Supporting Information

Unusual Reactivity of 4-vinyl isoxazoles in the Copper-Mediated Synthesis of Pyridines, employing DMSO as a One-Carbon Surrogate.

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

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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 and toluene were distilled from sodium and benzophenone, whereas dry dimethyl sulfoxide, was distilled 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), 70 eV) 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 were collected using a Bruker SMART APEX II CCD diffractometer with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation at different low temperatures for each crystal.

(2) General procedures:

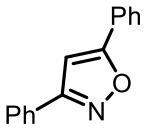
(I) Preparation of 3, 5-diaryl isoxazoles:

(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:[3]

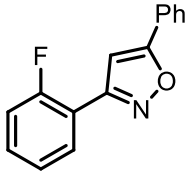
Aryl acetylene (1.5 equiv, 5.25 mmol) was added to a solution of aldoxime (1.0 equiv, 3.5 mmol) in water (15 mL) at room temperature, KCl (1.0 equiv, 3.5 mmol) was added portion-wise followed by oxone (1.5 equiv, 5.25 mmol). The resulting mixture was stirred at room temperature for 12 h till the reaction was 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):[3,4]



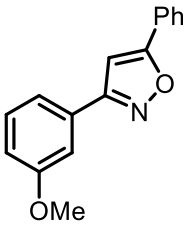
Prepared according to the general procedure and the title compound was isolated in 73% (564 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

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



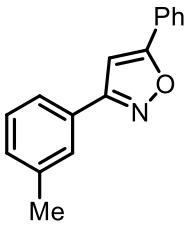
Prepared according to the general procedure and the title compound was isolated in 52% (435 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

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



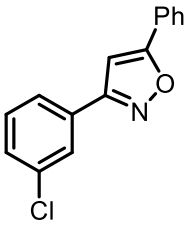
Prepared according to the general procedure and the title compound was isolated in 56% (493 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

5-phenyl-3-(*m*-tolyl)isoxazole (1d):[6]



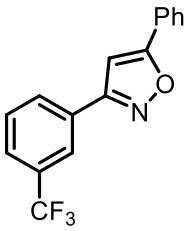
Prepared according to the general procedure and the title compound was isolated in 52% (428 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(3-chlorophenyl)-5-phenylisoxazole (1e):



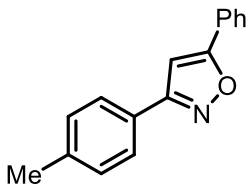
Yield: 44% (394 mg); Physical appearance: Colorless solid; M.p. 113–115 ^{o}C; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 – 7.85 (m, 3H), 7.81 – 7.76 (m, 1H), 7.54 – 7.44 (m, 5H), 6.84 (s, 1H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 170.8, 161.9, 134.9, 130.9, 130.4, 130.2, 130.0, 129.1, 127.3, 126.9, 125.9, 124.9, 97.4; **IR** (KBr, cm^{-1}): 3115, 1578, 1450, 1081, 899, 692; **ESI–HRMS**: Calculated for $C_{15}H_{11}ClNO^{+}$ $[M+H]^{+}$ 256.0524, found 256.0514.

5-phenyl-3-(3-(trifluoromethyl)phenyl)isoxazole (1f):



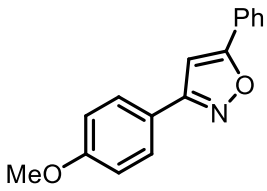
Yield: 46% (465 mg); Physical appearance: Colorless solid; M.p. 62–64 ^{o}C; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.15 (s, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.91 – 7.85 (m, 2H), 7.75 (d, J = 7.8 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.57 – 7.47 (m, 3H), 6.90 (s, 1H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 171.1, 161.8, 131.6, 131.4, 130.5, 130.0, 129.9, 129.53, 129.1, 127.2, 126.6 (q, J = 3.8 Hz), 125.9, 124.9, 123.7 (q, J = 3.9 Hz), 122.8, 97.3; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –62.8; **IR** (KBr, cm^{-1}): 3420, 3120, 1614, 1389, 1169, 810, 692; **ESI–HRMS**: Calculated for $C_{16}H_{11}F_3NO^{+}$ $[M+H]^{+}$ 290.0787, found 290.0775.

5-phenyl-3-(*p*-tolyl)isoxazole (1g):[7]



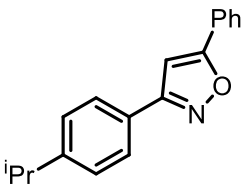
Prepared according to the general procedure and the title compound was isolated in 75% (618 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-methoxyphenyl)-5-phenylisoxazole (1h):[7]



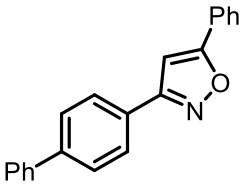
Prepared according to the general procedure and the title compound was isolated in 76% (667 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-isopropylphenyl)-5-phenylisoxazole (1i):[8]



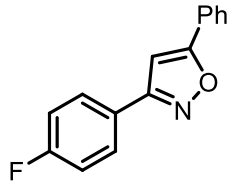
Prepared according to the general procedure and the title compound was isolated in 61% (562 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-([1,1'-biphenyl]-4-yl)-5-phenylisoxazole (1j):[9]



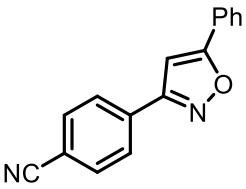
Prepared according to the general procedure and the title compound was isolated in 54% (562 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

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



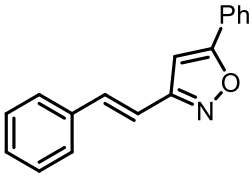
Prepared according to the general procedure and the title compound was isolated in 51% (427 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

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



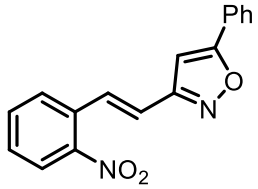
Prepared according to the general procedure and the title compound was isolated in 45% (388 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

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



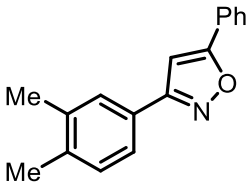
Prepared according to the general procedure and the title compound was isolated in 57% (493 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

(*E*)-3-(2-nitrostyryl)-5-phenylisoxazole (1n):[10]



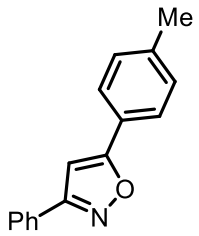
Prepared according to the general procedure and the title compound was isolated in 50% (511 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(3,4-dimethylphenyl)-5-phenylisoxazole (1o):



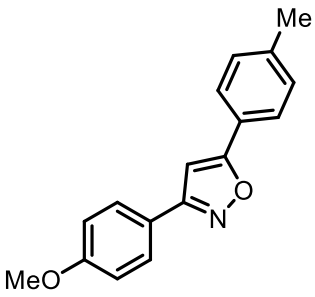
Yield: 72% (628 mg); Physical appearance: Colorless solid; M.p. 80–82 ^{o}C; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.90 – 7.84 (m, 2H), 7.70 (s, 1H), 7.62 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.54 – 7.45 (m, 3H), 7.27 (d, *J* = 7.8 Hz, 1H), 6.84 (s, 1H), 2.37 (s, 3H) 2.35 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 170.1, 163.0, 138.8, 137.3, 130.2, 130.1, 128.9, 127.9, 127.6, 126.6, 125.8, 124.3, 97.5, 19.8, 19.8; **IR** (KBr, cm^{-1}): 3415, 2437, 1612, 1461, 1365, 1261, 1049, 762; **ESI–HRMS**: Calculated for $C_{17}H_{16}NO^{+}$ $[M+H]^{+}$ 250.1226, found 250.1206.

3-phenyl-5-(*p*-tolyl)isoxazole (1p):[11]



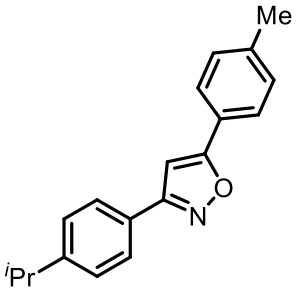
Prepared according to the general procedure and the title compound was isolated in 63% (519 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-methoxyphenyl)-5-(*p*-tolyl)isoxazole (1q):[12]



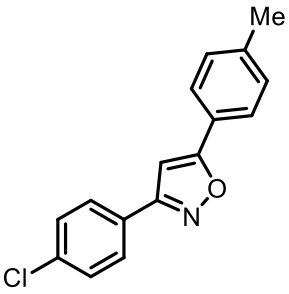
Prepared according to the general procedure and the title compound was isolated in 62% (576 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-isopropylphenyl)-5-(*p*-tolyl)isoxazole (1r):



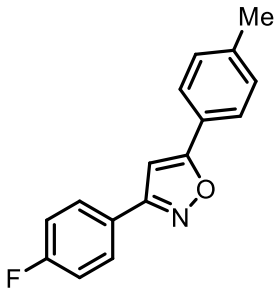
Yield: 61% (592 mg); Physical appearance: Colorless solid; M.p. 101–103 °C; TLC R_f 0.4 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, , $CDCl_3$): δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 6.78 (s, 1H), 3.00 (sept, *J* = 6.9 Hz, 1H), 2.44 (s, 3H), 1.32 (d, *J* = 6.9 Hz, 6H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 170.4, 162.9, 150.9, 140.4, 129.7, 127.0, 126.8, 126.8, 125.8, 124.9, 96.9, 34.1, 23.9, 21.5; **IR** (KBr, cm^{-1}): 3424, 2963, 1615, 1434, 1115, 839, 814, 516; **ESI–HRMS**: Calculated for $C_{19}H_{20}NO^+$ $[M+H]^+$ 278.1539, found 278.1524.

3-(4-chlorophenyl)-5-(*p*-tolyl)isoxazole (1s):[3,13]



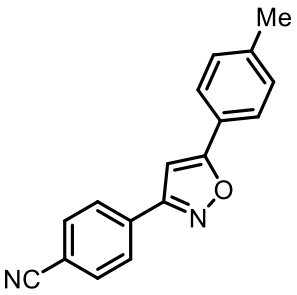
Prepared according to the general procedure and the title compound was isolated in 55% (518 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-(4-fluorophenyl)-5-(*p*-tolyl)isoxazole (1t):[13]



Prepared according to the general procedure and the title compound was isolated in 47% (416 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

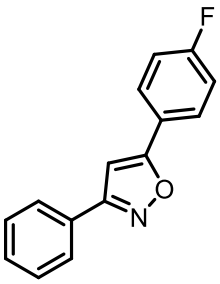
4-(5-(*p*-tolyl)isoxazol-3-yl)benzonitrile (1u):



Yield: 47% (428 mg); Physical appearance: Colorless solid; M.p. 145–147 °C; TLC R_f 0.2 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.83 – 7.79 (m, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 6.83 (s, 1H), 2.45 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 171.5,

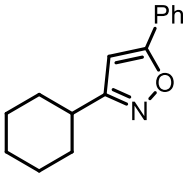
161.41, 141.1, 133.6, 132.7, 129.8, 127.4, 125.84, 124.3, 118.4, 113.6, 96.7, 21.5; **IR** (KBr, cm^{-1}): 3396, 1598, 1047, 849, 805, 557; **ESI–HRMS**: Calculated for $C_{17}H_{13}N_2O^+$ $[M+H]^+$ 261.1022, found 261.1019.

5-(4-fluorophenyl)-3-phenylisoxazole (1v):[14]



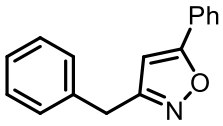
Prepared according to the general procedure and the title compound was isolated in 51% (427 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-cyclohexyl-5-phenylisoxazole (1w):[15]



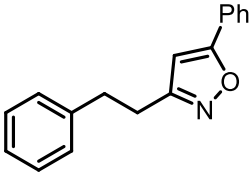
Prepared according to the general procedure and the title compound was isolated in 44% (350 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-benzyl-5-phenylisoxazole (1x):[16]



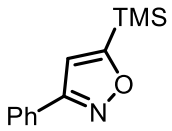
Prepared according to the general procedure and the title compound was isolated in 42% (345 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-phenethyl-5-phenylisoxazole (1y):[17]



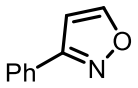
Prepared according to the general procedure and the title compound was isolated in 45% (392 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-phenyl-5-(trimethylsilyl)isoxazole (1z):[18]



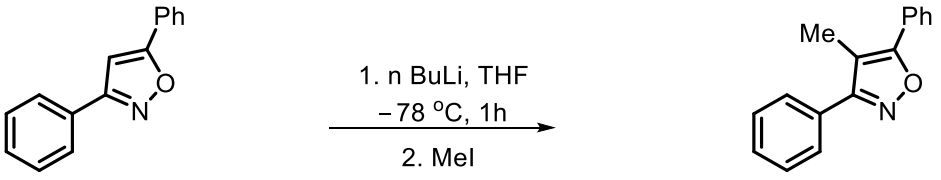
Prepared according to the general procedure and the title compound was isolated in 55% (418 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

3-phenylisoxazole (1aa):[3]



Prepared according to the general procedure and the title compound was isolated in 95% (317 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

4-methyl-3,5-diphenylisoxazole (1ab):

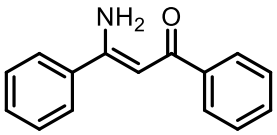


1a **1ab** 96%

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 (195 mg) in 92% yield.

Physical appearance: Colorless solid; M.p. 91–93 °C; TLC R_f 0.5 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 – 7.76 (m, 2H), 7.75 – 7.68 (m, 2H), 7.61 – 7.44 (m, 6H), 2.35 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 165.8, 163.9, 129.6, 129.5, 129.4, 128.9, 128.8, 128.6, 128.4, 126.9, 108.7, 9.4; **IR** (KBr, cm^{-1}): 3404, 1598, 1443, 1073, 771, 696; **ESI–HRMS**: Calculated for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1070, found 236.1075.

(*Z*)-3-amino-1,3-diphenylprop-2-en-1-one (1a'):[19]

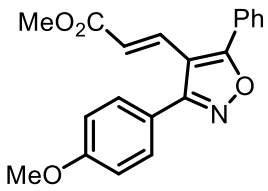


Procedure: To an oven-dried round bottom flask, 1,3-diphenylpropane-1,3-dione (224 mg, 1.0 equiv), was dissolved in EtOH (10 mL) fallowed by addition of NH_4OAc (385 mg, 5.0 equiv). The reaction mixture was heated (oil bath) to reflux for overnight. After cooling to room temperature, EtOH was removed. H_2O was added and the mixture was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (5:1 hexanes:EtOAc) to afford the title compound (160 mg) in 72% yield as a yellow solid. Spectral data obtained were in good agreement with those reported in the literature.

(II) General procedure for the Pd-catalyzed C-H olefination of isoxazole:[3]

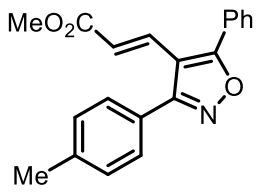
In a pressure tube equipped with a stir bar, isoxazole (1.0 equiv, 0.2 mmol) was dissolved in dry tetrahydrofuran (2.0 mL). This was followed by the addition of olefin (2.0 equiv, 0.40 mmol), $Pd(OAc)_2$ (0.1 equiv, 0.02 mmol), AgOAc (1.0 equiv, 0.2 mmol) and Ag_2CO_3 (2.0 equiv, 0.40 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 110 ^oC (oil bath) and allowed to stir for 24–30 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.

Methyl (*E*)-3-(3-(4-methoxyphenyl)-5-phenylisoxazol-4-yl)acrylate (4a):[3]



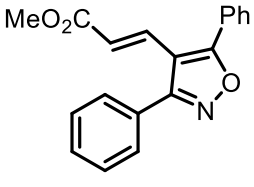
Prepared according to the general procedure and the title compound was isolated in 60% (40 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Methyl (*E*)-3-(5-phenyl-3-(p-tolyl)isoxazol-4-yl)acrylate (4b):[3]



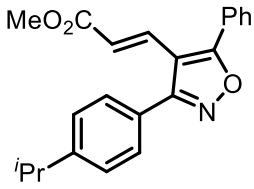
Prepared according to the general procedure and the title compound was isolated in 61% (39 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Methyl (*E*)-3-(3, 5-diphenylisoxazol-4-yl)acrylate (4c):[3]



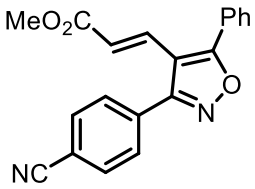
Prepared according to the general procedure and the title compound was isolated in 57% (35 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Methyl (*E*)-3-(3-(4-isopropylphenyl)-5-phenylisoxazol-4-yl)acrylate (4d):[3]



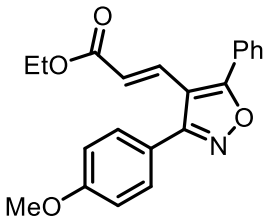
Prepared according to the general procedure and the title compound was isolated in 52% (36 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Methyl (*E*)-3-(3-(4-cyanophenyl)-5-phenylisoxazol-4-yl)acrylate (4e):[3]



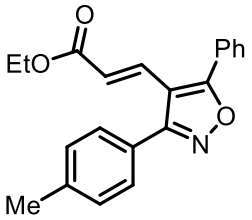
Prepared according to the general procedure and the title compound was isolated in 48% (32 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Ethyl (*E*)-3-(3-(4-methoxyphenyl)-5-phenylisoxazol-4-yl)acrylate (4f):



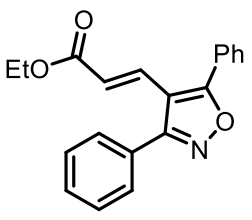
Yield: 64% (44 mg); Physical appearance: Colorless solid; M.p. 93–95 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77– 7.72 (m, 2H), 7.69 (d, *J* = 16.2 Hz, 1H), 7.58 – 7.50 (m, 5H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.03 (d, *J* = 16.2 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H),1.27 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 169.1, 166.6, 162.1, 160.9, 132.5, 130.8, 130.2, 129.1, 128.12, 127.3, 121.7, 120.8, 114.4, 110.3, 60.6, 55.4, 14.3; **IR** (KBr, cm^{-1}): 2928, 1713, 1613, 1429, 1254, 1179, 1031, 836, 697; **ESI–HRMS**: Calculated for $C_{21}H_{20}NO_4^+$ $[M+H]^+$ 350.1387, found 350.1388.

Ethyl (*E*)-3-(5-phenyl-3-(*p*-tolyl)isoxazol-4-yl)acrylate (4g):



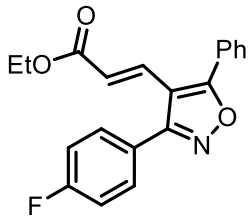
Yield: 62% (41 mg); Physical appearance: Colorless solid; M.p. 92–94 °C; TLC R_f 0.4 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79–7.72 (m, 2H), 7.68 (d, *J* = 16.2 Hz, 1H), 7.58 – 7.52 (m, 3H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 6.01 (d, *J* = 16.2 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 169.2, 166.6, 162.4, 140.1, 132.4, 130.8, 129.6, 129.2, 128.7, 128.1, 127.3, 125.6, 121.7, 110.4, 60.6, 21.5, 14.2; **IR** (KBr, cm^{-1}): 3417, 2981, 1714, 1643, 1272, 1034, 695; **ESI–HRMS**: Calculated for $C_{21}H_{20}NO_3^+$ $[M+H]^+$ 334.1438, found 334.1421.

Ethyl (*E*)-3-(3,5-diphenylisoxazol-4-yl)acrylate (4h):[3]



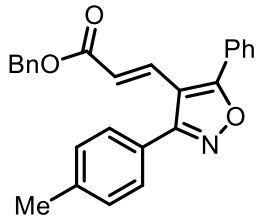
Prepared according to the general procedure and the title compound was isolated in 50% (37 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Ethyl (*E*)-3-(3-(4-fluorophenyl)-5-phenylisoxazol-4-yl)acrylate (4i):



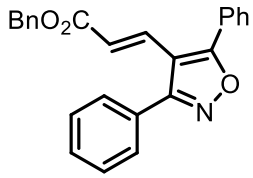
Yield: 49% (33 mg); Physical appearance: Colorless solid; M.p. 98–100 ^{o}C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 – 7.74 (m, 2H), 7.66 (d, *J* = 16.2 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.57 – 7.52 (m, 3H), 7.31 – 7.24 (m, 2H), 6.00 (d, *J* = 16.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 168.2, 166.4,164.1 (d, *J* = 252.6 Hz), 162.5, 131.9, 130.3 (d, *J* = 8.7 Hz), 130.1, 128.9, 128.9, 128.5, 123.5 (d, *J* = 3.5 Hz), 122.1, 116.5 (d, *J* = 22.2 Hz), 110.3, 60.7, 14.2; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –108.1; **ESI–HRMS**: Calculated for $C_{20}H_{17}FNO_3^+$ $[M+H]^+$ 338.1187, found 338.1169.

Benzyl (*E*)-3-(5-phenyl-3-(*p*-tolyl)isoxazol-4-yl)acrylate (4j):



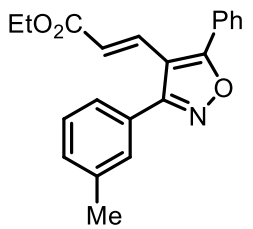
Yield: 55% (43 mg); Physical appearance: Colorless solid; M.p. 139–141 ^{o}C; TLC R_f 0.4 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 – 7.70 (m, 3H), 7.58–7.51 (m, 3H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.40 – 7.28 (m, 7H), 6.06 (d, *J* = 16.2 Hz, 1H), 5.18 (s, 2H), 2.44 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 169.4, 166.4, 162.4, 140.2, 135.9, 133.1, 130.9, 129.7, 129.2, 128.7, 128.6, 128.3, 128.2, 127.2, 125.5, 121.1, 110.3, 66.5, 21.5; **IR** (KBr, cm^{-1}): 3397, 2917, 1708, 1419, 1274, 1017, 6958; **ESI–HRMS**: Calculated for $C_{26}H_{22}NO_3^+$ $[M+H]^+$ 396.1594, found 396.1601.

Benzyl (*E*)-3-(3, 5-diphenylisoxazol-4-yl)acrylate (4k):[3]



Prepared according to the general procedure and the title compound was isolated in 53% (40 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

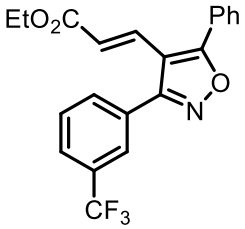
Ethyl (*E*)-3-(5-phenyl-3-(*m*-tolyl)isoxazol-4-yl)acrylate (4l):



Yield: 53% (35 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 – 7.74 (m, 2H), 7.70 (d, *J* = 16.2 Hz, 1H), 7.61 – 7.54 (m, 3H), 7.45 (s, 1H), 7.44 – 7.33 (m, 3H), 6.02 (d, *J* = 16.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.46 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz,

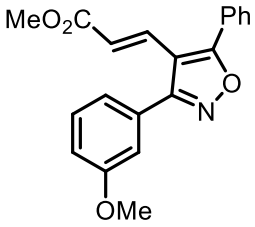
$CDCl_3$) δ 169.2, 166.6, 162.5, 138.8, 132.3, 130.8, 130.7, 129.5, 129.2, 128.8, 128.5, 128.2, 127.3, 125.9, 121.7, 110.4, 60.6, 21.4, 14.2; **IR** (KBr, cm^{-1}): 3421, 2924, 1718, 1273, 1181, 694; **ESI–HRMS**: Calculated for $C_{21}H_{20}NO_3^+$ $[M+H]^+$ 334.1438, found 334.1433.

Ethyl (*E*)-3-(5-phenyl-3-(3-(trifluoromethyl)phenyl)isoxazol-4-yl)acrylate (4m):



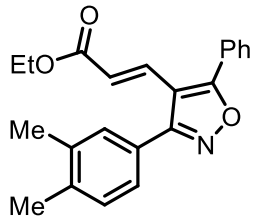
Yield: 48% (37 mg); Physical appearance: Colorless solid; M.p. 72–74 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.86 – 7.75 (m, 4H), 7.74 – 7.65 (m, 2H), 7.62 – 7.55 (m, 3H), 5.97 (d, *J* = 16.3 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.29 (d, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 169.6, 166.2, 161.1, 132.2, 131.7, 131.7, 131.4, 131.1, 129.6, 129.5, 129.3, 128.1, 126.9, 126.8 (q, *J* = 3.4 Hz), 125.9 (q, *J* = 3.7 Hz), 122.5, 110.2, 60.8, 14.2; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –62.8; **IR** (KBr, cm^{-1}): 3418, 2918, 1716, 1667, 1448, 1260, 1022, 698; **ESI–HRMS**: Calculated for $C_{21}H_{17}F_3NO_3^+$ $[M+H]^+$ 388.1155, found 388.1140.

Methyl (*E*)-3-(3-(3-methoxyphenyl)-5-phenylisoxazol-4-yl)acrylate (4n):[3]



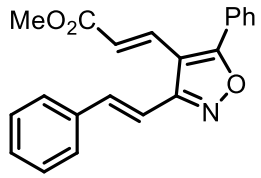
Prepared according to the general procedure and the title compound was isolated in 51% (34 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Ethyl (*E*)-3-(3-(3,4-dimethylphenyl)-5-phenylisoxazol-4-yl)acrylate (4o):



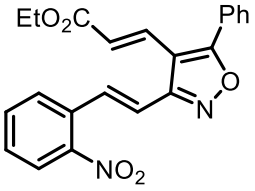
Yield: 63% (44 mg); Physical appearance: Colorless solid; M.p. 64–66 °C; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 – 7.74 (m, 2H), 7.71 (d, *J* = 16.2 Hz, 1H), 7.60 – 7.54 (m, 3H), 7.41 (s, 1H), 7.37 – 7.25 (m, 2H), 6.06 (d, *J* = 16.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.36 (d, *J* = 4.8 Hz, 6H), 1.29 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 169.1, 166.6, 162.5, 138.8, 137.3, 132.49, 130.8, 130.1, 129.9, 129.1, 128.1, 127.4, 126.3, 125.9, 121.7, 110.4, 60.6, 19.8, 19.8, 14.3; **IR** (KBr, cm^{-1}): 3420, 2958, 2839, 1721, 1614, 1507, 1170, 592; **ESI–HRMS**: Calculated for $C_{22}H_{22}NO_3^+$ $[M+H]^+$ 348.1594, found 348.1586.

Methyl (*E*)-3-(5-phenyl-3-((*E*)-styryl)isoxazol-4-yl)acrylate (4p):[3]



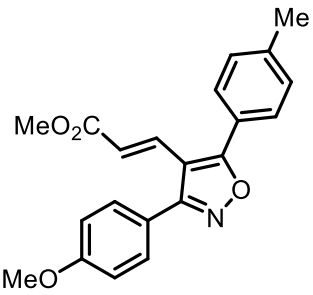
Prepared according to the general procedure and the title compound was isolated in 68% (45 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Ethyl (*E*)-3-(3-((*E*)-2-nitrostyryl)-5-phenylisoxazol-4-yl)acrylate (4q):



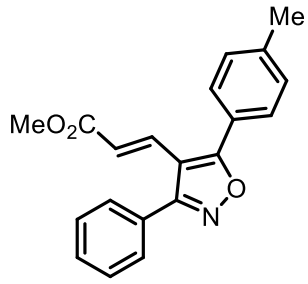
Yield: 48% (37 mg); Physical appearance: Yellow gel; TLC R_f 0.1 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.01 (d, *J* = 16.1 Hz, 1H), 7.80 – 7.71 (m, 5H), 7.59 – 7.53 (m, 4H), 6.97 (d, *J* = 16.0 Hz, 1H), 6.33 (d, *J* = 16.2 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 169.2, 166.3, 158.8, 148.2, 133.5, 132.7, 132.4, 131.8, 130.9, 129.5, 129.2, 129.1, 127.9, 126.9, 124.9, 122.7, 118.8, 110.6, 60.8, 14.3; **IR** (KBr, cm^{-1}): 2924, 1718, 1524, 1180, 1033, 695; **ESI–HRMS**: Calculated for $C_{22}H_{19}N_2O_5^+$ $[M+H]^+$ 391.1288, found 391.1281.

Methyl (*E*)-3-(3-(4-methoxyphenyl)-5-(*p*-tolyl)isoxazol-4-yl)acrylate (4r):



Yield: 56% (39 mg); Physical appearance: Colorless solid; M.p.128–130 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 16.2 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.02 (d, *J* = 16.2 Hz, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 2.45 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 169.5, 167.1, 162.1, 160.9, 141.29, 132.9, 130.2, 129.9, 128.0, 124.5, 120.9, 120.8, 114.4, 109.9, 55.4, 51.7, 21.6; **IR** (KBr, cm^{-1}): 2955, 2837, 1720, 1642, 1614, 1428, 1173, 590; **ESI–HRMS**: Calculated for $C_{21}H_{20}NO_4^+$ $[M+H]^+$ 350.1387, found 350.1386.

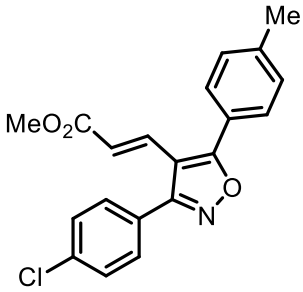
Methyl (*E*)-3-(3-phenyl-5-(*p*-tolyl)isoxazol-4-yl)acrylate (4s):



Yield: 57% (36 mg); Physical appearance: Colorless solid; M.p. 104–106 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 16.2 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.61 – 7.56 (m, 2H), 7.54 – 7.48 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.96 (d, *J* = 16.2 Hz, 1H), 3.71 (s, 3H), 2.45 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 169.6, 166.9, 162.4, 141.4, 132.7, 129.9, 129.9, 128.9, 128.9, 128.7, 128.0, 124.4, 120.9, 109.9, 51.7, 21.6; **IR** (KBr,

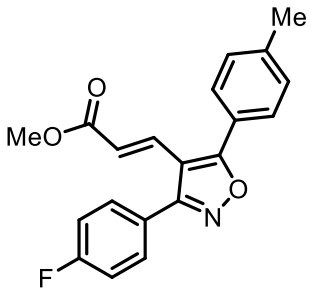
cm^{-1}): 3417, 2949, 1716, 1429, 1270, 1170, 823, 701; **ESI–HRMS**: Calculated for $C_{20}H_{18}NO_3^+$ $[M+H]^+$ 320.1281, found 320.1273.

Methyl (*E*)-3-(3-(4-chlorophenyl)-5-(*p*-tolyl)isoxazol-4-yl)acrylate (4t):[3]



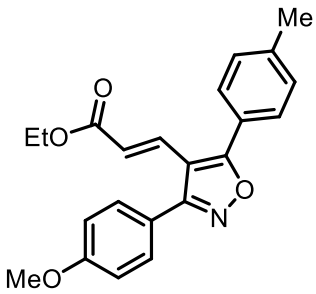
Prepared according to the general procedure and the title compound was isolated in 46% (33 mg) yield. Spectral data obtained were in good agreement with those reported in the literature.

Methyl (*E*)-3-(3-(4-fluorophenyl)-5-(*p*-tolyl)isoxazol-4-yl)acrylate (4u):



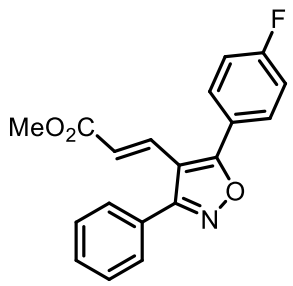
Yield: 50% (34 mg); Physical appearance: Colorless solid; M.p. 87–89 ^oC; TLC R_f 0.4 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 – 7.55 (m, 5H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 8.6 Hz, 2H), 5.95 (d, *J* = 16.2 Hz, 1H), 3.73 (s, 3H), 2.45 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 169.7, 166.9, 163.8 (d, *J* = 250.2 Hz), 161.5, 141.5, 132.6, 130.7 (d, *J* = 8.5 Hz), 129.9, 128.0, 124.7 (d, *J* = 3.4 Hz), 124.2, 121.2, 116.2 (d, *J* = 22.0 Hz), 109.8, 51.7, 21.6; **IR** (KBr, cm^{-1}): 2918, 1717, 1419, 1170, 822, 698; **ESI–HRMS**: Calculated for $C_{20}H_{17}FNO_3^+$ $[M+H]^+$ 338.1187, found 338.1186.

Ethyl (*E*)-3-(3-(4-methoxyphenyl)-5-(*p*-tolyl)isoxazol-4-yl)acrylate (4v):



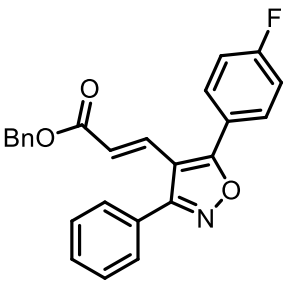
Yield: 63% (46 mg); Physical appearance: Colorless solid; M.p. 90–92 ^oC; TLC R_f 0.3 (10:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 16.2 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.02 (d, *J* = 16.2 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 2.45 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 169.4, 166.7, 162.1, 160.9, 141.24 132.72 130.22 129.8, 128.0, 124.5, 121.3, 120.9, 114.4, 109.9, 60.6, 55.4, 21.6, 14.3; **IR** (KBr, cm^{-1}): 3397, 1713, 1613, 1428, 1254, 1028, 822, 591; **ESI–HRMS**: Calculated for $C_{22}H_{22}NO_4^+$ $[M+H]^+$ 364.1543, found 364.1539.

Methyl (*E*)-3-(5-(4-fluorophenyl)-3-phenylisoxazol-4-yl)acrylate (4w):



Yield: 49% (32 mg); Physical appearance: Colorless solid; M.p. 99–101 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 – 7.74 (m, 2H), 7.67 (d, *J* = 16.2 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.57 – 7.51 (m, 3H), 7.31 – 7.24 (m, 2H), 6.00 (d, *J* = 16.2 Hz, 1H), 3.75 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 168.2, 166.8, 164.2 (d, *J* = 252.9 Hz), 162.4, 132.2, 130.3 (d, *J* = 8.7 Hz), 130.1, 128.9, 128.8, 128.5, 123.4 (d, *J* = 3.4 Hz), 121.7, 116.6 (d, *J* = 22.1 Hz), 110.3, 51.8; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –107.9; **IR** (KBr, cm^{-1}): 3430, 2924, 1719, 1170, 820, 692; **ESI–HRMS**: Calculated for $C_{19}H_{15}FNO_3^+$ $[M+H]^+$ 324.1030, found 324.1025.

Benzyl (*E*)-3-(5-(4-fluorophenyl)-3-phenylisoxazol-4-yl)acrylate (4x):



Yield: 48% (38 mg); Physical appearance: Colorless solid; M.p. 75–77 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 – 7.68 (m, 3H), 7.65 – 7.48 (m, 5H), 7.42 – 7.30 (m, 5H), 7.28 – 7.22 (m, 2H), 6.05 (d, *J* = 16.2 Hz, 1H), 5.20 (s, 2H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 168.4, 166.2, 164.2 (d, *J* = 253.0 Hz), 162.5, 135.8, 132.6, 130.3 (d, *J* = 8.7 Hz), 130.2, 128.9, 128.84, 128.6, 128.4, 128.3, 128.2, 123.4 (d, *J* = 3.6 Hz), 121.6, 116.6 (d, *J* = 22.2 Hz), 110.3, 66.5; **IR** (KBr, cm^{-1}): 3413, 2923, 2852, 1715, 1505, 1267, 1160, 957, 697; **ESI–HRMS**: Calculated for $C_{25}H_{19}FNO_3^+$ $[M+H]^+$ 400.1343, found 400.1352.

(III) General procedure for the Cu-mediated synthesis of pyridines:

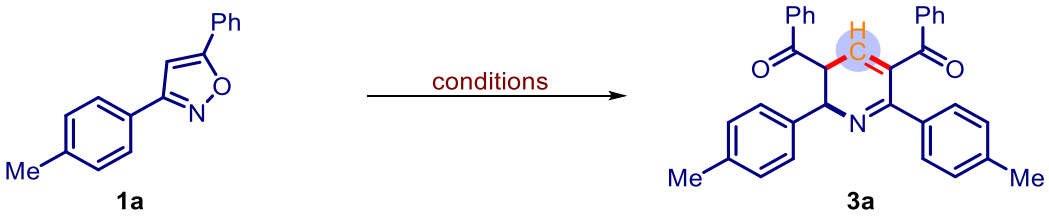
In a pressure tube equipped with a stir bar, isoxazole (1.0 equiv, 0.15 mmol) was dissolved in dry DMSO (1.5 mL) and acetic acid (2.0 equiv, 0.30 mmol) was added. The reaction mixture was stirred for 10 min followed by the addition of the $Cu(OTf)_2$ (2.0 equiv, 0.30 mmol). The tube was fitted with a Teflon screw cap under an argon flow and the reaction mixture was heated to 130 °C (oil bath) and allowed to stir for 6–26 h. The progress of the reaction was followed by TLC. 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.

(IV) General procedure for the Cu-mediated cyclization of 4-alkenyl-3, 5-diaryisoxazole to pyridines:

In a pressure tube equipped with a stir bar, 4-alkenyl-3, 5-diarylisoxazole (1.0 equiv, 0.10 mmol) was dissolved in dry DMSO (1.5 mL). The reaction mixture was stirred for 10 min followed by the addition of acetic acid (2.0 equiv, 0.20 mmol) and $Cu(OTf)_2$ (2.0 equiv, 0.20 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 130 ^oC (oil bath) and allowed to stir for 8–24 h. The progress of the reaction was followed by TLC. 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.

(i) Optimization studies for the cyclization to form pyridines



1a 3a

Table-S1

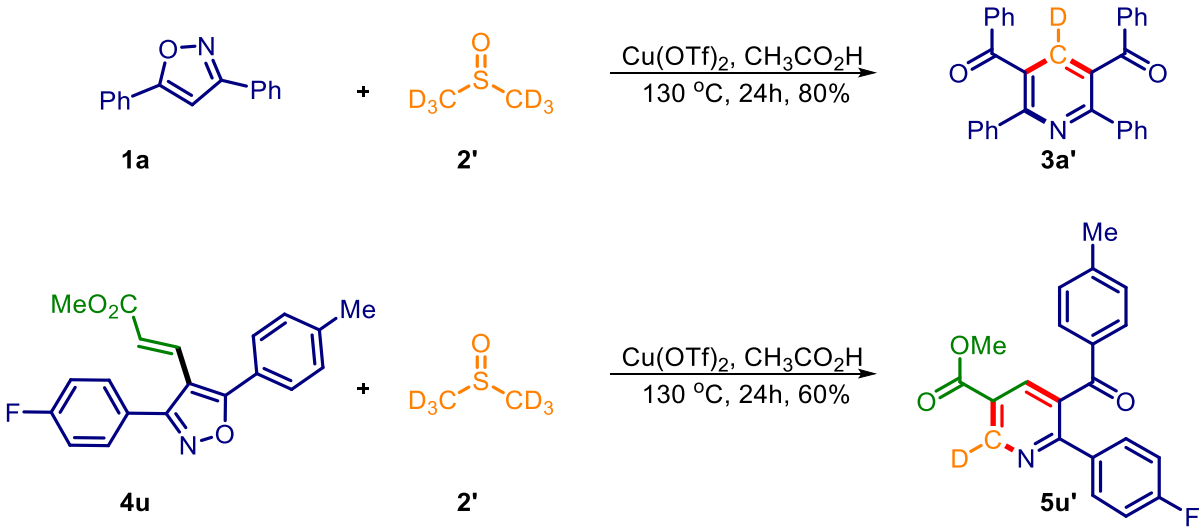
Entry	Conditions	Yield[a] (3a%)
1	$Cu(OTf)_2$ (1 equiv)/DMSO/100 ^oC/24 h	0
2	$Cu(OTf)_2$ (1 equiv)/DMSO/110 ^oC/24 h	0
3	$Cu(OTf)_2$ (1 equiv)/DMSO/130 ^oC/24 h	0
4	$Cu(OTf)_2$ (1 equiv)/AcOH (1 equiv)/DMSO/130 ^oC/24 h	51
5	$Cu(OTf)_2$ (10 mol%.)/AcOH (2 equiv)/DMSO/130 ^oC/24 h	0
6	AcOH (1 equiv)/DMSO/130 ^oC/24 h	0
7	CF_3SO_3H (1 equiv)/DMSO/130 ^oC/24 h	0
8	$Cu(OTf)_2$ (2 equiv)/AcOH (1 equiv)/DMSO/130 ^oC/24 h	82
9	$Cu(OTf)_2$ (2 equiv)/ CF_3SO_3H (1 equiv)/DMSO/130 ^oC/24 h	65
10	$Cu(OAc)_2$ (2 equiv)/AcOH (2 equiv)/DMSO/130 ^oC/24 h	28
11	$Cu(OAc)_2.H_2O$ (2 equiv)/AcOH (2 equiv)/DMSO/130 ^oC/24 h	20

12	**$Cu(OTf)_2$ (2 equiv)/AcOH (2 equiv)/DMSO/130 °C/14 h**	**95**
13	CuF_2 (1 equiv)/AcOH (2 equiv)/DMSO/130 °C/24 h	10
14	$CuCl_2$ (1 equiv)/AcOH (2 equiv)/DMSO/130 °C/24 h	5
15	$Sc(OTf)_3$ (1 equiv)/AcOH (2 equiv)/DMSO/130 °C/24 h	0
16	$Zn(OTf)_2$ (1 equiv)/AcOH (2 equiv)/DMSO/130 °C/24 h	50
17	CuI (1 equiv)/AcOH (2 equiv)/DMSO/130 °C/24 h	6
18	CuCl (1 equiv)/AcOH (2 equiv)/DMSO/130 °C/24 h	5
19	$Ni(OAc)_2{\cdot}4H_2O$ (1 equiv)/AcOH (2 equiv)/DMSO/130 °C/24 h	0
20	$RuCl_3{\cdot}xH_2O$ (10 mol%)/$AgSbF_6$ (20 mol%)/DMSO/130 °C/24 h	0
21	$[RuCl_2(p\text{-cym})]_2$ (10 mol%)/$AgSbF_6$ (20 mol%)/$Cu(OAc)_2.H_2O$ /DMSO/130 °C/24 h	0

[a]Isolated yield.

(V) Mechanistic Studies:

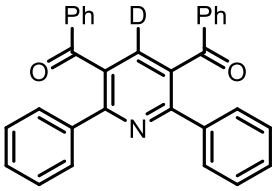
(a) Deuterium-labelling experiments:



Procedure: In a pressure tube equipped with a stir bar, 3, 5-diaryisoxazole or 4-alkenyl-3, 5-diaryisoxazole (1.0 equiv, 0.1 mmol) was dissolved in dry DMSO-d_6 (1.0 mL). The reaction mixture was stirred for 10-15 min followed by the addition of AcOH (2.0 equiv, 0.2 mmol) and $Cu(OTf)_2$ (2.0 equiv, 0.2 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 130 °C (oil bath) and allowed to stir for 24 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

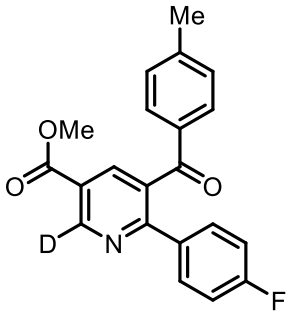
under reduced pressure. The crude product was purified by a silica gel flash column chromatography to result in the desired product.

(2,6-diphenylpyridine-3,5-diyl-4-*d*)bis(phenylmethanone) (3a'):



Yield: 80% (27 mg); Physical appearance: Colorless solid; M.p. 126–128 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 – 7.63 (m, 8H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.35 – 7.25 (m, 10H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.6, 158.1, 138.6, 136.4, 133.5, 131.8, 129.9, 129.6, 129.4, 128.5, 128.4; **IR** (KBr, cm^{-1}): 3393, 2852, 1663, 1559, 1260, 1012; **ESI–HRMS**: Calculated for $C_{31}H_{21}DNO_2^+$ $[M+H]^+$ 441.1708, found 441.1687.

Methyl 6-(4-fluorophenyl)-5-(4-methylbenzoyl)nicotinate-2-*d* (5u'):

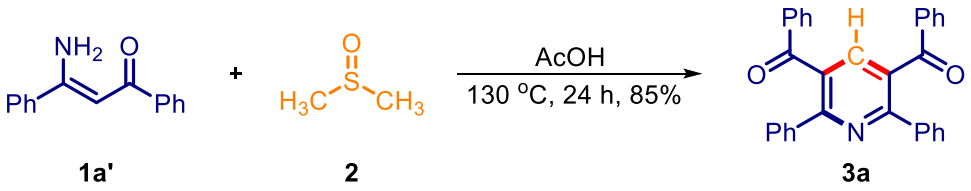


Yield: 60% (21 mg); Physical appearance: Colorless solid; M.p. 108–110 °C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.61– 7.52 (m, 4H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.96 (t, *J* = 8.7 Hz, 1H), 3.97 (s, 3H), 2.35 (s, 3H).); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 195.7, 165.1, 163.6 (d, *J* = 250.4 Hz), 159.4, 151.4, 145.1, 138.0, 134.5 (d, *J* = 3.4 Hz), 134.1, 133.6, 131.3 (d, *J* = 8.6 Hz), 130.1, 129.4, 123.8, 115.6 (d, *J* = 21.8 Hz), 52.6, 21.8; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –111.1; **IR** (KBr, cm^{-1}): 1728, 1664, 1414, 1241, 845, 474; **ESI–HRMS**: Calculated for $C_{21}H_{16}DFNO_3^+$ $[M+H]^+$ 351.1250, found 351.1233.

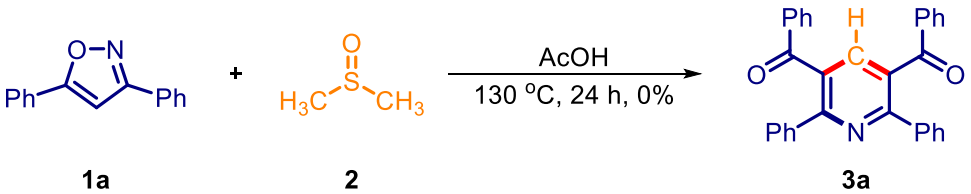
(b) Reaction in absence of copper triflate:

Procedure: In a pressure tube equipped with a stir bar, 3-amino-1,3-diphenylprop-2-en-1-one or 3, 5-diphenylisoxazole (1.0 equiv, 0.1 mmol) was dissolved in dry DMSO (1.0 mL). The reaction mixture was stirred for 10–15 min followed by the addition of AcOH (2.0 equiv, 0.2 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 130 °C (oil bath) and allowed to stir for 12–24 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.

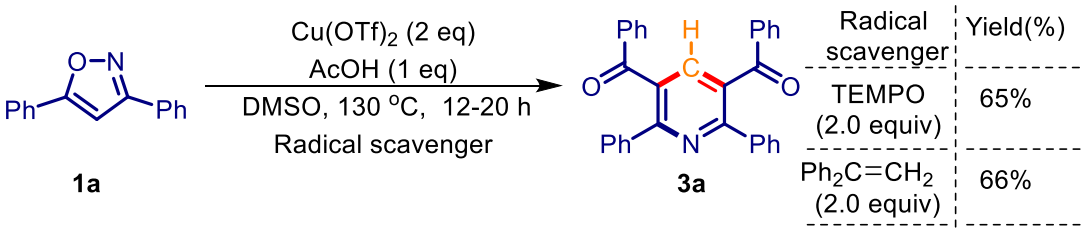


1a' **2** **3a**



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

(c) Radical trap experiments:



1a **3a**

Procedure: In a pressure tube equipped with a stir bar, 3, 5-diaryisoxazole (1.0 equiv, 0.15 mmol) was dissolved in dry DMSO (1.5 mL). The reaction mixture was stirred for 10–15 min followed by the addition of AcOH (2.0 equiv, 0.30 mmol), $Cu(OTf)_2$ (2.0 equiv, 0.30 mmol) and radical trap agent (2.0 equiv, 0.30 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 130 °C (oil bath) and allowed to stir for 12–20 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 yield the desired product.

(d) Procedure for cross-over experiments.

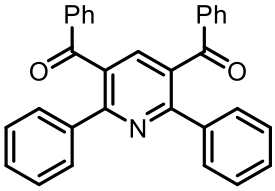
Procedure: In a pressure tube equipped with a stir bar, 3-(4-methoxyphenyl)-5-phenylisoxazole (1.0 equiv, 0.15 mmol) was dissolved in dry DMSO (1.5 mL) and acetic acid (2.0 equiv, 0.30 mmol) was added. The reaction mixture was stirred for 10 min followed by

the addition of 3-(4-fluorophenyl)-5-phenylisoxazole (1.0 equiv, 0.15 mmol) and $Cu(OTf)_2$ (2.0 equiv, 0.30 mmol). The tube was fitted with a Teflon screw cap under an argon flow and the reaction mixture was heated to 130 ^oC (oil bath) and allowed to stir for 20 h. The progress of the reaction was followed by TLC. 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.

(e) Reaction with 2,4-dibenzoyl-1,5-diphenylpentane-1,5-dione.

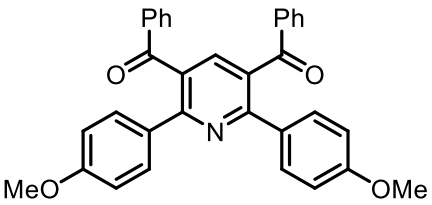
In a pressure tube equipped with a stir bar, 2,4-dibenzoyl-1,5-diphenylpentane-1,5-dione (1.0 equiv, 0.15 mmol) was dissolved in dry DMSO (1.5 mL) and acetic acid (2.0 equiv, 0.30 mmol) was added. The reaction mixture was stirred for 10 min followed by the addition of isoxazoles (1.0 equiv, 0.15 mmol) and $Cu(OTf)_2$ (2.0 equiv, 0.30 mmol). The tube was fitted with a Teflon screw cap under an argon flow and the reaction mixture was heated to 130 ^oC (oil bath) and allowed to stir for 20 h. The progress of the reaction was followed by TLC. 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.

(2,6-diphenylpyridine-3,5-diyl)bis(phenylmethanone) (3a):[20]



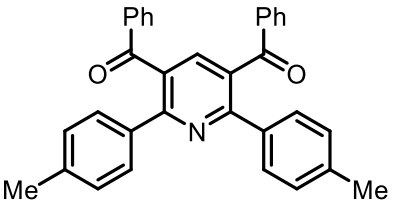
Yield: 96% (32 mg); Physical appearance: Colorless solid; M.p. 193–195 ^oC; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.73 (d, J = 7.8 Hz, 4H), 7.70 – 7.64 (m, 4H), 7.45 (t, J = 7.4 Hz, 2H), 7.34 – 7.25 (m, 10H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.6, 158.0, 138.8, 138.6, 136.4, 133.5, 131.9, 129.9, 129.6, 129.4, 128.48, 128.4; **ESI–HRMS**: Calculated for $C_{31}H_{22}NO_2^+$ $[M+H]^+$ 440.1645, found 440.1667.

(2,6-bis(4-methoxyphenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3b:3b') (5:1) 3b:



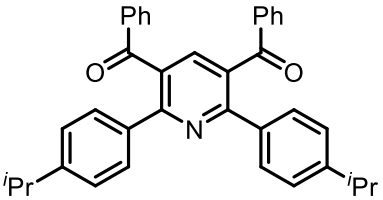
Yield: 95% (36 mg); Physical appearance: Colorless solid; M.p. 126–128 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 4H), 7.64 (d, *J* = 8.6 Hz, 4H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 4H), 6.78 (d, *J* = 8.8 Hz, 4H), 3.74 (s, 6H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 197.0, 160.7, 157.4, 139.1, 136.5, 133.5, 131.25, 131.1, 130.6, 129.9, 128.5, 113.9, 55.3; **IR** (KBr, cm^{-1}): 2838, 1656, 1502, 1252, 1174, 1015, 840, 699; **ESI–HRMS**: Calculated for $C_{33}H_{26}NO_4^+$ $[M+H]^+$ 500.1856, found 500.1877.

(2,6-di-*p*-tolylpyridine-3,5-diyl)bis(phenylmethanone) (3c:3c') (9:1) (3c):



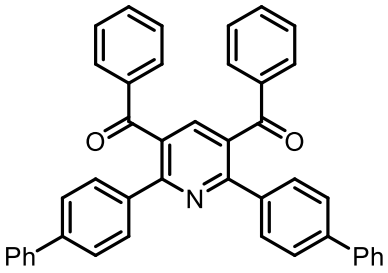
Yield: 95% (33 mg); Physical appearance: Colorless solid; M.p. 104–106 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 4H), 7.57 (d, *J* = 8.1 Hz, 4H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.7 Hz, 4H), 7.07 (d, *J* = 8.0 Hz, 4H), 2.27 (s, 6H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.9, 157.9, 139.5, 138.7, 136.5, 135.9, 133.5, 131.3, 129.9, 129.5, 129.1, 128.5, 21.3; **IR** (KBr, cm^{-1}): 3058, 2921, 1661, 1580, 1423, 1240, 1180, 1010, 618; **ESI–HRMS**: Calculated for $C_{33}H_{26}NO_2^+$ $[M+H]^+$ 468.1958, found 468.1960.

(2,6-bis(4-isopropylphenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3d:3d') (10:1) (3d):



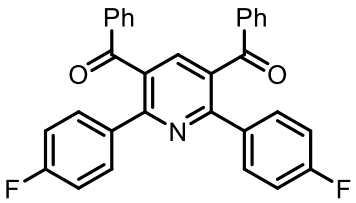
Yield: 65% (26 mg); Physical appearance: Colorless solid; M.p. 101–103 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 4H), 7.58 (d, *J* = 8.0 Hz, 4H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 4H), 7.10 (d, *J* = 8.1 Hz, 4H), 2.81 (sept, *J* = 6.9 Hz, 2H), 1.15 (d, *J* = 6.9 Hz, 12H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.9, 158.2, 150.3, 138.8, 136.6, 136.2, 133.3, 131.3, 129.9, 129.6, 128.4, 126.5, 33.9, 23.7; **IR** (KBr, cm^{-1}): 3057, 2961, 1912, 1664, 1426, 1317, 1257, 1009, 845, 698; **ESI–HRMS**: Calculated for $C_{37}H_{34}NO_2^+$ $[M+H]^+$ 524.2584, found 524.2572.

(2,6-di([1,1'-biphenyl]-4-yl)pyridine-3,5-diyl)bis(phenylmethanone) (3e:3e') (8:1) (3e):



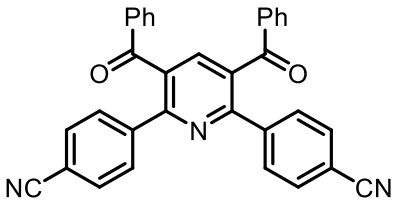
Yield: 63% (28 mg); Physical appearance: Colorless solid; M.p. 90–92 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.82 (d, *J* = 8.2 Hz, 8H), 7.60 – 7.53 (m, 8H), 7.53 – 7.42 (m, 6H), 7.40 – 7.34 (m, 6H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.7, 157.7, 142.2, 140.3, 138.9, 137.5, 136.4, 133.6, 131.6, 130.0, 130.0, 128.79, 128.6, 127.7, 127.1, 127.1; **IR** (KBr, cm^{-1}): 3036, 1661, 1574, 1258, 1007, 762, 697, 632; **ESI–HRMS**: Calculated for $C_{43}H_{30}NO_2^+$ $[M+H]^+$ 592.2271, found 592.2290.

(2,6-bis(4-fluorophenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3f:3f') (10:1) (3f):



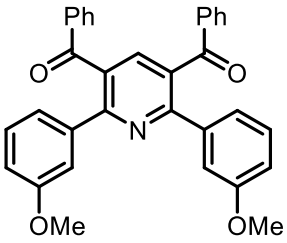
Yield: 58% (20 mg); Physical appearance: Colorless solid; M.p. 140–142 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.77 – 7.73 (m, 4H), 7.71 – 7.66 (m, 4H), 7.55 – 7.49 (m, 2H), 7.41 – 7.34 (m, 4H), 7.04 – 6.96 (m, 4H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.4, 163.6 (d, *J* = 250.5 Hz), 156.8, 138.9, 136.2, 134.6 (d, *J* = 3.2 Hz), 133.8, 131.8, 131.5 (d, *J* = 8.5 Hz), 129.9, 128.62, 115.6 (d, *J* = 21.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): δ –111.3; **IR** (KBr, cm^{-1}): 3060, 1665, 1597, 1504, 1318, 1237, 1010, 845, 700; **ESI–HRMS**: Calculated for $C_{31}H_{19}F_2NaNO_2^+$ $[M+Na]^+$ 498.1276, found 498.1301.

4,4'-(3,5-dibenzoylpyridine-2,6-diyl)dibenzonitrile (3g:3g') (11:1) (3g):



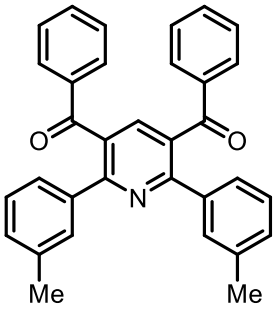
Yield: 55% (20 mg); Physical appearance: Colorless solid; M.p. 164–166 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.79 – 7.69 (m, 8H), 7.59 (d, *J* = 8.2 Hz, 4H), 7.54 (t, *J* = 7.4 Hz, 2 H), 7.38 (t, *J* = 7.8 Hz, 4H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 195.4, 156.304, 142.304, 138.9, 135.8, 134.4, 133.2, 132.2, 130.0, 129.9, 128.9, 118.2, 113.3; **IR** (KBr, cm^{-1}): 3061, 2229, 1666, 1580, 1427, 1259, 1009, 699; **ESI–HRMS**: Calculated for $C_{33}H_{20}N_3O_2^+$ $[M+H]^+$ 490.1550, found 490.1531.

(2,6-bis(3-methoxyphenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3h:3h') (12:1) (3h):



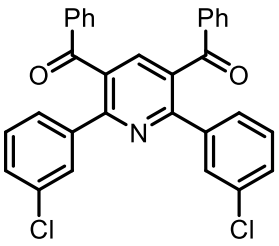
Yield: 75% (28 mg); Physical appearance: Pale-yellow solid; M.p. 47–49 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (s, 1H), 7.73 (d, *J* = 7.8 Hz, 4H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.7 Hz, 4H), 7.23 – 7.07 (m, 6H), 6.80 (d, *J* = 8.3 Hz, 2H), 3.71 (s, 6H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.6, 159.5, 157.7, 139.9, 138.6, 136.4, 133.6, 132.1, 129.8, 129.5, 128.5, 122.2, 115.7, 114.5, 55.3; **IR** (KBr, cm^{-1}): 2934, 1663, 1449, 1261, 1015, 699; **ESI–HRMS**: Calculated for $C_{33}H_{26}NO_4^+$ $[M+H]^+$ 500.1856, found 500.1839.

(2,6-di-*m*-tolylpyridine-3,5-diyl)bis(phenylmethanone) (3i:3i') (11:1) (3i):



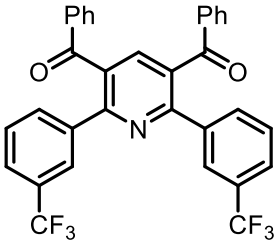
Yield: 72% (25 mg); Physical appearance: Colorless solid; M.p. 113–115 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.74 (d, *J* = 7.8 Hz, 4H), 7.53 (s, 2H), 7.50 – 7.43 (m, 4H), 7.34 (t, *J* = 7.8 Hz, 4H), 7.17 (t, *J* = 7.6 Hz, 2H), 7.10 (d, *J* = 7.6 Hz, 2H), 2.30 (s, 6H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.8, 158.3, 138.8, 138.6, 138.1, 136.5, 133.4, 131.9, 130.3, 130.2, 129.8, 128.4, 128.3, 126.7, 21.3; **IR** (KBr, cm^{-1}): 3037, 1663, 1572, 1318, 1259, 773, 699; **ESI–HRMS**: Calculated for $C_{33}H_{26}NO_2^+$ $[M+H]^+$ 468.1958, found 468.1937.

(2,6-bis(3-chlorophenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3j:3j') (10:1) (3j):



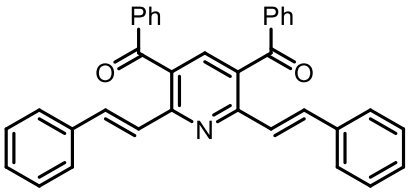
Yield: 70% (27 mg); Physical appearance: Colorless solid; M.p. 101–103 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.75 – 7.67 (m, 6H), 7.52 – 7.42 (m, 4H), 7.34 (t, *J* = 7.7 Hz, 4H), 7.27–7.24 (m, 2H), 7.18 (t, *J* = 7.8 Hz, 2H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.0, 156.6, 140.0, 138.9, 136.2, 134.6, 133.9, 132.5, 129.8, 129.6, 129.6, 129.5, 128.7, 127.6; **IR** (KBr, cm^{-1}): 3063, 2925, 1664, 1578, 1429, 1397, 1259, 1615, 912, 738; **ESI–HRMS**: Calculated for $C_{31}H_{20}Cl_2NO_2^+$ $[M+H]^+$ 508.0866, found 508.0869.

(2,6-bis(3-(trifluoromethyl)phenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3k:3k') (11:1) (3k):



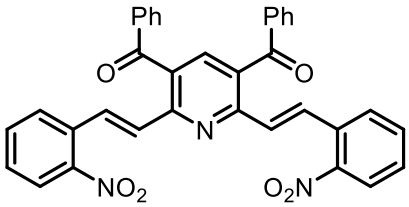
Yield: 68% (29 mg); Physical appearance: Colorless solid; M.p. 136–138 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.96 (s, 2H), 7.85 (d, *J* = 7.9 Hz, 2H), 7.76 – 7.71 (m, 4H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.54 – 7.48 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 4H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 195.9, 156.7, 139.2, 138.9, 136.1, 133.9, 132.8, 132.6, 131.1, 130.8, 129.8, 128.9, 128.7, 126.5 (d, *J* = 3.9 Hz), 126.1 (d, *J* = 3.7 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): δ –62.9; **IR** (KBr, cm^{-1}): 3065, 1664, 1578, 1331, 1128, 1074, 911, 698; **ESI–HRMS**: Calculated for $C_{33}H_{20}F_6NO_2^+$ $[M+H]^+$ 576.1393, found 576.1394.

(2,6-di((*E*)-styryl)pyridine-3,5-diyl)bis(phenylmethanone) (3l):



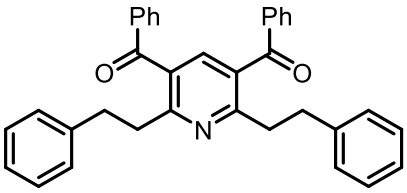
Yield: 86% (32 mg); Physical appearance: Yellow solid; M.p. 101–103 °C; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 15.6 Hz, 2H), 7.85 (d, *J* = 7.9 Hz, 4H), 7.73 (s, 1H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.53 – 7.43 (m, 8H), 7.36 – 7.26 (m, 8H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 195.9, 154.3, 138.5, 137.2, 137.1, 136.3, 133.9, 130.2, 130.1, 128.9, 128.8, 128.7, 127.7, 124.3; **IR** (KBr, cm^{-1}): 3063, 1656, 1563, 1292, 1177, 1072, 922, 690; **ESI–HRMS**: Calculated for $C_{35}H_{26}NO_2^+$ $[M+H]^+$ 492.1958, found 492.1961.

(2,6-bis((*E*)-2-nitrostyryl)pyridine-3,5-diyl)bis(phenylmethanone) (3m):



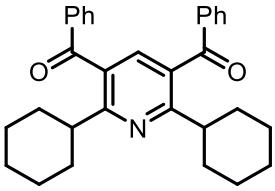
Yield: 77% (34 mg); Physical appearance: Yellow solid; M.p. 52–54 °C; TLC R_f 0.2 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 15.4 Hz, 2H), 8.04 (d, *J* = 8.2 Hz, 2H), 7.88 (d, *J* = 8.01 Hz, 4H), 7.82 (s, 1H), 7.68 – 7.63 (m, 2H), 7.60 – 7.56 (m, 4H), 7.55–7.44(m, 7H), 7.25 (s, 1H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 195.6, 153.7, 148.4, 138.6, 136.9, 134.1, 133.2, 132.5, 130.9, 130.3, 129.1, 129.0, 128.9, 128.5, 124.9; **IR** (KBr, cm^{-1}): 3058, 2925, 1659, 1821, 1343, 1256, 1178, 970, 784, 735; **ESI–HRMS**: Calculated for $C_{35}H_{23}N_3NaO_6^+$ $[M+Na]^+$ 604.1479, found 604.1489.

(2,6-diphenethylpyridine-3,5-diyl)bis(phenylmethanone) (3o):



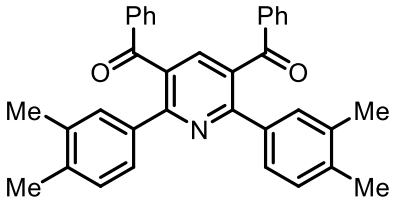
Yield: 51% (19 mg); Physical appearance: Brown gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.72 – 7.64 (m, 4H), 7.63 – 7.58 (m, 2H), 7.50 (s, 1H), 7.47 – 7.42 (m, 4H), 7.25 – 7.20 (m, 4H), 7.18 – 7.12 (m, 6H), 3.28– 3.20 (m, 4H), 3.16 – 3.09 (m, 4H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$): δ 196.3, 160.9, 141.4, 136.9, 136.4, 133.7, 130.6, 130.0, 128.7, 128.5, 128.3, 125.9, 37.8, 35.5; **IR** (KBr, cm^{-1}): 3027, 2928, 1664, 1596, 1449, 1258, 1071, 905, 699; **ESI–HRMS**: Calculated for $C_{35}H_{30}NO_2^+$ $[M+H]^+$ 496.2271, found 496.2244.

(2,6-dicyclohexylpyridine-3,5-diyl)bis(phenylmethanone) (3p):



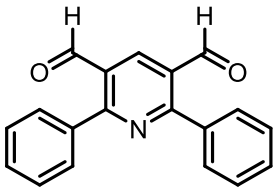
Yield: 51% (17 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.3 (19:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 – 7.80 (m, 4H), 7.64 – 7.58 (m, 2H), 7.50 – 7.46 (m, 4H), 7.43 (s, 1H), 2.94– 2.84 (m, 2H), 1.85 – 1.78 (m, 11H), 1.33 – 1.24 (m, 9H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.9, 165.2, 137.3, 135.5, 133.7, 130.1, 129.4, 128.6, 43.4, 32.4, 26.3, 25.9; **IR** (KBr, cm^{-1}): 3025, 2927, 1720, 1666, 1582, 1260, 1073, 699; **ESI–HRMS**: Calculated for $C_{31}H_{34}NO_2^+$ $[M+H]^+$ 452.2584, found 452.2587.

(2,6-bis(3,4-dimethylphenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3q:3q') (8:1) (3q):



Yield: 70% (26 mg); Physical appearance: Colorless solid; M.p. 140–142 °C; TLC R_f0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.77 (d, J = 7.6 Hz, 4H), 7.54 – 7.45 (m, 4H), 7.41 – 7.32 (m, 6H), 7.04 (d, J = 7.8 Hz, 2H), 2.21 (s, 12H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.9, 158.2, 138.6, 138.1, 136.6, 136.3, 133.3, 131.2, 130.8, 129.9, 129.6, 128.4, 127.0, 19.7, 19.6; **IR** (KBr, cm^{-1}): 3059, 2073, 1654, 1426, 1259, 911, 698; **ESI–HRMS**: Calculated for $C_{35}H_{30}NO_2^+$ $[M+H]^+$ 496.2271, found 496.2266.

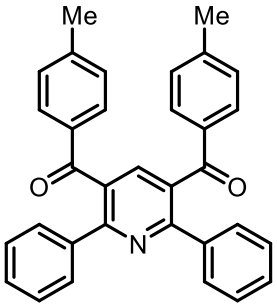
2,6-diphenylpyridine-3,5-dicarbaldehyde (3t):



Yield: 40% (8 mg); Physical appearance: Colorless solid; M.p. 118–120 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR**

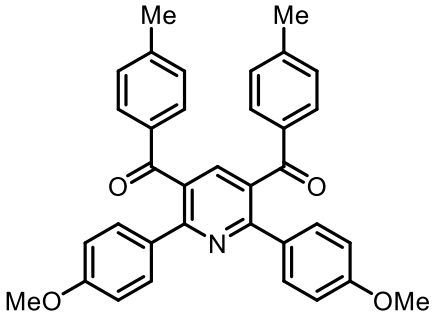
(400 MHz, $CDCl_3$): δ 10.17 (s, 2H), 8.93 (s, 1H), 7.79 – 7.71 (m, 4H), 7.63 – 7.56 (m, 6H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 190.48, 164.25, 137.22, 136.50, 130.69, 130.50, 128.83, 128.15; **IR** (KBr, cm^{-1}): 1695, 1570, 1380, 1140, 755, 700; **ESI–HRMS**: Calculated for $C_{19}H_{14}NO_2^+$ $[M+H]^+$ 288.1019, found 288.0997.

(2,6-diphenylpyridine-3,5-diyl)bis(*p*-tolylmethanone) (3u:3u') (8:1) (3u):



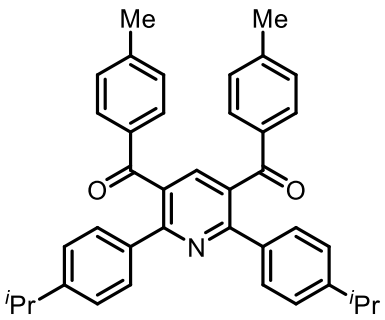
Yield: 84% (29 mg); Physical appearance: Colorless solid; M.p. 170–172 °C; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.75 – 7.70 (m, 4H), 7.68 (d, *J* = 8.2 Hz, 4H), 7.34 – 7.30 (m, 6H), 7.15 (d, *J* = 8.0 Hz, 4H), 2.36 (s, 6H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.3, 157.7, 144.6, 138.7, 138.4, 133.9, 132.1, 130.1, 129.5, 129.3, 129.3, 128.4, 21.7; **IR** (KBr, cm^{-1}): 3057, 1661, 1604, 1420, 1263, 1011, 751, 698; **ESI–HRMS**: Calculated for $C_{33}H_{26}NO_2^+$ $[M+H]^+$ 468.1958, found 468.1956.

(2,6-bis(4-methoxyphenyl)pyridine-3,5-diyl)bis(*p*-tolylmethanone) (3v:3v') (5:1) (3v):



Yield: 71% (28 mg); Physical appearance: Pale-yellow solid; M.p. 127–129 °C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.68 – 7.62 (m, 8H), 7.11 (d, *J* = 8.0 Hz, 4H), 6.80 (d, *J* = 8.8 Hz, 4H), 3.75 (s, 6H), 2.33 (s, 6H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.7, 160.6, 156.9, 144.5, 138.6, 134.0, 131.4, 130.9, 130.8, 130.1, 129.2, 113.9, 55.3, 21.7; **IR** (KBr, cm^{-1}): 2993, 1604, 1306, 1176, 1023, 840, 739; **ESI–HRMS**: Calculated for $C_{35}H_{30}NO_4^+$ $[M+H]^+$ 528.2169, found 528.2174.

