Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Ruthenium-Catalyzed Oxidative Coupling of Vinylene Carbonate with Isoxazoles: Access to Fused Anthranils

Pravin Kumar and Manmohan Kapur*

Department of Chemistry, Indian Institute of Science Education and Research Bhopal, Bhopal Bypass Road, Bhauri, Bhopal 462066, MP, India

mk@iiserb.ac.in

Table of contents

Experimental:

1 General Methods:

All commercially available compounds were used without purification. Unless otherwise noted, all reactions were performed in oven-dried glassware. All reactions were run under argon or nitrogen atmosphere. All solvents used in the reactions were purified before use. Dry tetrahydrofuran, toluene and diethyl ether were distilled from sodium and benzophenone, whereas dry dimethyl sulfoxide and dimethyl formamide were distilled under reduced pressure from CaH_2.[1] Petroleum ether with a boiling range of 40–60 °C was used. Melting points are uncorrected. ^{1}H, ^{13}C and ^{19}F NMR: Recorded on Bruker Avance III 400 MHz NMR Spectrometer, Bruker Avance III 500 MHz NMR Spectrometer and Bruker Avance III 700 MHz NMR Spectrometer; spectra were recorded at 295 K in $CDCl_3$; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (^{1}H δ 7.26; ^{13}C δ 77.0). HRMS: Bruker Daltonics MicroTOF Q-II with electron spray ionization (ESI) and Atmospheric Pressure Chemical Ionization (APCI). GC–HRMS: Performed on Agilent 7200 GC–QToF (with Electron Impact (EI), 70eV) with 7890A GC using DB-5 column. GC–LRMS: Performed on Agilent 7890A GC with Agilent 5975C MS (EI 70 eV) using DB–5 column. IR: Perkin Elmer Spectrum BX FTIR, Shimadzu IRAffinity–1 FTIR and were recorded as thin films between KBr plates. Single-crystal X-ray diffraction data was collected using a Bruker SMART APEX II CCD diffractometer with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation at low temperature.

(2) General procedures:

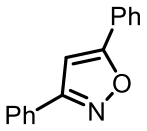
I) Preparation of 3,5-diaryl isoxazoles:

Ia) General procedure for the synthesis of oximes:[2] $NaHCO_3$ (1.2 equiv, 12.97 mmol) was added to a solution of $NH_2OH.HCl$ (1.2 equiv, 12.97 mmol) in water (20 mL). The resulting solution was then added to a vigorously stirred suspension of the aldehyde (1.0 equiv, 10.81 mmol) in EtOH (20 mL) at room temperature. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was concentrated under reduced pressure to remove the solvent and the residue was diluted with CH_2Cl_2 and washed with brine. The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was used as such without any purification.

Ib) General procedure for the synthesis of 3, 5-diaryl isoxazoles from the aldoxime:[2]

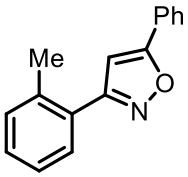
Aryl acetylene (1.5 equiv, 5.25 mmol) was added to a solution of aldoxime (1.0 equiv, 3.5 mmol) in water (15 mL) at room temperature. KCl (1.0 equiv, 3.5 mmol) was added portion-wise followed by oxone (1.5 equiv, 5.25 mmol). The resulting mixture was stirred at room temperature for 12 h till the reaction was found to be complete. The mixture was poured into a separatory funnel and extracted with ethyl acetate, followed by washing with brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to result in the desired product.

3, 5-diphenylisoxazole (1a):[2,]



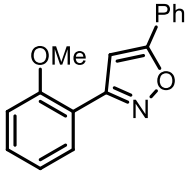
Prepared according to the general procedure and the title compound was isolated in 73% (564 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

5-phenyl-3-(*o*-tolyl)isoxazole (1b):[2]



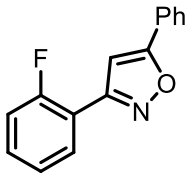
Prepared according to the general procedure and the title compound was isolated in 60% (493 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(2-methoxyphenyl)-5-phenylisoxazole (1c):[2]



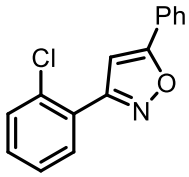
Prepared according to the general procedure and the title compound was isolated in 62% (545 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(2-fluorophenyl)-5-phenylisoxazole (1d):[2]



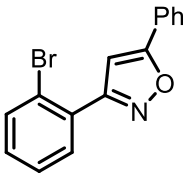
Prepared according to the general procedure and the title compound was isolated in 52% (435 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(2-chlorophenyl)-5-phenylisoxazole (1e):[2]



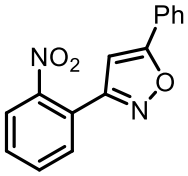
Prepared according to the general procedure and the title compound was isolated in 47% (420 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(2-bromophenyl)-5-phenylisoxazole (1f):[2]



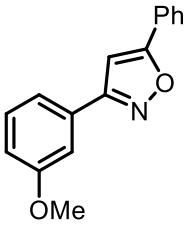
Prepared according to the general procedure and the title compound was isolated in 53% (556 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(2-nitrophenyl)-5-phenylisoxazole (1g):[2]



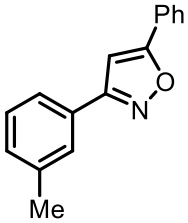
Prepared according to the general procedure and the title compound was isolated in 52% (484 mg) yield; Spectral data obtained were in good agreement with those reported in the literature.

3-(3-methoxyphenyl)-5-phenylisoxazole (1h):[2]



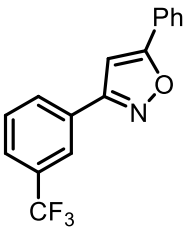
Prepared according to the general procedure and the title compound was isolated in 56% (493 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

5-phenyl-3-(*m*-tolyl)isoxazole (1i):[2]



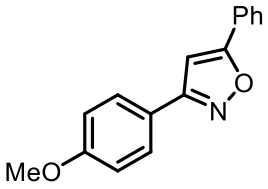
Prepared according to the general procedure and the title compound was isolated in 52% (428 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

5-phenyl-3-(3-(trifluoromethyl)phenyl)isoxazole (1j):[2]



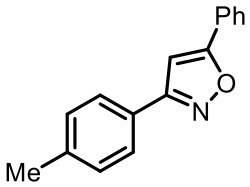
Prepared according to the general procedure and the title compound was isolated in 46% (465 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-methoxyphenyl)-5-phenylisoxazole (1k):[2]



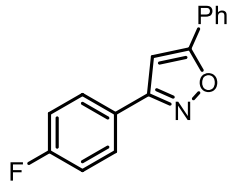
Prepared according to the general procedure and the title compound was isolated in 76% (667 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

5-phenyl-3-(*p*-tolyl)isoxazole (1l):[2]



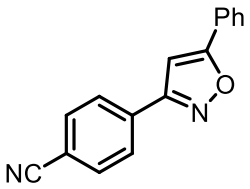
Prepared according to the general procedure and the title compound was isolated in 75% (618 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-fluorophenyl)-5-phenylisoxazole (1m):[2]



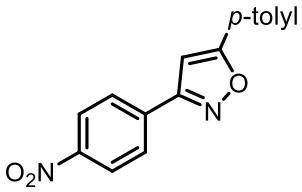
Prepared according to the general procedure and the title compound was isolated in 51% (427 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

4-(5-phenylisoxazol-3-yl)benzonitrile (1n):[2]



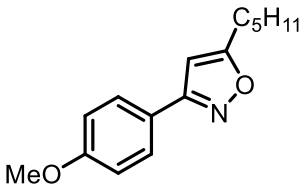
Prepared according to the general procedure and the title compound was isolated in 45% (388 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-nitrophenyl)-5-phenylisoxazole (1o):[2]



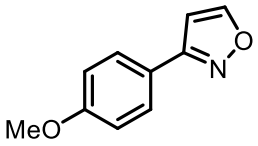
Prepared according to the general procedure and the title compound was isolated in 35% (343 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-methoxyphenyl)-5-pentylisoxazole (1p):[2,3]



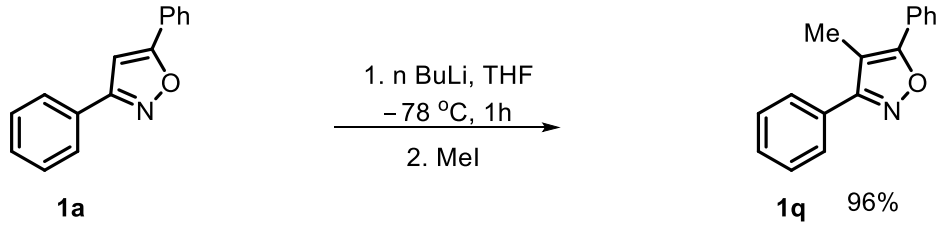
Prepared according to the general procedure and the title compound was isolated in 48% (412 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-methoxyphenyl)isoxazole (1q):[2,4]



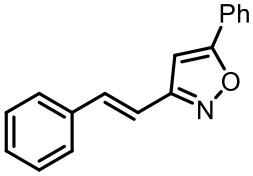
Prepared according to reported literature procedure and the title compound was isolated in 94% (332 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

4-methyl-3,5-diphenylisoxazole (1r):[5]



Procedure: To a stirred solution of isoxazole **1a** (1.0 equiv, 0.9 mmol) in THF (20 mL) was added dropwise a solution of *n*-butyllithium (1.6 mL of 2.0 M in THF, 3.16 mmol) at −78 °C. The resulting reaction mixture was stirred at this temperature for 1 h and quenched with MeI (0.20 mL) to give the desired compound (194 mg) in 90% yield. Spectral data obtained were in good agreement with those reported in the literature.

(*E*)-5-phenyl-3-styrylisoxazole (1s):[2]



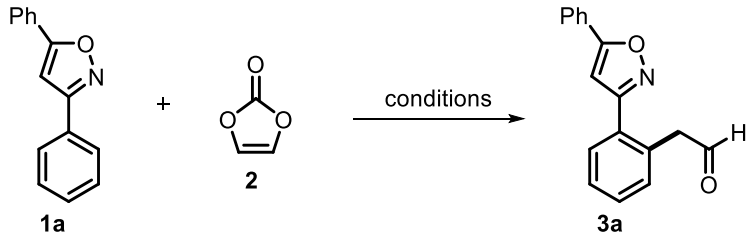
Prepared according to the general procedure and the title compound was isolated in 57% (493 mg) yield. Spectral data obtained were in good agreement with that reported in the literature.

3) General procedure for the Ru-catalyzed C-H formyl methylation at 3-aryl ring of isoxazoles:

In a pressure tube equipped with a stir bar, isoxazole (1.0 equiv, 0.1 mmol) was dissolved in HFIP (1.0 mL). The reaction mixture was degassed with nitrogen for 10 min followed by the addition of the vinylene carbonate (2.0 equiv, 0.20 mmol), $[RuCl_2(p\text{-cym})]_2$ (5 mol%, 0.005

mmol), $AgSbF_6$ (0.50 equiv, 0.05 mmol) and PivOH (0.50 equiv, 0.05 mmol). The tube was fitted with a Teflon screw cap under a nitrogen flow, and the reaction mixture was heated to 90 ^oC and allowed to stir for 24-30 h at that temperature. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was washed with a saturated solution of $NaHCO_3$ and brine. The organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to result in the desired product.

Table 1: Optimization studies[a,b]



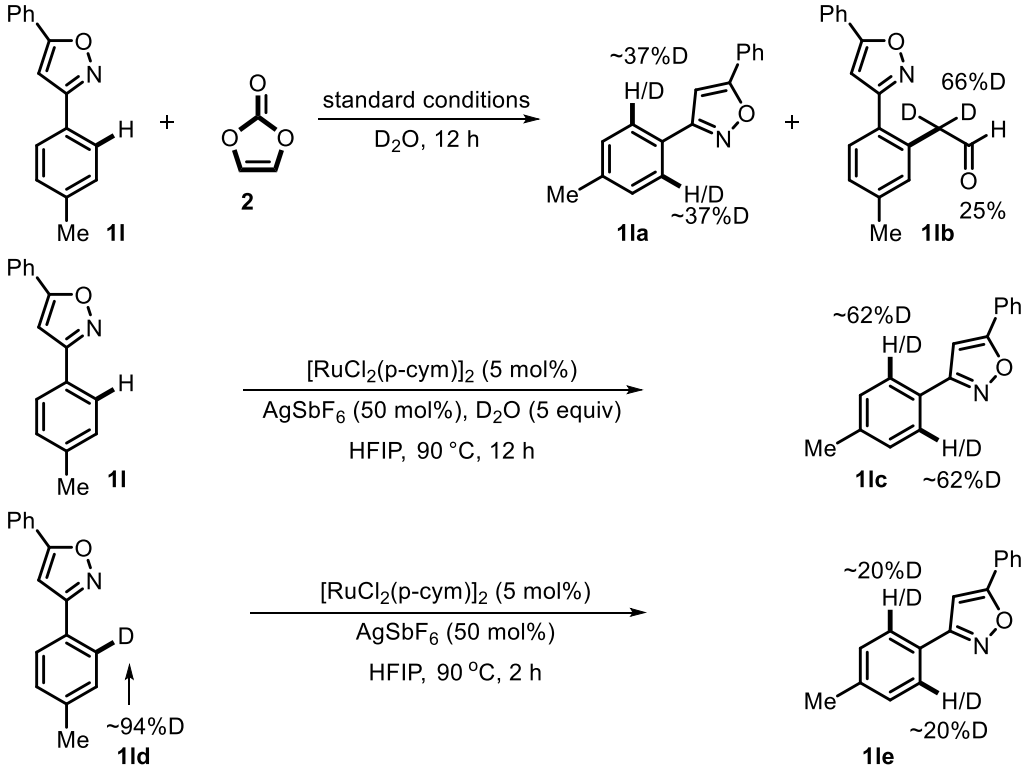
Entry	Conditions	Yield[b] (%)
1	$[RhCl_2Cp^*]_2$ (2 mol%)/$AgSbF_6$ (20 mol%)/DCE/24 h	30
2	$[RhCl_2Cp^*]_2$ (2 mol%)/$AgSbF_6$ (50 mol%)/DCE/24 h	35
3	$[Cp^*Co(CO)I_2]$ (10 mol%)/$AgSbF_6$ (20 mol%)/DCE/24 h	n.d.
4	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (20 mol%)/DCE/24 h	15
5	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (20 mol%)/TFE/24 h	20
6	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (20 mol%)/HFIP/24 h	30
7	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (20 mol%)/*t*-BuOH/24 h	trace
8	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (20 mol%)/MeOH/24 h	n.d.
9	$[RuCl_2(p\text{-cym})]_2$/KPF_6 (10 mol%)/HFIP/24 h	n.d.
10	$[RuCl_2(p\text{-cym})]_2$/AgOAc (20 mol%)/HFIP/24 h	trace
11	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (20 mol%)/AcOH (10 mol%)/HFIP/24 h	trace
12	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (20 mol%)/AgOAc (10 mol%)/HFIP/24 h	trace
13	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (50 mol%)/HFIP/24 h	70
14	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (50 mol%)/AcOH (50 mol%)/HFIP/24 h	71
15	**$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$ (50 mol%)/PivOH (50 mol%)/HFIP/24 h**	**75**
16	$AgSbF_6$ (50 mol%)/HFIP/24 h	n.d.

[a]Unless otherwise specified, all reactions were carried out using **1a** (0.10 mmol), **2** (0.20 mmol), catalyst (0.005 mmol.), additive (0.05 mmol.) PivOH (0.05 mmol.) at 90 ^oC for 24 h under N_2; [b]Isolated yields; n.d. = Not detected.

3.1) Mechanistic studies

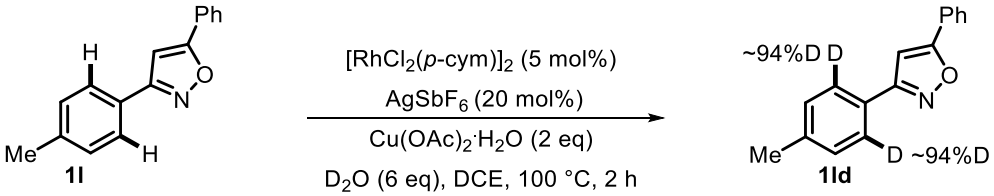
3.1.1) Deuterium exchange experiment:

To check the reversibility of C-H bond cleavage, we performed the reversibility studies. These studies revealed that the C-H bond cleavage is a reversible step.



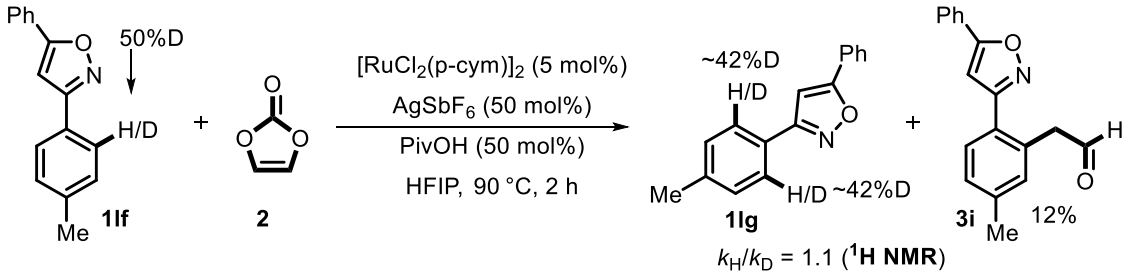
Procedure: In a pressure tube equipped with a stir bar, isoxazole (1.0 equiv, 0.1 mmol) was dissolved in HFIP (1.0 mL). The reaction mixture was degassed with nitrogen for 10 min followed by the addition of the vinylene carbonate (2.0 equiv, 0.20 mmol), $[RuCl_2(p\text{-cym})]_2$ (5 mol%, 0.005 mmol), $AgSbF_6$ (0.50 equiv, 0.05 mmol), and D_2O (5.0 equiv, 0.50 mmol) The tube was fitted with a Teflon screw cap under a nitrogen flow, and the reaction mixture was heated to 90 °C and allowed to stir for 2-12 h. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was washed with saturated solution of $NaHCO_3$ and brine. The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to result in the desired product. The same procedure was followed for the other reaction in which no vinylene carbonate was added to the reaction mixture.

3.1.2) Deuteration at the *ortho*-position of 3-aryl ring of isoxazole:[2]



Procedure: In a pressure tube equipped with a stir bar, isoxazole (1.0 equiv, 0.452 mmol) was dissolved in dry dichloroethane (2.0 mL). The reaction mixture was degassed with nitrogen for 10 min followed by the addition of $[RuCl_2(p\text{-cym})]_2$ (5 mol%, 0.0226 mmol), $AgSbF_6$ (0.20 equiv, 0.09 mmol), $Cu(OAc)_2.H_2O$ (2.0 equiv, 0.90 mmol) and D_2O (6.0 equiv, 2.71mmol). The tube was fitted with a Teflon screw cap under a nitrogen flow, and the reaction mixture was heated to 100 ^oC and allowed to stir for 2 h. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was washed with a saturated solution of $NaHCO_3$ and brine. The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to result in the desired deuterated product. This experiment was repeated till complete deuteration of the desired compound.

3.1.3) Determination of the kinetic isotope effect (k_H/k_D): (Competition experiment):

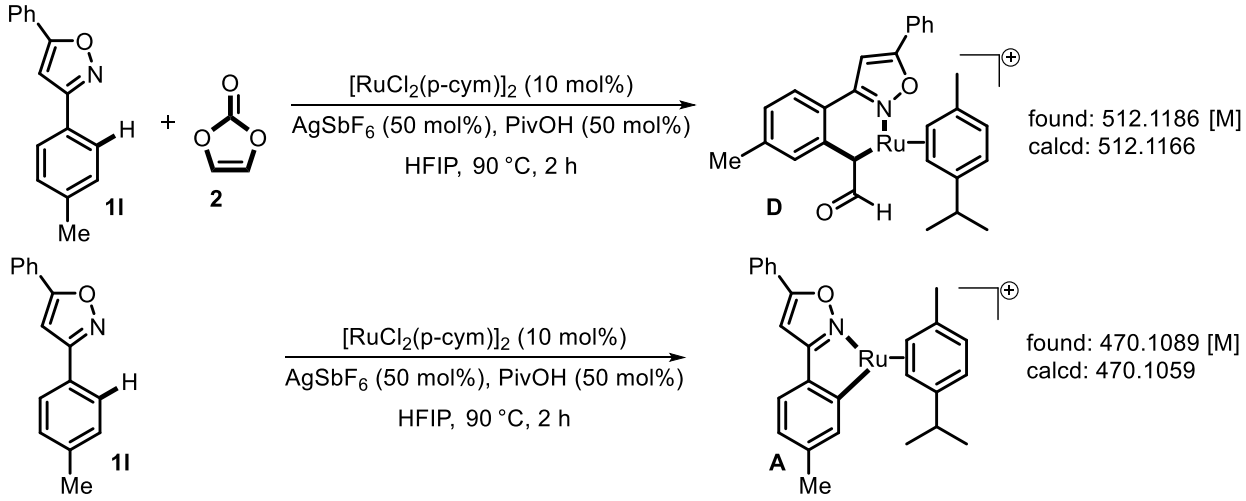


Procedure: In a pressure tube equipped with a stir bar, isoxazole 1lf (1.0 equiv, 0.1 mmol) was dissolved in HFIP (1.0 mL). The reaction mixture was stirred for 10 min followed by the addition of the vinylene carbonate (2.0 equiv, 0.20 mmol), $[RuCl_2(p\text{-cym})]_2$ (0.05 equiv, 0.005 mmol), $AgSbF_6$ (0.50 equiv, 0.05 mmol) and PivOH (0.50 equiv, 0.05 mmol). The tube was fitted with a Teflon screw cap under nitrogen flow, and the reaction mixture was heated to 90 ^oC and allowed to stir for 2 h. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was washed with a saturated solution of $NaHCO_3$ and brine. The organic extract was dried over anhydrous

Na_2SO_4, filtered, and concentrated under reduced pressure and the remaining starting materials (C-H and C-D substrates) were recovered and analyzed by ^{1}H NMR. This experiment indicated a value of 1.1 for k_H/k_D, which in turn indicated that the C-H metalation step may not be rate-limiting.

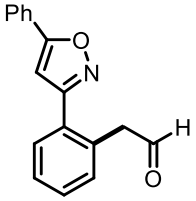
3.1.4) Mass spectrometry studies for detecting intermediates:

Procedure: In a pressure tube equipped with a stir bar, the isoxazole (1.0 equiv, 0.1 mmol) was dissolved in HFIP (1.0 mL). The reaction mixture was stirred for 10 min followed by the addition of the vinylene carbonate (2.0 equiv, 0.20 mmol), $[RuCl_2(p\text{-cym})]_2$ (0.1 equiv, 0.01 mmol), $AgSbF_6$ (0.50 equiv, 0.05 mmol) and PivOH (0.50 equiv, 0.05 mmol). The tube was fitted with a Teflon screw cap under nitrogen flow, and the reaction mixture was heated to 90 ^{o}C and allowed to stir for 10 min. This reaction mixture was subjected to mass spectrometry (ESI-HRMS). The same procedure was followed for another reaction in which no coupling partner was added.



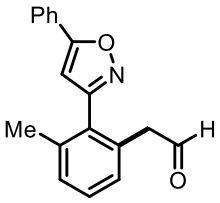
Analytical data:

2-(2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3a)



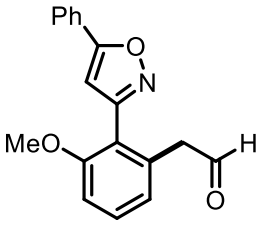
Yield: 75 % (20 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (700 MHz, $CDCl_3$): δ 9.85 (s, 1H), 7.86 (d, J = 7.4 Hz, 2H), 7.67 (d, J = 7.3 Hz, 1H), 7.54 – 7.45 (m, 5H), 7.36 (d, J = 7.3 Hz, 1H), 6.76 (s, 1H), 4.11 (s, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.64, 170.01, 163.02, 132.08, 131.60, 130.40, 129.98, 129.89, 129.26, 129.08, 127.85, 127.19, 125.89, 99.68, 49.26; **ESI−HRMS**: Calculated for $C_{17}H_{14}NO_2^+$ $[M+H]^+$ 264.1019, found 264.0996.

2-(3-methyl-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3b):

Yield: 69% (19 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); 

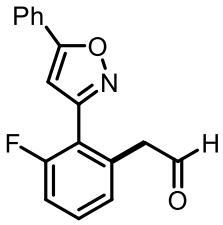
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (t, *J* = 1.7 Hz, 1H), 7.89 – 7.84 (m, 2H), 7.56 – 7.47 (m, 3H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 6.52 (s, 1H), 3.68 (d, *J* = 1.8 Hz, 2H), 2.30 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.31, 170.38, 162.12, 138.22, 131.90, 130.46, 129.78, 129.67, 129.52, 129.09, 128.23, 127.20, 125.93, 100.95, 48.72, 20.54; **ESI−HRMS**: Calculated for $C_{18}H_{15}NNaO_2^+$ $[M+Na]^+$ 300.0995, found 300.1003.

2-(3-methoxy-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3c):



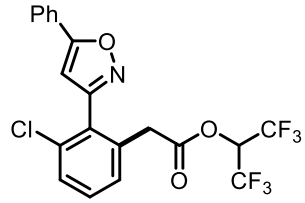
Yield: 71% (20 mg); Physical appearance: Yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.76 (t, *J* = 1.7 Hz, 1H), 7.86 (d, *J* = 6.8 Hz, 2H), 7.52 – 7.43 (m, 4H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.71 (s, 1H), 3.86 (s, 3H), 3.83 (d, *J* = 1.5 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 199.40, 169.35, 159.74, 158.29, 133.66, 130.83, 130.13, 128.98, 127.53, 125.87, 123.44, 118.95, 110.23, 102.19, 55.86, 48.71; **ESI−HRMS**: Calculated for $C_{18}H_{16}NO_3^+$ $[M+H]^+$ 294.1125, found 294.1111.

2-(3-fluoro-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3d):



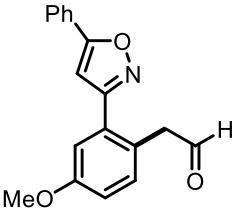
Yield: 54% (15 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.81 (d, *J* = 1.4 Hz, 1H), 7.88 – 7.84 (m, 2H), 7.54 – 7.44 (m, 4H), 7.20 (t, *J* = 9.2 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 3.2 Hz, 1H), 4.03 (d, *J* = 1.4 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 198.70, 169.96, 161.03 (d, *J* = 250.0 Hz), 157.56, 134.37 (d, *J* = 2.4 Hz), 131.15 (d, *J* = 9.1 Hz), 130.41, 129.06, 127.41 (d, *J* = 3.2 Hz), 127.14, 125.90, 117.88 (d, *J* = 14.0 Hz), 115.21 (d, *J* = 22.3 Hz), 101.52 (d, *J* = 6.3 Hz), 48.79; **ESI−HRMS**: Calculated for $C_{17}H_{13}FNO_2^+$ $[M+H]^+$ 282.0925, found 282.0920.

1,1,1,3,3,3-hexafluoropropan-2-yl 2-(3-chloro-2-(5-phenylisoxazol-3-yl)phenyl)acetate (3e):



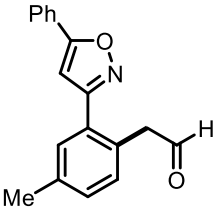
Yield: 51% (23 mg); Physical appearance: Colorless solid; M.p. 67−69 ºC; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.56 – 7.49 (m, 4H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 9.0 Hz, 1H), 6.68 (s, 1H), 5.70 (sept, *J* = 6.1 Hz, 1H), 3.96 (s, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 170.25, 167.90, 160.17, 134.85, 133.85, 130.71, 130.43, 129.65, 129.24, 129.22, 129.05, 127.14, 125.89, 101.52, 66.96, 66.77, 66.57, 66.37, 38.46; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −73.25; **ESI−HRMS**: Calculated for $C_{20}H_{12}ClF_6NNaO_3^+$ $[M+H]^+$ 486.0302, found 486.0297.

2-(4-methoxy-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3f):



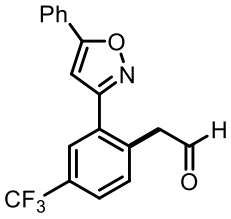
Yield: 78% (23 mg); Physical appearance: Yellow gel; TLC R_f 0.2 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.78 (t, *J* = 1.5 Hz, 1H), 7.88 – 7.83 (m, 2H), 7.55 – 7.47 (m, 3H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 6.7 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 6.69 (s, 1H), 4.05 (d, *J* = 1.4 Hz, 2H), 3.90 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 200.14, 169.95, 162.98, 158.27, 130.95, 130.35, 129.05, 128.66, 127.24, 125.89, 121.95, 121.01, 111.55, 100.29, 55.84, 42.46; **ESI−HRMS**: Calculated for $C_{18}H_{15}NNaO_3^+$ $[M+Na]^+$ 316.0944, found 316.0950.

2-(4-methyl-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3g):



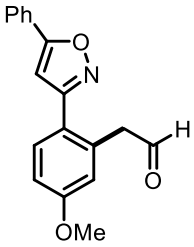
Yield: 71% (20 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.83 (t, *J* = 1.4 Hz, 1H), 7.89 – 7.84 (m, 2H), 7.55 – 7.46 (m, 4H), 7.32 – 7.28 (m, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 6.75 (s, 1H), 4.06 (d, *J* = 1.2 Hz, 2H), 2.45 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.92, 169.91, 163.11, 137.63, 131.97, 130.74, 130.54, 130.36, 129.06, 129.04, 128.47, 127.24, 125.88, 99.70, 48.84, 21.06; **ESI−HRMS**: Calculated for $C_{18}H_{15}NNaO_2^+$ $[M+Na]^+$ 300.0995, found 300.0989.

2-(2-(5-phenylisoxazol-3-yl)-4-(trifluoromethyl)phenyl)acetaldehyde (3h):



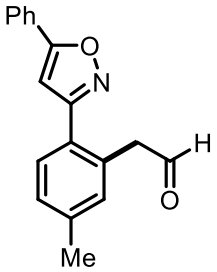
Yield: 66% (22 mg); Physical appearance: Yellow gel; TLC R_f 0.2 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.87 (t, *J* = 1.3 Hz, 1H), 7.91 (s, 1H), 7.89 – 7.85 (m, 2H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.48 (m, 4H), 6.80 (s, 1H), 4.22 (s, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 198.20, 170.59, 162.01, 135.72, 132.75, 130.66, 130.43, 130.24, 130.06, 129.15, 126.88, 126.63 (q, *J* = 3.8 Hz), 126.48 (q, *J* = 3.4 Hz), 125.94, 124.48, 122.94, 99.44, 49.18; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −62.71; **ESI−HRMS**: Calculated for $C_{18}H_{13}F_3NO_2^+$ $[M+H]^+$ 331.0890, found 331.0900.

