Divergent Synthesis of Isoxazoles and 6*H*-1,2-Oxazines via Hypervalent Iodine Mediated Intramolecular Oxygenation of Alkenes

Yuhang Chen, Dingcheng Zhang, Mingze Sun and Zhenhua Ding*
Jiangsu Key Laboratory of Drug Design and Optimization, Department of Medicinal Chemistry, School of Pharmacy, China Pharmaceutical University, Nanjing 210009, China

Supporting Information

Table of contents

1. General information

All purchased reagents and solvents were used without further purification unless otherwise noted.

Flash column chromatography was carried out using commercially available silica gel (300-400 mesh) under pressure.

Analytical thin layer chromatography was performed by using commercially prepared silica gel plates (HSGF254) and visualization was effected at 254 nm.

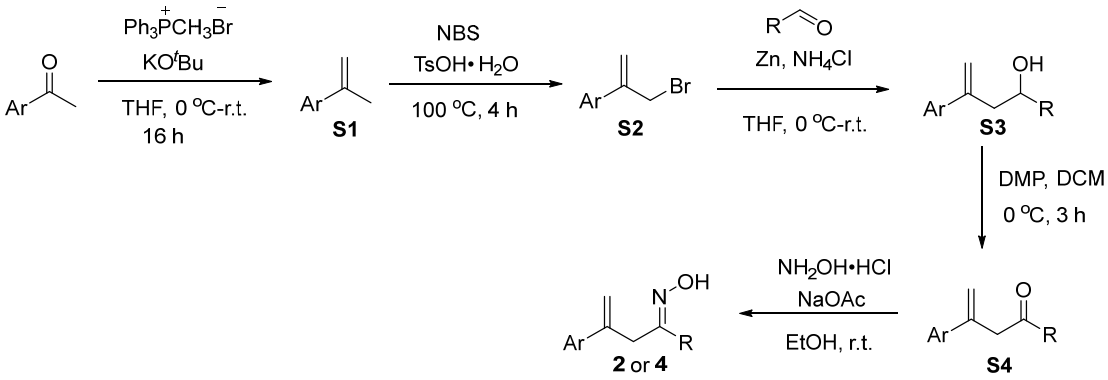
Melting points were measured using ShenGuang WRS-2 melting point apparatus.

^{1}H NMR, $^{13}C\{H\}$ NMR and $^{19}F\{H\}$ NMR spectra were recorded on a Bruker AV-300 (300 MHz) NMR spectrometer with $CDCl_3$ as the solvent. Chemical shifts (δ) were reported in ppm from tetramethylsilane with the solvent resonance as internal standard (^{1}H: δ=7.26 ppm, ^{13}C: δ=77.0 ppm).

High-resolution mass spectrometry (HRMS) was performed on Agilent QTOF 6520 mass spectrometer with an electrospray ionization (ESI) source.

2. General procedures

2.1 General procedure for synthesis of substrates 2 and 4



S1: To a dried flask were added methyl triphenylphosphonium bromide (1.2 equiv.) and anhydrous THF (1.6 mL/mmol). The suspension was cooled to 0 °C, KO^{t}Bu (1.2 equiv.) was added and the resulting yellow suspension was allowed to stir at 0 °C for 45 min. To this suspension, a solution of ketone (1.0 equiv.) in THF (0.7 mL/mmol) was added dropwise and the resulting mixture was warmed gradually to r.t. and allowed to stir for 16 h. The reaction mixture was concentrated under reduced pressure and filtered over Celite®. The filtrate was concentrated under reduced pressure to yield a yellow oil. Purification by column chromatography over silica gel (300-400 mesh) using petroleum ether as eluent afforded **S1**.[1]

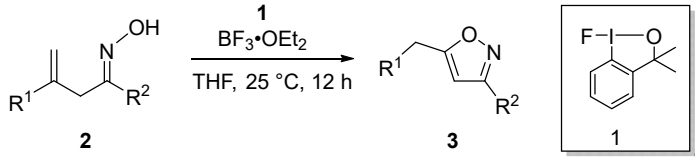
S2: In a dried flask, **S1** (1.0 equiv.) and THF (3.0 mL/mmol) were added. To the resulting solution, *N*-Bromosuccinimide (1.05 equiv.) and TsOH·H2O (0.1 equiv.) were added and the solution was refluxed at 100 °C for 4 h. The reaction mixture was cooled to ambient temperature and the reaction mixture was diluted with petroleum ether (15 mL/mmol) and washed with H2O (15 mL × 3). The organic phase was dried over anhydrous Na_2SO_4, concentrated under reduced pressure to obtain a yellow oil. Purification by column chromatography over silica gel (300-400 mesh) using petroleum ether as eluent afforded **S2**.[1]

S3: In a flask **S2** (1.2 equiv.), the aldehyde (1.0 equiv.) and THF (4 mL/mmol of **S2**) were added and the resulting mixture was allowed to stir at 0 °C, followed by the addition of Zinc powder (1.2 equiv.) and sat. aqueous NH_4Cl (0.5 mL/mmol). The reaction mixture was warmed to ambient temperature and allowed to stir for 3 h. The resulting suspension was quenched by water (10 ml/mmol) and filtered over Celite®. The filtrate was extracted with ethyl acetate 3 times. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography over silica gel (300-400 mesh) to give **S3**.[2]

S4: In an oven dried flask **S3** (1.0 equiv.) was taken and to this dry DCM (4.0 mL/mmol) was added. The resulting solution was cooled to 0 °C. To this Dess-Martin periodinane (1.5 equiv.) was added. The resulting suspension was stirred at 0 °C for 3 h. The reaction mixture was diluted with DCM (10.0 mL/mmol) and sat. aqueous $NaHCO_3$ (10 mL/mmol). Organic was separated and the aqueous layer was extracted with DCM 3 times. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography over silica gel (300-400 mesh) to give **S4**.[1]

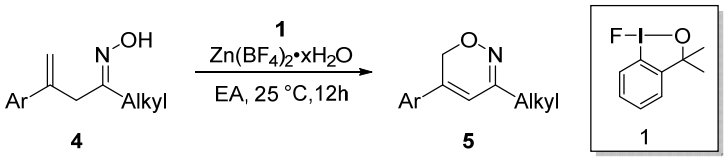
2 or **4**: To a stirred solution of **S4** (1.0 equiv.) in EtOH (2 mL/mmol), hydroxylamine hydrochloride (5.0 equiv.), NaOAc (7.0 equiv.) was added at r.t.. The mixture was stirred at the room temperature until the reaction was completed, monitored by TLC. Then, the solvent was removed and the residue was purified by flash column chromatography to give **2** or **4**.[3]

2.2 General procedure for synthesis of products 3a-3x



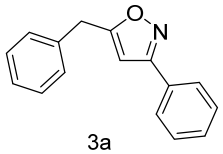
1 (0.24 mmol, 1.2 equiv.), **2** (0.2 mmol, 1.0 equiv.), BF_3•OEt_2 (0.01 mmol, 5 mol%), and THF (2 mL) were added to an oven-dried Schlenk tube and stirred at 25 °C for 12 h, and the reaction was monitored by TLC. The resulting solution was concentrated and purified by flash column chromatography to give corresponding product.

2.3 General procedure for synthesis of products 5a-5k



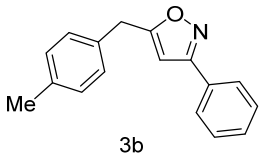
1 (0.36 mmol, 1.2 equiv.), **4** (0.3 mmol, 1.0 equiv.), $Zn(BF_4)_2$•xH_2O (0.015 mmol, 5 mol%), and EA (3 mL) were added to an oven-dried Schlenk tube and stirred at 25 °C for 12 h, and the reaction was monitored by TLC. The resulting solution was concentrated and purified by flash column chromatography to give corresponding product.

3. Characterization data of products



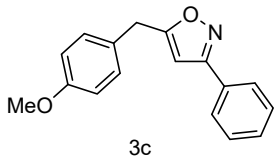
3a

*5-Benzyl-3-phenylisoxazole **(3a)***. White solid (38 mg, 81%); m.p. 78.6－78.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.44 – 7.38 (m, 3H), 7.36 – 7.26 (m, 5H), 6.20 (t, *J* = 0.9 Hz, 1H), 4.11 (s, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.8, 162.5, 136.0, 129.9, 129.2, 128.9, 128.9, 128.5, 127.2, 126.8, 100.0, 33.4; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{14}NO$ 236.1075, found 236.1073.



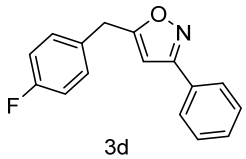
3b

*5-(4-Methylbenzyl)-3-phenylisoxazole **(3b)***. White solid (42 mg, 84%); m.p. 78.9－79.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.49 – 7.33 (m, 3H), 7.23 – 7.09 (m, 4H), 6.18 (t, *J* = 0.9 Hz, 1H), 4.06 (s, 2H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 173.1, 162.5, 136.9, 132.9, 129.9, 129.6, 129.3, 128.9, 128.8, 126.8, 99.9, 33.0, 21.1; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1228.



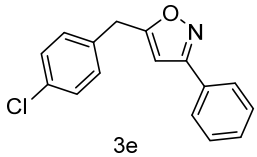
3c

*5-(4-Methoxybenzyl)-3-phenylisoxazole **(3c)***. White solid (42 mg, 79%); m.p. 104.6－107.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.48 – 7.35 (m, 3H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.18 (t, *J* = 1.0 Hz, 1H), 4.05 (s, 2H), 3.80 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 173.3, 162.5, 158.8, 130.0, 129.9, 129.2, 128.9, 128.0, 126.8, 114.3, 99.9, 55.3, 32.5; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO_2$ 266.1181, found 266.1175.



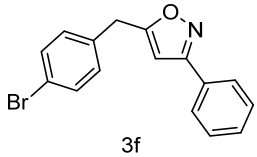
3d

*5-(4-Fluorobenzyl)-3-phenylisoxazole **(3d)***. White solid (39 mg, 77%); m.p. 78.2－80.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.47 – 7.36 (m, 3H), 7.25 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.20 (t, *J* = 0.9 Hz, 1H), 4.08 (s, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.4, 162.5, 162.0 (d, $^{1}J_{C\text{-}F}$ = 245.8 Hz), 131.7 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 130.5 (d, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 130.0, 129.1, 128.9, 126.8, 115.8 (d, $^{2}J_{C\text{-}F}$ = 21.4 Hz), 100.1, 32.5; ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -115.4; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}FNO$ 254.0981, found 254.0979.



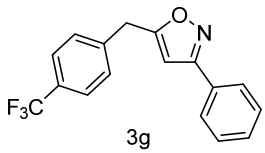
3e

5-(4-Chlorobenzyl)-3-phenylisoxazole ***(3e)***. White solid (46 mg, 85%); m.p. 118.9—122.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.49 – 7.37 (m, 3H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.21 (t, *J* = 0.9 Hz, 1H), 4.07 (s, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.0, 162.5, 134.4, 133.2, 130.3, 130.0, 129.0, 128.9, 126.8, 100.2, 32.7; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}ClNO$ 270.0686, found 270.0685.



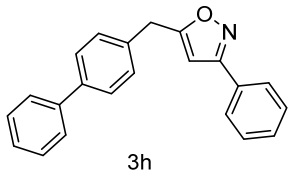
3f

5-(4-Bromobenzyl)-3-phenylisoxazole ***(3f)***. White solid (52 mg, 83%); m.p. 107.7—110.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.44 – 7.38 (m, 3H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.21 (s, 1H), 4.06 (s, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.9, 162.5, 134.9, 132.0, 130.6, 130.0, 129.0, 128.9, 126.8, 121.2, 100.2, 32.7; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}BrNO$ 314.0181, found 314.0179.



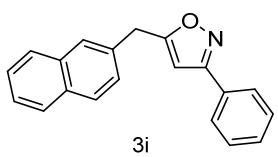
3g

3-Phenyl-5-(4-(trifluoromethyl)benzyl)isoxazole ***(3g)***. White solid (28 mg, 46%); m.p. 89.6—90.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 6.8, 2.9 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.49 – 7.37 (m, 5H), 6.25 (s, 1H), 4.18 (s, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.4, 162.6, 139.9, 130.1 (q, $^{2}J_{C\text{-}F}$ = 32.4 Hz), 130.0, 129.3, 128.9, 126.8, 125.8 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 124.1 (q, $^{1}J_{C\text{-}F}$ = 270.8 Hz), 100.3, 33.1; ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -62.5; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}F_3NO$ 304.0949, found 304.0948.



3h

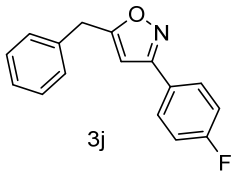
5-([1,1'-Biphenyl]-4-ylmethyl)-3-phenylisoxazole ***(3h)***. White solid (51 mg, 82%); m.p. 137.0—138.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.56 (dd, *J* = 7.9, 3.4 Hz, 4H), 7.46 – 7.37 (m, 5H), 7.34 (d, *J* = 7.9 Hz, 3H), 6.23 (s, 1H), 4.13 (s, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.6, 162.6, 140.7, 140.2, 135.0, 130.0, 129.4, 129.2, 128.9, 127.6, 127.4, 127.1, 126.8, 100.1, 33.0; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{18}NO$ 312.1388, found 312.1386.



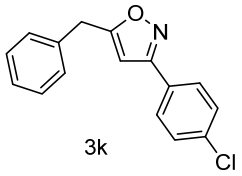
3i

5-(Naphthalen-2-ylmethyl)-3-phenylisoxazole ***(3i)***. White solid (49 mg, 86%); m.p. 112.9—116.6 °C; ^{1}H NMR (300

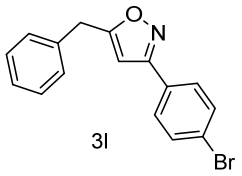
MHz, $CDCl_3$) δ 7.79 (t, *J* = 7.9 Hz, 3H), 7.76 – 7.69 (m, 3H), 7.49 – 7.43 (m, 2H), 7.38 (dd, *J* = 6.5, 2.8 Hz, 4H), 6.19 (s, 1H), 4.24 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 172.7, 162.5, 133.6, 133.4, 132.6, 129.9, 129.2, 128.9, 128.7, 127.8, 127.7, 127.6, 127.0, 126.8, 126.4, 126.0, 100.2, 33.5; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{16}NO$ 286.1232, found 286.1228.



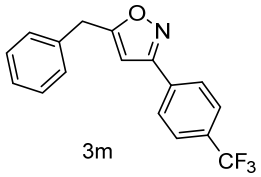
5-Benzyl-3-(4-fluorophenyl)isoxazole ***(3j)***. White solid (46 mg, 91%); m.p. 71.2—71.8 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.9, 5.3 Hz, 2H), 7.41 – 7.24 (m, 5H), 7.10 (t, *J* = 8.7 Hz, 2H), 6.16 (t, *J* = 0.9 Hz, 1H), 4.12 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 173.0, 163.7 (d, $^1J_{C\text{-}F}$ = 249.8 Hz), 161.6, 135.9, 128.9, 128.7 (d, $^3J_{C\text{-}F}$ = 8.5 Hz), 127.3, 125.4 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 116.0 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 99.9, 33.3; $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$) δ -110.8; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}FNO$ 254.0981, found 254.0978.



5-Benzyl-3-(4-chlorophenyl)isoxazole ***(3k)***. White solid (48 mg, 89%); m.p. 73.6—74.6 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 7.36 – 7.25 (m, 5H), 6.17 (t, *J* = 0.9 Hz, 1H), 4.11 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 173.1, 161.5, 135.9, 135.8, 129.1, 128.9, 128.1, 127.7, 127.3, 99.9, 33.3; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}ClNO$ 270.0686, found 270.0682.

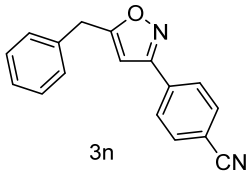


5-Benzyl-3-(4-bromophenyl)isoxazole ***(3l)***. White solid (52 mg, 83%); m.p. 88.7—90.1 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.41 – 7.22 (m, 5H), 6.16 (s, 1H), 4.10 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 173.2, 161.6, 135.8, 132.1, 128.9, 128.3, 128.2, 127.3, 124.2, 99.9, 33.3; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}BrNO$ 314.0181, found 314.0176.

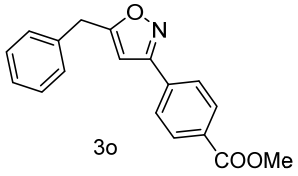


5-Benzyl-3-(4-(trifluoromethyl)phenyl)isoxazole ***(3m)***. White solid (40 mg, 66%); m.p. 78.3—81.1 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.42 – 7.26 (m, 5H), 6.24 (s, 1H), 4.14 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 173.5, 161.4, 135.7, 132.7, 131.7 (q, $^2J_{C\text{-}F}$ = 32.6 Hz), 129.0, 128.9, 127.4, 127.1,

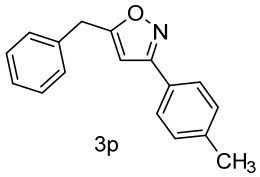
125.9 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 123.9 (q, $^{1}J_{C\text{-}F}$ = 272.5 Hz), 100.1, 33.4; $^{19}F\{^{1}H\}$ NMR (282 MHz, $CDCl_3$) δ -62.8; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}F_3NO$ 304.0949, found 304.0942.



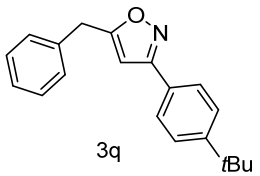
4-(5-Benzylisoxazol-3-yl)benzonitrile ***(3n)***. White solid (49 mg, 94%); m.p. 93.9—94.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.6 Hz, 2H), 7.69 (d, *J* = 8.6 Hz, 2H), 7.43 – 7.24 (m, 5H), 6.25 (t, *J* = 0.9 Hz, 1H), 4.14 (s, 2H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 173.8, 161.0, 135.6, 133.5, 132.7, 129.0, 128.9, 127.4, 127.3, 118.4, 113.4, 100.0, 33.3; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}N_2O$ 261.1028, found 261.1308.



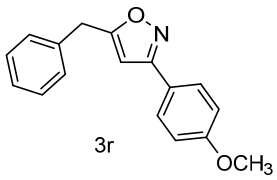
Methyl 4-(5-Benzylisoxazol-3-yl)benzoate ***(3o)***. White solid (54 mg, 92%); m.p. 127.8—128.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.39 – 7.24 (m, 5H), 6.25 (s, 1H), 4.12 (s, 2H), 3.92 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 173.3, 166.5, 161.6, 135.7, 133.4, 131.3, 130.1, 128.93, 128.91, 127.3, 126.7, 100.2, 52.3, 33.3; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{16}NO_3$ 294.1130, found 294.1129.



5-Benzyl-3-(p-tolyl)isoxazole ***(3p)***. White solid (35 mg, 70%); m.p. 86.0—88.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.39 – 7.27 (m, 5H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.17 (s, 1H), 4.11 (s, 2H), 2.37 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 172.5, 162.4, 140.0, 136.0, 129.6, 128.92, 128.86, 127.2, 126.7, 126.3, 100.0, 33.4, 21.44; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1228.

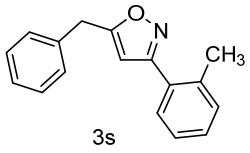


5-Benzyl-3-(4-(tert-butyl)phenyl)isoxazole ***(3q)***. White solid (46 mg, 79%); m.p. 52.8—54.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.38 – 7.24 (m, 5H), 6.18 (t, *J* = 0.9 Hz, 1H), 4.10 (s, 2H), 1.33 (s, 9H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 172.5, 162.4, 153.2, 136.1, 128.93, 128.87, 127.2, 126.5, 126.4, 125.8, 100.0, 34.8, 33.3, 31.3; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{22}NO$ 292.1701, found 292.1700.



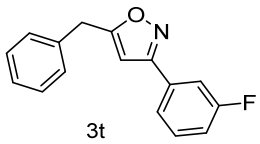
3r

5-Benzyl-3-(4-methoxyphenyl)isoxazole ***(3r)***. White solid (44 mg, 83%); m.p. 75.2—76.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.50 – 7.36 (m, 5H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.26 (s, 1H), 4.21 (s, 2H), 3.94 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.5, 162.2, 161.0, 136.1, 129.0, 128.9, 128.2, 127.2, 121.8, 114.3, 99.9, 55.4, 33.4; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO_2$ 266.1181, found 266.1178.



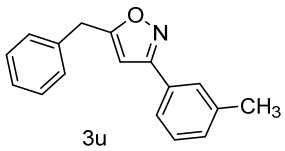
3s

5-Benzyl-3-(o-tolyl)isoxazole ***(3s)***. Yellow oil (24 mg, 48%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.39 – 7.26 (m, 7H), 7.22 (dd, *J* = 7.0, 2.0 Hz, 1H), 6.08 (s, 1H), 4.14 (s, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.7, 163.1, 136.8, 136.0, 131.0, 129.4, 129.3, 128.92, 128.89, 128.8, 127.2, 125.9, 102.6, 33.3, 21.1; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1226.



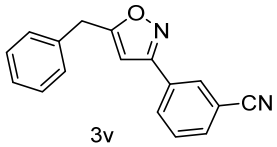
3t

5-Benzyl-3-(3-fluorophenyl)isoxazole ***(3t)***. White solid (40 mg, 79%); m.p. 56.8—57.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.8 Hz, 1H), 7.46 (dt, *J* = 9.7, 2.1 Hz, 1H), 7.42 – 7.23 (m, 6H), 7.09 (td, *J* = 8.4, 2.7 Hz, 1H), 6.18 (s, 1H), 4.11 (s, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 173.2, 163.0 (d, $^{1}J_{C\text{-}F}$ = 246.5 Hz), 161.6 (d, $^{4}J_{C\text{-}F}$ = 2.4 Hz), 135.8, 131.3 (d, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 130.5 (d, $^{3}J'_{C\text{-}F}$ = 8.3 Hz), 128.9, 127.3, 122.5 (d, $^{4}J'_{C\text{-}F}$ = 3.1 Hz), 116.8 (d, $^{2}J_{C\text{-}F}$ = 21.3 Hz), 113.8 (d, $^{2}J'_{C\text{-}F}$ = 23.1 Hz), 100.0, 33.3; ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ -112.2; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}FNO$ 254.0981, found 254.0979.



3u

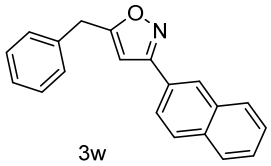
5-Benzyl-3-(m-tolyl)isoxazole ***(3u)***. White solid (42 mg, 84%); m.p. 81.1—83.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.38 – 7.24 (m, 6H), 7.20 (d, *J* = 7.7 Hz, 1H), 6.18 (s, 1H), 4.09 (s, 2H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.6, 162.6, 138.6, 136.0, 130.7, 129.1, 128.93, 128.88, 128.8, 127.4, 127.2, 123.9, 100.1, 33.4, 21.4; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1230.



3v

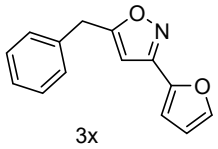
3-(5-Benzylisoxazol-3-yl)benzonitrile ***(3v)***. White solid (49 mg, 94%); m.p. 54.7—55.6 °C; ^{1}H NMR (300 MHz,

$CDCl_3$) δ 8.07 – 7.94 (m, 2H), 7.67 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.53 (td, *J* = 7.7, 0.9 Hz, 1H), 7.42 – 7.23 (m, 5H), 6.23 (t, *J* = 1.0 Hz, 1H), 4.13 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 173.8, 160.7, 135.6, 133.2, 130.9, 130.6, 130.3, 129.8, 129.0, 128.9, 127.4, 118.2, 113.2, 99.9, 33.3; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}N_2O$ 261.1028, found 261.1227.



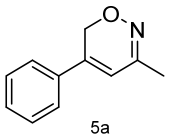
3w

5-Benzyl-3-(naphthalen-2-yl)isoxazole ***(3w)***. White solid (50 mg, 88%); m.p. 128.9—129.4 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.99 – 7.75 (m, 4H), 7.55 – 7.43 (m, 2H), 7.41 – 7.24 (m, 5H), 6.31 (s, 1H), 4.12 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 172.9, 162.5, 136.0, 134.0, 133.2, 129.0, 128.9, 128.7, 128.5, 127.9, 127.3, 127.0, 126.6, 126.5, 124.0, 100.2, 33.4; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{16}NO$ 286.1232, found 286.1231.



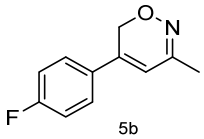
3x

5-Benzyl-3-(furan-2-yl)isoxazole ***(3x)***. White solid (27 mg, 60%); m.p. 37.5—40.9 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.43 – 7.22 (m, 5H), 6.84 (dd, *J* = 3.4, 0.8 Hz, 1H), 6.48 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.16 (t, *J* = 0.9 Hz, 1H), 4.10 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 172.5, 154.9, 144.4, 143.8, 135.7, 128.9, 127.3, 111.7, 110.1, 99.6, 33.2; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{12}NO_2$ 226.0868, found 226.0867.



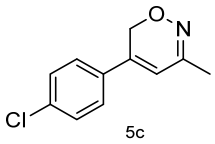
5a

3-Methyl-5-phenyl-6H-1,2-oxazine ***(5a)***. White solid (37 mg, 71%); m.p. 93.8—94.9 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 2H), 7.44 – 7.38 (m, 3H), 6.20 (s, 1H), 4.76 (s, 2H), 2.13 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 156.5, 140.2, 134.6, 129.8, 129.0, 125.6, 111.7, 64.0, 19.5; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{12}NO$ 174.0919, found 174.0915.



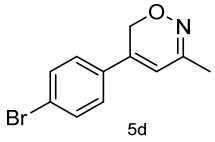
5b

5-(4-Fluorophenyl)-3-methyl-6H-1,2-oxazine ***(5b)***. Yellow solid (34 mg, 59%); m.p. 77.4—78.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 8.9, 5.2 Hz, 2H), 7.11 (t, *J* = 8.6 Hz, 2H), 6.14 (t, *J* = 1.3 Hz, 1H), 4.72 (d, *J* = 1.2 Hz, 2H), 2.12 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 163.6 (d, $^1J_{C\text{-}F}$ = 250.6 Hz), 156.4, 139.2, 130.9 (d, $^4J_{C\text{-}F}$ = 3.7 Hz), 127.6 (d, $^3J_{C\text{-}F}$ = 8.3 Hz), 116.2 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 111.6, 64.0, 19.5; $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$) δ -110.3; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{11}FNO$ 192.0825, found 192.0821.



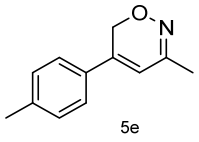
5c

*5-(4-Chlorophenyl)-3-methyl-6H-1,2-oxazine (**5c**)*. Yellow solid (51 mg, 82%); m.p. 60.4—63.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (s, 4H), 6.18 (t, *J* = 1.3 Hz, 1H), 4.71 (d, *J* = 1.3 Hz, 2H), 2.13 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 156.3, 138.9, 135.7, 133.0, 129.3, 126.9, 112.0, 63.7, 19.4; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{11}ClNO$ 208.0529, found 208.0525.



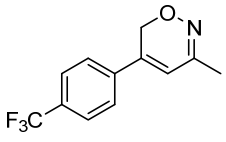
5d

*5-(4-Bromophenyl)-3-methyl-6H-1,2-oxazine (**5d**)*. White solid (42 mg, 56%); m.p. 61.3—62.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H), 6.19 (t, *J* = 1.3 Hz, 1H), 4.71 (d, *J* = 1.3 Hz, 2H), 2.13 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 156.3, 139.0, 133.5, 132.2, 127.1, 124.0, 112.1, 63.7, 19.4; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{11}BrNO$ 252.0024, found 252.0018.



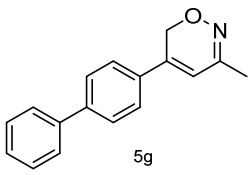
5e

*3-Methyl-5-(p-tolyl)-6H-1,2-oxazine (**5e**)*. Yellow oil (22 mg, 39%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.17 (t, *J* = 1.3 Hz, 1H), 4.74 (d, *J* = 1.2 Hz, 2H), 2.38 (s, 3H), 2.12 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 156.6, 140.3, 140.1, 131.6, 129.7, 125.5, 110.8, 64.0, 21.4, 19.5; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{14}NO$ 188.1075, found 188.1072.