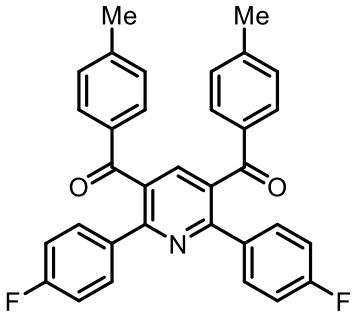
(2,6-bis(4-isopropylphenyl)pyridine-3,5-diyl)bis(*p*-tolylmethanone) (3w:3w') (6:1) (3w):



Yield: 62% (26 mg); Physical appearance: Colorless solid; M.p. 131–133 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.61 (dd, *J* = 17.1, 8.0 Hz, 8H), 7.11 (d, *J* = 8.0 Hz, 8H), 2.82 (sept, *J* = 6.9 Hz, 2H), 2.32 (s, 6H), 1.16 (d, *J* = 6.9 Hz, 12H); **^{13}C {^{1}H}**

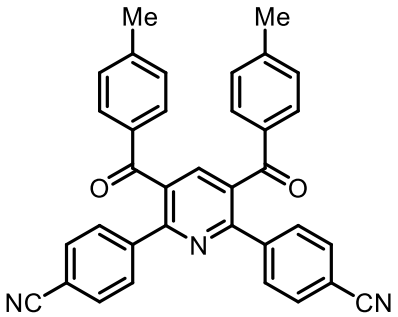
NMR (125 MHz, $CDCl_3$): δ 196.5, 157.8, 150.2, 144.3, 138.5, 136.3, 134.2, 131.4, 130.2, 129.6, 129.1, 126.4, 33.9, 23.7, 21.6; **IR** (KBr, cm^{-1}): 3029, 2960, 1663, 1579, 1500, 1314, 1179, 1010, 913, 741; **ESI–HRMS**: Calculated for $C_{39}H_{38}NO_2^+$ $[M+H]^+$ 552.2897, found 552.2920.

(2,6-bis(4-fluorophenyl)pyridine-3,5-diyl)bis(*p*-tolylmethanone) (3x:3x') (11:1) (3x):



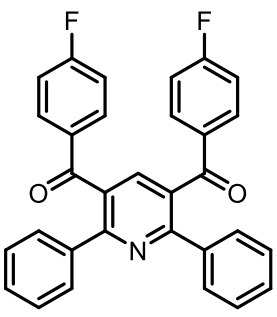
Yield: 56% (21 mg); Physical appearance: Colorless solid; M.p. 131–133 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.71 – 7.58 (m, 8H), 7.13 (d, *J* = 8.0 Hz, 4H), 6.97 (t, *J* = 8.6 Hz, 4H), 2.34 (s, 6H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.0, 163.5 (d, *J* = 250.1 Hz), 156.5, 144.9, 138.6, 134.7 (d, *J* = 3.0 Hz), 133.7, 131.9, 131.4 (d, *J* = 8.6 Hz), 130.1, 129.37, 115.5 (d, *J* = 21.8 Hz), 21.73; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –111.6; **IR** (KBr, cm^{-1}): 3028, 1603, 1262, 845; **ESI–HRMS**: Calculated for $C_{33}H_{24}F_2NO_2^+$ $[M+H]^+$ 504.1770, found 504.1751.

4,4'-(3,5-bis(4-methylbenzoyl)pyridine-2,6-diyl)dibenzonitrile (3y:3y') (12:1) (3y):



Yield: 52% (20 mg); Physical appearance: Pale-yellow solid; M.p. 192–194 °C; TLC R_f 0.1 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.76 (d, *J* = 8.3 Hz, 4H), 7.66 – 7.55 (m, 8H), 7.17 (d, *J* = 8.0 Hz, 4H), 2.37 (s, 6H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 194.9, 155.9, 145.7, 142.4, 138.6, 133.5, 133.4, 132.2, 130.1, 129.9, 129.6, 118.3, 113.2, 21.8; **IR** (KBr, cm^{-1}): 3064, 1660, 1263, 1010, 850, 562; **ESI–HRMS**: Calculated for $C_{35}H_{24}N_3O_2^+$ $[M+H]^+$ 518.1863, found 518.1840.

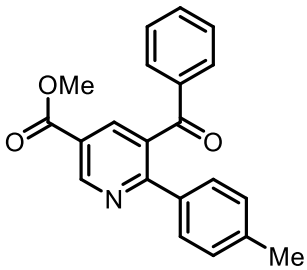
(2,6-diphenylpyridine-3,5-diyl)bis((4-fluorophenyl)methanone) (3z:3z') (9:1) (3z):



Yield: 64% (23 mg); Physical appearance: Colorless solid; M.p. 218–220 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10 (s, 1H), 7.79 – 7.73 (m, 4H), 7.72 – 7.67 (m, 4H), 7.34 – 7.30 (m, 6H), 7.03 – 6.96 (m, 4H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 195.1, 165.8 (d, *J* = 256.5 Hz), 157.9, 138.9, 138.4,132.7 (d, *J* = 2.7 Hz), 132.5 (d, *J* = 9.6 Hz), 131.8, 129.7,

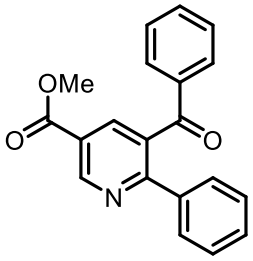
129.5, 128.5, 115.7 (d, J = 22.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): δ –103.6; **IR** (KBr, cm^{-1}): 3057, 1593, 1253, 1141, 855, 759; **ESI–HRMS**: Calculated for $C_{31}H_{20}F_2NO_2^+$ $[M+H]^+$ 476.1457, found 476.1478.

Methyl 5-benzoyl-6-(*p*-tolyl)nicotinate (5a):



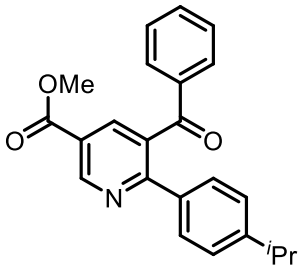
Yield: 78% (26 mg); Physical appearance: Colorless solid; M.p. 125–127 ^oC; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.37 (d, J = 1.9 Hz, 1H), 8.37 (d, J = 1.9 Hz, 1H), 7.66 (d, J = 7.9 Hz, 2H), 7.51 – 7.41 (m, 3H), 7.32 (t, J = 7.7 Hz, 2H), 7.06 (d, J = 7.9 Hz, 2H), 3.96 (s, 3H), 2.25 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.4, 165.2, 160.8, 151.5, 139.9, 138.0, 136.2, 135.5, 133.7, 133.6, 129.9, 129.3, 128.6, 123.5, 52.6, 21.3; **IR** (KBr, cm^{-1}): 1728, 1667, 1539, 1430, 1304, 1128, 780; **ESI–HRMS**: Calculated for $C_{21}H_{18}NO_3^+$ $[M+H]^+$ 332.1281, found 332.1257.

Methyl 5-benzoyl-6-phenylnicotinate (5b):



Yield: 70% (22 mg); Physical appearance: Yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.43 (d, J = 2.0 Hz, 1H), 8.46 (d, J = 2.0 Hz, 1H), 7.68 (d, J = 7.8 Hz, 2H), 7.61 – 7.57 (m, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.35 (t, J = 8.0 Hz, 2H), 7.31 – 7.29 (m, 3H), 4.02 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.2, 165.16, 160.8, 151.6, 138.3, 138.1, 136.2, 134.0, 133.7, 129.9, 129.6, 129.3, 128.5, 128.4, 123.9, 52.6; **IR** (KBr, cm^{-1}): 3060, 2928, 1727, 1594, 1430, 1305, 1252, 1129, 934, 695; **ESI–HRMS**: Calculated for $C_{20}H_{16}NO_3^+$ $[M+H]^+$ 318.1125, found 318.1114.

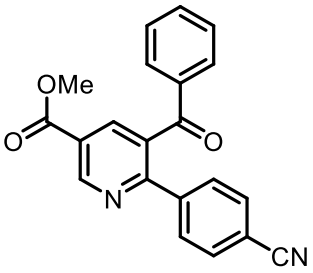
Methyl 5-benzoyl-6-(4-isopropylphenyl)nicotinate (5c):



Yield: 67% (24 mg); Physical appearance: Colorless solid; M.p. 113–115 ^oC; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.41 (s, 1H), 8.43 (s, 1H), 7.69 (d, J = 8.1 Hz, 2H), 7.54 -7.46 (m, 3H), 7.35 (t, J = 7.6 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 4.01 (s, 3H), 2.84 (h, J = 7.0 Hz, 1H), 1.17 (d, J = 67.0 Hz, 6H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.4, 165.3, 160.9, 151.5, 150.7, 138.1, 136.3, 135.8, 133.8, 133.5, 129.9, 129.4, 128.5, 126.6, 123.5, 52.6, 33.8, 23.7; **IR** (KBr, cm^{-1}):

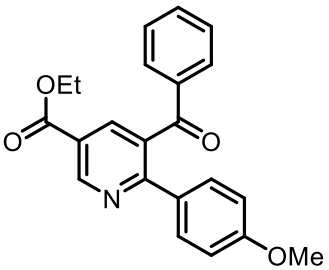
2962, 1725, 1593, 1303, 1129, 929, 711; **ESI–HRMS**: Calculated for $C_{23}H_{22}NO_3^+$ $[M+H]^+$ 360.1594, found 360.1592.

Methyl 5-benzoyl-6-(4-cyanophenyl)nicotinate (5d):



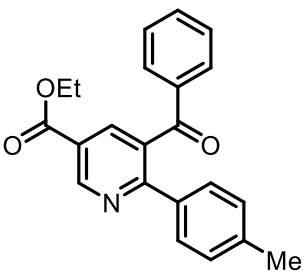
Yield: 53% (18 mg); Physical appearance: Yellow semi-solid; TLC R_f 0.2 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz,$CDCl_3$): δ 9.44 (d, *J* = 2.0 Hz, 1H), 8.48 (d, *J* = 2.0 Hz, 1H), 7.74 – 7.65 (m, 4H), 7.63 – 7.53 (m, 3H), 7.41 (t, *J* = 7.7 Hz, 2H), 4.03 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 195.5, 164.8, 158.7, 151.7, 142.5, 138.3, 135.9, 134.4, 134.3, 132.2, 129.9, 129.9, 128.9, 124.8, 118.2, 113.2, 52.8; **IR** (KBr, cm^{-1}): 3033, 2229, 1728, 1595, 1305, 1130, 847; **ESI–HRMS**: Calculated for $C_{21}H_{15}N_2O_3^+$ $[M+H]^+$ 343.1077, found 343.1082.

Ethyl 5-benzoyl-6-(4-methoxyphenyl)nicotinate (5e):



Yield: 83% (30 mg); Physical appearance: Pale-yellow solid; M.p. 69–71 ^{o}C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.40 (d, *J* = 2.0 Hz, 1H), 8.41 (d, *J* = 2.0 Hz, 1H), 7.69 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 8.1 Hz, 2H), 6.81 (d, *J* = 8.9 Hz, 2H), 4.47 (q, *J* = 7.1 Hz, 2H), 3.77 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.7, 164.8, 160.9, 160.1, 151.5, 138.1, 136.2, 133.7, 133.37, 130.9, 130.9, 129.9, 128.6, 123.6, 114.0, 61.6, 55.3, 14.3; **IR** (KBr, cm^{-1}): 3053, 1720, 1592, 1438, 1253, 1176, 1021, 840; **ESI–HRMS**: Calculated for $C_{22}H_{20}NO_4^+$ $[M+H]^+$ 362.1387, found 362.1411.

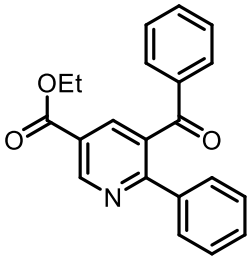
Ethyl 5-benzoyl-6-(*p*-tolyl)nicotinate (5f):



Yield: 77% (27 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.42 (d, *J* = 2.1 Hz, 1H), 8.45 (d, *J* = 2.1 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.44 (s, 1H), 7.34 (t, *J* = 7.7 Hz, 3H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 7.7 Hz, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.5, 164.7, 160.8, 151.6, 138.2, 138.1, 133.9, 133.6, 130.4, 129.9,

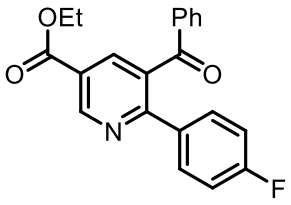
129.7, 128.5, 128.3, 126.5, 124.1, 61.7, 21.3, 14.3; **IR** (KBr, cm^{-1}): 2918, 1723, 1594, 1449, 1302, 1253, 1127, 880; **ESI–HRMS**: Calculated for $C_{22}H_{20}NO_3^+$ $[M+H]^+$ 346.1438, found 346.1432.

Ethyl 5-benzoyl-6-phenylnicotinate (5g):



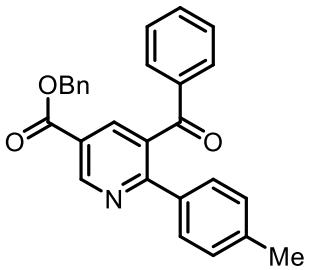
Yield: 68% (23 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.43 (d, *J* = 2.1 Hz, 1H), 8.46 (d, *J* = 2.1 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.61 – 7.56 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.31 – 7.26 (m, 3H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.4, 164.7, 160.7, 151.6, 138.4, 138.1, 136.2, 133.9, 133.7, 129.9, 129.6, 129.3, 128.5, 128.5, 124.2, 61.8, 14.3; **IR** (KBr, cm^{-1}): 3025, 1722, 1594, 1301, 1129, 876, 695; **ESI–HRMS**: Calculated for $C_{21}H_{18}NO_3^+$ $[M+H]^+$ 332.1281, found 332.1306.

Ethyl 5-benzoyl-6-(4-fluorophenyl)nicotinate (5h):



Yield: 64% (22 mg); Physical appearance: Yellow gel; TLC R_f0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.44 (d, *J* = 2.1 Hz, 1H), 8.46 (d, *J* = 2.1 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.60 – 7.54 (m, 2H), 7.33 – 7.29 (m, 3H), 7.03 – 7.95 (m, 2H), 4.48 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H); **^{13}C {^{1}H} NMR** (125MHz, $CDCl_3$): δ 196.3, 163.6 (d, *J* = 251.9 Hz), 159.4, 151.6, 138.1, 136.1, 134.5 (d, *J* = 3.2 Hz), 133.9, 133.8, 131.3 (d, *J* = 8.6 Hz), 129.8, 128.6, 124.3, 115.6 (d, *J* = 21.8 Hz), 61.8, 14.3; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –111.0; **IR** (KBr, cm^{-1}): 2982, 1722, 1595, 1441, 1250, 1015, 846, 649; **ESI–HRMS**: Calculated for $C_{21}H_{17}FNO_3^+$ $[M+H]^+$ 350.1187, found 350.1177.

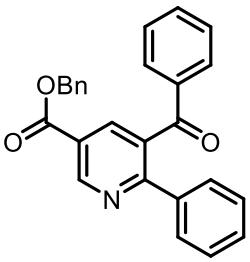
Benzyl 5-benzoyl-6-(*p*-tolyl)nicotinate (5i):



Yield: 72% (29 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.44 (d, *J* = 2.0 Hz, 1H), 8.43 (d, *J* = 2.0 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.50 – 7.32 (m, 10H), 7.09 (d, *J* = 7.9 Hz, 2H), 5.45 (s, 2H), 2.29 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.4,

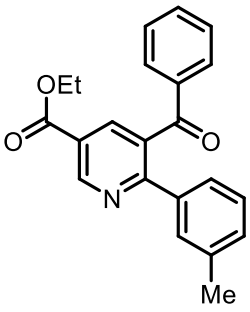
164.6, 160.8, 151.6, 139.9, 138.0, 136.2, 135.5, 135.4, 133.8, 133.6, 129.9, 129.3, 129.2, 128.7, 128.6, 128.5, 128.4, 123.6, 67.3, 21.3; **IR** (KBr, cm^{-1}): 3033, 1724, 1593, 1439, 1299, 1115, 829, 694; **ESI–HRMS**: Calculated for $C_{27}H_{22}NO_3^+$ $[M+H]^+$ 408.1594, found 408.1610.

Benzyl 5-benzoyl-6-phenylnicotinate (5j):



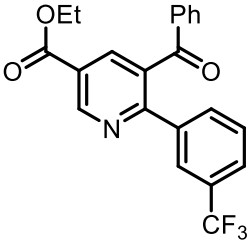
Yield: 65% (26 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.47 (d, *J* = 2.1 Hz, 1H), 8.47 (d, *J* = 2.1 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.61 – 7.56 (m, 2H), 7.52 – 7.45 (m, 3H), 7.44 – 7.38 (m, 3H), 7.35 – 7.27 (m, 5H), 5.46 (s, 2H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.3, 164.6, 160.8, 151.7, 138.3, 138.2, 136.2, 135.3, 134.0, 133.7, 129.8, 129.7, 129.3, 128.7, 128.6, 128.5, 128.4, 128.3, 123.9, 67.4; **IR** (KBr, cm^{-1}): 2925, 1723, 1594, 1294, 1126, 695; **ESI–HRMS**: Calculated for $C_{26}H_{20}NO_3^+$ $[M+H]^+$ 394.1438, found 394.1421.

Ethyl 5-benzoyl-6-(*m*-tolyl)nicotinate (5k):



Yield: 68% (24 mg); Physical appearance: Colorless gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.42 (d, *J* = 2.1 Hz, 1H), 8.45 (d, *J* = 2.1 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.44 (s, 1H), 7.34 (t, *J* = 7.9 Hz, 3H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.11–7.07 (m, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.5, 164.7, 160.8, 151.6, 138.3, 138.2, 138.1, 136.3, 133.9, 133.6, 130.4, 129.9, 129.7, 128.5, 128.3, 126.5, 124.1, 61.7, 21.3, 14.3; **IR** (KBr, cm^{-1}): 3022, 1723, 1594, 1302, 1025, 772; **ESI–HRMS**: Calculated for $C_{22}H_{20}NO_3^+$ $[M+H]^+$ 346.1438, found 346.1453.

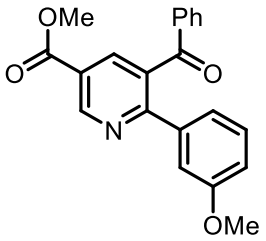
Ethyl 5-benzoyl-6-(3-(trifluoromethyl)phenyl)nicotinate (5l):



Yield: 53% (21 mg); Physical appearance: Colorless gel; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.45 (d, *J* = 2.1 Hz, 1H), 8.51 (d, *J* = 2.1 Hz, 1H), 7.89 (s, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.56 – 7.48 (m, 2H), 7.43 – 7.32 (m, 3H), 4.49 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 195.9, 164.4, 158.9, 151.7, 139.1, 138.3, 136.0, 134.2, 133.9, 132.5, 131.1, 130.8, 129.8, 128.9, 128.7, 126.3 (d, *J* = 3.7 Hz), 126.1 (d, *J* = 3.6 Hz), 124.9, 61.9, 14.3;**^{19}F**

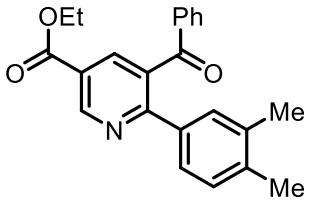
NMR (376 MHz, $CDCl_3$): δ –62.9; **IR** (KBr, cm^{-1}): 3044, 1728, 1595, 1336, 1128, 909, 699; **ESI–HRMS**: Calculated for $C_{22}H_{17}F_3NO_3^+$ $[M+H]^+$ 400.1155, found 400.1134.

Methyl 5-benzoyl-6-(3-methoxyphenyl)nicotinate (5m):



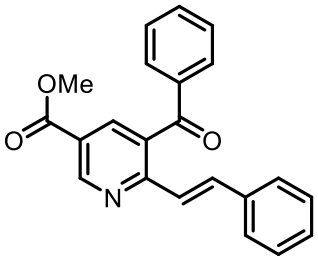
Yield: 67% (23 mg); Physical appearance: Yellow solid; M.p. 89–91 °C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.42 (d, *J* = 2.1 Hz, 1H), 8.44 (d, *J* = 2.1 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.21 – 7.10 (m, 3H), 6.86 – 6.81 (m, 1H), 4.01 (s, 3H), 3.74 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.2, 165.1, 160.6, 159.6, 151.5, 139.6, 138.0, 136.2, 134.1, 133.7, 129.8, 129.6, 128.6, 123.9, 121.9, 116.2, 114.1, 55.2, 52.6; **IR** (KBr, cm^{-1}): 2924, 1728, 1595, 1547, 1431, 1304, 1254, 1031, 876, 776, 694; **ESI–HRMS**: Calculated for $C_{21}H_{18}NO_4^+$ $[M+H]^+$ 348.1230, found 348.1222.

Ethyl 5-benzoyl-6-(3,4-dimethylphenyl)nicotinate (5n):



Yield: 80% (28 mg); Physical appearance: Yellow gel; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.40 (d, *J* = 2.1 Hz, 1H), 8.41 (d, *J* = 2.1 Hz, 1H), 7.69 (d, *J* = 7.3 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.42 (s, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 2.19 (d, *J* = 2.4 Hz, 6H), 1.44 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.6, 164.8, 160.8, 151.5, 138.5, 137.9, 136.3, 135.9, 133.7, 133.5, 130.5, 129.8, 129.7, 128.5, 126.8, 123.7, 61.7, 19.7, 19.6, 14.3; **IR** (KBr, cm^{-1}): 2920, 1722, 1593, 1449, 1252, 1124, 1022, 708, 648; **ESI–HRMS**: Calculated for $C_{23}H_{22}NO_3^+$ $[M+H]^+$ 360.1594, found 360.1580.

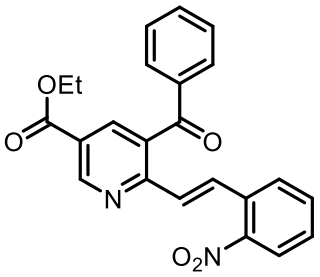
Methyl (*E*)-5-benzoyl-6-styrylnicotinate (5o):



Yield: 70% (24 mg); Physical appearance: Pale-yellow solid; M.p. 109–111 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.33 (d, *J* = 1.9 Hz, 1H), 8.29 (d, *J* = 2.0 Hz, 1H), 8.07 (d, *J* = 15.6 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 2H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.58 – 7.45 (m, 4H), 7.37 – 7.30 (m, 3H), 7.23 (d, *J* = 15.6 Hz, 1H), 3.98 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 195.9, 165.2, 156.8, 151.7, 138.1, 137.8, 136.9, 136.0, 134.1, 132.5, 130.2, 129.2, 128.9, 128.7, 127.8, 123.6, 123.0,

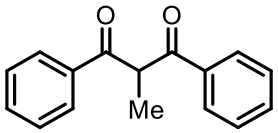
52.5; **IR** (KBr, cm^{-1}): 2952, 2081, 1664, 1590, 1430, 1124, 935, 781; **ESI–HRMS**: Calculated for $C_{22}H_{18}NO_3^+$ $[M+H]^+$ 344.1281, found 343.1263.

Ethyl (*E*)-5-benzoyl-6-(2-nitrostyryl)nicotinate (5p):



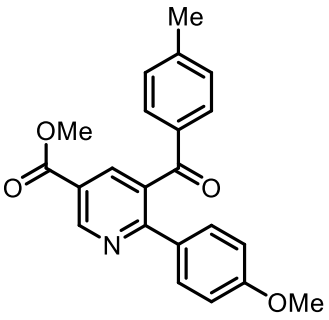
Yield: 61% (24 mg); Physical appearance: Yellow solid; M.p. 94–96 °C; TLC R_f 0.2 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.37 (d, *J* = 2.1 Hz, 1H), 8.50 (d, *J* = 15.3 Hz, 1H), 8.32 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.85 (d, *J* = 7.3 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.59 – 7.51 (m, 4H), 7.49 – 7.42 (m, 1H), 7.22 (d, *J* = 15.3 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 195.8, 164.6, 155.8, 151.9, 148.5, 137.8, 136.7, 134.2, 133.2, 132.9, 132.8, 132.1, 130.3, 129.2, 128.9, 128.8, 128.4, 124.7, 124.1, 61.7, 14.3; **IR** (KBr, cm^{-1}): 3032, 2080, 1643, 1246, 1122, 712; **ESI–HRMS**: Calculated for $C_{23}H_{19}N_2O_5^+$ $[M+H]^+$ 403.1288, found 403.1303.

2-methyl-1,3-diphenylpropane-1,3-dione (5q):[21]



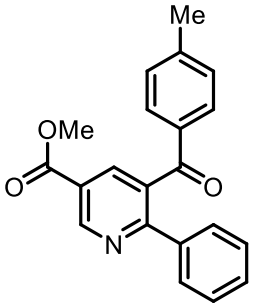
Yield: 8% (2 mg); Physical appearance: Colorless solid; M.p. 76–79°C; TLC R_f 0.4 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.03 – 7.93 (m, 4H), 7.63 – 7.56 (m, 2H), 7.52 – 7.43 (m, 4H), 5.29 (q, *J* = 7.0 Hz, 1H), 1.63 (d, *J* = 7.0 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 197.2, 135.7, 133.5, 128.9, 128.6, 51.1, 14.4; **GC–LRMS**: 238 (100%, M^+).

Methyl 6-(4-methoxyphenyl)-5-(4-methylbenzoyl)nicotinate (5r):



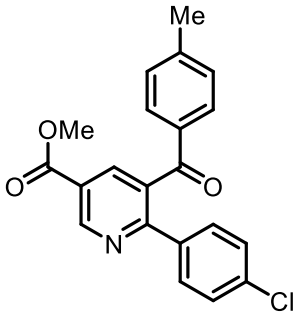
Yield: 75% (27 mg); Physical appearance: Colorless solid; M.p. 90–92 °C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.33 (d, *J* = 2.0 Hz, 1H), 8.33 (d, *J* = 2.0 Hz, 1H), 7.61 – 7.51 (m, 4H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 3.95 (s, 3H), 3.74 (s, 3H), 2.34 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 196.13, 165.30, 160.84, 160.08, 151.3, 144.8, 137.9, 133.7, 133.6, 130.8, 130.1, 129.4, 123.1, 114.0, 55.3, 52.5, 21.7; **IR** (KBr, cm^{-1}): 2953, 1727, 1663, 1592, 1516, 1430, 1395, 1256, 1129, 934; **ESI–HRMS**: Calculated for $C_{22}H_{20}NO_4^+$ $[M+H]^+$ 362.1387, found 362.1366.

Methyl 5-(4-methylbenzoyl)-6-phenylnicotinate (5s):



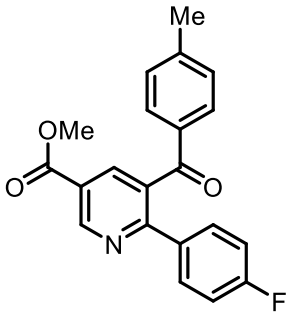
Yield: 66% (22 mg); Physical appearance: Colorless solid; M.p. 91–93 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.42 (s, 1H), 8.42 (s, 1H), 7.63 – 7.57 (m, 4H), 7.33 – 7.29 (m, 3H), 7.16 (d, *J* = 7.9 Hz, 2H), 4.01 (s, 3H), 2.37 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 195.8, 165.2, 160.7, 151.4, 144.8, 138.4, 137.9, 134.3, 133.7, 130.1, 129.6, 129.3, 129.3, 128.5, 123.8, 52.6, 21.7; **IR** (KBr, cm^{-1}): 2924, 1727, 1664, 1430, 1306, 1257, 1128, 934, 756; **ESI–HRMS**: Calculated for $C_{21}H_{18}NO_3^+$ $[M+H]^+$ 332.1281, found 332.1259.

Methyl 6-(4-chlorophenyl)-5-(4-methylbenzoyl)nicotinate (5t):



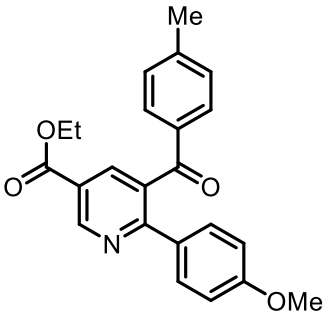
Yield: 63% (23 mg); Physical appearance: Colorless solid; M.p. 123–125 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.36 (d, *J* = 2.0 Hz, 1H), 8.36 (d, *J* = 2.0 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.27- 7.22 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 3.97 (s, 3H), 2.36 (s, 3H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$): δ 195.6, 165.1, 159.3, 151.4, 145.2, 137.9, 136.8, 135.9, 134.2, 133.5, 130.6, 130.1, 129.5, 128.8, 123.9, 52.7, 21.8; **IR** (KBr, cm^{-1}): 2953, 1728, 1593, 1430, 1258, 429, 1011, 839; **ESI–HRMS**: Calculated for $C_{21}H_{17}ClNO_3^+$ $[M+H]^+$ 366.0891, found 366.0872.

Methyl 6-(4-fluorophenyl)-5-(4-methylbenzoyl)nicotinate (5u):



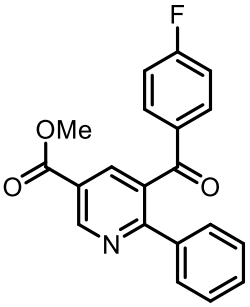
Yield: 61% (21 mg); Physical appearance: Colorless solid; M.p. 99–101 °C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.40 (d, *J* = 2.0 Hz, 1H), 8.41 (d, *J* = 2.0 Hz, 1H), 7.63 – 7.57 (m, 4H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 4.01 (s, 3H), 2.39 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 195.7, 165.1, 163.6 (d, *J* = 250.4 Hz), 159.4, 151.4, 145.1, 138.0, 134.5 (d, *J* = 3.4 Hz), 134.1, 133.6, 131.3 (d, *J* = 8.6 Hz), 130.1, 129.4, 123.8, 115.6 (d, *J* = 21.8 Hz), 52.6, 21.8; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –111.1; **IR** (KBr, cm^{-1}): 2953, 2345, 1728, 1663, 1431, 1305, 1258, 1128, 1001, 844, 616; **ESI–HRMS**: Calculated for $C_{21}H_{17}FNO_3^+$ $[M+H]^+$ 350.1187, found 350.1174.

Ethyl 6-(4-methoxyphenyl)-5-(4-methylbenzoyl)nicotinate (5v):



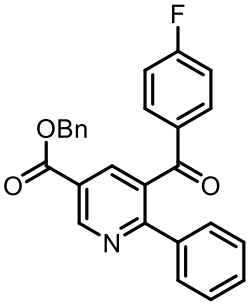
Yield: 74% (28 mg); Physical appearance: Pale-yellow solid; M.p. 74–76 °C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.38 (d, *J* = 2.0 Hz, 1H), 8.37 (d, *J* = 2.0 Hz, 1H), 7.63–7.56 (m, 4H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.46 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.38 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.28, 164.85, 160.82, 159.93, 151.36, 144.78, 137.88, 133.73, 133.61, 130.95, 130.88, 130.09, 129.35, 123.46, 114.00, 61.61, 55.27, 21.74, 14.30; **IR** (KBr, cm^{-1}): 3022, 1723, 1592, 1438, 1254, 1176, 1021, 840; **ESI–HRMS**: Calculated for $C_{23}H_{22}NO_4^+$ $[M+H]^+$ 376.1543, found 376.1537.

Methyl 5-(4-fluorobenzoyl)-6-phenylnicotinate (5w):



Yield: 72% (24 mg); Physical appearance: Pale-yellow solid; M.p. 108–110 °C; TLC R_f 0.2 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.43 (d, *J* = 2.1 Hz, 1H), 8.46 (d, *J* = 2.1 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.60 – 7.55 (m, 2H), 7.33 – 7.28 (m, 3H), 7.04 – 6.96 (m, 2H), 4.02 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 194.7, 165.9 (d, *J* = 226.8 Hz), 165.1, 160.6, 151.7, 138.2, 138.1, 133.7, 132.6 (d, *J* = 2.7 Hz), 132.5 (d, *J* = 9.5 Hz), 129.8, 129.3, 128.6, 124.0, 115.8 (d, *J* = 22.2 Hz), 52.67; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –103.4; **IR** (KBr, cm^{-1}): 3038, 1726, 1663, 1594, 1431, 1225, 1128, 935, 760; **ESI–HRMS**: Calculated for $C_{20}H_{15}FNO_3^+$ $[M+H]^+$ 336.1030, found 336.1010.

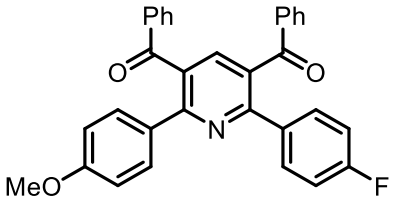
Benzyl 5-(4-fluorobenzoyl)-6-phenylnicotinate (5x):



Yield: 65% (28 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.3 (9:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.47 (d, *J* = 2.1 Hz, 1H), 8.47 (d, *J* = 2.1 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.59 – 7.53 (m, 2H), 7.51 – 7.38 (m, 5H), 7.30 (d, *J* = 1.9 Hz, 3H), 6.98 (t, *J* = 8.6 Hz, 2H), 5.46 (s, 2H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 194.8, 165.9 (d, *J* = 256.5 Hz), 164.5, 160.6, 151.8, 138.2, 138.2, 135.3, 133.7, 132.6 (d, *J* = 2.7 Hz), 132.4 (d, *J* = 9.7 Hz), 129.8, 129.3, 128.7, 128.6, 128.6, 128.5, 124.1, 115.8 (d, *J* = 22.1 Hz), 67.4; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –103.4; **IR** (KBr, cm^{-1}): 2917,

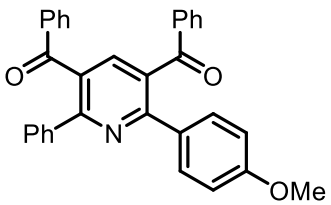
1724, 1595, 1439, 1250, 852, 758; **ESI–HRMS**: Calculated for $C_{26}H_{19}FNO_3^+$ $[M+H]^+$ 412.1343, found 412.1367.

(2-(4-fluorophenyl)-6-(4-methoxyphenyl)pyridine-3,5-diyl)bis(phenylmethanone) (3hk):



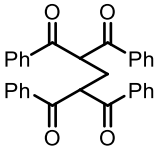
Yield: 18% (13 mg); Physical appearance: Colorless solid; M.p. 141–143 °C; TLC R_f 0.2 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.80 – 7.73 (m, 4H), 7.72 – 7.64 (m, 4H), 7.54 – 7.47 (m, 2H), 7.36 (t, *J* = 7.7 Hz, 4H), 6.99 (t, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H); **^{13}C {^{1}H} NMR** (175 MHz, $CDCl_3$): δ 196.84, 196.67, 163.48 (d, *J* = 250.1 Hz), 162.77, 160.77, 157.52, 156.75, 139.04, 136.34, 136.30,134.86 (d, *J* = 3.2 Hz), 133.68, 133.63, 131.47 (d, *J* = 8.5 Hz), 131.30, 131.05, 130.97, 129.93, 129.90, 128.57, 128.55, 115.48 (d, *J* = 21.7 Hz), 113.95, 55.30; **^{19}F** NMR (376 MHz, $CDCl_3$) δ –111.59; **IR** (KBr, cm^{-1}): 2990, 1608, 1310, 1165, 1020, 739; **ESI–HRMS**: Calculated for $C_{32}H_{23}FNO_3^+$ $[M+H]^+$ 488.1656, found 488.1678.

(2-(4-methoxyphenyl)-6-phenylpyridine-3,5-diyl)bis(phenylmethanone) (3ah):



Yield: 67% (47 mg); Physical appearance: Colorless solid; M.p. 42–44 °C; TLC R_f 0.3 (4:1, Petroleum ether: EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.80 – 7.73 (m, 4H), 7.72 – 7.66 (m, 4H), 7.52 – 7.45 (m, 2H), 7.39 – 7.29 (m, 7H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.78 (s, 3H); **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$): δ 196.94, 196.75, 160.72, 157.96, 157.46, 138.95, 138.71, 136.50, 136.38, 133.56, 133.45, 131.25, 131.12, 131.08, 129.94, 129.91, 129.56, 129.37, 128.52, 128.44, 128.37, 113.91, 55.28; **IR** (KBr, cm^{-1}): 2995, 1601, 1406, 1180, 1030, 845, 720; **ESI–HRMS**: Calculated for $C_{32}H_{24}NO_3^+$ $[M+H]^+$ 470.1751, found 470.1729.

Preparation of 2,4-dibenzoyl-1,5-diphenylpentane-1,5-dione (6):



Despite all efforts to prepare compound **7** (i.e., dibenzoyl ethylene), we were not able to synthesize it and each time we ended up with compound **6**.[22,23] Therefore, we used compound **6** as a precursor of dibenzoyl ethylene (**7**).

Procedure:1,3-diphenylpropane-1,3-dione (493 mg, 2.2 mmol), AcOH (0.4 mL, 6.6 mmol) and 5 mL of DMSO were weighed in air and placed in a 10 mL Schlenk tube with magnetic stirring. The mixture was stirred at 120 ^{o}C (oil bath) under air atmosphere. After completing reaction, the mixture was diluted with dichlormethane (10 mL) and washed with water (3 × 10 mL). The organic phase was dried over anhydrous Na_2SO_4 and filtered. The solvents were evaporated, and the residue was purified by silica gel column chromatography with EA/petroleum ether (1:50) as the eluent to give the desired compound (420 mg) in 83% yield. Spectral data obtained were in good agreement with those reported in the literature.[24]

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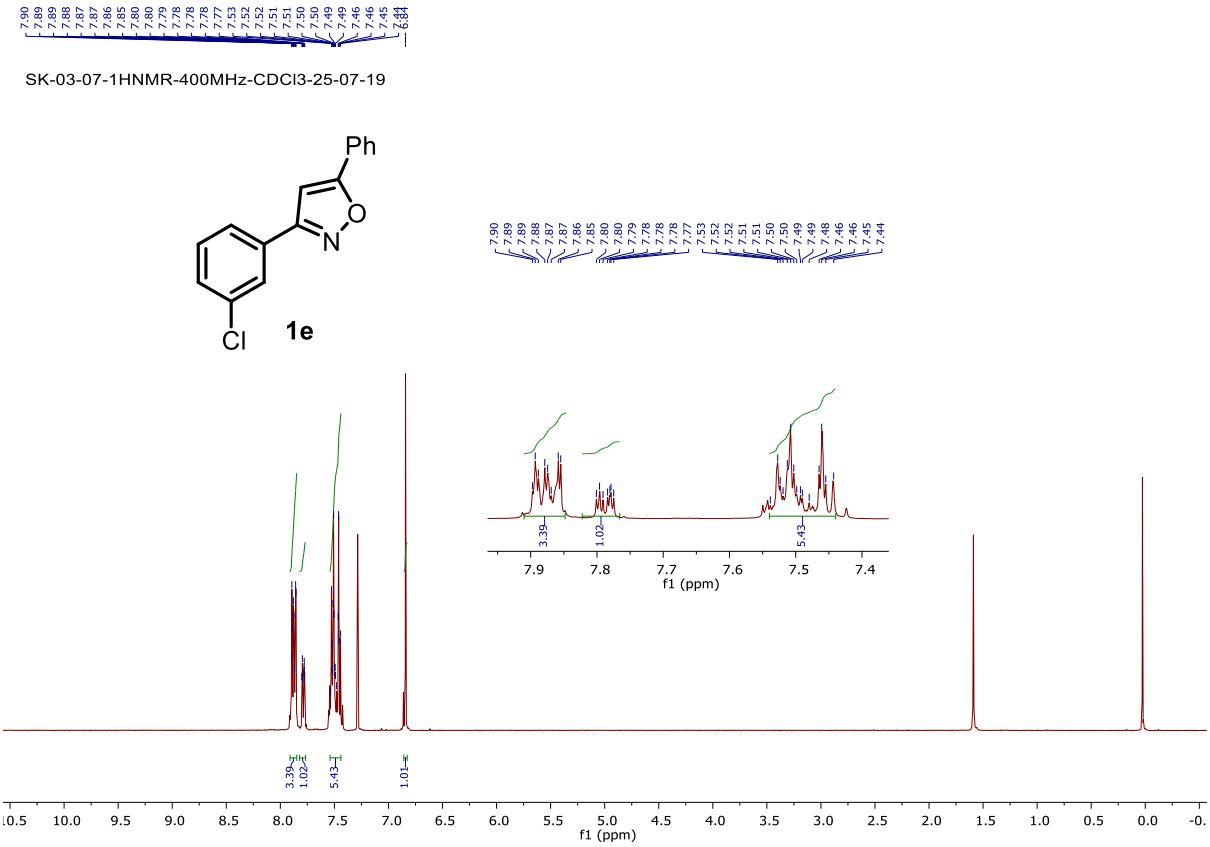
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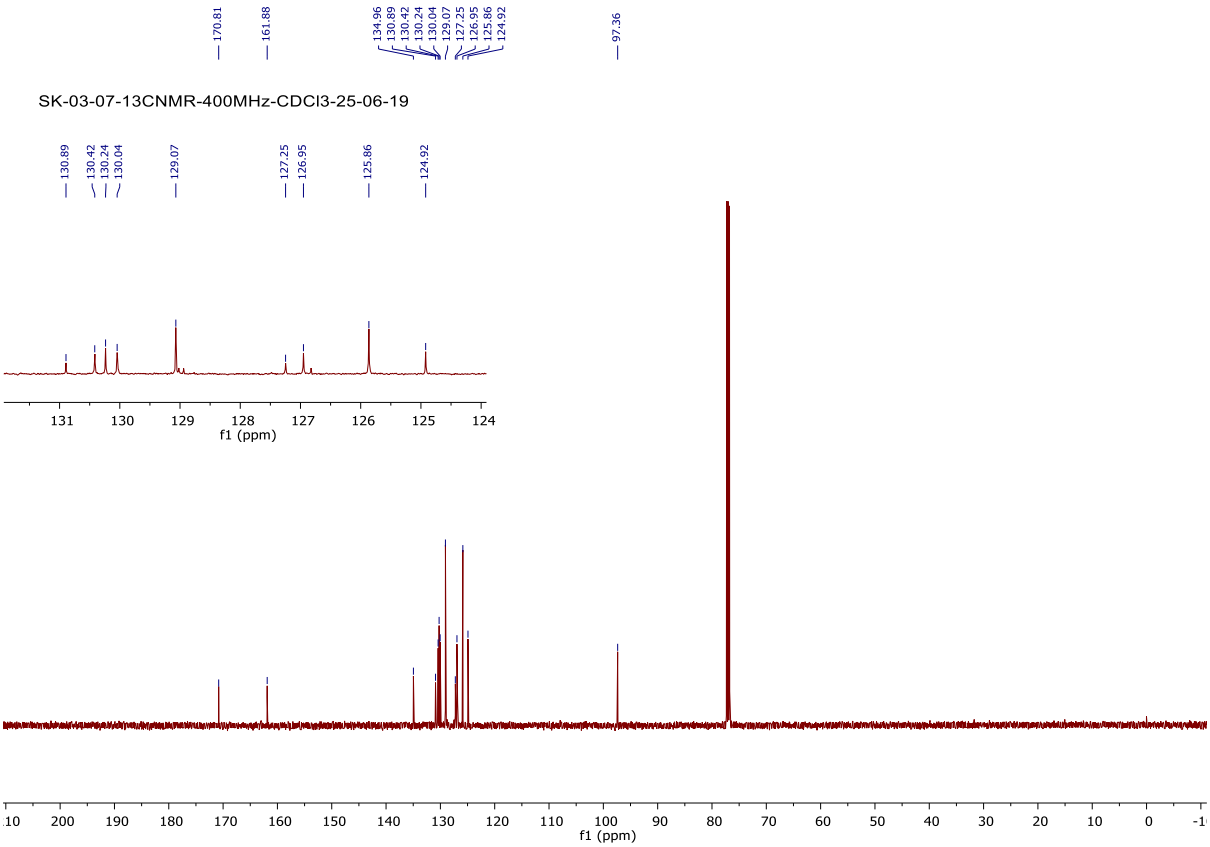
Ph
O
N
Cl
1e
f1 (ppm)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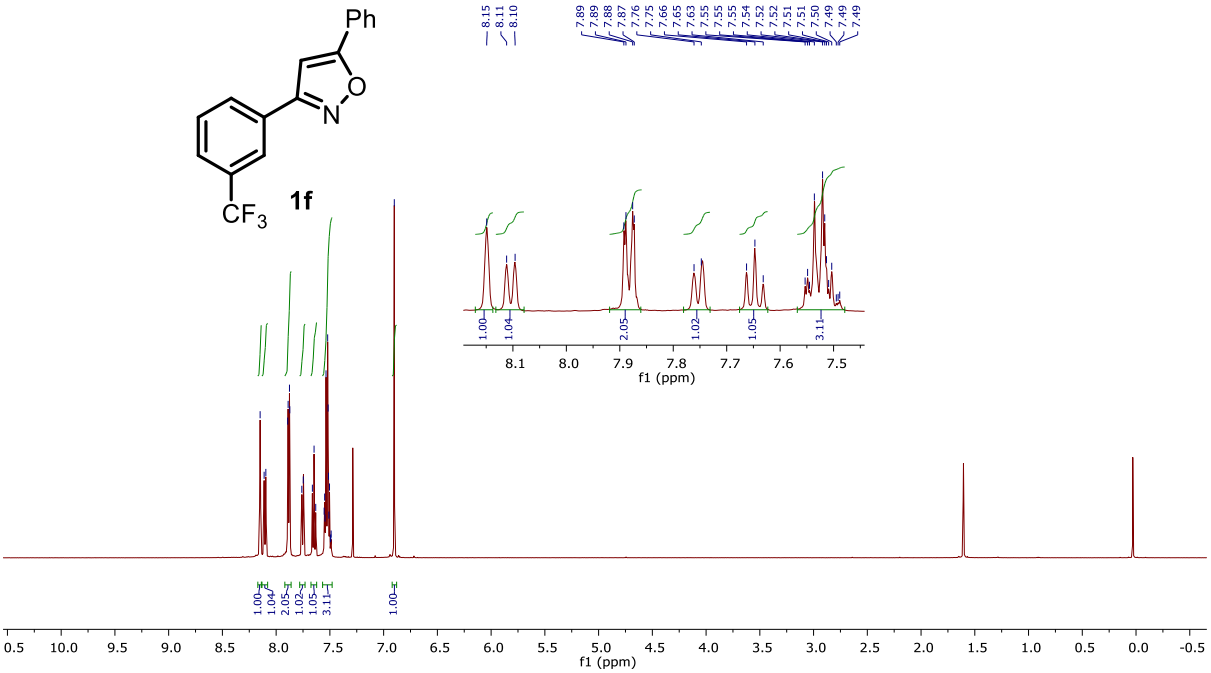
f1 (ppm)

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



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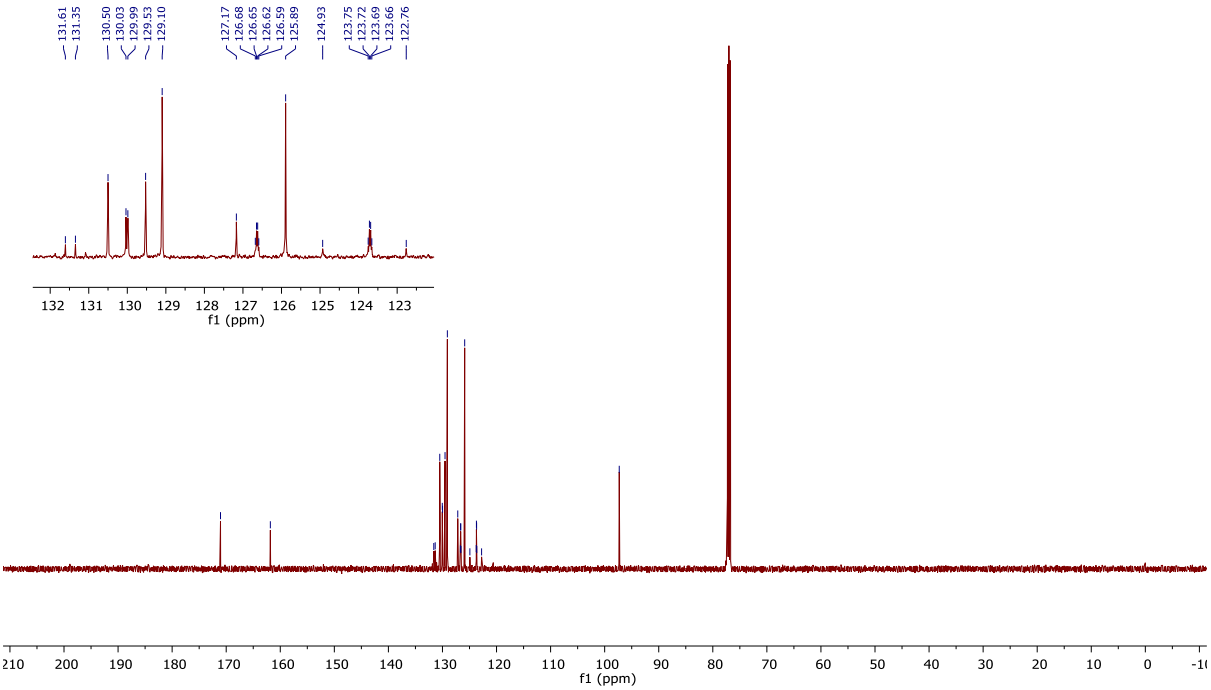

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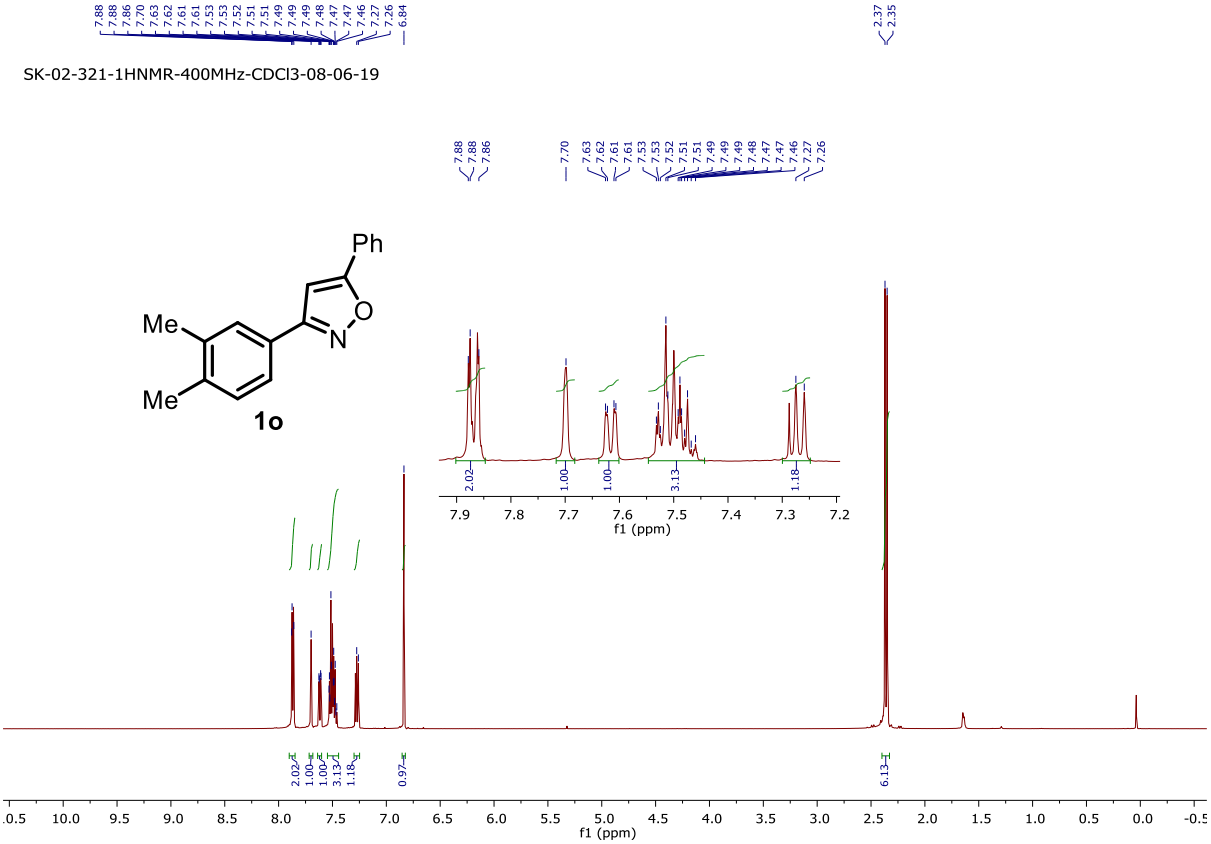

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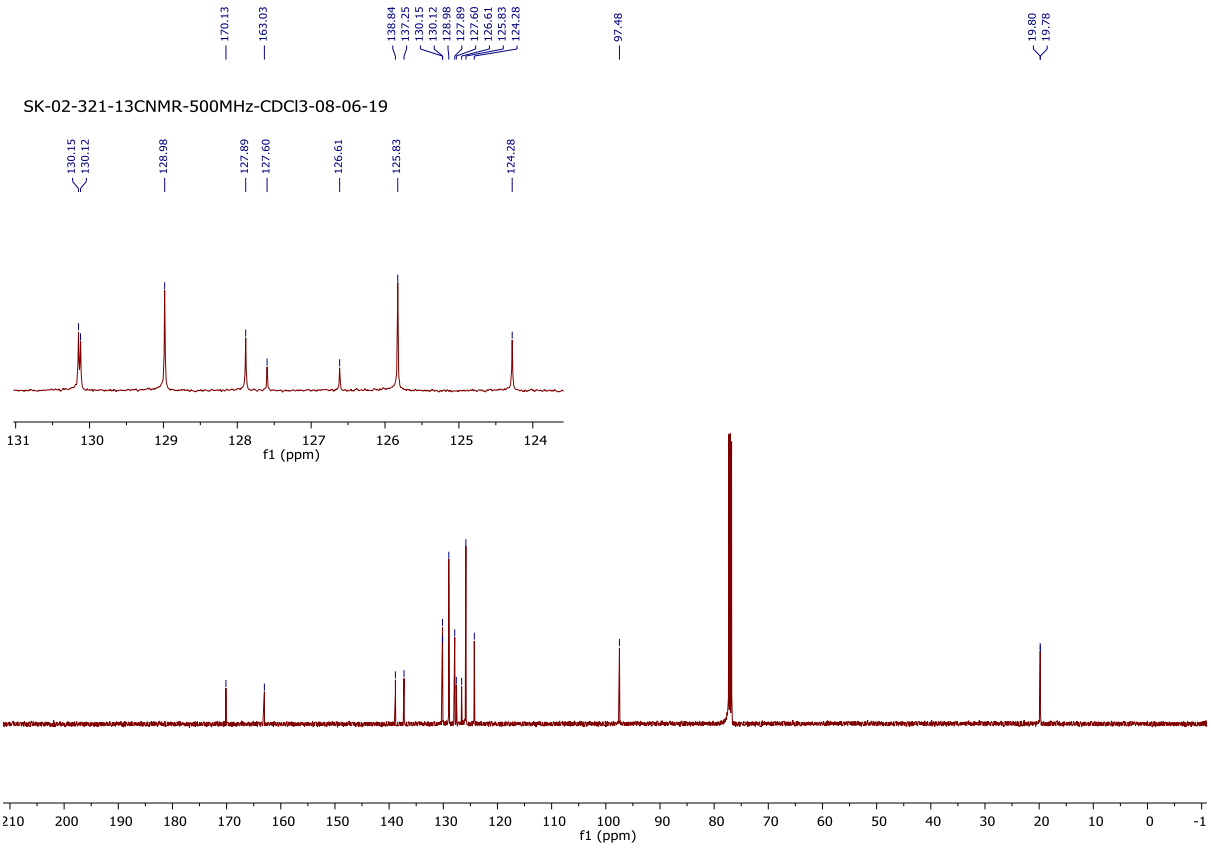

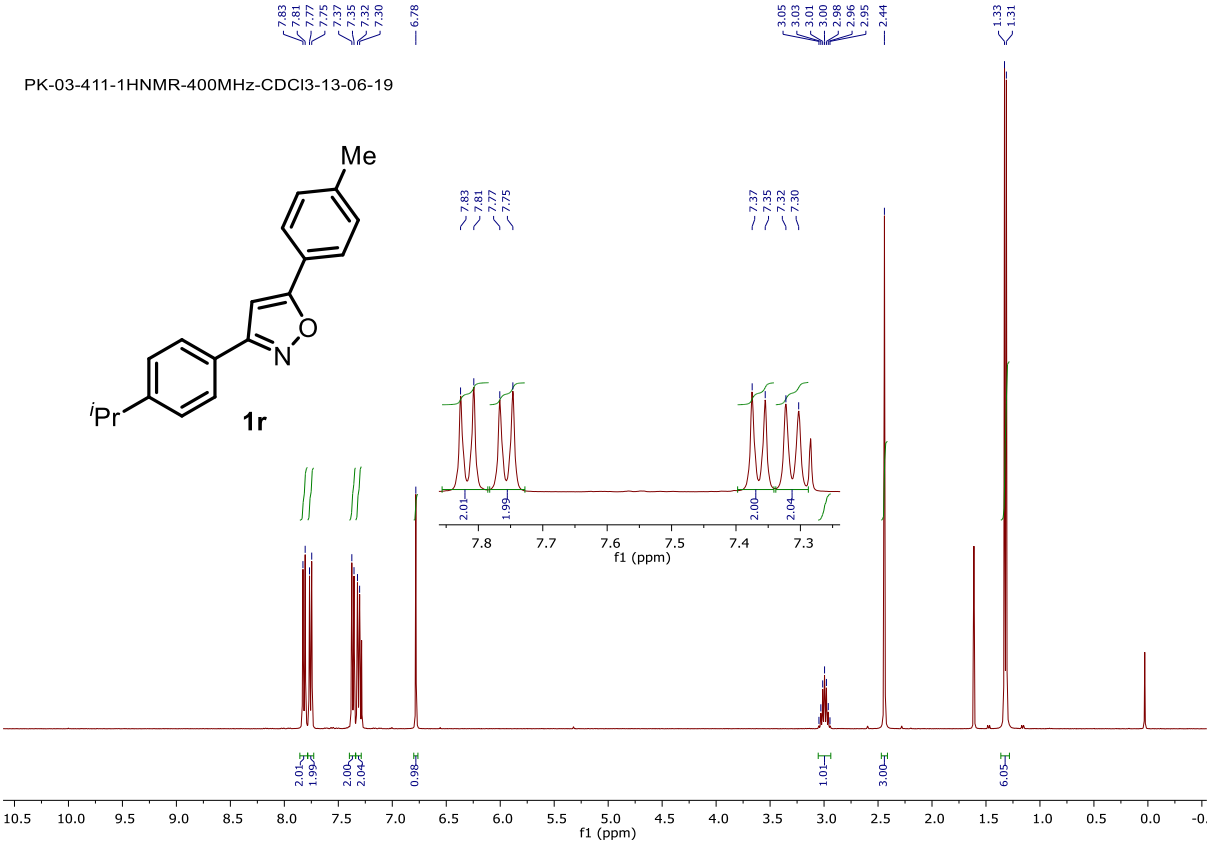
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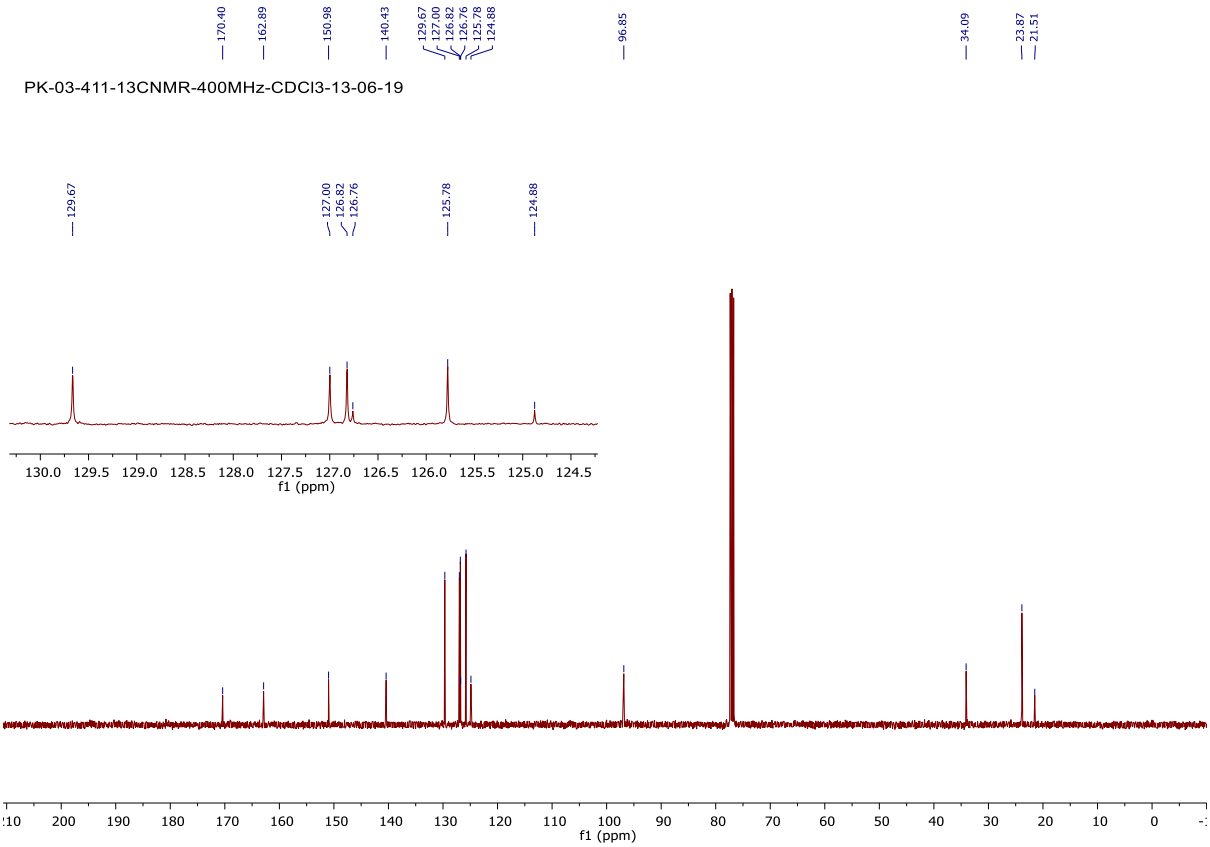
Me
^{i}Pr
1r
f1 (ppm)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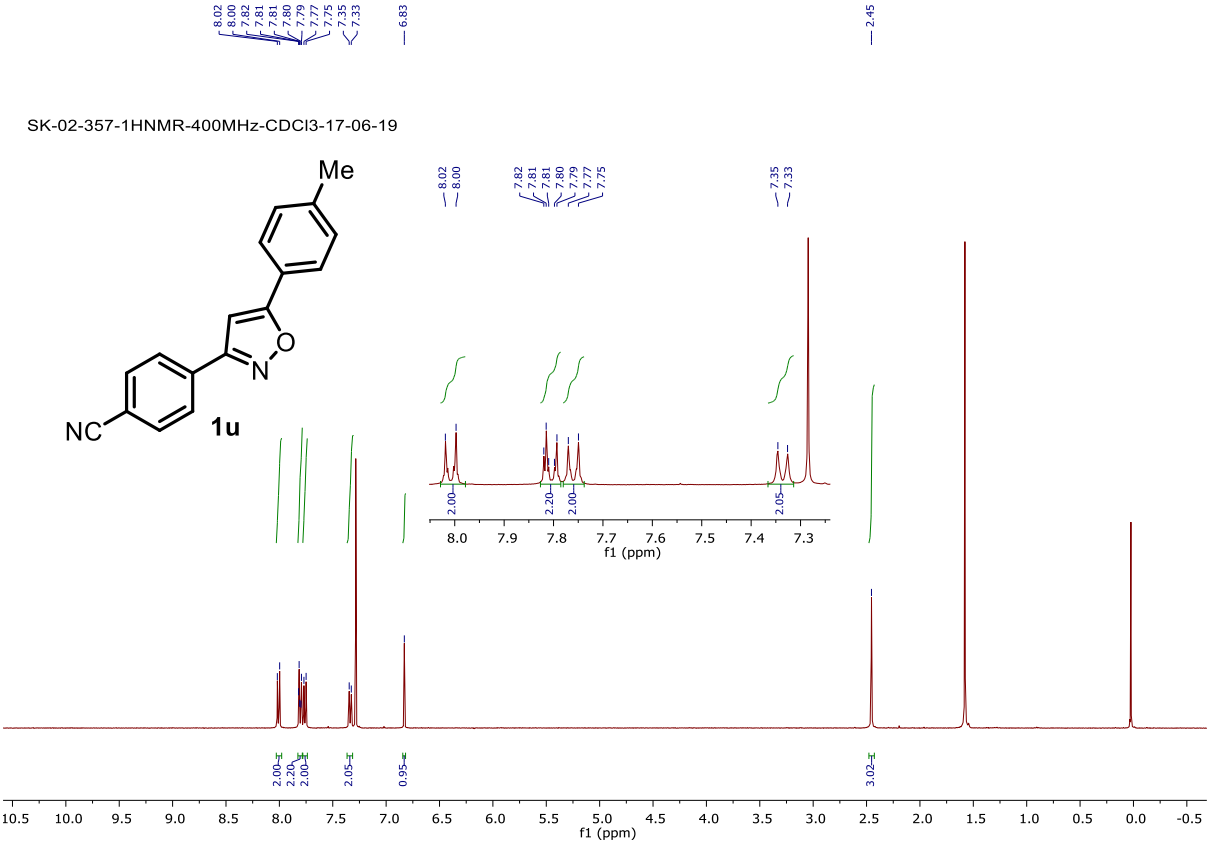
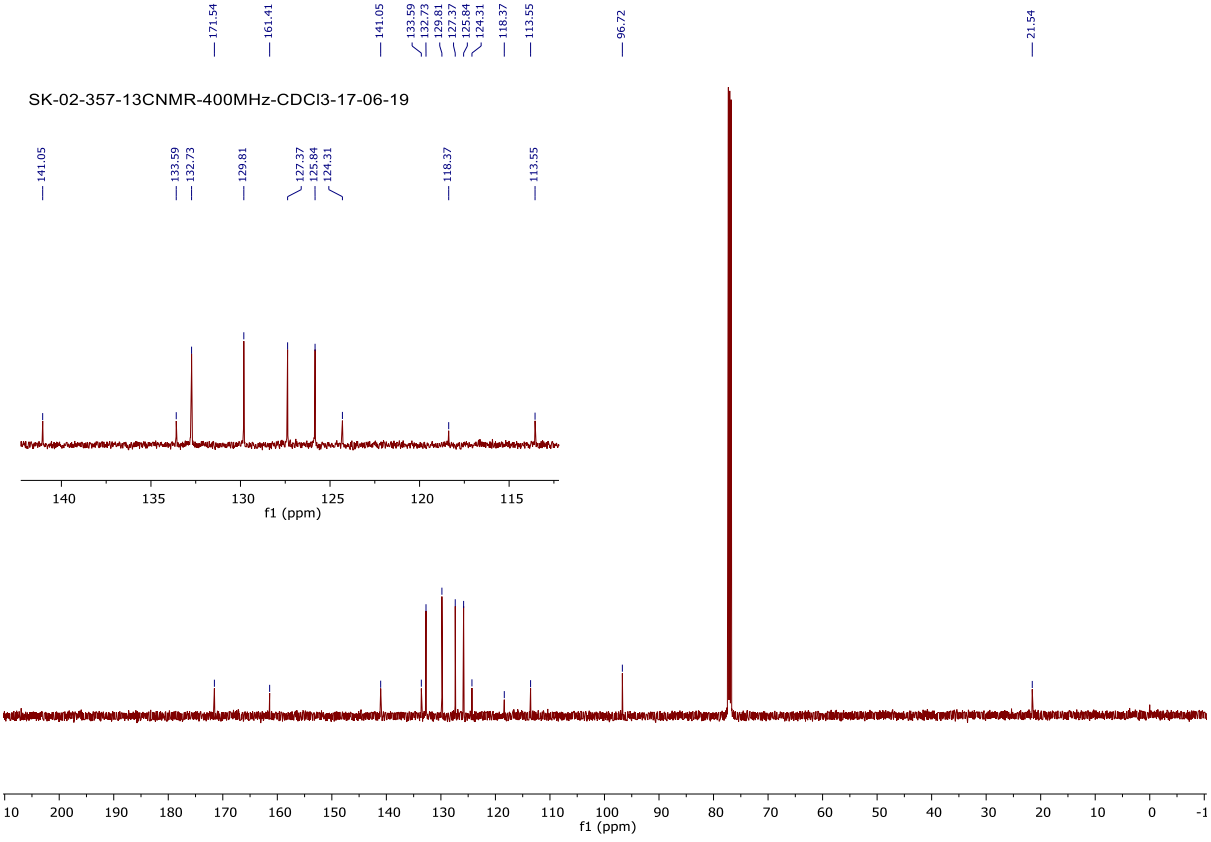
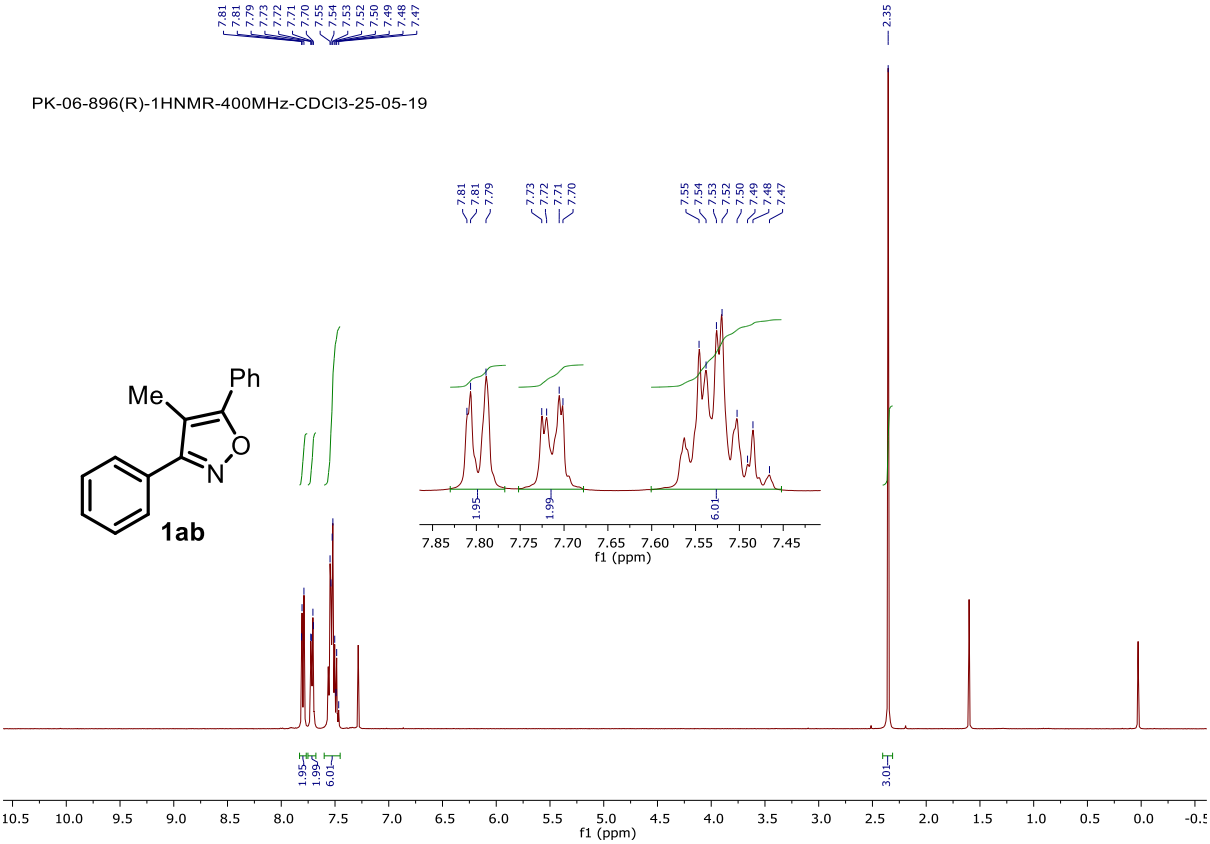
f1 (ppm)


8.02
8.00
7.82
7.81
7.81
7.80
7.79
7.77
7.75
7.35
7.33
6.83
2.45
SK-02-357-1HNMR-400MHz-CDCl3-17-06-19
Me
NC
1u
f1 (ppm)


