Electronic Supplementary Material (ESI) for ChemComm.

A Ru-catalyzed aminomethylation of arenes with O-tosyl-hydroxamates

Authors: Guobao Li, Tilo Lübken, Bernd Plietker*

Affiliations:

Professur für Organische Chemie I, Fakultät Chemie und Lebensmittelchemie, Technische Universität Dresden, Bergstraße 66, DE-01069 Dresden, Germany.

*Corresponding author. Email: bernd.plietker@tu-dresden.de.

Content

1. General Remarks

The solvent compositions used are given as volume ratios. All solvents except H_2O, *n*-pentane, *n*-heptane, and EtOAc were distilled before use. The dried solvents DCM, diethyl ether, toluene, acetonitrile, and *n*-pentane were obtained from a solvent drying plant (SPS). THF used was distilled over sodium using benzophenone as an indicator. The solvents DMF, chloroform, MeOH, EtOH, triethylamine, 1,2-DCE, 1,4-dioxane, and DMSO, were distilled over suitable desiccants and stored under an inert atmosphere - unless explicitly marked otherwise. The reagents used were obtained from Sigma Aldrich, TCI, Alfa Aesar, Acros Organics, Fluka, Porphychem, abcr, BLD, and ChemPur and, unless otherwise stated, used without further purification. All water and air-sensitive reactions were performed under an inert N_2 or Ar atmosphere using standard Schlenk techniques. Glassware was dried by extensive heating under a high vacuum.

NMR spectra were recorded on a Bruker Avance II 300 spectrometer at 300 MHz (^{1}H NMR), 75 MHz (^{13}C NMR), 282 MHz (^{19}F NMR), a Bruker Ascend 400 spectrometer at 400 MHz (^{1}H NMR), 376 MHz (^{19}F NMR), 101 MHz (^{13}C NMR), a Bruker DRX 500 spectrometer at 500 MHz (^{1}H NMR), 126 MHz (^{13}C NMR), 202 MHz (^{31}P NMR), a Bruker Avance III 600 spectrometer at 600 MHz (^{1}H), 150 MHz (^{13}C NMR) or a Bruker 700 spectrometer at 700 MHz (^{1}H NMR), 176 MHz (^{13}C NMR). Chemical shifts are reported in ppm relative to tetramethylsilane. Residual solvent signals were used as reference. Coupling constants *J* are given in Hz. The following abbreviations are used in the analysis of NMR spectra: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *hept* = heptet, *sept* = septet, These abbreviations are combined whenever more than one coupling is observed. IR spectra were measured on a Bruker Vector 22 FT-IR spectrometer in ATR mode. The measured values are given in reciprocal wavelength (cm^{-1}). The intensity of the observed peaks is given in parenthesis: *s* = strong, *m* = medium, *w* = weak. Mass spectra were measured using electrospray ionization on a Bruker micrOTOF-Q.

Thin-layer chromatography was carried out on TLC aluminum foil (silica gel 60, F254) from Macherey-Nagel. UV light was used to detect the individual spots, and the TLC foils were treated with sulfuric $KMnO_4$ solution, or 10% molybdophosphoric acid solution in EtOH. Column chromatographic purifications were carried out on silica gel (0.040–0.063 mm, 230 – 400 mesh) from Macherey-Nagel, silica gel 60 (230-400 mesh) from Fluka or Alox (N). Some compounds were purified using semi-preparative High-performance liquid chromatography

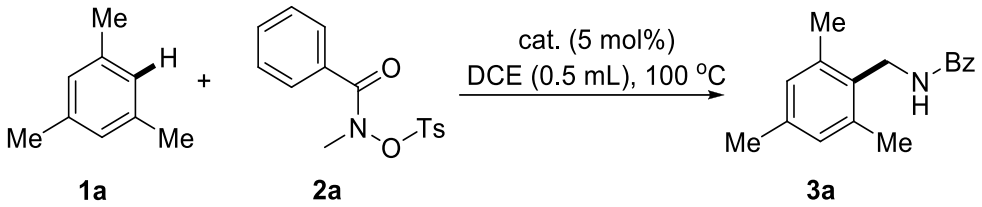
(HPLC). The K-501 pump and the RI detector K-2400 from Knauer were used in connection with a column of the type VP 250/21 Nucleodur 100-5 C18 from Macherey-Nagel. Mixtures of ethyl acetate and petroleum ether or isohexane were used as eluents, and a flow rate of 10 mL/min was set.

High-resolution mass analysis was performed by Claudia Guttroff and analytic department of University of Stuttgart on the devices MAT 95 from Finnigan (EI) and micro-TOF-Q from Bruker (ESI). High-resolution mass analysis was also performed by Dr. Ingmar Bauer and Anne Jäger using an LC-MS coupling from Hewlett Packard (HPLC: 1100, mass detector: Esquire-LC, ESI).

Enantiomeric excess (ee) was measured on an Agilent HPLC 1100 Series system equipped with the Daicel Chiralpak column.

2. Optimization

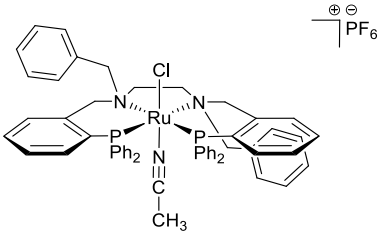
Table S1. Screening of catalysts



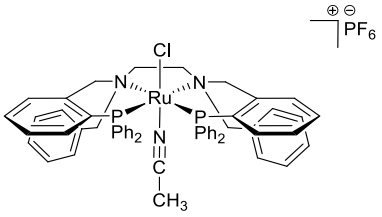
1a **2a** **3a**

entry	Catalyst	result[a]
1	*trans*-Ru(PNNP)PF_6	30%
2	$Ru(PPh_3)_2(CO)HCl$	13%
3	*cis*-Ru(PNNP)PF_6	30%
5	Ru(NNNN)PF_6	35%
6	$RuCl_3$	trace
7	[Ru(*p*-cymene)Cl_2]$_2$	11%
8	$Ru(DMSO)_4Cl_2$	24%
9	$Ru(PMe)_3Cl_2$	trace
10	$Ru(PPh_3)_3Cl_2$	65%
11	$Ru(PPh_3)_3H_2$	trace
12	Ru(P(*4*-ClPh)$_3$)$_3$$Cl_2$	18%
13[b]	$Ru(PPh_3)_3Cl_2$	72%
14[b]	Ru(NNNN)PF_6	47%
15[b]	*trans*-Ru(PNNP)PF_6	33%
16	$Rh(PPh_3)_3Cl$	0%
17	$Pd(PPh_3)_2Cl_2$	0%

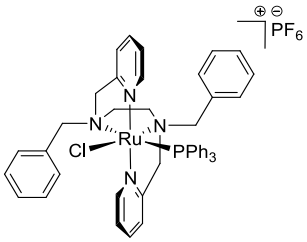
[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.1 mmol), catalyst (5 mol%), in DCE (0.5 mL) at 100 °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard. [b] using 1.5 equiv **2a**.



***trans*-Ru(PNNP)**

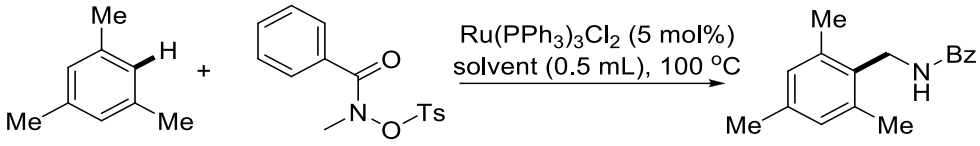


***cis*-Ru(PNNP)**



Ru(NNNN)

Table S2. Screening of solvents



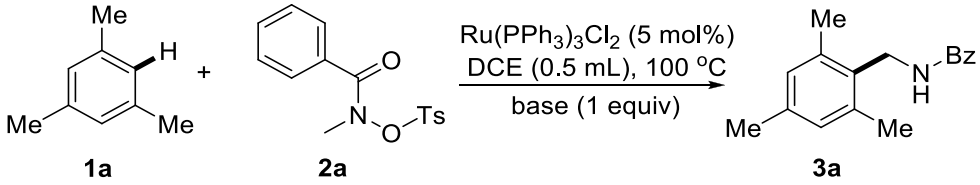
1a **2a** **3a**

entry	solvent	result[a]
1	DCE	65%
2	THF	trace
3	DMF	n.r.
4	1,4-dioxane	trace
5	ArF_6	11%
6	DCM	38%
7	chloroform	32%
8	trifluorotoluene	16%.
9	fluorobenzene	18%
10	CCl_4	n.d.
11	MeCN	trace
12	cyclohexane	trace
13	DMSO	n.r.
14	*iso*-propanol	trace
15	1,2-dichlorobenzene	35%
16	EtOAc	n.r.
17	acetone	n.r.
18[b]	DCM	50%
19[b]	THF	trace
20[b]	ArF_6	12%

21[b]	cyclohexane	trace
22[c]	DCE	65%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.1 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%), in solvent (0.5 mL) at 100 °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard. [b] using 1.5 equiv **2a**. [c] using dry DCE under Ar in a Schlenk tube.

Table S3. Screening of base

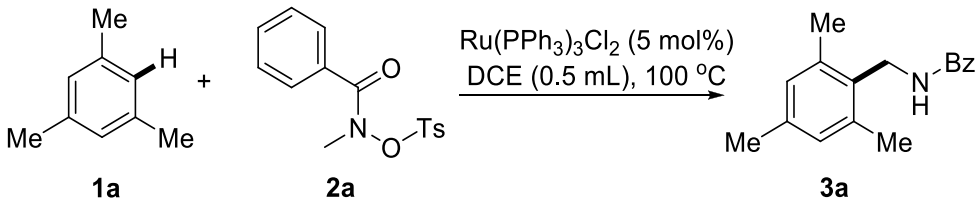


1a **2a** **3a**

entry	base	result[a]
1	K_2CO_3	trace
2	Cs_2CO_3	n.r.
3	Li_2CO_3	n.r.
4	$KHCO_3$	5%
5	KOAc	58%
6	K_3PO_4	n.r.
7	Et_3N	n.r.
8	none	65%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.1 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%), base (1 equiv) in DCE (0.5 mL) at 100 °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard.

Table S4. Screening of amount of **2a**



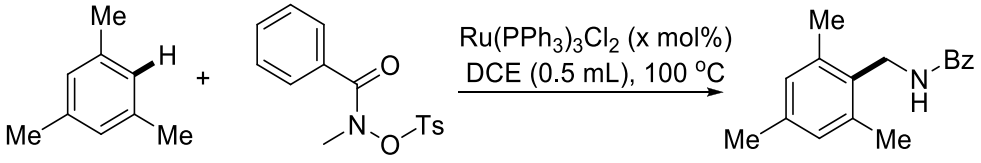
1a **2a** **3a**

entry	amount of **2a**	result[a]
1	1.0 equiv **2a**	65%
2	1.5 equiv **2a**	72%

3	2.0 equiv **2a**	73%
4	2.5 equiv **2a**	55%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (x mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%) in DCE (0.5 mL) at 100 °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard.

Table S5. Screening of amount of catalyst

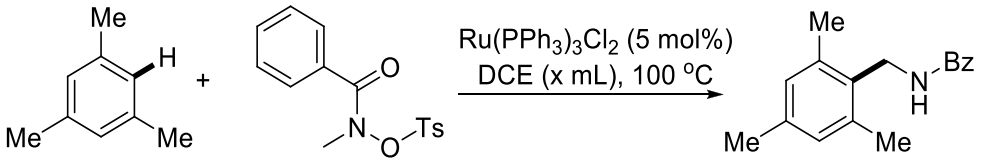


1a **2a** **3a**

entry	amount of cat. (mol%)	result[a]
1	0.50	15%
2	1.00	28%
3	2.50	41%
4	5.00	72%
5	7.50	66%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.15 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%) in DCE (0.5 mL) at 100 °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard.

Table S6. Screening amount of solvent

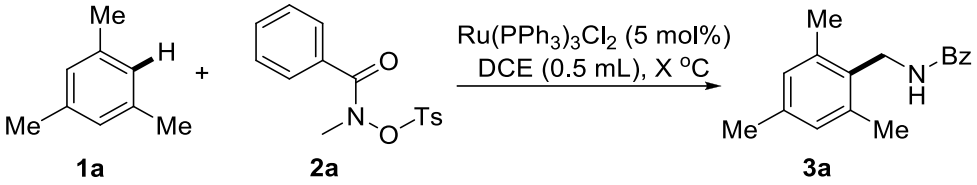


1a **2a** **3a**

entry	amount of DCE	result[a]
1	0.1 mL	38%
2	0.5 mL	72%
3	1.0 mL	55%
4	2.0 mL	28%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.15 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%) in DCE (x mL) at 100 °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard.

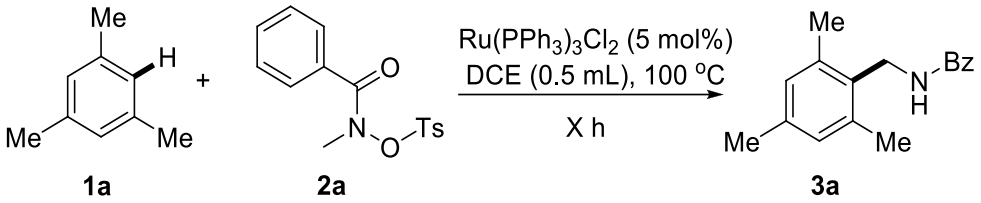
Table S7. Screening temperature



entry	temp. (°C)	result[a]
1	40	trace
2	60	3%
3	80	13%
4	90	62%
5	100	72%
6	110	58%
7	130	18%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.15 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%) in DCE (0.5 mL) at X °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard.

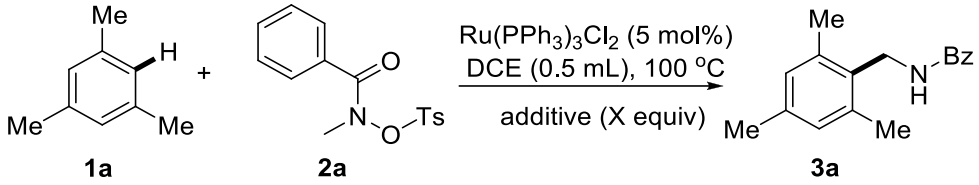
Table S8. Screening reaction time



entry	time	result[a]
1	1 h	64%
2	8 h	69%
3	18 h	72%
4	24 h	72%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.15 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%) in DCE (0.5 mL) at 100 °C for X h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard.

Table S9. Screening additive

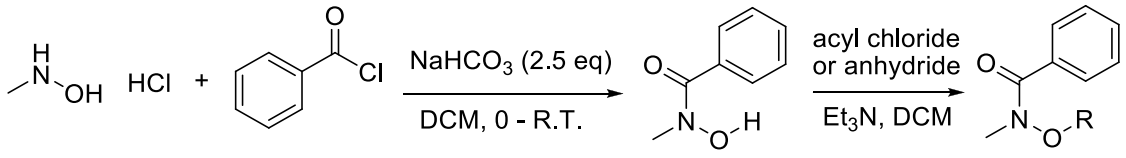


entry	amount of additive	result[a]
1.	PivOH (0.3 eq)	40%
2.	TsOH (0.3 eq)	45%
3.	MesCOOH (0.3 eq)	34%
4.	$AgNTf_2$ (0.2 eq)	trace
5.	AgOTf (0.2 eq)	12%
6.	$AgBF_4$ (0.2 eq)	trace
7.	$AgPF_6$ (0.2 eq)	trace
8.	4Å MS (100 mg)	n.r.
9.	TfOH (0.3 eq)	trace
10.	TFA (0.3 eq)	27%
11.	H_2O (1 eq)	41%
12.	AgOAc (0.5 eq)	n.r.
13.	$Cu(OAc)_2$ (0.5 eq)	18%
14.	BQ (0.5 eq)	trace
15.	$K_2S_2O_8$ (0.5 eq)	28%
16.	O_2 (1 atm)	65%
17.	PCy_3 (0.3 eq)	trace
18.	$P(4\text{-}MeOPh)_3$ (0.2 eq)	28%
19.	$P(4\text{-}FPh)_3$ (0.2 eq)	34%
20.	DPPE (0.2 eq)	10%
21.	Phen (0.2 eq)	20%

[a] Reaction condition: **1a** (0.1 mmol), **2a** (0.15 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%) and additive (X equiv) in DCE (0.5 mL) at 100 °C for 18 h under air in a sealed tube. Yield is determined by GC analysis using dodecane as internal standard.

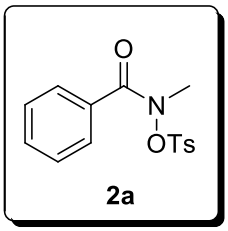
3. Preparation of substrates

3.1. General procedure (GP-1) for preparation of 2a, 4a-4c



Step 1: $NaHCO_3$ (4.2 g, 50 mmol, 2.5 equiv) was added to a solution of MeNHOH·HCl (1.8 g, 22 mmol, 1.1 equiv) in DCM (140 mL) at room temperature. Then the mixture was cooled to 0 °C and a solution of benzoyl chloride (2.8 g, 20 mmol, 1.0 equiv) in DCM (70 mL) was added. The resulting reaction mixture was stirred overnight at room temperature and filtered off the insoluble precipitate. The filtrate was washed with water 3 times, then the organic layers were dried (Na_2SO_4) and evaporated *in vacuo* to afford the crude compound as a light yellow oil, which was used without further purification.[1]

Step 2: Corresponding acyl chloride or anhydride (5.5 mmol, 1.1 equiv) and Et_3N (0.76 g, 7.5 mmol, 1.5 equiv) were added to a solution of *N*-hydroxy-*N*-methylbenzamide (0.75 g, 5 mmol, 1 equiv) in DCM (50 mL) at 0 °C. The resulting reaction mixture was stirred at room temperature overnight. The solvent was removed *in vacuo* and the crude mixture was purified by flash column chromatography on silica gel isohexane/EtOAc (v/v=7:1) to obtain the product.[2]



According to GP-1, *N*-hydroxy-*N*-methylbenzamide (5.0 mmol, 0.75 g), Et_3N (7.5 mmol, 1.05 mL), TsCl (5.5 mmol, 1.05 g) in DCM (50 mL) afforded 2a as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

***N*-methyl-*N*-(tosyloxy)benzamide**

Yield: 1.14 g (3.75 mmol, 75%).

Physical State: white solid.

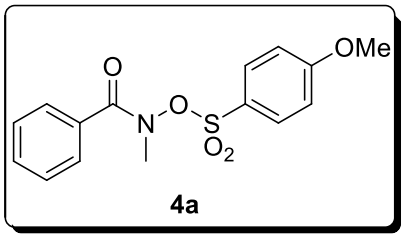
R_f Value: 0.25 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.22 (m, 5H), 7.14 (d, *J* = 8.1 Hz, 2H), 3.52 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.21, 146.18, 132.47, 131.39, 130.22, 129.79, 129.21, 128.47, 128.10, 40.53, 21.81.

IR (ATR in $CDCl_3$) *v*2948 (s), 1722 (s), 1453 (s), 1282(s), 1159 (s), 1028 (m), 812 (w), 715 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{16}NO_4$ [$M+H^+$]: 306.0795, found: 306.0801.



4a

According to GP-1, *N*-hydroxy-*N*-methylbenzamide (2.0 mmol, 0.30 g), Et_3N (3.0 mmol, 0.42 mL), 4-methoxybenzenesulfonyl chloride (2.2 mmol, 0.45 g) in DCM (20 mL) afforded 4a as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

***N*-(((4-methoxyphenyl)sulfonyl)oxy)-*N*-methylbenzamide**

Yield: 534 mg (1.7 mmol, 83%).

Physical State: white solid.

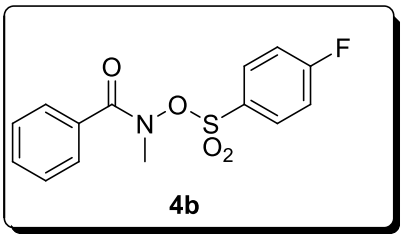
R_f Value: 0.25 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.55 (m, 2H), 7.42 – 7.20 (m, 5H), 6.81 – 6.73 (m, 2H), 6.82 – 6.72 (m, 2H), 3.80 (s, 3H), 3.52 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.17, 164.71, 132.66, 131.58, 131.38, 128.56, 128.19, 124.30, 114.47, 55.87, 40.42.

IR (ATR in $CDCl_3$) *v*3063 (m), 2948 (w), 1703 (s), 1595 (s), 1498 (m), 1379 (m), 1192 (s), 1025 (m), 894 (m), 808 (w), 715 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{16}NO_5S$ [$M+H^+$]: 322.0744, found: 322.0751.



4b

According to GP-1, *N*-hydroxy-*N*-methylbenzamide (2.0 mmol, 0.30 g), Et_3N (3.0 mmol, 0.42 mL), 4-fluorobenzenesulfonyl chloride (2.2 mmol, 0.43 g) in DCM (20 mL) afforded 4b as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

***N*-(((4-fluorophenyl)sulfonyl)oxy)-*N*-methylbenzamide**

Yield: 420 mg (1.4 mmol, 70%).

Physical State: white solid.

R_f Value: 0.25 (isohexane/EtOAc – 5/1).

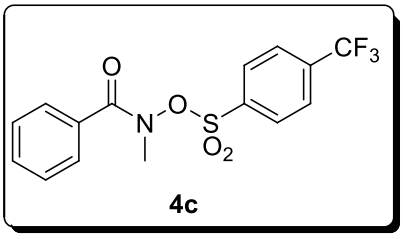
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 – 7.70 (m, 2H), 7.45 – 7.40 (m, 1H), 7.36 – 7.28 (m, 4H), 7.07 – 6.98 (m, 2H), 3.57 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.24, 166.49 (d, *J* = 258.7 Hz), 132.35, 132.30, 132.16, 131.68, 128.49, 128.38, 128.06, 116.63 (d, *J* = 22.9 Hz), 40.89.

^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -100.80.

IR (ATR in $CDCl_3$) *v*3075 (m), 2981 (w), 1699 (s), 1591 (s), 1386 (m), 1192 (s), 1021 (m), 838 (w), 711 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{14}H_{13}FNO_4S$ [$M+H^+$]: 310.0549, found: 310.0548.



4c

According to GP-1, *N*-hydroxy-*N*-methylbenzamide (2.0 mmol, 0.30 g), Et_3N (3.0 mmol, 0.42 mL), 4-trifluoromethylbenzenesulfonyl chloride (2.2 mmol, 0.54 g) in DCM (20 mL) afforded 4c as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

***N*-methyl-*N*-(((4-(trifluoromethyl)phenyl)sulfonyl)oxy)benzamide**

Yield: 580 mg (1.6 mmol, 80%).

Physical State: white solid.

R_f Value: 0.25 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.45 – 7.23 (m, 5H), 3.60 (s, 3H).

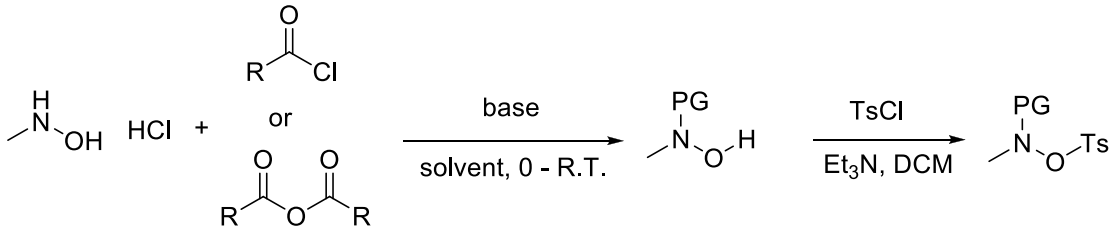
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.18, 136.98, 136.20 (q, *J* = 33.3 Hz), 132.10, 131.70, 129.76, 128.42, 128.40, 126.22 (q, *J* = 3.7 Hz), 122.94 (q, *J* = 271.5 Hz), 40.90.

^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -63.49.

IR (ATR in $CDCl_3$) *v*3071 (s), 1707 (s), 1431 (w), 1334 (s), 1174 (s), 1133 (s), 1066 (m), 842 (w), 719 (m) cm^{-1}.

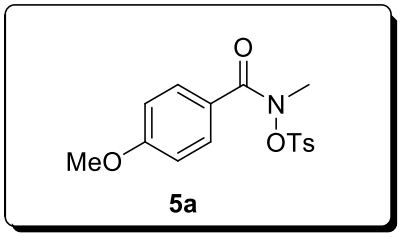
HRMS (ESI MS) calcd for $C_{15}H_{13}F_3NO_4S$ [M+H^+]: 360.0517, found: 360.0519.

3.2. General procedure (GP-2) for preparation of 5a-5d



Step 1: $NaHCO_3$ (4.2 g, 50 mmol, 2.5 equiv) was added to a solution of MeNHOH·HCl (1.8 g, 22 mmol, 1.1 equiv) in DCM (140 mL) at room temperature. Then the mixture was cooled to 0 °C and a solution of corresponding acyl chloride or anhydride (20 mmol, 1.0 equiv) in DCM (70 mL) was added. The resulting reaction mixture was stirred overnight at room temperature and filtered off the insoluble precipitate. The filtrate was washed with water 3 times, then the organic layers were dried (Na_2SO_4) and evaporated *in vacuo* to afford the crude compound as a light yellow oil, which was used without further purification.[1]

Step 2: TsCl (1.05 g, 5.5 mmol, 1.1 equiv) and Et_3N (0.76 g, 7.5 mmol, 1.5 equiv) were added to a solution of *N*-hydroxy-*N*-protected amide (5 mmol, 1 equiv) in DCM (50 mL) at 0 °C. The resulting reaction mixture was stirred at room temperature overnight. The solvent was removed *in vacuo* and the crude mixture was purified by flash column chromatography on silica gel isohexane/EtOAc (v/v=7:1) to obtain the product.[2]



5a

N-hydroxy-*N*-methyl-(4-methoxyl)benzamide was obtained according to modified procedure (GP-2, step 1). According to GP-2, *N*-hydroxy-*N*-methyl-(4-methoxyl)benzamide (5 mmol, 0.91 g), Et_3N (7.5 mmol, 1.05 mL), TsCl (5.5 mmol, 1.05 g) in DCM (50 mL) afforded 5a as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

4-methoxy-*N*-methyl-*N*-(tosyloxy)benzamide

Yield: 1.44 g (3.95 mmol, 79%).

Physical State: white solid.

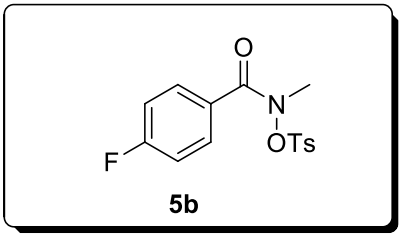
R_f Value: 0.25 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.7 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H), 3.46 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.02, 162.21, 146.04, 130.67, 130.38, 129.64, 129.10, 124.28, 113.37, 55.42, 40.99, 21.72.

IR (ATR in $CDCl_3$) *v*3015 (s), 2952 (s), 2840 (m), 1710 (s), 1602 (s), 1513 (m), 1435 (s), 1252 (s), 1167 (s), 1103 (s), 1028 (w), 846 (m), 767 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{16}H_{18}NO_5S$ $[M+H^+]$: 366.0906, found: 366.0910.



5b

N-hydroxy-*N*-methyl-(4-fluoro)benzamide was obtained according to modified procedure (GP-2, step 1). According to GP-2, *N*-hydroxy-*N*-(4-fluoro)benzamide (5 mmol, 0.85 g), Et_3N (7.5 mmol, 1.05 mL), TsCl (5.5 mmol, 1.05 g) in DCM (50 mL) afforded 5b as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

4-fluoro-*N*-methyl-*N*-(tosyloxy)benzamide

Yield: 1.16 g (3.60 mmol, 72%).

Physical State: white solid.

R_f Value: 0.25 (isohexane/EtOAc – 5/1).

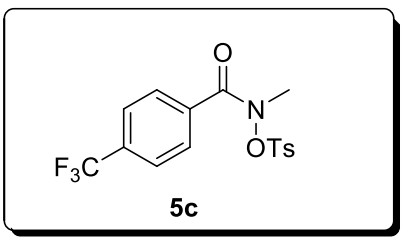
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 – 7.52 (m, 2H), 7.40 – 7.32 (m, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 6.99 – 6.89 (m, 2H), 3.54 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.05, 164.40 (d, *J* = 252.8 Hz), 146.42, 131.10 (d, *J* = 8.9 Hz), 130.25, 129.84, 129.21, 128.60 (d, *J* = 3.4 Hz), 115.20 (d, *J* = 21.9 Hz), 40.21, 21.85.

^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -107.92.

IR (ATR in $CDCl_3$) *v*3172 (s), 3063 (s), 1722 (s), 1602 (m), 1453 (m), 1282 (s), 1155 (s), 1036 (m), 812 (w), 685 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{15}FNO_4S$ [$M+H^+$]: 324.0706, found: 324.0708.



5c

N-hydroxy-*N*-methyl-(4-trifluoromethyl)benzamide was obtained according to modified procedure (GP-2, step 1). According to GP-2, *N*-hydroxy-*N*-methyl-(4-trifluoromethyl)benzamide (5 mmol, 1.10 g), Et_3N (7.5 mmol, 1.05 mL), TsCl (5.5 mmol, 1.05

g) in DCM (50 mL) afforded 5c as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

***N*-methyl-*N*-(tosyloxy)-4-(trifluoromethyl)benzamide**

Yield: 1.44 g (3.8 mmol, 76%).

Physical State: white solid.

R_f Value: 0.25 (isohexane/EtOAc – 5/1).

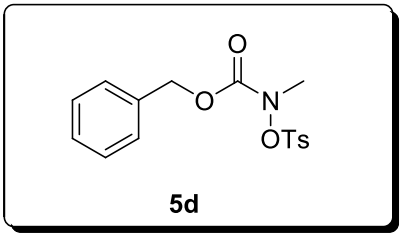
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (t, *J* = 7.9 Hz, 4H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 3.59 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.50, 146.60, 135.97, 132.62 (q, *J* = 32.8 Hz), 129.97, 129.92, 129.07, 128.88, 124.85 (q, *J* = 3.8 Hz), 123.60 (q, *J* = 270.7 Hz), 39.55, 21.74.

^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -63.15.

IR (ATR in $CDCl_3$) *v*3168 (s), 3063 (s), 1725 (s), 1453 (s), 1326 (m), 1155 (s), 1036 (w), 1010 (w), 812 (s), 689 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{16}H_{15}F_3NO_4S$ [M+H^+]: 374.0668, found: 374.0666.



5d

N-hydroxy-*N*-methyl-Cbz-amide was obtained according to modified procedure (GP-2, step 1). According to GP-2, *N*-hydroxy-*N*-Cbz amide (5 mmol, 0.90 g), Et_3N (7.5 mmol, 1.05 mL), TsCl (5.5 mmol, 1.05 g) in DCM (50 mL) afforded 5d as a white solid after purification on silica gel (isohexanes: EtOAc = 7:1). Reaction time: 12 h.

benzyl methyl(tosyloxy)carbamate

Yield: 1.42 g (4.25 mmol, 85%).

Physical State: white solid.

R_f Value: 0.25 (isohexane/EtOAc – 5/1).

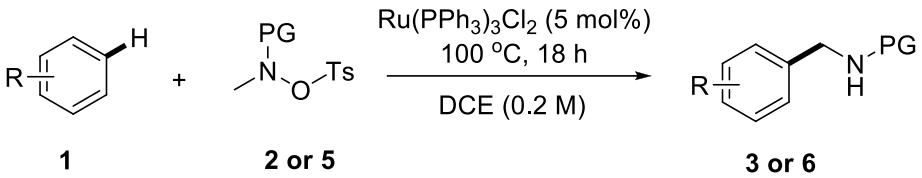
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.33 (dd, *J* = 4.9, 1.8 Hz, 3H), 7.17 (d, *J* = 8.6 Hz, 4H), 4.90 (s, 2H), 3.30 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.37, 145.89, 134.91, 130.89, 129.65, 128.63, 128.59, 128.31, 68.93, 40.48, 21.94.

IR (ATR in $CDCl_3$) *v*3000 (s), 2952 (s), 2855 (s), 1729(s), 1457 (w), 1379 (s), 1308 (m), 1177 (s), 816 (s), 752 (m) cm^{-1}.

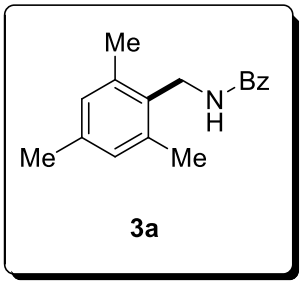
HRMS (ESI MS) calcd for $C_{16}H_{18}NO_5S$ [$M+H^+$]: 366.0906, found: 366.0908.

3.3. General procedure (GP-3) for preparation of 3a-3r, 6a-6d



1 **2 or 5** **3 or 6**

A mixture of **1** (0.2 mmol), *N*-protected-*N*-methyl-hydroxylamine **2** (0.3 mmol), $Ru(PPh_3)_3Cl_2$ (5 mol%), and 1 mL DCE in a 15 mL sealed glass vial was heated at 100 °C under air with vigorous stirring for 18 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated *in vacuo* and purified by column chromatography on silica gel (isohexane/EA = 10/1 to 5/1) to give the corresponding product.



3a

According to GP-3, mesitylene (0.2 mmol, 24.0 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3a after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(2,4,6-trimethylbenzyl)benzamide**

Yield: 36 mg (0.14 mmol, 72%).

Physical State: white solid.

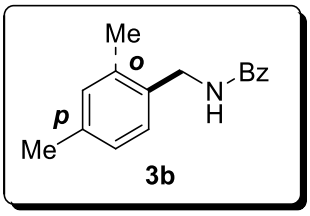
R_f Value: 0.27 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 – 7.69 (m, 2H), 7.52 – 7.44 (m, 1H), 7.44 – 7.36 (m, 2H), 6.91 (s, 2H), 5.88 (s, 1H), 4.63 (d, *J* = 4.5 Hz, 2H), 2.37 (s, 6H), 2.28 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.52, 137.89, 137.75, 134.50, 131.61, 130.93, 129.41, 128.71, 127.04, 38.89, 21.08, 19.81.

IR (ATR in $CDCl_3$) *v*3280 (s), 2955 (s), 2918 (m), 1628 (s), 1535 (s), 1453 (w), 1036 (m), 746 (m), 689 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{17}H_{20}NO$ [M+H^+]: 154.1545, found: 154.1543.



According to GP-3, *N*-methyl-*N*-(tosyloxy)benzamide (0.2 mmol, 61.0 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in toluene (1 mL) afforded 3b as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(4-methylbenzyl)benzamide** and ***N*-(2-methylbenzyl)benzamide**

Yield: 29 mg (0.13 mmol, 65%).

Physical State: white solid.

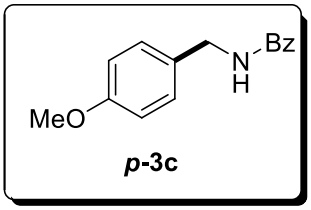
R_f Value: 0.18 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 – 7.74 (m, 2H), 7.54 – 7.47 (m, 1H), 7.46 – 7.39 (m, 2H), 7.27 – 7.15 (m, 4H), 6.32 (s, 0.76H), 6.19 (s, 0.27H), 4.65 (d, *J* = 5.3 Hz, 0.5H), 4.61 (d, *J* = 5.6 Hz, 1.5H), 2.38 (s, 0.72H), 2.35 (s, 2.28H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.41, 167.34, 137.50, 136.78, 135.89, 135.27, 134.60, 134.51, 131.67, 131.63, 130.79, 129.59, 128.88, 128.74, 128.70, 128.09, 127.07, 126.43, 44.06, 42.50, 21.24, 19.20.

IR (ATR in $CDCl_3$) *v*3309 (s), 2922 (s), 1640 (s), 1535 (m), 1297 (w), 1028 (w), 805 (w), 745 (m), 693 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{16}NO$ $[M+H^+]$: 226.1232, found: 226.1230.



***p*-3c**

According to GP-3, anisole (0.2 mmol, 21.6 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded *p*-3c and *o*-3c as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(4-methoxybenzyl)benzamide**

Yield: 25 mg (0.10 mmol, 51%).

Physical State: white solid.

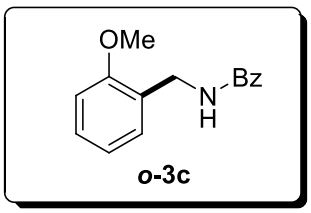
R_f Value: 0.15 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 – 7.74 (m, 2H), 7.48 (dd, *J* = 5.0, 3.6 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.31 – 7.26 (m, 2H), 6.92 – 6.86 (m, 2H), 6.36 (s, 1H), 4.58 (d, *J* = 5.6 Hz, 2H), 3.80 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.38, 159.28, 134.60, 131.64, 130.38, 129.46, 128.72, 127.06, 114.31, 55.46, 43.79.

IR (ATR in $CDCl_3$) *v*3309 (s), 2929 (s), 2832 (s), 1640 (s), 1535 (s), 1300 (m), 1248 (s), 1032 (m), 831 (w), 697 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{16}NO_2$ $[M+H^+]$: 242.1176, found: 242.1181.



***o*-3c**

***N*-(2-methoxybenzyl)benzamide**

Yield: 8 mg (0.04 mmol, 18%).

Physical State: white solid.

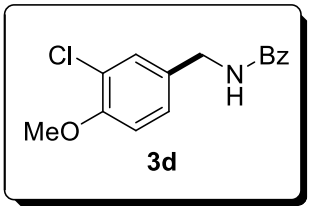
R_f Value: 0.20 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 2H), 7.50 – 7.34 (m, 4H), 7.30 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.93 (dd, *J* = 14.4, 7.8 Hz, 2H), 6.64 (s, 1H), 4.65 (d, *J* = 5.8 Hz, 2H), 3.89 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.83, 134.98, 131.45, 130.20, 129.15, 128.66, 127.07, 126.31, 120.97, 110.54, 55.57, 40.21.

IR (ATR in $CDCl_3$) *v*3309 (s), 2929 (s), 2834 (s), 1640 (s), 1535 (s), 1330 (m), 1156 (s), 1036 (m), 868 (w), 693 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{15}NO_2$ [$M+H^+$]: 242.1176, found: 242.1178.



3d

According to GP-3, 2-chloroanisole (0.2 mmol, 28.4 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3d as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(3-chloro-4-methoxybenzyl)benzamide**

Yield: 51 mg (0.18 mmol, 93%).

Physical State: white solid.

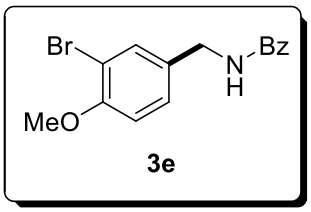
R_f Value: 0.11 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.52 – 7.45 (m, 1H), 7.44 – 7.36 (m, 2H), 7.33 (d, *J* = 2.1 Hz, 1H), 7.18 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.73 (s, 1H), 4.51 (d, *J* = 5.8 Hz, 2H), 3.86 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.55, 154.47, 134.25, 131.72, 131.57, 129.81, 128.68, 127.47, 127.11, 122.60, 112.26, 77.58, 77.16, 76.74, 56.29, 43.14.

IR (ATR in $CDCl_3$) *v*3317 (s), 2933 (m), 2840 (w), 1640 (s), 1535 (m), 1502 (s), 1282 (s), 1066 (m), 879 (w), 805 (w), 693 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{15}ClNO_2$ [M+H$^+$]: 276.0791, found: 276.0790.



3e

According to GP-3, 2-bromoanisole (0.2 mmol, 37.0 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3e as a brown solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(3-bromo-4-methoxybenzyl)benzamide**

Yield: 51 mg (0.16 mmol, 81%).

Physical State: brown solid.

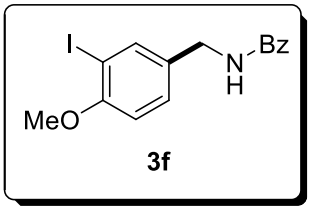
R_f Value: 0.10 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 2H), 7.49 (dd, *J* = 7.9, 4.7 Hz, 2H), 7.44 – 7.37 (m, 2H), 7.27 – 7.19 (m, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.71 (s, 1H), 4.52 (d, *J* = 5.8 Hz, 2H), 3.85 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.52, 155.38, 134.25, 132.89, 132.03, 131.73, 128.69, 128.30, 127.11, 112.11, 77.58, 77.16, 76.74, 56.39, 43.05.

IR (ATR in $CDCl_3$) *v*3313 (s), 2937 (s), 2836 (m), 1640 (s), 1535 (s), 1494 (s), 1256 (s), 1054 (s), 1021 (s), 711 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{15}BrNO_2$ [M+H$^+$]: 320.0281, found: 320.0277.



3f

According to GP-3, 2-iodoanisole (0.2 mmol, 46.8 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3f as a yellow oil after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(3-iodo-4-methoxybenzyl)benzamide**

Yield: 41 mg (0.11 mmol, 56%).

Physical State: yellow oil.

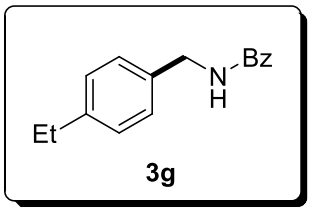
R_f Value: 0.10 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 – 7.72 (m, 3H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.30 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.60 (d, *J* = 19.1 Hz, 1H), 4.52 (d, *J* = 5.7 Hz, 2H), 3.85 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.48, 157.71, 139.03, 134.29, 132.57, 131.73, 129.47, 128.71, 127.11, 111.06, 86.20, 56.55, 42.92.

IR (ATR in $CDCl_3$) *v*3309 (s), 2937 (m), 2836 (w), 1636 (s), 1535 (m), 1487 (s), 1278 (s), 1047 (m), 883 (w), 805 (w), 708 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{15}H_{15}INO_2$ [$M+H^+$]: 368.0142, found: 368.0143.



3g

According to GP-3, ethylbenzene (0.2 mmol, 21.2 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3g as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(4-ethylbenzyl)benzamide**

Yield: 27 mg (0.11 mmol, 58%).

Physical State: white solid.

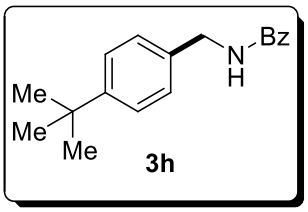
R_f Value: 0.20 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 2H), 7.52 – 7.47 (m, 1H), 7.47 – 7.38 (m, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 6.35 (s, 1H), 4.62 (d, *J* = 5.5 Hz, 2H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.41, 143.96, 135.49, 134.62, 131.64, 128.73, 128.45, 128.20, 127.07, 44.12, 28.69, 15.77.

IR (ATR in $CDCl_3$) *v*3308 (s), 2959 (s), 2199 (m), 1640 (s), 1539 (m), 1248 (w), 730 (m), 700 (w) cm^{-1}.

HRMS (ESI MS) calcd for $C_{16}H_{18}NO$ [M+H^+]: 240.1388, found: 240.1389.



3h

According to GP-3, *tert*-butylbenzene (0.2 mmol, 26.8 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3h as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(4-(tert-butyl)benzyl)benzamide**

Yield: 39 mg (0.15 mmol, 74%).

Physical State: white solid.

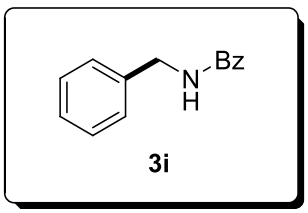
R_f Value: 0.21 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 – 7.74 (m, 2H), 7.48 (dd, *J* = 5.0, 3.6 Hz, 1H), 7.46 – 7.35 (m, 4H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.36 (s, 1H), 4.62 (d, *J* = 5.5 Hz, 2H), 1.32 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.42, 150.86, 135.24, 134.61, 131.64, 128.72, 127.94, 127.08, 125.88, 44.02, 34.69, 31.47.

IR (ATR in $CDCl_3$) *v*3304 (s), 2939 (s), 1641 (s), 1439 (m), 1118 (w), 1069 (w), 737 (m), 716 (w) cm^{-1}.

HRMS (ESI MS) calcd for $C_{18}H_{22}NO$ [M+H^+]: 268.1701, found: 268.1703.



3i

According to GP-3, *N*-methyl-*N*-(tosyloxy)benzamide (0.2 mmol, 61.0 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in benzene (1 mL) afforded 3i as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-benzylbenzamide**

Yield: 20 mg (0.08 mmol, 43%).

Physical State: white solid.

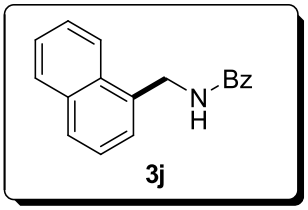
R_f Value: 0.18 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 2H), 7.53 – 7.47 (m, 1H), 7.46 – 7.40 (m, 2H), 7.40 – 7.28 (m, 5H), 6.38 (s, 1H), 4.66 (d, *J* = 5.7 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.47, 138.30, 134.55, 131.72, 128.97, 128.77, 128.10, 127.82, 127.09, 44.33.

IR (ATR in $CDCl_3$) *v*3302 (s), 2967 (s), 1640 (s), 1539 (m), 1457 (w), 1300 (m), 712 (s), 700 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{14}H_{14}NO$ [$M+H^+$]: 212.1075, found: 212.1076.



3j

According to GP-3, naphthalene (0.2 mmol, 25.6 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3j as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(naphthalen-1-ylmethyl)benzamide**

Yield: 20 mg (0.08 mmol, 39%).

Physical State: white solid.

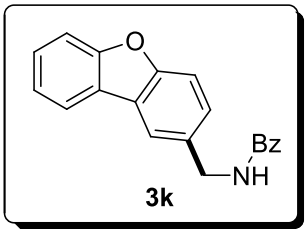
R_f Value: 0.1 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 – 8.04 (m, 1H), 7.92 – 7.82 (m, 2H), 7.75 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.58 – 7.45 (m, 5H), 7.43 – 7.37 (m, 2H), 6.34 (s, 1H), 5.10 (d, *J* = 5.2 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.29, 134.45, 134.09, 133.51, 131.70, 131.65, 128.97, 128.78, 128.73, 127.15, 127.10, 126.94, 126.23, 125.58, 123.67, 42.59.

IR (ATR in $CDCl_3$) *v*3321 (s), 3063 (s) 2926 (m), 1640 (s), 1535 (s), 1293 (s), 1148 (w), 1028 (m), 805 (w), 745 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{18}H_{16}NO_2$ [M+H$^+$]: 262.1232, found: 262.1233.



According to GP-3, dibenzofuran (0.2 mmol, 33.6 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3k as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(dibenzo[b,d]furan-2-ylmethyl)benzamide**

Yield: 35 mg (0.11 mmol, 58%).

Physical State: white solid.

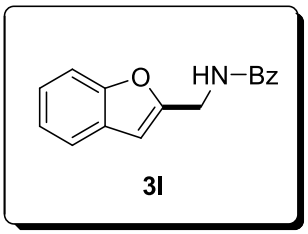
R_f Value: 0.15 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.6 Hz, 2H), 7.85 – 7.80 (m, 2H), 7.58 – 7.42 (m, 7H), 7.34 (td, *J* = 7.6, 1.0 Hz, 1H), 6.57 (s, 1H), 4.79 (d, *J* = 5.7 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.50, 156.72, 155.79, 134.47, 132.93, 131.76, 128.77, 127.52, 127.35, 127.13, 122.95, 120.90, 120.42, 111.98, 111.87, 44.36.

IR (ATR in $CDCl_3$) *v*3324 (s), 3060 (m), 2926 (m), 1640 (s), 1449 (s), 1535 (s), 1483 (s), 1304 (m), 1196 (s), 1025 (m), 909 (m), 842 (m), 749 (s), 711 (w) cm^{-1}.

HRMS (ESI MS) calcd for $C_{20}H_{16}NO_2$ [M+H$^+$]: 302.1181, found: 302.1178.



3l

According to GP-3, benzofuran (0.2 mmol, 23.6 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3l as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(benzofuran-2-ylmethyl)benzamide**

Yield: 26 mg (0.10 mmol, 52%).

Physical State: white solid.

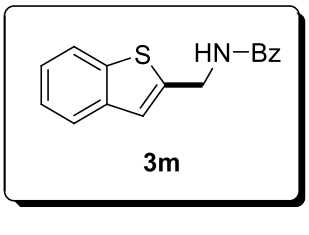
R_f Value: 0.17 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 – 7.76 (m, 2H), 7.56 – 7.48 (m, 2H), 7.47 – 7.41 (m, 3H), 7.30 – 7.18 (m, 2H), 6.69 (s, 1H), 6.56 (s, 1H), 4.80 (d, *J* = 5.1 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.43, 155.11, 153.99, 134.17, 131.91, 128.80, 128.37, 127.17, 124.42, 123.06, 121.19, 111.26, 104.60, 37.62.

IR (ATR in $CDCl_3$) *ν*3321 (s), 1640 (s), 1535 (s), 1487 (s), 1297 (m), 1177 (m), 939 (m), 808 (s), 697 (w) cm^{-1}.

HRMS (ESI MS) calcd for $C_{16}H_{14}NO_2$ $[M+H^+]$: 252.1019, found: 252.1025.



3m

According to GP-3, benzothiophene (0.2 mmol, 26.8 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3m as a yellow solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(benzothiophen-2-ylmethyl)benzamide**

Yield: 28 mg (0.11 mmol, 53%).

Physical State: yellow solid.

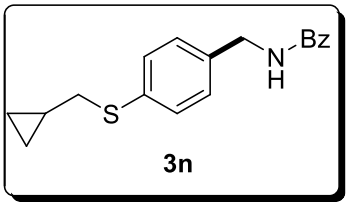
R_f Value: 0.17 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 – 7.83 (m, 2H), 7.80 – 7.72 (m, 2H), 7.48 (dd, *J* = 4.9, 3.6 Hz, 1H), 7.45 – 7.35 (m, 5H), 6.36 (s, 1H), 4.91 (d, *J* = 5.4 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.50, 140.84, 137.93, 134.37, 132.82, 131.79, 128.77, 127.09, 124.92, 124.87, 124.65, 123.13, 121.95, 38.21.

IR (ATR in $CDCl_3$) *v*3309 (s), 3060 (m), 2926 (m), 1640 (s), 1535 (s), 1293 (s), 1159 (w), 760 (w), 693 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{16}H_{14}NOS$ [M+H$^+$]: 268.0796, found: 268.0794.



3n

According to GP-3, cyclopropylmethyl phenyl sulfide (0.2 mmol, 32.8 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3n as a yellow oil after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(4-((cyclopropylmethyl)thio)benzyl)benzamide**

Yield: 39 mg (0.14 mmol, 69%).

Physical State: yellow oil.

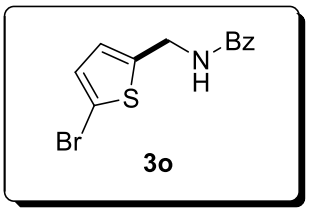
R_f Value: 0.16 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 2H), 7.51 – 7.41 (m, 3H), 7.36 – 7.26 (m, 4H), 6.41 (s, 1H), 4.61 (d, *J* = 5.7 Hz, 2H), 2.85 (d, *J* = 7.0 Hz, 2H), 1.12 – 0.98 (m, 1H), 0.67 – 0.45 (m, 2H), 0.34 – 0.17 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.46, 136.67, 136.01, 134.47, 131.74, 129.77, 128.76, 128.56, 127.08, 43.83, 39.78, 10.77, 5.77.

IR (ATR in $CDCl_3$) *v*3309 (s), 3071 (m), 3004 (m), 2914 (m), 1640 (s), 1535 (s), 1289 (s), 1092 (m), 1017 (m), 827 (w), 793 (m), 693 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{18}H_{20}NOS$ [M+H$^+$]: 298.1266, found: 298.1267.



According to GP-3, 2-bromothiophene (0.2 mmol, 32.6 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3o as a yellow solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-((5-bromothiophen-2-yl)methyl)benzamide**

Yield: 39 mg (0.13 mmol, 67%).

Physical State: yellow solid.

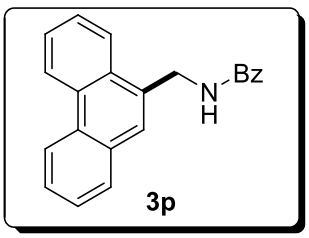
R_f Value: 0.16 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 – 7.72 (m, 2H), 7.54 – 7.47 (m, 1H), 7.47 – 7.40 (m, 2H), 6.90 (d, *J* = 3.7 Hz, 1H), 6.79 (d, *J* = 3.7 Hz, 1H), 6.51 (s, 1H), 4.72 (d, *J* = 6.4 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.38, 142.78, 134.02, 131.95, 129.69, 128.80, 127.13, 126.68, 112.07, 39.17.

IR (ATR in $CDCl_3$) *v*3328(s), 2922 (s), 2855 (m), 1641 (s), 1420 (m), 1222 (s), 1140 (m), 972 (m), 735 (w), 397 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{12}H_{11}BrNOS$ [$M+H^+$]: 295.9739, found: 295.9737.



