Access to hexahydroazepinone heterocycles via palladium-catalysed C(sp^3)–H alkenylation/ring-opening of cyclopropanes

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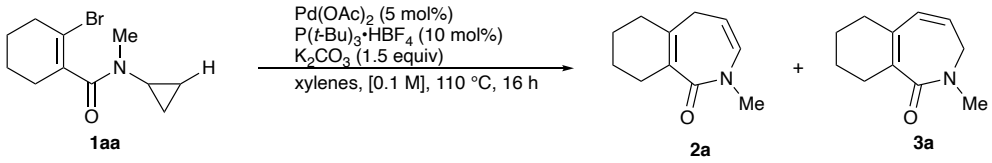
General Methods: Commercial reagents were used as supplied or purified by standard techniques where necessary.[1] All non-aqueous reactions were run under argon atmosphere with flame-dried glassware using standard techniques for manipulating air-sensitive compounds.[2] Anhydrous solvents were obtained by filtration through drying columns according to the method of Grubbs[3] or by distillation over calcium hydride or sodium. Flash chromatography was performed using 230-400 mesh silica according to the method of Still[4] or on an automatic purification system (Santai Sepabean) using pre-packed normal phase silica cartridges SepaFlash® HP from Santai Technologies, Inc. Analytical thin-layer chromatography (TLC) was performed on pre-coated, glass-backed silica gel plates (Merck 60 F254) and visualized by UV absorbance (254 nm), potassium permanganate ($KMnO_4$), and/or cerium ammonium molybdate (CAM) stains.

Nuclear magnetic resonance spectra were recorded on an Avance AV400 MHz, Avance AV 300 MHZ, or DRX 400 MHz (^1H,^{13}C, ^{19}F, 1D NOESY) spectrometer. Chemical shifts for ^1H NMR spectra are recorded in parts per million (ppm) from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CHCl_3$, $\delta = 7.26$ ppm). The data was reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, br = broad, d = doublet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, ddd = doublet of doublets of doublets, t = triplet, q = quadruplet, quintet = quint, m = multiplet), integration, coupling constant (Hz) and assignment. Chemical shifts for ^{13}C NMR spectra were recorded in parts per million from tetramethylsilane using the central peak of $CDCl_3$ (77.16 ppm) as the internal standard. All ^{13}C NMR spectra were obtained with complete proton decoupling. Starting materials were reported as a mixture of rotamers. Infrared spectra were taken on a Bruker Alpha Platinum ATR (neat) and are reported in reciprocal centimeters (cm^{-1}). Melting points were obtained using a Büchi melting point apparatus and are uncorrected. High-resolution mass spectra were performed by the Centre régional de spectrométrie de masse de l'Université de Montréal.

Selected optimization and control experiments

Table S1: Control experiments

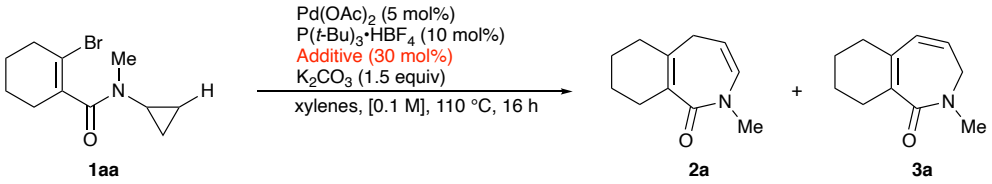


Entry	Variation from Standard Conditions	Yield (%)[a]
1	No $Pd(OAc)_2$	0 (100)[b]
2	No $tBu_3P•HBF_4$	0 (100)[b]
3	No K_2CO_3	0 (100)[b]

[a]Yields were calculated based on ^1H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]Unreacted starting material.

Procedure: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), $tBu_3P•HBF_4$ (5.78 mg, 0.020 mmol) and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further rinsed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^1H NMR signals of the product relative to those of the internal standard.

Table S2: Additive screening



Entry	Additive	Yield (%)[a]
1	PivOH	86 (0)[c]
2	AdOH	88 (0)[c]
3	Ag_2CO_3[b]	89 (0)[c]

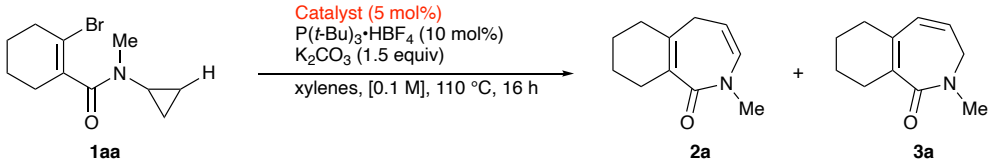
[a]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]0.5 equivalents were used. [c]Unreacted starting material.

Procedure for entry 1 and 2: A 5.0-mL microwave vial containing an oven dried stirring bar was charged with **1aa** (51.6 mg, 0.20 mmol) and 30 mol% of Additive and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), *t*Bu_3P•HBF_4 (5.78 mg, 0.020 mmol), and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard.

Procedure for entry 3: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), *t*Bu_3P•HBF_4 (5.78 mg, 0.020 mmol), K_2CO_3 (41.5 mg, 0.30 mmol), and **Ag_2CO_3** (27.6 mg, 0.10 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an

internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^1H NMR signals of the product relative to those of the internal standard.

Table S3: Catalyst screening

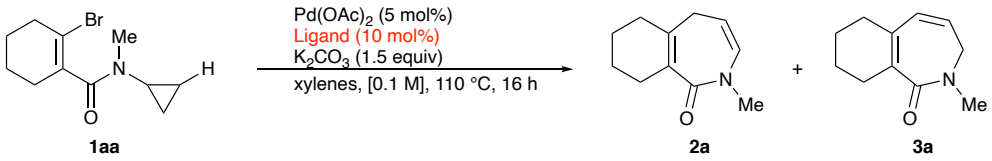


Entry	Catalyst	Yield (%)[a]
1	$Pd(dba)_2$	3 (93)[b]
2[c]	$Pd(dba)_2$	92 (0)[b]
3	Pd_2dba_3	3 (93)[b]
4	$Pd(TFA)_2$	66 (15)[b]
5	$PdCl_2$	9 (85)[b]
6	$Pd(OAc)_2$	88 (0)[b]

[a]Yields were calculated based on ^1H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]Unreacted starting material.[c]Entry performed using 30 mol% pivalic acid as an additive.

Procedure: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. The Catalyst (0.010 mmol, 5 mol%), tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol), and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^1H NMR signals of the product relative to those of the internal standard.

Table S4: Ligand screening

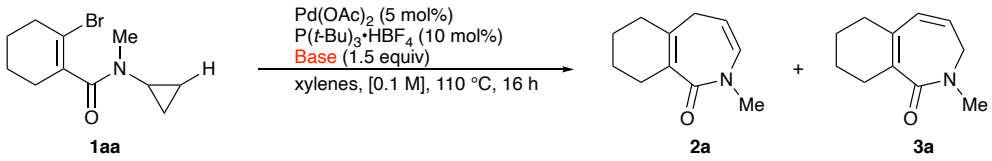


Entry	Ligand	Yield (%)[a]
1	Xphos	65 (0)[b]
2	Davephos	47 (44)[b]
3	Xantphos	88 (0)[b]
4	PCy_3	91 (0)[b]
5	tBu$_3$P •HBF$_4$	88 (0)[b]
6	tBu$_2$MeP•HBF$_4$	47 (52)[b]
7	PPh_3	53 (28)[b]
8	dppf	57 (28)[b]
9	*rac*-BINAP	96 (0)[b]
10	P(4-FC$_6$H$_4$)$_3$	16 (75)[b]
11	P(4-MeOC$_6$H$_4$)$_3$	28 (62)[b]
12[c]	tBu$_3$P •HBF$_4$	85 (2)[d]
13[c]	PCy_3	78 (0)[d]
14[c]	PPh_3	12 (73)[b]
15[c]	DavePhos	77 (10)[d]
16[e]	Xantphos	8 (87)[b]
17[f]	Xantphos	0 (99)[b]

[a]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]Unreacted starting material. [c]DMF as solvent. [d]Yield of the other isomer (**3a**). [e]Pd(dba)$_2$ was used as catalyst. [f]30 mol% of pivalic acid was used as an additive.

Procedure: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. Pd(OAc)$_2$ (2.27 mg, 0.010 mmol), the Ligand (0.020 mmol, 10 mol%), and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard.

Table S5: Base screening



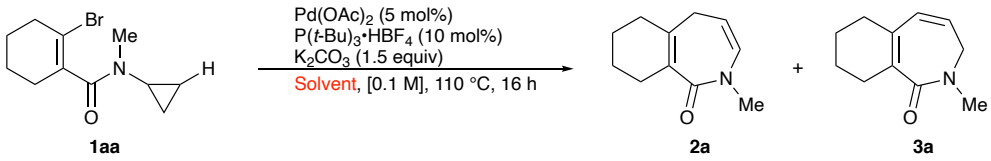
Entry	Base	Yield (%)[a]
1	K_2CO_3	88 (0)[b]
2	Na_2CO_3	14 (84)[b]
3	Cs_2CO_3	93 (0)[b]
4	Rb_2CO_3	92 (0)[b]
5	KOtBu	23 (0)[b]
6	K_3PO_4	30 (69)[b]
7	KOAc	93 (0)[b]
8	DIPEA	81 (8)[d]
9[c]	DIPEA	79 (8)[d]
10[e]	Cs_2CO_3	78 (0)[b]
11[e]	KOAc	40 (56)[b]
12[f]	Et_3N	17 (83)[b]
13	Matrix Innov. MP-carbonate resin	95 (0)[b]

[a]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]Unreacted starting material. [c]DMF was used as solvent. [d]Yield of the other isomer **3a**. [e]PCy_3 was used as ligand. [f]Et_3N was used as a solvent.

Procedure (entries 1-7, 10, 11, 13): A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) and the Base (0.30 mmol, 1.5 equiv) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylene (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard.

Procedure (entries 8-9, 10, 12): A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol) and tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. The solvent (2.00 mL) and the base (0.30 mmol, 1.5 equiv) were then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard.

Table S6: Solvent screening



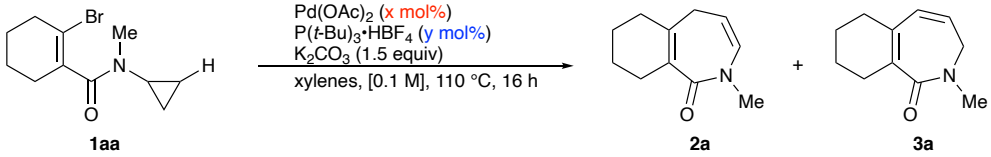
Entry	Solvent	Yield(%)[a]
1	Chlorobenzene	13 (83)[b]
2	DMF	85 (2)[c]
3	Dioxane	89 (0)[b]
4	Isobutanol	27 (60)[b]
5	Benzene	84 (0)[b]
6	DMA	80 (0)[b]
7	Xylenes	88 (0)[b]
8	Toluene	70 (0)[b]
9	CPME	68 (32)[b]

[a]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]Unreacted starting material. [c]Yield of the other isomer **3a**.

Procedure: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. The Solvent

(2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^1H NMR signals of the product relative to those of the internal standard.

Table S7: Catalyst and ligand loading

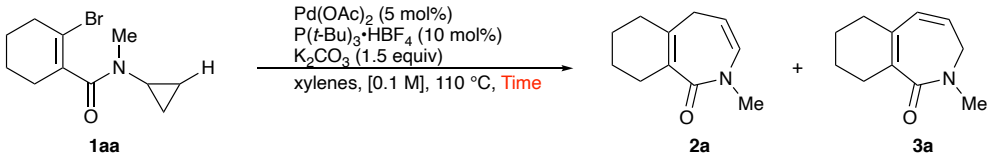


Entry	Pd (x mol%): L (y mol%)	Yield (%)[a]
1	5:5	88 (0)[b]
2	10:10	83 (0)[b]
3	2.5:5	89 (0)[b]
4	10:20	85 (0)[b]
5	5:10	88 (0)[b]

[a]Yields were calculated based on ^1H NMR using 1,3,5-trimethoxybenzene (TMB) as an internal standard.[b]Unreacted Starting material.

Procedure: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (x mmol), tBu$_3$P•HBF$_4$ (y mmol) and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^1H NMR signals of the product relative to those of the internal standard.

Table S8: Yield vs time for the reactions in xylenes and DMF

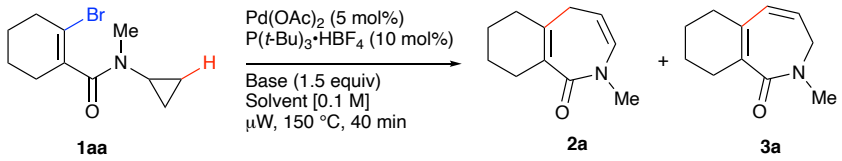


Entry	Time (h)	Yield in Xylenes (%)	Yield in DMF (%)
1	0.5	0 (91)[b]	28 (70)[b]
2	1	19 (81)[b]	52 (45)[b]
3	3	20 (76)[b]	88 (0)[b]
4	6	56 (40)[b]	90 (0)[b]
5	9	88 (0)[b]	---
6	16	88 (0)[b]	85 (2)[c]
7	48	---	77 (10)[c]

[a]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]Unreacted starting material. [c]Yield of the other isomer **3a**.

Procedure: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes or DMF (2.00 mL) was then added and the reaction was heated to 110 °C for Time. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard.

Table S9: Microwave reaction



Entry	Base	Solvent	Yield in DMF (%)
1	DIPEA	DMF	55 (30)[b]
2	K_2CO_3	Xylenes: DMF (17:3)	88 (0)[c]

[a]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]Yield of the other isomer **3a**. [c]Unreacted starting material.

Procedure (entry 1): A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol) and tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) and DIPEA (52 μL, 0.30 mmol) were then added and the reaction was heated to 150 °C for 40 min under microwave irradiation (Biotage Initiator® microwave). The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard.

Procedure (entry 2): A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) was then added and the reaction was heated to 150 °C for 40 min under microwave irradiation (Biotage Initiator® microwave). The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further washed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole mixture was dissolved in

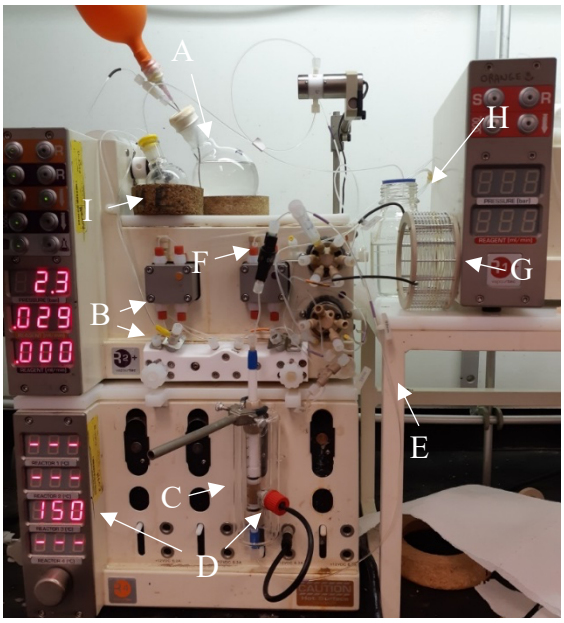
$CDCl_3$. The yield was calculated based on the integration of ^1H NMR signals of the product relative to those of the internal standard.

Note: *Caution must be taken when performing reactions under microwave irradiation as specific reaction conditions might cause formation of a palladium mirror and/or deposit of palladium black which upon intense heating led to the cracking of the reaction vial.*

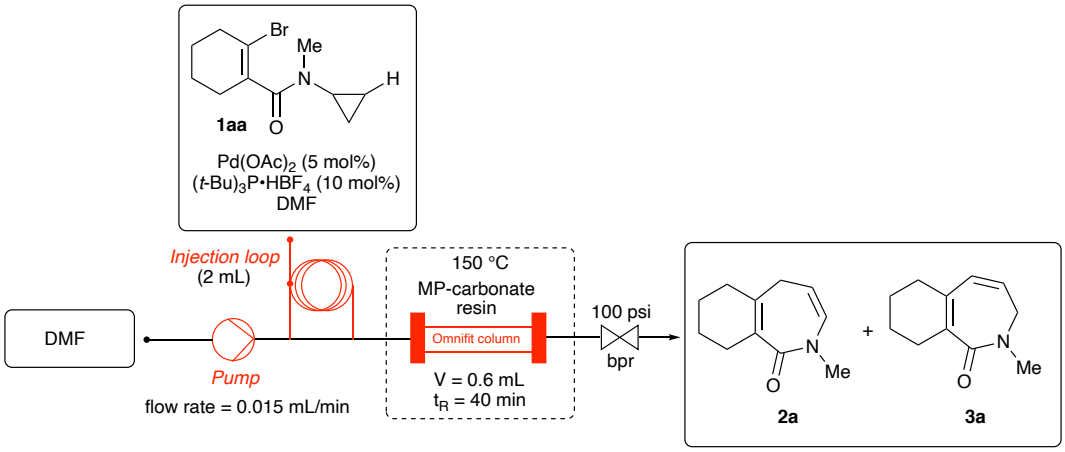
Optimization of the continuous flow reaction

Use of a packed bed column filled with the supported base (injection loop):

To optimize the reaction conditions under continuous flow, a R-Series Vapourtec® flow system (R2+ pump, R4 heating module), an Omnifit® glass column, and standard 1/16'' x 0.04'' tubing PFA tubing were used. The set-up is shown below:



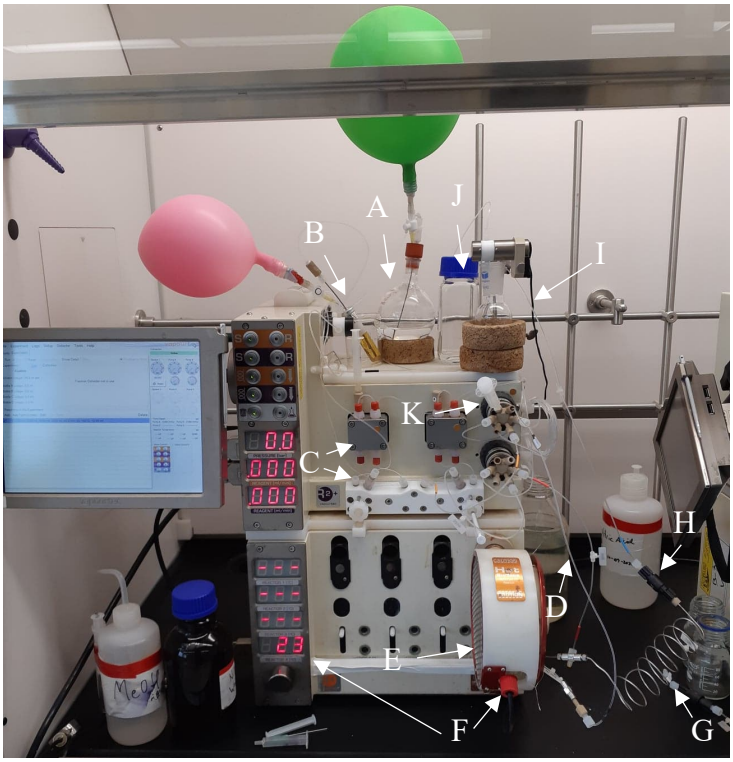
A. Solvent feed tank under argon atmosphere; **B.** HPLC pump and pressure sensor; **C.** Omnifit® column; **D.** Temperature controller; **E.** 40 cm drop tubing; **F.** 100 psi back pressure regulator; **G.** Six-way valve with 2-mL injection loop; **H.** Waste; **I.** Collection flask



Procedure: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol) and tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. DMF (2.00 mL) was then added and the homogeneous solution was loaded into the injection loop and pumped (flow rate = 0.015 mL/min) through the pre-heated (150 °C) Omnifit® packed bed column containing Matrix Innovation MP-carbonate supported resin (>0.5 mmol/g, V = 0.6 mL) (residence time = 40 min). The whole reaction mixture was collected in a flask (5 mL) and the mixture was concentrated under reduced pressure. The resulting solid was dissolved in a 1:1 mixture of water: EtOAc (10 mL) and transferred into a separatory funnel. The layer separated and the aqueous layer was washed with EtOAc (2 x 5 mL). The combined organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard. Product **2a** was obtained in 23% NMR yield along with 69% of unreacted starting material **1aa**.

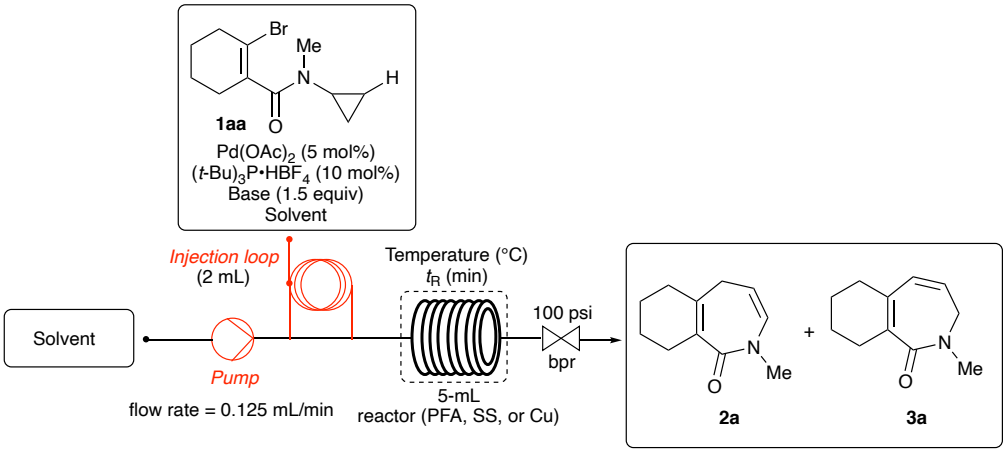
Homogeneous conditions (injection loop and reagent feed tank):

To optimize the conditions in flow chemistry, a R-Series Vapourtec® flow system (R2+ pump, R4 heating module) and standard 1/16'' x 0.04'' tubing PFA tubing were used. The set-up used for both optimization (loop) and scale-up (bottle reagent) is shown below.



A. Solvent feed tank under argon atmosphere; **B.** Reaction feed tank: reaction mixture under argon atmosphere; **C.** HPLC pump and pressure sensor; **D.** 40 cm drop tubing; **E.** Coil reactor (Stainless steel, PFA or Copper); **F.** Temperature controller; **G.** 100 cm cooling loop; **H.** 100 psi back pressure regulator; **I.** Collection flask; **J.** Waste; **K.** Six-way valve with 2-mL injection loop (used for optimization).

General procedure for the optimization study of the continuous flow reaction under homogeneous conditions (injection loop) (Table S10-S14)



General procedure for the optimization: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol) and tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. The solvent (2.00 mL) and base (1.5 equiv) were then added and the homogeneous solution was loaded into the injection loop and pumped through the reactor coil that was pre-heated at the selected temperature. The reaction solvent was used as the carrier solvent. The whole reaction mixture was collected in a flask (5 mL) and the mixture was concentrated under reduced pressure. The resulting solid was dissolved in a 1:1 mixture of water: EtOAc (10 mL) and transferred into a separatory funnel. The layer separated and the aqueous layer was washed with EtOAc (2 x 5 mL). The combined organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude product. 1,3,5-Trimethoxybenzene was then added as an internal standard, the whole was dissolved in $CDCl_3$. The yield was calculated based on the integration of ^{1}H NMR signals of the product relative to those of the internal standard.

Table S10: Solvent mixture screening[a]

Entry	Solvent	Yield (%)[b]
1[c]	DMF	41 (40)[d]
2	Xylenes: DMF (1:3)	53 (34)[d]
3	Xylenes: DMF (1:1)	31 (53)[d]
4	Xylenes: DMF (3:1)	78 (19)[d]
5	Xylenes: DMF (17:3)	23 (69)[d]
6	Toluene: DMF (3:1)	26 (44)[d]

[a] Unless otherwise noted: base: DIPEA, reactor: stainless steel, reactor temperature: 150 °C, residence time: 40 min, flow rate: 0.125 mL/min. [b]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [c]Performed at 140 °C.[d] Yield of unreacted starting material.

Table S11: Temperature screening[a]

Entry	Temperature (°C)	Yield (%)[b]
1	110	<5 (83)[c]
2	140	51 (43)[c]
3	150	78 (19)[c]
4	160	53 (19)[c]
5	180	59 (21)[c]
6	190[d]	63 (17)[c]

[a] Unless otherwise noted: solvent: xylenes:DMF (3:1), base: DIPEA, reactor: stainless steel, residence time: 40 min, flow rate: 0.125 mL/min. [b]Yields were calculated based on ^{1}H NMR using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [c]Yield of unreacted starting material.[d]20 min as residence time.

Table S12: Residence time screening[a]

Entry	Residence time (min)/ Flow rates (mL/min)	Yield (%)[b]
1	20/0.250	31 (65)[c]
2	30/0.175	43 (49)[c]
3	40/0.125	78 (19)[c]
4	60/0.075	37 (50)[c]

[a] Unless otherwise noted: solvent: xylenes:DMF (3:1), base: DIPEA, reactor: stainless steel, reactor temperature: 150 °C. [b]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [c]Yield of unreacted starting material.

Table S13: Base screening[a]

Entry	Base	Yield (%)[a]
1[b]	DIPEA	47 (40)[c]
2	DIPEA	78 (19)[c]
3[d]	DIPEA	79 (10)[c]
4	Et_3N	---[e]
5	iPr_2NH	33 (39)
6	2,6-Lutidine	7 (78)

[a] Unless otherwise noted: solvent: xylenes:DMF (3:1), reactor: stainless steel, reactor temperature: 150 °C, residence time: 40 min, flow rate: 0.125 mL/min.[a]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [b]1.1 equiv used. [c]Yield of unreacted starting material. [d]4.5 equiv used. [e]Clogging was observed.

Table S14: Reactor material screening and other miscellaneous conditions[a]

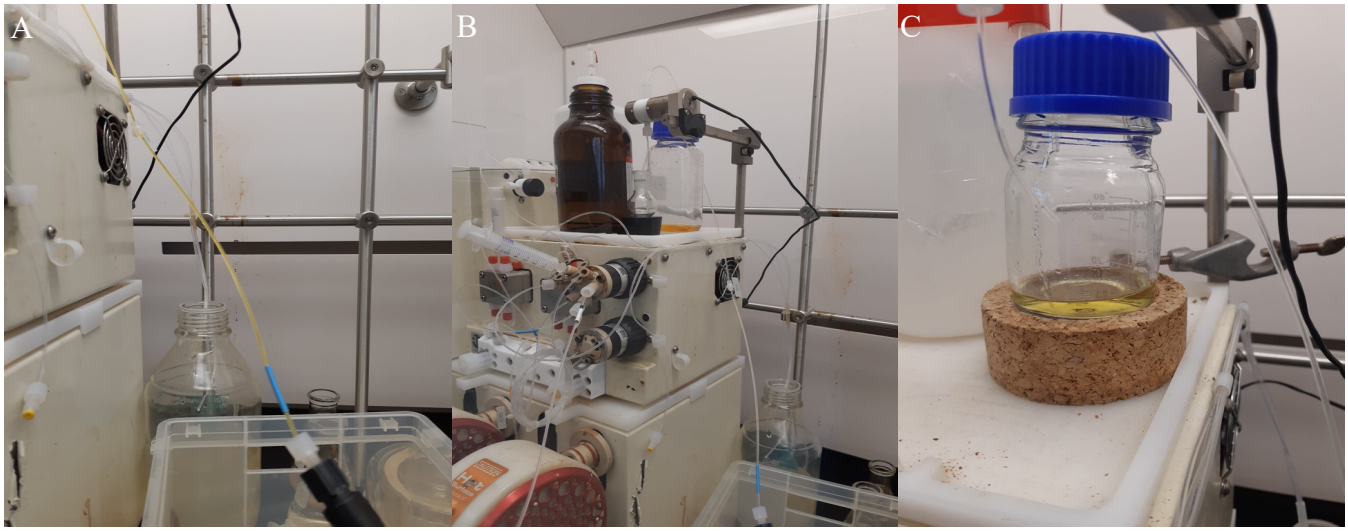
Entry	5-mL Reactor material	Yield (%)[b]
1	PFA	---[c]
2	Stainless steel	78 (19)[c]
3[d]	Stainless steel	63 (0)[c]
4[e]	Stainless steel	74 (0) [c]
5	Copper	---[f]
6[g]	Stainless steel	85 (0)

[a] Unless otherwise noted: solvent: xylenes:DMF (3:1), base: DIPEA, reactor temperature: 150 °C, residence time: 40 min, flow rate: 0.125 mL/min. [b]Yields were calculated based on ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (TMB) as an internal standard. [c]Unreacted starting material. [d]Increased catalytic loading, $Pd(OAc)_2$ 10 mol% and 20 mol% P(*t*Bu)$_3$•HBF4. [e] Increased catalytic loading, $Pd(OAc)_2$ 10 mol% and 20 mol% P(*t*Bu)$_3$•HBF4 and nitric acid wash as described above. [f]High amount of copper leaching into the reaction mixture. [g] Increased reaction scale 0.6 mmol.

During the optimization and as observed by others, palladium (0) deposition on the stainless-steel reactor coil was suspected, thus leading to diminished reaction yield and reproducibility issues. As mentioned by Kappe[5], it is possible to clean the reactor in between runs by washing it with diluted nitric acid. The following procedure was used.

Nitric acid wash procedure:

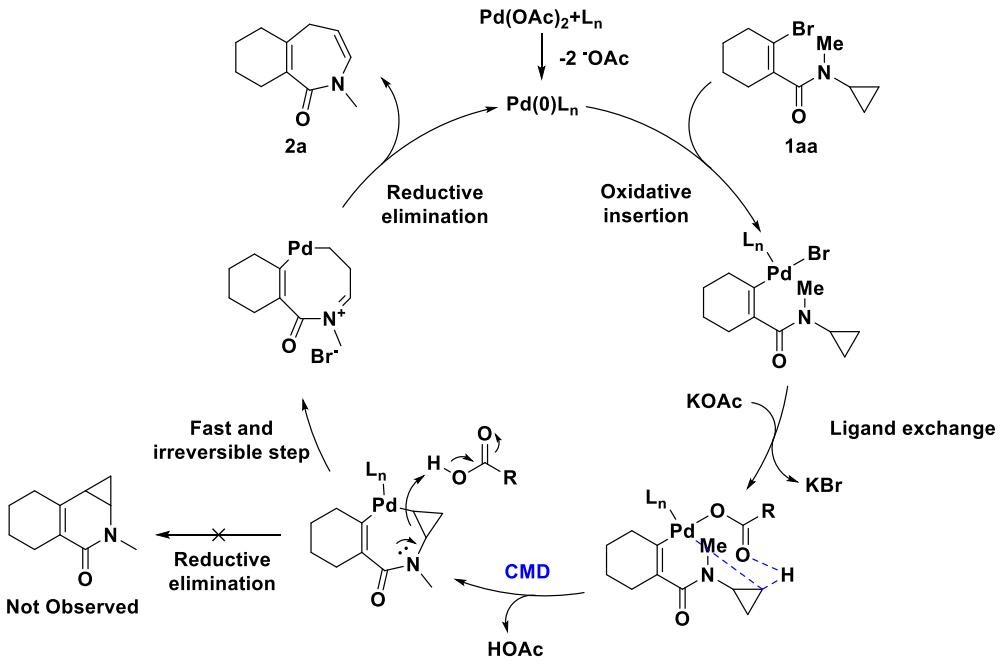
After the reaction, the whole set-up was washed with MeOH (flow rate of 2.50 mL/min) for 5 min. The reactor was heated to 60 °C and then washed with 20% aqueous nitric acid (flow rate of 2.50 mL/min) for 5 min or until the yellow solution (indicative of dissolved palladium particle) became colorless. The system was then washed with MeOH as above and after which it was ready to be used in the next reaction.



A. Reaction stream (yellow) while washing the reactor coil with 20% aqueous nitric acid (flow rate: 2.50 mL/min, 60 °C); **B.** Reaction stream (colorless) after washing; **C.** Collected solution of the aqueous nitric acid and MeOH wash.

Mechanism

The proposed mechanism of the optimized reaction is as followed:

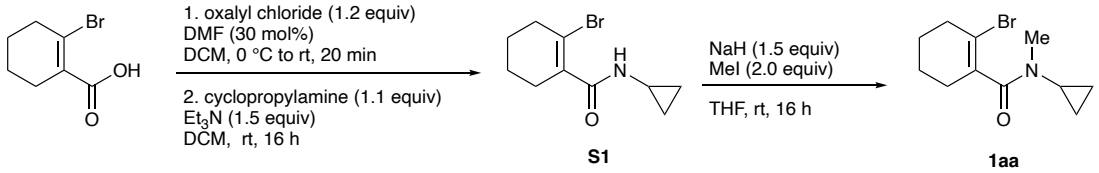


Reaction mechanism for the formation of hexahydroazepinone via a CMD transition state.

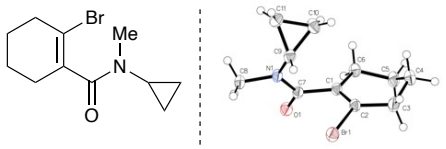
Experimental procedures and characterization data

General procedure 1 for synthesis of the starting materials and characterization data (1aa, 1ab, 1ac, 1b-r) (procedure for 1aa shown below). Starting materials not listed below were obtained commercially and the reagents were used without further purification. 2-Halocycloalkenyl carboxylic acids were synthesized via a Vilsmeier-Haack formylation[5] followed by Pinnick oxidation as reported in the literature (Scheme 1).[6,7]

The precursors to the ring opening reaction were reported as a mixture of rotamers.[8,9]

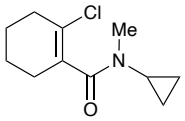


2-Bromo-*N*-cyclopropylcyclohex-1-ene-1-carboxamide (S1). To a flamed-dried, 100-mL flask and cooled under argon was added DCM (60 mL), cat. DMF (0.23 mL, 2.93 mmol), and 2-bromocyclohex-1-ene-1-carboxylic acid (2.00 g, 9.75 mmol). To this was slowly added oxalyl chloride (1.5 mL, 17.97 mmol) and bubbling was immediately observed. The reaction was stirred for 1 h and it turned yellow, then cyclopropylamine (0.75 mL, 10.7 mmol) was added followed by Et_3N (2.04 mL, 14.6 mmol) leading to the formation of a white gas over the reaction mixture that disappeared after a few moments. The reaction mixture was stirred for 16 h and then transferred to a separatory funnel. The organics were washed with Na_2CO_3 (3x50 mL) and brine (1x50 mL). The combined organic layers were dried over Mg_2SO_4, filtered, and concentrated under reduced pressure to give a brownish oil. The residue was dissolved in DCM and purified by flash chromatography (40% EtOAc:hexanes) as eluent to give **S1** as a white solid (2.09 g, 88%). **A** can also be purified via trituration using hexanes as solvent. **mp**: 98-101 °C; $\mathbf{R_f}$: 0.18 (30% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 6.07-5.97 (brs, 1H, **N-H**), 2.77 (dtt, J = 7.5, 3.4, 3.4 Hz, 1H, N-**CH**$_{cyclopropane}$), 2.51-2.35 (m, 4H, **CH$_2$**-C(-Br)=C and **CH$_2$**-C(-C=O)=C-), 1.75-1.66 (m, 4H, CH_2-**CH$_2$-CH$_2$**-$CH_{2cyclohexene}$), 0.87-0.77 (m, 2H, **CH$_2$-CH$_{2cyclopropane}$**), 0.64-0.56 (m, 2H, **CH$_2$-CH$_{2cyclopropane}$**); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.6, 135.2, 120.8, 36.2, 29.1, 24.1, 22.6, 18.4, 6.5; **FTIR** (cm-1) (neat): 3267, 2940, 2922, 1627, 1536, 1444, 1301, 1058, 1014, 726, 673; **HRMS** (ESI, Pos) calc. for $C_{10}H_{15}[^{79}Br]NO$ (M+H)+: 244.03315 found: 244.03343 m/z, calc. for $C_{10}H_{15}[^{81}Br]NO$ (M+H)+: 246.03144 found: 246.03111 m/z.



1aa CCDC 2104751

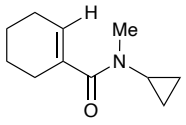
2-Bromo-*N*-cyclopropyl-*N*-methylcyclohex-1-ene-1-carboxamide (1aa). To a 250-mL round bottomed flask containing 50 mL of THF was added intermediate **S1** (2.09 g, 8.55 mmol). The reaction was cooled to 0 ºC and NaH, 54% wt. oil dispersion (396 mg, 9.40 mmol) was added. After stirring for 15 min, MeI (1.08 mL, 17.1 mmol) was added dropwise. The reaction stirred for 16 h before quenching with 75 mL brine and 75 mL of EtOAc. The reaction was transferred to a 250-mL separatory funnel. The layers were then separated, and the aq. layer was then washed with EtOAc (3x50 mL). The combined organics were then washed with brine (1x50 mL), dried over Na_2SO_4 anhydrous, filtered and concentrated under reduced pressure to give **1aa** as white solid (97% yield, 2.14 g, 8.29 mmol) after flash chromatography (0-30% hexanes:ethyl acetate). All starting materials are reported as mixtures of rotamers. **mp:** 50-52 °C; $\mathbf{R_f}$: 0.29 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 3.00-2.68 (m, 4H, N-**CH_3** and N-**$CH_{cyclopropane}$**), 2.61-2.45 (m, 2H, **CH_2**-C(-Br)=C), 2.38-2.11 (m, 2H, **CH_2**-C(-C=O)=C-), 1.84-1.70 (m, 4H, CH_2-**CH_2-CH_2**-$CH_{2cyclohexene}$), 0.89-0.67 (m, 4H, **CH_2-$CH_{2cyclopropane}$**); **^{13}C NMR** (CD_3OD, 400 MHz): δ 174.9, 174.4, 137.1, 136.1, 36.6, 36.3, 35.9, 33.9, 32.6, 30.7, 30.0, 29.4, 25.3, 25.1, 22.5, 22.4, 8.8, 7.2, 6.9, 6.7; **FTIR** (cm^{-1}) (neat): 2933, 2885, 1635, 1381, 1363, 1025, 756; **HRMS** (ESI, Pos) calc. for $C_{11}H_{17}[^{79}Br]NO$ $(M+H)^+$ 258.04880: found: 258.04842 *m/z*, calc. for $C_{11}H_{17}[^{81}Br]NO$ $(M+H)^+$ 260.04676 : found 260.04712 *m/z.*



1ab

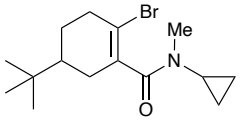
2-Chloro-*N*-cyclopropyl-*N*-methylcyclohex-1-ene-1-carboxamide (1ab). The title compound **1ab** was prepared according to the general procedure on a 6.23 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1ab** as a light yellow oil (1.08 g, 5.17 mmol, 83% over 2 steps). $\mathbf{R_f}$: 0.30 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 2.98-2.69 (m, 4H, N-**CH_3** and N-**$CH_{cyclopropane}$**), 2.47-2.09 (m, 4H, **CH_2**-C(-Cl)=C(-C=O)-**CH_2**), 1.84-1.66 (m, 4H, CH_2-**CH_2-CH_2**-$CH_{2cyclohexene}$), 0.89-0.65 (m, 4H, **CH_2-$CH_{2cyclopropane}$**); **^{13}C NMR** (CD_3OD, 101 MHz): δ 174.3, 173.7, 133.8, 132.9, 130.0, 129.7, 35.7, 33.9, 33.7, 32.3, 30.6, 29.1,

28.5, 24.5, 24.4, 22.5, 22.4, 8.8, 7.2, 6.8; **FTIR** (cm^{-1}) (neat): 2933, 2860, 1633, 1435, 1383, 1364, 1026, 986, 737; **HRMS** (ESI, Pos) calc. for $C_{11}H_{17}[^{35}Cl]NO$ $(M+H)^+$: 214.09932 found: 214.09933 *m/z*, calc. for $C_{11}H_{17}[^{37}Cl]NO$ $(M+H)^+$: 216.09637 found: 216.09714 *m/z*.



1ac

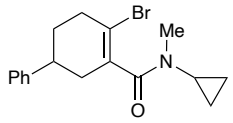
***N*-Cyclopropyl-*N*-methylcyclohex-1-ene-1-carboxamide (1ac).** The title compound **1ac** was prepared according to the general procedure on a 7.93 mmol-scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give 1ac as a light yellow oil (1.28 g, 7.14 mmol, 90% over two steps). **R_f:** 0.15 (20% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 5.94 (s(br), 1H, CH_2-C(**-H**)=C(C=O)), 2.96 (s, 3H, N-**CH_3**), 2.74-2.68 (m, 1H, N-**$CH_{cyclopropane}$**), 2.27-2.11 (m, 4H, **CH_2**-C(-H)=C(-C=O)-**CH_2**), 1.77-1.61 (m, 4H, CH_2-**CH_2-CH_2**-$CH_{2cyclohexene}$), 0.85-0.76 (m, 2H, **C**H_{trans}**H_{cis}**-**C**H_{trans}**H_{cis}**$_{cyclopropane}$), 0.69-0.62 (m, 2H, **$CH_{trans}H_{cis}$**-**$CH_{trans}H_{cis}$**$_{cyclopropane}$); **^{13}C NMR** (CD_3OD, 101 MHz): δ 176.8, 136.2, 130.4, 35.3, 33.5, 26.6, 25.8, 23.3, 22.8, 9.2; **FTIR** (cm^{-1}) (neat): 2928, 2857, 1620, 1434, 1382, 1359, 1026, 642.8, 459.1; **HRMS** (ESI, Pos) calc. for $C_{11}H_{18}NO$ $(M+H)^+$: 180.13829 found: 180.13876 *m/z*.



1b

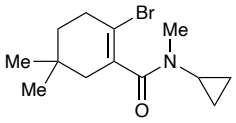
2-Bromo-5-(*tert*-butyl)-*N*-cyclopropyl-*N*-methylcyclohex-1-ene-1-carboxamide (1b). The title compound **1b** was prepared using the general procedure on a 3.36 mmol-scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1b** as a white solid (276 mg, 0.820 mmol, 25% over two steps). **mp:** 57-61 °C; **R_f**: 0.63 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 3.03-2.69 (m, 4H, N-**CH_3** and N-**$CH_{cyclopropyl}$**), 2.65-2.51 (m, 2H, **C-$H_{cyclohexene}$**), 2.39-1.84 (m, 3H, **C-$H_{cyclohexene}$**), 1.51-1.37 (m, 2H, **C-$H_{cyclohexene}$**), 0.96-0.67 (m, 13H, **CH_2-$CH_{2cyclopropyl}$** and C-**$(CH_3)_3$**); **^{13}C NMR** (CD_3OD, 101 MHz): δ 175.1, 174.8, 174.5, 174.3, 137.0, 136.9, 136.2, 135.9, 121.0, 120.9, 120.6, 120.4, 44.68, 44.63, 44.5, 44.3, 38.1, 38.0, 37.8, 37.7, 37.5, 36.1, 35.8, 34.0, 33.9, 33.0, 32.6, 31.83, 31.75, 31.21, 31.15, 30.74, 30.65, 27.6, 27.5, 26.9, 26.83, 26.78, 26.68, 9.3, 8.6, 7.3, 7.2, 7.1, 6.7, 6.6; **FTIR** (cm^{-1}) (neat): 2957, 2867, 1637,

1434, 1364, 1024, 749; **HRMS** (ESI, Pos) calc. for $C_{15}H_{25}[^{79}Br]NO$ $(M+H)^+$: 314.11140 found: 314.11217 *m/z,* calc. for $C_{15}H_{25}[^{81}Br]NO$ $(M+H)^+$: 316.10936 found: 316.10956 *m/z.*



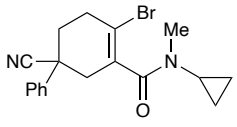
1c

4-Bromo-*N*-cyclopropyl-*N*-methyl-1,2,5,6-tetrahydro-[1,1'-biphenyl]-3-carboxamide (1c). The title compound **1c** was prepared using the general procedure on a 2.13 mmol-scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1c** as a white solid (389 mg, 1.16 mmol, 55% over two steps). **mp:** 62-65 °C; **R_f**: 0.27 (20% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.33-7.16 (m, 5H, **C-H**$_{aryl}$), 3.07-2.25 (m, 9H, N-**CH$_3$**, N-**CH**$_{cyclopropyl}$ and **C-H**$_{cyclohexene}$), 2.07-1.91 (m, 2H, **C-H**$_{cyclohexene}$), 0.93-0.66 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 172.3, 172.1, 171.5, 171.4, 144.8, 144.7, 144.5, 135.8, 135.6, 135.0, 134.5, 128.7, 126.8, 126.71, 126.66, 119.3, 119.1, 118.9; **FTIR** (cm^{-1}) (neat): 3058, 3024, 2923, 1634, 1383, 1027, 952, 699; **HRMS** (ESI, Pos) calc. for $C_{17}H_{21}[^{79}Br]NO$ $(M+H)^+$: 334.08010 found: 334.08090 *m/z*, calc. for $C_{17}H_{21}[^{81}Br]NO$ $(M+H)^+$: 336.07806 found: 336.07893 *m/z.*



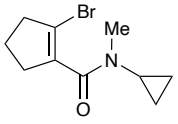
1d

2-Bromo-*N*-cyclopropyl-*N*-5,5-trimethylcyclohex-1-ene-1-carboxamide (1d). The title compound **1d** was prepared using the general procedure on a 1.84 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1d** as a light yellow oil (325 mg, 1.14 mmol, 62% over two steps). **R_f**: 0.38 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 2.98-2.68 (m, 4H, N-**CH$_3$**, N-**CH**$_{cyclopropyl}$), 2.59-2.49 (m, 2H, **C-H**$_{cyclohexene}$), 2.16-1.90 (m, 2H, **C-H**$_{cyclohexene}$), 1.59-1.50 (m, 2H, **C-H**$_{cyclohexene}$), 1.06-0.97 (m, 6H, CH_2-C-**(CH$_3$)$_2$**-CH_2), 0.92-0.66 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** (CD_3OD, 101 MHz): δ 174.8, 174.2, 136.2, 135.2, 119.8, 119.6, 43.2, 42.8, 37.9, 37.7, 35.9, 34.5, 34.2, 34.0, 32.5, 30.7, 29.5, 28.2, 28.0, 27.7, 9.0, 7.2, 6.8; **FTIR** (cm^{-1}) (neat): 2951, 2924, 1635, 1383, 1364, 1031, 560; **HRMS** (ESI, Pos) calc. for $C_{13}H_{21}[^{79}Br]NO$ $(M+H)^+$: 286.08010 found: 286.08048 *m/z,* calc. for $C_{13}H_{21}[^{81}Br]NO$ $(M+H)^+$: 288.07806 found: 288.07854 *m/z.*



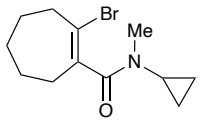
1e

4-Bromo-1-cyano-*N*-cyclopropyl-*N*-methyl-1,2,5,6-tetrahydro-[1,1'-biphenyl]-3-carboxamide (1e). The title compound **1e** was prepared using the general procedure on a 1.14 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1e** as a white solid (233 mg, 0.570 mmol, 50% over two steps). **mp:** 141-144 °C; **R_f**: 0.14 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.49 (t, *J* = 7.8 Hz, 2H, **C-H**$_{aryl}$), 7.43-7.31 (m, 3H, **C-H**$_{aryl}$), 3.11-2.59 (m, 8H, N-**CH$_3$**, N-**CH**$_{cyclopropyl}$ and **C-H**$_{cyclohexene}$), 2.39-2.16 (m, 2H, **C-H**$_{cyclohexene}$), 1.06-0.63 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): 170.9, 170.1, 138.6, 138.3, 133.1, 132.2, 129.4, 129.3, 128.69, 128.65, 125.63, 125.59, 121.9, 121.8, 118.8, 118.3, 40.7, 40.5, 40.0, 39.9, 35.2, 34.3, 34.1, 33.7, 33.6, 33.5, 31.3, 29.8, 8.7, 6.8, 6.6, 6.4; **FTIR** (cm^{-1}) (neat): 3091, 3009, 2967, 2940, 2224, 1638, 1604, 1497, 1420, 1208, 772, 741, 698, 550; **HRMS** (ESI, Pos) calc. for $C_{18}H_{20}[^{79}Br]N_2O$ $(M+H)^+$: 359.07535 found: 359.07611 *m/z,* calc. for $C_{18}H_{20}[^{81}Br]N_2O$ $(M+H)^+$: 361.07331 found: 361.07404 *m/z.*



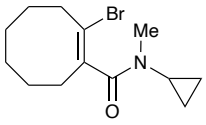
1f

2-Bromo-*N*-cyclopropyl-*N*-methylcyclopent-1-ene-1-carboxamide (1f). The title compound **1f** was prepared using the general procedure on a 5.23 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1f** as a light yellow oil (984 mg, 4.03 mmol, 77% over two steps). **R_f:** 0.25 (30% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 2.99-2.55 (m, 8H, N-**CH$_3$**, N-**CH**$_{cyclopropyl}$ and **C-H**$_{cyclopentene}$), 2.06-1.94 (m, 2H, **C-H**$_{cyclohexene}$), 0.85-0.58 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.0, 138.6, 119.4, 118.9, 40.6, 35.6, 34.7, 34.3, 33.7, 31.1, 29.5, 22.8, 22.3, 7.8, 6.6; **FTIR** (cm^{-1}) (neat): 2929, 2852, 1624, 1422, 1107, 1027, 740; **HRMS** (ESI, Pos) calc. for $C_{10}H_{15}[^{79}Br]NO$ $(M+H)^+$: 244.03315 found: 244.03378 *m/z,* calc. for $C_{10}H_{15}[^{81}Br]NO$ $(M+H)^+$: 246.03111 found: 246.03159 *m/z.*



1g

2-Bromo-*N*-cyclopropyl-*N*-methylcyclohept-1-ene-1-carboxamide (1g). The title compound **1g** was prepared using the general procedure on a 1.83 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1g** as a light yellow oil (258 mg, 0.945 mmol, 53% over two steps). **R_f:** 0.26 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 3.00-2.66 (m, 6H, N-**CH_3**, N-**$CH_{cyclopropyl}$** and **C-$H_{cycloheptane}$**), 2.46-2.25 (m, 2H, **C-$H_{cycloheptane}$**), 1.91-1.59 (m, 6H, **C-$H_{cycloheptane}$**), 0.90-0.66 (m, 4H, **CH_2-$CH_{2cyclopropyl}$**); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 173.9, 173.1, 140.6, 139.4, 137.0, 131.9, 123.1, 122.7, 41.4, 41.2, 39.0, 38.8, 35.4, 35.3, 33.6, 32.1, 31.6, 31.2, 31.1, 30.9, 30.8, 30.7, 30.6, 29.50, 29.45, 26.5, 26.44, 26.38, 26.3, 25.6, 25.3, 9.1, 6.4, 6.6, 6.3; **FTIR** (cm^{-1}) (neat): 2923, 2851, 1635, 1380, 1026, 740; **HRMS** (ESI, Pos) calc. for $C_{12}H_{19}[^{79}Br]NO$ $(M+H)^+$: 272.06445 found: 272.06449 *m/z*, calc. for $C_{12}H_{19}[^{81}Br]NO$ $(M+H)^+$: 274.06241 found: 274.06277 *m/z.*

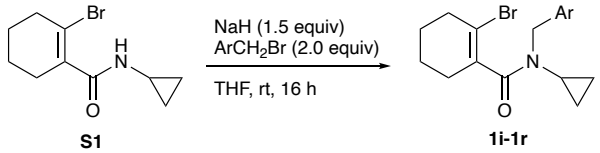


1h

(*Z*)-2-Bromo-*N*-cyclopropyl-*N*-methylcyclooct-1-ene-1-carboxamide (1h). The title compound **1h** was prepared using the general procedure on a 3.72 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1h** as a light yellow oil (827 mg, 2.90 mmol, 78% over two steps). **R_f:** 0.37 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 3.09-2.66 (m, 5H, N-**CH_3**, N-**$CH_{cyclopropyl}$** and **C-$H_{cyclooctene}$**), 2.62-2.37 (m, 2H, **C-$H_{cyclooctene}$**), 2.23-2.12 (m, 1H, **C-$H_{cyclooctene}$**), 1.83-1.41 (m, 8H, **C-$H_{cyclooctene}$**), 0.87-0.66 (m, 4H, **CH_2-$CH_{2cyclopropyl}$**); **^{13}C NMR** (CD_3OD, 101 MHz): δ 175.2, 174.6, 139.2, 138.2, 37.1, 37.0, 35.9, 33.7, 32.43, 32.36, 31.8, 31.1, 30.8, 30.6, 29.1, 27.5, 27.4, 26.4, 9.2, 7.3, 6.9, 6.7; **FTIR** (cm^{-1}) (neat): 2925, 2850, 1634, 1381, 1027, 663; **HRMS** (ESI, Pos) calc. for $C_{13}H_{21}[^{79}Br]NO$ $(M+H)^+$: 286.08010 found:

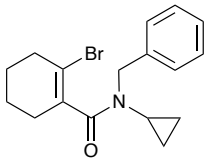
286.08061 *m/z*, calc. for $C_{13}H_{21}[^{81}Br]NO$ $(M+H)^+$: 288.07806 found: 288.07861 *m/z.*

Synthesis benzylic substituted 2-halocycloalkenyl amides (1i-r)



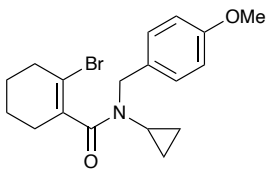
S1 **1i-1r**

Using the arylmethyl bromide and amide **S1**, the *N*-arylmethyl-substituted compounds were prepared using the general alkylation procedure described for **1aa**.



