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

Organocatalytic synthesis of β-enaminyl radicals as the single-electron donors for phenyliodine(III) dicarboxylates: Direct one-pot alkylation-aminoxidation of styrenes

Nagaraju Sakkani, Nouraan Sadiq, and John C.-G. Zhao*

Department of Chemistry, University of Texas at San Antonio

Supporting Information

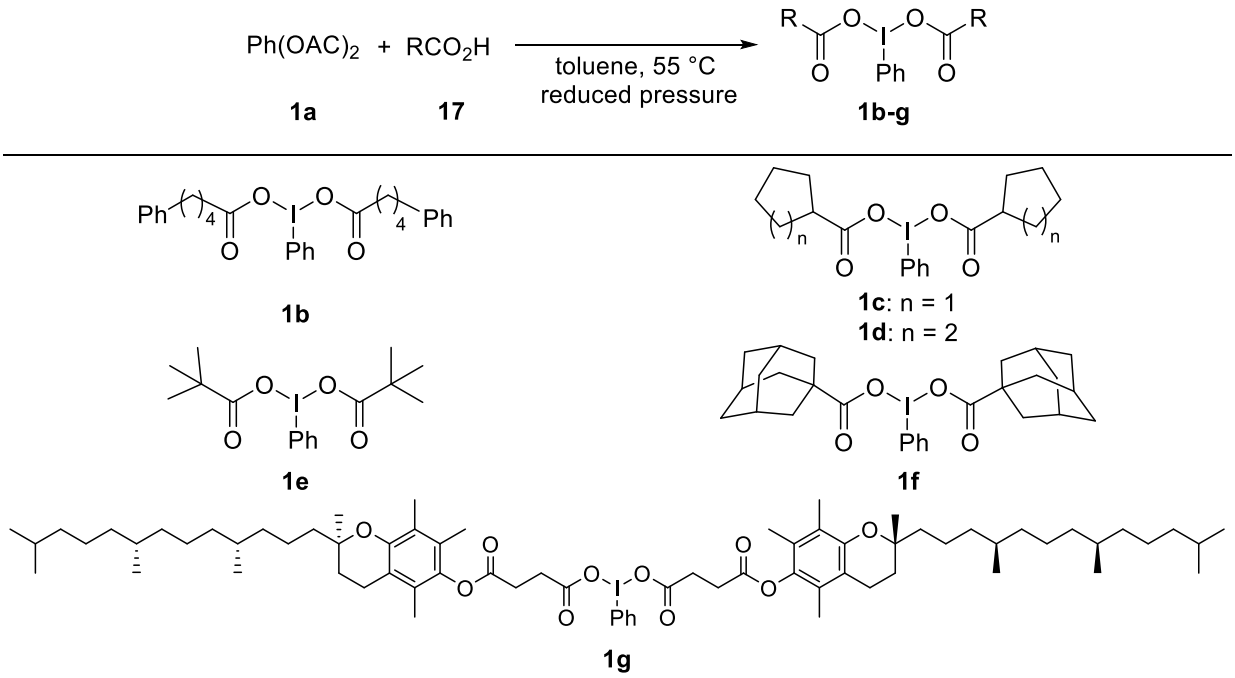
Table of Contents

General Information

Unless otherwise specified, all reactions were monitored by TLC on silica gel aluminum plates (200 μm) and visualized by UV. Column chromatography was performed on silica gel (40-63μm). ^{1}H NMR spectra were recorded on a 500 MHz or a 300 MHz spectrometer (126 MHz or 75 MHz for ^{13}C NMR). All deuterated solvents were purchased form Cambridge Isotope Laboratories. Infrared spectra were measured on a Bruker Vector 22 instrument. Melting points were recorded on MEL-TEMP melting point apparatus in open capillaries and uncorrected. HRMS were conducted by the RCMI Core Facilities, Department of Chemistry, UTSA. Unless specified below, all chemicals are commercial products and were used as received. All the styrenes used in this study are known compounds and were either commercially available or synthesized according to the literature procedures.[33]

Experimental Procedures

General procedure for the preparation of phenyliodine(III) dicarboxylates[34]



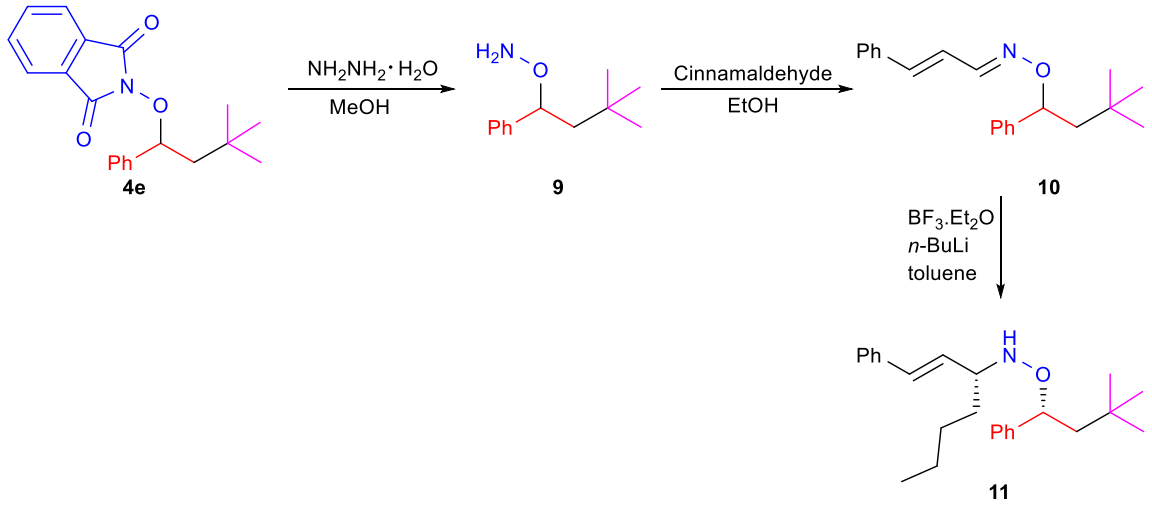
Scheme S-1. Preparation of phenyliodine(III) dicarboxylates **1b-1g**.

To a 50-mL flame-dried round-bottom flask were added $PhI(OAc)_2$ (**1a**, 0.322 mg, 1.0 mmol), the required carboxylic acid (2.1 mmol, 2.1 equiv.), and toluene (20 mL). The flask was then attached a rotary evaporator, and toluene and the generated acetic acid were evaporated at 55 °C for 10 min. Then, another 20 mL of toluene was added to the flask and the liquid was evaporated at the same temperature for the same amount of time. This procedure was repeated for another three times to yield the pure phenyliodine(III) dicarboxylate with almost a quantitative yield. The synthesized phenyliodine(III) dicarboxylate is pure enough to use in the reaction without further purification. Phenyliodine(III) dicarboxylates **1c**[34a], **1d**[34b], **1e**[34b], and **1f**[34b] are known in the literature.

Derivatization of the reaction product 4e

1. Synthesis of *O*-(3,3-dimethyl-1-phenylbutyl)hydroxylamine (9)

To a solution of **4e** (323 mg, 1.0 mmol) in methanol (5.0 mL) was added hydrazine mono hydrate (300 mg, 6.0 mmol), and the reaction mixture was allowed to stir at 60 °C for 40 min. After completion of the reaction, solvent was removed under reduced pressure. The resulted crude reaction mixture was purified by flash chromatography using 1 to 3% methanol in dichloromethane to give the desired hydroxylamine compound **9** (120 mg, 62% yield).



Scheme S-2. Derivatization of the reaction product **4e**.

2. Synthesis of (1*E*,2*E*)-cinnamaldehyde *O*-(3,3-dimethyl-1-phenylbutyl) oxime (10)

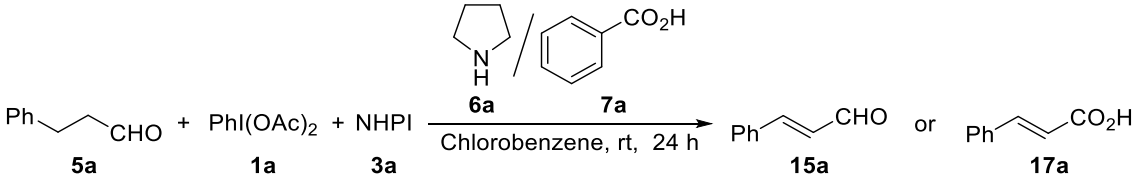
To a solution of **9** (193 mg, 1.0 mmol) in EtOH (5.0 mL), cinnamaldehyde (145 mg, 1.1 mmol) was added. The resulted solution was allowed to stir at room temperature overnight.

After the completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography with 1-5% EtOAc in hexane as the eluent to give the desired compound **10** (190 mg, 62% yield).

3. Synthesis of *O*-[(*R**)-3,3-dimethyl-1-phenylbutyl]-*N*-[(*R*,E*)-1-phenylhept-1-en-3-yl]hydroxylamine (11)

A flame-dried round-bottom flask was evacuated and backfilled with argon three times. A solution of **10** (76 mg, 0.25 mmol) in toluene (3.0 mL) added and then cooled to -78 °C under argon. To the above solution $BF_3.Et_2O$ (106 mg, 0.75 mmol) was added and the mixture was stirred for 15 min before *n*-BuLi (2.0 M in hexane, 0.75 mmol) was added dropwise. Upon completion, the mixture was further stirred for 30 min. Water (0.5 mL) was then added and the reaction mixture was allowed to warm to room temperature, extracted with diethyl ether (5 mL × 3). K_2CO_3 was added to the combined organic layer, filtered, and dried with Na_2SO_4, and then solvent was evaporated. The residue was purified by flash chromatography using 3 to 5% EtOAc in hexane as the eluent to give compound **11** (71 mg, 78% yield; dr = 90:10). The relative stereochemistry of compound **11** was assigned according to a similar product reported in the literature.[32]

Table S-1. Oxidation of 3-phenylpropionaldehyde (**5a**) by $PhI(OAc)_2$ (**1a**) in the presence of NHPI (**3a**)[a]



Entry	**3a** (equiv.)	**1a** (equiv.)	**6a** (equiv.)	**7a** (equiv.)	Conversion (%)[b]
1	0	1.0	0.1	0.1	0[c]
2	0.1	1.0	0.1	0.1	9
3	0.3	1.0	0.1	0.1	28
4	1.0	1.0	0.1	0.1	44
5	1.0	1.25	0.1	0.1	73
6	0.1	2.0	0.1	0.1	10
7	1.5	2.0	0.1	0.1	100[d]

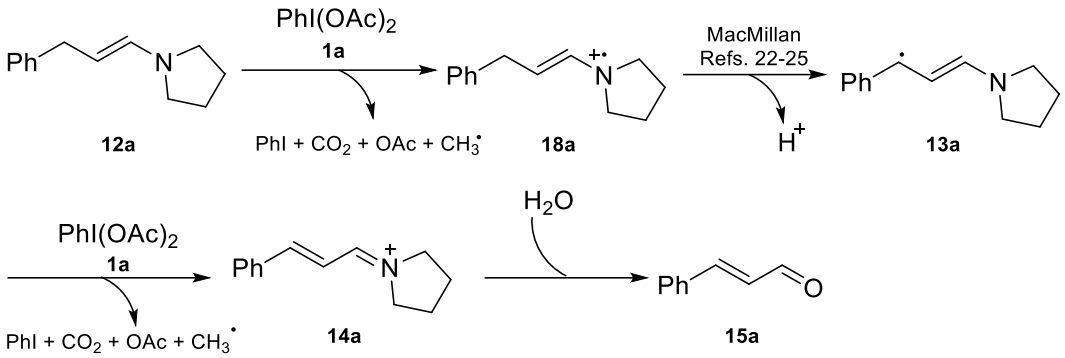
[a]Unless otherwise specified, all reactions were carried out with **5a** (1.0 mmol), **1a**, NHPI (**3a**), pyrrolidine (**6a**, 0.10 mmol), and benzoic acid (**7a**, 0.10 mmol) in chlorobenzene (5.0 mL) at rt for 24 h.

[b]Conversion of **5a** to **16a** was determined by analysis of the ^{1}H NMR of the crude reaction mixture.

[c]Aldehyde **5a** and its self-condensation product (65:35) were recovered in 96%.

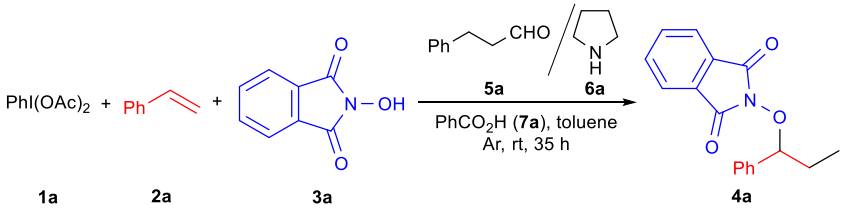
[d]Only *trans*-cinnamic acid (**17a**) was obtained in this case.

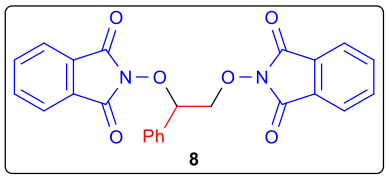
The above results show that **NO** conversion of the aldehyde **5a** to **15a** was achieved without NHPI (Table S-1, entry 1), which indicates that the direct oxidation of enamine **12a** by $PhI(OAc)_2$ (**1a**) is **NOT** happening. Otherwise, **12a** will be oxidized by **1a** to the enamine radical cation **18a**, which based on MacMillan's results,[22-25] will be converted to β-enaminyl radical **13a**, and then further oxidized by **1a** to **15a** (Scheme S-3).



Scheme S-3. Conversion of **12a** to **15a** should be **possible without NHPI** if **12a** can be **directly oxidized** by $PhI(OAc)_2$ (**1a**).

Table S-2. Direct one-pot alkylation-aminoxidation of styrene (**2a**) conducted in toluene[a]





Entry	**3a** (mmol)	**5a** (equiv.)	**2a** (equiv.)	**1a** (equiv.)	**6a** (equiv.)	**7a** (equiv.)	Yield of **4a** (%)[b]
1	0.5	2.0	2.0	4.0	0.2	0.2	14
2	0.5	2.0	2.0	---	0.2	0.2	---
3	0.5	2.0	---	4.0	0.2	0.2	---
4	0.5	---	2.0	4.0	0.2	0.2	---[c]
5	--	2.0	2.0	4.0	0.2	0.2	---
6	0.5	2.0	2.0	4.0	---	0.2	---[c]
7	0.5	2.0	2.0	4.0	0.2	---	---[c]
8	1.0	2.0	2.0	1.0	0.2	0.2	05
9	1.0	2.0	2.0	2.0	0.2	0.2	27
10	1.0	2.0	2.0	3.0	0.2	0.2	21
11	1.0	2.0	2.0	5.0	0.2	0.2	14
12	1.0	2.0	1.0	2.0	0.2	0.2	10
13	1.0	2.0	3.0	2.0	0.2	0.2	31
14	1.0	2.0	4.0	2.0	0.2	0.2	28
15	1.0	1.0	3.0	2.0	0.1	0.1	13
16	1.0	0.8	3.0	2.0	0.1	0.1	11
17	**1.0**	**3.0**	**3.0**	**2.0**	**0.3**	**0.3**	**39**

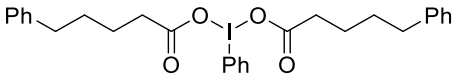
[a]Unless otherwise indicated, all reactions were carried out under argon in toluene (5.0 mL) at the room temperature for 35 h.

[b]Yield of the isolated product after column chromatography.

[c]The double addition to styrene product **8** was obtained.

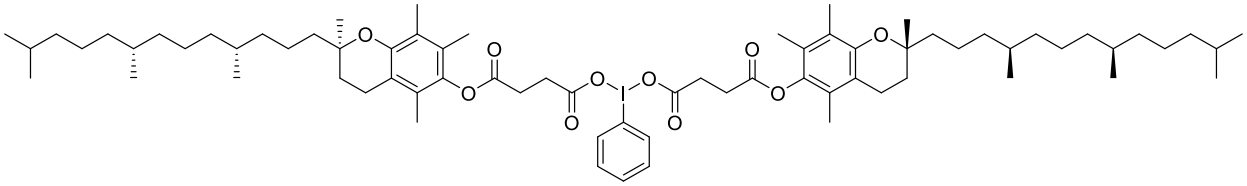
Compound Characterization Data

Phenyl-λ^3-iodanediyl bis(5-phenylpentanoate) (1b)



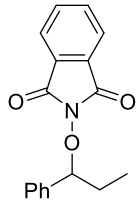
White liquid; 554 mg, 99% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14–8.09 (m, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 4H), 7.27–7.16 (m, 6H), 2.64 (t, *J* = 7.1 Hz, 4H), 2.36 (t, *J* = 6.9 Hz, 4H), 1.72–1.59 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.7, 134.9, 130.9, 128.4, 128.3, 128.3, 125.7, 121.8, 35.6, 33.9, 31.0, 25.3. ν_{max} (neat, cm^{-1}): 3025, 2939, 1647, 1440, 1200, 1154. HRMS (ESI, m/z) calcd. for $C_{28}H_{31}INaO_4$ ([M+Na]$^+$): 581.1159; found: 581.1138.

O,*O*'-(Phenyl-λ^3-iodanediyl) bis{(*R*)-2,5,7,8-tetramethyl-2-[(4*R*,8*R*)-4,8,12-trimethyltridecyl]chroman-6-yl} disuccinate (1g)



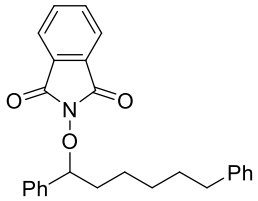
White solid; 1,244 mg, 98% yield, m.p. 106-107 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 27.1, 7.6 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.52–7.45 (m, 2H), 2.96 (t, *J* = 6.6 Hz, 1H), 2.87 (dd, *J* = 15.0, 8.2 Hz, 4H), 2.73 (t, *J* = 6.8 Hz, 3H), 2.60 (t, *J* = 6.4 Hz, 4H), 2.10 (s, 6H), 1.98 (d, *J* = 17.0 Hz, 12H), 1.80 (ddt, *J* = 25.9, 13.0, 6.7 Hz, 4H), 1.59–1.06 (m, 50H), 0.88 (dd, *J* = 11.2, 6.4 Hz, 24H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 171.0, 149.3, 140.4, 134.8, 134.4, 131.7, 131.2, 130.9, 126.7, 124.9, 122.9, 121.7, 117.3, 75.0, 39.3, 37.4, 37.2, 32.8, 32.7, 31.1, 29.7, 28.8, 27.9, 24.8, 24.4, 22.7, 22.6, 21.0, 20.6, 19.7, 19.6, 12.9, 12.1 11.8. ν_{max} (neat, cm^{-1}): 2953, 2843, 1741, 1663, 1474, 1440, 1363, 1211, 1154. HRMS (ESI, *m*/*z*) calcd. for $C_{72}H_{111}INaO_{10}$ ([M+Na]$^+$): 1,285.7114; found: 1,285.7117.

2-(1-Phenylpropoxy)isoindoline-1,3-dione (4a)[35]



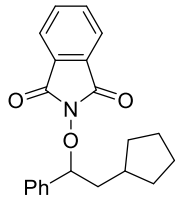
White solid; 165 mg, 59% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77–7.72 (m, 2H), 7.72–7.67 (m, 2H), 7.52–7.44 (m, 2H), 7.37–7.31 (m, 3H), 5.30–5.24 (m, 1H), 2.29–2.19 (m, 1H), 2.03–1.94 (m, 1H), 1.00 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 137.9, 134.2, 128.9, 128.2, 128.1, 123.3, 90.6, 27.8, 10.1.

2-[(1,6-Diphenylhexyl)oxy]isoindoline-1,3-dione (4b)



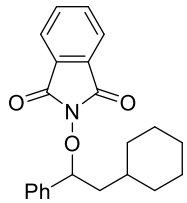
Colorless liquid; 189 mg, 47% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.47 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.31 (ddd, *J* = 14.9, 11.6, 7.5 Hz, 5H), 7.19 (t, *J* = 8.1 Hz, 3H), 5.34 (t, *J* = 7.1 Hz, 1H), 2.61 (t, *J* = 7.7 Hz, 2H), 2.21 (ddt, *J* = 12.0, 9.8, 6.0 Hz, 1H), 1.99–1.89 (m, 1H), 1.66–1.36 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 142.6, 138.1, 134.2, 128.9, 128.8, 128.3, 128.3, 128.2, 128.1, 125.6, 123.3, 89.2, 35.8, 34.7, 31.2, 29.0, 25.5. ν_{max} (neat, cm^{-1}): 2862, 2524, 1732, 1372, 1237, 1161. HRMS (ESI, *m*/*z*) calcd. for $C_{26}H_{25}NNaO_3$ ($[M+Na]^+$): 422.1727; found: 422.1713.

2-(2-Cyclopentyl-1-phenylethoxy)isoindoline-1,3-dione (4c)



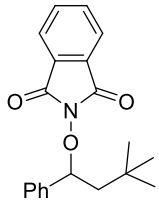
Colorless liquid; 219 mg, 65% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (ddd, *J* = 25.1, 5.7, 3.1 Hz, 4H), 7.48 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 3H), 5.39 (t, *J* = 7.1 Hz, 1H), 2.29–2.19 (m, 1H), 2.00–1.80 (m, 4H), 1.67–1.60 (m, 2H), 1.58–1.48 (m, 2H), 1.26–1.11 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 138.4, 134.2, 128.9, 128.8, 128.2, 128.1, 123.2, 88.8, 41.1, 36.6, 32.9, 32.6, 25.1, 25.0. ν_{max} (neat, cm^{-1}): 2874, 2514, 1725, 1385, 1252, 1152. HRMS (ESI, *m*/*z*) calcd. for $C_{21}H_{21}NNaO_3$ ($[M+Na]^+$): 358.1414 ; found: 358.1415.

2-(2-Cyclohexyl-1-phenylethoxy)isoindoline-1,3-dione (4d)



Colorless liquid; 224 mg, 64% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (ddd, *J* = 23.8, 5.5, 3.2 Hz, 4H), 7.47 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.31 (dd, *J* = 14.3, 8.9 Hz, 3H), 5.49 (dd, *J* = 7.7, 6.5 Hz, 1H), 2.20–2.07 (m, 1H), 1.97 (d, *J* = 12.7 Hz, 1H), 1.86–1.63 (m, 5H), 1.54 (dtd, *J* = 18.0, 7.3, 3.5 Hz, 1H), 1.31–1.16 (m, 3H), 1.05–0.96 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 138.6, 134.1, 128.9, 128.2, 128.1, 123.3, 123.2, 87.0, 42.7, 34.2, 33.4, 33.1, 26.5, 26.1. ν_{max} (neat, cm^{-1}): 2919, 2845, 1791, 725, 1700, 1374, 1189. HRMS (ESI, *m*/*z*) calcd. for $C_{22}H_{23}KNO_3$ $[M+K]^+$: 388.1310; found: 388.1297.

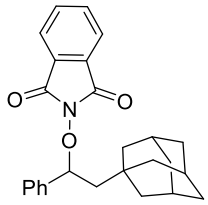
2-(3,3-Dimethyl-1-phenylbutoxy)isoindoline-1,3-dione (4e)[35]



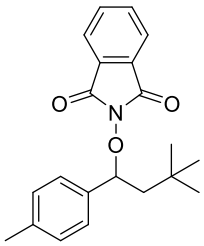
White solid; 217 mg, 67%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73–7.62 (m, 4H), 7.46 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.35–7.25 (m, 3H), 5.55 (dd, *J* = 7.5, 4.2 Hz, 1H), 2.22 (dd, *J* = 14.9, 7.6 Hz, 1H), 1.80 (dd, *J* = 14.9, 4.2 Hz, 1H), 1.08 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 139.6 134.1, 128.8, 128.2, 128.1, 123.2, 86.8, 48.8, 30.5, 30.0.

2-{2-[(3*r*,5*r*,7*r*)-Adamantan-1-yl]-1-phenylethoxy}isoindoline-1,3-dione (4f)

White solid; 245 mg, 61% yield, m.p. 125-126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.64 (m, 4H), 7.49–7.42 (m, 2H), 7.33–7.29 (m, 2H), 7.28 (s, 1H), 5.60 (dd, *J* = 7.5, 4.2 Hz, 1H), 2.09 (dd, *J* = 15.0, 7.5 Hz, 1H), 2.00 (s, 3H), 1.76–1.64 (m, 13H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 139.8,134.1, 128.8, 128.7, 128.2, 128.1, 123.2, 85.4, 49.6, 42.7, 36.9, 32.4, 28.7. ν_{max} (neat, cm^{-1}): 2852, 1723, 1485, 1361, 1256. HRMS (ESI, *m*/*z*) calcd. for $C_{26}H_{27}NNaO_3$ ($[M+Na]^+$): 424.1883; found: 424.1884.

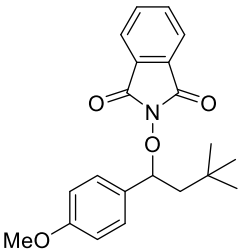


2-[3,3-Dimethyl-1-(*p*-tolyl)butoxy]isoindoline-1,3-dione (4g)



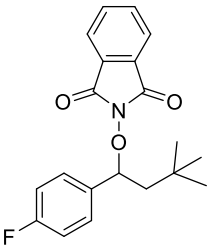
Colorless liquid; 224 mg, 66% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.63 (m, 4H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 5.51 (dd, *J* = 7.4, 4.3 Hz, 1H), 2.30 (s, 3H), 2.21 (dd, *J* = 14.8, 7.5 Hz, 1H), 1.78 (dd, *J* = 14.8, 4.3 Hz, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 138.6, 136.6, 134.1, 128.9, 128.8, 128.1, 123.2, 86.7, 48.7, 30.4, 30.0, 21.2. ν_{max} (neat, cm^{-1}): 2954, 1788, 1706, 1374, 1185, 1125. HRMS (ESI, *m*/*z*) calcd. for $C_{21}H_{23}KNO_3$ ($[M+K]^+$): 376.1310; found: 376.1296.

2-[1-(4-Methoxyphenyl)-3,3-dimethylbutoxy]isoindoline-1,3-dione (4h)



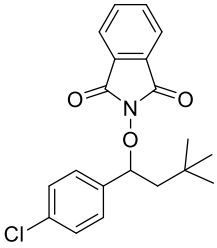
Colorless liquid; 381 mg, 60% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.64 (m, 4H), 7.37 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.49 (dd, *J* = 7.2, 4.7 Hz, 1H), 3.77 (s, 3H), 2.21 (dd, *J* = 14.7, 7.2 Hz, 1H), 1.81 (dd, *J* = 14.7, 4.7 Hz, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 159.9, 134.1, 131.6, 129.6, 128.8, 123.2, 113.5, 86.4, 55.1, 48.5, 30.4, 30.0. ν_{max} (neat, cm^{-1}): 2952, 1820, 1610, 1513, 1246, 1185. HRMS (ESI, *m*/*z*) calcd. for $C_{21}H_{23}NNaO_4$ ($[M+Na]^+$): 376.1519; found: 376.1521.

2-[1-(4-Fluorophenyl)-3,3-dimethylbutoxy]isoindoline-1,3-dione (4i)[35]



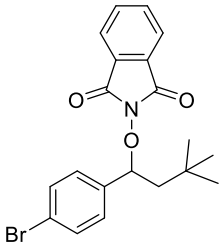
White solid; 240 mg, 70% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72–7.64 (m, 4H), 7.45–7.39 (m, 2H), 6.97 (t, *J* = 8.7 Hz, 2H), 5.49 (dd, *J* = 7.5, 4.3 Hz, 1H), 2.18 (dd, *J* = 14.8, 7.5 Hz, 1H), 1.74 (dd, *J* = 14.8, 4.4 Hz, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 162.9 (d, $J_{C\text{-}F}$ = 248.2 Hz), 135.5 (d, $J_{C\text{-}F}$ = 3.7 Hz), 134.2, 129.9 (d, $J_{C\text{-}F}$ = 8.8 Hz), 128.7, 123.2, 115.2 (d, $J_{C\text{-}F}$ = 21.4 Hz), 86.1, 48.8, 30.4, 30.0.

2-[1-(4-Chlorophenyl)-3,3-dimethylbutoxy]isoindoline-1,3-dione (4j)[35]



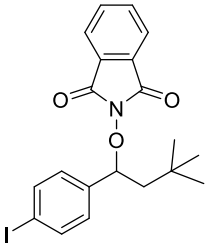
White solid; 245 mg, 69% yield, 1H NMR (500 MHz, $CDCl_3$) δ 7.76–7.64 (m, 4H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 5.52 (dd, *J* = 7.6, 4.2 Hz, 1H), 2.18 (dd, *J* = 14.9, 7.6 Hz, 1H), 1.73 (dd, *J* = 14.9, 4.2 Hz, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.63, 138.37, 134.62, 134.30, 129.46, 128.73, 128.50, 123.32, 86.11, 49.01, 30.52, 30.03.

2-[1-(4-Bromophenyl)-3,3-dimethylbutoxy]isoindoline-1,3-dione (4k)[35]



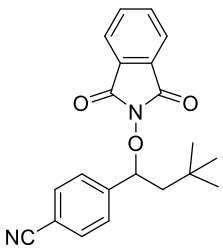
White solid; 271 mg, 67% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.65 (m, 4H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 5.51 (dd, *J* = 7.7, 4.1 Hz, 1H), 2.17 (dd, *J* = 14.9, 7.7 Hz, 1H), 1.72 (dd, *J* = 14.9, 4.1 Hz, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 138.9, 134.3, 131.4, 129.7, 128.7, 123.3, 122.8, 86.1, 49.0, 30.5, 30.0.