2-(5-methoxy-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3i):



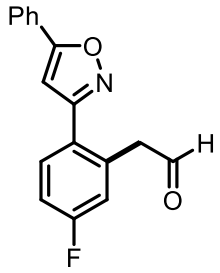
Yield: 77% (22 mg); Physical appearance: Colorless solid; M.p. 79–81 °C; TLC R_f 0.2 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.85 (s, 1H), 7.87 – 7.83 (m, 2H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.54 – 7.46 (m, 3H), 6.98 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.87 (d, *J* = 2.6 Hz, 1H), 6.72 (s, 1H), 4.10 (d, *J* = 1.3 Hz, 2H), 3.89 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.58, 169.71, 162.74, 160.59, 133.26, 131.24, 130.31, 129.04, 127.28, 125.86, 121.58, 117.51, 113.24, 99.50, 55.43, 49.51; **ESI−HRMS**: Calculated for $C_{18}H_{15}NNaO_3^+$ $[M+Na]^+$ 316.0944, found 316.0936.

2-(5-methyl-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3j):



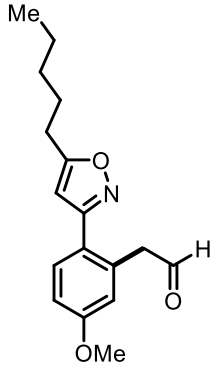
Yield: 73% (20 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.85 (t, *J* = 1.6 Hz, 1H), 7.87 – 7.83 (m, 2H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.54 – 7.47 (m, 3H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.17 (s, 1H), 6.74 (s, 1H), 4.08 (d, *J* = 1.6 Hz, 2H), 2.44 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.85, 169.81, 162.99, 140.14, 132.86, 131.38, 130.33, 129.80, 129.05, 128.59, 127.26, 126.31, 125.87, 99.61, 49.28, 21.25; **ESI−HRMS**: Calculated for $C_{18}H_{16}NO_3^+$ $[M+H]^+$ 278.1176, found 278.1183.

2-(5-fluoro-2-(5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3k):



Yield: 55% (15 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.85 (t, *J* = 1.5 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.67 – 7.62 (m, 1H), 7.55 – 7.47 (m, 3H), 7.19 – 7.13 (m, 1H), 7.08 (dd, *J* = 9.2, 2.7 Hz, 1H), 6.72 (s, 1H), 4.12 (d, *J* = 1.5 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 198.60, 170.15, 163.19 (d, *J* = 250.7 Hz), 162.23, 134.29 (d, *J* = 8.2 Hz), 131.69 (d, *J* = 8.8 Hz), 130.49, 129.10, 127.07, 125.89, 125.44, 125.42, 119.02 (d, *J* = 21.7 Hz), 114.93 (d, *J* = 21.5 Hz), 99.56, 49.12; **^{19}F NMR** (376 MHz, $CDCl_3$) δ −110.88; **ESI−HRMS**: Calculated for $C_{17}H_{13}FNO_2^+$ $[M+H]^+$ 282.0925, found 282.0935.

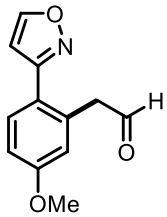
2-(5-methoxy-2-(5-pentylisoxazol-3-yl)phenyl)acetaldehyde (3n):



Yield: 76% (22 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.79 (t, *J* = 1.6 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 6.94 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.83 (d, *J* = 2.6 Hz, 1H), 6.16 (s, 1H), 4.05 (d, *J* = 1.5 Hz, 2H), 3.87 (s, 3H), 2.79 (t, *J* = 7.7 Hz, 2H), 1.81 – 1.72 (m, 2H), 1.44 – 1.37 (m, 4H), 0.94 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.70, 173.58, 162.03, 160.38, 133.14, 131.16, 121.90, 117.38, 113.13, 100.75, 55.38, 49.46, 31.28, 27.19, 26.65, 22.31, 13.93; **ESI−HRMS**: Calculated for $C_{17}H_{21}NNaO_3^+$ $[M+Na]^+$ 310.1414, found 310.1417.

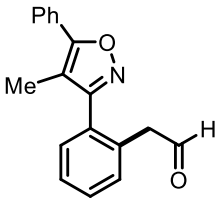
2-(2-(isoxazol-3-yl)-5-methoxyphenyl)acetaldehyde (3o):

Yield: 70% (15 mg); Physical appearance: Yellow gel; TLC R_f 0.2 (4:1, Petroleum ether:



EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.80 (t, *J* = 1.5 Hz, 1H), 8.46 (d, *J* = 1.6 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 6.96 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.86 (d, *J* = 2.6 Hz, 1H), 6.56 (d, *J* = 1.6 Hz, 1H), 4.06 (d, *J* = 1.5 Hz, 2H), 3.88 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.49, 161.18, 160.59, 158.21, 133.29, 131.28, 121.24, 117.54, 113.22, 104.47, 55.41, 49.47; **ESI−HRMS**: Calculated for $C_{12}H_{11}NNaO_3^+$ $[M+Na]^+$ 240.0631, found 240.0638.

2-(2-(4-methyl-5-phenylisoxazol-3-yl)phenyl)acetaldehyde (3p):



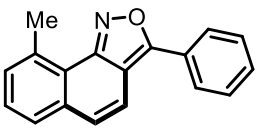
Yield: 61% (17 mg); Physical appearance: Yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.75 (t, *J* = 1.8 Hz, 1H), 7.84 – 7.80 (m, 2H), 7.57 – 7.44 (m, 6H), 7.39 (d, *J* = 7.8 Hz, 1H), 3.85 (d, *J* = 1.7 Hz, 2H), 2.18 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.18, 165.39, 163.70, 132.03, 131.32, 130.43, 129.84, 129.66, 129.51, 128.92, 128.33, 127.62, 126.72, 109.63, 48.34, 8.89; **ESI−HRMS**: Calculated for $C_{18}H_{16}NO_2^+$ $[M+H]^+$ 278.1176, found 278.1154.

3.6.1.2 General procedure for the Ru-catalyzed synthesis of anthranils:

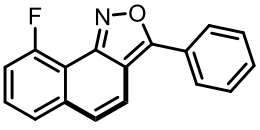
In a pressure tube equipped with a stir bar, the isoxazole (1.0 equiv, 0.1 mmol) was dissolved in HFIP (1.0 mL). The reaction mixture was degassed with nitrogen for 10 min followed by the addition of the vinylene carbonate (2.0 equiv, 0.20 mmol), $[RuCl_2(p\text{-cym})]_2$ (5 mol%, 0.005 mmol), and $AgSbF_6$ (0.50 equiv, 0.05 mmol). The tube was fitted with a Teflon screw cap under a nitrogen flow, and the reaction mixture was heated to 90 °C and allowed to stir for 24-26 h. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was washed with a saturated solution of $NaHCO_3$ and brine. The organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to result in the desired product.

9-methyl-3-phenylnaphtho[1,2-c]isoxazole (4a):

Yield: 68% (18 mg); Physical appearance: Colorless solid; M.p. 113−115 °C; TLC R_f 0.5 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.06 (d, *J* = 7.2 Hz, 2H), 7.67 – 7.47 (m, 7H), 7.36 (d, *J* = 9.2 Hz, 1H), 3.08 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 162.29, 158.09, 138.02, 134.78, 130.17, 130.03, 129.24, 128.94, 128.51, 128.25, 126.76, 126.34, 121.95, 116.99, 113.13, 24.11; **ESI−HRMS**: Calculated for $C_{18}H_{14}NO^+$ $[M+H]^+$ 260.1070, found 260.1059.



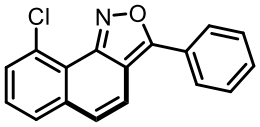
9-fluoro-3-phenylnaphtho[1,2-c]isoxazole (4b):



Yield: 62% (16 mg); Physical appearance: Colorless solid; M.p. 124−126 °C; TLC R_f 0.4 (9:1, Petroleum ether: EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 – 8.03 (m, 2H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.67 – 7.53 (m, 5H), 7.43 – 7.35 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 163.30, 160.00 (d, *J* =

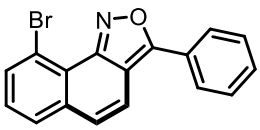
257.7 Hz), 154.28 (d, *J* = 5.1 Hz), 135.97 (d, *J* = 4.3 Hz), 130.39, 130.23 (d, *J* = 8.8 Hz), 129.30, 128.14, 126.89, 126.58 (d, *J* = 2.9 Hz),124.05 (d, *J* = 3.7 Hz), 118.55, 114.45 (d, *J* = 20.1 Hz), 112.44, 111.56 (d, *J* = 15.2 Hz); **ESI−HRMS**: Calculated for $C_{17}H_{10}FNO^+$ $[M+H]^+$ 264.0819, found 264.0810.

9-chloro-3-phenylnaphtho[1,2-c]isoxazole (4c):



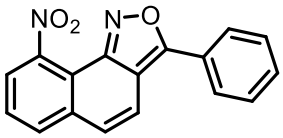
Yield: 65% (18 mg); Physical appearance: Colorless solid; M.p. 153–155 °C; TLC R_f 0.4 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.07 – 8.03 (m, 2H), 7.76 – 7.68 (m, 3H), 7.64 – 7.53 (m, 4H), 7.36 (d, *J* = 9.2 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 163.24, 156.03, 136.20, 132.65, 130.37, 129.98, 129.50, 129.32, 128.16, 127.26, 127.24, 126.89, 121.15, 118.41, 113.26; **ESI−HRMS**: Calculated for $C_{17}H_{11}ClNO^+$ $[M+H]^+$ 280.0524, found 280.0527.

9-bromo-3-phenylnaphtho[1,2-c]isoxazole (4d):



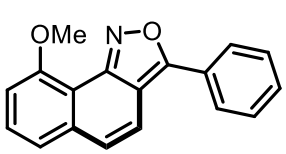
Yield: 61% (20 mg); Physical appearance: Colorless solid; M.p. 154–156 °C; TLC R_f 0.4 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.04 (d, *J* = 7.1 Hz, 2H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.70 (d, *J* = 9.1 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.57 – 7.52 (m, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 9.2 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 163.32, 156.16, 136.49, 133.77, 130.36, 129.69, 129.32, 128.15, 127.93, 127.40, 126.86, 122.78, 120.53, 118.34, 113.28; **ESI−HRMS**: Calculated for $C_{17}H_{11}BrNO^+$ $[M+H]^+$ 324.0019, found 324.0015.

9-nitro-3-phenylnaphtho[1,2-c]isoxazole (4e):



Yield: 54% (15 mg); Physical appearance: Yellow solid; M.p. 203–205 °C; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.02 (d, *J* = 7.4 Hz, 2H), 7.95 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.82 – 7.70 (m, 3H), 7.64 – 7.53 (m, 3H), 7.41 (d, *J* = 9.3 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 164.37, 152.73, 147.81, 135.21, 131.08, 130.75, 129.41, 127.70, 126.89, 126.12, 121.57, 119.78, 113.24, 112.64; **ESI−HRMS**: Calculated for $C_{17}H_{11}N_2O_3^+$ $[M+H]^+$ 291.0764, found 291.0793.

9-methoxy-3-phenylnaphtho[1,2-c]isoxazole (4f):



Yield: 63% (17 mg); Physical appearance: Colorless solid; M.p. 140–142 °C; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.3 Hz, 2H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.65-7.57 (m, 3H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 9.2 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 1H), 4.20 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$): δ 162.49, 157.80, 155.78, 135.88, 130.07, 130.07, 129.21, 128.51, 127.37, 126.85, 120.77, 117.98, 112.94, 112.48, 109.25, 56.17; **ESI−HRMS**: Calculated for $C_{18}H_{14}NO_2^+$ $[M+H]^+$ 276.1019, found 276.1026.

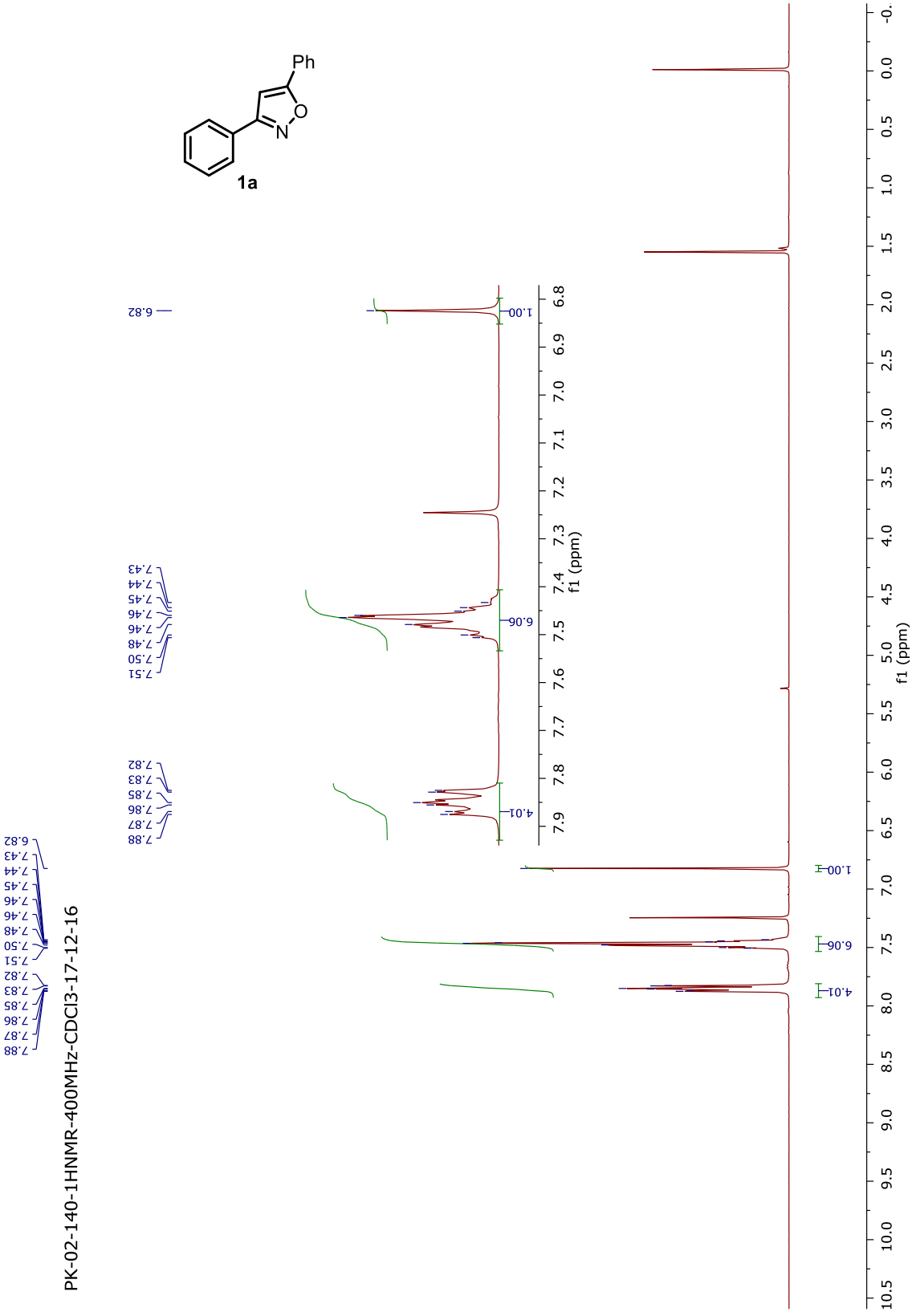
4) Procedure for the TsOH-mediated cyclization of formylmethyl isoxazoles.

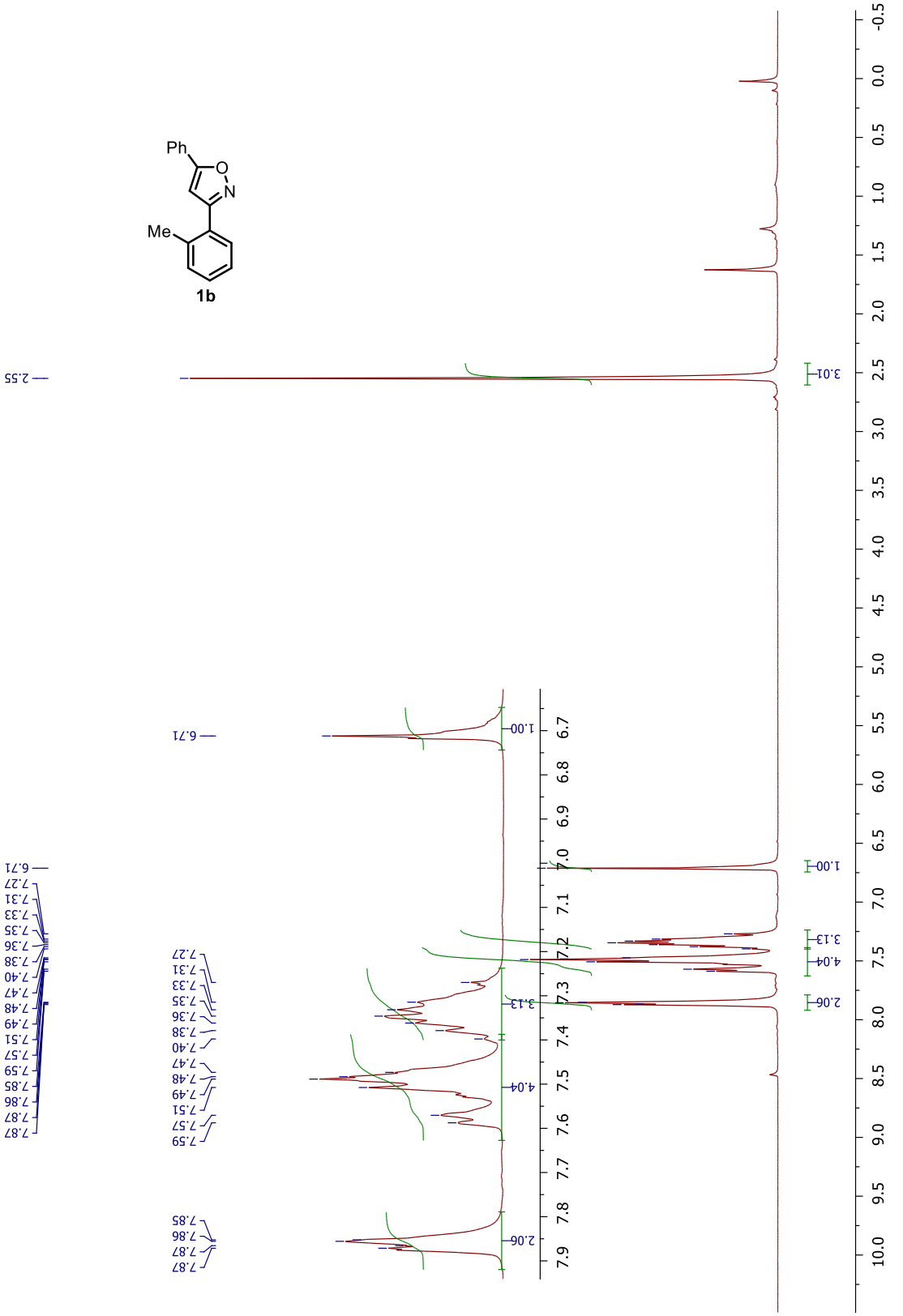
In a pressure tube equipped with a stir bar, the crude formylmethyl isoxazole (**3c**, **3d**) were dissolved in DCE (1.0 mL) followed by the addition of *p*-TSA (1.0 equiv). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 100 °C and allowed to stir for 12 h. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was washed with a saturated solution of $NaHCO_3$ and brine. The organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to result in the desired product.

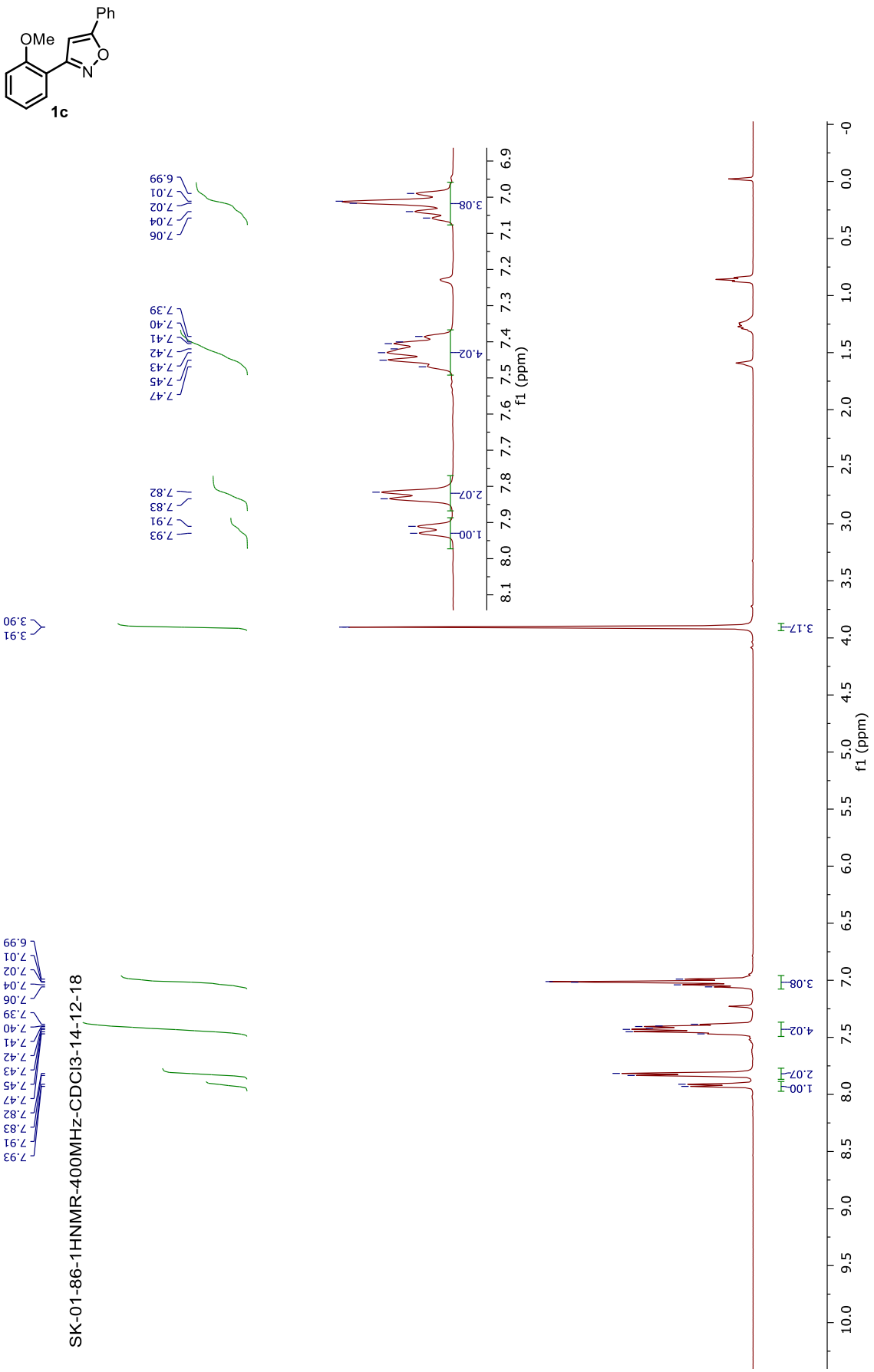
5) References

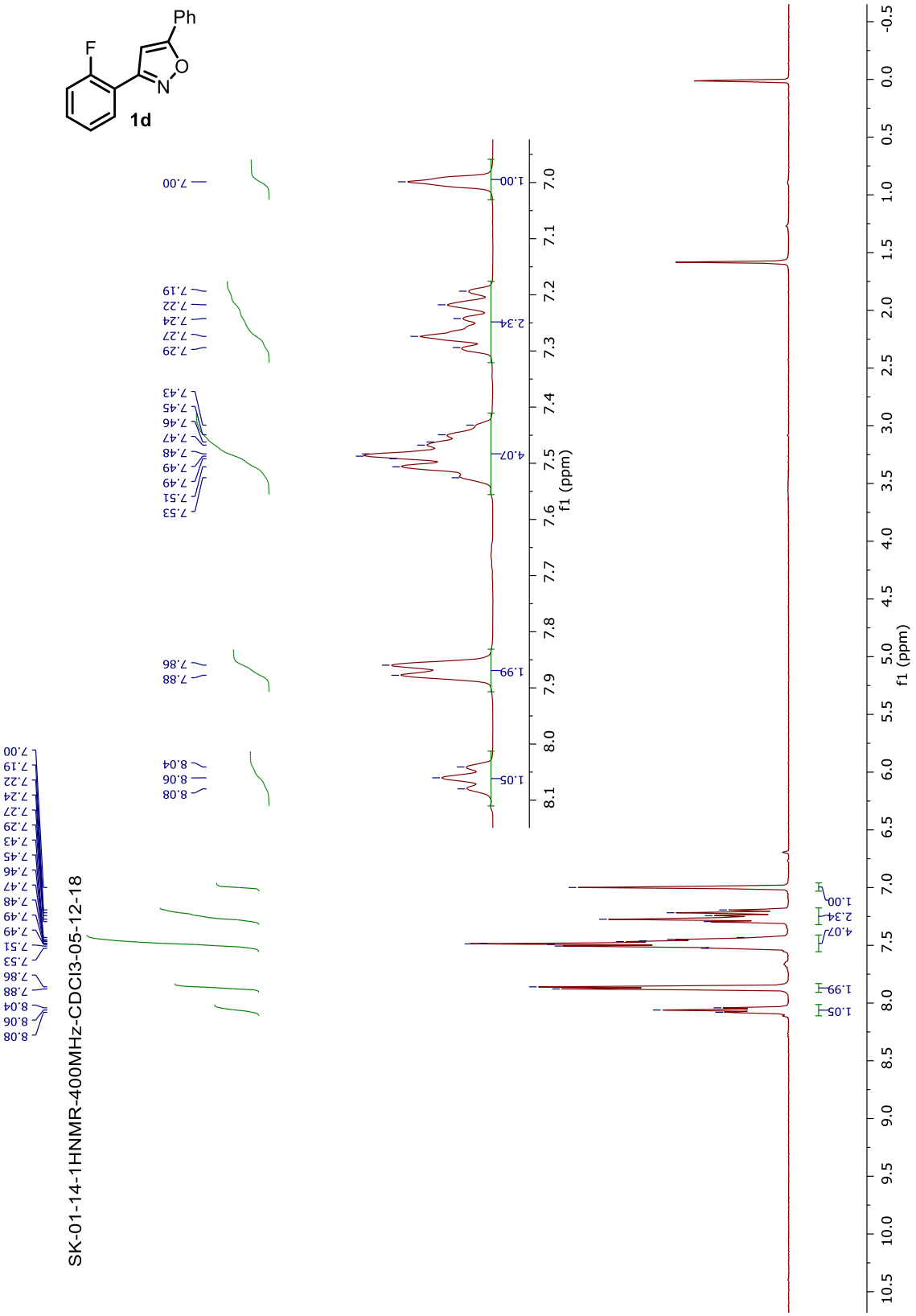
(1) W. L. F. Armarego, *Purification of Laboratory Chemicals*; 8th Edition; Butterworth-Heinemann, **2017**.
(2) P. Kumar, M. Kapur, *Org. Lett.* **2019**, *21*, 2134.
(3) P. Kumar, S. K. Keshri, M. Kapur, *Org. Biomol. Chem.* **2021**, *19*, 3428.
(4) M. S. Ledovskaya, K. S. Rodygin and V. P. Ananikov, *Org. Chem. Front.* **2018**, *5*, 226.
(5) P. Kumar, M. Kapur, *Org. Lett.* **2021**, *23*, 5855.