According to GP-3, phenanthrene (0.2 mmol, 35.6 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3p as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(phenanthren-9-ylmethyl)benzamide**

Yield: 40 mg (0.13 mmol, 64%).

Physical State: white solid.

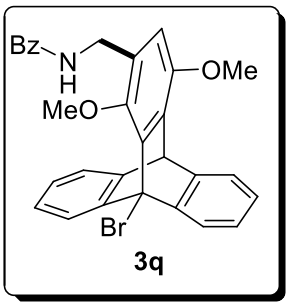
R_f Value: 0.11 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 – 8.65 (m, 2H), 8.18 – 8.09 (m, 1H), 7.91 – 7.83 (m, 1H), 7.81 – 7.73 (m, 3H), 7.71 – 7.58 (m, 4H), 7.53 – 7.44 (m, 1H), 7.44 – 7.36 (m, 2H), 6.41 (s, 1H), 5.14 (d, *J* = 5.3 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.36, 134.43, 131.82, 131.73, 131.44, 131.04, 130.64, 130.42, 128.75, 128.68, 128.02, 127.39, 127.18, 127.12, 127.07, 126.94, 124.38, 123.47, 122.71, 43.03.

IR (ATR in $CDCl_3$) *v*3313 (s), 3056 (s) 2922 (m), 1640 (s), 1535 (s), 1487 (m), 1297 (s), 1177 (w), 1073 (m), 790 (w), 693 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{22}H_{18}NO_2$ [$M+H^+$]: 312.1383, found: 312.1385.



3q

According to GP-3, triptycene (0.1 mmol, 39.2 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.15 mmol, 45.8 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 4.8 mg) in DCE (0.5 mL) afforded 3q as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(((9r,10r)-9-bromo-1,4-dimethoxy-9,10-dihydro-9,10-[1,2]benzenoanthracen-2-yl)methyl)benzamide**

Yield: 35 mg (0.07 mmol, 66%).

Physical State: white solid.

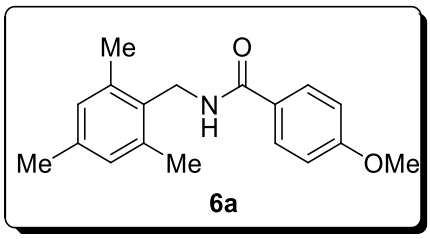
R_f Value: 0.31 (DCM/MeOH – 10/1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.94 (m, 2H), 7.74 – 7.69 (m, 2H), 7.49 – 7.44 (m, 1H), 7.39 (ddd, *J* = 13.8, 7.2, 1.4 Hz, 4H), 7.13 – 7.05 (m, 4H), 6.72 (s, 1H), 6.56 (t, *J* = 5.2 Hz, 1H), 5.92 (s, 1H), 4.60 (d, *J* = 5.6 Hz, 2H), 3.82 (s, 3H), 3.77 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.45, 150.03, 148.65, 145.16, 143.58, 137.03, 134.57, 134.45, 131.59, 130.67, 128.65, 127.10, 126.48, 125.50, 125.02, 123.33, 111.70, 65.93, 63.97, 56.27, 46.43, 39.81.

IR (ATR in $CDCl_3$) *v*3309 (s), 3063 (m), 2937 (m), 2832 (w), 1640 (s), 1528 (m), 1468 (s), 1293 (m), 1226 (m), 1043 (m), 909 (m), 730 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{30}H_{25}BrNO_3$ [M+H^+]: 526.1012, found: 526.1014.



6a

According to GP-3, mesitylene (0.2 mmol, 24.0 mg), 4-methoxy-*N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 100.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 6a as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

4-methoxy-*N*-(2,4,6-trimethylbenzyl)benzamide

Yield: 50 mg (0.18 mmol, 91%).

Physical State: white solid.

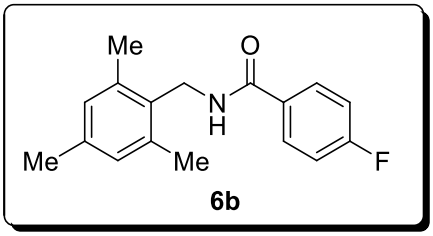
R_f Value: 0.24 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 – 7.69 (m, 2H), 7.12 – 7.03 (m, 2H), 6.91 (s, 2H), 5.82 (s, 1H), 4.62 (d, *J* = 4.5 Hz, 2H), 2.37 (s, 6H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.01, 162.29, 137.80, 137.76, 131.10, 129.37, 128.82, 126.76, 113.85, 55.53, 38.81, 21.06, 19.80.

IR (ATR in $CDCl_3$) *v*3309 (s), 2948 (w), 1621 (s), 1528 (w), 1505 (m), 1312 (w), 1263 (s), 1028 (w), 835 (m), 717 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{18}H_{22}NO_2$ [M+H^+]: 284.1651, found: 284.1670.



6b

According to GP-3, mesitylene (0.2 mmol, 24.0 mg), 4-fluoro-*N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 96.9 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 6b as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

4-fluoro-*N*-(2,4,6-trimethylbenzyl)benzamide

Yield: 27 mg (0.1 mmol, 50%).

Physical State: white solid.

R_f Value: 0.26 (isohexane/EtOAc – 5/1).

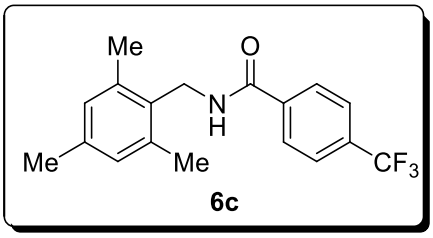
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 – 7.69 (m, 2H), 7.12 – 7.03 (m, 2H), 6.91 (s, 2H), 5.82 (s, 1H), 4.62 (d, *J* = 4.5 Hz, 2H), 2.37 (s, 6H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.43, 164.86 (d, *J* = 249.7 Hz), 137.97, 137.72, 130.80, 129.44, 129.41, 129.29, 115.73 (d, *J* = 21.7 Hz), 38.93, 21.07, 19.80.

^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -108.89.

IR (ATR in $CDCl_3$) *v*3268 (s), 2948 (w), 2914 (m), 1632 (s), 1546 (w), 1502 (s), 1304 (w), 1226 (s), 1155 (w), 909 (s), 849 (s), 738 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{17}H_{19}FNO$ [$M+H^+$]: 272.1451, found: 272.1449.



6c

According to GP-3, mesitylene (0.2 mmol, 24.0 mg), 4-trifluoromethyl-*N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 100.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL)

afforded 6c as a yellow oil after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

4-(trifluoromethyl)-*N*-(2,4,6-trimethylbenzyl)benzamide

Yield: 23 mg (0.07 mmol, 36%).

Physical State: yellow oil.

R_f Value: 0.26 (isohexane/EtOAc – 5/1).

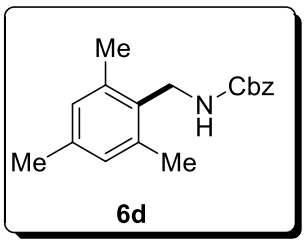
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.1 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 6.92 (s, 2H), 5.94 (s, 1H), 4.64 (d, *J* = 4.6 Hz, 2H), 2.37 (s, 6H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.17, 138.10, 137.72, 133.36 (q, *J* = 32.8 Hz), 130.51, 129.69, 129.48, 127.54, 125.75 (q, *J* = 3.8 Hz), 123.77 (q, *J* = 270.7 Hz), 39.03, 21.06, 19.81.

^{19}F{^{1}H}NMR (282 MHz, $CDCl_3$) δ -62.96.

IR (ATR in $CDCl_3$) *v*3308 (s), 2949(w), 2904 (m), 1639 (s), 1584 (w), 1432 (s), 1321 (w), 1066 (w), 913 (s), 837 (w), 752 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{18}H_{19}F_3NO$ [M+H$^+$]: 322.1419, found: 322.1418.



6d

According to GP-3, mesitylene (0.2 mmol, 24.0 mg), benzyl methyl(tosyloxy)carbamate (0.3 mmol, 100.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 6d as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

benzyl (2,4,6-trimethylbenzyl)carbamate

Yield: 28 mg (0.1 mmol, 49%).

Physical State: white solid.

R_f Value: 0.45 (isohexane/EtOAc – 5/1).

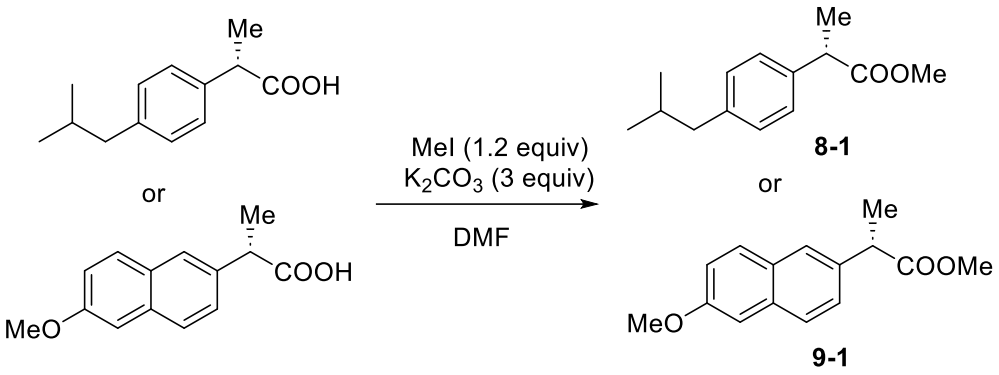
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 5H), 6.86 (s, 2H), 5.12 (s, 2H), 4.60 (s, 1H), 4.39 (d, *J* = 4.8 Hz, 2H), 2.33 (s, 6H), 2.26 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.27, 137.69, 137.42, 136.72, 131.09, 129.32, 128.66, 128.25, 128.21, 66.87, 39.49, 21.04, 19.71.

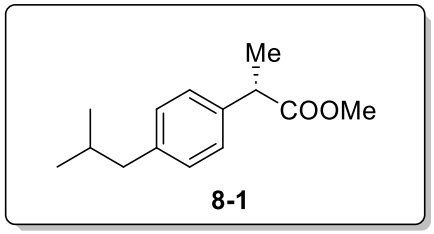
IR (ATR in $CDCl_3$) *v*3317 (s), 2922 (s), 1681 (s), 1524 (s), 1353 (m), 1284 (s), 1047 (m), 853 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{18}H_{22}NO_2$ [$M+H^+$]: 284.1651, found: 284.1654.

3.4. General procedure (GP-4) for preparation of 8-1, 9-1



MeI (0.51 g, 3.6 mmol, 1.2 equiv) was added to a solution of S(+)-Ibuprofen (618 mg, 3 mmol) or S(+)-Naproxen (690 mg, 3 mmol) and K_2CO_3 (1.24 g, 9 mmol, 3 equiv) in DMF (10 mL) at room temperature. The mixture was allowed to stir overnight at room temperature. After pouring 10 mL of water, the mixture was extracted by EtOAc (10 mL × 3). The combined organic layer was washed by brine and dried over anhydrous Na_2SO_4. The residue was purified by silica gel chromatography using isohexane/EtOAc = (10/1) to obtain pure product **8-1**.[3]



methyl (S)-2-(4-isobutylphenyl)propanoate

Yield: 646 mg (2.94 mmol, 98%).

Physical State: colorless oil.

R_f Value: 0.35 (isohexane/EtOAc – 5/1).

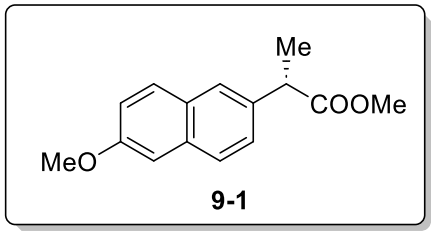
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 – 7.77 (m, 2H), 7.56 – 7.40 (m, 3H), 7.27 (td, *J* = 7.3, 2.4 Hz, 3H), 7.20 – 7.13 (m, 2H), 7.00 (d, *J* = 8.6 Hz, 1H), 6.93 – 6.79 (m, 3H), 2.32 (s, 6H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.32, 140.66, 137.87, 129.46, 127.24, 52.06, 45.16, 45.13, 30.29, 22.50, 18.73.

IR (ATR in $CDCl_3$) *v*2952 (s), 2870 (m), 1736 (s), 1461 (m), 1334 (m), 1207 (s), 1161 (s), 1069 (m), 857 (m), 797 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{14}H_{21}O_2$ [$M+H^+$]: 221.1536, found: 221.1542.

Enantiomer ratio was determinted by HPLC using a Daicel Chiralpak OJ column (flow rate 0.8 mL/min, *n*-hexane/*i*-PrOH = 99.9/0.1, λ = 230.4 nm), t_R = 11.76 min (major), t_R = 12.89 min (minor); 98% *ee*.



9-1

methyl (S)-2-(6-methoxynaphthalen-2-yl)propanoate

Yield: 577 mg (2.36 mmol, 79%).

Physical State: white solid.

R_f Value: 0.55 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 12.1, 5.1 Hz, 3H), 7.41 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.14 (dt, *J* = 7.0, 2.4 Hz, 2H), 3.91 (d, *J* = 4.1 Hz, 3H), 3.90 – 3.83 (m, 1H), 3.67 (s, 3H), 1.58 (d, *J* = 7.2 Hz, 3H).

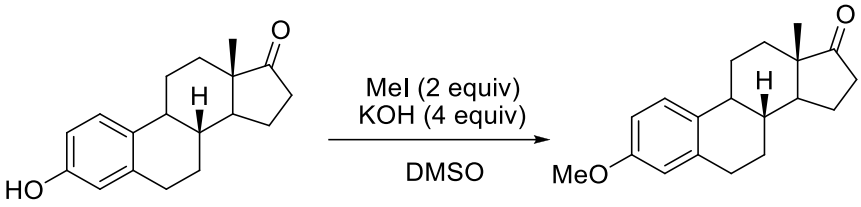
^{13}C NMR (75 MHz, $CDCl_3$) δ 175.27, 157.77, 135.80, 133.82, 129.40, 129.05, 127.30, 126.31, 126.06, 119.12, 105.70, 55.42, 52.17, 45.47, 18.72.

IR (ATR in $CDCl_3$) *v*2985 (m), 2940 (m), 1736 (s), 1602 (s), 1438 (s), 1267 (m), 1174 (s), 1028 (m), 857 (m), 823 (s) cm^{-1}.

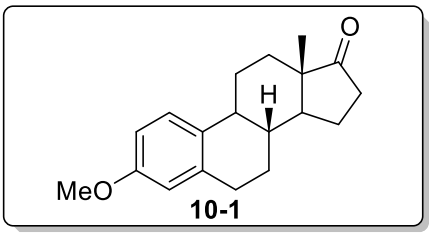
HRMS (ESI MS) calcd for $C_{15}H_{17}O_3$ [$M+H^+$]: 245.1172, found: 245.1178.

Enantiomer ratio was determinted by HPLC using a Daicel Chiralpak OD-H column (flow rate 1.0 mL/min, *n*-hexane/*i*-PrOH = 99.0/1.0, λ = 230.4 nm), t_R = 9.25 min (minor), t_R = 10.96 min (major); 99% *ee*.

3.5. Preparation of 10-1



Add estrone (568 mg, 2 mmol) and MeI (6.85 mL, 110 mmol) to a solution of KOH (448 mg, 8 mmol) in DMSO (3.6 mL) at room temperature. Stir the reaction mixture at room temperature for 3 hours. Filter the reaction mixture. Wash the reaction mixture with water to obtain (8R,9S,13S,14S)-3-methoxy-13-methyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]-phenanthren-17(14H)-one **10-1**.[4]



(8R,13S)-3-methoxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]-phenanthren-17-one

Yield: 511 mg (0.18 mmol, 92%).

Physical State: white solid.

R_f Value: 0.32 (isohexane/EtOAc – 5/1).

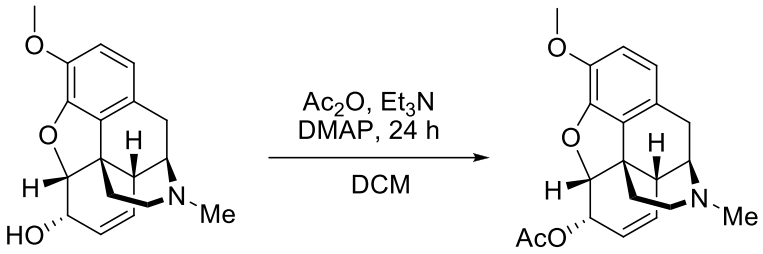
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.5 Hz, 1H), 6.74 – 6.59 (m, 2H), 3.78 (s, 3H), 2.93 – 2.86 (m, 2H), 2.55 – 2.37 (m, 2H), 2.25 - 2.18 (m, 1H), 2.08 – 1.95 (m, 3H), 1.65 – 1.42 (m, 7H), 0.91 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 221.25, 157.70, 137.87, 132.14, 126.47, 114.00, 111.69, 77.58, 77.16, 76.74, 55.34, 50.52, 48.16, 44.09, 38.49, 36.01, 31.69, 29.79, 26.67, 26.05, 21.71, 13.98.

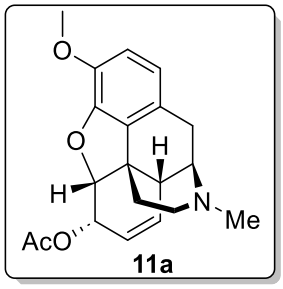
IR (ATR in $CDCl_3$) *v*2926 (s), 2858 (m), 1736 (s), 1610 (m), 1498 (s), 1282 (m), 1054 (m), 868 (w), 816 (m), 782 (m), 730 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{19}H_{25}O_2$ $[M+H^+]$: 285.1855, found: 285.1661.

3.6. Preparation of 11-a



To a mixture of Codeine hydrochloride salt (0.3 g, 1.0 mmol) and dimethylaminopyridine (DMAP, 0.244 g, 2.0 mmol, 2.0 equiv) in dry DCM (10.5 mL) at rt were added triethylamine (0.41 mL, 3 mmol, 3.0 equiv) and Ac_2O (0.28 mL, 3.0 mmol, 3.0 equiv) respectively. The resulting solution was stirred for 24 h, then poured into half saturated brine (20 mL), and extracted with DCM (3 × 10 mL). The combined organic extracts was dried over anhydrous Na_2SO_4, decanted and concentrated by rotary evaporation. The residue was purified by silica gel chromatography using DCM/MeOH = (20/1 to 10/1) to obtain pure product.[5]



***N*-((4-oxo-2-phenylchroman-6-yl)methyl)benzamide**

Yield: 220 mg (0.6 mmol, 65%).

Physical State: light yellow solid.

R_f Value: 0.50 (DCM/MeOH – 10/1).

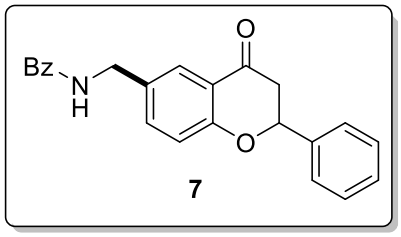
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.65 (d, *J* = 8.2 Hz, 1H), 6.53 (d, *J* = 8.2 Hz, 1H), 5.69 – 5.57 (m, 1H), 5.47 – 5.37 (m, 1H), 5.18 (ddd, *J* = 8.2, 5.2, 2.8 Hz, 1H), 5.11 – 5.01 (m, 1H), 3.84 (s, 3H), 3.36 (dd, *J* = 5.9, 3.3 Hz, 1H), 3.03 (d, *J* = 18.6 Hz, 1H), 2.79 – 2.68 (m, 1H), 2.59 (dd, *J* = 12.2, 3.8 Hz, 1H), 2.43 (d, *J* = 5.1 Hz, 3H), 2.41 – 2.23 (m, 2H), 2.15 (s, 3H), 2.05 (td, *J* = 12.3, 5.1 Hz, 1H), 1.86 (dd, *J* = 12.6, 1.8 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.71, 146.87, 142.24, 130.71, 129.71, 128.55, 127.07, 119.25, 113.90, 88.22, 59.17, 56.73, 46.77, 43.17, 42.87, 40.83, 35.49, 20.99, 20.46.

IR (ATR in $CDCl_3$) *v*2914 (w), 2814 (w), 1750 (s), 1636 (s), 1435 (s), 1230 (s), 1170 (w), 1043 (s), 902 (m), 782 (m), 697 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{20}H_{24}NO_4$ [M+H$^+$]: 342.1705, found: 342.1707.

3.7. Preparation of 7-11



7

According to GP-3, flavanone (0.2 mmol, 44.8 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded **7** after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-((4-oxo-2-phenylchroman-6-yl)methyl)benzamide**

Yield: 20 mg (0.06 mmol, 29%).

Physical State: yellow solid.

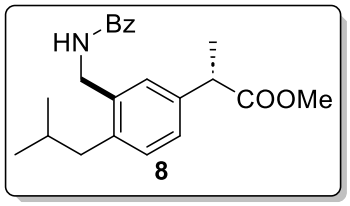
R_f Value: 0.40 (isohexane/EtOAc – 1/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.3 Hz, 1H), 7.79 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.58 – 7.41 (m, 9H), 7.06 (d, *J* = 8.5 Hz, 1H), 6.52 (s, 1H), 5.47 (dd, *J* = 13.1, 3.1 Hz, 1H), 4.63 (d, *J* = 5.8 Hz, 2H), 3.08 (dd, *J* = 16.9, 13.1 Hz, 1H), 2.89 (dd, *J* = 16.9, 3.1 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 191.97, 167.57, 161.17, 138.67, 136.35, 134.32, 131.94, 131.82, 129.02, 128.99, 128.78, 127.13, 126.29, 126.06, 120.86, 118.96, 79.81, 44.65, 43.38.

IR (ATR in $CDCl_3$) *v*3354 (s), 2981 (s), 1692 (s), 1643 (s), 1539 (s), 1490 (s), 1297 (s), 1230 (s), 909 (m), 805 (w), 760 (w), 700 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{23}H_{20}NO_3$ [M+H$^+$]: 358.1438, found: 358.1439.



According to GP-3, S(+)-Ibuprofen methyl ester **8-1** (0.2 mmol, 44.0 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded **8** as a colorless oil after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

methyl (S)-2-(3-(benzamidomethyl)-4-isobutylphenyl)propanoate

Yield: 28 mg (0.08 mmol, 41%).

Physical State: colorless oil.

R_f Value: 0.3 (isohexane/EtOAc – 3/1).

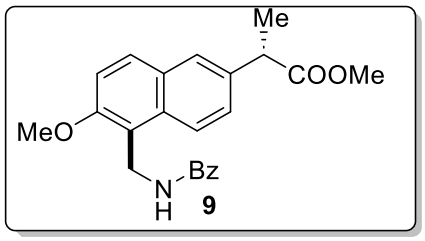
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 5.2, 3.4 Hz, 2H), 7.50 (ddd, *J* = 6.6, 3.8, 1.2 Hz, 1H), 7.43 (dd, *J* = 10.4, 4.7 Hz, 2H), 7.23 (d, *J* = 1.7 Hz, 1H), 7.19 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.15 (d, *J* = 7.9 Hz, 1H), 6.17 (s, 1H), 4.65 (d, *J* = 5.2 Hz, 2H), 3.70 (q, *J* = 7.2 Hz, 1H), 3.66 (s, 3H), 2.53 (d, *J* = 7.2 Hz, 2H), 1.92 – 1.81 (m, 1H), 1.49 (d, *J* = 7.2 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.17, 167.29, 139.33, 138.67, 136.02, 134.58, 131.68, 131.13, 128.77, 128.51, 127.07, 126.81, 52.20, 45.11, 42.01, 41.50, 30.10, 22.72, 18.76.

IR (ATR in $CDCl_3$) *v*3317 (s), 2952 (s), 2870 (m), 1736 (s), 1640 (s), 1535 (s), 1289 (m), 1162 (m), 846 (w), 693 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{22}H_{28}NO_3[M+H^+]$: 354.2069, found: 354.2066.

Enantiomer ratio was determinted by HPLC using a Daicel Chiralpak AS-H column (flow rate 1.0 mL/min, *n*-hexane/*i*-PrOH = 98.0/2.0, λ = 230.4 nm), t_R = 118.70 min (minor), t_R = 129.01 min (major); 99% *ee*.



According to GP-3, S(+)-Naproxen methyl ester **9-1** (0.2 mmol, 48.8 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded **9** as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

methyl (S)-2-(5-(benzamidomethyl)-6-methoxynaphthalen-2-yl)propanoate

Yield: 41 mg (0.11 mmol, 54%).

Physical State: white solid.

R_f Value: 0.15 (isohexane/EtOAc – 5/1).

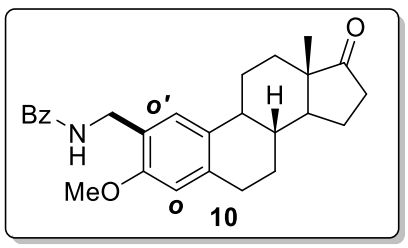
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.9 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.74 – 7.70 (m, 3H), 7.49 – 7.32 (m, 5H), 6.37 (s, 1H), 5.12 (d, *J* = 5.3 Hz, 2H), 4.00 (s, 3H), 3.89 – 3.85 (m, 1H), 3.66 (s, 3H), 1.57 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.13, 167.31, 155.72, 136.03, 134.76, 132.17, 131.45, 130.06, 129.30, 128.61, 127.49, 127.09, 126.64, 124.02, 118.60, 113.29, 56.68, 52.23, 45.34, 34.68, 18.64.

IR (ATR in $CDCl_3$) *v*3350 (s), 2974 (m), 2948 (s), 1840 (m), 1733 (s), 1643 (s), 1505 (s), 1457 (m), 1252 (s), 1162 (m), 1095 (w), 890 (m), 805 (w), 715 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{23}H_{24}NO_4$ [$M+H^+$]: 378.1705, found: 378.1714.

Enantiomer ratio was determinted by HPLC using a Daicel Chiralpak OD-H column (flow rate 1.0 mL/min, *n*-hexane/*i*-PrOH = 95.0/5.0, λ = 230.4 nm), t_R = 52.09 min (minor), t_R = 71.60 min (major); 79% *ee*.



According to GP-3, methyl estrone (0.2 mmol, 56.8 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.3 mmol, 91.5 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 9.6 mg) in DCE (1 mL) afforded 3w as a white solid after purification on silica gel (isohexane/EA = 10/1 to 5/1). Reaction time: 18 h.

***N*-(((8R,13S)-3-methoxy-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-2-yl)methyl)benzamide *o*-10** and ***N*-(((8R,13S)-3-methoxy-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-4-yl)methyl)benzamide *p*-10**

Yield: 58 mg (0.14 mmol, 71%).

Physical State: white solid.

R_f Value: 0.30 (isohexane/EtOAc – 5/1).

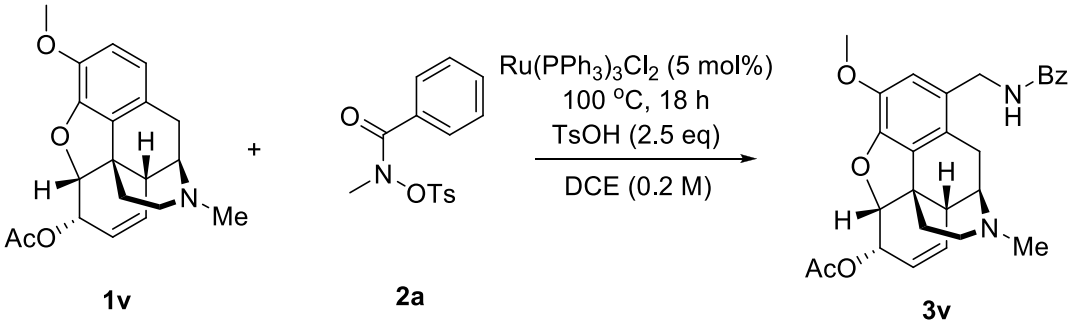
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 – 7.68 (m, 2H), 7.49 – 7.37 (m, 3H), 7.28 (s, 0.77H), 6.79 (d, *J* = 8.7 Hz, 0.23H), 6.65 - 6.60 (m, 1H), 4.71 (dd, *J* = 5.5, 4.1 Hz, 0.43H), 4.60 (dd, *J* = 5.7, 1.4 Hz, 1.57H), 3.88 (s, 0.70H), 3.86 (s, 2.30H), 3.05 – 2.83 (m, 2H), 2.54 – 2.41 (m, 2H), 2.16 – 1.93 (m, 4H), 1.67 – 1.37 (m, 7H), 0.93 – 0.87 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 220.90, 167.12, 156.52, 155.91, 137.43, 136.92, 135.05, 134.88, 132.09, 131.40, 131.37, 128.60, 127.64, 127.04, 125.93, 124.28, 123.80, 111.02, 108.22, 55.75, 55.61, 50.55, 50.48, 48.13, 48.01, 44.44, 44.04, 40.31, 38.51, 37.64, 35.98, 35.57, 31.72, 31.68, 29.87, 26.72, 26.65, 26.09, 21.70, 13.98, 13.92.

IR (ATR in $CDCl_3$) *v*3399 (s), 2929 (s), 2840 (m), 1736 (s), 1651 (m), 1505 (s), 1267 (m), 1088 (m), 861 (w), 678 (m) cm^{-1}.

HRMS (ESI MS) calcd for $C_{27}H_{32}NO_3$ [$M+H^+$]: 418.2382, found: 418.2389.

3.8. Procedure for preparation of 11



1v **2a** **3v**

A mixture of codeine acetate **11-1** (0.1 mmol, 34.1 mg), *N*-methyl-*N*-(tosyloxy)benzamide (0.15 mmol, 45.8 mg) and $Ru(PPh_3)_3Cl_2$ (5 mol%, 4.8 mg) in DCE (0.5 mL) in a 15 mL sealed glass vial was heated at 100 ^oC under air with vigorous stirring for 18 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated *in vacuo* and purified by column chromatography on silica gel (DCM/MeOH – 20/1 to 10/1)to give the corresponding product **11**.

methyl (S)-2-(5-(benzamidomethyl)-6-methoxynaphthalen-2-yl)propanoate

Yield: 10 mg (0.02 mmol, 21%).

Physical State: white solid.

R_f Value: 0.45 (DCM/MeOH – 10/1).

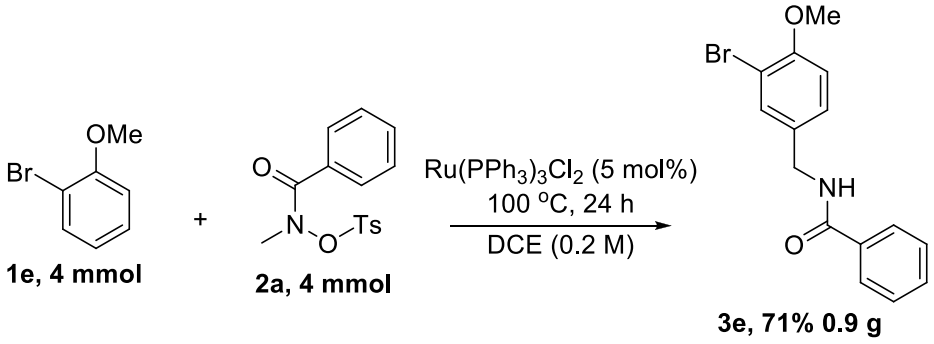
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 – 7.72 (m, 2H), 7.55 – 7.48 (m, 1H), 7.47 – 7.39 (m, 2H), 6.68 (s, 1H), 6.16 (s, 1H), 5.65 (d, *J* = 10.0 Hz, 1H), 5.49 – 5.39 (m, 1H), 5.19 (dt, *J* = 5.1, 2.8 Hz, 1H), 5.09 (d, *J* = 6.1 Hz, 1H), 4.62 (dd, *J* = 14.5, 5.8 Hz, 1H), 4.43 (dd, *J* = 14.5, 4.9 Hz, 1H), 3.86 (s, 3H), 3.43 – 3.31 (m, 1H), 3.06 (d, *J* = 18.6 Hz, 1H), 2.78 (s, 1H), 2.66 – 2.58 (m, 1H), 2.41 (s, 3H), 2.27 (dd, *J* = 18.8, 6.6 Hz, 2H), 2.15 (s, 3H), 1.85 (d, *J* = 10.9 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.69, 167.31, 146.51, 142.29, 134.45, 131.78, 131.52, 129.54, 128.83, 127.47, 127.00, 114.83, 88.20, 68.10, 59.00, 56.94, 46.89, 43.17, 42.82, 41.15, 40.32, 40.30, 35.34, 20.97, 18.67.

IR (ATR in $CDCl_3$) *v*3309 (s), 2937 (m), 1733 (m), 1636 (s), 1505 (s), 1446 (m), 1371 (s), 1241 (s), 1121 (w), 1054 (w), 909 (m), 697 (s), 667 (s) cm^{-1}.

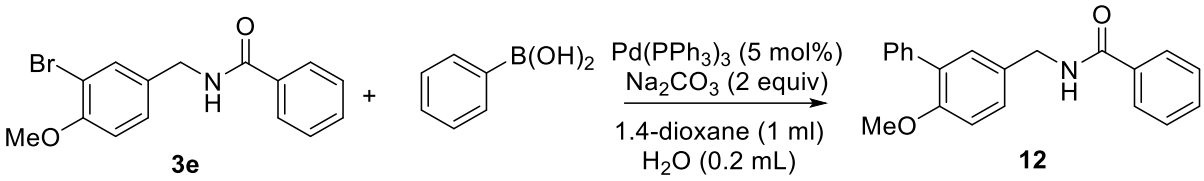
HRMS (ESI MS) calcd for $C_{28}H_{31}N_2O_5$ [$M+H^+$]: 475.2233, found: 475.2230

3.9. Scale-up reaction

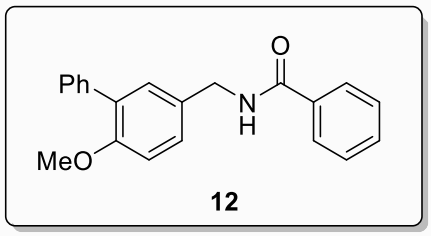


A mixture of **1e** (0.74 g, 4.0 mmol, 1.0 equiv), *N*-benzoyl-*O*-tosyl-*N*-methylhydroxylamine **2a** (1.2 g, 4.0 mmol, 1.0 equiv), $Ru(PPh_3)_3Cl_2$ (191 mg, 0.2 mmol, 5 mol%), and 20 mL DCE in a 100 mL sealed high-pressure glass tube was heated at 100 ^oC under air with vigorous stirring for 24 hours. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through celite. The filtrate was concentrated *in vacuo* and purified by column chromatography on silica gel (isohexane/EA = 10/1 to 5/1) to give the product.

3.10. Further transformation-Heck reaction



An argon-flooded Schlenk tube containing phenylboronic acid (29.2 mg, 0.24 mmol, 1.2 equiv) in dry 1.4-dioxane (1 mL) was charged with sodium carbonate (42.4 mg, 0.4 mmol, 2 equiv), deionized water (0.4 mL) the *N*-(3-bromo-4-methoxybenzyl)benzamide **3e** (63.8 mg, 0.2 mmol, 1 equiv), and $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol, 0.05 equiv). After refluxing for 18 h, the crude mixture was cooled to room temperature and filtered through a short pad of celite. After the addition of brine (50 mL) and extraction with toluene (3 x 50 mL) the organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/isohexane = 1:7) to provide the product.[6]



***N*-((6-methoxy-[1,1'-biphenyl]-3-yl)methyl)benzamide**

Yield: 59 mg (0.19 mmol, 94%).

Physical State: white solid.

R_f Value: 0.27 (isohexane/EtOAc – 5/1).

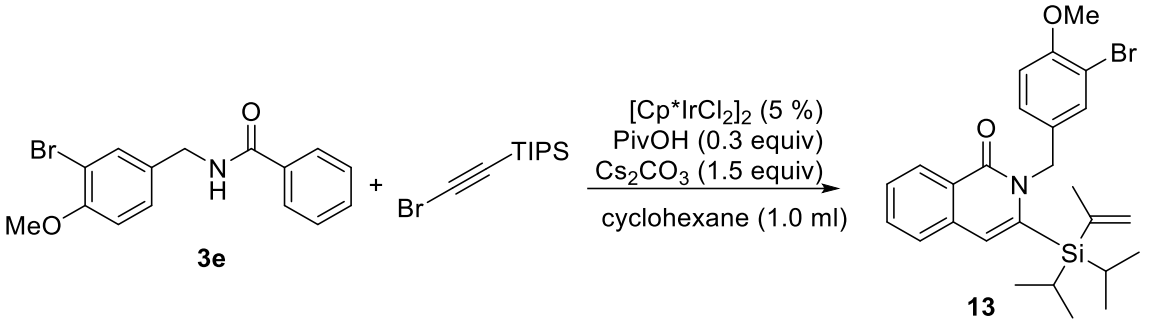
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.73 (m, 2H), 7.55 – 7.46 (m, 3H), 7.44 – 7.37 (m, 4H), 7.36 – 7.29 (m, 3H), 6.96 (d, *J* = 8.7 Hz, 1H), 6.51 (s, 1H), 4.62 (d, *J* = 5.6 Hz, 2H), 3.80 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.39, 156.13, 138.23, 134.55, 131.60, 131.15, 130.79, 130.56, 129.59, 128.67, 128.44, 128.16, 127.23, 127.08, 111.65, 55.84, 43.78.

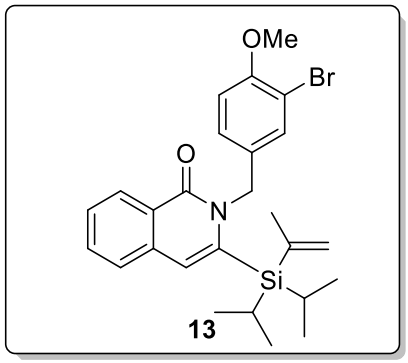
IR (ATR in $CDCl_3$) *v*3306 (s), 3060 (m), 2933 (s), 2832 (m), 1640 (s), 1539 (s), 1487 (s), 1297 (m), 1263 (s), 1148 (w), 1028 (m), 805 (m), 775 (w), 700 (s) cm^{-1}.

HRMS (ESI MS) calcd for $C_{21}H_{20}NO_2$ [$M+H^+$]: 318.1494, found: 318.1500.

3.11. Further transformation-C-H activation



A mixture of required *N*-(3-bromo-4-methoxybenzyl)benzamide **3e** (63.8 mg, 0.2 mmol, 1 equiv), (2-bromoethynyl)triisopropylsilane (78 mg, 0.3 mmol, 1.5 equiv), $[Cp^*IrCl_2]_2$ (8.0 mg, 5 mol%), Cs_2CO_3 (97.6 mg, 0.3 mmol, 1.5 equiv), PivOH (6.0 mg, 0.06 mmol, 0.3 equiv) and 1 mL cyclohexane in a 15 mL sealed glass tube was heated at 80 ^oC under air with vigorous stirring for 18 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated *in vacuo* and purified by column chromatography on silica gel (isohexane/EA = 20/1 to 5/1) to give the corresponding product.[7]



2-(3-bromo-4-methoxybenzyl)-3-(diisopropyl(prop-1-en-2-yl)silyl)isoquinolin-1(2H)-one

Yield: 39 mg (0.08 mmol, 81%).

Physical State: yellow oil.

R_f Value: 0.24 (isohexane/EtOAc – 5/1).

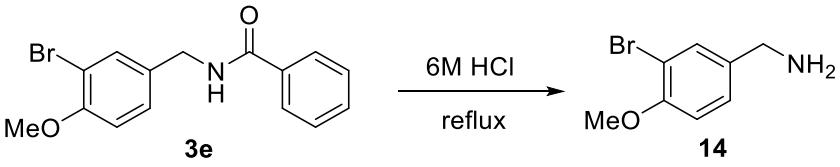
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.60 – 7.52 (m, 2H), 7.48 – 7.43 (m, 1H), 7.31 – 7.27 (m, 1H), 7.12 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 5.90 (dd, *J* = 3.0, 1.6 Hz, 1H), 5.47 (dd, *J* = 2.9, 1.2 Hz, 1H), 5.14 (s, 2H), 3.87 (s, 3H), 1.83 (s, 3H), 1.45 – 1.35 (m, 2H), 1.02 – 0.97 (m, 12H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.33, 155.75, 142.10, 140.64, 139.23, 133.21, 132.17, 131.81, 130.67, 129.95, 128.70, 128.29, 127.99, 126.68, 112.22, 112.08, 107.48, 56.46, 51.01, 24.53, 18.75, 18.42, 18.16, 11.34, 11.02.

IR (ATR in $CDCl_3$) *v*2870 (m), 2183 (w), 1640 (s), 1408 (m), 1148 (w), 1006 (m), 916 (s), 853 (m), 752 (w) cm^{-1}.

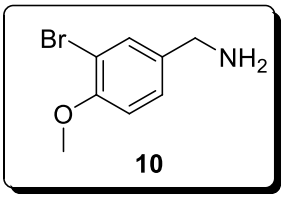
HRMS (ESI MS) calcd for $C_{26}H_{33}BrNO_2Si$ [$M+H^+$]: 498.1464, found: 498.1464.

3.12. Further transformation-Bz removal



Reflux a suspension of *N*-(3-bromo-4-methoxybenzyl)benzamide **3e** (63.8 mg, 0.2 mmol, 1 equiv) in 6 M HCl (13 mL, 80 mmol) until a clear solution was obtained (18 hours). The reaction mixture was cooled to room temperature. Then add NaOH solution solwly basified the resulting

solution, then exacted with DCM (3 times), dry it with K_2CO_3, evaporate to get the pure amine as yellow oil.[8]



(3-bromo-4-methoxyphenyl)methanamine

Yield: 33 mg (0.14 mmol, 95%).

Physical State: yellow oil.

R_f Value: 0.05 (isohexane/EtOAc – 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 2.0 Hz, 1H), 7.24 – 7.20 (m, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 3.90 – 3.82 (m, 5H), 2.17 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.90, 133.67, 132.31, 127.31, 112.10, 111.80, 56.46, 31.07.

IR (ATR in $CDCl_3$) *v*3350 (s), 2922 (s), 2840 (m), 1602 (w), 1494 (s), 1256 (s), 1054 (s), 1021 (w), 808 (m), 738 (w) cm^{-1}.

HRMS (ESI MS) calcd for [$C_8H_{10}BrNO + H^+ - NH_3$]: 200.9738, found: 200.9739.

4. References

[1] G. Cecere, C. M. König, J. L. Alleva, D. W. C. MacMillan, *J. Am. Chem. Soc.* 2013, **135**, 11521–11524.

[2] X. Ma, I. R. Hazelden, T. Langer, R. H. Munday, J. F. Bower, *J. Am. Chem. Soc.* 2019, **141**, 3356–3360.

[3] S. Wang, E. Miao, H. Wang, B. Song, W. Huang, W. Yang, *Chem. Commun.* 2021, **57**, 5929–5932.

[4] Q. Guo, X. Ren, Z. Lu, *Org. Lett.* 2019, **21**, 880–884.

[5] M. P. Paudyal, A. M. Adebesin, S. R. Burt, D. H. Ess, Z. Ma, L. Kürti, J. R. Falck, *Science.* 2016, **353**, 1144–1147.

[6] S. Bhowmik, S. Khanna, K. Srivastava, M. Hasanain, J. Sarkar, S. Verma, S. Batra, *ChemMedChem* 2013, **8**, 1767–1772.

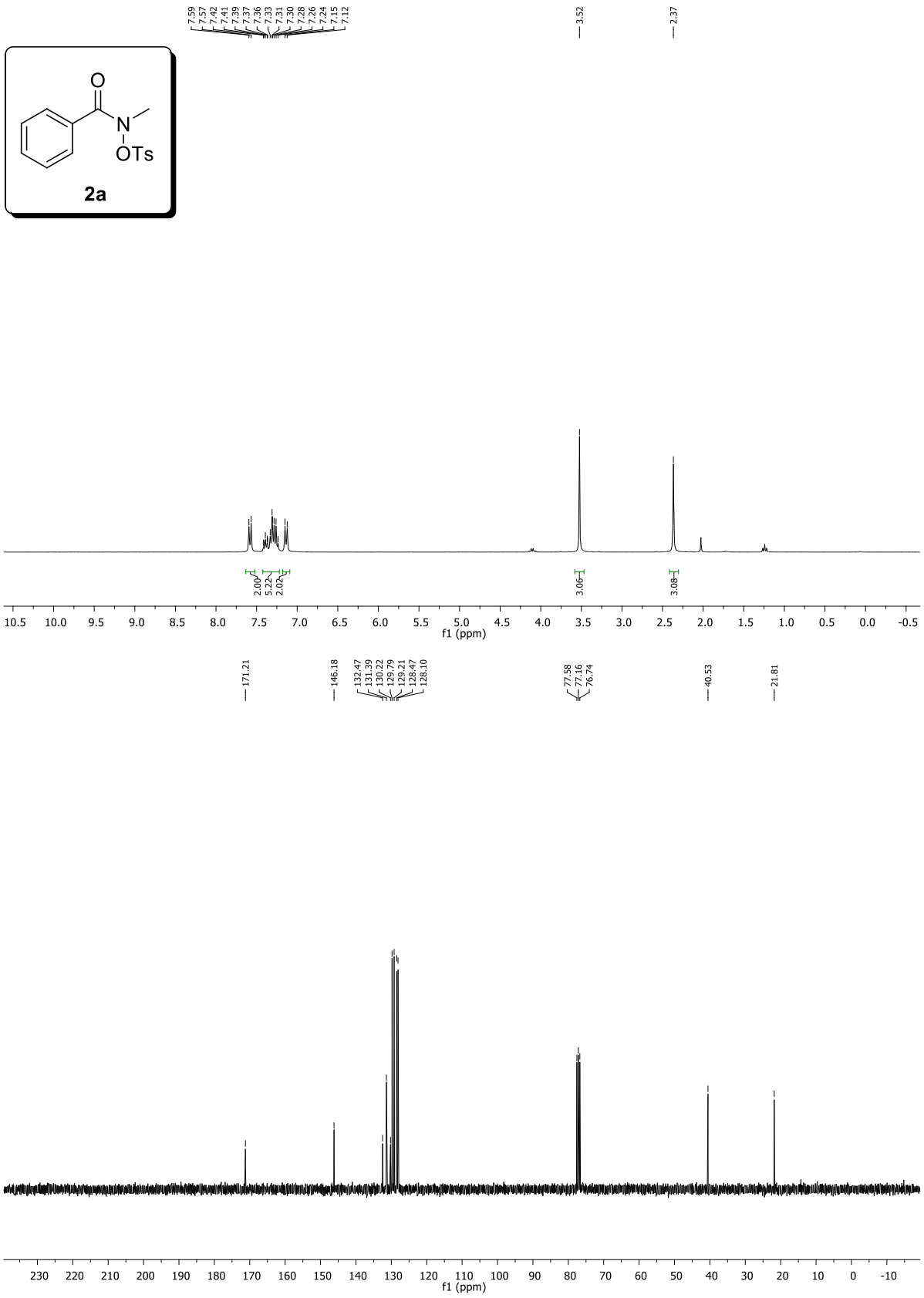
[7] G. Li, J. Hu, R. Zeng, D.-Q. Shi, Y. Zhao, *Org. Lett.* 2018, **20**, 2454–2458.

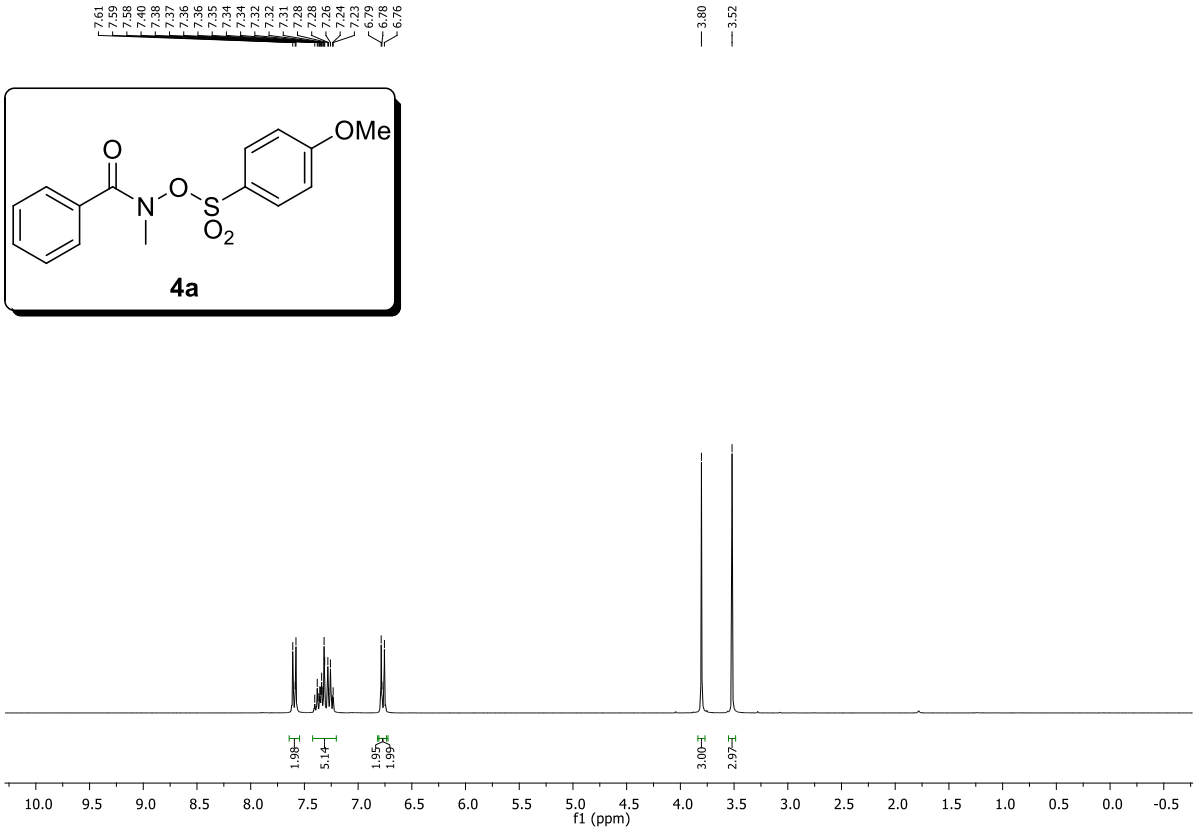
[8] M. Gait, N. Seeman, D. Liu, O. Seitz, M. Komiyama, J. Micklefield, *Org. Biomol. Chem.* 2012, **10**, 8660–8668.

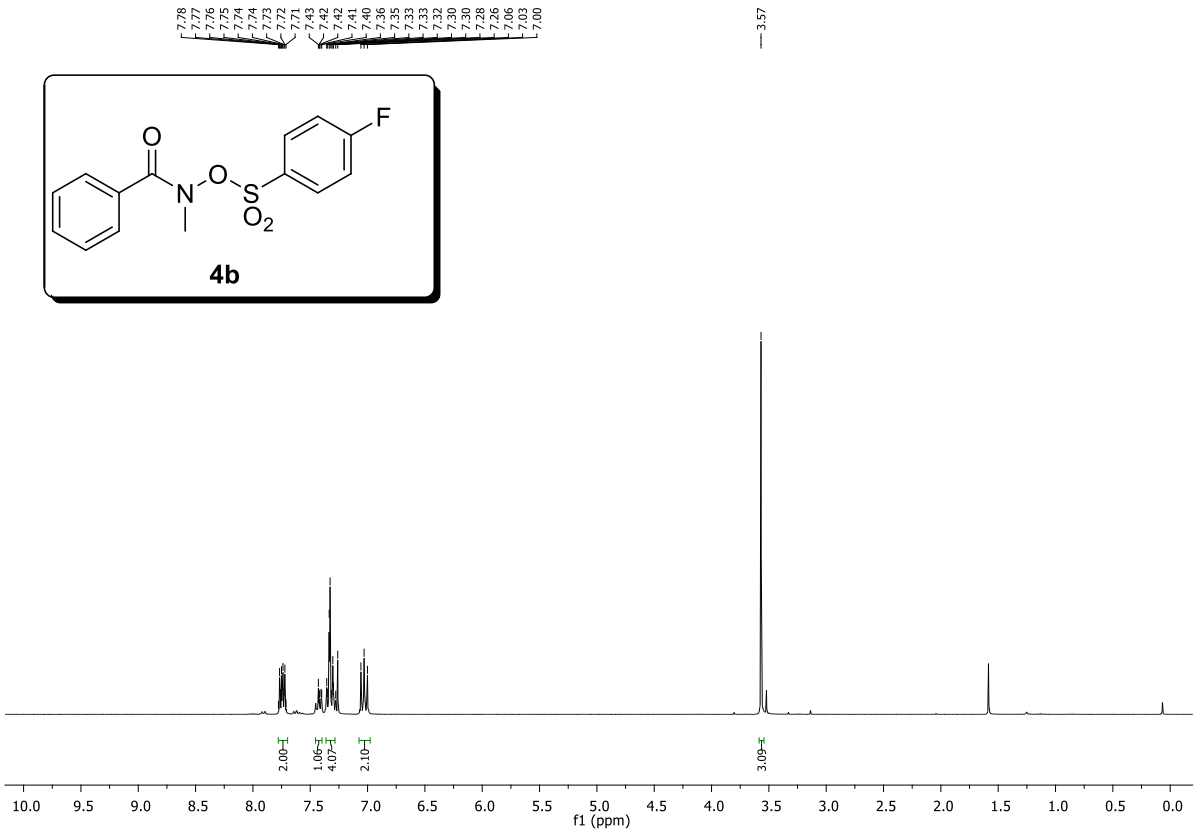
[9] W. Lau, J. K. Kochi, *J. Am. Chem. Soc.* 2002, **106**, 7100–7112.