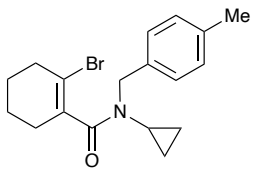
1i

***N*-Benzyl-2-bromo-*N*-cyclopropylcyclohex-1-ene-1-carboxamide (1i).** The title compound **1i** was prepared from amide **S1** on a 1.84 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1i** as a light yellow oil (412 mg, 1.23 mmol, 67%). $\mathbf{R_f}$: 0.51 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.40-7.21 (m, 5H, **C-H**$_{aryl}$), 4.82-4.66 (m, 1H, **C-H**$_{benzylic}$), 4.52-4.40 (m, 1H, **C-H**$_{benzylic}$), 2.80-2.73 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.59-2.43 (m, 2H, **C-H**$_{cyclohexene}$), 2.39-2.27 (m, 2H, **C-H**$_{cyclohexene}$), 1.85-1.57 (m, 4H, **C-H**$_{cyclohexene}$), 0.94-0.67 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** (CD_3OD, 101 MHz): δ 175.0, 138.7, 138.5, 136.9, 135.8, 129.8, 129.4, 129.2, 128.7, 128.5, 128.4, 122.0, 120.9, 53.8, 50.7, 36.6, 36.5, 31.3, 30.2, 30.1, 29.8, 25.2, 25.0, 22.5, 22.3, 8.8, 7.4, 7.2; **FTIR** (cm^{-1}) (neat): 3062, 2932, 1632, 1433, 1400, 1027, 698; **HRMS** (ESI, Pos) calc. for $C_{17}H_{21}[^{79}Br]NO$ $(M+H)^+$: 334.08010 found: 334.08065 *m/z*, calc. for $C_{17}H_{21}[^{81}Br]NO$ $(M+H)^+$: 336.07806 found: 336.07877 *m/z.*



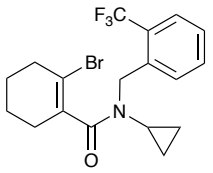
1j

2-Bromo-*N*-cyclopropyl-*N*-(4-methoxybenzyl)cyclohex-1-ene-1-carboxamide (1j). The title compound **1j** was prepared from amide **S1** using DMF at 70 °C for 16 h on a 1.43 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1j** as a light yellow oil (425 mg, 1.16 mmol, 81%). **R_f**: 0.39 (30% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.30-7.20 (m, 2H, **C-H**$_{aryl,\ o\text{-}CH2}$), 6.89-6.78 (m, 2H, **C-H**$_{aryl,\ o\text{-}OMe}$), 4.82-4.21 (m, 2H, **C-H**$_{benzylic}$), 3.81-3.74 (m, 3H, O-**CH_3**), 2.68-2.60 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.53-2.13 (m, 4H, **C-H**$_{cyclohexene}$), 2.00-1.55 (m, 4H, **C-H**$_{cyclohexene}$), 0.95-0.60 (m, 4H, **CH_2-CH_2**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 172.6, 172.3, 159.2, 159.1, 158.9, 135.8, 134.8, 133.4, 129.9, 129.8, 129.7, 129.3, 128.6, 120.3, 119.4, 114.1, 114.0, 113.7, 65.0, 55.4, 55.3, 52.2, 49.1, 35.62, 35.57, 29.6, 29.33, 29.29, 28.2, 24.3, 24.1, 21.5, 21.4, 8.5, 8.4, 6.8, 6.7; **FTIR** (cm^{-1}) (neat): 3006, 2934, 1631, 1612, 1600, 1510, 1243, 1174, 1030, 813; **HRMS** (ESI, Pos) calc. for $C_{18}H_{23}[^{79}Br]NO_2$ $(M+H)^+$: 364.09067 found: 364.09204 *m/z,* calc. for $C_{18}H_{23}[^{81}Br]NO_2$ $(M+H)^+$: 366.08862 found: 366.08936 *m/z.*



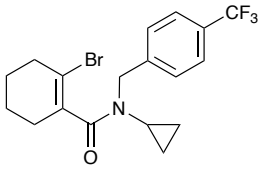
1k

2-Bromo-*N*-cyclopropyl-*N*-(4-methylbenzyl)cyclohex-1-ene-1-carboxamide (1k). The title compound **1k** was prepared from amide **S1** on a 0.819 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1k** a light yellow oil (205 mg, 0.589 mmol, 72%). **R_f**: 0.52 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.25-7.07 (m, 4H, **C-H**$_{aryl}$), 4.77-4.62 (m, 1H, **C-H**$_{benzylic}$), 4.47-4.34 (m, 1H, **C-H**$_{benzylic}$), 2.77-2.69 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.59-2.44 (m, 2H, **C-H**$_{cyclohexene}$), 2.41-2.25 (m, 5H, C_{aryl}-**CH_3** and **C-H**$_{cyclohexene}$), 1.85-1.58 (m, 4H, **C-H**$_{cyclohexene}$), 0.92-0.66 (m, 4H, **CH_2-CH_2**$_{cyclopropyl}$); **^{13}C NMR** (CD_3OD, 101 MHz): δ 175.0, 138.6, 138.1, 137.0, 135.9, 135.6, 135.3, 130.4, 130.0, 129.3, 128.5, 121.9, 120.8, 53.6, 50.4, 36.6, 36.5, 31.2, 30.2, 30.1, 29.7, 25.3, 25.1, 22.5, 22.4, 21.13, 21.10, 8.8, 7.4, 7.2; **FTIR** (cm^{-1}) (neat): 3009, 2935, 1633, 1514, 1397, 1056, 1025, 754; **HRMS** (ESI, Pos) calc. for $C_{18}H_{23}[^{79}Br]NO$ $(M+H)^+$: 348.09575 found: 348.09578 *m/z*, calc. for $C_{18}H_{23}[^{81}Br]NO$ $(M+H)^+$: 350.09371 found: 350.09431 *m/z.*



1l

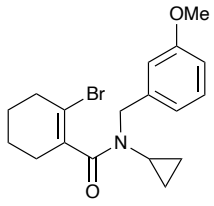
2-Bromo-*N*-cyclopropyl-*N*-(2-(trifluoromethyl)benzyl)cyclohex-1-ene-1-carboxamide (1l). The title compound **1l** was prepared from amide **S1** on a 1.23 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1l** as a white solid (437 mg, 1.08 mmol, 88%). **mp:** 44-48 °C; $\mathbf{R_f}$: 0.26 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.69-7.28 (m, 4H, **C-H**$_{aryl}$), 5.00-4.49 (m, 2H, **CH$_2$**$_{benzylic}$), 2.90-2.74 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.60-2.26 (m, 4H, **C-H**$_{cyclohexene}$), 1.89-1.40 (m, 4H, **C-H**$_{cyclohexene}$), 0.99-0.54 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 173.3, 173.0, 136.9, 135.8, 134.4, 132.3, 132.1, 128.4, 127.7, 127.6 (q, J = 30.1 Hz), 127.4, 126.9, 126.3 (q, J = 5.8 Hz), 125.8 (q, J = 5.8 Hz), 124.5 (q, J = 274.3 Hz), 121.0, 119.9, 48.8 (q, J = 3.3 Hz), 46.4 (q, J = 3.3 Hz), 35.7, 35.5, 30.7, 29.4, 29.2, 29.1, 24.3, 24.0, 21.5, 21.3, 7.9, 6.5; **^{19}F NMR** ($CDCl_3$, 400 MHz): -61.42; **FTIR** (cm^{-1}) (neat): 3014, 2938, 2863, 1639, 1608, 1457, 1309, 1161, 1111, 1035, 767, 651; **HRMS** (ESI, Pos) calc. for $C_{18}H_{20}[^{79}Br]F_3NO$ $(M+H)^+$: 402.06749 found: 402.06820 *m/z*, calc. for $C_{18}H_{20}[^{81}Br]F_3NO$ $(M+H)^+$: 404.06616 found: 404.06544 *m/z.*



1m

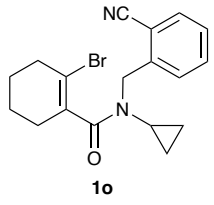
2-Bromo-*N*-cyclopropyl-*N*-(4-(trifluoromethyl)benzyl)cyclohex-1-ene-1-carboxamide (1p). The title compound **1m** was prepared from amide **S1** on a 0.819 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1m** as a light golden oil (291 mg, 0.721 mmol, 88%). $\mathbf{R_f}$: 0.56 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.71-7.48 (m, 4H, **C-H**$_{aryl}$), 4.94-4.86 (m, 1H, **CH**$_{benzylic}$), 4.60-4.46 (m, 1H, **CH**$_{benzylic}$), 2.87-2.79 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.61-2.46 (m, 2H, **C-H**$_{cyclohexene}$), 2.41-2.32 (m, 2H, **C-H**$_{cyclohexene}$), 1.86-1.60 (m, 4H, **C-H**$_{cyclohexene}$), 0.93-0.70 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 172.6, 172.1, 141.8, 141.4, 135.3, 134.3, 129.1 (q, J = 32.2 Hz), 128.3, 127.4, 125.5 (q, J = 3.6 Hz), 125.1 (q, J = 3.6 Hz), 124.0 (q, J = 272.1 Hz), 120.6, 52.1, 49.3, 35.34, 35.27, 29.8, 29.0, 28.1, 24.0, 23.8,

21.2, 21.1, 8.2, 8.1, 6.5; **^{19}F NMR** (CD_3OD, 400 MHz): -63.86; **FTIR** (cm^{-1}) (neat): 3012, 2934, 1634, 1397, 1110, 1064, 814; **HRMS** (ESI, Pos) calc. for $C_{18}H_{20}[^{79}Br]F_3NO$ $(M+H)^+$: 402.06749 found: 402.06750 *m/z*, calc. for $C_{18}H_{20}[^{81}Br]F_3NO$ $(M+H)^+$: 404.06544 found: 404.06613 *m/z.*



1n

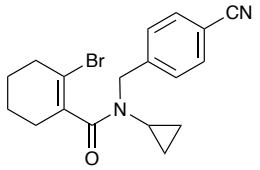
2-Bromo-*N*-cyclopropyl-*N*-(3-methoxybenzyl)cyclohex-1-ene-1-carboxamide (1n). The title compound **1n** was prepared from amide **S1** on a 1.23 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1n** as a light yellow oil (406 mg, 1.12 mmol, 91%). **R_f**: 0.40 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.30-7.18 (m, 1H, **C-H**$_{aryl}$), 6.93-6.79 (m, 3H, **C-H**$_{aryl}$), 4.80-4.64 (m, 1H, **CH**$_{benzylic}$), 4.46-4.38 (m, 1H, **CH**$_{benzylic}$), 3.80-3.74 (m, 3H, O-**CH$_3$**), 2.82-2.74 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.60-2.29 (m, 4H, **C-H**$_{cyclohexene}$), 1.84-1.59 (m, 4H, **C-H**$_{cyclohexene}$), 0.93-0.69 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** (CD_3OD, 101 MHz): δ175.0, 174.9, 140.3, 140.1, 137.0, 135.8, 130.9, 130.4, 122.0, 121.4, 120.9, 120.6, 114.5, 114.2, 114.0, 55.71, 55.66, 53.7, 50.64, 36.6, 36.5, 31.3, 30.23, 30.15, 29.8, 25.2, 25.0, 22.5, 22.4, 8.7, 7.4 **FTIR** (cm^{-1}) (neat): 3009, 2936, 2860, 1628, 1611, 1601, 1489, 1401, 1259, 1042, 982, 780, 744, 695; **HRMS** (ESI, Pos) calc. for $C_{18}H_{23}[^{79}Br]NO_2$ $(M+H)^+$: 364.09067 found: 364.09227 *m/z*, calc. for $C_{18}H_{23}[^{81}Br]NO_2$ $(M+H)^+$: 366.09011 found: 366.08862 *m/z.*



1o

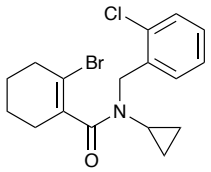
2-Bromo-*N*-(2-cyanobenzyl)-*N*-cyclopropylcyclohex-1-ene-1-carboxamide (1o). The title compound **1o** was prepared from amide **S1** on a 1.23 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1o** as a white solid (370 mg, 1.03 mmol, 84%). **mp:** 44-48 °C; **R_f:** 0.20 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.69-7.57 (m, 2H, **C-H**$_{aryl,\ o,p\text{-}CN}$), 7.53 (td, J_1 = 7.4 Hz, J_2 = 1.3 Hz, 1H, **C-H**$_{aryl,\ m\text{-}CN}$), 7.46-7.31 (m, 1H, **C-H**$_{aryl,\ o\text{-}CH2}$), 5.08 (d, J_1 = 15.3 Hz, 1H, **CH**$_{benzylic}$), 4.69-4.57 (m, 1H, **CH**$_{benzylic}$), 2.78 (tt, J_1 = 7.0 Hz, J_2

= 4.3 Hz, 1H, N-**CH**$_{cyclopropyl}$), 2.56-2.17 (m, 4H, **C-H**$_{cyclohexene}$), 1.87-1.66 (m, 4H, **C-H**$_{cyclohexene}$), 0.97-0.62 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 173.0, 141.5, 135.3, 133.24, 133.17, 133.03, 132.6, 129.6, 128.1, 128.0, 127.8, 120.0, 117.7, 111.8, 50.7, 48.0, 35.6, 35.5, 30.3, 29.3, 29.2, 28.8, 24.2, 24.0, 21.4, 21.3, 8.8, 7.1; **FTIR** (cm^{-1}) (neat): 3052, 2932, 2858, 2224, 1660, 1609, 1357, 1257, 726; **HRMS** (ESI, Pos) calc. for $C_{18}H_{20}[^{79}Br]N_2O$ $(M+H)^+$: 359.07535 found: 359.07602 *m/z*, calc. for $C_{18}H_{20}[^{81}Br]N_2O$ $(M+H)^+$: 361.07331 found: 361.07410 *m/z*.



1p

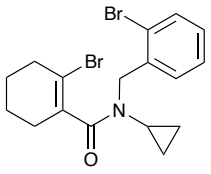
2-Bromo-*N*-(4-cyanobenzyl)-*N*-cyclopropylcyclohex-1-ene-1-carboxamide (1p). The title compound **1p** was prepared from amide **S1** on a 1.23 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1p** as a white solid (371 mg, 1.03 mmol, 84%). **mp:** 83-86 °C; **R$_f$**: 0.17 (20% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.77-7.64 (m, 2H, **C-H**$_{aryl,\ o\text{-}CN}$), 7.56-7.46 (m, 2H, **C-H**$_{aryl,\ m\text{-}CN}$), 4.94-4.83 (m, 1H, **CH**$_{benzylic}$), 4.59-4.44 (m, 1H, **CH**$_{benzylic}$), 2.88-2.79 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.62-2.44 (m, 2H, **C-H**$_{cyclohexene}$), 2.41-2.30 (m, 2H, **C-H**$_{cyclohexene}$), 1.86-1.57 (m, 4H, **C-H**$_{cyclohexene}$), 0.94-0.68 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** (CD_3OD, 101 MHz): δ 175.2, 144.7, 136.7, 133.7, 133.4, 130.0, 129.5, 121.2, 199.6, 112.1, 50.7, 36.6, 31.6, 30.1, 25.2, 22.5, 9.0, 7.3; **FTIR** (cm^{-1}) (neat): 3004, 2937, 2223, 1636, 1600, 1452, 1302, 1031, 763; **HRMS** (ESI, Pos) calc. for $C_{18}H_{20}[^{79}Br]N_2O$ $(M+H)^+$: 359.07535 found: 359.07610 *m/z*, calc. for $C_{18}H_{20}[^{81}Br]N_2O$ $(M+H)^+$: 361.07331 found: 361.07414 *m/z.*



1q

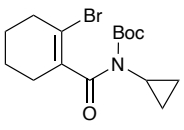
2-Bromo-*N*-(2-chlorobenzyl)-*N*-cyclopropylcyclohex-1-ene-1-carboxamide (1q). The title compound **1q** was prepared from amide **S1** on a 0.819 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give 1q as a white solid (272 mg, 0.737 mmol, 90%). **mp:** 59-61 °C; **R$_f$**: 0.47 (30% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.44-7.22 (m, 4H, **C-H**$_{aryl}$), 4.77-4.50 (m, 2H, **CH$_2$**$_{benzylic}$), 2.91-2.64 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.60-2.23 (m, 4H, **C-**

H$_{cyclohexene}$), 1.85-1.52 (m, 4H, **C-H**$_{cyclohexene}$), 0.95-0.68 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 172.9, 135.8, 135.3, 133.2, 129.9, 129.5, 129.4, 128.8, 128.6, 128.4, 127.2, 127.0, 119.8, 50.0, 47.4, 35.7, 30.5, 29.4, 29.1, 29.0, 24.3, 24.2, 21.6, 21.4, 8.3, 7.0; **FTIR** (cm^{-1}) (neat): 3012, 2934, 2860, 1635, 1396, 1298, 1036, 748, 643; **HRMS** (ESI, Pos) calc. for $C_{17}H_{20}[^{79}Br][^{35}Cl]NO$ $(M+H)^+$: 368.04113 found: 368.04144 *m/z*, calc. for $C_{17}H_{20}[^{81}Br][^{35}Cl]NO$ $(M+H)^+$: 370.03908 found: 370.03945 *m/z*, calc. for $C_{17}H_{20}[^{79}Br][^{37}Cl]NO$ $(M+H)^+$: 370.03818 found: 370.03945 *m/z*, calc. for $C_{17}H_{20}[^{81}Br][^{37}Cl]NO$ $(M+H)^+$: 372.03613 found: 372.03713 *m/z*.



1r

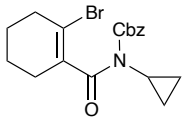
2-Bromo-*N*-(2-bromobenzyl)-*N*-cyclopropylcyclohex-1-ene-1-carboxamide (1r). The title compound **1r** was prepared from amide **S1** on a 0.819 mmol scale and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **1r** as a white solid (300 mg, 0.729 mmol, 89%). **mp:** 84-87 °C; **R$_f$**: 0.46 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.63-7.14 (m, 4H, **C-H**$_{aryl}$), 4.89-4.83 (m, 2H, **CH$_2$**$_{benzylic}$), 2.94-2.71 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.62-2.19 (m, 4H, **C-H**$_{cyclohexene}$), 1.86-1.50 (m, 4H, **C-H**$_{cyclohexene}$), 0.98-0.70 (m, 4H, **CH$_2$-CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** (CD_3OD, 101 MHz): δ 175.1, 137.8, 137.7, 137.0, 135.7, 134.2, 133.9, 130.4, 130.1, 130.0, 129.1, 128.6, 123.83, 123.78, 122.3, 121.3, 53.8, 51.4, 36.6, 32.0, 30.6, 30.1, 30.0, 25.2, 25.0, 22.5, 22.3, 8.7, 8.5, 7.6, 7.2; **FTIR** (cm^{-1}) (neat): 3006, 2966, 2863, 1637, 1567, 1463, 1398, 1296, 1057, 1032, 750; **HRMS** (ESI, Pos) calc. for $C_{17}H_{20}[^{79}Br]_2NO$ $(M+H)^+$: 411.99062 found: 411.99068 *m/z*, calc. for $C_{17}H_{20}[^{79}Br][^{81}Br]NO$ $(M+H)^+$: 413.98857 found: 413.98917 *m/z*, calc. for $C_{17}H_{20}[^{81}Br]_2NO$ $(M+H)^+$: 415.98652 found: 415.98708 *m/z*.



S2

***tert*-Butyl (2-bromocyclohex-1-ene-1-carbonyl)(cyclopropyl)carbamate (S2).** To a solution of amide **S1** (450 mg, 1.84 mmol) in ACN (10 mL) was sequentially added di-*tert*-butyl dicarbonate (443 mg, 2.03 mmol) and 4-dimethylaminopyridine (11.3 mg, 0.092 mmol). When

TLC analysis showed complete consumption of starting material (overnight), the reaction mixture was concentrated to dryness. The residue was dissolved in DCM and purified by flash chromatography using a gradient of 0-40% (EtOAc:hexanes) to afford **S2** as a colorless oil (343 mg, 1.00 mmol, 54%). **R_f**: 0.7 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 2.65-2.57 (m, 1H, N-**CH**$_{cyclopropyl}$), 2.50-2.42 (m, 2H, **C-H**$_{cyclohexene}$), 2.33-2.24 (m, 2H, **C-H**$_{cyclohexene}$), 1.80-1.67 (m, 4H, **C-H**$_{cyclohexene}$), 1.53 (s, 9H, C-(**CH$_3$**)$_3$), 1.02-0.93 (m, 2H, CH_2-**CH$_2$**$_{cyclopropyl}$), 0.72-0.65 (m, 2H, **CH$_2$**-$CH_{2cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 172.0, 154.1, 135.6, 134.6, 128.3, 128.1, 117.7, 68.4, 35.1, 28.6, 27.0, 23.4, 20.6, 8.5, 8.0; **FTIR (cm^{-1})** (neat): 2978, 2935, 1736, 1690, 1675, 1282, 1249, 1160, 1143, 1108, 729; **HRMS** (ESI, Pos) calc. for $C_{15}H_{22}[^{79}Br]NNaO_3$ $(M+Na)^+$: 366.06753 found: 366.06854 *m/z*, calc. for $C_{15}H_{22}[^{81}Br]NNaO_3$ $(M+Na)^+$: 368.06548 found: 368.06572 *m/z*.



S3

Benzyl (2-bromocyclohex-1-ene-1-carbonyl)(cyclopropyl)carbamate (S3) . To a flame-dried, 100-mL round bottom and cooled in an acetone/dry ice bath under argon, was sequentially added amide **S1** (500 mg, 2.05 mmol), THF (20 mL) and *n*-butyllithium (2.5 M solution in hexanes (1.07 mL, 2.25 mmol). The resulting mixture was stirred for 30 min. Then benzyl chloroformate (0.32 mL, 2.25 mmol) was added and the reaction mixture stirred for 16 h at room temperature. The reaction mixture was diluted with equal parts of ethyl acetate and brine, and then the aqueous layer was washed with EtOAc (3x50 mL). The combined organics were washed with brine, dried over Na_2SO_4 anhydrous, filtered and concentrated under reduced pressure to give a rusty brown oil. The residue was dissolved in DCM and purified by flash chromatography using 10% EtOAc:hexanes as the eluent to afford **S3** as a colorless oil (542 mg, 1.43 mmol, 70%). **R_f:** 0.55 (30% EtOAc:hexanes); **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.46-7.31 (m, 5H, **C-H**$_{aryl}$), 5.28-5.15 (m, 2H, **CH$_2$**$_{benzylic}$), 2.66 (tt, *J* = 7.0, 3.9 Hz, 1H, N-**CH**$_{cyclopropyl}$), 2.36-1.98 (m, 4H, **C-H**$_{cyclohexene}$), 1.60-1.45 (m, 4H, **C-H**$_{cyclohexene}$), 1.01-0.85 (m, 2H, CH_2-**CH$_2$**$_{cyclopropyl}$), 0.77-0.67 (m, 2H, CH_2-**CH$_2$**$_{cyclopropyl}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 172.5, 154.5, 136.1, 135.11, 128.8, 128.6, 118.2, 68.9, 35.5, 29.1, 27.5, 23.9, 21.1, 9.0, 8.5; **FTIR** (cm^{-1}) (neat): 3032, 2937, 1736, 1682, 1272, 1232,

1185, 728, 696; **HRMS** (ESI, Pos) calc. for $C_{18}H_{21}[^{79}Br]NO_3$ $(M+H)^+$: 378.06993 found: 378.07077 *m/z*, calc. for $C_{18}H_{21}[^{81}Br]NO_3$ $(M+H)^+$: 380.06789found: 380.06896*m/z.*

General Procedures for the Pd-catalyzed cyclization under batch conditions

Procedure A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with 2-cycloalkenyl bromide (0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) or DMF (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further rinsed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product that was then purified by flash chromatography over silica gel using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give products **2a-4r.**

Procedure B: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with 2-cycloalkenyl bromide (0.20 mmol) and pivalic acid (30 mol%, 0.06 mmol, 6.1 mg) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol), tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) and K_2CO_3 (41.5 mg, 0.30 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) or DMF (2.00 mL) was then added and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further rinsed with EtOAc (10 mL). The filtrate was concentrated under reduced pressure to yield the crude product that was then purified by flash chromatography over silica gel using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give products **2a-4r.**

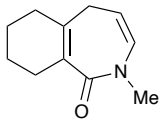
Procedure C: A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (51.6 mg, 0.20 mmol) and taken into a glovebox. $Pd(OAc)_2$ (2.27 mg, 0.010 mmol) and tBu$_3$P•HBF$_4$ (5.78 mg, 0.020 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. Xylenes (2.00 mL) or DMF (2.00 mL) was then added followed by DIPEA (0.053 mL, 0.30 mmol) and the reaction was heated to 110 °C for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (5 mL), filtered over a cotton-Celite® plug that was further rinsed with EtOAc (10 mL). The filtrate was concentrated under

reduced pressure to yield the crude product that was then purified by flash chromatography over silica gel using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give products **2a-4r.**

Procedure for the 0.6 mmol scale under continuous flow conditions (feed tank).

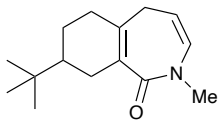
A 5.0-mL microwave vial containing an oven-dried magnetic stir bar was charged with **1aa** (154.8 mg, 0.6 mmol) and taken into a glovebox. $Pd(OAc)_2$ (13.6 mg, 0.060 mmol) and tBu$_3$P•HBF$_4$ (34.7 mg, 0.120 mmol) were then sequentially added to the vial that was then crimp-sealed and taken out of the glovebox. A 3:1 (v/v) mixture of xylenes and DMF (6.00 mL) was then added followed by DIPEA (468 μL, 2.7 mmol). The reaction mixture was stirred at room temperature until the solution became homogeneous (ca. 5 min). A color change was observed going from colorless to orange then to light yellow. Using the afore mentioned set-up for homogeneous conditions, the reaction mixture was pumped (flow rate = 0.125 mL/min) through the 5 mL stainless steel reactor (bottle reagent) that was pre-heated to 150 °C (residence time = 40 min). The volume corresponding to the reaction mixture was collected in a flask (15 mL) and the mixture was concentrated under reduced pressure. The resulting solid was dissolved with a mixture of water:EtOAc (1:1, 10 mL) and transferred into a separatory funnel. The layer were separated and the aqueous layer was washed with EtOAc (2x5 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude product. Flash chromatography over silica gel using a solvent gradient of 10% to 50% ethyl acetate/hexanes afforded product **2a** as a brownish oil (90 mg, 85%).

Characterization data for compounds 2a-4r.



2a

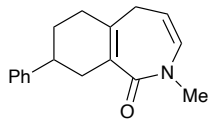
2-Methyl-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepin-1-one (2a). The title compound **2a** was prepared by the general procedure **A** using xylenes as the solvent on a 0.200 mmol scale (51.6 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **2a** as a golden oil (31.5 mg, 0.178 mmol, 89%). Reaction was also run on a 2.0 mmol (516 mg) scale to give **2a** in 91% (0.324 g, 1.82 mmol) using general procedure **A**. The reaction was conducted in flow chemistry using general procedure **D** on a 2.0 mmol (516 mg) scale to yield 74% of **2a** (0.264 g, 1.48 mmol), reaction performed twice. **R_f:** 0.29 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.89 (d, *J* = 7.4 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.39 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 3.14 (s, 3H, N-**CH_3**), 2.49 (dd, *J* = 7.2, 0.6 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.36-2.29 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.24-2.16 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.64-1.55 (m, 4H, CH_2-**CH_2-CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.9, 147.2, 130.9, 127.7, 115.7, 36.0, 31.8, 30.9, 26.5, 22.6, 22.2; **FTIR** (cm^{-1}) (neat):2929, 2858, 1660, 1604, 1431, 1343, 1244, 1040, 775, 718; **HRMS** (ESI, Pos) calc. for $C_{11}H_{15}NO$ $(M+H)^+$: 178.12264 found: 178.12251 *m/z*.



2b

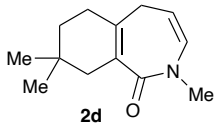
8-(*tert*-Butyl)-2-methyl-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepin-1-one (2b). The title compound **2b** was prepared by the general procedure **B** using xylenes as the solvent on a 0.200 mmol scale (62.9 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **2b** as a white solid (44.5 mg, 0.190 mmol, 95%). **mp:** 70-73°C; **R_f**: 0.33 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.94 (d, *J* = 7.4 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.43 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 3.19 (s, 3H, N-**CH_3**), 2.62-2.53 (m, 1H, C-$H_{cyclohexene/azepinone}$), 2.51-2.37 (m, 2H, C-$H_{cyclohexene/azepinone}$), 2.36-2.17 (m, 2H, C-$H_{cyclohexene/azepinone}$), 2.09-1.97 (m, 1H, C-$H_{cyclohexene/azepinone}$), 1.27-1.09 (m, 1H, C-$H_{cyclohexene/azepinone}$), 0.87 (s, 9H, **$(CH_3)_3$**-C); **^{13}C NMR**

($CDCl_3$, 101 MHz): δ 171.1, 146.9, 131.1, 128.1, 115.7, 44.0, 36.2, 33.5, 32.4, 30.5, 28.3, 27.4, 24.1; **FTIR** (cm^{-1}) (neat): 2972, 2948, 1661, 1600, 1427, 1269, 1053, 1032, 1010, 752; **HRMS** (ESI, Pos) calc. for $C_{15}H_{24}NO$ $(M+H)^+$: 234.18524 found: 234.18537 *m/z.*



2c

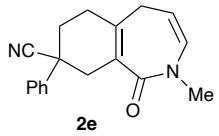
2-Methyl-8-phenyl-2,5,6,7,8,9-hexahydro-1H-benzo[c]azepin-1-one (2c). The title compound **2c** was prepared by the general procedure **A** using xylenes as the solvent on a 0.200 mmol scale (66.9 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **2c** as an orange oil (50.6 mg, 0.200 mmol, 100%). **mp:** 76-80 °C; **R_f**: 0.20 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.33-7.15 (m, 5H, C-**H_{aryl}**), 5.98 (d, *J* = 7.4 Hz, 1H, N-C(-**H**)=C(-H)-CH_2), 5.45 (q, *J* = 7.4 Hz, 1H, N-C(-H)=C(-**H**)-CH_2), 3.21 (s, 3H, N-**CH_3**), 2.81-2.68 (m, 2H, C-$H_{cyclohexene/azepinone}$), 2.66-2.58 (m, 1H, C-$H_{cyclohexene/azepinone}$), 2.54-2.38 (m, 3H, C-$H_{cyclohexene/azepinone}$), 2.35-2.30 (m, 1H, C-$H_{cyclohexene/azepinone}$), 1.99-1.91 (m, 1H, C-$H_{cyclohexene/azepinone}$), 1.81-1.71 (m, 1H, C-$H_{cyclohexene/azepinone}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.5, 146.8, 146.2, 131.2, 128.5, 127.7, 127.0, 126.2, 115.6, 39.7, 36.2, 34.3, 32.6, 30.6, 29.8; **FTIR** (cm^{-1}) (neat): 3008, 2974, 2965, 1653, 1593, 1372, 1255, 1055, 702; **HRMS** (ESI, Pos) calc. for $C_{17}H_{20}NO$ $(M+H)^+$: 254.15394 found: 254.15414 *m/z.*



2d

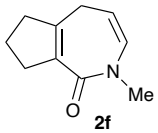
2,8,8-Trimethyl-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepin-1-one (2d). The title compound **2d** was prepared by the general procedure **A** using xylenes as the solvent on a 0.200 mmol scale (57.2 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give **2d** an orange oil (35.0 mg, 0.170 mmol, 85%). **R_f**: 0.35 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.90 (d, *J* = 7.4 Hz, 1H, N-C(-**H**)=C(-H)-CH_2), 5.42 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(-**H**)-CH_2), 3.16 (s, 3H, N-**CH_3**), 2.51 (d, *J* = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.23 (td, *J* = 6.5, 2.2 Hz, 2H, **CH_2**-CH_2-$C(CH_3)_2$-$CH_{2Cyclohexene}$), 2.13 (br s, 2H, CH_2-CH_2-$C(CH_3)_2$-**CH_2**$_{Cyclohexene}$ 1.38 (t, *J* = 6.5 Hz, 2H, CH_2-**CH_2**-$C(CH_3)_2$-$CH_{2Cyclohexene}$), 0.90 (s, 6H, CH_2-CH_2-C(**CH_3**$)_2$-

$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 171.0, 145.8, 131.1, 126.8, 115.7, 40.2, 36.2, 35.4, 30.6, 30.0, 28.7, 27.9; **FTIR** (cm^{-1}) (neat): 2950, 2922, 1719, 1659, 1607, 1273, 1263, 1050, 1012, 691; **HRMS** (ESI, Pos) calc. for $C_{13}H_{20}NO$ $(M+H)^+$: 206.15394 found: 206.15419 *m/z.*



2e

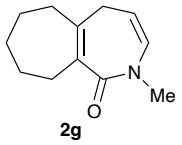
2-Methyl-1-oxo-8-phenyl-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepine-8-carbonitrile (2e). The title compound **2e** was prepared by the general procedure **A** using xylenes as the solvent on a 0.200 mmol scale (71.9 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give a yellow oil in 95% yield (53.0 mg, 0.190 mmol). **R_f:** 0.18 (30% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.51-7.45 (m, 2H, C-**H**$_{aryl}$), 7.42-7.35 (m, 2H, C-**H**$_{aryl}$), 7.34-7.29 (m, 1H, C-**H**$_{aryl}$), 5.97 (dd, *J* = 7.4, 1.0 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.48 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 3.18 (s, 3H, N-**CH_3**), 3.03-2.68 (m, 4H, C-$H_{cyclohexene/azepinone}$), 2.56-2.47 (m, 1H, C-$H_{cyclohexene/azepinone}$), 2.43-2.33 (m, 1H, C-$H_{cyclohexene/azepinone}$), 2.26-2.18 (m, 1H, C-$H_{cyclohexene/azepinone}$), 2.15-2.03 (m. 1H, C-$H_{cyclohexene/azepinone}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.3, 146.6, 139.6, 131.3, 129.4, 129.1, 128.3, 125.9, 125.8, 125.0, 122.4, 115.5, 40.9, 38.1, 36.2, 32.7, 30.4, 30.1; **FTIR** (cm^{-1}) (neat): 3058, 2957, 2938, 2234, 1747, 1661, 1600, 1496, 1388, 1263, 1052, 697; **HRMS** (ESI, Pos) calc. for C18H19N2O $(M+H)^+$: 279.14919 found: 279.14913 *m/z.*



2f

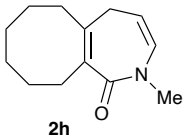
2-Methyl-3,6,7,8-tetrahydrocyclopenta[*c*]azepin-1(2*H*)-one (2f). The title compound **2f** was prepared by the general procedure **B** using xylenes as the solvent on a 0.200 mmol scale (48.8 mg) and then purified by flash chromatography (40% Et_2O in pentane to give an orange oil in 65% yield (21.3 mg, 0.130 mmol). **R_f:** 0.15 (20% Et_2O in Hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.86 (d, *J* = 8.3 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.13 (dt, *J* = 8.3, 6.3 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 3.14 (s, 3H, N-**CH_3**), 2.76-2.67 (m, 4H, C=C-**CH_2**-C(-H)=C and **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.54 (t, *J* = 7.6 Hz, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.85 (quint, *J* = 7.6 Hz, 4H, CH_2-**CH_2**-$CH_{2Cyclopentene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 166.9, 153.3, 132.8, 131.5, 39.4, 36.4, 34.4, 26.2,

21.8; **FTIR** (cm^{-1}) (neat): 2953, 2853, 2220, 1721, 1651, 1602, 1538, 1437, 1408, 1305, 727; **HRMS** (ESI, Pos) calc. for $C_{10}H_{14}NO$ $(M+H)^+$: 164.10699 found: 164.10709 *m/z.*



2g

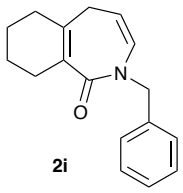
2-Methyl-3,6,7,8,9,10-hexahydrocyclohepta[*c*]azepin-1(2*H*)-one (2g). The title compound **2g** was prepared by the general procedure **B** using xylenes as the solvent on a 0.200 mmol scale (54.4 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give an pale yellow oil in 69% yield (24.6 mg, 0.138 mmol). $\mathbf{R_f}$: 0.29 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.92 (d, *J* = 7.2 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.48 (q, *J* = 7.3 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 3.16 (s, 3H, N-**CH_3**), 2.56 (d, *J* = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.48-2.43 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.41-2.36 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.77-1.69 (m, 2H, CH_2-**CH_2**-$CH_{2Cycloheptene}$), 1.56-1.46 (m, 4H, **CH_2**-CH_2-**$CH_{2Cycloheptene}$**); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 171.7, 153.0, 133.4, 131.0, 116.5, 37.8, 36.0, 33.5, 32.3, 30.8, 26.9, 26.2; **FTIR** (cm^{-1}) (neat): 2924, 2853, 1707, 1644, 1590, 1443, 1388, 1268, 1164, 1047, 969, 728; HRMS (ESI, Pos) calc. for $C_{12}H_{18}NO$ $(M+H)^+$: 192.13830 found: 192.13830 *m/z.*



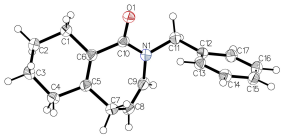
2h

(*Z*)-2-Methyl-2,3,6,7,8,9,10,11-octahydro-1*H*-cycloocta[*c*]azepin-1-one (2h). The title compound **2h** was prepared by the general procedure **C** using xylenes as the solvent on a 0.200 mmol scale (57.2 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give an orange oil in 67% yield (27.6 mg, 0.134 mmol). $\mathbf{R_f}$: 0.29 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.96 (d, *J* = 7.2 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.47 (q, *J* = 7.3 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 3.18 (s, 3H, N-**CH_3**), 2.54 (d, *J* = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.45-2.41 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.35-2.31 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.66-1.57 (m, 4H, CH_2-**CH_2-CH_2**-$CH_{2Cyclooctene}$), 1.50-1.41 (m, 4H, **CH_2**-CH_2-CH_2-**$CH_{2Cyclooctene}$**); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 171.4, 149.2, 131.1, 130.5, 116.0, 36.2, 34.2, 31.2, 30.9, 29.8, 28.6, 26.8, 26.4; **FTIR** (cm^{-1}) (neat): 2921, 2848, 1655, 1645, 1604, 1364, 1058, 711; **HRMS** (ESI, Pos)

calc. for $C_{13}H_{20}NO$ $(M+H)^+$: 206.15394 found: 206.15291 *m/z*.

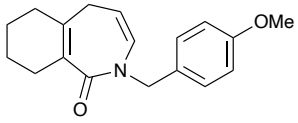


2i



CCDC 2104750

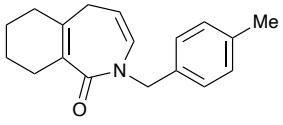
2-Benzyl-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepin-1-one (2i,). The title compound **2i** was prepared by the general procedure **A** using xylenes as the solvent on a 0.200 mmol scale (66.9 mg) and then purified by flash chromatography (0%-20% EtOAc:hexanes) to give a white solid in 90% yield (45.5 mg, 0.179 mmol). **mp:** 68-71 °C; **R_f**: 0.43 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.32-722 (m, 5H, Ar-**H**), 5.94 (d, *J* = 7.4 Hz, 1H, N-C(-**H**)=C(-H)-CH_2), 5.46 (q, *J* = 7.3 Hz, 1H, N-C(-H)=C(-**H**)-CH_2), 4.82 (s, 2H, N-**CH_2**-Ph), 2.48 (d, *J* = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.42-2.34 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.25-2.16 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.61 (quint, *J* = 3.1 Hz, 4H, CH_2-**CH_2-CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.7, 147.4, 138.1, 130.14, 128.6, 128.0, 127.9, 127.4, 116.9, 51.5, 32.0, 31.2, 26.8, 22.8, 22.4; **FTIR** (cm^{-1}) (neat): 3033, 2930, 2900, 1662, 1601, 1494, 746; **HRMS** (ESI, Pos) calc. for $C_{17}H_{20}NO$ $(M+H)^+$: 254.15394, found: 254.15438.



2j

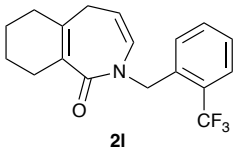
2-(4-Methoxybenzyl)-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepin-1-one (2j). The title compound **2j** was prepared by the general procedure **A** using DMF as the solvent on a 0.200 mmol scale (72.9 mg) and then purified by flash chromatography (0-20% EtOAc:hexanes) to give a pale yellow oil in 95% yield (54.0 mg, 0.190 mmol). **R_f**: 0.51 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.25-7.20 (m, 2H, **C-H**$_{Aryl,\ m\text{-}OMe}$), 6.85-6.80 (m, 2H,**C-H**$_{Aryl,\ o\text{-}OMe}$), 5.93 (d, *J* = 7.4 Hz, 1H, N-C(-**H**)=C(-H)-CH_2), 5.44 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(-**H**)-CH_2), 4.74 (s, 2H, N-**CH_2**-Ph) 3.77 (s, 3H, -O-**CH_3**), 2.45 (d, *J* = 7.1 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.39-2.33 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.22-2.15 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.60 (quint, *J* = 3.1, 4H, CH_2-**CH_2-CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.6, 159.0, 147.3,

130.36, 130.03, 129.32, 128.0, 116.9, 114.0, 55.4, 50.9, 31.9, 31.2, 26.8, 22.7, 22.3; **FTIR** (cm^{-1}) (neat): 3050, 3005, 2997, 2931, 2858, 1659, 1605, 1510, 1402, 1300, 1241, 1033, 970, 726; **HRMS** (ESI, Pos) calc. for $C_{18}H_{22}NO_2$ $(M+H)^+$: 284.16451 found: 284.16574 *m/z.*



2k

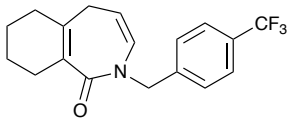
2-(4-Methylbenzyl)-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepin-1-one (2k). The title compound **2k** was prepared by the general procedure **A** using DMF as the solvent on a 0.200 mmol scale (69.7 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give a pale yellow oil in 95% yield (50.7 mg, 0.190 mmol). $\mathbf{R_f}$: 0.50 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.18 (d, *J* = 8.0 Hz, 2H, **C-H**$_{Aryl,\ m\text{-}Me}$), 7.10 (d, *J* = 7.8 Hz, 2H, **C-H**$_{Aryl,\ o\text{-}Me}$), 5.93 (d, *J* = 7.4, 1H, N-C(**-H**)=C(-H)-CH_2), 5.44 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 4.77 (s, 2H, N-**CH_2**-Ar), 2.47 (d, *J* = 7.0 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.40-2.34 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.31 (s, 3H, Ar-**CH_3**), 2.23-2.17 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.60 (quint, *J* = 3.1 Hz, 4H, CH_2-**CH_2**-**CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.7, 147.3, 137.0, 135.2, 130.1, 129.3, 128.0, 127.9, 116.9, 51.2, 32.0, 31.2, 26.8, 22.8, 22.4, 21.2; **FTIR** (cm^{-1}) (neat): 3004, 2924, 1659, 1606, 1514, 1211, 1180, 703; **HRMS** (ESI, Pos) calc. for $C_{18}H_{22}NO$ $(M+H)^+$: 268.16959 found: 268.16927 *m/z.*



2l

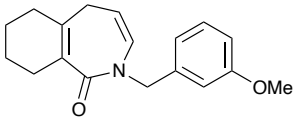
2-(2-(Trifluoromethyl)benzyl)-2,3,6,7,8,9-hexahydro-1H-benzo[c]azepin-1-one (2l). The title compound **2l** was prepared by the general procedure **A** using DMF as the solvent on a 0.200 mmol scale (80.5 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give an yellow pale oil in 89% yield (57.4 mg, 0.178 mmol). $\mathbf{R_f}$**:** 0.34 (30% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.64 (d, *J* = 7.7 Hz, 1H, **C-H**$_{Aryl,\ o\text{-}CF3}$), 7.48 (t, *J* = 7.5 Hz, 1H, **C-H**$_{Aryl,\ m\text{-}CF3}$), 7.36-7.31 (m, 2H, **C-H**$_{Aryl}$), 5.88 (d, *J* = 7.4 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.48 (q, *J* = 7.3 Hz ,1H, N-C(-H)=C(**-H**)-CH_2), 5.07 (s, 2H, N-**CH_2**-Ar), 2.59 (d, *J* = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.43-2.36 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.28-2.22 (m, 2H, CH_2-C(-CH_2)=C(-

C=O)-**CH₂**), 1.64 (qt, *J* = 3.2 Hz, 4H, CH_2-**CH_2-CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 171.0, 147.8, 136.5, 132.3, 130.1, 128.1 (q, *J* = 30.7 Hz), 128.0, 127.9, 127.1, 126.0 (q, 6.1 Hz), 124.5 (q, 274.0 Hz), 117.1, 47.8, (q, *J* = 3.2 Hz), 32.1, 31.3, 26.9, 22.7, 22.3; **^{19}F NMR** ($CDCl_3$, 400 MHz): δ -59.81; **FTIR** (cm^{-1}) (neat): 3051, 2933, 2860, 1660, 1609, 1457, 1311, 1157, 1109, 1035, 764, 717; **HRMS** (ESI, Pos) calc. for $C_{18}H_{19}F_3NO$ $(M+H)^+$: 322.14133 found: 322.14160 *m/z*.



2m

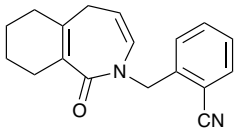
2-(4-(Trifluoromethyl)benzyl)-2,3,6,7,8,9-hexahydro-1*H*-benzo[*c*]azepin-1-one (2m). The title compound **2m** was prepared by the general procedure **A** using xylenes as the solvent on a 0.200 mmol scale (80.5 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give a pale light oil in 96% yield (61.6 mg, 0.192 mmol). **R_f**: 0.44 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.55 (d, *J* = 8.0 Hz, 2H, **C-H**$_{Aryl,\ o\text{-}CF3}$), 7.39 (d, *J* = 8.0 Hz, 2H, **C-H**$_{Aryl,\ m\text{-}CF3}$), 5.94 (d, *J* = 7.4 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.49 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 4.84 (s, 2H, N-**CH_2**-Ar), 2.49 (d, *J* = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.39-2.31 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.25-2.17 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.60 (quint, *J* = 3.13 Hz, 4H, CH_2-**CH_2-CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.6, 147.8, 142.2, 130.0, 129.6 (q, *J* = 33.3 Hz), 128.0, 127.9, 125.6 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 272.0 Hz), 117.3, 51.3, 32.0, 31.2, 26.8, 22.7, 22.3; **^{19}F NMR** ($CDCl_3$, 400 MHz): δ -62.50; **FTIR** (cm^{-1}) (neat): 3053, 2933, 2861, 1660, 1608, 1321, 1117, 1104, 1064, 1017, 715; **HRMS** (ESI, Pos) calc. for $C_{18}H_{19}F_3NO$ $(M+H)^+$: 322.14133 found: 322.13994 *m/z*.



2n

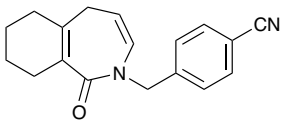
2-(3-Methoxybenzyl)-2,3,6,7,8,9-hexahydro-1H-benzo[c]azepin-1-one (2n). The title compound **2n** was prepared by the general procedure **A** using DMF as solvent on a 0.200 mmol scale (72.9 mg) and then purified by flash chromatography (30% EtOAc:hexanes) to give a yellow pale oil in 93% yield (52.5 mg, 0.186 mmol). **R_f**: 0.37 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.21 (t, *J* = 7.9 Hz, 2H, **C-H**$_{Aryl,\ m\text{-}OMe}$), 6.86 (d, *J* = 7.6 Hz, 2H, **C-H**$_{Aryl,\ p\text{-}OMe}$), 6.83

(br s, 1H, **C-H**$_{\text{Aryl, }o\text{-OMe and }o\text{-CH2}}$), 6.78 (dd, J = 8.3, 2.5 Hz, 1H, **C-H**$_{\text{Aryl, }o\text{-OMe}}$), 5.94 (d, J = 7.4 Hz, 1H, N-C(-**H**)=C(-H)-CH_2), 5.46 (q, J = 7.2 Hz ,1H, N-C(-H)=C(-**H**)-CH_2), 4.80 (s, 2H, N-**CH_2**-Ar), 3.78 (s, 3H, O-**CH_3**), 2.50 (d, J = 7.1 Hz, 1H, C=C-**CH_2**-C(-H)=C), 2.40-2.33 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.23-2.17 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.63-1.58 (m. 4H, CH_2-**CH_2**-**CH_2**-$CH_{2\text{Cyclohexene}}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.7, 159.9, 147.4, 139.7, 130.2, 129.6, 128.0, 120.2, 116.9, 113.3, 113.0, 55.3, 51.4, 32.0, 31.2, 26.8, 22.8, 22.4; **FTIR** (cm^{-1}) (neat): 3012, 2994, 2918, 1656, 1256, 1148, 1046, 751, 729; **HRMS** (ESI, Pos) calc. for $C_{18}H_{22}NO_2$ $(M+H)^+$: 284.16451 found: 284.16452 *m/z.*



2o

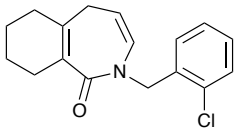
2-((1-Oxo-1,3,6,7,8,9-hexahydro-2*H*-benzo[*c*]azepin-2-yl)methyl)benzonitrile (2o). The title compound **2o** was prepared by the general procedure **A** using DMF as the solvent on a 0.200 mmol scale (71.9 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give a colorless oil in 86 % yield (48.0 mg, 0.172 mmol). **R_f**: 0.28 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.63 (dd, J = 7.6, 1.0 Hz, 1H, **C-H**$_{\text{Aryl, }o\text{-CN}}$), 7.54 (td, J = 7.6, 1.3 Hz, 1H, **C-H**$_{\text{Aryl, }p\text{-CN}}$), 7.48 (br d, J = 7.6 Hz, 1H, **C-H**$_{\text{Aryl, o-CH}}$), 7.35 (td, J = 7.6, 1.2 Hz, 1H, **C-H**$_{\text{Aryl, }m\text{-CN}}$), 6.00 (d, J = 7.4 Hz, 1H, N-C(-**H**)=C(-H)-CH_2), 5.51 (q, J = 7.2 Hz, 1H, N-C(-H)=C(-**H**)-CH_2), 5.04 (s, 2H, N-**CH_2**-Ar), 2.51 (d. J = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.42-2.34 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.26-2.16 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**) 1.61 (quint, J = 3.1 Hz, 4H, CH_2-**CH_2**-**CH_2**-$CH_{2\text{Cyclohexene}}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.7, 148.1, 141.8, 133.3, 132.9, 130.0, 128.8, 127.9, 127.8, 117.7, 117.6, 111.9, 49.7, 32.1, 31.2, 26.8, 22.7, 22.3; **FTIR** (cm^{-1}) (neat):3052, 2932, 2858, 2224, 1660, 1609, 1485, 1281, 1257, 759, 726, 705; **HRMS** (ESI, Pos) calc. for $C_{18}H_{19}N_2O$ $(M+H)^+$: 279.14919 found: 279.14958 *m/z.*



2p

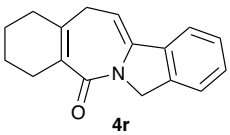
4-((1-Oxo-1,3,6,7,8,9-hexahydro-2*H*-benzo[*c*]azepin-2-yl)methyl)benzonitrile (2p). The title compound **2p** was prepared by the general procedure **A** using xylenes as the solvent on a 0.200 mmol scale (71.9 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes)

to give a light yellow oil in 99% yield (55.0 mg, 0.198mmol). **R_f**: 0.19 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.59 (d, *J* = 8.2 Hz, 2H, **C-H**$_{Aryl,\ o\text{-}CN}$), 7.39 (d, *J* = 8.2 Hz, 2H, **C-H**$_{Aryl,\ m\text{-}CN}$), 5.94 (d, *J* = 7.4 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.50 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 4.83 (s, 2H, N-**CH_2**-Ar), 2.50 (d, *J* = 7.2 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.39-2.30 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.26-2.18 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.61 (quint, *J* = 3.0 Hz, 4H, CH_2-**CH_2**-**CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 170.6, 148.1, 143.7, 132.5, 130.0, 128.4, 127.8, 118.9, 117.5, 111.3, 51.6, 32.1, 31.2, 26.7, 22.7, 22.3; **FTIR** (cm^{-1}) (neat): 3052, 2930, 2857, 2227, 1659, 1605, 1400, 1210, 1163, 724, 547; **HRMS** (ESI, Pos) calc. for $C_{18}H_{19}N_2O$ $(M+H)^+$: 279.14919 found: 279.14907 *m/z.*



2o

2-(2-Chlorobenzyl)-2,3,6,7,8,9-hexahydro-1H-benzo[c]azepin-1-one (2q). The title compound **2q** was prepared by the general procedure **A** using DMF as the solvent on a 0.200 mmol scale (73.7 mg) and then purified by Preparative TLC using 30% EtOAc:hexanes to give a colorless oil in 80% yield (60.0 mg, 0.160 mmol). **R_f**: 0.22; **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.37-32 (m, 1H, **C-H**$_{Aryl\ o\text{-}Cl}$), 7.28-7.15 (m, 3H, **C-H**$_{Aryl\ m,p\text{-}Cl}$), 5.93 (d, *J* = 7.4 Hz, 1H, N-C(**-H**)=C(-H)-CH_2), 5.46 (q, *J* = 7.2 Hz, 1H, N-C(-H)=C(**-H**)-CH_2), 4.96 (s, 2H, N-**CH_2**-Ar), 2.56 (d, *J* = 7.1 Hz, 2H, C=C-**CH_2**-C(-H)=C), 2.41-2.36 (m, 2H, **CH_2**-C(-CH_2)=C(-C=O)-CH_2), 2.26-2.20 (m, 2H, CH_2-C(-CH_2)=C(-C=O)-**CH_2**), 1.68-1.57 (m. 4H, CH_2-**CH_2**-**CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ170.8, 147.8, 135.2, 133.5, 130.3, 129.6, 129.0, 128.6, 128.0, 127.1, 116.9, 49.2, 32.1, 31.3, 26.9, 22.8, 22.3; **FTIR** (cm^{-1}) (neat): 3058, 2929, 2856, 1659, 1609, 1573, 1471, 1440, 1401, 1281, 1007, 747, 730, 443; **HRMS** (ESI, Pos) calc. for $C_{17}H_{19}{}^{[35}Cl]NO$ $(M+H)^+$: 288.11497 found: 288.11551 *m/z*, calc. for $C_{17}H_{19}{}^{[37}Cl]NO$ $(M+H)^+$: 290.11202 found: 290.11295 *m/z.*



4r

1,2,3,4,7,13-Hexahydro-5H-benzo[5,6]azepino[2,1-a]isoindol-5-one (4r). The title compound **4r** was prepared by the general procedure **A** using DMF as the solvent on a 0.200 mmol scale (82.6 mg) and then purified by flash chromatography (0-30% EtOAc:hexanes) to give an

orange oil in 70% yield (35.8 mg, 0.140 mmol). **R_f**: 0.25 (20% EtOAc:hexanes); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.38-7.33 (m, 1H, **C-H**$_{Aryl}$), 7.25-7.18 (m, 2H, **C-H**$_{Aryl}$), 7.17-7.13 (m, 1H, **C-H**$_{Aryl}$), 5.48 (t, *J* = 6.5, 1H, **C-H**$_{alkene}$), 4.91 (s, 2H, N-**CH_2**-Ar), 3.68 (d, *J* = 6.5, 2H, C=C-**CH_2**-C(-H)=C), 2.31-2.23 (m, 4H, **CH_2**-C(-CH_2)=C(-C=O)-**CH_2**), 1.73-1.64 (m, 4H, CH_2-**CH_2**-**CH_2**-$CH_{2Cyclohexene}$); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.3, 142.2, 140.7, 140.4, 135.7, 129.8, 129.4, 128.6, 128.3, 127.4, 106.0, 43.7, 31.4, 22.2, 20.7, 20.3; **FTIR** (cm^{-1}) (neat): 3064, 3025, 2930, 2857, 2243, 1677, 1654, 1401, 1129, 1060, 968, 728; **HRMS** (ESI, Pos) calc. for $C_{17}H_{18}NO$ $(M+H)^+$: 252.13829 found: 252.13878 *m/z.*

References:

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X-Ray Data

Crystal properties for 1aa (CCDC 2104571)

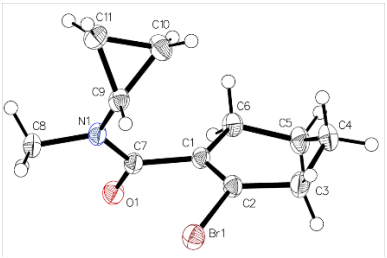


Table 1 Crystal data and structure refinement for CHA233.

Identification code	CHA233
Empirical formula	$C_{11}H_{16}BrNO$
Formula weight	258.16
Temperature/K	120
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.6041(4)
b/Å	9.5540(3)
c/Å	11.2772(4)
α/°	90
β/°	99.1440(10)
γ/°	90
Volume/Å^3	1127.99(7)
Z	4
ρ_{calc}g/cm^3	1.520
μ/mm^{-1}	3.114
F(000)	528.0
Crystal size/mm^3	0.17 × 0.12 × 0.05
Radiation	GaKα (λ = 1.34139)
2Θ range for data collection/°	7.346 to 146.936
Index ranges	$-15 \le h \le 15$, $-13 \le k \le 12$, $-15 \le l \le 16$
Reflections collected	27326
Independent reflections	3440 [R_{int} = 0.0425, R_{sigma} = 0.0264]
Data/restraints/parameters	3440/0/128
Goodness-of-fit on F^2	1.096
Final R indexes [I>=2σ (I)]	R_1 = 0.0284, wR_2 = 0.0739
Final R indexes [all data]	R_1 = 0.0304, wR_2 = 0.0751
Largest diff. peak/hole / e Å^{-3}	0.47/-0.41

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for CHA233. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Br1	4692.0(2)	6927.6(2)	5092.2(2)	29.16(7)
O1	1049.6(11)	6660.9(11)	3881.0(9)	26.6(2)
N1	1896.5(11)	5196.0(11)	5384.3(11)	22.5(2)
C1	2249.7(13)	7736.7(13)	5575.6(11)	20.7(2)
C2	3481.9(14)	8074.8(13)	5738.5(13)	22.5(2)
C3	4068.3(15)	9347.6(16)	6375.3(15)	29.6(3)
C4	3109.6(16)	10119.4(16)	7016.0(15)	31.3(3)
C5	1818.1(16)	10206.8(15)	6203.9(14)	29.6(3)
C6	1273.7(14)	8740.8(14)	5940.2(13)	24.8(3)
C7	1699.3(13)	6478.6(13)	4877.8(12)	20.9(2)
C8	1503.2(15)	3959.0(14)	4653.4(14)	27.5(3)
C9	2664.8(14)	4936.6(13)	6537.1(13)	24.5(2)
C10	2346.7(19)	5600.1(16)	7650.8(14)	33.5(3)
C11	2107.6(17)	4061.1(16)	7435.8(14)	30.5(3)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for CHA233. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	25.40(9)	25.21(9)	37.73(10)	−3.91(5)	7.70(6)	1.31(5)
O1	30.3(5)	25.0(4)	23.0(4)	1.2(4)	−0.6(4)	−3.1(4)
N1	27.1(5)	15.8(4)	23.7(5)	−1.5(4)	2.0(4)	−1.8(4)
C1	25.9(6)	14.8(5)	20.8(5)	0.3(4)	1.6(4)	0.4(4)
C2	25.6(6)	17.4(5)	24.4(6)	−1.3(4)	3.8(5)	0.9(4)
C3	29.6(7)	24.0(6)	34.8(7)	−6.3(5)	4.1(6)	−6.3(5)
C4	37.0(7)	23.2(6)	33.0(7)	−7.6(5)	2.9(6)	−1.0(6)
C5	37.7(7)	17.3(5)	32.6(7)	−2.7(5)	1.7(6)	4.3(5)
C6	26.4(6)	19.1(5)	28.4(6)	−0.6(5)	3.1(5)	3.6(5)
C7	21.4(5)	18.0(5)	23.5(5)	−1.2(4)	3.8(4)	−0.9(4)
C8	32.4(7)	19.2(6)	31.3(7)	−5.8(5)	6.3(5)	−5.1(5)
C9	28.6(6)	18.5(5)	25.5(6)	2.2(4)	1.4(5)	1.5(5)
C10	52.4(10)	22.3(6)	24.4(6)	0.4(5)	1.7(6)	6.5(6)
C11	38.3(8)	22.2(6)	30.9(7)	6.0(5)	5.4(6)	1.3(5)

Table 4 Bond Lengths for CHA233.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Br1	C2	1.9174(14)	C2	C3	1.4965(19)
O1	C7	1.2339(17)	C3	C4	1.527(2)
N1	C7	1.3542(17)	C4	C5	1.524(2)
N1	C8	1.4631(17)	C5	C6	1.5261(19)
N1	C9	1.4417(18)	C9	C10	1.492(2)
C1	C2	1.330(2)	C9	C11	1.505(2)
C1	C6	1.5151(19)	C10	C11	1.505(2)
C1	C7	1.5029(18)			

Table 5 Bond Angles for CHA233.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C7	N1	C8	118.83(12)	C4	C5	C6	110.04(12)
C7	N1	C9	124.28(11)	C1	C6	C5	112.36(12)
C9	N1	C8	116.03(11)	O1	C7	N1	122.58(12)
C2	C1	C6	120.48(12)	O1	C7	C1	118.58(12)
C2	C1	C7	123.90(12)	N1	C7	C1	118.80(11)
C7	C1	C6	115.04(11)	N1	C9	C10	120.99(12)
C1	C2	Br1	120.72(10)	N1	C9	C11	118.46(12)
C1	C2	C3	126.00(13)	C10	C9	C11	60.27(10)
C3	C2	Br1	113.25(11)	C9	C10	C11	60.29(10)
C2	C3	C4	111.24(13)	C10	C11	C9	59.44(10)
C5	C4	C3	110.14(12)				

Table 6 Torsion Angles for CHA233.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Br1	C2	C3	C4	−172.36(10)	C6	C1	C7	N1	−113.84(14)
N1	C9	C10	C11	107.29(15)	C7	N1	C9	C10	59.48(19)
N1	C9	C11	C10	−111.40(15)	C7	N1	C9	C11	130.07(14)
C1	C2	C3	C4	9.6(2)	C7	C1	C2	Br1	−0.93(19)
C2	C1	C6	C5	13.31(18)	C7	C1	C2	C3	176.99(13)
C2	C1	C7	O1	−107.47(16)	C7	C1	C6	C5	−158.29(12)
C2	C1	C7	N1	74.88(18)	C8	N1	C7	O1	10.1(2)
C2	C3	C4	C5	−43.59(17)	C8	N1	C7	C1	−172.36(12)

Table 6 Torsion Angles for CHA233.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C3	C4	C5	C6	63.49(17)	C8	N1	C9	C10	−131.35(14)
C4	C5	C6	C1	−47.28(17)	C8	N1	C9	C11	−60.77(17)
C6	C1	C2	Br1	−171.76(10)	C9	N1	C7	O1	178.98(13)
C6	C1	C2	C3	6.2(2)	C9	N1	C7	C1	−3.5(2)
C6	C1	C7	O1	63.80(17)					

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for CHA233.