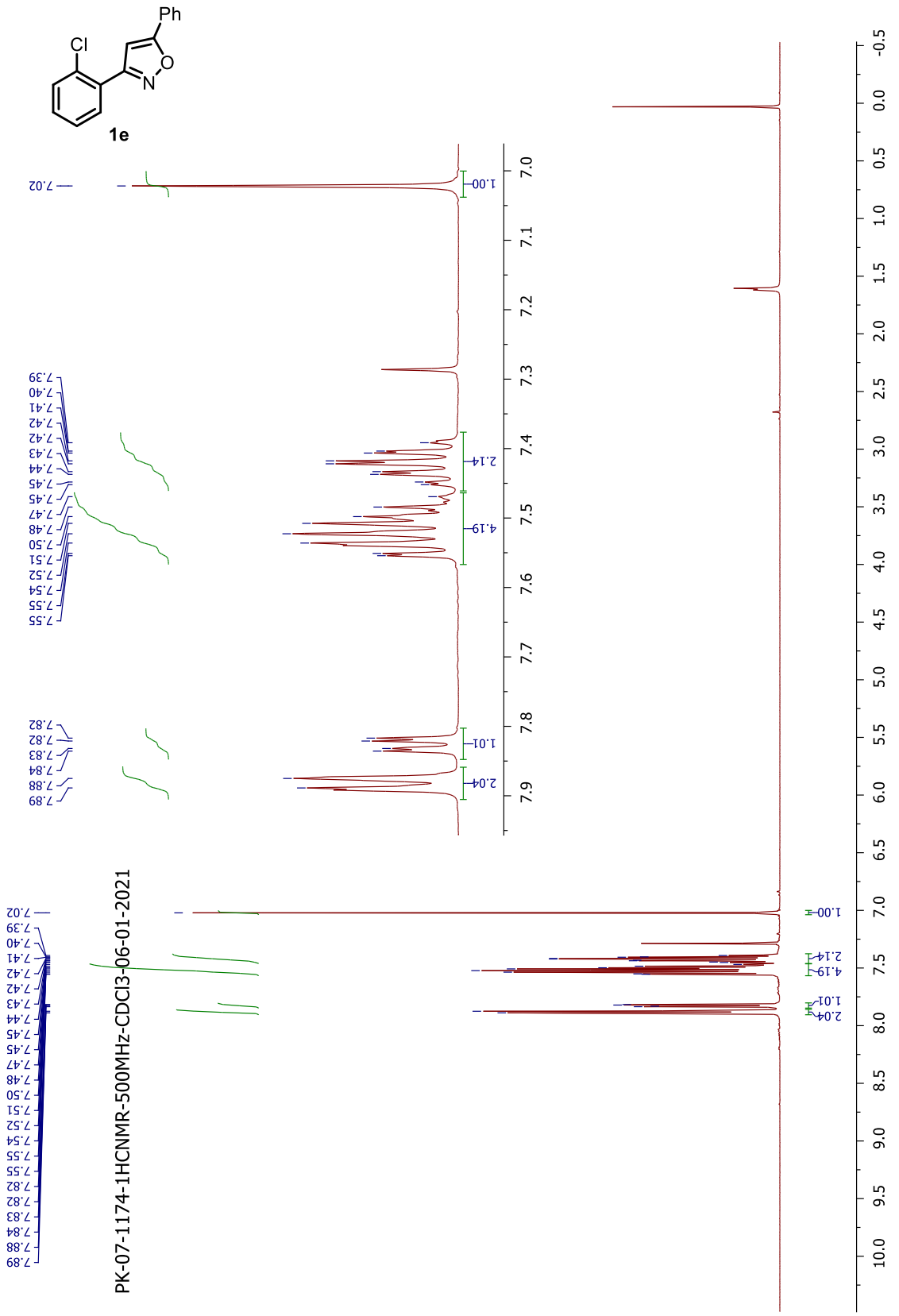
6) Representative Spectra

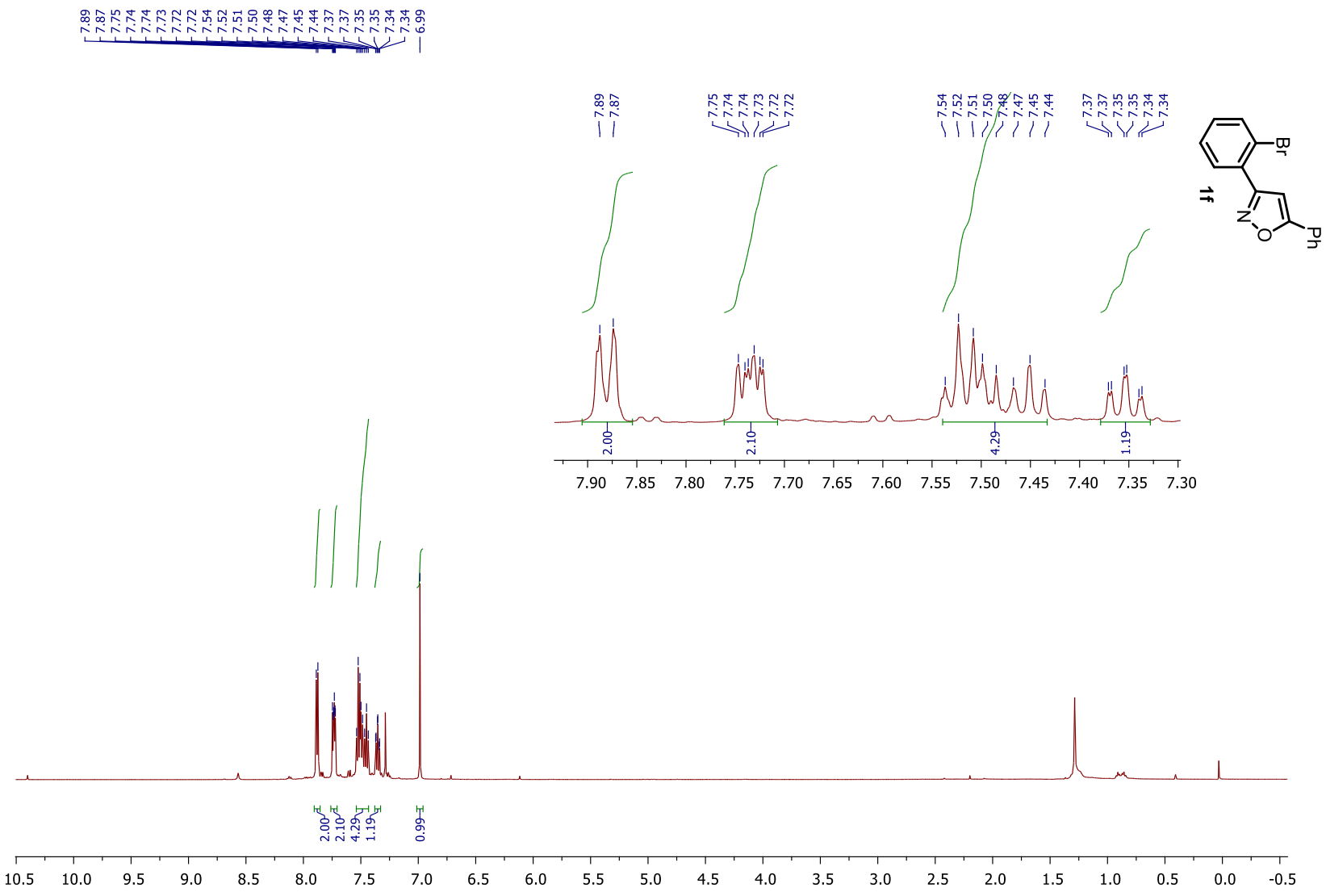



Ph
O
N
Me
1b

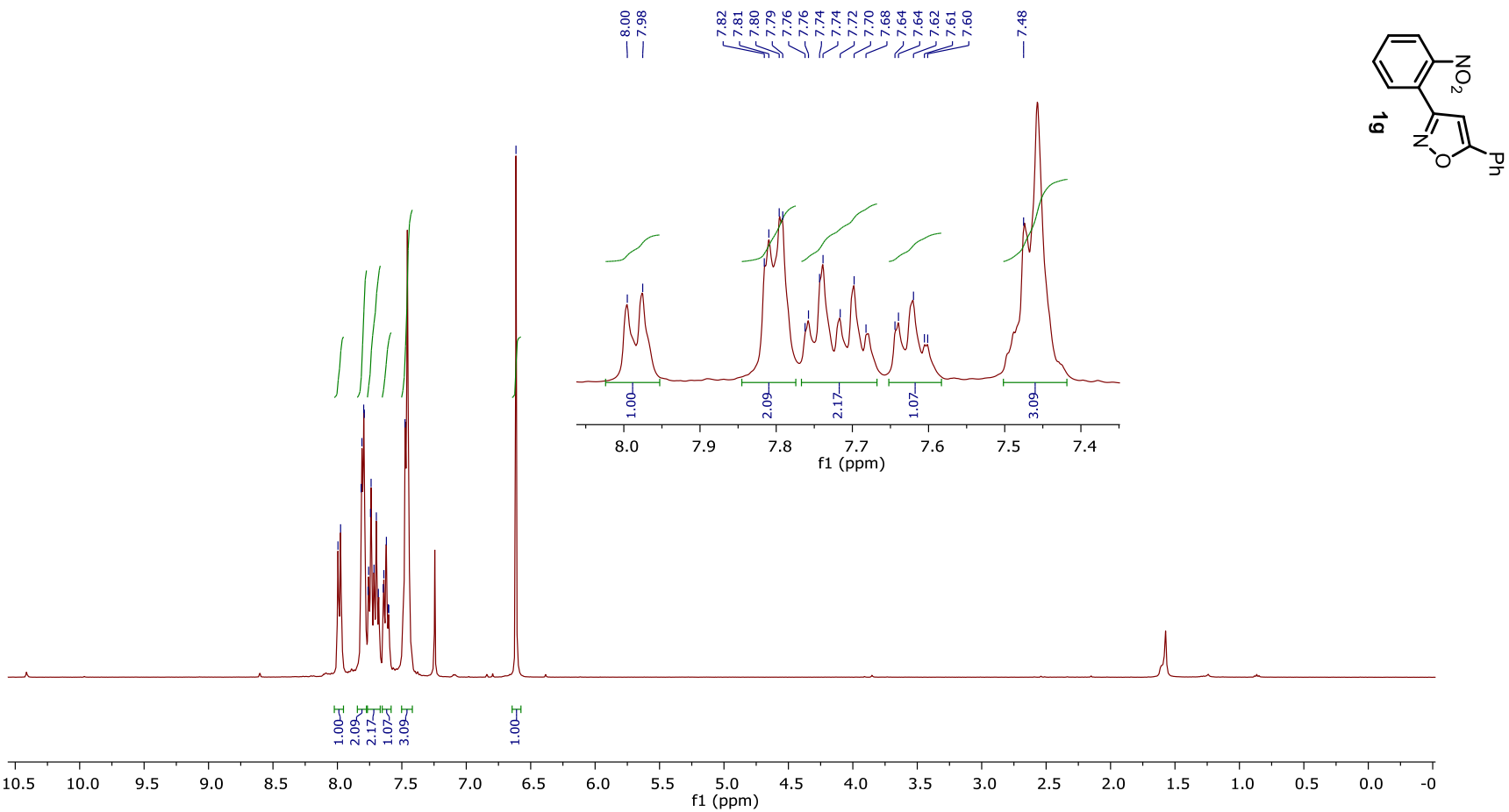

Ph
OMe
O
N
1c
SK-01-86-1HNMR-400MHz-CDCl3-14-12-18
f1 (ppm)
3.17
3.08
4.02
2.07
1.00

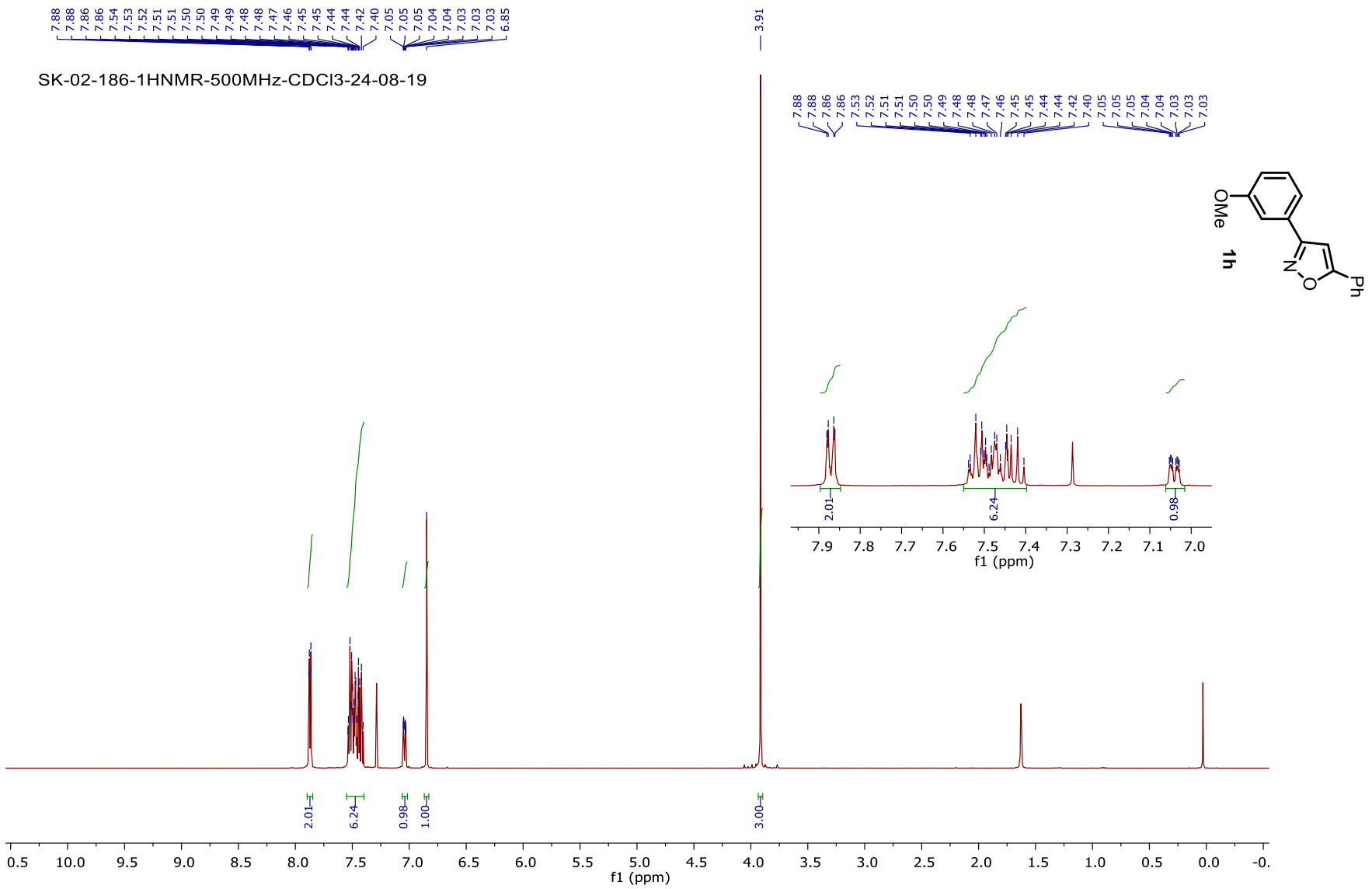

Ph
F
O
N
1d
SK-01-14-1HNMR-400MHz-CDCl3-05-12-18
f1 (ppm)

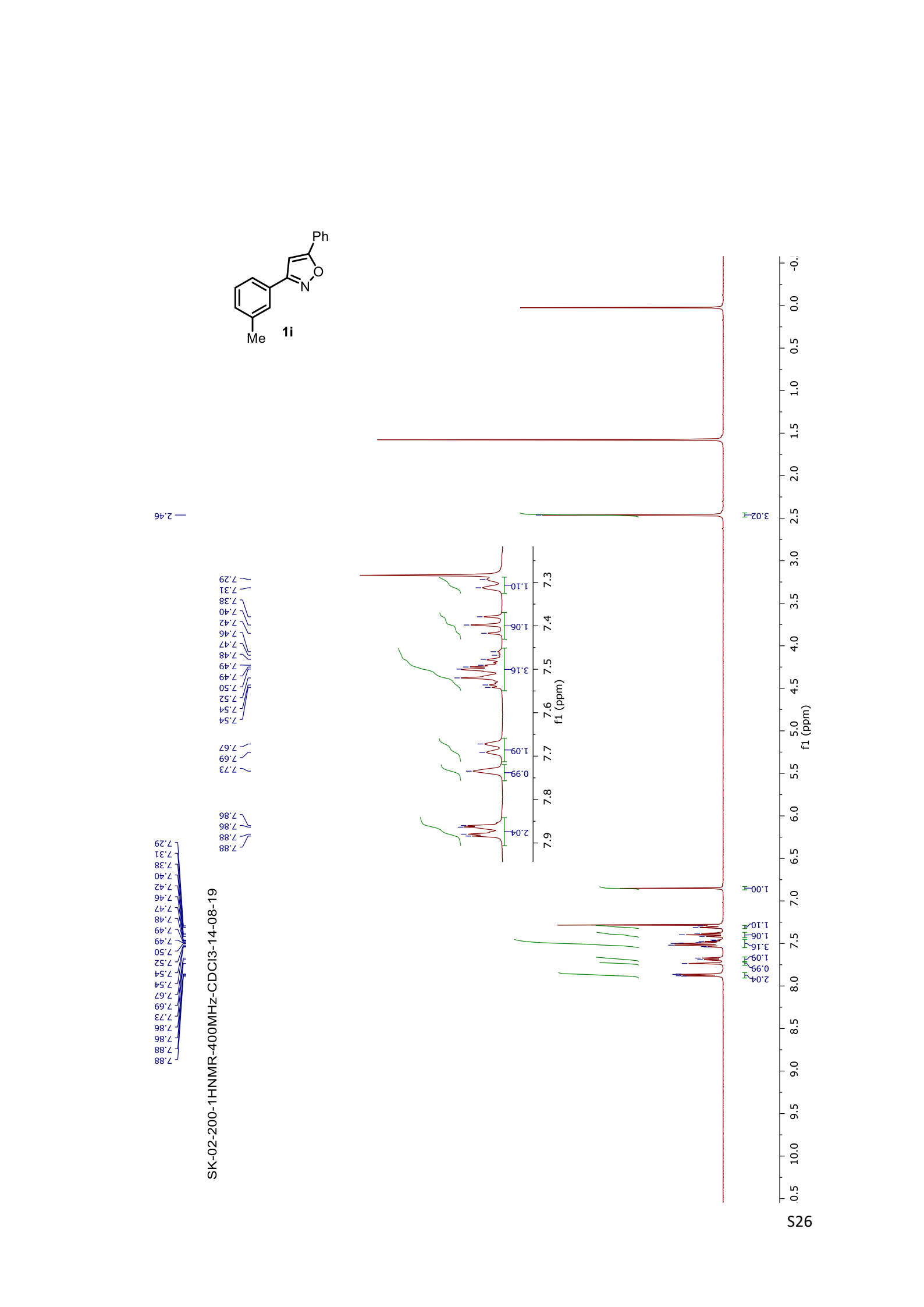

Ph
Cl
O
N
1e
PK-07-1174-1HCNMR-500MHz-CDCl3-06-01-2021


7.89
7.87
7.75
7.74
7.74
7.73
7.72
7.72
7.54
7.52
7.51
7.50
7.48
7.47
7.45
7.44
7.37
7.37
7.35
7.34
7.34
6.99
2.00
2.10
4.29
1.19
0.99
Br
Ph
N
O
1f

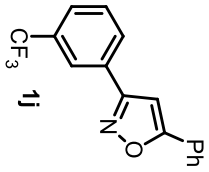
PK-04-456-1HNMR-400MHz-CDCl3-17-01-18

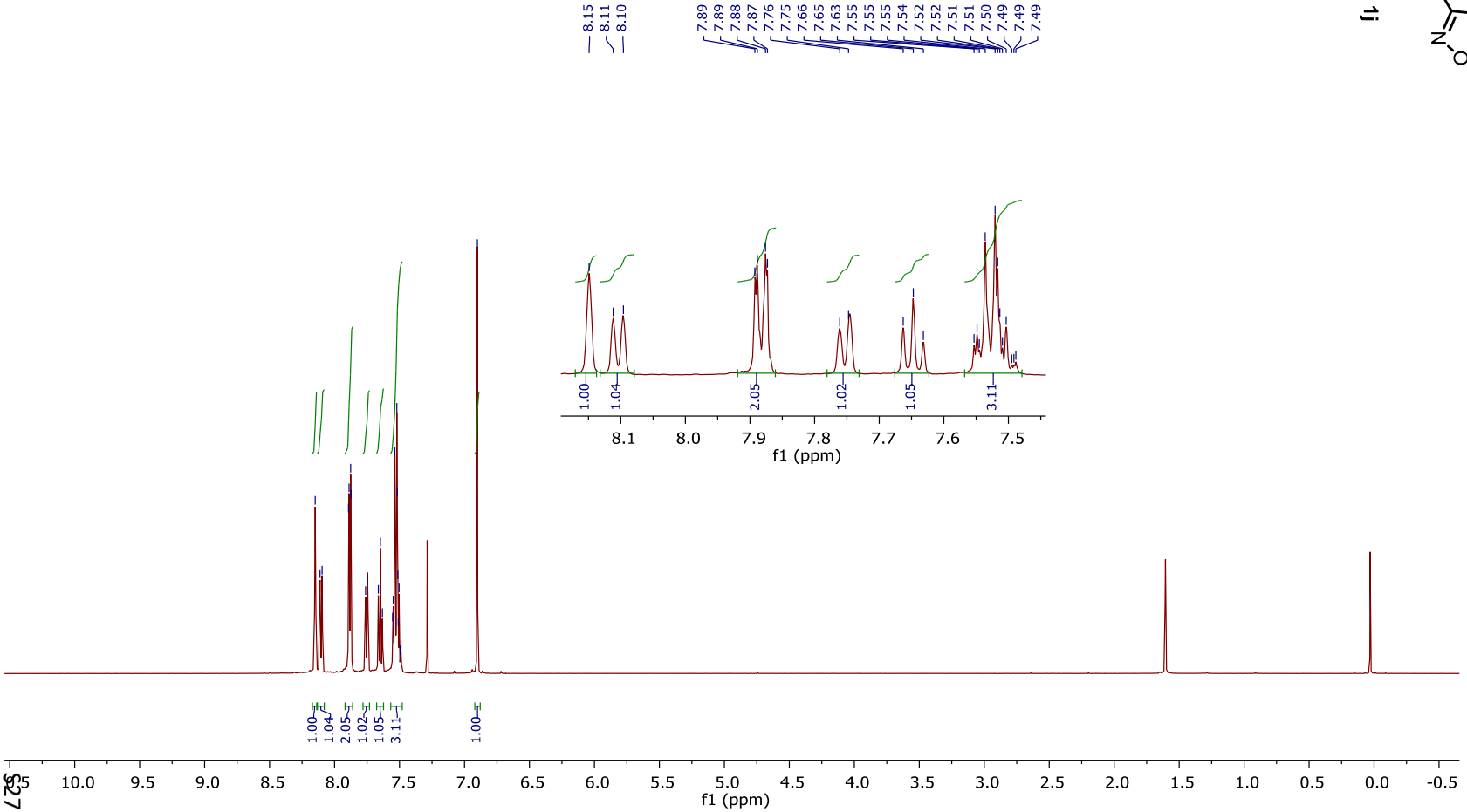


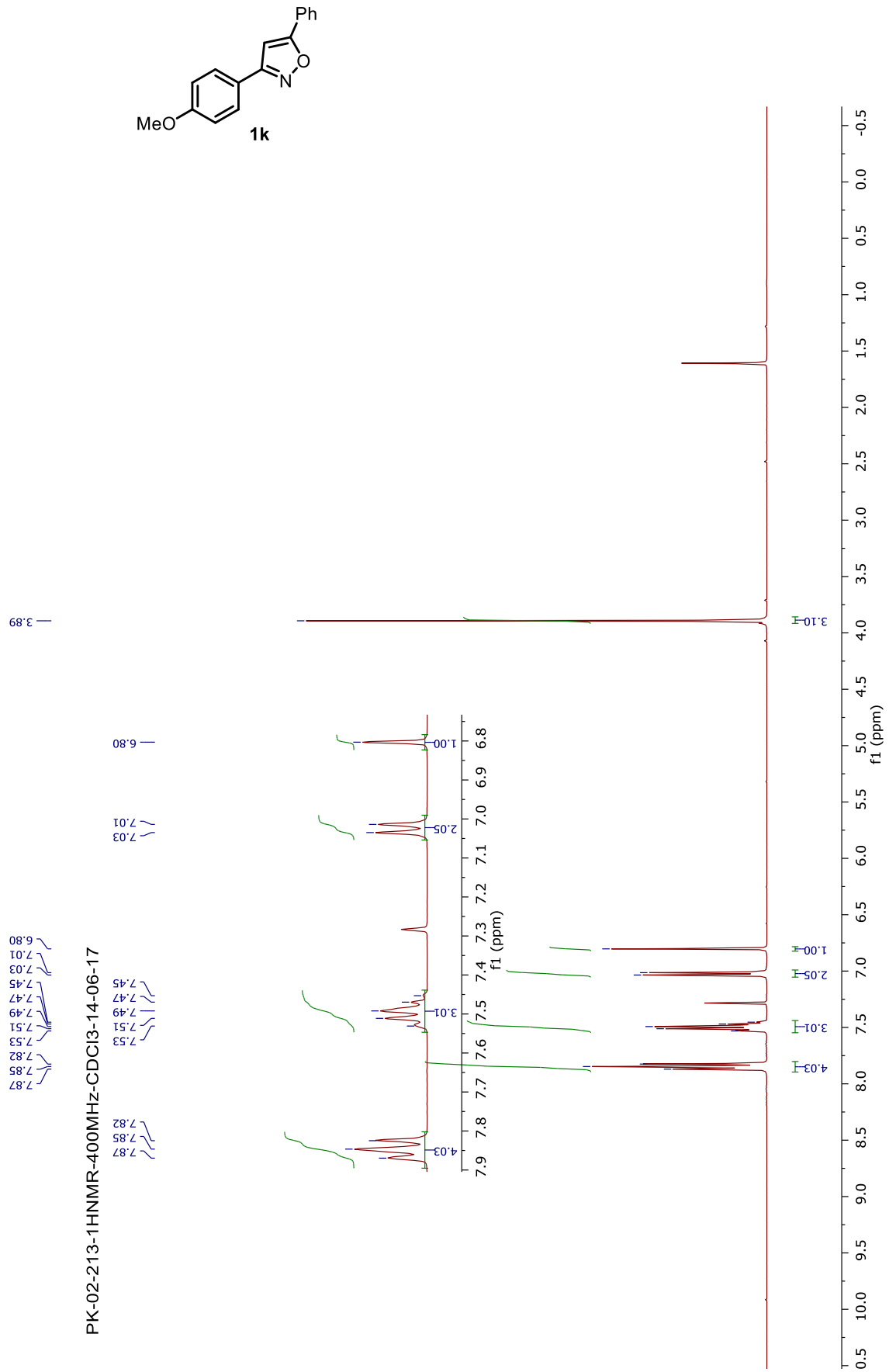

SK-02-186-1HNMR-500MHz-CDCl3-24-08-19
7.88 7.88 7.86 7.86 7.54 7.53 7.52 7.51 7.51 7.50 7.50 7.49 7.49 7.48 7.48 7.47 7.46 7.45 7.45 7.44 7.44 7.42 7.40 7.05 7.05 7.04 7.04 7.03 7.03 6.85
3.91
OMe
1h
Ph
2.01
6.24
0.98
1.00
3.00
f1 (ppm)

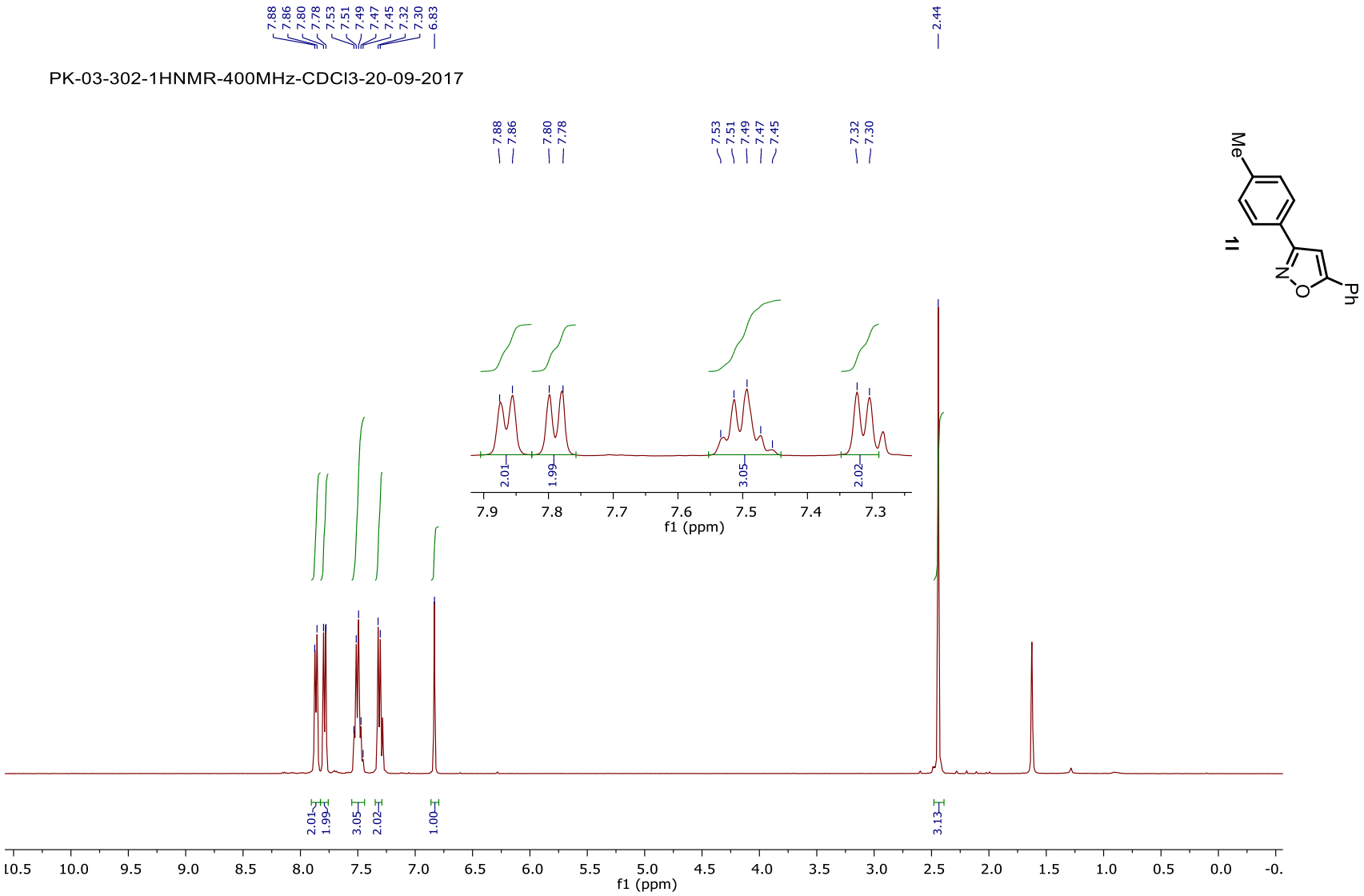

Ph
O
N
Me
1i
SK-02-200-1HNMR-400MHz-CDCl3-14-08-19
f1 (ppm)