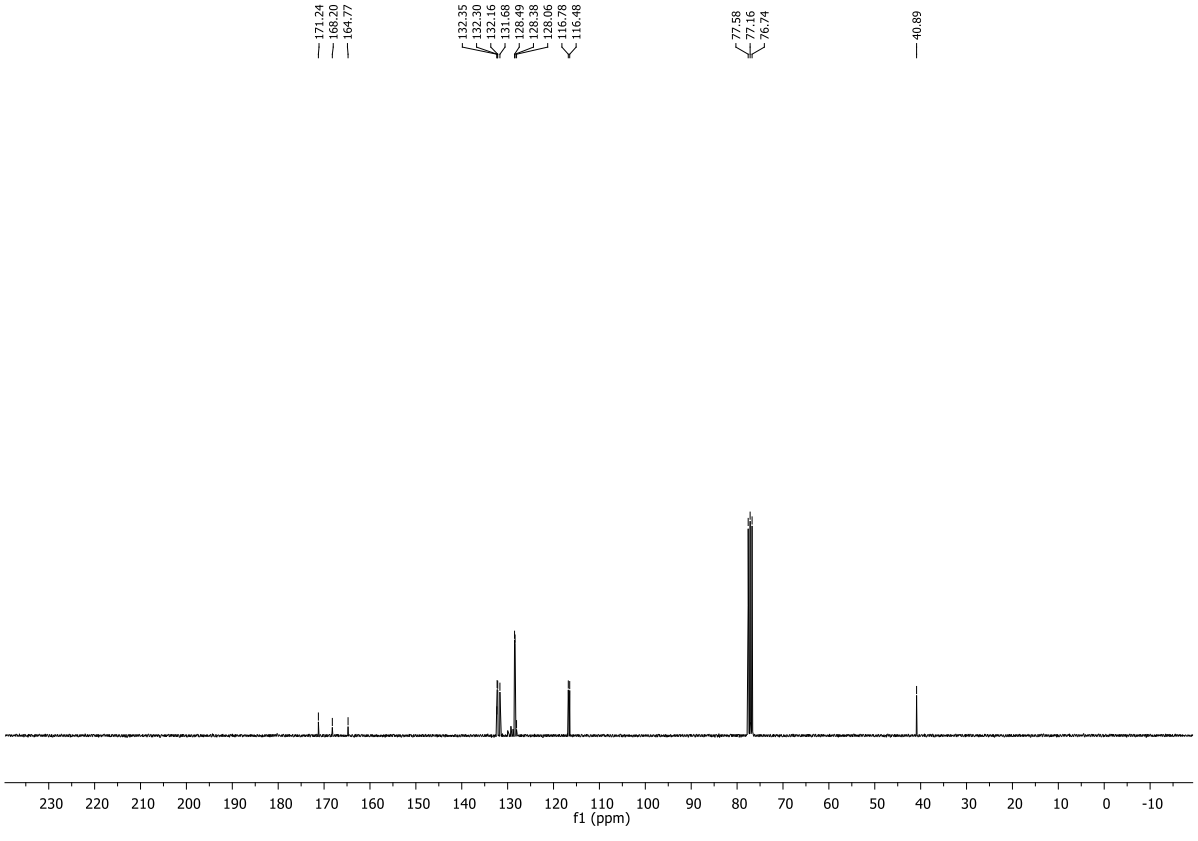
[10] C.-Z. Yao, Z.-F. Xiao, J. Liu, X.-S. Ning, Y.-B. Kang, *Org. Lett.* 2014, **16**, 2498–2501.

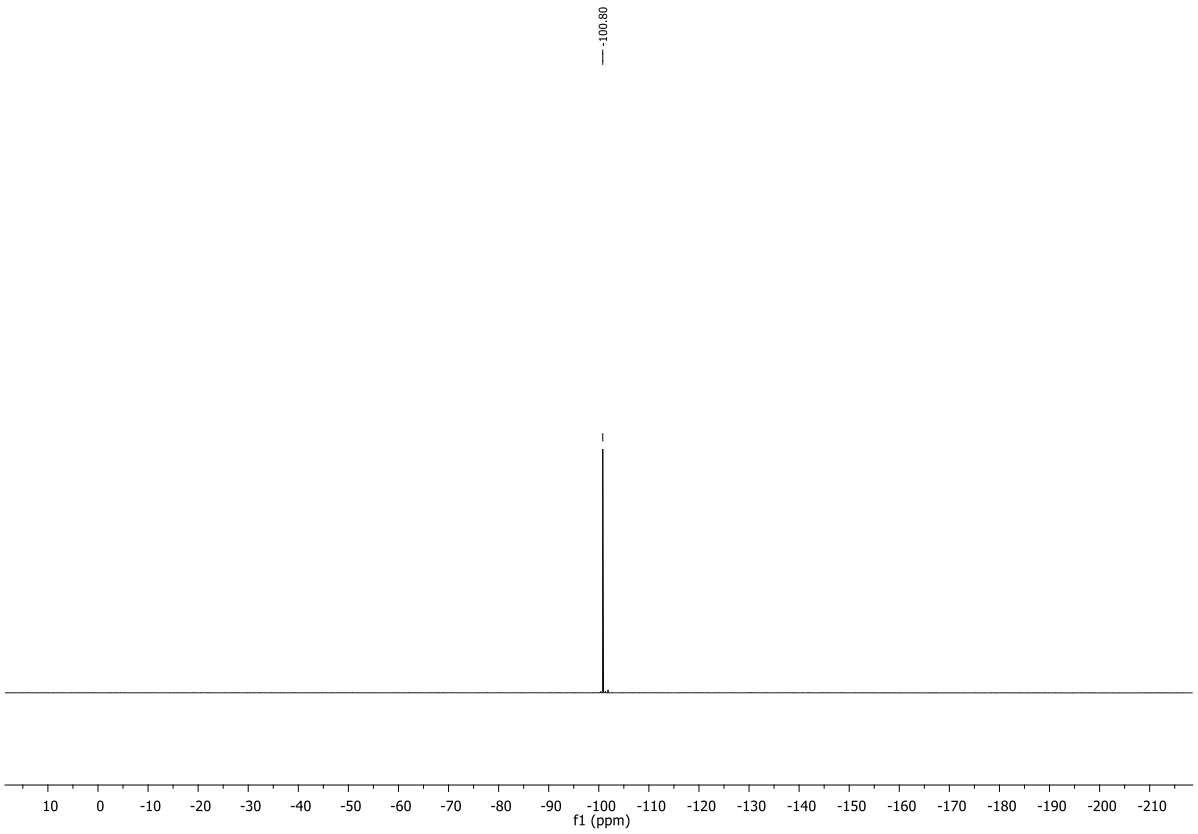
5. ^{1}H-, ^{13}C-, ^{19}F- NMR Spectra

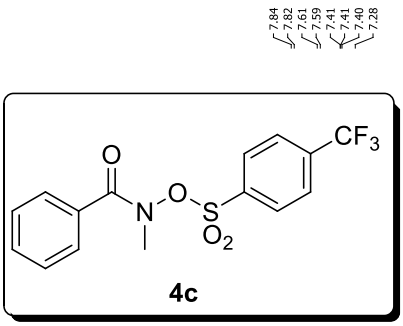



7.61
7.59
7.58
7.40
7.38
7.37
7.36
7.36
7.35
7.34
7.34
7.32
7.32
7.31
7.28
7.28
7.26
7.24
7.23
6.79
6.78
6.76
3.80
3.52
OMe
O
N
O
S
O2
4a
1.98
5.14
1.95
1.99
3.00
2.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
171.17
164.71
132.66
131.58
131.38
128.56
128.19
124.30
114.47
77.58
77.16
76.74
55.87
40.42
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.78
7.77
7.76
7.75
7.74
7.74
7.73
7.72
7.71
7.43
7.42
7.42
7.41
7.40
7.36
7.35
7.33
7.33
7.32
7.30
7.30
7.28
7.26
7.06
7.03
7.00
3.57
O
N
O
S
O2
F
4b
2.00
1.06
4.07
2.10
3.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

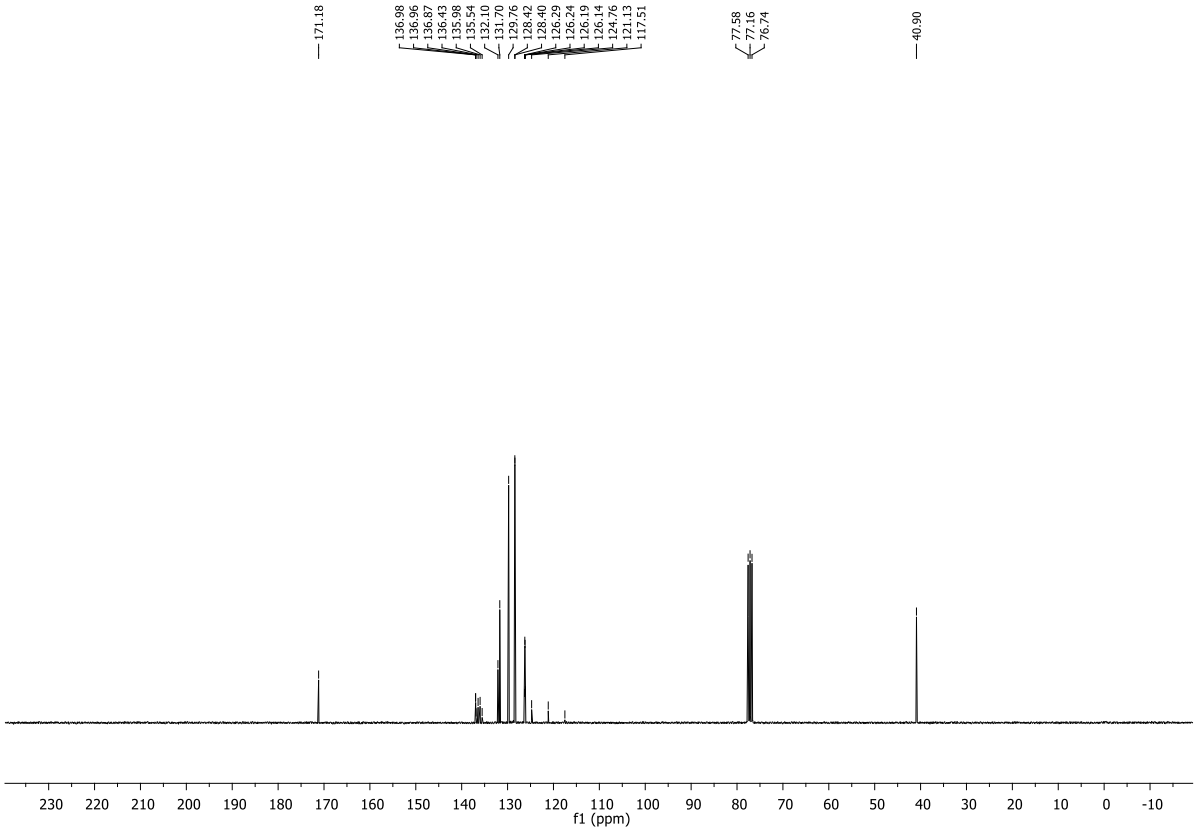

171.24
168.20
164.77
132.35
132.30
132.16
131.68
128.49
128.38
128.06
116.78
116.48
77.58
77.16
76.74
40.89
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

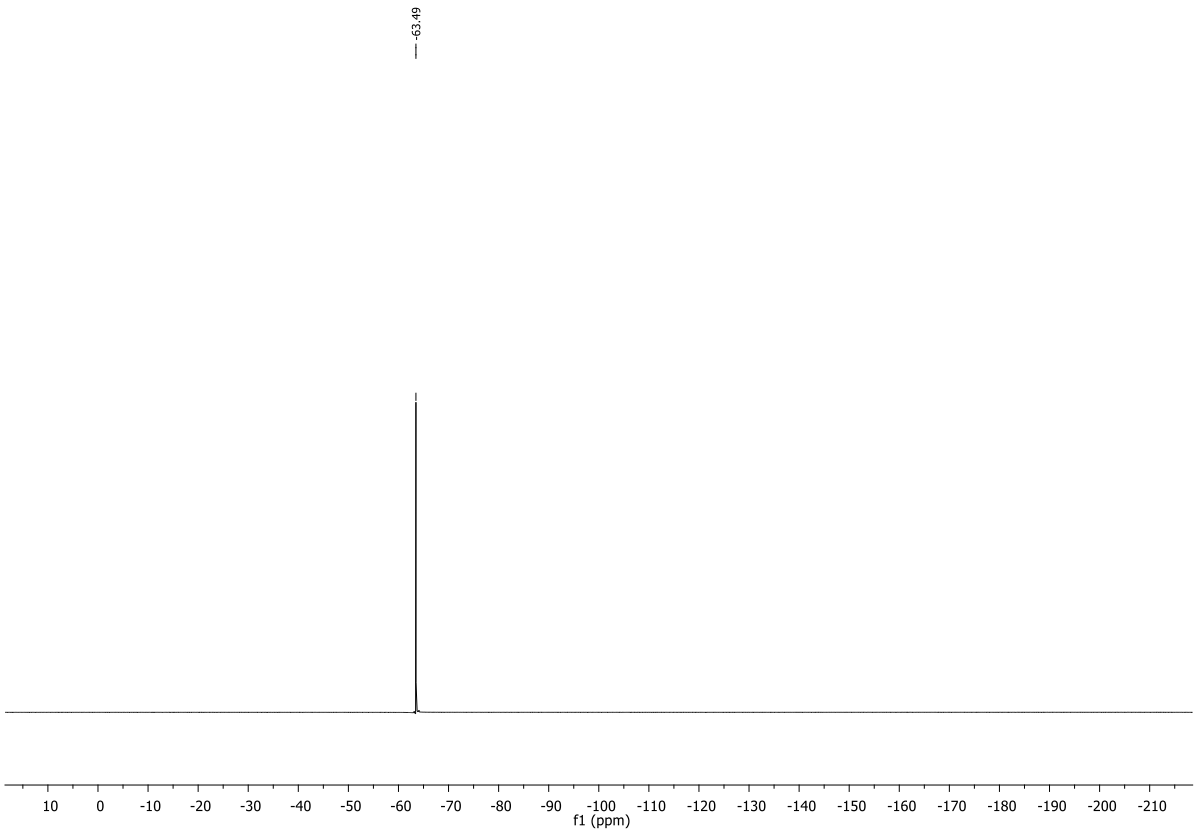

— -100.80
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

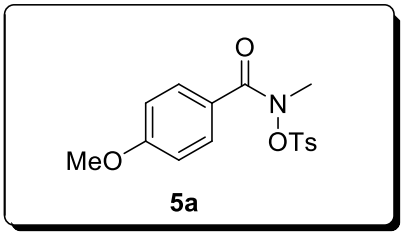

O
N
O
S
O2
CF3

4c

7.84
7.82
7.61
7.59
7.41
7.41
7.40
7.28
3.60
1.96
2.00
5.07
3.00
f1 (ppm)

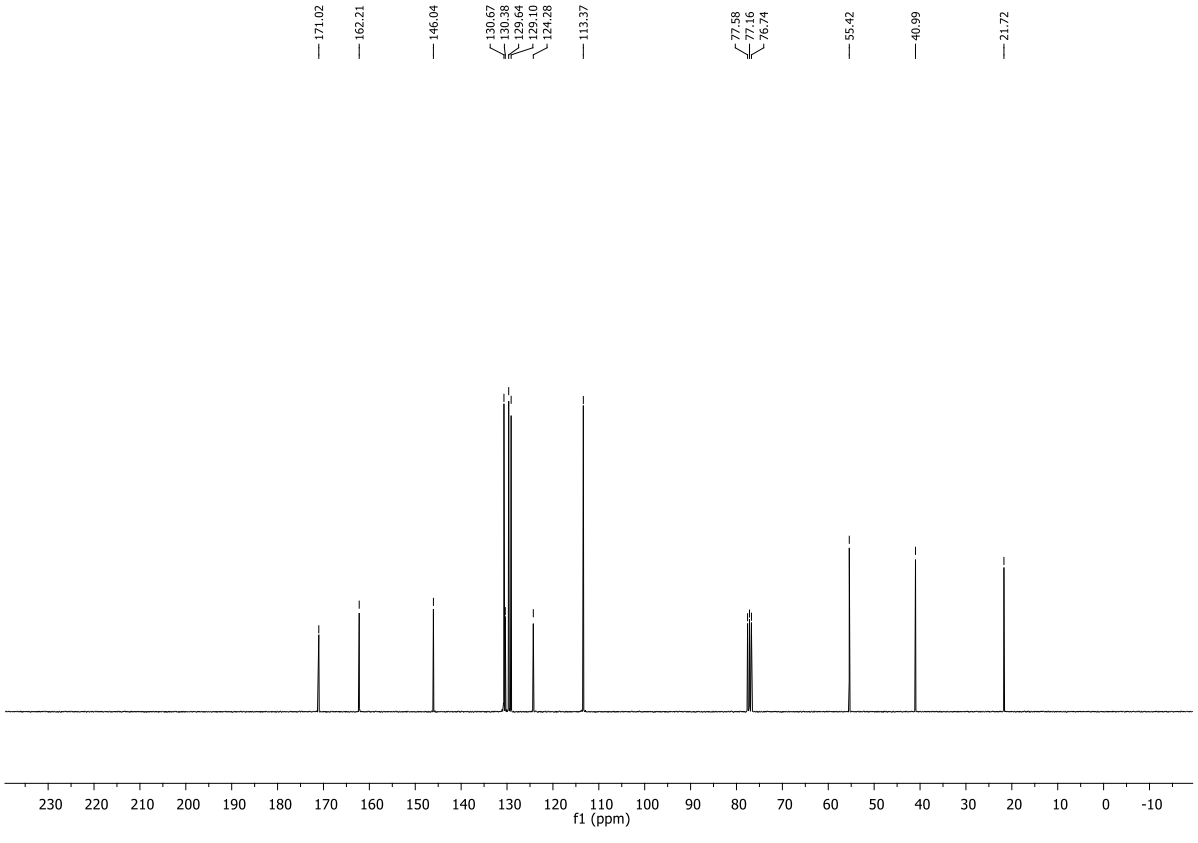

171.18
136.98
136.96
136.87
136.43
135.98
135.54
132.10
131.70
129.76
128.42
128.40
126.29
126.24
126.19
126.14
124.76
121.13
117.51
77.58
77.16
76.74
40.90
f1 (ppm)

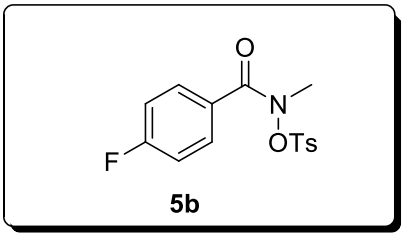

-63.49
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


O
N
OTs
MeO

5a

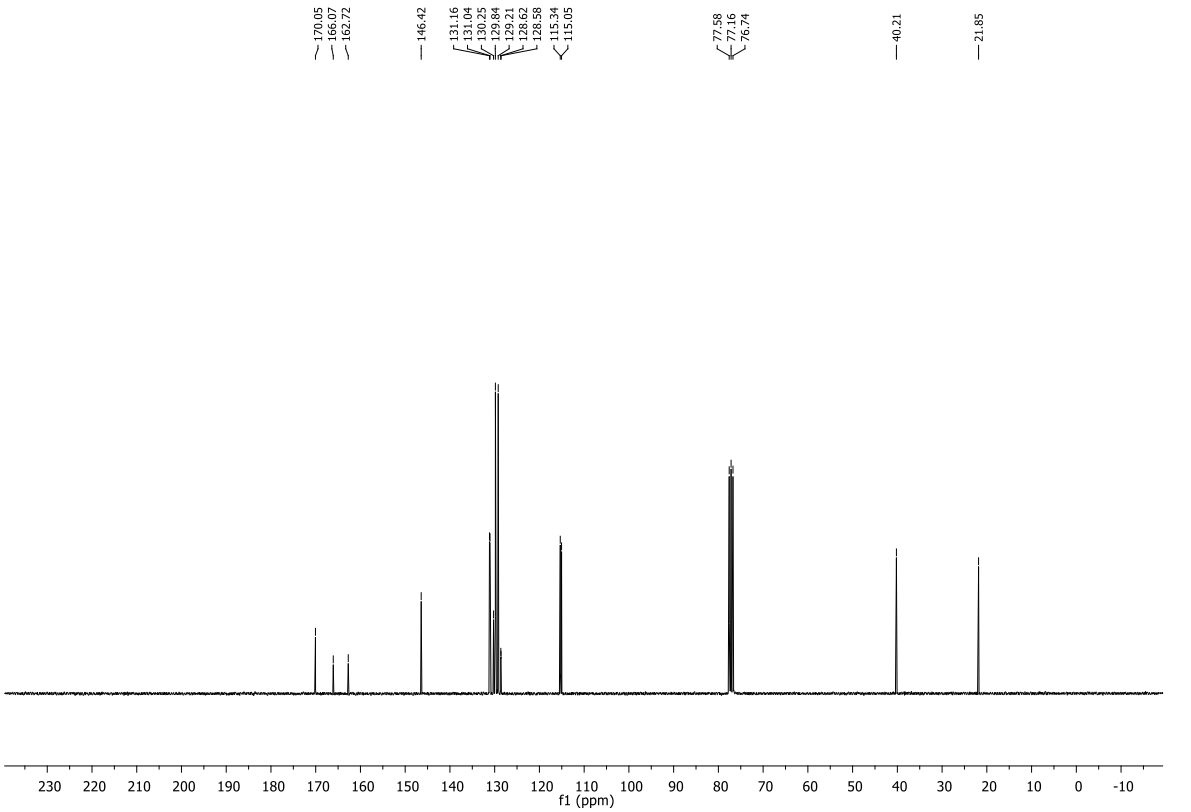
7.63
7.61
7.35
7.32
7.16
7.13
6.77
6.74
3.79
3.46
2.34
2.00
2.03
1.95
2.01
3.03
3.11
3.06
f1 (ppm)

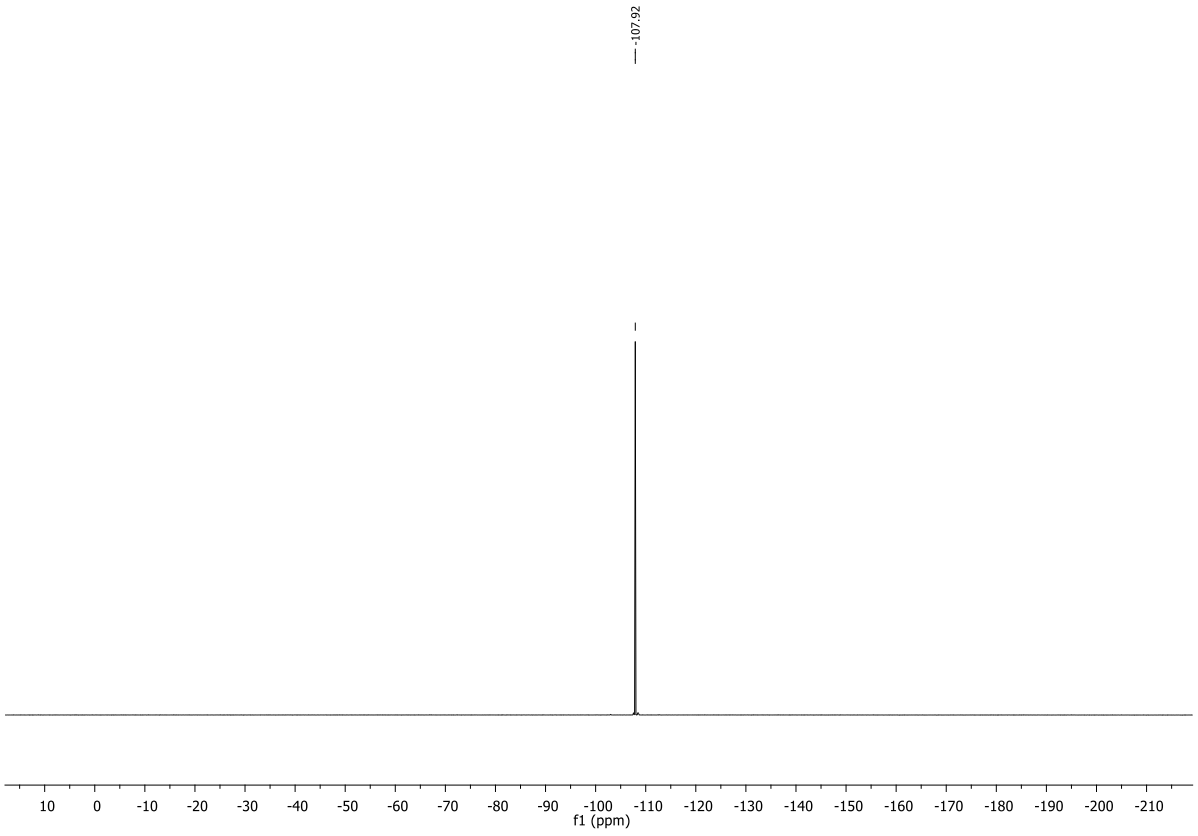

171.02
162.21
146.04
130.67
130.38
129.64
129.10
124.28
113.37
77.58
77.16
76.74
55.42
40.99
21.72
f1 (ppm)

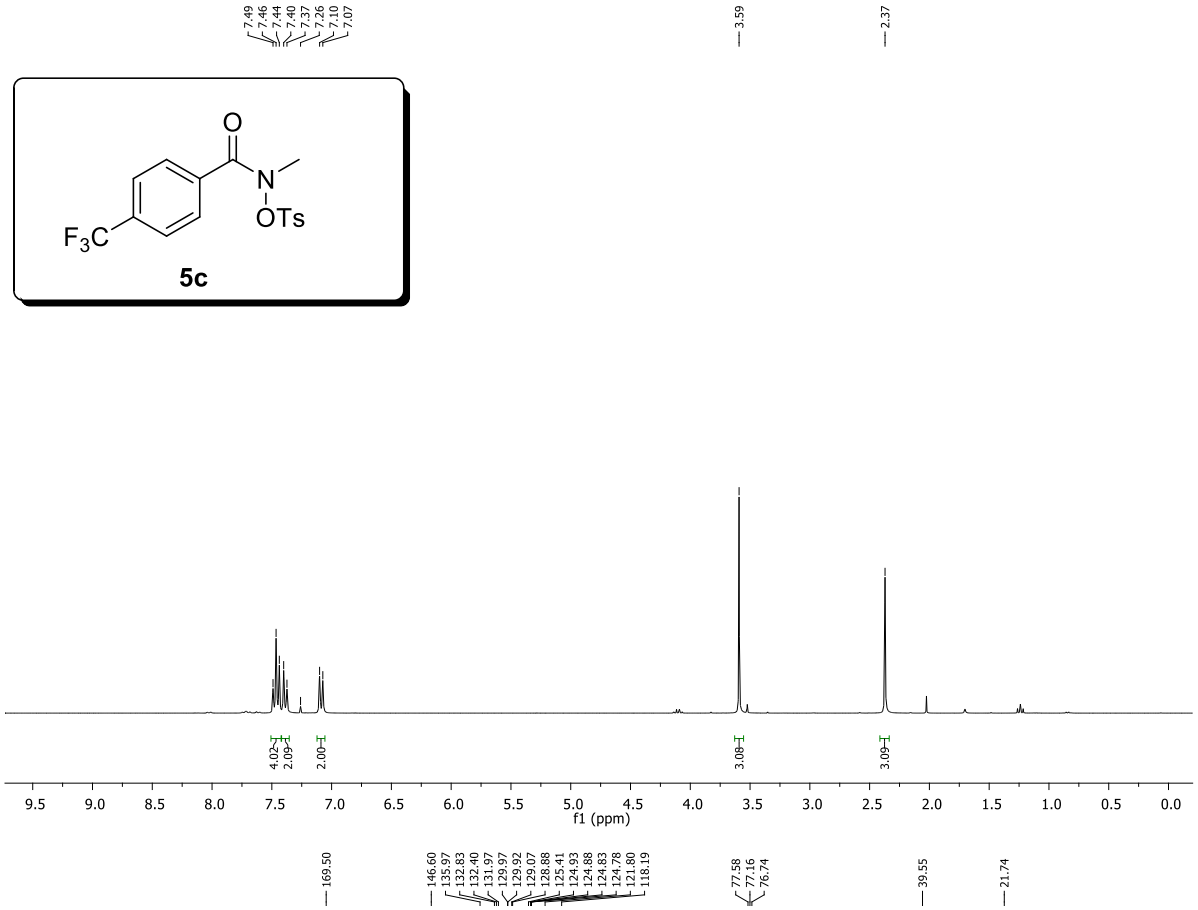

O
N
OTs
F

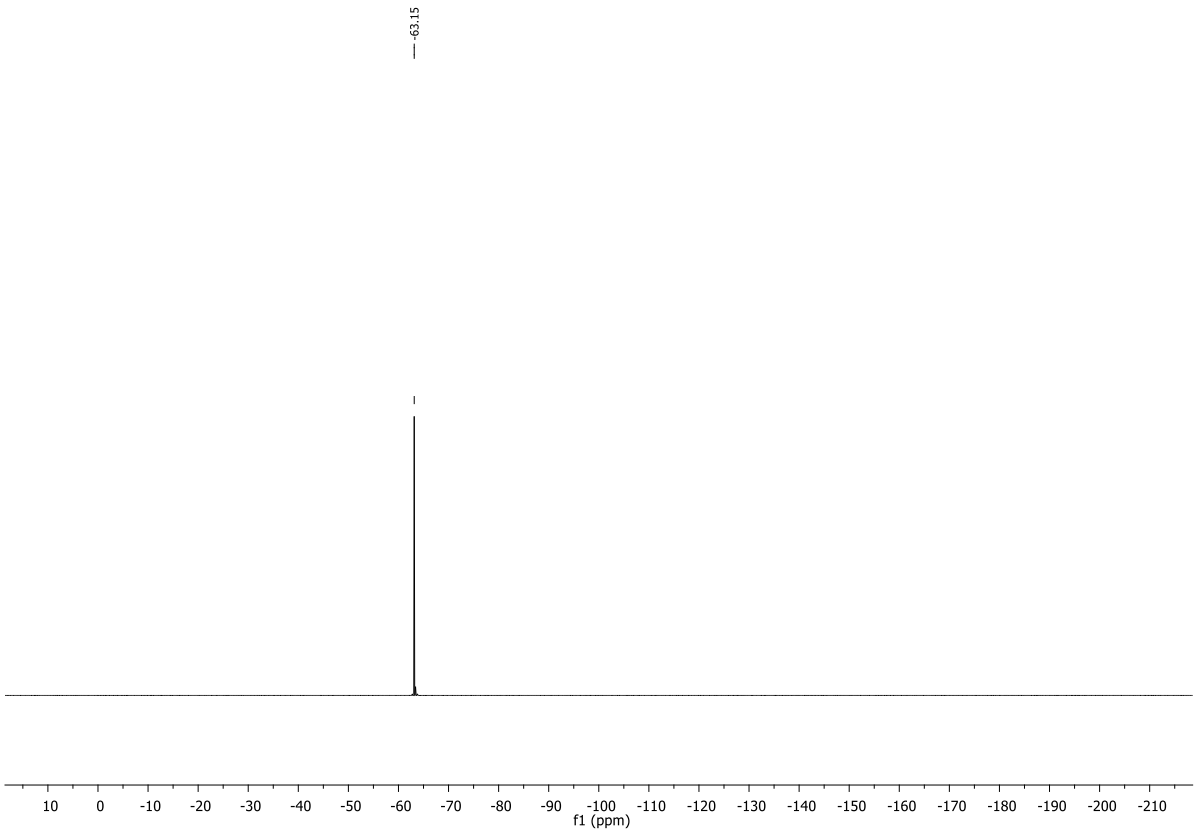
5b

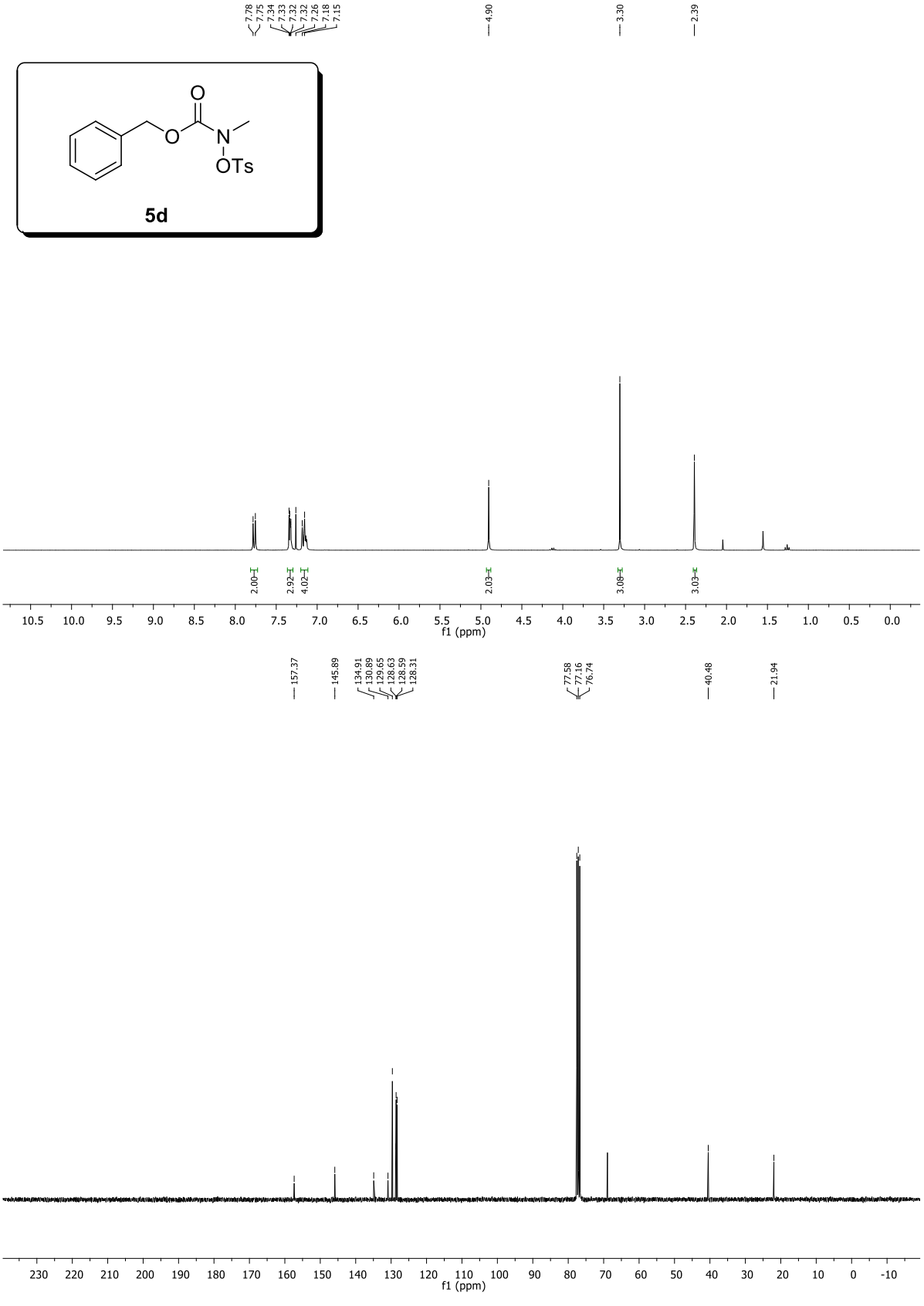
7.58
7.57
7.56
7.55
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.26
7.17
7.15
6.97
6.96
6.95
6.94
6.94
6.92
6.91
3.54
2.39
2.00
2.01
2.05
2.07
3.03
3.07
f1 (ppm)

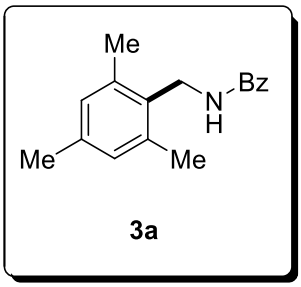

170.05
166.07
162.72
146.42
131.16
131.04
130.25
129.84
129.21
128.62
128.58
115.34
115.05
77.58
77.16
76.74
40.21
21.85
f1 (ppm)


-107.92
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

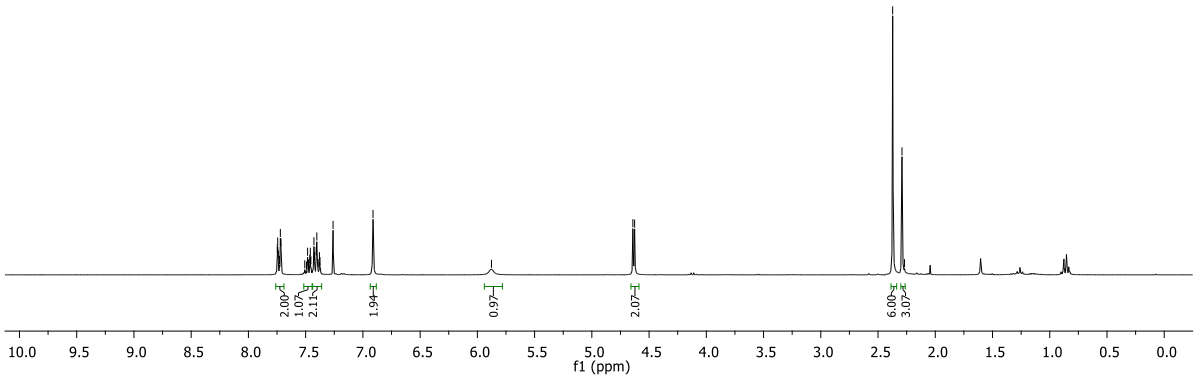

7.49
7.46
7.44
7.40
7.37
7.26
7.10
7.07
3.59
2.37
O
N
OTs
F3C
5c
4.02
2.09
2.00
3.08
3.09
f1 (ppm)
169.50
146.60
135.97
132.83
132.40
131.97
129.97
129.92
129.07
128.88
125.41
124.93
124.88
124.83
124.78
121.80
118.19
77.58
77.16
76.74
39.55
21.74
f1 (ppm)

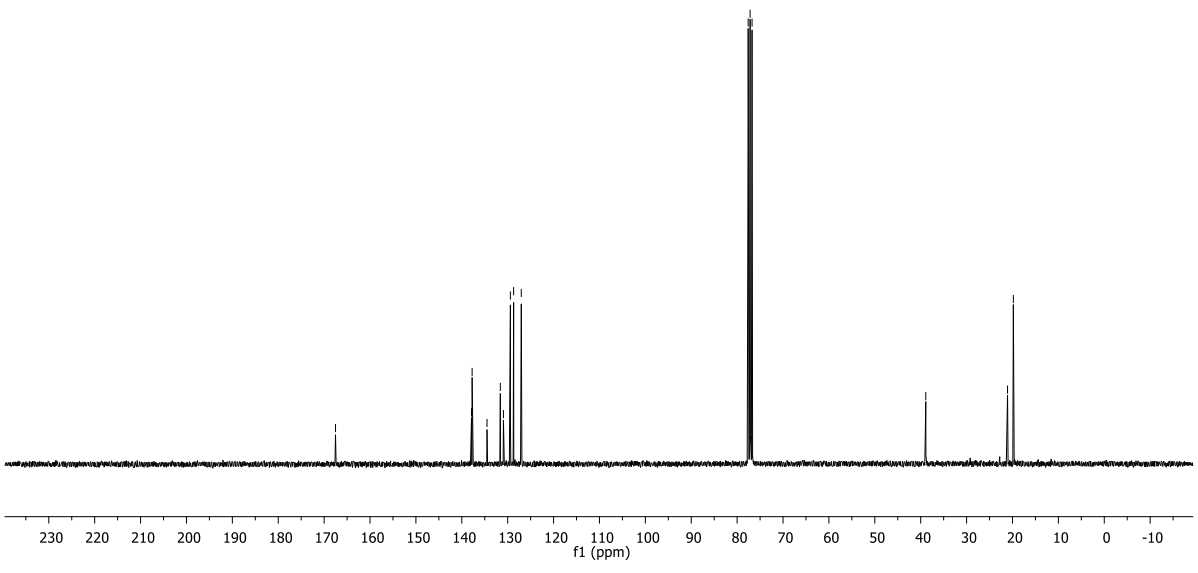

-63.15
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

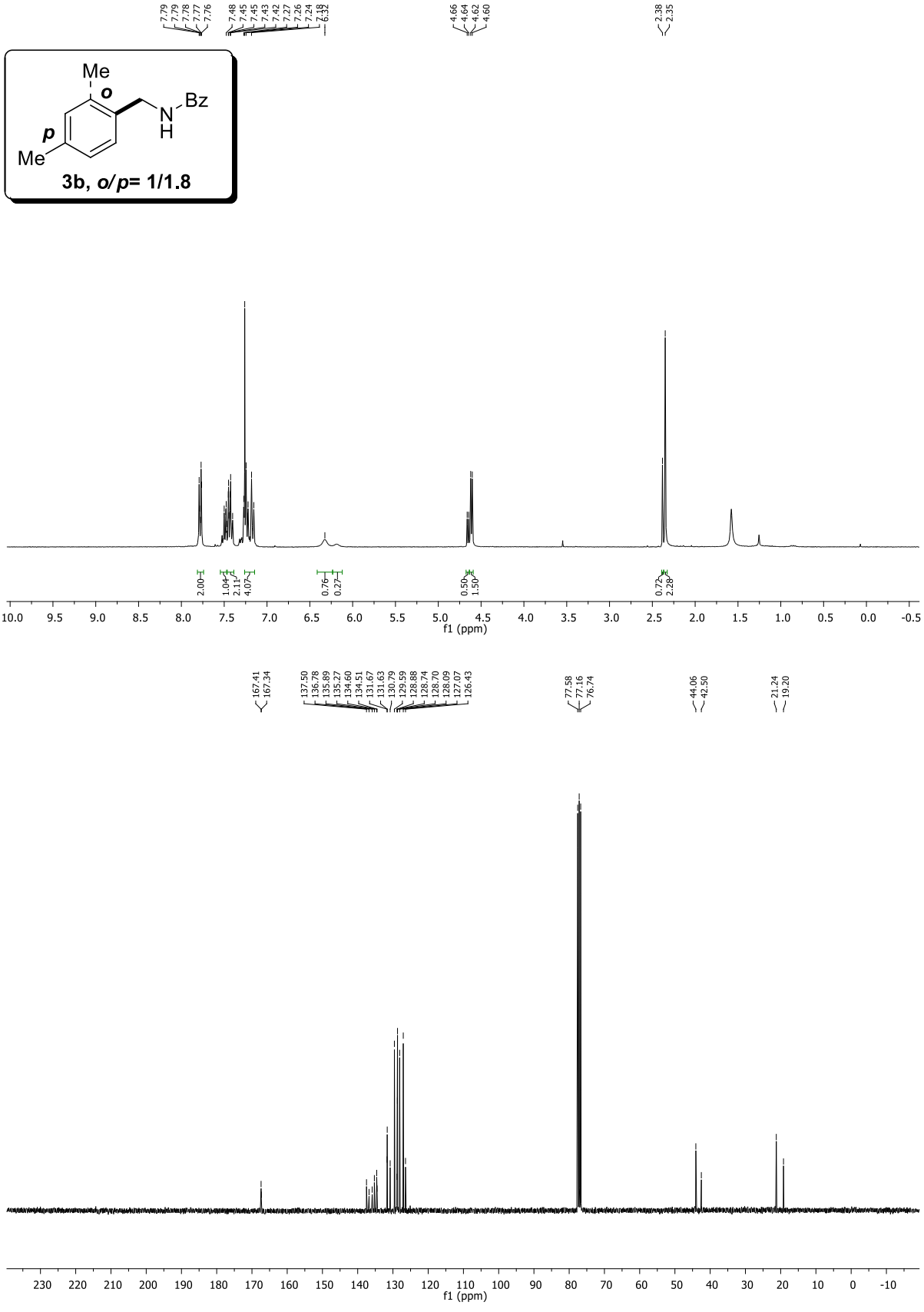

7.78
7.75
7.34
7.33
7.32
7.32
7.26
7.18
7.15
4.90
3.30
2.39
O
O
N
OTs
5d
2.00
2.92
4.02
2.03
3.08
3.03
f1 (ppm)
157.37
145.89
134.91
130.89
129.65
128.63
128.59
128.31
77.58
77.16
76.74
40.48
21.94
f1 (ppm)