171.54
161.41
141.05
133.59
132.73
129.81
127.37
125.84
124.31
118.37
113.55
96.72
21.54
SK-02-357-13CNMR-400MHz-CDCl3-17-06-19
f1 (ppm)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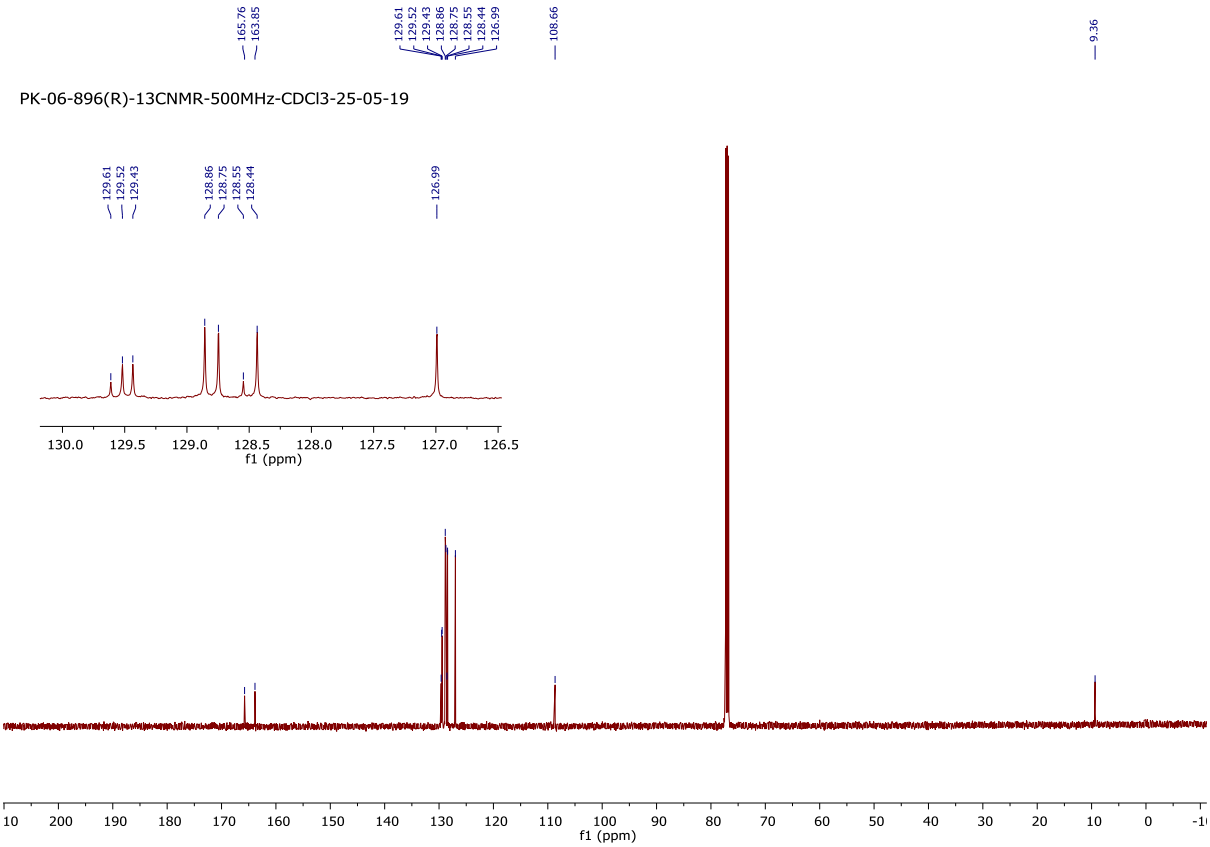
Me
Ph
O
N
1ab
f1 (ppm)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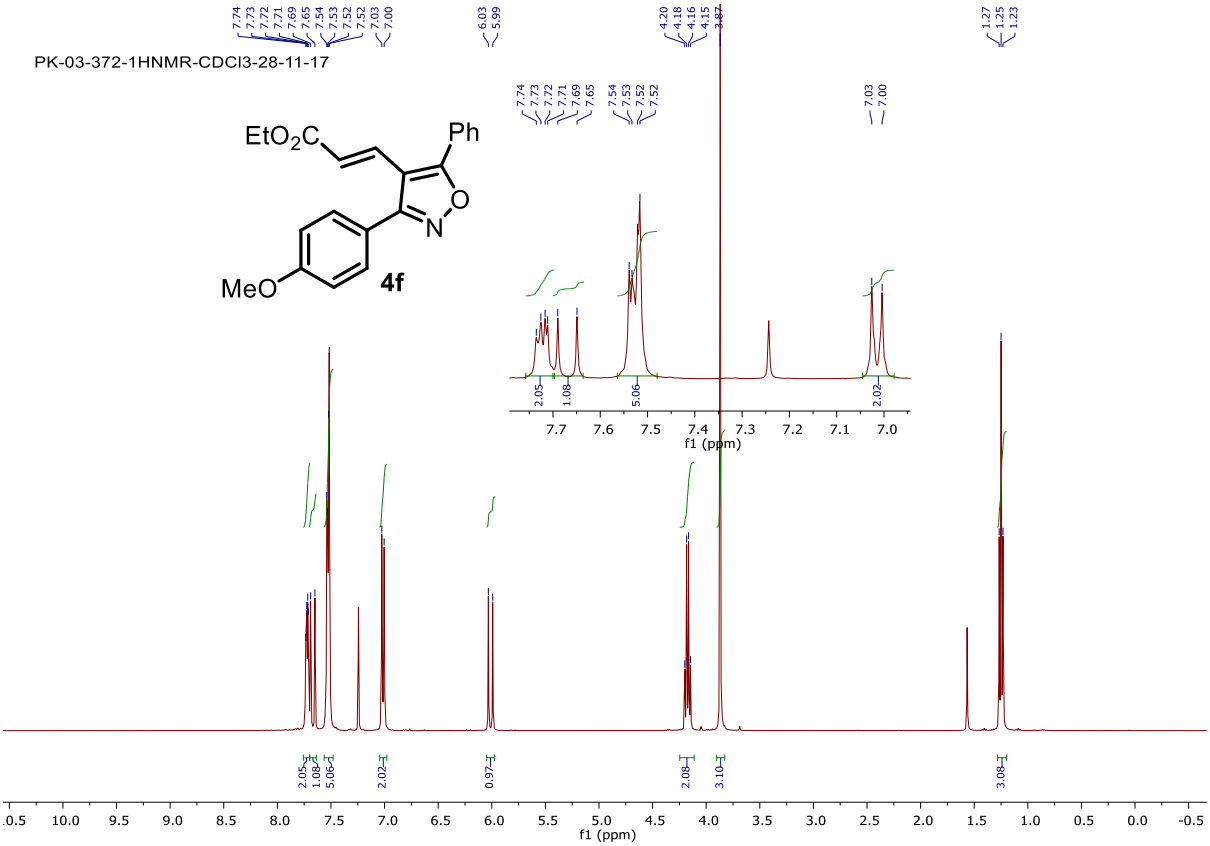
f1 (ppm)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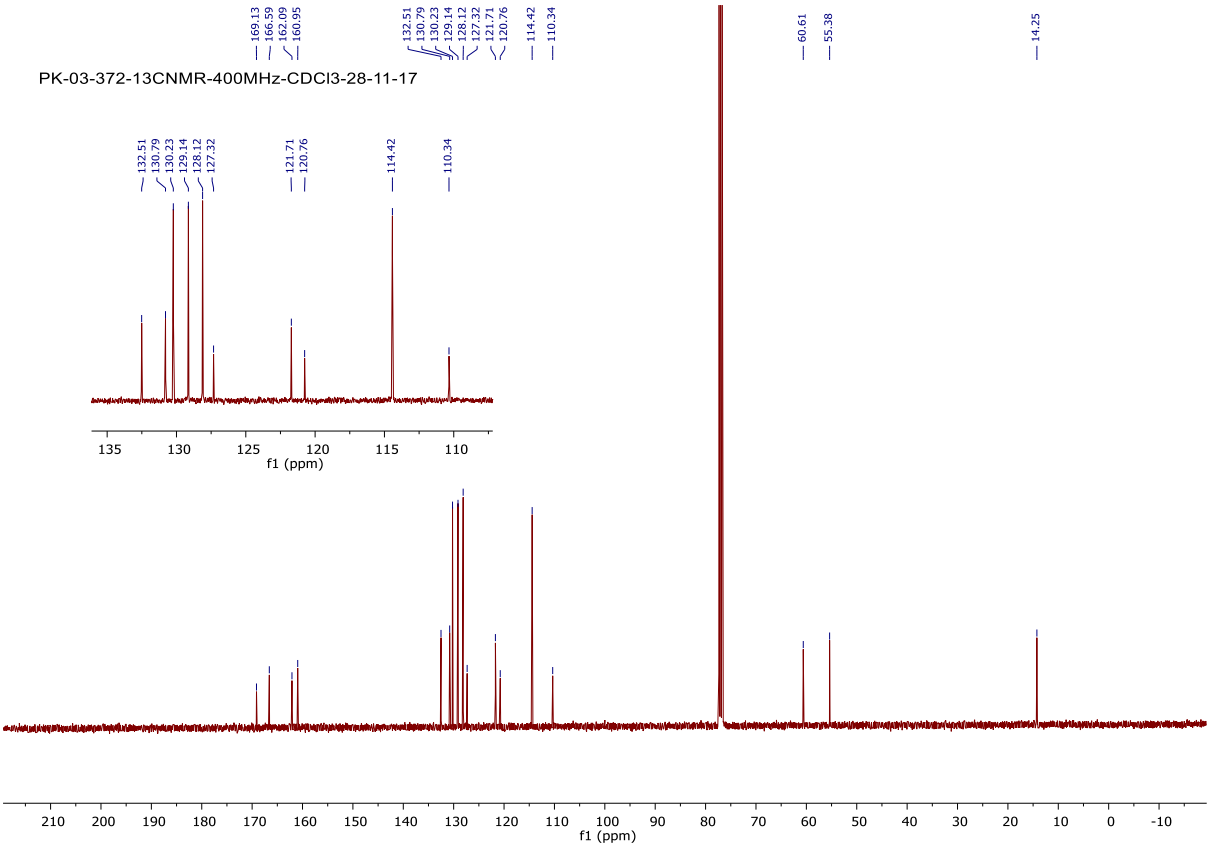
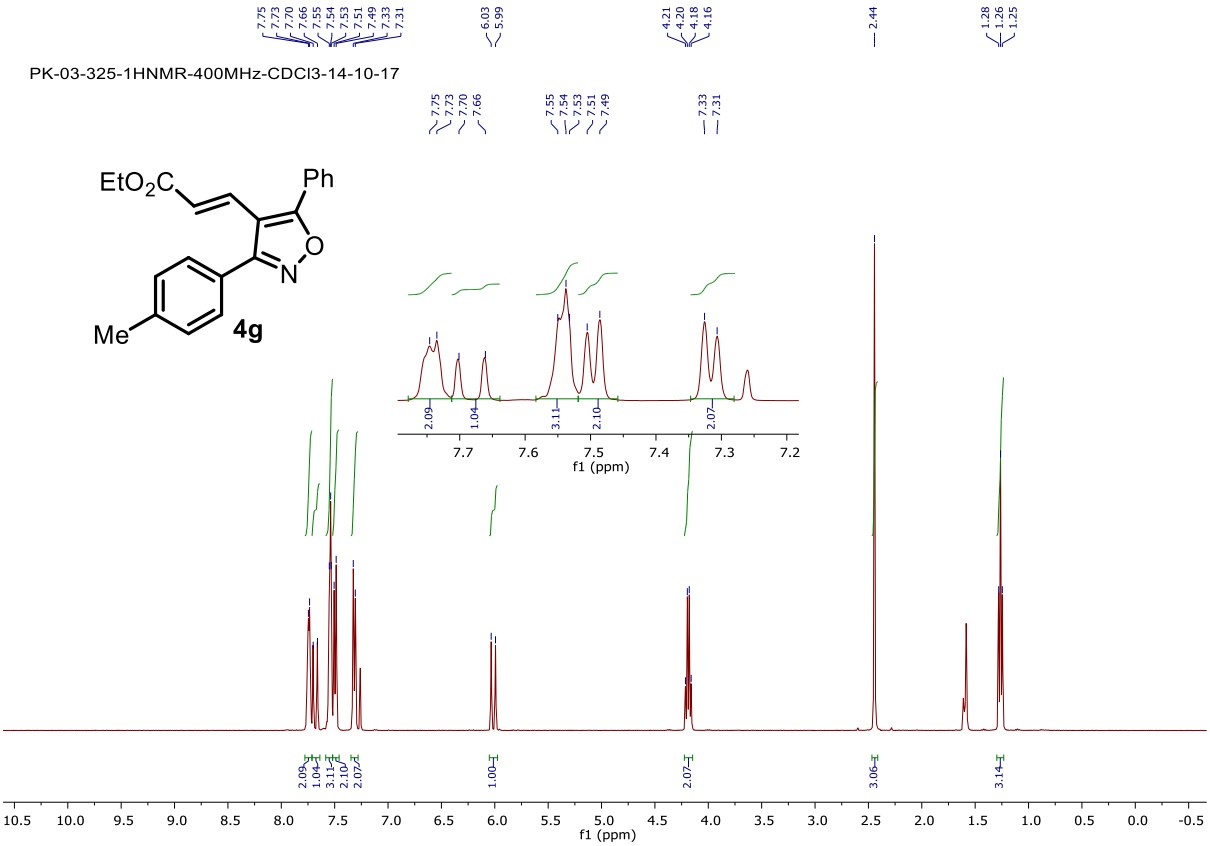
EtO2C
Ph
O
N
MeO
4f
f1 (ppm)


PK-03-372-13CNMR-400MHz-CDCl3-28-11-17
f1 (ppm)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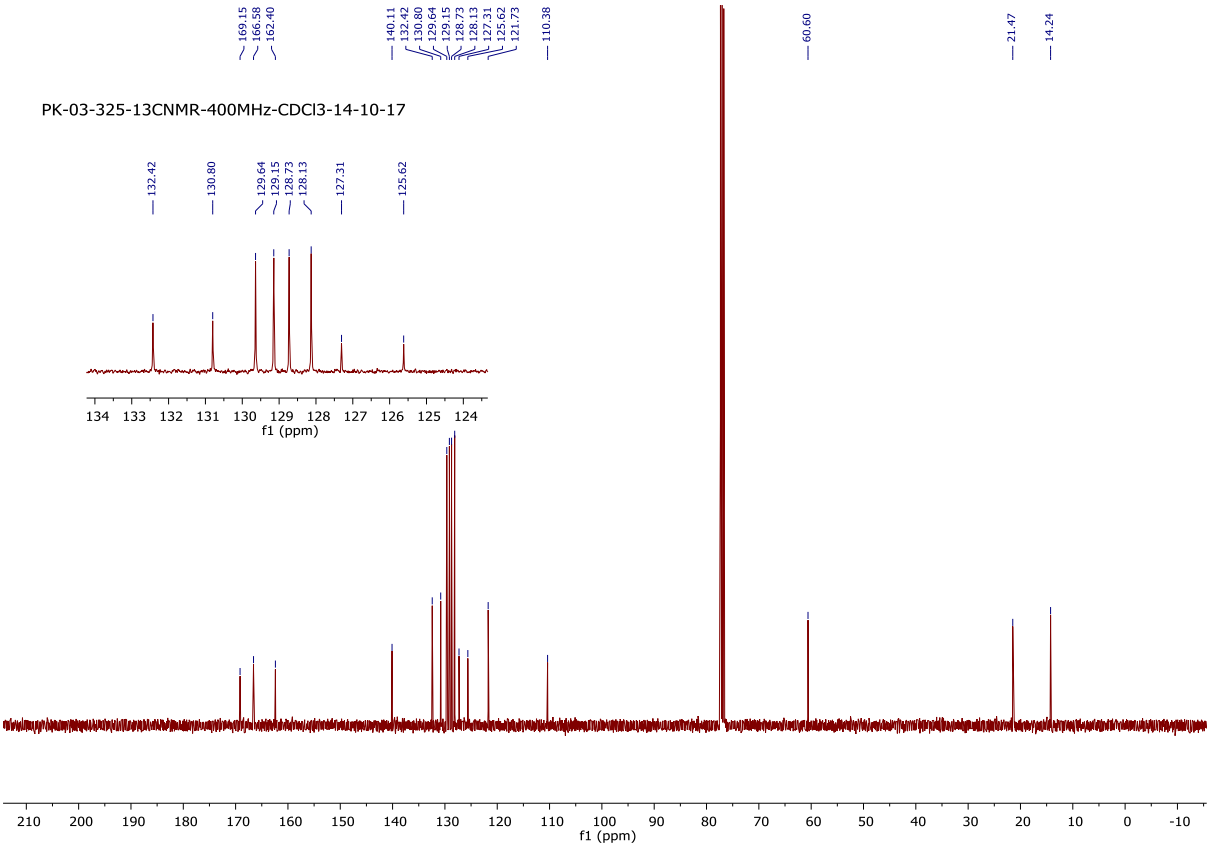
EtO2C
Ph
O
N
Me
4g
f1 (ppm)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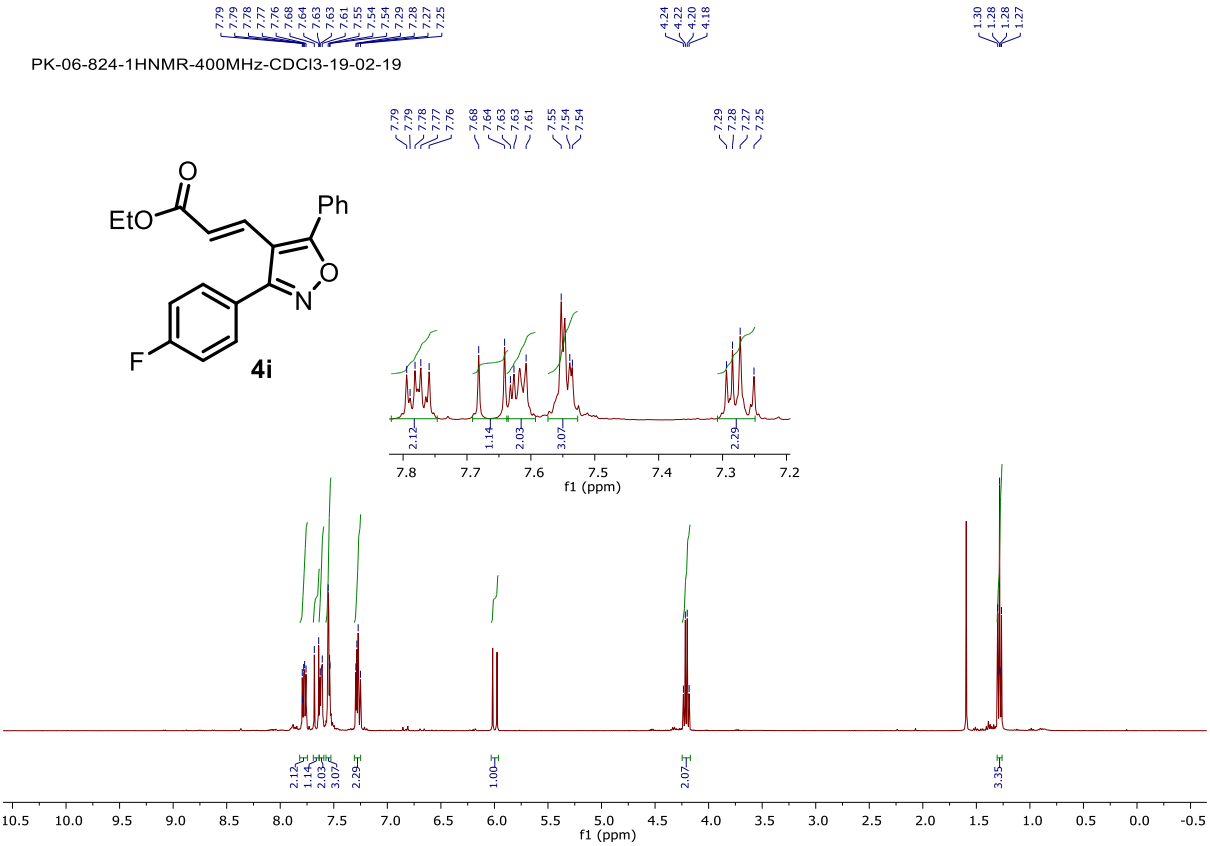
f1 (ppm)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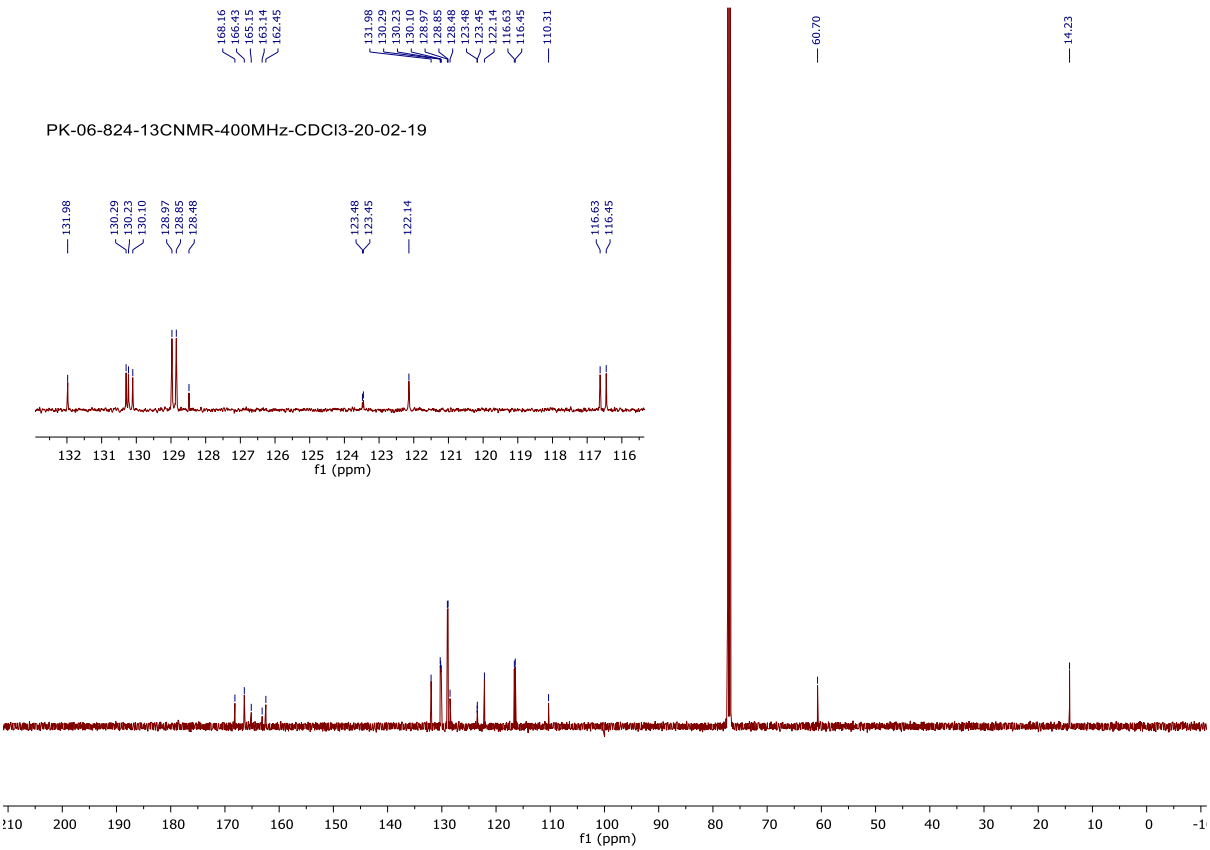
EtO
O
Ph
O
N
F
4i
f1 (ppm)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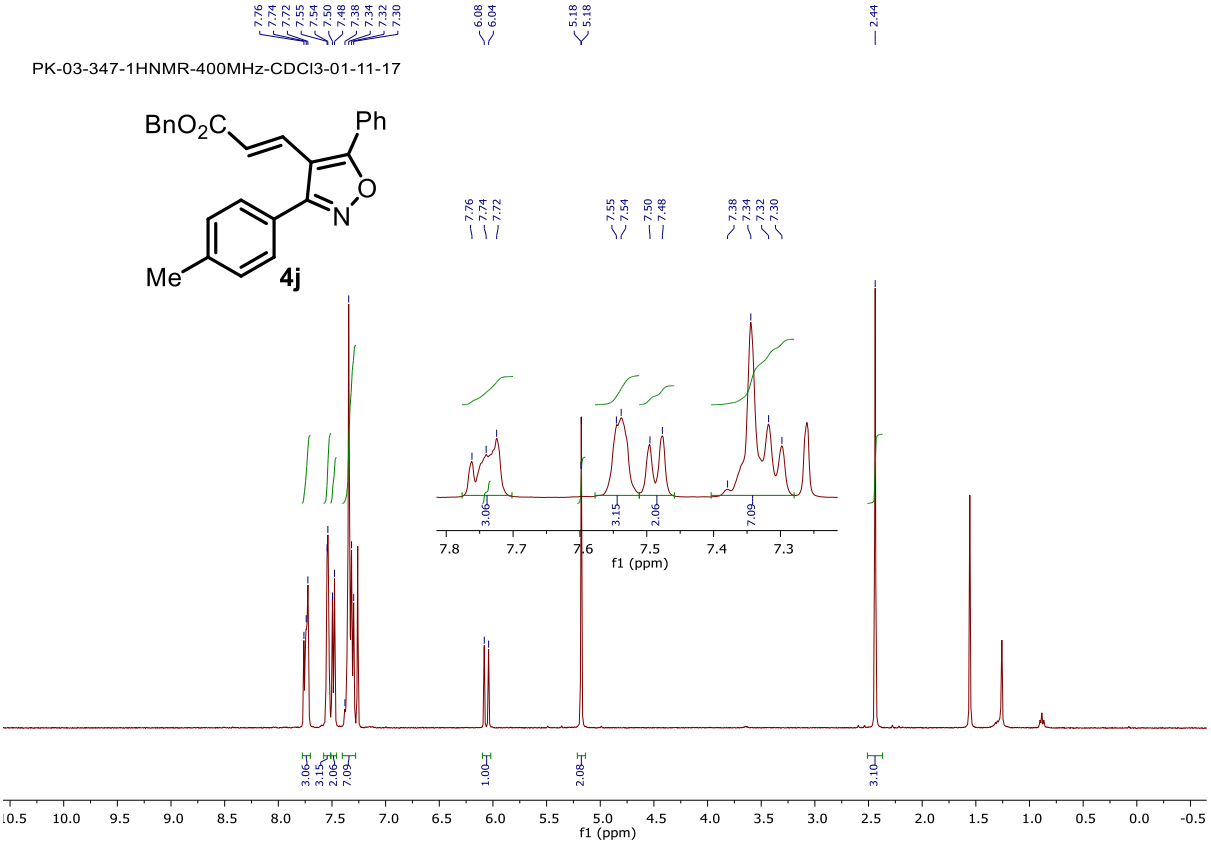
f1 (ppm)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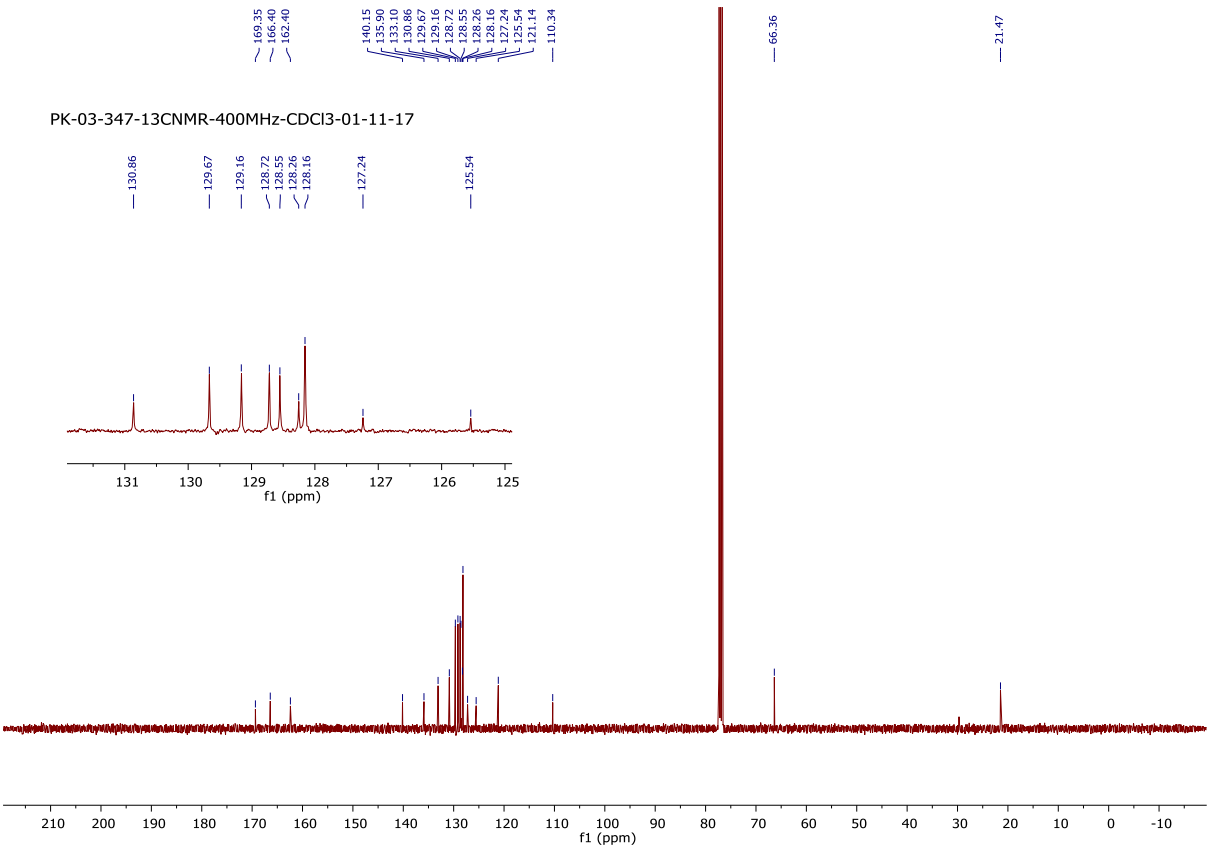
BnO2C
Ph
N
O
Me
4j
f1 (ppm)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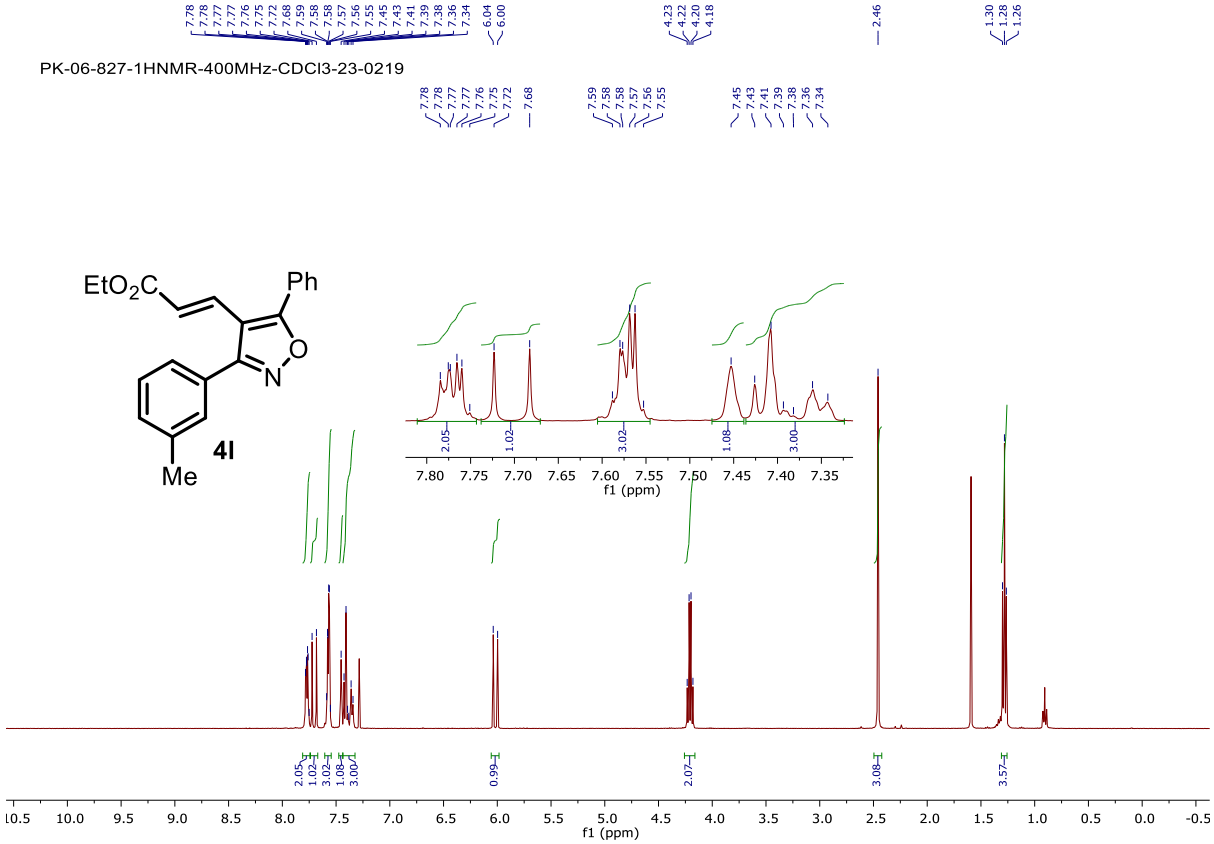
f1 (ppm)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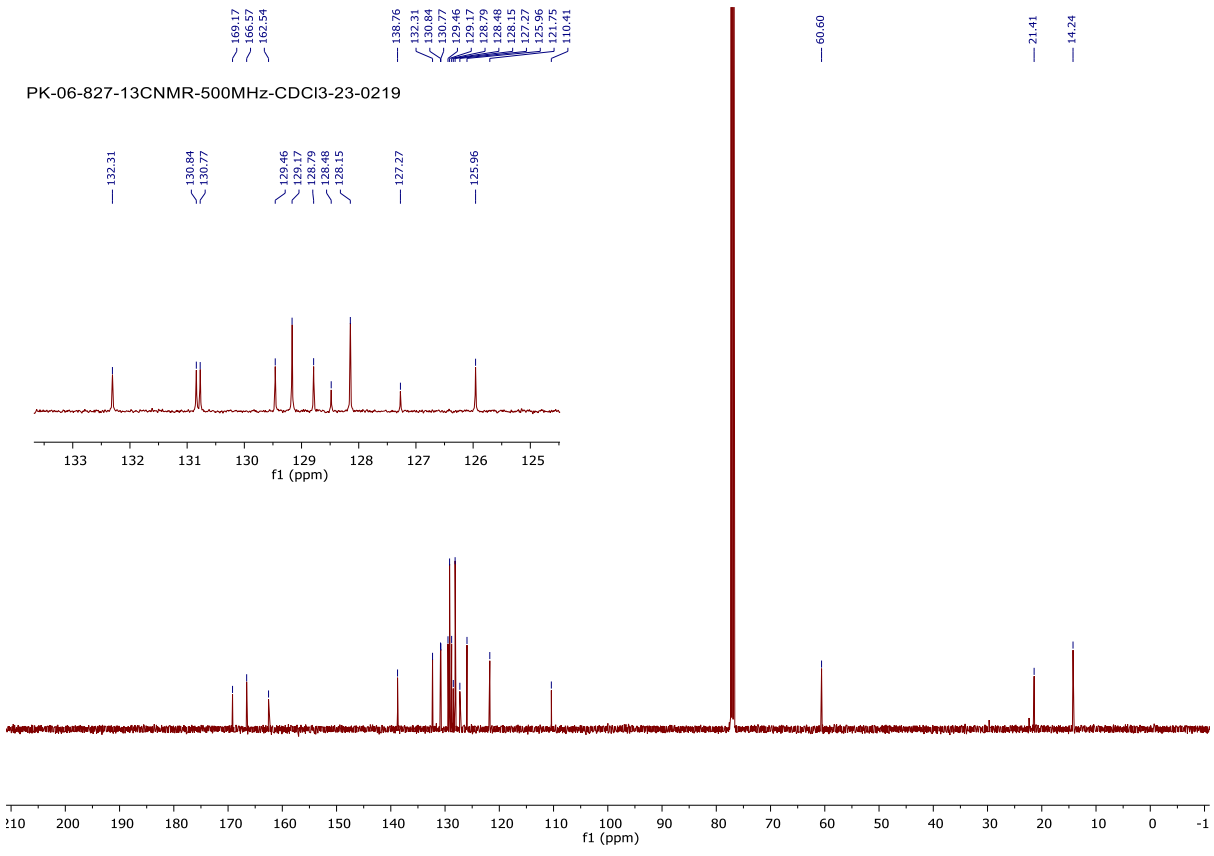
EtO2C
Ph
O
N
Me
4l
f1 (ppm)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f1 (ppm)

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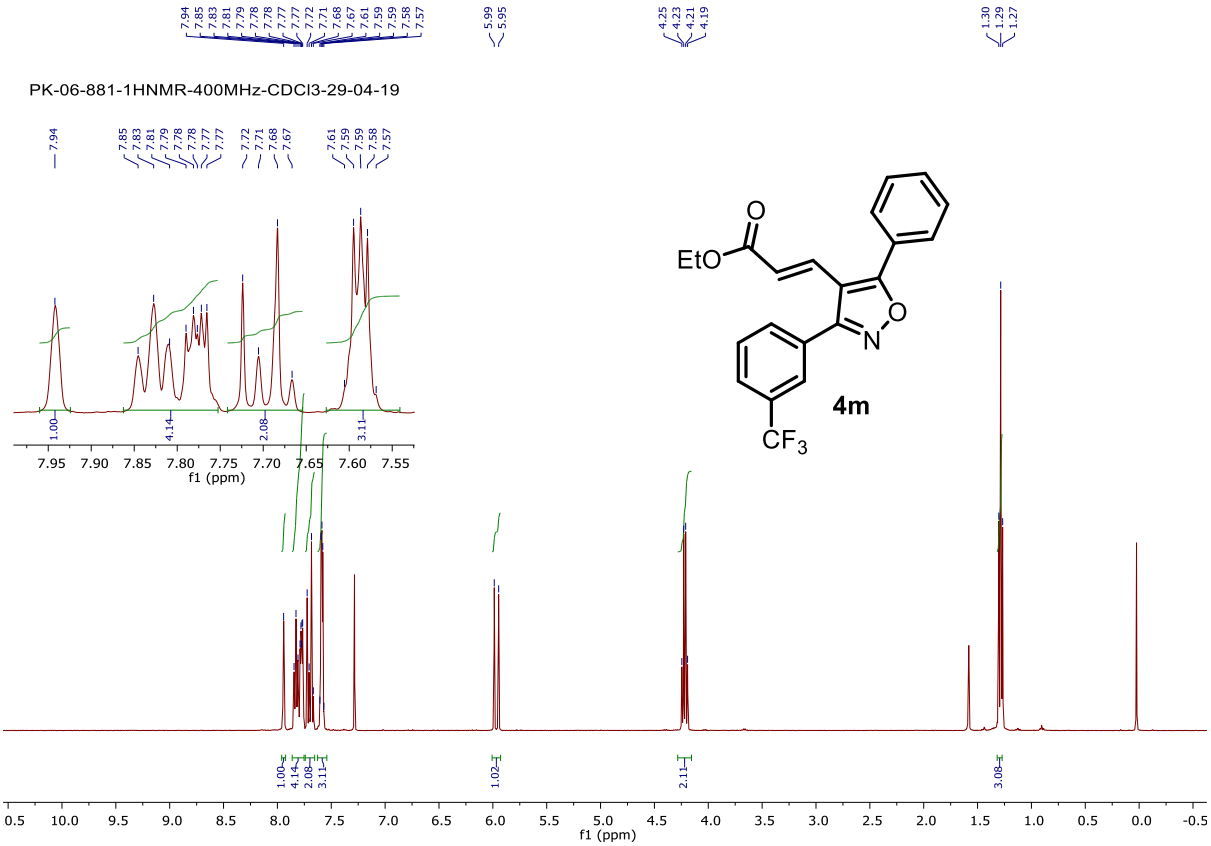
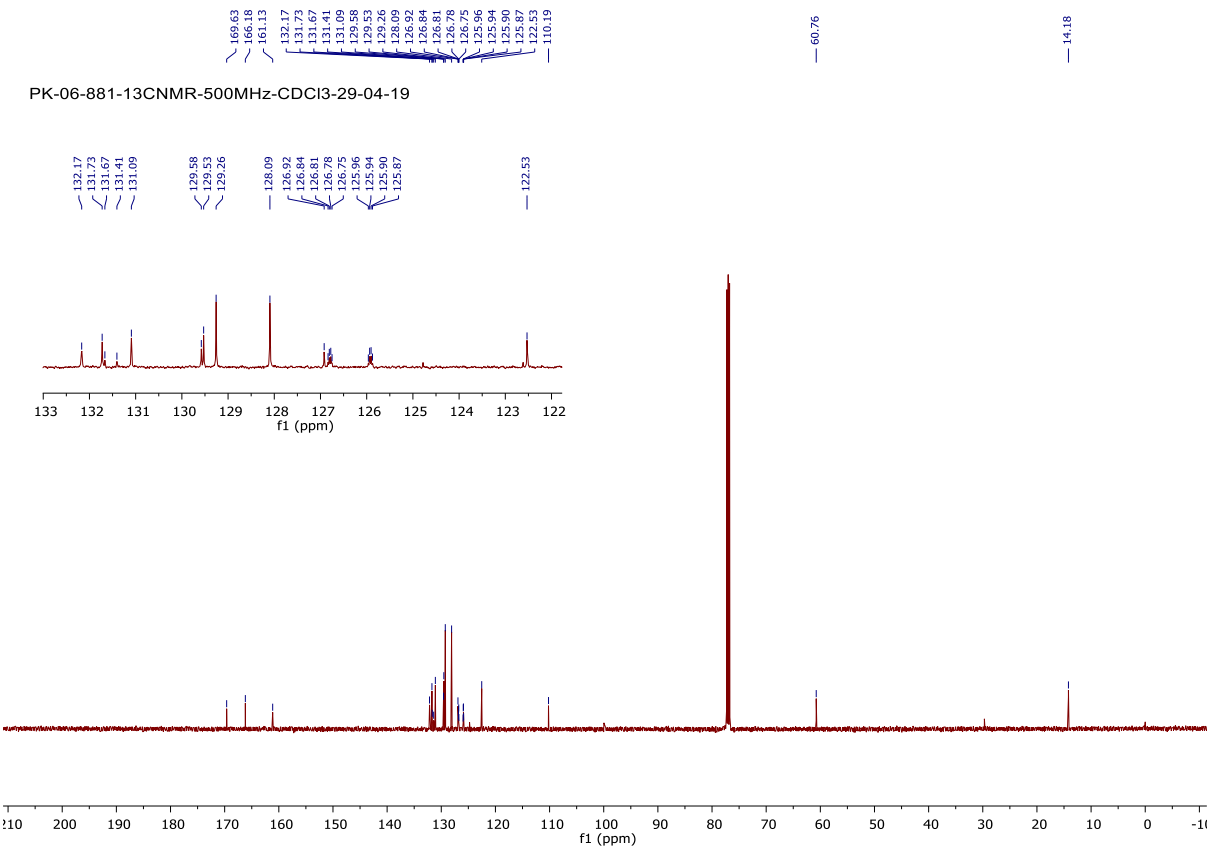


4m

PK-06-881-13CNMR-500MHz-CDCl3-29-04-19



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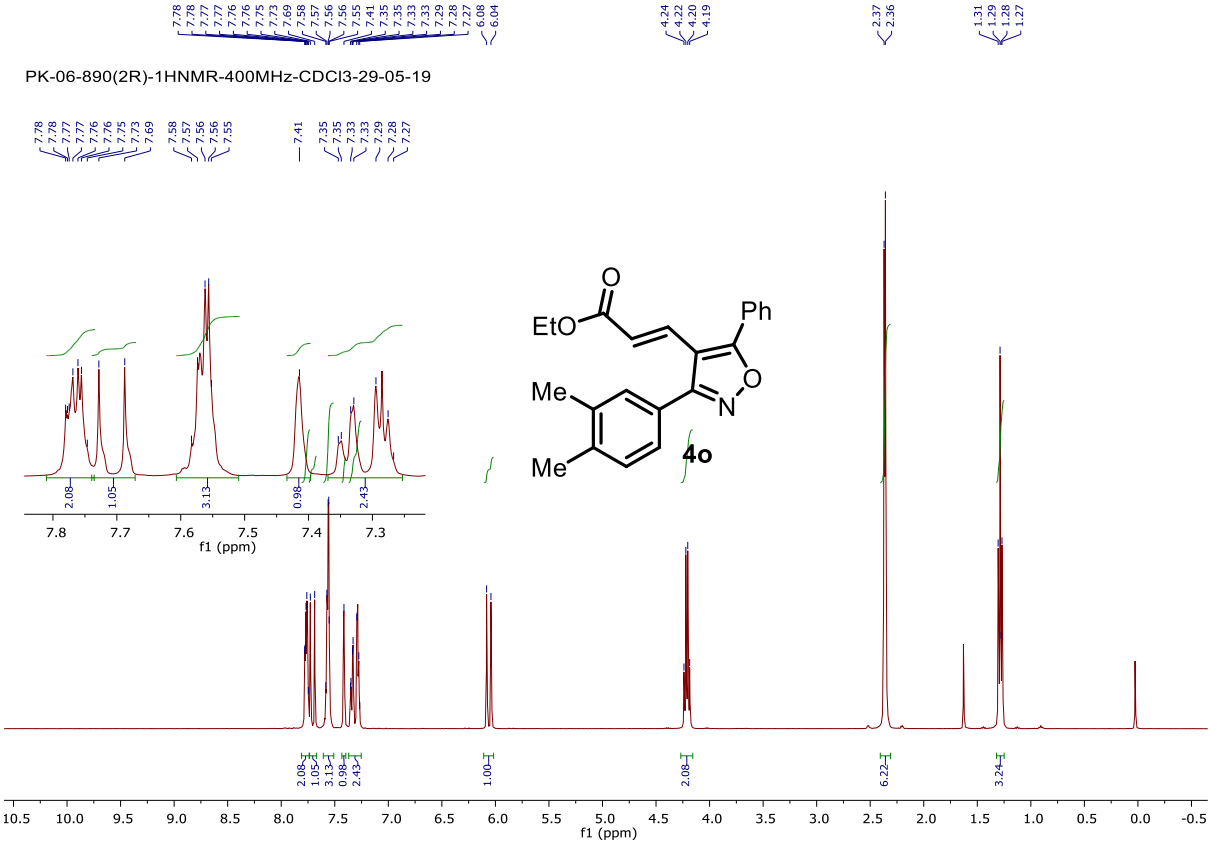

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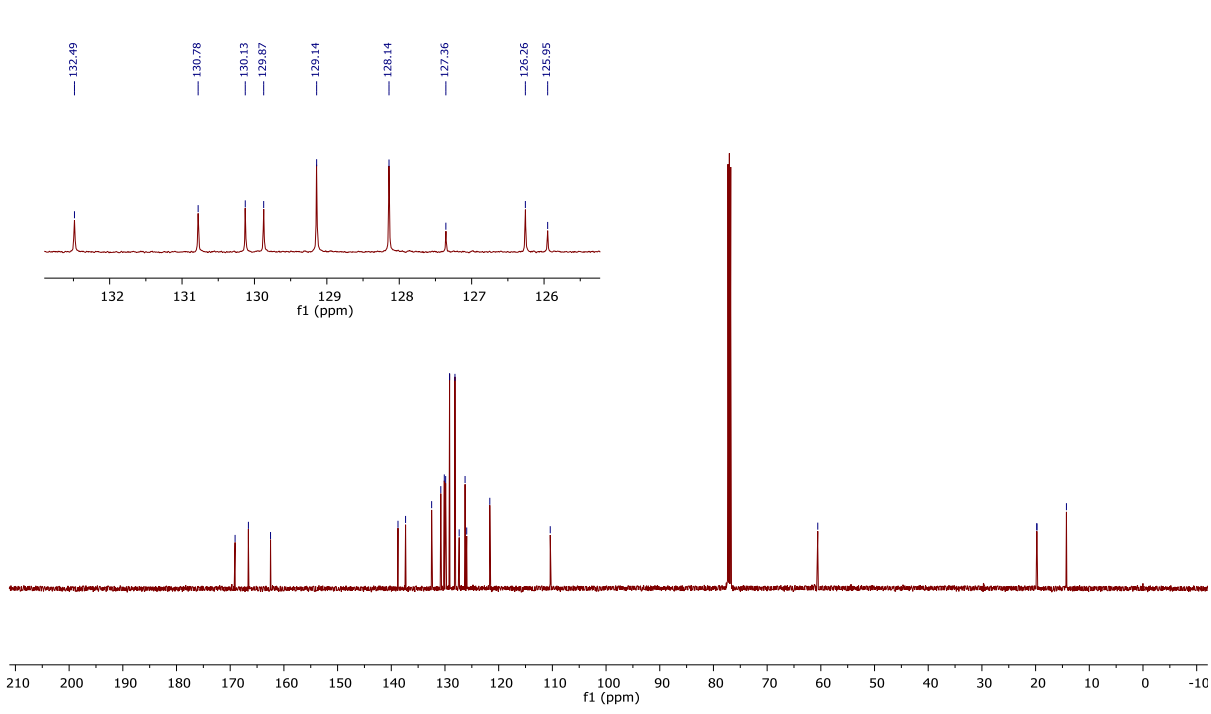
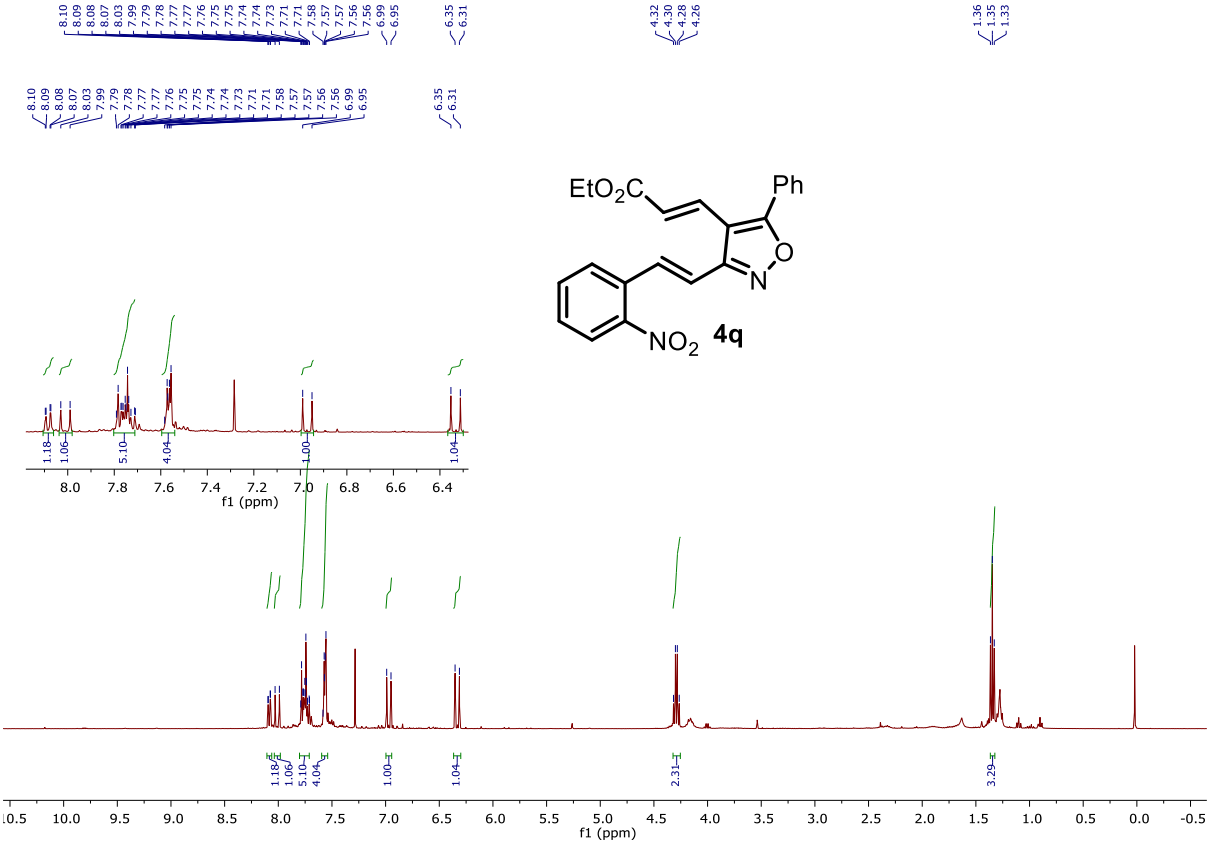
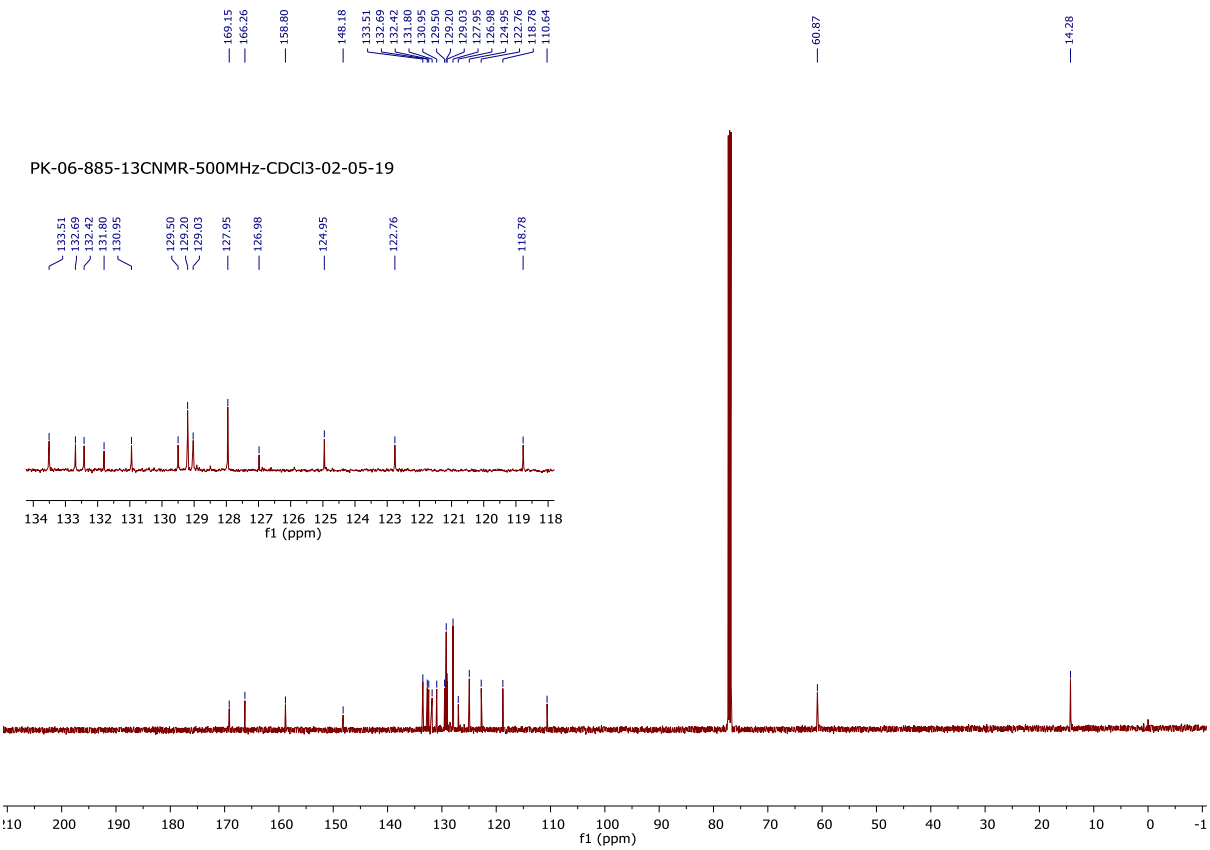



EtO2C
Ph
O
N
NO2
4q
f1 (ppm)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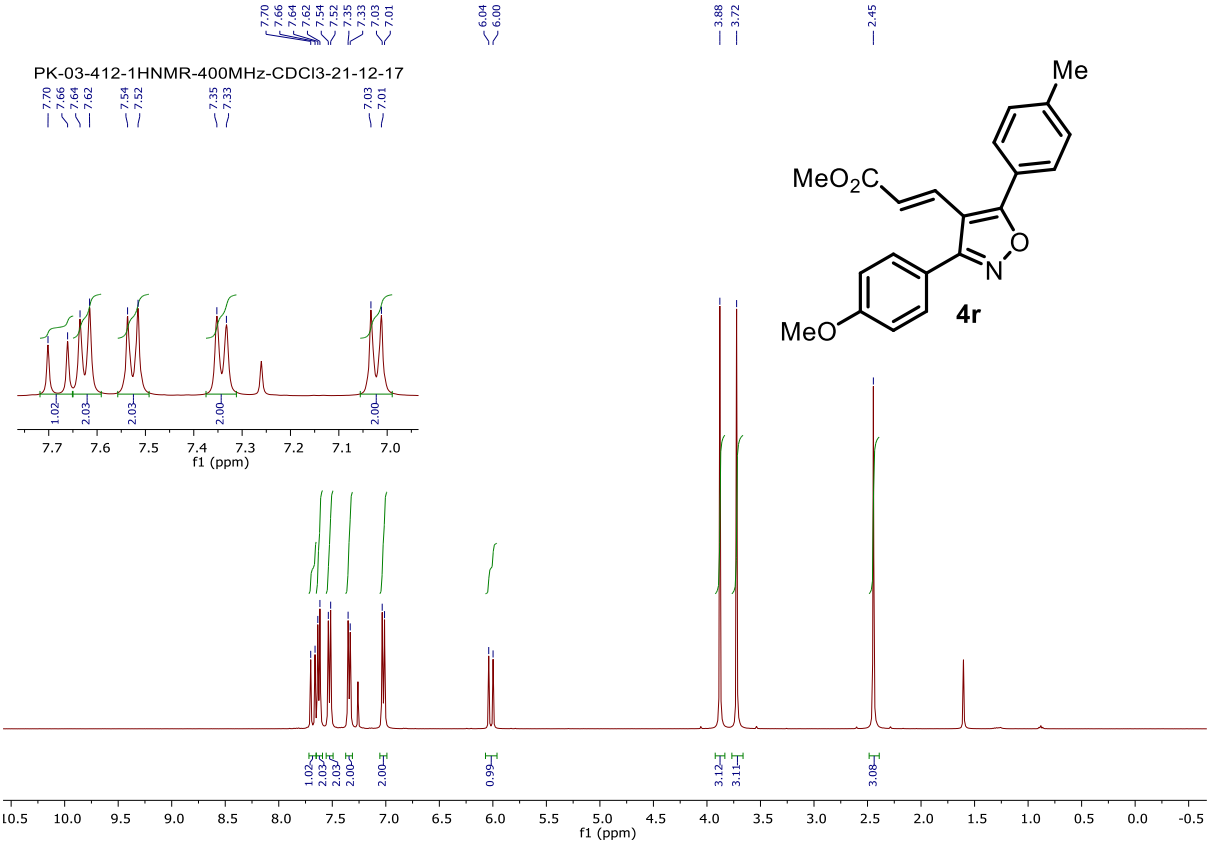
f1 (ppm)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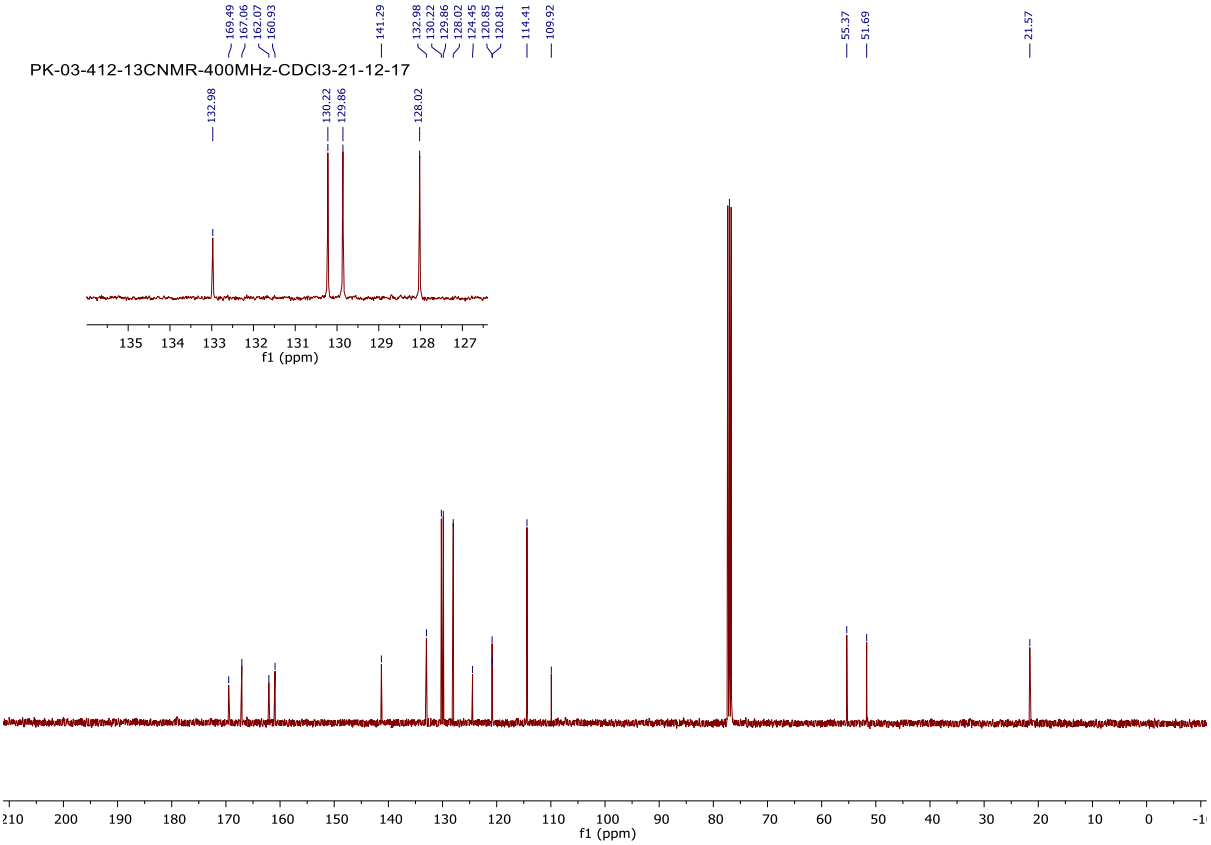
O
N
MeO
4r
f1 (ppm)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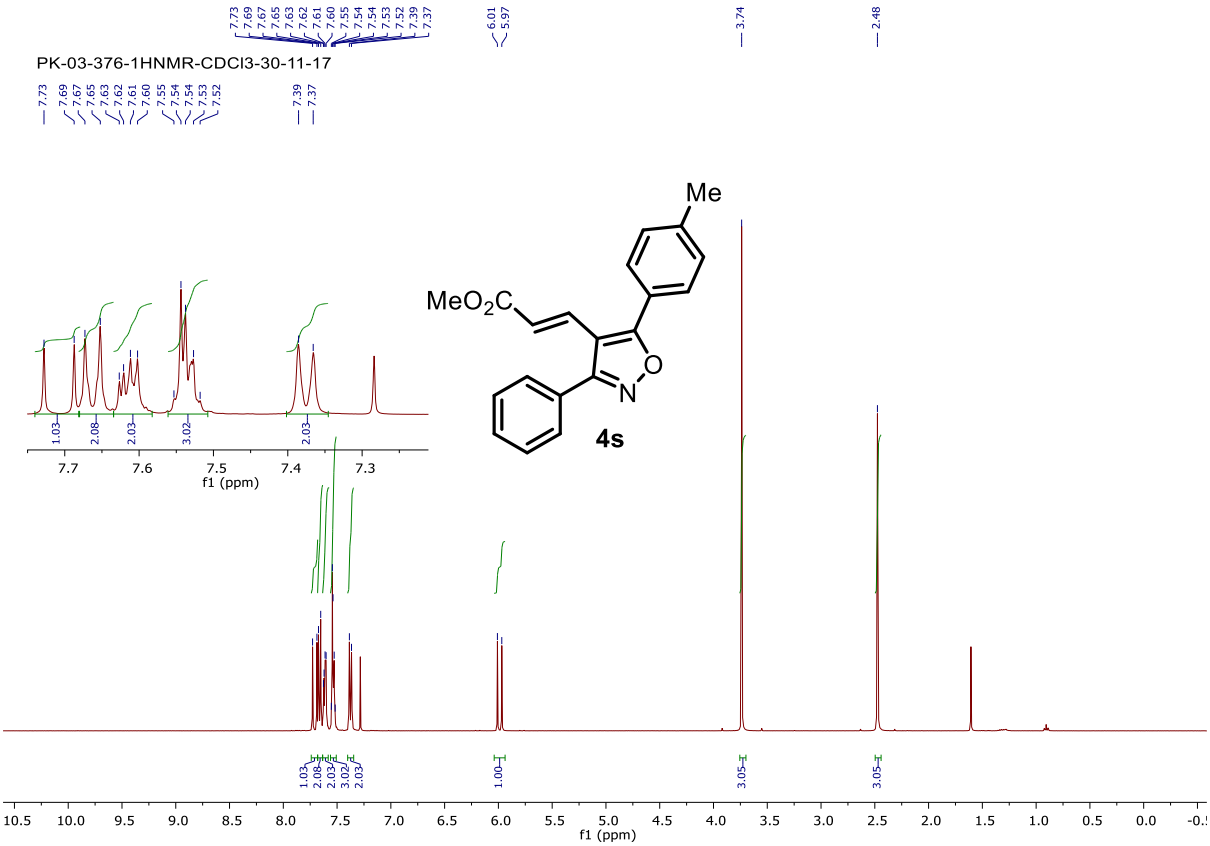
f1 (ppm)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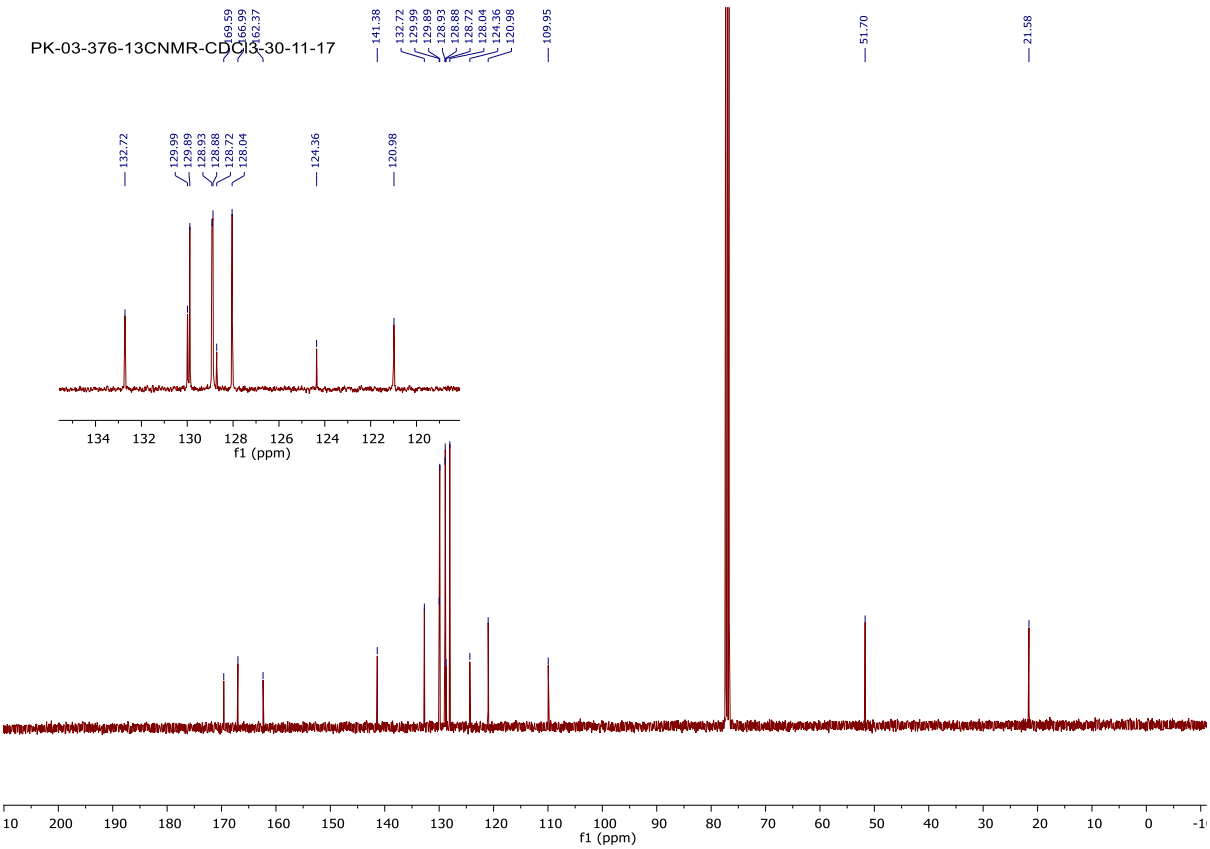
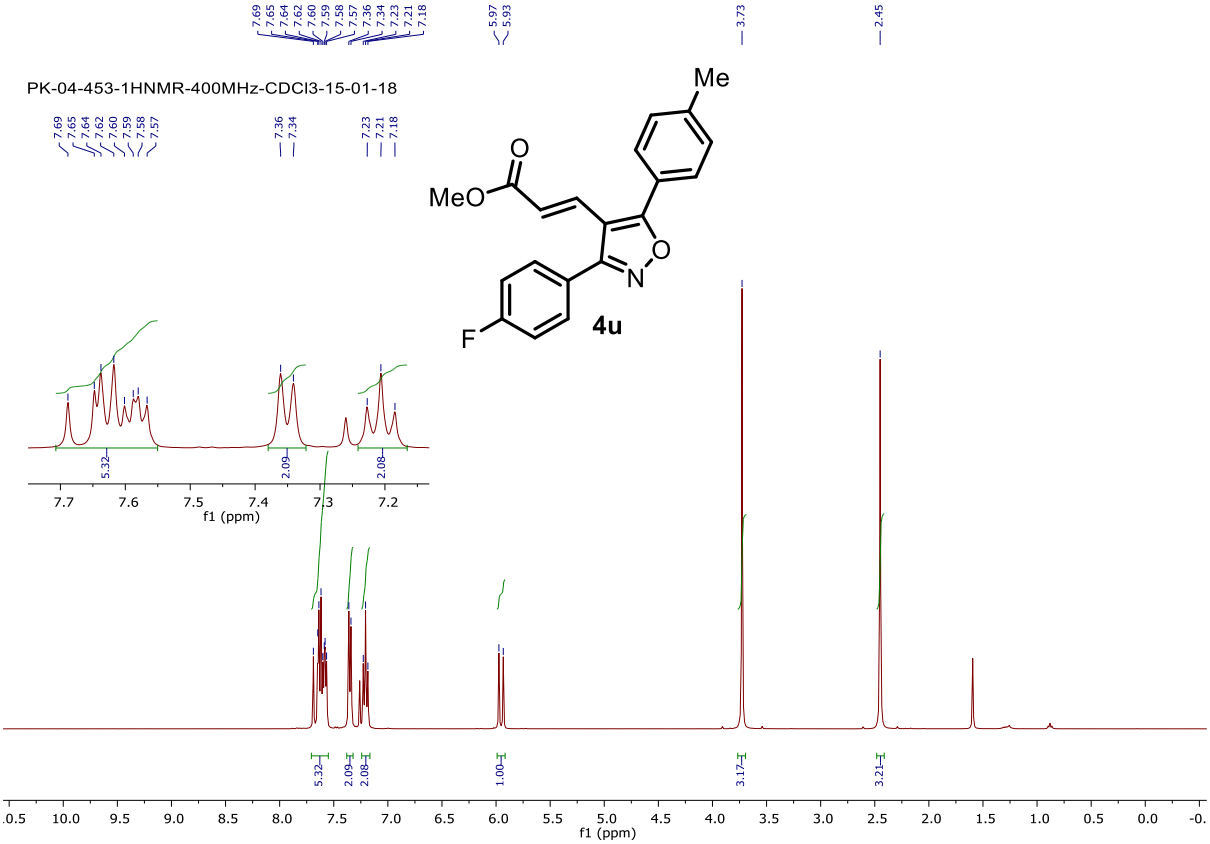
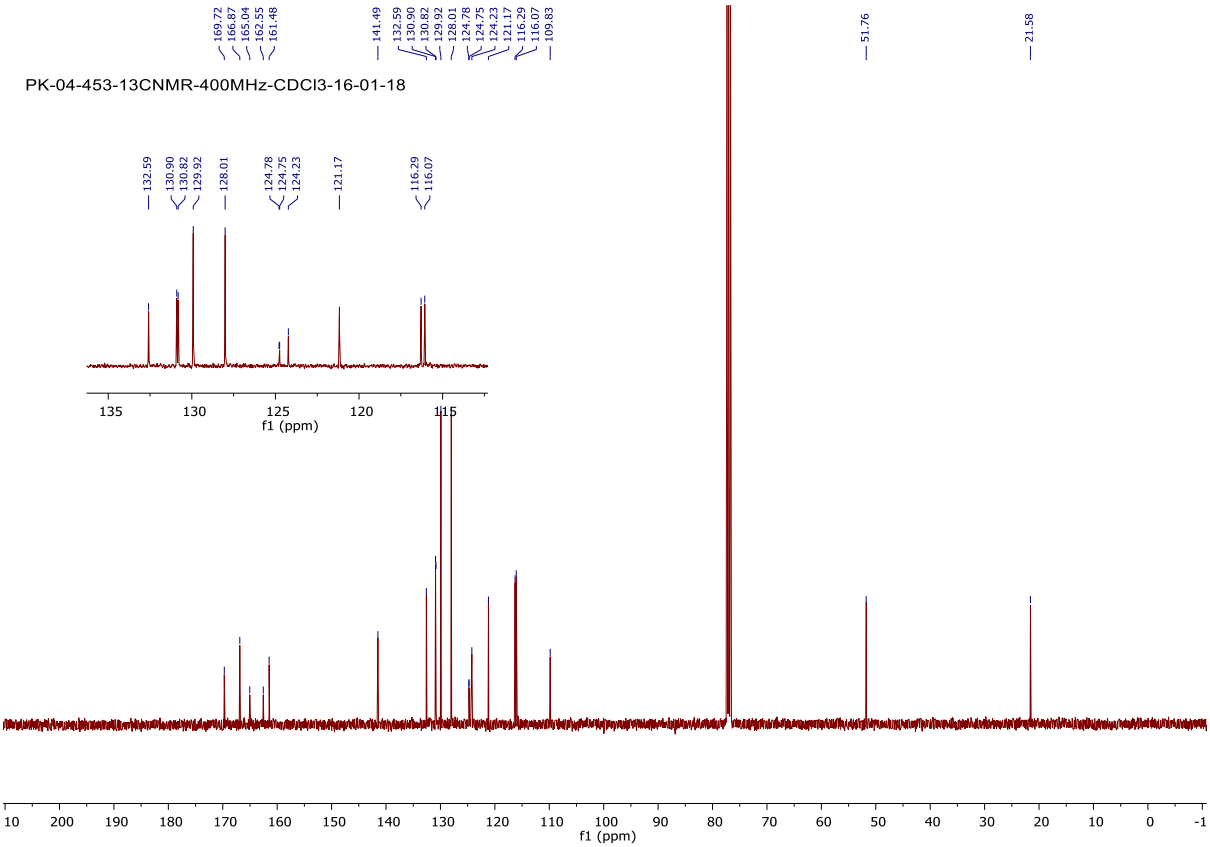
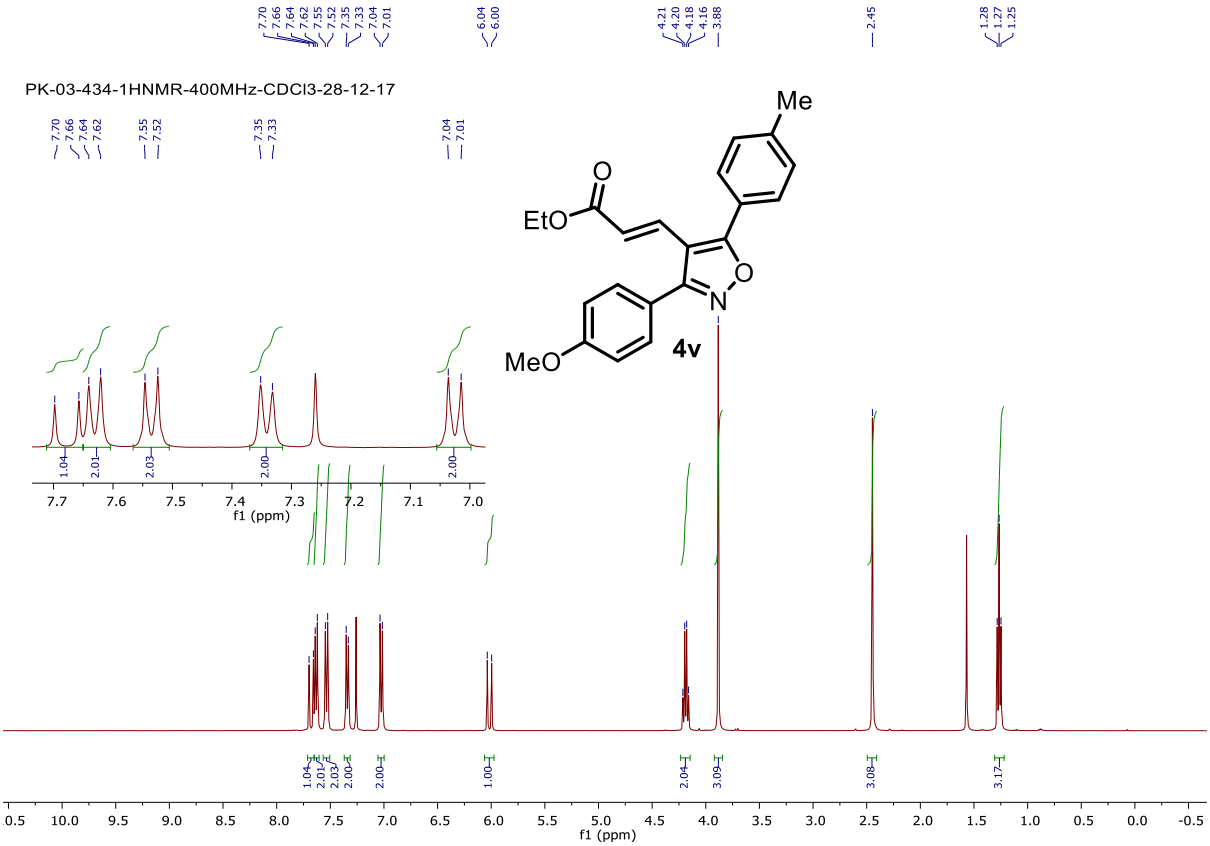
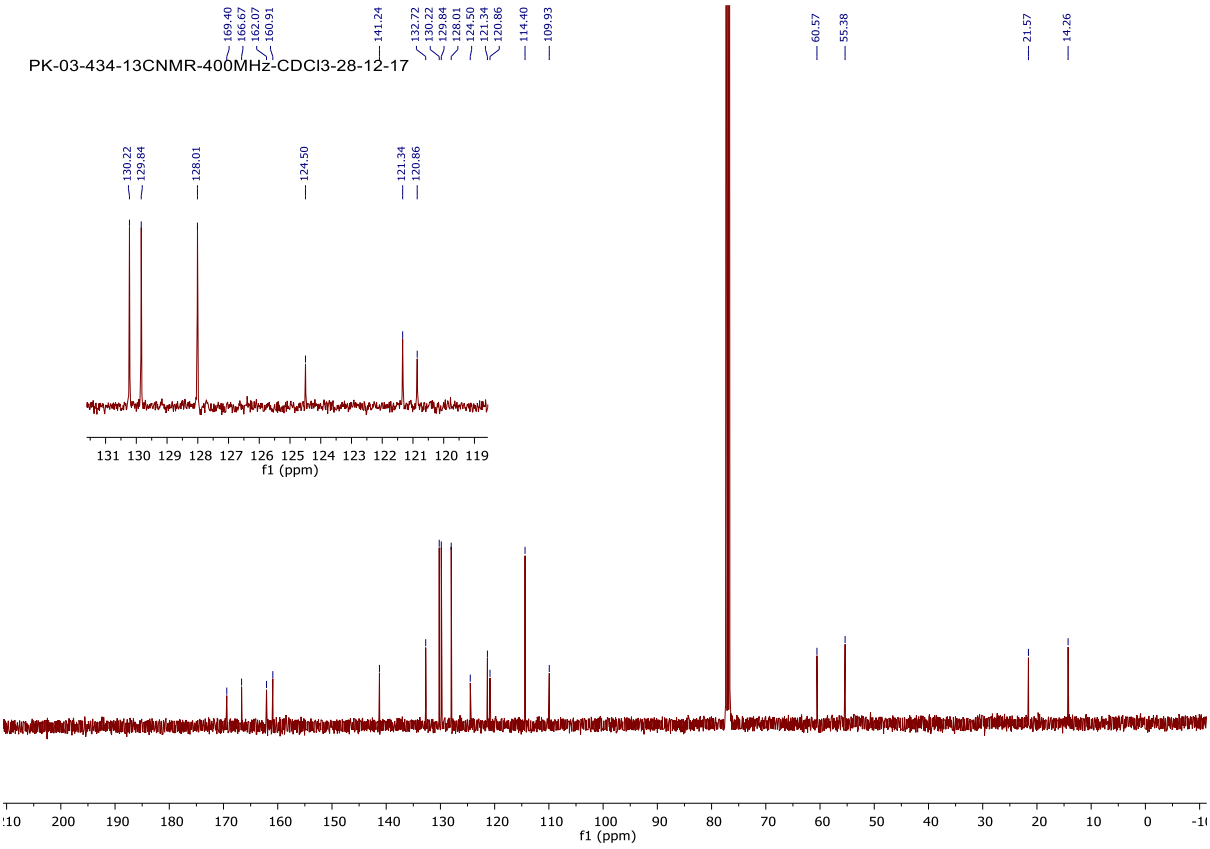
O
N
4s
f1 (ppm)

