

Supporting Information

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1. General information

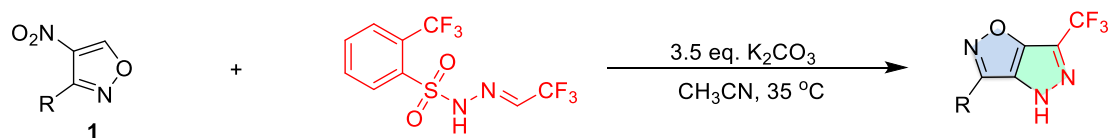
All experiments were carried out under an atmosphere of air. Flash column chromatography was performed over silica gel 48-75 μm . ^1H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded on Bruker-AV (500 MHz, 471 MHz and 126 MHz, respectively) instrument internally referenced to SiMe_4 or chloroform signals. HRMS was recorded using waters G2-Xs qtof mass spectrometer. The new compounds were characterized by ^1H NMR, ^{19}F NMR, ^{13}C NMR, MS and HRMS. The structures of known compounds were further corroborated by comparing their ^1H NMR, ^{19}F NMR, ^{13}C NMR data and MS data with those of literature. The Substrates **1**¹ and **TFHZ-Tfs**² was synthesized according to the reported methods.

Trichloromethane (CHCl_3), dichloromethane, dichloroethane and ethyl acetate were freshly distilled from CaH_2 ; tetrahydrofuran (THF), toluene and ether were dried with sodium benzophenone and distilled before use.

Reactions were monitored by thin layer chromatography (TLC) using silicycle pre-coated silica gel plates. Flash column chromatography was performed on silica gel 60 (particle size 300-400 mesh ASTM, purchased from Yantai, China) and eluted with petroleum ether/ethyl acetate. All reagents and solvents were used as received from commercial sources (*Energy Chemical*, *J&K*[®], *Adamas-beta*[®], *Bidepharm*) without further purification.

2. Experimental procedure

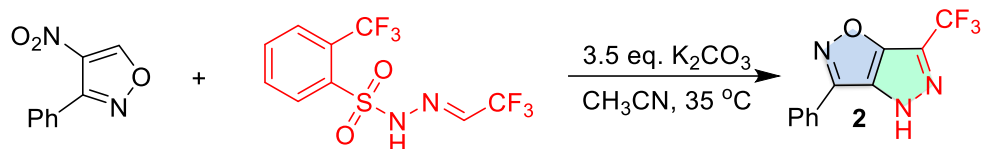
2.1 K_2CO_3 -Promoted [3 + 2] annulation of in situ formed trifluorodiazaoethane with 4-nitroisoxazoles



In a 10 mL of sealed tube, a mixture of 4-nitroisoxazoles **1** (0.2 mmol), **TFHZ-Tfs** (0.4 mmol, 128.0 mg), K_2CO_3 (0.7 mmol, 96.7 mg) and CH_3CN (2 mL) was stirred at $35\text{ }^\circ\text{C}$ for 6-12 h. After completion of the reaction (detected by TLC), the reaction mixture was concentrated under reduced pressure. The residue was separated by

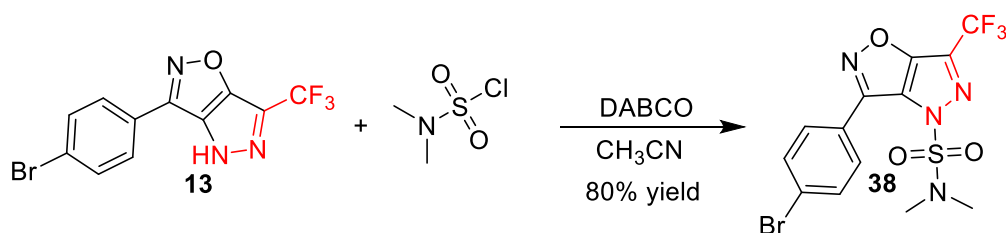
column chromatography on silica gel with ethyl acetate/petroleum ether as the eluent to afford **2-40**.

2.2 Scaled-Up version of **2**.

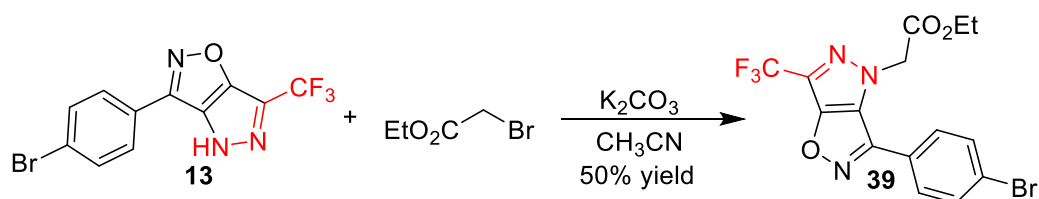


In a 100 mL of sealed tube, a mixture of 4-nitro-3-phenylisoxazole (5.0 mmol, 0.95 g), **TFHZ-Tfs** (10 mmol, 3.2 g), K_2CO_3 (17.5 mmol, 2.42 g) and CH_3CN (30 mL) was stirred at $35\text{ }^\circ\text{C}$ for 12 h. After completion of the reaction (detected by TLC), the reaction mixture was concentrated under reduced pressure. The residue was separated by column chromatography on silica gel with ethyl acetate/petroleum ether as the eluent to afford **2** in 1.08 g, 85% yield.

2.3 The transformation of the Product **38**.



To compound **13** (60.2 mg, 0.2 mmol) in 3 mL CH_3CN was added DABCO (26.9 mg, 0.24 mmol) at rt. Then the reaction was stirred for 13 h at rt. The aqueous solution was extracted with DCM three times. The combined organic layers were dried over Na_2SO_4 . After evaporation of the solvent, the resulting crude mixture was purified by flash chromatography on silica gel to afford compound **38** in 80% yield.



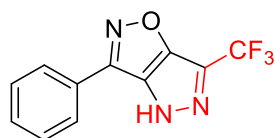
To compound **13** (60.2 mg, 0.2 mmol) in 3 mL CH_3CN was added K_2CO_3 (82.9 mg, 0.6 mmol) at rt, the reaction was stirred for 2 h at rt. The resulting mixture was

extracted with EA three times. The combined organic layers were dried over Na₂SO₄. After evaporation of solvent, the resulting crude mixture was purified by flash chromatography on silica gel to afford compound **39** in 50% yield.

3. Characterization data of the products

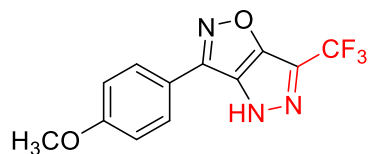
NOTE: When deuterated DMSO as a solvent, the ¹³C NMR signal of the C(sp²) bonded to the CF₃ are sometimes not visible in the ¹³C NMR spectra.

3-phenyl-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (**2**)



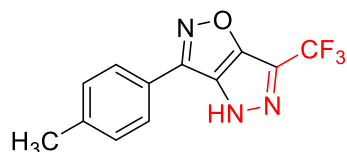
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **2** as a yellow solid (48.0 mg, 95% yield); ¹H NMR (500 MHz, DMSO) δ 14.81 (s, 1H), 8.04 – 8.02 (m, 2H), 7.65 – 7.64 (m, 3H); ¹⁹F NMR (471 MHz, DMSO) δ -59.11; ¹³C NMR (126 MHz, DMSO) δ 157.05, 148.36, 135.96, 132.00, 129.99, 127.89, 126.06, 120.87 (q, *J* = 266.8 Hz); HRMS (ESI) *m/z* calcd. for C₁₁H₇F₃N₃O⁺ [M+H]⁺ = 254.0536, found 254.0536.

3-(4-methoxyphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (**3**)



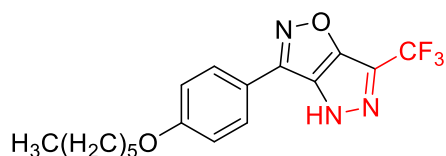
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **3** as a white solid (45.9 mg, 81% yield); ¹H NMR (500 MHz, DMSO) δ 14.72 (s, 1H), 7.95 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H); ¹⁹F NMR (471 MHz, DMSO) δ -59.20; ¹³C NMR (126 MHz, DMSO) δ 162.10, 156.83, 147.87, 135.87, 129.45, 120.91 (q, *J* = 267.2 Hz), 119.75 (q, *J* = 40.3 Hz), 118.24, 115.31, 55.91; HRMS (ESI) *m/z* calcd. for C₁₂H₉F₃N₃O₂⁺ [M+H]⁺ = 284.0641, found 284.0644.

3-(p-tolyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (4)



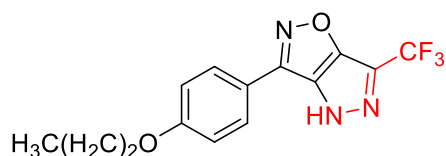
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **4** as a white solid (44.9 mg, 84% yield). ¹H NMR (500 MHz, DMSO) δ 14.74 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.9 Hz, 2H), 2.42 (s, 3H); ¹⁹F NMR (471 MHz, DMSO) δ -59.17; ¹³C NMR (126 MHz, DMSO) δ 156.89, 148.20, 141.98, 135.91, 130.42, 127.70, 123.19, 120.87 (q, *J* = 267.3 Hz), 21.48; HRMS (ESI) *m/z* calcd. for C₁₂H₉F₃N₃O⁺ [M+H]⁺ = 268.0692, found 268.0692.

3-(4-(hexyloxy)phenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (5)



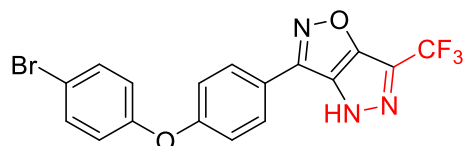
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **4** as a white solid (60.7 mg, 86% yield); ¹H NMR (500 MHz, DMSO) δ 7.64 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 3.75 (t, *J* = 6.5 Hz, 2H), 1.48 – 1.42 (m, 2H), 1.15 – 1.12 (m, 2H), 1.03 (d, *J* = 3.5 Hz, 4H), 0.60 (t, *J* = 6.7 Hz, 3H); ¹⁹F NMR (471 MHz, DMSO) δ -59.24; ¹³C NMR (126 MHz, DMSO) δ 161.51, 156.69, 147.92, 136.13, 129.35, 120.87 (q, *J* = 267.3 Hz), 118.06, 115.60, 68.22, 31.45, 28.98, 25.57, 22.48, 14.20; HRMS (ESI) *m/z* calcd. for C₁₇H₁₉F₃N₃O₂⁺ [M+H]⁺ = 354.1424, found 354.1420.

3-(4-propoxyphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (6)



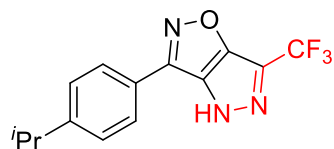
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **6** as a white solid (54.1 mg, 87% yield); ^1H NMR (500 MHz, DMSO) δ 14.74 (s, 1H), 7.95 (d, J = 8.6 Hz, 2H), 7.16 (d, J = 8.7 Hz, 2H), 4.05 (t, J = 6.5 Hz, 2H), 1.79 (dd, J = 14.0, 6.9 Hz, 2H), 1.03 (t, J = 7.4 Hz, 3H); ^{19}F NMR (471 MHz, DMSO) δ -59.16; ^{13}C NMR (126 MHz, DMSO) δ 161.61, 156.80, 148.01, 135.99, 129.50, 120.90 (q, J = 267.2 Hz), 118.10, 115.79, 69.77, 22.40, 10.75; HRMS (ESI) m/z calcd. for $\text{C}_{14}\text{H}_{13}\text{F}_3\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+ = 312.0954$, found 312.0953.

3-(4-(4-bromophenoxy)phenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (7)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **7** as a white solid (37.2 mg, 44% yield); ^1H NMR (500 MHz, DMSO) δ 8.04 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H), 7.11 (d, J = 8.8 Hz, 2H); ^{19}F NMR (471 MHz, CDCl_3) δ -54.33; ^{13}C NMR (126 MHz, DMSO) δ 159.48, 156.93, 155.46, 147.78, 136.05, 133.57, 130.05, 122.09, 121.24, 120.87 (q, J = 267.1 Hz), 119.55, 116.70; HRMS (ESI) m/z calcd. for $\text{C}_{17}\text{H}_{10}\text{BrF}_3\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+ = 423.9903$, found 423.9904.

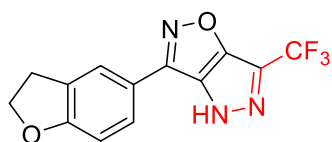
3-(4-isopropylphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (8)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **8** as a white solid (55.4 mg, 94% yield); ^1H NMR (500 MHz, DMSO) δ 7.95 (d, J = 8.3 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H), 3.03 – 2.97 (m, 1H), 1.27 (d, J = 6.9 Hz, 6H); ^{19}F NMR (471

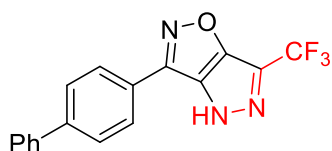
MHz, DMSO) δ -59.20; ^{13}C NMR (126 MHz, DMSO) δ 156.87, 152.63, 148.24, 136.08, 127.90, 127.82, 123.61, 120.87 (q, J = 267.3 Hz), 60.18, 33.92, 23.93; HRMS (ESI) m/z calcd. for $\text{C}_{14}\text{H}_{13}\text{F}_3\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 296.1005$, found 296.1003.

3-(2,3-dihydrobenzofuran-5-yl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (9)



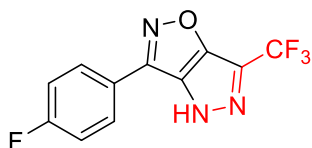
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **9** as a yellow solid (35.9 mg, 61% yield); ^1H NMR (500 MHz, DMSO) δ 7.85 (s, 1H), 7.75 (d, J = 8.3 Hz, 1H), 6.97 (d, J = 8.3 Hz, 1H), 4.66 (t, J = 8.8 Hz, 2H), 3.29 (t, J = 8.7 Hz, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.14; ^{13}C NMR (126 MHz, DMSO) δ 162.82, 156.59, 148.22, 136.11, 129.56, 128.57, 124.56, 120.90 (q, J = 267.1 Hz), 118.05, 110.13, 72.25, 29.06; HRMS (ESI) m/z calcd. for $\text{C}_{13}\text{H}_9\text{F}_3\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+ = 296.0641$, found 296.0640.

3-([1,1'-biphenyl]-4-yl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (10)



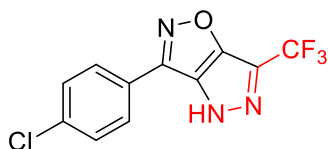
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **10** as a white solid (47.4 mg, 72% yield); ^1H NMR (500 MHz, DMSO) δ 14.83 (s, 1H), 8.10 (d, J = 8.2 Hz, 2H), 7.92 (d, J = 8.2 Hz, 2H), 7.78 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.6 Hz, 2H), 7.45 (t, J = 7.3 Hz, 1H); ^{19}F NMR (471 MHz, DMSO) δ -59.11; ^{13}C NMR (126 MHz, DMSO) δ 157.01, 148.07, 143.44, 139.32, 136.12, 129.52, 128.72, 128.43, 128.05, 127.33, 124.99, 120.87 (q, J = 267.4 Hz); HRMS (ESI) m/z calcd. for $\text{C}_{17}\text{H}_{11}\text{F}_3\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 330.0849$, found 330.0849.

3-(4-fluorophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (11)



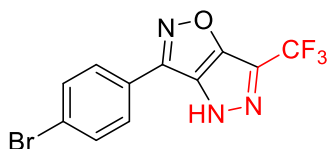
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **11** as a white solid (45.0 mg, 83% yield); ^1H NMR (500 MHz, DMSO) δ 7.97 (dd, $J = 7.9, 5.5$ Hz, 2H), 7.39 (t, $J = 8.5$ Hz, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.29, -108.48; ^{13}C NMR (126 MHz, DMSO) δ 164.20 (d, $J = 249.9$ Hz), 156.94, 147.28, 135.83, 130.15 (d, $J = 9.0$ Hz), 122.55 (d, $J = 3.5$ Hz), 120.78 (q, $J = 267.3$ Hz), 116.94 (d, $J = 22.2$ Hz); HRMS (ESI) m/z calcd. for $\text{C}_{11}\text{H}_6\text{F}_4\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 272.0442$, found 272.0440.

3-(4-chlorophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (**12**)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **12** as a white solid (39.6 mg, 69% yield); ^1H NMR (500 MHz, DMSO) δ 7.99 (d, $J = 8.5$ Hz, 2H), 7.68 (d, $J = 8.5$ Hz, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.23; ^{13}C NMR (126 MHz, DMSO) δ 157.10, 147.34, 136.67, 135.70, 129.95, 129.48, 124.90, 120.78 (q, $J = 267.4$ Hz); HRMS (ESI) m/z calcd. for $\text{C}_{11}\text{H}_6\text{ClF}_3\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 288.0146$, found 288.0147.

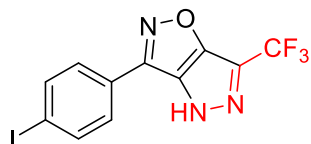
3-(4-bromophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (**13**)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **13** as a white solid (60.9 mg, 92% yield); ^1H NMR (500 MHz, DMSO) δ 7.94 (d, $J = 8.4$

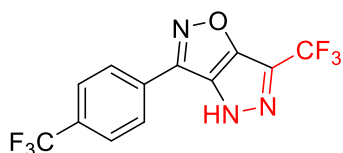
Hz, 2H), 7.84 (d, $J = 8.3$ Hz, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.13; ^{13}C NMR (126 MHz, DMSO) δ 157.13, 147.57, 135.80, 132.96, 129.72, 125.54, 125.28, 120.81 (q, $J = 267.1$ Hz); HRMS (ESI) m/z calcd. for $\text{C}_{11}\text{H}_6\text{BrF}_3\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 331.9641$, found 331.9641.

3-(4-iodophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (14)



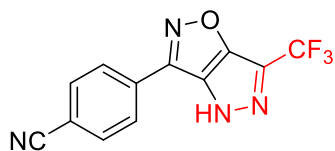
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **14** as a white solid (69.0 mg, 91% yield); ^1H NMR (500 MHz, DMSO) δ 7.99 – 7.94 (m, 2H), 7.76 – 7.71 (m, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.10; ^{13}C NMR (126 MHz, DMSO) δ 157.04, 147.75, 138.73, 135.86, 129.45, 125.47, 120.79 (q, $J = 267.2$ Hz), 99.30; HRMS (ESI) m/z calcd. for $\text{C}_{11}\text{H}_6\text{F}_3\text{IN}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 379.9502$, found 379.9505.

6-(trifluoromethyl)-3-(4-(trifluoromethyl)phenyl)-4H-pyrazolo[3,4-d]isoxazole (15)



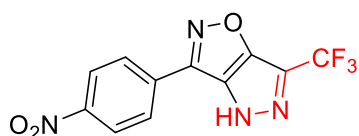
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **15** as a white solid (59.7 mg, 93% yield); ^1H NMR (500 MHz, DMSO) δ 14.85 (s, 1H), 8.17 (d, $J = 8.1$ Hz, 2H), 7.95 (d, $J = 8.2$ Hz, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.27, -61.63; ^{13}C NMR (126 MHz, DMSO) δ 157.35, 147.21, 135.67, 131.69 (q, $J = 32.3$ Hz), 131.00, 129.98, 128.61, 126.75 (q, $J = 3.7$ Hz), 124.21 (q, $J = 272.7$ Hz), 120.75 (q, $J = 267.0$ Hz); HRMS (ESI) m/z calcd. for $\text{C}_{12}\text{H}_6\text{F}_6\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 322.0410$, found 322.0412.

4-(6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazol-3-yl)benzotrile (16)



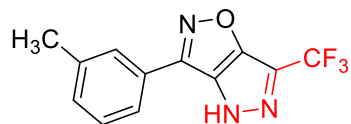
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **16** as a yellow solid (50.0 mg, 90% yield); ^1H NMR (500 MHz, DMSO) δ 8.15 (d, J = 8.1 Hz, 2H), 8.10 (d, J = 8.2 Hz, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.16; ^{13}C NMR (126 MHz, DMSO) δ 157.34, 147.21, 135.79, 133.79, 130.33, 128.56, 120.74 (q, J = 267.4 Hz), 118.58, 114.22; HRMS (ESI) m/z calcd. for $\text{C}_{12}\text{H}_6\text{F}_3\text{N}_4\text{O}^+$ $[\text{M}+\text{H}]^+ = 279.0488$, found 279.0486.

3-(4-nitrophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (**17**)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **17** as a yellow solid (38.1 mg, 64% yield); ^1H NMR (500 MHz, DMSO) δ 8.42 – 8.40 (m, 2H), 8.23 – 8.21 (m, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.12; ^{13}C NMR (126 MHz, DMSO) δ 157.39, 149.35, 146.93, 135.91, 132.04, 129.14, 124.95, 120.73 (q, J = 267.1 Hz); HRMS (ESI) m/z calcd. for $\text{C}_{11}\text{H}_6\text{F}_3\text{N}_4\text{O}_3^+$ $[\text{M}+\text{H}]^+ = 299.0387$, found 299.0389.

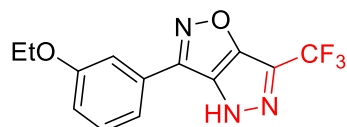
3-(*m*-tolyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (**18**)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **18** as a white solid (52.3 mg, 98% yield); ^1H NMR (500 MHz, MeOD) δ 7.73 (s, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 2.42 (s, 3H); ^{19}F NMR

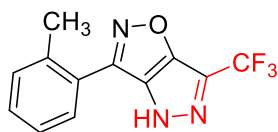
(471 MHz, MeOD) δ -61.98; ^{13}C NMR (126 MHz, MeOD) δ 156.96, 148.00, 139.18, 135.76, 131.56, 129.61, 128.88, 127.45, 126.00, 124.00, 120.44 (q, $J = 266.7$ Hz), 19.89; HRMS (ESI) m/z calcd. for $\text{C}_{12}\text{H}_9\text{F}_3\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 268.0692$, found 268.0692.

3-(3-ethoxyphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (19)



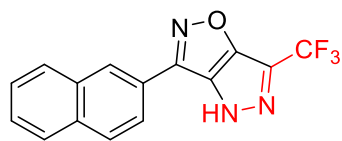
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **19** as a white solid (24.4 mg, 41% yield); ^1H NMR (500 MHz, DMSO) δ 14.55 (s, 1H), 7.69 (d, $J = 8.9$ Hz, 2H), 7.39 (d, $J = 2.9$ Hz, 1H), 7.28 (dd, $J = 8.9, 3.0$ Hz, 1H), 4.16 (q, $J = 6.9$ Hz, 1H), 1.40 (t, $J = 6.9$ Hz, 3H); ^{19}F NMR (471 MHz, DMSO) δ -59.21; ^{13}C NMR (126 MHz, DMSO) δ 158.05, 156.65, 156.49, 147.09, 136.55, 131.84, 125.94, 123.66, 120.82 (q, $J = 267.2$ Hz), 119.51, 117.54, 64.42, 14.91; HRMS (ESI) m/z calcd. for $\text{C}_{13}\text{H}_{11}\text{F}_3\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+ = 298.0798$, found 298.0796.

3-(o-tolyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (20)



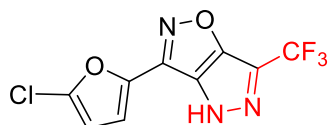
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **20** as a white solid (52.8 mg, 99% yield); ^1H NMR (500 MHz, CDCl_3) δ 11.33 (s, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.43-7.40 (m, 1H), 7.36 (d, $J = 7.5$ Hz, 1H), 7.31 (t, $J = 7.4$ Hz, 1H), 2.54 (s, 3H); ^{19}F NMR (471 MHz, CDCl_3) δ -60.67; ^{13}C NMR (126 MHz, CDCl_3) δ 156.62, 148.77, 137.58, 137.37, 131.73, 130.81, 129.76, 126.46, 125.17, 121.89 (q, $J = 41.4$ Hz), 119.89 (q, $J = 268.1$ Hz), 21.20; HRMS (ESI) m/z calcd. for $\text{C}_{12}\text{H}_9\text{F}_3\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 268.0692$, found 268.0692.

3-(naphthalen-2-yl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (21)



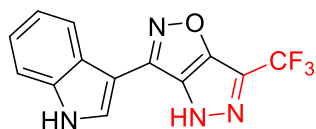
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **21** as a yellow solid (50.9 mg, 84% yield); ^1H NMR (500 MHz, DMSO) δ 14.66 (s, 1H), 8.58 (d, $J = 7.6$ Hz, 1H), 8.22 (d, $J = 8.2$ Hz, 1H), 8.11 (d, $J = 7.6$ Hz, 1H), 8.05 (d, $J = 6.0$ Hz, 1H), 7.75 – 7.66 (m, 3H); ^{19}F NMR (471 MHz, DMSO) δ -59.17; ^{13}C NMR (126 MHz, DMSO) δ 156.36, 148.84, 137.70, 134.02, 132.24, 130.21, 130.17, 129.33, 128.53, 127.31, 125.93, 125.78, 122.93, 120.95 (q, $J = 267.5$ Hz), 119.86 (q, $J = 41.2$ Hz); HRMS (ESI) m/z calcd. for $\text{C}_{15}\text{H}_8\text{F}_3\text{N}_3\text{NaO}^+$ $[\text{M}+\text{Na}]^+ = 326.0512$, found 326.0510.

3-(5-chlorofuran-2-yl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (22)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **22** as a yellow solid (42.7 mg, 77% yield); ^1H NMR (500 MHz, DMSO) δ 14.75 (s, 1H), 7.50 – 7.39 (m, 1H), 6.94 – 6.82 (m, 1H); ^{19}F NMR (471 MHz, DMSO) δ -59.33; ^{13}C NMR (126 MHz, CDCl_3) δ 157.15, 141.00, 140.02, 139.30, 134.46, 120.12 (q, $J = 267.7$ Hz), 115.48, 109.20, 39.81 (q, $J = 21.0$ Hz); HRMS (ESI) m/z calcd. for $\text{C}_9\text{H}_4\text{ClF}_3\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+ = 277.9939$, found 277.9938.

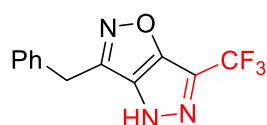
3-(1H-indol-3-yl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (23)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **23** as a yellow solid

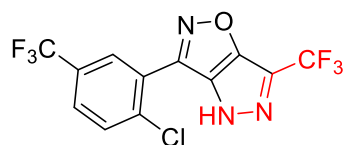
(35.6 mg, 61% yield); ^1H NMR (500 MHz, DMSO) δ 14.54 (s, 1H), 12.09 (s, 1H), 8.33 (s, 1H), 8.10 (d, $J = 7.7$ Hz, 1H), 7.56 (d, $J = 7.8$ Hz, 1H), 7.29-7.22 (m, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.07; ^{13}C NMR (126 MHz, DMSO) δ 155.47, 145.12, 137.30, 136.69, 130.03, 124.34, 123.52, 121.74, 121.61, 121.08 (q, $J = 267.0$ Hz), 119.73 (q, $J = 40.9$ Hz), 112.79, 101.94; HRMS (ESI) m/z calcd. for $\text{C}_{13}\text{H}_8\text{F}_3\text{N}_4\text{O}^+$ $[\text{M}+\text{H}]^+ = 293.0645$, found 293.0648.

3-benzyl-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (24)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **24** as a yellow solid (37.9 mg, 71% yield); ^1H NMR (500 MHz, CDCl_3) δ 10.29 (s, 1H), 7.28 – 7.18 (m, 5H), 4.13 (s, 2H); ^{19}F NMR (471 MHz, CDCl_3) δ -60.70; ^{13}C NMR (126 MHz, CDCl_3) δ 156.91, 148.79, 136.70, 135.07, 129.37, 128.76, 127.94, 121.93 (q, $J = 41.6$ Hz), 119.88 (q, $J = 266.3$ Hz), 31.15; HRMS calcd. for: $\text{C}_{12}\text{H}_9\text{F}_3\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 268.0692$, found 268.0692.

3-(2-chloro-5-(trifluoromethyl)phenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (25)

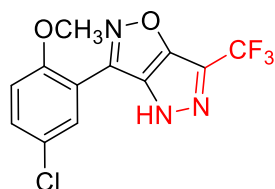


The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **25** as a white solid (52.5 mg, 74% yield); ^1H NMR (500 MHz, DMSO) δ 14.48 (s, 1H), 8.17 (s, 1H), 8.06 – 8.03 (m, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.32, -61.42; ^{13}C NMR (126 MHz, CDCl_3) δ 161.66, 150.90, 149.40, 142.00, 141.07, 136.87, 134.59, 133.83 (q, $J = 33.1$

Hz), 133.65, 131.32, 128.53 (q, $J = 272.3$ Hz), 125.51 (q, $J = 267.0$ Hz); HRMS calcd. for: $C_{12}H_5ClF_6N_3O^+$ $[M+H]^+ = 356.0020$, found 356.0020.

3-(5-chloro-2-methoxyphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole

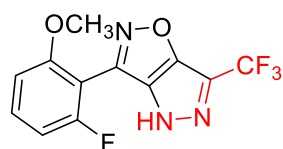
(26)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **26** as a yellow solid (42.9 mg, 65% yield); 1H NMR (500 MHz, DMSO) δ 14.00 (s, 1H), 7.82 (d, $J = 2.7$ Hz, 1H), 7.66 (dd, $J = 9.0, 2.7$ Hz, 1H), 7.34 (d, $J = 9.0$ Hz, 1H), 3.97 (s, 3H); ^{19}F NMR (471 MHz, DMSO) δ -59.21; ^{13}C NMR (126 MHz, DMSO) δ 156.62, 156.35, 144.62, 136.54, 133.04, 128.36, 125.27, 120.89 (q, $J = 266.8$ Hz), 116.12, 114.65, 57.44; HRMS calcd. for: $C_{12}H_8ClF_3N_3O_2^+$ $[M+H]^+ = 318.0252$, found 318.0253.

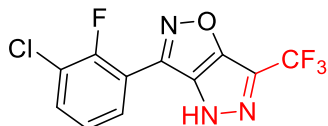
3-(2-fluoro-6-methoxyphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole

(27)



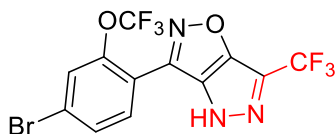
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **27** as a yellow solid (49.4 mg, 82% yield); 1H NMR (500 MHz, MeOD) δ 7.59-7.54 (m, 1H), 7.07 (d, $J = 8.5$ Hz, 1H), 6.95 (t, $J = 9.2$ Hz, 1H), 3.97 (s, 3H); ^{19}F NMR (471 MHz, MeOD) δ -62.11, -112.27; ^{13}C NMR (126 MHz, MeOD) δ 160.79 (d, $J = 253.0$ Hz), 158.88 (d, $J = 5.6$ Hz), 156.00, 140.94, 137.18, 133.01 (d, $J = 11.0$ Hz), 120.55 (q, $J = 268.1$ Hz), 108.27 (d, $J = 22.2$ Hz), 107.14 (d, $J = 3.1$ Hz), 103.31 (d, $J = 15.7$ Hz), 55.89; HRMS calcd. for: $C_{12}H_8F_4N_3O_2^+$ $[M+H]^+ = 302.0547$, found 302.0549.

3-(3-chloro-2-fluorophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (28)



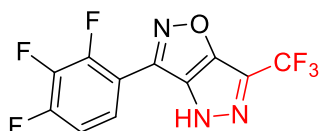
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **28** as a white solid (40.3 mg, 66% yield); ^1H NMR (500 MHz, DMSO) δ 8.00 (t, J = 7.0 Hz, 1H), 7.89 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 8.0 Hz, 1H); ^{19}F NMR (471 MHz, DMSO) δ -59.21, -115.46; ^{13}C NMR (126 MHz, DMSO) δ 157.09, 155.27 (d, J = 253.9 Hz), 143.09, 136.20, 134.03, 128.36, 126.85 (d, J = 4.2 Hz), 121.40 (d, J = 17.3 Hz), 120.82 (q, J = 267.3 Hz), 119.45 (q, J = 39.5 Hz), 116.06 (d, J = 12.2 Hz); HRMS calcd. for: $\text{C}_{11}\text{H}_5\text{ClF}_4\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 306.0052$, found 306.0054.

3-(4-bromo-2-(trifluoromethoxy)phenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (**29**)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **29** as a yellow solid (62.2 mg, 75% yield); ^1H NMR (500 MHz, DMSO) δ 14.53 (s, 1H), 7.99 – 7.94 (m, 2H), 7.91 – 7.86 (m, 1H); ^{19}F NMR (471 MHz, DMSO) δ -57.16, -59.59; ^{13}C NMR (126 MHz, DMSO) δ 156.90, 146.45, 144.31, 136.10, 132.69, 132.25, 125.76 (d, J = 24.2 Hz), 123.89, 121.77, 120.26 (q, J = 259.7 Hz), 119.63, 117.52; HRMS calcd. for: $\text{C}_{12}\text{H}_5\text{BrF}_6\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+ = 415.9464$, found 415.9467.

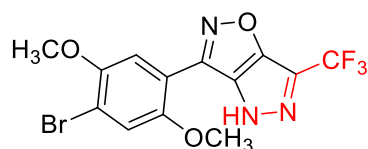
6-(trifluoromethyl)-3-(2,3,4-trifluorophenyl)-4H-pyrazolo[3,4-d]isoxazole (**30**)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **30** as a white solid

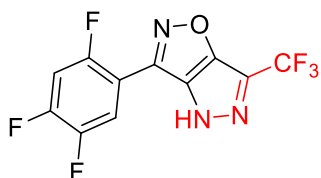
(56.5 mg, 92% yield); ^1H NMR (500 MHz, MeOD) δ 7.95 – 7.90 (m, 1H), 7.48-7.43 (m, 1H); ^{19}F NMR (471 MHz, MeOD) δ -62.22 (s), -117.49 (s), -130.05 (dd, J = 21.0, 6.1 Hz), -142.62 (dd, J = 20.9, 15.0 Hz); ^{13}C NMR (126 MHz, DMSO) δ 157.12, 155.77 (dd, J = 252.2, 9.7 Hz), 151.81 (dt, J = 254.7, 13.8 Hz), 147.08 (dd, J = 244.7, 12.9 Hz), 142.14, 135.62, 120.69 (q, J = 267.3 Hz), 119.52 (q, J = 40.7 Hz), 116.99 (dd, J = 21.3, 3.3 Hz), 111.08 (ddd, J = 15.1, 6.7, 4.2 Hz), 107.91 (dd, J = 28.1, 22.0 Hz); HRMS calcd. for: $\text{C}_{11}\text{H}_4\text{F}_6\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 308.0253$, found 308.0254.

3-(4-bromo-2,5-dimethoxyphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (31)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **31** as a white solid (49.3 mg, 63% yield); ^1H NMR (500 MHz, MeOD) δ 7.52 (s, 1H), 7.43 (s, 1H), 3.97 (s, 3H), 3.89 (s, 3H); ^{19}F NMR (471 MHz, MeOD) δ -62.10; ^{13}C NMR (126 MHz, MeOD) δ 156.86, 151.55, 150.66, 144.38, 136.05, 123.73, 120.56 (q, J = 266.6 Hz), 117.32, 115.55, 114.41, 111.01, 56.33, 55.88; HRMS calcd. for: $\text{C}_{13}\text{H}_{10}\text{BrF}_3\text{N}_3\text{O}_3^+$ $[\text{M}+\text{H}]^+ = 391.9852$, found 391.9853.

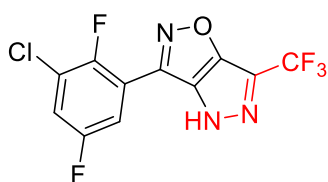
6-(trifluoromethyl)-3-(2,4,5-trifluorophenyl)-4H-pyrazolo[3,4-d]isoxazole (32)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **32** as a white solid (49.7 mg, 81% yield); ^1H NMR (500 MHz, DMSO) δ 14.50 (s, 1H), 8.09 – 8.04 (m, 1H), 8.01-7.96 (m, 1H); ^{19}F NMR (471 MHz, DMSO) δ -59.39, -113.27, -128.45 (dd,

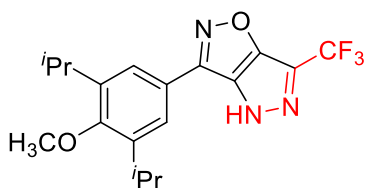
$J = 22.6, 6.6$ Hz), -141.04 ; ^{13}C NMR (126 MHz, DMSO) δ 157.18, 155.82 (dd, $J = 250.6, 9.8$ Hz), 151.85 (dt, $J = 254.7, 13.7$ Hz) 147.13 (ddd, $J = 244.5, 12.9, 3.1$ Hz), 142.25, 135.66, 120.74 (q, $J = 268.9$ Hz), 119.65 (q, $J = 40.6$ Hz), 117.17 (dd, $J = 21.3, 2.8$ Hz), 111.14 (ddd, $J = 14.7, 6.8, 3.8$ Hz), 108.00 (dd, $J = 28.2, 22.0$ Hz); HRMS calcd. for: $\text{C}_{11}\text{H}_4\text{F}_6\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 308.0253$, found 308.0254.

3-(3-chloro-2,5-difluorophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (33)



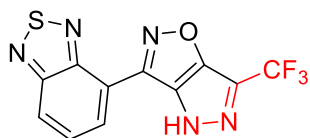
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **33** as a yellow solid (37.5 mg, 58% yield); ^1H NMR (500 MHz, DMSO) δ 8.07 (dd, $J = 9.9, 6.1$ Hz, 1H), 8.01 (dd, $J = 9.2, 6.1$ Hz, 1H); ^{19}F NMR (471 MHz, DMSO) δ -59.31 (s), -115.42 (d, $J = 12.7$ Hz), -119.63 (d, $J = 15.4$ Hz); ^{13}C NMR (126 MHz, DMSO) δ 157.19, 156.66 (d, $J = 2.1$ Hz), 155.54 (d, $J = 2.5$ Hz), 154.66 (d, $J = 2.3$ Hz), 153.59 (d, $J = 2.7$ Hz), 142.32, 135.74, 124.41 (dd, $J = 20.0, 11.6$ Hz), 120.72 (q, $J = 267.4$ Hz), 119.73 (d, $J = 27.3$ Hz), 119.36, 118.45 (d, $J = 230.3$ Hz), 116.32 (dd, $J = 25.7, 3.4$ Hz), 114.52 (dd, $J = 15.0, 8.0$ Hz); HRMS calcd. for: $\text{C}_{11}\text{H}_4\text{ClF}_5\text{N}_3\text{O}^+$ $[\text{M}+\text{H}]^+ = 323.9958$, found 323.9954.

3-(3,5-diisopropyl-4-methoxyphenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (34)



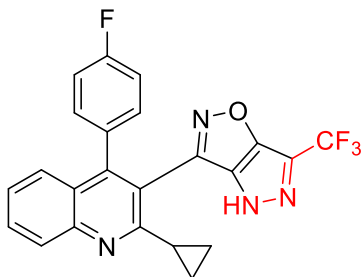
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **34** as a yellow solid (54.3 mg, 74% yield); ^1H NMR (500 MHz, DMSO) δ 14.86 (s, 1H), 7.69 (s, 2H), 3.71 (s, 3H), 3.34 – 3.28 (m, 2H), 1.25 (d, J = 7.0 Hz, 12H); ^{19}F NMR (471 MHz, DMSO) δ -59.08; ^{13}C NMR (126 MHz, DMSO) δ 157.33, 157.06, 148.22, 143.45, 135.72, 123.94, 122.40, 120.91 (q, J = 267.1 Hz), 62.61, 26.69, 24.04; HRMS calcd. for: $\text{C}_{18}\text{H}_{21}\text{F}_3\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+ = 368.1580$, found 368.1581.

3-(benzo[c][1,2,5]thiadiazol-4-yl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (35)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **35** as a white solid (24.9 mg, 40% yield); ^1H NMR (500 MHz, DMSO) δ 14.38 (s, 1H), 8.55 – 8.48 (m, 1H), 8.40 (d, J = 8.1 Hz, 1H), 7.99 – 7.92 (m, 1H); ^{19}F NMR (471 MHz, DMSO) δ -59.13; ^{13}C NMR (126 MHz, DMSO) δ 157.32, 154.93, 151.98, 144.98, 136.78, 130.52, 128.61, 124.67, 123.23 (q, J = 266.8 Hz), 119.04; HRMS calcd. for: $\text{C}_{11}\text{H}_5\text{F}_3\text{N}_5\text{O}^+$ $[\text{M}+\text{H}]^+ = 312.0161$, found 312.0161.

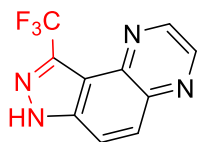
3-(2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole (36)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **36** as a yellow oil

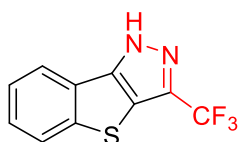
(49.9 mg, 57% yield); ^1H NMR (500 MHz, DMSO) δ 14.16 (s, 1H), 8.07 (d, $J = 8.4$ Hz, 1H), 7.90 – 7.86 (m, 1H), 7.60 – 7.56 (m, 1H), 7.49 (d, $J = 8.4$ Hz, 1H), 7.40 – 7.36 (m, 2H), 7.29 – 7.25 (m, 2H), 2.08 – 2.04 (m, 1H), 1.33 – 1.25 (m, 2H), 1.01 (d, $J = 4.4$ Hz, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.20, -112.82; ^{13}C NMR (126 MHz, DMSO) δ 162.43 (d, $J = 245.9$ Hz), 160.63, 156.17, 148.61, 148.34, 146.78, 138.29, 132.03, 131.65, 131.39, 131.36, 129.17, 127.24, 126.55, 125.18, 120.68 (q, $J = 267.3$ Hz), 118.63, 115.82 (d, $J = 21.7$ Hz), 15.84, 11.69; HRMS calcd. for: $\text{C}_{23}\text{H}_{15}\text{F}_4\text{N}_4\text{O}^+$ $[\text{M}+\text{H}]^+ = 439.1177$, found 439.1176.

3-(trifluoromethyl)-1H-pyrazolo[3,4-f]quinoxaline (37)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:5) to afford **37** as a yellow solid (18.0 mg, 38% yield); ^1H NMR (500 MHz, DMSO) δ 14.60 (s, 1H), 9.08 (d, $J = 2.1$ Hz, 1H), 9.01 (d, $J = 2.0$ Hz, 1H), 8.14 (d, $J = 9.2$ Hz, 1H), 8.07 (d, $J = 9.3$ Hz, 1H); ^{19}F NMR (471 MHz, DMSO) δ -60.44; ^{13}C NMR (126 MHz, DMSO) δ 145.48, 144.39, 142.14, 141.06, 137.66, 135.83 (q, $J = 38.6$ Hz), 130.10, 122.32 (q, $J = 268.2$ Hz), 116.83, 114.90; HRMS calcd. for: $\text{C}_{10}\text{H}_6\text{F}_3\text{N}_4^+$ $[\text{M}+\text{H}]^+ = 239.0539$, found 239.0541.

