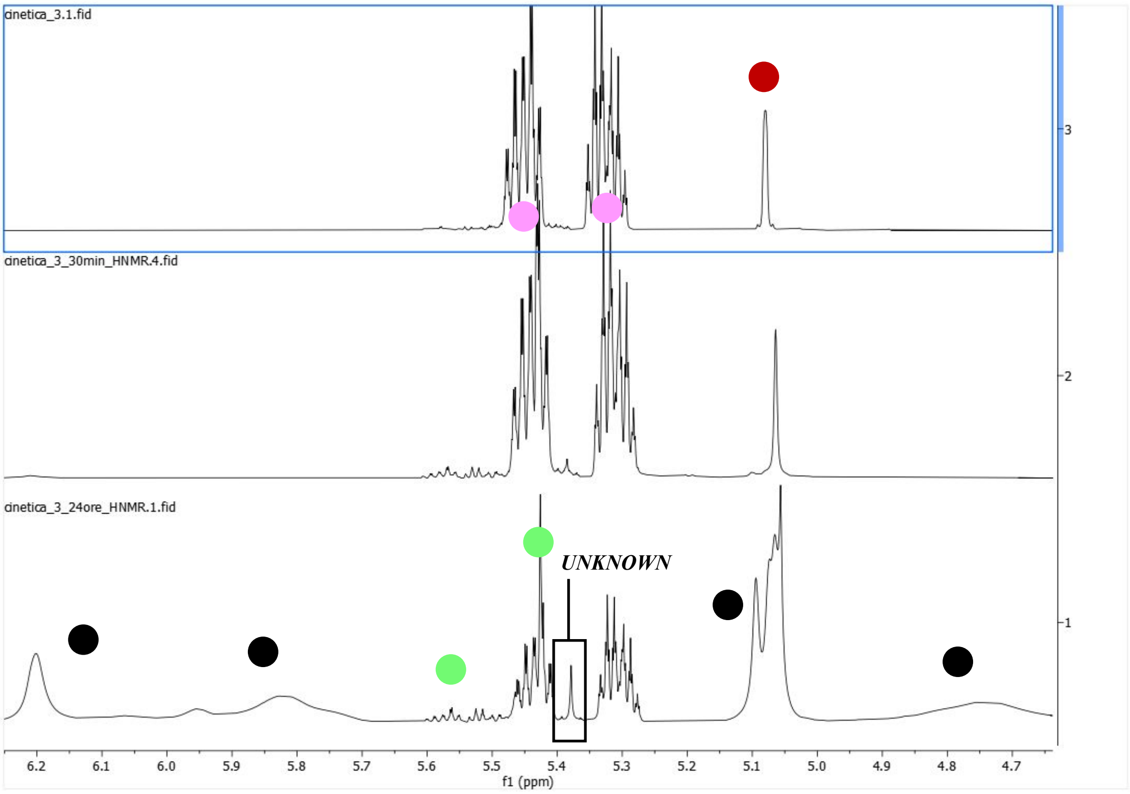
N-1c


H
Boc
N
N
Boc
Me

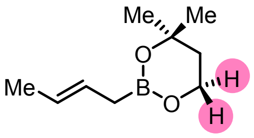
3a


I
H
HO
H
OH
I

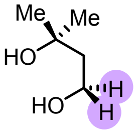
N


cinetica_3.1.fid
cinetica_3_30min_HNMR.4.fid
cinetica_3_24ore_HNMR.1.fid
UNKNOWN
3
2
1
6.2
6.1
6.0
5.9
5.8
5.7
5.6
5.5
5.4
5.3
5.2
5.1
5.0
4.9
4.8
4.7
f1 (ppm)

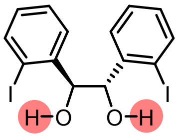
The signal of isopropanol partially overlaps with the peaks corresponding to the CH_2 (pink) of the ligand of **1ca**. After 24 hours in that region another signal appears that seems to be similar to the CH_2 of the ligand, while also the multiplet of the isopropanol shifts to 4.30 ppm. Therefore, the 3-methylbutane-1,3-diol **12**, unlike the catalyst, seems to be almost totally bonded with the boron atom together with some molecules of isopropanol.



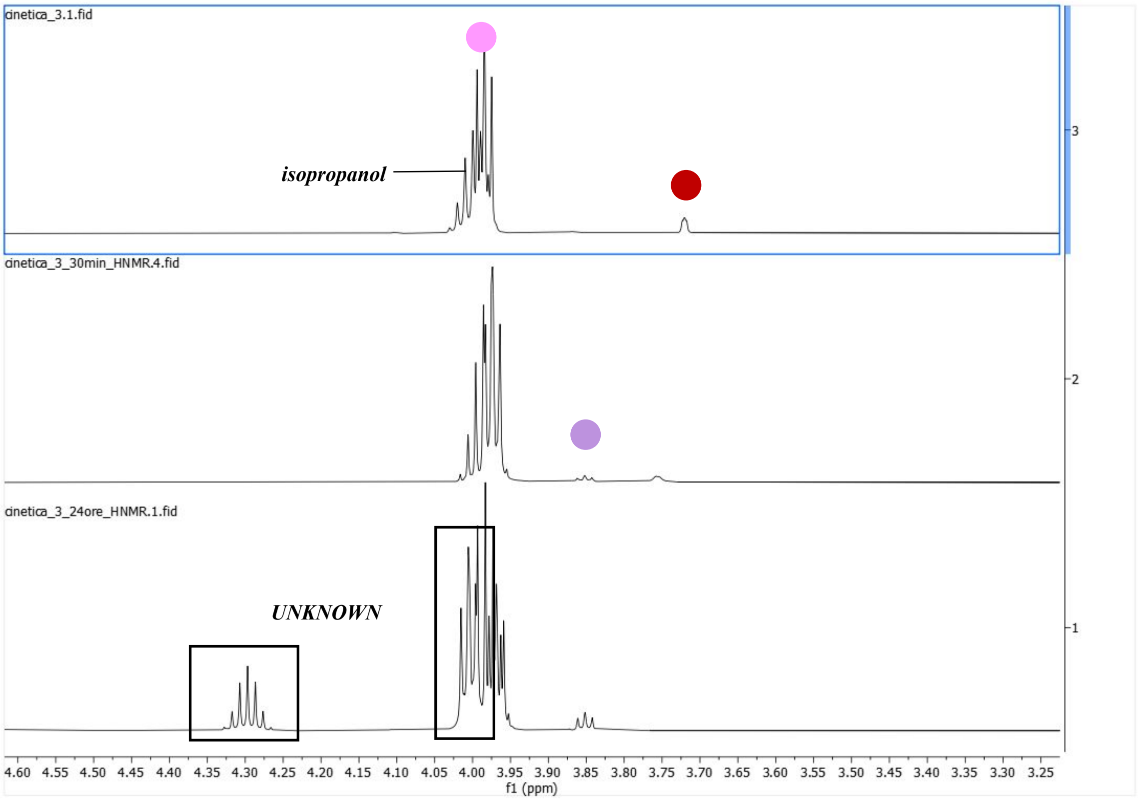
1ca



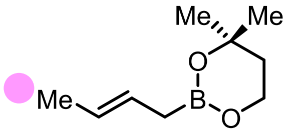
12



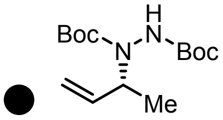
N



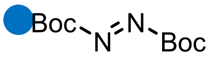
The same trend is visible in the most shielded area of the spectra. After 24h, each signal of **12** is duplicated as well as those belonging to the isopropanol.