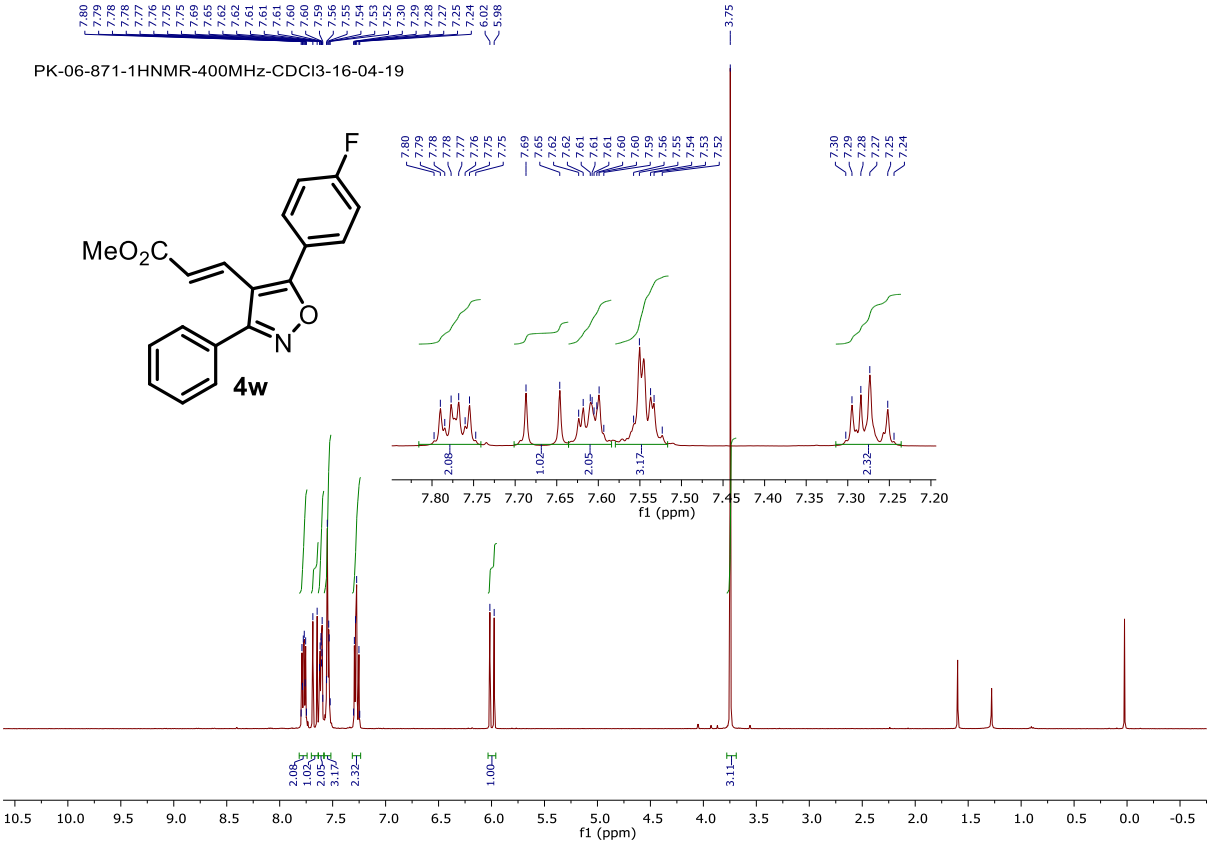

PK-03-376-13CNMR-CDCl3-30-11-17
f1 (ppm)

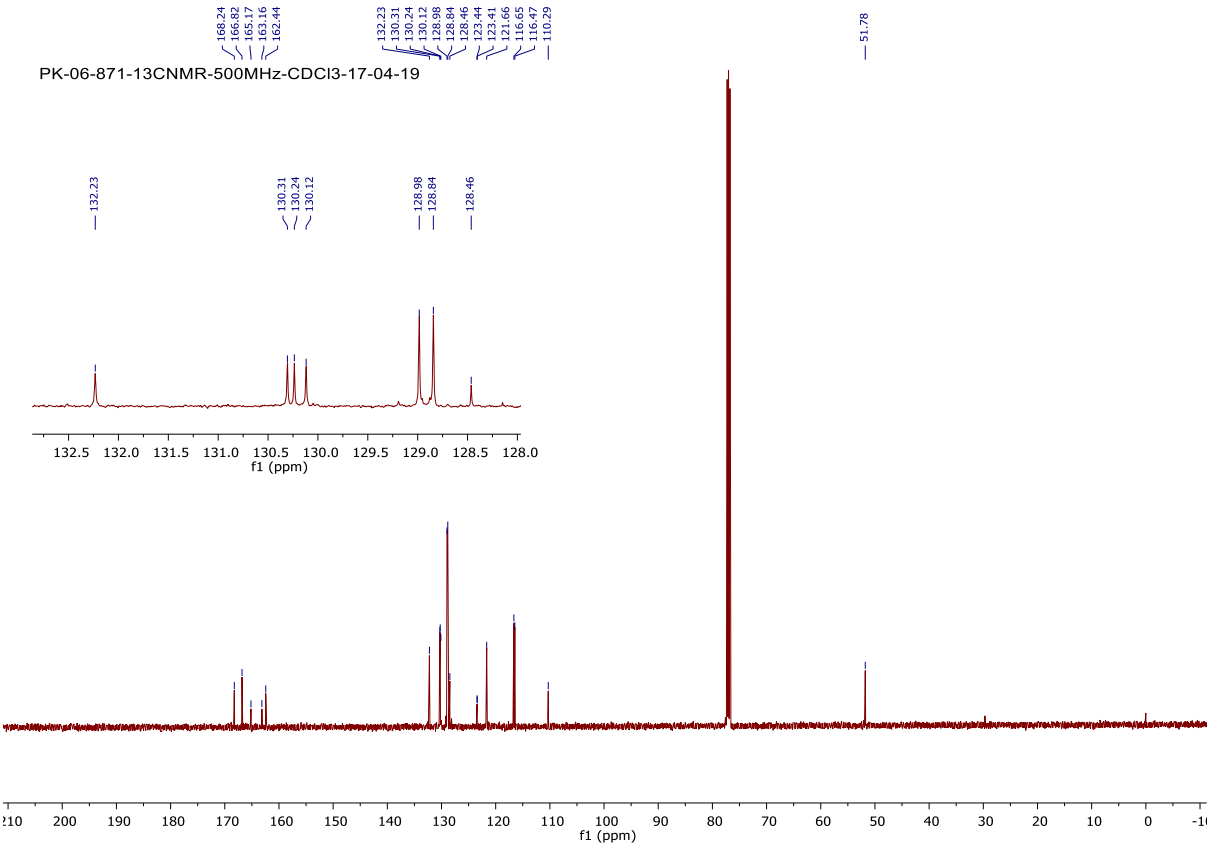

PK-04-453-1HNMR-400MHz-CDCl3-15-01-18
Me
MeO
O
O
N
F
4u
f1 (ppm)

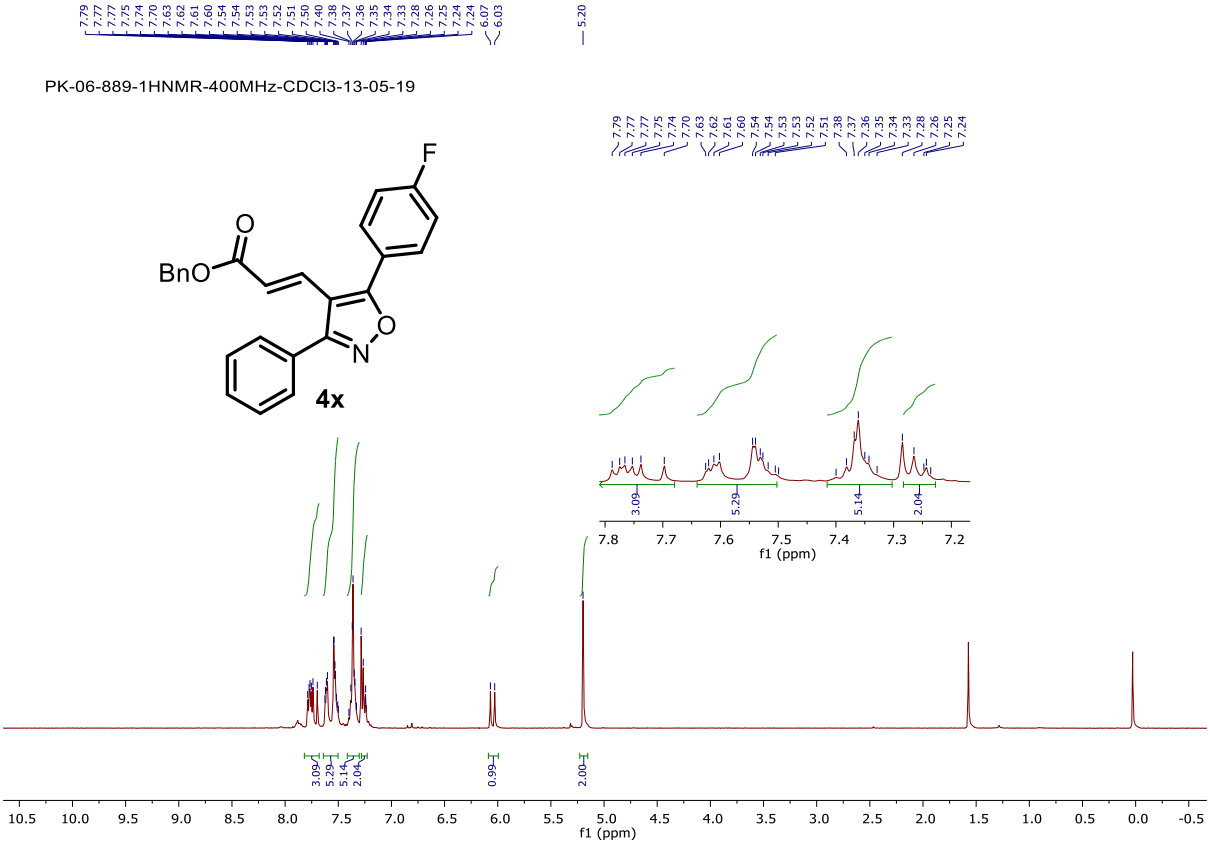

PK-04-453-13CNMR-400MHz-CDCl3-16-01-18
f1 (ppm)

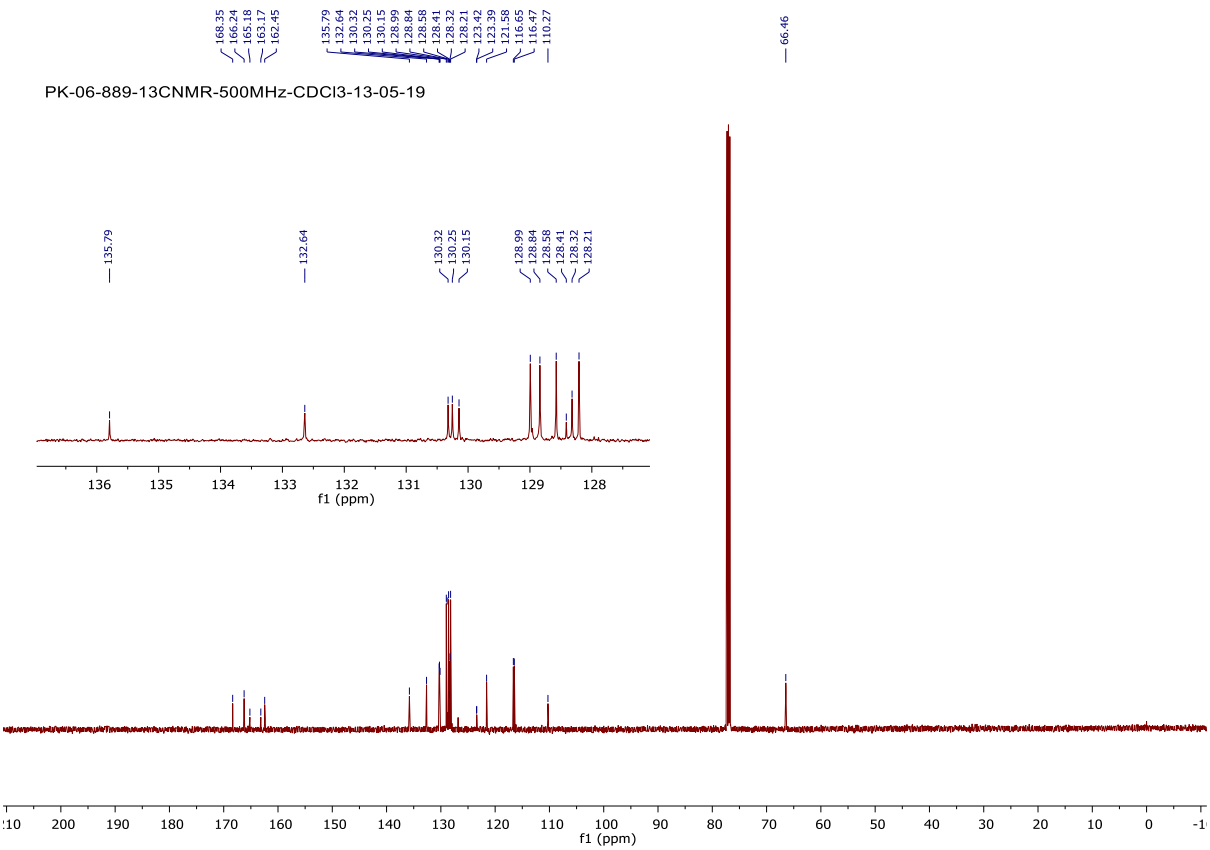

PK-03-434-1HNMR-400MHz-CDCl3-28-12-17
Me
EtO
O
N
O
MeO
4v
f1 (ppm)

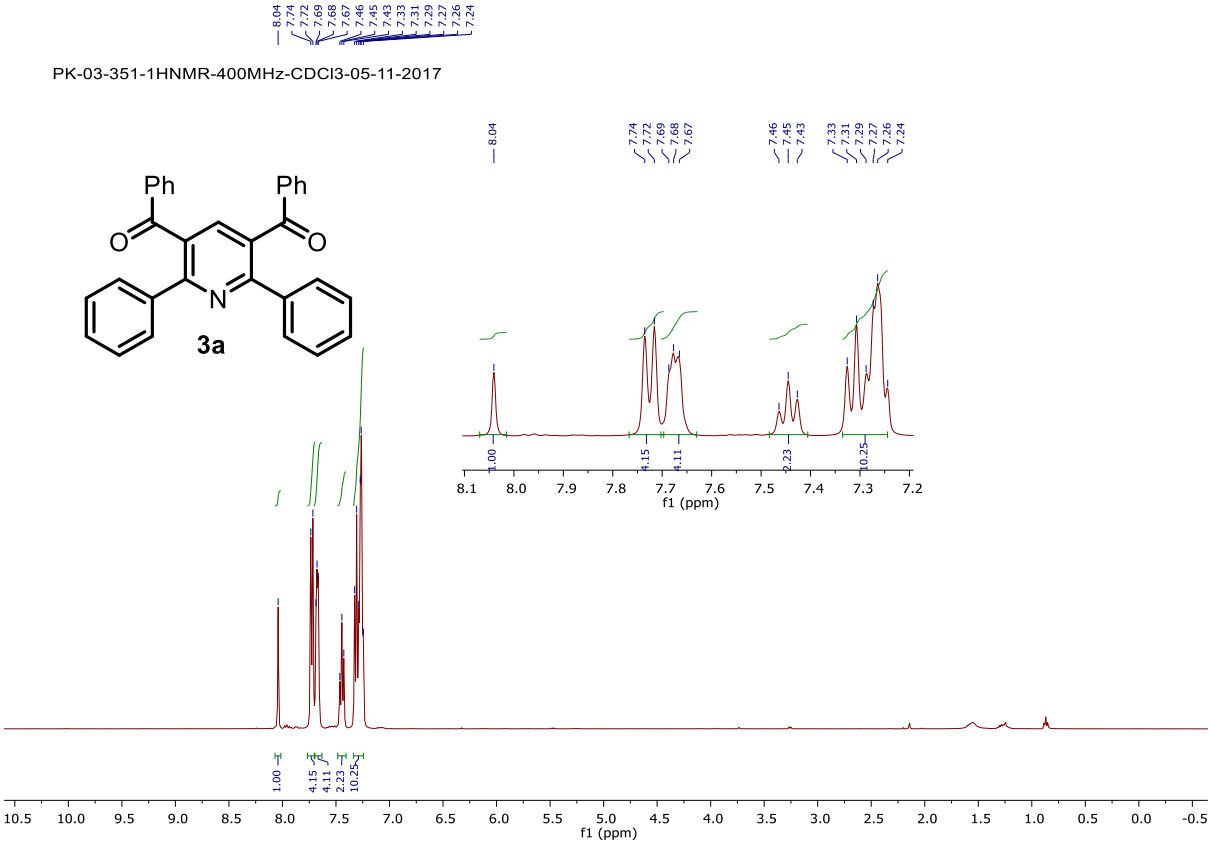

PK-03-434-13CNMR-400MHz-CDCl3-28-12-17
f1 (ppm)

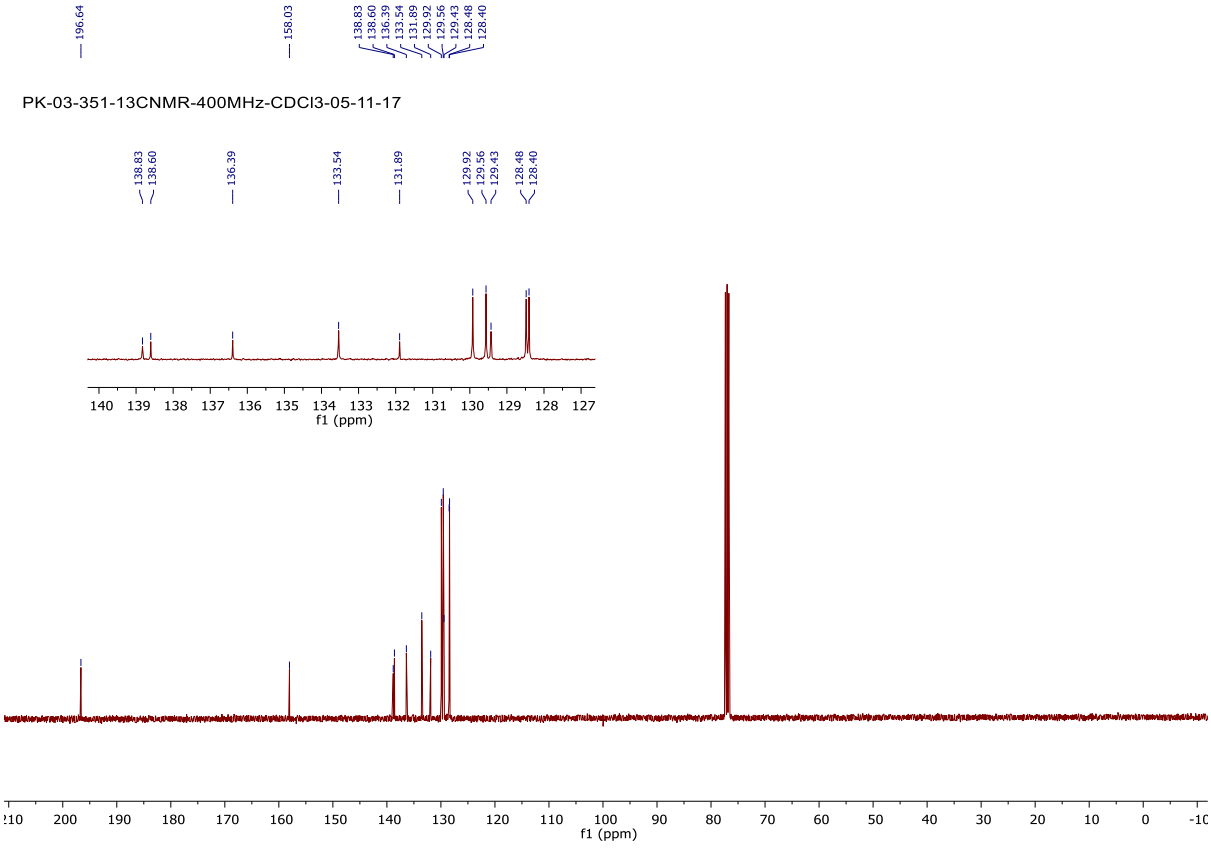

PK-06-871-1HNMR-400MHz-CDCl3-16-04-19
MeO2C
F
N
O
4w
f1 (ppm)


PK-06-871-13CNMR-500MHz-CDCl3-17-04-19
f1 (ppm)

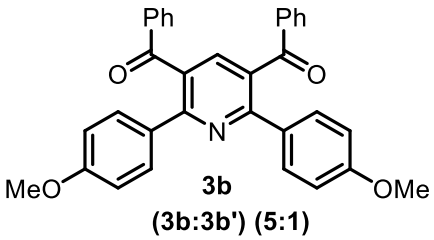

PK-06-889-1HNMR-400MHz-CDCl3-13-05-19
BnO
O
O
N
F
4x
f1 (ppm)


PK-06-889-13CNMR-500MHz-CDCl3-13-05-19
f1 (ppm)


8.04
7.74
7.72
7.69
7.68
7.67
7.46
7.45
7.43
7.33
7.31
7.29
7.27
7.26
7.24
PK-03-351-1HNMR-400MHz-CDCl3-05-11-2017
Ph
Ph
O
O
N
3a
1.00
4.15
4.11
2.23
10.25
f1 (ppm)


196.64
158.03
138.83
138.60
136.39
133.54
131.89
129.92
129.56
129.43
128.48
128.40
PK-03-351-13CNMR-400MHz-CDCl3-05-11-17
f1 (ppm)

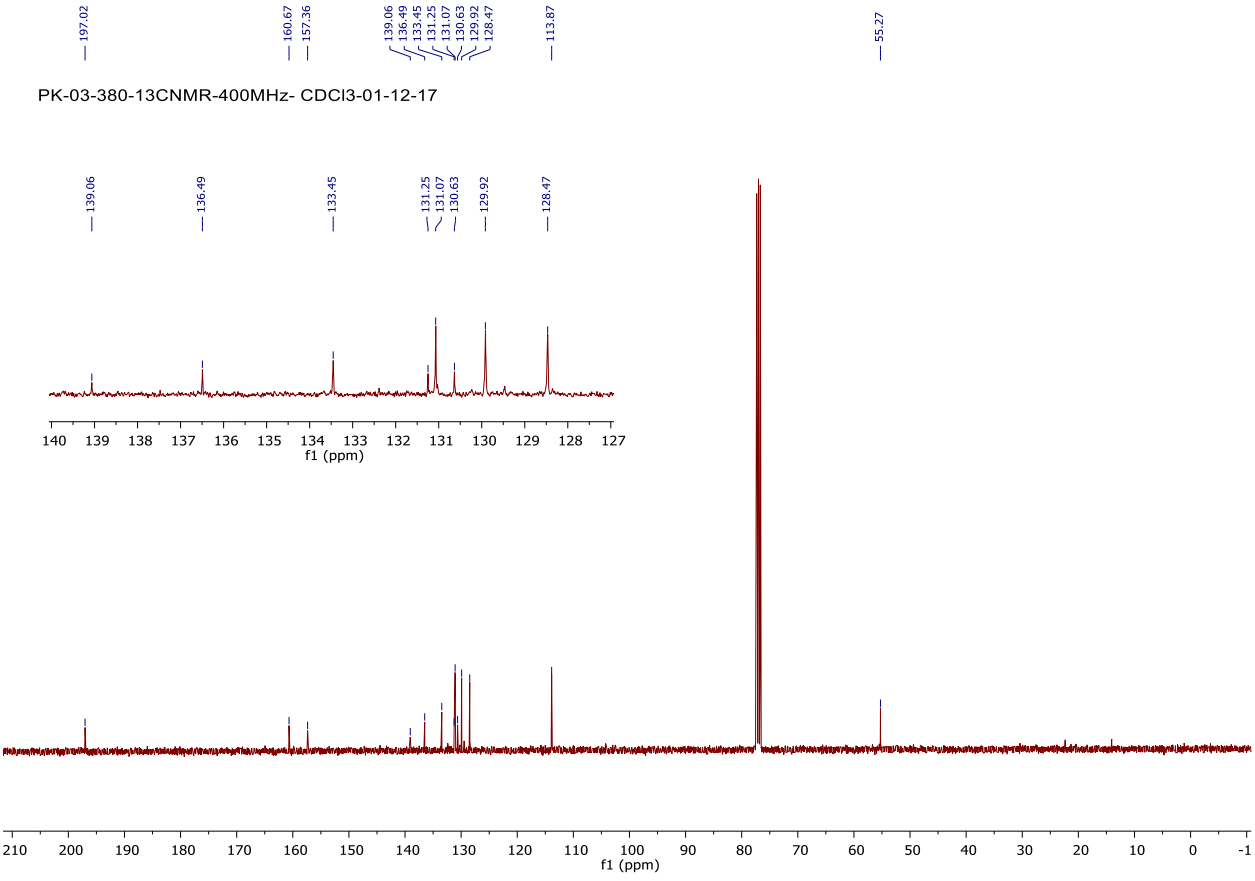
PK-03-380-1HNMR-400MHz-CDCl3-01-12-17

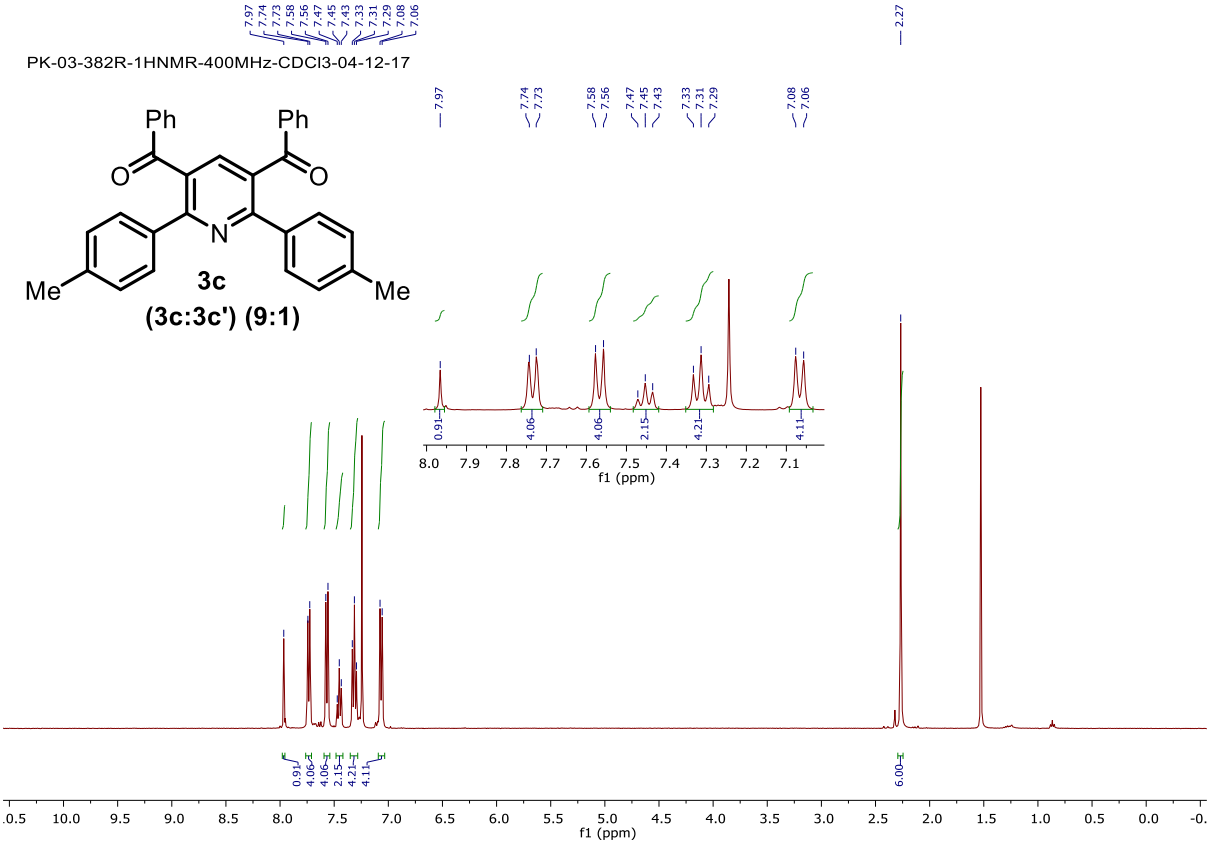


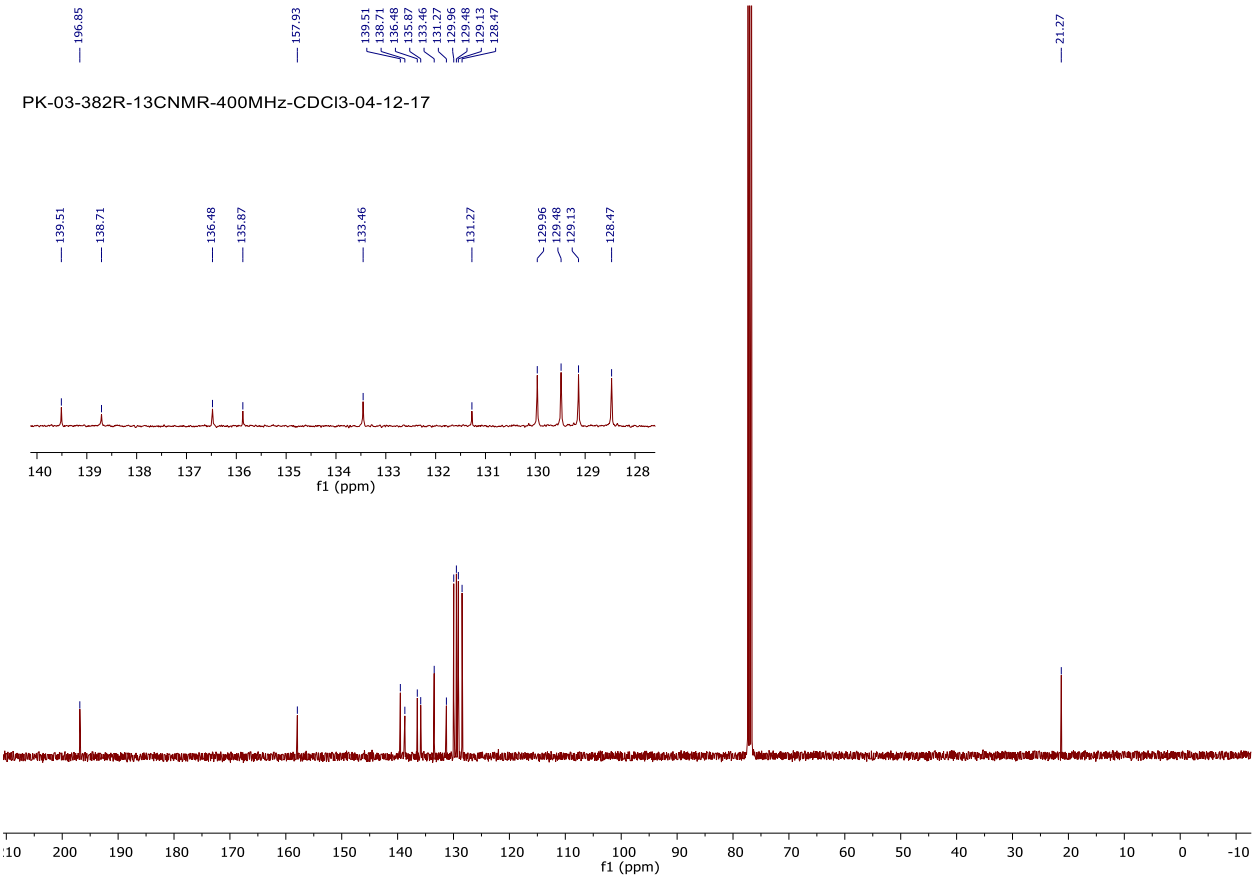
3b

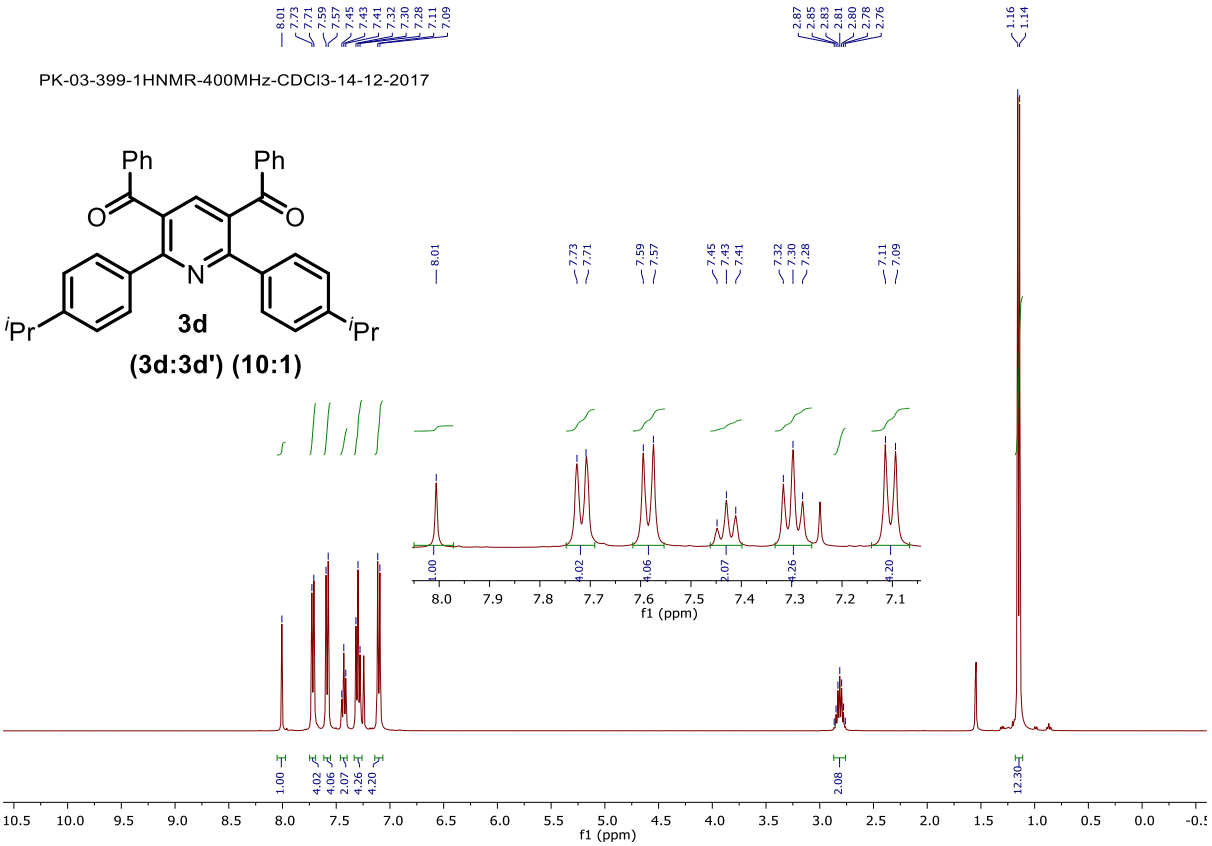
(3b:3b') (5:1)

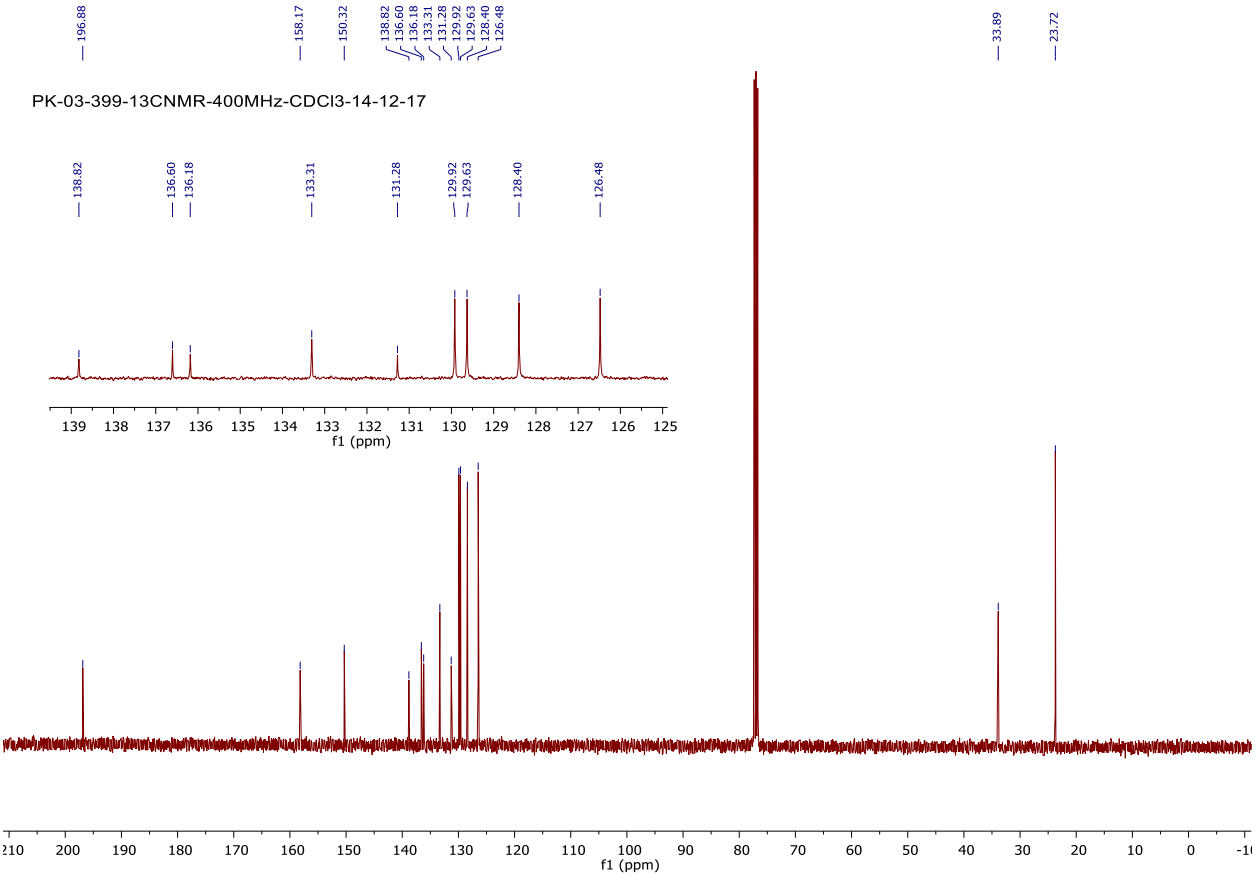
PK-03-380-13CNMR-400MHz- CDCl3-01-12-17

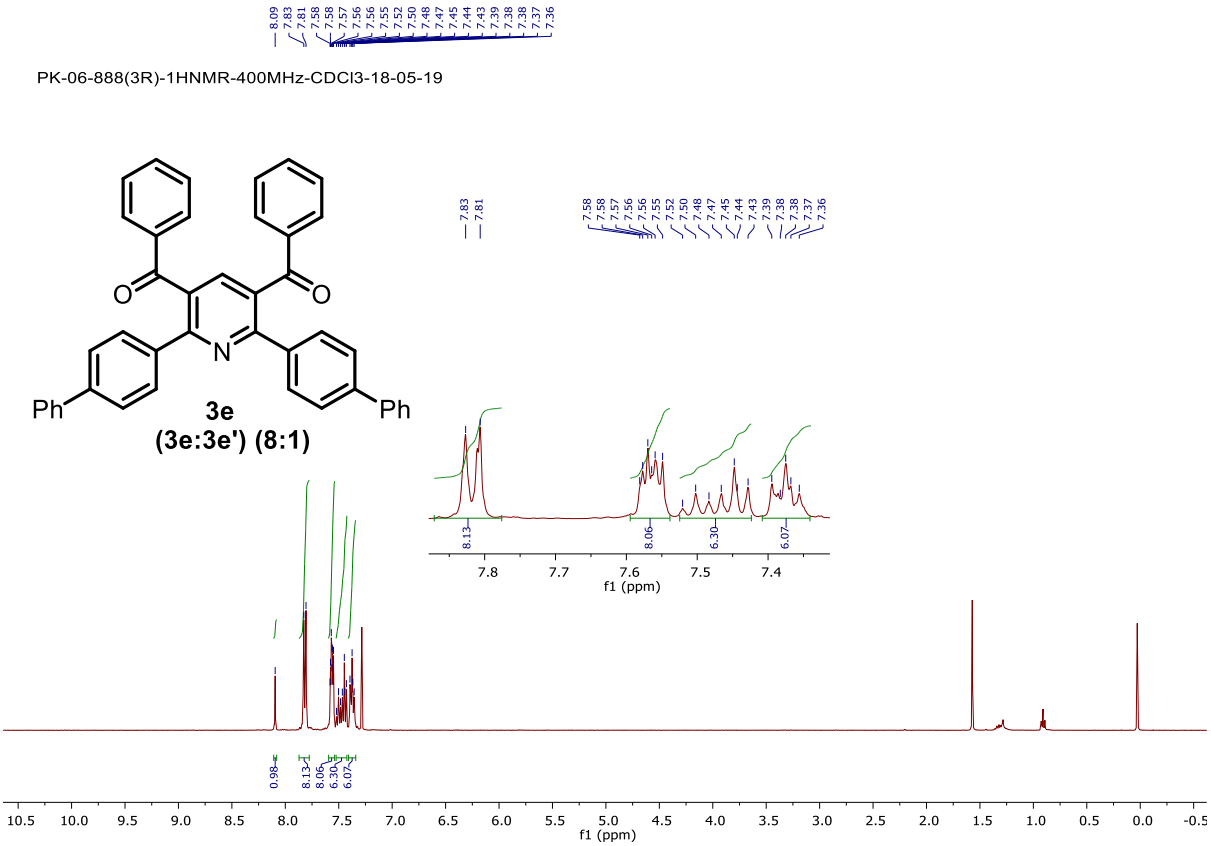


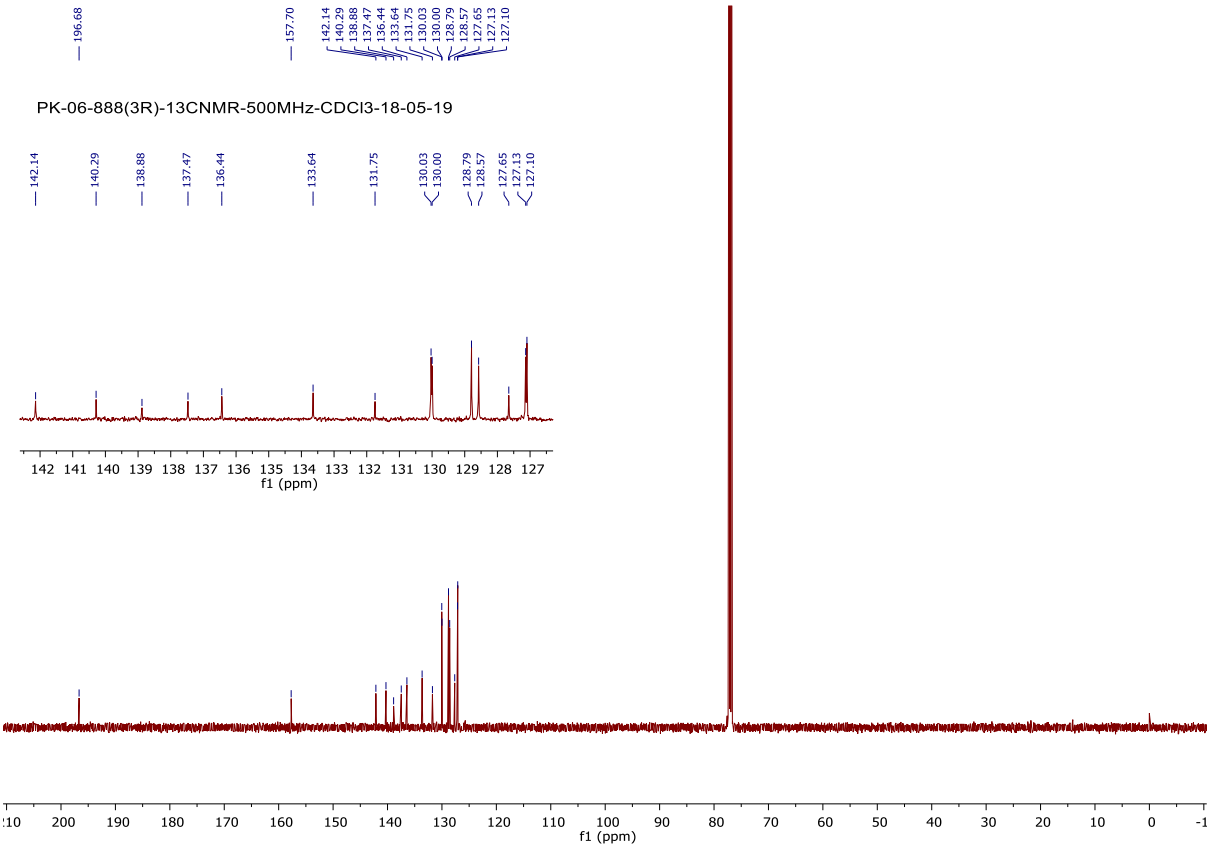

PK-03-382R-1HNMR-400MHz-CDCl3-04-12-17
Ph
Ph
O
O
N
Me
Me
3c
(3c:3c') (9:1)
f1 (ppm)


PK-03-382R-13CNMR-400MHz-CDCl3-04-12-17
f1 (ppm)

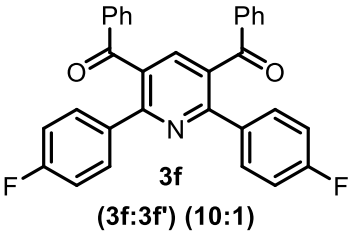

PK-03-399-1HNMR-400MHz-CDCl3-14-12-2017
Ph
Ph
O
O
N
3d
(3d:3d') (10:1)
f1 (ppm)


PK-03-399-13CNMR-400MHz-CDCl3-14-12-17
f1 (ppm)


8.09
7.83
7.81
7.58
7.57
7.56
7.55
7.52
7.50
7.48
7.47
7.45
7.44
7.43
7.39
7.38
7.38
7.37
7.36
PK-06-888(3R)-1HNMR-400MHz-CDCl3-18-05-19
O
O
N
Ph
Ph
3e
(3e:3e') (8:1)
8.13
8.06
6.30
6.07
f1 (ppm)
0.98
f1 (ppm)

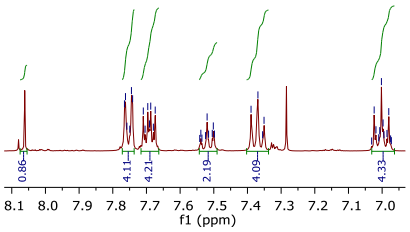

196.68
157.70
142.14
140.29
138.88
137.47
136.44
133.64
131.75
130.03
130.00
128.79
128.57
127.65
127.13
127.10
PK-06-888(3R)-13CNMR-500MHz-CDCl3-18-05-19
f1 (ppm)
f1 (ppm)

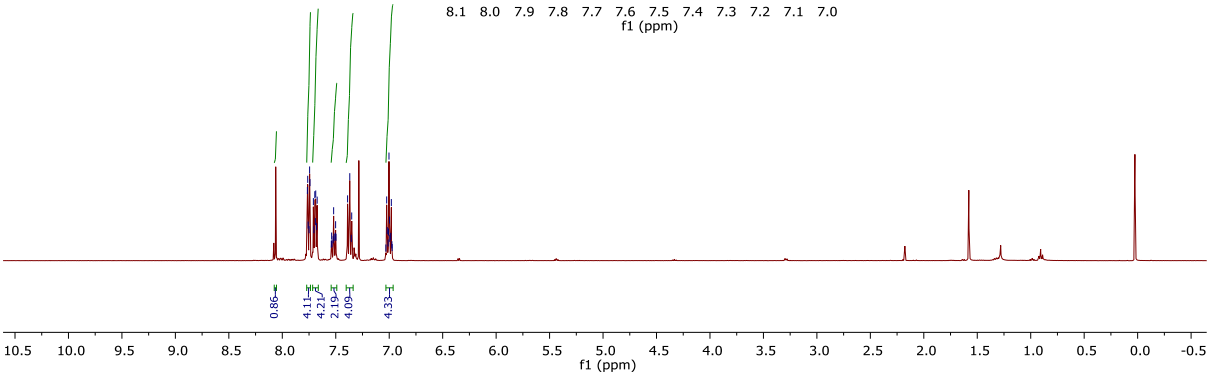
PK-06-860-1HNMR-400MHz-CDCl3-08-04-19



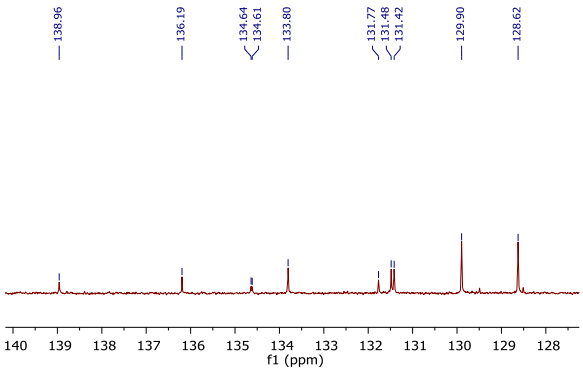
3f

(3f:3f') (10:1)

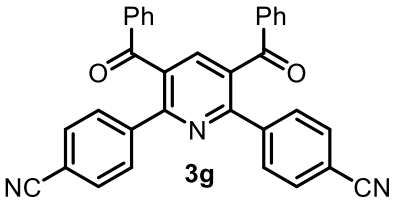




PK-06-860-13CNMR-500MHz-CDCl3-08-04-19

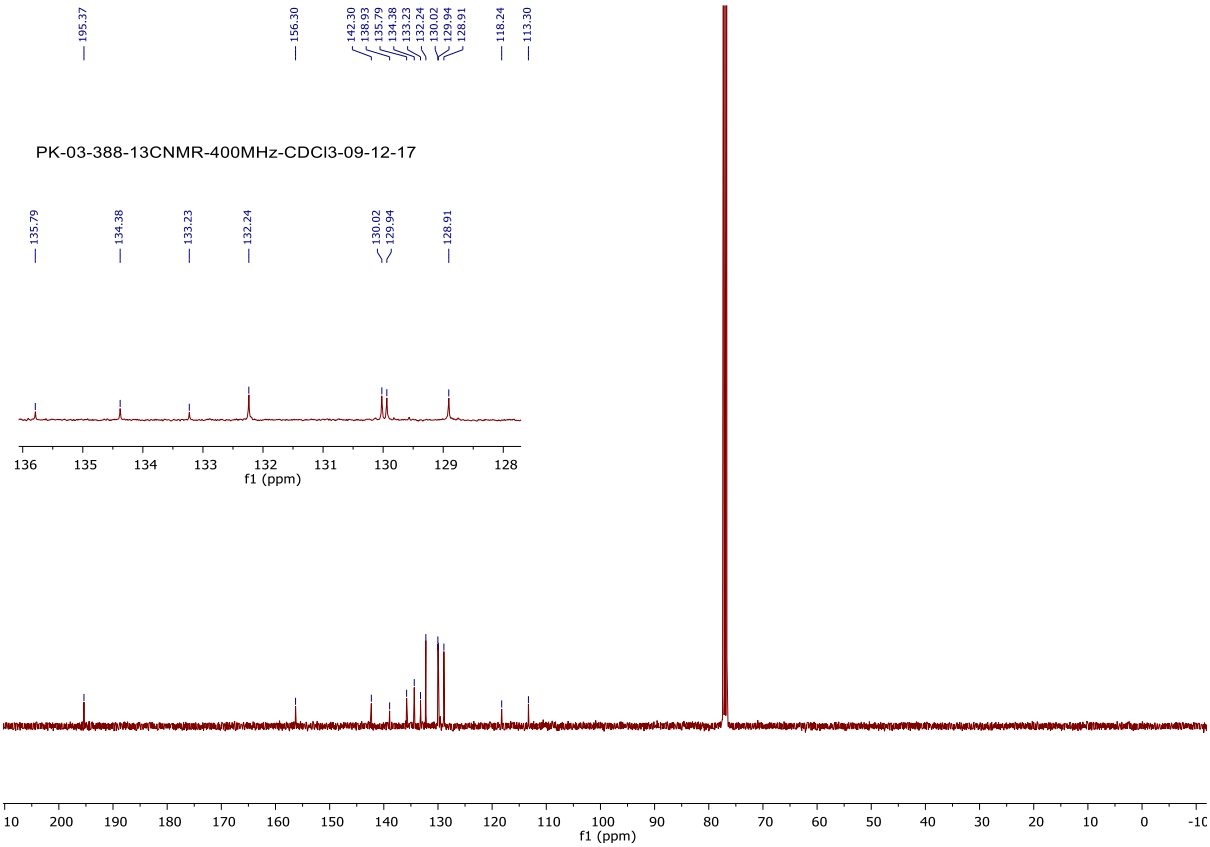


PK-03-388-1HNMR-400MHz-CDCl3-08-12-17

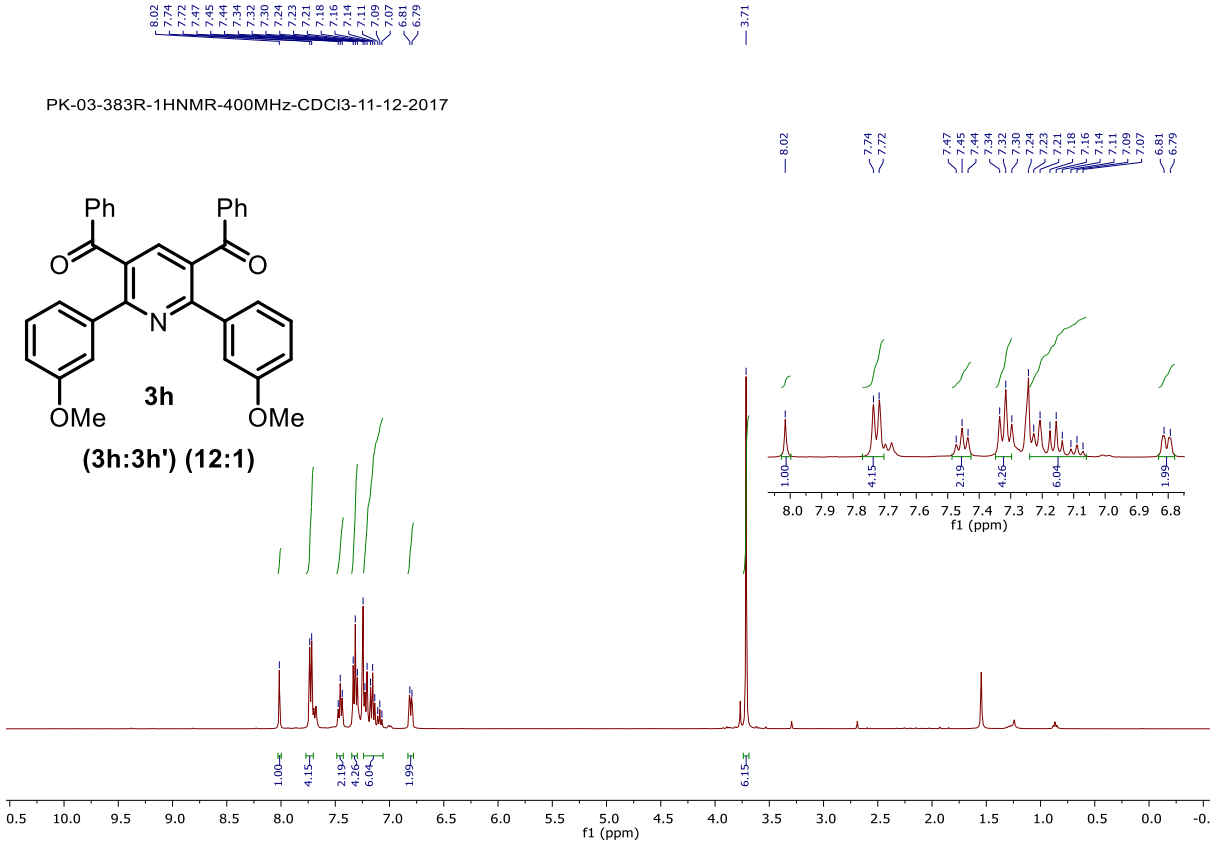


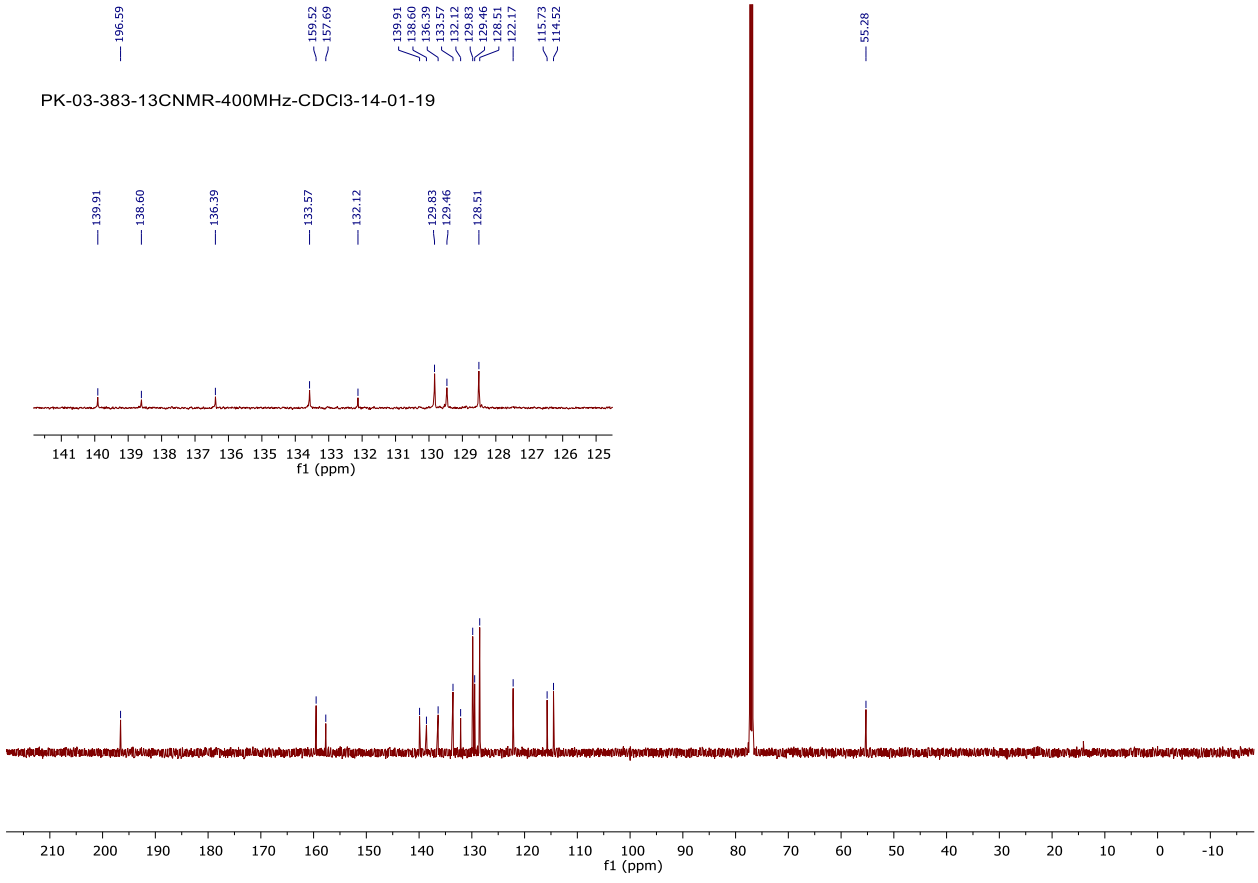
3g

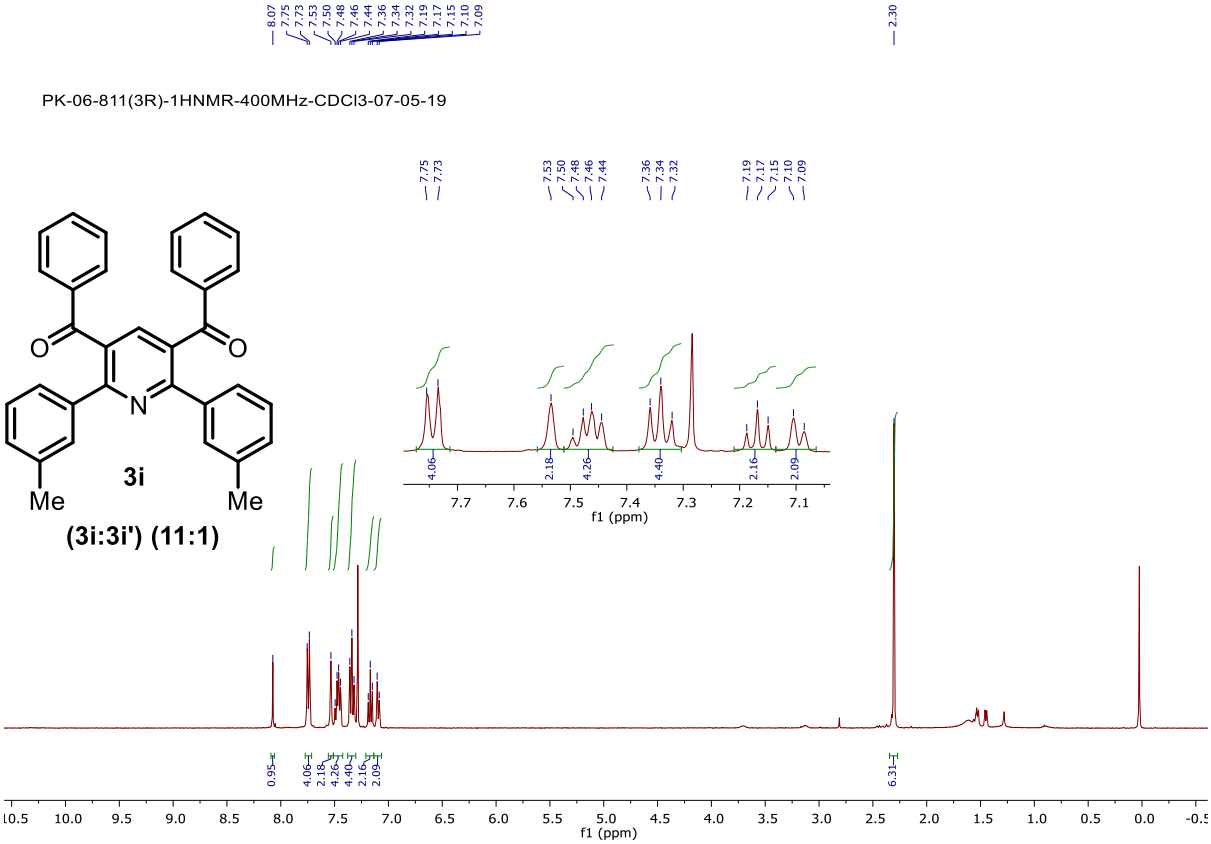
(3g:3g') (11:1)