2-[1-(4-Iodophenyl)-3,3-dimethylbutoxy]isoindoline-1,3-dione (4l)



White solid; 210 mg, 47% yield, m.p. 89-90 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.66 (m, 4H), 7.65–7.61 (m, 2H), 7.25–7.19 (m, 2H), 5.50 (dd, *J* = 7.7, 4.0 Hz, 1H), 2.16 (dd, *J* = 14.9, 7.7 Hz, 1H), 1.70 (dd, J = 14.9, 4.1 Hz, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 139.6, 137.4, 134.3, 129.8, 128.7, 123.3, 94.7, 86.2, 49.1, 30.5, 30.0. ν_{max} (neat, cm^{-1}): 2937, 2868, 1791, 1724, 1465. HRMS (ESI, *m/z*) calcd. for $C_{20}H_{20}IKNO_3$ ($[M+K]^+$): 488.0119; found: 488.0113.

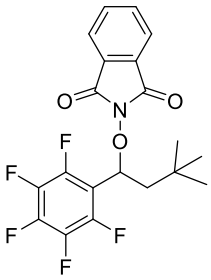
4-{1-[(1,3-Dioxoisoindolin-2-yl)oxy]-3,3-dimethylbutyl}benzonitrile (4m)



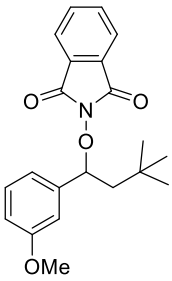
White solid; 251 mg, 72% yield, m.p. 178-179 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77–7.67 (m, 3H), 7.62 (s, 3H), 5.59 (dd, *J* = 8.0, 3.7 Hz, 1H), 2.17 (dd, *J* = 15.0, 8.0 Hz, 1H), 1.68 (dd, *J* = 15.0, 3.7 Hz, 1H), 1.10 (s, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 145.3, 134.5, 132.1, 128.6, 128.6, 123.4, 118.5, 112.5, 86.1, 49.3, 30.6, 29.9. ν_{max} (neat, cm^{-1}): 2846, 2247, 1670, 1425, 1350, 1225. HRMS (ESI, *m*/*z*) calcd for $C_{21}H_{20}N_2NaO_3$ ($[M+Na]^+$): 371.1366; found: 371.1353.

2-[3,3-Dimethyl-1-(perfluorophenyl)butoxy]isoindoline-1,3-dione (4n)

White solid; 251 mg, 61% yield, m.p. 118-119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80–7.70 (m, 4H), 5.68 (dd, *J* = 7.2, 4.5 Hz, 1H), 2.47 (dd, *J* = 15.1, 7.3 Hz, 1H), 1.89 (dd, *J* = 15.1, 4.5 Hz, 1H), 1.08 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4, 146.8, 144.8, 142.6 (m), 140.5 (m), 138.3, 136.3, 134.6, 128.5, 123.6, 113.67 (m), 77.8, 46.1, 30.5, 29.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ -152.38 (tt, *J* = 21.0, 2.6 Hz, 5F). ν_{max} (neat, cm^{-1}): 2970, 1781. 1522. 1466, 1325, 1129. HRMS (ESI, *m*/*z*) calcd. for $C_{20}H_{16}F_5KNO_3$ ($[M+K]^+$): 452.0682; found: 452.0680.

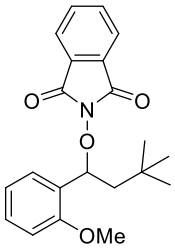


2-[1-(3-Methoxyphenyl)-3,3-dimethylbutoxy]isoindoline-1,3-dione (4o)



Colorless liquid; 162 mg, 45% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.63 (m, 4H), 7.19 (t, *J* = 7.9 Hz, 1H), 7.11–7.06 (m, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.82 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 5.57 (dd, *J* = 7.8, 3.9 Hz, 1H), 3.83 (s, 3H), 2.18 (dd, *J* = 14.9, 7.8 Hz, 1H), 1.76 (dd, *J* = 14.9, 3.9 Hz, 1H), 1.09 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 159.4, 141.4, 134.1, 129.1, 128.8, 123.2, 120.2, 114.8, 112.7, 86.7, 55.2, 49.2, 30.5, 30.0. ν_{max} (neat, cm^{-1}): 2952, 1788, 1600, 1490, 1466, 1366, 1042. HRMS (ESI, *m*/*z*) calcd. for $C_{21}H_{23}NNaO_4$ ($[M+Na]^+$): 376.1519; found 376.1516.

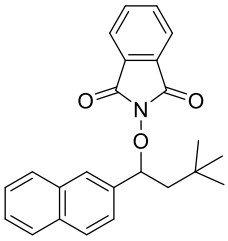
2-[1-(2-Methoxyphenyl)-3,3-dimethylbutoxy]isoindoline-1,3-dione (4p)



White solid; 121 mg, 34% yield, m.p. 96-97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77–7.62 (m, 5H), 7.27–7.22 (m, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.11 (dd, *J* = 7.4, 3.7 Hz, 1H), 3.63 (s, 3H), 2.20 (dd, *J* = 14.9, 7.7 Hz, 1H), 1.78 (dd, *J* = 14.9, 3.9 Hz, 1H), 1.10 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 157.2, 134.0, 129.6, 129.1, 129.8, 128.2, 123.0, 120.6, 110.2, 80.1, 55.2,

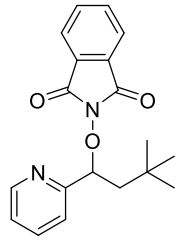
47.9, 30.6, 29.9. ν_{max} (neat, cm^{-1}): 2948, 1787, 1725, 1369, 1245. HRMS (ESI, *m*/*z*) calcd for $C_{21}H_{23}NNaO_4$ ($[M+Na]^+$): 376.1519 ; found: 376.1514.

2-[3,3-Dimethyl-1-(naphthalen-2-yl)butoxy]isoindoline-1,3-dione (4q)



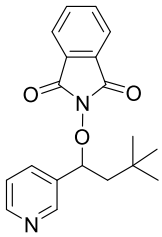
White solid; 261 mg, 70% yield, m.p. 158-159°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90–7.72 (m, 5H), 7.70–7.59 (m, 4H), 7.52–7.41 (m, 2H), 5.75 (dd, *J* = 7.5, 4.1 Hz, 1H), 2.31 (dd, *J* = 14.9, 7.6 Hz, 1H), 1.85 (dd, *J* = 14.9, 4.1 Hz, 1H), 1.12 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 137.3, 134.1, 133.5, 132.7, 128.7, 128.2, 128.0, 127.7, 127.5, 126.2, 126.1, 125.3, 123.2, 87.0, 49.0, 30.6, 30.0. ν_{max} (neat, cm^{-1}): 2955, 1788, 1469, 1369, 1186. HRMS (ESI, *m*/*z*) calcd. for $C_{24}H_{23}NNaO_3$ ($[M+Na]^+$): 396.1570; found: 396.1560.

2-[3,3-Dimethyl-1-(pyridin-2-yl)butoxy]isoindoline-1,3-dione (4r)



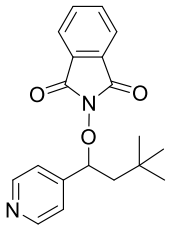
White solid; 142 mg, 44% yield, m.p. 118-119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51–8.46 (m, 1H), 7.76–7.66 (m, 5H), 7.22 (ddd, *J* = 6.8, 4.8, 2.0 Hz, 2H), 5.59 (dd, *J* = 8.0, 4.2 Hz, 1H), 2.20 (dd, *J* = 14.9, 8.0 Hz, 1H), 1.86 (dd, *J* = 14.9, 4.2 Hz, 1H), 1.12 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$) δ 163.5, 159.5, 148.7, 136.6, 134.2, 129.2, 128.8, 128.6, 123.5, 123.4, 123.3, 122.6, 88.3, 47.8, 30.5, 30.0. ν_{max} (neat, cm^{-1}): 2851, 1732, 1420, 1250, 1121. HRMS (ESI, *m*/*z*) calcd. for $C_{19}H_{21}N_2O_3$ ($[M+H]^+$): 325.1547; found: 325.1540.

2-[3,3-Dimethyl-1-(pyridin-3-yl)butoxy]isoindoline-1,3-dione (4s)



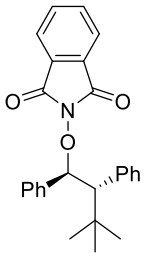
Greyish white jelly; 98 mg, 30% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 – 8.43 (m, 2H), 7.97 (dq, J = 8.1, 1.6 Hz, 1H), 7.74 – 7.56 (m, 4H), 7.29 (dd, J = 8.0, 4.8 Hz, 1H), 5.50 (dd, J = 8.2, 4.0 Hz, 1H), 2.21 (dd, J = 15.0, 7.9 Hz, 1H), 1.71 (dd, J = 15.6, 3.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 150.4, 149.4, 135.7, 135.4, 134.4, 128.7, 123.6, 123.4, 84.5, 48.8, 30.6, 30.0. ν_{max} (neat, cm^{-1}): 1784, 1723, 1466, 1426, 1374, 1186, 1124, 1083. HRMS (ESI, *m*/*z*) calcd. for $C_{19}H_{21}N_2O_3$ ($[M+H]^+$): 325.1547; found: 325.1536.

2-[3,3-Dimethyl-1-(pyridin-4-yl)butoxy]isoindoline-1,3-dione (4t)



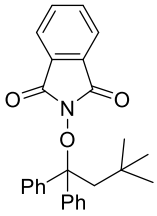
Greyish white jelly; 68 mg, 21% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 5.0 Hz, 2H), 7.73 – 7.64 (m, 4H), 7.44 – 7.35 (m, 2H), 5.55 (dd, *J* = 8.2, 3.4 Hz, 1H), 2.13 (dd, *J* = 15.1, 8.2 Hz, 1H), 1.64 (dd, *J* = 15.1, 3.4 Hz, 1H), 1.09 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 150.0, 148.9, 134.5, 128.7, 123.4, 122.5, 85.6, 49.3, 30.7, 30.0. ν_{max} (neat, cm^{-1}): 1793, 1727, 1599, 1469, 1364, 1188, 1083. HRMS (ESI, *m*/*z*) calcd. for $C_{19}H_{21}N_2O_3$ ($[M+H]^+$): 325.1547; found: 325.1537.

2-[(1*S,2*S**)-3,3-Dimethyl-1,2-diphenylbutoxy]isoindoline-1,3-dione (4u)**[35]



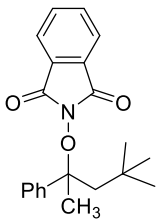
White solid; 175 mg, 37% yield (*syn*/*anti* = 70:30). Major isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.60 (m, 4H), 7.22–7.16 (m, 2H), 7.14–6.88 (m, 8H), 5.97 (d, *J* = 10.2 Hz, 1H), 3.29 (d, *J* = 10.2 Hz, 1H), 1.21 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.5, 140.7, 137.6, 134.1, 129.3, 128.5, 128.2, 127.3, 125.8, 123.1, 90.3, 60.2, 34.6, 29.9.

2-[3,3-Dimethyl-1,1-diphenylbutoxy]isoindoline-1,3-dione (4v)



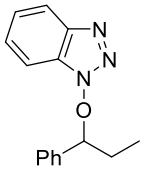
Colorless liquid; 198 mg, 50% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (s, 4H), 7.57–7.50 (m, 4H), 7.22 (dd, *J* = 5.3, 4.0 Hz, 6H), 2.97 (s, 2H), 0.88 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 142.4, 133.9, 128.7, 128.5, 127.7, 127.3, 122.8, 95.8, 50.6, 31.9, 31.5. ν_{max} (neat, cm^{-1}): 2891, 1735, 1365, 1216, 1205, 1189. HRMS (ESI, *m*/*z*) calcd. for $C_{26}H_{25}KNO_3$ ($[M+K]^+$): 438.1466; found: 438.1461.

2-[(4,4-Dimethyl-2-phenylpentan-2-yl)oxy]isoindoline-1,3-dione (4w)



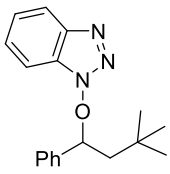
Colorless liquid; 139 mg, 41% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (dt, *J* = 7.0, 3.5 Hz, 2H), 7.75–7.68 (m, 4H), 7.40–7.28 (m, 3H), 2.47 (d, *J* = 14.3 Hz, 1H), 2.10 (d, *J* = 14.3 Hz, 1H), 1.94 (s, 3H), 0.81 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 142.0, 134.3, 129.3, 128.0, 127.6, 123.3, 92.0, 53.1, 31.4, 30.8, 24.0. ν_{max} (neat, cm^{-1}): 2981, 1726, 1466, 1365, 1216, 965, 875, 697. HRMS (ESI, *m*/*z*) calcd. for $C_{21}H_{23}KNO_3$ ($[M+K]^+$): 376.1310; found: 376.1305.

1-(1-Phenylpropoxy)-1*H*-benzo[*d*][1,2,3]triazole (4x)



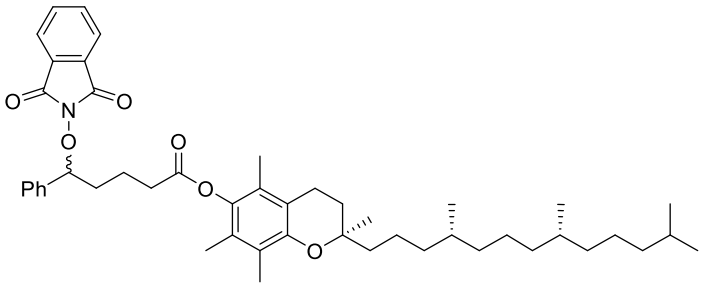
Colorless liquid; 198 mg, 67% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95–7.85 (m, 1H), 7.34–7.23 (m, 7H), 7.13–7.02 (m, 1H), 5.48 (t, *J* = 7.2 Hz, 1H), 2.42 (dt, *J* = 14.3, 7.2 Hz, 1H), 2.13 (dt, *J* = 14.0, 7.4 Hz, 1H), 1.12 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.15 (s), 137.3, 129.3, 128.6, 127.8, 127.4, 124.1, 119.8, 108.9, 94.6, 27.2, 10.2. ν_{max} (neat, cm^{-1}): 2920, 1733, 1456, 1374, 1239, 1082. HRMS (ESI, *m*/*z*) calcd. for $C_{15}H_{17}N_3O$ ($[M+H]^+$): 254.1288; found: 254.1281.

1-(3,3-Dimethyl-1-phenylbutoxy)-1*H*-benzo[*d*][1,2,3]triazole (4y)



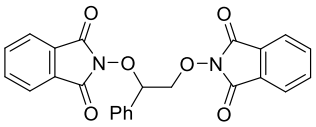
Colorless liquid; 210 mg, 71% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91–7.84 (m, 1H), 7.32–7.17 (m, 7H), 6.99–6.90 (m, 1H), 5.73 (dd, *J* = 7.5, 4.7 Hz, 1H), 2.45 (dd, *J* = 14.8, 7.5 Hz, 1H), 1.99 (dd, *J* = 14.8, 4.7 Hz, 1H), 1.14 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 138.9, 129.3, 128.6, 127.9, 127.2, 123.9, 119.7, 108.9, 91.3, 47.5, 30.6, 30.1. ν_{max} (neat, cm^{-1}) 2952, 1734, 1456, 1366, 1087. HRMS (ESI, *m*/*z*) calcd. for $C_{18}H_{22}N_3O$ ($[M+H]^+$): 296.1757; found: 296.1753.

(*R*)-2,5,7,8-Tetramethyl-2-[(4*R*,8*R*)-4,8,12-trimethyltridecyl]chroman-6-yl 5-[(1,3-dioxoiso-indolin-2-yl)oxy]-5-phenylpentanoate (4aa)



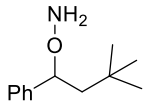
Colorless liquid; 347 mg, 46% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (ddd, *J* = 28.0, 5.3, 3.2 Hz, 4H), 7.51 (d, *J* = 6.5 Hz, 2H), 7.35 (q, *J* = 6.2 Hz, 3H), 5.42 (t, *J* = 6.7 Hz, 1H), 2.75 (t, *J* = 7.2 Hz, 2H), 2.60 (t, *J* = 6.4 Hz, 2H), 2.39–2.32 (m, 1H), 2.10–1.92 (m, 12H), 1.85–1.75 (m, 2H), 1.58–1.08 (m, 25H), 0.88 (dd, *J* = 11.0, 6.4 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 171.8, 163.6, 149.3, 140.4, 137.8, 134.2, 129.1, 128.8, 128.4, 128.0, 126.6, 124.8, 123.3, 122.9, 117.3, 88.7, 75.0, 39.3, 37.4, 37.3, 34.3, 33.5, 32.8, 32.7, 29.7, 28.0, 24.8, 24.4, 22.7, 22.6, 21.3, 21.0, 20.6, 19.7, 19.6, 13.0, 12.1, 11.8. ν_{max} (neat, cm^{-1} 2922, 1731, 1653, 1456, 1374, 1110. HRMS (ESI, *m*/*z*) calcd. for $C_{48}H_{65}NNaO_6$ ($[M+Na]^+$): 774.4704; found: 774.4706.

2,2'-[(1-Phenylethane-1,2-diyl)bis(oxy)]bis(isoindoline-1,3-dione) (8)[29]



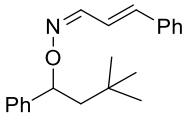
White solid; 45 mg, 21% yield (Table 1, entry 6); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 – 7.65 (m, 8H), 7.58 (d, *J* = 6.7 Hz, 2H), 7.43 – 7.31 (m, 3H), 5.87 (dd, *J* = 7.4, 3.7 Hz, 1H), 4.94 (dd, *J* = 11.5, 7.4 Hz, 1H), 4.58 (dd, *J* = 11.6, 3.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.5, 163.2, 134.6, 134.3, 134.2, 129.7, 128.9, 128.8, 128.7, 128.2, 123.7, 123.6, 123.5, 85.7, 79.4.

_O_-(3,3-Dimethyl-1-phenylbutyl)hydroxylamine (9)[35]



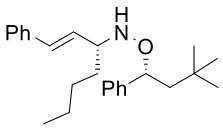
Colorless liquid; 120 mg, 62% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.21 (m, 5H), 4.79 (s, 2H), 4.64 (dd, *J* =8.4, 3.5 Hz, 1H), 1.79 (dd, *J* = 14.7, 8.4 Hz, 1H), 1.49 (dd, *J* =14.7, 3.5 Hz, 1H), 1.00 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 128.5, 127.5, 126.5, 85.4, 50.1, 30.4, 30.1.

(1*Z*,2*E*)-Cinnamaldehyde _O_-(3,3-dimethyl-1-phenylbutyl) oxime (10)



White solid; 190 mg, 62% yield, m.p. 65-66 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.8 Hz, 1H), 7.44 (d, *J* = 7.3 Hz, 2H), 7.37 (dd, *J* = 14.8, 7.1 Hz, 6H), 7.31 (s, 2H), 6.89–6.77 (m, 2H), 5.32 (dd, *J* = 9.1, 3.1 Hz, 1H), 2.01 (dd, *J* = 14.8, 9.1 Hz, 1H), 1.65 (dd, *J* = 14.8, 3.1 Hz, 1H), 1.08 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.6, 144.3, 138.1, 136.1, 128.7, 128.7, 128.3, 127.2, 126.8, 126.4, 122.4, 83.6, 50.2, 30.6, 30.2. ν_{max} (neat, cm^{-1}): 2851, 1753, 1452, 1385, 1265. HRMS (ESI, m/z) calcd. for $C_{21}H_{26}NO$ ($[M+H]^+$): 308.2009; found: 308.2004.

_O_-[(*R)-(3,3-Dimethyl-1-phenylbutyl)-_N_-[(*R**,*E*)-1-phenylhept-1-en-3-yl]hydroxylamine (11)**



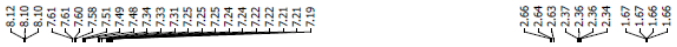
Colorless liquid; 71 mg, 78% yield; dr = 90:10. Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.33 (m, 6H), 7.32–7.29 (m, 2H), 7.27 (dd, *J* = 11.4, 4.1 Hz, 2H), 6.52 (d, *J* = 15.9 Hz, 1H), 6.03 (dd, *J* = 15.9, 8.3 Hz, 1H), 4.80 (dt, *J* = 14.7, 7.3 Hz, 1H), 3.59 (tt, *J* = 16.9, 8.5 Hz, 1H), 1.86–1.77 (m, 2H), 1.54–1.48 (m, 2H), 1.41–1.32 (m, 4H), 1.04 (d, *J* = 10.4 Hz, 9H), 0.95 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.4, 137.0, 132.1, 130.4, 128.45, 128.44, 127.3, 127.2, 126.6, 126.3, 83.1, 63.5, 50.4, 32.3, 30.2, 28.0, 22.7, 14.0. ν_{max} (neat, cm^{-1}): 2951, 2865, 1452, 1365, 1214. HRMS (ESI, *m*/*z*) calcd. for $C_{25}H_{36}NO$ ($[M+H]^+$): 366.2791; found: 366.2782.

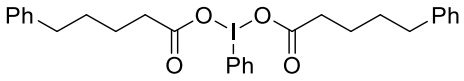
Additional References

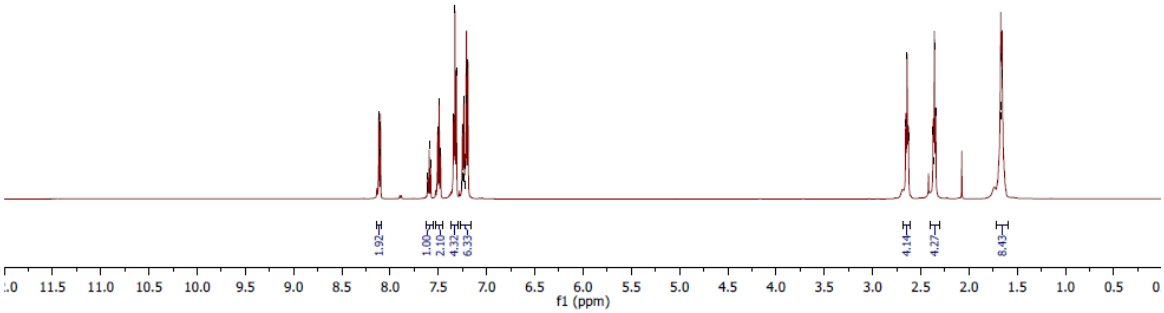
33. Ratushnyy, M.; Kamenova, M.; Gevorgyan, V. *Chem. Sci.* **2018**, *9*, 7193– 7197.
34. a) Wang, Z.; Kanai, M.; Kuninobu, Y. *Org. Lett.* **2017**, *19*, 2398– 2401; b). Xie, L.-Y.; Jiang, L.-L.; Tan, J.-X.; Wang, Y.; Xu, X.-Q.; Zhang, B.; Cao, Z.; He, W.-M. *ACS Sustainable Chem. Eng.* **2019**, *7*, 14153–14160.
35. Li, Y.-X.; Wang, Q.-Q.; Yang, L. *Org. Biomol. Chem*. **2017**, *15*, 1338– 1342.

