Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information for:

One-shot access to α,β-difunctionalized azepenes and dehydropiperidines by reductive cross-coupling of α-selenonyl-β-selenyl enamides with organic bromides

Timothy K. Beng, Ann Wens V. Silaire, Amir Alwali, and Daniel P. Bassler*

Department of Chemistry, Susquehanna University, Selinsgrove,
PA 17870, USA
beng@susqu.edu

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1. General Information and Procedures

All experiments involving air- and moisture-sensitive reagents such as transition metal precatalysts were carried out under an inert atmosphere of argon or nitrogen, using freshly distilled solvents. Dichloromethane was distilled from $MgSO_4$. Organic bromides and other simple reagents were obtained from commercial sources. All electrophiles that were not newly purchased were distilled immediately before use. TMEDA was distilled on a short path, over CaH_2. Column chromatography was performed on silica gel (230-400 mesh). Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed on silica plates. Visualization of the TLC plates was aided by UV irradiation at 254 nm or by $KMnO_4$, CAM, and *p*-anisaldehyde staining. Unless otherwise indicated, ^1H, ^{13}C, and DEPT-135 spectra were acquired using C_6D_6 or $CDCl_3$ as solvent, at room temperature. Chemical shifts are quoted in parts per million (ppm). HRMS-EI^+ data were obtained using either electrospray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using Excalibur). High resolution EI was obtained on an Autospec (magnetic sector; analyzed using MassLynx).

General Procedure A: Selenation of enecarbamates with PhSeSePh

To an oven-dried, septum-capped round bottom flask equipped with a stir bar, was added freshly distilled TMEDA (0.09 mL, 0.6 mmol, 1.2 equiv) and a solution of the enecarbamate (0.5 mmol, 1.0 equiv) in THF (5 mL) under argon. The mixture was cooled to –60 °C and a solution of *n*-BuLi (0.24 mL, 2.5 M in hexanes, 0.6 mmol, 1.2 equiv) was added slowly. After 2 h at this temperature, the mixture was quenched with PhSeSePh (2 equiv). The mixture was slowly warmed to room temperature and *sat*. NH_4Cl was added. The layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered and evaporated to obtain the crude product, which was oxidized immediately without further purification.

General Procedure B1: Selenation of α-bromo eneformamides with PhSeSePh

Sodium borohydride (6 mmol) was added to a solution of diphenyl diselenide (3 mmol) in DMF (8 mL) at 120 ^oC. After 1 h, a solution of the bromo eneformamide (1 mmol) was added. After 5 h (TLC monitoring), the reaction mixture was poured into *sat* $NH_4Cl_{(aq)}$ solution and extracted with Et_2O. The combined organic layers were washed with water, then with brine, dried over Na_2SO_4, filtered, and evaporated under reduced pressure to obtain the crude products.

General Procedure B2: Diphenyldiselenide (1.2 mmol) was added to a solution of the bromoeneformamide (1 mmol) in dry acetonitrile (8 mL) at room temperature and the mixture was heated to 80 ^{o}C. After 4 h, the mixture was directly evaporated. To the resulting residue, potassium *tert*-butoxide (2 mmol) in THF (8 mL) was added and the mixture was allowed to stand for 1 h at room temperature. The reaction mixtures were poured into aqueous NH_4Cl solution and extracted with Et_2O. The organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to obtain the crude selenide, which was immediately oxidized.

General Procedure C: Oxidation of Selenides

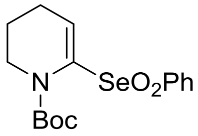
The crude selenide (1 mmol) was dissolved in CH_2Cl_2 (4 mL) and MeOH (4 mL) at room temperature and *m*-CPBA (4 mmol) was added. Following complete consumption of the selenide (TLC monitoring), the mixture was poured onto 10% Na_2CO_3 solution, and extracted with Et_2O. The organic layers were washed with water, dried, and evaporated. Purification was carried out by flash chromatography on silica (pretreated with 1% Et_3N).

Procedure D: Alkylative deselenonation with Grignard reagents: To an oven-dried, septum-capped two-necked flask equipped with a stir bar were added freshly distilled TMEDA (0.90 mL, 6.00 mmol, 6.0 equiv), PhMgBr (3.0 M in Et_2O, 1.00 mL, 3.00 mmol, 3.0 equiv) diluted with anhydrous tert-butyl methyl ether (TBME, 3.0 mL) via syringe under an argon atmosphere. One of the septa was opened and $Fe(acac)_3$ (7.1 mg, 0.020 mmol, 2 mol%) was rapidly introduced and the suspension was diluted with TBME (5.0 mL) was added. After several minutes (~5 min), α-selenonyl enecarbamate **1a** (371 mg, 1.00 mmol, 1.0 equiv) in TBME (5.0 mL) was added. The suspension was sonicated until a clear solution was obtained (~10 min, longer time required for less suluble Grignard reagents). After 5 h at rt (TLC and GC-MS monitoring), the mixture was quenched by slow addition of *sat* NH_4Cl. It was then filtered through a pad of Celite under vacuum and the remaining residue was rinsed with EtOAc. The filtrate was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc and the combined organic extracts were dried over Na_2SO_4 (30 min), filtered, and concentrated in under reduced pressure to give the crude product.

General Procedure E: (β-regioselective lithiation/heterosubstitution): To an oven-dried, septum-capped round bottom flask equipped with a stir bar, was added freshly distilled TMEDA (1.8 mL, 1.2 mmol, 1.2 equiv) and a solution of the enecarbamate (1 mmol, 1.0 equiv) in THF (10 mL) under argon. The mixture was cooled to –78 °C and a solution of *t*-BuLi (1.2 mL, 1.0 M in pentane, 1.2 mmol, 1.2 equiv; in the case of eneformamides) or *n*-BuLi (0.5 mL, 2.0 M in hexanes; in the case of enecarbamates) was added slowly. After 1 h at this temperature, the mixture was quenched with the desired electrophile (2 equiv). The mixture was slowly warmed to room temperature and *sat*. NH_4Cl was added. The layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered and evaporated to obtain the crude product.

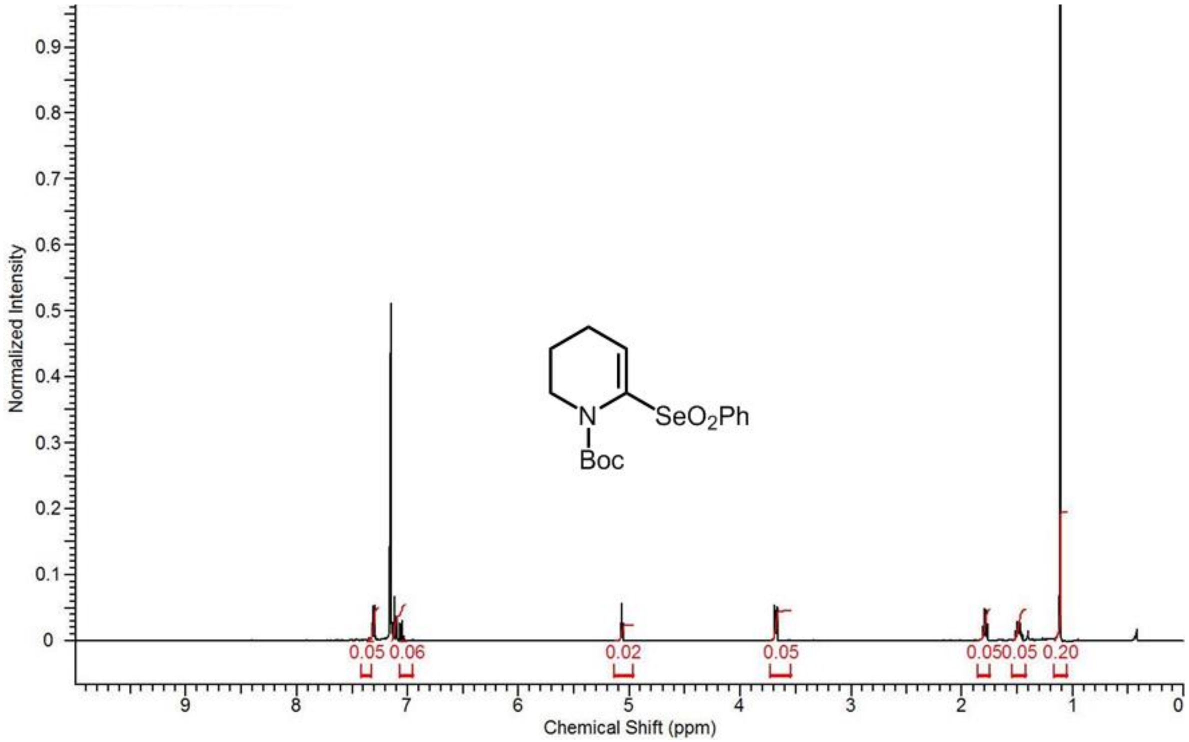
General Procedure F: To a solution of $CoBr_2$ (22 mg, 0.10 mmol, 10 mol%), bis-1,2-diphenylphosphinopropane (41.2 mg, 0.10 mmol, 10 mol%), and manganese powder (165 mg, 3 mmol, 3 equiv) in acetonitrile (5 mL) was added the aryl bromide (2 mmol, 2 equiv) at the desired temperature (rt for the bromo eneformamides or 40 ^{o}C for the bromo enecarbamates). A solution of the bromo eneformamide (1 mmol, 1 equiv) in acetonitrile (5 mL) was added slowly. After completion (as judged by TLC and GC-MS), the reaction mixture was treated with a mild acid such as 10% H_3PO_4 (aq) and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the desired coupling product as an oil. Purification was carried out by flash chromatography on silica (pretreated with 1% Et_3N).

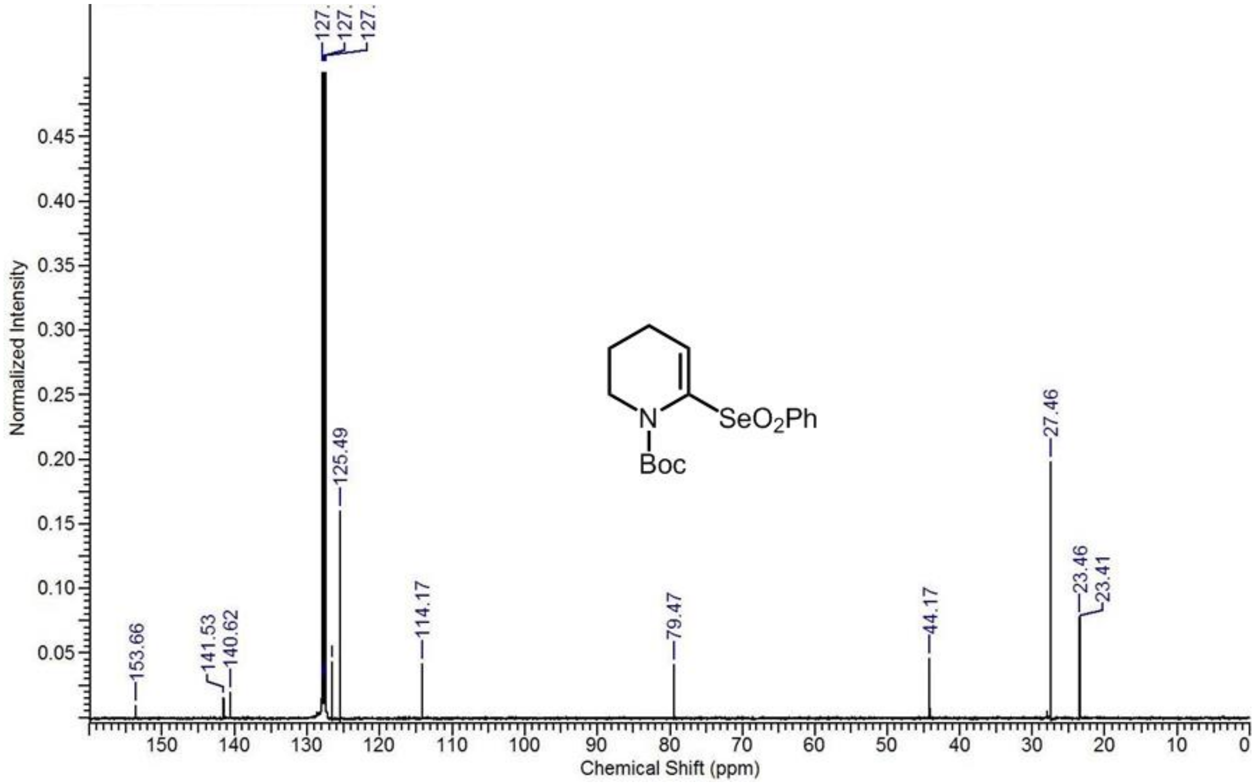
2. Preparation of α-selenonyl dehydropiperidines and azepenes

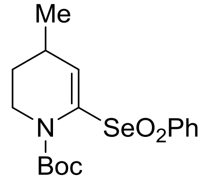


1a

Prepared from **6a** (183 mg, 1.0 mmol) using **General Procedures A** and **C.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (2:1). Yield = 289 mg; 78%. ^1H NMR (400 MHz, C_6D_6) δ 7.33 to 7.28 (2H, m), 7.18 to 7.06 (3H, m), 5.09 to 5.06 (1H, t), 3.70 to 3.64 (2H, dd), 1.82 to 1.73 (2H, m), 1.53 to 1.44 (2H, m), 1.10 (9H, s). ^{13}C NMR (101 MHz, C_6D_6) δ 153.7, 141.5, 140.6, 127.0, 125.5, 114.2, 79.5, 44.2, 27.5, 23.5, 23.4. HRMS calc for $C_{16}H_{21}NO_4Se$ 371.0636, found 371.0631.

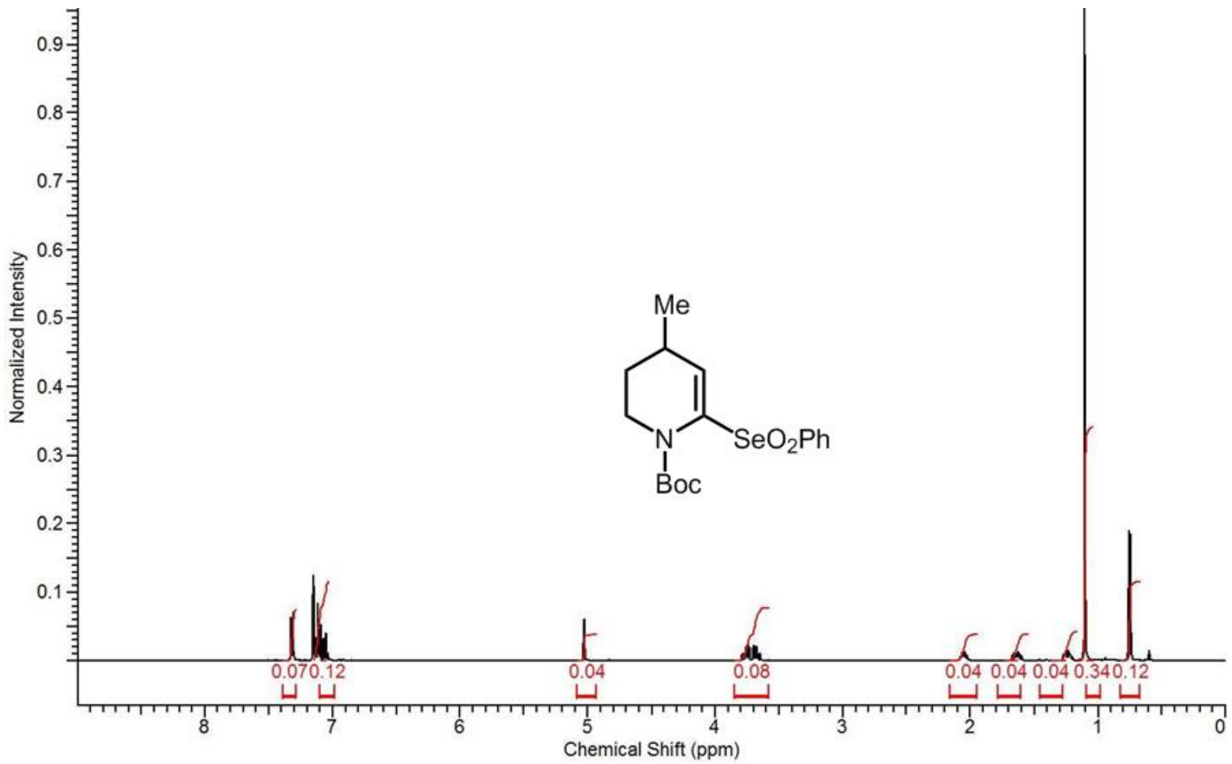






1b

Prepared from **6b** (197 mg, 1 mmol) using **General Procedures A** and **C.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N). PE/DCM (2:1). Yield = 324 mg; 84%. ^1H NMR (400 MHz, C_6D_6, mixture of rotamers) δ 7.45 (1H, d) 7.18 to 6.99 (4H, m), 5.01 (1H, t), 3.91 to 3.55 (2H, dd), 2.09 to 2.03 (1H, m), 1.68 to 1.50 (1H, m), 1.46 to 1.02 (11H, m), 0.86 to 0.60 (3H, d). ^{13}C NMR (101 MHz, C_6D_6, mixture of rotamers) δ 153.55, 141.36, 141.31, 139.53, 128.67, 127.09, 126.63, 125.63, 120.02, 79.52, 78.33, 42.77, 31.54, 28.84, 28.21, 27.96, 27.42, 21.58, 21.16. HRMS calc for $C_{17}H_{23}NO_4Se$ 385.0792, found 385.0796.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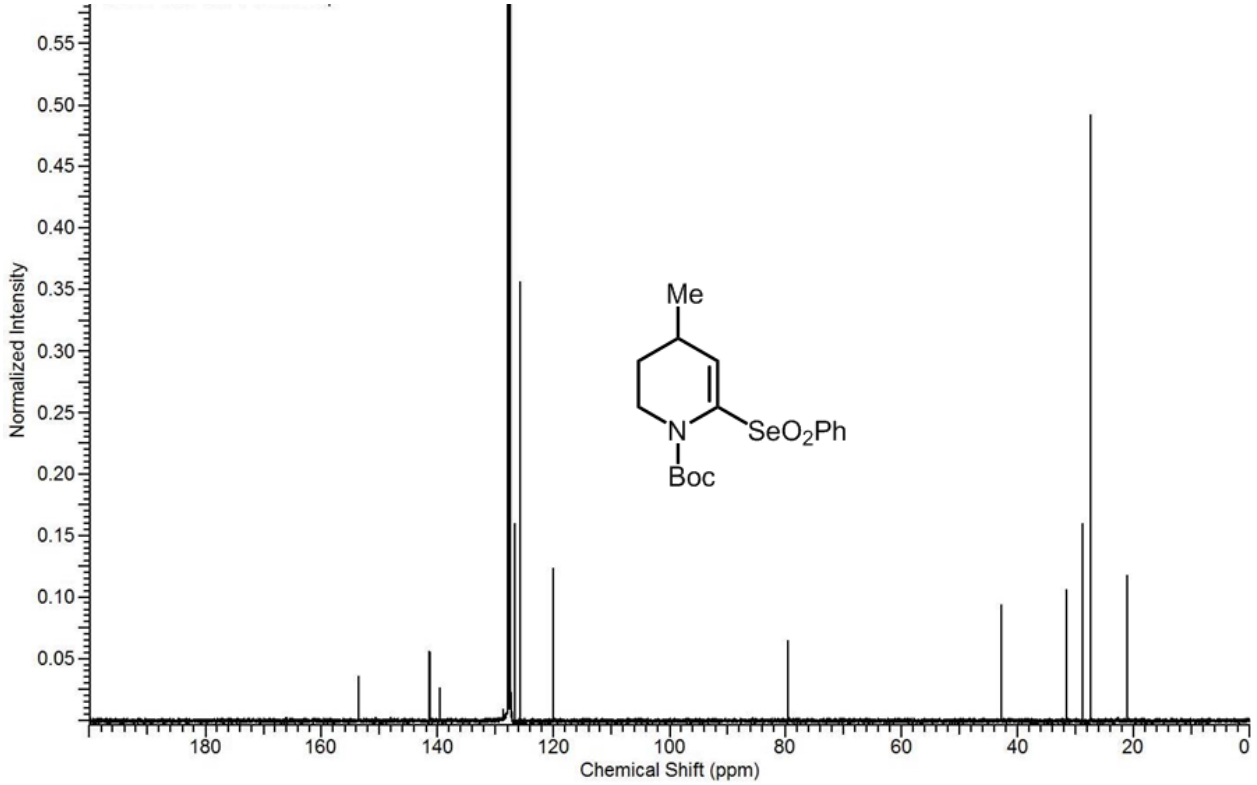
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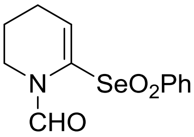
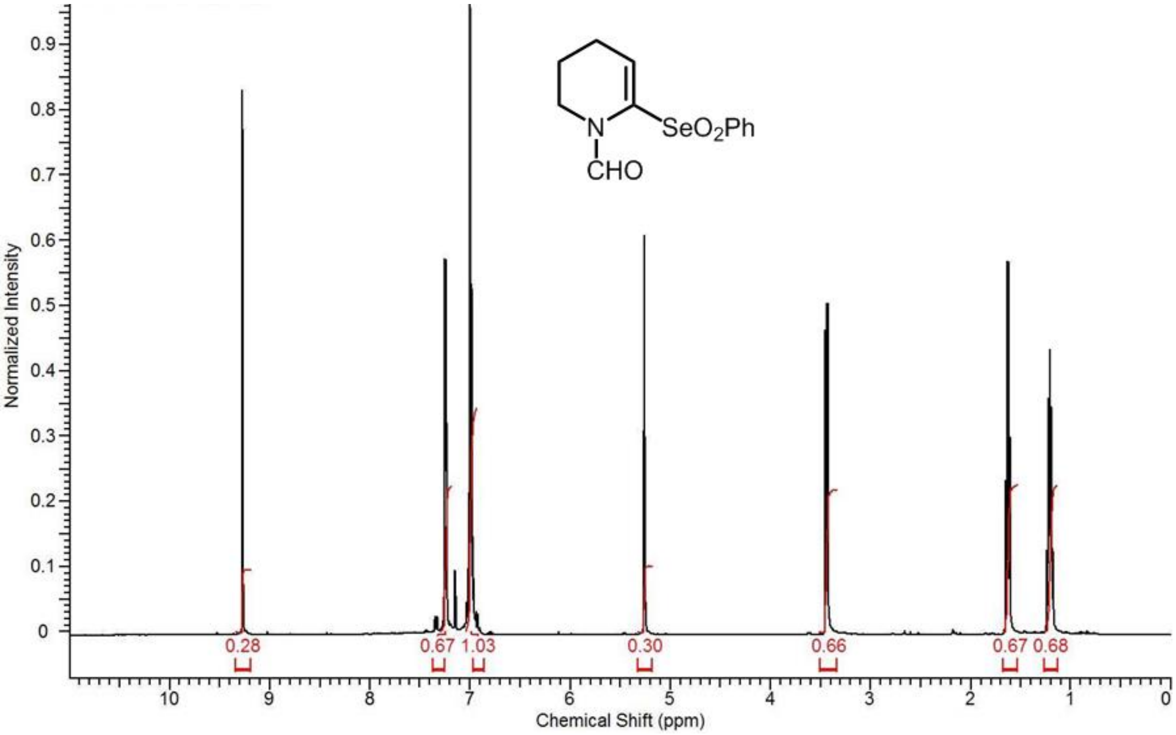
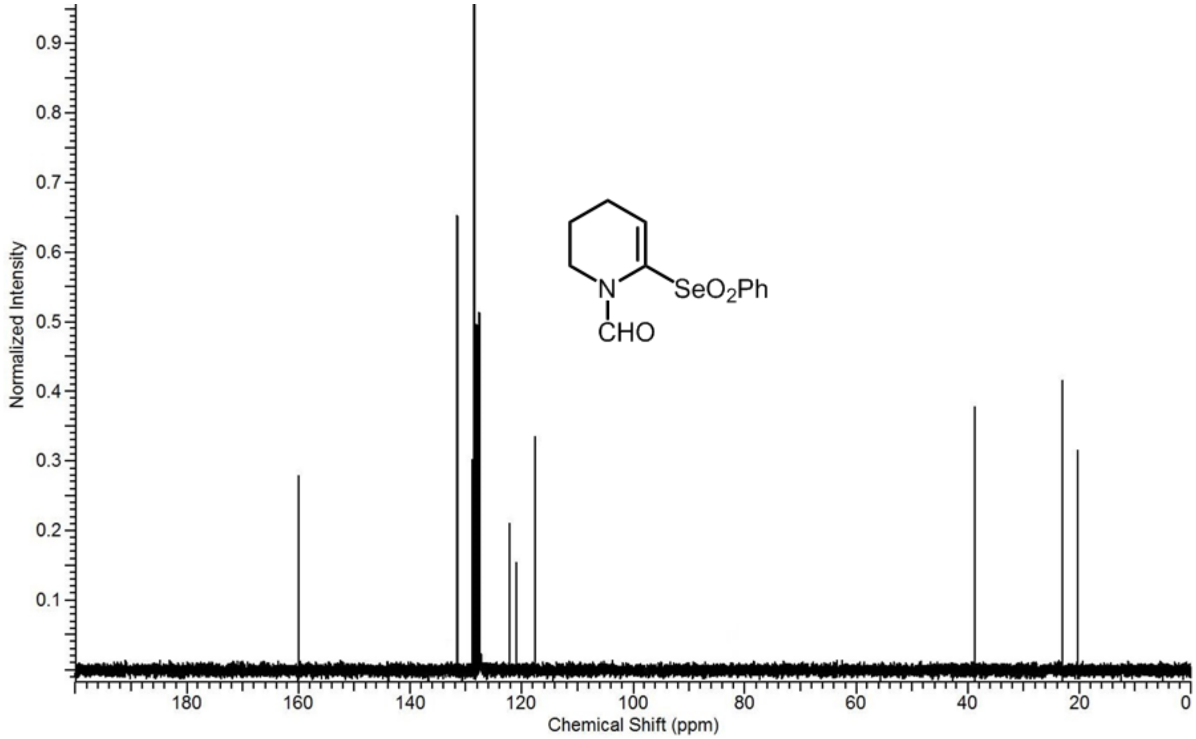
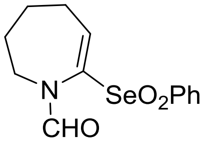


1c

Prepared from **7a** (189 mg, 1 mmol) using **General Procedures B1** and **C.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 213 mg, 71%. ^{1}H NMR (400 MHz, C_6D_6) δ 9.35 (1H, s), 7.28 to 7.21 (2H, m), 7.00 to 6.93 (3H, m), 5.28 to 5.25 (1H, t), 3.46 to 3.43 (2H, dd), 1.60 to 1.52 (2H, m), 1.20 to 1.14 (2H, m). ^{13}C NMR (101 MHz, C_6D6) δ 160.6, 132.1, 129.3, 129.0, 122.7, 121.58, 118.0, 93.4, 83.0, 39.3, 23.6, 20.9. HRMS calc for $C_{12}H_{13}NO_3Se$ 299.0061, found 299.0065.