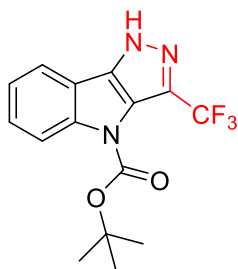
3-(trifluoromethyl)-1H-benzo[4,5]thieno[3,2-c]pyrazole (38)



The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **38** as a yellow solid (26.3 mg, 54% yield); ^1H NMR (500 MHz, DMSO) δ 14.68 (s, 1H), 8.04 (dd, $J = 17.8, 7.8$ Hz, 2H), 7.56 – 7.50 (m, 2H); ^{19}F NMR (471 MHz, DMSO) δ -59.93; ^{13}C

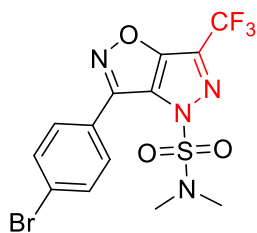
NMR (126 MHz, DMSO) δ 145.44, 144.85, 132.90 (q, $J = 38.9$ Hz), 127.42, 125.97, 125.43, 123.49, 122.01 (q, $J = 267.8$ Hz), 121.75, 117.13; HRMS calcd. for: $C_{10}H_6F_3N_2S^+$ $[M+H]^+ = 243.0198$, found 243.0199.

tert-butyl 3-(trifluoromethyl)pyrazolo[4,3-b]indole-4(1H)-carboxylate (39)³



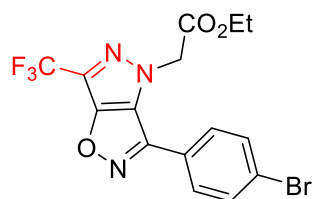
The general procedure was followed and then purified by silica column chromatography (ethyl acetate/petroleum ether = 1:30) to afford **39** as a yellow solid (39.0 mg, 30% yield); 1H NMR (500 MHz, DMSO) δ 14.20 (s, 1H), 8.17 (d, $J = 8.5$ Hz, 1H), 7.84 (d, $J = 7.7$ Hz, 1H), 7.54 (t, $J = 8.2$ Hz, 1H), 7.43 (t, $J = 7.5$ Hz, 1H), 1.65 (s, 9H); ^{19}F NMR (471 MHz, DMSO) δ -56.32; ^{13}C NMR (126 MHz, DMSO) δ 149.61, 141.95, 136.80, 127.64, 124.98 (q, $J = 37.5$ Hz), 124.05, 123.84, 121.82 (q, $J = 267.3$ Hz), 119.79, 117.40, 115.60, 85.36, 28.19.

3-(4-bromophenyl)-N,N-dimethyl-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazole-4-sulfonamide (40)



40, a yellow solid (69.3 mg, 80% yield); 1H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, $J = 19.3, 8.5$ Hz, 4H), 3.03 (s, 6H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -61.47; ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.12, 149.33, 135.02, 131.92, 131.08, 125.81, 124.17, 124.00 (q, $J = 43.4$ Hz), 119.13 (q, $J = 269.9$ Hz), 39.31; HRMS calcd. for: $C_{13}H_{11}BrF_3N_4O_3S^+$ $[M+H]^+ = 438.9682$, found 438.9680.

Ethyl-2-(3-(4-bromophenyl)-6-(trifluoromethyl)-4H-pyrazolo[3,4-d]isoxazol-4-yl) acetate (41)

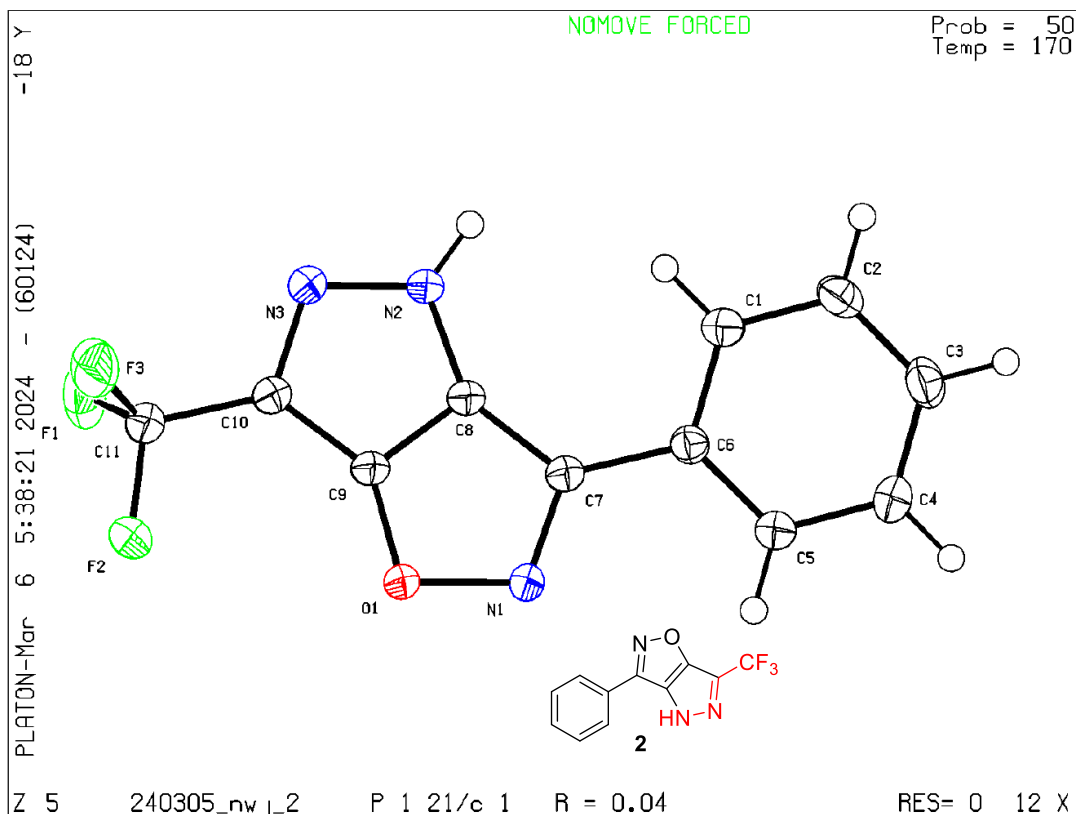


41, a yellow solid (40.1 mg, 48% yield); ^1H NMR (500 MHz, CDCl_3) δ 7.68 (d, $J = 8.5$ Hz, 2H), 7.55 (d, $J = 8.5$ Hz, 2H), 5.05 (s, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 1.21 (t, $J = 7.1$ Hz, 3H); ^{19}F NMR (471 MHz, CDCl_3) δ -60.75; ^{13}C NMR (126 MHz, CDCl_3) δ 166.31, 158.31, 147.93, 135.79, 132.78, 129.50, 125.65, 125.16, 121.68 (q, $J = 43.8$ Hz), 119.65 (q, $J = 268.4$ Hz), 62.73, 53.59, 13.98; HRMS calcd. for: $\text{C}_{15}\text{H}_{12}\text{BrF}_3\text{N}_3\text{O}_3^+$ $[\text{M}+\text{H}]^+ = 418.0009$, found 418.0009.

4. X-ray Crystal Structure for **2**, **26**, and **37**

Suitable crystals of compound **2**, **26**, and **37** were obtained by slowly evaporating a mixture of dichloromethane and hexane solution at ambient temperature. A colorless crystal of **2**, **26** and **37** was mounted on a glass fiber at a random orientation.

A Single colourless needle-shaped crystals of **2**, **26** and **37** were used as supplied. A suitable crystal with dimensions $0.40 \times 0.15 \times 0.05$ mm³ was selected and mounted on a Bruker D8 Venture diffractometer. The crystal was kept at a steady $T = 170.00$ K during data collection. The structure was solved with the ShelXT 2018/2 (Sheldrick, 2018) solution program using dual methods and by using Olex2 1.5 (Dolomanov et al., 2009) as the graphical interface. The model was refined with ShelXL 2019/2 (Sheldrick, 2015) using full matrix least squares minimisation on F². The ellipsoids are shown at 30% probability levels. Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Center and allocated with the deposition numbers: CCDC 2373144 for compound **2**, CCDC 2373145 for compound **26**, CCDC 2373147 for compound **37**.



Bond precision: C-C = 0.0018 Å

Wavelength=1.34139

Cell: a=12.0758 (5)
alpha=90

b=12.1758 (6)
beta=97.473 (2)

c=6.8549 (3)
gamma=90

Temperature: 170 K

	Calculated	Reported
Volume	999.33 (8)	999.33 (8)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C11 H6 F3 N3 O	C11 H6 F3 N3 O
Sum formula	C11 H6 F3 N3 O	C11 H6 F3 N3 O
Mr	253.19	253.19
Dx, g cm ⁻³	1.683	1.683
Z	4	4
Mu (mm ⁻¹)	0.844	0.844
F000	512.0	512.0
F000'	513.64	
h, k, lmax	15, 15, 8	15, 15, 8
Nref	2295	2284
Tmin, Tmax	0.960, 0.975	0.664, 0.752
Tmin'	0.943	

Correction method= # Reported T Limits: Tmin=0.664 Tmax=0.752
AbsCorr = MULTI-SCAN

Data completeness= 0.995

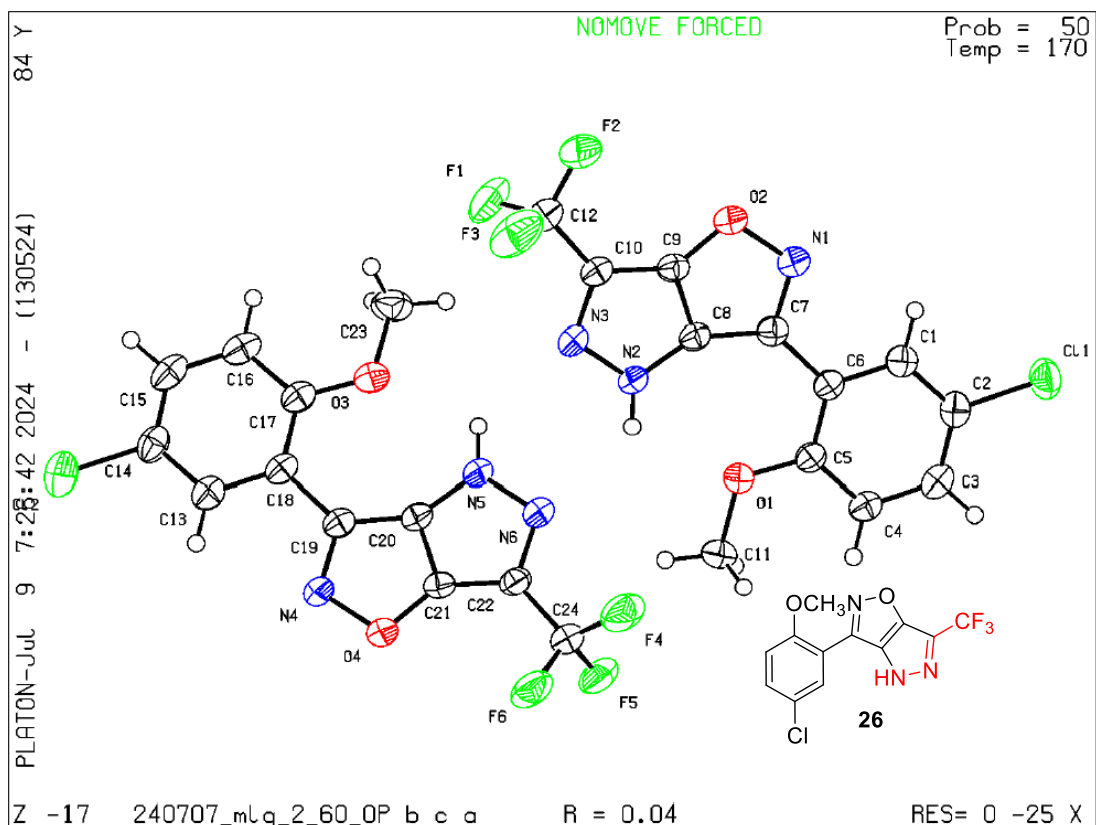
Theta(max)= 60.702

R(reflections)= 0.0371 (2031)

wR2(reflections)=
0.1040 (2284)

S = 1.102

Npar= 163



Bond precision: C-C = 0.0027 Å

Wavelength=1.34139

Cell: a=7.0457 (6)

b=23.6493 (19)

c=30.637 (3)

alpha=90

beta=90

gamma=90

Temperature: 170 K

	Calculated	Reported
Volume	5104.9 (8)	5104.9 (7)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C12 H7 Cl F3 N3 O2	C12 H7 Cl F3 N3 O2
Sum formula	C12 H7 Cl F3 N3 O2	C12 H7 Cl F3 N3 O2
Mr	317.66	317.66
Dx, g cm ⁻³	1.653	1.653
Z	16	16
Mu (mm ⁻¹)	2.044	2.044
F000	2560.0	2560.0
F000'	2572.65	
h, k, lmax	9, 30, 39	9, 30, 39
Nref	5867	5844
Tmin, Tmax	0.885, 0.941	0.599, 0.752
Tmin'	0.767	

Correction method= # Reported T Limits: Tmin=0.599 Tmax=0.752

AbsCorr = MULTI-SCAN

Data completeness= 0.996

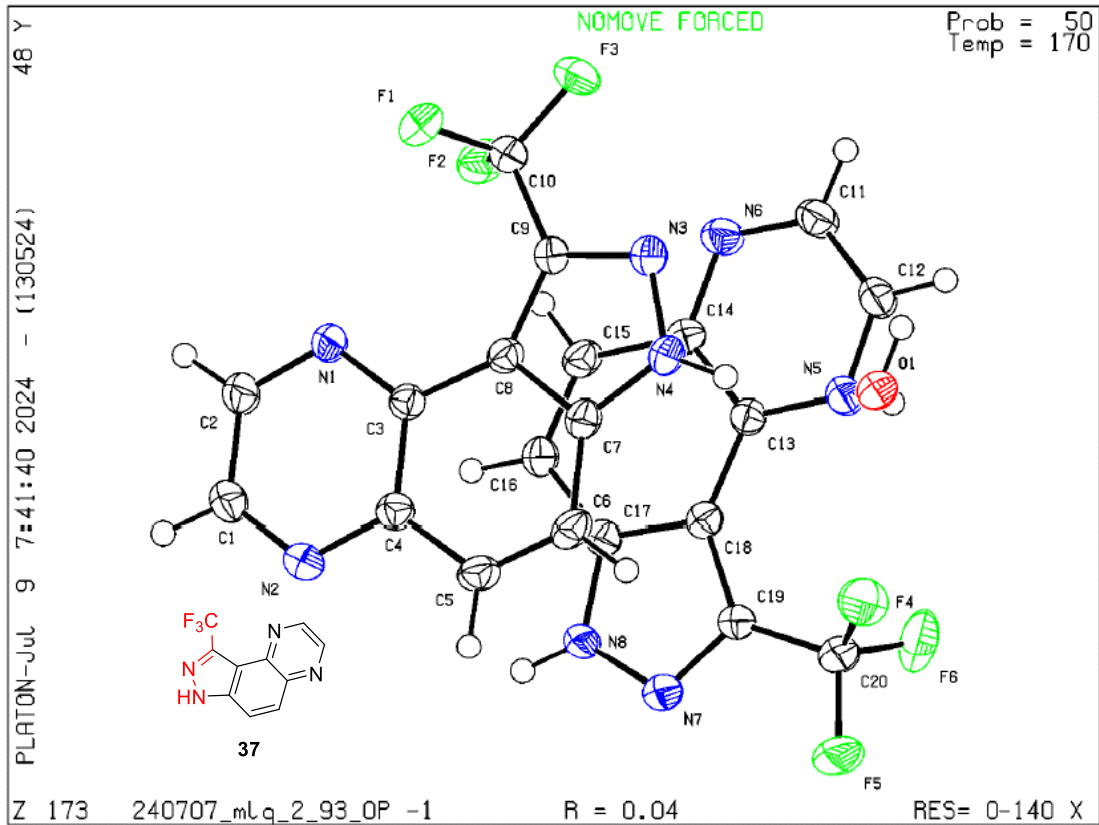
Theta(max)= 60.679

R(reflections)= 0.0417 (4496)

wR2(reflections)
0.1156 (5844)

S = 1.026

Npar= 381



Bond precision: C-C = 0.0019 Å

Wavelength=1.34139

Cell: a=7.5837(6) b=8.1452(7) c=16.1468(13)
 alpha=95.204(3) beta=93.854(3) gamma=90.608(4)
 Temperature: 170 K

	Calculated	Reported
Volume	990.90(14)	990.90(14)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	2(C10 H5 F3 N4), H2 O	H2 O, 2(C10 H5 F3 N4)
Sum formula	C20 H12 F6 N8 O	C20 H12 F6 N8 O
Mr	494.38	494.38
Dx, g cm ⁻³	1.657	1.657
Z	2	2
Mu (mm ⁻¹)	0.833	0.833
F000	500.0	500.0
F000'	501.58	
h, k, lmax	9, 10, 20	9, 10, 20
Nref	4051	3971
Tmin, Tmax	0.951, 0.975	0.641, 0.752
Tmin'	0.890	

Correction method= # Reported T Limits: Tmin=0.641 Tmax=0.752
 AbsCorr = MULTI-SCAN

Data completeness= 0.980 Theta(max)= 56.962

R(reflections)= 0.0400(3267)

wR2(reflections)=
0.1049(3971)

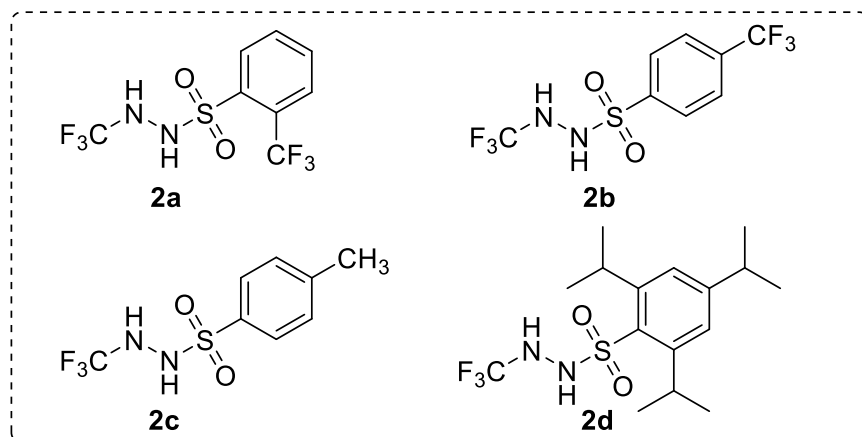
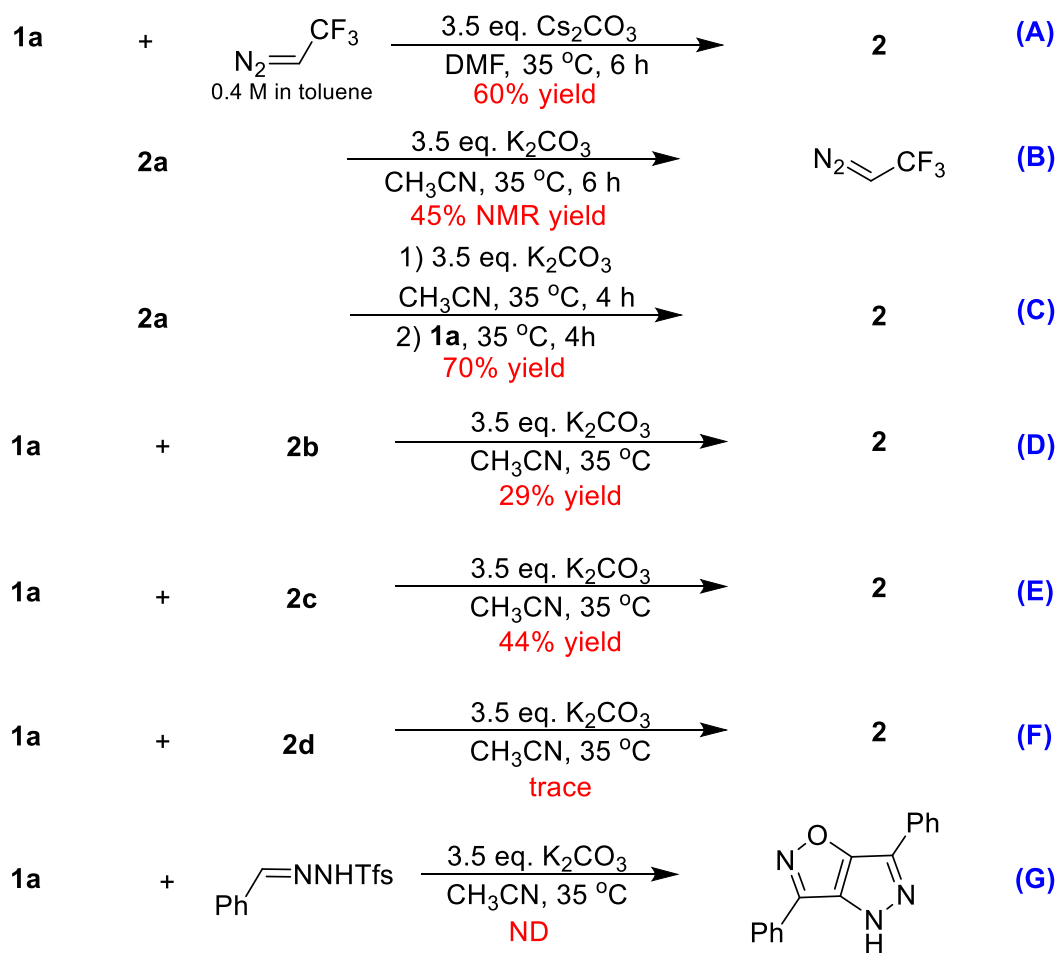
S = 1.073

Npar= 319

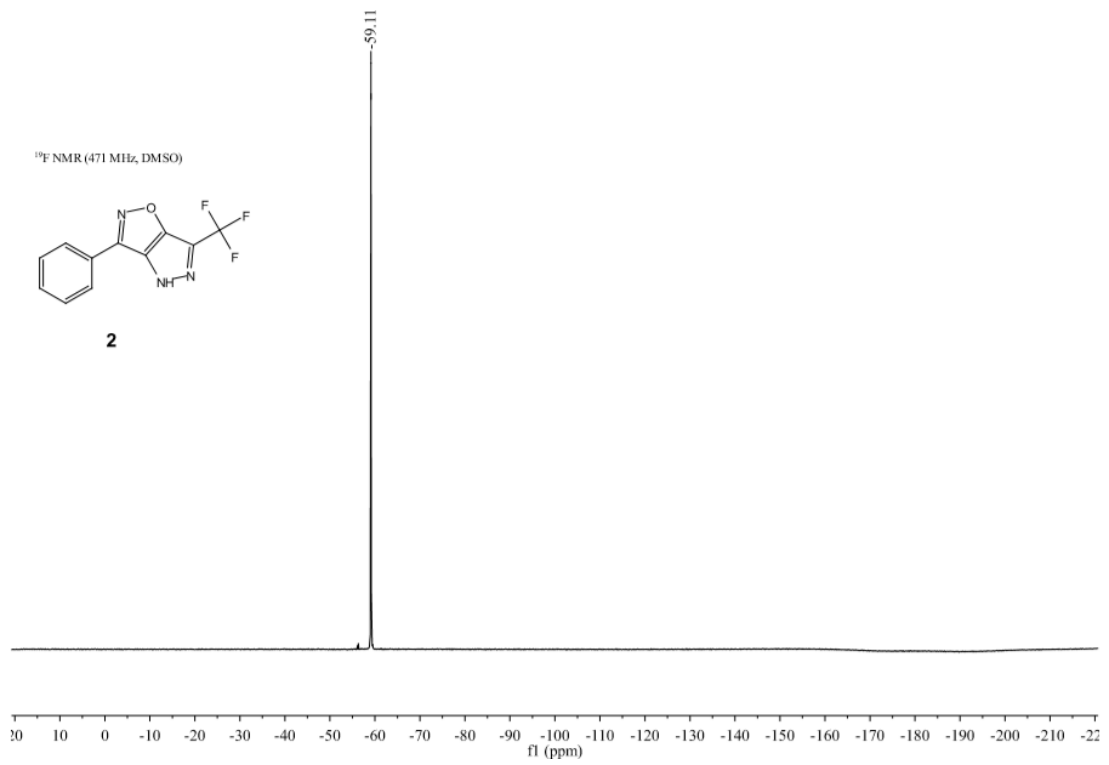
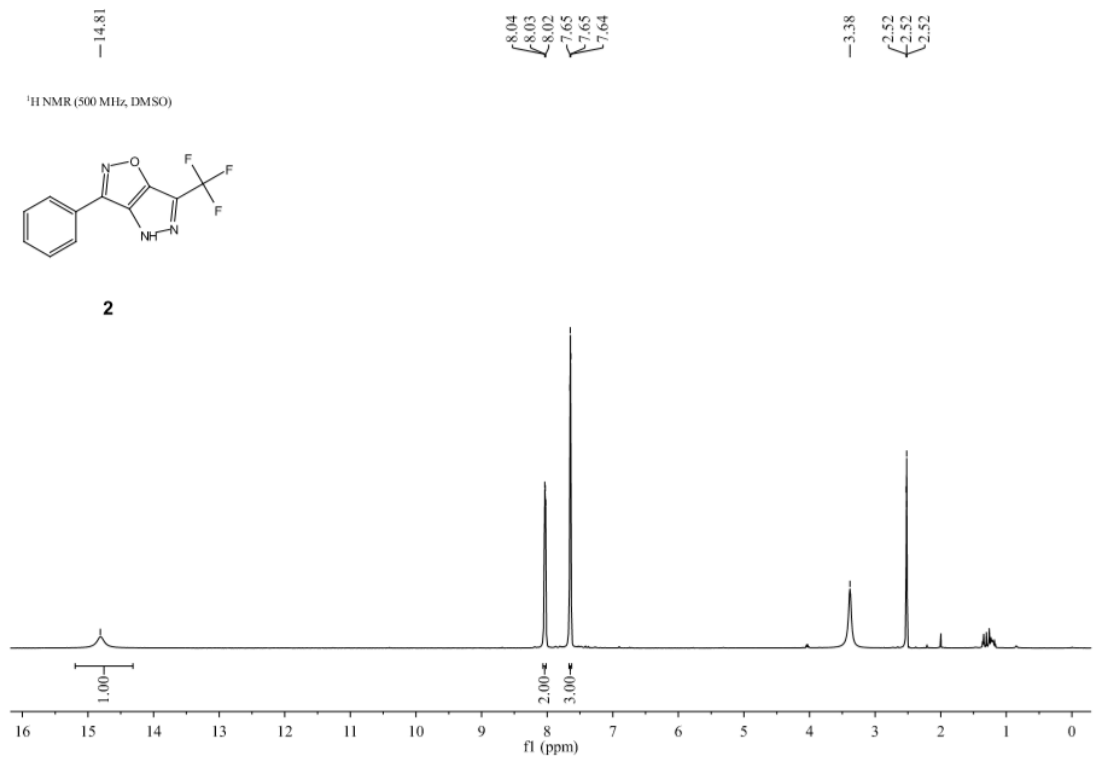
5. Reference

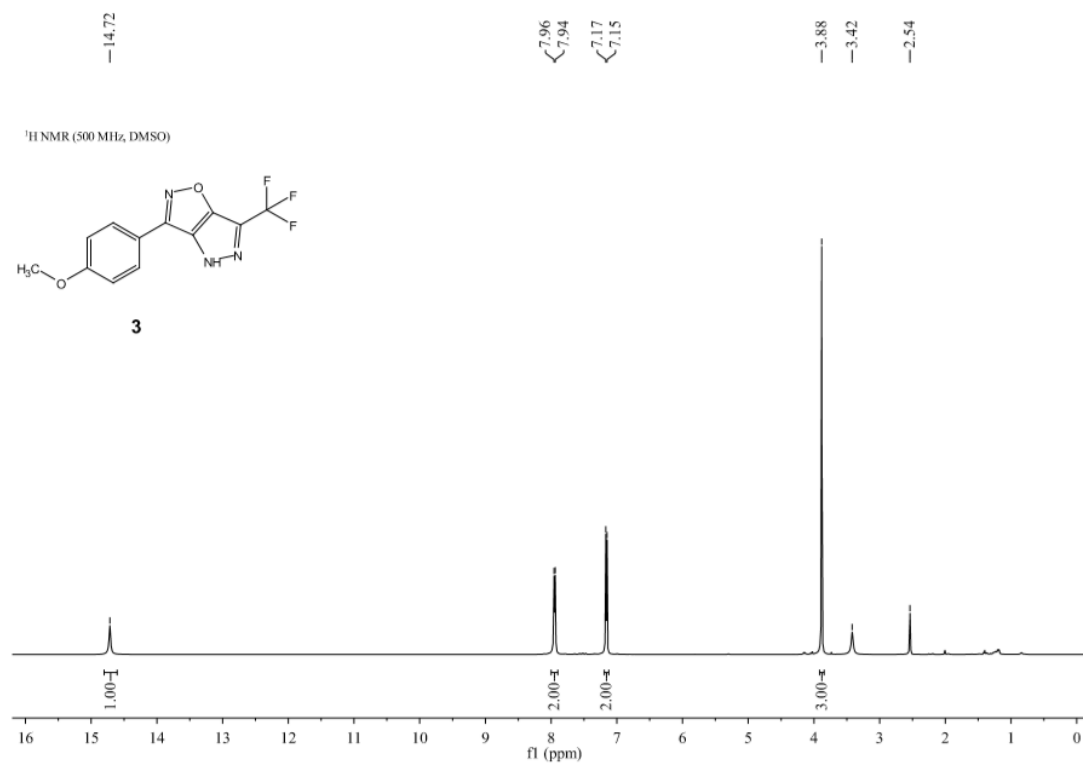
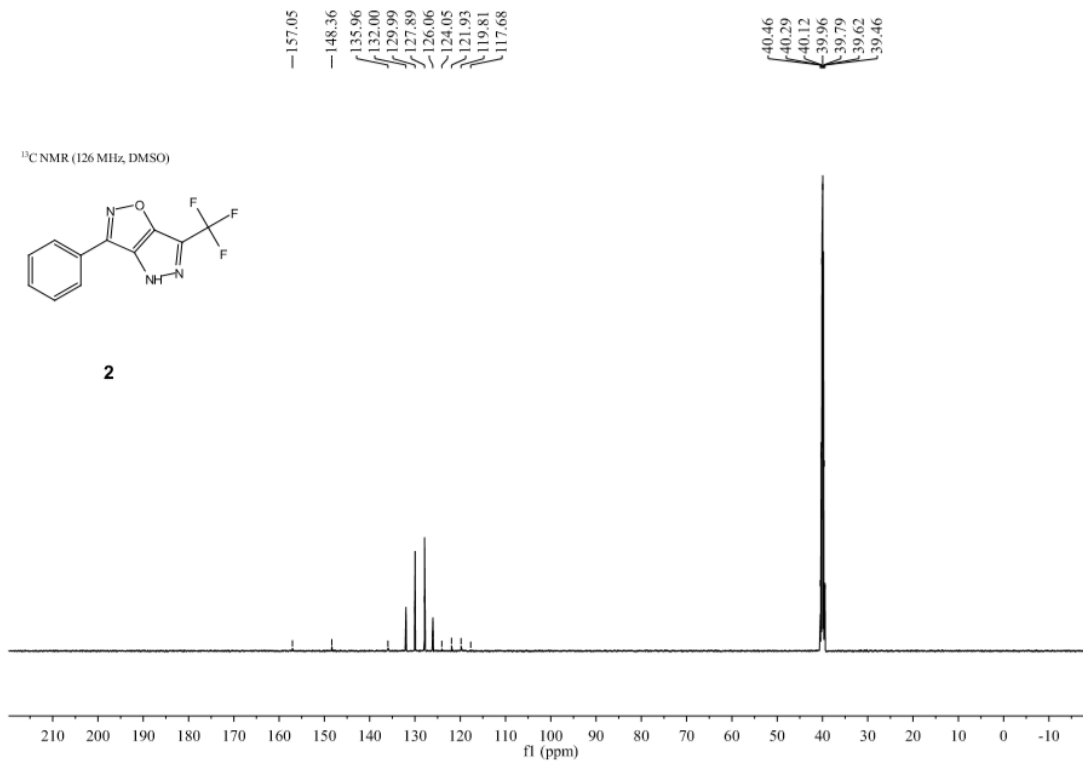
1. T. Morita, N. Ito and H. Nakamura, Asymmetric Synthesis of Bicyclic Isoxazolines via Dearomative Cycloaddition of 4-Nitroisoxazoles with Zwitterionic π -Allyl Palladium Species. *Org. Lett.*, 2023, **25**, 26, 4787–4791.
2. H. Wang, Y. Ning, Y. Sun, P. Sivaguru and X. Bi, Cycloaddition of Trifluoroacetaldehyde N-Triflylhydrazones (TFHZ-Tfs) with Alkynes for Synthesizing -Trifluoromethylpyrazoles. *Org. Lett.*, 2020, **22**, 2012–2016.
3. S. Kumar, L. Fatma, N. Vaishanv, K. Mohanan, CsF-Mediated Reaction of Trifluorodiazethane with 3-Nitroindoles Enables Access to Trifluoromethylpyrazolo[4,3-b]indoles. *J. Org. Chem.*, 2024, **89**, 761–769.

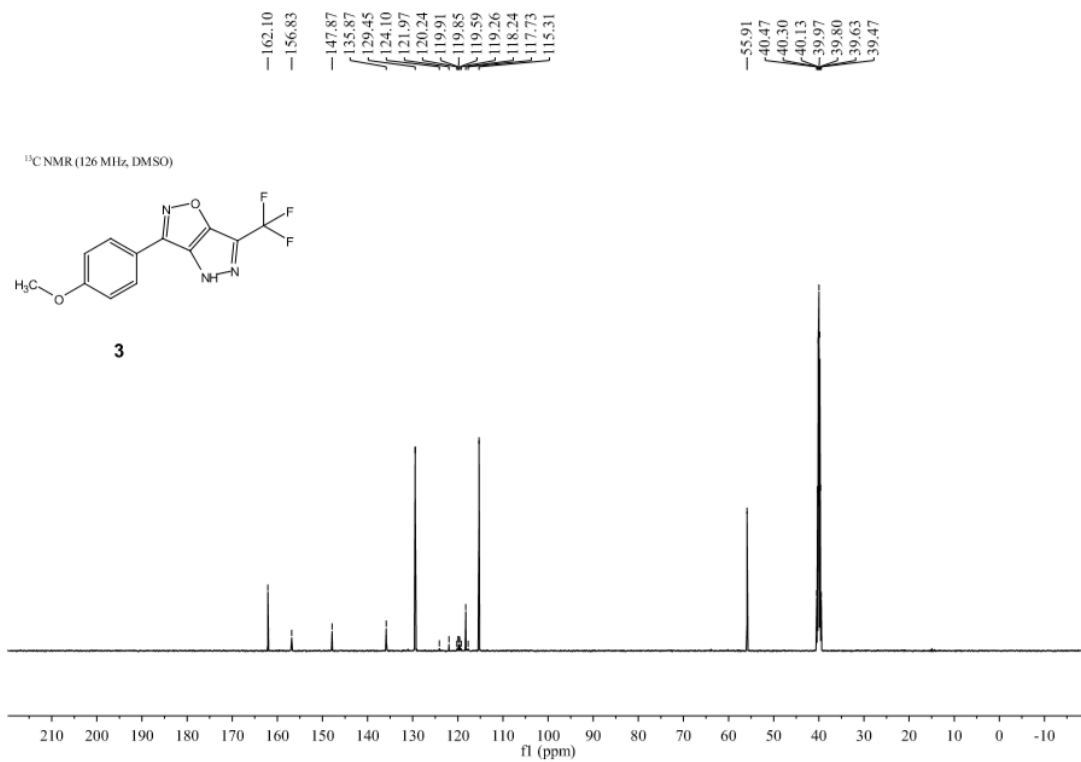
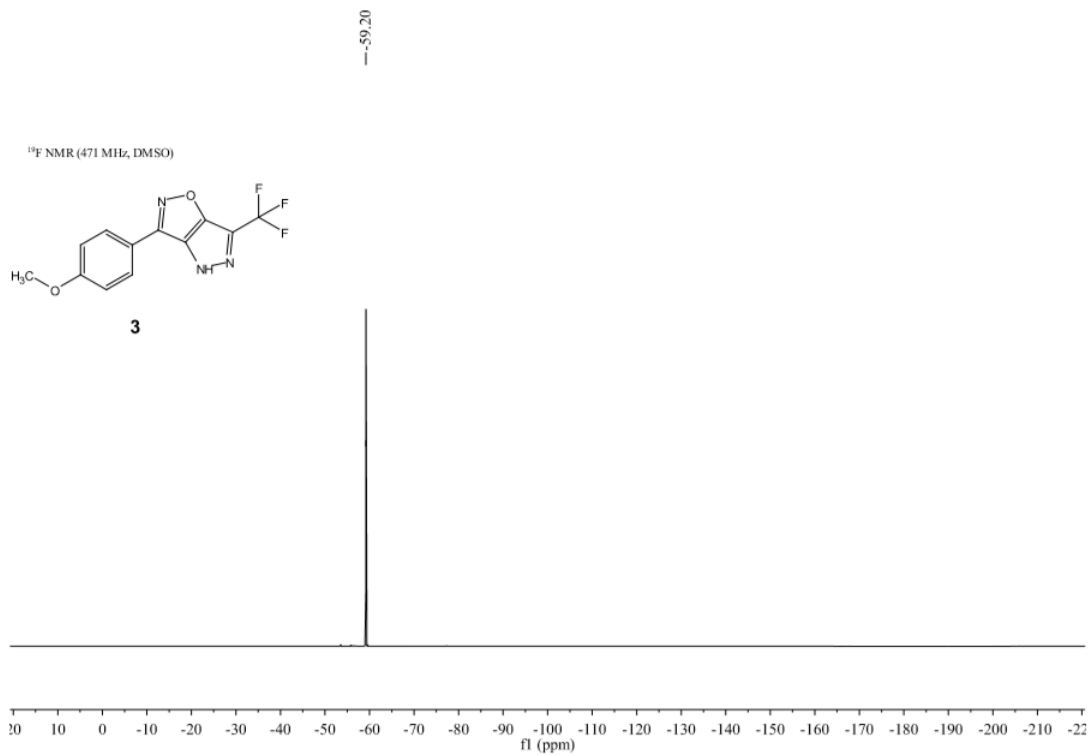
6. Control Experiments

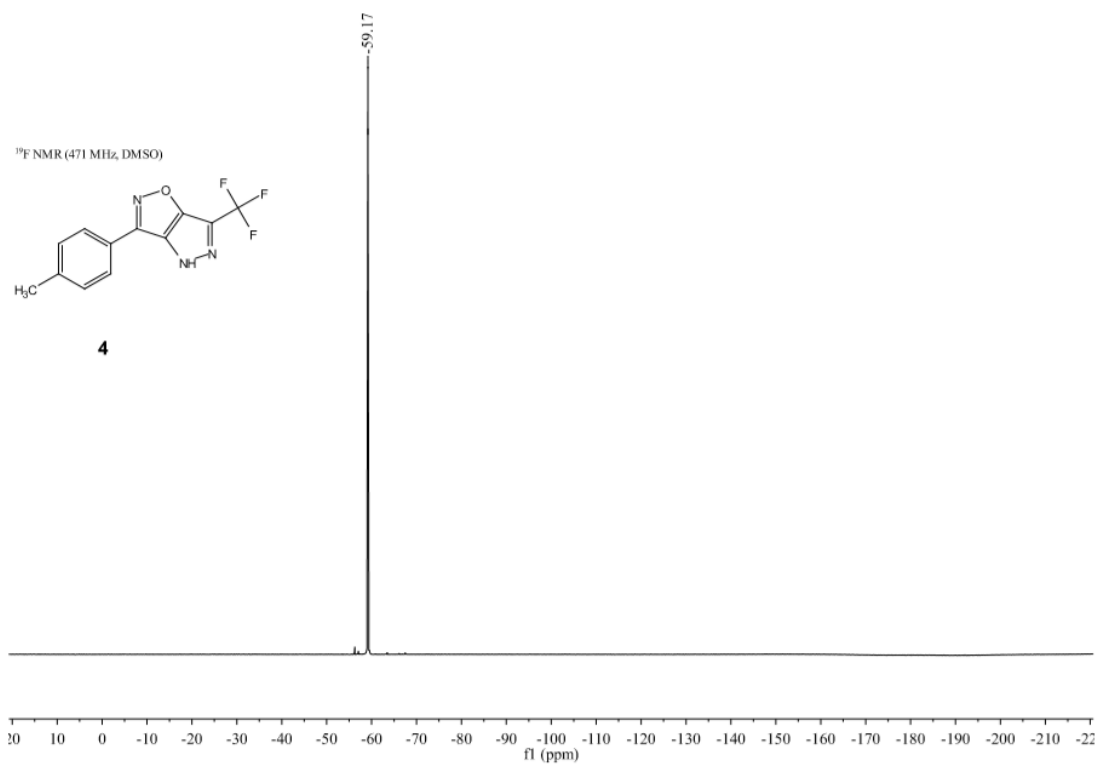
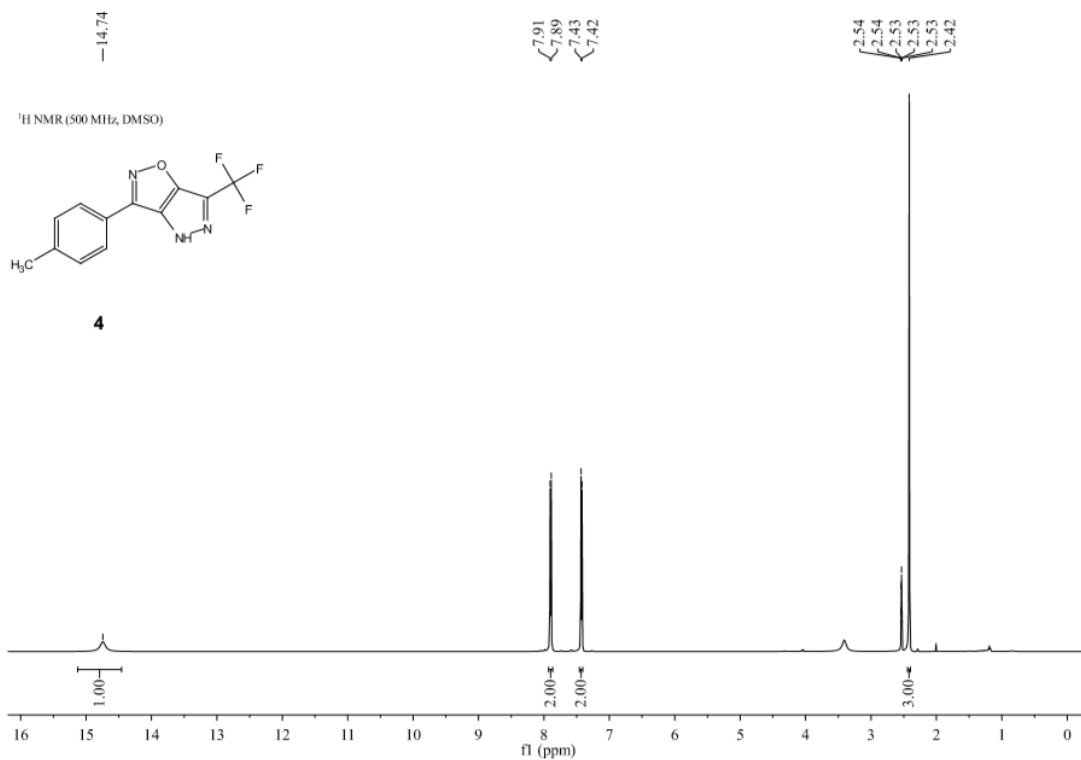


