

A Catalyst Facile Synthesis of 2-(dihydropyridyl)benzothiazoles from (Benzothiazol-2-yl)acrylonitriles: A Green Route

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Supporting Information (SI)

Table of Contents

1. General Information	S2
2. Preparation of Substrates	S2
3. General Procedure for 2-(Benzo[<i>d</i>]thiazol-2-yl)acrylonitriles 1	S3
4. General Procedure for Preparation of Cyclic 1,1-enediamines 2	S4
5. Procedure for Optimisation of Reaction Conditions for Synthesis of 3a	S6
6. General Procedure for Catalyst-Free [3+3] Annulation of Benzothiazole-Based Acceptors with Cyclic 1,1-enediamines (<i>GP1</i>)	S8
7. Procedure for Optimization of Reaction Conditions for the Synthesis of 6	S9
8. General Procedure for Synthesis of <i>N</i> -benzyl imidazo[1,2- <i>a</i>]pyridine-benzothiazole hybrids (<i>GP2</i>)	S10
9. Spectroscopic Data of Compounds	S10
10. Gram-scale Synthesis	S31
11. One-pot Synthesis	S31
12. Control Experiments:	S32
13. Calculation of Green Matrix	S33
14. X-ray Crystallographic Analysis	S34
15. Optimised Structures and coordinated of optimised structure of Compounds 3a	S37
16. References	S39
17. Copies of NMR Spectra of Synthesized Compounds	S40

1. General Information

Unless specified, all reactions were performed in oven-dried glassware equipped with magnetic stir bar. Reagents and solvents were of analytical grade and used as received from AVRA, GLR, and BLD Pharma without further purification. Reaction progress was monitored using thin-layer chromatography (TLC) on 0.2 mm commercial silica gel 60 F₂₅₄ plates, with visualization under UV light. All compounds are fully characterized. ¹H NMR, ¹³C NMR, and ¹⁹F NMR spectra were recorded on a JEOL ECZ500R/S1 spectrometer operating at 500, 126, and 471 MHz, respectively, at room temperature. Chemical shifts (δ) are reported in parts per million (ppm) relative to the reference DMSO-*d*₆ ($\delta = 2.50$ for ¹H, $\delta = 39.52$ for ¹³C{¹H}) and TMS ($\delta = 0.00$ for ¹H). A residual signal at $\delta = 3.33$ ppm indicates moisture in DMSO-*d*₆. Multiplicities are given as s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), and m (multiplet), with coupling constants (*J*) reported in hertz (Hz). High-resolution mass spectra (HRMS) were obtained using a time-of-flight (TOF) mass spectrometer with electrospray ionization (ESI). Melting points were determined using a digital melting point apparatus. All reactions used a silicone oil bath as the heat source.

2. Preparation of Substrates

2.1 Substrates studied in this report

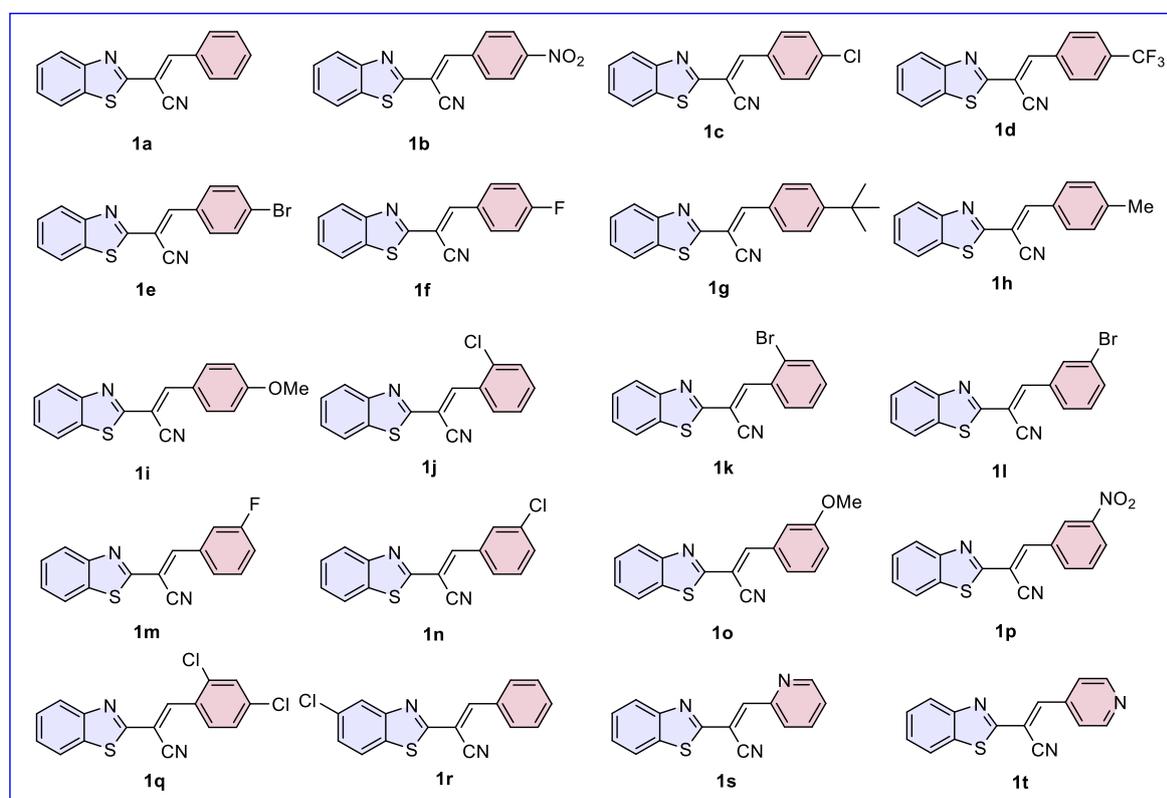


Figure S1. Representative examples of substrates **1**

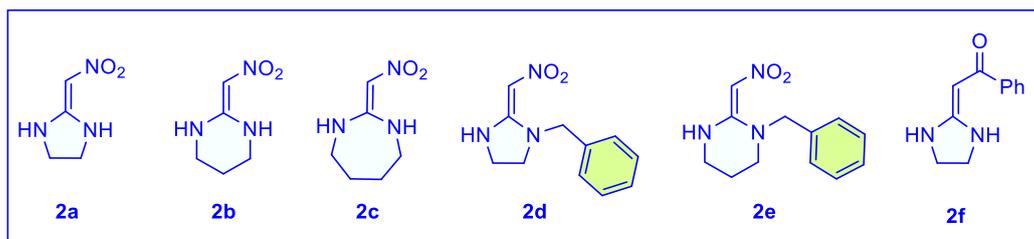


Figure S2. Representative examples of cyclic 1,1-enediamines **2a–2f**.

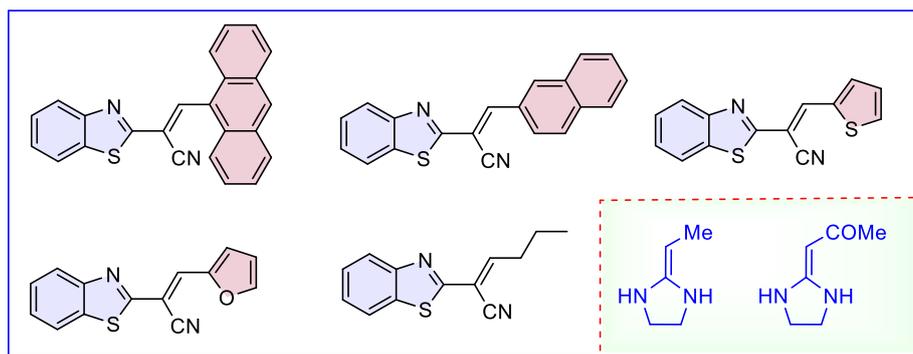
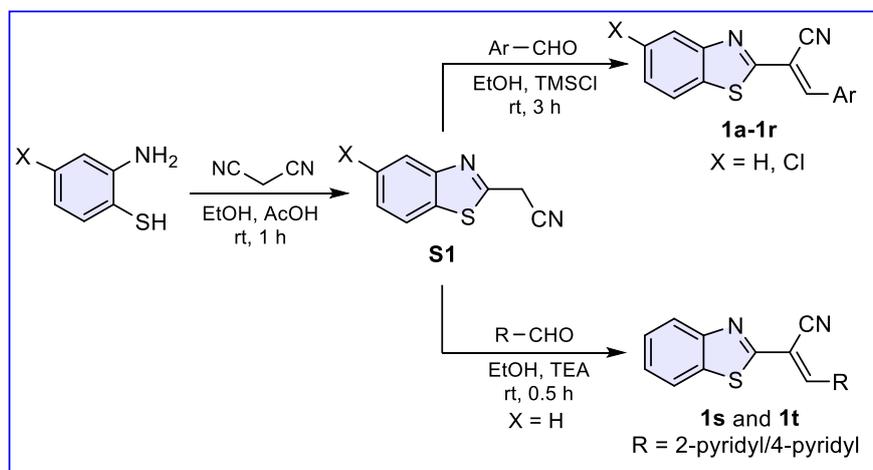


Figure S3. Unsuccessful substrates.

3. General Procedure for 2-(Benzo[*d*]thiazol-2-yl)acrylonitriles **1**



Scheme S1. Preparation of benzothiazole-based Michael acceptors **1**

Preparation of substrates 1a-1r¹

A mixture of 2-aminothiophenol (30 mmol), malononitrile (30 mmol), and acetic acid (30 mmol) in ethanol (50 mL) was stirred at room temperature for one hour. The resulting precipitate was filtered and recrystallized from ethanol, yielding benzothiazol-2-yl acetonitrile (**S1**). Next, a solution containing an aldehyde (5 mmol), benzothiazol-2-yl acetonitrile (**S1**) (5 mmol), and

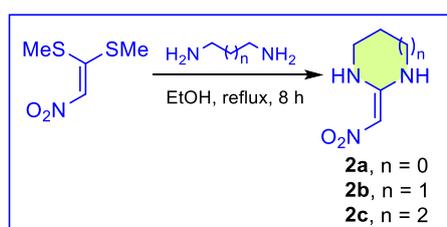
TMSCl (1.3 mL) in EtOH (10 mL) was stirred at room temperature for three hours. The precipitated solid was filtered and washed with isopropanol to obtain the products (**1a–1r**) as shown in Scheme S1.

Preparation of substrates **1s** and **1t**²

1s and **1t** were obtained by Knoevenagel condensation between equimolar amounts of 2-(benzo[*d*]thiazol-2-yl)acrylonitrile (**S1**) and hetaryl aldehydes, using ethanol as solvent and catalytic amounts of triethylamine (TEA), as shown in Scheme S1. The reaction was carried out with stirring at room temperature for a short duration. The adducts were obtained as brown solids with excellent purities and high yields. All the substrates **1** are listed in Figure S1.

4. General Procedure for Preparation of Cyclic 1,1-enediamines **2**

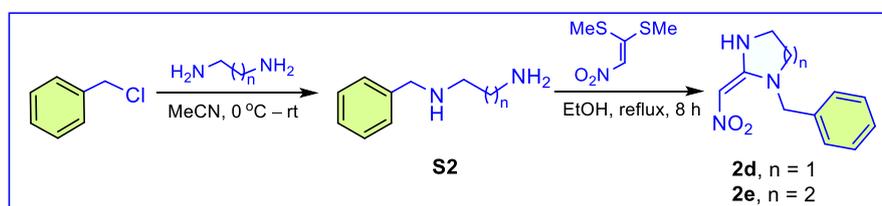
Preparation of **2a–2c**³



Scheme S2. Preparation of substrates **2a–2c**

A solution of (2-nitroethene-1,1-diyl)bis(methylsulfane) (1.65 g, 10 mmol) and diaminoalkane (12 mmol) in 40 mL of ethanol was stirred for approximately 8 h at reflux. After cooling to room temperature, the resulting product was obtained by filtration and collected as a white solid (**2a–2c**), yielding 80–85% (Scheme S2).

Preparation of **2d** and **2e**⁴



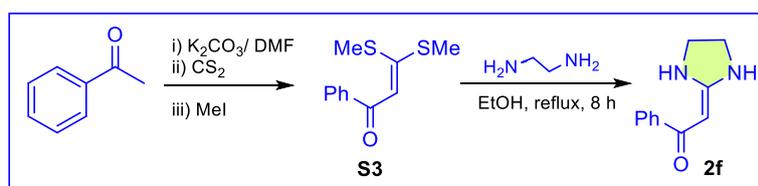
Scheme S3. Preparation of substrates **2d** and **2e**

For **S2**: The solution of benzyl chloride (20 mmol) in acetonitrile (50 mL) was added dropwise to a solution of diamine (100 mmol) in acetonitrile (30 mL) that had been cooled in a salt-ice

bath maintained at a temperature between $-15\text{ }^{\circ}\text{C}$ and $-10\text{ }^{\circ}\text{C}$. Subsequently, the mixture was allowed to warm to room temperature and was stirred for 8 h. Following this, the solvent was removed under reduced pressure. Water (50 mL) was then added to the resulting liquid, after which extraction was performed using DCM ($30\text{ mL} \times 5$). The combined organic layer was thoroughly dried over anhydrous Na_2SO_4 and subsequently filtered. The solvent was removed under reduced pressure to yield substituted diethylene amine **S2**, which was utilized in the subsequent step without further purification.