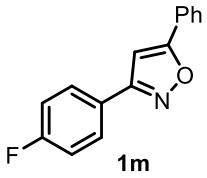
SK-02-297-1HNMR-400MHz-CDCl3-08-06-19



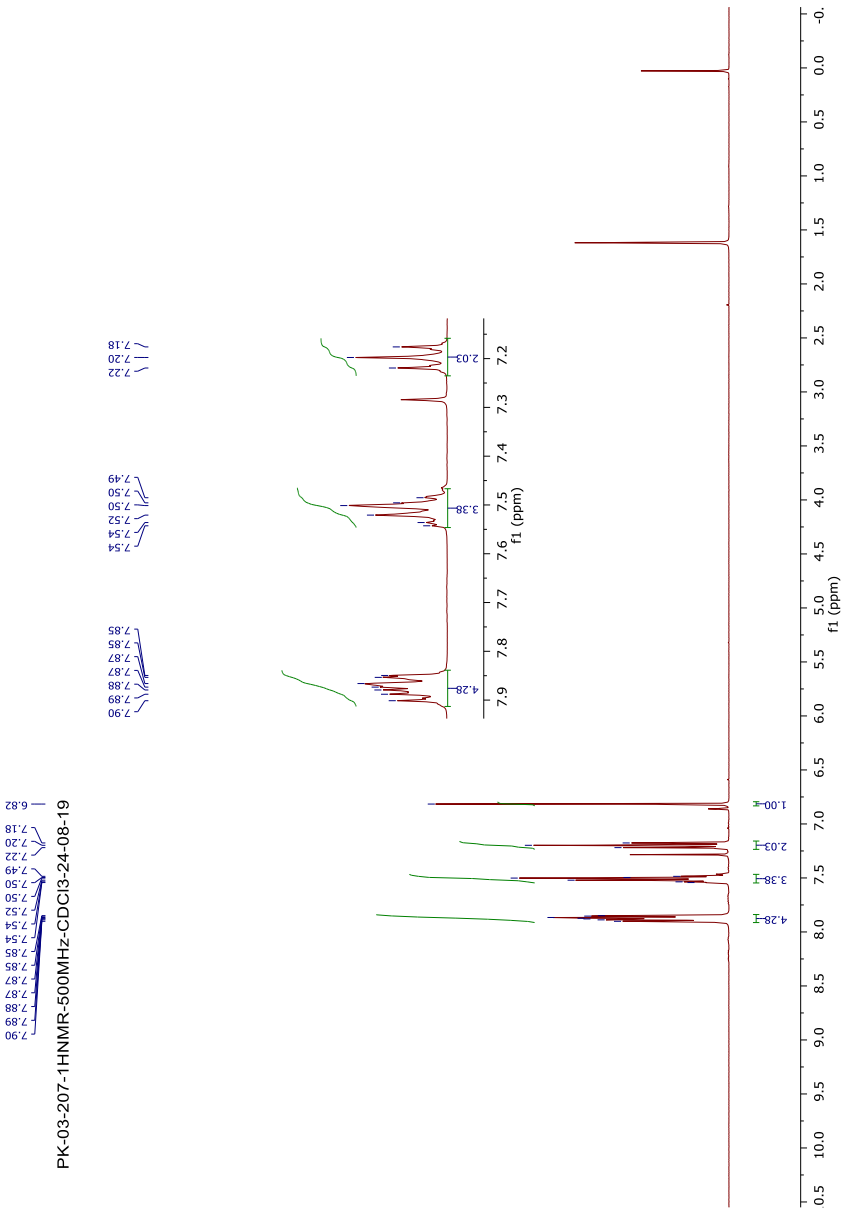


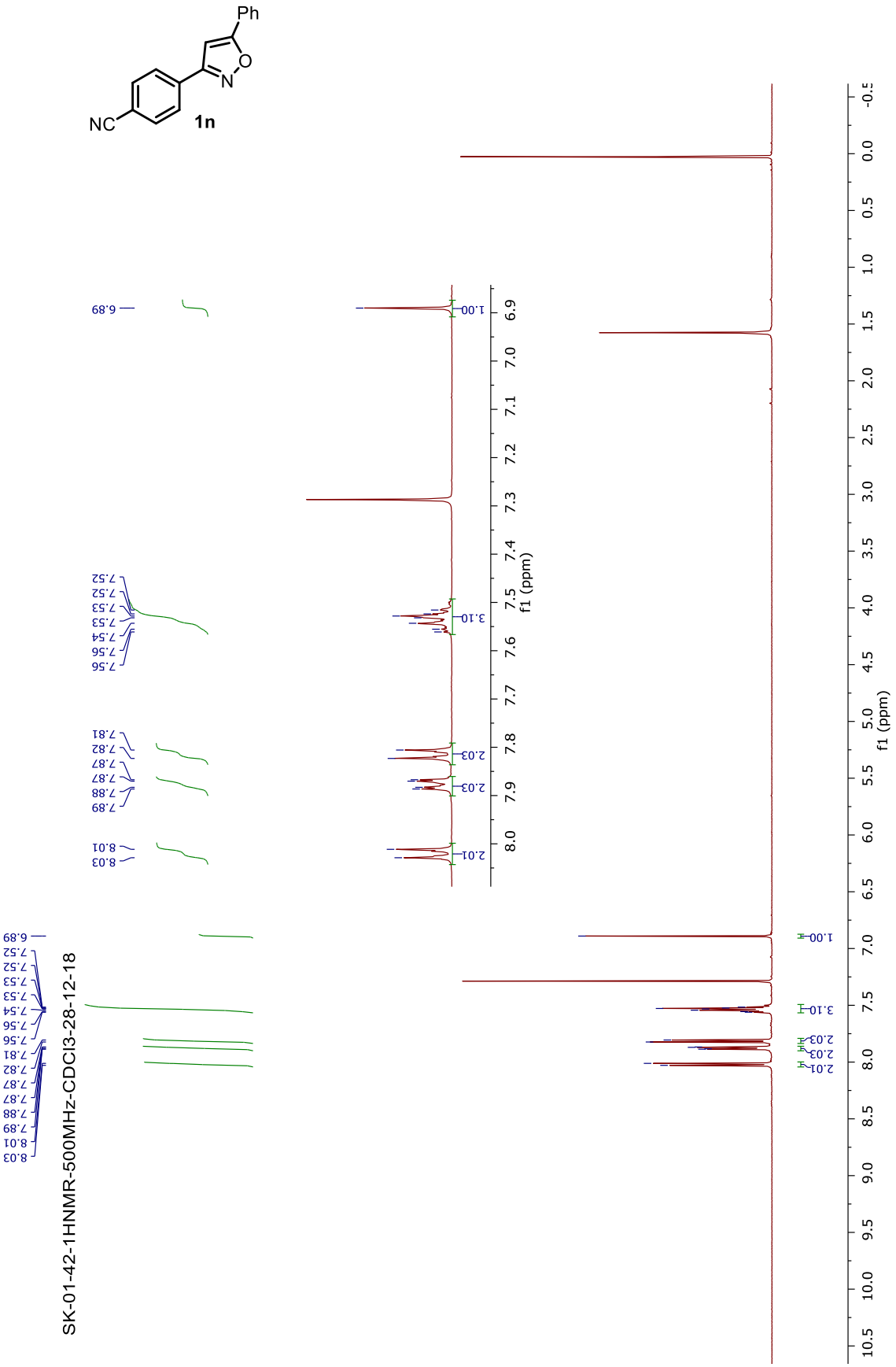

Ph
O
N
MeO
1k
PK-02-213-1HNMR-400MHz-CDCl3-14-06-17
f1 (ppm)

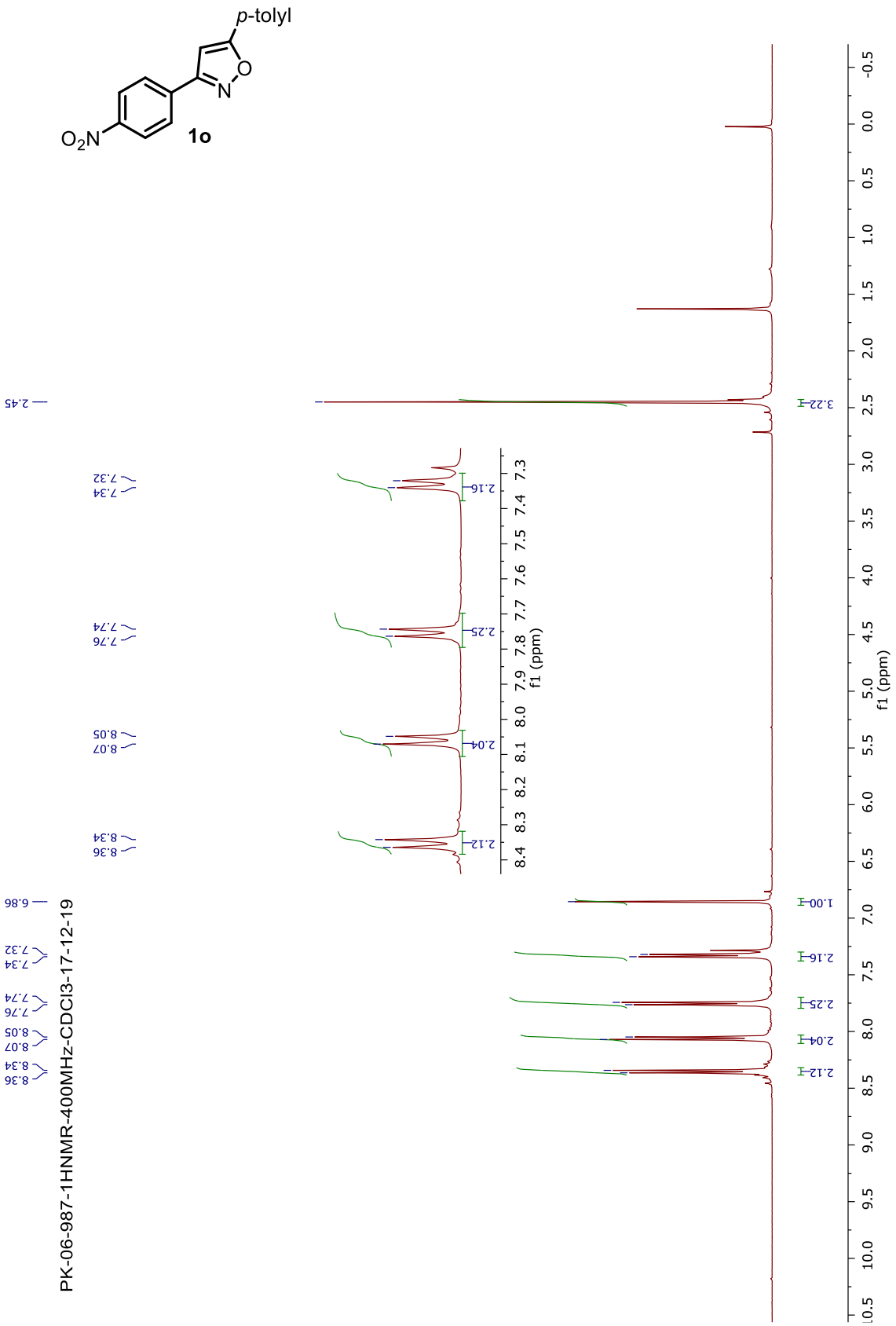

7.88
7.86
7.80
7.78
7.53
7.51
7.49
7.47
7.45
7.32
7.30
6.83
2.44
PK-03-302-1HNMR-400MHz-CDCl3-20-09-2017
Me
Ph
N
O
11
2.01
1.99
3.05
2.02
1.00
3.13
f1 (ppm)

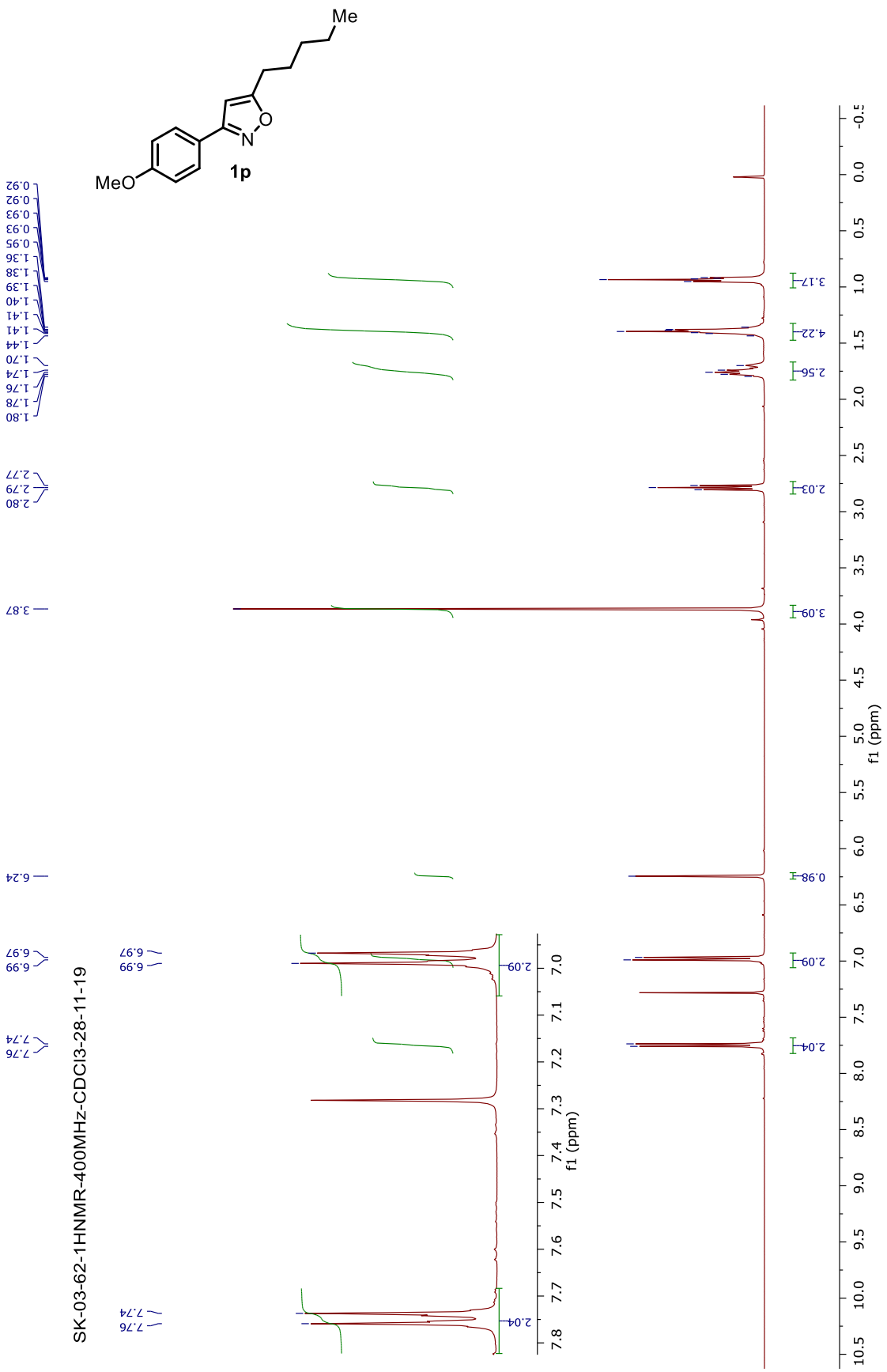

Ph
O
N
F

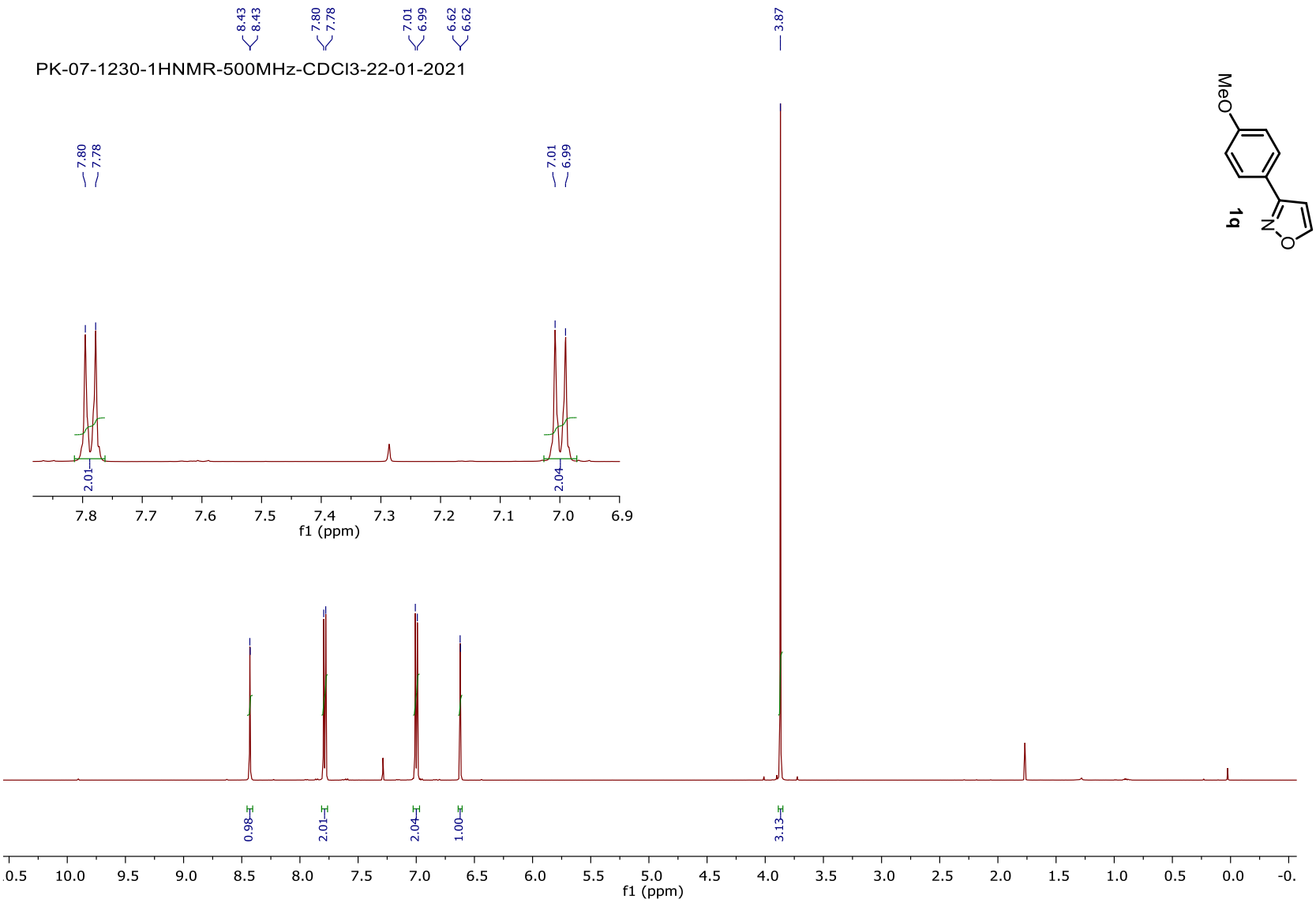
1m

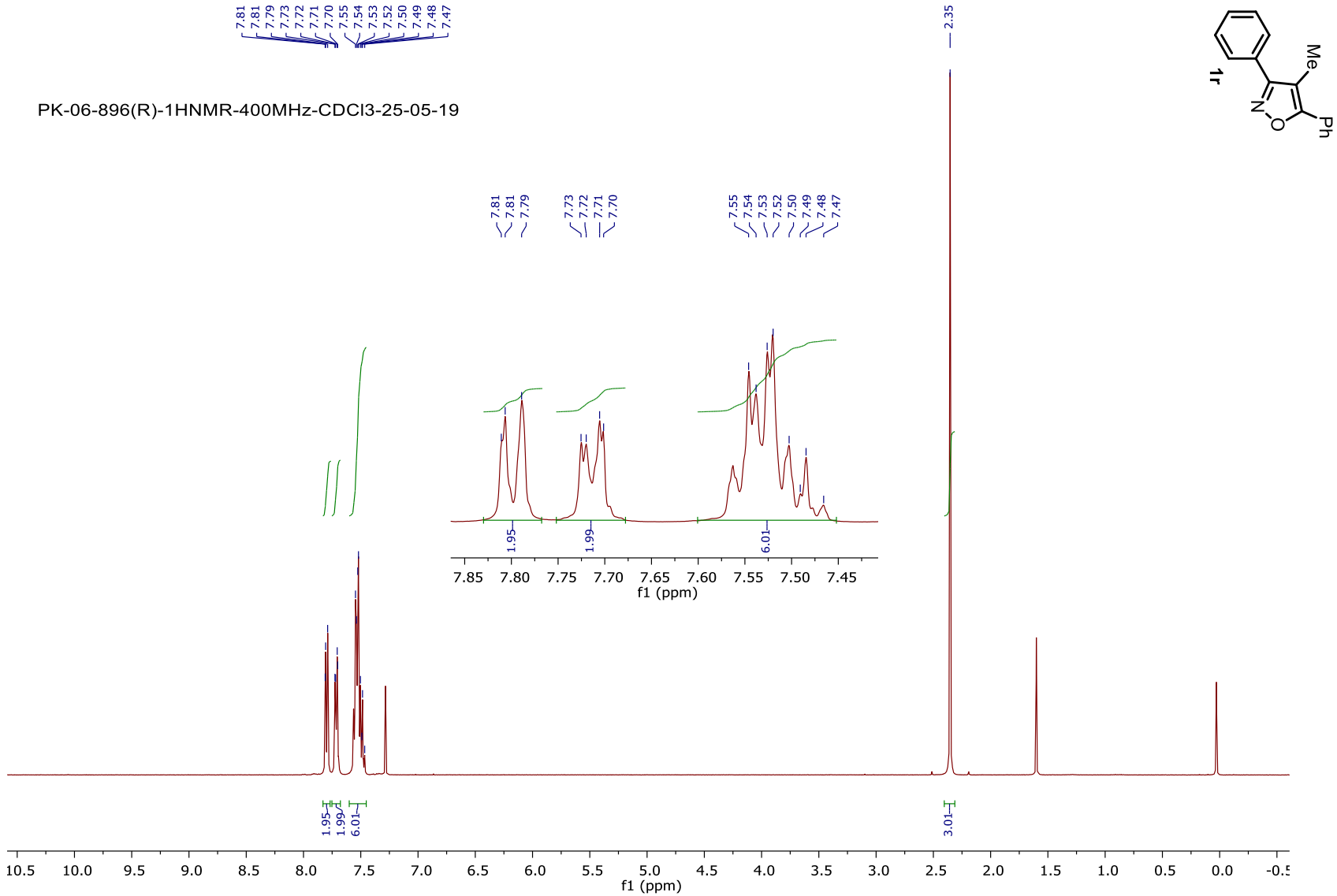

PK-03-207-1HNMR-500MHz-CDCl3-24-08-19
f1 (ppm)
1.00
2.03
3.38
4.28

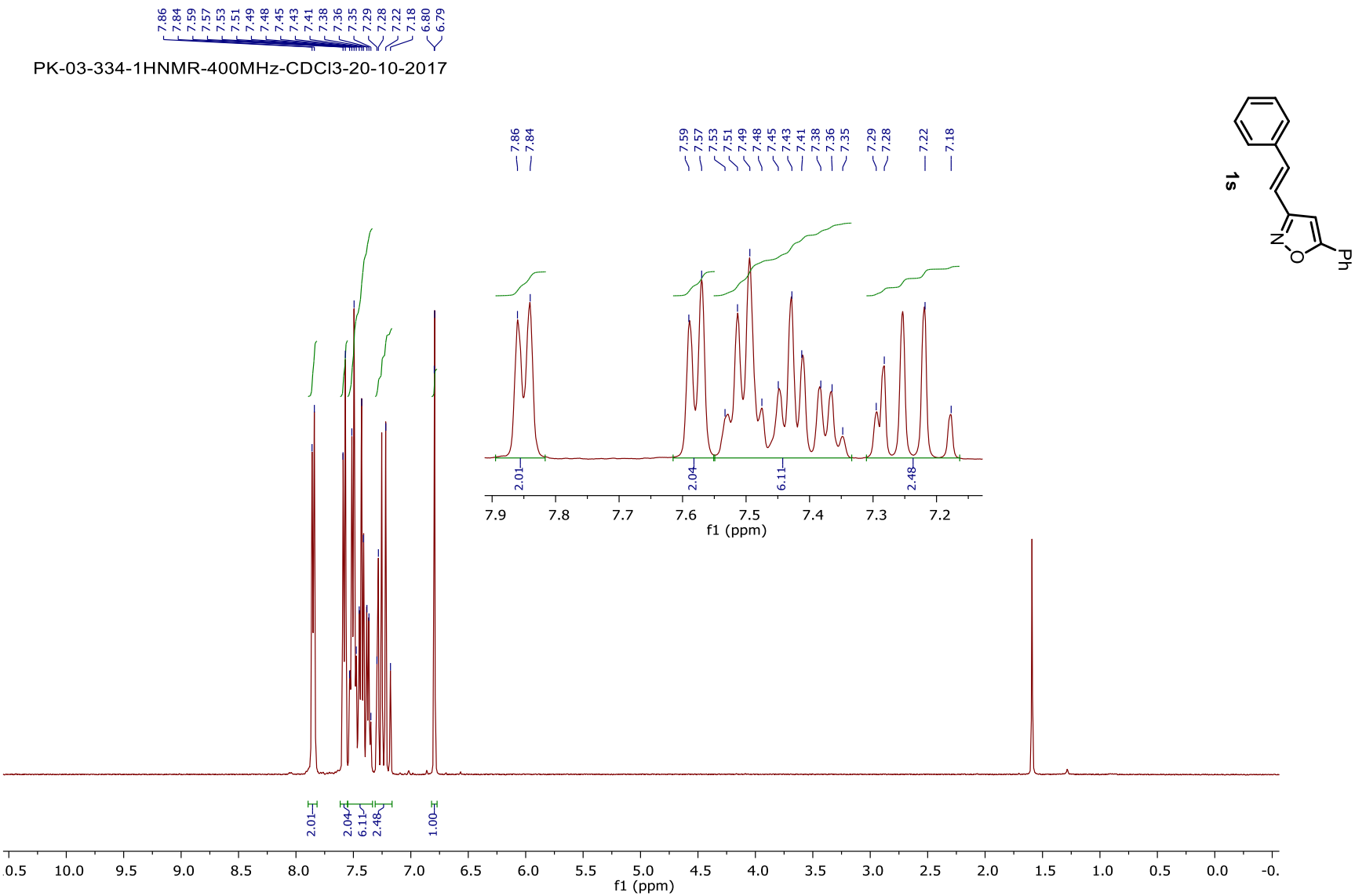

Ph
O
N
NC
1n
SK-01-42-1HNMR-500MHz-CDCl3-28-12-18
f1 (ppm)

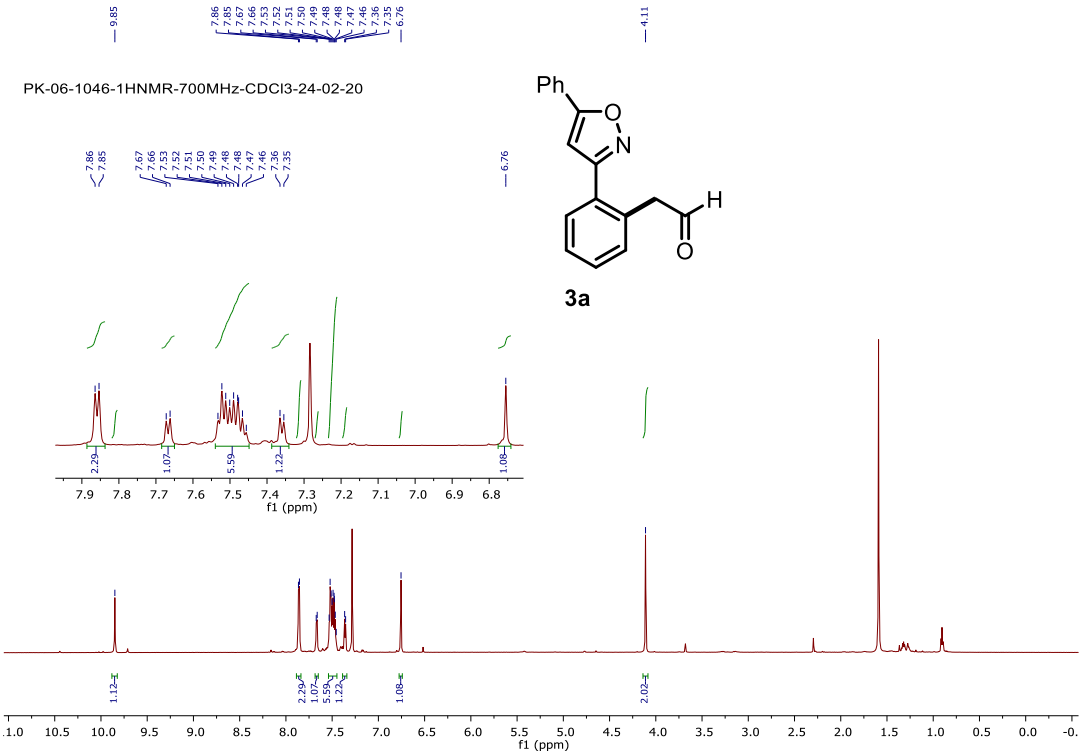

p-tolyl
O2N
1o
PK-06-987-1HNMR-400MHz-CDCl3-17-12-19
f1 (ppm)

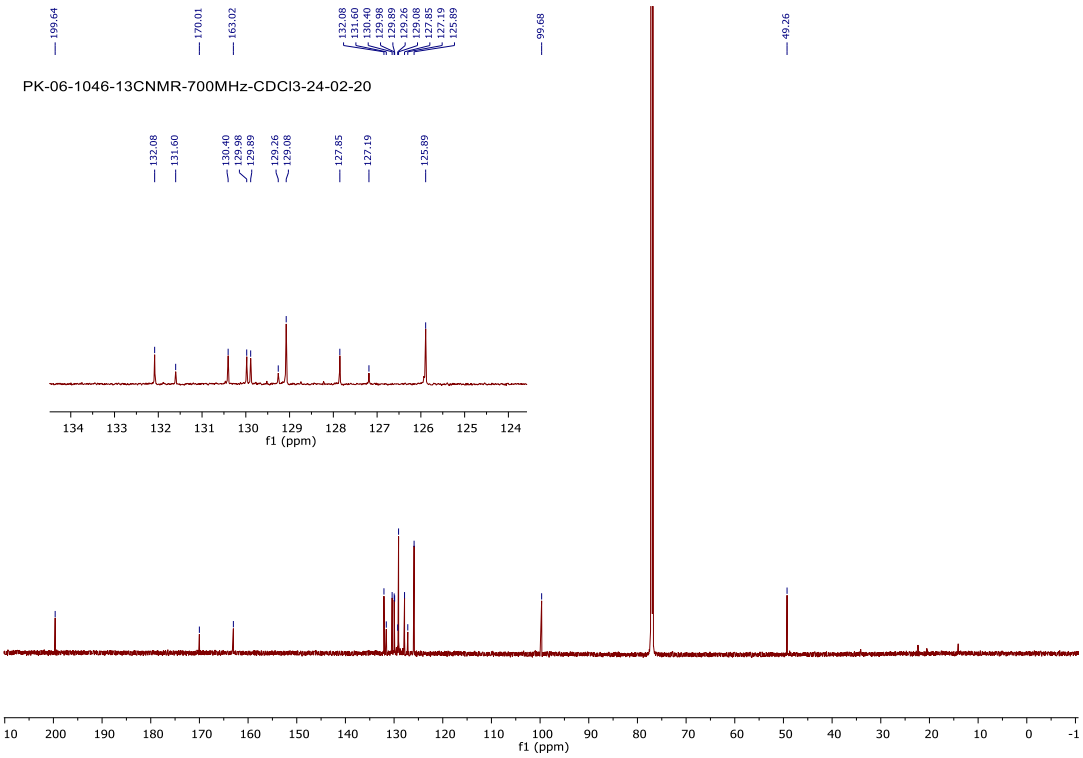

Me
O
N
O
MeO
1p
SK-03-62-1HNMR-400MHz-CDCl3-28-11-19
f1 (ppm)

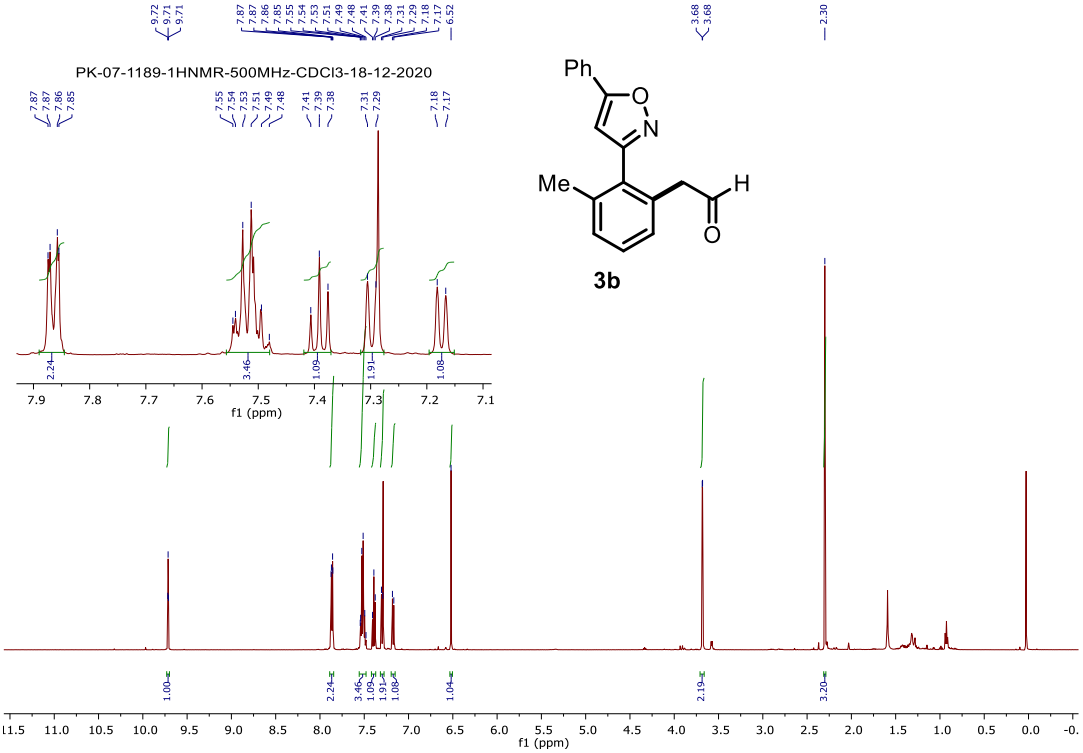

PK-07-1230-1HNMR-500MHz-CDCl3-22-01-2021
8.43
8.43
7.80
7.78
7.01
6.99
6.62
6.62
3.87
MeO
1q
2.01
2.04
f1 (ppm)
0.98
2.01
2.04
1.00
3.13
f1 (ppm)