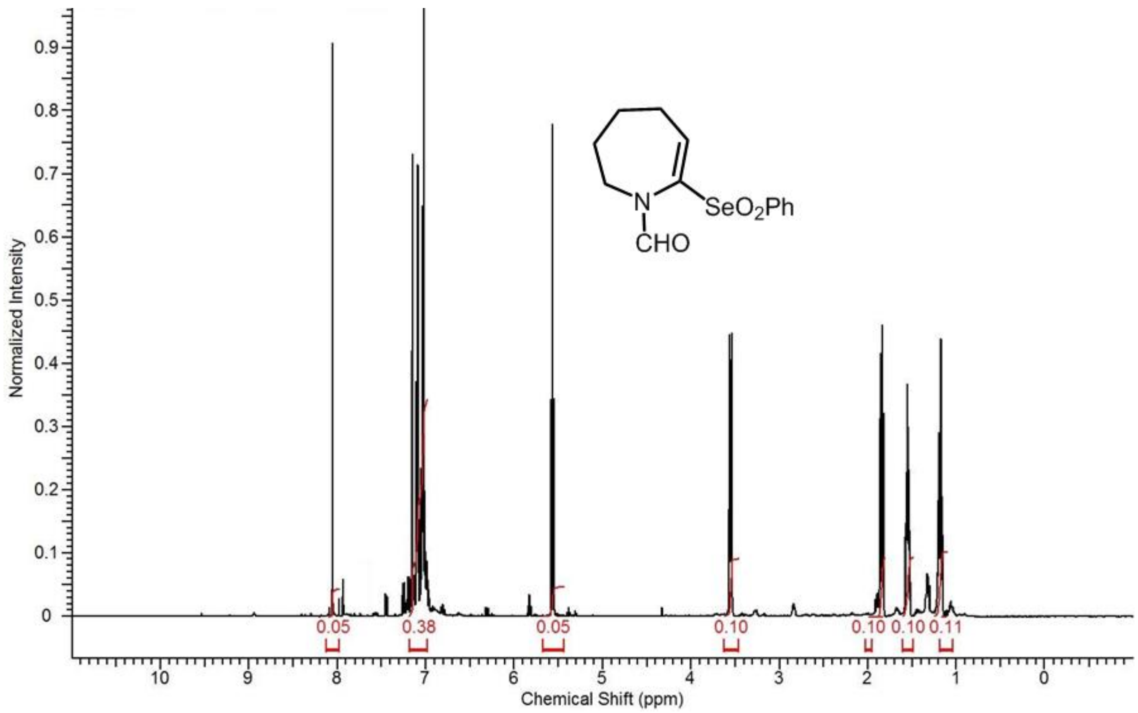






1d

Prepared from **7b** (203 mg, 1 mmol) using **General Procedures B2** and **C.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 235 mg, 75%. ^{1}H NMR (400 MHz, C_6D_6, mixture of rotamers) δ 8.07 (1H, s), 7.11 to 7.01 (5H, m), 5.58 to 5.54 (1H, t), 3.58 to 3.55 (2H, dd), 1.86 to 1.82 (2H, m), 1.59 to 1.53 (2H, m), 1.21 to 1.15 (2H, m).^{13}C NMR (101 MHz, C_6D_6) δ 161.8, 143.0, 138.5, 131.4, 128.6, 125.9, 123.3, 44.2, 28.7, 27.2, 24.1. HRMS calc for $C_{13}H_{15}NO_3Se$ 313.0217, found 313.0221.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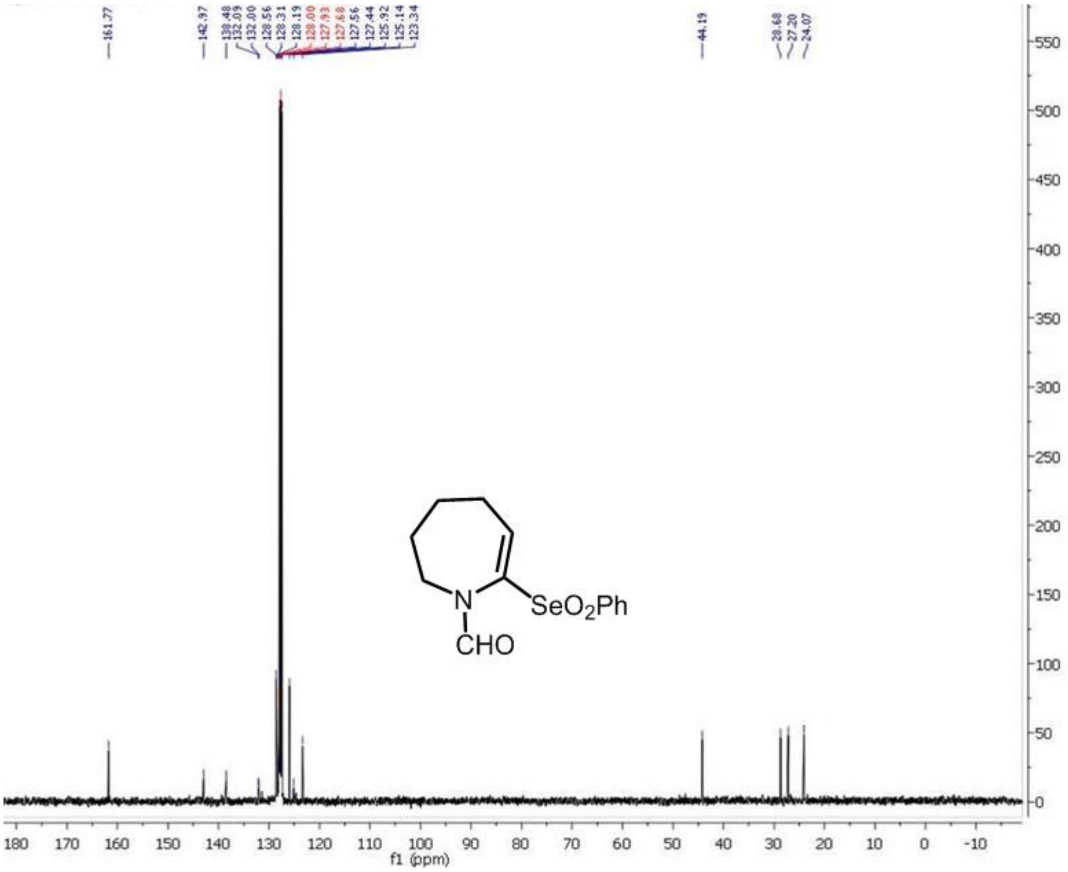
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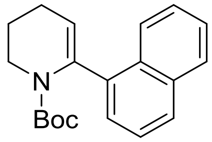
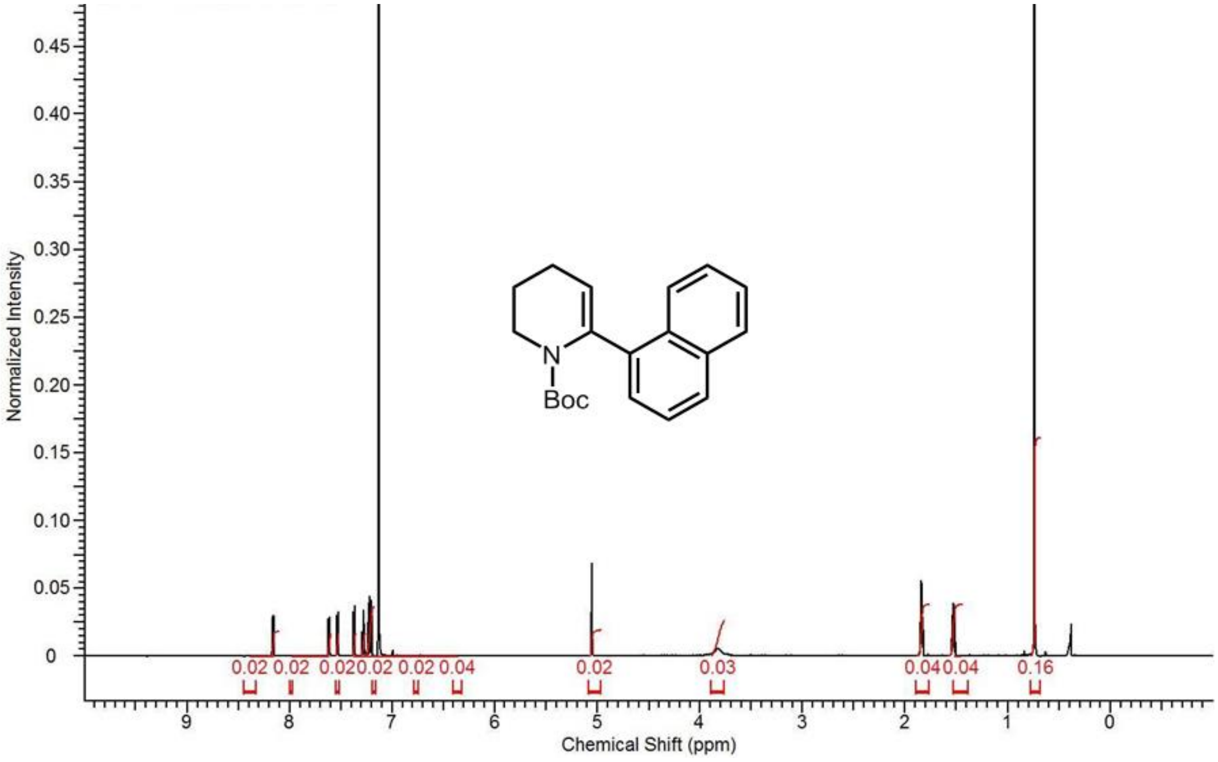
f1 (ppm)

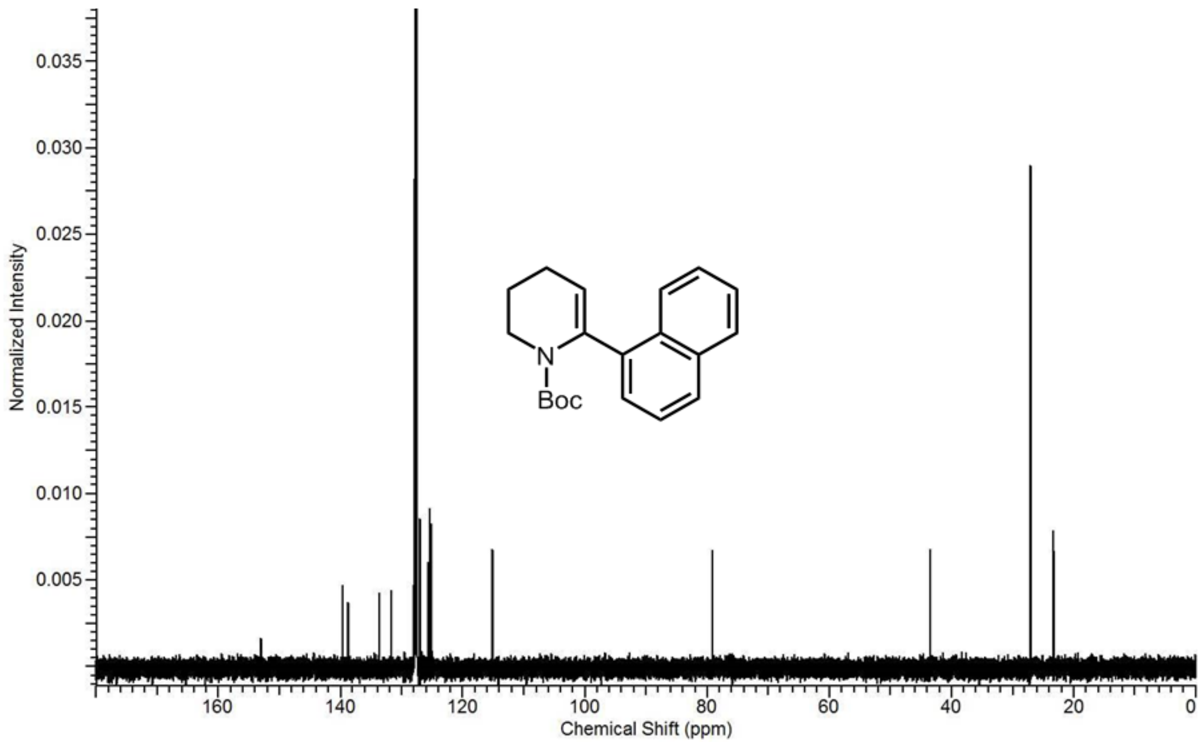
3. Preparation of α-carbofunctionalized dehydropiperidines and azepenes

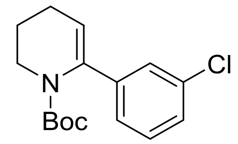


2a

Prepared from **1a** (371 mg, 1 mmol) and 1-naphthylmagnesium bromide (3 equiv) using **General Procedure D.** Purification: Flash chromatography on silica (pretreated with 1% Et$_3$N) eluting with PE/DCM (2:1). Yield = 216 mg; 70%. ^{1}H NMR (400 MHz, C$_6$D$_6$) δ 8.16 (1H, d), 7.81 to 7.85 (6H, m), 5.18 to 5.17 (1H, t), 3.79 to 3.71 (2H, dd), 1.88 to 1.83 (2H, m), 1.55 to 1.52 (2H, m), 0.98 (9H, s). ^{13}C NMR (101 MHz, C$_6$D$_6$) δ 153.7, 140.5, 138.9, 133.6, 132.7, 128.5, 128.2, 127.8, 127.5, 127.2, 126.0, 125.3, 124.5, 123.7, 114.9, 79.5, 44.2, 27.3, 23.6, 23.4. HRMS calc for $C_{20}H_{23}NO_2$ 309.1729, found 309.1733.

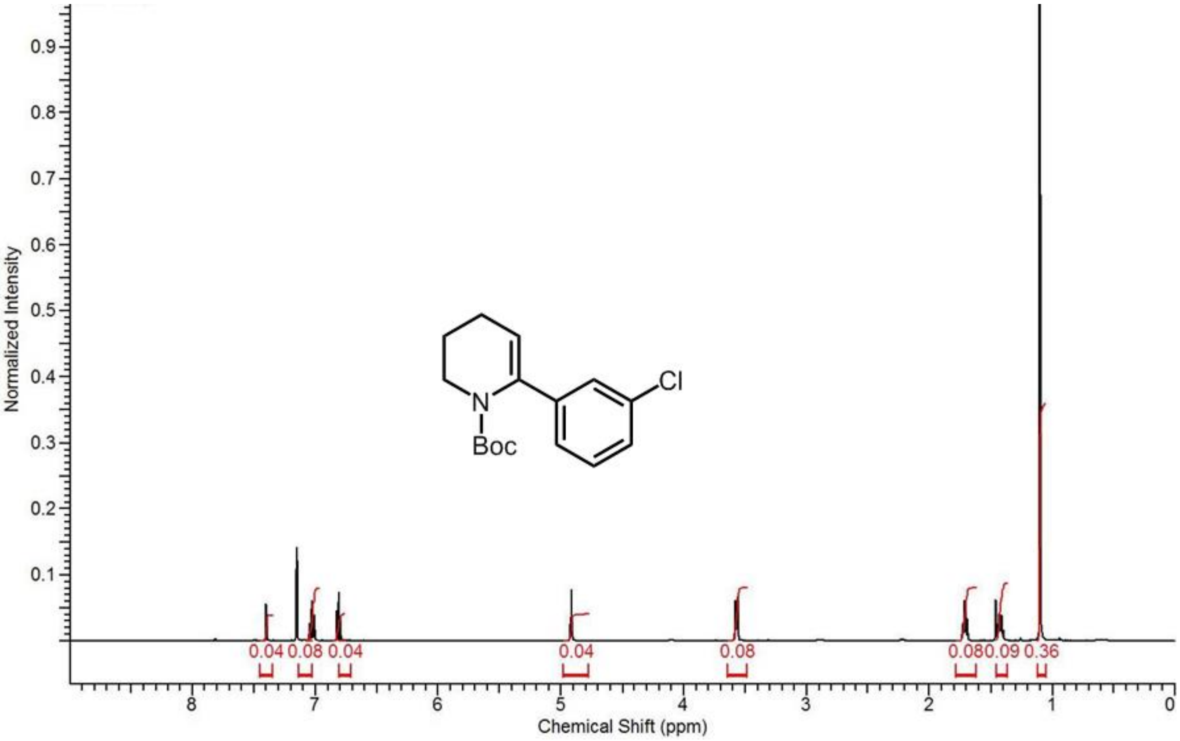






2b

Prepared from **1a** (371 mg, 1.0 mmol) and 3-chlorophenylmagnesium bromide (3 equiv) using **General Procedure D.** Temp = 50 °C, time = 22 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (1:1). Yield = 229 mg; 78%. ^{1}H NMR (400 MHz, C_6D6) δ 7.22 (1H, s), 7.18 to 6.96 (2H, m), 6.80 to 6.71 (1H, t), 5.14 to 5.12 (1H, t), 3.68 to 3.66 (2H, dd), 1.82 to 1.78 (2H, m), 1.52 to 1.46 (2H, m), 1.14 (9H, s). ^{13}C NMR (101 MHz, C_6D_6) δ 153.3, 143.3, 139.2, 133.8, 129.0, 126.5, 125.8, 123.5, 115.2, 79.8, 44.0, 27.4, 23.4, 23.1. HRMS calc for $C_{16}H_{20}ClNO_2$ 293.1183, found 293.1178.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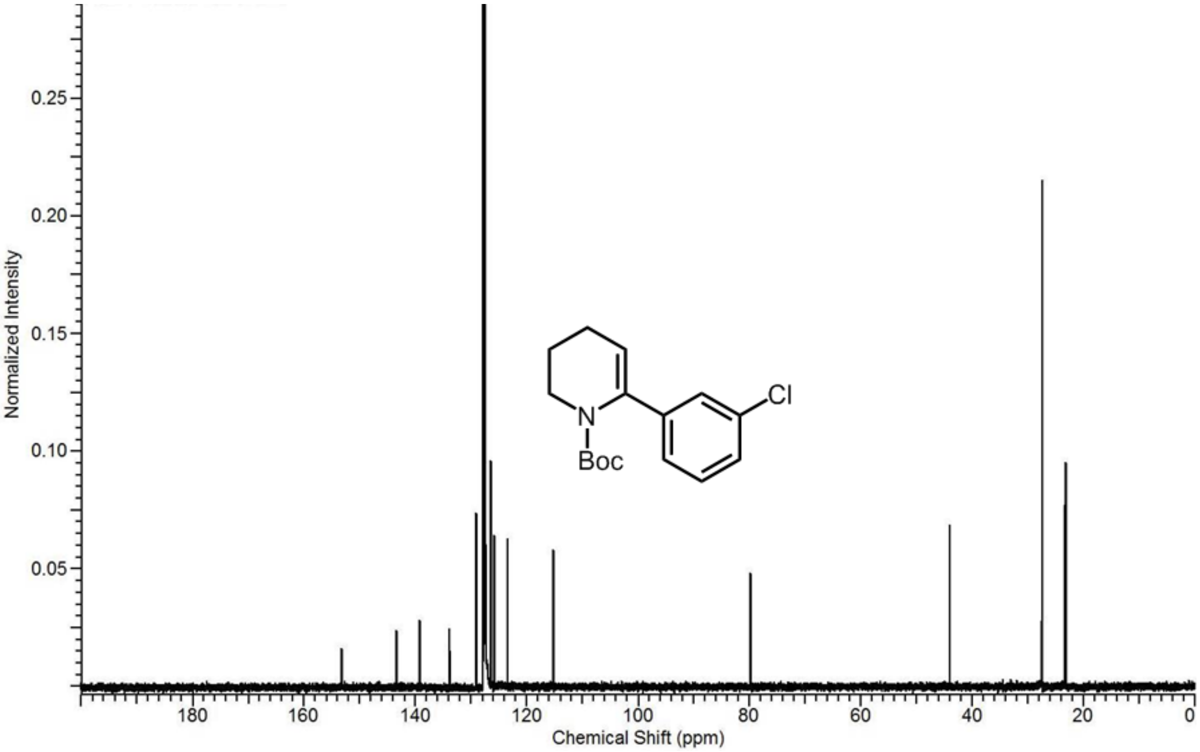
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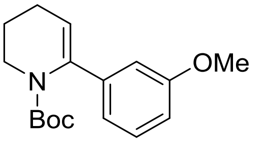
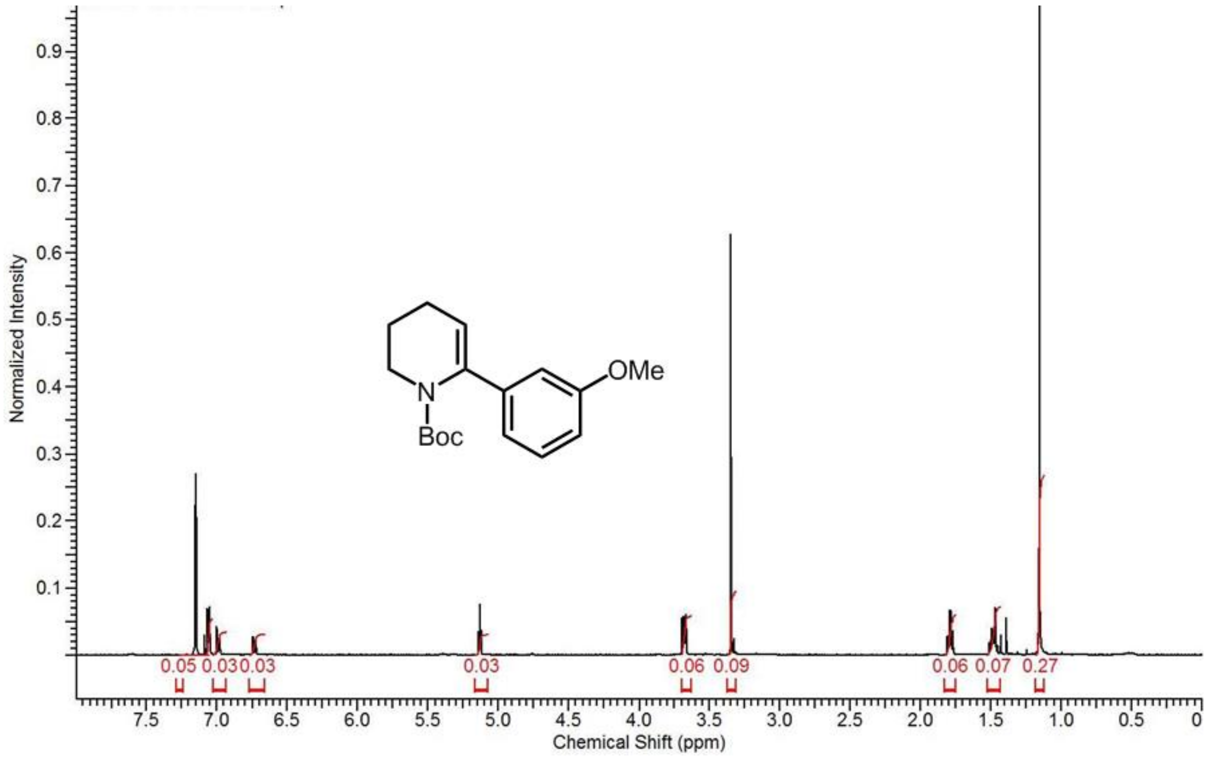
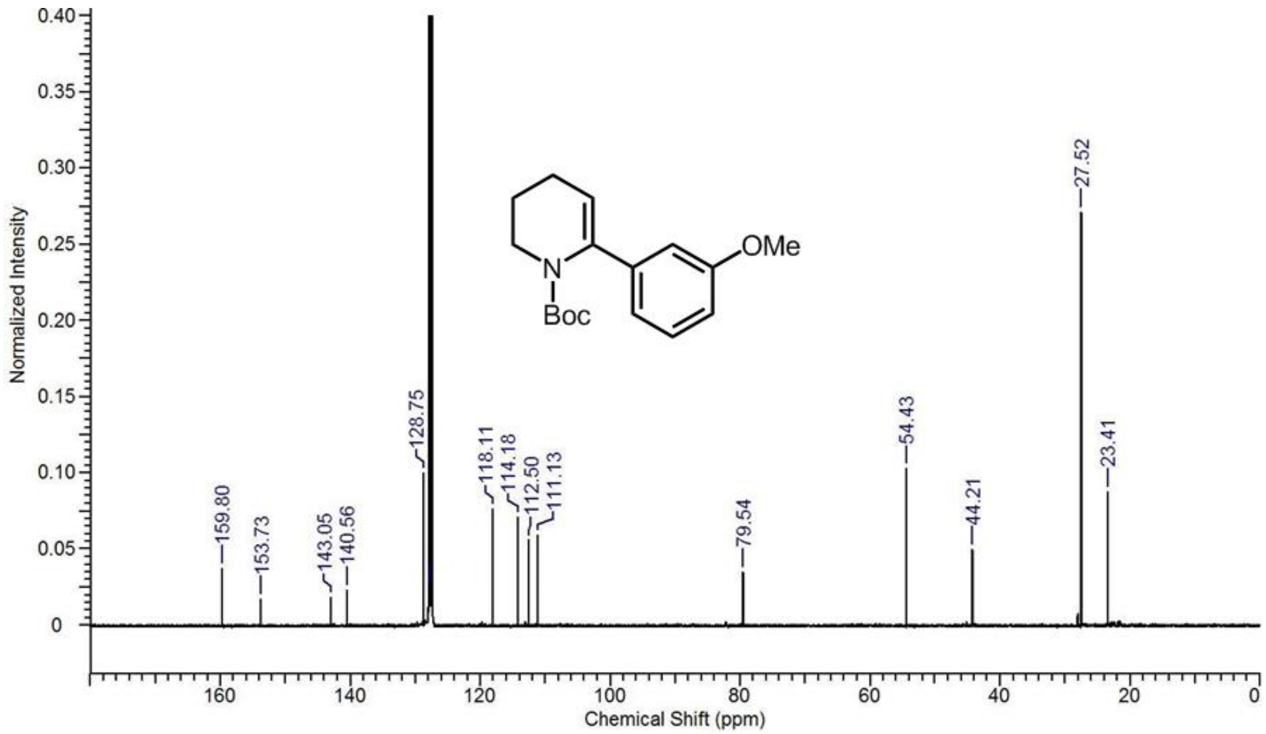
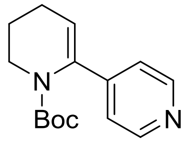


2c

Prepared from **1a** (371 mg, 1.0 mmol) and 3-methoxyphenylmagnesium bromide (3 equiv) using **General Procedure D**. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (1:1). Yield = 237 mg; 82%. ^{1}H NMR (400 MHz, C_6D_6) δ 7.22 (1H, s), 7.18 to 6.96 (2H, m), 6.80 to 6.71 (2H, t), 5.14 to 5.12 (1H, t), 3.68 to 3.66 (2H, dd), 3.34 (3H, s), 1.82 to 1.78 (2H, m), 1.52 to 1.46 (2H, m), 1.14 (9H, s). ^{13}C NMR (101 MHz, C_6D6) δ 160.3, 153.7, 142.9, 140.5, 129.7, 119.6, 112.9, 112.9, 112.4, 79.5, 54.4, 44.2, 27.5, 23.4, 23.4. HRMS calc for $C_{17}H_{23}NO_3$ 289.1678, found 289.1600.