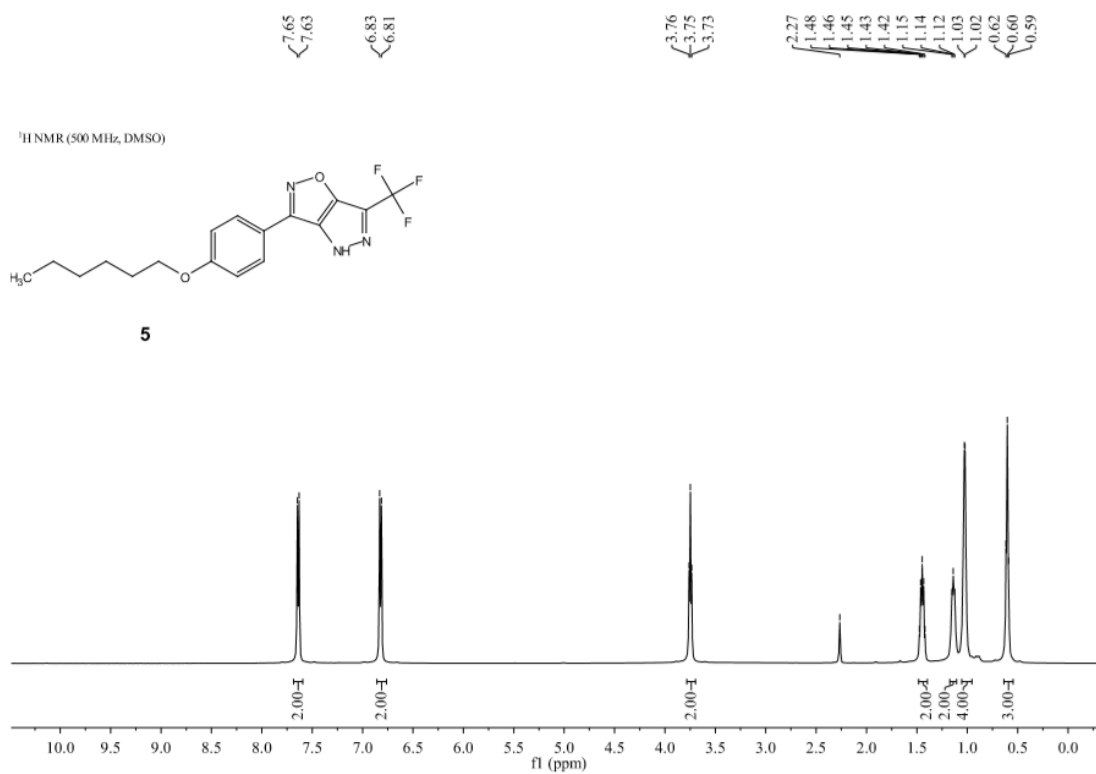
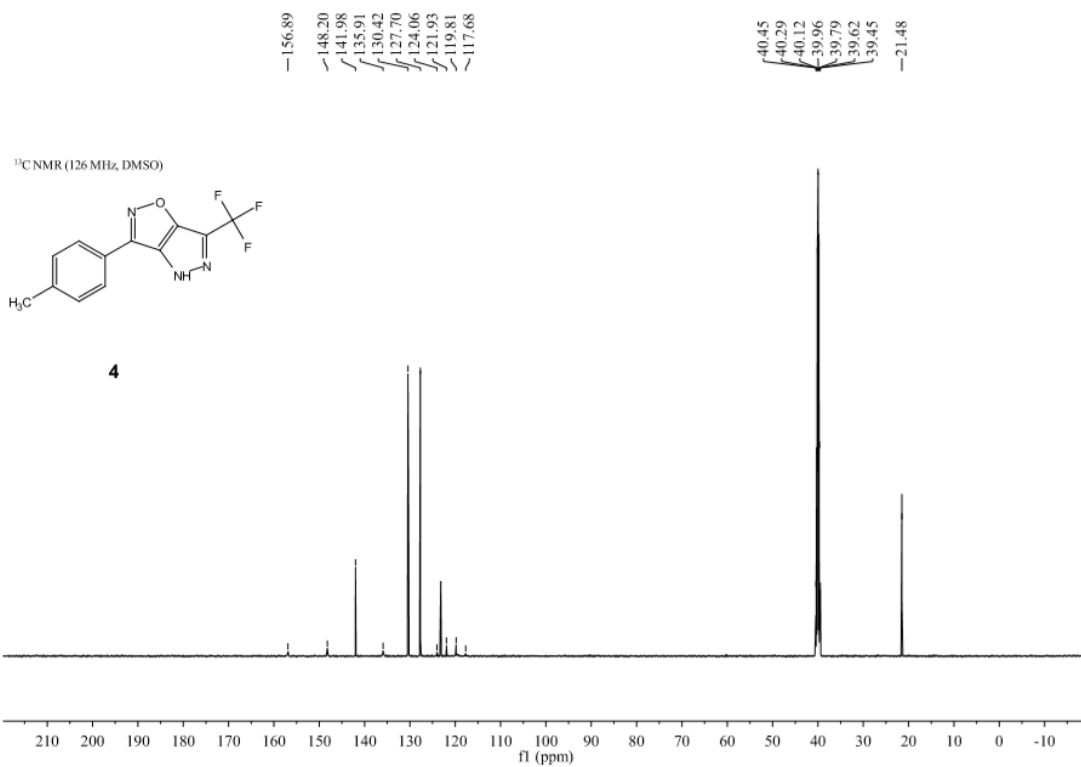
7. ^1H , ^{13}C , ^{19}F NMR spectra of compounds

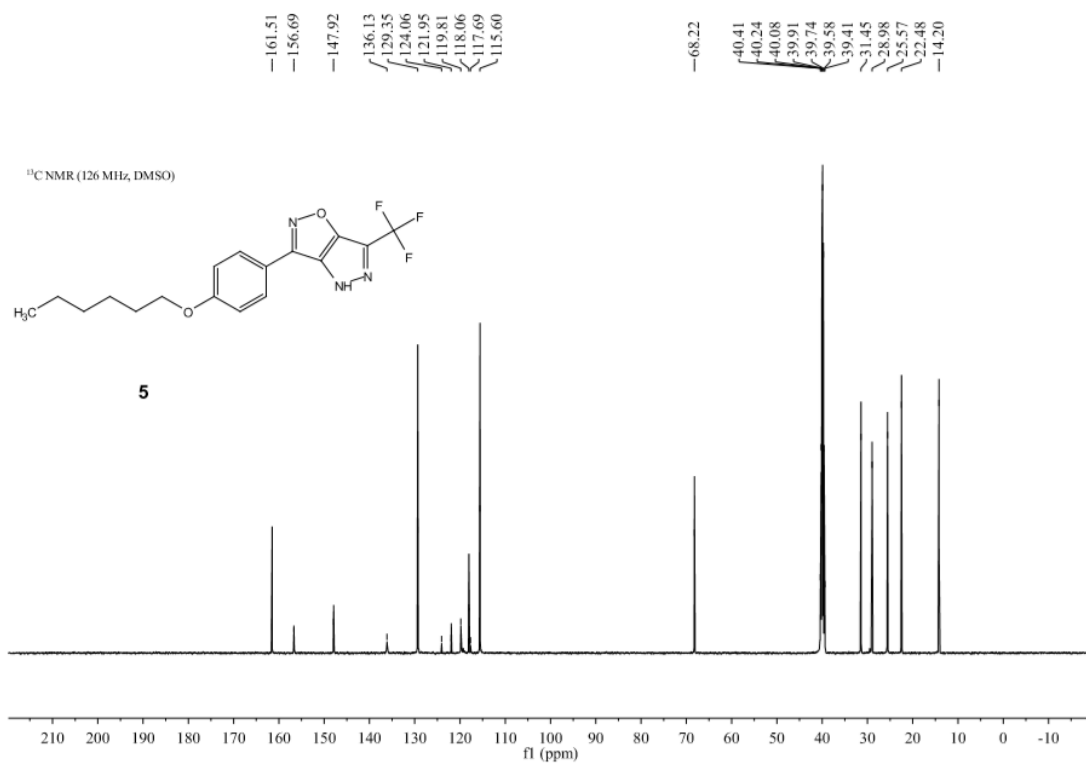
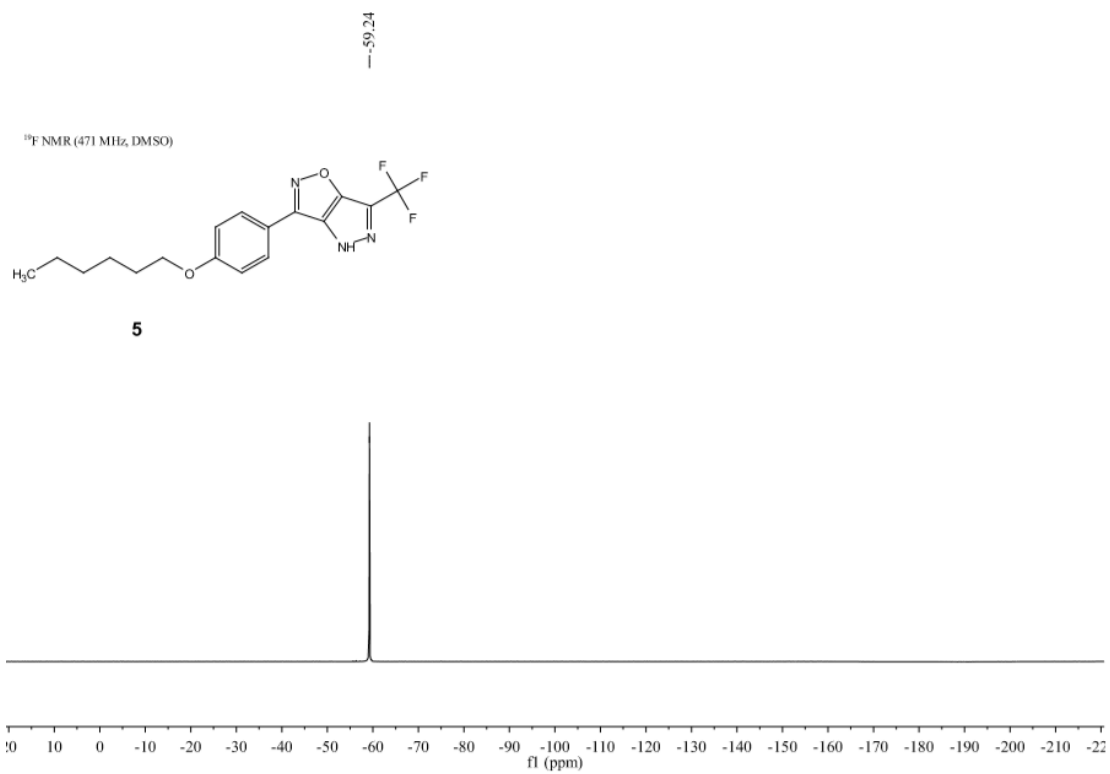


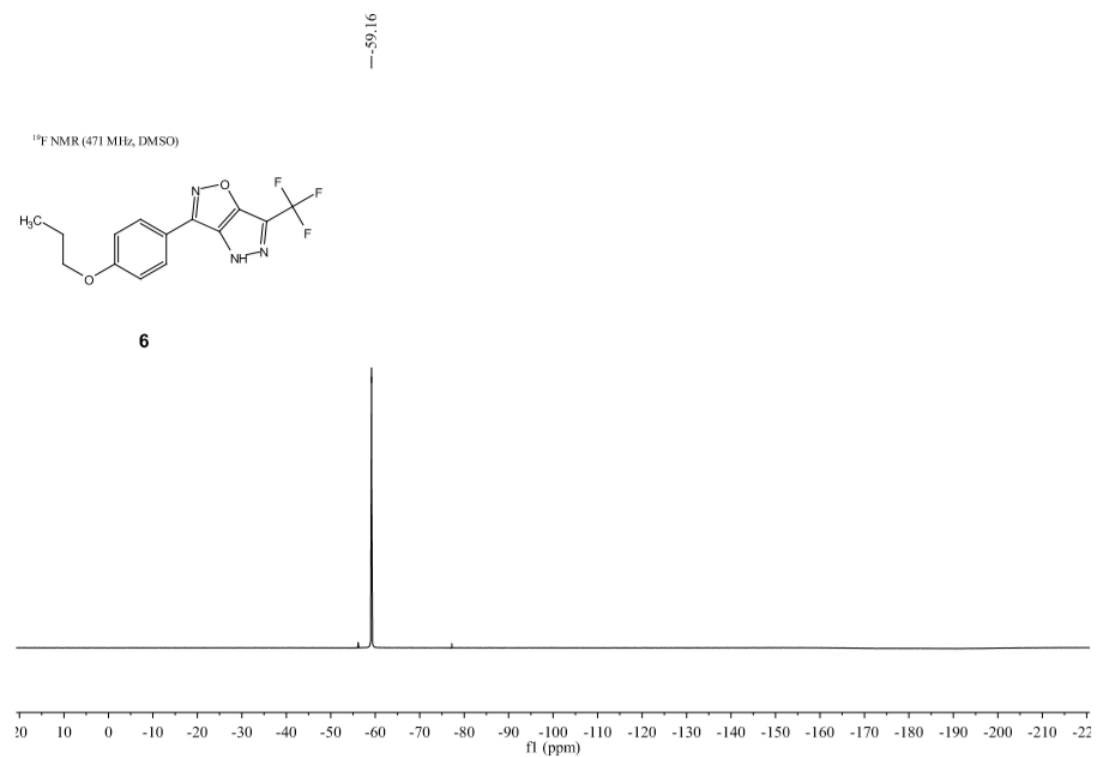
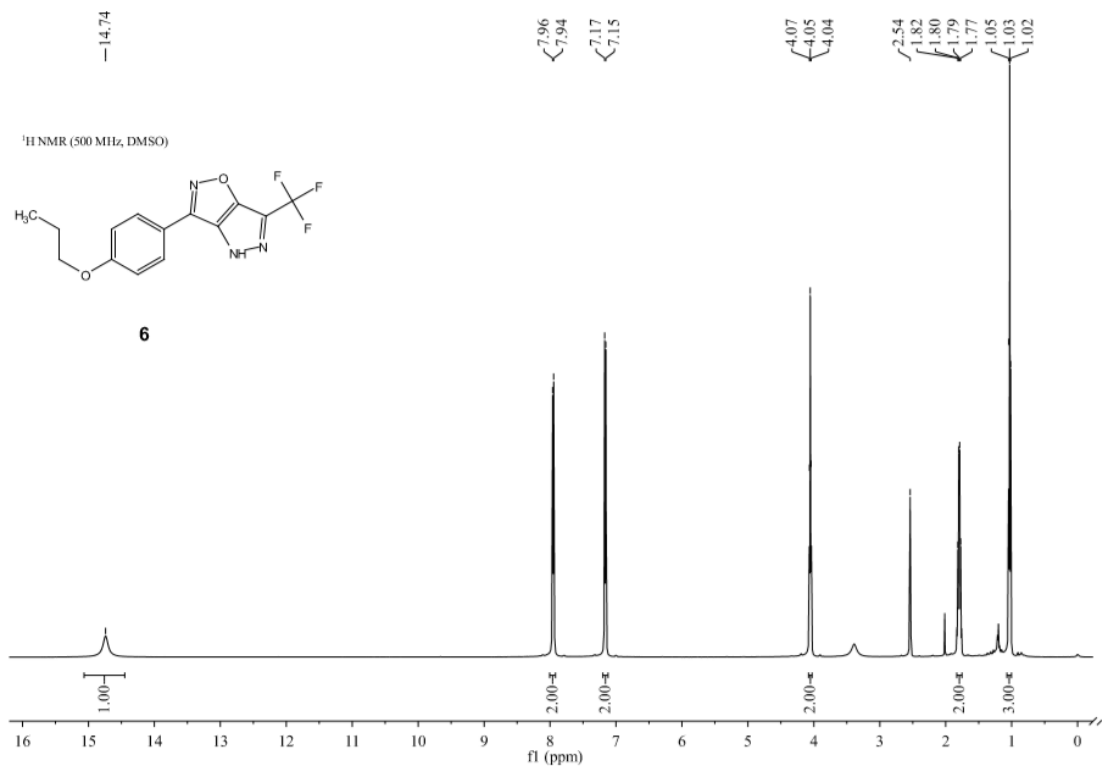


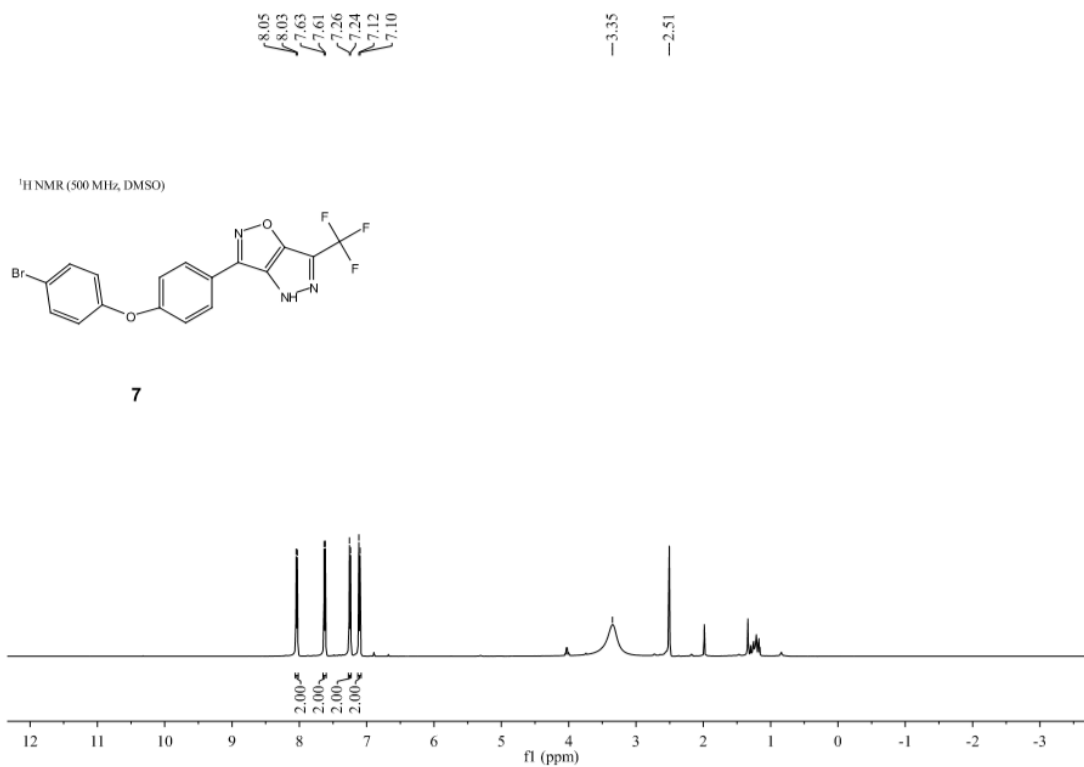
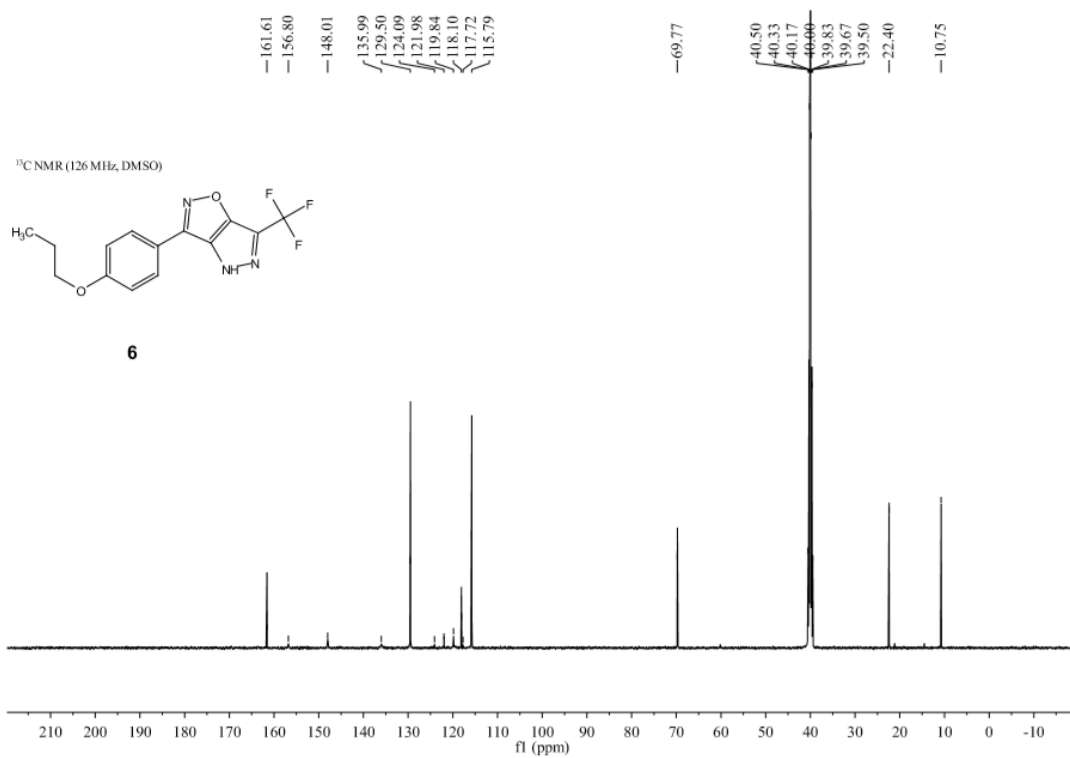


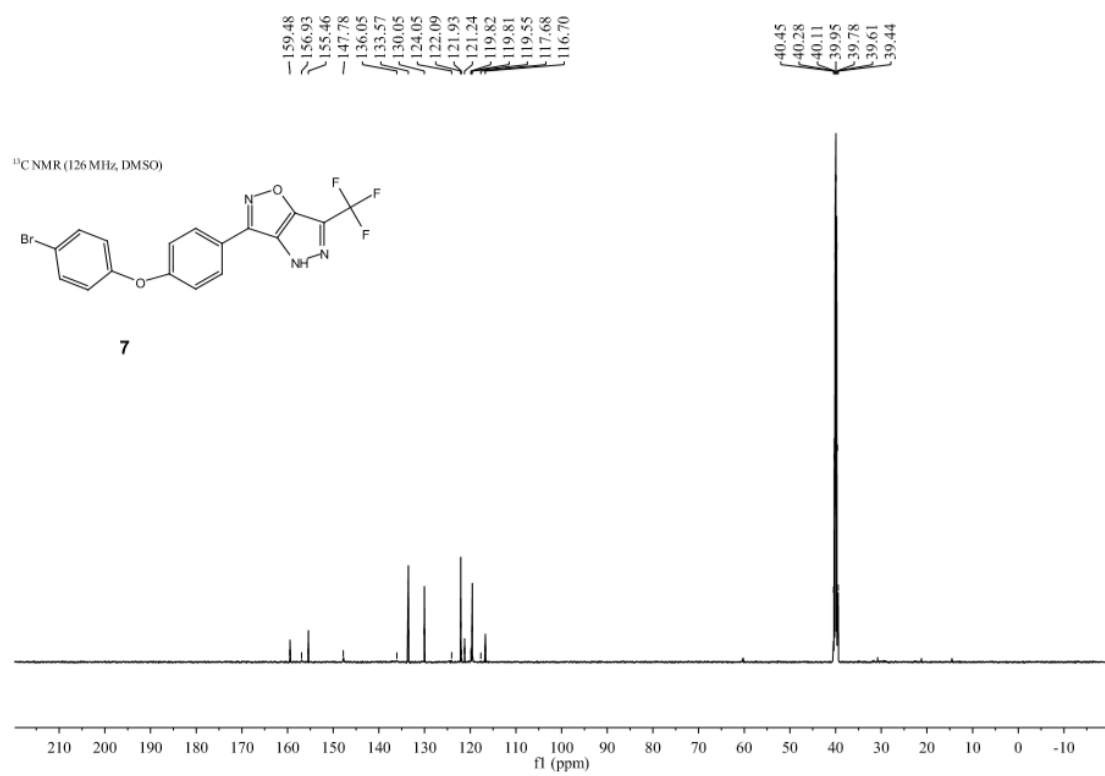
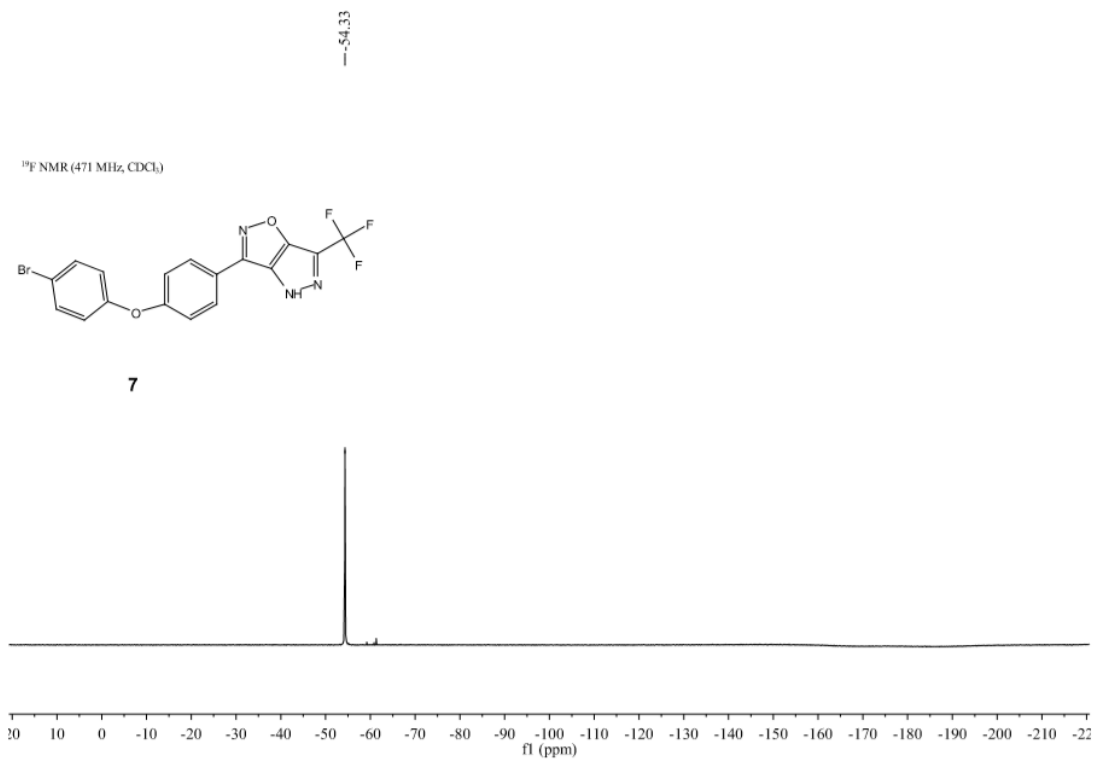


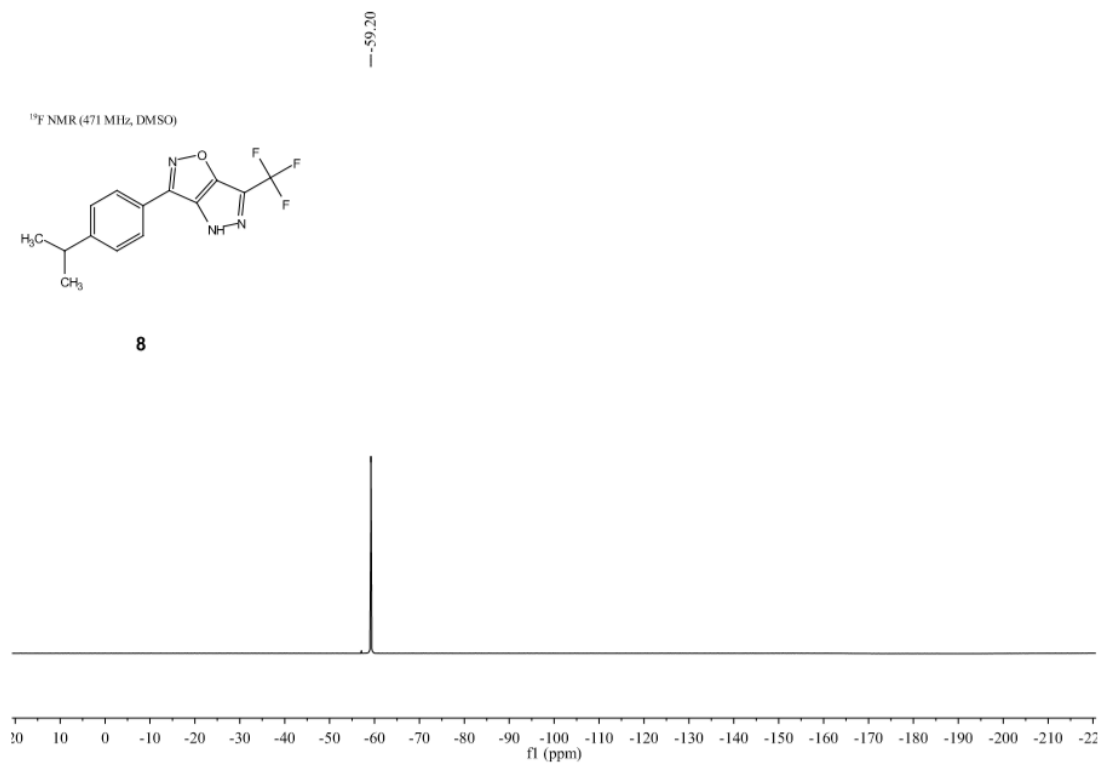
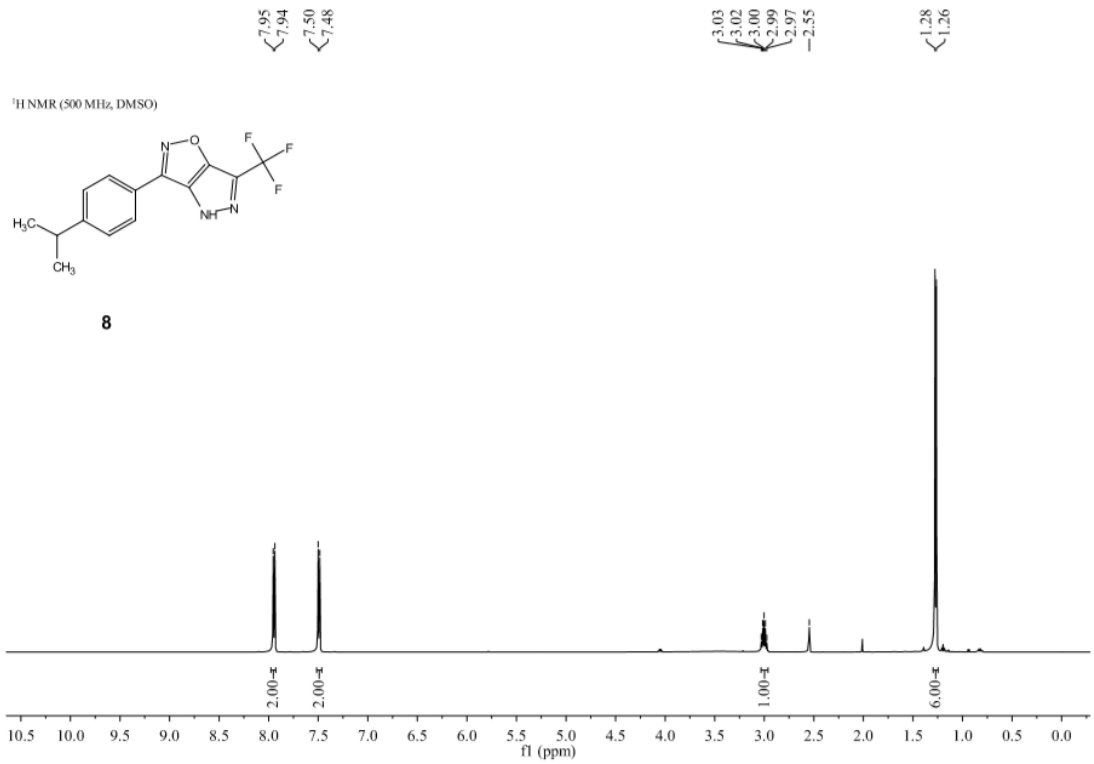


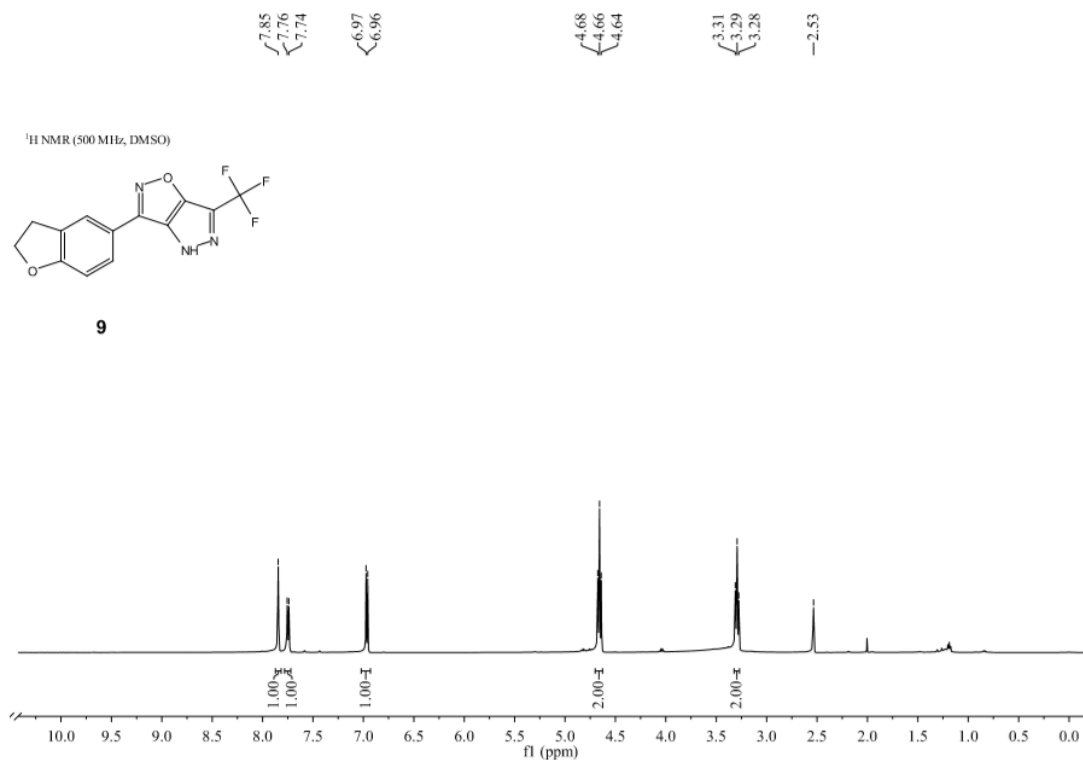
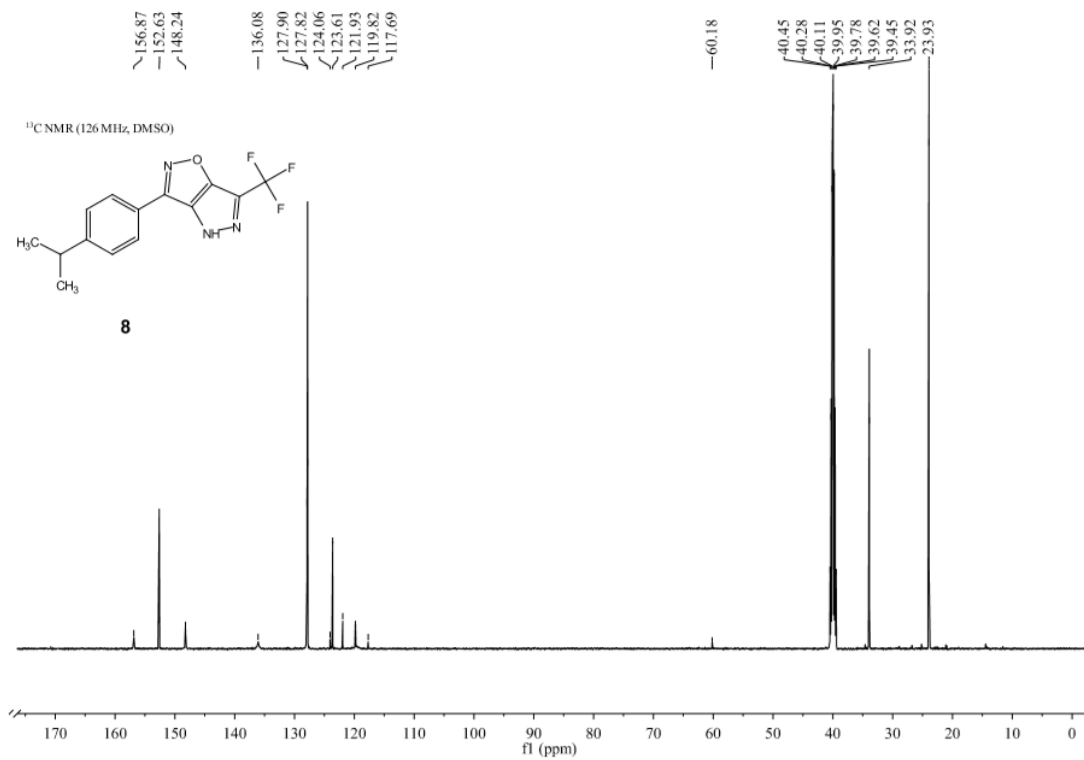


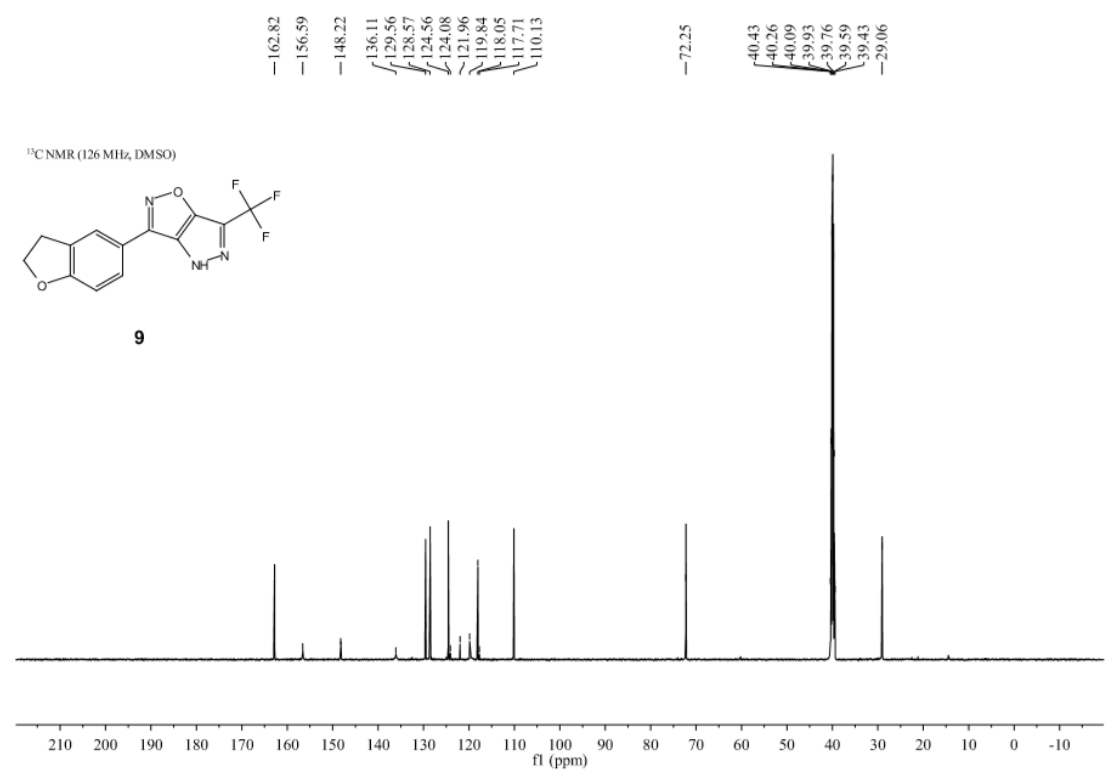
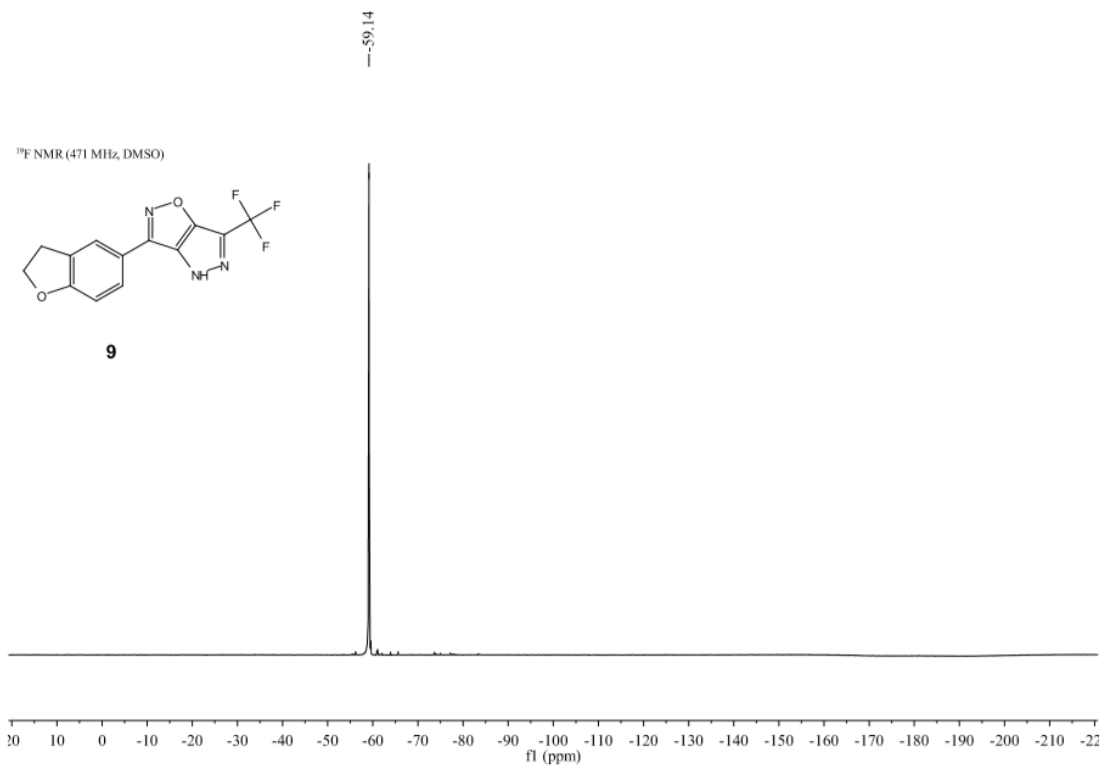