Atom	*x*	*y*	*z*	U(eq)
H3A	4365.39	9970.91	5799.21	35
H3B	4800.66	9073.01	6957.46	35
H4A	3016.7	9628.67	7750.14	38
H4B	3420.88	11055.38	7228.48	38
H5A	1916.23	10667.02	5457.26	36
H5B	1232.77	10757.22	6593.04	36
H6A	973.43	8381.39	6649.89	30
H6B	546.93	8794.46	5299.99	30
H8A	955.37	4238.3	3931.2	41
H8B	1051.2	3328.47	5098.96	41
H8C	2244.89	3498.7	4450.53	41
H9	3577.63	4794.46	6523.58	29
H10A	1611.04	6216.26	7570.78	40
H10B	3049.61	5869.69	8267.5	40
H11A	1229.05	3752.98	7223.63	37
H11B	2668.44	3406.2	7920.75	37

Crystal properties for 2i (CCDC 2104570)

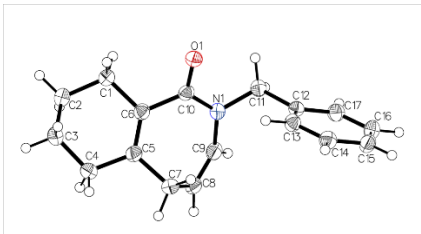


Table 1 Crystal data and structure refinement for lauvin2.

Identification code	lauvin2
Empirical formula	$C_{17}H_{19}NO$
Formula weight	253.33
Temperature/K	100
Crystal system	orthorhombic
Space group	$Pna2_1$
a/Å	9.1178(3)
b/Å	18.3487(7)
c/Å	8.0923(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1353.84(8)
Z	4
ρ_{calc}g/cm^3	1.243
μ/mm^{-1}	0.596
F(000)	544.0
Crystal size/mm^3	0.23 × 0.1 × 0.09
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	10.834 to 144.098
Index ranges	$-11 \le h \le 11$, $-21 \le k \le 18$, $-9 \le l \le 9$
Reflections collected	17932
Independent reflections	2599 [R_{int} = 0.0431, R_{sigma} = 0.0281]
Data/restraints/parameters	2599/1/173
Goodness-of-fit on F^2	1.048
Final R indexes [I>=2σ (I)]	R_1 = 0.0351, wR_2 = 0.0915
Final R indexes [all data]	R_1 = 0.0355, wR_2 = 0.0923
Largest diff. peak/hole / e Å^{-3}	0.18/-0.20
Flack parameter	0.1(3)

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for lauvin2. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	4945.8(14)	1745.3(7)	6668.0(17)	29.4(3)
N1	3926.8(16)	2767.7(9)	5605.8(18)	26.3(3)
C1	4331(2)	937.7(10)	3804(2)	29.8(4)
C2	4139(2)	630.2(11)	2069(3)	32.9(4)
C3	5410(2)	868.7(11)	967(3)	33.7(4)
C4	5461(2)	1694.4(11)	822(3)	34.1(4)
C5	5200(2)	2085.0(10)	2436(2)	27.6(4)
C6	4681(2)	1744.2(10)	3773(3)	26.8(4)
C7	5557(2)	2890.5(10)	2477(3)	31.8(4)
C8	4203(2)	3318.6(10)	2891(2)	30.9(4)
C9	3499(2)	3240.5(9)	4312(2)	30.0(4)
C10	4559.2(18)	2090.6(10)	5439(2)	25.3(4)
C11	3606(2)	3041.9(10)	7278(2)	29.2(4)
C12	4622.0(19)	3652.7(10)	7804(2)	25.7(4)
C13	6130.1(19)	3613.8(10)	7523(2)	29.3(4)
C14	7050(2)	4164.3(10)	8063(2)	31.8(4)
C15	6478(2)	4761.4(11)	8898(2)	33.6(4)
C16	4981(2)	4810.0(10)	9177(3)	35.2(5)
C17	4057(2)	4256.4(10)	8626(3)	31.4(4)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for lauvin2. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	34.4(6)	28.0(7)	25.7(7)	2.6(5)	−2.3(5)	−0.2(5)
N1	28.7(7)	25.0(8)	25.3(8)	−1.8(6)	−0.4(6)	−1.3(5)
C1	36.5(9)	24.9(10)	28.1(9)	−0.1(7)	−0.3(8)	−2.2(7)
C2	39.7(9)	26.9(9)	32.0(9)	−4.1(7)	−0.1(8)	−2.9(8)
C3	42.3(11)	30.8(10)	28.0(9)	−5.2(7)	2.1(8)	1.5(7)
C4	46.7(11)	30.2(11)	25.6(9)	1.3(7)	2.5(9)	1.0(7)
C5	30.8(8)	24.3(9)	27.8(9)	1.4(7)	−1.7(7)	1.0(6)
C6	29.5(8)	24.3(9)	26.7(9)	−0.3(7)	−2.3(7)	0.9(7)
C7	39.7(10)	27.0(10)	28.7(9)	3.3(7)	1.4(8)	−4.5(7)
C8	42.1(10)	21.4(9)	29.3(10)	2.6(7)	−6.0(8)	−1.2(7)
C9	33.1(9)	23.8(9)	33.0(10)	−1.8(7)	−6.0(8)	0.8(7)
C10	25.0(8)	23.5(9)	27.5(9)	1.0(7)	−1.2(7)	−4.9(6)
C11	32.1(8)	28.1(9)	27.4(9)	−2.6(7)	1.9(7)	−1.9(7)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for lauvin2. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C12	31.1(9)	23.5(9)	22.5(9)	0.8(6)	-0.5(6)	1.0(6)
C13	32.1(9)	26.5(9)	29.4(9)	-2.4(7)	-0.3(8)	4.5(7)
C14	31.5(9)	32.0(9)	31.9(9)	-1.0(7)	-3.3(8)	1.1(7)
C15	40.5(11)	25.7(10)	34.6(11)	-2.2(7)	-4.5(8)	-3.1(7)
C16	43.7(10)	26.1(10)	35.9(11)	-5.8(8)	3.0(8)	3.2(8)
C17	33.4(9)	29.6(9)	31.2(9)	-0.7(8)	3.5(8)	2.5(7)

Table 4 Bond Lengths for lauvin2.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C10	1.231(2)	C6	C10	1.495(3)
N1	C9	1.414(2)	C7	C8	1.501(3)
N1	C10	1.376(2)	C8	C9	1.325(3)
N1	C11	1.473(2)	C11	C12	1.515(2)
C1	C2	1.523(3)	C12	C13	1.396(2)
C1	C6	1.514(3)	C12	C17	1.391(3)
C2	C3	1.526(3)	C13	C14	1.384(3)
C3	C4	1.520(3)	C14	C15	1.389(3)
C4	C5	1.509(3)	C15	C16	1.386(3)
C5	C6	1.336(3)	C16	C17	1.393(3)
C5	C7	1.514(2)			

Table 5 Bond Angles for lauvin2.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C9	N1	C11	114.56(15)	C9	C8	C7	122.40(17)
C10	N1	C9	126.62(16)	C8	C9	N1	125.11(17)
C10	N1	C11	118.80(15)	O1	C10	N1	120.34(18)
C6	C1	C2	111.79(16)	O1	C10	C6	119.25(16)
C1	C2	C3	110.17(16)	N1	C10	C6	120.25(15)
C4	C3	C2	110.72(16)	N1	C11	C12	112.90(15)
C5	C4	C3	113.70(17)	C13	C12	C11	121.25(16)
C4	C5	C7	116.68(17)	C17	C12	C11	119.80(16)
C6	C5	C4	122.29(17)	C17	C12	C13	118.92(17)
C6	C5	C7	121.03(18)	C14	C13	C12	120.56(17)
C5	C6	C1	123.06(18)	C13	C14	C15	120.09(17)
C5	C6	C10	123.88(16)	C16	C15	C14	120.02(18)

Table 5 Bond Angles for lauvin2.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	C6	C1	112.65(16)	C15	C16	C17	119.76(17)
C8	C7	C5	109.83(16)	C12	C17	C16	120.65(18)

Table 6 Torsion Angles for lauvin2.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
N1	C11	C12	C13	-44.1(2)	C7	C5	C6	C10	-6.8(3)
N1	C11	C12	C17	137.71(18)	C7	C8	C9	N1	1.1(3)
C1	C2	C3	C4	-61.2(2)	C9	N1	C10	O1	176.56(16)
C1	C6	C10	O1	36.8(2)	C9	N1	C10	C6	-8.0(3)
C1	C6	C10	N1	−138.64(16)	C9	N1	C11	C12	-73.42(19)
C2	C1	C6	C5	-19.3(3)	C10	N1	C9	C8	-35.6(3)
C2	C1	C6	C10	167.73(16)	C10	N1	C11	C12	108.16(17)
C2	C3	C4	C5	42.5(2)	C11	N1	C9	C8	146.13(19)
C3	C4	C5	C6	-12.9(3)	C11	N1	C10	O1	-5.2(2)
C3	C4	C5	C7	167.08(16)	C11	N1	C10	C6	170.20(16)
C4	C5	C6	C1	1.0(3)	C11	C12	C13	C14	−177.67(18)
C4	C5	C6	C10	173.19(18)	C11	C12	C17	C16	177.46(17)
C4	C5	C7	C8	119.92(19)	C12	C13	C14	C15	0.2(3)
C5	C6	C10	O1	−136.04(18)	C13	C12	C17	C16	-0.7(3)
C5	C6	C10	N1	48.5(3)	C13	C14	C15	C16	-0.6(3)
C5	C7	C8	C9	62.0(2)	C14	C15	C16	C17	0.3(3)
C6	C1	C2	C3	48.5(2)	C15	C16	C17	C12	0.3(3)
C6	C5	C7	C8	-60.1(2)	C17	C12	C13	C14	0.5(3)
C7	C5	C6	C1	−178.98(17)					

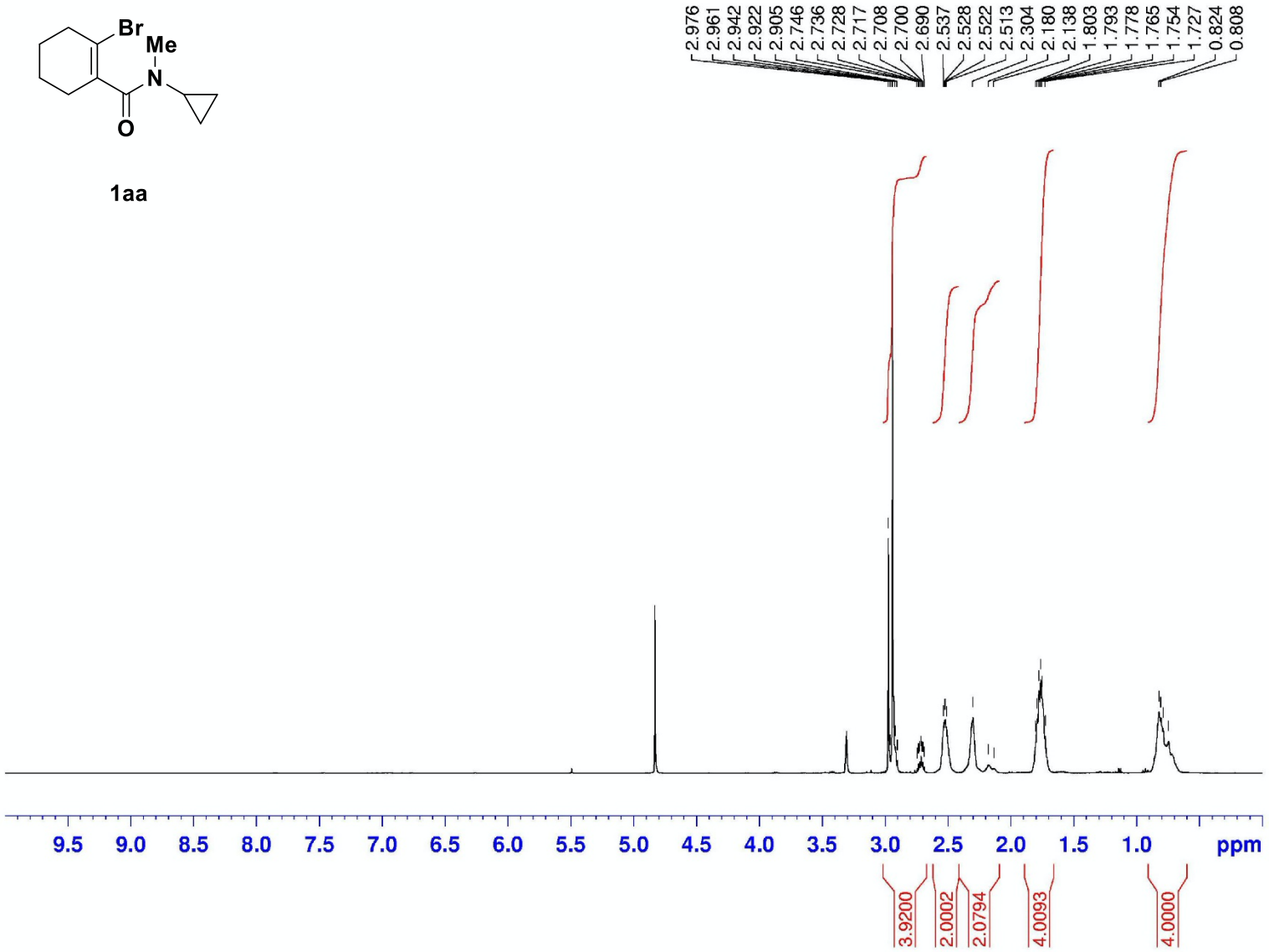
Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for lauvin2.

Atom	*x*	*y*	*z*	U(eq)
H1A	3419.5	858.1	4442.56	36
H1B	5134.75	673.84	4368.86	36
H2A	3202.05	805.51	1595.3	39
H2B	4102.5	91.43	2119.28	39
H3A	6345.04	689.89	1438.42	40
H3B	5292.52	651.77	-145.27	40

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for lauvin2.

Atom	*x*	*y*	*z*	U(eq)
H4A	6431.61	1839.41	384.63	41
H4B	4709.42	1852.87	15.12	41
H7A	6324.4	2984.7	3314.76	38
H7B	5937.45	3045.85	1386.46	38
H8	3837.66	3657.85	2105.8	37
H9	2639.94	3524.37	4475.54	36
H11A	3692.69	2635.08	8076.19	35
H11B	2581.1	3219.57	7312.77	35
H13	6528.32	3206.1	6955.08	35
H14	8075.22	4133.63	7863.16	38
H15	7111.76	5136.6	9276.97	40
H16	4586.97	5219.31	9742.55	42
H17	3030.91	4291.59	8813.75	38

NMR spectra of novel compounds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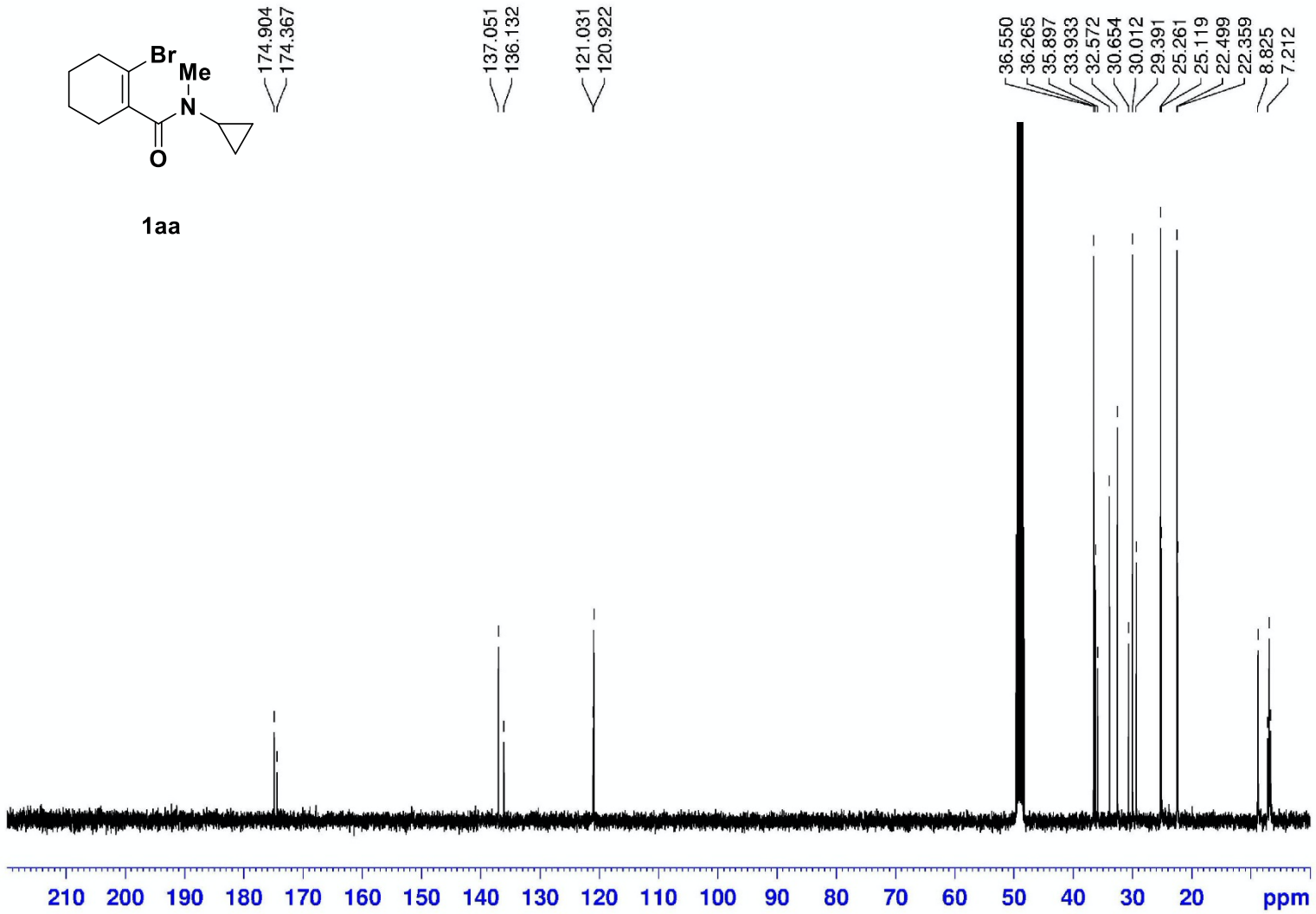
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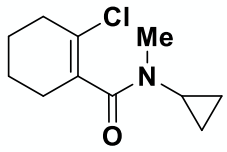
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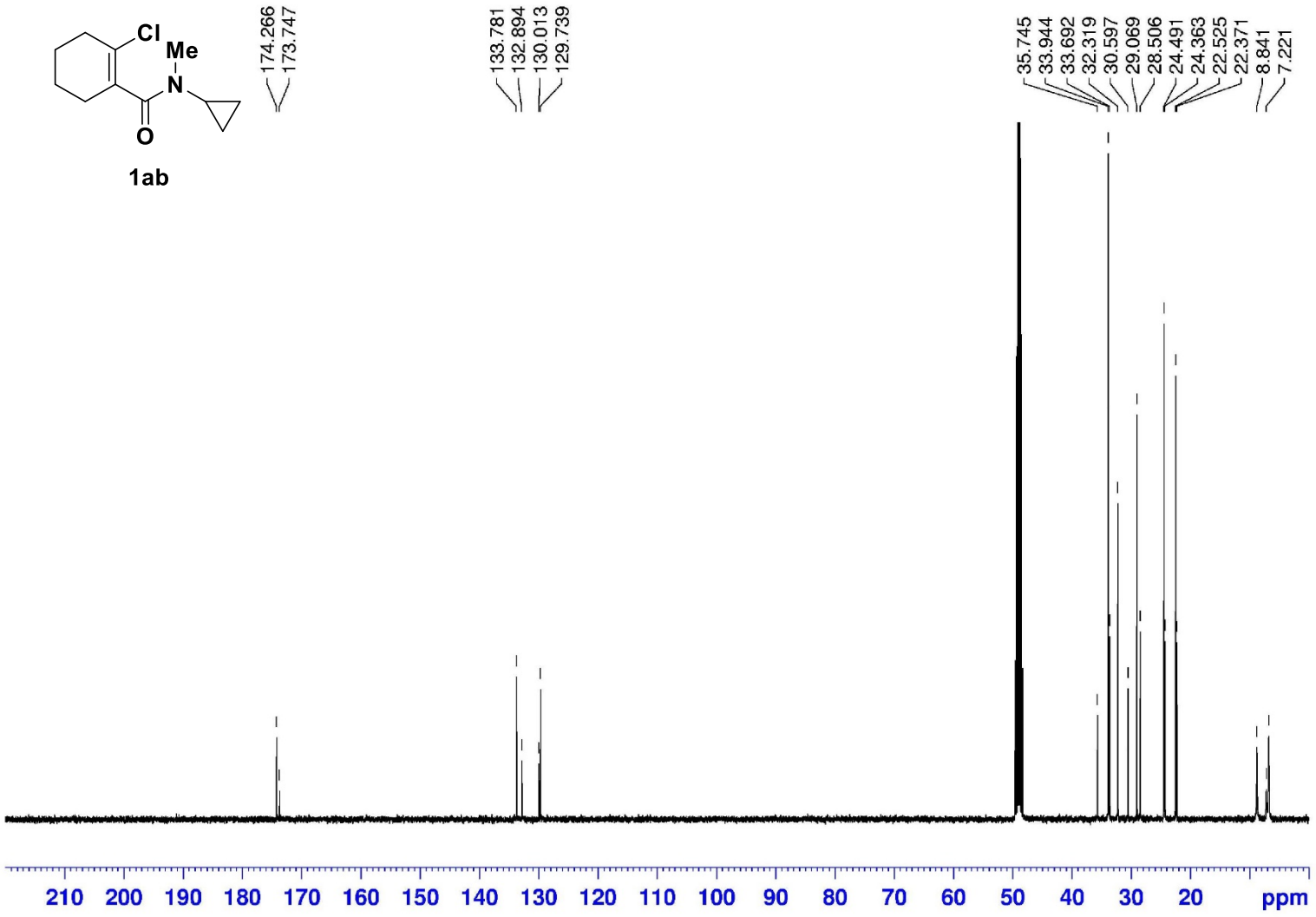
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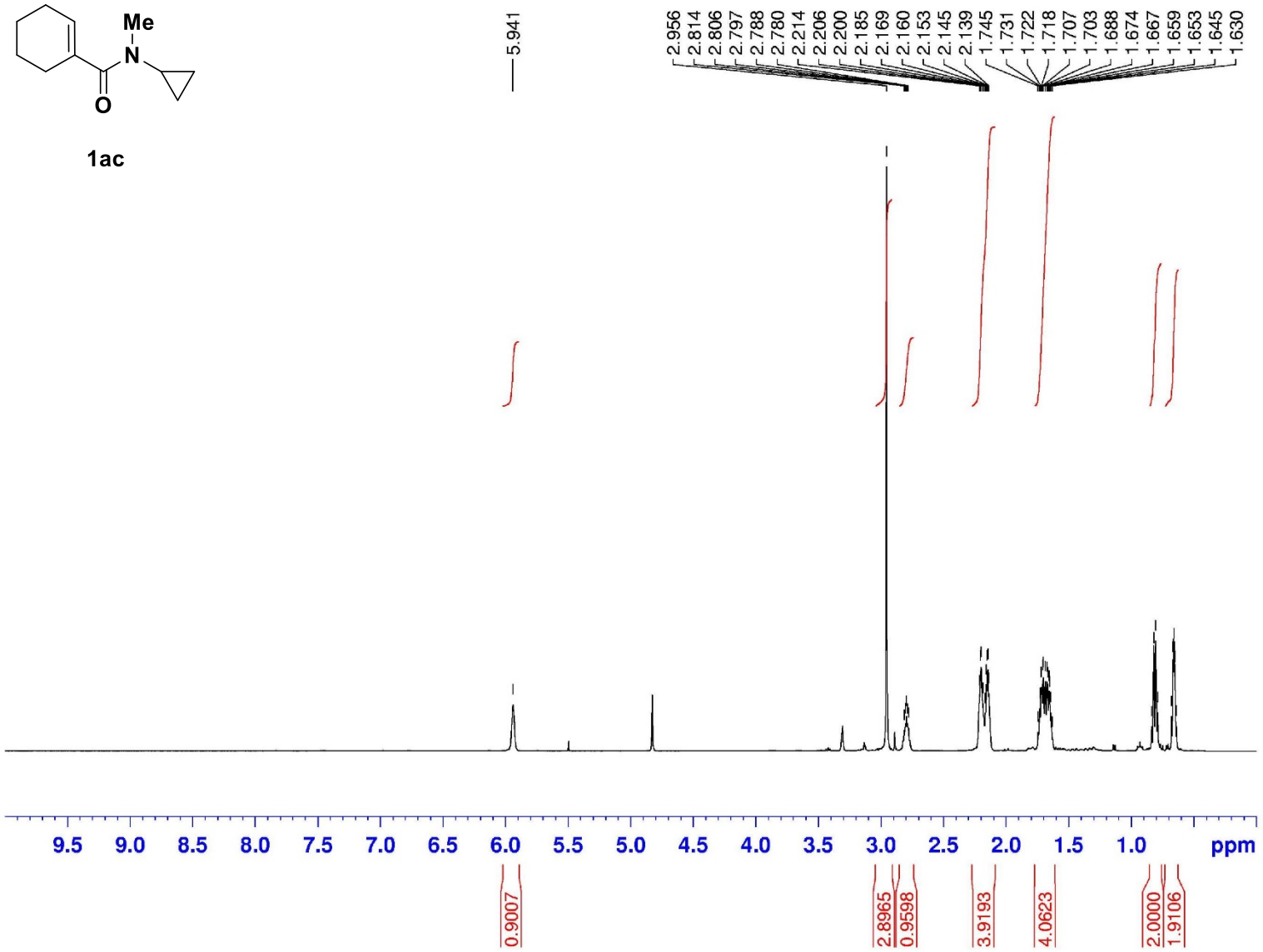
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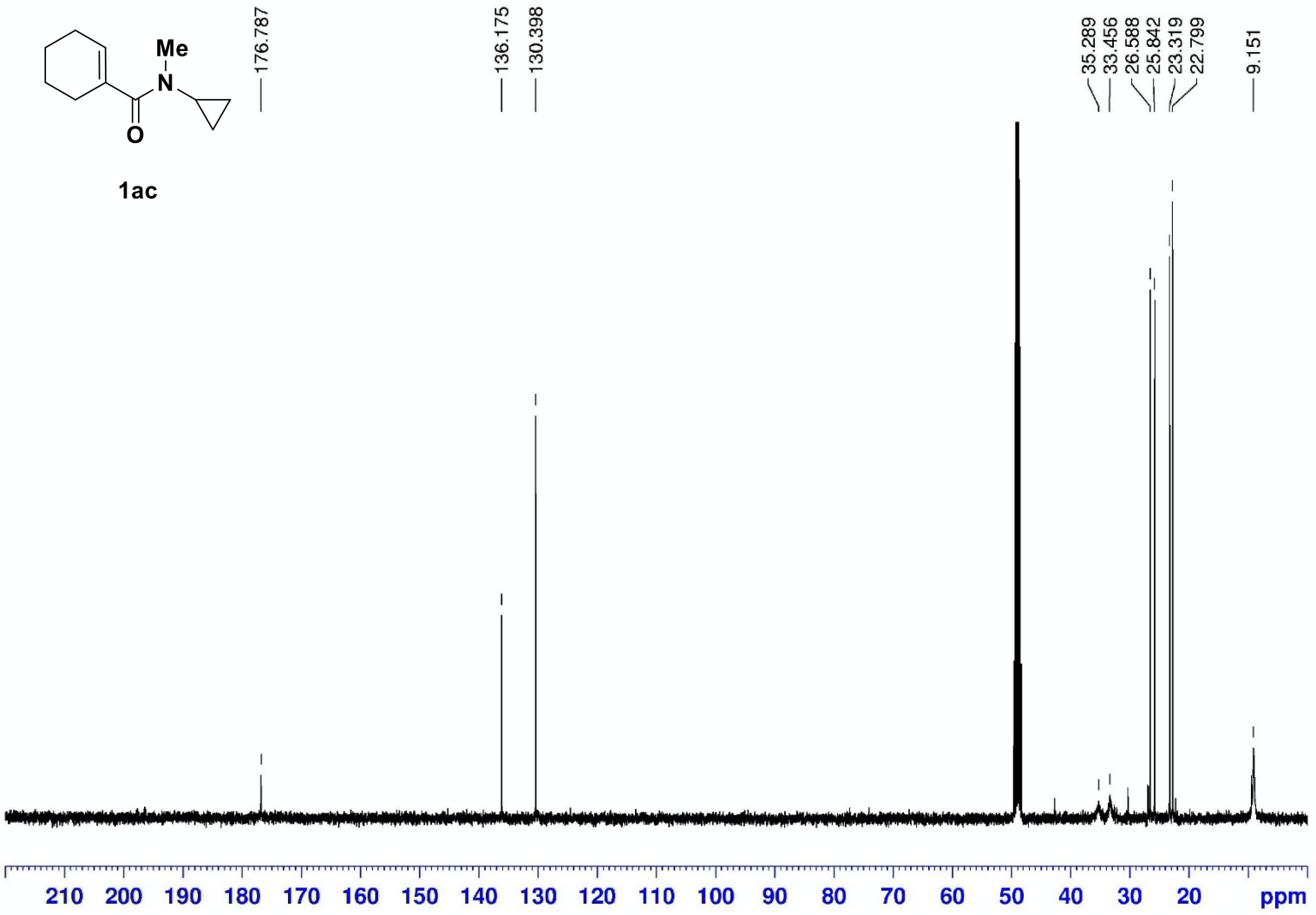
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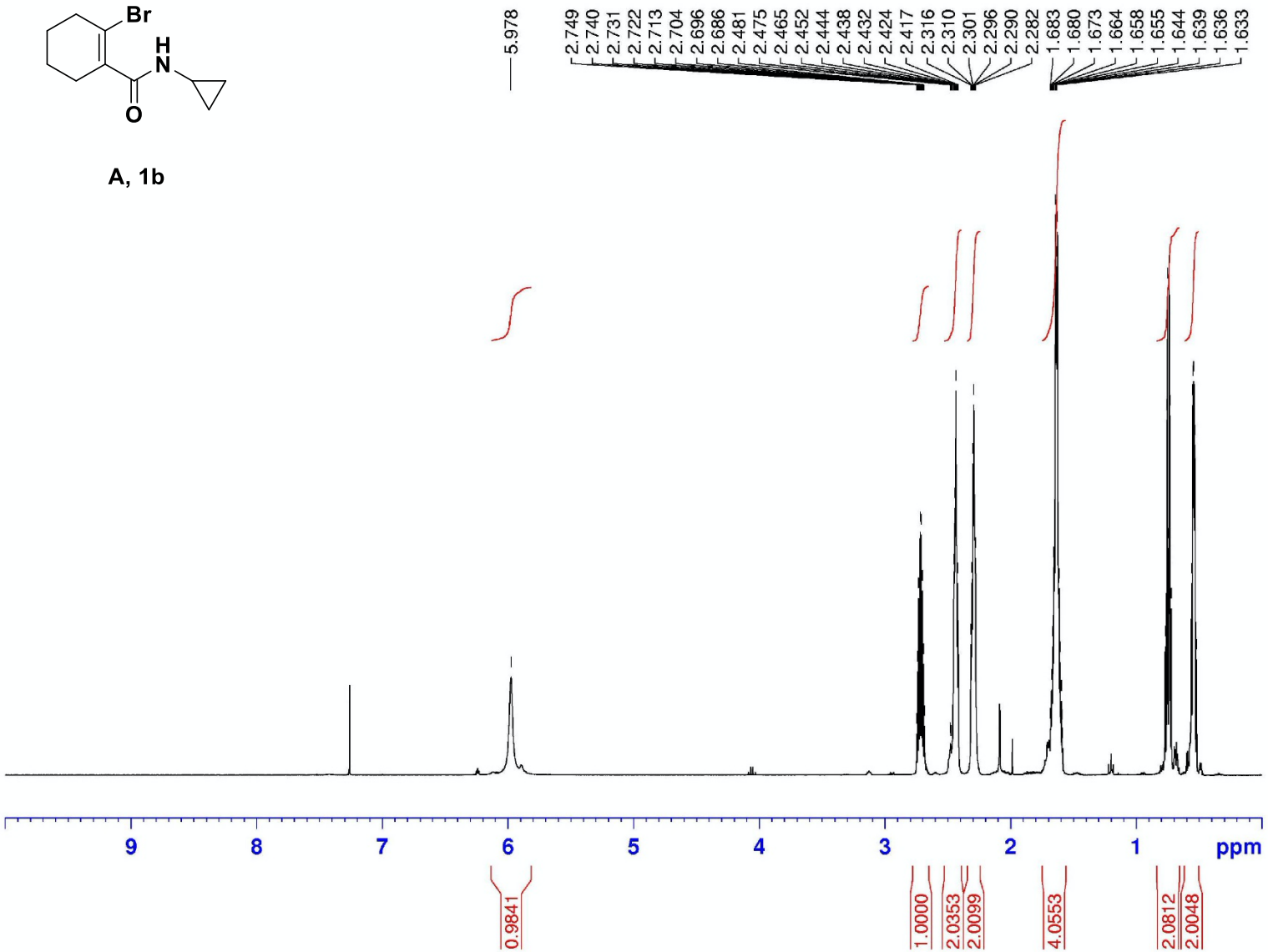
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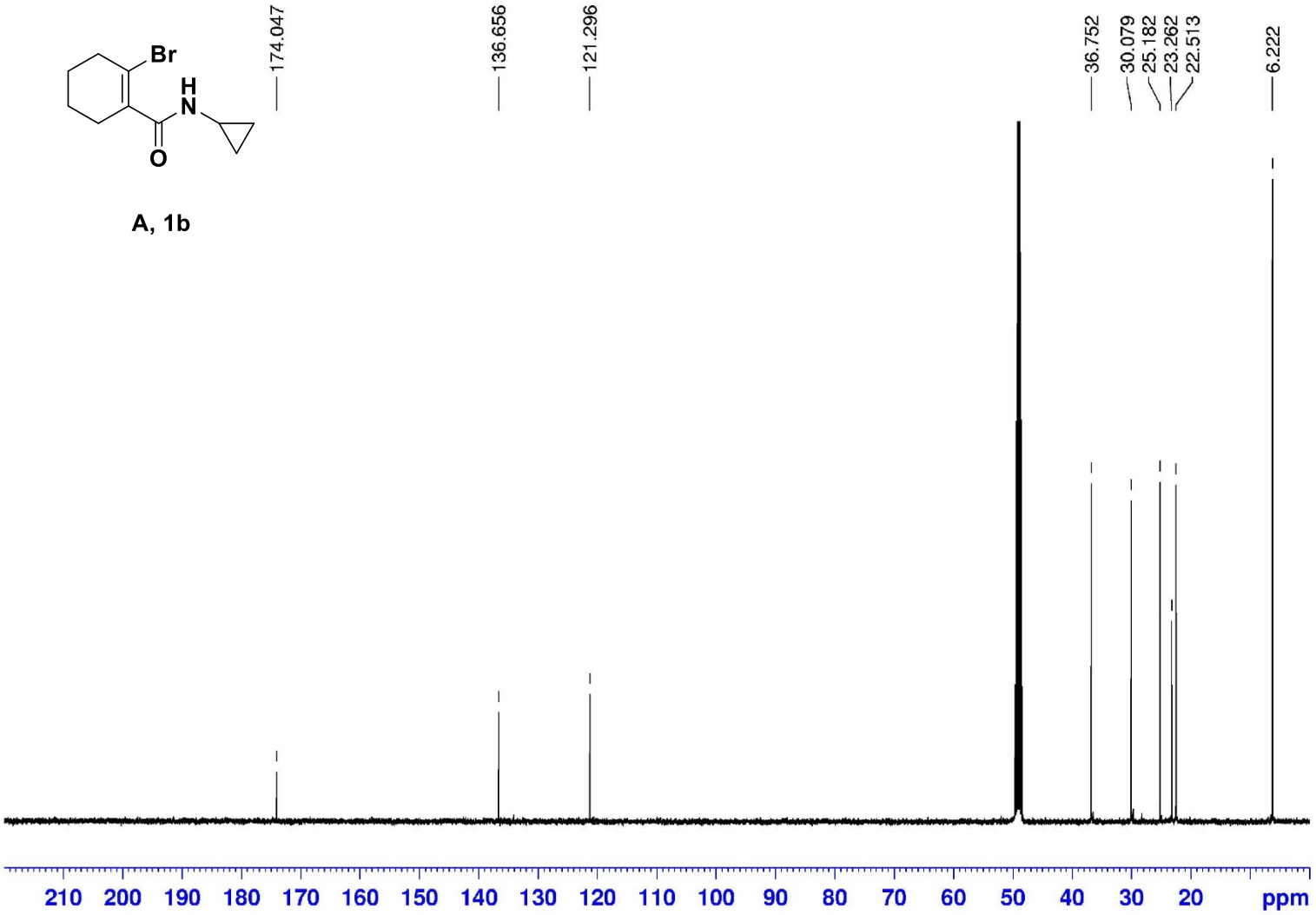
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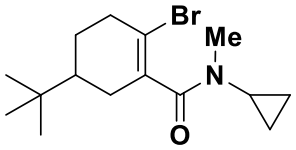
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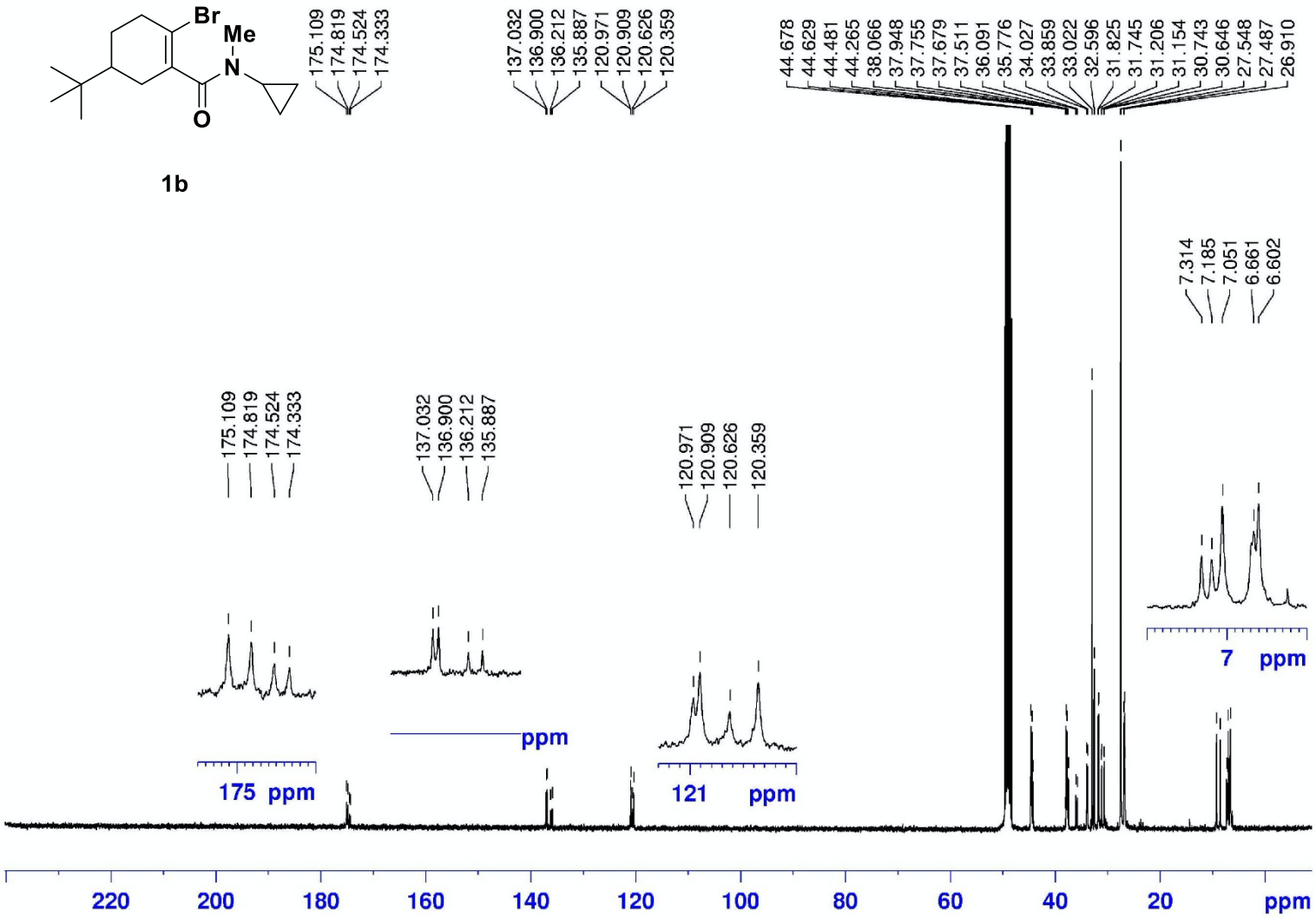
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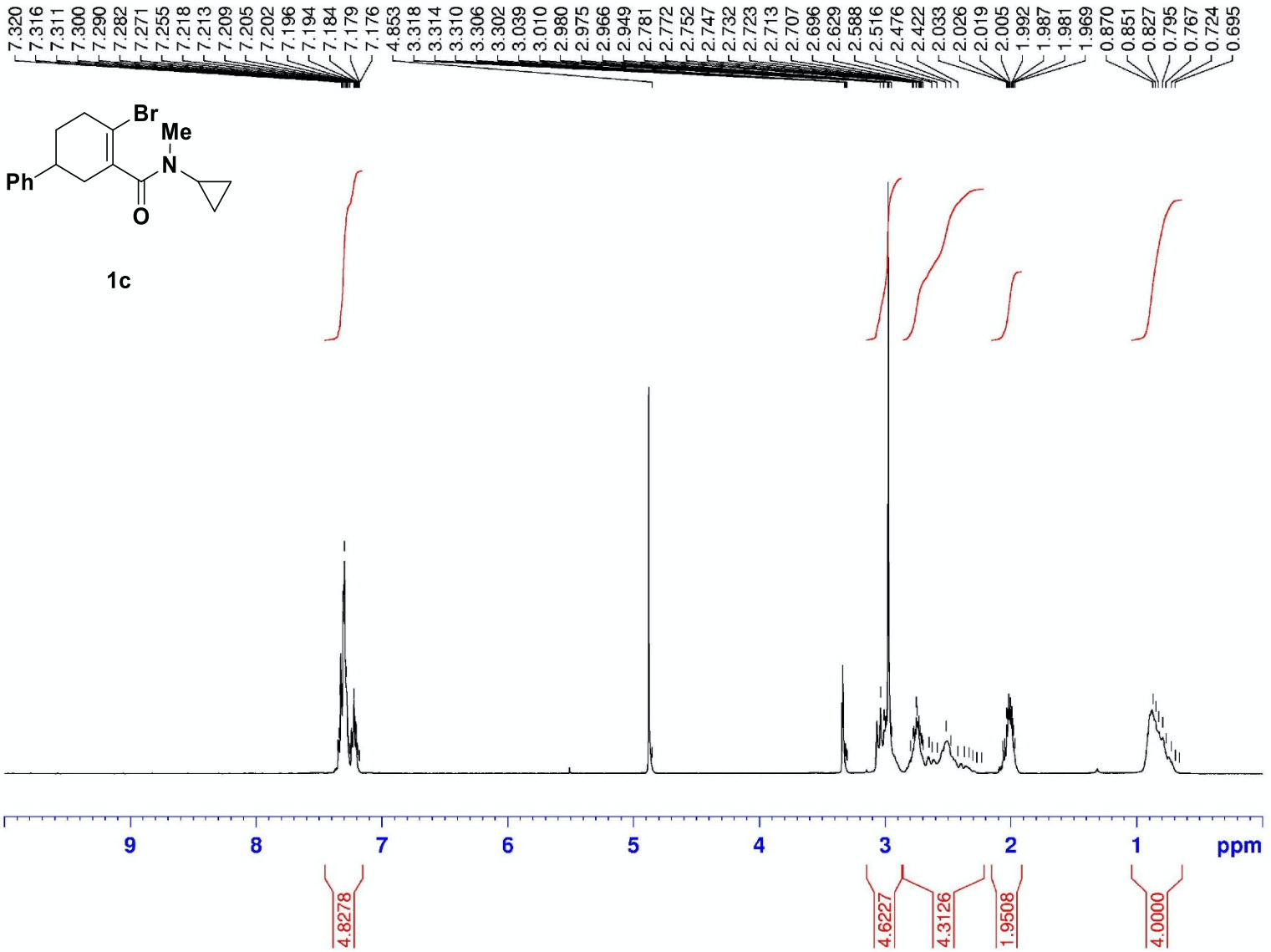
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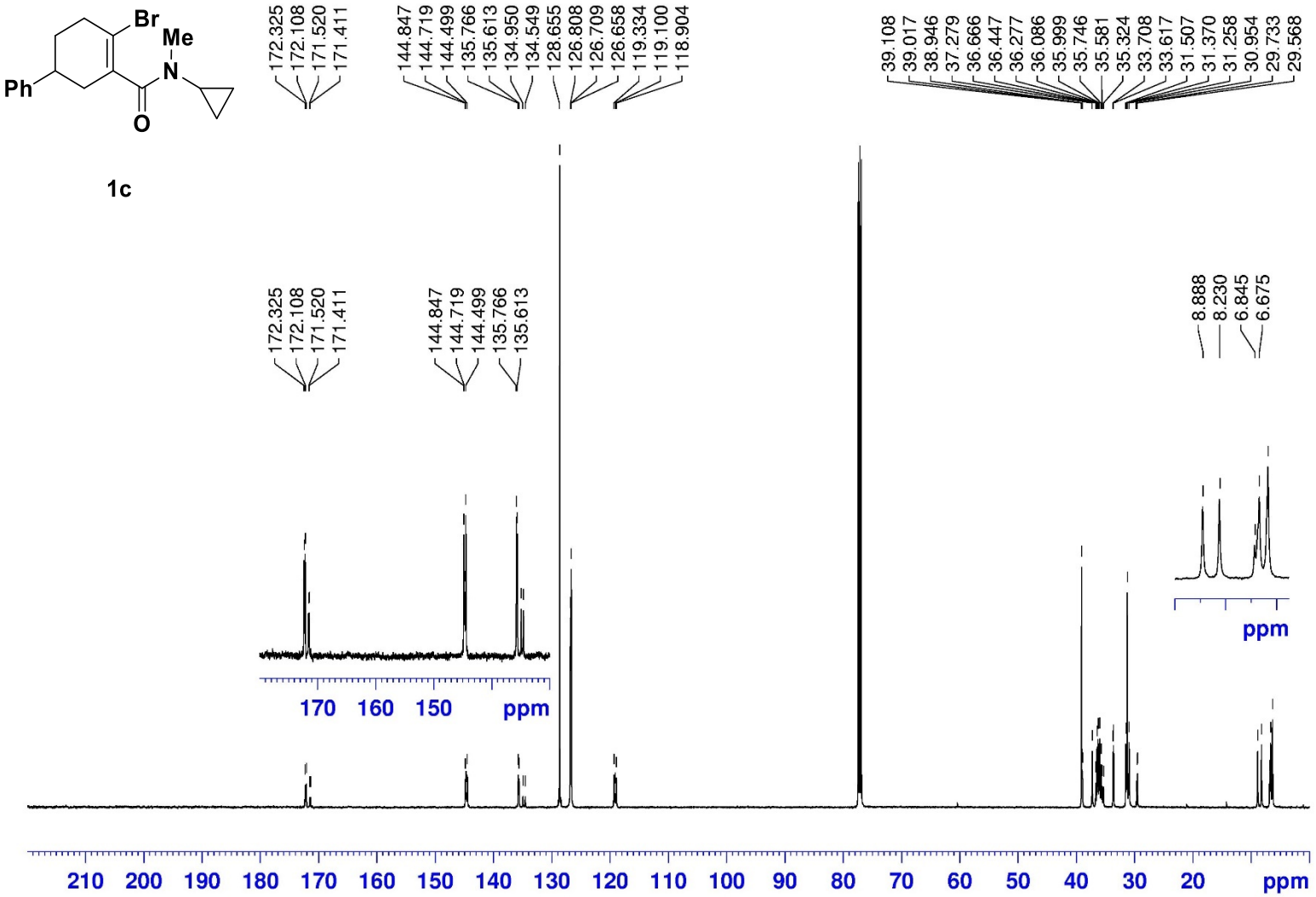
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Me
N
Ph
O
1c
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172.108
171.520
171.411
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144.499
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135.613
134.950
134.549
128.655
126.808
126.709
126.658
119.334
119.100
118.904
39.108
39.017
38.946
37.279
36.666
36.447
36.277
36.086
35.999
35.746
35.581
35.324
33.708
33.617
31.507
31.370
31.258
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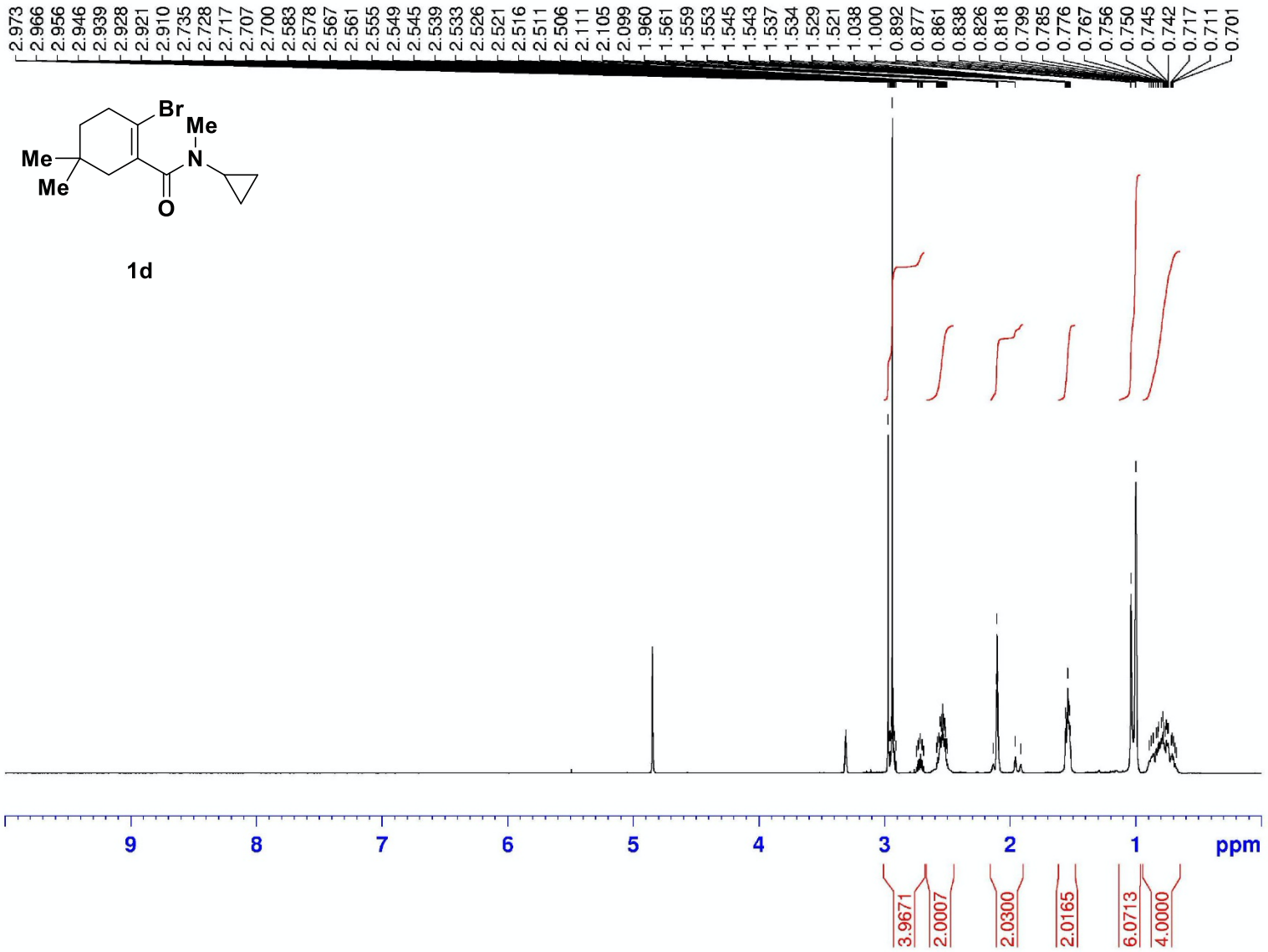
8.888
8.230
6.845
6.675
ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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2.928
2.921
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2.728
2.717
2.707
2.700
2.583
2.578
2.567
2.561
2.555
2.549
2.545
2.539
2.533
2.526
2.521
2.516
2.511
2.506
2.111
2.105
2.099
1.960
1.561
1.559
1.553
1.545
1.543
1.537
1.534
1.529
1.521
1.038
1.000
0.892
0.877
0.861
0.838
0.826
0.818
0.799
0.785
0.776
0.767
0.756
0.750
0.745
0.742
0.717
0.711
0.701
Br
Me
Me
N
Me
O
9
8
7
6
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3
2
1
ppm
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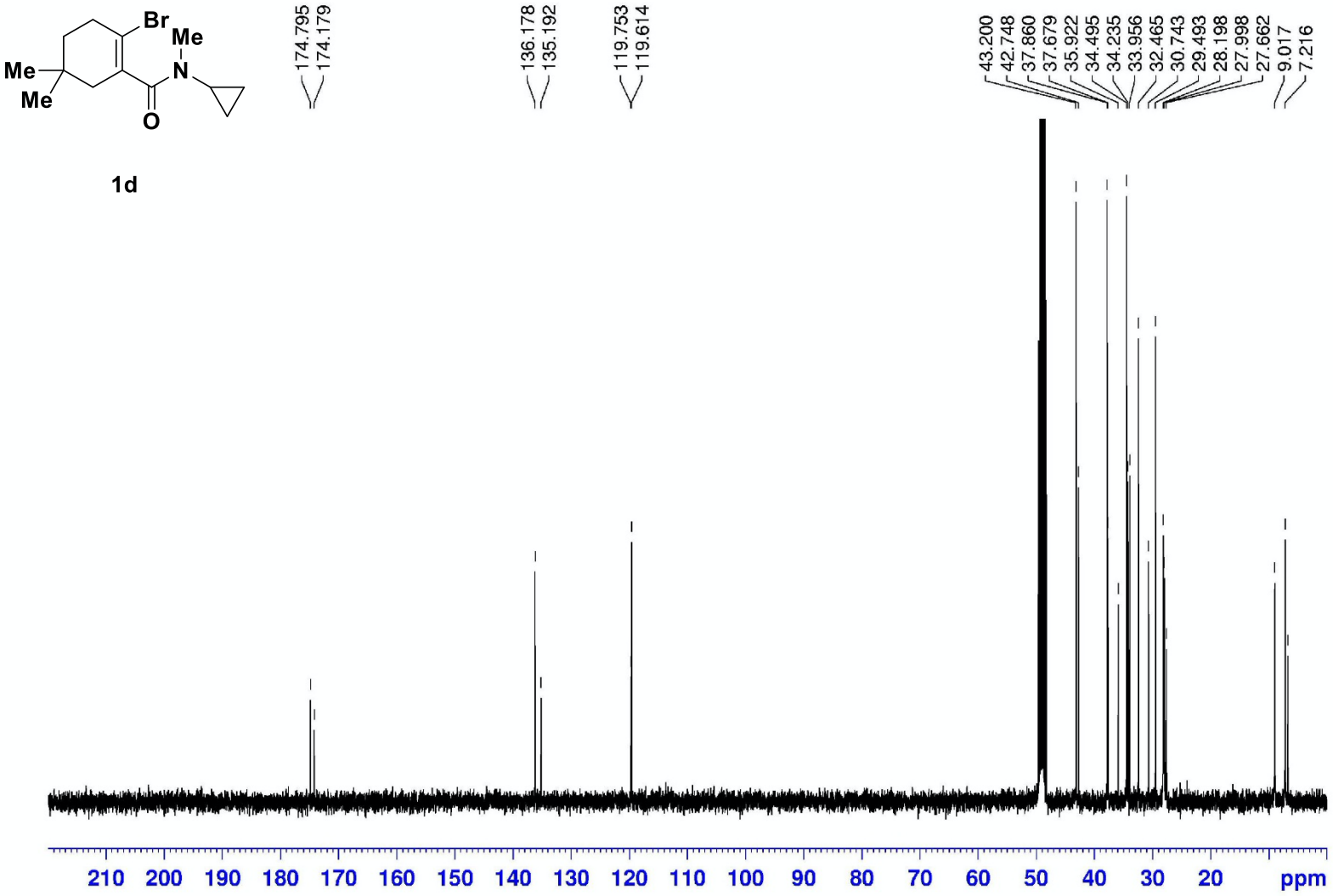
1d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Me
Me
N
Me
O
1d
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42.748
37.860
37.679
35.922
34.495
34.235
33.956
32.465
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28.198
27.998
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9.017
7.216
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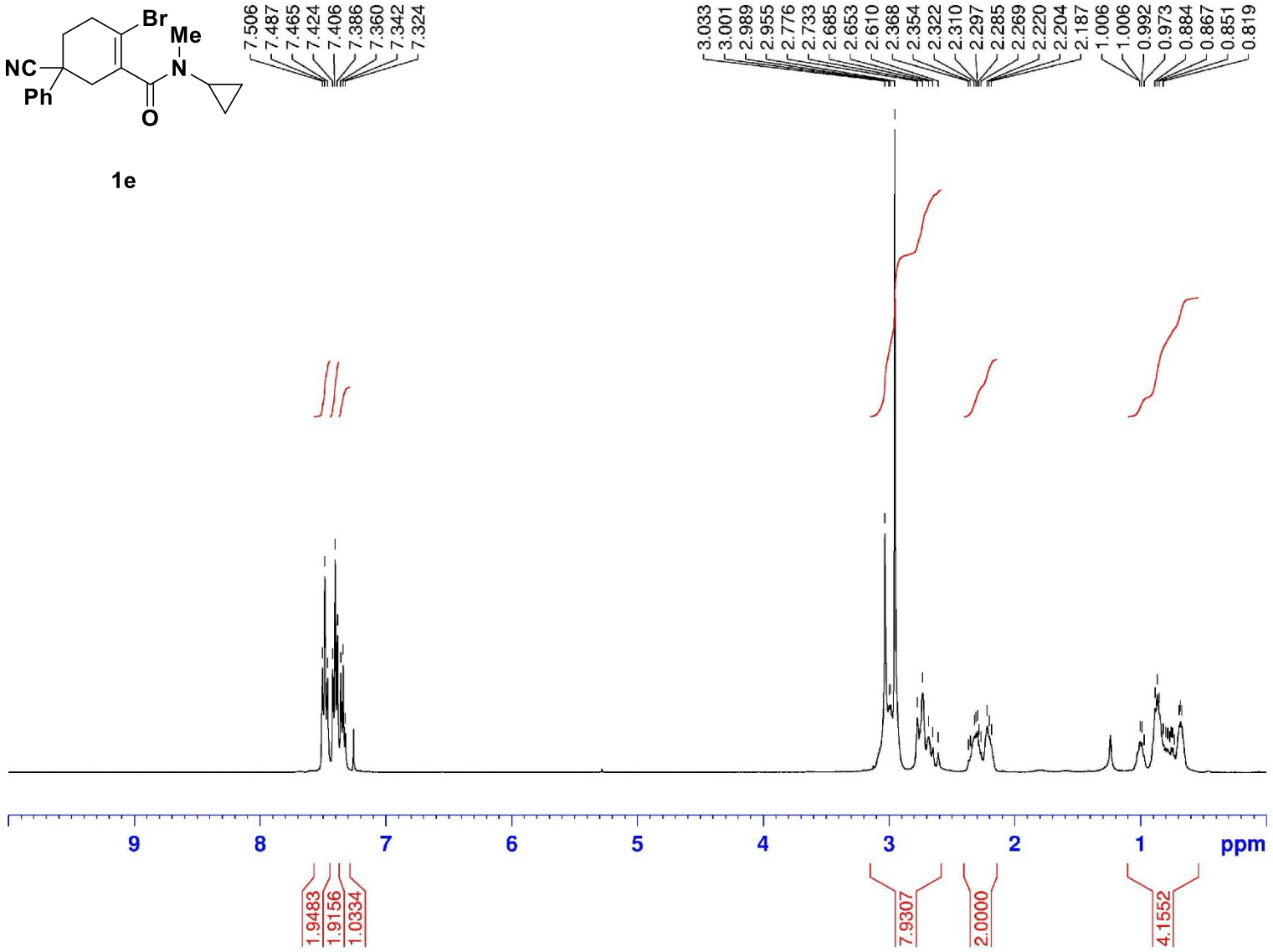
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Me
NC
N
Ph
O
1e
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7.342
7.324
3.033
3.001
2.989
2.955
2.776
2.733
2.685
2.653
2.610
2.368
2.354
2.322
2.310
2.297
2.285
2.269
2.220
2.204
2.187
1.006
1.006
0.992
0.973
0.884
0.867
0.851
0.819
9
8
7
6
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4
3
2
1
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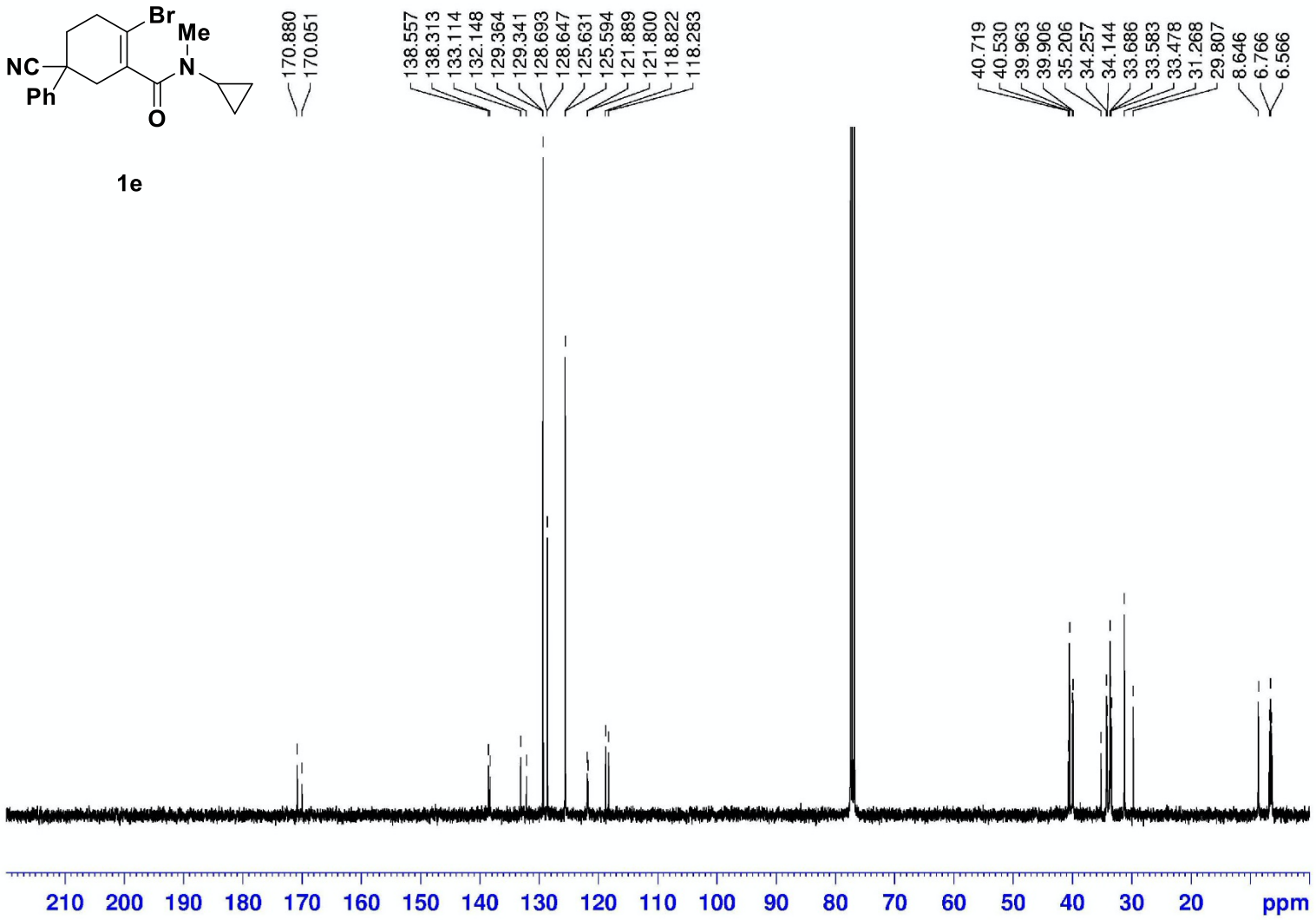
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Me
NC
N
Ph
O
1e
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170.051
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138.313
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132.148
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128.693
128.647
125.631
125.594
121.889
121.800
118.822
118.283
40.719
40.530
39.963
39.906
35.206
34.257
34.144
33.686
33.583
33.478
31.268
29.807
8.646
6.766
6.566
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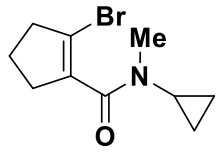
Br
Me
N
O