For compounds **2d** and **2e**: The reaction mixture consisting of compound substituted diamine **S2** (10 mmol) and ketene dithioacetal (10 mmol) in ethanol (20 mL) was subjected to reflux for 8 h. The precipitate formed was filtered, washed with a small amount of ethanol, and dried to furnish the products **2d** and **2e** (Scheme S3).

Preparation of 2f

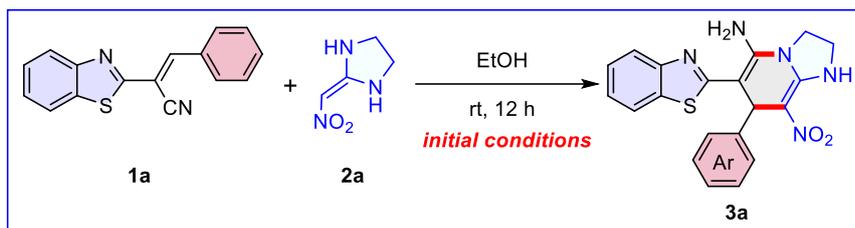


Scheme S4. Preparation of substrate 2f

For **S3**: To a well-stirred suspension of acetophenone (1.00 g, 10 mmol), K_2CO_3 (3.45 g, 25 mmol) and DMF (20 mL) was added CS_2 (0.66 mL, 11 mmol) at $0\text{ }^{\circ}\text{C}$. After the reaction mixture was stirred at $0\text{ }^{\circ}\text{C}$ for 1 h, MeI (1.37 mL, 22 mmol) was added dropwise within 15 min. The mixture was allowed to warm to room temperature and stirred for 24 h, and then poured into ice-water (50 mL) under stirring and extracted with CH_2Cl_2 ($3 \times 20\text{ mL}$). The combined organic phase was washed with water ($3 \times 20\text{ mL}$), dried over MgSO_4 and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, petroleum ether/ethyl acetate: 20/1, v/v) to give **S3** (1.90 g, 92%) as a white solid.

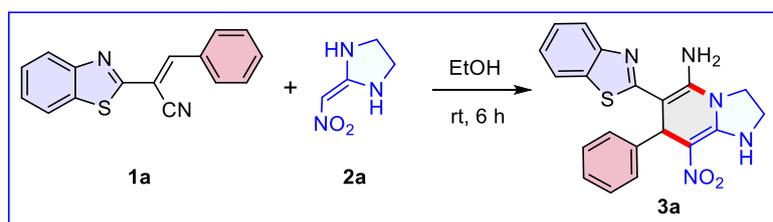
For **2f**: The reaction mixture consisting of compound ketene dithioacetal **S3** (10 mmol) and ethylene diamine (10 mmol) in ethanol (20 mL) was subjected to reflux for 8 h. The precipitate formed was filtered, washed with a small amount of ethanol, and dried to furnish the products **2f** (Scheme S4). All the substrates are listed in Figure S2.

5. Procedure for Optimisation of Reaction Conditions for Synthesis of 3a



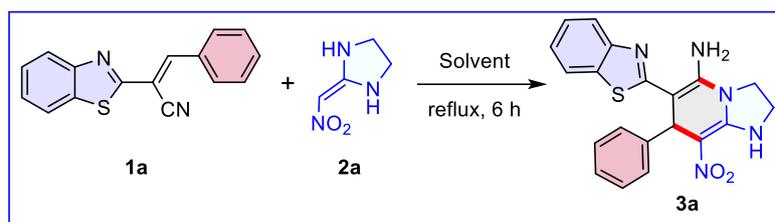
In a 10 mL round-bottom flask equipped with a magnetic stir bar, compound **1a** (0.25 mmol, 1 equiv) and 2-(nitromethylene)imidazolidine **2a** (0.25 mmol, 1 equiv) were dissolved in ethanol (2 mL). The reaction mixture was stirred at room temperature for 12 h under ambient conditions. Reaction progress monitored by thin-layer chromatography. Upon completion of the reaction, as monitored by TLC, a yellow precipitate was formed. The solid product was collected by filtration, washed with cold ethanol, and dried to afford the pure compound **3a**.

Table S1. Optimisation of Base^a



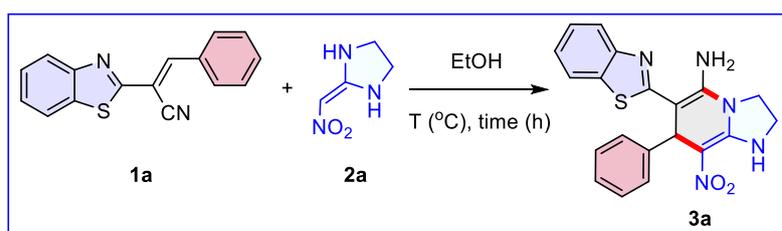
entry	base	yield (%) of 3a ^b
1	Piperidine	25
2	Pyridine	28
3	DABCO	30
4	Et ₃ N	33
5	DBU	35
6^c	DBU	37

^aReaction conditions: All the reactions were performed using **1a** (0.25 mmol, 1 equiv), **2a** (0.25 mmol, 1 equiv), and base (1 equiv) in ethanol (2 mL) at rt (25 °C) under air for 6 h. ^bisolated yield. ^cReaction time 12 h.

Table S2. Optimisation of Solvent^a

entry	solvent	yield (%) of 3a ^b
1	EtOH	68
2	MeOH	63
3	DCE	nr
4	Dioxane	nr
5	H ₂ O	nr
6	THF	Traces
7	ACN	nr
8	DMF	60

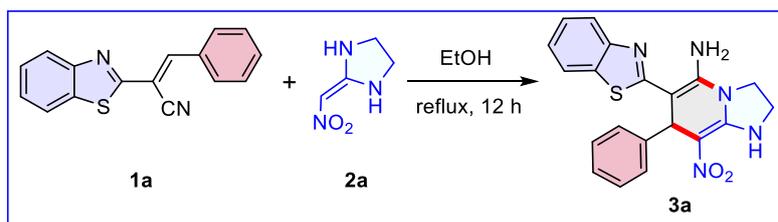
^aReaction conditions: All the reactions were performed using **1a** (0.25 mmol, 1 equiv), **2a** (0.25 mmol, 1 equiv), in solvent (2 mL) at reflux (25 °C) for 6 h. ^bisolated yield.

Table S3. Optimisation of Reaction Temperature and Time^a

entry	temp (°C)	time (h)	yield (%) of 3a ^b
1	reflux	6	68
2	reflux	8	70
3	reflux	12	96
4	40	12	49
5	60	12	51

^aReaction conditions: All the reactions were performed using **1a** (0.25 mmol, 1 equiv), **2a** (0.25 mmol, 1 equiv), and base (1 equiv) in ethanol (2 mL) under air. ^bisolated yield.

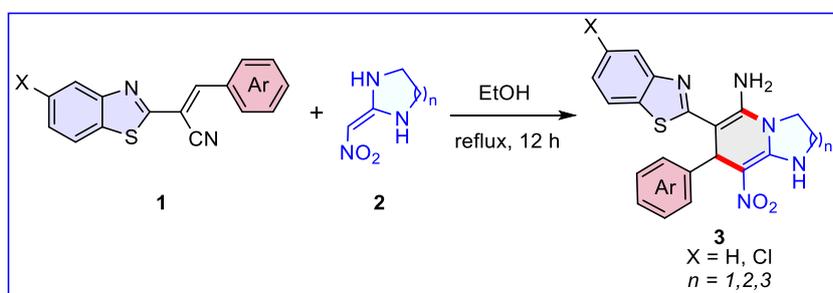
Table S4. Optimisation of Stoichiometry^a



entry	equiv of 1a	equiv of 2a	yield (%) of 3a ^b
1	1	1	96
2	1.25	1	96
3	1	1.25	96

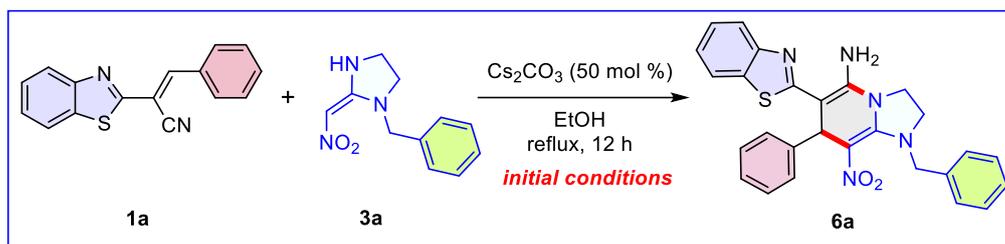
^aReaction conditions: All the reactions were performed using **1a** (0.25 mmol, 1 equiv), **2a** (0.25 mmol, 1 equiv), and base (1 equiv) in ethanol (2 mL) at reflux for 12 h. ^bisolated yield.

6. General Procedure for Catalyst-Free [3+3] Annulation of Benzothiazole-Based Acceptors with Cyclic 1,1-enediamines (GPI)



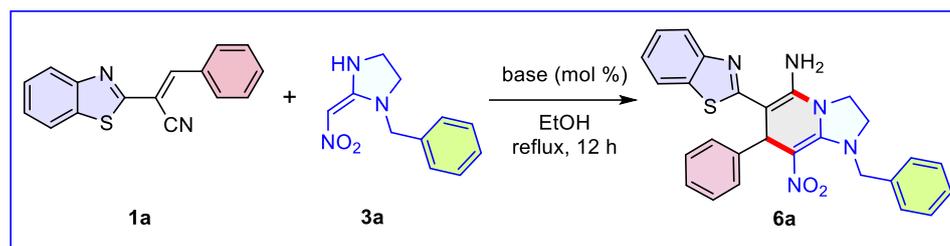
In a 10 mL round-bottom flask equipped with a magnetic stir bar, compound **1** (0.25 mmol, 1 equiv) and 2-(nitromethylene)imidazolidine **2** (0.25 mmol, 1 equiv) were dissolved in ethanol (2 mL). The reaction mixture was stirred at reflux for 12 h. After completion of the reaction (as monitored by TLC), the solid product was collected by filtration, washed with cold ethanol, and dried to afford the corresponding imidazo[1,2-*a*]pyridine–benzothiazole hybrids.

7. Procedure for Optimization of Reaction Conditions for the Synthesis of 6a



To a 10 mL round-bottom flask equipped with a magnetic stir bar, compound **1a** (0.37 mmol, 1.5 equiv.) and 1-benzyl-2-(nitromethylene)imidazolidine **3a** were added along with a catalytic amount of Cs_2CO_3 (0.146 mmol, 20 mol%) in ethanol (2 mL). The reaction mixture was then heated under reflux for 12 h. Upon completion, the mixture was allowed to cool to room temperature, forming a precipitate. The solid product was collected by filtration, washed with cold ethanol, and dried to afford the pure compound **6a** with 89% yield.

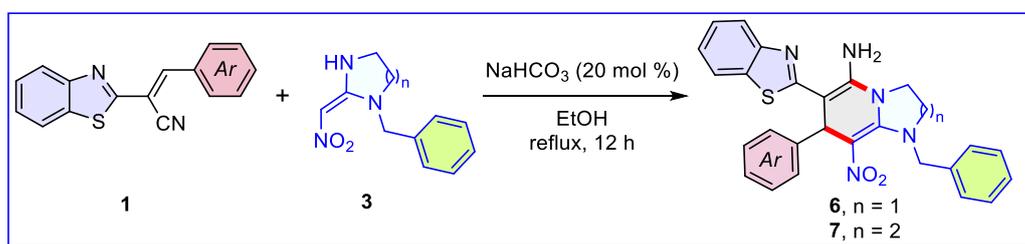
Table S5. Optimisation of Reaction Conditions



entry	solvent	base (mol%)	yield (%) of 6a ^b
1	EtOH	Cs_2CO_3 (50)	89
2	EtOH	NaHCO_3 (50)	90
3	EtOH	NaHCO_3 (30)	90
4	EtOH	NaHCO_3 (20)	90
5	EtOH	NaHCO_3 (10)	80

^aReaction conditions: All the reactions were performed using **1a** (0.35 mmol, 1.5 equiv), **3a** (0.25 mmol, 1 equiv), and base (x mol%) in ethanol (2 mL) at reflux for 12 h. ^bisolated yield.

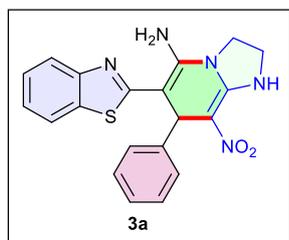
8. General Procedure for Synthesis of *N*-benzyl imidazo[1,2-*a*]pyridine-benzothiazole hybrids (GP2)



To a 10 mL round-bottom flask equipped with a magnetic stir bar, compound **1** (0.37 mmol, 1.5 equiv) and 1-benzyl-2-(nitromethylene)imidazolidine **3** were added along with a catalytic amount (0.146 mmol, 20 mol%) of NaHCO₃ in ethanol (2 mL). The reaction mixture was then heated under reflux for 12 h. Upon completion, the mixture was allowed to cool to room temperature, forming a precipitate. The solid product was collected by filtration, washed with cold ethanol, and dried to afford the corresponding pure *N*-benzyl imidazo[1,2-*a*]pyridine-benzothiazole hybrids **6** and **7**.