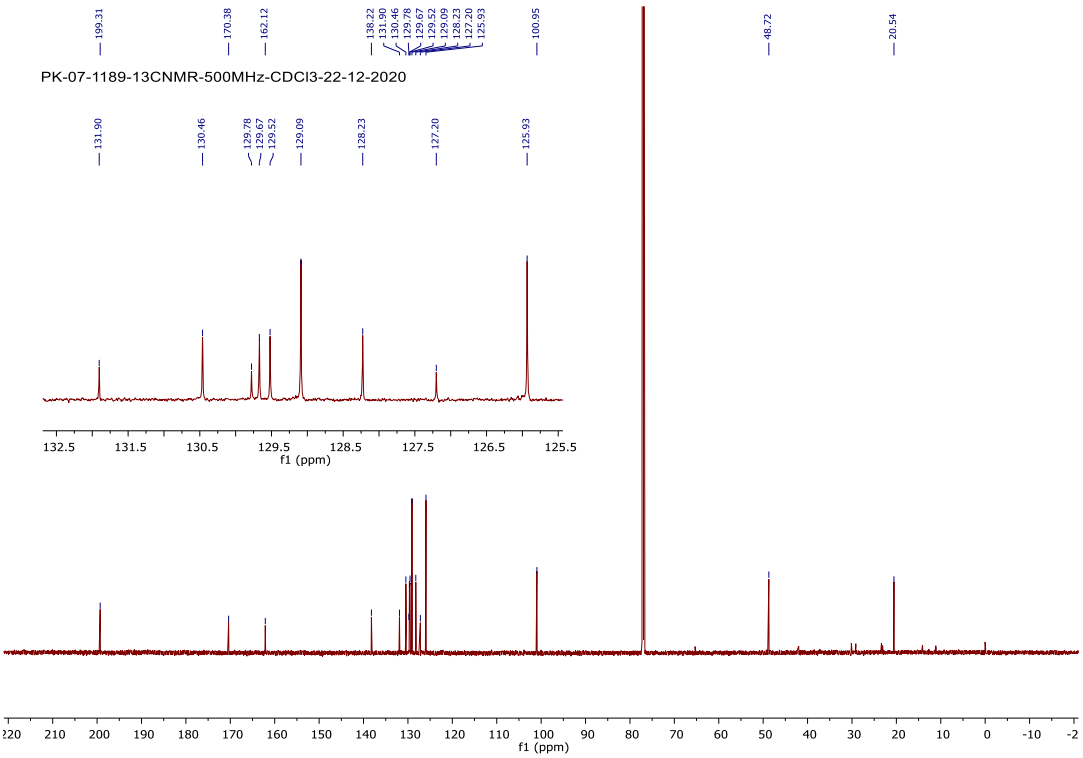

7.81
7.81
7.79
7.73
7.72
7.71
7.70
7.55
7.54
7.53
7.52
7.50
7.49
7.48
7.47
2.35
PK-06-896(R)-1HNMR-400MHz-CDCl3-25-05-19
1r
Me
Ph
N
O
1.95
1.99
6.01
3.01
f1 (ppm)

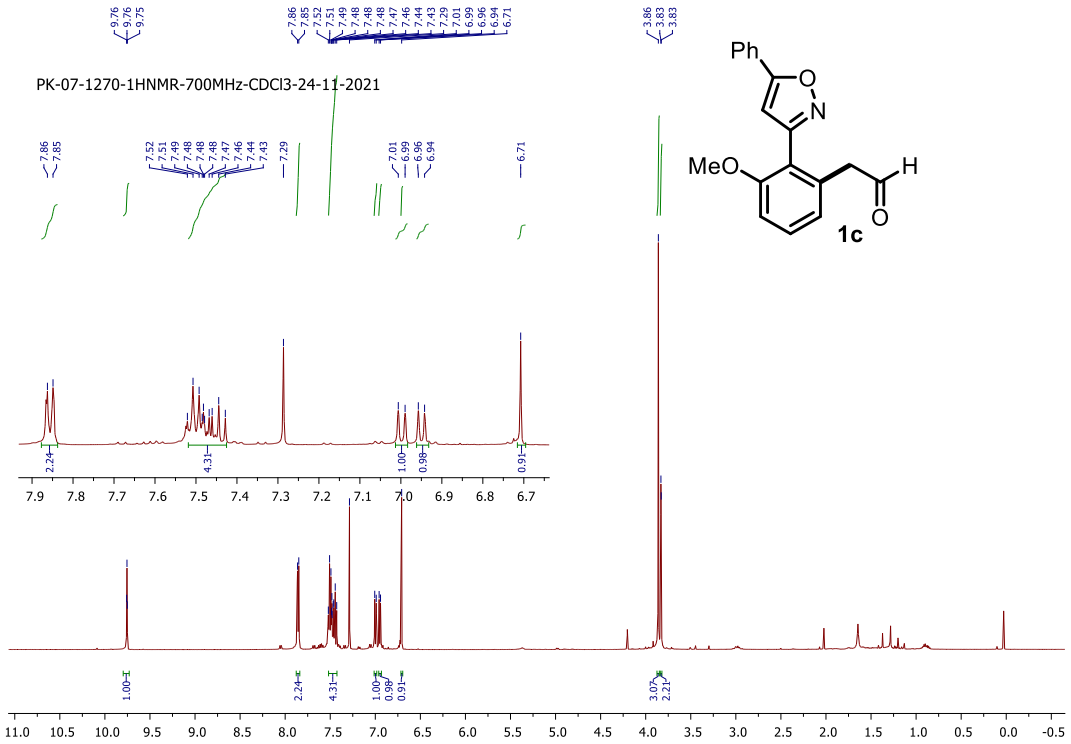

7.86
7.84
7.59
7.57
7.53
7.51
7.49
7.48
7.45
7.43
7.41
7.38
7.36
7.35
7.29
7.28
7.22
7.18
6.80
6.79
PK-03-334-1HNMR-400MHz-CDCl3-20-10-2017
1s
N
O
Ph
2.01
2.04
6.11
2.48
1.00
f1 (ppm)

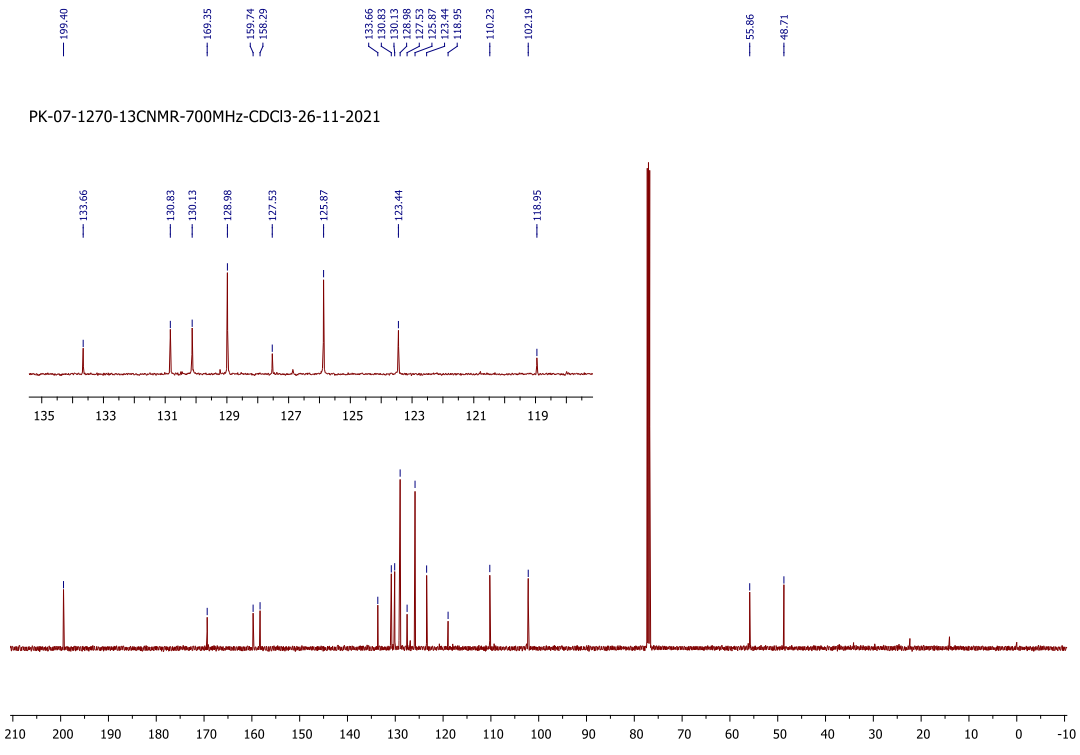

PK-06-1046-1HNMR-700MHz-CDCl3-24-02-20
Ph
O
N
H
O
3a
f1 (ppm)

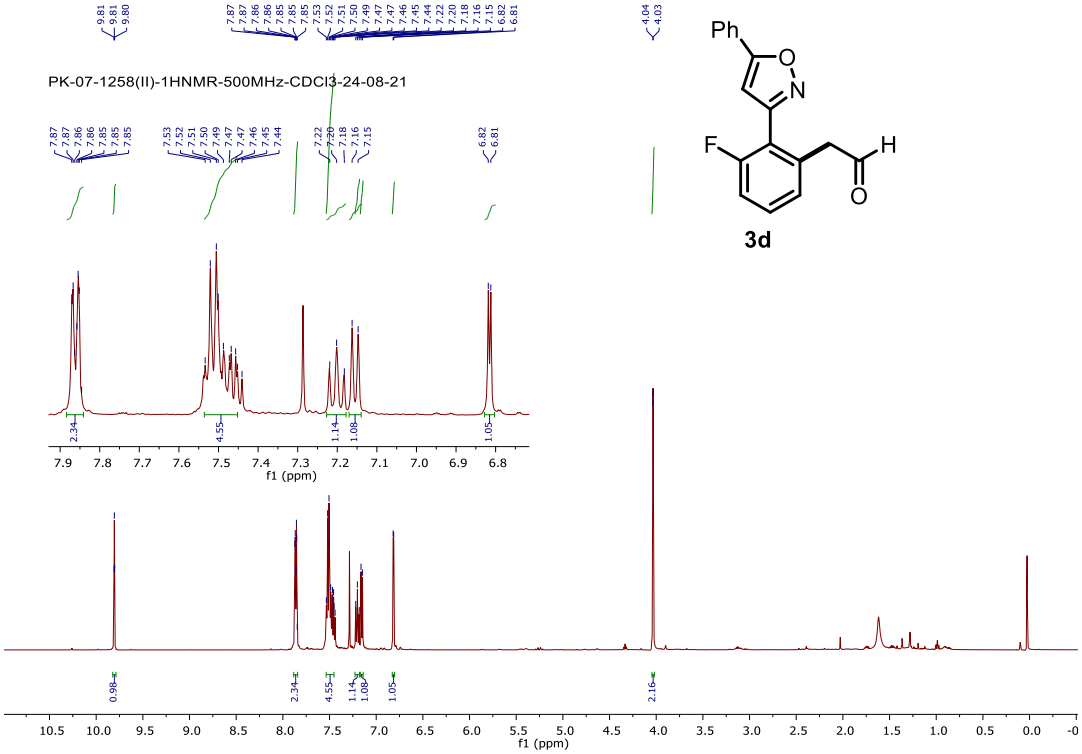

PK-06-1046-13CNMR-700MHz-CDCl3-24-02-20
f1 (ppm)

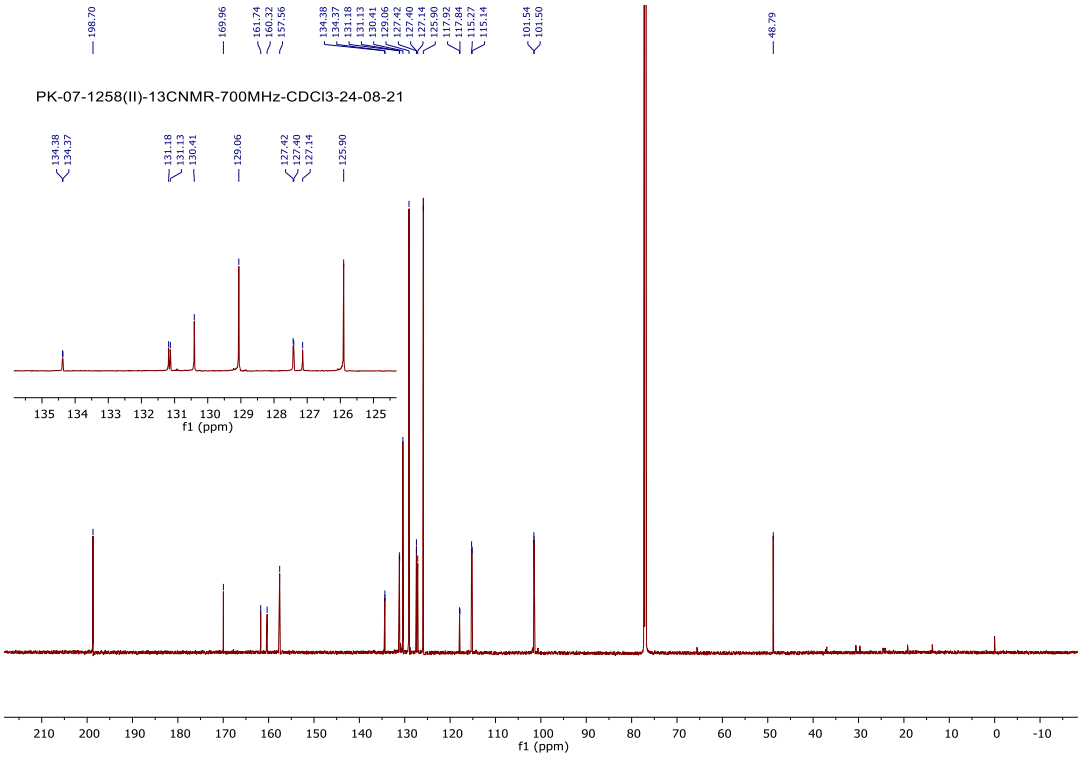

PK-07-1189-1HNMR-500MHz-CDCl3-18-12-2020
Ph
O
N
Me
H
O
3b
f1 (ppm)

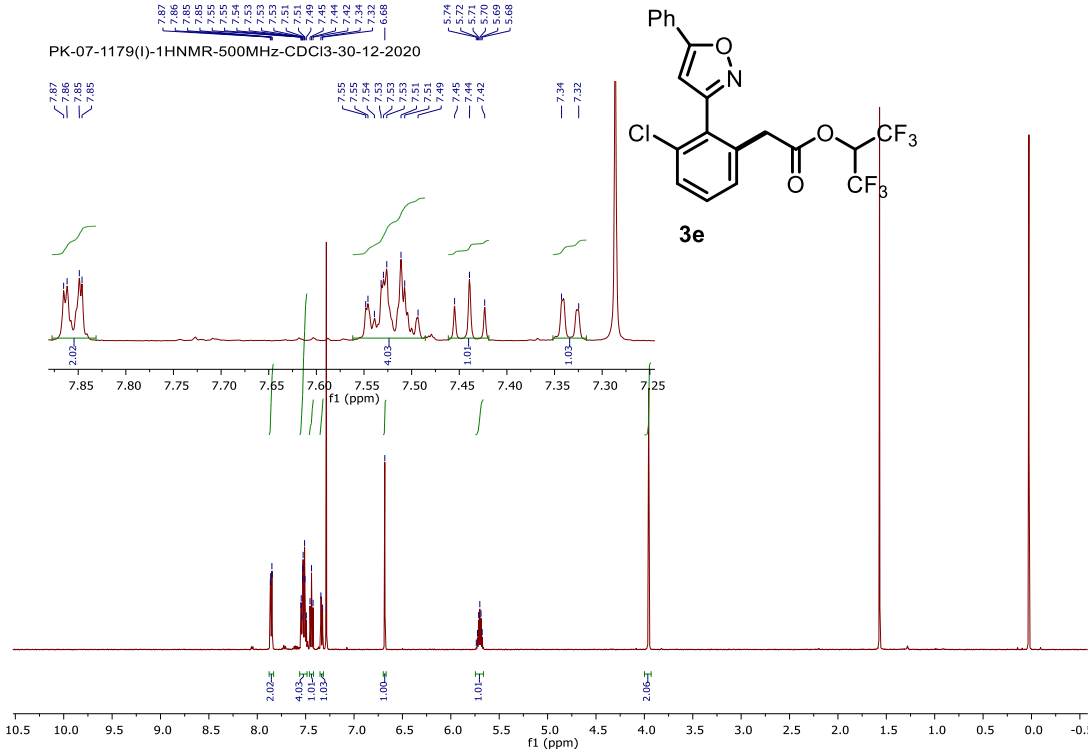

PK-07-1189-13CNMR-500MHz-CDCl3-22-12-2020
f1 (ppm)

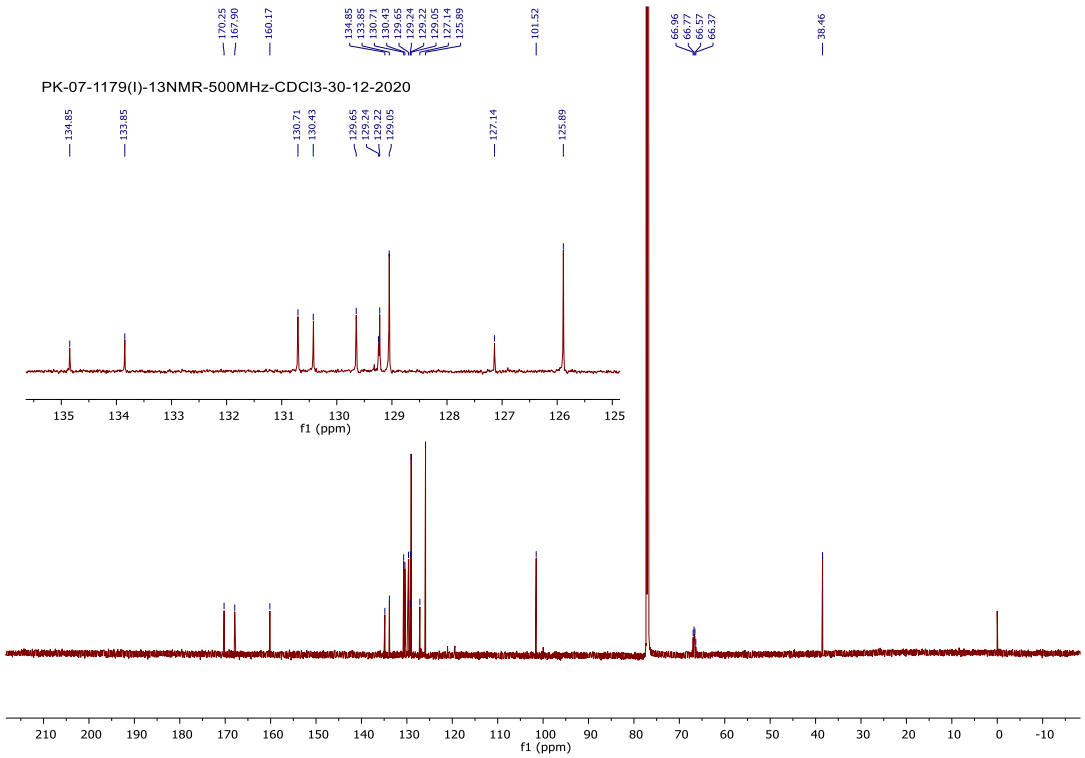

PK-07-1270-1HNMR-700MHz-CDCl3-24-11-2021
Ph
O
N
MeO
H
O
1c

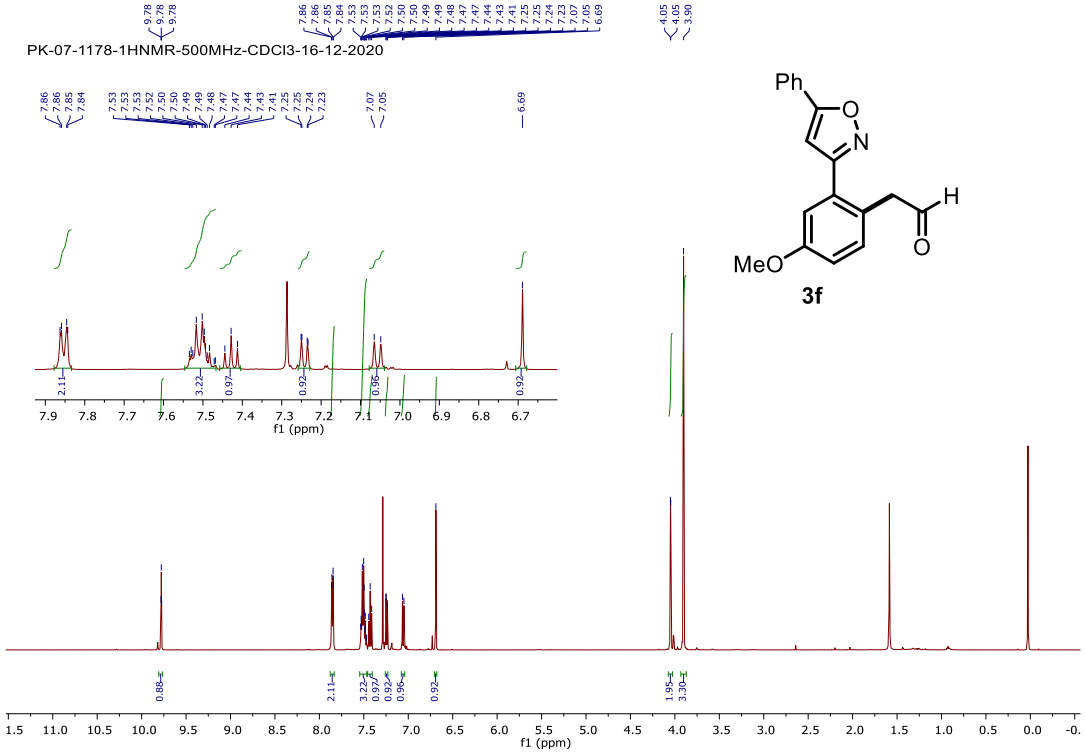

PK-07-1270-13CNMR-700MHz-CDCl3-26-11-2021

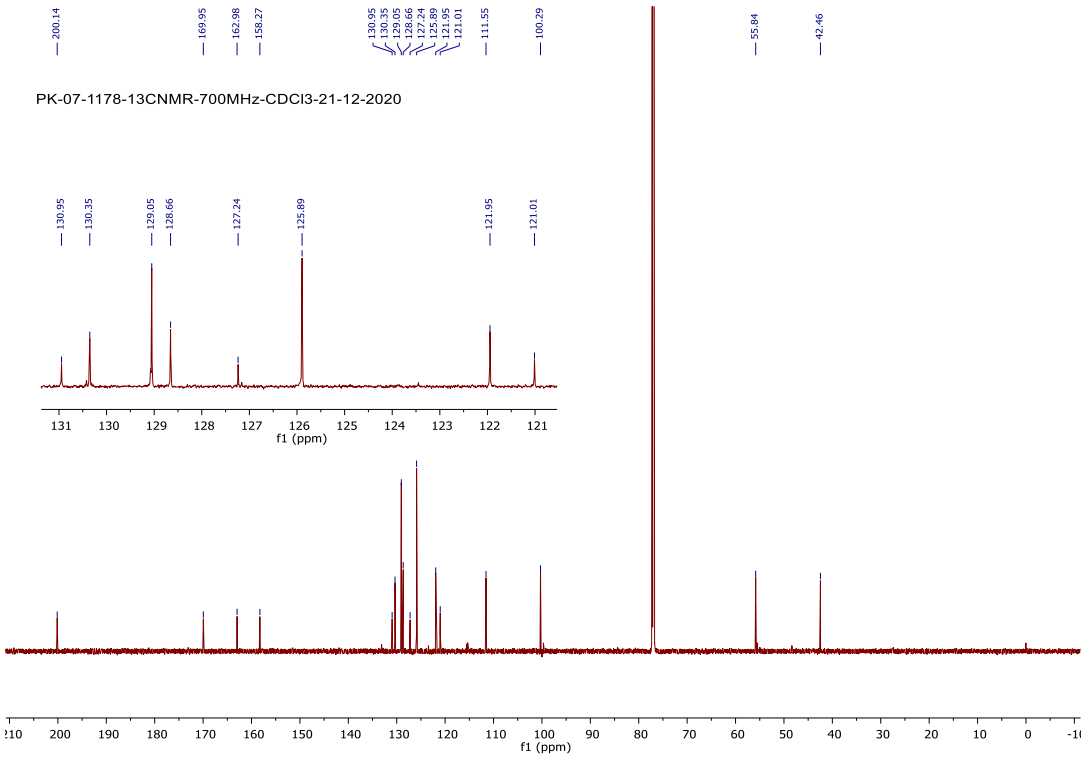

PK-07-1258(II)-1HNMR-500MHz-CDCl3-24-08-21
Ph
O
N
F
H
O
3d
f1 (ppm)

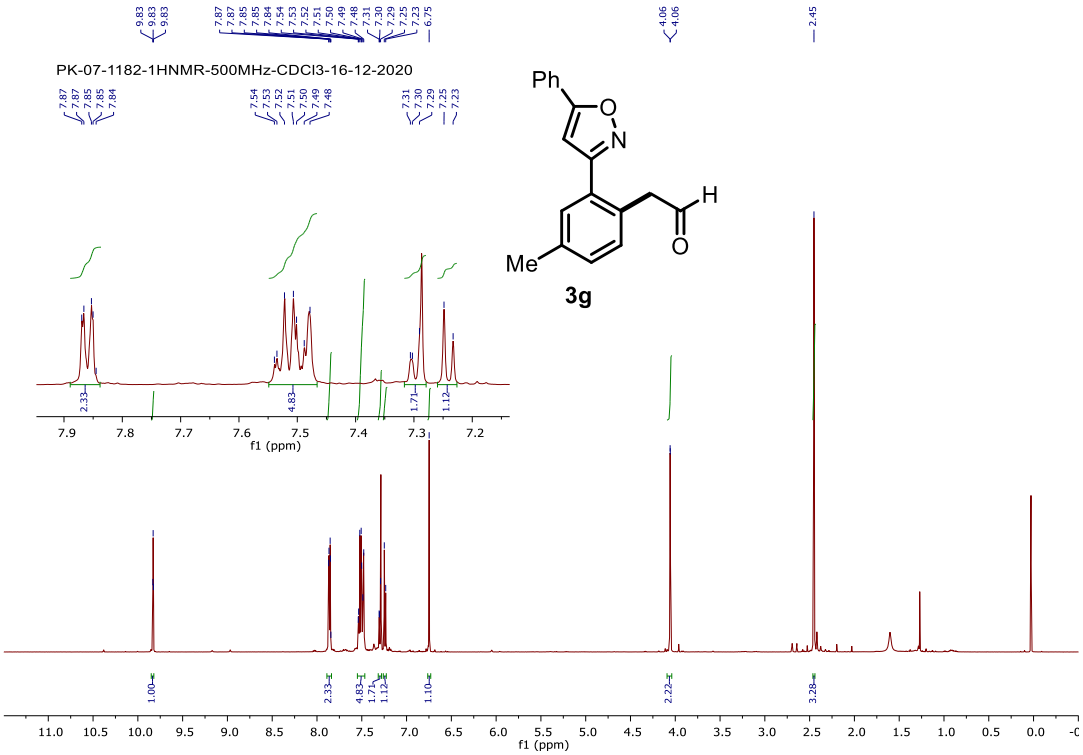

PK-07-1258(II)-13CNMR-700MHz-CDCl3-24-08-21
f1 (ppm)

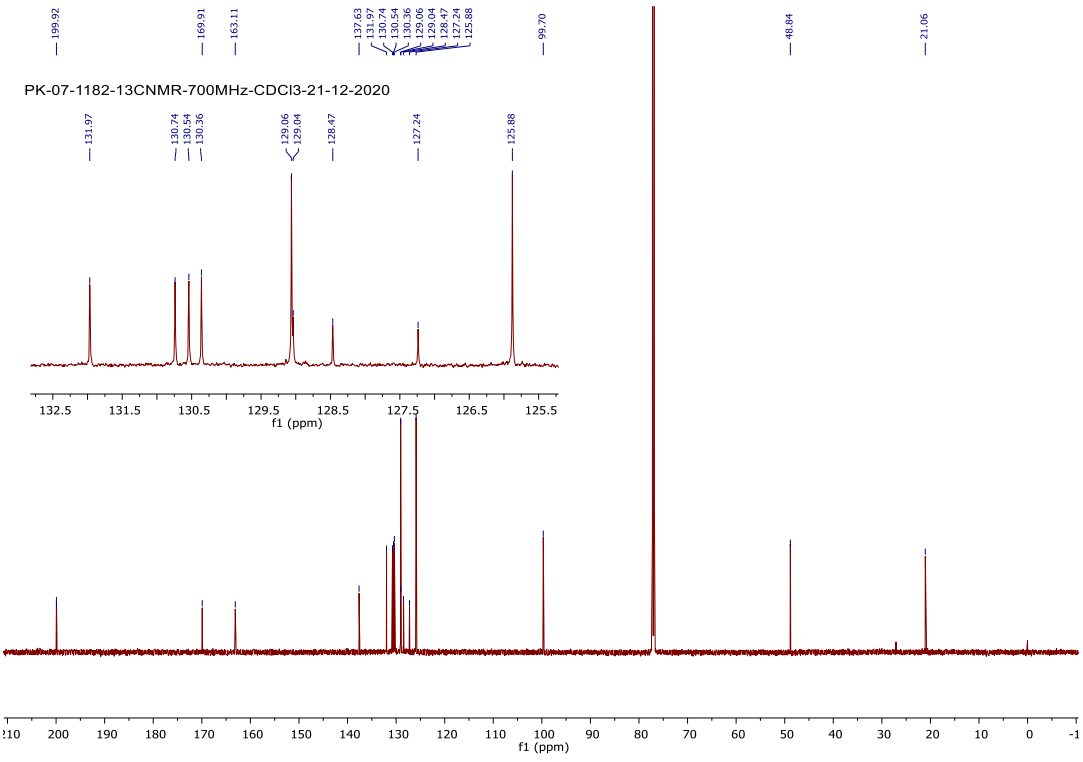

PK-07-1179(I)-1HNMR-500MHz-CDCl3-30-12-2020
Ph
O
N
Cl
O
O
CF3
CF3
3e
f1 (ppm)