1f

2.986
2.942
2.910
2.900
2.892
2.882
2.874
2.866
2.855
2.725
2.719
2.707
2.694
2.688
2.661
2.643
2.631
2.625
2.074
2.055
2.037
2.019
2.000
0.845
0.832
0.830
0.764
0.748
9
8
7
6
5
4
3
2
1
ppm
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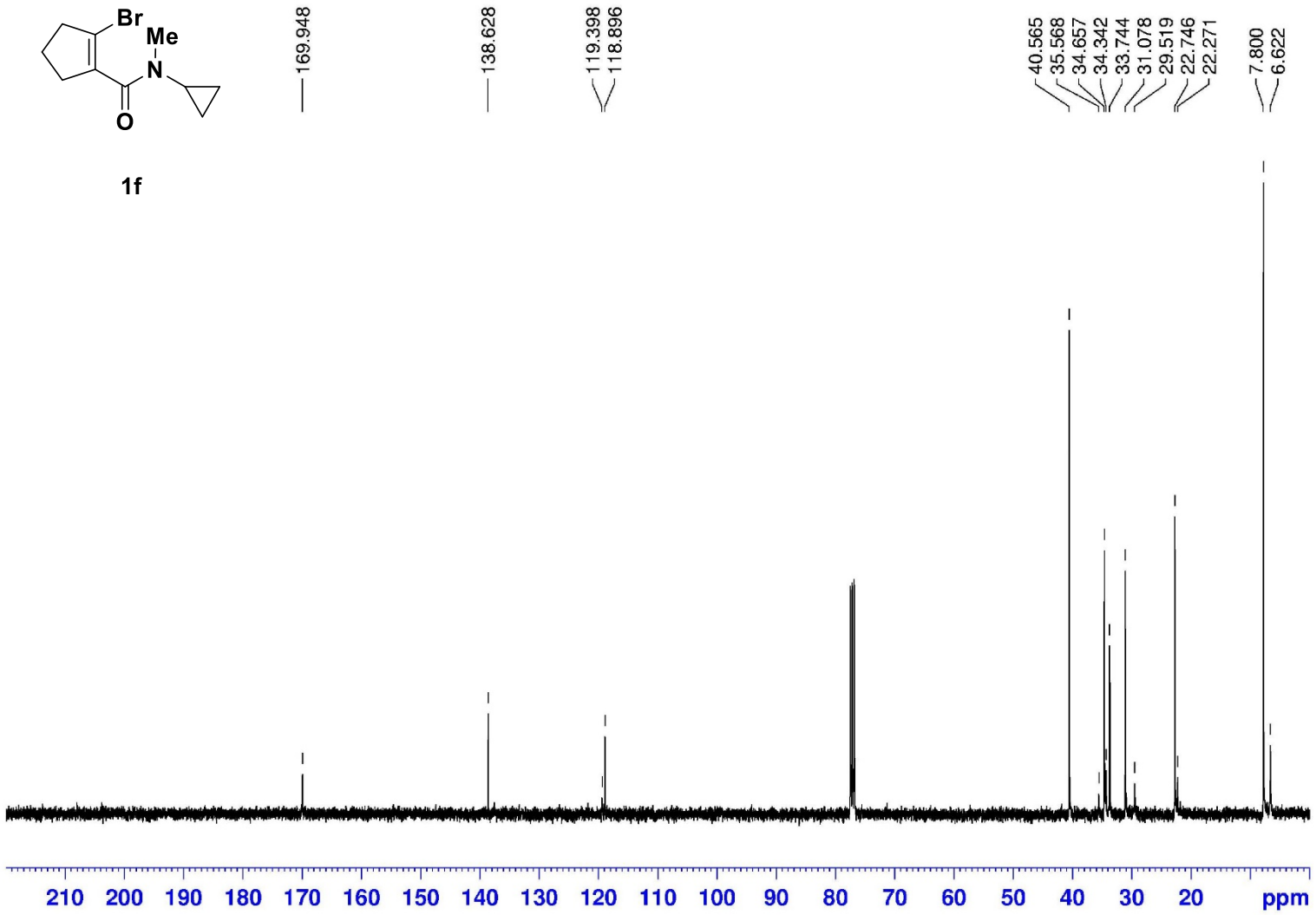
4.1793
2.0042
3.9870


Br
Me
N
O
1f
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40.565
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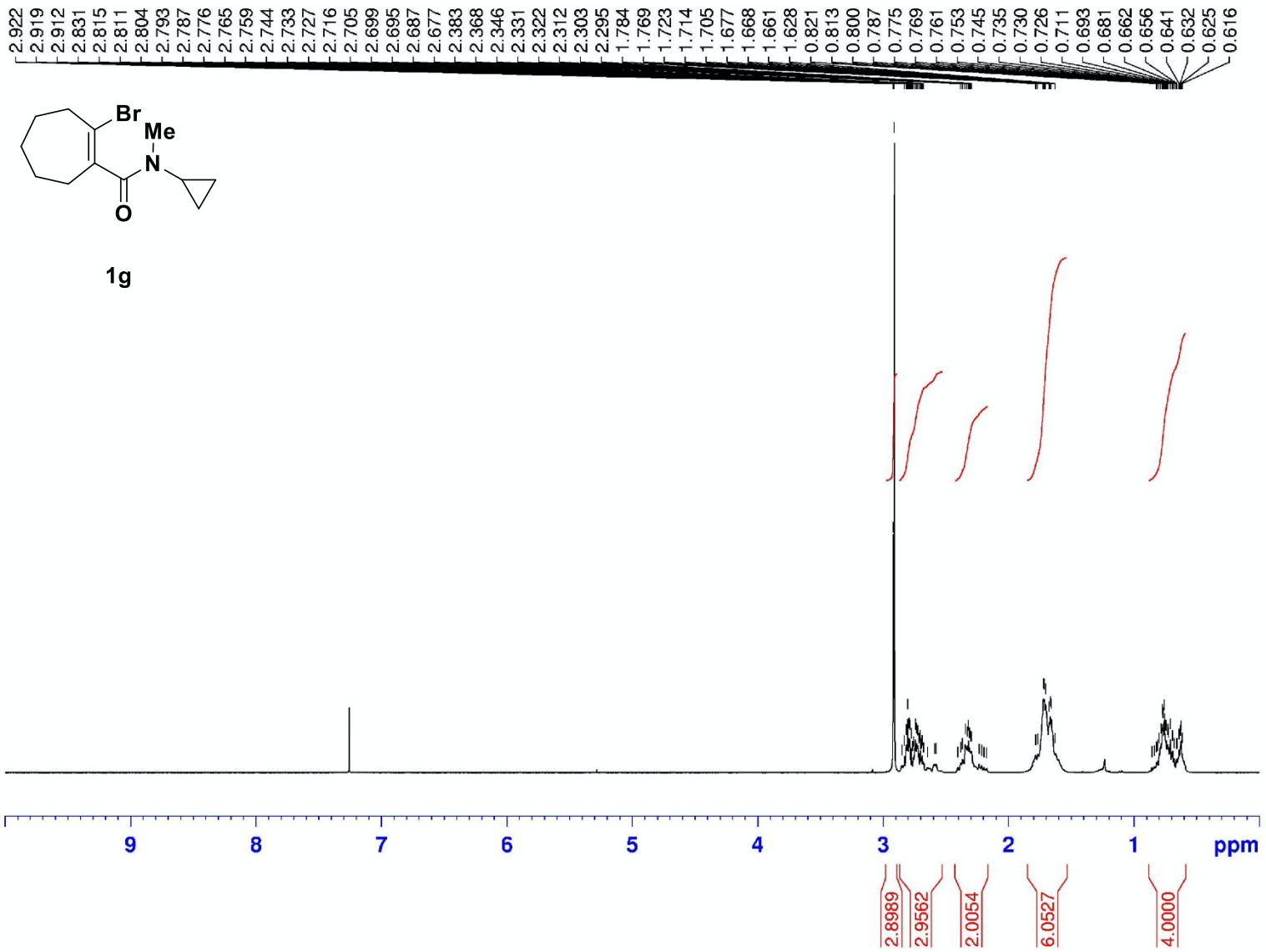
34.657
34.342
33.744
31.078
29.519
22.746
22.271
7.800
6.622
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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2.919
2.912
2.831
2.815
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2.776
2.765
2.759
2.744
2.733
2.727
2.716
2.705
2.699
2.695
2.687
2.677
2.383
2.368
2.346
2.331
2.322
2.312
2.303
2.295
1.784
1.769
1.723
1.714
1.705
1.677
1.668
1.661
1.628
0.821
0.813
0.800
0.787
0.775
0.769
0.761
0.753
0.745
0.735
0.730
0.726
0.711
0.693
0.681
0.662
0.656
0.641
0.632
0.625
0.616
Br
Me
N
O
1g
9
8
7
6
5
4
3
2
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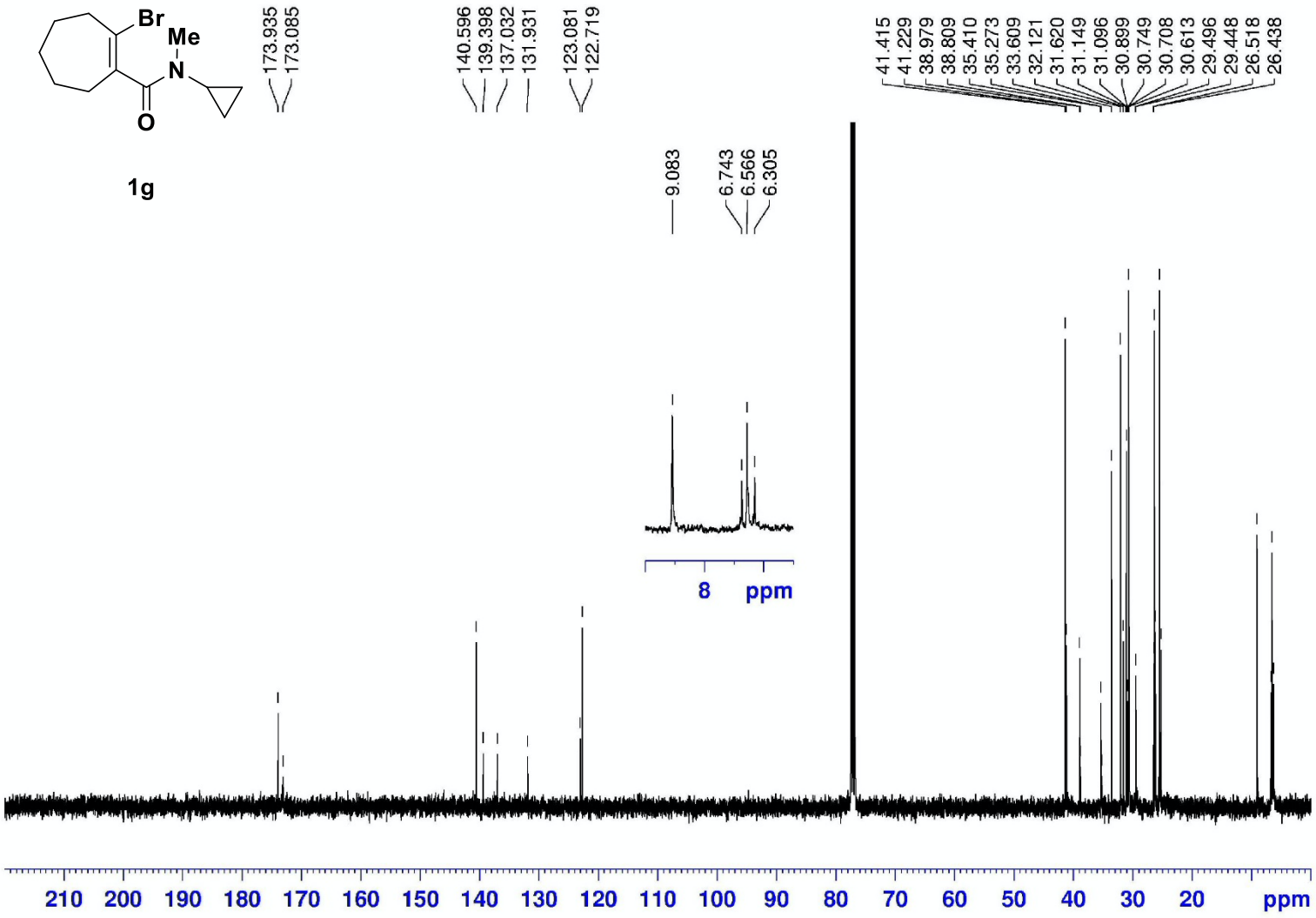
6.0527
4.0000


Br
Me
N
O
1g
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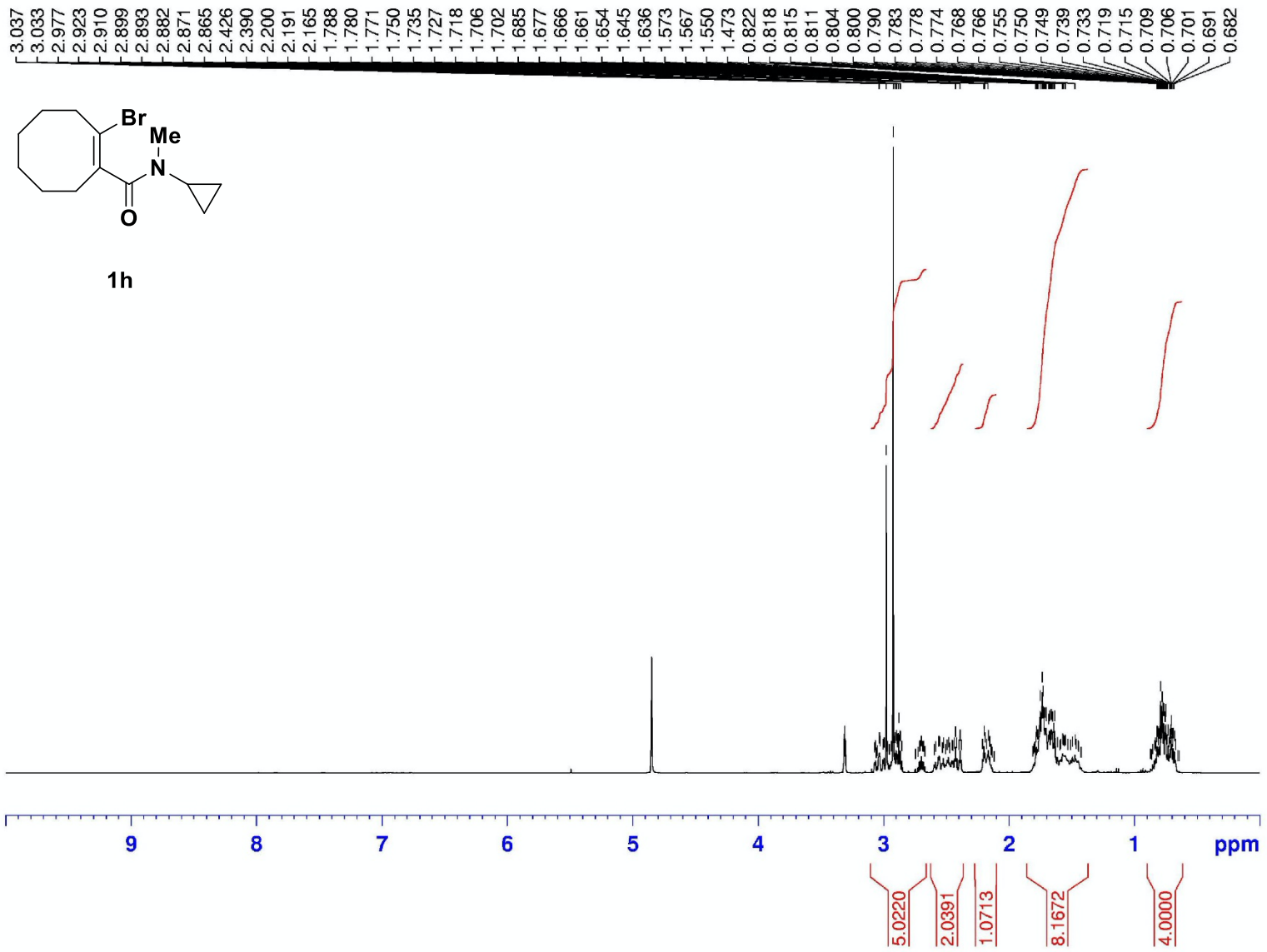
173.085
140.596
139.398
137.032
131.931
123.081
122.719
41.415
41.229
38.979
38.809
35.410
35.273
33.609
32.121
31.620
31.149
31.096
30.899
30.749
30.708
30.613
29.496
29.448
26.518
26.438
9.083
6.743
6.566
6.305
8 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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3.033
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2.923
2.910
2.899
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2.882
2.871
2.865
2.426
2.390
2.200
2.191
2.165
1.788
1.780
1.771
1.750
1.735
1.727
1.718
1.706
1.702
1.685
1.677
1.666
1.661
1.654
1.645
1.636
1.573
1.567
1.550
1.473
0.822
0.818
0.815
0.811
0.804
0.800
0.790
0.783
0.778
0.774
0.768
0.766
0.755
0.750
0.749
0.739
0.733
0.719
0.715
0.709
0.706
0.701
0.691
0.682
Br
Me
N
O
1h
9
8
7
6
5
4
3
2
1
ppm
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2.0391
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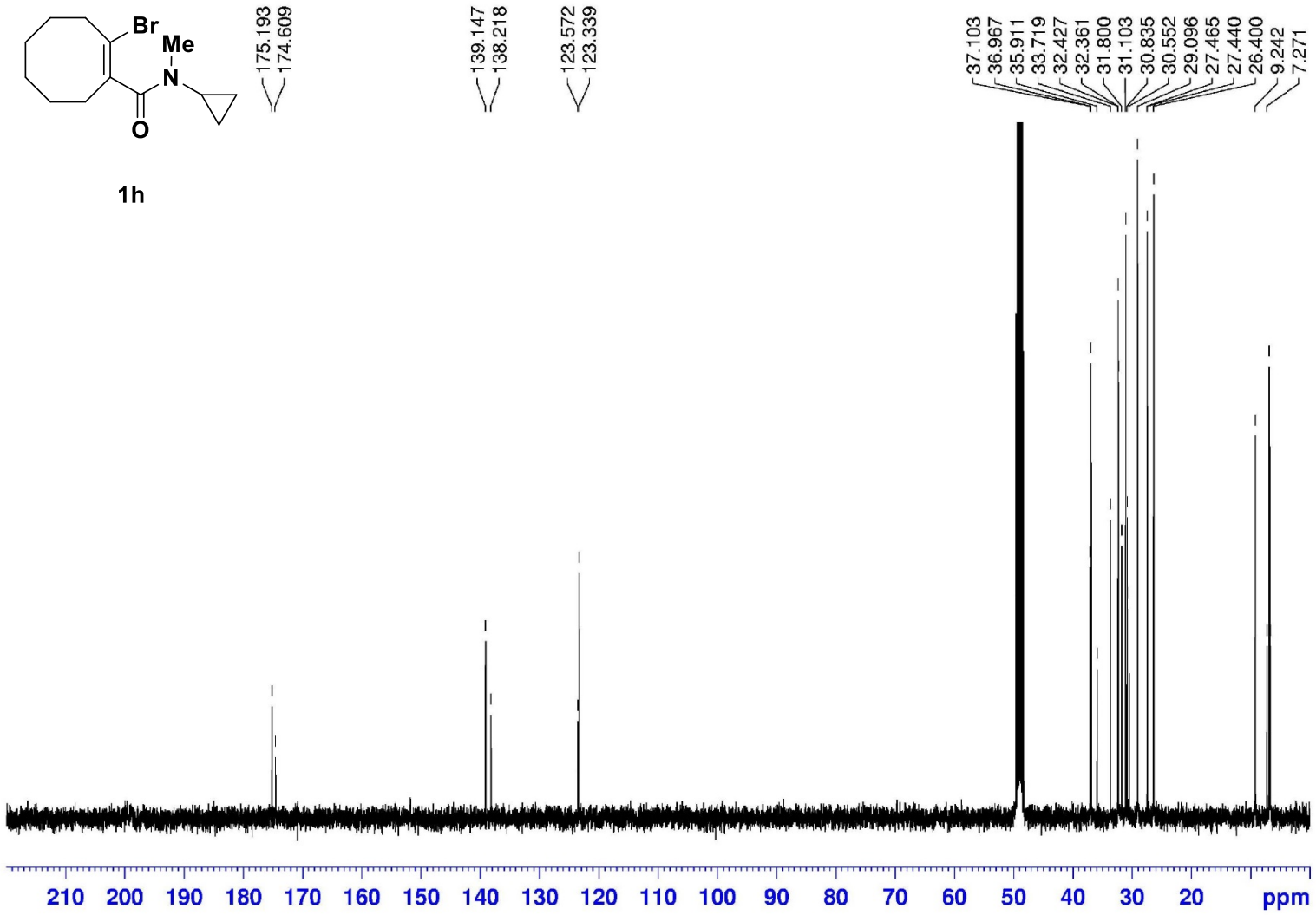
4.0000


Br
Me
N
O
1h
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123.572
123.339
37.103
36.967
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33.719
32.427
32.361
31.800
31.103
30.835
30.552
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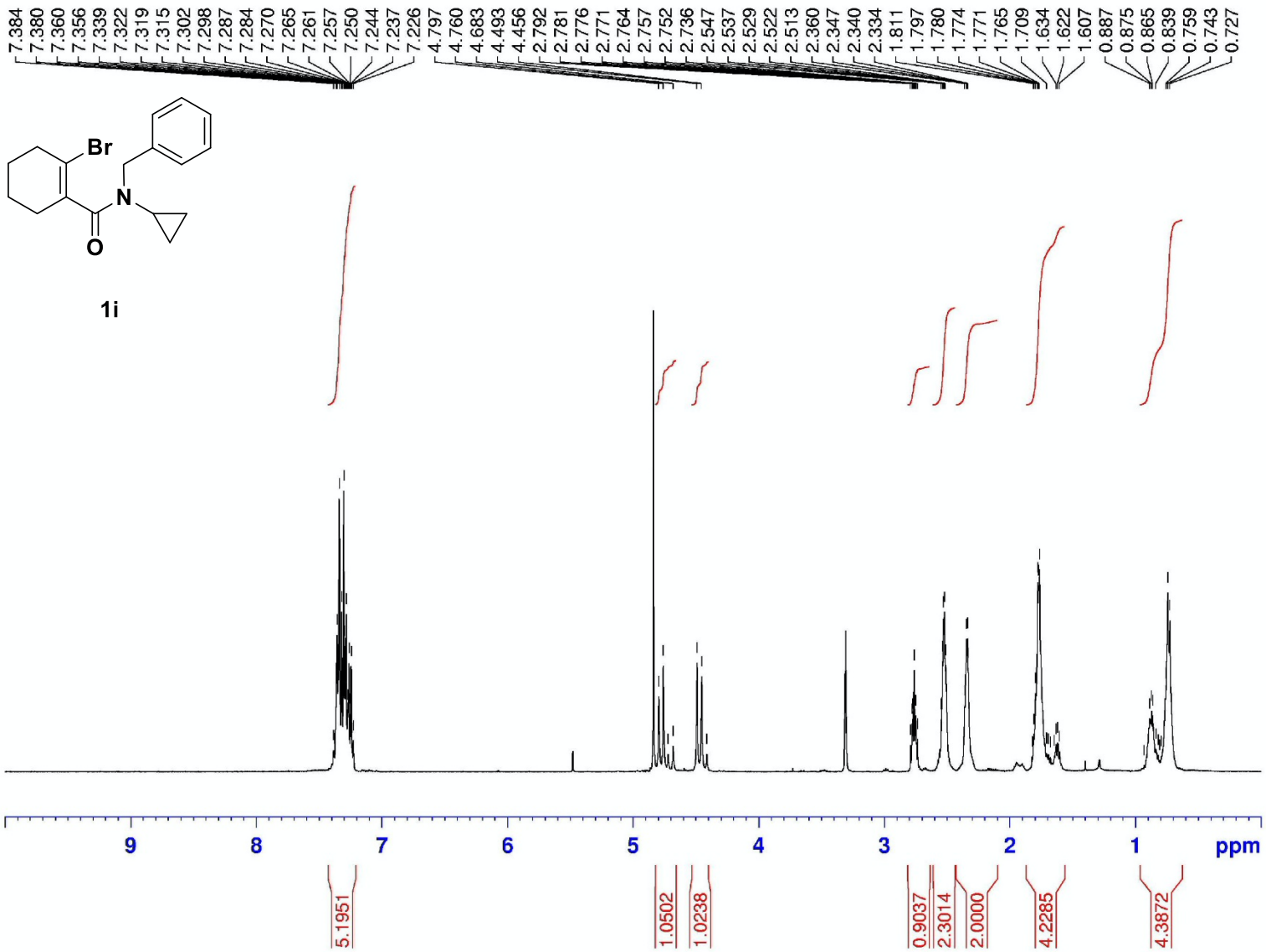
27.465
27.440
26.400
9.242
7.271
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.322
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7.284
7.270
7.265
7.261
7.257
7.250
7.244
7.237
7.226
4.797
4.760
4.683
4.493
4.456
2.792
2.781
2.776
2.771
2.764
2.757
2.752
2.736
2.547
2.537
2.529
2.522
2.513
2.360
2.347
2.340
2.334
1.811
1.797
1.780
1.774
1.771
1.765
1.709
1.634
1.622
1.607
0.887
0.875
0.865
0.839
0.759
0.743
0.727
Br
N
O
1i
9
8
7
6
5
4
3
2
1
ppm
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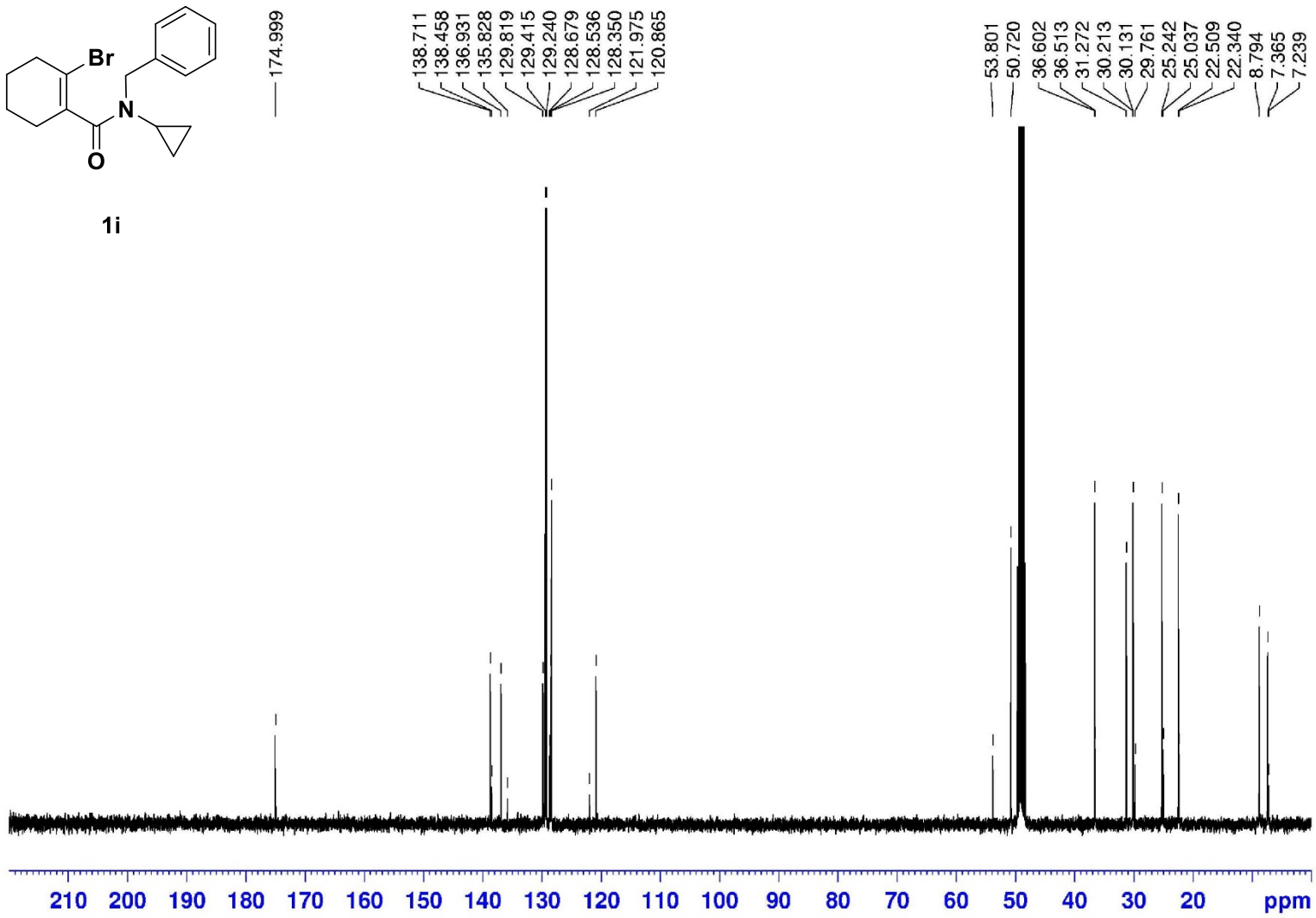
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N
O
1i
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135.828
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128.536
128.350
121.975
120.865
53.801
50.720
36.602
36.513
31.272
30.213
30.131
29.761
25.242
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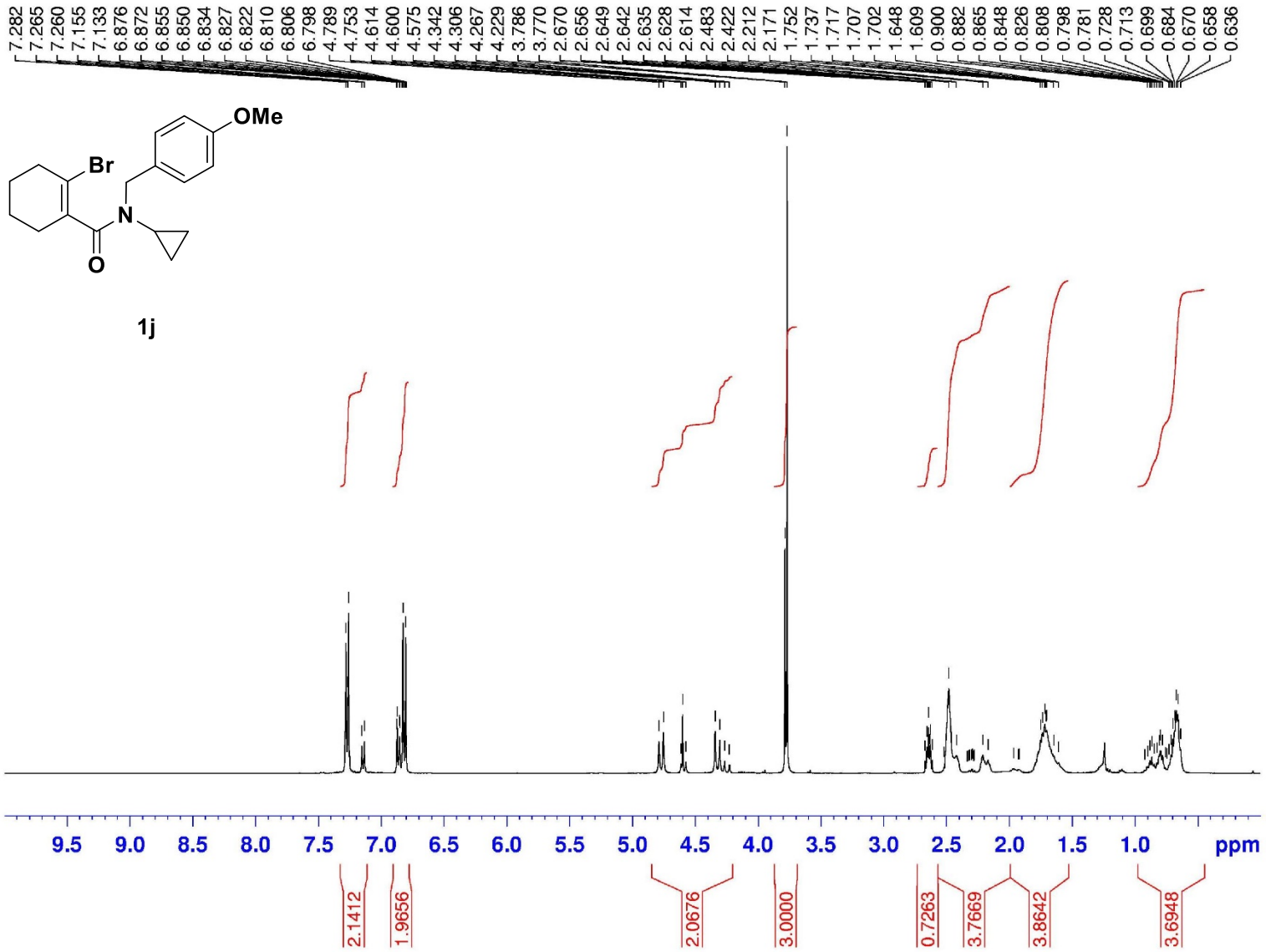
22.509
22.340
8.794
7.365
7.239
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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6.872
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6.850
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6.827
6.822
6.810
6.806
6.798
4.789
4.753
4.614
4.600
4.575
4.342
4.306
4.267
4.229
3.786
3.770
2.670
2.656
2.649
2.642
2.635
2.628
2.614
2.483
2.422
2.212
2.171
1.752
1.737
1.717
1.707
1.702
1.648
1.609
0.900
0.882
0.865
0.848
0.826
0.808
0.798
0.781
0.728
0.713
0.699
0.684
0.670
0.658
0.636
OMe
Br
N
O
1j
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
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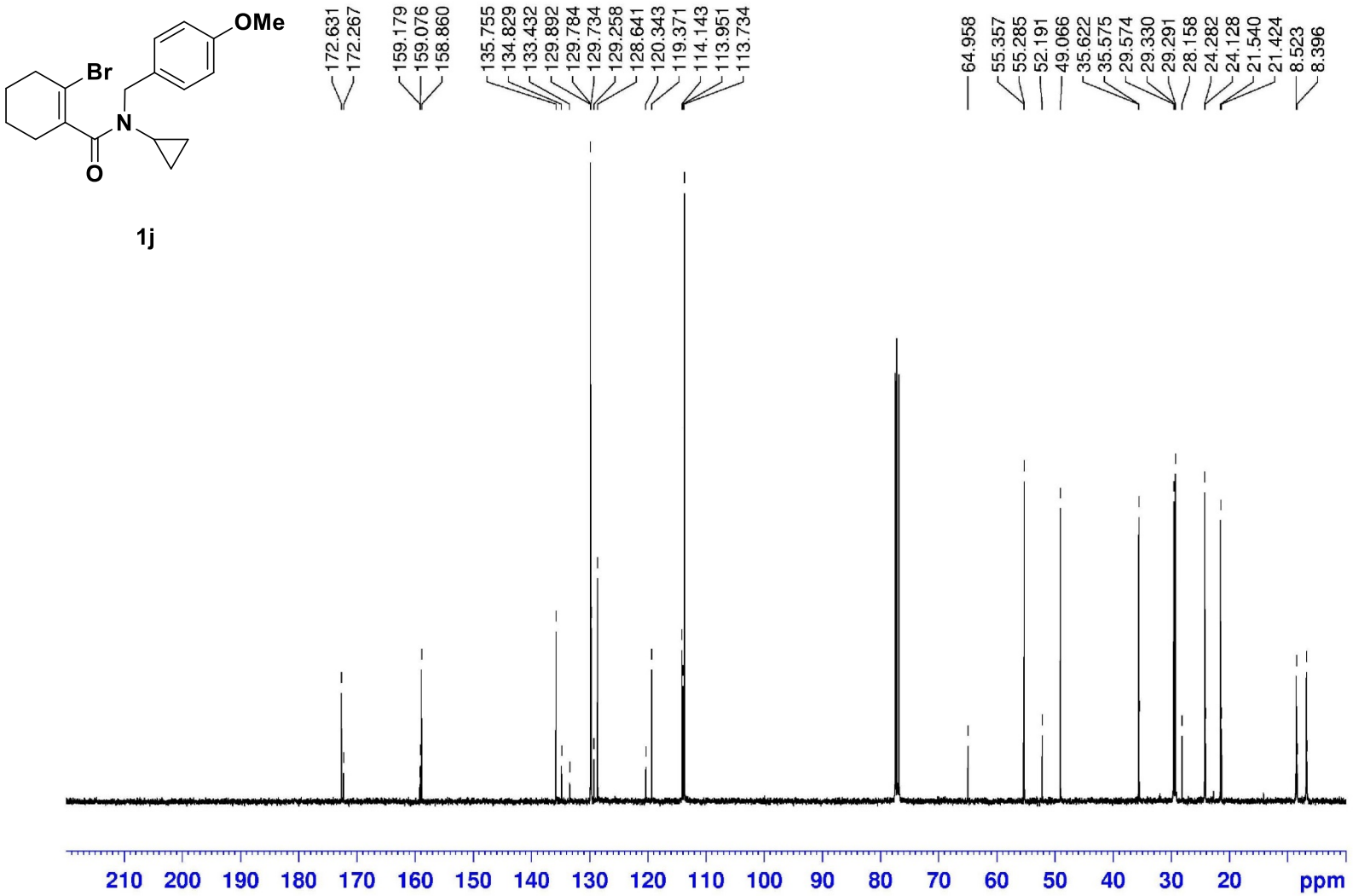
OMe
Br
N
O
1j
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159.076
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134.829
133.432
129.892
129.784
129.734
129.258
128.641
120.343
119.371
114.143
113.951
113.734
64.958
55.357
55.285
52.191
49.066
35.622
35.575
29.574
29.330
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24.128
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21.424
8.523
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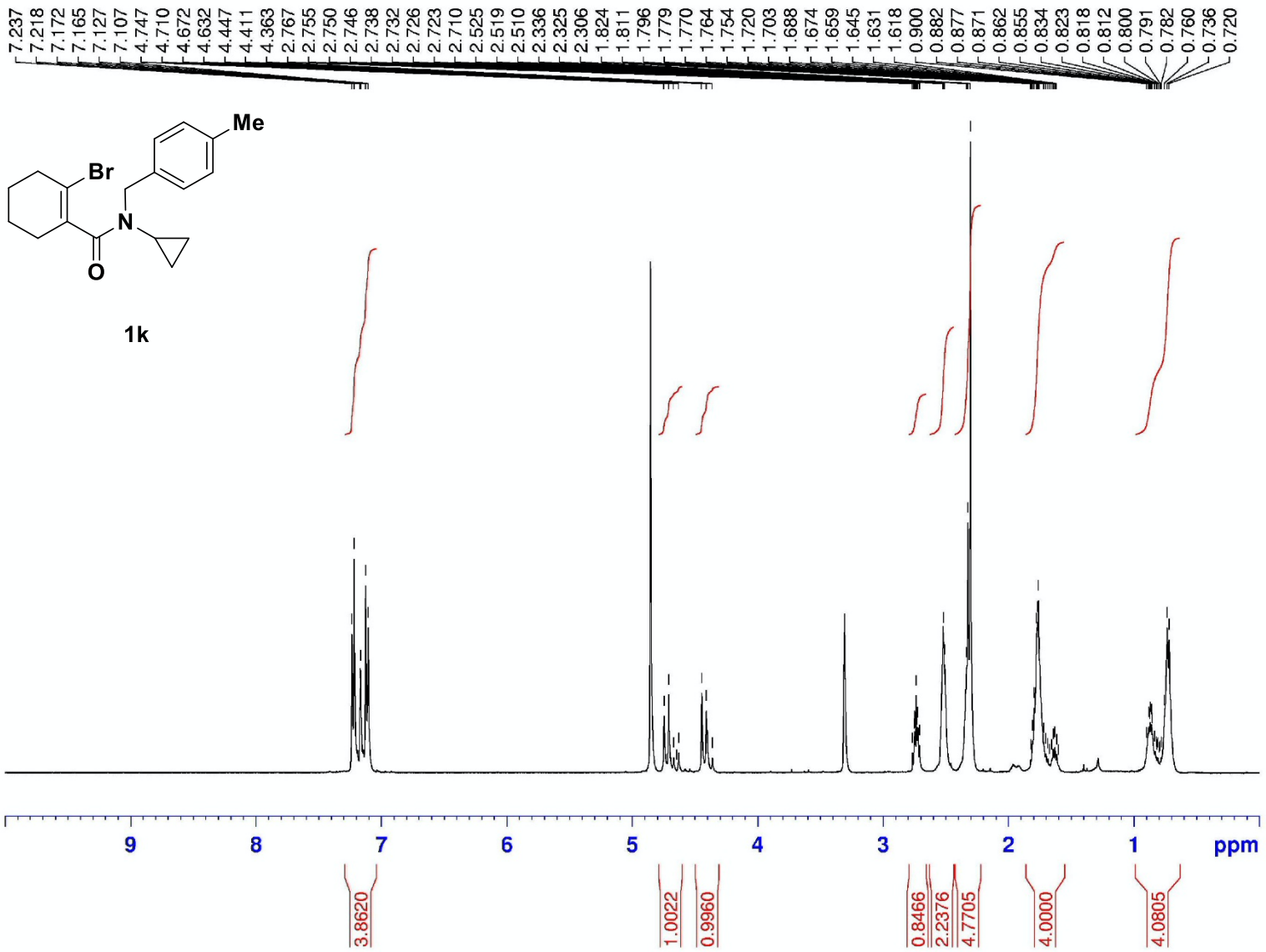
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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4.632
4.447
4.411
4.363
2.767
2.755
2.750
2.746
2.738
2.732
2.726
2.723
2.710
2.525
2.519
2.510
2.336
2.325
2.306
1.824
1.811
1.796
1.779
1.770
1.764
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1.720
1.703
1.688
1.674
1.659
1.645
1.631
1.618
0.900
0.882
0.877
0.871
0.862
0.855
0.834
0.823
0.818
0.812
0.800
0.791
0.782
0.760
0.736
0.720
Me
Br
N
O
1k
9
8
7
6
5
4
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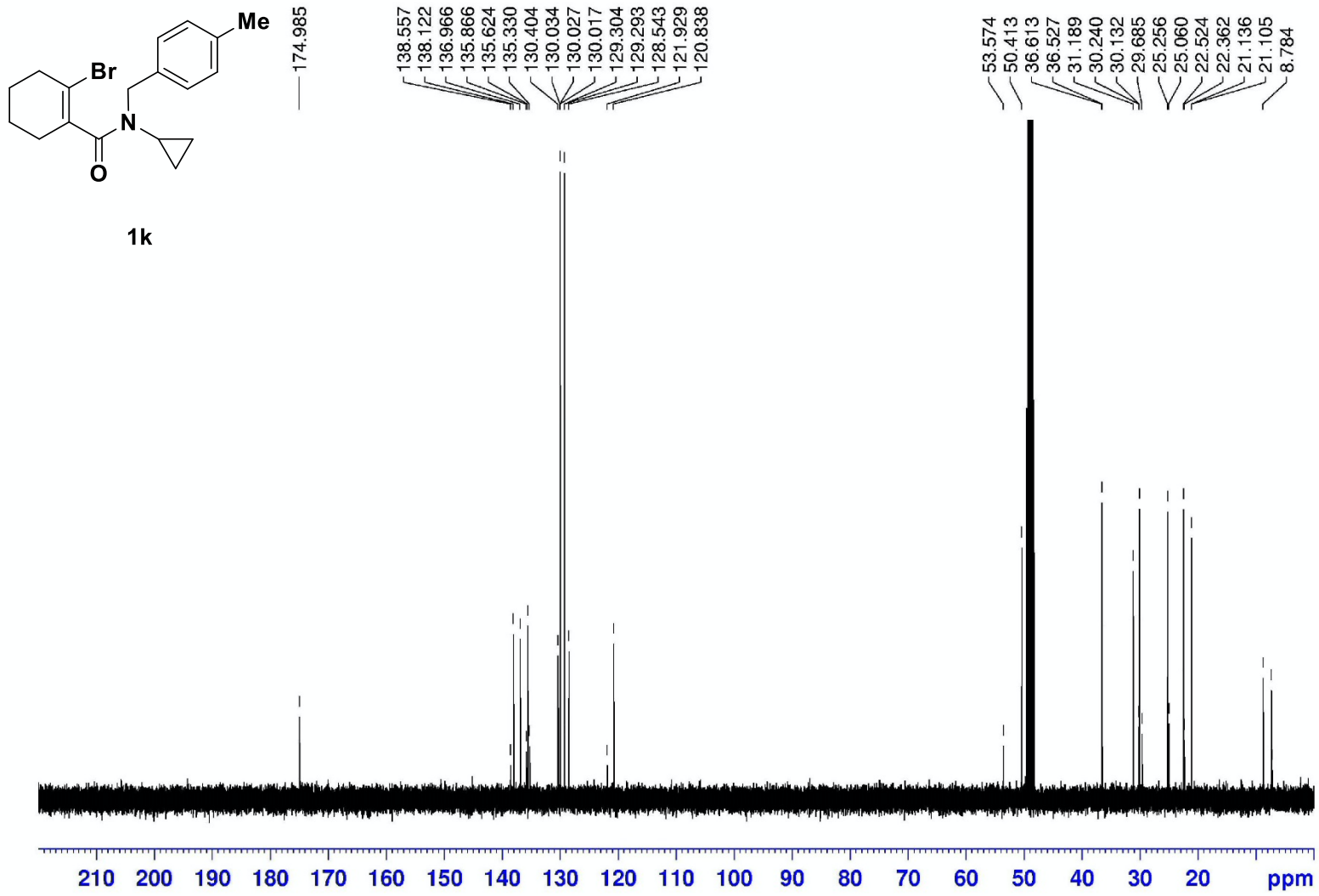
Me
Br
N
O
1k
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135.866
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135.330
130.404
130.034
130.027
130.017
129.304
129.293
128.543
121.929
120.838
53.574
50.413
36.613
36.527
31.189
30.240
30.132
29.685
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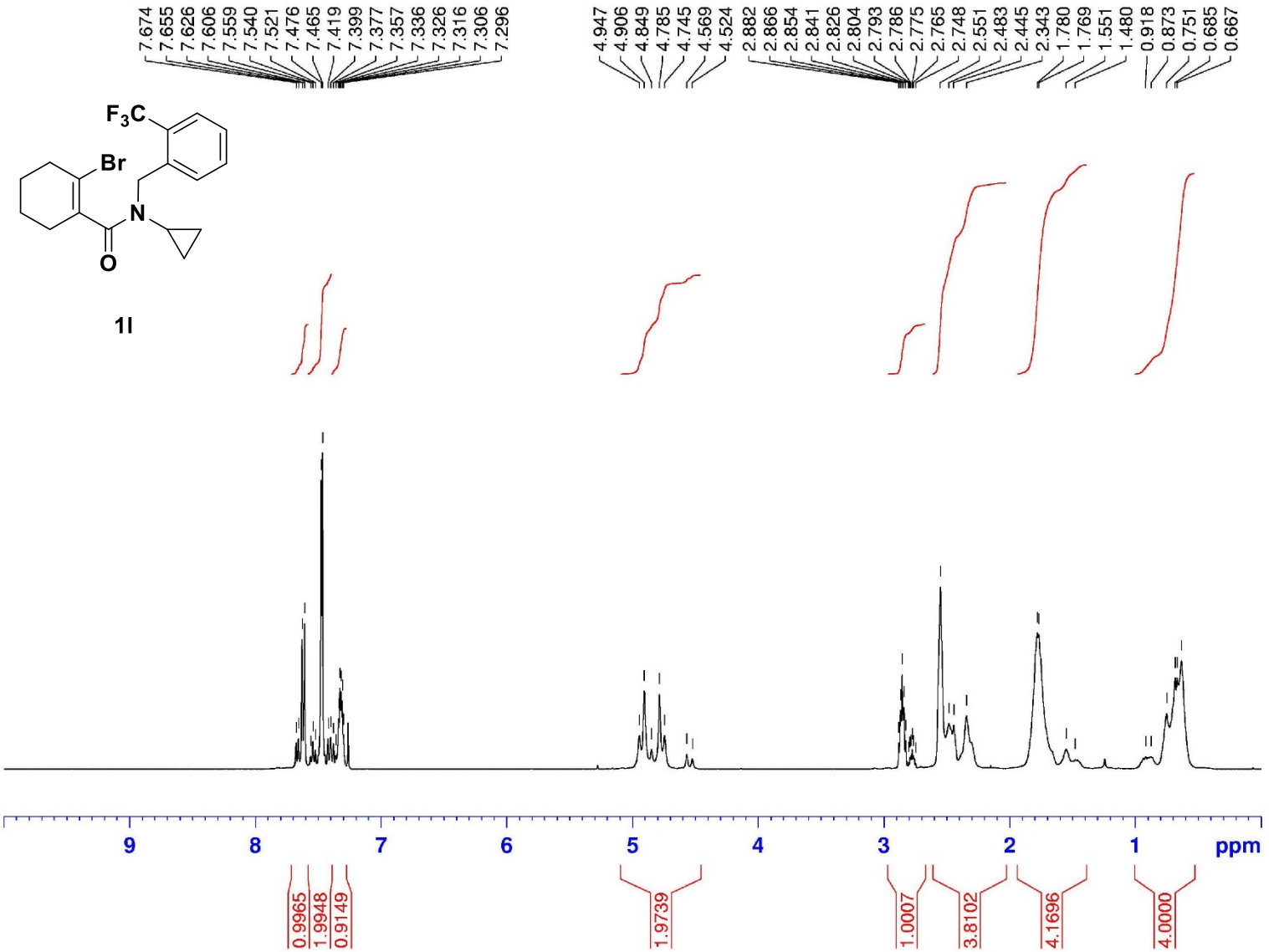
22.524
22.362
21.136
21.105
8.784
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.476
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7.419
7.399
7.377
7.357
7.336
7.326
7.316
7.306
7.296
4.947
4.906
4.849
4.785
4.745
4.569
4.524
2.882
2.866
2.854
2.841
2.826
2.804
2.793
2.786
2.775
2.765
2.748
2.551
2.483
2.445
2.343
1.780
1.769
1.551
1.480
0.918
0.873
0.751
0.685
0.667
F3C
Br
N
O
1l
9
8
7
6
5
4
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1
ppm
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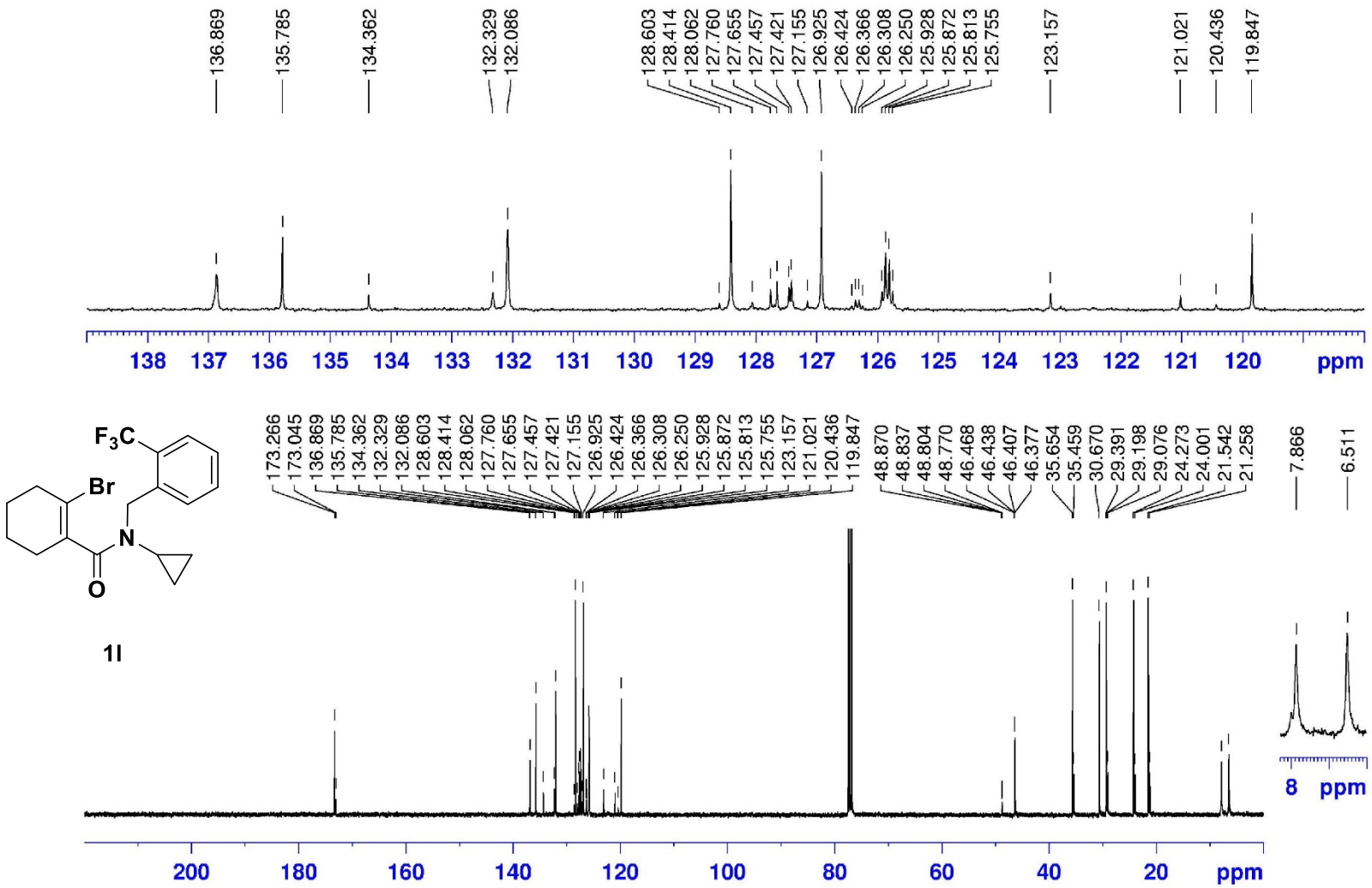
4.0000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127.655
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127.421
127.155
126.925
126.424
126.366
126.308
126.250
125.928
125.872
125.813
125.755
123.157
121.021
120.436
119.847
138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 ppm
F3C
Br
N
O
1l
173.266
173.045
136.869
135.785
134.362
132.329
132.086
128.603
128.414
128.062
127.760
127.655
127.457
127.421
127.155
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125.813
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123.157
121.021
120.436
119.847
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48.837
48.804
48.770
46.468
46.438
46.407
46.377
35.654
35.459
30.670
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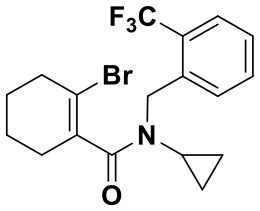
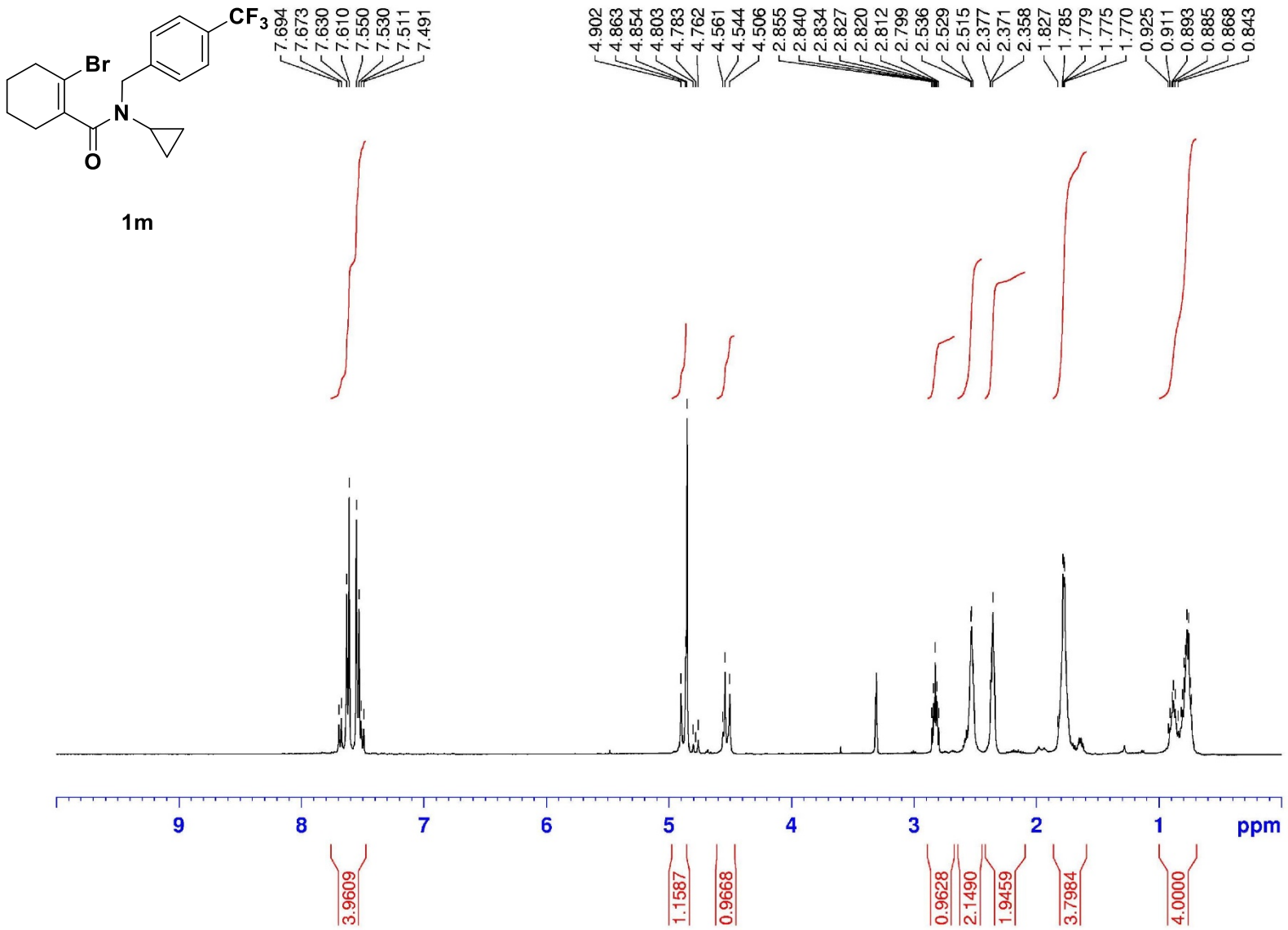
24.273
24.001
21.542
21.258
7.866
6.511
8 ppm
200 180 160 140 120 100 80 60 40 20 ppm