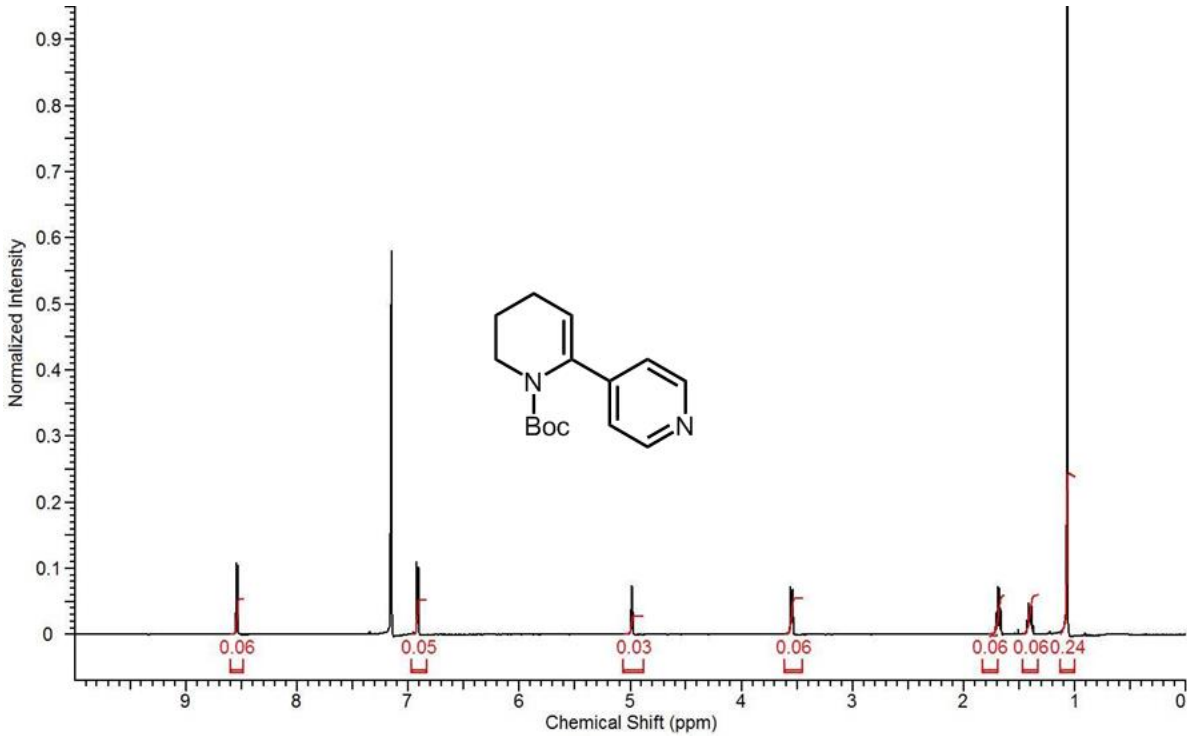






2d

Prepared from **1a** (371 mg, 0.10 mmol) and 4-pyridylmagnesium bromide (3 equiv) using **General Procedure D**. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with DCM/MeOH (95:5). Yield = 146 mg; 56%. ^{1}H NMR (400 MHz, C_6D_6) δ 8.56 to 8.55 (2H), 6.92 to 6.90 (2H), 4.99 to 4.97 (1H), 3.56 to 3.53 (2H), 1.71 to 1.66 (2H), 1.45 to 1.37 (2H), 1.07 (9H). ^{13}C NMR (101 MHz, C_6D_6) δ 153.1, 149.8, 148.1, 138.6, 119.9, 116.9, 80.2, 43.9, 27.4, 23.4, 23.0. HRMS calc for $C_{15}H_{20}N_2O_2$ 260.1525, found 260.1521.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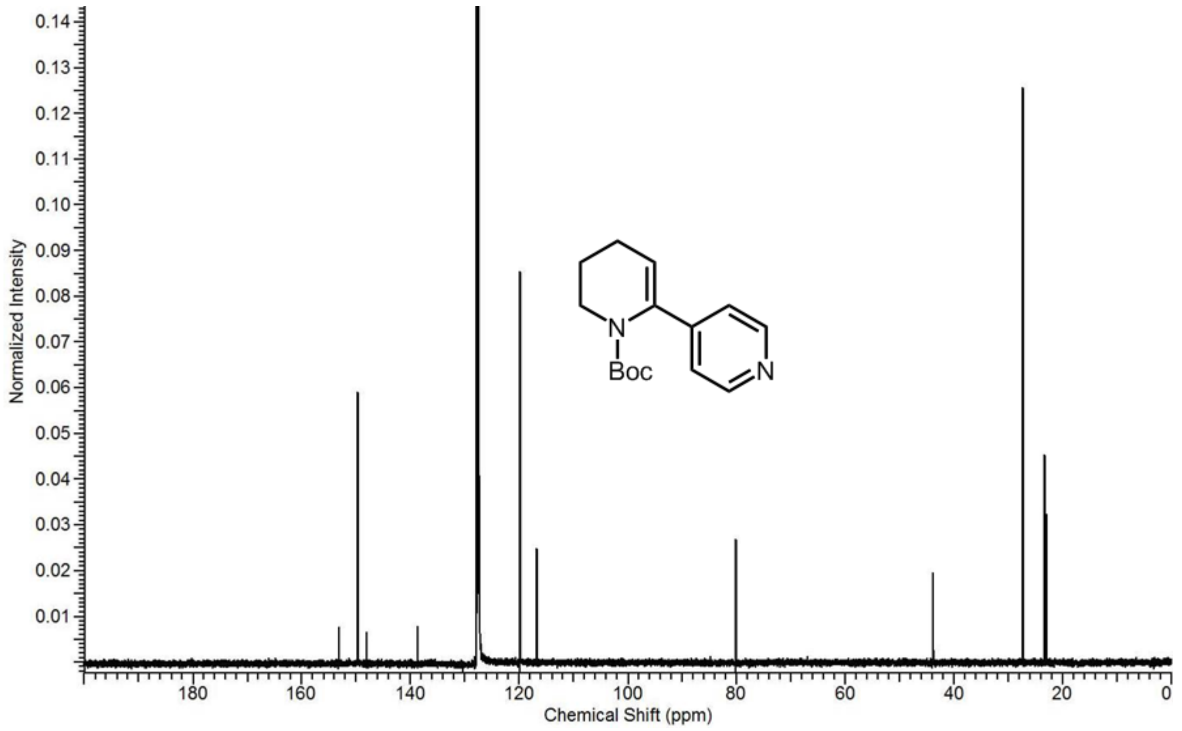
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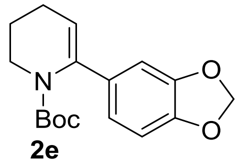
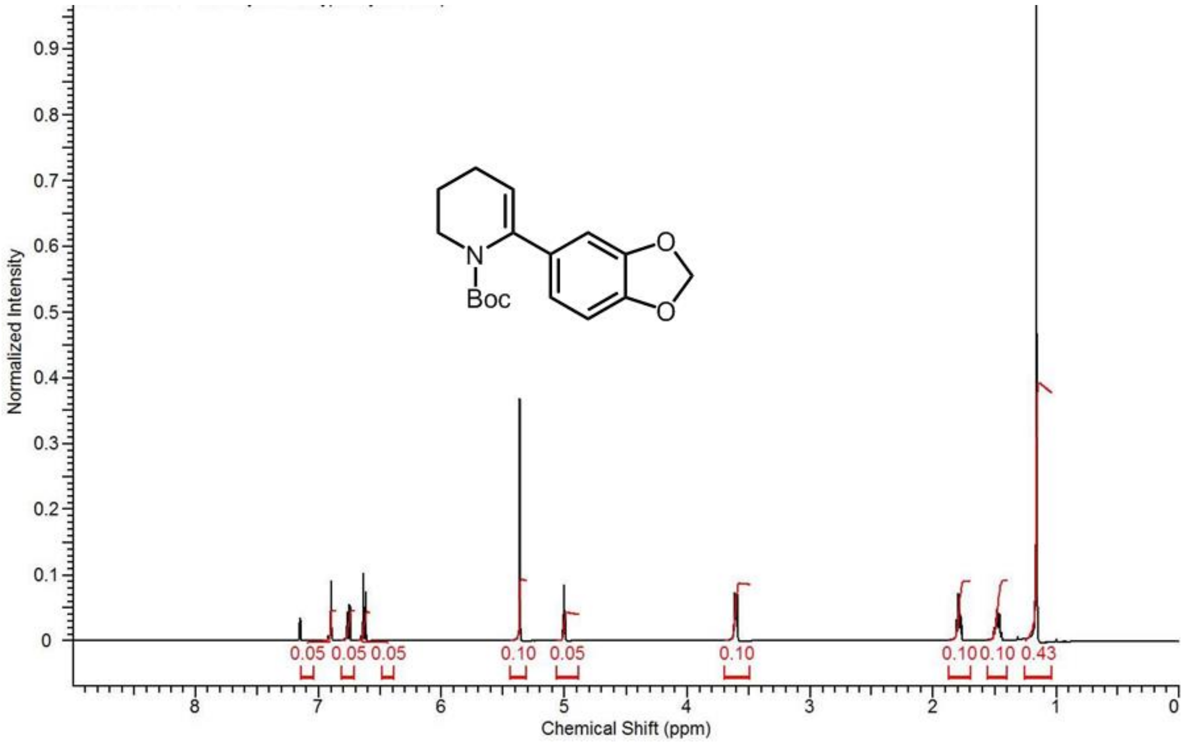
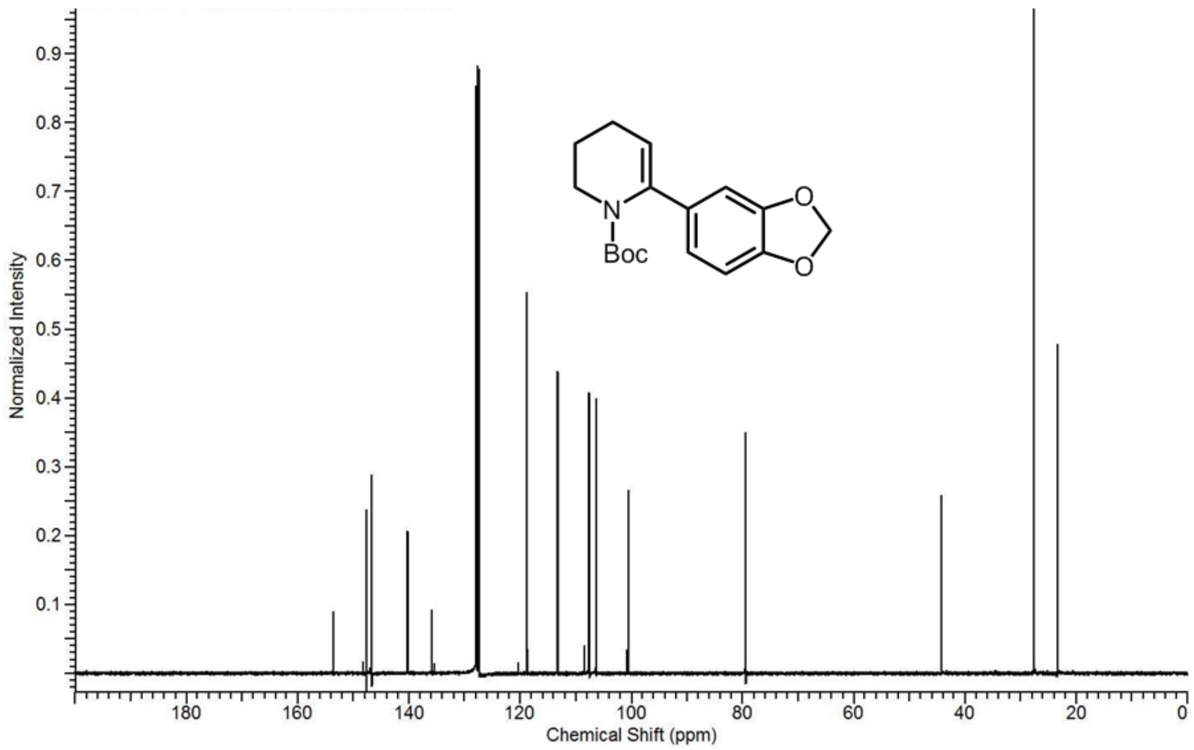
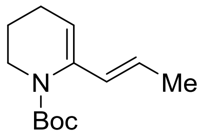


2e

Prepared from **1a** (371 mg, 1 mmol) and 5-benzo[*d*][1,3]dioxolylmagnesium bromide (3 equiv) using **General Procedure D**. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (1:3). Yield = 256 mg; 85%. ^{1}H NMR (400 MHz, C_6D_6) δ 6.94 (1H), 6.79 to 6.63 (1H), 5.33 (1H), 5.02 to 5.00 (2H), 3.65 to 3.62 (2H), 1.80 to 1.76 (2H), 1.52 to 1.19 (11H). ^{13}C NMR (101 MHz, C_6D_6) δ 154.4, 148.3, 147.3, 140.9, 136.1, 119.5, 114.0, 109.1, 107.1, 101.3, 80.1, 44.9, 28.3, 24.1, 24.1. HRMS calc for $C_{17}H_{21}NO_4$ 303.1471, found 303.1466.

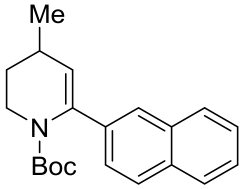






2f

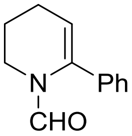
Prepared from **1a** (371 mg, 1 mmol) and 1-propenylmagnesium bromide (3 equiv) using **General Procedure D**. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (2:1). Yield = 150 mg; 67%. Data as reported by us.[1]



2g

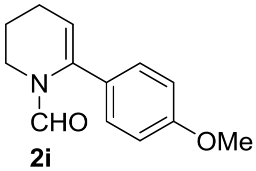
Prepared from **1b** (385 mg, 1 mmol) and 2-naphthylmagnesium bromide (3 equiv) using **General Procedure D.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N). PE/DCM (2:1). Yield = 258.5 mg; 80%. ^{1}H NMR (400 MHz, C_6D_6, mixture of rotamers) δ 8.03 to 7.84 (1H), 7.76 to 7.21 (6H), 5.17 & 5.16 (1H), 3.81 to 3.76 (2H), 2.16 to 2.09 (1H), 1.74 to

1.66 (1H), 1.52 to 0.98 (11H), 0.82 to 0.65 (3H). ^{13}C NMR (101 MHz, C_6D_6) δ 153.6, 139.5, 138.8, 133.6, 132.8, 127.8, 127.6, 127.2, 126.0, 125.4, 124.7, 123.9, 120.7, 79.7, 42.9, 31.6, 29.0, 27.4, 21.1. HRMS calc for $C_{21}H_{25}NO_2$ 323.1885, found 323.1879. Data as reported by us.[1]



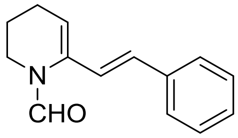
2h

Prepared from **1c** (299 mg, 1 mmol) and PhMgBr (3 equiv) using **General Procedure D**, T = 23 °C, time = 4 h; Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 150 mg, 80%. Data as reported by us.[1]



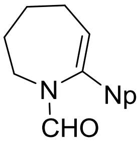
2i

Prepared from **1c** (299 mg, 1 mmol) and 4-methoxyphenylmagnesium bromide (3 equiv) using **General Procedure D.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 173.6 mg, 80%. Data as reported.[1]



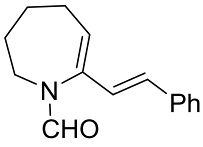
2j

Prepared from **1c** (299 mg, 1 mmol) and β-styrenyl magnesium bromide (3 equiv) using General Procedure D**.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 151 mg, 71%. Data as reported.[1]



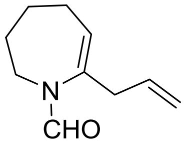
2k

Prepared from **1d** (313 mg, 1 mmol) and 1-naphthylmagnesium bromide (3 equiv) using **Procedure D**. Time = 6 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (70:30). Yield = 189 mg, 75%. Data as reported.[2]



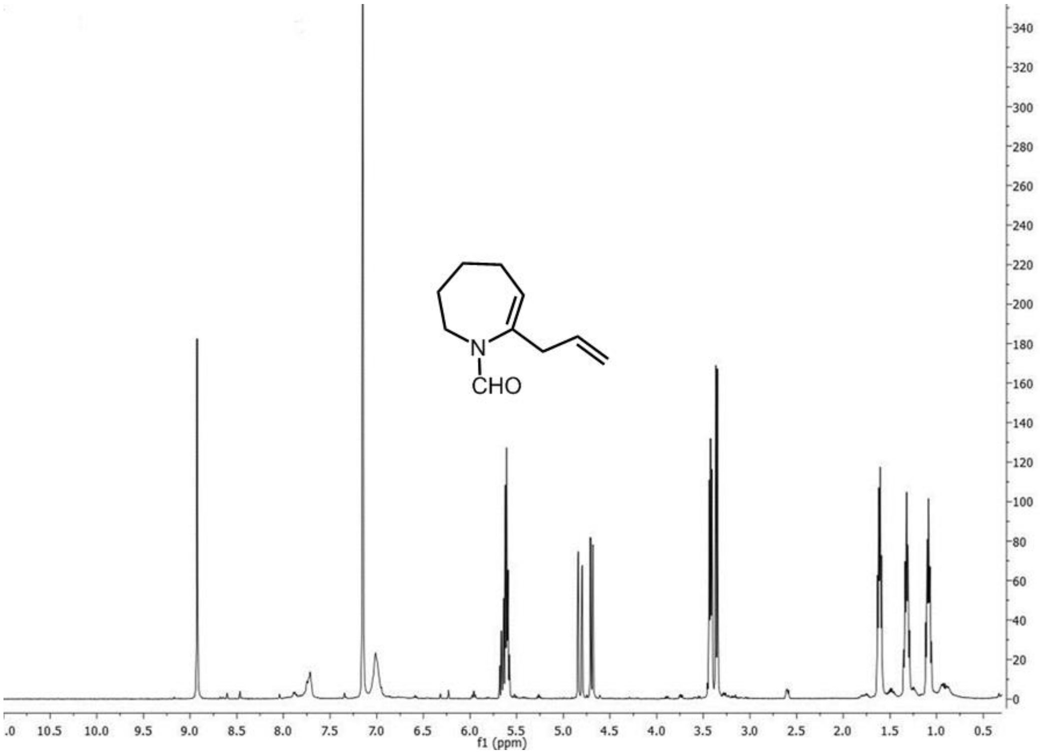
2l

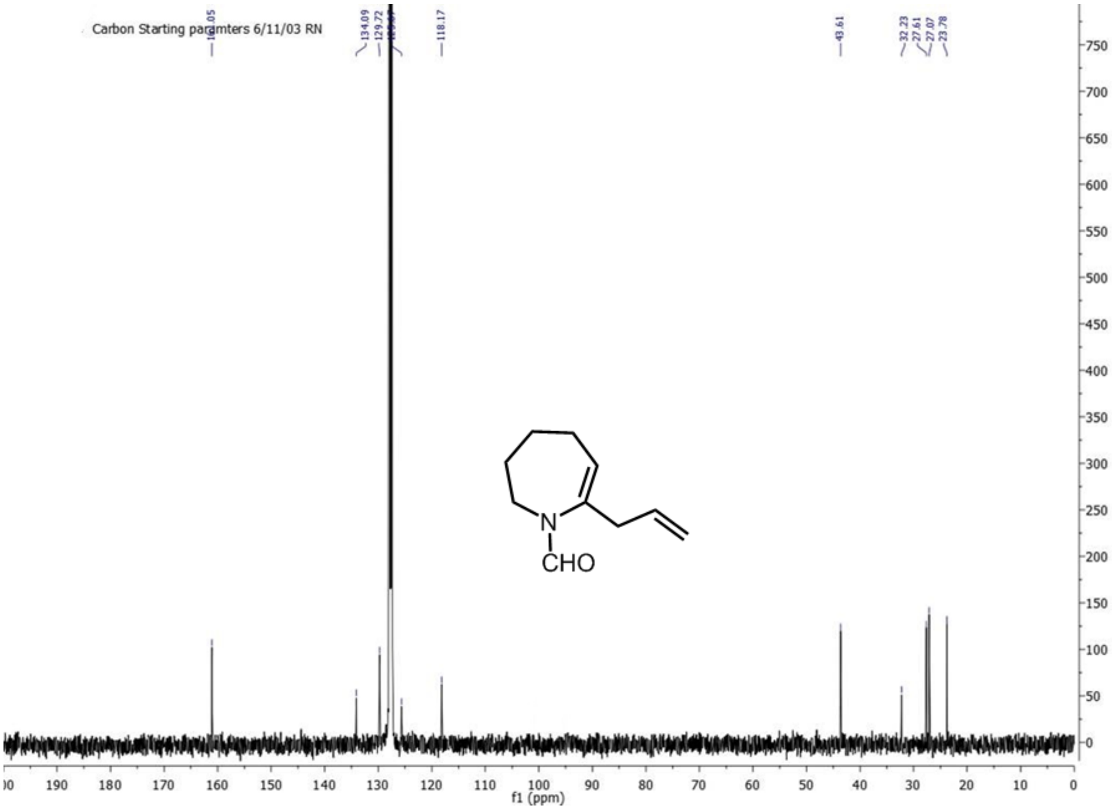
Prepared from **1d** (313 mg, 1 mmol) and β-styrenylmagnesium bromide (3 equiv) using **Procedure D**. Time = 8 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 177 mg, 78%. Data as reported by us.[2]

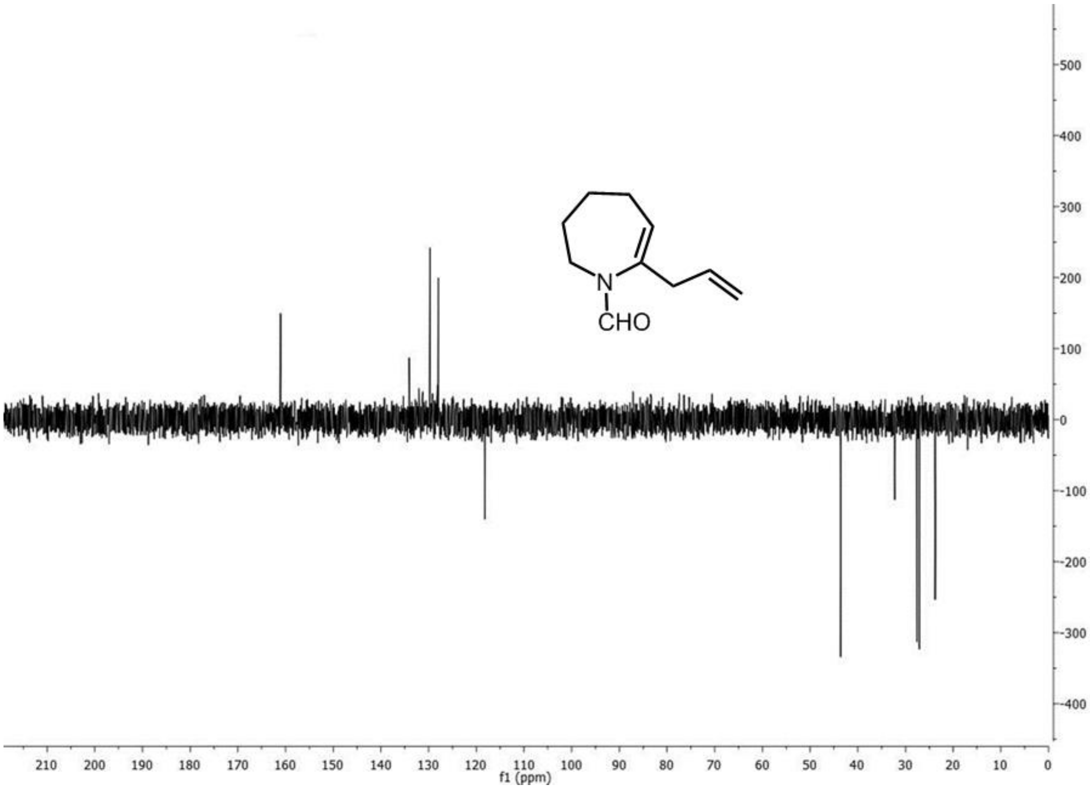


2m

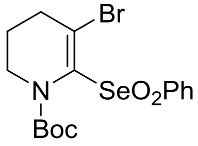
Prepared from **1d** (313 mg, 1 mmol) and allylmagnesium bromide (3.0 mL, 1.0 M in Et_2O, 3 equiv) using **Procedure D**. Time = 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 88 mg; 53%. ^{1}H NMR (400 MHz, C_6D_6) δ 8.92 (1H, s), 5.68 to 5.58 (2H, m), 4.85 to 4.68 (2H, dd), 3.44 to 3.35 (4H, m), 1.64 to 1.58 (2H, m), 1.35 to 1.29 (2H, m), 1.12 to 1.06 (2H, m). ^{13}C NMR (101 MHz, C_6D6) δ 161.0, 134.1, 129.7, 125.7, 118.2, 43.6, 32.2, 27.6, 27.1, 23.8. HRMS calc for $C_{10}H_{15}NO$ 165.1154, found 165.1158.


N
CHO
f1 (ppm)
.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0


Carbon Starting paramters 6/11/03 RN
134.09
129.72
118.17
43.61
32.23
27.61
27.07
23.78
N
CHO
f1 (ppm)
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0

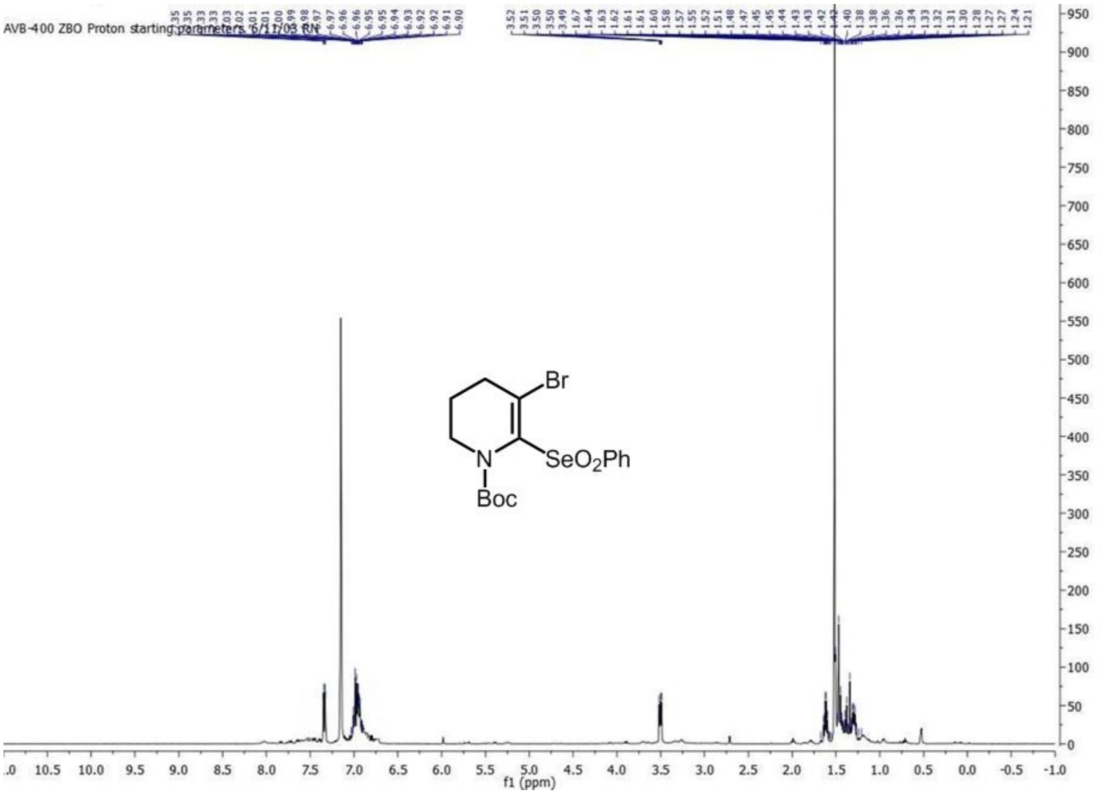


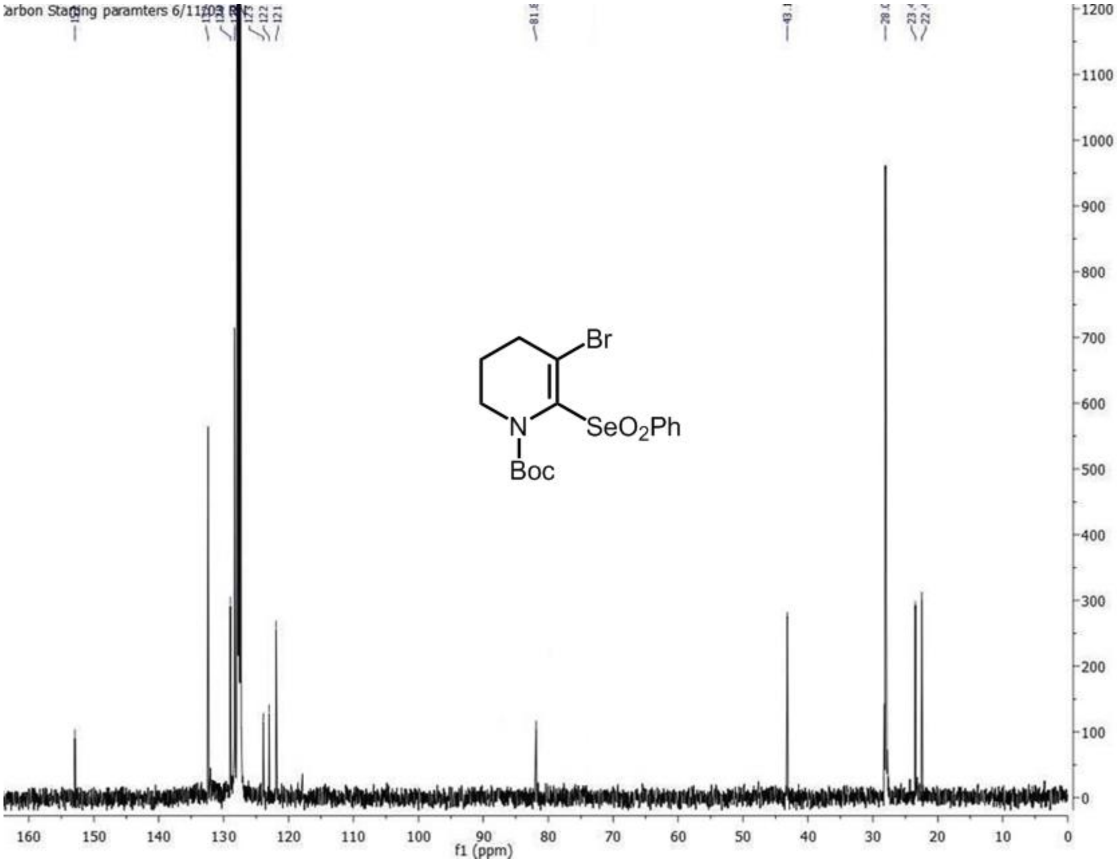
4. Preparation of α-selenonyl-β-heterofunctionalized dehydropiperidines and azepenes

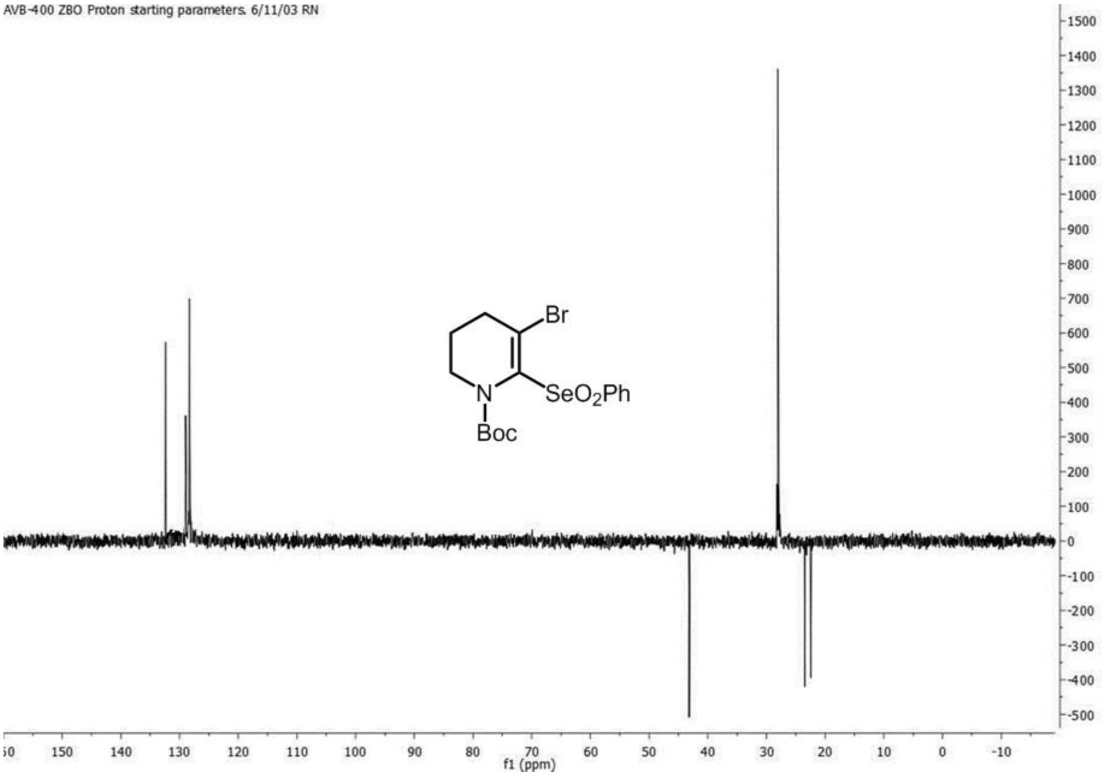


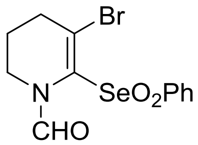
3a

Prepared from **1a** (371 mg, 1 mmol), and $C_2F_4Br_2$ (516 mg, 2 equiv) using **General Procedure E.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane:EtOAc (95:5). Yield = 391 mg; 87%. ^{1}H NMR (400 MHz, C_6D_6) δ 7.34 (1H, d), 7.03, to 6.90 (4H, m), 3.52 to 3.49 (2H, dd), 1.67 to 1.21 (13H, m). ^{13}C NMR (101 MHz, C_6D6) δ 152.9, 132.4, 128.9, 128.3, 123.9, 122.9, 121.9, 81.9, 80.3, 74.6, 43.2, 28.1, 23.4, 22.4. HRMS calc for $C_{16}H_{20}BrNO_4Se$ 448.9741, found 448.9745.