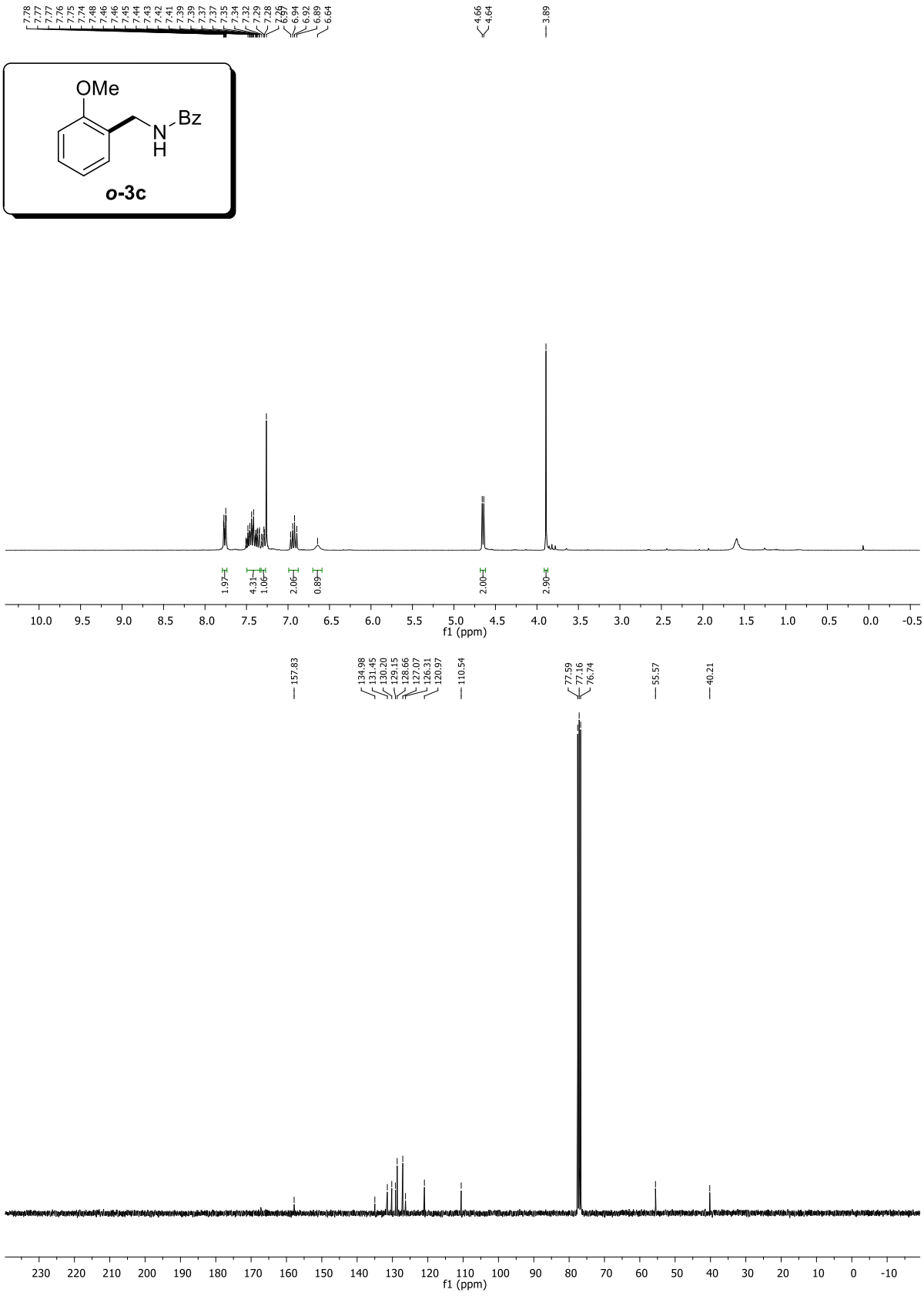


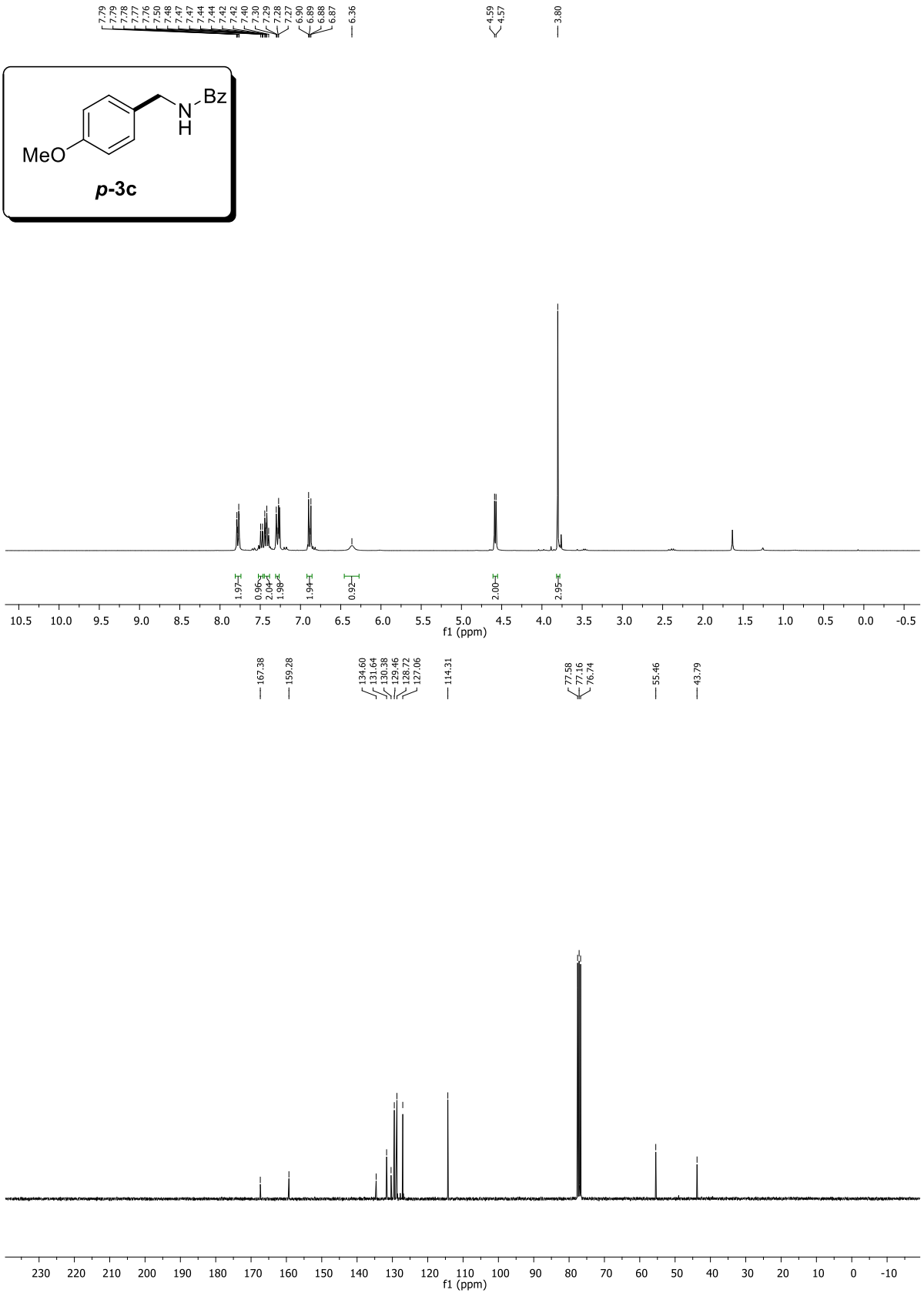
3a

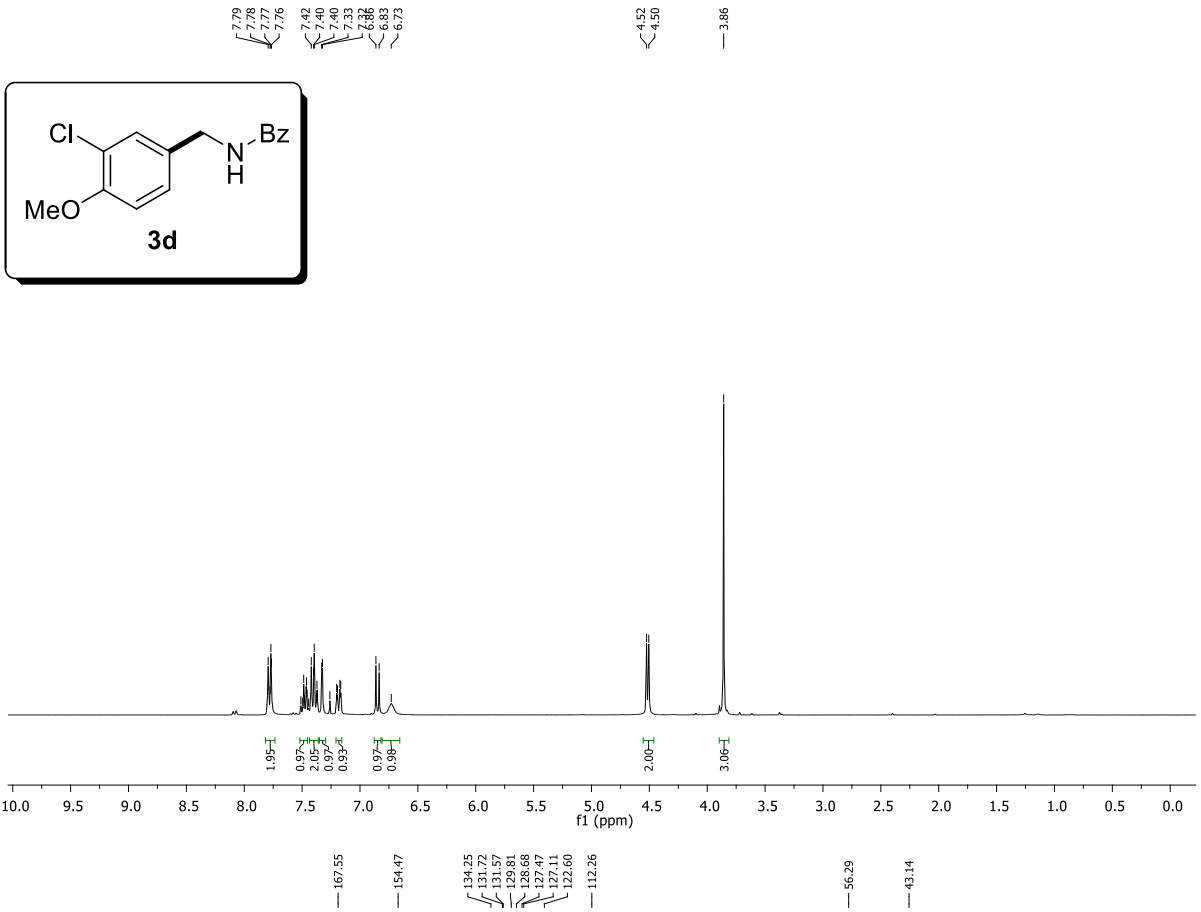


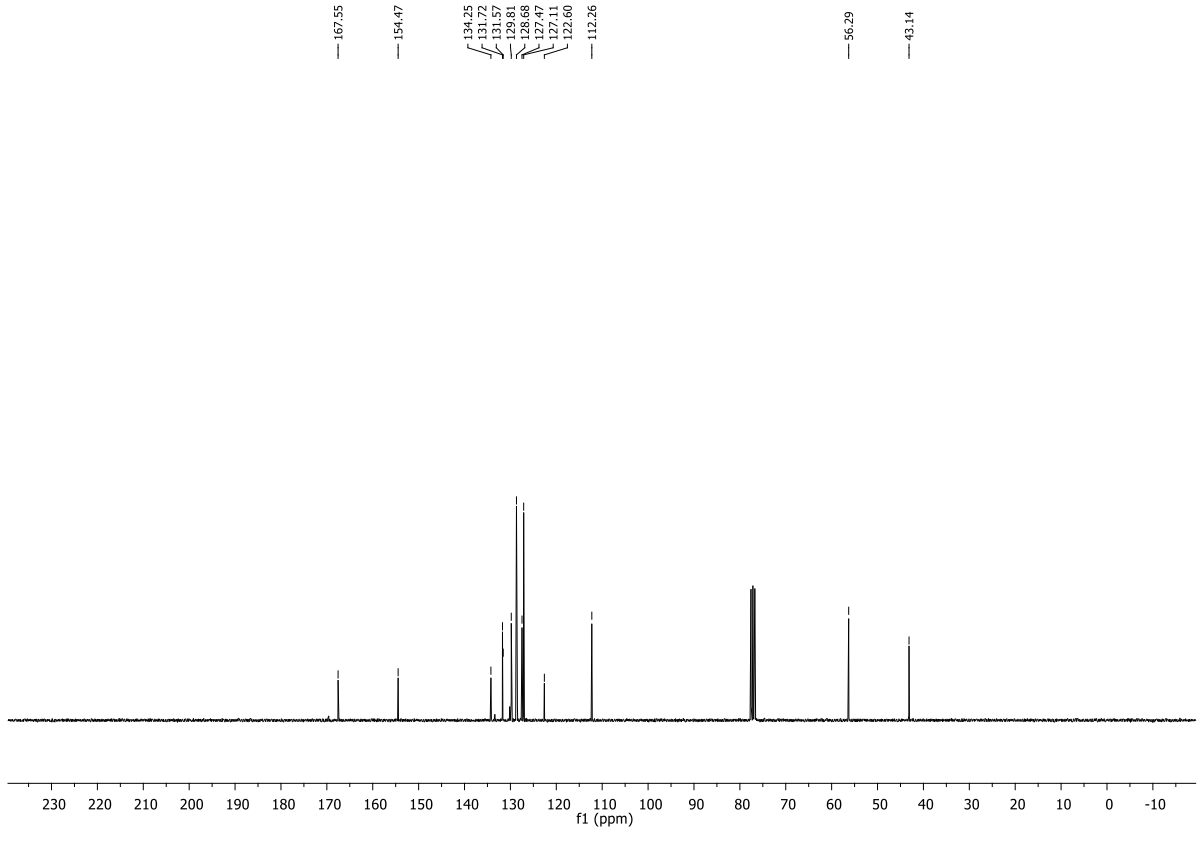


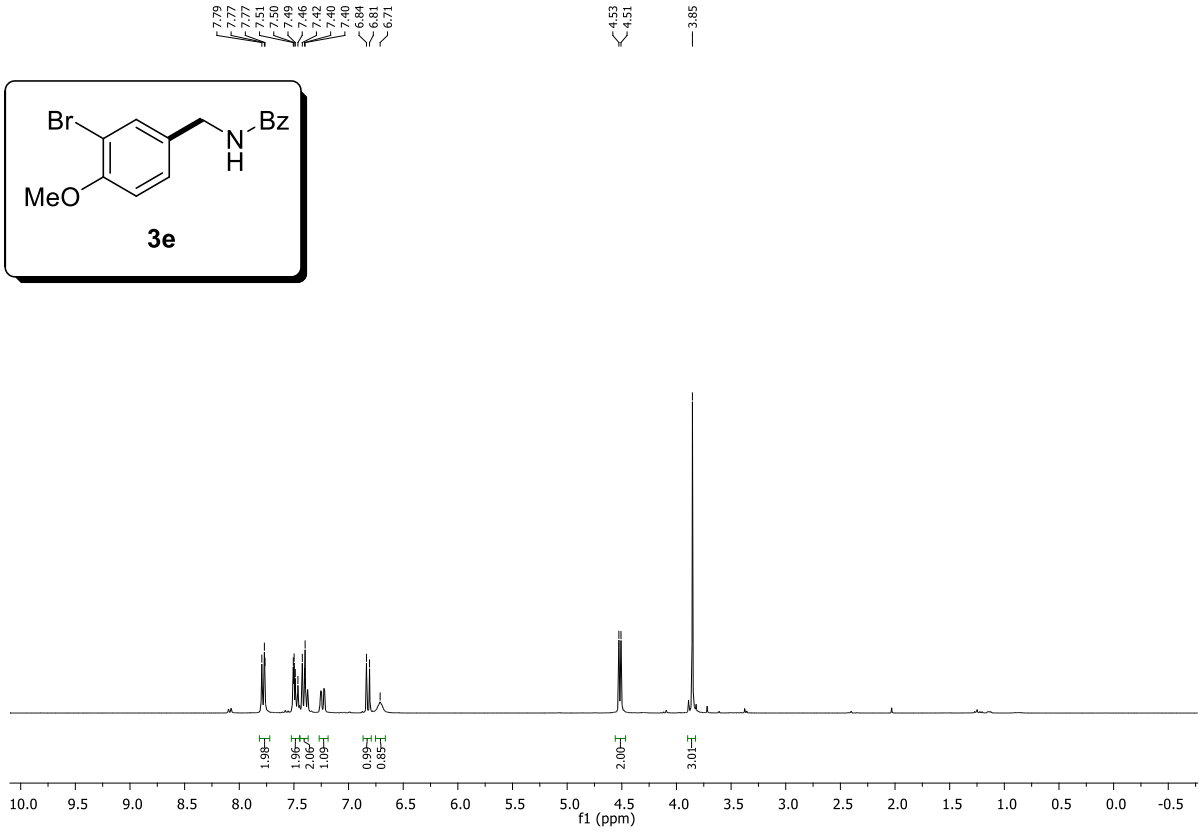

7.79
7.79
7.78
7.77
7.76
7.48
7.45
7.45
7.43
7.42
7.27
7.26
7.24
7.18
6.32
4.66
4.64
4.62
4.60
2.38
2.35
Me
o
Bz
N
H
p
Me
3b, o/p= 1/1.8
2.00
1.04
2.11
4.07
0.76
0.27
0.50
1.50
0.72
2.28
f1 (ppm)
167.41
167.34
137.50
136.78
135.89
135.27
134.60
134.51
131.67
131.63
130.79
129.59
128.88
128.74
128.70
128.09
127.07
126.43
77.58
77.16
76.74
44.06
42.50
21.24
19.20
f1 (ppm)

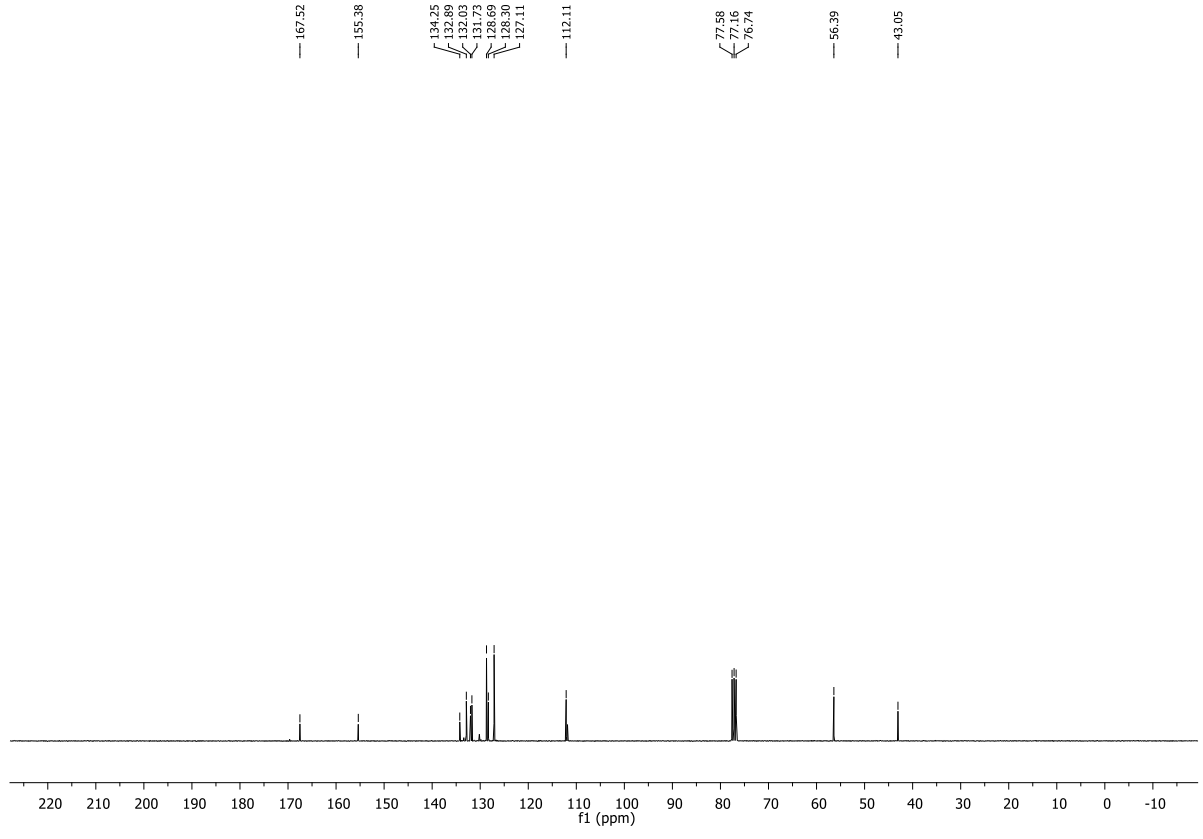

7.78
7.77
7.77
7.76
7.75
7.74
7.48
7.46
7.46
7.45
7.44
7.43
7.42
7.41
7.39
7.39
7.37
7.37
7.35
7.34
7.32
7.29
7.28
7.26
6.97
6.94
6.92
6.89
6.64
4.66
4.64
3.89
OMe
Bz
N
H
o-3c
1.97
4.31
1.06
2.06
0.89
2.00
2.90
f1 (ppm)
157.83
134.98
131.45
130.20
129.15
128.66
127.07
126.31
120.97
110.54
77.59
77.16
76.74
55.57
40.21
f1 (ppm)

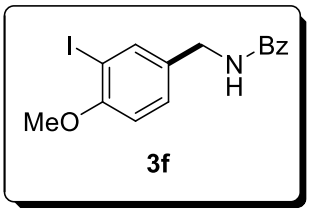

7.79
7.79
7.78
7.77
7.76
7.50
7.48
7.47
7.47
7.44
7.44
7.42
7.42
7.40
7.30
7.29
7.28
7.27
6.90
6.89
6.88
6.87
6.36
4.59
4.57
3.80
Bz
N
H
MeO
p-3c
1.97
0.96
2.04
1.98
1.94
0.92
2.00
2.95
f1 (ppm)
167.38
159.28
134.60
131.64
130.38
129.46
128.72
127.06
114.31
77.58
77.16
76.74
55.46
43.79
f1 (ppm)


7.79
7.78
7.77
7.76
7.42
7.40
7.40
7.33
6.86
6.83
6.73
4.52
4.50
3.86
Cl
N
H
Bz
MeO
3d
1.95
0.97
2.05
0.97
0.93
0.97
0.98
2.00
3.06
f1 (ppm)


167.55
154.47
134.25
131.72
131.57
129.81
128.68
127.47
127.11
122.60
112.26
56.29
43.14
f1 (ppm)

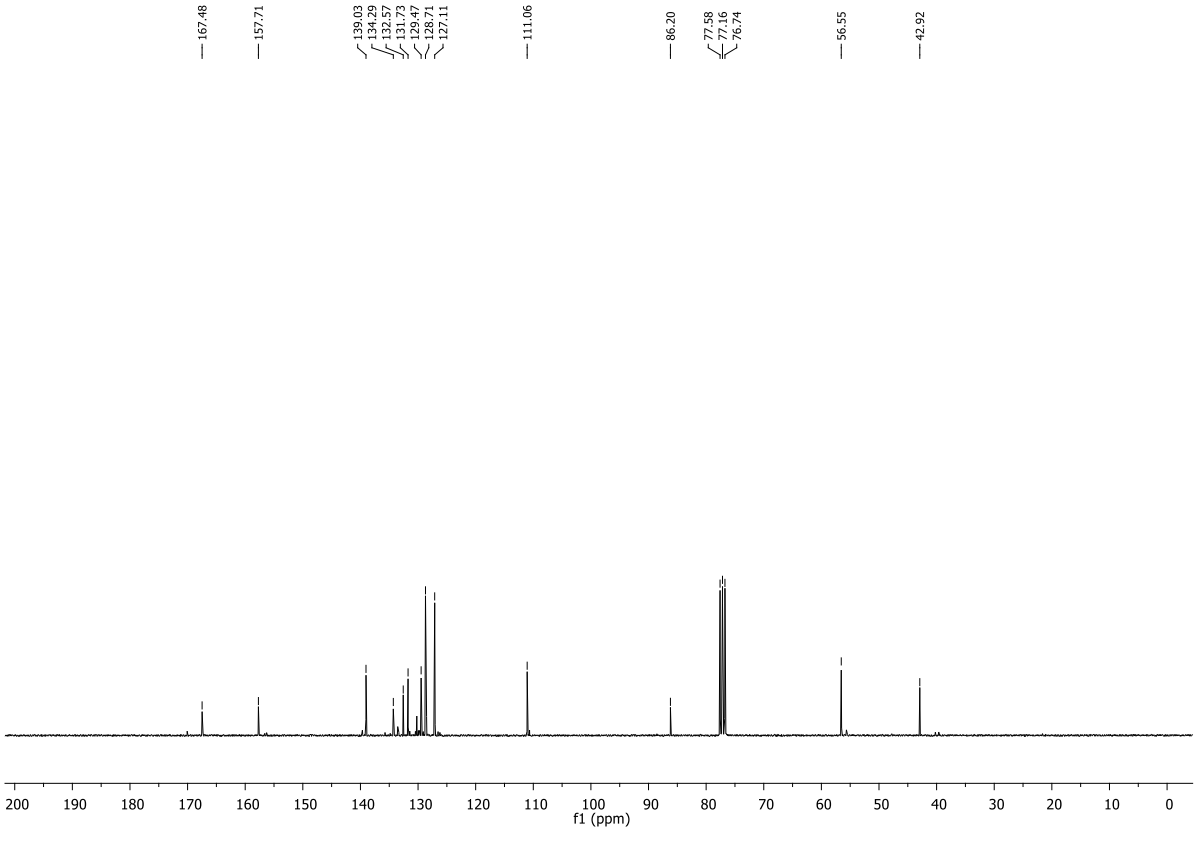

7.79
7.77
7.77
7.77
7.51
7.50
7.49
7.46
7.42
7.40
7.40
6.84
6.81
6.71
4.53
4.51
3.85
Br
N
H
Bz
MeO
3e
1.98
1.96
2.06
1.09
0.99
0.85
2.00
3.01
f1 (ppm)

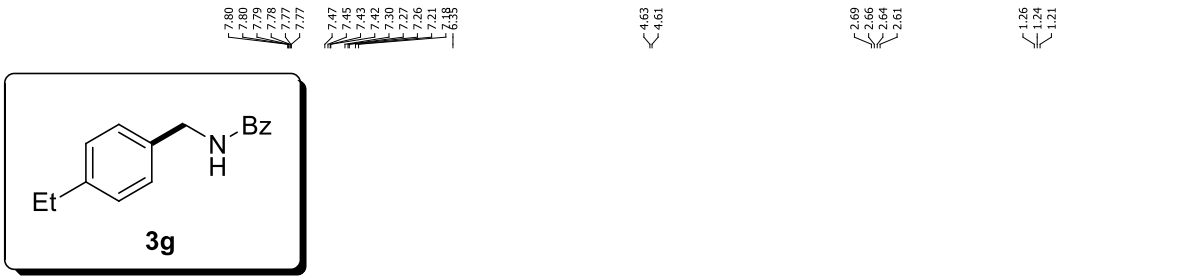

167.52
155.38
134.25
132.89
132.03
131.73
128.69
128.30
127.11
112.11
77.58
77.16
76.74
56.39
43.05
f1 (ppm)

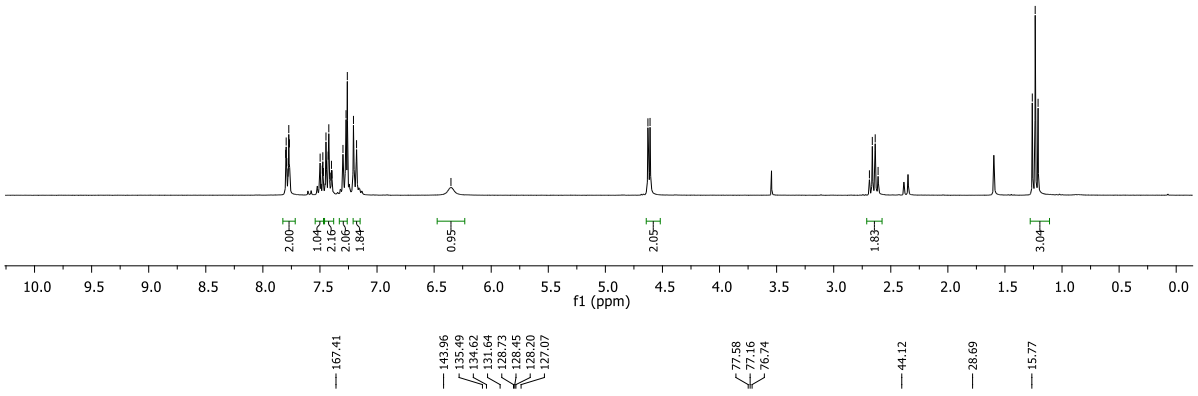

I
Bz
N
H
MeO

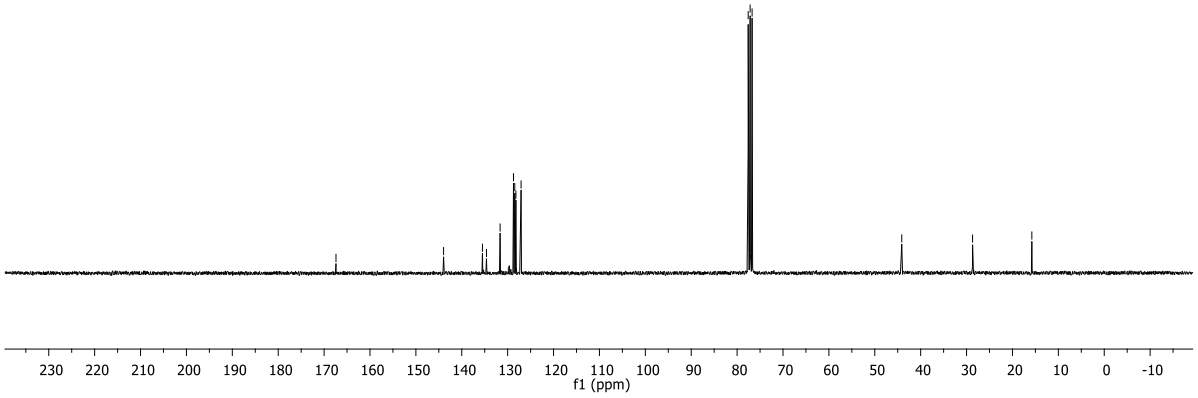
3f

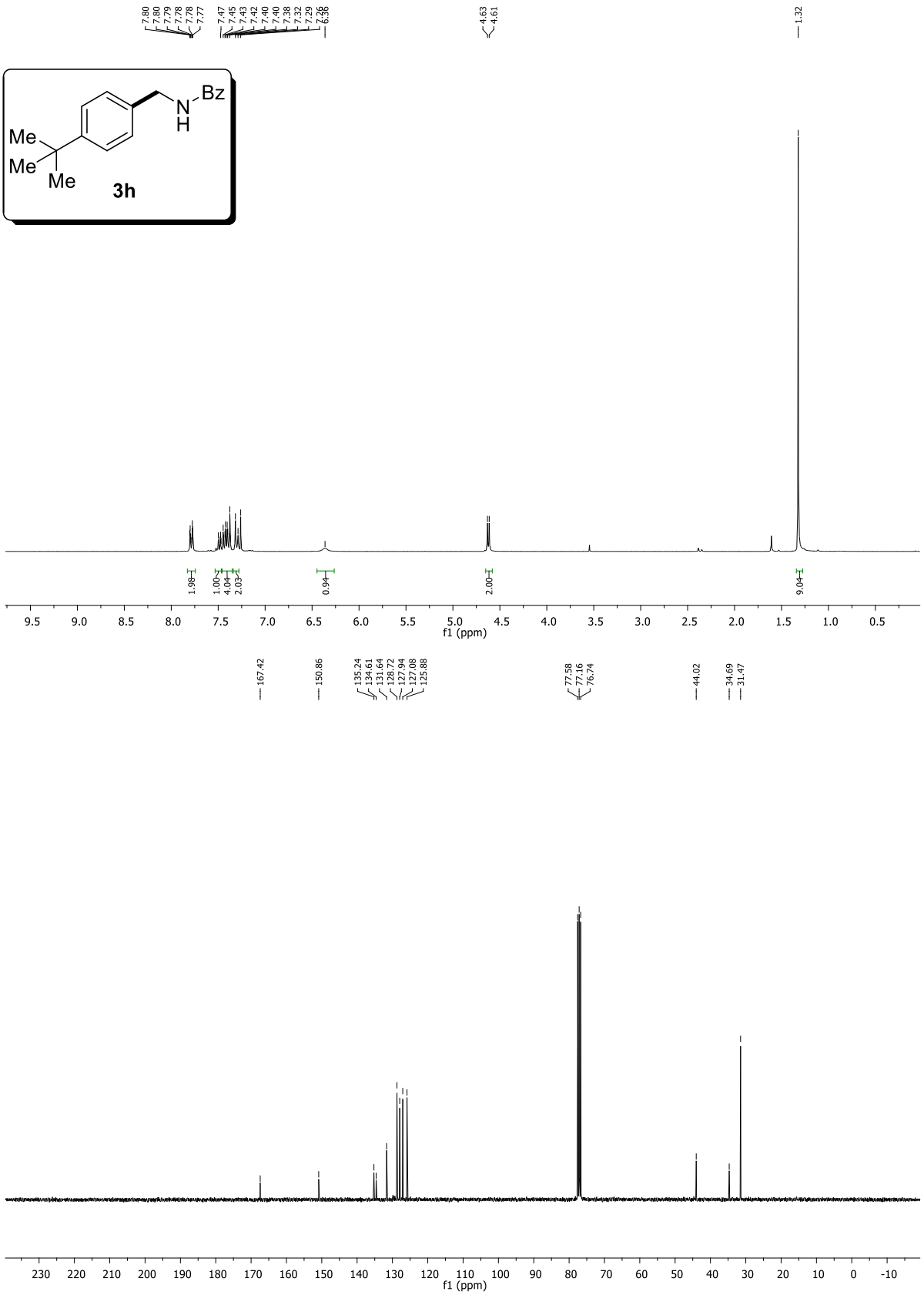
7.80
7.77
7.77
7.75
7.74
7.50
7.47
7.44
7.42
7.41
7.32
7.31
7.29
7.28
7.26
6.78
6.75
4.53
4.51
3.85
2.92
1.03
2.07
0.99
0.94
0.91
2.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

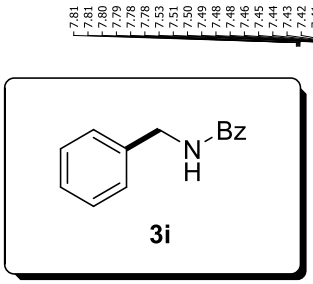

167.48
157.71
139.03
134.29
132.57
131.73
129.47
128.71
127.11
111.06
86.20
77.58
77.16
76.74
56.55
42.92
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

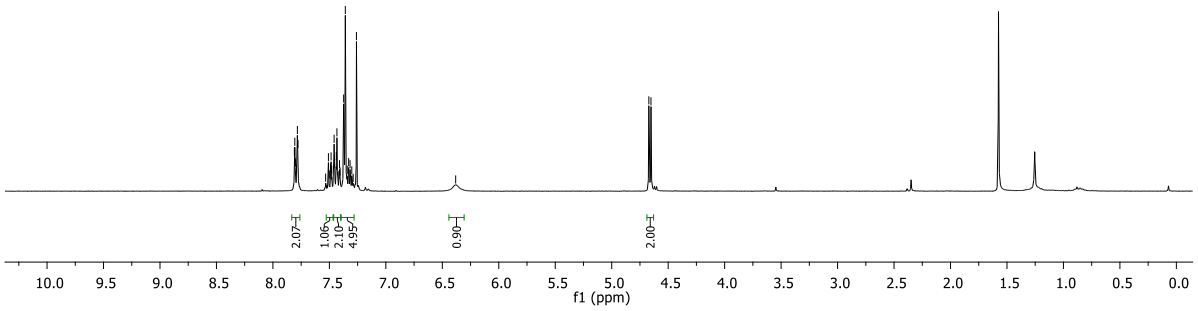

Et
N
H
Bz
3g

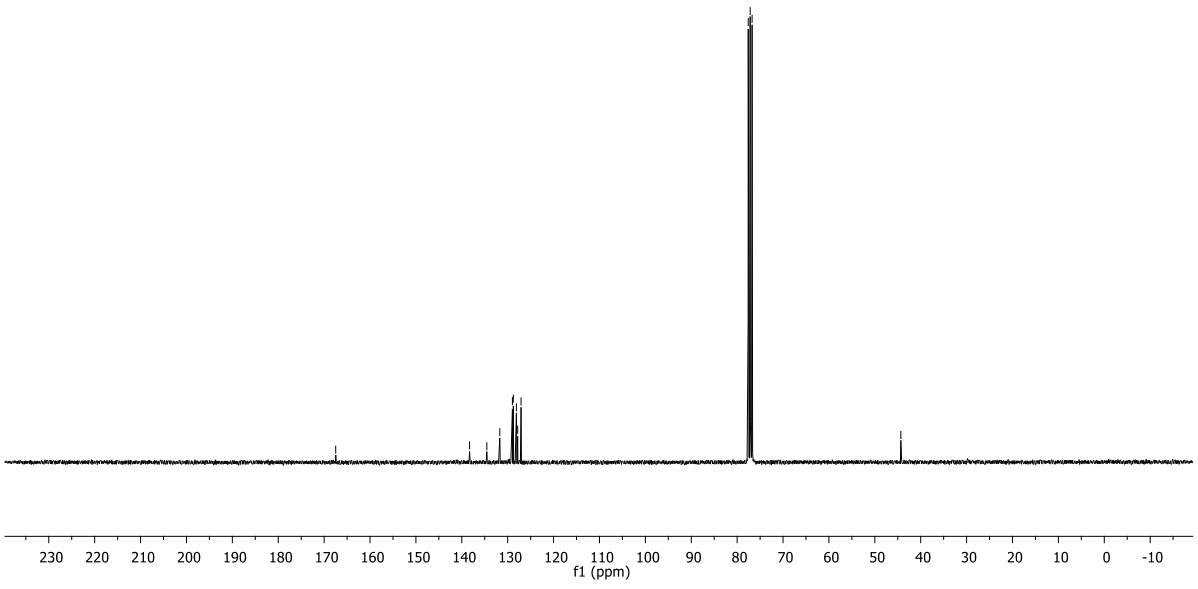

f1 (ppm)

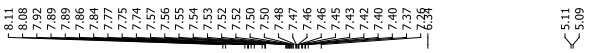

f1 (ppm)

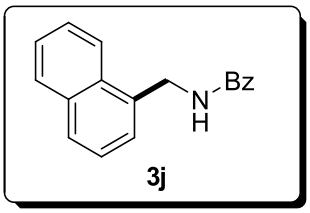

7.80
7.80
7.79
7.78
7.78
7.77
7.47
7.45
7.43
7.42
7.40
7.40
7.38
7.32
7.29
7.26
6.38
4.63
4.61
1.32
Bz
N
H
Me
Me
Me
3h
1.98
1.00
4.04
2.03
0.94
2.00
9.04
f1 (ppm)
167.42
150.86
135.24
134.61
131.64
128.72
127.94
127.08
125.88
77.58
77.16
76.74
44.02
34.69
31.47
f1 (ppm)

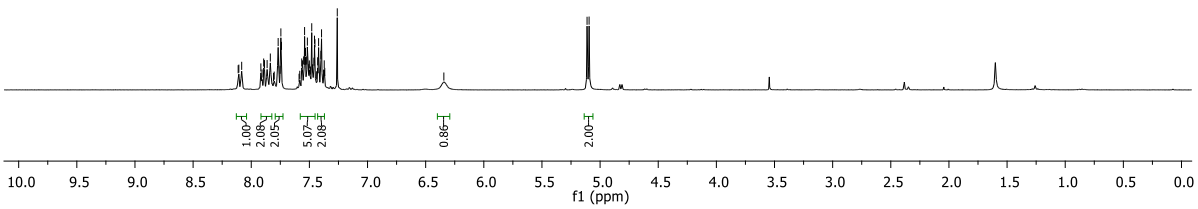

Bz
N
H
3i


2.07
1.06
2.10
4.95
0.90
2.00
f1 (ppm)

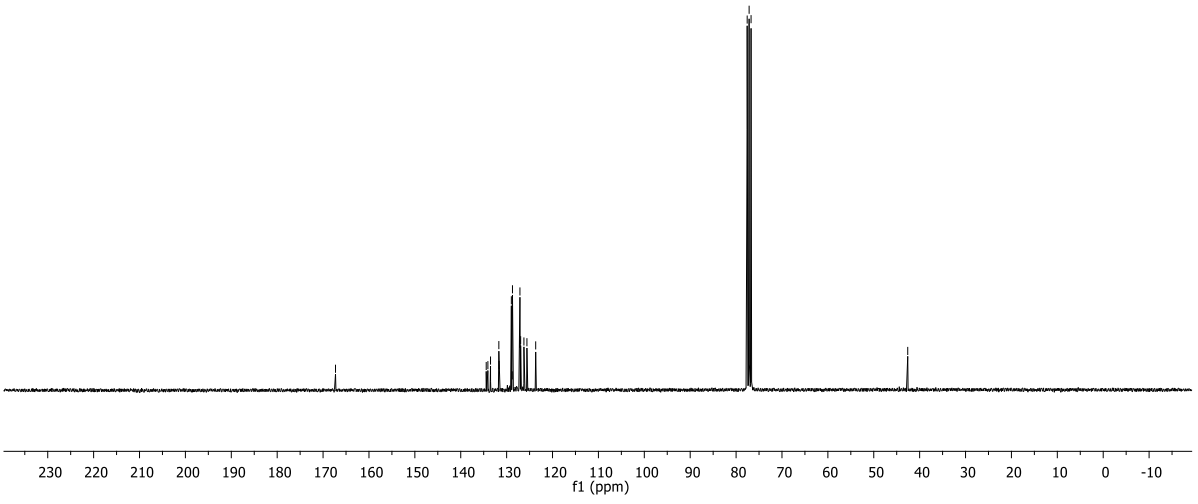

f1 (ppm)

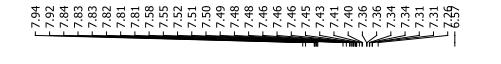

8.11
8.08
7.92
7.89
7.89
7.86
7.84
7.77
7.75
7.74
7.57
7.56
7.55
7.54
7.53
7.52
7.52
7.50
7.50
7.48
7.47
7.46
7.46
7.45
7.43
7.42
7.40
7.40
7.37
7.36
7.35
5.11
5.09

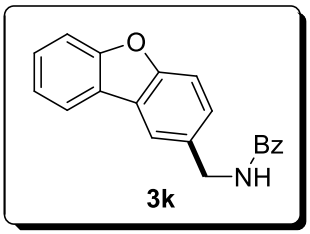

Bz
N
H
3j

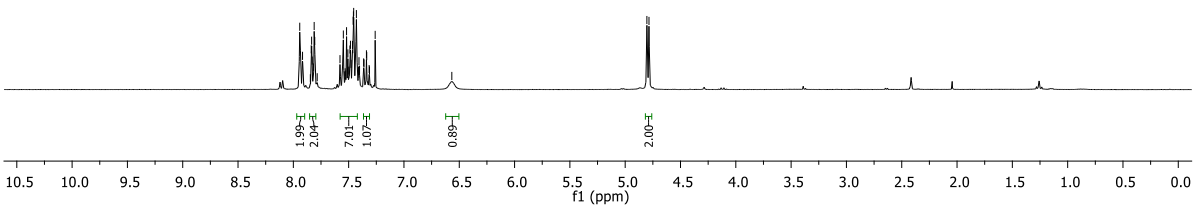

1.00
2.08
2.05
5.07
2.08
0.86
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.29
134.45
134.09
133.51
131.70
131.65
128.97
128.78
128.73
127.15
127.10
126.94
126.23
125.58
123.67
77.58
77.16
76.74
42.59

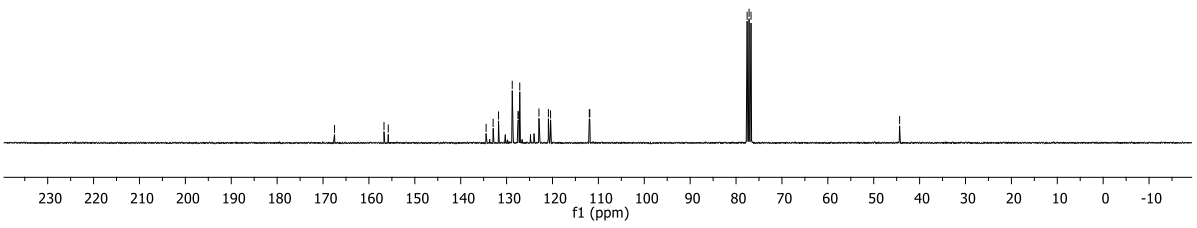

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

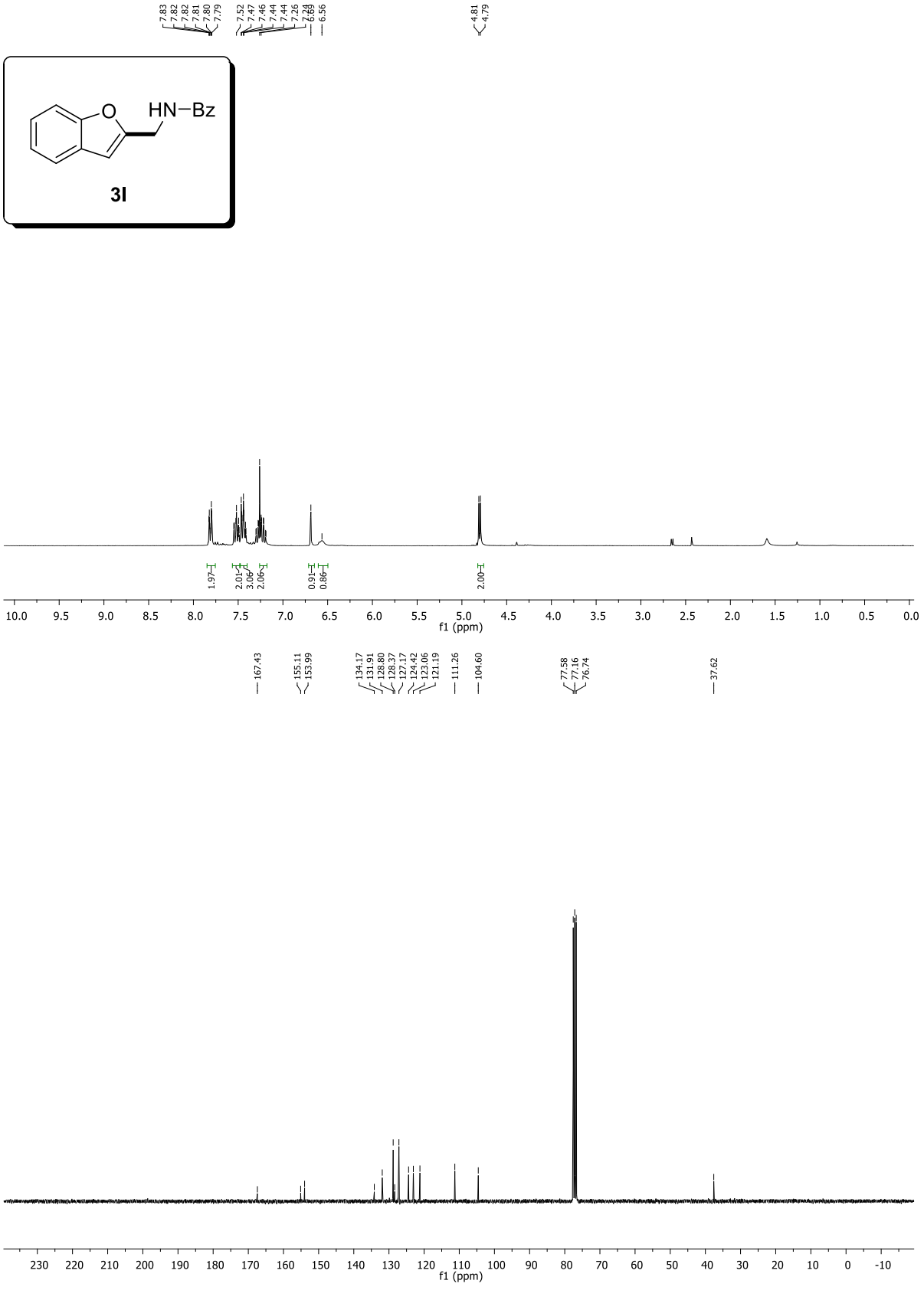

7.94
7.92
7.84
7.83
7.83
7.82
7.81
7.81
7.58
7.55
7.52
7.51
7.50
7.49
7.48
7.48
7.46
7.46
7.46
7.45
7.43
7.41
7.40
7.36
7.36
7.34
7.34
7.31
7.31
7.26
6.57
4.80
4.78

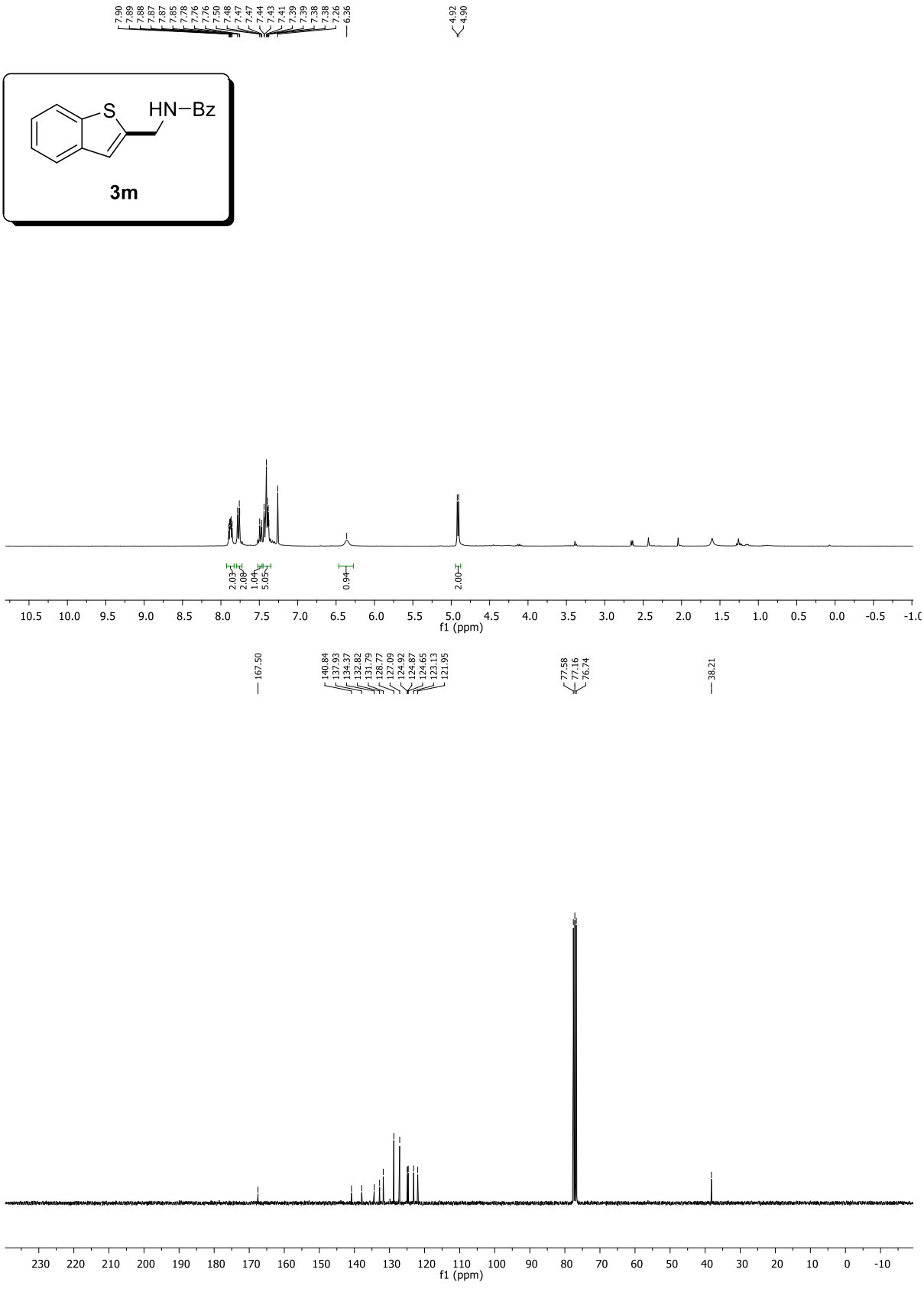

O
Bz
NH
3k

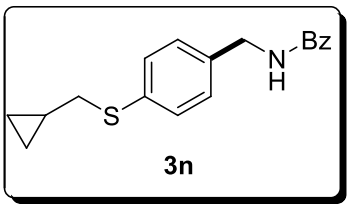

1.99
2.04
7.01
1.07
0.89
2.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.50
156.72
155.79
134.47
132.93
131.76
128.77
127.52
127.35
127.13
122.95
120.90
120.42
111.98
111.87
77.58
77.16
76.74
44.36

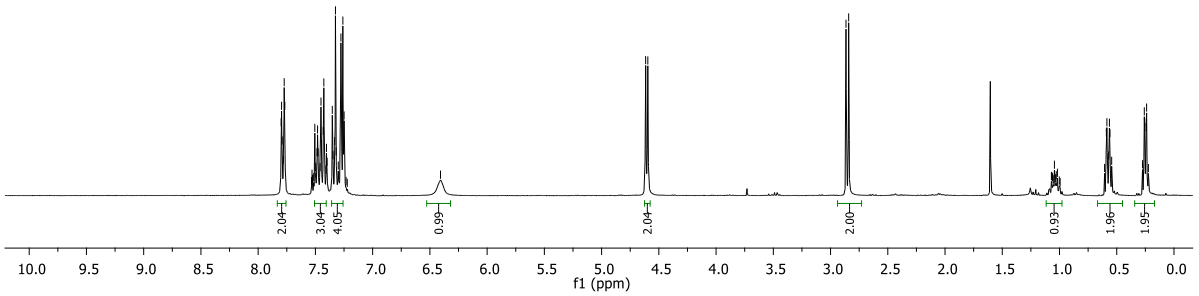

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

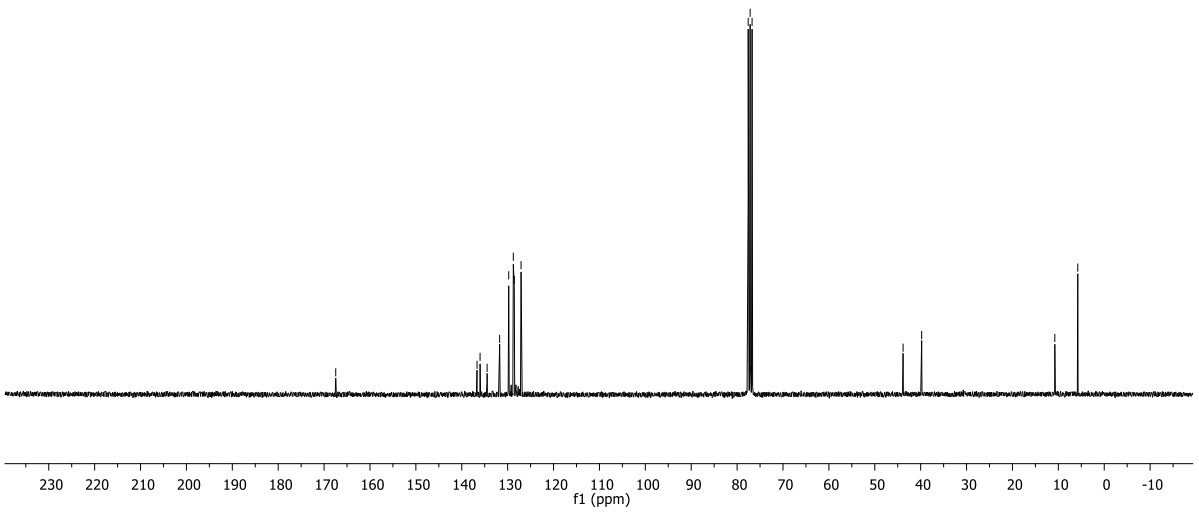

7.83
7.82
7.82
7.81
7.80
7.79
7.52
7.47
7.46
7.44
7.44
7.26
6.56
4.81
4.79
O
HN−Bz
3l
1.97
2.01
3.06
2.06
0.91
0.86
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
167.43
155.11
153.99
134.17
131.91
128.80
128.37
127.17
124.42
123.06
121.19
111.26
104.60
77.58
77.16
76.74
37.62
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

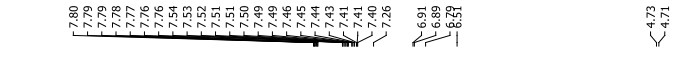

7.90
7.89
7.88
7.87
7.87
7.85
7.78
7.76
7.76
7.50
7.48
7.47
7.47
7.44
7.43
7.41
7.39
7.39
7.38
7.38
7.26
6.36
4.92
4.90
S
HN−Bz
3m
2.03
2.08
1.04
5.05
0.94
2.00
f1 (ppm)
167.50
140.84
137.93
134.37
132.82
131.79
128.77
127.09
124.92
124.87
124.65
123.13
121.95
77.58
77.16
76.74
38.21
f1 (ppm)

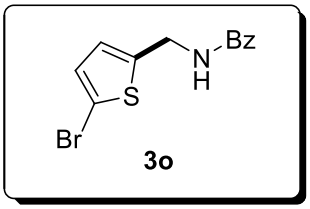


3n

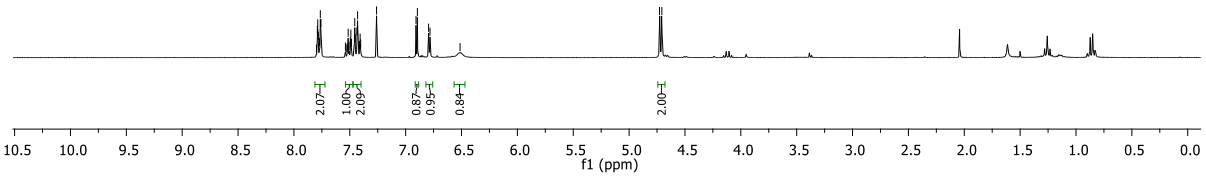




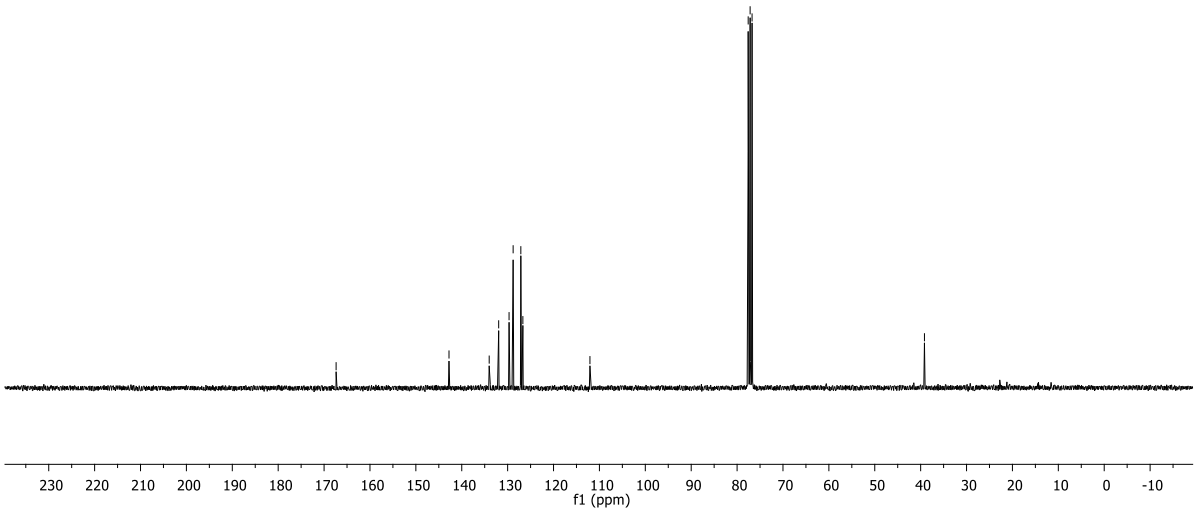

7.80
7.79
7.79
7.78
7.77
7.76
7.76
7.54
7.53
7.52
7.51
7.51
7.50
7.49
7.49
7.46
7.45
7.44
7.43
7.41
7.41
7.40
7.26
6.91
6.89
6.79
6.51
4.73
4.71