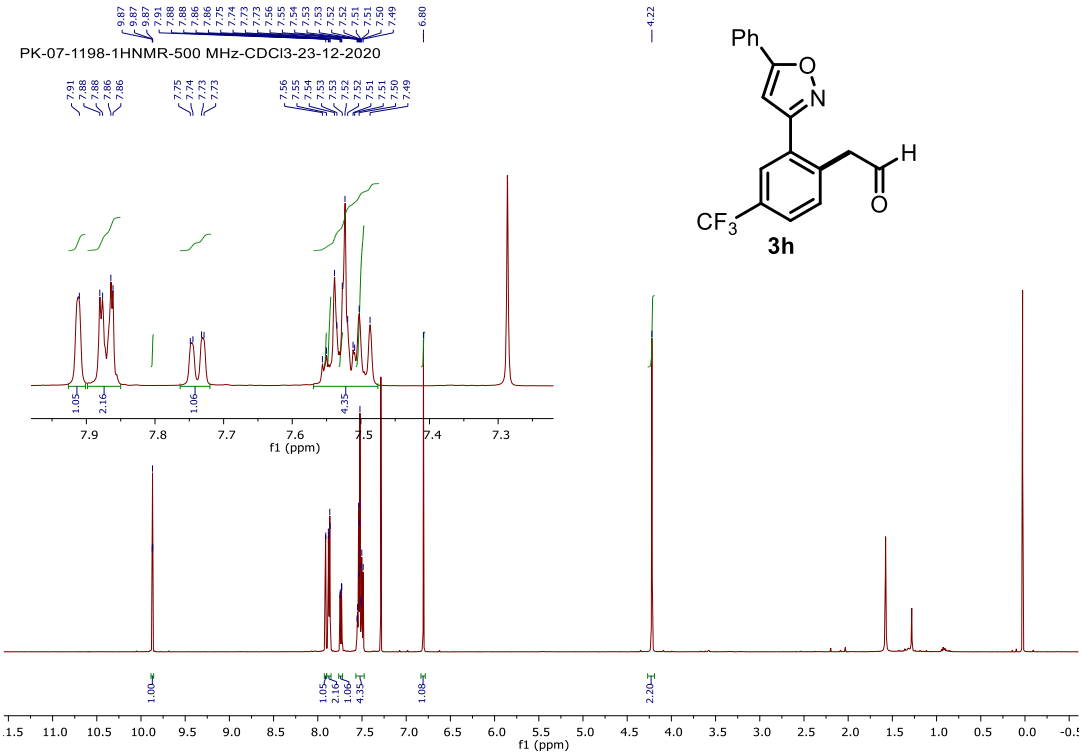

PK-07-1179(I)-13NMR-500MHz-CDCl3-30-12-2020
f1 (ppm)

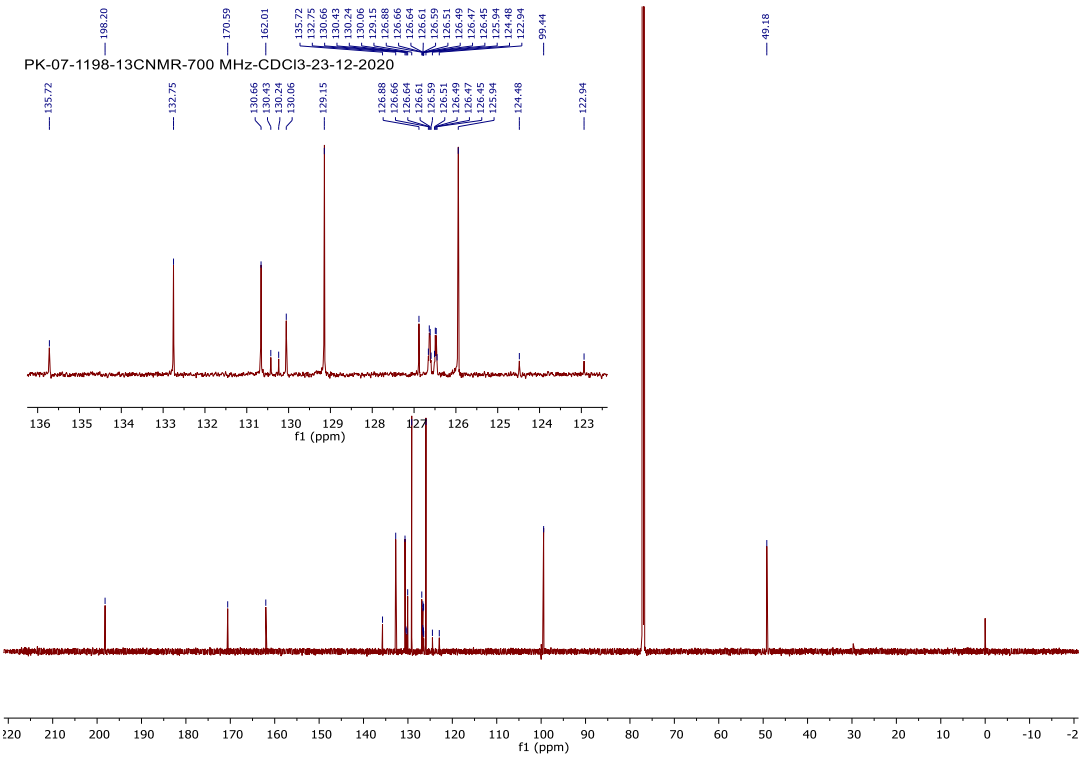

PK-07-1178-1HNMR-500MHz-CDCl3-16-12-2020
Ph
O
N
H
O
MeO
3f
f1 (ppm)

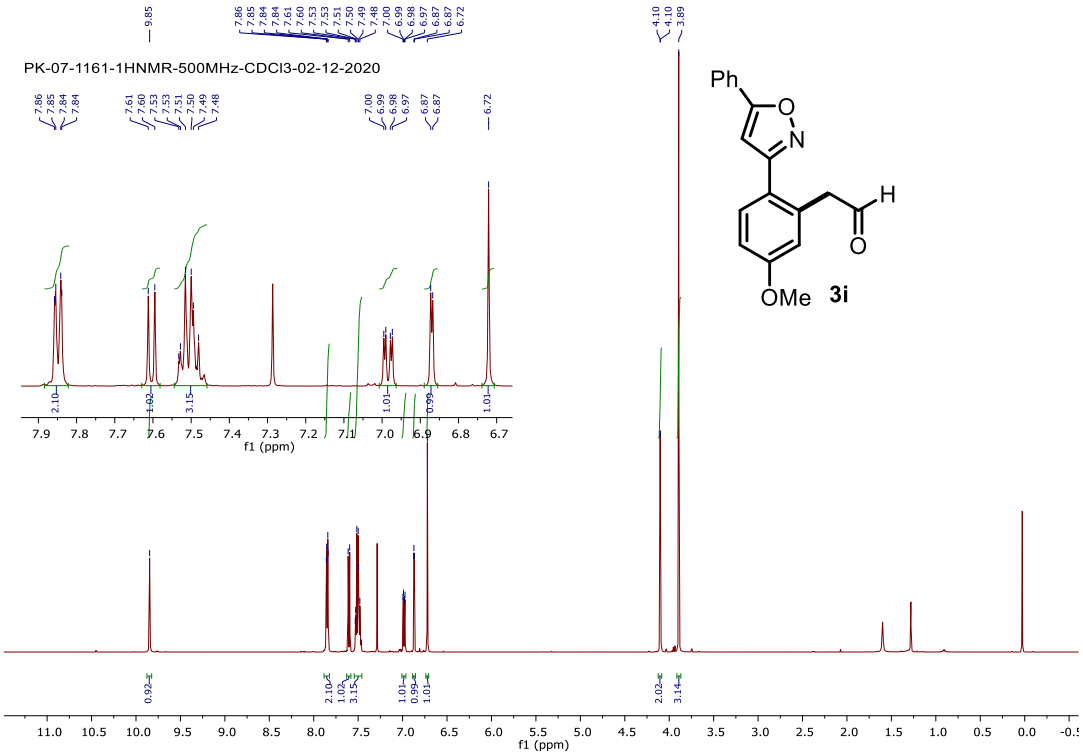

PK-07-1178-13CNMR-700MHz-CDCl3-21-12-2020
f1 (ppm)

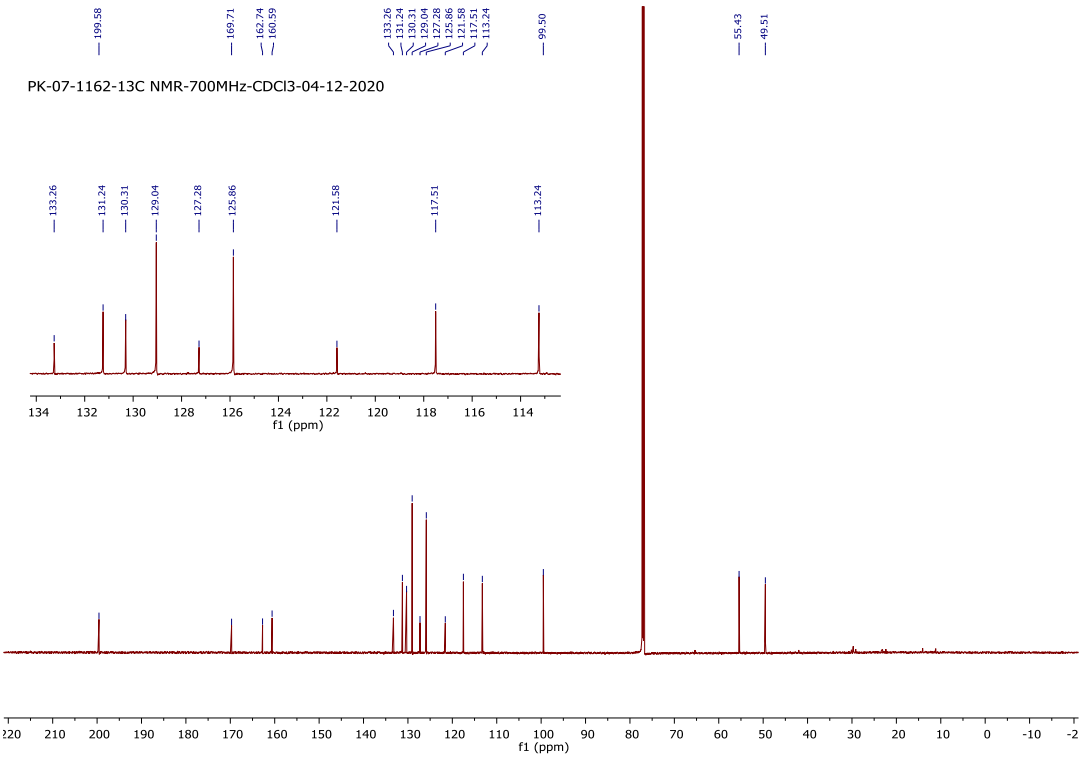

PK-07-1182-1HNMR-500MHz-CDCl3-16-12-2020
Ph
O
N
H
O
Me
3g
f1 (ppm)

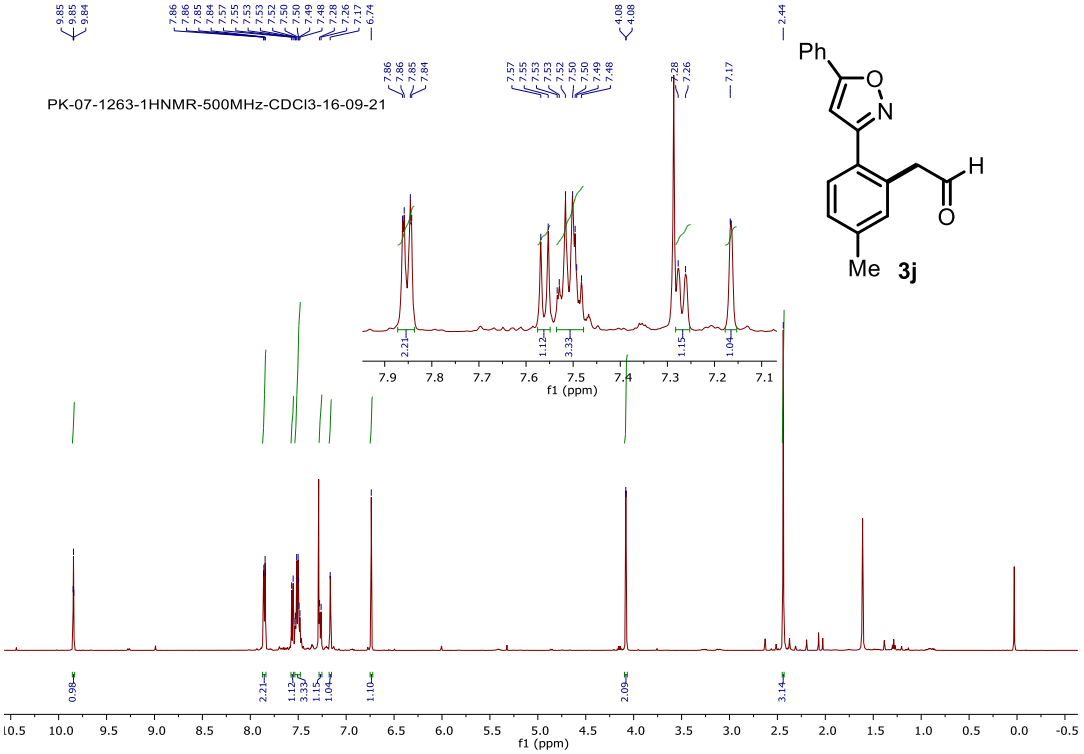

PK-07-1182-13CNMR-700MHz-CDCl3-21-12-2020
f1 (ppm)

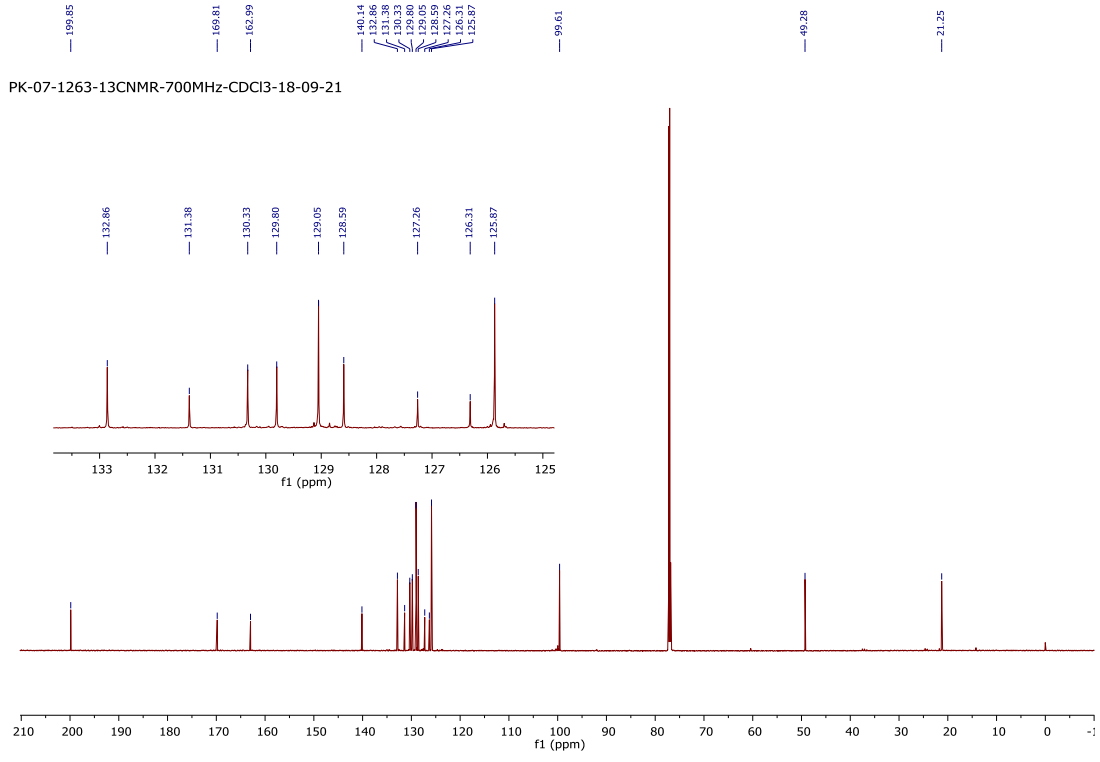

PK-07-1198-1HNMR-500 MHz-CDCl3-23-12-2020
Ph
O
N
H
O
CF3
3h
f1 (ppm)

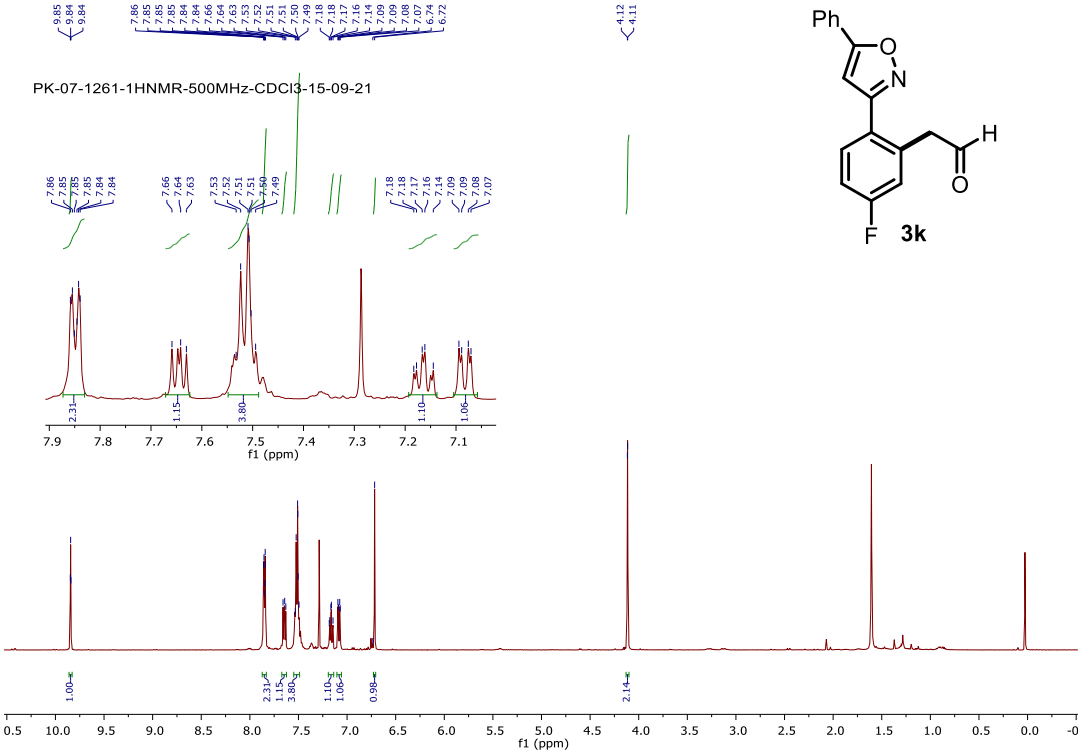

PK-07-1198-13CNMR-700 MHz-CDCl3-23-12-2020
f1 (ppm)

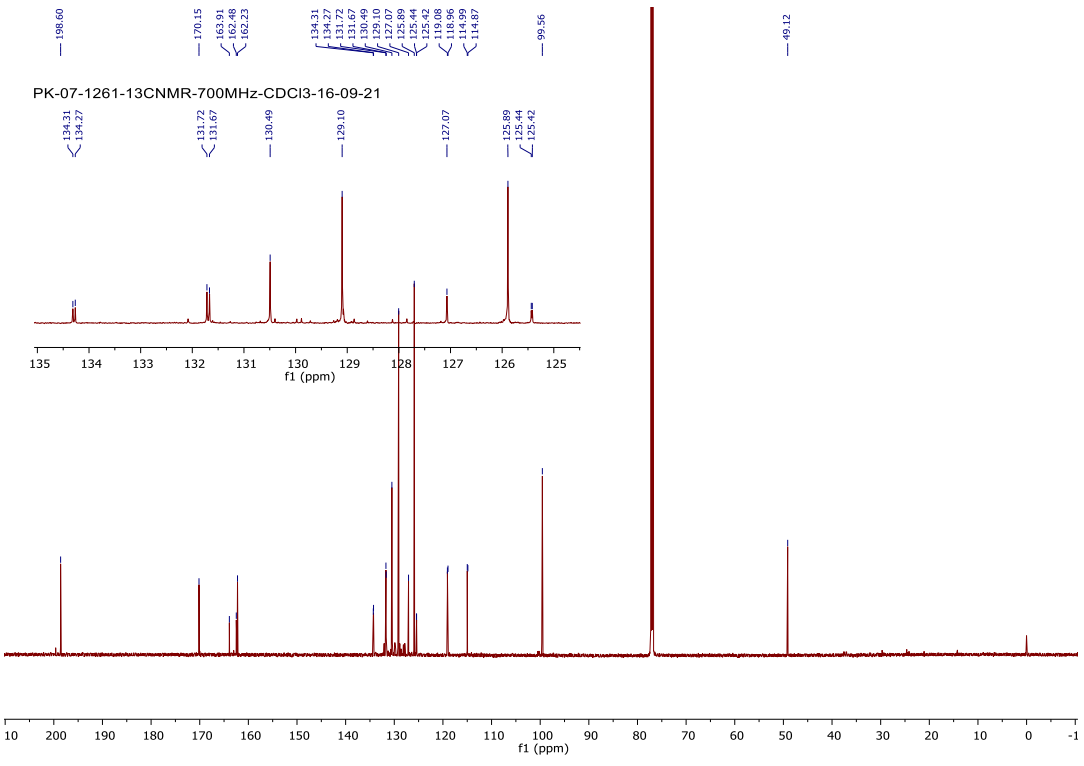

PK-07-1161-1HNMR-500MHz-CDCl3-02-12-2020
Ph
O
N
H
O
OMe
3i
f1 (ppm)

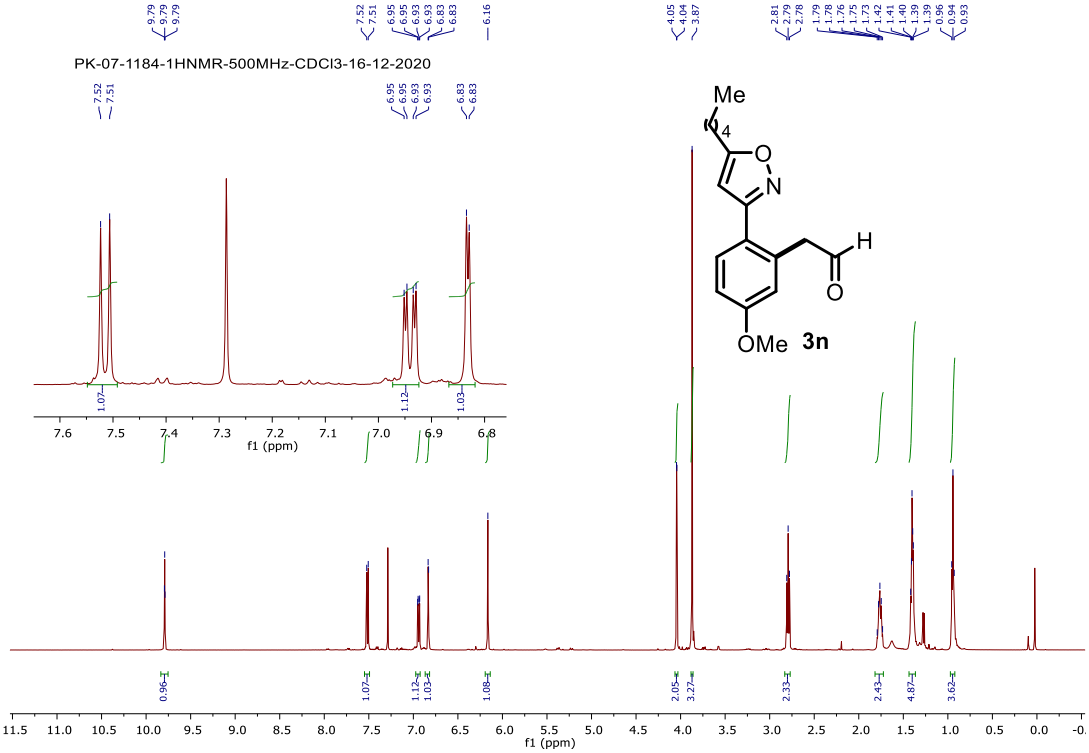

PK-07-1162-13C NMR-700MHz-CDCl3-04-12-2020
f1 (ppm)

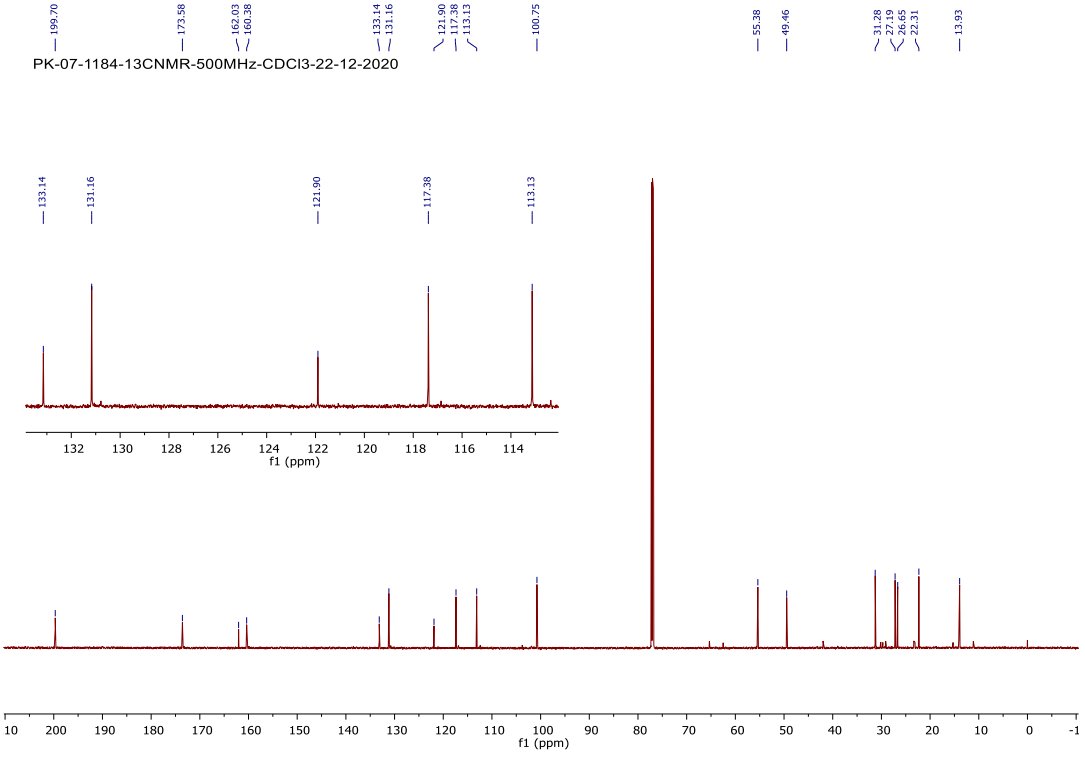

PK-07-1263-1HNMR-500MHz-CDCl3-16-09-21
Ph
O
N
H
O
Me
3j
f1 (ppm)

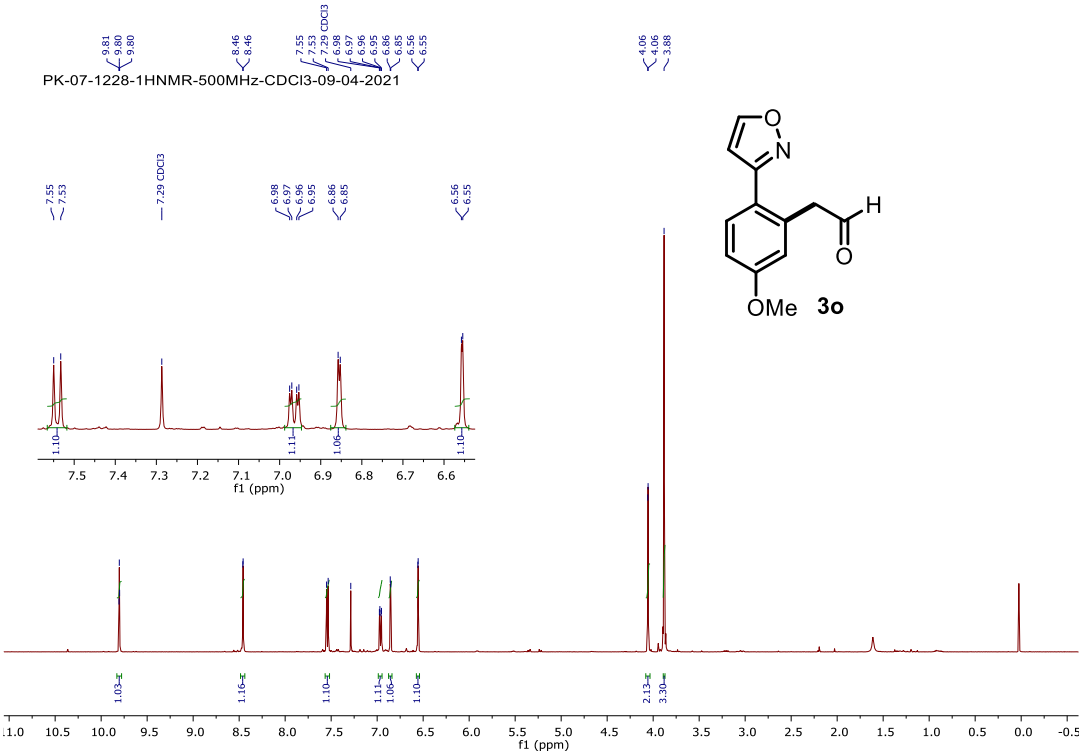

PK-07-1263-13CNMR-700MHz-CDCl3-18-09-21
f1 (ppm)

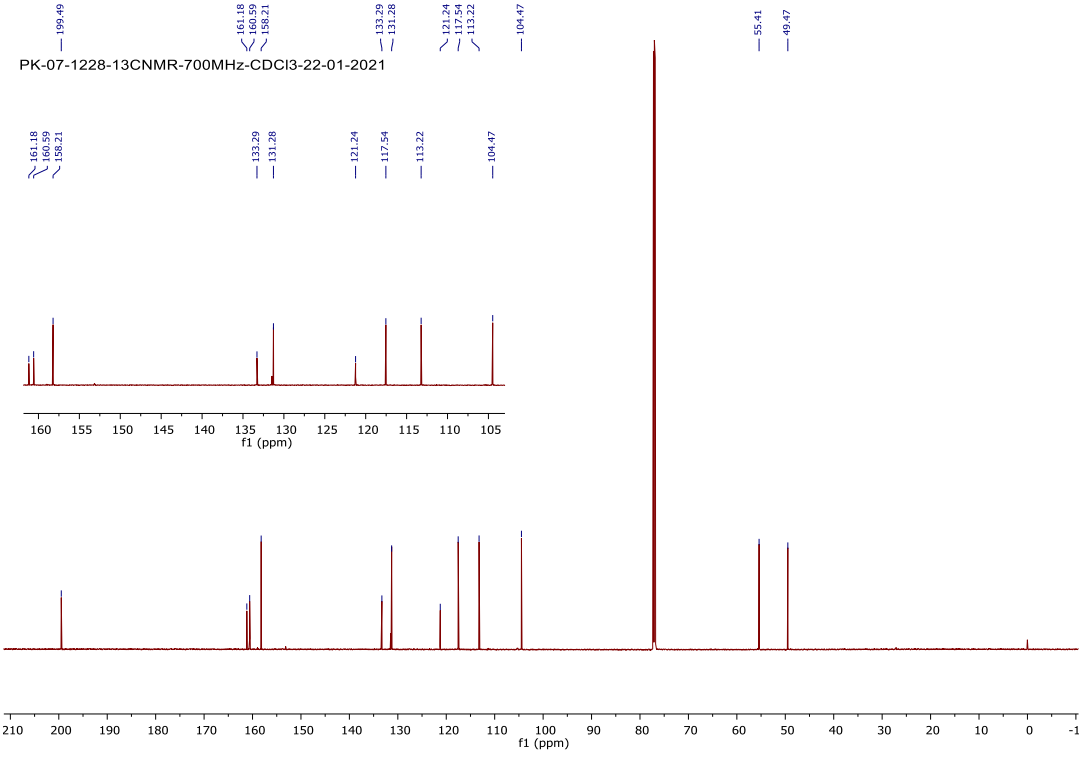

PK-07-1261-1HNMR-500MHz-CDCl3-15-09-21
Ph
O
N
H
O
F
3k
f1 (ppm)