AVB-400 ZBO Proton starting parameters 6/11/03 RN
7.35 7.35 7.33 7.33 7.03 7.02 7.01 7.01 7.00 6.99 6.98 6.97 6.97 6.96 6.96 6.95 6.95 6.94 6.93 6.92 6.92 6.91 6.90
3.52 3.51 3.50 3.50 3.49 1.67 1.64 1.63 1.62 1.61 1.61 1.60 1.58 1.57 1.55 1.52 1.51 1.48 1.47 1.45 1.45 1.44 1.43 1.43 1.42 1.42 1.40 1.38 1.38 1.36 1.36 1.34 1.33 1.32 1.31 1.30 1.28 1.27 1.27 1.24 1.21
Br
N
SeO2Ph
Boc
f1 (ppm)
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
950 900 850 800 750 700 650 600 550 500 450 400 350 300 250 200 150 100 50 0

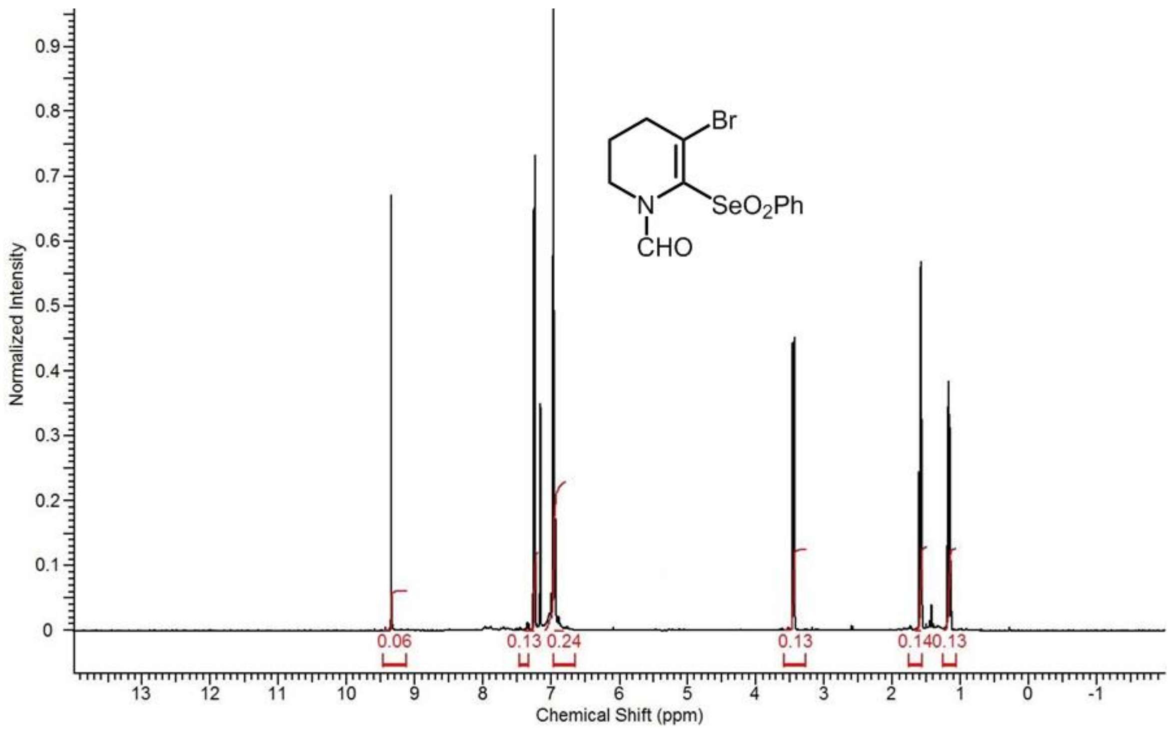

Carbon Starting paramters 6/11/03 RN
123
122
121
81.8
43.1
28.0
23.4
22.4
Br
N
SeO2Ph
Boc
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
1200 1100 1000 900 800 700 600 500 400 300 200 100 0

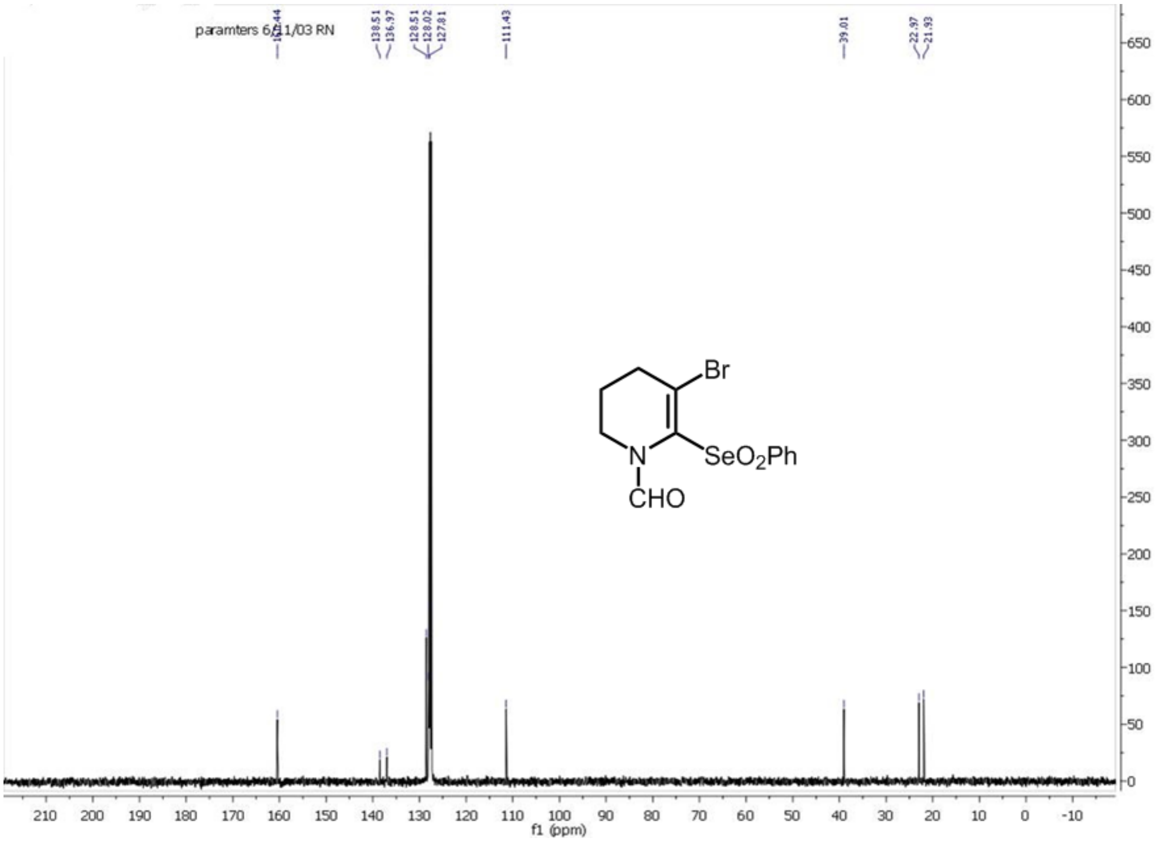


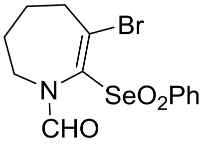


3b

Prepared from **1c** (299 mg, 1 mmol), and $C_2F_4Br_2$ (516 mg, 2 equiv) using **General Procedure E.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane:EtOAc (80:20). Yield = 196 mg; 52%. ^{1}H NMR (400 MHz, C_6D_6) δ 9.35 (1H, s), 7.28 to 7.21 (2H, m), 7.00 to 6.93 (3H, m), 3.46 to 3.43 (2H, dd), 1.60 to 1.52 (2H, m), 1.20 to 1.14 (2H, m). ^{13}C NMR (101 MHz, C_6D_6) δ 160.4, 138.5, 136.9, 128.5, 128.0, 127.8, 111.4, 39.0, 22.9, 21.9. HRMS calc for $C_{12}H_{12}BrNO_3Se$ 376.9166, found 376.9162.

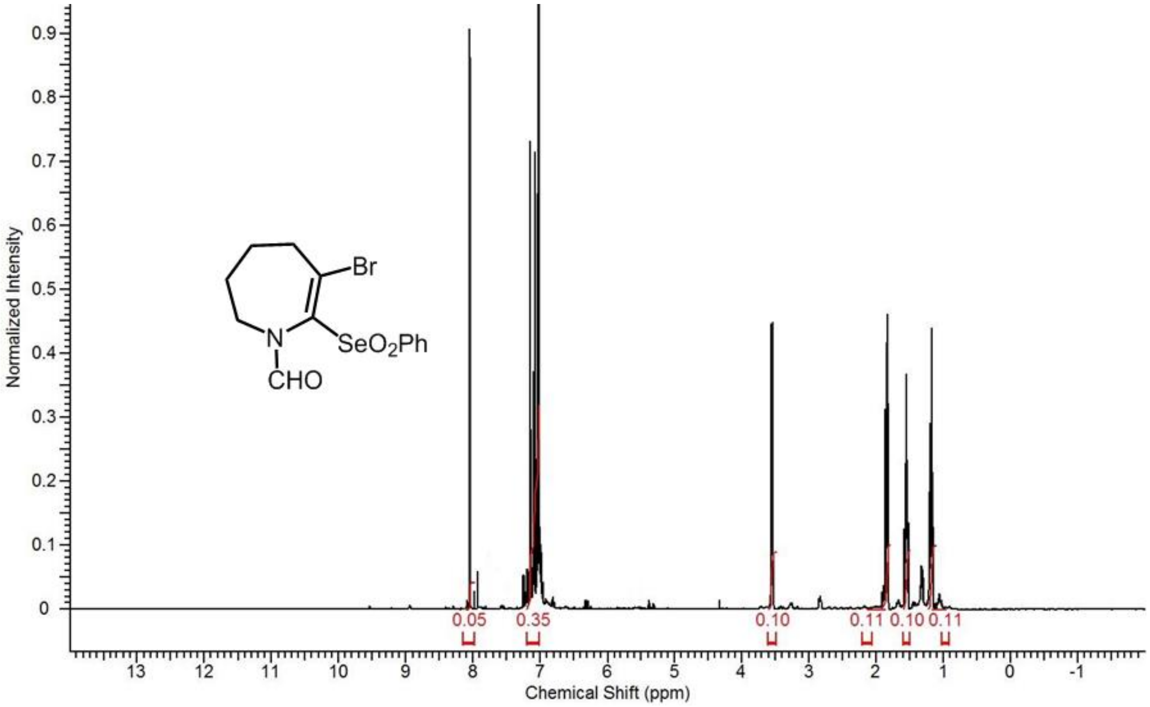

Br
SeO2Ph
N
CHO
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.06
0.13
0.24
0.13
0.14
0.13
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
Chemical Shift (ppm)

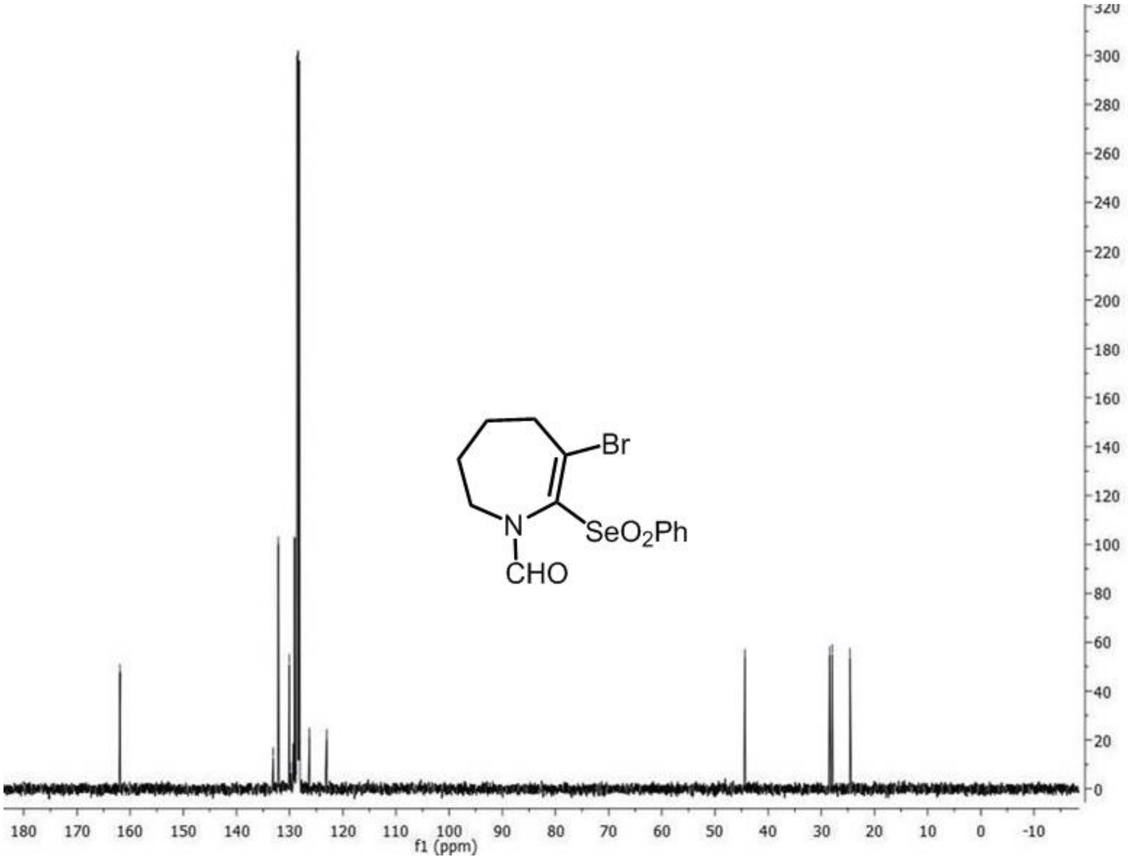

paramters 6/11/03 RN
160.44
138.51
136.97
128.51
128.02
127.81
111.43
39.01
22.97
21.93
Br
SeO2Ph
N
CHO
650
600
550
500
450
400
350
300
250
200
150
100
50
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

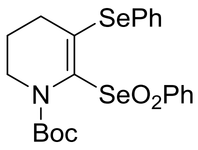


3c

Prepared from **1d** (313 mg, 1 mmol), and $C_2F_4Br_2$ (516 mg, 2 equiv) using **General Procedure E.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane:EtOAc (80:20). Yield = 188 mg; 48%. ^{1}H NMR (400 MHz, C_6D_6) δ 8.94 (1H, s), 7.31 to 7.26 (2H, m), 6.96 to 6.90 (3H, m), 3.52 to 3.50 (2H, dd), 1.72 to 1.68 (2H, m), 1.42 to 1.36 (2H, m), 1.18 to 1.12 (2H, m). ^{13}C NMR (101 MHz, C_6D_6) δ 161.9, 133.1, 132.1, 130.1, 129.7, 126.3, 123.0, 44.4, 28.4, 27.9, 24.6. HRMS calc for $C_{13}H_{14}BrNO_3Se$ 390.9322, found 390.9326.

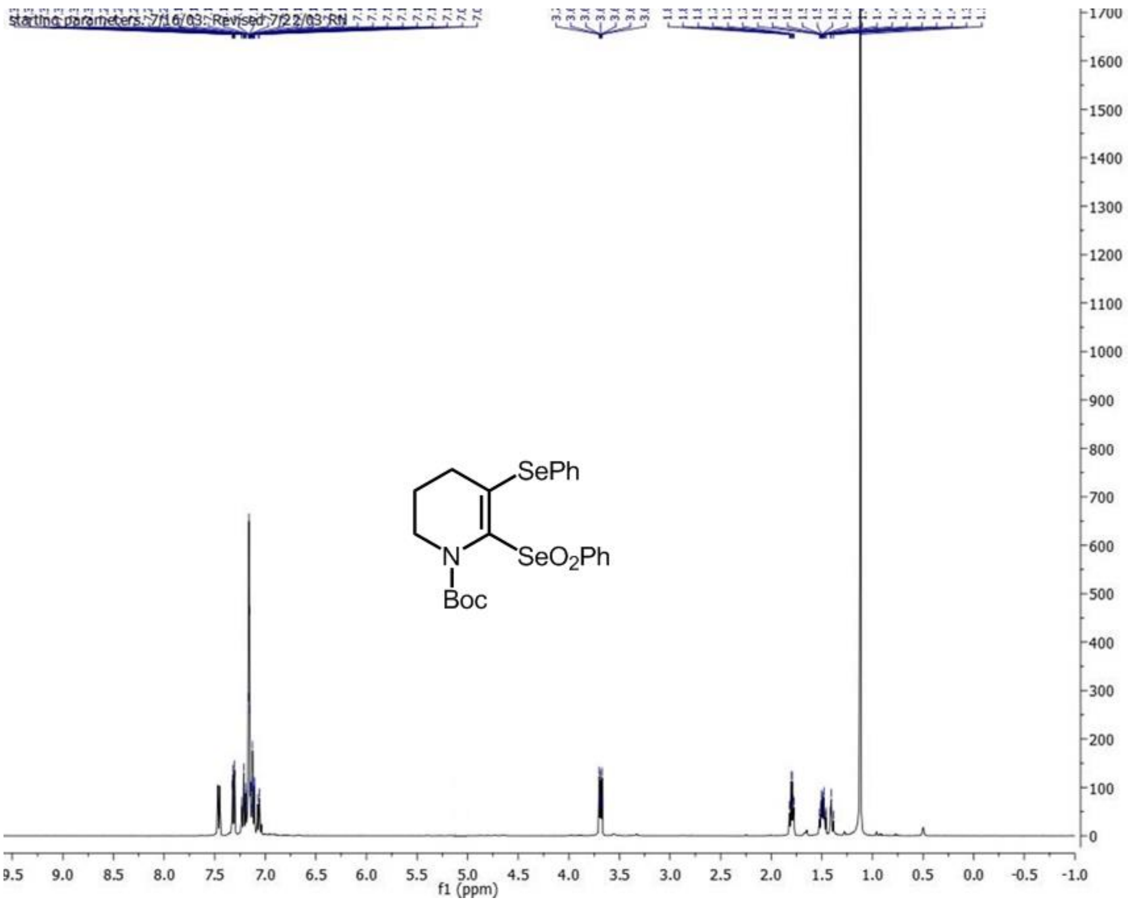


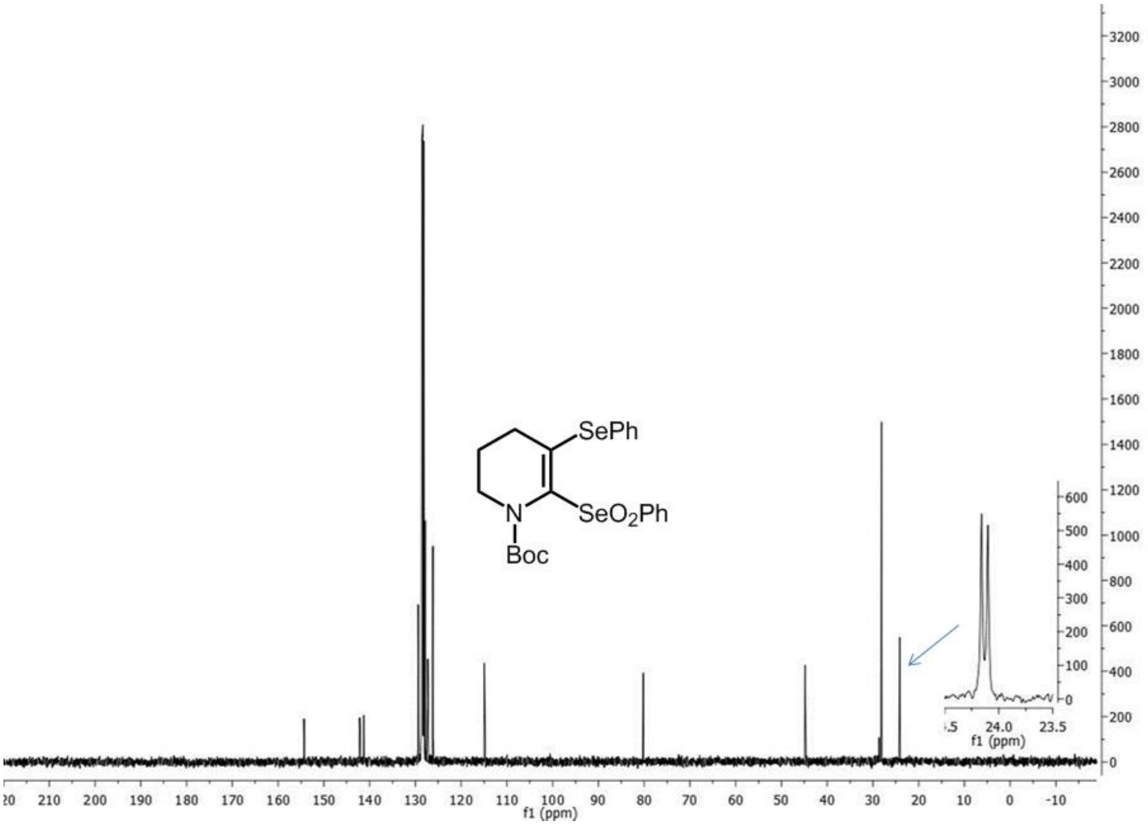


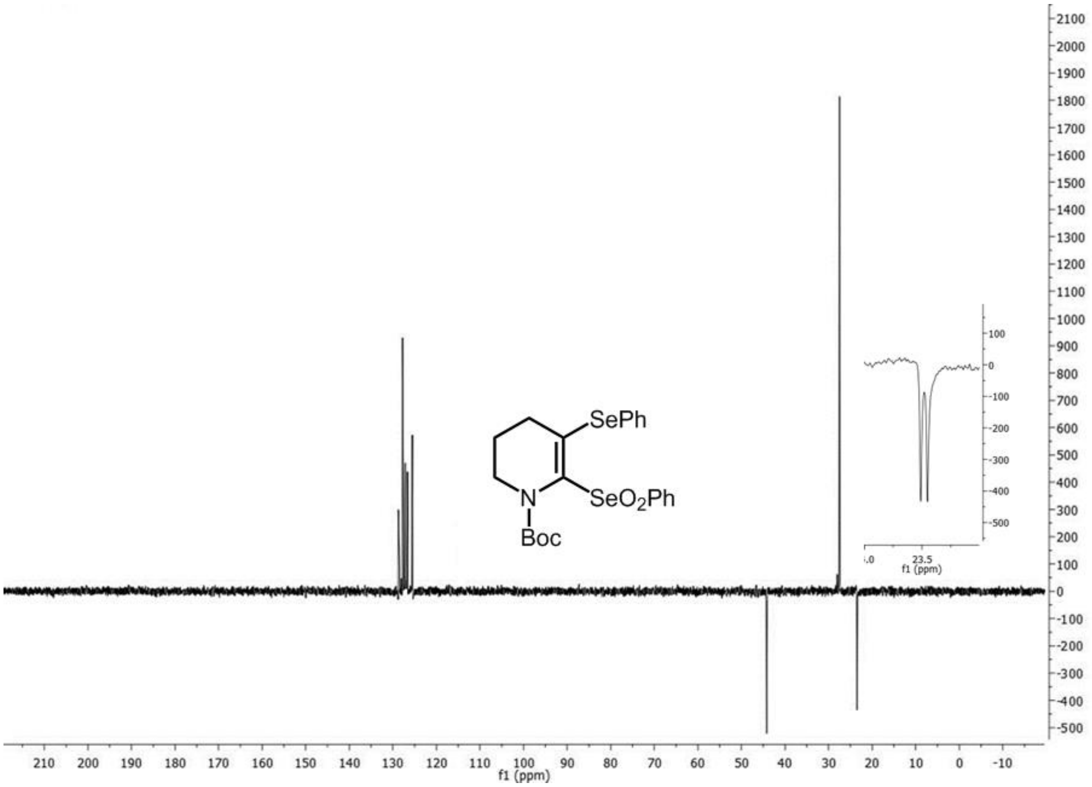


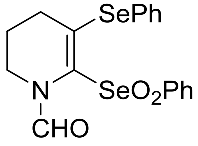
3d

Prepared from **1a** (371 mg, 1 mmol) and PhSeSePh (628 mg, 2 equiv) using **General Procedure E.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane:EtOAc (95:5). Yield = 406 mg; 77%. ^1H NMR (400 MHz, C_6D_6) δ 7.39 (1H, d), 7.32 to 7.06 (9H, m), 3.70 to 3.67 (2H, dd), 1.82 to 1.78 (2H, m), 1.52 to 1.39 (2H, m), 1.12 (9H, s). ^{13}C NMR (101 MHz, C_6D_6) δ 154.3, 142.1, 141.2, 129.4, 127.8, 127.3, 126.1, 114.9, 80.2, 44.8, 28.1, 24.1, 24.1. HRMS calc for $C_{22}H_{25}NO_4Se_2$ 527.0114, found 527.0117.


starting parameters. 7/16/03; Revised 7/22/03 RN
SePh
SeO2Ph
N
Boc
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)
1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0

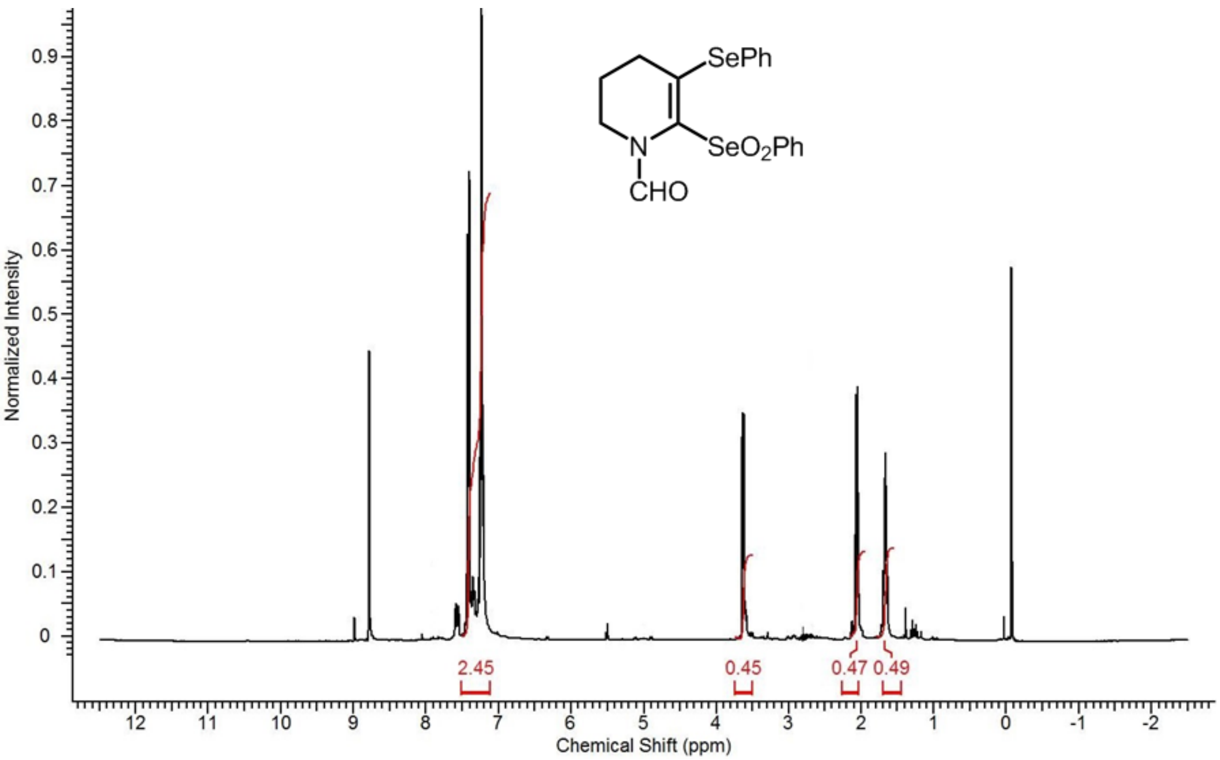

SePh
SeO2Ph
N
Boc
24.0 23.5
f1 (ppm)
600 500 400 300 200 100 0
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0

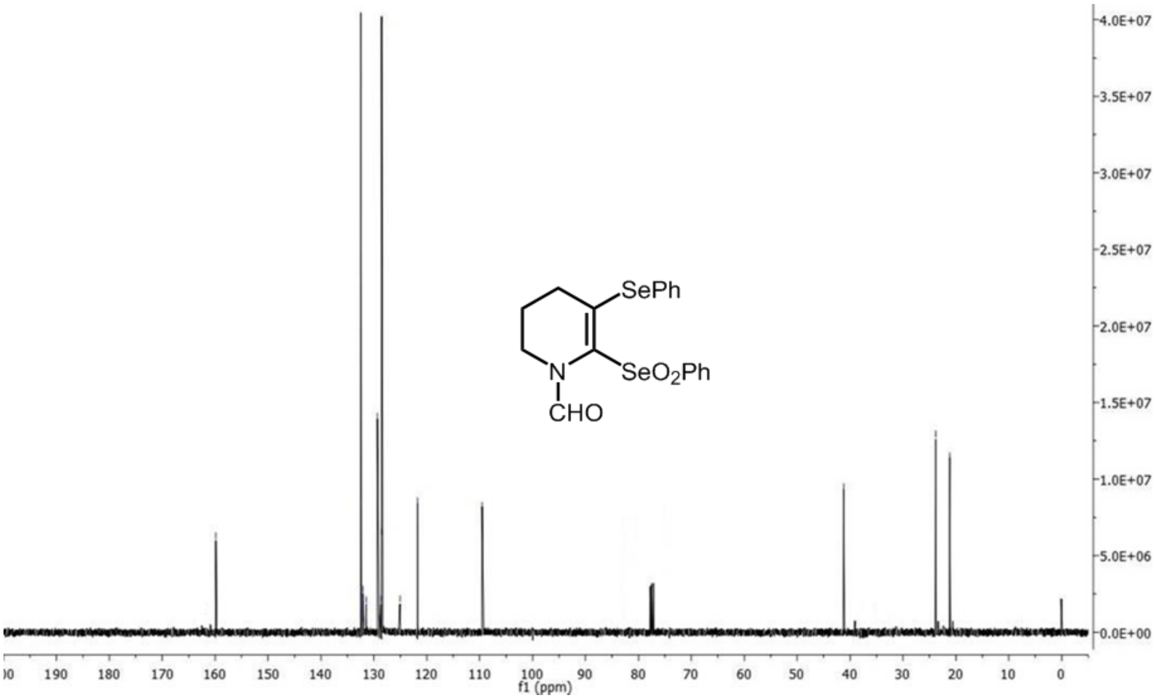


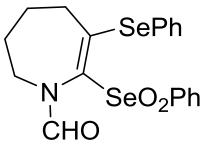


3e

Prepared from **1c** (299 mg, 1 mmol) and PhSeSePh (628 mg, 2 equiv) using **General Procedure E.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane:EtOAc (80:20). Yield = 273 mg; 60%. ^{1}H NMR (400 MHz, CHLOROFORM-*D*) δ 8.78 (1H, s), 7.43 to 7.22 (10H, m), 3.64 to 3.61 (2H, dd), 2.08 to 2.04 (2H, m), 1.69 to 1.63 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 132.5, 132.4, 132.1, 132.0, 131.9, 131.9, 131.5, 129.3, 129.0, 128.7, 128.5, 128.5, 125.1, 121.7, 109.5, 41.2, 23.8, 21.1. HRMS calc for $C_{18}H_{17}NO_3Se_2$ 454.9539, found 454.9544.