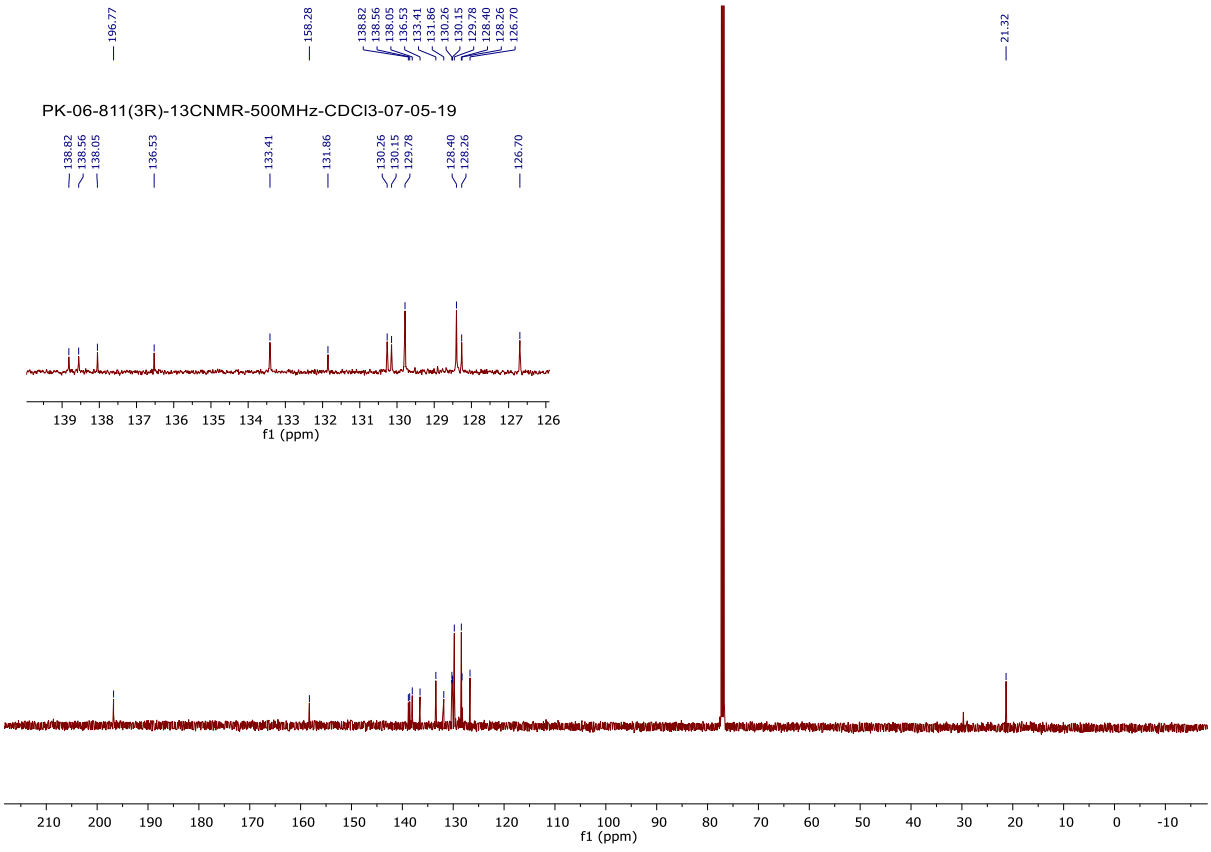


PK-03-388-13CNMR-400MHz-CDCl3-09-12-17

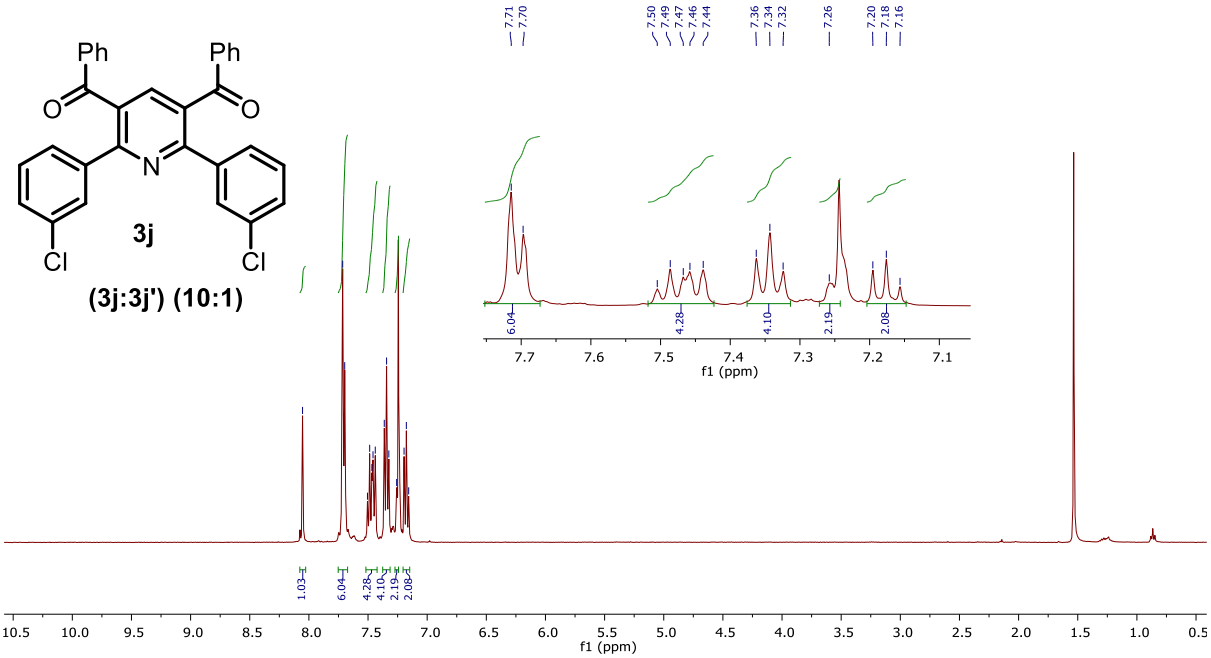

8.02
7.74
7.72
7.47
7.45
7.44
7.34
7.32
7.30
7.24
7.23
7.21
7.18
7.16
7.14
7.11
7.09
7.07
6.81
6.79
3.71
PK-03-383R-1HNMR-400MHz-CDCl3-11-12-2017
Ph
Ph
O
O
N
OMe
OMe
3h
(3h:3h') (12:1)
1.00
4.15
2.19
4.26
6.04
1.99
6.15
f1 (ppm)

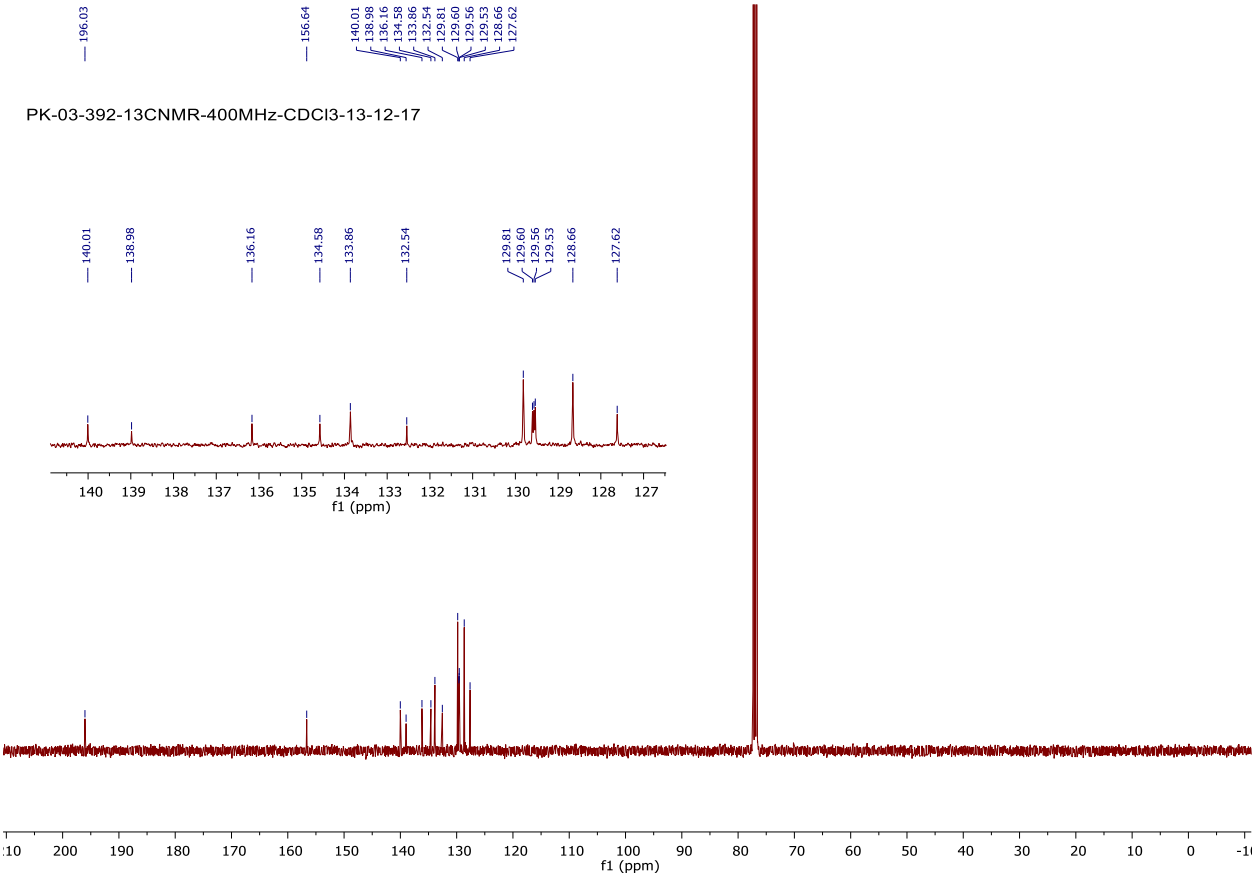

196.59
159.52
157.69
139.91
138.60
136.39
133.57
132.12
129.83
129.46
128.51
122.17
115.73
114.52
55.28
PK-03-383-13CNMR-400MHz-CDCl3-14-01-19
f1 (ppm)


PK-06-811(3R)-1HNMR-400MHz-CDCl3-07-05-19
3i
Me
Me
(3i:3i') (11:1)
f1 (ppm)

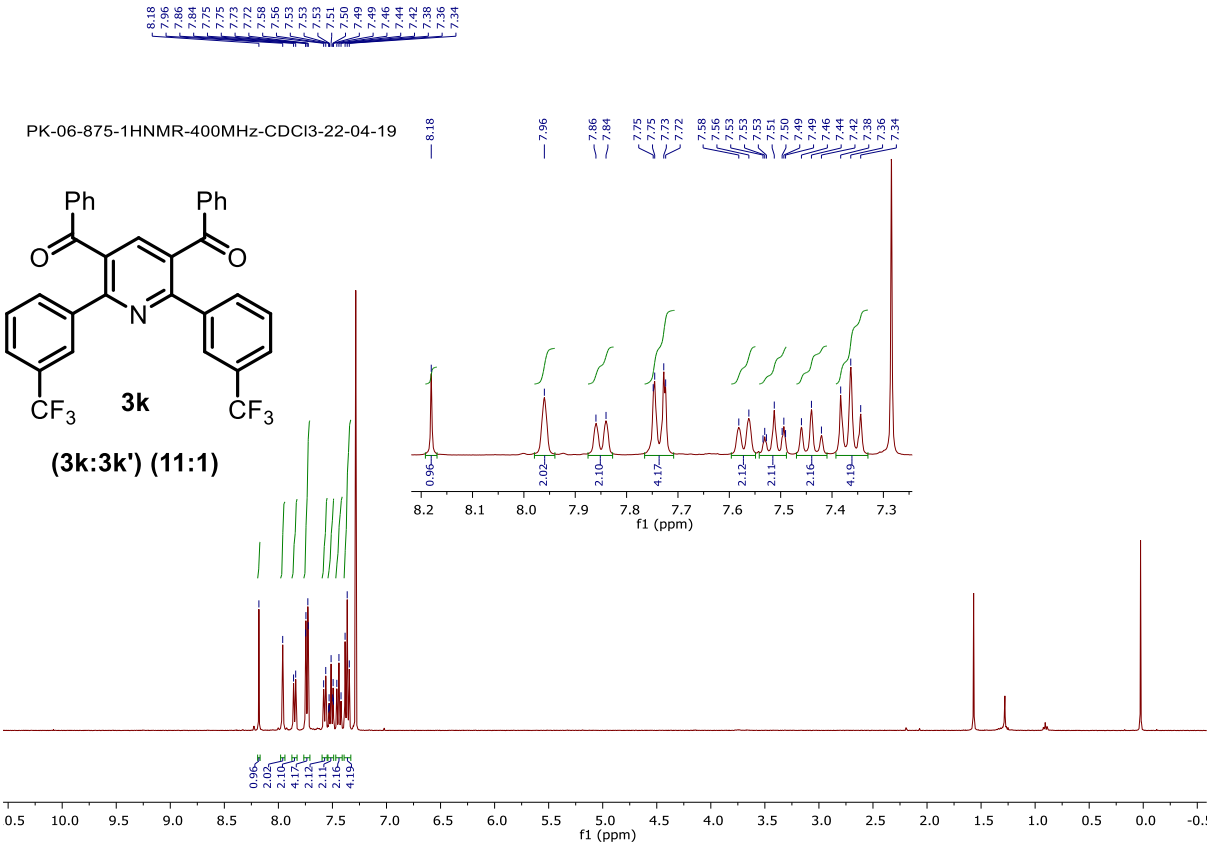

PK-06-811(3R)-13CNMR-500MHz-CDCl3-07-05-19
f1 (ppm)

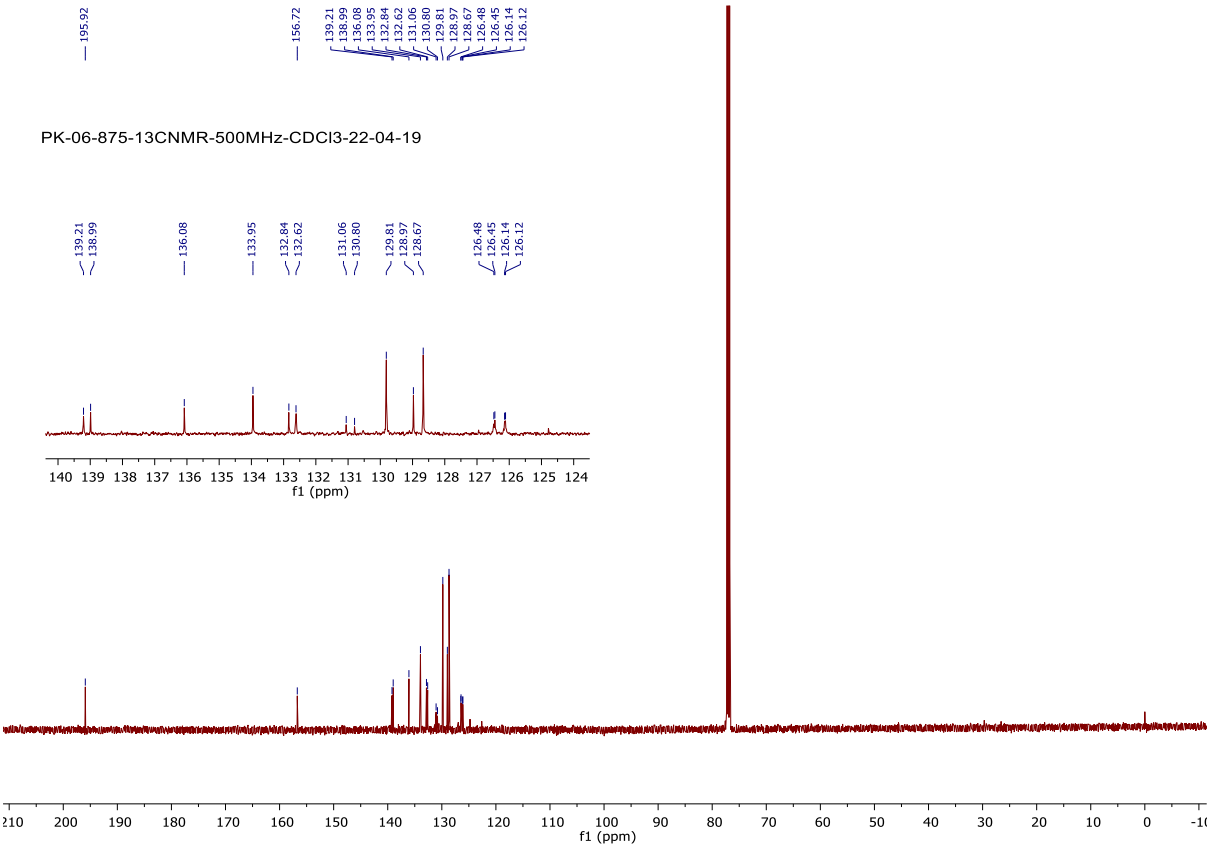
PK-03-392R-1HNMR-400MHz-CDCl3-12-12-17



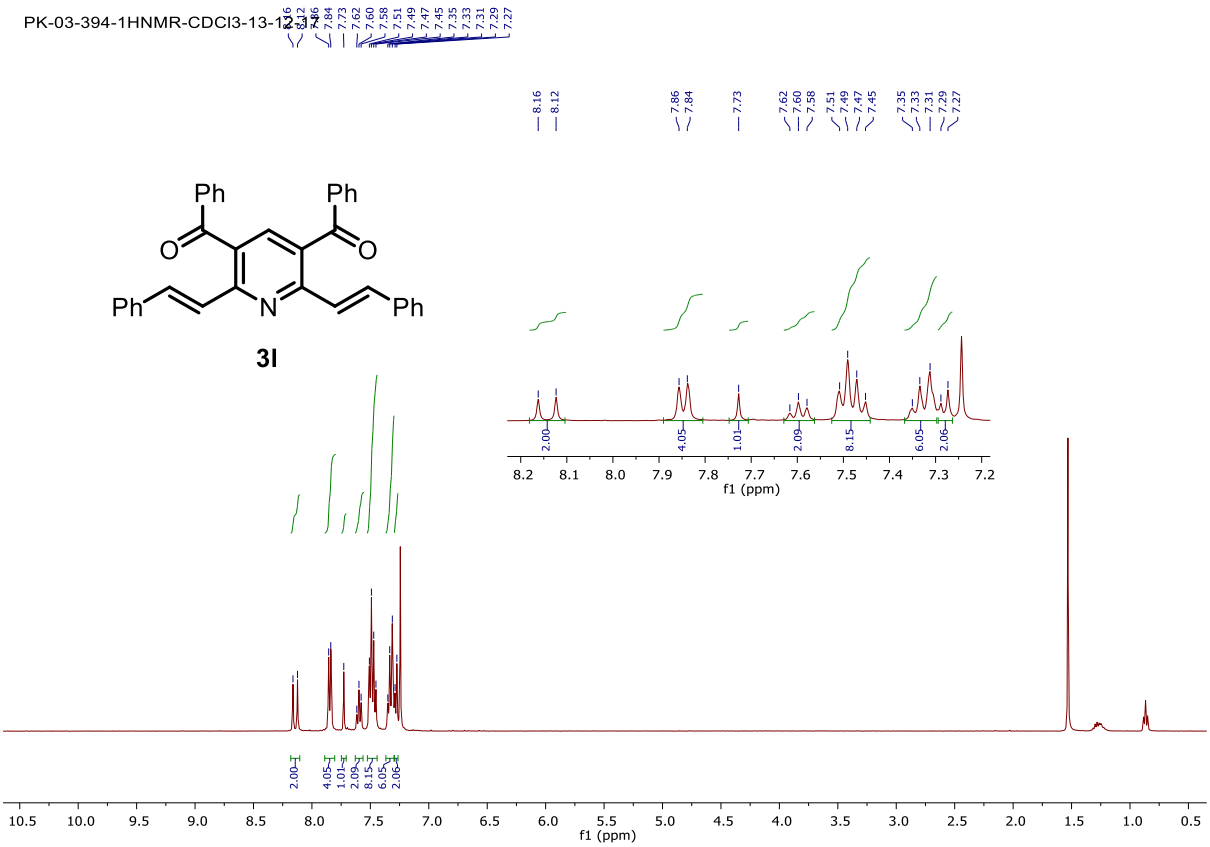


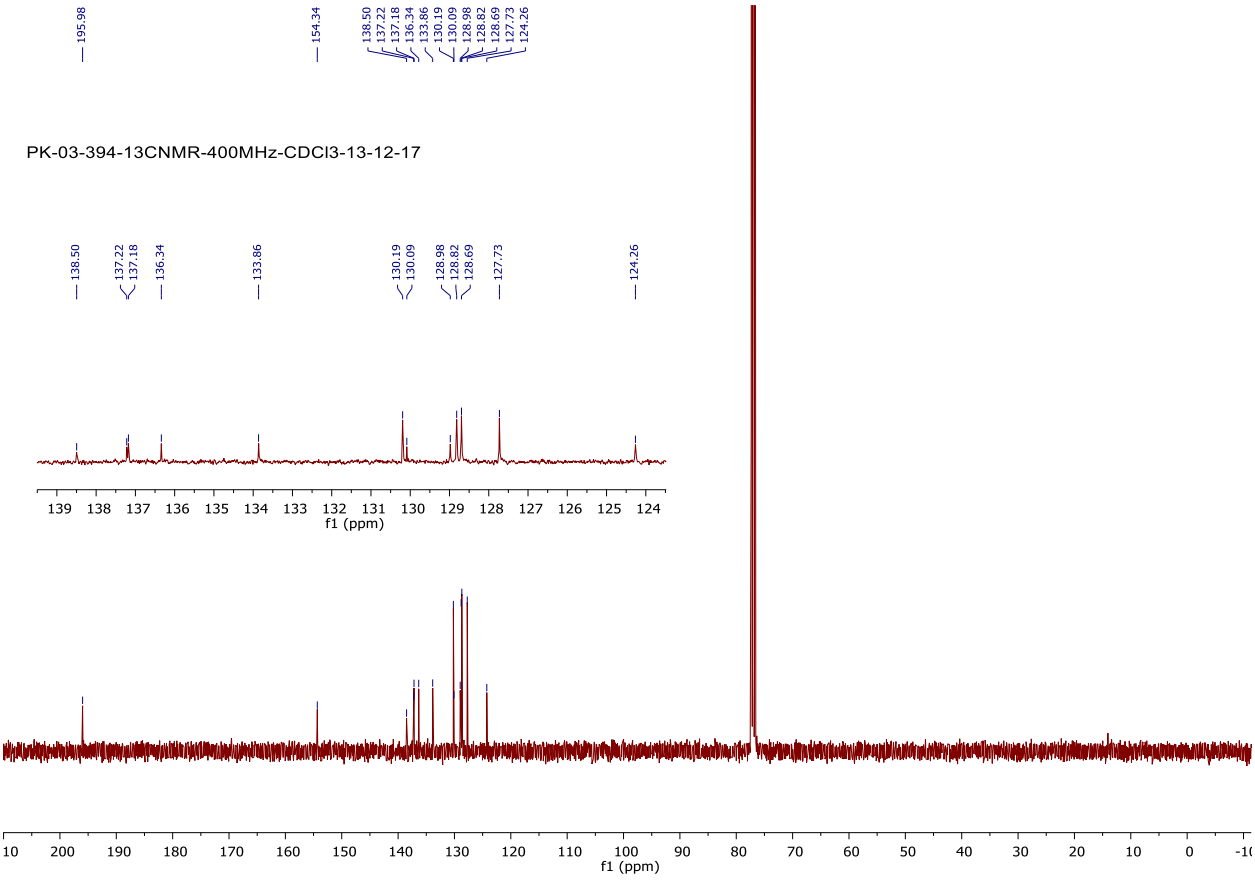
PK-03-392-13CNMR-400MHz-CDCl3-13-12-17


PK-06-875-1HNMR-400MHz-CDCl3-22-04-19
Ph
Ph
O
O
N
CF3
CF3
3k
(3k:3k') (11:1)
f1 (ppm)

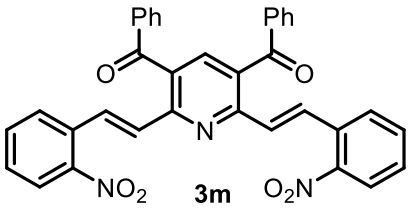

PK-06-875-13CNMR-500MHz-CDCl3-22-04-19
f1 (ppm)

PK-03-394-1HNMR-CDCl3-13-12-17

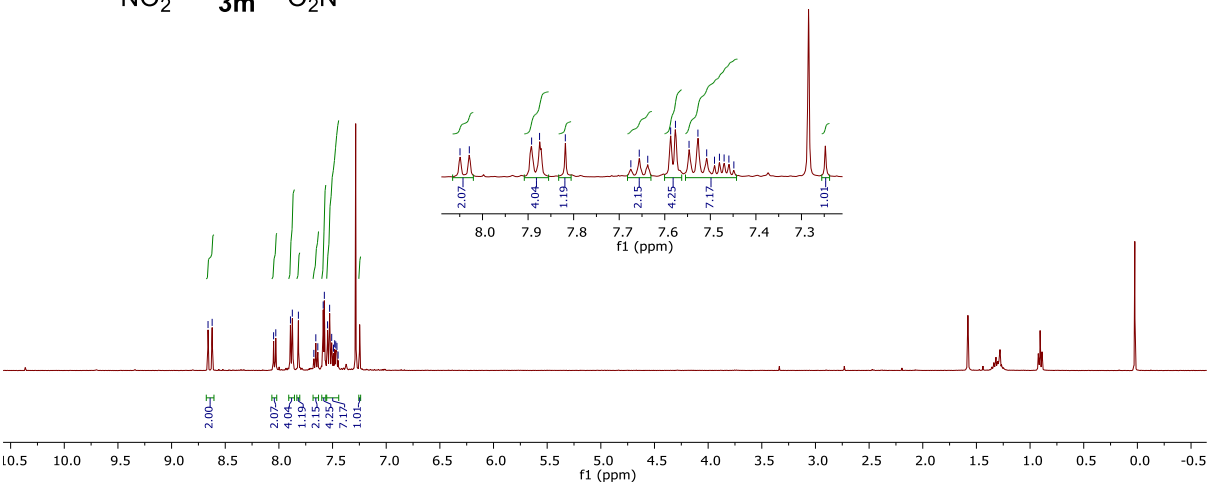




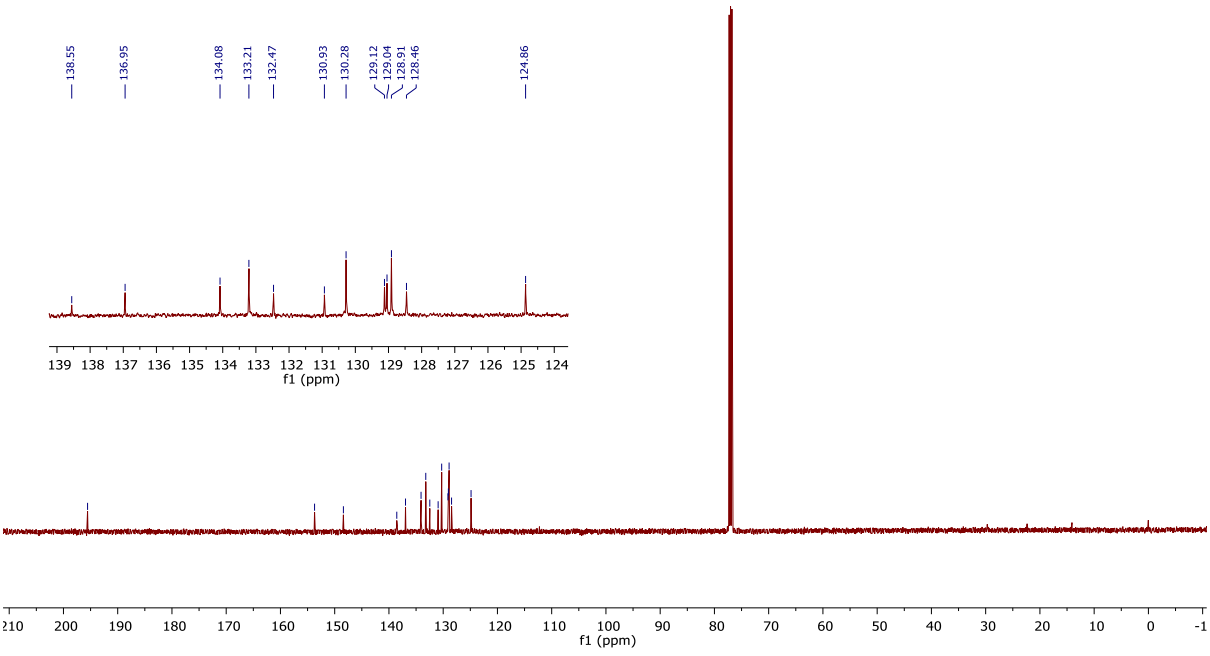
PK-06-870-1HNMR-400MHz-CDCl3-24-04-19

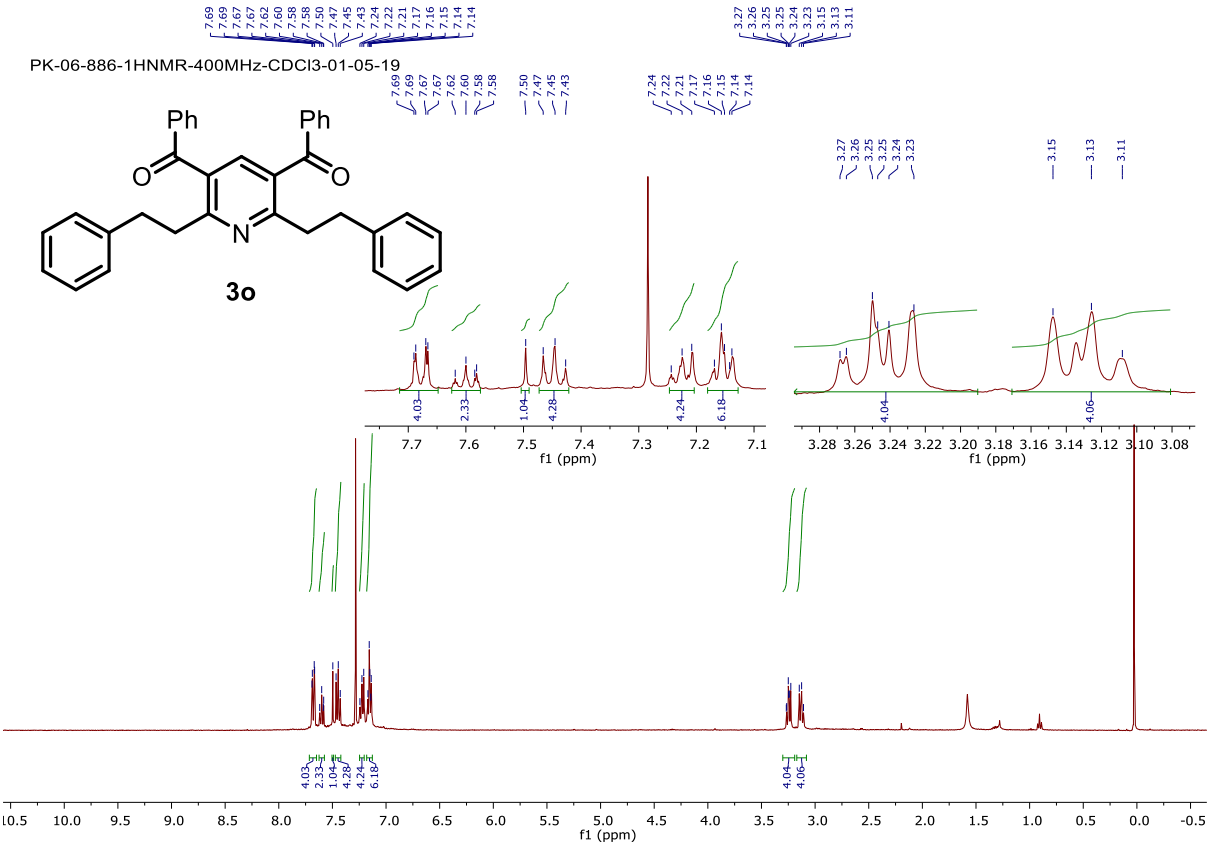


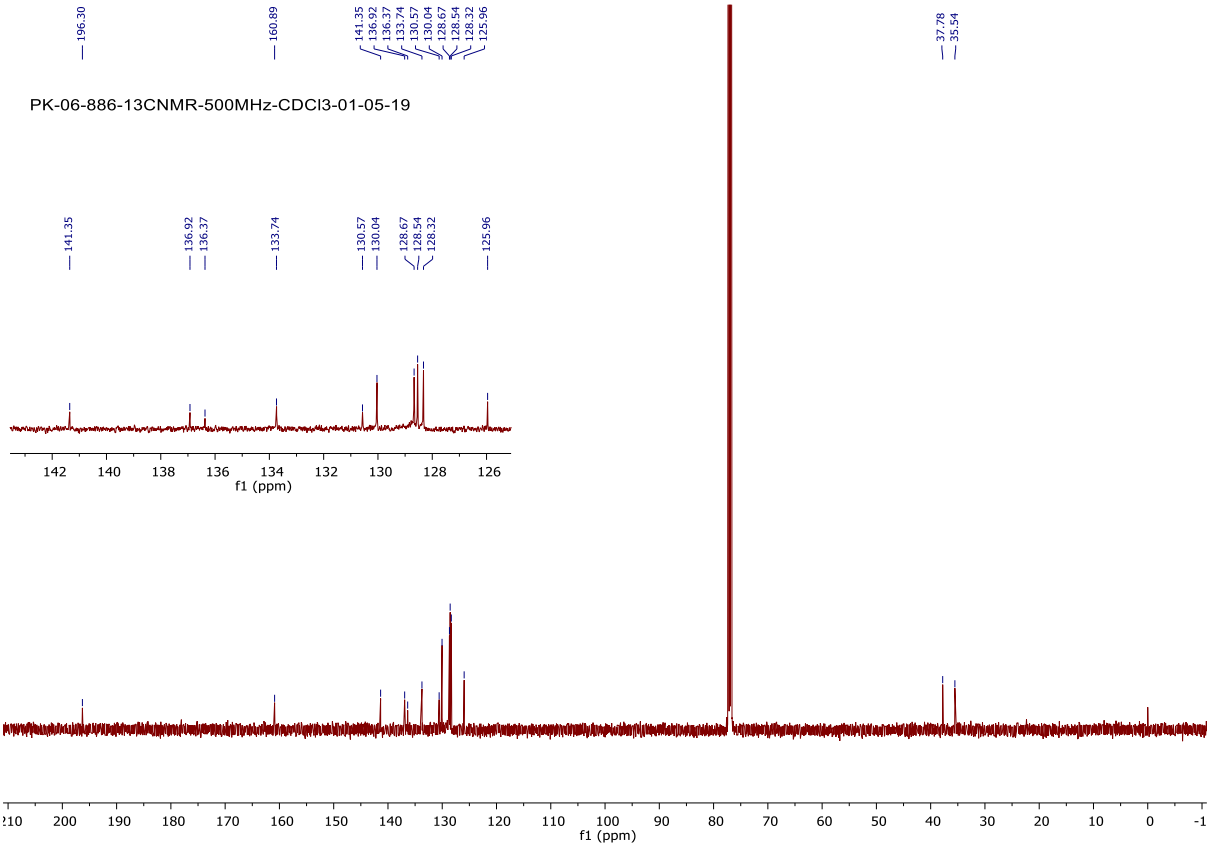
3m



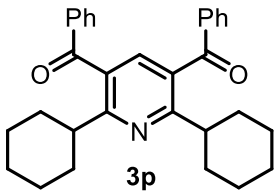
PK-06-870-13CNMR-500MHz-CDCl3-24-04-19



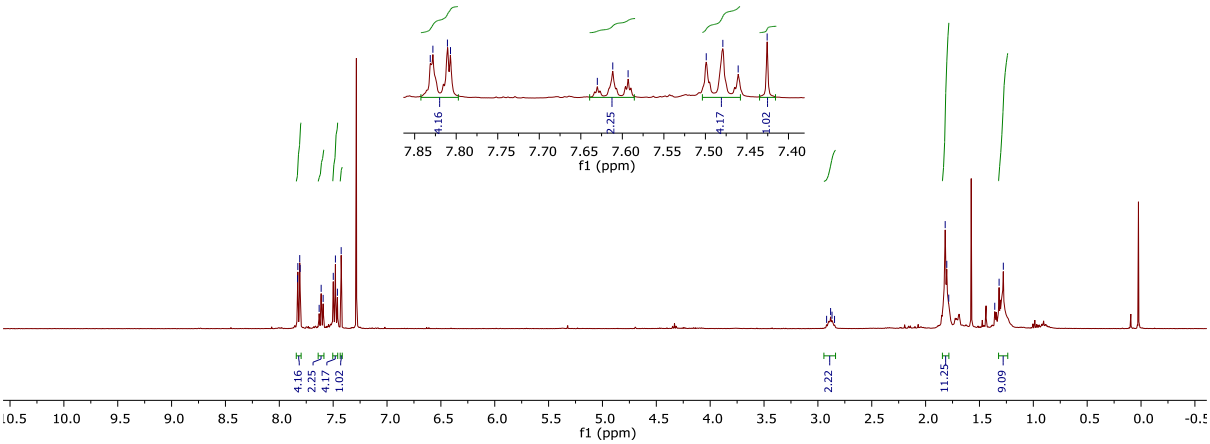

PK-06-886-1HNMR-400MHz-CDCl3-01-05-19
Ph
Ph
O
O
N
3o
f1 (ppm)


PK-06-886-13CNMR-500MHz-CDCl3-01-05-19
f1 (ppm)

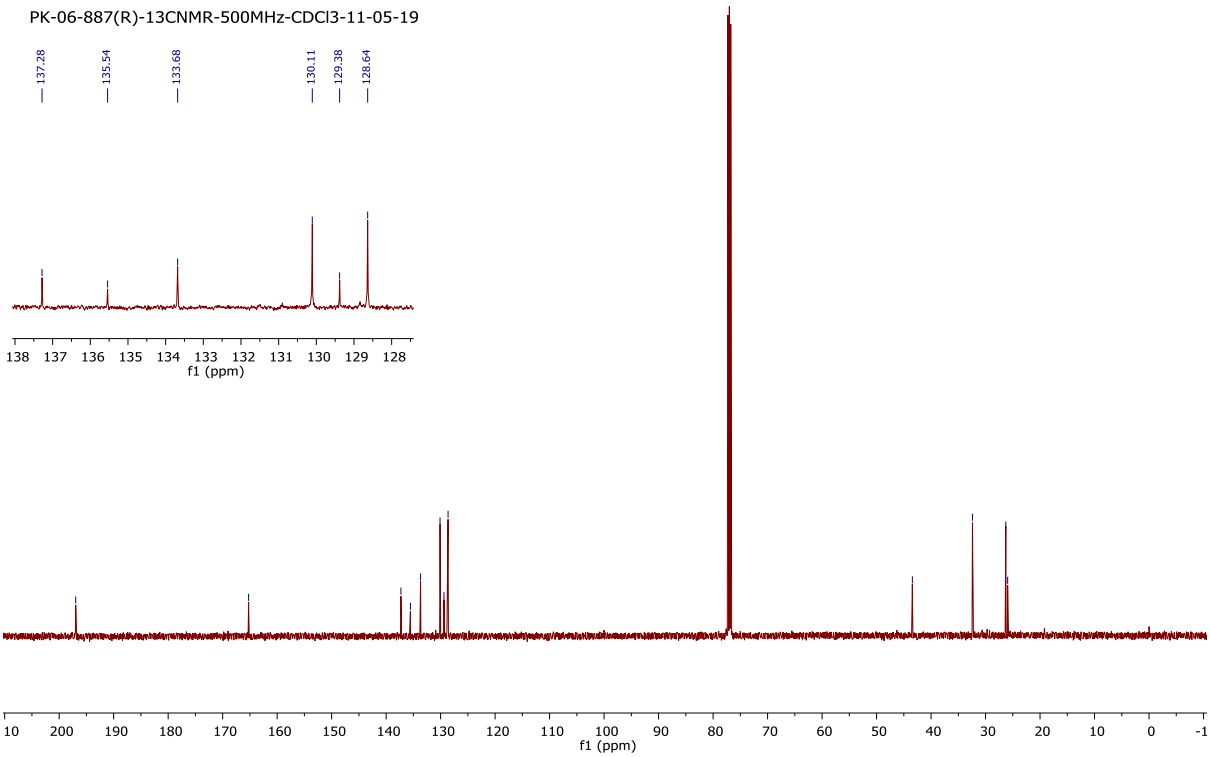
PK-06-887(4R)-1HMR-400MHz-CDCl3-11-05-19

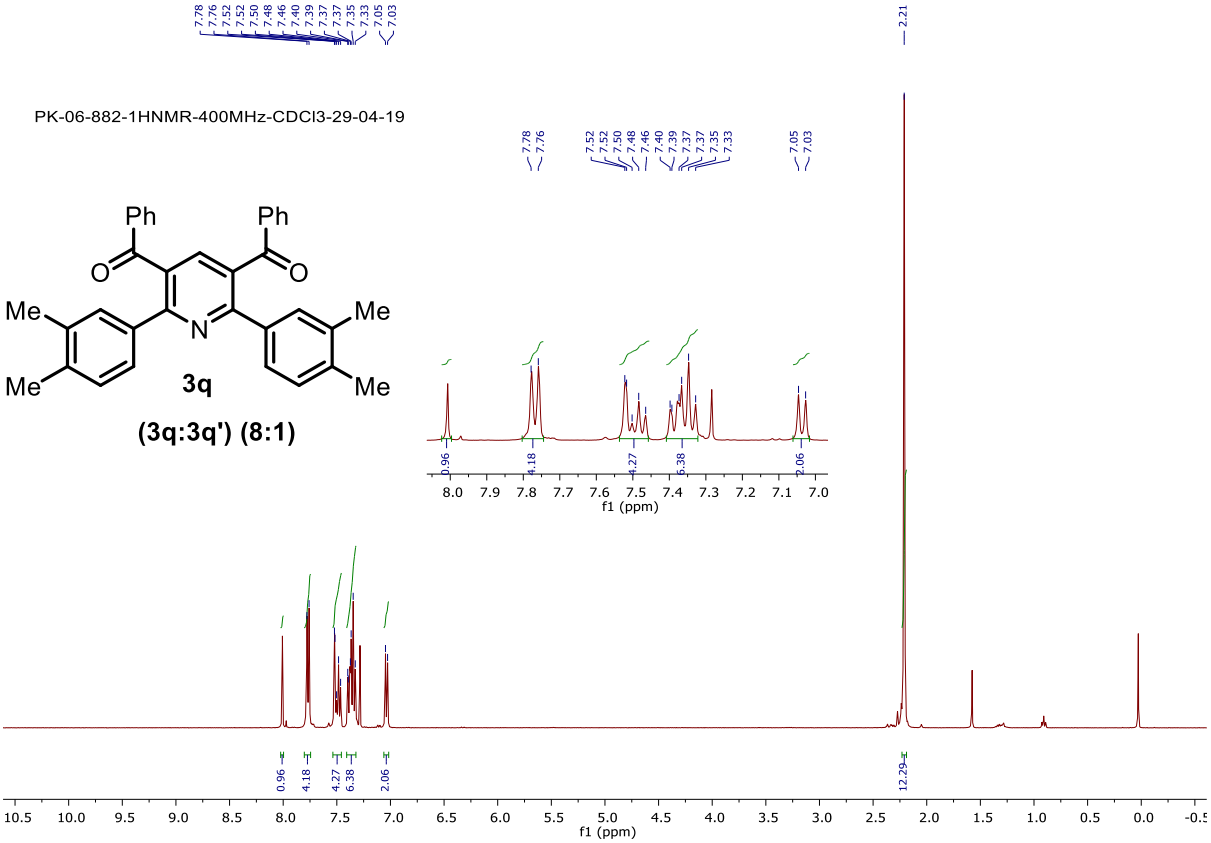


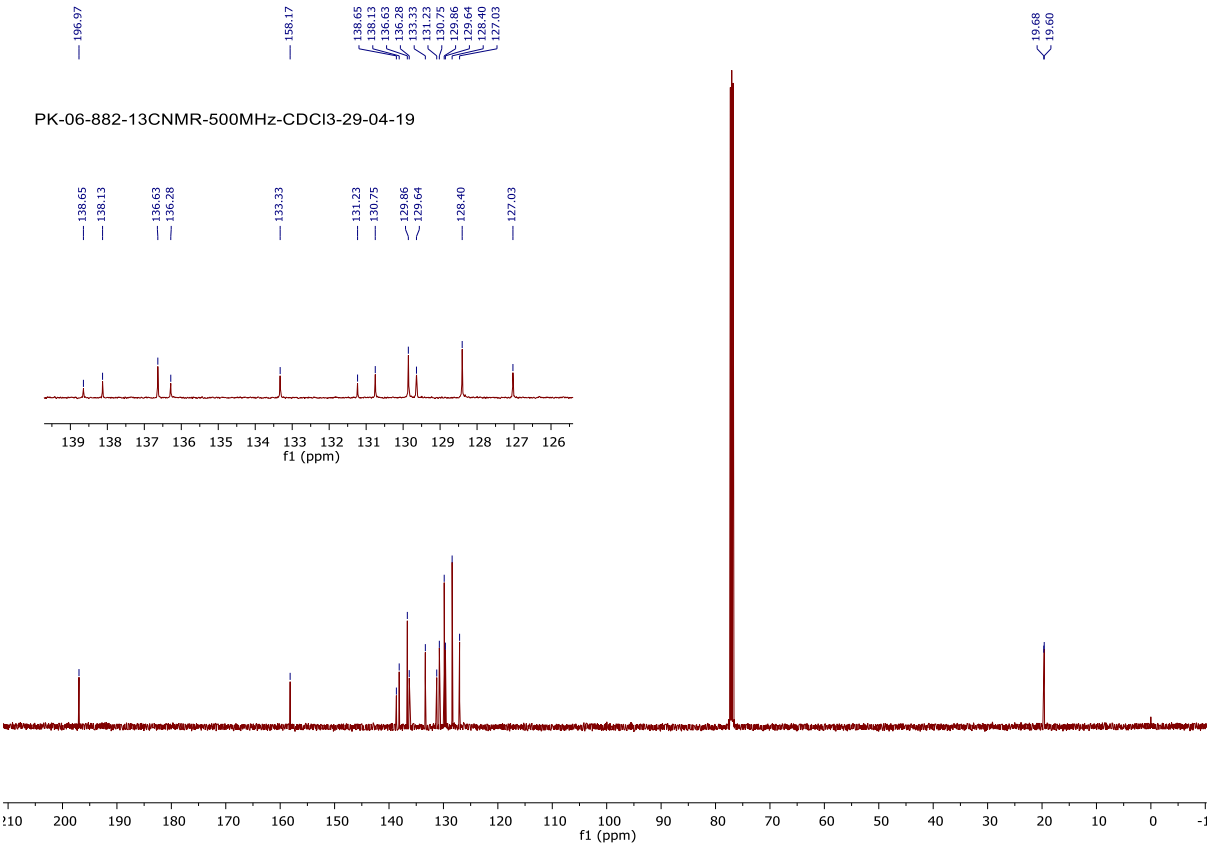
3p



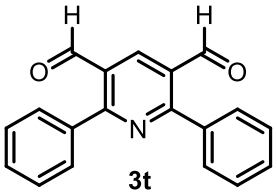
PK-06-887(R)-13CNMR-500MHz-CDCl3-11-05-19



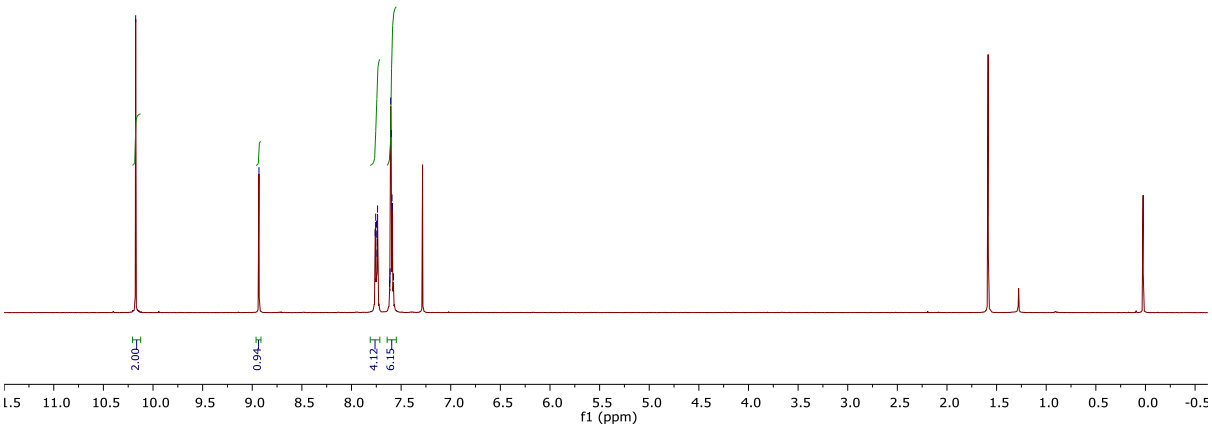

PK-06-882-1HNMR-400MHz-CDCl3-29-04-19
Ph
Ph
O
O
Me
Me
N
Me
Me
3q
(3q:3q') (8:1)
f1 (ppm)


PK-06-882-13CNMR-500MHz-CDCl3-29-04-19
f1 (ppm)

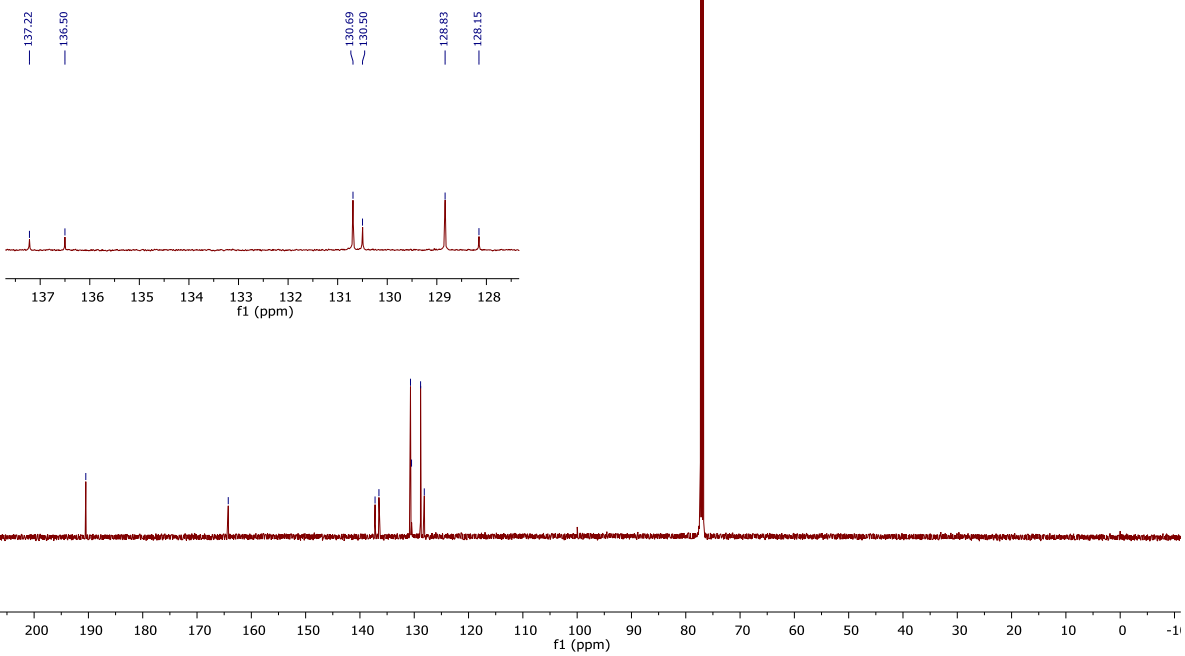
PK-06-904-1HNMR-400MHz-CDCl3-13-06-19

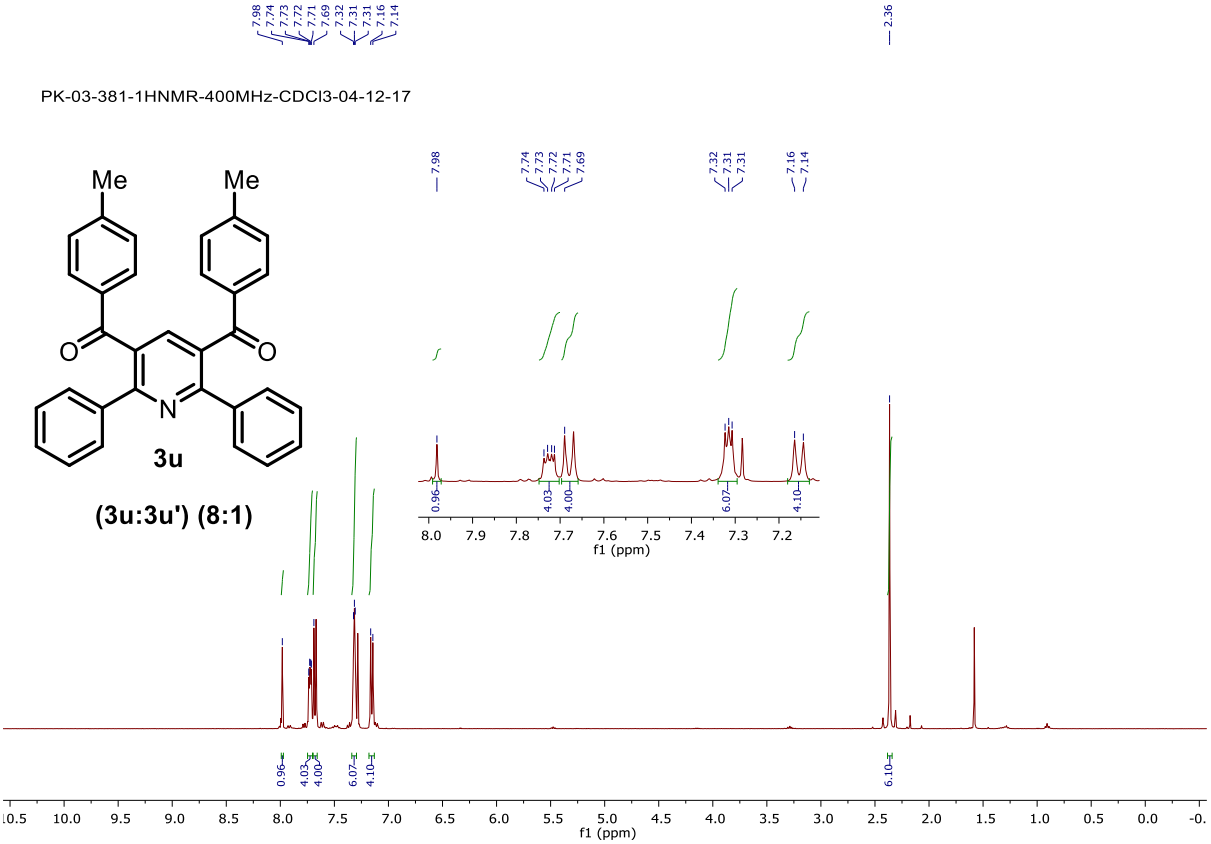


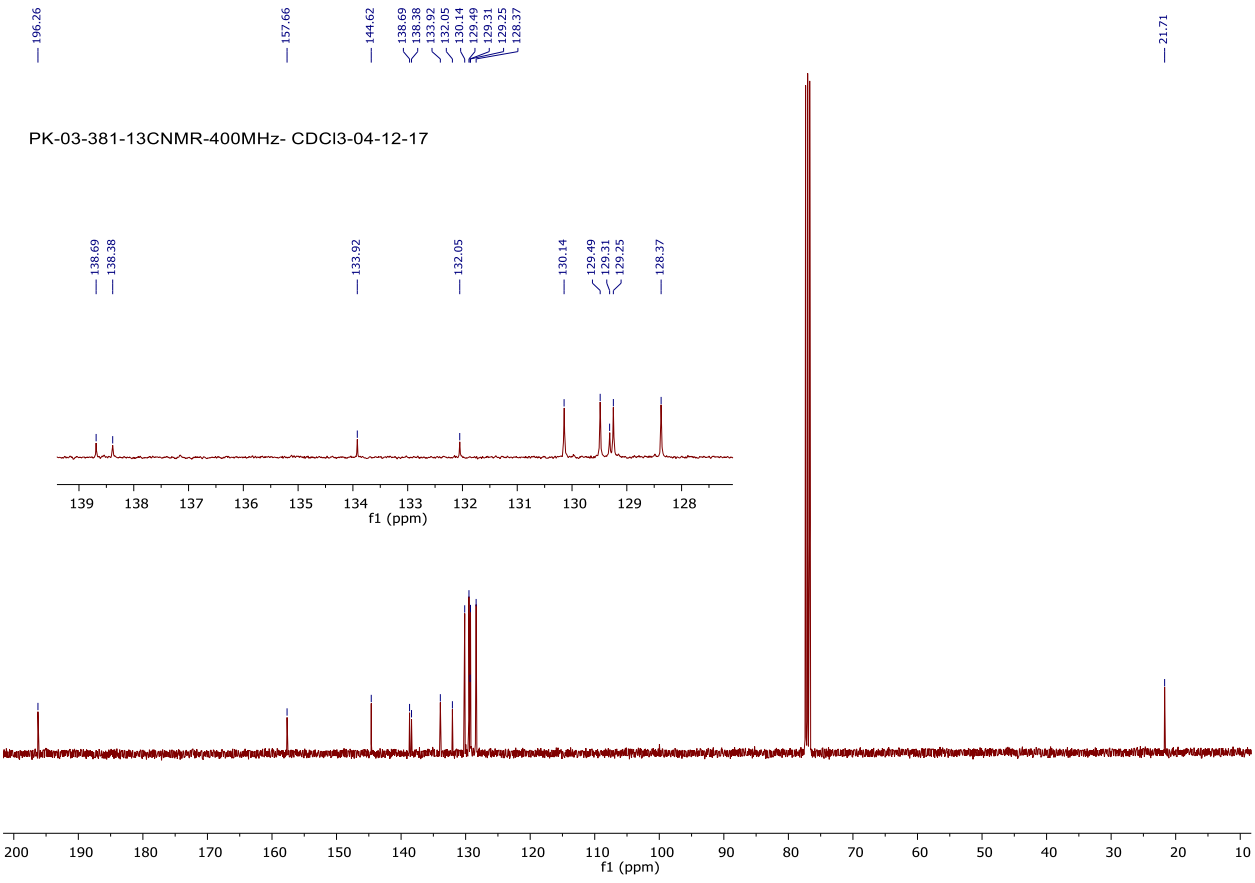
3t

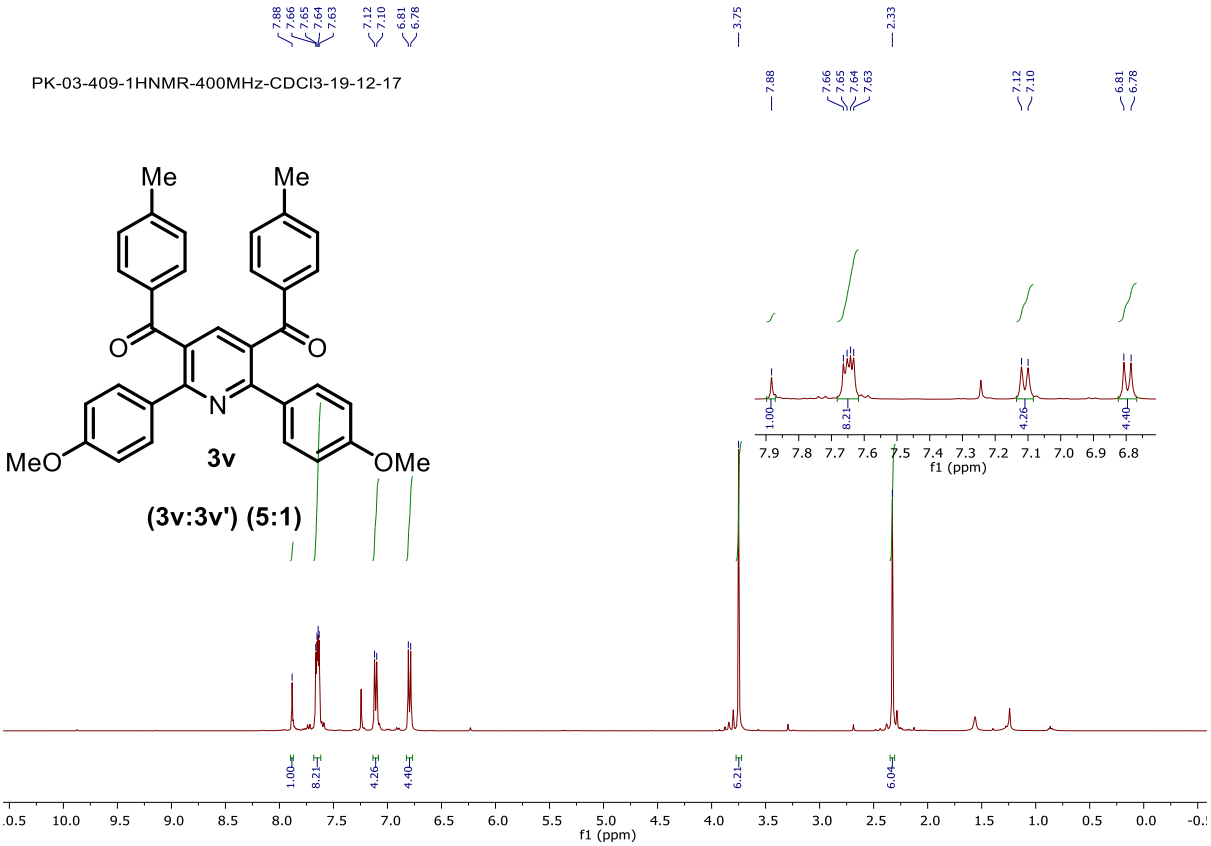


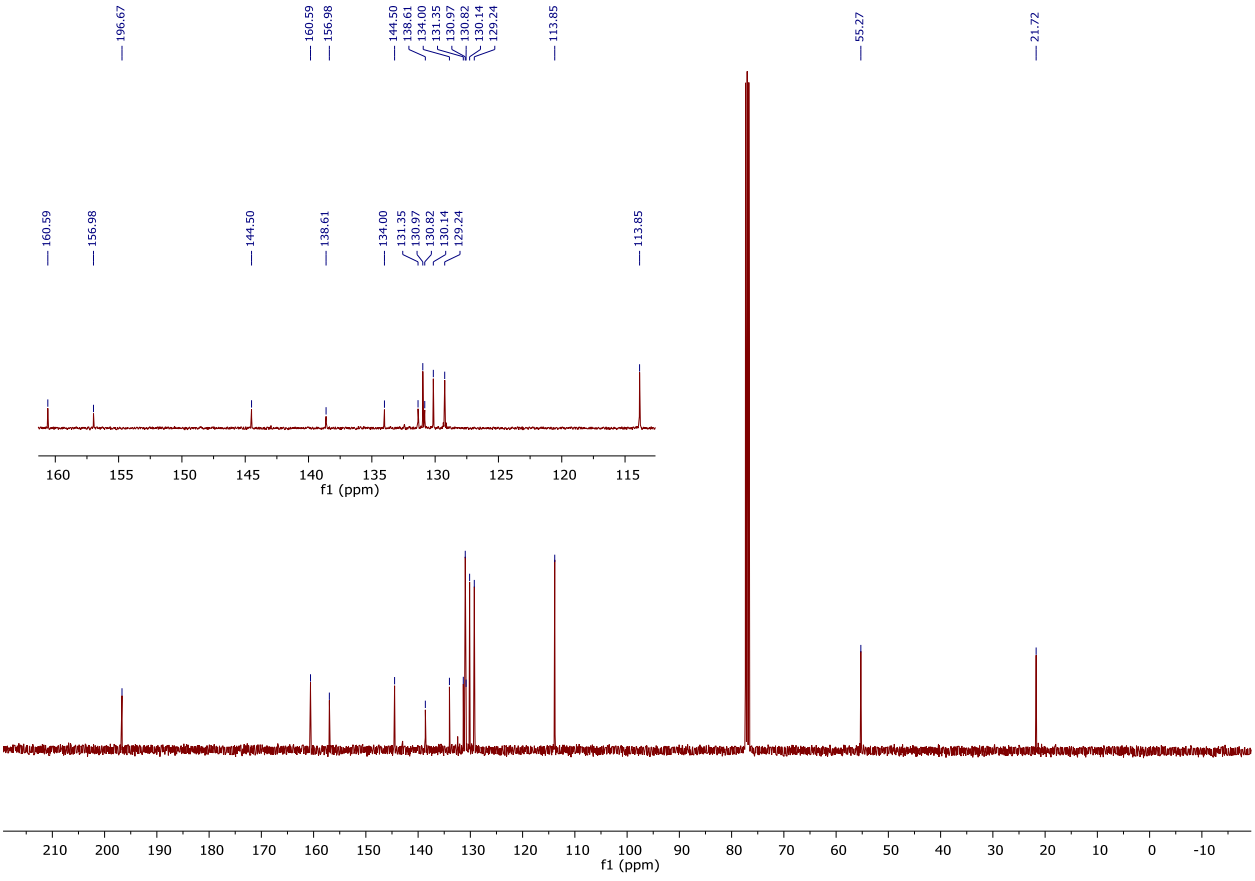
PK-06-904-13CNMR-500MHz-CDCl3-13-06-19



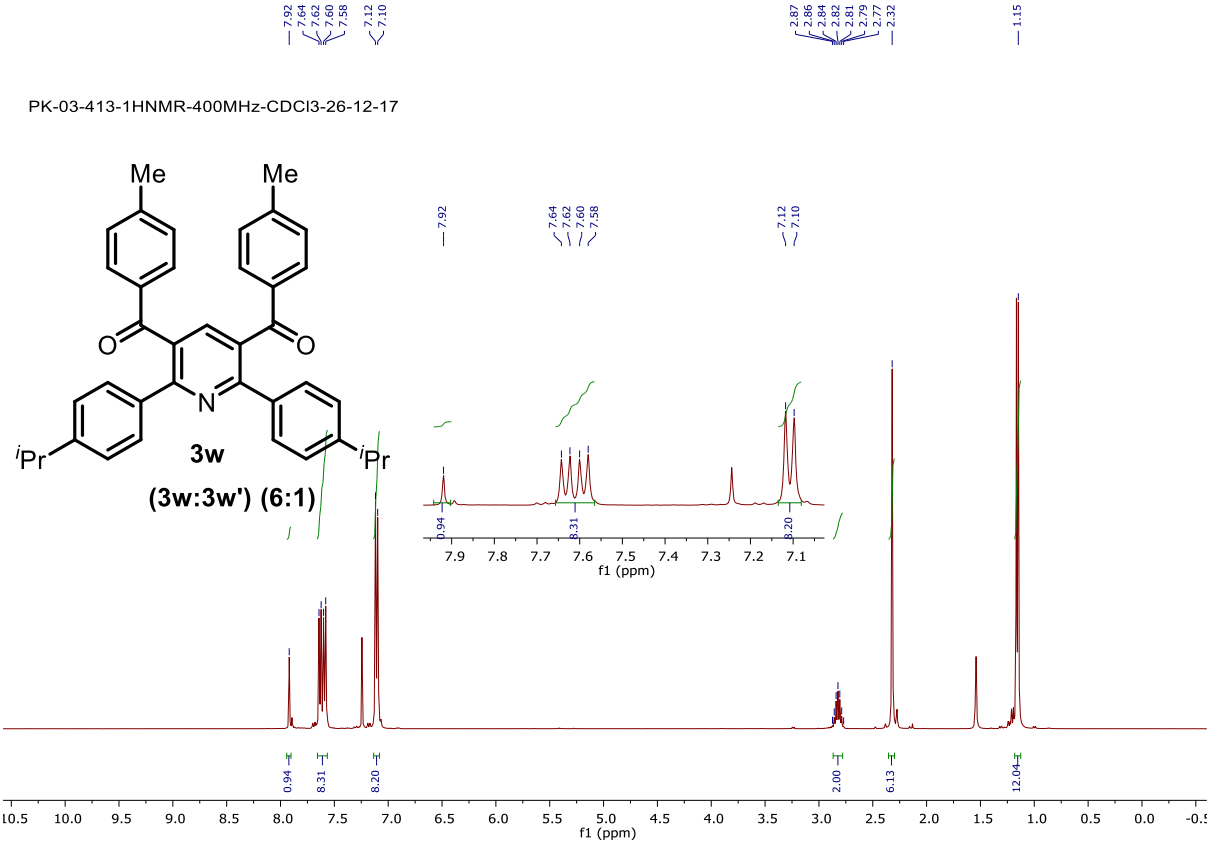

PK-03-381-1HNMR-400MHz-CDCl3-04-12-17
Me
Me
O
O
N
3u
(3u:3u') (8:1)
f1 (ppm)


PK-03-381-13CNMR-400MHz- CDCl3-04-12-17
f1 (ppm)