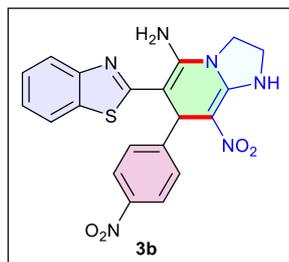
9. Spectroscopic Data of Compounds

6-(Benzo[*d*]thiazol-2-yl)-8-nitro-7-phenyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (**3a**)



3a was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-phenylacrylonitrile **1a** (62 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (92.0 mg, 95%) m.p.: 278.9–280.2 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.16 (s, 1H), 8.25 (s, 2H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 2H), 7.04 (t, *J* = 5.8 Hz, 2H), 5.05 (s, 1H), 4.27–4.06 (m, 2H), 4.01–3.80 (m, 2H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 169.00, 153.5, 151.5, 146.0, 144.5, 131.3, 128.8, 128.2, 126.9, 126.4, 122.7, 121.6, 119.7, 108.00, 84.3, 49.1, 45.1, 43.9, 43.1; HRMS (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₀H₁₈N₅O₂S: 392.1176, Found: 392.1175.

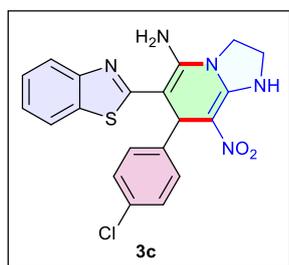
6-(Benzo[*d*]thiazol-2-yl)-8-nitro-7-(4-nitrophenyl)-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3b)



3b was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-nitrophenyl)acrylonitrile **1b** (76 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (104.8 mg, 96%) m.p.: 297.5–298.0 °C $^1\text{H NMR}$

(500 MHz, DMSO-*d*₆) δ 9.46 (s, 1H), 8.51 (s, 2H), 7.83 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 7.8 Hz, 1H), 7.41 (t, J = 7.6 Hz, 3H), 7.31 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 5.01 (s, 1H), 4.20–4.14 (m, 2H), 3.92–3.86 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO-*d*₆) δ 168.5, 153.5, 152.0, 151.4, 146.6, 146.2, 131.0, 130.0, 126.5, 123.5, 122.8, 121.6, 119.8, 106.9, 83.0, 45.1, 44.0, 43.2; **HRMS** (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for C₂₀H₁₇N₆O₄S: 437.1027, Found: 437.1027.

6-(Benzo[*d*]thiazol-2-yl)-7-(4-chlorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3c)

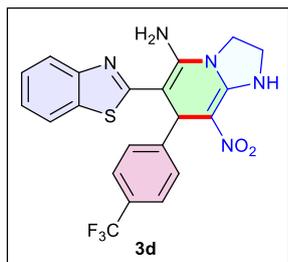


3c was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-chlorophenyl)acrylonitrile **1c** (74 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (88.3 mg, 83 %) m.p.: 301.7–302.5 °C; $^1\text{H NMR}$ (500

MHz, DMSO-*d*₆) δ 9.48 (s, 1H), 8.53 (s, 2H), 7.82 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.13 (t, J = 7.5 Hz, 1H), 4.99 (s, 1H), 4.28–4.06 (m, 2H), 4.01–3.79 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO-*d*₆) δ 168.1, 152.8, 150.7, 145.4, 142.7, 130.8, 130.5, 129.1, 127.5, 125.8, 122.1, 120.9, 119.1, 106.9, 83.0, 44.4, 43.2, 42.0; **HRMS** (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for C₂₀H₁₇³⁵ClN₅O₂S: 426.0786, Found: 426.0785.

6-(Benzo[*d*]thiazol-2-yl)-8-nitro-7-(4-(trifluoromethyl)phenyl)-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3d)

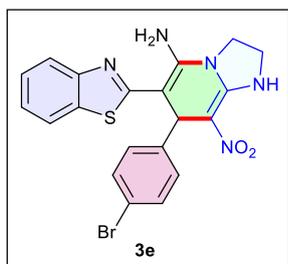
3d was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-(trifluoromethyl)phenyl)acrylonitrile **1d** (82 mg, 0.25 mmol) and 2-(nitromethy-



lene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (100 mg, 87%) m.p.: 321.1–321.6; $^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ 9.51 (s, 1H), 8.56 (s, 2H), 7.81 (d, $J = 7.8$ Hz, 1H), 7.67 (d, $J = 8.0$ Hz, 1H), 7.59 (d, $J = 9.4$ Hz, 4H), 7.34–7.29 (m, 1H), 7.15–7.09 (m, 1H), 5.09 (s, 1H), 4.25–4.13 (m, 2H), 3.97–3.85 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz,

DMSO- d_6) δ 168.7, 153.5, 151.20 (d, $J_{\text{C-F}} = 432.2$), 146.1, 131.1, 129.5, 127.8 (q, $J_{\text{C-F}} = 31.3$ Hz), 126.3, 125.5, 125.0, 124.0, 122.6, 121.5, 119.7, 107.4, 83.5, 45.0, 44.0, 43.1; **HRMS** (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{17}\text{F}_3\text{N}_5\text{O}_2\text{S}$: 460.1050, Found: 460.1058, $^{19}\text{F NMR}$ (471 MHz, DMSO- d_6) δ -60.71 (s, 1F).

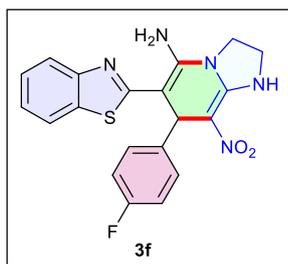
6-(Benzo[*d*]thiazol-2-yl)-7-(4-bromophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3e)



3e was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-bromophenyl)acrylonitrile **1e** (85 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (94 mg, 80%) m.p.: 298.3–298.9; $^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ 9.49 (s, 1H), 8.53 (s, 2H), 7.83–7.75 (m, 1H),

7.66 (d, $J = 8.1$ Hz, 1H), 7.42 (d, $J = 1.8$ Hz, 1H), 7.41–7.39 (m, 1H), 7.35 (d, $J = 1.9$ Hz, 1H), 7.34–7.32 (m, 1H), 7.30 (dd, $J = 8.1, 1.0$ Hz, 1H), 7.14–7.08 (m, 1H), 4.99 (s, 1H), 4.26–4.05 (m, 2H), 3.91 (ddd, $J = 25.3, 15.1, 7.9$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.7, 153.4, 151.3, 146.0, 143.7, 131.2, 131.0, 131.0, 126.4, 122.7, 121.5, 120.0, 119.7, 107.5, 83.6, 45.0, 43.8, 42.7; **HRMS** (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{17}^{79}\text{BrN}_5\text{O}_2\text{S}$: 470.0281, Found: 470.0281.

6-(Benzo[*d*]thiazol-2-yl)-7-(4-fluorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3f)

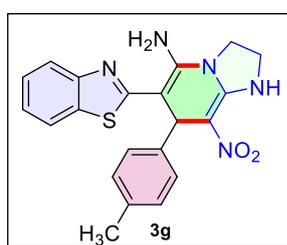


3f was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-fluorophenyl)acrylonitrile **1f** (70 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (71.6 mg, 70%) m.p.: 272.8–274 °C; $^1\text{H NMR}$ (500

MHz, DMSO- d_6) δ 9.46 (s, 1H), 8.51 (s, 2H), 7.82 (d, $J = 7.8$ Hz, 1H), 7.67 (d, $J = 8.0$ Hz,

1H), 7.39 (dt, $J = 34.1, 17.1$ Hz, 2H), 7.32 (t, $J = 7.6$ Hz, 1H), 7.12 (t, $J = 7.5$ Hz, 1H), 7.04 (t, $J = 8.7$ Hz, 2H), 5.01 (s, 1H), 4.27–4.08 (m, 2H), 4.01–3.63 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.9, 161.3 (d, $J_{\text{C-F}} = 242.3$ Hz), 153.5, 151.4, 146.0, 140.5, 131.2, 130.5 (d, $J_{\text{C-F}} = 7.7$ Hz), 126.4, 122.7, 121.6, 119.8, 115.0, 114.8 (d, $J_{\text{C-F}} = 21.2$ Hz), 107.8, 84.0, 45.0, 43.9, 42.4, 40.5, 40.3, 40.1, 40.0, 39.9, 39.7; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{17}\text{FN}_5\text{O}_2\text{S}$: 410.1082, Found: 410.1080; ^{19}F NMR (471 MHz, DMSO- d_6): δ -116.21 to -116.24 (m, 1F).

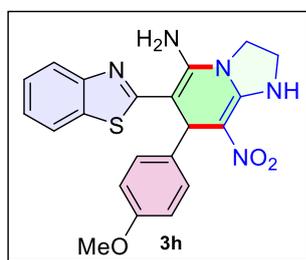
6-(benzo[*d*]thiazol-2-yl)-8-nitro-7-(*p*-tolyl)-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3g)



3g was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(*p*-tolyl)acrylonitrile **1h** (69 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (50.0 mg, 49%) m.p.: 236–238 °C; ^1H NMR (500 MHz, DMSO- d_6) δ 9.42

(s, 1H), 8.47 (s, 1H), 7.81 (d, $J = 7.8$ Hz, 1H), 7.66 (d, $J = 8.1$ Hz, 1H), 7.30 (dd, $J = 15.4, 7.8$ Hz, 2H), 7.26 (s, 1H), 7.12 (t, $J = 7.6$ Hz, 1H), 7.02 (d, $J = 7.9$ Hz, 2H), 4.99 (s, 1H), 4.36 – 4.10 (m, 2H), 3.88 (s, 1H), 2.18 (s, 3H); ^{13}C NMR (126 MHz, DMSO- D_6) 169.07, 153.52, 151.50, 145.93, 141.48, 135.99, 131.37, 128.76, 128.70, 126.35, 122.63, 121.56, 119.73, 108.14, 84.41, 45.09, 43.86, 42.72, 40.54, 40.37, 40.20, 40.03, 39.87, 39.70, 39.53, 21.13; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{20}\text{N}_5\text{O}_2\text{S}$: 406.1332, Found: 406.1333.

6-(benzo[*d*]thiazol-2-yl)-7-(4-methoxyphenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3h)

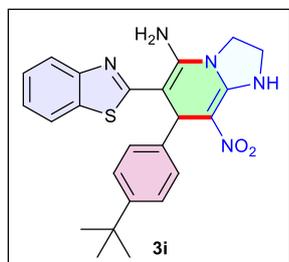


3h was prepared by following the general procedure **GP1** using (*Z*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-methoxyphenyl)acrylonitrile **1i** (73 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (60.4 mg, 56%) m.p.: 255–255.9 °C; ^1H NMR (500 MHz, DMSO- d_6) δ 9.41 (s, 1H), 8.45 (s, 1H), 7.82 (d, $J = 7.8$ Hz, 1H), 7.66

(d, $J = 8.1$ Hz, 1H), 7.32 (d, $J = 7.3$ Hz, 1H), 7.28 (d, $J = 8.7$ Hz, 2H), 7.12 (t, $J = 7.6$ Hz, 1H), 6.77 (d, $J = 8.7$ Hz, 2H), 4.96 (s, 1H), 4.33 – 4.06 (m, 1H), 3.88 (d, $J = 10.2$ Hz, 1H), 3.65 (s, 4H); ^{13}C NMR (126 MHz, DMSO- D_6) δ 169.0, 158.3, 153.5, 151.4, 145.9, 136.5, 131.4, 129.8, 126.4, 122.6, 121.6, 119.7, 113.6, 108.2, 84.5, 55.5, 45.1, 43.8, 42.3, 40.5, 40.4, 40.2, 40.0,

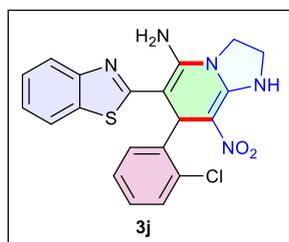
39.9, 39.7, 39.5; **HRMS** (ESI/Q-TOF) m/z : $[M+H]^+$ Calcd for $C_{21}H_{20}N_5O_3S$: 422.1281, Found: 422.1282.

6-(Benzo[*d*]thiazol-2-yl)-7-(4-(*tert*-butyl)phenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3i)



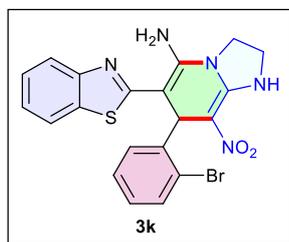
3i was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-(*tert*-butyl)phenyl)acrylonitrile **1g** (79 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (76.0 mg, 68%) m.p.: 288.2–289.0 °C; 1H NMR (500 MHz, DMSO-*d*₆) δ 9.44 (s, 1H), 8.44 (d, $J = 25.1$ Hz, 2H), 7.83 (d, $J = 7.7$ Hz, 1H), 7.66 (d, $J = 7.7$ Hz, 1H), 7.36–7.27 (m, 3H), 7.23 (d, $J = 7.9$ Hz, 2H), 7.16–7.06 (m, 1H), 4.97 (s, 1H), 4.27–4.04 (m, 2H), 4.04–3.79 (m, 2H), 1.19 (s, 9H); $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-*d*₆) δ 169.0, 153.6, 151.6, 149.1, 146.0, 141.5, 131.3, 128.3, 126.4, 125.0, 122.7, 121.7, 119.7, 108.1, 84.3, 45.0, 43.9, 42.6, 34.5, 31.6; **HRMS** (ESI/Q-TOF) m/z : $[M+H]^+$ Calcd for $C_{24}H_{26}N_5O_2S$: 448.1802, Found: 448.1782.