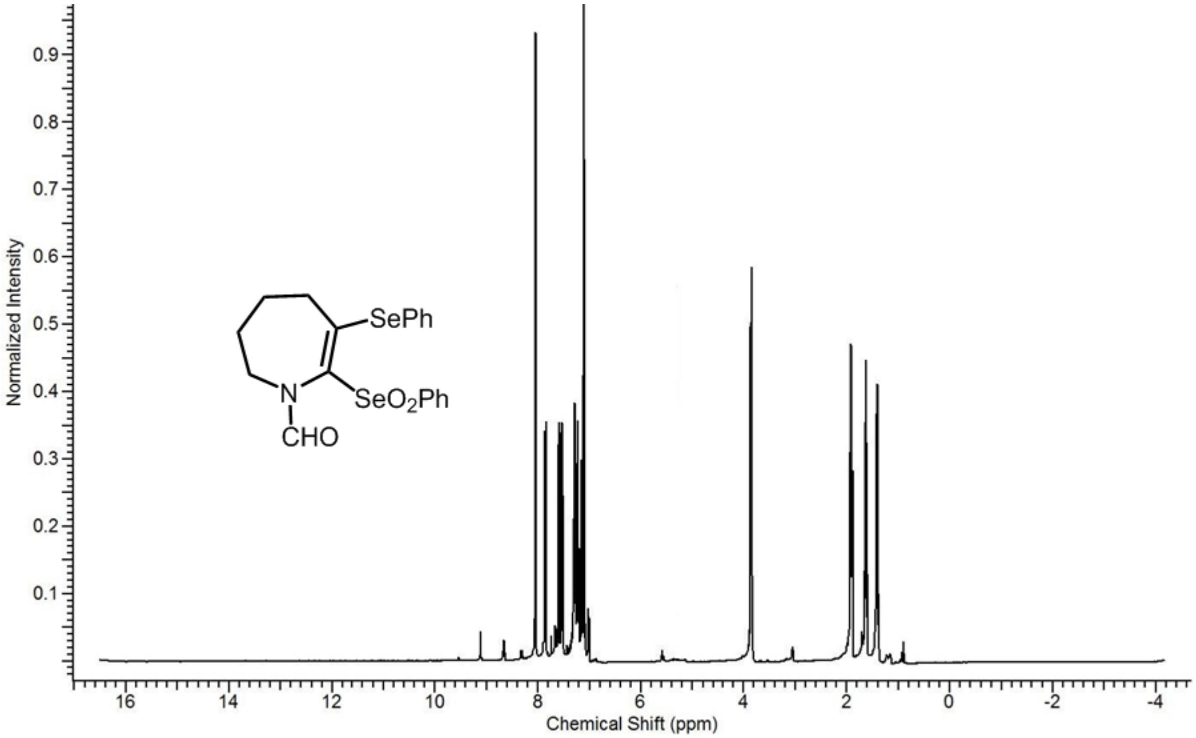

SePh
SeO2Ph
N
CHO
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
2.45
0.45
0.47
0.49
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Chemical Shift (ppm)

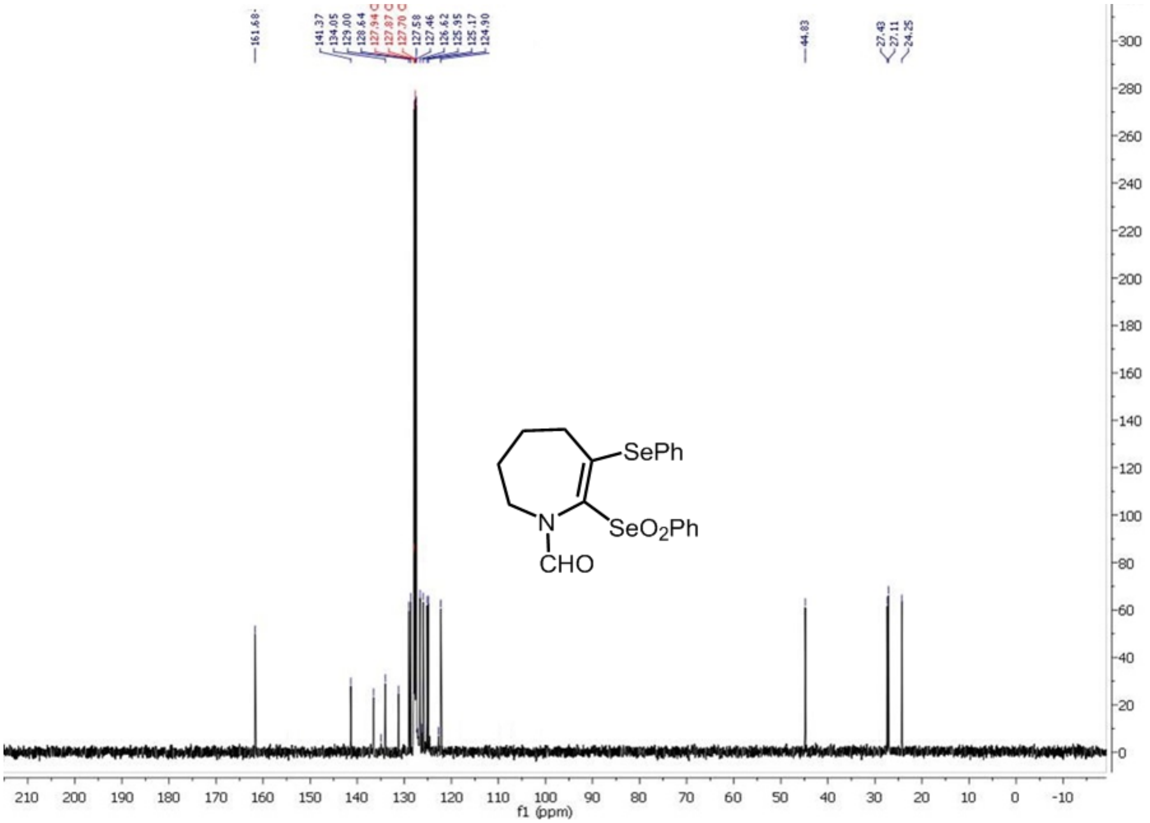

SePh
SeO2Ph
N
CHO
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

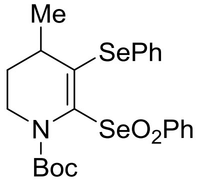


3f

Prepared from **1d** (313 mg, 1 mmol) and PhSeSePh (628 mg, 2 equiv) using **General Procedure E.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane:EtOAc (80:20). Yield = 296 mg; 63%. ^{1}H NMR (400 MHz, C_6D_6) δ 8.07 (1H, s), 7.91 to 7.86 (1H, d), 7.61 to 7.09 (10H, m), 3.92 to 3.86 (2H, dd), 1.97 to 1.91 (2H, m), 1.67 to 1.61 (2H, m), 1.46 to 1.40 (2H, m). ^{13}C NMR (101 MHz, C_6D6) δ 161.7, 141.4, 136.5, 134.0, 131.2, 129.0, 128.6, 126.6, 125.9, 125.2, 124.9, 122.2, 44.8, 27.4, 27.1, 24.2. HRMS calc for $C_{19}H_{19}NO_3Se_2$ 468.9695, found 468.9699.

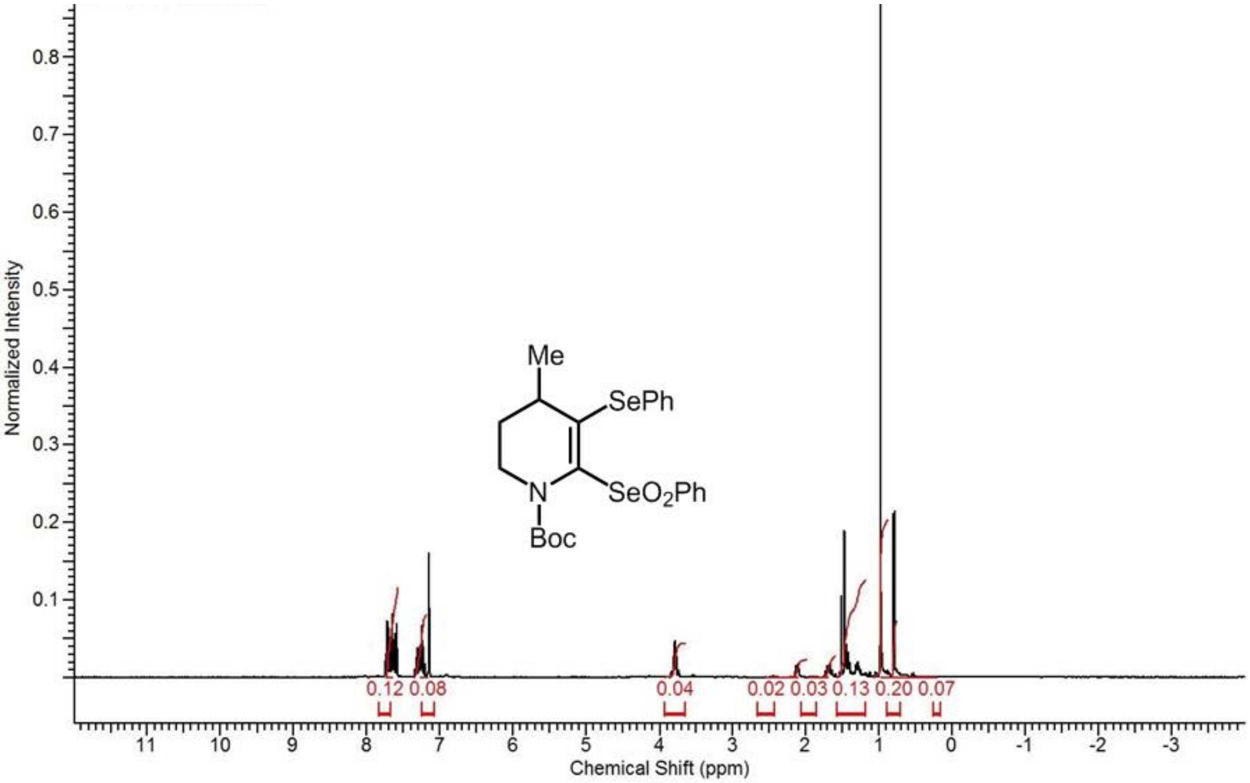






3g

Prepared from **1a** (371 mg, 1 mmol) and PhSeSePh (628 mg, 2 equiv) using **General Procedure E.** Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane:EtOAc (95:5). Yield = 423 mg; 78%. δ 7.45 to 6.99 (10H), 3.91 to 3.55 (2H), 2.09 to 2.03 (1H), 1.68 to 1.50 (1H), 1.46 to 1.02 (11H), 0.86 to 0.60 (3H). ^{13}C NMR (101 MHz, C_6D_6, mixture of rotamers) δ 153.5, 141.4, 141.3, 139.5, 128.7, 127.1, 126.6, 125.6, 120.0, 79.5, 78.3, 42.8, 31.5, 28.8, 28.2, 27.9, 27.4, 21.6, 21.2. HRMS calc for $C_{23}H_{27}NO_4Se_2$ 541.0271, found 541.0275.


Normalized Intensity
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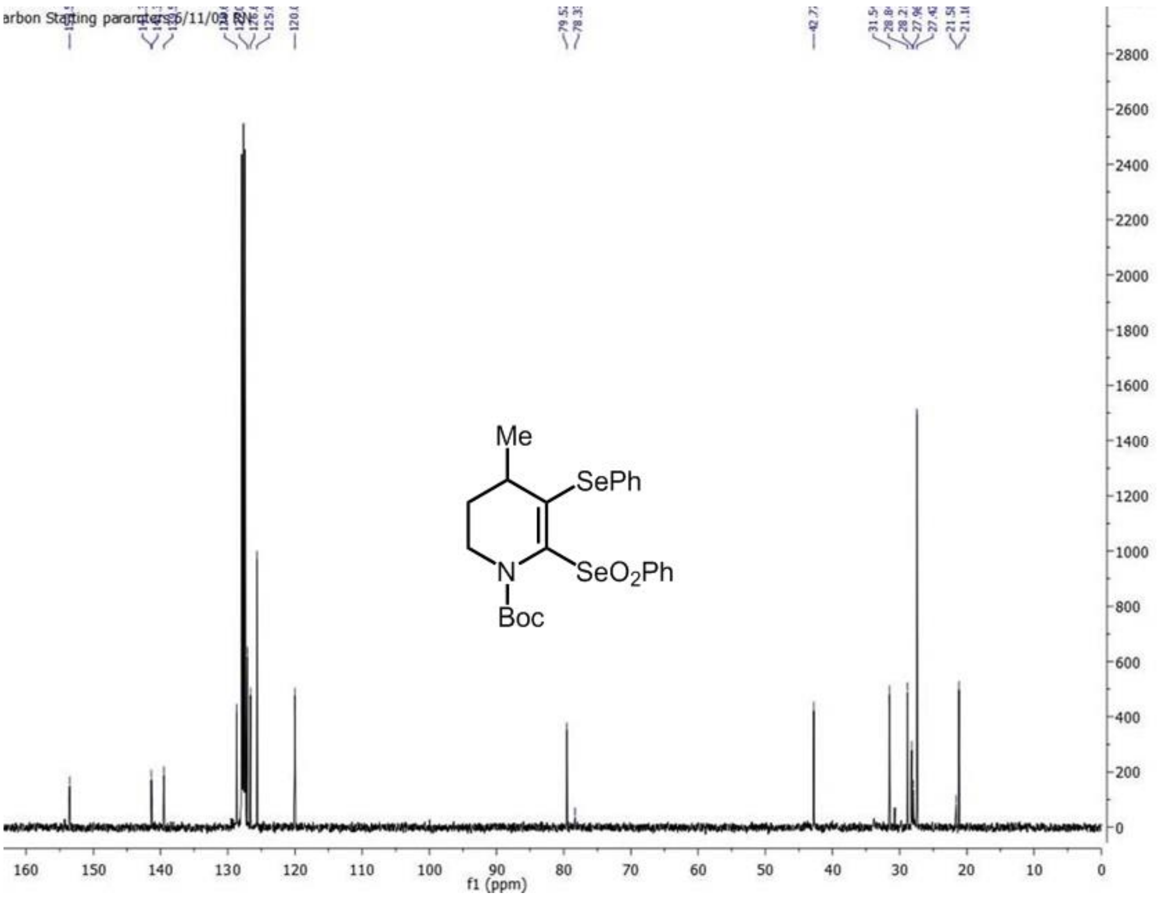
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Me
SePh
SeO2Ph
N
Boc
0.12
0.08
0.04
0.02
0.03
0.13
0.20
0.07
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
Chemical Shift (ppm)


arbon Starting paramters 6/11/03 RN
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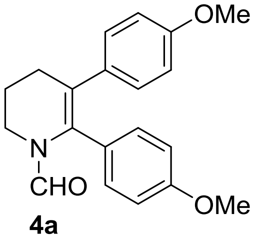
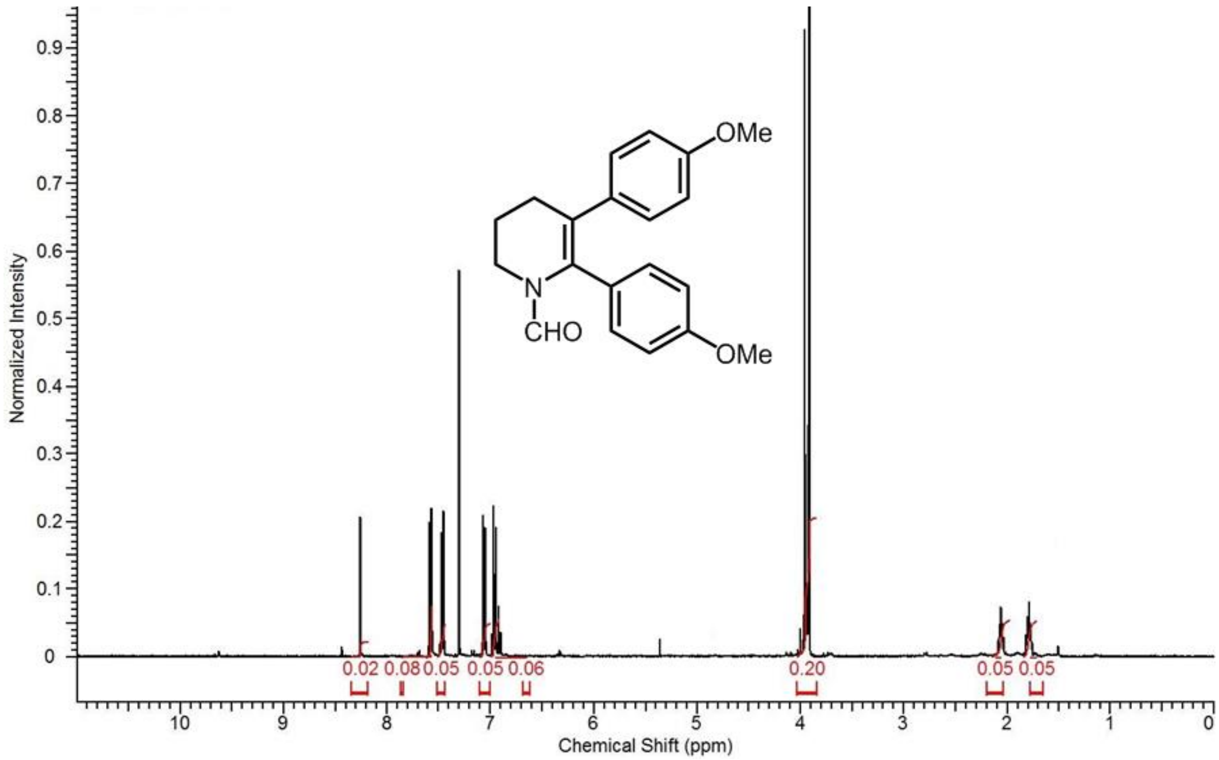
125.8
79.52
78.33
42.73
31.54
28.84
28.23
27.96
27.42
21.58
21.16
Me
SePh
SeO2Ph
N
Boc
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

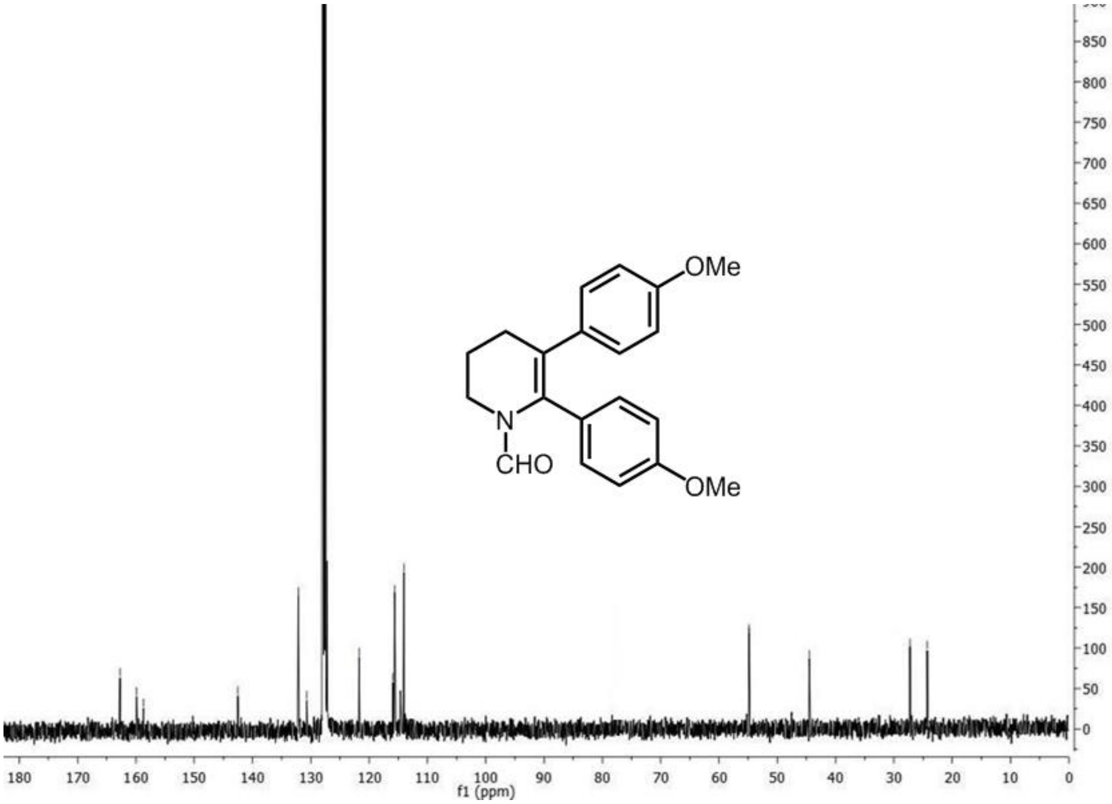
5. Cobalt-catalyzed reductive cross-coupling

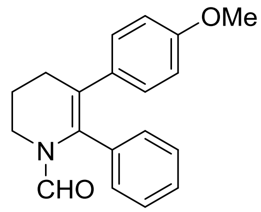


4a

Prepared from **3e** (455 mg, 1 mmol) and *p*-bromoanisole (561 mg, 3 equiv), using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h; Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20 to 50:50). Yield = 246 mg, 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (1H, s), 7.52 (2H, d), 7.39 (2H, d), 6.99 (2H, d), 6.88 (2H, d), 3.90 to 3.85 (8H, m), 2.03 to 1.97 (2H, m), 1.76 to 1.70 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 159.8, 158.6, 142.5, 132.1, 130.6, 121.7, 115.9, 115.6, 114.0, 54.8, 54.8, 44.5, 28.6, 27.2, 24.2. HRMS calc for $C_{19}H_{19}NO_2$ 323.1521, found 323.1524.

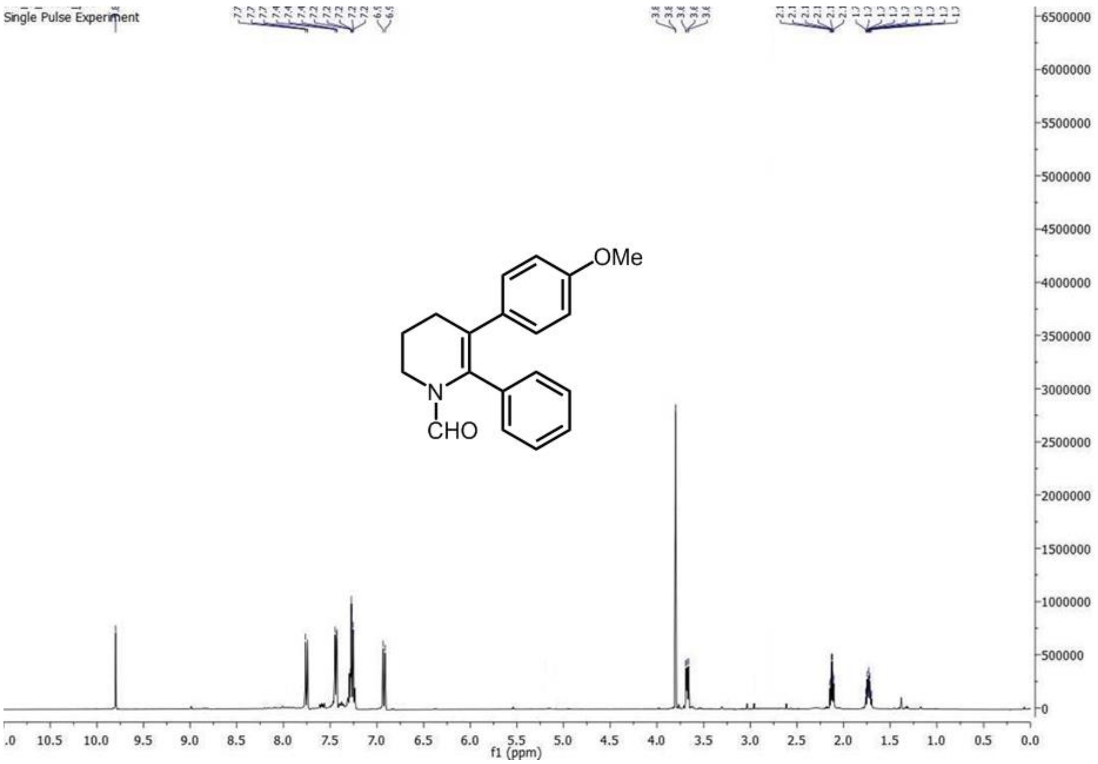






4b

Prepared from **3e** (455 mg, 1 mmol), phenyl bromide (189 mg, 1.2 equiv) and *p*-bromoanisole (374 mg, 2 equiv), using General Procedure F. T = 23 ^{o}C for 8 h, then 40 ^{o}C for 16 h; Purification: Flash chromatography on silica (pretreated with 1% Et$_3$N) eluting with hexane/EtOAc (80:20 to 50:50). Yield = 208 mg, 71%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.80 (1H, s), 7.7 (2H, d), 7.45 (2H, m), 7.28 to 7.25 (3H, m), 6.92 (2H, d), 3.80 (3H, s), 3.69 to 3.66 (2H, dd), 2.15 to 2.10 (2H, m), 1.76 to 1.70 (2H, m). ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.5, 159.9, 132.5, 131.9, 129.3, 128.5, 125.1, 121.7, 114.4, 109.5, 55.6, 41.2, 23.8, 21.1. HRMS calc for C$_{19}$H$_{19}$NO$_2$ 293.1416, found 293.1420.


Single Pulse Experiment
OMe
N
CHO
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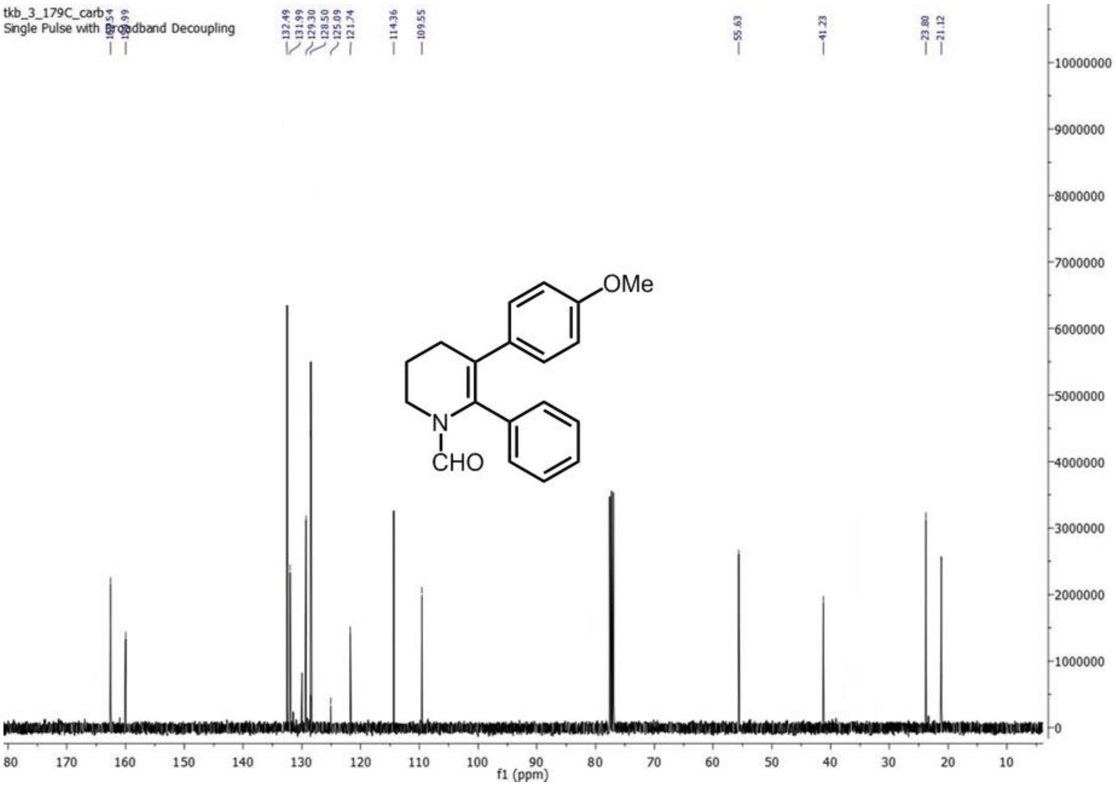
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


tkb_3_179C_carb
Single Pulse with Broadband Decoupling
162.54
159.99
132.49
131.99
129.30
128.50
125.09
121.74
114.36
109.55
55.63
41.23
23.80
21.12
OMe
N
CHO
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
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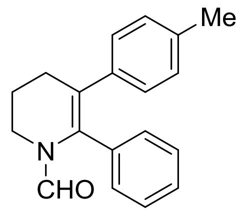
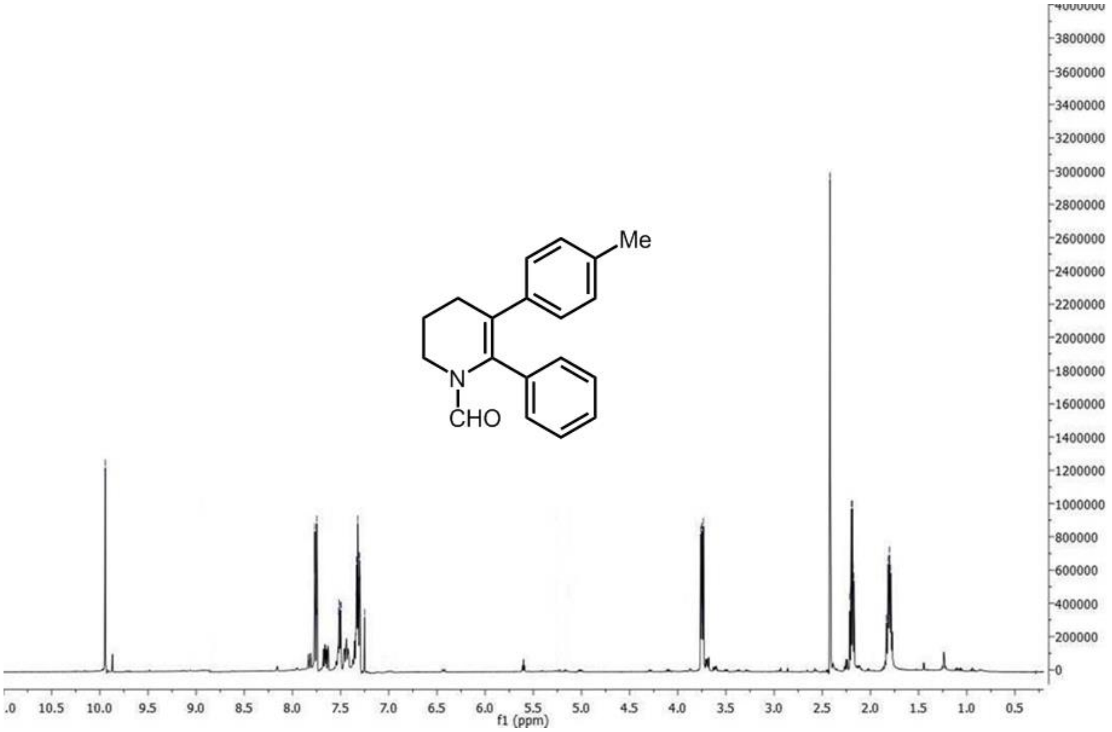
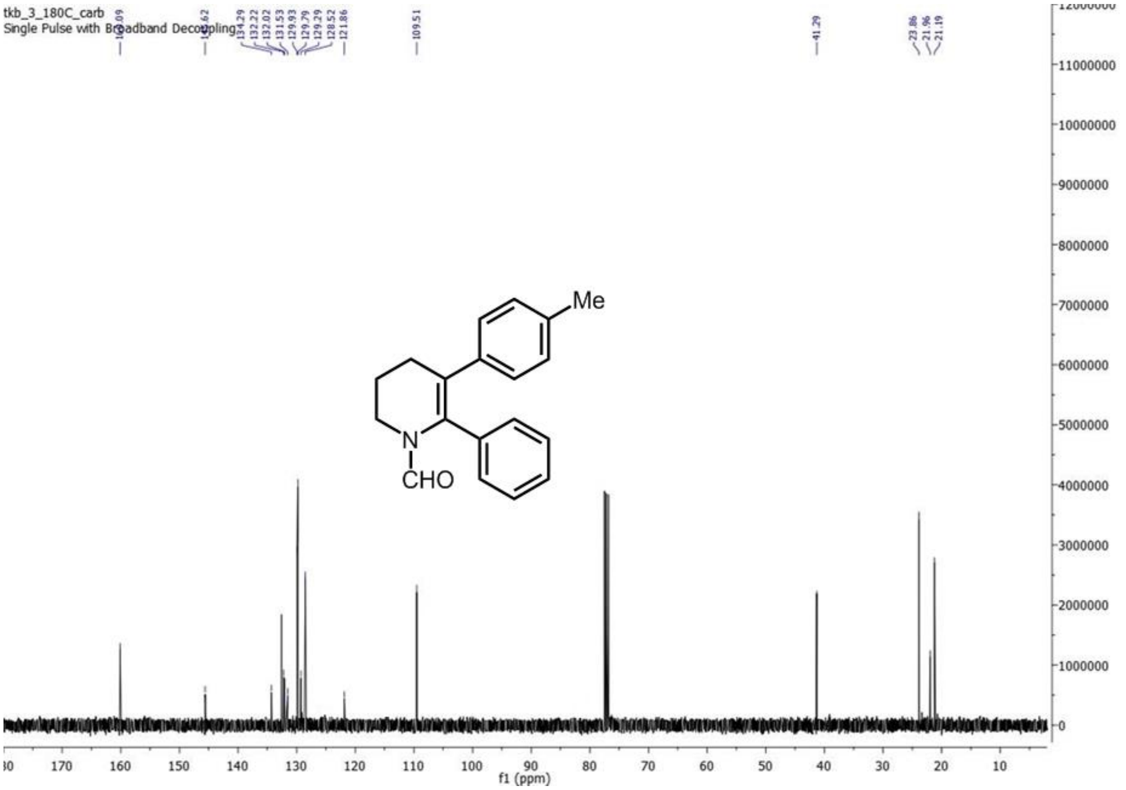
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

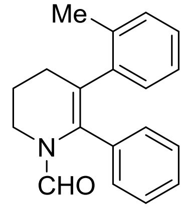


4c

Prepared from **3e** (455 mg, 1 mmol), phenyl bromide (189 mg, 1.2 equiv) and *p*-bromotoluene (340 mg, 2 equiv), using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h; Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 172 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (1H, s), 7.77 to 7.25 (9H, m), 3.76 to 3.73 (2H, dd), 2.42 (3H, s), 2.21 to 2.17 (2H, m), 1.83 to 1.79 (2H, m). ^{13}C NMR (101 MHz, CHLOROFORM-*D*) δ 160.1, 145.6, 134.3, 132.2, 132.0, 131.5, 129.8, 129.3, 128.5, 121.9, 109.5, 41.3, 23.9, 21.9, 21.2. HRMS calc for $C_{19}H_{19}NO$ 277.1467, found 277.1465.