Copy of NMR Spectra

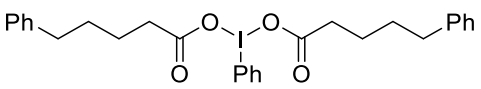
III-NS-430-1.1.fid

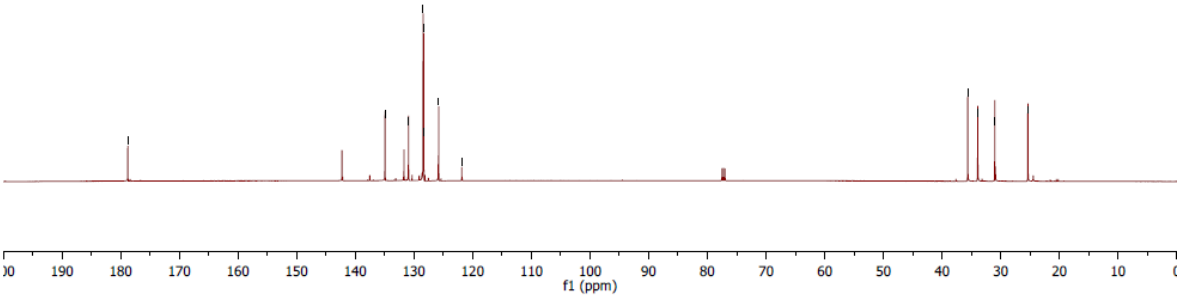


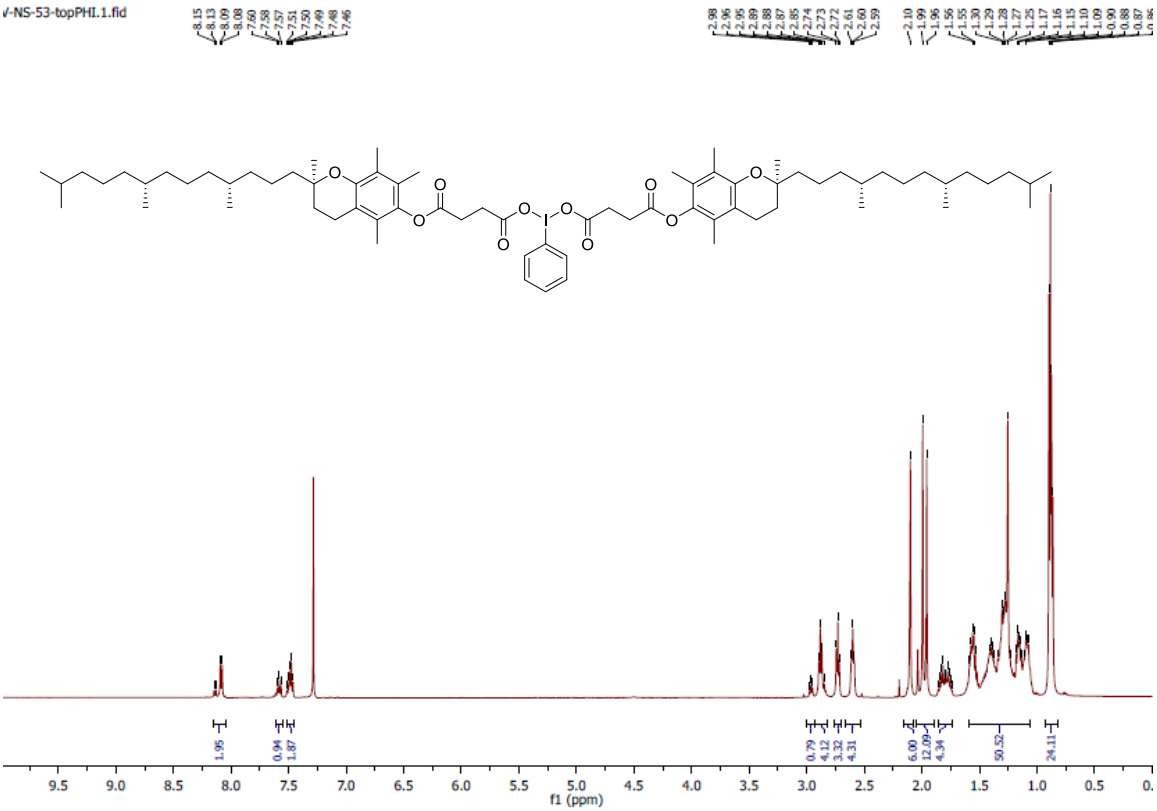


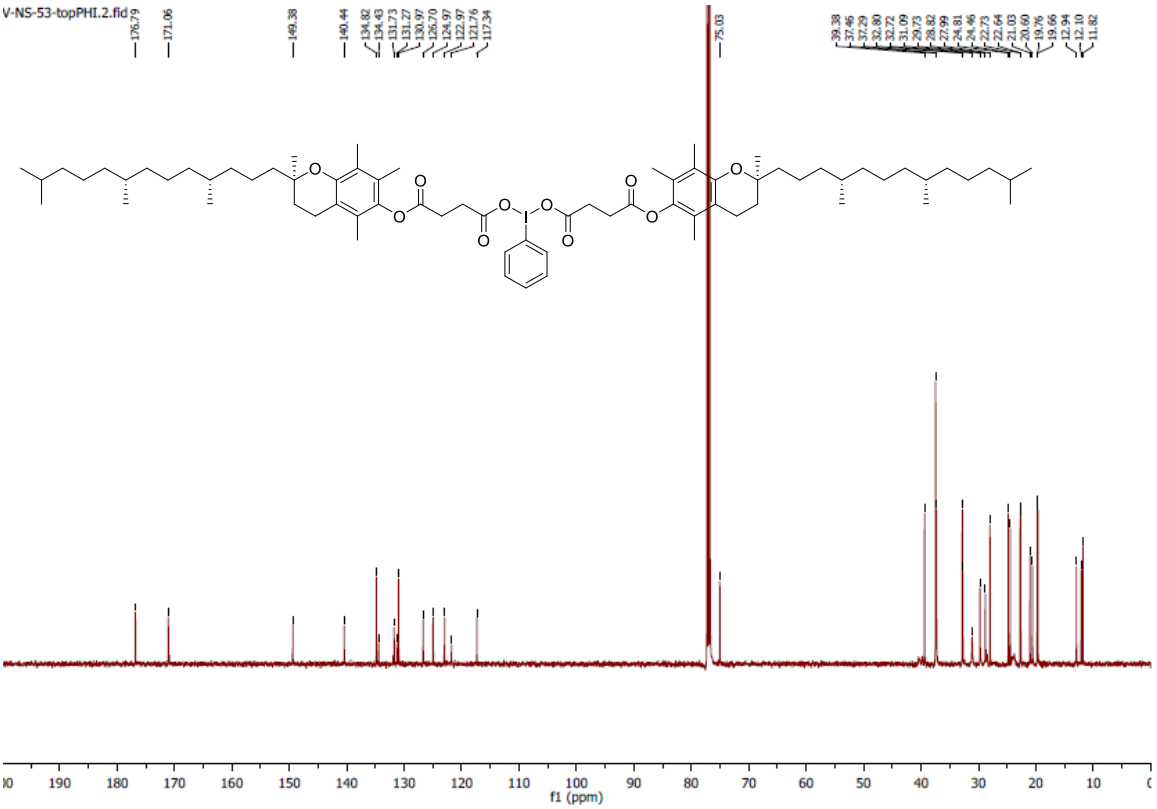


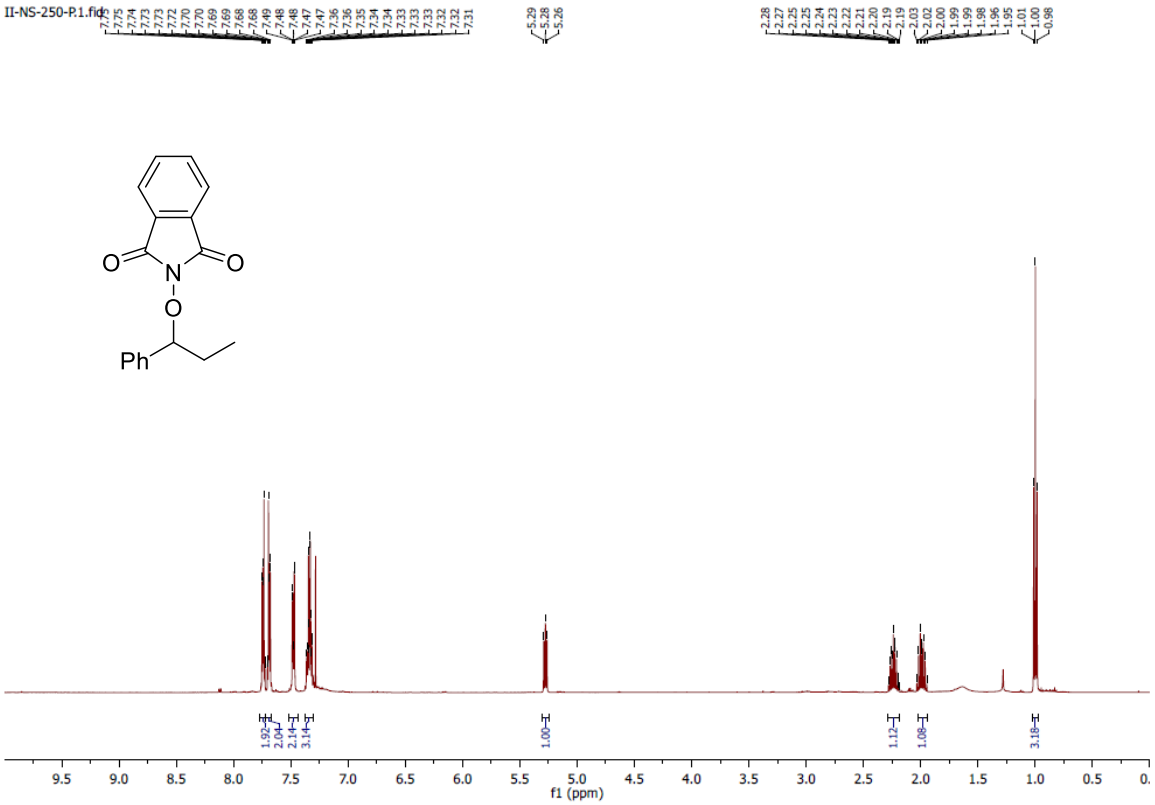
III-NS-430-P.2.fid

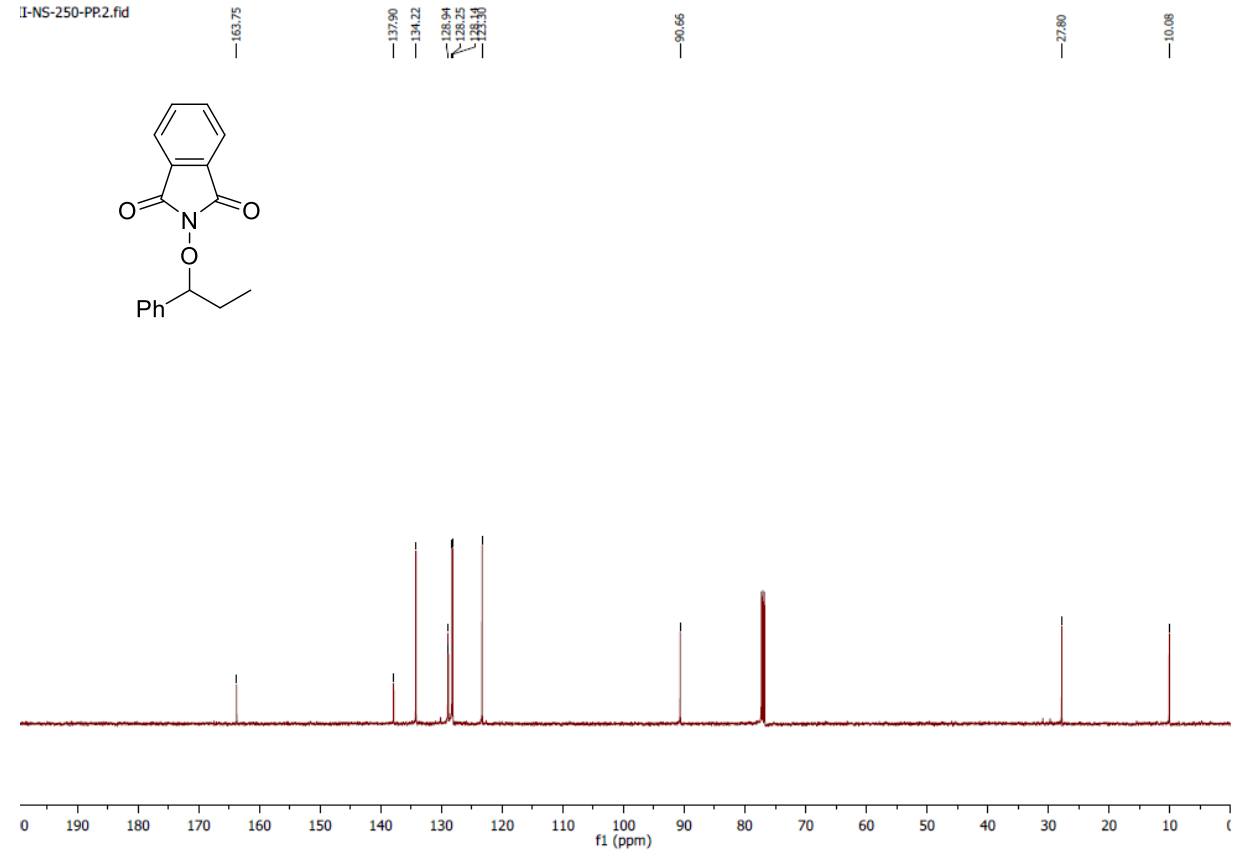




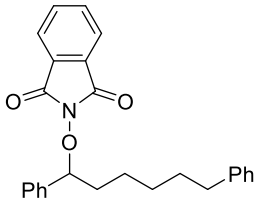

V-NS-53-topPHI.1.fid
f1 (ppm)

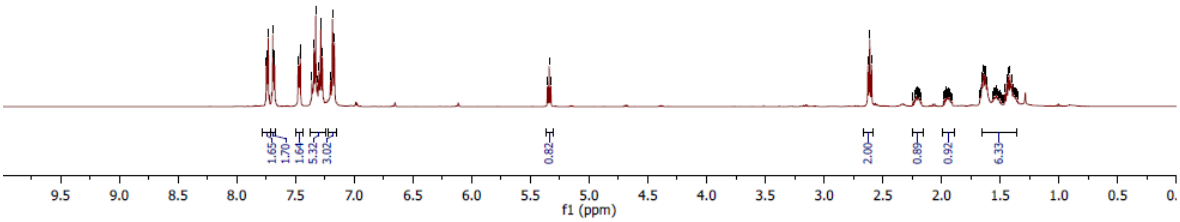

V-NS-53-topPHI.2.fid
f1 (ppm)


II-NS-250-P1.fid
O
N
O
O
Ph
f1 (ppm)

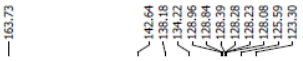

I-NS-250-PP.2.fid
163.75
137.90
134.22
128.94
128.25
123.30
90.66
27.80
10.08
O
N
O
O
Ph
f1 (ppm)

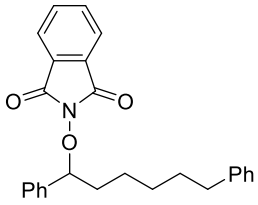
III-NS-437-P.1.fid

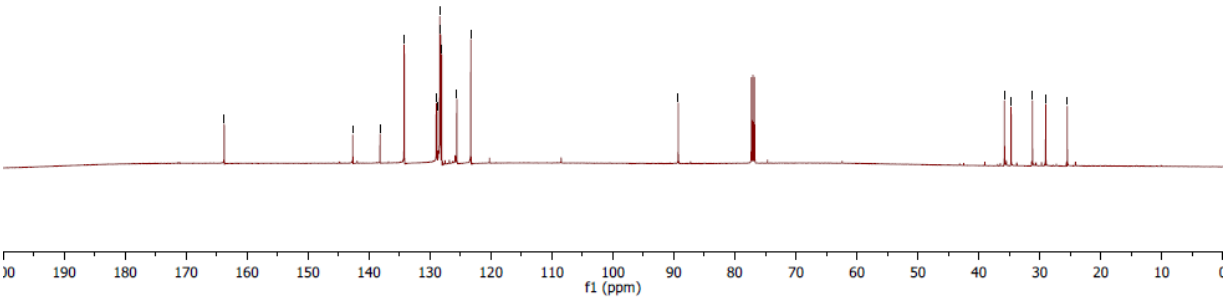


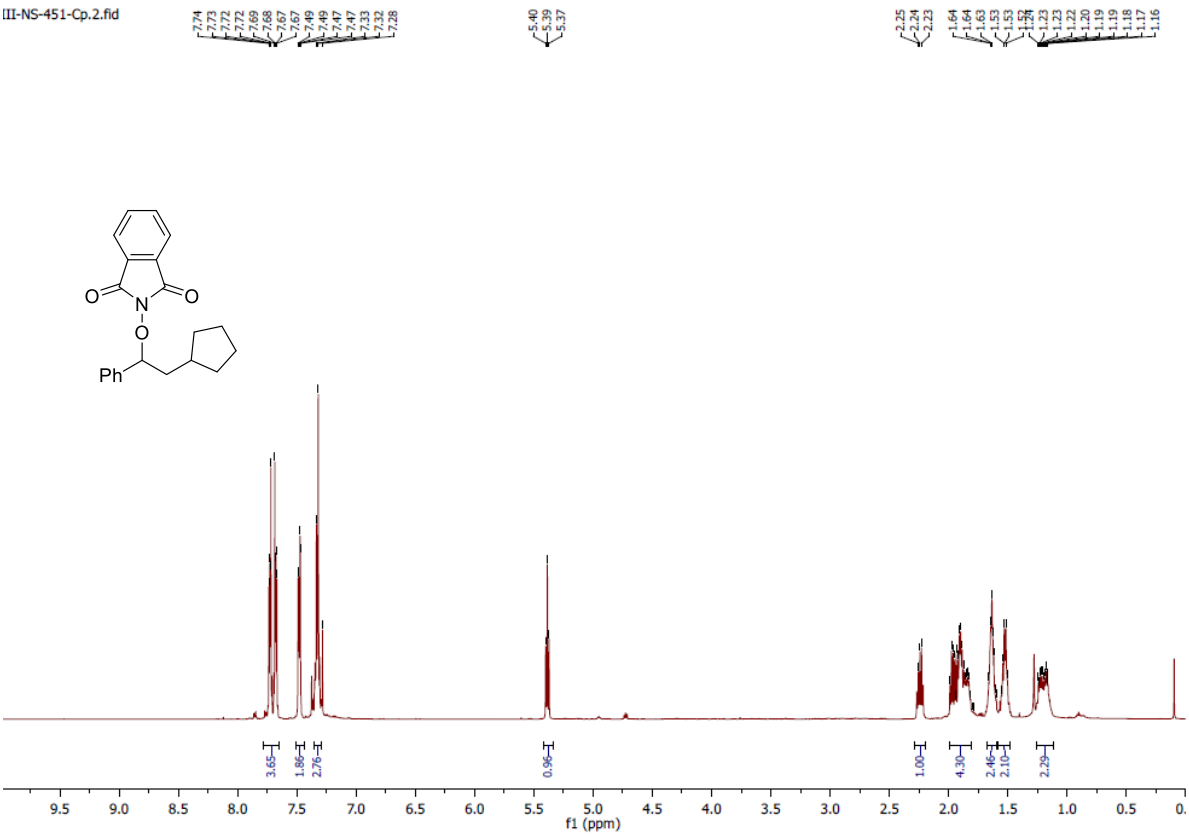


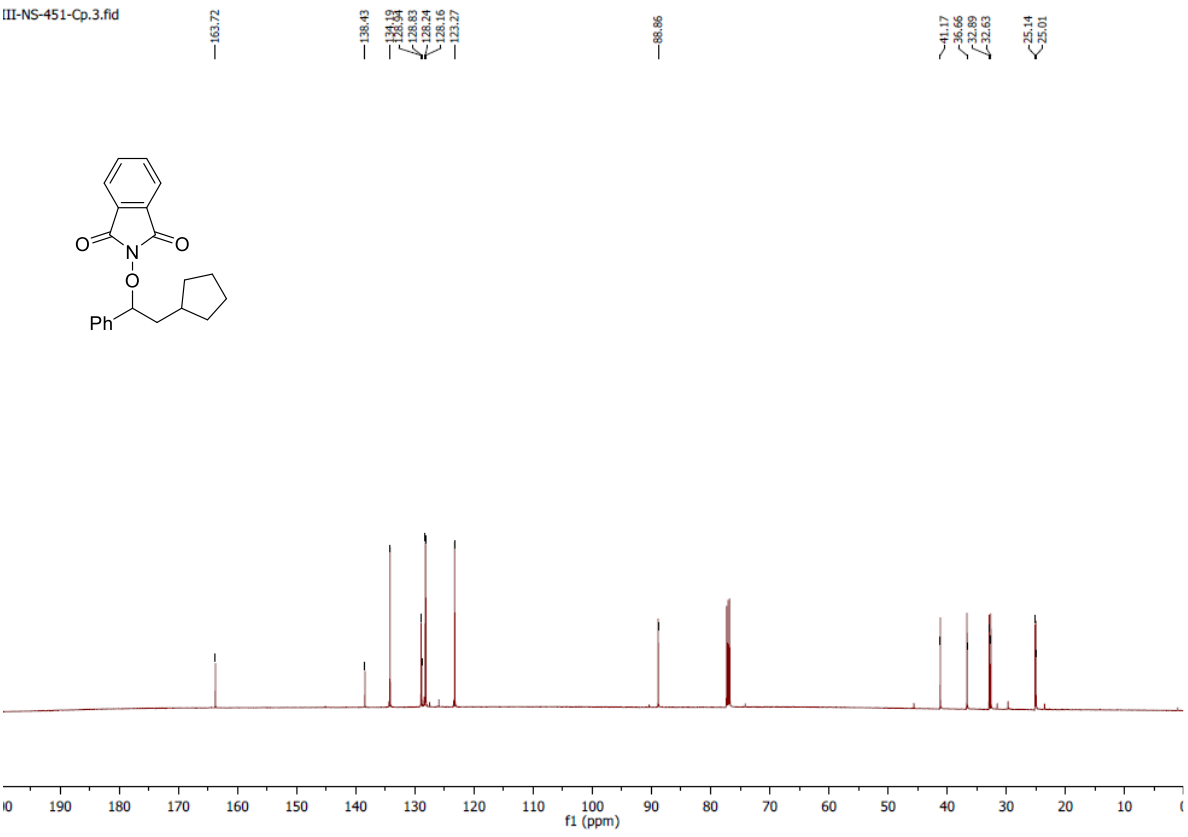
III-NS-437-P.3.fid

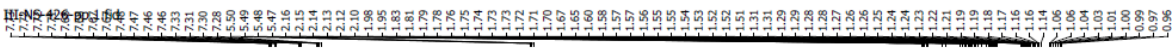


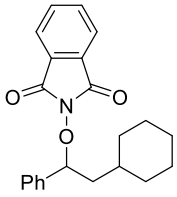


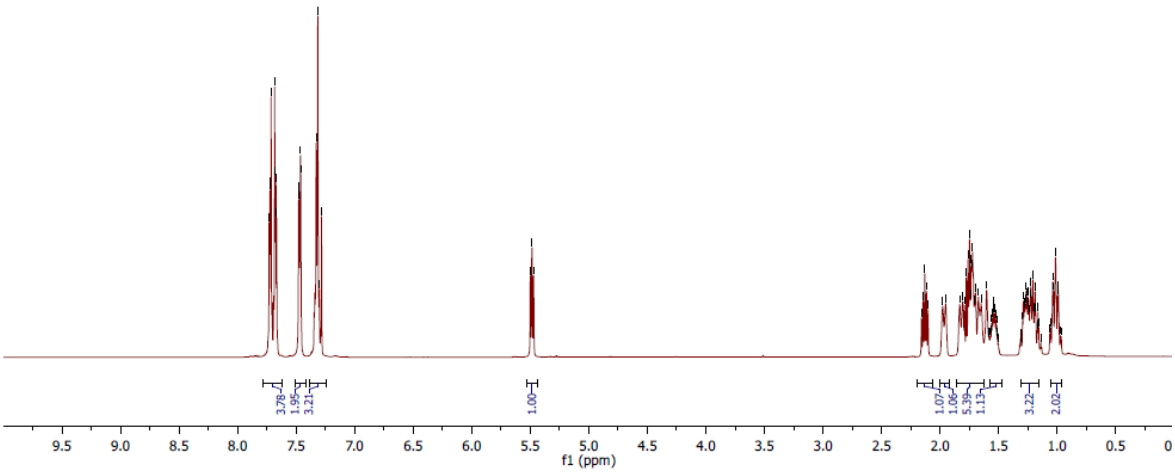



III-NS-451-Cp.2.fid
7.74
7.73
7.72
7.72
7.69
7.68
7.67
7.67
7.49
7.49
7.47
7.47
7.33
7.32
7.28
5.40
5.39
5.37
2.25
2.24
2.23
1.64
1.64
1.63
1.53
1.53
1.52
1.24
1.23
1.23
1.22
1.20
1.19
1.19
1.18
1.17
1.16
O
N
O
O
Ph
3.65
1.86
2.76
0.96
1.00
4.30
2.46
2.10
2.29
f1 (ppm)

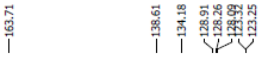

III-NS-451-Cp.3.fid
163.72
138.43
134.13
134.04
128.83
128.24
126.16
123.27
88.86
41.17
36.66
32.89
32.63
25.14
25.01
O
N
O
O
Ph
f1 (ppm)

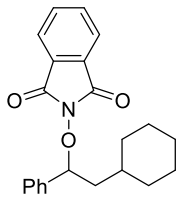


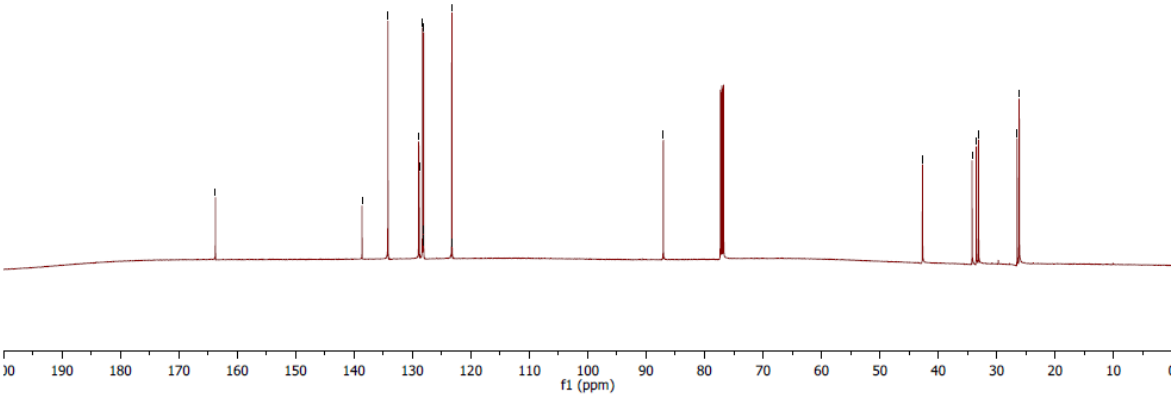


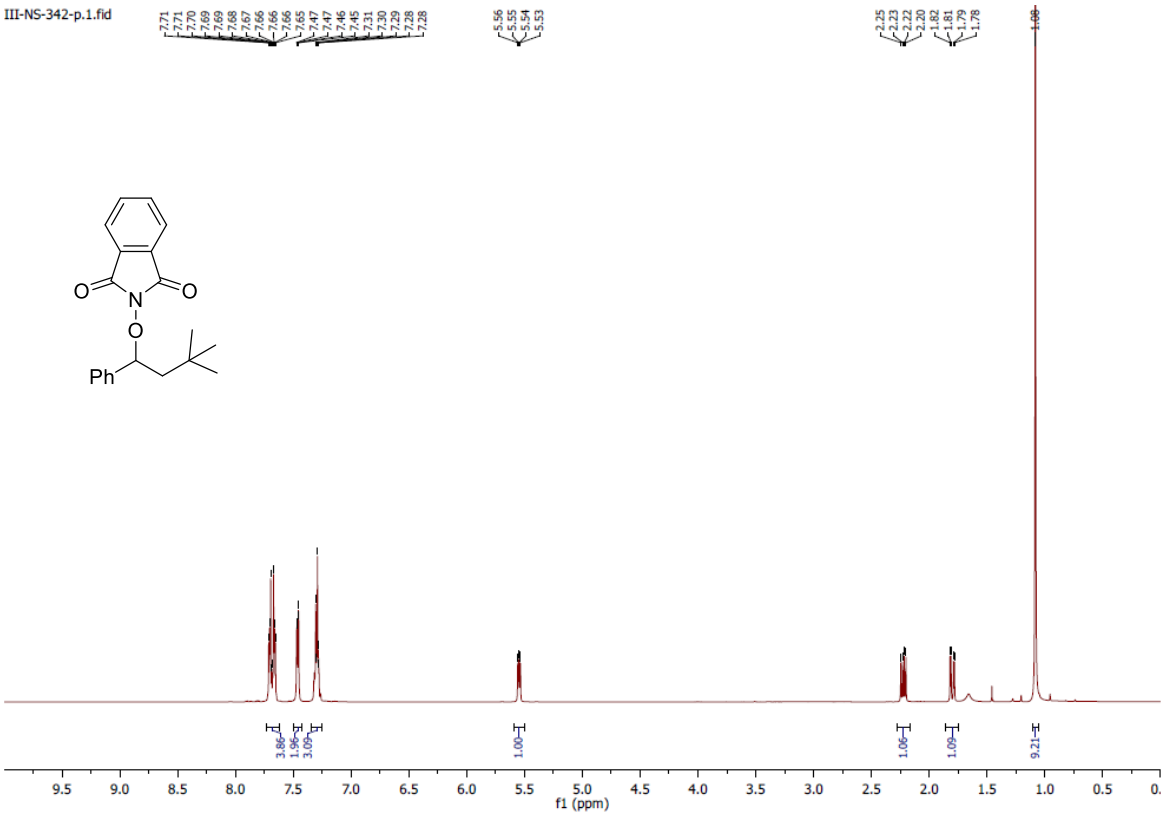


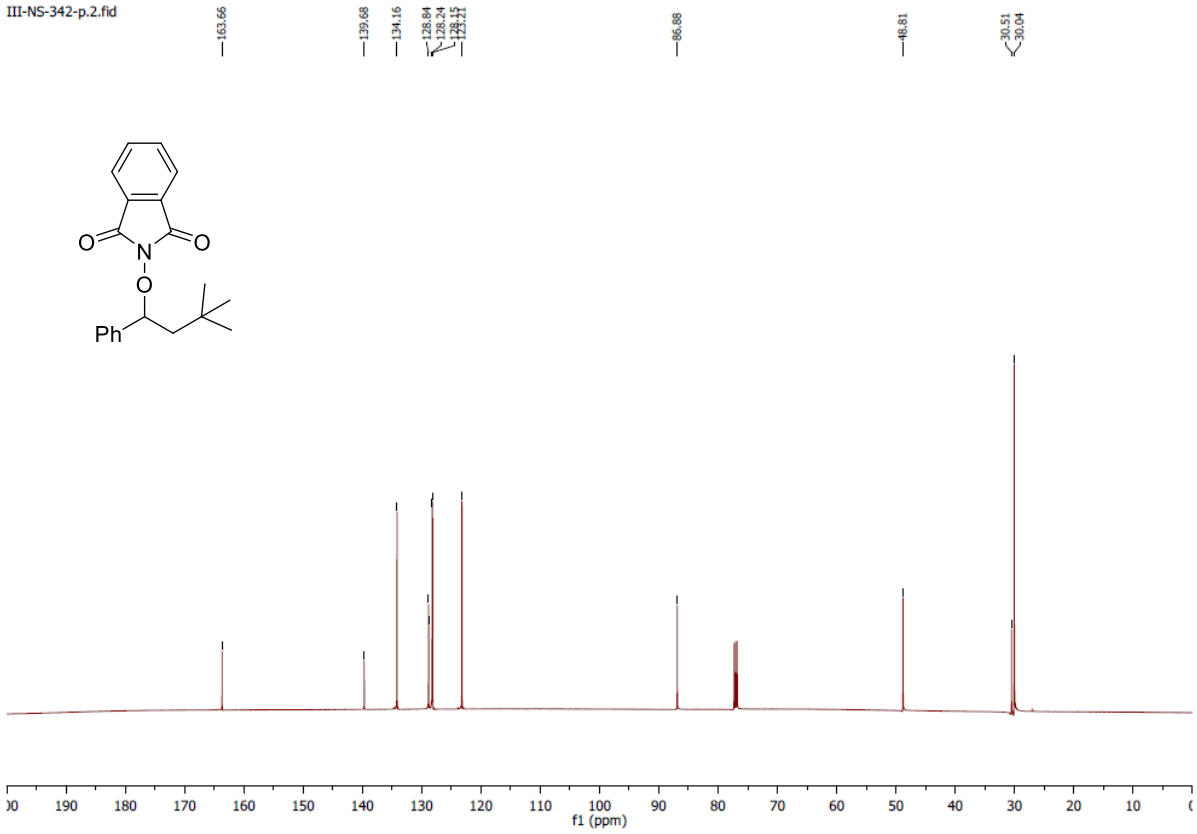
III-NS-426-pp.2.fid



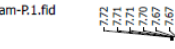


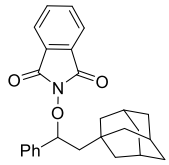


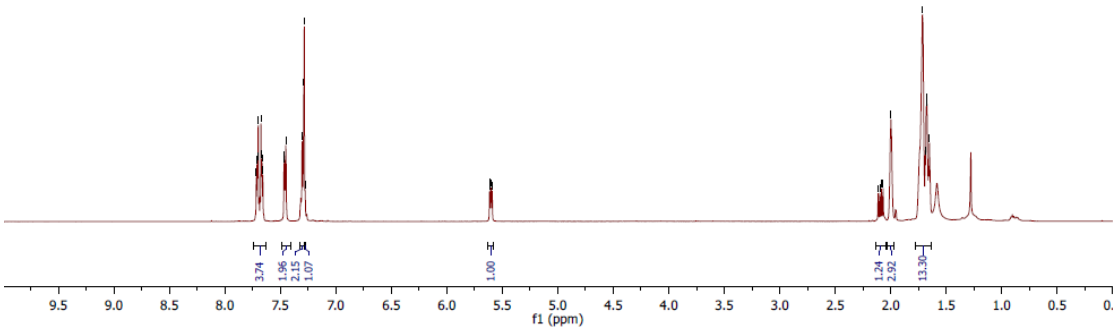

III-NS-342-p.1.fid
7.71
7.71
7.70
7.69
7.69
7.68
7.67
7.66
7.66
7.65
7.47
7.47
7.46
7.45
7.31
7.30
7.29
7.28
7.28
5.56
5.55
5.54
5.53
2.25
2.23
2.22
2.20
1.82
1.81
1.79
1.78
1.00
O
N
O
O
Ph
3.86
1.96
3.09
1.00
1.06
1.09
9.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


III-NS-342-p.2.fid
163.66
139.68
134.16
128.84
128.24
123.15
123.11
86.88
48.81
30.51
30.04
O
N
O
O
Ph
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