5f

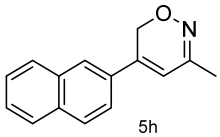
*3-Methyl-5-(4-(trifluoromethyl)phenyl)-6H-1,2-oxazine (**5f**)*. White solid (44 mg, 61%); m.p. 71.8—75.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 6.26 (t, *J* = 1.2 Hz, 1H), 4.76 (d, *J* = 1.3 Hz, 2H), 2.15 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 156.2, 138.6, 138.2, 131.4 (q, $^{2}J_{C\text{-}F}$ = 32.6 Hz), 126.0, 126.0, 123.8 (q, $^{1}J_{C\text{-}F}$ = 272.2 Hz), 113.5, 63.7, 19.4; $^{19}F\{^{1}H\}$ NMR (282 MHz, $CDCl_3$) δ -62.9; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{10}F_3NO$ 242.0793, found 242.0786.



5g

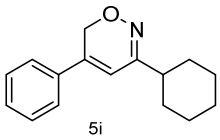
*5-([1,1'-Biphenyl]-4-yl)-3-methyl-6H-1,2-oxazine (**5g**)*. Yellow solid (35 mg, 47%); m.p. 138.1—140.2 °C; ^{1}H NMR

(300 MHz, $CDCl_3$) δ 7.69 – 7.57 (m, 4H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.41 – 7.33 (m, 1H), 6.24 (t, *J* = 1.3 Hz, 1H), 4.78 (d, *J* = 1.3 Hz, 2H), 2.14 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 156.5, 142.6, 140.0, 139.8, 133.3, 129.0, 127.9, 127.6, 127.0, 126.1, 111.5, 63.9, 19.5; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1229.



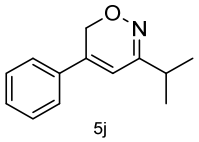
5h

*3-Methyl-5-(naphthalen-2-yl)-6H-1,2-oxazine (**5h**)*. Yellow solid (21 mg, 31%); m.p. 117.5—119.4 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.92 – 7.79 (m, 4H), 7.62 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.52 (dd, *J* = 6.3, 3.2 Hz, 2H), 6.32 (s, 1H), 4.88 (d, *J* = 1.3 Hz 2H), 2.16 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 156.5, 139.9, 133.8, 133.2, 131.7, 128.9, 128.5, 127.8, 127.2, 126.9, 125.3, 122.8, 112.0, 64.0, 19.5; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{14}NO$ 224.1075, found 224.1071.



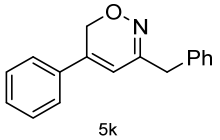
5i

*3-Cyclohexyl-5-phenyl-6H-1,2-oxazine (**5i**)*. Yellow oil (28 mg, 39%); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 – 7.37 (m, 5H), 6.25 (t, *J* = 1.5 Hz, 1H), 4.75 (d, *J* = 1.4 Hz, 2H), 2.49 – 2.32 (m, 1H), 1.92 – 1.79 (m, 4H), 1.77 – 1.69 (m, 1H), 1.49 – 1.28 (m, 5H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ163.44, 140.56, 134.97, 129.69, 129.00, 125.58, 109.98, 64.31, 42.54, 30.50, 26.08, 25.96; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{20}NO$ 242.1545, found 242.1541.



5j

*3-Isopropyl-5-phenyl-6H-1,2-oxazine (**5j**)*. Yellow oil (21 mg, 35%); ^1H NMR (300 MHz, $CDCl_3$) δ 7.52 – 7.44 (m, 3H), 7.42 (d, *J* = 6.2 Hz, 2H), 6.26 (t, *J* = 1.4 Hz, 1H), 4.76 (d, *J* = 1.4 Hz, 2H), 2.82 – 2.65 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 164.0, 140.7, 129.7, 129.0, 128.7, 125.6, 109.4, 64.3, 32.7, 20.2; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_{16}NO$ 202.1232, found 202.1227.



5k

*3-Benzyl-5-phenyl-6H-1,2-oxazine (**5k**)*. Yellow oil (30 mg, 40%); ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 10H), 6.10 (t, *J* = 1.3 Hz, 1H), 4.79 (d, *J* = 1.3 Hz, 2H), 3.73 (s, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.7, 140.4, 136.3, 134.6, 129.8, 129.0, 128.9, 128.8, 127.1, 125.6, 110.6, 64.4, 39.6; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1229.

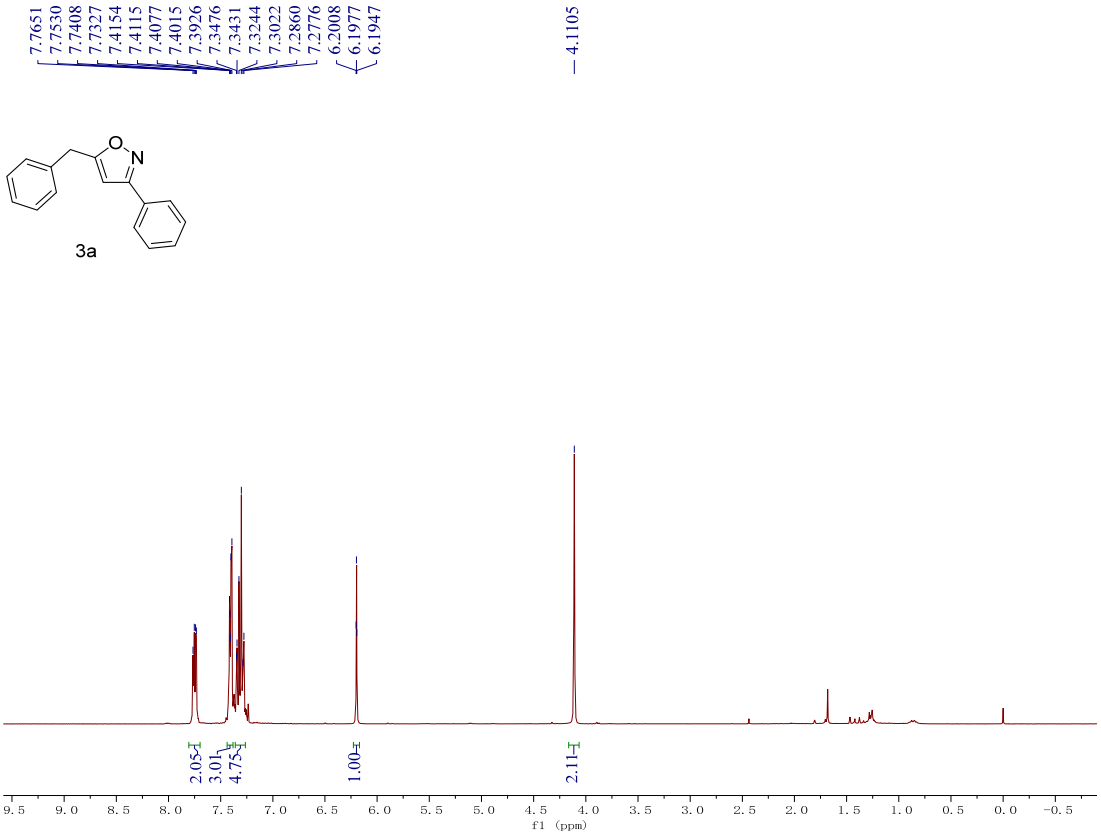
4. References

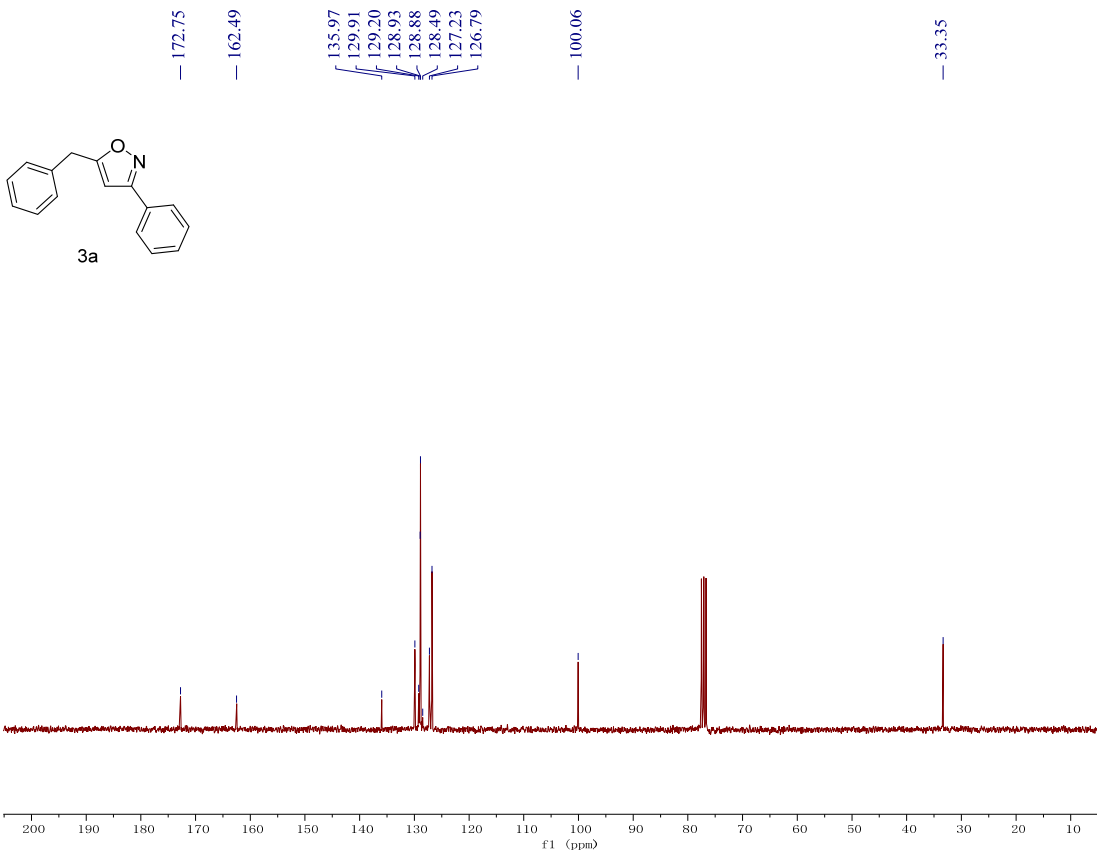
(1) C. B. Tripathi and S. Mukherjee, Catalytic Enantioselective Iodoetherification of Oximes, *Angew. Chem. Int. Ed.,* 2013, **52** ,8450−8453.

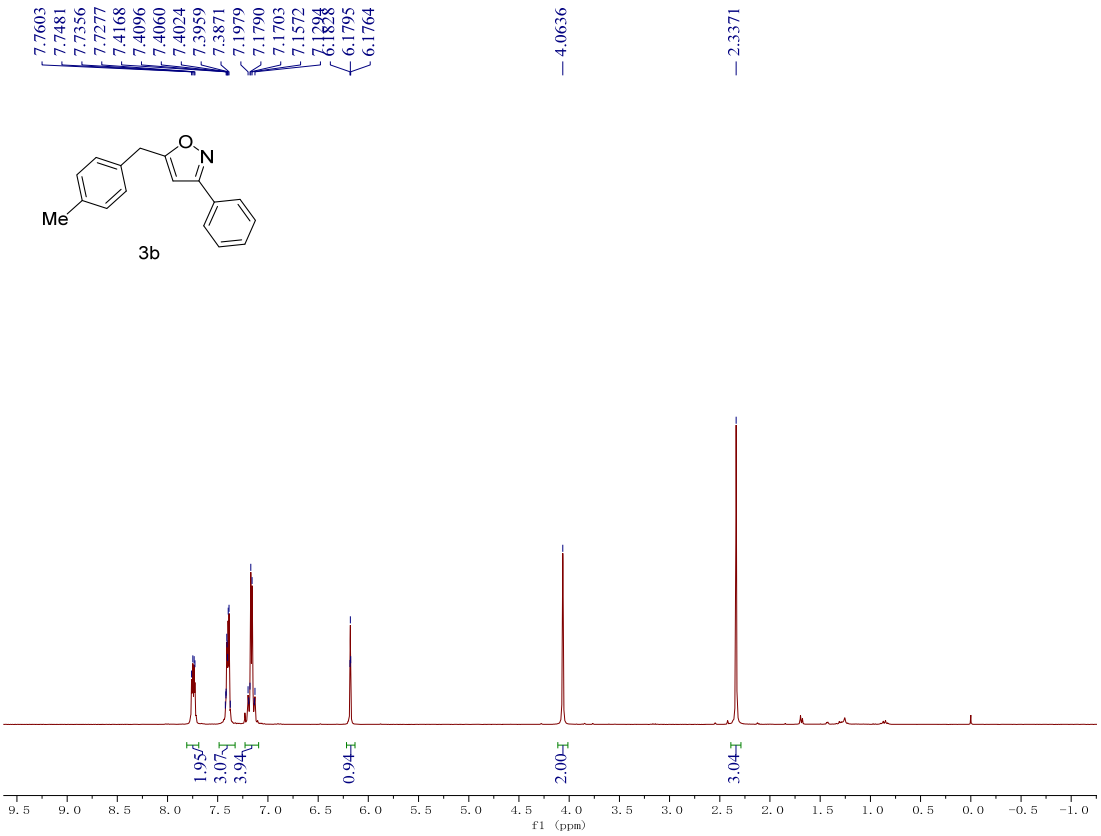
(2) R.-Z. Huang, K. K. Lau, Z. Li, T.-L. Liu and Y. Zhao, Rhodium-Catalyzed Enantioconvergent Isomerization of Homoallylic and Bishomoallylic Secondary Alcohols, *J. Am. Chem. Soc.*, 2018, **140**, 14647−14654.

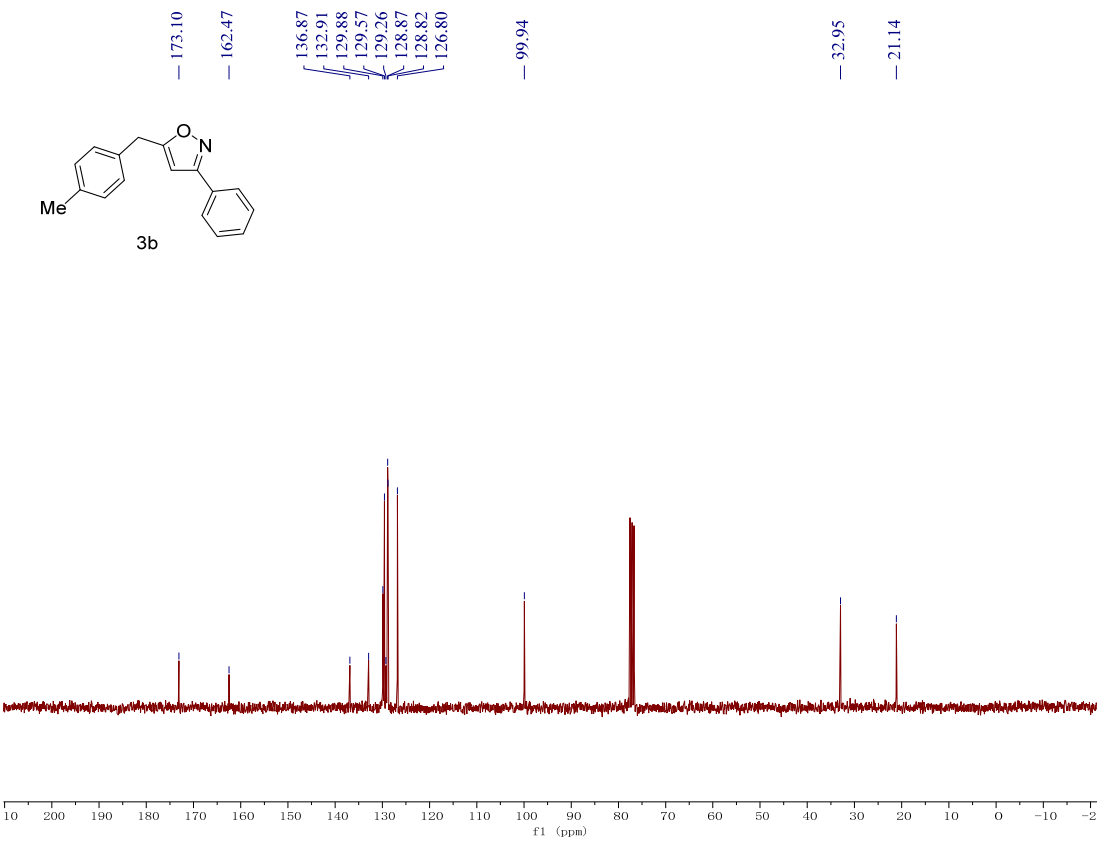
(3) Q. Wei, J.-R. Chen, X.-Q. Hu, X.-C. Yang, B. Lu and W.-J. Xiao, Photocatalytic Radical Trifluoromethylation/Cyclization Cascade: Synthesis of CF_3-Containing Pyrazolines and Isoxazolines, *Org. Lett.*, 2015, **17**, 4464−4467.

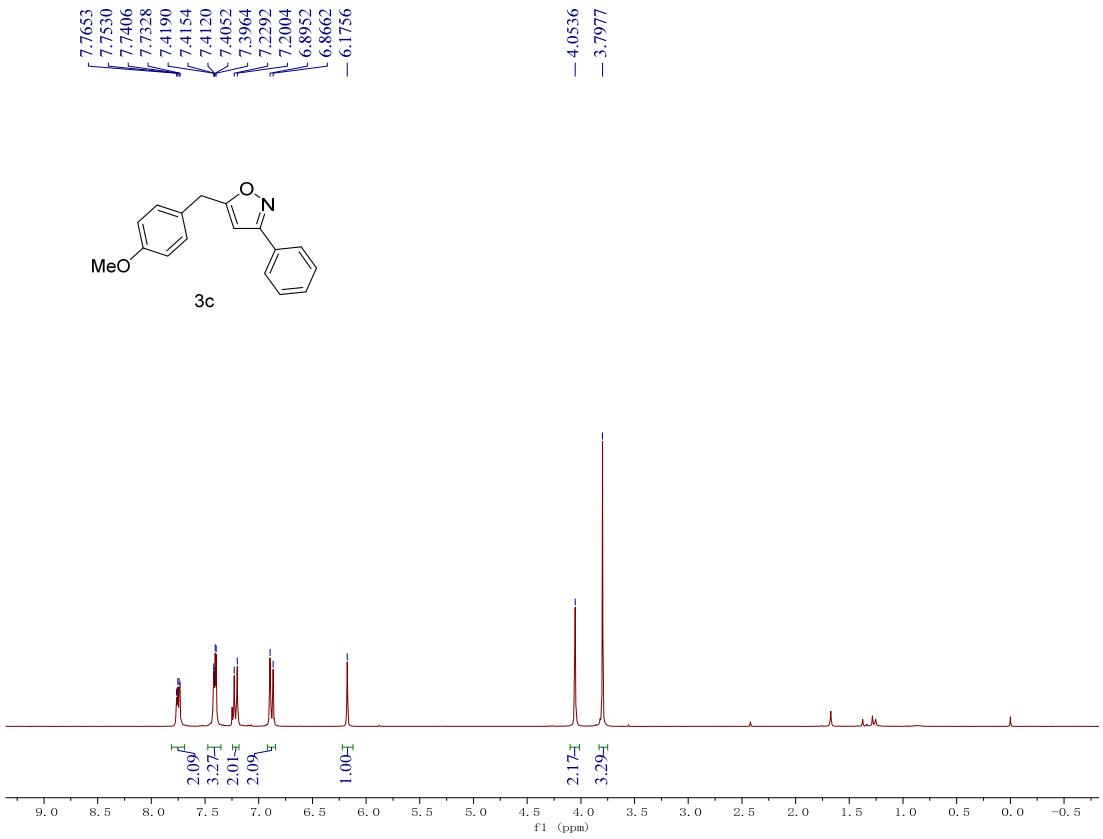
5. Copies of NMR spectra

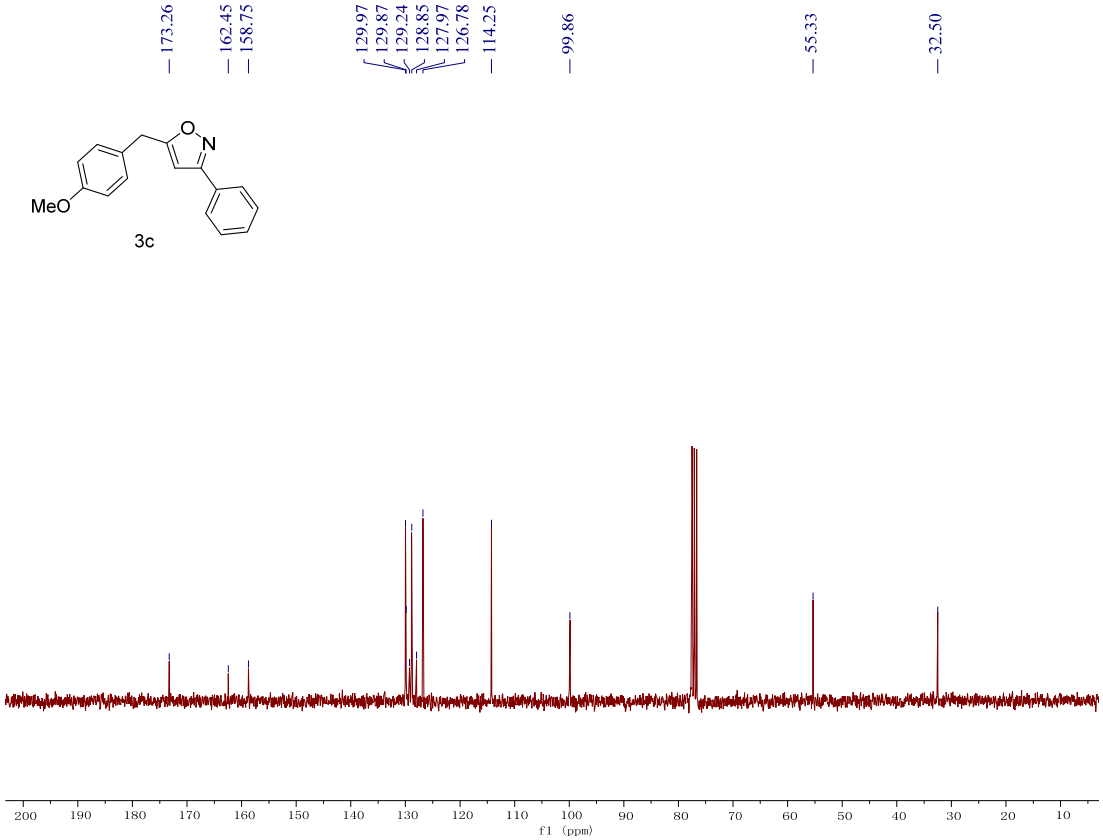




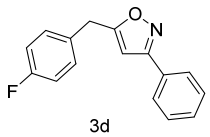

7.7603
7.7481
7.7356
7.7277
7.4168
7.4096
7.4060
7.4024
7.3959
7.3871
7.1979
7.1790
7.1703
7.1572
7.1294
6.1828
6.1795
6.1764
4.0636
2.3371
O
N
Me
3b
1.95
3.07
3.94
0.94
2.00
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


173.10
162.47
136.87
132.91
129.88
129.57
129.26
128.87
128.82
126.80
99.94
32.95
21.14
O
N
Me
3b
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -2
f1 (ppm)

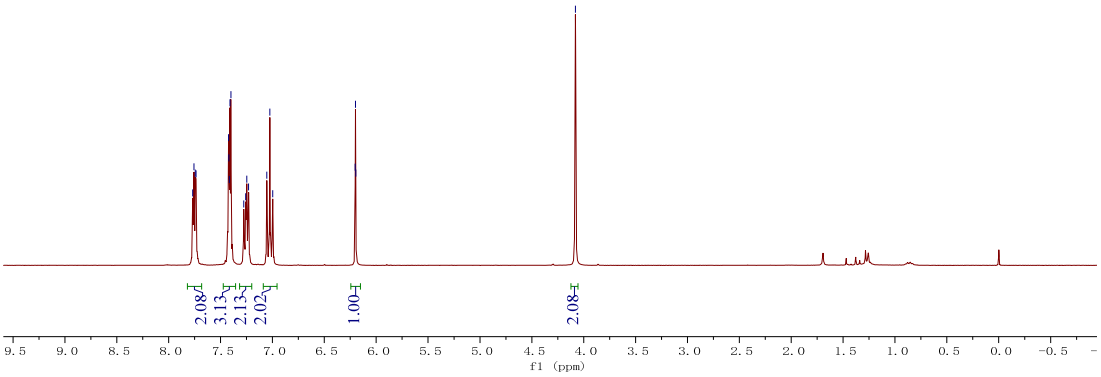

7.7653
7.7530
7.7406
7.7328
7.4190
7.4154
7.4120
7.4052
7.3964
7.2292
7.2004
6.8952
6.8662
6.1756
4.0536
3.7977
MeO
3c
2.09
3.27
2.01
2.09
1.00
2.17
3.29
f1 (ppm)


173.26
162.45
158.75
129.97
129.87
129.24
128.85
127.97
126.78
114.25
99.86
55.33
32.50
MeO
3c
f1 (ppm)

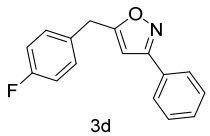

7.7682
7.7560
7.7441
7.7359
7.4231
7.4197
7.4154
7.4097
7.4006
7.2761
7.2580
7.2474
7.2297
7.0546
7.0257
6.9967
6.2024
6.1994
6.1964
4.0804


O
N
F

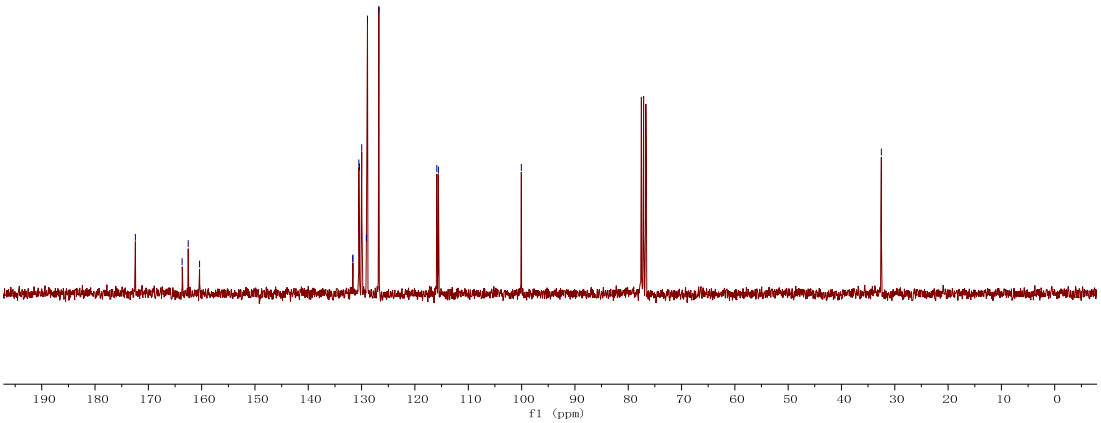
3d

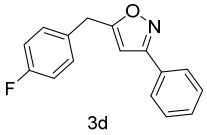

2.08
3.13
2.13
2.02
1.00
2.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


172.44
163.66
162.52
160.40
131.68
131.64
130.51
130.41
129.98
129.11
128.90
126.78
115.89
115.61
100.06
32.53