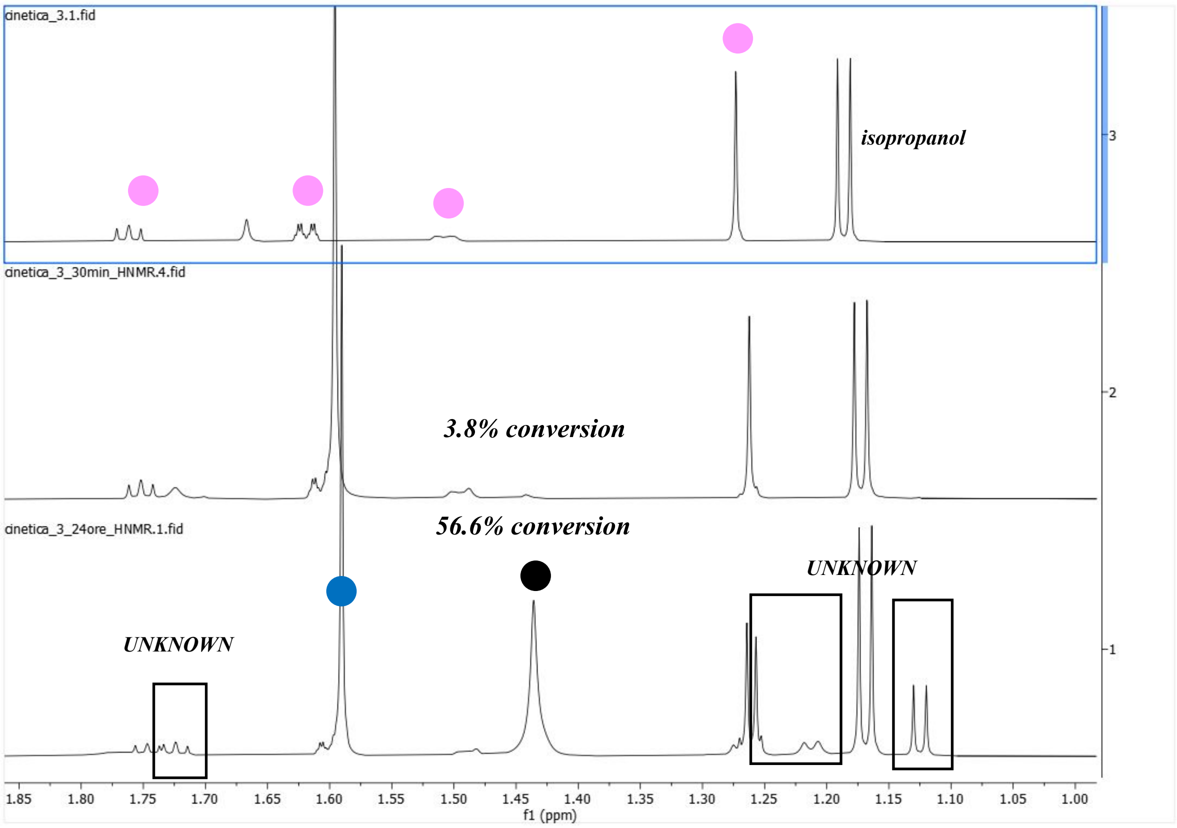
1ca

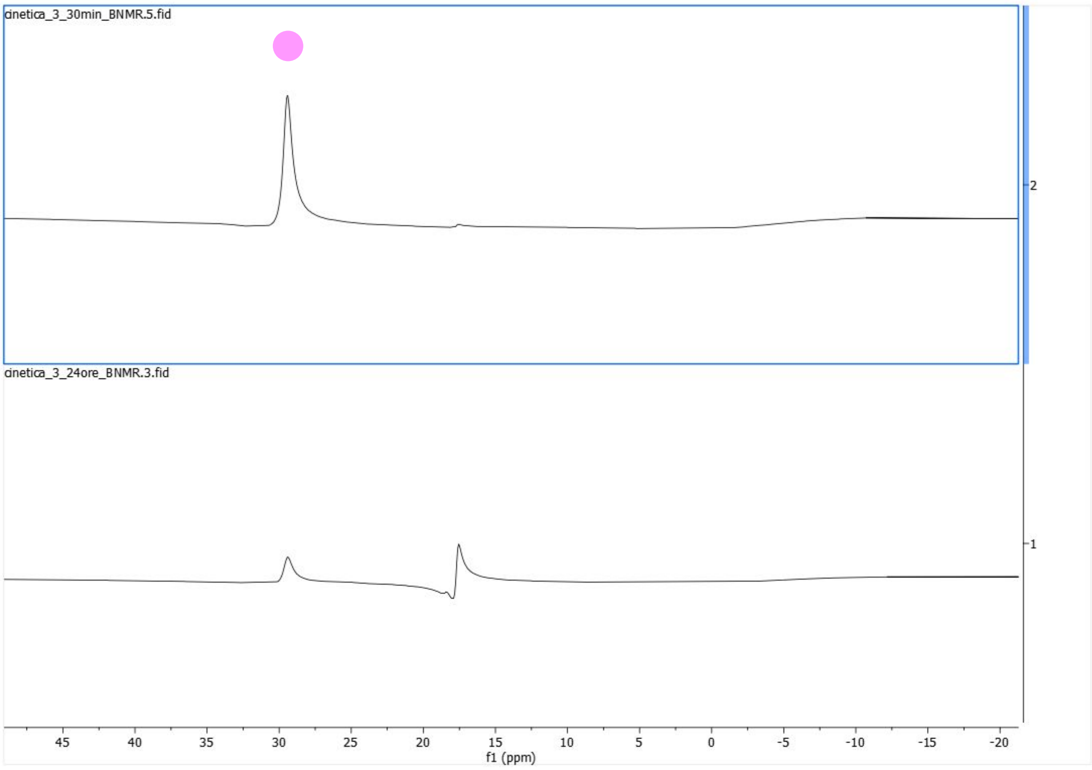


3a



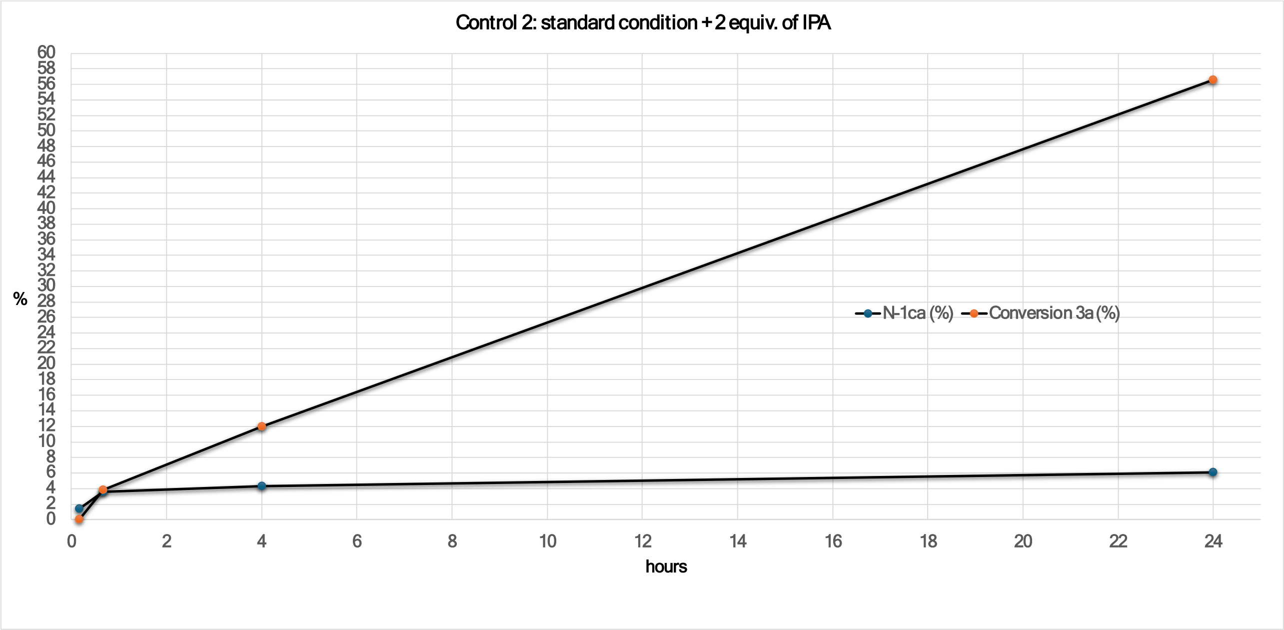
2a





In conclusion, the main effect of the isopropanol seems to be the releasing of **N**, beside favouring the formation of a species which involves **12** with the boron atom. This is also beneficial toward the formation of **N-1ca** which accumulates over time. The e.r of the isolated product is 96:4. The percentage of **N-1ca** refers to the initial amount of **N**.

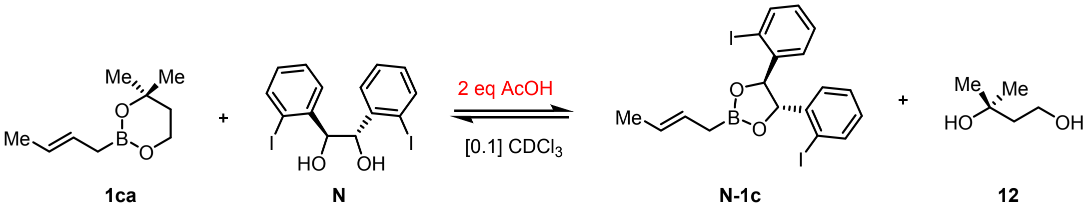
Time (h)	N-1ca	3a
0.17	14	/
0.67	36	3.8
3	43	8
24	61	56.6



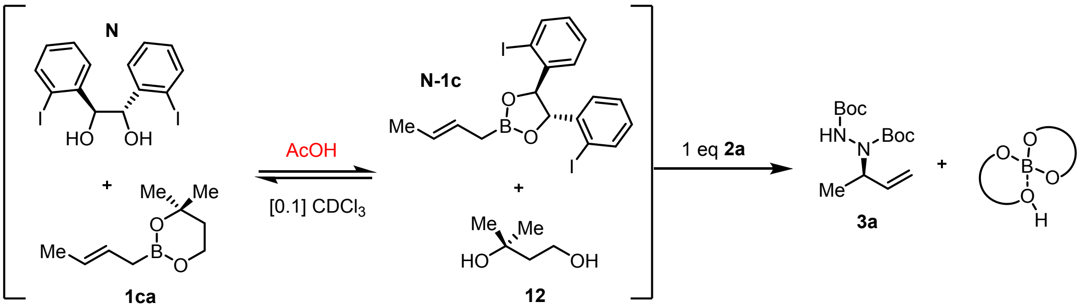
NMRs EXPERIMENT n4

This experiment aims to understand the role of the acetic acid.

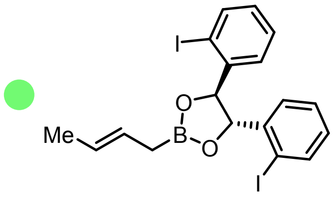
Conditions: In a screw cap vial provided of a magnetic stir bar were added 25.5 mg of **1ca** (0.15 mmol), 0.65 mL of $CDCl_3$, 7 mg of **N** (0.015 mmol) and 17 µL of acetic acid (0.3 mmol). The reaction was stirred for 10 minutes, then a ^1H NMR of the mixture was recorded.



