

Supporting Information

Synthesis of multifunctional lactam-substituted alkyl sulfones using rongalite as electron donor, sulfone source, and C1 synthon

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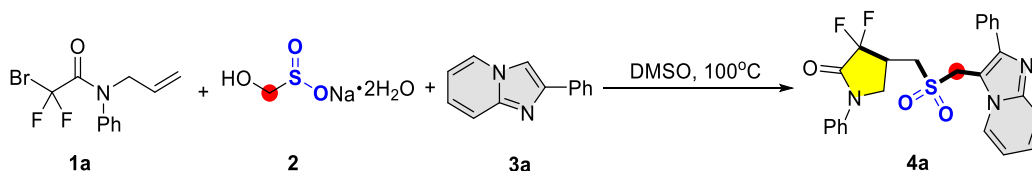
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1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh). ^1H spectra were recorded in $\text{DMSO}-d_6$ or CDCl_3 on 400 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C spectra were recorded in $\text{DMSO}-d_6$ or CDCl_3 on 100 MHz NMR spectrometers and resonances (δ) are given in ppm. ^{19}F spectra were recorded in $\text{DMSO}-d_6$ or CDCl_3 on 376 MHz NMR spectrometers and resonances (δ) are given in ppm. HRMS were obtained on a Bruker 7-tesla FT-ICR MS or an Agilent 1290 LC/MS with the TOF analyzer. Melting points were determined using XT-4 apparatus and not corrected. *N*-allylbromoacetamides **1** and imidazo[1,2-*a*]pyridines (or indoles) **3** were known compounds, and prepared according to the reported procedures.^{1, 2}

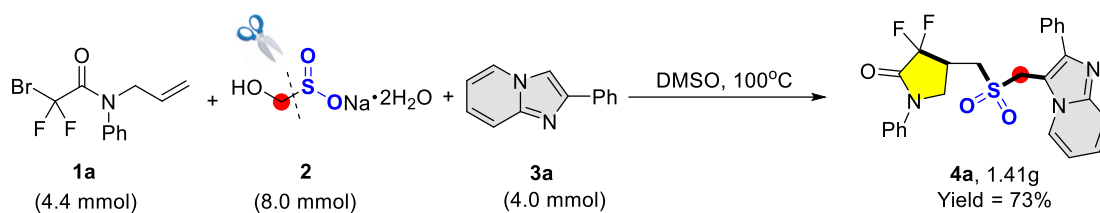
2. Experimental Section

(1) General procedure for the synthesis of 4 (4a as an example).



A mixture of *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide (**1a**) (0.22 mmol, 63.9 mg), rongalite (**2**) (0.4 mmol, 61.6 mg), and 2-phenylimidazo[1,2-*a*]pyridine (**3a**) (0.2 mmol, 38.8 mg) in DMSO (2.0 mL) was stirred at 100 °C in an oil bath for 2.0 h in a pressure vessel. The resulting mixture was dropped into 30 mL H_2O and extracted with EtOAc 3 times (3×30 mL). The organic extract was dried with anhydrous Na_2SO_4 , filtered and concentrated. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) to afford the product 3,3-difluoro-1-phenyl-4-(((2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)sulfonyl)methyl pyrrolidin-2-one (**4a**) as white solid (79.0 mg, 82%).

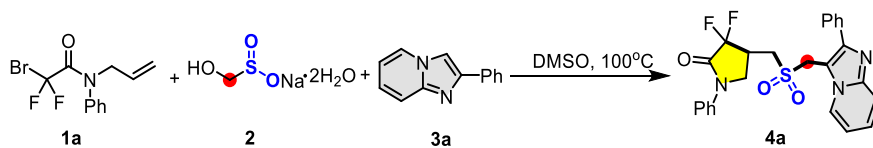
(2) As for gram-scale reaction.



A mixture of *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide (**1a**) (4.40 mmol, 1.28 g), rongalite (**2**) (8.0 mmol, 1.23 g), and 2-phenylimidazo[1,2-*a*]pyridine (**3a**) (4.0 mmol, 0.77 g) in DMSO (40 mL) was stirred at 100 °C in an oil bath for 2.0 h in a pressure vessel. The resulting mixture was dropped into 200 mL H₂O and extracted with EtOAc 3 times (3 × 100). The organic extract was dried with anhydrous Na₂SO₄, filtered and concentrated. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) to afford the product 3,3-difluoro-1-phenyl-4-(((2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)sulfonyl)methyl pyrrolidin-2-one (**4a**) as white solid (1.41 g, 73%).

3. Optimization of the Reaction Conditions.

Table S1. Optimization of the Reaction Conditions. ^a

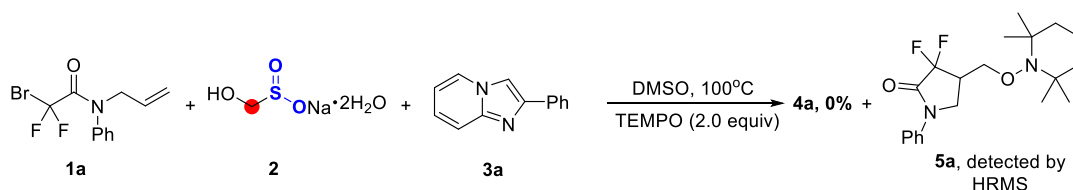


Entry	Variation from the standard conditions	Yield of 4a ^b (%)
1	None	82
2	With Na ₂ CO ₃ / Cs ₂ CO ₃ / DBU / Et ₃ N	0 / 0 / trace/ 0
3	With 0.5 equiv FeCl ₃ / Fe(OTf) ₃ / Cu(OTf) ₂	78 / 75 / 80
4	DMF instead of DMSO	67
5	1,4-dioxane instead of DMSO	0
6	PhMe instead of DMSO	0
7	DCE instead of DMSO	0
8	At 90 °C / 110 °C	75 / 69
9	Rongalite loading: 1.0 / 1.5 / 2.5 equiv.	68 / 74 / 78

^aReactions conditions: **1a** (0.22 mmol), **2** (0.40 mmol), and **3a** (0.20 mmol) were heated in 2.0 mL DMSO in a sealed vessel at 100 °C in an oil bath for 2 h. ^bIsolated yield based on **3a**.

4. Evidence in support of the mechanism

a Radical-trapping experiment with TEMPO



A mixture of *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide (**1a**) (0.22 mmol, 63.9 mg), rongalite (**2**) (0.4 mmol, 61.6 mg), 2-phenylimidazo[1,2-a]pyridine (**3a**, 38.8 mg) and TEMPO (0.4 mmol, 62.5 mg) in DMSO (2.0 mL) was stirred at 100°C in an oil bath for 2.0 h in a pressure vessel. After the above operation, the desired product **4a** was not obtained, while the radical trapping product α,α -difluoro- γ -lactam-TEMPO (**5a**) was detected by HRMS (Figure S1).

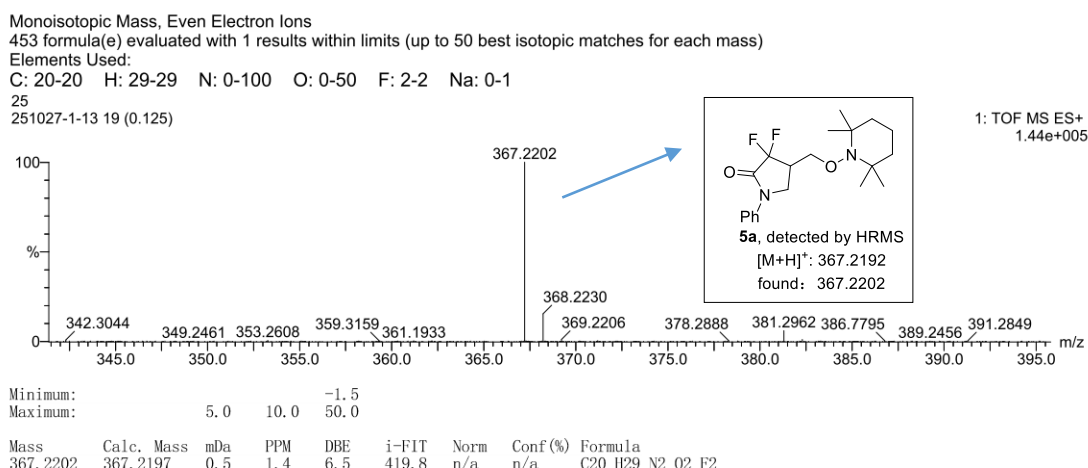
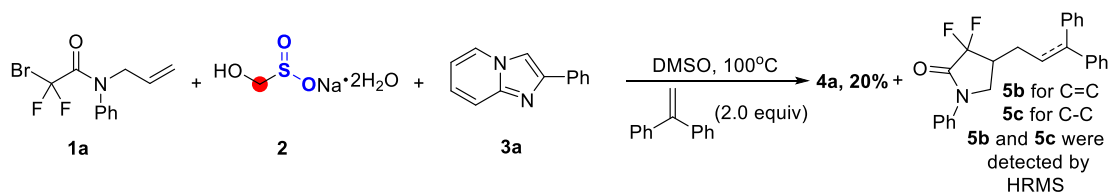


Figure S1 HRMS of **5a**

b Radical-trapping experiment with 1,1-diphenylethylene



A mixture of *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide (**1a**) (0.22 mmol, 63.9 mg), rongalite (**2**) (0.4 mmol, 61.6 mg), 2-phenylimidazo[1,2-a]pyridine (**3a**, 38.8 mg), and 1,1-diphenylethylene (0.4 mmol, 72.1 mg) in DMSO (2.0 mL) was stirred at 100°C in an oil bath for 2.0 h in a pressure vessel. After the above operation, the generation of desired product **4a** was significantly inhibited, while the radical trapping product α,α -difluoro- γ -lactam-1,1-diphenylethylene (**5b**) and α,α -difluoro- γ -lactam-1,1-diphenylethylene (**5c**) were detected by HRMS (Figure S2).

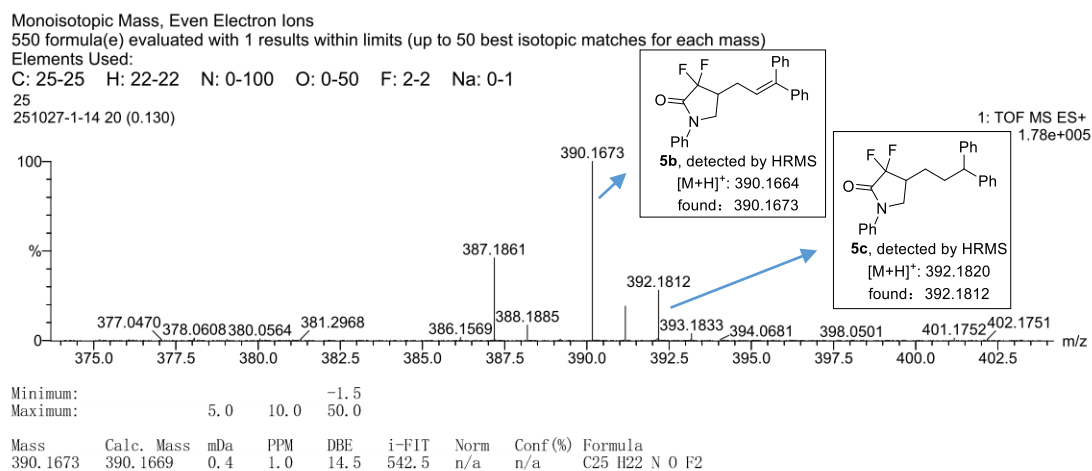
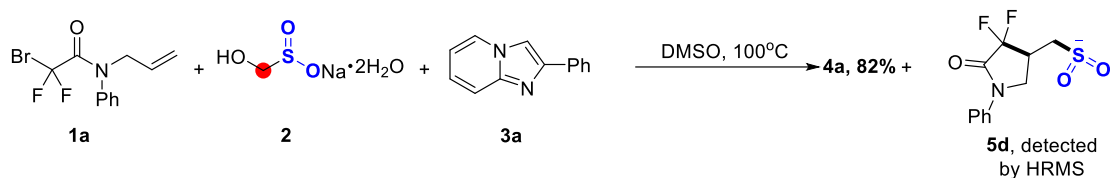


Figure S2 HRMS of **5b** and **5c**

c Detection experiment of intermediate sulfinate anion



A mixture of *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide (**1a**) (0.22 mmol, 63.9 mg), rongalite (**2**) (0.4 mmol, 61.6 mg), 2-phenylimidazo[1,2-*a*]pyridine (**3a**, 38.8 mg) in DMSO (2.0 mL) was stirred at 100°C for 2.0 h in a pressure vessel. After the above operation, the generation of desired product **4a** was obtained in 70% yield, and the intermediate sulfinate anion **5e** was detected by HRMS (Figure S4).

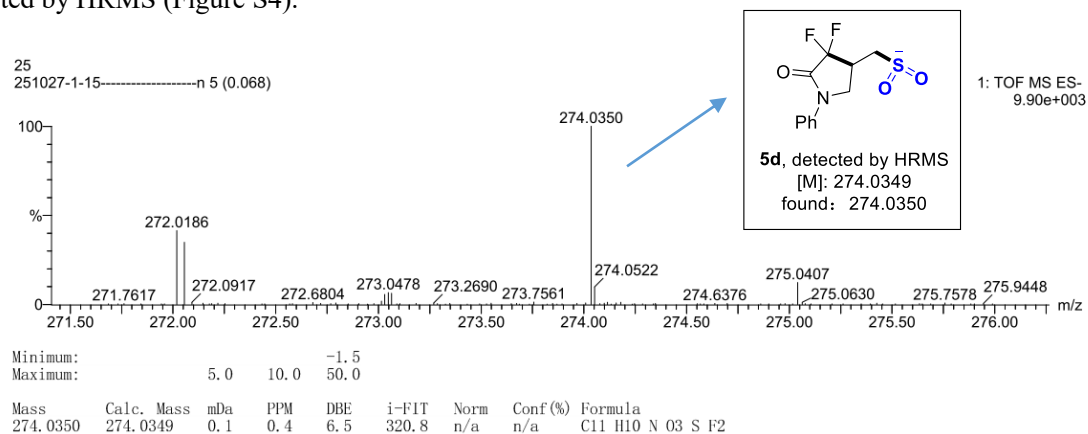
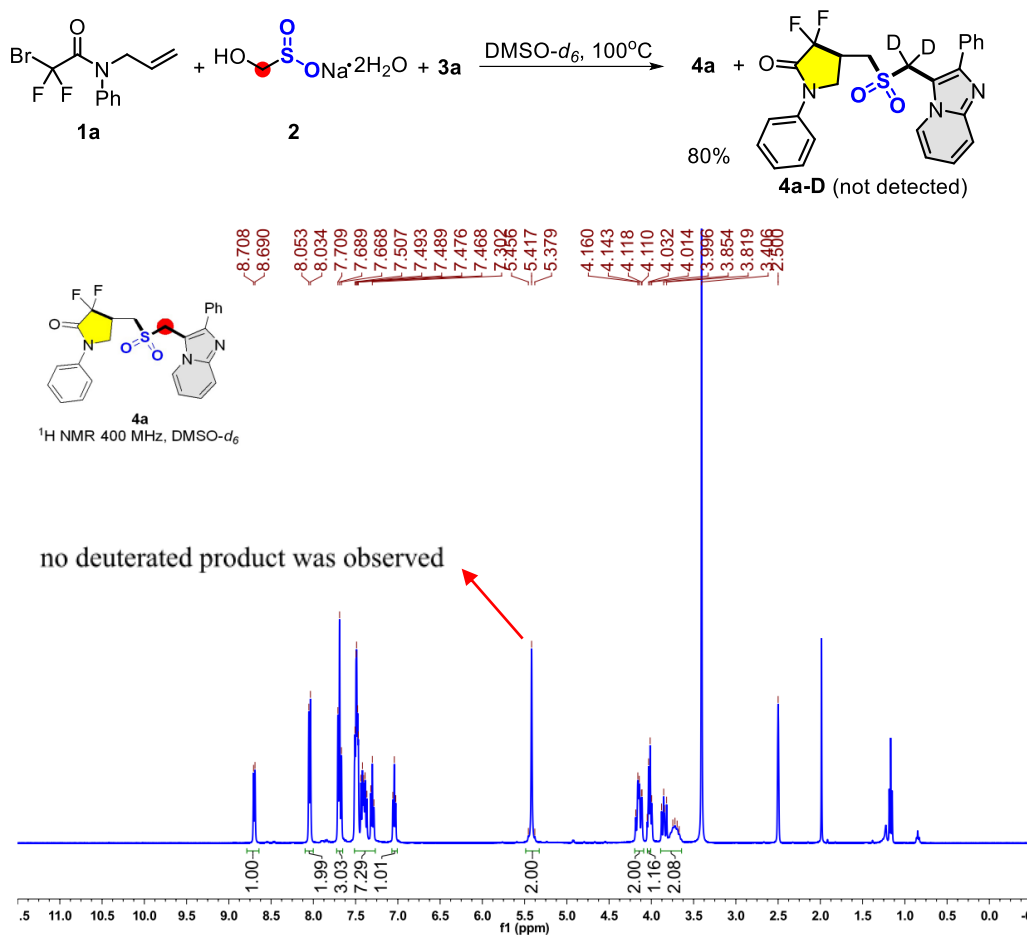


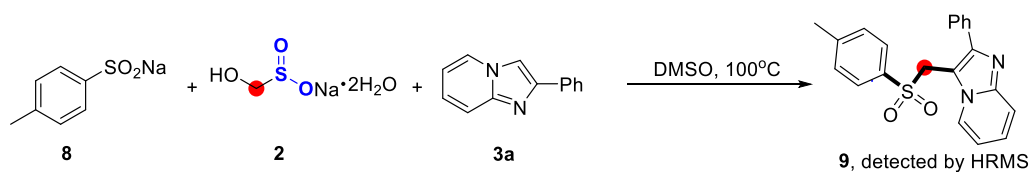
Figure S3 HRMS of **5d**

d DMSO-*d*₆ as the solvent for the reaction of **1a**, **2** and **3a**

We performed the reaction of *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide (**1a**), rongalite (**2**), and 2-phenylimidazo[1,2-*a*]pyridine (**3a**) in DMSO-*d*₆ and observed no deuterated product, thereby excluding DMSO as the possible C1 source.



e Experiment for the detection of intermediates by HRMS



A mixture of *p*-toluenesulfonate (**8**) (0.2 mmol, 35.6 mg), rongalite (**2**) (0.4 mmol, 61.6 mg), and 2-phenylimidazo[1,2-*a*]pyridine (**3a**, 38.8 mg) in DMSO (2.0 mL) was stirred at 100°C for 1.0 h in a pressure vessel. After the above operation, the compound **9** was detected by HRMS (Figure S4).

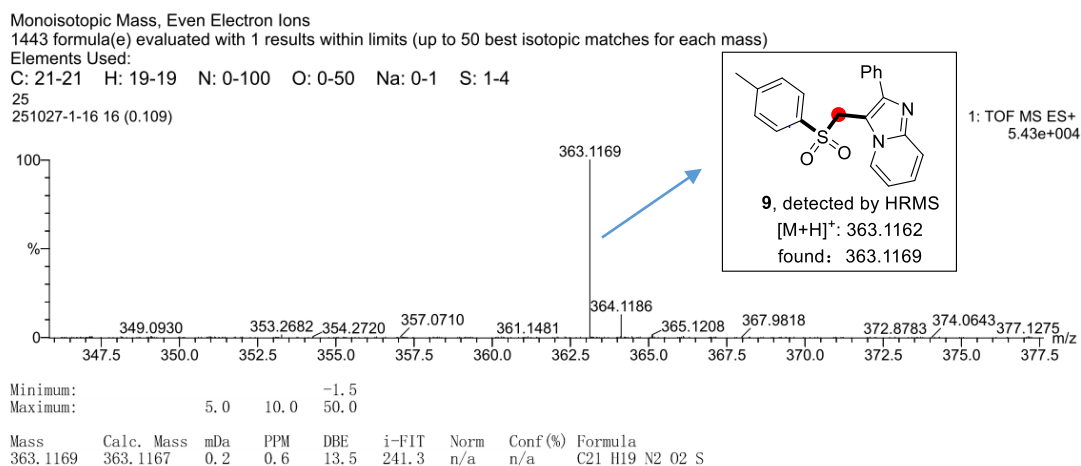


Figure S4 HRMS of **9**

f Experiment of HCHO Detection

We employed the well-established acetylacetone method to detect formaldehyde released from rongalite. The ultraviolet absorption experiment showed a distinct strong absorption peak at 415 nm when rongalite reacted with the acetylacetone reagent.

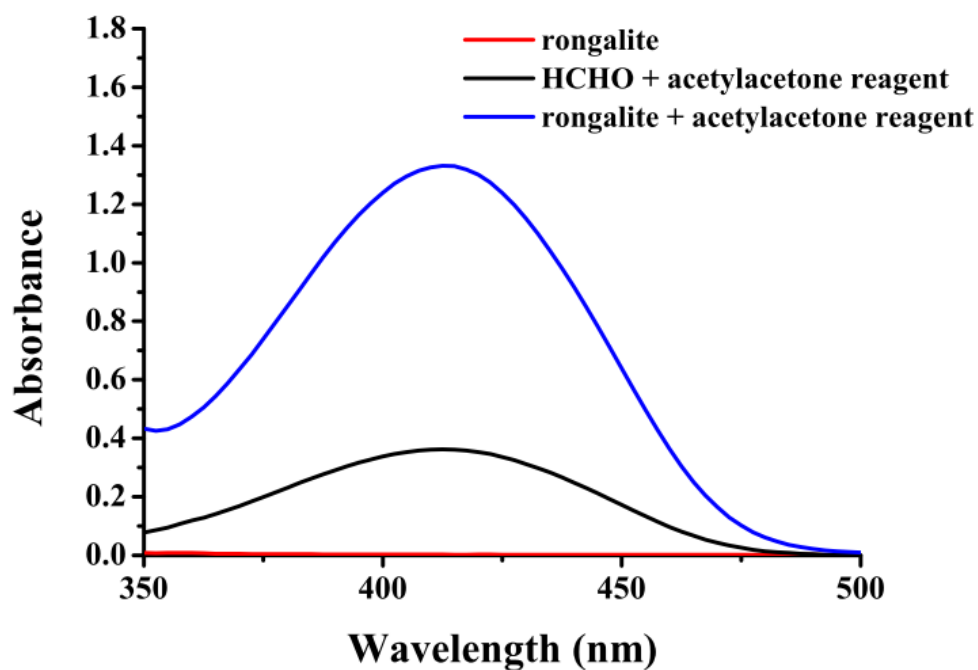
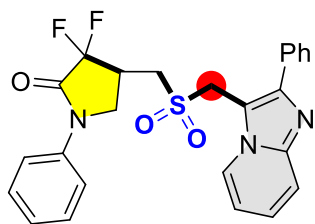


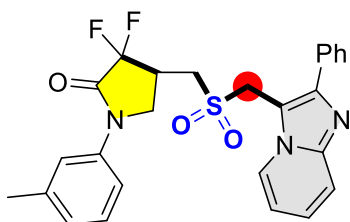
Figure S5 Ultraviolet absorption experiment

5. Characterization data for target compound



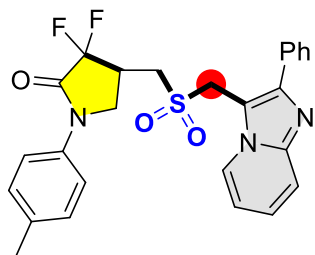
3,3-difluoro-1-phenyl-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4a**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (79.0 mg, 82%); mp: 198.6–200.1 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.70 (s, 1H), 8.05 (d, J = 5.6 Hz, 2H), 7.70 (s, 3H), 7.50–7.31 (m, 7H), 7.05 (s, 1H), 5.42 (s, 2H), 4.15–4.02 (m, 3H), 3.85–3.73 (m, 2H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.6 (t, J = 31.6 Hz), 146.3, 145.3, 137.6, 133.5, 129.1, 128.6, 128.2, 128.1, 126.2, 126.0, 120.3, 117.3 (t, J = 247.3 Hz), 116.7, 112.1, 107.2, 48.7, 48.6, 47.8 (d, J = 6.1 Hz), 33.1 (m); ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.1 (d, J = 262.1 Hz), -112.8 (d, J = 261.7 Hz); HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{22}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 482.1344, found 482.1353.



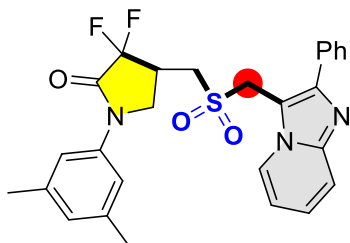
3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-(4-methylphenyl)pyrrolidin-2-one (**4b**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (77.3 mg, 78%); mp: 216.0–216.2 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.72 (d, J = 6.8 Hz, 1H), 8.04 (d, J = 7.6 Hz, 2H), 7.69 (d, J = 9.2 Hz, 1H), 7.50 (s, 4H), 7.44–7.34 (m, 3H), 7.13–7.05 (m, 2H), 5.42 (s, 2H), 4.14 (t, J = 9.6 Hz, 2H), 3.99 (t, J = 8.4 Hz, 1H), 3.88–3.81 (m, 1H), 3.75–3.66 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.6 (t, J = 31.2 Hz), 145.9, 145.1, 138.6, 137.6, 133.2, 129.0, 128.6, 128.3, 128.2, 126.9, 126.4, 126.3, 120.8, 117.6, 117.4 (t, J = 247.1 Hz), 116.5, 112.4, 107.3, 48.7, 48.6, 47.9 (d, J = 5.8 Hz), 33.2 (m), 21.1; ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.1 (d, J = 262.1 Hz), -112.8 (d, J = 262.1 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 496.1501, found 496.1509.



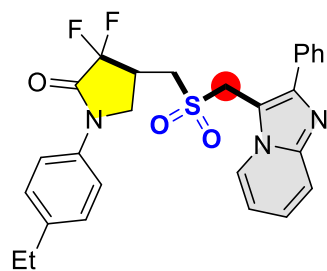
3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-(p-tolyl)pyrrolidin-2-one (**4c**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (75.3 mg, 76%); mp: 121.7–122.5 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.82 (d, J = 6.8 Hz, 1H), 8.02 (d, J = 7.2 Hz, 2H), 7.78 (d, J = 9.2 Hz, 1H), 7.58–7.48 (m, 6H), 7.29 (d, J = 8.0 Hz, 2H), 7.22 (t, J = 6.8 Hz, 1H), 5.45 (s, 2H), 4.12 (t, J = 9.2 Hz, 2H), 4.00–3.94 (m, 1H), 3.88–3.82 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.45 (t, J = 30.8 Hz), 146.3, 145.3, 135.6, 135.2, 133.5, 129.5, 128.6, 128.2, 128.1, 126.2, 126.0, 120.2, 117.4 (t, J = 247.6 Hz), 116.7, 112.1, 107.2, 48.7, 48.5, 47.8 (d, J = 6.1 Hz), 33.1 (m), 20.5; ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.0 (d, J = 261.7 Hz), -112.7 (d, J = 262.1 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 496.1501, found 496.1508.



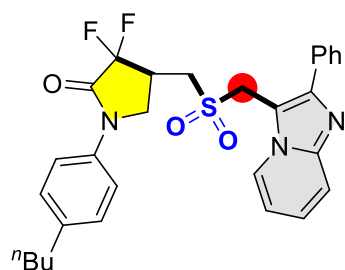
1-(3,5-dimethylphenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4d**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (65.2 mg, 64%); mp: 69.9–71.0 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.71 (d, J = 6.8 Hz, 1H), 8.04 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 8.8 Hz, 1H), 7.50 (t, J = 7.2 Hz, 2H), 7.41 (dd, J = 15.6, 8.0 Hz, 2H), 7.30 (s, 2H), 7.05 (t, J = 6.8 Hz, 1H), 6.94 (s, 1H), 5.42 (s, 2H), 4.11 (d, J = 9.2 Hz, 2H), 3.96 (t, J = 8.4 Hz, 1H), 3.85–3.79 (m, 1H), 3.70 (dd, J = 17.6, 8.8 Hz, 1H), 2.31 (s, 6H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.5 (t, J = 31.7 Hz), 146.1, 145.1, 138.3, 137.5, 133.3, 128.6, 128.2, 128.1, 127.7, 126.2, 118.1, 117.4 (t, J = 247.2 Hz), 116.6, 112.3, 107.3, 48.7, 48.5, 48.0 (d, J = 6.0 Hz), 33.2 (m), 21.0; ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.2 (d, J = 261.7 Hz), -112.9 (d, J = 261.7 Hz); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{26}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 510.1657, found 510.1666.



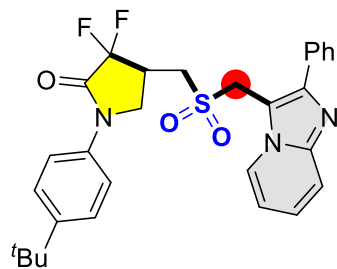
1-(4-ethylphenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4e**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (66.2 mg, 65%); mp: 202.5–203.7 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.37 (d, J = 6.8 Hz, 1H), 7.74 (d, J = 7.2 Hz, 3H), 7.51 (t, J = 7.6 Hz, 2H), 7.44 (d, J = 8.4 Hz, 3H), 7.38–7.34 (m, 1H), 7.20 (d, J = 8.4 Hz, 2H), 6.97 (t, J = 6.8 Hz, 1H), 4.97–4.89 (m, 2H), 4.03–3.99 (m, 1H), 3.63 (t, J = 9.2 Hz, 1H), 3.22 (d, J = 13.2 Hz, 1H), 3.13–3.02 (m, 1H), 2.97 (t, J = 12.4 Hz, 1H), 2.62 (q, J = 7.6 Hz, 2H), 1.20 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.3 (t, J = 29.6 Hz), 147.7, 146.3, 142.9, 134.8, 132.8, 129.3, 129.1, 128.5, 128.4, 126.6, 124.7, 120.1, 117.7, 116.1 (t, J = 248.5 Hz), 113.4, 106.8, 50.6, 47.8 (d, J = 7.1 Hz), 47.7 (d, J = 5.5 Hz), 34.0 (m), 28.3, 15.5; ^{19}F NMR (376 MHz, CDCl_3) δ -110.2 (d, J = 265.5 Hz), -114.9 (d, J = 265.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{26}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 510.1657, found 510.1667.



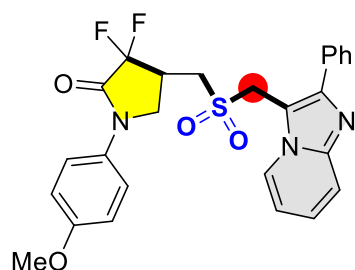
1-(4-butylphenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4f**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (75.3 mg, 70%); mp: 195.1–196.4 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.70 (d, J = 6.8 Hz, 1H), 8.05 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 9.2 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.44–7.36 (m, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.04 (t, J = 6.8 Hz, 1H), 5.43 (d, J = 15.2 Hz, 2H), 4.13 (dd, J = 17.2, 9.2 Hz, 2H), 3.98 (t, J = 8.4 Hz, 1H), 3.86–3.81 (m, 1H), 3.69 (dd, J = 19.2, 9.6 Hz, 1H), 2.58 (t, J = 7.6 Hz, 2H), 1.60–1.49 (m, 2H), 1.29 (dd, J = 14.8, 7.6 Hz, 2H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 160.5 (t, J = 31.3 Hz), 146.3, 145.3, 140.5, 135.3, 133.5, 128.9, 128.6, 128.1, 128.1, 126.2, 126.0, 120.3, 117.4 (t, J = 247.0 Hz), 116.7, 112.1, 107.2, 48.7, 48.6, 47.8 (d, J = 5.8 Hz), 34.2, 33.2 (m), 33.0, 21.6, 13.7; ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$) δ -108.0 (d, J = 262.1 Hz), -112.8 (d, J = 261.7 Hz); HRMS (ESI) m/z calcd for $\text{C}_{29}\text{H}_{30}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 538.1970, found 538.1979.



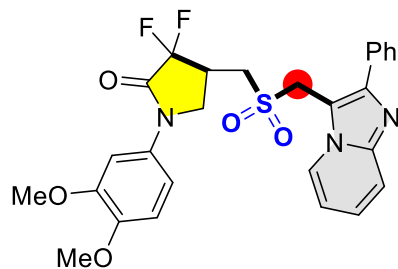
1-(4-(tert-butyl)phenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4g**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (73.1 mg, 68%); mp: 68.6–69.9 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.70 (d, J = 6.8 Hz, 1H), 8.05 (d, J = 7.6 Hz, 2H), 7.68 (d, J = 9.2 Hz, 1H), 7.61 (d, J = 8.8 Hz, 2H), 7.50 (t, J = 7.2 Hz, 4H), 7.44–7.36 (m, 2H), 7.04 (t, J = 6.8 Hz, 1H), 5.46–5.38 (m, 2H), 4.17–4.10 (m, 2H), 3.98 (t, J = 8.4 Hz, 1H), 3.88–3.82 (m, 1H), 3.69 (dd, J = 18.8, 9.2 Hz, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 16.5 (t, J = 31.8 Hz), 148.7, 146.3, 145.3, 135.1, 133.5, 128.6, 128.1, 128.1, 126.2, 126.0, 125.8, 120.1, 117.4 (t, J = 247.1 Hz), 116.7, 112.1, 107.2, 48.7, 48.6, 47.8 (d, J = 5.7 Hz), 34.2, 33.3 (m), 31.0; ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.0 (d, J = 262.1 Hz), -112.8 (d, J = 262.4 Hz); HRMS (ESI) m/z calcd for $\text{C}_{29}\text{H}_{30}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 538.1970, found 538.1979.



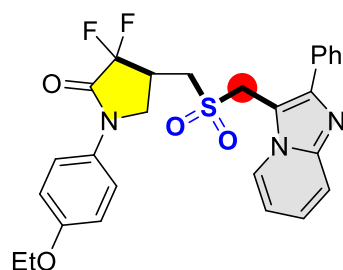
3,3-difluoro-1-(4-methoxyphenyl)-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4h**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (64.5 mg, 63%); mp: 96.3–98.1 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.68 (d, J = 6.8 Hz, 1H), 8.03 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 9.2 Hz, 1H), 7.59 (d, J = 8.8 Hz, 2H), 7.49 (t, J = 7.2 Hz, 2H), 7.44–7.36 (m, 2H), 7.04 (d, J = 9.2 Hz, 3H), 5.38 (d, J = 15.6 Hz, 2H), 4.11–4.07 (m, 2H), 3.95 (t, J = 8.4 Hz, 1H), 3.83 (d, J = 10.4 Hz, 1H), 3.77 (s, 3H), 3.71–3.65 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.2 (t, J = 31.1 Hz), 157.9, 146.9, 145.8, 132.1, 130.2, 129.4, 129.4, 128.4, 127.2, 124.9, 121.7, 117.3, 116.2 (t, J = 248.5 Hz), 114.3, 113.7, 107.0, 55.5, 50.5, 47.9 (d, J = 5.0 Hz), 34.0 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -110.0 (d, J = 265.8 Hz), -114.6 (d, J = 265.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_4\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 512.1450, found 512.1459.



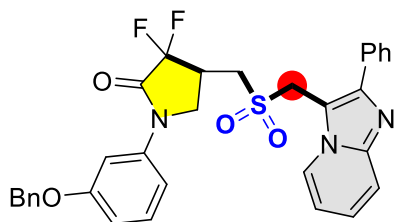
1-(3,4-dimethoxyphenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4i**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (56.3 mg, 52%); mp: 89.7–91.3 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.38 (d, J = 6.8 Hz, 1H), 7.72 (t, J = 8.0 Hz, 3H), 7.50 (t, J = 7.6 Hz, 2H), 7.45–7.40 (m, 2H), 7.37–7.33 (m, 1H), 6.96 (t, J = 6.8 Hz, 1H), 6.82 (d, J = 8.0 Hz, 2H), 4.98–4.90 (m, 2H), 4.03–3.98 (m, 1H), 3.85 (d, J = 2.8 Hz, 6H), 3.63 (t, J = 9.2 Hz, 1H), 3.23 (dd, J = 13.6, 2.4 Hz, 1H), 3.15–3.04 (m, 1H), 3.01–2.96 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.2 (t, J = 31.5 Hz), 149.0, 147.5, 146.2, 132.6, 130.6, 129.3, 129.1, 128.4, 126.7, 124.7, 118.5 (t, J = 210.7 Hz), 117.6, 113.4, 111.9, 110.8, 106.8, 104.8, 56.0, 55.9(6), 50.6, 48.0 (d, J = 5.7 Hz), 47.8 (d, J = 7.1 Hz), 33.9 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -110.0 (d, J = 265.8 Hz), -114.7 (d, J = 265.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{26}\text{F}_2\text{N}_3\text{O}_5\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 542.1556, found 542.1564.



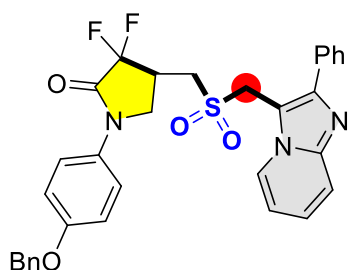
1-(4-ethoxyphenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4j**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (78.8 mg, 75%); mp: 95.2–96.3 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.41 (d, J = 6.8 Hz, 1H), 7.76 (t, J = 8.8 Hz, 3H), 7.52 (t, J = 7.6 Hz, 2H), 7.42 (dt, J = 16.4, 7.6 Hz, 4H), 7.00 (t, J = 6.8 Hz, 1H), 6.88 (d, J = 8.4 Hz, 2H), 4.99–4.91 (m, 2H), 4.01 (q, J = 6.4 Hz, 3H), 3.63 (t, J = 8.8 Hz, 1H), 3.24 (d, J = 12.8 Hz, 1H), 3.16–3.07 (m, 1H), 2.99 (t, J = 12.0 Hz, 1H), 1.40 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 160.1 (t, J = 30.3 Hz), 157.3, 147.3, 146.1, 132.4, 130.1, 129.4, 129.3, 128.5, 127.0, 124.8, 121.8, 118.7 (t, J = 237.8 Hz), 117.6, 114.9, 113.6, 106.9, 63.7, 50.7, 48.0 (d, J = 5.7 Hz), 34.2 (m), 29.7, 14.7; ^{19}F NMR (376 MHz, CDCl_3) δ -110.1 (d, J = 265.8 Hz), -114.8 (d, J = 265.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{26}\text{F}_2\text{N}_3\text{O}_4\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 526.1607, found 526.1616.



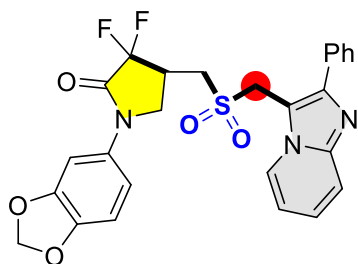
1-(3-(benzyloxy)phenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfo-nyl)methyl)pyrrolidin-2-one (**4k**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (84.5 mg, 72%); mp: 170.3–171.1 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.35 (d, J = 6.8 Hz, 1H), 7.72 (dd, J = 13.2, 8.4 Hz, 3H), 7.50 (t, J = 7.6 Hz, 2H), 7.44–7.31 (m, 8H), 7.26 (t, J = 8.4 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 6.94 (t, J = 6.8 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 5.07–5.01 (m, 2H), 4.96–4.85 (m, 2H), 4.02–3.97 (m, 1H), 3.59 (t, J = 9.2 Hz, 1H), 3.22 (d, J = 11.6 Hz, 1H), 3.08 (dd, J = 19.2, 8.8 Hz, 1H), 3.01–2.94 (m, 1H); ^{13}C NMR (100 MHz, DMSO) δ 160.8 (t, J = 31.5 Hz), 158.7, 146.4, 145.3, 138.8, 136.7, 133.6, 130.0, 128.6, 128.5, 128.2, 127.9, 127.7, 126.1, 126.0, 117.4 (t, J = 247.6 Hz), 117.3, 116.7, 112.7, 112.3, 112.2, 107.4, 107.2, 69.4, 48.8, 48.7 (d, J = 6.9 Hz), 47.9 (d, J = 4.7 Hz), 33.2 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -108.1 (d, J = 262.4 Hz), -112.8 (d, J = 262.1 Hz); HRMS (ESI) m/z calcd for $\text{C}_{32}\text{H}_{28}\text{F}_2\text{N}_3\text{O}_4\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 588.1763, found 588.1772.



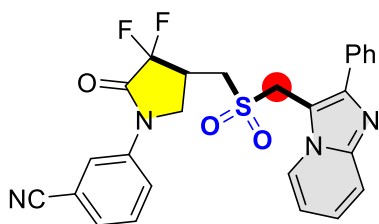
1-(4-(benzyloxy)phenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfo-nyl)methyl)pyrrolidin-2-one (**4l**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow oil (79.1 mg, 67%); ^1H NMR (400 MHz, CDCl_3) δ 8.35 (d, J = 6.8 Hz, 1H), 7.73 (t, J = 7.2 Hz, 3H), 7.51 (t, J = 7.6 Hz, 2H), 7.46–7.32 (m, 9H), 6.98–6.95 (m, 3H), 5.04 (s, 2H), 4.92 (s, 2H), 4.00–3.95 (m, 1H), 3.60 (t, J = 9.2 Hz, 1H), 3.20 (d, J = 11.6 Hz, 1H), 3.13–3.03 (m, 1H), 2.96 (t, J = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 160.3 (t, J = 31.9 Hz), 156.3, 146.4, 145.3, 136.8, 133.5, 130.8, 128.6, 128.5, 128.2, 128.1, 127.9, 127.7, 126.2, 126.0, 122.1, 117.5 (t, J = 247.3 Hz), 116.7, 115.1, 112.2, 107.2, 69.4, 48.7, 48.1 (d, J = 6.0 Hz), 42.1, 33.2 (m); ^{19}F NMR (376 MHz, DMSO- d_6) δ -107.9 (d, J = 262.1 Hz), -112.6 (d, J = 250.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{32}\text{H}_{28}\text{F}_2\text{N}_3\text{O}_4\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 588.1763, found 588.1772.



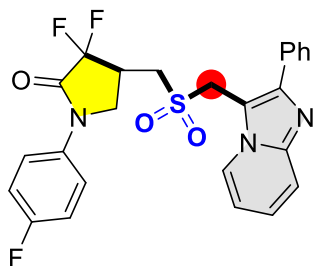
3,3-difluoro-1-(4-methoxyphenyl)-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4m**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (78.8 mg, 75%); mp: 131.5–132.3 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.34 (d, J = 6.8 Hz, 1H), 7.71 (dd, J = 13.6, 8.4 Hz, 3H), 7.49 (t, J = 7.2 Hz, 2H), 7.45–7.39 (m, 1H), 7.35–7.31 (m, 1H), 7.19 (s, 1H), 6.93 (t, J = 6.8 Hz, 1H), 6.77 (dd, J = 22.0, 8.4 Hz, 2H), 5.95 (s, 2H), 4.95–4.87 (m, 2H), 3.93 (t, J = 9.2 Hz, 1H), 3.57 (t, J = 9.2 Hz, 1H), 3.20 (d, J = 13.2 Hz, 1H), 3.11–3.01 (m, 1H), 2.97 (d, J = 10.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.2 (t, J = 29.5 Hz), 148.1, 147.8, 146.4, 146.0, 132.9, 131.3, 129.3, 129.0, 128.4, 126.4, 124.6, 118.5 (t, J = 227.5 Hz), 117.8, 113.5, 113.3, 108.1, 106.7, 102.6, 101.7, 50.6, 48.2 (d, J = 5.6 Hz), 47.7 (d, J = 6.9 Hz), 42.6, 34.0 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -110.1 (d, J = 265.8 Hz), -114.8 (d, J = 265.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{22}\text{F}_2\text{N}_3\text{O}_5\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 526.1243, found 526.1249.



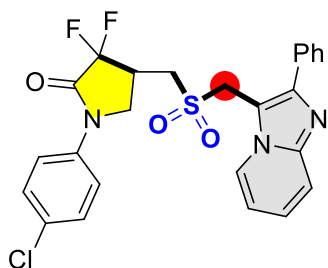
3-(3,3-difluoro-2-oxo-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-1-yl)benzonitrile (**4n**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (50.7 mg, 50%); mp: 94.8–96.2 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.69 (d, J = 6.8 Hz, 1H), 8.16 (s, 1H), 8.13–7.97 (m, 3H), 7.82–7.65 (m, 3H), 7.54–7.36 (m, 4H), 7.04 (t, J = 6.8 Hz, 1H), 5.41 (s, 2H), 4.23–4.19 (m, 1H), 4.13–4.00 (m, 2H), 3.86–3.67 (m, 2H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 161.1 (t, J = 31.7 Hz), 146.3, 145.3, 138.3, 133.5, 130.5, 129.7, 128.6, 128.2, 128.1, 126.2, 126.0, 125.0, 123.5, 118.2, 117.1 (t, J = 246.6 Hz), 116.7, 112.1, 112.0, 107.1, 48.8, 48.7 (d, J = 7.8 Hz), 47.7 (d, J = 6.1 Hz), 33.1 (m); ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$) δ -108.5 (d, J = 262.8 Hz), -112.8 (d, J = 263.2 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{21}\text{F}_2\text{N}_4\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 507.1297, found 507.1306.



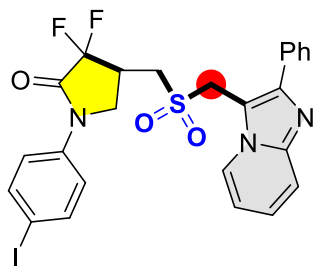
3,3-difluoro-1-(4-fluorophenyl)-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)m-ethyl)pyrrolidin-2-one (**4o**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (79.9 mg, 80%); mp: 121.6–121.8 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.35 (d, J = 6.0 Hz, 1H), 7.71 (t, J = 10.0 Hz, 3H), 7.49–7.42 (m, 5H), 7.35–7.32 (m, 1H), 7.05 (t, J = 8.0 Hz, 2H), 6.94 (d, J = 6.0 Hz, 1H), 4.92 (s, 2H), 3.98 (t, J = 8.8 Hz, 1H), 3.61 (t, J = 8.4 Hz, 1H), 3.22 (d, J = 13.2 Hz, 1H), 3.07 (dd, J = 17.6, 9.2 Hz, 1H), 3.00–2.94 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.3 (t, J = 30.3 Hz), 160.5 (d, J = 245.7 Hz), 147.6, 146.2, 133.2, 132.7, 129.3, 129.1, 128.4, 126.6, 124.7, 121.9 (d, J = 8.2 Hz), 118.3 (t, J = 218.4 Hz), 117.6, 116.0 (d, J = 22.6 Hz), 113.3, 106.7, 50.5, 47.7 (d, J = 5.4 Hz), 47.6 (d, J = 6.9 Hz) 33.9 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -110.3 (d, J = 266.2 Hz), -114.9 (d, J = 266.2 Hz); HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{21}\text{F}_3\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 500.1250, found 500.1259.



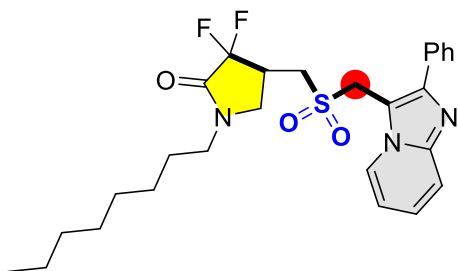
1-(4-chlorophenyl)-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)m-ethyl)pyrrolidin-2-one (**4p**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (74.3 mg, 72%); mp: 93.3–94.0 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.36 (d, J = 6.4 Hz, 1H), 7.71 (t, J = 8.0 Hz, 3H), 7.50 (d, J = 6.8 Hz, 4H), 7.43 (d, J = 7.2 Hz, 1H), 7.34 (t, J = 10.0 Hz, 3H), 6.95 (t, J = 6.8 Hz, 1H), 4.98–4.89 (m, 2H), 3.99 (t, J = 9.2 Hz, 1H), 3.61 (t, J = 8.8 Hz, 1H), 3.22 (d, J = 13.2 Hz, 1H), 3.13–3.04 (m, 1H), 3.00–2.95 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.4 (t, J = 30.9 Hz), 147.5, 146.2, 135.7, 132.7, 131.8, 129.3, 129.2, 129.1, 128.4, 126.6, 124.7, 121.1, 118.2 (t, J = 201.7 Hz), 117.6, 113.4, 106.8, 50.6, 47.7 (d, J = 7.0 Hz), 47.4 (d, J = 5.6 Hz), 33.9 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -110.3 (d, J = 266.6 Hz), -114.8 (d, J = 265.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{21}\text{ClF}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 516.0955, found 516.0962.



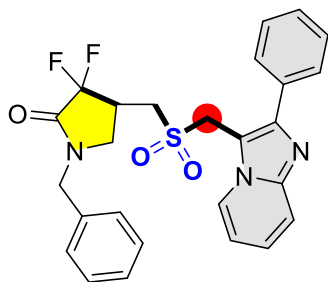
3,3-difluoro-1-(4-iodophenyl)-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4q**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (75.3 mg, 62%); mp: 75.9–76.4 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.72 (d, J = 6.8 Hz, 1H), 8.07 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 9.2 Hz, 1H), 7.56–7.49 (m, 4H), 7.44–7.36 (m, 2H), 7.04 (t, J = 6.8 Hz, 1H), 5.44 (s, 2H), 4.19–4.12 (m, 2H), 4.00 (t, J = 8.4 Hz, 1H), 3.88–3.82 (m, 1H), 3.71 (d, J = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.7 (t, J = 31.5 Hz), 146.4, 145.3, 137.8, 137.4, 133.5, 128.6, 128.1, 126.1, 126.0, 122.2, 117.2 (t, J = 247.2 Hz), 116.7, 112.1, 107.1, 90.8, 48.8, 48.6 (d, J = 6.9 Hz), 47.6 (d, J = 5.8 Hz), 33.0 (m); ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.0 (d, J = 262.4 Hz), -112.6 (d, J = 262.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{21}\text{F}_2\text{IN}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 608.0311, found 608.0318.



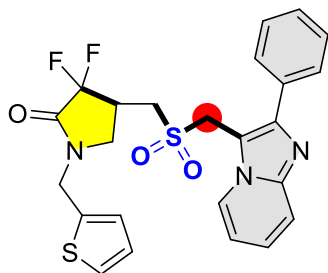
3,3-difluoro-1-octyl-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4r**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as brown solid (67.3 mg, 65%); mp: 85.2–87.3 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.25 (d, J = 6.0 Hz, 1H), 7.65 (t, J = 6.8 Hz, 3H), 7.43 (t, J = 7.6 Hz, 2H), 7.39–7.35 (m, 1H), 7.30–7.26 (m, 1H), 6.88 (t, J = 6.8 Hz, 1H), 4.87–4.79 (m, 2H), 3.52–3.47 (m, 1H), 3.26–3.10 (m, 4H), 2.96–2.81 (m, 2H), 1.45–1.38 (m, 2H), 1.17 (s, 10H), 0.80 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.5 (t, J = 30.3 Hz), 147.7, 146.3, 132.8, 129.3, 129.0, 128.4, 126.5, 124.6, 117.7, 116.5 (t, J = 248.9 Hz), 113.3, 106.8, 50.6, 47.9 (d, J = 7.6 Hz), 46.5 (d, J = 5.9 Hz), 43.5, 34.3 (m), 31.6, 29.0, 26.6, 26.5, 22.5, 14.0; ^{19}F NMR (376 MHz, CDCl_3) δ -111.4 (d, J = 265.4 Hz), -115.0 (d, J = 265.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{34}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 518.2283, found 518.2291.



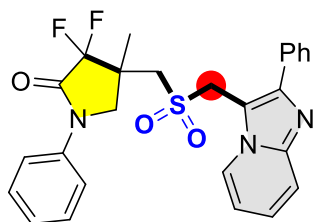
1-benzyl-3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4s**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (77.3 mg, 78%); mp: 65.9–66.8 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.63 (d, J = 6.8 Hz, 1H), 7.99 (d, J = 7.6 Hz, 2H), 7.66 (d, J = 9.2 Hz, 1H), 7.47–7.35 (m, 7H), 7.29 (d, J = 7.6 Hz, 2H), 7.01 (t, J = 6.8 Hz, 1H), 5.33 (q, J = 15.2 Hz, 2H), 4.54 (dd, J = 61.6, 14.8 Hz, 2H), 4.03–3.99 (m, 1H), 3.78–3.72 (m, 1H), 3.63 (t, J = 8.8 Hz, 1H), 3.51 (dd, J = 19.6, 11.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 162.1 (t, J = 30.2 Hz), 146.2, 145.2, 135.1, 133.4, 128.8, 128.5, 128.1, 128.0, 127.9, 127.8, 126.0, 126.0, 118.2 (t, J = 246.7 Hz), 116.6, 112.1, 107.1, 48.5 (d, J = 8.1 Hz), 46.3 (d, J = 4.6 Hz), 34.0 (m); ^{19}F NMR (376 MHz, DMSO- d_6) δ -110.0 (d, J = 261.3 Hz), -113.1 (d, J = 261.3 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 496.1501, found 496.1508.