O
N
F

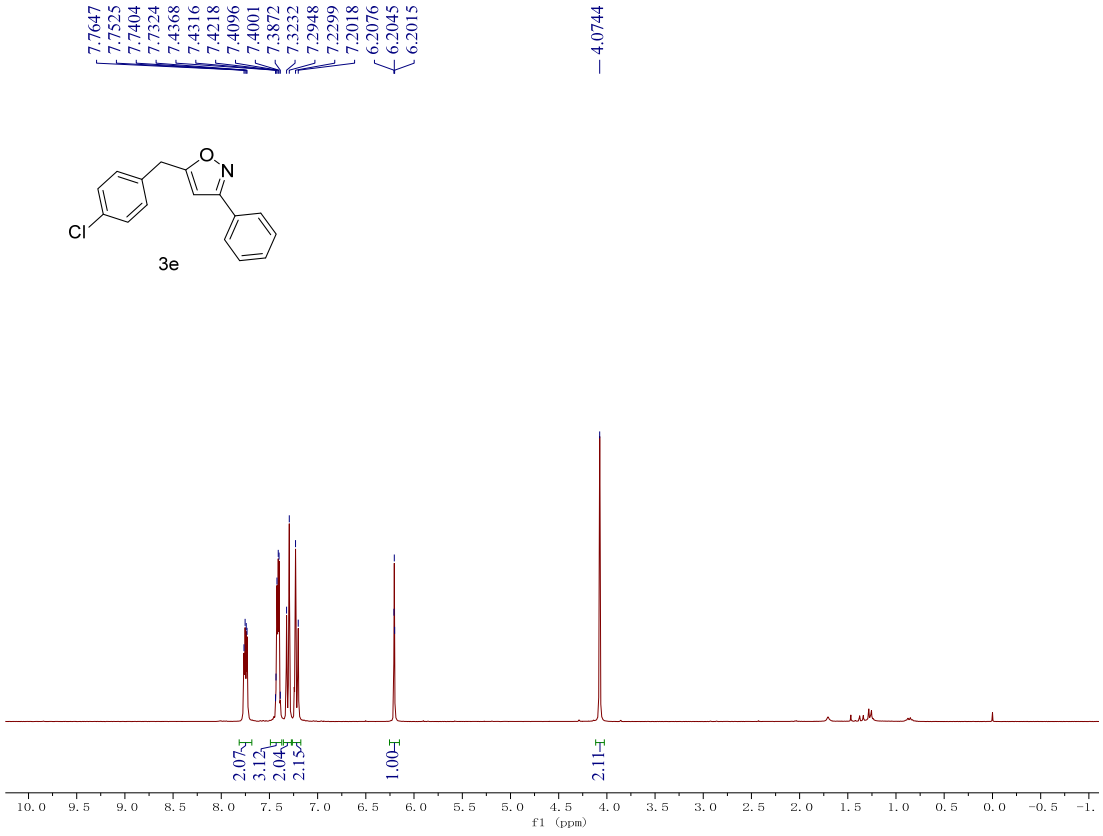
3d

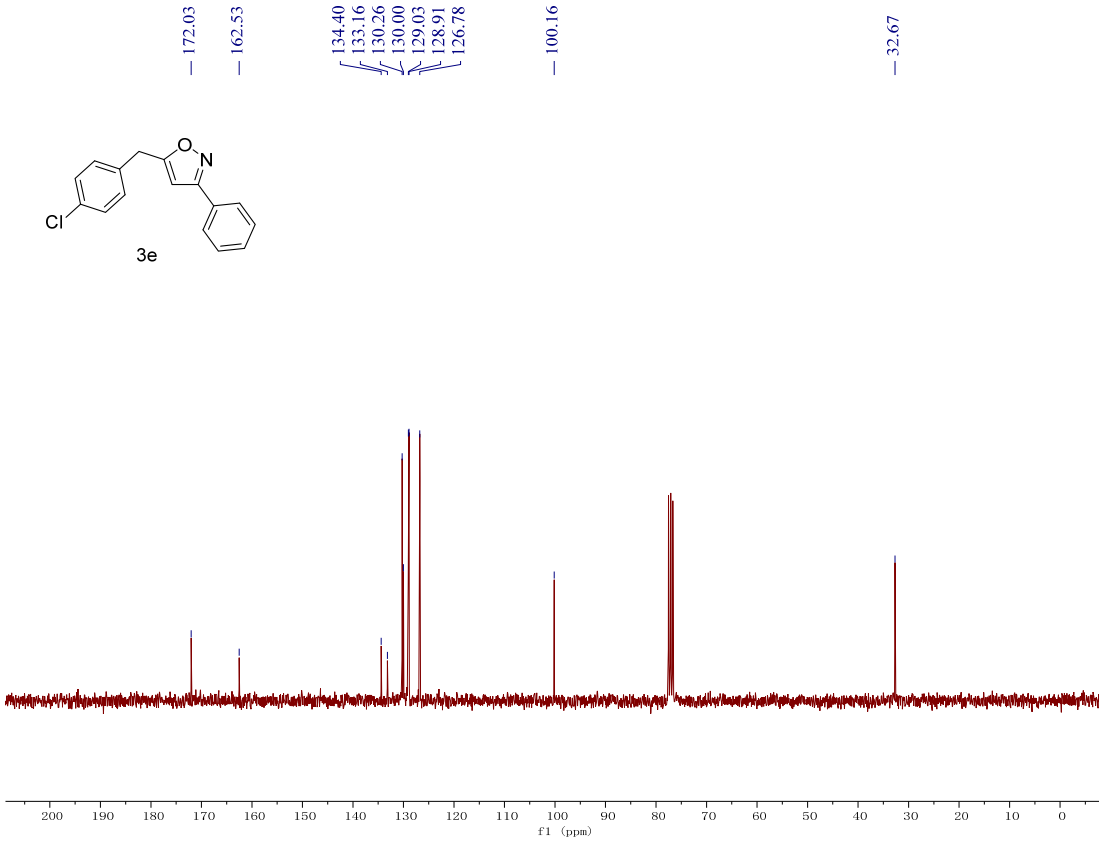

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

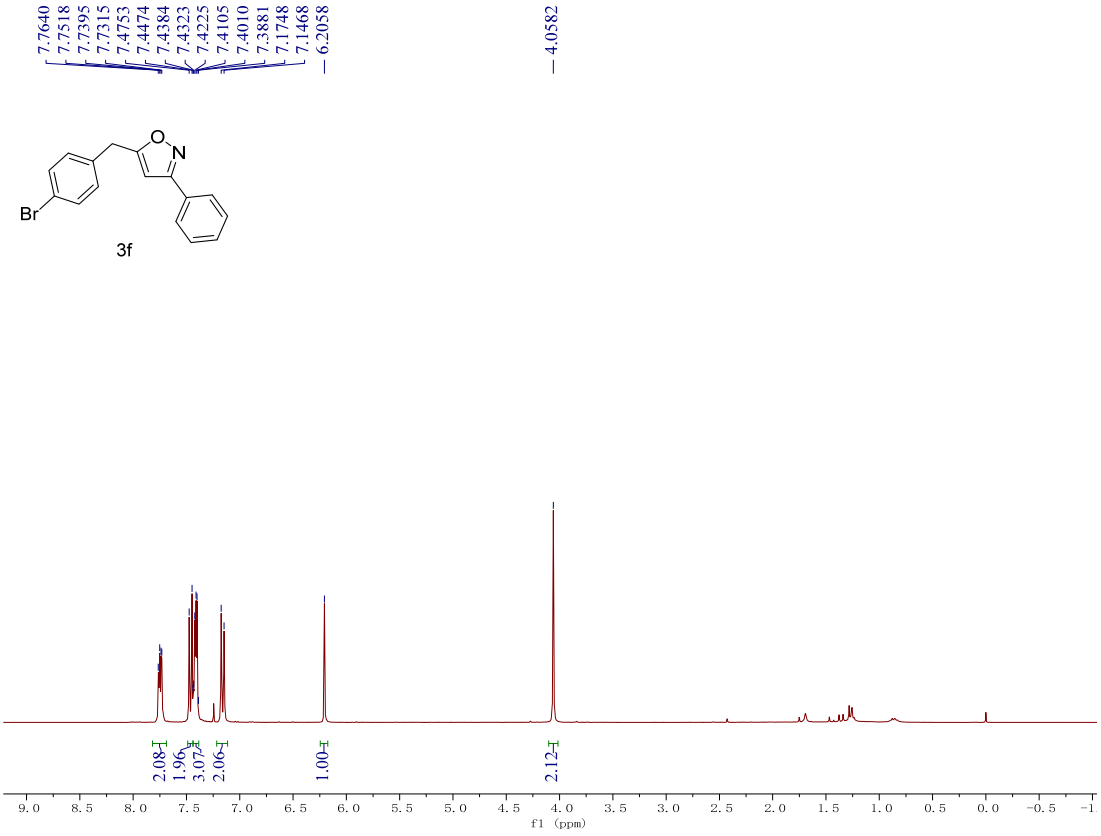

O
N
F

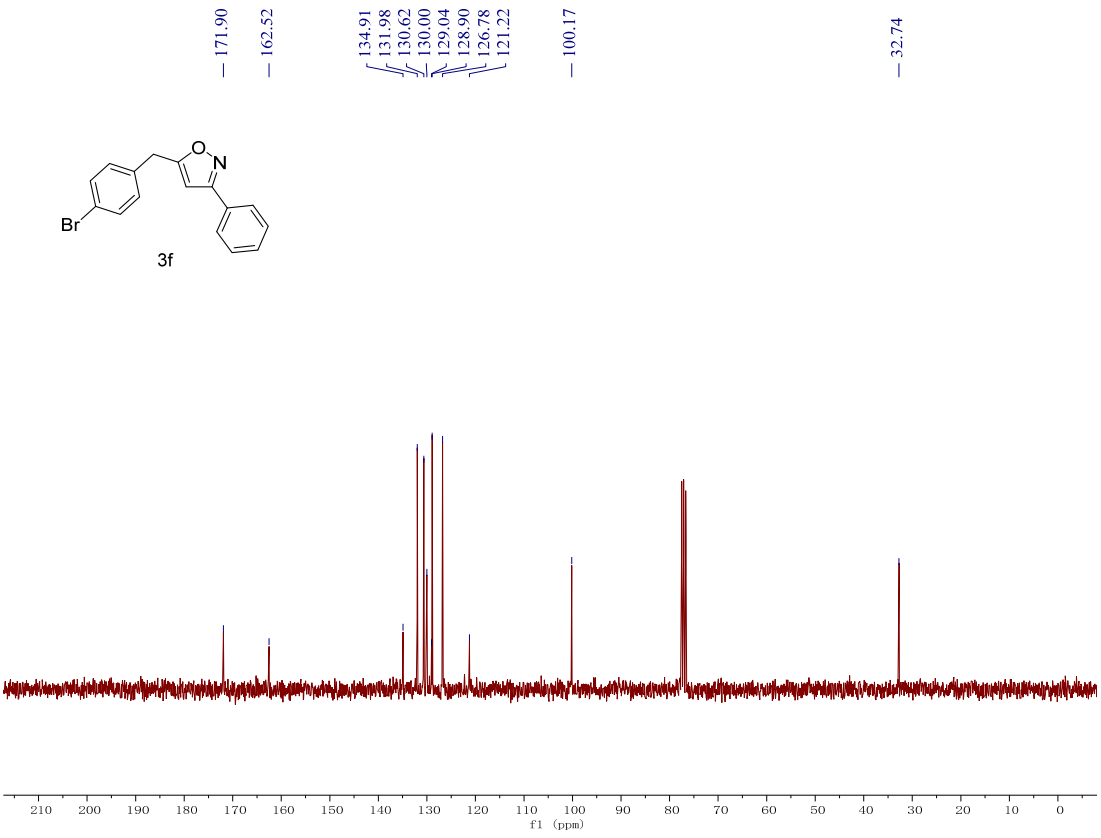
3d

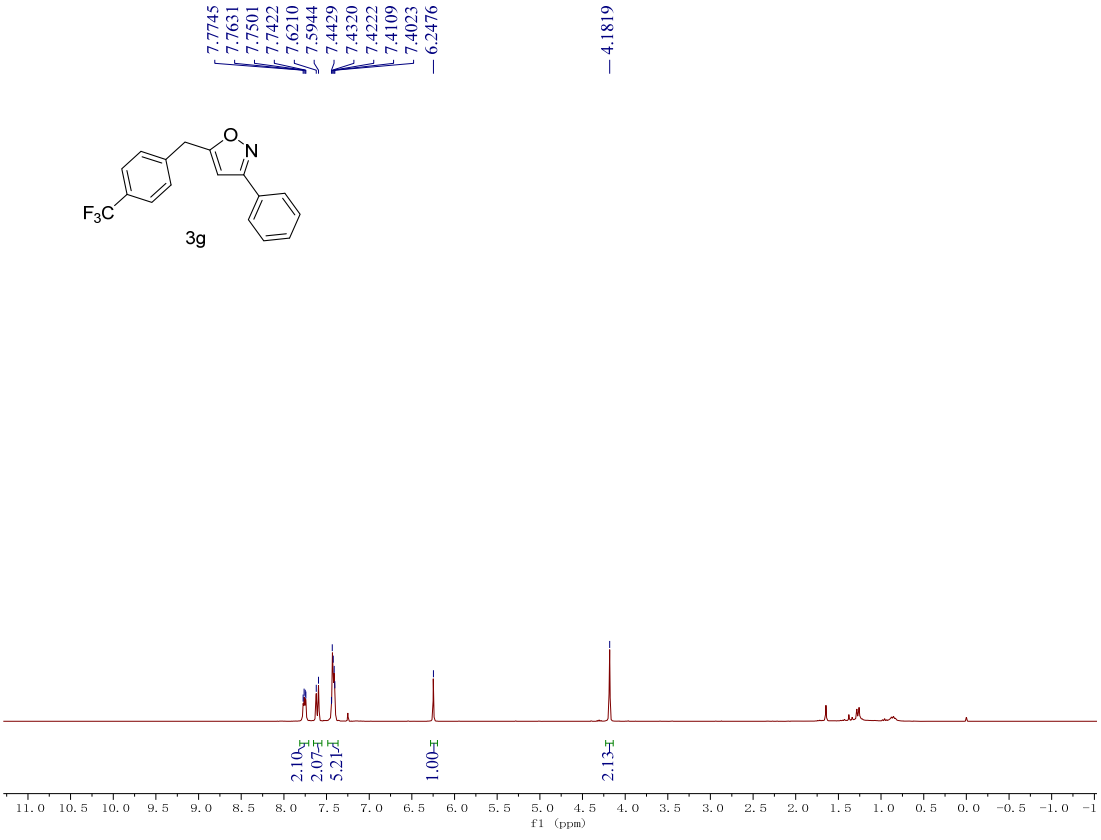
-115.42
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

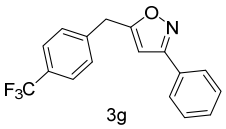

7.7647
7.7525
7.7404
7.7324
7.4368
7.4316
7.4218
7.4096
7.4001
7.3872
7.3232
7.2948
7.2299
7.2018
6.2076
6.2045
6.2015
4.0744
O
N
Cl
3e
2.07
3.12
2.04
2.15
1.00
2.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


172.03
162.53
134.40
133.16
130.26
130.00
129.03
128.91
126.78
100.16
32.67
O
N
Cl
3e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.7640
7.7518
7.7395
7.7315
7.4753
7.4474
7.4384
7.4323
7.4225
7.4105
7.4010
7.3881
7.1748
7.1468
6.2058
4.0582
O
N
Br
3f
2.08
1.96
3.07
2.06
1.00
2.12
f1 (ppm)

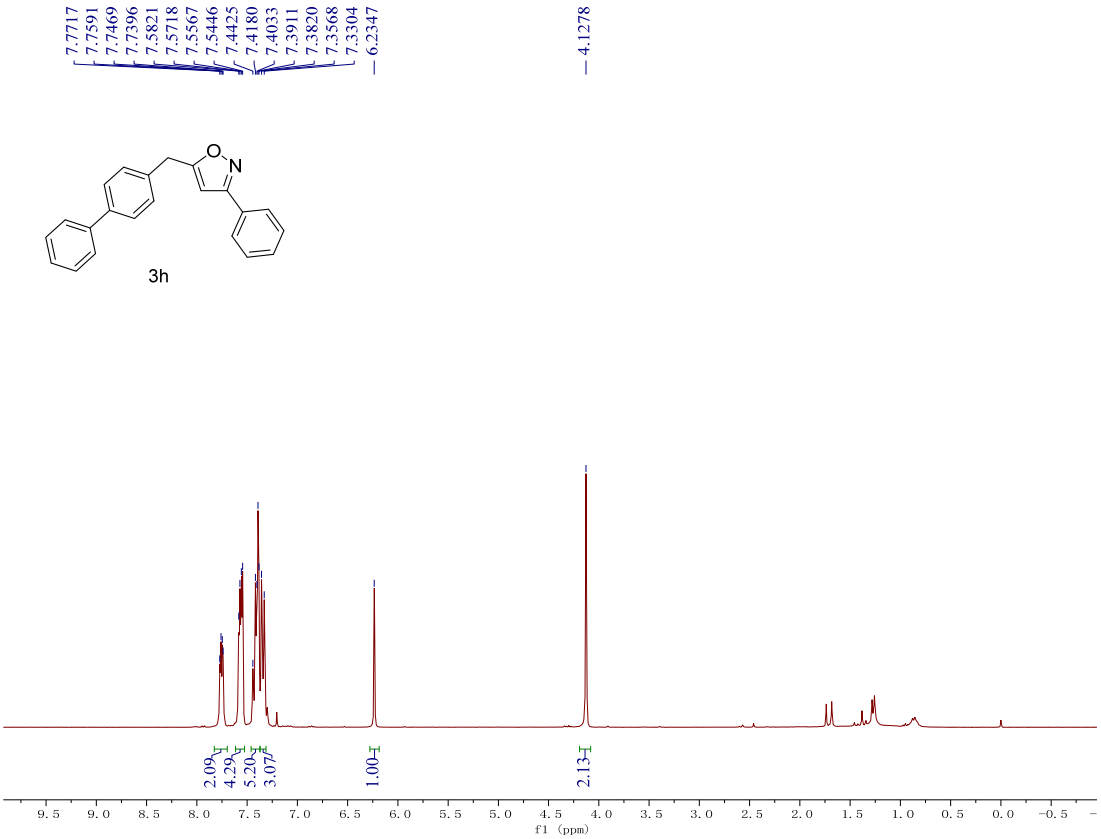

171.90
162.52
134.91
131.98
130.62
130.00
129.04
128.90
126.78
121.22
100.17
32.74
O
N
Br
3f
f1 (ppm)

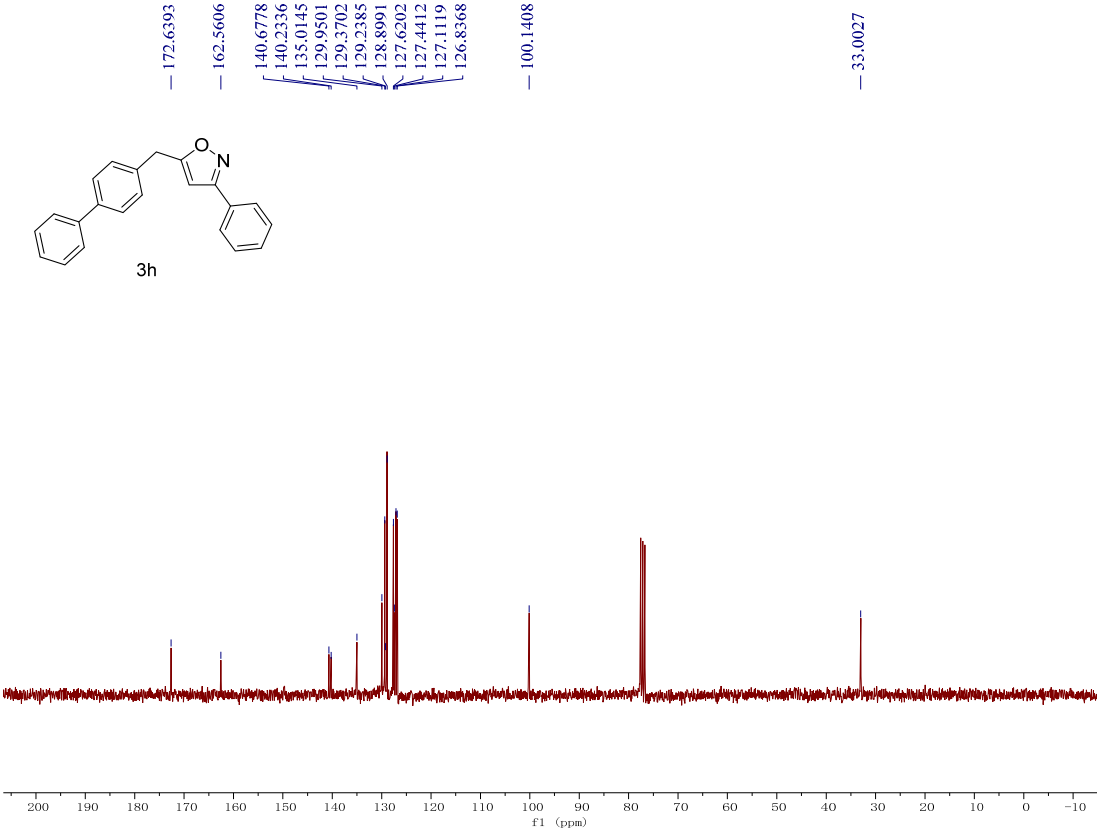

7.7745
7.7631
7.7501
7.7422
7.6210
7.5944
7.4429
7.4320
7.4222
7.4109
7.4023
6.2476
4.1819
O
N
F3C
3g
2.10
2.07
5.21
1.00
2.13
f1 (ppm)
171.35
162.58
139.92
130.62
130.27
130.04
129.84
129.49
129.40
129.25
128.91
126.76
125.90
125.85
125.80
125.75
122.28
118.67
100.34
33.06
O
N
F3C
3g
f1 (ppm)

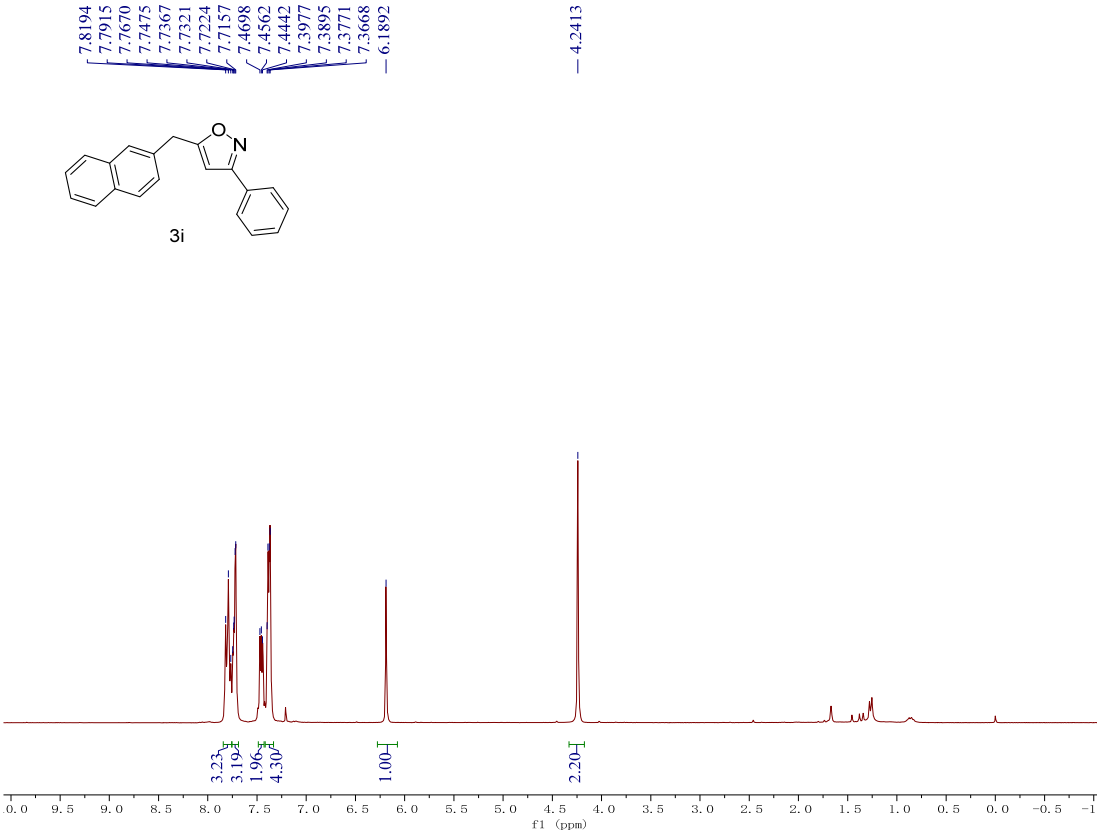

O
N
F3C

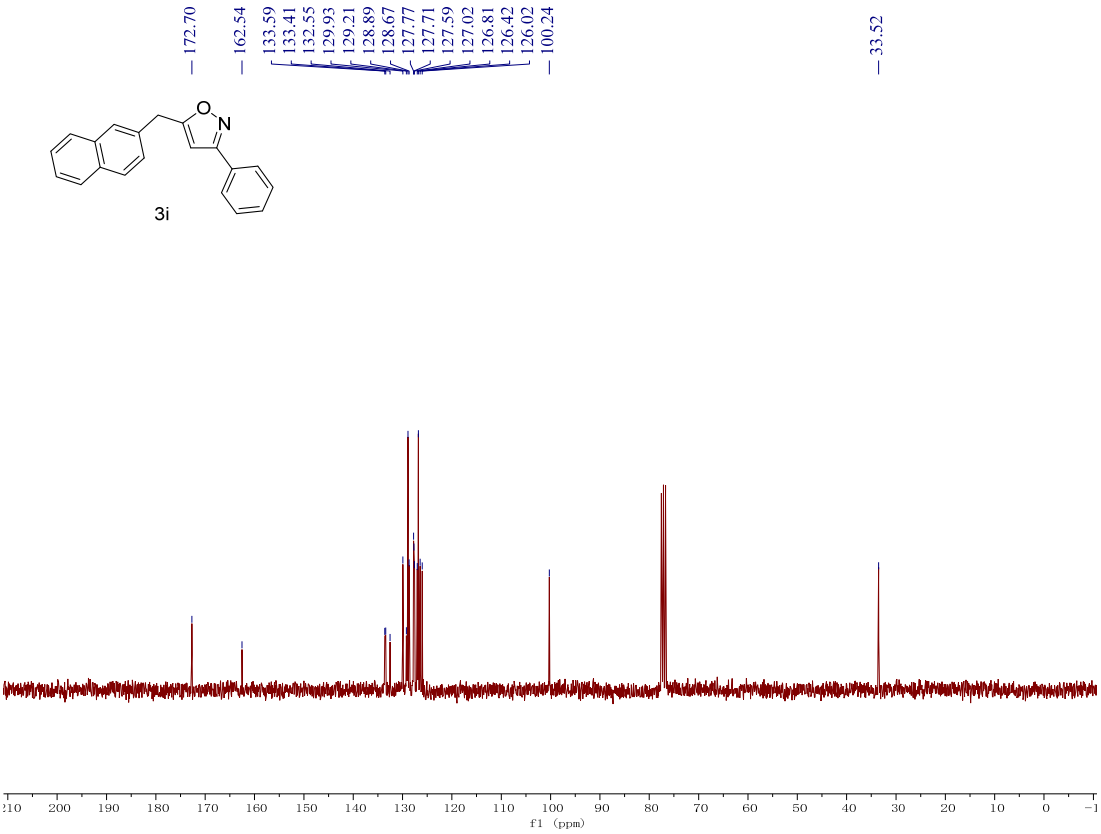
3g

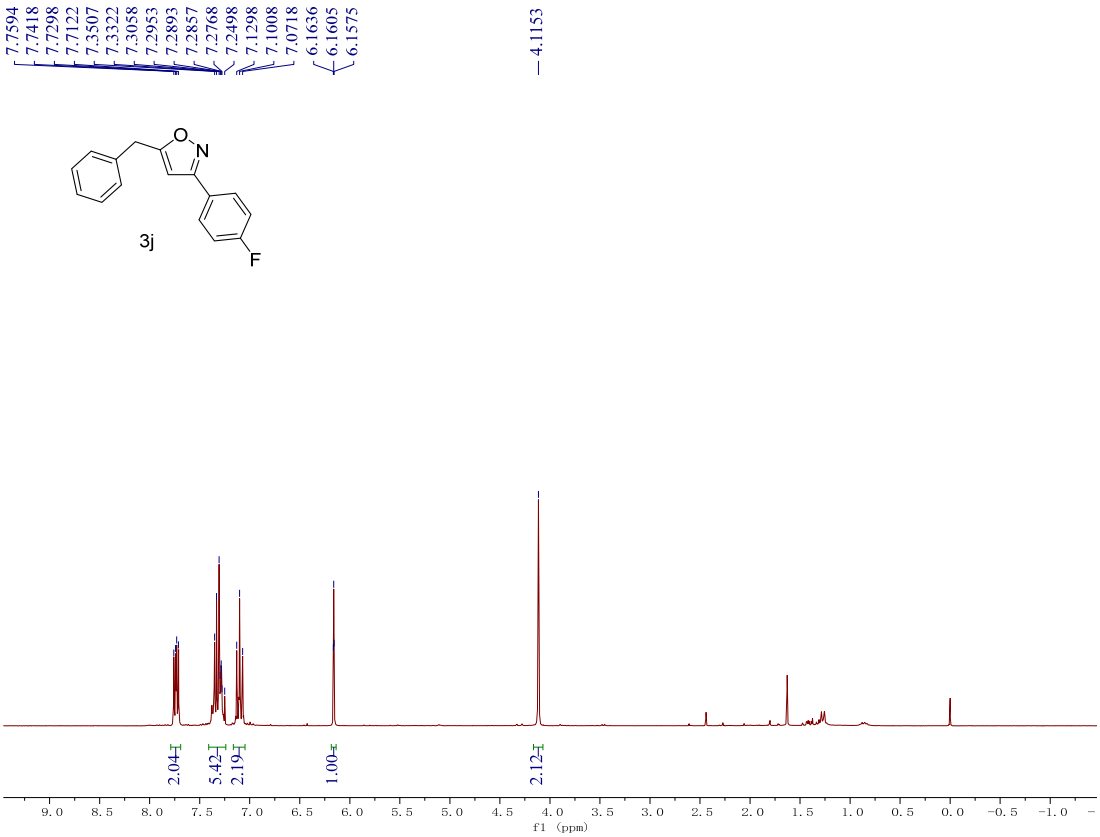
-62.54
-5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140
f1 (ppm)