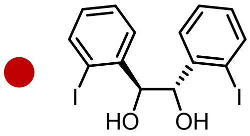
Then 34.5 mg (0.15 mmol) of **2a** were added to the reaction mixture and the stirring was continued at 25°C.



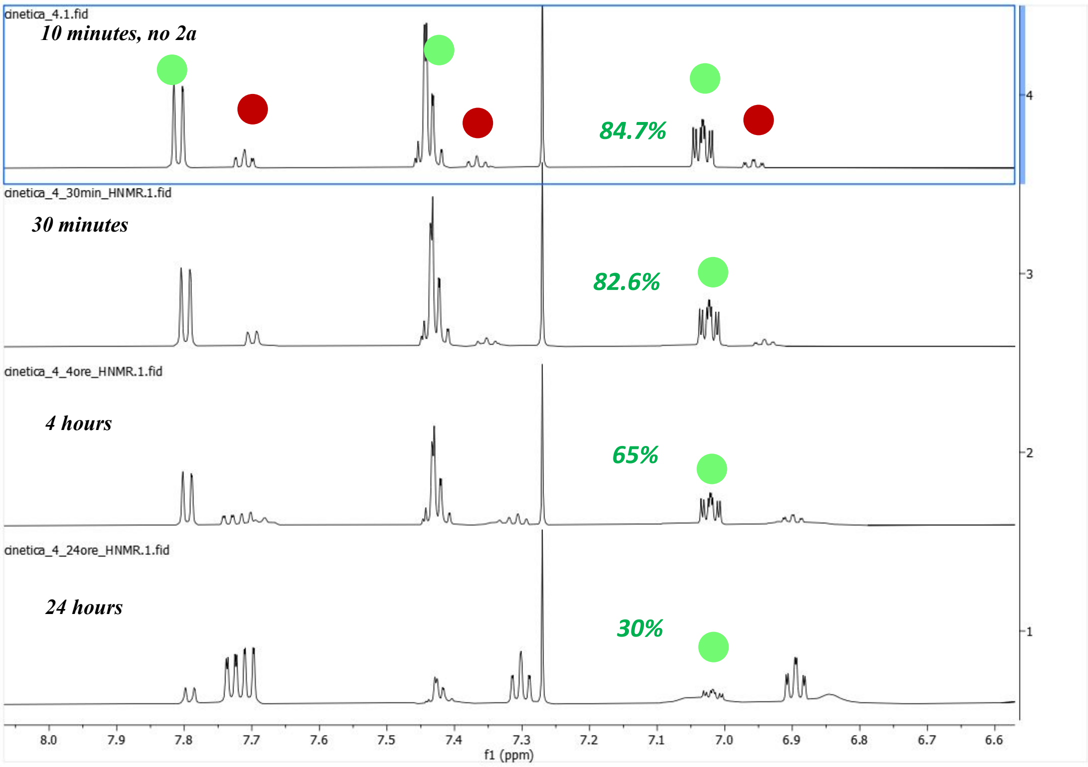
Unlike the previous cases, **N-1ca** is already the 85% of the starting **N** within 10 minutes. Nevertheless, this is the first case where its concentration constantly decreases during the reaction coordinate. After 4 hours the aromatic region is already contaminated by a co-product and even the signals of the catalyst slightly shift, like the case of **NMRs experiments n2**, which may indicate that no free catalyst is anymore available in the solution. This strongly affect the formation of **N-1ca** that is only 30% after 24 hours.


Me
B
O
O
I
I

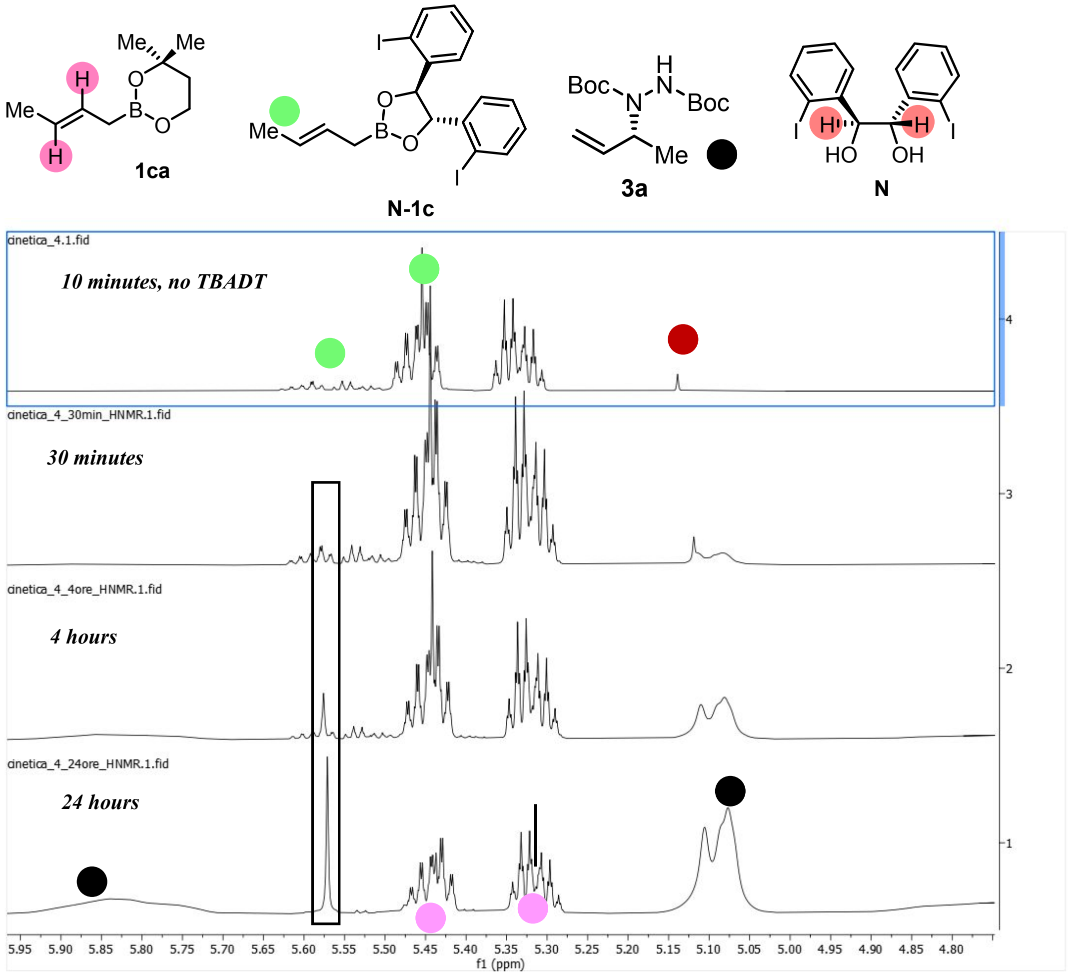
N-1c

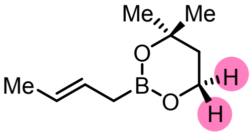

I
I
HO
OH

N

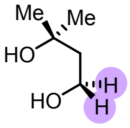

cinetica_4.1.fid
10 minutes, no 2a
84.7%
cinetica_4_30min_HNMR.1.fid
30 minutes
82.6%
cinetica_4_4ore_HNMR.1.fid
4 hours
65%
cinetica_4_24ore_HNMR.1.fid
24 hours
30%
4
3
2
1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
f1 (ppm)

Indeed, these spectra share the same co-products of those detected in the **NMRs experiments n2**: there is the same singlet at 5.55 ppm and between 4.15 ppm and 3-37 ppm a kind of similar multiple signals arises over 24 hours.