6-(Benzo[*d*]thiazol-2-yl)-7-(2-chlorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3j)



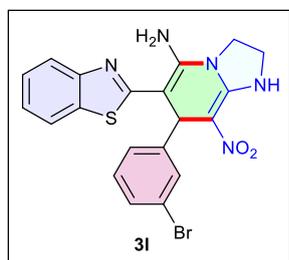
3j was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(2-chlorophenyl)acrylonitrile **1j** (74 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (72.2 mg, 68%) m.p.: 299.9–301.4; 1H NMR (500 MHz, DMSO-*d*₆) δ 9.46 (s, 1H), 8.57 (s, 2H), 7.79 (d, $J = 7.8$ Hz, 1H), 7.61 (d, $J = 8.0$ Hz, 1H), 7.50 (d, $J = 7.2$ Hz, 1H), 7.27 (t, $J = 7.6$ Hz, 1H), 7.20 (dd, $J = 17.6, 7.8$ Hz, 2H), 7.08 (dd, $J = 14.1, 6.8$ Hz, 2H), 5.24 (s, 1H), 4.16 (dd, $J = 15.9, 8.1$ Hz, 2H), 3.87 (t, $J = 8.2$ Hz, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-*d*₆) δ 168.4, 162.1, 152.8, 145.9, 140.6, 133.8, 133.2, 131.4, 130.3, 128.6, 126.8, 126.4, 122.7, 121.5, 119.7, 106.5, 82.9, 44.3, 43.2, 41.6; **HRMS** (ESI/Q-TOF) m/z : $[M+H]^+$ Calcd for $C_{20}H_{17}^{35}ClN_5O_2S$: 426.0786, Found: 426.0787.

6-(Benzo[d]thiazol-2-yl)-7-(2-bromophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-a]pyridin-5-amine (3k)



3k was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(2-bromophenyl)acrylonitrile **1k** (85 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (74 mg, 63%) m.p.: 292.6–293.1; $^1\text{H NMR}$ (500 MHz, DMSO-*d*₆) δ 9.51 (s, 1H), 8.64 (s, 2H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.57 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.43 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.34–7.29 (m, 1H), 7.31–7.22 (m, 1H), 7.18–7.08 (m, 1H), 7.04 (td, *J* = 7.8, 1.6 Hz, 1H), 5.25 (s, 1H), 4.22 (td, *J* = 8.9, 3.0 Hz, 2H), 3.90 (t, *J* = 8.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO-*d*₆) δ 168.4, 152.5, 151.0, 146.0, 141.4, 134.0, 133.2, 131.4, 128.3, 126.6, 125.9, 122.8, 122.1, 120.9, 119.1, 106.0, 82.4, 44.3, 43.7, 43.2; **HRMS** (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₀H₁₇⁷⁹BrN₅O₂S: 470.0281, Found: 470.0284.

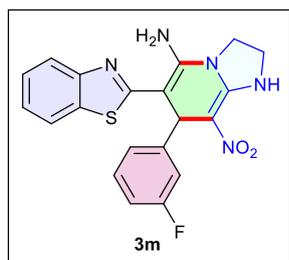
6-(Benzo[d]thiazol-2-yl)-7-(3-bromophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-a]pyridin-5-amine (3l)



3l was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(3-bromophenyl)acrylonitrile **1l** (85 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (129 mg, 96 %) m.p.: 280.5–282.3 °C; $^1\text{H NMR}$ (500 MHz, DMSO-*d*₆) δ 9.50 (s, 1H), 8.54 (s, 2H), 7.83 (d, *J* = 3.3 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.52 (s, 1H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 6.5 Hz, 1H), 5.01 (s, 1H), 4.31–4.16 (m, 1H), 4.14 (dd, *J* = 19.0, 9.4 Hz, 1H), 3.90 (dd, *J* = 19.6, 9.8 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO-*d*₆) δ 168.2, 153.0, 150.9, 146.5, 145.6, 130.7, 130.6, 130.0, 129.9, 127.3, 125.9, 122.7, 121.2, 121.1, 119.2, 106.8, 82.8, 44.5, 43.3, 42.4; **HRMS** (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₀H₁₇⁷⁹BrN₅O₂S: 470.0281, Found: 470.0279.

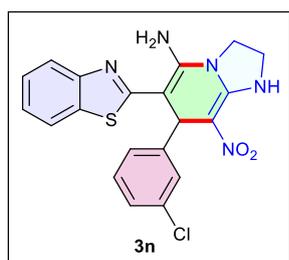
6-(Benzo[d]thiazol-2-yl)-7-(3-fluorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-a]pyridin-5-amine (3m)

3m was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(3-fluorophenyl)acrylonitrile **1m** (70 mg, 0.25 mmol) and 2-(nitromethylene)-



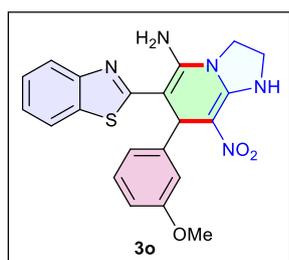
imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (81.82 mg, 80 %) m.p.: 321.4–321.9; $^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ 9.43 (s, 1H), 8.48 (s, 2H), 7.80 (d, $J = 7.8$ Hz, 1H), 7.63 (d, $J = 8.1$ Hz, 1H), 7.33 (t, $J = 7.6$ Hz, 1H), 7.29–7.20 (m, 2H), 7.13 (dd, $J = 8.7, 5.6$ Hz, 2H), 7.00–6.92 (m, 1H), 5.00 (s, 1H), 4.19–07 (m, 2H), 3.89–3.82 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.8, 161.3, 153.5, 151.4, 147.3, 147.2, 146.1 (d, $J_{\text{C-F}} = 242.9$ Hz), 131.2, 130.0 (d, $J_{\text{C-F}} = 7.9$ Hz), 126.4, 124.8, 124.8, 122.7, 121.6, 119.8, 115.4, 115.3, 113.9 (d, $J_{\text{C-F}} = 21.1$ Hz), 113.7, 107.4, 83.5, 45.0, 43.9, 42.9; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{17}\text{FN}_5\text{O}_2\text{S}$: 410.1082, Found: 410.1085; $^{19}\text{F NMR}$ (471 MHz, DMSO- d_6): δ -113.86 to -113.91 (m, 1F).

6-(Benzo[*d*]thiazol-2-yl)-7-(3-chlorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (**3n**)



3n was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(3-chlorophenyl)acrylonitrile **1n** (74 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (71.6 mg, 70%) m.p.: 253.7–254.6 °C; $^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ 9.49 (s, 1H), 8.54 (s, 1H), 7.85 (d, $J = 7.0$ Hz, 1H), 7.68 (d, $J = 7.2$ Hz, 1H), 7.37 (s, 1H), 7.34 (d, $J = 6.7$ Hz, 2H), 7.27 (t, $J = 6.3$ Hz, 1H), 7.20 (d, $J = 7.0$ Hz, 1H), 7.14 (s, 1H), 5.02 (s, 1H), 4.22 (s, 1H), 4.14 (d, $J = 9.3$ Hz, 1H), 3.90 (dd, $J = 23.0, 11.8$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.2, 153.0, 150.8, 146.7, 146.2, 132.8, 131.2, 130.1, 128.4, 127.4, 127.0, 126.4, 122.7, 121.6, 119.8, 106.8, 82.8, 44.6, 43.4, 42.5; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{17}^{35}\text{ClN}_5\text{O}_2\text{S}$: 426.0786, Found: 426.0785.

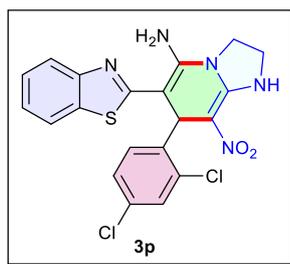
6-(Benzo[*d*]thiazol-2-yl)-7-(3-methoxyphenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (**3o**)



3o was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(3-methoxyphenyl)acrylonitrile **1o** (73 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (68.4 mg, 65%) m.p.: 255–255.9 °C; $^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ 9.45 (s, 1H), 8.49 (s, 2H), 7.83 (d, $J = 7.8$ Hz, 1H), 7.67 (d, $J = 8.0$ Hz,

1H), 7.32 (t, $J = 7.6$ Hz, 1H), 7.13 (q, $J = 8.0$ Hz, 2H), 6.94 (d, $J = 7.6$ Hz, 1H), 6.90 (s, 1H), 6.78–6.64 (m, 1H), 5.01 (s, 1H), 4.26–4.05 (m, 2H), 4.00–3.76 (m, 2H), 3.68 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 169.0, 159.2, 153.5, 151.5, 146.0, 145.9, 131.3, 129.3, 126.4, 122.6, 121.6, 120.9, 119.7, 115.6, 111.2, 107.8, 84.0, 55.4, 45.0, 43.8, 43.0; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{20}\text{N}_5\text{O}_3\text{S}$: 422.1281, Found: 422.1288.

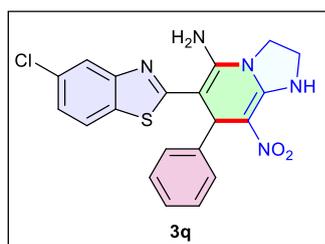
6-(Benzo[*d*]thiazol-2-yl)-7-(2,4-dichlorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3p)



3p was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(2,4-dichlorophenyl)acrylonitrile **1p** (82 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (81.7 mg, 71%) m.p.: 224.6–225.1 °C; ^1H

NMR (500 MHz, DMSO- d_6) δ 9.56 (s, 1H), 8.68 (s, 2H), 7.88 (d, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 7.9$ Hz, 1H), 7.59 (d, $J = 8.3$ Hz, 1H), 7.44 (s, 1H), 7.37 (t, $J = 8.0$ Hz, 2H), 7.18 (t, $J = 7.3$ Hz, 1H), 5.31 (s, 1H), 4.25 (dd, $J = 15.3, 7.9$ Hz, 2H), 4.01–3.88 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.6, 153.1, 151.4, 146.4, 139.6, 134.9, 134.1, 132.1, 131.2, 129.4, 126.9, 126.3, 122.6, 121.5, 119.6, 106.1, 82.3, 44.9, 43.7, 41.8; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{Cl}_2\text{N}_5\text{O}_2\text{S}$: 460.0396, Found: 460.0404.

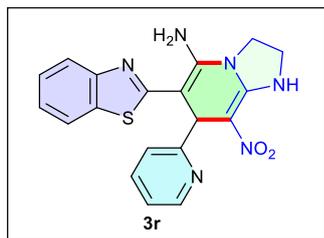
6-(4-Chlorobenzo[*d*]thiazol-2-yl)-8-nitro-7-phenyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (3q)



3q was prepared by following the general procedure **GP1** using (*E*)-2-(5-chlorobenzo[*d*]thiazol-2-yl)-3-phenylacrylonitrile **1q** (74 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h., followed by filtration. Orange solid (93.6 mg, 88 %) m.p.: 285.8–286.2 °C;

^1H NMR (500 MHz, DMSO- d_6) δ 9.48 (s, 1H), 8.59 (s, 2H), 7.82 (d, $J = 8.3$ Hz, 1H), 7.71 (s, 1H), 7.36 (d, $J = 7.1$ Hz, 2H), 7.22 (t, $J = 7.0$ Hz, 2H), 7.13 (d, $J = 7.4$ Hz, 2H), 4.96 (s, 1H), 4.16 (dt, $J = 18.6, 7.3$ Hz, 2H), 3.98–3.78 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 170.2, 154.2, 150.8, 146.3, 143.7, 130.5, 130.3, 129.5, 129.3, 128.3, 127.7, 126.5, 122.3, 121.7, 118.4, 107.4, 83.9, 44.6, 43.4, 42.5; HRMS (ESI/Q-TOF) m/z , $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{17}^{35}\text{ClN}_5\text{O}_2\text{SNa}$: 448.0605 Found: 448.0617.

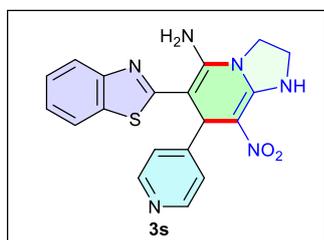
6-(Benzo[d]thiazol-2-yl)-8-nitro-7-(pyridin-2-yl)-1,2,3,7-tetrahydroimidazo[1,2-a]pyridin-5-amine (3r)



3r was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(pyridin-2-yl)acrylonitrile **1r** (65 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (92.9 mg, 97%) m.p.: 292.6–293.4 °C;

¹H NMR (500 MHz, DMSO-*d*₆) δ 9.49 (s, 1H), 8.47 (s, 2H), 8.39 (d, *J* = 4.4 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.65 (ddd, *J* = 8.0, 6.7, 2.7 Hz, 2H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 6.8 Hz, 2H), 5.11 (s, 1H), 4.28–4.07 (m, 2H), 3.98–3.78 (m, 2H); **¹³C{¹H} NMR** (126 MHz, DMSO-*d*₆) δ 168.8, 162.0, 153.6, 152.0, 149.8, 146.5, 135.8, 131.1, 126.4, 124.5, 122.5, 122.3, 121.5, 119.6, 107.1, 83.7, 45.5, 45.0, 43.8; **HRMS** (ESI/Q-TOF) *m/z*, [M+H]⁺ Calcd for C₁₉H₁₇N₆O₂S: 393.1128, Found: 393.1127.