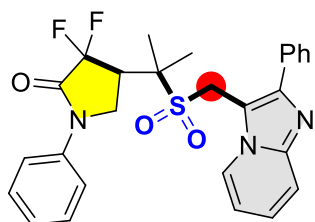
3,3-difluoro-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-(thiophen-2-ylmethyl)pyrrolidin-2-one (**4t**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (66.2 mg, 66%); mp: 73.8–75.6 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.63 (d, J = 6.8 Hz, 1H), 8.00 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 8.8 Hz, 1H), 7.54 (d, J = 4.4 Hz, 1H), 7.42 (ddd, J = 21.2, 14.8, 7.6 Hz, 4H), 7.13 (s, 1H), 7.04–7.0 (m, 2H), 5.34 (q, J = 15.2 Hz, 2H), 4.73 (dd, J = 60.8, 15.2 Hz, 2H), 4.00 (d, J = 14.0 Hz, 1H), 3.78–3.68 (m, 2H), 3.55–3.49 (m, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 161.6 (t, J = 29.5 Hz), 146.2, 145.2, 136.9, 133.4, 128.5, 128.1, 128.0, 127.8, 127.1, 126.7, 126.0, 125.9, 117.5 (t, J = 252 Hz), 116.6, 112.1, 107.1, 48.6, 48.5 (d, J = 7.3 Hz), 46.1 (d, J = 6.5 Hz), 41.0, 33.5 (m); ^{19}F NMR (376 MHz, DMSO- d_6) δ -110.0 (d, J = 261.7 Hz), -113.6 (d, J = 261.7 Hz); HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{22}\text{F}_2\text{N}_3\text{O}_3\text{S}_2^+$ ($\text{M}+\text{H}$) $^+$ 502.1065, found 502.1074.



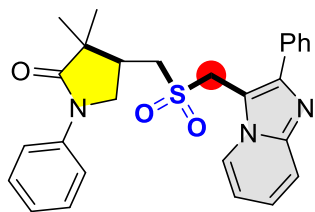
3,3-difluoro-4-methyl-1-phenyl-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)m-ethyl)pyrrolidin-2-one (**4u**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 2/1) affords the title compound as white solid (58.4 mg, 59%); mp: 89.0–91.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.26 (d, *J* = 6.8 Hz, 1H), 7.62 (dd, *J* = 18.0, 8.0 Hz, 3H), 7.41 (dd, *J* = 16.4, 8.0 Hz, 4H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.30–7.20 (m, 3H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.83 (t, *J* = 6.8 Hz, 1H), 4.79 (t, *J* = 8.8 Hz, 2H), 3.85 (d, *J* = 10.8 Hz, 1H), 3.66 (dd, *J* = 10.8, 1.6 Hz, 1H), 3.02 (dd, *J* = 31.2, 14.0 Hz, 2H), 1.30 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.3 (t, *J* = 31.5 Hz), 147.8, 146.3, 137.4, 132.9, 129.2, 129.1, 129.0, 128.4, 126.4, 126.3, 124.7, 120.0, 117.6, 117.1 (t, *J* = 256.6 Hz), 113.1, 107.1, 54.0, 52.3 (d, *J* = 8.2 Hz), 52.1, 40.6 (m), 17.7 (d, *J* = 6.1 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -114.2 (d, *J* = 260.2 Hz), -123.9 (d, *J* = 259.8 Hz); HRMS (ESI) *m/z* calcd for C₂₆H₂₄F₂N₃O₃S⁺ (M+H)⁺ 496.1501, found 496.1507.



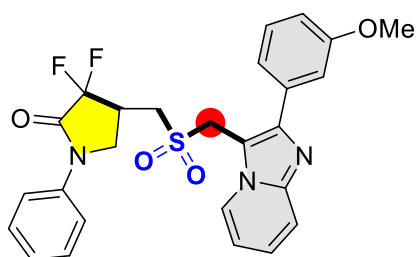
3,3-difluoro-1-phenyl-4-(2-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)propyl)pyrrolidin-2-one (**4v**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 2/1) affords the title compound as white solid (62.2 mg, 61%); mp: 241.8–242.2 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.57 (d, *J* = 7.2 Hz, 1H), 8.01–7.99 (m, 2H), 7.75 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.39–7.31 (m, 3H), 7.05 (td, *J* = 6.8, 1.2 Hz, 1H), 5.37 (q, *J* = 14.8 Hz, 2H), 4.29 (t, *J* = 9.2 Hz, 1H), 4.05 (dd, *J* = 12.0, 8.0 Hz, 1H), 3.78 (ddt, *J* = 22.8, 14.0, 8.8 Hz, 1H), 1.84 (s, 3H), 1.69 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 160.3 (t, *J* = 28.8 Hz), 147.1, 145.4, 137.7, 133.7, 129.1, 128.5, 128.2, 128.1, 126.3, 126.1, 120.5, 118.6 (t, *J* = 254.3 Hz), 116.7, 112.2, 106.7, 62.9, 45.2 (d, *J* = 6.2 Hz), 43.1, 41.0 (m), 20.8, 17.0 (d, *J* = 6.0 Hz); ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -101.2 (d, *J* = 262.1 Hz), -112.4 (d, *J* = 262.1 Hz); HRMS (ESI) *m/z* calcd for C₂₇H₂₆F₂N₃O₃S⁺ (M+H)⁺ 510.1657, found 510.1664.



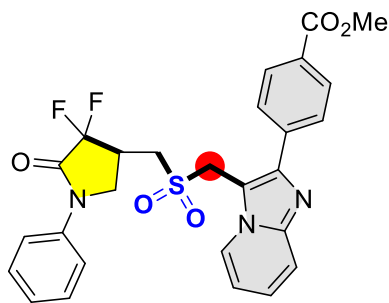
3,3-dimethyl-1-phenyl-4-((((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4w**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (66.3 mg, 70%); mp: 111.4–112.3 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.38 (d, J = 6.8 Hz, 1H), 7.74 (t, J = 8.0 Hz, 3H), 7.53–7.51 (m, 4H), 7.44 (t, J = 7.2 Hz, 1H), 7.33 (dt, J = 15.6, 7.6 Hz, 3H), 7.11 (t, J = 7.6 Hz, 1H), 6.97 (t, J = 6.8 Hz, 1H), 4.97–4.89 (m, 2H), 3.91 (dd, J = 10.0, 7.6 Hz, 1H), 3.46 (t, J = 10.0 Hz, 1H), 3.10–2.65 (m, 4H), 2.610–2.503 (m, 1H), 1.03 (s, 3H), 0.69 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.5, 146.5, 146.1, 138.8, 133.0, 129.4, 129.1, 128.8, 128.3, 126.7, 124.7, 124.7, 119.8, 117.5, 113.4, 107.6, 50.3, 50.2, 49.7, 44.2, 36.2, 23.1, 18.5; HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{28}\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 474.1846, found 474.1851.



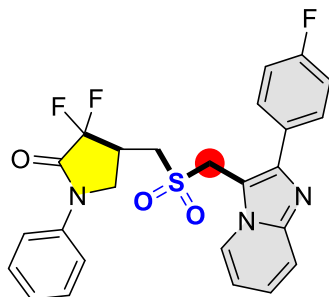
3,3-difluoro-4-((((2-(3-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-phenylpyrrolidin-2-one (**4x**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (66.5 mg, 65%); mp: 108.1–109.9 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.69 (d, J = 6.8 Hz, 1H), 7.67 (dd, J = 17.6, 9.2 Hz, 4H), 7.59 (d, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.39 (dd, J = 14.0, 6.8 Hz, 2H), 7.31 (t, J = 7.2 Hz, 1H), 7.04 (t, J = 6.8 Hz, 1H), 6.99 (d, J = 6.8 Hz, 1H), 5.40 (s, 2H), 4.19 (t, J = 9.2 Hz, 1H), 4.12 (dd, J = 14.0, 2.8 Hz, 1H), 4.01 (t, J = 8.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 3.82 (s, 3H), 3.70 (dd, J = 24.4, 14.8 Hz, 1H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 161.1 (t, J = 29.7 Hz), 159.4, 146.4, 145.2, 137.6, 134.8, 129.6, 129.1, 126.2, 126.1, 126.0, 120.5, 120.3, 117.6 (t, J = 210.8 Hz), 116.7, 114.2, 113.2, 112.1, 107.2, 55.0, 54.8, 49.3 (d, J = 6.3 Hz), 48.3 (d, J = 5.8 Hz), 33.7 (m); ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$) δ -108.1 (d, J = 262.1 Hz), -112.9 (d, J = 262.1 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_4\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 512.1450, found 512.1457.



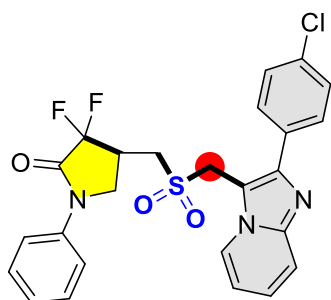
methyl(s)-4-(3-((((4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)methyl)sulfonyl)methyl)imidazo[1,2-a]pyridin-2-yl)benzoate (**4y**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (72.3 mg, 67%); mp: 200.6–202.6 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.38 (d, J = 6.8 Hz, 1H), 8.17 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 9.2 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.39 (t, J = 8.0 Hz, 3H), 7.23 (d, J = 7.6 Hz, 1H), 6.98 (t, J = 6.8 Hz, 1H), 4.93 (s, 2H), 4.10 (t, J = 9.2 Hz, 1H), 3.93 (s, 3H), 3.75–3.71 (m, 1H), 3.36 (dd, J = 13.2, 2.4 Hz, 1H), 3.24–3.15 (m, 1H), 3.11–3.05 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.6, 160.4 (t, J = 30.9 Hz), 147.0, 146.6, 137.5, 137.2, 130.5, 130.4, 129.3, 128.4, 126.8, 126.6, 124.7, 120.1, 118.0, 113.6, 107.1, 52.3, 50.9, 48.3 (d, J = 6.8 Hz), 47.7 (d, J = 5.3 Hz), 34.2 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -108.0 (d, J = 262.1 Hz), -112.8 (d, J = 261.7 Hz); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_5\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 540.1399, found 540.1408.



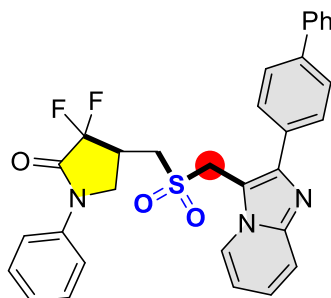
3,3-difluoro-4-((((2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-phenylpyrrolidin-2-one (**4z**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (74.9 mg, 75%); mp: 160.0–161.1 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.70 (d, J = 6.8 Hz, 1H), 8.09 (dd, J = 8.0, 6.0 Hz, 2H), 7.69 (t, J = 10.8 Hz, 3H), 7.48 (t, J = 8.0 Hz, 2H), 7.41–7.28 (m, 4H), 7.05 (t, J = 6.8 Hz, 1H), 5.42 (s, 2H), 4.21–4.13 (m, 2H), 4.03 (t, J = 7.2 Hz, 1H), 3.90–3.84 (m, 1H), 3.72 (dd, J = 25.6, 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 162.3 (d, J = 243.8 Hz), 160.7 (t, J = 29.9 Hz), 145.4, 145.2, 137.6, 130.2 (d, J = 8.2 Hz), 130.0, 129.9, 129.1, 126.2, 120.3, 117.4 (t, J = 250.5 Hz), 116.6, 115.5 (d, J = 21.2 Hz), 112.3, 107.1, 59.8, 48.6 (d, J = 10.4 Hz), 47.8 (d, J = 5.5 Hz), 33.2 (m); ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$) δ -108.1 (d, J = 262.1 Hz), -113.5 (d, J = 268.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{21}\text{F}_3\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 500.1250, found 500.1259.



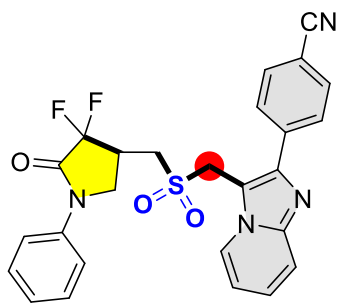
4-((((2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (**4aa**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (81.2 mg, 78%); mp: 167.1–169.1 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.68 (d, J = 6.8 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H), 7.69 (t, J = 9.6 Hz, 3H), 7.54 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.42–7.38 (m, 1H), 7.30 (t, J = 7.2 Hz, 1H), 7.05 (t, J = 6.8 Hz, 1H), 5.41 (s, 2H), 4.19–4.10 (m, 2H), 4.01 (t, J = 8.8 Hz, 1H), 3.87–3.81 (m, 1H), 3.72 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.6 (t, J = 31.8 Hz), 145.3, 145.1, 137.6, 133.0, 132.4, 129.8, 129.1, 128.6, 126.2, 126.2, 126.1, 120.3, 117.3 (t, J = 253.2 Hz), 116.7, 112.3, 107.4, 48.6 (d, J = 7.0 Hz), 48.4, 47.8 (d, J = 5.7 Hz), 33.1 (m); ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.0 (d, J = 261.7 Hz), -112.8 (d, J = 261.7 Hz); HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{21}\text{ClF}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 516.0955, found 516.0963.



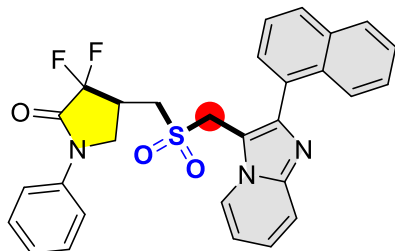
4-((((2-([1,1'-biphenyl]-4-yl)imidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (**4ab**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (81.3 mg, 73%); mp: 72.0–74.2 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.73 (d, J = 6.8 Hz, 1H), 8.14 (d, J = 8.4 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.74–7.69 (m, 5H), 7.49 (dd, J = 15.2, 7.6 Hz, 4H), 7.41 (dd, J = 16.8, 9.2 Hz, 2H), 7.30 (t, J = 7.6 Hz, 1H), 7.09 (t, J = 6.8 Hz, 1H), 5.47 (s, 2H), 4.20–4.13 (m), 4.05–4.00 (m, 1H), 3.87 (dd, J = 13.6, 10.4 Hz, 1H), 3.73 (dd, J = 18.8, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.7 (t, J = 31.6 Hz), 146.0, 145.4, 139.7, 139.6, 137.6, 132.7, 129.1, 129.0, 128.7, 127.6, 126.8, 126.6, 126.2, 126.1, 126.1, 120.3, 117.4 (t, J = 247.0 Hz), 116.7, 112.2, 107.3, 52.2, 48.7, 47.8 (d, J = 5.6 Hz), 33.2 (m); ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.1 (d, J = 262.1 Hz), -112.8 (d, J = 261.7 Hz); HRMS (ESI) m/z calcd for $\text{C}_{31}\text{H}_{26}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 558.1657, found 558.1667.



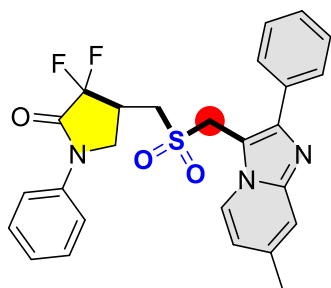
4-(3-((((4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)methyl)sulfonyl)methyl)imidazo[1,2-a]pyridin-2-yl)benzonitrile (**4ac**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (59.8 mg, 58%); mp: 249.1–251.4 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.71 (d, *J* = 6.4 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.94 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 3H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.44–7.40 (m, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.08 (t, *J* = 6.4 Hz, 1H), 5.47 (s, 2H), 4.16 (dd, *J* = 19.6, 11.2 Hz, 2H), 4.03–4.00 (m, 1H), 3.89–3.83 (m, 1H), 3.72 (dd, *J* = 27.2, 13.6 Hz, 1H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 160.6 (t, *J* = 29.5 Hz), 145.4, 144.2, 138.1, 137.6, 132.5, 132.5, 129.1, 128.6, 126.7, 126.2, 120.3, 118.8, 117.3 (t, *J* = 246.7 Hz), 116.8, 112.6, 110.5, 108.6, 48.7 (d, *J* = 7.3 Hz), 48.3, 47.8 (d, *J* = 5.5 Hz), 33.1 (m); ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -108.0 (d, *J* = 261.7 Hz), -112.8 (d, *J* = 261.7 Hz); HRMS (ESI) *m/z* calcd for C₂₆H₂₁F₂N₄O₃S⁺ (M+H)⁺ 507.1297, found 507.1304.



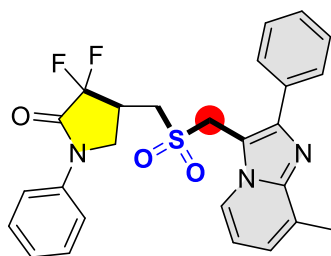
3,3-difluoro-4-((((2-(naphthalen-1-yl)imidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-phenylpyrrolidin-2-one (**4ad**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (68.0 mg, 63%); mp: 198.7–200.2 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.78 (d, *J* = 6.8 Hz, 1H), 8.00 (t, *J* = 9.2 Hz, 3H), 7.82 (d, *J* = 6.8 Hz, 1H), 7.73 (d, *J* = 9.2 Hz, 1H), 7.62 (dd, *J* = 7.2, 5.2 Hz, 3H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.46 (dt, *J* = 16.4, 6.0 Hz, 4H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 6.4 Hz, 1H), 5.25–5.17 (m, 2H), 3.95 (t, *J* = 8.8 Hz, 1H), 3.75 (d, *J* = 10.0 Hz, 2H), 3.53–3.47 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 160.5 (t, *J* = 29.9 Hz), 146.3, 145.1, 137.5, 133.4, 131.8, 130.7, 129.1, 128.7, 128.3, 128.1, 126.4, 126.2, 126.2, 126.1, 126.0, 125.9, 125.3, 120.2, 117.0 (t, *J* = 247.7 Hz), 116.8, 112.2, 109.7, 48.5, 48.0 (d, *J* = 7.0 Hz), 47.5 (d, *J* = 6.1 Hz), 32.9 (m); ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -108.3 (d, *J* = 262.4 Hz), -113.0 (d, *J* = 262.1 Hz); HRMS (ESI) *m/z* calcd for C₂₉H₂₄F₂N₃O₃S⁺ (M+H)⁺ 532.1501, found 532.1509.



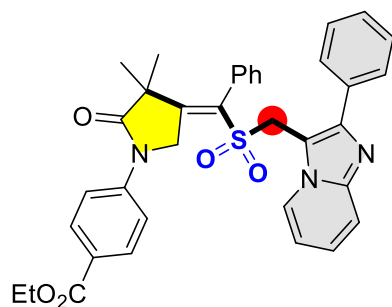
3,3-difluoro-4-((((7-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-phenylpyrrolidin-2-one (**4ae**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (64.4 mg, 65%); mp: 166.2–167.5 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.56 (d, J = 7.2 Hz, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.50–7.38 (m, 6H), 7.31 (d, J = 6.8 Hz, 1H), 6.89 (d, J = 7.2 Hz, 1H), 5.36 (s, 2H), 4.17–4.07 (m, 2H), 4.00 (t, J = 8.4 Hz, 1H), 3.85–3.79 (m, 1H), 3.69 (dd, J = 20.8, 10.0 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.5 (t, J = 31.7 Hz), 146.1, 145.1, 138.3, 137.5, 133.3, 128.6, 128.2, 128.1, 127.7, 126.2, 118.1, 117.4 (t, J = 247.2 Hz), 116.6, 112.3, 107.3, 48.7, 48.0 (d, J = 6.0 Hz), 42.1, 33.2 (m), 21.0; ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.1 (d, J = 262.1 Hz), -112.9 (d, J = 262.1 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 496.1501, found 496.1509.



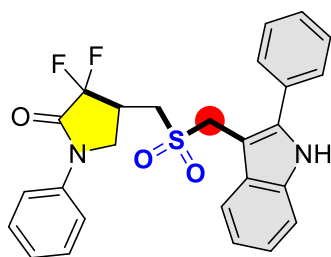
3,3-difluoro-4-((((8-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methyl)-1-phenylpyrrolidin-2-one (**4af**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (68.7 mg, 69%); mp: 77.5–79.3 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 8.55 (d, J = 6.8 Hz, 1H), 8.04 (d, J = 7.6 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 2.8 Hz, 4H), 7.43–7.40 (m, 1H), 7.30 (t, J = 7.2 Hz, 1H), 7.19 (d, J = 6.8 Hz, 1H), 6.94 (t, J = 6.8 Hz, 1H), 5.39 (s, 2H), 4.18–4.07 (m, 2H), 4.00 (t, J = 8.4 Hz, 1H), 3.85–3.79 (m, 1H), 3.73–3.65 (m, 1H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.6 (t, J = 30.3 Hz), 145.8, 145.6, 137.6, 133.7, 129.1, 128.5, 128.2, 128.0, 127.9, 126.2, 124.4, 123.9, 120.3, 117.3 (t, J = 246.1 Hz), 112.1, 107.6, 48.8, 48.6 (d, J = 6.6 Hz), 47.8 (d, J = 6.2 Hz), 33.1 (m), 16.5; ^{19}F NMR (376 MHz, DMSO- d_6) δ -108.1 (d, J = 262.1 Hz), -112.8 (d, J = 262.1 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{N}_3\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 496.1501, found 496.1507.



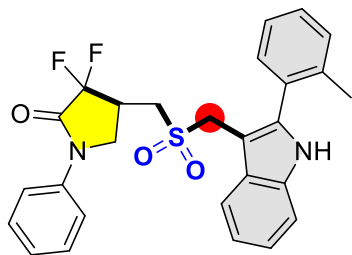
ethyl(Z)-4-(3,3-dimethyl-2-oxo-4-(phenyl(((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)sulfonyl)methylene)pyrrolidin-1-yl)benzoate (**4ag**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as yellow solid (48.3 mg, 39%); mp: 76.7–79.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, *J* = 6.8 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.69 (dd, *J* = 13.2, 7.6 Hz, 4H), 7.61 (d, *J* = 9.2 Hz, 1H), 7.46–7.29 (m, 8H), 6.98 (d, *J* = 7.2 Hz, 2H), 6.91 (t, *J* = 6.8 Hz, 1H), 4.81 (s, 2H), 4.69 (s, 2H), 4.41 (dd, *J* = 14.0, 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H), 1.01 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 175.2, 166.0, 154.0, 147.9, 146.1, 141.9, 136.1, 133.0, 131.4, 130.6, 130.5, 129.8, 129.0, 128.8, 128.6, 128.4, 126.5, 126.2, 125.2, 118.7, 117.5, 113.0, 106.7, 61.0, 50.2, 49.7, 49.0, 24.8, 14.3; HRMS (ESI) *m/z* calcd for C₃₆H₃₄N₃O₅S⁺ (*M*+H)⁺ 620.2214, found 620.2217.



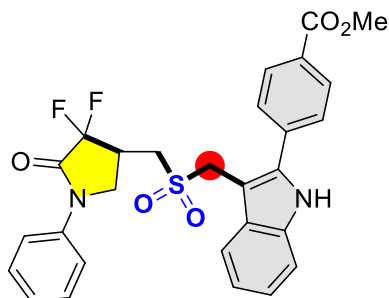
3,3-difluoro-1-phenyl-4-((((2-phenyl-1*H*-indol-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4ah**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as pink solid (57.7 mg, 60%); mp: 116.5–118.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.49 (s, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.46 (t, *J* = 8.0 Hz, 4H), 7.40–7.36 (m, 2H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.25–7.19 (m, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 4.63 (s, 2H), 4.00–3.95 (m, 1H), 3.58–3.54 (m, 1H), 3.13 (dd, *J* = 13.2, 2.0 Hz, 1H), 2.97 (dd, *J* = 19.2, 11.2 Hz, 1H), 2.90–2.84 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.7 (t, *J* = 30.7 Hz), 139.1, 137.3, 135.7, 131.2, 129.6, 129.3, 129.2, 128.5, 128.0, 126.4, 123.5, 121.3, 120.0, 119.5, 116.3 (t, *J* = 30.7 Hz), 111.4, 98.7, 52.7, 47.8 (d, *J* = 5.6 Hz), 47.5 (d, *J* = 6.7 Hz), 34.2 (m); ¹⁹F NMR (376 MHz, CDCl₃) δ -115.1 (d, *J* = 265.8 Hz), -119.8 (d, *J* = 265.2 Hz); HRMS (ESI) *m/z* calcd for C₂₆H₂₂F₂N₂O₃SN⁺ (*M*+Na)⁺ 503.1220, found 503.1214.



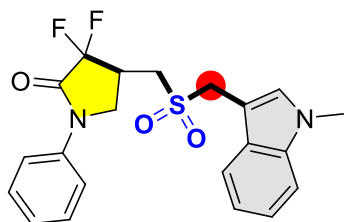
3,3-difluoro-1-phenyl-4-((((2-(o-tolyl)-1H-indol-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4ai**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 3/1) affords the title compound as pink solid (48.5 mg, 49%); mp: 108.9–110.1 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.43 (s, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 7.6 Hz, 1H), 7.32–7.18 (m, 8H), 7.16 (d, J = 7.6 Hz, 1H), 4.40 (s, 2H), 3.97–3.93 (m, 1H), 3.51 (t, J = 9.2 Hz, 1H), 3.05–2.91 (m, 2H), 2.78 (t, J = 12.4 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.7 (t, J = 29.7 Hz), 138.6, 137.4, 137.3, 135.7, 131.1, 130.6, 130.1, 129.8, 129.1, 127.3, 126.4, 126.4, 123.2, 121.1, 120.0, 119.6, 116.4 (t, J = 29.7 Hz), 111.3, 99.9, 52.7, 47.7 (d, J = 5.6 Hz), 46.7 (d, J = 6.7 Hz), 34.0 (m), 19.8; ^{19}F NMR (376 MHz, CDCl_3) δ -115.2 (d, J = 265.5 Hz), -119.6 (d, J = 265.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{24}\text{F}_2\text{N}_2\text{O}_3\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 517.1368, found 517.1372.



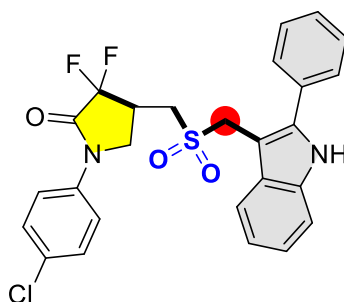
Methyl-4-(3-((((4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)methyl)sulfonyl)methyl)-1H-indol-2-yl)benzoate (**4aj**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 2/1) affords the title compound as pink solid (56.0 mg, 52%); mp: 136.2–138.2 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.68 (s, 1H), 8.10 (d, J = 8.4 Hz, 2H), 7.68 (dd, J = 13.6, 8.0 Hz, 3H), 7.47 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 8.0 Hz, 2H), 7.26–7.20 (m, 2H), 7.19–7.15 (m, 1H), 4.63 (s, 2H), 4.06–4.02 (m, 1H), 3.89 (s, 3H), 3.66–3.62 (m, 1H), 3.25 (dd, J = 13.2, 2.0 Hz, 1H), 3.10–3.05 (m, 1H), 3.00–2.94 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.4, 160.6 (t, J = 32.1 Hz), 137.9, 137.3, 136.0, 135.6, 130.6, 130.6, 129.2, 128.3, 128.0, 126.5, 124.0, 121.5, 120.1, 119.5, 116.4 (t, J = 249.9 Hz), 111.6, 99.4, 52.6, 52.4, 48.0 (d, J = 6.8 Hz), 47.9 (d, J = 5.8 Hz), 34.3 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -114.9 (d, J = 271.1 Hz), -119.7 (d, J = 269.1 Hz); HRMS (ESI) m/z calcd for $\text{C}_{28}\text{H}_{25}\text{F}_2\text{N}_2\text{O}_5\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 539.1447, found 539.1451.



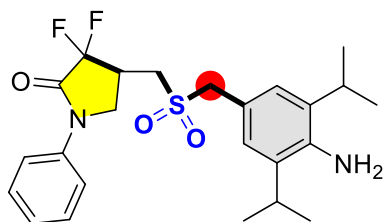
3,3-difluoro-4-((((1-methyl-1*H*-indol-3-yl)methyl)sulfonyl)methyl)-1-phenylpyrrolidin-2-one(**4ak**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 2/1) affords the title compound as yellow solid (46.0 mg, 55%); mp: 82.3–84.6 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.70 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.43 (t, J = 8.0 Hz, 3H), 7.36 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 6.8 Hz, 3H), 4.60 (s, 2H), 4.22–4.18 (m, 1H), 3.88 (s, 3H), 3.79–3.75 (m, 1H), 3.48 (d, J = 13.6 Hz, 1H), 3.29–3.19 (m, 1H), 3.15–3.09 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.7 (t, J = 29.7 Hz), 137.4, 137.0, 130.3, 129.2, 127.0, 126.5, 122.8, 120.7, 120.0, 118.5, 116.5 (t, J = 252.3 Hz), 110.0, 99.9, 52.8, 48.0 (d, J = 5.8 Hz), 46.6 (d, J = 6.6 Hz), 34.4 (m), 33.2; ^{19}F NMR (376 MHz, CDCl_3) δ -110.4 (d, J = 265.8 Hz), -115.1 (d, J = 270.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{20}\text{F}_2\text{N}_2\text{O}_3\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 441.1055, found 441.1063.



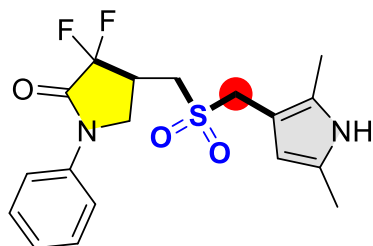
1-(4-chlorophenyl)-3,3-difluoro-4-((((2-phenyl-1*H*-indol-3-yl)methyl)sulfonyl)methyl)pyrrolidin-2-one (**4al**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as red oil (58.7 mg, 57%); ^1H NMR (400 MHz, CDCl_3) δ 8.61 (s, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.2 Hz, 2H), 7.52–7.44 (m, 4H), 7.33 (dd, J = 13.2, 8.8 Hz, 4H), 4.77–4.67 (m, 2H), 4.05–4.00 (m, 1H), 3.60 (t, J = 9.2 Hz, 1H), 3.21 (d, J = 11.6 Hz, 1H), 3.11–3.02 (m, 1H), 2.98–2.92 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.7 (t, J = 30.3 Hz), 139.1, 135.9, 135.7, 131.8, 131.2, 129.6, 129.4, 129.2, 128.5, 127.9, 123.5, 121.3, 121.1, 119.5, 116.2 (t, J = 247.7 Hz), 111.4, 98.7, 52.7, 47.7 (d, J = 5.9 Hz), 47.4 (d, J = 6.5 Hz), 34.1 (m); ^{19}F NMR (376 MHz, CDCl_3) δ -110.6 (d, J = 265.8 Hz), -115.0 (d, J = 265.8 Hz); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{21}\text{ClF}_2\text{N}_2\text{O}_3\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 537.0822, found 537.0826.



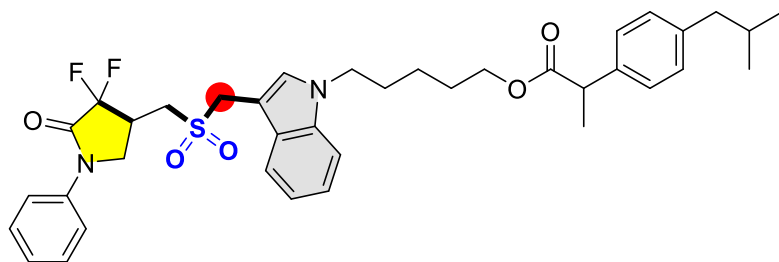
4-(((4-amino-3,5-diisopropylbenzyl)sulfonyl)methyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (**4am**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as green solid (68.0 mg, 73%); mp: 60.0–60.5 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.51 (d, J = 8.0 Hz, 2H), 7.32 (t, J = 8.0 Hz, 2H), 7.17 (d, J = 7.6 Hz, 1H), 6.97 (s, 2H), 4.24–4.16 (m, 2H), 4.06 (dd, J = 10.8, 8.0 Hz, 1H), 3.66–3.62 (m, 1H), 3.35 (d, J = 11.6 Hz, 3H), 3.04–2.94 (m, 2H), 2.83 (dt, J = 13.6, 6.8 Hz, 2H), 1.19 (t, J = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.7 (t, J = 30.9 Hz), 141.3, 137.3, 133.3, 129.2, 126.5, 125.2, 120.0, 116.4 (t, J = 278.9 Hz), 61.4, 47.9 (d, J = 5.6 Hz), 46.6 (d, J = 6.9 Hz), 34.6 (m), 27.9, 22.3, 22.2; ^{19}F NMR (376 MHz, CDCl_3) δ -110.4 (d, J = 265.5 Hz), -115.6 (d, J = 265.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{30}\text{F}_2\text{N}_2\text{O}_3\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 487.1837, found 487.1845.



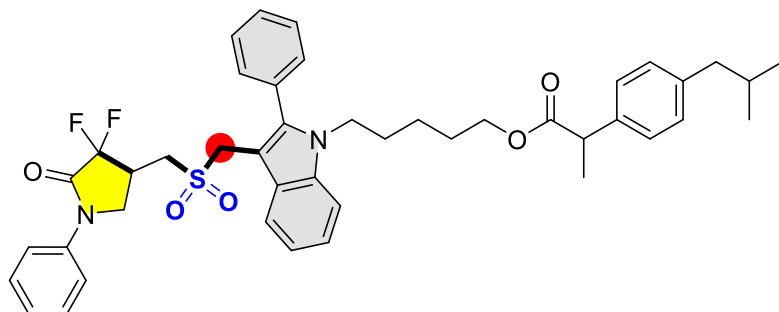
4-(((2,5-dimethyl-1H-pyrrol-3-yl)methyl)sulfonyl)methyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (**4an**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 1/1) affords the title compound as white solid (21.3 mg, 28%); mp: 121.4–121.6 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.83 (s, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.40 (t, J = 7.6 Hz, 3H), 7.24 – 7.23 (m, 1H), 4.18 (t, J = 9.2 Hz, 1H), 4.05 (s, 2H), 3.80 – 3.67 (m, 2H), 3.20 – 3.12 (m, 2H), 2.21 (s, 3H), 2.13 (d, J = 3.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.8 (t, J = 29.8 Hz), 137.4, 129.2, 126.5, 126.4, 123.3, 120.0, 117.4 (t, J = 245.4 Hz), 116.8, 104.4, 52.4, 48.1 (d, J = 5.5 Hz), 46.5 (d, J = 6.5 Hz), 34.3 (m), 11.6, 11.1; ^{19}F NMR (376 MHz, CDCl_3) δ -110.21 (dd, J = 265.3, 7.5 Hz), -115.04 (dd, J = 265.5, 8.2 Hz); HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{21}\text{F}_2\text{N}_2\text{O}_3\text{S}^+$ ($\text{M}+\text{H}$) $^+$ 383.1235, found 383.1237.



5-(3-((((4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)methyl)sulfonyl)methyl)-1H-indol-1-yl)pentyl 2-(4-isobutylphenyl)propanoate (**4ao**):

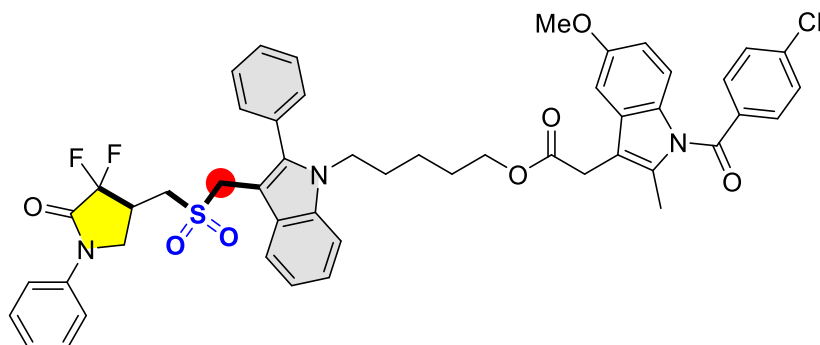
Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 3/1) affords the title compound as yellow oil (69.2 mg, 51%); ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.34–7.22 (m, 4H), 7.20–7.14 (m, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.0 Hz, 2H), 4.49 (s, 2H), 4.10–4.06 (m, 1H), 4.02–3.93 (m, 4H), 3.67–3.56 (m, 2H), 3.38–3.35 (m, 1H), 3.14–2.97 (m, 2H), 2.36 (d, J = 7.2 Hz, 2H), 1.79–1.69 (m, 3H), 1.56–1.48 (m, 4H), 1.39 (d, J = 7.2 Hz, 3H), 0.81 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 174.7, 160.6 (t, J = 27.5 Hz), 140.5, 137.8, 137.4, 136.3, 129.3, 129.2, 129.2, 127.1, 126.5, 122.7, 120.7, 120.0, 118.7, 115.4 (t, J = 270.3 Hz), 110.1, 100.0, 64.1, 52.8, 47.9 (d, J = 5.9 Hz), 46.6 (d, J = 6.9 Hz), 46.5, 45.1, 45.0, 34.5, 30.2, 29.6, 28.0, 23.2, 22.3, 18.4; ^{19}F NMR (376 MHz, CDCl_3) δ -115.2 (d, J = 265.5 Hz), -119.9 (d, J = 265.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{38}\text{H}_{44}\text{F}_2\text{N}_2\text{O}_5\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 701.2831, found 701.2833.



5-(3-((((4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)methyl)sulfonyl)methyl)-2-phenyl-1H-indol-1-yl)pentyl 2-(4-isobutylphenyl)propanoate (**4ap**):

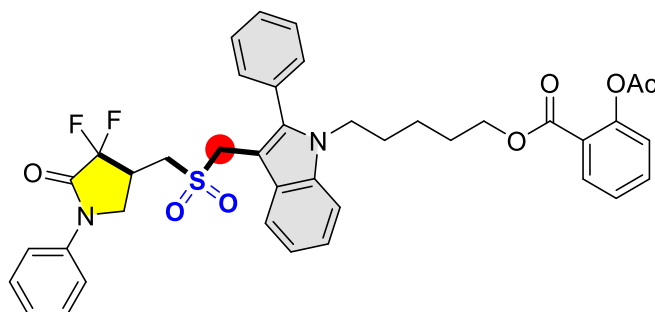
Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 3/1) affords the title compound as red solid (81.5 mg, 54%); mp: 52.0–52.2 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, J = 8.0 Hz, 1H), 7.60–7.54 (m, 5H), 7.43–7.34 (m, 6H), 7.28 (dt, J = 20.0, 7.6 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 4.54 (s, 2H), 4.09–4.00 (m, 3H), 3.94 (t, J = 6.4 Hz, 2H), 3.68–3.61 (m, 2H), 3.14–3.01 (m, 2H), 2.89 (t, J = 12.8 Hz, 1H), 2.46 (d, J = 7.2 Hz, 2H), 1.85 (dt, J = 13.6, 6.8 Hz, 1H), 1.61 (dd, J = 15.2, 7.6 Hz, 2H), 1.47 (d, J = 7.2 Hz, 3H), 1.41 (dd, J = 14.8, 6.8 Hz, 2H), 1.13–1.05 (m, 2H), 0.91 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 174.6, 160.6 (t, J = 29.8 Hz), 141.3, 140.5, 137.7, 137.3, 136.2, 130.4, 130.2, 129.5, 129.3, 129.2, 129.1, 127.1, 127.0, 126.4, 122.9, 120.9, 120.0, 119.7, 116.5 (t, J = 256.0 Hz), 110.2, 99.2, 64.0, 52.9, 47.7 (d, J = 5.7 Hz), 47.1 (d, J = 6.7 Hz), 45.1,

45.0, 43.9, 34.1 (m), 30.1, 29.3, 27.9, 22.9, 22.3, 18.4; ^{19}F NMR (376 MHz, CDCl_3) δ -115.1 (d, $J = 265.5$ Hz), -119.6 (d, $J = 265.5$ Hz); HRMS (ESI) m/z calcd for $\text{C}_{44}\text{H}_{48}\text{F}_2\text{N}_2\text{O}_5\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 777.3144, found 777.3142.



5-(3-((((4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)methyl)sulfonyl)methyl)-2-phenyl-1*H*-indol-1-yl)pentyl-2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate(**4aq**):

Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 2/1) affords the title compound as brown solid (96.3 mg, 53%); mp: 64.0–64.3 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, $J = 7.6$ Hz, 1H), 7.54 (d, $J = 8.4$ Hz, 2H), 7.49–7.43 (m, 5H), 7.37 (d, $J = 8.4$ Hz, 2H), 7.33–7.20 (m, 7H), 7.15 (t, $J = 7.6$ Hz, 1H), 6.86 (d, $J = 2.4$ Hz, 1H), 6.77 (d, $J = 9.2$ Hz, 1H), 6.59 (dd, $J = 9.2, 2.4$ Hz, 1H), 4.43 (s, 2H), 3.98–3.93 (m, 1H), 3.89 (dd, $J = 13.6, 7.2$ Hz, 4H), 3.72 (s, 3H), 3.55–3.51 (m, 3H), 3.05–2.91 (m, 2H), 2.80 (t, $J = 12.8$ Hz, 1H), 2.27 (s, 3H), 1.39–1.32 (m, 2H), 1.21 (d, $J = 15.2$ Hz, 2H), 1.07–0.99 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 168.2, 160.9 (t, $J = 23.2$ Hz), 156.0, 141.3, 139.3, 137.3, 136.2, 135.9, 133.8, 131.1, 130.8, 130.6, 130.4, 130.2, 129.5, 129.3, 129.1, 129.1, 127.0, 126.4, 123.0, 121.0, 120.0, 119.7, 116.5 (t, $J = 255.7$ Hz), 114.9, 112.6, 111.4, 110.2, 101.5, 99.3, 64.4, 55.7, 52.9, 47.7 (d, $J = 5.8$ Hz), 47.1 (d, $J = 6.6$ Hz), 43.8, 34.1 (m), 30.3, 29.4, 28.0, 23.0, 13.3; ^{19}F NMR (376 MHz, CDCl_3) δ -115.1 (d, $J = 265.5$ Hz), -119.7 (d, $J = 265.5$ Hz); HRMS (ESI) m/z calcd for $\text{C}_{50}\text{H}_{46}\text{ClF}_2\text{N}_3\text{O}_7\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 928.2605, found 928.2601.

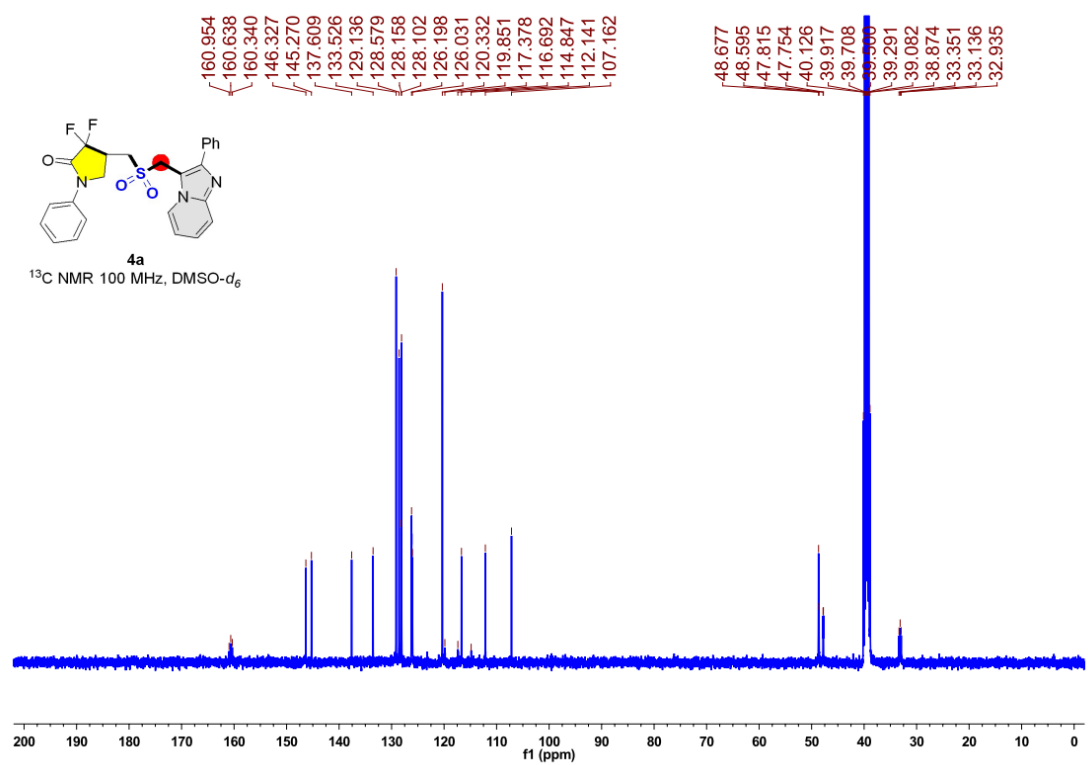
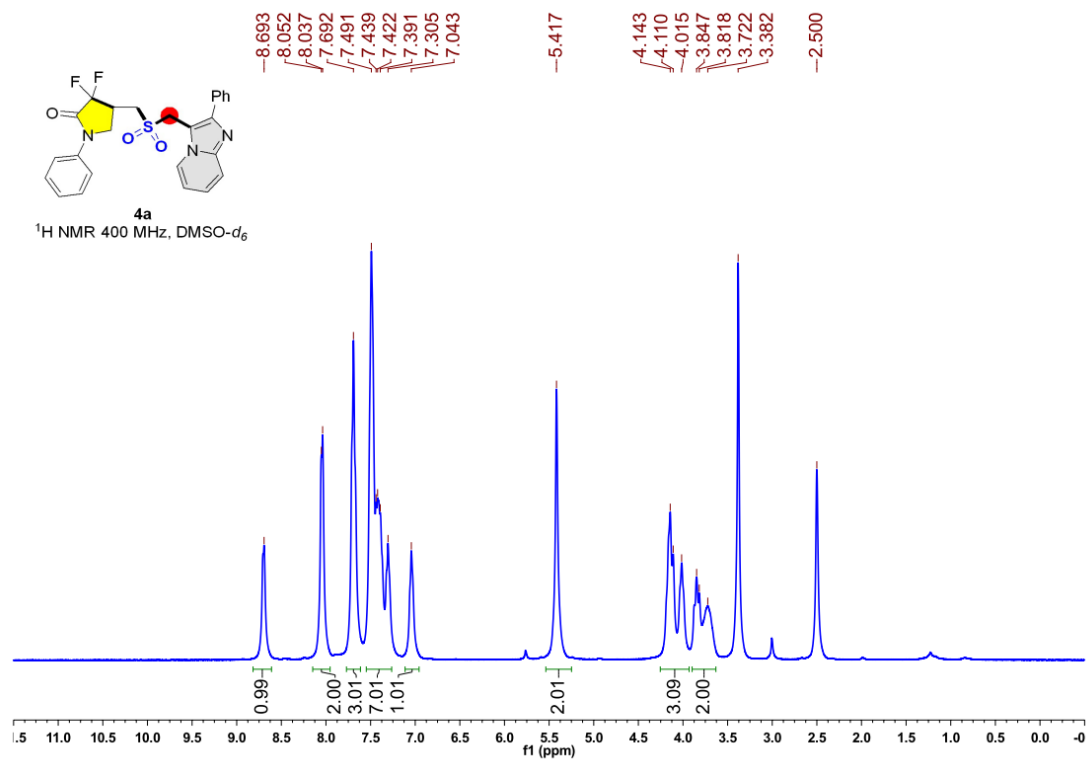


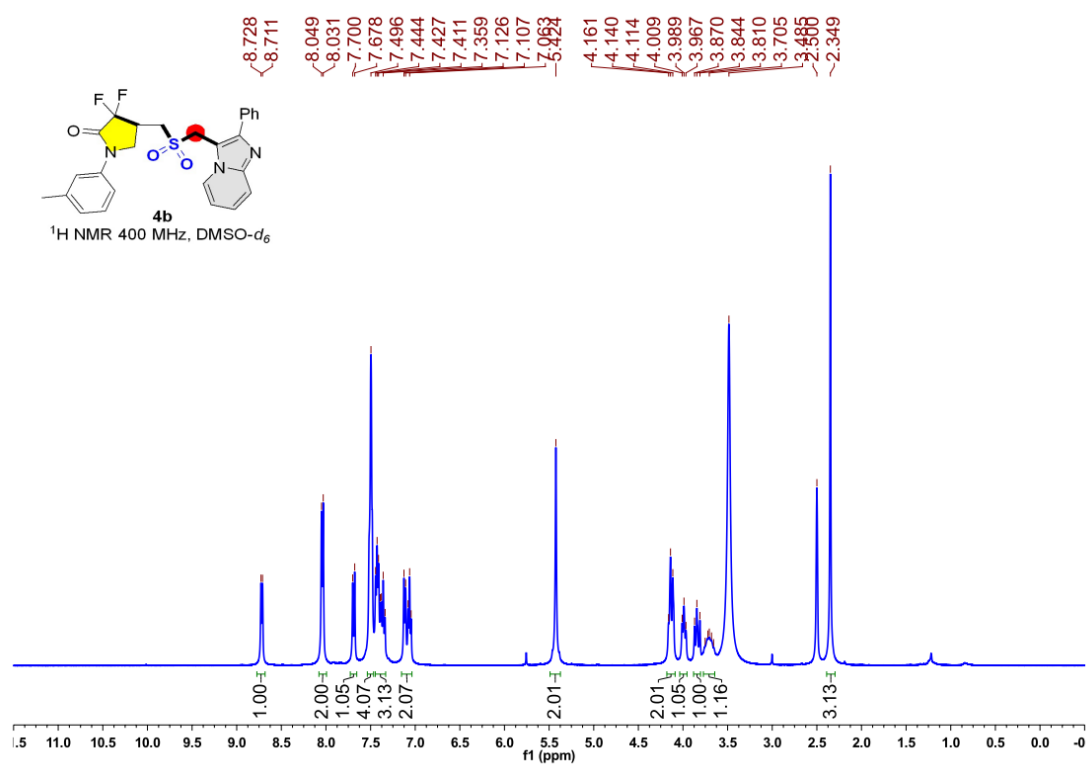
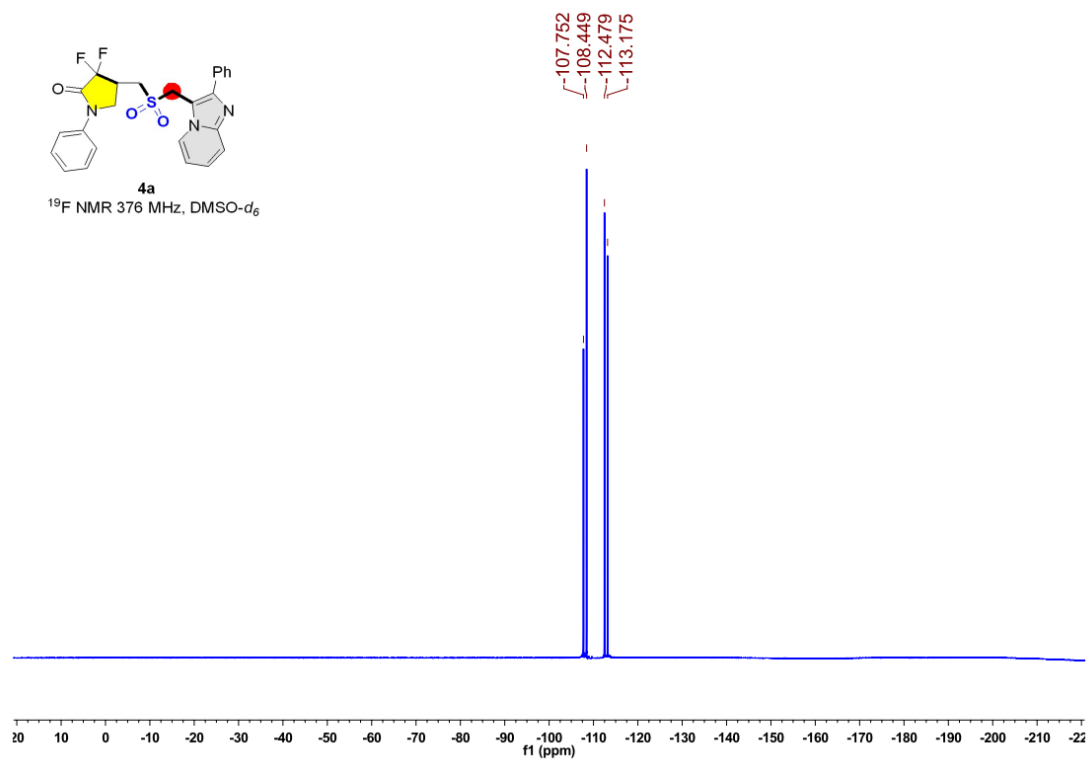
5-(3-((((4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)methyl)sulfonyl)methyl)-2-phenyl-1*H*-indol-1-yl)pentyl 2-acetoxybenzoate(**4ar**):