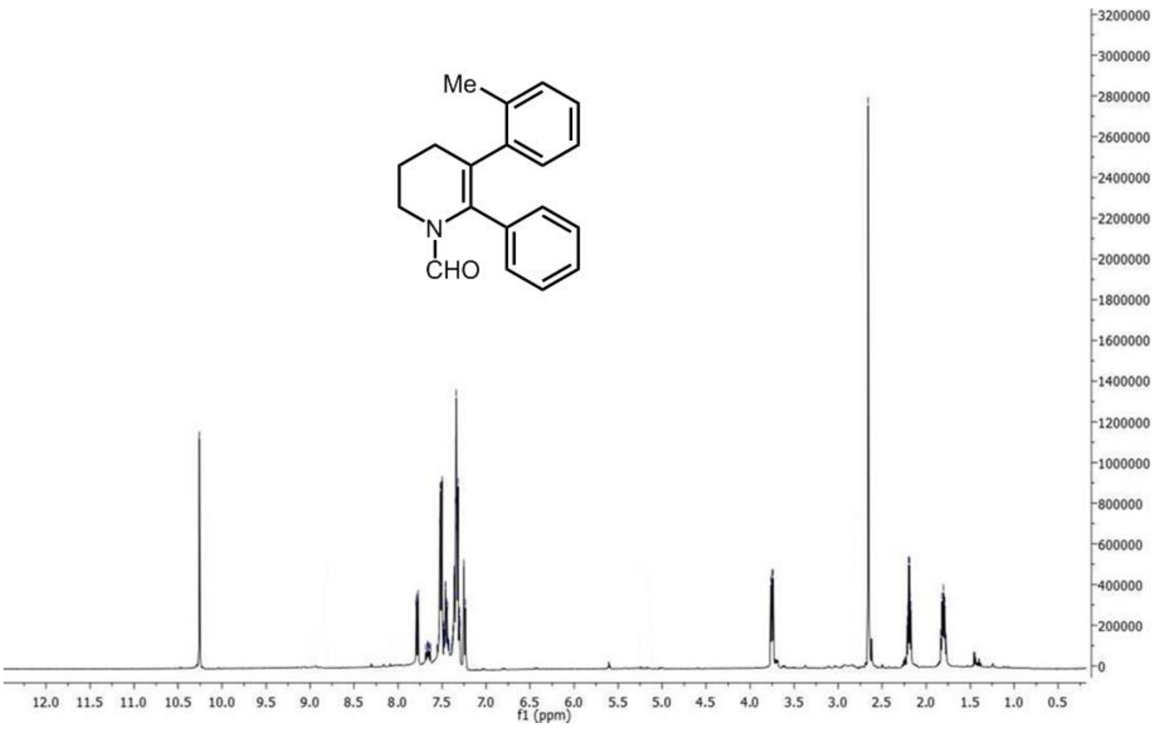






4d

Prepared from **3e** (455 mg, 1 mmol), phenyl bromide (189 mg, 1.2 equiv) and *o*-bromotoluene (340 mg, 2 equiv), using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h; Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 100 mg, 36%. ^{1}H NMR (400 MHz, CHLOROFORM-*D*) δ 10.26 (1H, s), 7.79 to 7.24 (9H, m), 3.77 to 3.74 (2H, dd), 2.66 (3H, s), 2.22 to 2.17 (2H, m), 1.83 to 1.77 (2H, m). ^{13}C NMR (101 MHz, CHLOROFORM-*D*) δ 160.1, 140.7, 134.2, 133.7, 132.6, 132.1, 131.8, 129.3, 128.5, 126.4, 121.9, 109.5, 41.3, 23.8, 21.2, 19.6. HRMS calc for $C_{19}H_{19}NO$ 277.1467, found 277.1465.


Me
N
CHO
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f1 (ppm)
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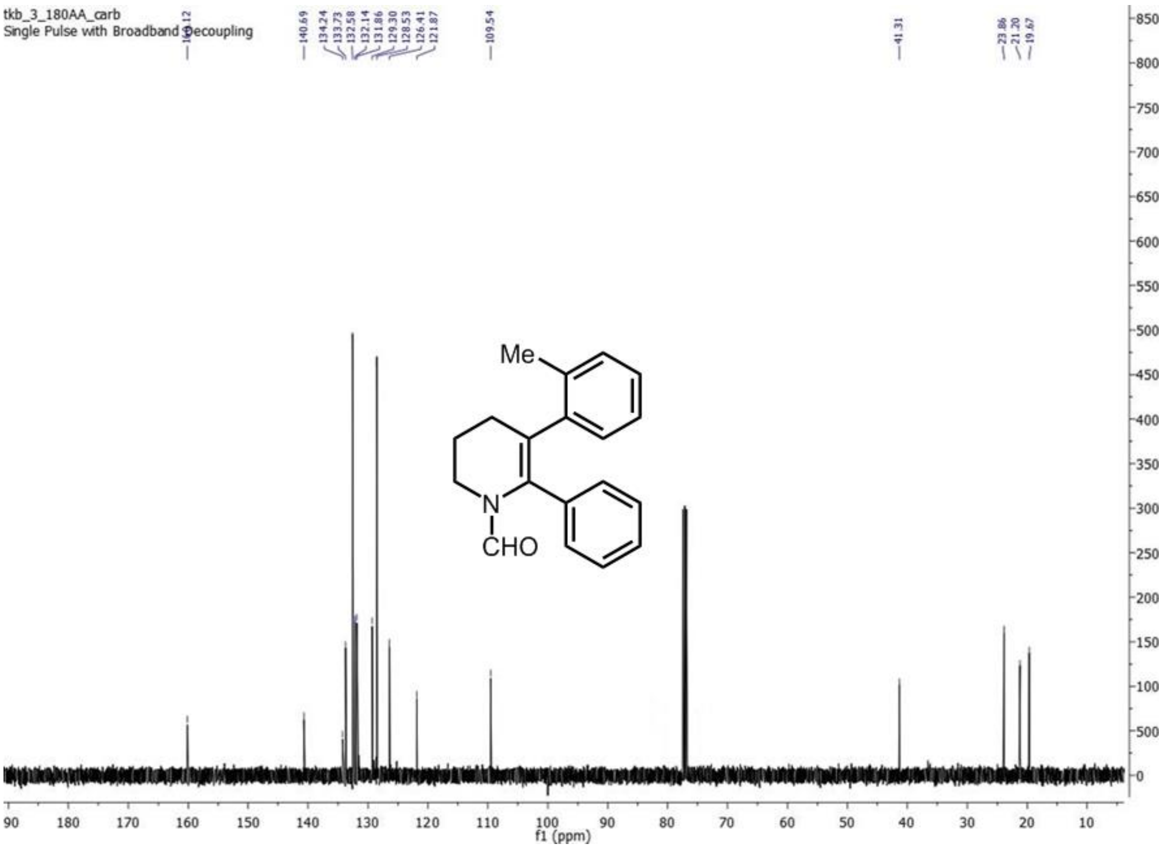
tkb_3_180AA_carb
Single Pulse with Broadband Decoupling
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140.69
134.24
133.73
132.58
132.14
131.86
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109.54
41.31
23.86
21.20
19.67
Me
N
CHO
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)
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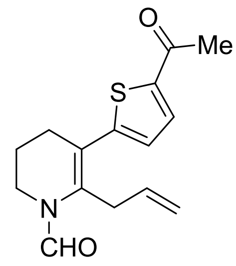
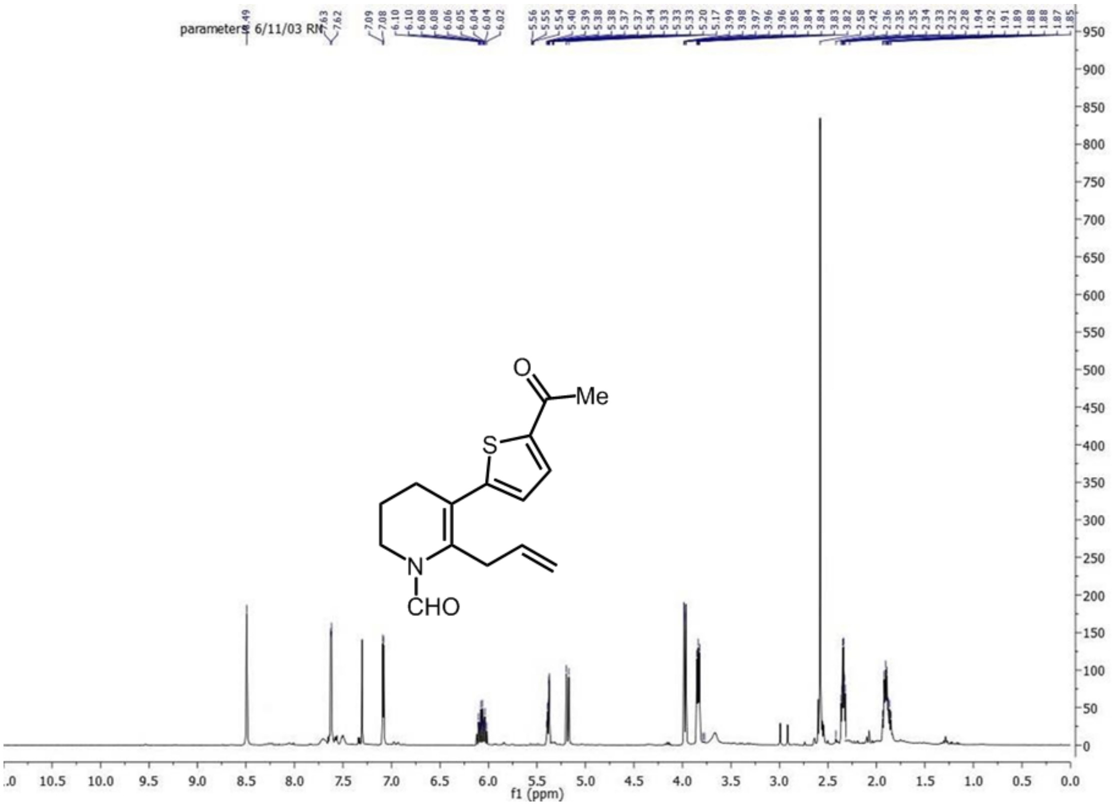
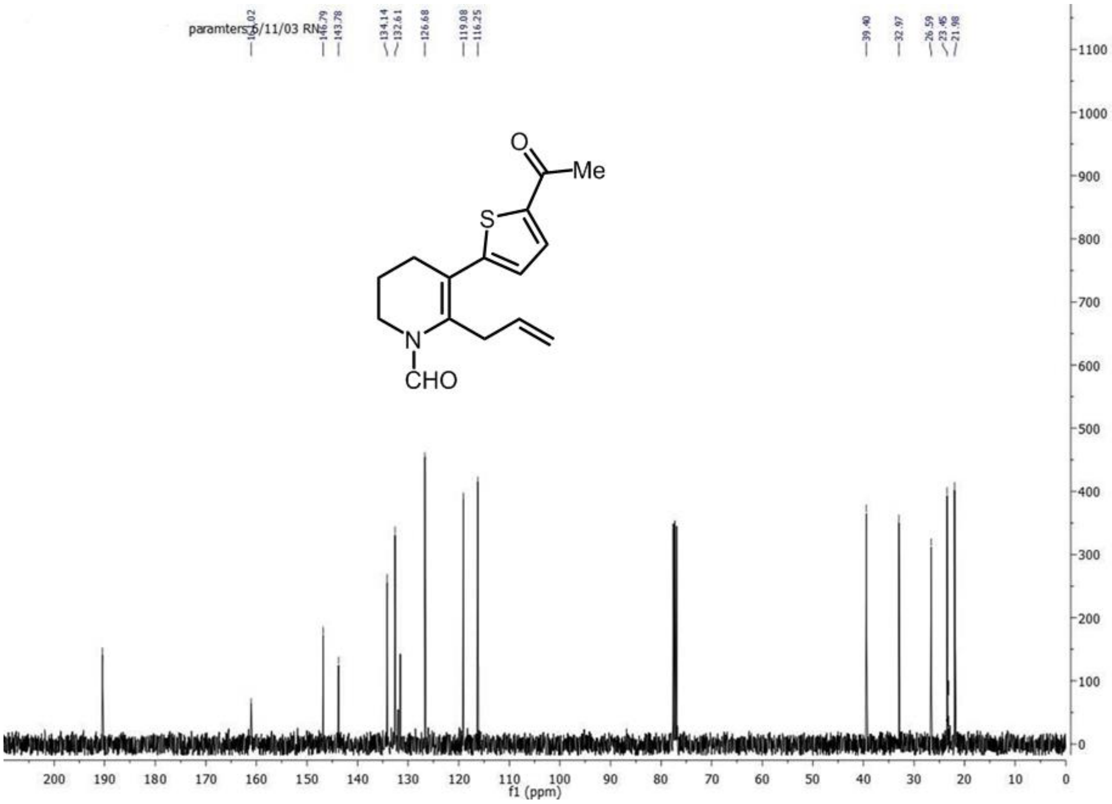
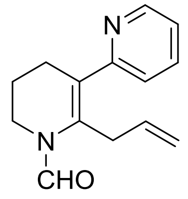


4e

Prepared from **3e** (455 mg, 1 mmol), allyl bromide (180 mg, 1.5 mmol, 1.5 equiv) and 2-acetyl-5-bromothiophene (406 mg, 2 mmol, 2 equiv) using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50). Yield = 223 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (1H, s), 7.63 to 7.62 (1H, d), 7.09 to 7.08 (1H, d), 6.10 to 6.02 (1H, m), 5.40 to 5.37 (1H, dd), 5.20 to 5.17 (1H, dd), 3.99 to 3.77 (4H, m), 2.58 (3H, s), 2.42 to 2.28 (2H, m), 1.94 to 1.85 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.4, 161.0, 146.8, 143.8, 134.1, 132.6, 126.7, 119.1, 116.2, 39.4, 33.0, 26.6, 23.4, 22.0. HRMS calc for $C_{15}H_{17}NO_2S$ 275.0980, found 275.0983.

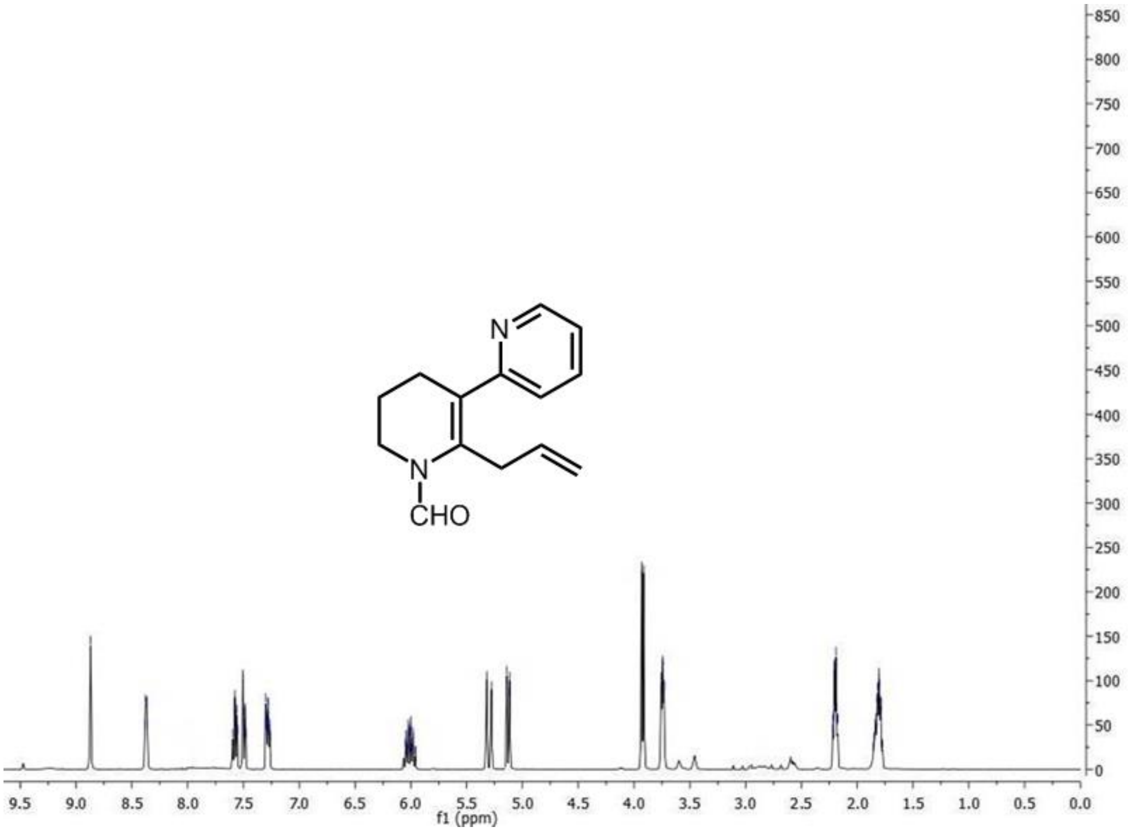






4f

Prepared from **3e** (455 mg, 1 mmol), allyl bromide (180 mg, 1.5 mmol, 1.5 equiv) and 2-bromopyridine (314 mg, 2 mmol, 2 equiv) using General Procedure F. T = 23 °C for 8 h then 40 °C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (20:80 to 0:100). Yield = 96 mg, 42%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (1H), 8.38 to 8.36 (1H), 7.60 to 7.48 (2H), 7.30 to 7.26 (1H), 6.05 to 5.96 (1H), 5.32 to 5.28 (1H), 5.14 to 5.11 (1H), 3.93 to 3.73 (4H), 2.22 to 2.17 (2H), 1.86 to 1.77 (2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 149.9, 141.8, 138.9, 134.1, 128.4, 125.0, 122.7, 119.1, 109.5, 41.2, 36.5, 23.7, 21.1. HRMS calc for $C_{14}H_{16}N_2O$ 228.1263, found 228.1265.


N
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750
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550
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450
400
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0
9.5
9.0
8.5
8.0
7.5
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6.5
6.0
5.5
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1.0
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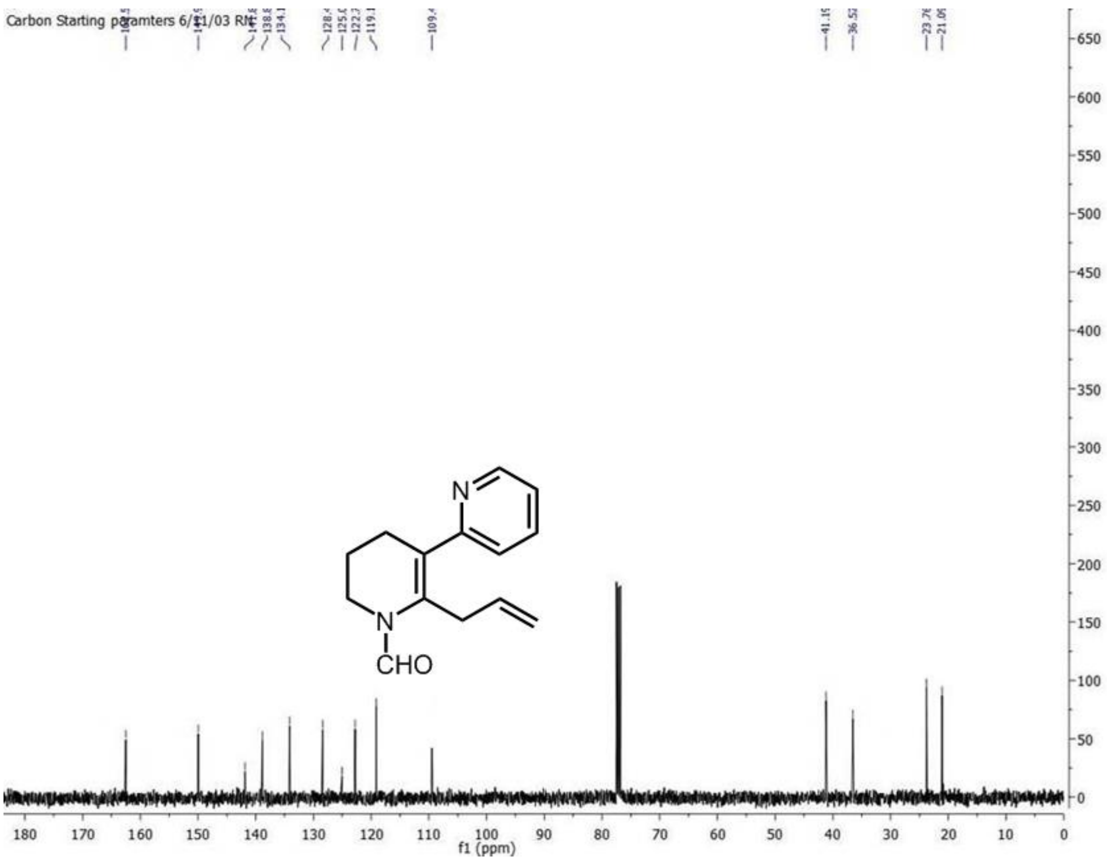
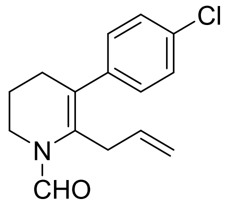
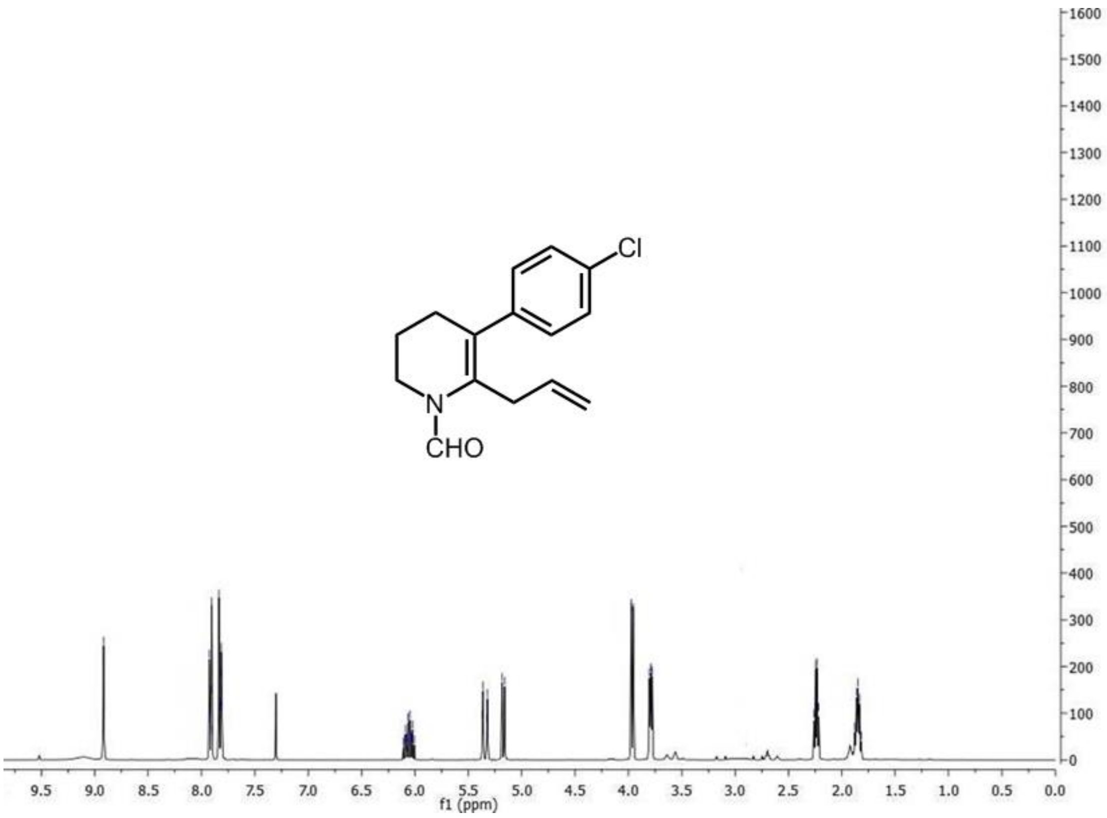
0.0
f1 (ppm)





4g

Prepared from **3e** (455 mg, 1 mmol), allyl bromide (180 mg, 1.5 mmol, 1.5 equiv) and *p*-chlorobromobenzene (380 mg, 2 mmol, 2 equiv) using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20 to 60:40). Yield = 173 mg, 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (1H, s), 7.91 (2H, d), 7.82 (2H, d), 6.11 to 6.00 (1H, m), 5.36 (1H, d), 5.32 (1H, d), 3.96 (2H, d), 3.80 to 3.78 (2H, dd), 2.26 to 2.22 (2H, m), 1.88 to 1.82 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 138.4, 134.2, 132.7, 132.4, 125.1, 119.1, 109.5, 104.3, 41.2, 32.9, 23.8, 21.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{16}H_{16}ClNO$ [M^+] 261.0920, found 261.0924.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9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.0
1.5
1.0
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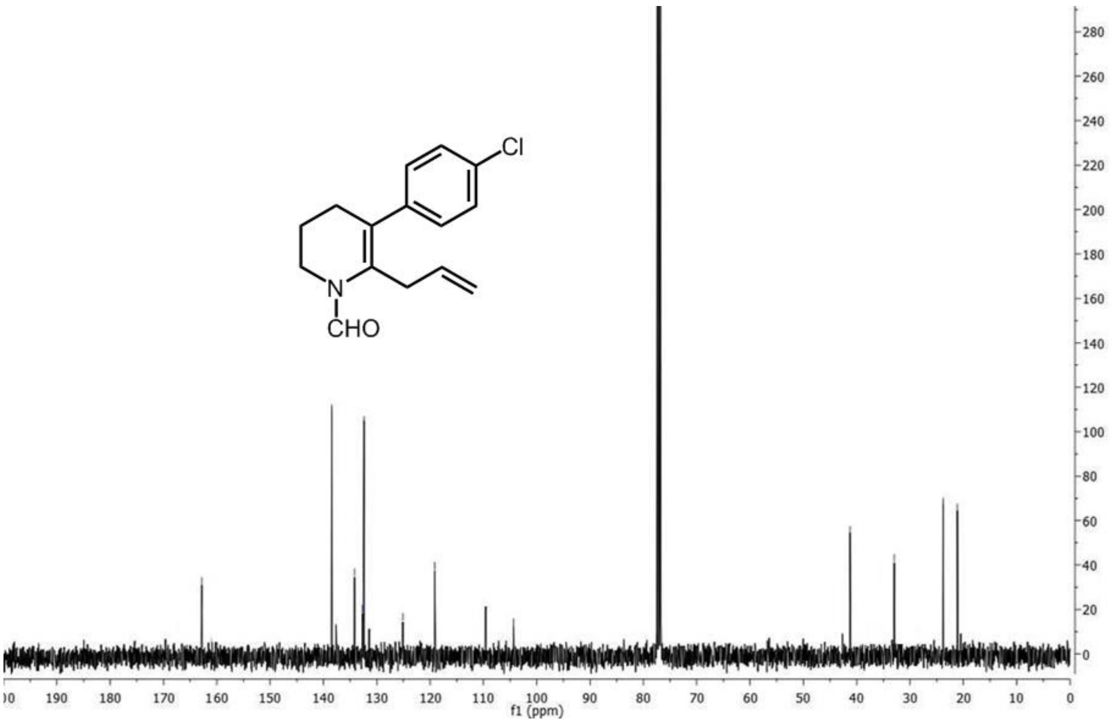
0.0
f1 (ppm)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180
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110
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90
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70
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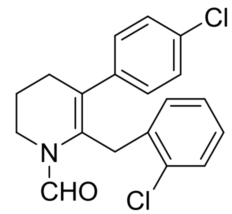
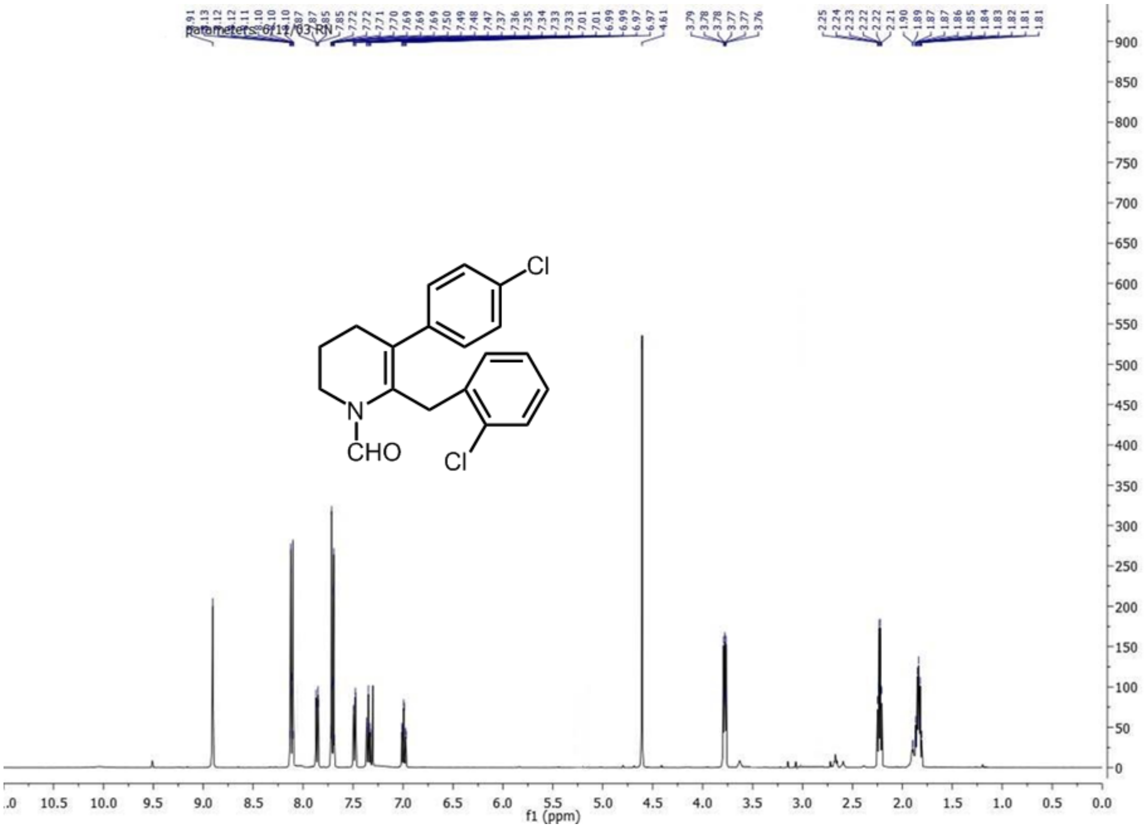
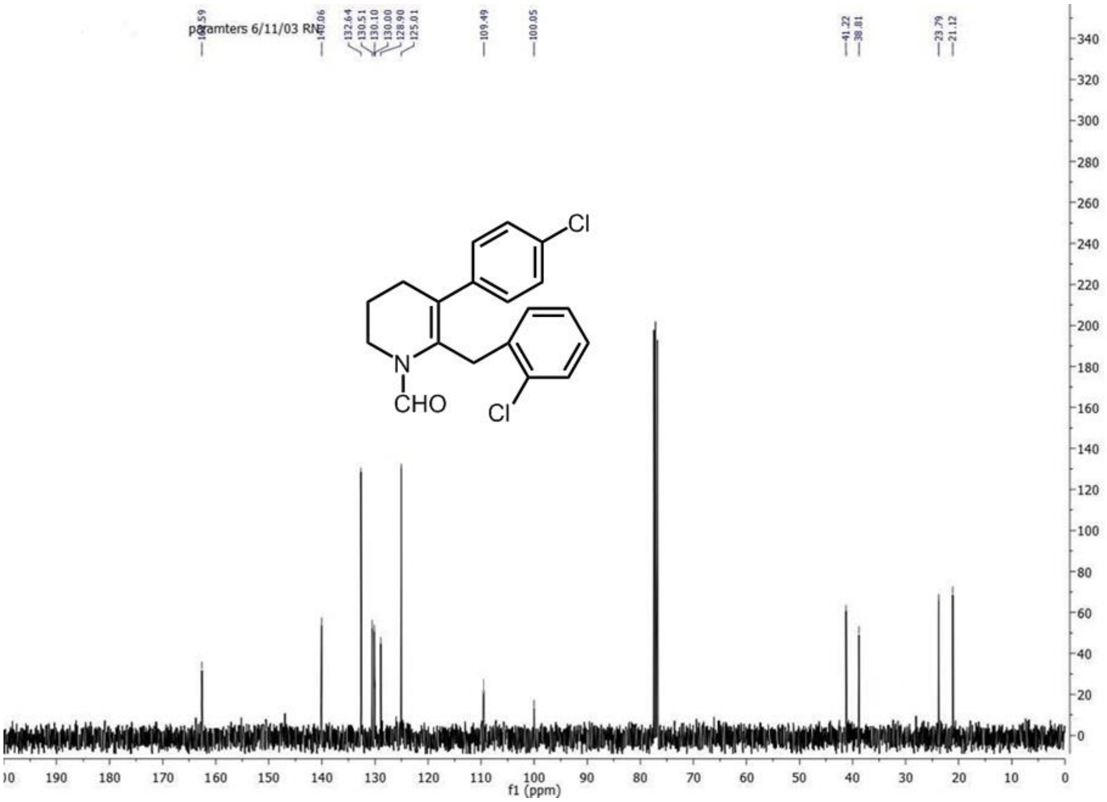
50
40
30
20
10
0
f1 (ppm)