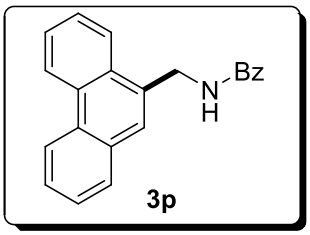

Bz
N
H
S
Br

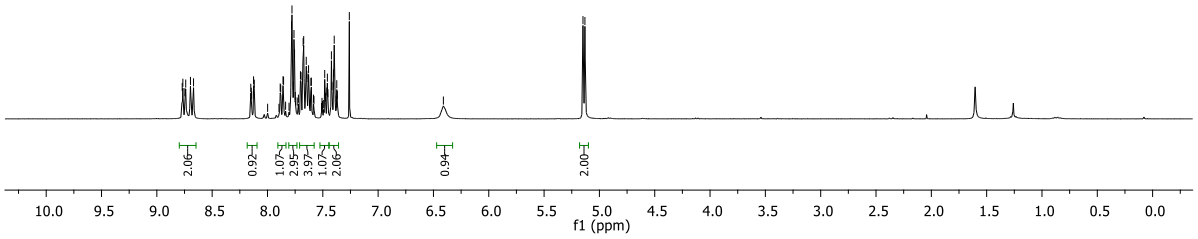
3o

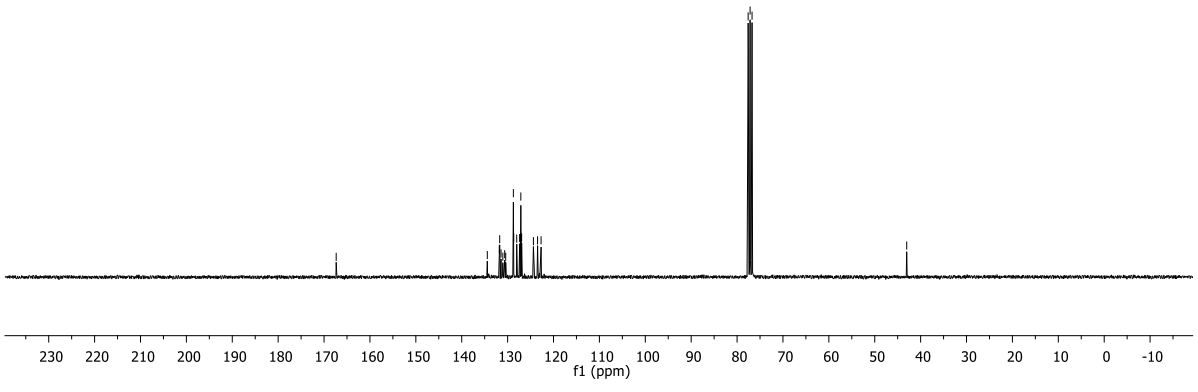

2.07
1.00
2.09
0.87
0.95
0.84
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


167.38
142.78
134.02
131.95
129.69
128.80
127.13
126.68
112.07
77.58
77.16
76.74
39.17

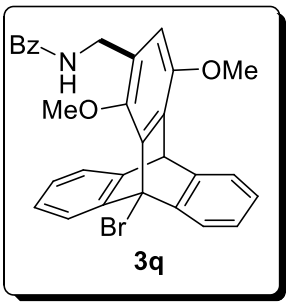

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Bz
N
H
3p

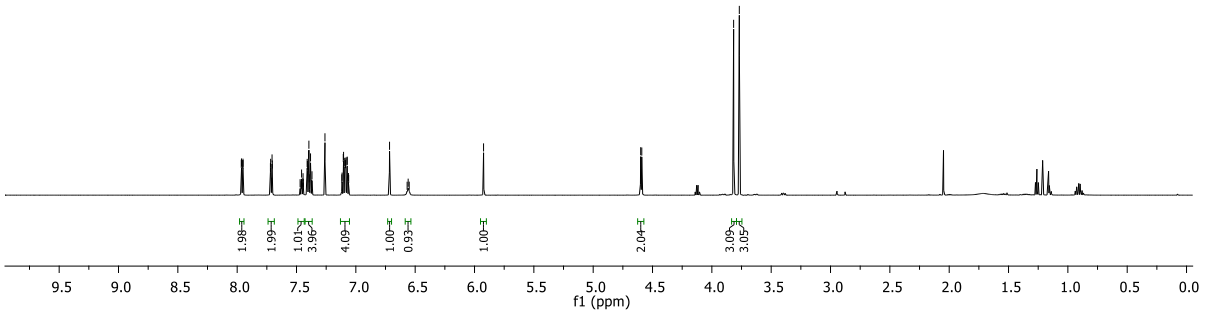

2.06
0.92
1.07
2.95
3.97
1.07
2.06
0.94
2.00
f1 (ppm)

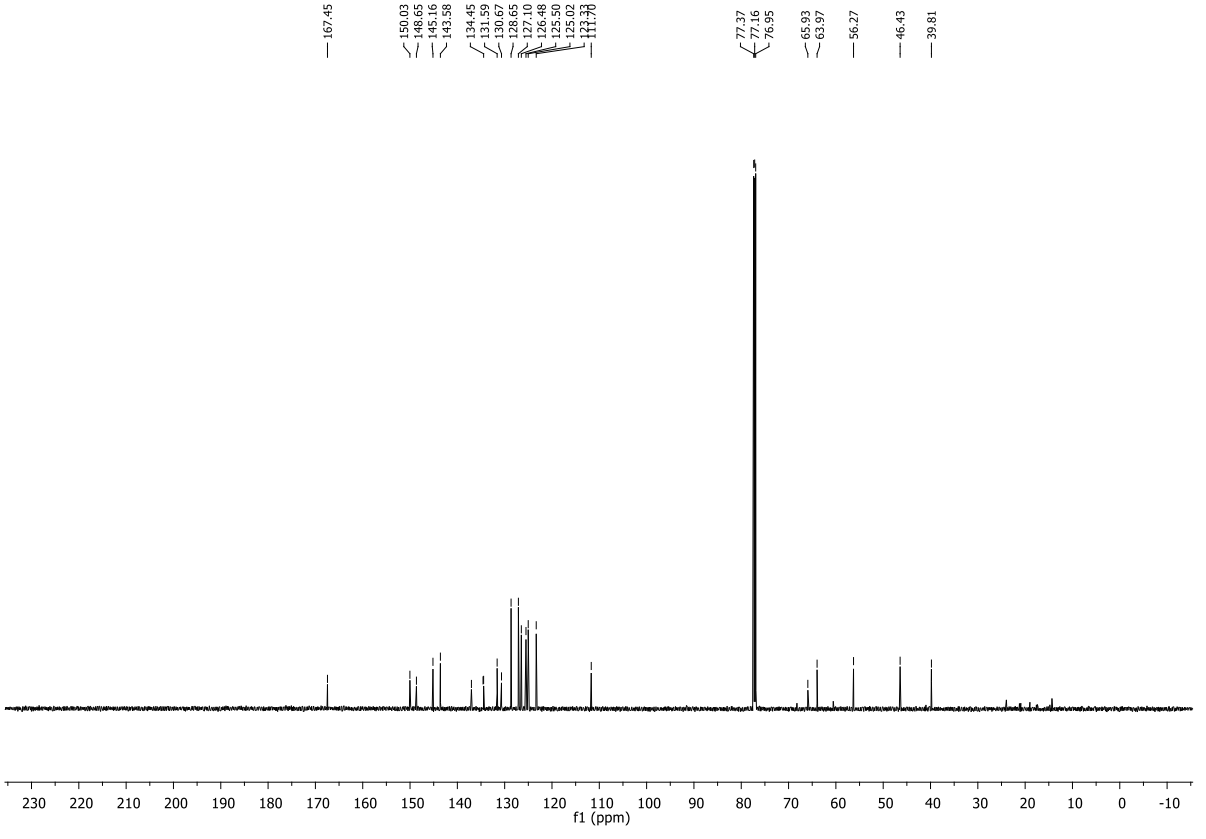

f1 (ppm)

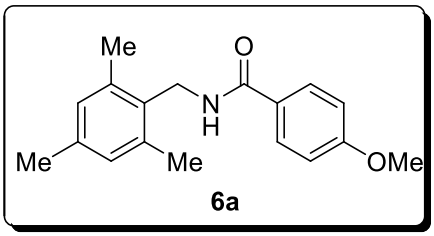

7.97
7.96
7.95
7.95
7.95
7.72
7.72
7.71
7.70
7.46
7.41
7.41
7.40
7.40
7.38
7.37
7.26
7.11
7.10
7.09
7.09
7.09
7.08
7.07
7.02
6.57
6.56
6.55
5.92
4.60
4.59
3.82
3.77


Bz
N
H
MeO
OMe
Br

3q

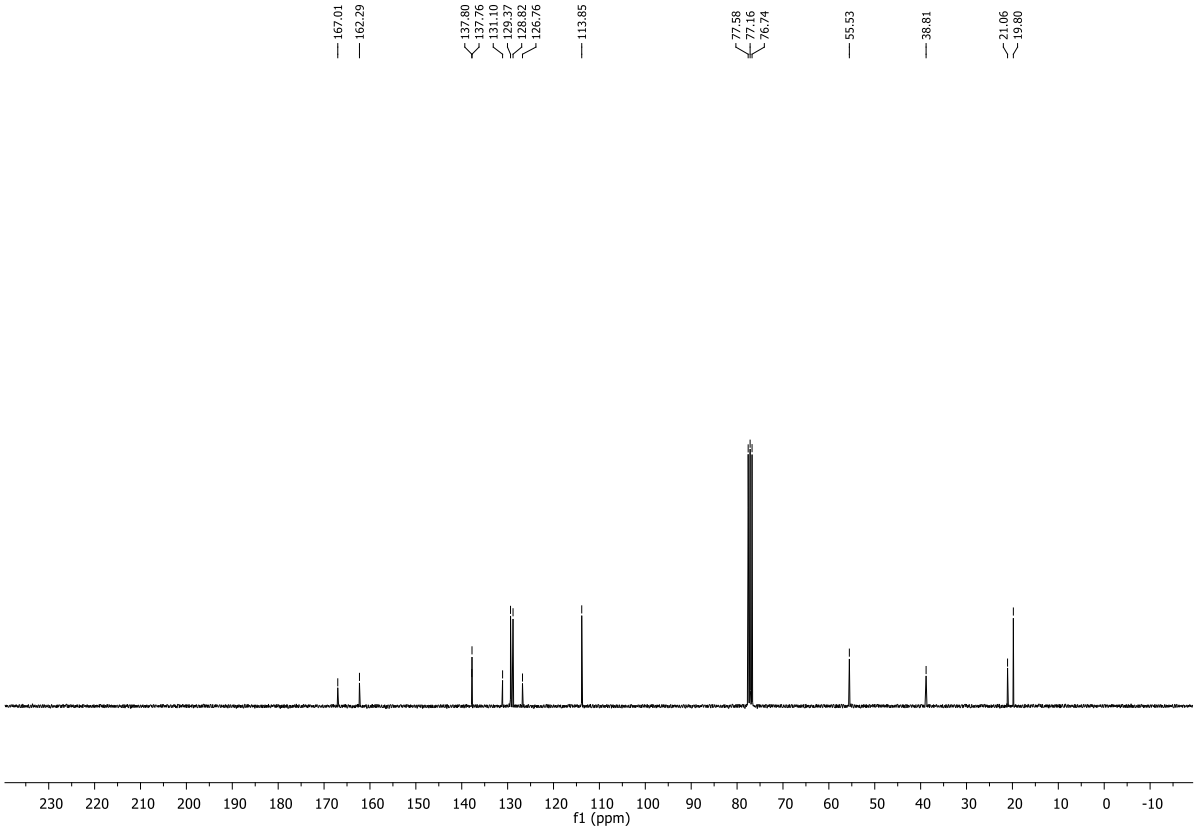

1.98
1.99
1.01
3.96
4.09
1.00
0.93
1.00
2.04
3.09
3.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

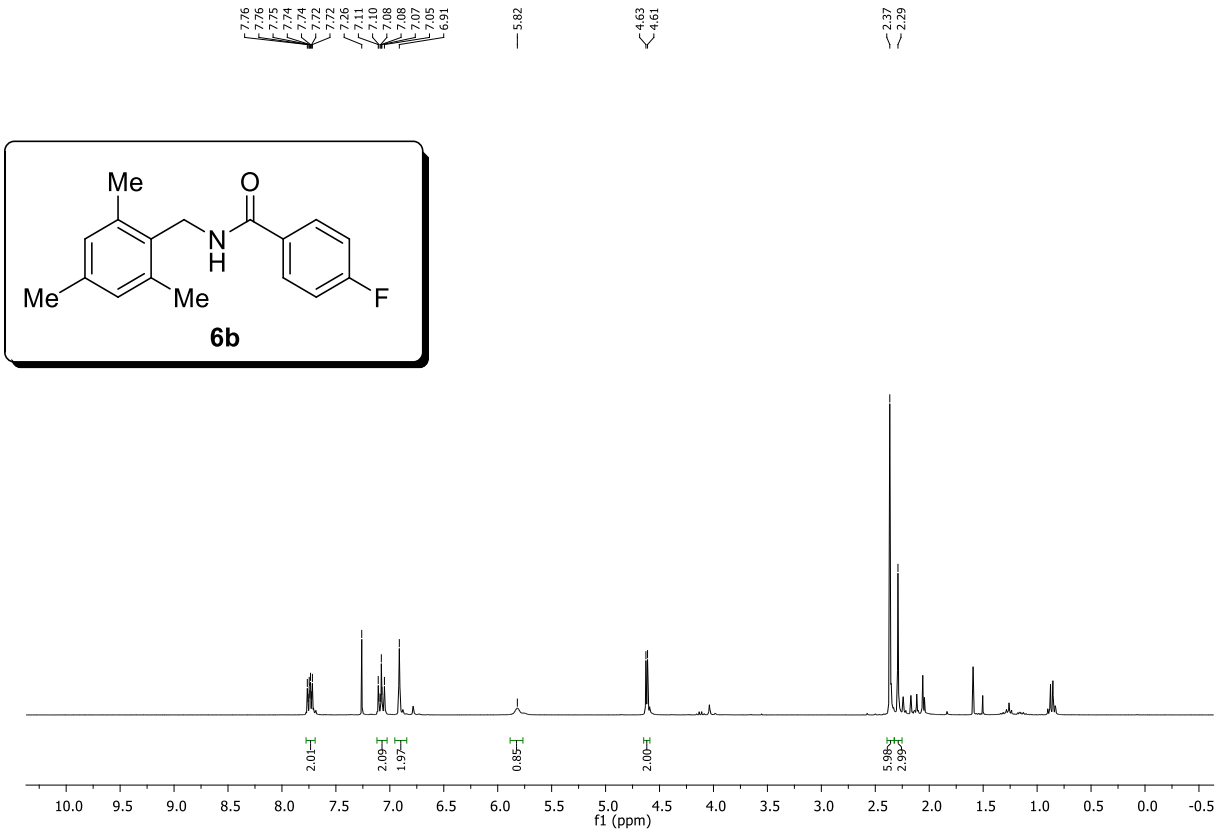

167.45
150.03
148.65
145.16
143.58
134.45
131.59
130.67
128.65
127.10
126.48
125.50
125.02
77.37
77.16
76.95
65.93
63.97
56.27
46.43
39.81
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

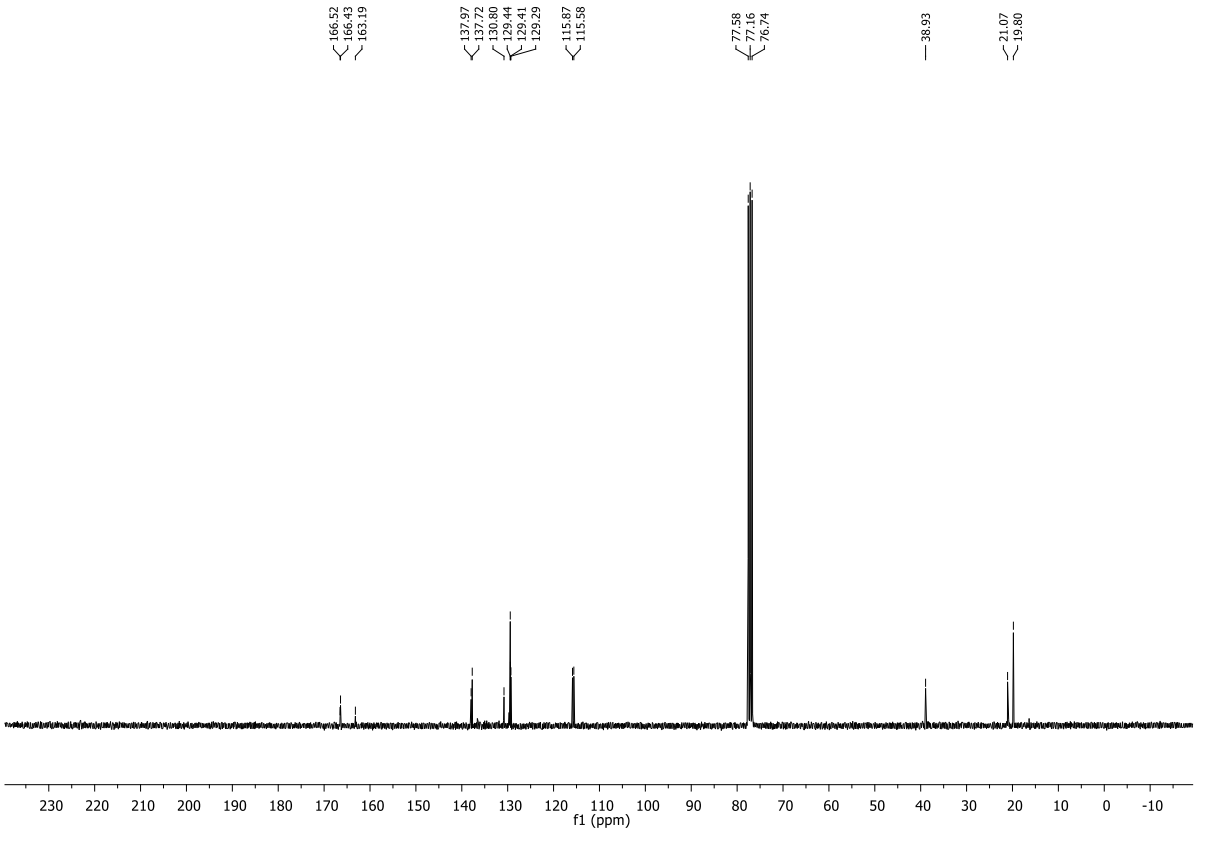

Me
O
N
H
Me
Me
OMe

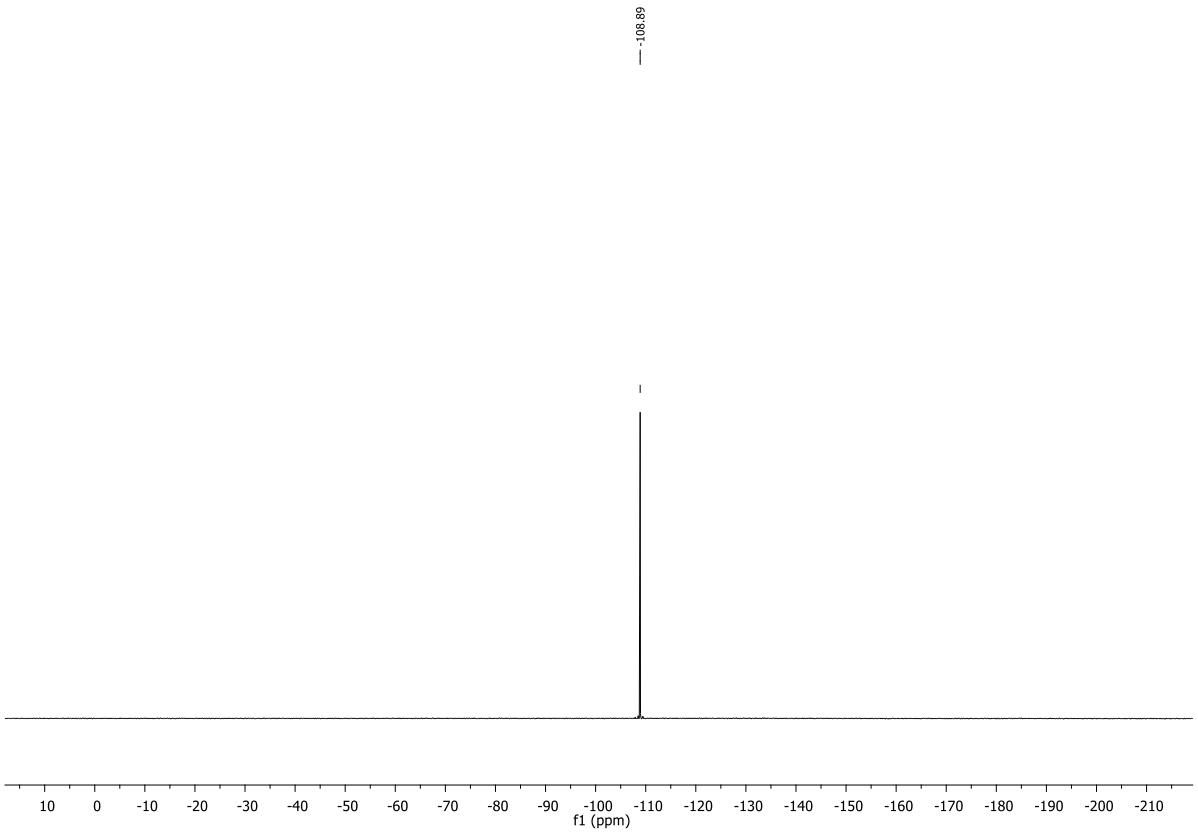
6a

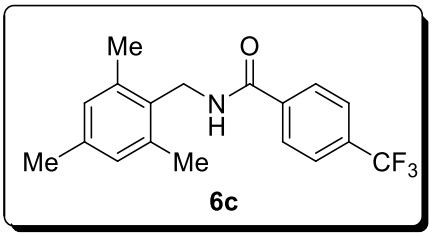
7.71
7.68
7.26
6.91
6.88
5.79
4.62
4.60
3.83
2.37
2.29
2.08
4.01
0.93
2.00
3.02
6.04
3.04
f1 (ppm)


167.01
162.29
137.80
137.76
131.10
129.37
128.82
126.76
113.85
77.58
77.16
76.74
55.53
38.81
21.06
19.80
f1 (ppm)


7.76
7.76
7.75
7.74
7.74
7.72
7.72
7.26
7.11
7.10
7.08
7.08
7.07
7.05
6.91
5.82
4.63
4.61
2.37
2.29
Me
O
N
H
Me
Me
F
6b
2.01
2.09
1.97
0.85
2.00
5.98
2.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

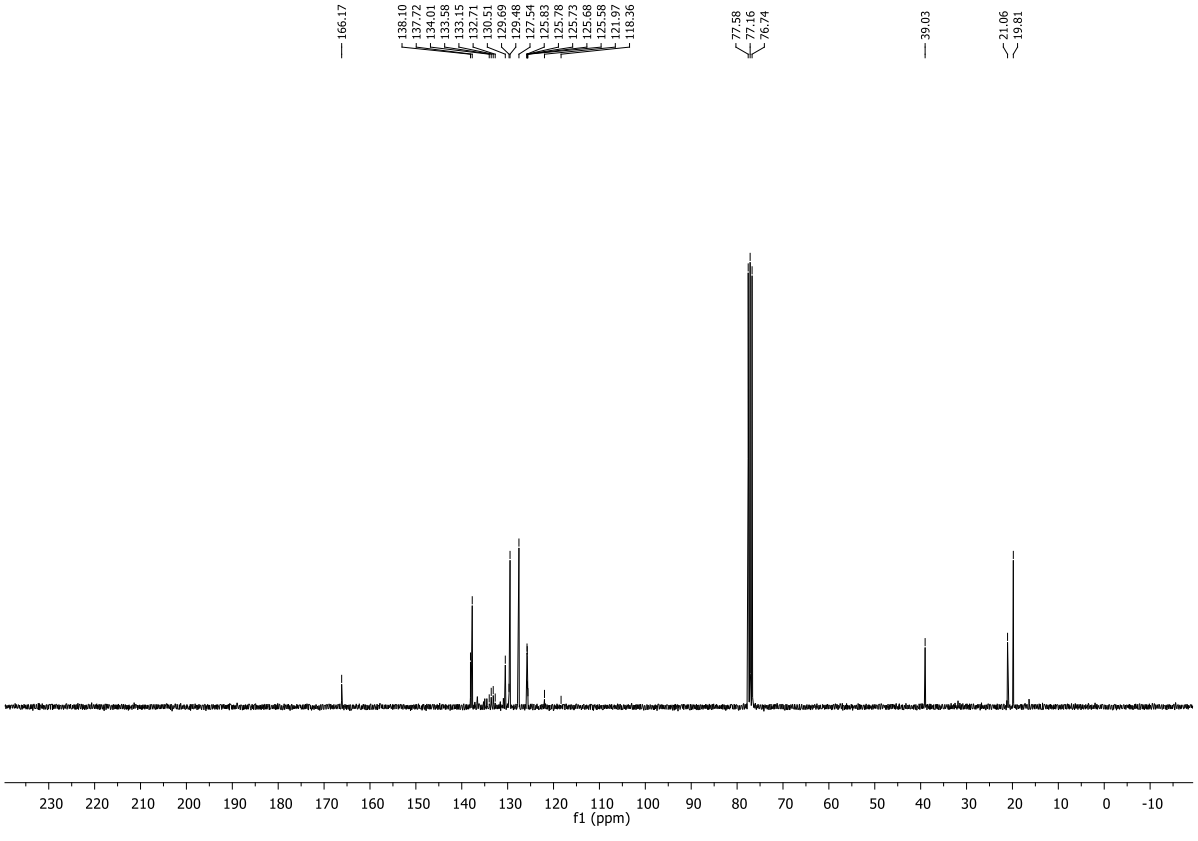

166.52
166.43
163.19
137.97
137.72
130.80
129.44
129.41
129.29
115.87
115.58
77.58
77.16
76.74
38.93
21.07
19.80
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

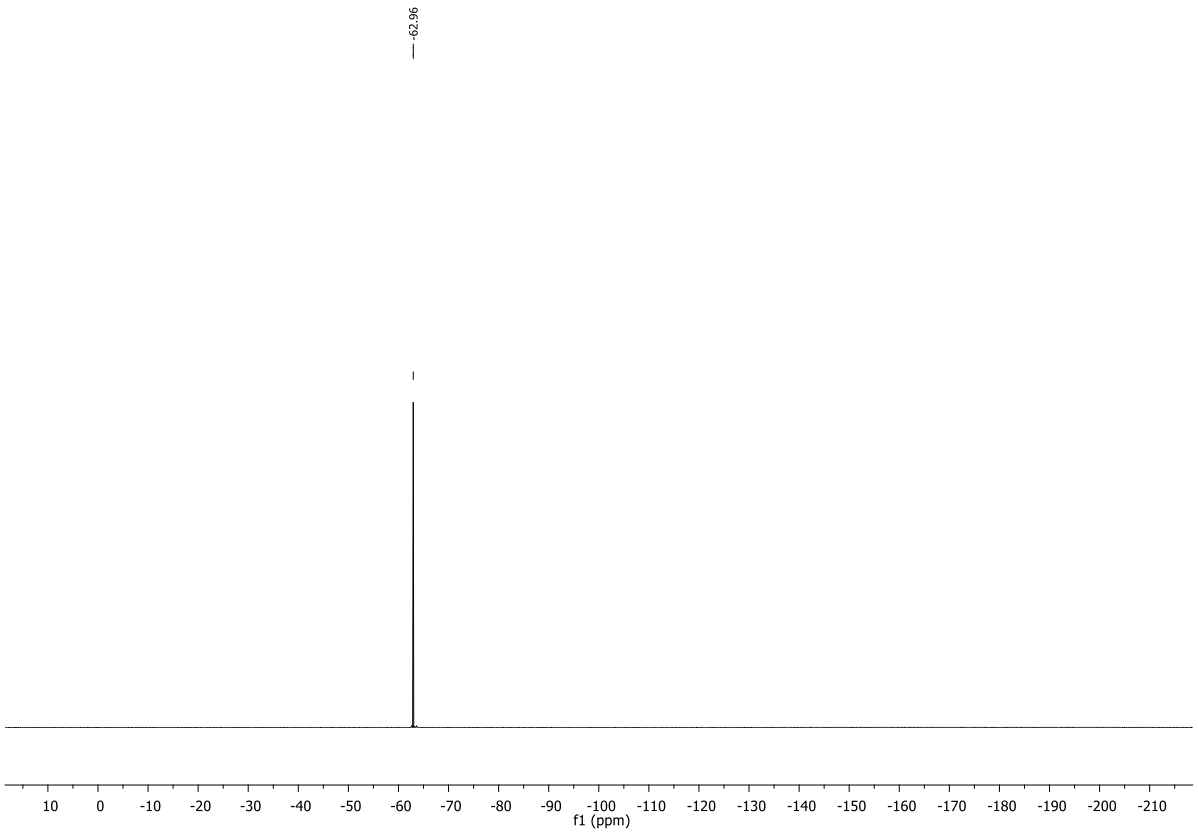

-108.89
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

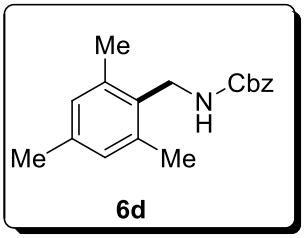

Me
O
N
H
Me
Me
CF3

6c

7.85
7.83
7.68
7.65
7.26
6.92
5.94
4.65
4.63
2.37
2.29
1.93
2.00
1.87
0.90
2.02
5.84
2.97
f1 (ppm)

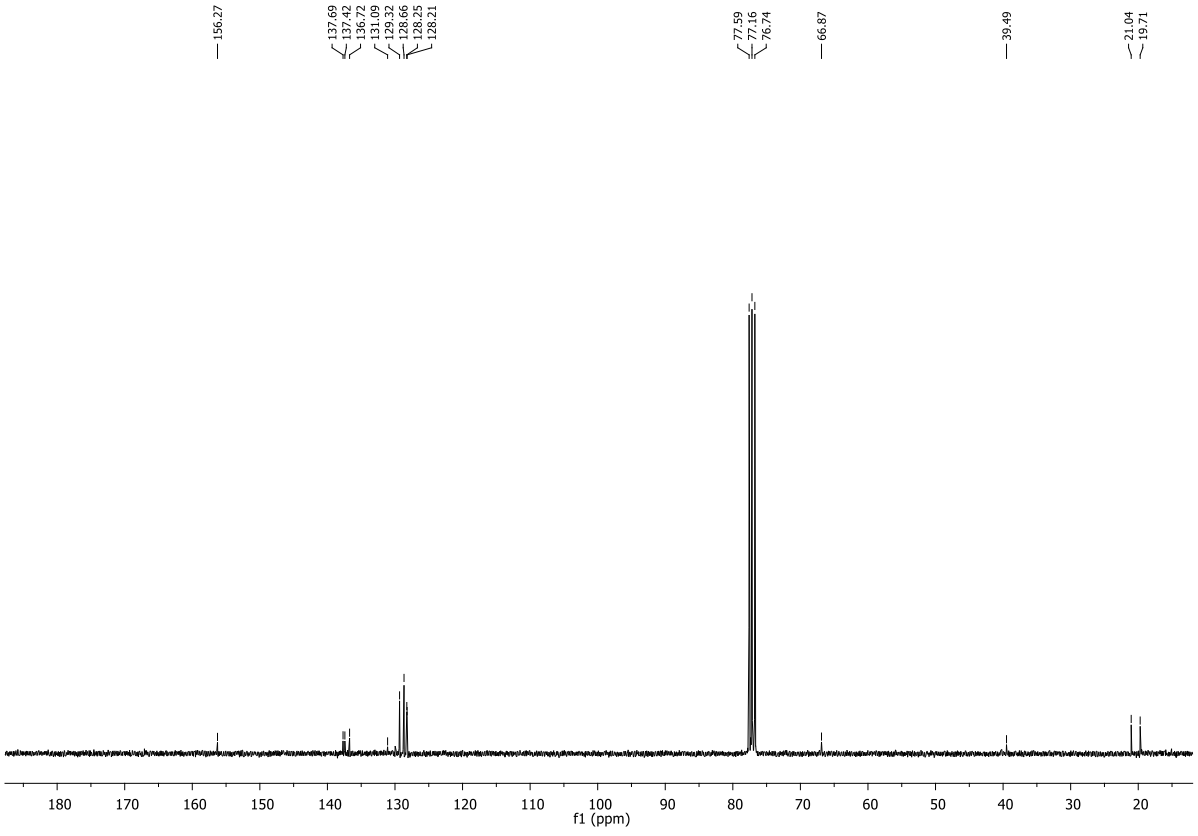

166.17
138.10
137.72
134.01
133.58
133.15
132.71
130.51
129.69
129.48
127.54
125.83
125.78
125.73
125.68
125.58
121.97
118.36
77.58
77.16
76.74
39.03
21.06
19.81
f1 (ppm)

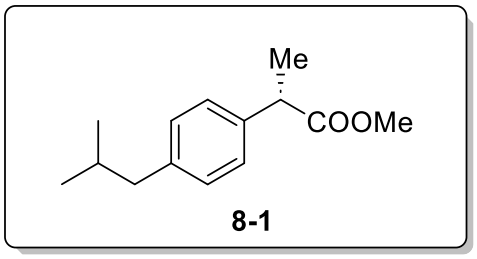

-62.96
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


Me
Cbz
N
H
Me
Me

6d

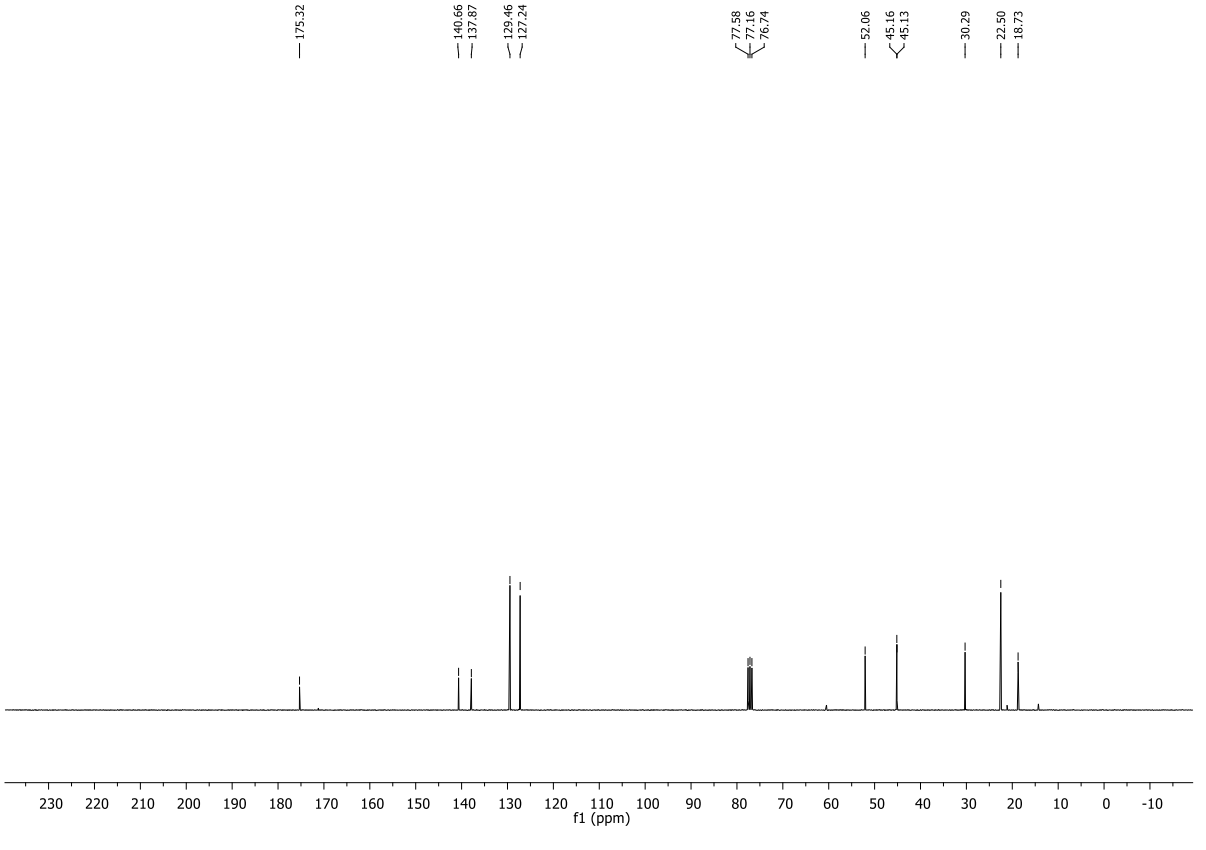
7.34
7.32
7.30
7.26
6.86
5.12
4.60
4.40
4.38
2.33
2.26
5.07
2.00
2.02
0.84
2.09
6.02
3.02
f1 (ppm)

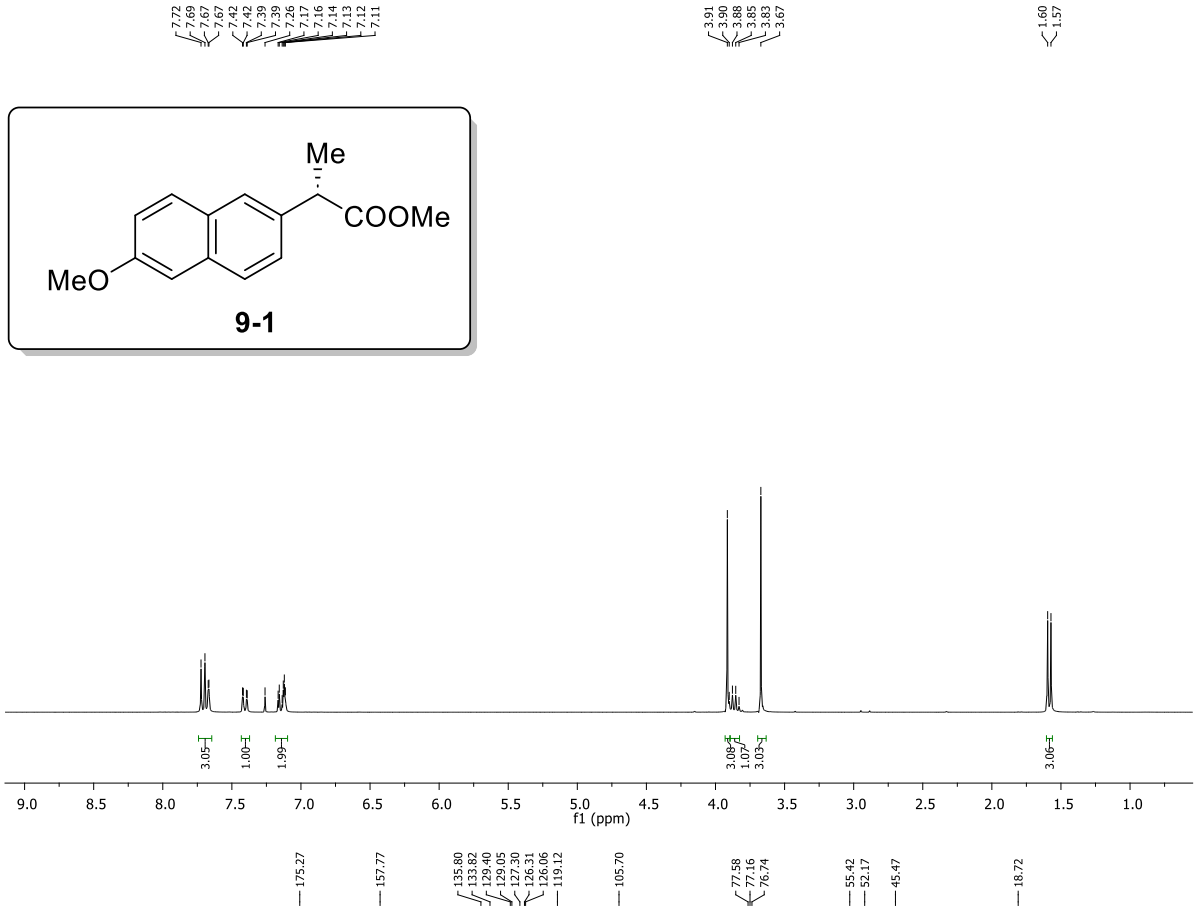

156.27
137.69
137.42
136.72
131.09
129.32
128.66
128.25
128.21
77.59
77.16
76.74
66.87
39.49
21.04
19.71
f1 (ppm)

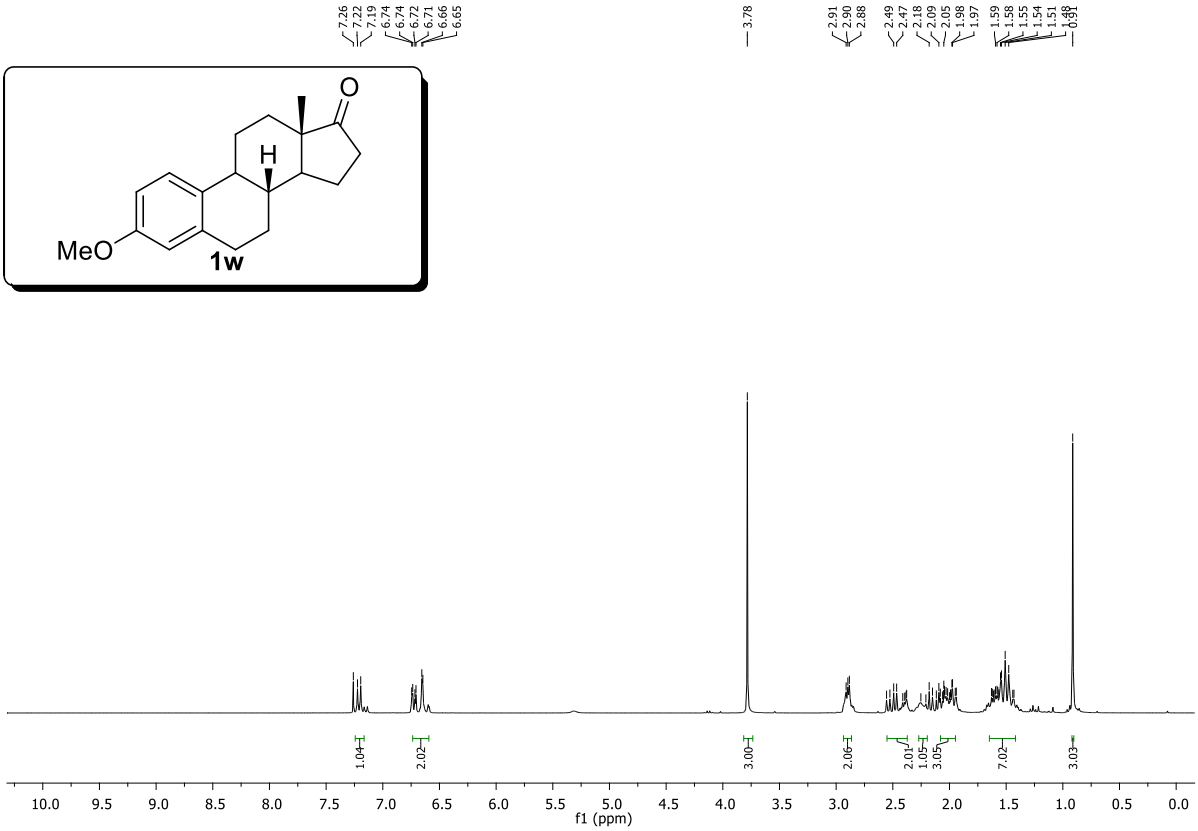

Me
COOMe

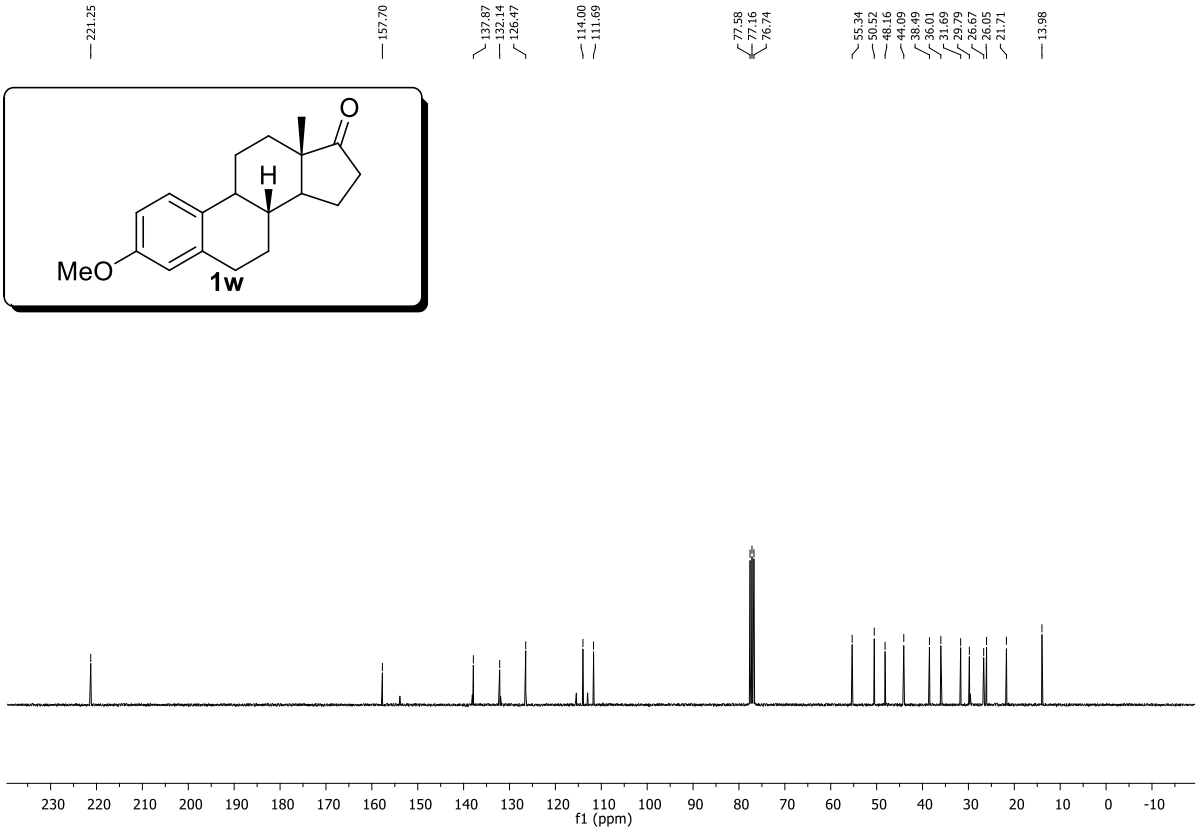
8-1

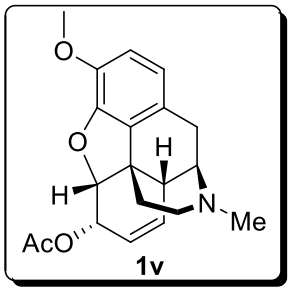
7.22
7.21
7.20
7.19
7.11
7.09
3.72
3.69
3.66
2.46
2.44
1.90
1.87
1.85
1.83
1.81
1.50
1.48
0.92
0.89
2.03
2.00
0.90
3.01
2.08
0.88
3.02
6.09
f1 (ppm)


175.32
140.66
137.87
129.46
127.24
77.58
77.16
76.74
52.06
45.16
45.13
30.29
22.50
18.73
f1 (ppm)

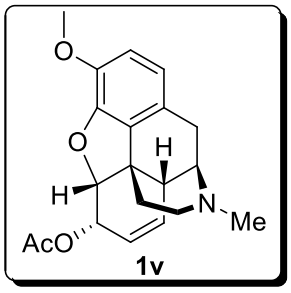

7.72
7.69
7.67
7.67
7.42
7.42
7.39
7.39
7.26
7.17
7.16
7.14
7.13
7.12
7.11
3.91
3.90
3.88
3.85
3.83
3.67
1.60
1.57
Me
COOMe
MeO
9-1
3.05
1.00
1.99
3.08
1.07
3.03
3.06
f1 (ppm)
175.27
157.77
135.80
133.82
129.40
129.05
127.30
126.31
126.06
119.12
105.70
77.58
77.16
76.74
55.42
52.17
45.47
18.72
f1 (ppm)


7.26
7.22
7.19
6.74
6.74
6.72
6.71
6.66
6.65
3.78
2.91
2.90
2.88
2.49
2.47
2.18
2.09
2.05
1.98
1.97
1.59
1.58
1.55
1.54
1.51
1.48
0.91
O
H
MeO
1w
1.04
2.02
3.00
2.06
2.01
1.05
3.05
7.02
3.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

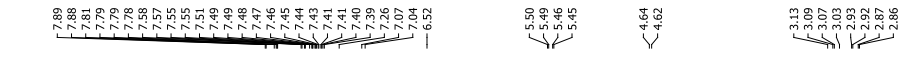

221.25
157.70
137.87
132.14
126.47
114.00
111.69
77.58
77.16
76.74
55.34
50.52
48.16
44.09
38.49
36.01
31.69
29.79
26.67
26.05
21.71
13.98
O
H
MeO
1w
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

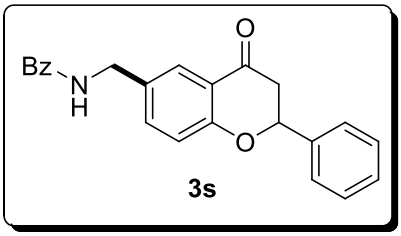

O
O
H
H
N
Me
AcO
1v

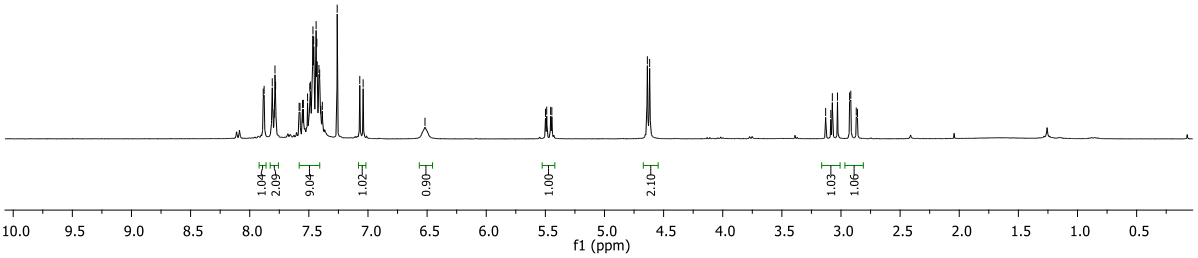
7.26
6.66
6.64
6.55
6.52
5.64
5.63
5.61
5.60
5.60
5.45
5.44
5.42
5.41
5.40
5.19
5.18
5.18
5.17
5.16
5.15
5.07
5.05
3.84
3.37
3.36
3.35
3.34
3.06
3.00
2.75
2.74
2.73
2.60
2.57
2.56
2.44
2.42
2.41
2.38
2.37
2.34
2.33
2.32
2.27
2.25
2.15
2.05
2.04
2.01
1.88
1.88
1.84
1.83
1.00
0.98
1.01
1.02
1.00
1.01
3.04
1.05
1.06
1.04
1.04
3.08
2.07
2.92
1.13
1.07
f1 (ppm)

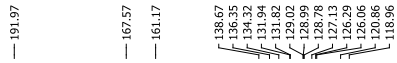

O
O
H
H
N
Me
AcO
1v

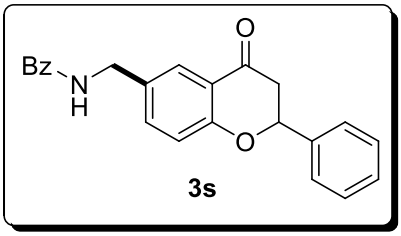
170.71
146.87
142.24
130.71
129.71
128.55
127.07
119.25
113.90
88.22
59.17
56.73
46.77
43.17
42.87
40.83
35.49
20.99
20.46
f1 (ppm)

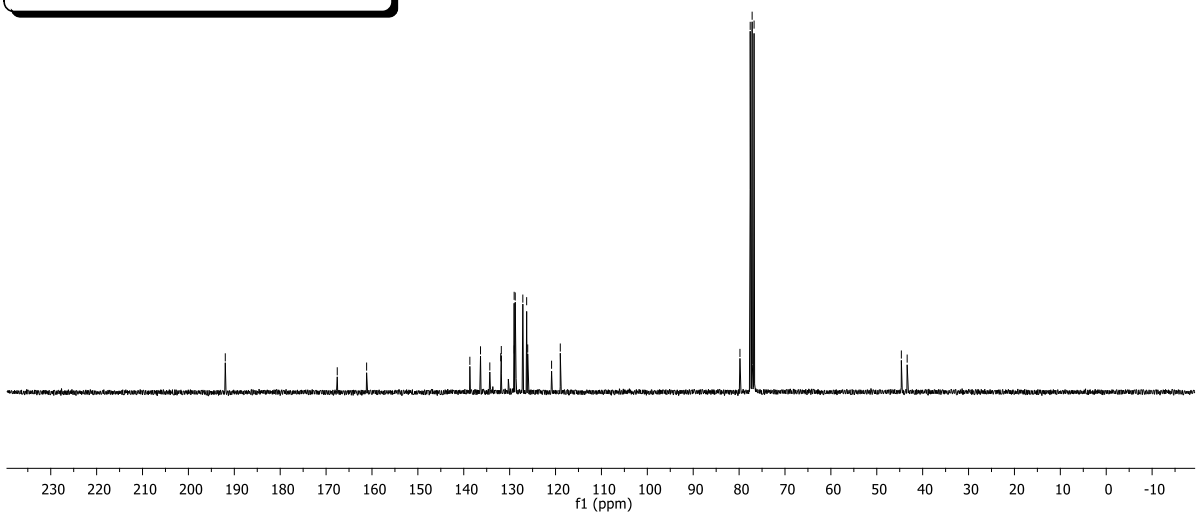

7.89
7.88
7.81
7.79
7.79
7.78
7.58
7.57
7.55
7.55
7.51
7.49
7.49
7.48
7.47
7.46
7.45
7.44
7.43
7.41
7.41
7.40
7.39
7.26
7.07
7.04
6.52
5.50
5.49
5.46
5.45
4.64
4.62
3.13
3.09
3.07
3.03
2.93
2.92
2.87
2.86