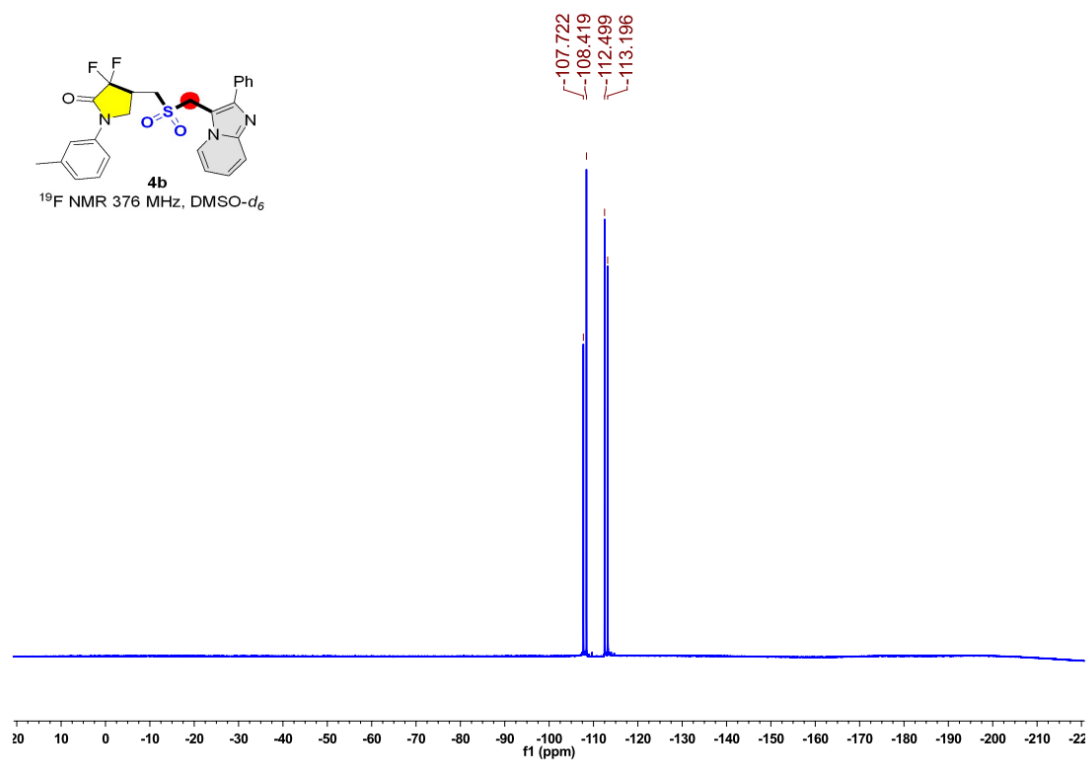
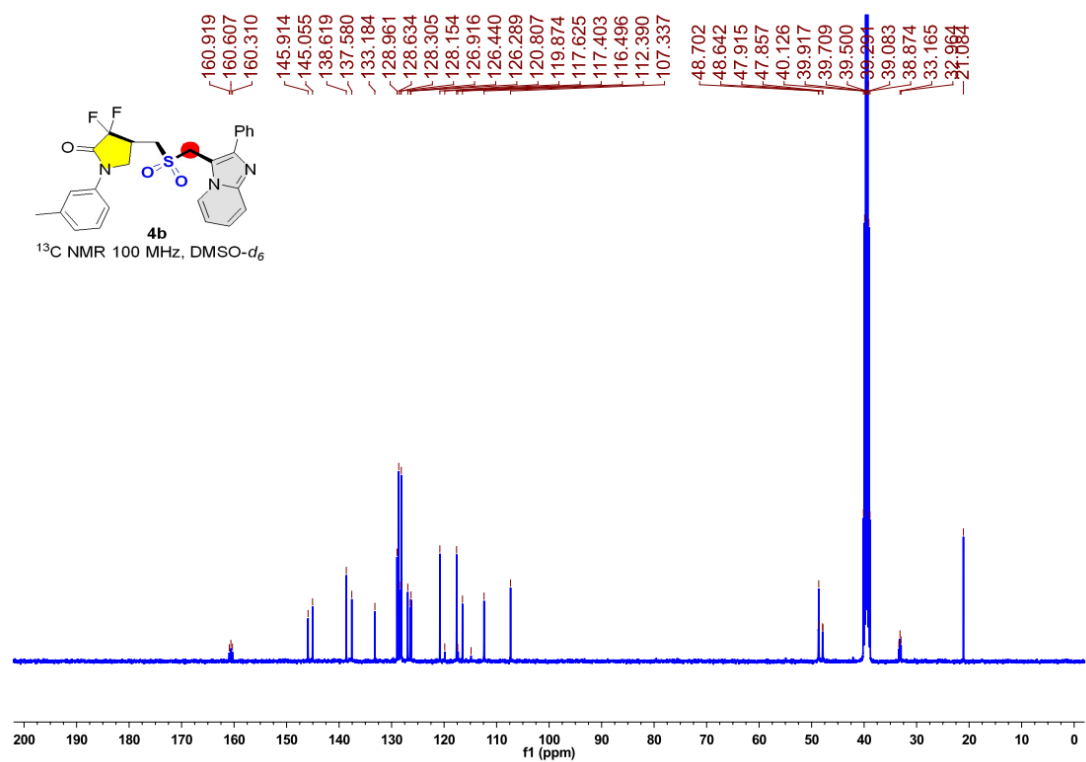
Purification by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 2/1) affords the title compound as yellow solid (62.7 mg, 43%); mp: 50.8–

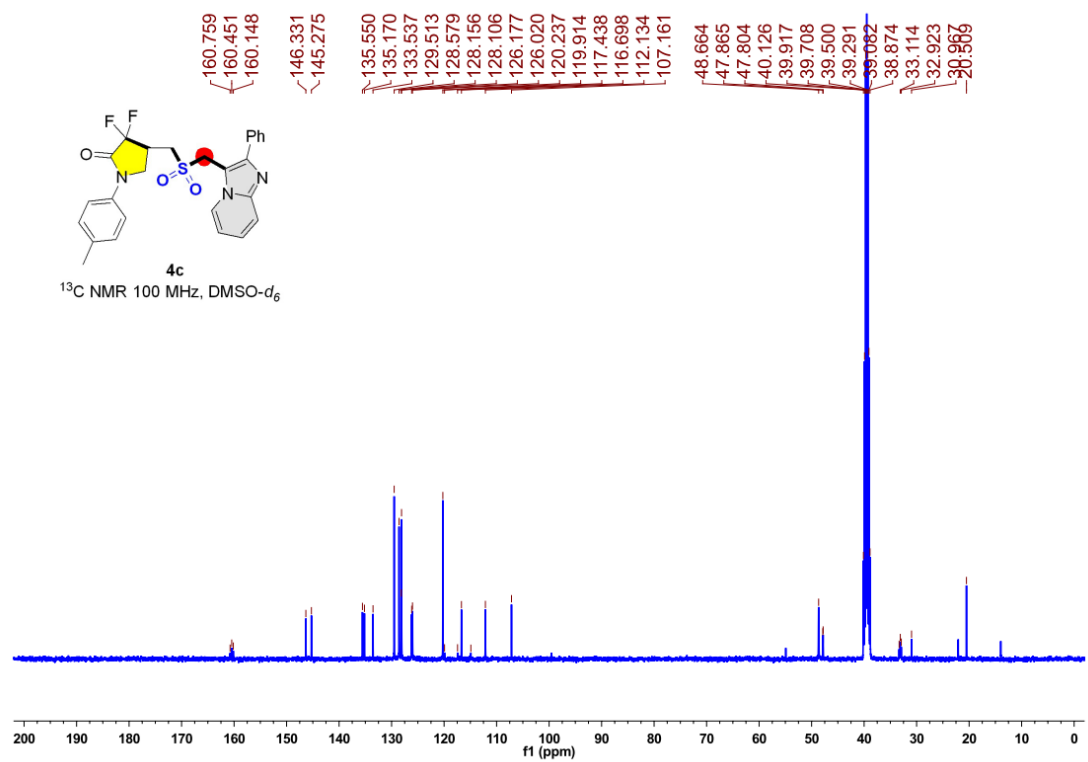
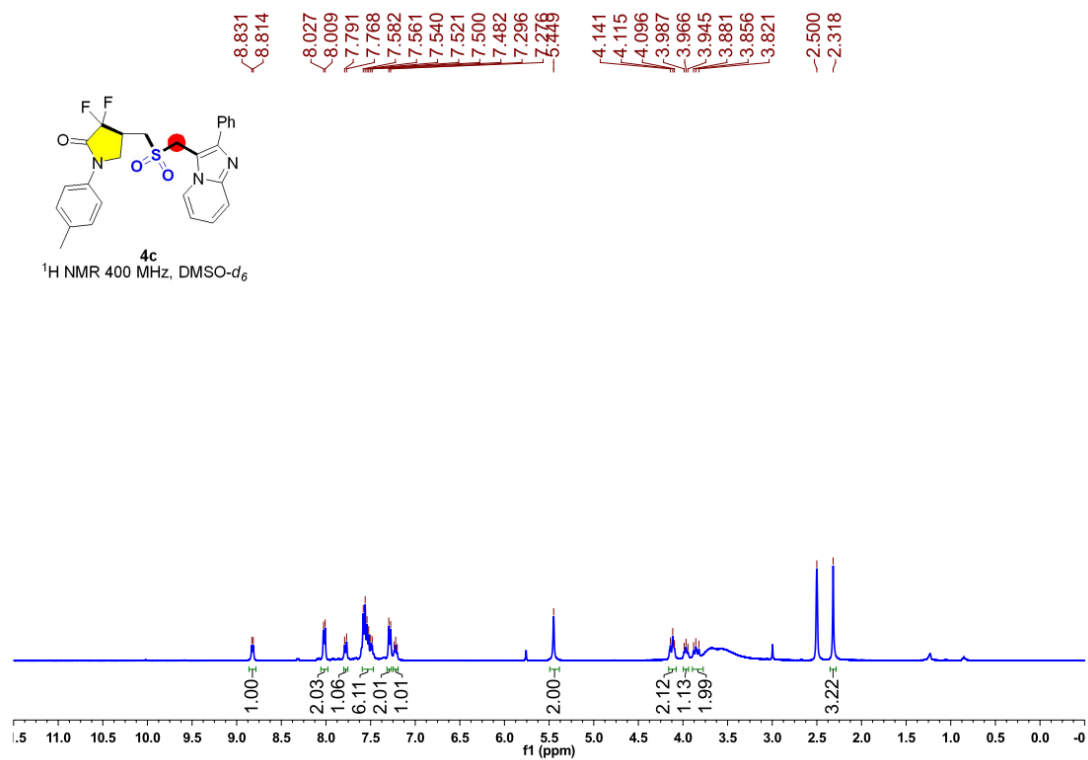
51.2 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.87–7.80 (m, 1H), 7.77–7.70 (m, 1H), 7.46 (dd, $J = 12.0, 6.0$ Hz, 6H), 7.32 (dt, $J = 14.0, 6.8$ Hz, 5H), 7.25–7.15 (m, 4H), 7.05–7.01 (m, 1H), 4.43 (d, $J = 4.8$ Hz, 2H), 4.01 (ddd, $J = 30.0, 17.6, 8.0$ Hz, 5H), 3.53–3.49 (m, 1H), 2.96 (dd, $J = 38.8, 18.4$ Hz, 2H), 2.77 (t, $J = 12.4$ Hz, 1H), 2.22 (s, 3H), 1.53 (dd, $J = 34.8, 13.2$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 169.6, 164.3, 160.6 (t, $J = 31.0$ Hz), 150.7, 141.3, 137.3, 136.2, 133.8, 131.6, 130.4, 130.2, 129.5, 129.4, 129.1, 127.0, 126.4, 126.0, 123.8, 123.2, 123.0, 121.0, 120.0, 119.7, 116.5 (t, $J = 256.3$ Hz), 110.3, 99.3, 64.5, 52.8, 47.7 (d, $J = 5.6$ Hz), 47.1 (d, $J = 6.6$ Hz), 43.9, 34.1 (m), 29.4, 28.0, 23.1, 21.0; ^{19}F NMR (376 MHz, CDCl_3) δ -115.1 (d, $J = 267.1$ Hz), -119.7 (d, $J = 269.6$ Hz); HRMS (ESI) m/z calcd for $\text{C}_{40}\text{H}_{38}\text{F}_2\text{N}_2\text{O}_7\text{SNa}^+$ ($\text{M}+\text{Na}$) $^+$ 751.2260, found 751.2267.

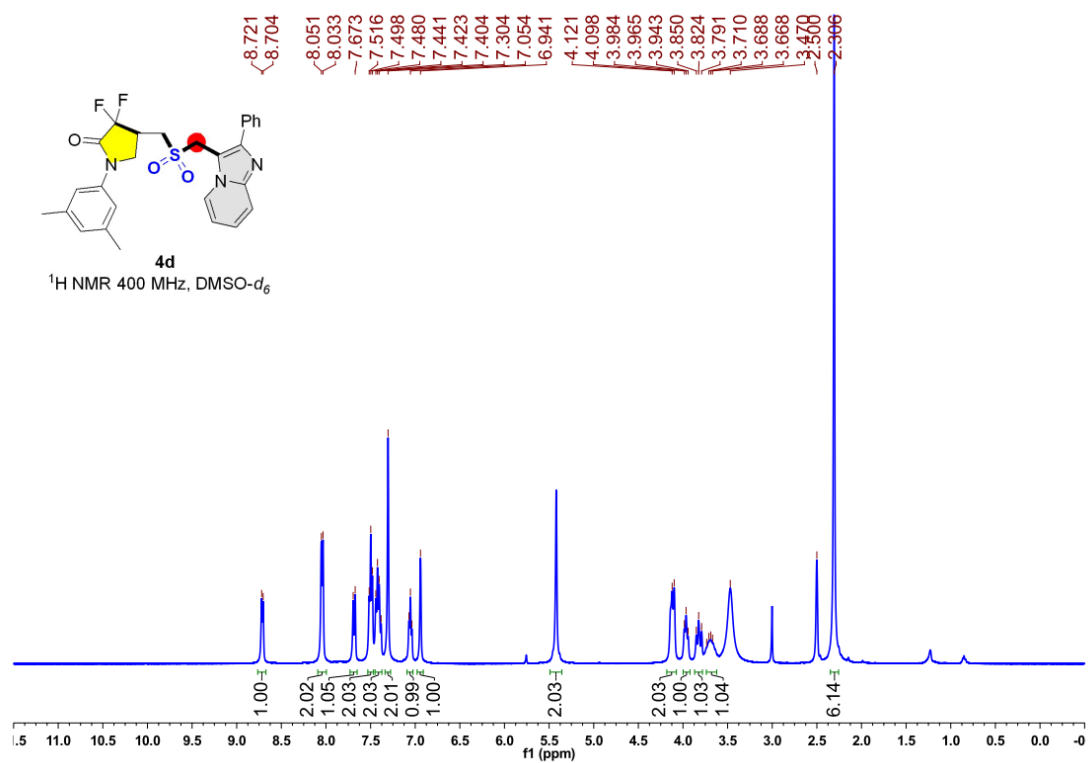
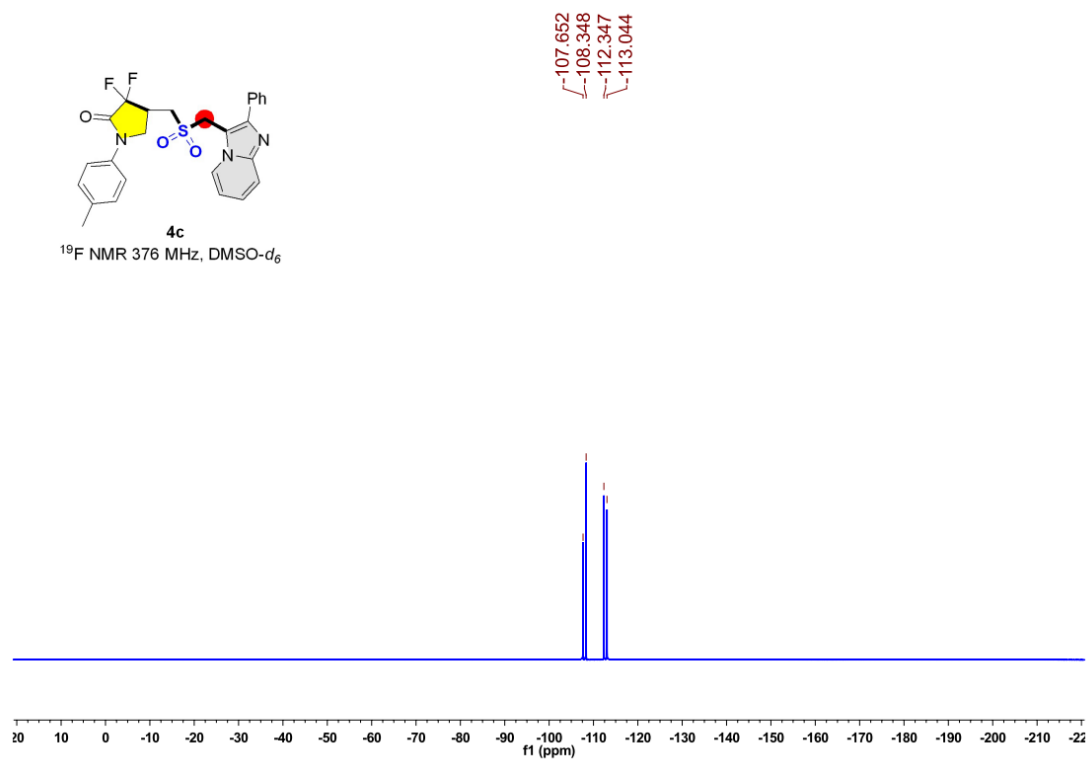
6. Copies of ^1H NMR, ^{13}C NMR, ^{19}F NMR

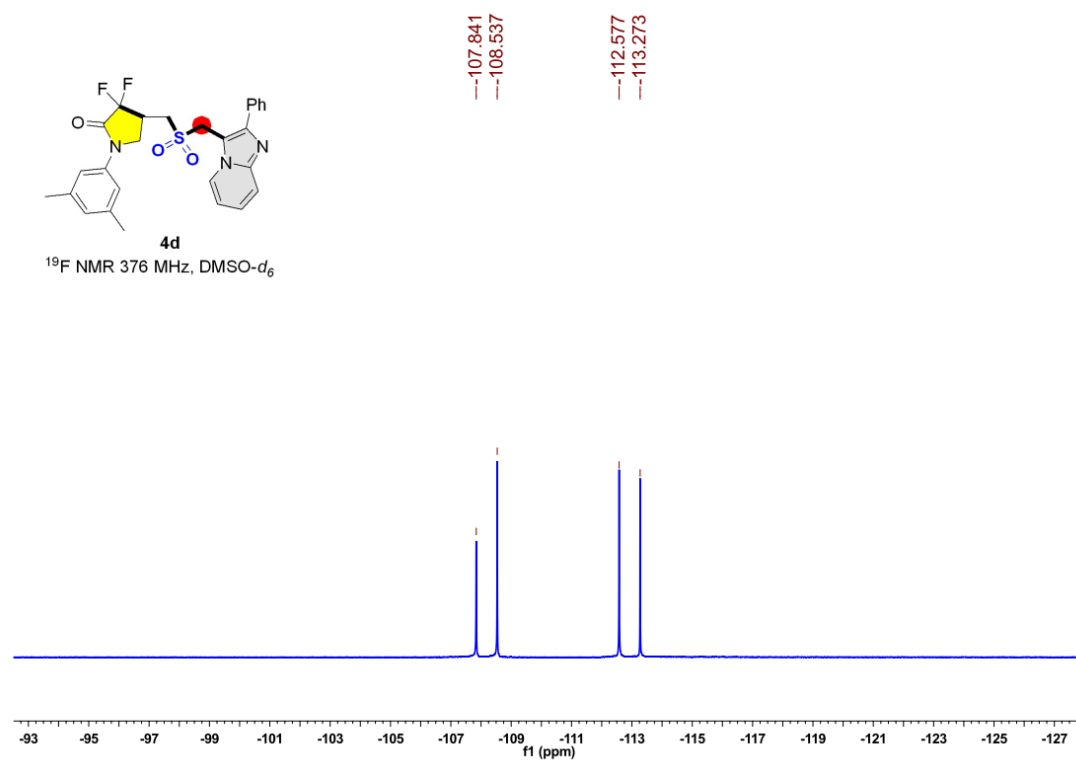
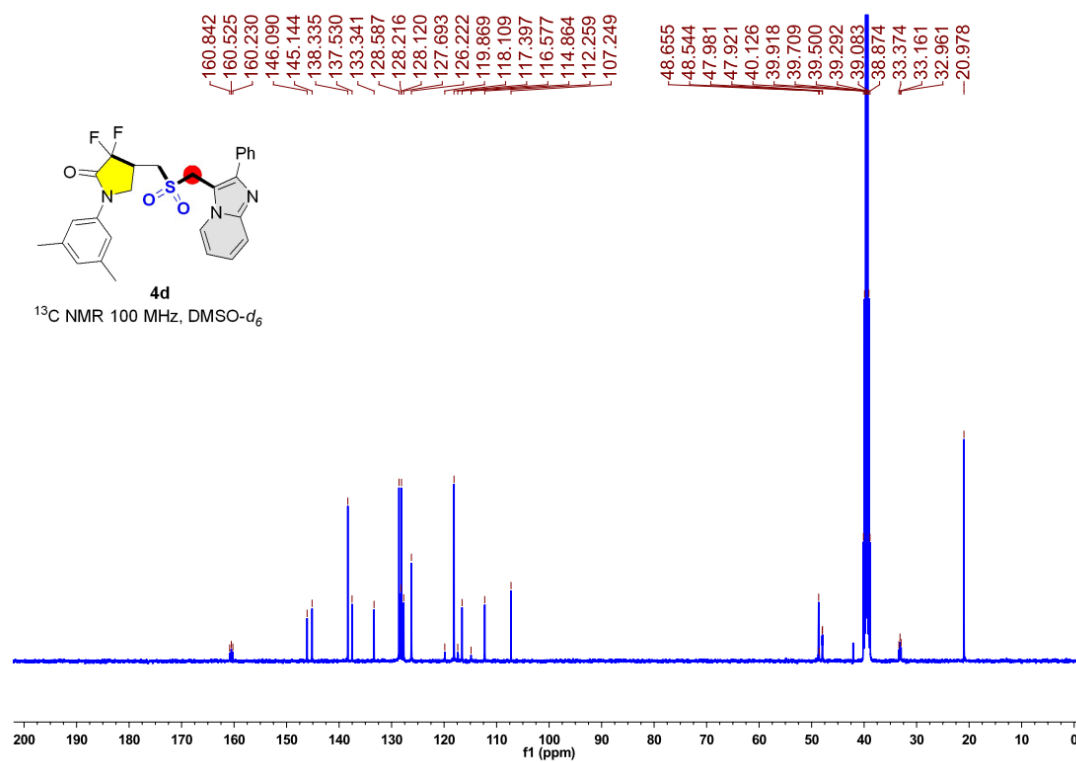


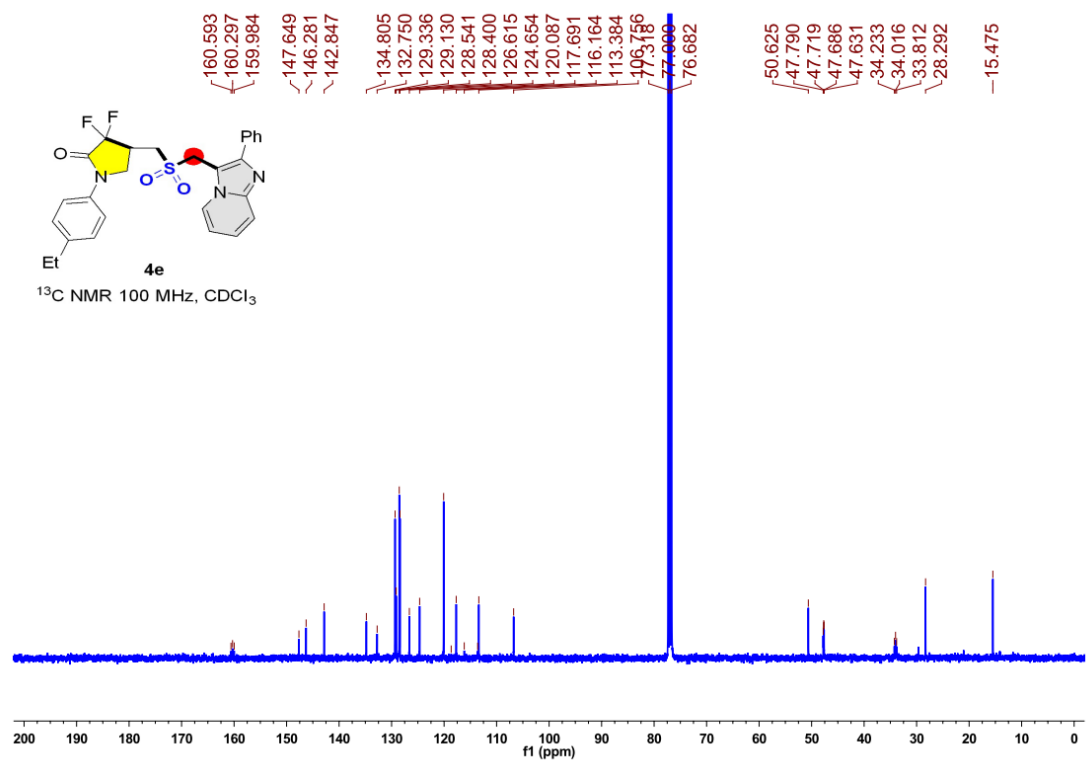
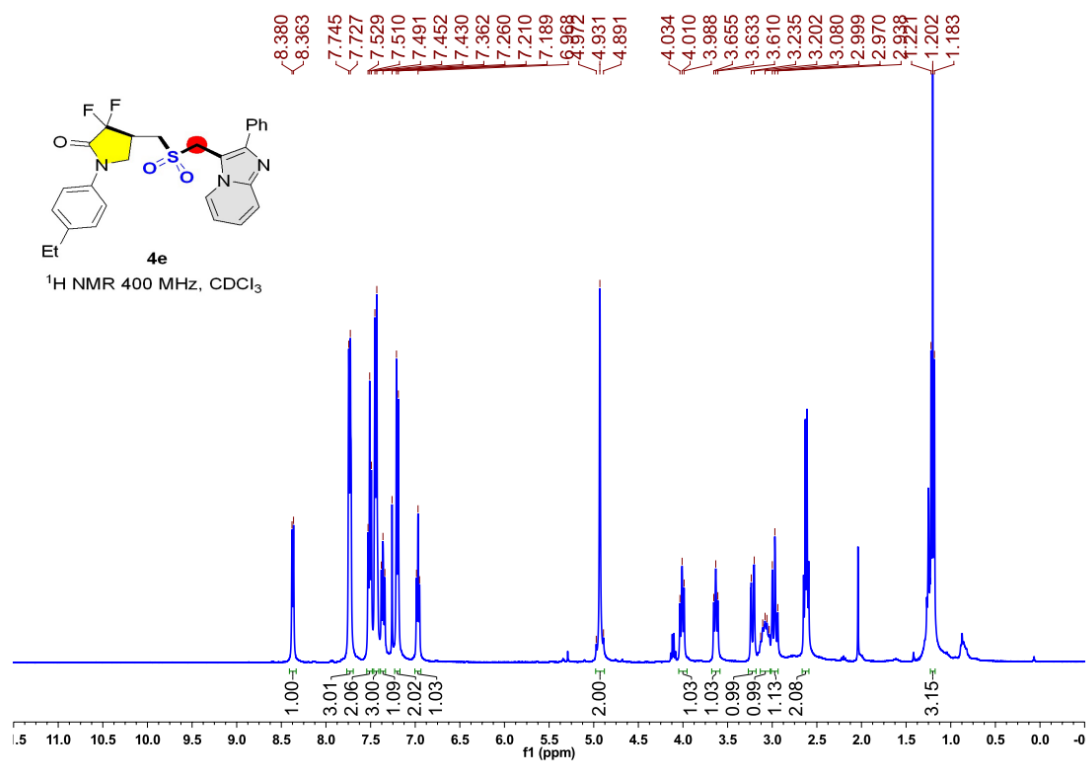


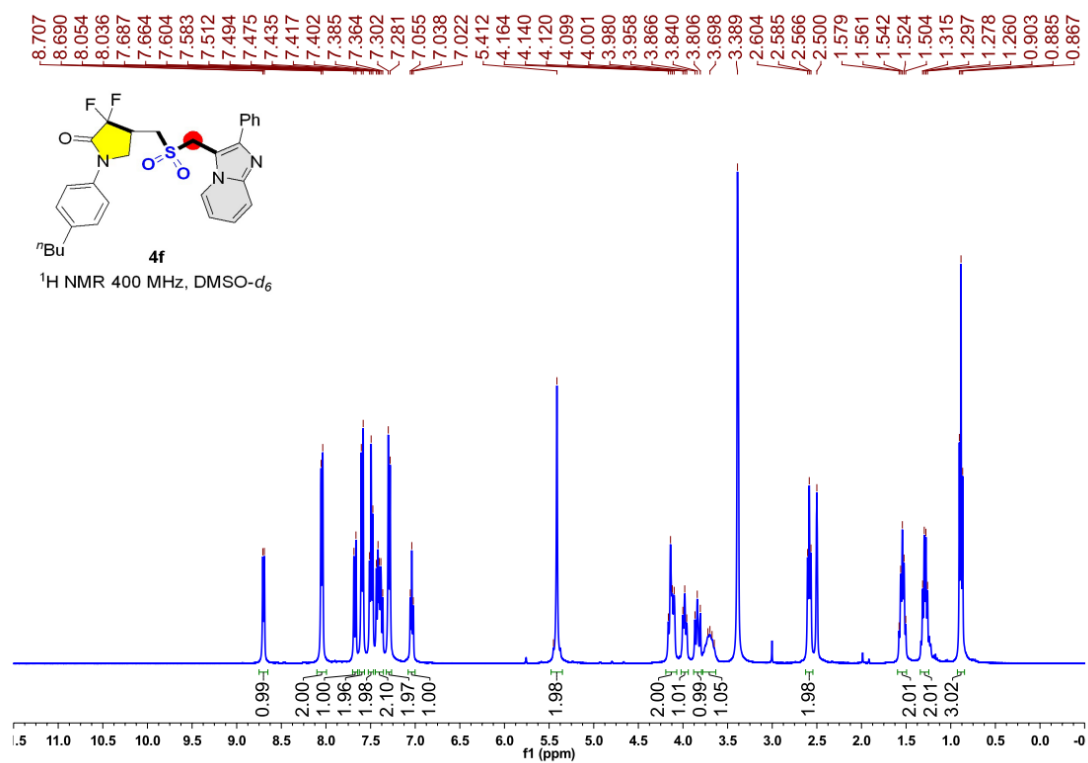
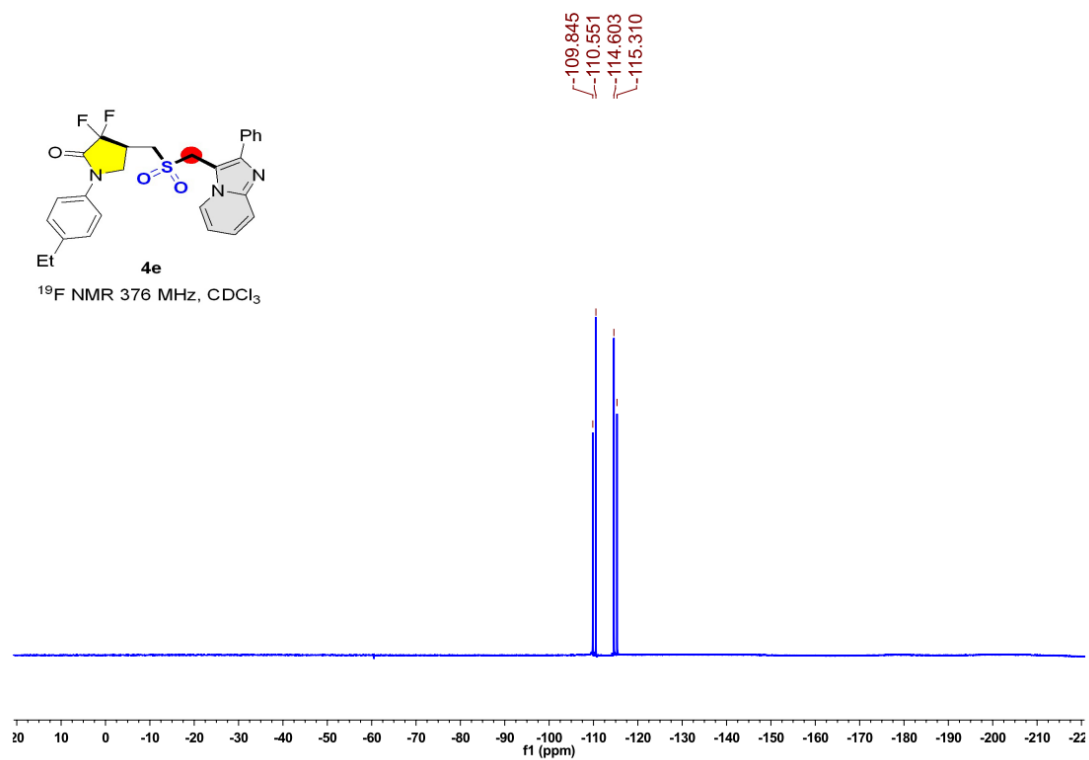


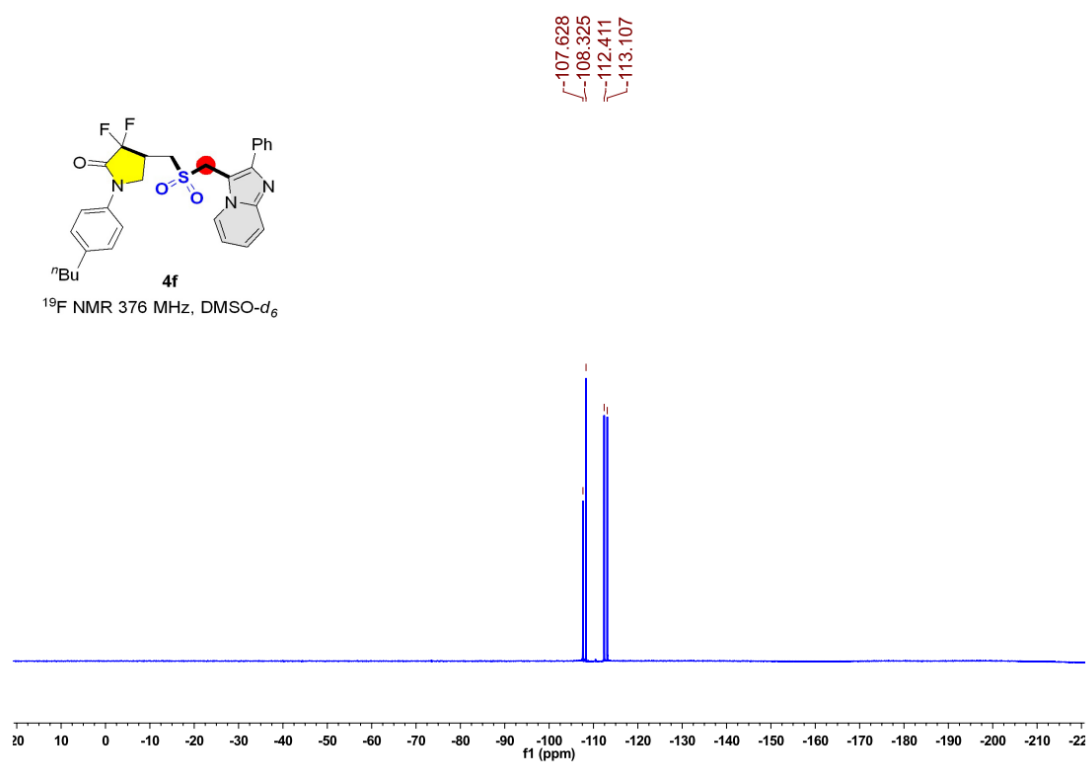
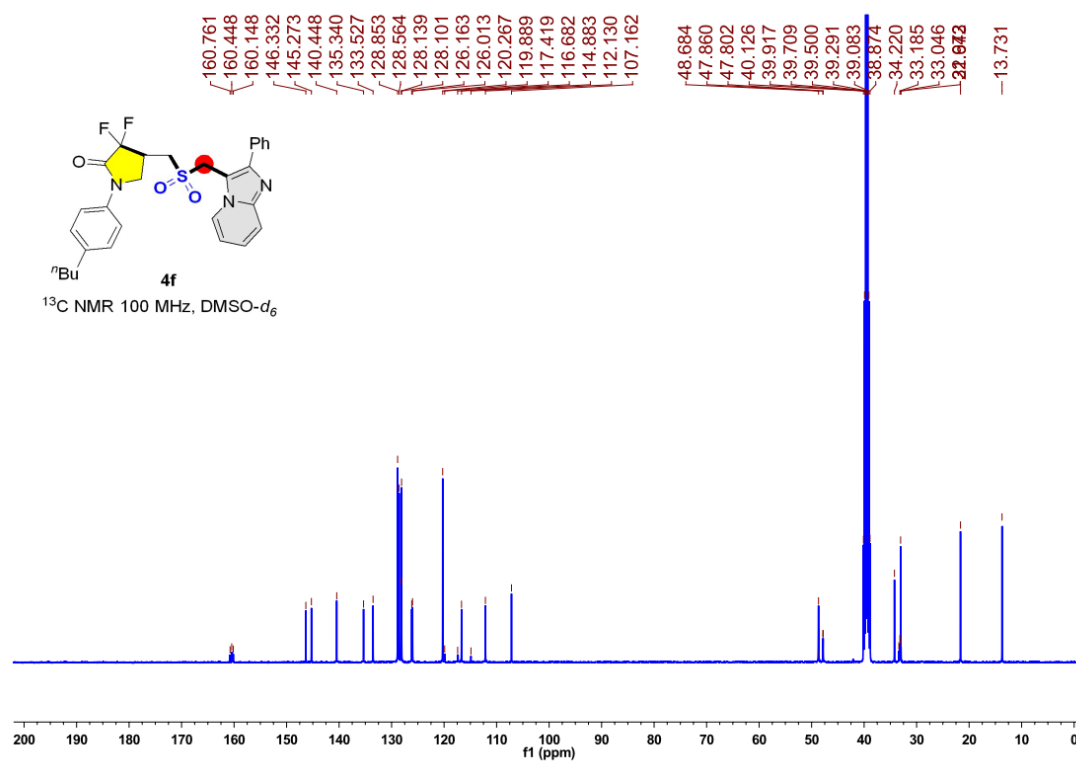


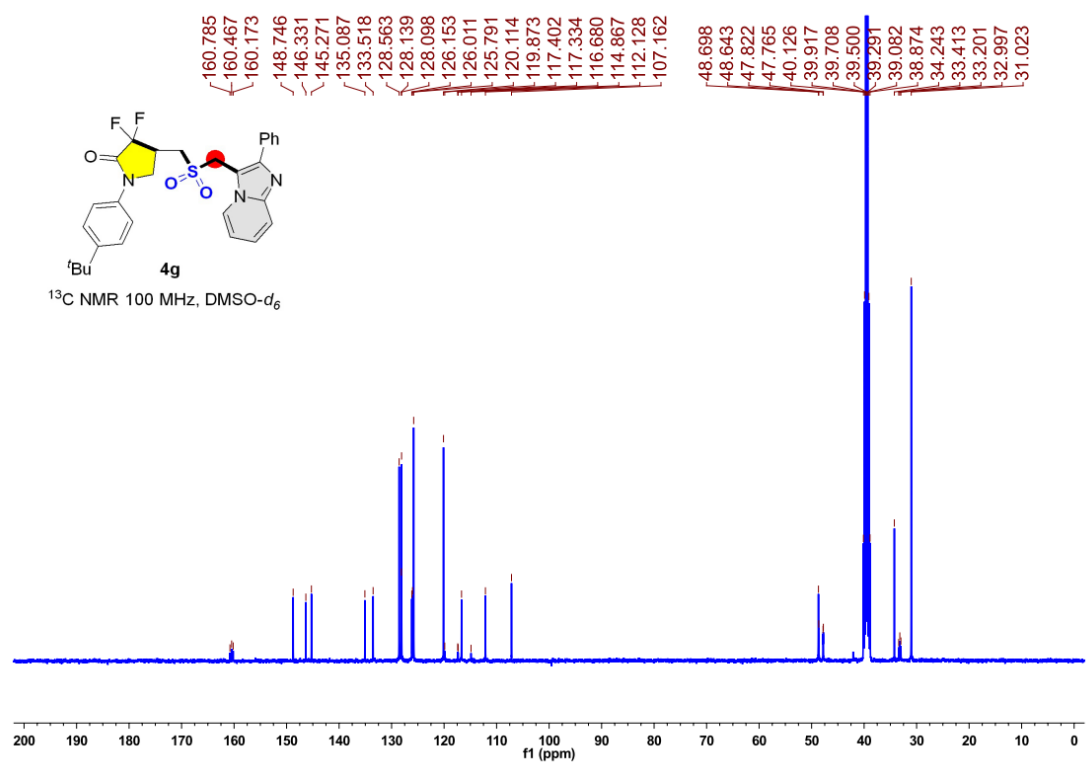
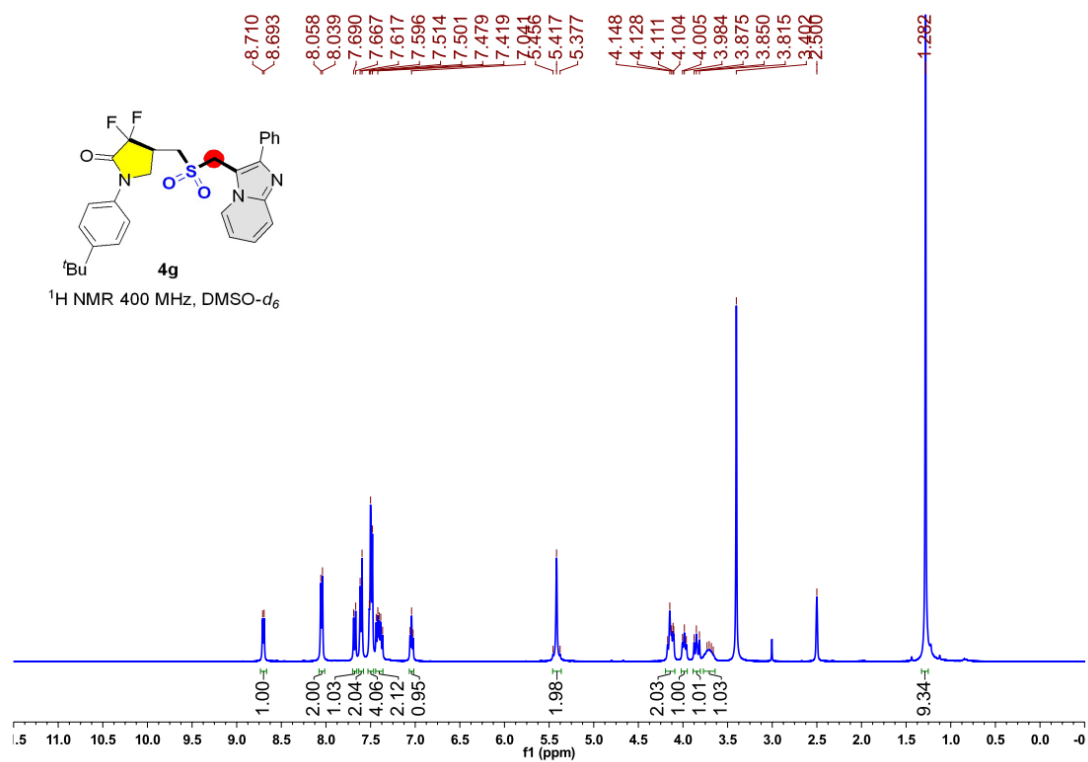


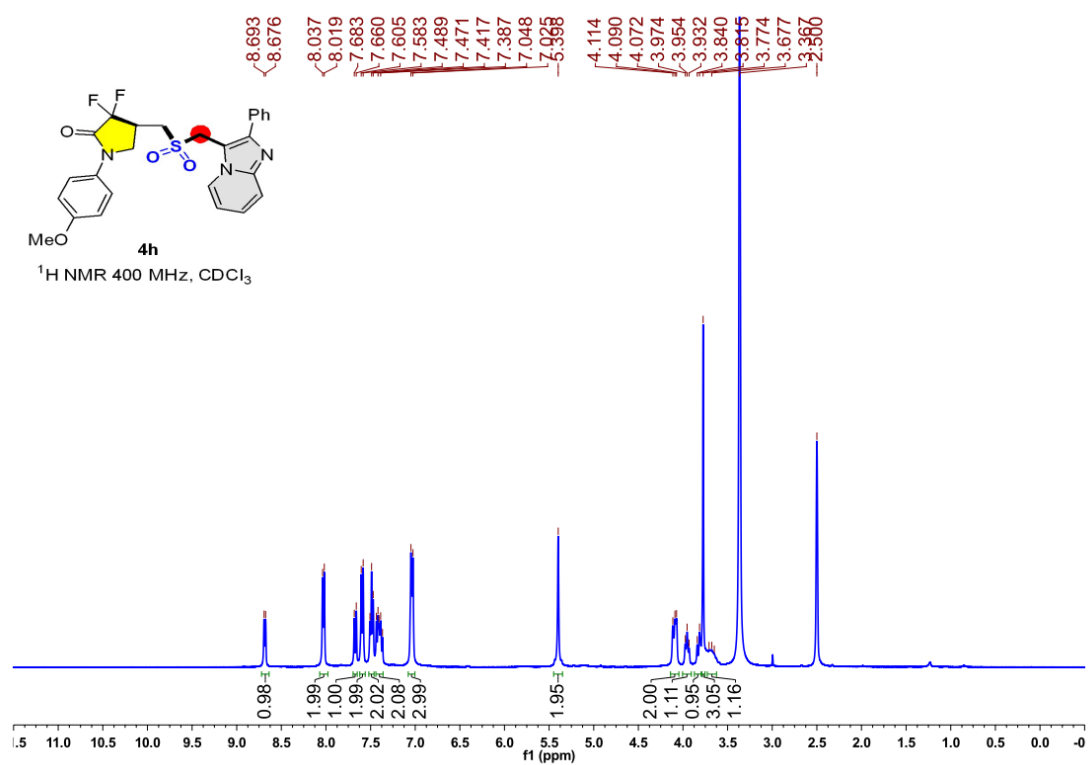
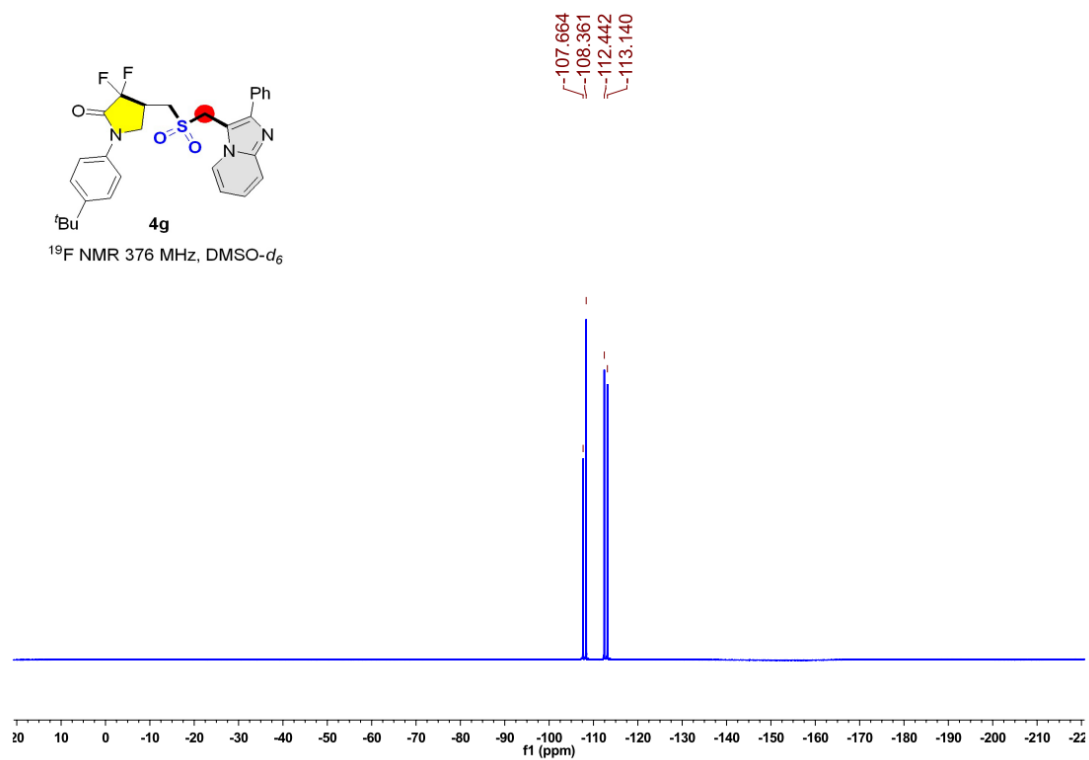


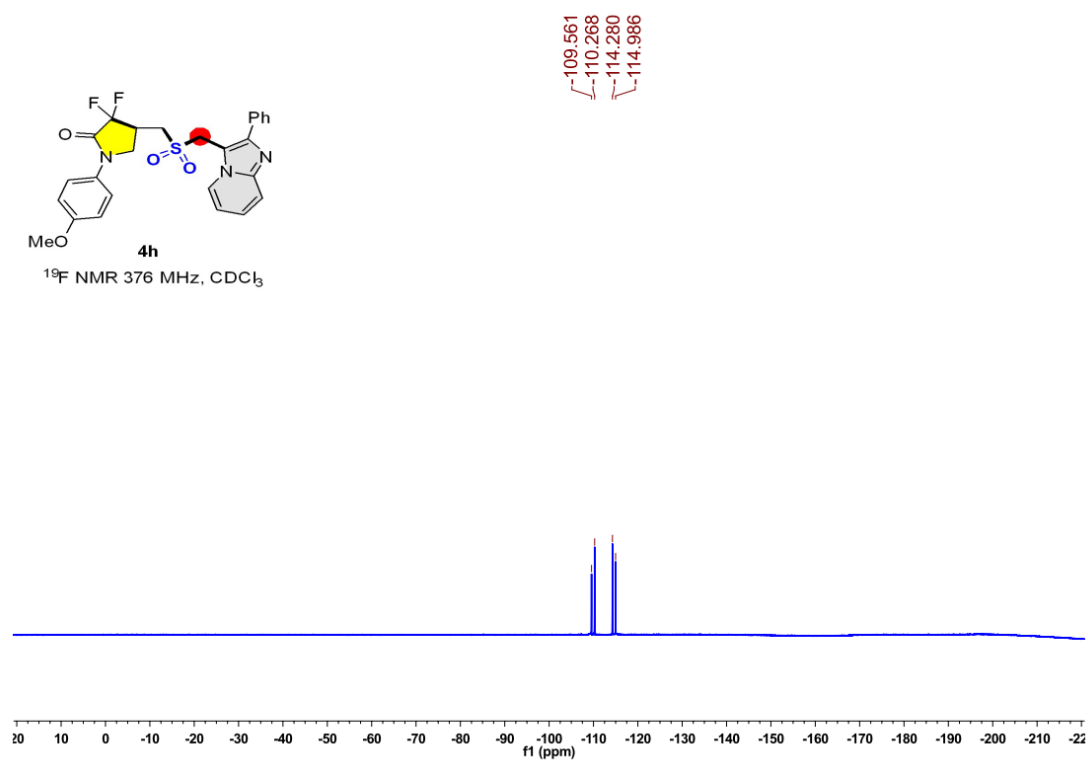
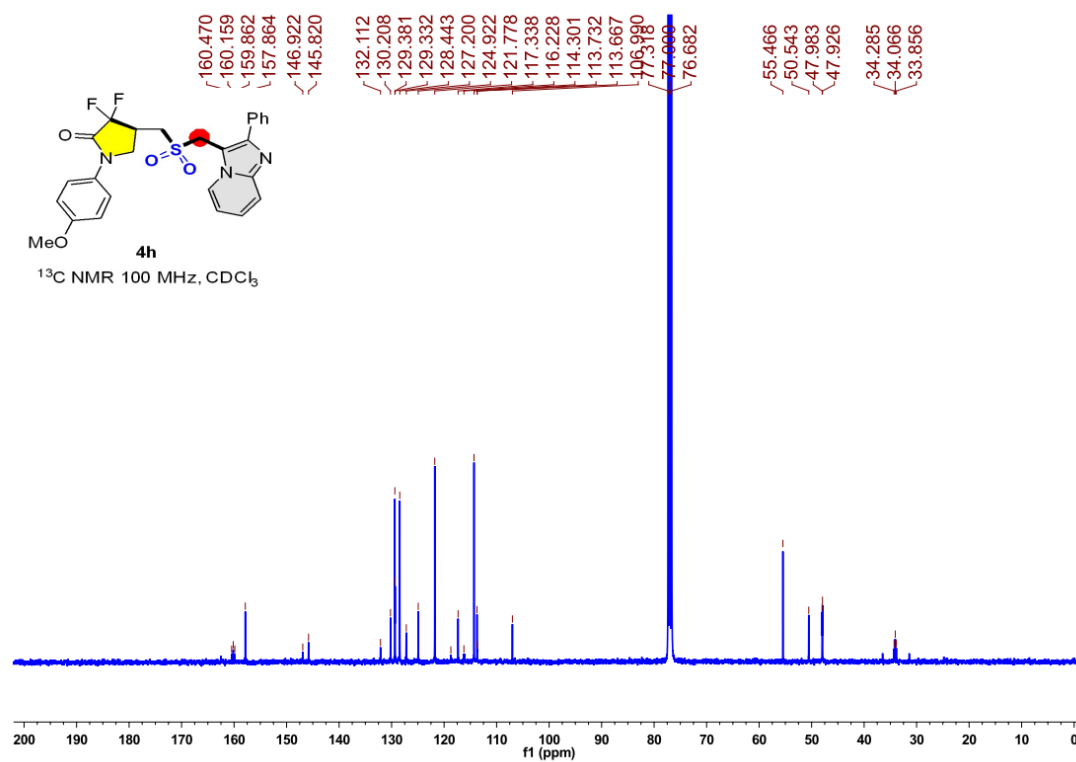