6-(Benzo[d]thiazol-2-yl)-8-nitro-7-(pyridin-4-yl)-1,2,3,7-tetrahydroimidazo[1,2-a]pyridin-5-amine (3s)

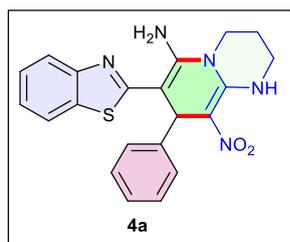


3s was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(pyridin-4-yl)acrylonitrile **1s** (65 mg, 0.25 mmol) and 2-(nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (120.0 mg, 80%) m.p.: 278.1–279.2 °C

¹H NMR (500 MHz, DMSO-*d*₆) δ 9.48 (s, 1H), 8.53 (s, 1H), 8.38 (dd, *J* = 4.5, 1.5 Hz, 2H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 4.5, 1.5 Hz, 2H), 7.3–7.26 (m, 1H), 7.15–6.99 (m, 1H), 4.97 (s, 1H), 4.24–4.02 (m, 2H), 3.94–3.75 (m, 2H); **¹³C{¹H} NMR** (126 MHz, DMSO-*d*₆) δ 168.0, 153.0, 152.2, 151.0, 149.1, 146.0, 130.5, 126.0, 123.4, 122.2, 121.7, 119.2, 106.1, 82.2, 79.2, 44.6, 43.4, 42.2; **HRMS** (ESI/Q-TOF) *m/z* [M+H]⁺ Calcd for C₁₉H₁₇N₆O₂S: 393.1128, Found: 393.1140

7-(Benzo[d]thiazol-2-yl)-9-nitro-8-phenyl-1,3,4,8-tetrahydro-2H-pyrido[1,2-a]pyrimidin-6-amine (4a)

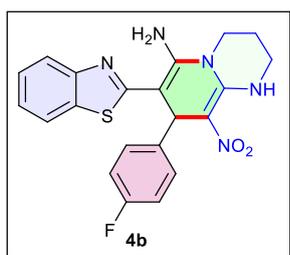
4a was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-phenylacrylonitrile **1a** (62 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid



(98.0 mg, 95 %) m.p.: 236–238 °C; $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 11.39 (d, $J = 4.2$ Hz, 1H), 8.44 (s, 2H), 7.82 (d, $J = 7.8$ Hz, 1H), 7.67 (d, $J = 8.0$ Hz, 1H), 7.33 (d, $J = 7.6$ Hz, 2H), 7.30 (d, $J = 7.7$ Hz, 1H), 7.19 (t, $J = 7.5$ Hz, 2H), 7.14–7.06 (m, 2H), 5.15 (s, 1H), 3.97 (d, $J = 8.1$ Hz, 1H), 3.86 (td, $J = 11.7, 3.9$ Hz, 1H), 3.59 (d, $J = 11.1$ Hz, 1H), 3.34 (s, 1H), 2.26–2.13 (m, 1H), 1.87 (dd, $J = 16.8, 7.6$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) δ 169.2, 153.5, 150.1, 146.9, 143.7, 131.4, 128.4, 128.2, 127.0, 126.5, 123.0, 121.7, 120.1, 110.0, 85.4, 43.4, 41.7, 38.8, 20.3; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{20}\text{N}_5\text{O}_2\text{S}$: 406.1332, Found: 406.1336.

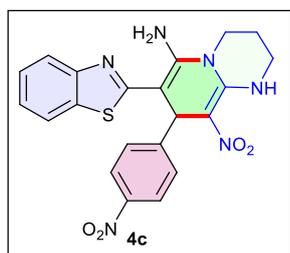
7-(Benzo[*d*]thiazol-2-yl)-8-(4-fluorophenyl)-9-nitro-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidin-6-amine (4b)

4b was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-fluorophenyl)acrylonitrile **1f** (70 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12



h followed by filtration. Yellow solid (63.5 mg, 60%) m.p.: 225.5–226.1 °C; $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 11.42 (s, 1H), 8.50 (s, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.39 (dd, $J = 8.6, 5.6$ Hz, 2H), 7.35 (t, $J = 7.8$ Hz, 1H), 7.17 (t, $J = 7.6$ Hz, 1H), 7.05 (t, $J = 8.8$ Hz, 2H), 5.17 (s, 1H), 4.02 (d, $J = 11.8$ Hz, 1H), 3.89 (td, $J = 11.8, 4.1$ Hz, 1H), 3.69–3.54 (m, 1H), 3.49–3.38 (m, 1H), 2.24 (dd, $J = 10.5, 3.1$ Hz, 1H), 2.01–1.80 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) δ 169.1, 161.4 (d, $J_{\text{C-F}} = 242.4$ Hz), 153.5, 150.0, 146.9, 139.8, 131.4, 130.10 (d, $J_{\text{C-F}} = 7.9$ Hz), 126.6, 123.1, 121.7, 120.1, 115.13 (d, $J_{\text{C-F}} = 21.1$ Hz), 109.9, 85.1, 43.5, 20.3; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{19}\text{FN}_5\text{O}_2\text{S}$: 424.1238, Found: 424.1237; $^{19}\text{F NMR}$ (471 MHz, $\text{DMSO-}d_6$): δ -111.21 to -111.27 (m, 1F).

7-(Benzo[*d*]thiazol-2-yl)-9-nitro-8-(4-nitrophenyl)-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidin-6-amine (4c)

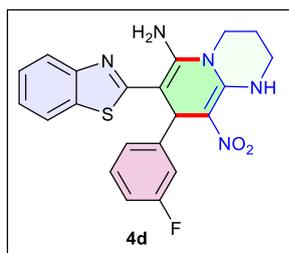


4c was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-nitrophenyl)acrylonitrile **1b** (76 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h followed by filtration. Orange solid (101.0 mg, 90%) m.p.: 237.2–238 °C; ^1H

NMR (500 MHz, DMSO-*d*₆) δ 11.32 (d, *J* = 4.4 Hz, 1H), 8.57 (s, 2H), 8.12 (s, 1H), 7.99 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 5.24 (s, 1H), 3.99 (d, *J* = 12.1 Hz, 1H), 3.88 (td, *J* = 11.7, 4.0 Hz, 1H), 3.61 (d, *J* = 11.6 Hz, 1H), 3.49–3.33 (m, 1H), 2.23 (d, *J* = 13.6 Hz, 1H), 2.04–1.79 (m, 1H); **¹³C{¹H} NMR** (126 MHz, DMSO-*d*₆) δ 168.7, 153.0, 149.5, 147.3, 146.7, 145.1, 134.1, 130.7, 129.8, 126.1, 122.7, 122.2, 121.8, 121.4, 120.2, 119.7, 83.6, 43.1, 41.2, 38.4, 19.7; **HRMS** (ESI/Q-TOF) *m/z*, [M+H]⁺ Calcd for C₂₁H₁₉N₆O₄S: 451.1183, Found: 451.1187.

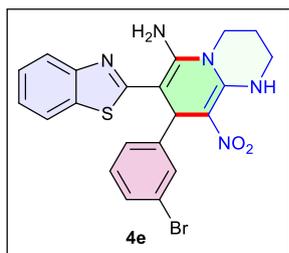
7-(Benzo[*d*]thiazol-2-yl)-8-(3-fluorophenyl)-9-nitro-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidin-6-amine (4d)

4d was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(3-fluorophenyl)acrylonitrile **1m** (70 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h followed by filtration.



Yellow solid (90.0 mg, 85 %) m.p.: 228.9-229.4; **¹H NMR** (500 MHz, DMSO-*d*₆) δ 11.40 (d, *J* = 4.6 Hz, 1H), 8.53 (s, 2H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.30–7.25 (m, 1H), 7.18 (dd, *J* = 16.3, 8.1 Hz, 2H), 7.11 (d, *J* = 10.0 Hz, 1H), 6.98 (td, *J* = 8.5, 2.5 Hz, 1H), 5.22 (s, 1H), 4.16–3.96 (m, 1H), 3.88 (td, *J* = 11.8, 4.1 Hz, 1H), 3.69–3.56 (m, 1H), 3.43 (s), 2.23 (dd, *J* = 10.3, 3.3 Hz, 1H), 1.93 (dd, *J* = 9.2, 4.3 Hz, 1H); **¹³C{¹H} NMR** (126 MHz, DMSO-*d*₆) δ 169.1, 163.3 (d, *J*_{C-F} = 243.7 Hz), 153.5, 150.0, 147.0, 147.0 (d, *J*_{C-F} = 6.1 Hz), 131.4, 130.6 (d, *J*_{C-F} = 8.5 Hz), 126.5, 124.2, 123.3, 121.8, 120.1, 114.9 (d, *J*_{C-F} = 21.3 Hz), 114.1, 109.5, 84.6, 43.5, 41.6, 38.9, 20.3; **HRMS** (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₁H₁₉FN₅O₂S: 424.1238, Found: 424.1241; **¹⁹F NMR** (471 MHz, DMSO-*d*₆): δ -113.55 (dd, 1F).

7-(Benzo[*d*]thiazol-2-yl)-8-(3-bromophenyl)-9-nitro-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidin-6-amine (4e)

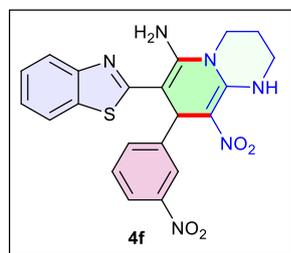


4e was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(3-bromophenyl)acrylonitrile **1l** (85 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (91.1 mg, 76%) m.p.: 235.1–235.9 °C; **¹H NMR** (500 MHz, DMSO-*d*₆) δ 11.38 (d, *J* = 4.4 Hz, 1H), 8.54 (s, 2H), 7.89 (d, *J* = 7.8 Hz,

1H), 7.72 (d, $J = 8.1$ Hz, 1H), 7.51 (s, 1H), 7.36 (t, $J = 7.4$ Hz, 2H), 7.31 (d, $J = 7.8$ Hz, 1H), 7.19 (dt, $J = 11.2, 7.7$ Hz, 2H), 5.17 (s, 1H), 4.02 (d, $J = 11.7$ Hz, 1H), 3.89 (td, $J = 11.8, 4.0$ Hz, 1H), 3.69–3.55 (m, 1H), 3.40 (dd, $J = 17.6, 6.9$ Hz, 1H), 2.34–2.15 (m, 1H), 2.03–1.83 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.9, 153.5, 150.0, 147.0, 146.3, 131.3, 131.1, 131.1, 130.1, 127.0, 126.6, 123.2, 121.9, 121.6, 120.2, 109.4, 84.4, 43.5, 41.6, 38.9, 20.3; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{19}^{79}\text{BrN}_5\text{O}_2\text{S}$: 484.0437, Found: 484.0449.

7-(Benzo[*d*]thiazol-2-yl)-9-nitro-8-(3-nitrophenyl)-1,3,4,8-tetrahydro-2H-pyrido[1,2-*a*]pyrimidin-6-amine (4f)

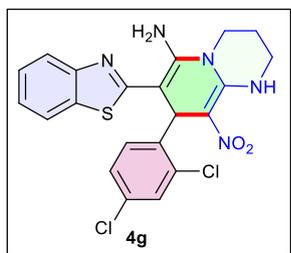
4f was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(3-nitrophenyl)acrylonitrile **1p** (76 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid, 96.1 mg, 86%, m.p.: 257.2–258 °C; ^1H NMR (500 MHz, DMSO- d_6) δ



11.38 (d, $J = 4.3$ Hz, 1H), 8.60 (s, 2H), 8.17 (s, 1H), 8.03 (d, $J = 8.1$ Hz, 1H), 7.87 (d, $J = 7.9$ Hz, 1H), 7.79 (d, $J = 7.7$ Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.54 (t, $J = 7.9$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.17 (t, $J = 7.5$ Hz, 1H), 5.29 (s, 1H), 4.03 (d, $J = 11.4$ Hz, 1H), 3.92 (td, $J = 11.7, 3.8$ Hz, 1H), 3.65 (d, $J = 10.5$ Hz, 1H), 3.43 (t, $J = 10.8$ Hz, 1H), 2.27 (d, $J = 13.5$ Hz, 1H), 1.96 (d, $J = 13.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.2, 153.0, 150.1, 146.5, 145.7, 130.8, 130.7, 130.0, 129.4, 127.3, 126.0, 122.2, 121.2, 121.0, 119.3, 106.8, 82.9, 59.8, 44.6, 43.4, 42.5, 20.8, 14.1; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for : $\text{C}_{21}\text{H}_{19}\text{N}_6\text{O}_4\text{S}$ 451.1183, Found: 451.1187.

8.1 Hz, 1H), 7.87 (d, $J = 7.9$ Hz, 1H), 7.79 (d, $J = 7.7$ Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.54 (t, $J = 7.9$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.17 (t, $J = 7.5$ Hz, 1H), 5.29 (s, 1H), 4.03 (d, $J = 11.4$ Hz, 1H), 3.92 (td, $J = 11.7, 3.8$ Hz, 1H), 3.65 (d, $J = 10.5$ Hz, 1H), 3.43 (t, $J = 10.8$ Hz, 1H), 2.27 (d, $J = 13.5$ Hz, 1H), 1.96 (d, $J = 13.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.2, 153.0, 150.1, 146.5, 145.7, 130.8, 130.7, 130.0, 129.4, 127.3, 126.0, 122.2, 121.2, 121.0, 119.3, 106.8, 82.9, 59.8, 44.6, 43.4, 42.5, 20.8, 14.1; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for : $\text{C}_{21}\text{H}_{19}\text{N}_6\text{O}_4\text{S}$ 451.1183, Found: 451.1187.