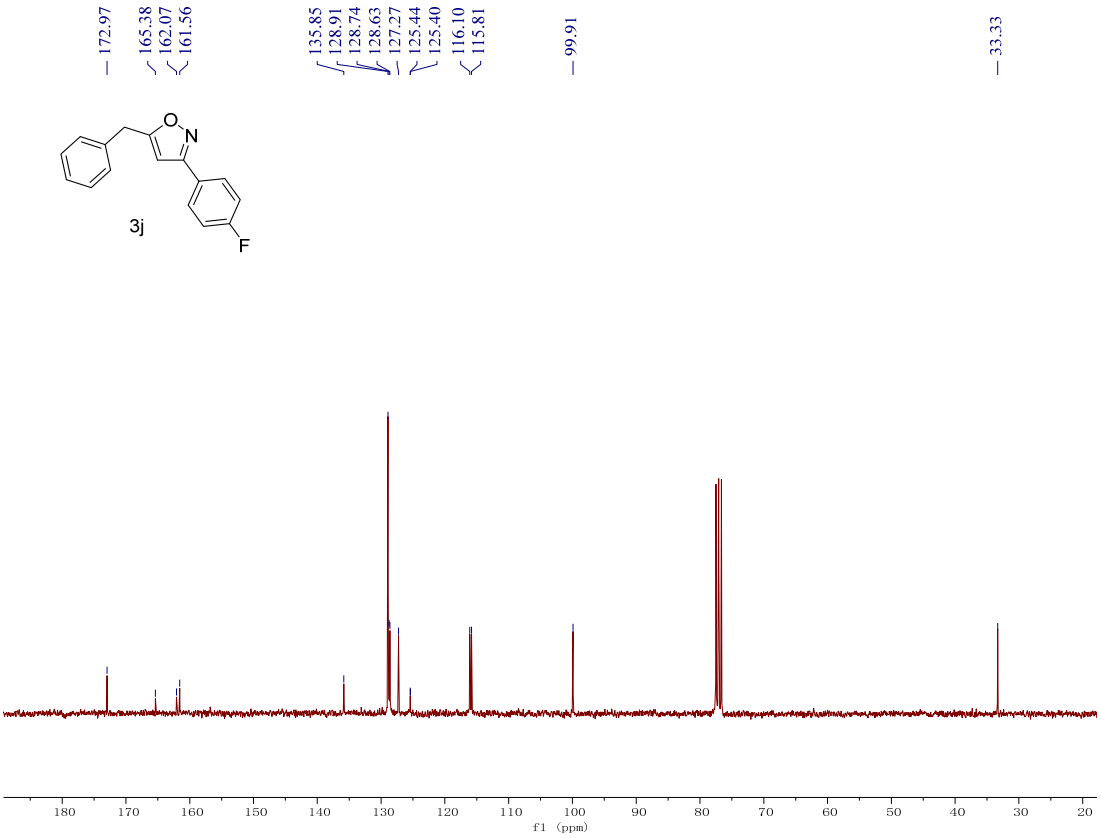

7.7717
7.7591
7.7469
7.7396
7.5821
7.5718
7.5567
7.5446
7.4425
7.4180
7.4033
7.3911
7.3820
7.3568
7.3304
6.2347
4.1278
O
N
3h
2.09
4.29
5.20
3.07
1.00
2.13
f1 (ppm)

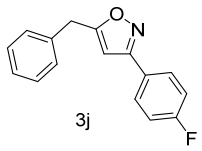

172.6393
162.5606
140.6778
140.2336
135.0145
129.9501
129.3702
129.2385
128.8991
127.6202
127.4412
127.1119
126.8368
100.1408
33.0027
O
N
3h
f1 (ppm)


7.8194
7.7915
7.7670
7.7475
7.7367
7.7321
7.7224
7.7157
7.4698
7.4562
7.4442
7.3977
7.3895
7.3771
7.3668
6.1892
4.2413
O
N
3i
3.23
3.19
1.96
4.30
1.00
2.20
f1 (ppm)


172.70
162.54
133.59
133.41
132.55
129.93
129.21
128.89
128.67
127.77
127.71
127.59
127.02
126.81
126.42
126.02
100.24
33.52
O
N
3i
f1 (ppm)

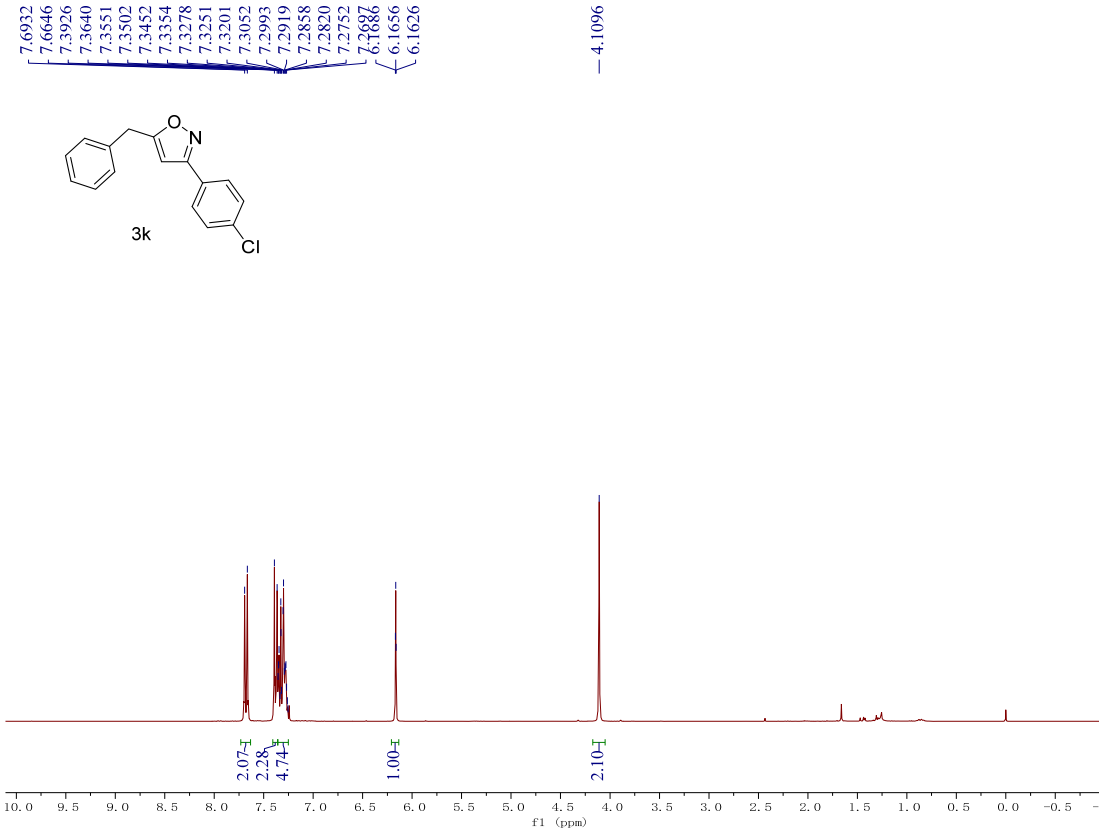

7.7594
7.7418
7.7298
7.7122
7.3507
7.3322
7.3058
7.2953
7.2893
7.2857
7.2768
7.2498
7.1298
7.1008
7.0718
6.1636
6.1605
6.1575
4.1153
O
N
F
3j
2.04
5.42
2.19
1.00
2.12
f1 (ppm)

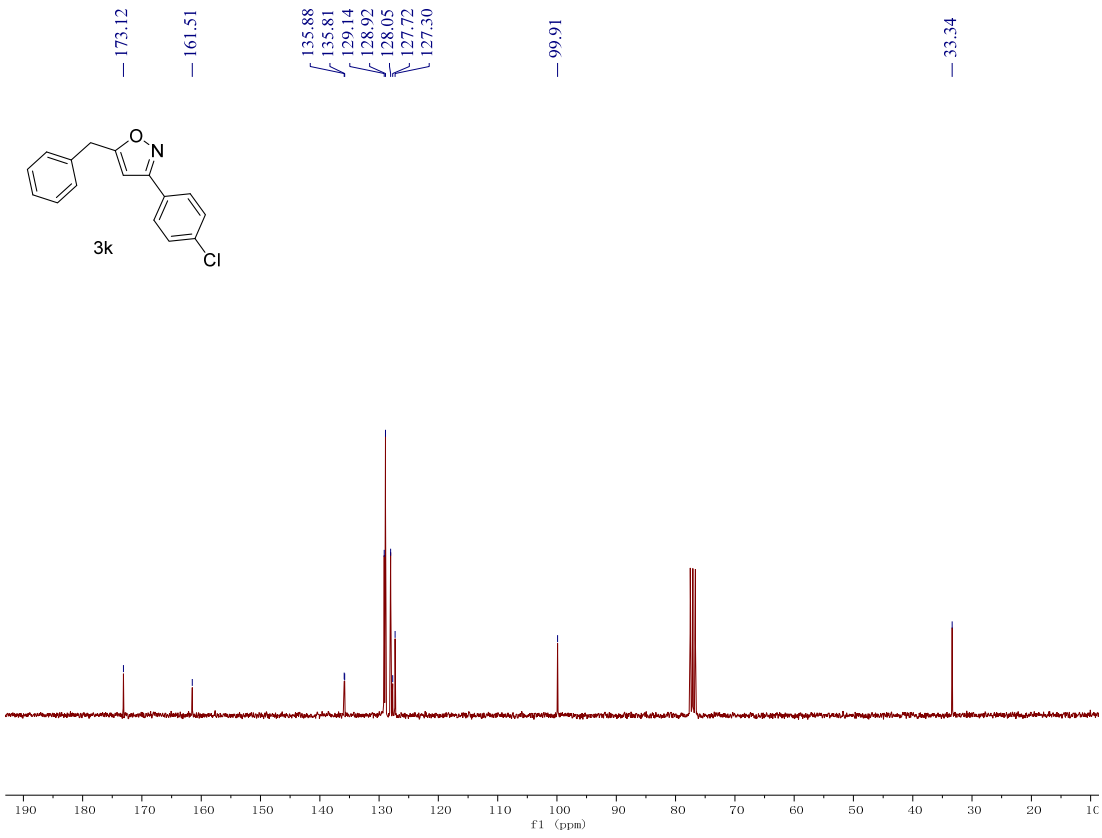

172.97
165.38
162.07
161.56
135.85
128.91
128.74
128.63
127.27
125.44
125.40
116.10
115.81
99.91
33.33
O
N
F
3j
f1 (ppm)

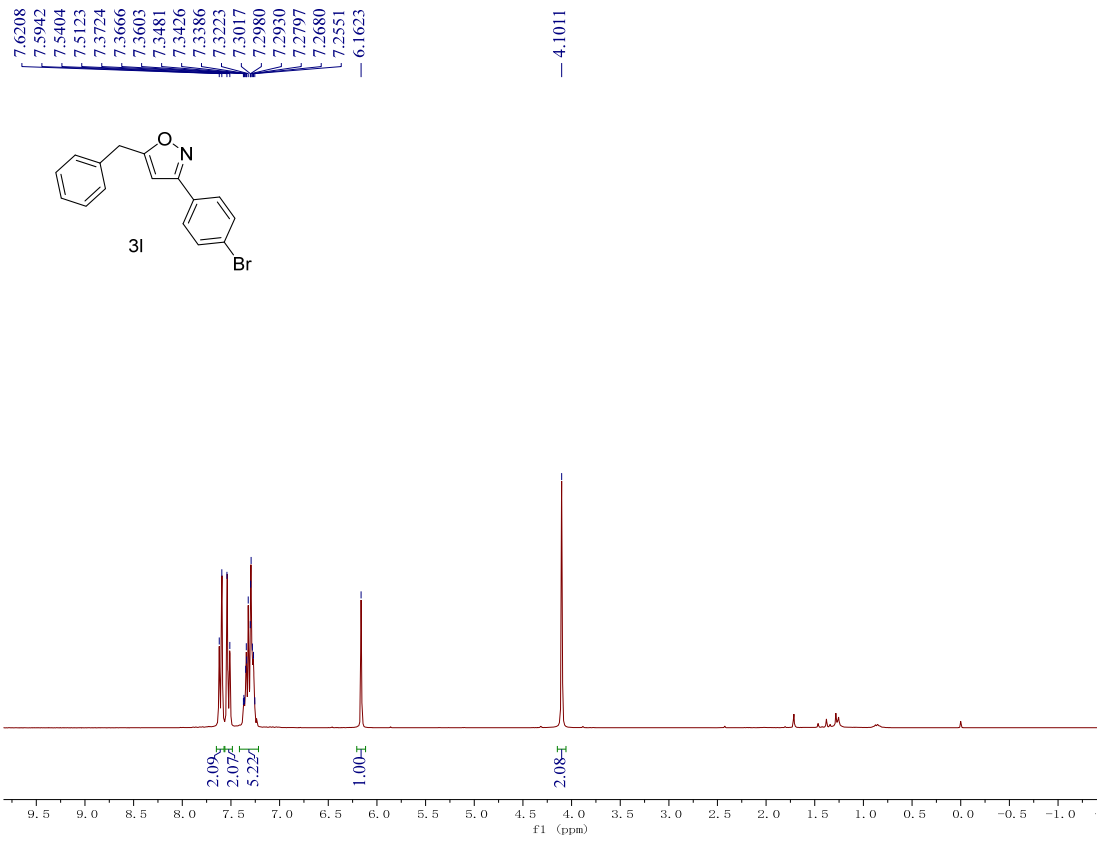

O
N
F

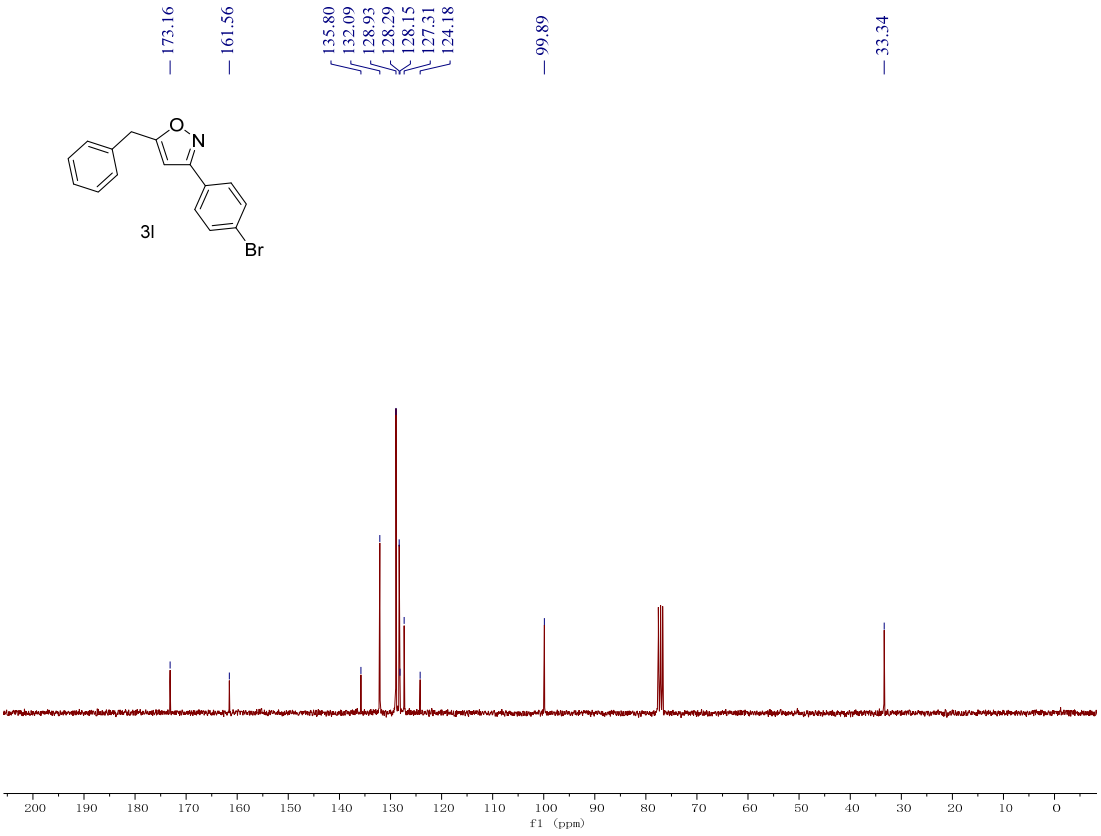
3j

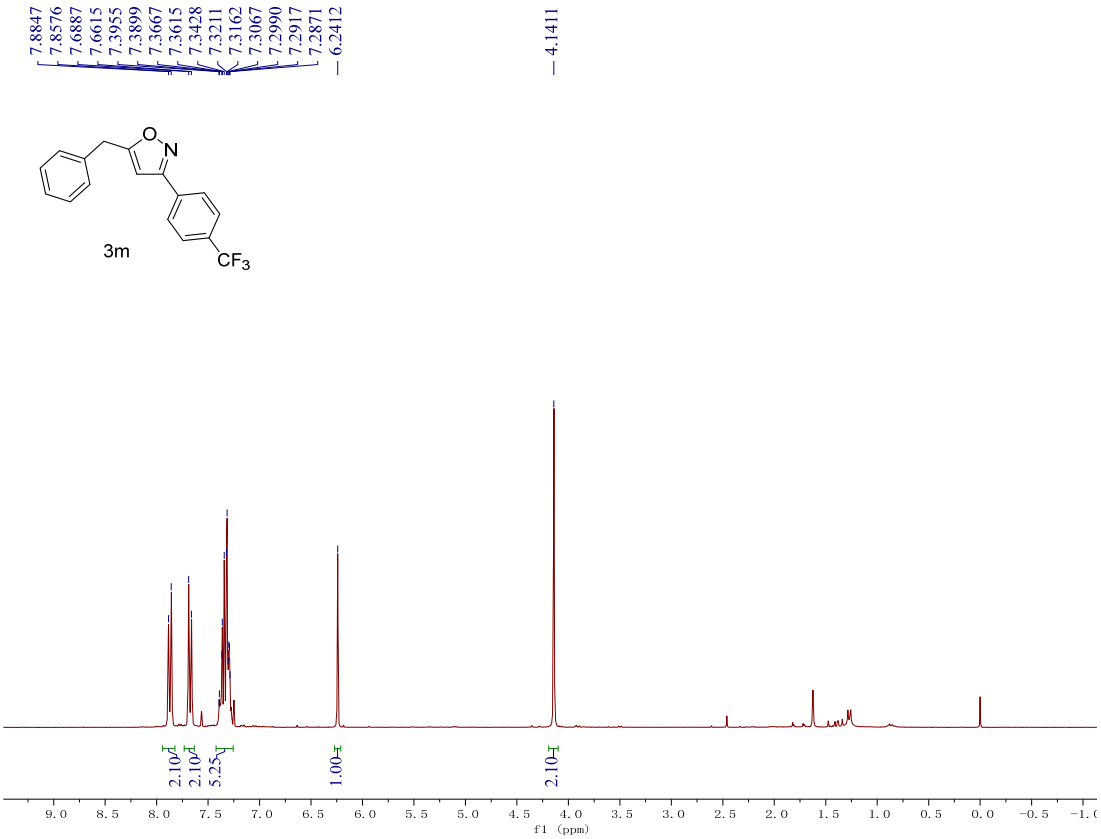
-110.81
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

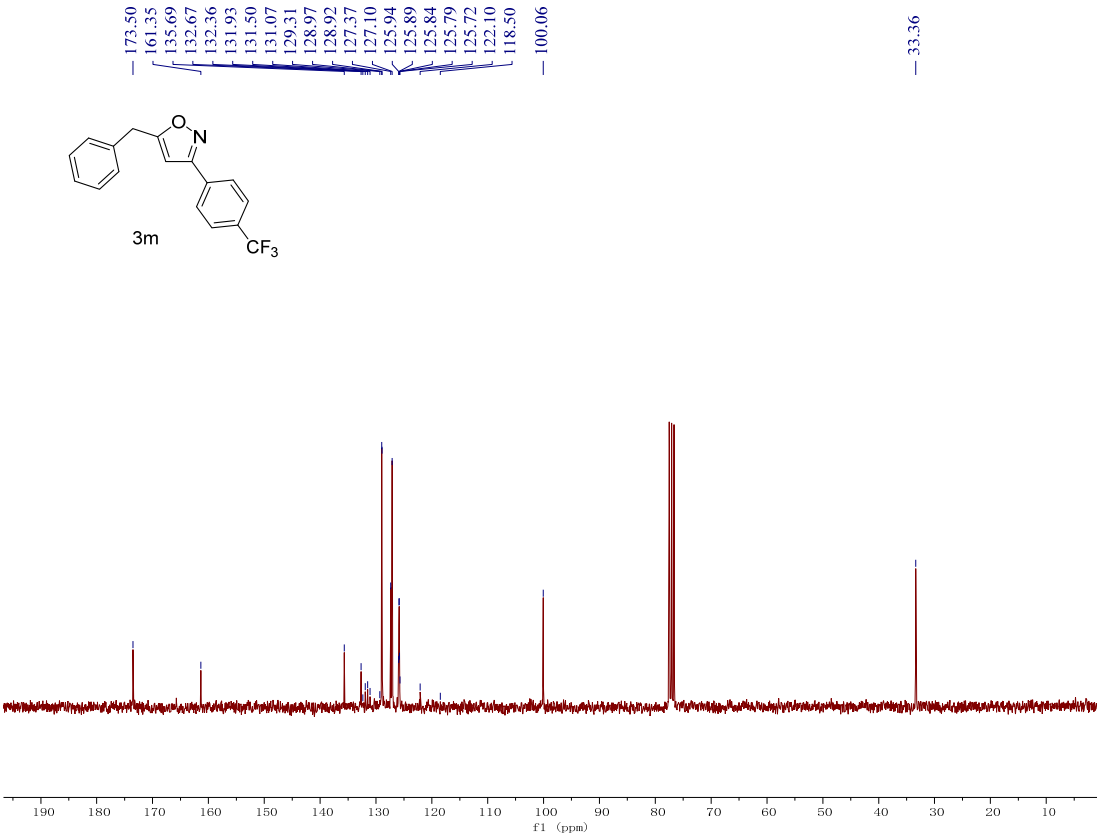

7.6932
7.6646
7.3926
7.3640
7.3551
7.3502
7.3452
7.3354
7.3278
7.3251
7.3201
7.3052
7.2993
7.2919
7.2858
7.2820
7.2752
7.2697
6.1686
6.1656
6.1626
4.1096
O
N
3k
Cl
2.07
2.28
4.74
1.00
2.10
f1 (ppm)

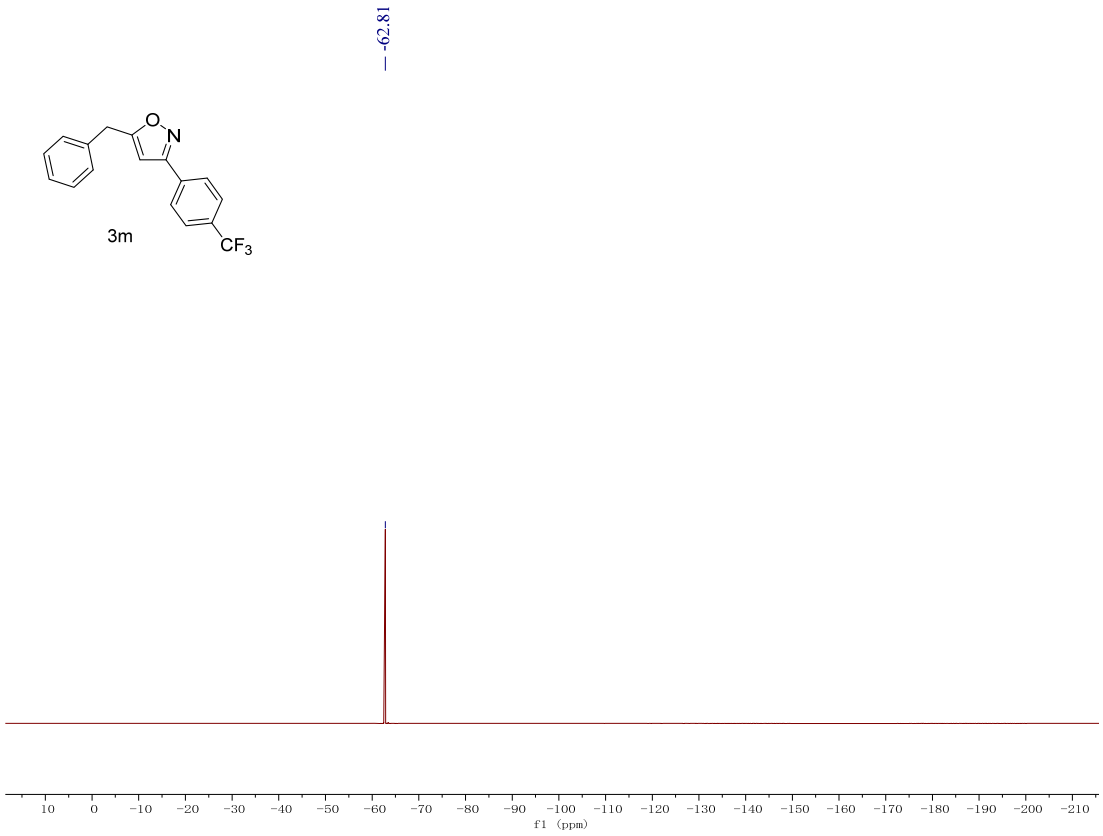

173.12
161.51
135.88
135.81
129.14
128.92
128.05
127.72
127.30
99.91
33.34
O
N
3k
Cl
f1 (ppm)