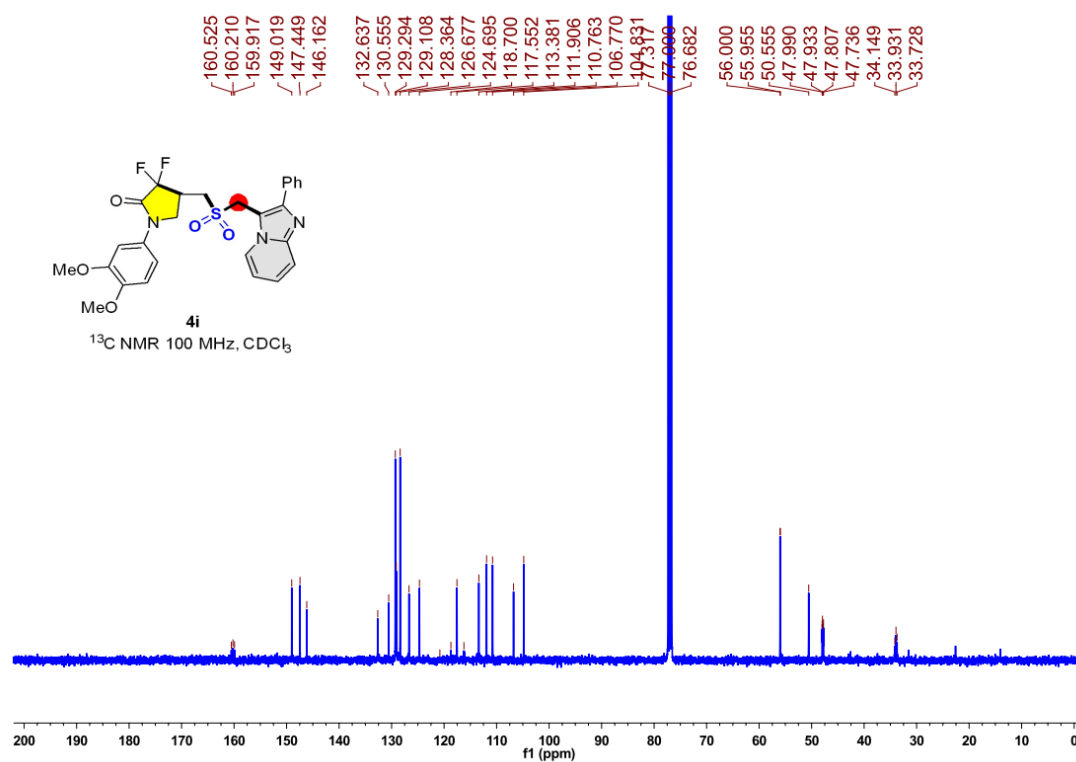
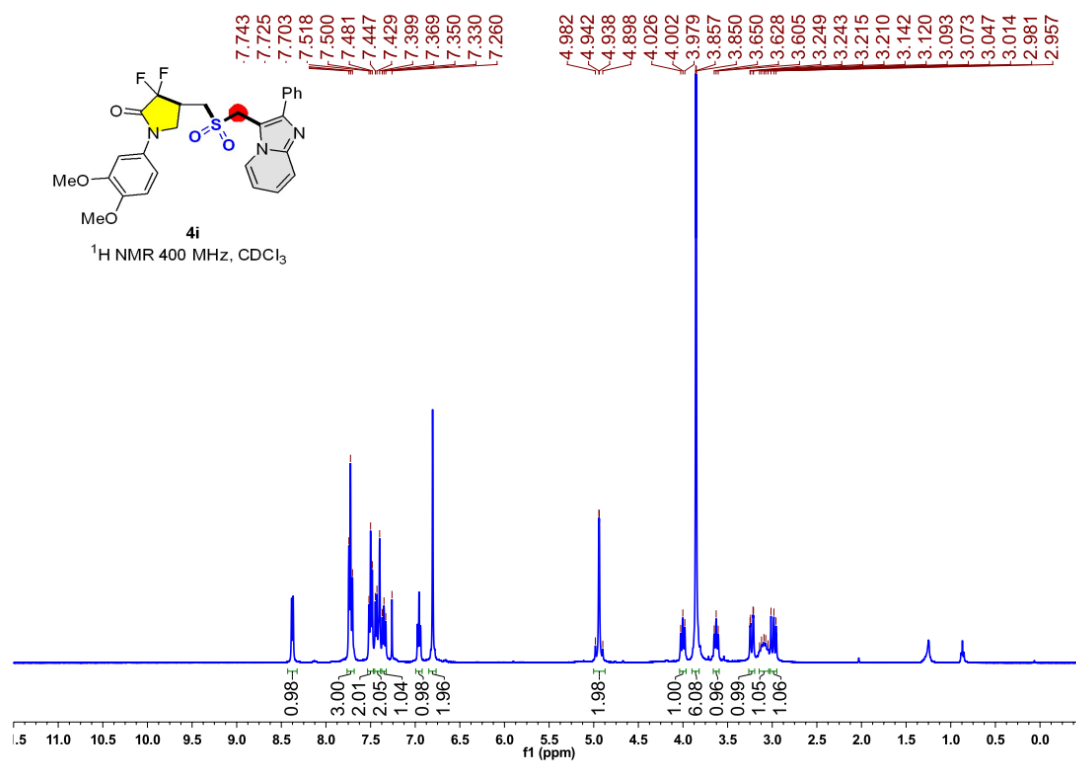


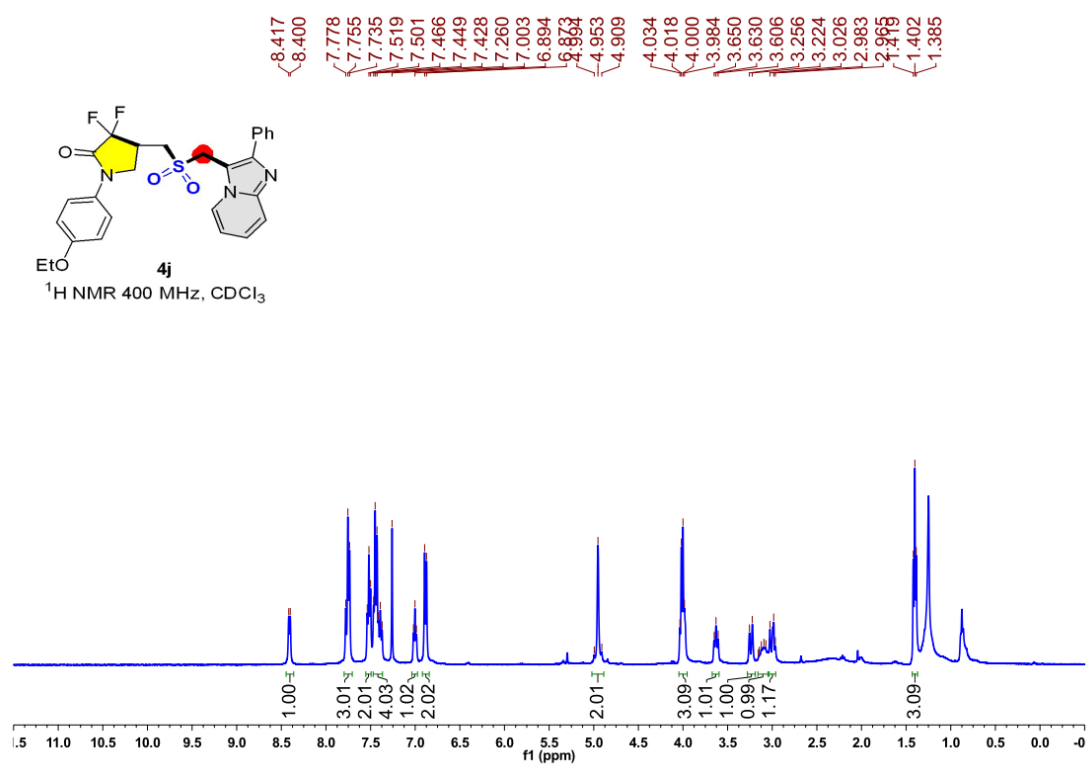
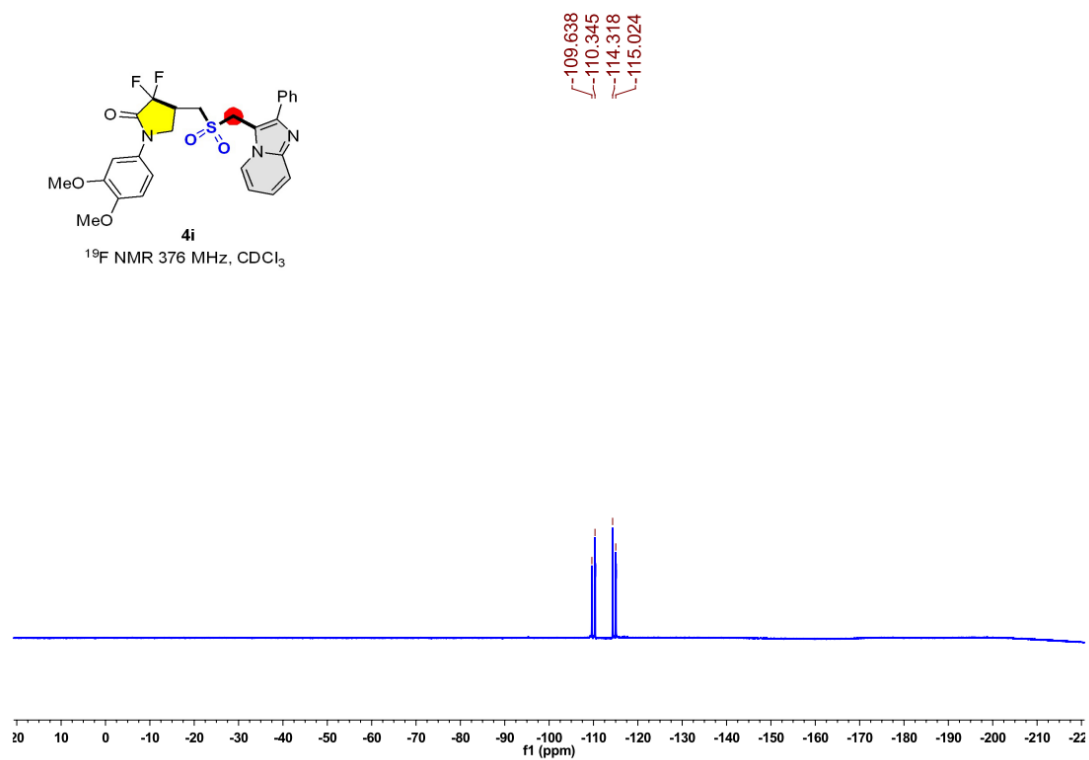


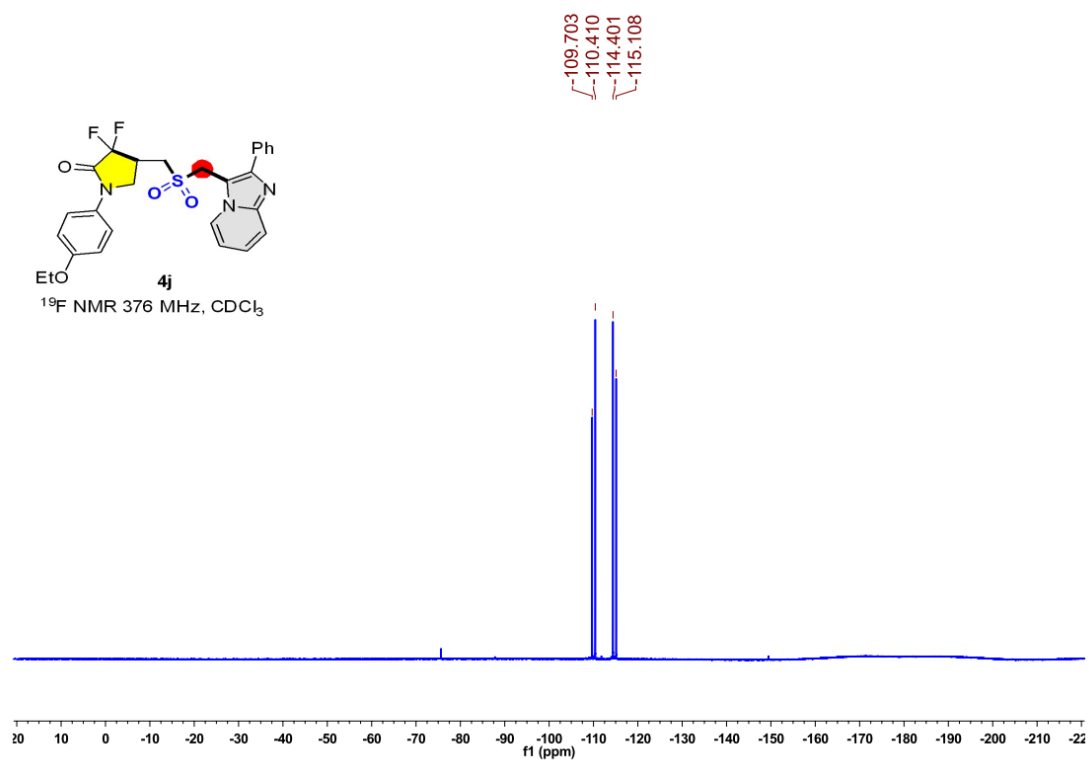
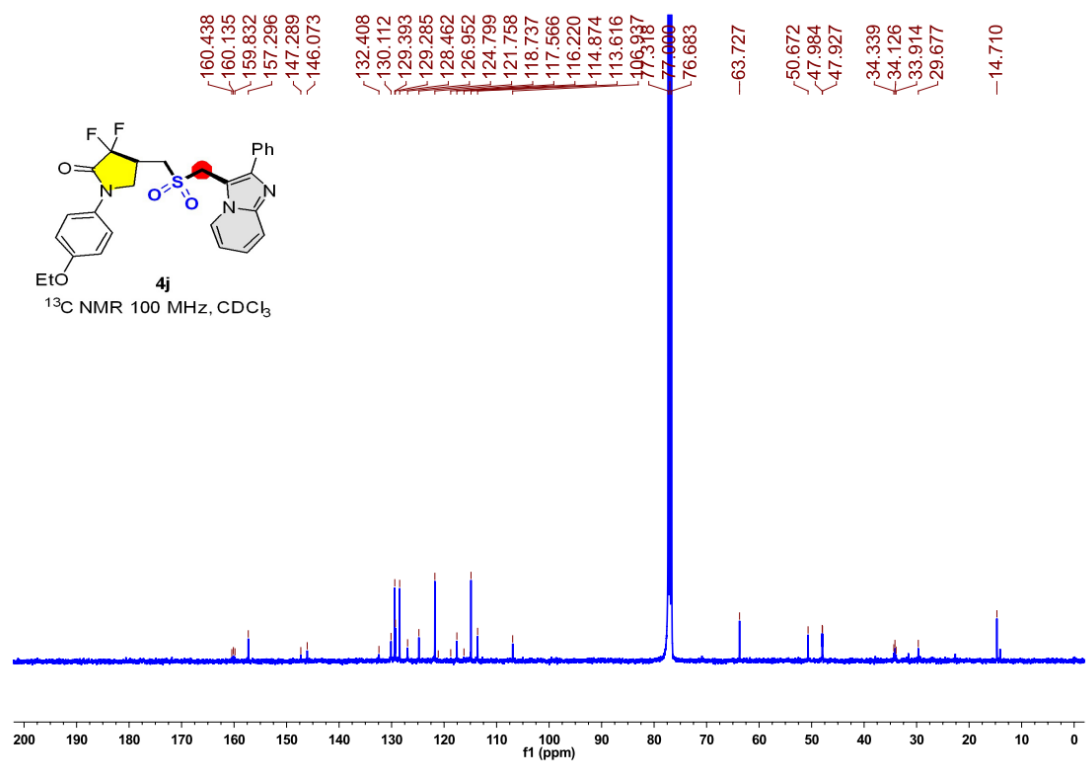


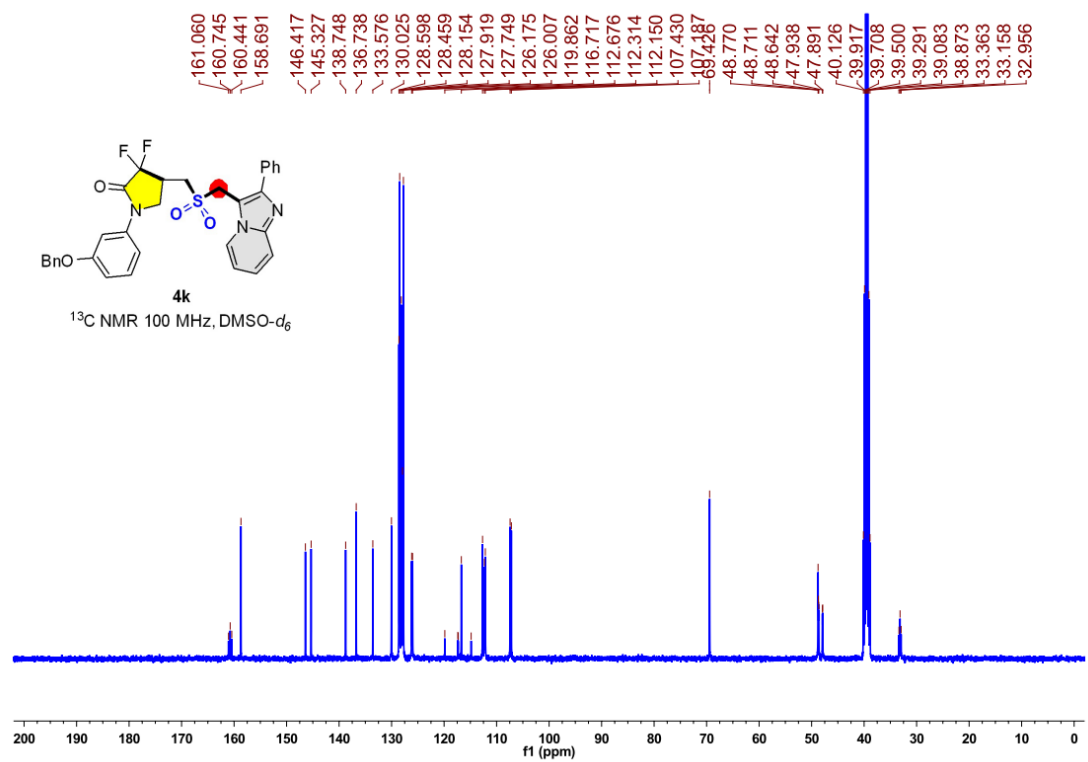
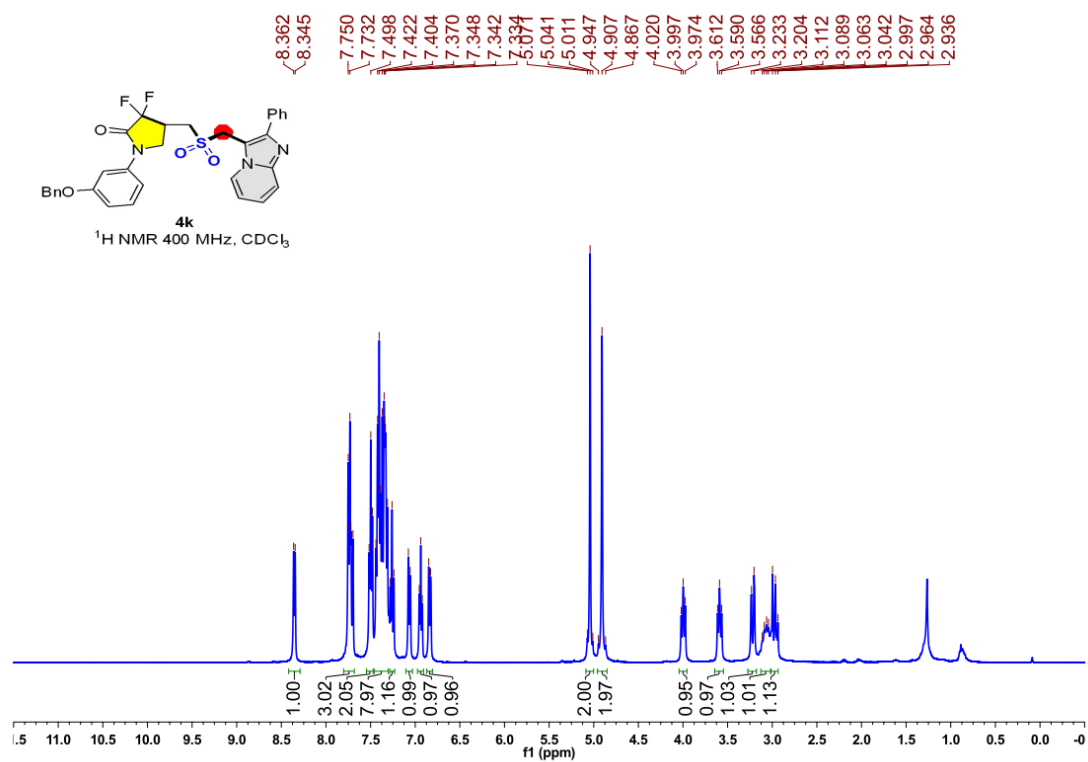


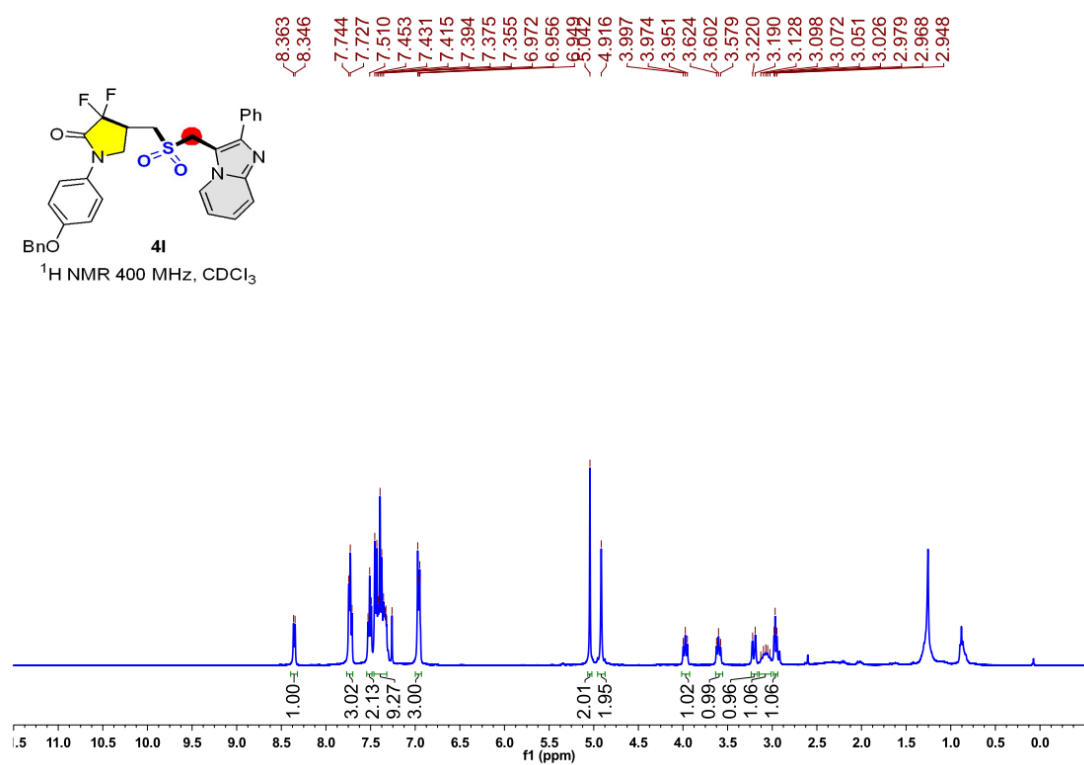
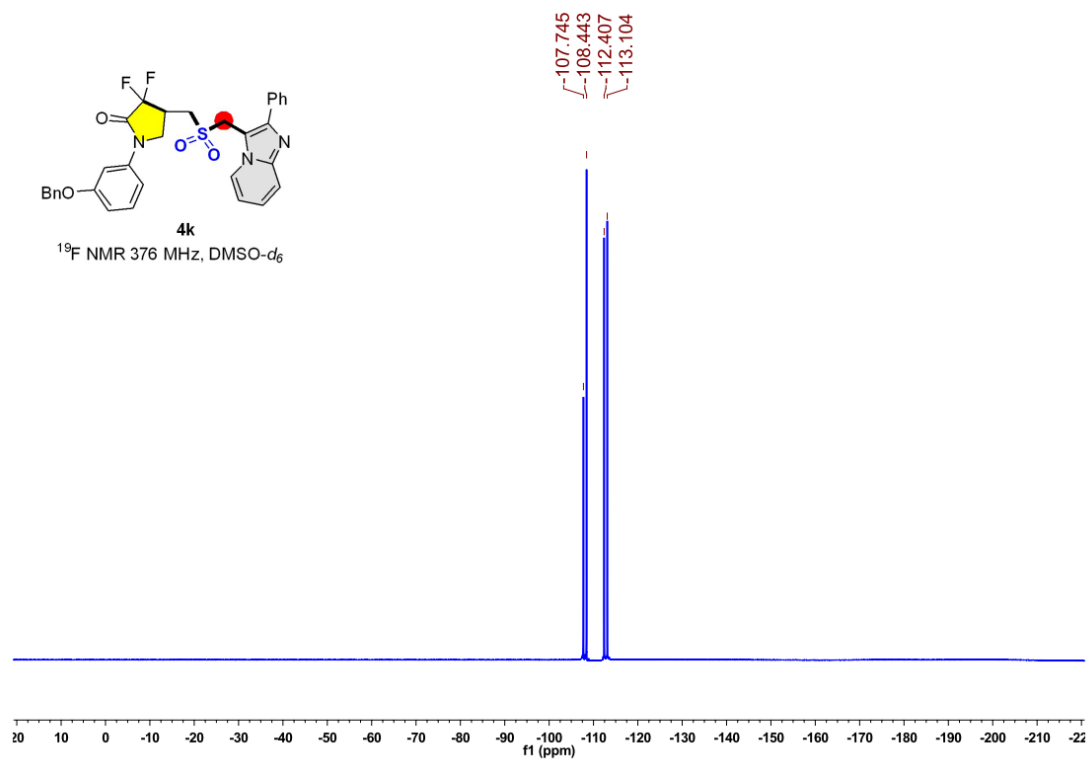


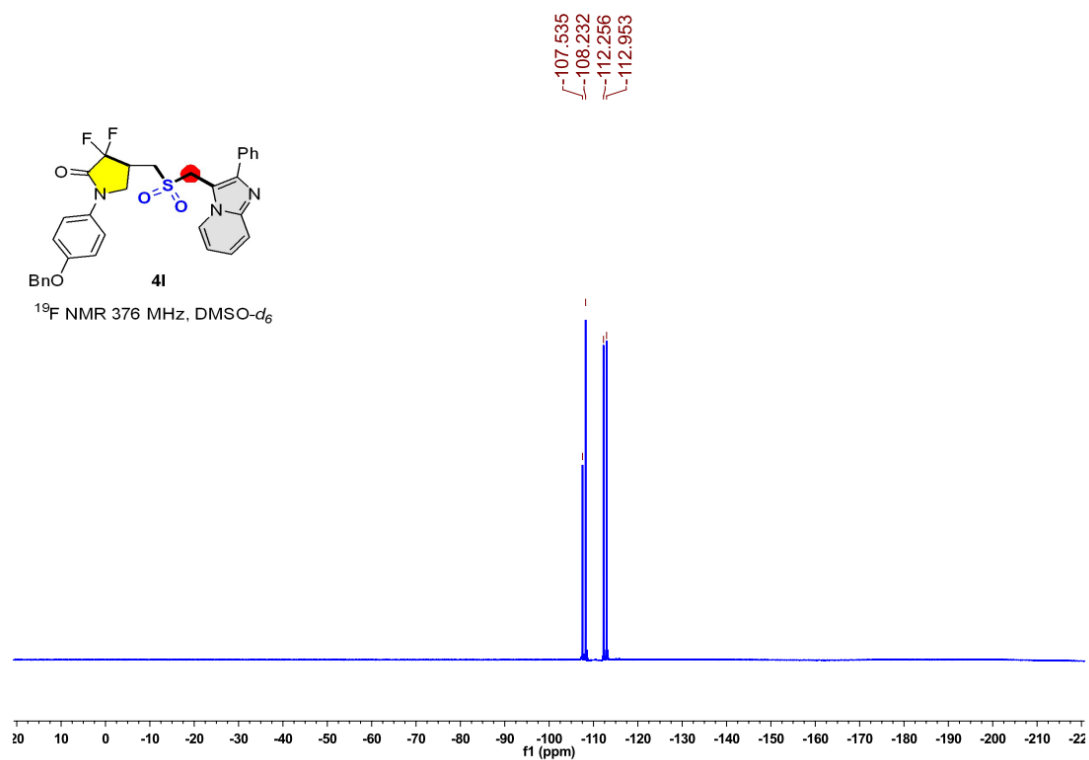
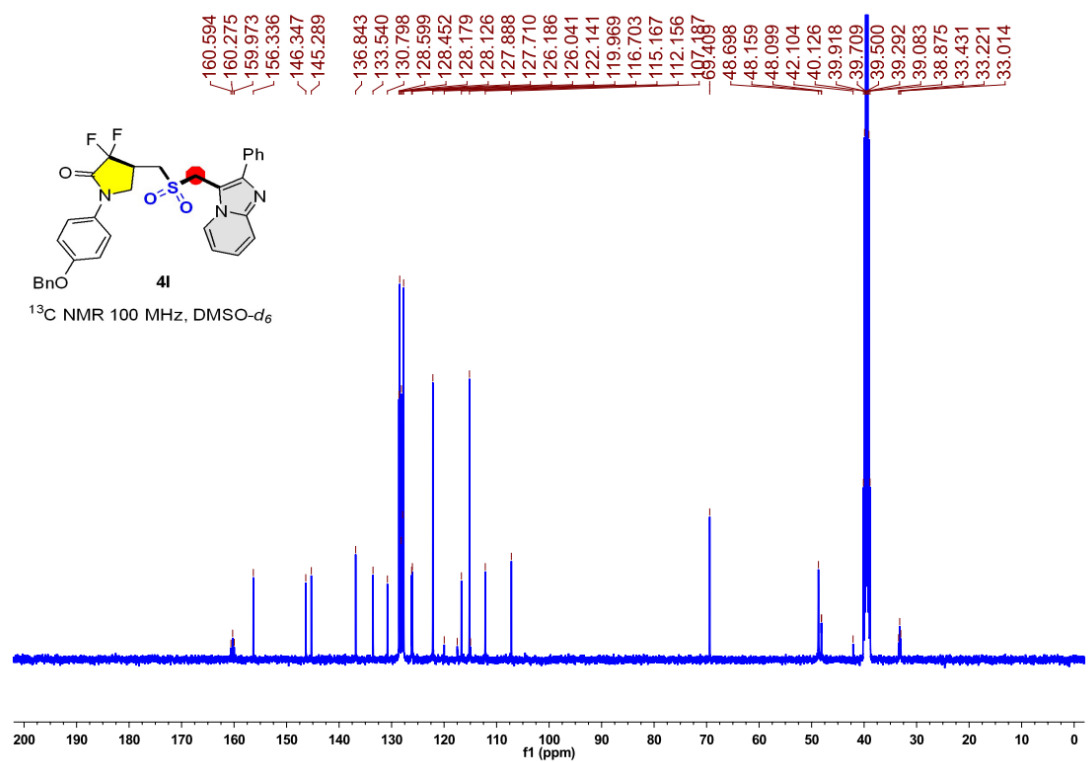


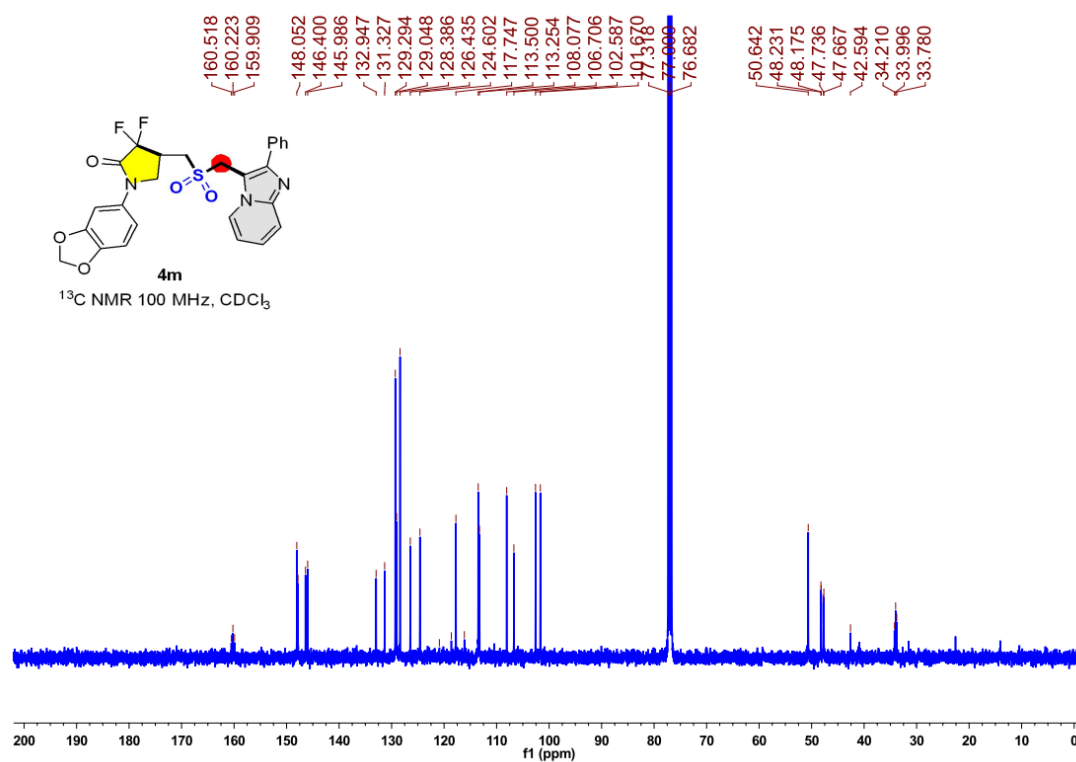
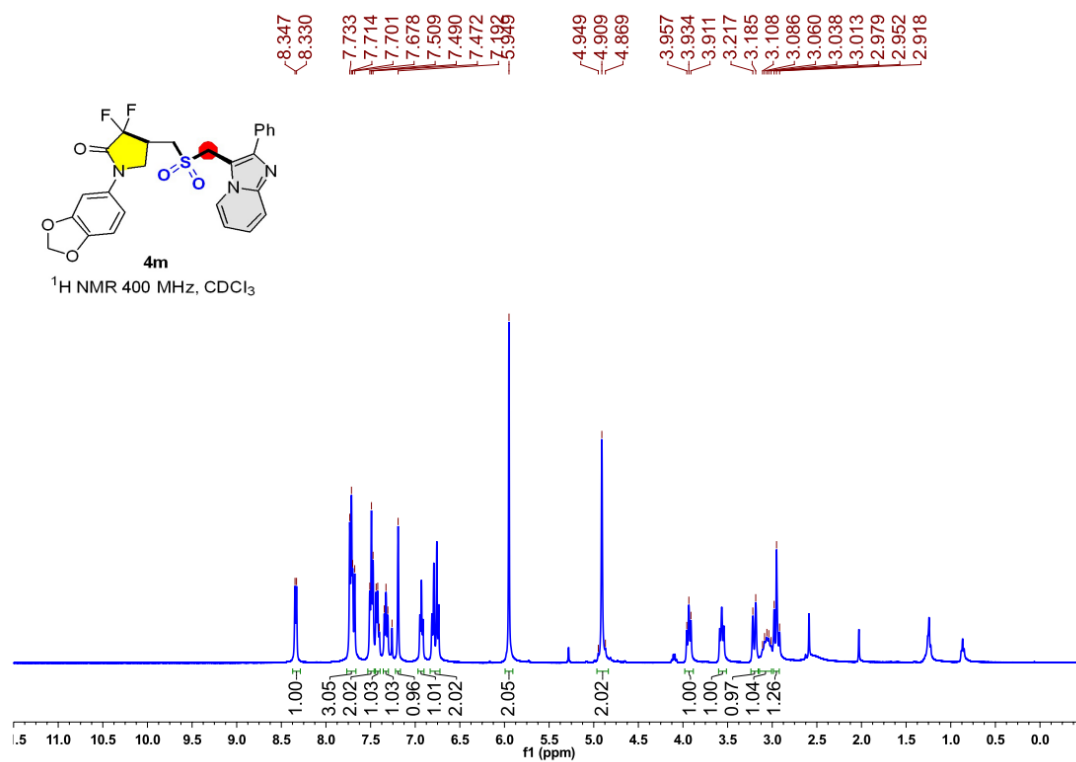


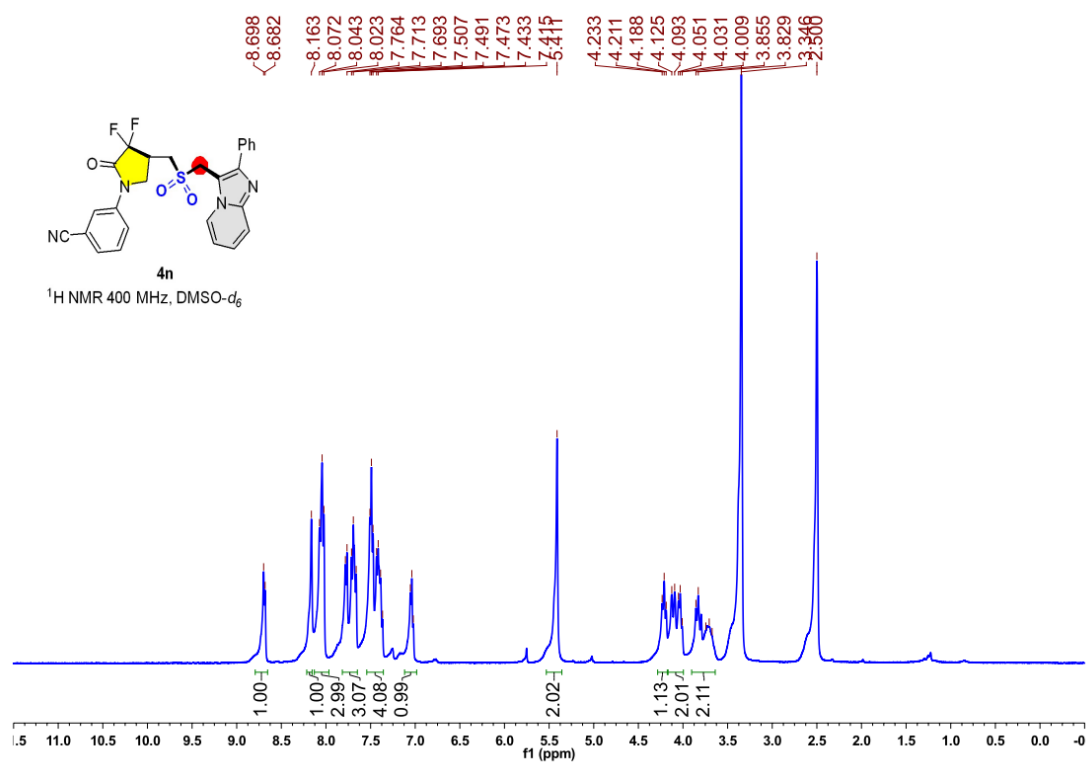
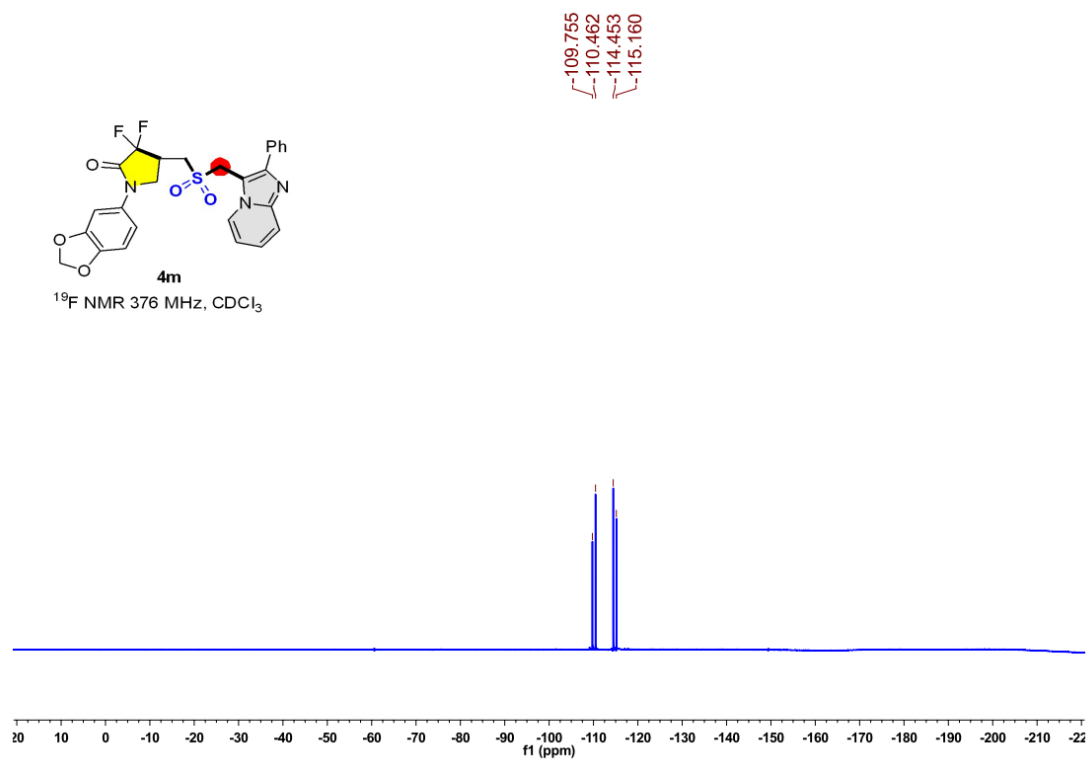


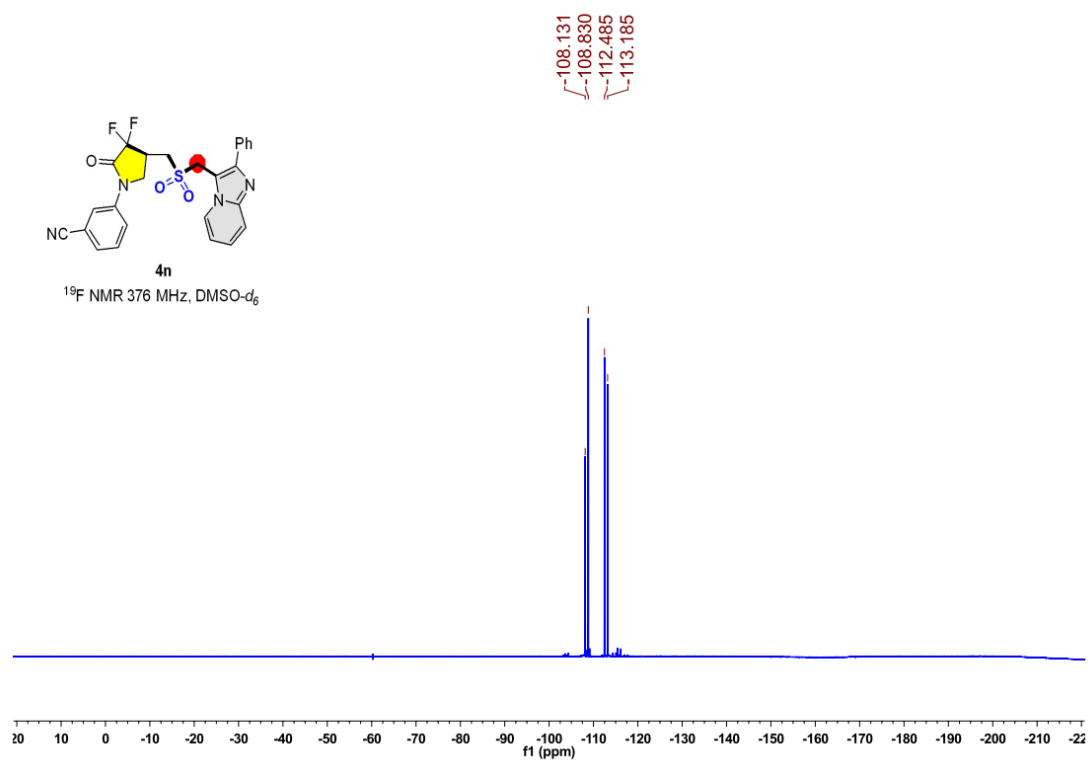
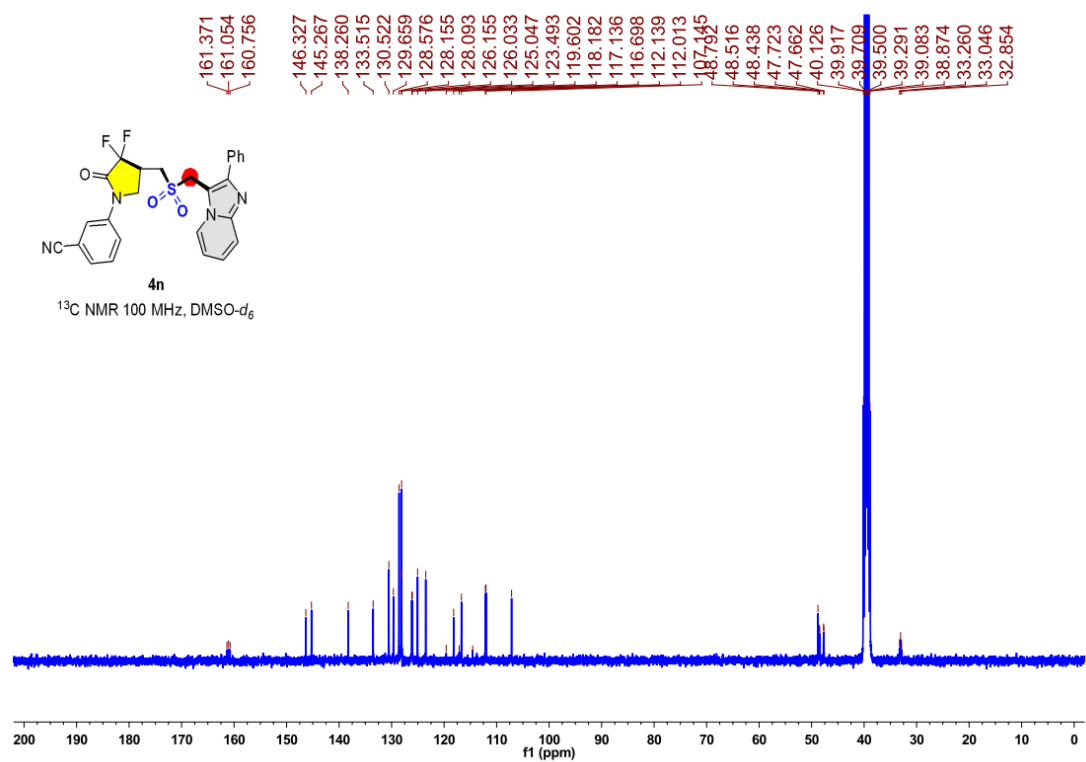


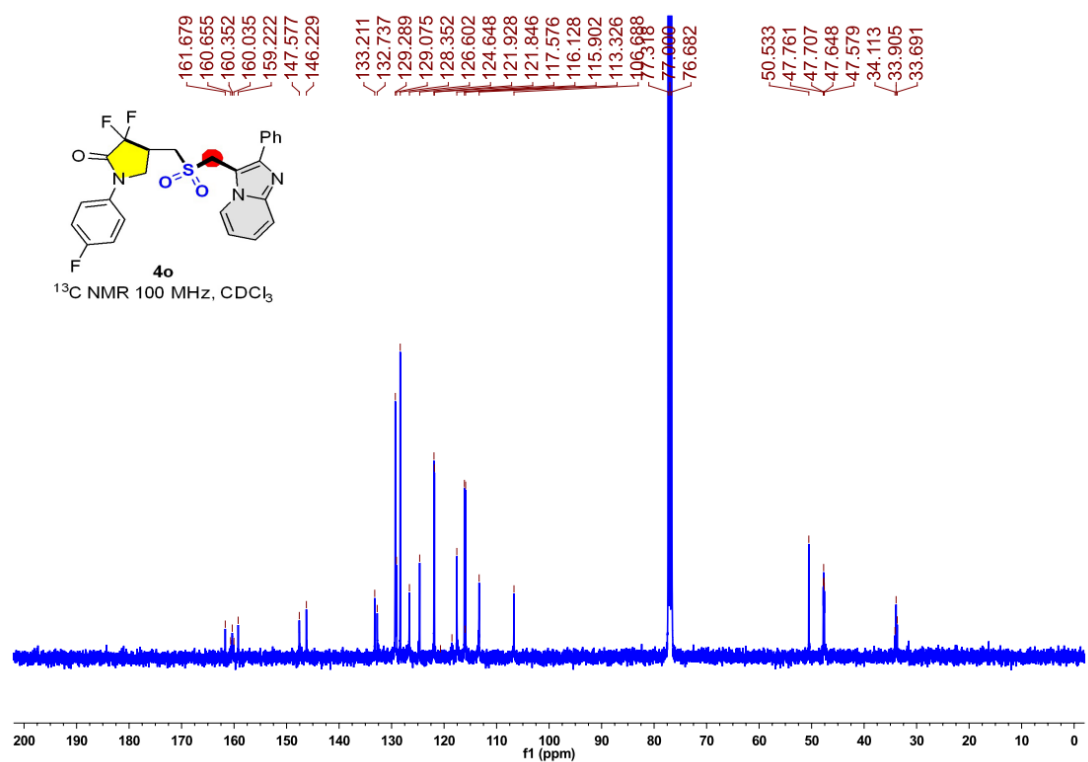
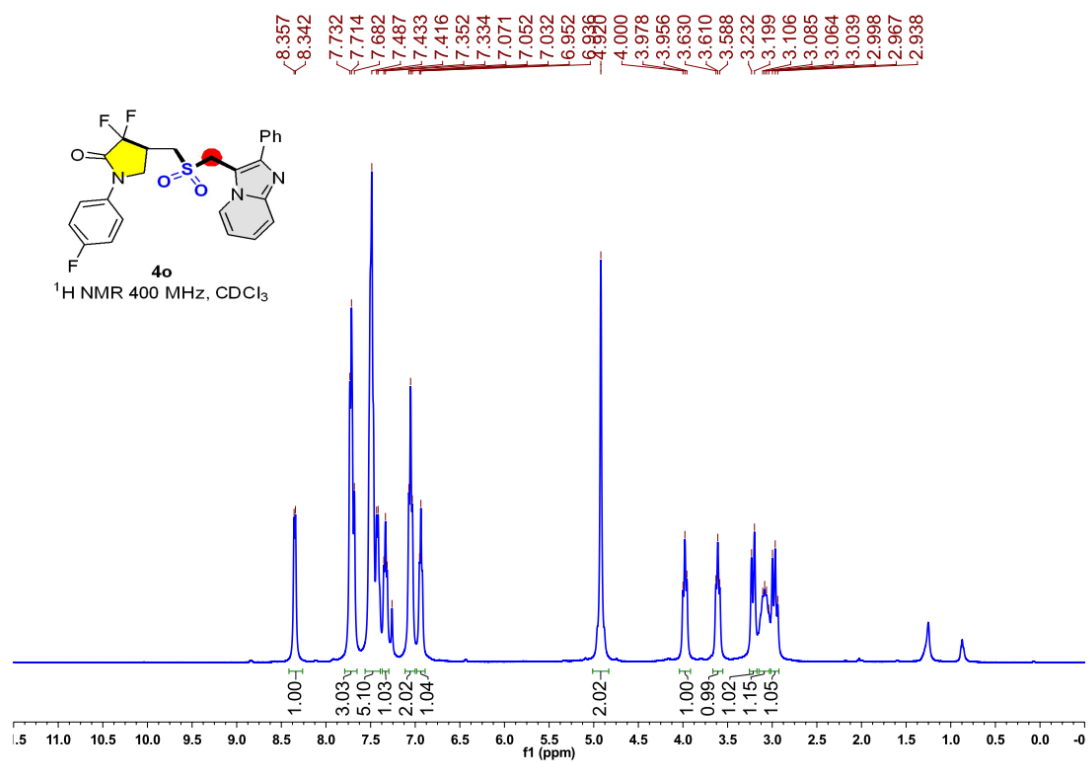