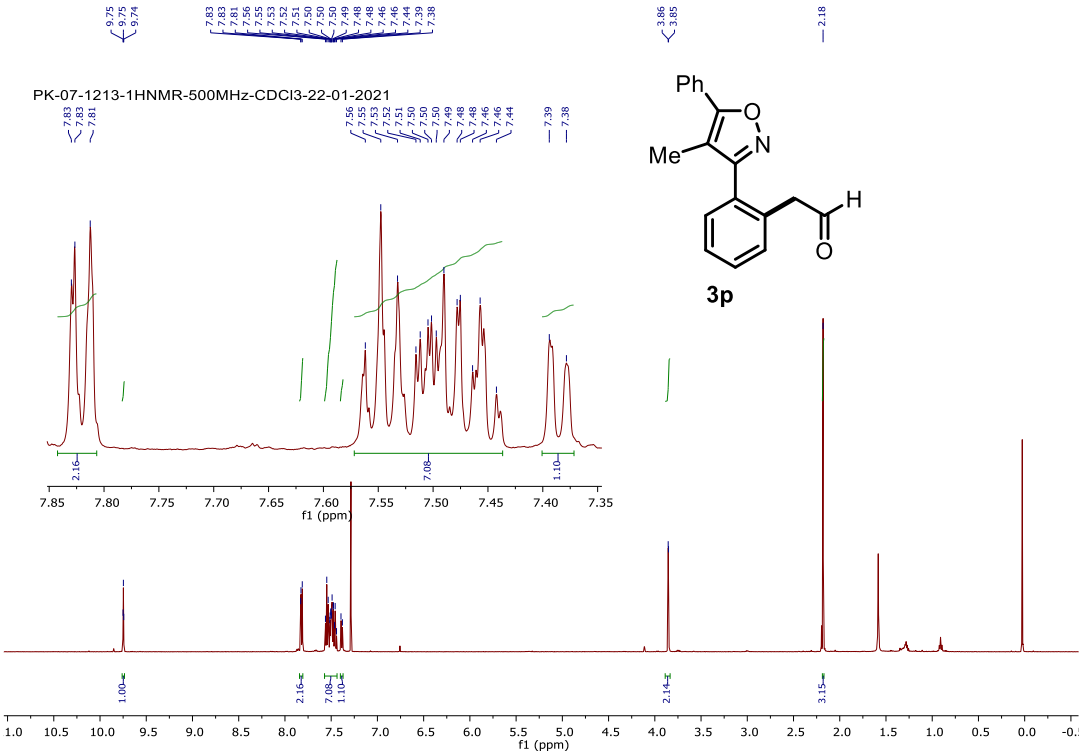

PK-07-1261-13CNMR-700MHz-CDCl3-16-09-21
f1 (ppm)

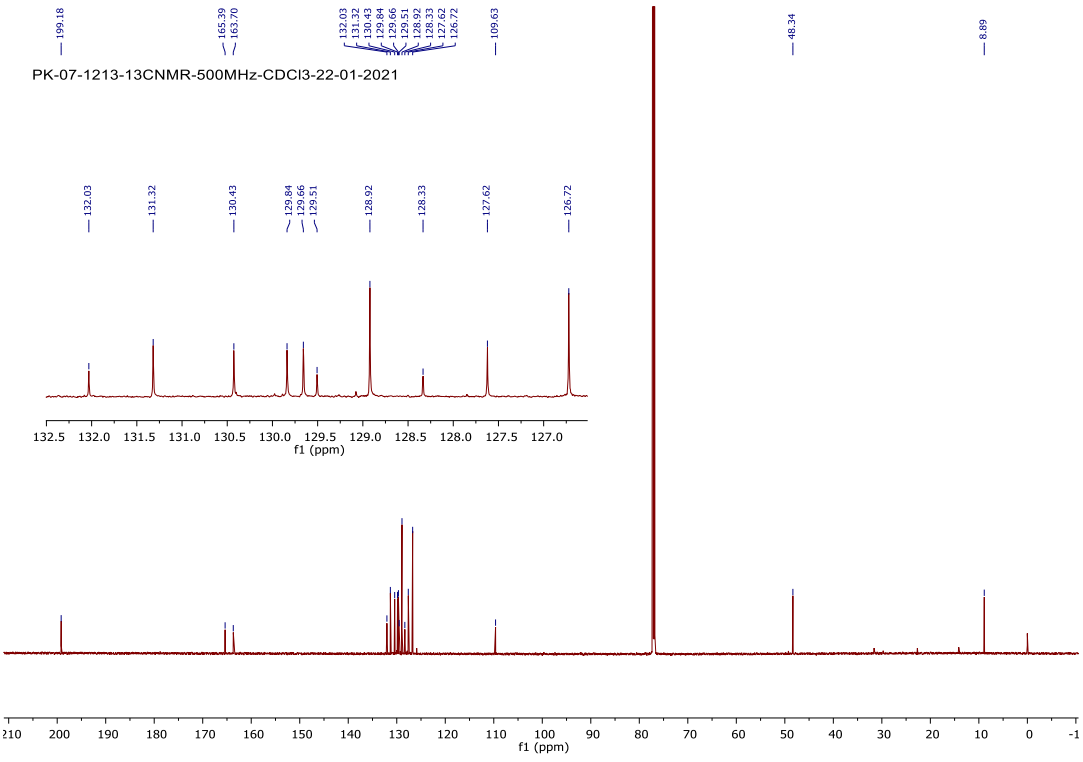

PK-07-1184-1HNMR-500MHz-CDCl3-16-12-2020
Me
O
N
H
O
OMe
3n
f1 (ppm)

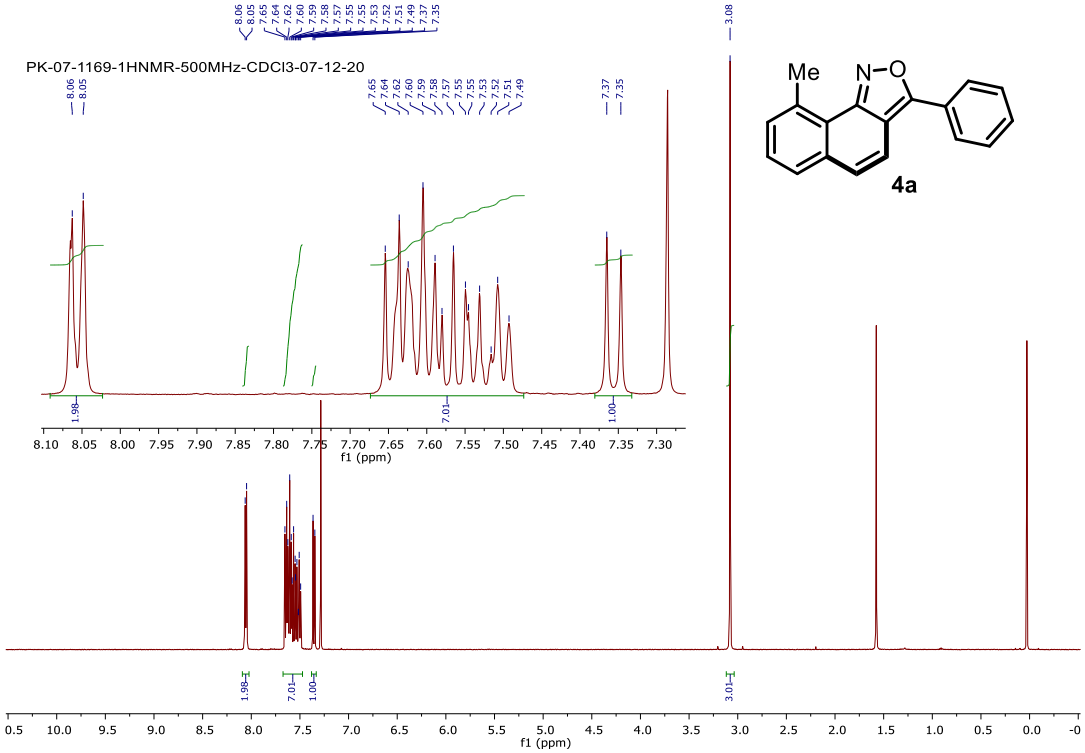

PK-07-1184-13CNMR-500MHz-CDCl3-22-12-2020
f1 (ppm)

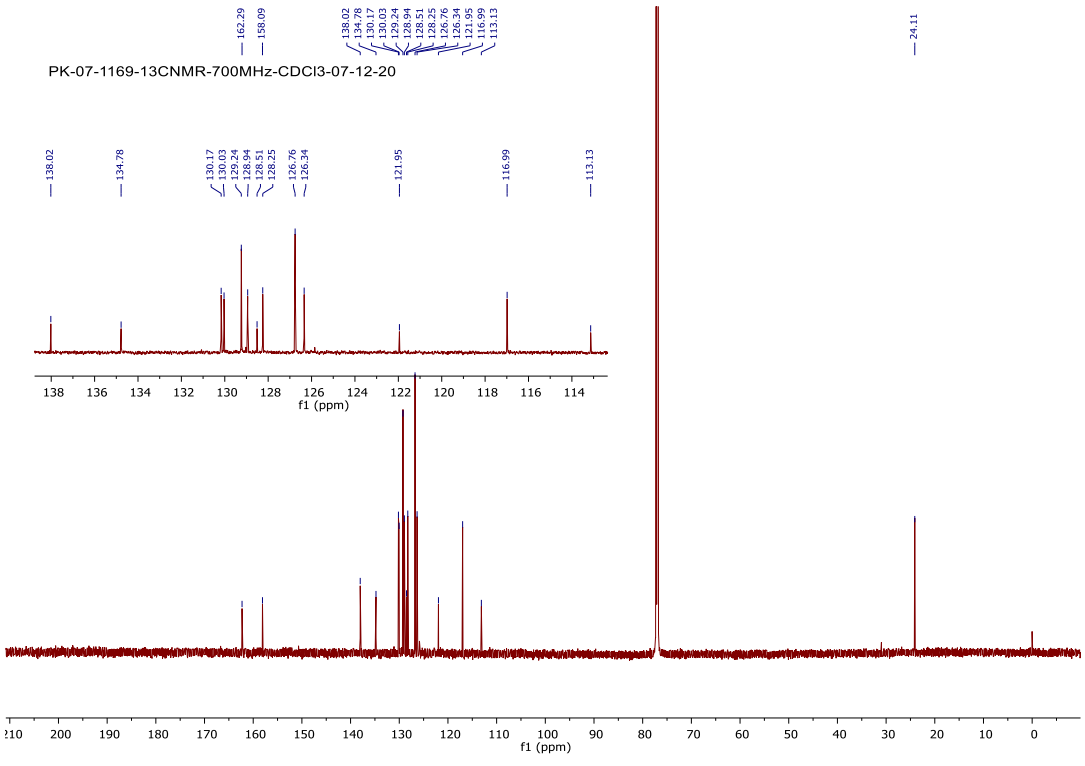

PK-07-1228-1HNMR-500MHz-CDCl3-09-04-2021
9.81
9.80
9.80
8.46
8.46
7.55
7.53
7.29 CDCl3
6.98
6.97
6.96
6.95
6.86
6.85
6.56
6.55
4.06
4.06
3.88
O
N
H
O
OMe
3o
f1 (ppm)

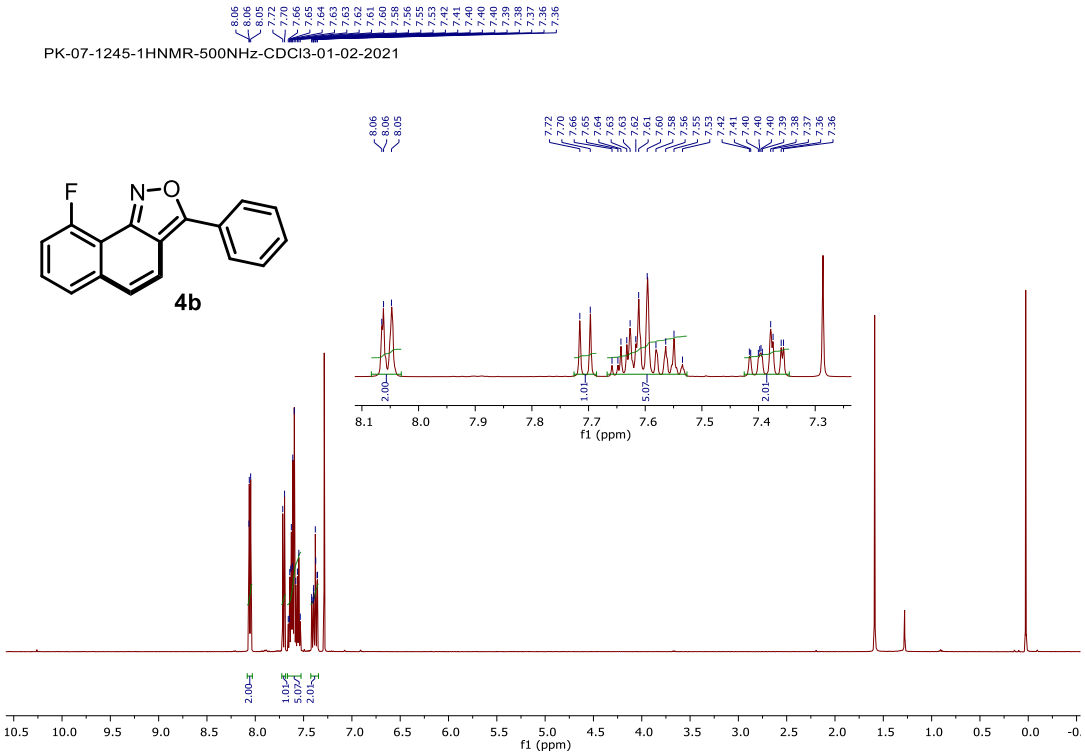

PK-07-1228-13CNMR-700MHz-CDCl3-22-01-2021
199.49
161.18
160.59
158.21
133.29
131.28
121.24
117.54
113.22
104.47
55.41
49.47
f1 (ppm)

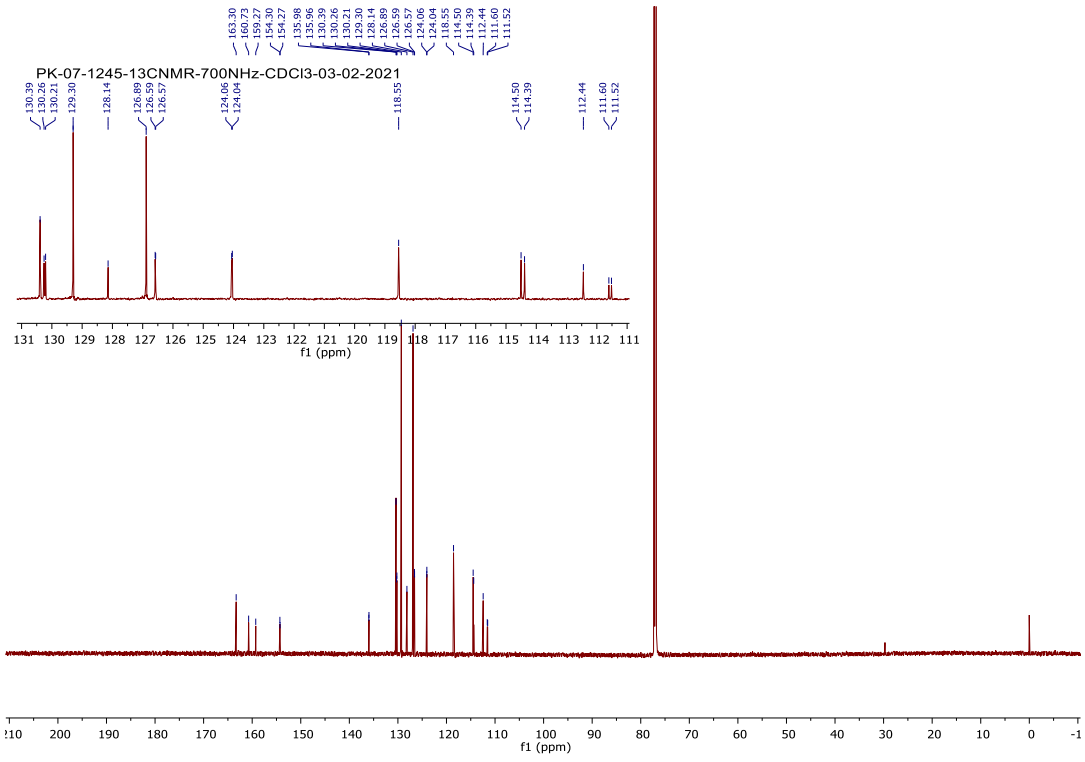

PK-07-1213-1HNMR-500MHz-CDCl3-22-01-2021
Ph
O
N
Me
H
O
3p
f1 (ppm)

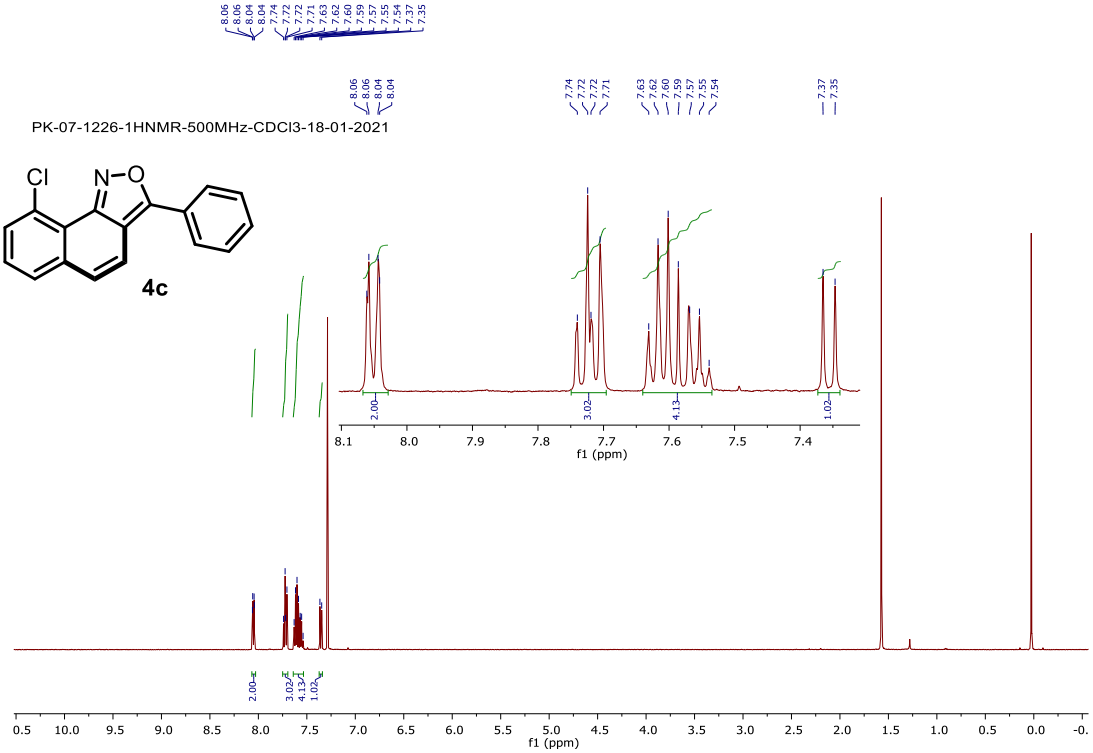

PK-07-1213-13CNMR-500MHz-CDCl3-22-01-2021
f1 (ppm)

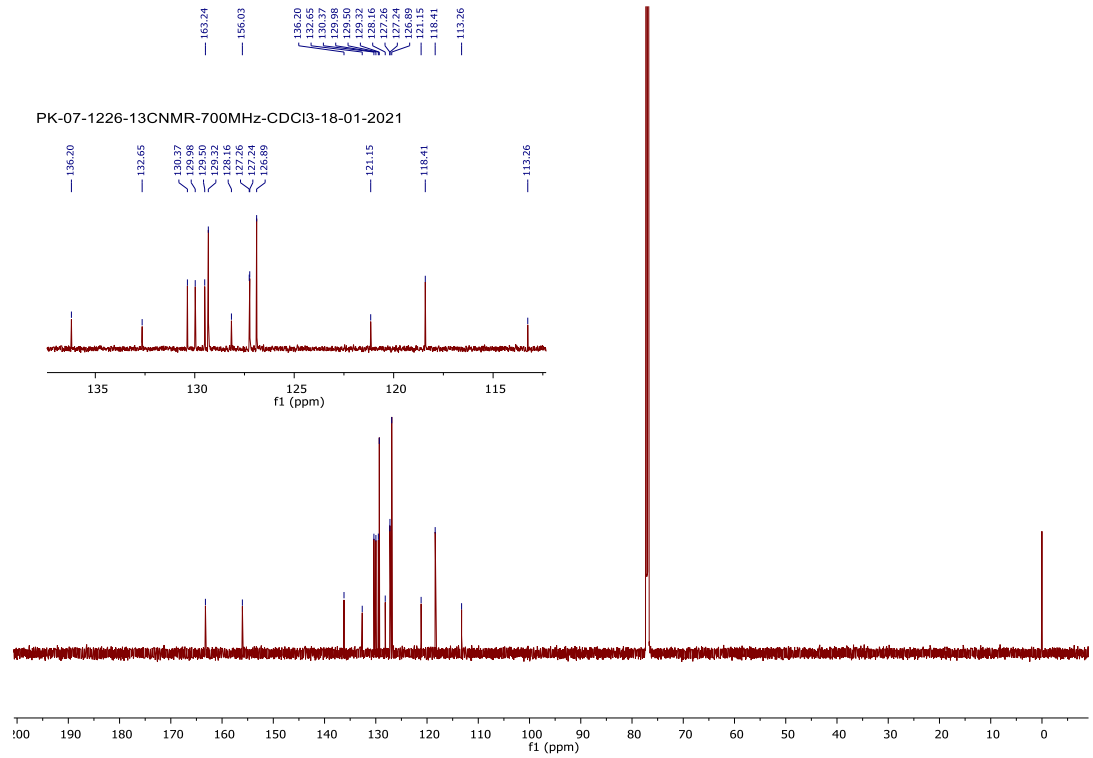

PK-07-1169-1HNMR-500MHz-CDCl3-07-12-20
Me
N
O
4a
f1 (ppm)

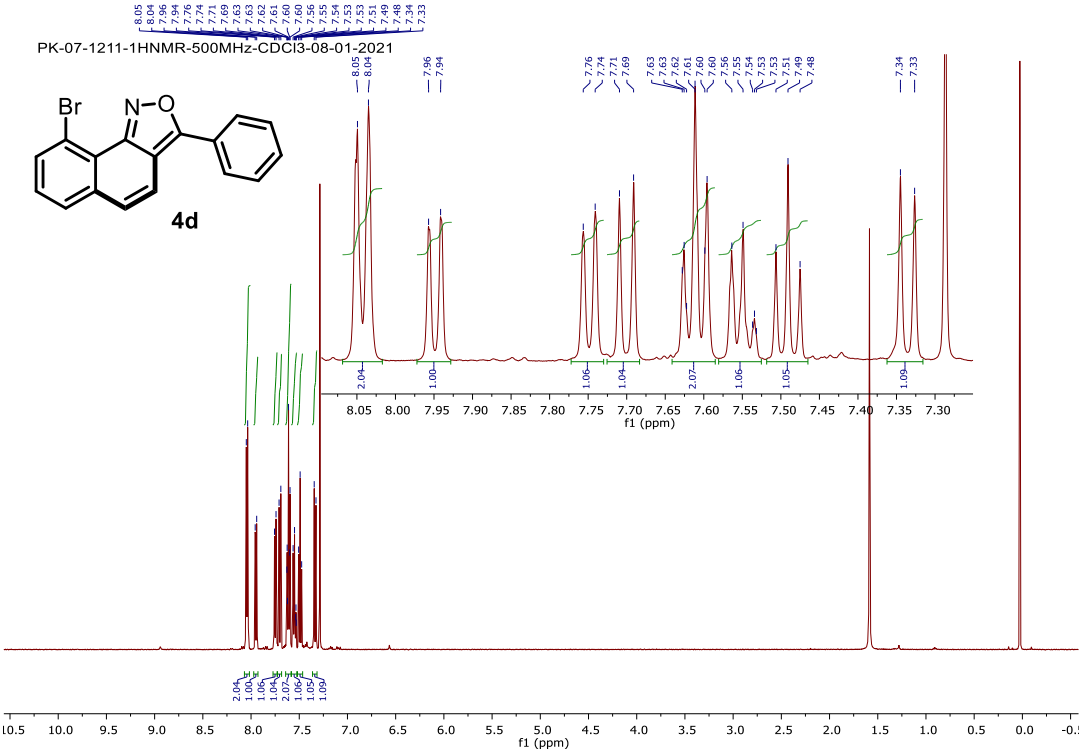

PK-07-1169-13CNMR-700MHz-CDCl3-07-12-20
f1 (ppm)

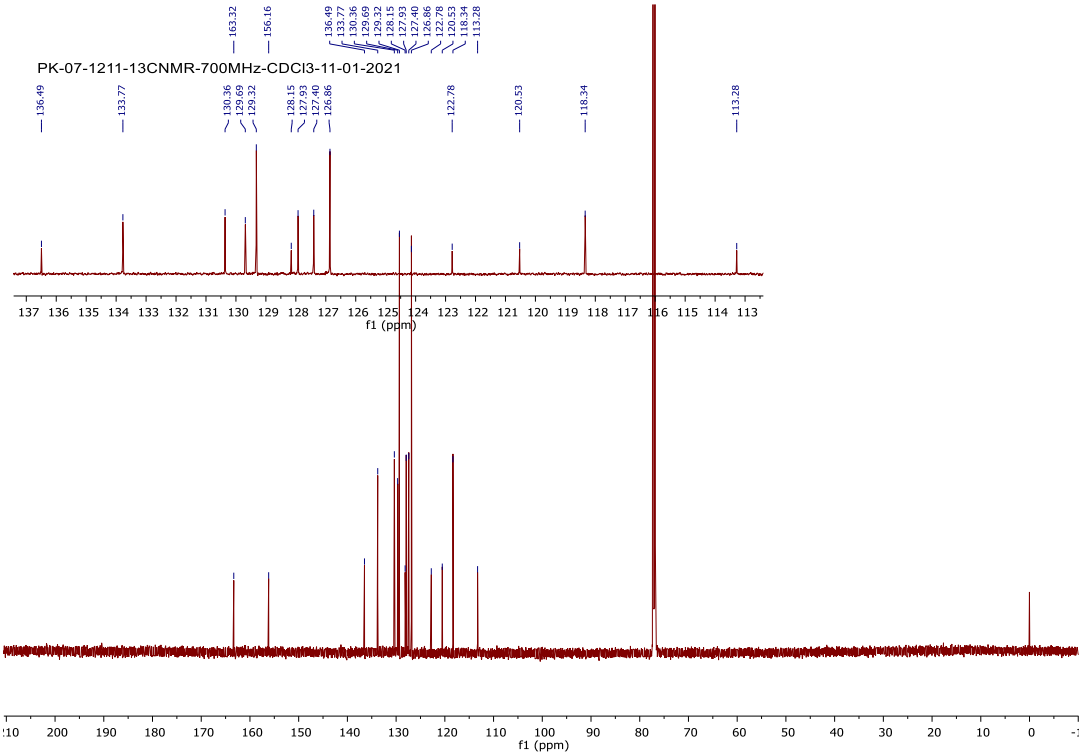

PK-07-1245-1HNMR-500NHz-CDCl3-01-02-2021
F
N
O
4b
f1 (ppm)

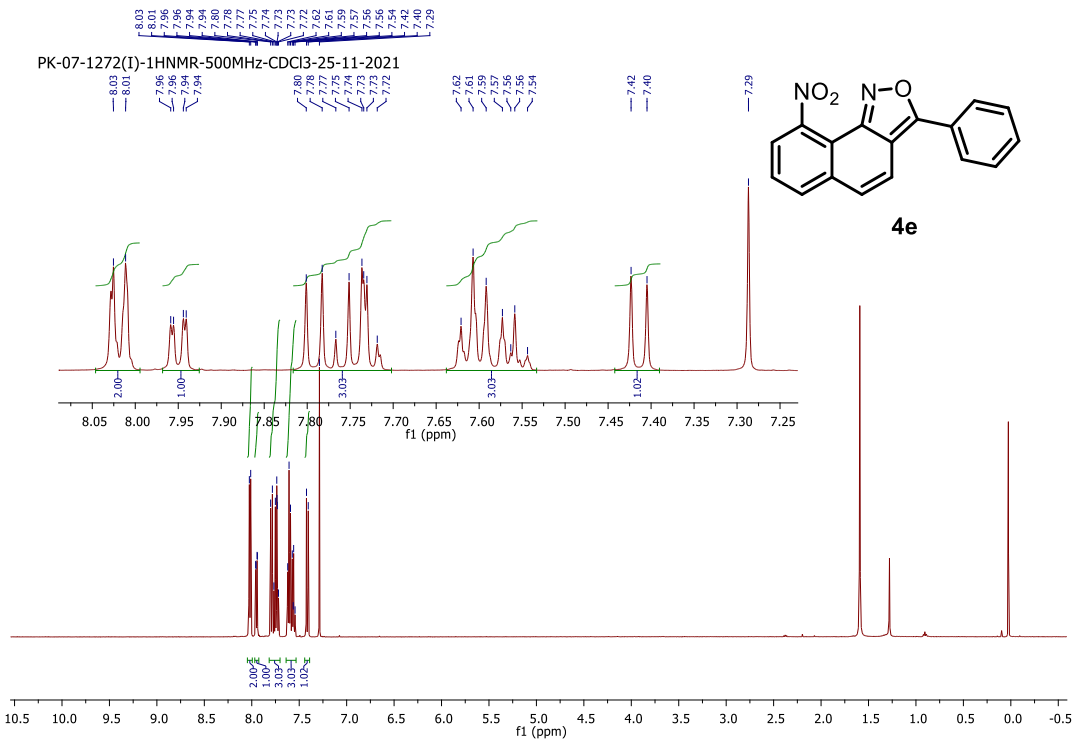

PK-07-1245-13CNMR-700NHz-CDCl3-03-02-2021
f1 (ppm)