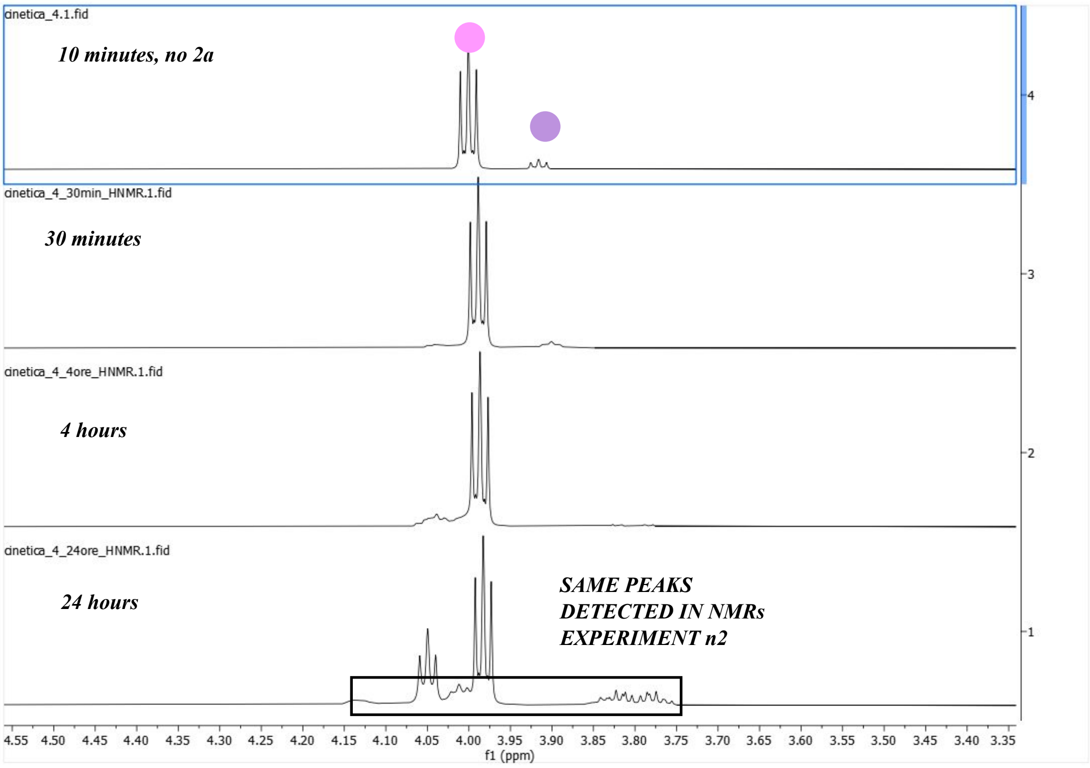




1ca



12



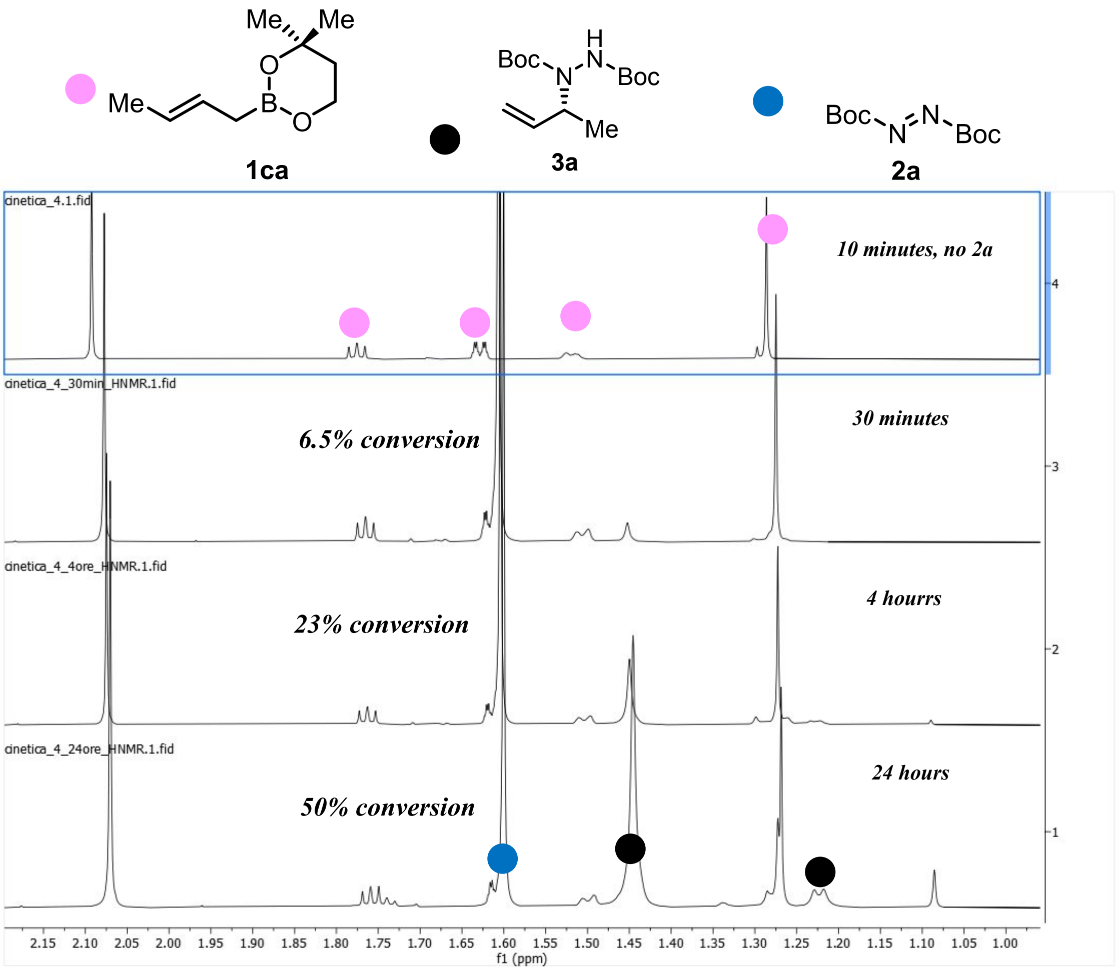
10 minutes, no 2a

30 minutes

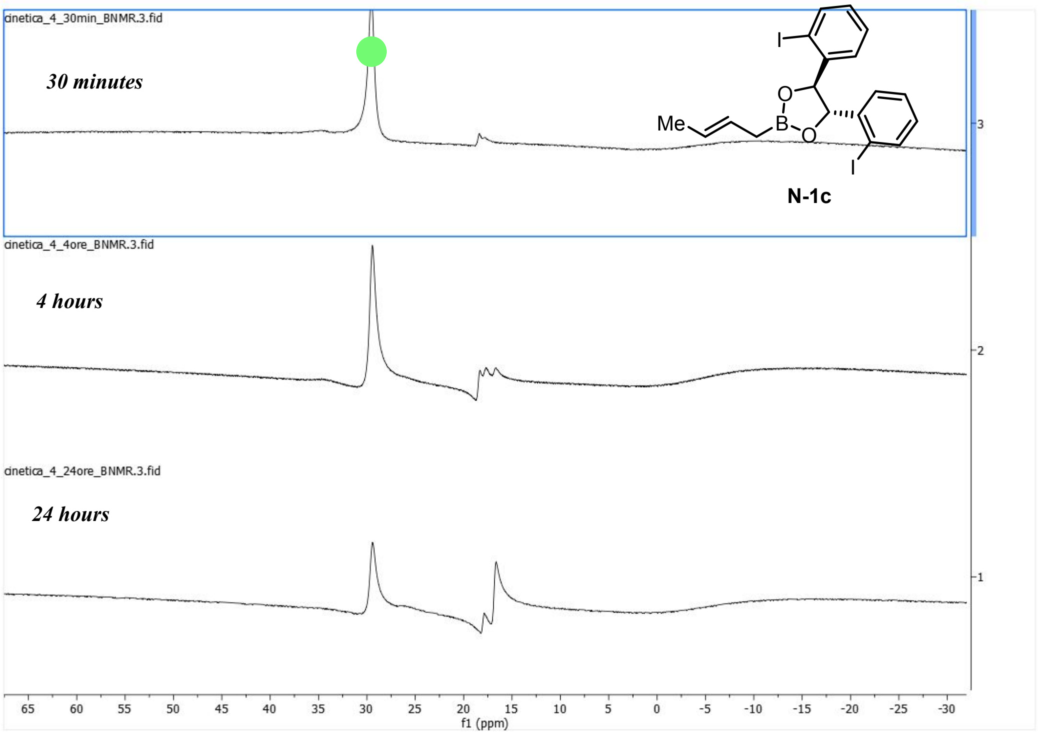
4 hours

24 hours

SAME PEAKS DETECTED IN NMRs EXPERIMENT n2

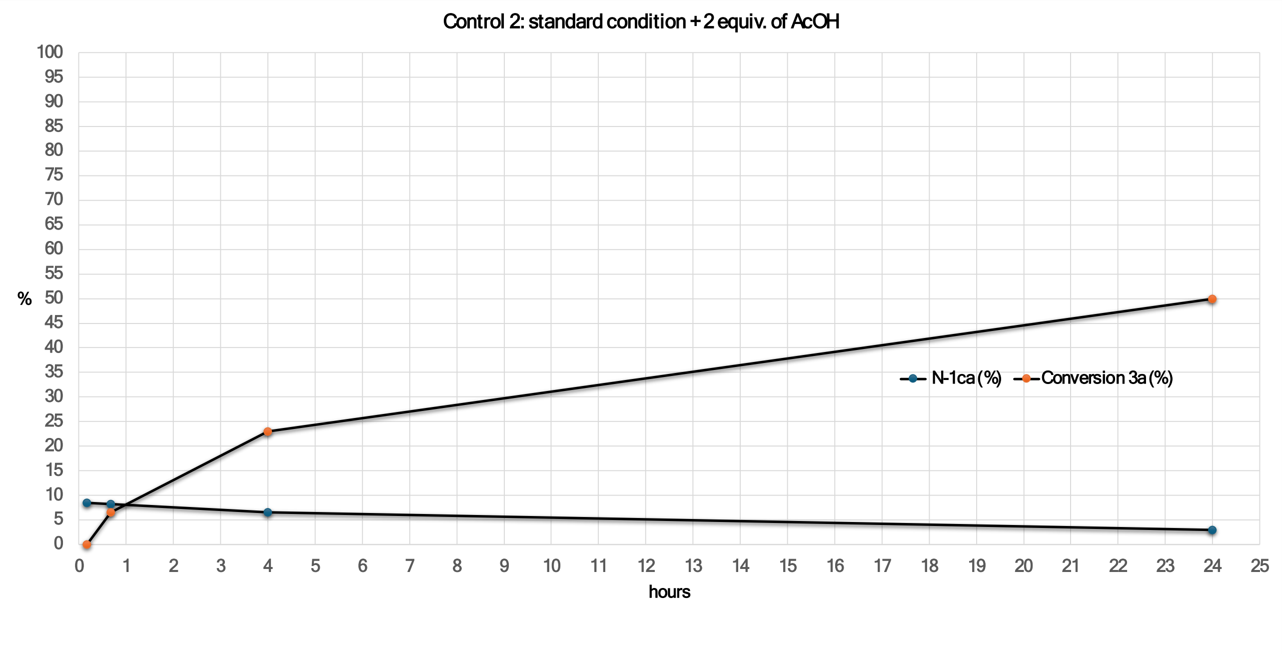


In contrast with **NMRs experiments n2**, the ^{11}B NMR after 24 hours shows a kind of convergence of different co-products into a predominant one. This might be due to the difference in conversion between the two experiments.