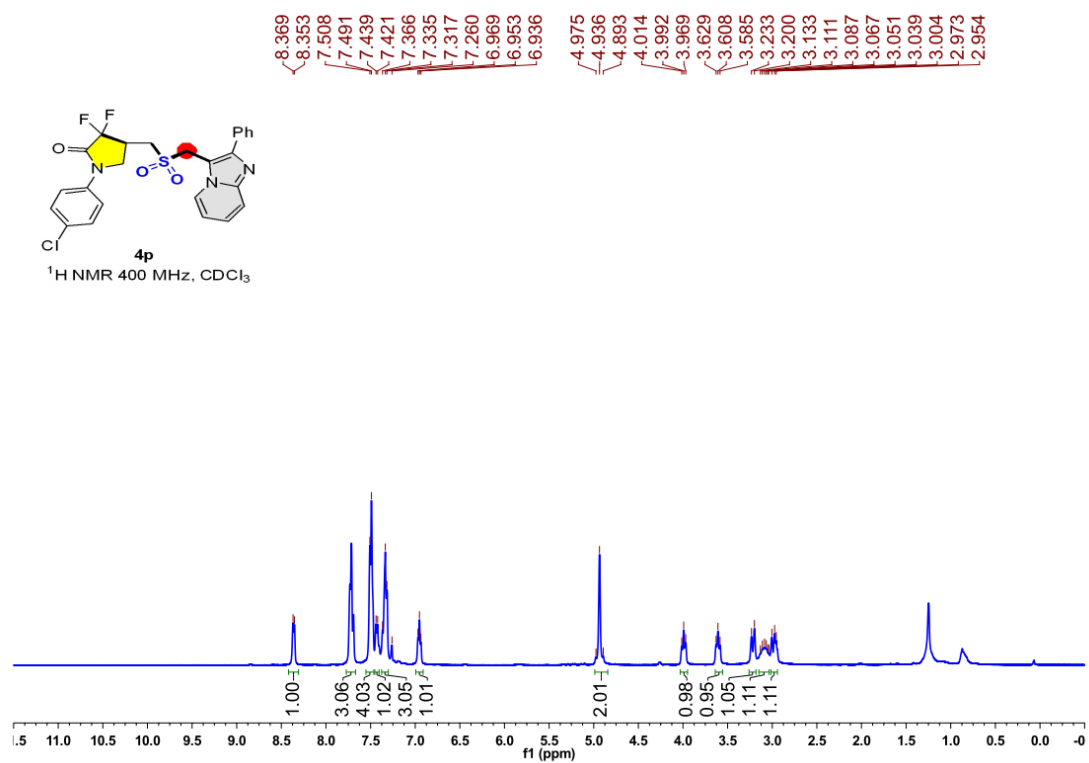
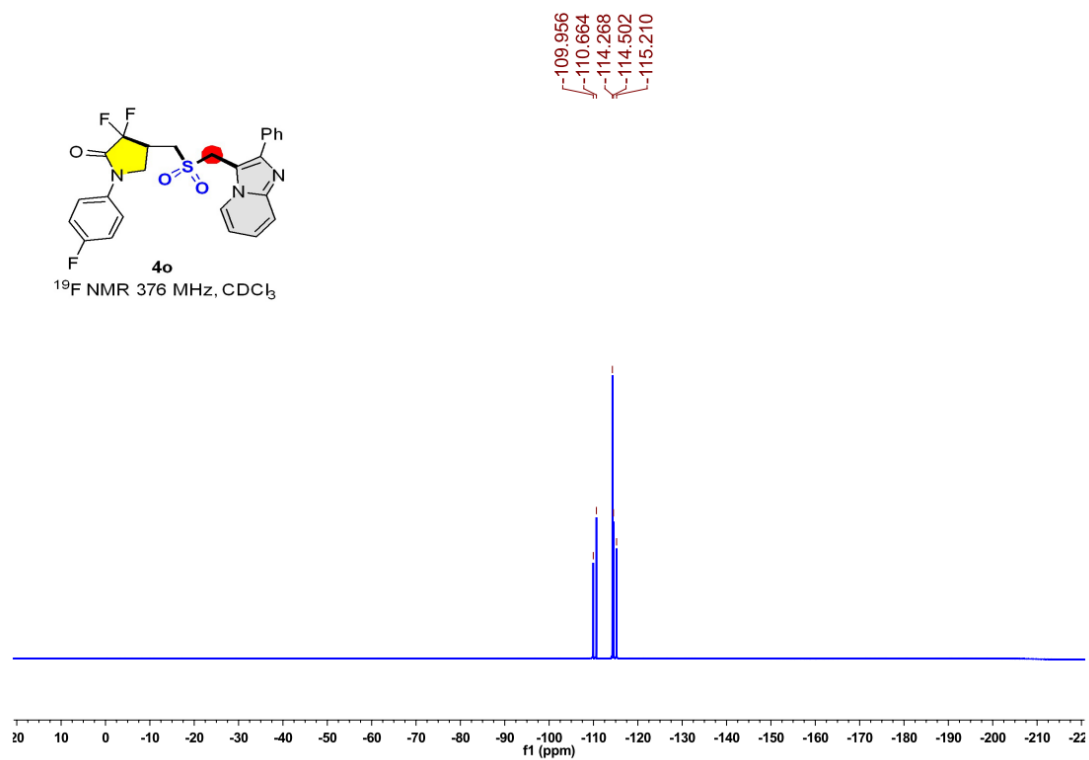


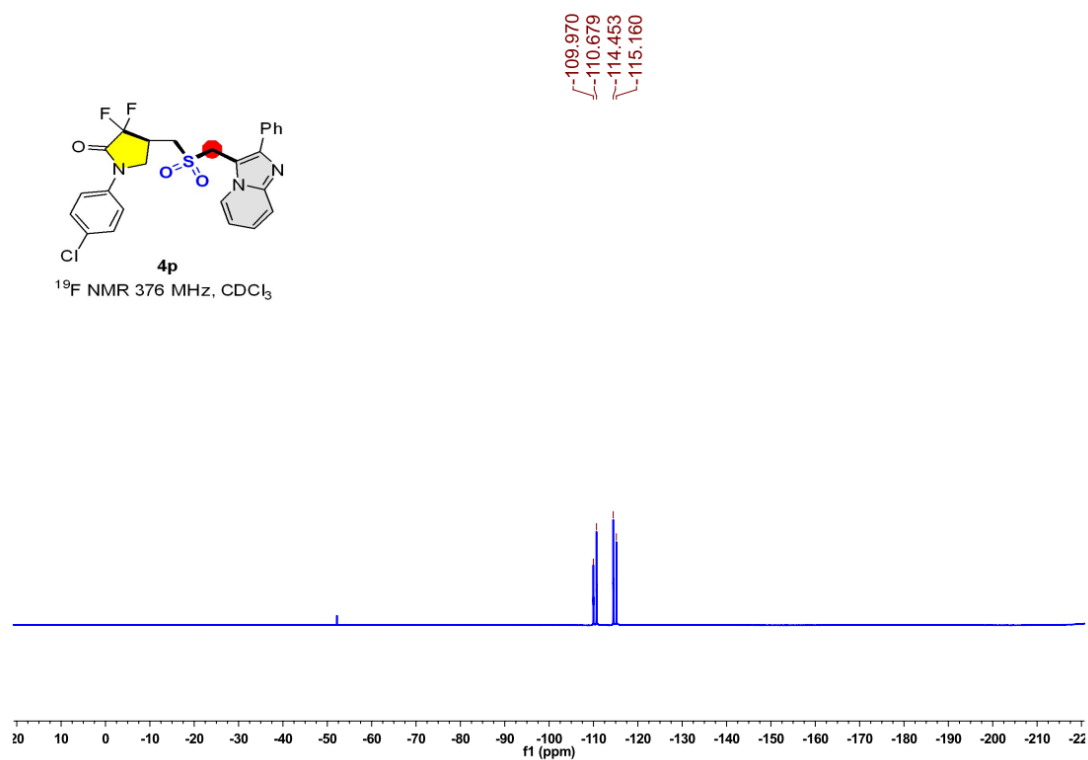
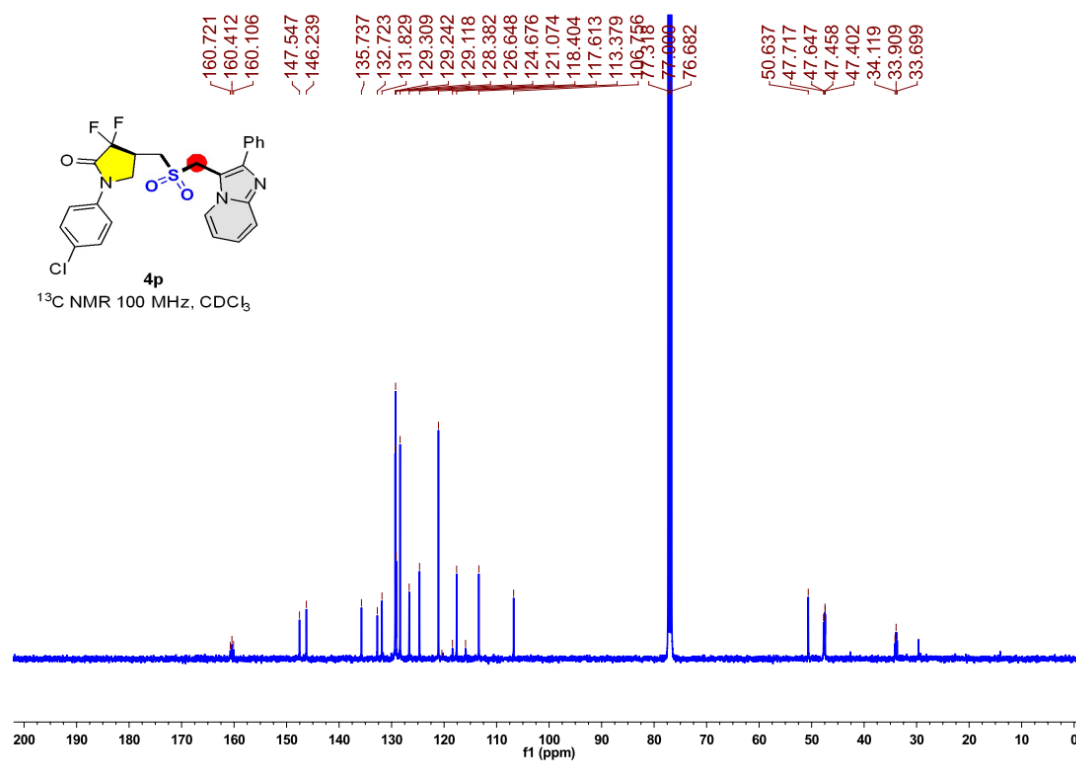


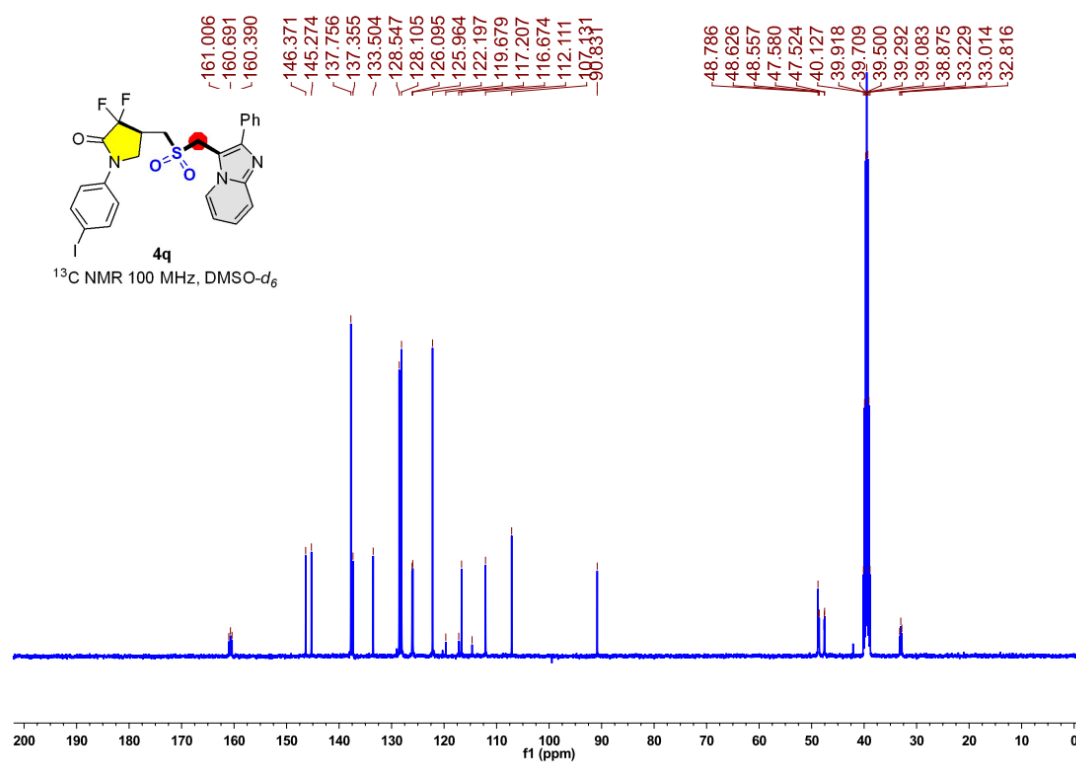
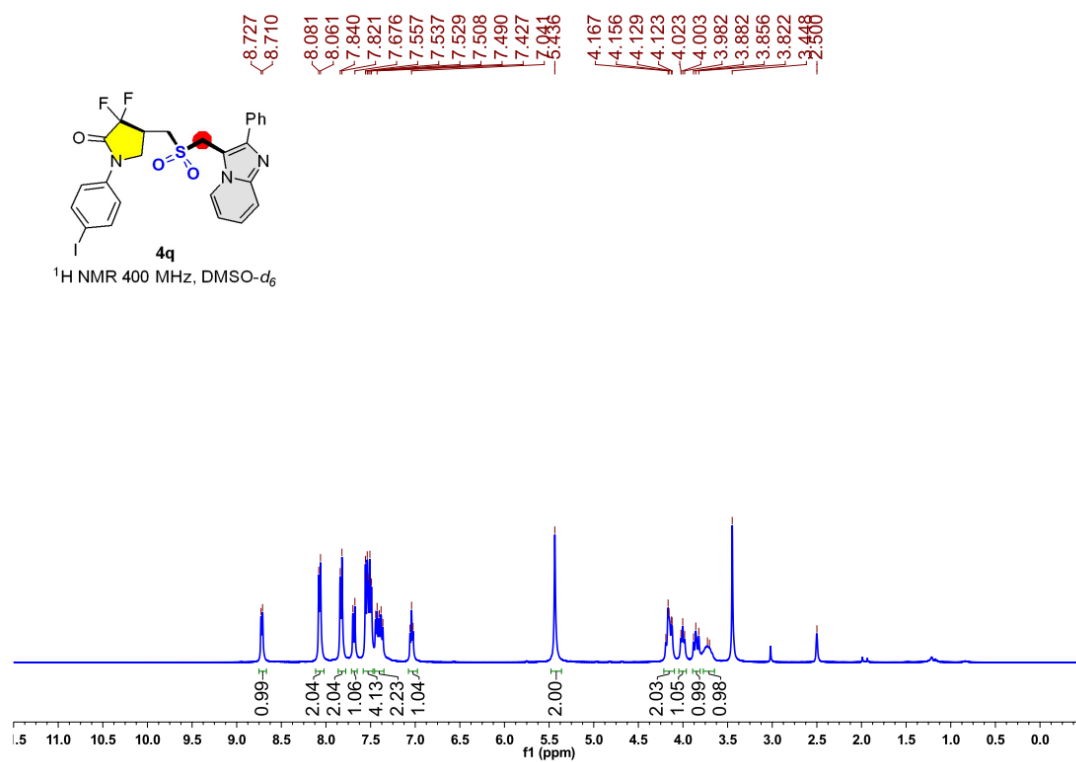


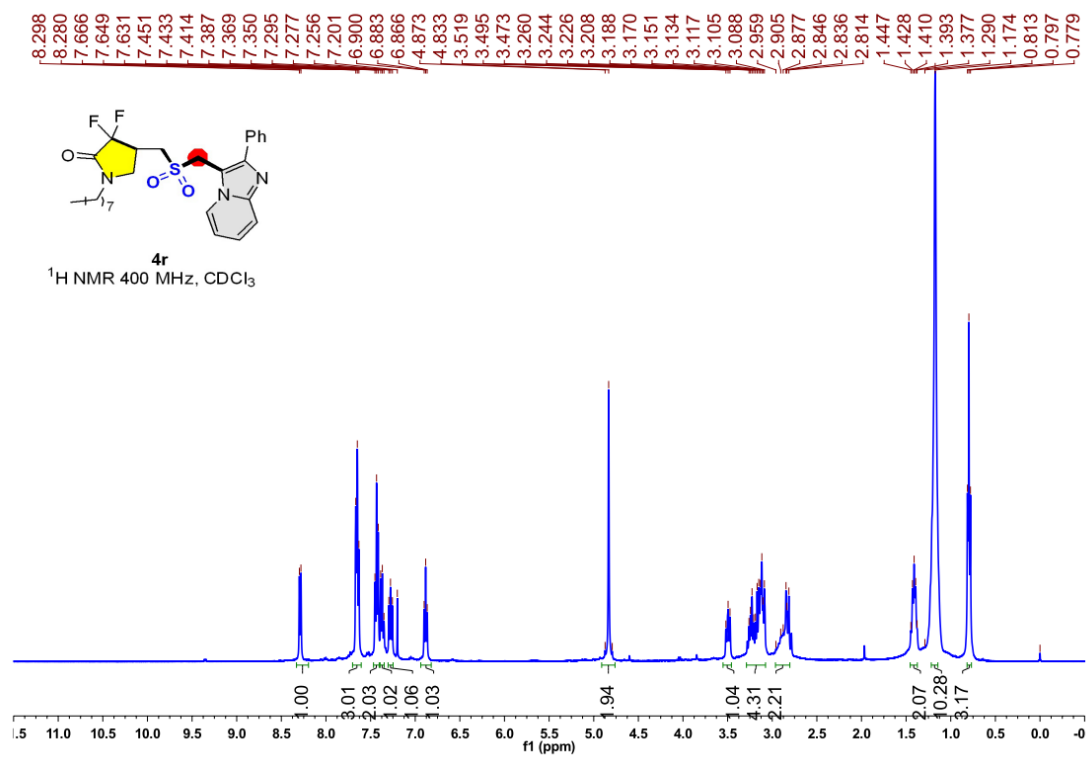
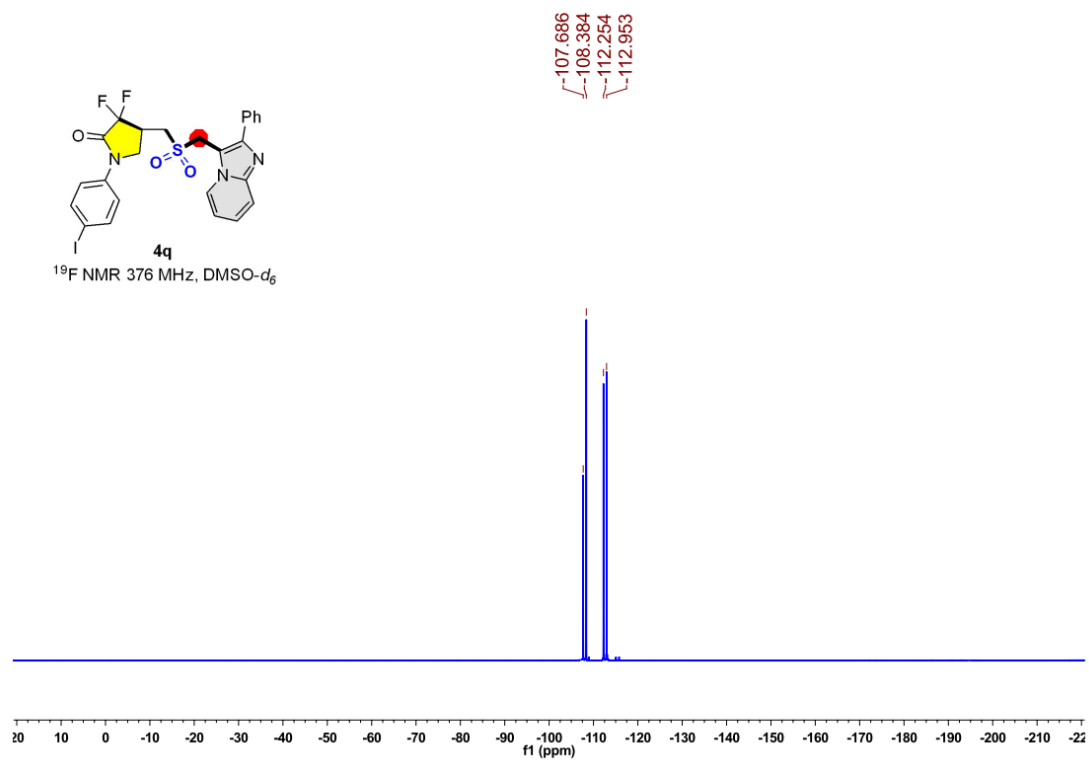


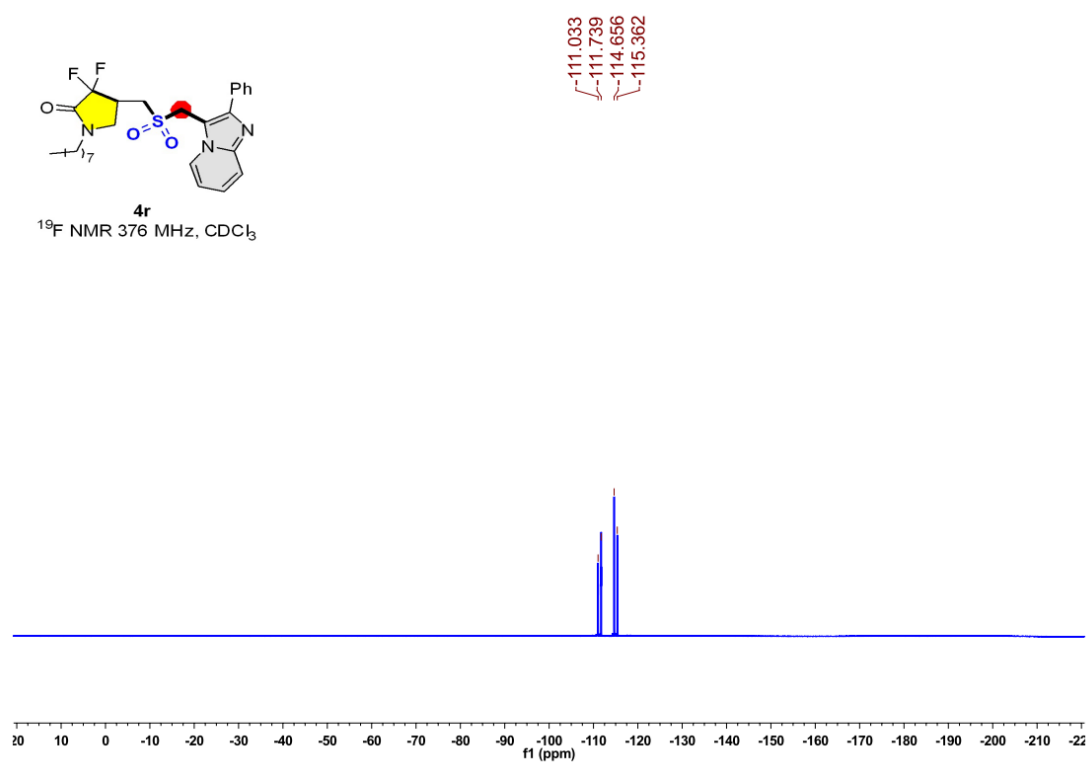
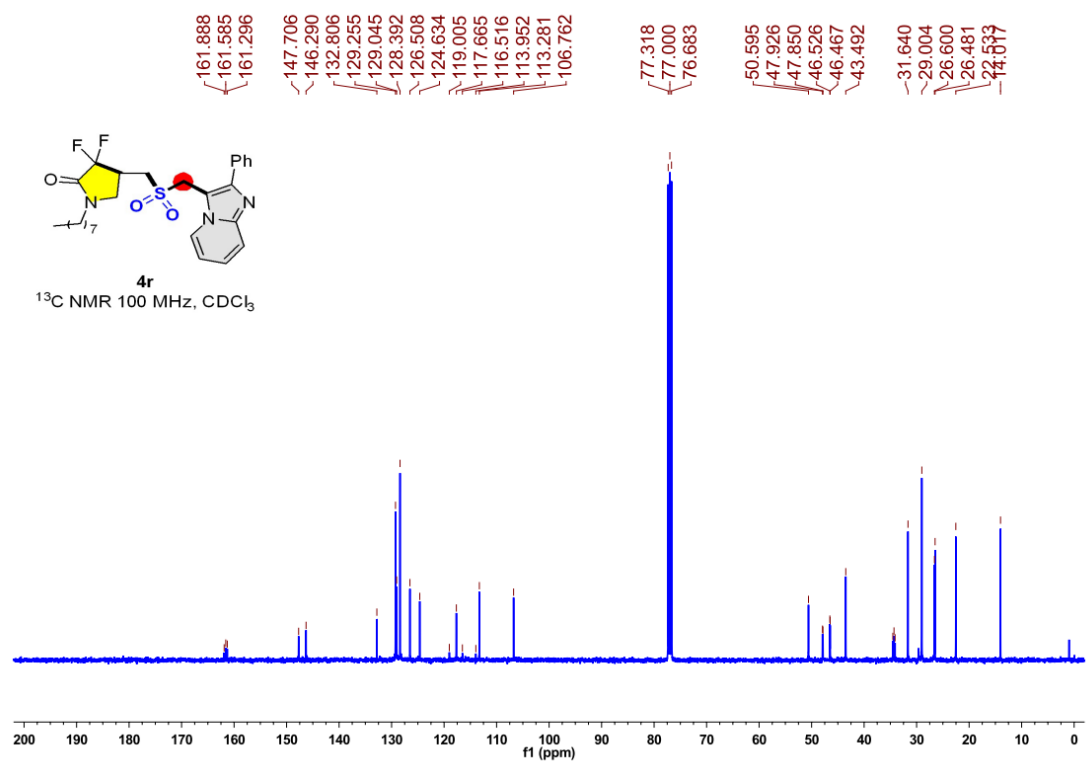


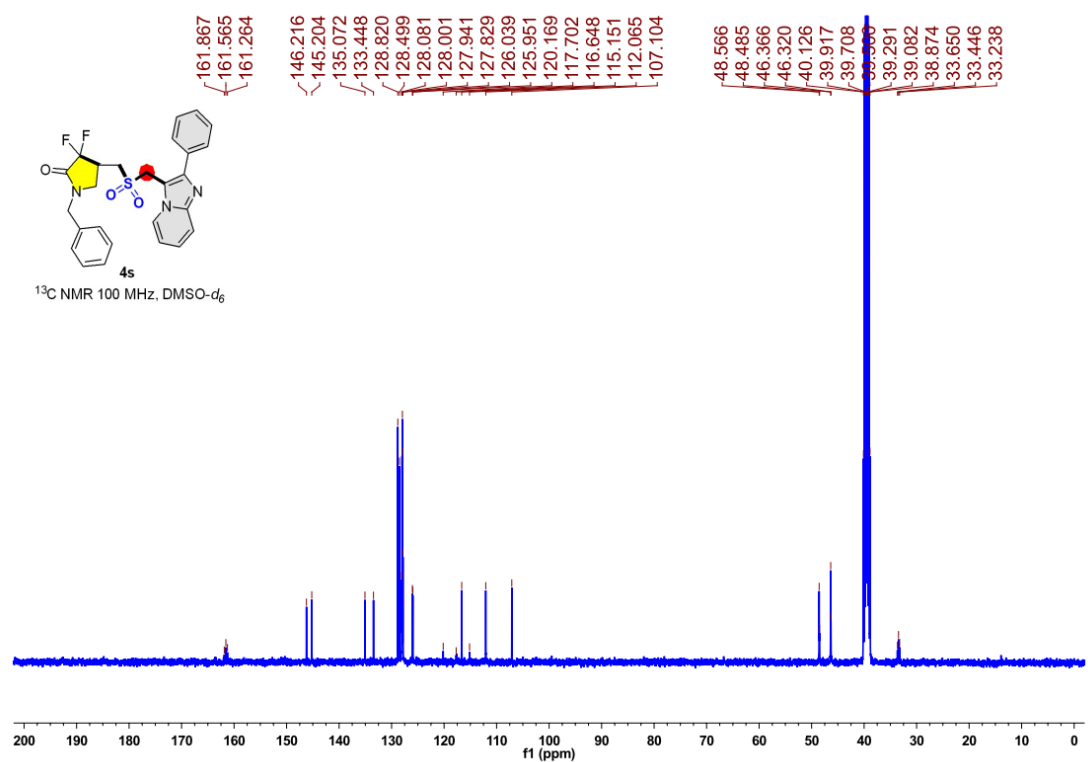
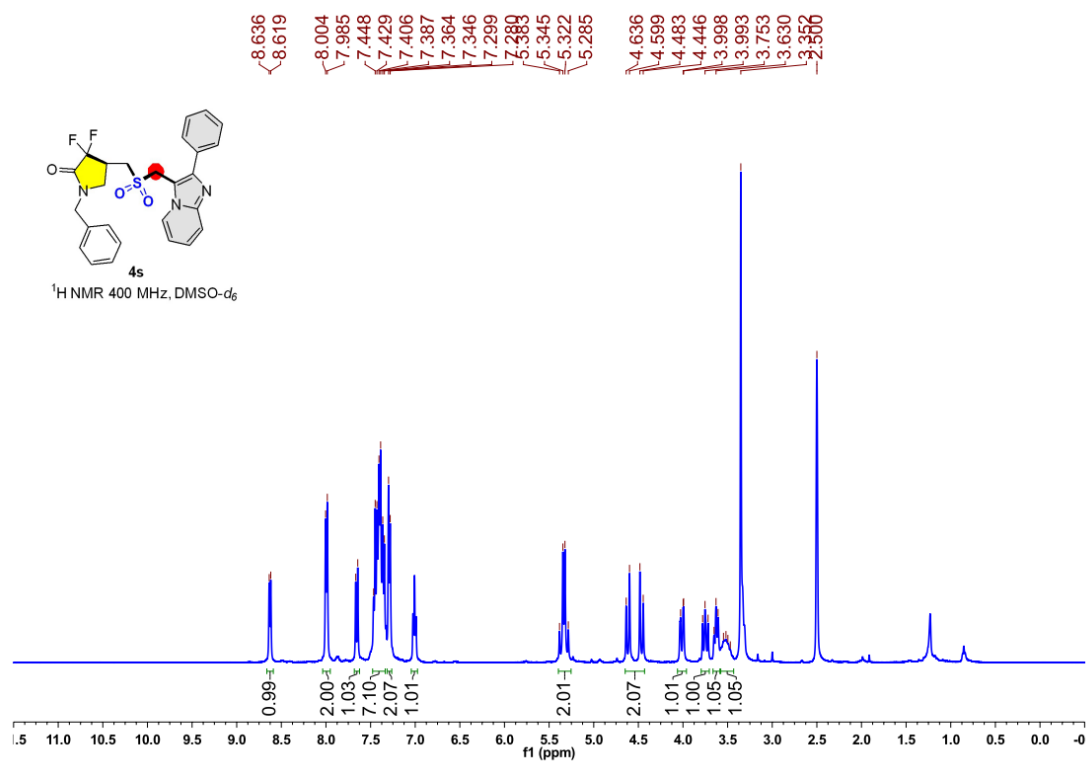


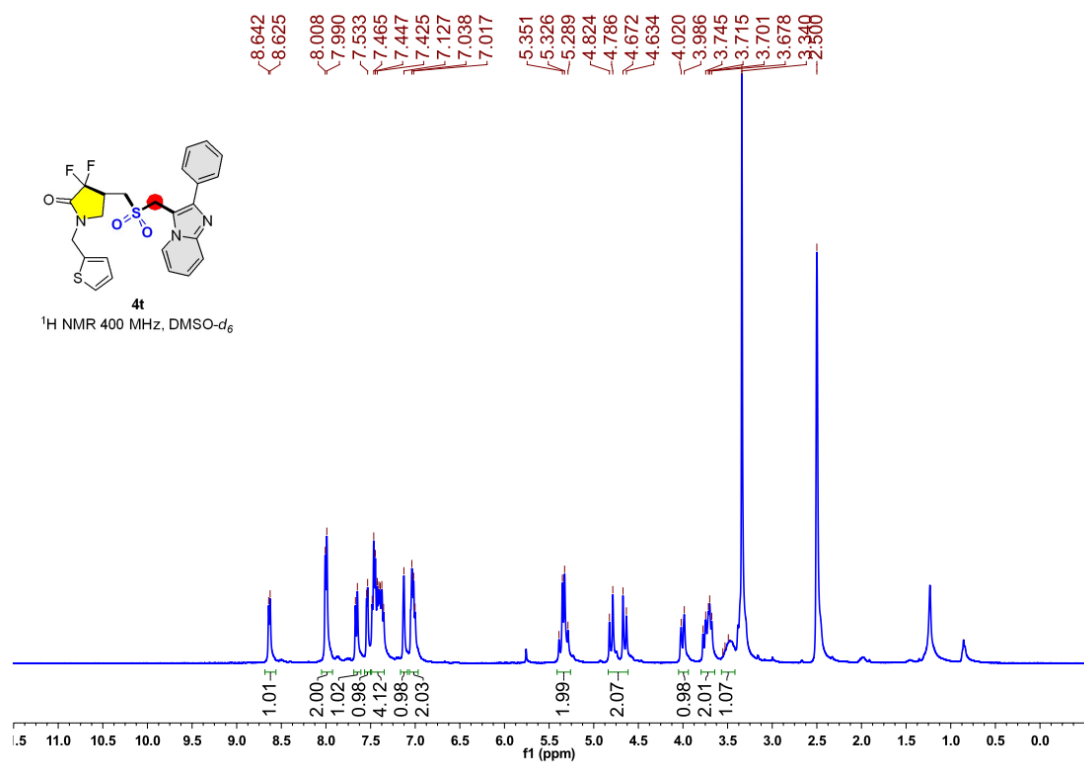
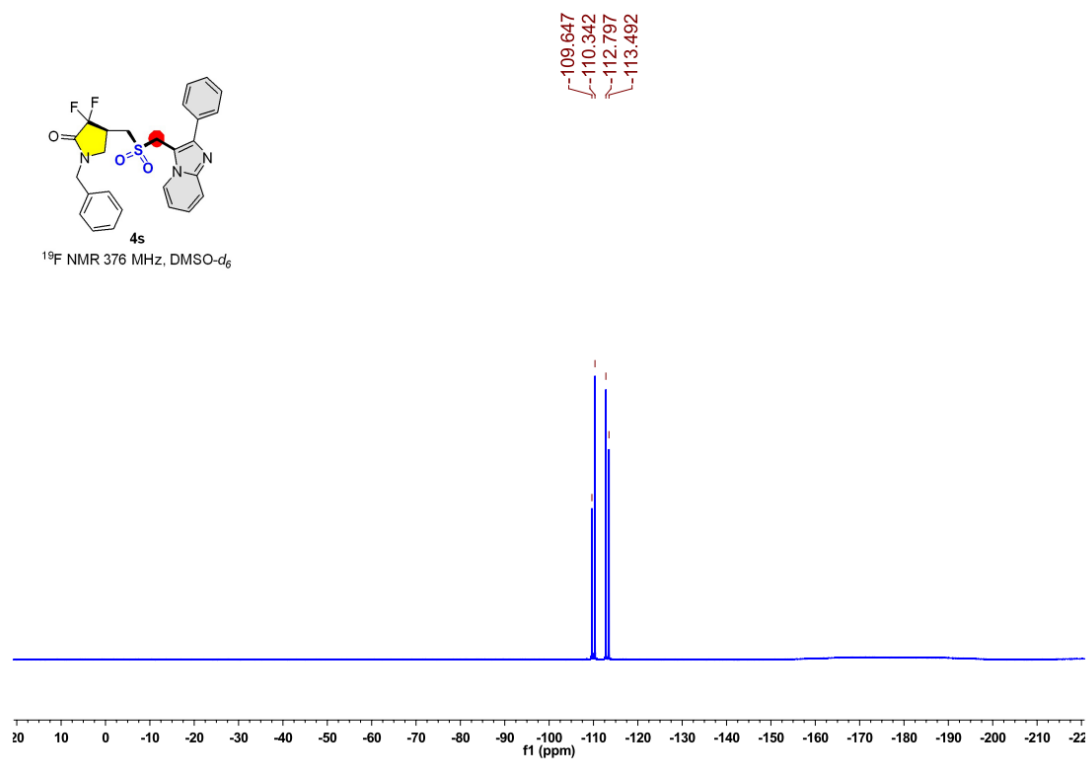


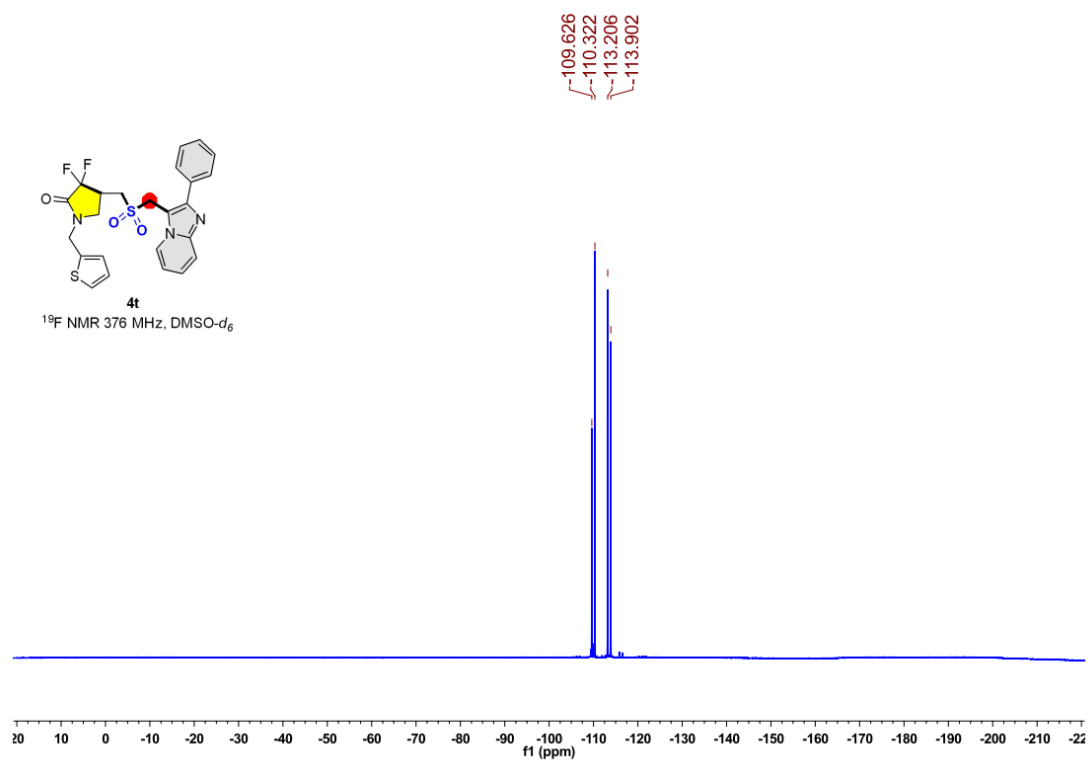
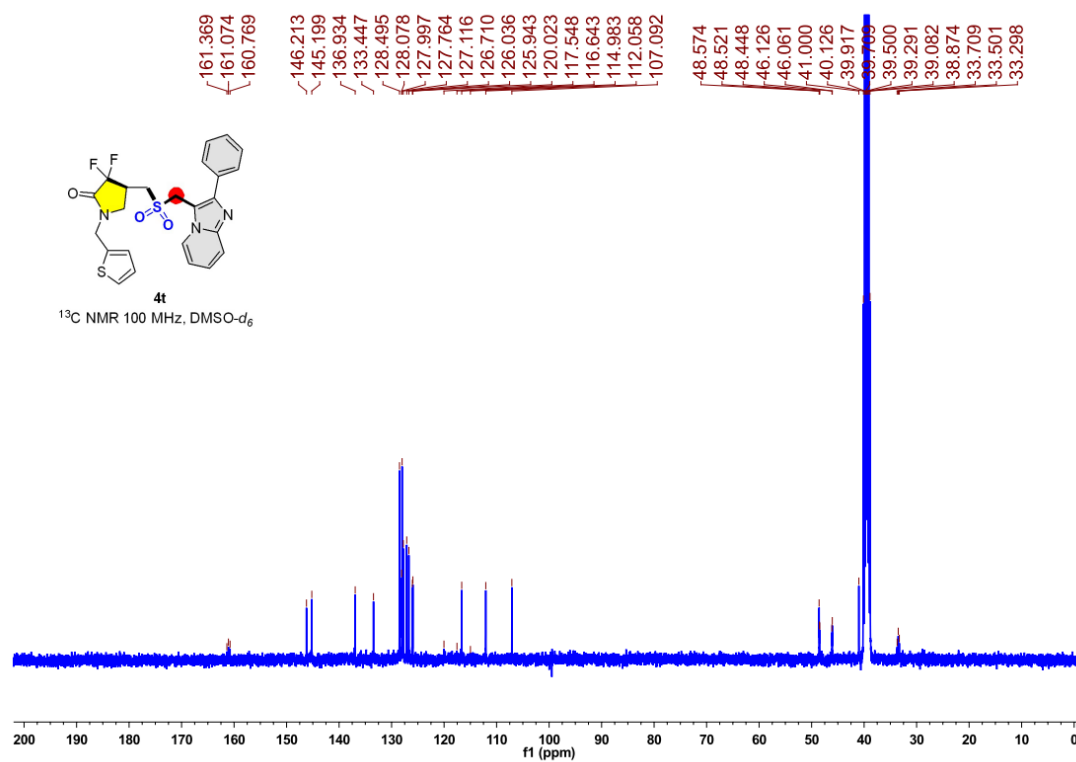


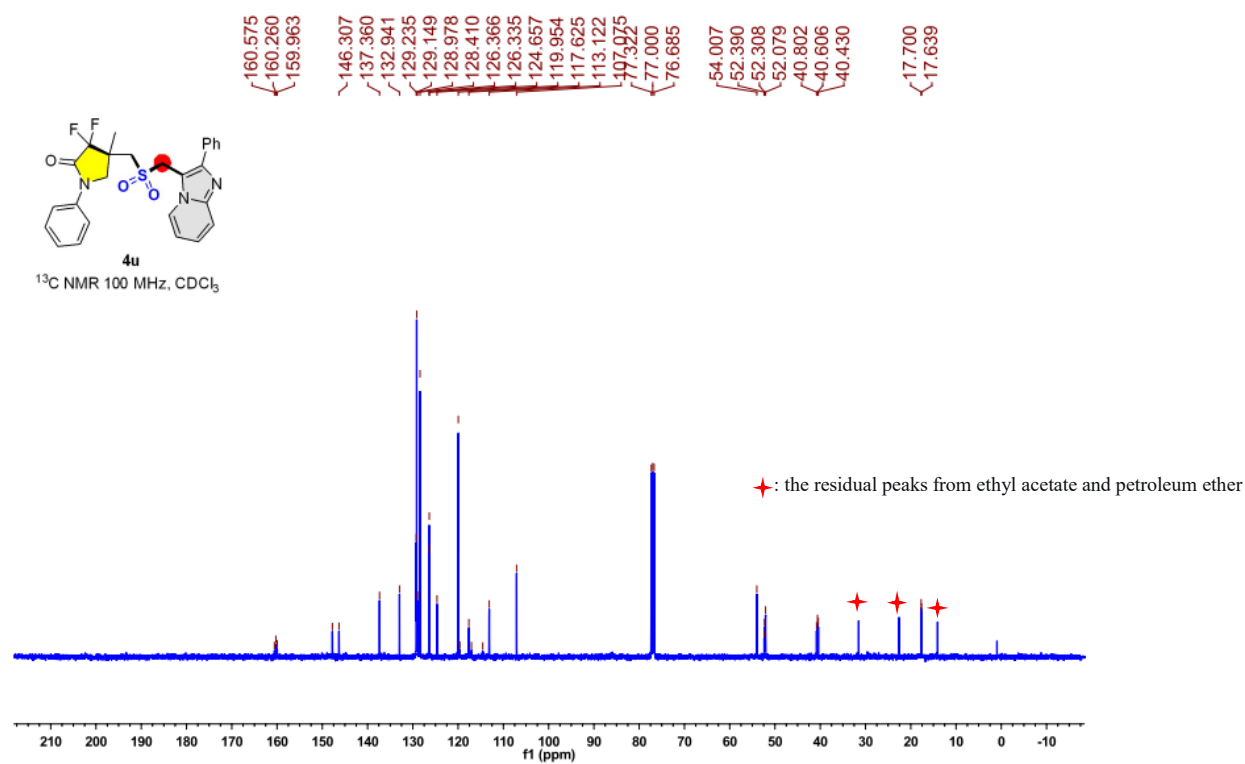
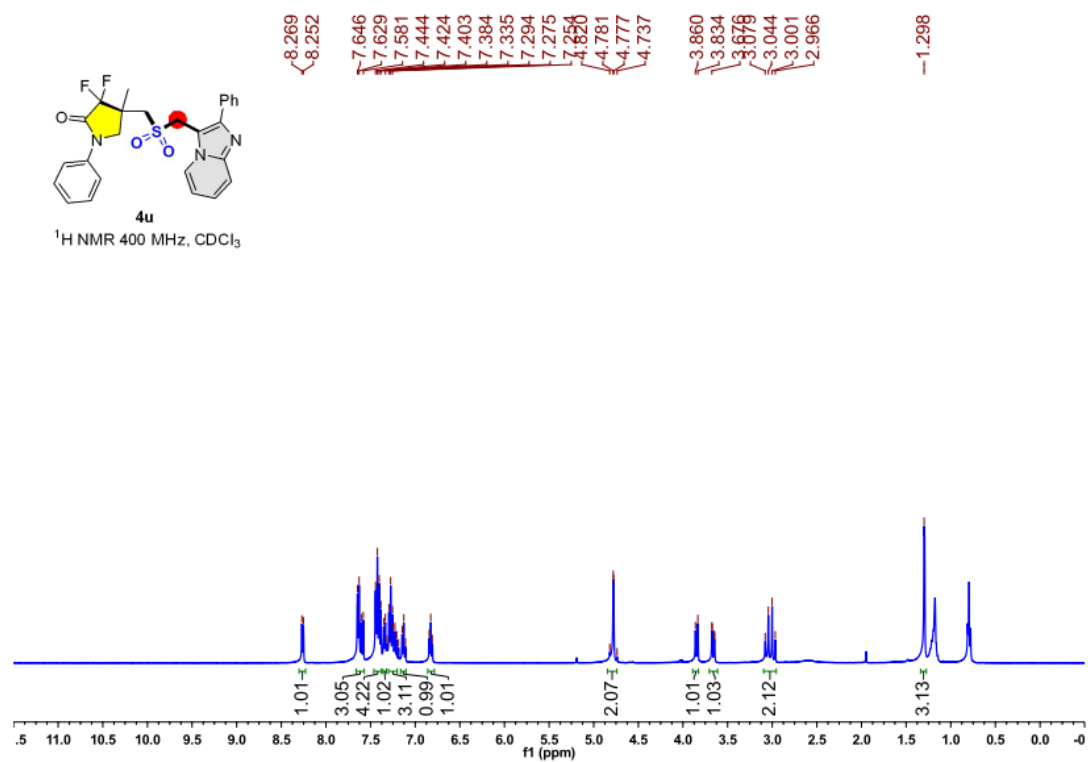


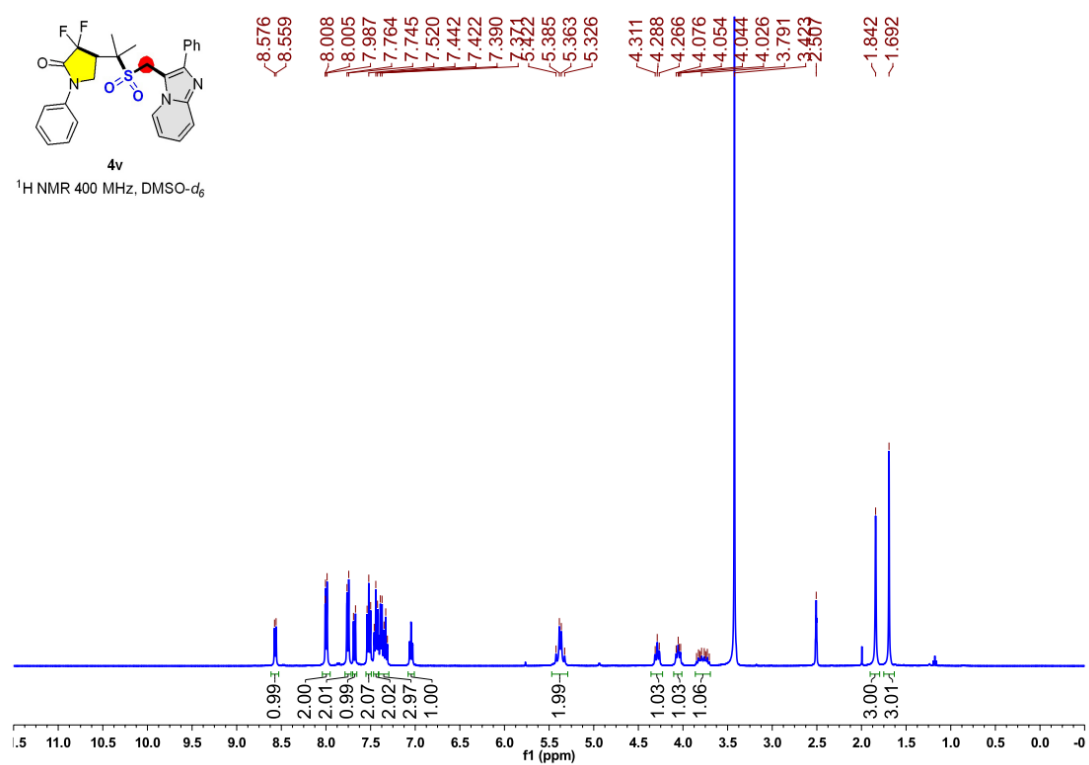
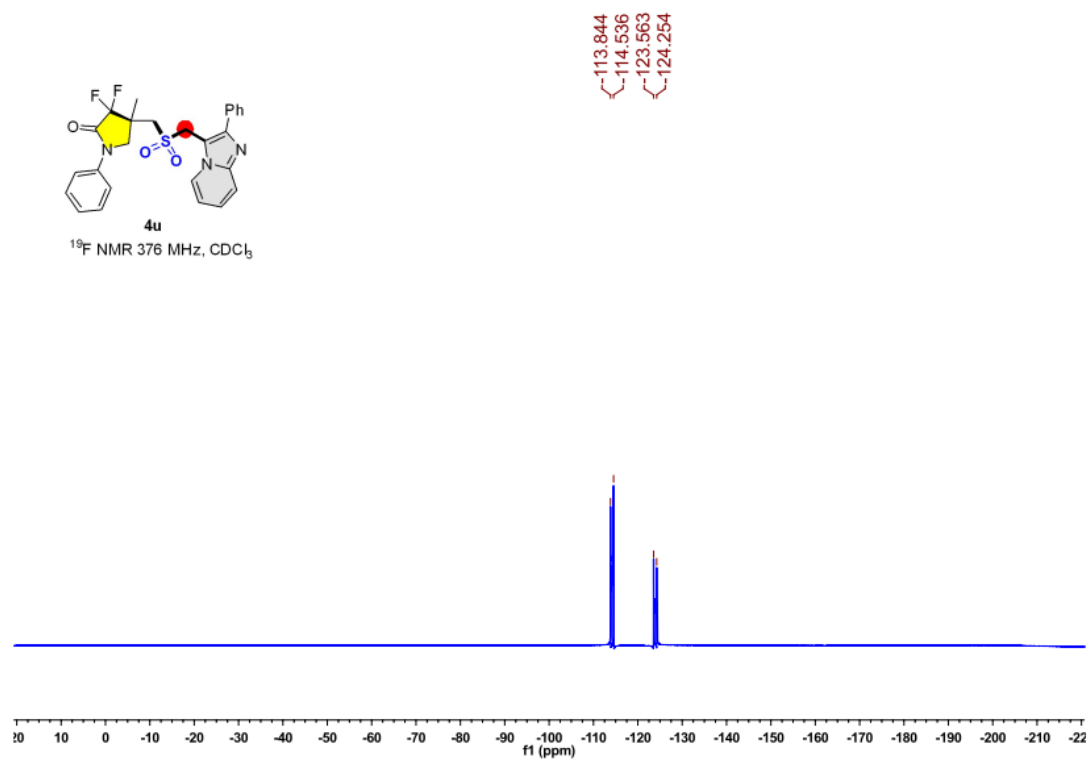