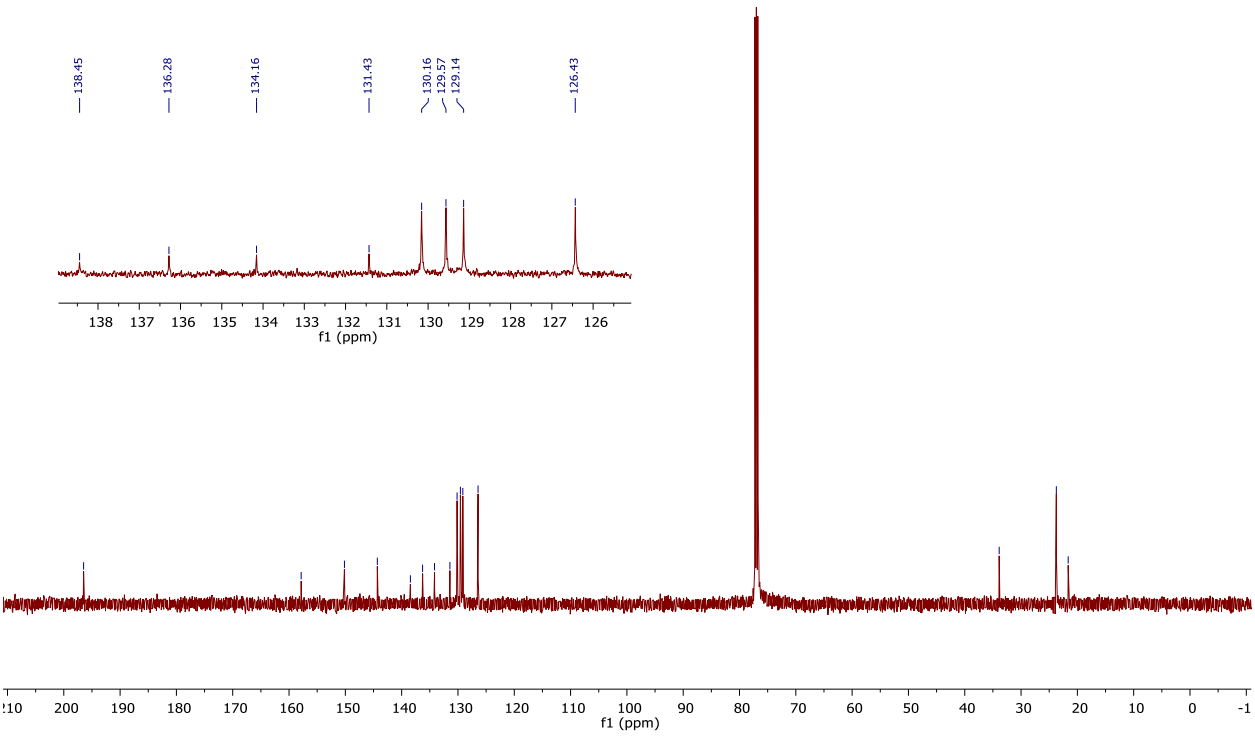

PK-03-409-1HNMR-400MHz-CDCl3-19-12-17
Me
Me
O
O
N
MeO
OMe
3v
(3v:3v') (5:1)
f1 (ppm)

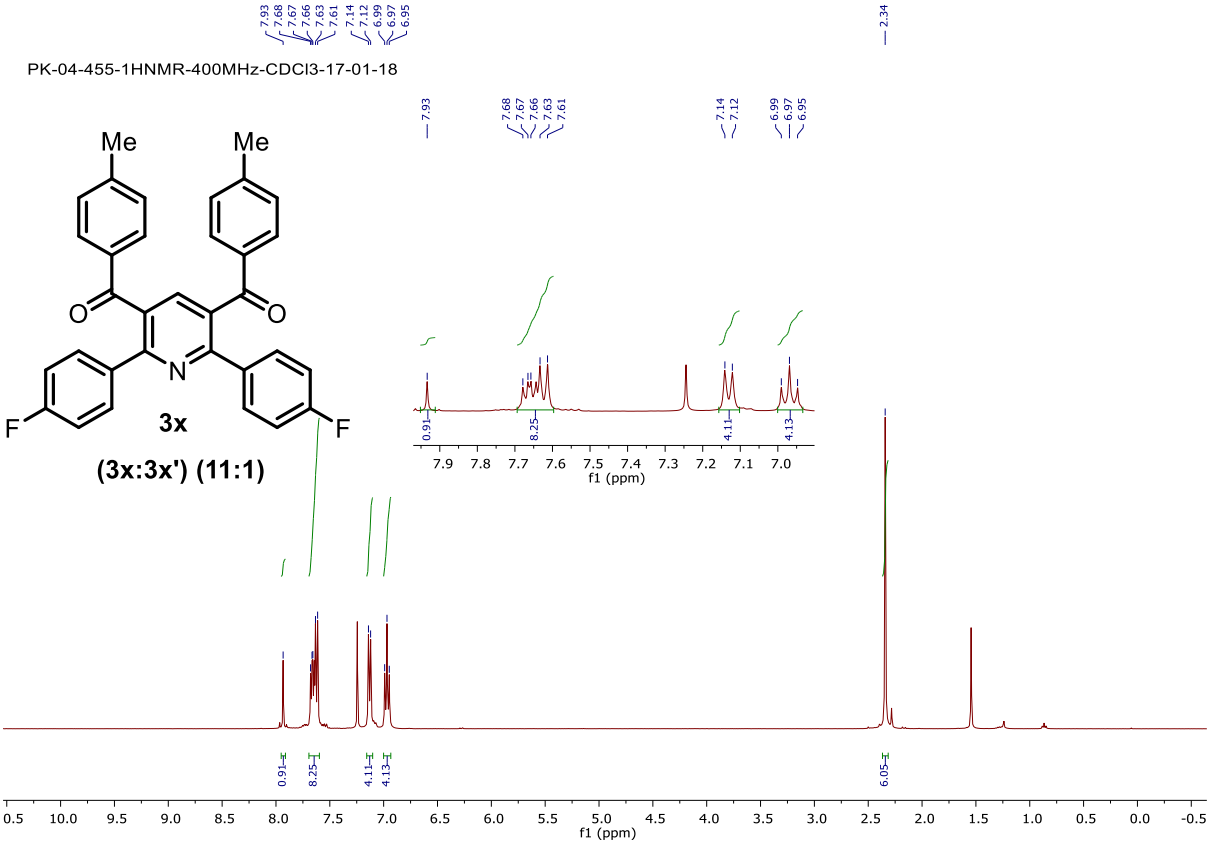

f1 (ppm)

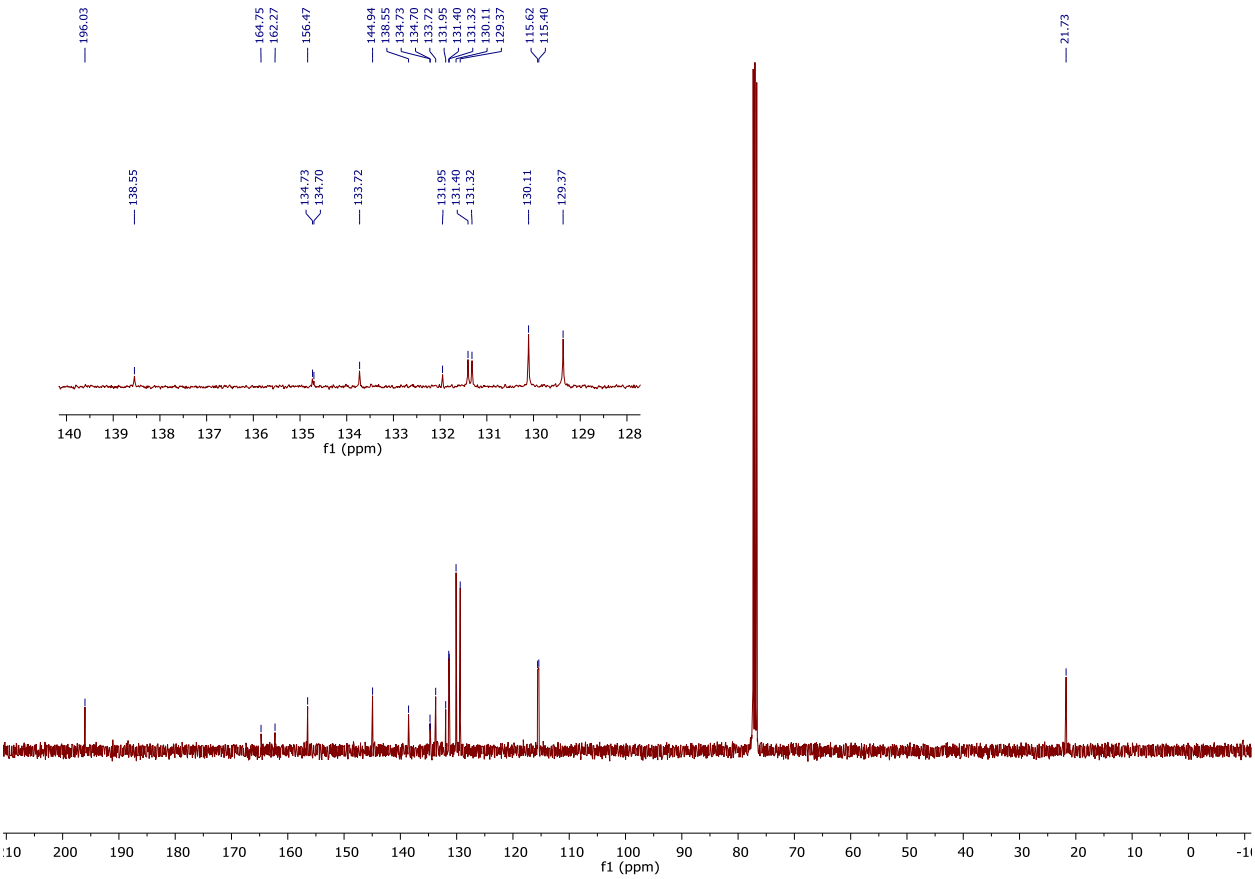
PK-03-413-1HNMR-400MHz-CDCl3-26-12-17

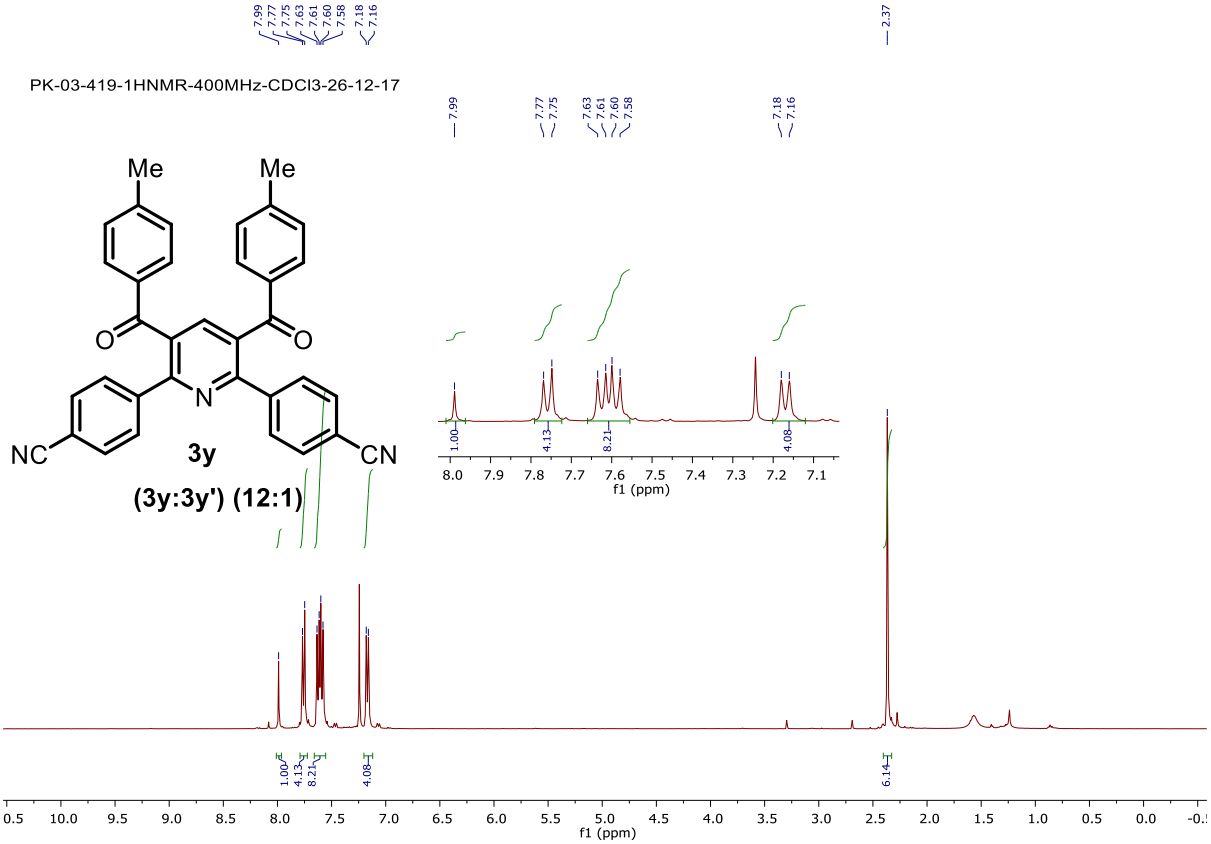


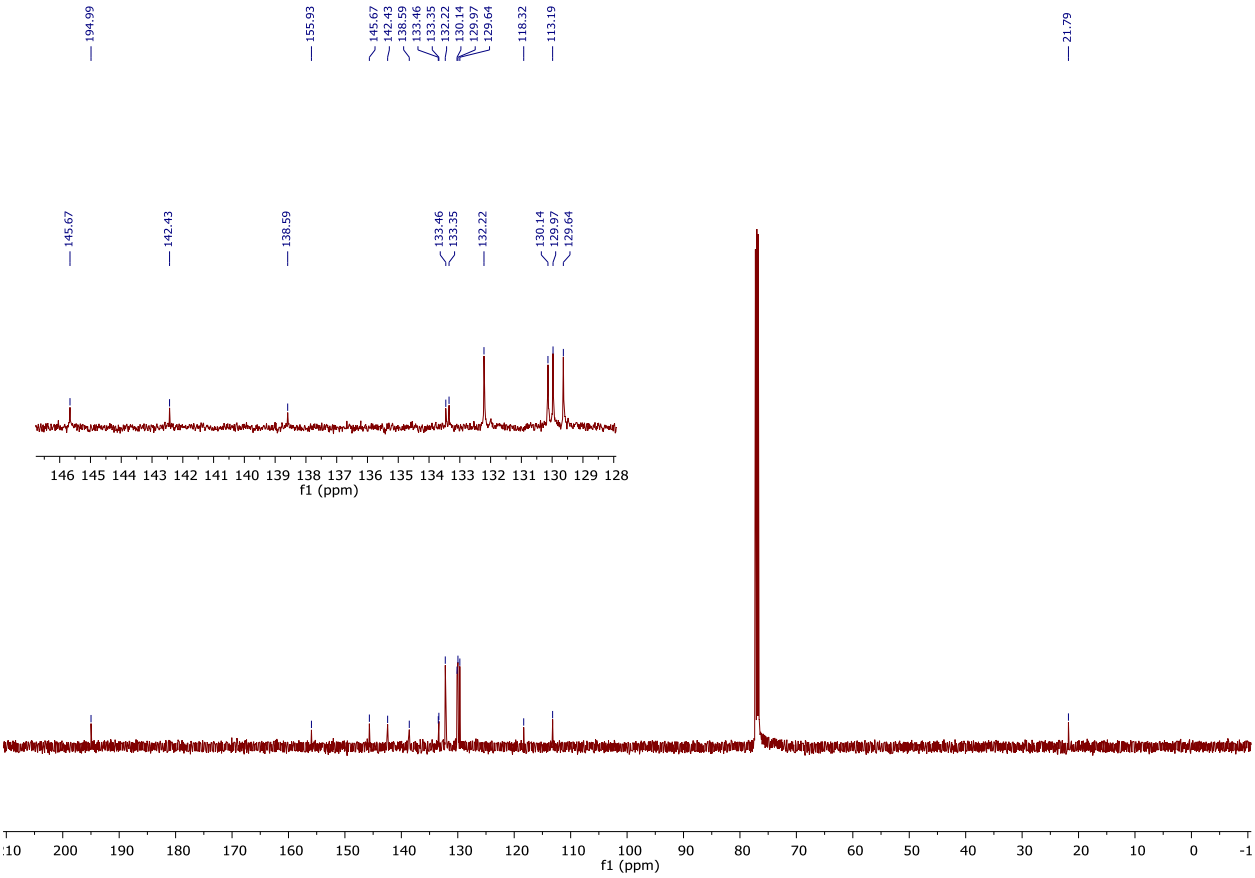
PK-03-413-13CNMR-400MHz-CDCl3-26-12-17

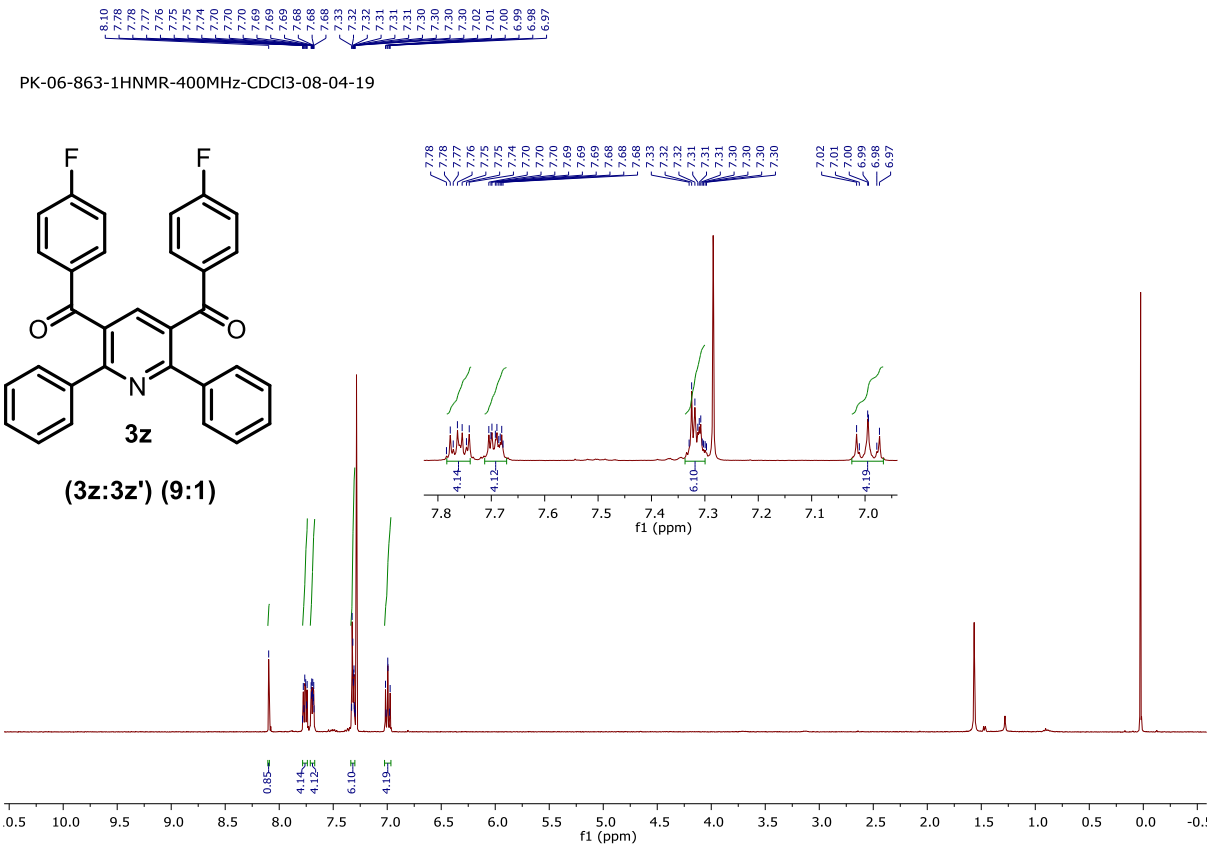


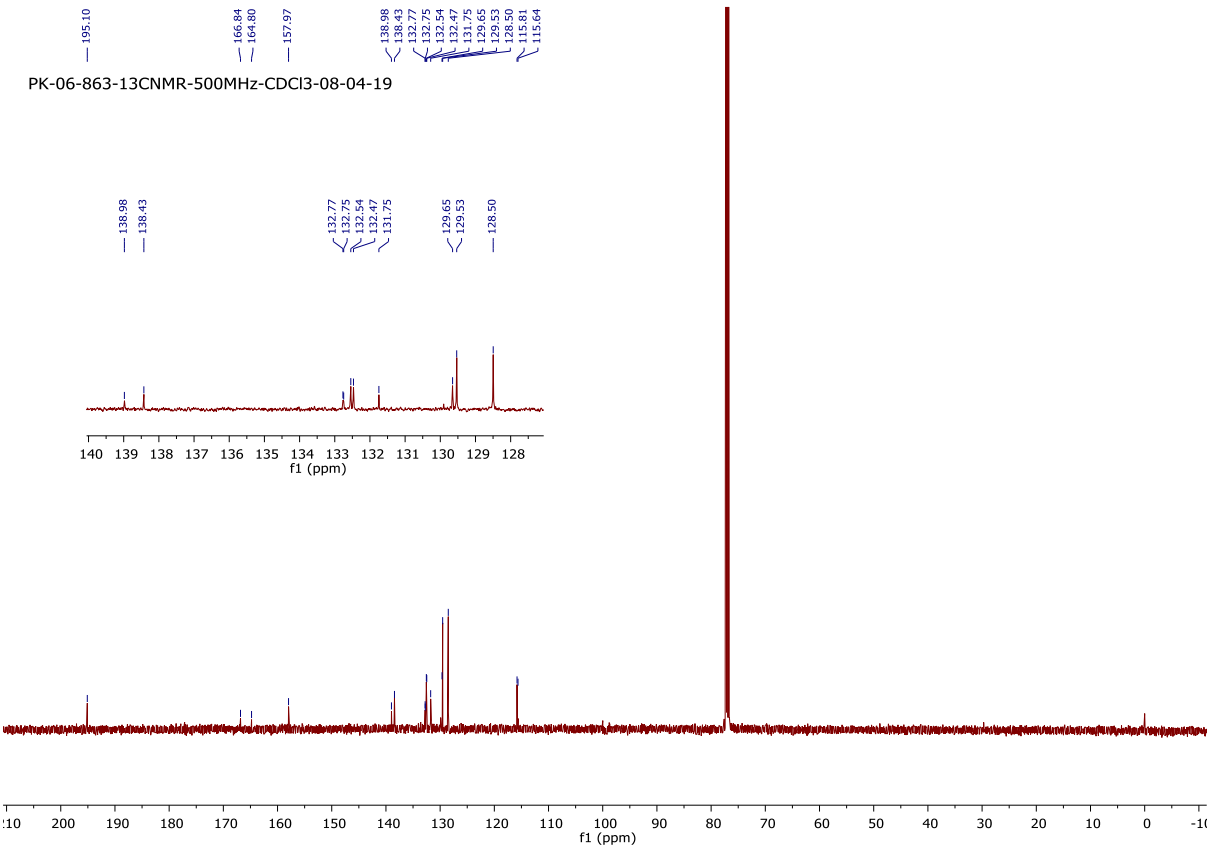

PK-04-455-1HNMR-400MHz-CDCl3-17-01-18
Me
Me
O
O
N
F
F
3x
(3x:3x') (11:1)
f1 (ppm)

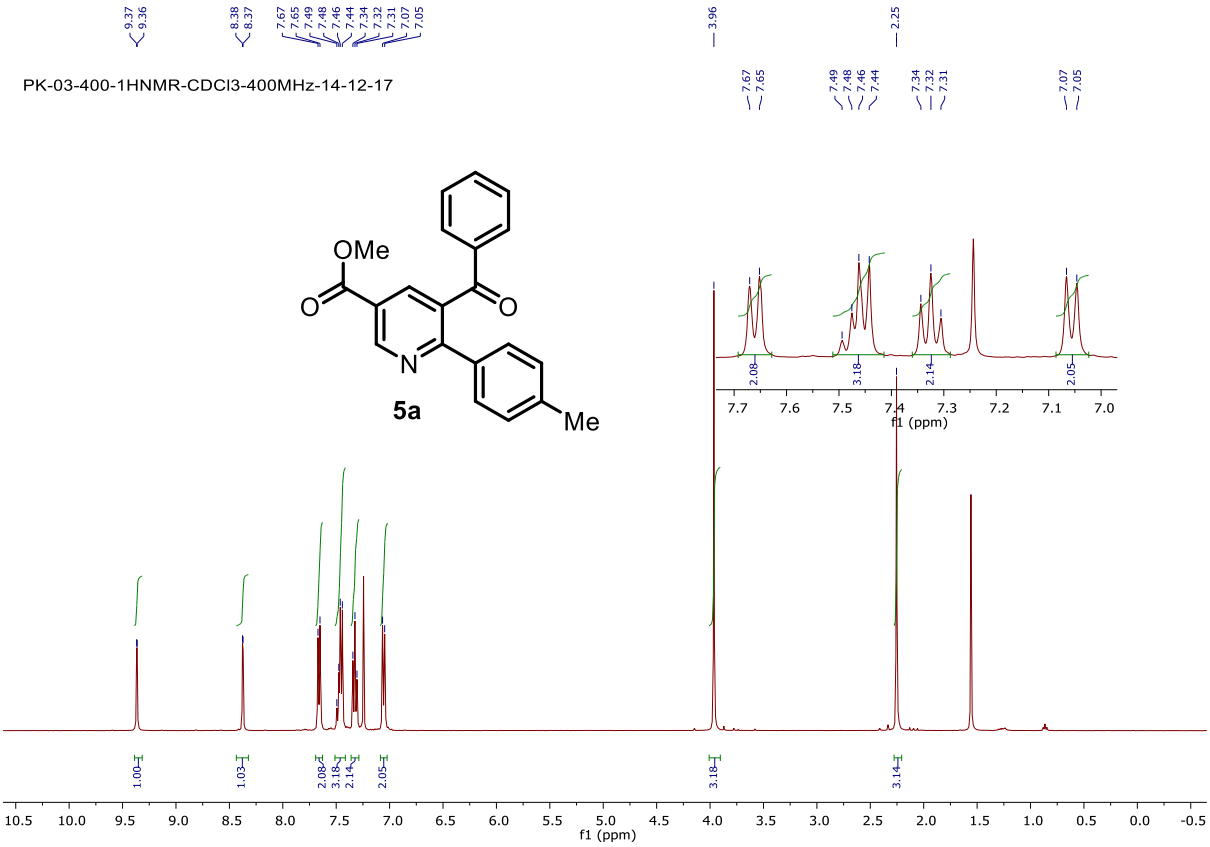

f1 (ppm)

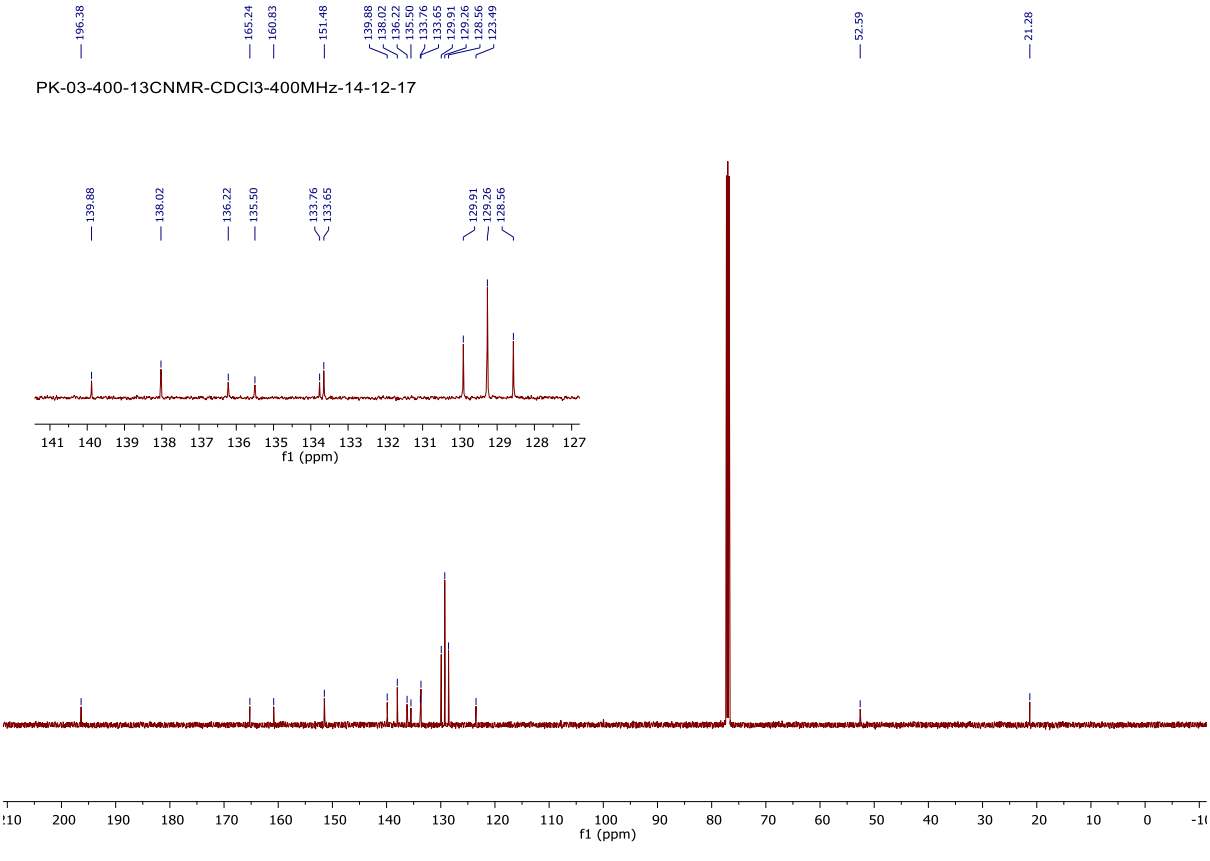

PK-03-419-1HNMR-400MHz-CDCl3-26-12-17
Me
Me
O
O
N
NC
CN
3y
(3y:3y') (12:1)
f1 (ppm)

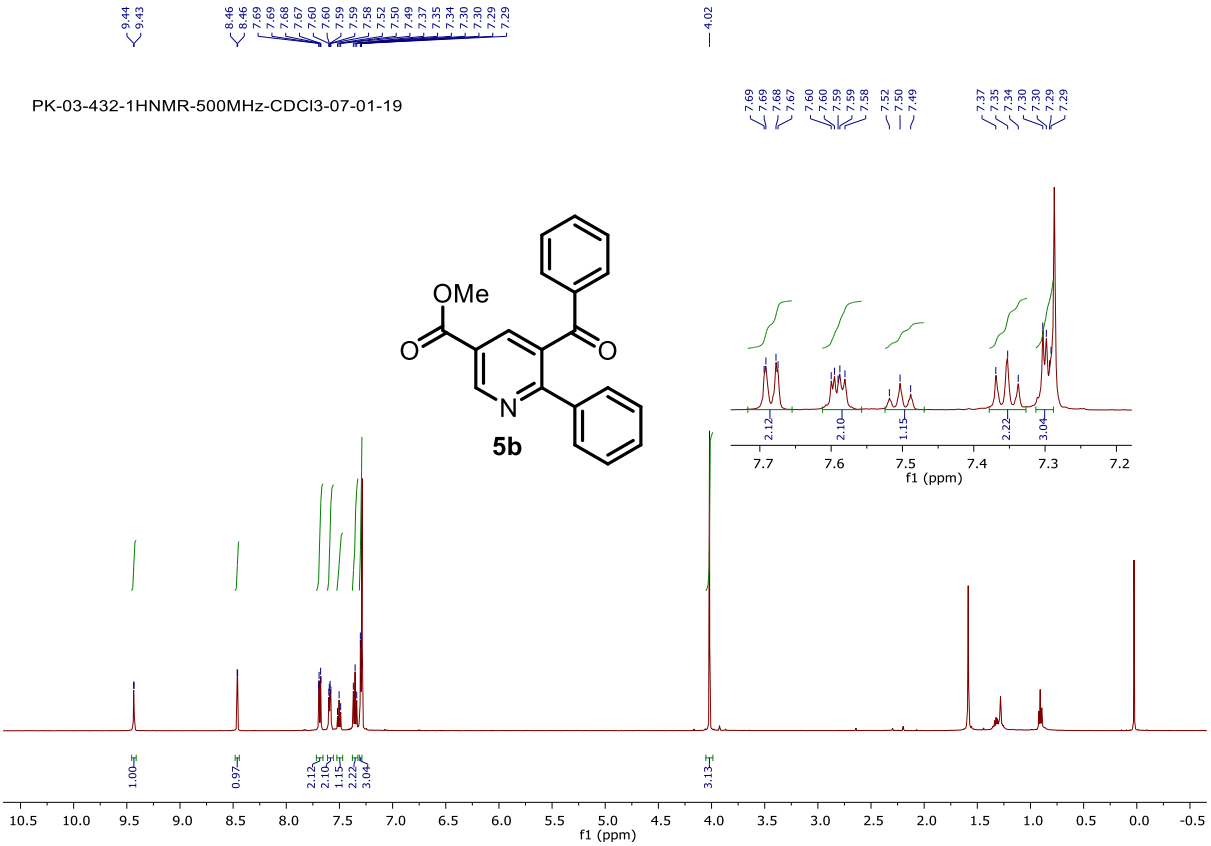

f1 (ppm)

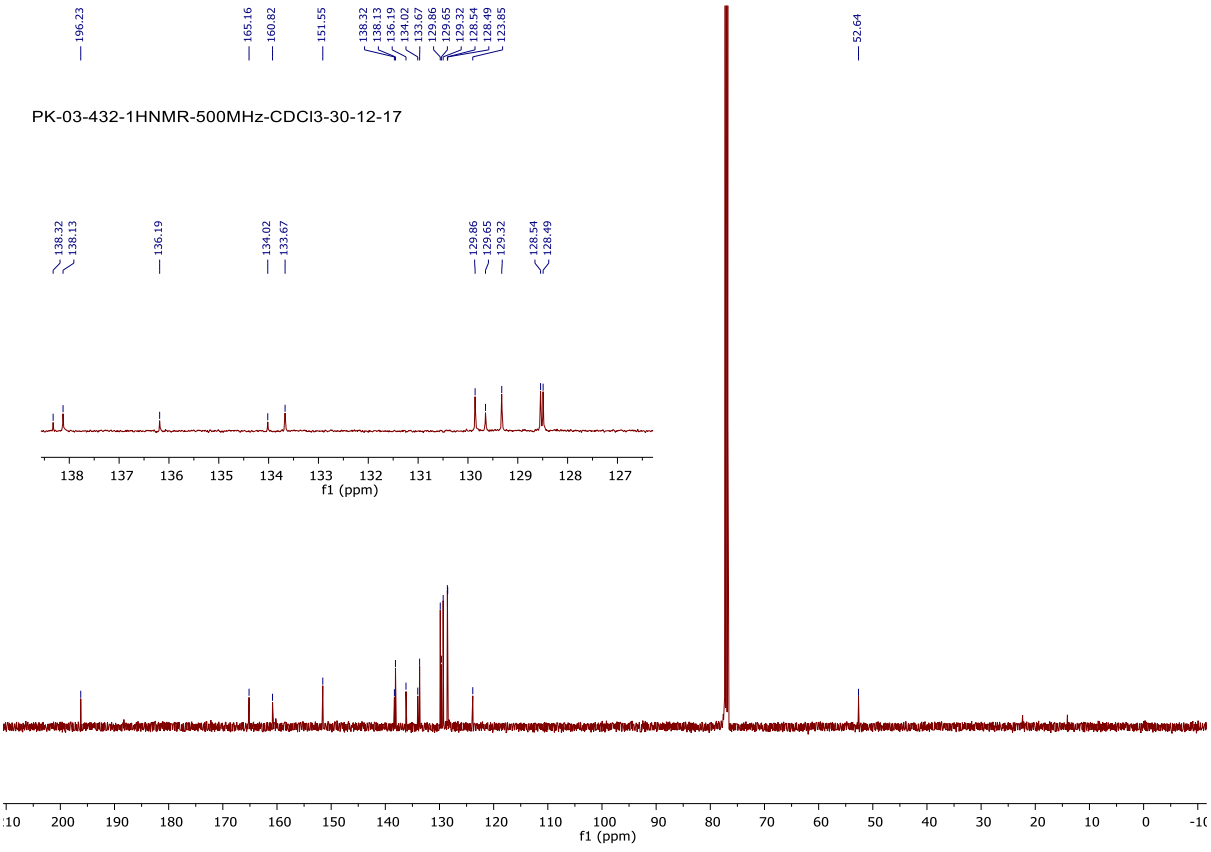

PK-06-863-1HNMR-400MHz-CDCl3-08-04-19
3z
(3z:3z') (9:1)
f1 (ppm)


PK-06-863-13CNMR-500MHz-CDCl3-08-04-19
f1 (ppm)

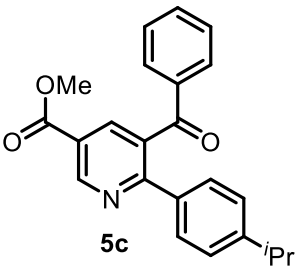

9.37
9.36
8.38
8.37
7.67
7.65
7.49
7.48
7.46
7.44
7.34
7.32
7.31
7.07
7.05
3.96
2.25
PK-03-400-1HNMR-CDCl3-400MHz-14-12-17
OMe
O
O
N
Me
5a
2.08
3.18
2.14
2.05
f1 (ppm)
1.00
1.03
3.18
3.14


196.38
165.24
160.83
151.48
139.88
138.02
136.22
135.50
133.76
133.65
129.91
129.26
128.56
123.49
52.59
21.28
PK-03-400-13CNMR-CDCl3-400MHz-14-12-17
f1 (ppm)

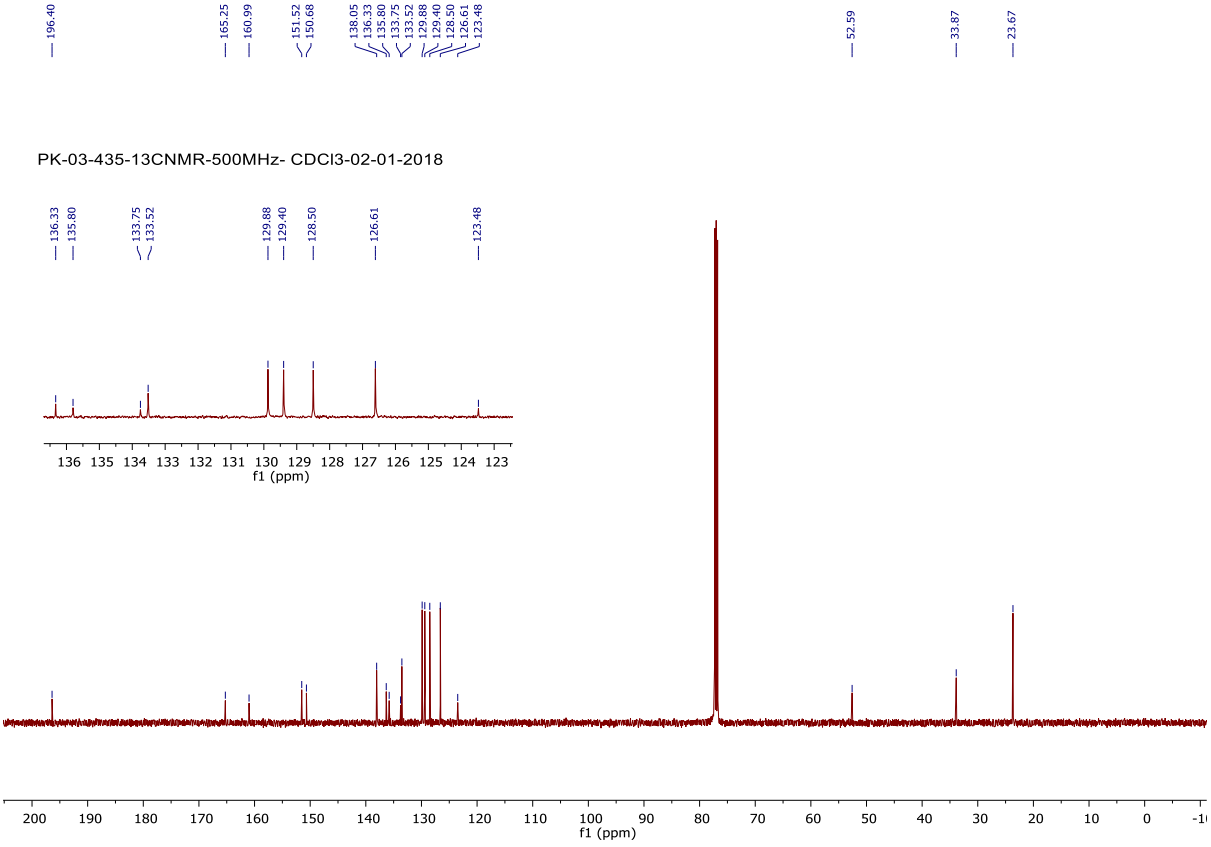

PK-03-432-1HNMR-500MHz-CDCl3-07-01-19
OMe
O
O
N
5b
f1 (ppm)

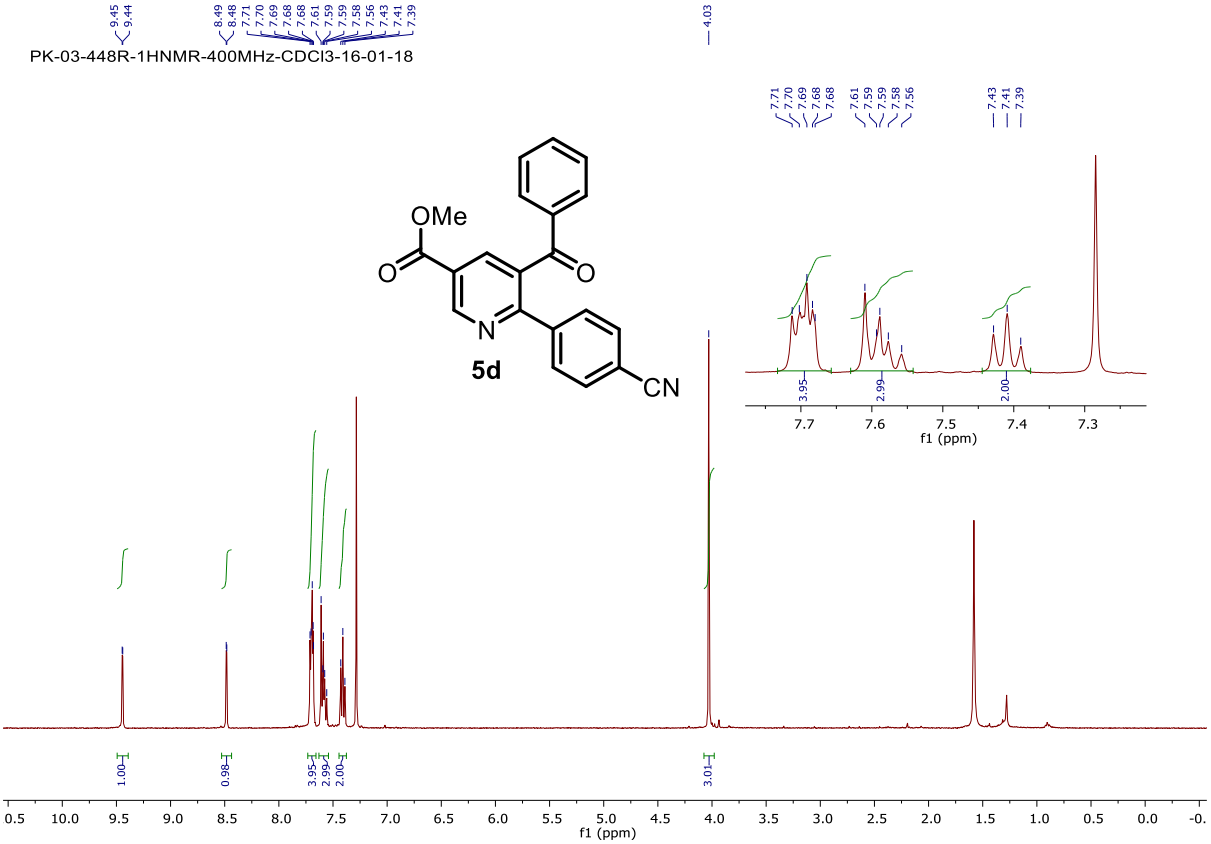

PK-03-432-1HNMR-500MHz-CDCl3-30-12-17
f1 (ppm)

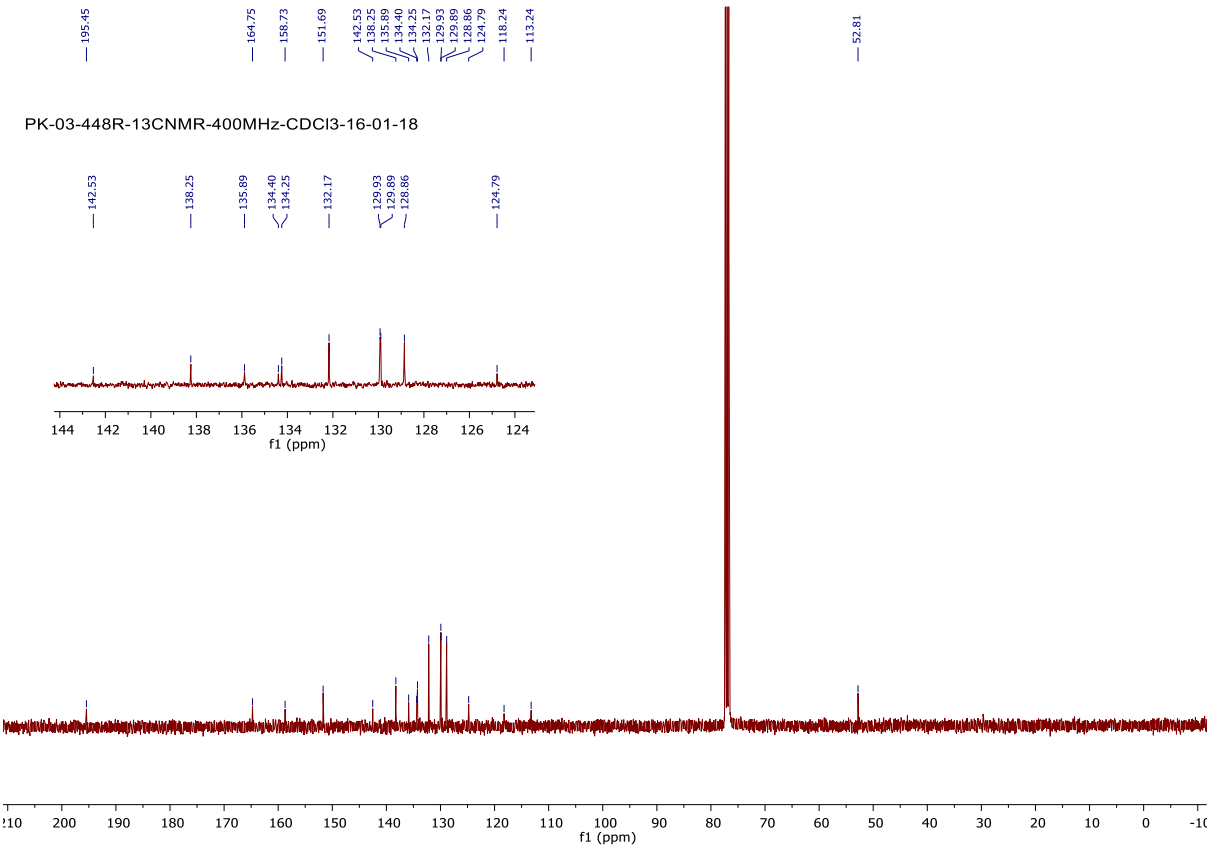
PK-03-435-1HNMR-400MHz-CDCl3-01-01-2018



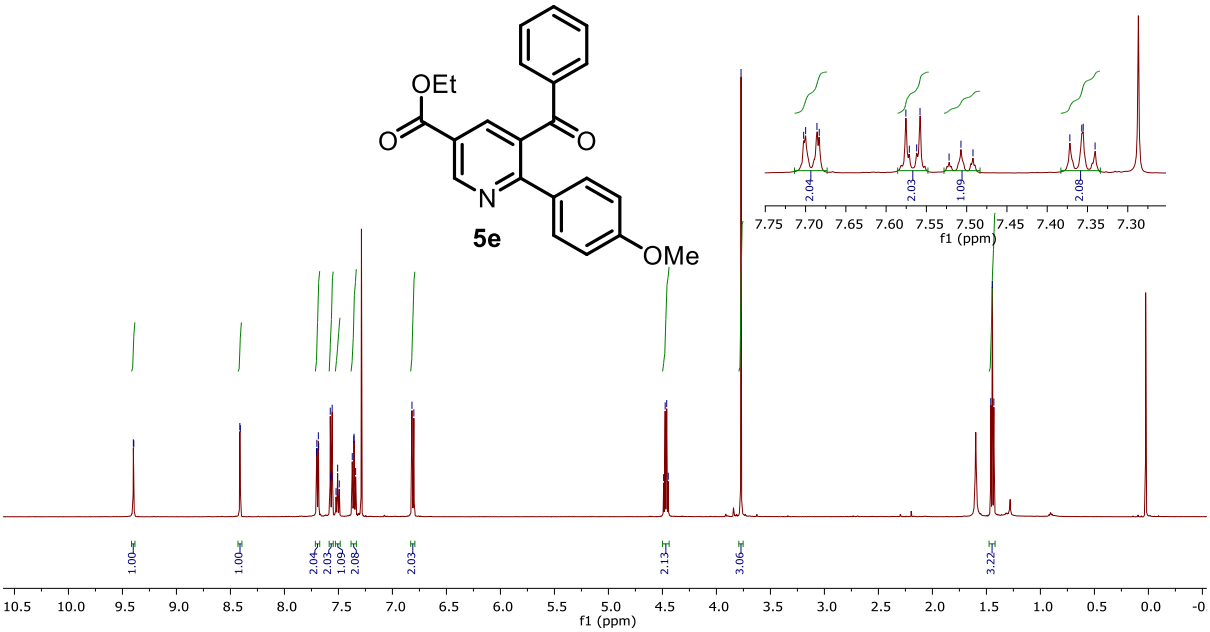
PK-03-435-13CNMR-500MHz- CDCl3-02-01-2018



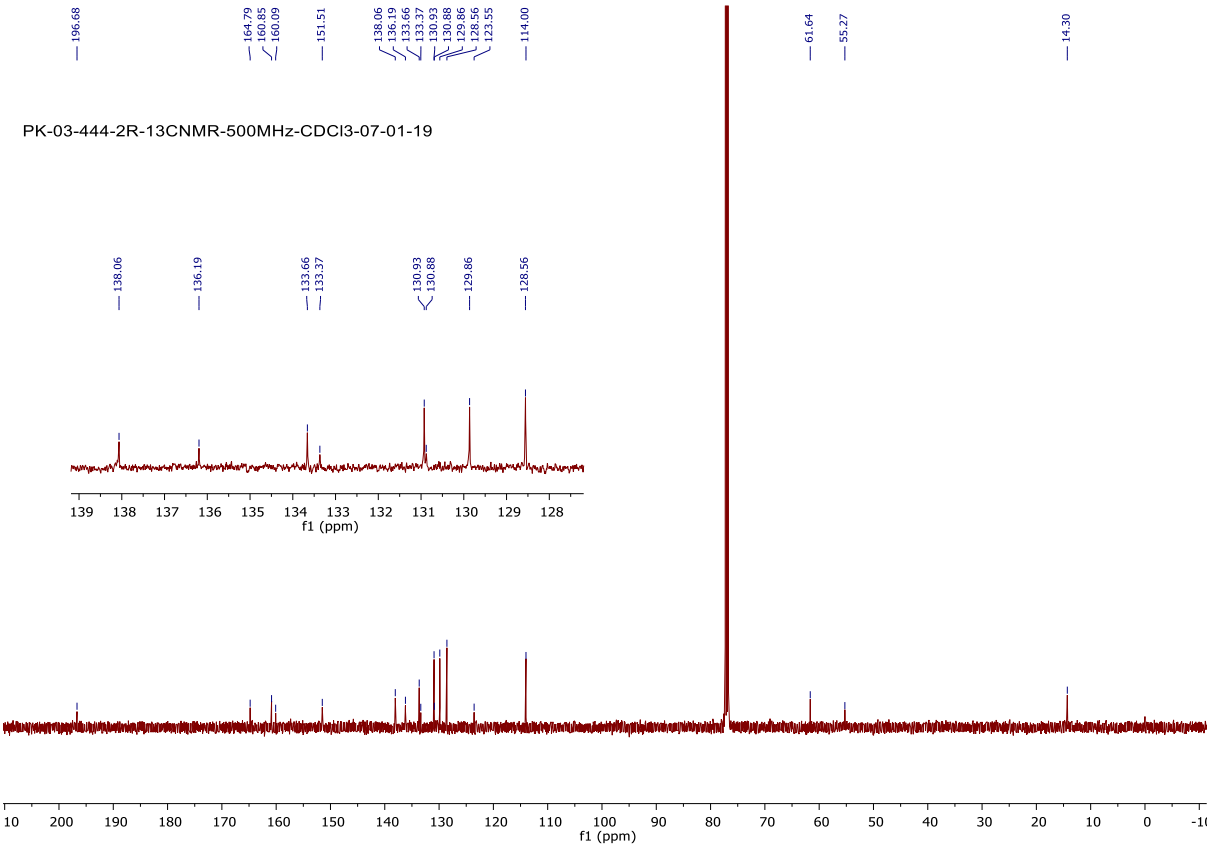

PK-03-448R-1HNMR-400MHz-CDCl3-16-01-18
9.45
9.44
8.49
8.48
7.71
7.70
7.69
7.68
7.68
7.61
7.59
7.59
7.58
7.56
7.43
7.41
7.39
4.03
OMe
O
O
N
5d
CN
1.00
0.98
3.95
2.99
2.00
3.01
f1 (ppm)


195.45
164.75
158.73
151.69
142.53
138.25
135.89
134.40
134.25
132.17
129.93
129.89
128.86
124.79
118.24
113.24
52.81
PK-03-448R-13CNMR-400MHz-CDCl3-16-01-18
f1 (ppm)

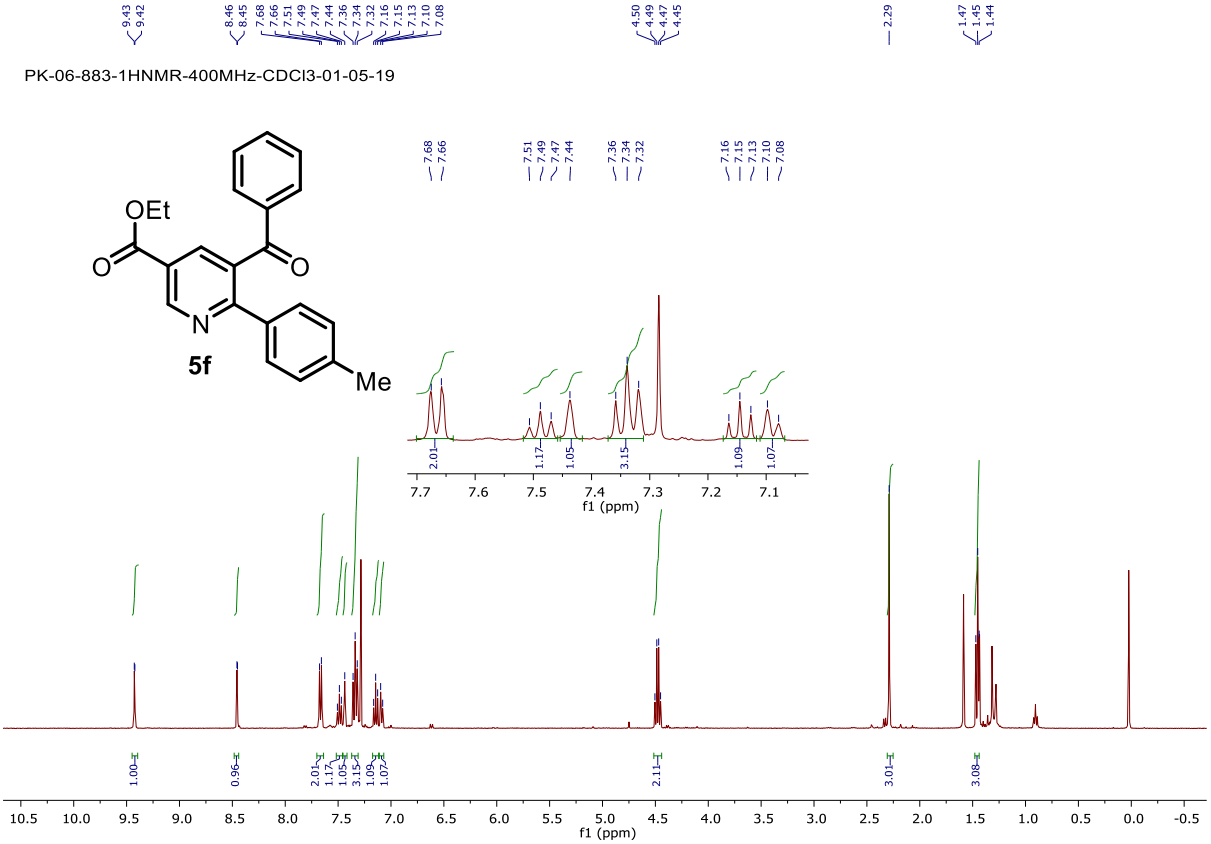
PK-03-444-2R-1HNMR-500MHz-CDCl3-07-01-19



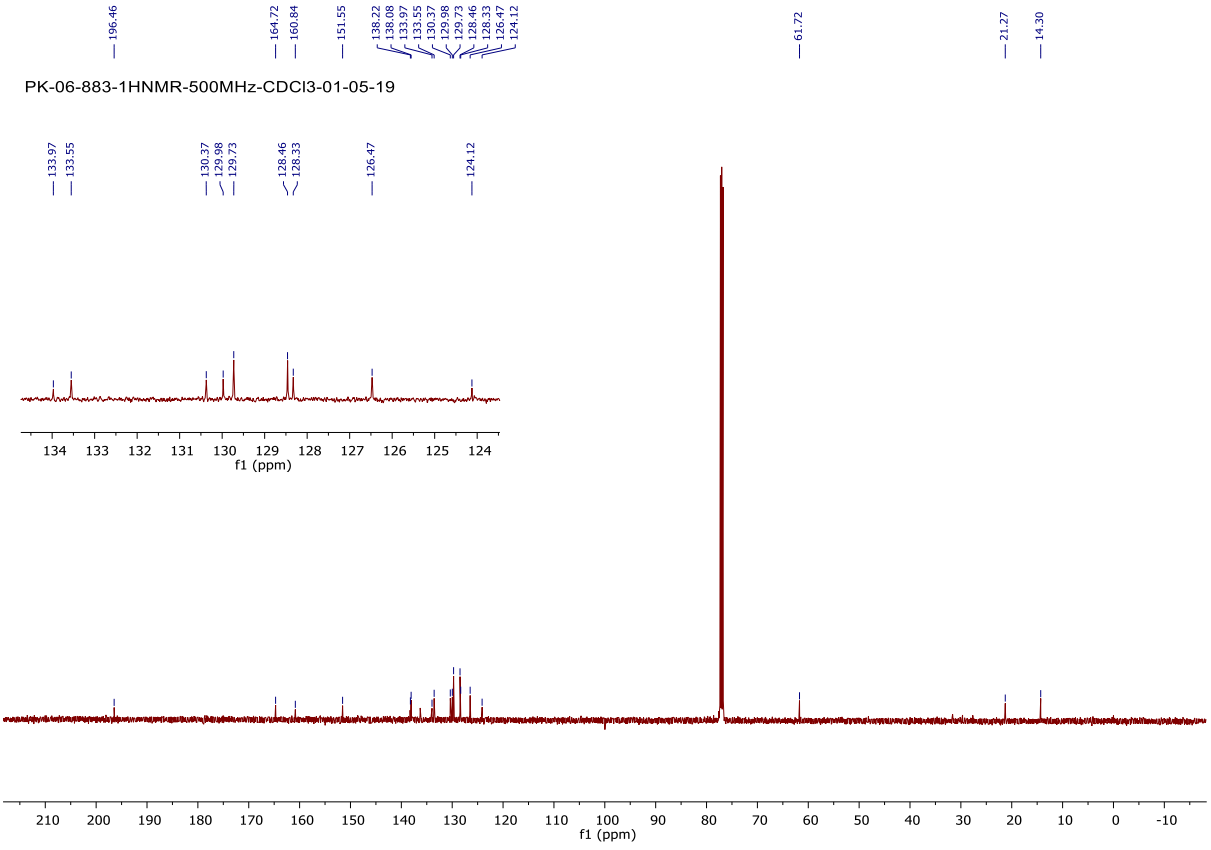
PK-03-444-2R-13CNMR-500MHz-CDCl3-07-01-19