4h

Prepared from **3e** (455 mg, 1 mmol), 2-chlorobenzyl bromide (245 mg, 1.2 mmol, 1.2 equiv) and *p*-chlorobromobenzene (380 mg, 2 mmol, 2 equiv) using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20). Yield = 217.5 mg, 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (1H, s), 8.13 to 8.10 (2H, d), 7.87 to 7.85 (1H, d), 7.72 to 7.69 (2H, d), 7.50 to 7.33 (2H, t), 7.01 to 6.97 (1H, t), 4.61 (2H, s), 3.79 to 3.76 (2H, dd), 2.25 to 2.21 (2H, m), 1.90 to 1.81 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 140.1, 132.6, 130.5, 130.1, 130.0, 128.9, 125.0, 109.5, 100.0, 41.2, 38.8, 23.8, 21.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{17}Cl_2NO$ [M^+] 345.0687, found 345.0690.

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125.01
109.49
100.05
41.22
38.81
23.79
21.12
Cl
N
CHO
Cl
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
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180
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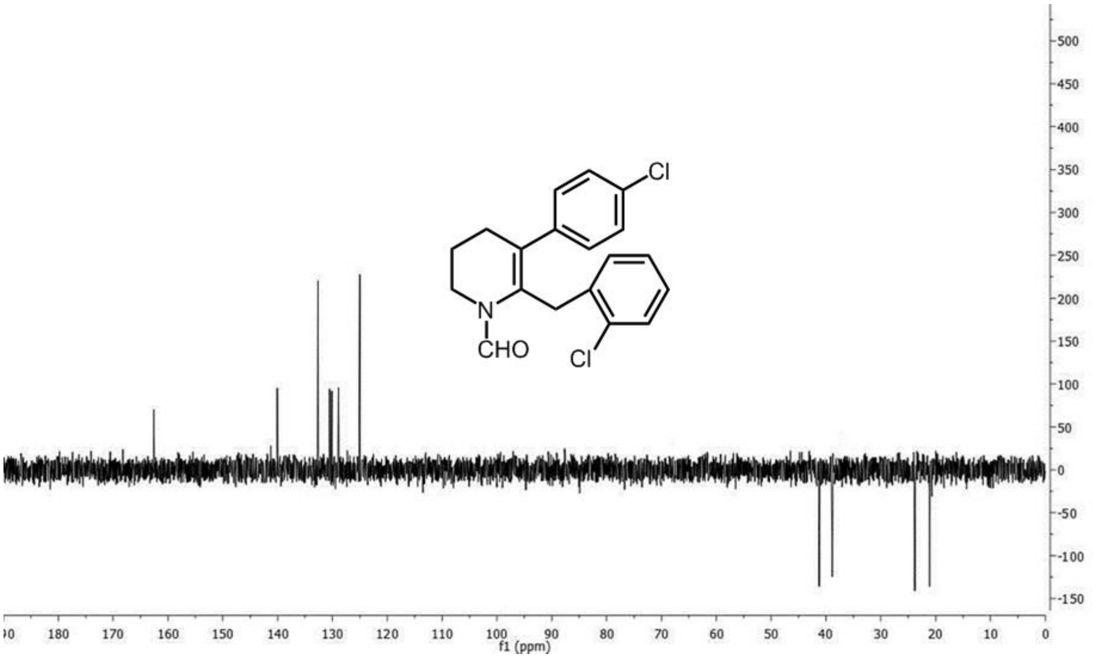
f1 (ppm)


Cl
N
CHO
Cl
500
450
400
350
300
250
200
150
100
50
0
-50
-100
-150
180
170
160
150
140
130
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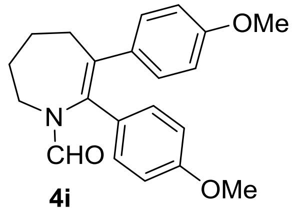
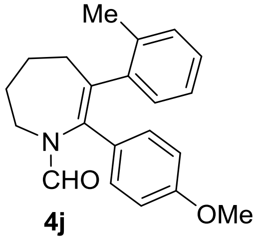
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



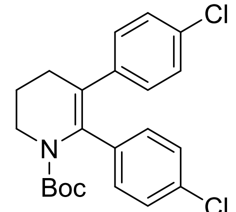
4i

Prepared from **3f** (469 mg, 1 mmol) and *p*-bromoanisole (561 mg, 3 equiv), using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (50:50 to 20:80). Yield = 273 mg, 81%. Data as reported by us.[3]



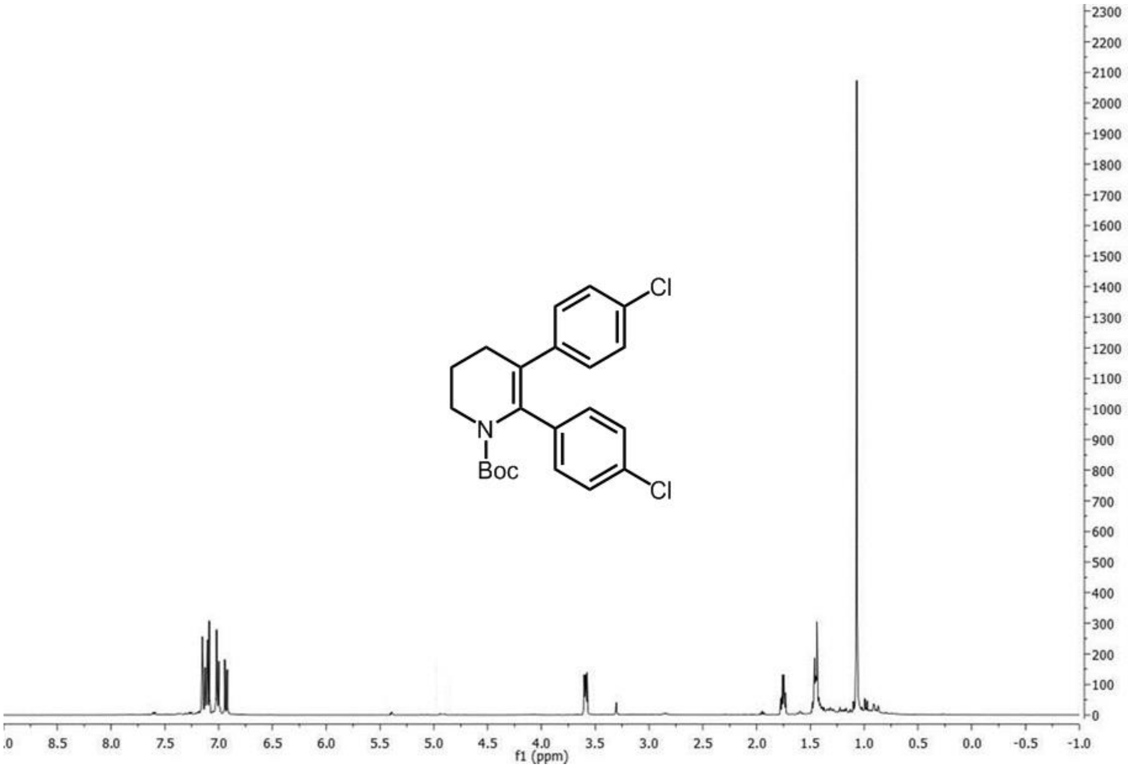
4j

Prepared from **3f** (469 mg, 1 mmol), *p*-bromoanisole (225 mg, 1.2 equiv), and 2-bromotoluene (340 mg, 2 equiv), using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (80:20 to 50:50). Yield = 145 mg, 45%. Data as reported by us.[3]



4k

Prepared from **3d** (527 mg, 1 mmol) and *p*-chlorobromobenzene (570 mg, 3 mmol, 3 equiv) using General Procedure F. T = 23 °C for 8 h, then 40 °C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (1:1). Yield = 234 mg; 58%. ^{1}H NMR (400 MHz, C_6D_6) δ 7.02 &7.00 (2H), 6.94 & 6.92 (2H), 3.60 to 3.58 (2H), 1.78 to 1.73 (2H), 1.48 to 1.42 (2H), 1.07 (9H). ^{13}C NMR (101 MHz, C_6D_6) δ 153.4, 139.8, 139.4, 132.2, 128.8, 128.1, 114.7, 79.7, 44.1, 27.4, 23.4, 23.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{23}Cl_2NO_2$ [M^+] 403.1106, found 403.1110


Cl
Cl
N
Boc
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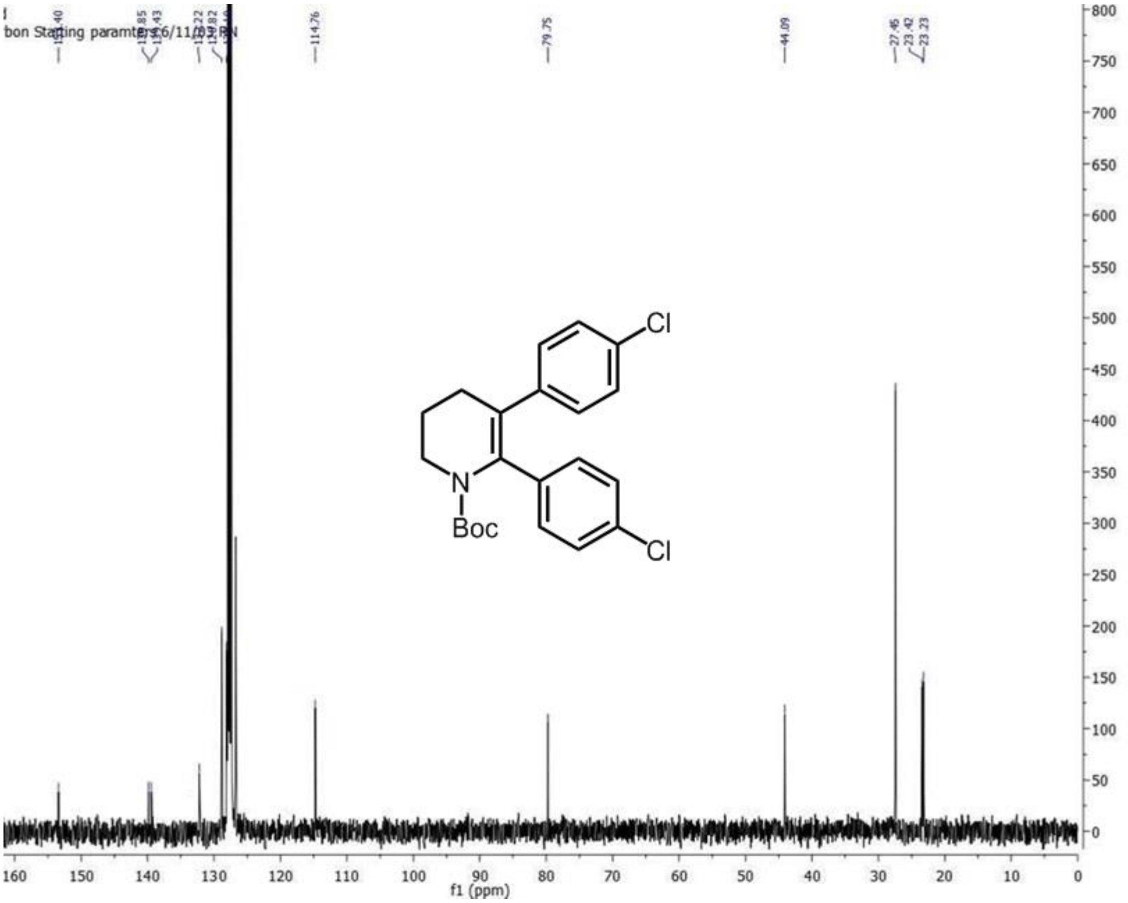
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


bon Starting paramters 6/11/03 PN
114.76
79.75
44.09
27.46
23.42
23.23
Cl
Cl
N
Boc
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
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150
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130
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100
90
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70
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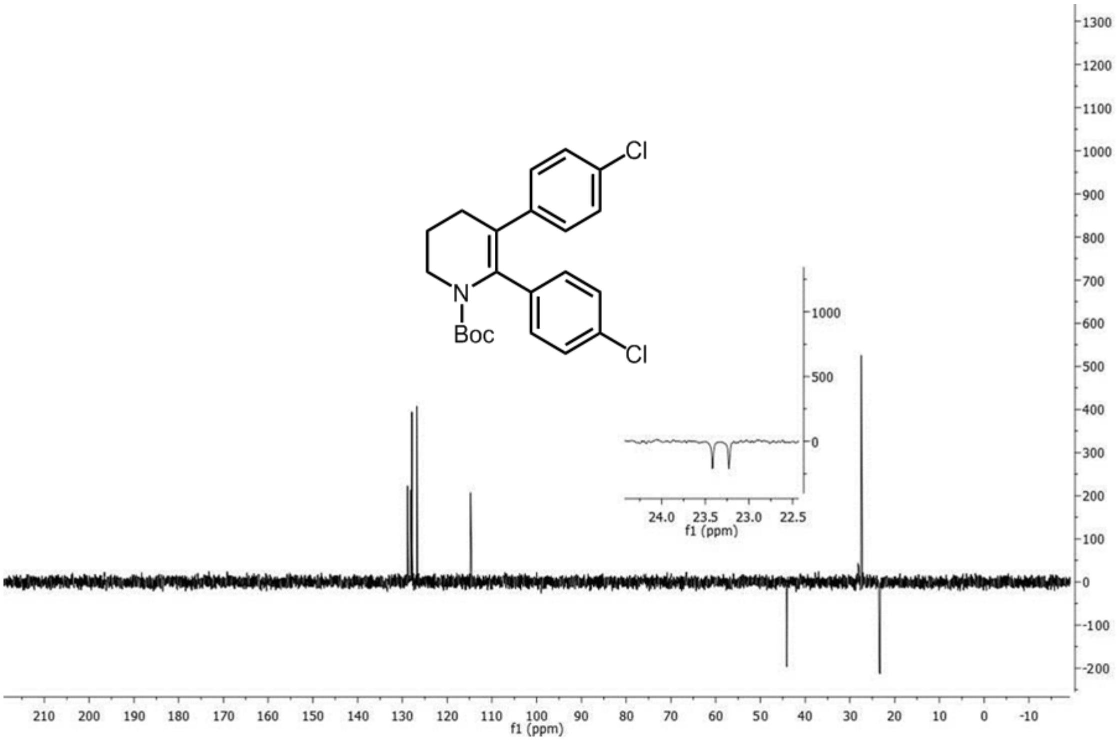
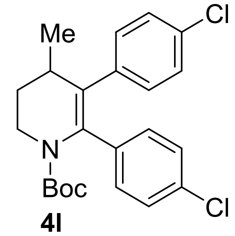
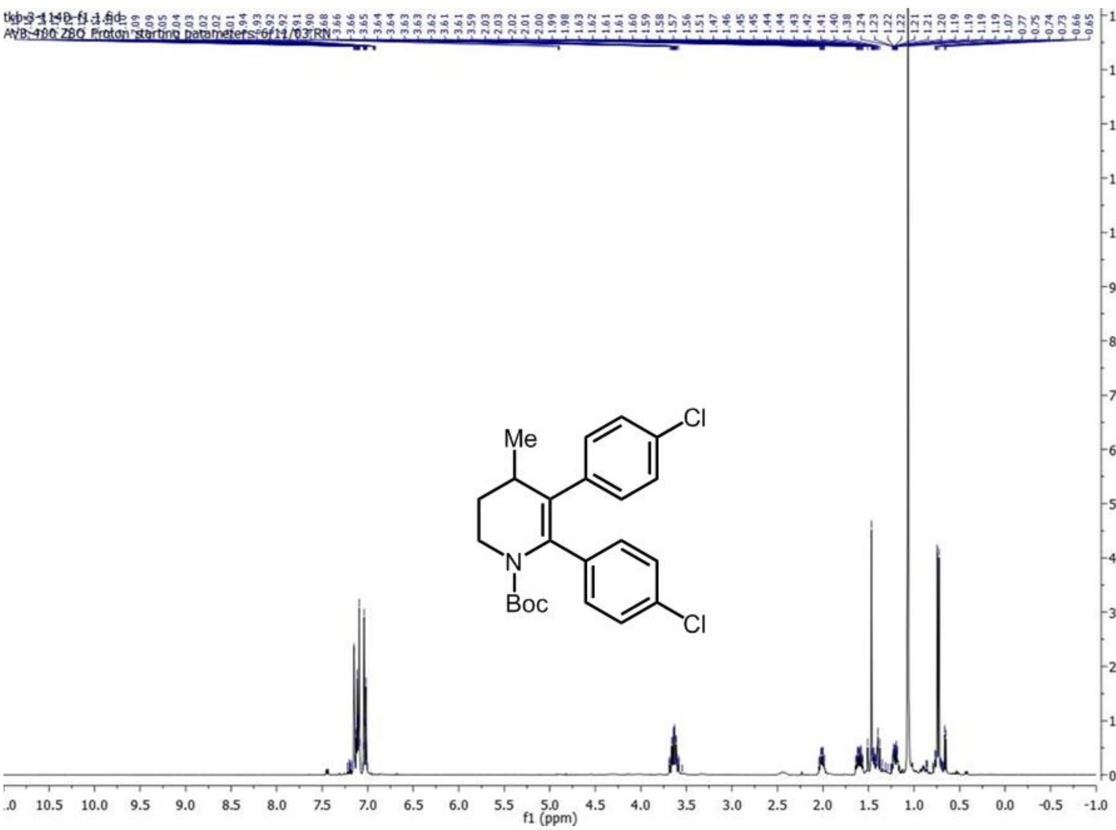
50
40
30
20
10
0
f1 (ppm)

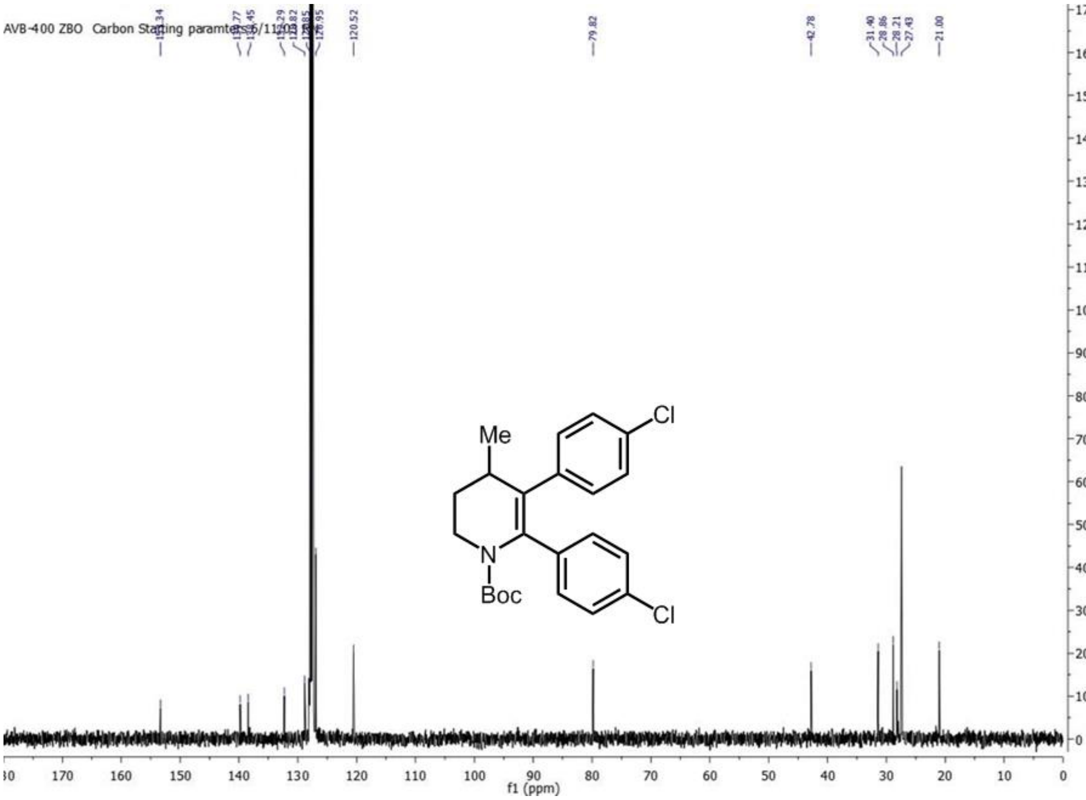




4l

Prepared from **3g** (541 mg, 1 mmol) and *p*-chlorobromobenzene (570 mg, 3 mmol, 3 equiv) using General Procedure F. T = 23 ^{o}C for 8 h, then 40 ^{o}C for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N). PE/DCM (2:1). Yield = 259 mg; 62%. ^{1}H NMR (400 MHz, C_6D_6, mixture of rotamers) δ 7.22 to 7.00 (2H, d), 6.95 to 6.90 (2H, d), 3.69 to 3.55 (2H, dd), 2.04 to 1.98 (1H, dd), 1.64 to 1.19 (11H, m), 0.87 to 0.65 (3H, d). ^{13}C NMR (101 MHz, C_6D6) δ 153.3, 139.7, 138.4, 132.3, 128.8, 127.8, 126.9, 120.5, 79.8, 42.7, 31.4, 28.8, 28.2, 27.4, 21.0. **HRMS-EI$^+$** (*m/z*): calc for $C_{17}H_{22}ClNO_2$ [M^+] 417.1262, found 417.1266.


tkb-3-114D-f1.1.fid
AVB-400 ZBO Proton starting parameters 6/11/03 RN
7.09 7.09 7.05 7.04 7.03 7.02 7.02 7.01 6.94 6.93 6.92 6.92 6.91 6.90 3.68 3.66 3.65 3.64 3.64 3.63 3.63 3.62 3.61 3.61 3.59 2.03 2.03 2.02 2.01 2.00 1.99 1.98 1.63 1.62 1.61 1.61 1.60 1.59 1.58 1.57 1.56 1.51 1.47 1.46 1.45 1.45 1.44 1.44 1.43 1.42 1.41 1.40 1.38 1.24 1.23 1.22 1.22 1.21 1.21 1.20 1.19 1.19 1.19 1.19 1.07 0.77 0.75 0.74 0.73 0.66 0.65
Me
Cl
N
Boc
Cl
f1 (ppm)


AVB-400 ZBO Carbon Starting paramters 6/11/03 RN
153.34
139.77
138.45
132.29
128.82
127.85
126.95
120.52
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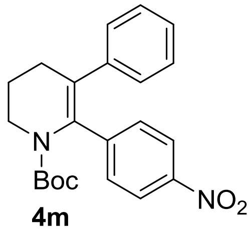
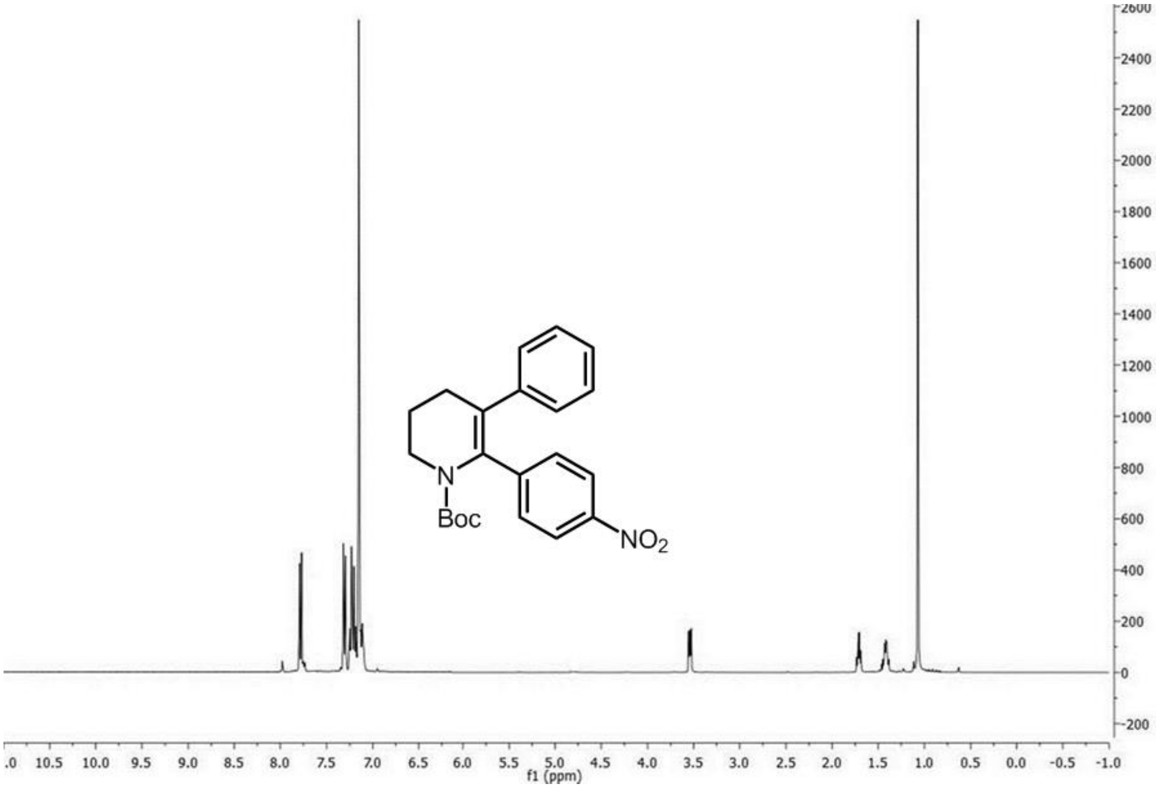
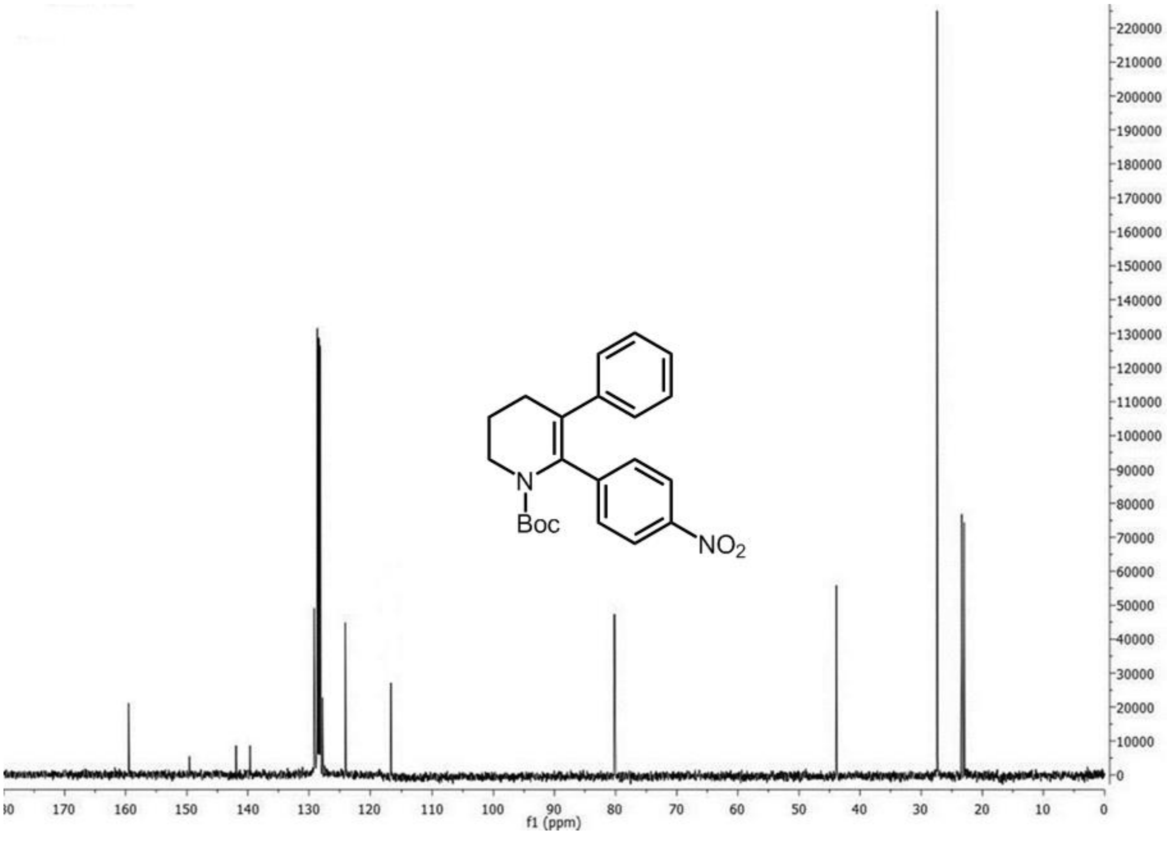
42.78
31.40
28.86
28.21
27.43
21.00
Me
Cl
N
Boc
Cl
f1 (ppm)

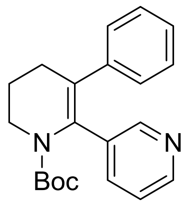


4m

Prepared from **3d** (527 mg, 1 mmol) and *p*-nitrobromobenzene (241 mg, 1.2 mmol, 1.2 equiv) and phenyl bromide (312 mg, 2 equiv) using General Procedure F. T = 23 °C for 8 h, then 40 °C, for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (1:1). Yield = 183 mg; 48%. ^{1}H NMR (400 MHz, C_6D_6) δ 7.78 (2H, d) 7.32 to 7.11 (7H, m), 3.55 to 3.53 (2H, dd), 1.73 to 1.69 (2H, m), 1.46 to 1.39 (2H, m), 1.07 (9H, s). ^{13}C NMR (101 MHz, C_6D_6) δ 159.5, 149.5, 141.9, 139.6, 129.2, 129.1, 129.0, 128.9, 128.6, 128.6, 128.4, 128.3, 128.1, 127.8, 124.0, 116.8, 80.2, 43.9, 27.4, 23.4, 23.0. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{24}N_2O_4$ [M$^+$] 380.1736, found 380.1739.