1l


CF3
Br
N
O
1m
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7.673
7.630
7.610
7.550
7.530
7.511
7.491
4.902
4.863
4.854
4.803
4.783
4.762
4.561
4.544
4.506
2.855
2.840
2.834
2.827
2.820
2.812
2.799
2.536
2.529
2.515
2.377
2.371
2.358
1.827
1.785
1.779
1.775
1.770
0.925
0.911
0.893
0.885
0.868
0.843
9
8
7
6
5
4
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0.9668
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2.1490
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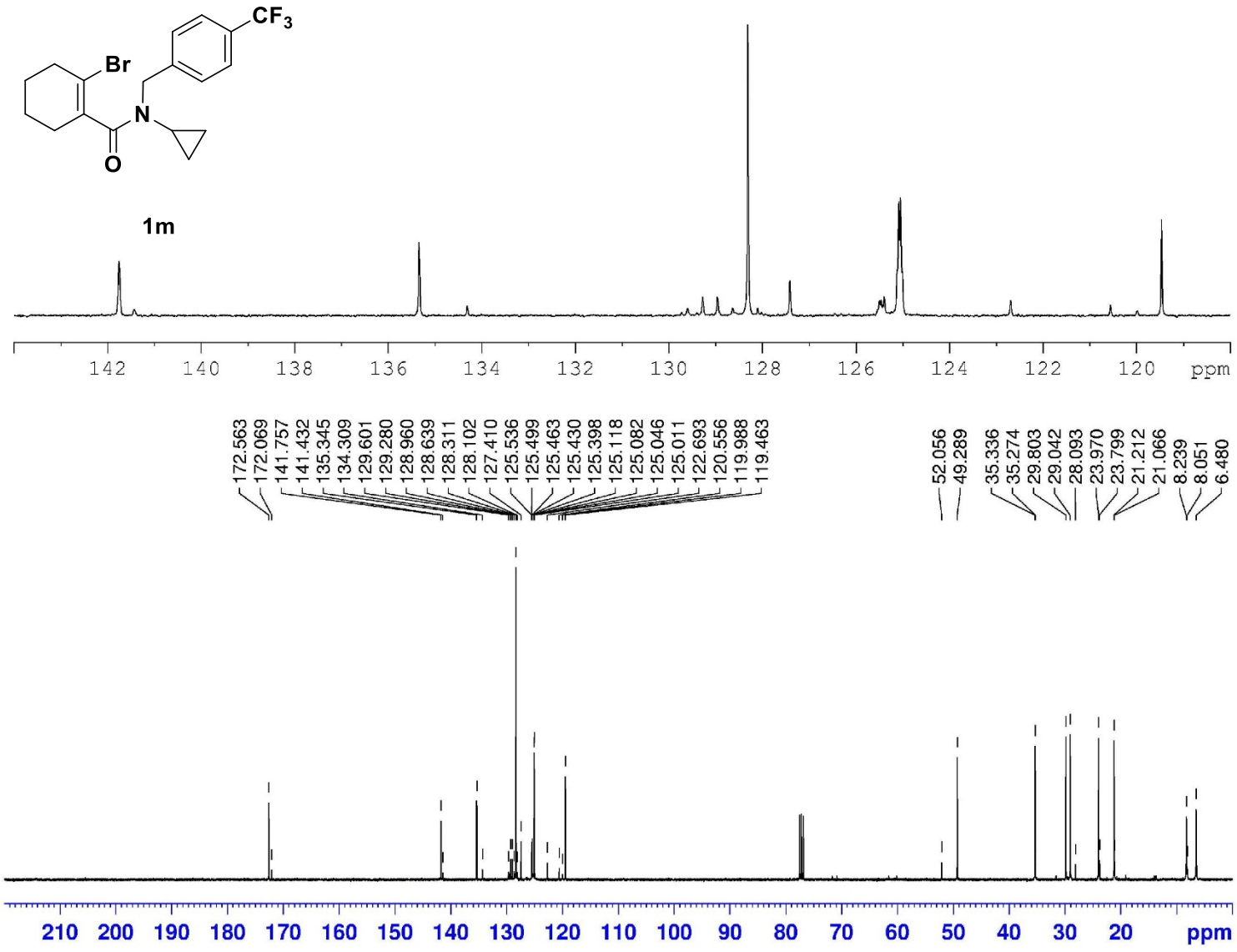
4.0000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Br
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O
1m
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136
134
132
130
128
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122
120
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172.069
141.757
141.432
135.345
134.309
129.601
129.280
128.960
128.639
128.311
128.102
127.410
125.536
125.499
125.463
125.430
125.398
125.118
125.082
125.046
125.011
122.693
120.556
119.988
119.463
52.056
49.289
35.336
35.274
29.803
29.042
28.093
23.970
23.799
21.212
21.066
8.239
8.051
6.480
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200
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160
150
140
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120
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80
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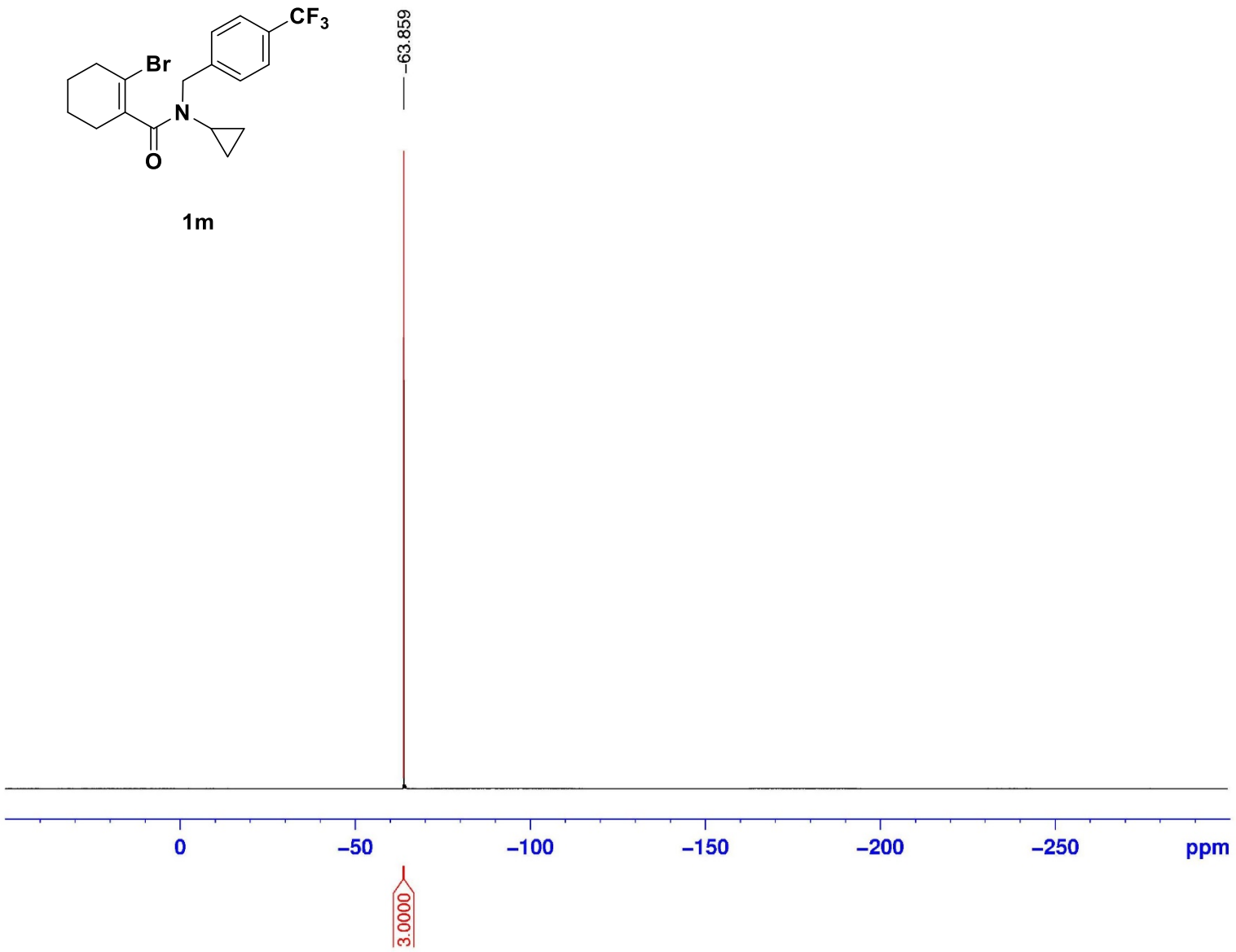
50
40
30
20
ppm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O
1m
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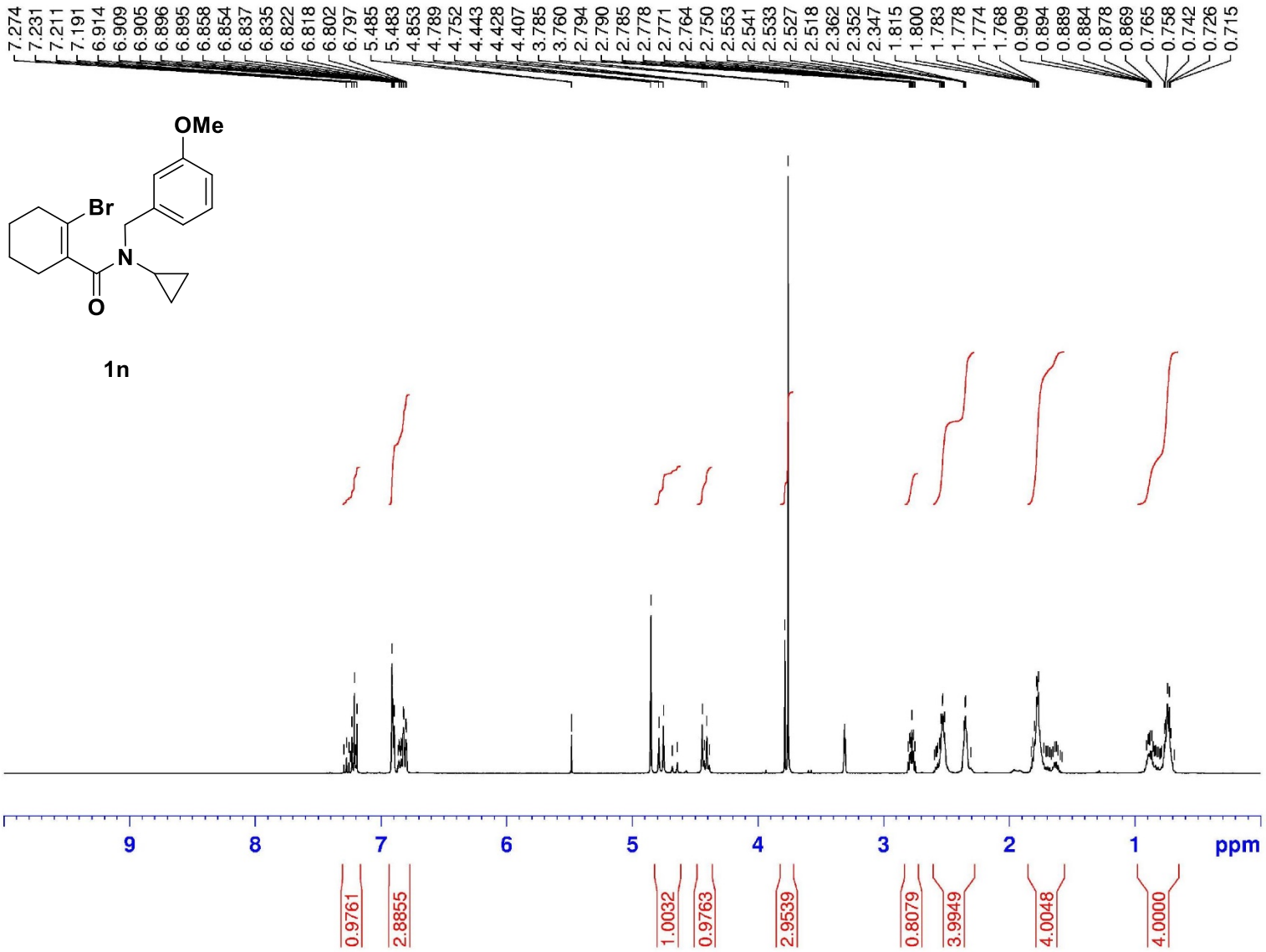
-100
-150
-200
-250
ppm
3.0000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7.231
7.211
7.191
6.914
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6.905
6.896
6.895
6.858
6.854
6.837
6.835
6.822
6.818
6.802
6.797
5.485
5.483
4.853
4.789
4.752
4.443
4.428
4.407
3.785
3.760
2.794
2.790
2.785
2.778
2.771
2.764
2.750
2.553
2.541
2.533
2.527
2.518
2.362
2.352
2.347
1.815
1.800
1.783
1.778
1.774
1.768
0.909
0.894
0.889
0.884
0.878
0.869
0.765
0.758
0.742
0.726
0.715
OMe
Br
N
O
1n
9
8
7
6
5
4
3
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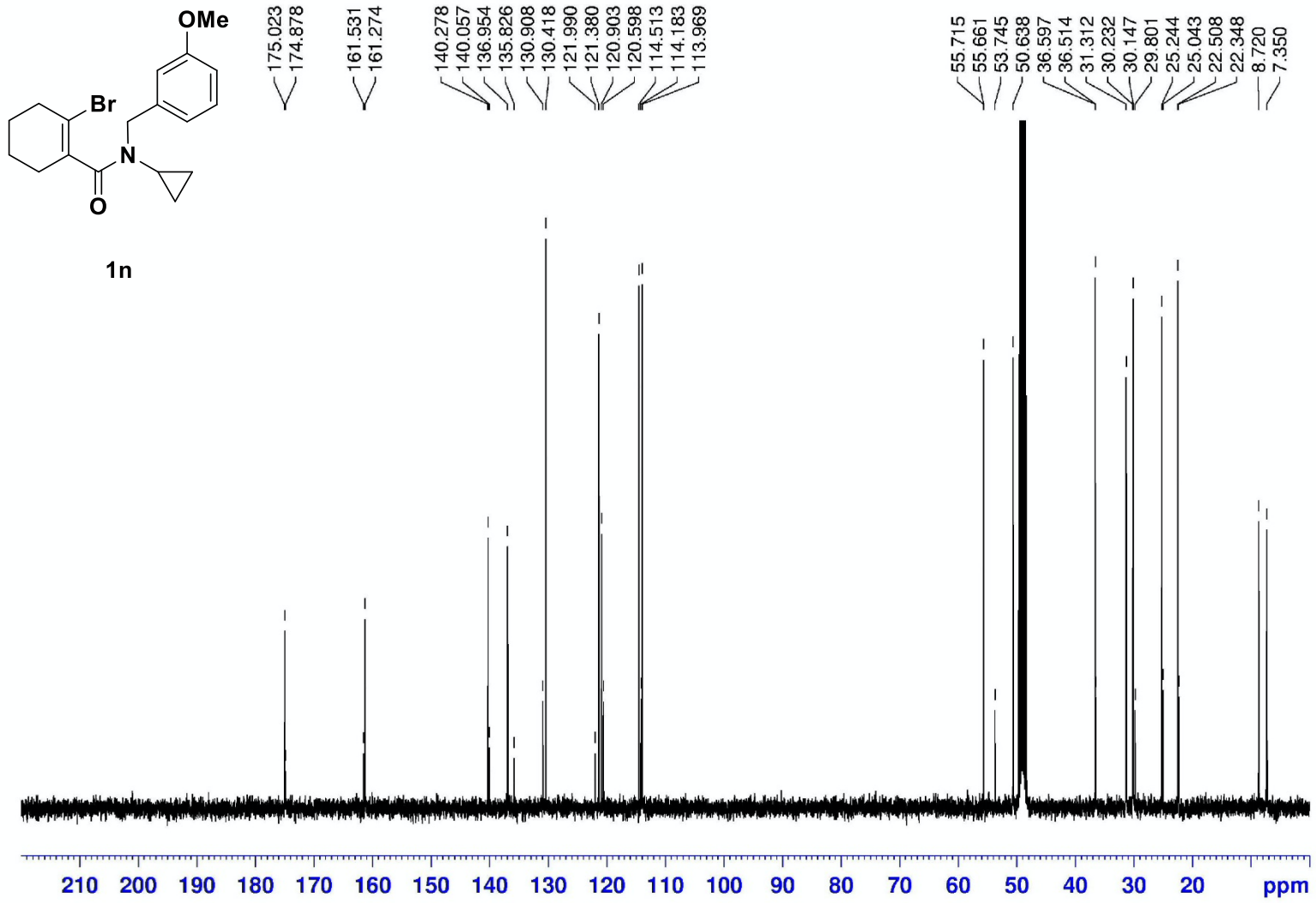
OMe
Br
N
O
1n
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161.274
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140.057
136.954
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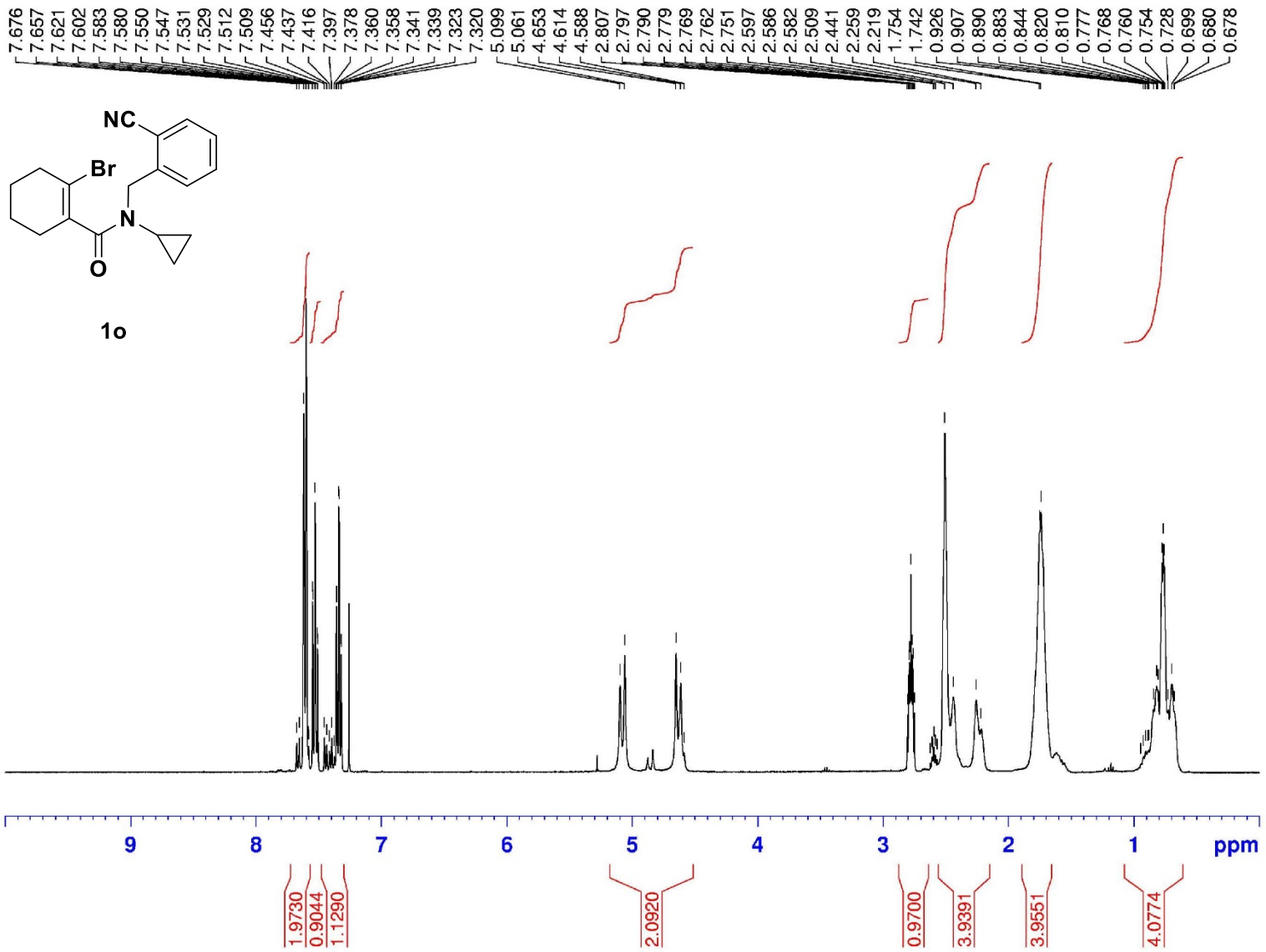
130.418
121.990
121.380
120.903
120.598
114.513
114.183
113.969
55.715
55.661
53.745
50.638
36.597
36.514
31.312
30.232
30.147
29.801
25.244
25.043
22.508
22.348
8.720
7.350
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.547
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7.529
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7.509
7.456
7.437
7.416
7.397
7.378
7.360
7.358
7.341
7.339
7.323
7.320
5.099
5.061
4.653
4.614
4.588
2.807
2.797
2.790
2.779
2.769
2.762
2.751
2.597
2.586
2.582
2.509
2.441
2.259
2.219
1.754
1.742
0.926
0.907
0.890
0.883
0.844
0.820
0.810
0.777
0.768
0.760
0.754
0.728
0.699
0.680
0.678
NC
Br
N
O
1o
9
8
7
6
5
4
3
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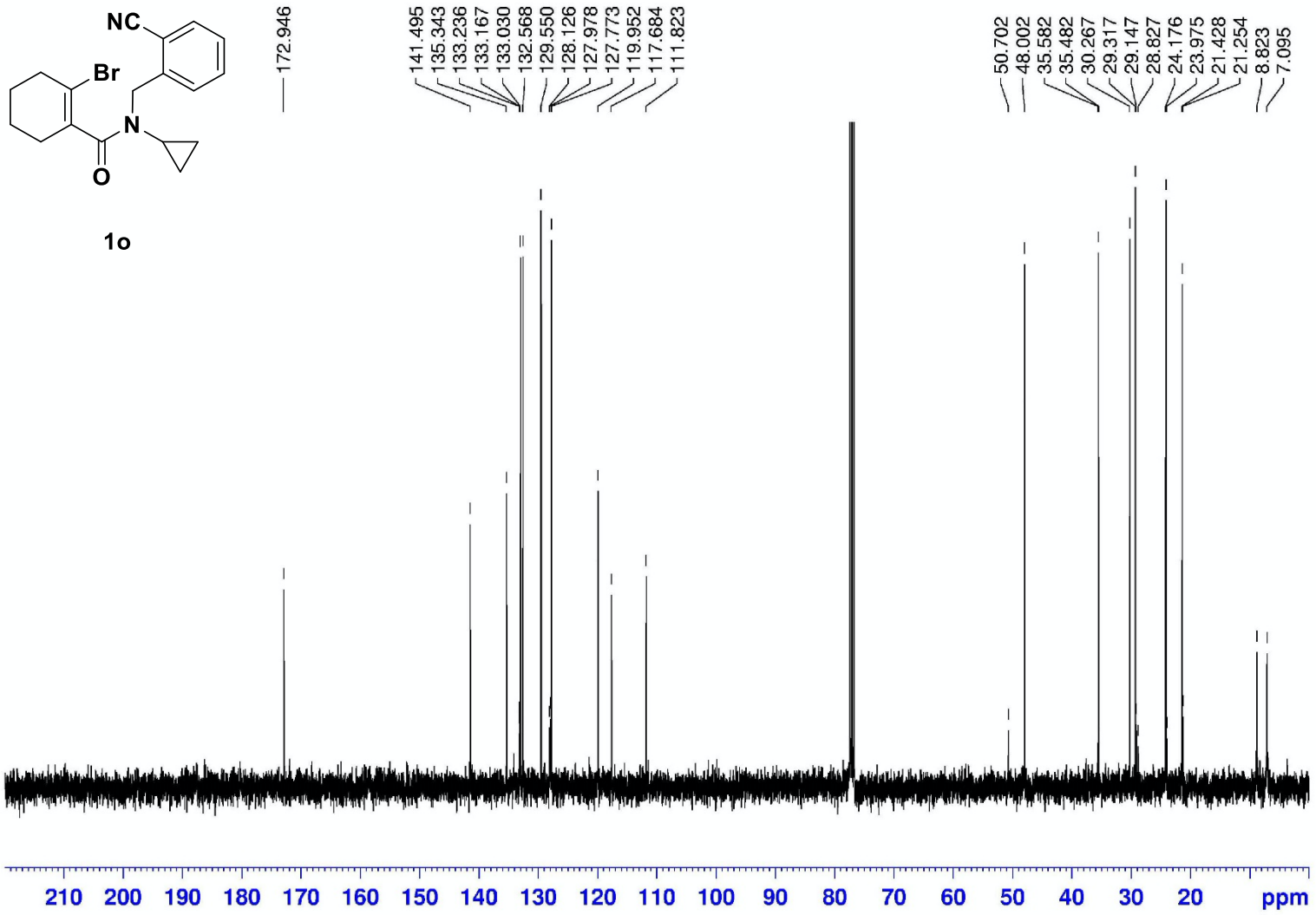
4.0774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Br
N
O
1o
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133.167
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132.568
129.550
128.126
127.978
127.773
119.952
117.684
111.823
50.702
48.002
35.582
35.482
30.267
29.317
29.147
28.827
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23.975
21.428
21.254
8.823
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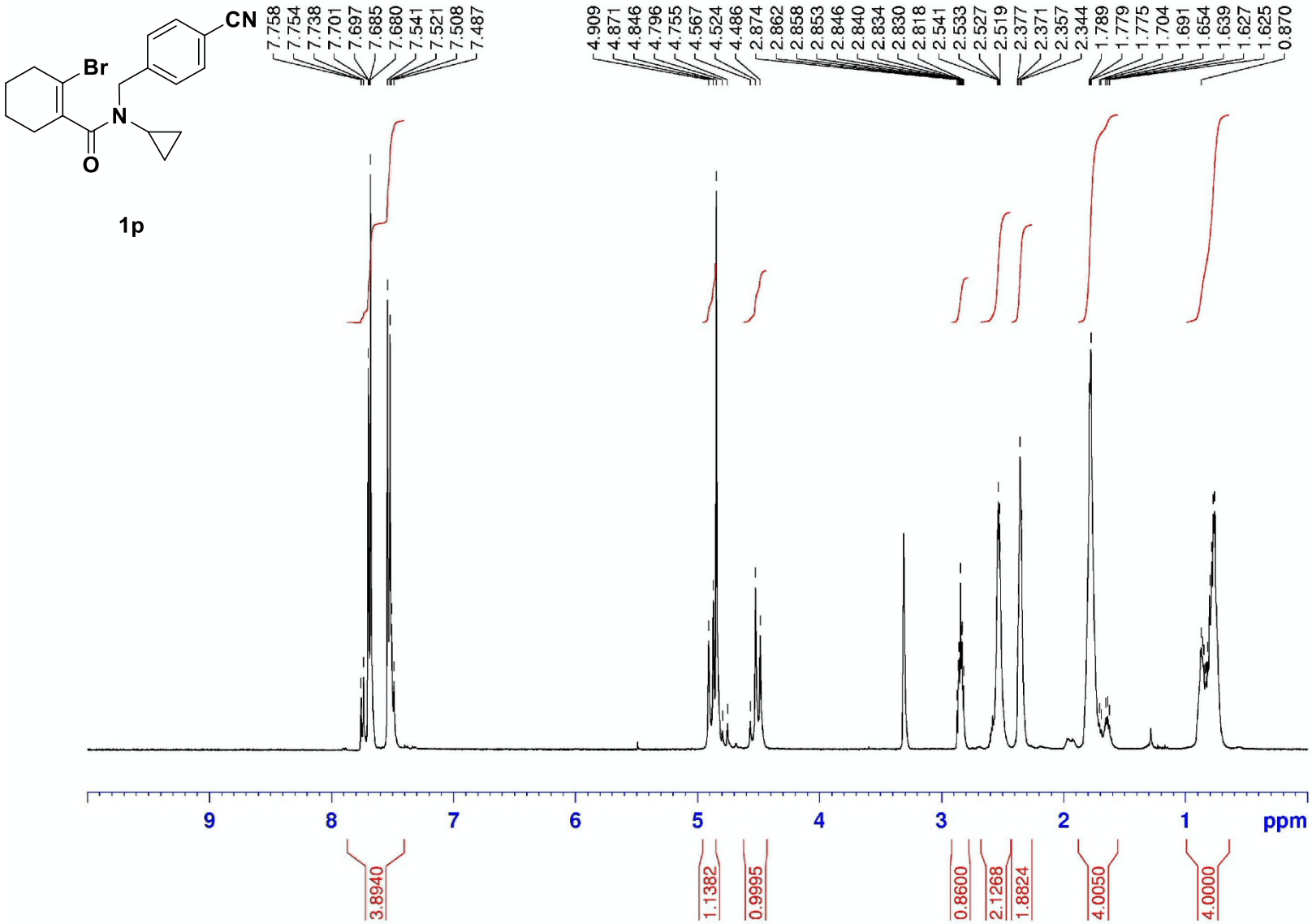
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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Br
N
O
1p
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7.738
7.701
7.697
7.685
7.680
7.541
7.521
7.508
7.487
4.909
4.871
4.846
4.796
4.755
4.567
4.524
4.486
2.874
2.862
2.858
2.853
2.846
2.840
2.834
2.830
2.818
2.541
2.533
2.527
2.519
2.377
2.371
2.357
2.344
1.789
1.779
1.775
1.704
1.691
1.654
1.639
1.627
1.625
0.870
9
8
7
6
5
4
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ppm
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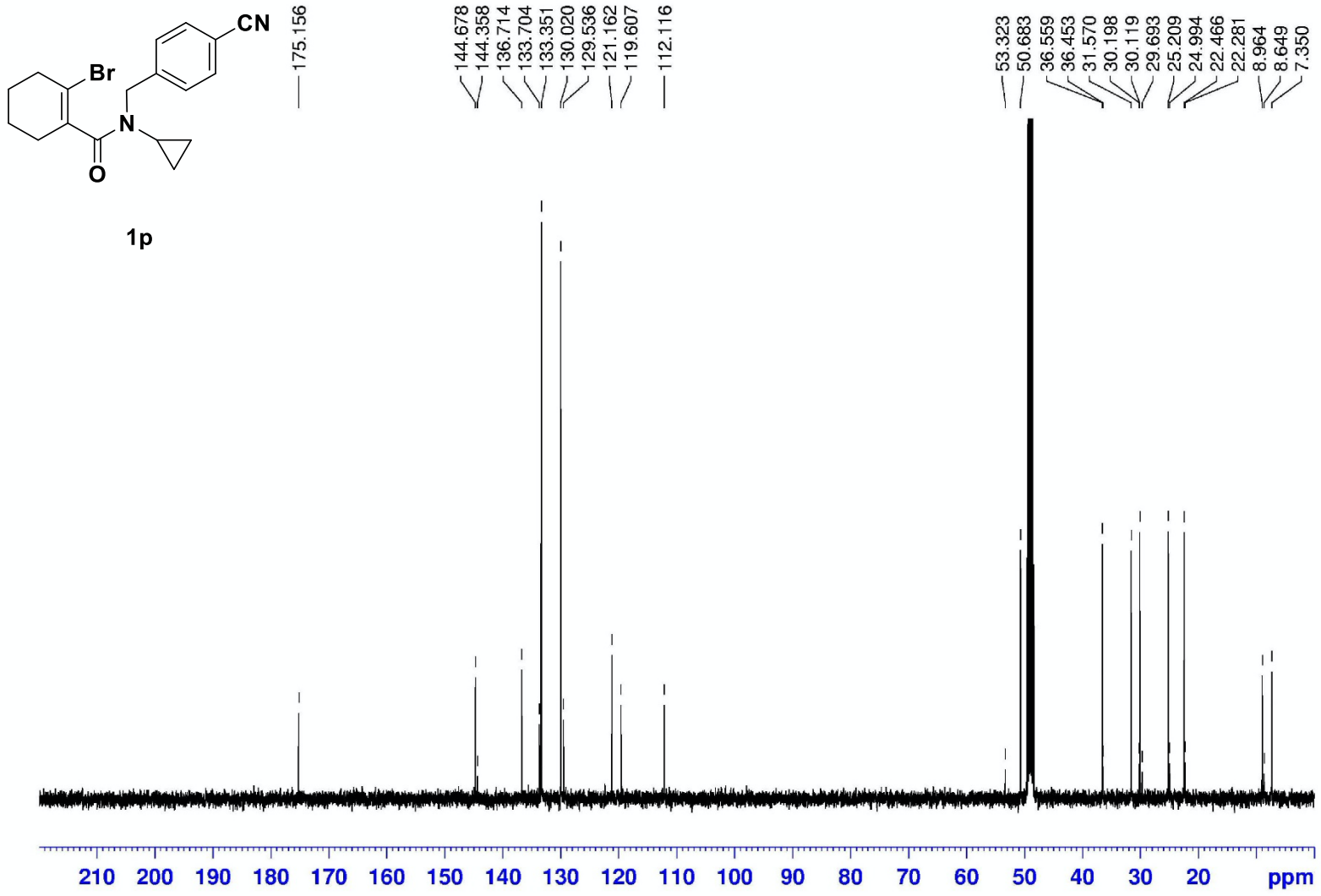
4.0000


CN
Br
N
O
1p
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144.358
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133.704
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130.020
129.536
121.162
119.607
112.116
53.323
50.683
36.559
36.453
31.570
30.198
30.119
29.693
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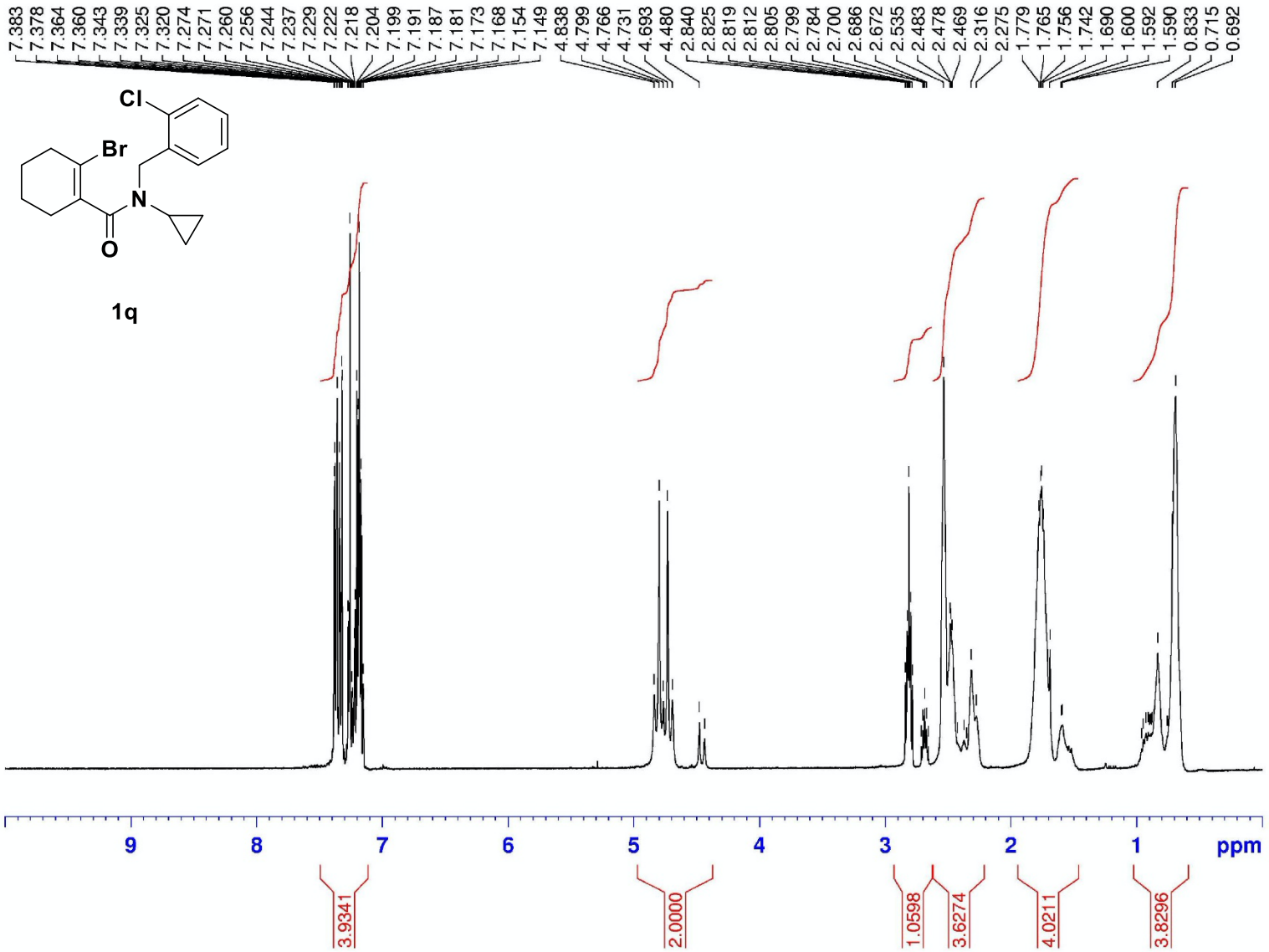
22.466
22.281
8.964
8.649
7.350
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.364
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7.343
7.339
7.325
7.320
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7.271
7.260
7.256
7.244
7.237
7.229
7.222
7.218
7.204
7.199
7.191
7.187
7.181
7.173
7.168
7.154
7.149
4.838
4.799
4.766
4.731
4.693
4.480
2.840
2.825
2.819
2.812
2.805
2.799
2.784
2.700
2.686
2.672
2.535
2.483
2.478
2.469
2.316
2.275
1.779
1.765
1.756
1.742
1.690
1.600
1.592
1.590
0.833
0.715
0.692
Cl
Br
N
O
1q
9
8
7
6
5
4
3
2
1
ppm
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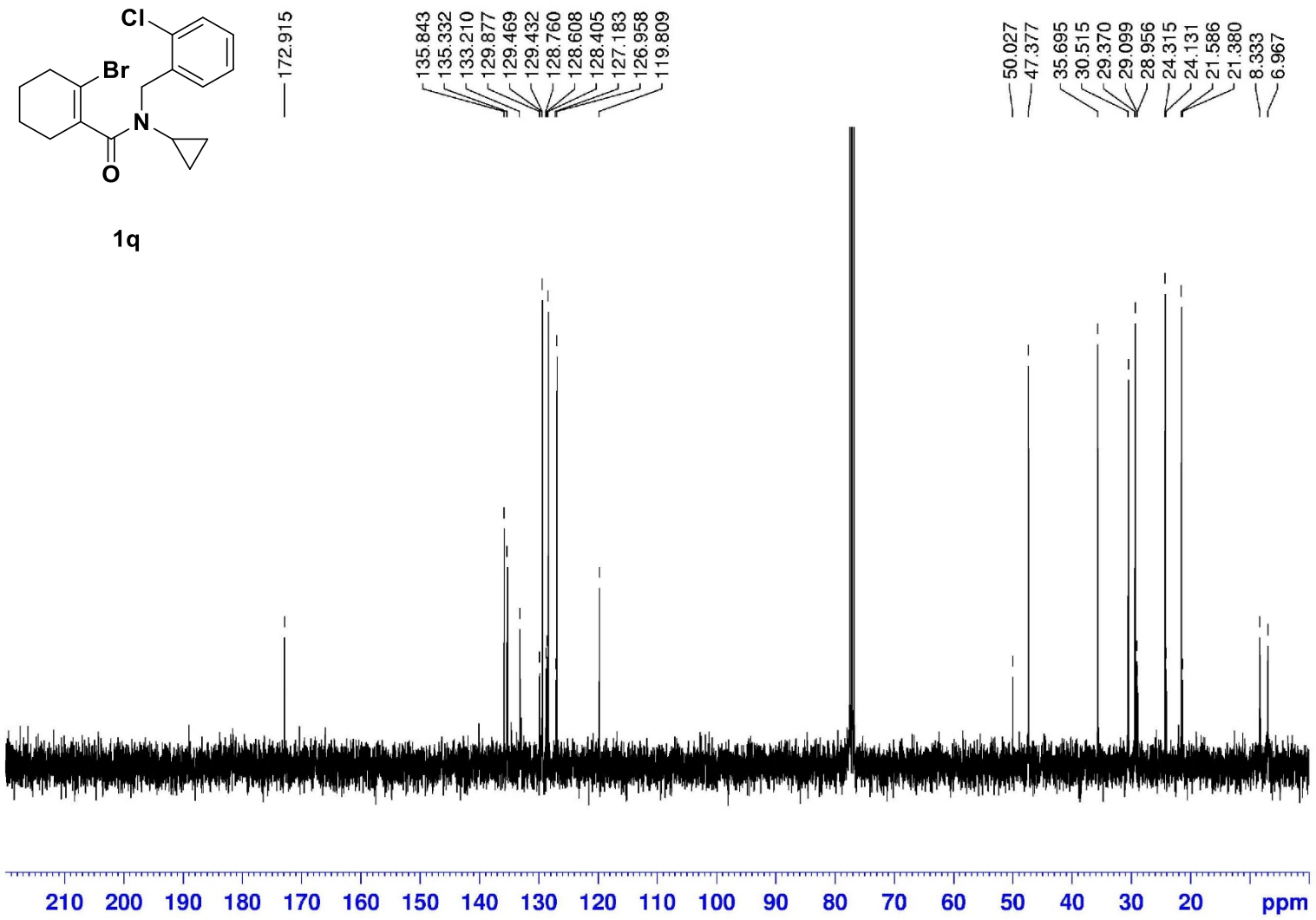
1.0598
3.6274
4.0211
3.8296


Cl
Br
N
O
1q
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135.332
133.210
129.877
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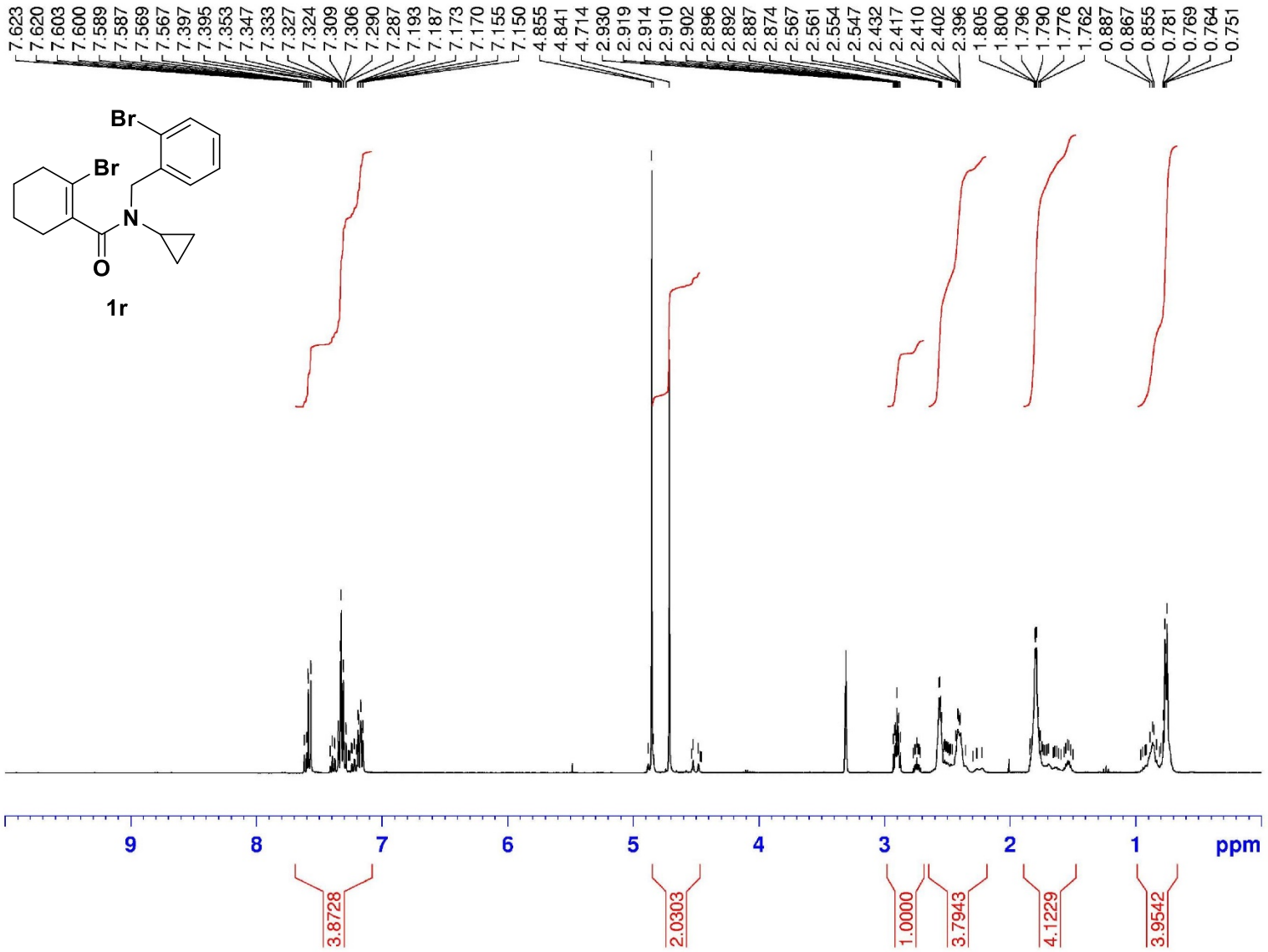
129.432
128.760
128.608
128.405
127.183
126.958
119.809
50.027
47.377
35.695
30.515
29.370
29.099
28.956
24.315
24.131
21.586
21.380
8.333
6.967
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.587
7.569
7.567
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7.395
7.353
7.347
7.333
7.327
7.324
7.309
7.306
7.290
7.287
7.193
7.187
7.173
7.170
7.155
7.150
4.855
4.841
4.714
2.930
2.919
2.914
2.910
2.902
2.896
2.892
2.887
2.874
2.567
2.561
2.554
2.547
2.432
2.417
2.410
2.402
2.396
1.805
1.800
1.796
1.790
1.776
1.762
0.887
0.867
0.855
0.781
0.769
0.764
0.751
Br
Br
N
O
1r
9
8
7
6
5
4
3
2
1
ppm
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1.0000
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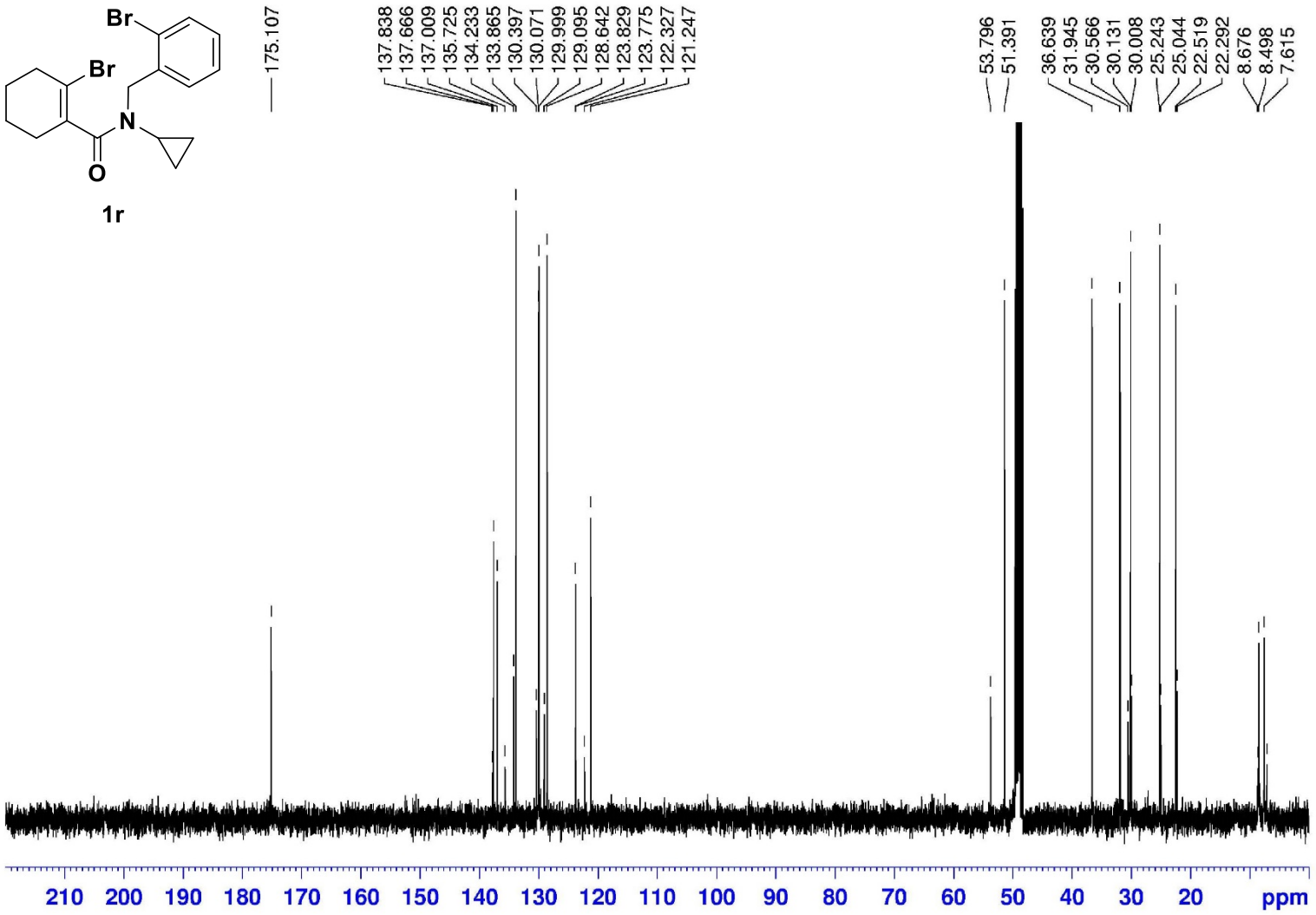
3.9542


Br
Br
N
O
1r
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137.009
135.725
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133.865
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129.999
129.095
128.642
123.829
123.775
122.327
121.247
53.796
51.391
36.639
31.945
30.566
30.131
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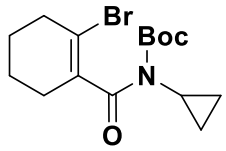
22.519
22.292
8.676
8.498
7.615
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