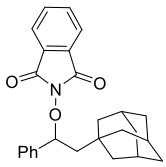
III-NS-491-adam-P.1.fid

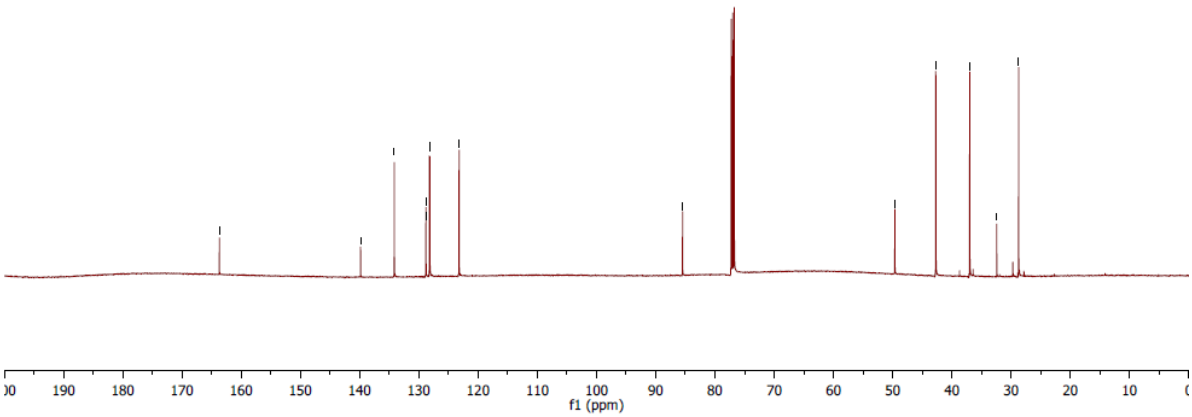


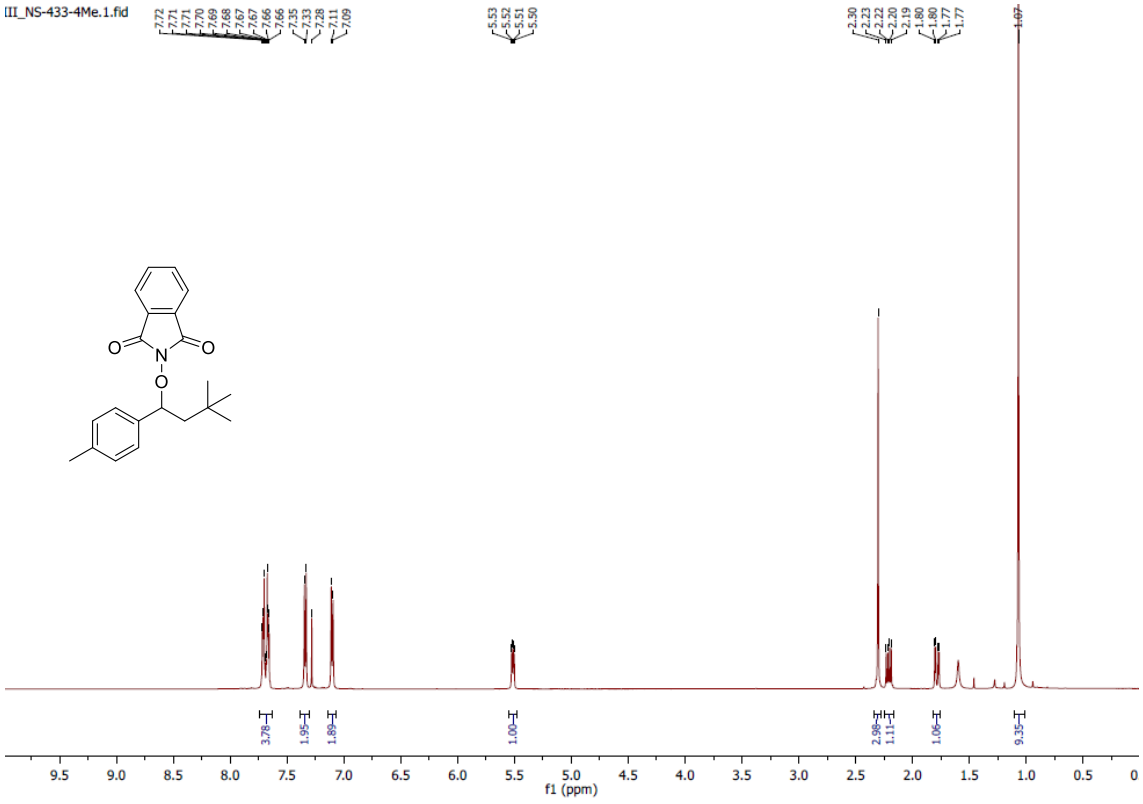


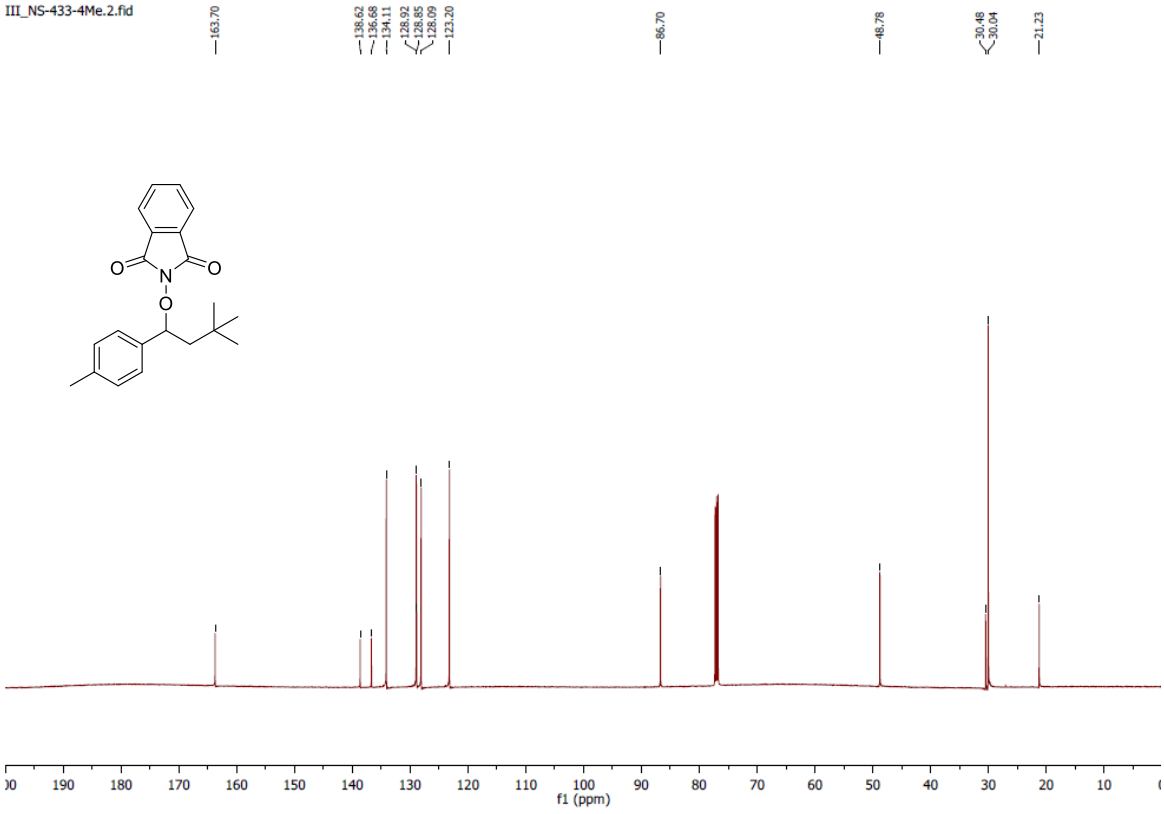


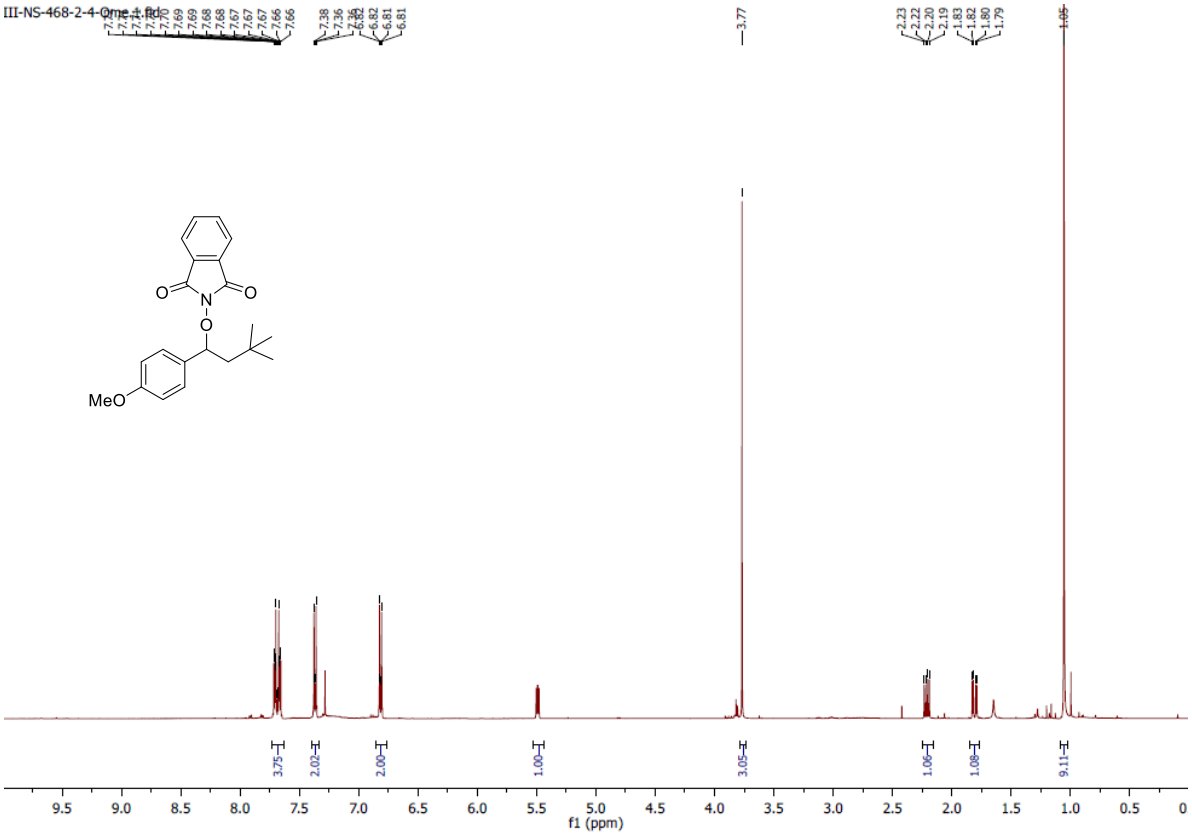
III-NS-491-adam-P.2.fid

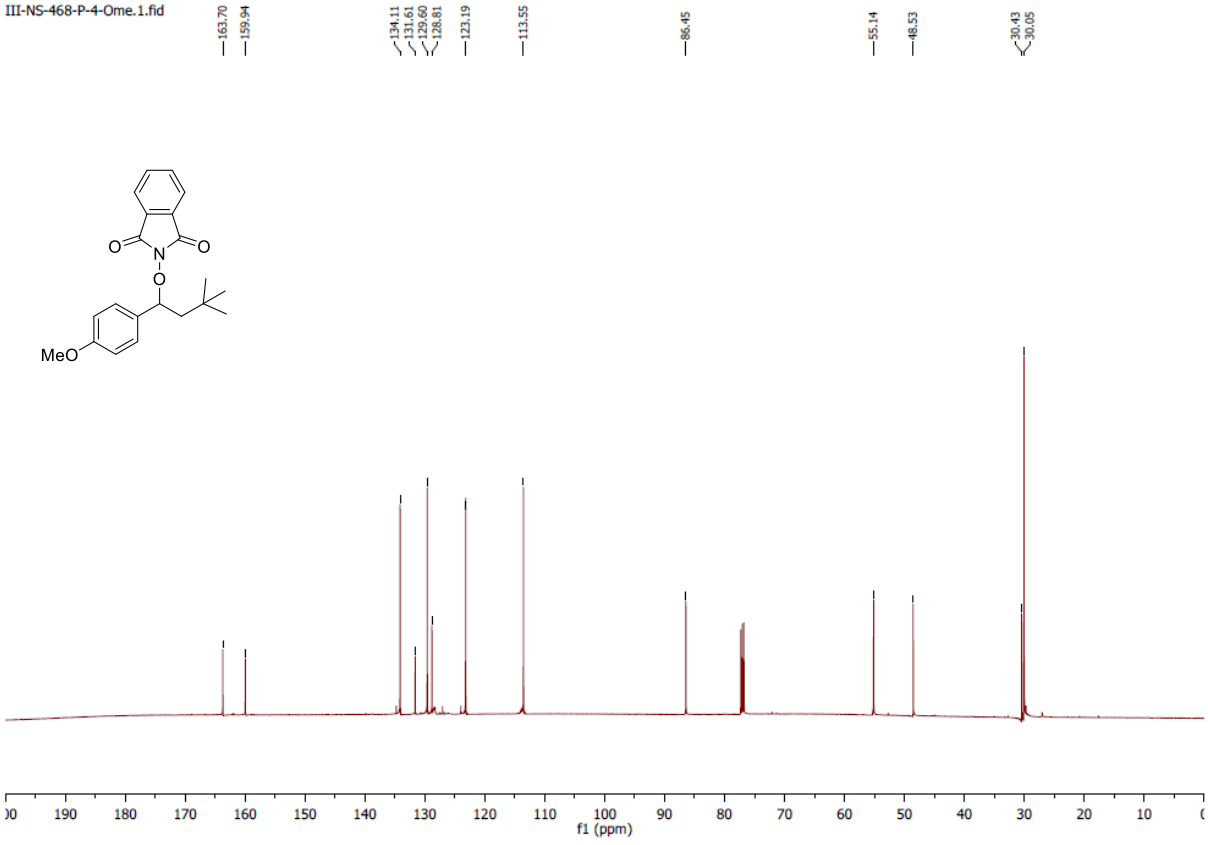


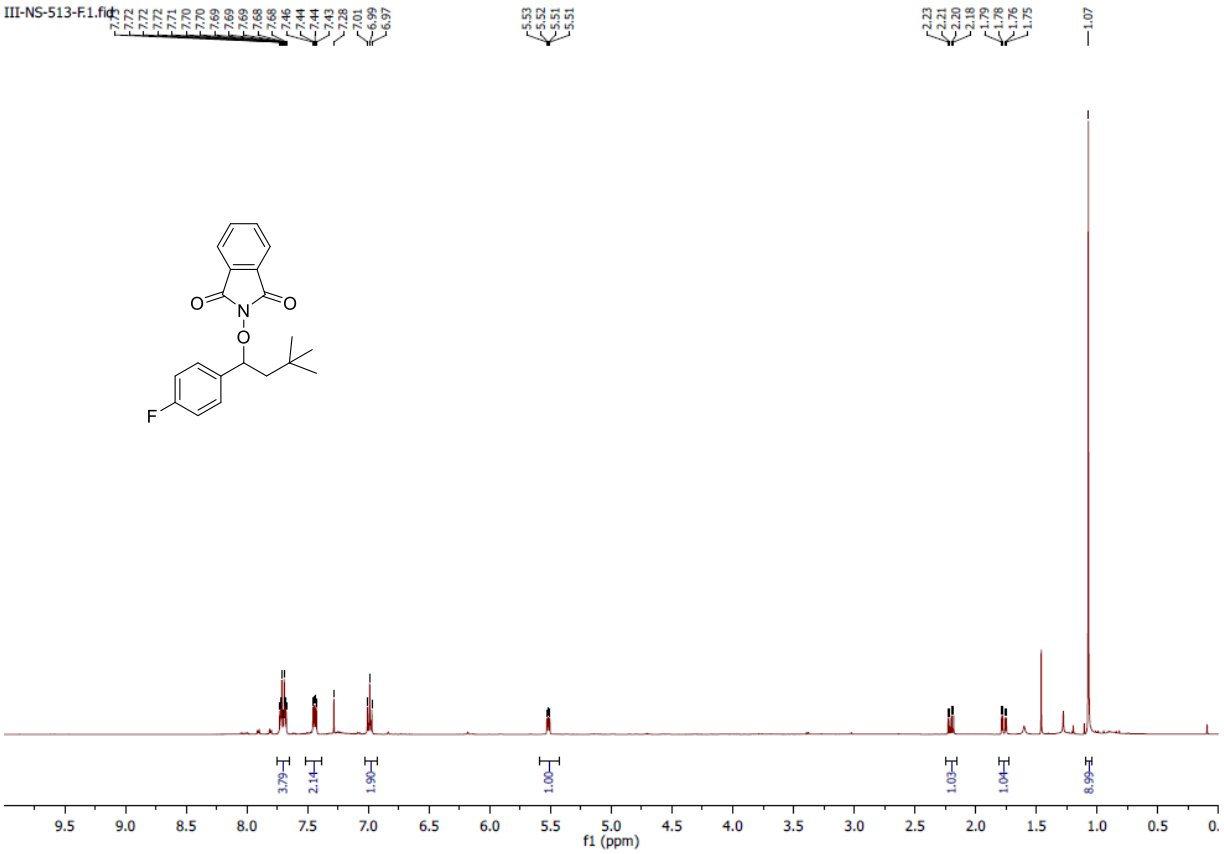


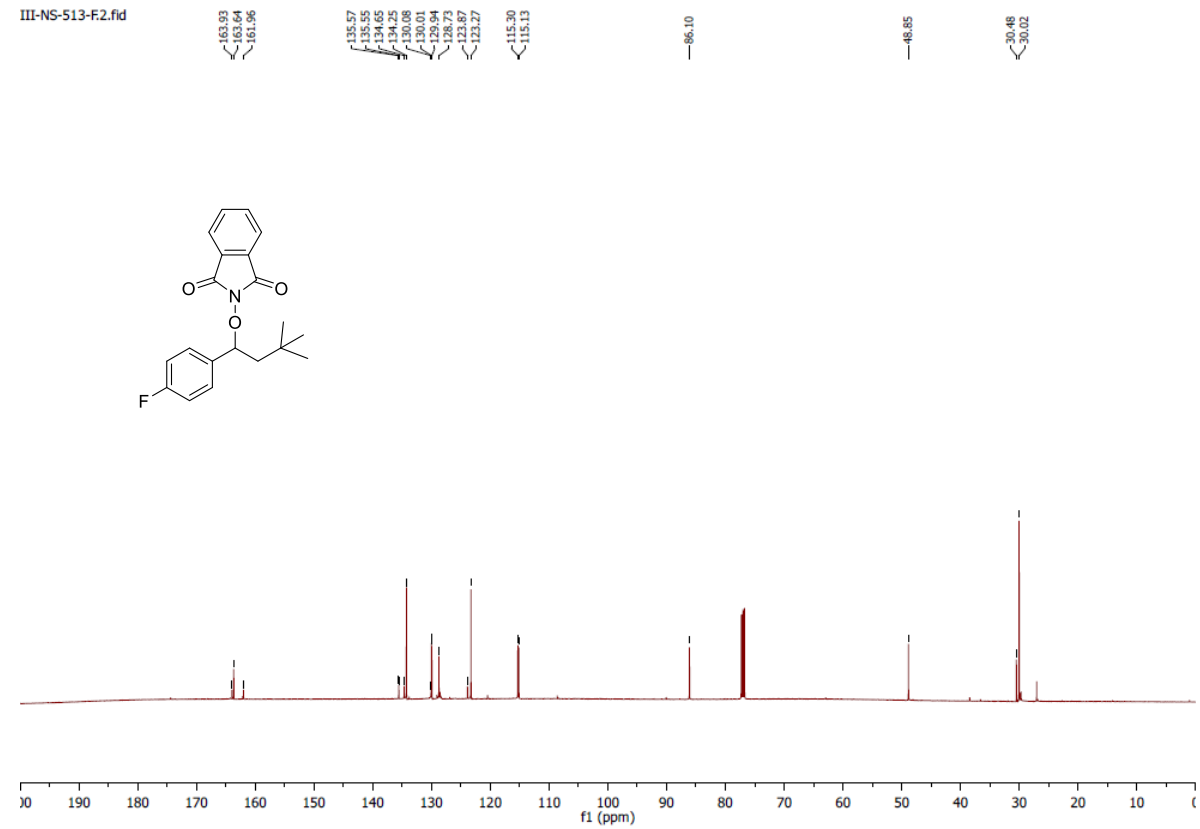

III_NS-433-4Me.1.fid
7.72
7.71
7.71
7.70
7.69
7.68
7.67
7.67
7.66
7.66
7.35
7.33
7.28
7.11
7.09
5.53
5.52
5.51
5.50
2.30
2.23
2.22
2.20
2.19
1.80
1.80
1.77
1.77
1.07
3.78
1.95
1.89
1.00
2.98
1.11
1.06
9.35
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

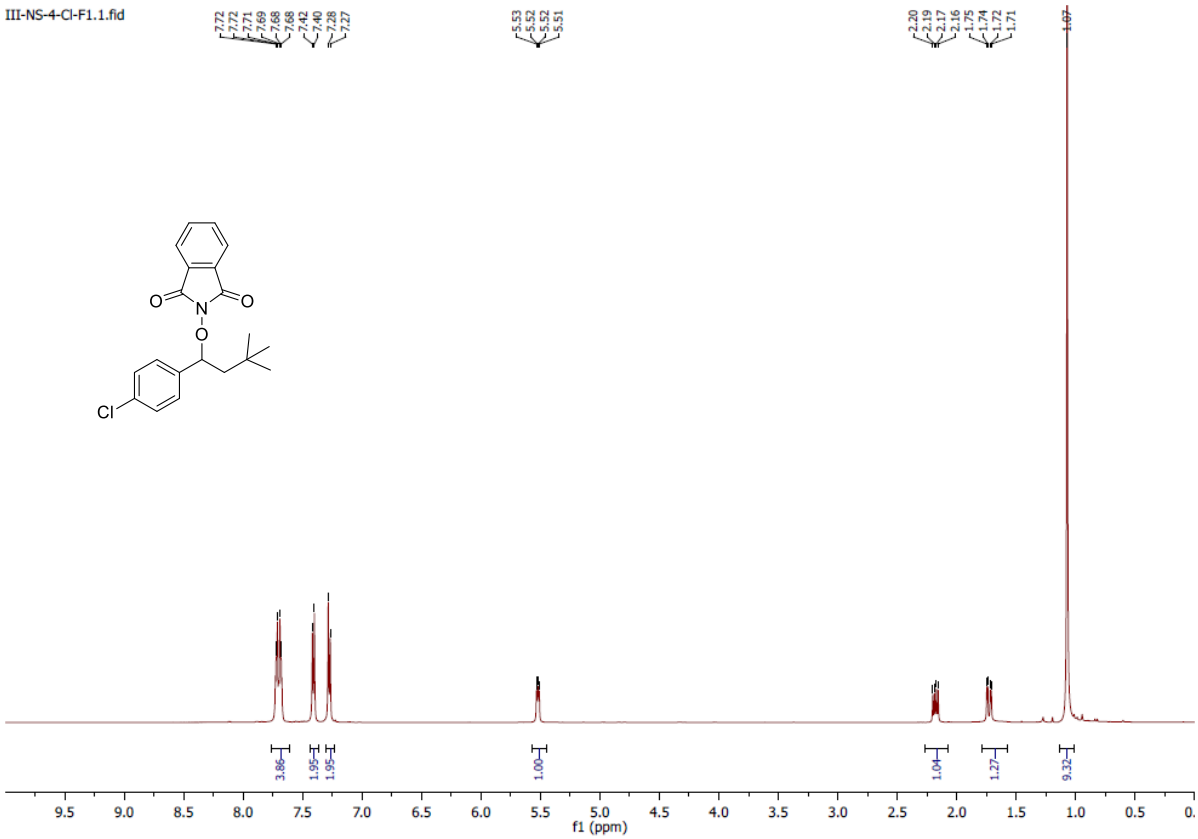

III_NS-433-4Me.2.fid
163.70
136.62
136.68
134.11
128.92
128.85
128.09
123.20
86.70
48.78
30.48
30.04
21.23
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

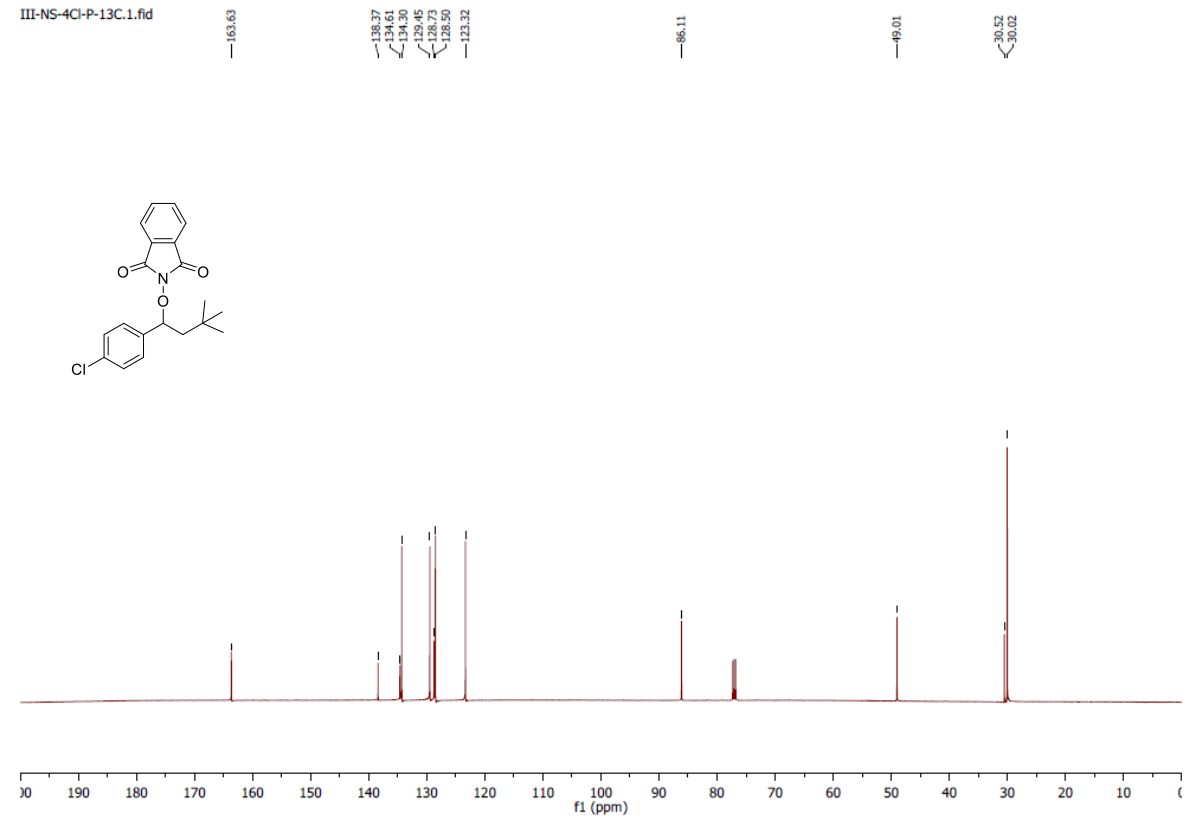

III-NS-468-2-4-Ome.1.fid
MeO
f1 (ppm)

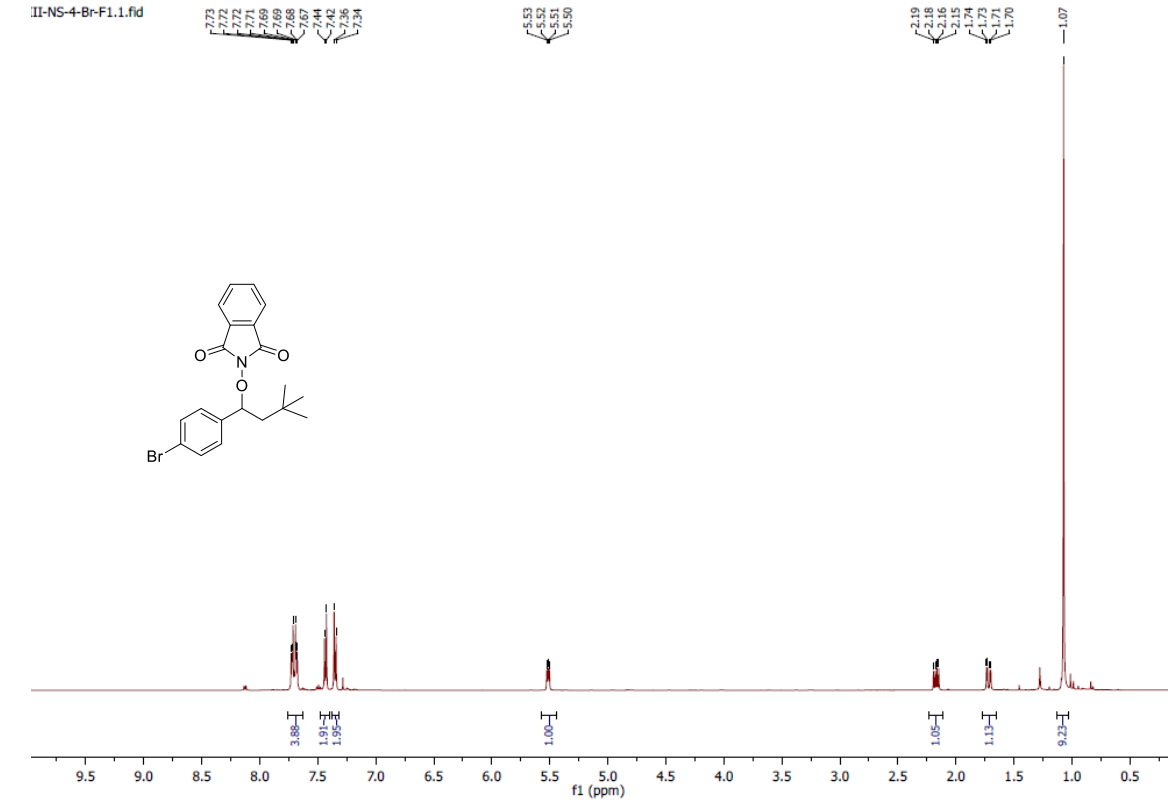

III-NS-468-P-4-Ome.1.fid
MeO
f1 (ppm)