In conclusion, this experiment clarified the role of the acetic acid in favouring the formation **N-1ca** and strongly evidenced that the isopropanol is strictly necessary to release the catalyst from the co-products. The conversion is comparable to that of **NMRs experiment n3** and the e.r. of the isolated product is 96:4, thus the background reaction does not affect the conversion. The percentage of **N-1ca** refers to the starting amount of N

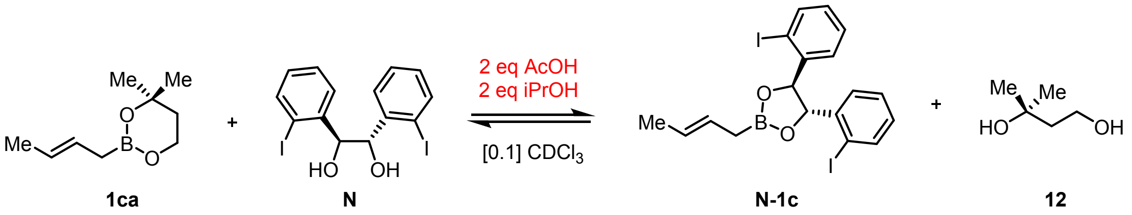
Time (h)	N-1ca	3a
0.17	84.7	/
0.67	82.6	6.5
4	65	23
24	30	50



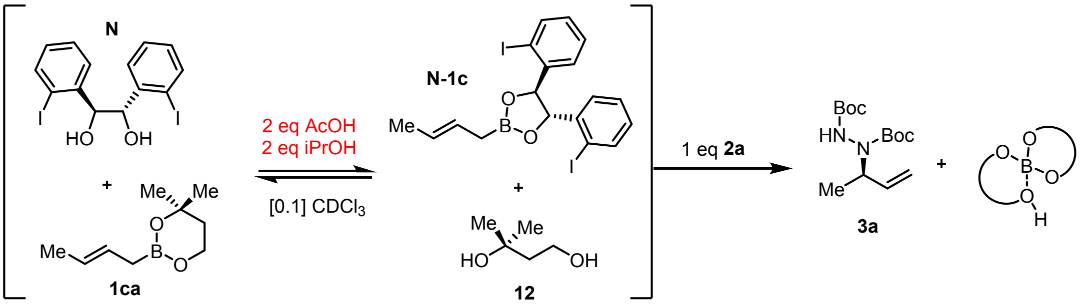
NMRs EXPERIMENT n5

This experiment was design to study the effect of the combination of isopropanol and acetic acid.

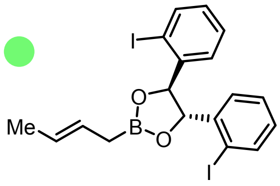
Conditions: In a screw cap vial provided of a magnetic stir bar 25.5 mg of **1ca** (0.15 mmol), 7 mg of the catalyst (0.015 mmol), 23 µL of iPrOH (0.3 mmol) and 17 µL of acetic acid (0.3 mmol) were added to 0.65 mL of $CDCl_3$. The reaction was stirred for 10 minutes, then a ^1H NMR of the mixture was recorded.



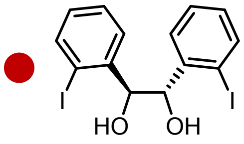
Then 34.5 mg (0.15 mmol) of **2a** were added to the reaction mixture and the stirring was continued at 25°C.



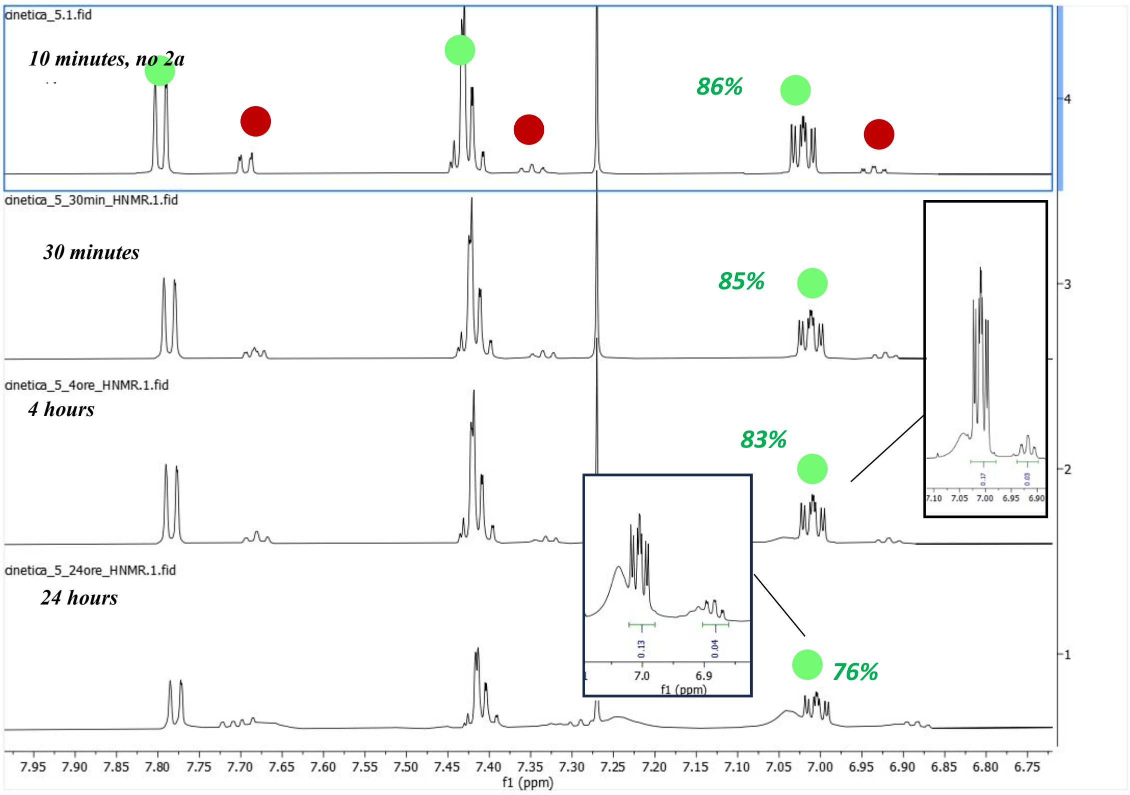
Within 10 minutes **N-1ca** is already 86% of the starting amount of the catalyst **N**, as in the case of **NMRs experiment n4** (2 eq. of acetic acid); but unlike that case its concentration is significantly lowered only after 24 hours, when 66% of **1ca** has been consumed. Interestingly, even in this case it seems that the free catalyst is no longer present in the solution after 24 hours; nevertheless, the reaction would proceed thanks to **N-1ca** which is still abundant.



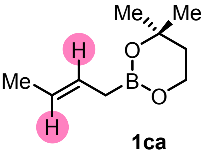
N-1c

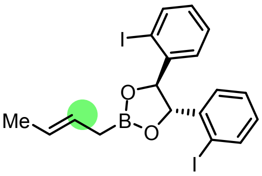


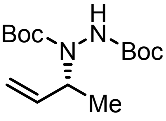
N

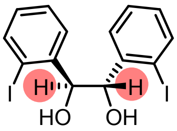

cinetica_5.1.fid
10 minutes, no 2a
86%
cinetica_5_30min_HNMR.1.fid
30 minutes
85%
cinetica_5_4ore_HNMR.1.fid
4 hours
83%
cinetica_5_24ore_HNMR.1.fid
24 hours
76%
0.17
0.03
7.10 7.05 7.00 6.95 6.90
0.13
0.04
7.0
6.9
f1 (ppm)
4
3
2
1
7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95 6.90 6.85 6.80 6.75
f1 (ppm)

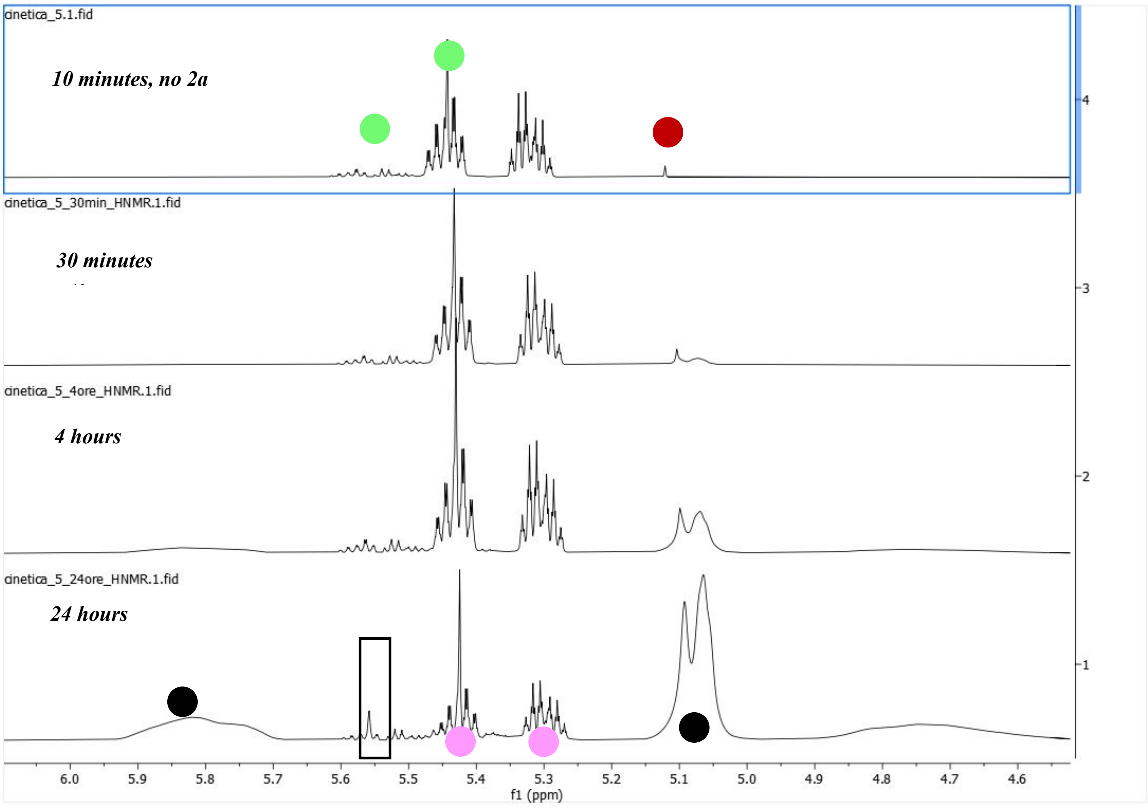
The following spectra shows the same co-products observed when 2 eq. of iPrOH and 2 eq. of AcOH have been used independently.