7-(Benzo[*d*]thiazol-2-yl)-8-(2,4-dichlorophenyl)-9-nitro-1,3,4,8-tetrahydro-2H-pyrido[1,2-*a*]pyrimidin-6-amine (4g)



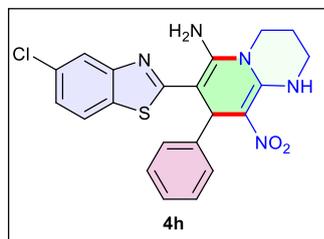
4g was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(2,4-dichlorophenyl)acrylonitrile **1q** (82 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h followed by filtration. Yellow solid (101.0 mg, 85%) m.p.: 206.3–207.1 °C;

^1H NMR (500 MHz, DMSO- d_6) δ 11.57 (d, $J = 4.0$ Hz), 8.65 (s), 7.87 (d, $J = 7.8$ Hz), 7.70 (d, $J = 8.1$ Hz), 7.57 (d, $J = 8.4$ Hz), 7.41 (d, $J = 1.6$ Hz), 7.34 (dd, $J = 18.0, 8.1$ Hz), 7.17 (t, $J = 7.5$ Hz), 5.35 (s), 4.04 (d, $J = 11.3$ Hz), 3.90 (td, $J = 11.6, 3.9$ Hz), 3.68 (d, $J = 10.4$

Hz), 3.42 (d, $J = 11.1$ Hz), 2.26 (d, $J = 13.2$ Hz), 1.93 (d, $J = 12.6$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 169.0, 153.0, 150.2, 147.6, 139.0, 135.3, 133.7, 132.3, 131.4, 129.7, 127.0, 126.6, 123.2, 121.7, 120.0, 108.1, 83.1, 43.7, 41.3, 38.7, 20.3; HRMS (ESI/Q-TOF) m/z , $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{17}^{35}\text{Cl}_2\text{N}_5\text{O}_2\text{S}$: 474.0553, Found: 474.0561.

7-(5-Chlorobenzo[*d*]thiazol-2-yl)-9-nitro-8-phenyl-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidin-6-amine (4h)

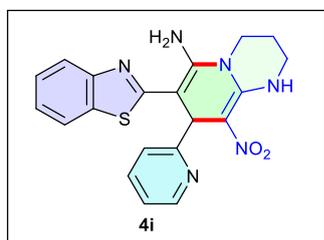
4h was prepared by following the general procedure **GP1** using (*E*)-2-(5-chlorobenzo[*d*]thiazol-2-yl)-3-phenylacrylonitrile **1r** (74 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h followed by filtration. Orange solid (93.6 mg, 88 %) m.p.: 256–258 °C; ^1H NMR (500 MHz,



DMSO- d_6) δ 11.42 (s, 1H), 8.57 (s, 2H), 7.86 (d, $J = 8.4$ Hz, 1H), 7.75 (s, 1H), 7.34 (d, $J = 7.4$ Hz, 2H), 7.22 (t, $J = 7.4$ Hz, 2H), 7.19–7.11 (m, 2H), 5.14 (s, 1H), 4.01 (d, $J = 10.6$ Hz, 1H), 3.89 (dd, $J = 11.6, 8.2$ Hz, 1H), 3.64 (d, $J = 10.7$ Hz, 1H), 3.41 (t, $J = 11.2$ Hz, 1H), 2.24 (d, $J = 13.4$ Hz, 1H), 1.93 (d, $J = 12.2$

Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 171.0, 154.6, 150.0, 147.6, 143.5, 131.2, 130.1, 128.5, 128.2, 127.1, 123.0, 122.7, 119.3, 109.9, 85.4, 43.5, 41.7, 40.2, 40.0, 39.8, 38.8, 20.3; HRMS (ESI/Q-TOF) m/z , $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{19}\text{ClN}_5\text{O}_2\text{S}$: 440.0943 Found: 440.0957.

7-(Benzo[*d*]thiazol-2-yl)-9-nitro-8-(pyridin-2-yl)-1,3,4,8-tetrahydro-2*H*-pyrido[1,2-*a*]pyrimidin-6-amine (4i)

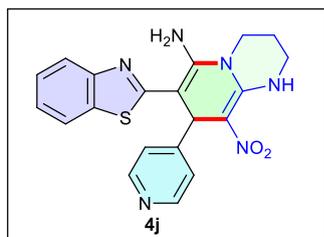


4i was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(pyridin-2-yl)acrylonitrile **1s** (65 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (100 mg, 98%) m.p.: 243.8–244.7 °C;

^1H NMR (500 MHz, DMSO- d_6) δ 11.46 (d, $J = 4.3$ Hz, 1H), 8.45 (s, 2H), 8.39 (d, $J = 4.2$ Hz, 1H), 7.87 (d, $J = 7.9$ Hz, 1H), 7.68 (d, $J = 8.1$ Hz, 1H), 7.64 (dd, $J = 7.6, 1.5$ Hz, 1H), 7.45 (d, $J = 7.8$ Hz, 1H), 7.34 (t, $J = 7.6$ Hz, 1H), 7.17 (d, $J = 7.6$ Hz, 1H), 7.16–7.11 (m, 1H), 5.26 (s, 1H), 3.90 (dd, $J = 9.4, 3.9$ Hz, 2H), 3.64 (d, $J = 3.9$ Hz, 1H), 3.42 (s, 1H), 2.23

(dd, $J = 10.2, 3.4$ Hz, 1H), 2.09–1.66 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO) δ 169.2, 161.8, 153.6, 151.0, 150.0, 147.3, 136.3, 131.3, 126.6, 123.5, 123.1, 122.5, 121.7, 120.0, 109.3, 84.8, 44.4, 43.5, 20.4; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{19}\text{N}_6\text{O}_2\text{S}$: 407.1285, Found : 407.1282.

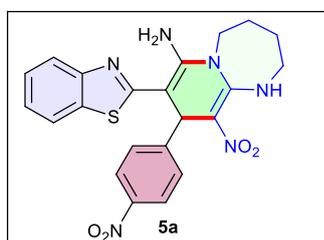
7-(benzo[d]thiazol-2-yl)-9-nitro-8-(pyridin-4-yl)-1,3,4,8-tetrahydro-2H-pyrido[1,2-a]pyrimidin-6-amine 4j



4j was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(pyridin-4-yl)acrylonitrile **1t** (65 mg, 0.25 mmol) and 2-(nitromethylene)hexahydropyrimidine **2b** (35 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (80.6 mg, 80%) m.p.: 250.7–251.4 °C ^1H

NMR (500 MHz, DMSO- d_6) δ 11.38 (s, 1H), 8.58 (s, 1H), 8.43 (d, $J = 5.5$ Hz, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.35 (t, $J = 6.6$ Hz, 3H), 7.17 (t, $J = 7.5$ Hz, 1H), 5.18 (s, 1H), 4.03 (d, $J = 11.1$ Hz, 1H), 3.96–3.81 (m, 1H), 3.64 (d, $J = 11.4$ Hz, 1H), 3.42 (d, $J = 10.9$ Hz, 1H), 2.24 (d, $J = 13.4$ Hz, 1H), 1.96 (dd, $J = 24.3, 11.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.3, 153.0, 151.4, 149.6, 149.4, 146.7, 130.7, 126.1, 122.7, 121.2, 119.6, 108.2, 83.3, 43.0, 40.9, 38.4, 19.7; HRMS (ESI/Q-TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{19}\text{N}_6\text{O}_2\text{S}$: 407.1285, Found: 407.1294.

8-(Benzo[d]thiazol-2-yl)-10-nitro-9-(4-nitrophenyl)-1,2,3,4,5,9-hexahydropyrido[1,2-a][1,3]diazepin-7-amine (5a)

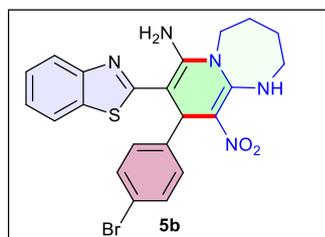


5a was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(4-nitrophenyl)acrylonitrile **1b** (76 mg, 0.25 mmol) and 2-(nitromethylene)-1,3-diazepane **2c** (39 mg, 0.25 mmol) in EtOH at reflux for 12 h followed by filtration. Orange solid (90.1 mg, 77%) m.p.: 242.4–243.1 °C;

^1H NMR (500 MHz, DMSO- d_6) δ 10.52 (s, 1H), 8.13 (d, $J = 8.5$ Hz, 4H), 7.89 (d, $J = 7.9$ Hz, 1H), 7.75 (d, $J = 8.1$ Hz, 1H), 7.55 (d, $J = 8.6$ Hz, 2H), 7.37 (t, $J = 7.6$ Hz, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 5.42 (s, 1H), 4.31 (d, $J = 14.0$ Hz, 1H), 3.80 (dd, $J = 8.6, 4.2$ Hz, 1H), 3.55 (t, $J = 12.4$ Hz, 1H), 3.37 (d, $J = 16.1$ Hz, 1H), 2.10 (d, $J = 9.3$ Hz, 1H), 1.89 (dd, $J = 23.0, 8.8$ Hz, 2H), 1.58 (d, $J = 8.3$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.4, 156.6,

153.7, 151.0, 149.7, 146.9, 131.4, 128.9, 126.7, 124.2, 123.5, 121.9, 120.5, 113.5, 87.6, 53.2, 45.4, 42.3, 26.6, 25.5. **HRMS** (ESI/Q-TOF) m/z , $[M+H]^+$ Calcd for $C_{22}H_{22}N_6O_4S$: 465.1340, Found: 465.1342.

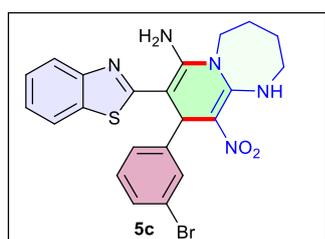
8-(Benzo[d]thiazol-2-yl)-9-(4-bromophenyl)-10-nitro-1,2,3,4,5,9-hexahydropyrido[1,2-a][1,3]diazepin-7-amine (5b)



5b was prepared by following the general procedure **GPI** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(4-bromophenyl)acrylonitrile **1e** (85 mg, 0.25 mmol) and 2-(nitromethylene)-1,3-diazepane **2c** (39 mg, 0.25 mmol) in EtOH at reflux for 12 h followed by filtration. Yellow solid (82.2 mg, 66%) m.p.: 251.7-252.1; 1H

NMR (500 MHz, $DMSO-d_6$) δ 10.50 (s, 1H), 8.08 (d, $J = 8.4$ Hz, 4H), 7.82 (d, $J = 7.7$ Hz, 1H), 7.70 (d, $J = 8.0$ Hz, 1H), 7.51 (d, $J = 8.3$ Hz, 2H), 7.31 (t, $J = 7.4$ Hz, 1H), 7.15 (d, $J = 7.4$ Hz, 1H), 5.38 (s, 1H), 4.28 (d, $J = 13.2$ Hz, 1H), 3.75 (d, $J = 4.3$ Hz, 1H), 3.51 (t, $J = 12.0$ Hz, 1H), 2.05 (s, 1H), 1.89–1.78 (m, 3H), 1.55 (s, 1H); $^{13}C\{^1H\}$ **NMR** 168.4, 153.7, 151.0, 149.7, 146.9, 131.4, 129.0, 128.9, 126.7, 124.3, 124.2, 124.2, 123.5, 121.9, 120.5, 113.5, 87.7, 60.3, 53.2, 45.4, 42.3, 26.6, 25.6, 21.3, 14.6; **HRMS** (ESI/Q-TOF) m/z , $[M+H]^+$ Calcd for $C_{22}H_{21}^{79}BrN_5O_2S$: 498.0594, Found: 498.0592.

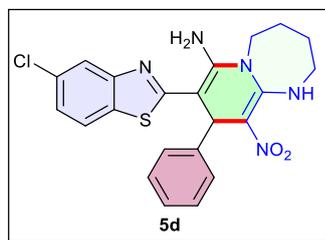
8-(Benzo[d]thiazol-2-yl)-10-nitro-9-(3-nitrophenyl)-1,2,3,4,5,9-hexahydropyrido[1,2-a][1,3]diazepin-7-amine (5c)



5c was prepared by following the general procedure **GPI** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(3-bromophenyl)acrylonitrile **1l** (85 mg, 0.25 mmol) and 2-(nitromethylene)-1,3-diazepane **2c** (39 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (122.2 mg, 92 %) m.p.: 223–235 °C; 1H

NMR (500 MHz, $DMSO-d_6$) δ 10.50 (s, 1H), 8.07 (s, 2H), 7.90 (d, $J = 8.0$ Hz, 1H), 7.75 (d, $J = 8.4$ Hz, 1H), 7.45 (s, 1H), 7.38 (d, $J = 7.8$ Hz, 2H), 7.34 – 7.14 (m, 3H), 5.30 (s, 1H), 4.28 (s, 1H), 3.78 (d, $J = 14.7$ Hz, 1H), 3.49 (m, $J = 25.8$ Hz, 2H), 2.08 (s, 1H), 1.87 (m, 2H), 1.57 (s, 1H). ^{13}C **NMR** (126 MHz, $DMSO-d_6$) δ 168.6, 156.6, 153.7, 149.5, 146.2, 131.5, 131.3, 130.5, 130.3, 126.7, 126.5, 123.5, 122.1, 122.0, 120.5, 114.1, 88.1, 79.7, 53.2, 45.5, 42.1, 26.7, 25.6; **HRMS** (ESI/Q-TOF) m/z , $[M+H]^+$ Calcd for $C_{22}H_{21}^{79}BrN_5O_2S$: 465.1340, Found: 465.1342.