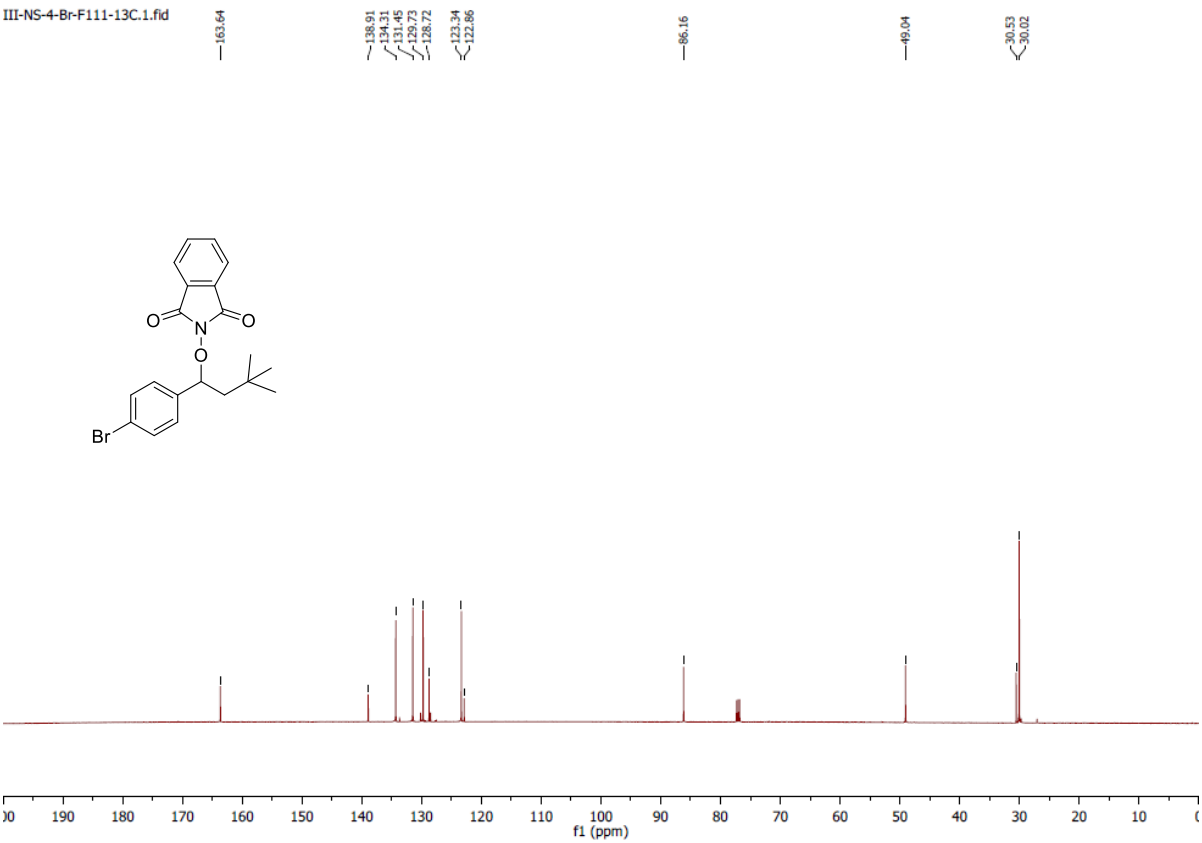

III-NS-513-F.1.fid
7.72
7.72
7.72
7.71
7.70
7.70
7.69
7.69
7.69
7.68
7.68
7.46
7.44
7.44
7.43
7.28
7.01
6.99
6.97
5.53
5.52
5.51
5.51
2.23
2.21
2.20
2.18
1.79
1.78
1.76
1.75
1.07
O
N
O
O
F
3.79
2.14
1.90
1.00
1.03
1.04
8.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

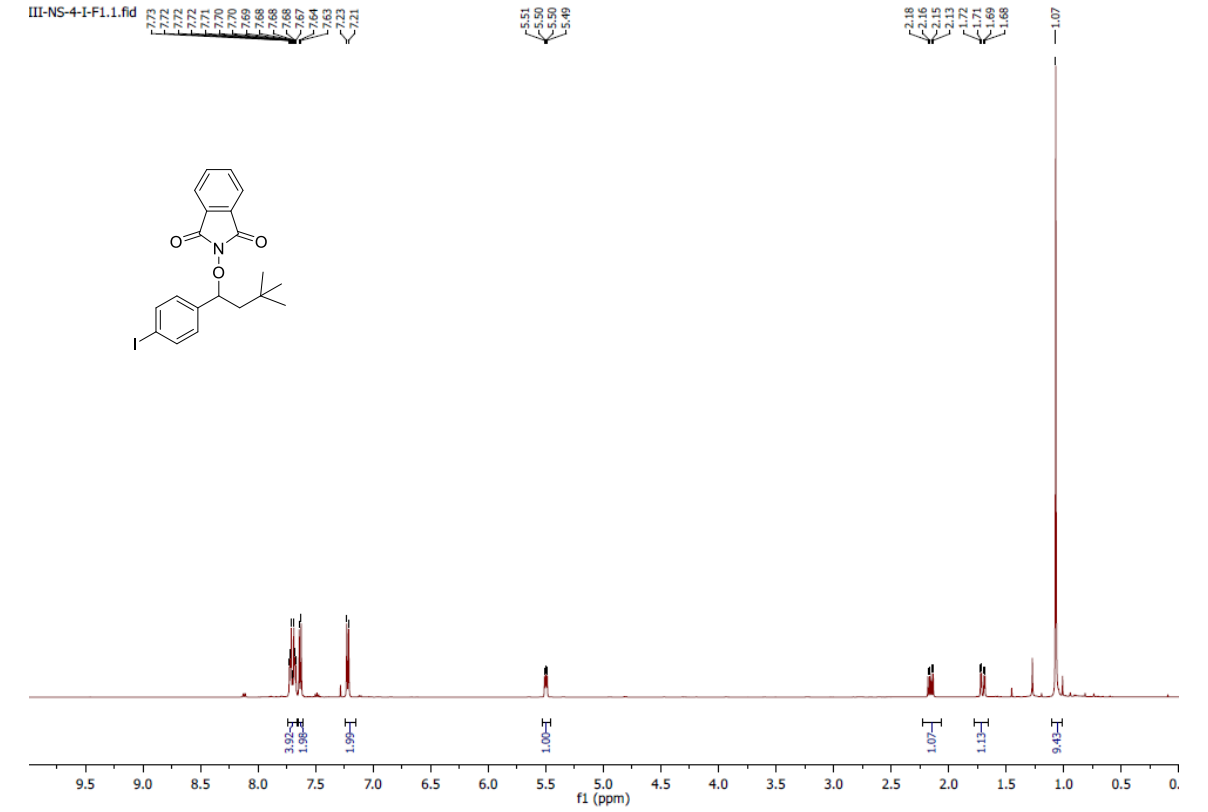

III-NS-513-F.2.fid
163.93
163.64
161.96
135.57
135.55
134.65
134.25
130.08
130.01
129.94
128.73
123.87
123.27
115.30
115.13
86.10
48.85
30.48
30.02
O
N
O
O
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

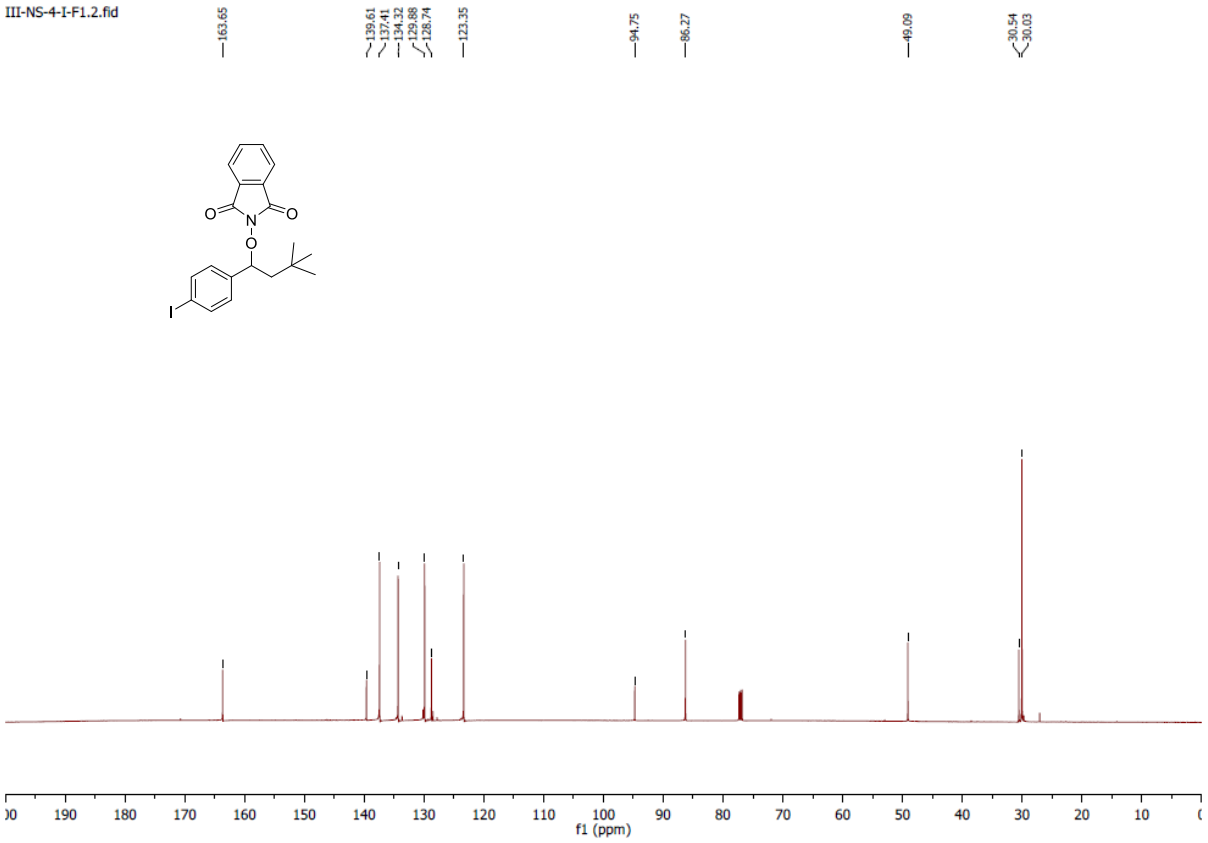

III-NS-4-Cl-F1.1.fid
7.72
7.72
7.71
7.71
7.69
7.68
7.68
7.42
7.40
7.28
7.27
5.53
5.52
5.52
5.51
2.20
2.19
2.17
2.16
1.75
1.74
1.72
1.71
1.67
O
N
O
O
Cl
3.86
1.95
1.95
1.00
1.04
1.27
9.32
f1 (ppm)

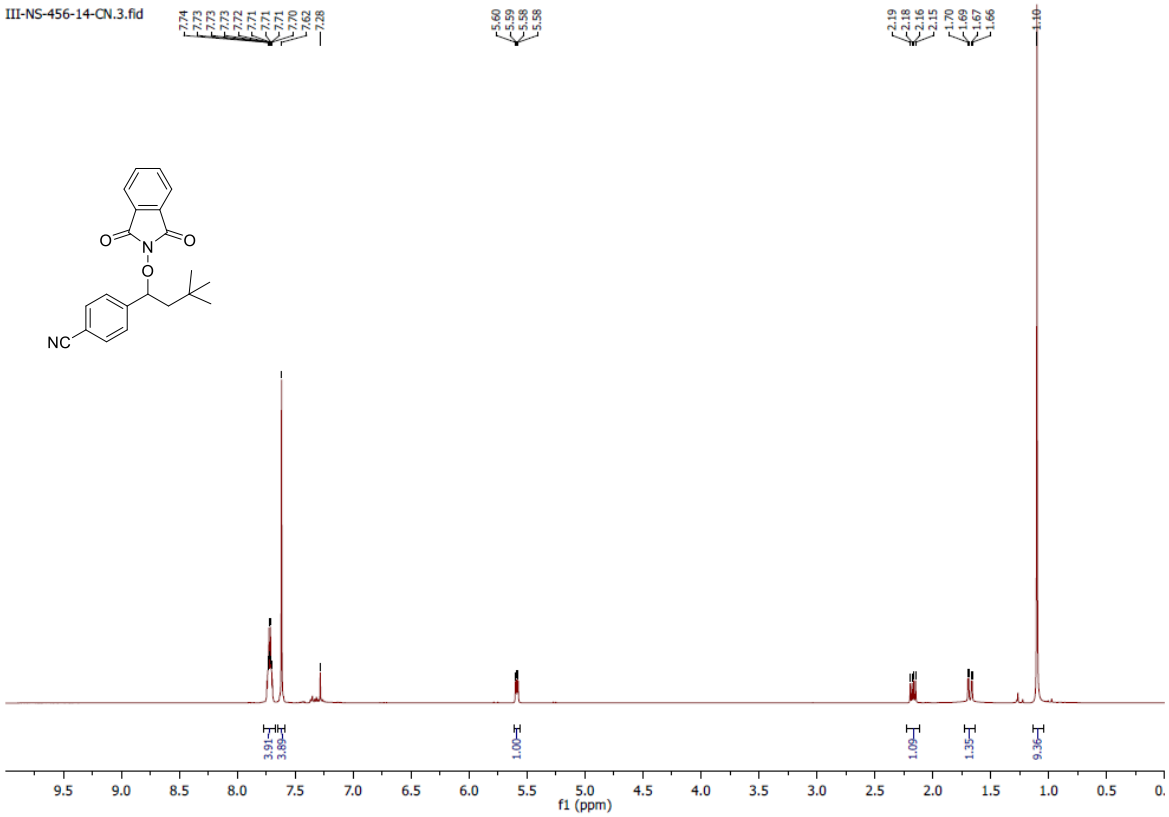

III-NS-4Cl-P-13C.1.fid
163.63
138.37
134.61
134.30
129.45
128.73
128.50
123.32
86.11
49.01
30.52
30.02
O
N
O
O
Cl
f1 (ppm)

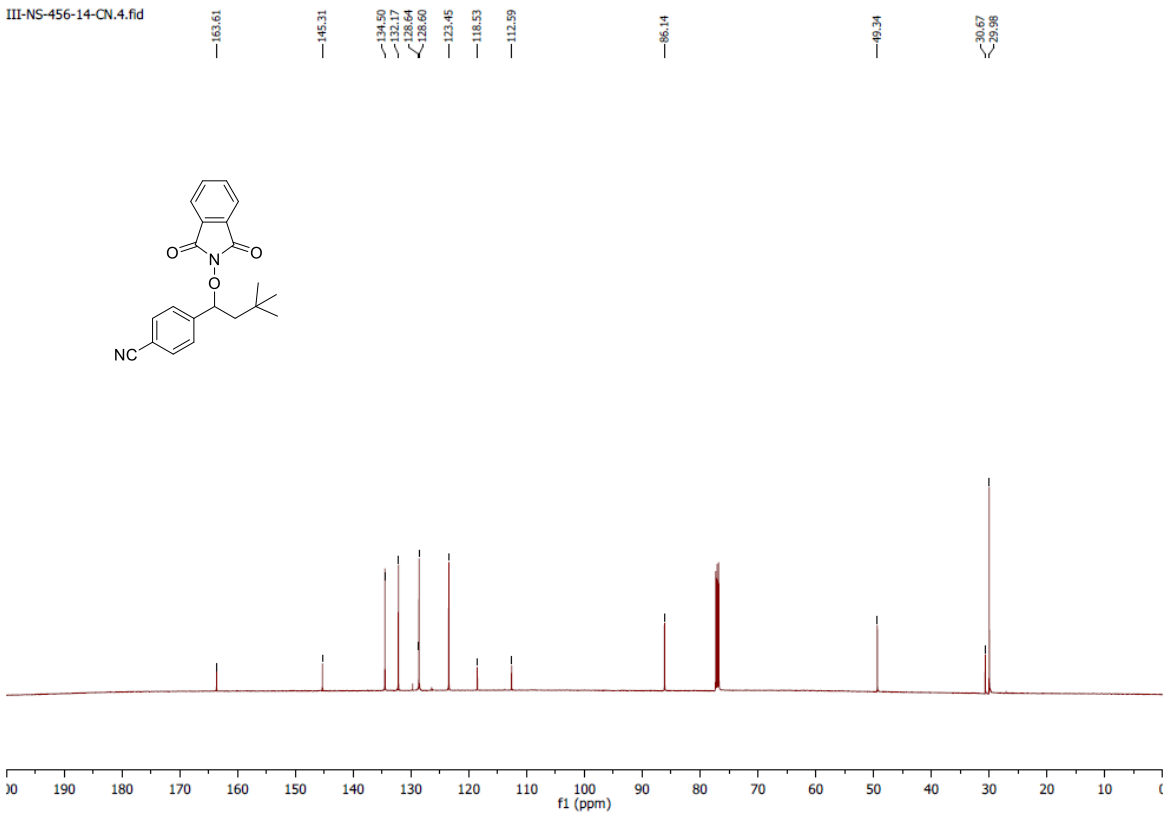

II-NS-4-Br-F1.1.fid
7.73
7.72
7.72
7.71
7.69
7.69
7.68
7.67
7.44
7.42
7.36
7.34
5.53
5.52
5.51
5.50
2.19
2.18
2.16
2.15
1.74
1.73
1.71
1.70
1.07
O
N
O
O
Br
3.88
1.91
1.95
1.00
1.05
1.13
9.23
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

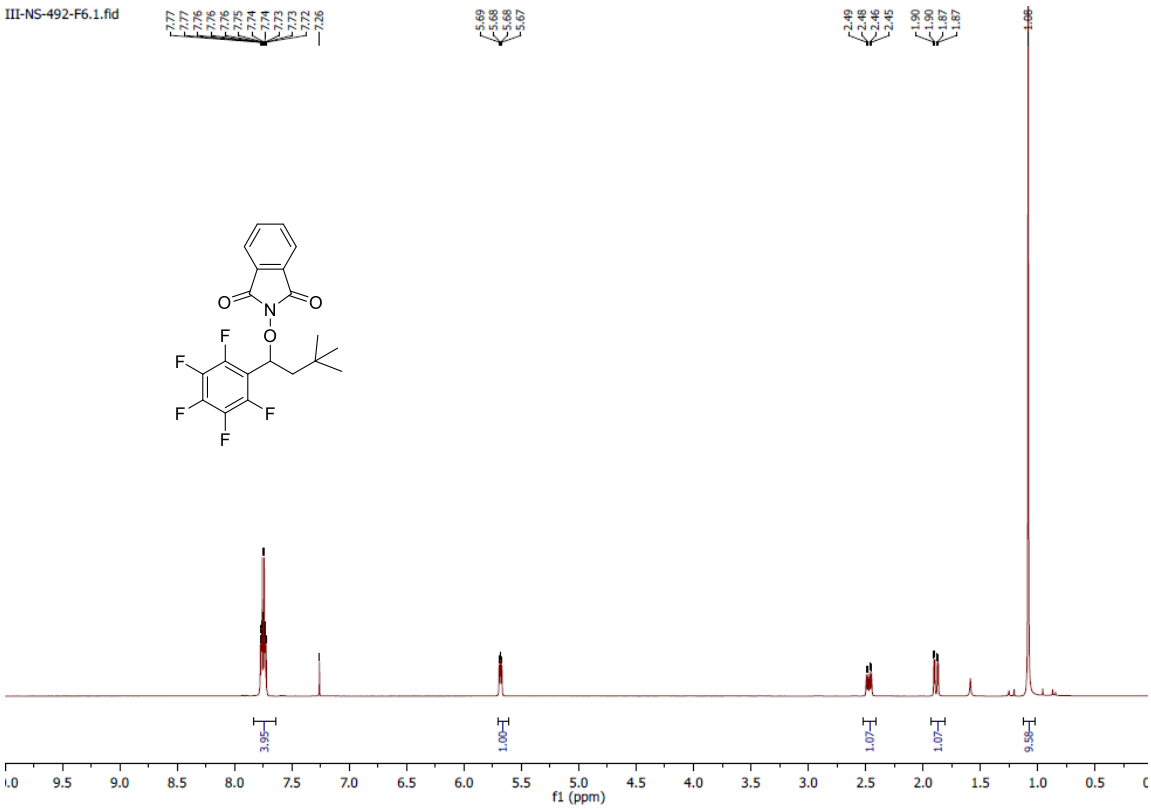

III-NS-4-Br-F111-13C.1.fid
163.64
138.91
134.31
131.45
129.73
128.72
123.34
122.86
86.16
49.04
30.53
30.02
O
N
O
O
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

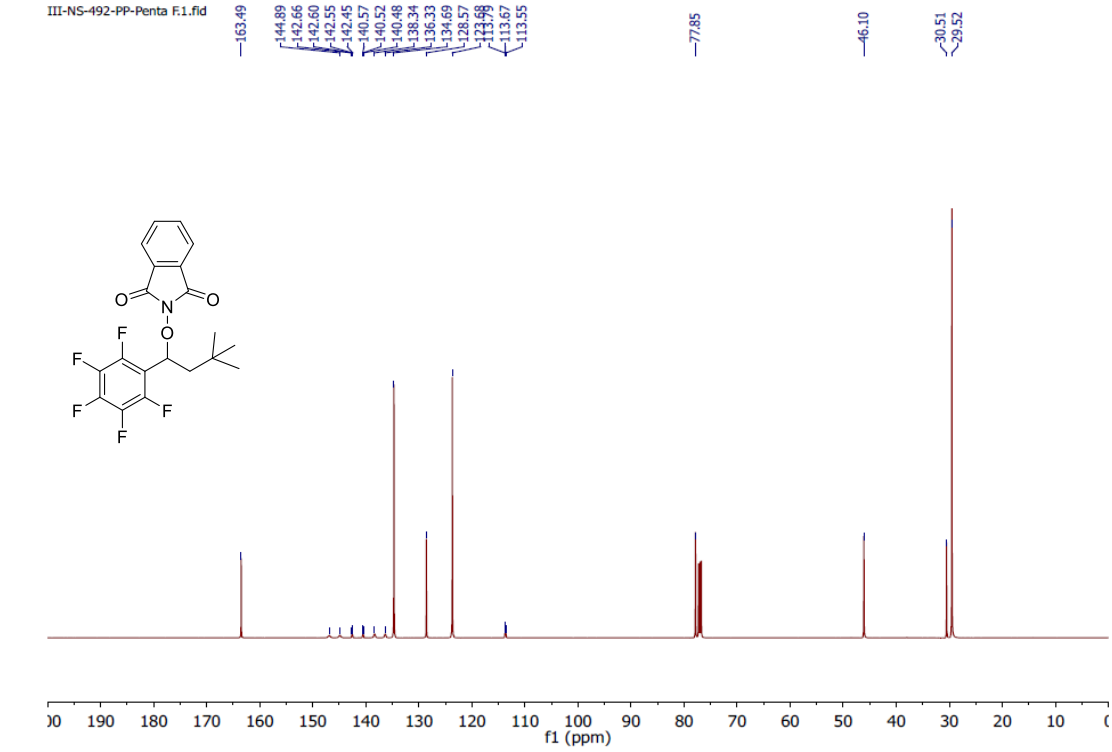

III-NS-4-I-F1.1.fid
7.73
7.72
7.72
7.72
7.72
7.71
7.70
7.70
7.69
7.68
7.68
7.68
7.67
7.64
7.63
7.23
7.21
5.51
5.50
5.50
5.49
2.18
2.16
2.15
2.13
2.12
1.71
1.69
1.68
1.07
3.92
1.98
1.99
1.00
1.07
1.13
9.43
f1 (ppm)


III-NS-4-I-F1.2.fid
163.65
139.61
137.41
134.32
129.88
128.74
123.35
94.75
86.27
49.09
30.54
30.03
f1 (ppm)

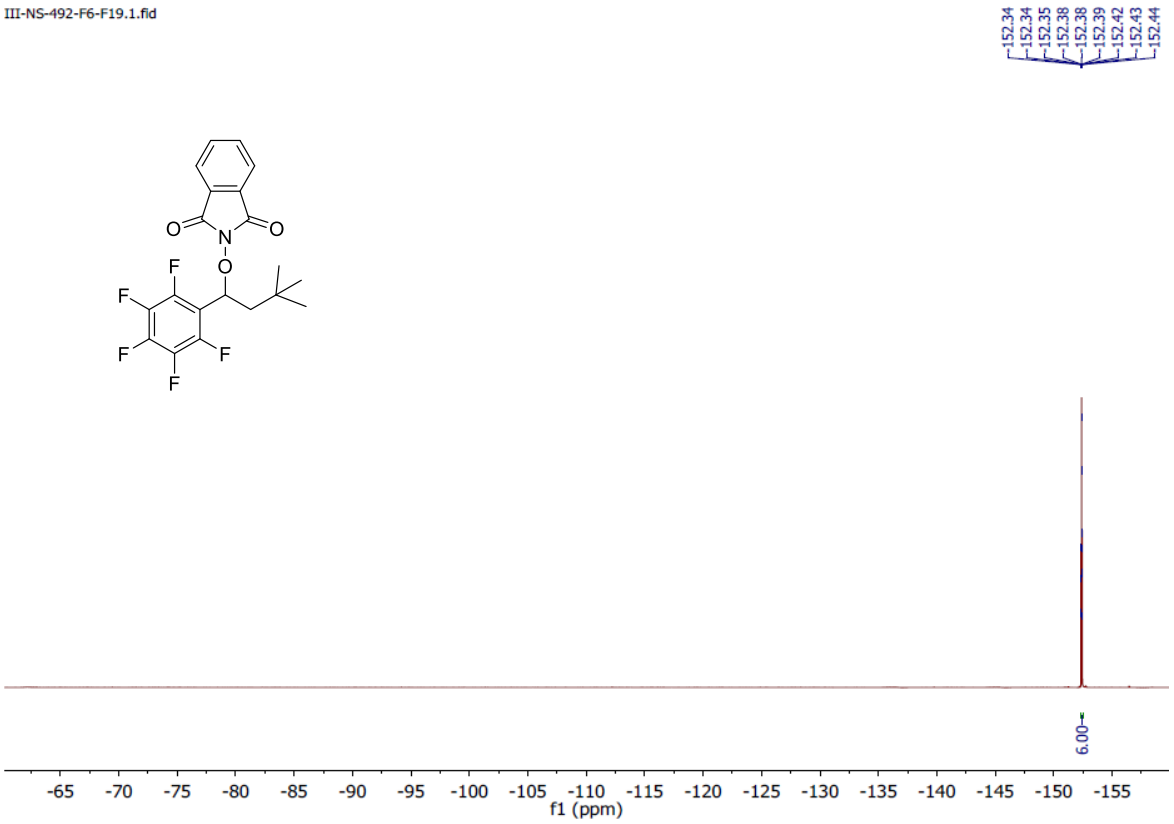

III-NS-456-14-CN.3.fid
7.74
7.73
7.73
7.73
7.72
7.71
7.71
7.71
7.70
7.62
7.28
5.60
5.59
5.58
5.58
5.58
2.19
2.18
2.16
2.15
1.70
1.69
1.67
1.66
1.10
O
N
O
O
NC
3.91
3.89
1.00
1.09
1.35
9.36
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