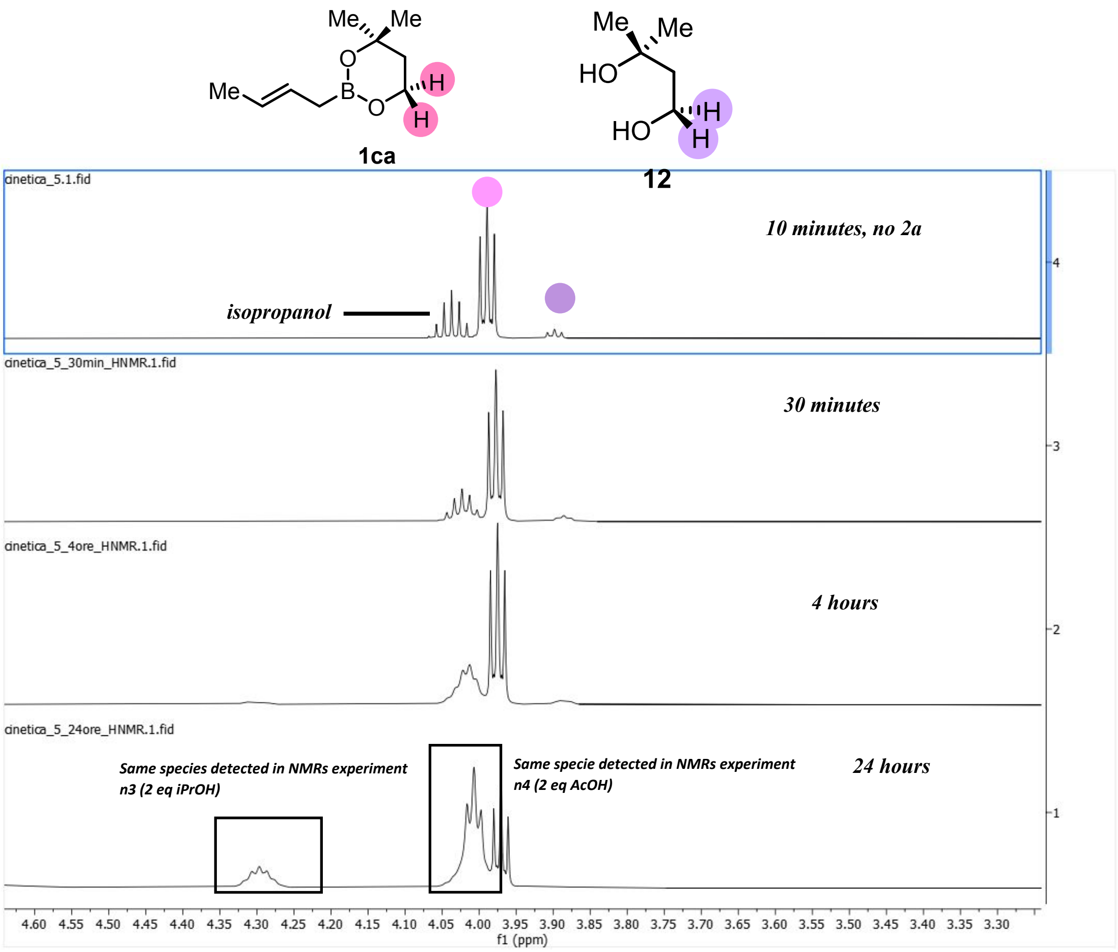

1ca


N-1c


3a ●


N





10 minutes, no 2a

isopropanol

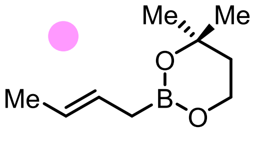
30 minutes

4 hours

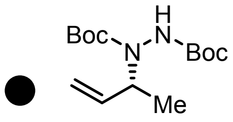
24 hours

Same species detected in NMRs experiment n3 (2 eq iPrOH)

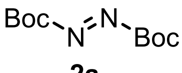
Same specie detected in NMRs experiment n4 (2 eq AcOH)