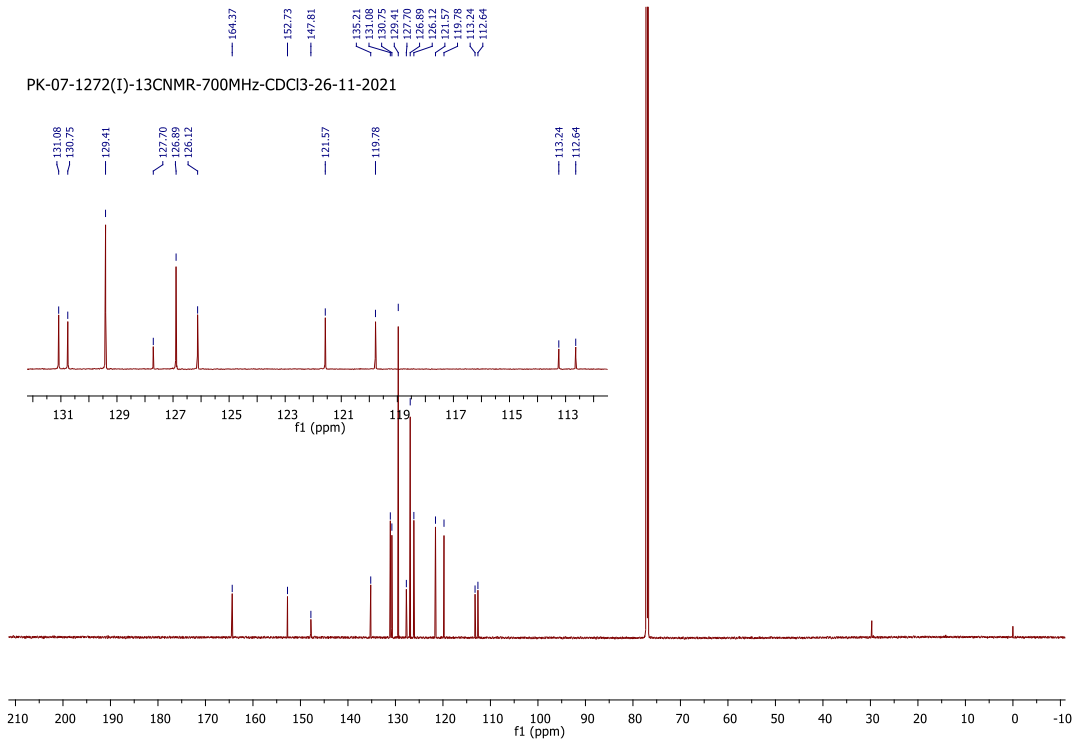

PK-07-1226-1HNMR-500MHz-CDCl3-18-01-2021
Cl
N
O
4c
f1 (ppm)

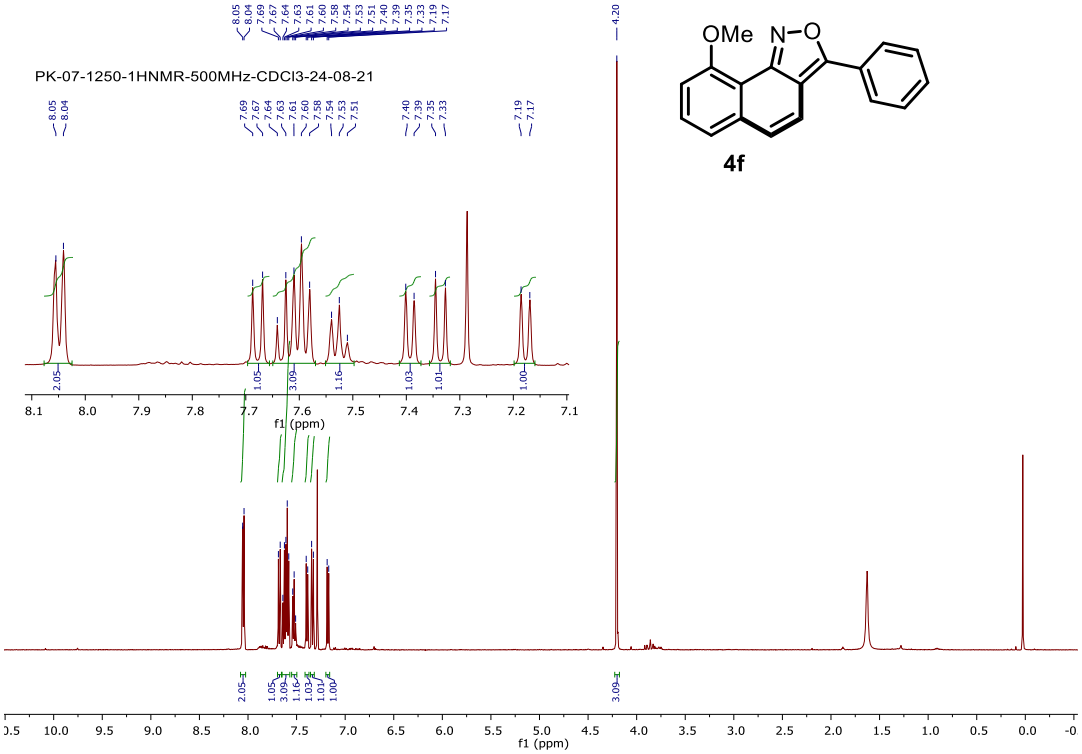

PK-07-1226-13CNMR-700MHz-CDCl3-18-01-2021
f1 (ppm)

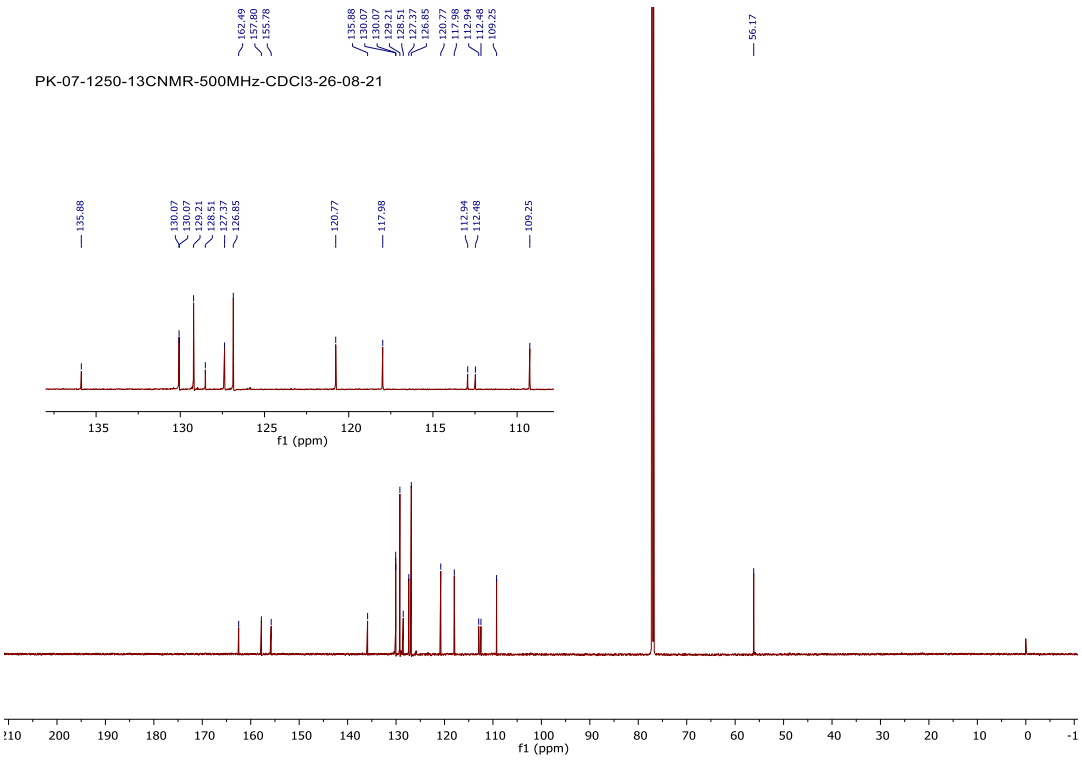

PK-07-1211-1HNMR-500MHz-CDCl3-08-01-2021
Br
N
O
4d
f1 (ppm)

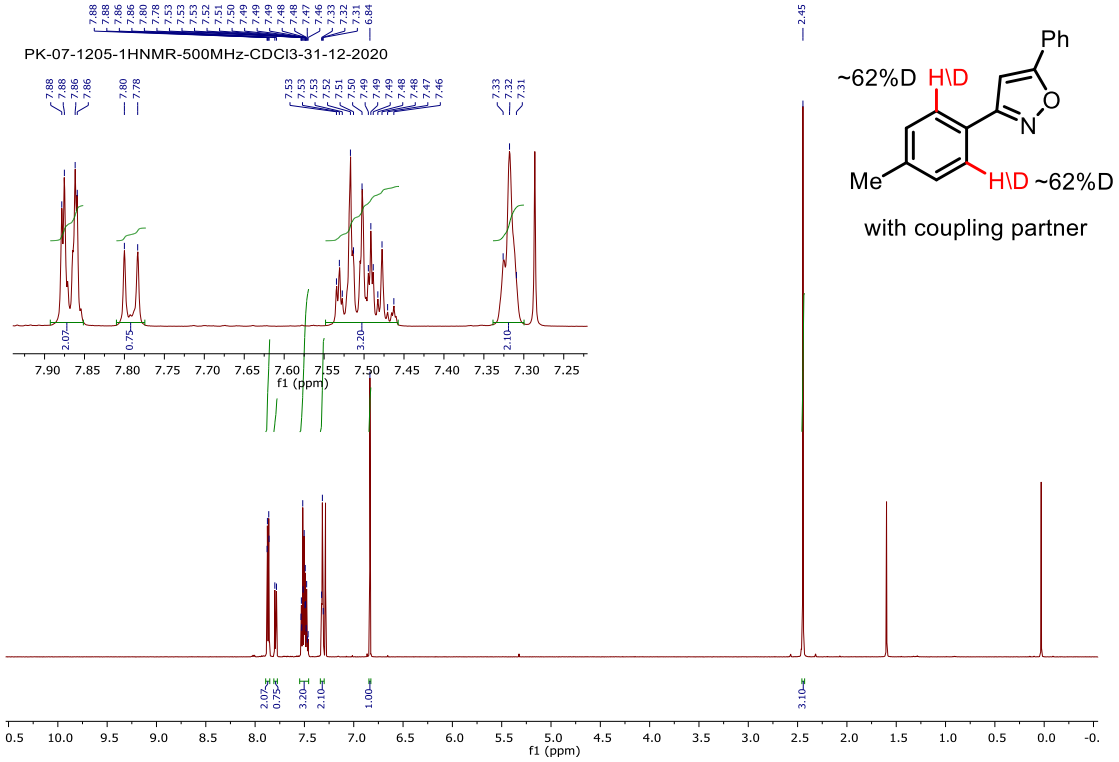

PK-07-1211-13CNMR-700MHz-CDCl3-11-01-2021
f1 (ppm)

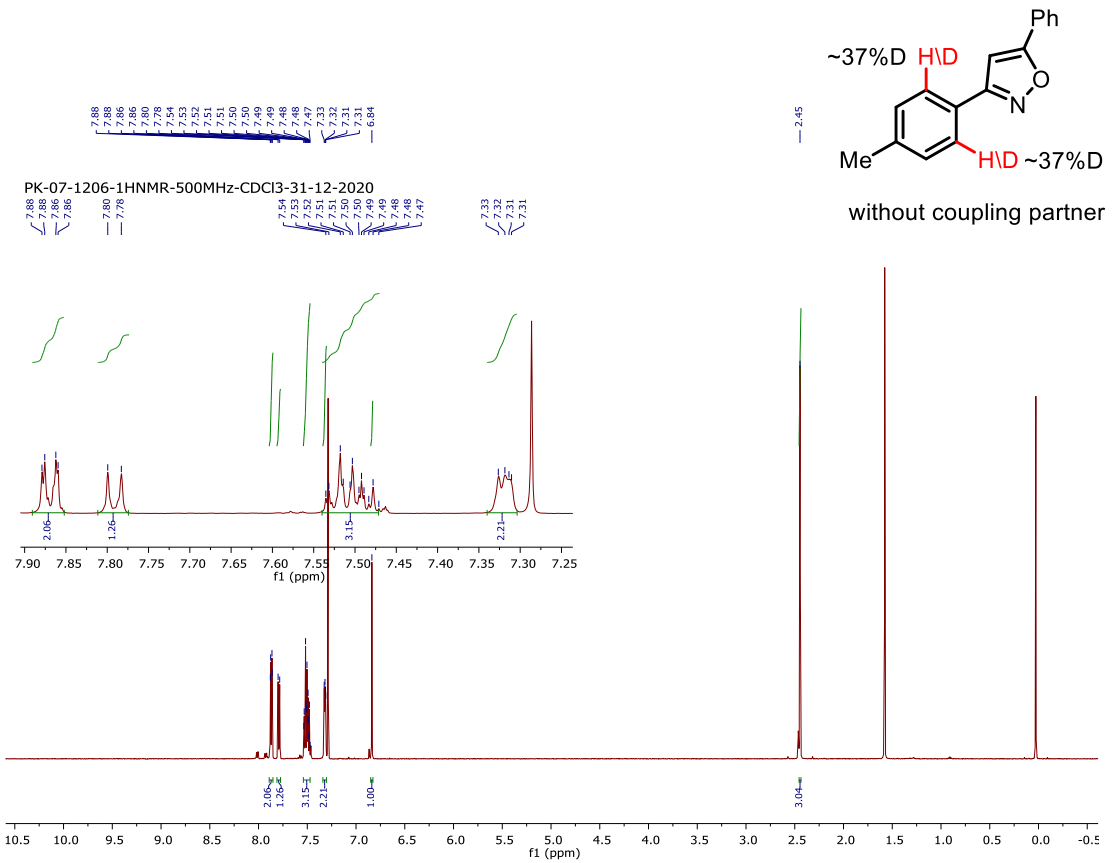

PK-07-1272(I)-1HNMR-500MHz-CDCl3-25-11-2021
NO2
N
O
4e
f1 (ppm)

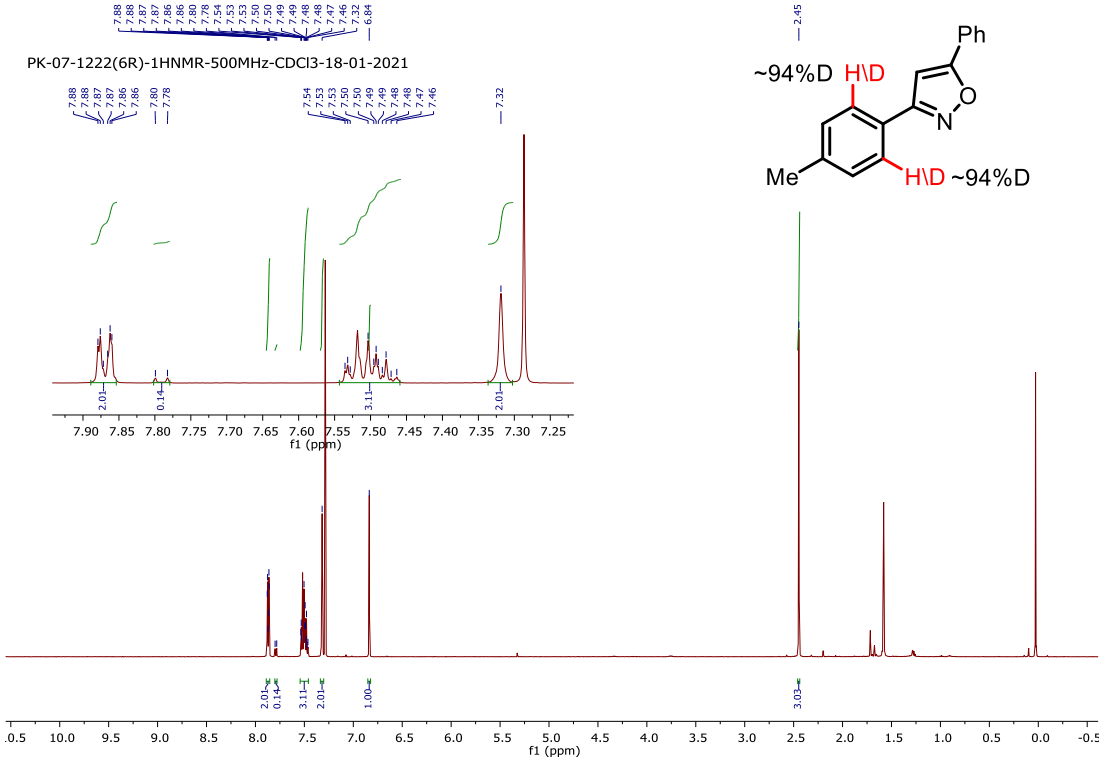

PK-07-1272(I)-13CNMR-700MHz-CDCl3-26-11-2021
f1 (ppm)

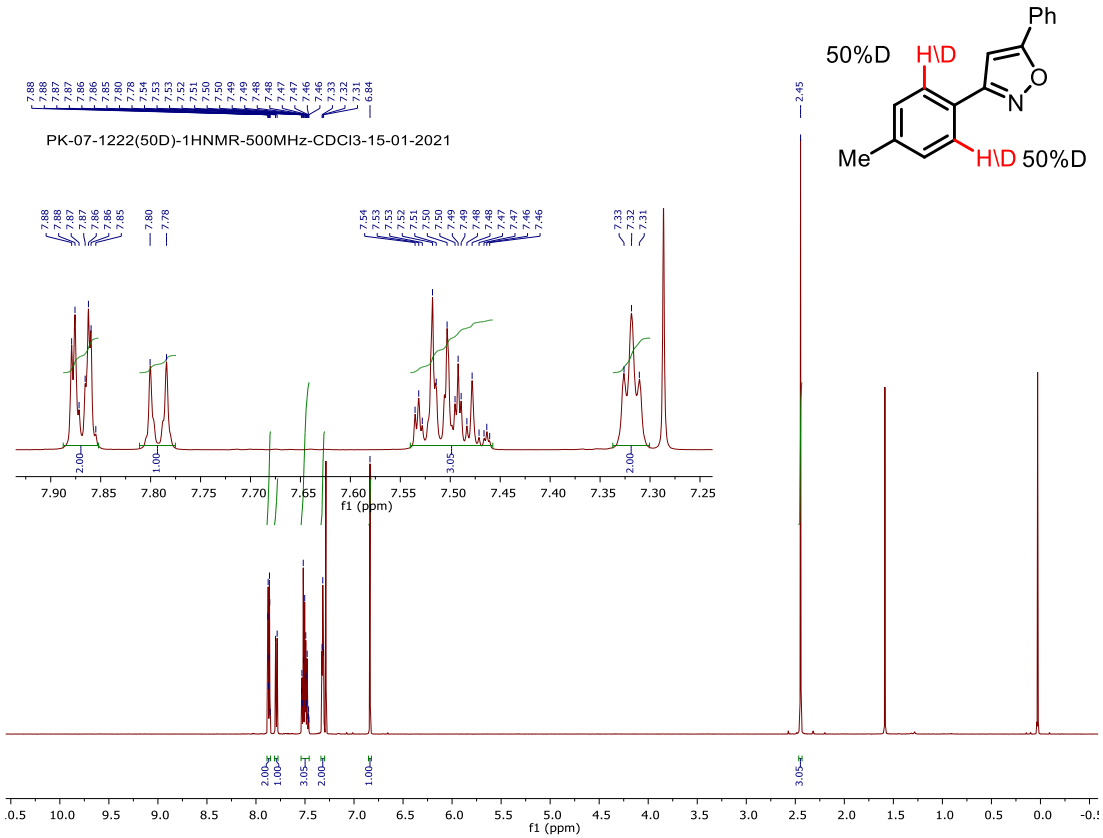

PK-07-1250-1HNMR-500MHz-CDCl3-24-08-21
OMe
N
O
4f
f1 (ppm)


PK-07-1250-13CNMR-500MHz-CDCl3-26-08-21
f1 (ppm)


PK-07-1205-1HNMR-500MHz-CDCl3-31-12-2020
f1 (ppm)
Ph
~62%D H\D
Me
H\D ~62%D
with coupling partner


PK-07-1206-1HNMR-500MHz-CDCl3-31-12-2020
f1 (ppm)
Ph
~37%D H\D
Me
H\D ~37%D
without coupling partner


PK-07-1222(6R)-1HNMR-500MHz-CDCl3-18-01-2021
~94%D H\D
Ph
O
N
Me
H\D ~94%D
f1 (ppm)


PK-07-1222(50D)-1HNMR-500MHz-CDCl3-15-01-2021
50%D H\D
Ph
O
N
Me
H\D 50%D
f1 (ppm)

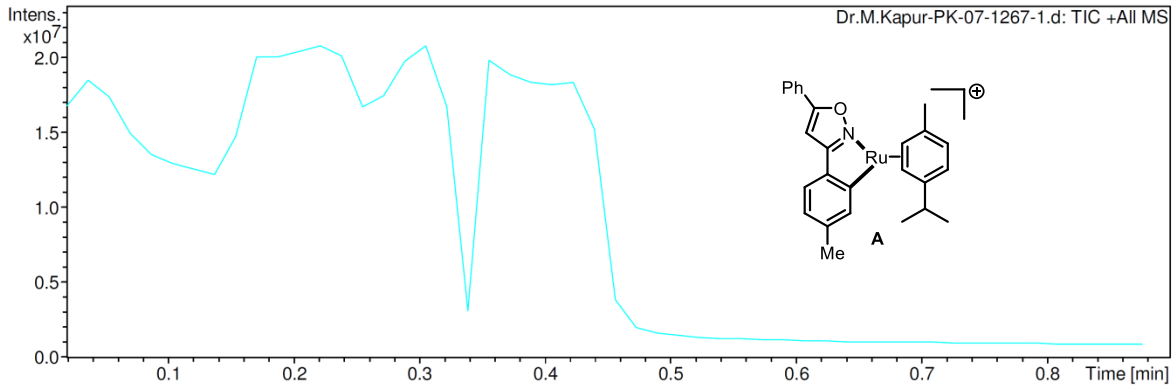
Display Report

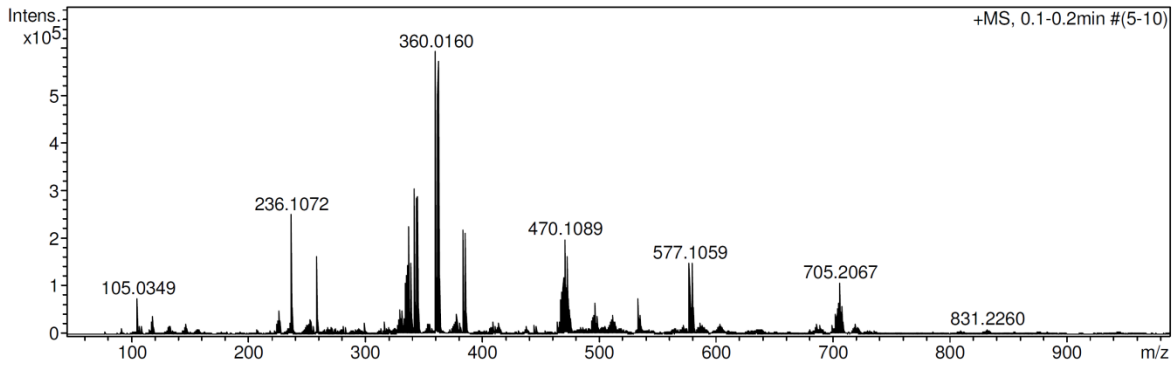
Analysis Info

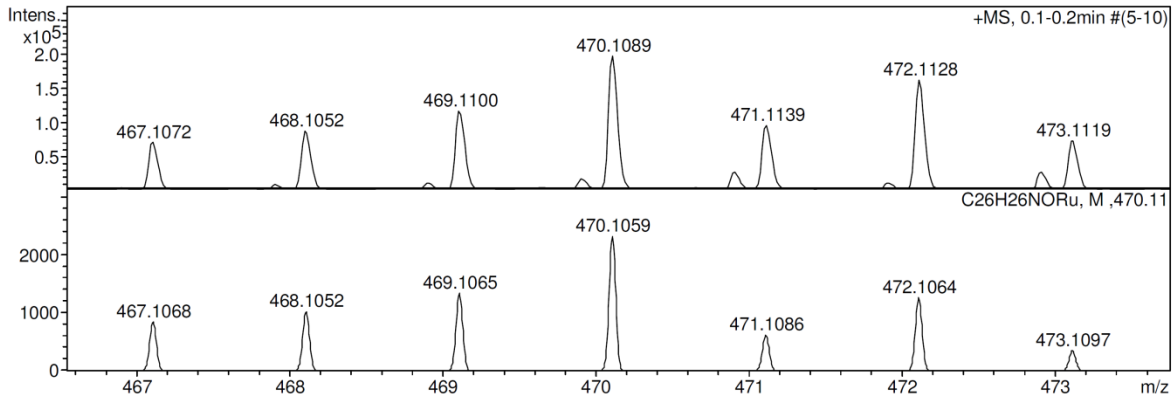
Analysis Name	D:\Data\new user data 2021\Oct-2021\12-Oct\Dr.M.Kapur-PK-07-1267-1.d	Acquisition Date	10/12/2021 11:41:09 AM
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	PK-07-1267-1	Instrument	micrOTOF-Q II 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste







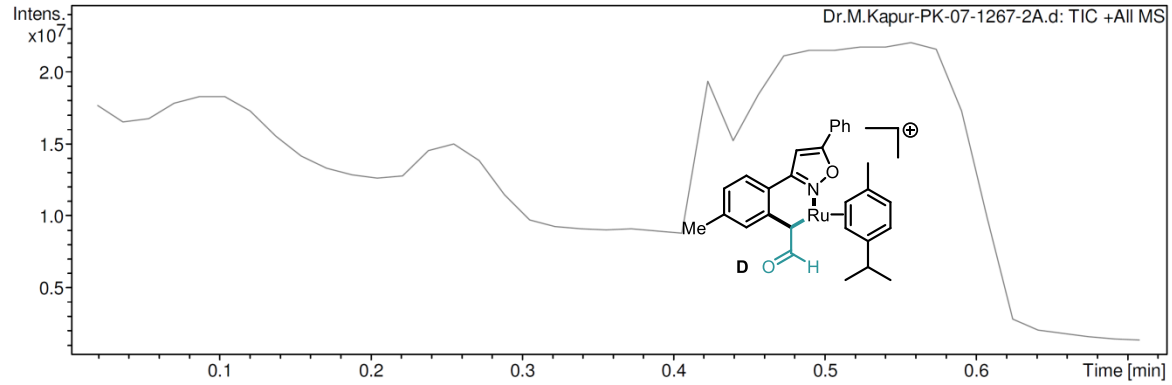
Display Report

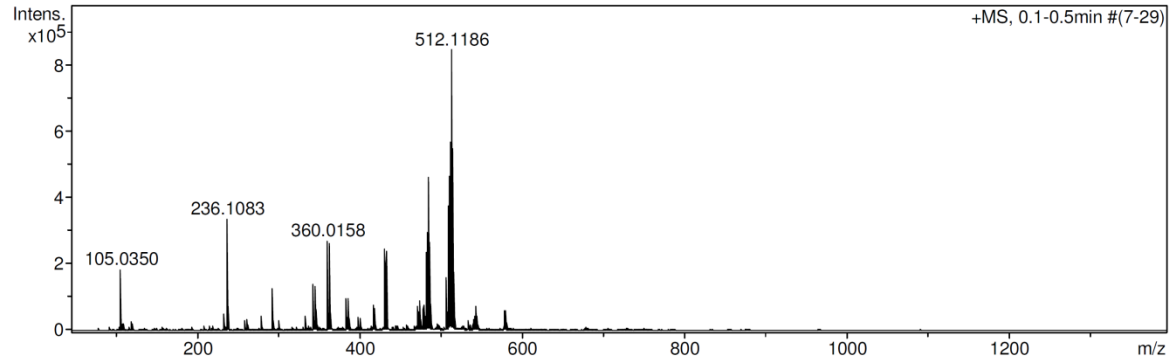
Analysis Info

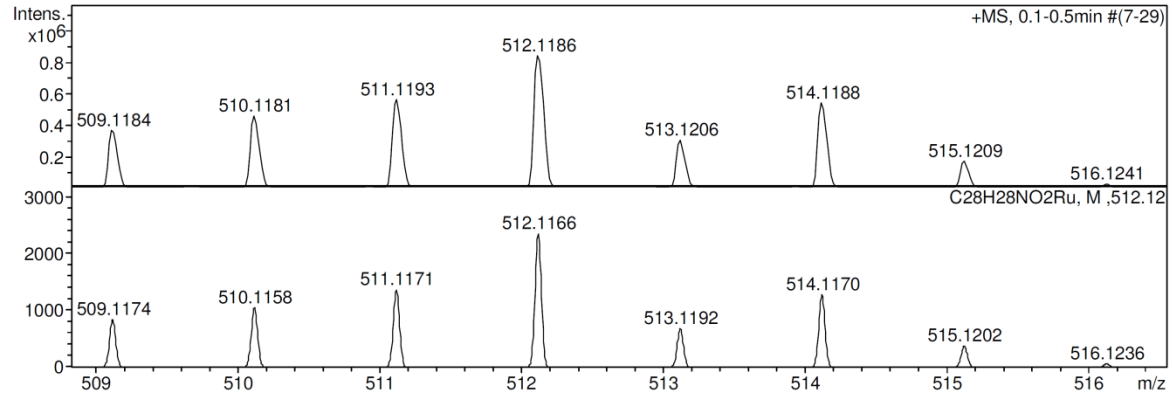
Analysis Name	D:\Data\new user data 2021\Oct-2021\12-Oct\Dr.M.Kapur-PK-07-1267-2A.d	Acquisition Date	10/12/2021 11:59:06 AM
Method	tune mix_low.New.021117.m	Operator	RUCHI
Sample Name	PK-07-1267-2A	Instrument	micrOTOF-Q II 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste



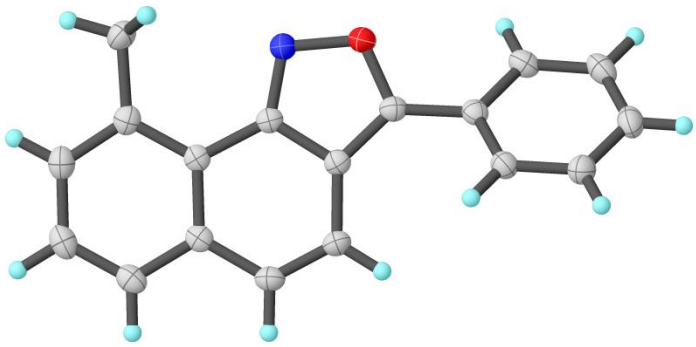




X-ray diffraction structural analysis data of 4a

Table 1: Crystal data and structure refinement for 4a.

CCDC	2115049
Identification code	FINAL
Empirical formula	$C_{18}H_{15}NO$
Formula weight	261.31
Temperature/K	140.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.2597(13)
b/Å	14.3246(16)
c/Å	8.6454(9)
α/°	90
β/°	91.870(4)
γ/°	90
Volume/Å^3	1269.9(3)
Z	4
ρ_{calc}g/cm^3	1.367
μ/mm^{-1}	0.085
F(000)	552.0
Crystal size/mm^3	? × ? × ?
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.886 to 60.154
Index ranges	$-14 \leq h \leq 14$, $-20 \leq k \leq 20$, $-12 \leq l \leq 11$
Reflections collected	40037
Independent reflections	3708 [R_{int} = 0.0536, R_{sigma} = 0.0246]
Data/restraints/parameters	3708/0/182
Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0413, wR_2 = 0.1075
Final R indexes [all data]	R_1 = 0.0475, wR_2 = 0.1129
Largest diff. peak/hole / e Å^{-3}	0.40/-0.18



Thermal ellipsoid shown at 50% probability level.

Figure S1. X-ray structure of (**4a)** i.e. (9-methyl-3-phenylnaphtho[1,2-c]isoxazole)