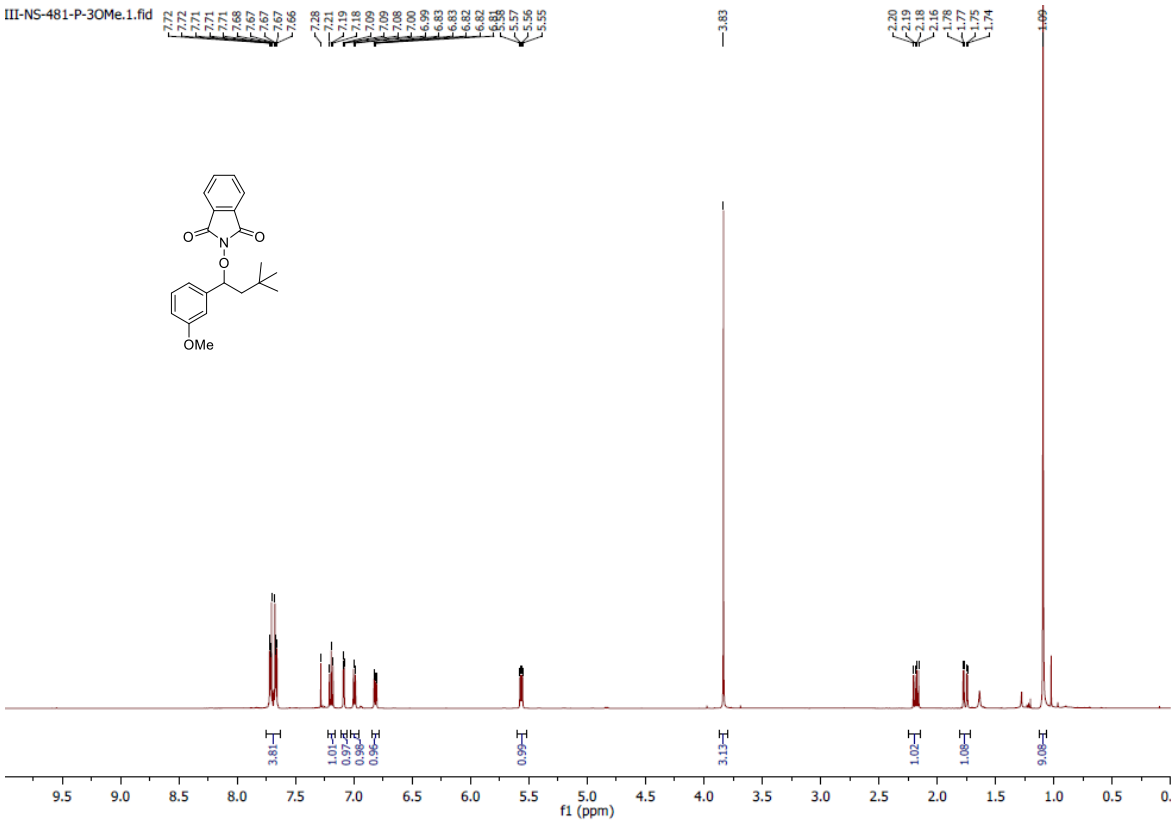

III-NS-456-14-CN.4.fid
163.61
145.31
134.50
132.17
128.64
128.60
123.45
118.53
112.59
86.14
49.34
30.67
29.98
O
N
O
O
NC
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

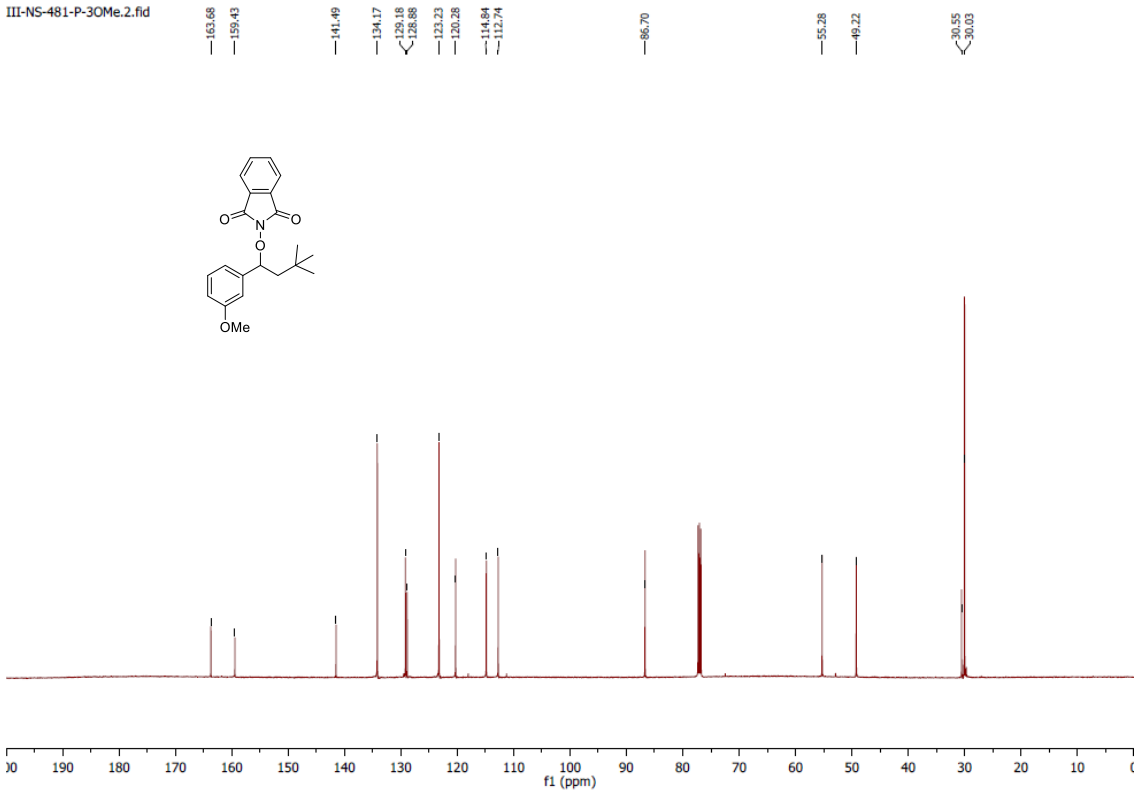

III-NS-492-F6.1.fid
f1 (ppm)

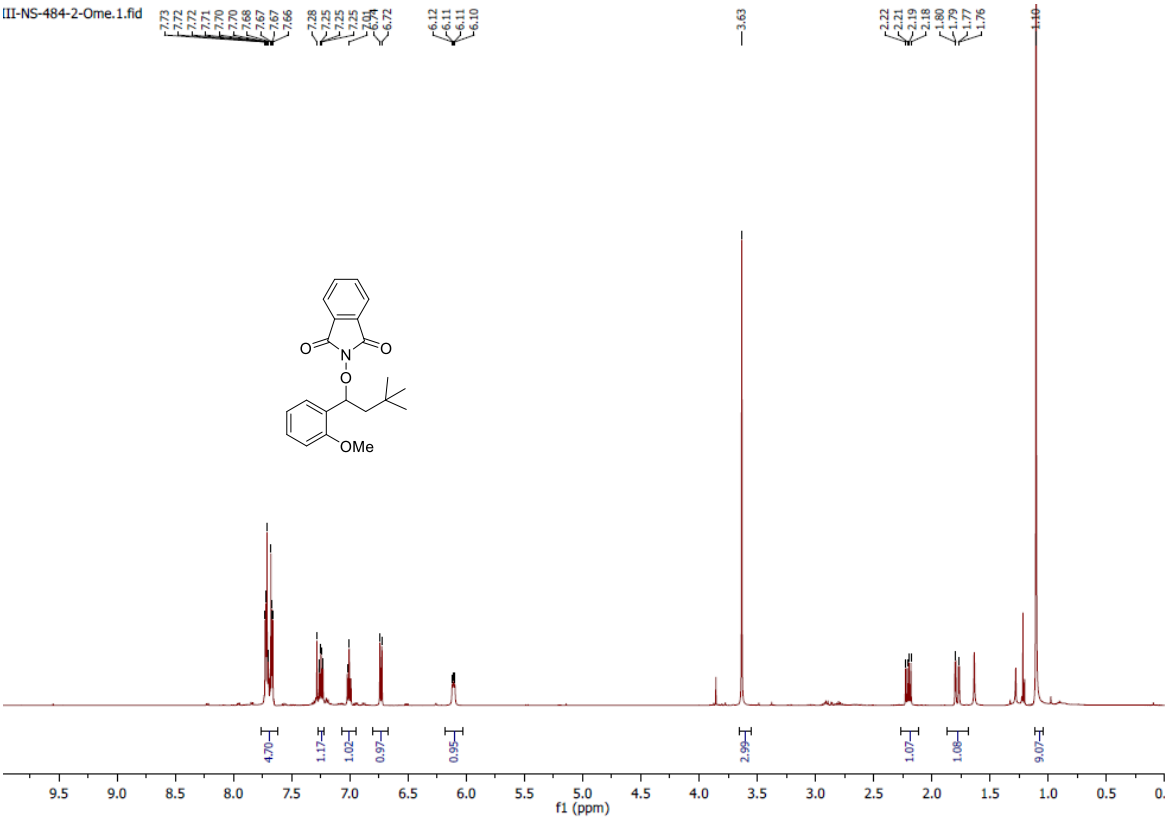

III-NS-492-PP-Penta F.1.fid
f1 (ppm)

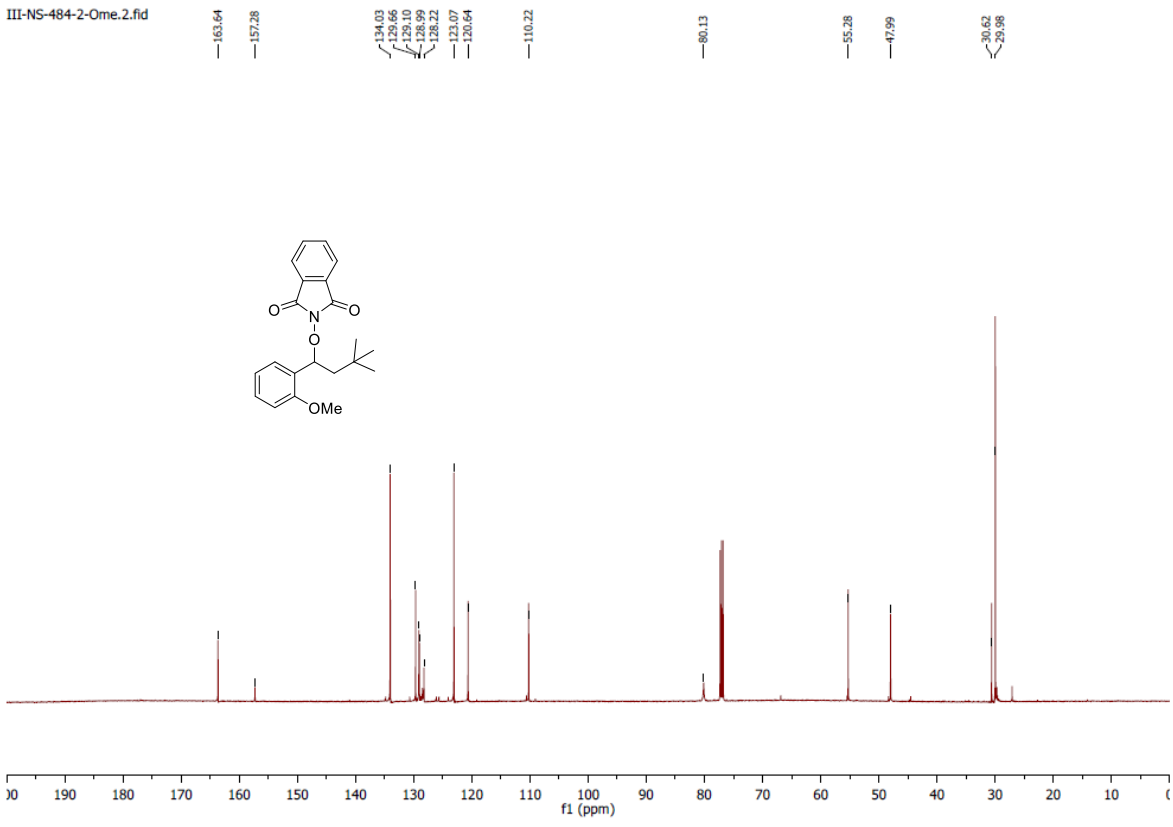
III-NS-492-F6-F19.1.fid

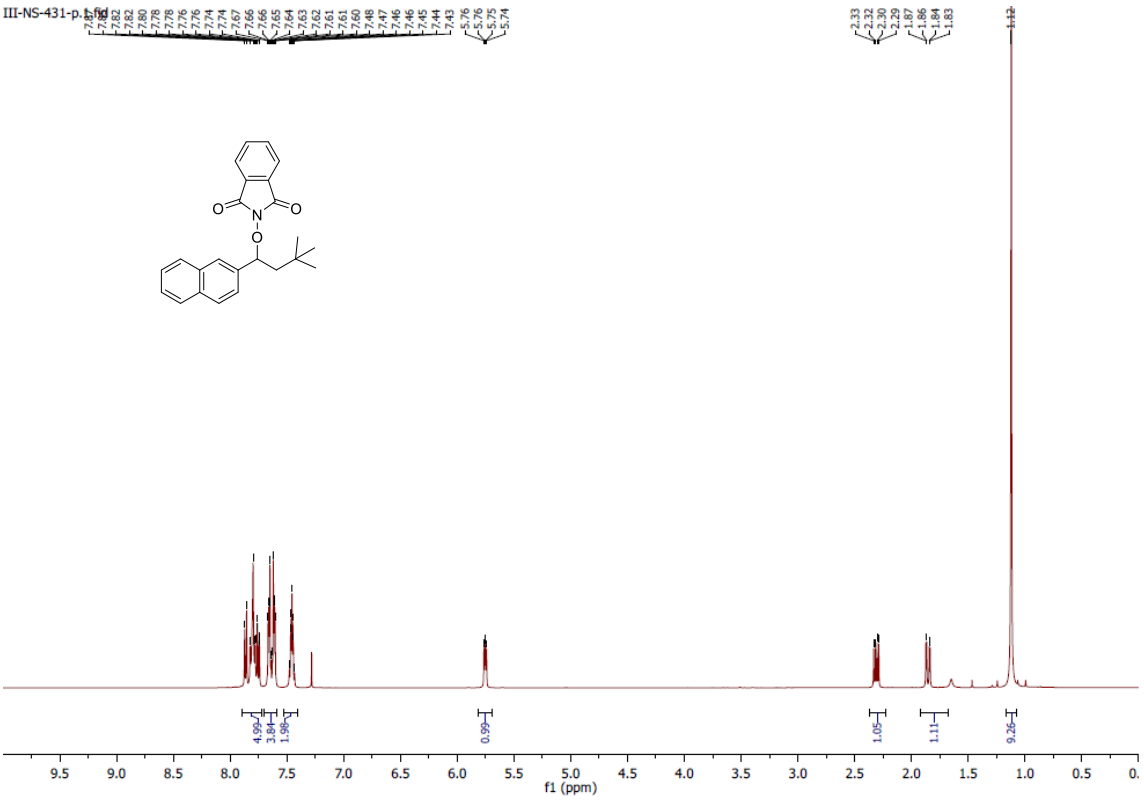


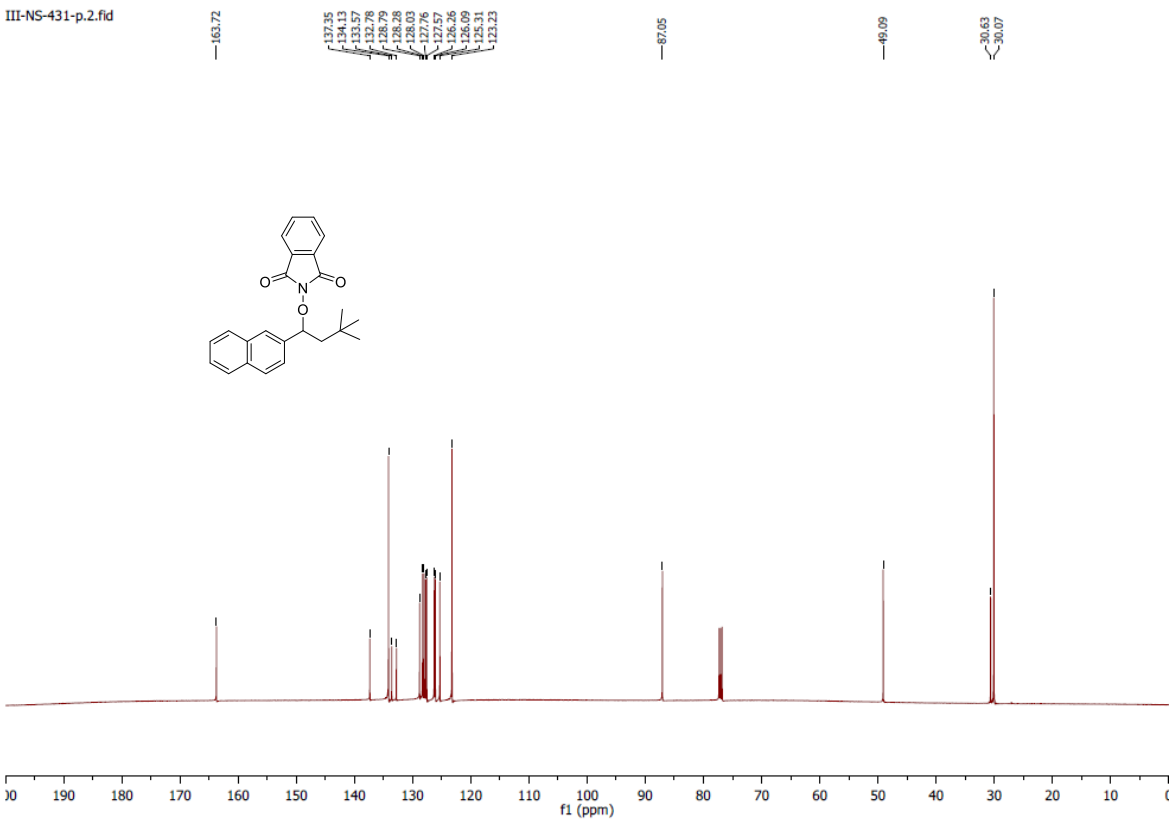

III-NS-481-P-3OMe.1.fid
OMe
f1 (ppm)

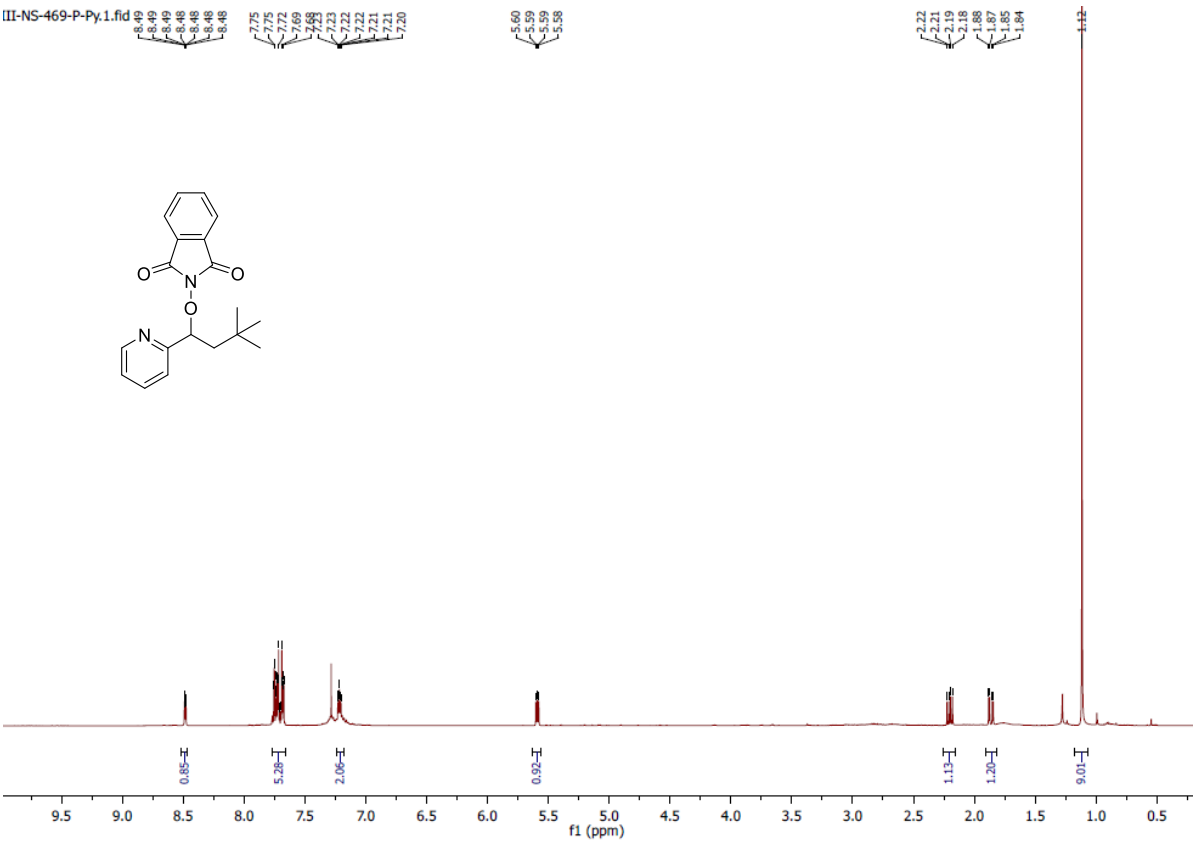

III-NS-481-P-3OMe.2.fid
OMe
f1 (ppm)

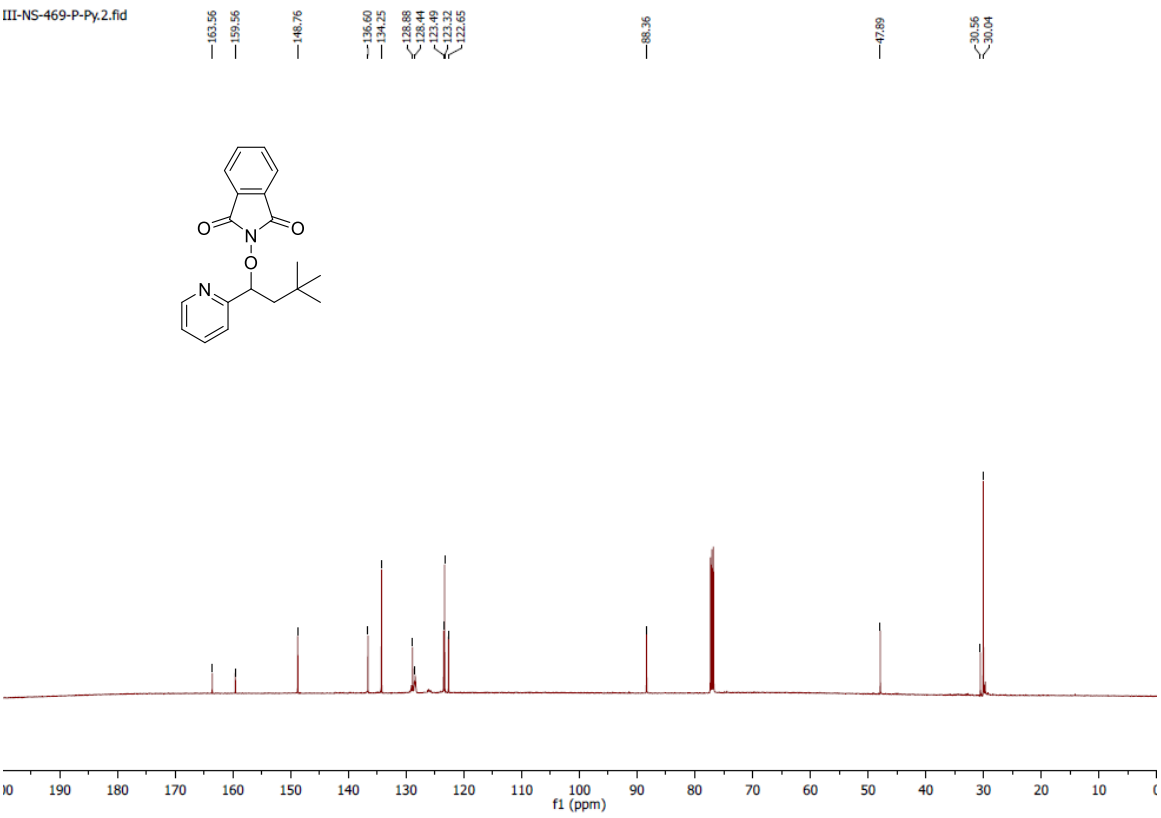

III-NS-484-2-Ome.1.fid
7.73
7.72
7.72
7.71
7.70
7.70
7.68
7.67
7.67
7.67
7.66
7.28
7.25
7.25
7.25
7.01
6.74
6.72
6.12
6.11
6.11
6.10
3.63
2.22
2.21
2.19
2.18
1.80
1.79
1.77
1.76
1.10
O
N
O
O
OMe
4.70
1.17
1.02
0.97
0.95
2.99
1.07
1.08
9.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

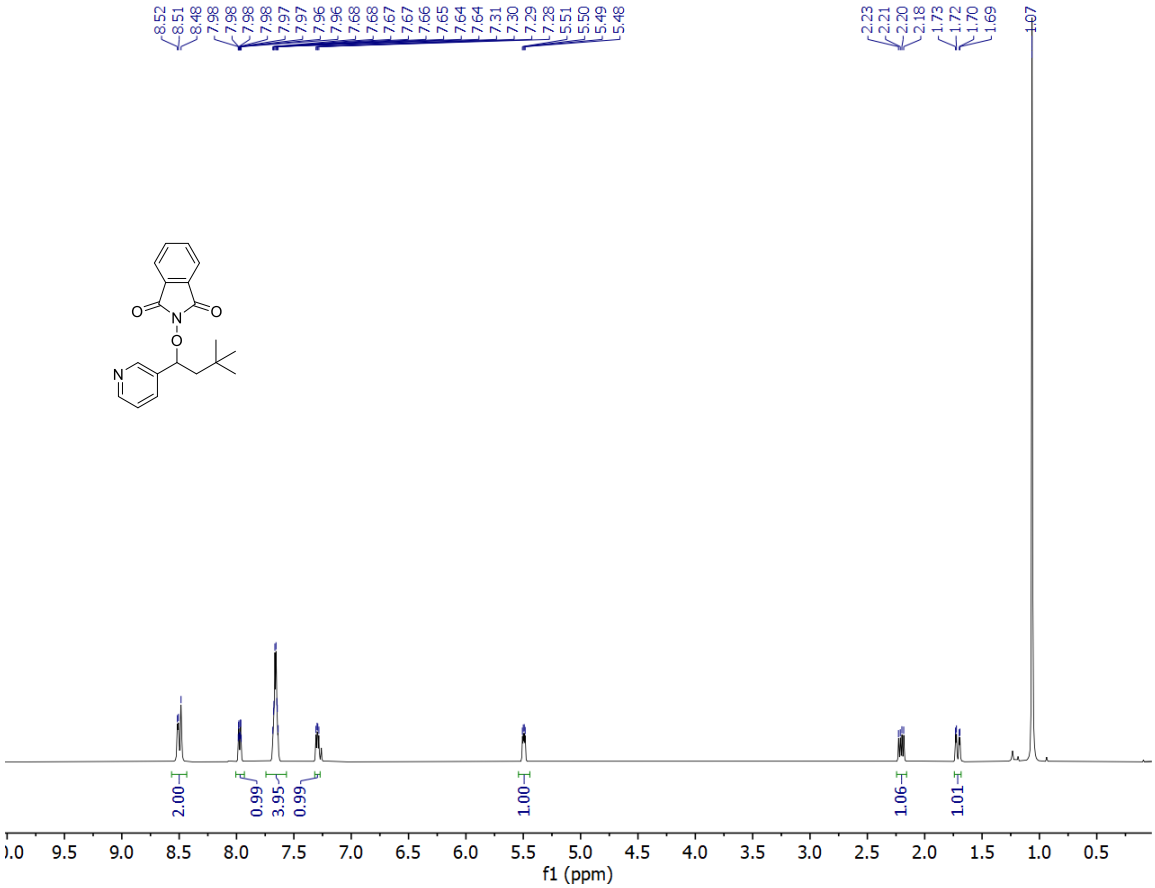

III-NS-484-2-Ome.2.fid
163.64
157.28
134.03
129.66
129.10
128.99
128.22
123.07
120.64
110.22
80.13
55.28
47.99
30.62
29.98
O
N
O
O
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

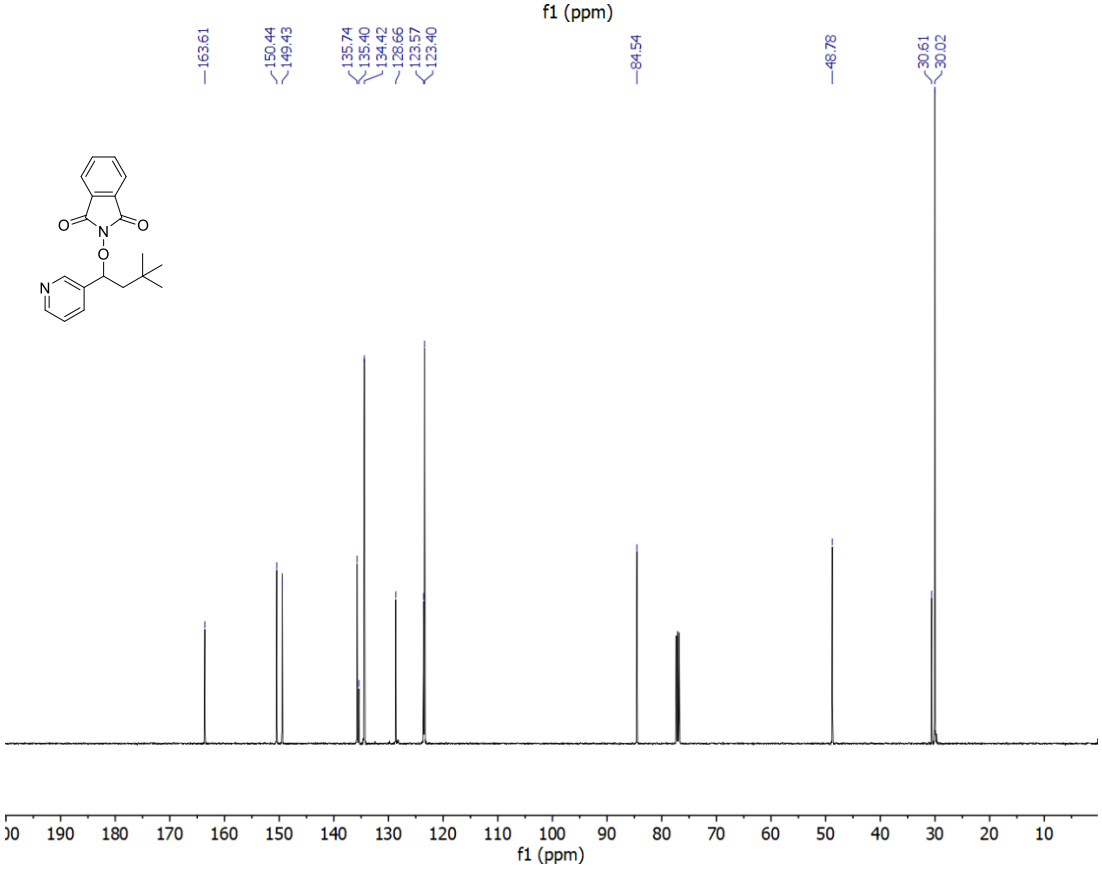

III-NS-431-p.1.fid
f1 (ppm)