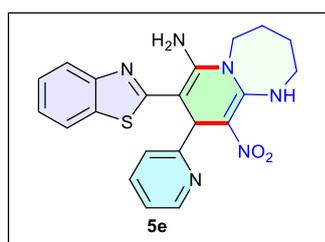
8-(5-Chlorobenzod[*d*]thiazol-2-yl)-10-nitro-9-phenyl-1,2,3,4,5,9-hexahydropyrido[1,2-*b*][1,3]diazepin-7-amine (5d)



5d was prepared by following the general procedure **GP1** using (*E*)-2-(5-chlorobenzod[*d*]thiazol-2-yl)-3-phenylacrylonitrile **1r** (74 mg, 0.25 mmol) and 2-(nitromethylene)-1,3-diazepane **2c** (39 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (79.4 mg, 70 %) m.p.: 255.9–256.7 °C;

¹H NMR (500 MHz, DMSO-*d*₆) δ 10.50 (s, 1H), 8.12 (s, 2H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.28 (t, *J* = 7.0 Hz, 3H), 7.25 (d, *J* = 7.8 Hz, 2H), 7.21 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.16 (t, *J* = 7.0 Hz, 1H), 5.27 (s, 1H), 4.30 (d, *J* = 13.9 Hz, 1H), 3.85–3.69 (m, 1H), 3.50 (t, *J* = 12.5 Hz, 1H), 3.38 (s, 1H), 2.10 (d, *J* = 9.5 Hz, 1H), 1.88 (dd, *J* = 23.8, 9.0 Hz, 2H), 1.57 (d, *J* = 8.8 Hz, 1H); **¹³C{¹H} NMR** (126 MHz, DMSO-*d*₆) δ 170.8, 156.5, 154.9, 150.1, 143.3, 131.3, 130.3, 128.9, 127.7, 127.3, 123.2, 123.1, 119.7, 114.7, 88.9, 53.3, 45.4, 42.2, 26.7, 25.7; **HRMS** (ESI/Q-TOF) *m/z*, [M+H]⁺ Calcd for C₂₂H₂₁³⁵ClN₅O₂S: 453.1021 Found: 453.1025.

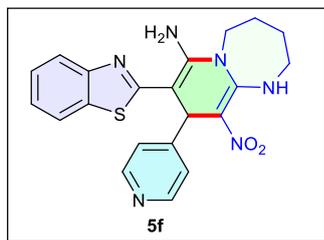
8-(Benzo[*d*]thiazol-2-yl)-10-nitro-9-(pyridin-2-yl)-1,2,3,4,5,9-hexahydropyrido[1,2-*b*][1,3]diazepin-7-amine (5e)



5e was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(pyridin-2-yl)acrylonitrile **1s** (65 mg, 0.25 mmol) and 2-(nitromethylene)-1,3-diazepane **2c** (39 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (85.6 mg, 80%) m.p.: 243.5–244.0 °C **¹H**

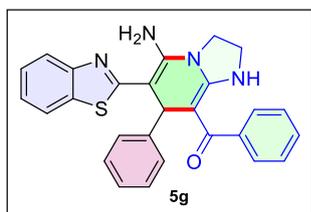
NMR (500 MHz, DMSO-*d*₆) δ 10.58 (s, 1H), 8.41 (d, *J* = 4.2 Hz, 1H), 7.98 (s, 2H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.67 (td, *J* = 7.7, 1.2 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.16 (dd, *J* = 7.2, 5.0 Hz, 1H), 5.33 (s, 1H), 4.26–4.02 (m, 1H), 3.89–3.62 (m, 1H), 3.46 (t, *J* = 12.4 Hz, 1H), 3.33 (s, 1H), 2.07 (d, *J* = 9.2 Hz, 1H), 1.94 (dd, *J* = 13.1, 4.8 Hz, 1H), 1.89–1.79 (m, 1H), 1.54 (d, *J* = 8.9 Hz, 1H); **¹³C{¹H} NMR** (126 MHz, DMSO-*d*₆) δ 168.7, 161.4, 158.0, 153.9, 150.5, 150.3, 136.7, 131.4, 126.6, 123.3, 122.9, 122.7, 121.8, 120.3, 114.0, 89.0, 54.5, 45.3, 44.7, 26.8, 25.8. **HRMS** (ESI/Q-TOF) *m/z* [M+H]⁺ Calcd for C₂₁H₂₁N₆O₂S: 421.1441, Found: 421.1440.

8-(Benzo[*d*]thiazol-2-yl)-10-nitro-9-(pyridin-4-yl)-1,2,3,4,5,9-hexahydropyrido[1,2-*a*][1,3]diazepin-7-amine (5f)



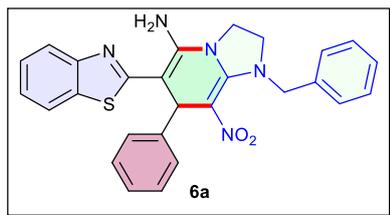
5f was prepared by following the general procedure **GP1** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(pyridin-4-yl)acrylonitrile **1t** (65 mg, 0.25 mmol) and 2-(nitromethylene)-1,3-diazepane (39 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (, 85%) m.p.: 251–251.8 °C ¹H NMR (500 MHz, DMSO-*d*₆) δ 10.51 (s, 1H), 8.45 (d, *J* = 5.8 Hz, 2H), 8.09 (s, 2H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 5.8 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 4.29 (d, *J* = 13.9 Hz, 1H), 3.79 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.52 (t, *J* = 12.3 Hz, 1H), 3.40 (s, 1H) 2.09 (d, *J* = 9.5 Hz, 1H), 1.87 (t, *J* = 13.4 Hz, 2H), 1.58 (d, *J* = 8.5 Hz, 1H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 168.5, 156.7, 153.8, 152.0, 150.3, 149.7, 131.4, 126.7, 123.5, 122.8, 121.9, 120.5, 113.4, 87.4, 79.7, 53.2, 45.5, 41.9, 26.7, 25.6. HRMS (ESI/Q-TOF) *m/z* [M+H]⁺ Calcd for C₂₁H₂₂N₆O₂S: 421.1441, Found: 421.1453.

(5-amino-6-(benzo[*d*]thiazol-2-yl)-7-phenyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-8-yl)(phenyl)methanone (5g)



5g was prepared by following the general procedure **GP1** using (2-(benzo[*d*]thiazol-2-yl)-3-phenylacrylonitrile **1a** (62 mg, 0.25 mmol) and 2-(imidazolidin-2-ylidene)-1-phenylethan-1-one **2f** (47 mg, 0.25 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (60 mg, 53%) m.p.: 296–296.9 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.15 (s, 1H), 8.39 (s, 2H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.51 – 7.41 (m, 3H), 7.32 – 7.20 (m, 3H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.99 (dq, *J* = 14.3, 7.4 Hz, 2H), 6.66 (d, *J* = 7.4 Hz, 2H), 4.81 (s, 1H), 4.09 (td, *J* = 9.5, 4.9 Hz, 1H), 4.02 (q, *J* = 9.5 Hz, 1H), 3.89 – 3.75 (m, 2H). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 190.6, 169.7, 155.3, 154.0, 148.2, 147.4, 142.7, 131.1, 129.4, 128.7, 128.3, 127.3, 127.0, 126.3, 126.2, 122.2, 121.5, 119.4, 89.7, 84.9, 44.0, 43.6, 43.4, 40.2, 40.1 39.9; HRMS (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₇H₂₃N₄OS: 451.1587, Found: 451.1586.

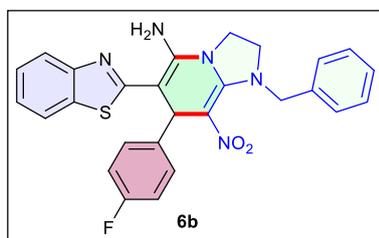
6-(Benzo[*d*]thiazol-2-yl)-1-benzyl-8-nitro-7-phenyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (6a)



6a was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-phenylacrylonitrile **1a** (98 mg, 0.37 mmol) and (1-benzyl-2-(nitromethylene)imidazolidine) **2d** (54 mg, 0.25 mmol) with NaHCO₃ (4 mg, 0.05 mmol) in EtOH at reflux for 12

h, followed by filtration. Orange solid (108.0 mg, 90%) m.p.: 257.7–258.2 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.33 (s, 2H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.20–7.16 (m, 2H), 7.14 (dd, *J* = 13.9, 6.6 Hz, 3H), 7.03 (d, *J* = 7.4 Hz, 2H), 5.35 (s, 1H), 4.87 (d, *J* = 15.4 Hz, 1H), 4.62 (d, *J* = 15.4 Hz, 1H), 4.32–4.17 (m, 1H), 4.08 (dd, *J* = 13.1, 6.8 Hz, 1H), 4.01–3.89 (m, 1H), 3.75 (q, *J* = 10.2 Hz, 1H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 168.9, 153.9, 153.3, 145.0, 144.0, 135.8, 131.6, 129.0, 128.8, 128.2, 128.0, 127.4, 127.1, 126.5, 123.0, 121.8, 120.0, 107.3, 85.2, 53.6, 49.7, 43.8, 43.5; HRMS (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₇H₂₄N₅O₂S: 482.1645, Found: 482.1651.

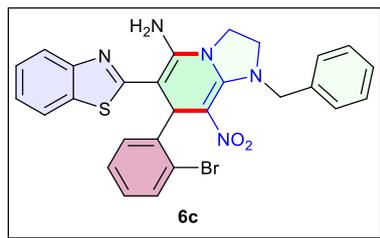
6-(Benzo[*d*]thiazol-2-yl)-1-benzyl-7-(4-fluorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (**6b**)



6b was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(4-fluorophenyl)acrylonitrile **1f** (103 mg, 0.25 mmol) and (1-benzyl-2-(nitromethylene)imidazolidine) **2d** (54 mg, 0.25 mmol) with NaHCO₃ (4 mg, 0.05 mmol) in EtOH at reflux for 12 h,

followed by filtration. Yellow solid (118.3 mg, 95 %) m.p.: 200–203 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.37 (s, 2H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.28–7.24 (m, 2H), 7.18 (dd, *J* = 12.7, 5.4 Hz, 1H), 7.13 (dd, *J* = 13.9, 6.4 Hz, 3H), 7.02 (dd, *J* = 10.1, 8.0 Hz, 4H), 5.31 (s, 1H), 4.88 (d, *J* = 15.4 Hz, 1H), 4.61 (d, *J* = 15.5 Hz, 1H), 4.28 (dd, *J* = 19.4, 9.9 Hz, 1H), 4.14–4.04 (m, 1H), 4.00 (td, *J* = 10.8, 6.3 Hz, 1H), 3.81 (q, *J* = 10.3 Hz, 1H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) 168.7, 162.5, 161.5 (d, *J*_{C-F} = 242.3 Hz), 160.6, 153.9, 153.4, 153.0, 145.0, 140.2, 135.9, 131.5, 129.3, 129.2 (d, *J*_{C-F} = 7.9 Hz), 128.9, 128.1, 128.0, 126.6, 123.0, 121.8, 120.1, 115.5 (d, *J*_{C-F} = 21.1 Hz), 115.4, 107.4, 85.0, 53.6, 50.1, 43.8, 42.9; HRMS (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₇H₂₃FN₅O₂S: 500.1551, Found: 500.1555; ¹⁹F NMR (471 MHz, DMSO-*d*₆): δ -111.50 to -111.60 (m, 1F).

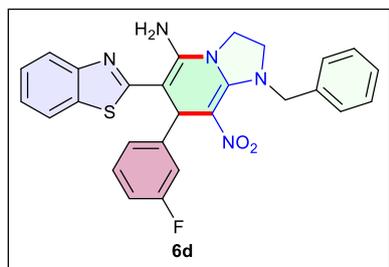
6-(Benzo[d]thiazol-2-yl)-1-benzyl-7-(2-bromophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-a]pyridin-5-amine (6c)



6c was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(2-bromophenyl)acrylonitrile **1i** (126 mg, 0.25 mmol) and (1-benzyl-2-(nitromethylene)imidazolidine) **2d** (54 mg, 0.25 mmol) with NaHCO₃ (4 mg, 0.05 mmol) in EtOH at reflux for 12 h,

followed by filtration. Orange solid (133.1 mg, 95%) m.p.: 246.8–247.9 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.46 (s, 2H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.22 (s, 5H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.3 Hz, 1H), 5.50 (s, 1H), 4.70 (q, *J* = 15.3 Hz, 2H), 4.42–4.24 (m, 1H), 4.14 (dd, *J* = 18.2, 9.9 Hz, 1H), 3.95 (dd, *J* = 18.7, 10.7 Hz, 1H), 3.78 (dt, *J* = 17.5, 8.9 Hz, 1H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 168.6, 153.5, 153.3, 145.4, 142.2, 135.7, 134.1, 133.3, 131.6, 129.0, 128.9, 128.5, 128.1, 127.7, 126.5, 123.0, 122.8, 121.7, 120.0, 105.0, 85.2, 54.5, 49.3, 45.3, 43.8; HRMS (ESI/Q-TOF) *m/z*: [M+H]⁺ Calcd for C₂₇H₂₃⁷⁹BrN₅O₂S: 560.0750, Found: 560.0752.