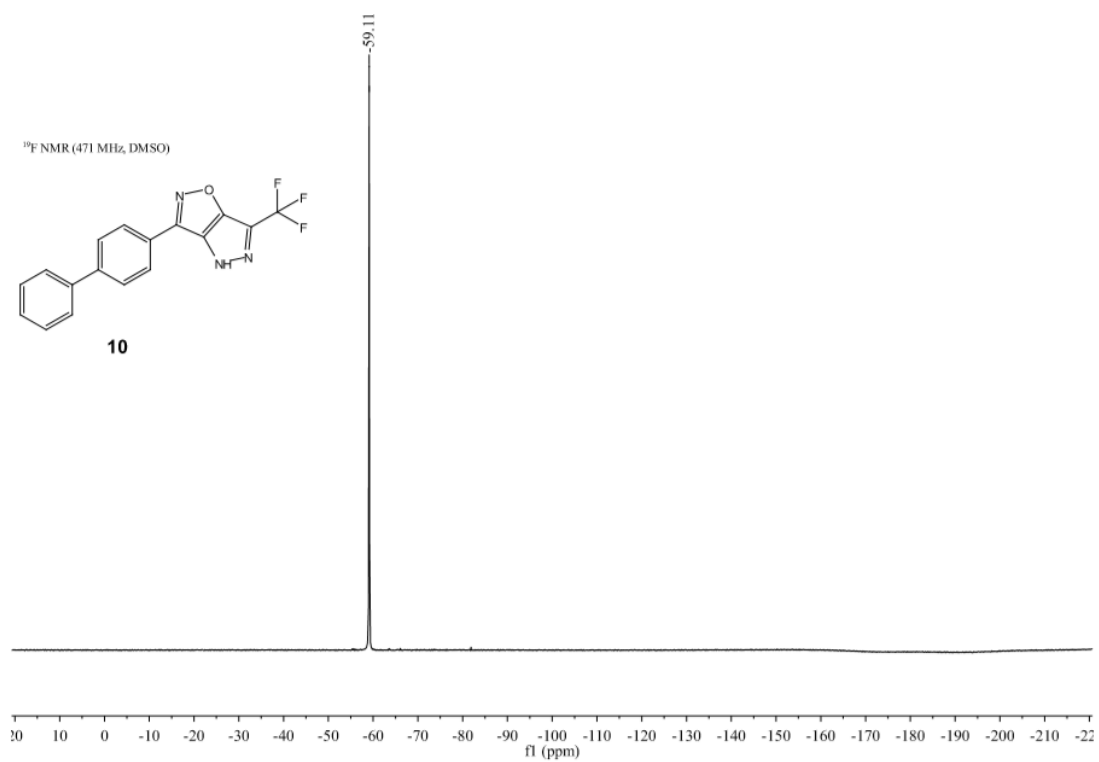
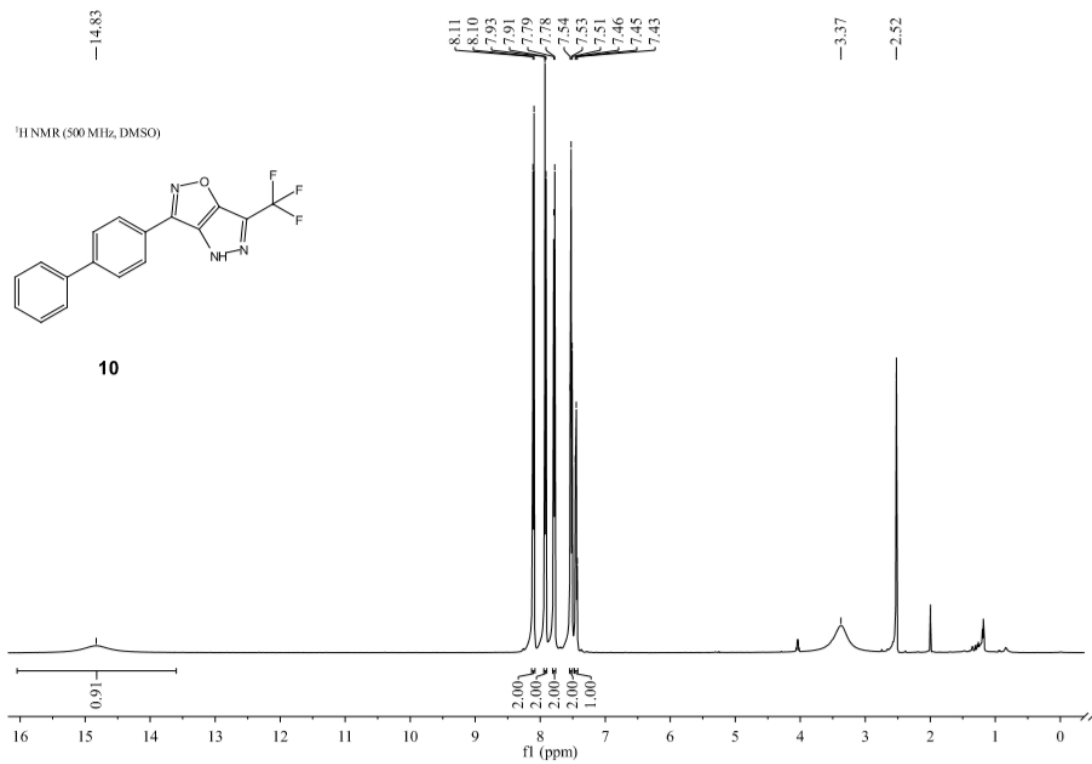


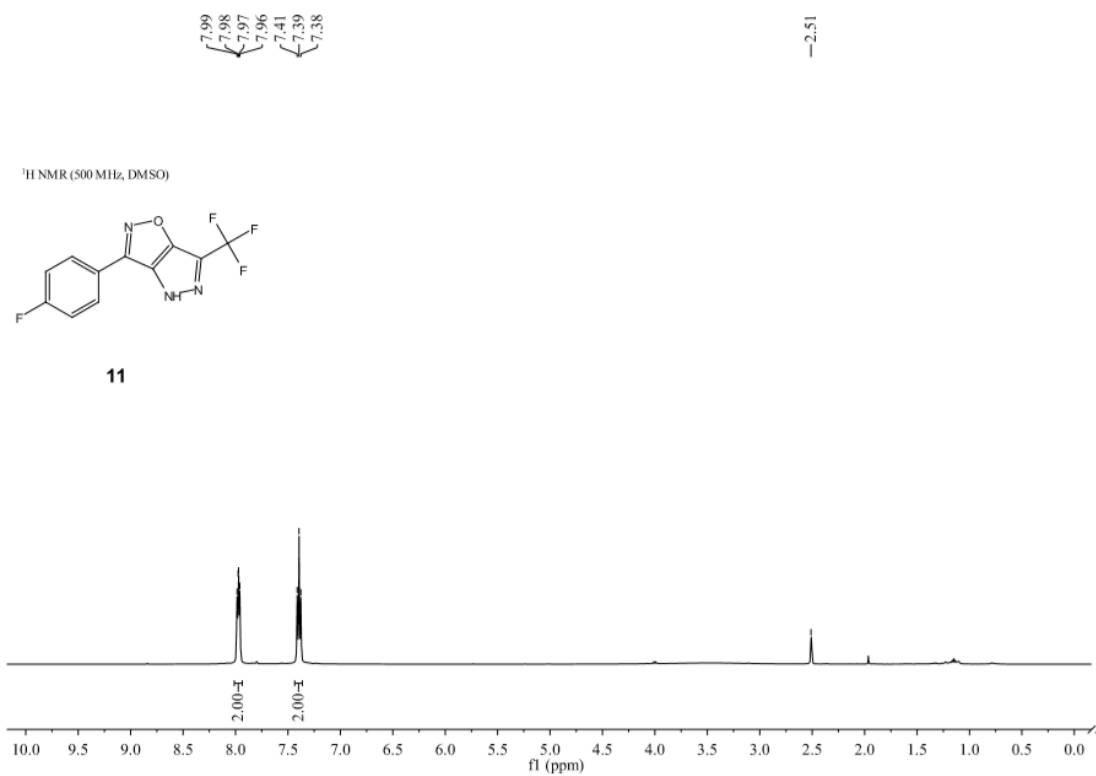
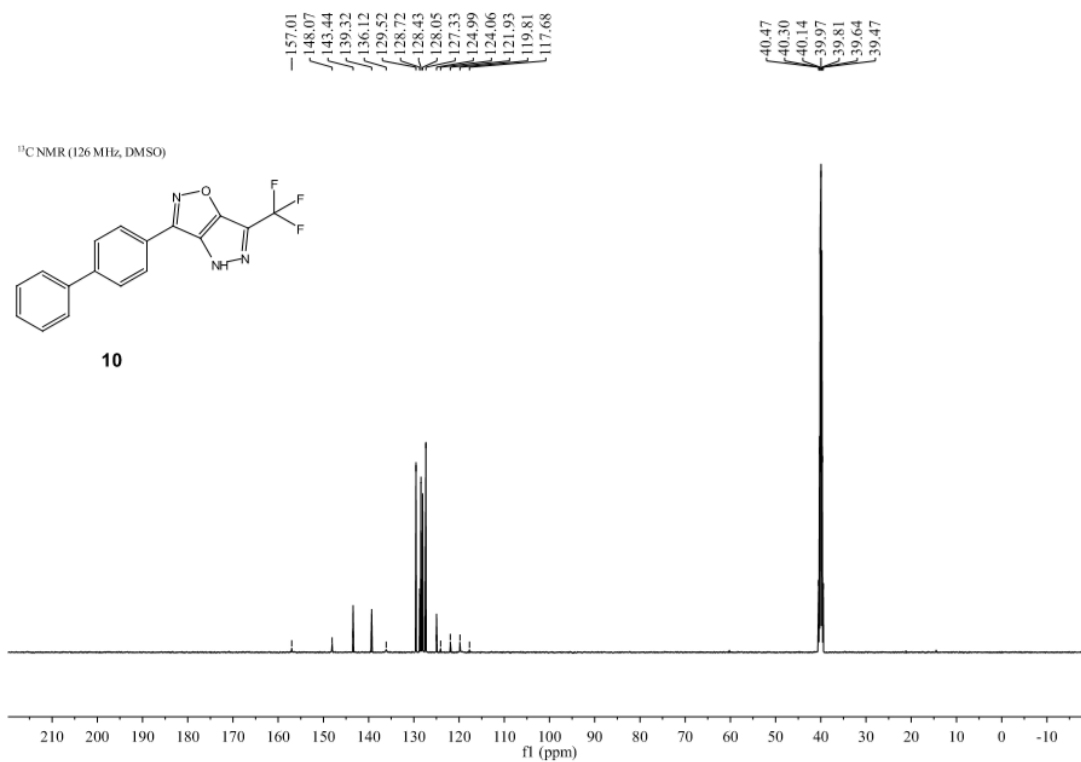


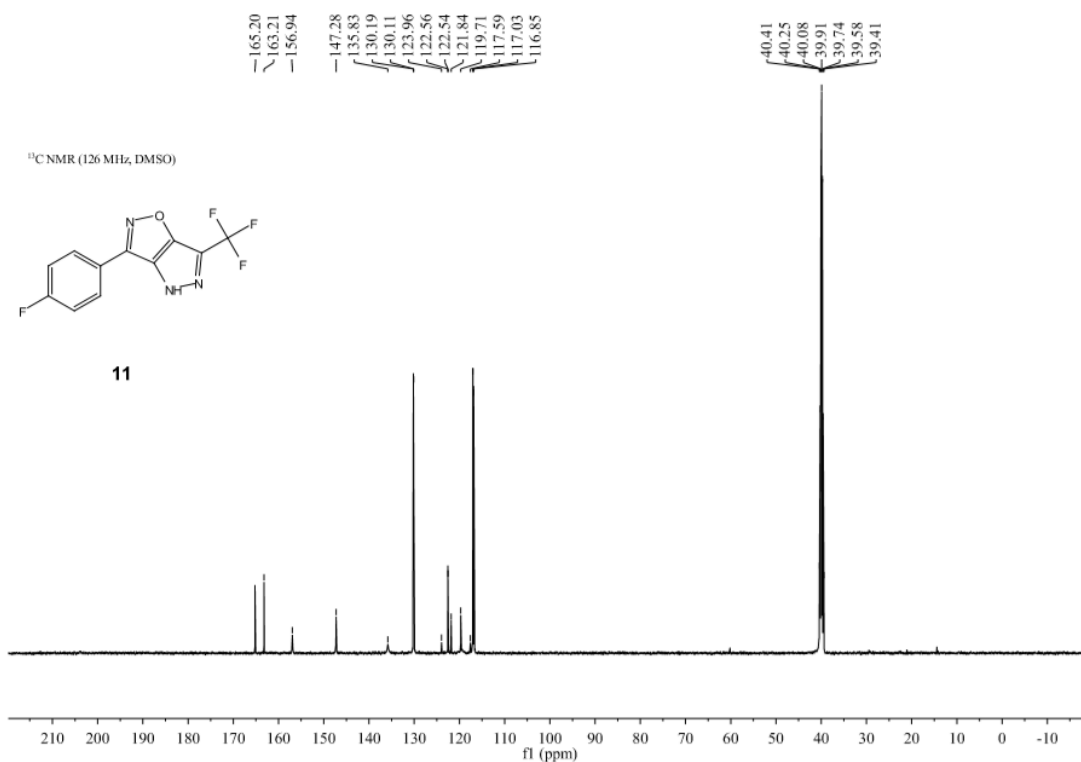
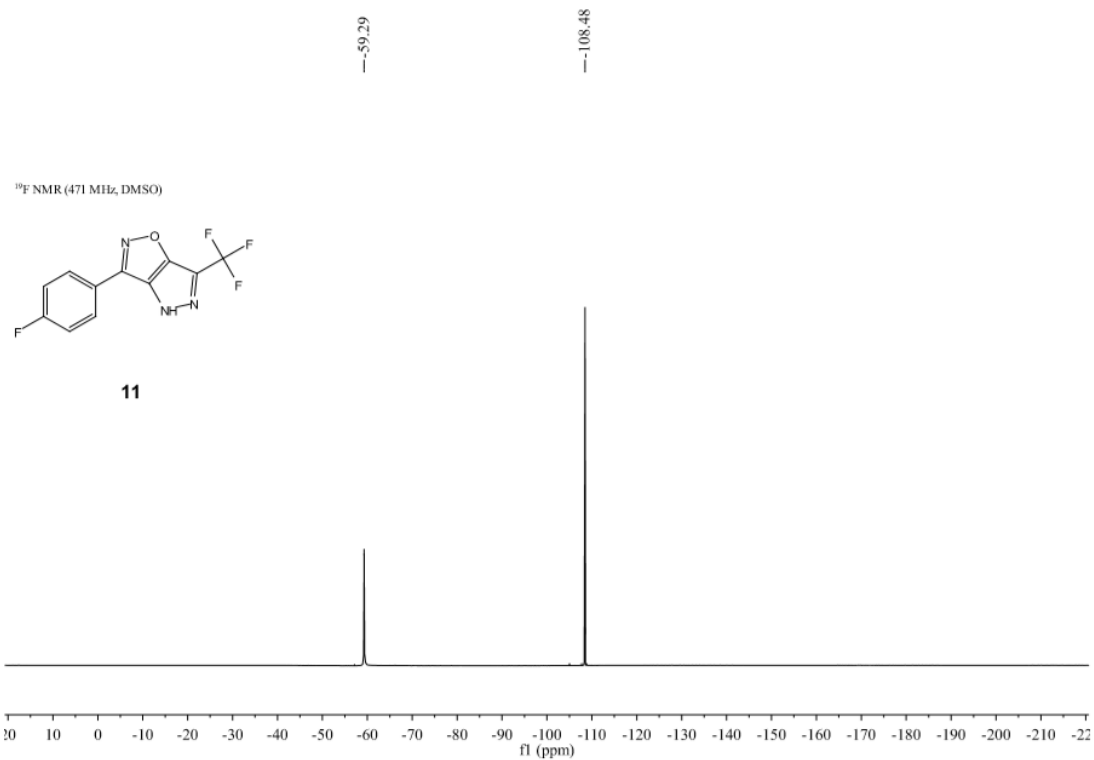


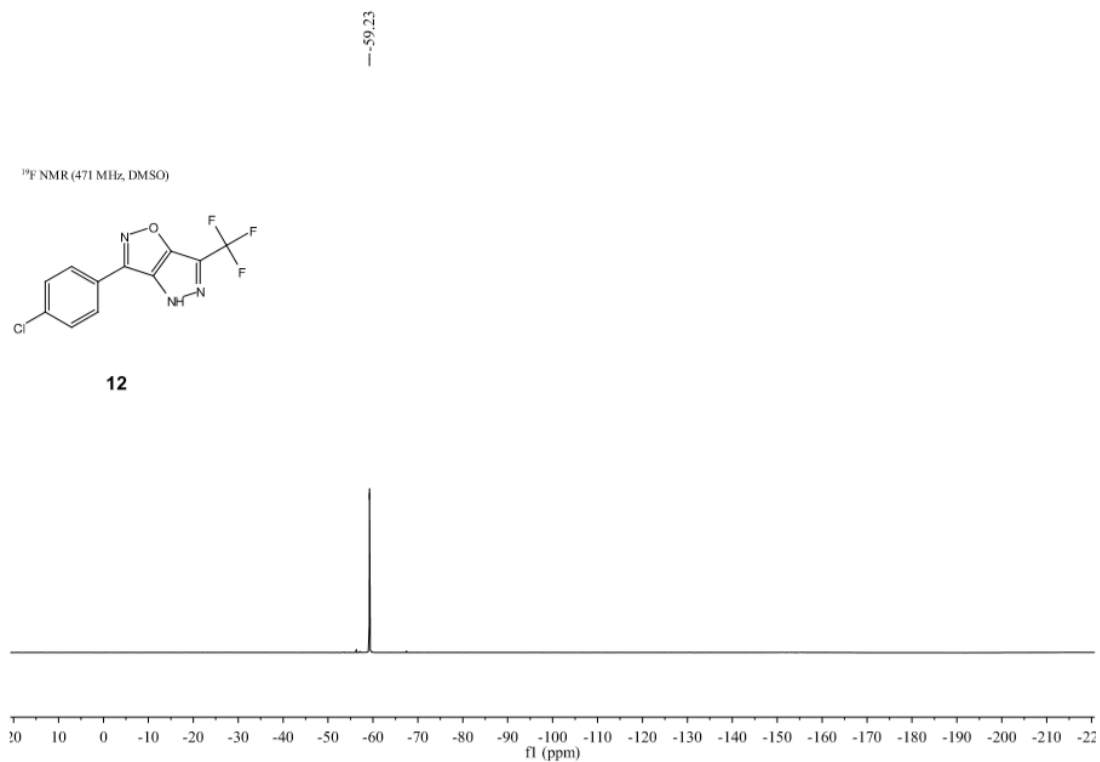
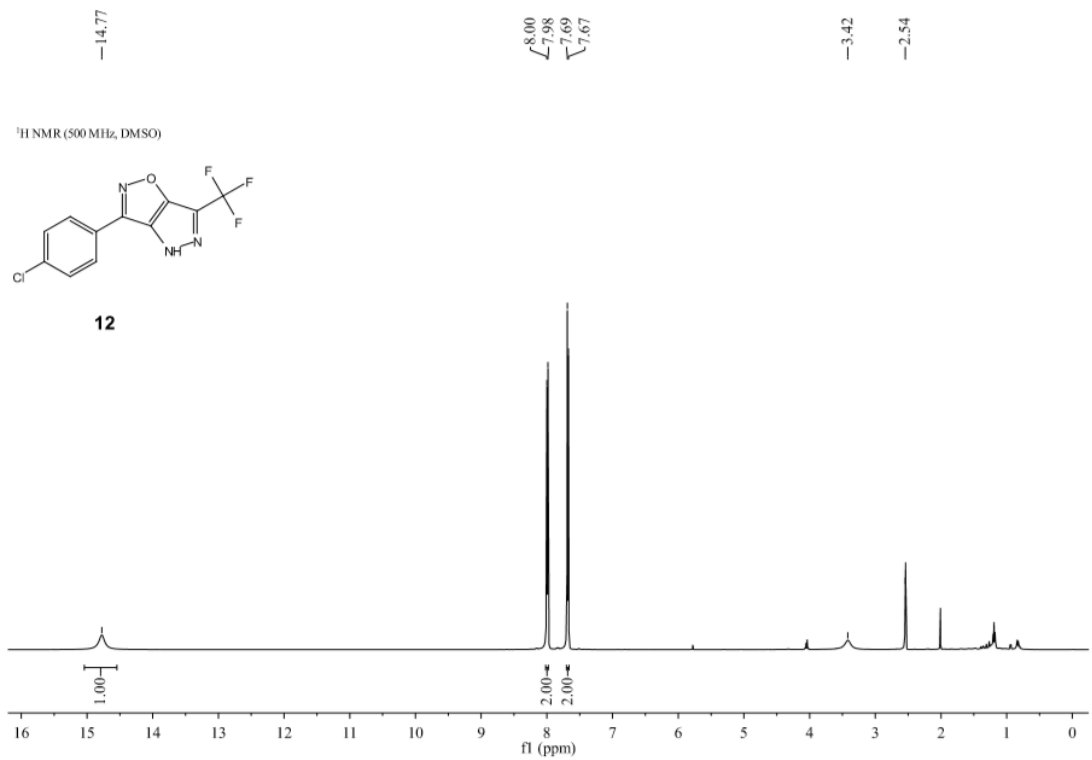


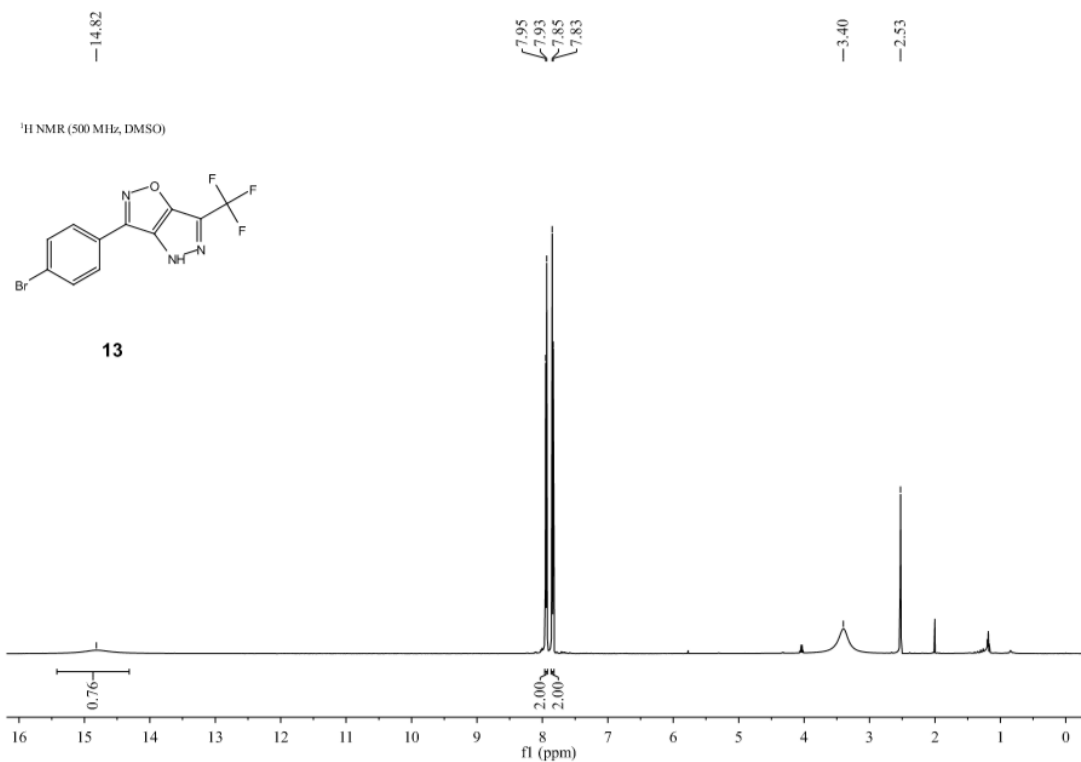
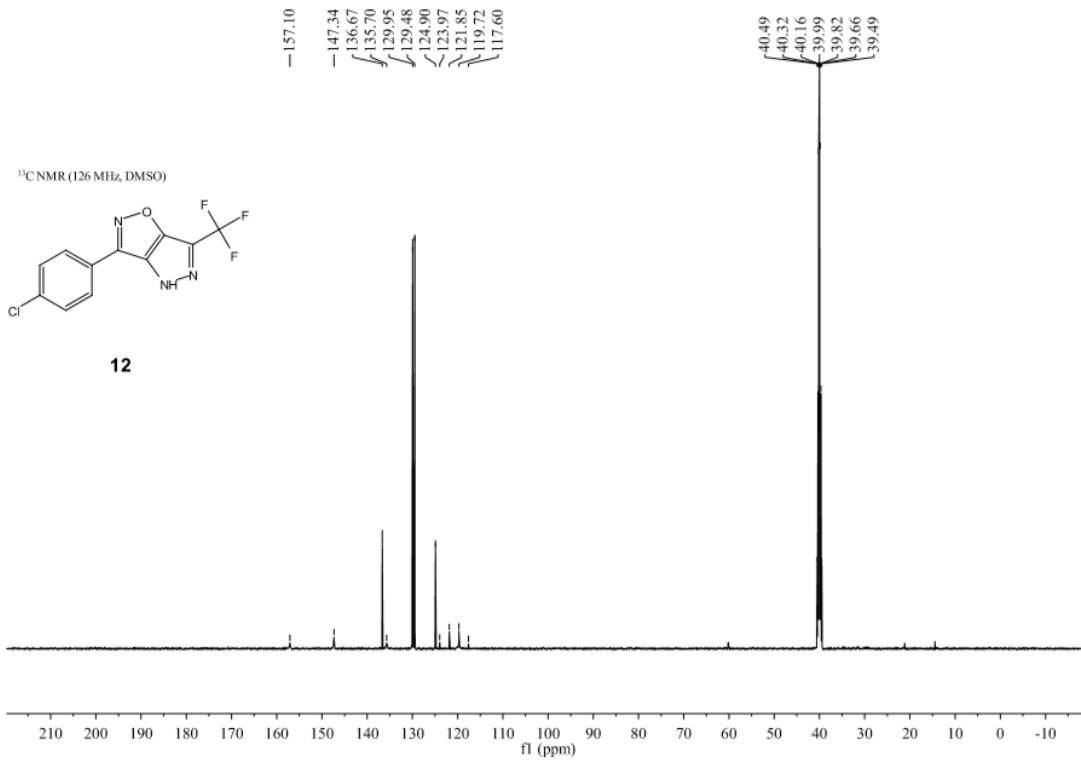


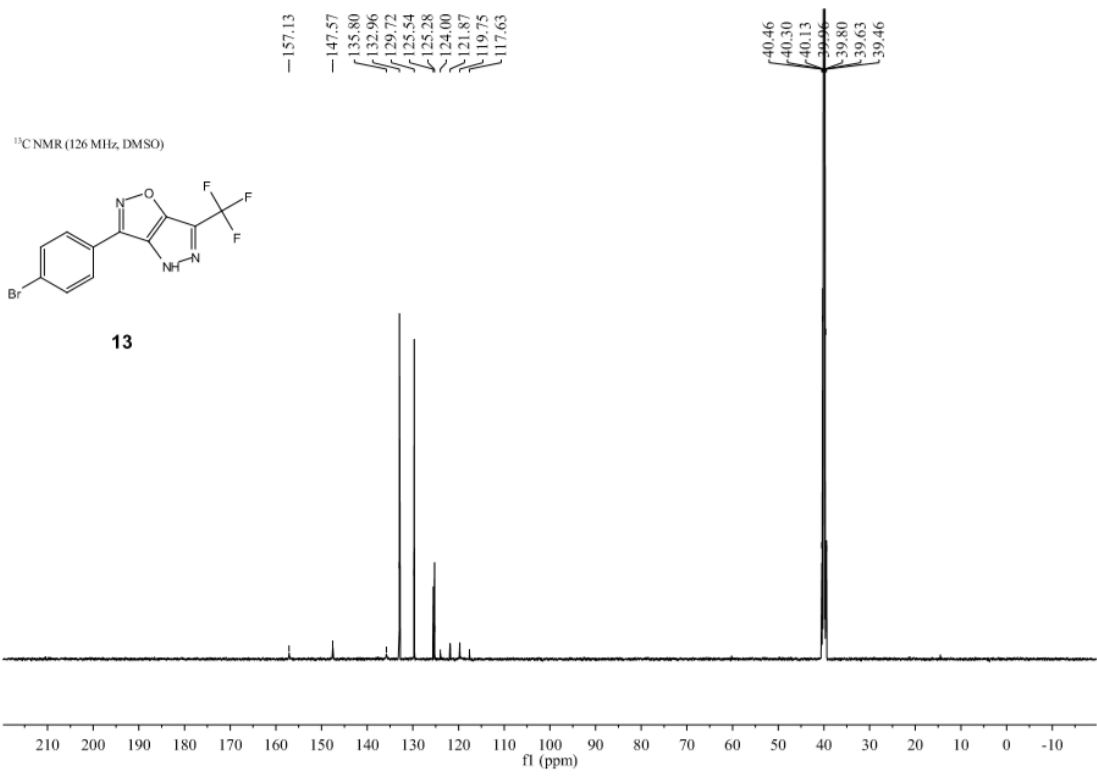
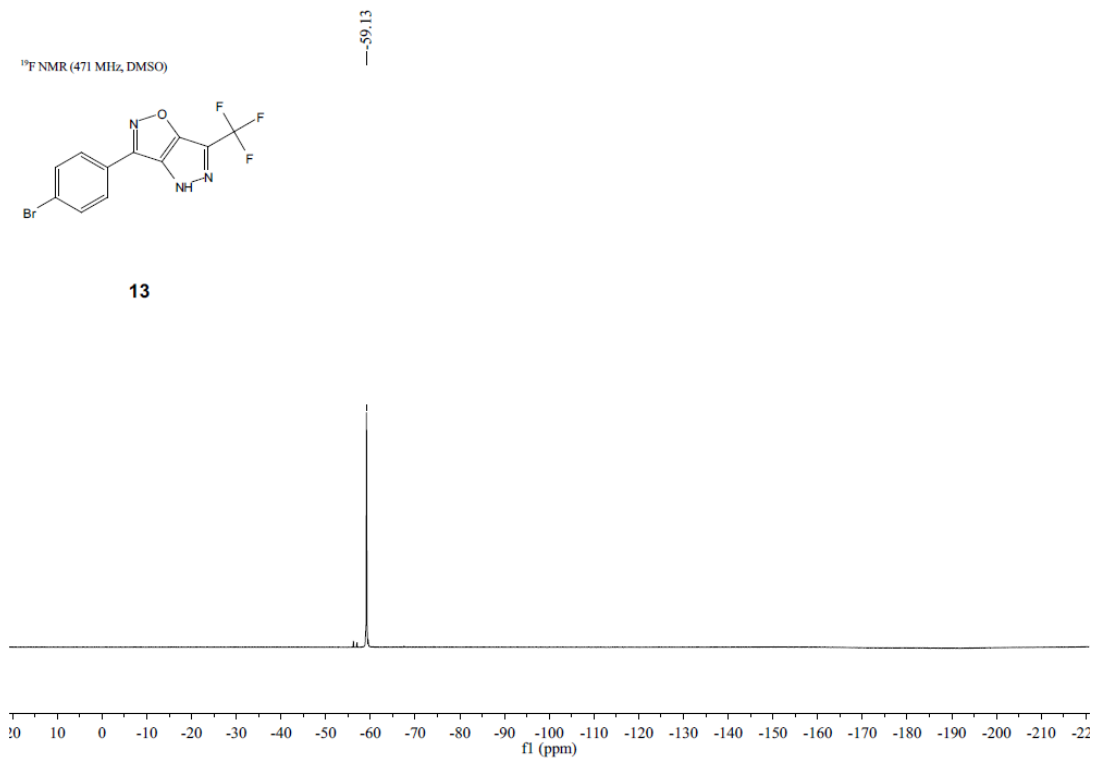


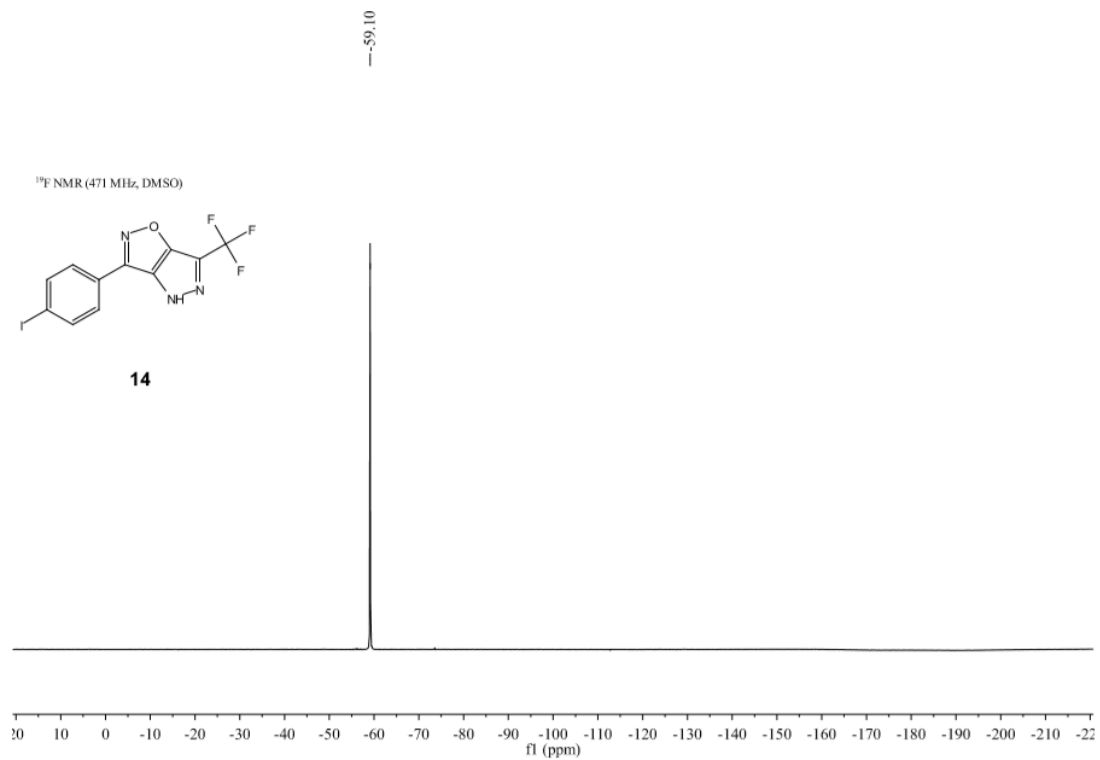
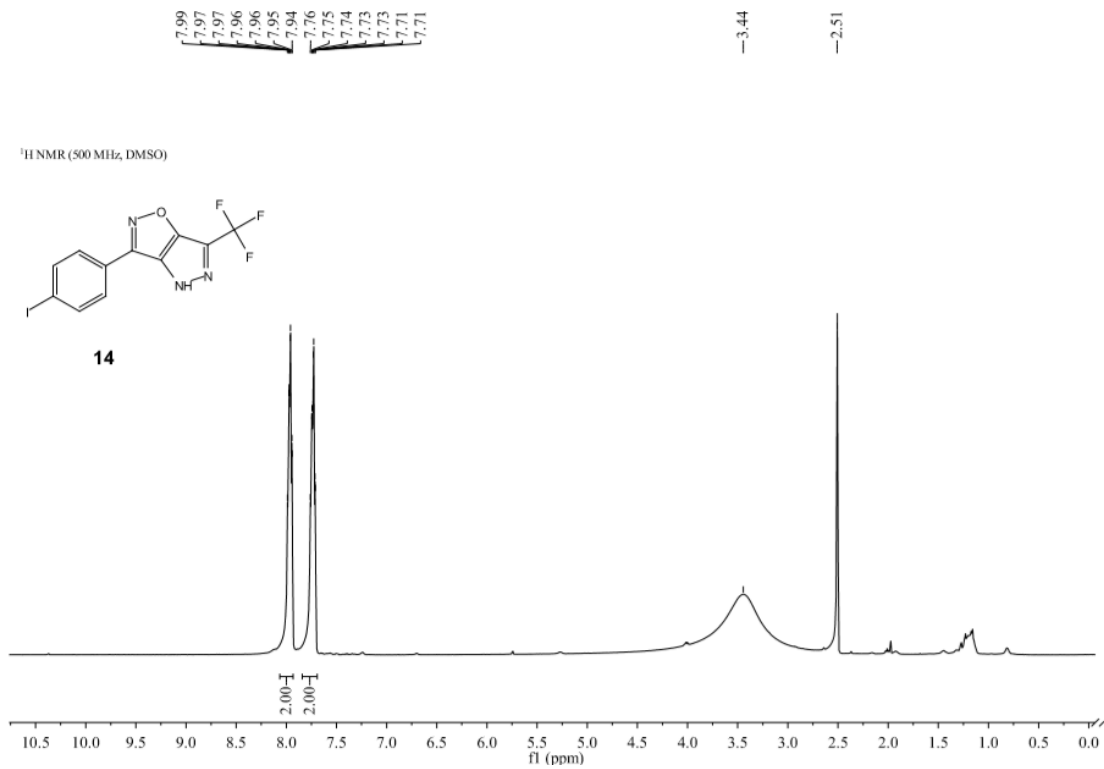


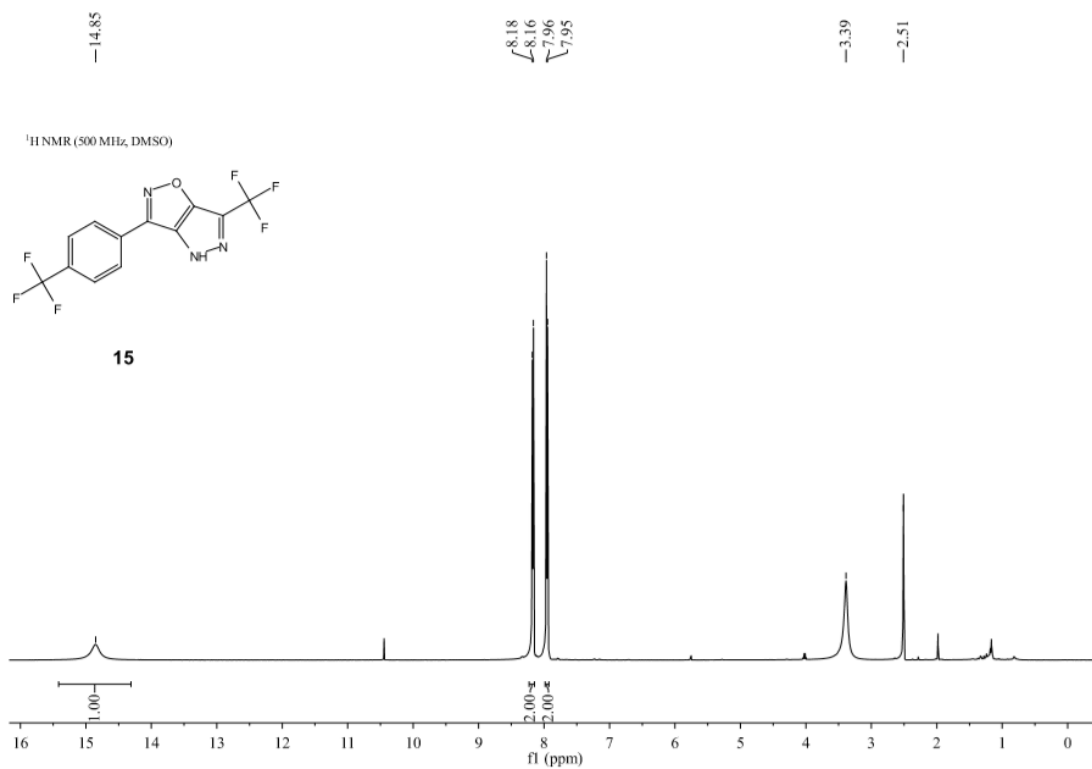
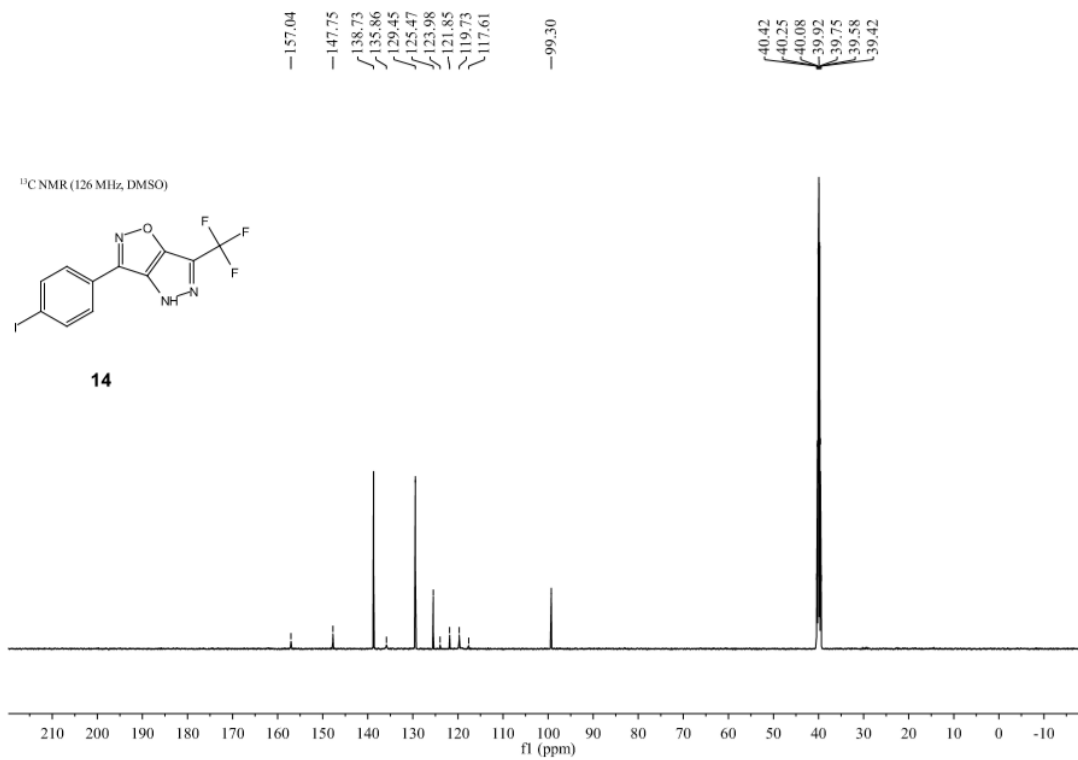