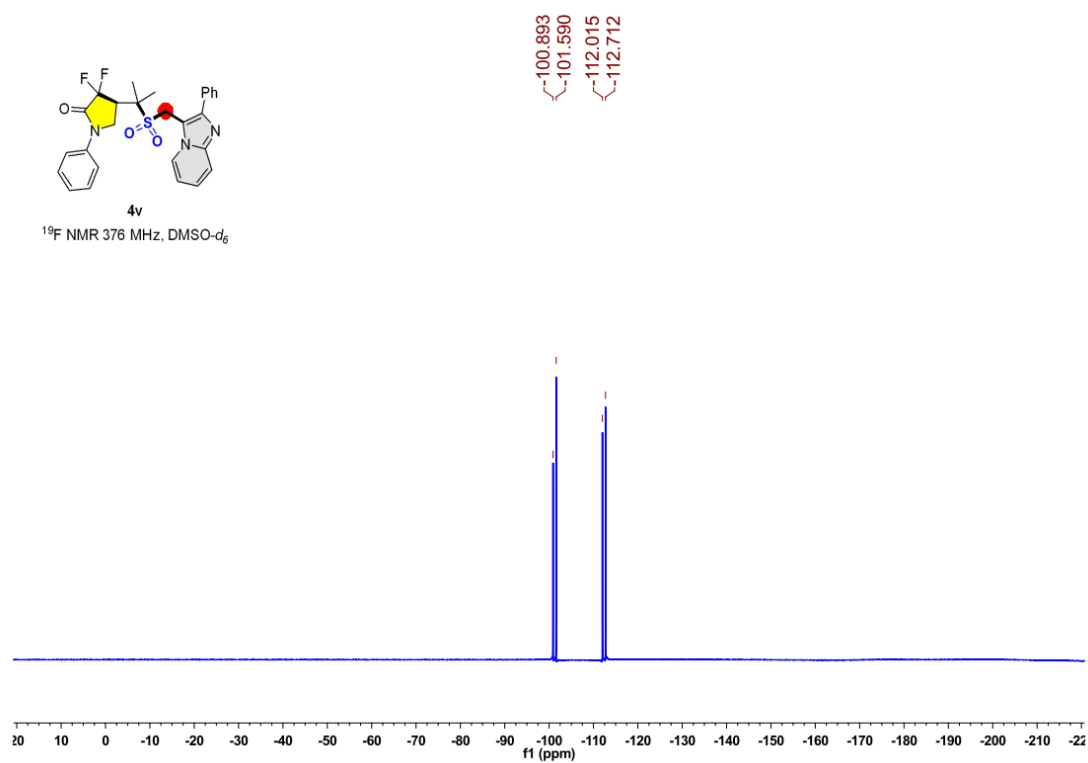
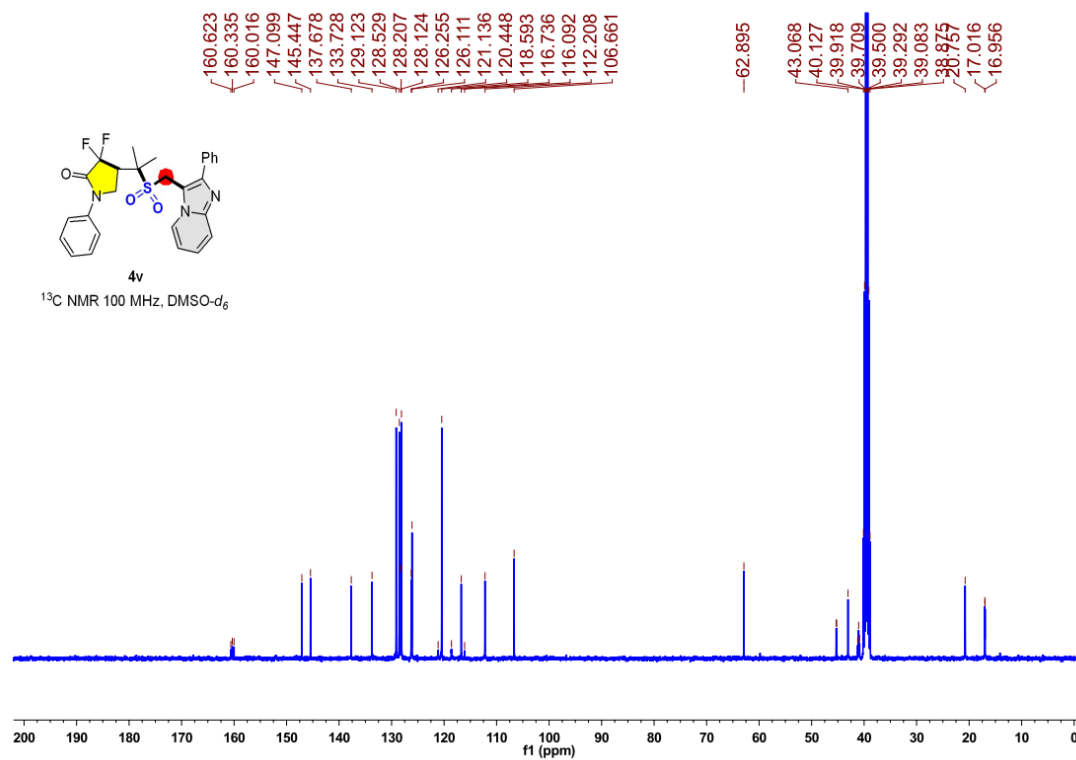


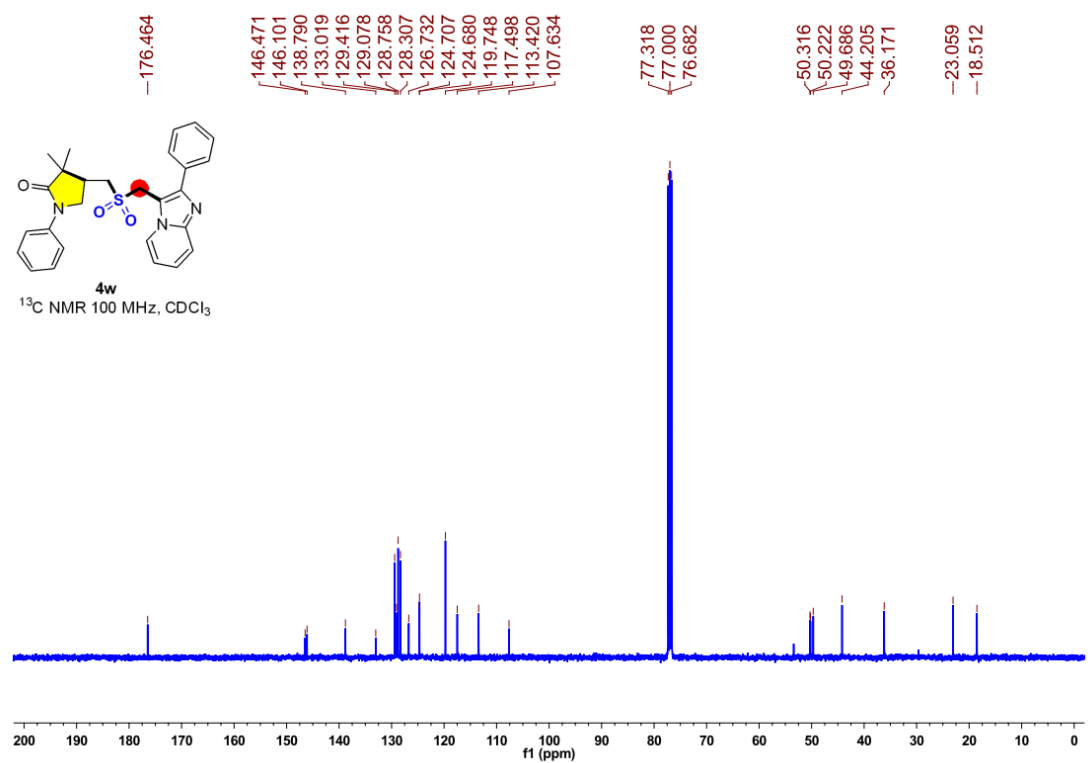
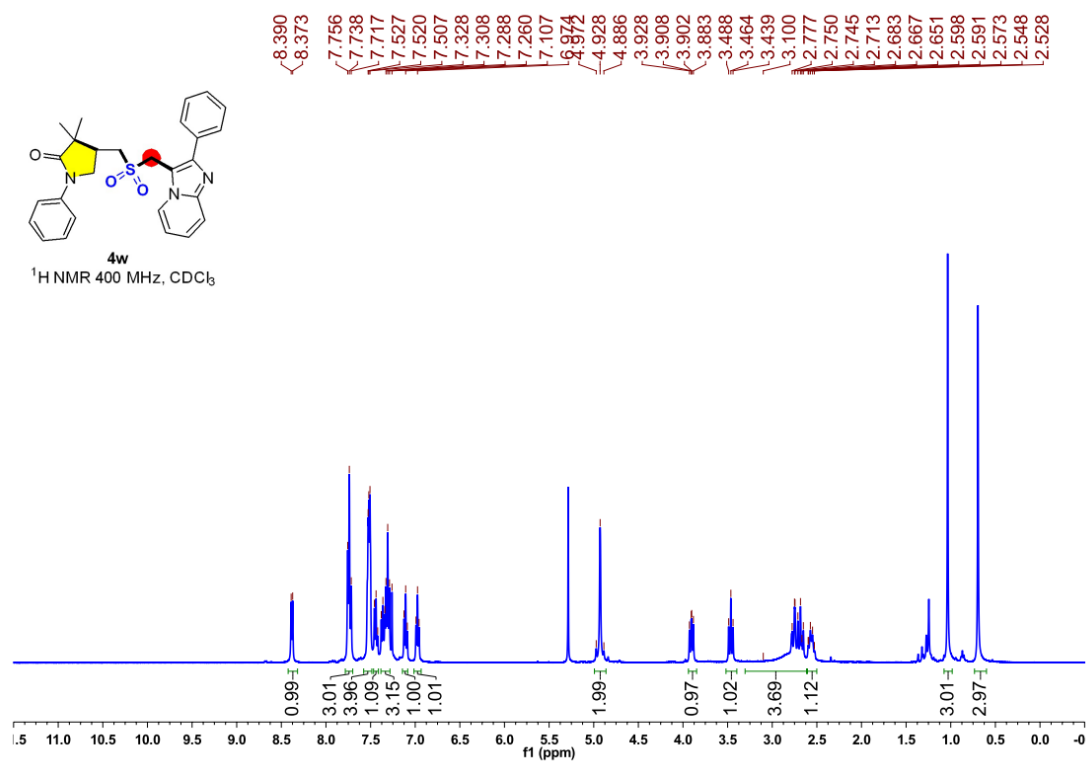


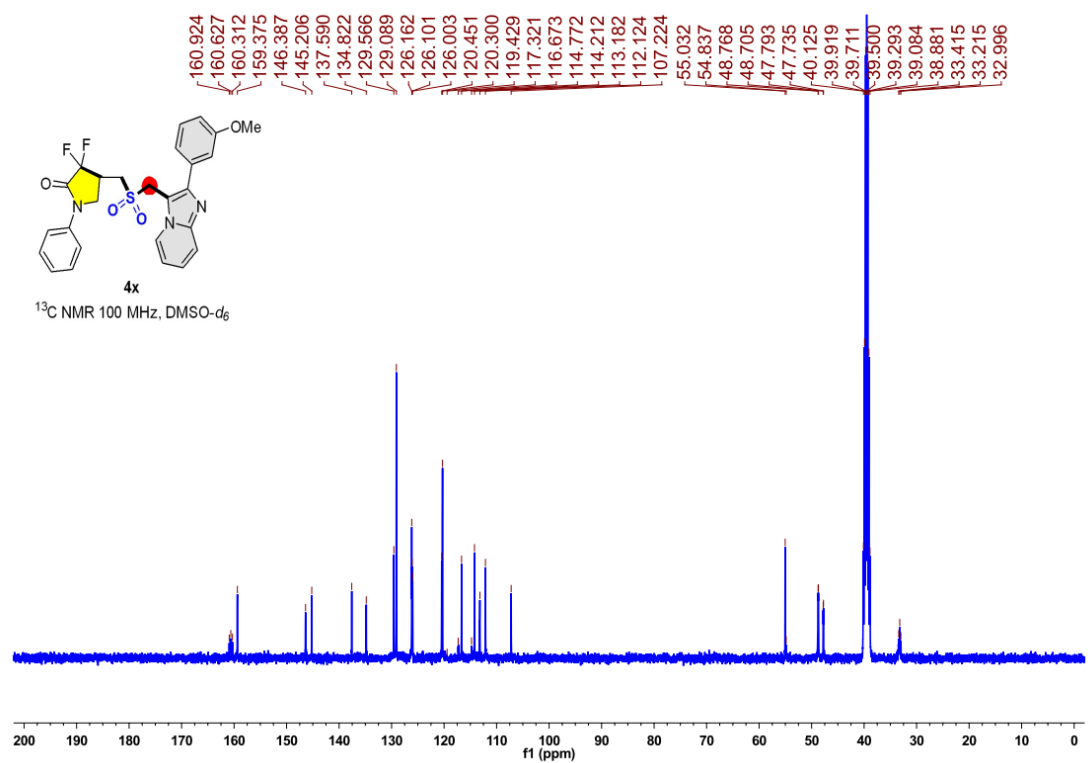
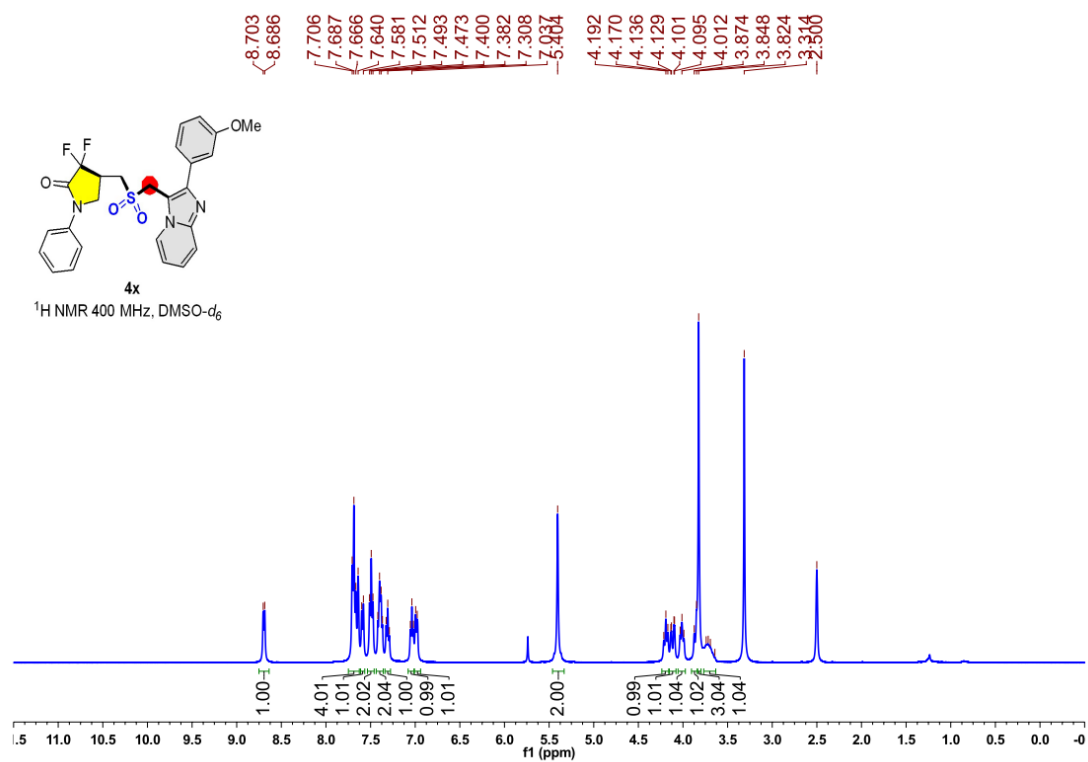


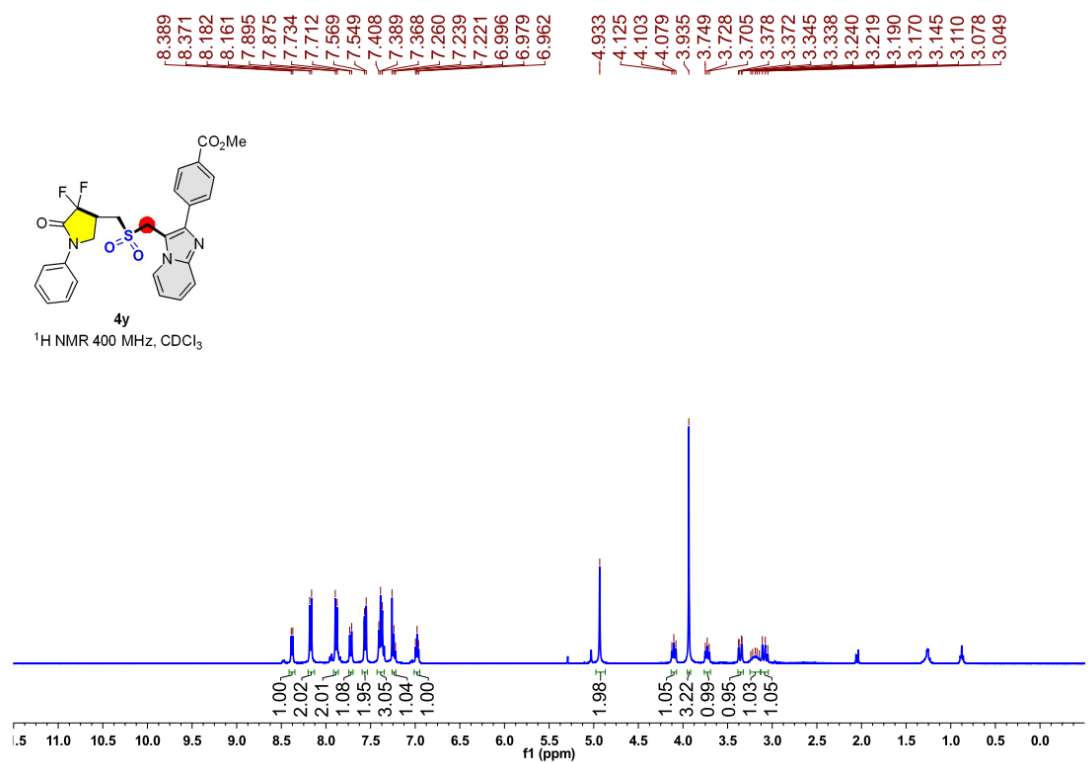
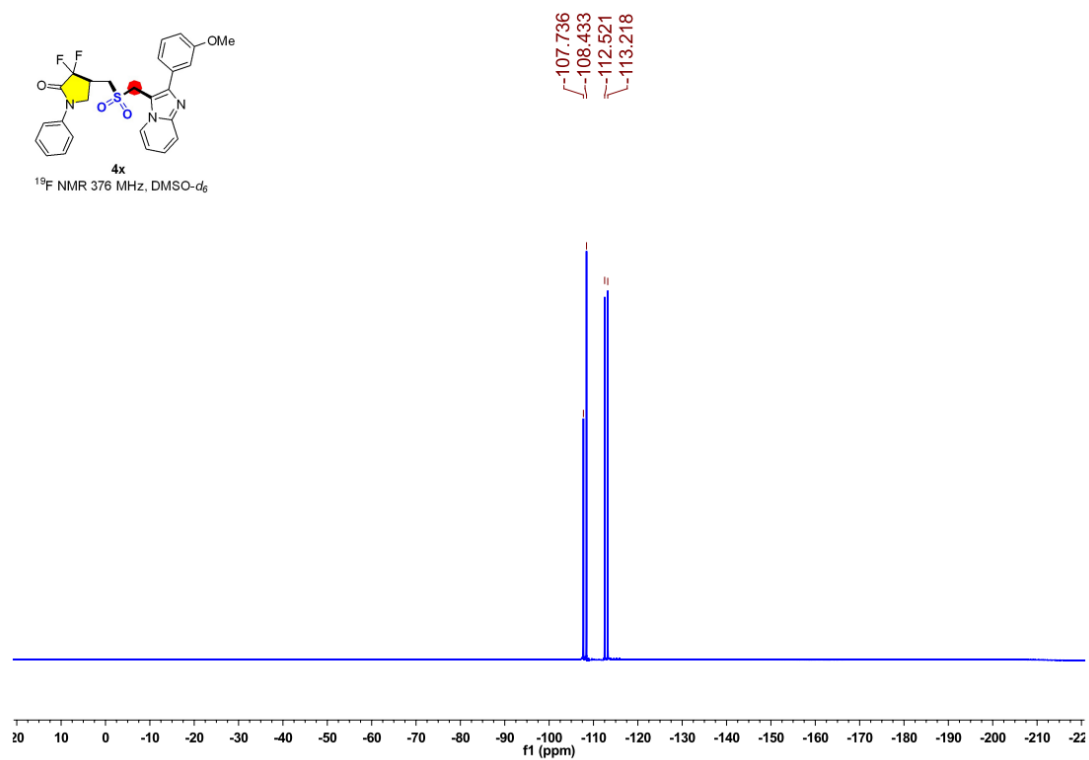


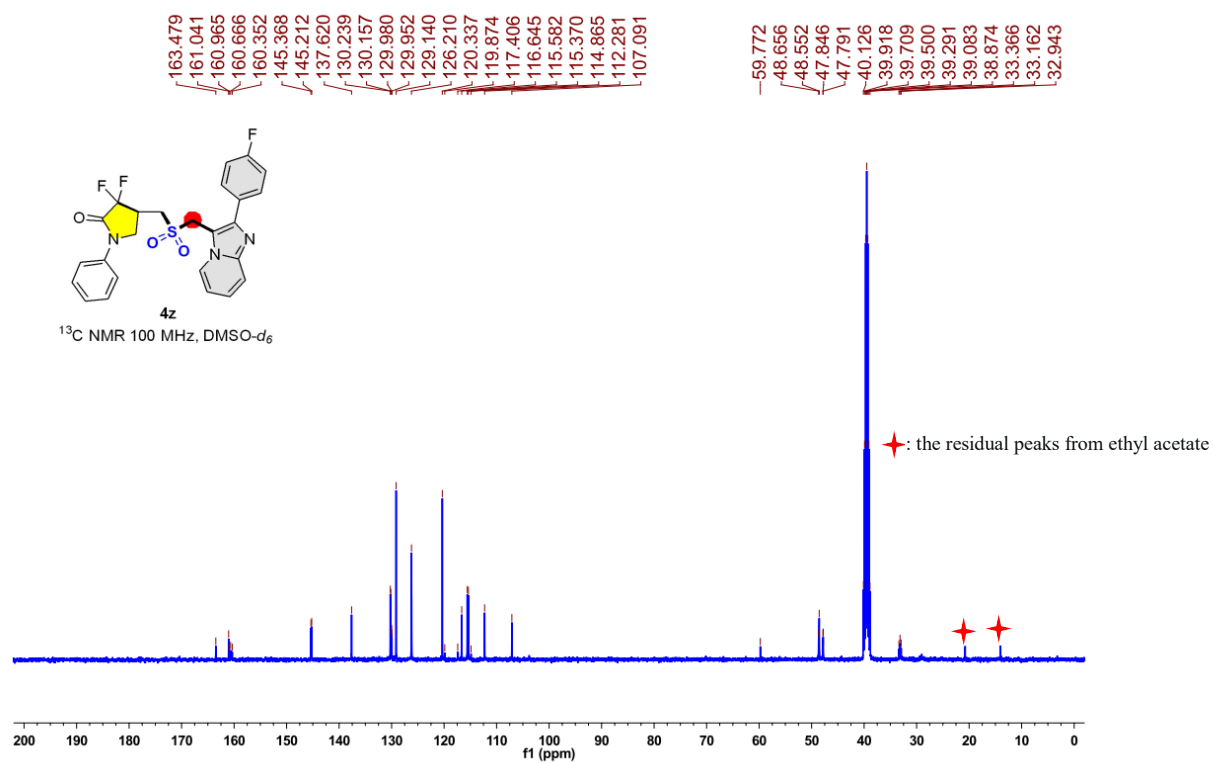
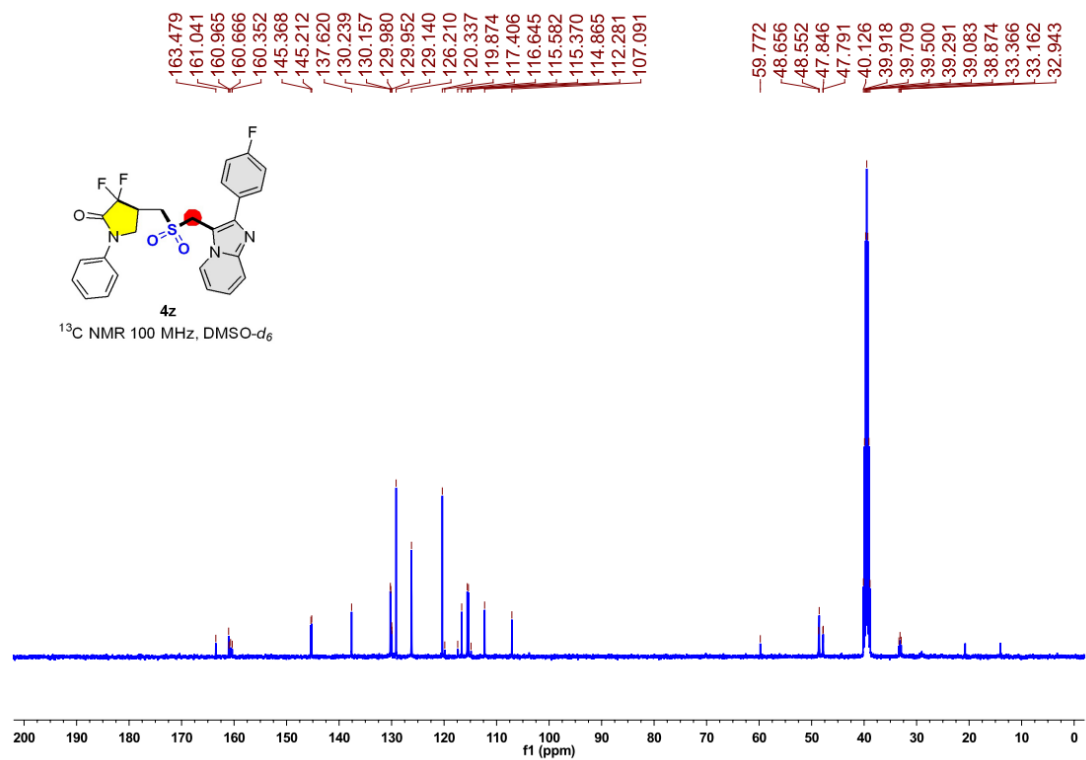


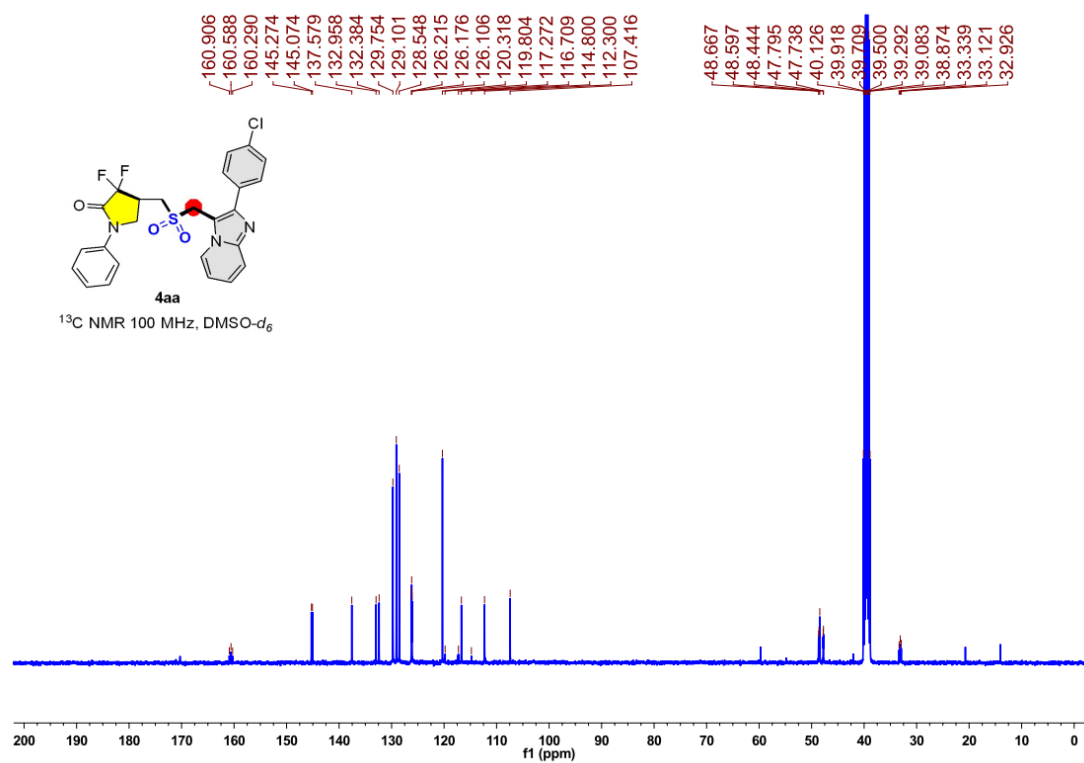
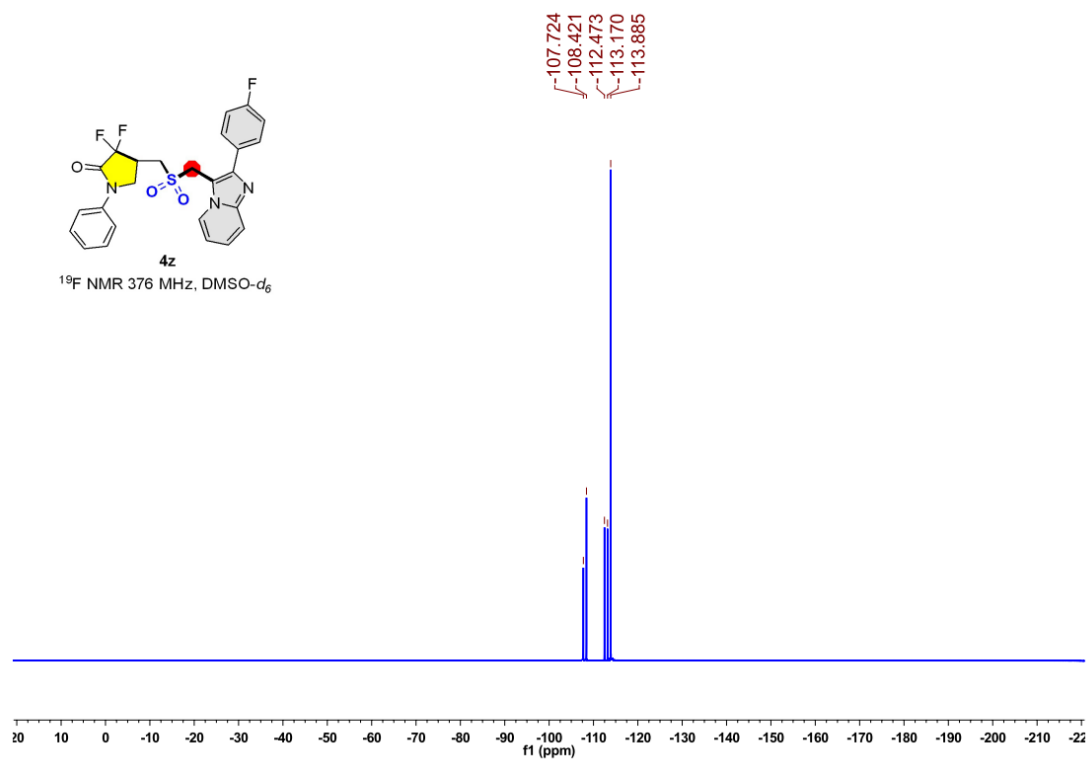


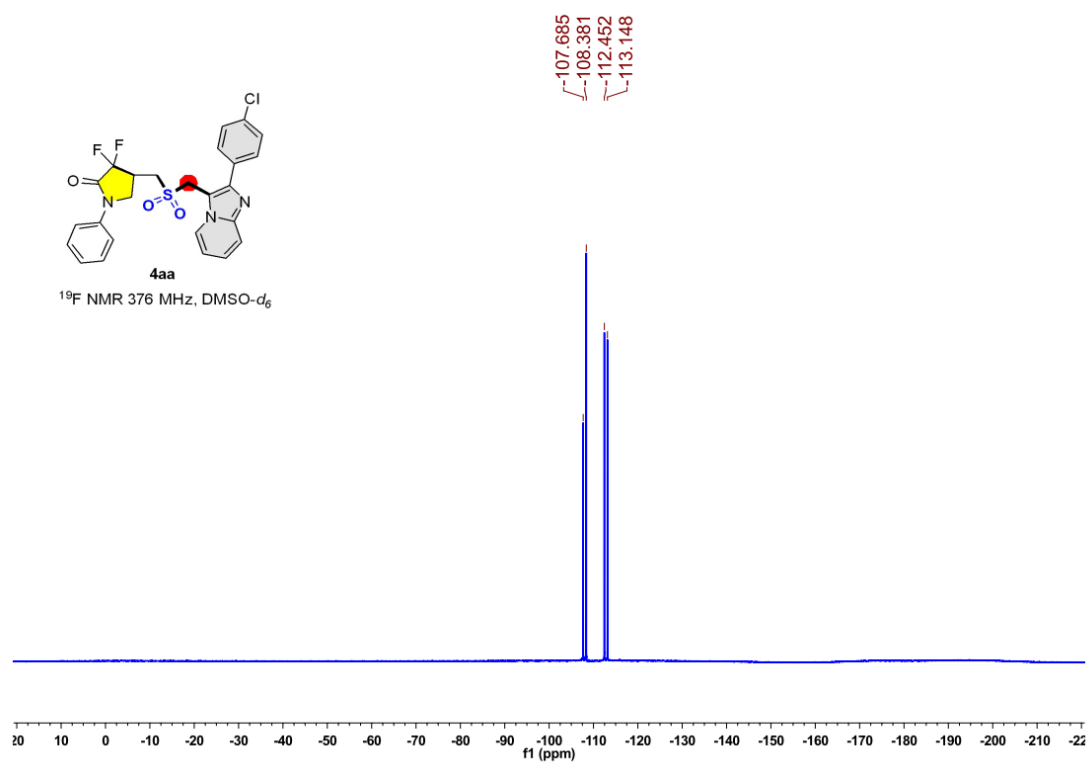
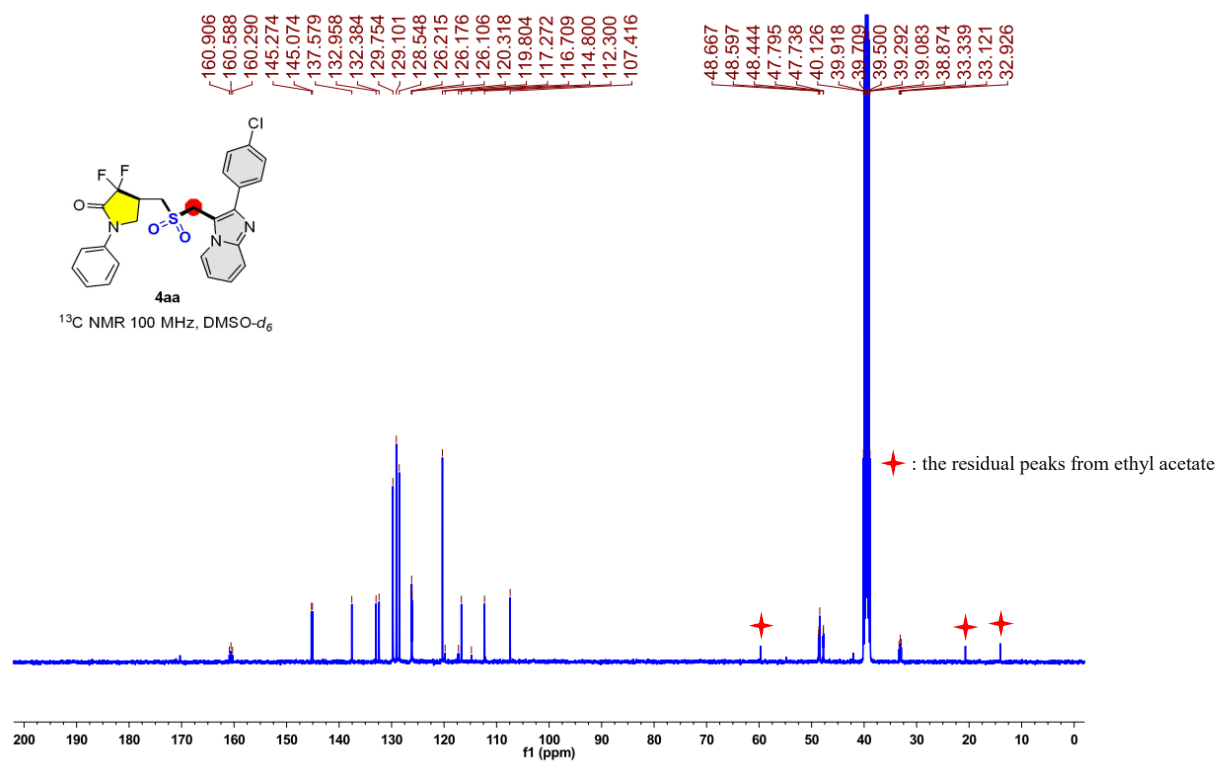


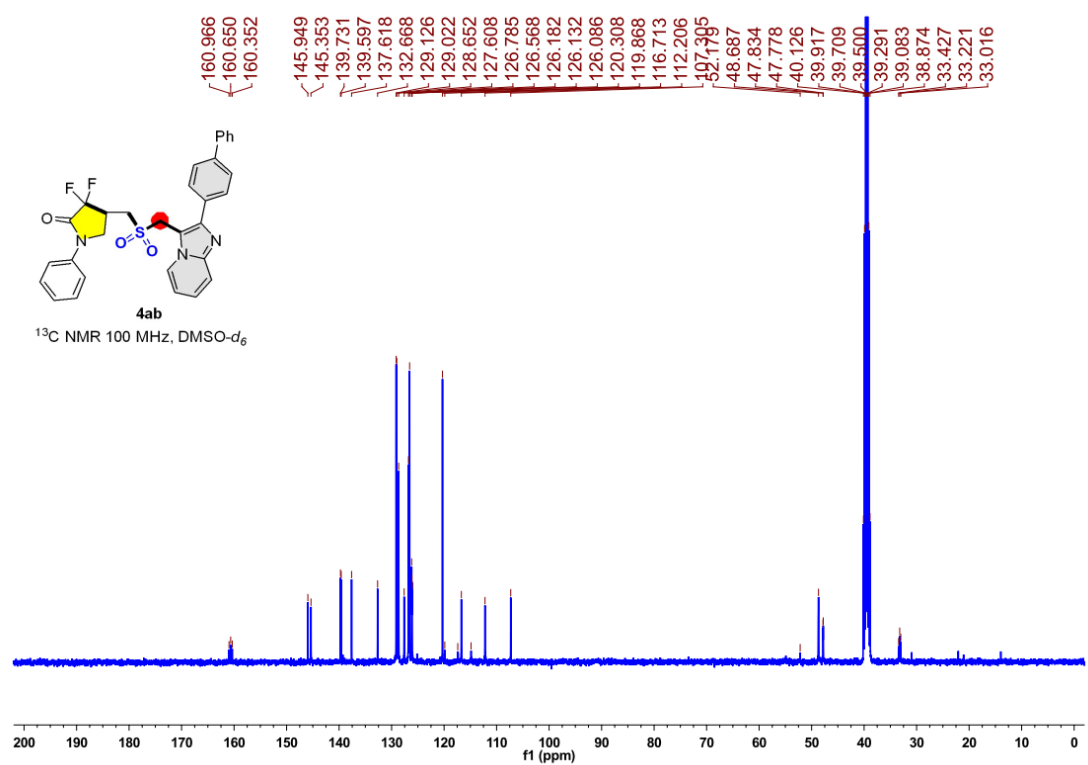
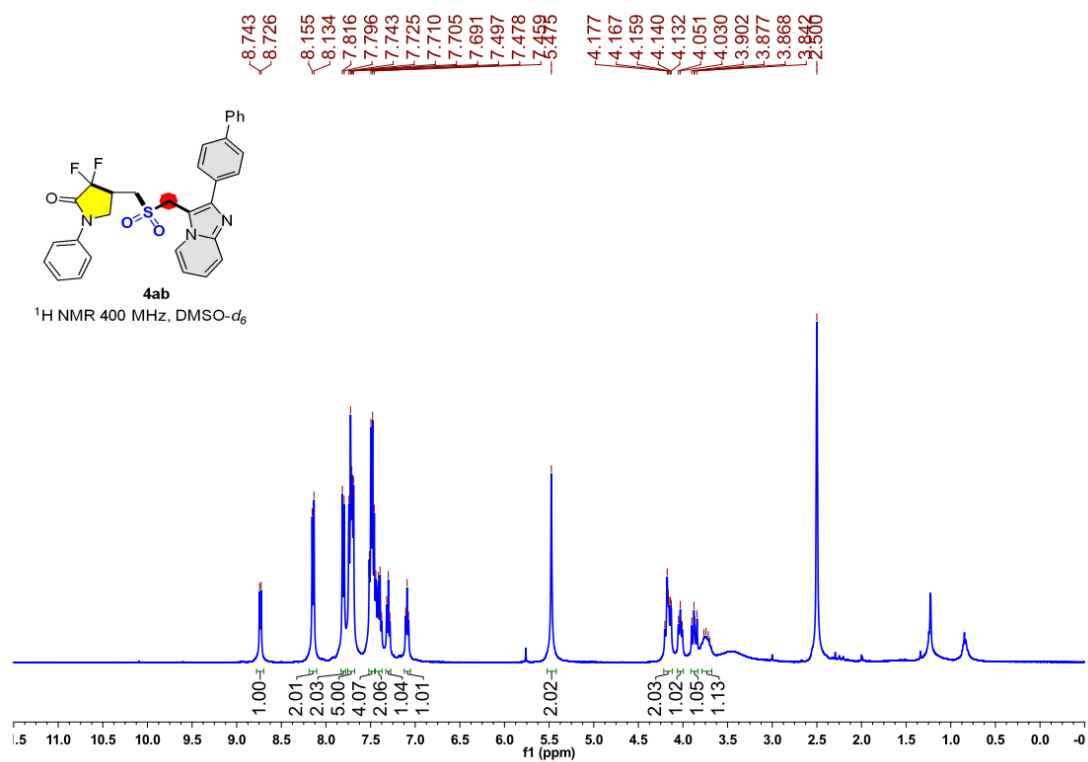


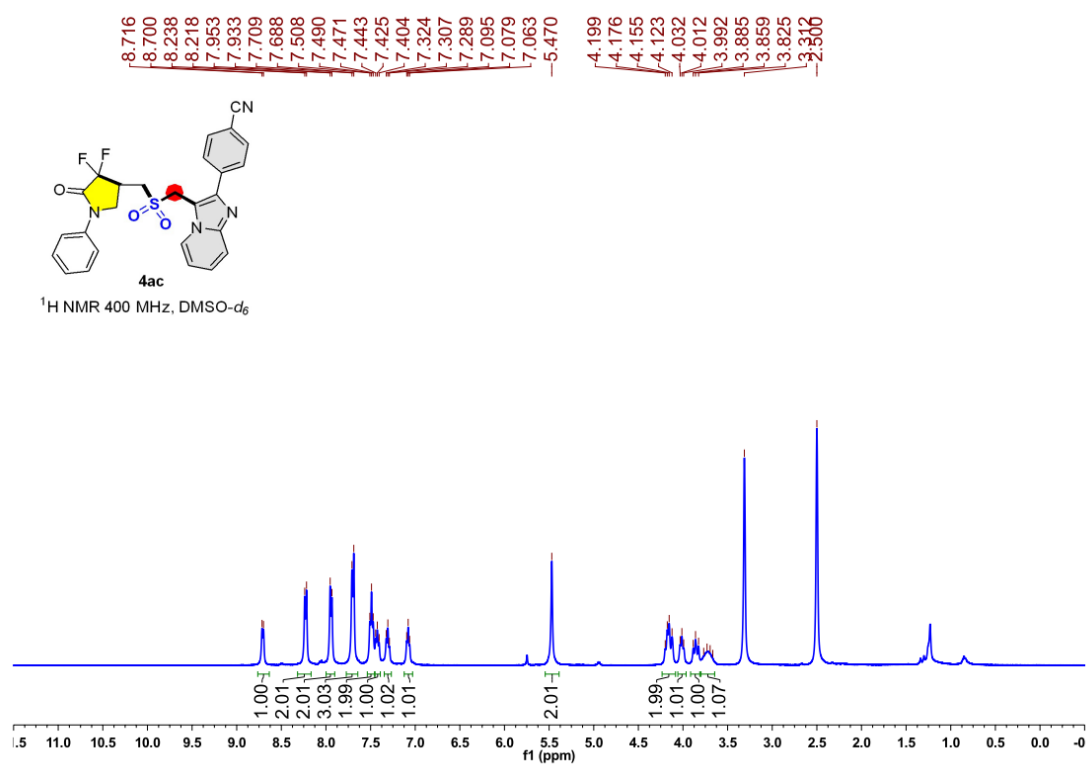
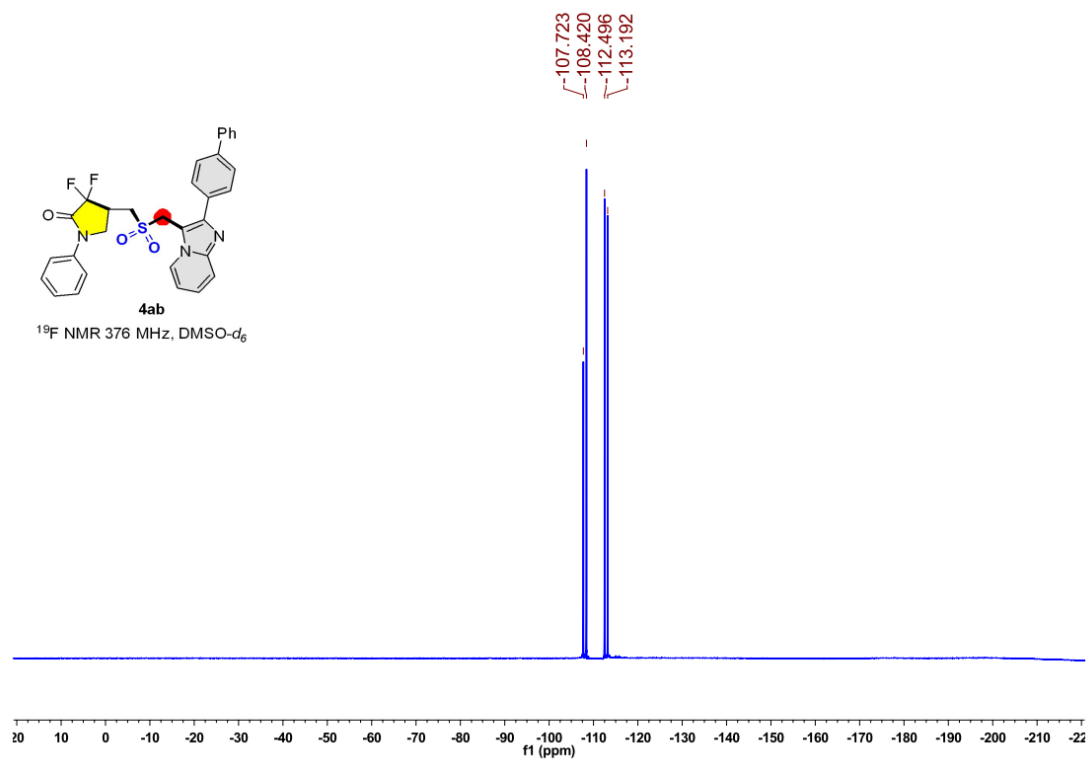


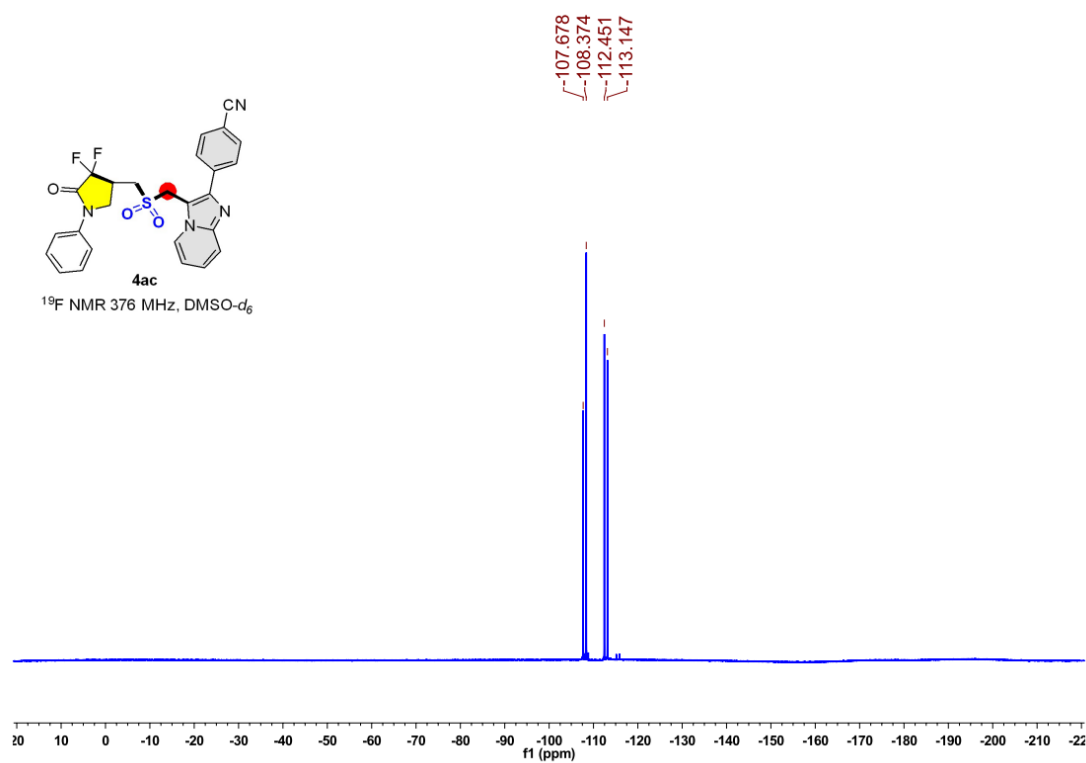
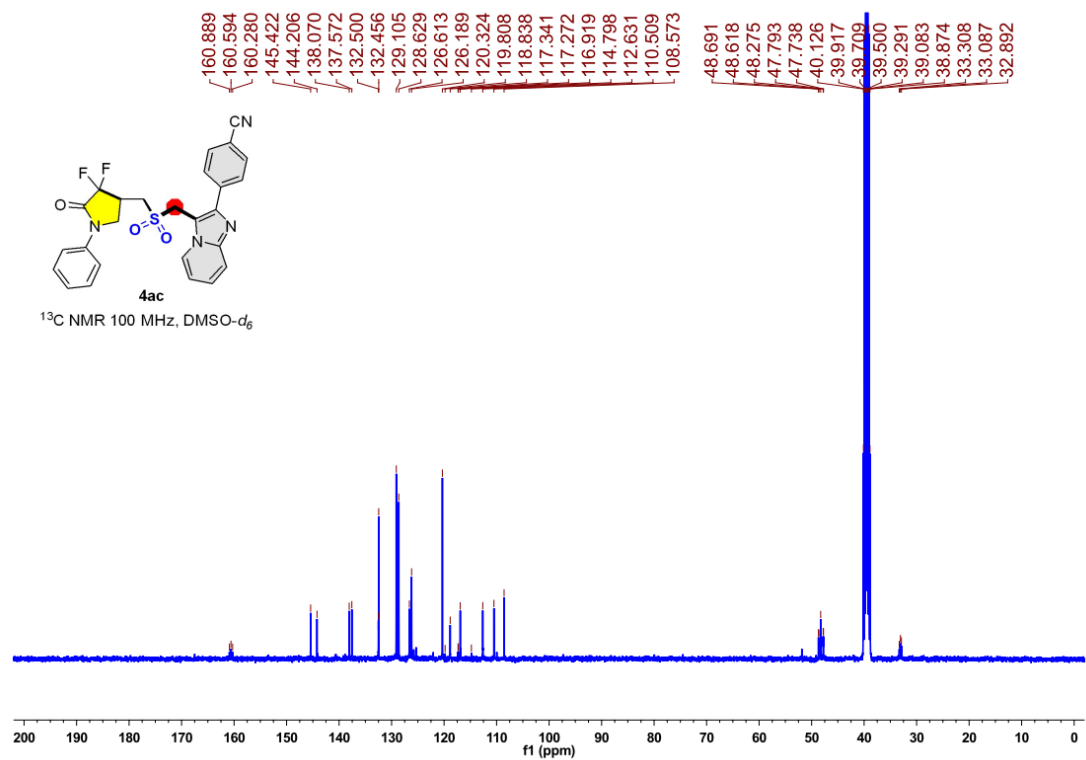