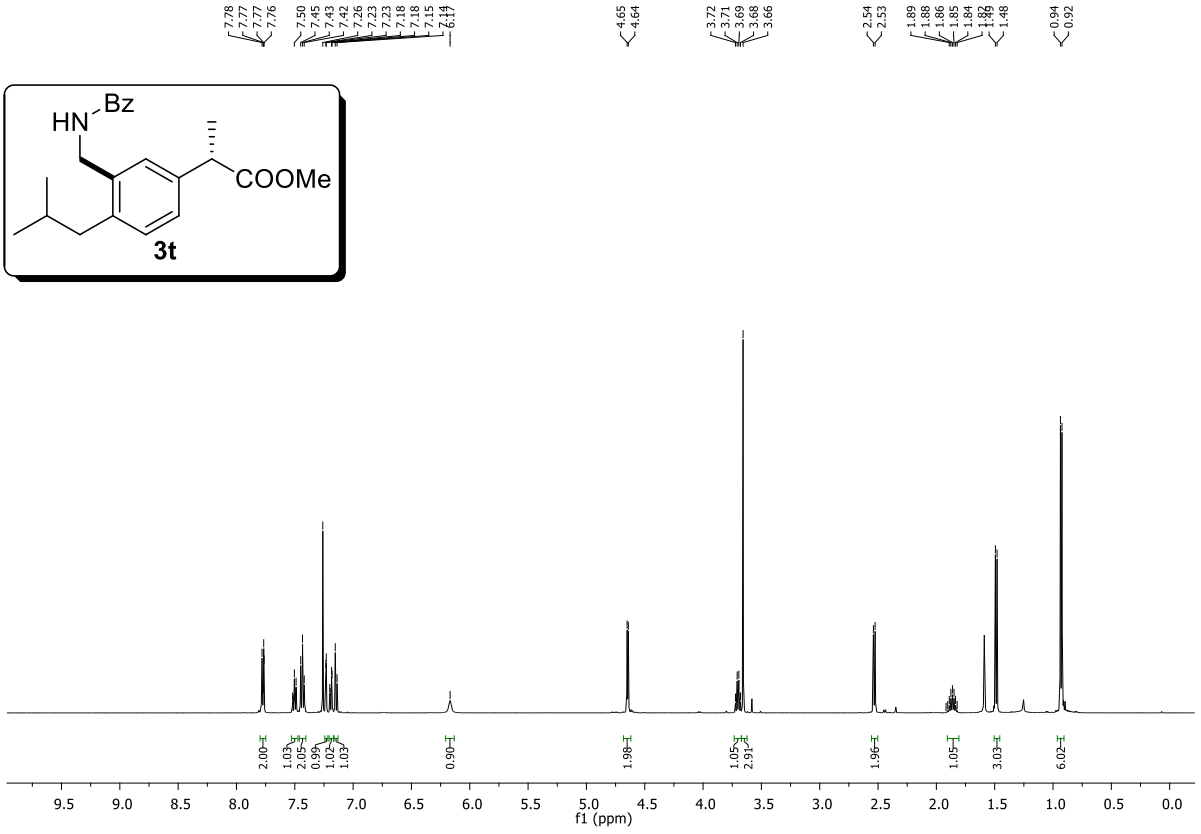

Bz
N
H
O
O
3s

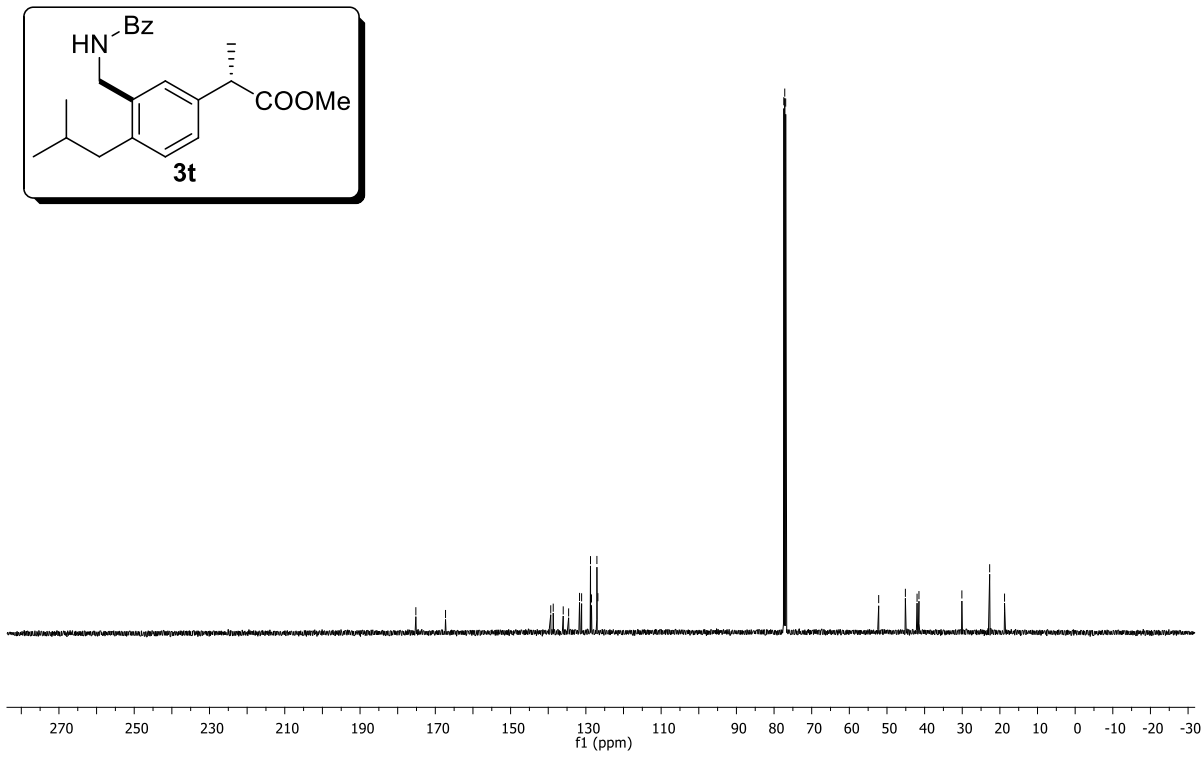

1.04
2.09
9.04
1.02
0.90
1.00
2.10
1.03
1.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

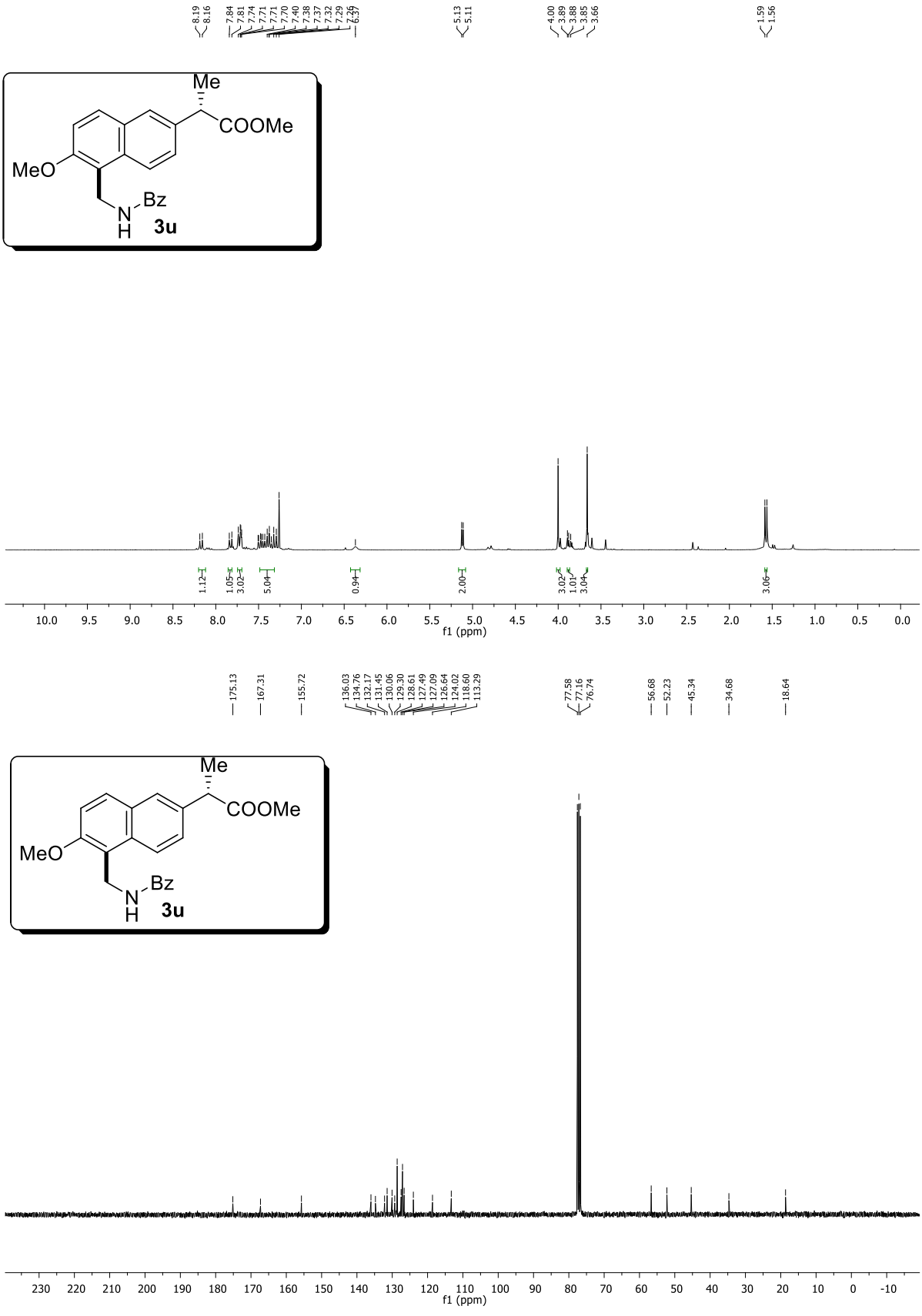

191.97
167.57
161.17
138.67
136.35
134.32
131.94
131.82
129.02
128.99
128.78
127.13
126.29
126.06
120.86
118.96
79.81
77.58
77.16
76.74
44.65
43.38

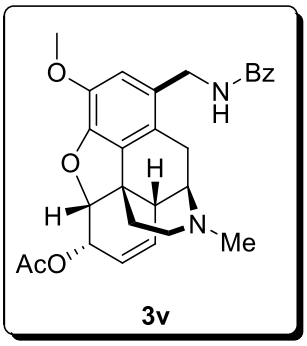

Bz
N
H
O
O
3s


230
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)

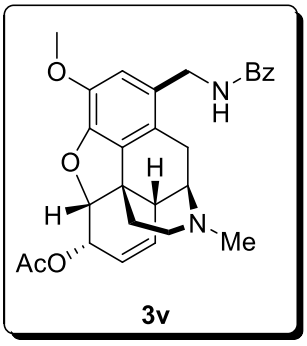

HN
Bz
COOMe
3t
f1 (ppm)


HN
Bz
COOMe
3t
f1 (ppm)

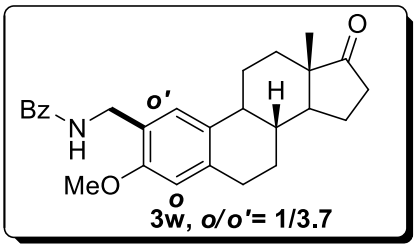

8.19
8.16
7.84
7.81
7.74
7.71
7.71
7.70
7.40
7.38
7.37
7.32
7.29
5.13
5.11
4.00
3.89
3.88
3.85
3.66
1.59
1.56
Me
COOMe
MeO
Bz
N
H
3u
1.12
1.05
3.02
5.04
0.94
2.00
3.02
1.01
3.04
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
175.13
167.31
155.72
136.03
134.76
132.17
131.45
130.06
129.30
128.61
127.49
127.09
126.64
124.02
118.60
113.29
77.58
77.16
76.74
56.68
52.23
45.34
34.68
18.64
Me
COOMe
MeO
Bz
N
H
3u
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



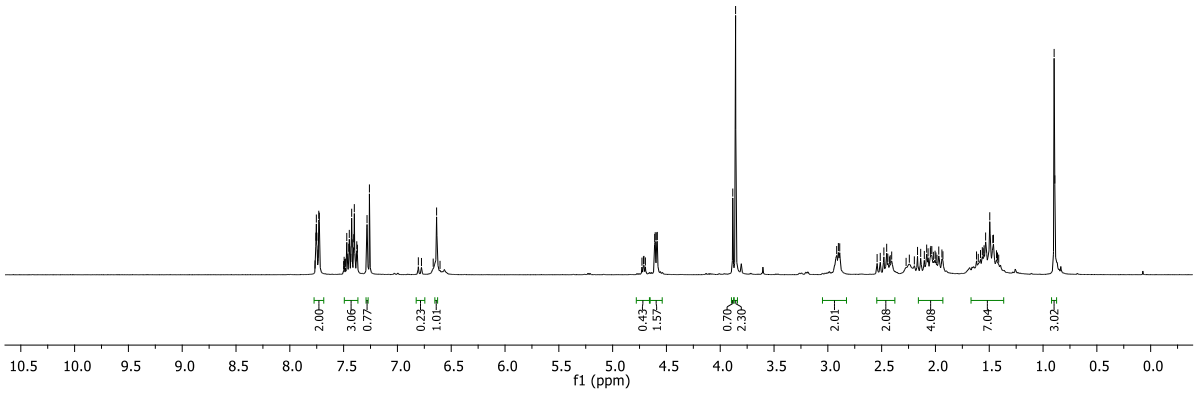
3v

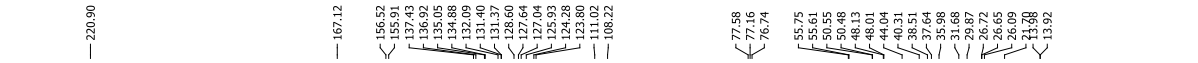


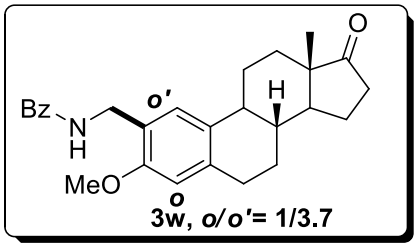
3v



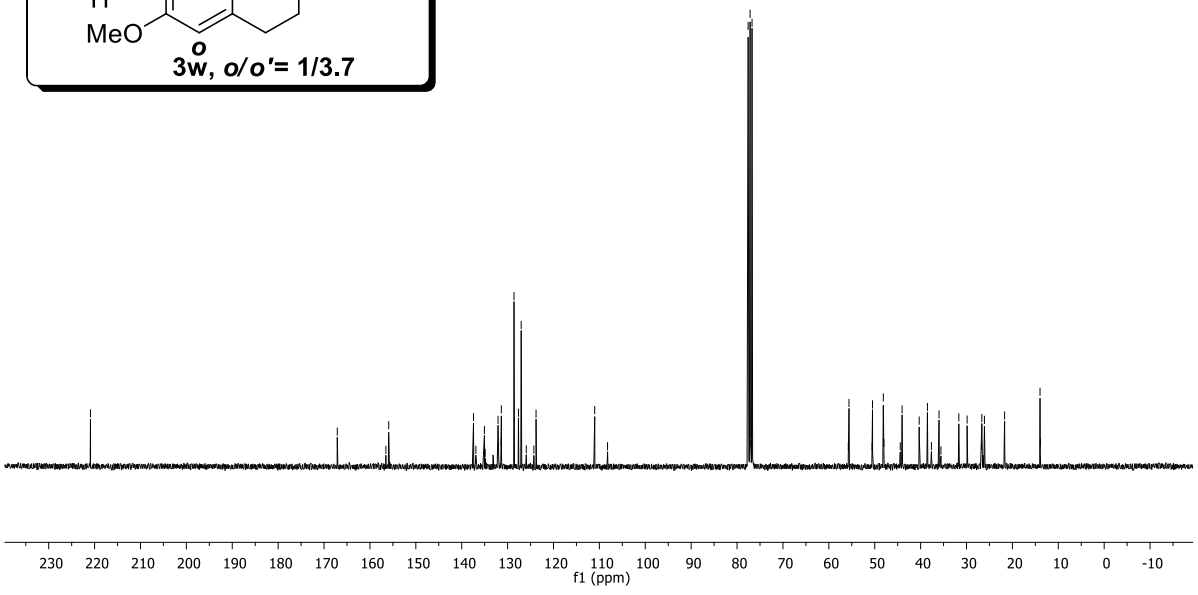
3w, *o*/*o*′= 1/3.7

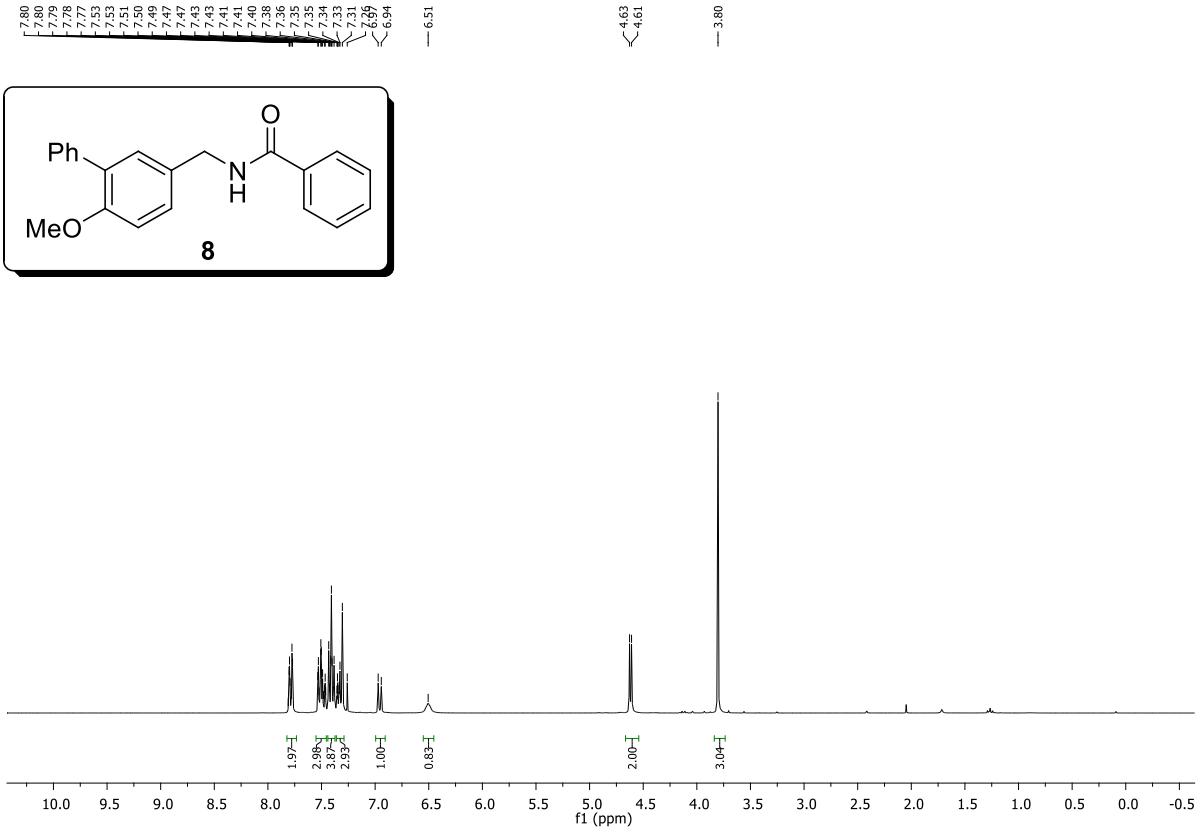


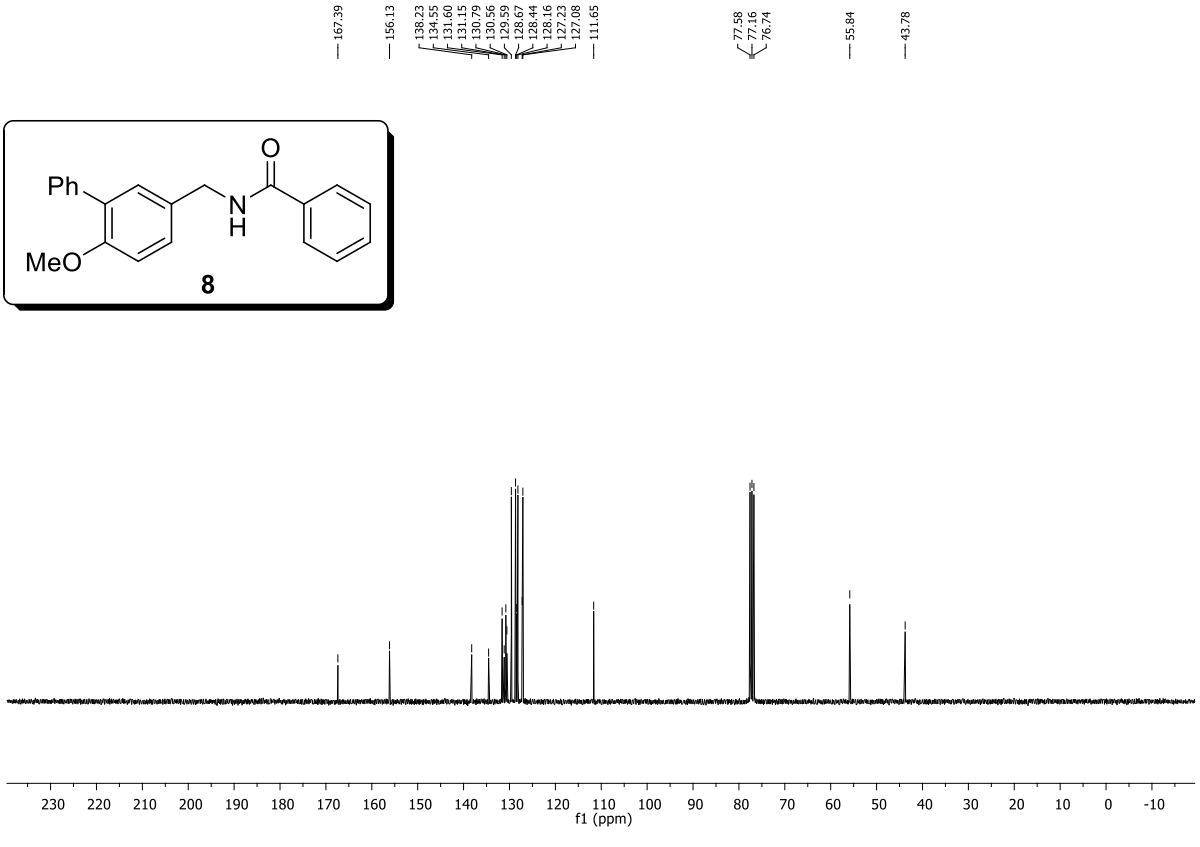


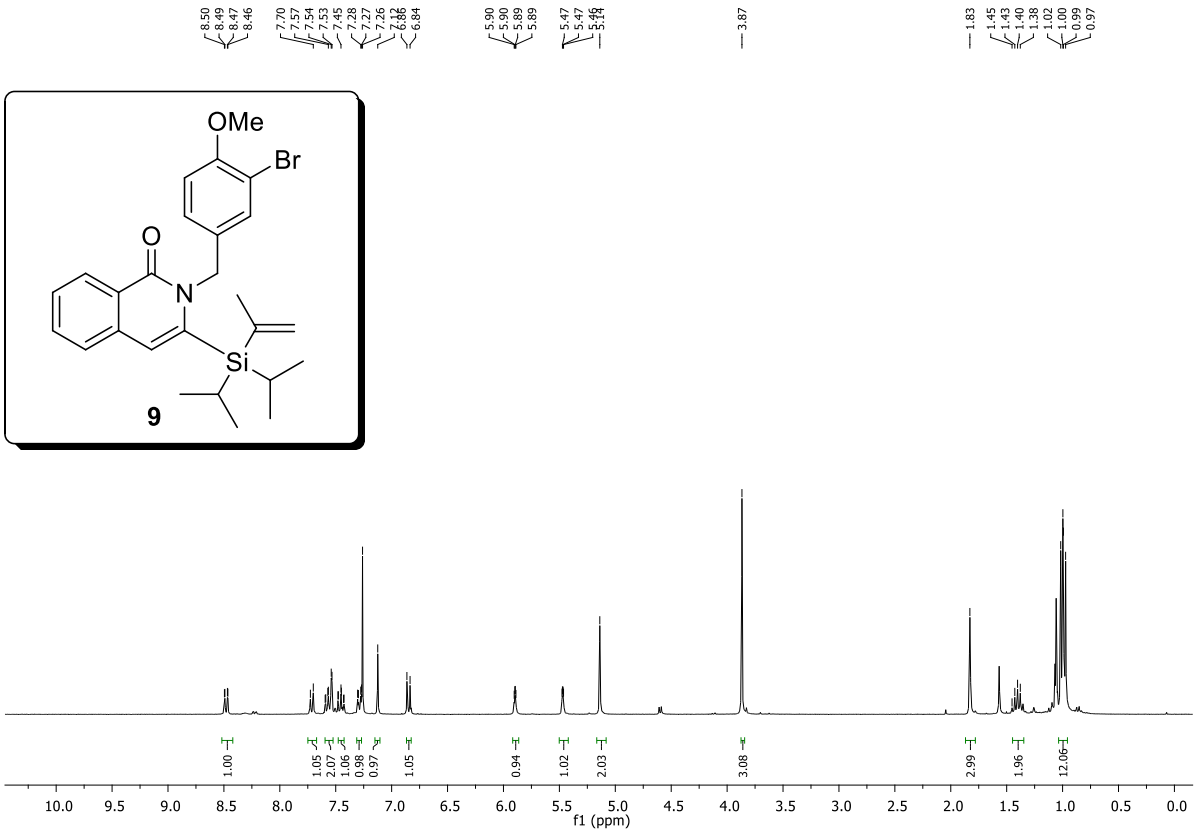


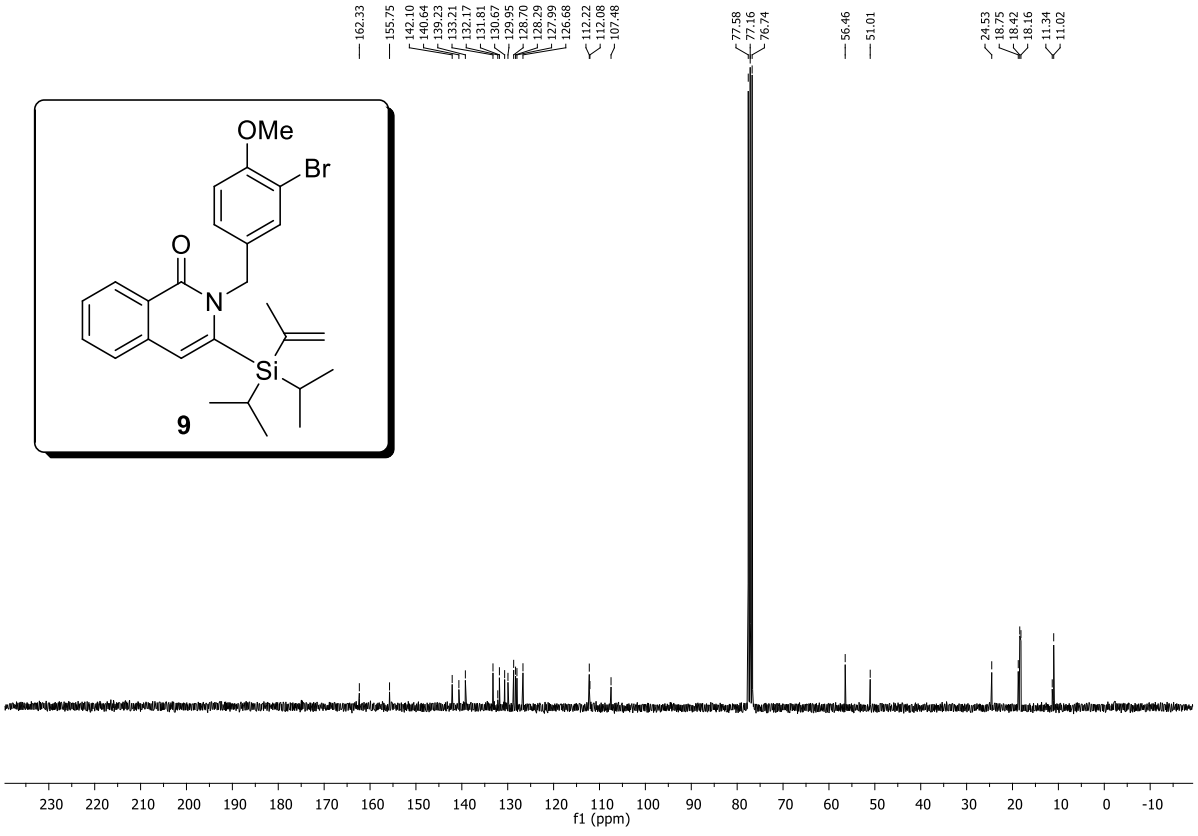
3w, *o*/*o*′= 1/3.7

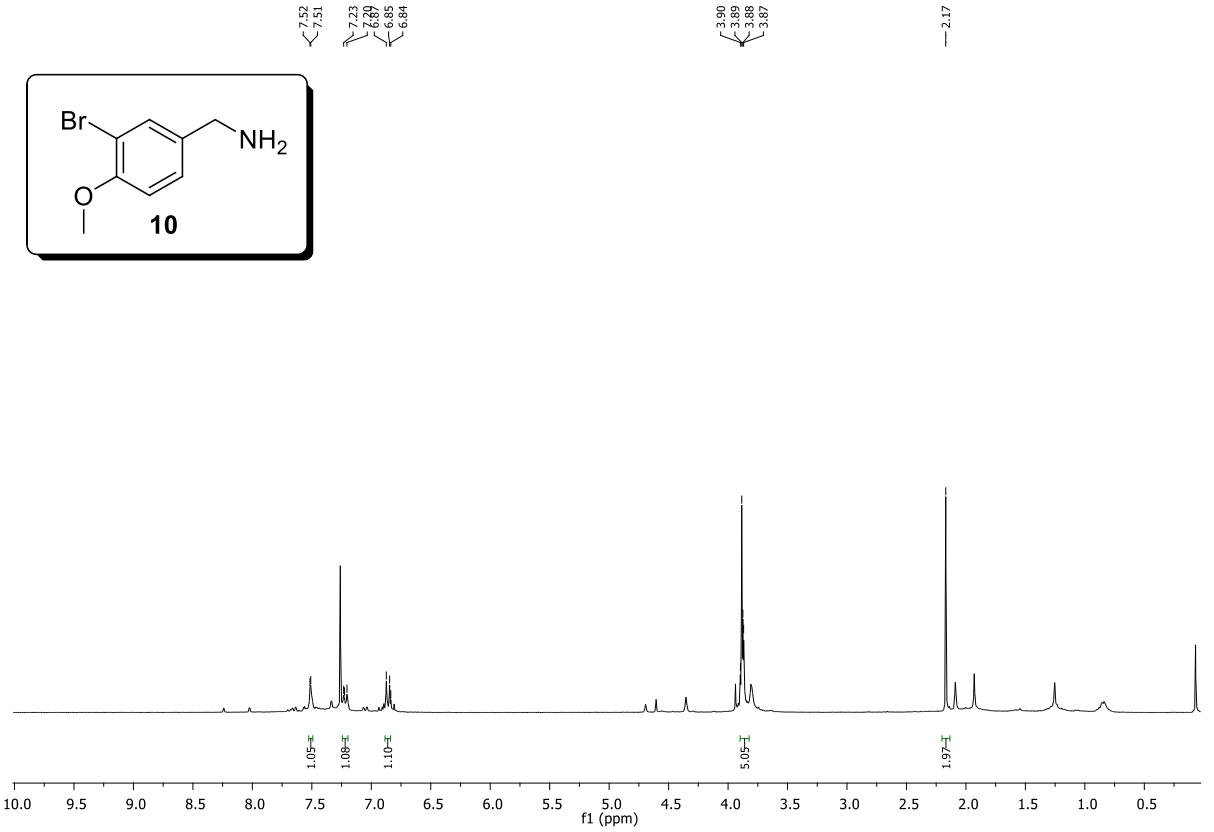


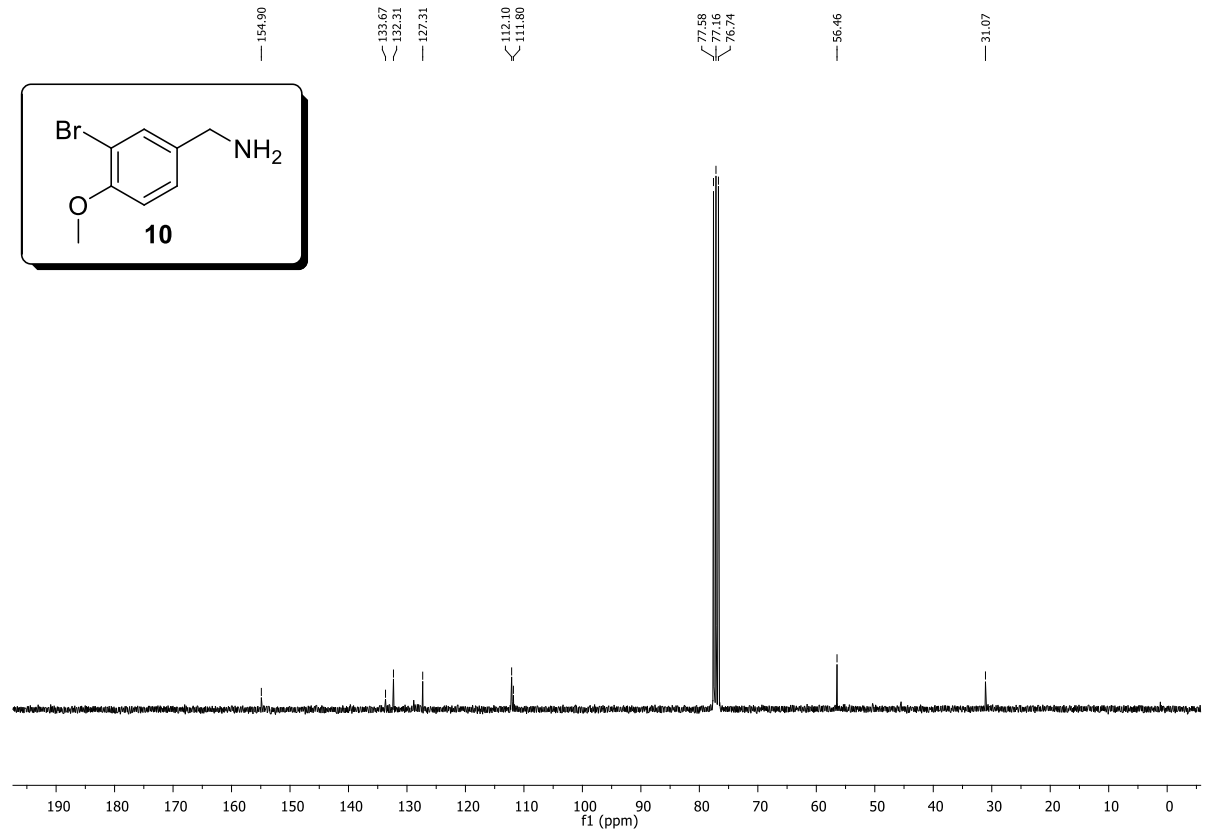

7.80
7.80
7.79
7.78
7.77
7.53
7.53
7.51
7.50
7.49
7.47
7.47
7.43
7.43
7.41
7.41
7.40
7.38
7.36
7.35
7.35
7.34
7.33
7.31
7.26
6.97
6.94
6.51
4.63
4.61
3.80
Ph
MeO
N
H
O
8
1.97
2.98
3.87
2.93
1.00
0.83
2.00
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


167.39
156.13
138.23
134.55
131.60
131.15
130.79
130.56
129.59
128.67
128.44
128.16
127.23
127.08
111.65
77.58
77.16
76.74
55.84
43.78
Ph
MeO
N
H
O
8
230
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)

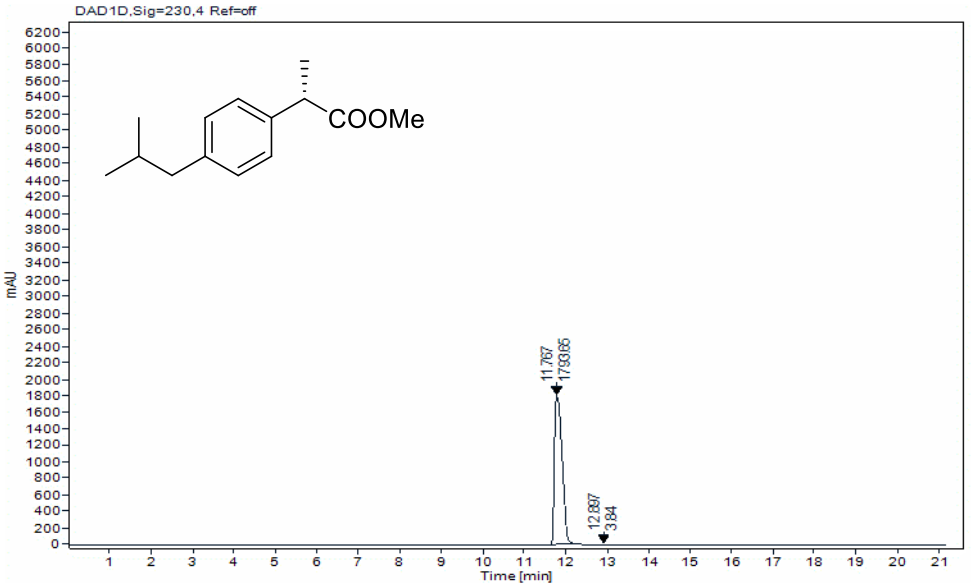

OMe
Br
O
N
Si
9
f1 (ppm)


OMe
Br
O
N
Si
9
f1 (ppm)

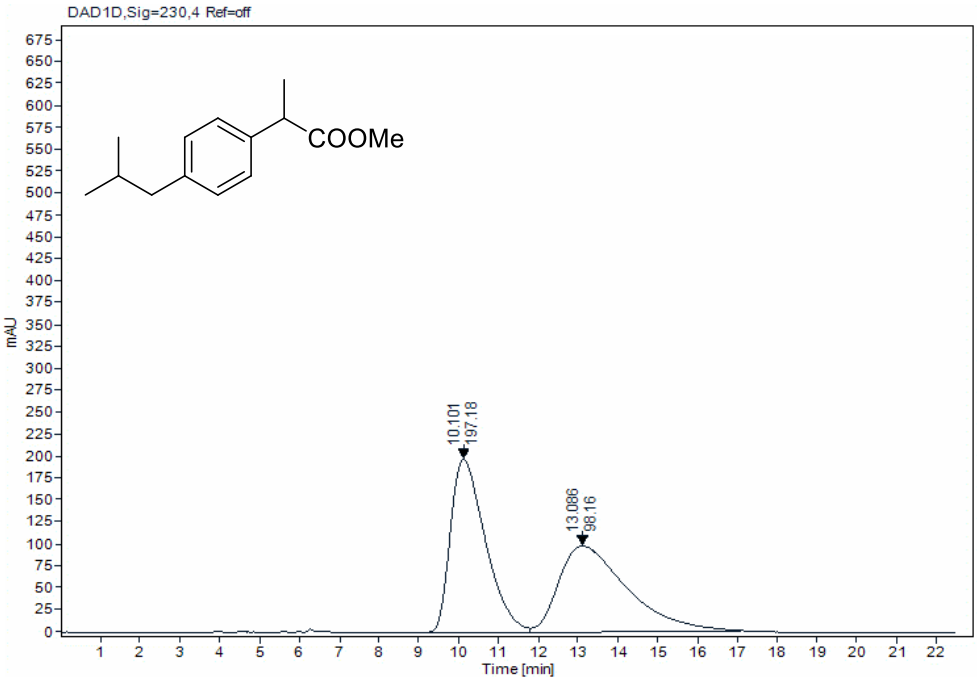

7.52
7.51
7.23
7.20
6.87
6.85
6.84
3.90
3.89
3.88
3.87
2.17
Br
NH2
O
10
1.05
1.08
1.10
5.05
1.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


154.90
133.67
132.31
127.31
112.10
111.80
77.58
77.16
76.74
56.46
31.07
Br
NH2
O
10
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

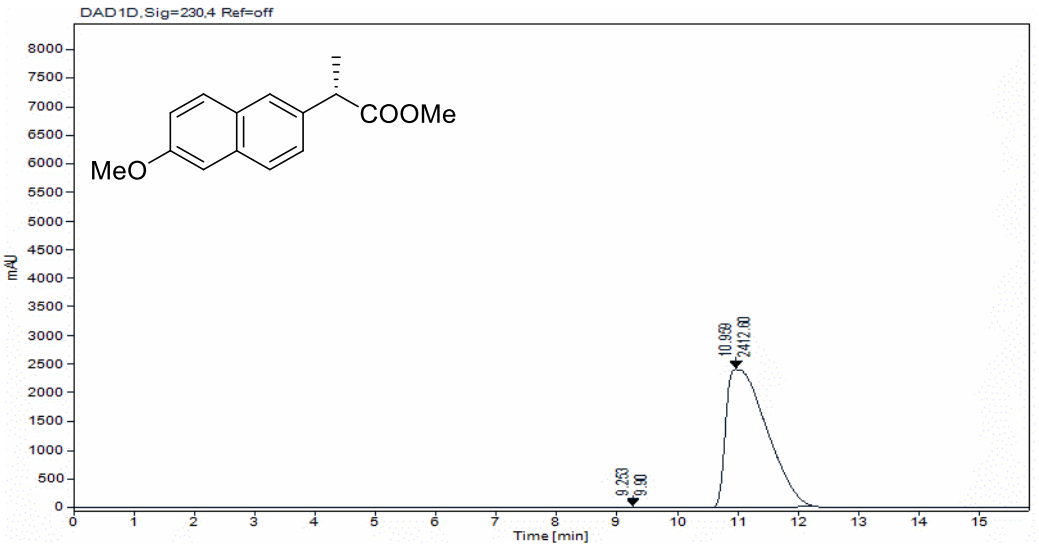
6. Chiral HPLC spectrums



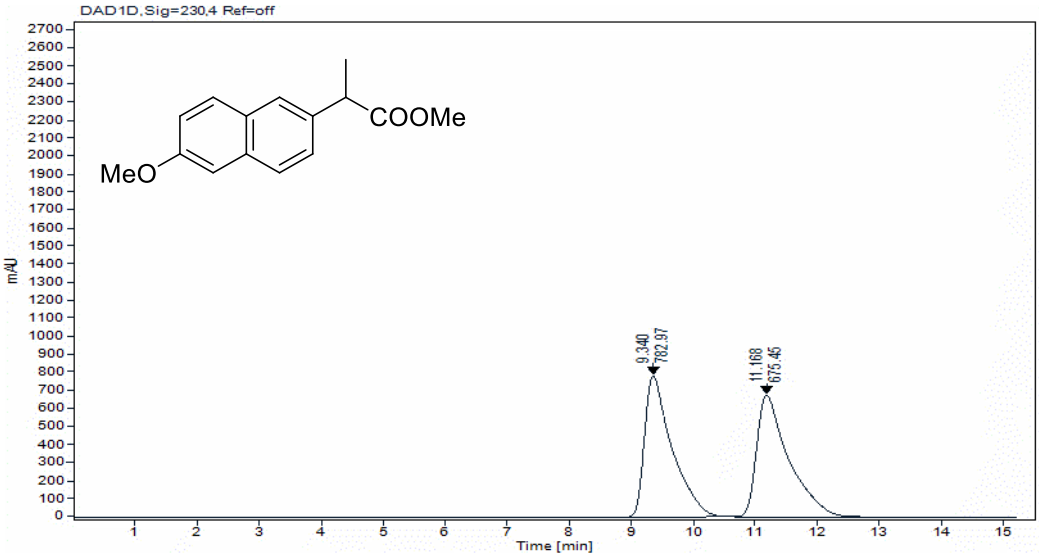
Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
11.767	0.7741	23074.7633	1793.6464	99.0574
12.897	1.5201	219.5656	3.8351	0.9426



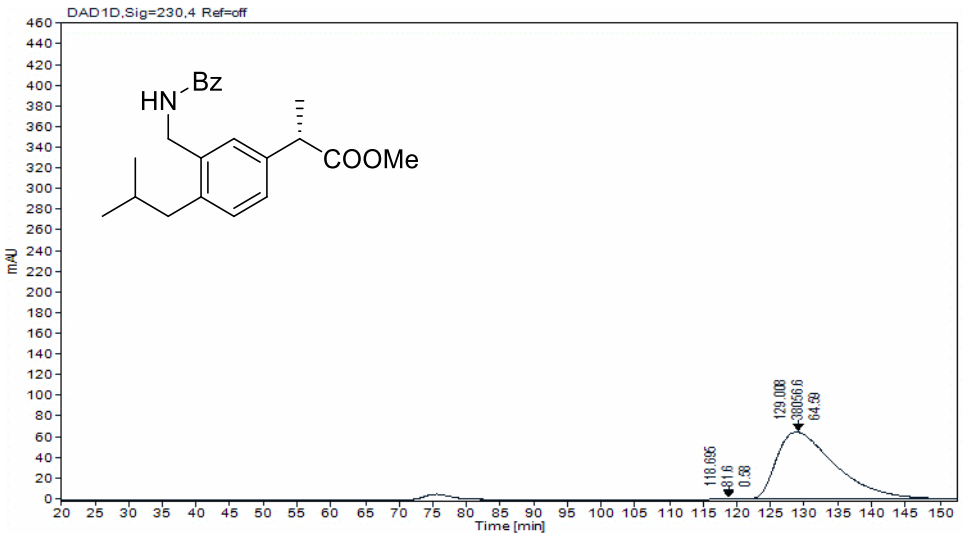
Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
10.101	2.5932	12073.261	197.1753	50.5183
13.086	5.2813	11825.51	98.1568	49.4817



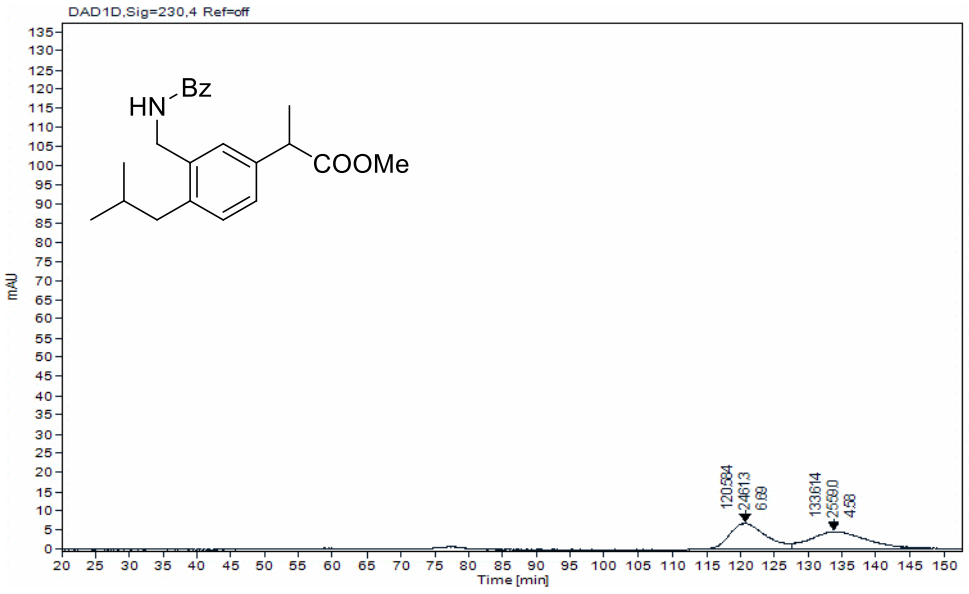
Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
9.253	1.3013	295.3429	9.9007	0.2605
10.959	1.8564	113080.17	2412.6	99.7395



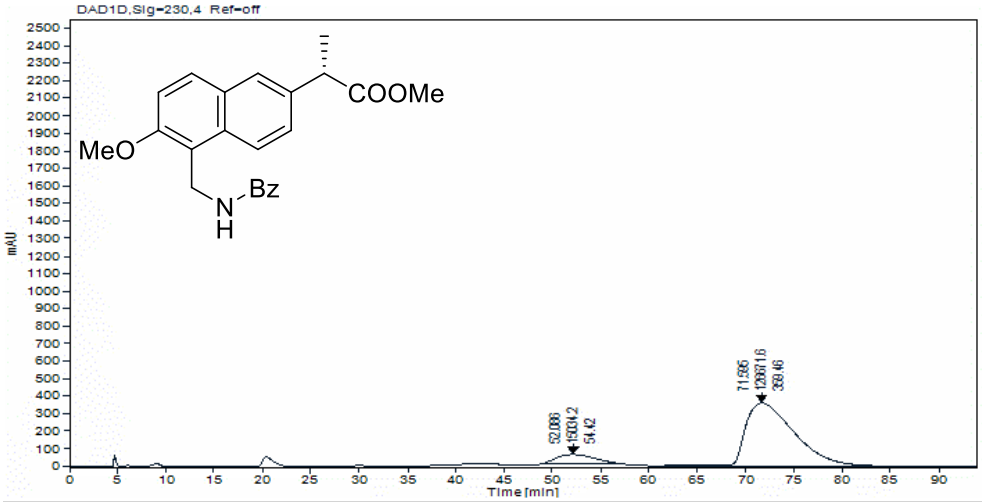
Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
9.34	1.7975	24050.205	782.9663	49.9862
11.168	2.0745	24063.476	675.4506	50.0138



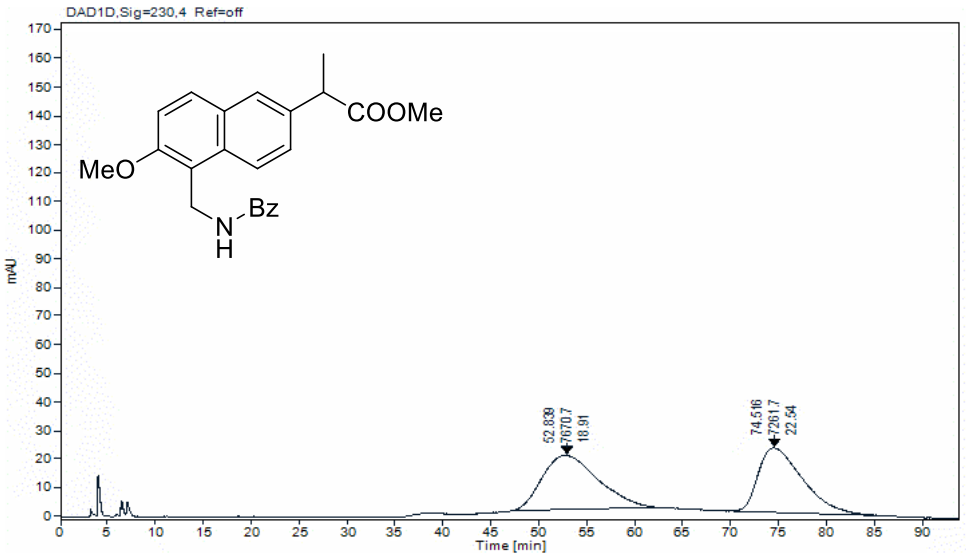
Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
118.695	5.45	81.6034	0.5777	0.214
129.008	26.3828	38056.584	64.592	99.786



Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
120.584	12.2272	2461.296	6.6928	49.0267
133.614	19.9129	2559.0206	4.5816	50.9733



Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
52.086	8.4119	15034.171	54.4174	10.6094
71.595	24.7219	126671.57	359.4567	89.3906



Signal:	DAD1D,Sig=230,4 Ref=off			
RT [min]	Width [min]	Area	Height	Area%
52.839	15.2954	7670.7384	18.9102	51.3696
74.516	18.358	7261.6945	22.5386	48.6304

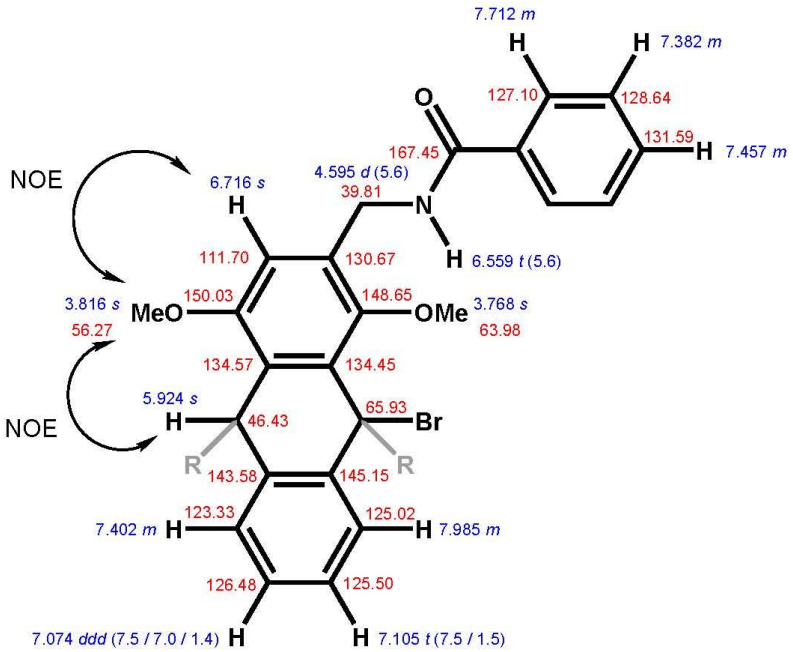
7. 2D- (^{1}H/^{1}H-, ^{1}H/^{13}C-) NMR Spectra

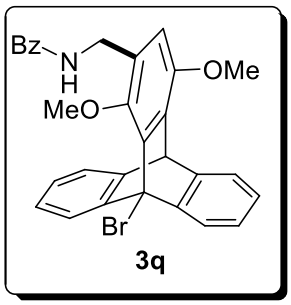
Li Guobao LGB-13-85-HPLC structure verification Avance600 2022-08-16

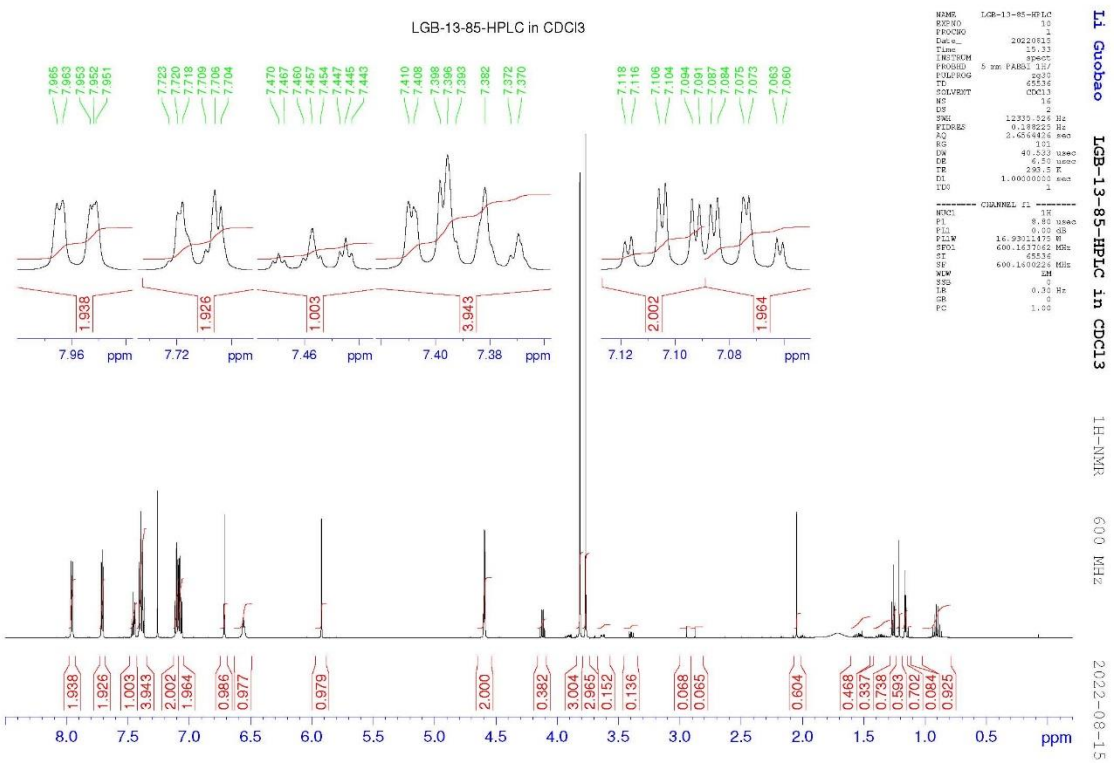
LGB-13-85 in $CDCl_3$

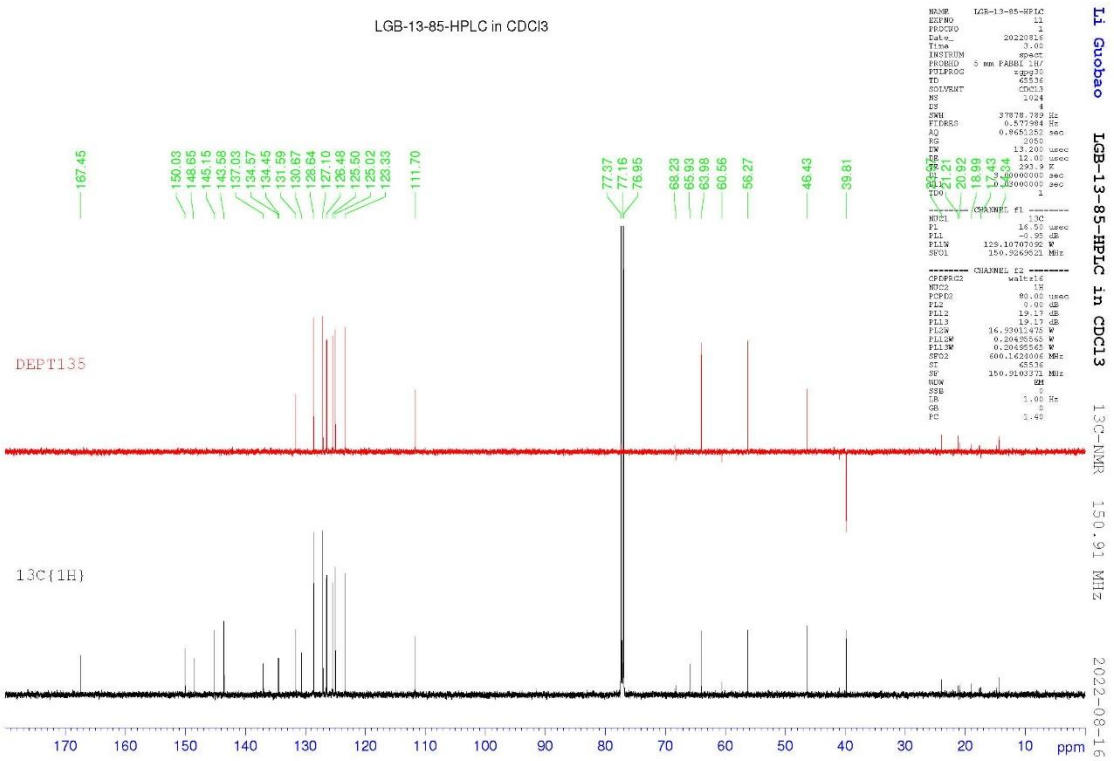
NMR Data were recorded at ambient temperature on a Bruker Avance III 600 spectrometer operating at 600.1 MHz for ^{1}H and 125.8 MHz for ^{13}C. Chemical shifts δ are given in ppm relative to TMS. The solvent signals were used as reference (^{1}H: δ_H 7.260 ppm residual $CHCl_3$, ^{13}C: δ_C 77.16 ppm). Coupling constants were given in Hertz and determined assuming first-order spin-spin coupling.