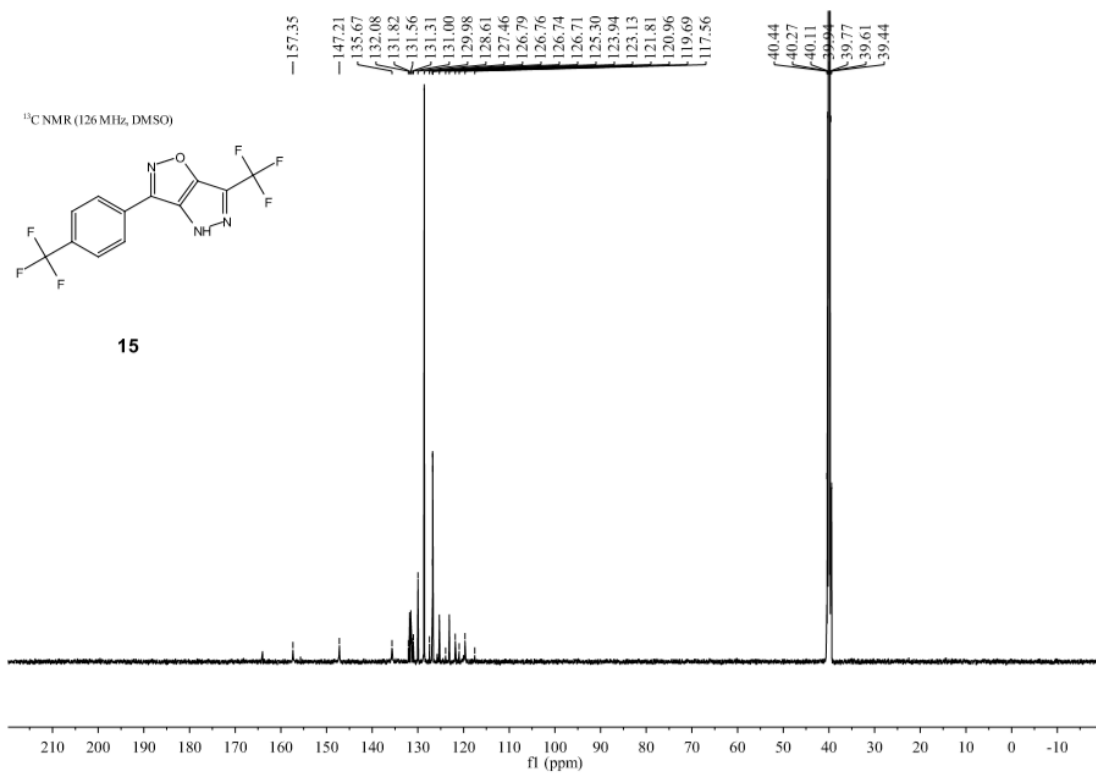
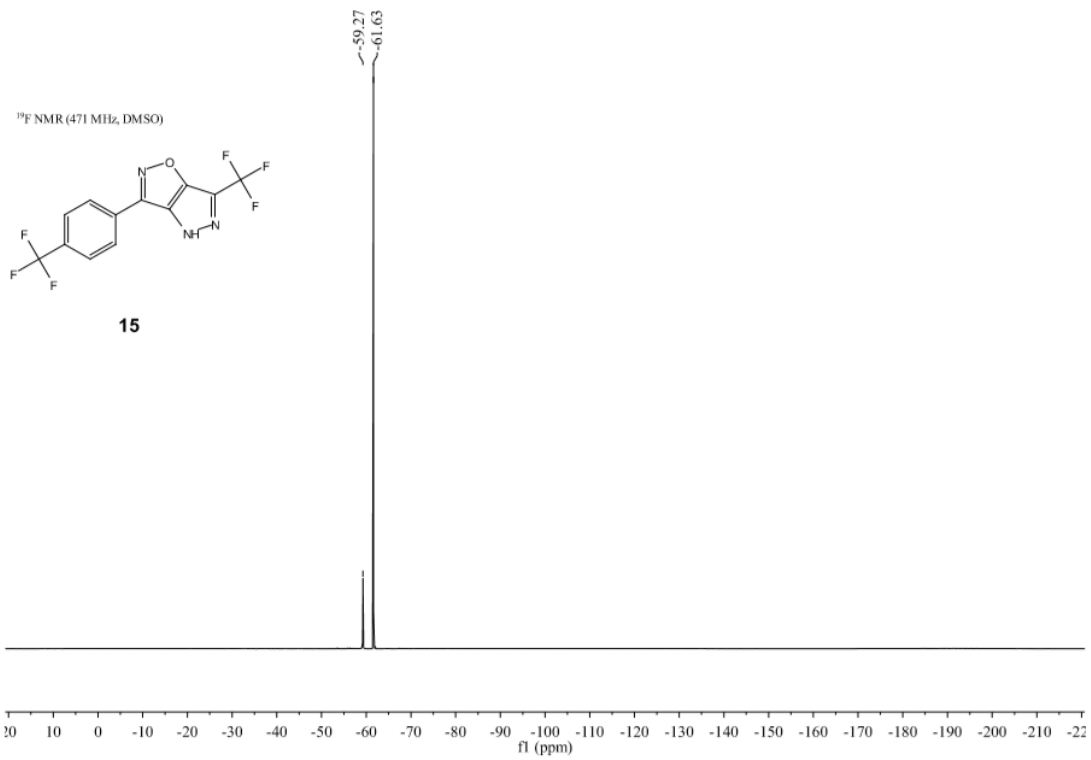


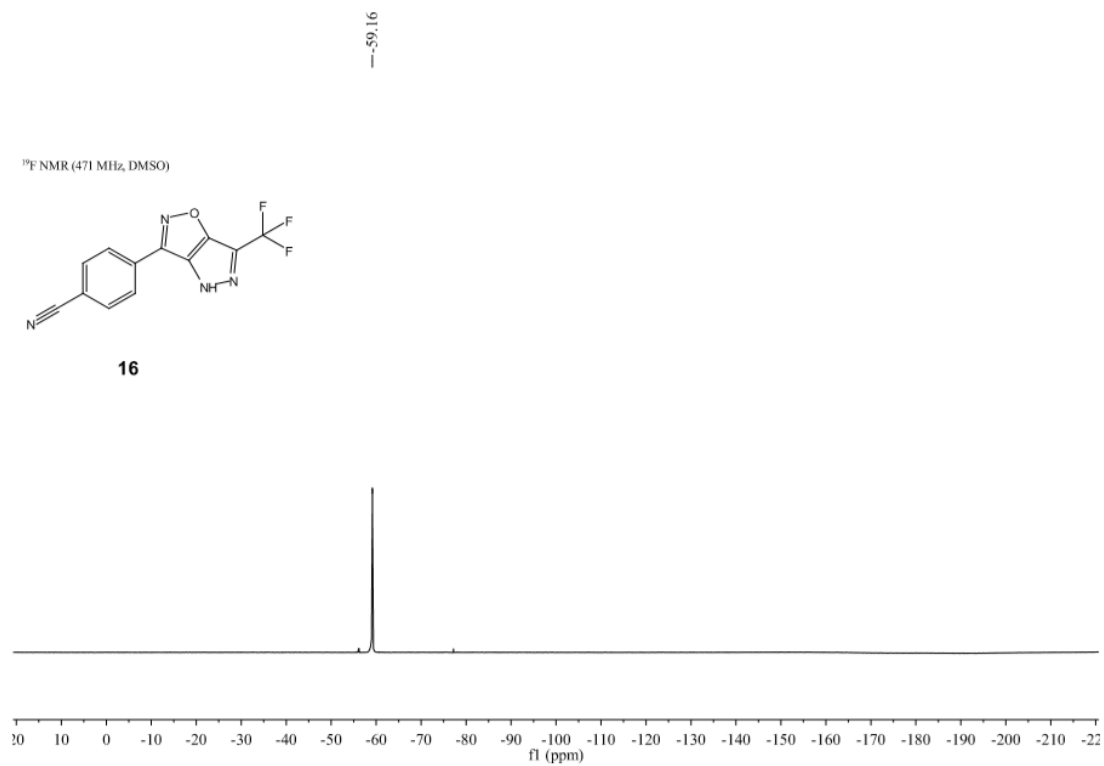
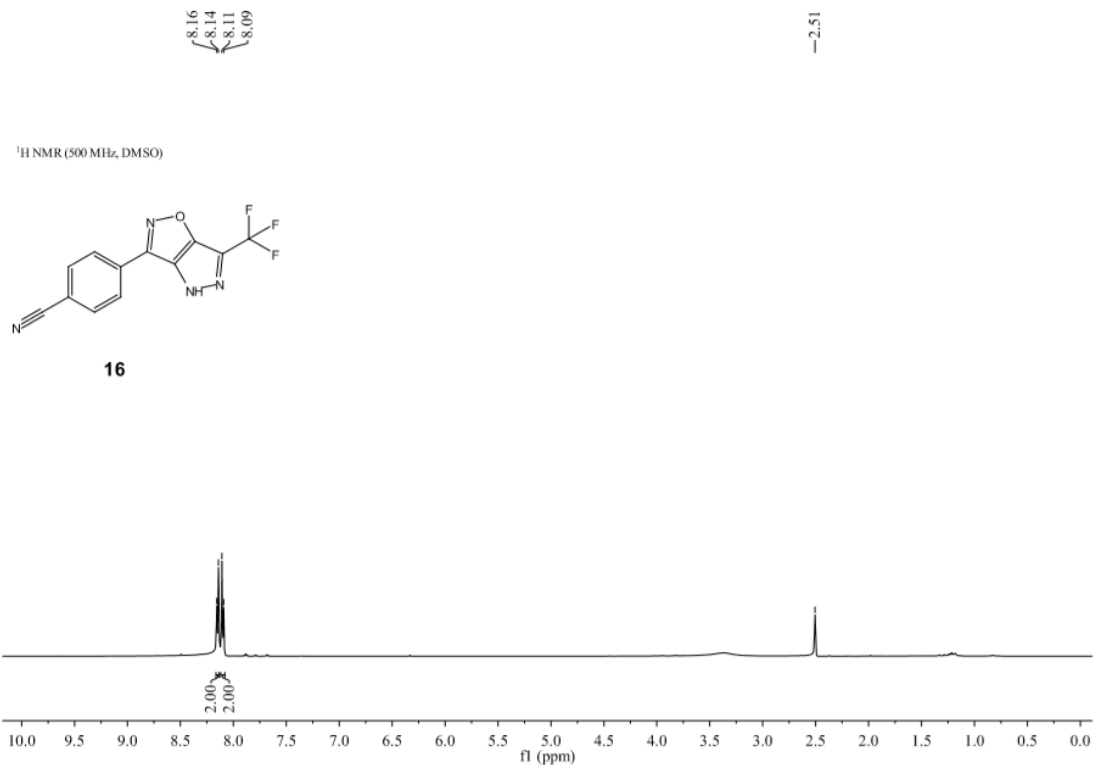


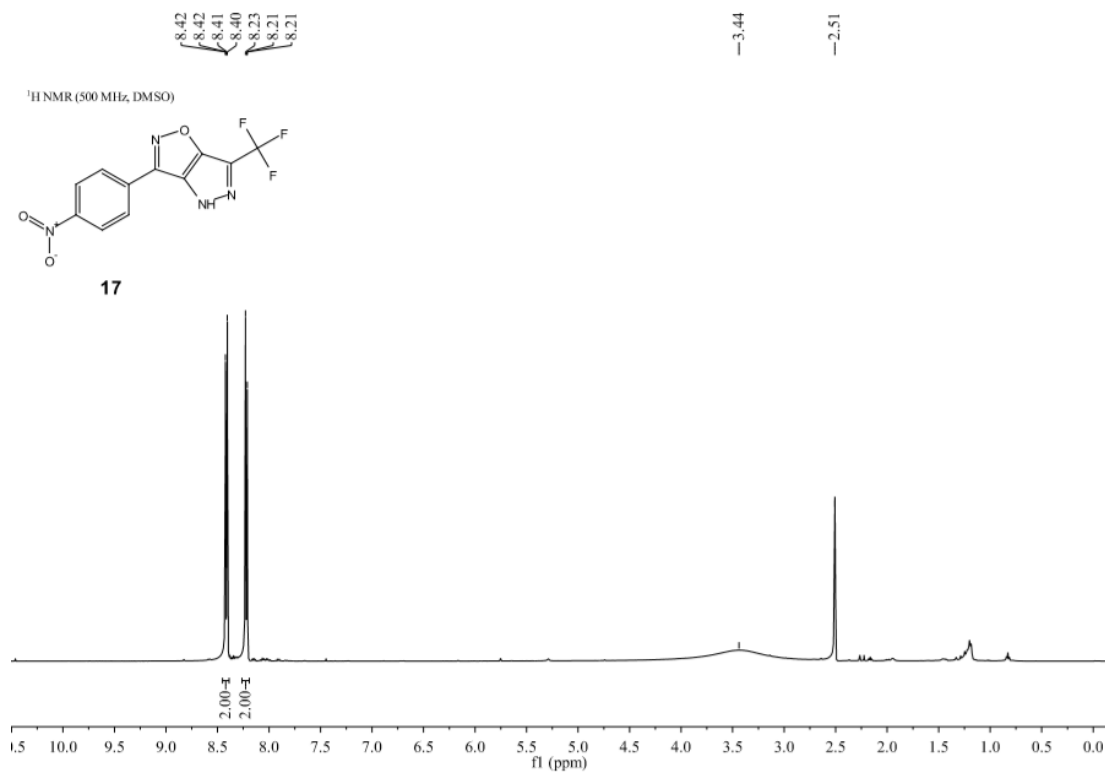
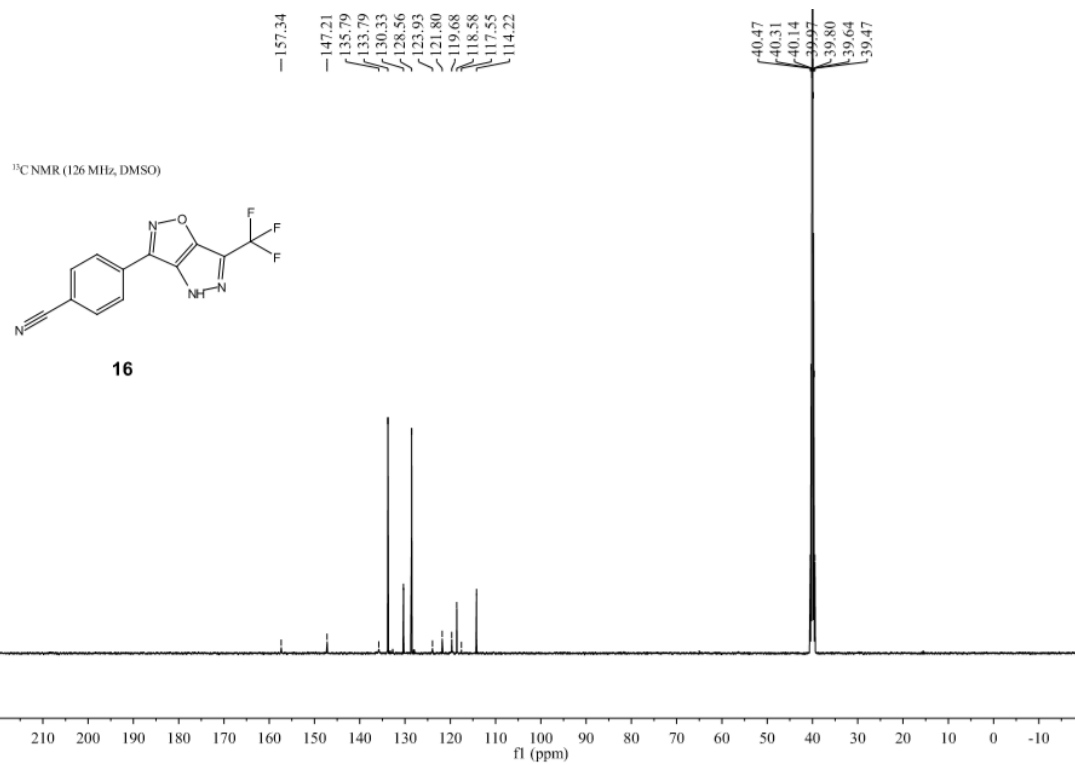


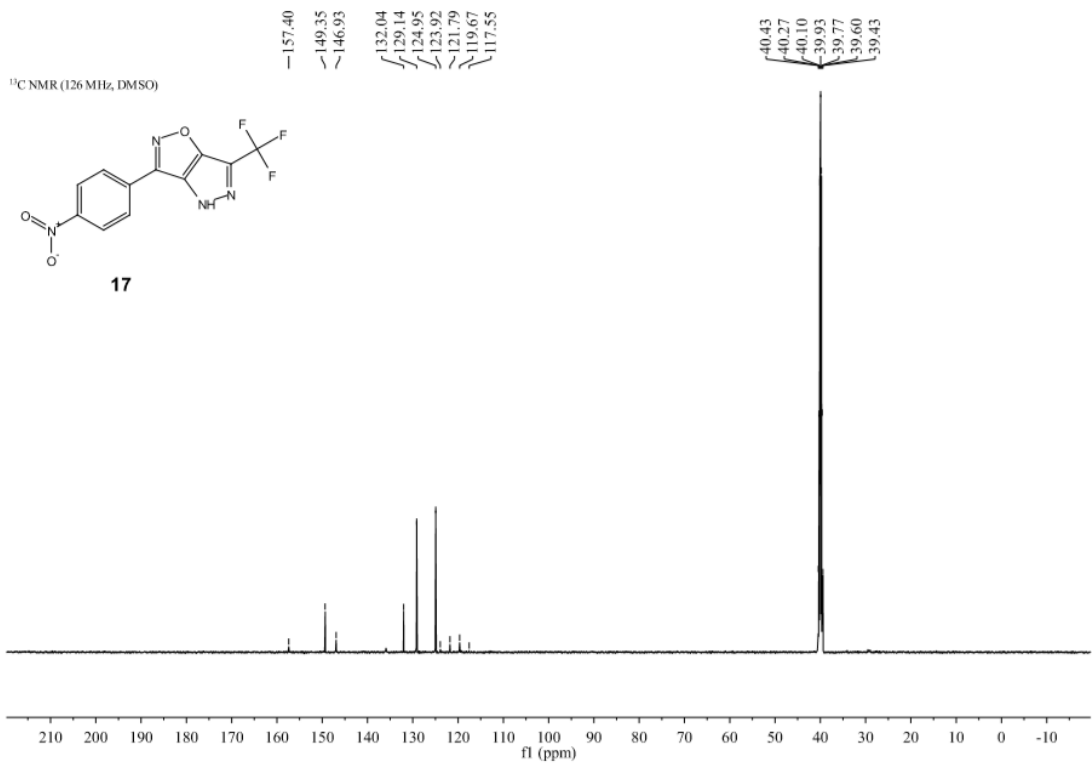
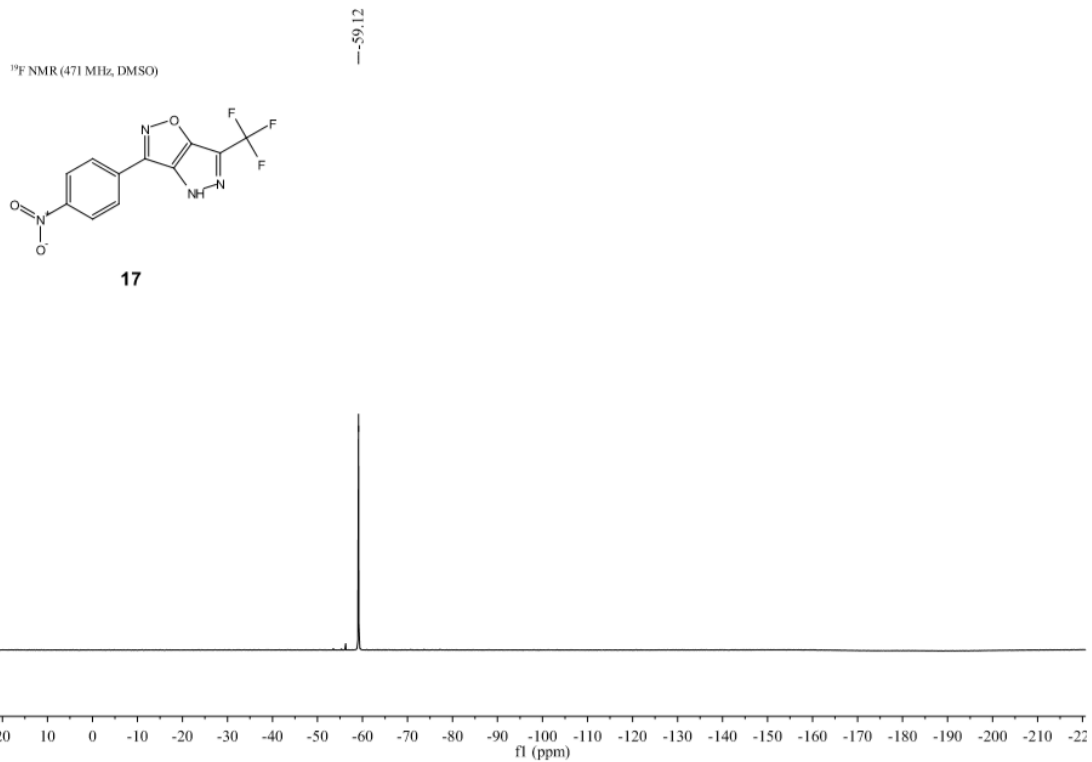


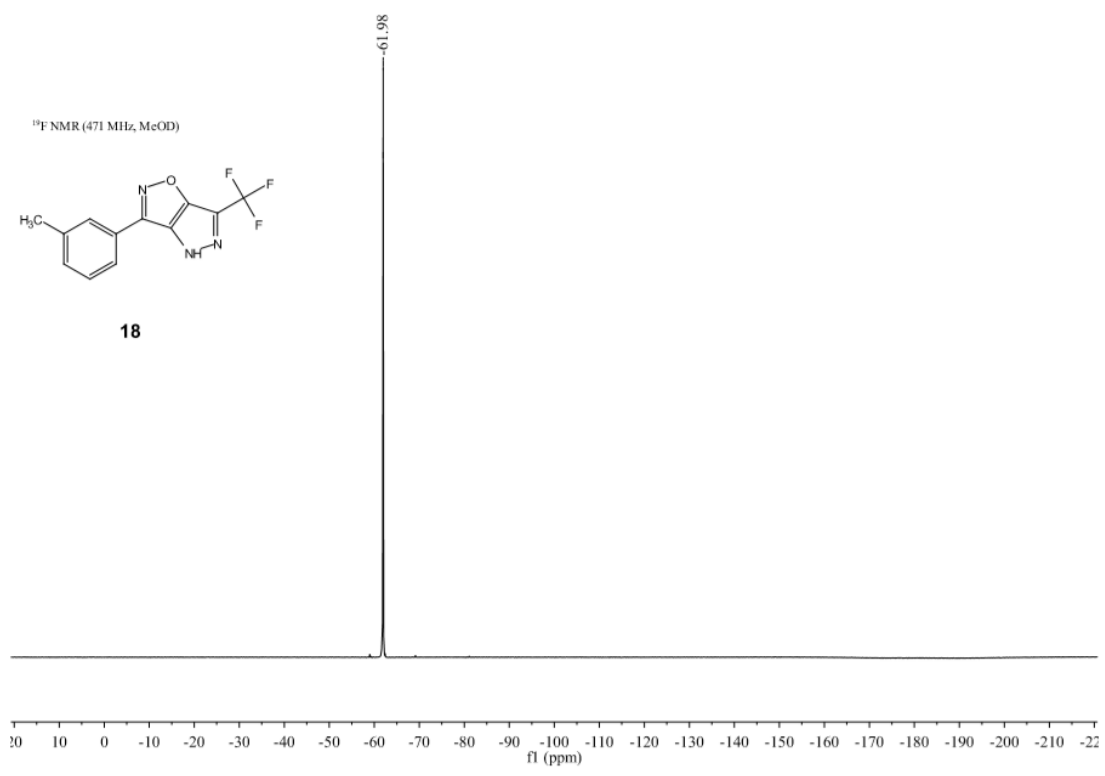
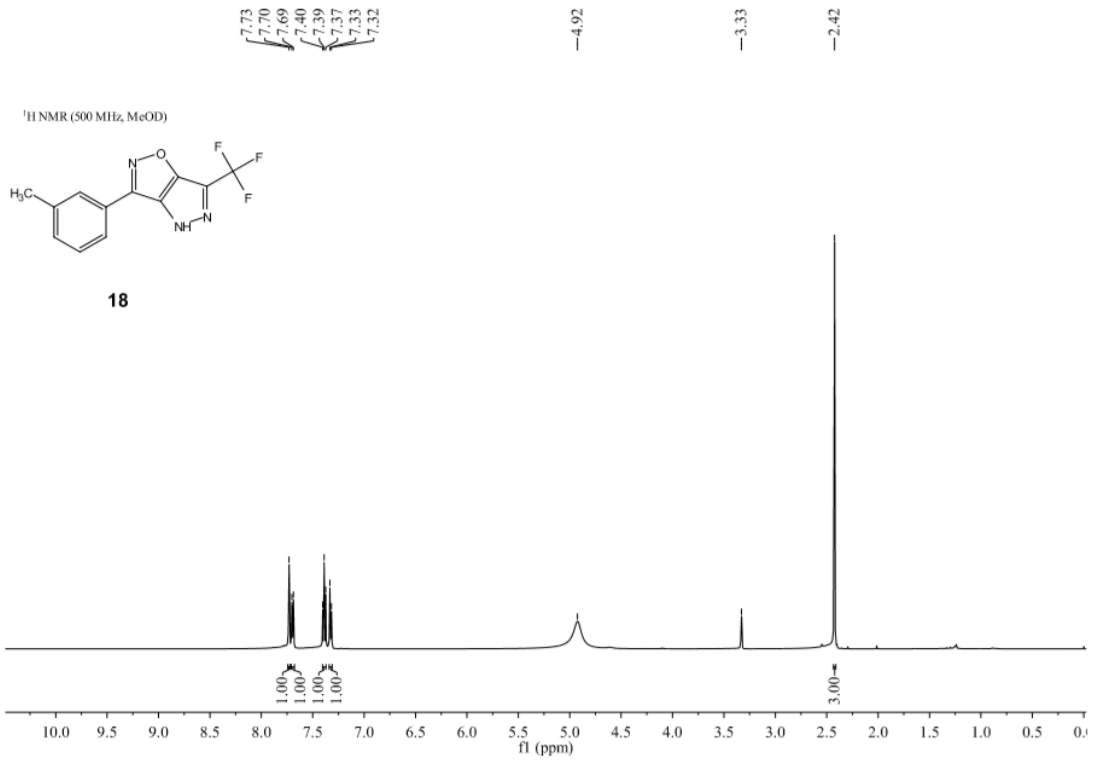


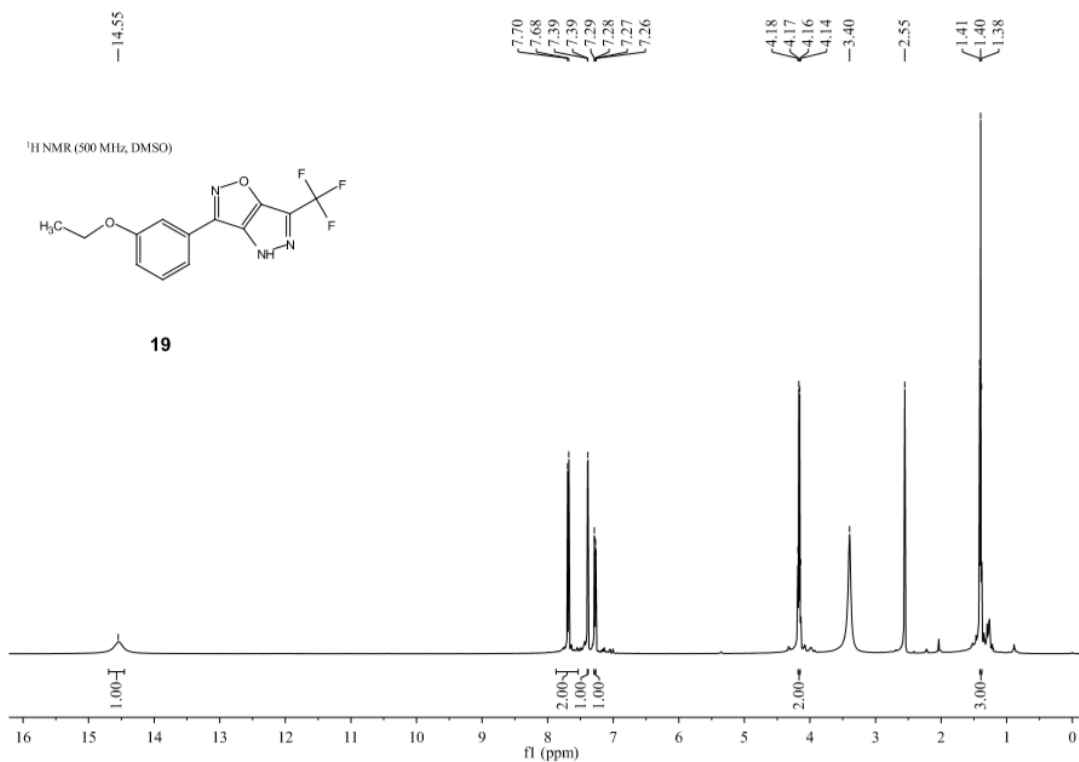
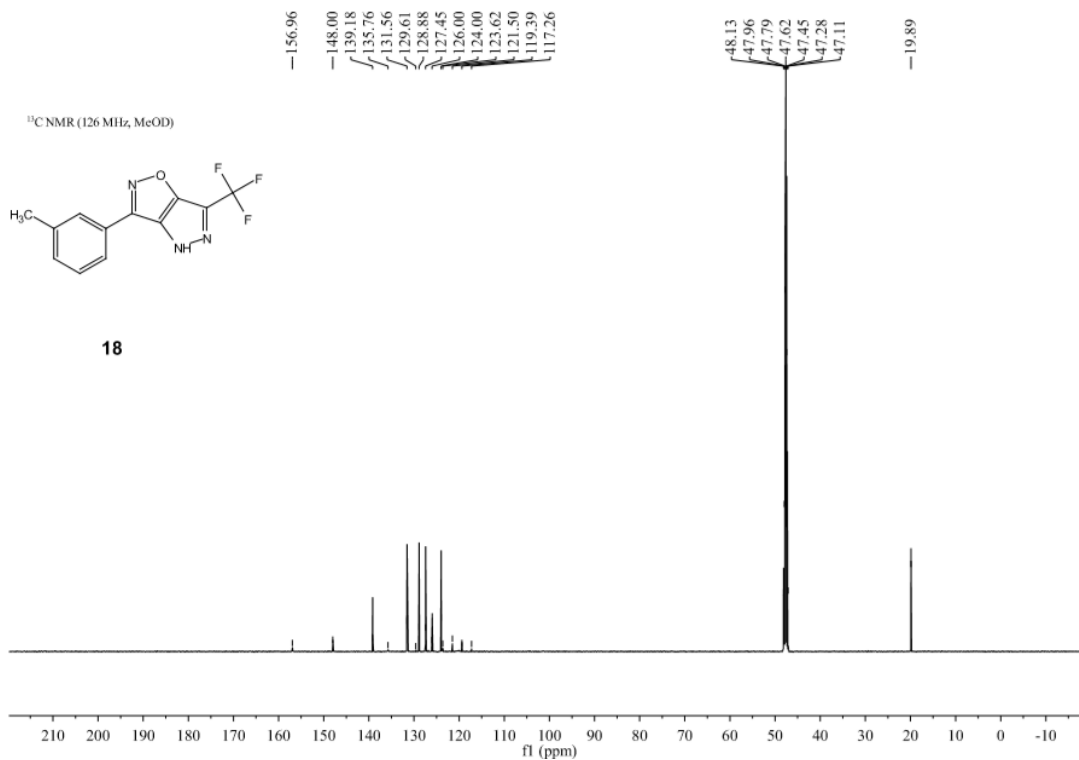


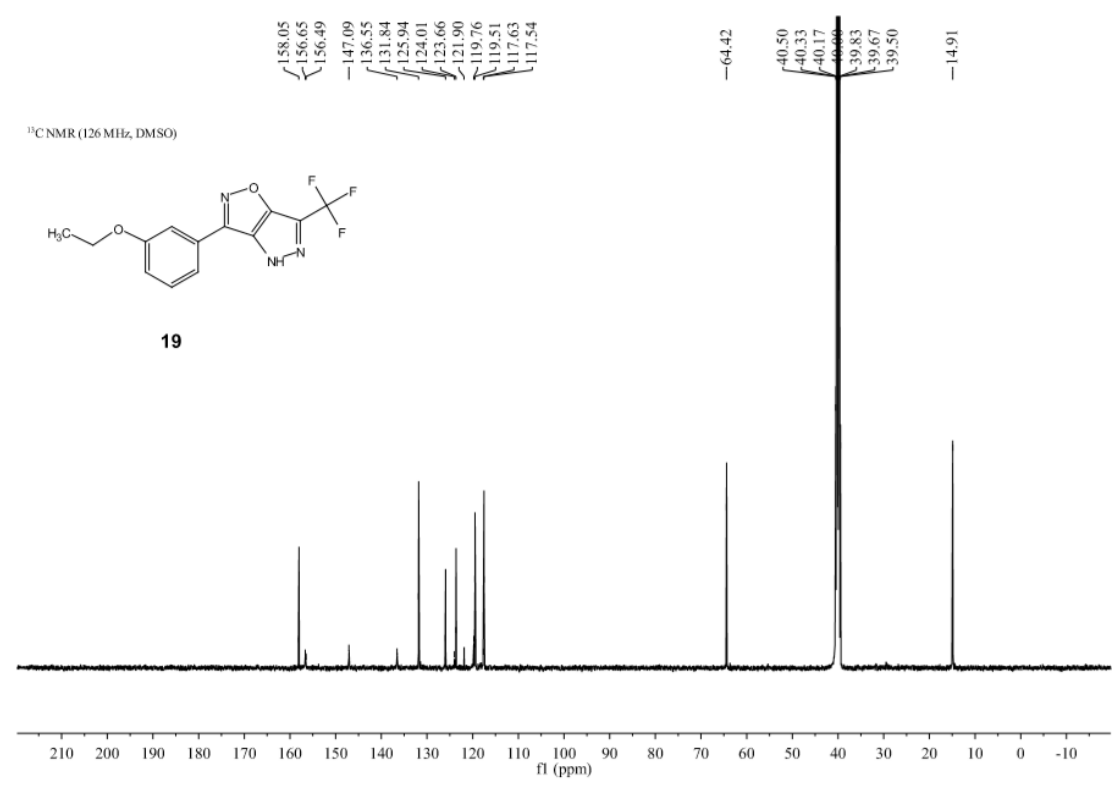
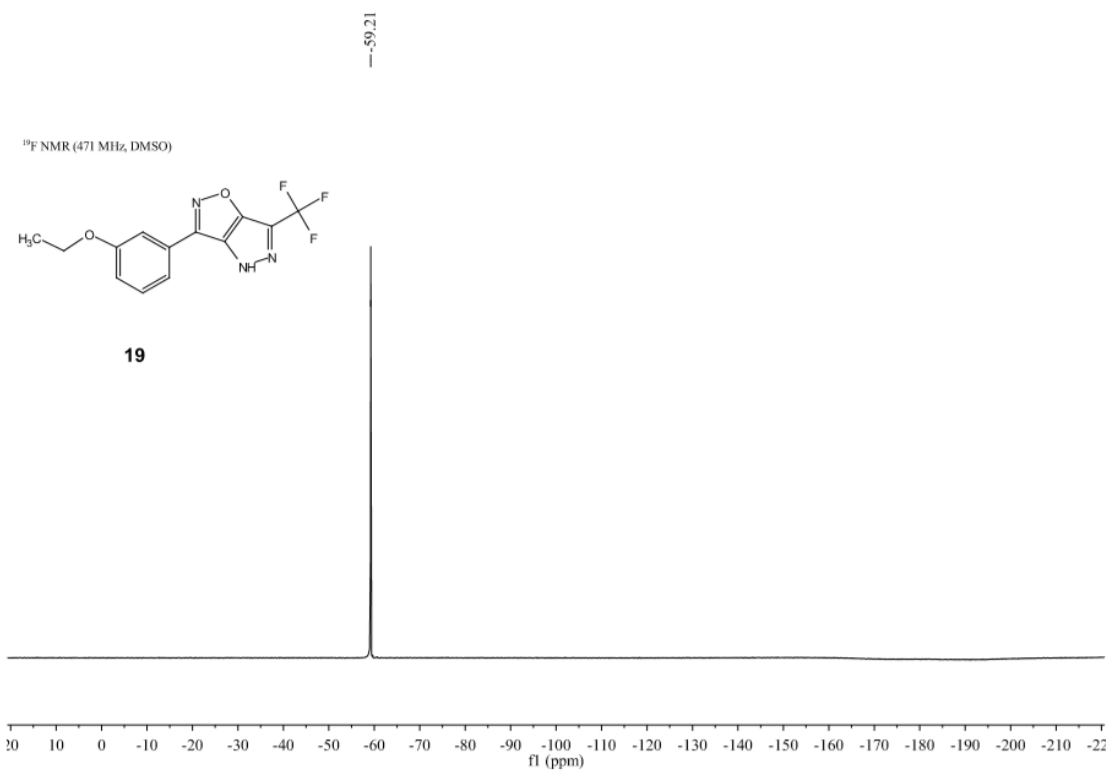


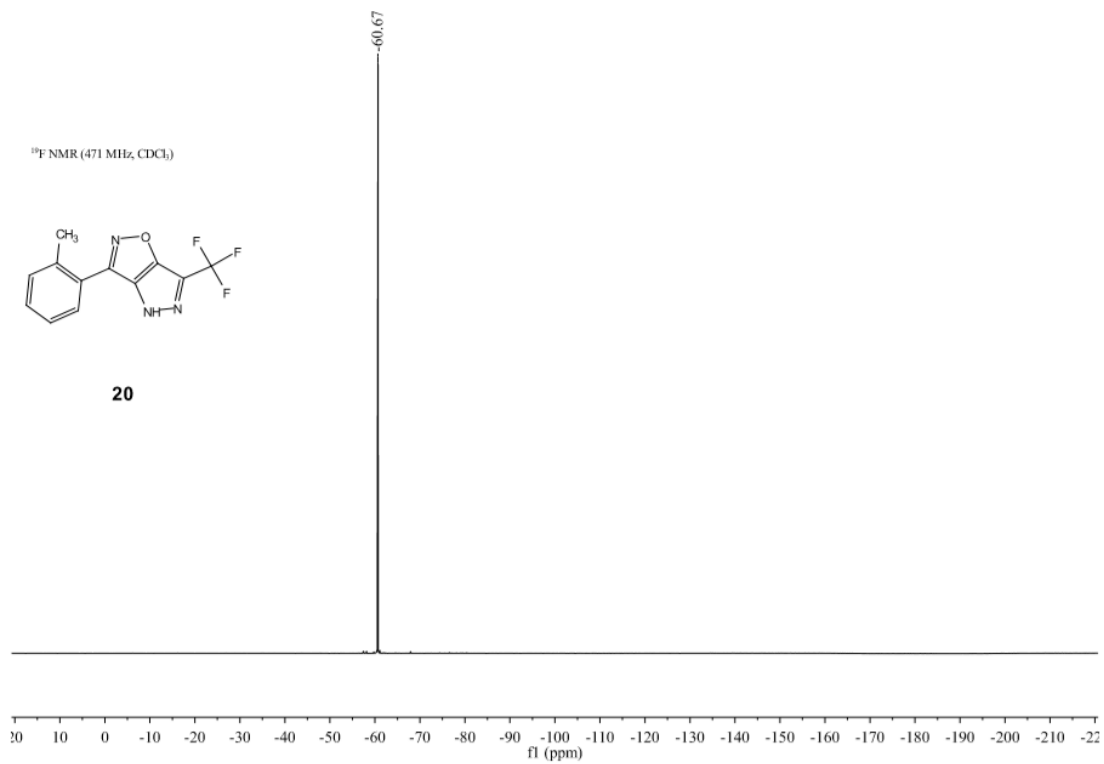
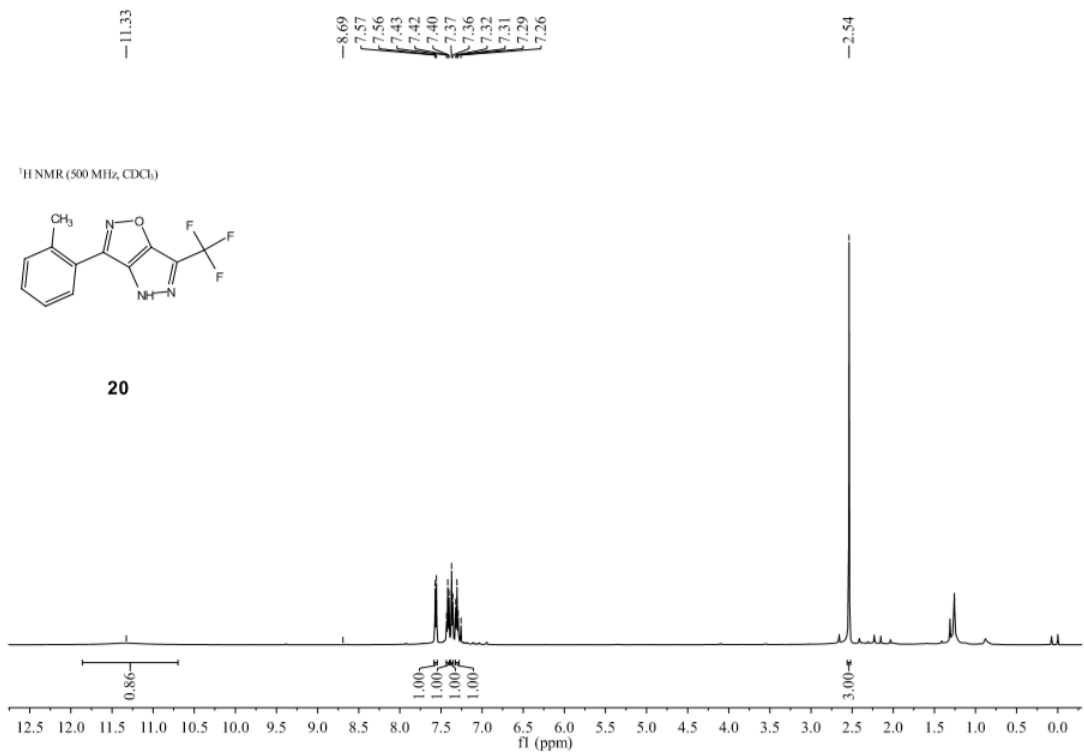