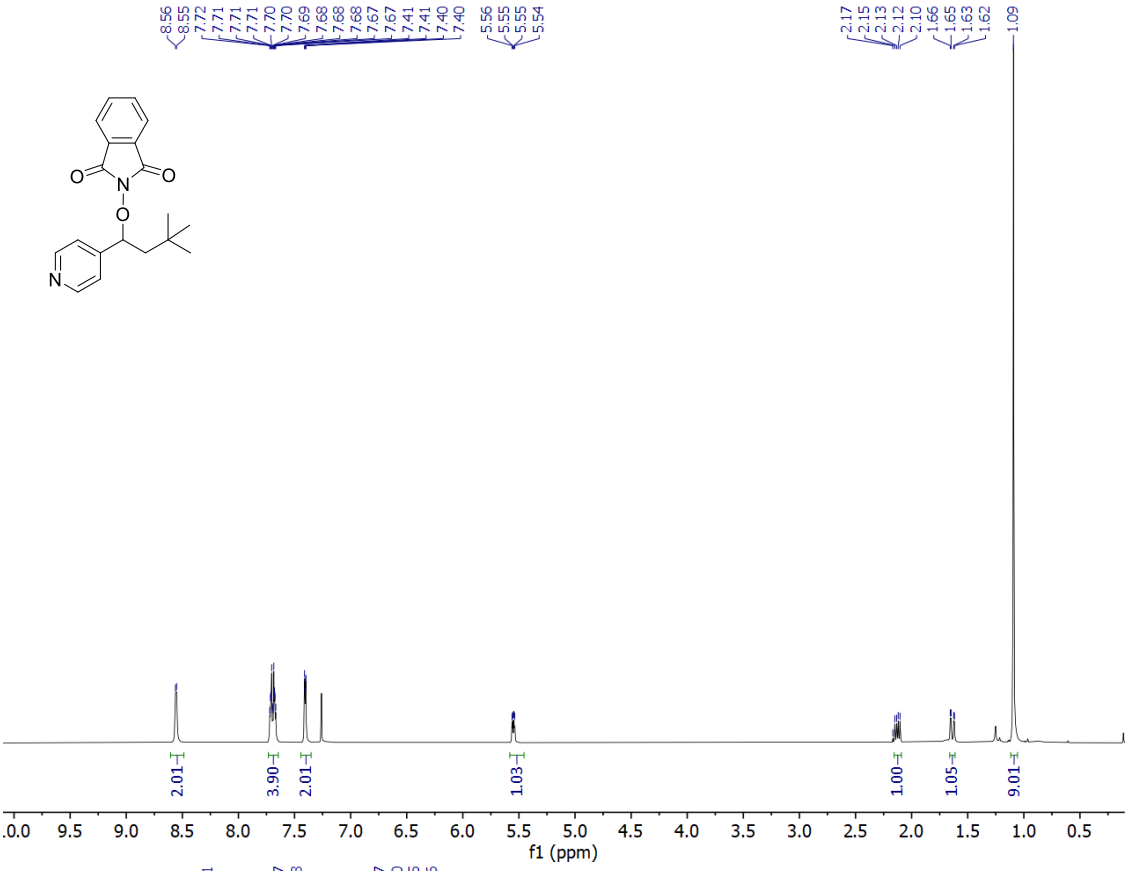

III-NS-431-p.2.fid
f1 (ppm)

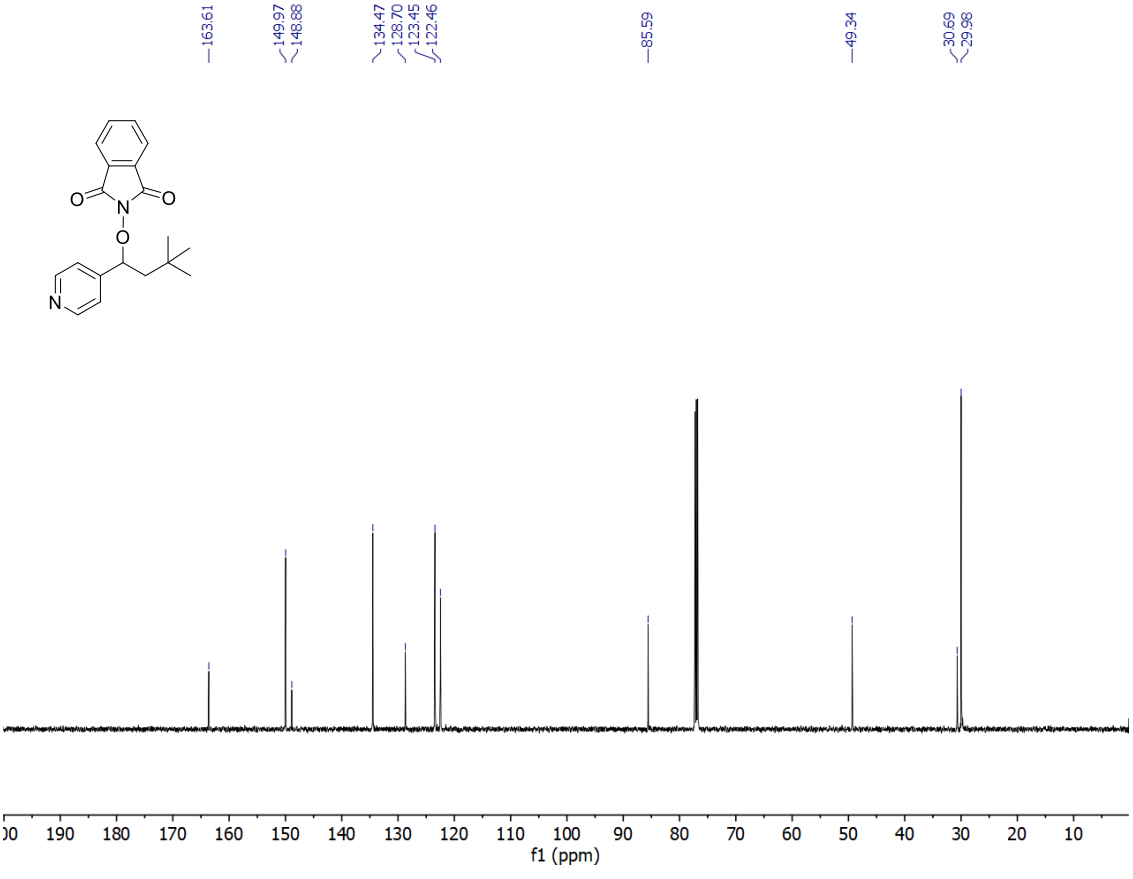

III-NS-469-P-Py.1.fid
8.49
8.49
8.49
8.48
8.48
8.48
8.48
7.75
7.75
7.72
7.69
7.68
7.23
7.22
7.22
7.21
7.21
7.20
5.60
5.59
5.59
5.58
2.22
2.21
2.19
2.18
1.88
1.87
1.85
1.84
1.12
0.85
5.28
2.06
0.92
1.13
1.20
9.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


III-NS-469-P-Py.2.fid
163.56
159.56
148.76
136.60
134.25
128.88
128.44
123.49
123.32
122.65
88.36
47.89
30.56
30.04
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

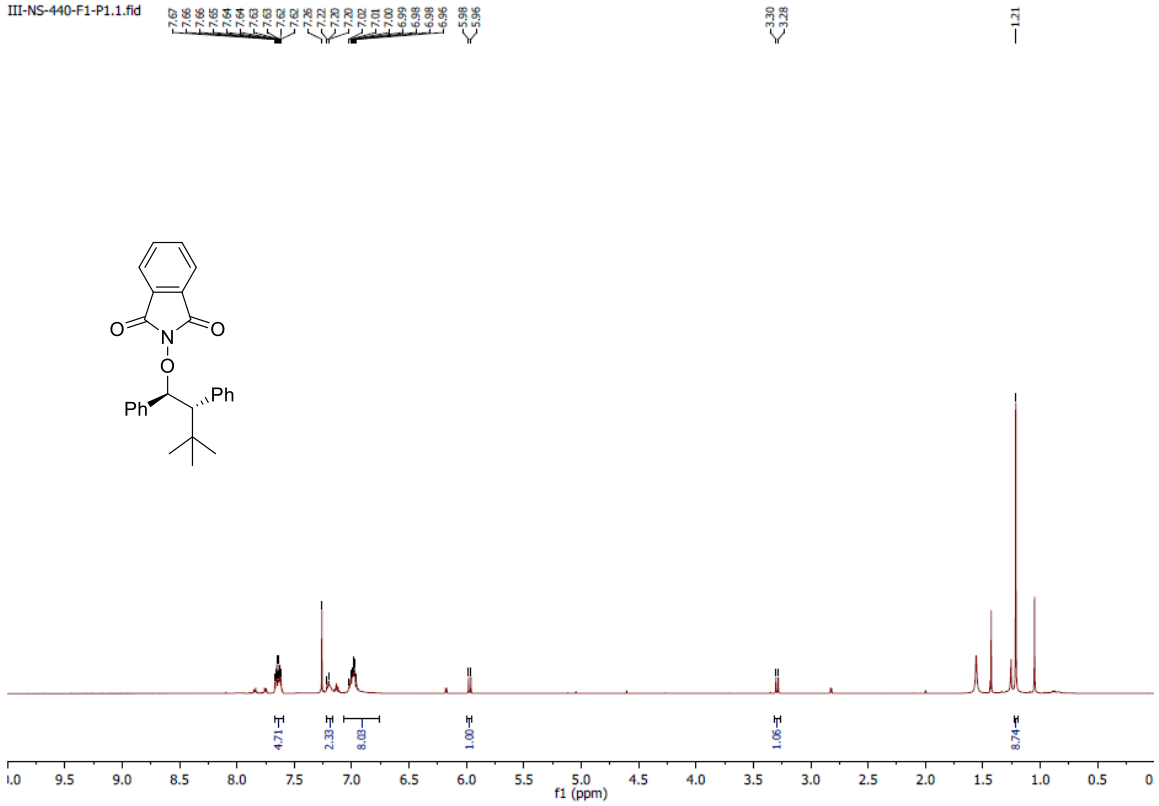

8.52
8.51
8.48
7.98
7.98
7.98
7.98
7.97
7.97
7.96
7.96
7.68
7.68
7.67
7.67
7.66
7.65
7.64
7.64
7.31
7.30
7.29
7.28
5.51
5.50
5.49
5.48
2.23
2.21
2.20
2.18
1.73
1.72
1.70
1.69
1.07
2.00
0.99
3.95
0.99
1.00
1.06
1.01
f1 (ppm)


163.61
150.44
149.43
135.74
135.40
134.42
128.66
123.57
123.40
84.54
48.78
30.61
30.02
f1 (ppm)

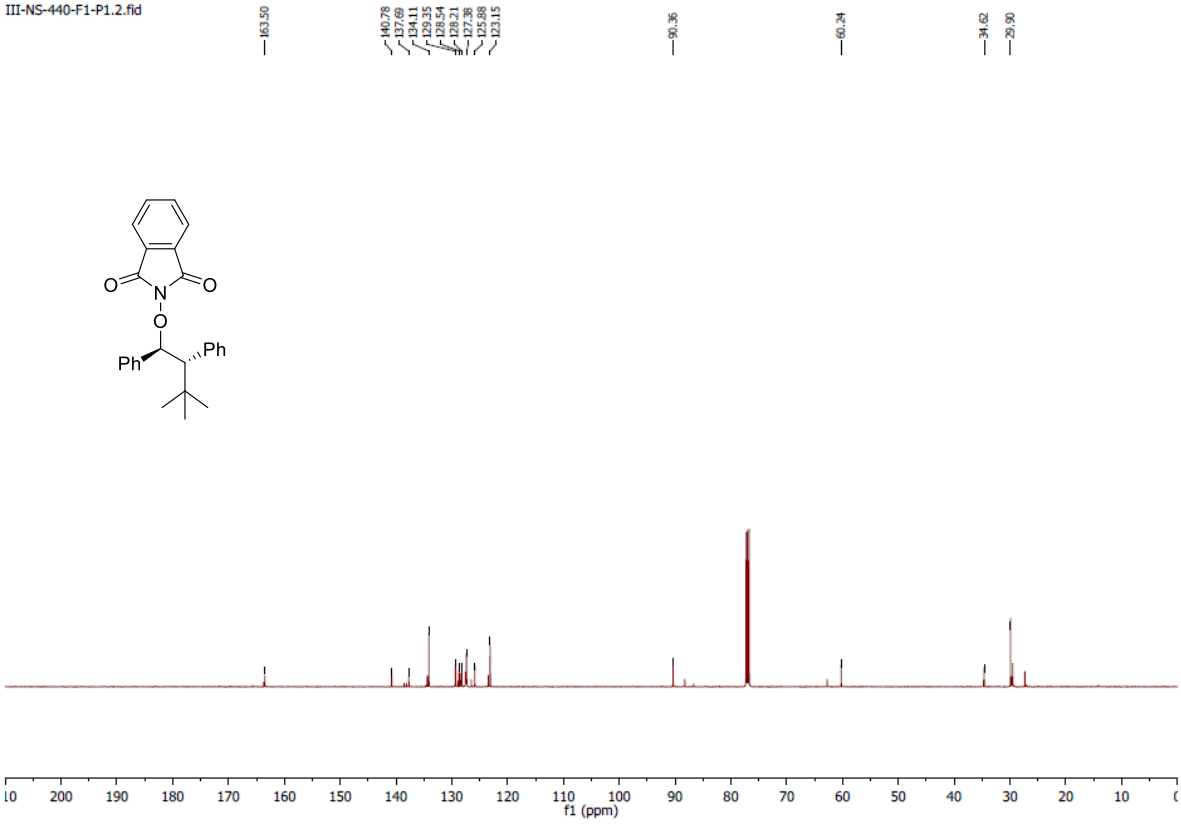

8.56
8.55
7.72
7.71
7.71
7.71
7.70
7.70
7.69
7.68
7.68
7.68
7.67
7.67
7.41
7.41
7.40
7.40
5.56
5.55
5.55
5.54
2.17
2.15
2.13
2.12
2.10
1.66
1.65
1.63
1.62
1.09
O
N
O
O
N
2.01
3.90
2.01
1.03
1.00
1.05
9.01
f1 (ppm)

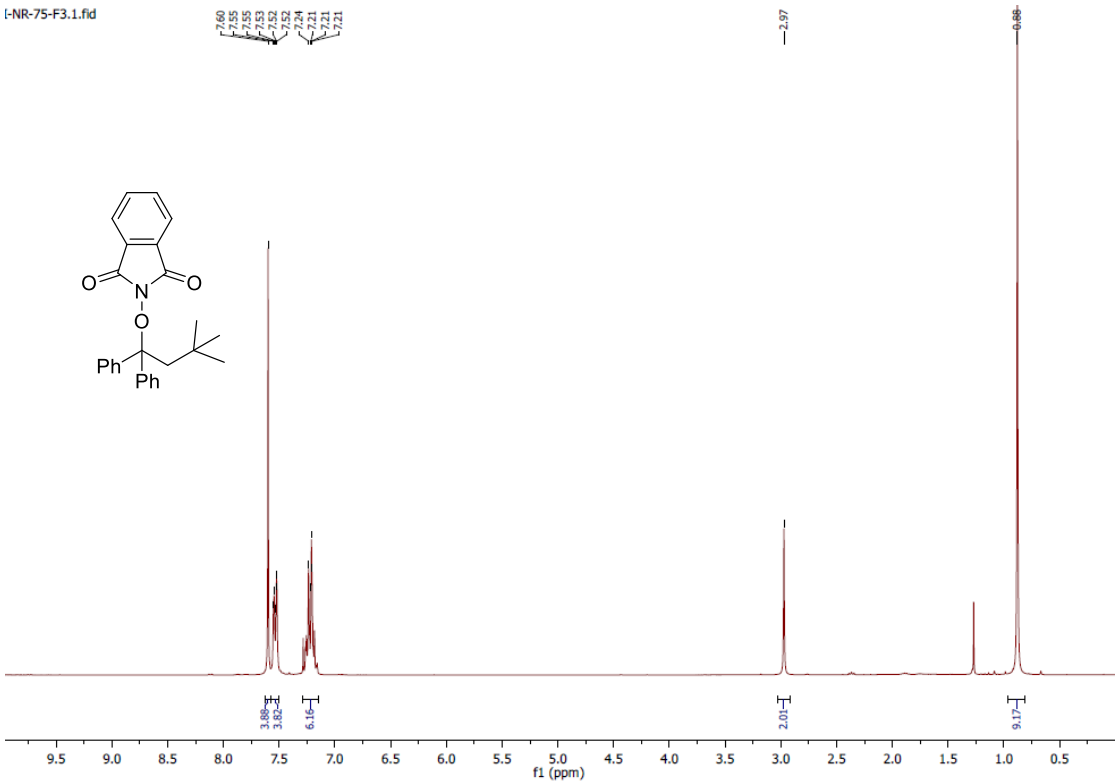

163.61
149.97
148.88
134.47
128.70
123.45
122.46
85.59
49.34
30.69
29.98
O
N
O
O
N
f1 (ppm)

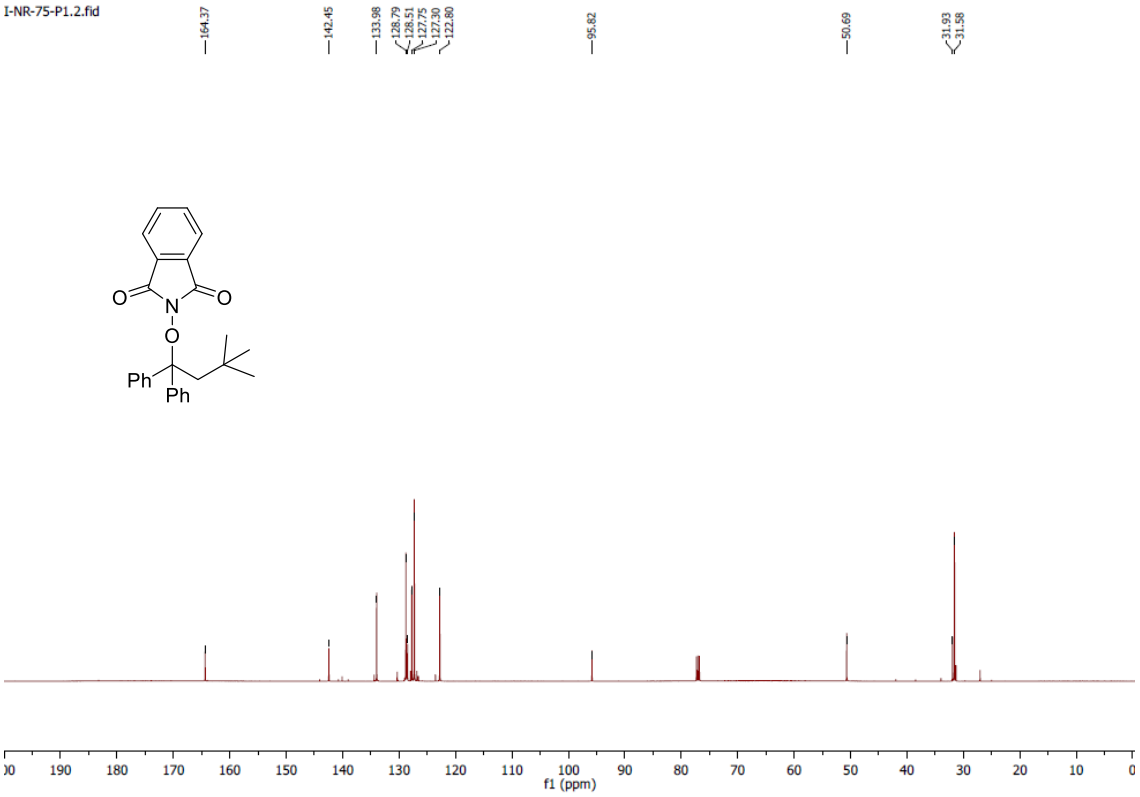
III-NS-440-F1-P1.1.fid

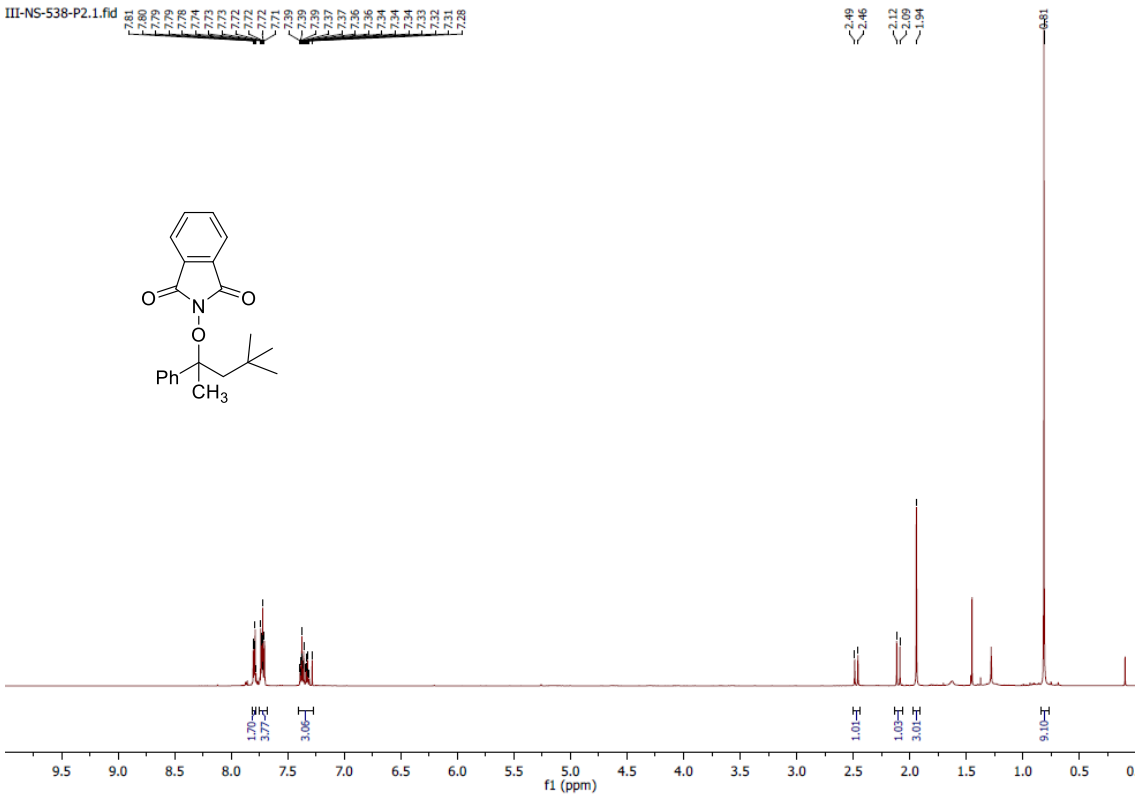


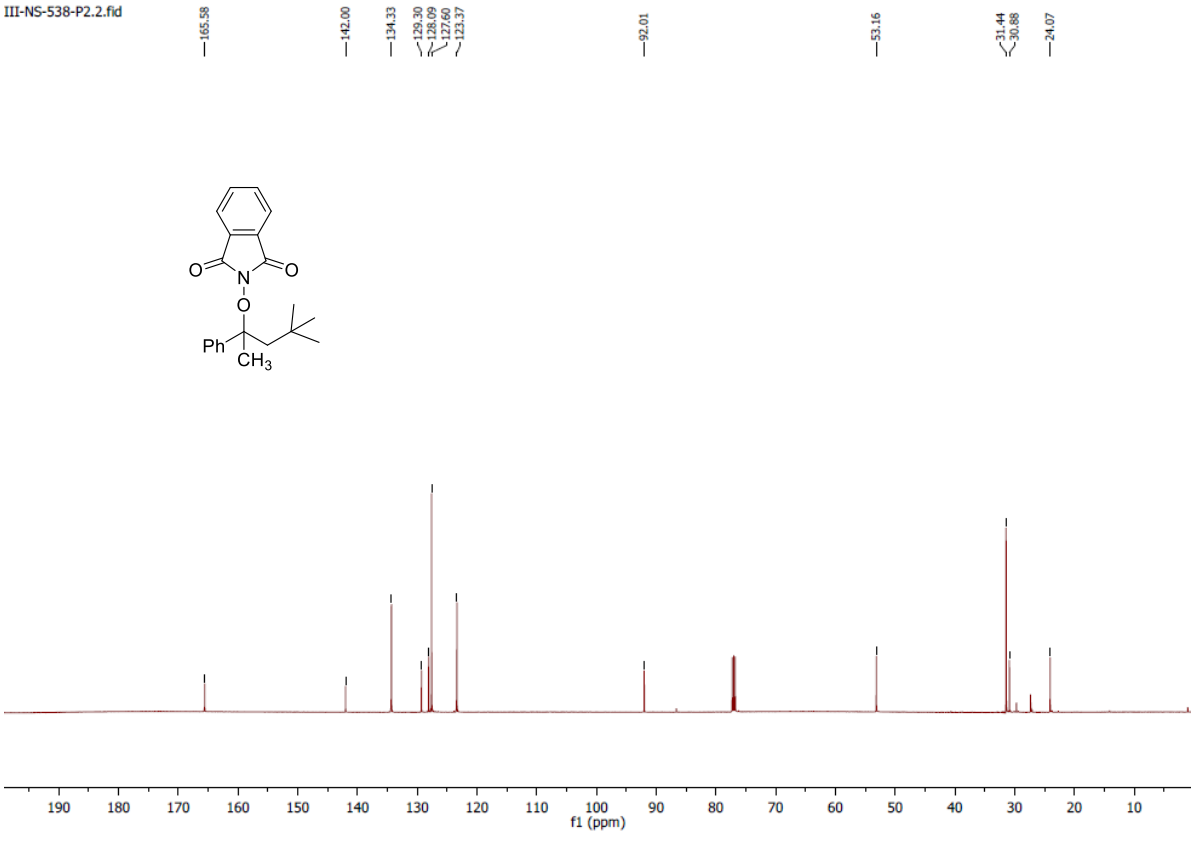
III-NS-440-F1-P1.2.fid



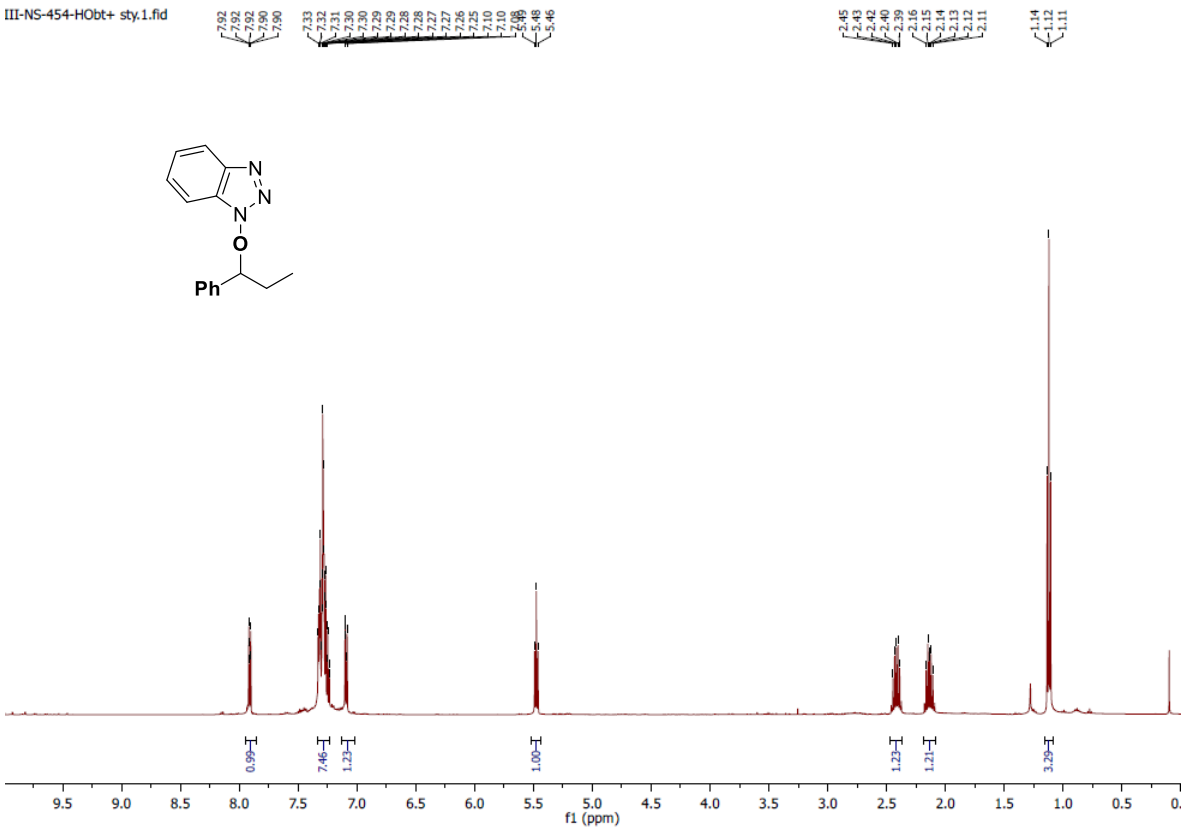

I-NR-75-F3.1.fid
7.60
7.55
7.55
7.53
7.52
7.52
7.24
7.21
7.21
7.21
2.97
0.68
O
N
O
O
Ph
Ph
3.88
3.82
6.16
2.01
9.17
f1 (ppm)