Me
Me
Me
O
B
O

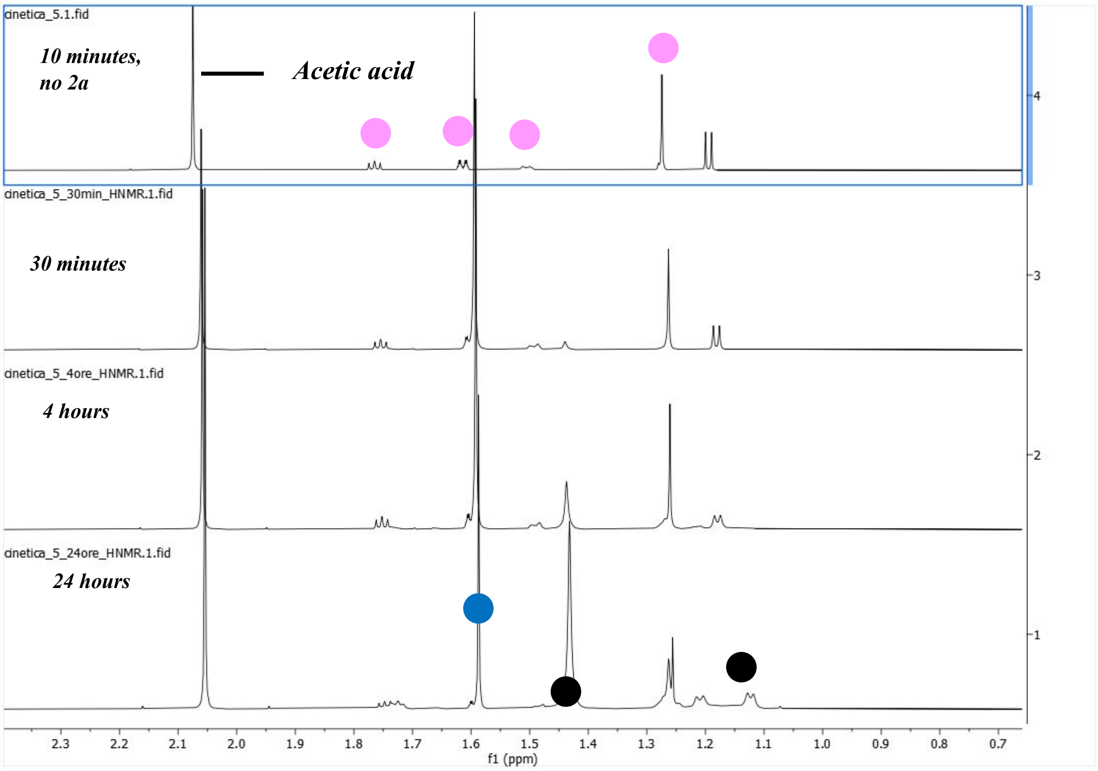
1ca

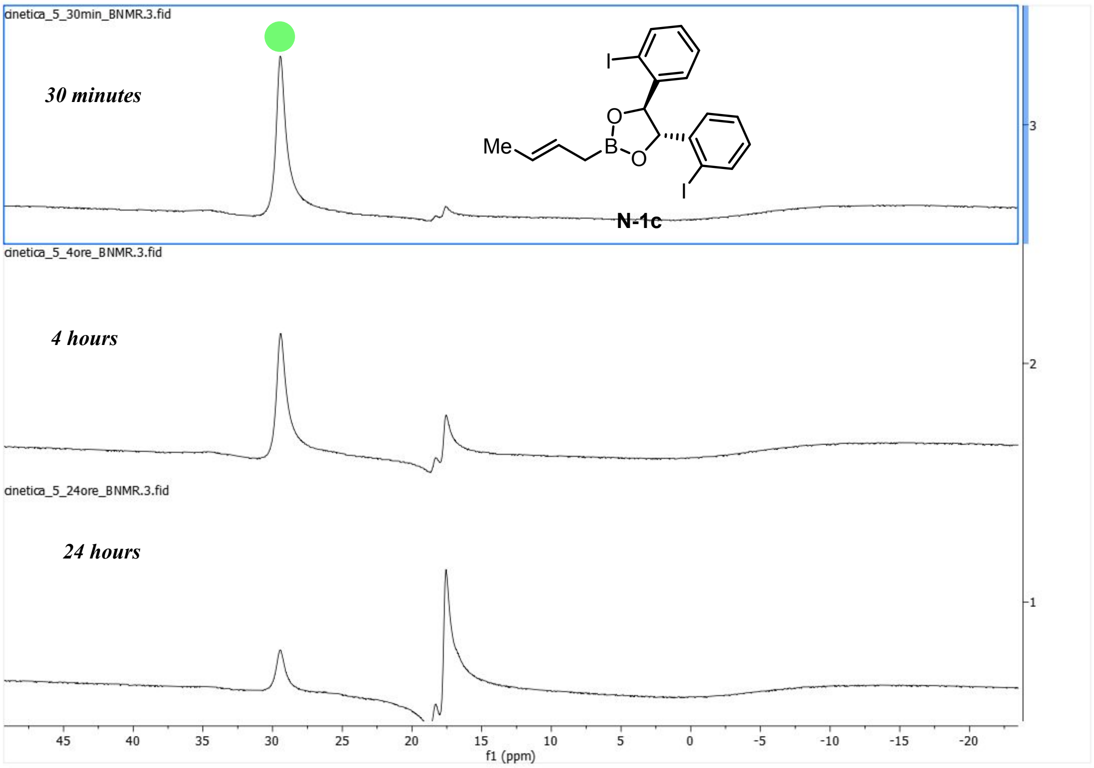

H
Boc
N
N
Boc
Me

3a


Boc
N
N
Boc

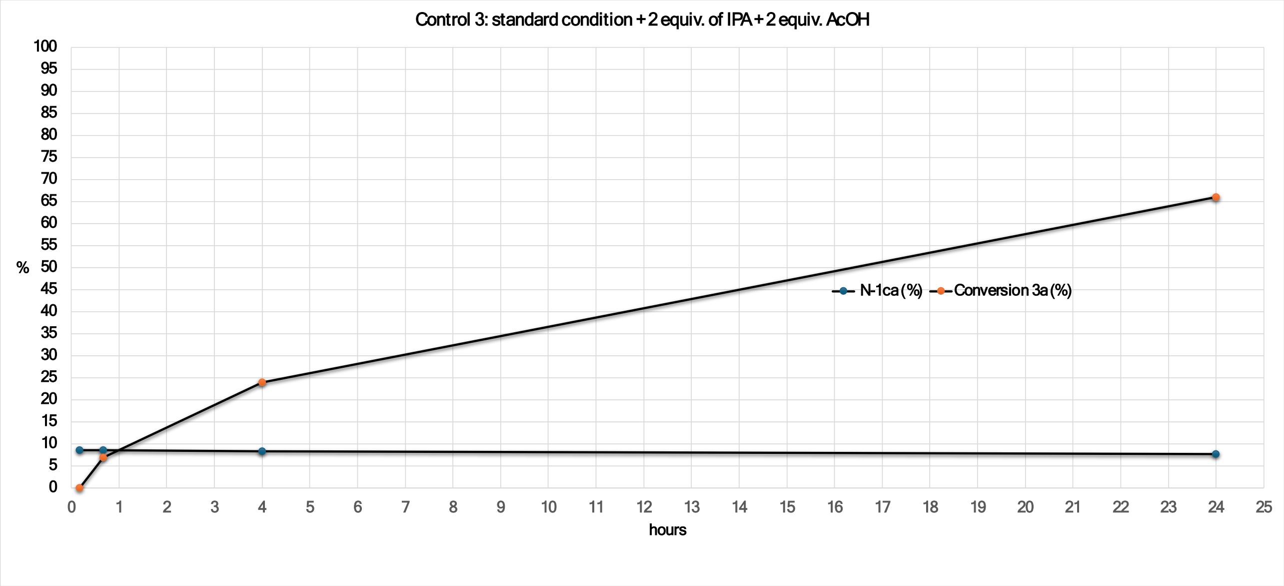
2a


cinetica_5.1.fid
10 minutes,
no 2a
Acetic acid
cinetica_5_30min_HNMR.1.fid
30 minutes
cinetica_5_4ore_HNMR.1.fid
4 hours
cinetica_5_24ore_HNMR.1.fid
24 hours
4
3
2
1
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
f1 (ppm)


cinetica_5_30min_BNMR.3.fid
30 minutes
I
O
Me
B
O
I
N-1c
cinetica_5_4ore_BNMR.3.fid
4 hours
cinetica_5_24ore_BNMR.3.fid
24 hours
3
2
1
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
f1 (ppm)

In conclusion, using a mixture of acetic acid and the isopropanol has the beneficial effects exhibited by those experiments in which they were used separately. Indeed, the concentration of **N-1ca** maintains high thanks to acetic acid while isopropanol accelerates the turnover of the catalyst. At the end, the conversion is higher than **NMRs experiments n3** and **n4**. The product was collected with an e.r. of 96:4. The percentage of **N-1ca** refers to the initial amount of **N**.

Time (h)	N-1ca	3a (%)
0.17	86	/
0.67	85	6.9
4	83	24
24	76	66

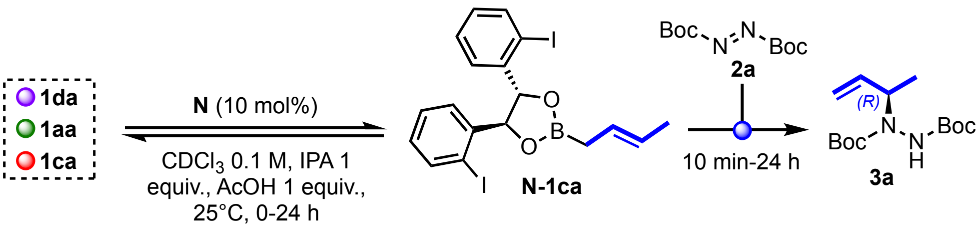


Comparative study for the reaction of boronates 1aa, 1da and 1ca

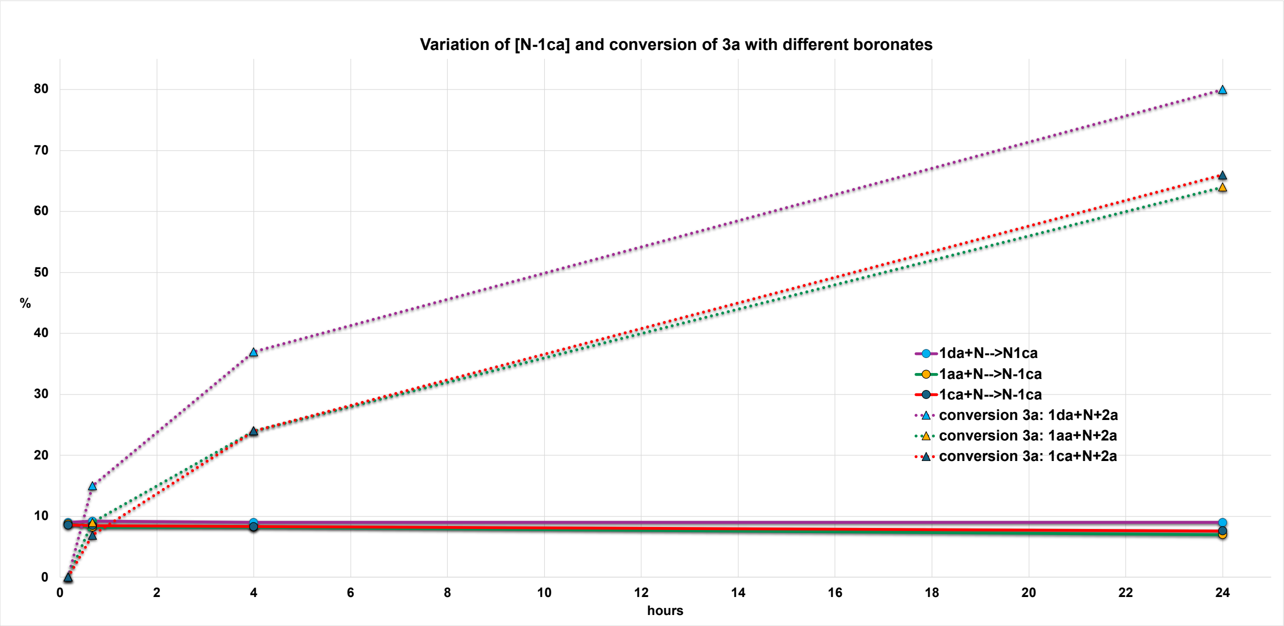
These experiments were design to compare the reactivity of boronates **1aa**, **1da** and **1ca** in the ligand exchange process with **N** to generate **N-1ca** and their reactivity with **2a**. Indeed, for each boronate the reaction with azodicarboxylate **2a** was studied without catalyst **N** and the results obtained have been compared with the catalytic reaction to clarify the effect of a background reaction.

First experiment

Conditions: In a screw cap vial provided of a magnetic stir bar boronate (0.15 mmol), 7 mg of the catalyst (0.015 mmol), 23 µL of iPrOH (0.3 mmol) and 17 µL of acetic acid (0.3 mmol) were added to 0.65 mL of $CDCl_3$. The reaction was stirred for 10 minutes, then a ^{1}H NMR of the mixture was recorded. Then 34.5 mg (0.15 mmol) of **2a** were added to the reaction mixture and the stirring was continued at 25°C. The conversion of **3a** and the concentration of **N-1ca** was monitored during time.