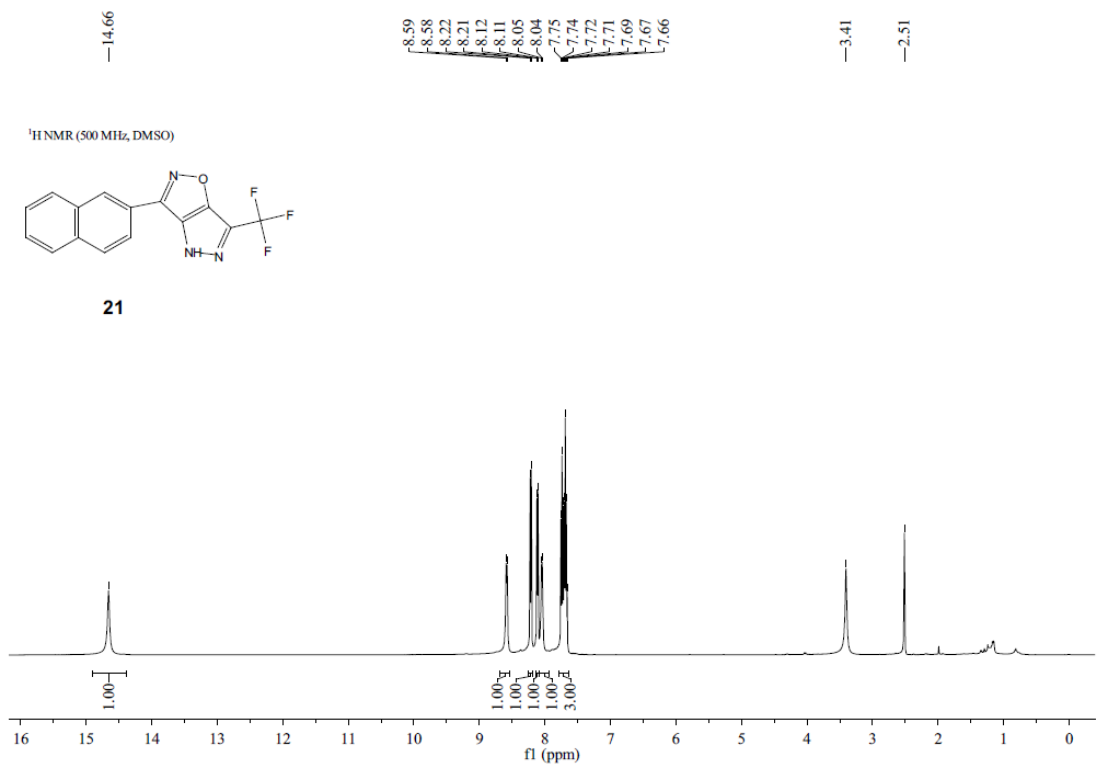
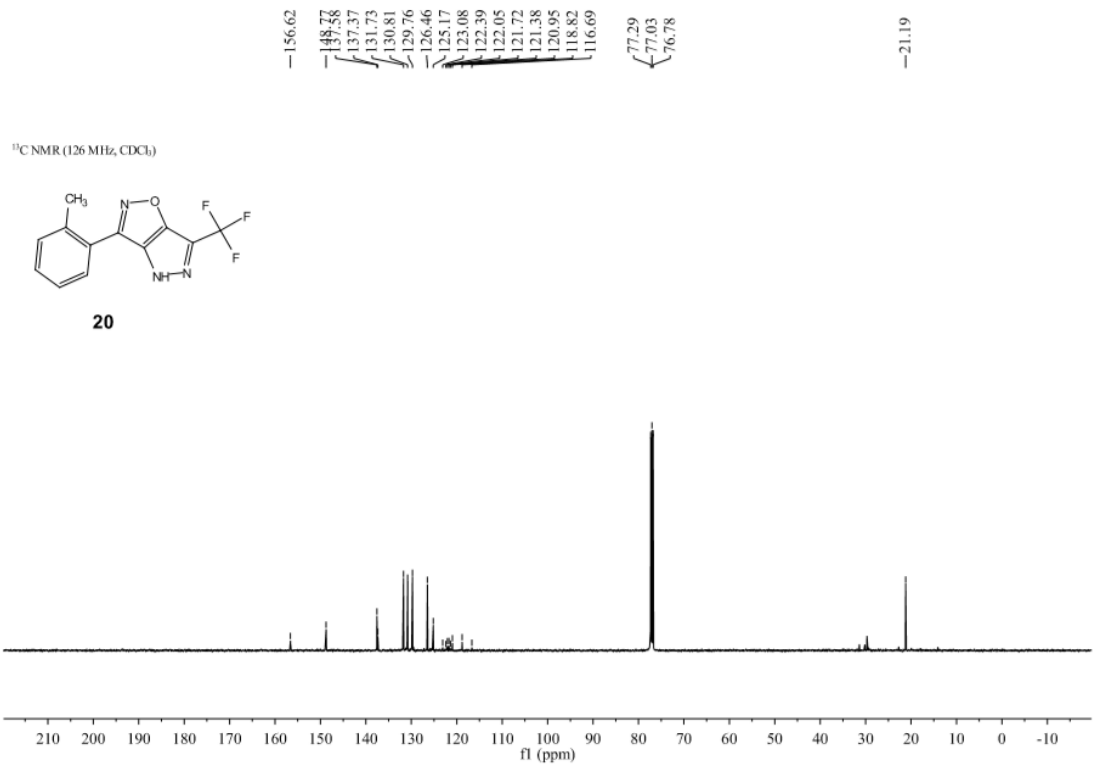


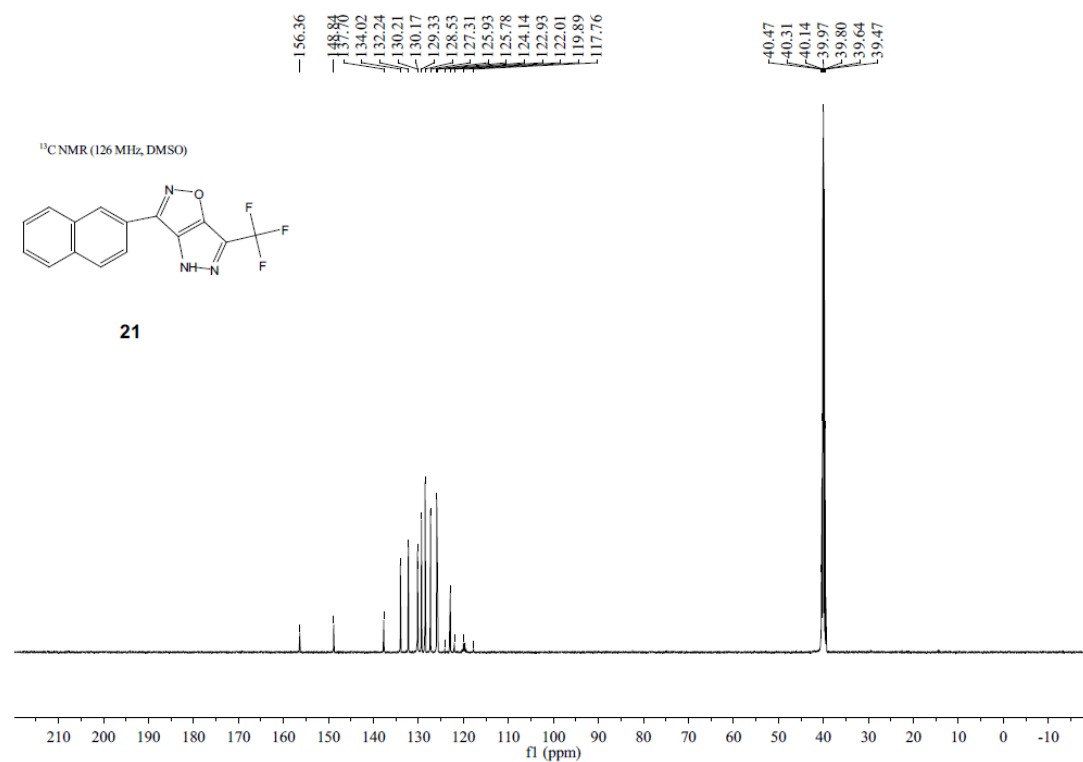
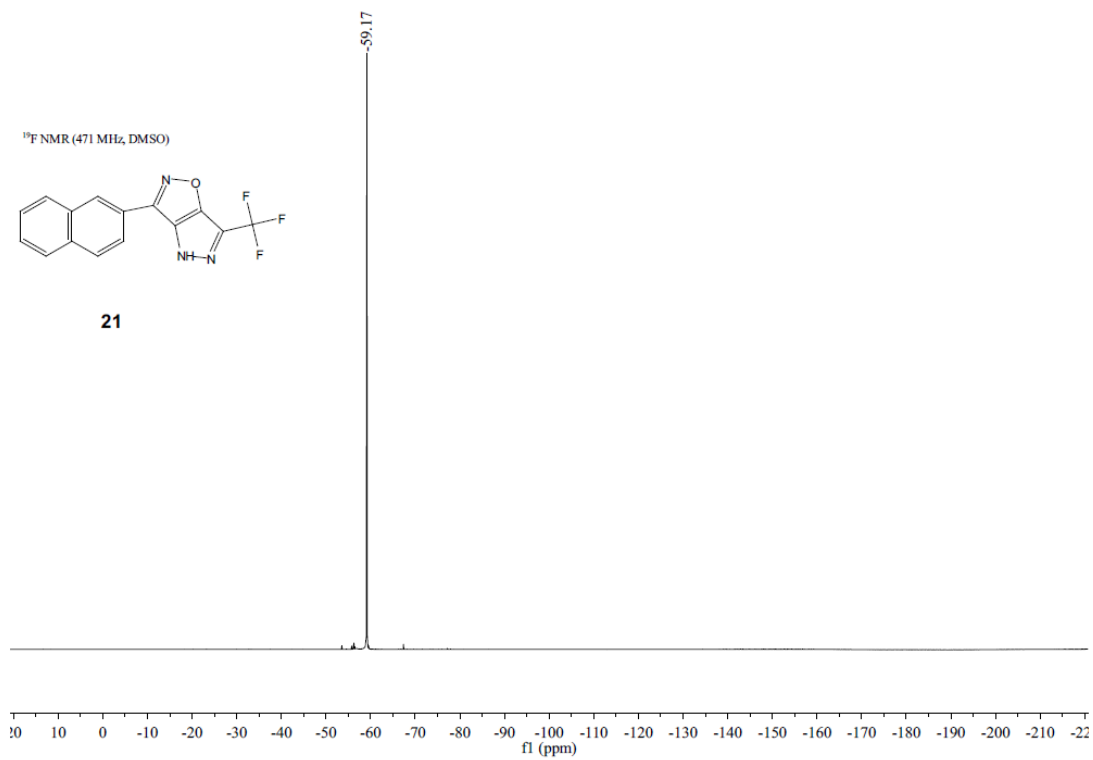


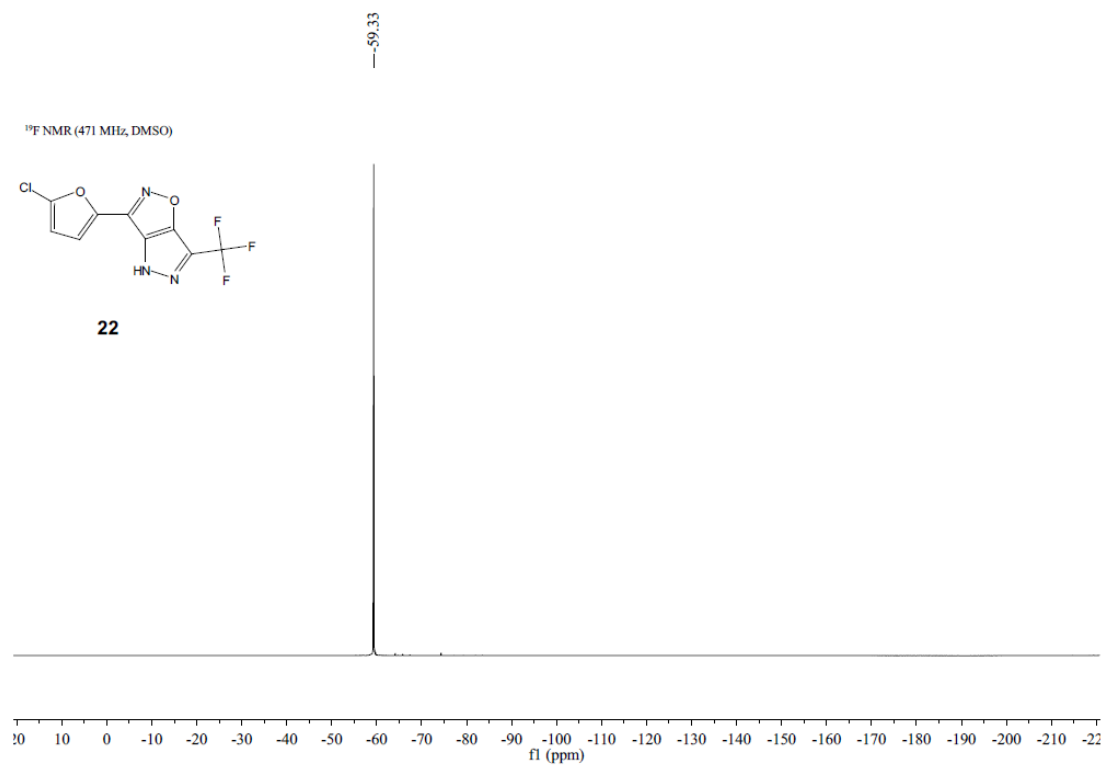
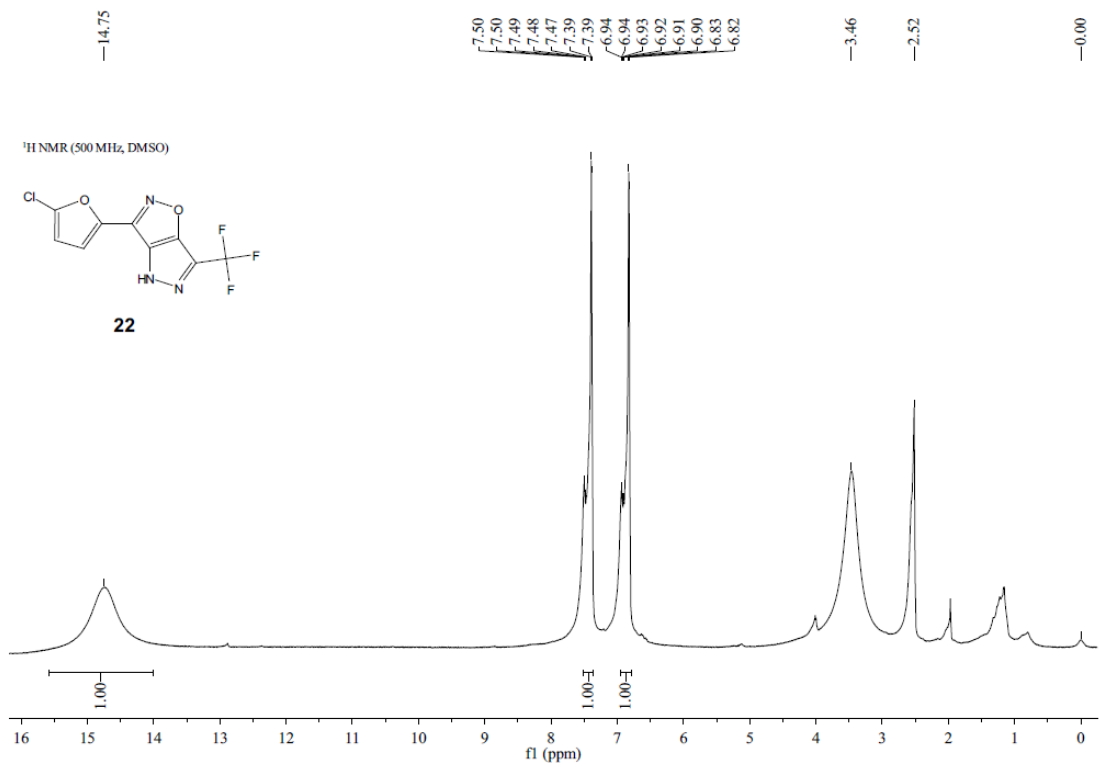


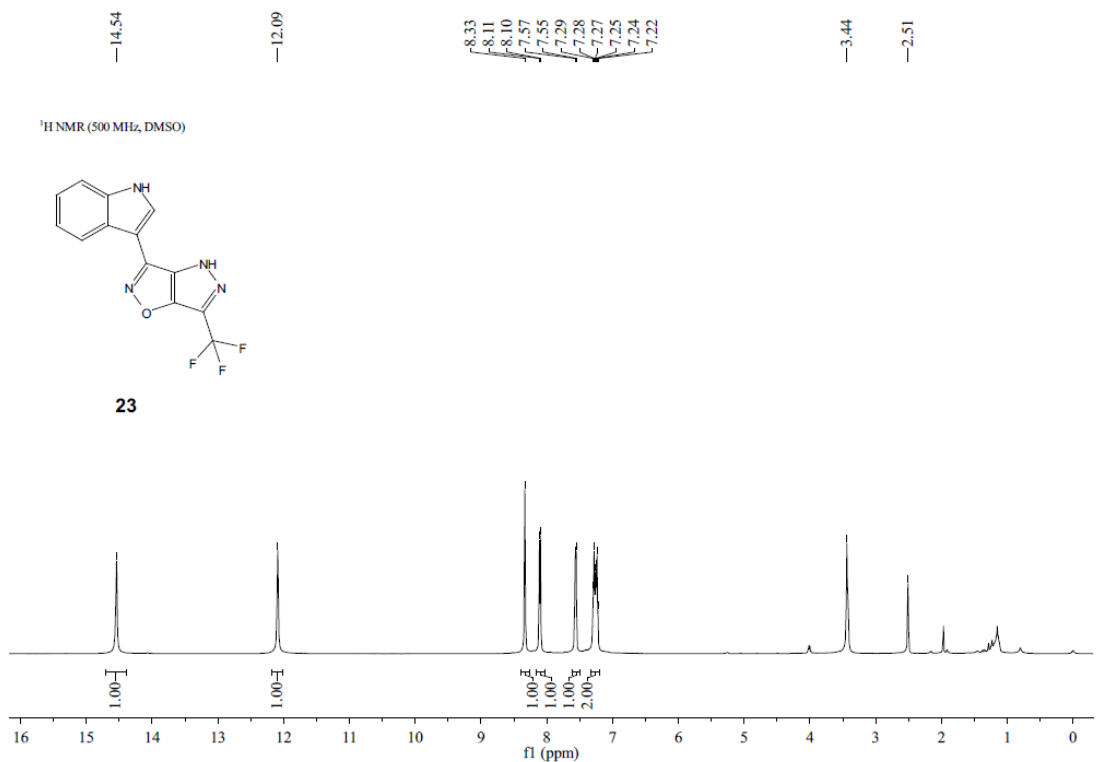
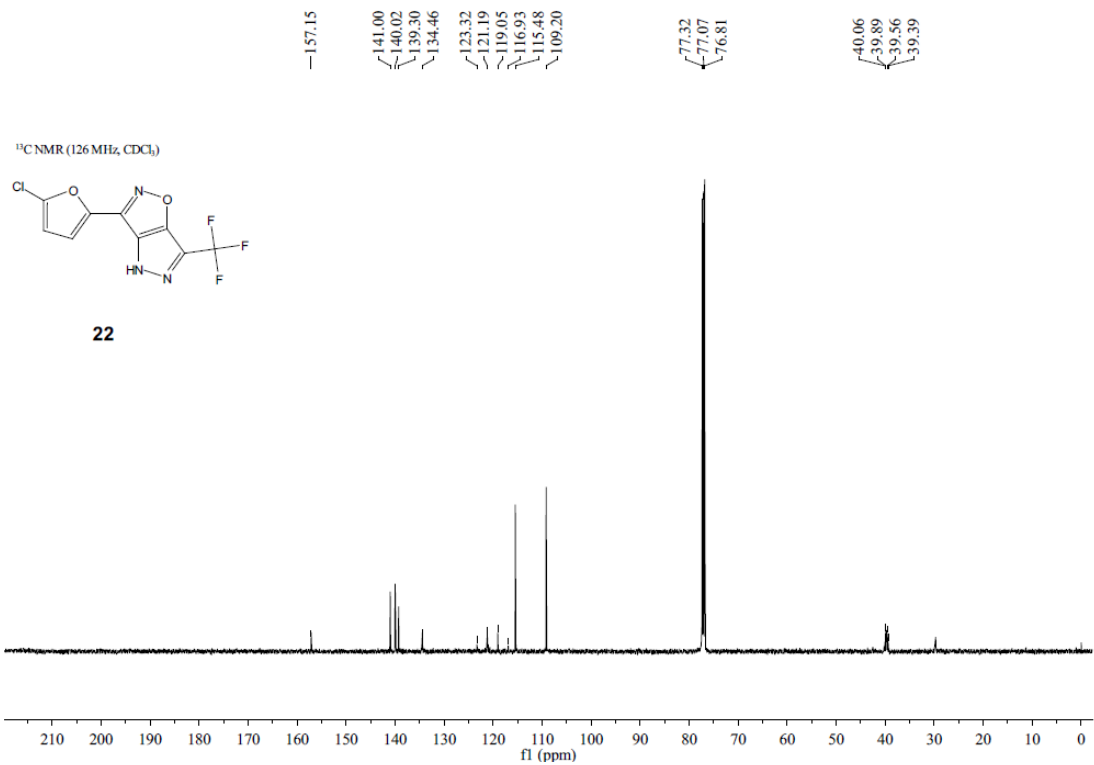


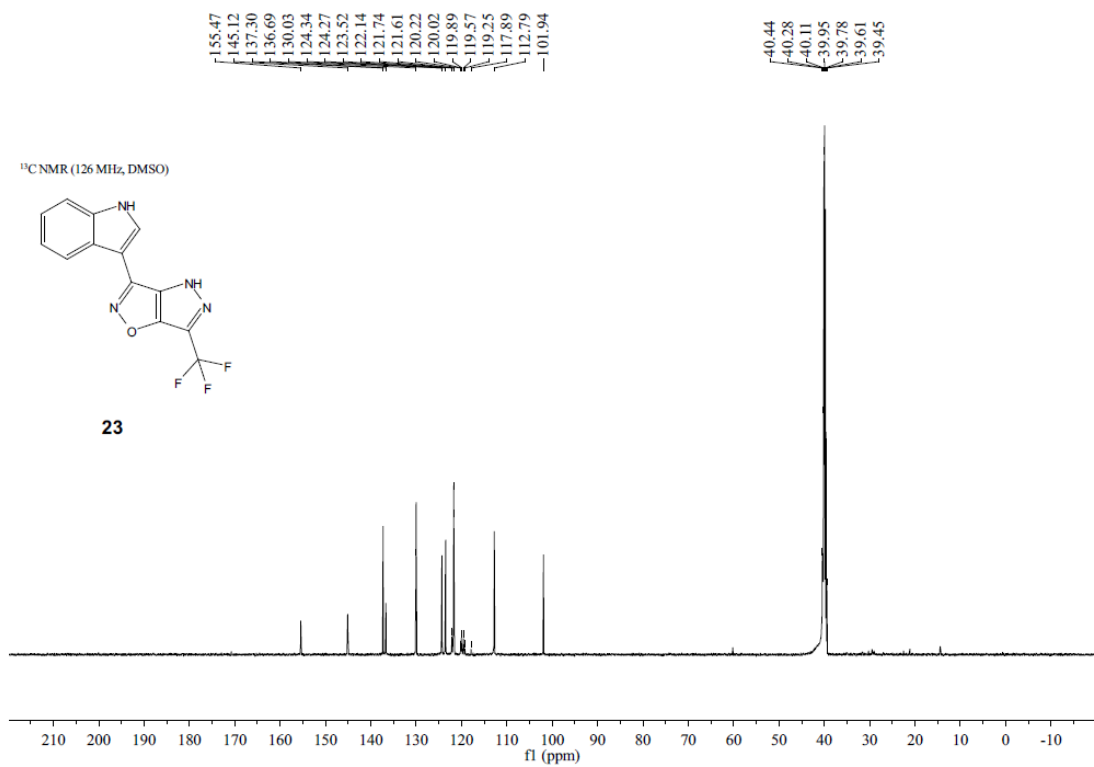
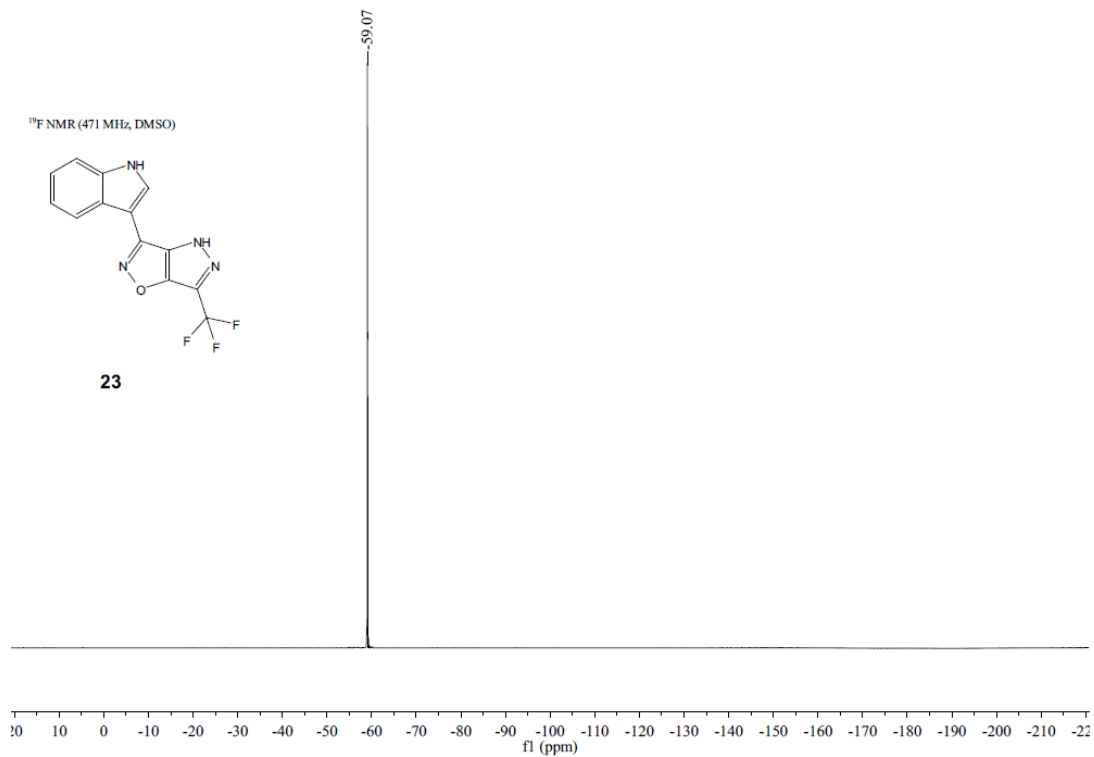


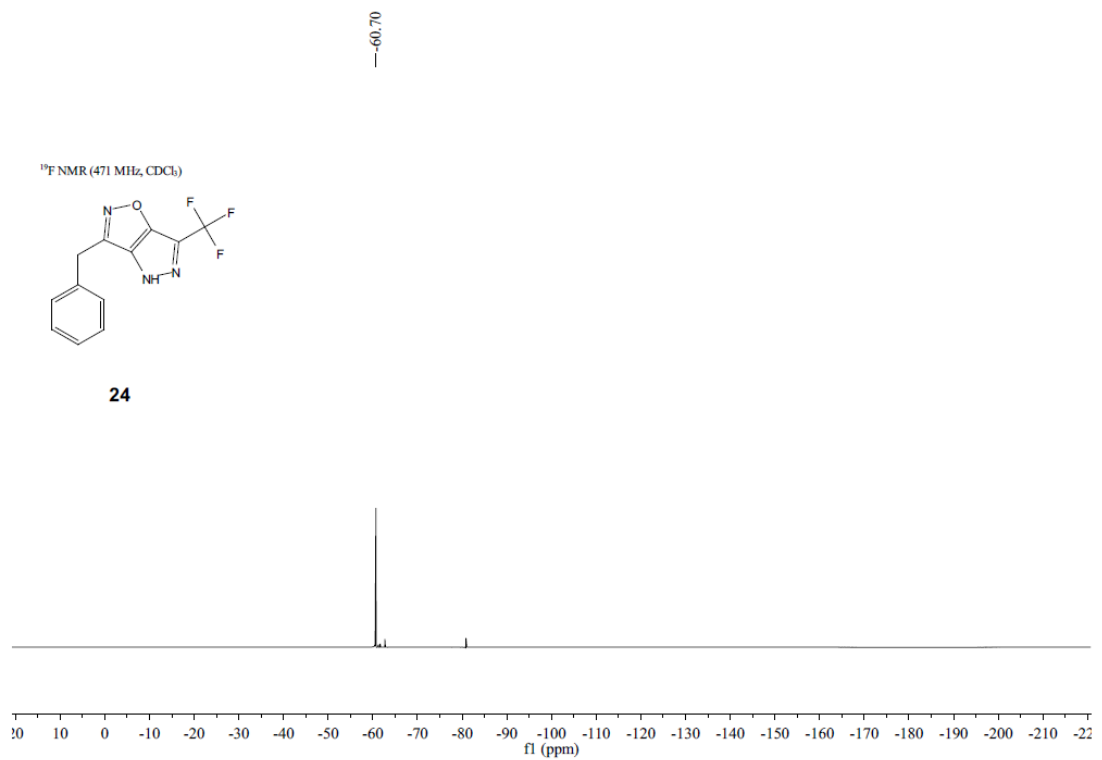
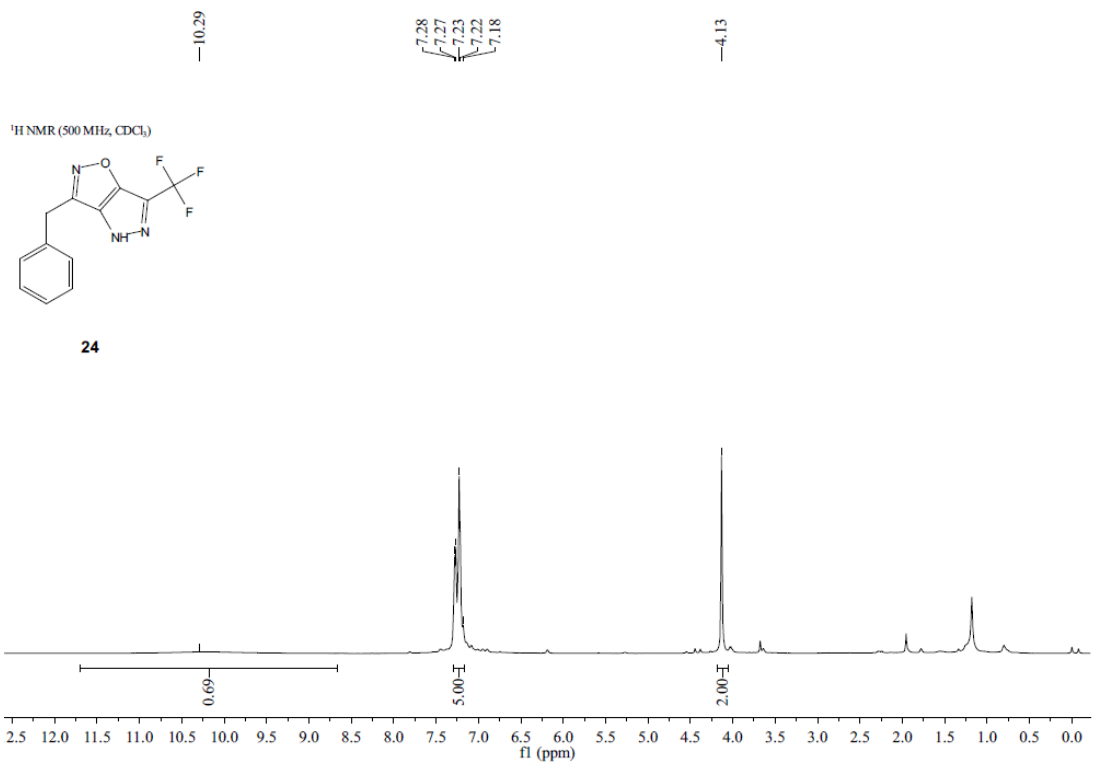


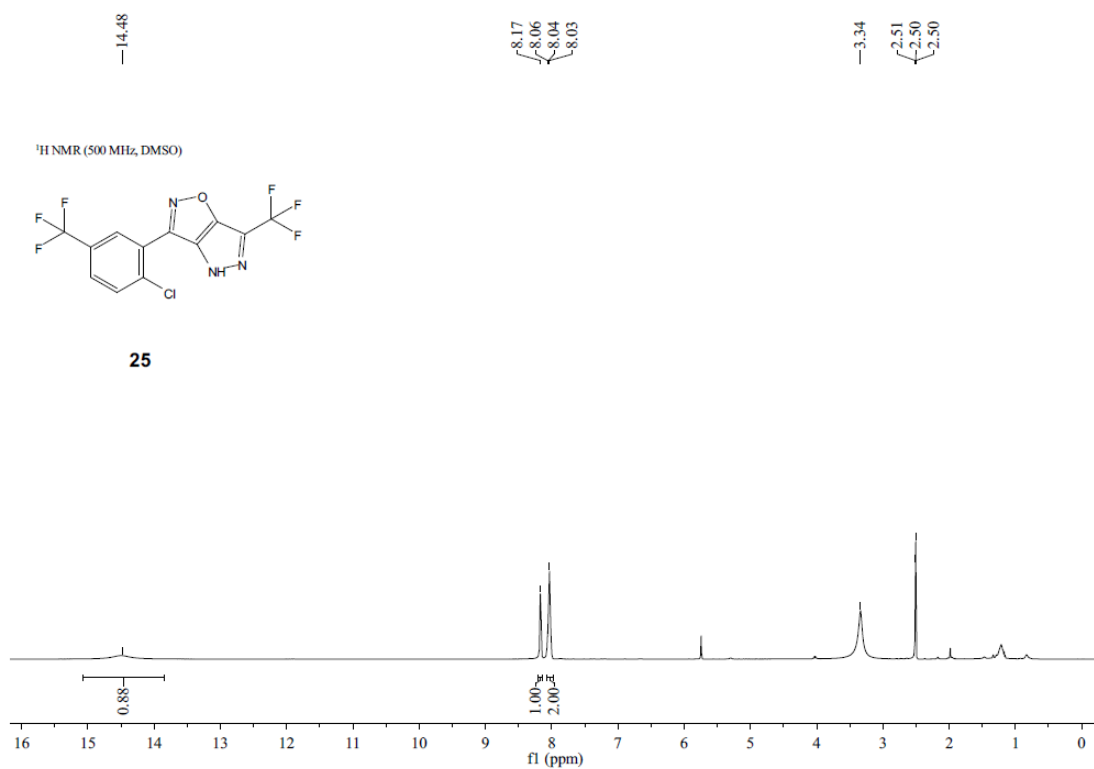
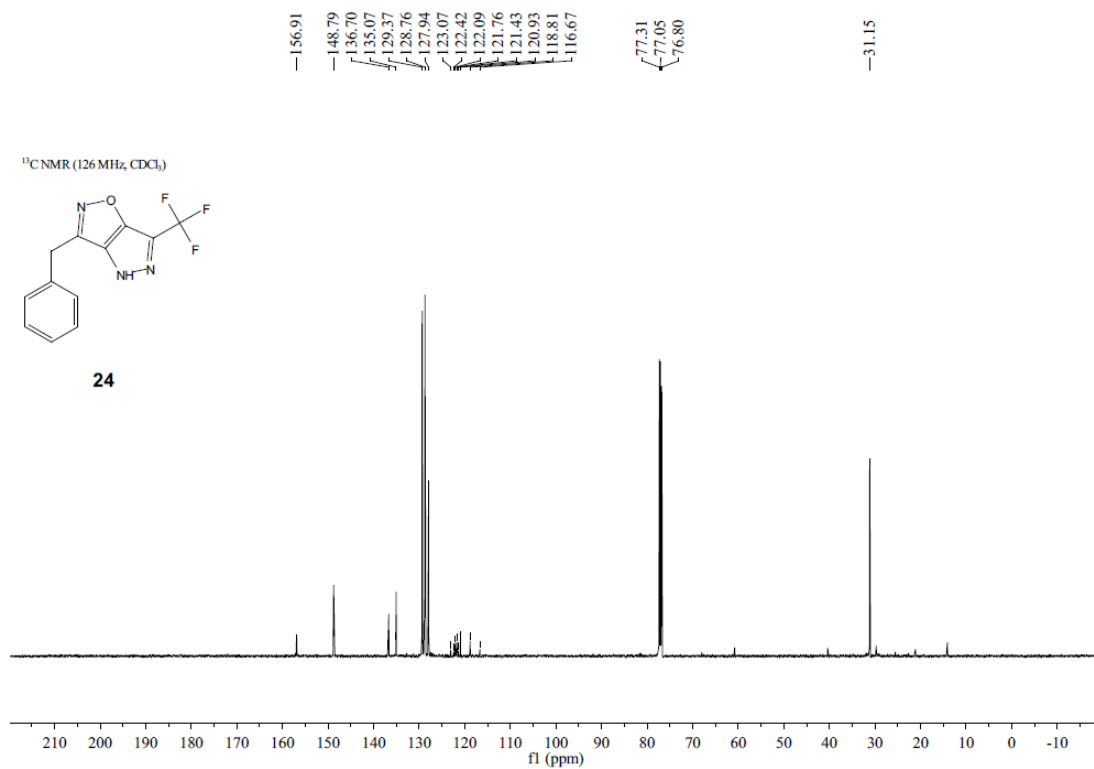


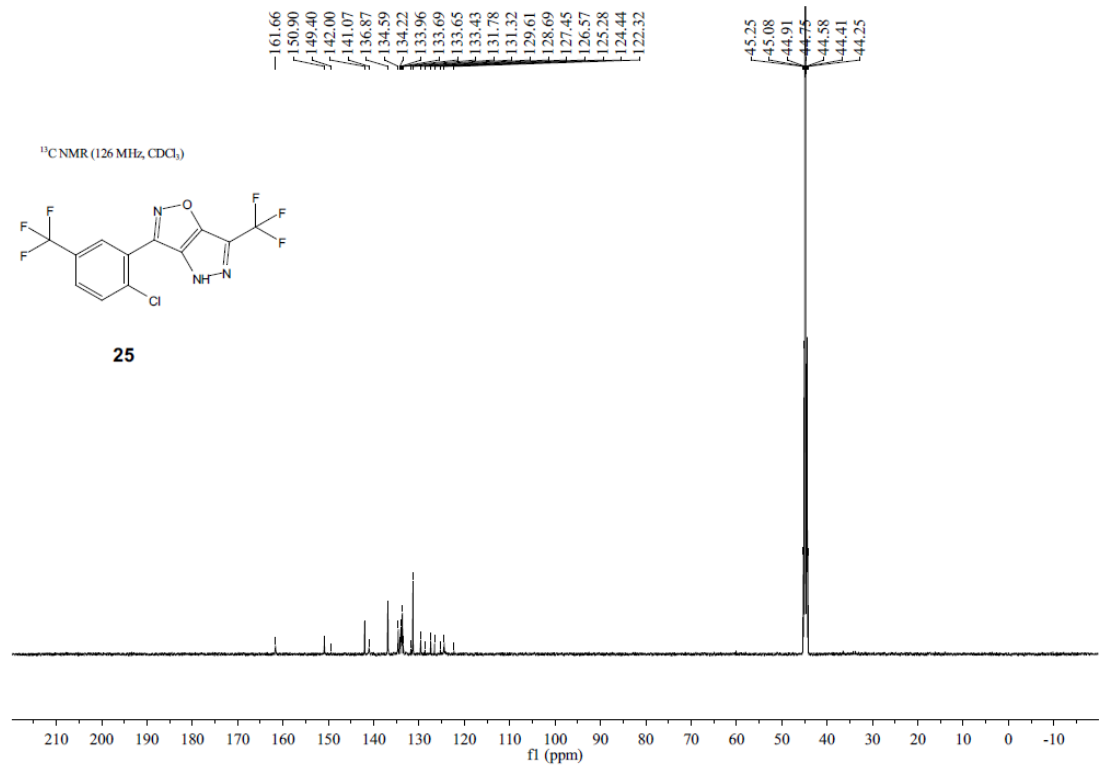
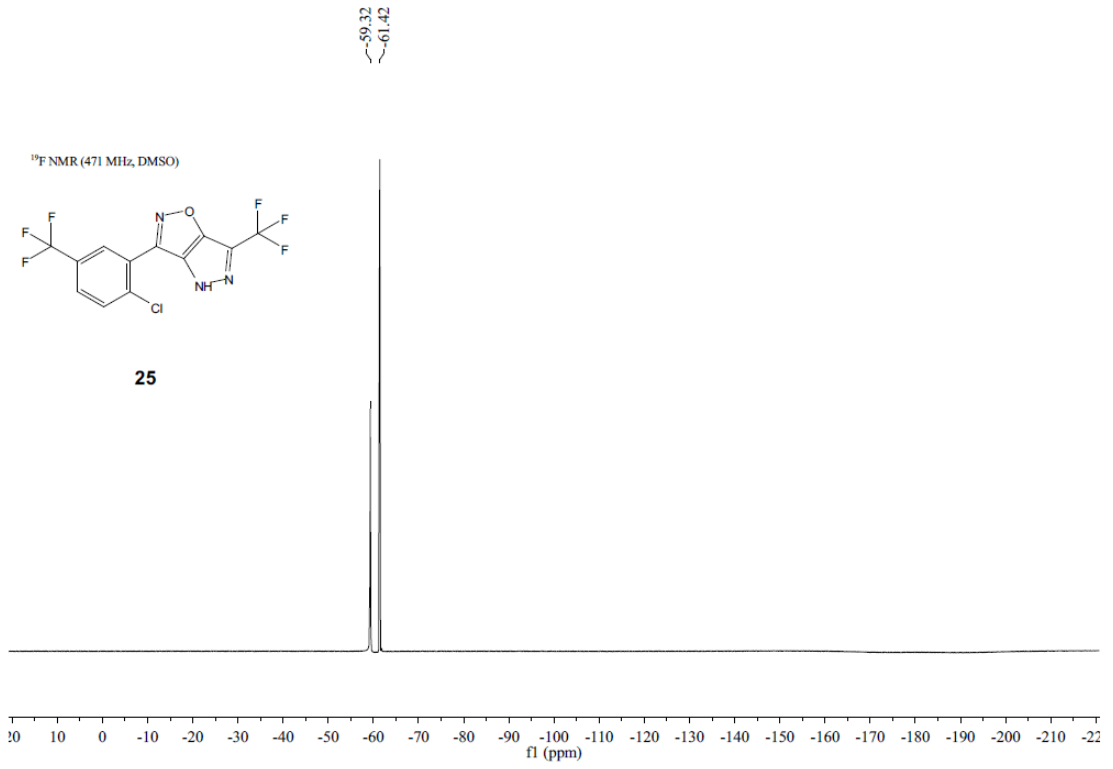