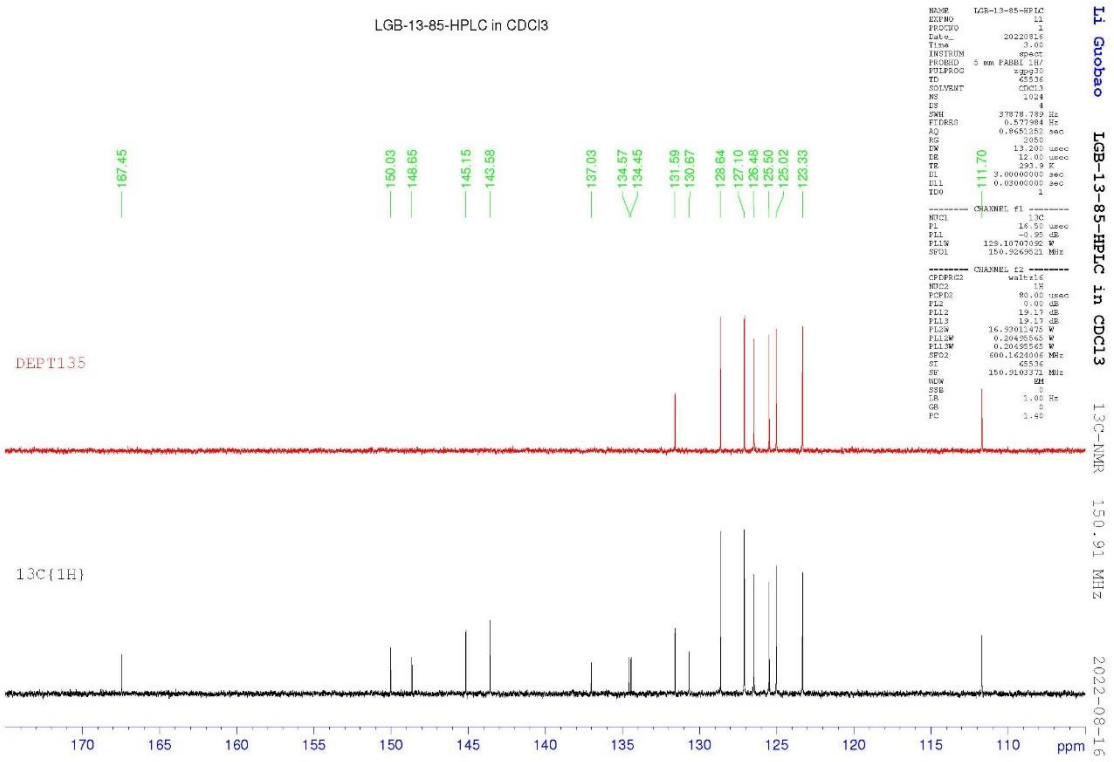
red ^{13}C chemical shift
blue ^{1}H chemical shift

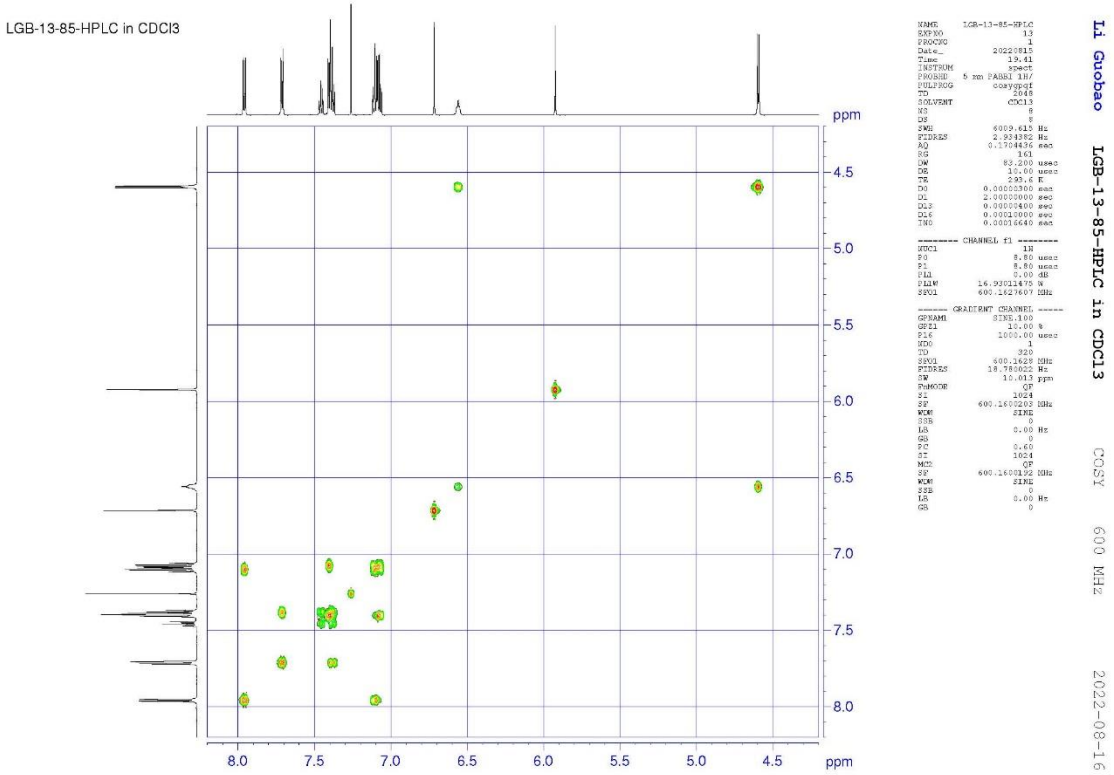


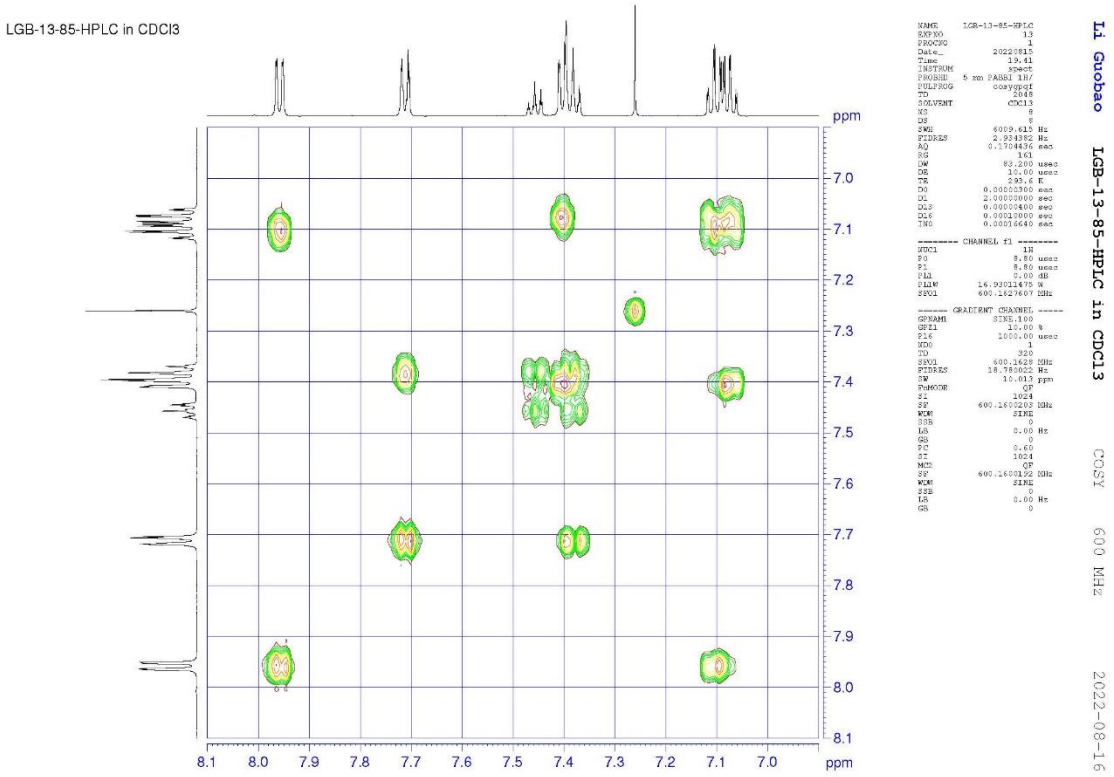


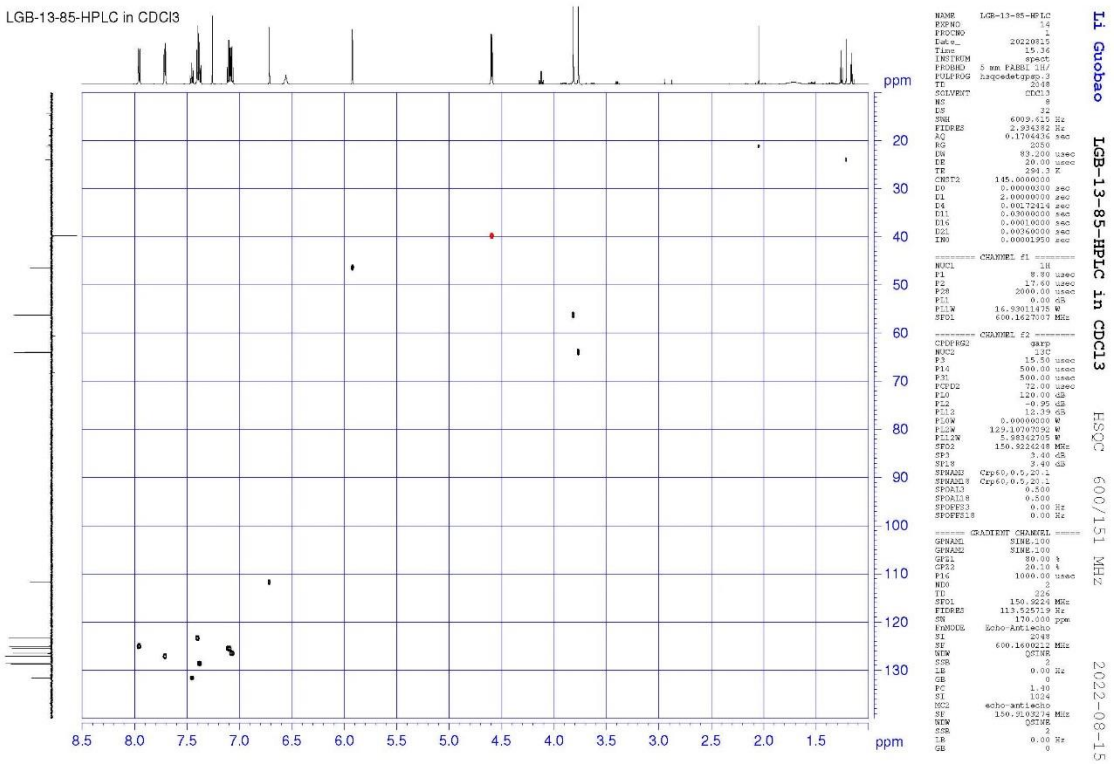

LGB-13-85-HPLC in CDCl3
Li Guobao
LGB-13-85-HPLC in CDCl3
1H-NMR
600 MHz
2022-08-15
ppm

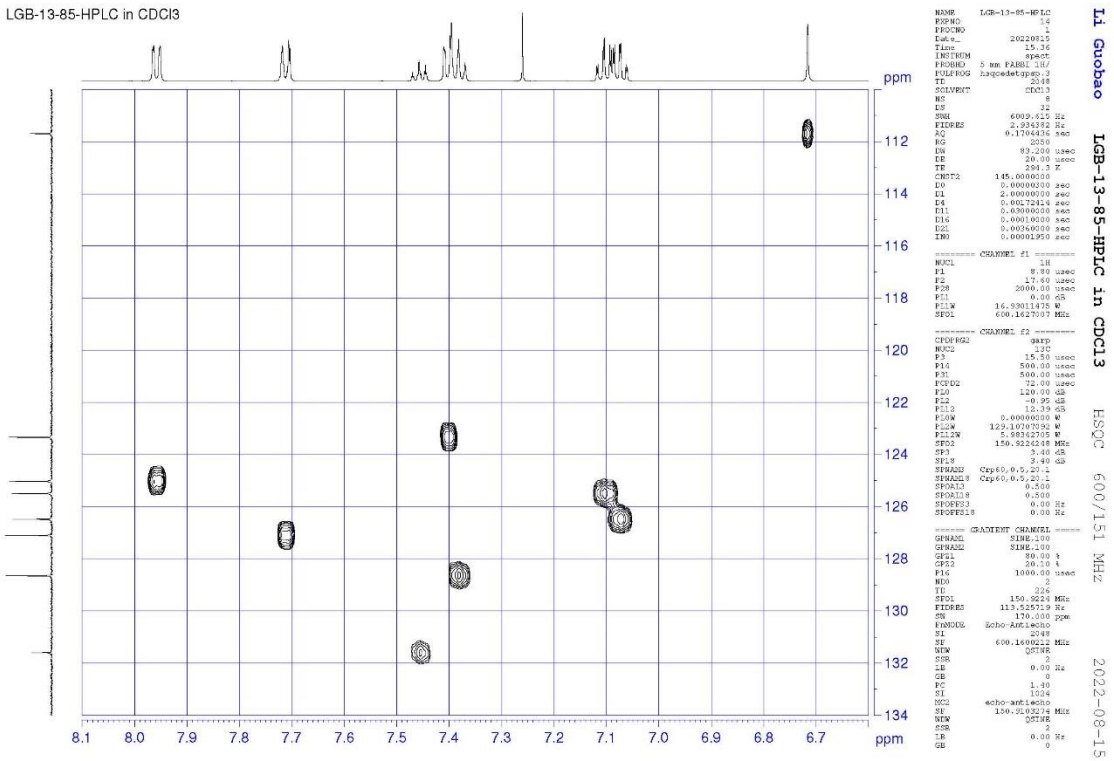

LGB-13-85-HPLC in CDCl3
Li Guobao
LGB-13-85-HPLC in CDCl3
DEPT135
13C{1H}
13C-NMR
150.91 MHz
2022-08-16
ppm

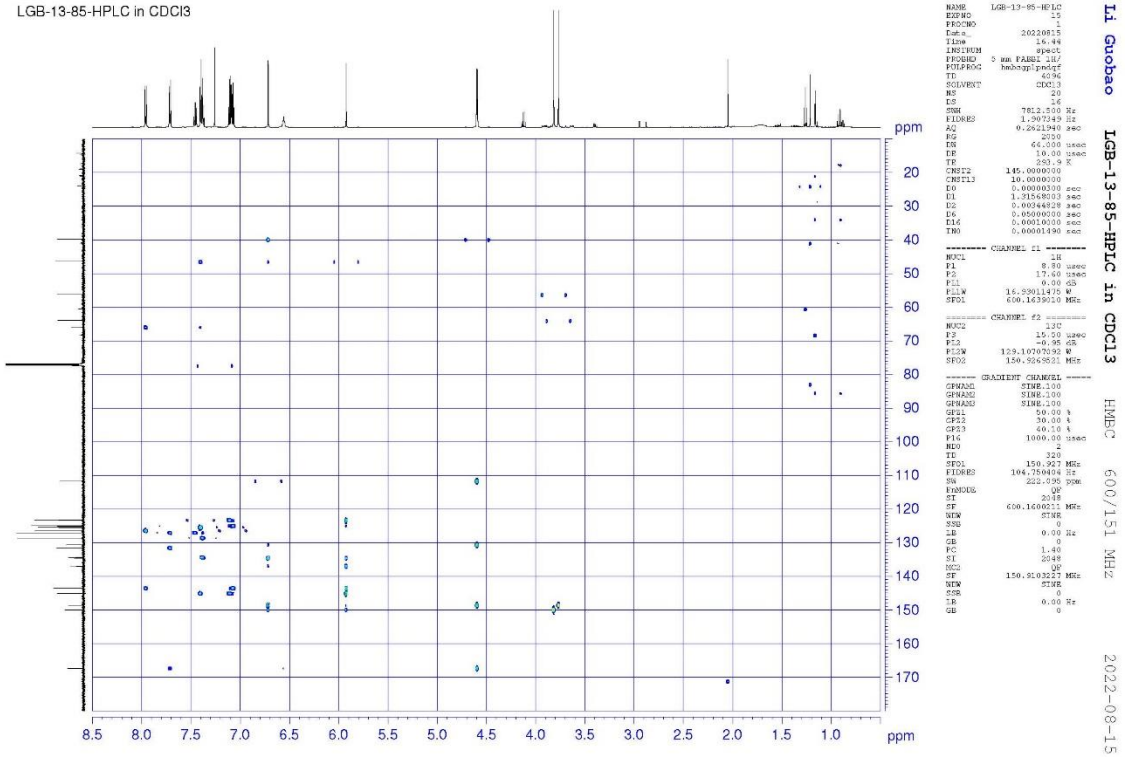

LGB-13-85-HPLC in CDCl3
DEPT135
13C{1H}
167.45
150.03
148.65
145.15
143.58
137.03
134.57
134.45
131.59
130.67
128.64
127.10
126.48
125.50
125.02
123.33
111.70
170
165
160
155
150
145
140
135
130
125
120
115
110
ppm
Li Guobao
LGB-13-85-HPLC in CDCl3
13C-NMR
150.91 MHz
2022-08-16

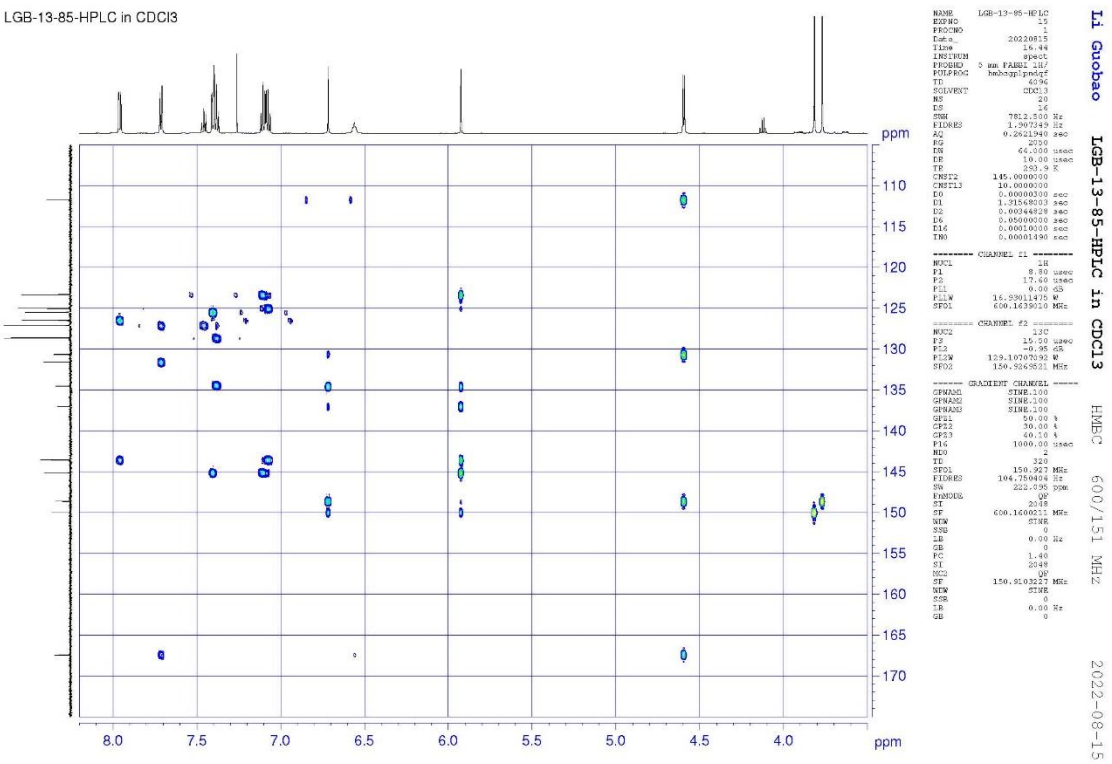

LGB-13-85-HPLC in CDCl3
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
ppm
Li Guobao
LGB-13-85-HPLC in CDCl3
COSY
600 MHz
2022-08-16

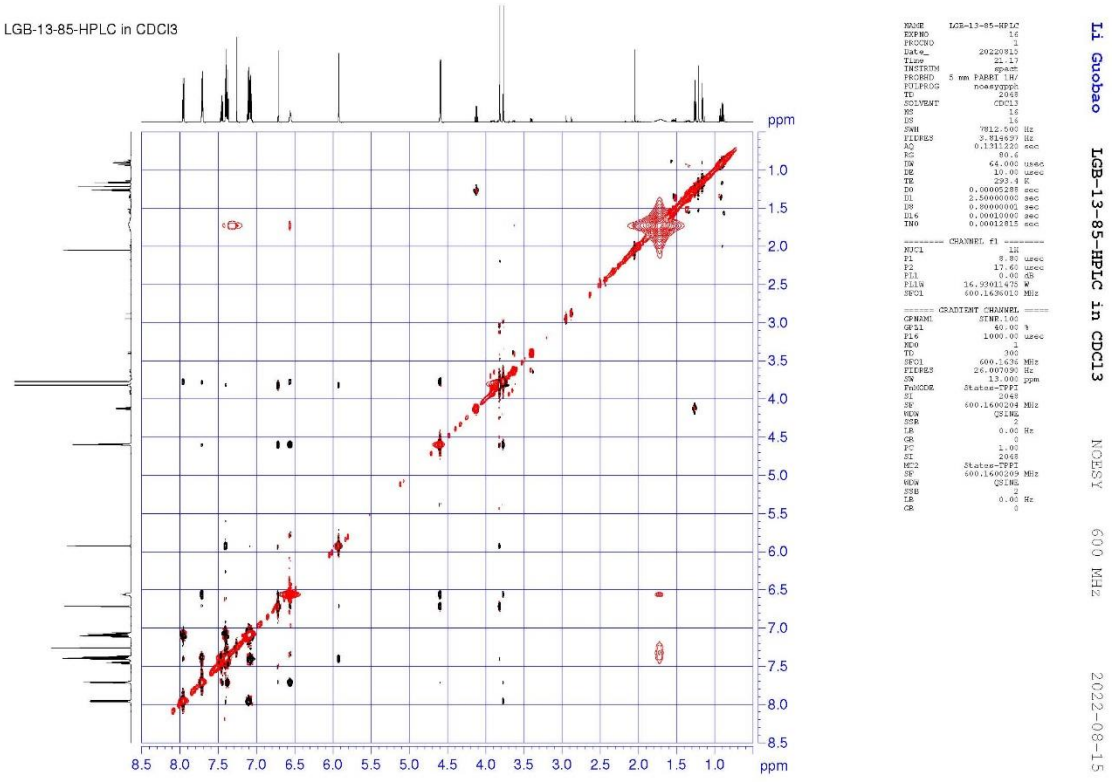

LGB-13-85-HPLC in CDCl3
Li Guobao LGB-13-85-HPLC in CDCl3 COSY 600 MHz 2022-08-16
ppm


LGB-13-85-HPLC in CDCl3
Li Guobao LGB-13-85-HPLC in CDCl3 HSQC 600/151 MHz 2022-08-15
ppm


LGB-13-85-HPLC in CDCl3
Li Guobao
LGB-13-85-HPLC in CDCl3 HSQC 600/151 MHz
2022-08-15
ppm


LGB-13-85-HPLC in CDCl3
Li Guobao
LGB-13-85-HPLC in CDCl3 HMBC 600/151 MHz
2022-08-15
ppm

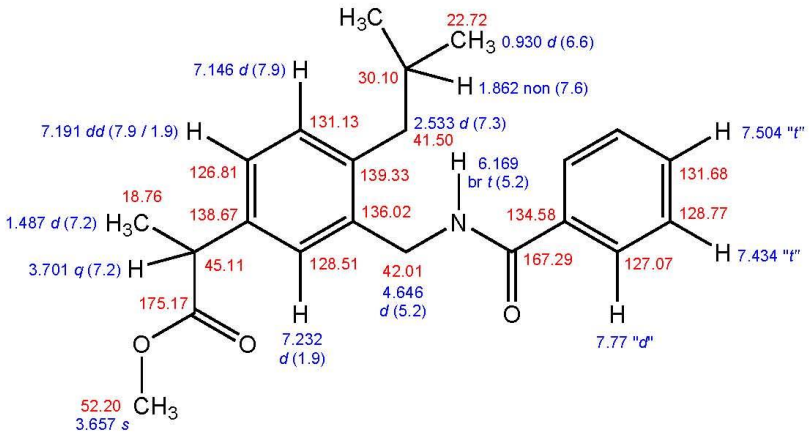

LGB-13-85-HPLC in CDCl3
Li Guobao
LGB-13-85-HPLC in CDCl3
HMBC 600/151 MHz
2022-08-15
ppm
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0
110 115 120 125 130 135 140 145 150 155 160 165 170

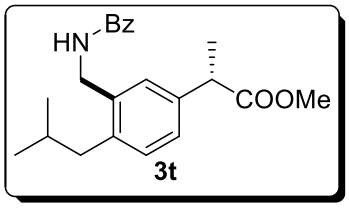

LGB-13-85-HPLC in CDCl3
Li Guobao
LGB-13-85-HPLC in CDCl3
NOESY 600 MHz
2022-08-15
ppm
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5

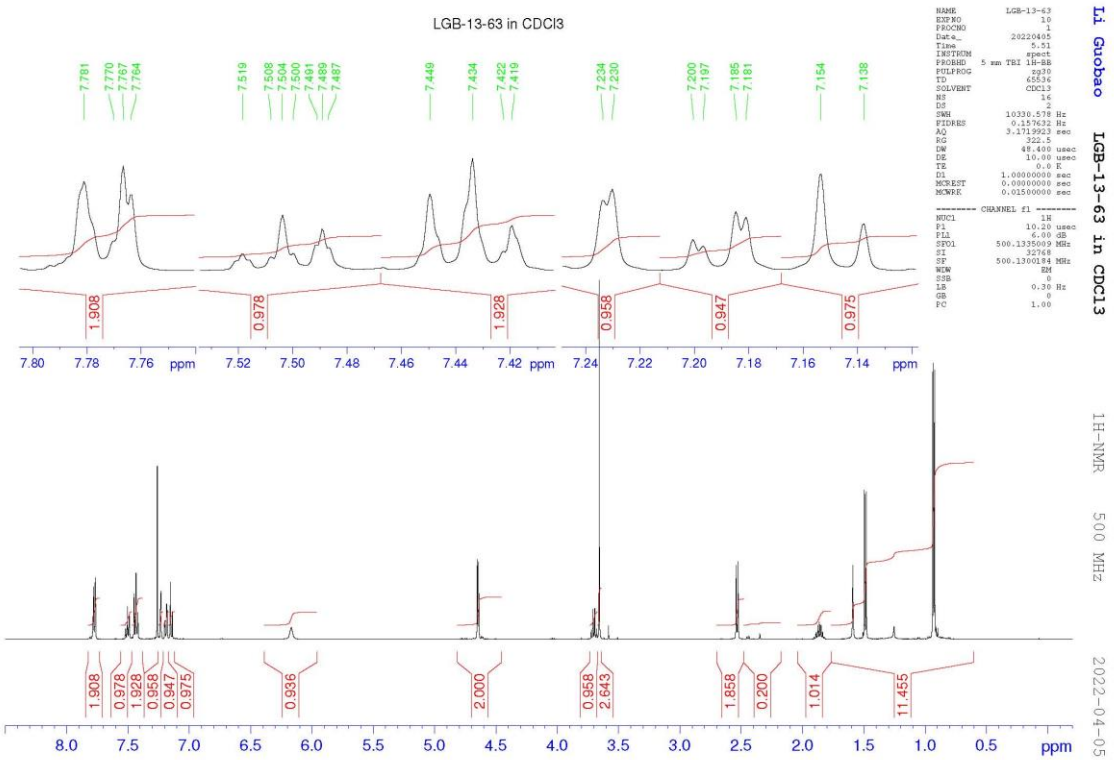
LGB-13-63 in $CDCl_3$

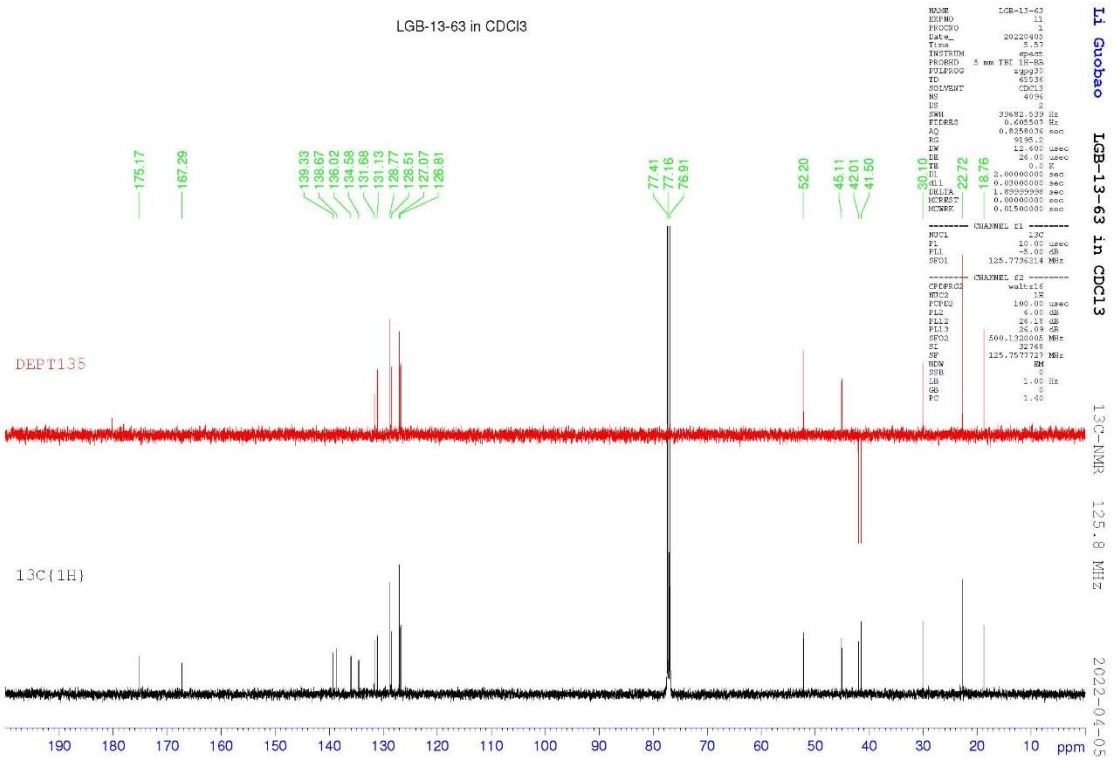
NMR Data were recorded at ambient temperature on a Bruker DRX 500 spectrometer operating at 500.1 MHz for ^1H and 125.8 MHz for ^{13}C. Chemical shifts δ are given in ppm relative to TMS. The solvent signals were used as reference (^1H: δ_H 7.260 ppm residual $CHCl_3$, ^{13}C: δ_C 77.16 ppm). Coupling constants were given in Hertz and determined assuming first-order spin-spin coupling.

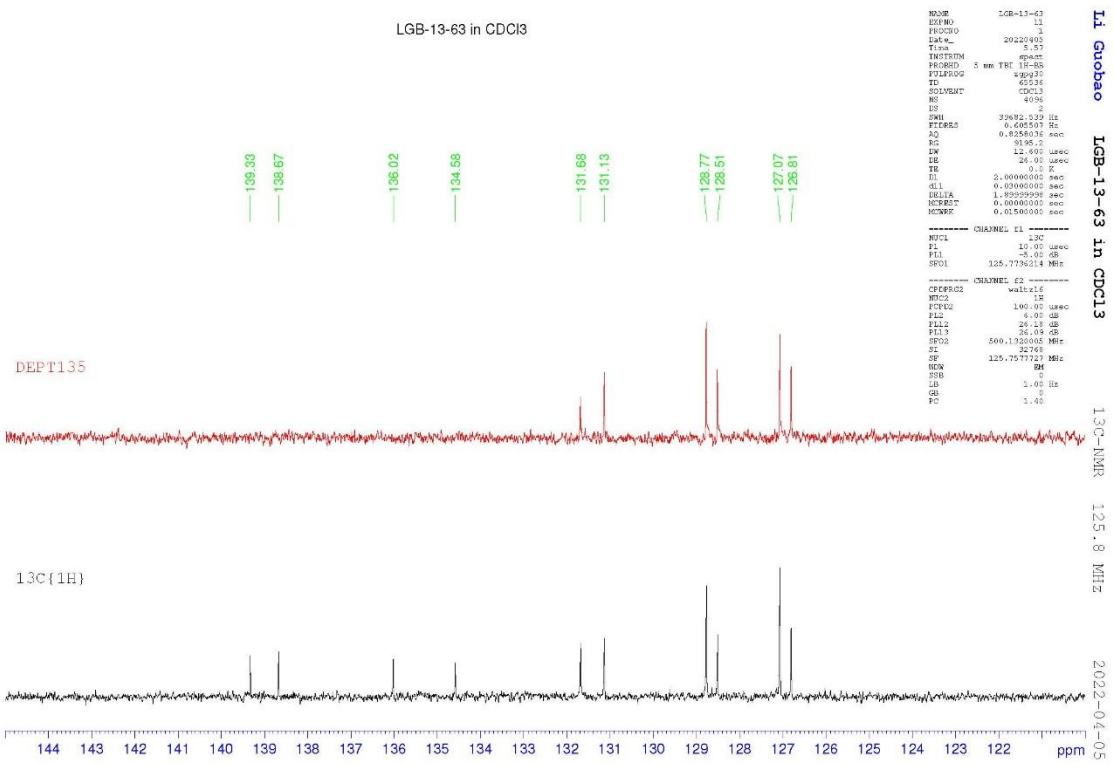
red ^{13}C chemical shift
blue ^1H chemical shift

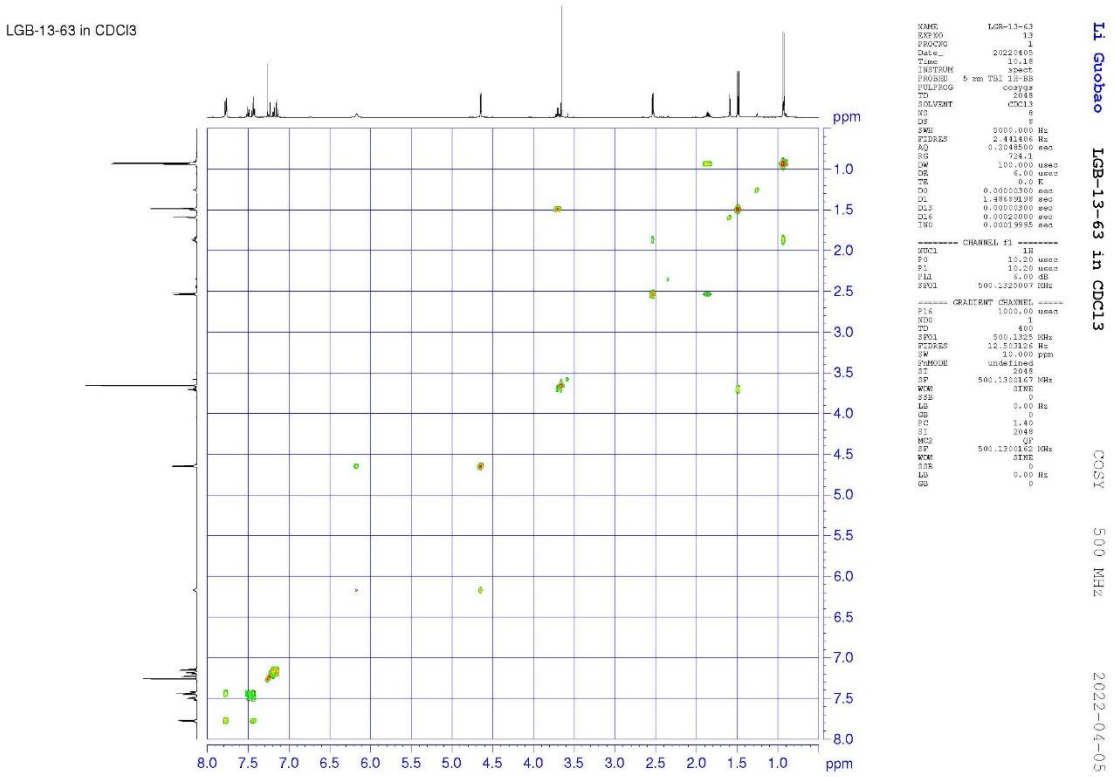


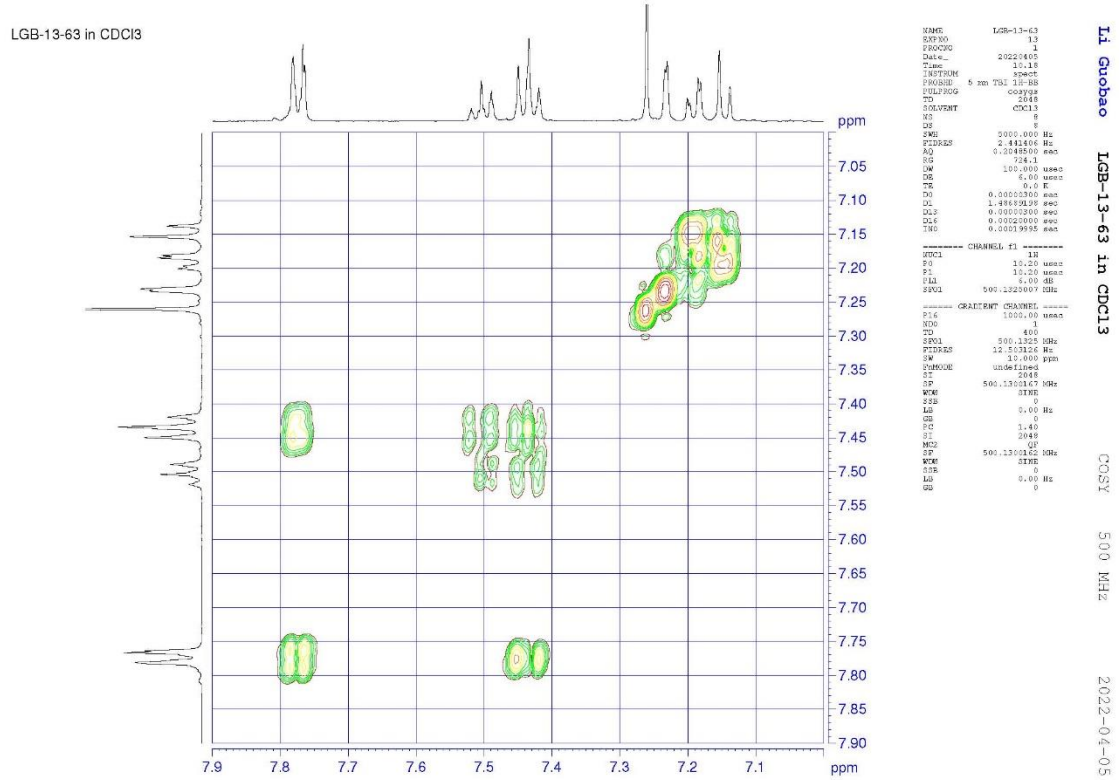


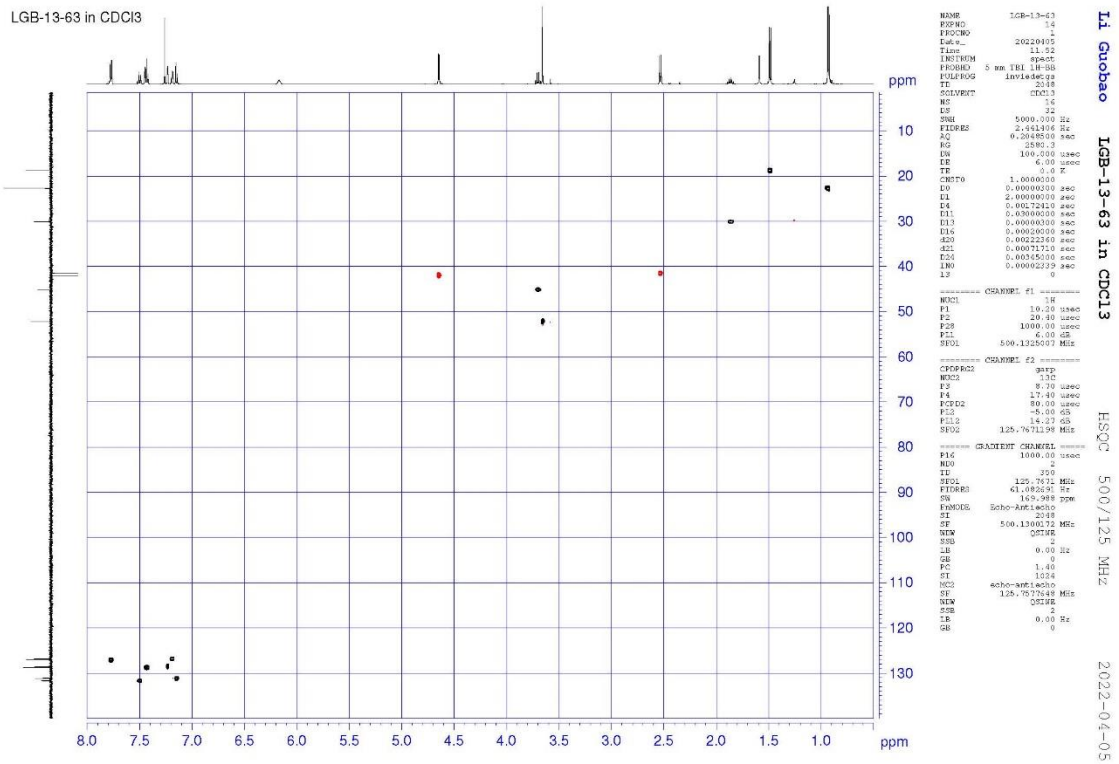

LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
1H-NMR
500 MHz
2022-04-05
ppm

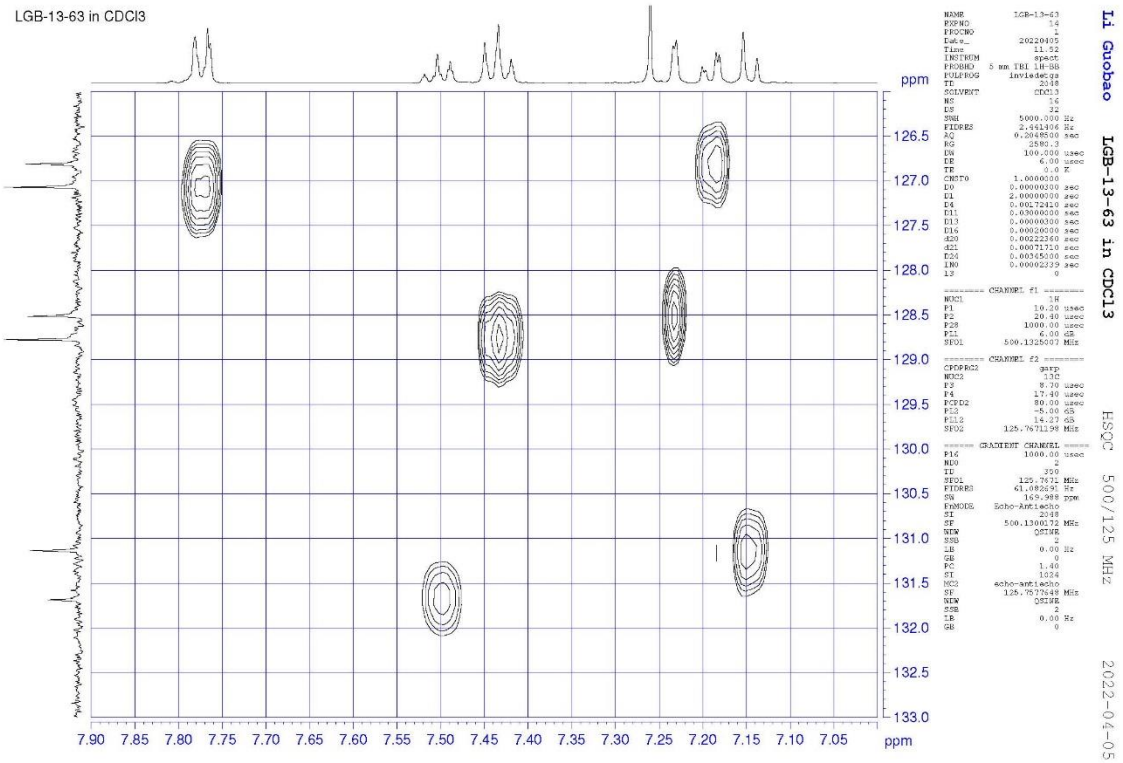

LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
DEPT135
13C{1H}
13C-NMR
125.8 MHz
2022-04-05
ppm