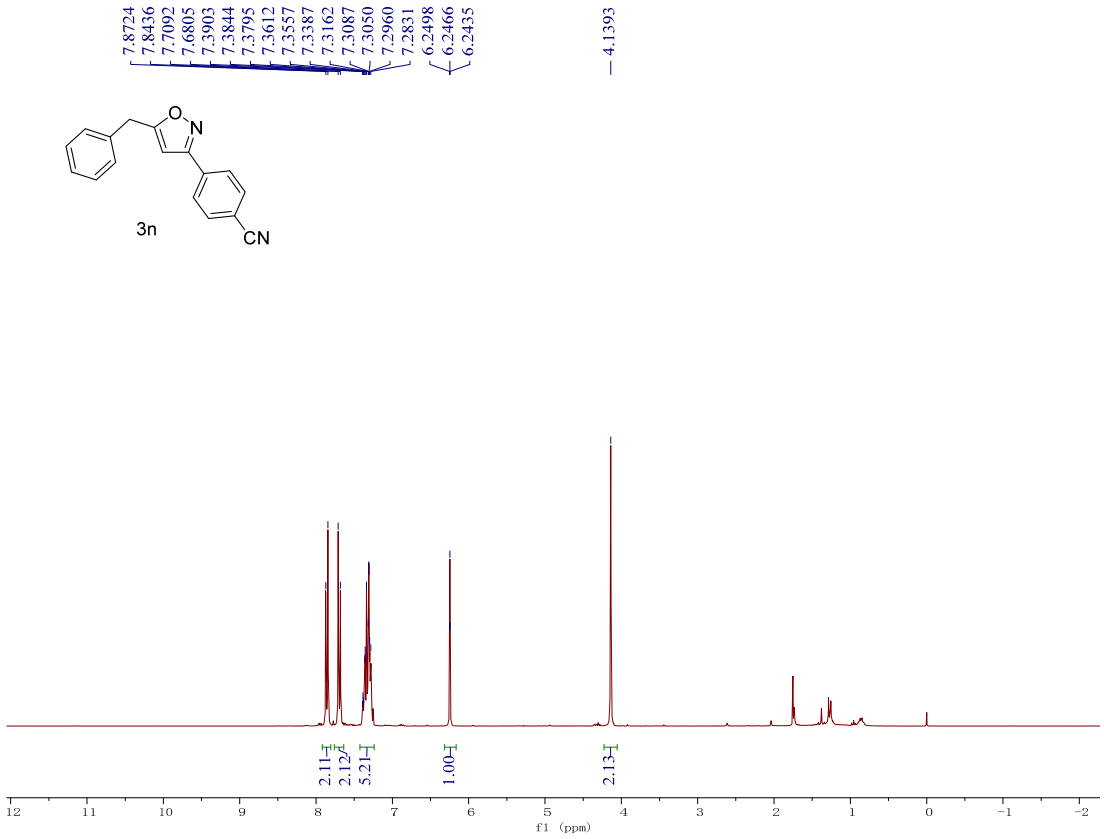

7.6208
7.5942
7.5404
7.5123
7.3724
7.3666
7.3603
7.3481
7.3426
7.3386
7.3223
7.3017
7.2980
7.2930
7.2797
7.2680
7.2551
6.1623
4.1011
O
N
Br
2.09
2.07
5.22
1.00
2.08
f1 (ppm)

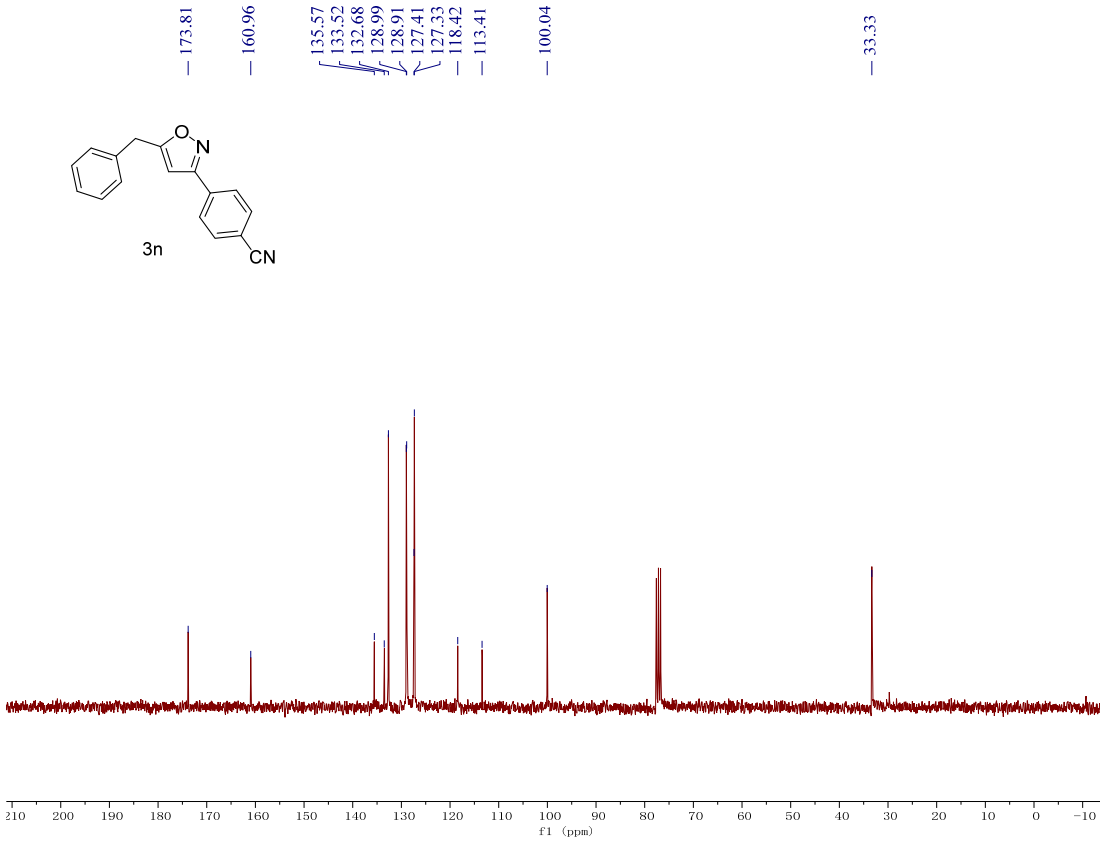

173.16
161.56
135.80
132.09
128.93
128.29
128.15
127.31
124.18
99.89
33.34
O
N
Br
f1 (ppm)

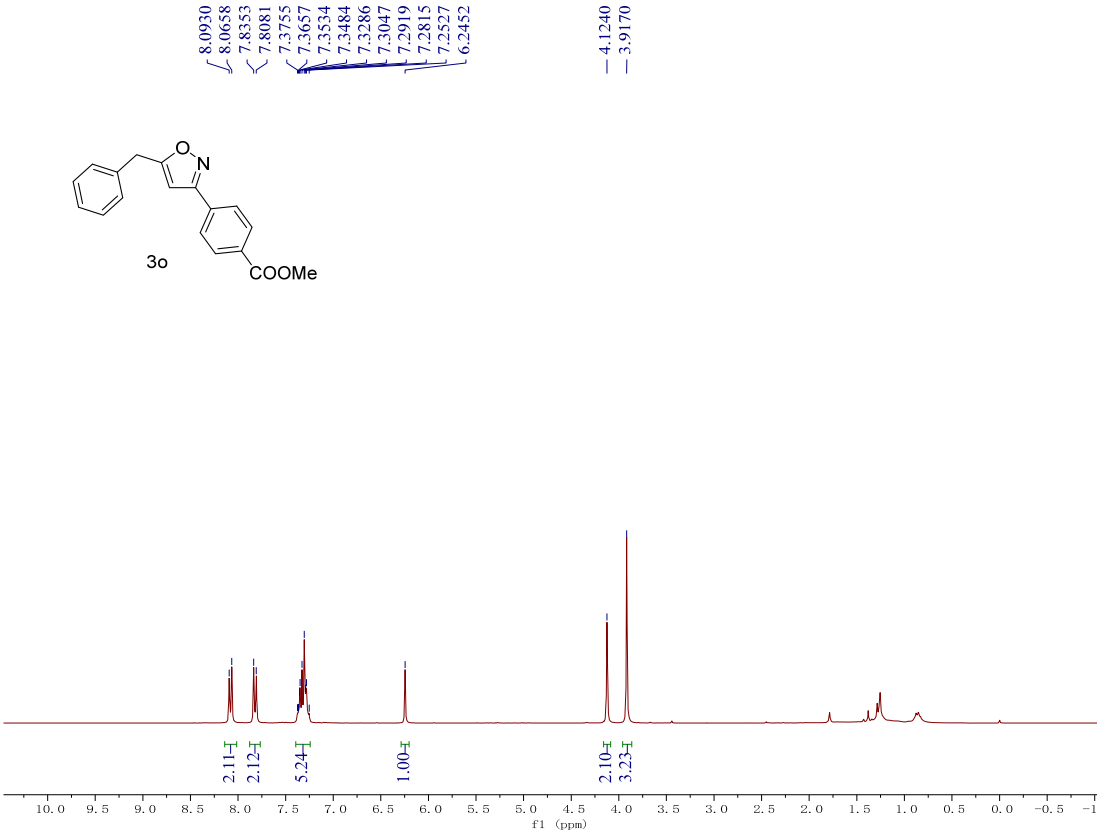

7.8847
7.8576
7.6887
7.6615
7.3955
7.3899
7.3667
7.3615
7.3428
7.3211
7.3162
7.3067
7.2990
7.2917
7.2871
6.2412
4.1411
3m
CF3
2.10
2.10
5.25
1.00
2.10
f1 (ppm)

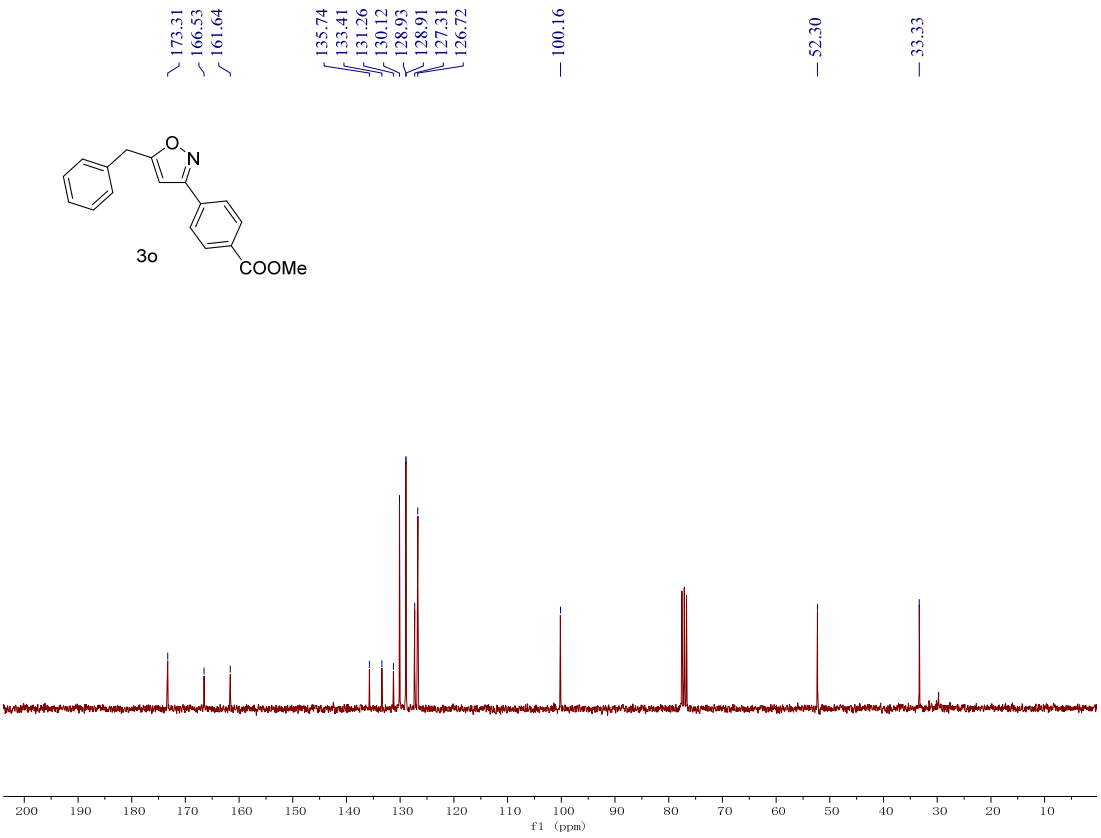

173.50
161.35
135.69
132.67
132.36
131.93
131.50
131.07
129.31
128.97
128.92
127.37
127.10
125.94
125.89
125.84
125.79
125.72
122.10
118.50
100.06
33.36
3m
CF3
f1 (ppm)

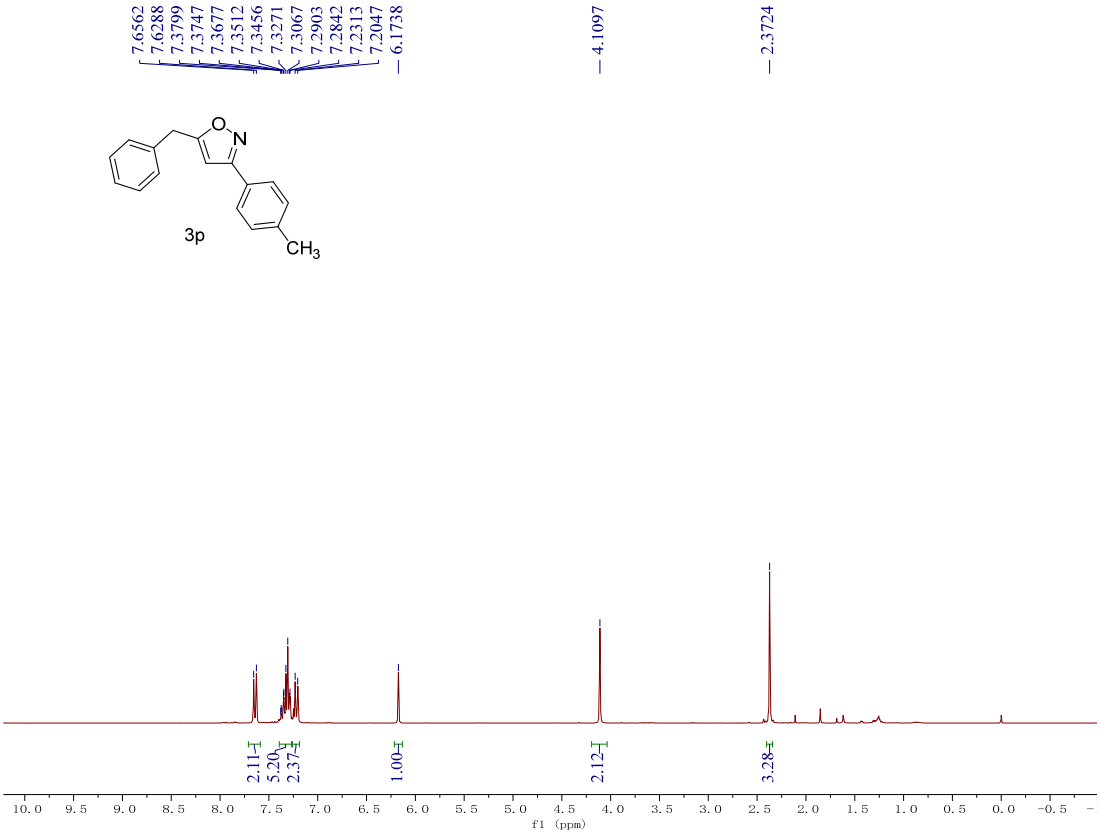

-62.81
O
N
3m
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

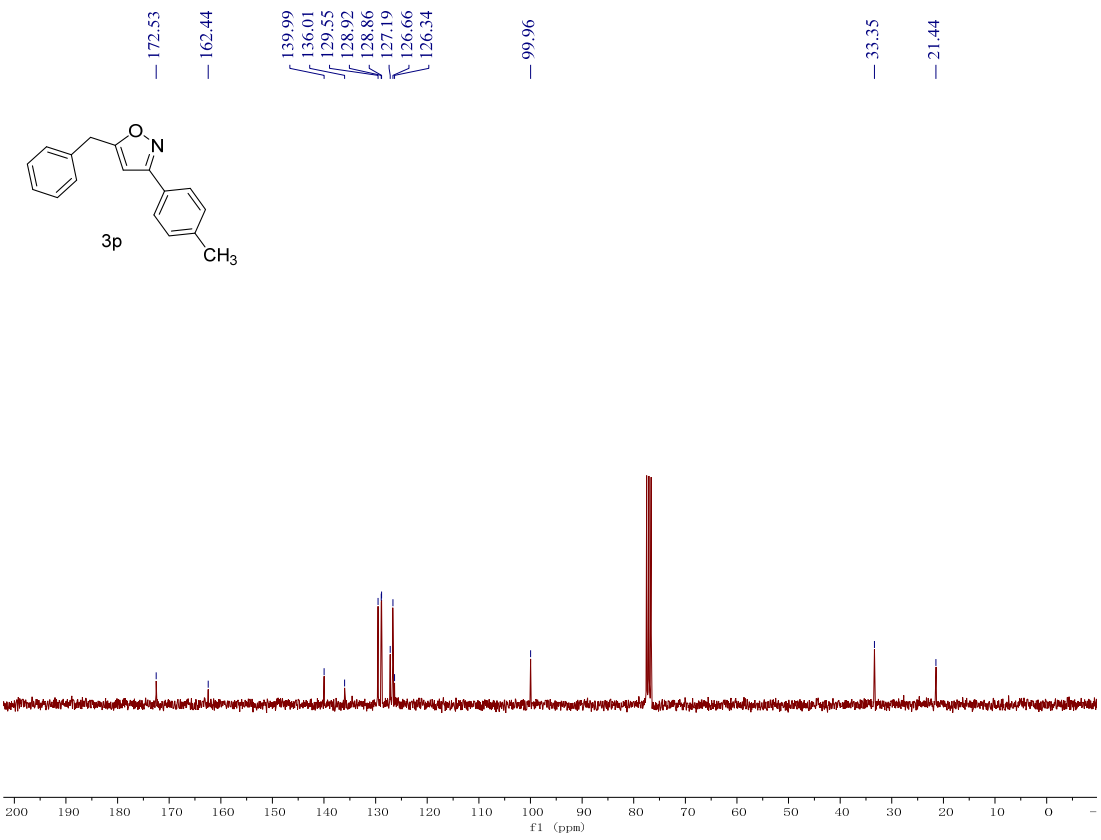

7.8724
7.8436
7.7092
7.6805
7.3903
7.3844
7.3795
7.3612
7.3557
7.3387
7.3162
7.3087
7.3050
7.2960
7.2831
6.2498
6.2466
6.2435
4.1393
O
N
3n
CN
2.11
2.12
5.21
1.00
2.13
f1 (ppm)

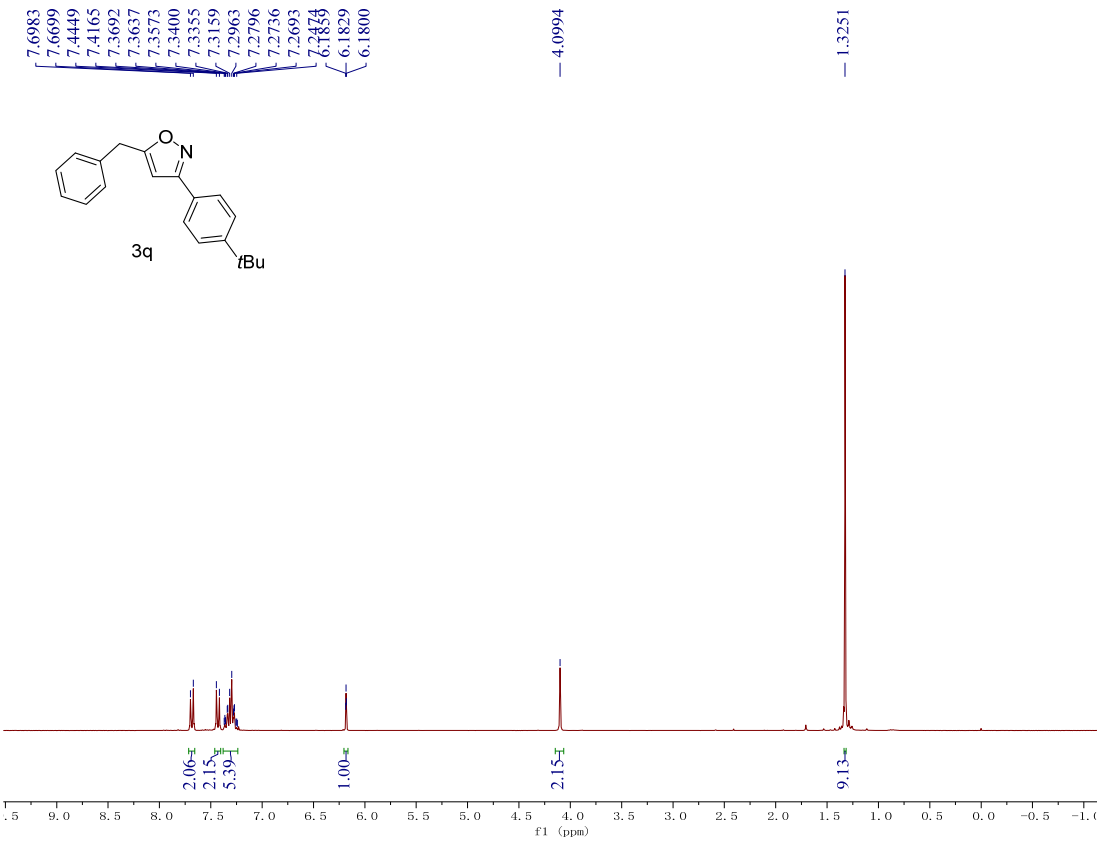

173.81
160.96
135.57
133.52
132.68
128.99
128.91
127.41
127.33
118.42
113.41
100.04
33.33
O
N
3n
CN
f1 (ppm)

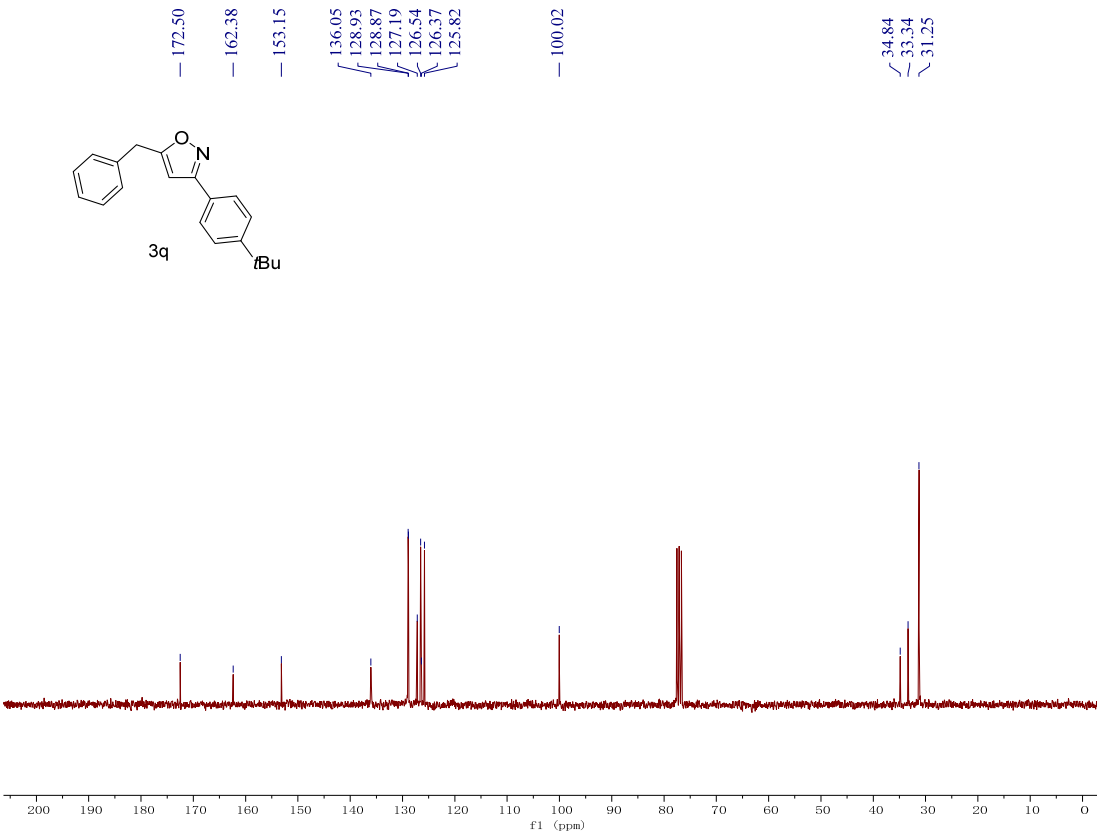

8.0930
8.0658
7.8353
7.8081
7.3755
7.3657
7.3534
7.3484
7.3286
7.3047
7.2919
7.2815
7.2527
6.2452
4.1240
3.9170
O
N
3o
COOMe
2.11
2.12
5.24
1.00
2.10
3.23
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1
f1 (ppm)

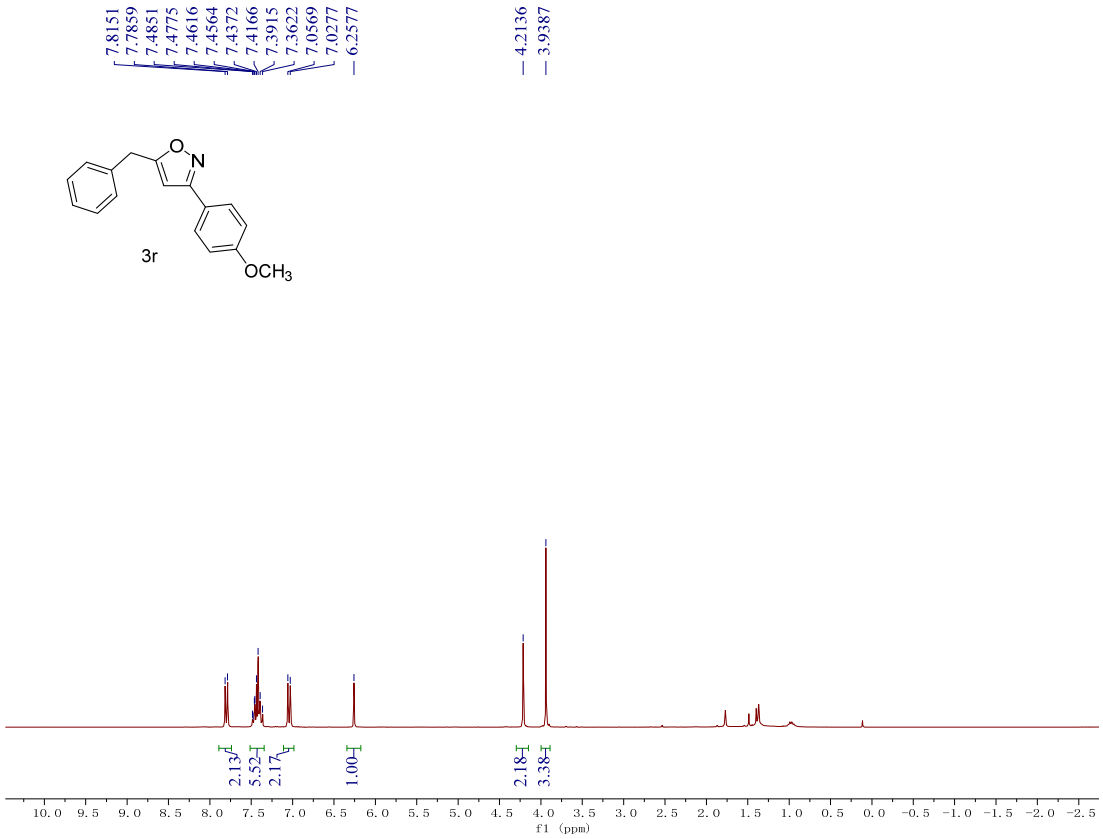

173.31
166.53
161.64
135.74
133.41
131.26
130.12
128.93
128.91
127.31
126.72
100.16
52.30
33.33
O
N
3o
COOMe
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