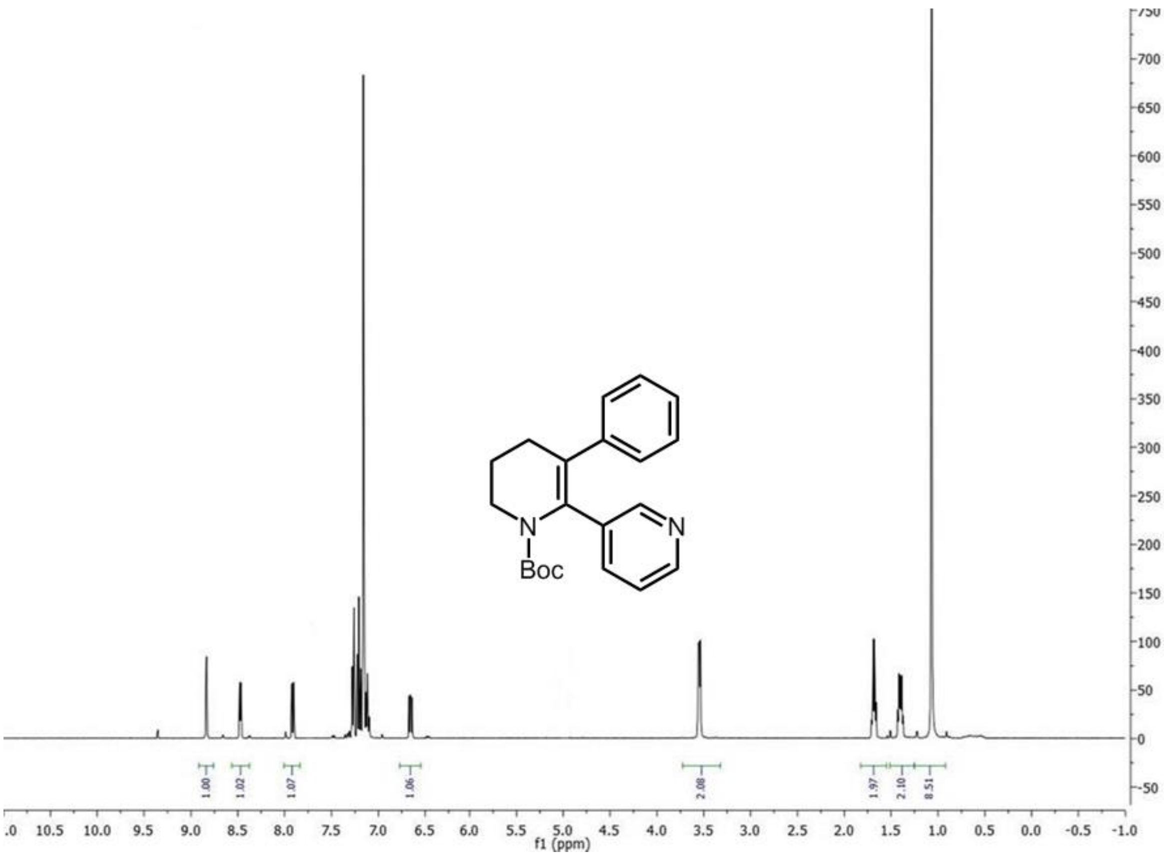






4n

Prepared from **3d** (527 mg, 1 mmol) and *m*-bromopyridine (188 mg, 1.2 mmol, 1.2 equiv) and phenyl bromide (312 mg, 2 equiv) using General Procedure F. T = 23 °C for 8 h, then 40 °C, for 16 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with PE/DCM (1:3). Yield = 182 mg; 54%. ^{1}H NMR (400 MHz, C_6D_6) δ 8.83 (1H, s), 8.48 (1H, d), 7.83 (1H, dd), 7.33 to 7.09 (5H, m), 6.66 (1H, dd), 3.56 to 3.53 (2H, dd), 1.70 to 1.66 (2H, m), 1.42 to 1.39 (2H, m), 1.06 (9H, s). ^{13}C NMR (101 MHz, C_6D6) δ 158.4, 151.6, 150.7, 139.4, 133.6, 131.7, 128.4, 128.3, 127.9, 127.9, 127.8, 127.7, 127.6, 127.4, 126.9, 123.2, 116.9, 80.3, 43.9, 27.4, 23.4 23.1. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{24}N_2O_2$ [M$^+$] 336.1838, found 336.1841.


N
Boc
N
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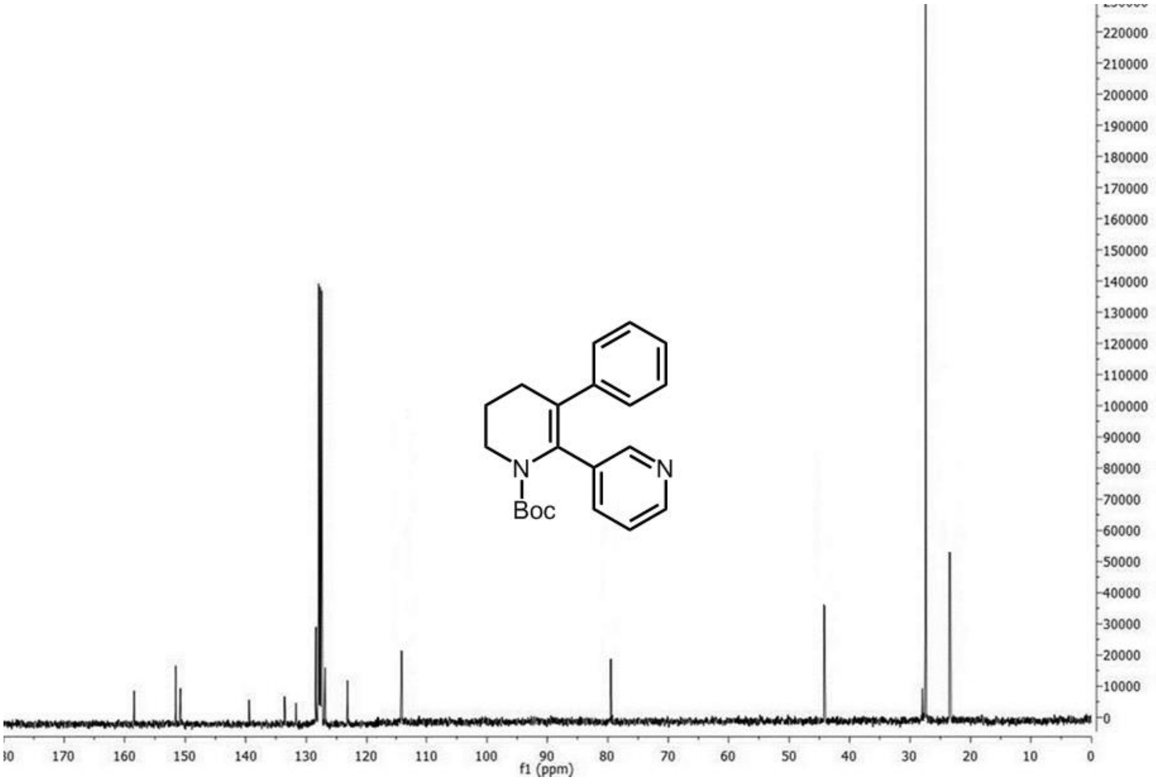
1.02
1.07
1.06
2.08
1.97
2.10
8.51
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


N
Boc
N
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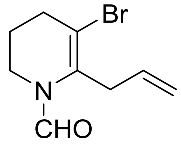
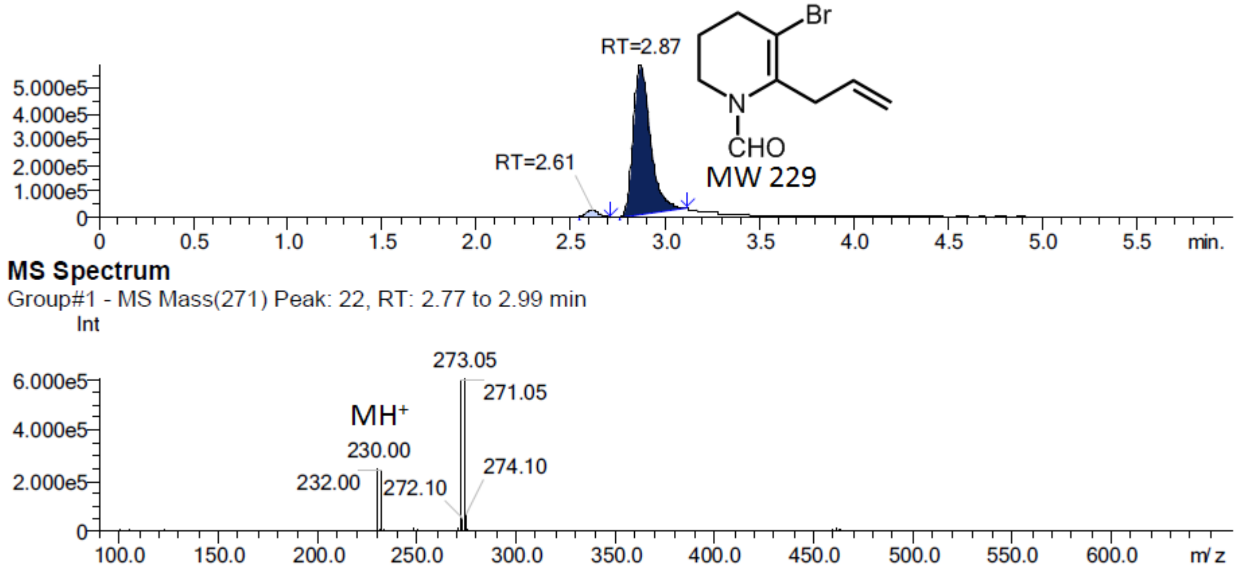
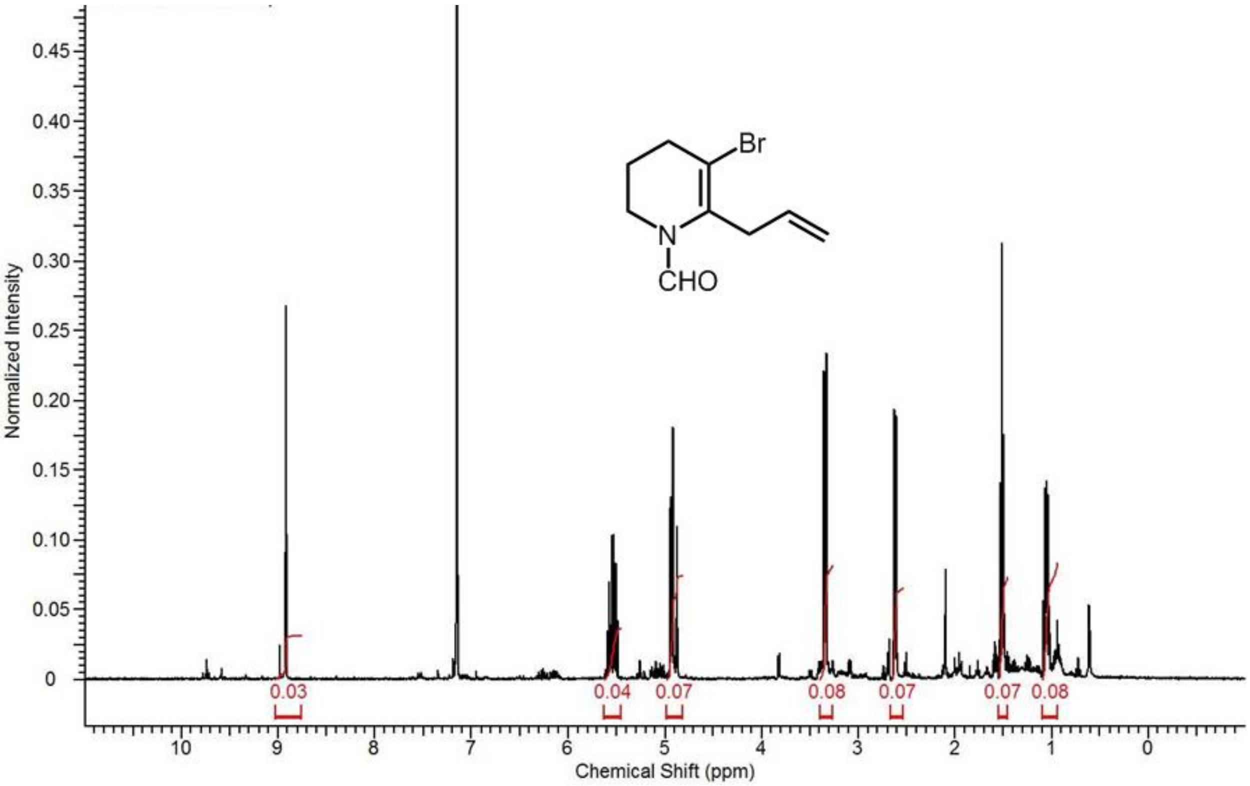
210000
200000
190000
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
30 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



4o

Prepared from **3b** (377 mg, 1 mmol) and allyl bromide (180 mg, 1.5 mmol, 1.5 equiv) using General Procedure F. T = 23 ^{o}C for 12 h. Purification: Flash chromatography on silica (pretreated with 1% Et$_3$N) eluting with hexane/EtOAc (90:10). Yield = 140 mg, 61%. ^{1}H NMR (400 MHz, C$_6$D$_6$) δ 8.93 (1H, s), 5.60 to 5.50 (1H, m), 4.96 to 4.88 (2H, m), 3.43 to 3.32 (2H, dd), 2.65 to 2.61 (2H, d), 1.57 to 1.46 (2H, m), 1.09 to 1.03 (2H, m). ^{13}C NMR (101 MHz, C$_6$D$_6$) δ 159.9, 134.6, 122.4, 117.2, 116.5, 41.3, 38.0, 28.4, 22.1. **HRMS-EI^{+}** (*m/z*): calc'd for C$_9$H$_{12}$BrNO 229.0102, found 229.0105.




Br
N
CHO
Normalized Intensity
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0.30
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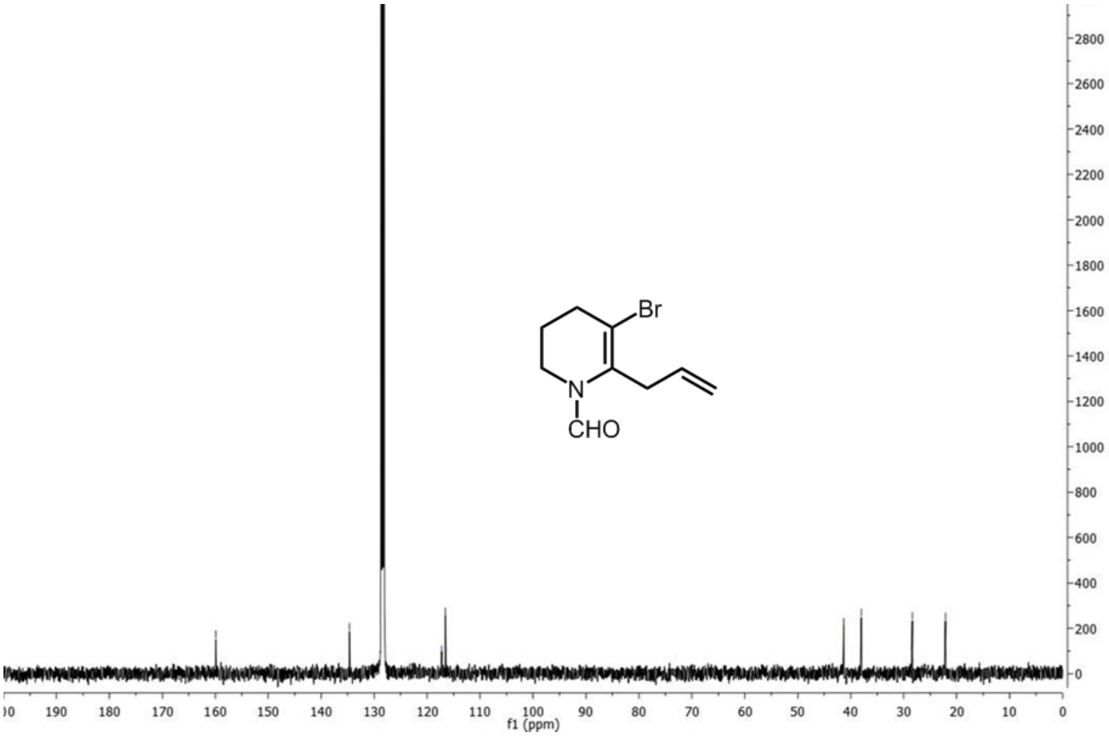
0.20
0.15
0.10
0.05
0
0.03
0.04
0.07
0.08
0.07
0.07
0.08
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


Br
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20
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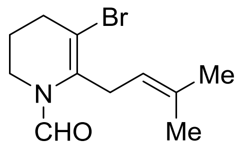
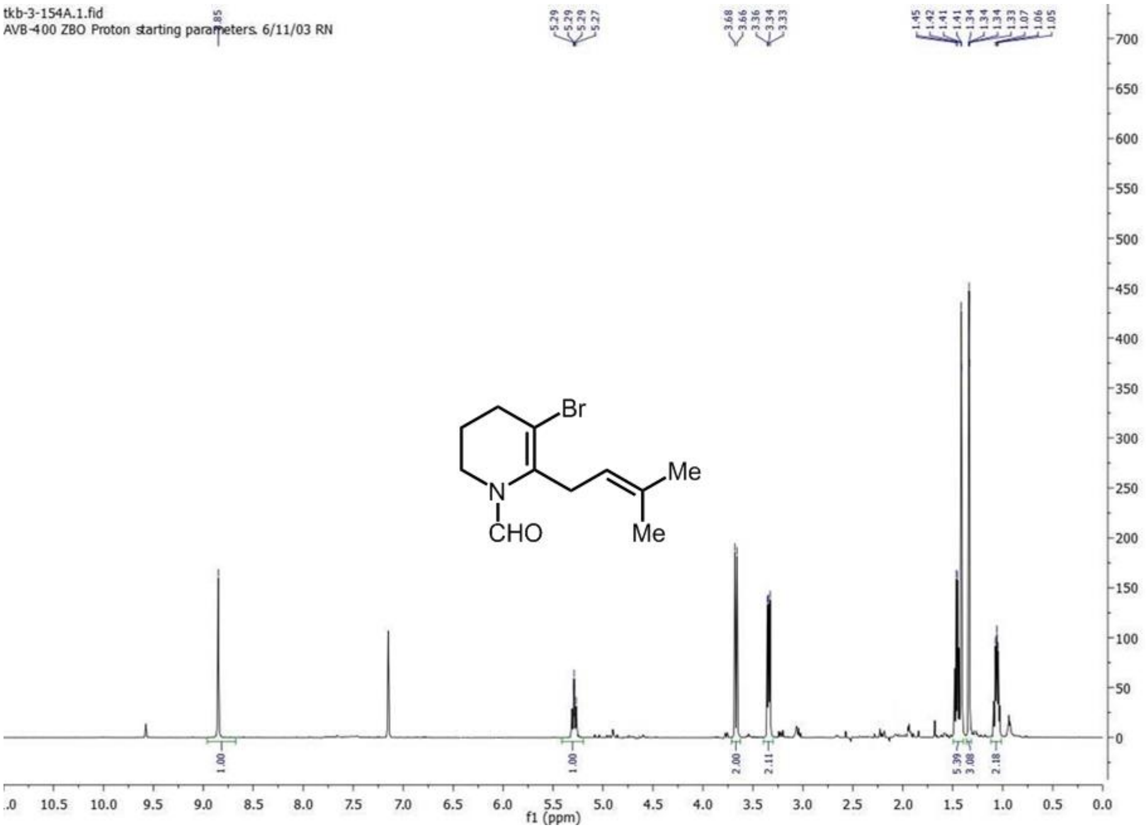
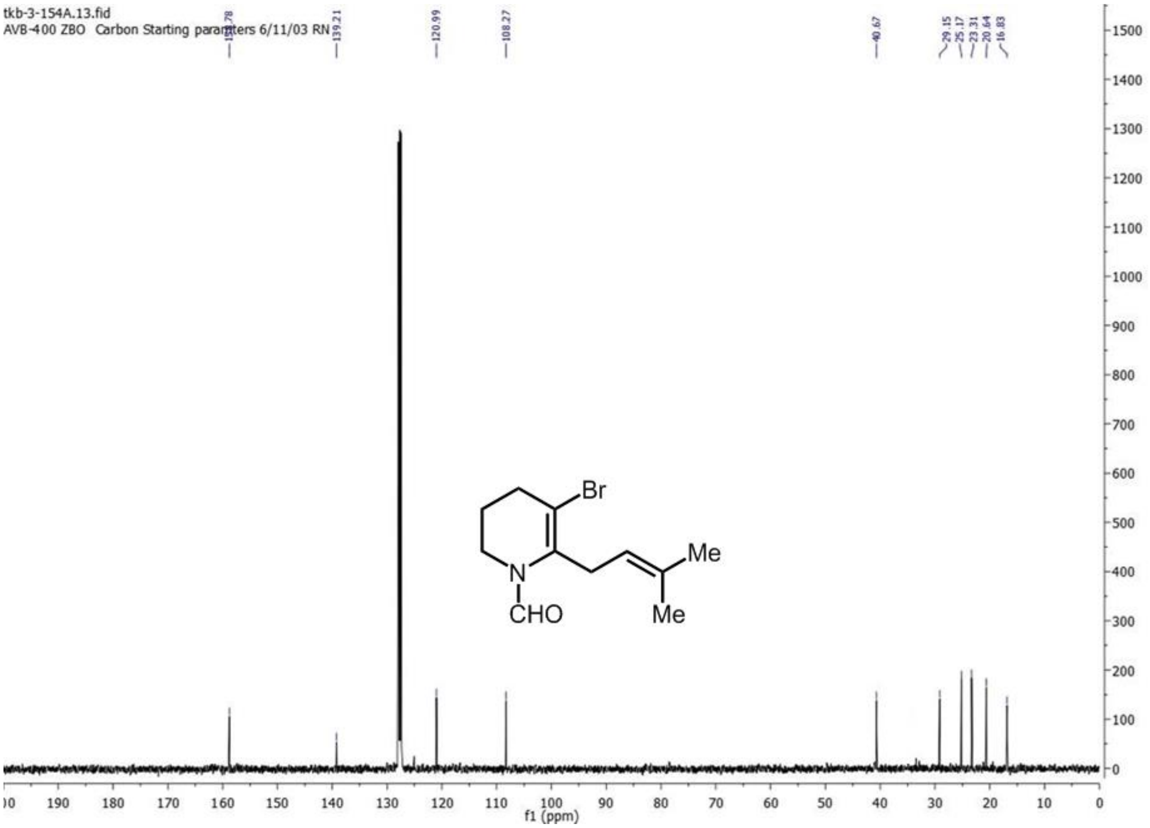
0
f1 (ppm)



4p

Prepared from **3b** (377 mg, 1 mmol) and dimethylallyl bromide (222 mg, 1.5 mmol, 1.5 equiv) using General Procedure F. T = 23 ^{o}C for 12 h. Purification: Flash chromatography on silica (pretreated with 1% Et_3N) eluting with hexane/EtOAc (90:10). Yield = 139 mg, 54%. ^{1}H NMR (400 MHz, C_6D_6) δ 8.85 (1H), 5.29 to 5.27 (1H), 3.68 to 3.66 (2H), 3.36 to 3.33 (2H), 1.46 to 1.41 (2H), 1.34 to 1.33 (6H), 1.07 to 1.04 (2H). ^{13}C NMR (101 MHz, C_6D_6) δ 158.78, 139.21, 125.05, 120.99, 108.27, 40.67, 29.15, 25.17, 23.31, 20.64, 16.83. **HRMS-EI$^+$** (*m/z*): calc for $C_{11}H_{16}BrNO$ $[M]^+$ 257.0415, found 257.0419.

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Br
Me
N
CHO
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1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
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0
190
180
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130
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110
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90
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70
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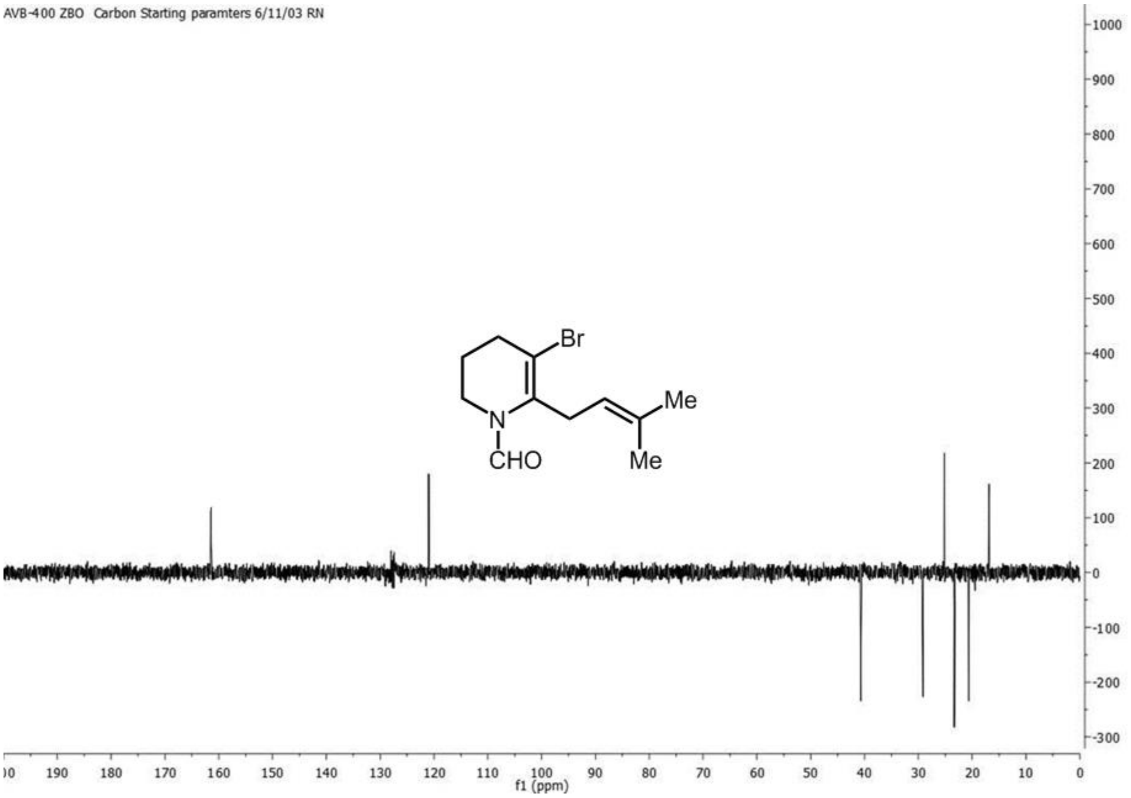
50
40
30
20
10
0
f1 (ppm)


AVB-400 ZBO Carbon Starting paramters 6/11/03 RN
Br
Me
N
CHO
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500
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200
100
0
-100
-200
-300
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180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

References

(1) Bassler, D. P.; Alwali, A.; Spence, L.; Beale, O.; Beng, T. K. *J. Organomet. Chem.* **2015**, *780*, 6.

(2) Beng, T. K.; Wilkerson-Hill, S. M.; Sarpong, R. *Org. Lett.* **2014**, *16*, 916.

(3) Bassler, D. P.; Spence, L.; Alwali, A.; Beale, O.; Beng, T. K. *Org. Biomol. Chem.* **2015**, *13*, 2285.