Br
Boc
N
O

1s

2.640
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2.611
2.601
2.592
2.584
2.574
2.470
2.465
2.459
2.450
2.444
2.316
2.310
2.301
2.296
2.290
1.782
1.750
1.743
1.735
1.720
1.714
1.705
1.687
1.530
0.995
9
8
7
6
5
4
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1
ppm
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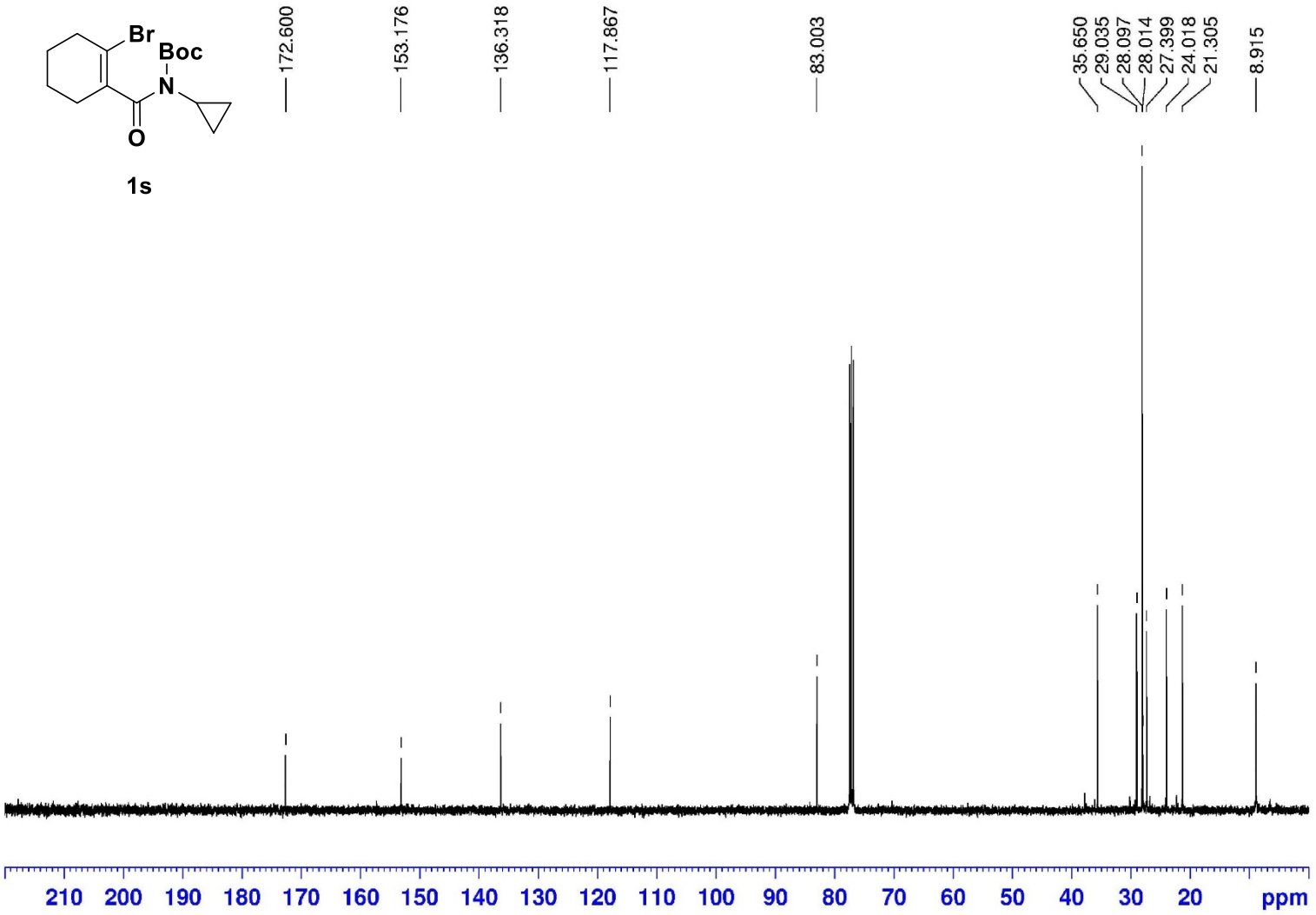
Br
Boc
N
O
1s
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83.003
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28.014
27.399
24.018
21.305
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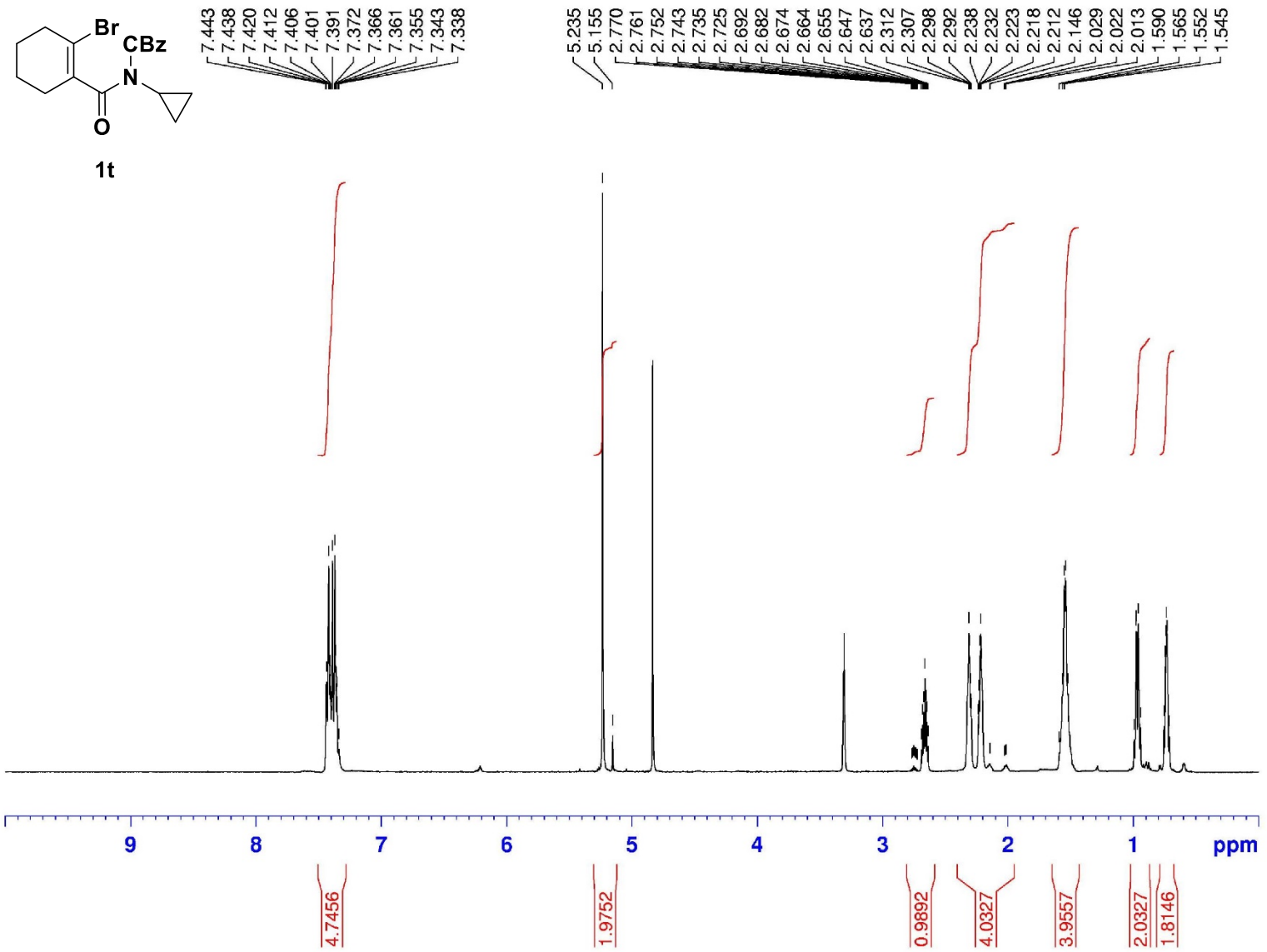
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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CBz
N
O
1t
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7.412
7.406
7.401
7.391
7.372
7.366
7.361
7.355
7.343
7.338
5.235
5.155
2.770
2.761
2.752
2.743
2.735
2.725
2.692
2.682
2.674
2.664
2.655
2.647
2.637
2.312
2.307
2.298
2.292
2.238
2.232
2.223
2.218
2.212
2.146
2.029
2.022
2.013
1.590
1.565
1.552
1.545
9
8
7
6
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4
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1
ppm
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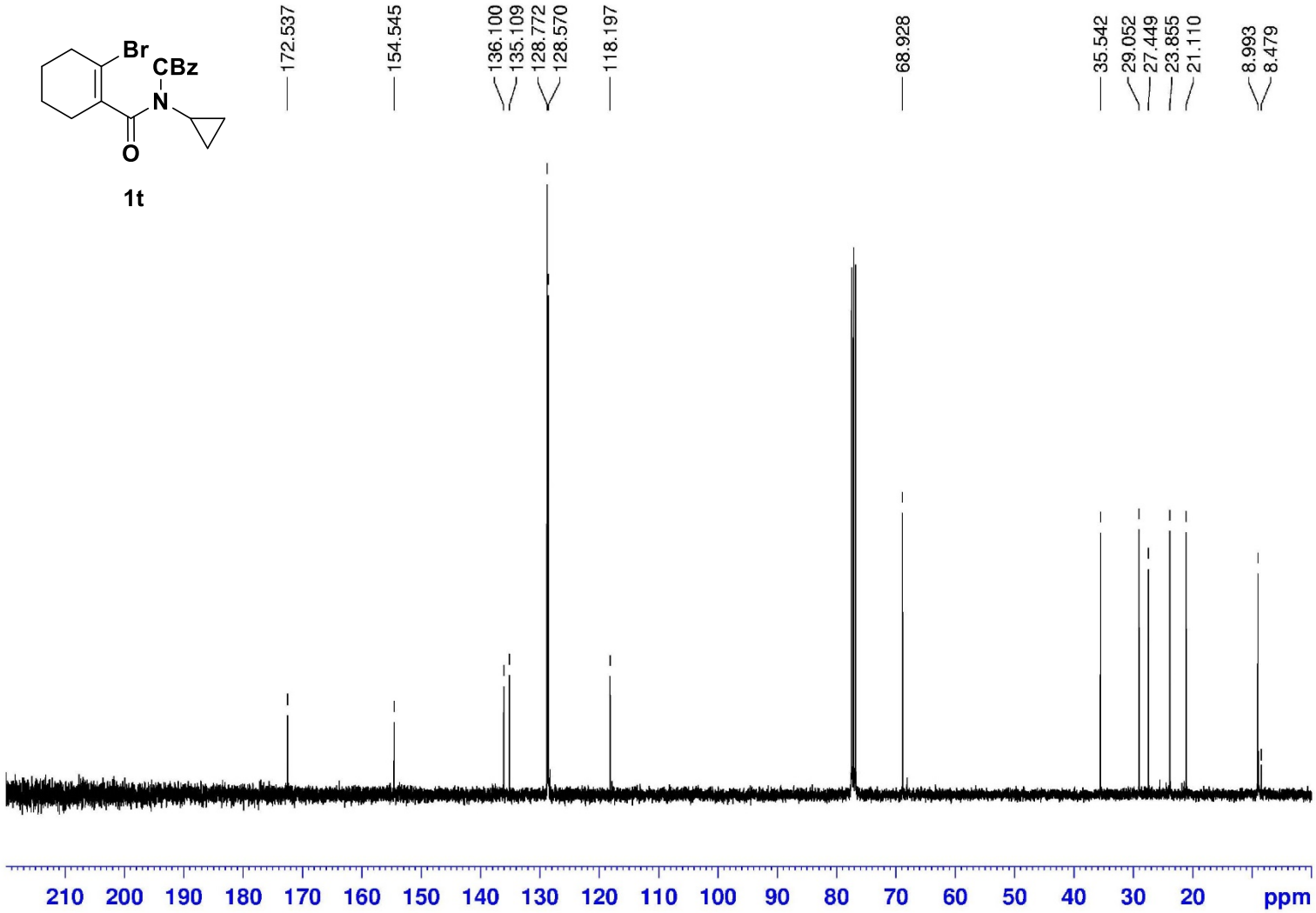
1.8146


Br
CBz
N
O
1t
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135.109
128.772
128.570
118.197
68.928
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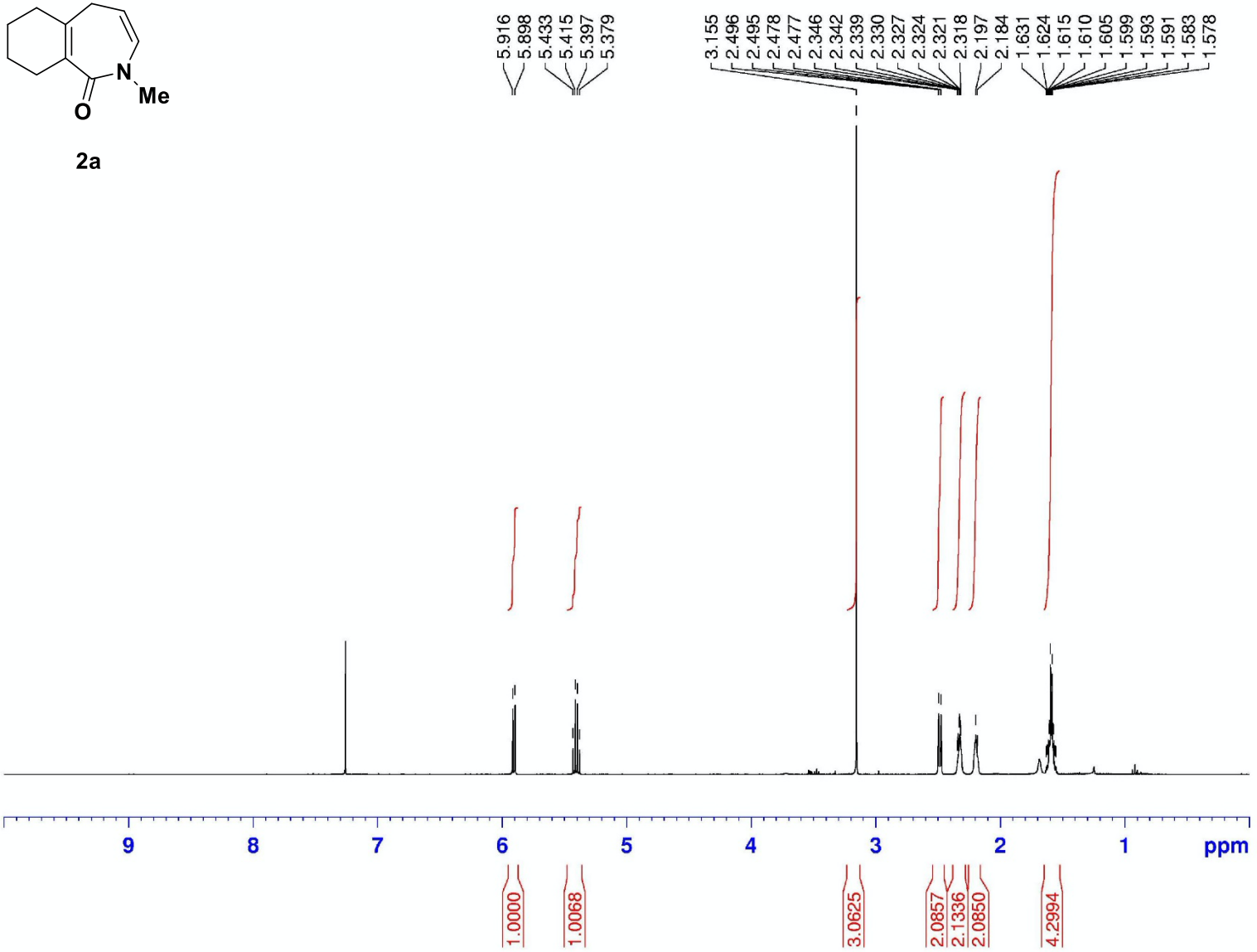
27.449
23.855
21.110
8.993
8.479
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


N
Me
O
2a
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5.415
5.397
5.379
3.155
2.496
2.495
2.478
2.477
2.346
2.342
2.339
2.330
2.327
2.324
2.321
2.318
2.197
2.184
1.631
1.624
1.615
1.610
1.605
1.599
1.593
1.591
1.583
1.578
9
8
7
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1
ppm
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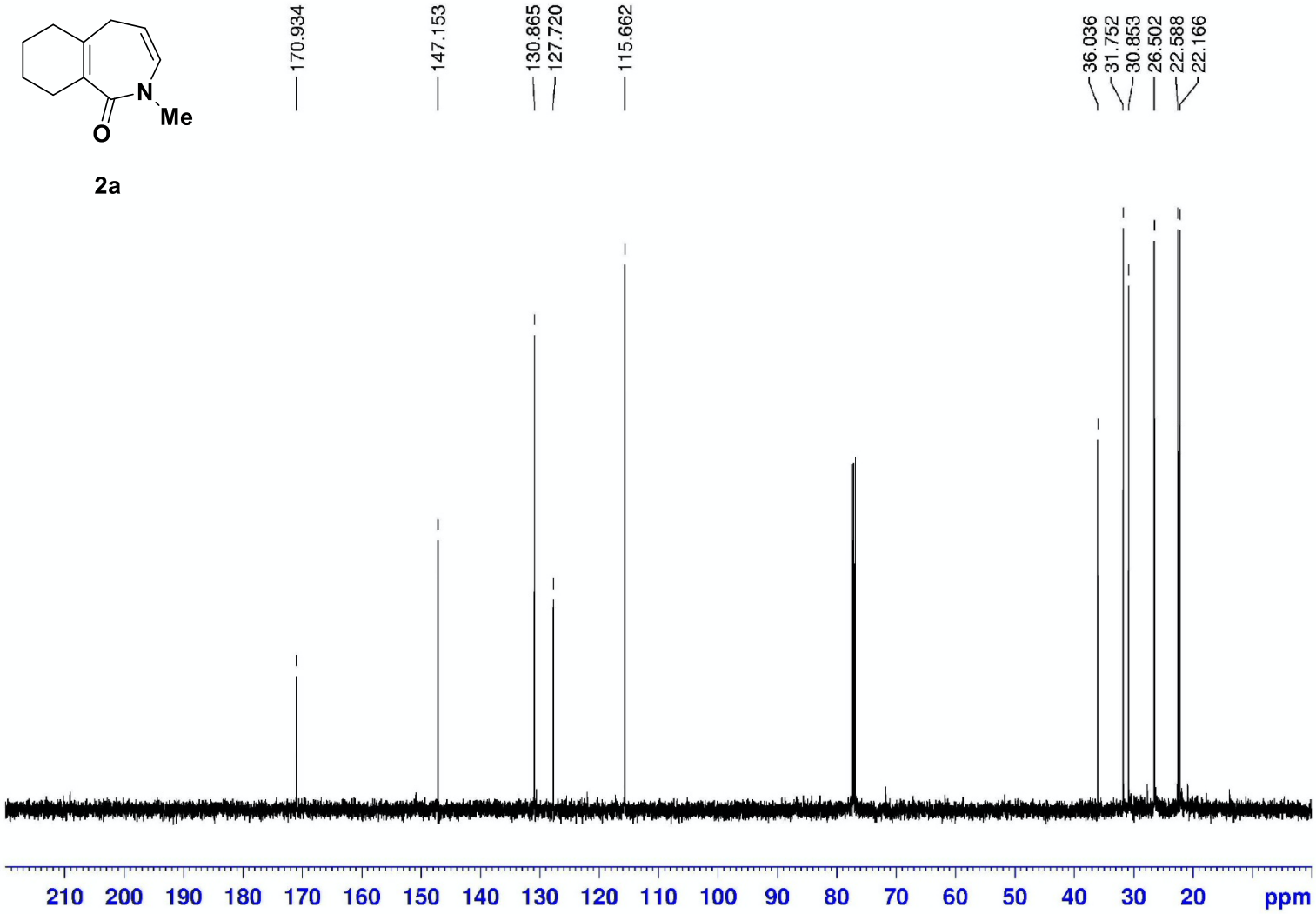
2.0850
4.2994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147.153
130.865
127.720
115.662
36.036
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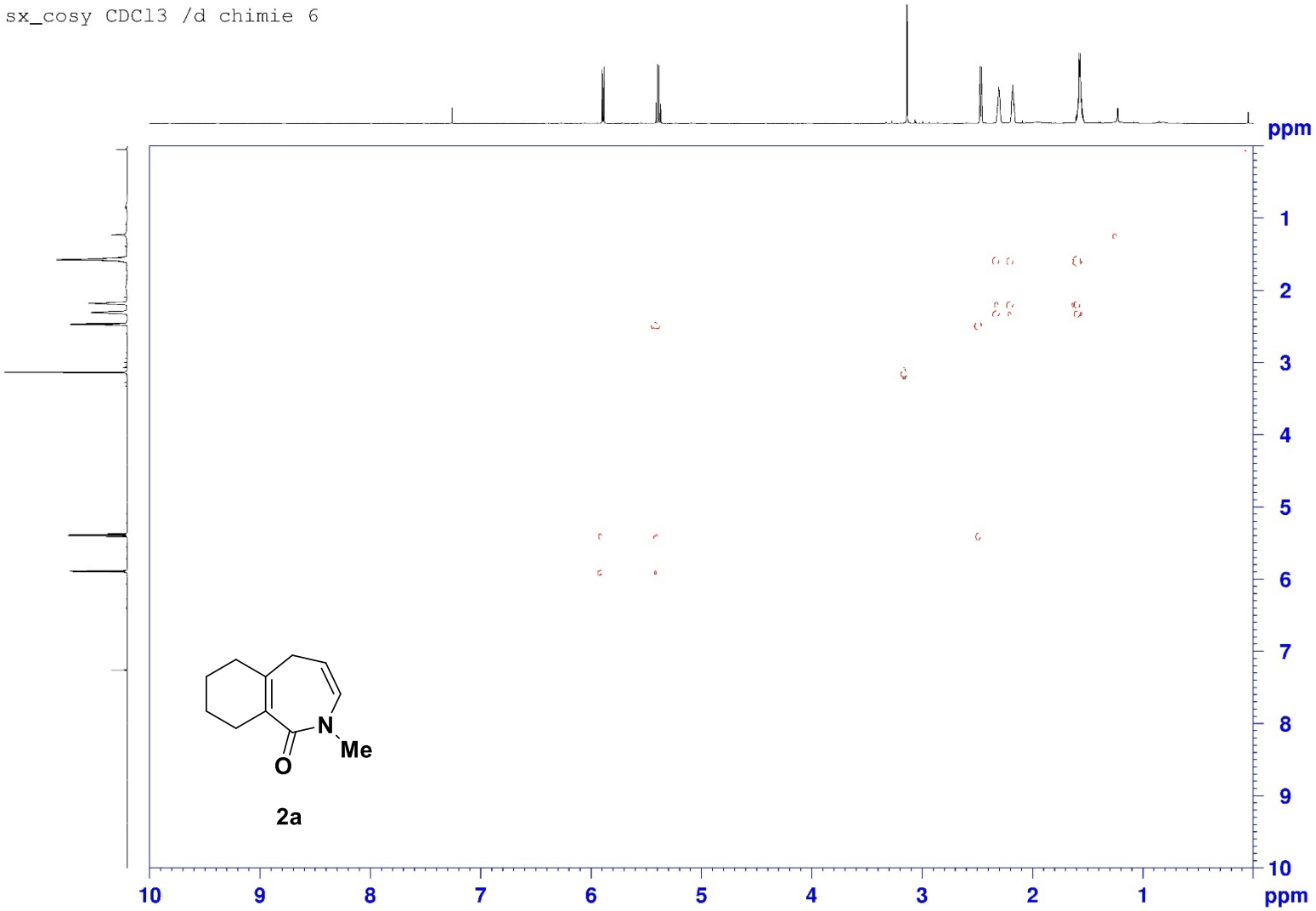
22.588
22.166
N
Me
O
2a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


sx_cosy CDCl3 /d chimie 6
ppm
1
2
3
4
5
6
7
8
9
10
10
9
8
7
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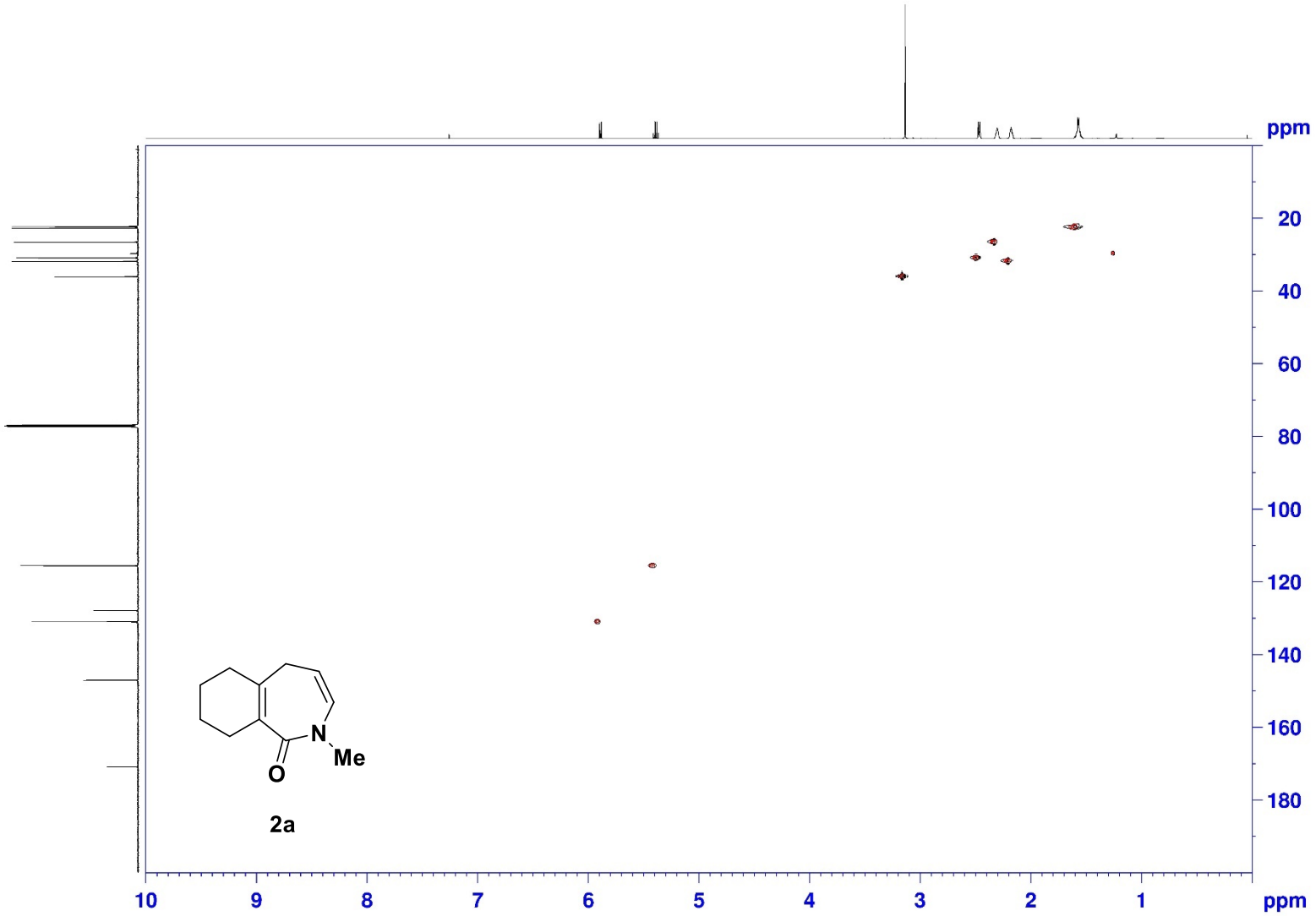
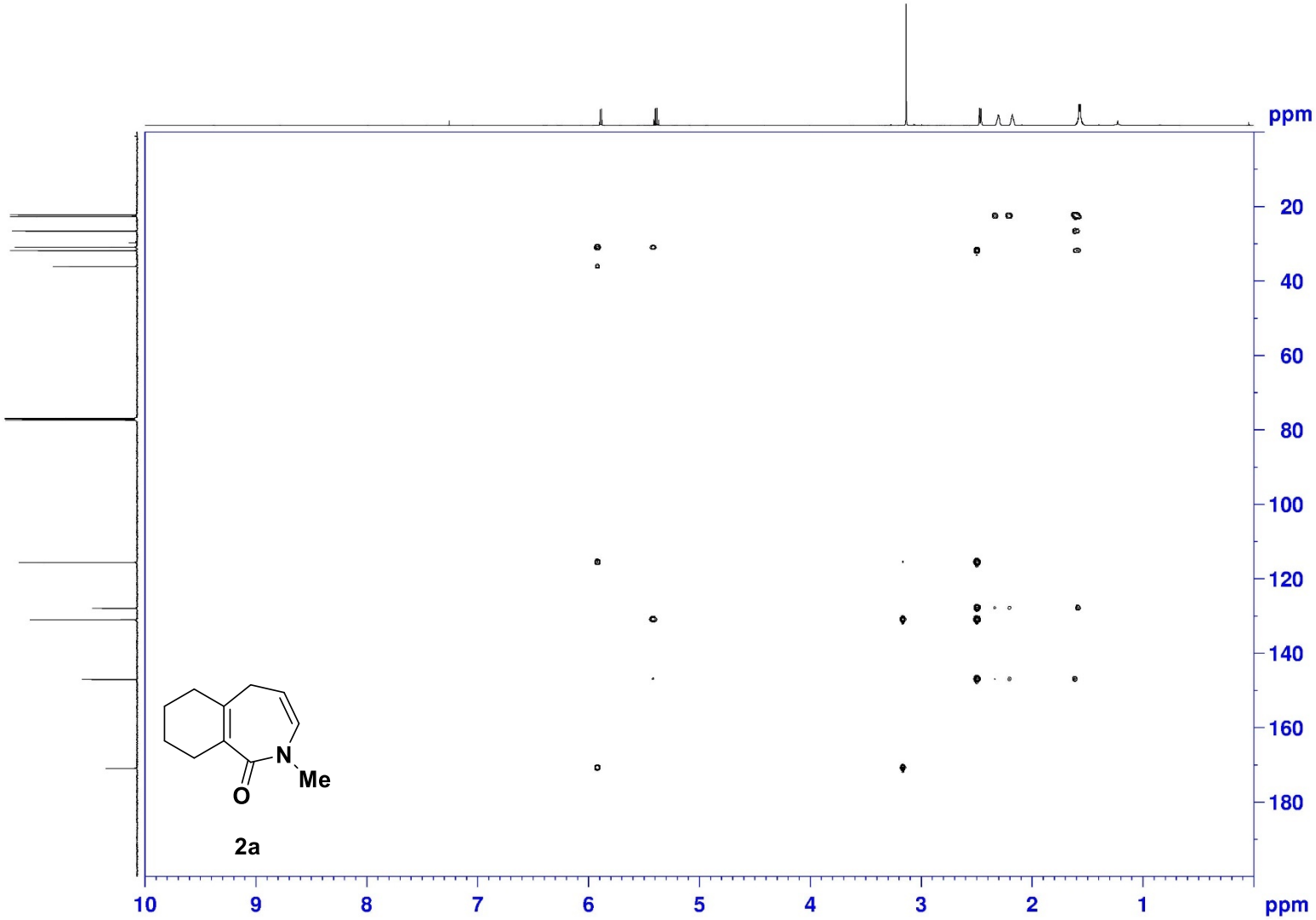
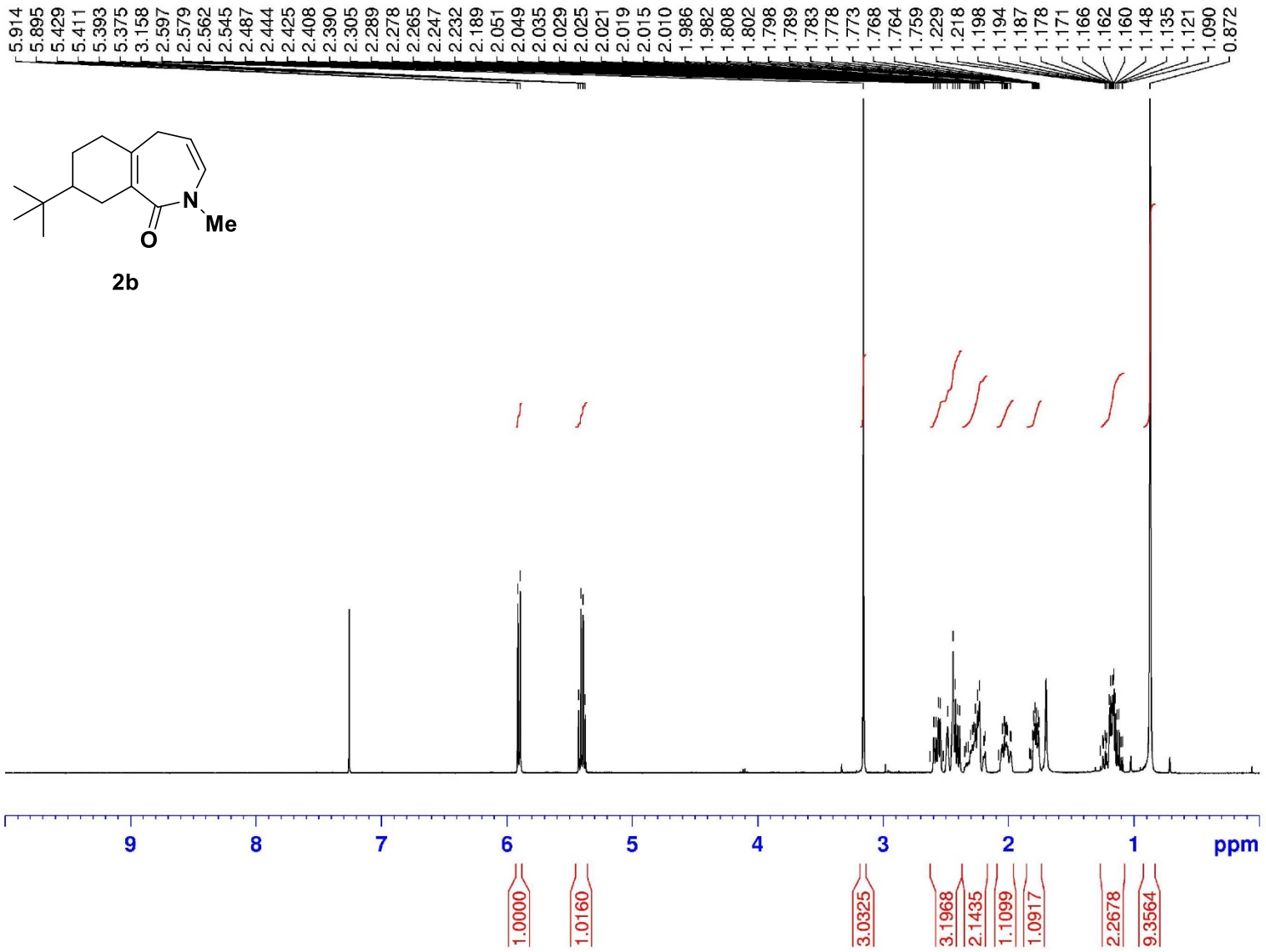
5
4
3
2
1
ppm
N
Me
O
2a


ppm
20
40
60
80
100
120
140
160
180
10
9
8
7
6
5
4
3
2
1
ppm
N
Me
O
2a


ppm
20
40
60
80
100
120
140
160
180
10
9
8
7
6
5
4
3
2
1
ppm
N
Me
O
2a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5.895
5.429
5.411
5.393
5.375
3.158
2.597
2.579
2.562
2.545
2.487
2.444
2.425
2.408
2.390
2.305
2.289
2.278
2.265
2.247
2.232
2.189
2.051
2.049
2.035
2.029
2.025
2.021
2.019
2.015
2.010
1.986
1.982
1.808
1.802
1.798
1.789
1.783
1.778
1.773
1.768
1.764
1.759
1.229
1.218
1.198
1.194
1.187
1.178
1.171
1.166
1.162
1.160
1.148
1.135
1.121
1.090
0.872
N
Me
O
2b
9
8
7
6
5
4
3
2
1
ppm
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3.0325
3.1968
2.1435
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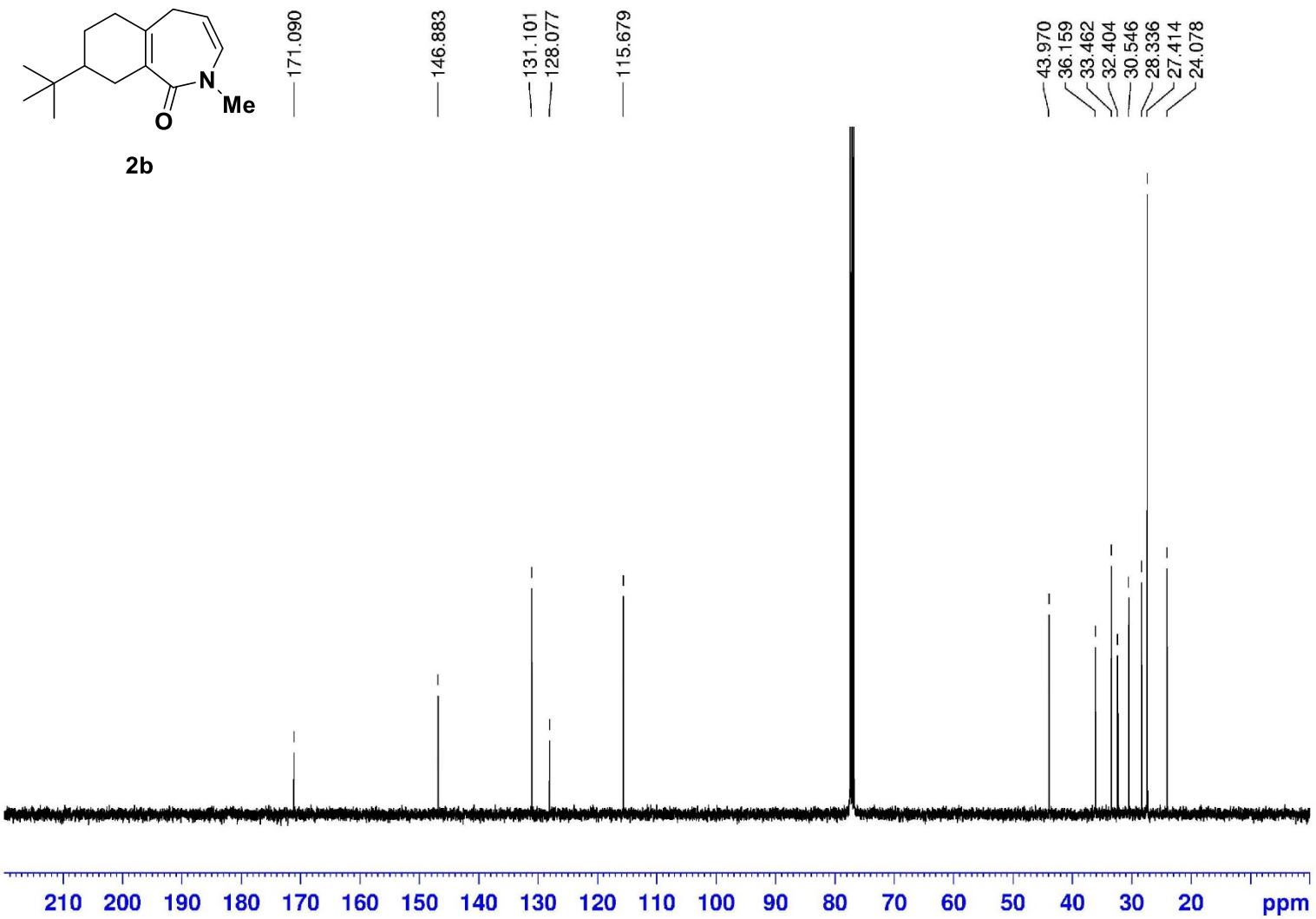
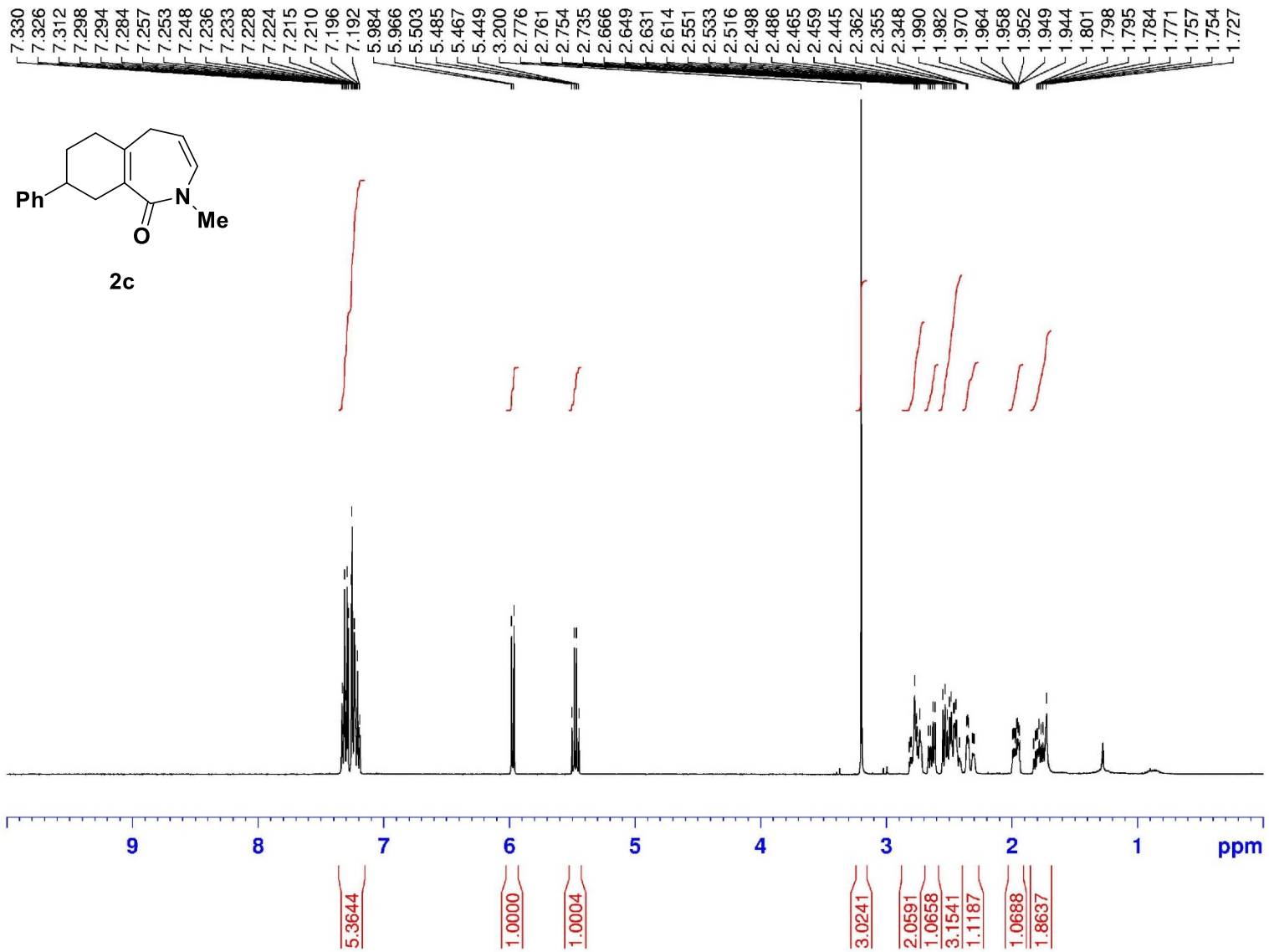
2.2678
9.3564


171.090
146.883
131.101
128.077
115.679
43.970
36.159
33.462
32.404
30.546
28.336
27.414
24.078
N
Me
O
2b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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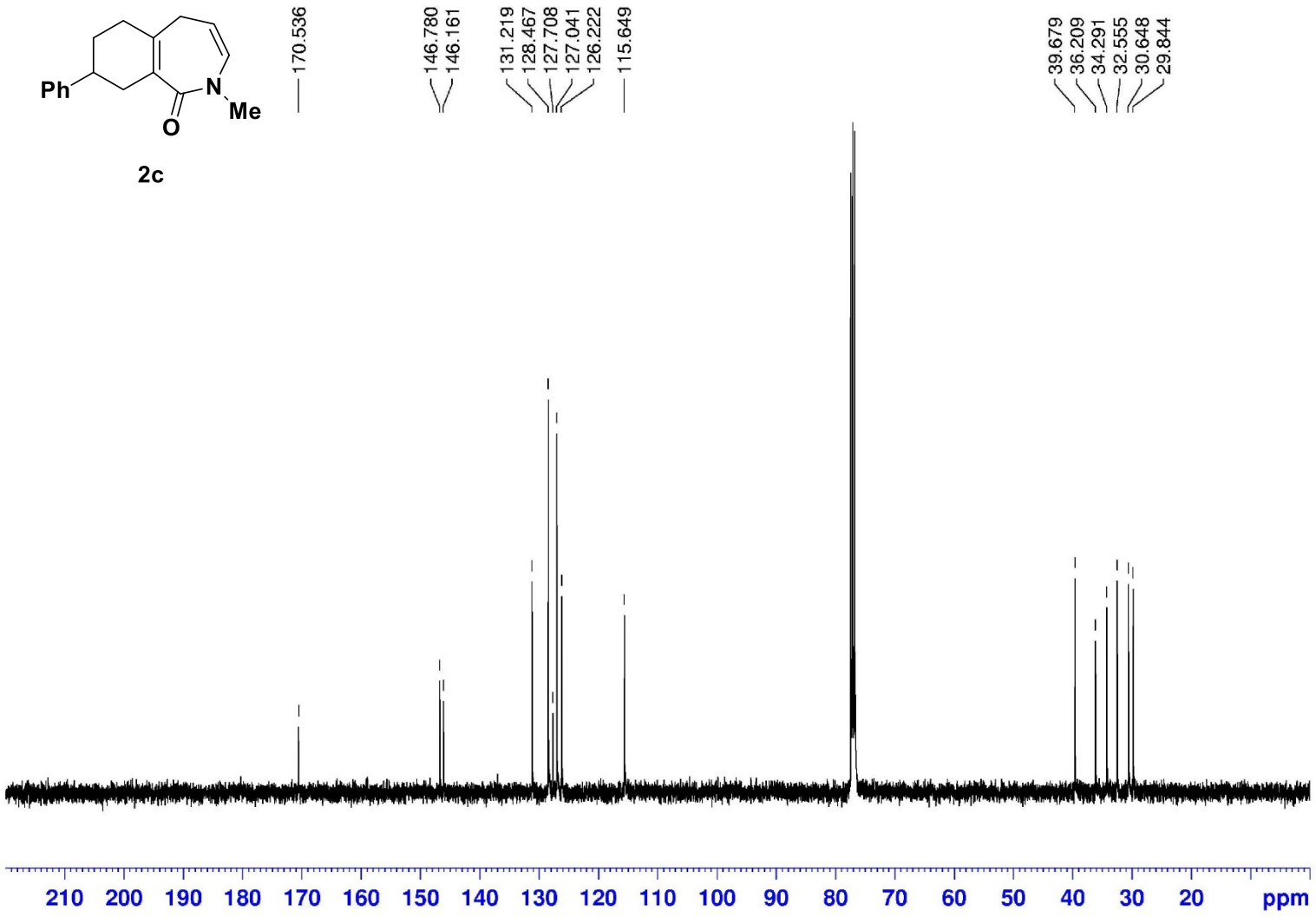
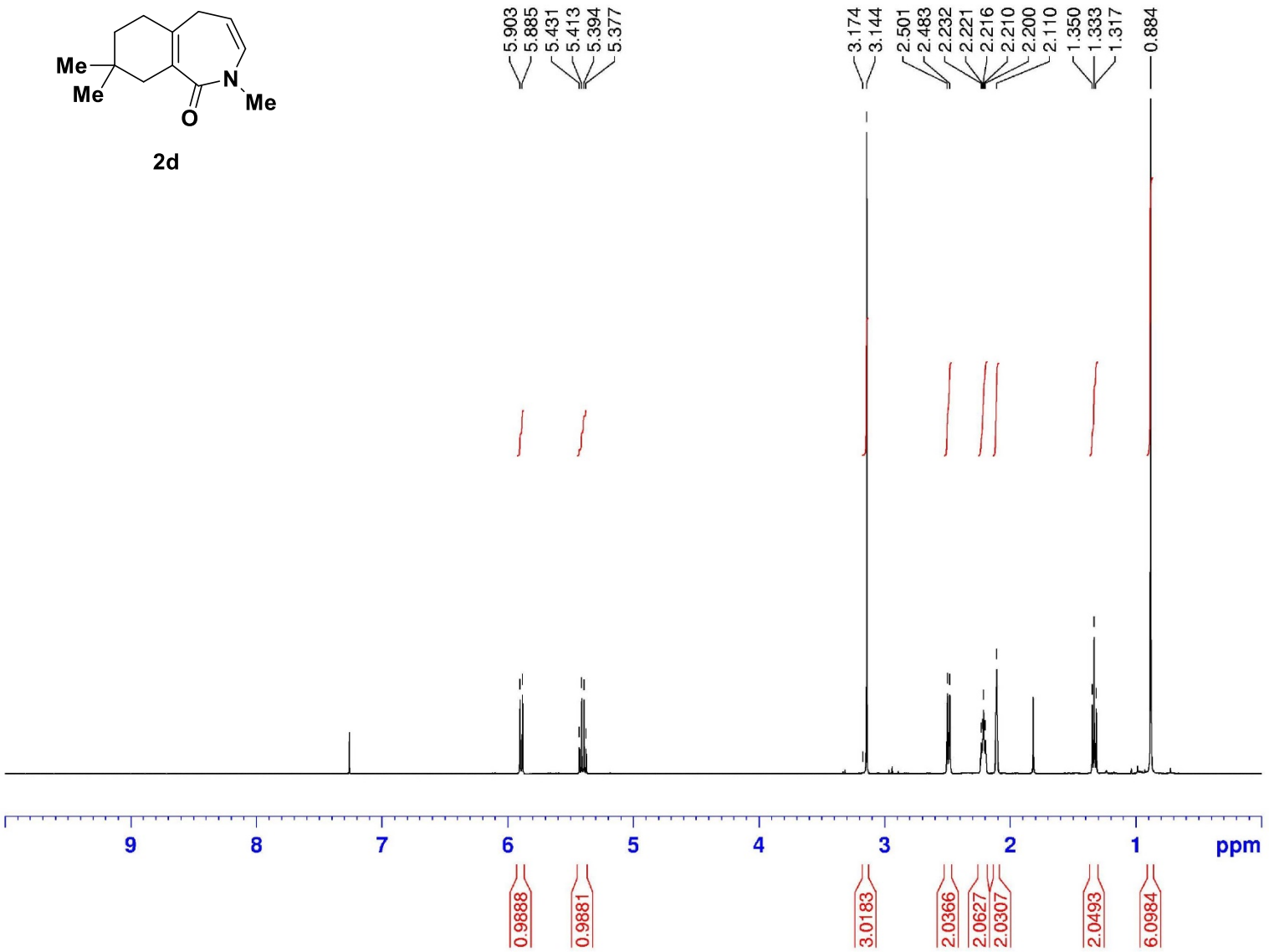
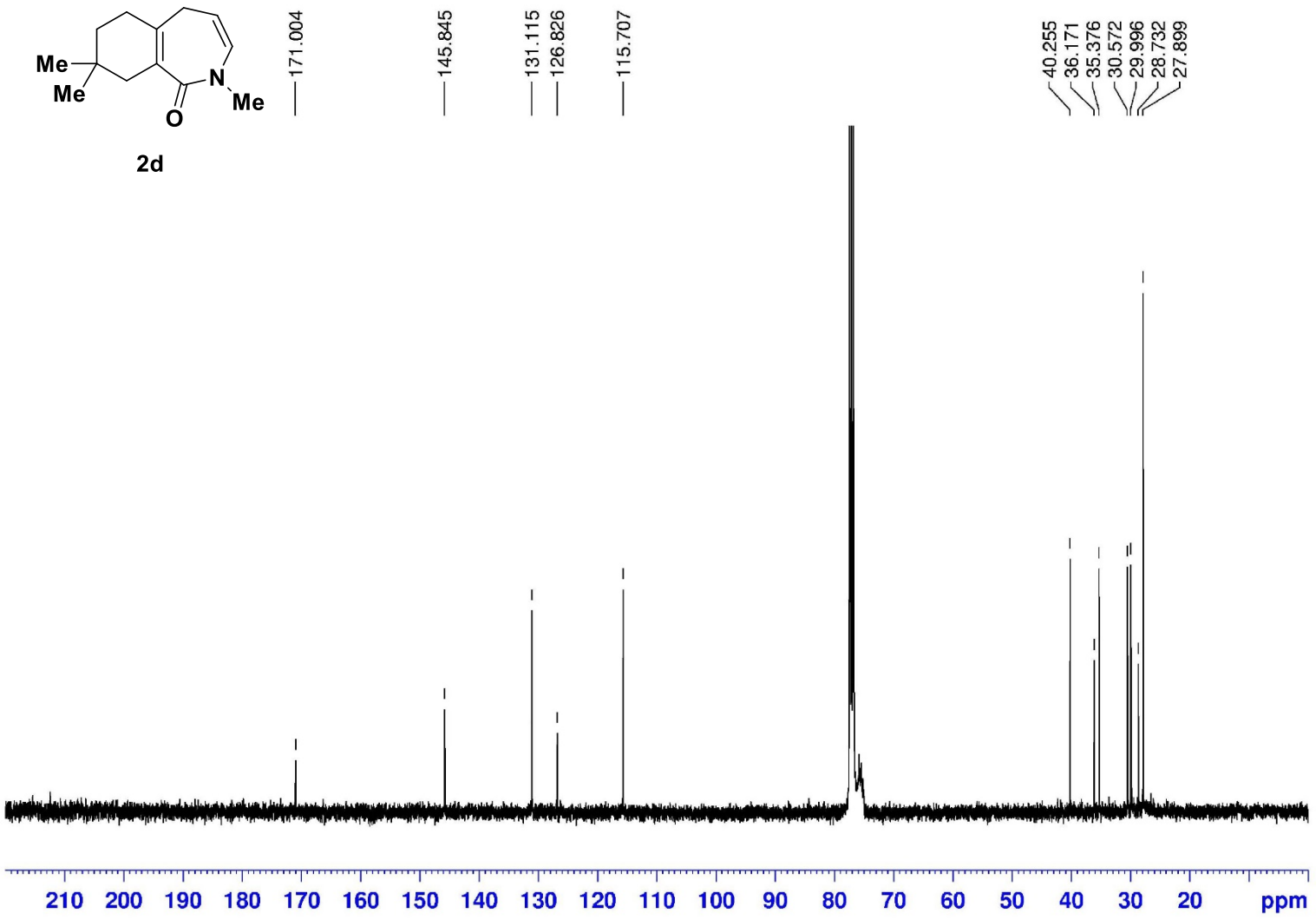
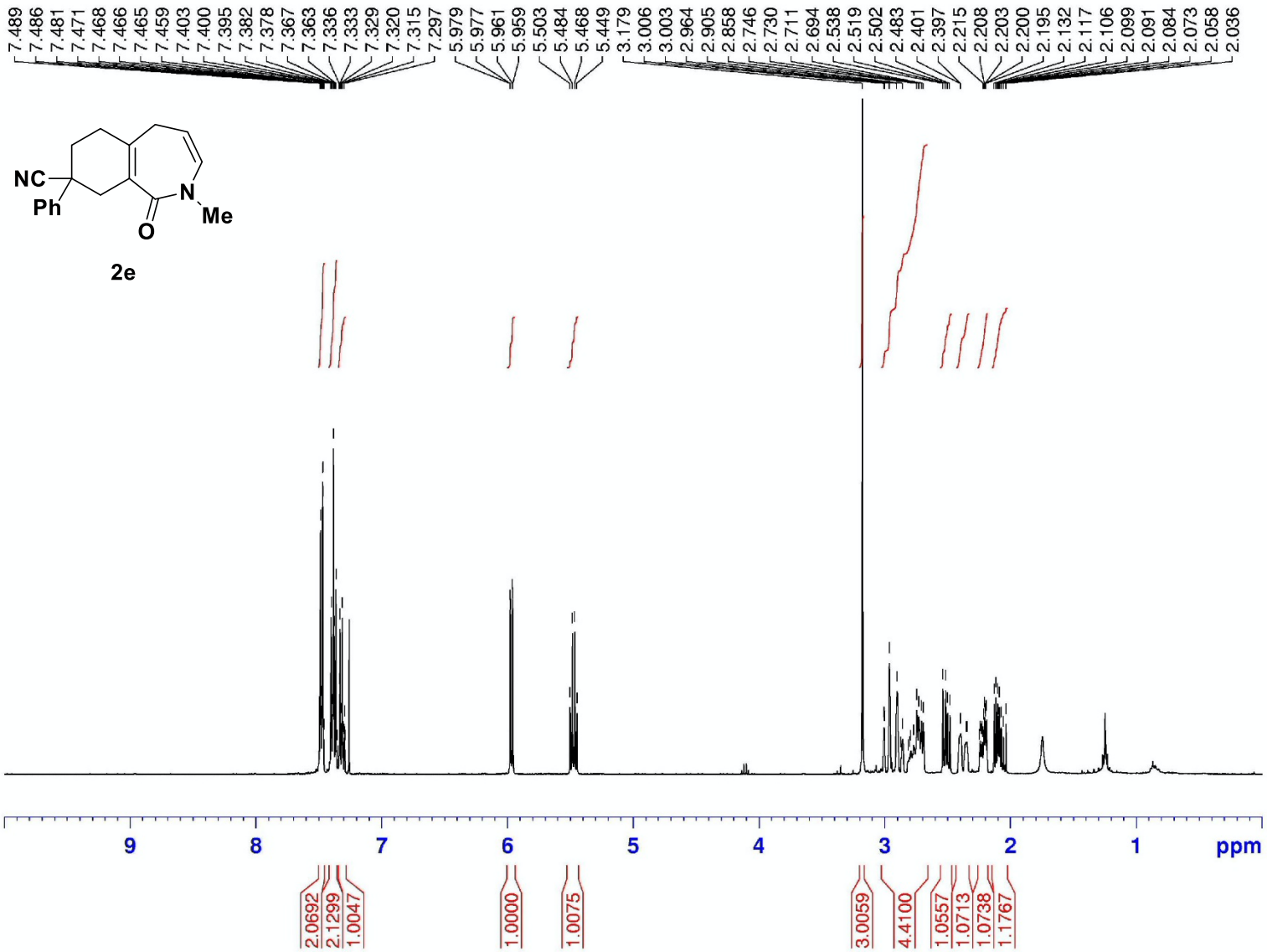
7.326
7.312
7.298
7.294
7.284
7.257
7.253
7.248
7.236
7.233
7.228
7.224
7.215
7.210
7.196
7.192
5.984
5.966
5.503
5.485
5.467
5.449
3.200
2.776
2.761
2.754
2.735
2.666
2.649
2.631
2.614
2.551
2.533
2.516
2.498
2.486
2.465
2.459
2.445
2.362
2.355
2.348
1.990
1.982
1.970
1.964
1.958
1.952
1.949
1.944
1.801
1.798
1.795
1.784
1.771
1.757
1.754
1.727
Ph
N
Me
O
2c
9
8
7
6
5
4
3
2
1
ppm
5.3644
1.0000
1.0004
3.0241
2.0591
1.0658
3.1541
1.1187
1.0688
1.8637


Ph
N
Me
O
2c
170.536
146.780
146.161
131.219
128.467
127.708
127.041
126.222
115.649
39.679
36.209
34.291
32.555
30.648
29.844
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


Me
Me
N
Me
O
2d
5.903
5.885
5.431
5.413
5.394
5.377
3.174
3.144
2.501
2.483
2.232
2.221
2.216
2.210
2.200
2.110
1.350
1.333
1.317
0.884
9
8
7
6
5
4
3
2
1
ppm
0.9888
0.9881
3.0183
2.0366
2.0627
2.0307
2.0493
6.0984