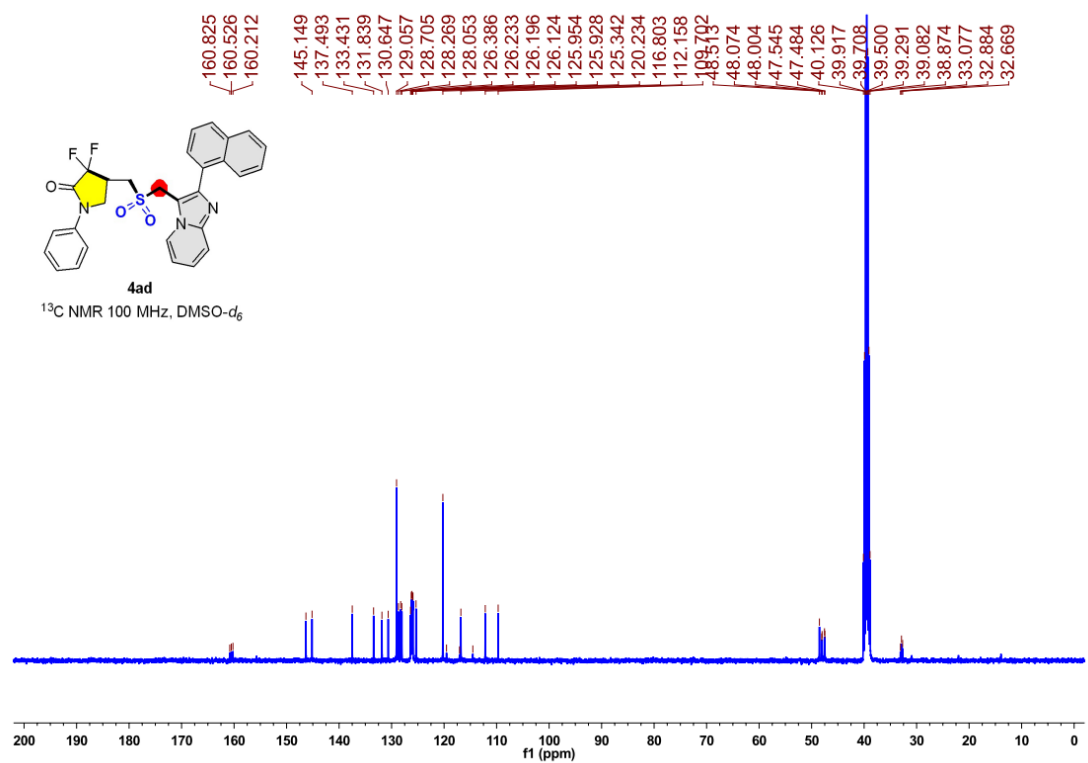
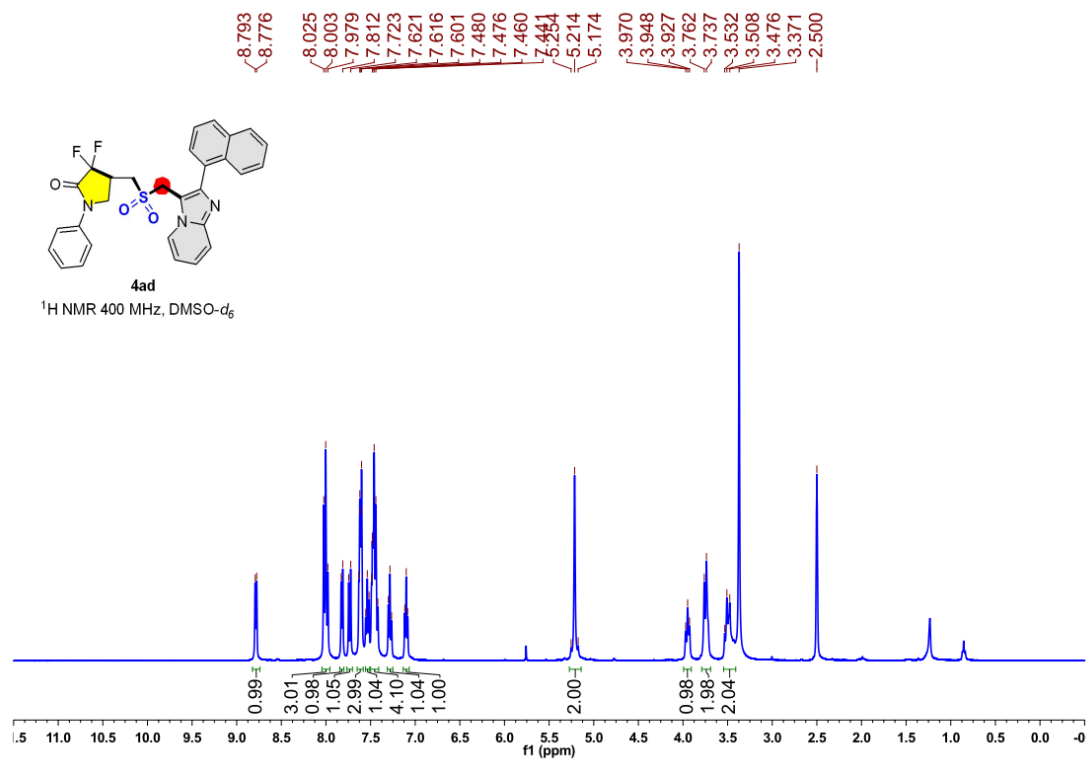


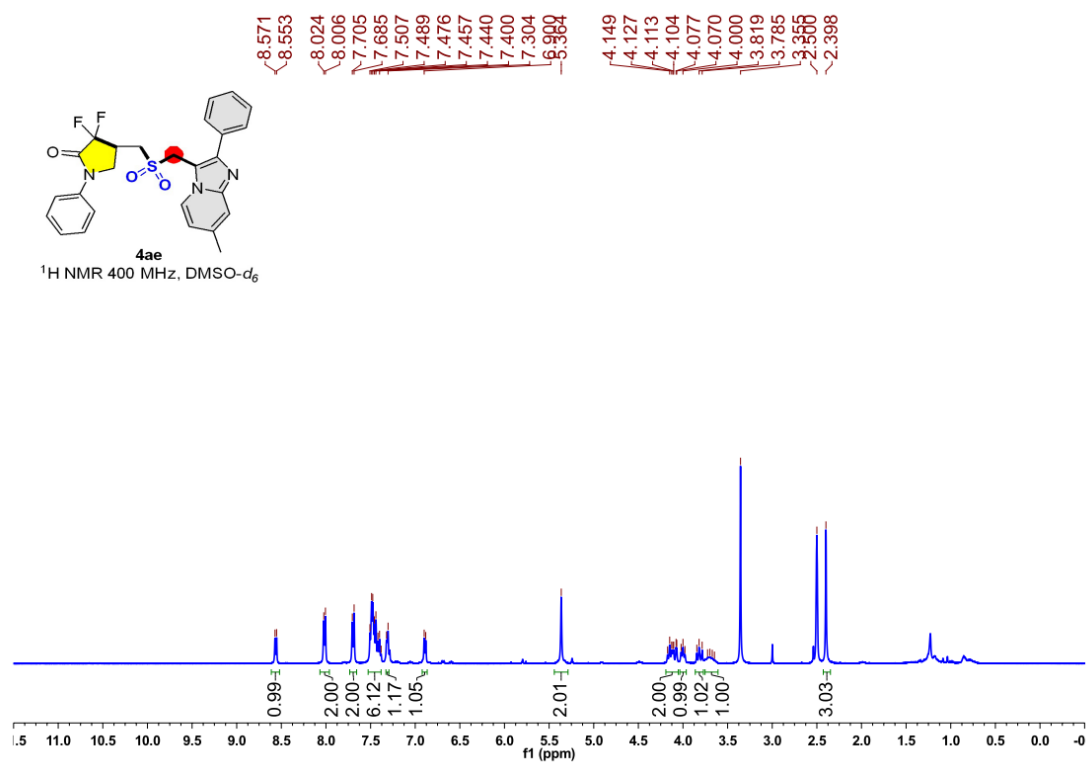
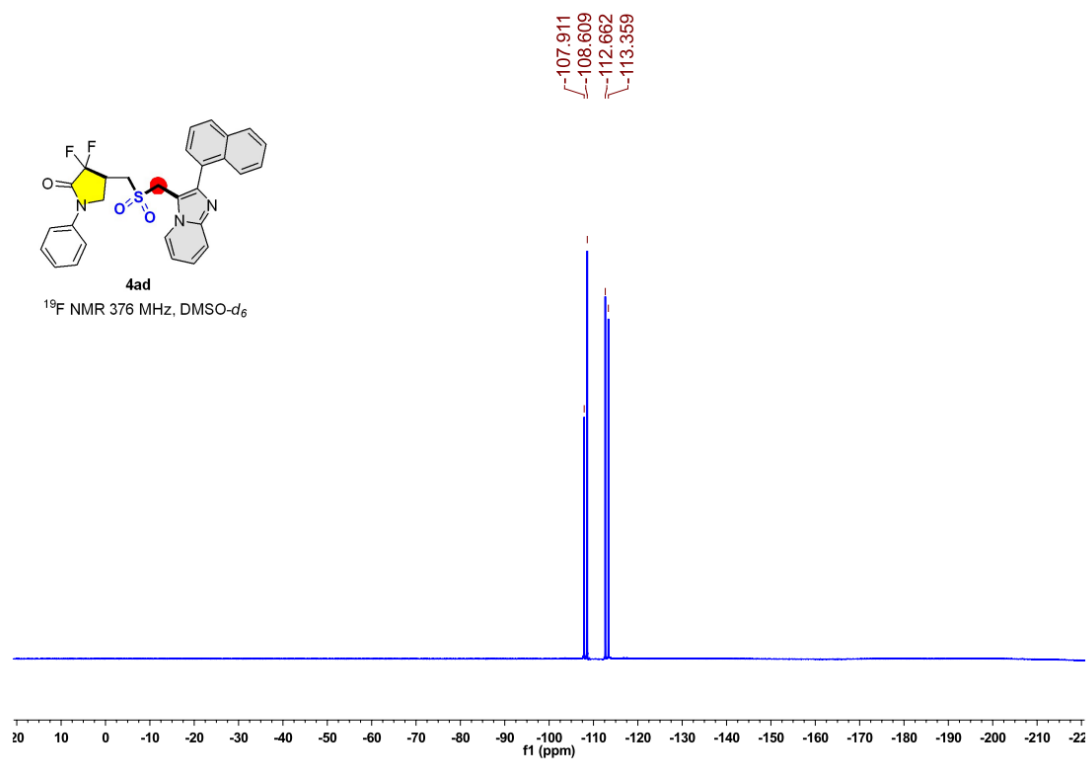


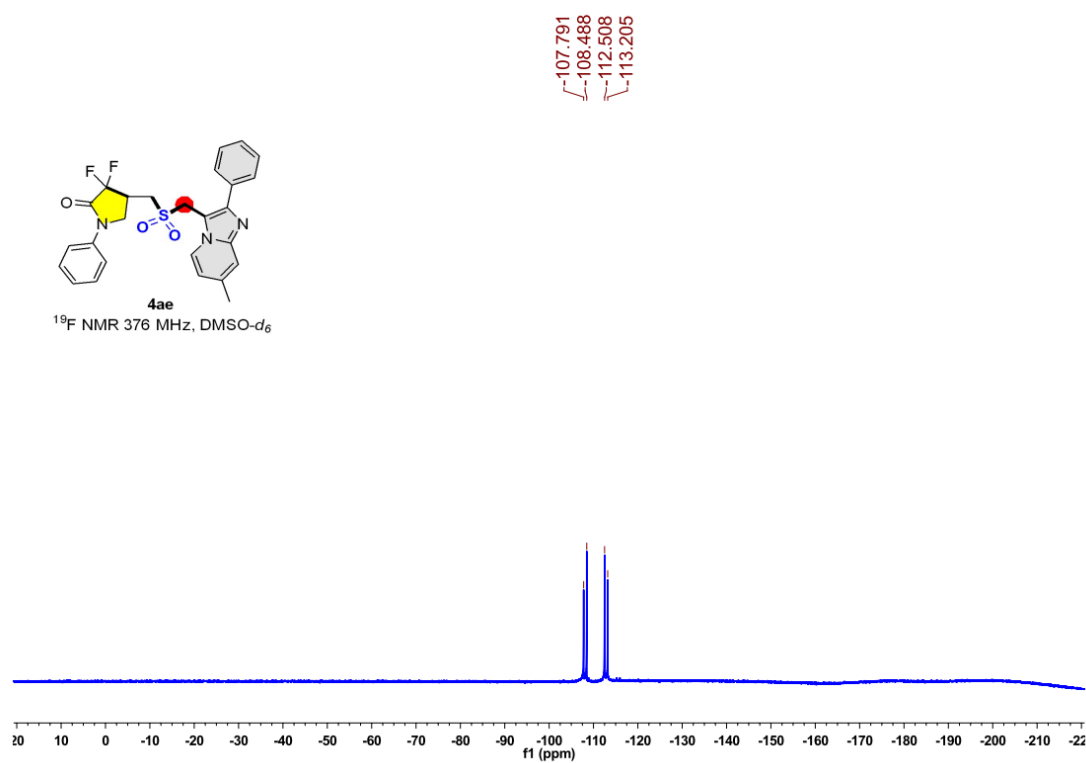
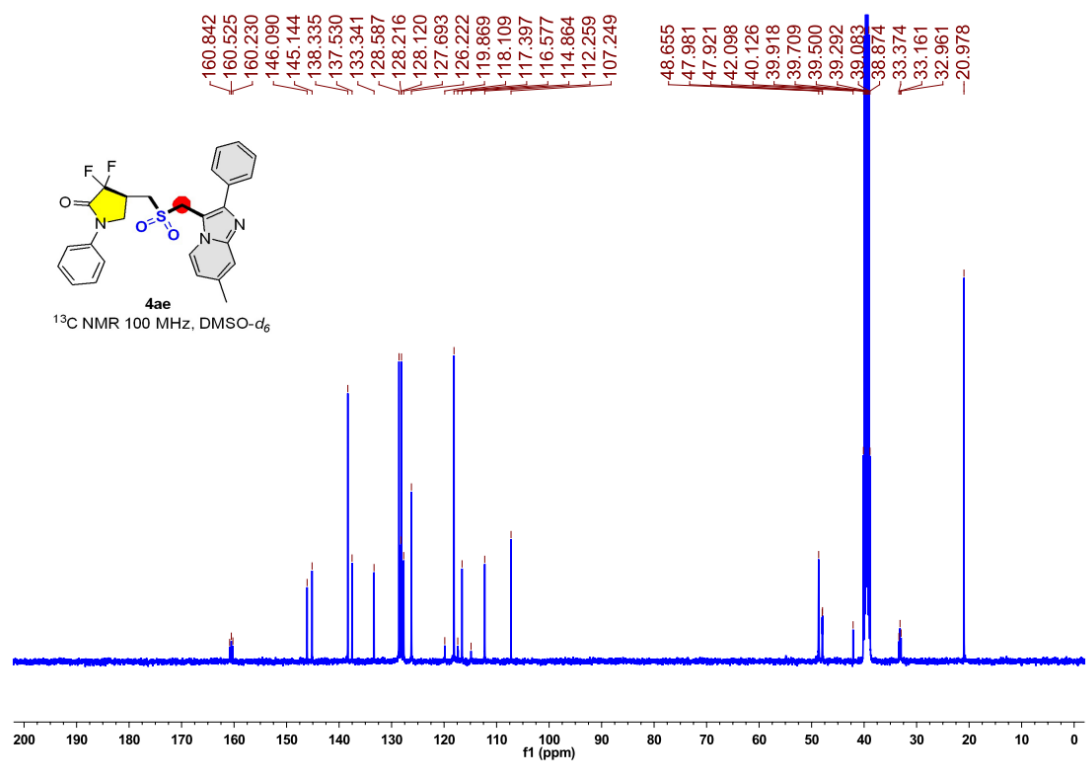


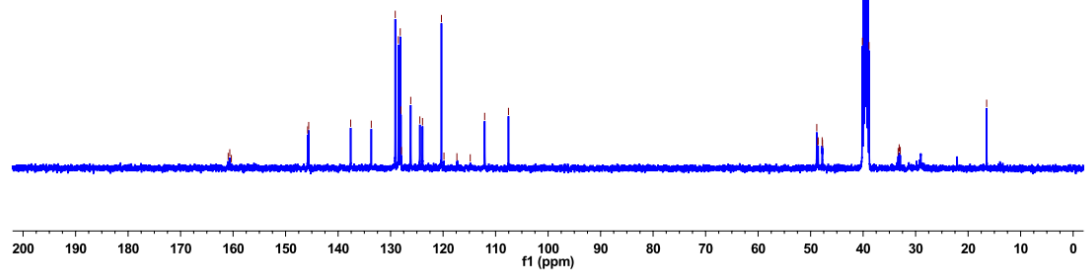
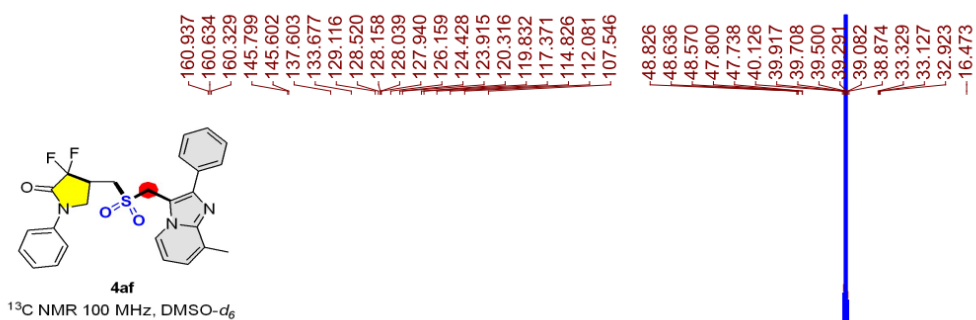
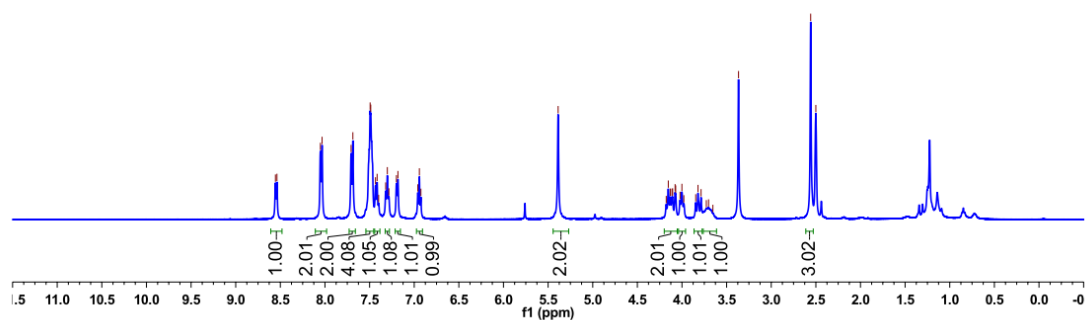
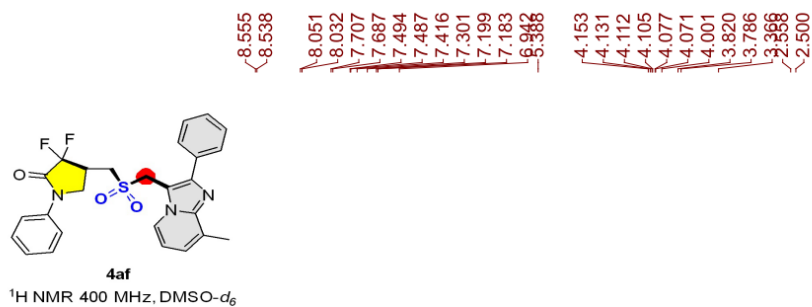


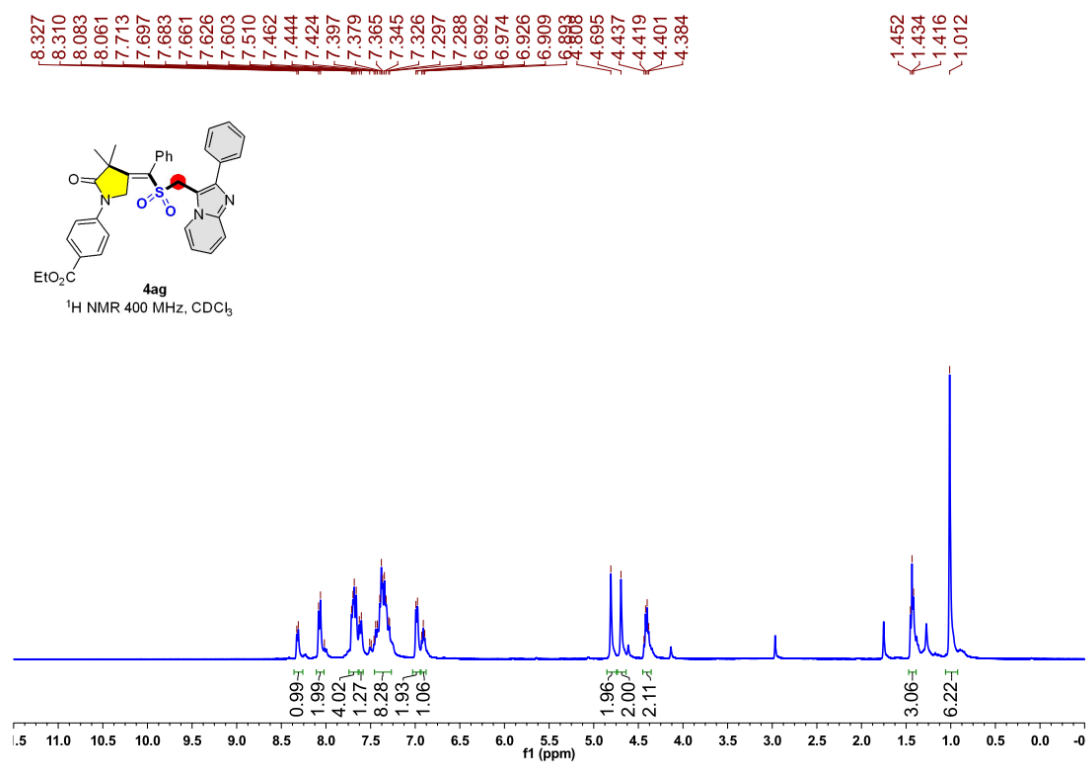
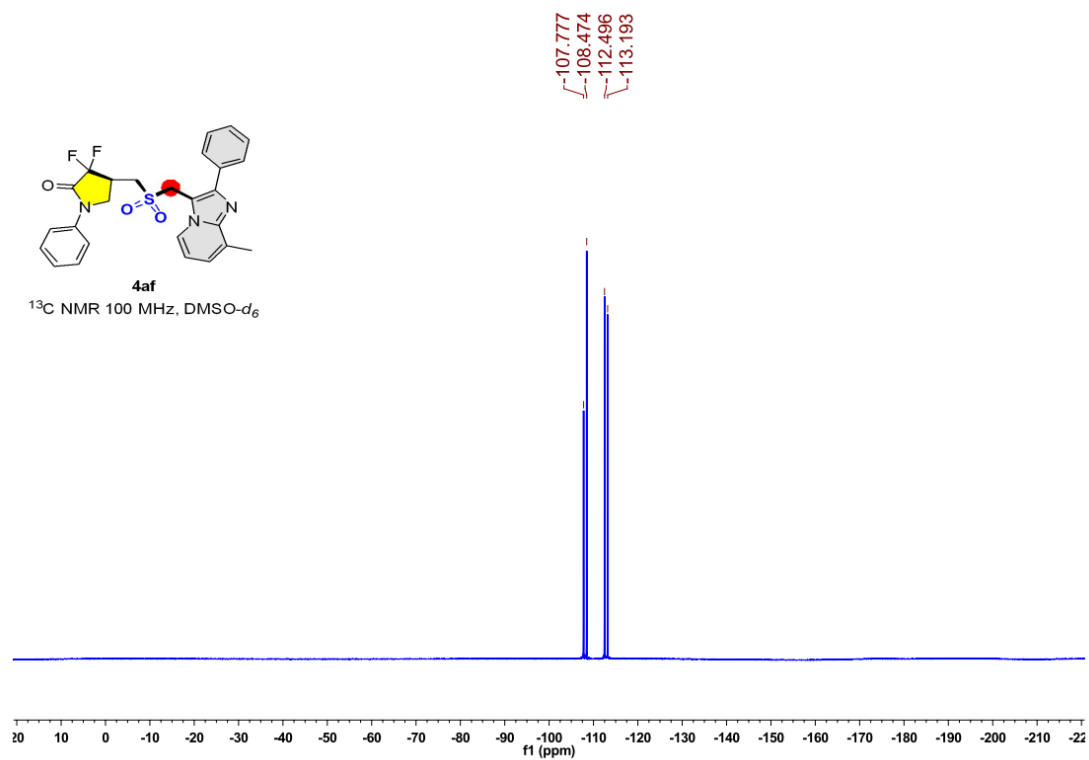


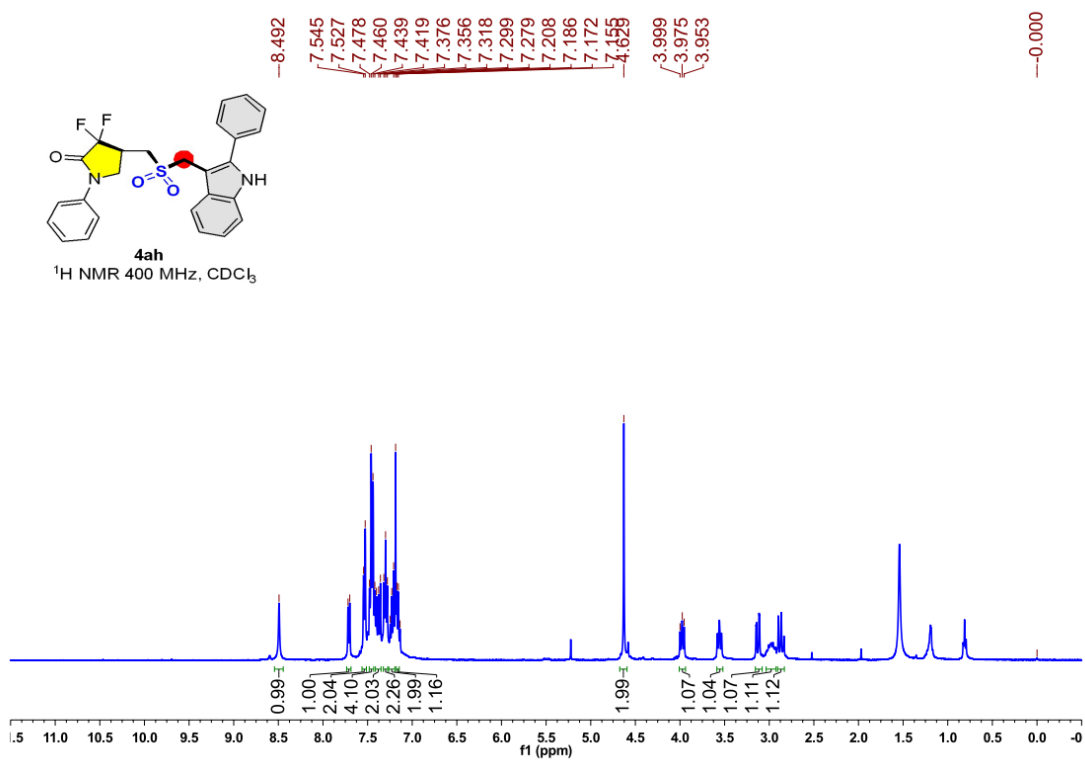
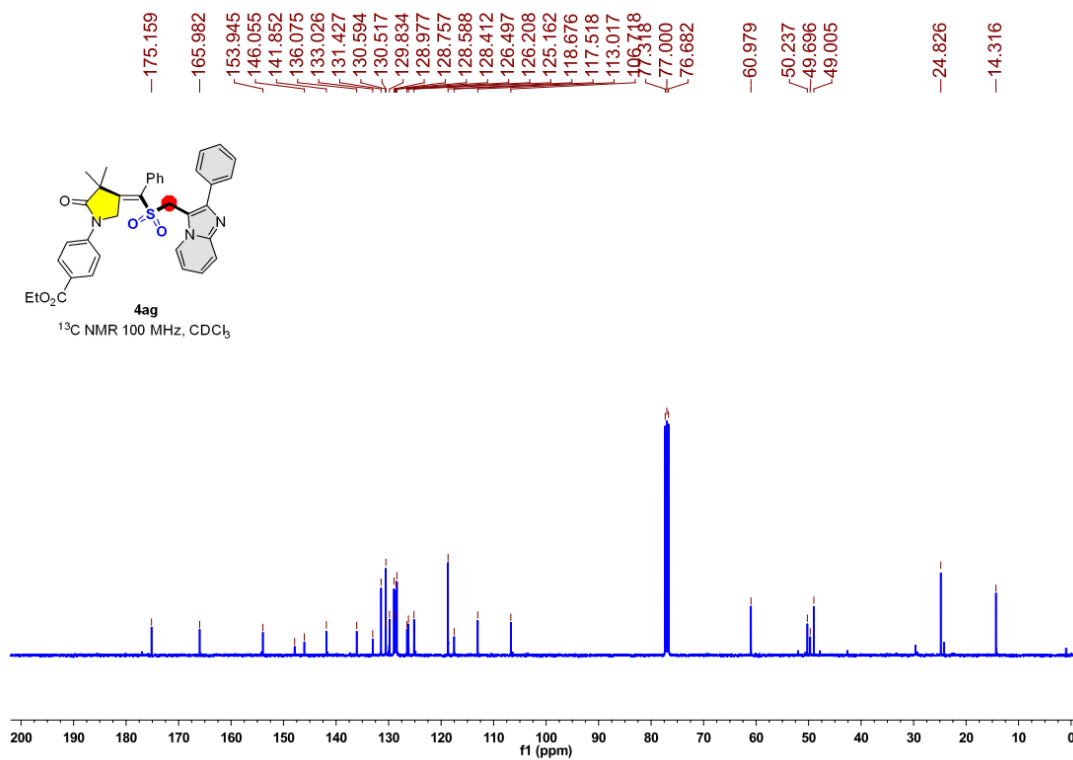


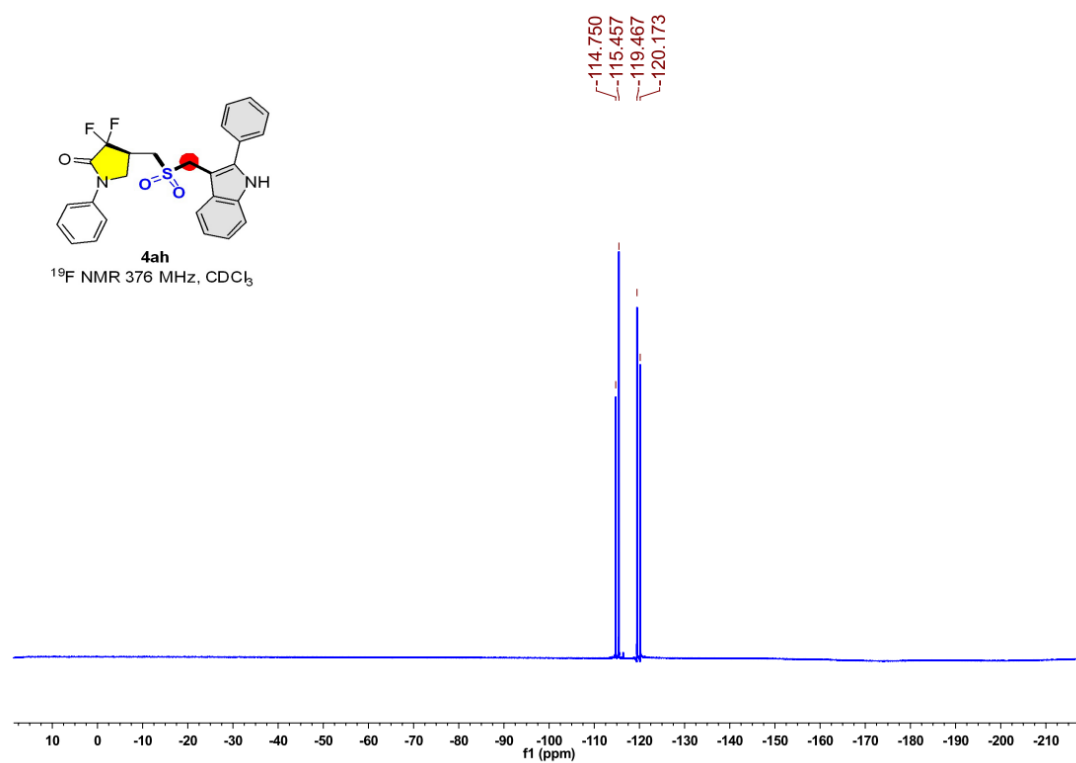
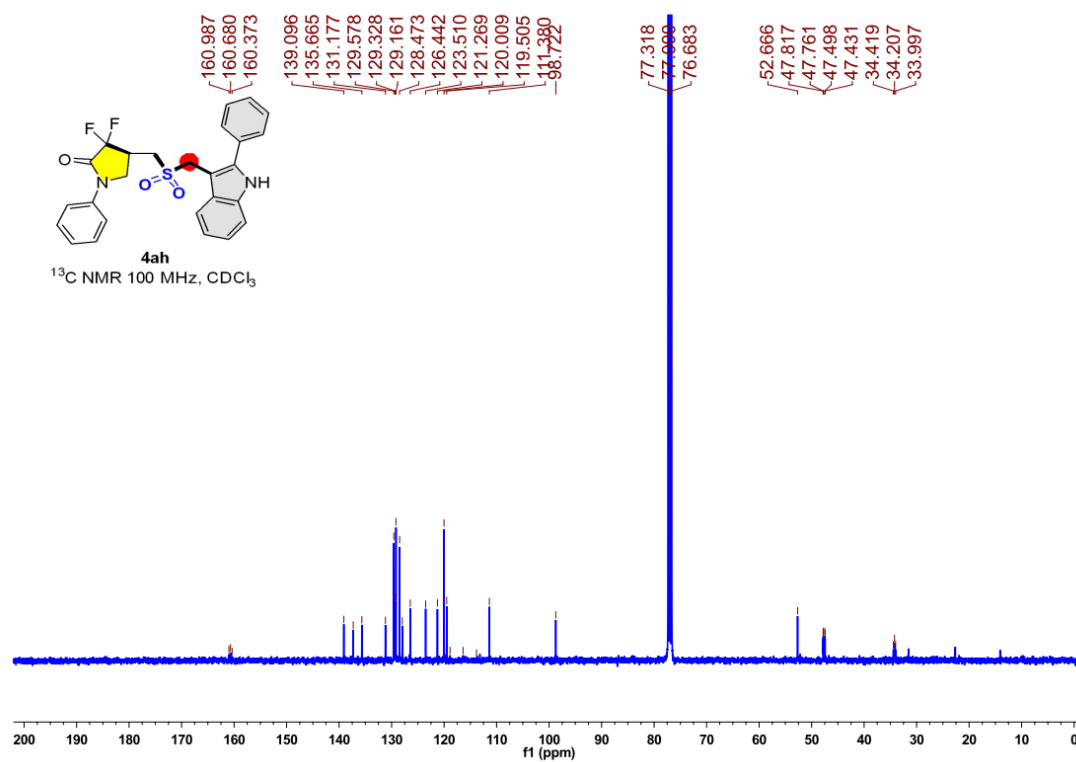


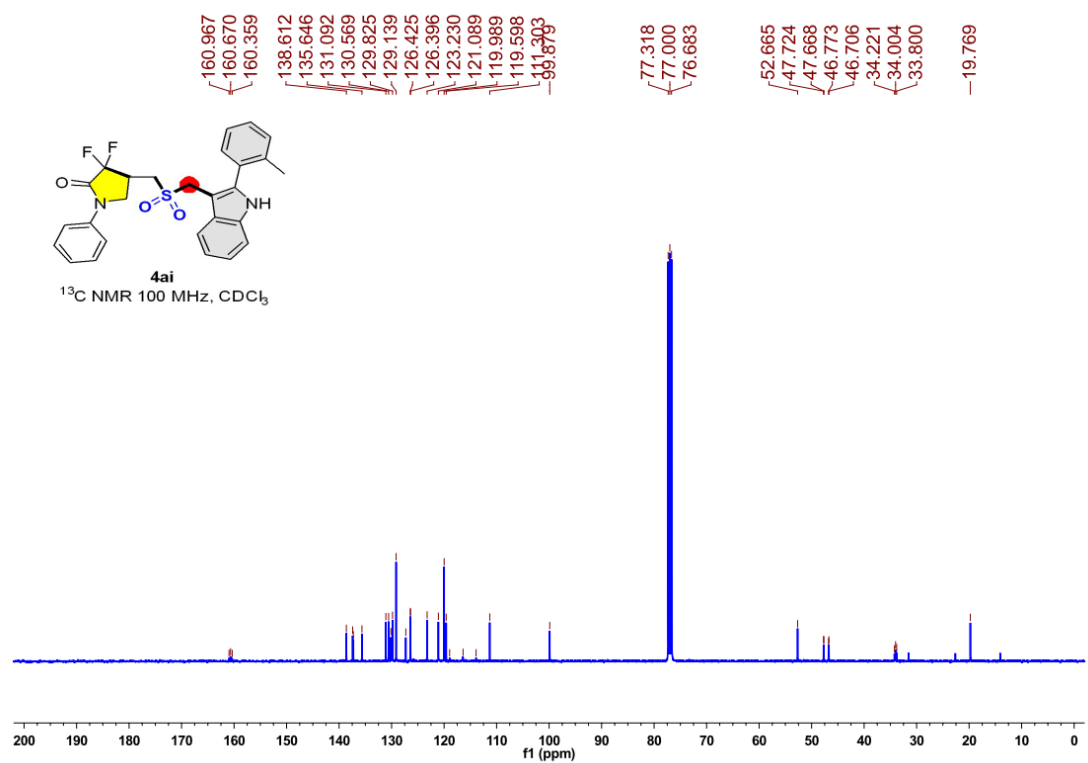
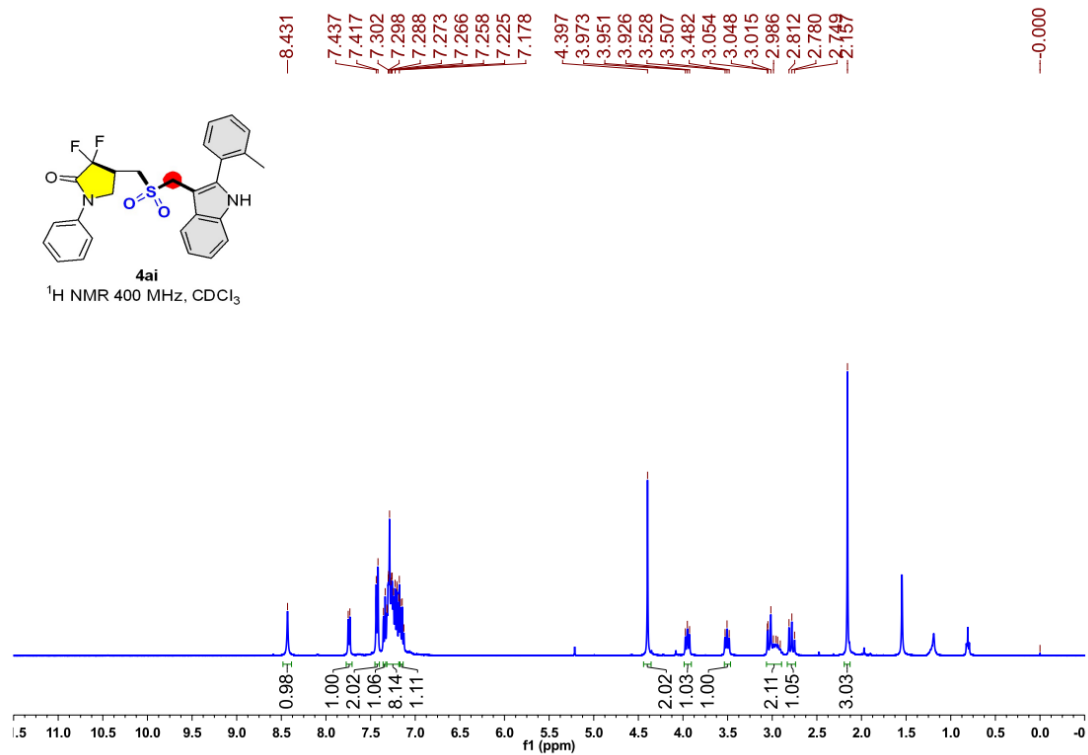


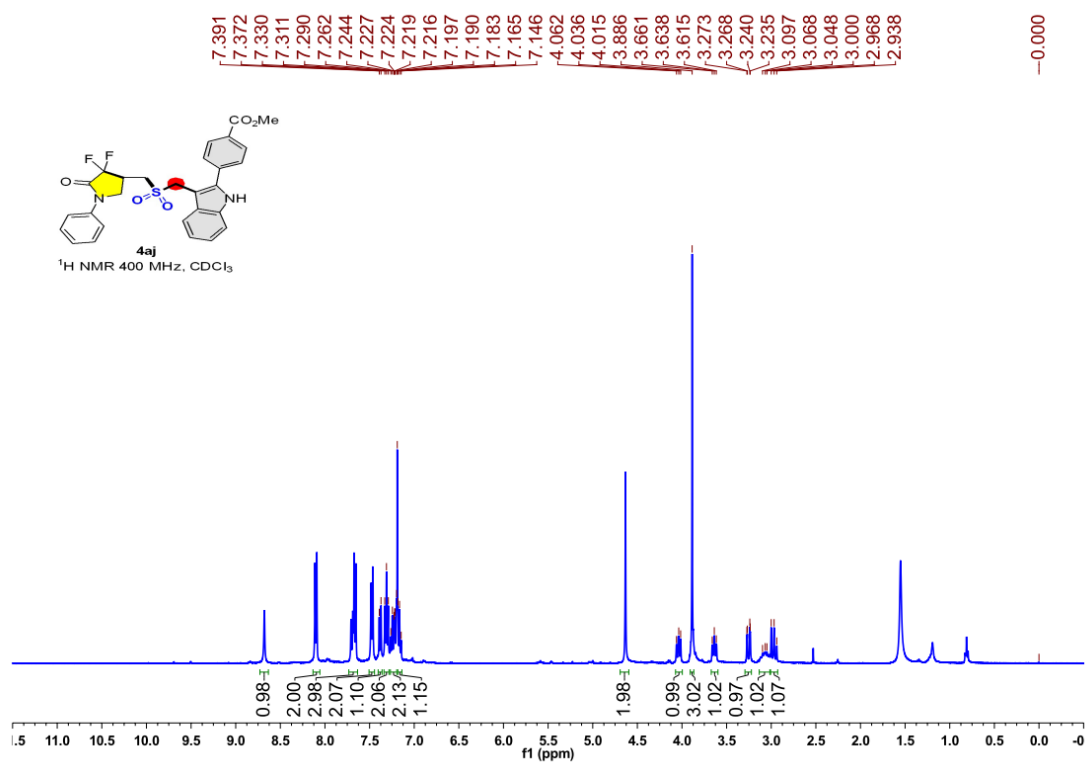
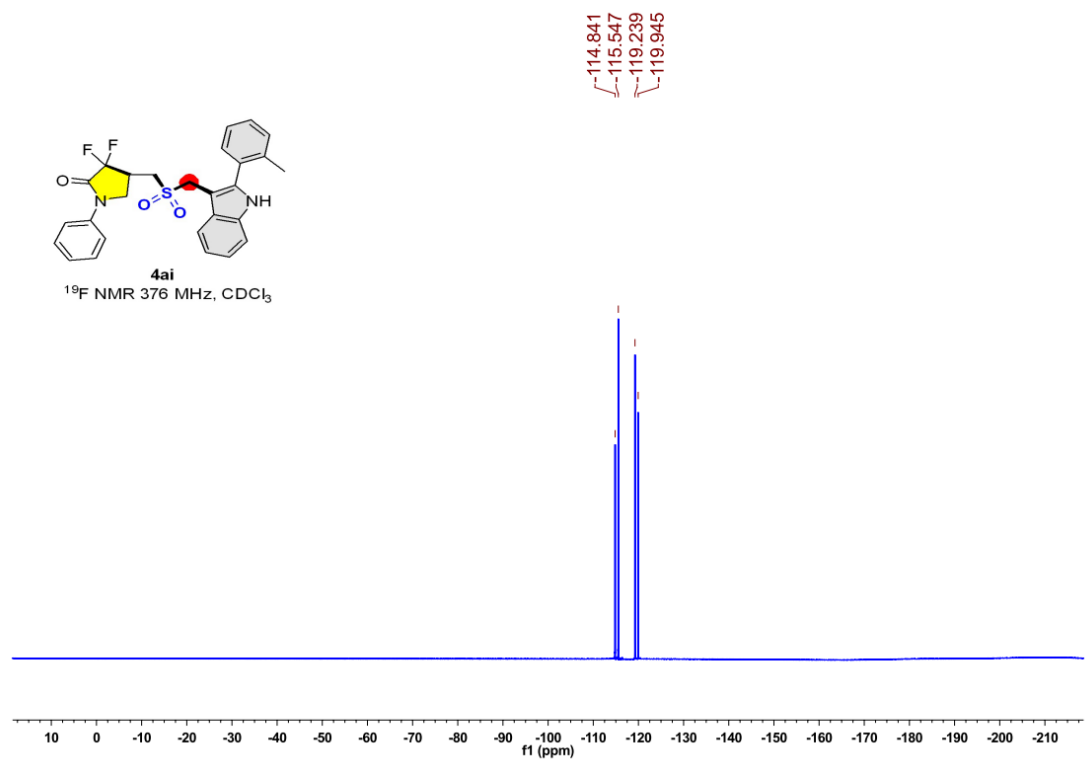


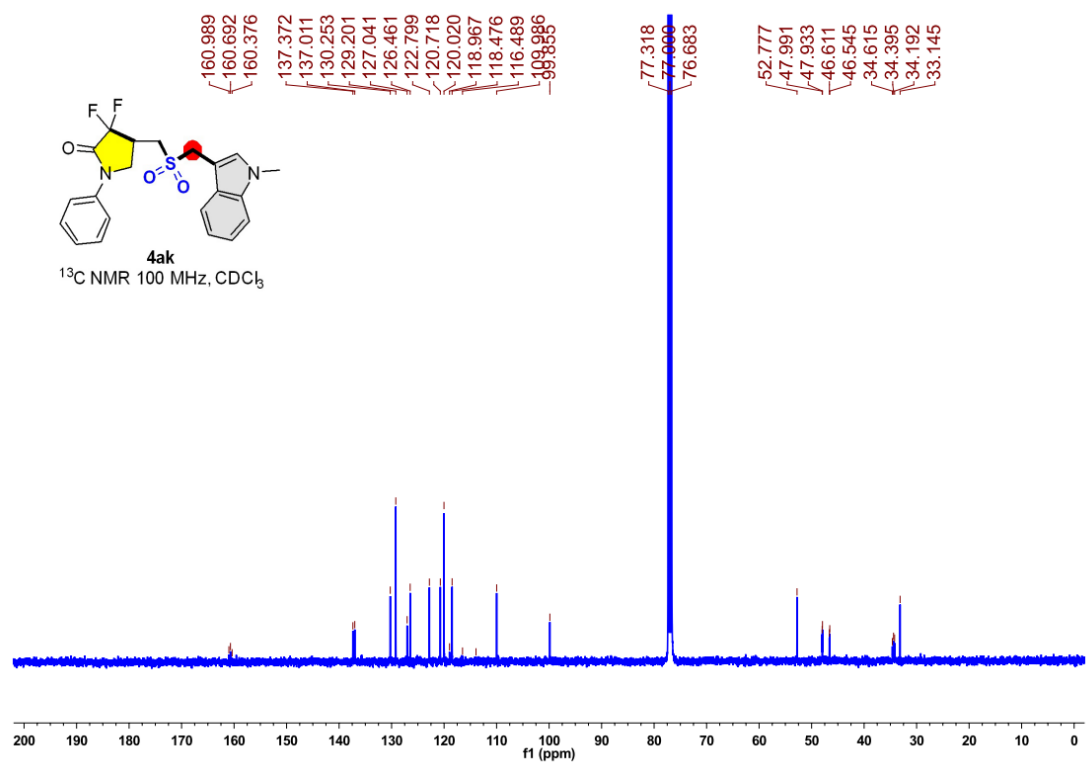
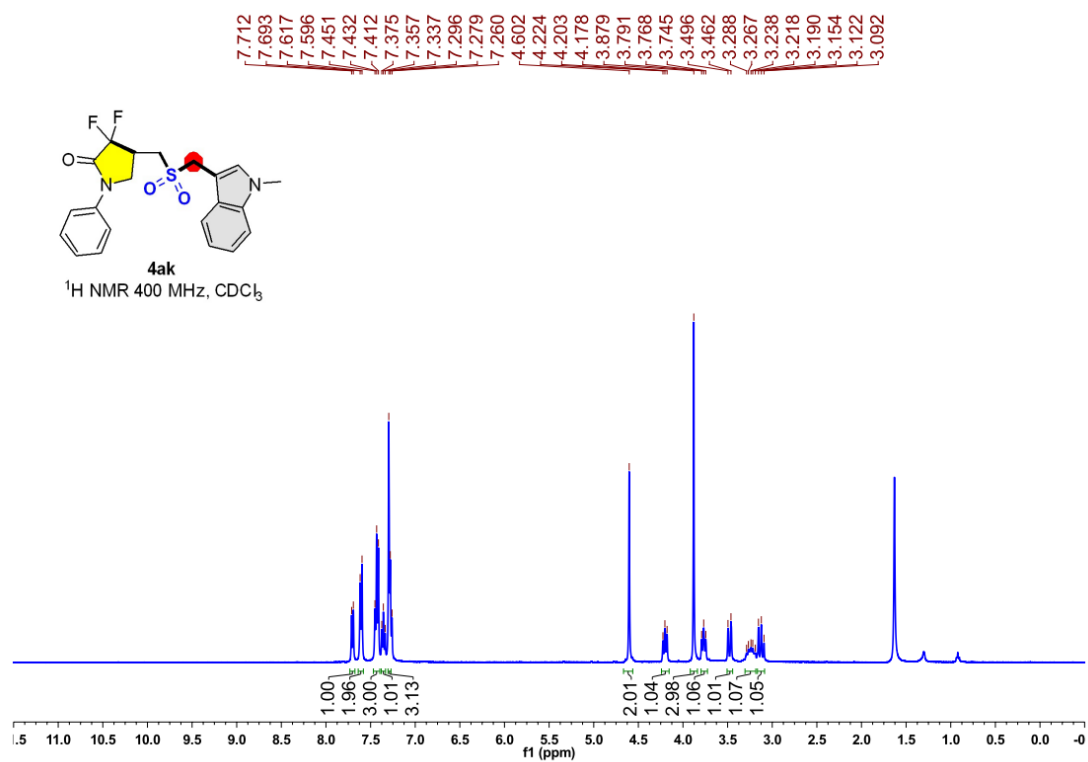


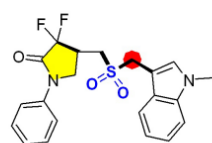








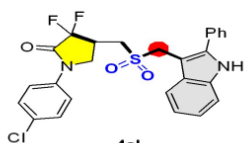
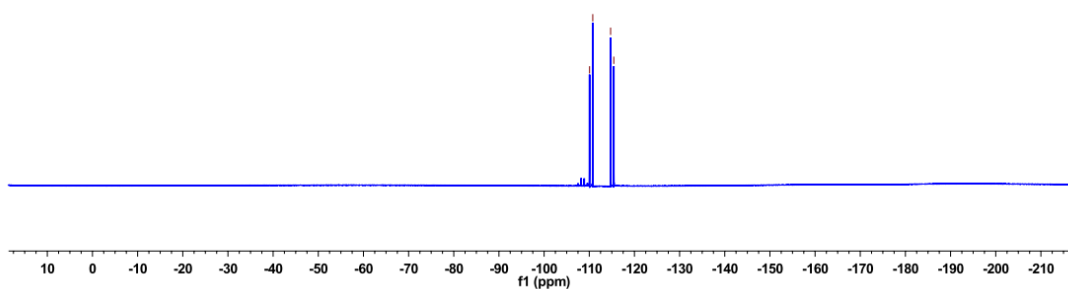