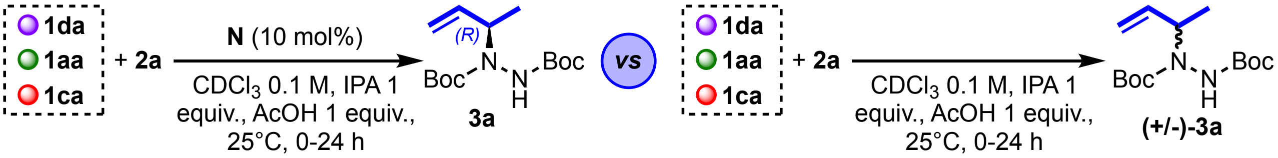
Time (h)	[N1ca] %			3a (%)		
	From 1da	From 1aa	From 1ca	From 1da	From 1aa	From 1ca
0,17	9	8,8	8,6	0	0	0
0,67	9,2	8,2	8,5	15	9	6,9
4	9	8,2	8,3	37	24	24
24	9	7	7,6	80	64	66



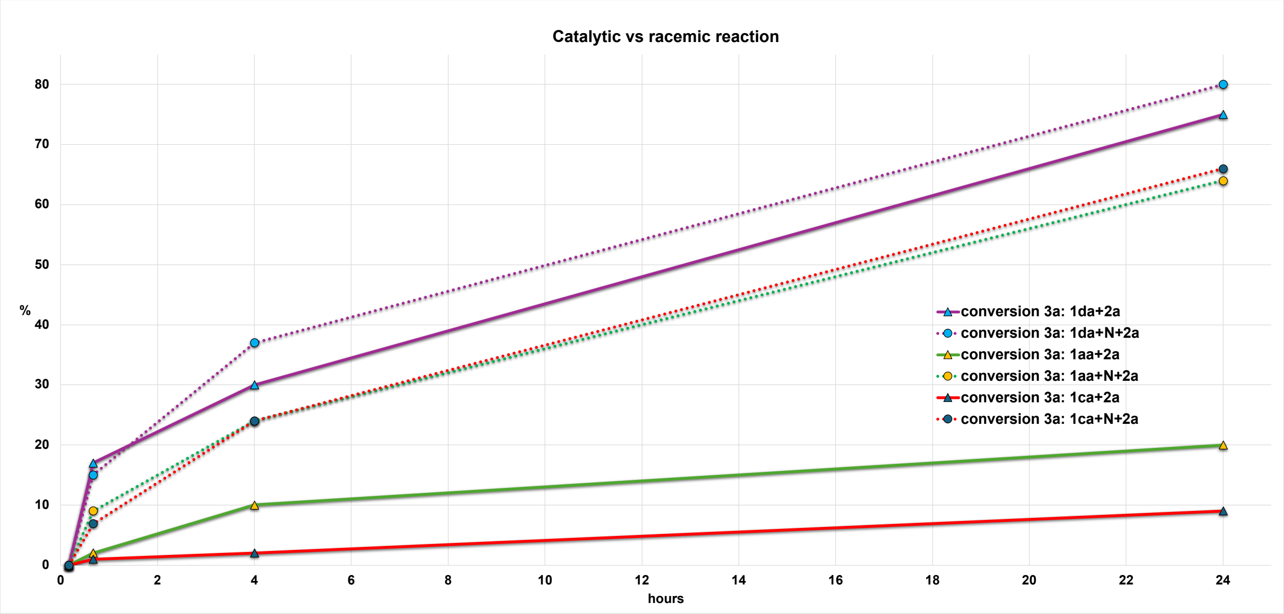
Within 10 minutes the concentration of **N-1ca** for the reaction of boronate **1aa** and **1da** is almost identical to the one of boronate **1ca**. The concentration of the catalytic species maintains constant during the reaction with **2a**. Boronate **1da** has the fastest kinetic profile while **1aa** and **1ca** show a similar trend even if at the beginning of the reaction with azodicarboxylate **1aa** produces **3a** in a larger amount than **1ca**. The e.r. for each reaction has been determined after 24 hours: 77:23 with **1da**, 92.5:7.5 with **1aa** and 96:4 with **1ca**.

Second experiment

__Conditions__: In a screw cap vial provided of a magnetic stir bar boronate (0.15 mmol), 23 µL of iPrOH (0.3 mmol) and 17 µL of acetic acid (0.3 mmol) were added to 0.65 mL of $CDCl_3$ then 34.5 mg (0.15 mmol) of **2a** were added to the reaction mixture and the stirring was continued at 25°C. The conversion of **3a** was monitored by ^{1}H NMR at the indicated time. The results obtained have been compared with those of catalytic reactions.



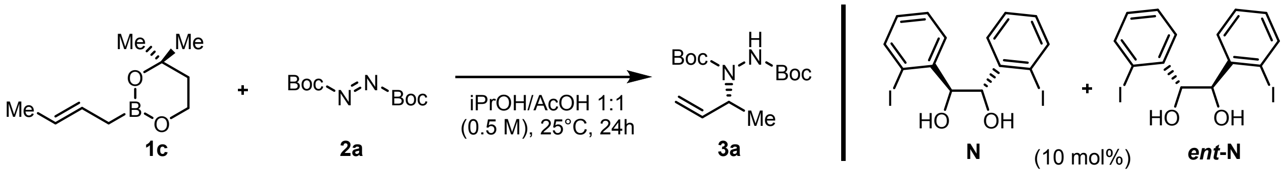
Time (h)	3a (%)-catalytic reaction			3a (%)-racemic reaction		
	From 1da	From 1aa	From 1ca	From 1da	From 1aa	From 1ca
0,5	15	9	6,9	17	2	1
4	37	24	24	30	10	2
24	80	64	66	75	20	9



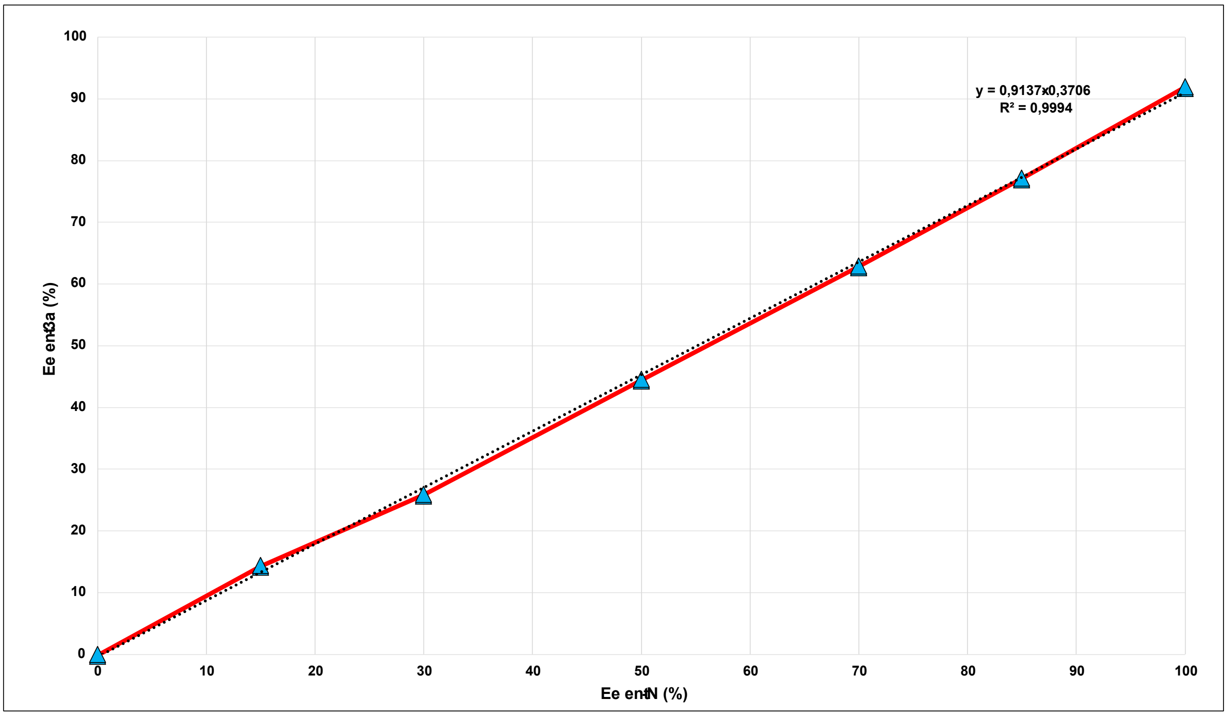
The results obtained clearly indicates how the background reaction contribute to convert boronates into allylic hydrazide for **1aa** and **1da** in a greater amount than what is observed for **1ca**. Despite the catalytic reaction is faster than the racemic one, if no background reaction took place the same value of e.r. should be obtained for each of catalytic reactions. This is because the amount of **N-1ca** is always the same and it has been clearly established that when **N-1ca** reacts with **2a** in a stoichiometric reaction the e.r. is 96:4.

NONLINEAR EFFECT

Procedure: solutions of the catalyst with different e.e. were prepared by mixing solutions of isopropanol containing **N** or **ent-N** in appropriate proportions. To this mixtures 0.1 mL of AcOH and 0.1 mmol of **1ca** were added and the solution was stirred for 10 minutes. Afterward, **2a** was introduced to the vessel and the reaction proceeded under stirring for 24 hours. The crude was diluted with hexane and flash chromatography was performed to isolate the product. GC-FID analysis provided the *e.e.* of the pure **3a**.



e.e. **N** (%)	*e.e.* **3a** (%)	*Yield (%)*
0	0	0
15	14.4	92
30	26	92
50	44.6	92
70	63	92
85	77.2	92
100	92	92



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