I-NR-75-P1.2.fid
164.37
142.45
133.98
128.79
128.51
127.75
127.30
122.80
95.82
50.69
31.93
31.58
O
N
O
O
Ph
Ph
f1 (ppm)

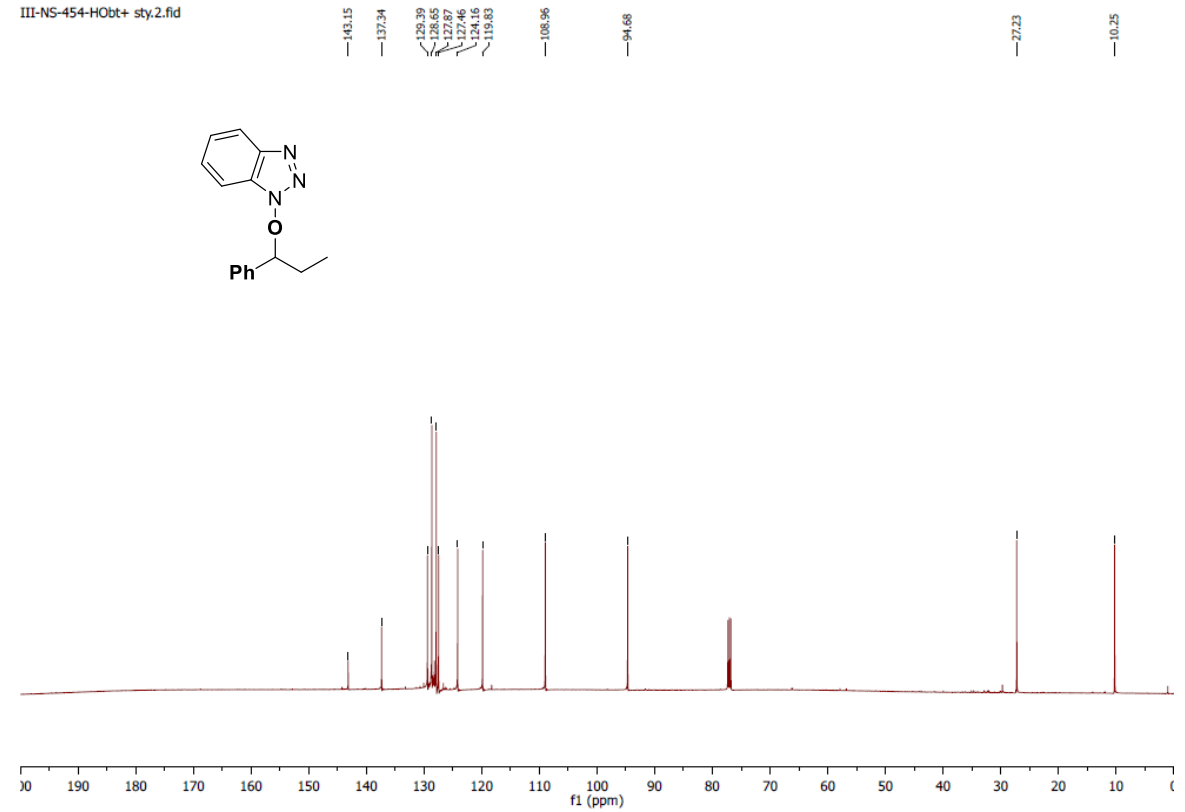

III-NS-538-P2.1.fid
7.81 7.80 7.79 7.79 7.78 7.74 7.73 7.73 7.72 7.72 7.72 7.71 7.39 7.39 7.39 7.37 7.37 7.36 7.34 7.34 7.33 7.32 7.31 7.28
2.49 2.46 2.12 2.09 1.94 0.81
O
N
O
O
Ph
CH3
1.70 3.77 3.06 1.01 1.03 3.01 9.10
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)


III-NS-538-P2.2.fid
165.58 142.00 134.33 129.30 128.09 127.60 123.37 92.01 53.16 31.44 30.88 24.07
O
N
O
O
Ph
CH3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

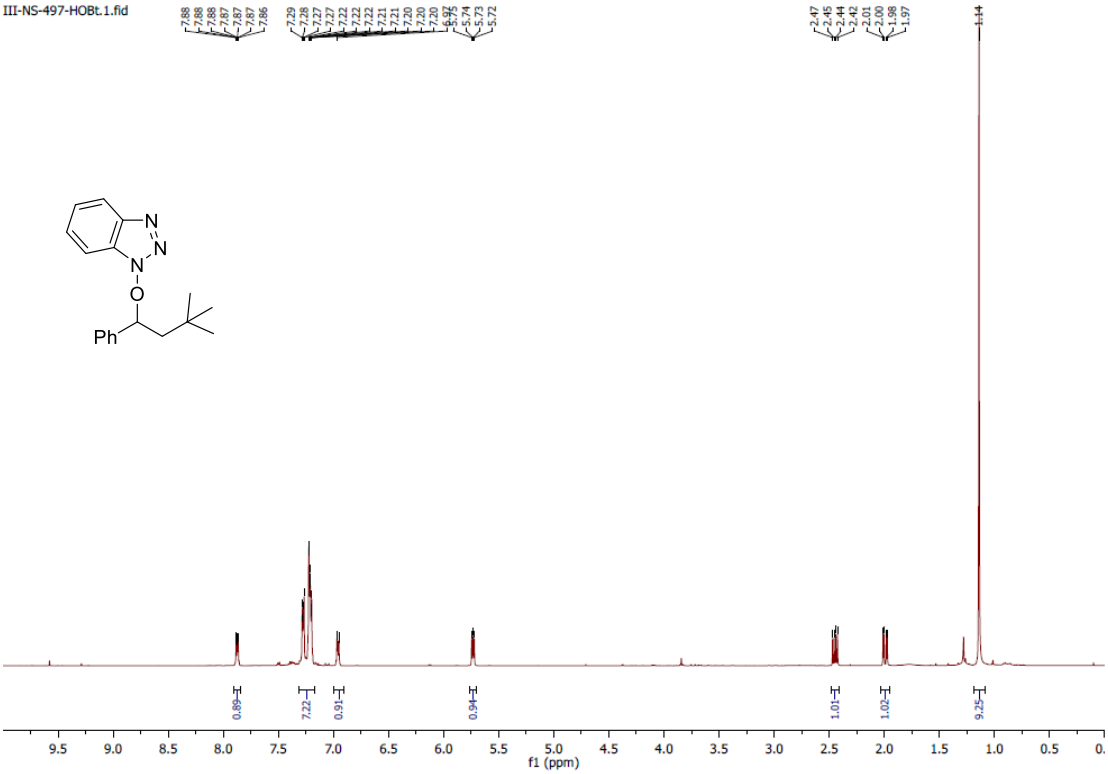
III-NS-454-HObt+ sty.1.fid



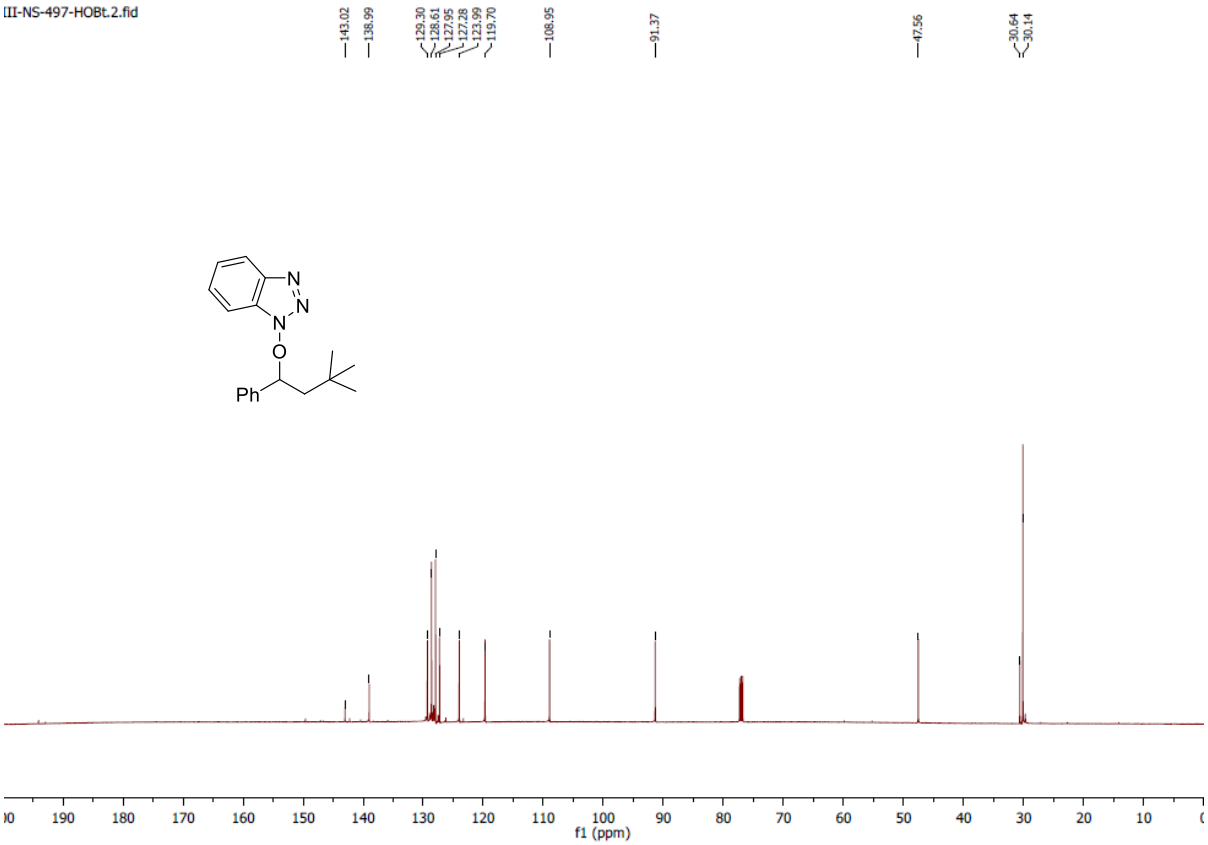
III-NS-454-HObt+ sty.2.fid

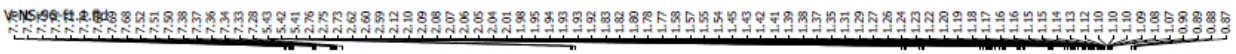


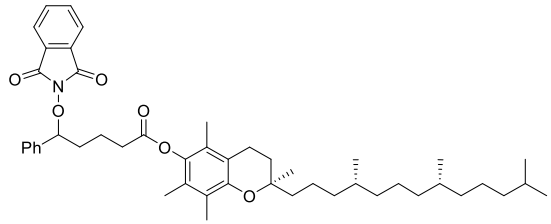
III-NS-497-HOBt.1.fid

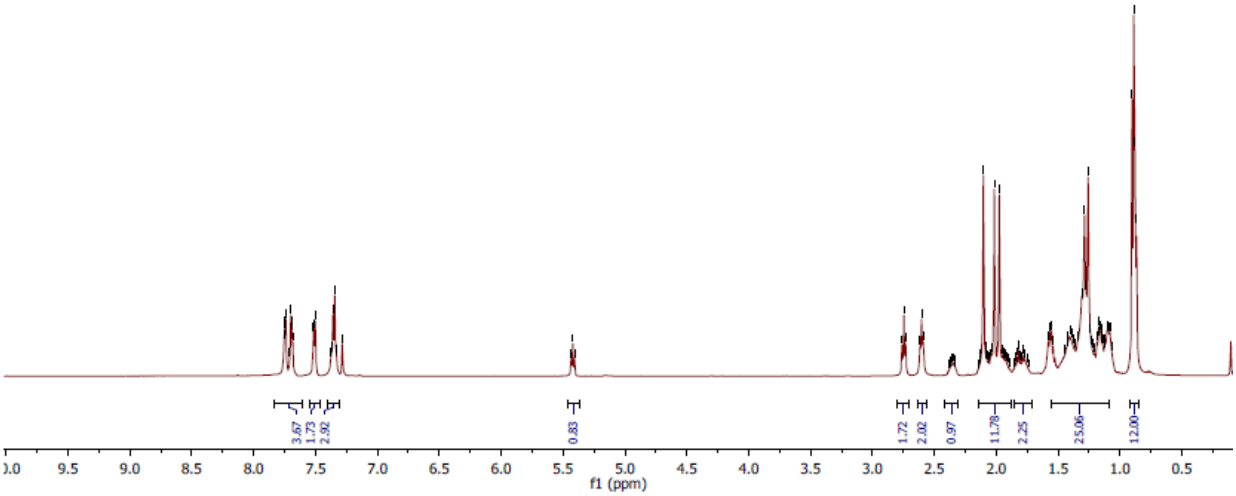


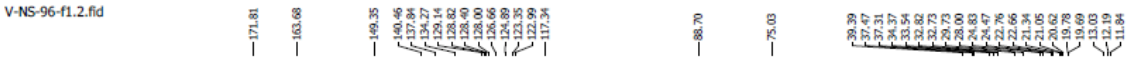
III-NS-497-HOBt.2.fid

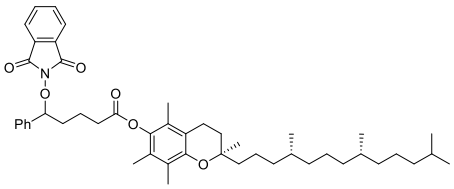


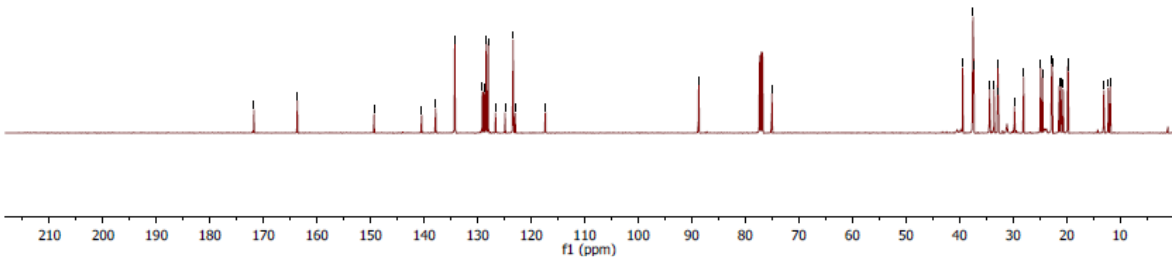


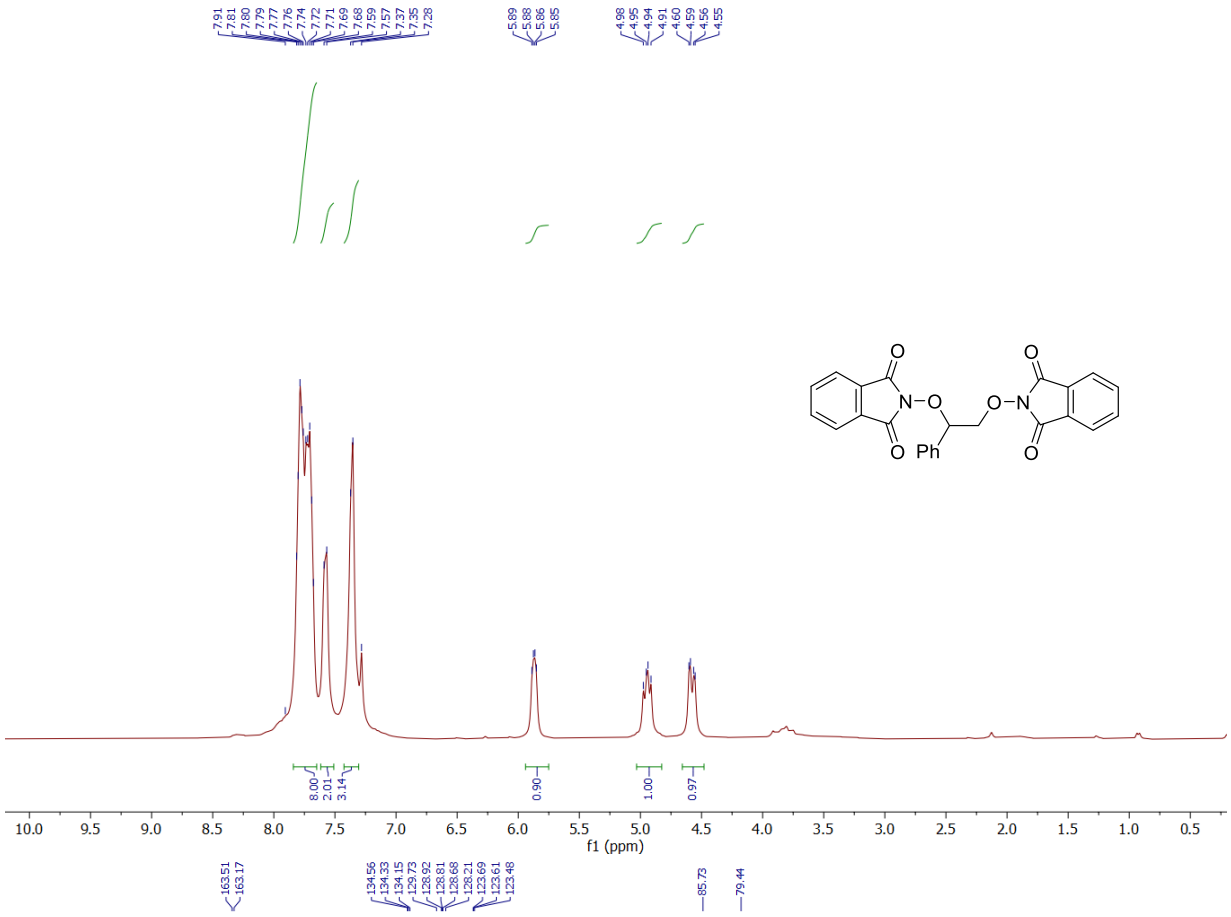

O
N
O
O
O
Ph
O
O

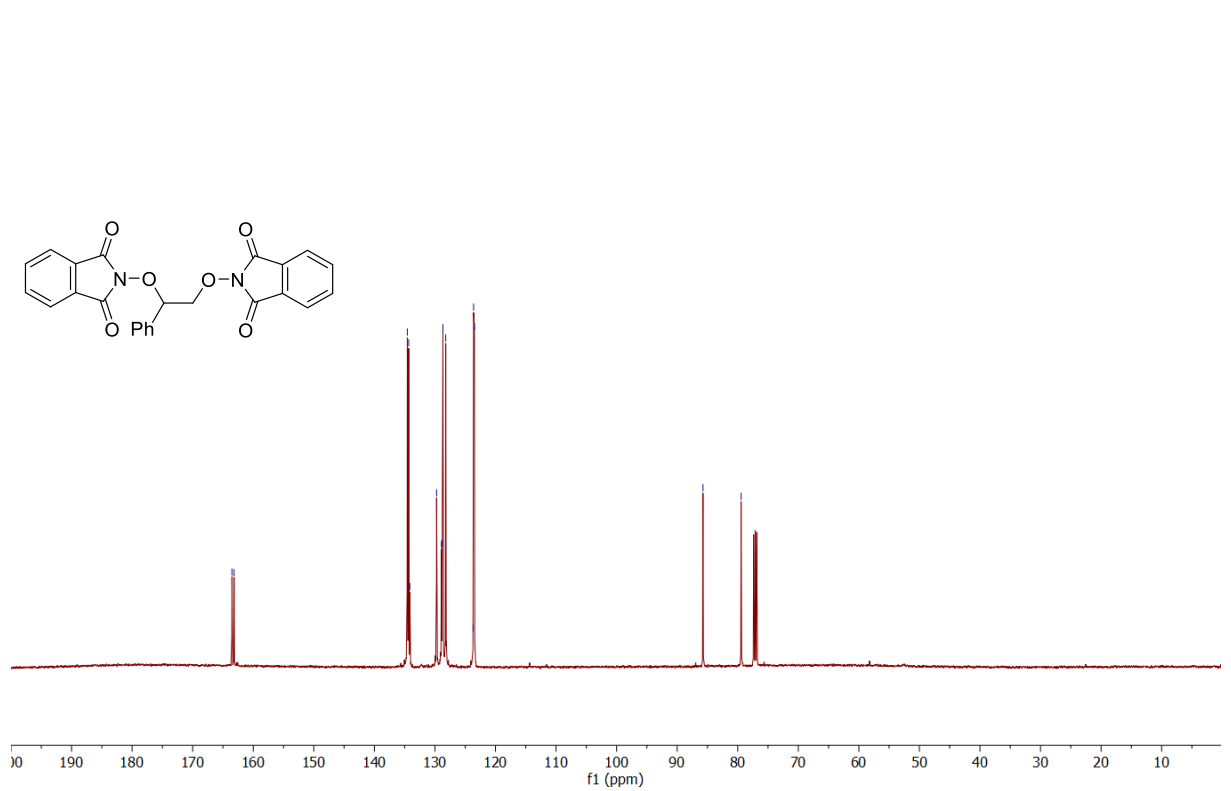

3.67
1.73
2.92
0.83
1.72
2.02
0.97
11.78
2.25
25.06
12.00
f1 (ppm)

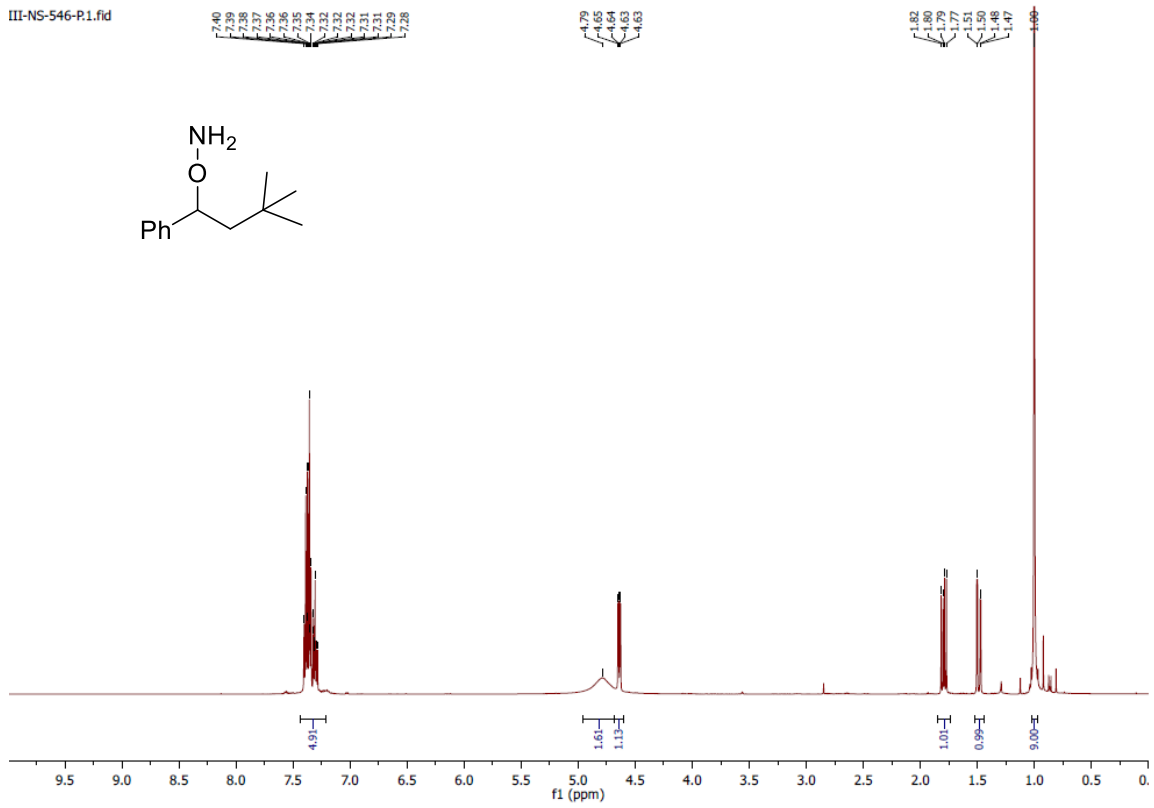

V-NS-96-f1.2.fid
171.81
163.68
149.35
140.46
137.84
134.27
129.14
128.82
128.40
128.00
126.66
124.89
123.35
122.99
117.34
88.70
75.03
39.39
37.47
37.31
34.37
33.54
32.82
32.73
29.73
28.00
24.83
24.47
22.76
22.66
21.34
21.05
20.62
19.78
19.69
13.03
12.19
11.84

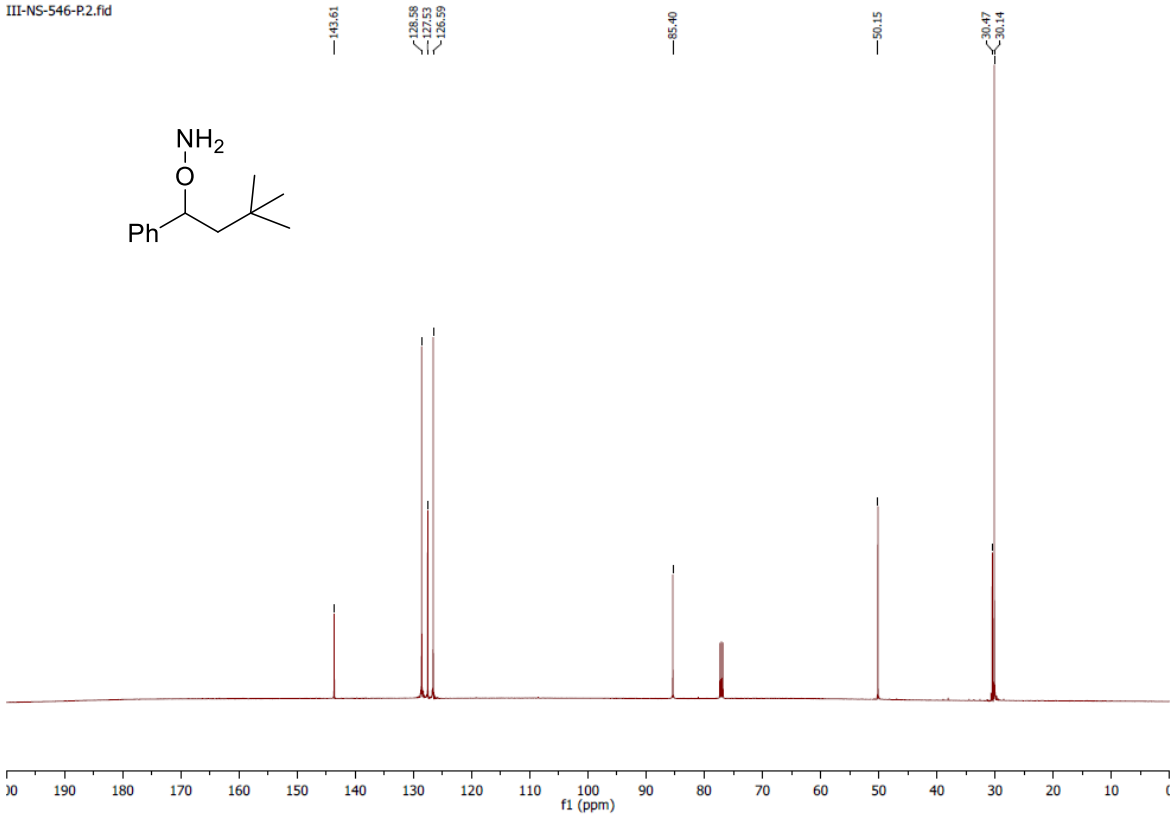

O
N
O
O
O
Ph
O
O


f1 (ppm)

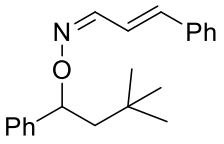

7.91
7.81
7.80
7.79
7.77
7.76
7.74
7.72
7.71
7.69
7.68
7.59
7.57
7.37
7.35
7.28
5.89
5.88
5.86
5.85
4.98
4.95
4.94
4.91
4.60
4.59
4.56
4.55
8.00
2.01
3.14
0.90
1.00
0.97
f1 (ppm)


163.51
163.17
134.56
134.33
134.15
129.73
128.92
128.81
128.68
128.21
123.69
123.61
123.48
85.73
79.44
f1 (ppm)

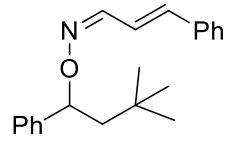

III-NS-546-P.1.fid
NH2
O
Ph
f1 (ppm)


III-NS-546-P.2.fid
NH2
O
Ph
f1 (ppm)

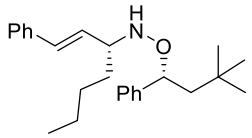
III-NS-548-P1.1.fid



III-NS-548-P1.2.fid



III-NS-566-P.1.fid



III-NS-566-P.3.fid