4ak

^{19}F NMR 376 MHz, CDCl_3

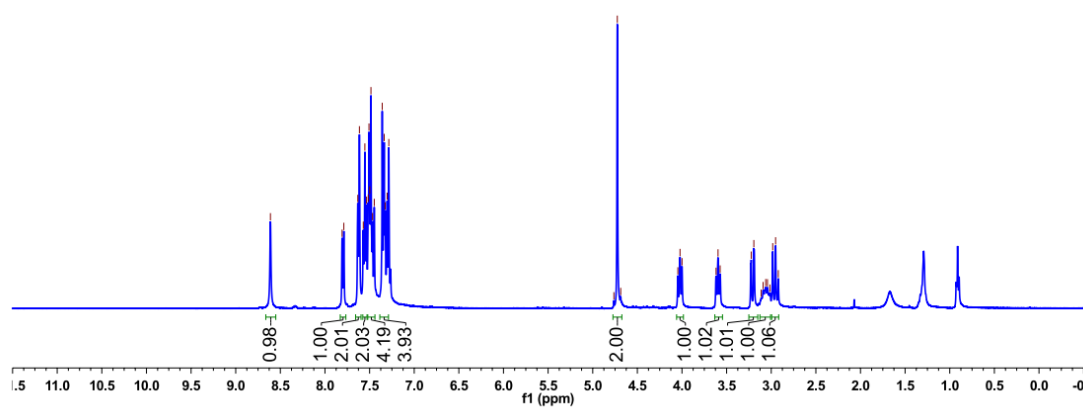
~110.067
~110.773
~114.725
~115.431

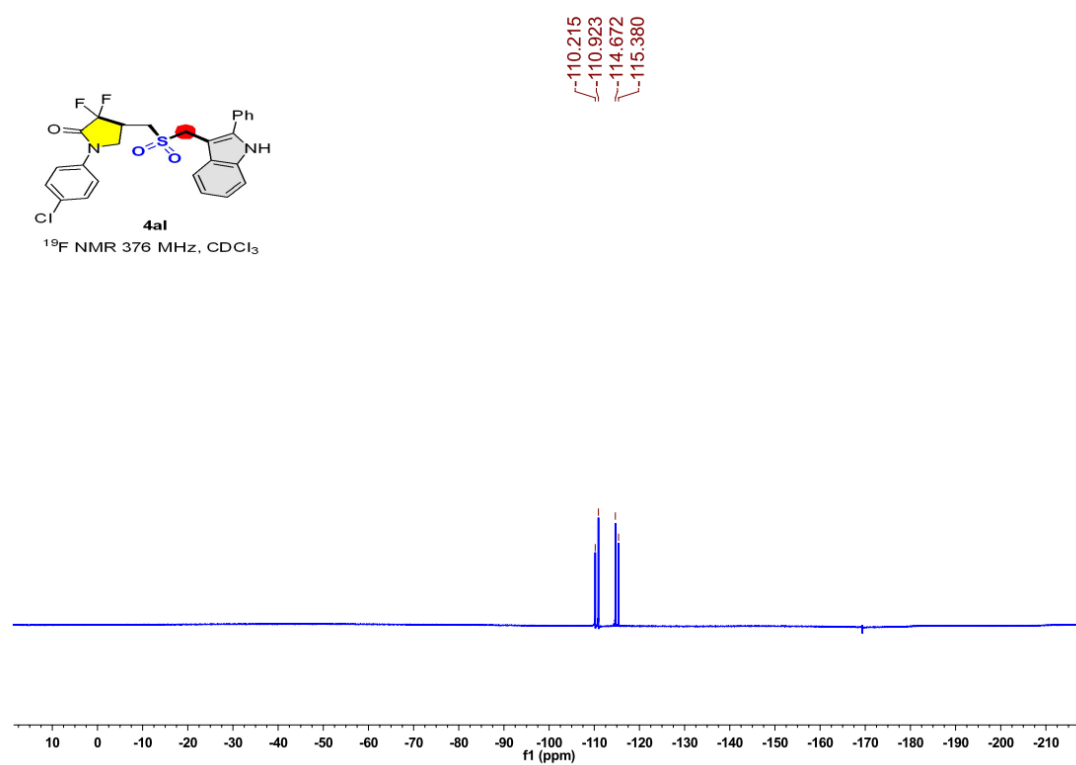
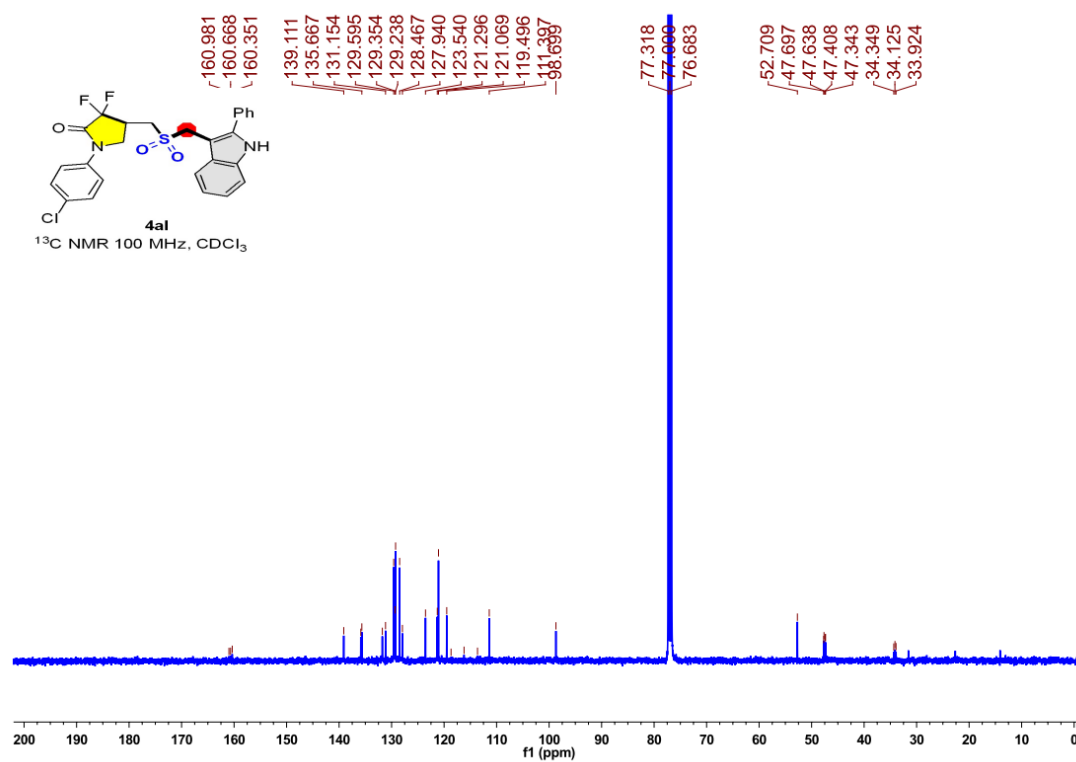


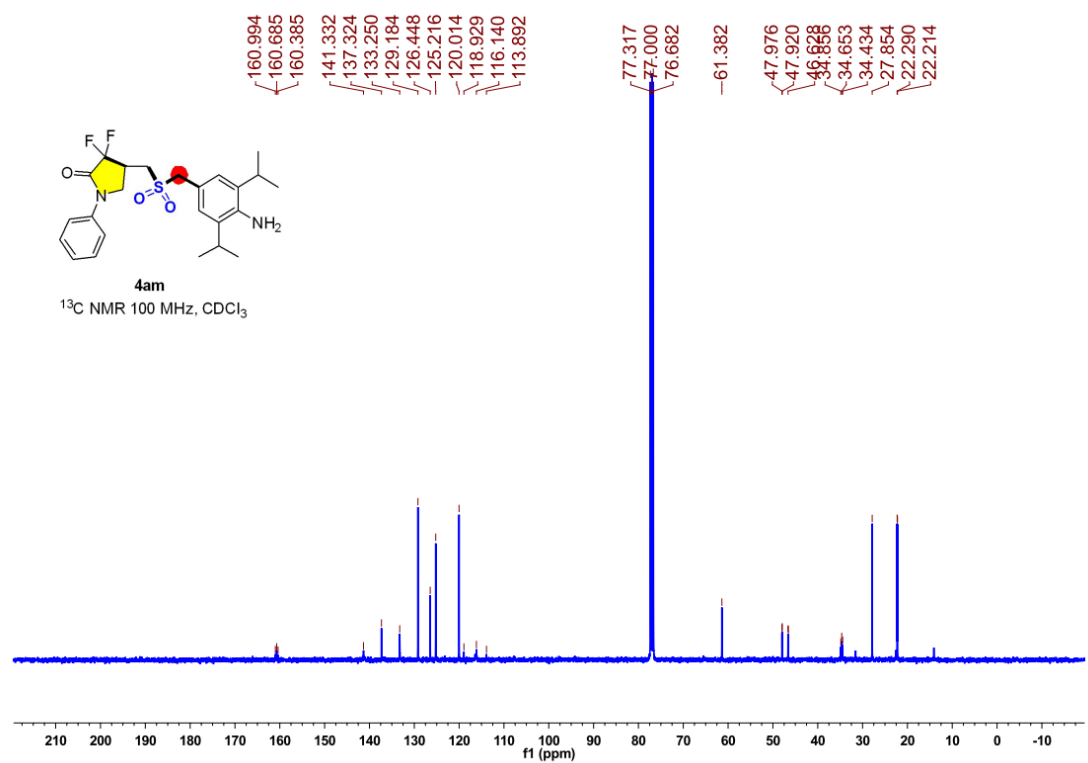
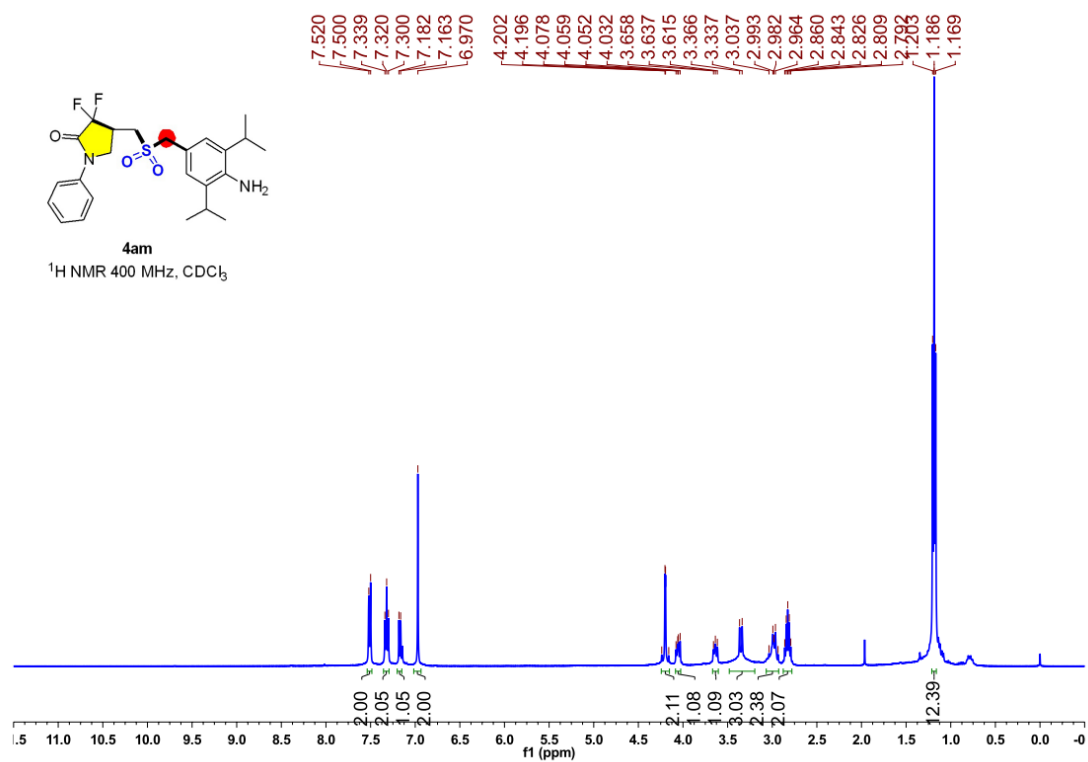
4al

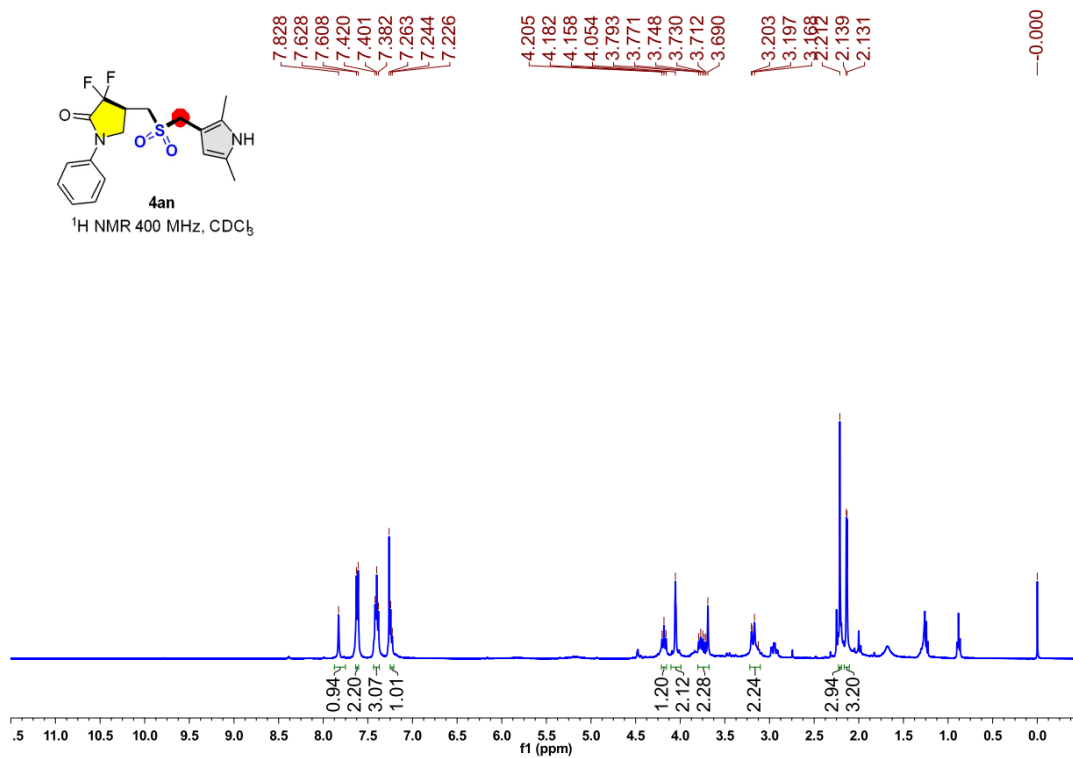
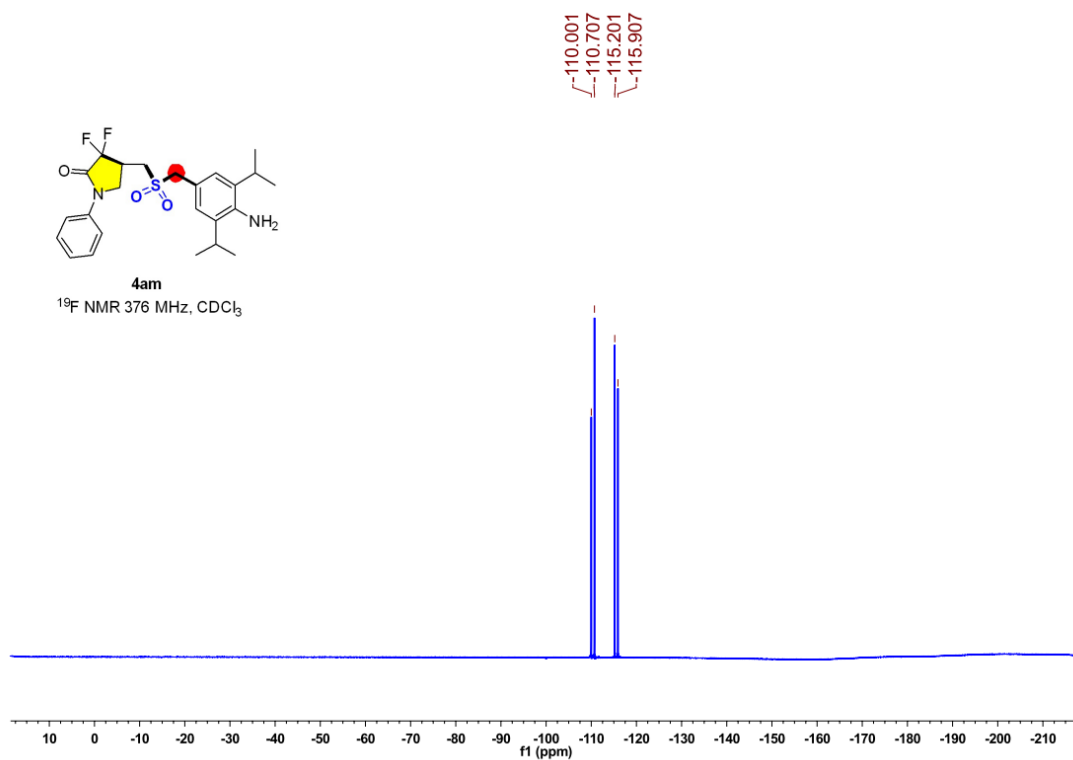
^1H NMR 400 MHz, CDCl_3

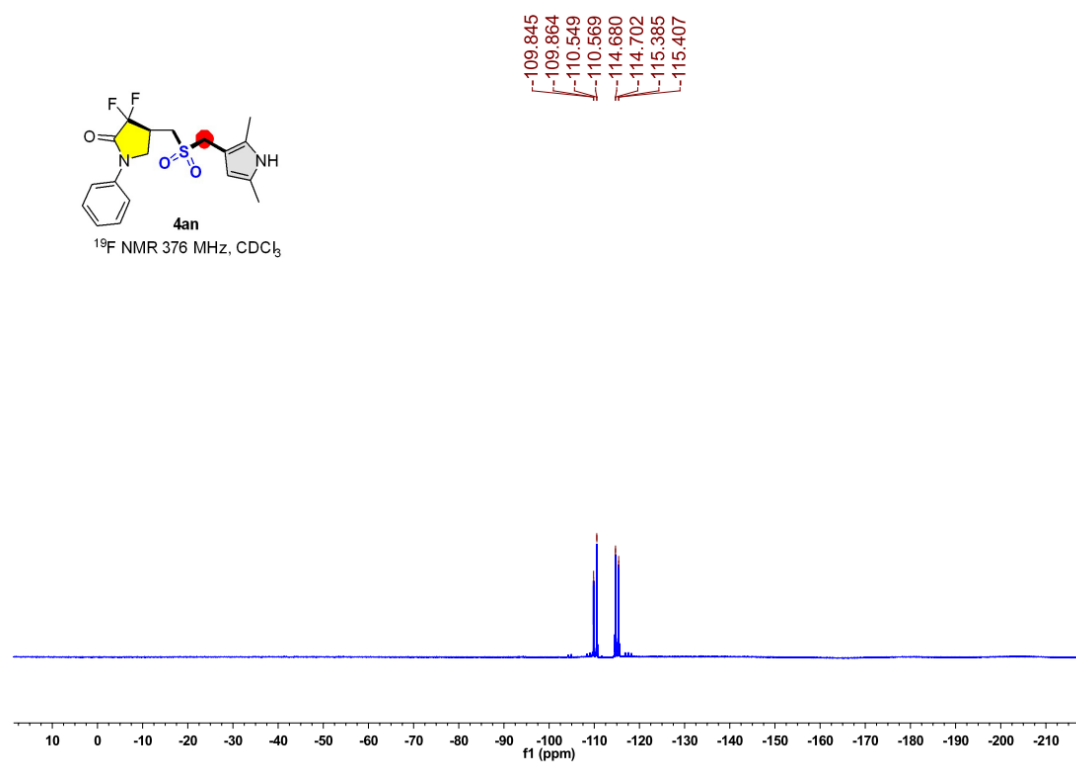
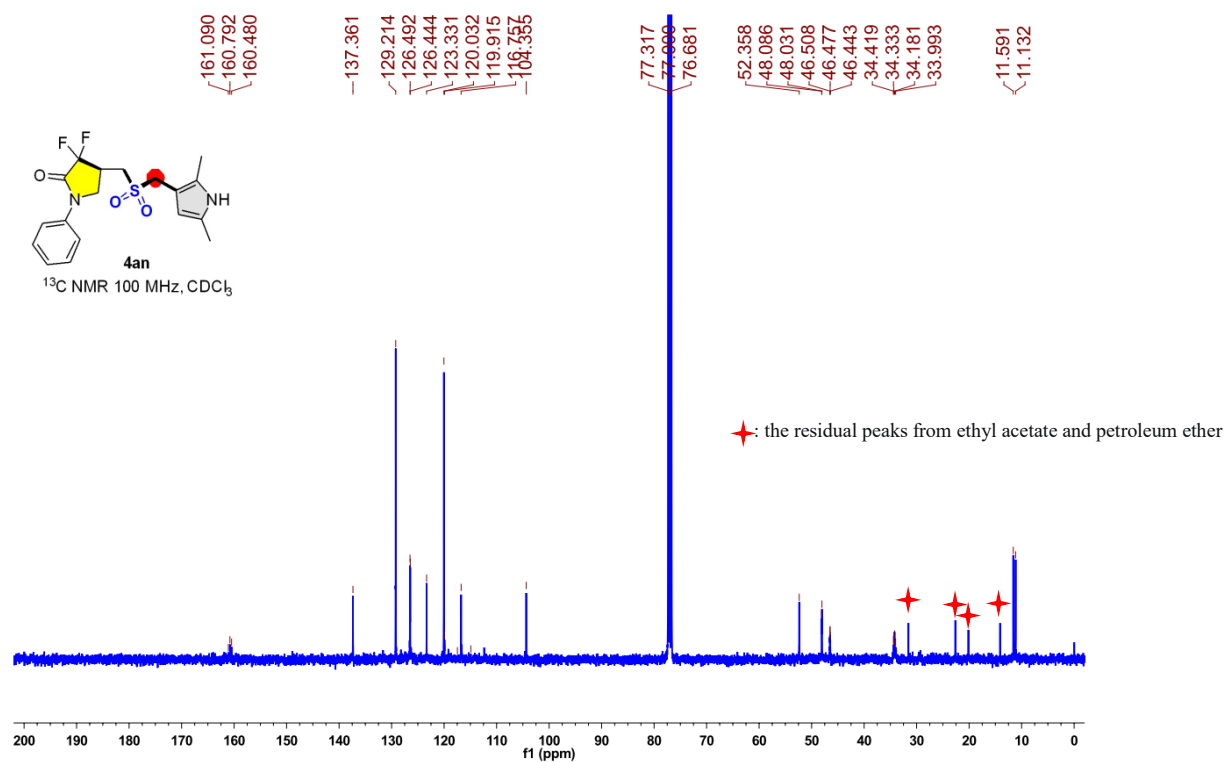
8.611
7.632
7.614
7.553
7.534
7.515
7.507
7.499
7.485
7.448
7.358
7.337
7.326
7.303
7.285
7.265
4.725
4.686
4.046
4.022
4.000
3.618
3.596
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3.113
3.091
3.062
3.042
3.015
2.983
2.951
2.921

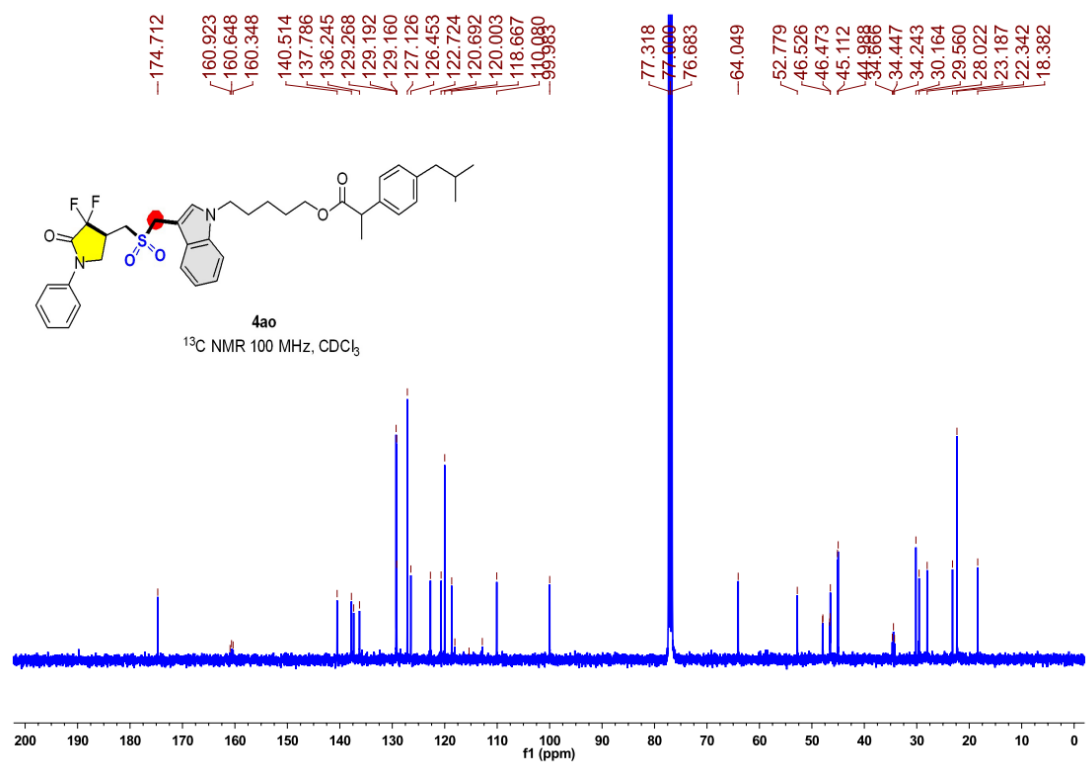
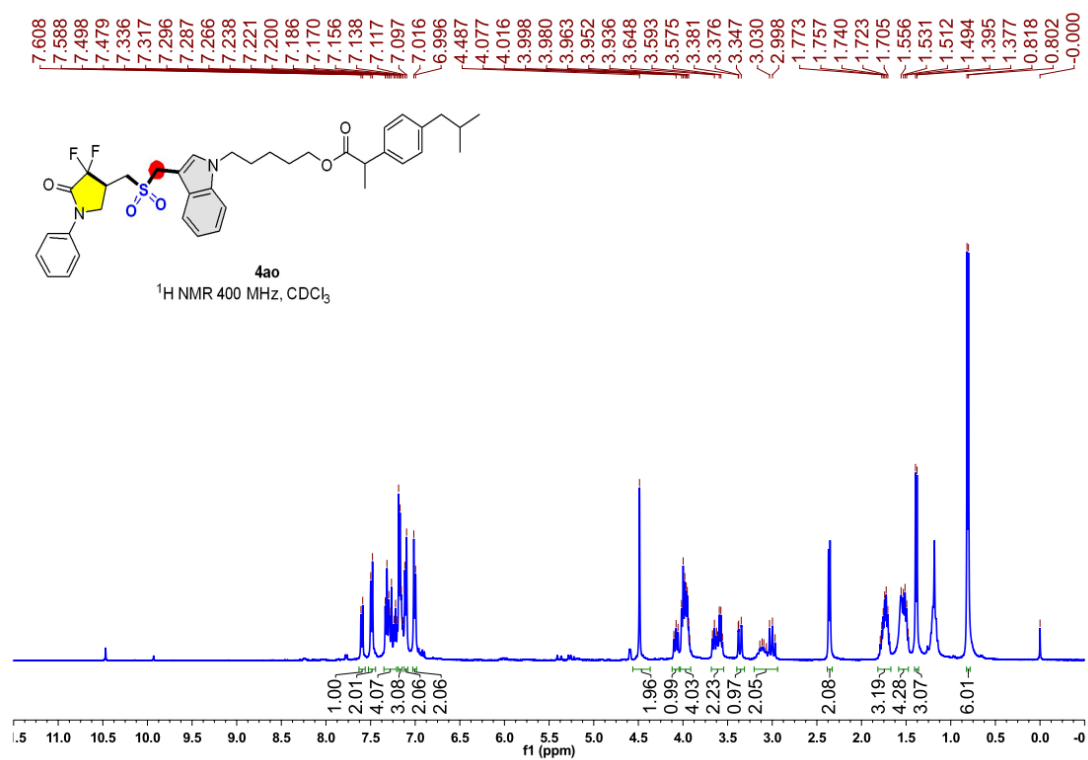


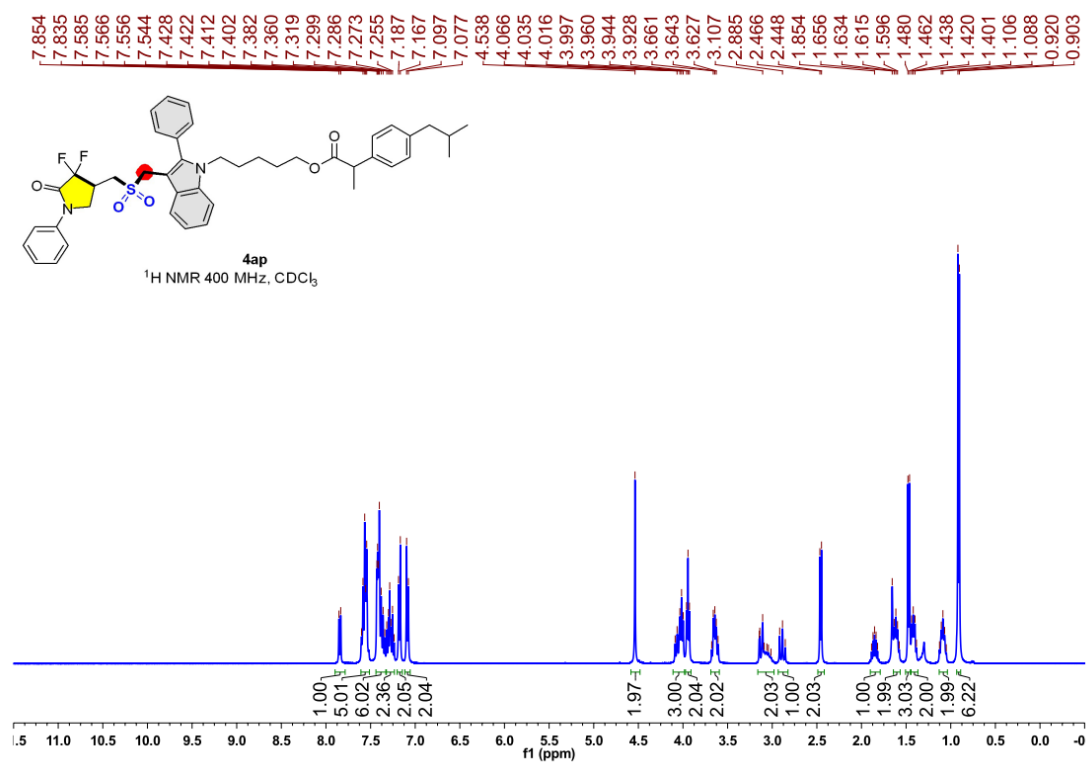
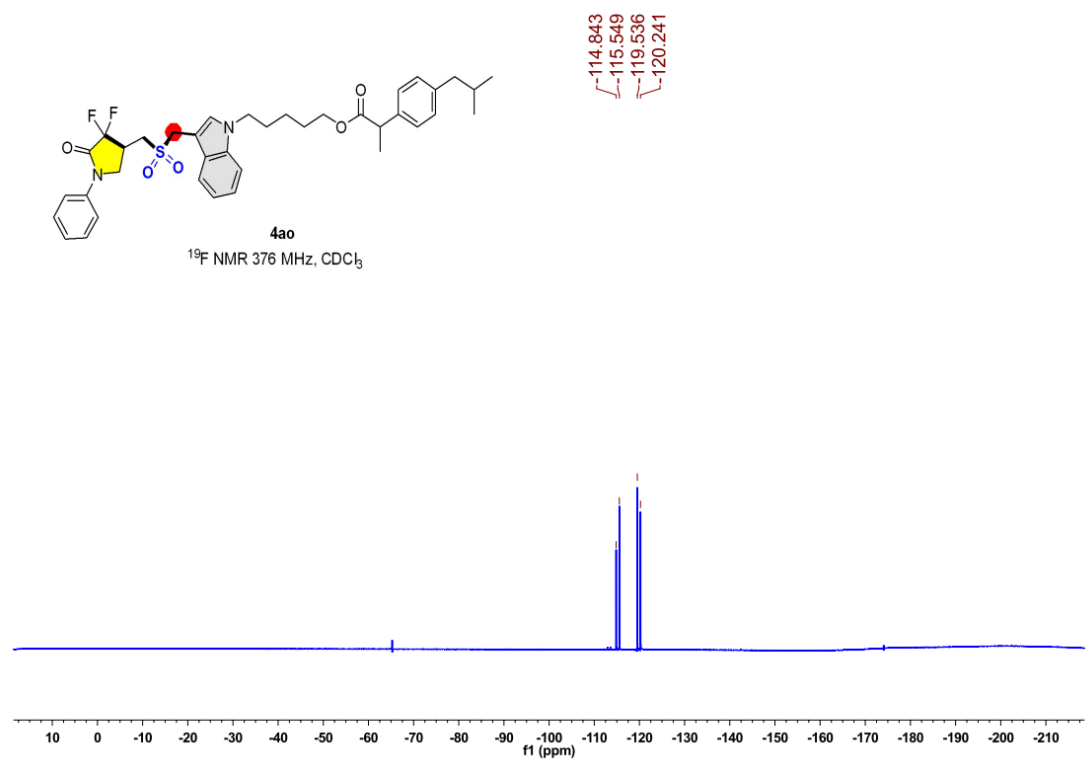


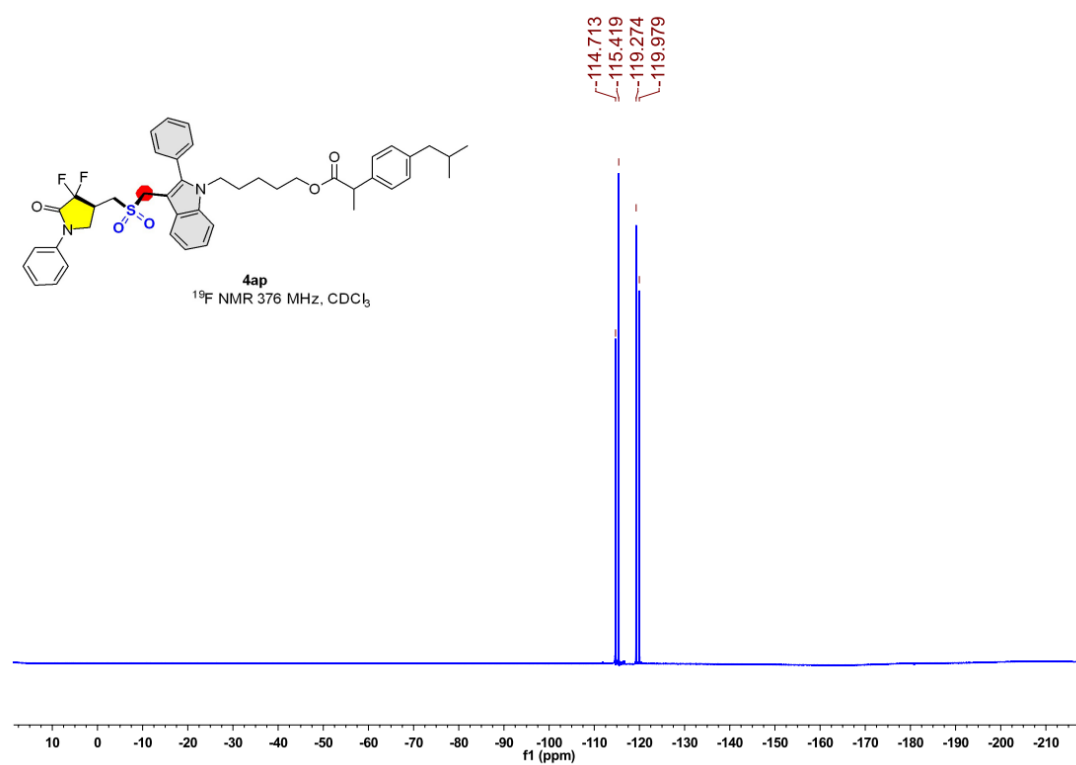
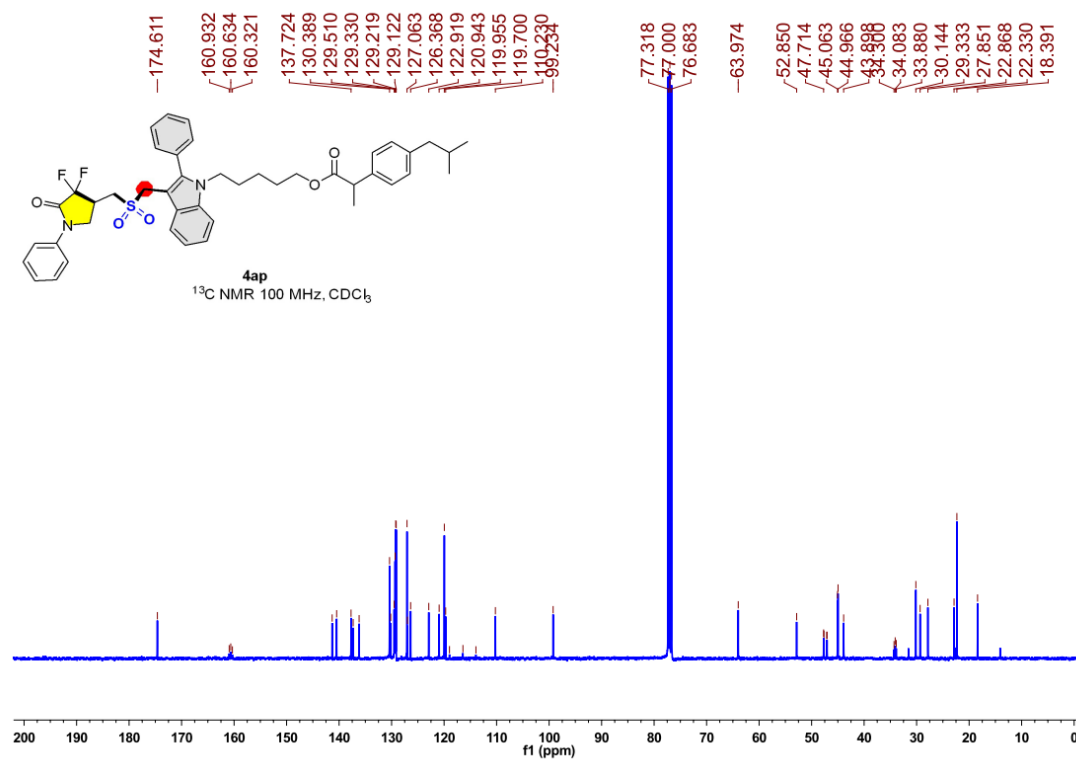


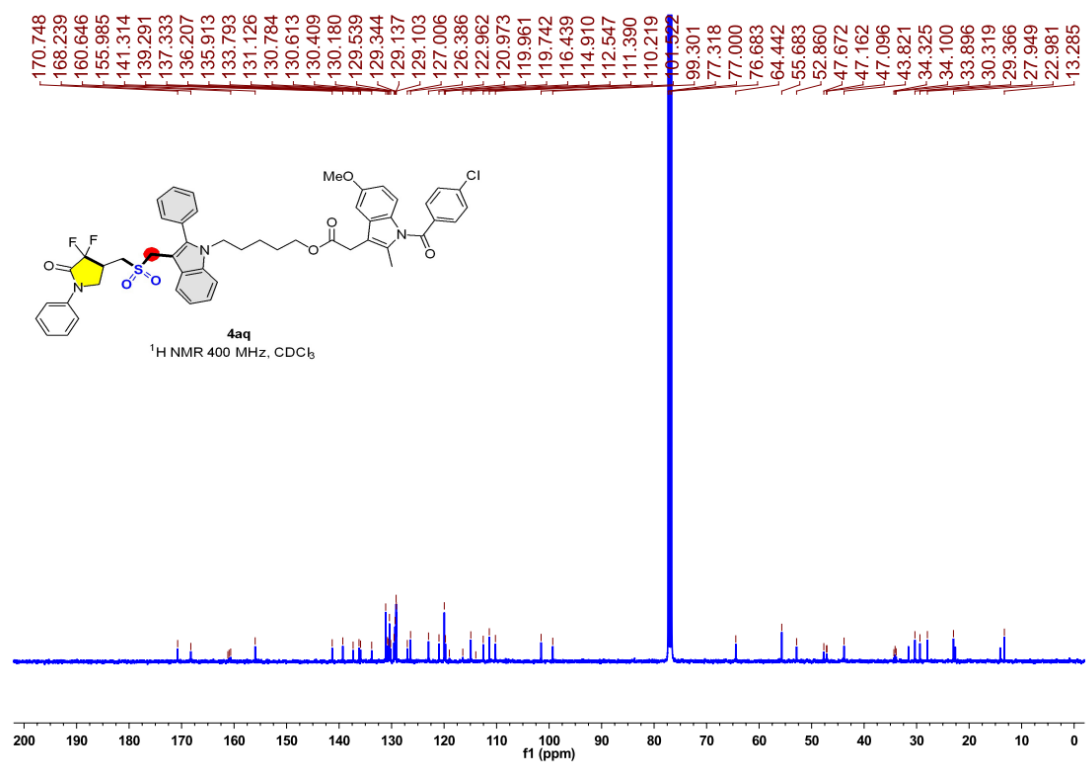
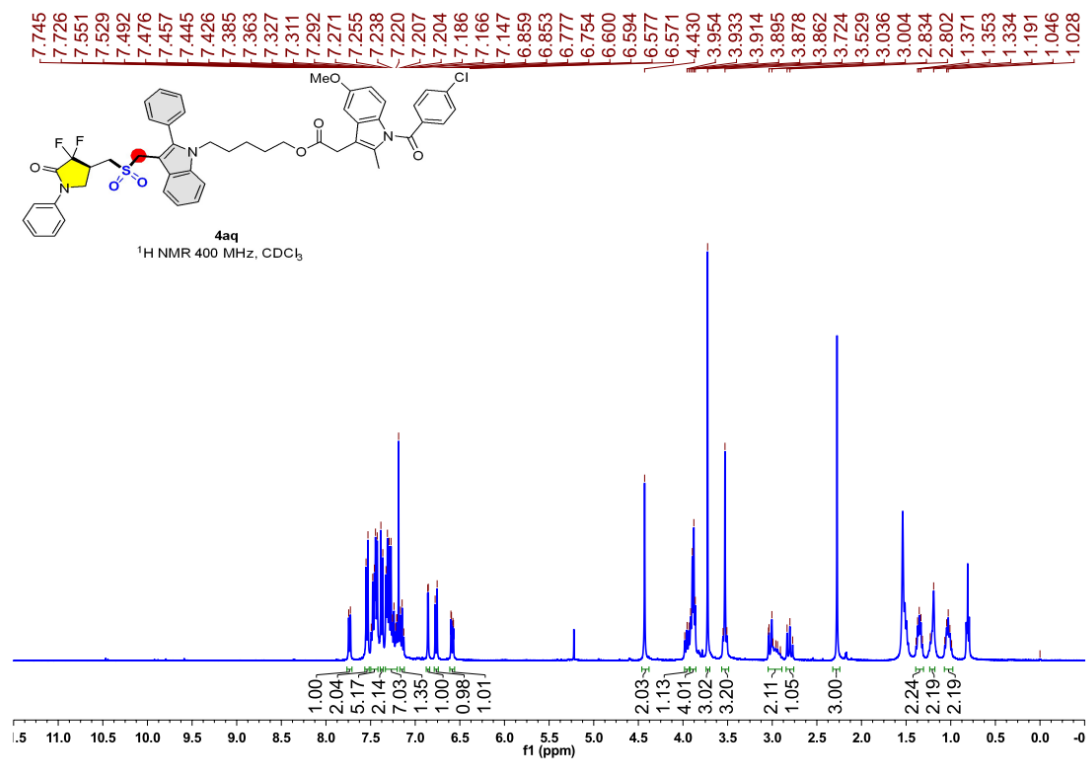


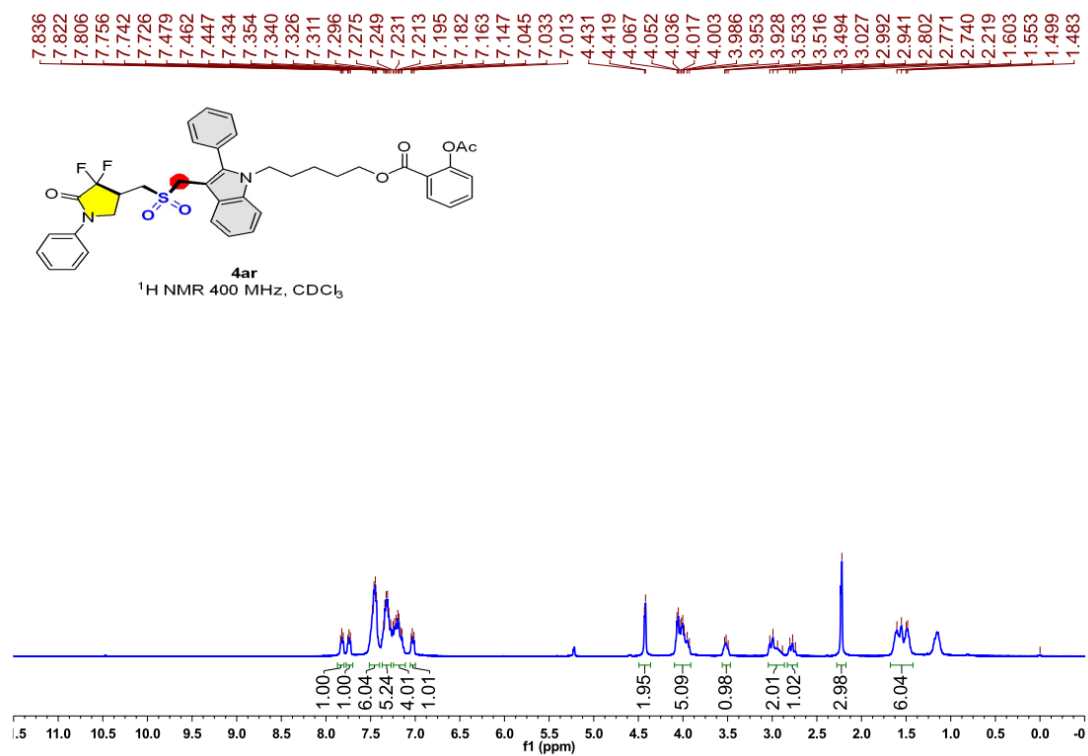
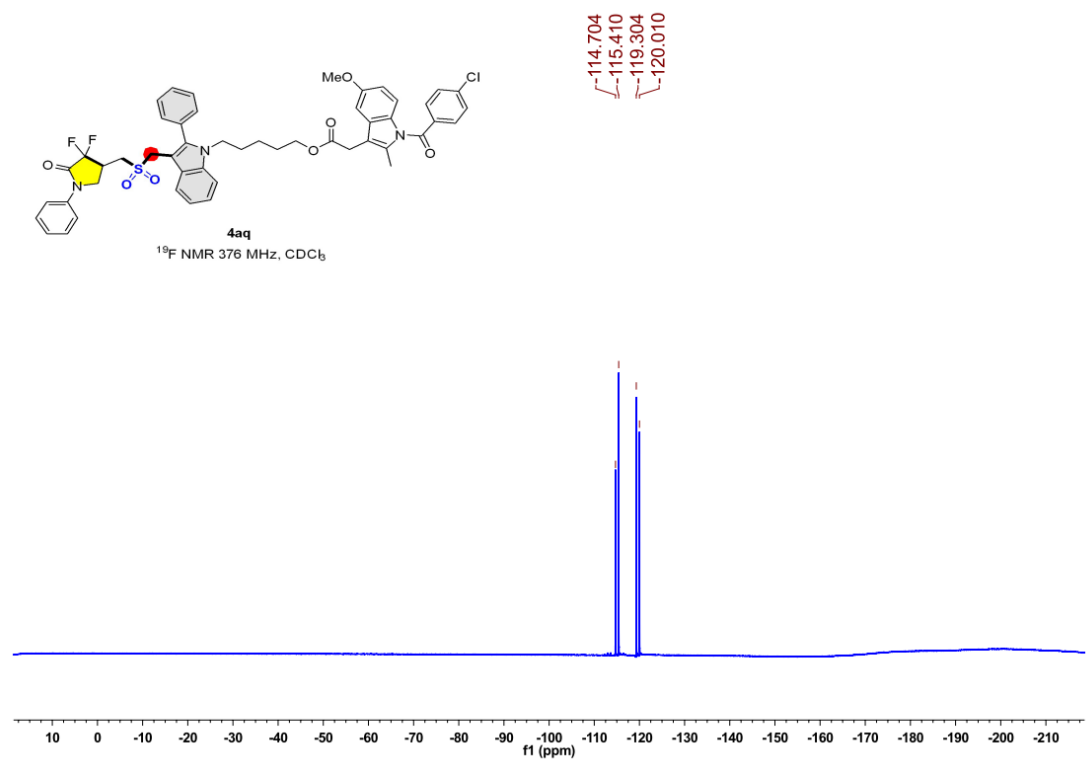


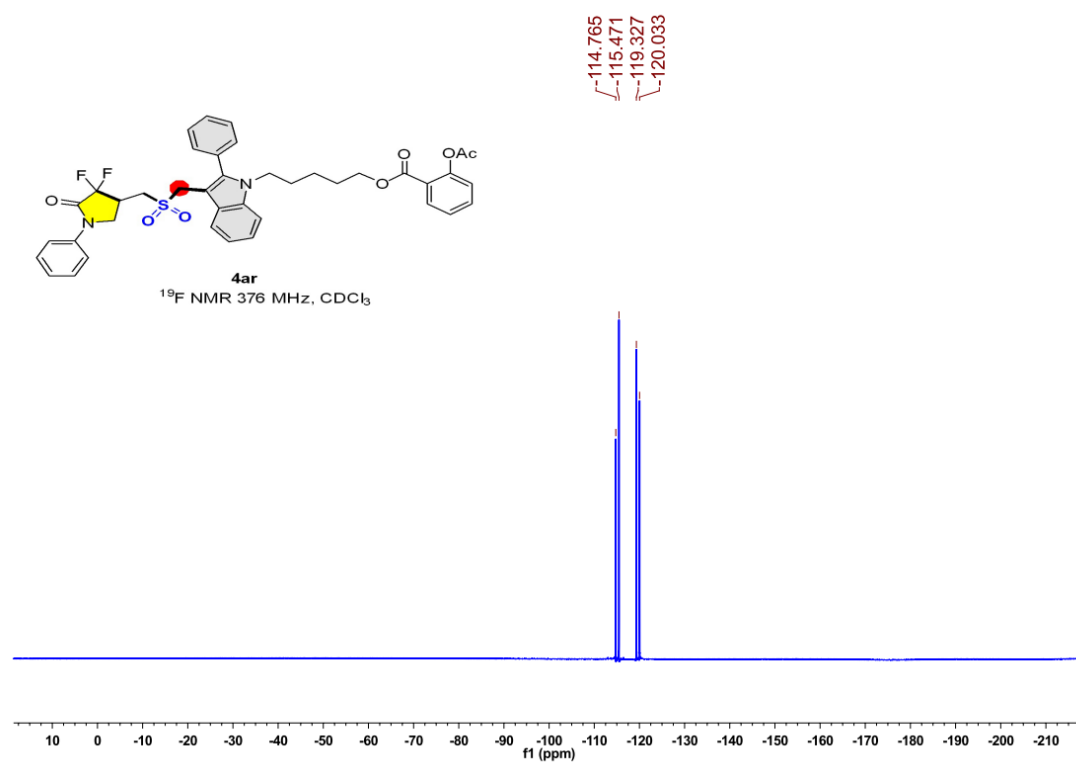
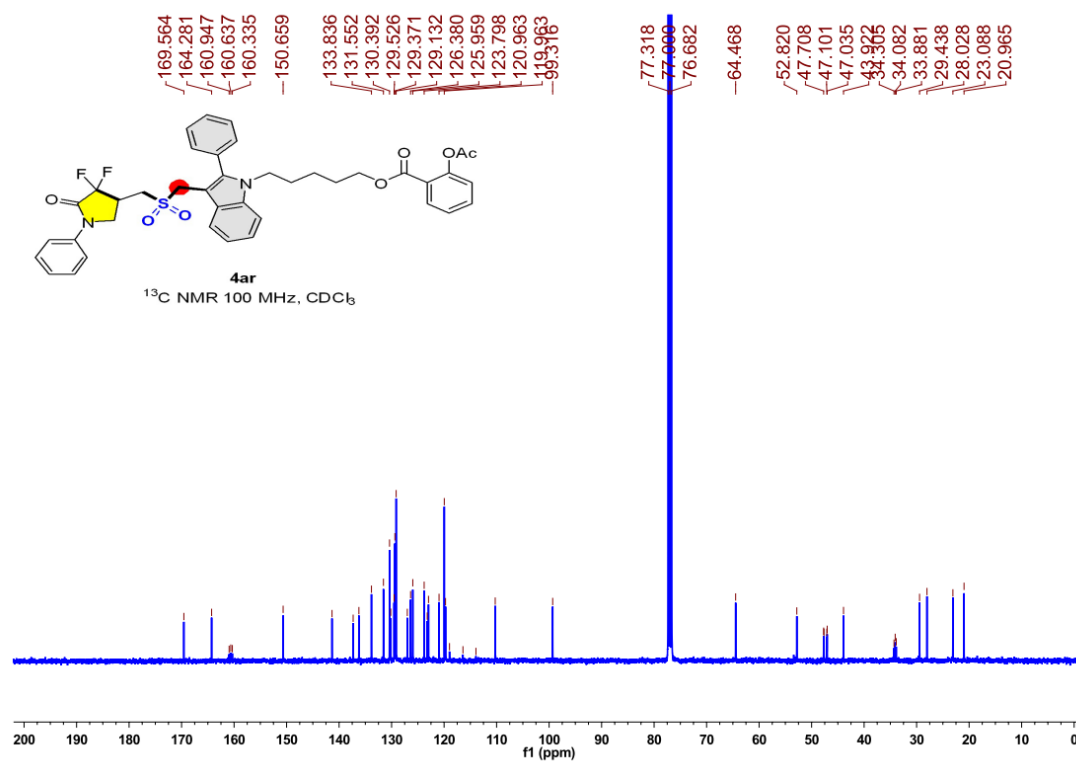












7. References

1. (a) N. N. Dai, Y. J. Lu, Z. Q. Wu, Y. Zhou, Y. Tong, K. Tang, Q. Li, J. Q. Zhang, Y. Liu and W. T. Wei, *Org. Lett.*, 2024, **26**, 3014–3019. (b) W. Lin, Y. Wang, J. Zou, Y. Zhao, J. Wang and X. Liu, *Adv. Synth. Catal.*, 2020, **362**, 5009–5013.
2. A. K. Bagdi, M. Rahman, S. Santra, A. Majee and A. Hajra, *Adv. Synth. Catal.*, 2013, **355**, 1741–1747.