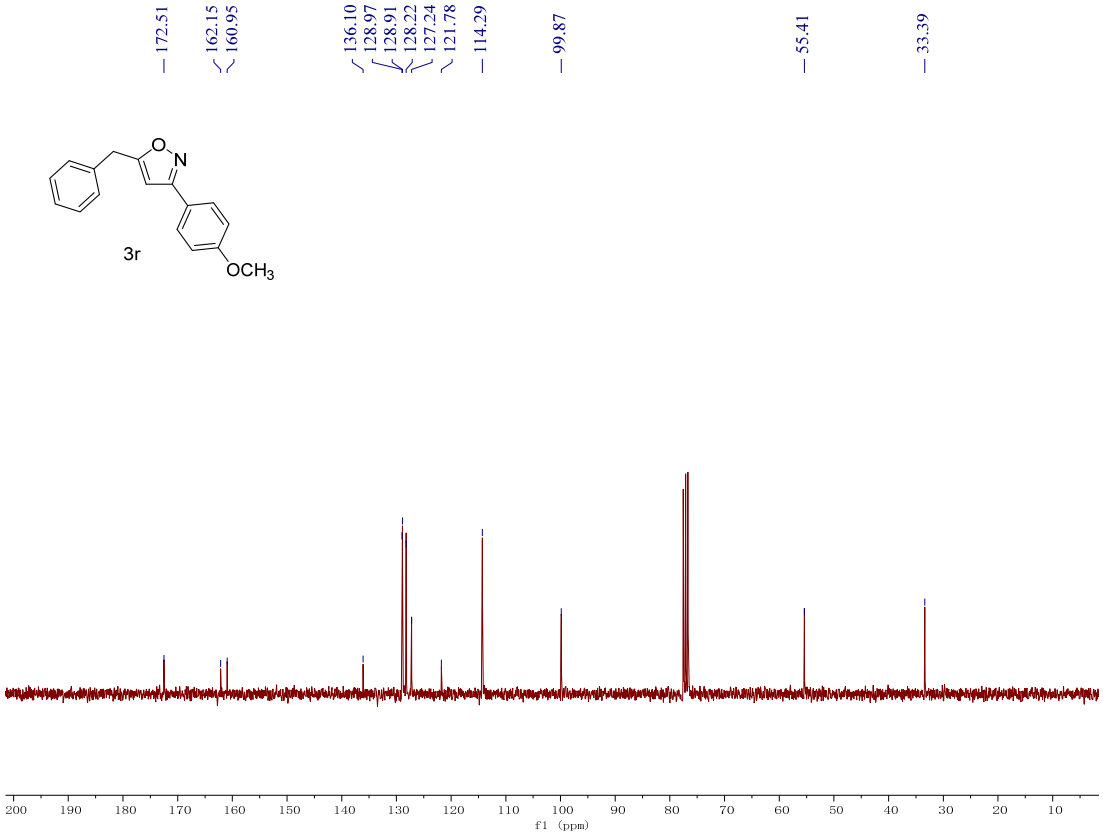

7.6562
7.6288
7.3799
7.3747
7.3677
7.3512
7.3456
7.3271
7.3067
7.2903
7.2842
7.2313
7.2047
6.1738
4.1097
2.3724
O
N
3p
CH3
2.11
5.20
2.37
1.00
2.12
3.28
f1 (ppm)

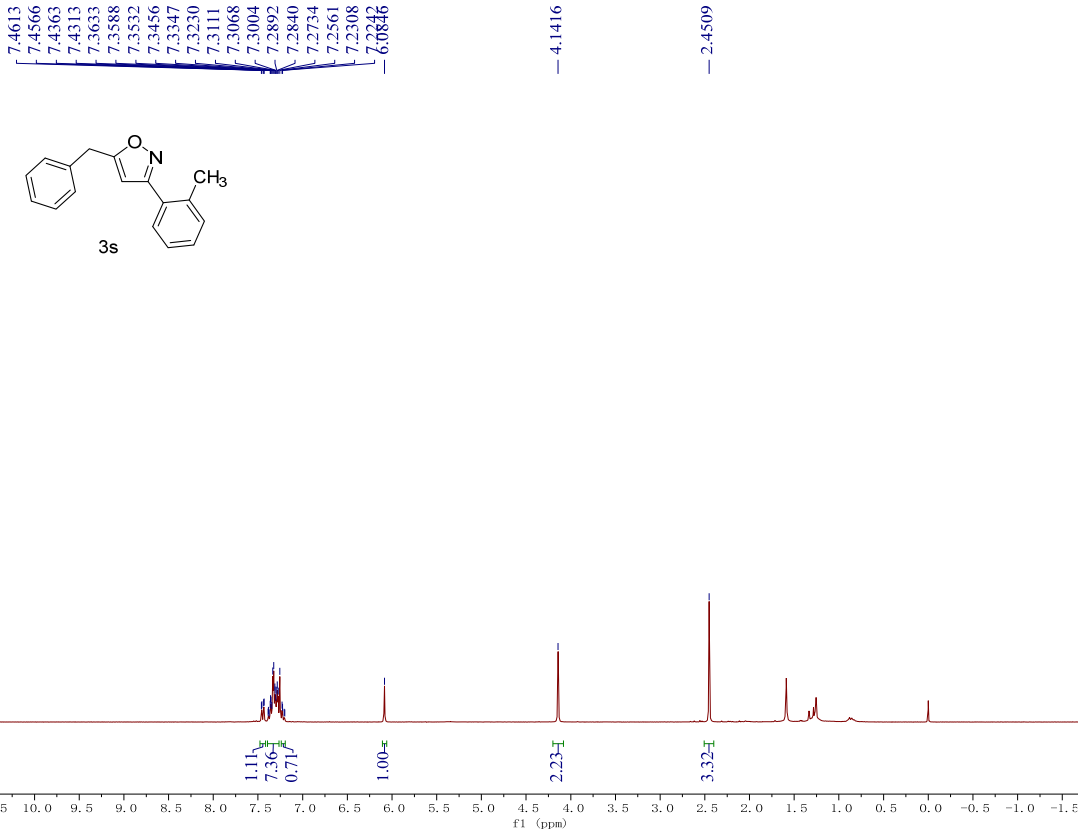

172.53
162.44
139.99
136.01
129.55
128.92
128.86
127.19
126.66
126.34
99.96
33.35
21.44
O
N
3p
CH3
f1 (ppm)


7.6983
7.6699
7.4449
7.4165
7.3692
7.3637
7.3573
7.3400
7.3355
7.3159
7.2963
7.2796
7.2736
7.2693
7.2474
6.1859
6.1829
6.1800
4.0994
1.3251
O
N
3q
tBu
2.06
2.15
5.39
1.00
2.15
9.13
f1 (ppm)

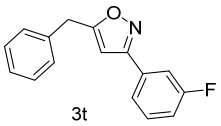

172.50
162.38
153.15
136.05
128.93
128.87
127.19
126.54
126.37
125.82
100.02
34.84
33.34
31.25
O
N
3q
tBu
f1 (ppm)


7.8151
7.7859
7.4851
7.4775
7.4616
7.4564
7.4372
7.4166
7.3915
7.3622
7.0569
7.0277
6.2577
4.2136
3.9387
O
N
3r
OCH3
2.13
5.52
2.17
1.00
2.18
3.38
f1 (ppm)

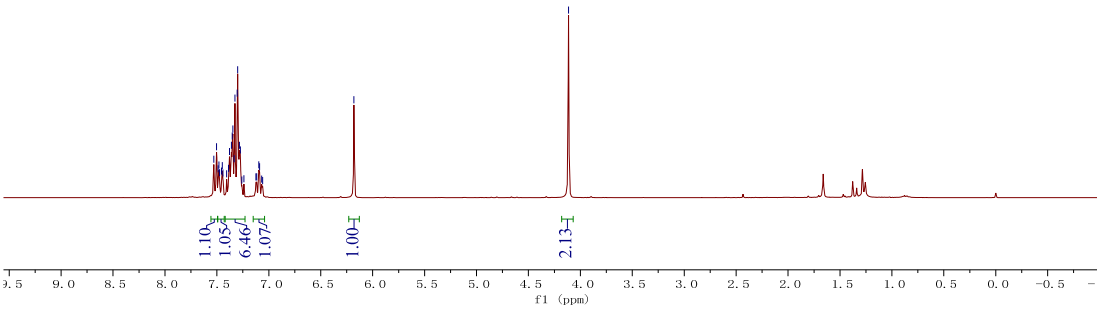

172.51
162.15
160.95
136.10
128.97
128.91
128.22
127.24
121.78
114.29
99.87
55.41
33.39
O
N
3r
OCH3
f1 (ppm)


7.4613
7.4566
7.4363
7.4313
7.3633
7.3588
7.3532
7.3456
7.3347
7.3230
7.3111
7.3068
7.3004
7.2892
7.2840
7.2734
7.2561
7.2308
7.2242
6.0846
4.1416
2.4509
O
N
CH3
3s
1.11
7.36
0.71
1.00
2.23
3.32
f1 (ppm)
171.70
163.11
136.84
135.99
130.99
129.40
129.33
128.92
128.89
128.84
127.17
125.89
102.62
33.28
21.11
O
N
CH3
3s
f1 (ppm)

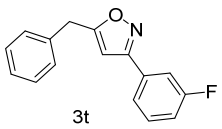

7.5295
7.5036
7.4874
7.4800
7.4743
7.4555
7.4483
7.4419
7.4061
7.3871
7.3788
7.3600
7.3516
7.3457
7.3346
7.3265
7.3045
7.2993
7.2825
7.2740
7.2601
7.2401
7.1246
7.1158
7.0966
7.0880
7.0689
7.0601
6.1802
4.1137


O
N
F

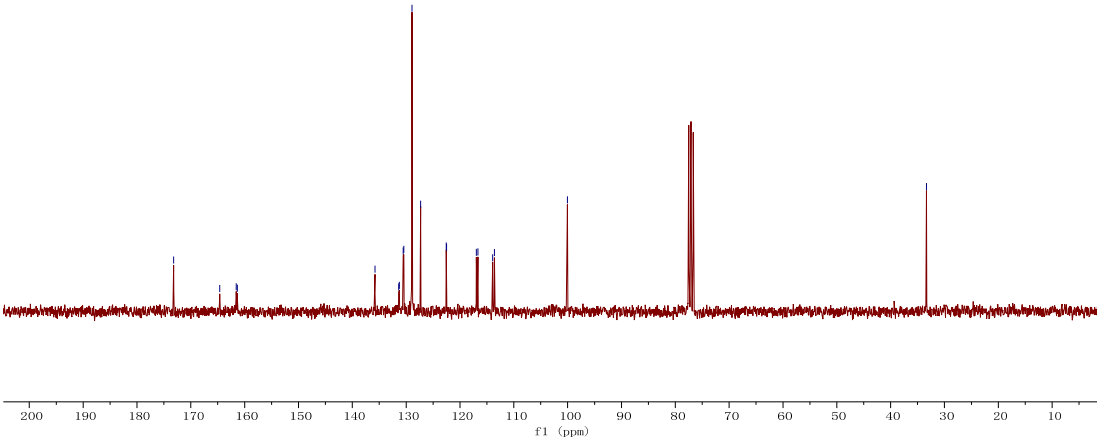
3t

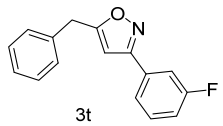

1.10
1.05
6.46
1.07
1.00
2.13
f1 (ppm)


173.19
164.62
161.56
161.36
135.79
131.38
131.27
130.56
130.45
128.92
127.31
122.54
122.50
116.95
116.67
113.92
113.61
100.04
33.34


O
N
F

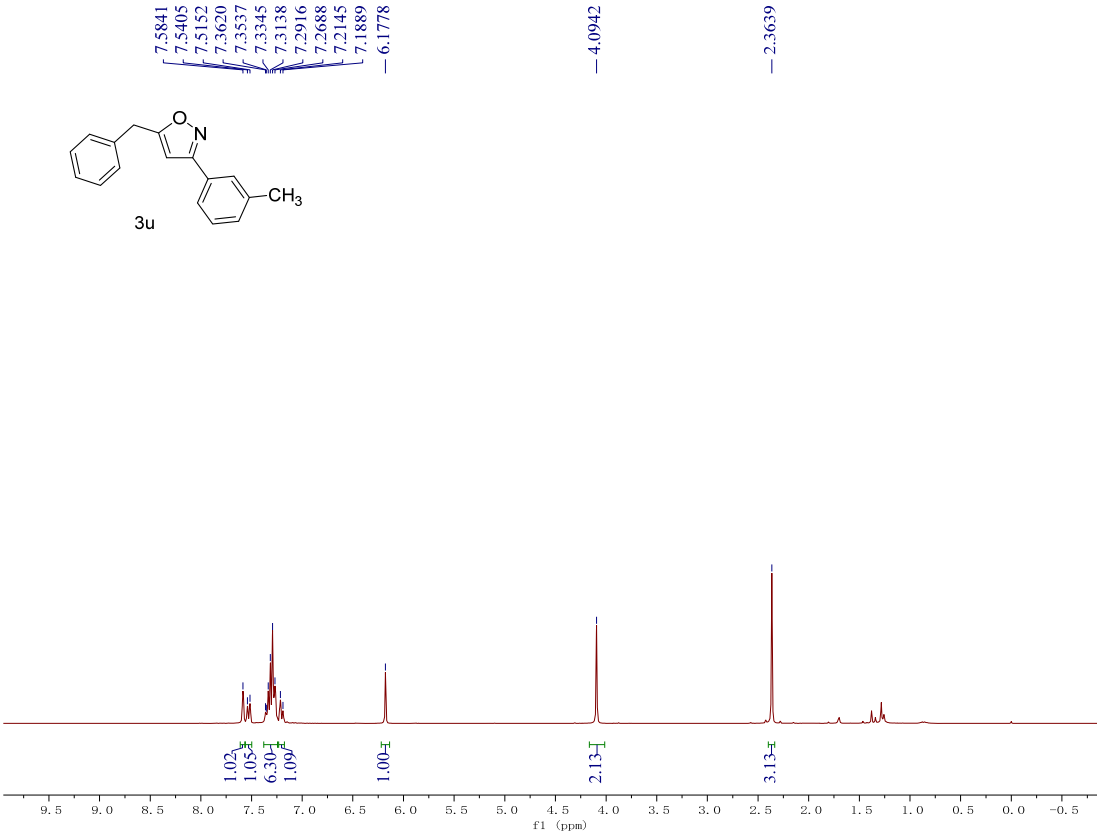
3t

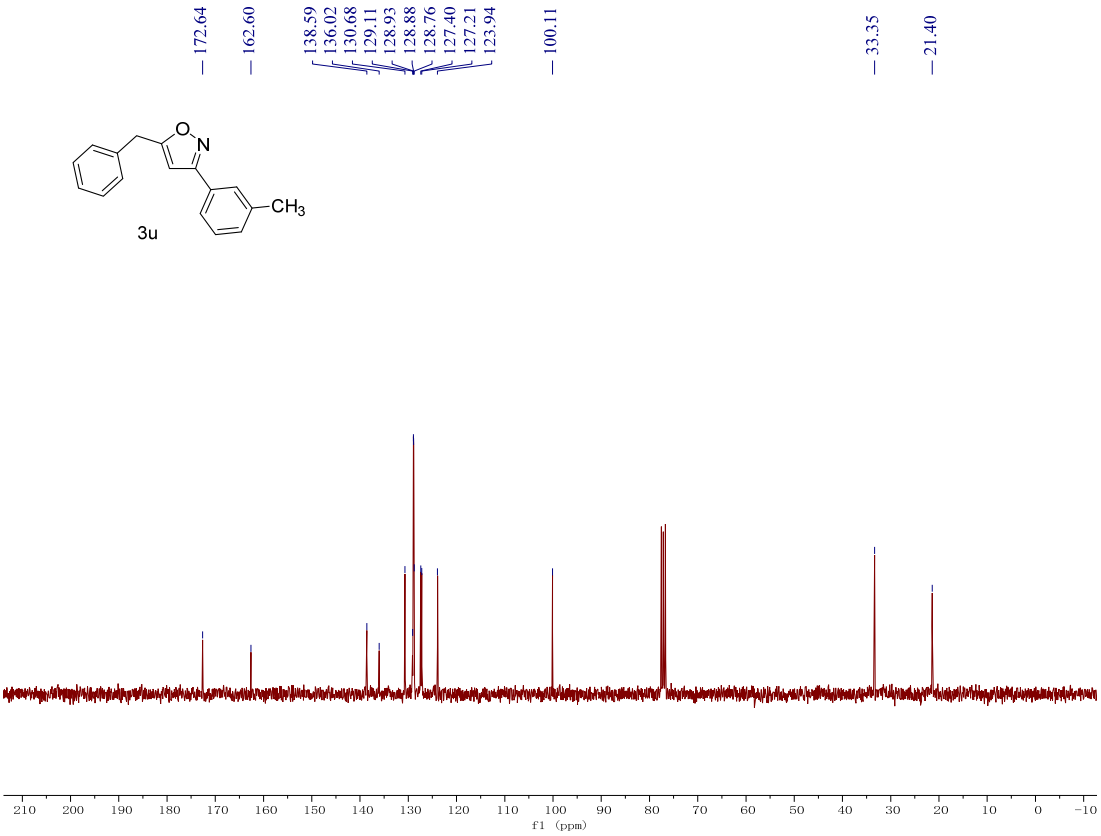

f1 (ppm)


O
N
F

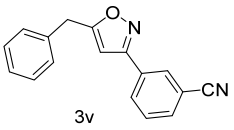
3t

-112.24
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

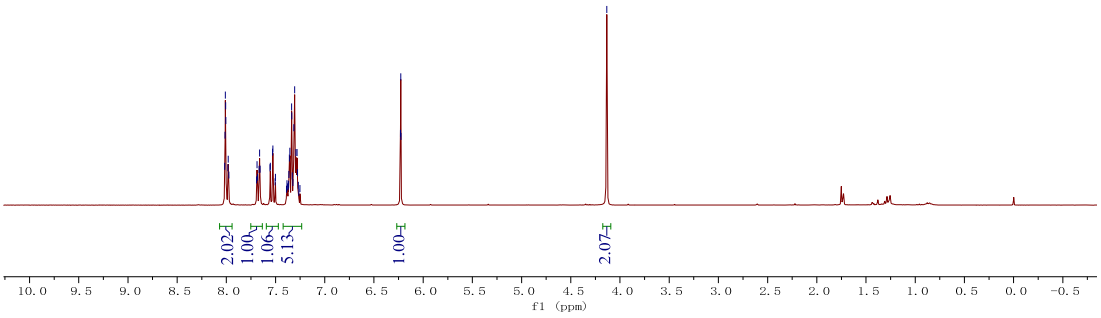

7.5841
7.5405
7.5152
7.3620
7.3557
7.3345
7.3138
7.2916
7.2688
7.2145
7.1889
6.1778
4.0942
2.3639
O
N
CH3
3u
1.02
1.05
6.30
1.09
1.00
2.13
3.13
f1 (ppm)

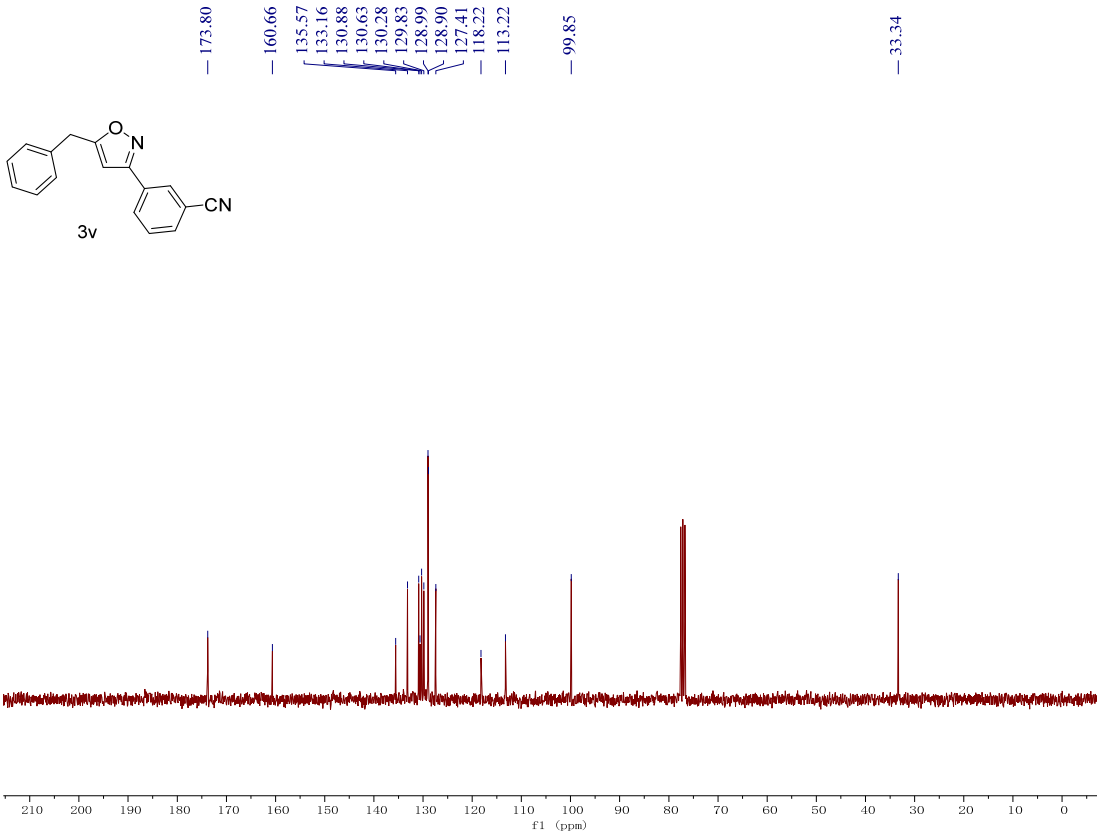

172.64
162.60
138.59
136.02
130.68
129.11
128.93
128.88
128.76
127.40
127.21
123.94
100.11
33.35
21.40
O
N
CH3
3u
f1 (ppm)


8.0162
8.0134
8.0105
8.0070
8.0052
7.9851
7.9804
7.9752
7.6928
7.6880
7.6831
7.6668
7.6619
7.6573
7.5560
7.5530
7.5303
7.5273
7.5051
7.5018
7.3893
7.3834
7.3777
7.3707
7.3674
7.3638
7.3595
7.3542
7.3373
7.3348
7.3298
7.3233
7.3139
7.3062
7.2936
7.2819
7.2764
7.2692
7.2641
7.2519
6.2313
6.2283
6.2251
4.1346


O
N
CN

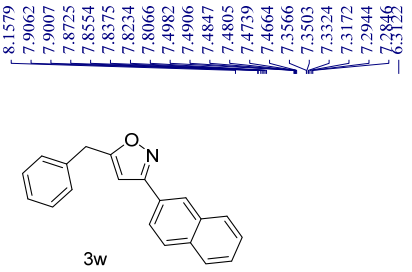
3v


2.02
1.00
1.06
5.13
1.00
2.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

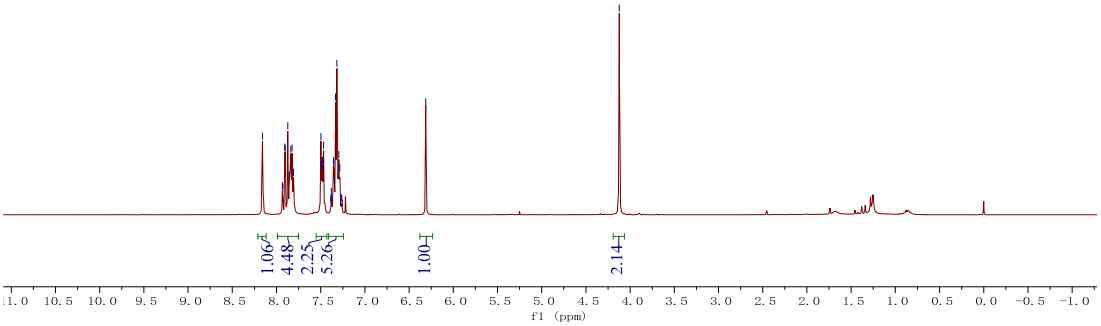

173.80
160.66
135.57
133.16
130.88
130.63
130.28
129.83
128.99
128.90
127.41
118.22
113.22
99.85
33.34
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

O
N
CN

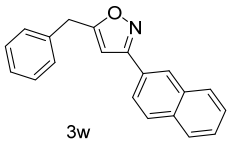
3v


8.1579
7.9062
7.9007
7.8725
7.8554
7.8375
7.8234
7.8066
7.4982
7.4906
7.4847
7.4805
7.4739
7.4664
7.3566
7.3503
7.3324
7.3172
7.2944
7.2846
6.3122
4.1230

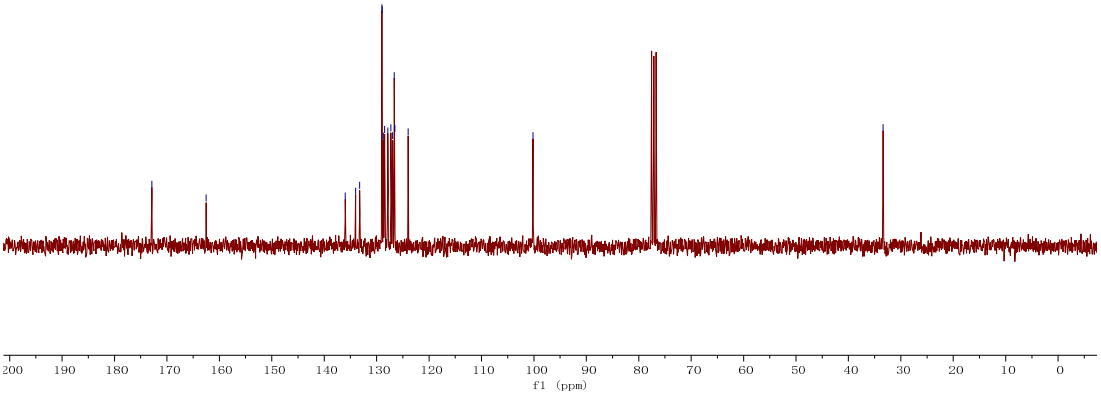
3w

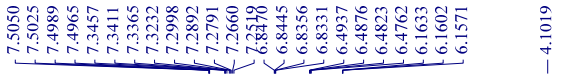

1.06
4.48
2.25
5.26
1.00
2.14
f1 (ppm)

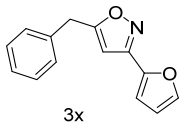

172.88
162.52
135.99
134.02
133.22
128.98
128.93
128.72
128.47
127.86
127.27
126.96
126.64
126.53
123.99
100.17
33.40



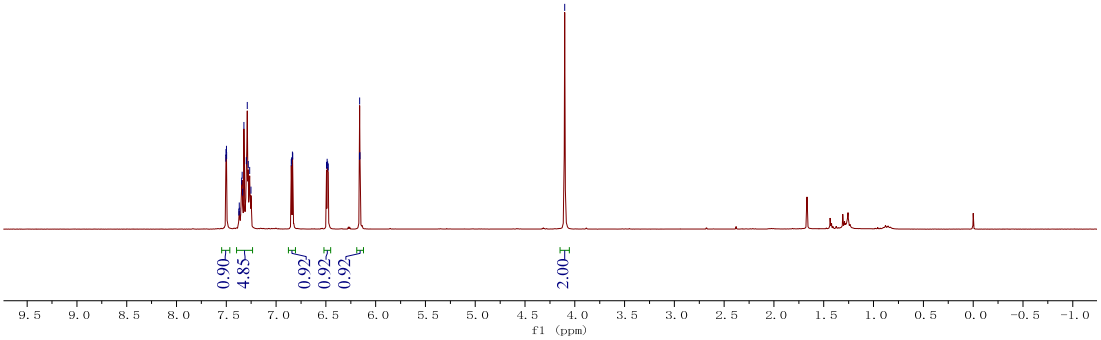
3w


f1 (ppm)

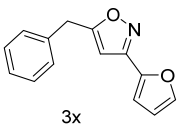

7.5050
7.5025
7.4989
7.4965
7.3457
7.3411
7.3365
7.3232
7.2998
7.2892
7.2791
7.2660
6.8445
6.8356
6.8331
6.4937
6.4876
6.4823
6.4762
6.1633
6.1602
6.1571
4.1019



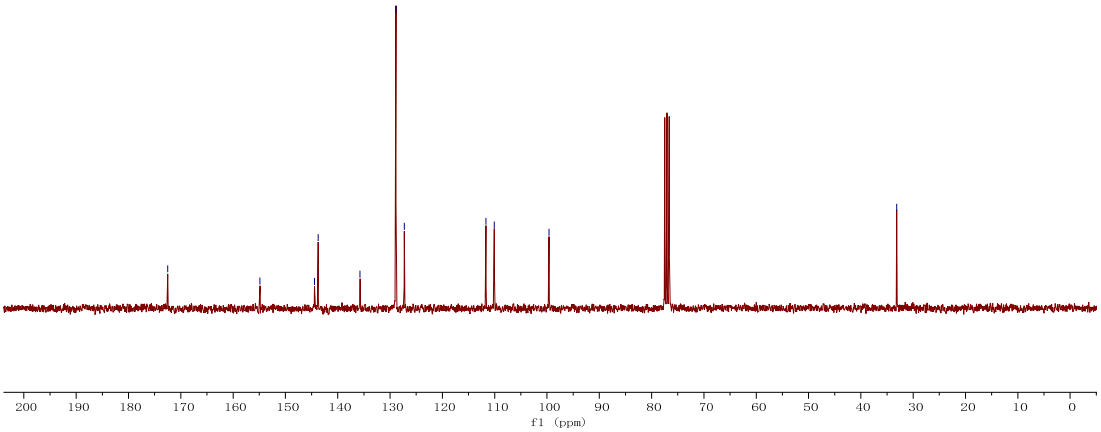
3x

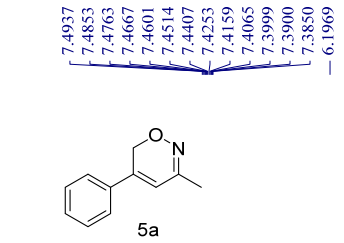

0.90
4.85
0.92
0.92
0.92
2.00
f1 (ppm)