Me
Me
N
Me
O
2d
171.004
145.845
131.115
126.826
115.707
40.255
36.171
35.376
30.572
29.996
28.732
27.899
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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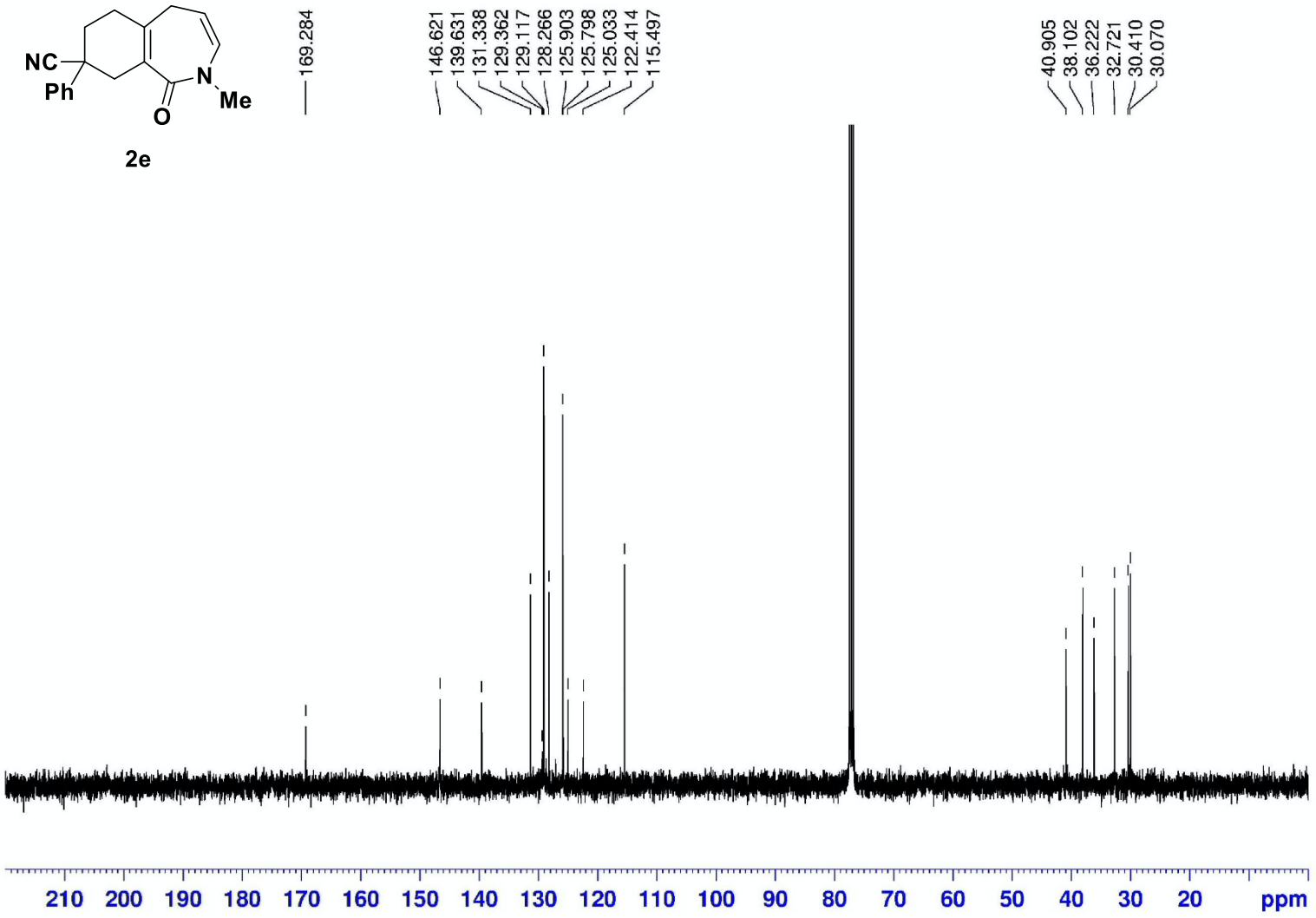
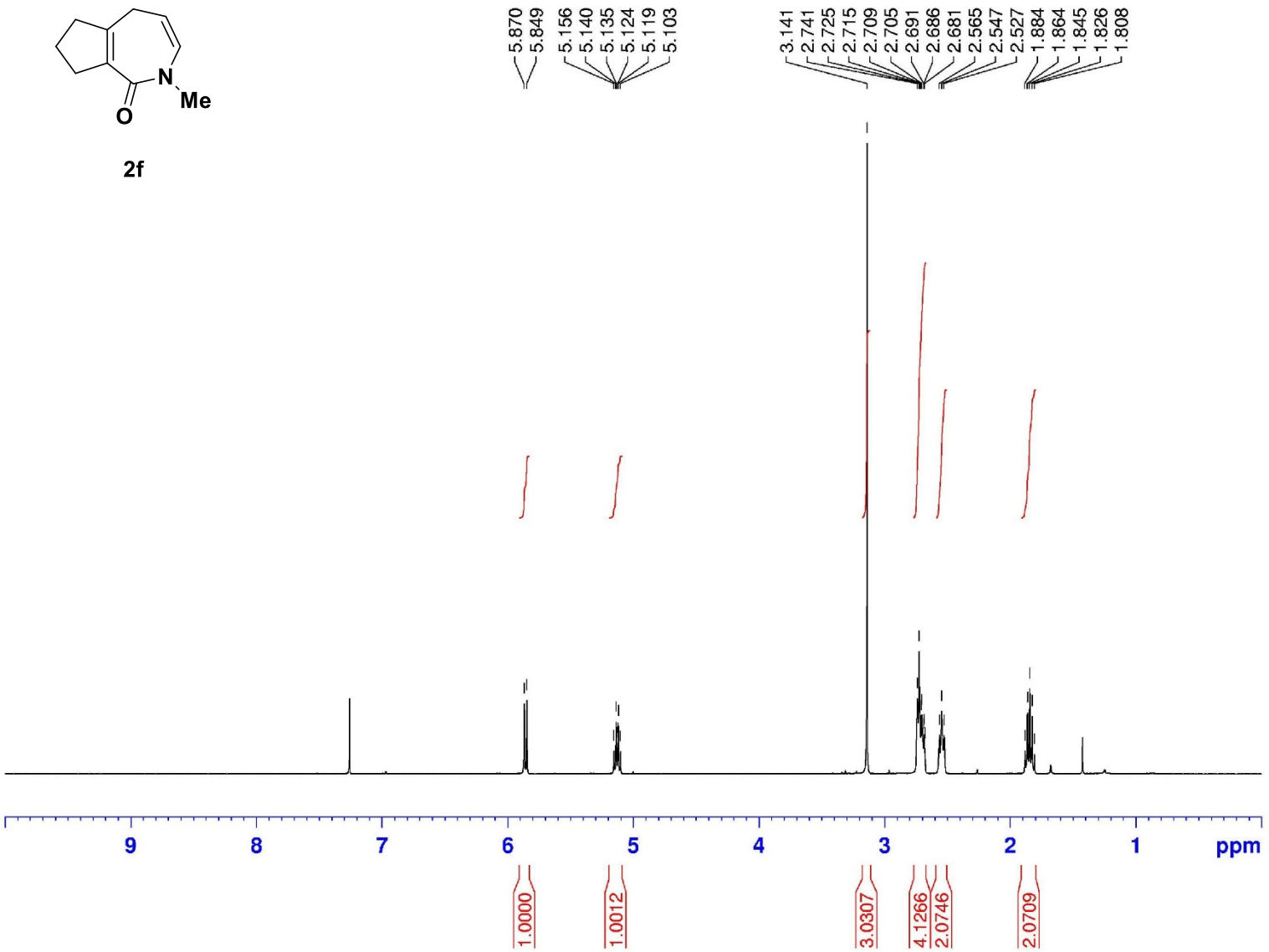
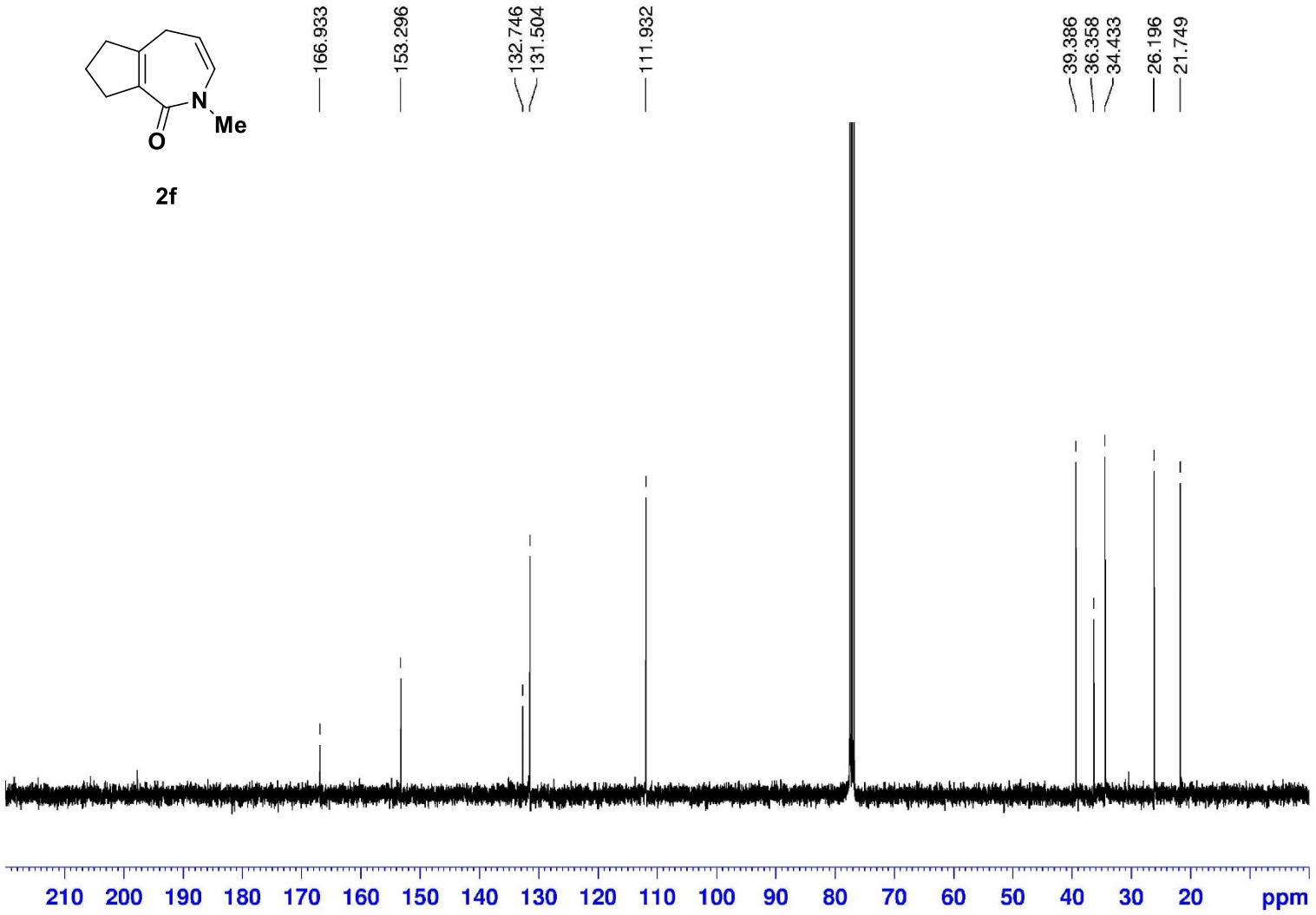
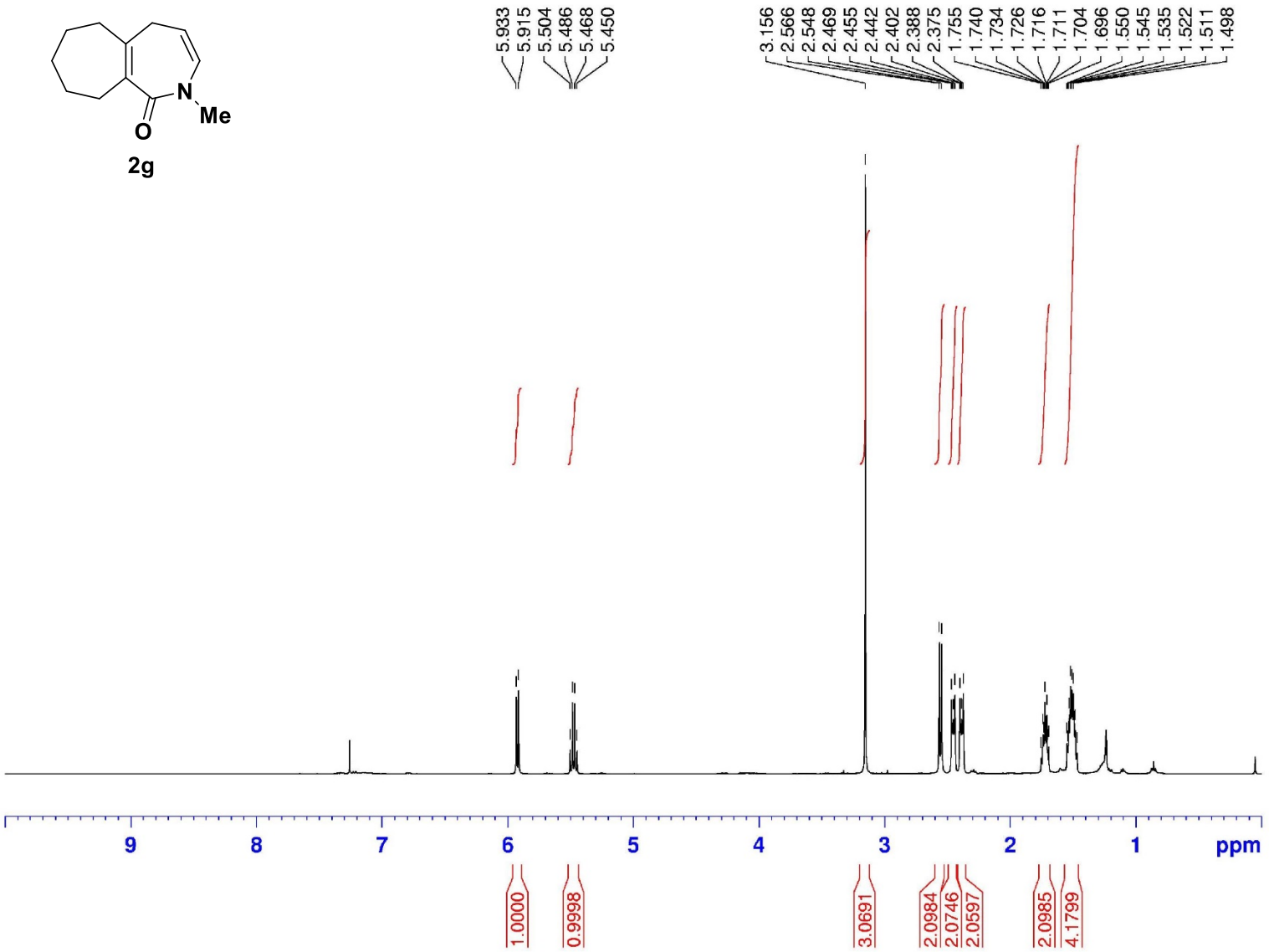
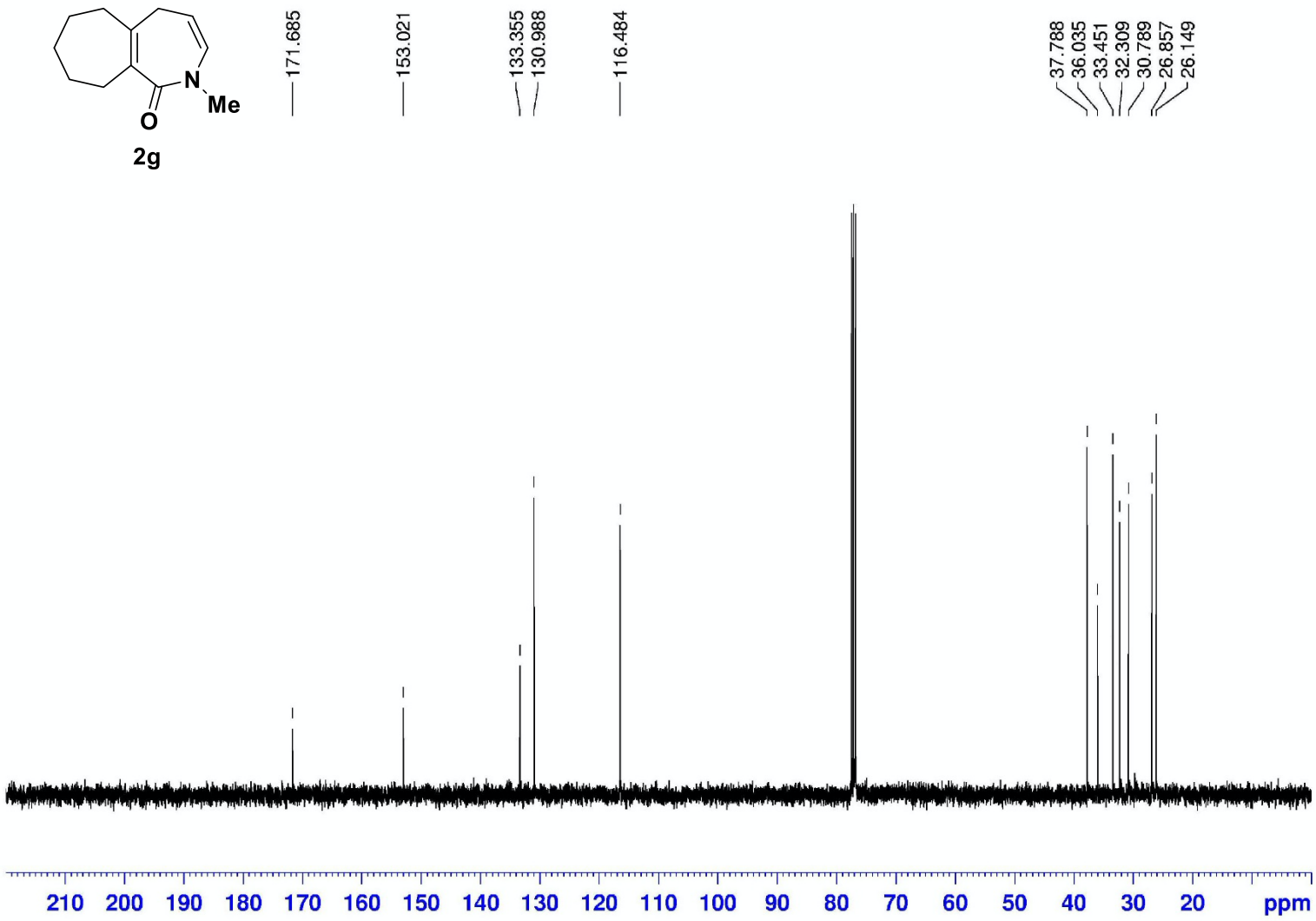
7.486
7.481
7.471
7.468
7.466
7.465
7.459
7.403
7.400
7.395
7.382
7.378
7.367
7.363
7.336
7.333
7.329
7.320
7.315
7.297
5.979
5.977
5.961
5.959
5.503
5.484
5.468
5.449
3.179
3.006
3.003
2.964
2.905
2.858
2.746
2.730
2.711
2.694
2.538
2.519
2.502
2.483
2.401
2.397
2.215
2.208
2.203
2.200
2.195
2.132
2.117
2.106
2.099
2.091
2.084
2.073
2.058
2.036
NC
Ph
N
Me
O
2e
9
8
7
6
5
4
3
2
1
ppm
2.0692
2.1299
1.0047
1.0000
1.0075
3.0059
4.4100
1.0557
1.0713
1.0738
1.1767

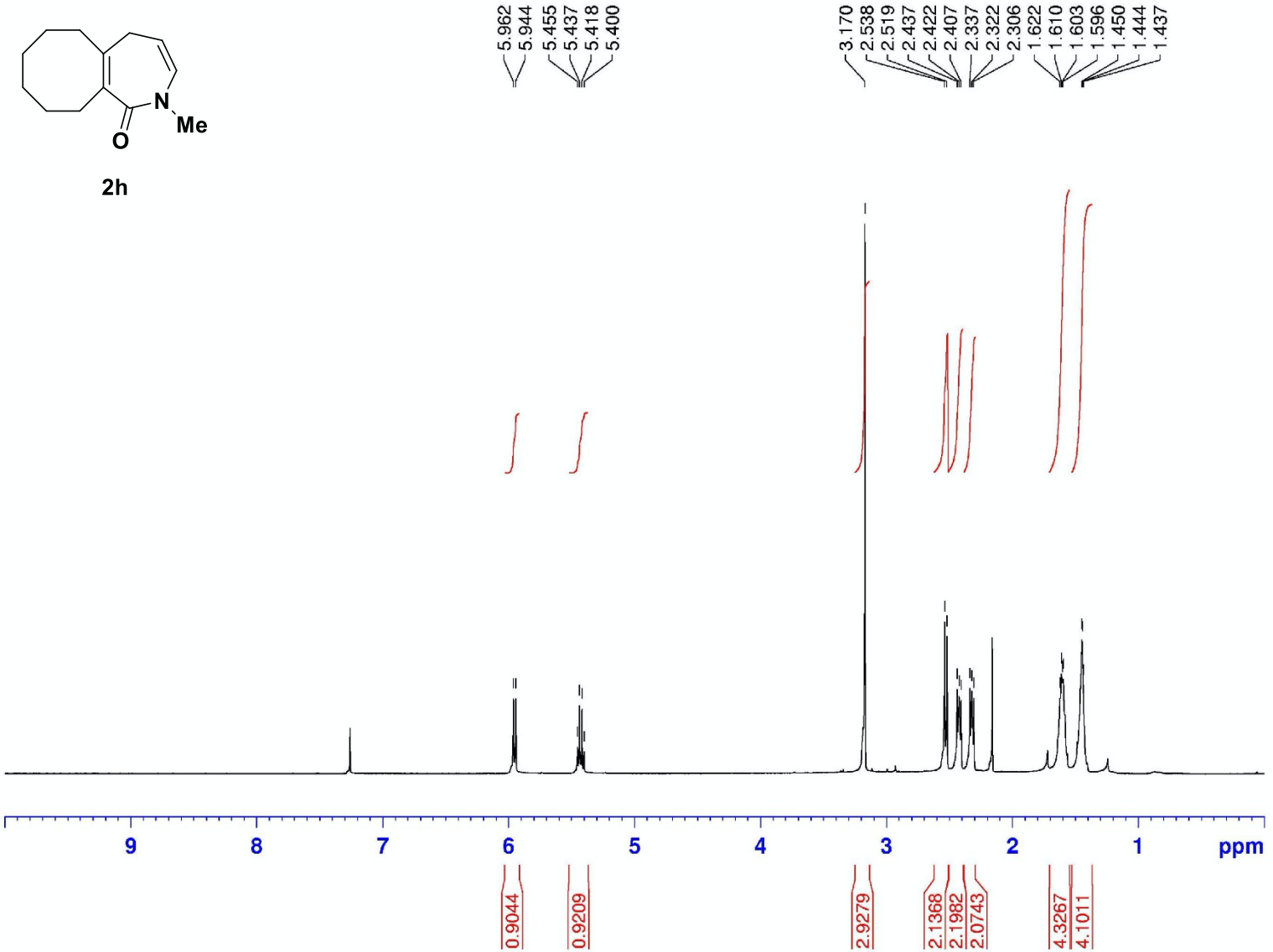

NC
Ph
N
Me
O
2e
169.284
146.621
139.631
131.338
129.362
129.117
128.266
125.903
125.798
125.033
122.414
115.497
40.905
38.102
36.222
32.721
30.410
30.070
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

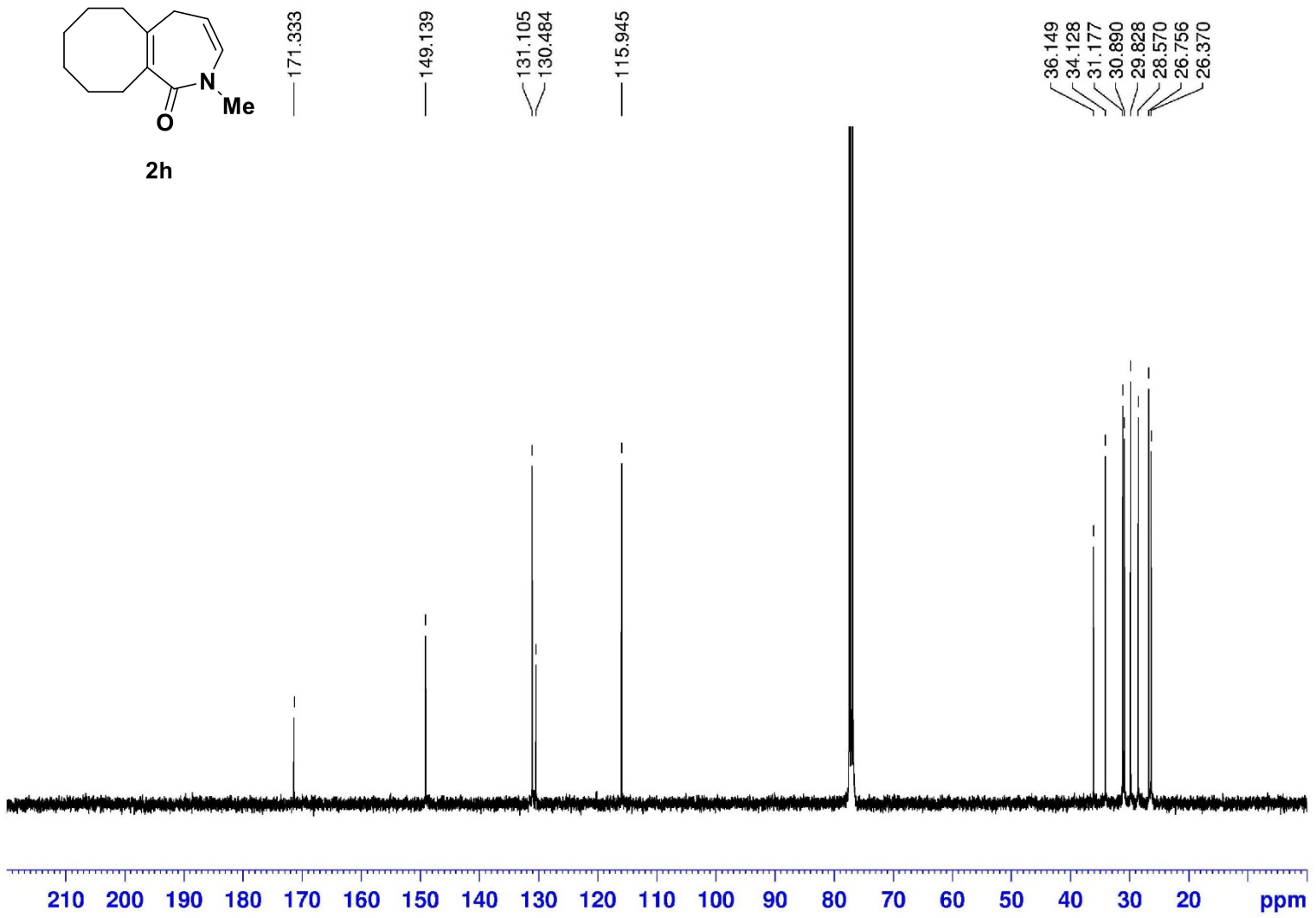

N
Me
O
2f
5.870
5.849
5.156
5.140
5.135
5.124
5.119
5.103
3.141
2.741
2.725
2.715
2.709
2.705
2.691
2.686
2.681
2.565
2.547
2.527
1.884
1.864
1.845
1.826
1.808
9
8
7
6
5
4
3
2
1
ppm
1.0000
1.0012
3.0307
4.1266
2.0746
2.0709

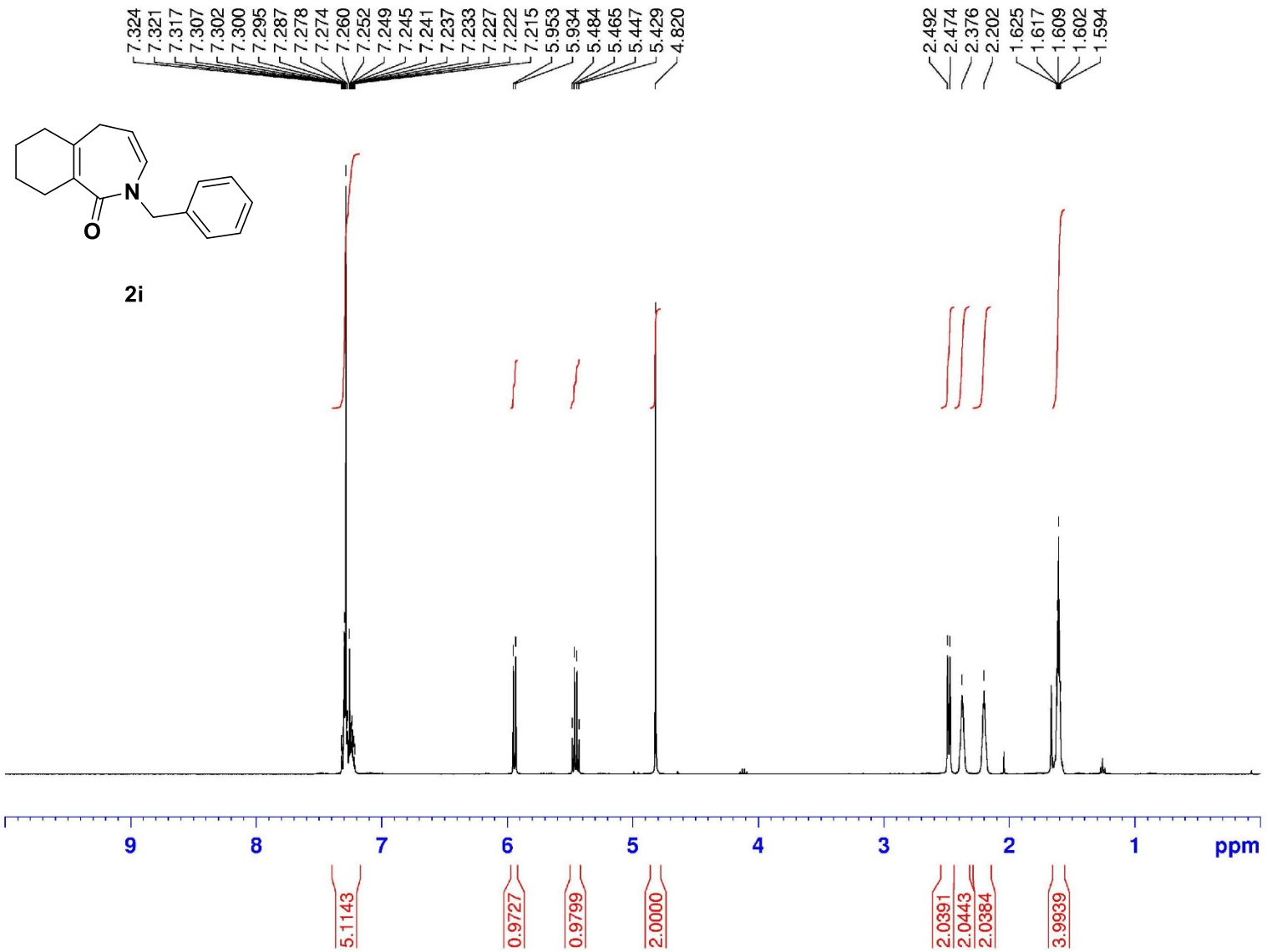

166.933
153.296
132.746
131.504
111.932
39.386
36.358
34.433
26.196
21.749
N
Me
O
2f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

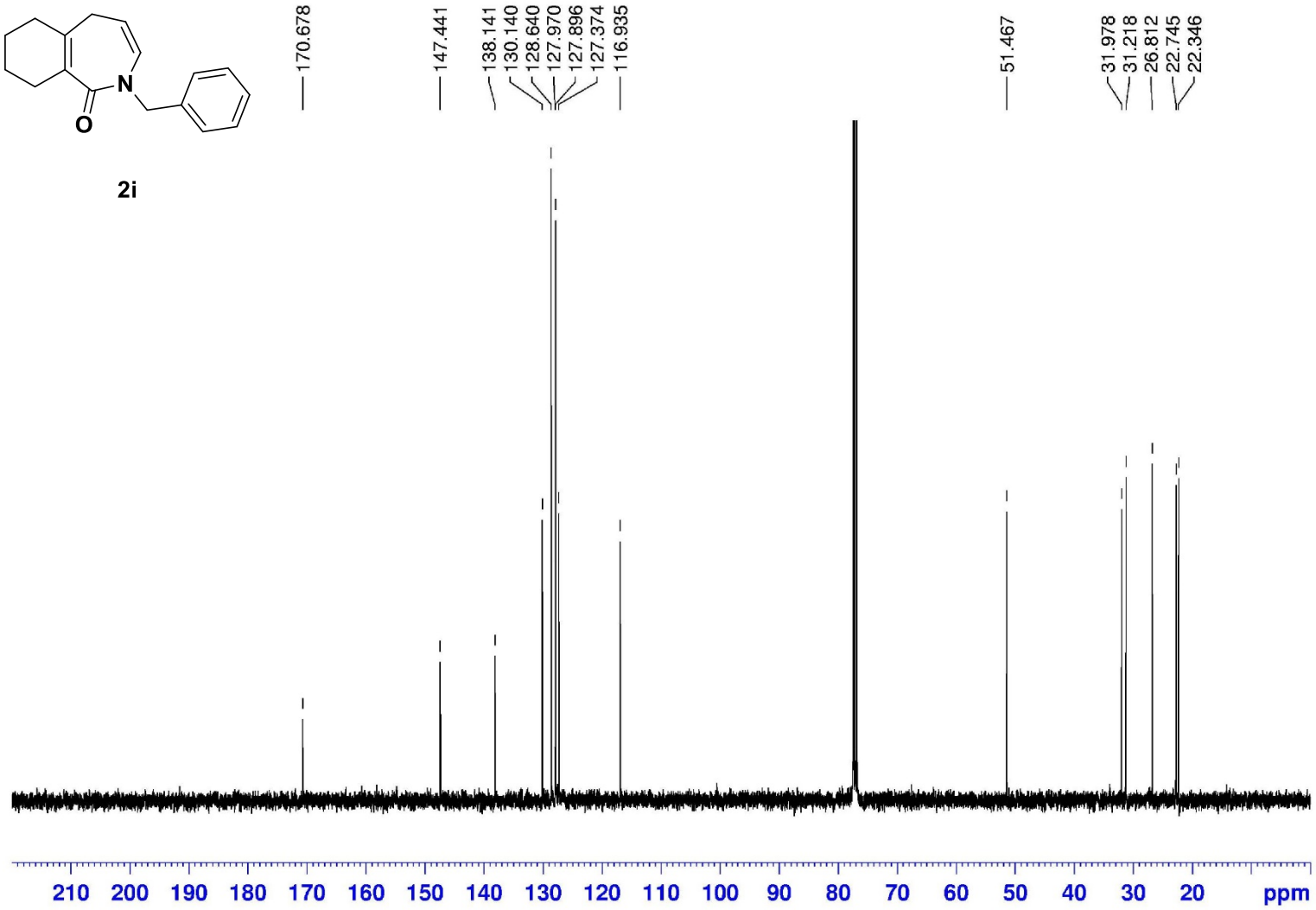

N
Me
O
2g
5.933
5.915
5.504
5.486
5.468
5.450
3.156
2.566
2.548
2.469
2.455
2.442
2.402
2.388
2.375
1.755
1.740
1.734
1.726
1.716
1.711
1.704
1.696
1.550
1.545
1.535
1.522
1.511
1.498
9
8
7
6
5
4
3
2
1
ppm
1.0000
0.9998
3.0691
2.0984
2.0746
2.0597
2.0985
4.1799

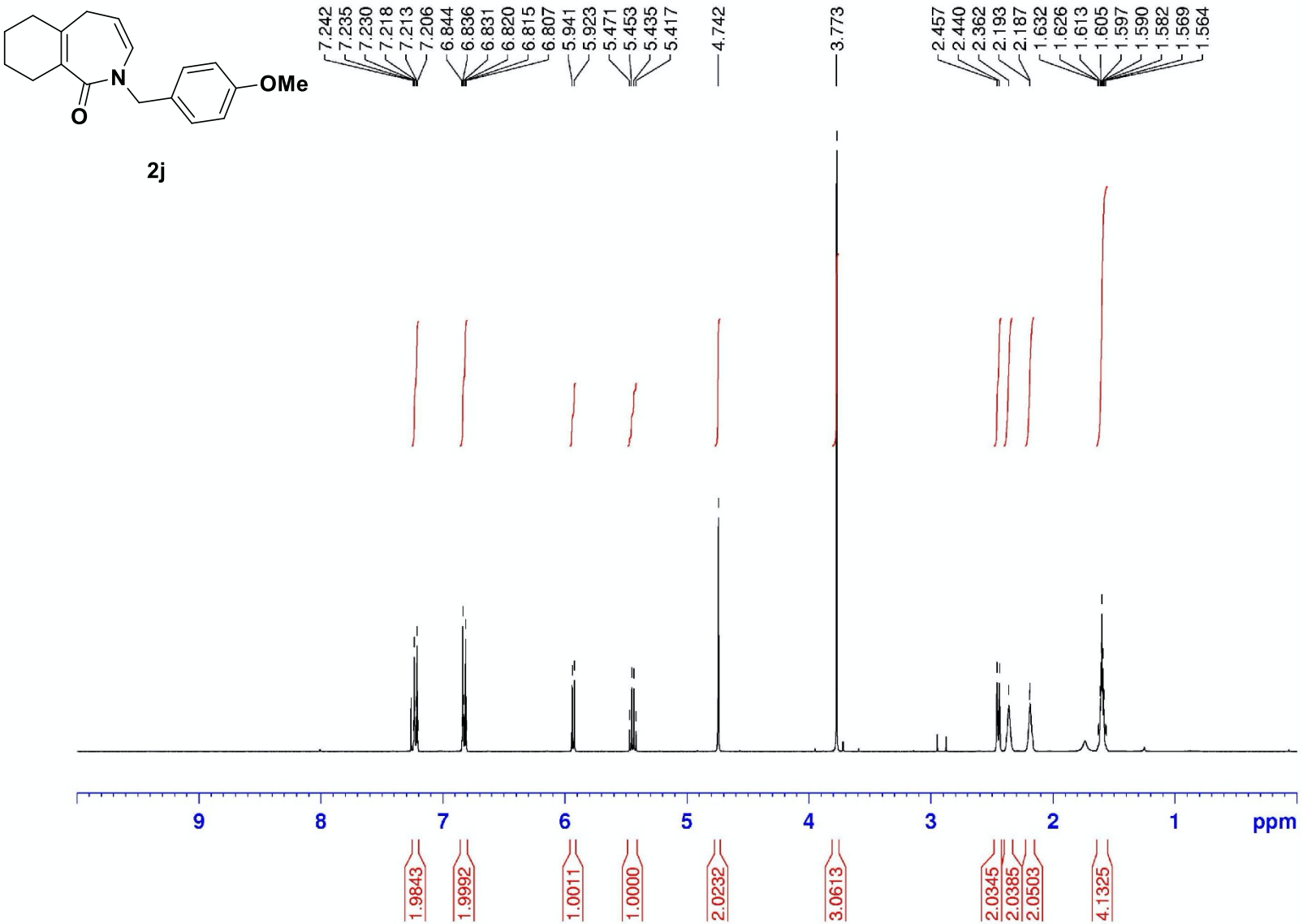

171.685
153.021
133.355
130.988
116.484
37.788
36.035
33.451
32.309
30.789
26.857
26.149
N
Me
O
2g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

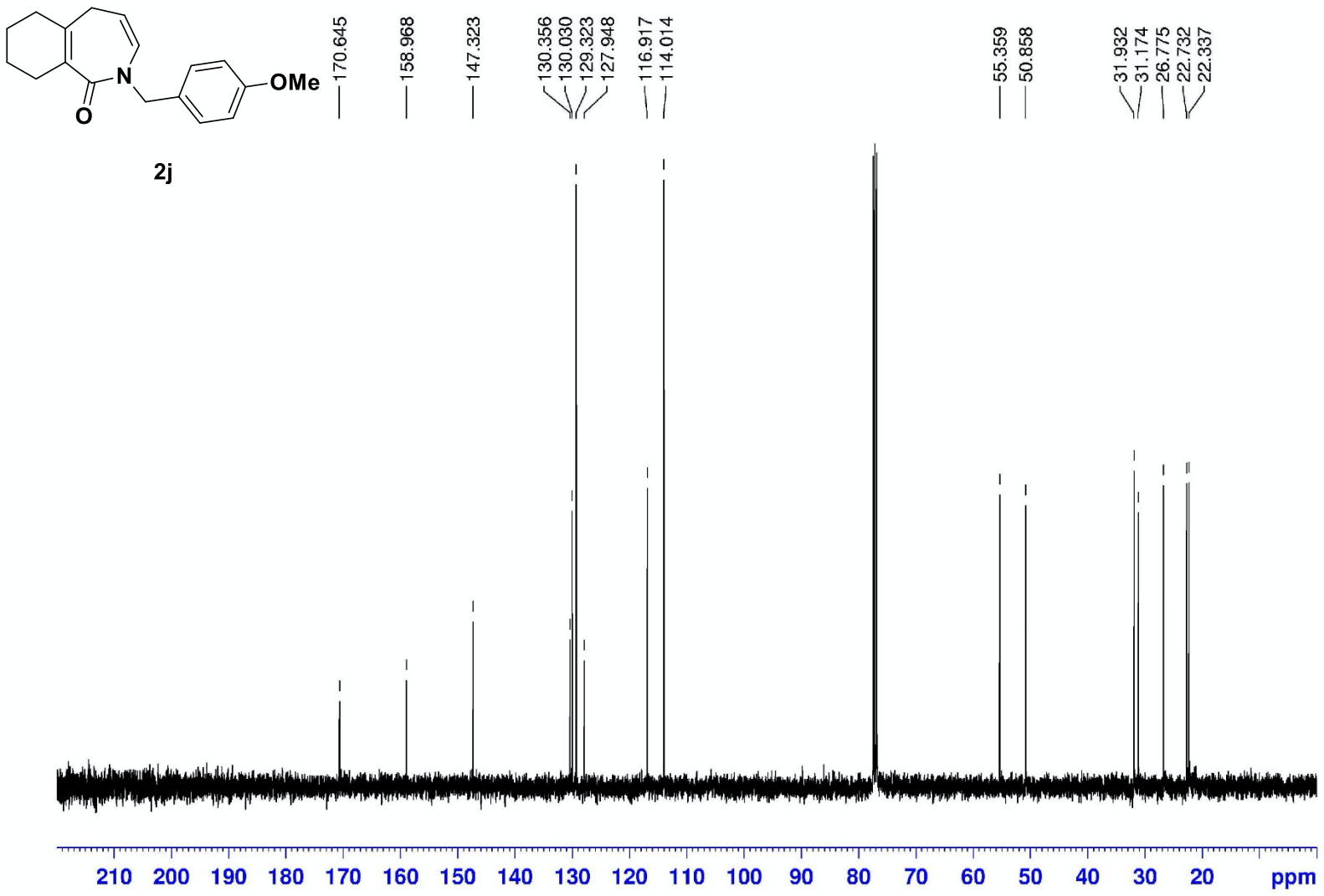

N
Me
O
2h
5.962
5.944
5.455
5.437
5.418
5.400
3.170
2.538
2.519
2.437
2.422
2.407
2.337
2.322
2.306
1.622
1.610
1.603
1.596
1.450
1.444
1.437
9
8
7
6
5
4
3
2
1
ppm
0.9044
0.9209
2.9279
2.1368
2.1982
2.0743
4.3267
4.1011

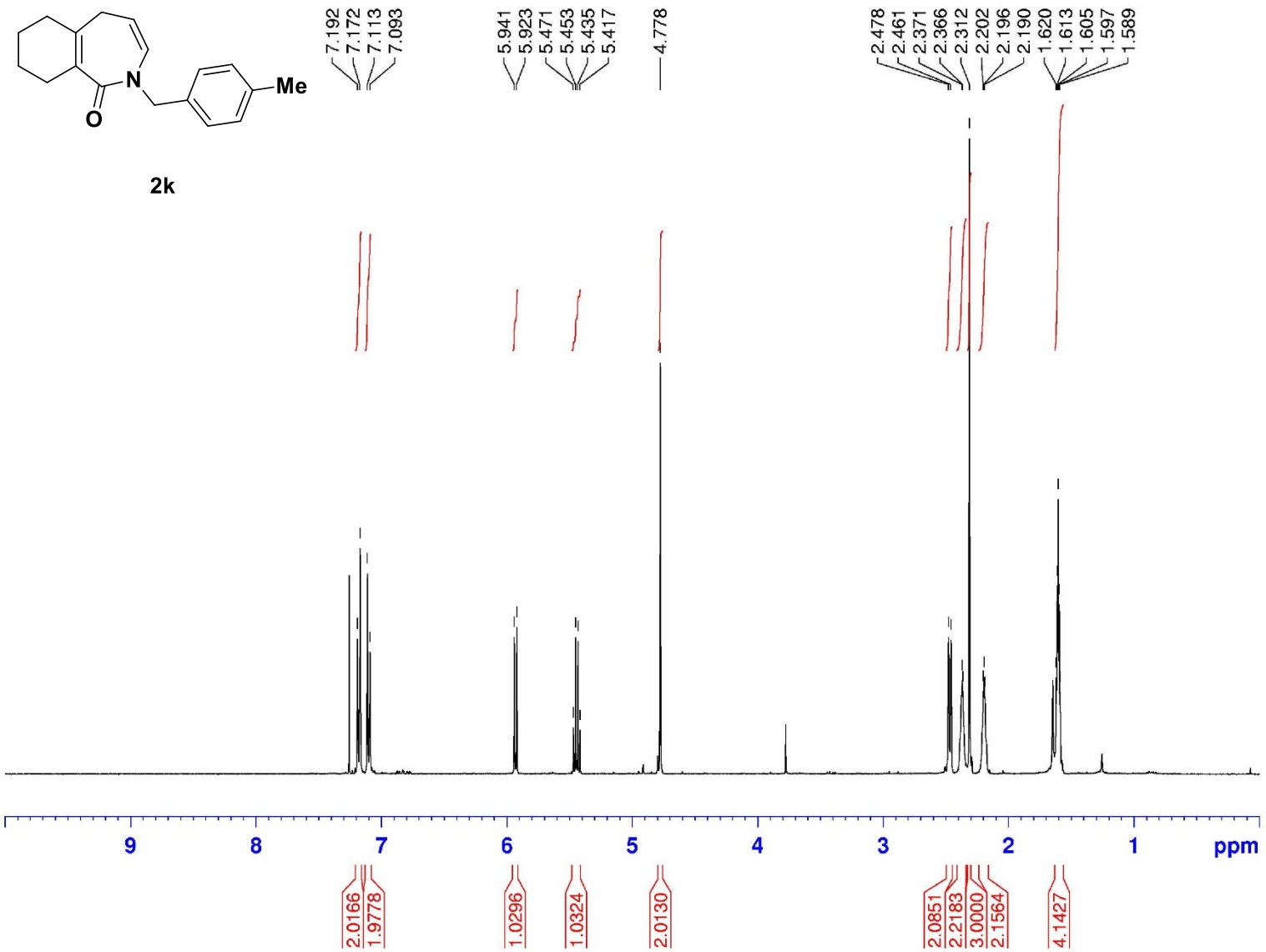

171.333
149.139
131.105
130.484
115.945
36.149
34.128
31.177
30.890
29.828
28.570
26.756
26.370
N
Me
O
2h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

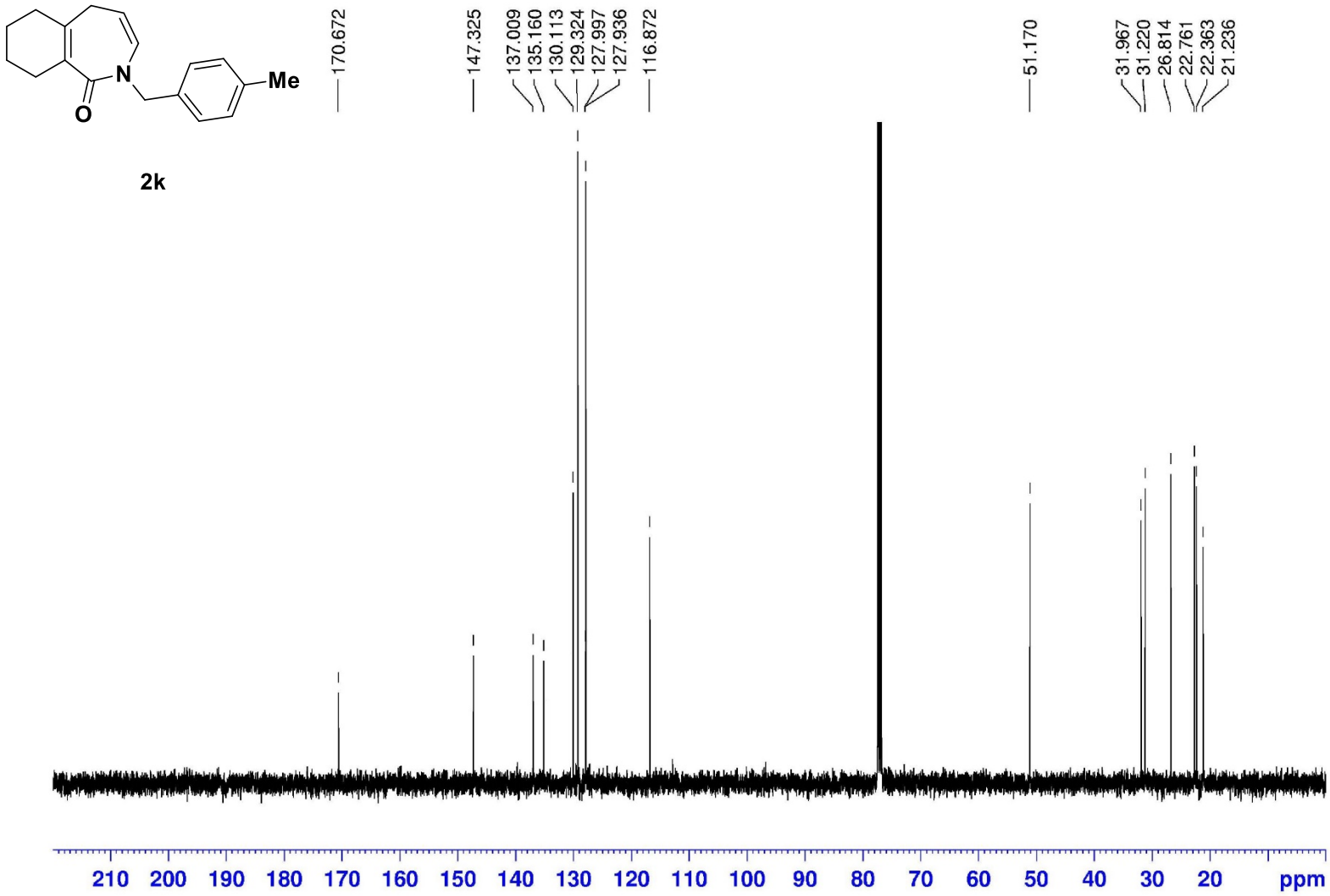

7.324
7.321
7.317
7.307
7.302
7.300
7.295
7.287
7.278
7.274
7.260
7.252
7.249
7.245
7.241
7.237
7.233
7.227
7.222
7.215
5.953
5.934
5.484
5.465
5.447
5.429
4.820
2.492
2.474
2.376
2.202
1.625
1.617
1.609
1.602
1.594
N
O
2i
9
8
7
6
5
4
3
2
1
ppm
5.1143
0.9727
0.9799
2.0000
2.0391
2.0443
2.0384
3.9939


170.678
147.441
138.141
130.140
128.640
127.970
127.896
127.374
116.935
51.467
31.978
31.218
26.812
22.745
22.346
N
O
2i
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.242
7.235
7.230
7.218
7.213
7.206
6.844
6.836
6.831
6.820
6.815
6.807
5.941
5.923
5.471
5.453
5.435
5.417
4.742
3.773
2.457
2.440
2.362
2.193
2.187
1.632
1.626
1.613
1.605
1.597
1.590
1.582
1.569
1.564
N
O
OMe
2j
9
8
7
6
5
4
3
2
1
ppm
1.9843
1.9992
1.0011
1.0000
2.0232
3.0613
2.0345
2.0385
2.0503
4.1325


N
O
OMe
2j
170.645
158.968
147.323
130.356
130.030
129.323
127.948
116.917
114.014
55.359
50.858
31.932
31.174
26.775
22.732
22.337
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.192
7.172
7.113
7.093
5.941
5.923
5.471
5.453
5.435
5.417
4.778
2.478
2.461
2.371
2.366
2.312
2.202
2.196
2.190
1.620
1.613
1.605
1.597
1.589
N
O
Me
2k
9
8
7
6
5
4
3
2
1
ppm
2.0166
1.9778
1.0296
1.0324
2.0130
2.0851
2.2183
3.0000
2.1564
4.1427


N
O
Me
2k
170.672
147.325
137.009
135.160
130.113
129.324
127.997
127.936
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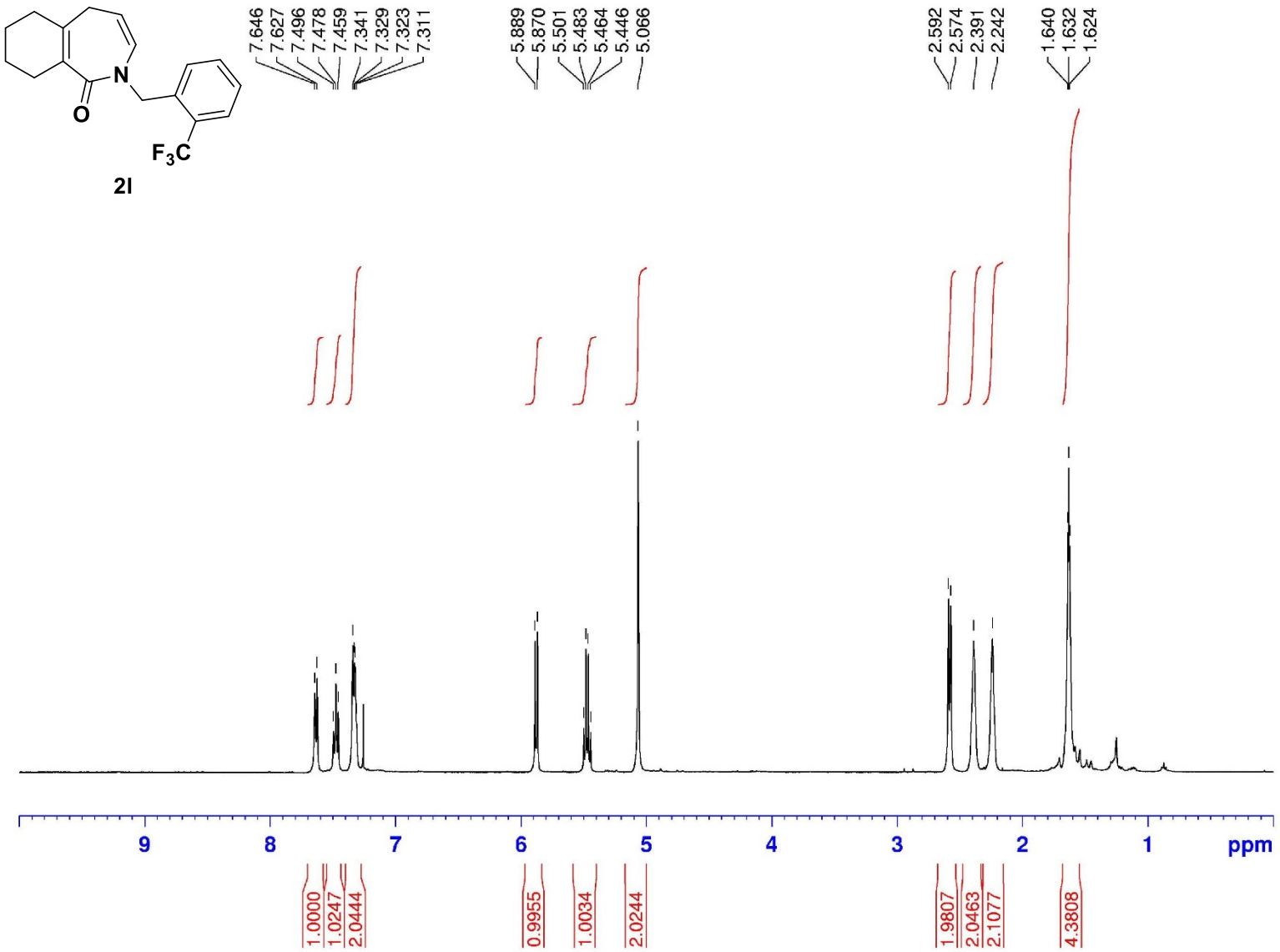
51.170
31.967
31.220
26.814
22.761
22.363
21.236
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.646
7.627
7.496
7.478
7.459
7.341
7.329
7.323
7.311
5.889
5.870
5.501
5.483
5.464
5.446
5.066
2.592
2.574
2.391
2.242
1.640
1.632
1.624
N
O
F3C
2l
9
8
7
6
5
4
3
2
1
ppm
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2.0444
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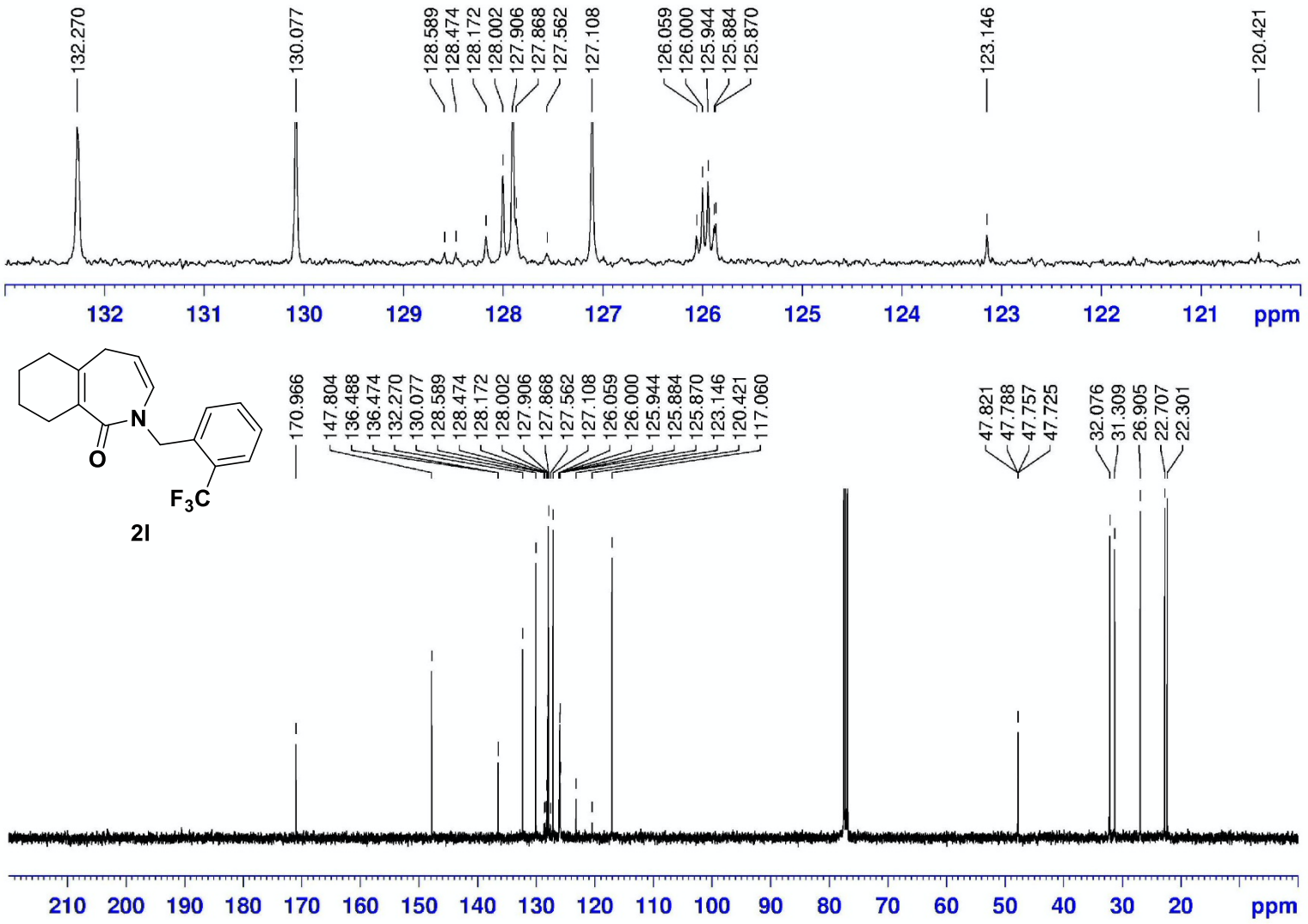
1.0034
2.0244
1.9807
2.0463
2.1077
4.3808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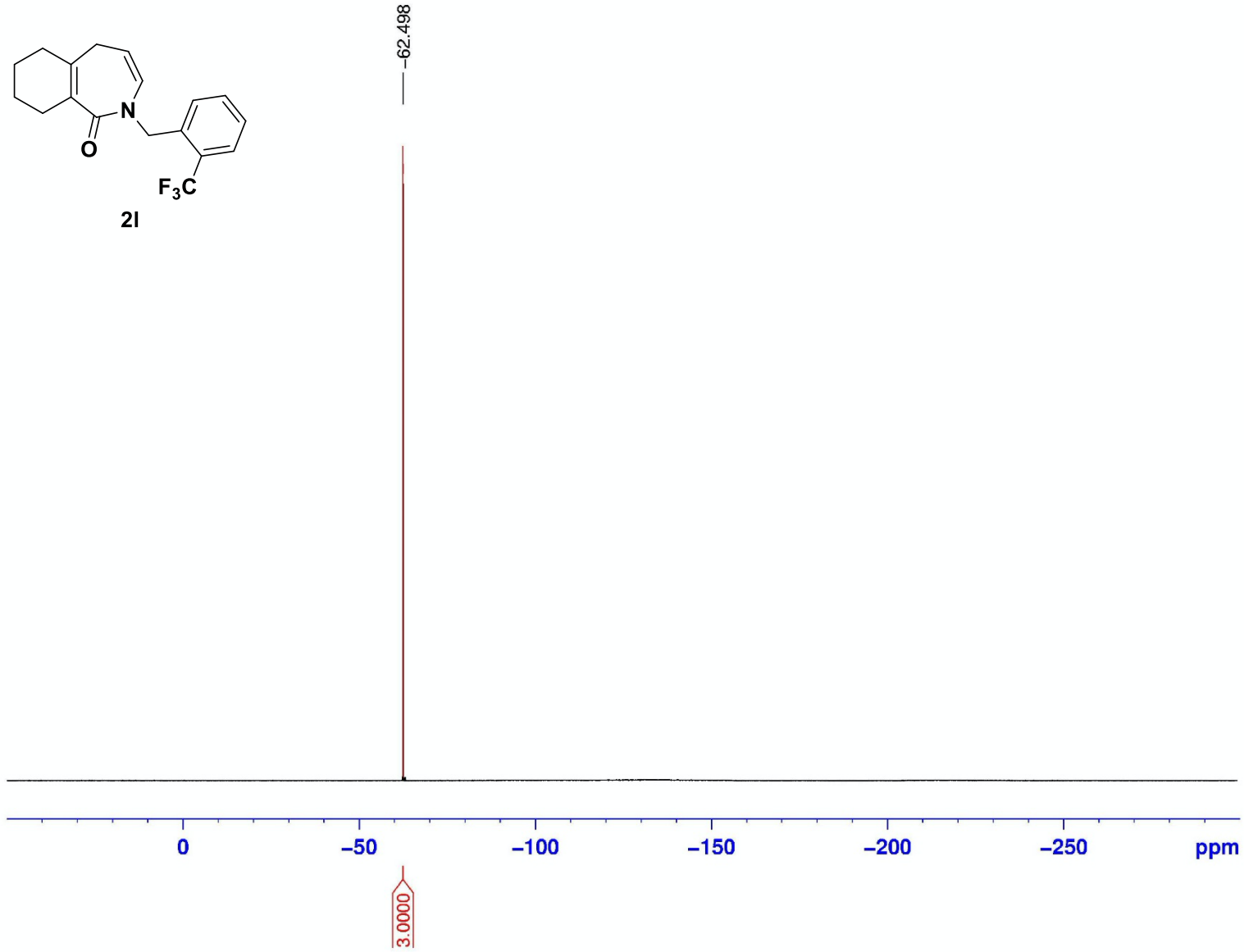
128.474
128.172
128.002
127.906
127.868
127.562
127.108
126.059
126.000
125.944
125.884
125.870
123.146
120.421
132
131
130
129
128
127
126
125
124
123
122
121
ppm
N
O
F3C
2l
170.966
147.804
136.488
136.474
132.270
130.077
128.589
128.474
128.172
128.002
127.906
127.868
127.562
127.108
126.059
126.000
125.944
125.884
125.870
123.146
120.421
117.060
47.821
47.788
47.757
47.725
32.076
31.309
26.905
22.707
22.301
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