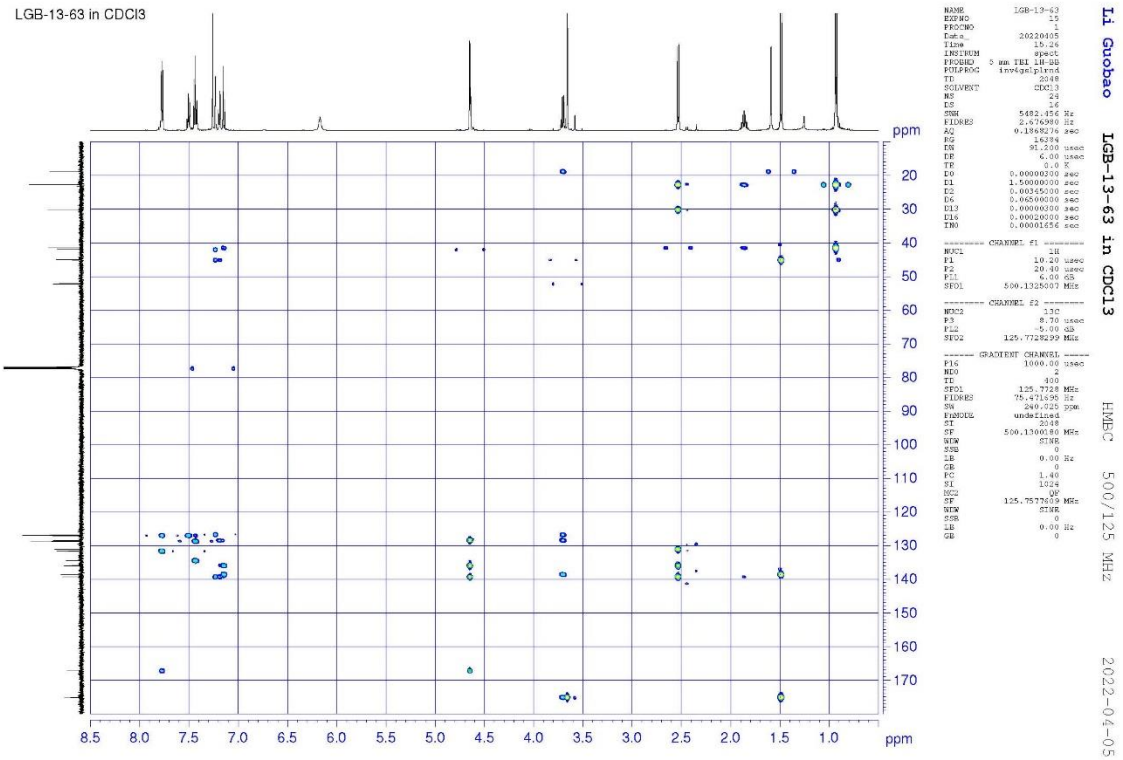

LGB-13-63 in CDCl3
139.33
138.67
136.02
134.58
131.68
131.13
128.77
128.51
127.07
126.81
DEPT135
13C{1H}
144 143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 ppm
Li Guobao
LGB-13-63 in CDCl3
13C-NMR
125.8 MHz
2022-04-05

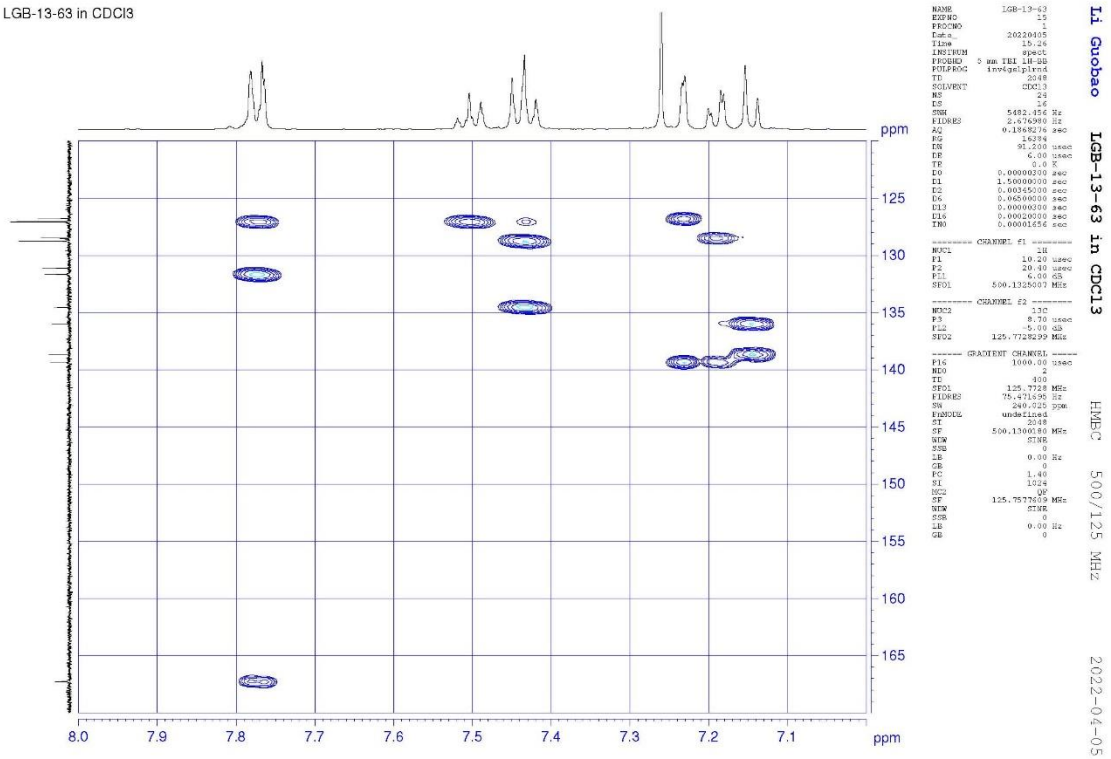

LGB-13-63 in CDCl3
ppm
1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
Li Guobao
LGB-13-63 in CDCl3
COSY
500 MHz
2022-04-05

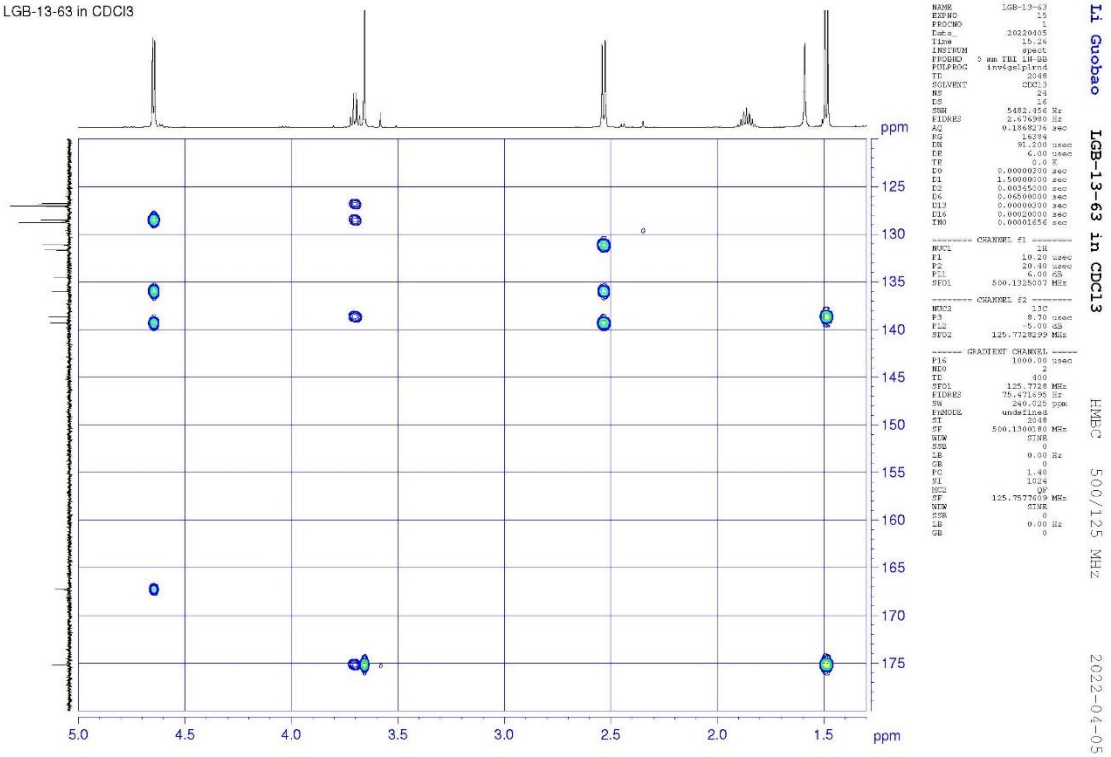

LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
COSY
500 MHz
2022-04-05
ppm

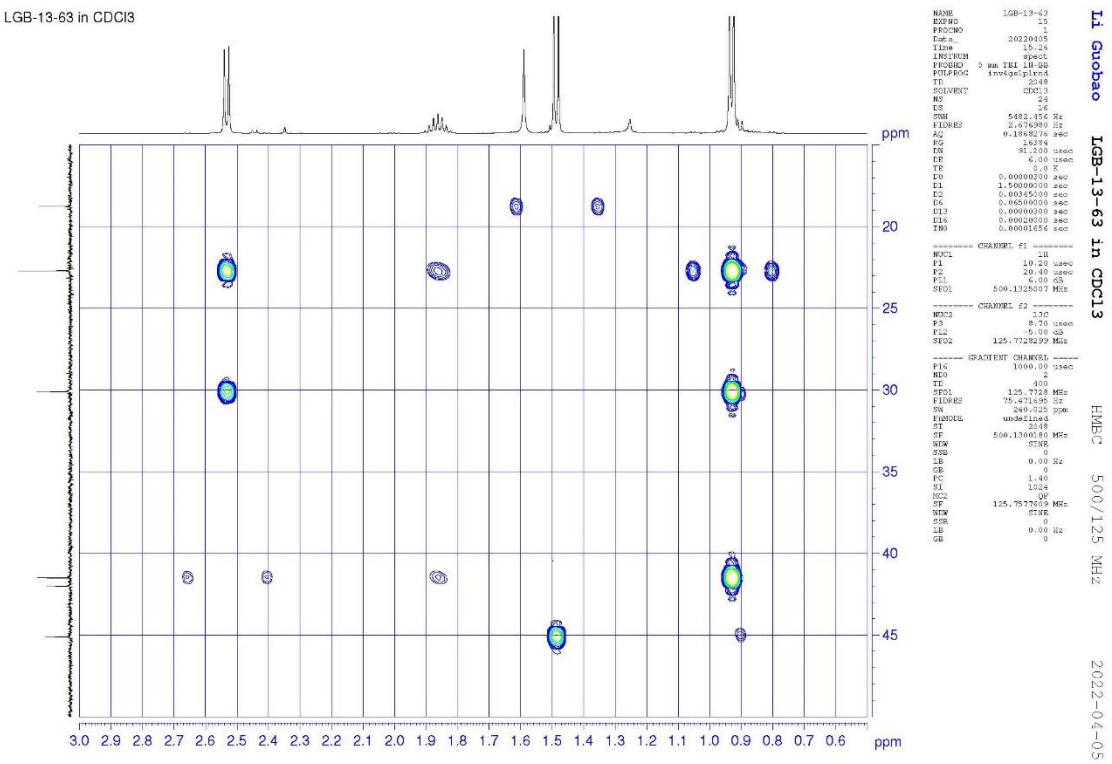

LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
HSQC
500/125 MHz
2022-04-05
ppm

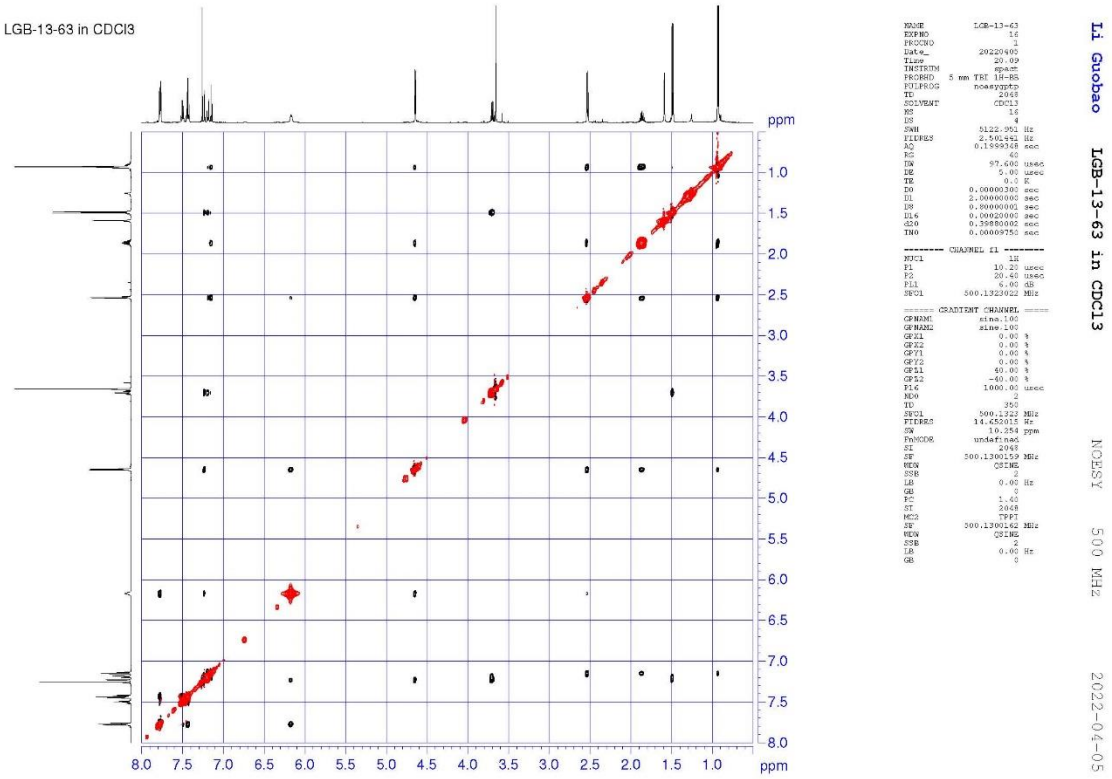

LGB-13-63 in CDCl3
Li Guobao LGB-13-63 in CDCl3 HSQC 500/125 MHz 2022-04-05


LGB-13-63 in CDCl3
Li Guobao LGB-13-63 in CDCl3 HMBC 500/125 MHz 2022-04-05


LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
HMBC 500/125 MHz
2022-04-05
ppm
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
125
130
135
140
145
150
155
160
165


LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
HMBC 500/125 MHz
2022-04-05
ppm
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
125
130
135
140
145
150
155
160
165
170
175


LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
HMBC 500/125 MHz
2022-04-05
ppm
3.0 2.9 2.8 2.7 2.6 2.5 2.4 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 0.6
20 25 30 35 40 45


LGB-13-63 in CDCl3
Li Guobao
LGB-13-63 in CDCl3
NOESY 500 MHz
2022-04-05
ppm
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

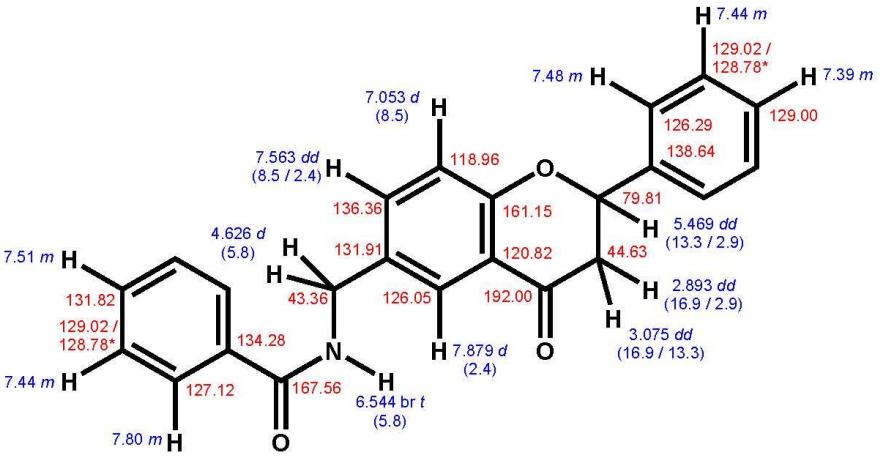
Li Guobao LGB-13-60 structure verification Avance600 2022-08-30

LGB-13-60 in $CDCl_3$

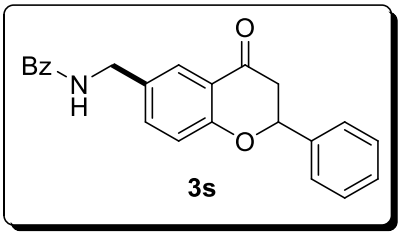
NMR Data were recorded at ambient temperature on a Bruker Avance III 600 spectrometer operating at 600.1 MHz for ^{1}H and 125.8 MHz for ^{13}C. Chemical shifts δ are given in ppm relative to TMS. The solvent signals were used as reference (^{1}H: δ_H 7.260 ppm residual $CHCl_3$, ^{13}C: δ_C 77.16 ppm). Coupling constants were given in Hertz and determined assuming first-order spin-spin coupling.

red ^{13}C chemical shift

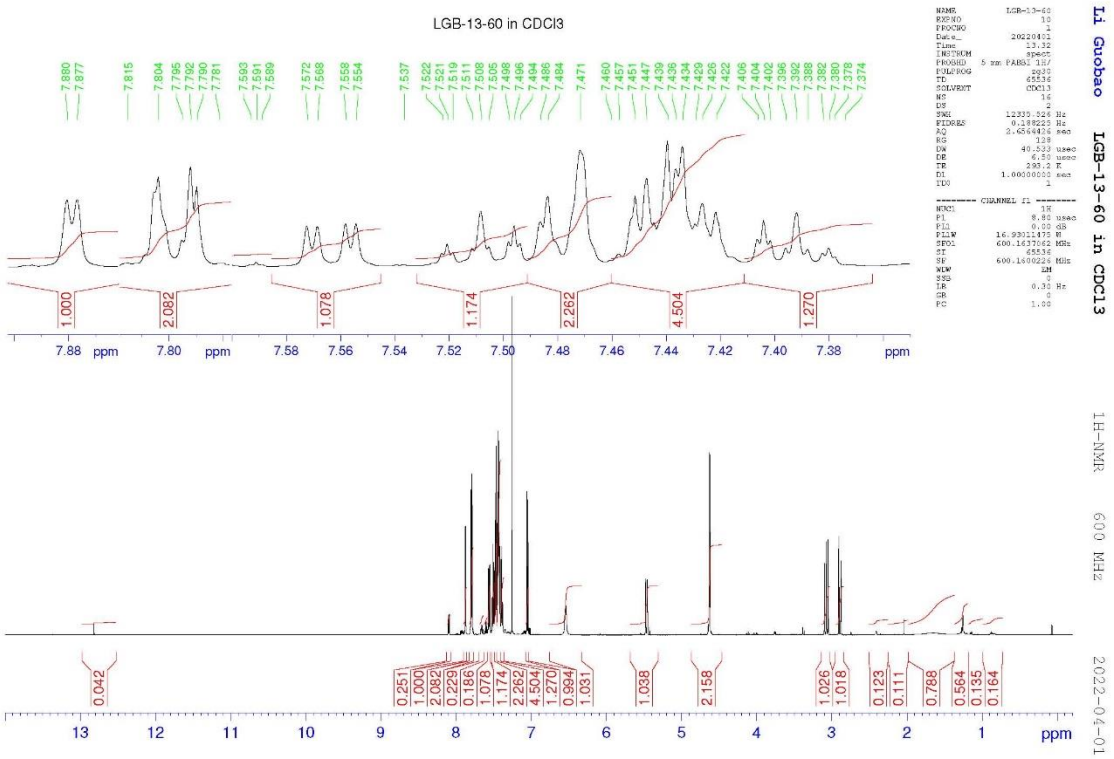
blue ^{1}H chemical shift

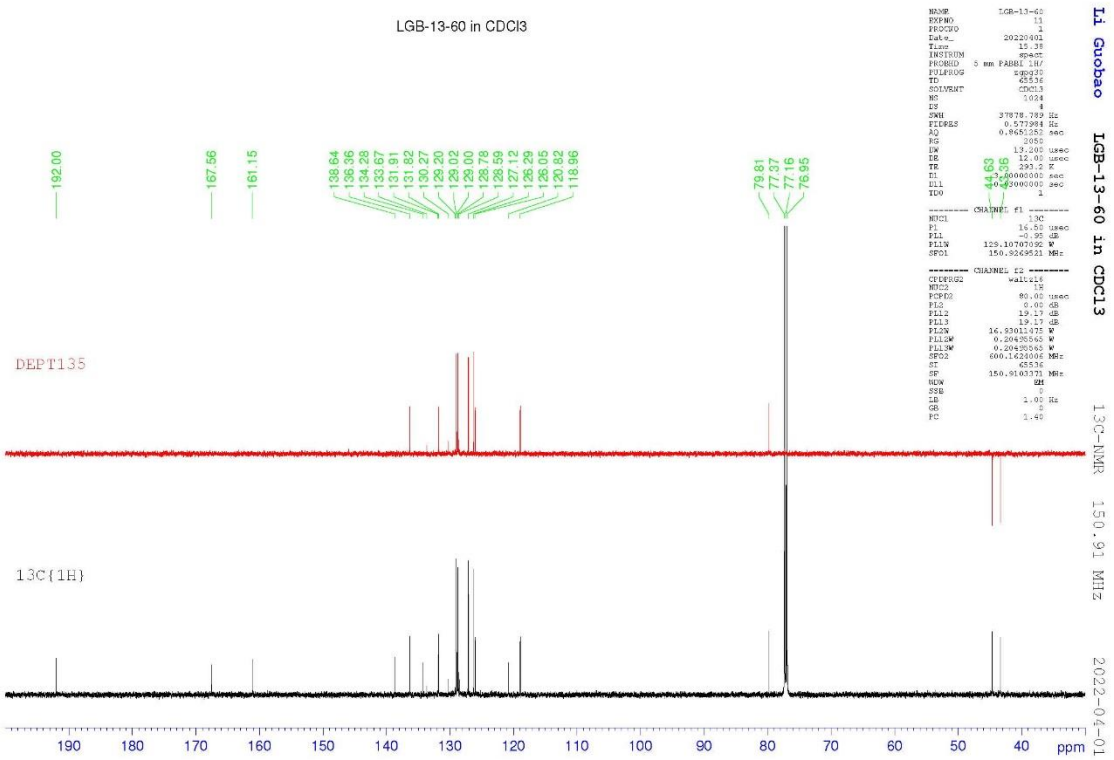


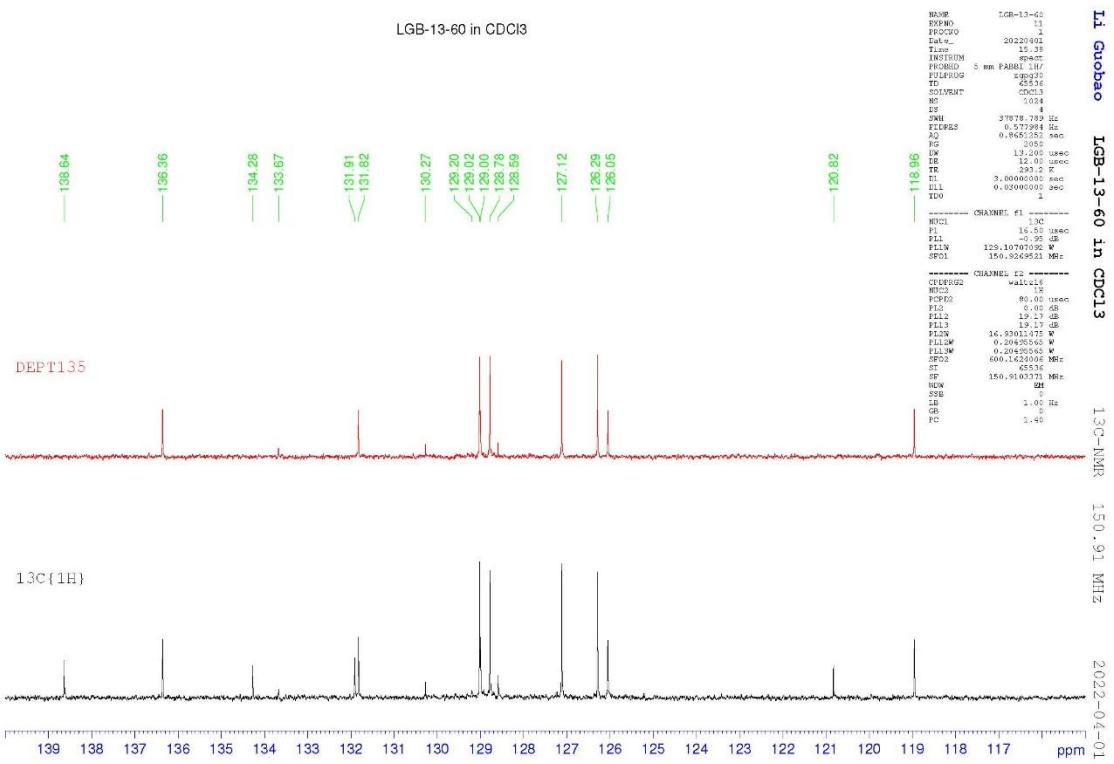
* signal assignment not unambiguous

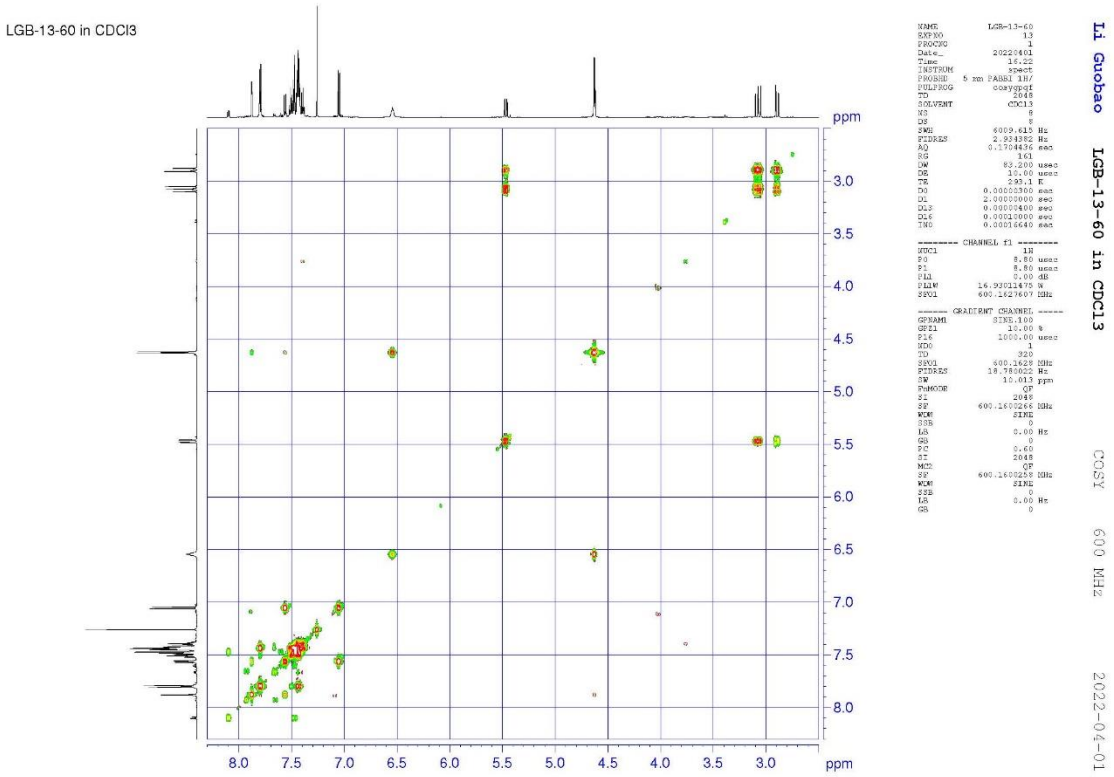


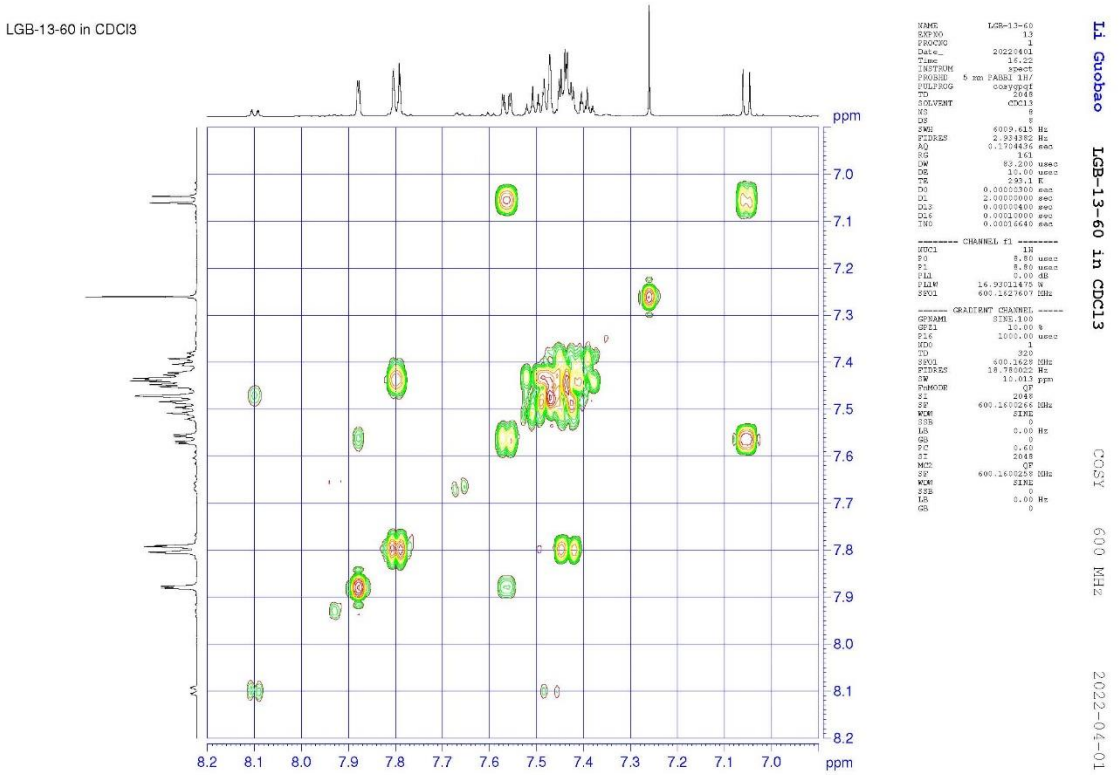
3s

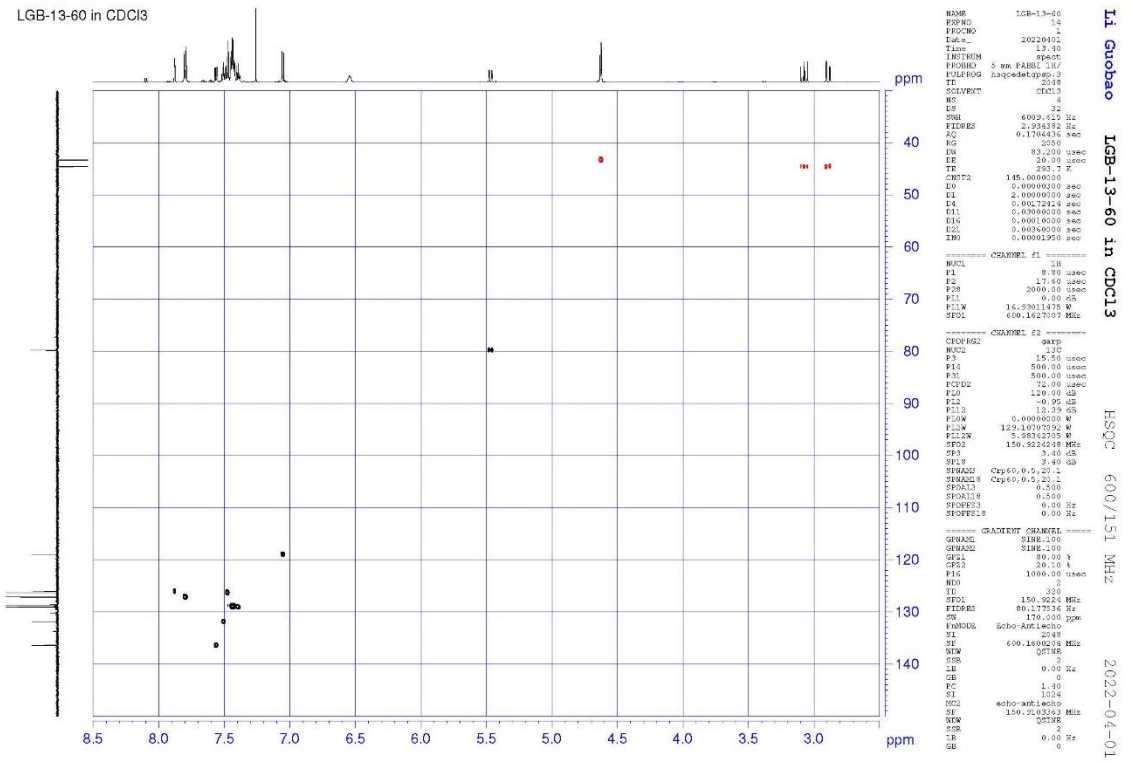

LGB-13-60 in CDCl3
Li Guobao
LGB-13-60 in CDCl3
1H-NMR
600 MHz
2022-04-01
ppm

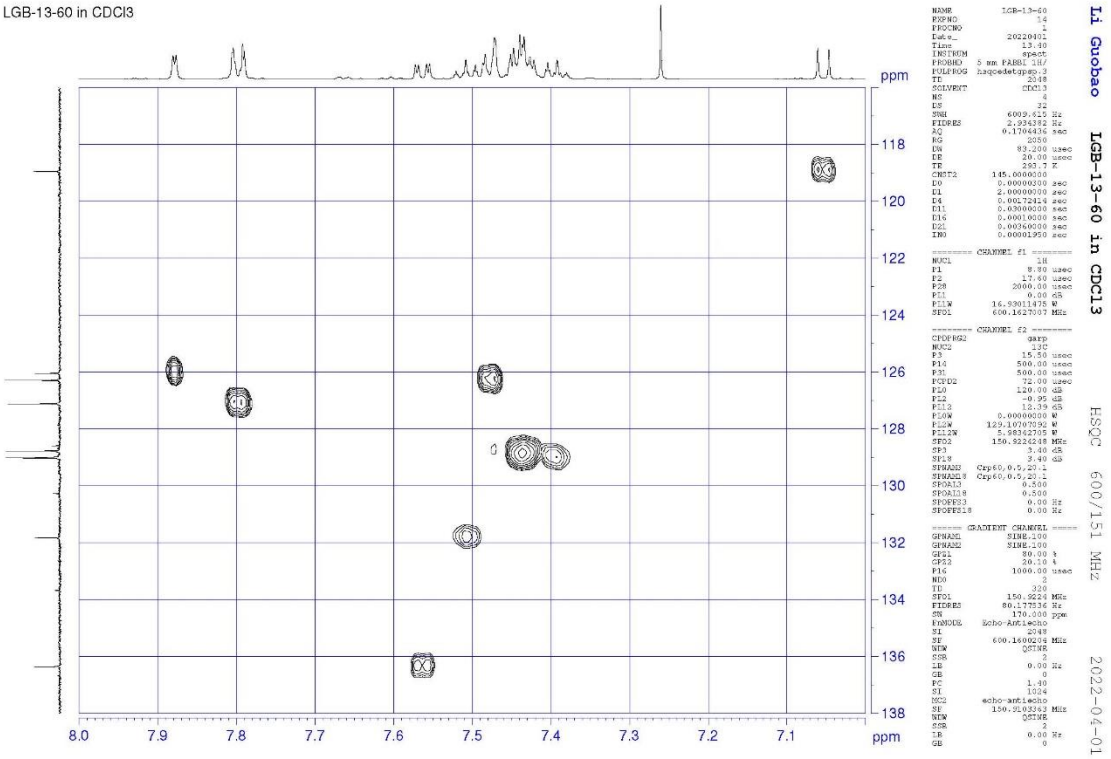

LGB-13-60 in CDCl3
Li Guobao
LGB-13-60 in CDCl3
DEPT135
13C{1H}
13C-NMR
150.91 MHz
2022-04-01
ppm

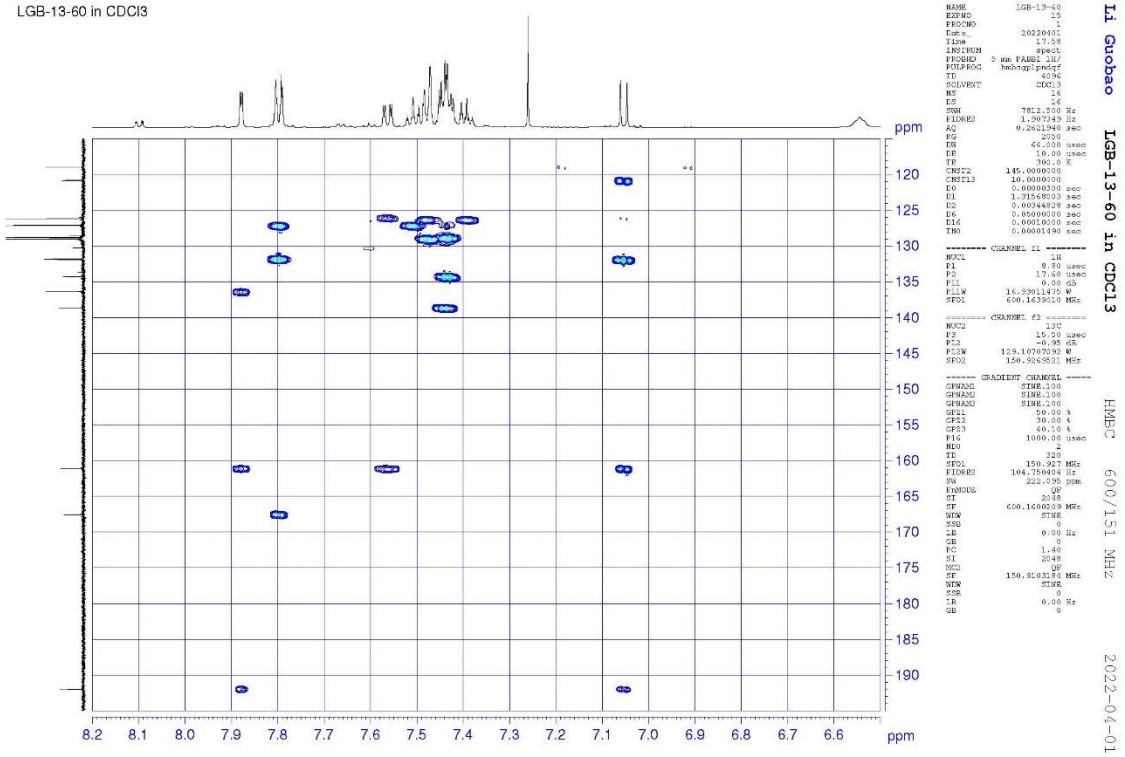

LGB-13-60 in CDCl3
138.64
136.36
134.28
133.67
131.91
131.82
130.27
129.20
129.02
129.00
128.78
128.59
127.12
126.29
126.05
120.82
118.96
DEPT135
13C{1H}
139 138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 ppm
Li Guobao
LGB-13-60 in CDCl3
13C-NMR
150.91 MHz
2022-04-01

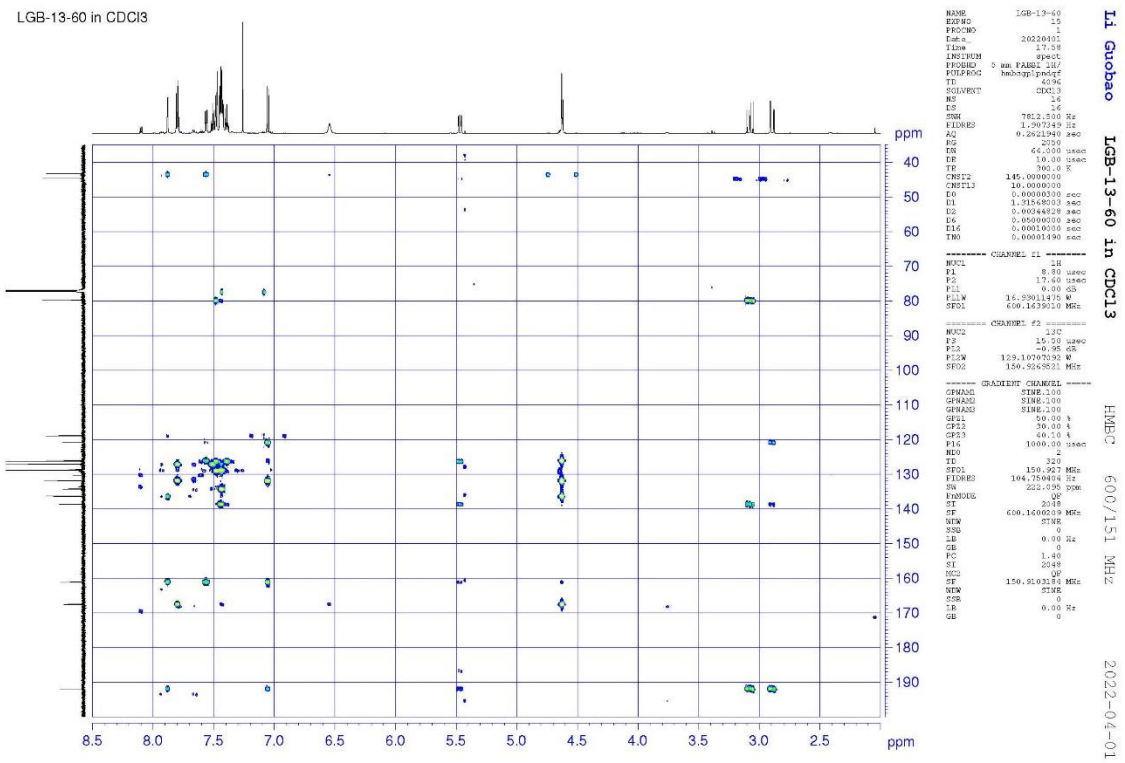

LGB-13-60 in CDCl3
ppm
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 ppm
Li Guobao
LGB-13-60 in CDCl3
COSY
600 MHz
2022-04-01

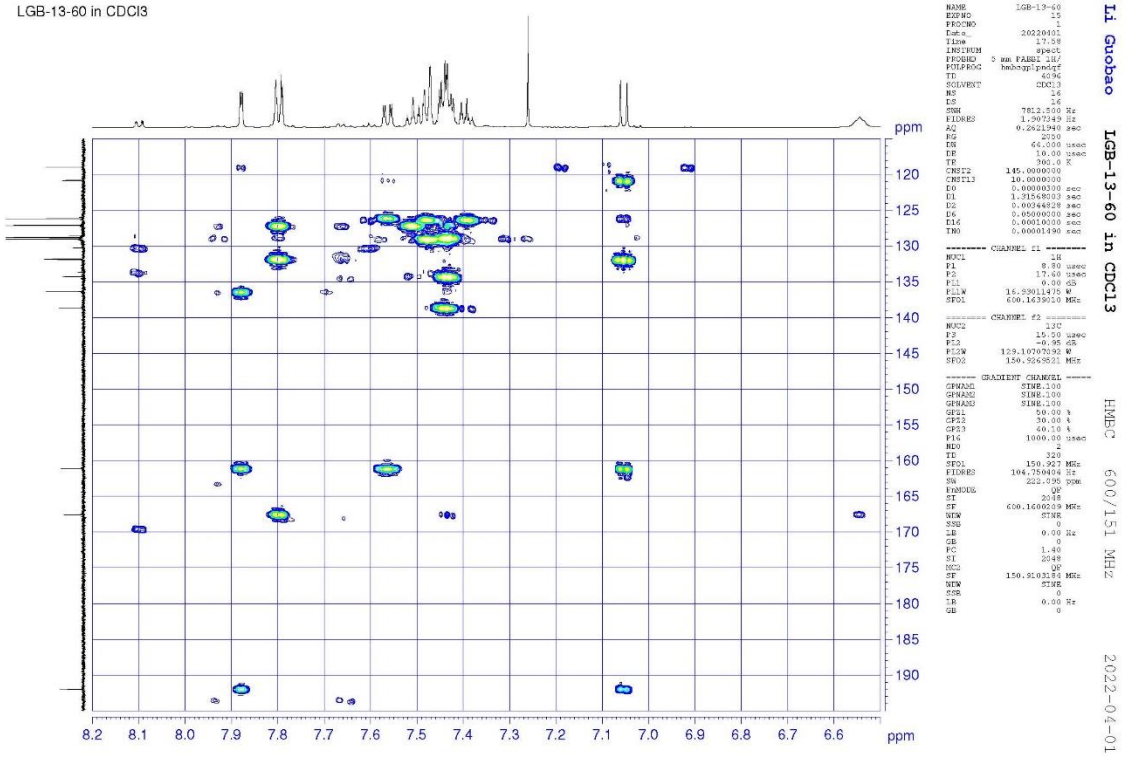

LGB-13-60 in CDCl3
Li Guobao LGB-13-60 in CDCl3 COSY 600 MHz 2022-04-01
ppm

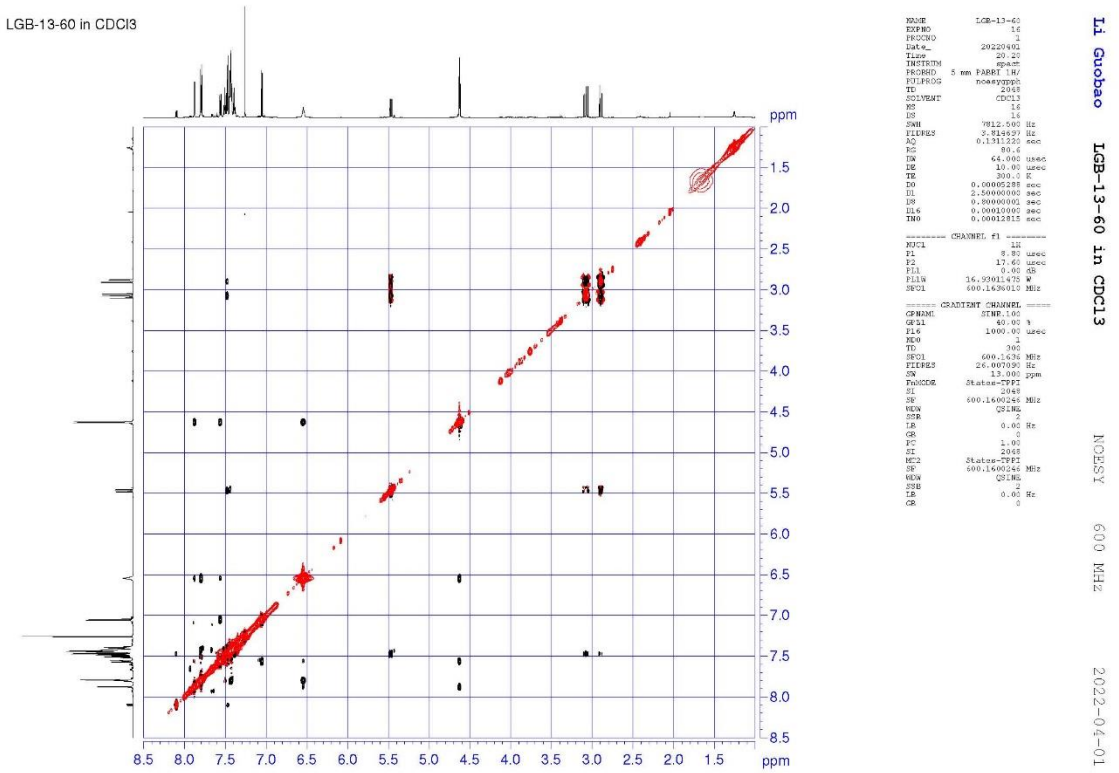

LGB-13-60 in CDCl3
Li Guobao LGB-13-60 in CDCl3 HSQC 600/151 MHz 2022-04-01
ppm


LGB-13-60 in CDCl3
Li Guobao LGB-13-60 in CDCl3 HSQC 600/151 MHz 2022-04-01
ppm
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1
118 120 122 124 126 128 130 132 134 136 138


LGB-13-60 in CDCl3
Li Guobao LGB-13-60 in CDCl3 HMBC 600/151 MHz 2022-04-01
ppm
8.2 8.1 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
120 125 130 135 140 145 150 155 160 165 170 175 180 185 190


LGB-13-60 in CDCl3
Li Guobao
LGB-13-60 in CDCl3
HMBC 600/151 MHz
2022-04-01
ppm
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
40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190


LGB-13-60 in CDCl3
Li Guobao
LGB-13-60 in CDCl3
HMBC 600/151 MHz
2022-04-01
ppm
8.2 8.1 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
120 125 130 135 140 145 150 155 160 165 170 175 180 185 190

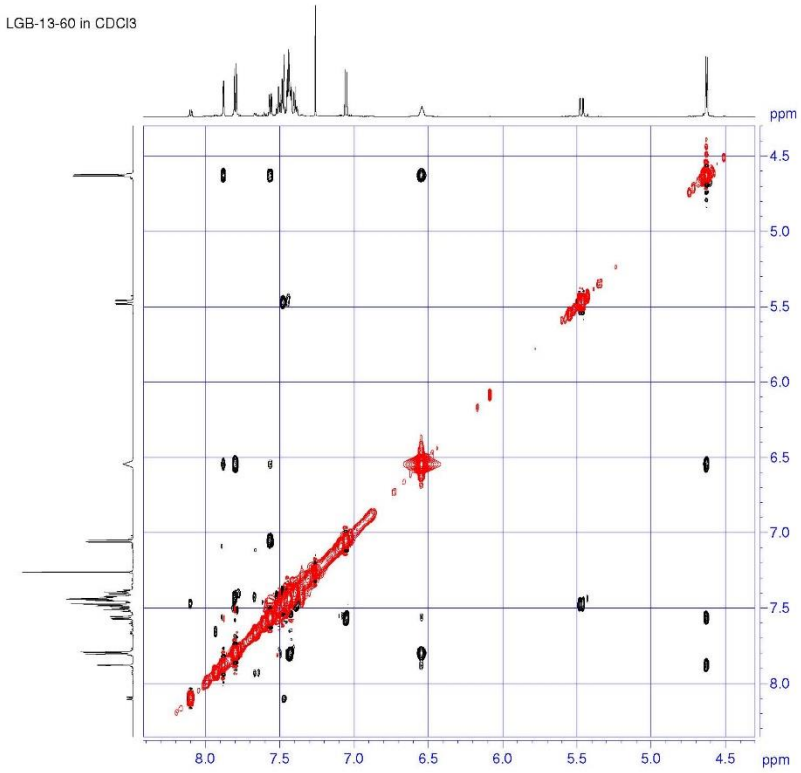


NAME LGB-13-60
EXPNO 16
PROCNO 1
Date_ 20220401
Time 20.20
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG noesygpph
TD 2048
SOLVENT CDCl3
NS 16
DS 16
SWH 7812.500 Hz
FIDRES 3.814697 Hz
AQ 0.1311220 sec
RG 80.6
DW 64.000 usec
DE 10.00 usec
TE 300.0 K
D0 0.00005288 sec
D1 2.50000000 sec
D8 0.80000001 sec
D16 0.00010000 sec
TD0 0.00012815 sec

======== CHANNEL f1 ========
NUC1 1H
P1 9.80 usec
P2 17.60 usec
PL1 0.00 dB
PLW 16.92901475 W
SFO1 600.1636010 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPZ1 40.00 %
P16 1000.00 usec
MD0 1
TD 300
SFO1 600.1636 MHz
FIDRES 26.007096 Hz
SW 13.000 ppm
FnMODE States-TPPI
SI 2048
SF 600.1600246 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.00
SI 2048
MC2 States-TPPI
SF 600.1600246 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

Li Guobao LGB-13-60 in CDCl3 NOESY 600 MHz 2022-04-01



NAME LGB-13-60
EXPNO 16
PROCNO 1
Date_ 20220401
Time 20.20
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG noesygpph
TD 2048
SOLVENT CDCl3
NS 16
DS 16
SWH 7812.500 Hz
FIDRES 3.814697 Hz
AQ 0.1311220 sec
RG 80.6
DW 64.000 usec
DE 10.00 usec
TE 300.0 K
D0 0.00005288 sec
D1 2.50000000 sec
D8 0.80000001 sec
D16 0.00010000 sec
TD0 0.00012815 sec

======== CHANNEL f1 ========
NUC1 1H
P1 9.80 usec
P2 17.60 usec
PL1 0.00 dB
PLW 16.92901475 W
SFO1 600.1636010 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPZ1 40.00 %
P16 1000.00 usec
MD0 1
TD 300
SFO1 600.1636 MHz
FIDRES 26.007096 Hz
SW 13.000 ppm
FnMODE States-TPPI
SI 2048
SF 600.1600246 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.00
SI 2048
MC2 States-TPPI
SF 600.1600246 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

Li Guobao LGB-13-60 in CDCl3 NOESY 600 MHz 2022-04-01