172.50
154.86
144.43
143.75
135.74
128.88
127.26
111.68
110.08
99.62
33.17

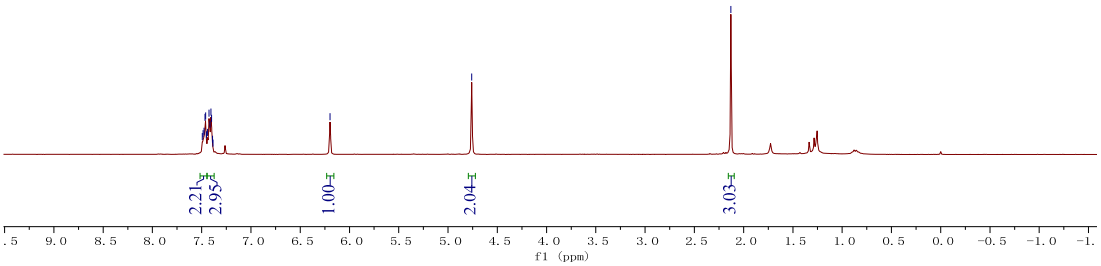


3x


f1 (ppm)

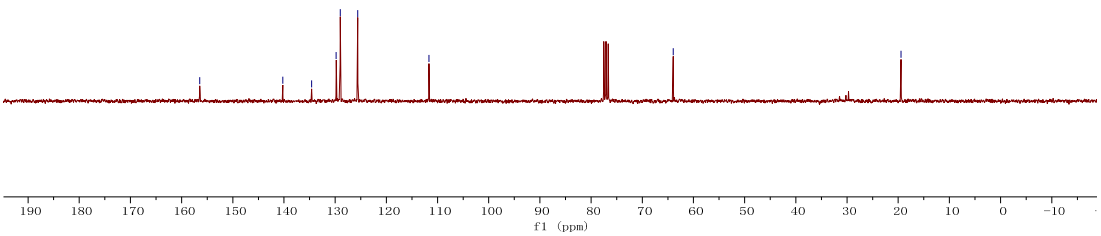

7.4937
7.4853
7.4763
7.4667
7.4601
7.4514
7.4407
7.4253
7.4159
7.4065
7.3999
7.3900
7.3850
6.1969
4.7593
2.1296
O
N

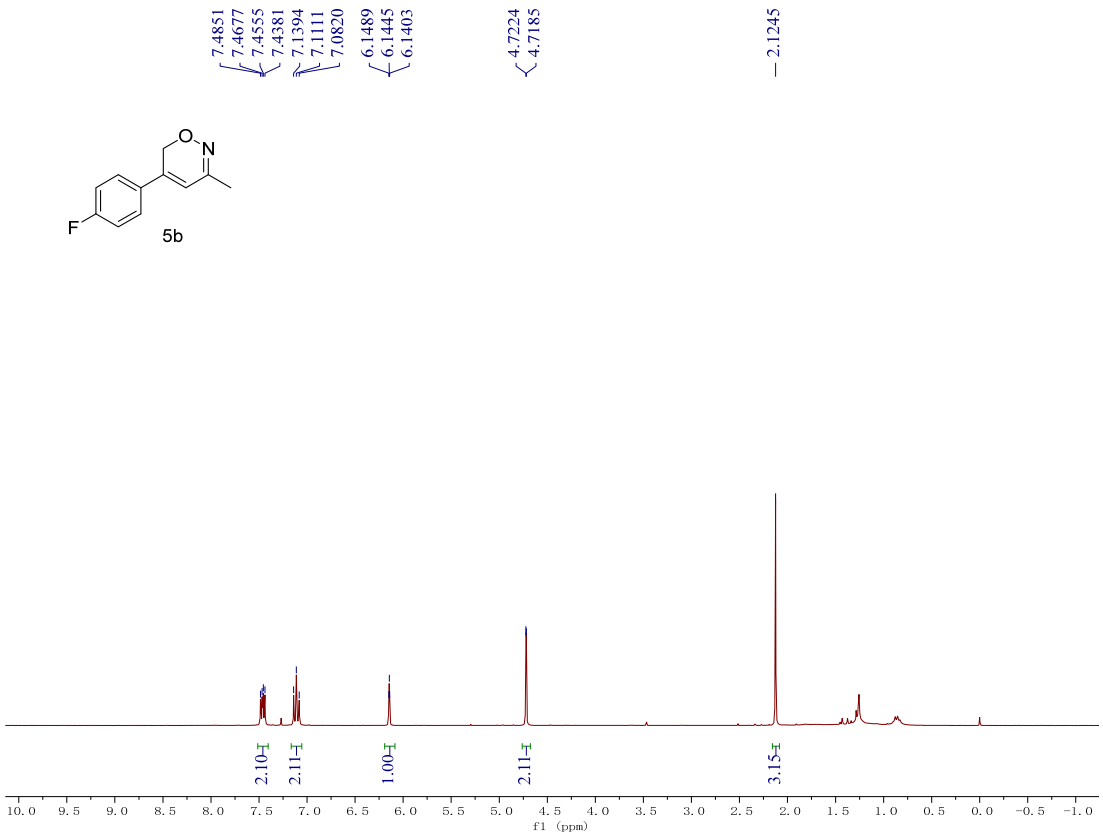
5a

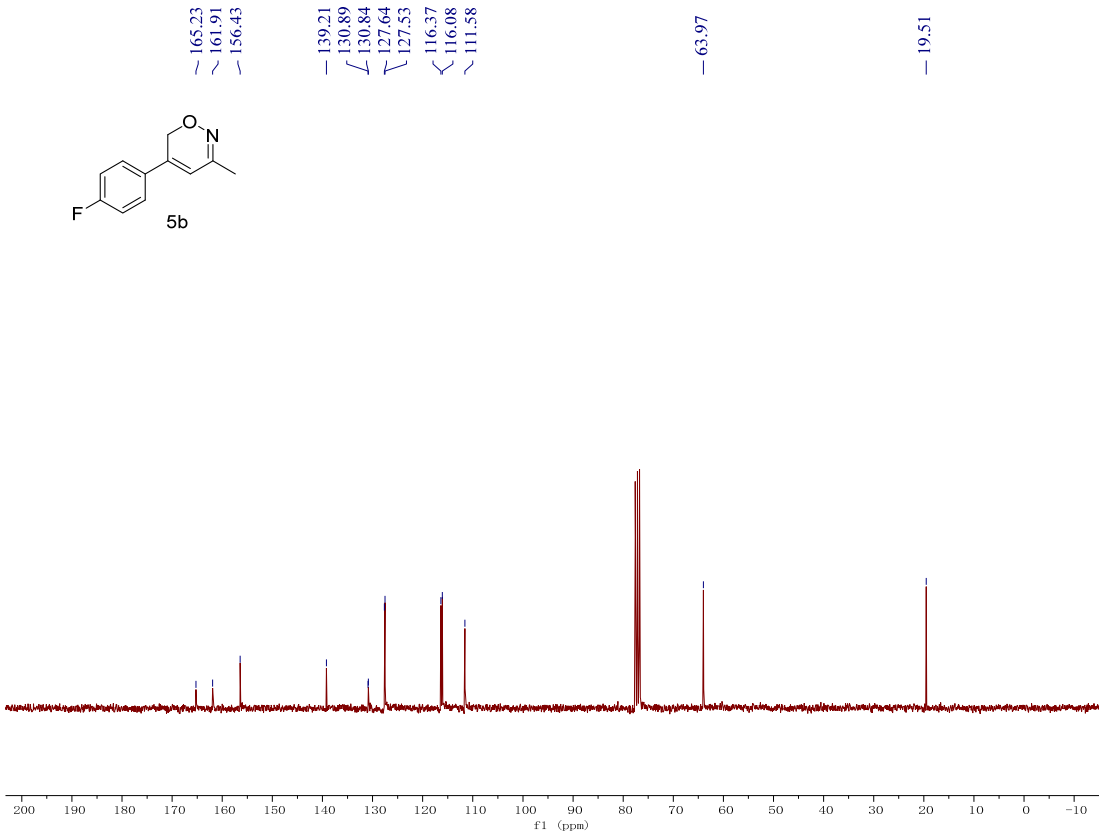

2.21
2.95
1.00
2.04
3.03
f1 (ppm)

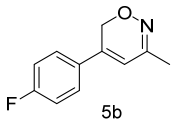

156.47
140.24
134.60
129.80
129.01
125.59
111.68
63.96
19.46
O
N

5a


f1 (ppm)

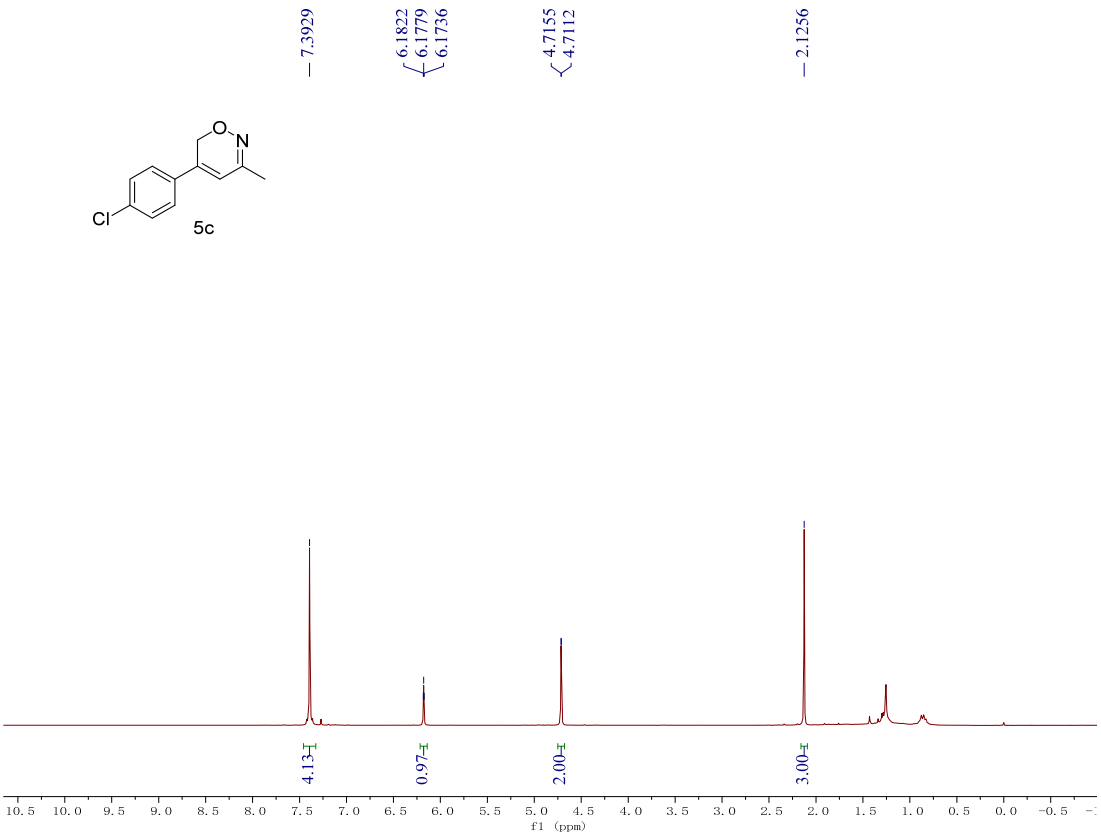

7.4851
7.4677
7.4555
7.4381
7.1394
7.1111
7.0820
6.1489
6.1445
6.1403
4.7224
4.7185
2.1245
O
N
F
5b
2.10
2.11
1.00
2.11
3.15
f1 (ppm)

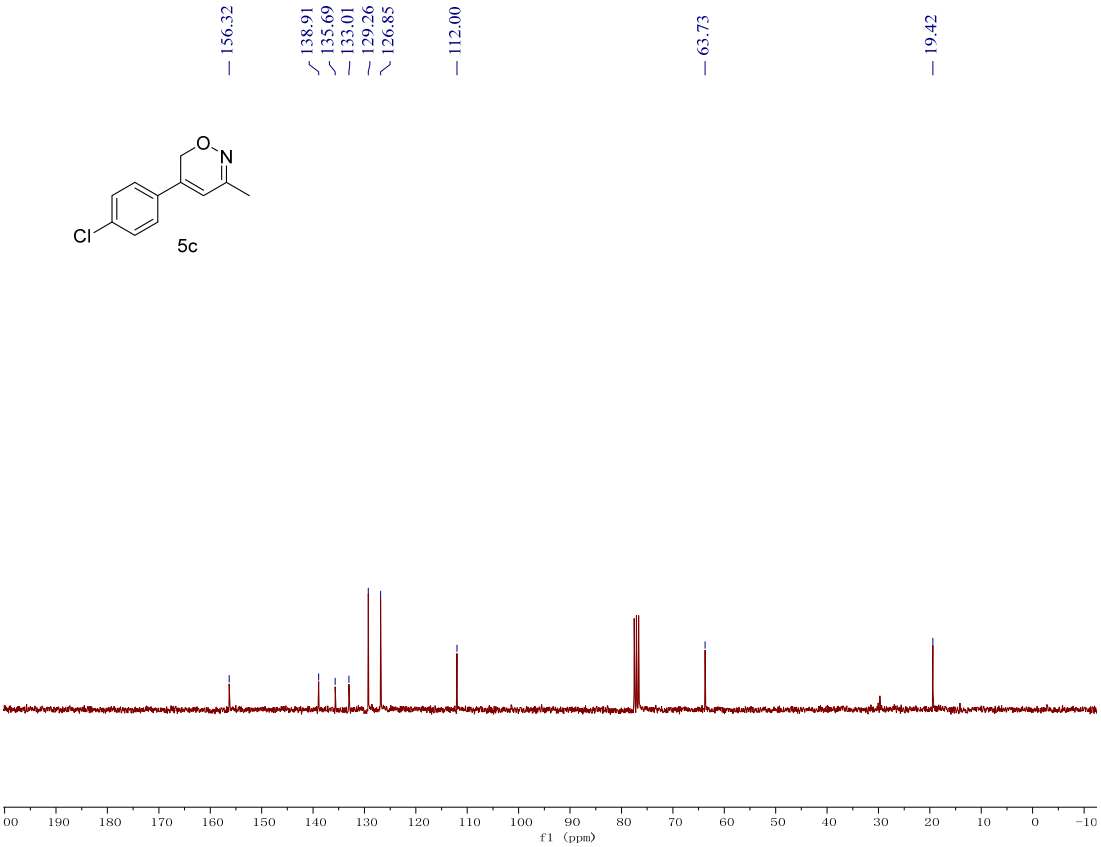

165.23
161.91
156.43
139.21
130.89
130.84
127.64
127.53
116.37
116.08
111.58
63.97
19.51
O
N
F
5b
f1 (ppm)

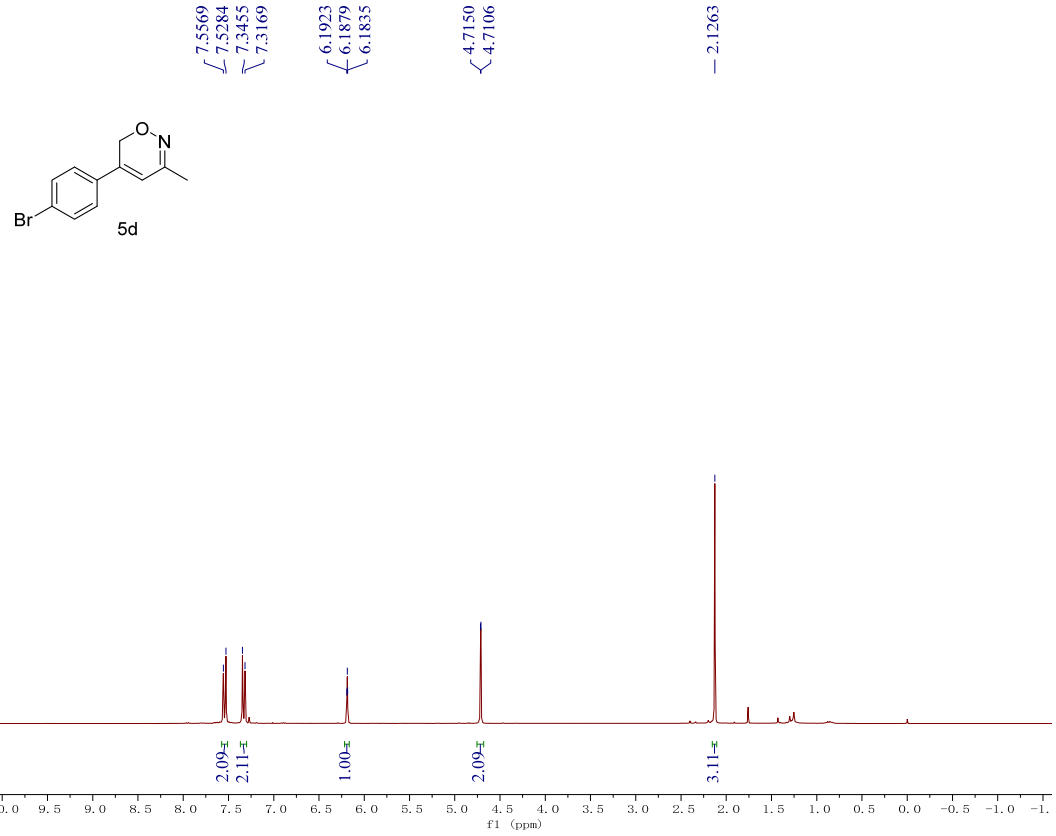

O
N
F

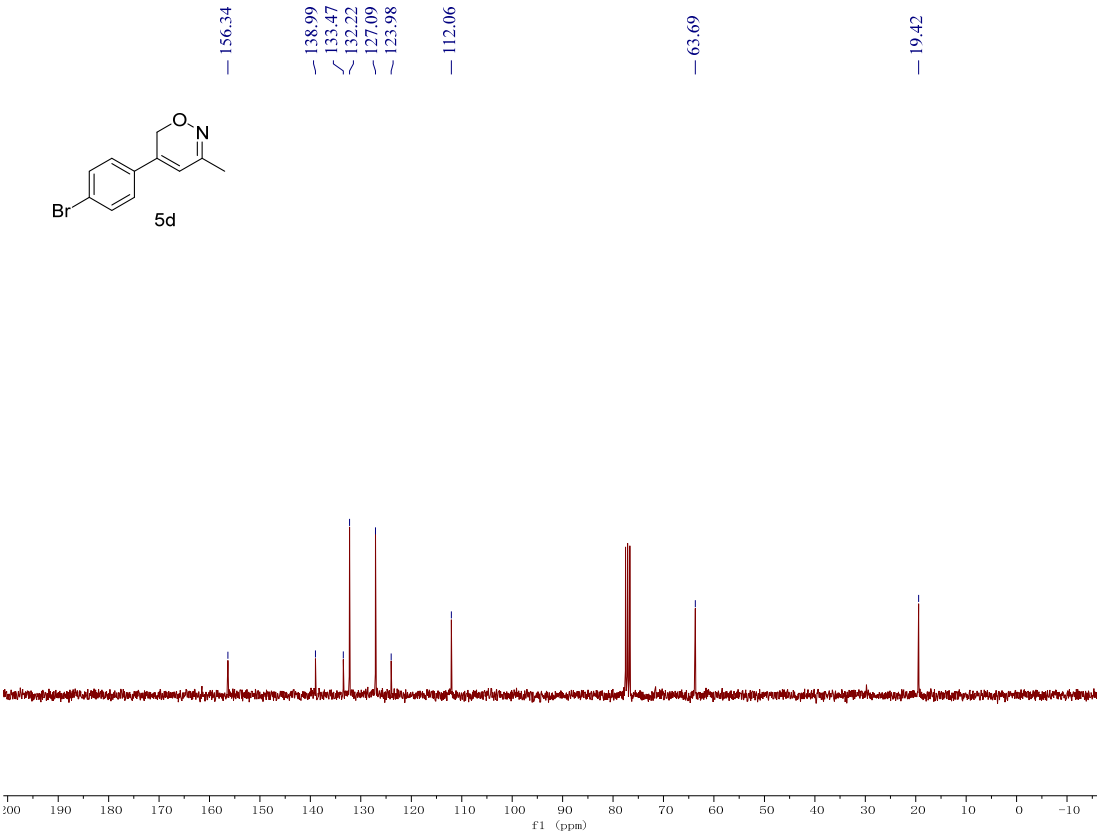
5b

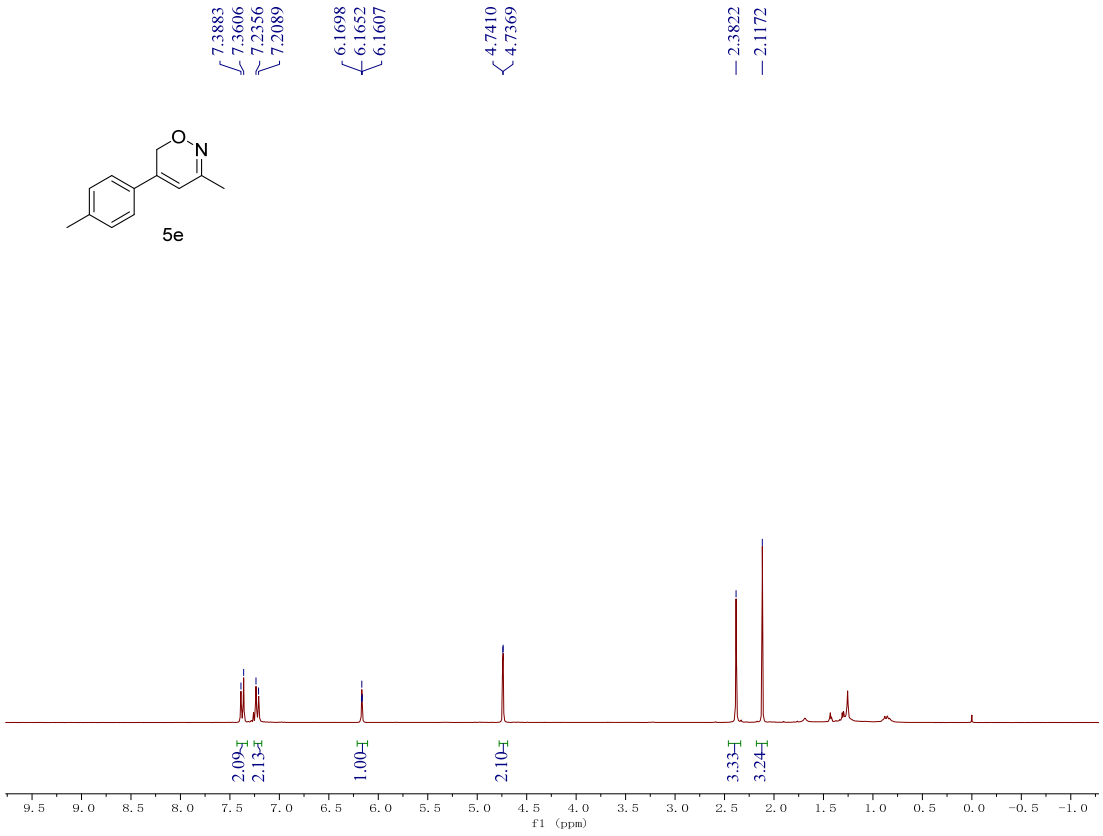
-110.34
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

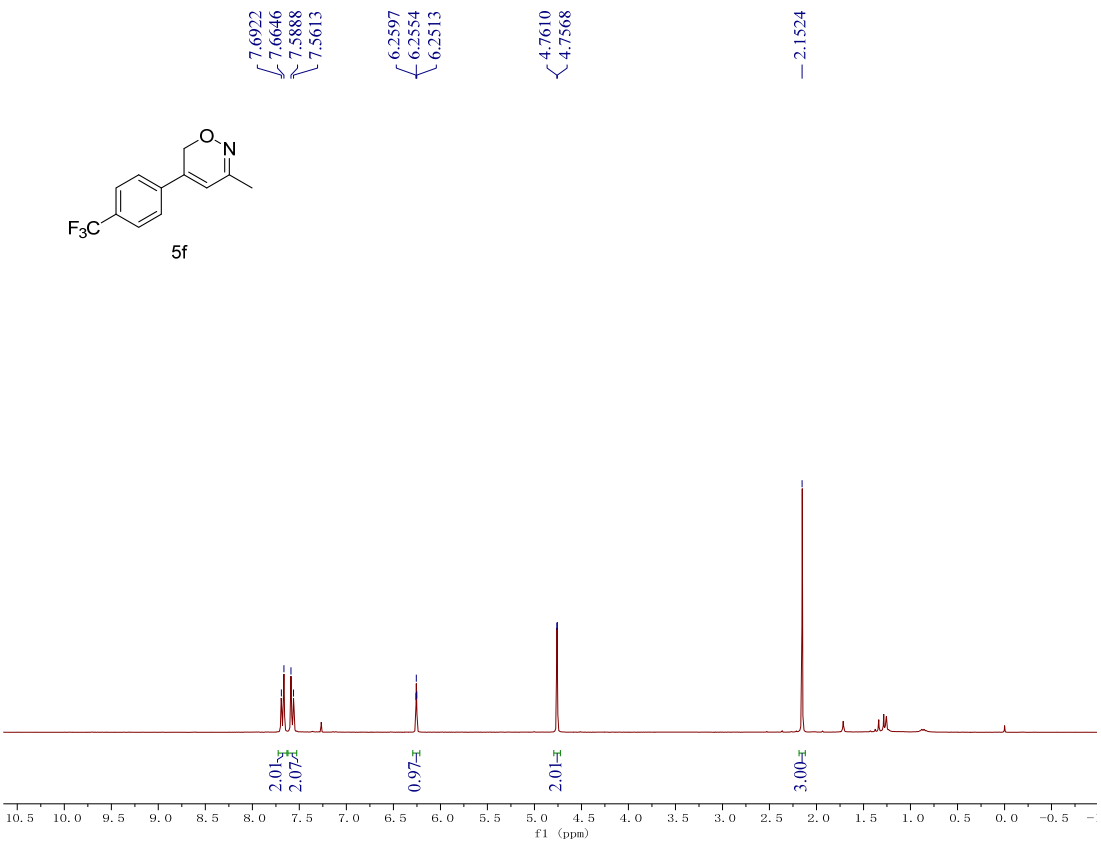

7.3929
6.1822
6.1779
6.1736
4.7155
4.7112
2.1256
O
N
Cl
5c
4.13
0.97
2.00
3.00
f1 (ppm)