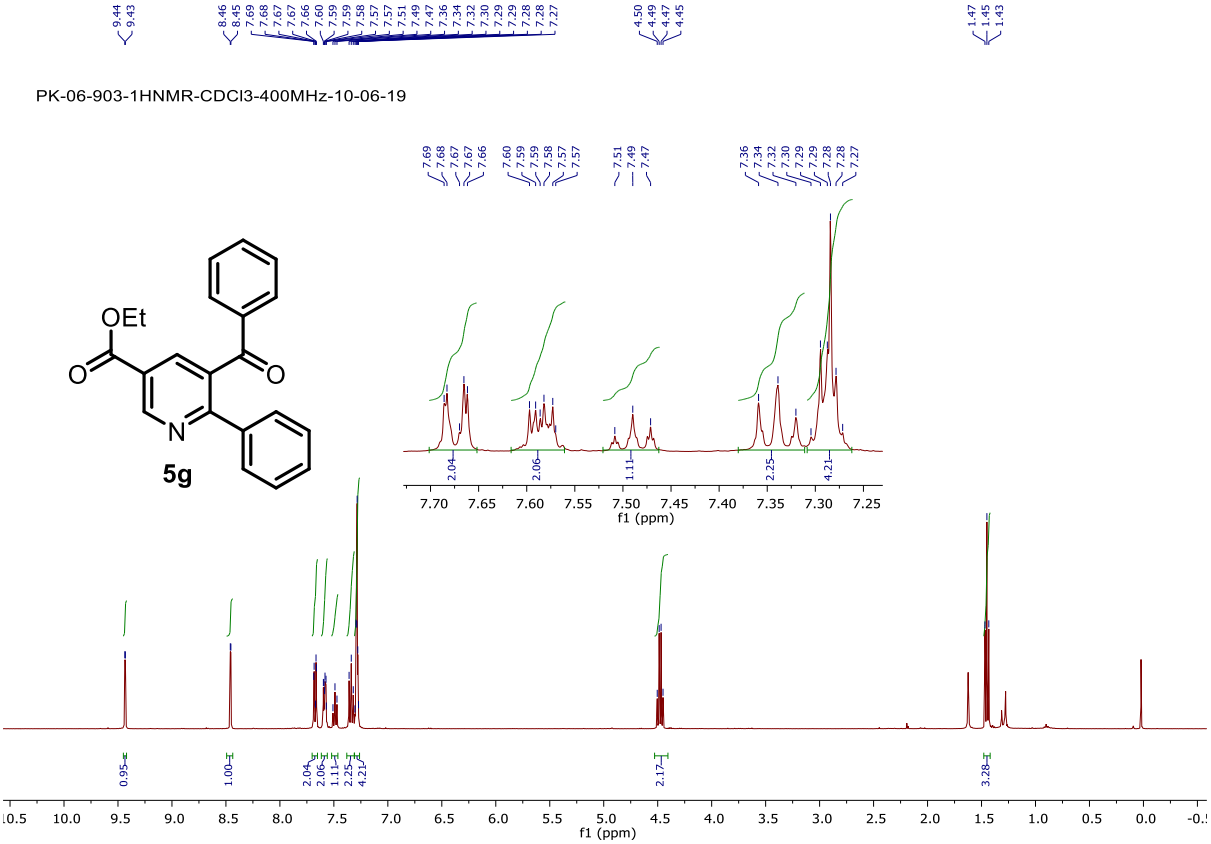
PK-06-883-1HNMR-400MHz-CDCl3-01-05-19



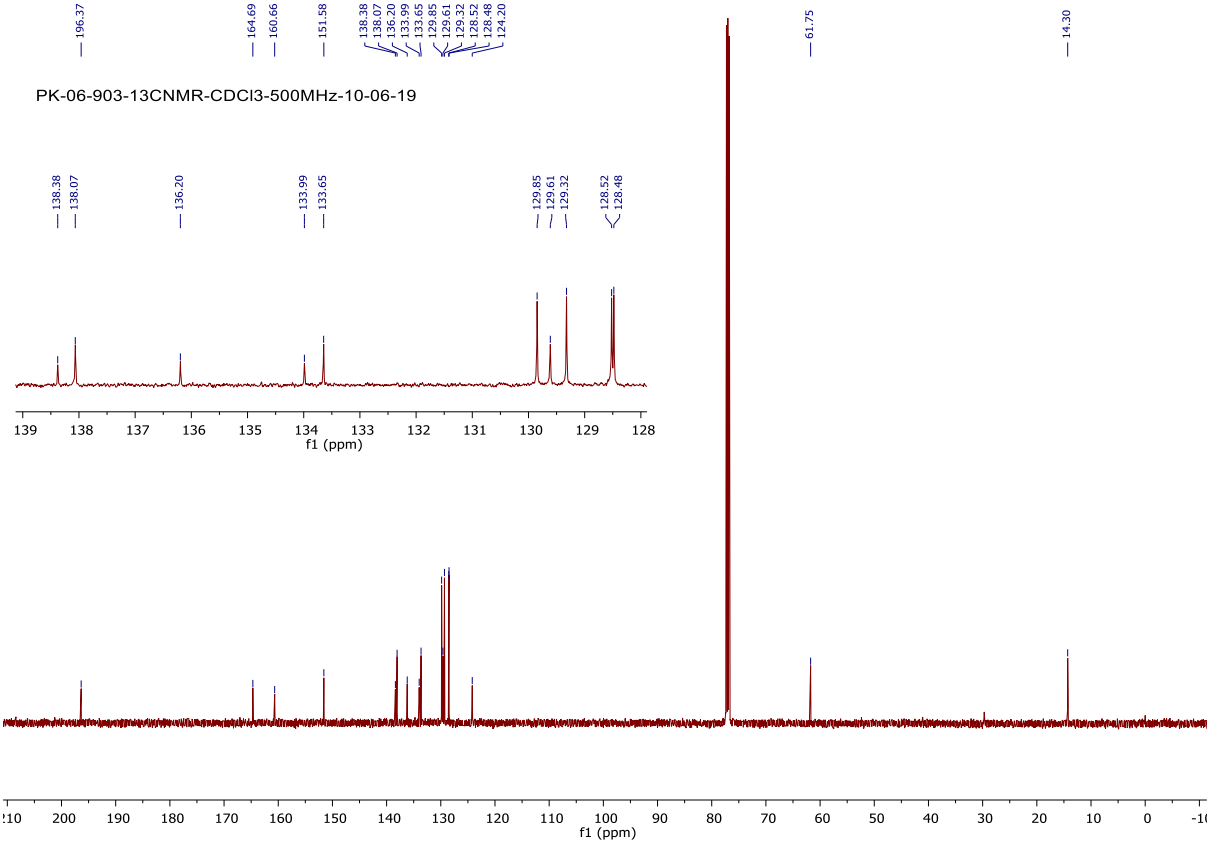
PK-06-883-1HNMR-500MHz-CDCl3-01-05-19



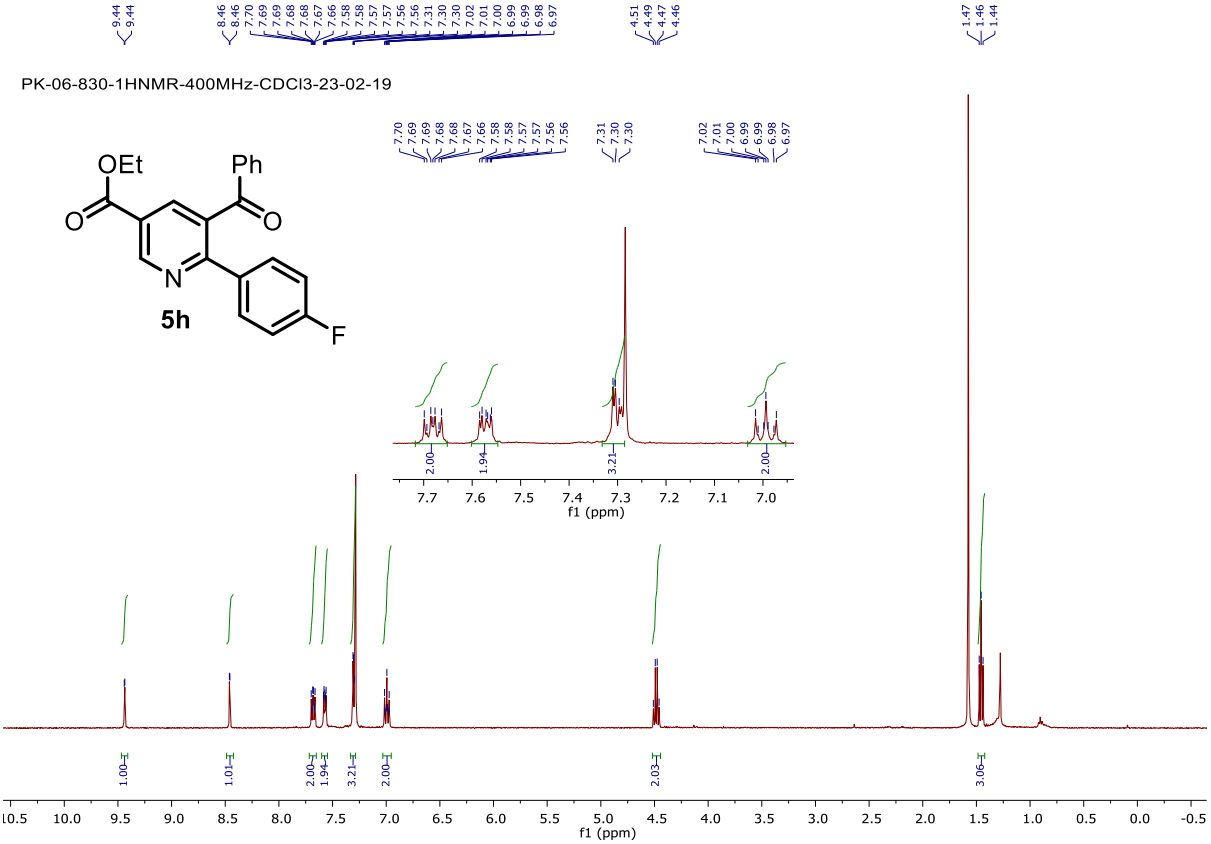
PK-06-903-1HNMR-CDCl3-400MHz-10-06-19



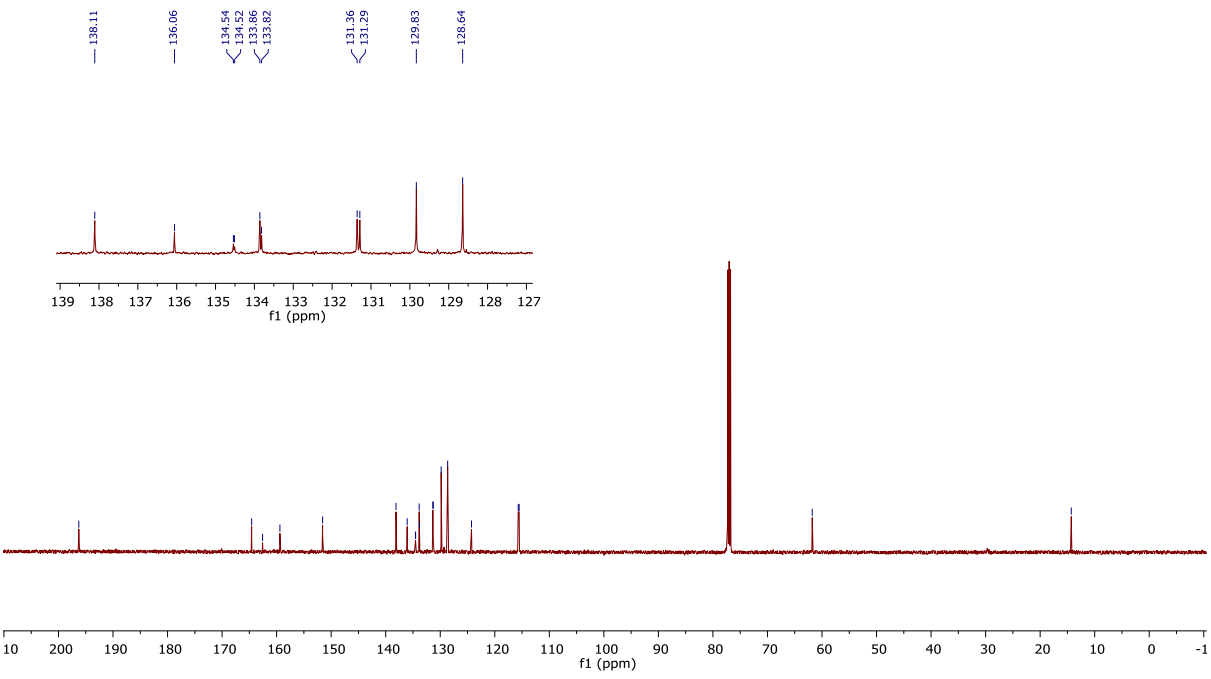
PK-06-903-13CNMR-CDCl3-500MHz-10-06-19



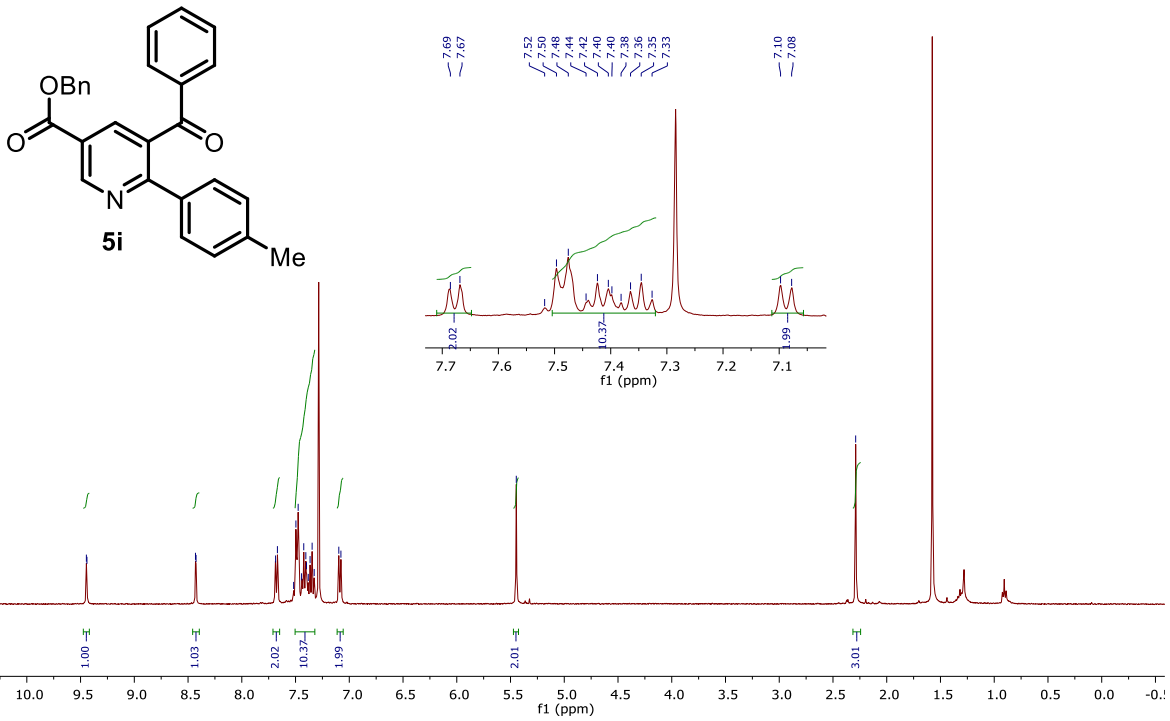
PK-06-830-1HNMR-400MHz-CDCl3-23-02-19



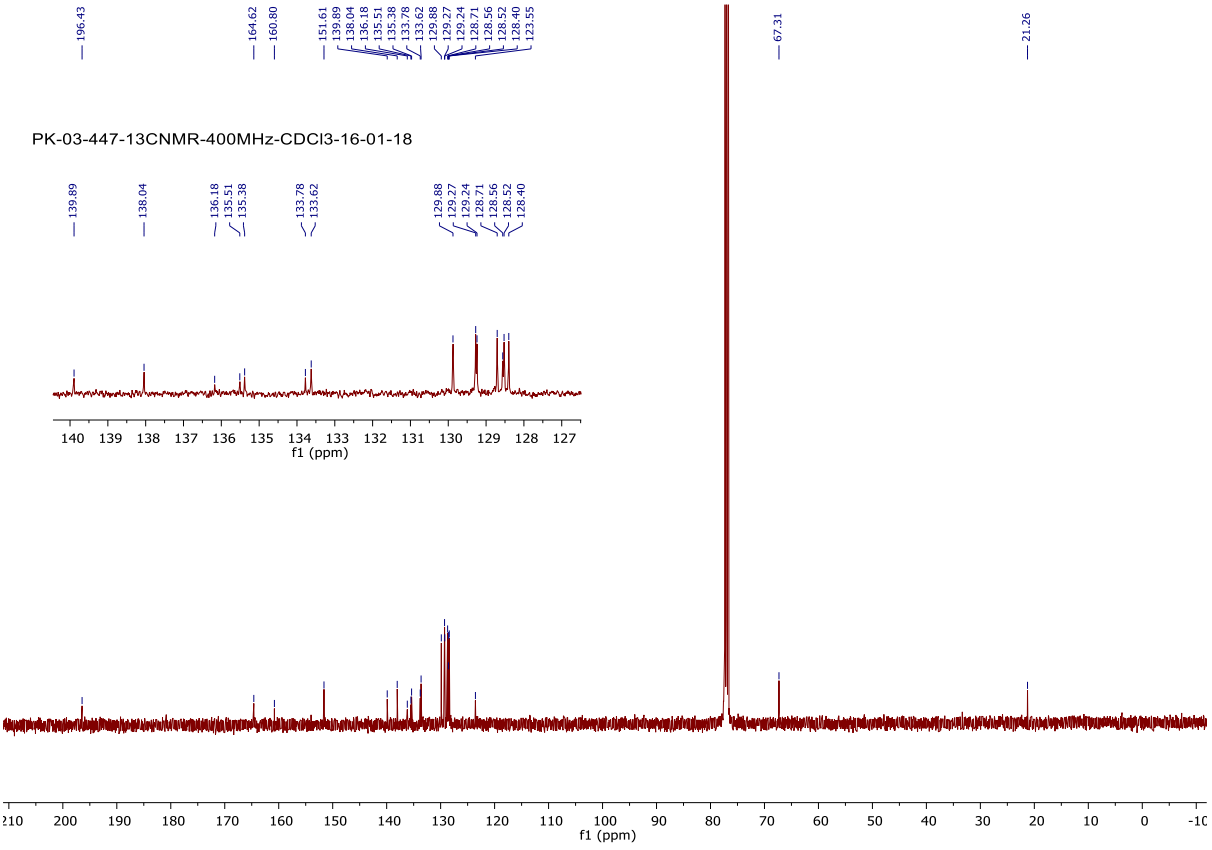
PK-06-830-13CNMR-500MHz-CDCl3-23-02-19

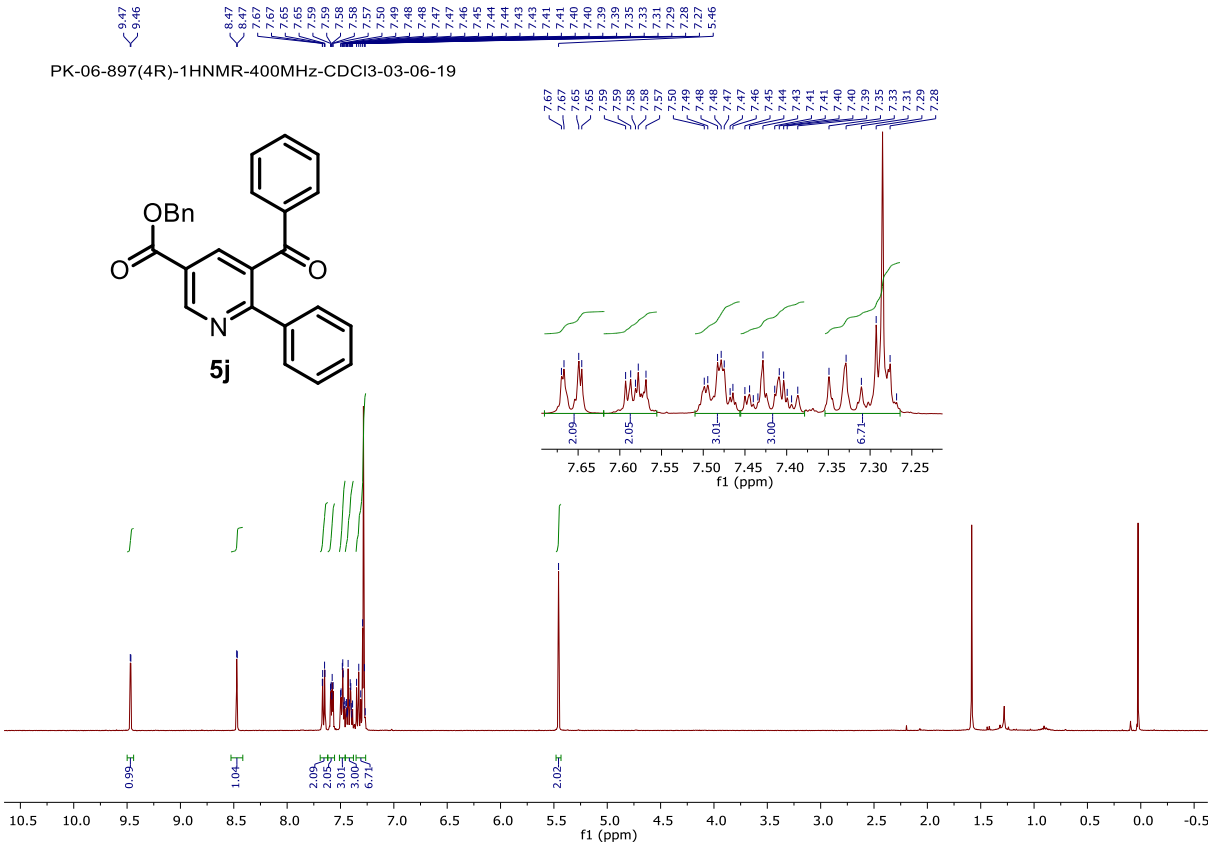


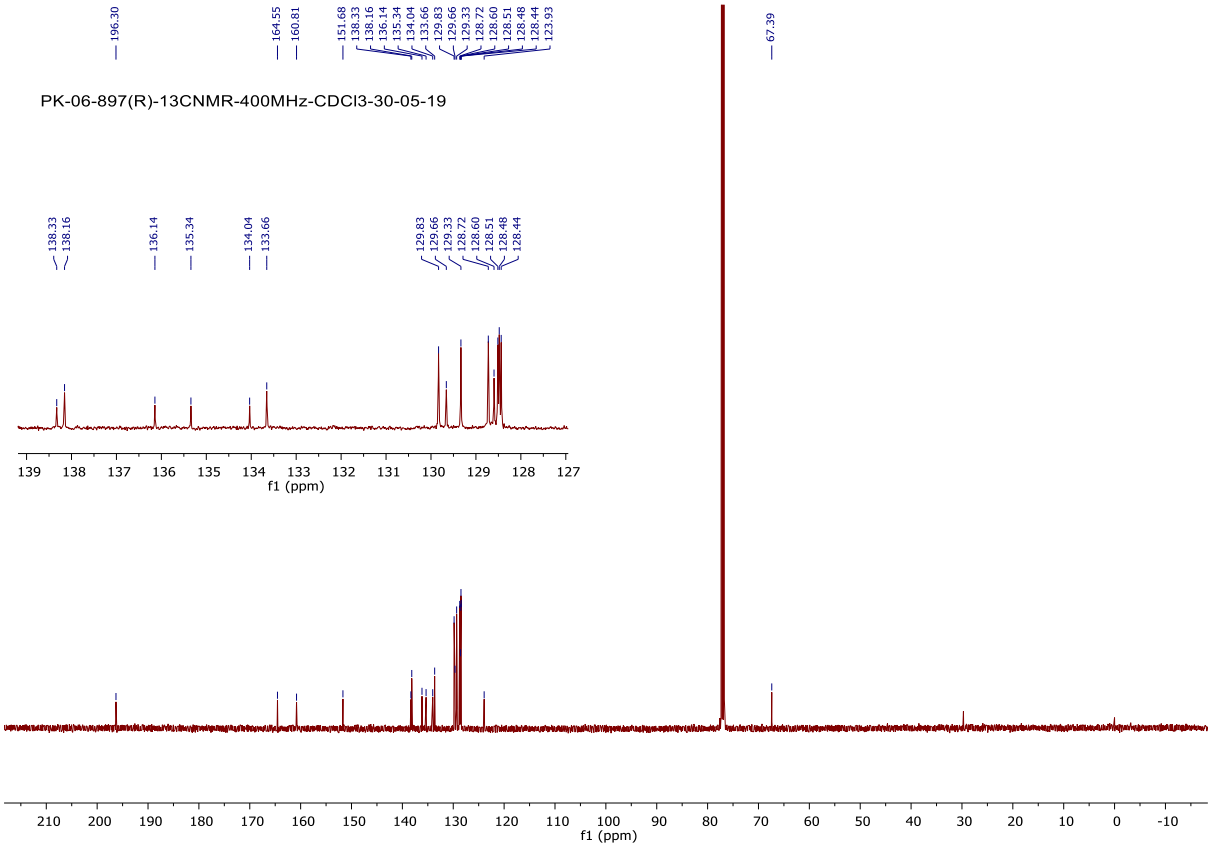
PK-03-447-1HNMR-400MHz-CDCl3-16-01-18

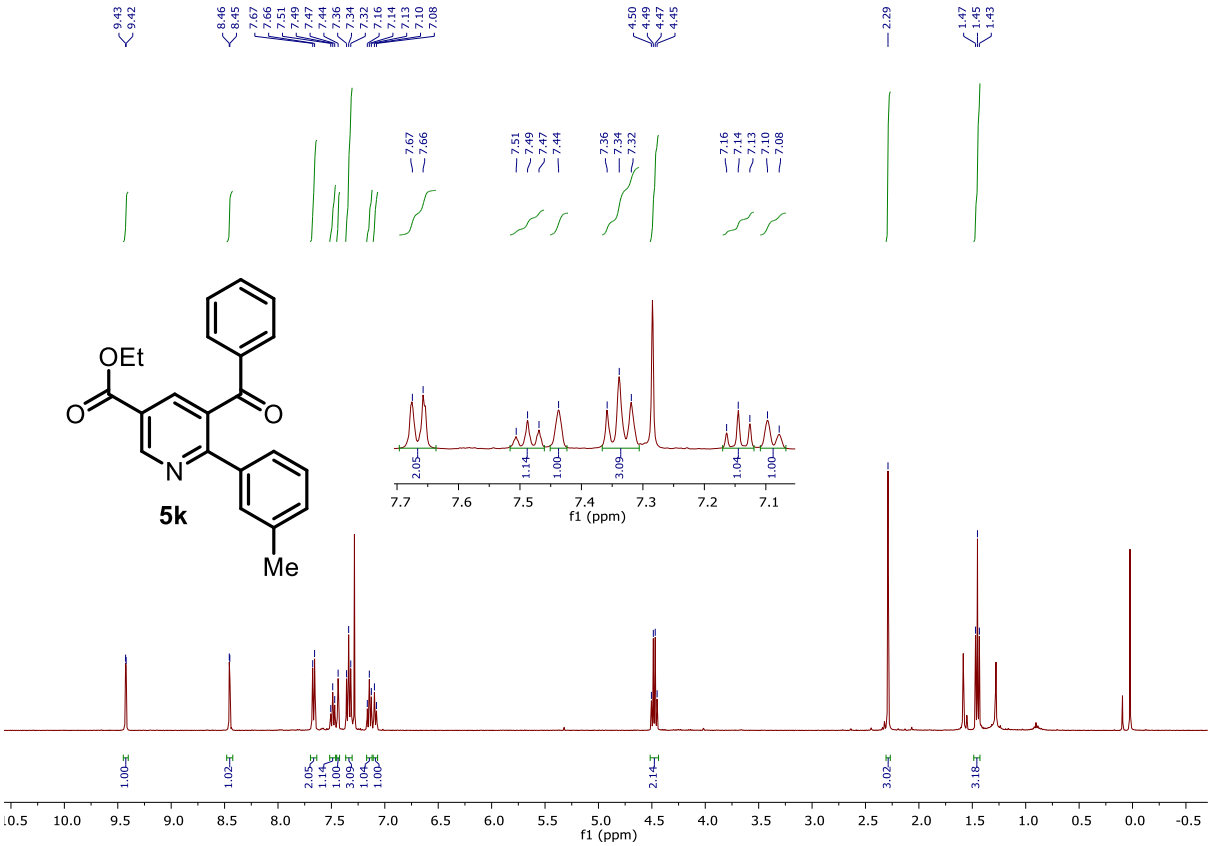


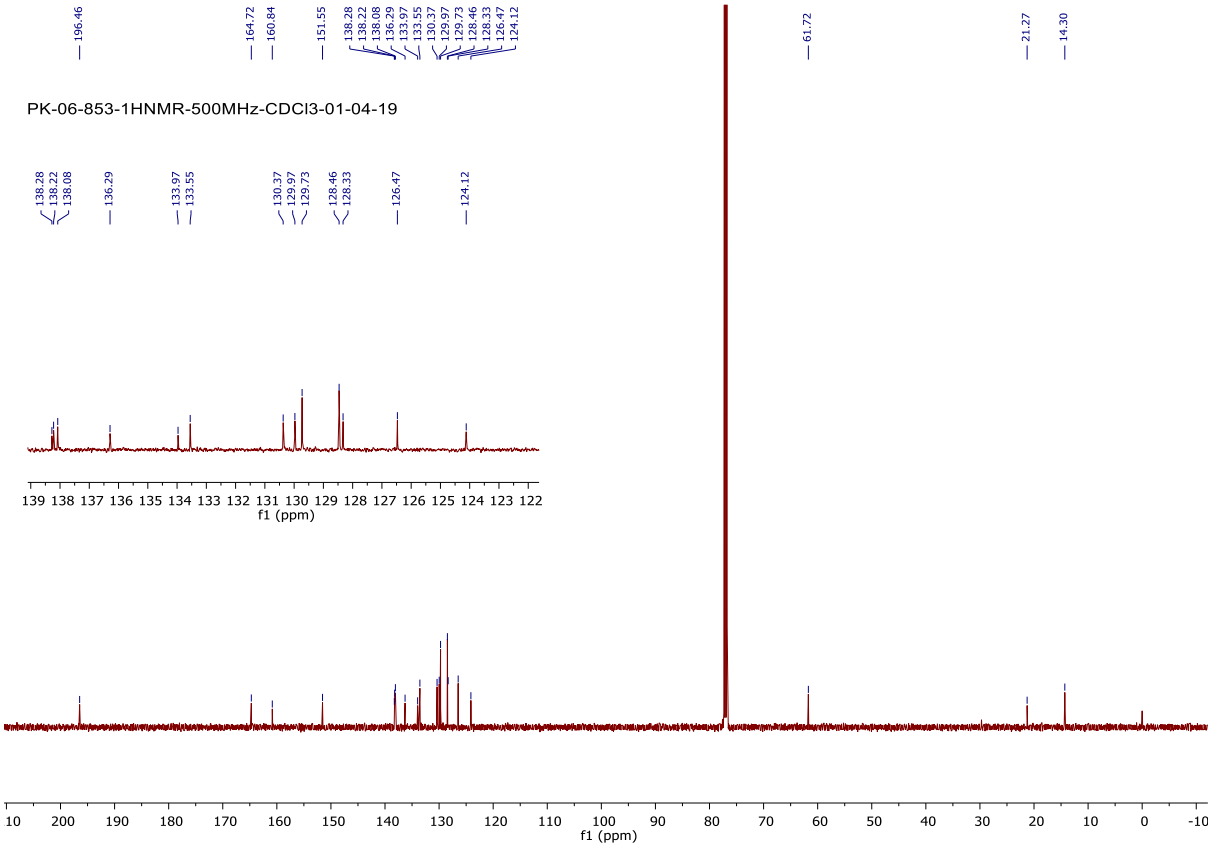
PK-03-447-13CNMR-400MHz-CDCl3-16-01-18



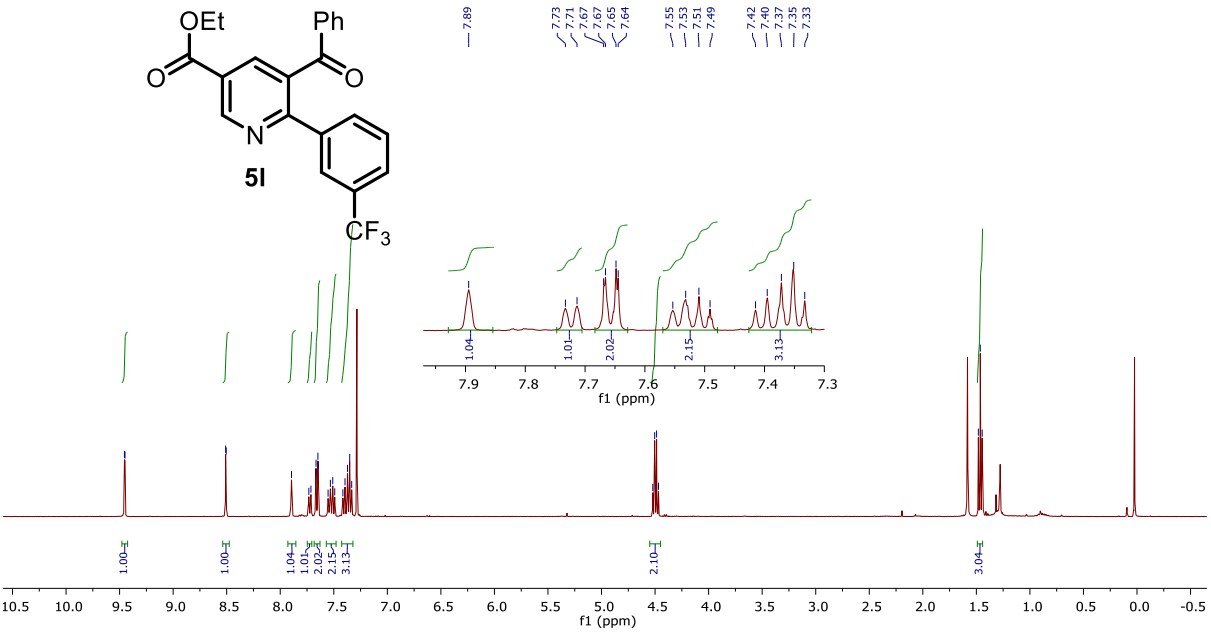

PK-06-897(4R)-1HNMR-400MHz-CDCl3-03-06-19
OBn
O
O
N
5j
f1 (ppm)


PK-06-897(R)-13CNMR-400MHz-CDCl3-30-05-19
f1 (ppm)

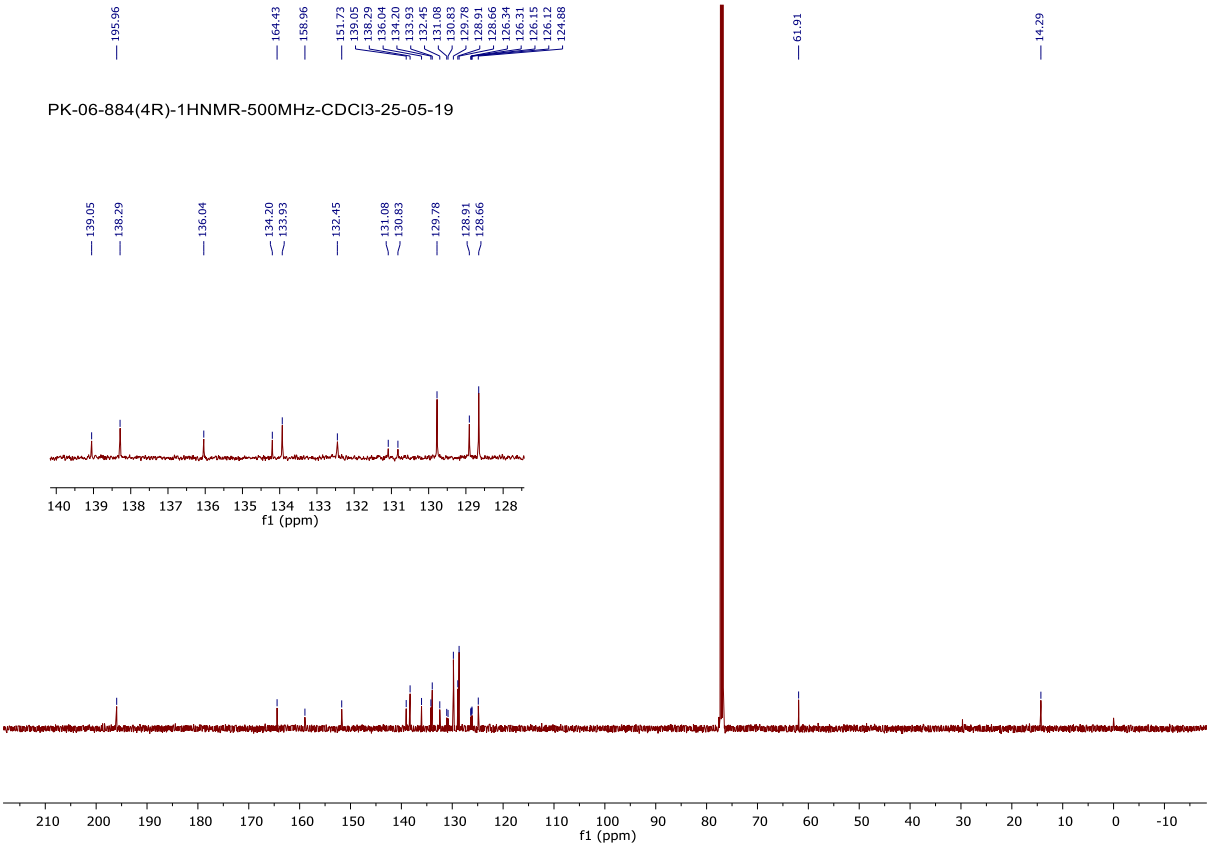

9.43
9.42
8.46
8.45
7.67
7.66
7.51
7.49
7.47
7.44
7.36
7.34
7.32
7.16
7.14
7.13
7.10
7.08
4.50
4.49
4.47
4.45
2.29
1.47
1.45
1.43
OEt
O
O
N
5k
Me
f1 (ppm)
f1 (ppm)

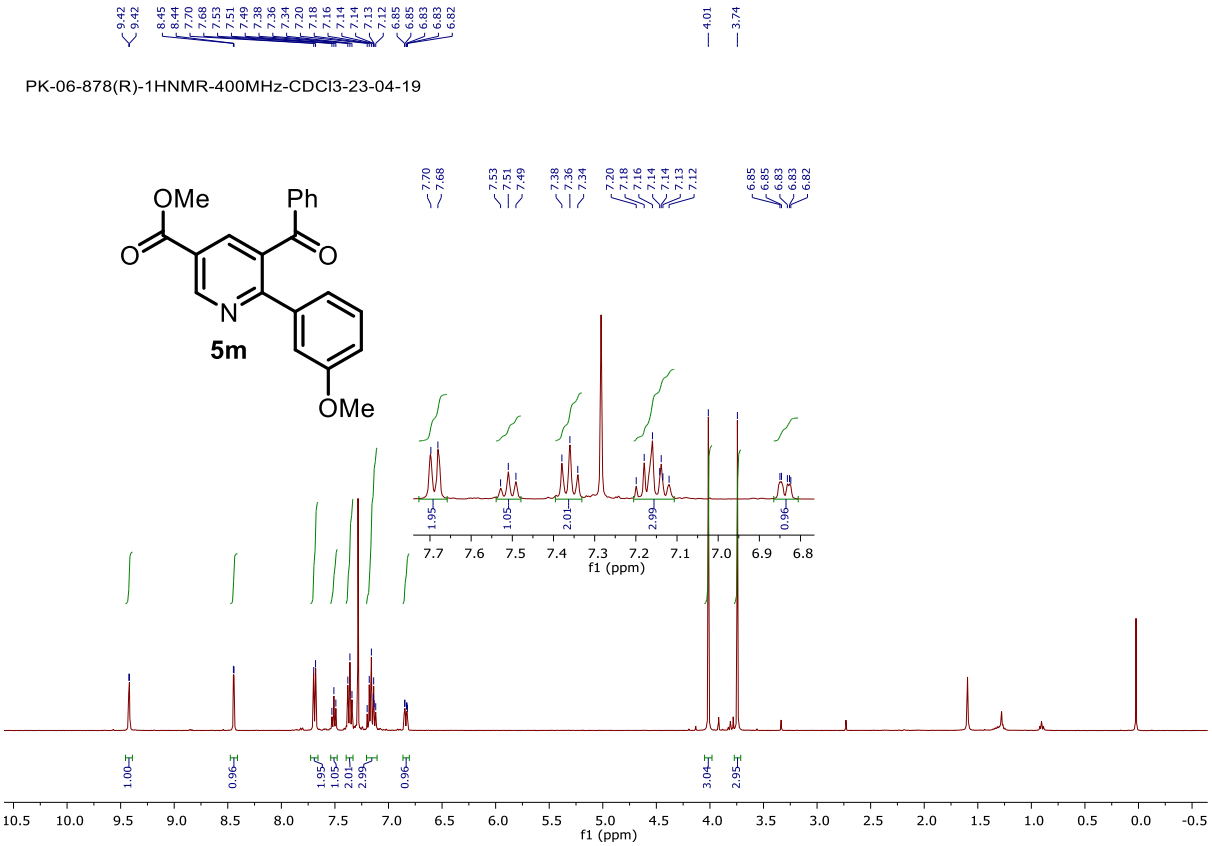

196.46
164.72
160.84
151.55
138.28
138.22
138.08
136.29
133.97
133.55
130.37
129.97
129.73
128.46
128.33
126.47
124.12
61.72
21.27
14.30
PK-06-853-1HNMR-500MHz-CDCl3-01-04-19
f1 (ppm)
f1 (ppm)

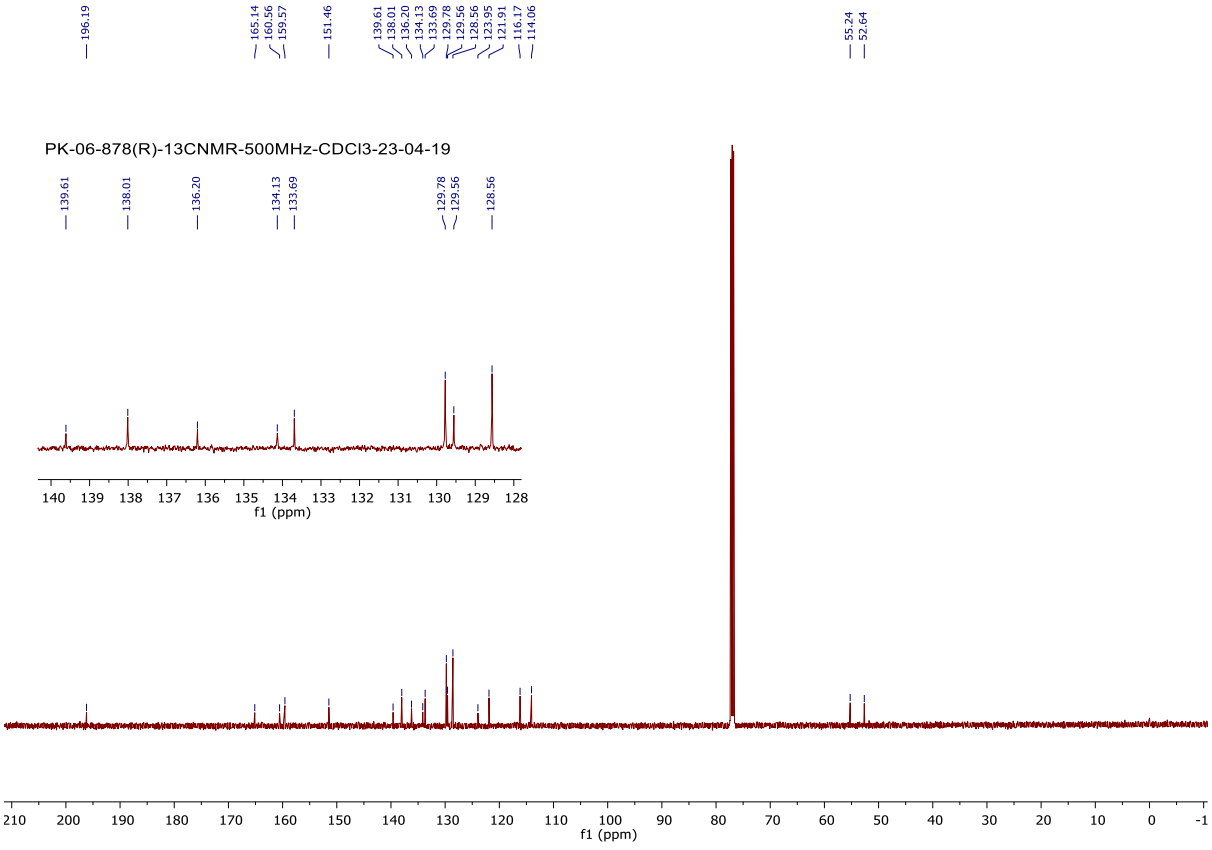
PK-06-884(4R)-1HNMR-400 MHz-CDCl3-24-05-19



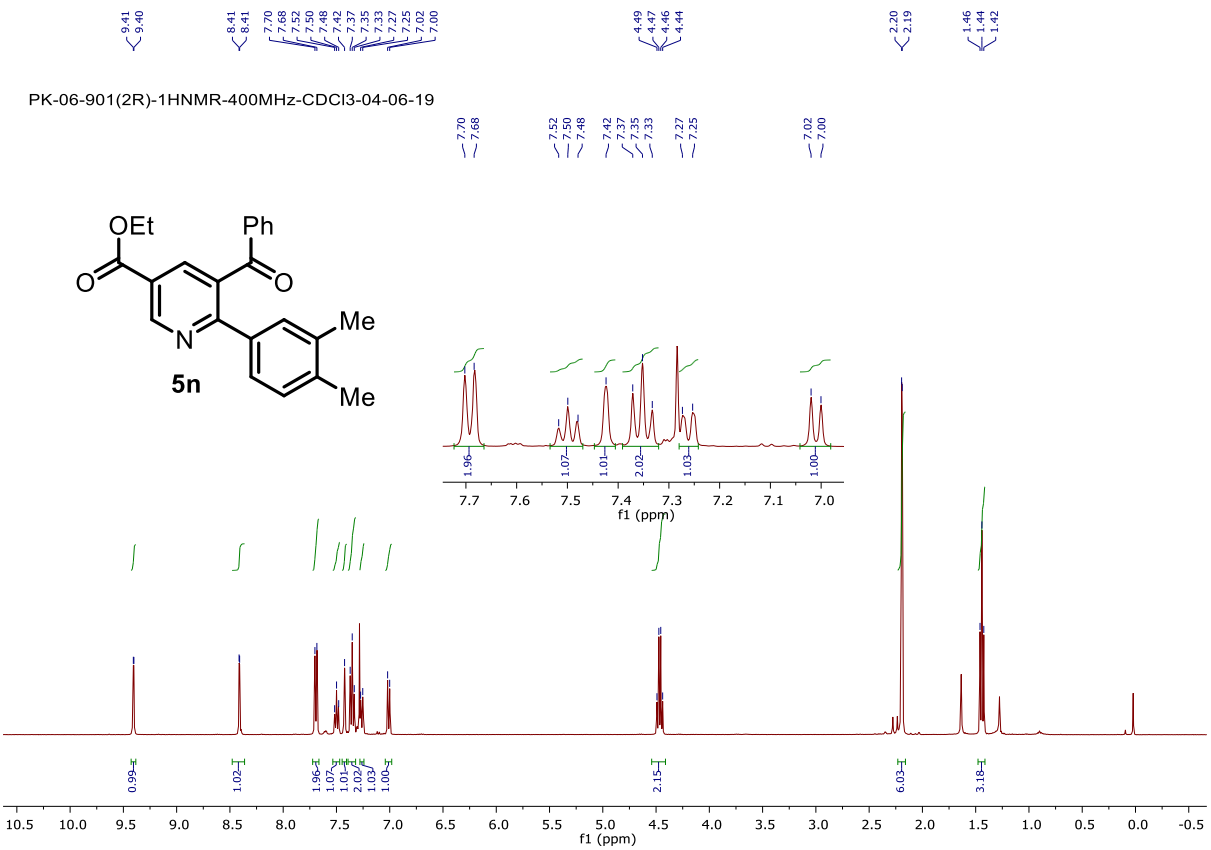
PK-06-884(4R)-1HNMR-500MHz-CDCl3-25-05-19



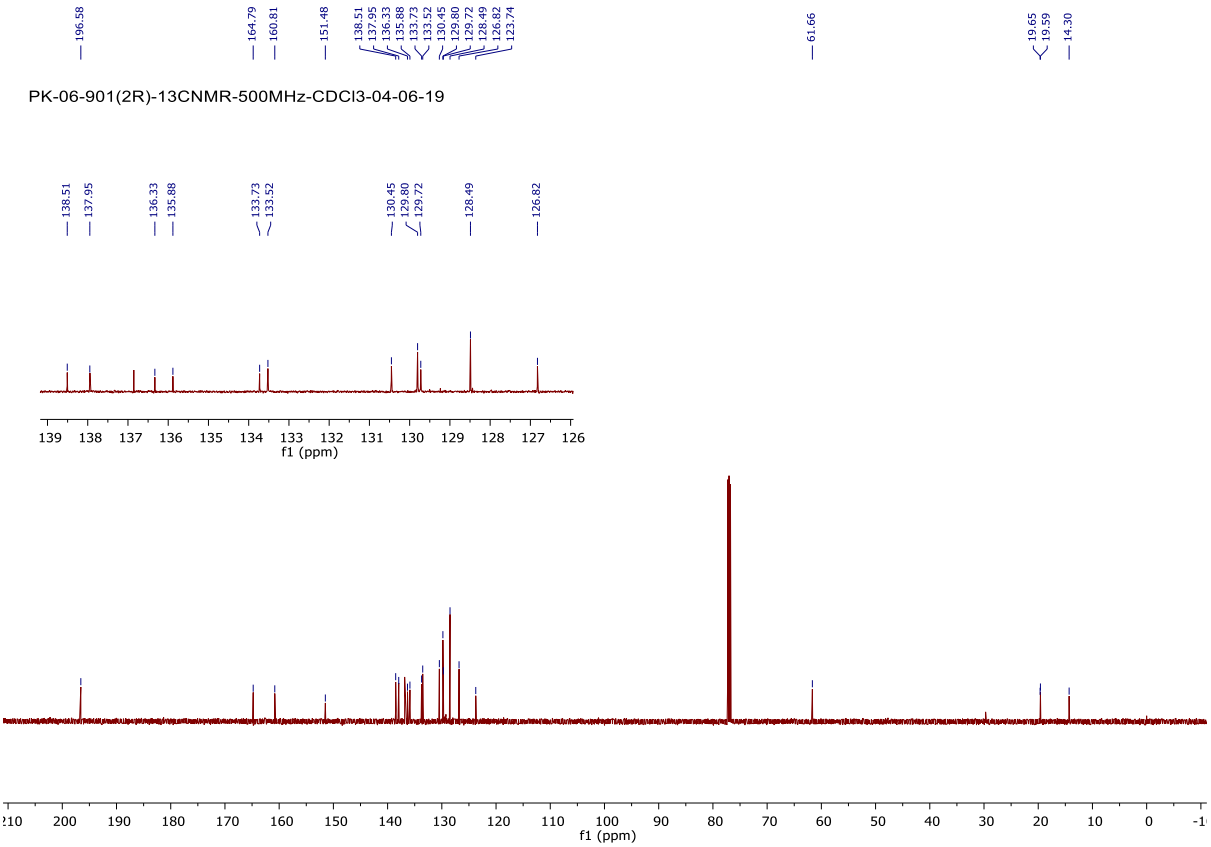

9.42
9.42
8.45
8.44
7.70
7.68
7.53
7.51
7.49
7.38
7.36
7.34
7.20
7.18
7.16
7.14
7.14
7.13
7.12
6.85
6.83
6.83
6.82
4.01
3.74
PK-06-878(R)-1HNMR-400MHz-CDCl3-23-04-19
OMe
Ph
O
O
N
5m
OMe
1.00
0.96
1.95
1.05
2.01
2.99
0.96
3.04
2.95
f1 (ppm)

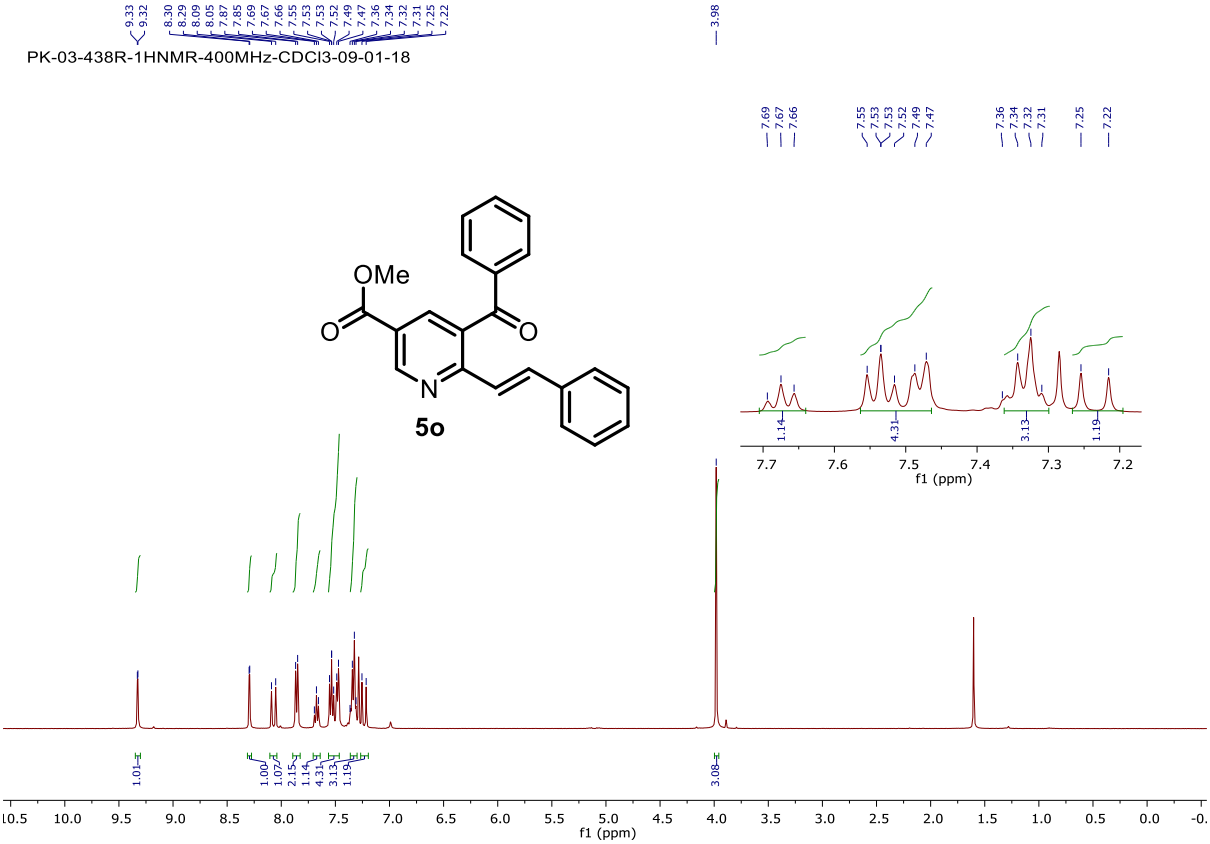

196.19
165.14
160.56
159.57
151.46
139.61
138.01
136.20
134.13
133.69
129.78
129.56
128.56
123.95
121.91
116.17
114.06
55.24
52.64
PK-06-878(R)-13CNMR-500MHz-CDCl3-23-04-19
f1 (ppm)

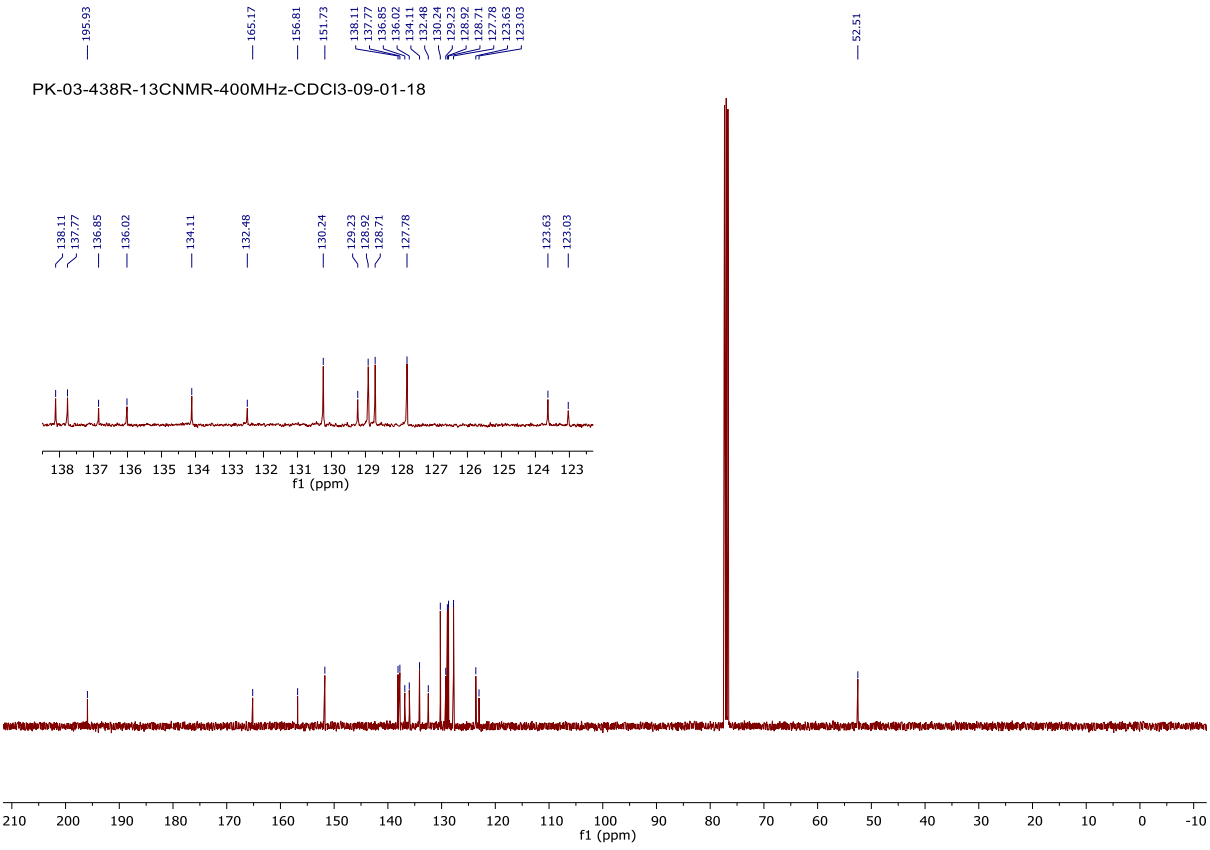
PK-06-901(2R)-1HNMR-400MHz-CDCl3-04-06-19



PK-06-901(2R)-13CNMR-500MHz-CDCl3-04-06-19




PK-03-438R-1HNMR-400MHz-CDCl3-09-01-18
OMe
O
O
N
5o
f1 (ppm)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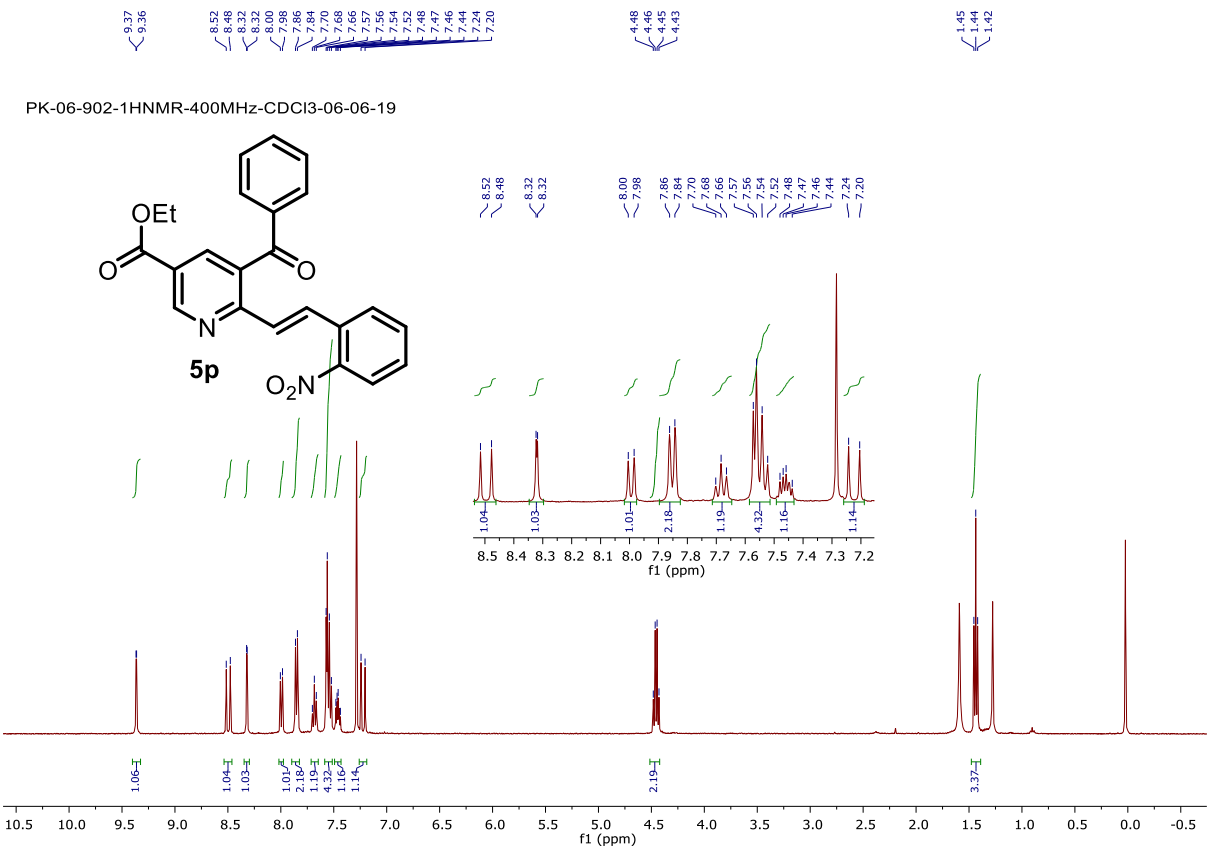
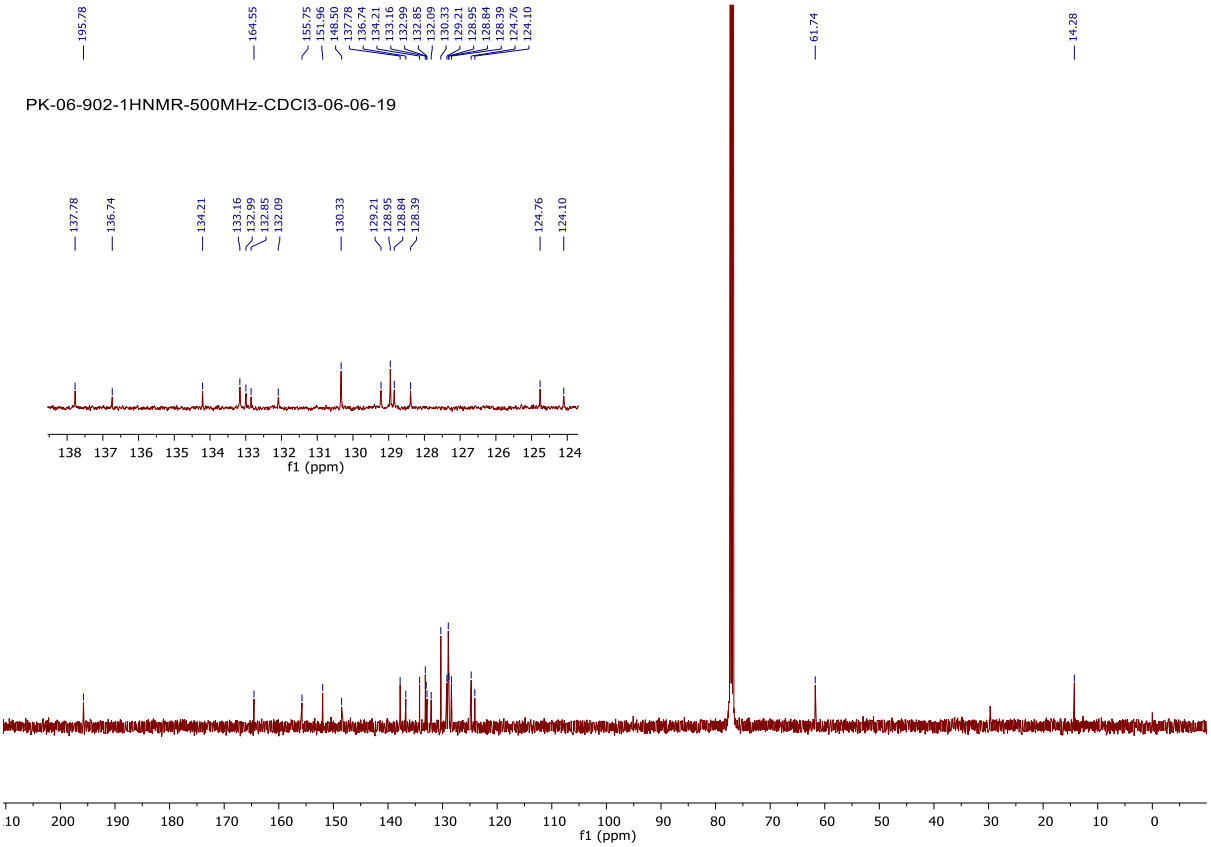
f1 (ppm)


PK-06-902-1HNMR-400MHz-CDCl3-06-06-19
OEt
O
O
N
5p
O2N
f1 (ppm)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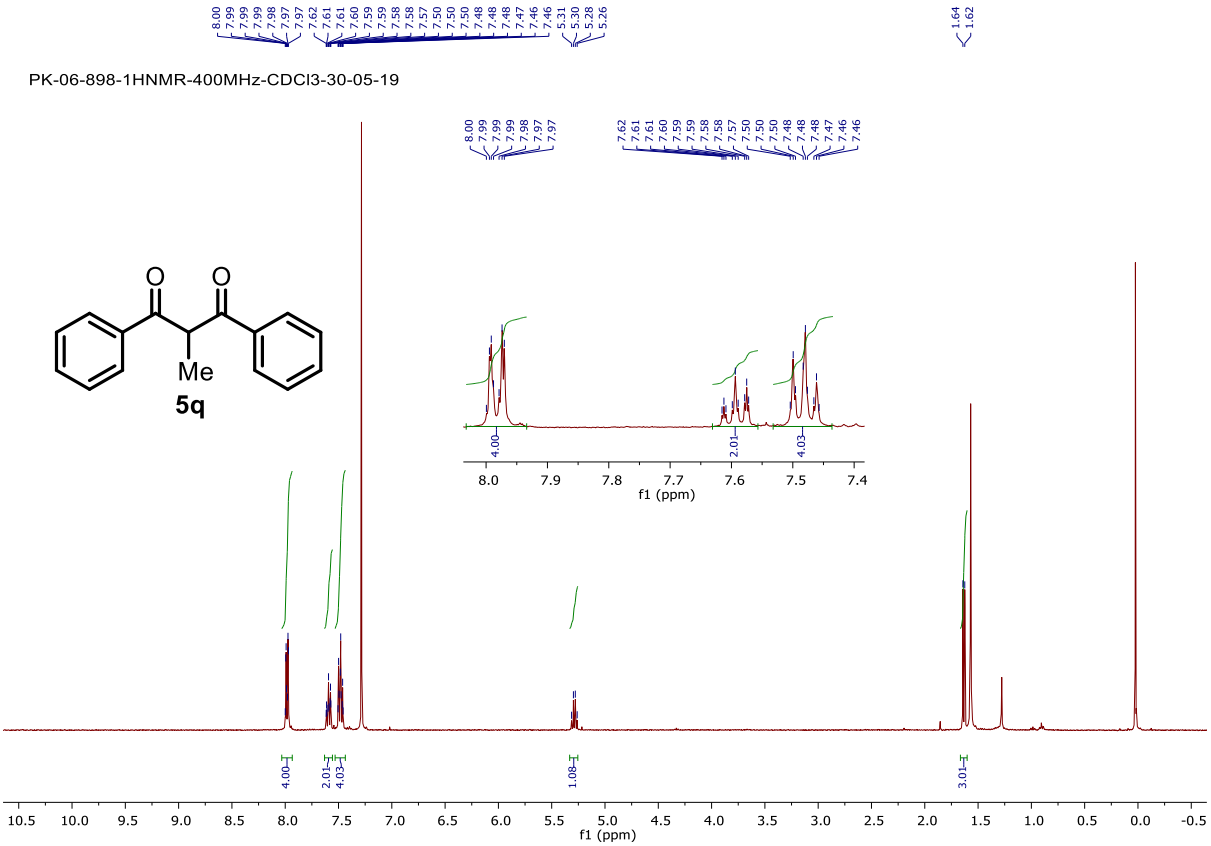
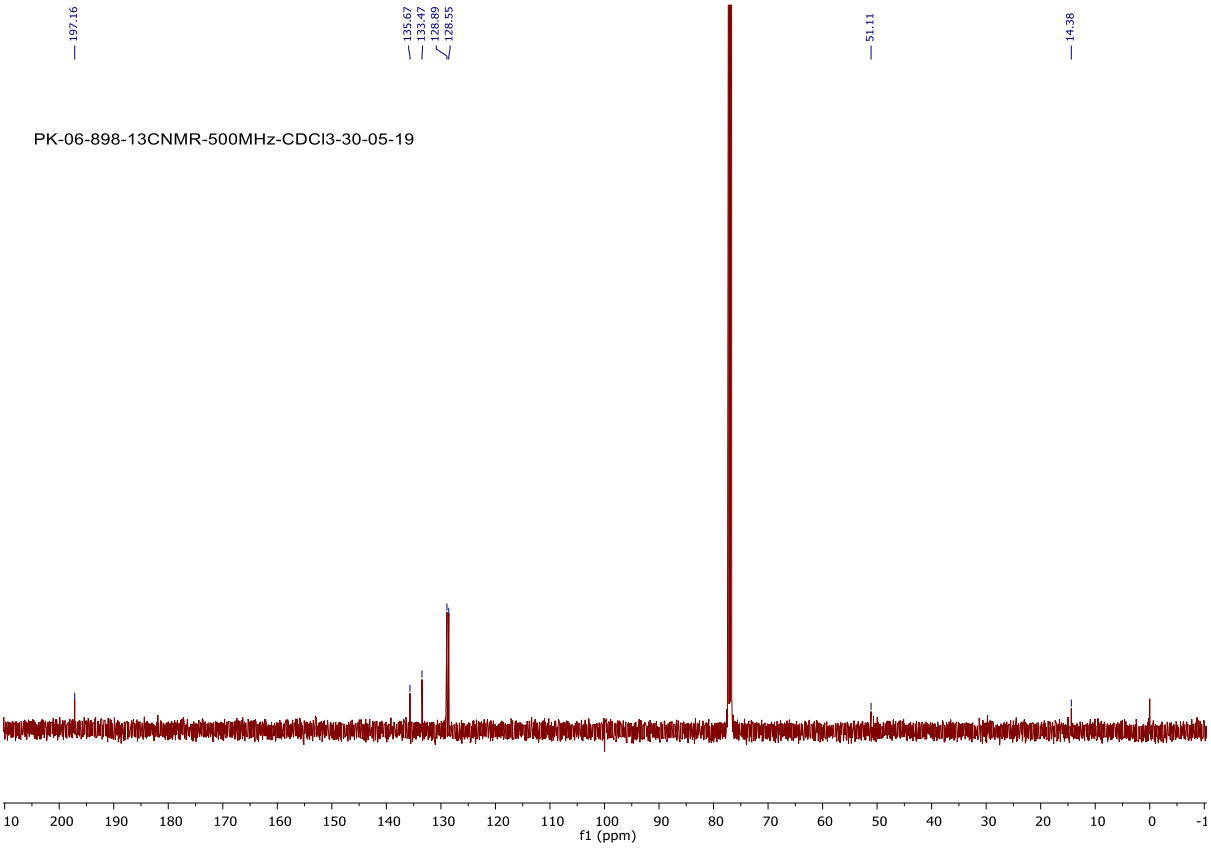
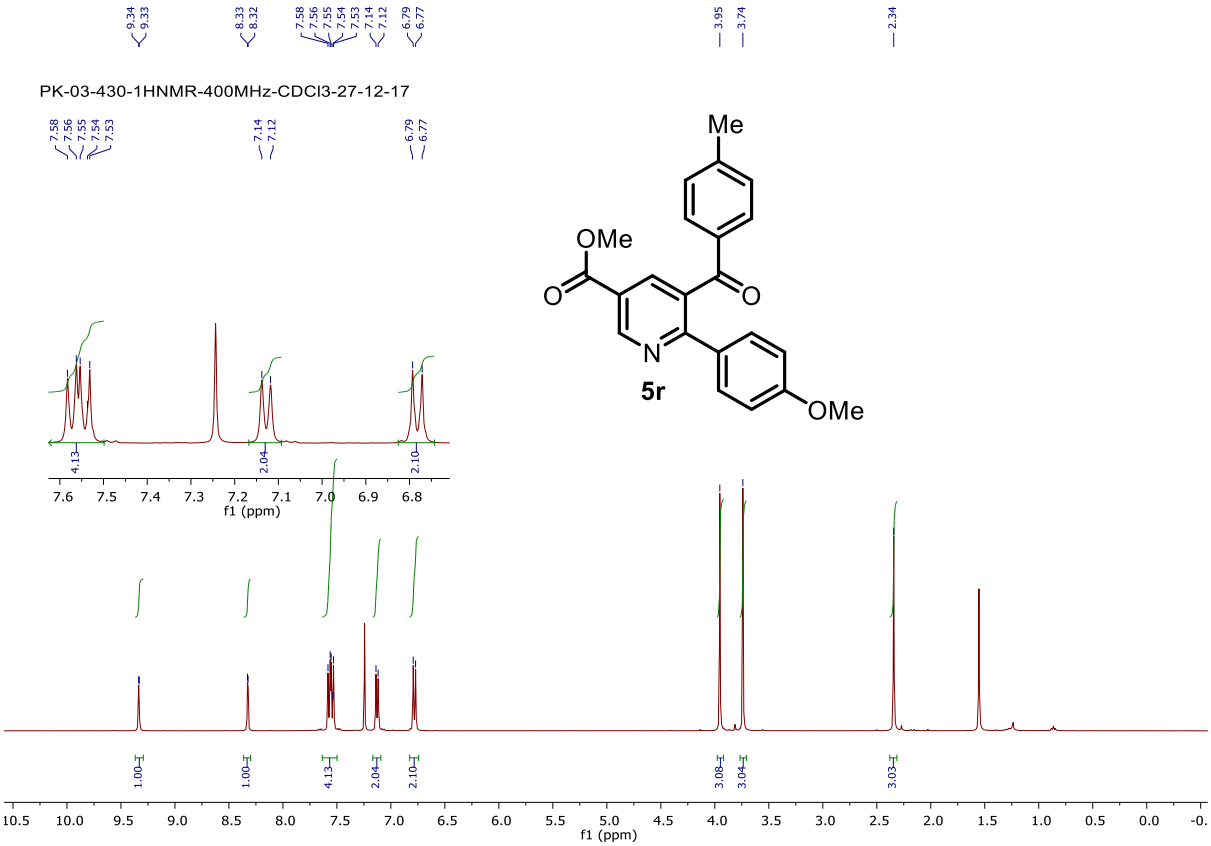
f1 (ppm)


8.00 7.99 7.99 7.99 7.98 7.97 7.97 7.62 7.61 7.61 7.60 7.59 7.59 7.58 7.58 7.57 7.50 7.50 7.48 7.48 7.47 7.46 7.46 5.31 5.30 5.28 5.26
1.64 1.62
PK-06-898-1HNMR-400MHz-CDCl3-30-05-19
O
O
Me
5q
4.00
2.01
4.03
1.08
3.01
f1 (ppm)


197.16
135.67 133.47 128.89 128.55
51.11
14.38
PK-06-898-13CNMR-500MHz-CDCl3-30-05-19
f1 (ppm)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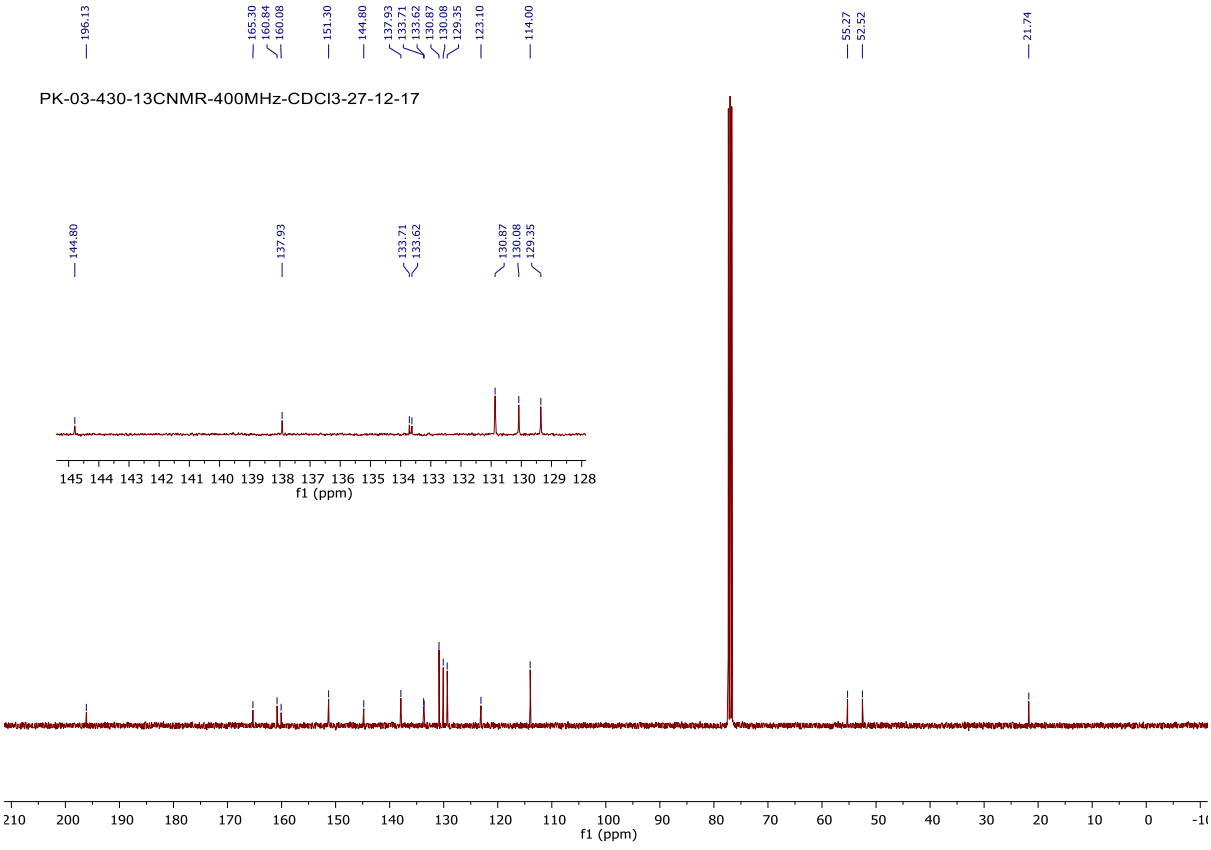
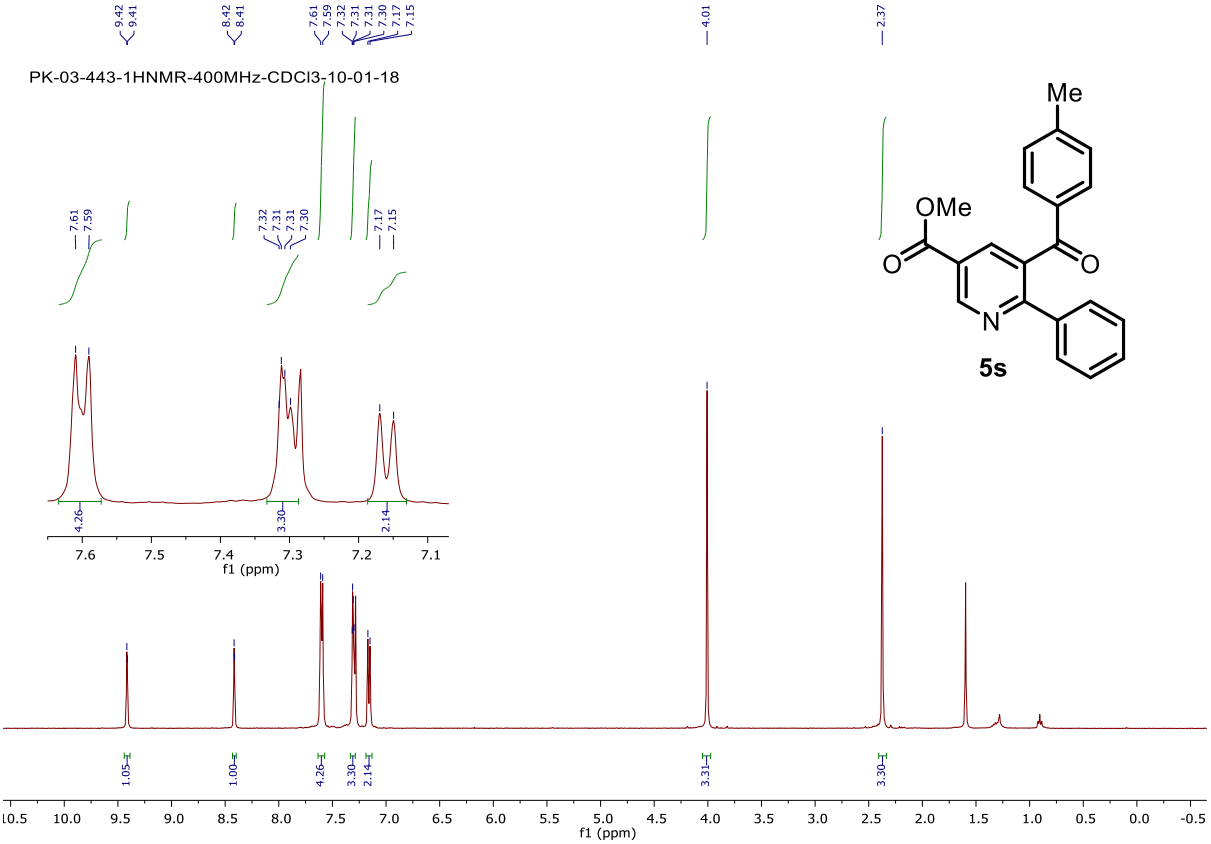
Me
OMe
O
O
N
5r
OMe
f1 (ppm)