N
O
F3C
2l
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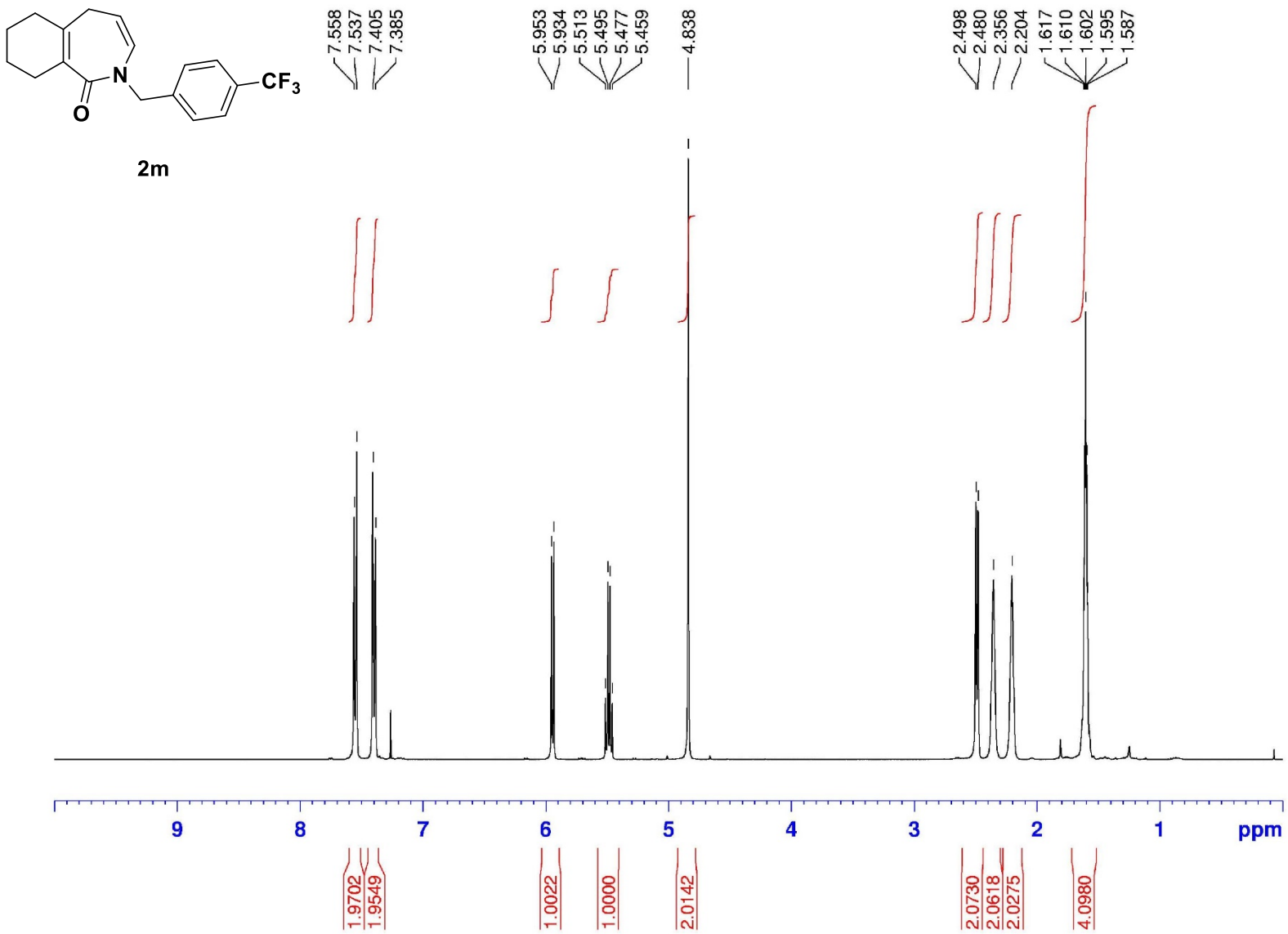
0
-50
-100
-150
-200
-250
ppm
3.0000


7.558
7.537
7.405
7.385
5.953
5.934
5.513
5.495
5.477
5.459
4.838
2.498
2.480
2.356
2.204
1.617
1.610
1.602
1.595
1.587
N
O
CF3
2m
9
8
7
6
5
4
3
2
1
ppm
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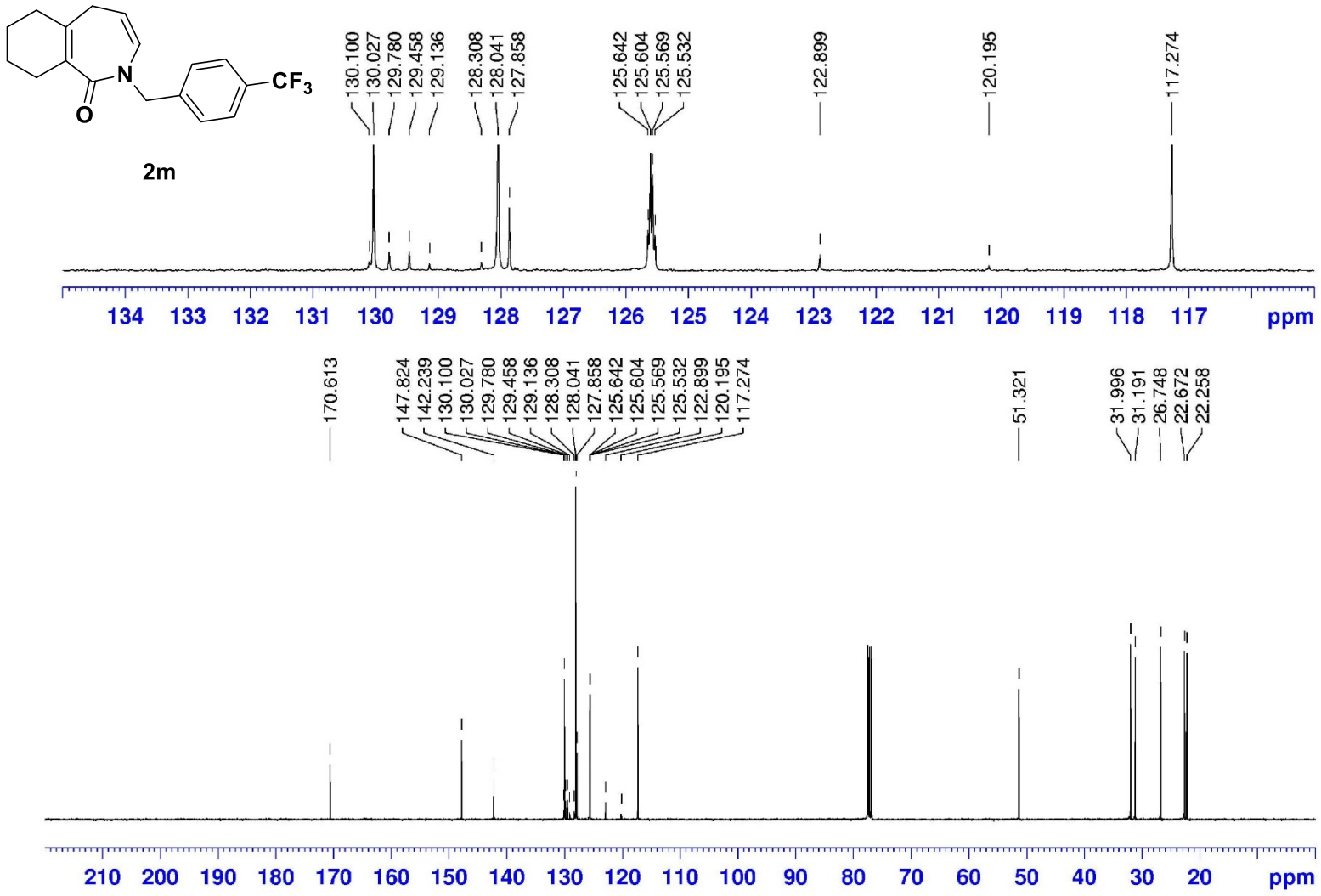
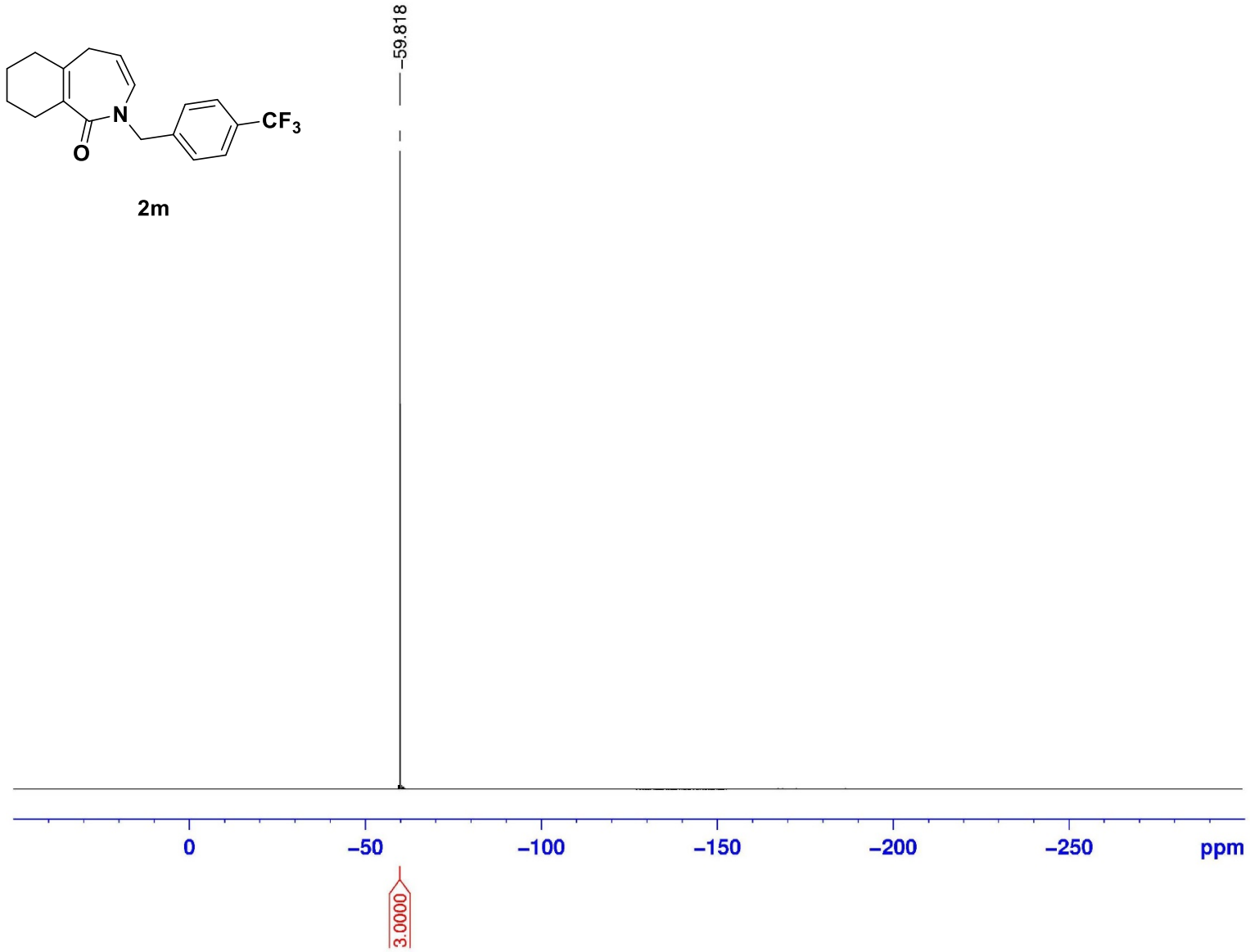
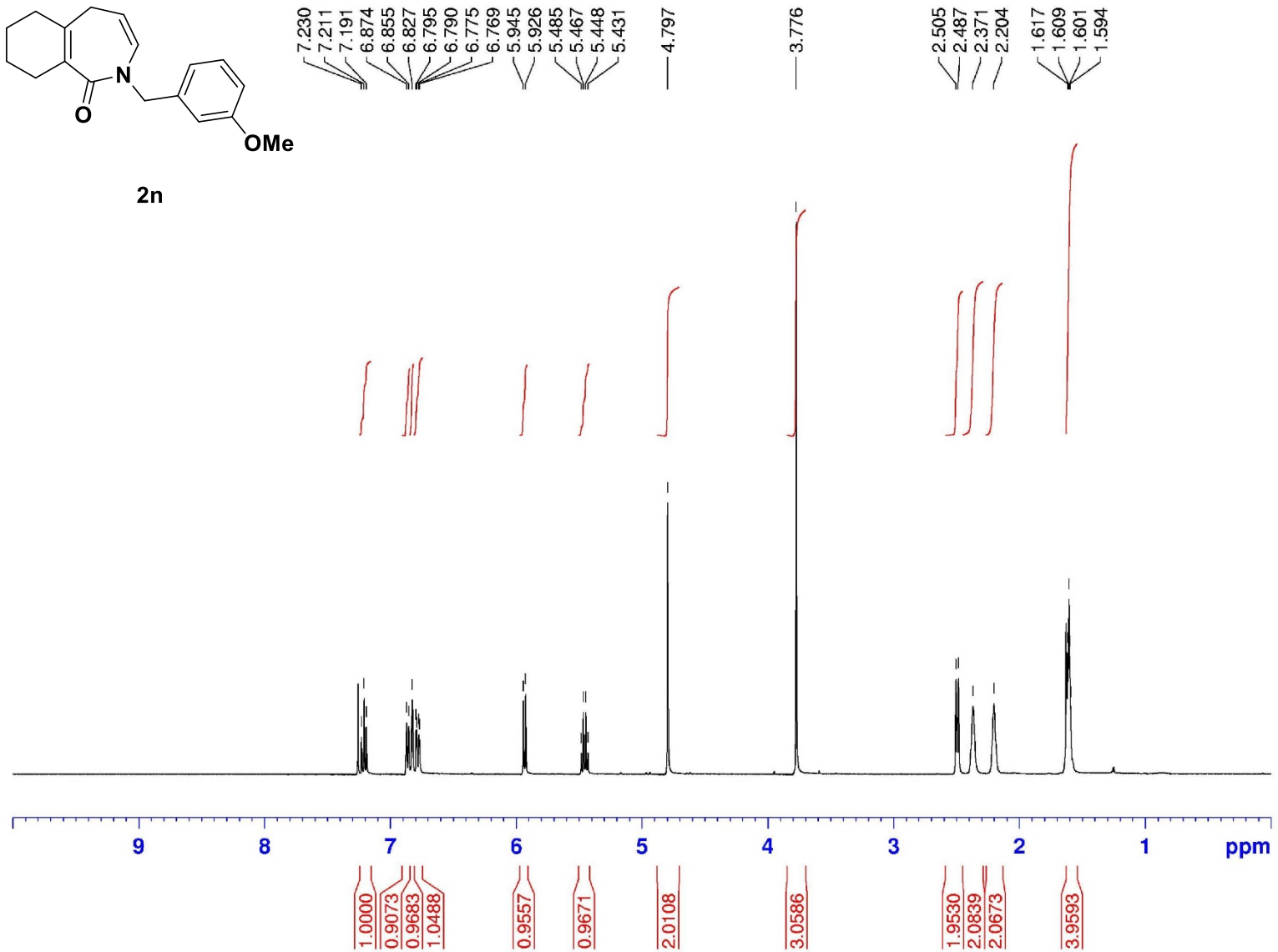
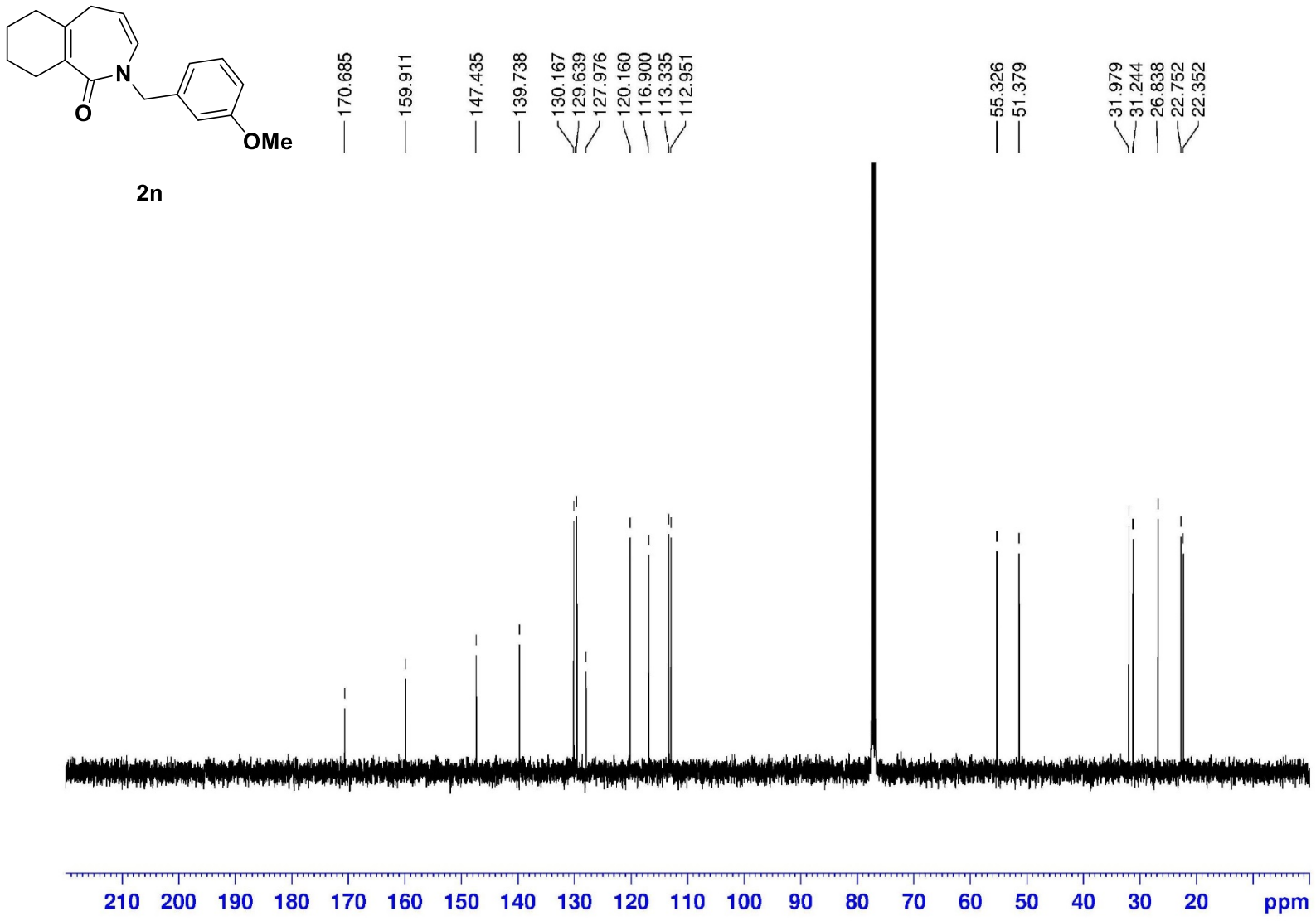
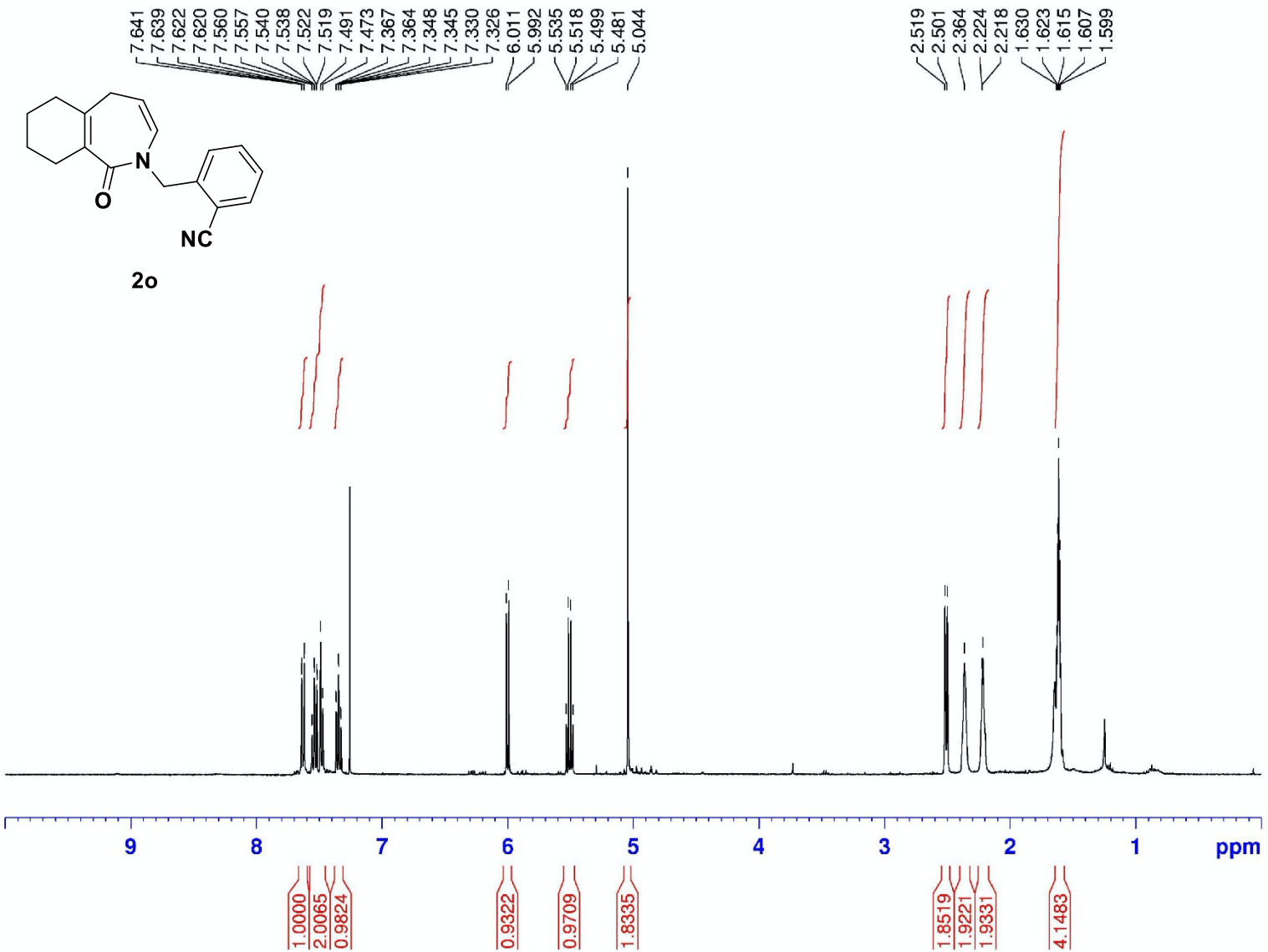
1.9549
1.0022
1.0000
2.0142
2.0730
2.0618
2.0275
4.0980

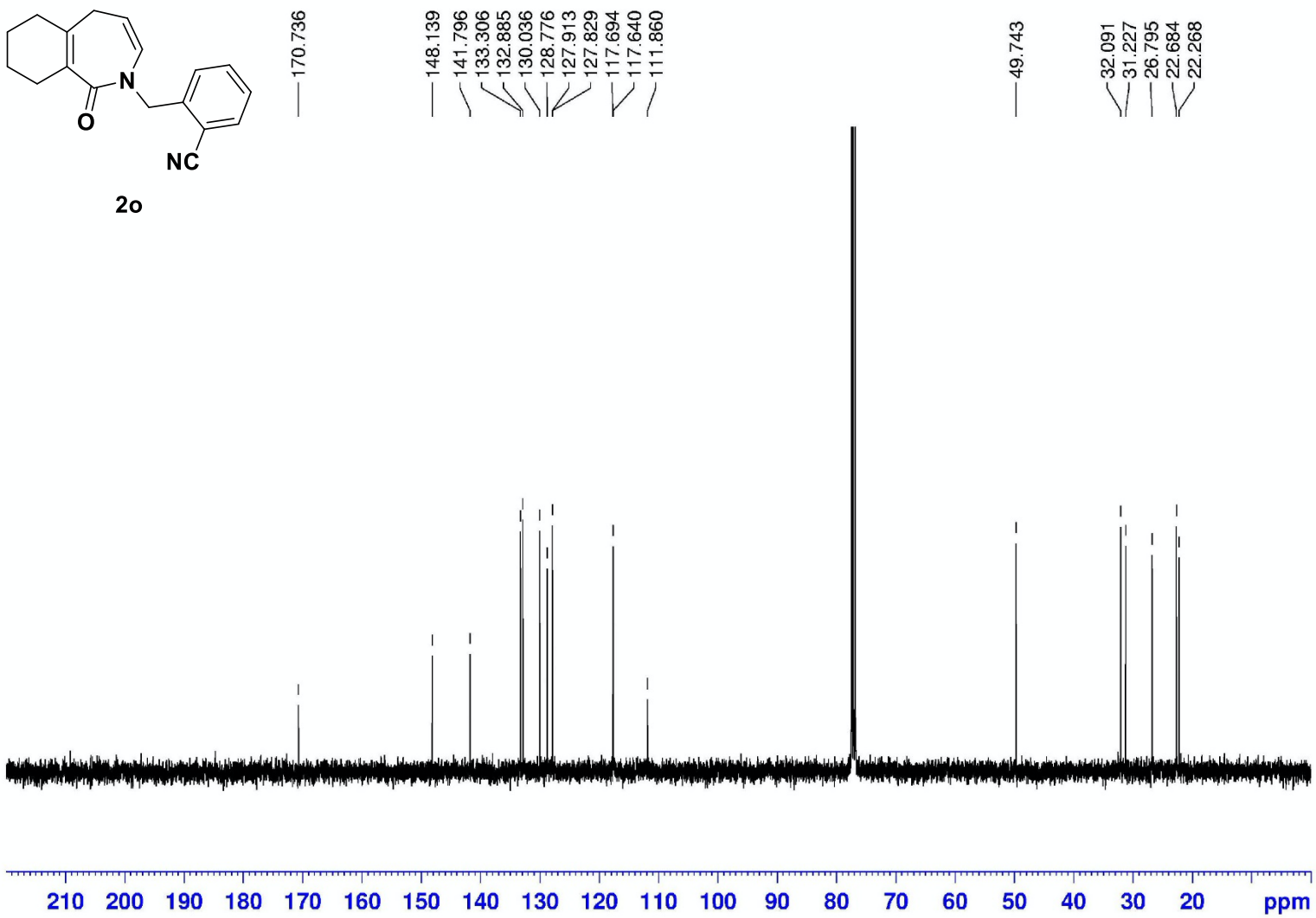

2m
130.100
130.027
129.780
129.458
129.136
128.308
128.041
127.858
125.642
125.604
125.569
125.532
122.899
120.195
117.274
134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 ppm
170.613
147.824
142.239
130.100
130.027
129.780
129.458
129.136
128.308
128.041
127.858
125.642
125.604
125.569
125.532
122.899
120.195
117.274
51.321
31.996
31.191
26.748
22.672
22.258
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

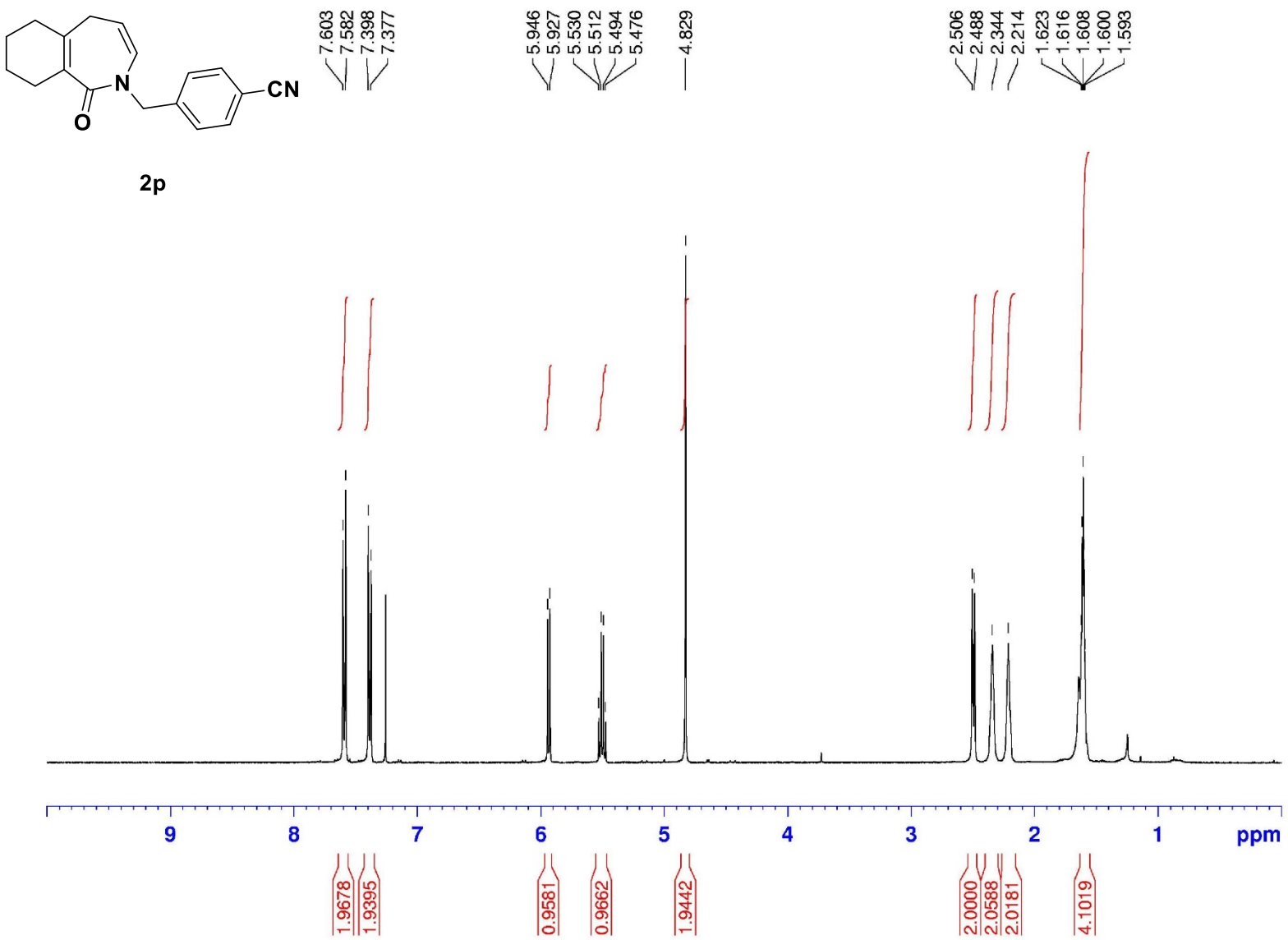

N
O
CF3
2m
-59.818
0
-50
-100
-150
-200
-250
ppm
3.0000

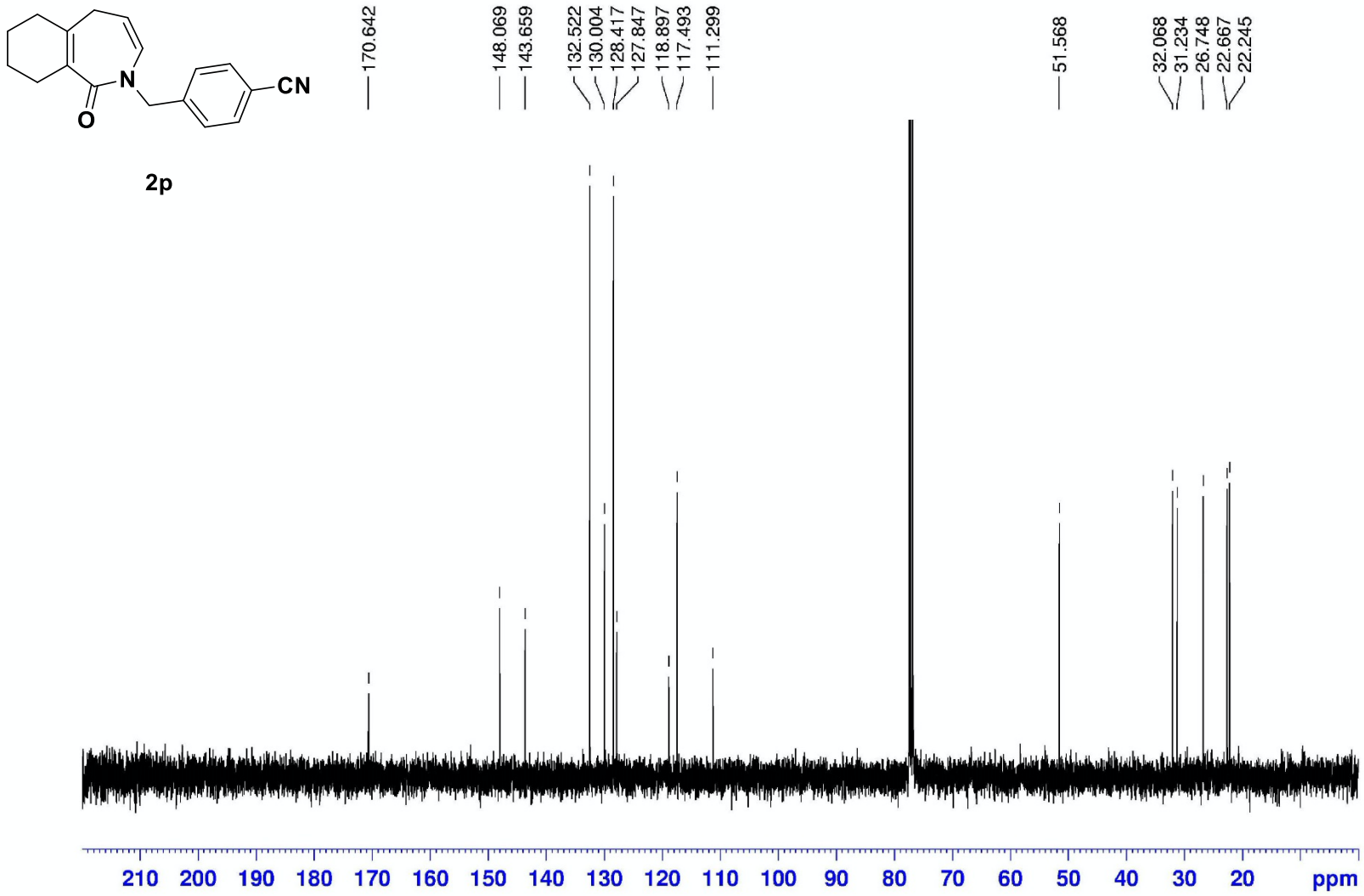

7.230
7.211
7.191
6.874
6.855
6.827
6.795
6.790
6.775
6.769
5.945
5.926
5.485
5.467
5.448
5.431
4.797
3.776
2.505
2.487
2.371
2.204
1.617
1.609
1.601
1.594
O
N
OMe
2n
9
8
7
6
5
4
3
2
1
ppm
1.0000
0.9073
0.9683
1.0488
0.9557
0.9671
2.0108
3.0586
1.9530
2.0839
2.0673
3.9593

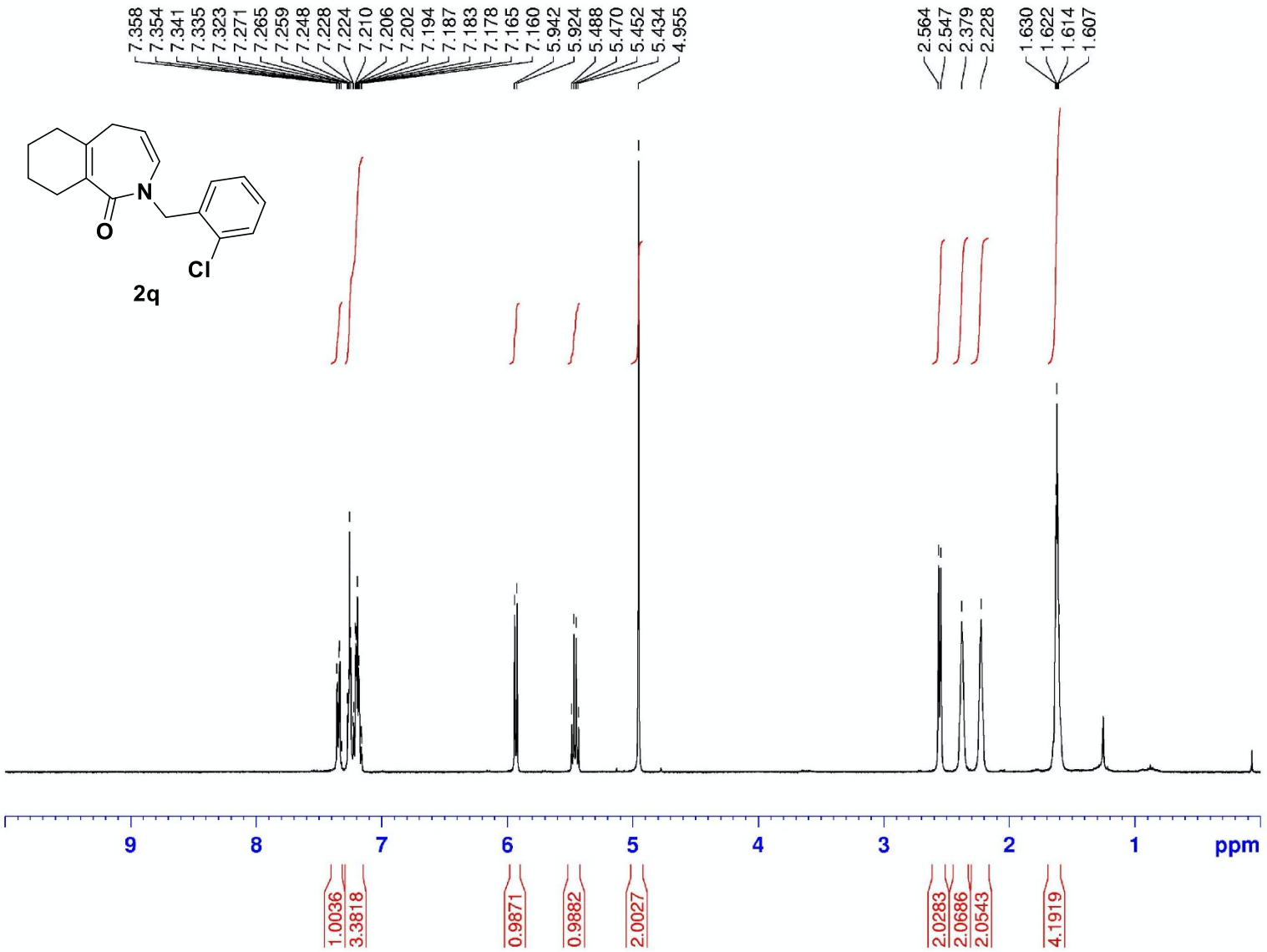

N
O
OMe
2n
170.685
159.911
147.435
139.738
130.167
129.639
127.976
120.160
116.900
113.335
112.951
55.326
51.379
31.979
31.244
26.838
22.752
22.352
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.641
7.639
7.622
7.620
7.560
7.557
7.540
7.538
7.522
7.519
7.491
7.473
7.367
7.364
7.348
7.345
7.330
7.326
6.011
5.992
5.535
5.518
5.499
5.481
5.044
2.519
2.501
2.364
2.224
2.218
1.630
1.623
1.615
1.607
1.599
N
O
NC
2o
9
8
7
6
5
4
3
2
1
ppm
1.0000
2.0065
0.9824
0.9322
0.9709
1.8335
1.8519
1.9221
1.9331
4.1483


170.736
148.139
141.796
133.306
132.885
130.036
128.776
127.913
127.829
117.694
117.640
111.860
49.743
32.091
31.227
26.795
22.684
22.268
O
N
NC
2o
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.603
7.582
7.398
7.377
5.946
5.927
5.530
5.512
5.494
5.476
4.829
2.506
2.488
2.344
2.214
1.623
1.616
1.608
1.600
1.593
N
O
CN
2p
9
8
7
6
5
4
3
2
1
ppm
1.9678
1.9395
0.9581
0.9662
1.9442
2.0000
2.0588
2.0181
4.1019


N
O
CN
2p
170.642
148.069
143.659
132.522
130.004
128.417
127.847
118.897
117.493
111.299
51.568
32.068
31.234
26.748
22.667
22.245
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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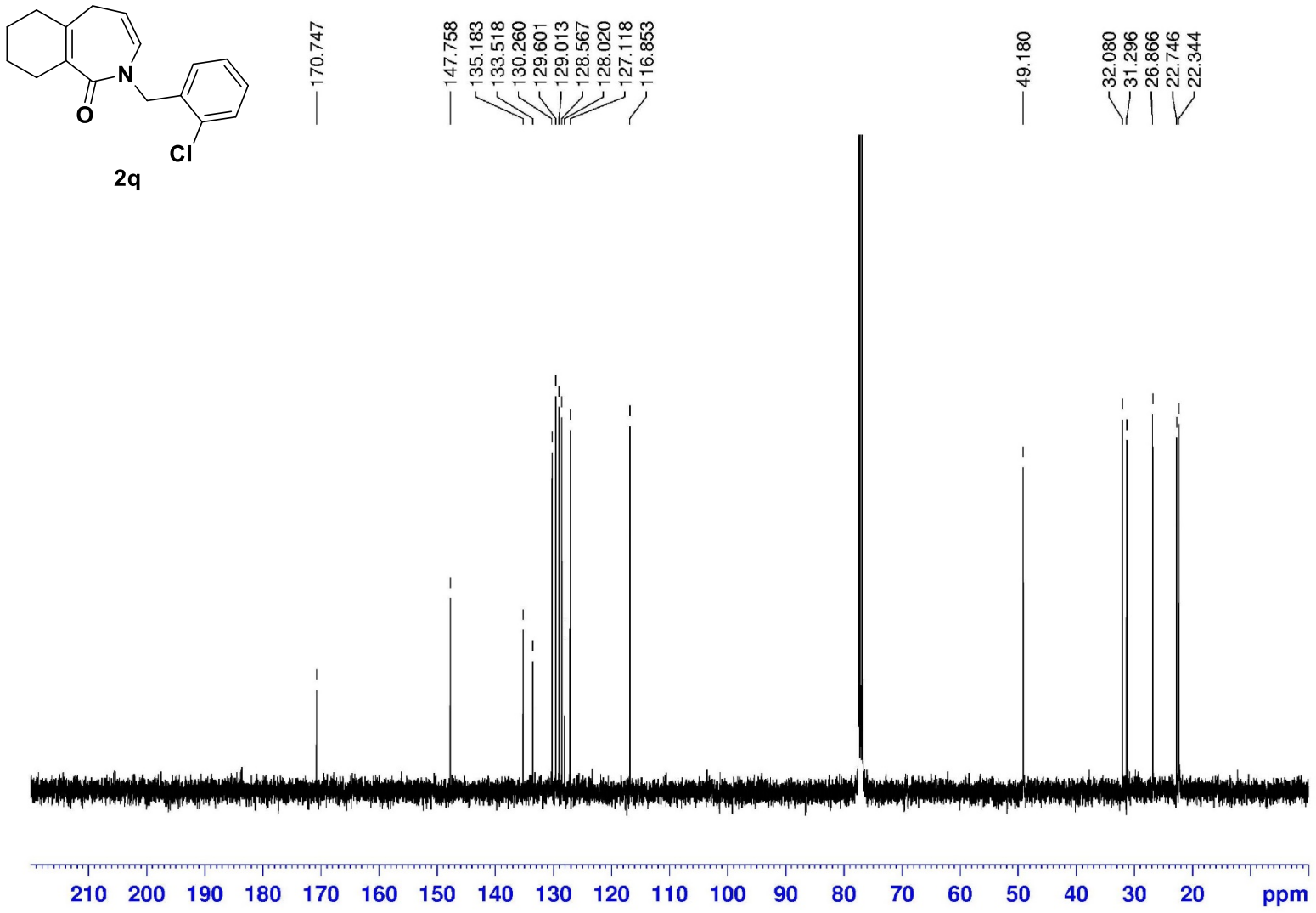
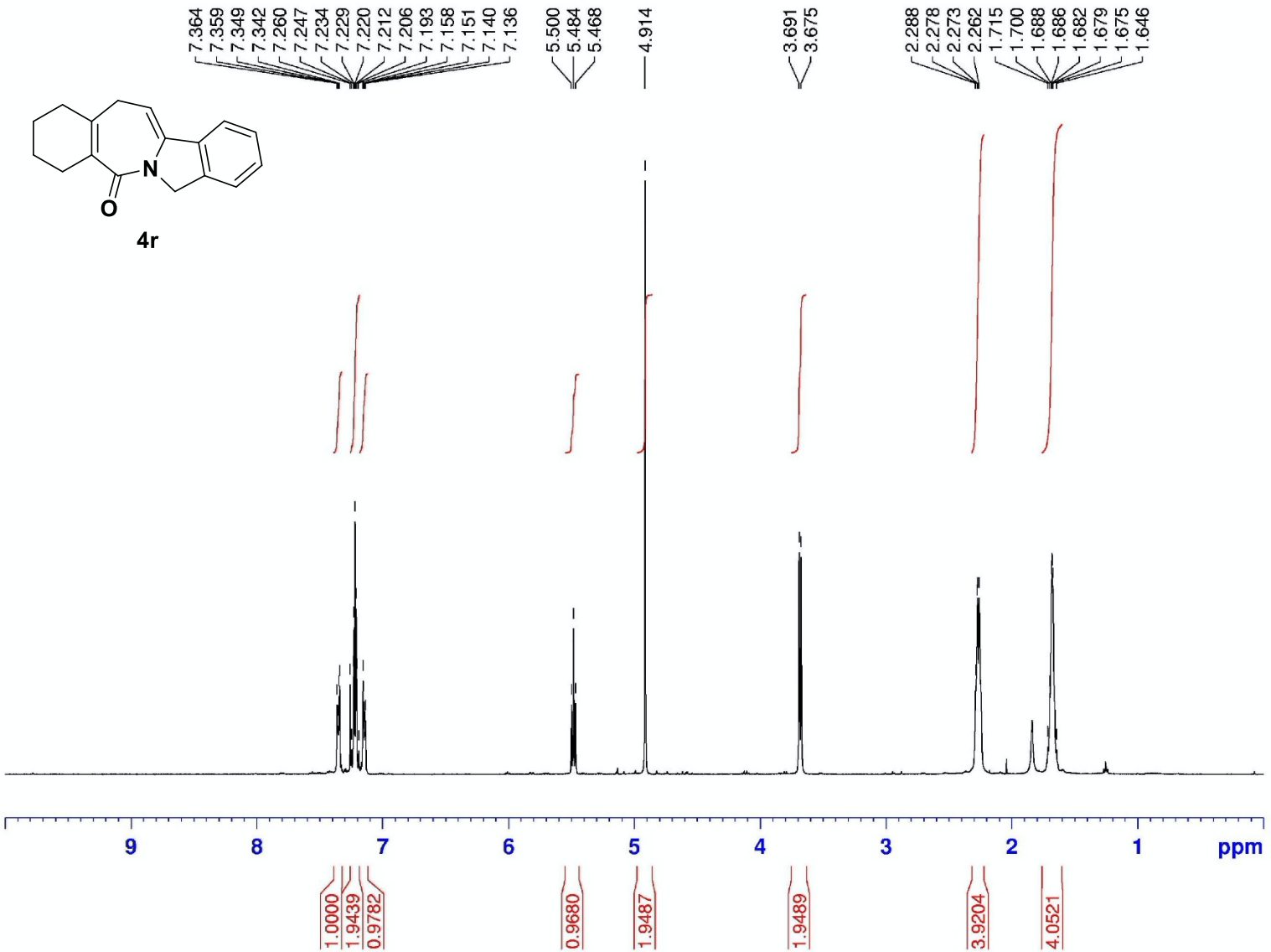
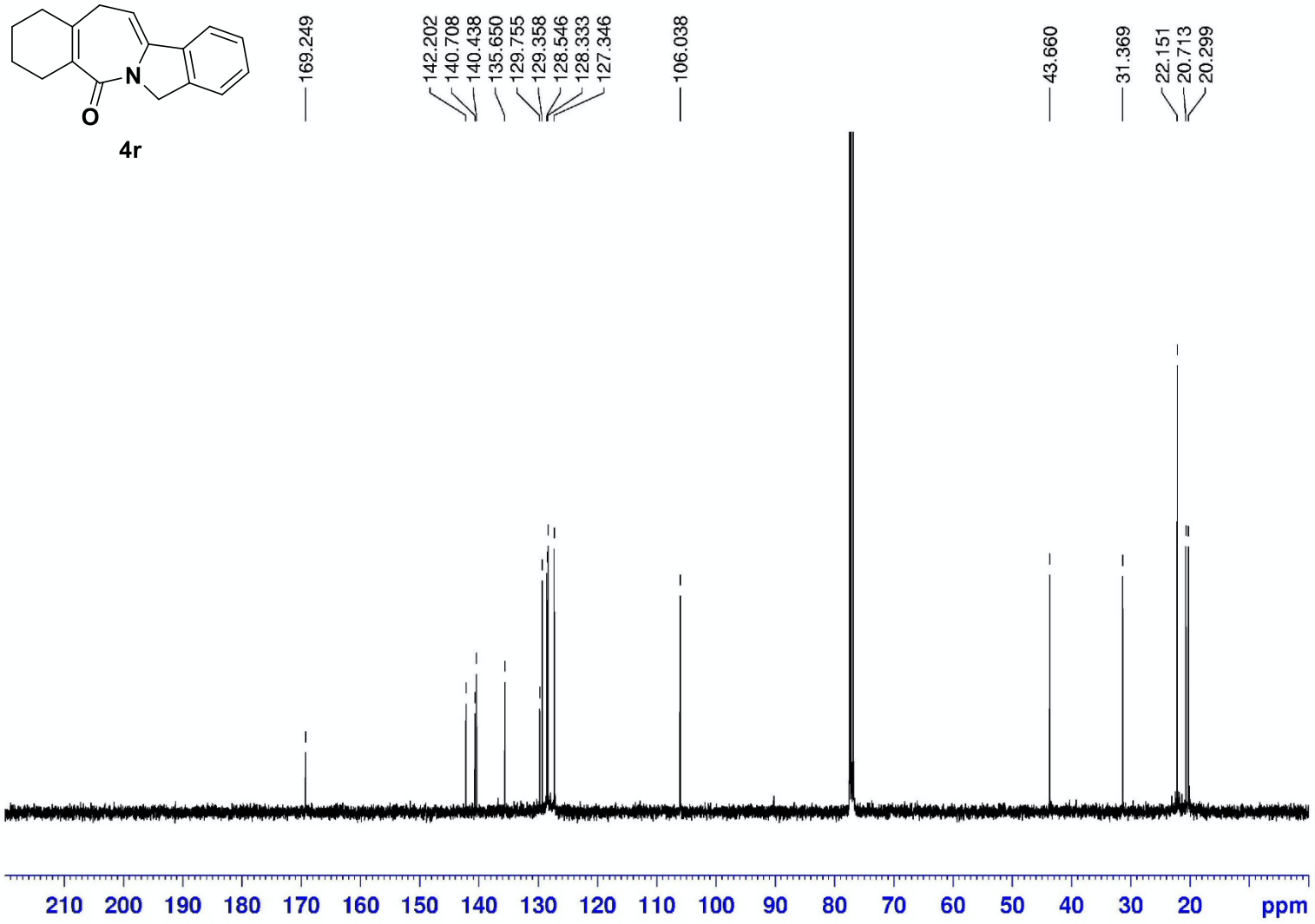
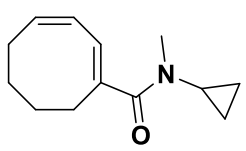
7.354
7.341
7.335
7.323
7.271
7.265
7.259
7.248
7.228
7.224
7.210
7.206
7.202
7.194
7.187
7.183
7.178
7.165
7.160
5.942
5.924
5.488
5.470
5.452
5.434
4.955
2.564
2.547
2.379
2.228
1.630
1.622
1.614
1.607
N
O
Cl
2q
9
8
7
6
5
4
3
2
1
ppm
1.0036
3.3818
0.9871
0.9882
2.0027
2.0283
2.0686
2.0543
4.1919


N
O
Cl
2q
170.747
147.758
135.183
133.518
130.260
129.601
129.013
128.567
128.020
127.118
116.853
49.180
32.080
31.296
26.866
22.746
22.344
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.364
7.359
7.349
7.342
7.260
7.247
7.234
7.229
7.220
7.212
7.206
7.193
7.158
7.151
7.140
7.136
5.500
5.484
5.468
4.914
3.691
3.675
2.288
2.278
2.273
2.262
1.715
1.700
1.688
1.686
1.682
1.679
1.675
1.646
N
O
4r
9
8
7
6
5
4
3
2
1
ppm
1.0000
1.9439
0.9782
0.9680
1.9487
1.9489
3.9204
4.0521


O
N
4r
169.249
142.202
140.708
140.438
135.650
129.755
129.358
128.546
128.333
127.346
106.038
43.660
31.369
22.151
20.713
20.299
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

NMR: Side product from the beta-hydride elimination reaction (SM: **5m**)



5m

NMR: Mixture of **2a:3a** with 1,3,5-trimethoxybenzene (TMB)(25.6 mg, 152 µmol) as an internal standard