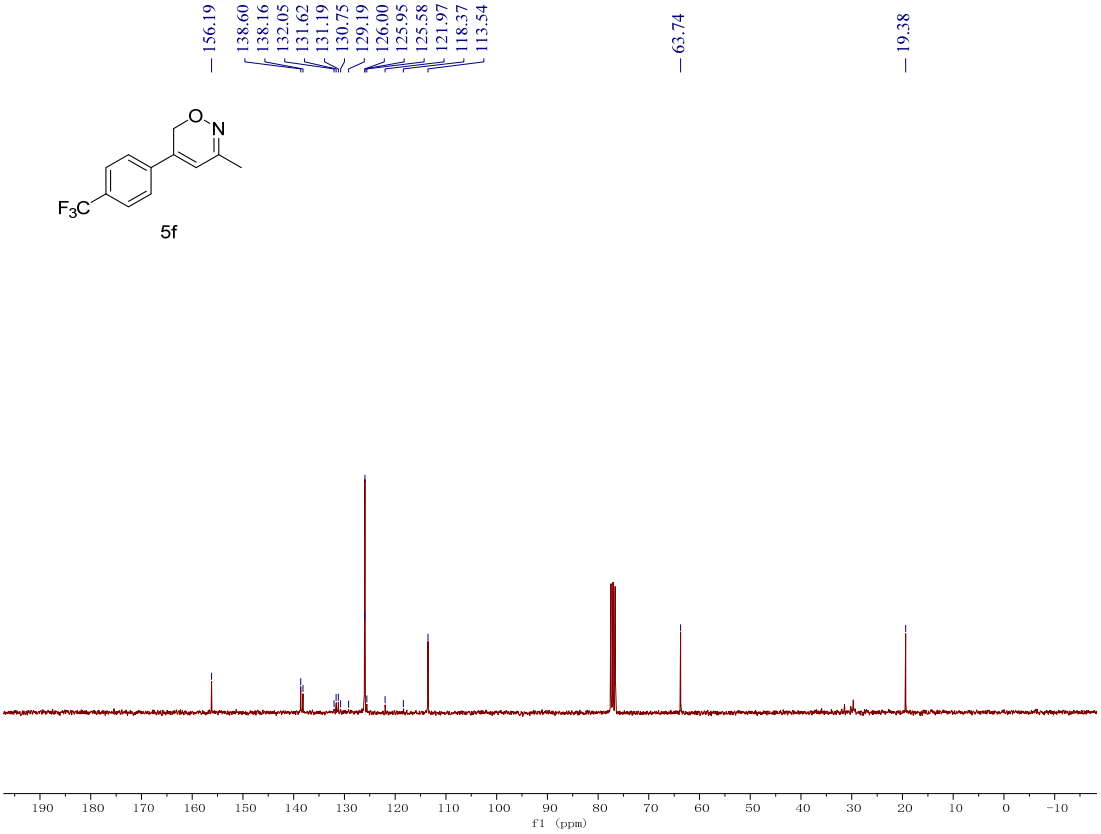

156.32
138.91
135.69
133.01
129.26
126.85
112.00
63.73
19.42
O
N
Cl
5c
f1 (ppm)

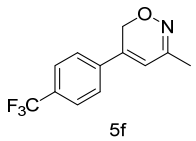

7.5569
7.5284
7.3455
7.3169
6.1923
6.1879
6.1835
4.7150
4.7106
2.1263
O
N
Br
5d
2.09
2.11
1.00
2.09
3.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.
f1 (ppm)


156.34
138.99
133.47
132.22
127.09
123.98
112.06
63.69
19.42
O
N
Br
5d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.3883
7.3606
7.2356
7.2089
6.1698
6.1652
6.1607
4.7410
4.7369
2.3822
2.1172
5e
2.09
2.13
1.00
2.10
3.33
3.24
f1 (ppm)
156.60
140.26
140.14
131.64
129.73
125.50
110.78
63.96
21.40
19.50
5e
f1 (ppm)

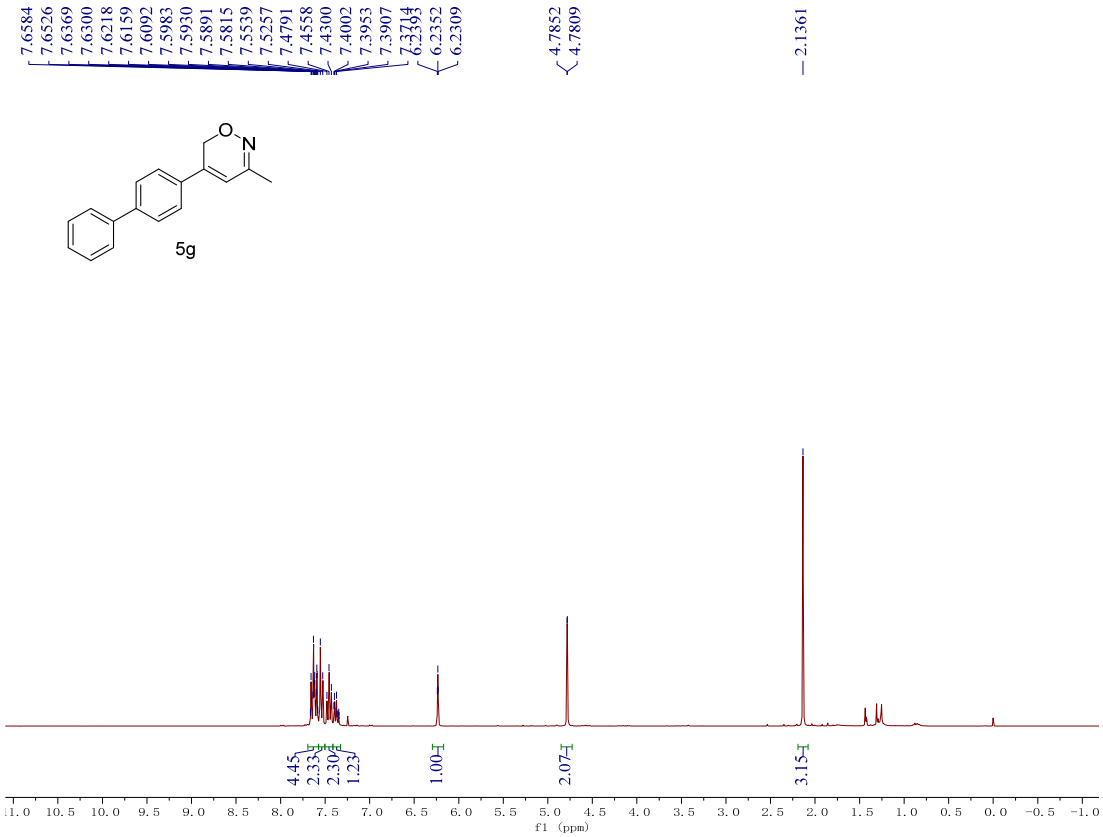

7.6922
7.6646
7.5888
7.5613
6.2597
6.2554
6.2513
4.7610
4.7568
2.1524
O
N
F3C
5f
2.01
2.07
0.97
2.01
3.00
f1 (ppm)

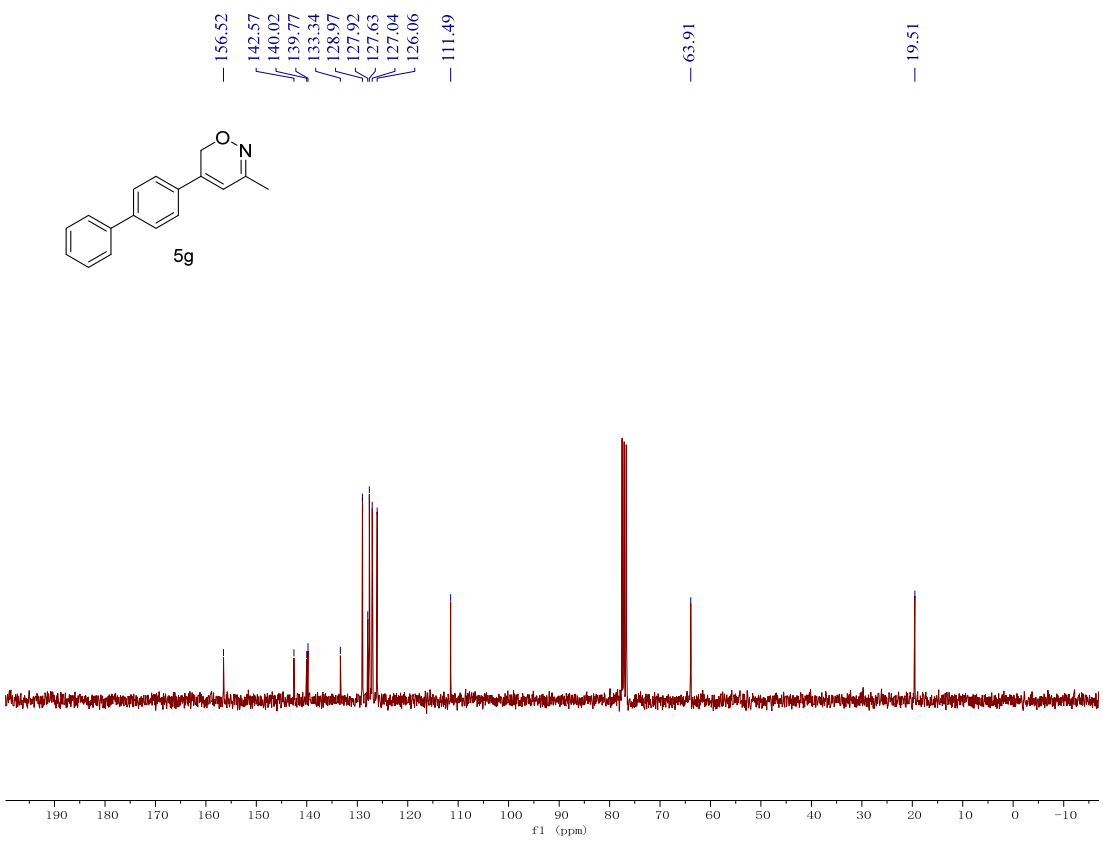

156.19
138.60
138.16
132.05
131.62
131.19
130.75
129.19
126.00
125.95
125.58
121.97
118.37
113.54
63.74
19.38
O
N
F3C
5f
f1 (ppm)

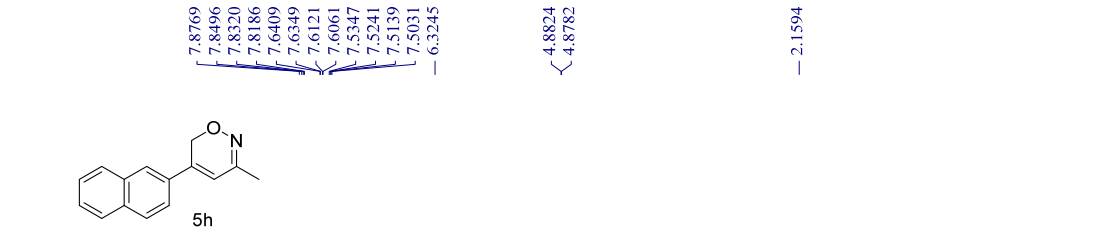

O
N
F3C

5f

-62.85
−15
−20
−25
−30
−35
−40
−45
−50
−55
−60
−65
−70
−75
−80
−85
−90
−95
−100
−105
−110
−115
f1 (ppm)

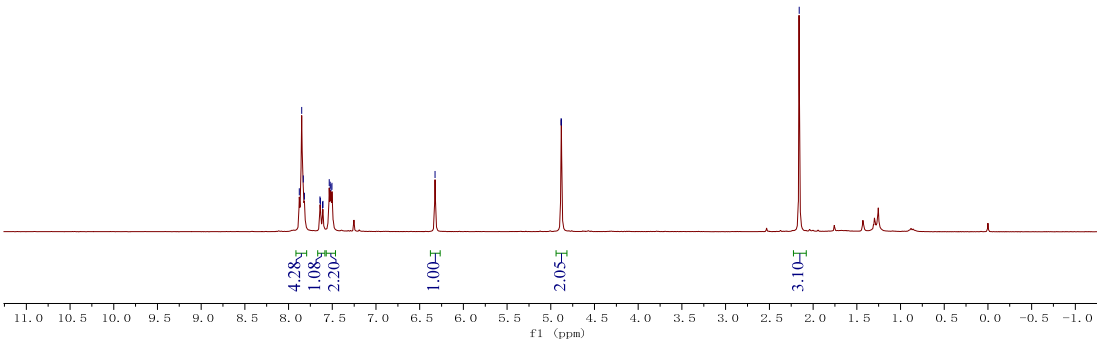

7.6584
7.6526
7.6369
7.6300
7.6218
7.6159
7.6092
7.5983
7.5930
7.5891
7.5815
7.5539
7.5257
7.4791
7.4558
7.4300
7.4002
7.3953
7.3907
7.3714
7.3393
6.2352
6.2309
4.7852
4.7809
2.1361
O
N
5g
4.45
2.33
2.30
1.23
1.00
2.07
3.15
f1 (ppm)

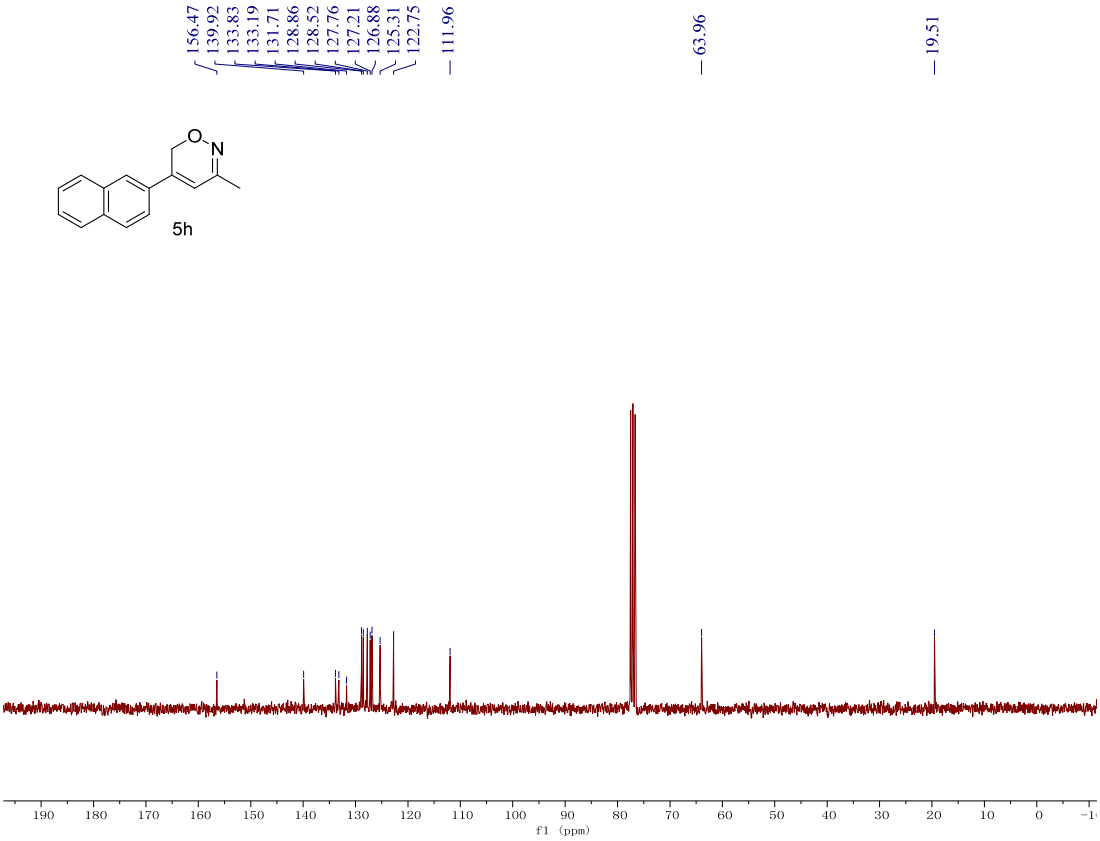

156.52
142.57
140.02
139.77
133.34
128.97
127.92
127.63
127.04
126.06
111.49
63.91
19.51
O
N
5g
f1 (ppm)


7.8769
7.8496
7.8320
7.8186
7.6409
7.6349
7.6121
7.6061
7.5347
7.5241
7.5139
7.5031
6.3245
4.8824
4.8782
2.1594

O
N

5h

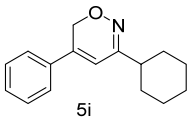

4.28
1.08
2.20
1.00
2.05
3.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


156.47
139.92
133.83
133.19
131.71
128.86
128.52
127.76
127.21
126.88
125.31
122.75
111.96
63.96
19.51
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

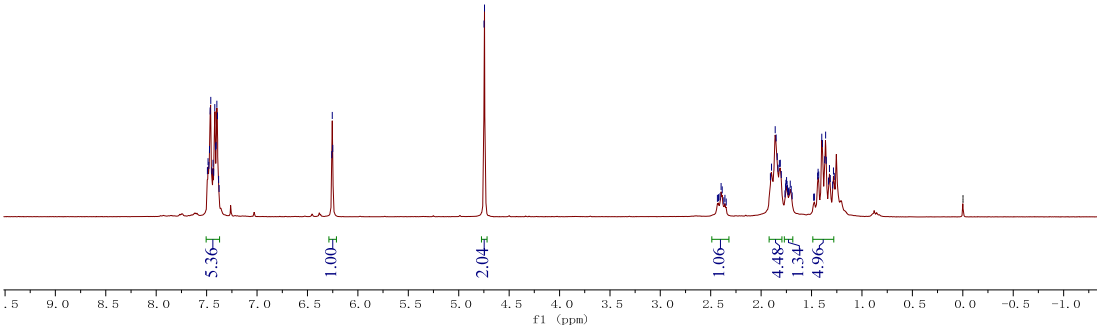
O
N

5h

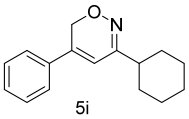

7.4928
7.4857
7.4783
7.4721
7.4659
7.4598
7.4487
7.4365
7.4302
7.4191
7.4122
7.4061
7.3988
7.3931
7.3812
7.3761
6.2593
6.2546
6.2495
4.7485
4.7439
2.3969
2.3858
1.9079
1.8974
1.8603
1.8510
1.8404
1.8323
1.8197
1.8103
1.8003
1.7580
1.7537
1.7485
1.7434
1.7388
1.7332
1.7225
1.7107
1.7014
1.4397
1.4350
1.4293
1.3993
1.3917
1.3694
1.3613
1.3536
1.3323
1.3232
1.3142
1.2913
1.2832


O
N

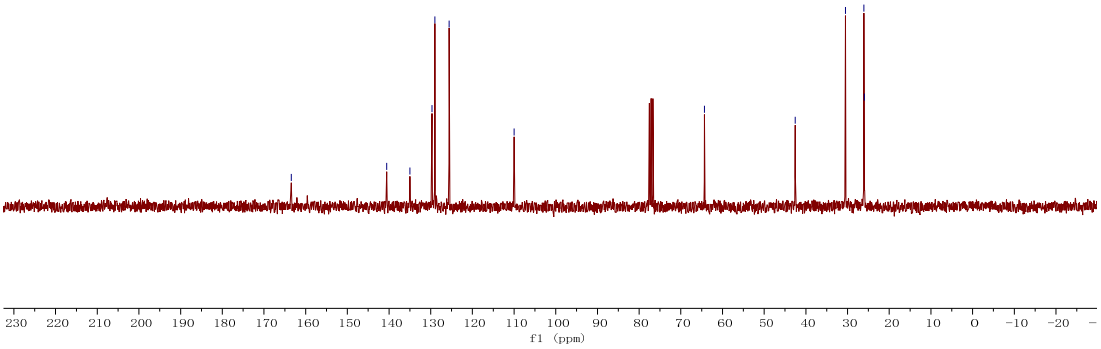
5i

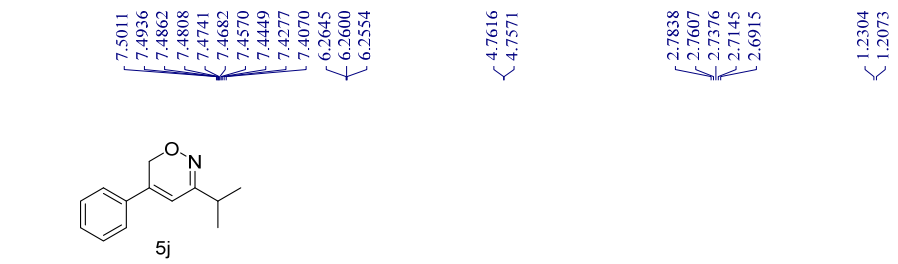

5.36
1.00
2.04
1.06
4.48
1.34
4.96
f1 (ppm)


163.44
140.56
134.97
129.69
129.00
125.58
109.98
64.31
42.54
30.50
26.08
25.96

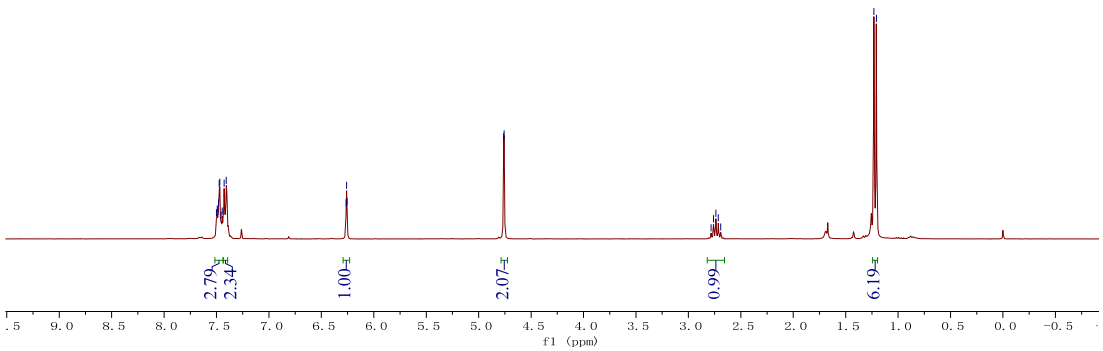

O
N

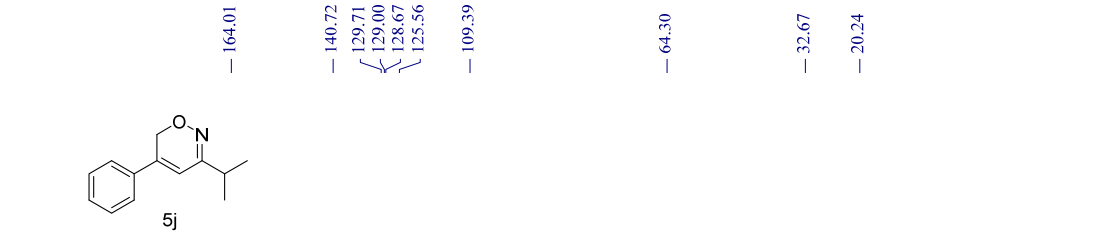
5i


f1 (ppm)

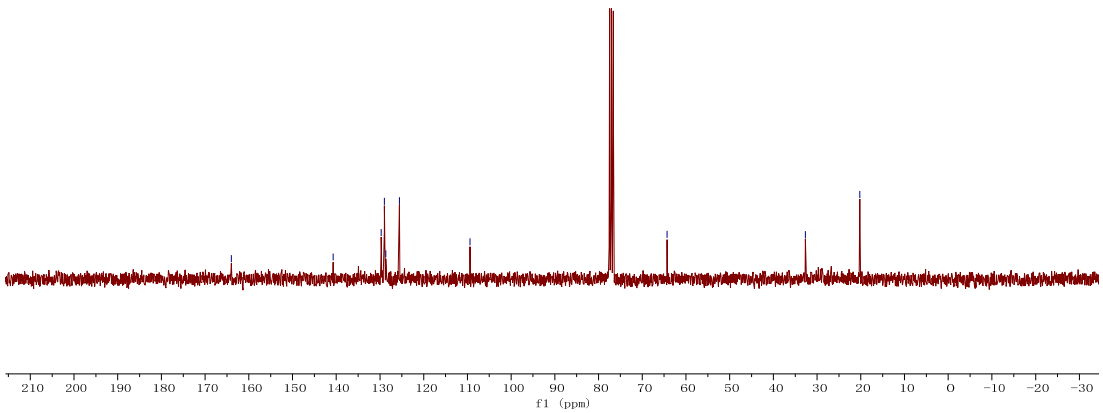

7.5011
7.4936
7.4862
7.4808
7.4741
7.4682
7.4570
7.4449
7.4277
7.4070
6.2645
6.2600
6.2554
4.7616
4.7571
2.7838
2.7607
2.7376
2.7145
2.6915
1.2304
1.2073

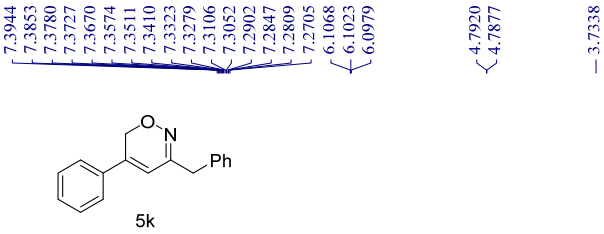
5j


2.79
2.34
1.00
2.07
0.99
6.19
f1 (ppm)

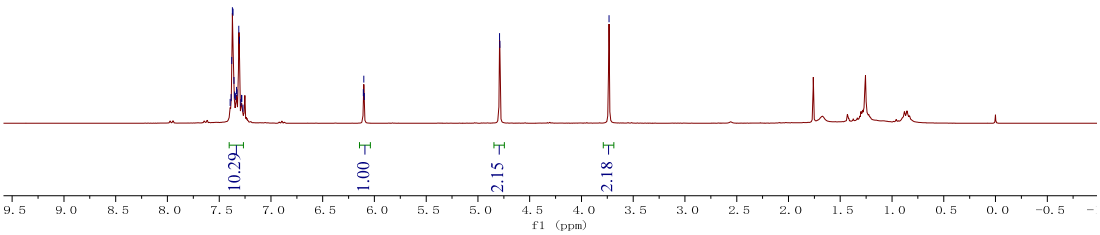

164.01
140.72
129.71
129.00
128.67
125.56
109.39
64.30
32.67
20.24

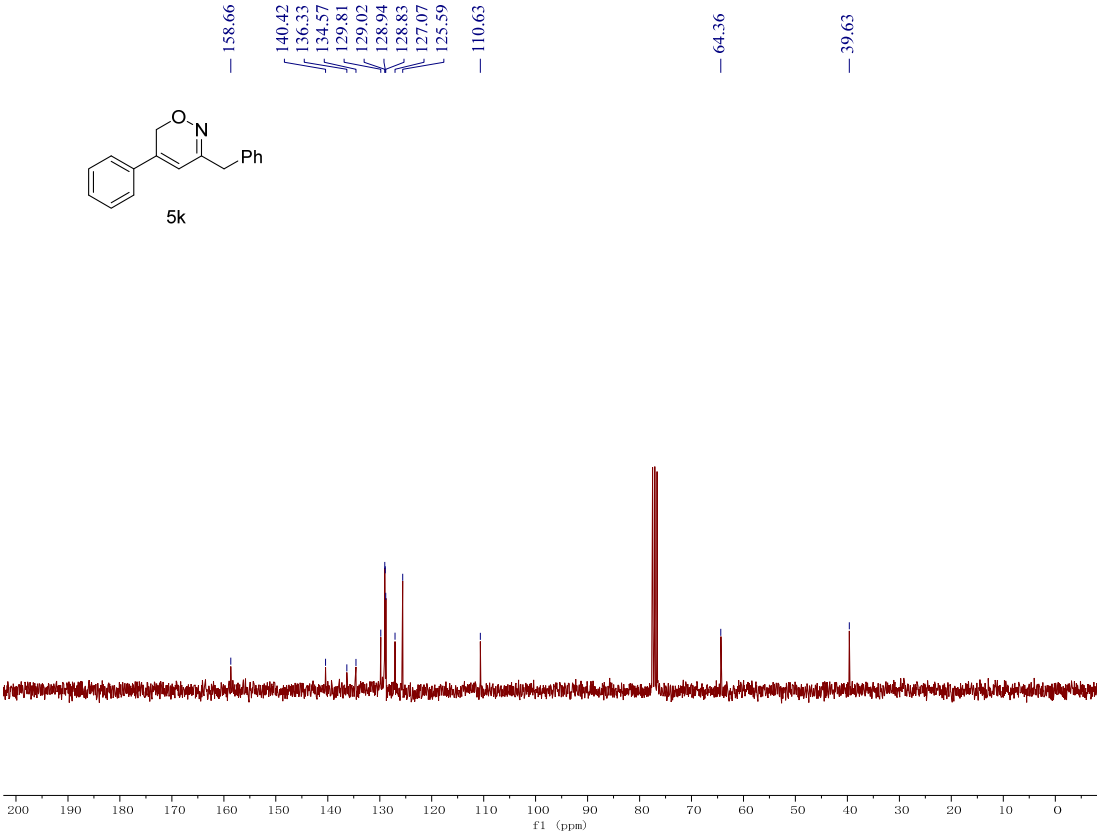
5j


f1 (ppm)


7.3944
7.3853
7.3780
7.3727
7.3670
7.3574
7.3511
7.3410
7.3323
7.3279
7.3106
7.3052
7.2902
7.2847
7.2809
7.2705
6.1068
6.1023
6.0979
4.7920
4.7877
3.7338
O
N
Ph

5k


10.29
1.00
2.15
2.18
f1 (ppm)


158.66
140.42
136.33
134.57
129.81
129.02
128.94
128.83
127.07
125.59
110.63
64.36
39.63
O
N
Ph
f1 (ppm)

5k