PK-03-430-13CNMR-400MHz-CDCl3-27-12-17
f1 (ppm)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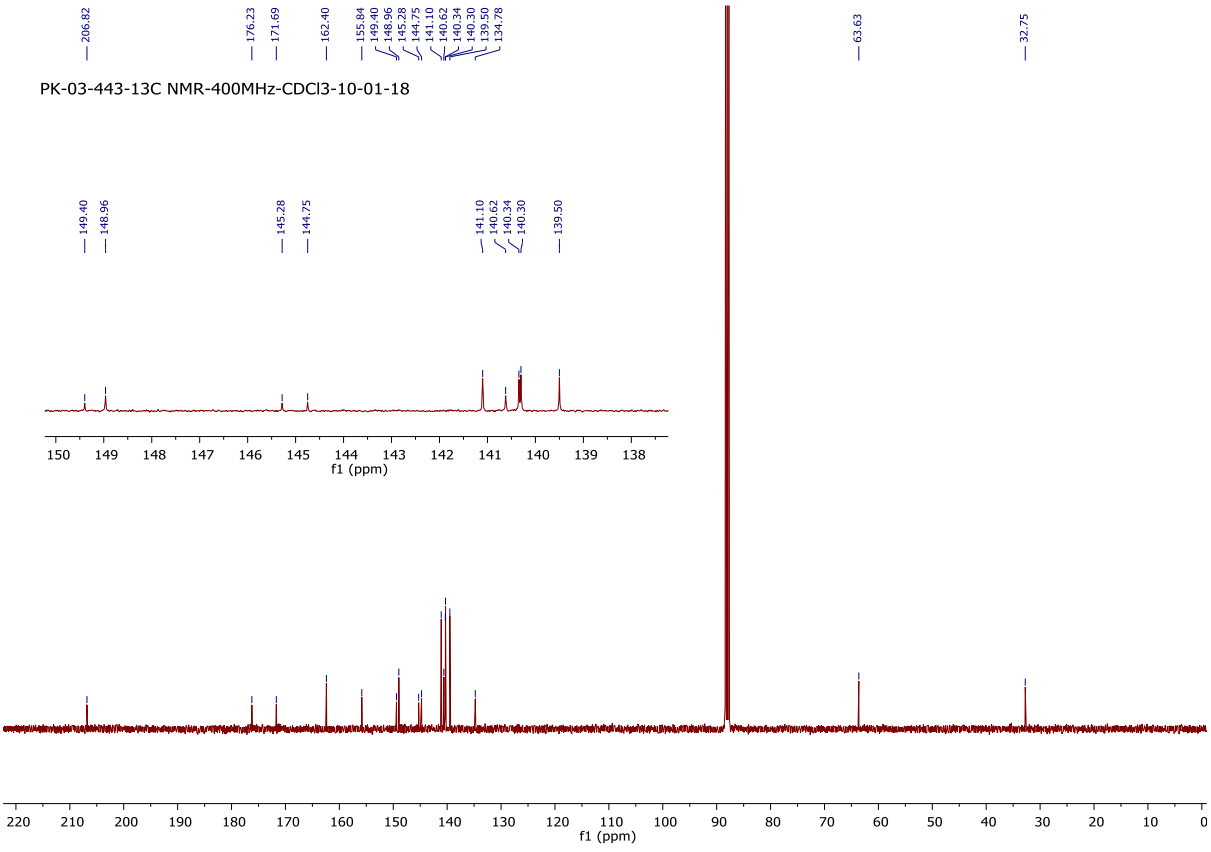
Me
OMe
O
O
N
5s
f1 (ppm)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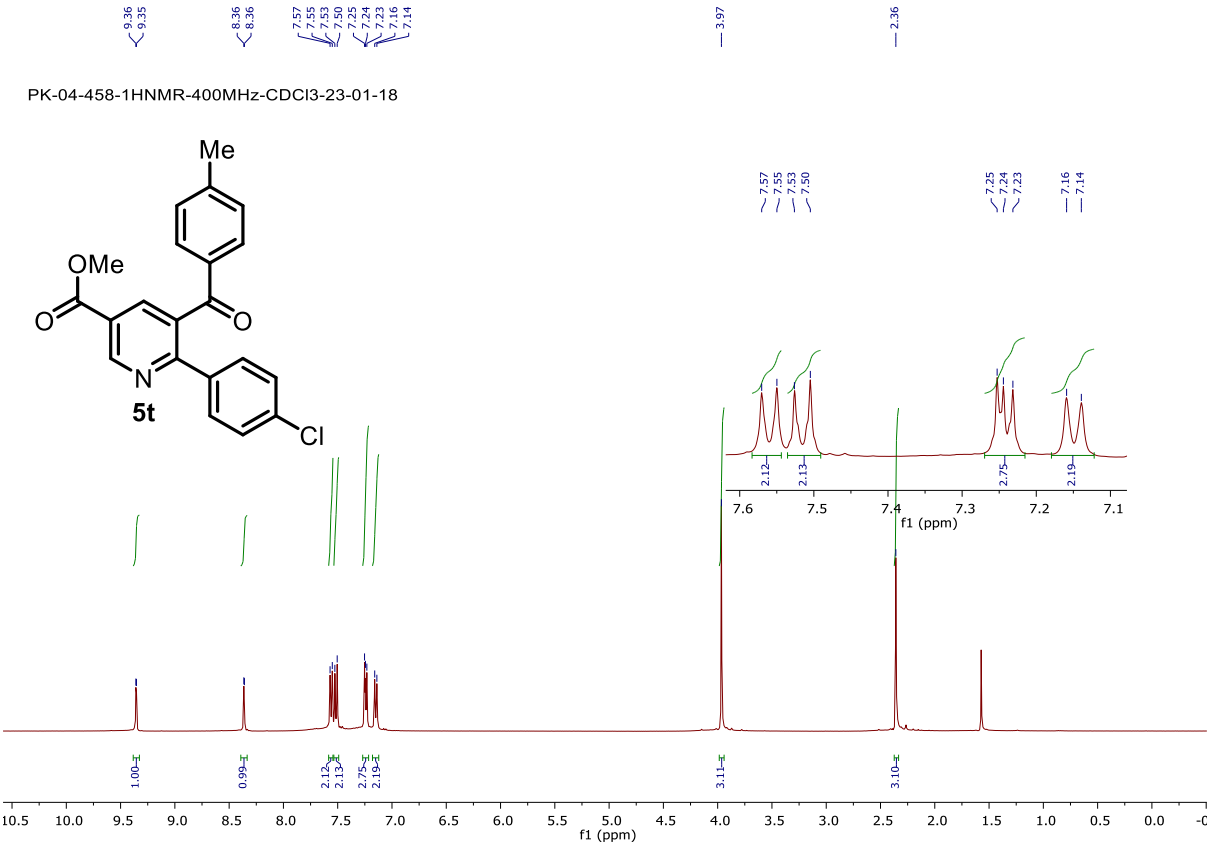
f1 (ppm)

PK-04-458-1HNMR-400MHz-CDCl3-23-01-18



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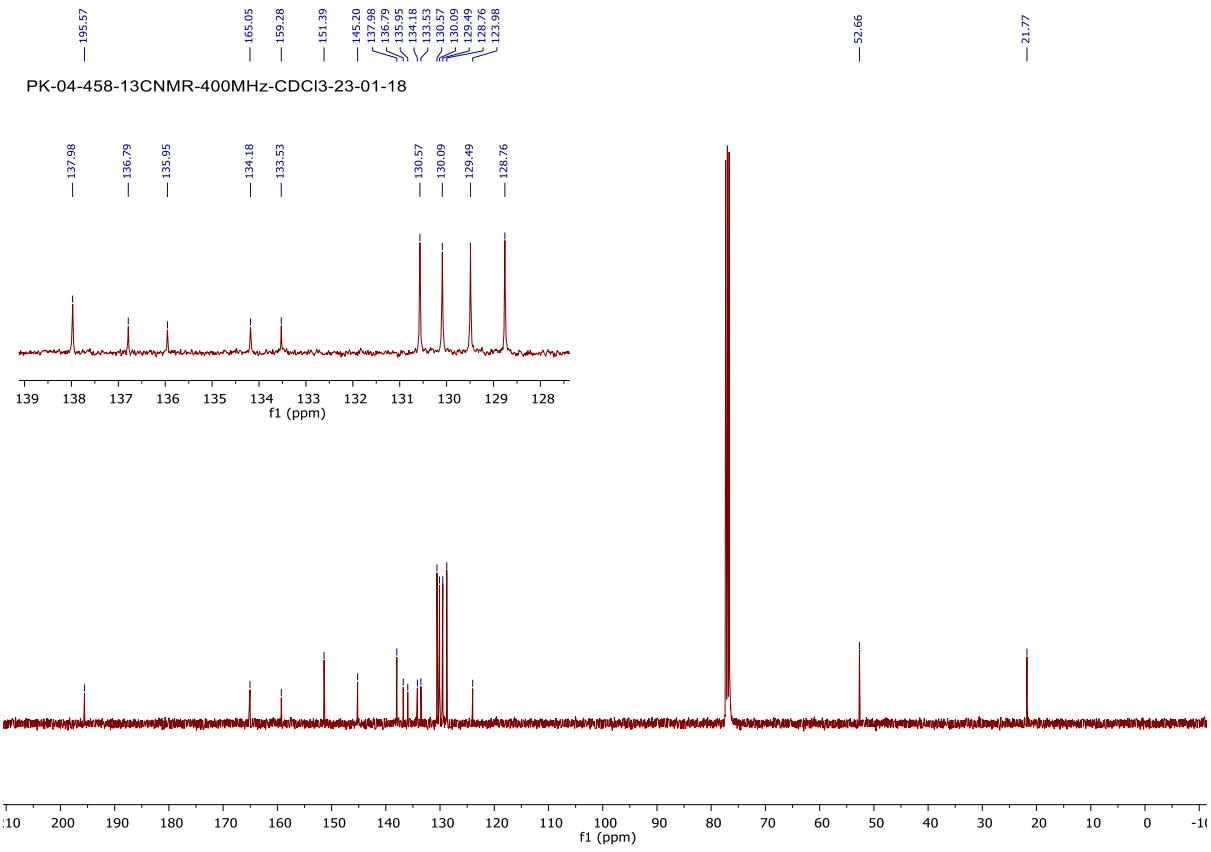
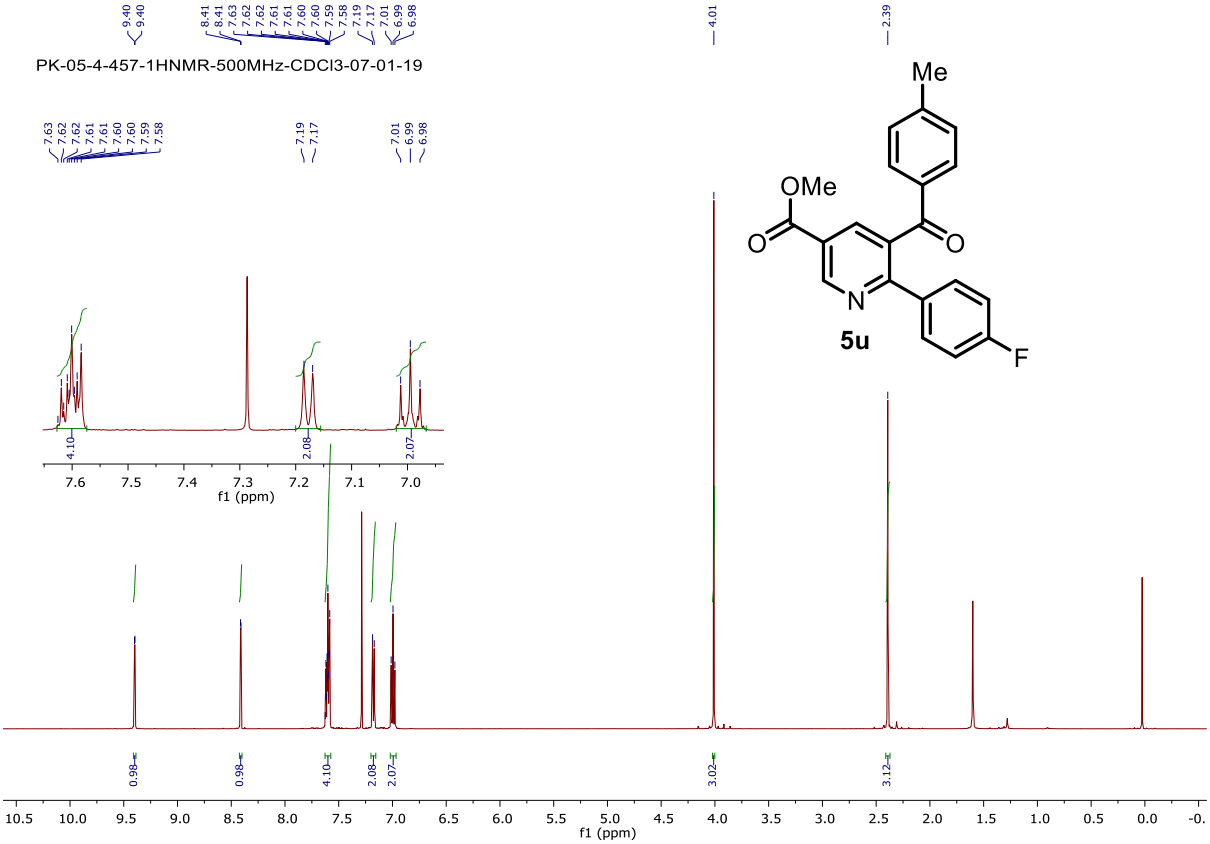
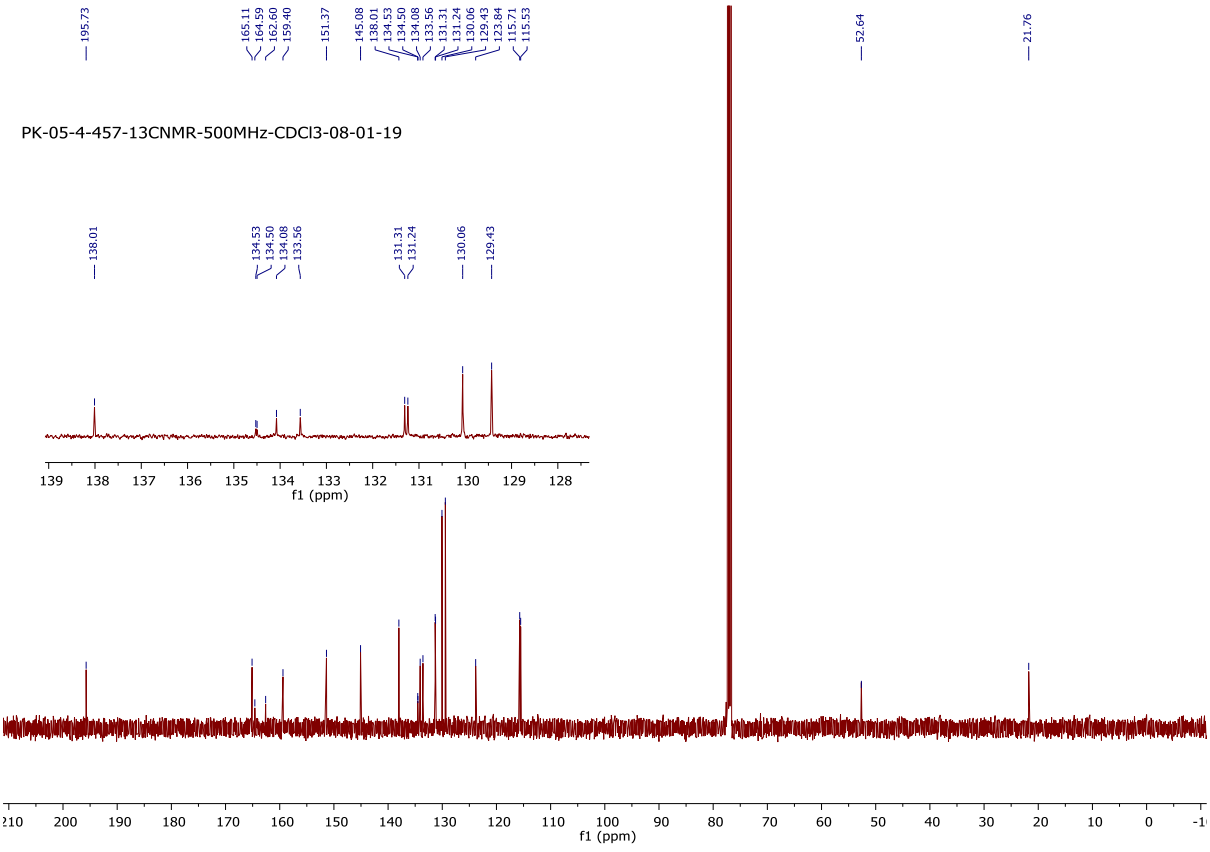
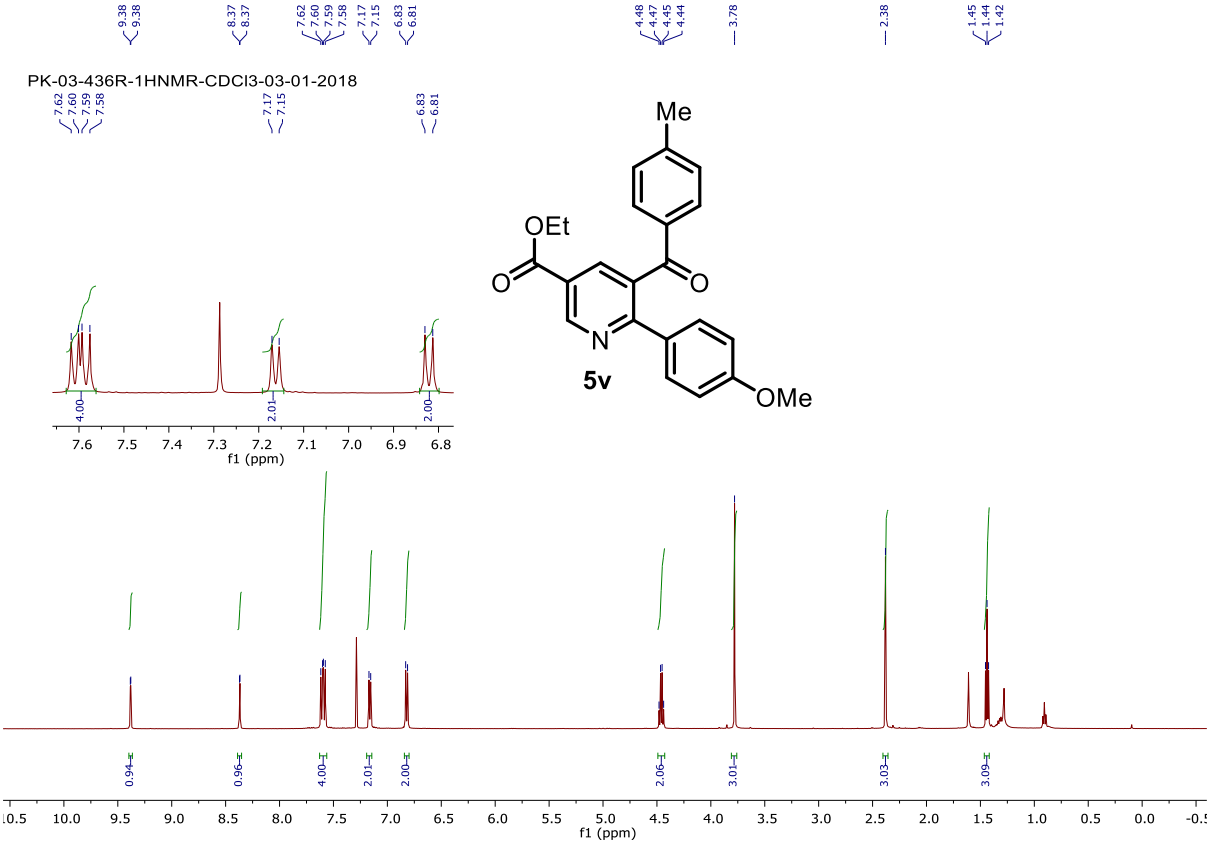
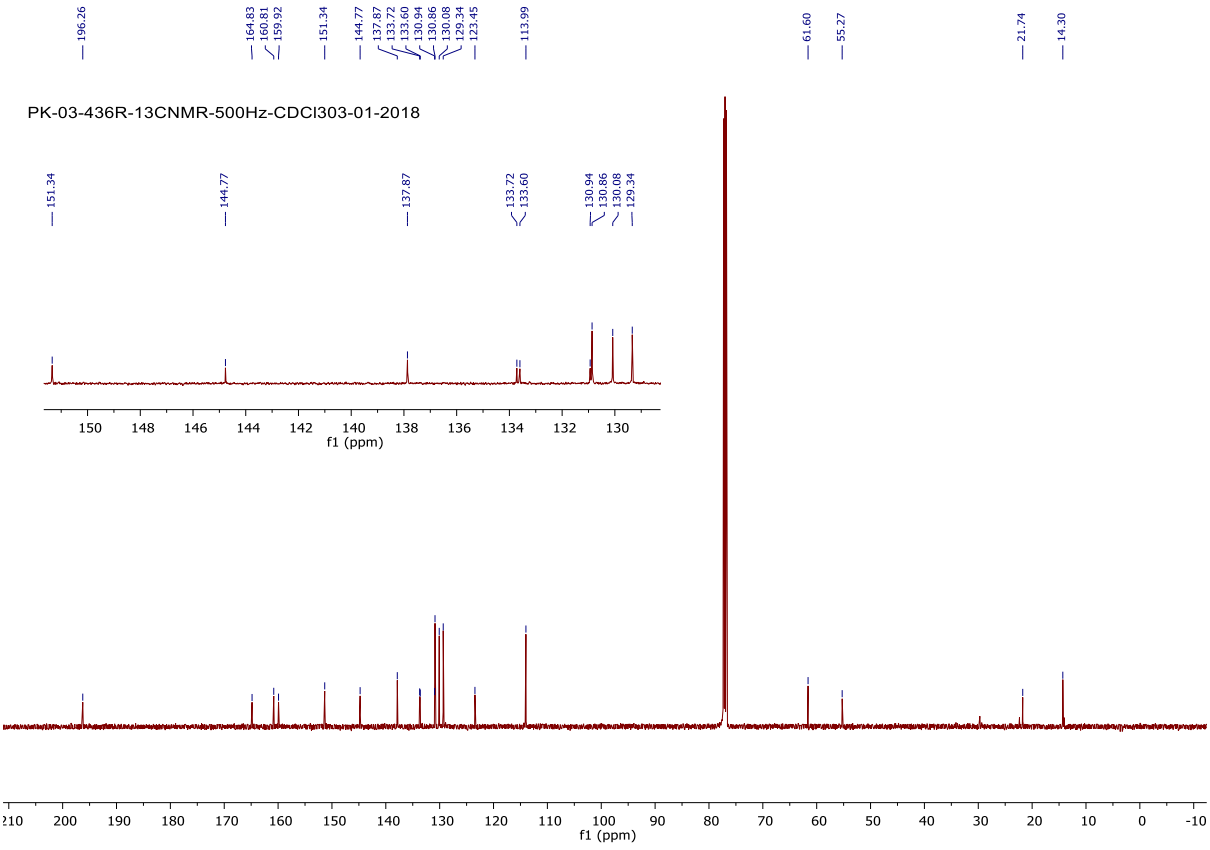


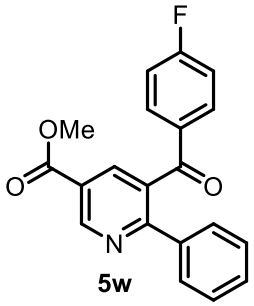

PK-05-4-457-1HNMR-500MHz-CDCl3-07-01-19
Me
OMe
O
O
N
F
5u
f1 (ppm)


PK-05-4-457-13CNMR-500MHz-CDCl3-08-01-19
f1 (ppm)


PK-03-436R-1HNMR-CDCl3-03-01-2018
Me
OEt
O
O
N
OMe
5v
f1 (ppm)

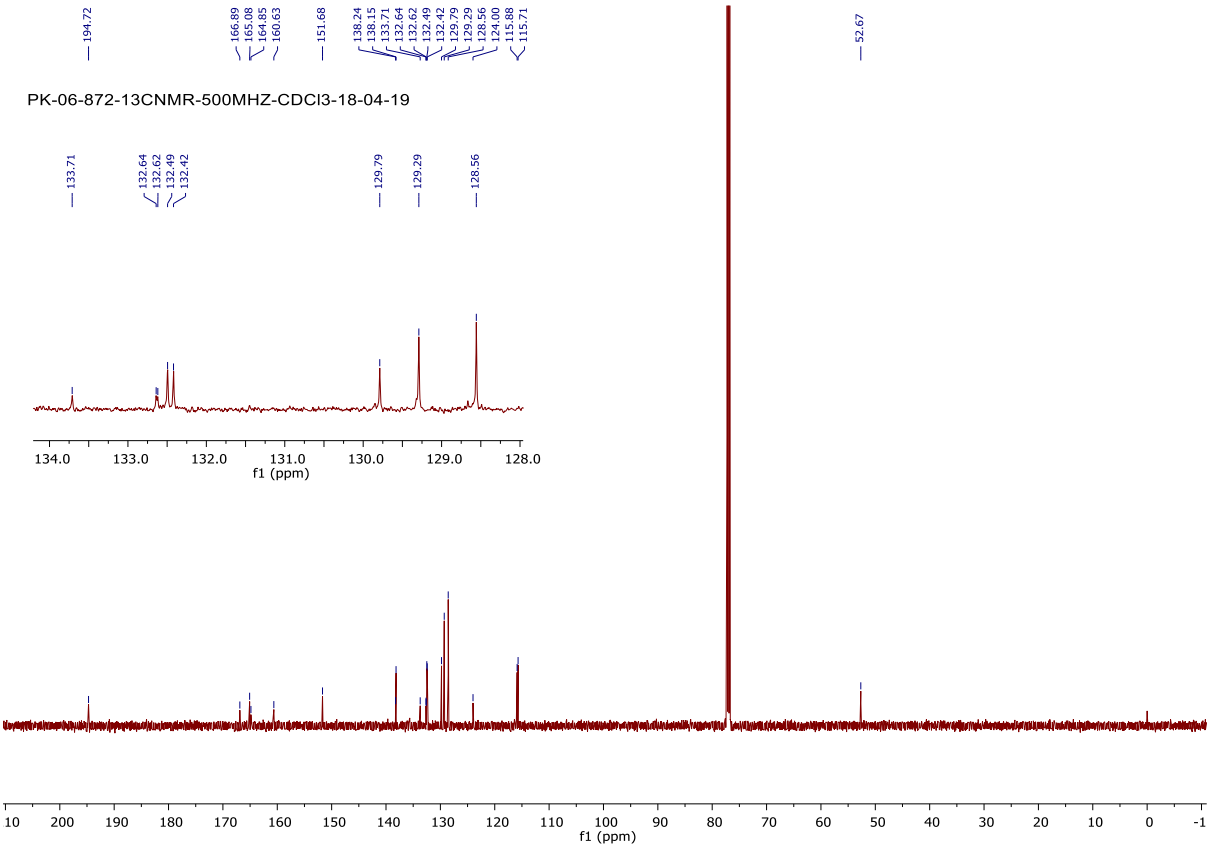

PK-03-436R-13CNMR-500Hz-CDCl303-01-2018
f1 (ppm)

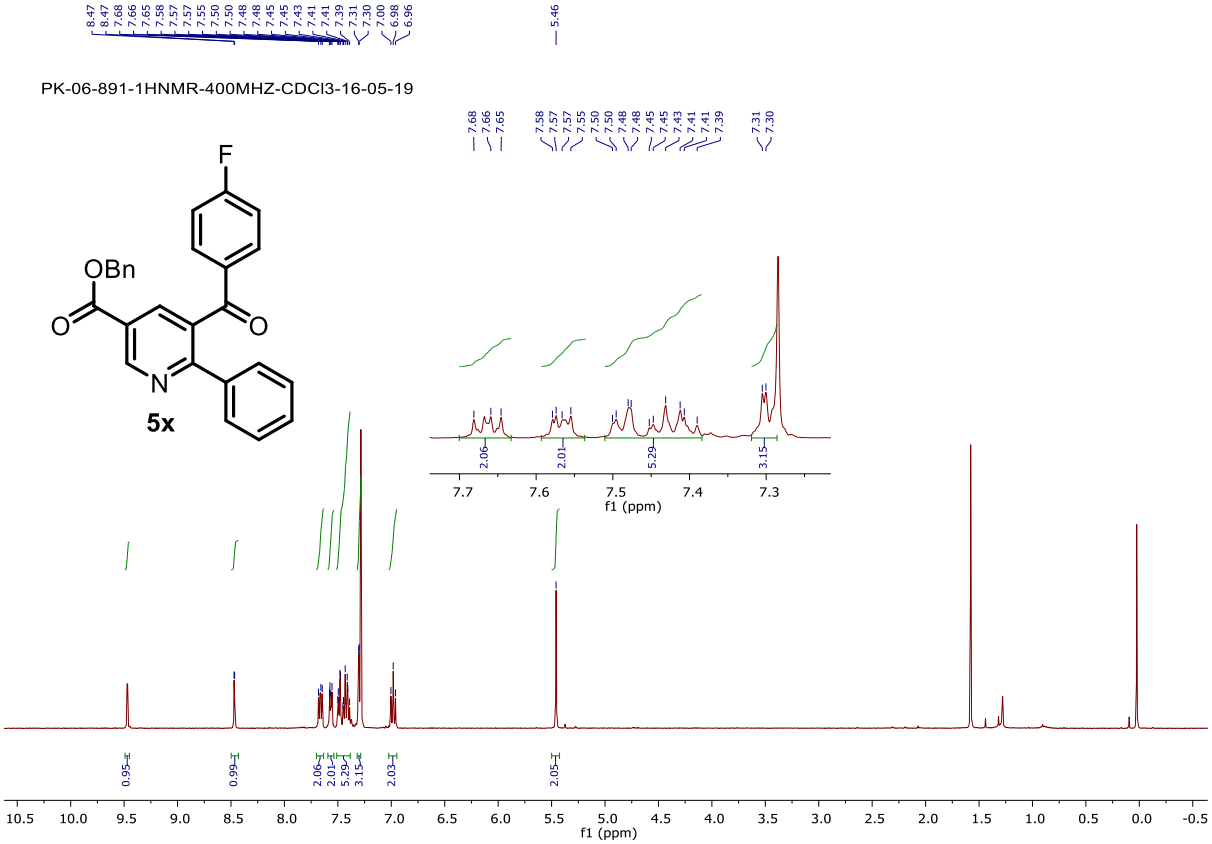
PK-06-872-1HNMR-400MHZ-CDCl3-18-04-19

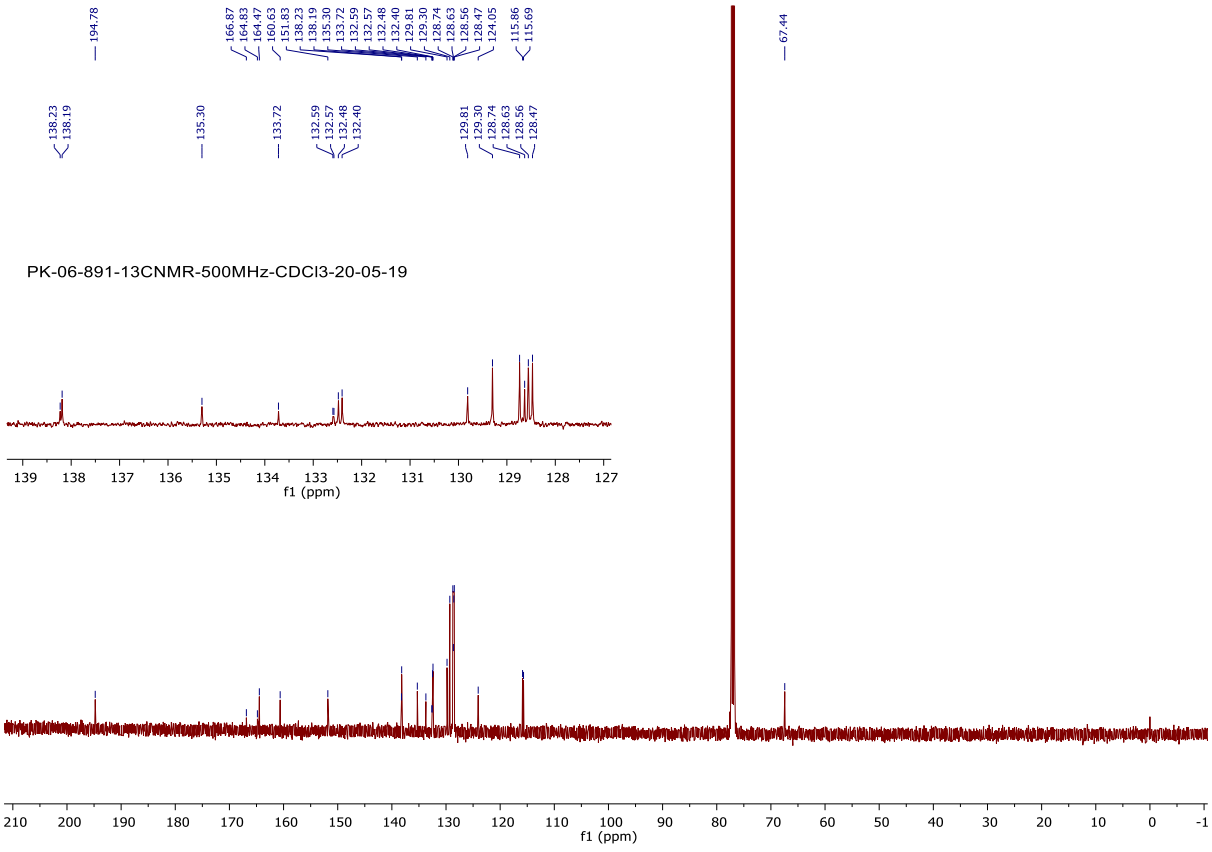


5w

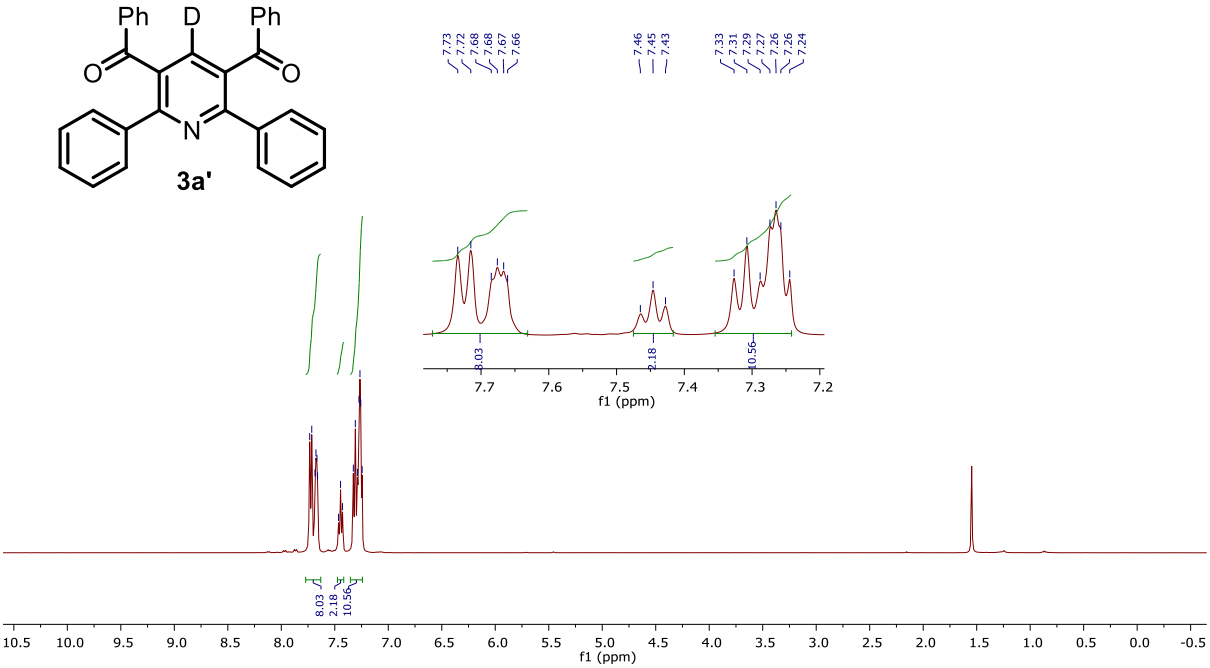
PK-06-872-13CNMR-500MHZ-CDCl3-18-04-19



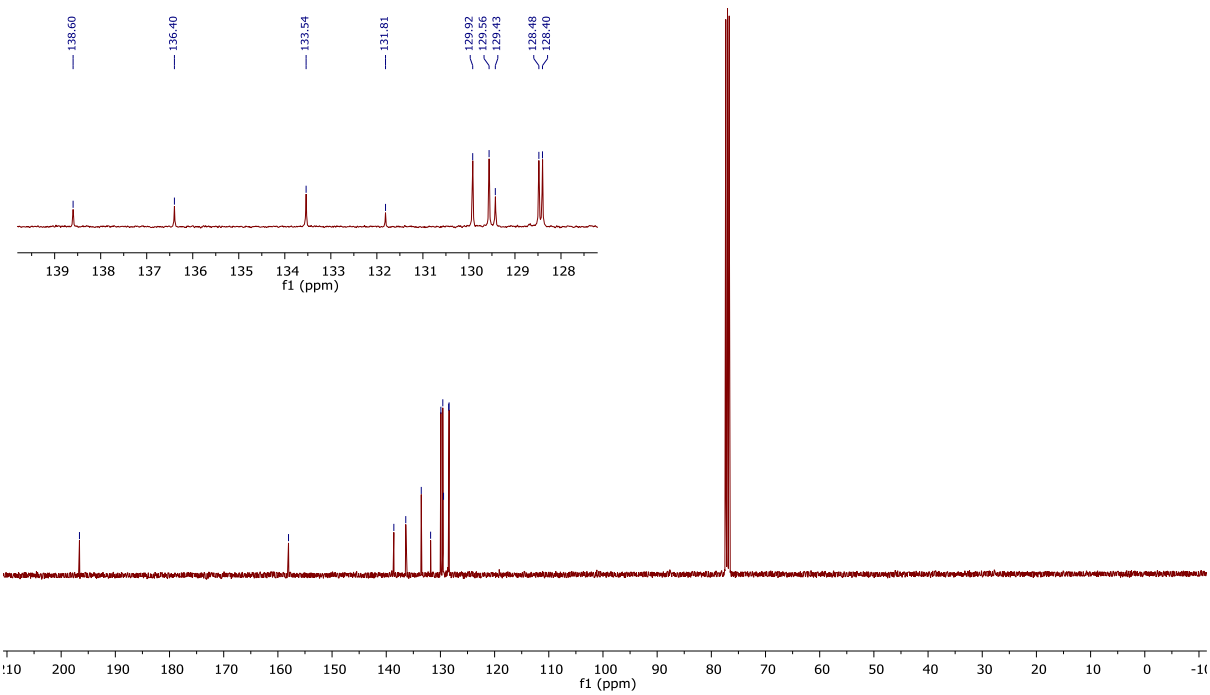

PK-06-891-1HNMR-400MHZ-CDCl3-16-05-19
OBn
F
O
O
N
5x
f1 (ppm)

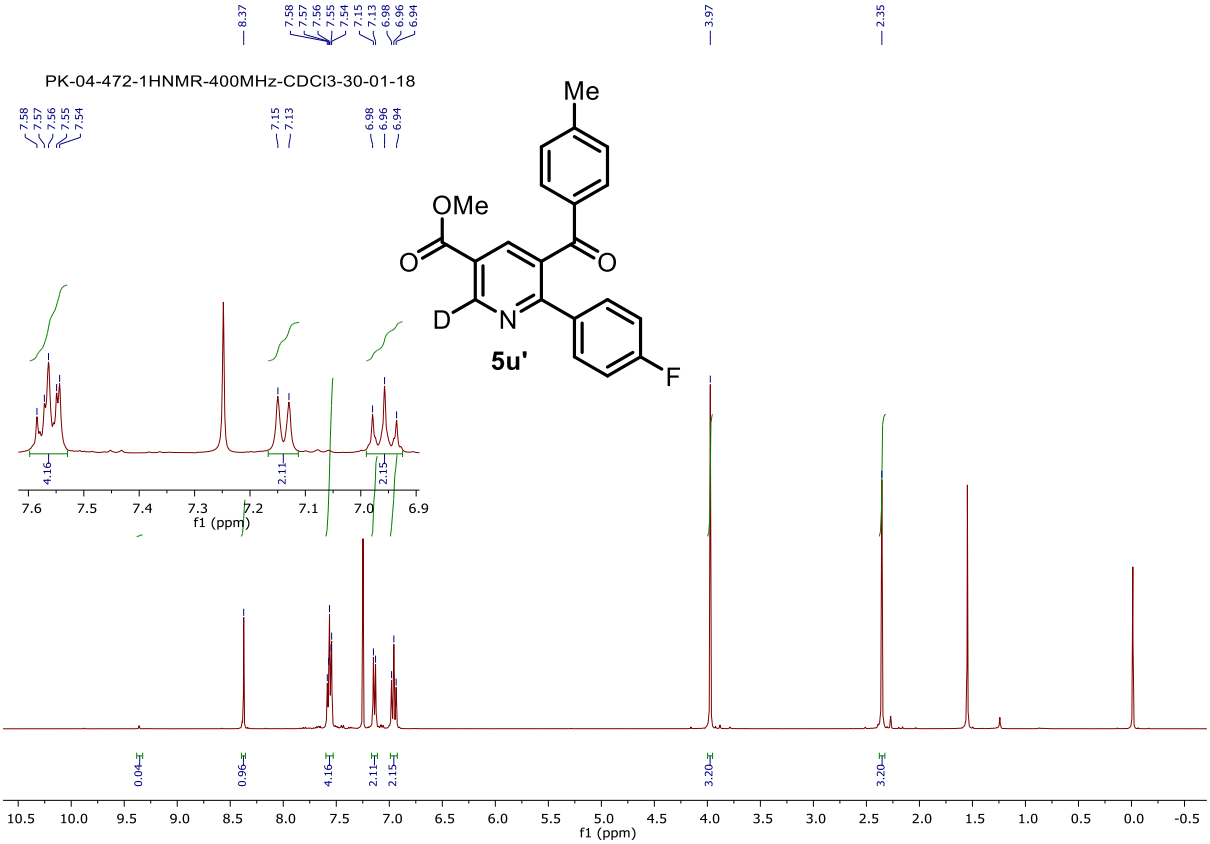

PK-06-891-13CNMR-500MHz-CDCl3-20-05-19
f1 (ppm)

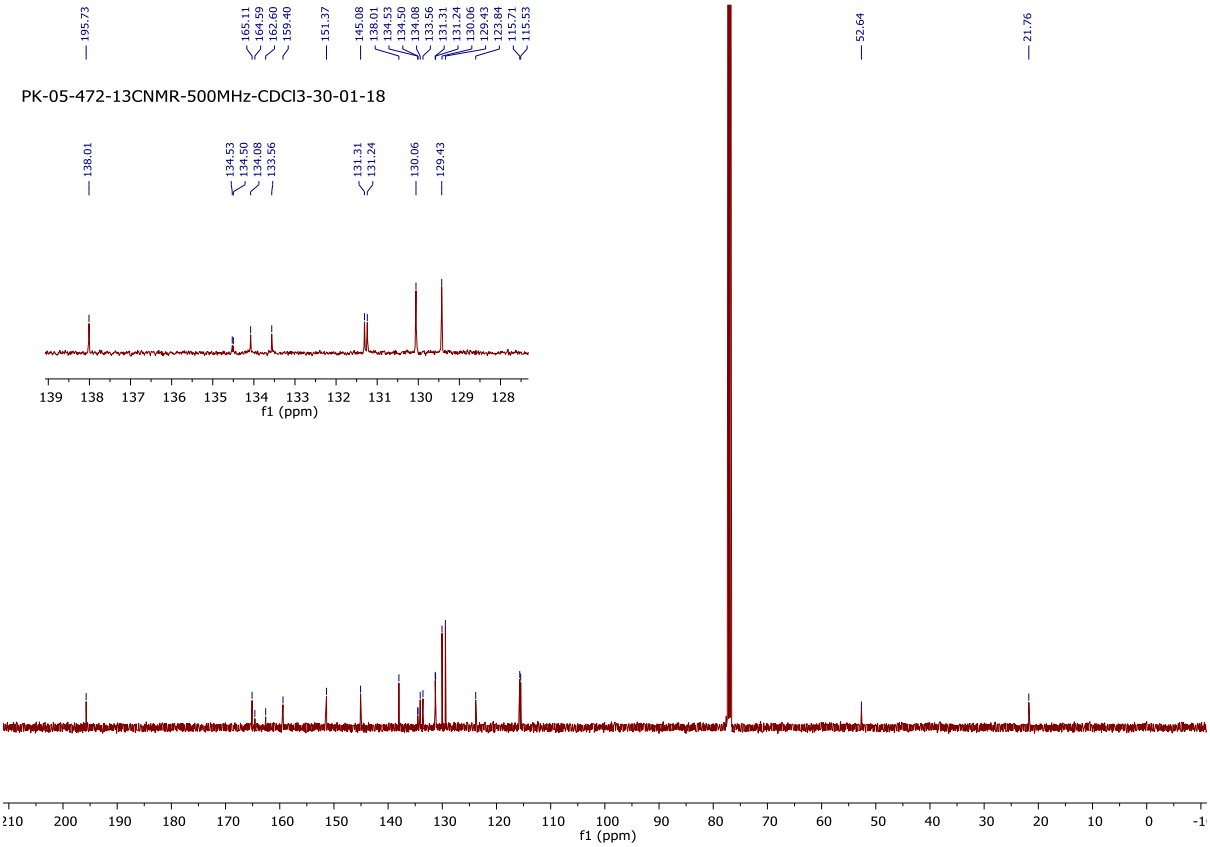
PK-03-440R-1HNMR-400MHz-CDCl3-09-01-18

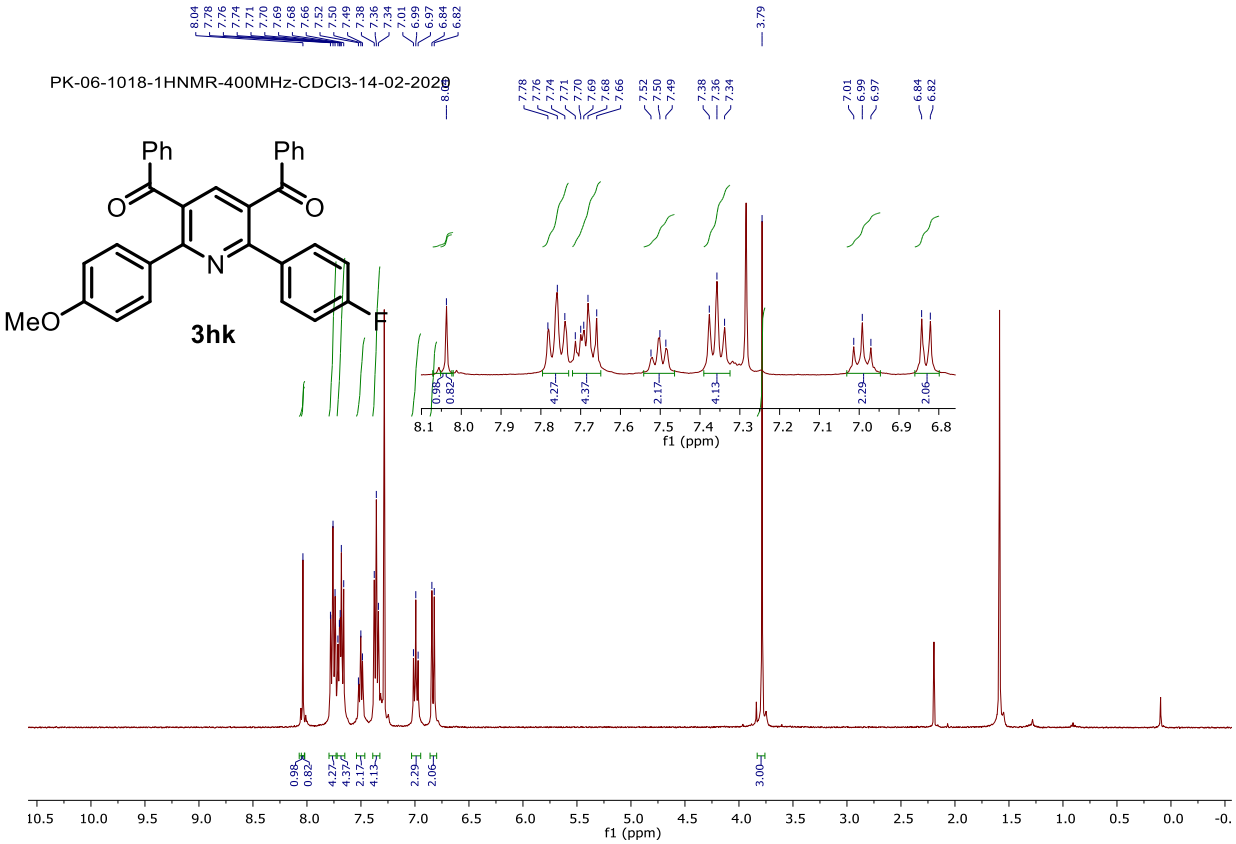


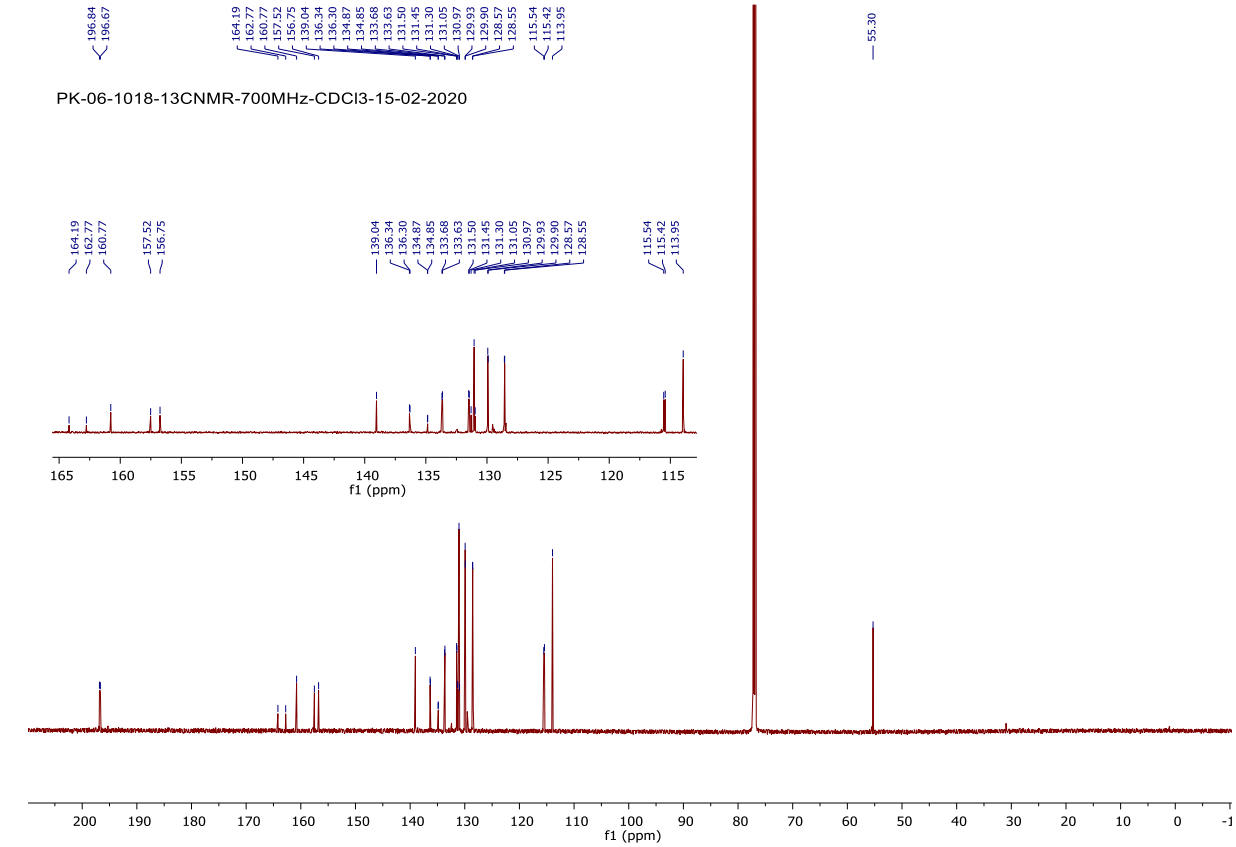
PK-03-440R-13CNMR-400MHz-CDCl3-09-01-18

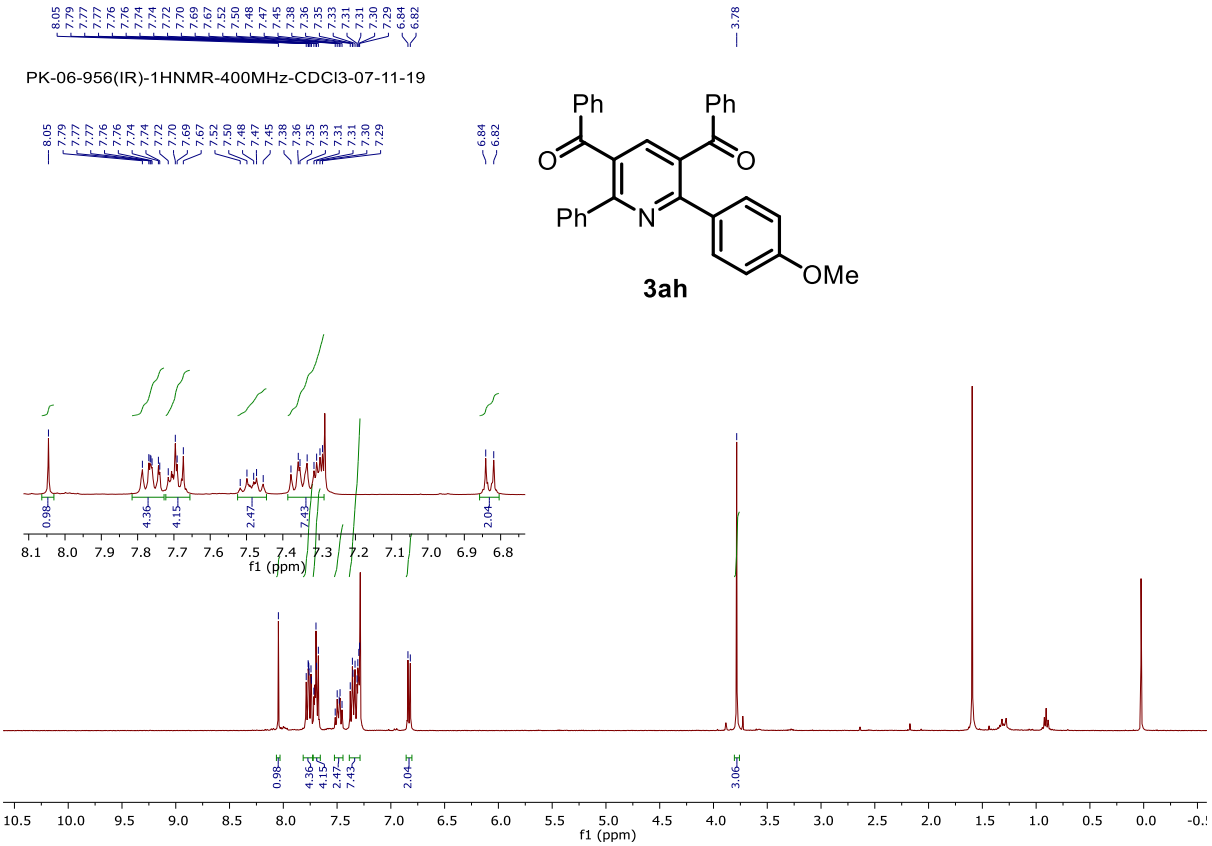


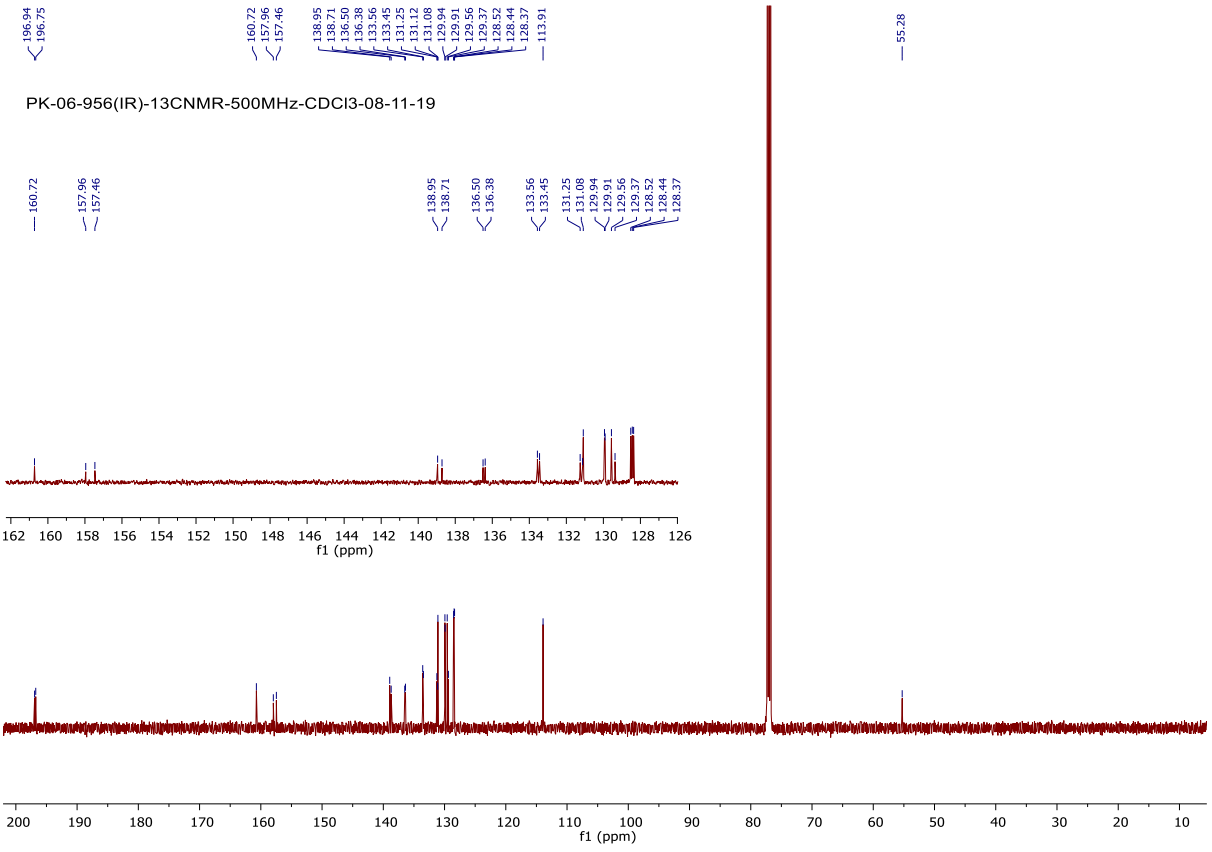

PK-04-472-1HNMR-400MHz-CDCl3-30-01-18
Me
OMe
O
O
D
N
F
5u'
f1 (ppm)

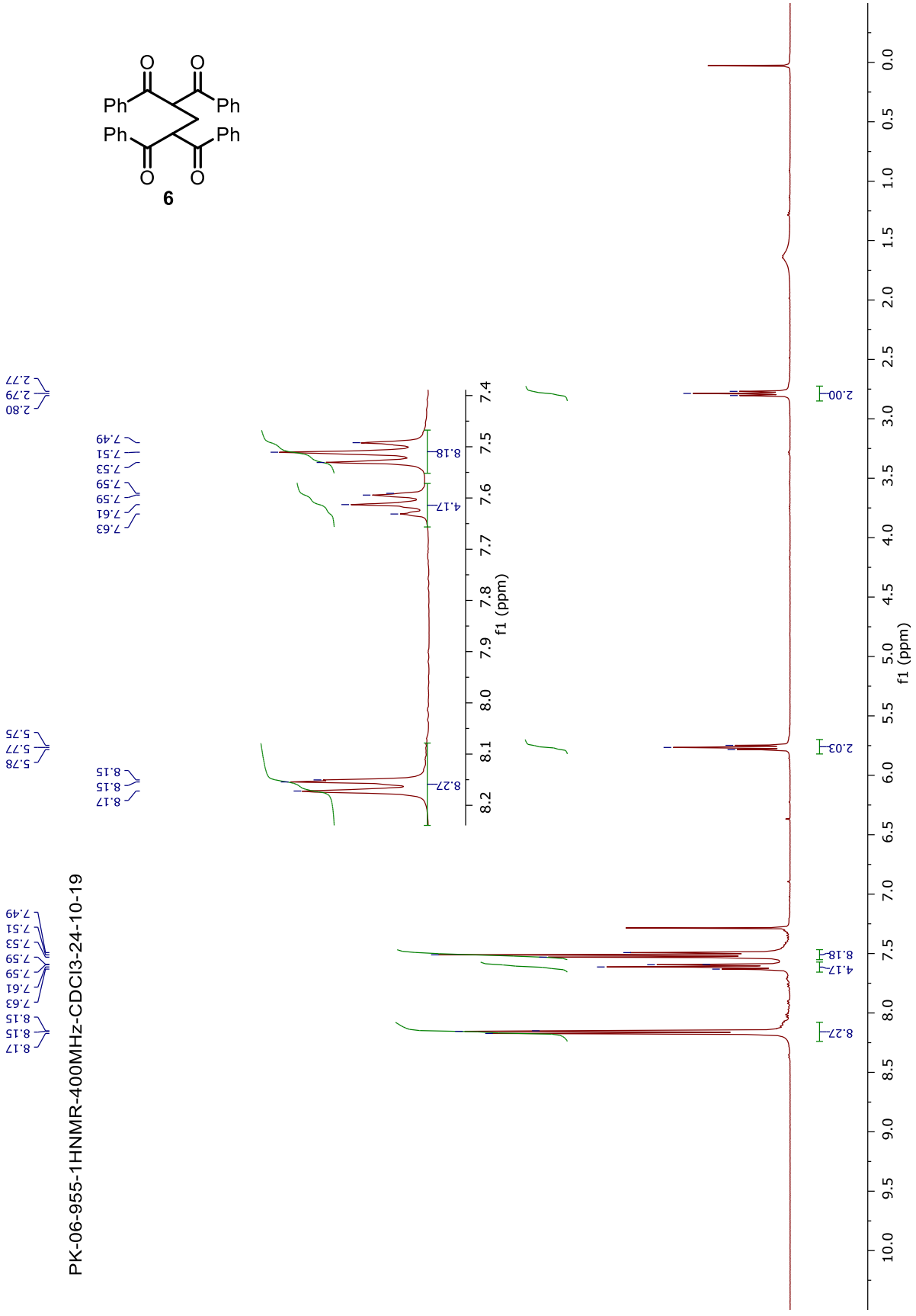

PK-05-472-13CNMR-500MHz-CDCl3-30-01-18
f1 (ppm)


PK-06-1018-1HNMR-400MHz-CDCl3-14-02-2020
Ph
Ph
O
O
N
MeO
F
3hk
f1 (ppm)


PK-06-1018-13CNMR-700MHz-CDCl3-15-02-2020
f1 (ppm)


PK-06-956(IR)-1HNMR-400MHz-CDCl3-07-11-19
Ph
Ph
O
O
Ph
N
OMe
3ah
f1 (ppm)


PK-06-956(IR)-13CNMR-500MHz-CDCl3-08-11-19
f1 (ppm)


Ph
Ph
Ph
Ph
O
O
O
O
6
PK-06-955-1HNMR-400MHz-CDCl3-24-10-19
f1 (ppm)
8.27
4.17
8.18
2.00
2.03

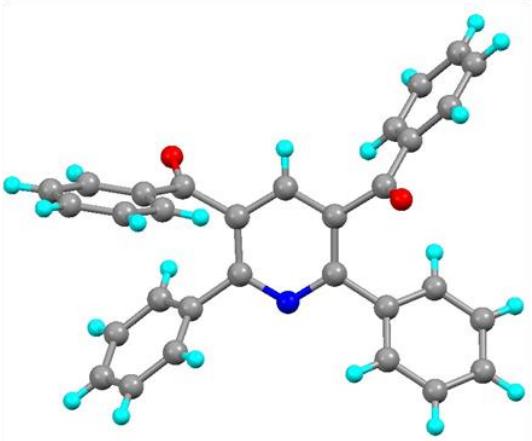
X-ray diffraction structural analysis data of 3a:

Sample preparation: 20 mg of **3a** (Colorless solid) was added to a 10 mL beaker and dissolved in minimal amount of chloroform. Hexane (3 mL) was added to the beaker along the wall. The beaker was capped loosely and kept at room temperature for slow evaporation. After 5 days, single crystal was obtained and then subjected to X-ray diffraction.

Table 1 Crystal data and structure refinement for 3a:

CCDC	1941419
Identification code	aa
Empirical formula	$C_{31}H_{21}NO_2$
Formula weight	439.49
Temperature/K	130.32
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	5.9798(9)
b/Å	20.690(3)
c/Å	18.016(3)
α/°	90
β/°	95.699(5)
γ/°	90
Volume/Å^3	2218.0(5)
Z	4
ρ_{calc}g/cm^3	1.316
μ/mm^{-1}	0.082
F(000)	920.0
Crystal size/mm^3	0.89 × 0.71 × 0.59
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.544 to 48.896
Index ranges	-6 ≤ h ≤ 6, -24 ≤ k ≤ 23, -20 ≤ l ≤ 20
Reflections collected	14821
Independent reflections	3629 [R_{int} = 0.1470, R_{sigma} =

	0.1287]
Data/restraints/parameters	3629/0/307
Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0615, wR_2 = 0.1123
Final R indexes [all data]	R_1 = 0.1290, wR_2 = 0.1368
Largest diff. peak/hole / e $Å^{-3}$	0.26/-0.29



Thermal ellipsoids shown at 50% probability level.

Figure S1. X-ray structure of (**3a)** i.e. (2,6-diphenylpyridine-3,5-diyl)bis(phenylmethanone).

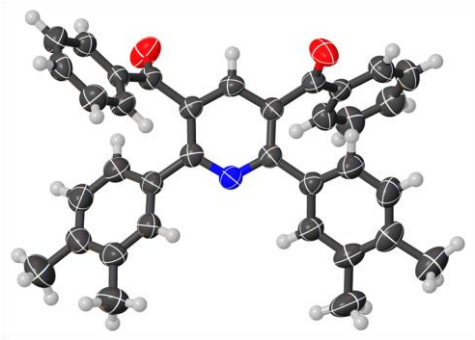
X-ray diffraction structural analysis data of 3q:

Sample preparation: 25 mg of **3q** (Colorless solid) was added to a 10 mL beaker and dissolved in minimal amount of chloroform. Hexane (3 mL) was added to the beaker along the wall. The beaker was capped loosely and kept at room temperature for slow evaporation. After 4 days, single crystal was obtained and then subjected to X-ray diffraction.

Table 1 Crystal data and structure refinement for 3q.

CCDC	1984052
Identification code	F1_a
Empirical formula	$C_{35}H_{29}NO_2$
Formula weight	495.59
Temperature/K	140.03
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	8.0729(5)
b/Å	25.2864(17)

c/Å	13.1642(9)
α/°	90
β/°	98.065(3)
γ/°	90
Volume/Å^3	2660.7(3)
Z	8
ρ_{calc}g/cm^3	1.2372
μ/mm^{-1}	0.076
F(000)	1048.0
Crystal size/mm^3	0.4 × 0.2 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	5.1 to 55.74
Index ranges	-10 ≤ h ≤ 10, -33 ≤ k ≤ 33, -17 ≤ l ≤ 14
Reflections collected	34635
Independent reflections	6345 [R_{int} = 0.0828, R_{sigma} = 0.0723]
Data/restraints/parameters	6345/0/347
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0598, wR_2 = 0.1117
Final R indexes [all data]	R_1 = 0.1137, wR_2 = 0.1311
Largest diff. peak/hole / e Å^{-3}	0.45/-0.47



Thermal ellipsoids shown at 50% probability level.

Figure S2. X-ray structure of (**3q)** i.e. (2,6-bis(3,4-dimethylphenyl)pyridine-3,5-diyl)bis(phenylmethanone).

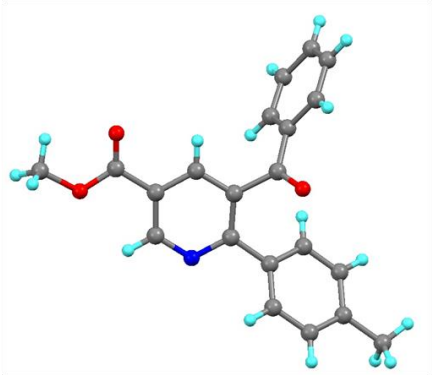
X-ray diffraction structural analysis data of 5a:

Sample preparation: 20 mg of **5a** (white solid) was added to a 10 mL beaker and dissolved in minimal amount of chloroform. Hexane (3 mL) was added to the beaker along the wall. The beaker was capped loosely and kept at room temperature for slow evaporation. After 4 days, single crystal was obtained and then subjected to X-ray diffraction.

Table 1 Crystal data and structure refinement for 5a.

CCDC	1884316
Identification code	M_a
Empirical formula	$C_{21}H_{17}NO_3$
Formula weight	331.36
Temperature/K	139.78
Crystal system	monoclinic
Space group	C2/c
a/Å	18.773(4)
b/Å	11.159(4)
c/Å	17.628(5)
α/°	90
β/°	115.428(13)
γ/°	90
Volume/Å^3	3334.9(16)
Z	8
ρ_{calc}g/cm^3	1.320
μ/mm^{-1}	0.089
F(000)	1392.0
Crystal size/mm^3	0.78 × 0.71 × 0.59
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.512 to 59.37
Index ranges	-26 ≤ h ≤ 26, -15 ≤ k ≤ 15, -24 ≤ l ≤ 22
Reflections collected	32932
Independent reflections	4715 [R_{int} = 0.1008, R_{sigma} =

	0.0905]
Data/restraints/parameters	4715/0/228
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0838, wR_2 = 0.1590
Final R indexes [all data]	R_1 = 0.1549, wR_2 = 0.1846
Largest diff. peak/hole / e $Å^{-3}$	0.64/-0.69



Thermal ellipsoids shown at 50% probability level.

Figure S3. X-ray structure of (**5a**) i.e. methyl 5-benzoyl-6-(*p*-tolyl)nicotinate.

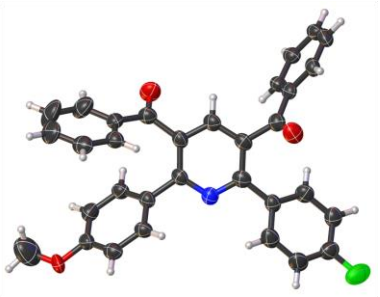
X-ray diffraction structural analysis data of 3hk:

Sample preparation: 15 mg of **3hk** (Colorless solid) was added to a 10 mL beaker and dissolved in minimal amount of dichloromethane and 2 drops of water was added. Hexane (4 mL) was added to the beaker along the wall. The beaker was capped loosely and kept at room temperature for slow evaporation. After 7 days, single crystal was obtained and then subjected to X-ray diffraction.

Table 1 Crystal data and structure refinement for 3hk.

CCDC	1984061
Identification code	MONOP
Empirical formula	$C_{32}H_{22}FNO_3$
Formula weight	487.51
Temperature/K	296.15
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	11.234(5)
b/Å	20.433(10)

c/Å	11.247(6)
α/°	90
β/°	107.484(10)
γ/°	90
Volume/Å^3	2462(2)
Z	4
ρ_{calc}g/cm^3	1.315
μ/mm^{-1}	0.089
F(000)	1016.0
Crystal size/mm^3	0.4 × 0.1 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	7.088 to 50.958
Index ranges	-13 ≤ h ≤ 12, -24 ≤ k ≤ 24, -12 ≤ l ≤ 13
Reflections collected	12972
Independent reflections	4573 [R_{int} = 0.1034, R_{sigma} = 0.1020]
Data/restraints/parameters	4573/2/335
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0837, wR_2 = 0.2101
Final R indexes [all data]	R_1 = 0.1579, wR_2 = 0.2530
Largest diff. peak/hole / e Å^{-3}	0.68/-0.43



Thermal ellipsoids shown at 50% probability level.

Figure S4. X-ray structure of (**3hk**) i.e. (2-(4-fluorophenyl)-6-(4-methoxyphenyl)pyridine-3,5-diyl)bis(phenylmethanone).