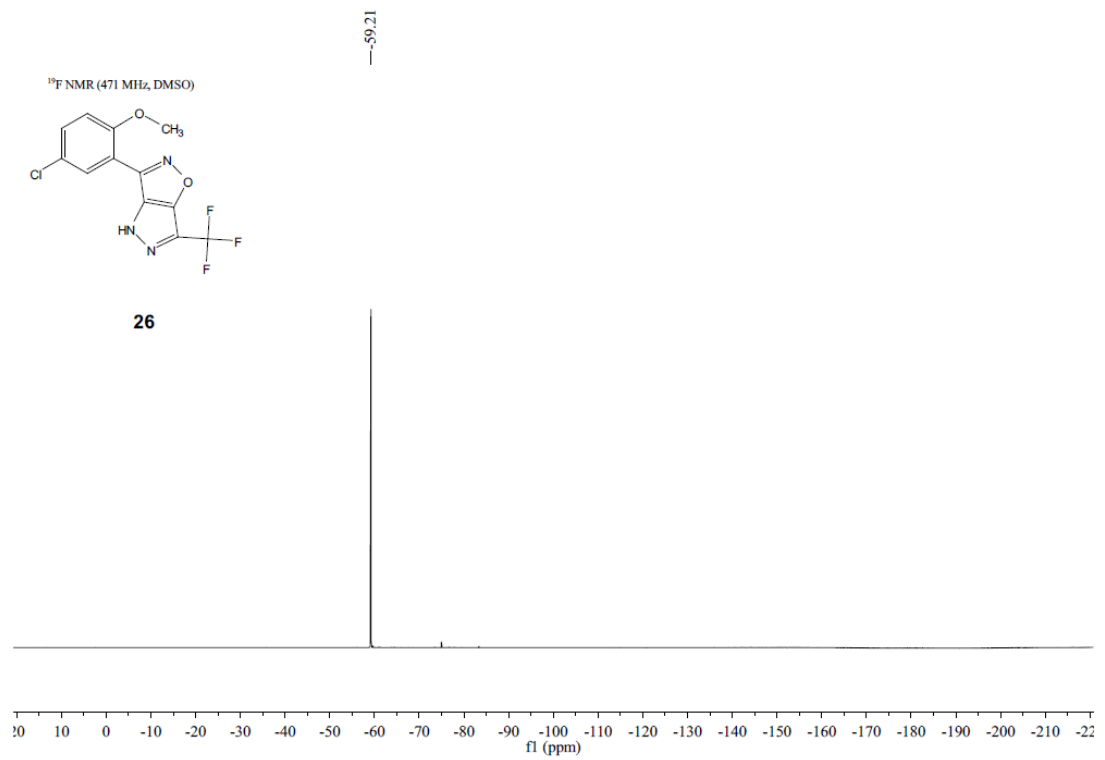
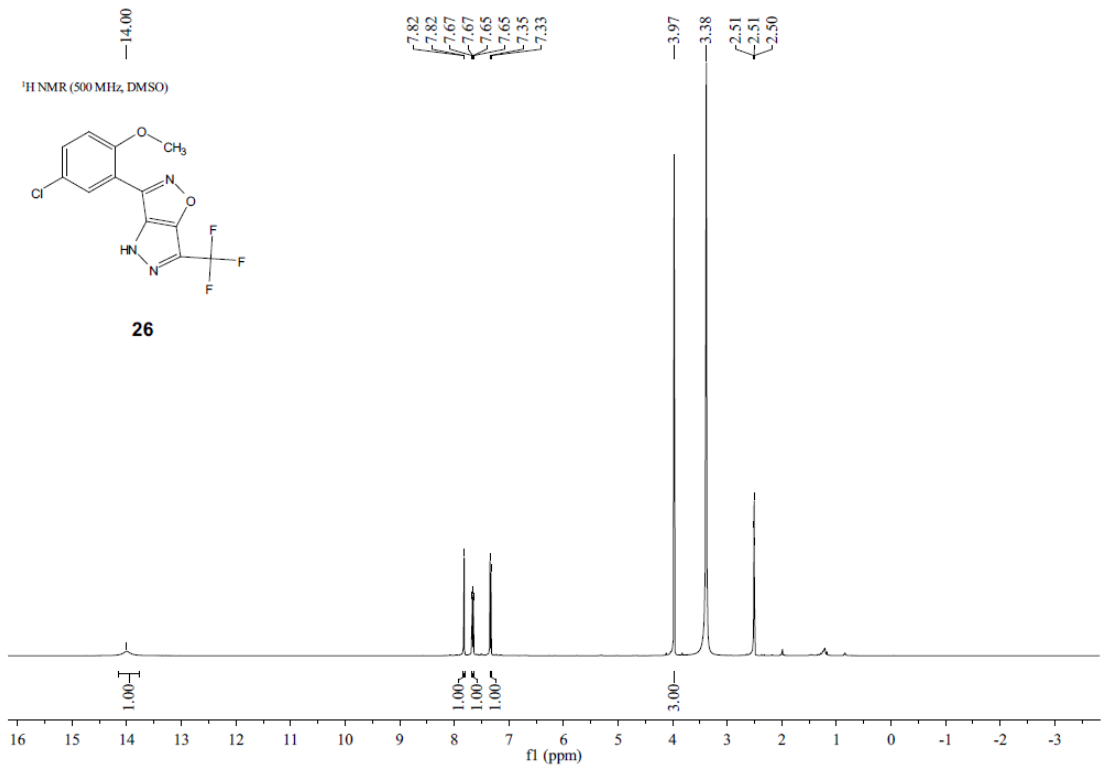


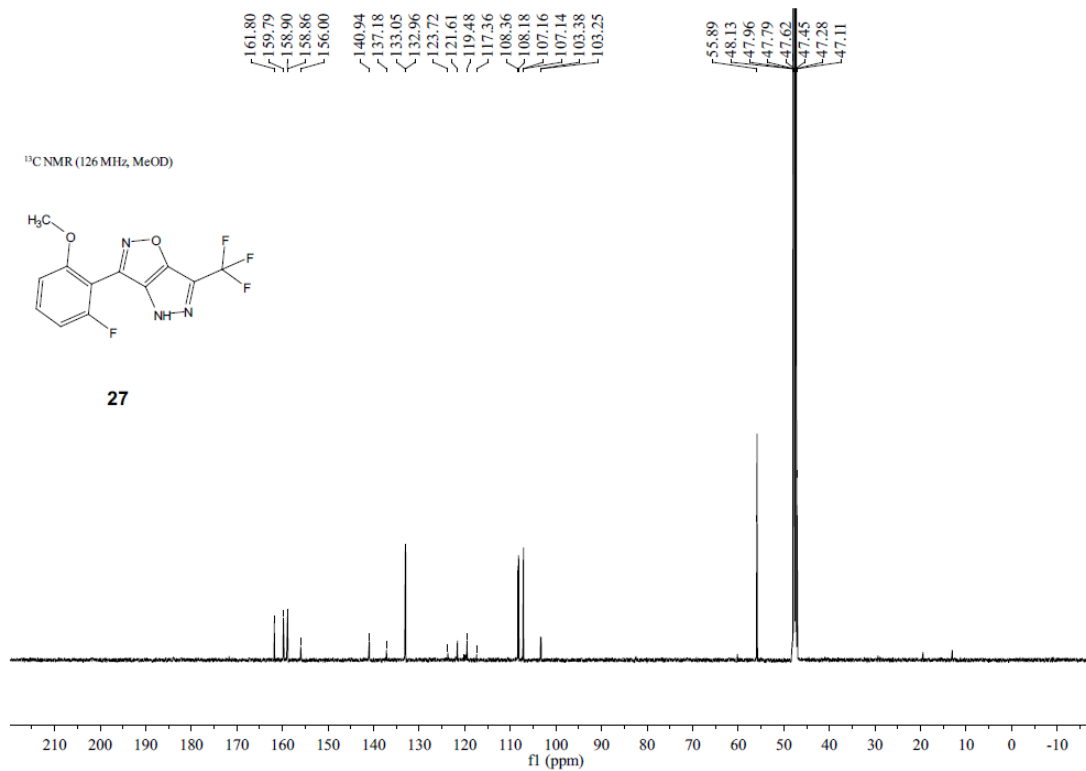
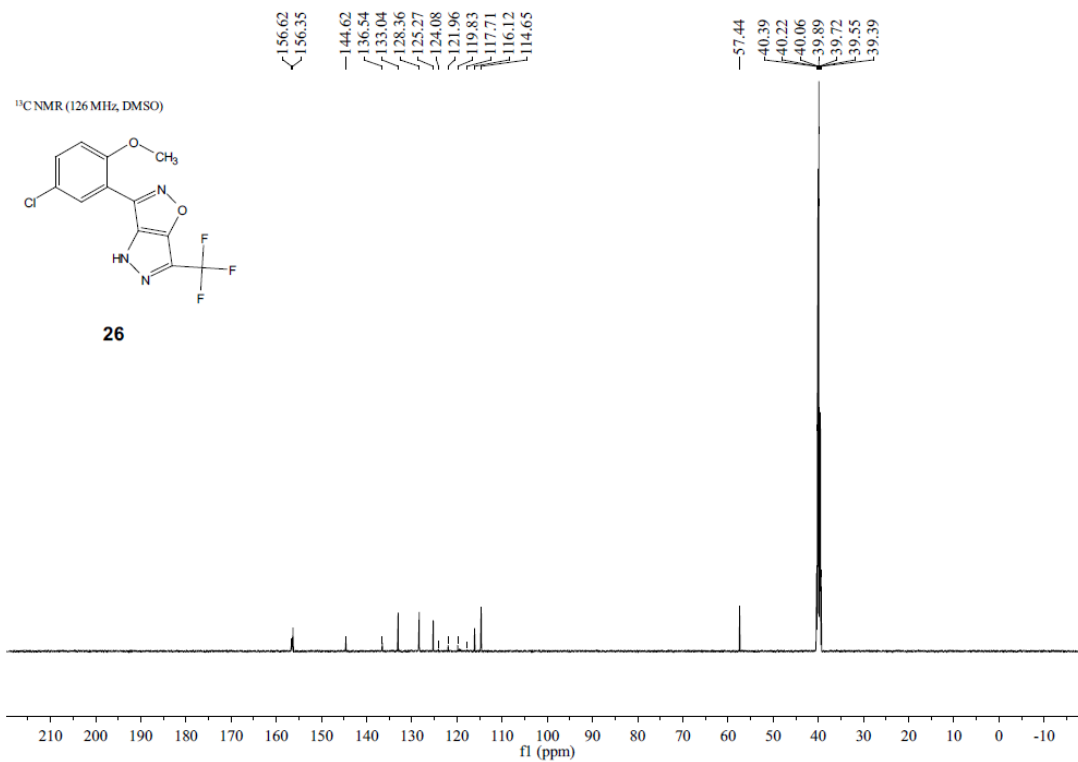


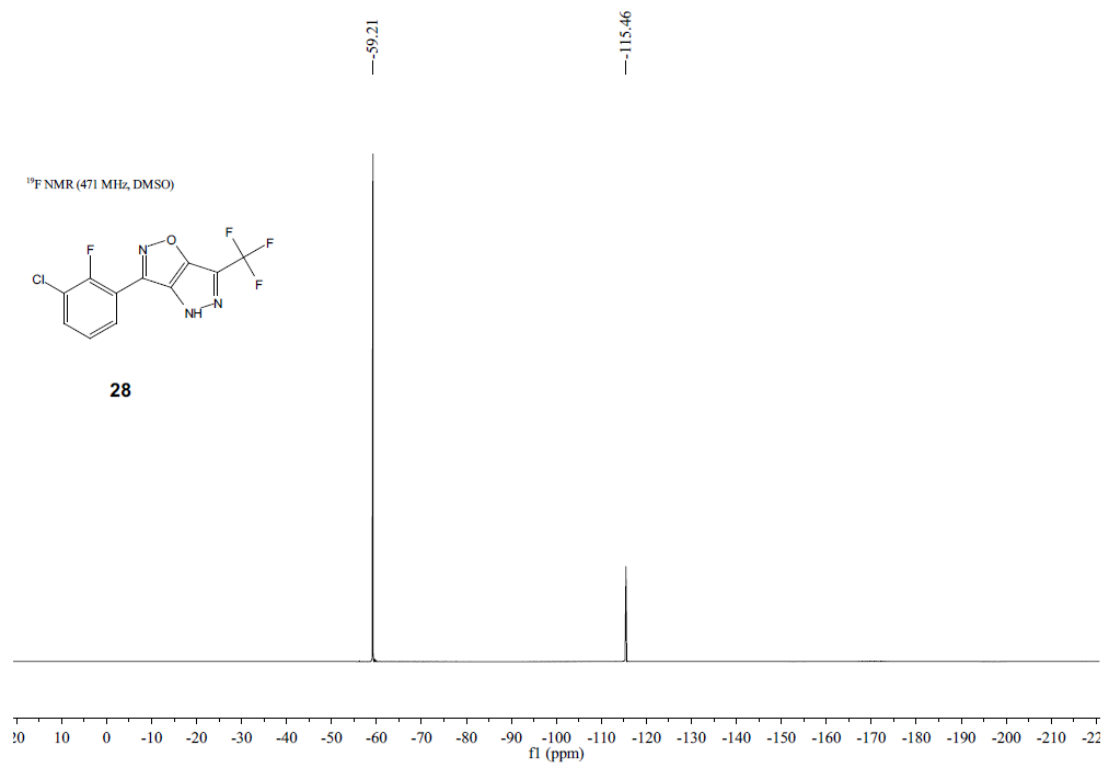
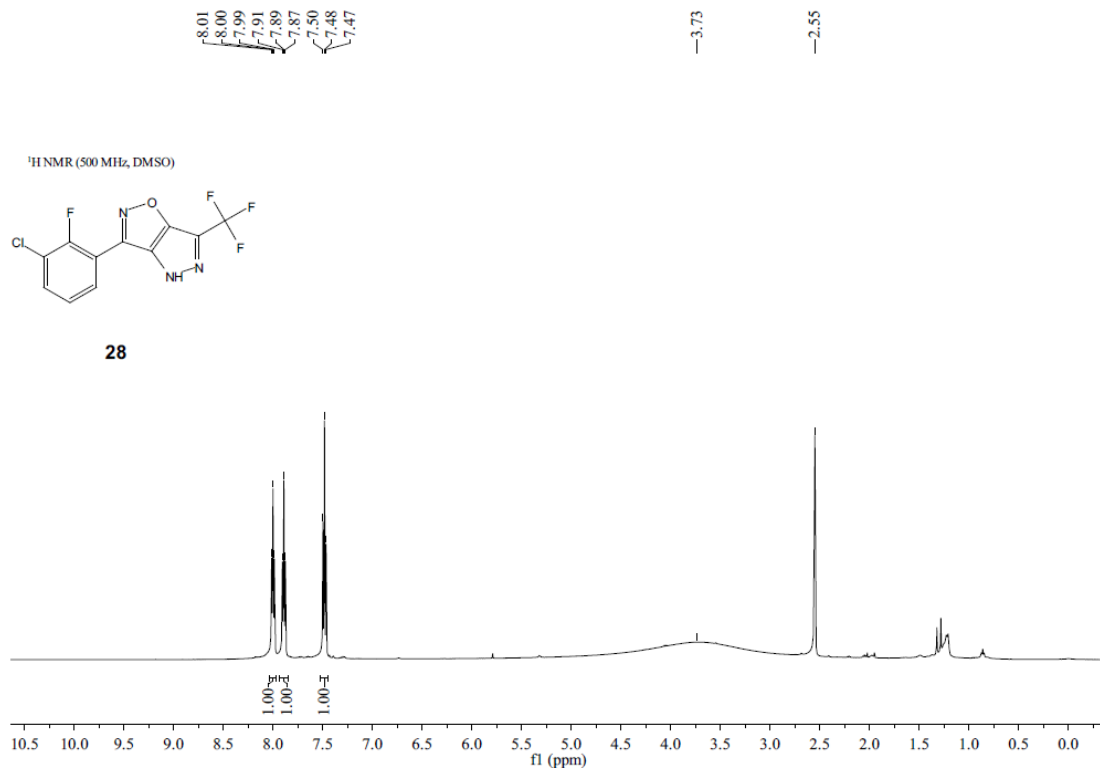


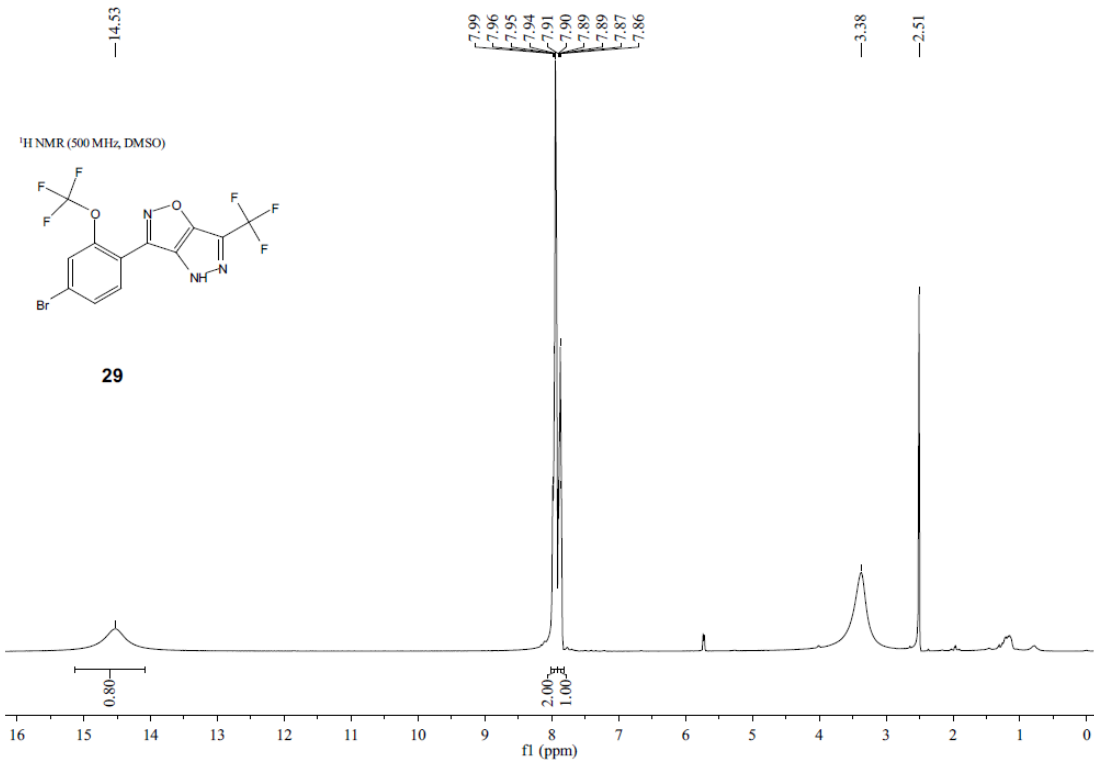
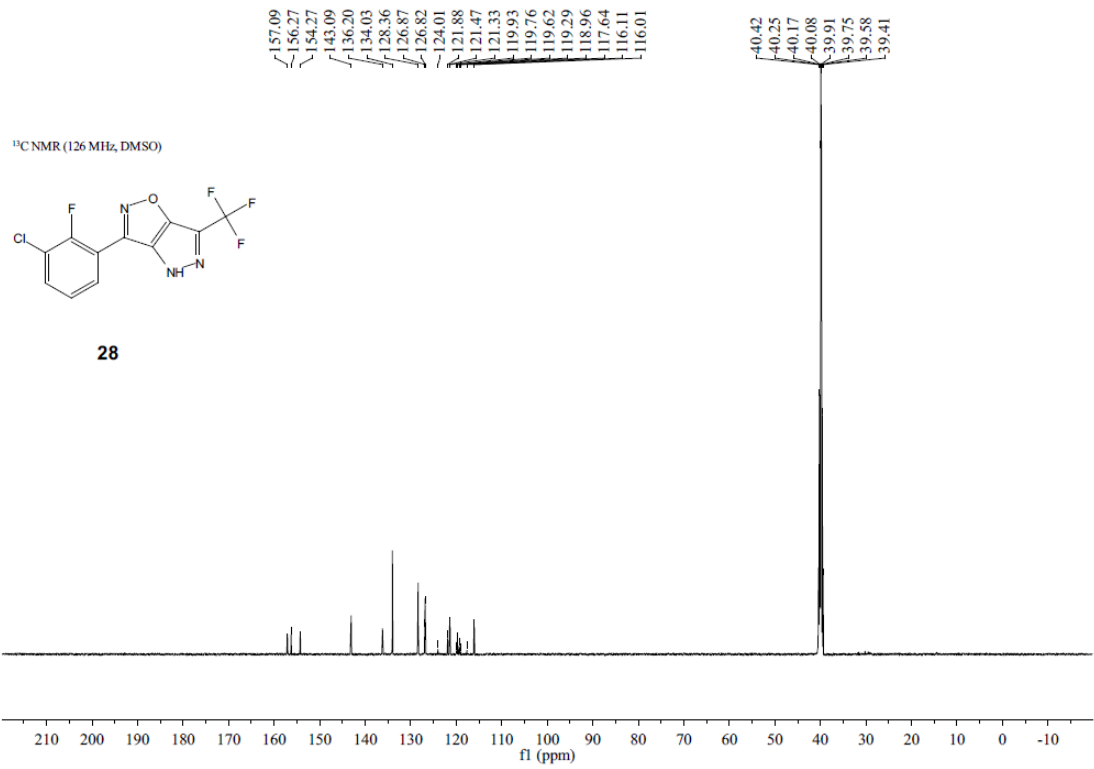


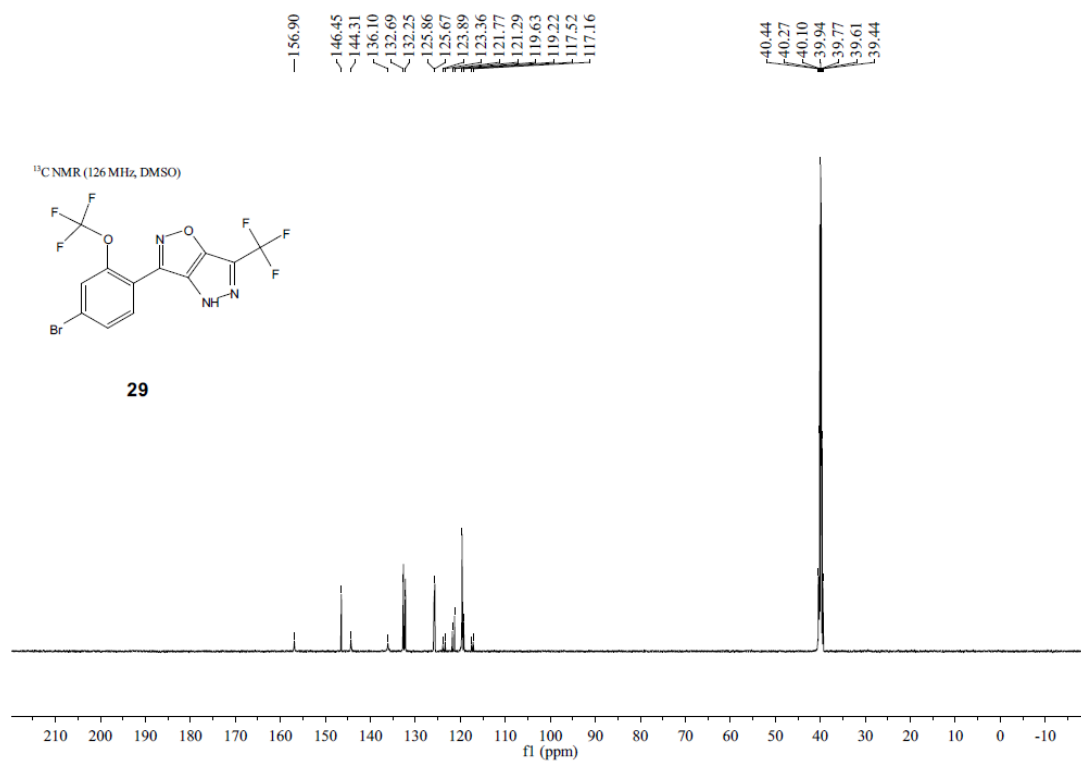
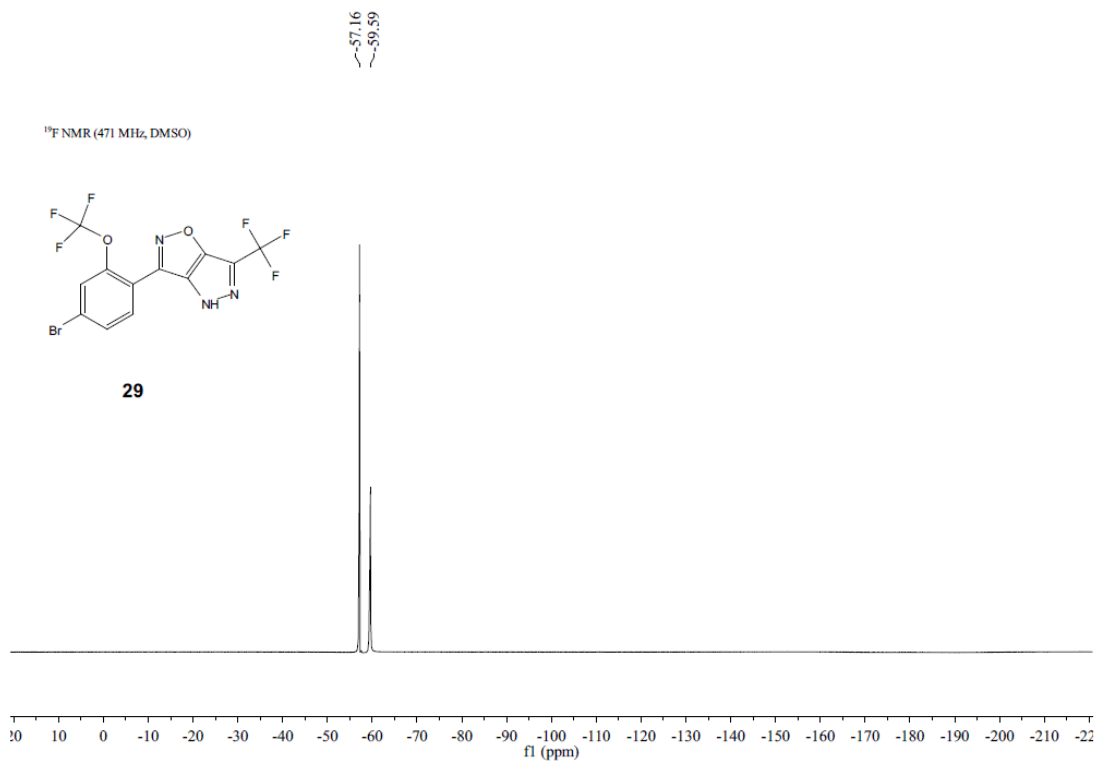










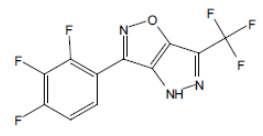


7.95
7.94
7.93
7.92
7.91
7.90
7.48
7.47
7.46
7.45
7.44
7.43

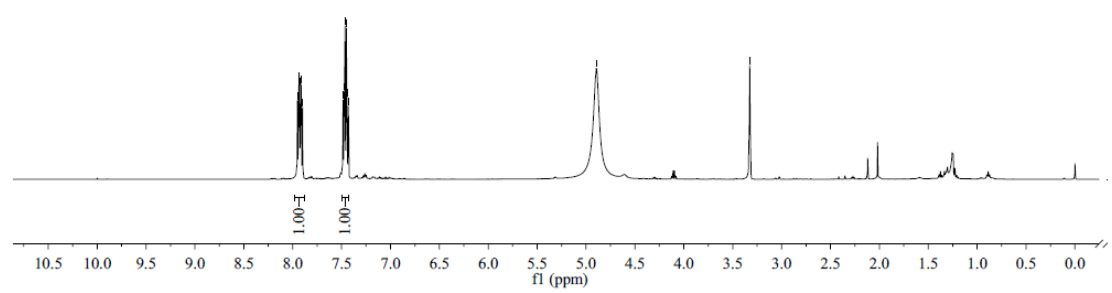
4.89

3.33

¹H NMR (500 MHz, MeOD)



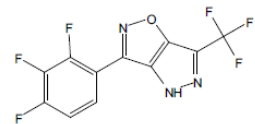
30



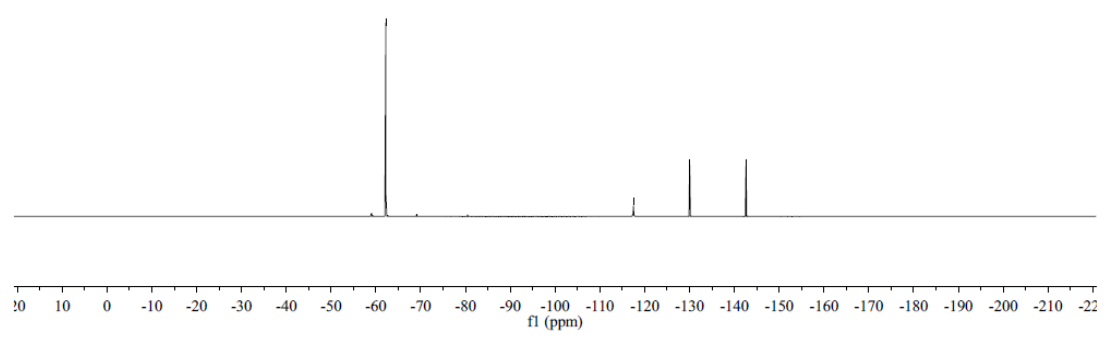
62.22

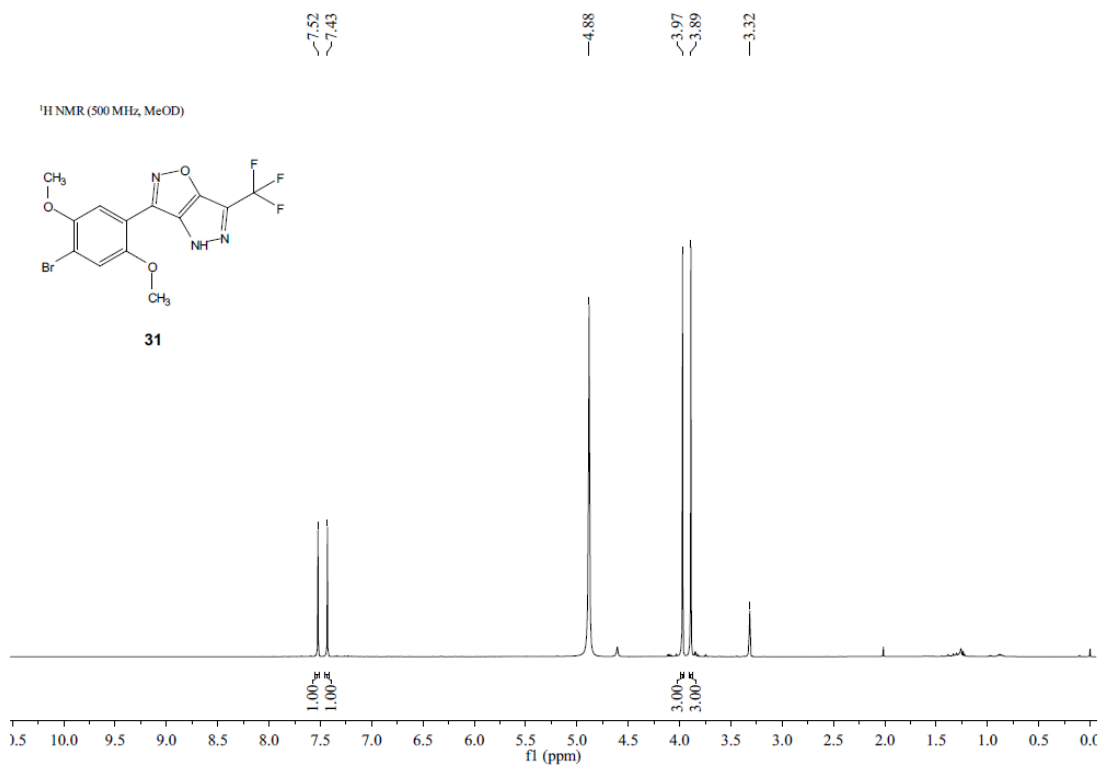
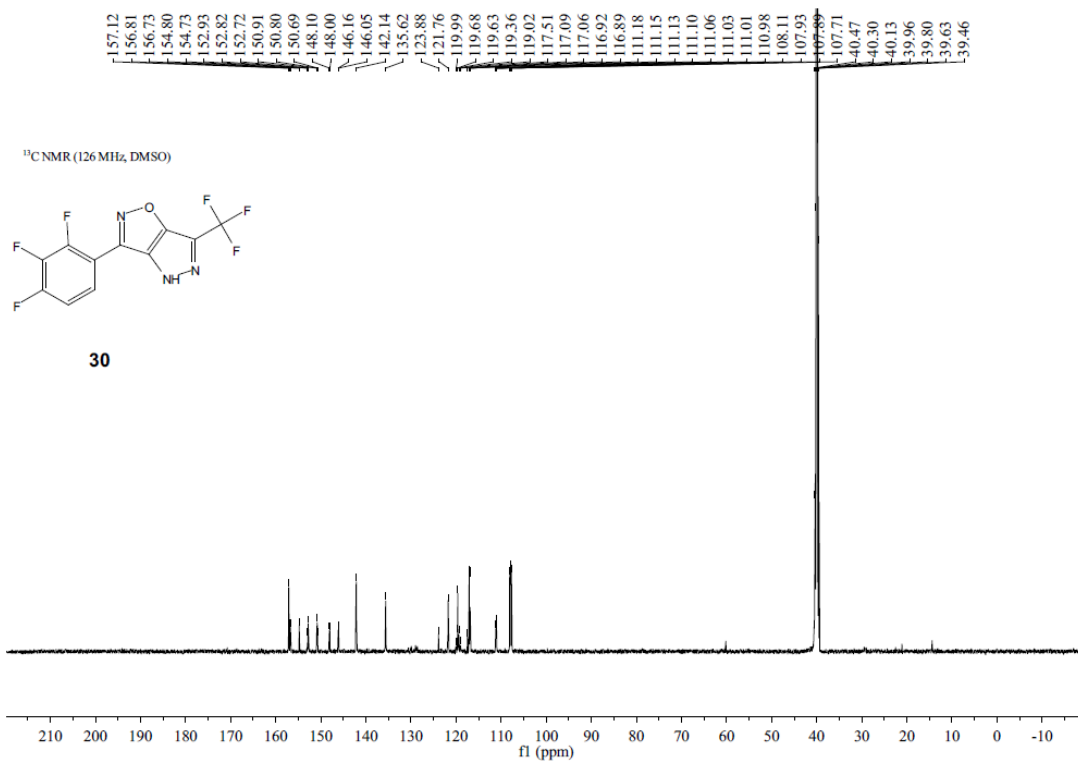
117.49
130.02
130.03
130.06
130.08
142.58
142.61
142.62
142.65

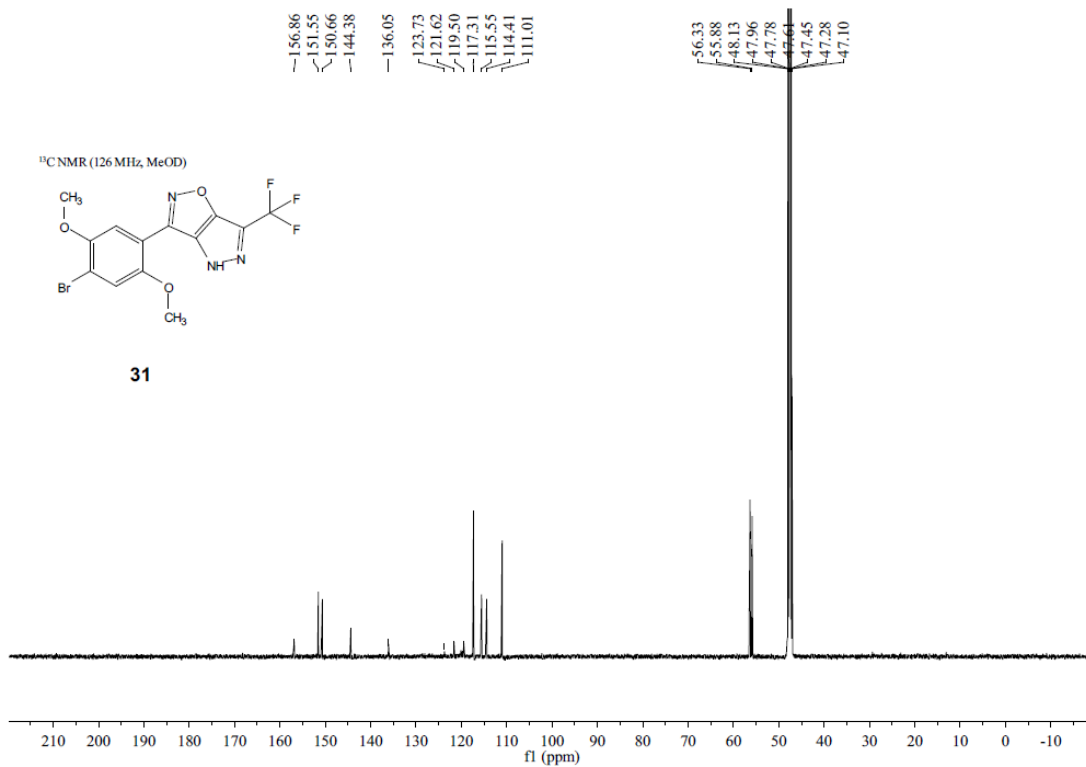
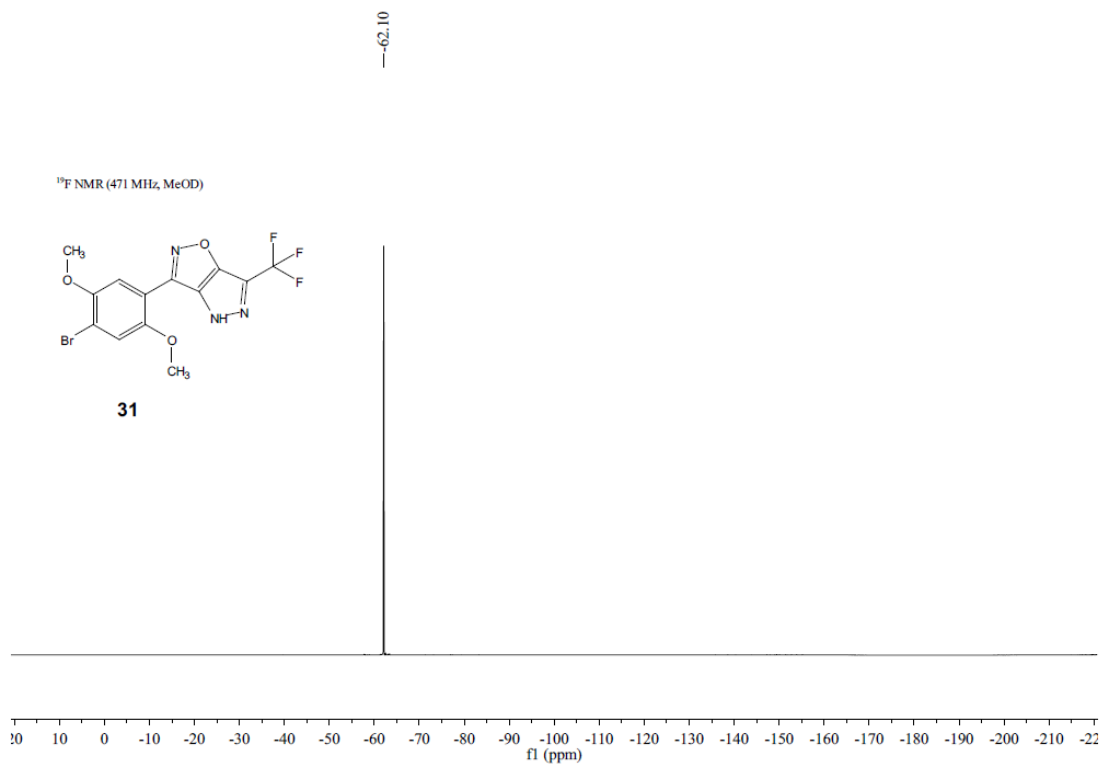
¹⁹F NMR (471 MHz, MeOD)

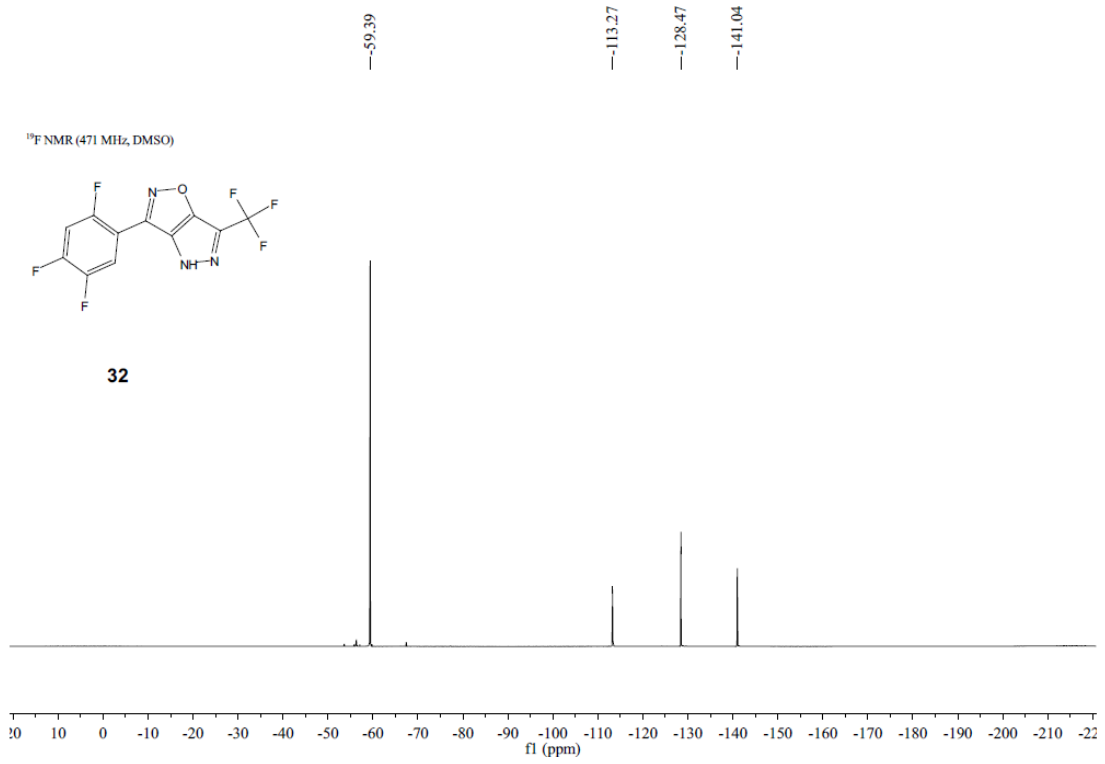
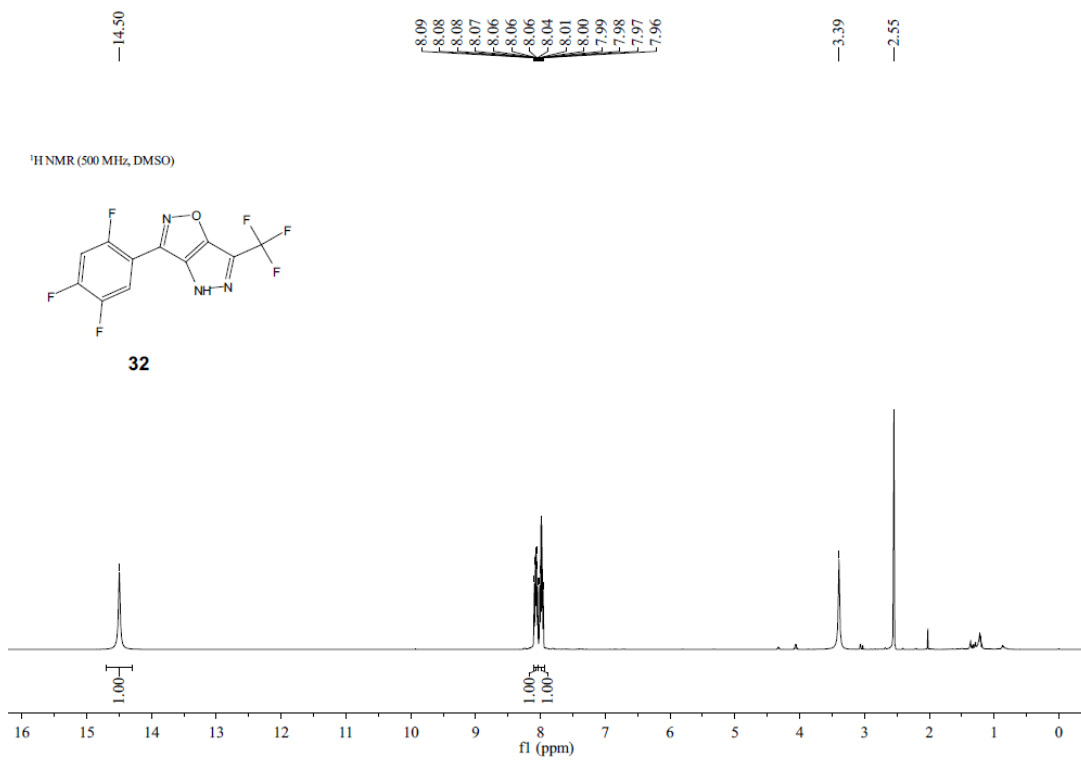


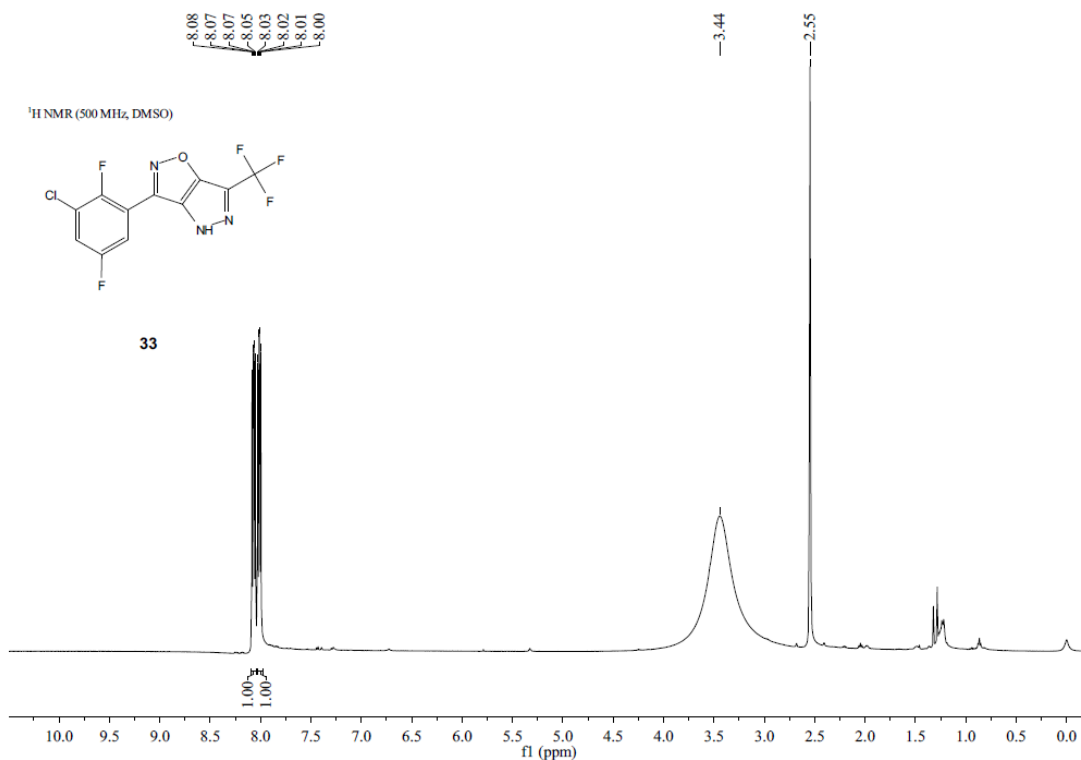
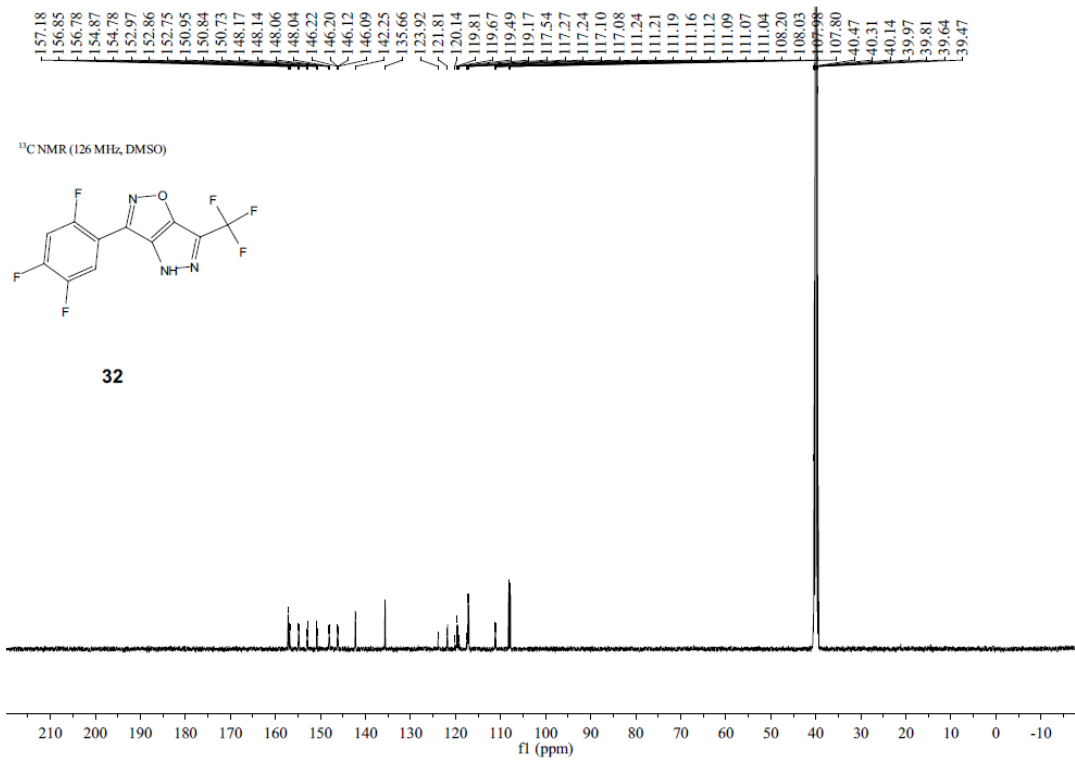
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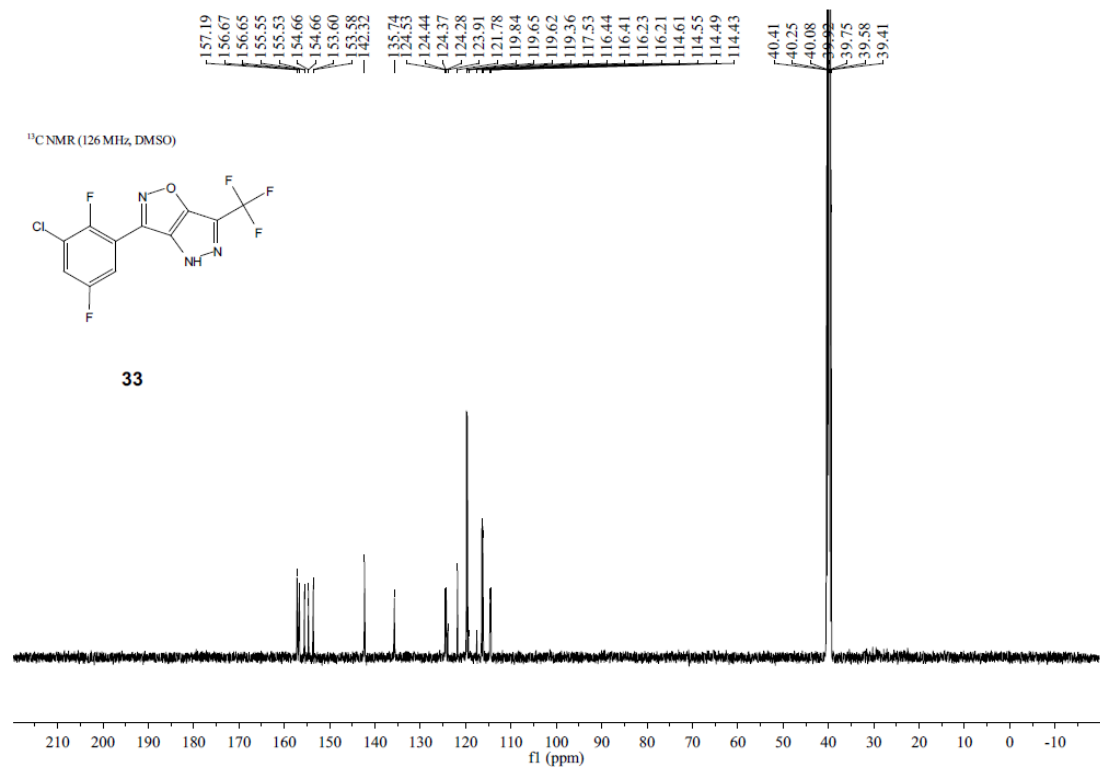
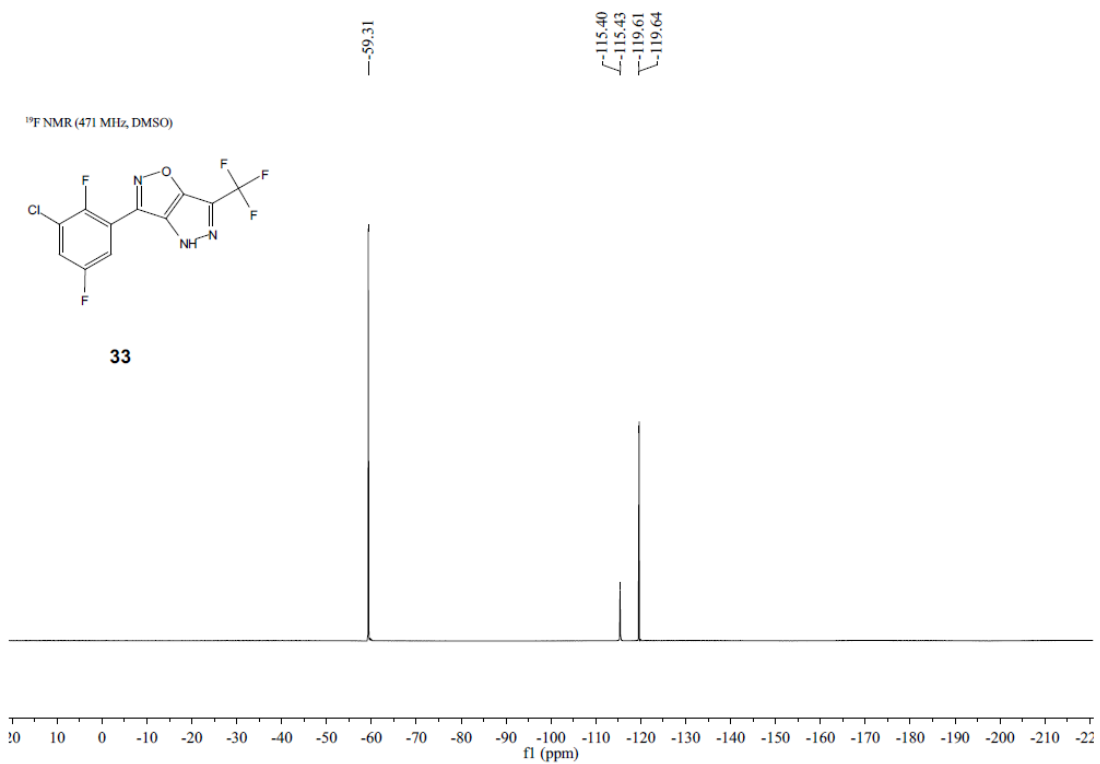


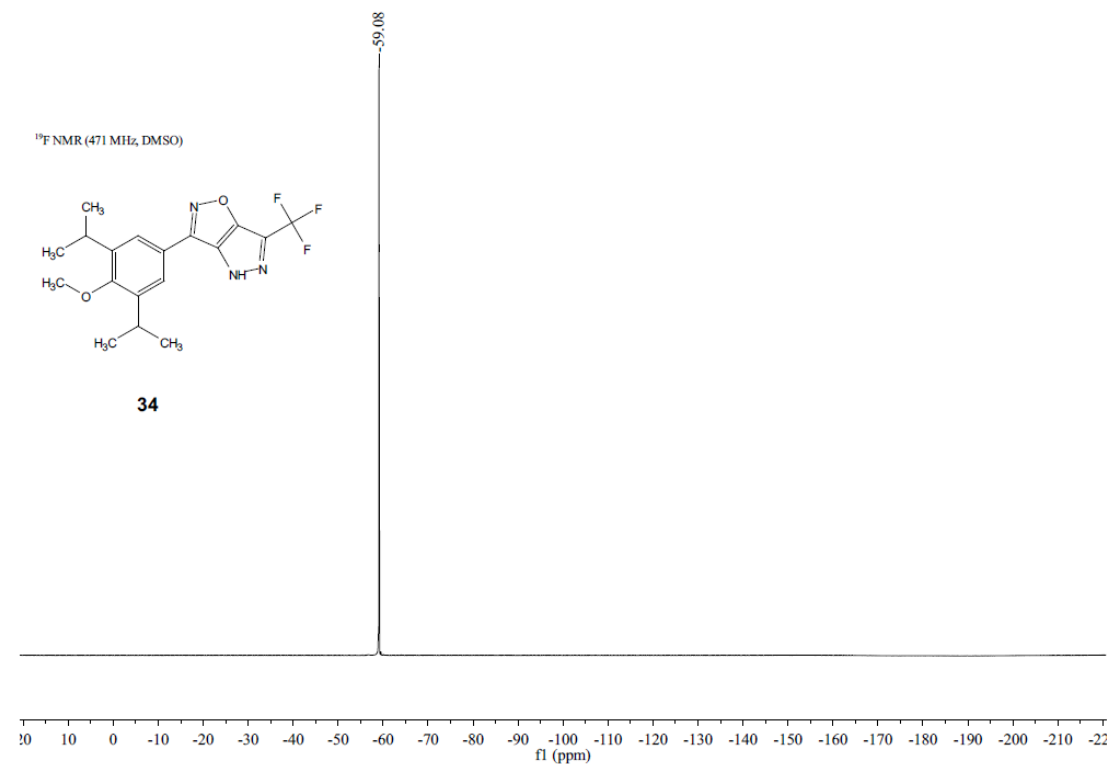
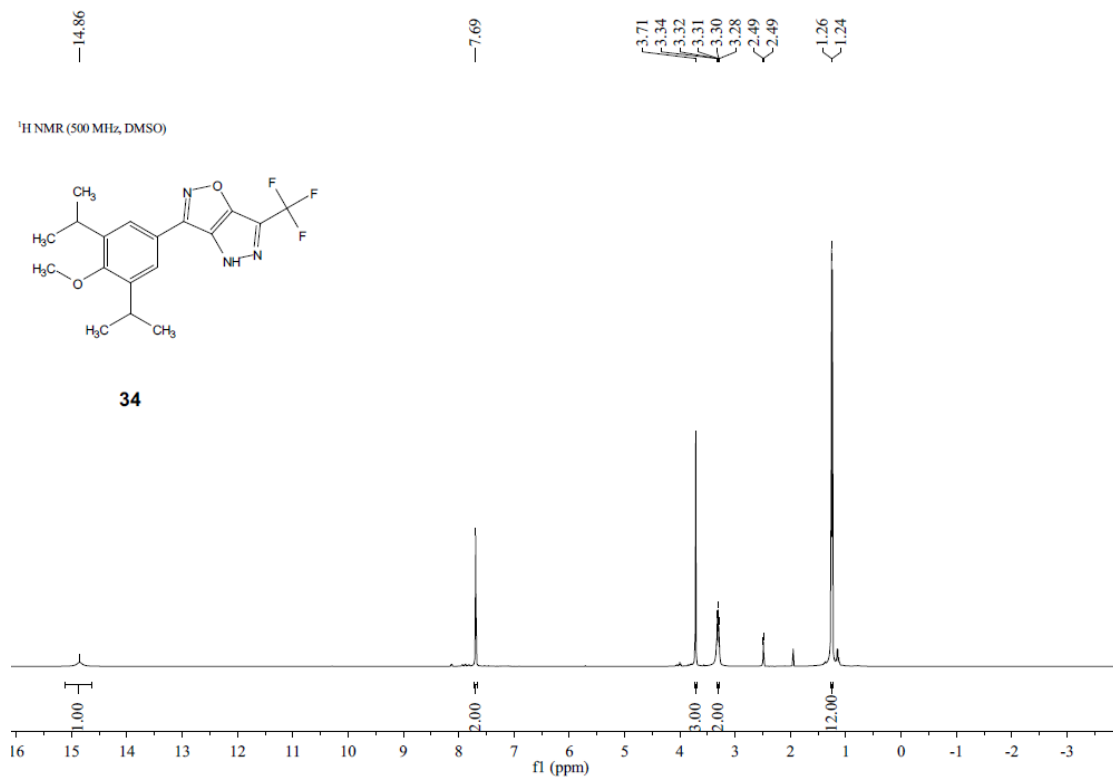


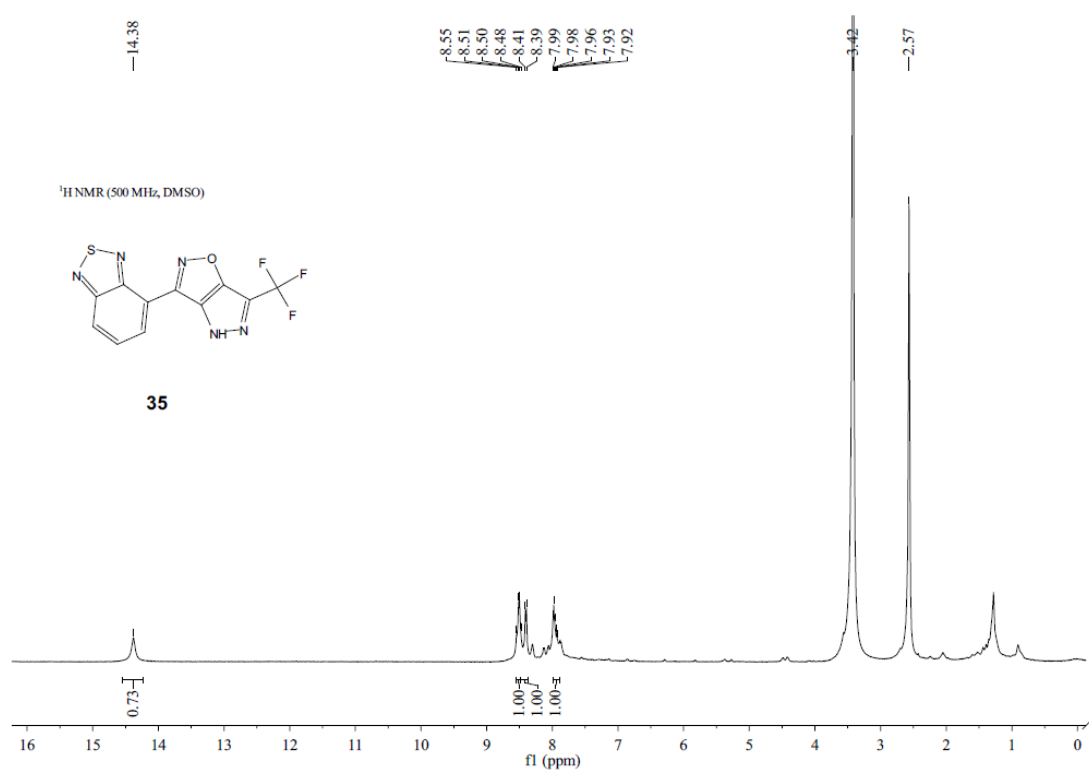
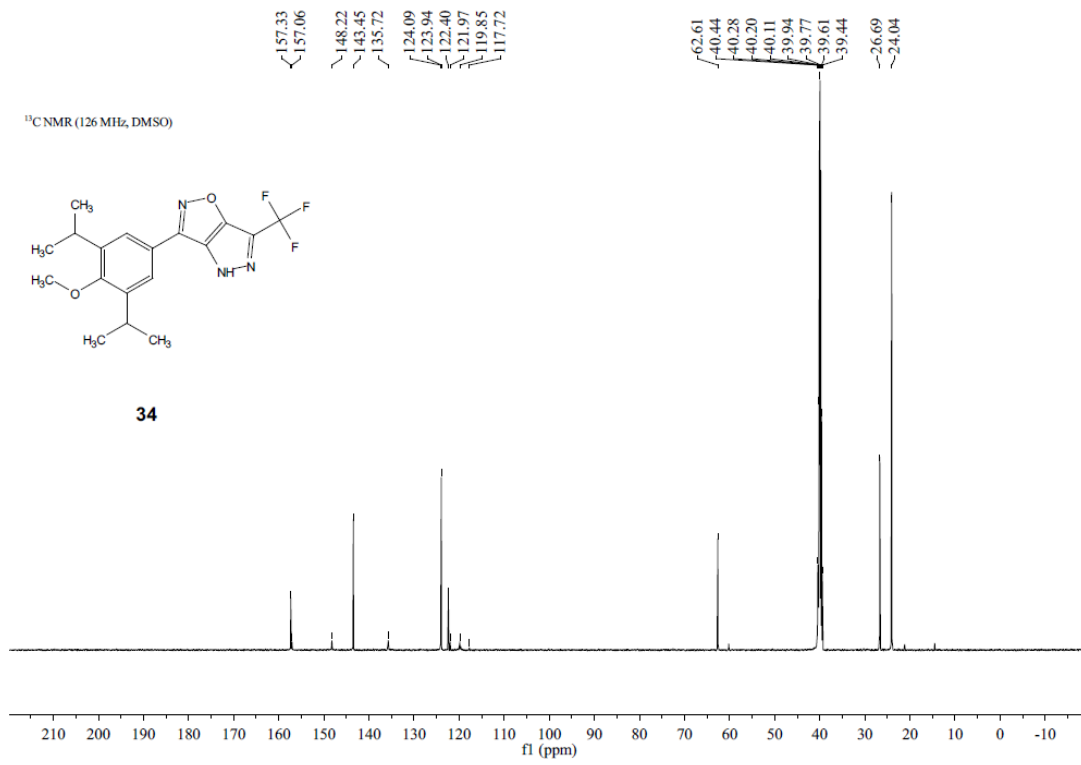






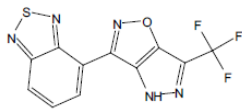




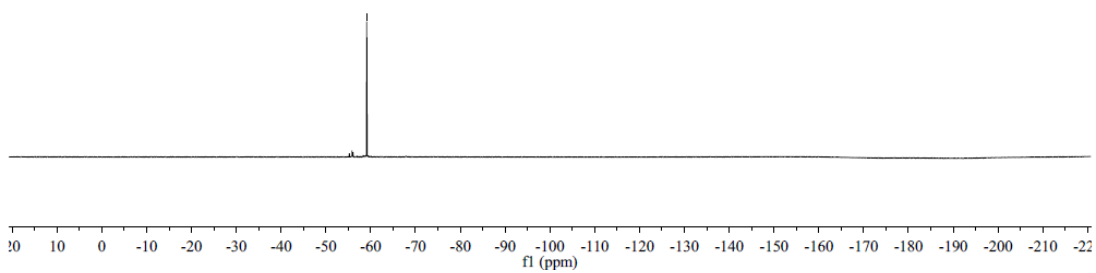


-59.13

¹⁹F NMR (471 MHz, DMSO)



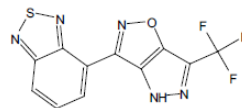
35



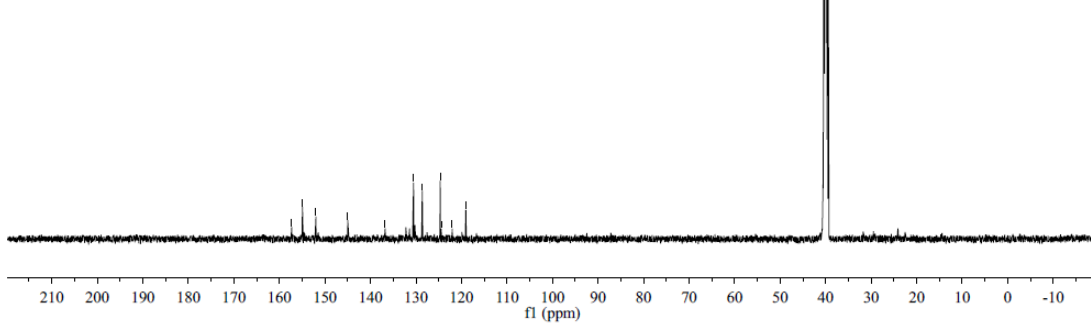
157.32
154.93
151.98
144.98
136.78
130.52
128.61
124.67
124.43
122.03
119.04

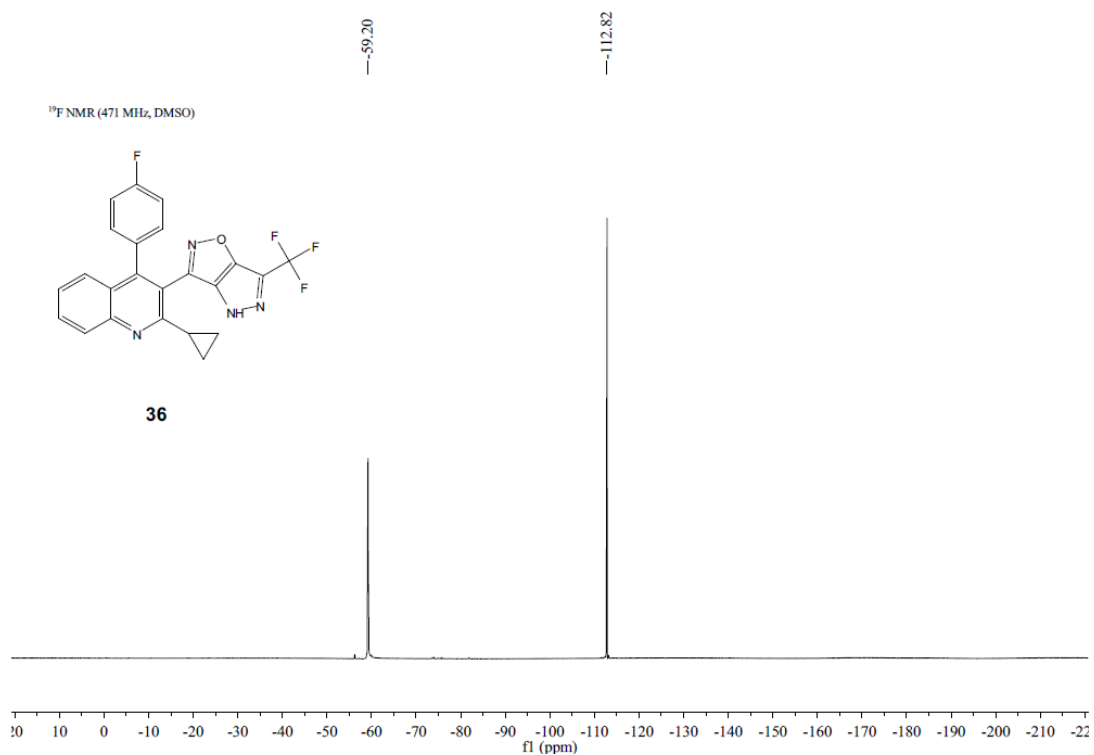
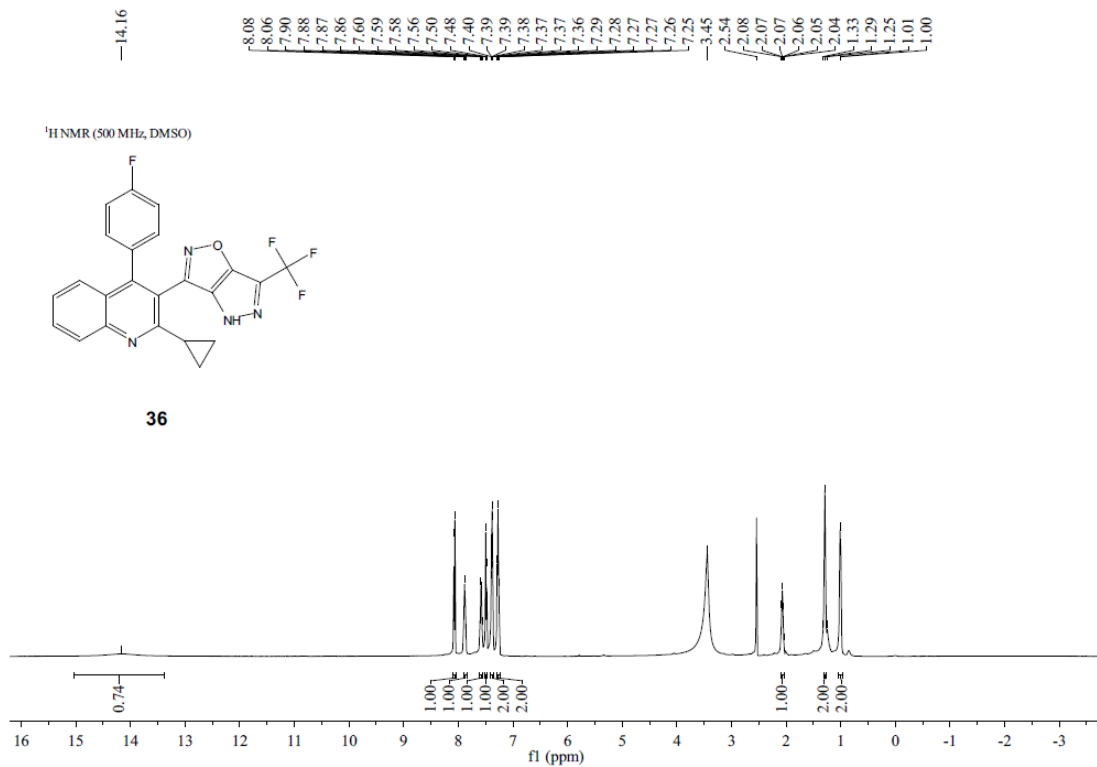
40.46
40.29
40.13
39.96
39.79
39.62
39.46

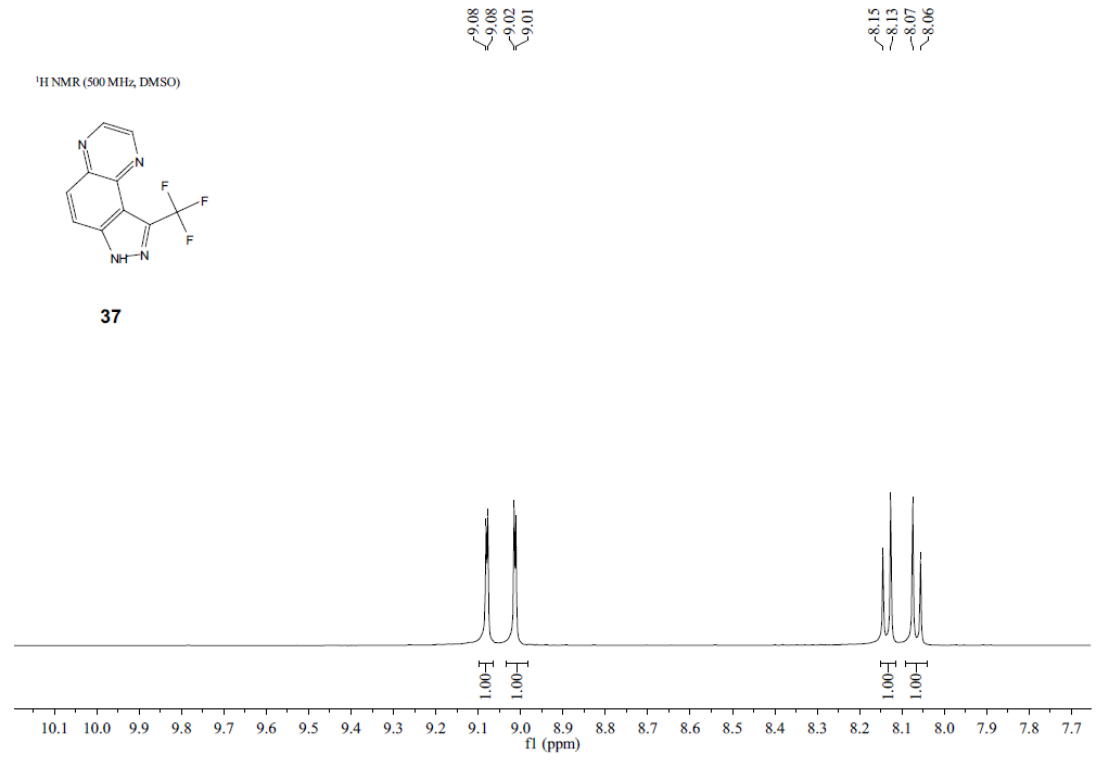
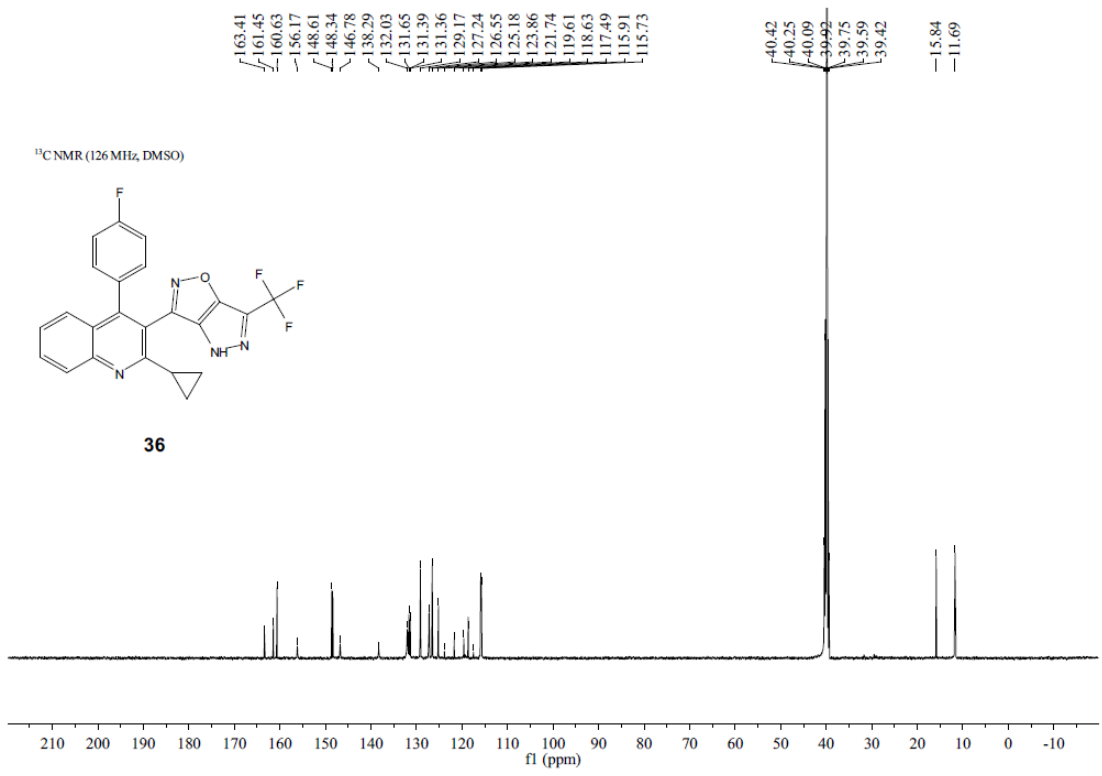
¹³C NMR (126 MHz, DMSO)

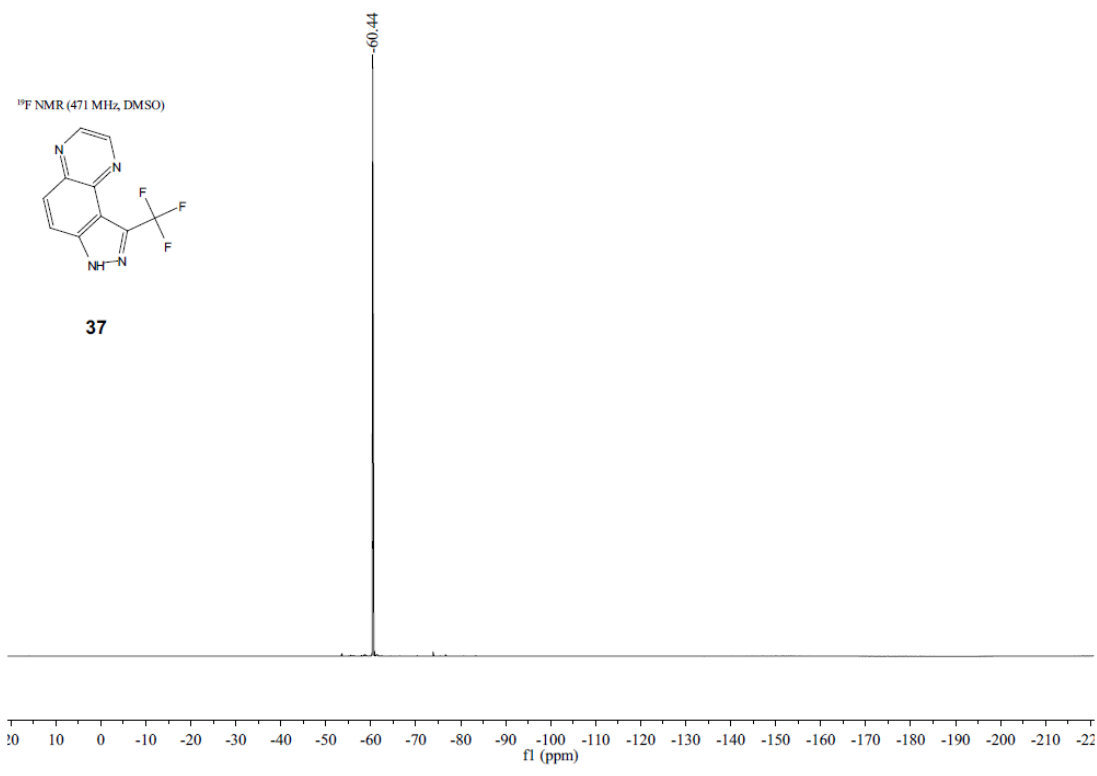


35

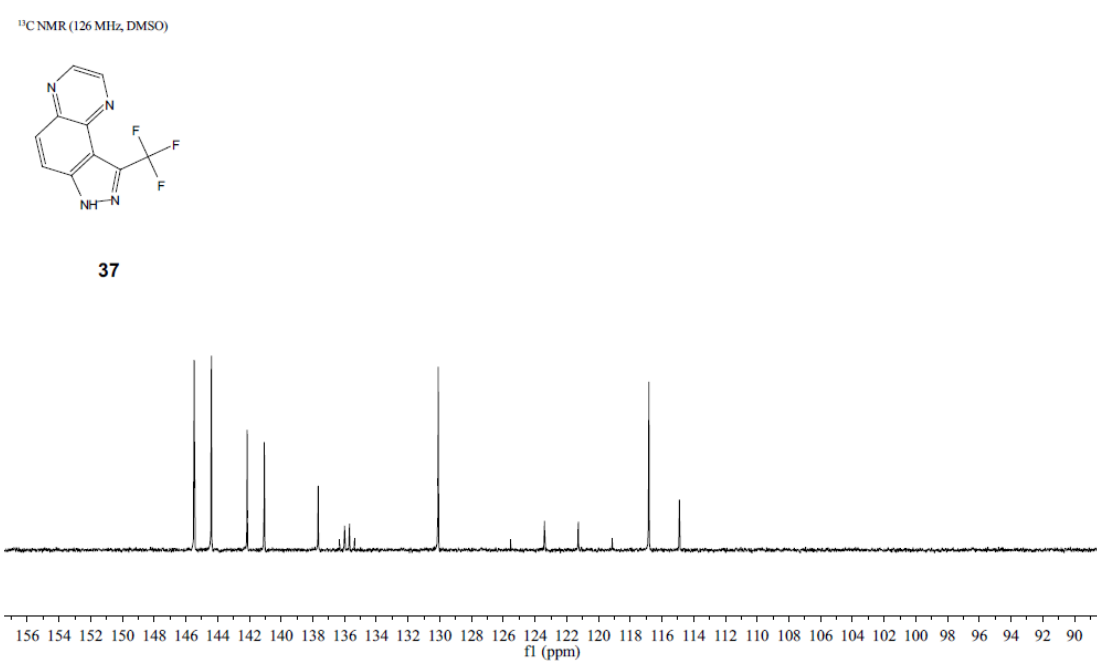








- 145.48
- 144.39
- 142.14
- 141.06
- 137.66
- 136.30
- 136.00
- 135.69
- 135.38
- 130.10
- 125.53
- 123.40
- 121.27
- 119.14
- 116.83
- 114.90

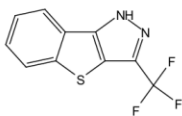


— 14.68

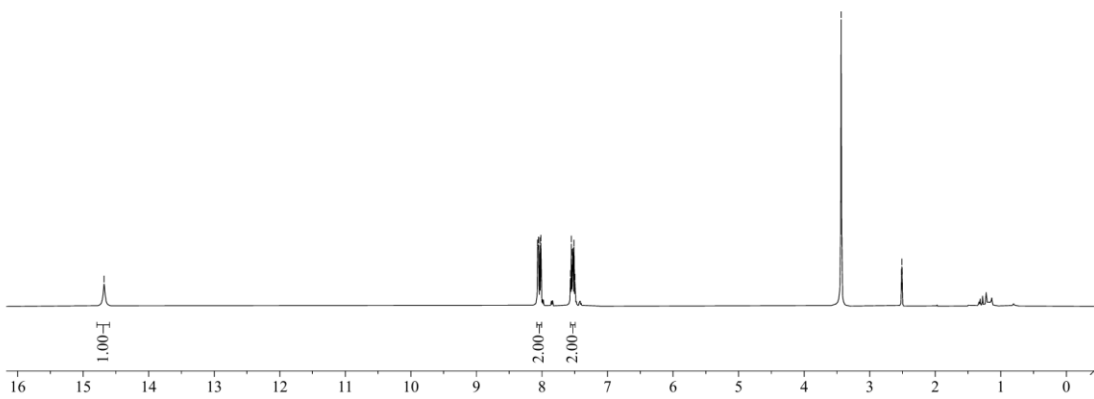
8.07
8.05
8.03
8.02
7.56
7.55
7.54
7.53
7.51
7.50

— 3.43
2.52
2.51
2.51
2.51
2.50

¹H NMR (500 MHz, DMSO)

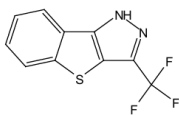


38



— 59.93

¹⁹F NMR (471 MHz, DMSO)



38