6-(Benzo[d]thiazol-2-yl)-1-benzyl-7-(4-fluorophenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-a]pyridin-5-amine (6d)

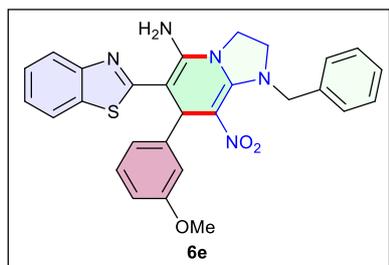


6d was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(3-fluorophenyl)acrylonitrile **1k** (103 mg, 0.25 mmol) and (1-benzyl-2-(nitromethylene)imidazolidine) **2d** (54 mg, 0.25 mmol) with NaHCO₃ (4 mg, 0.05 mmol) in EtOH at reflux for 12 h, followed by filtration. Orange solid (133.1 mg, 95%)

m.p.: 265.4–266.7 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.37 (s, 2H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.26 (dd, *J* = 14.5, 8.1 Hz, 1H), 7.19–7.13 (m, 2H), 7.10 (t, *J* = 6.8 Hz, 3H), 7.03 (d, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 5.35 (s, 1H), 4.90 (d, *J* = 15.4 Hz, 1H), 4.62 (d, *J* = 15.5 Hz, 1H), 4.27 (dd, *J* = 19.5, 9.8 Hz, 1H), 4.13 (dt, *J* = 16.0, 8.1 Hz, 1H), 4.01 (td, *J* = 10.7, 6.4 Hz, 1H), 3.84 (dd, *J* = 19.4, 10.2 Hz, 1H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 168.7, 162.17 (d, *J*_{C-F} = 243.7), 153.9, 153.0, 147.0, 147.0, 145.1, 135.8, 131.5, 130.1 (d, *J*_{C-F} = 8.1 Hz), 128.9, 128.9, 128.9, 128.8, 128.8, 128.8, 128.1, 128.1, 126.6, 123.5, 123.5, 123.0, 121.8, 120.1, 114.1, 113.9 (d, *J*_{C-F} =

21.1 Hz), 107.0, 84.4, 53.6, 50.2, 43.8, 43.4; **HRMS** (ESI/Q-TOF) m/z , $[M+H]^+$ Calcd for $C_{27}H_{23}FN_5O_2S$: 500.1551, Found: 500.1551; ^{19}F **NMR** (471 MHz, $DMSO-d_6$): δ -113.00 (dd, 1F).

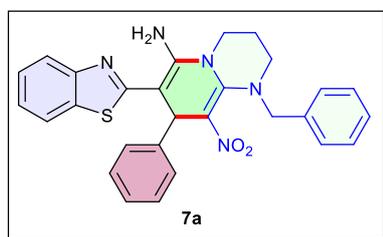
6-(Benzo[*d*]thiazol-2-yl)-1-benzyl-7-(3-methoxyphenyl)-8-nitro-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridin-5-amine (6e)



6e was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(3-methoxyphenyl)-acrylonitrile **1m** (108 mg, 0.25 mmol) and (1-benzyl-2-(nitromethylene)imidazolidine) **2d** (54 mg, 0.25 mmol) with $NaHCO_3$ (4 mg, 0.05 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (121.2 mg, 95%) m.p.:

278.9-279.3; 1H **NMR** (500 MHz, $DMSO-d_6$) δ 8.33 (s, 2H), 7.84 (d, $J = 7.9$ Hz, 1H), 7.72 (d, $J = 8.1$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.18 (dd, $J = 12.9, 7.4$ Hz, 3H), 7.14 (d, $J = 3.6$ Hz, 1H), 7.11 (d, $J = 7.4$ Hz, 1H), 7.02 (d, $J = 7.5$ Hz, 2H), 6.86 (d, $J = 7.7$ Hz, 1H), 6.82 (s, 1H), 6.76 (dd, $J = 8.1, 2.0$ Hz, 1H), 5.35 (s, 1H), 4.89 (d, $J = 15.4$ Hz, 1H), 4.60 (d, $J = 15.4$ Hz, 1H), 4.33-4.22 (m, 1H), 4.06 (dd, $J = 13.1, 6.8$ Hz, 1H), 4.01-3.91 (m, 1H), 3.78-3.69 (m, 1H), 3.66 (s, 3H); $^{13}C\{^1H\}$ **NMR** (126 MHz, $DMSO-d_6$) δ 168.8, 153.5, 150.0, 147.8, 147.3, 145.7, 134.7, 131.2, 130.3, 126.7, 123.2, 122.7, 122.3, 121.9, 120.2, 109.2, 84.1, 43.6, 41.7, 39.0, 20.2; **HRMS** (ESI/Q-TOF) m/z : $[M+H]^+$ Calcd for $C_{28}H_{26}N_5O_3S$: 512.1751, Found: 512.1751.

7-(Benzo[*d*]thiazol-2-yl)-1-benzyl-9-nitro-8-phenyl-1,3,4,8-tetrahydro-2H-pyrido[1,2-*a*]pyrimidin-6-amine (7a)

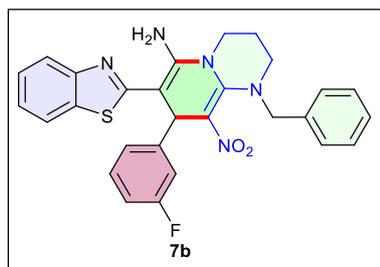


7a was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-phenylacrylonitrile **1a** (98 mg, 0.25 mmol) and (1-benzyl-2-(nitromethylene)hexahydropyrimidine) **2e** (58 mg, 0.25 mmol) with $NaHCO_3$ (4 mg, 0.05 mmol) in EtOH at reflux

for 12 h, followed by filtration. Yellow solid (111.2 mg, 90%) m.p.: 212.1-212.6; 1H **NMR** (500 MHz, $DMSO-d_6$) δ 8.33 (s, 1H), 7.90 (d, $J = 5.4$ Hz, 1H), 7.82 (d, $J = 5.9$ Hz, 1H), 7.41 (s, 1H), 7.31 (s, 1H), 7.28 (s, 1H), 7.23 (s, 1H), 7.14 (s, 1H), 7.14 (s, 1H), 6.71 (s, 1H), 5.74 (s, 1H), 4.26 (dd, $J = 38.2, 13.2$ Hz, 2H), 3.42 (s, 1H), 3.10 (s, 1H), 2.01 (d, $J = 21.8$ Hz, 1H), 1.64 (s, 1H); $^{13}C\{^1H\}$ **NMR** (126 MHz, $DMSO-d_6$) δ 168.4, 153.4, 153.1, 145.9, 142.6,

128.8, 128.5, 128.2, 128.0, 126.8, 126.1, 126.0, 123.0, 121.5, 120.1, 107.5, 89.4, 58.2, 44.7, 43.2, 41.5, 22.1. **HRMS** (ESI/Q-TOF) m/z : $[M+H]^+$ Calcd for $C_{28}H_{26}N_5O_2S$: 496.1802, Found: 496.1805.

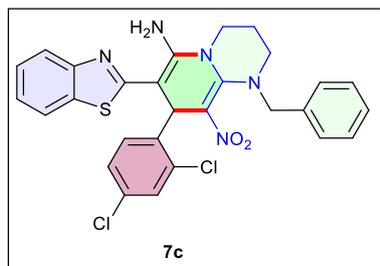
7-(Benzo[d]thiazol-2-yl)-1-benzyl-8-(3-fluorophenyl)-9-nitro-1,3,4,8-tetrahydro-2H-pyrido[1,2-a]pyrimidin-6-amine (7b)



7b was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(3-fluorophenyl)acrylonitrile **1k** (103 mg, 0.25 mmol) and (1-benzyl-2-(nitromethylene)hexahydropyrimidine **2e** (58 mg, 0.25 mmol) with $NaHCO_3$ (4 mg, 0.05 mmol) with $NaHCO_3$ (4 mg, 0.05 mmol) in EtOH at reflux for 12 h, followed by

filtration. Yellow solid (133.1 mg, 95%) m.p.: 216.6–217.1 °C; **1H NMR** (500 MHz, $DMSO-d_6$) δ 8.37 (s, 2H), 7.90 (d, $J = 7.9$ Hz, 1H), 7.81 (d, $J = 8.1$ Hz, 1H), 7.41 (t, $J = 7.7$ Hz, 1H), 7.35 (dd, $J = 14.1, 7.9$ Hz, 1H), 7.23 (td, $J = 7.4, 4.3$ Hz, 2H), 7.14 (t, $J = 7.6$ Hz, 2H), 7.11–7.06 (m, 2H), 6.96 (d, $J = 9.9$ Hz, 1H), 6.75 (d, $J = 7.5$ Hz, 2H), 5.72 (s, 1H), 4.30 (d, $J = 6.2$ Hz, 2H), 4.28–4.20 (m, 1H), 3.50–3.41 (m, 1H), 3.33 (d, $J = 8.3$ Hz, 1H), 3.16 (dt, $J = 13.7, 6.9$ Hz, 1H), 2.04 (ddd, $J = 13.0, 7.8, 2.6$ Hz, 1H), 1.69 (ddd, $J = 13.2, 6.7, 3.9$ Hz, 1H); **$^{13}C\{^1H\}$ NMR** (126 MHz, $DMSO-d_6$) δ 168.8, 153.4, 153.0 (d, $J_{C-F} = 244.3$ Hz), 146.6, 145.7, 128.5, 128.1, 128.0, (d, $J_{C-F} = 7.9$ Hz), 126.3, 123.1, 122.1, 121.5, 120.2, 112.6 (d, $J_{C-F} = 21.1$ Hz), 107.2, 88.7, 58.2, 45.2, 43.2, 41.4, 22.2; **HRMS** (ESI/Q-TOF) m/z : $[M+H]^+$ Calcd for $C_{28}H_{25}FN_5O_2S$: 514.1708, Found 514.1706; **^{19}F NMR** (471 MHz, $DMSO-d_6$): δ -112.55 (dd, 1F).

7-(Benzo[d]thiazol-2-yl)-1-benzyl-8-(2,4-dichlorophenyl)-9-nitro-1,3,4,8-tetrahydro-2H-pyrido[1,2-a]pyrimidin-6-amine (7c)

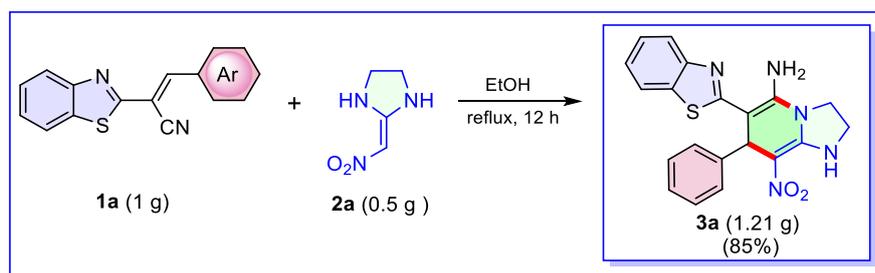


7c was prepared by following the general procedure **GP2** using (*E*)-2-(benzo[d]thiazol-2-yl)-3-(2,4-dichlorophenyl)acrylonitrile **1o** (122 mg, 0.25 mmol) and (1-benzyl-2-(nitromethylene)hexahydropyrimidine **2e** (58 mg, 0.25 mmol) with $NaHCO_3$ (4 mg, 0.05 mmol) in EtOH at reflux for 12 h, followed by filtration. Yellow solid (114 mg, 75%),

m.p.: 209.4–210.8 °C; **1H NMR** (500 MHz, $DMSO-d_6$) δ 8.40 (s, 2H), 7.90 (d, $J = 7.5$ Hz, 1H), 7.81 (d, $J = 8.0$ Hz, 1H), 7.59 (d, $J = 2.2$ Hz, 1H), 7.43–7.39 (m, 1H), 7.36 (dd, $J = 8.4,$

2.2 Hz, 1H), 7.23 (ddd, $J = 8.1, 4.3, 2.1$ Hz, 2H), 7.12 (d, $J = 2.7$ Hz, 1H), 7.12–7.08 (m, 2H), 6.59 (d, $J = 7.4$ Hz, 2H), 5.92 (s, 1H), 4.54 (d, $J = 14.8$ Hz, 1H), 4.34 (d, $J = 14.9$ Hz, 1H), 4.24 (ddd, $J = 12.9, 7.8, 4.9$ Hz, 1H), 3.48 (ddd, $J = 11.5, 6.2, 4.5$ Hz, 2H), 3.19–3.01 (m, 1H), 2.14–2.00 (m, 1H), 1.61–1.48 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 168.2, 154.1, 154.0, 147.0, 138.3, 135.5, 134.9, 132.8, 131.8, 130.2, 129.2, 128.9, 128.5, 128.2, 127.9, 126.8, 123.7, 122.0, 120.7, 103.9, 89.9, 59.1, 45.2, 43.7, 21.9; HRMS (ESI/Q-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{24}^{35}\text{Cl}_2\text{N}_5\text{O}_2\text{S}$: 564.1022, Found: 564.1027.

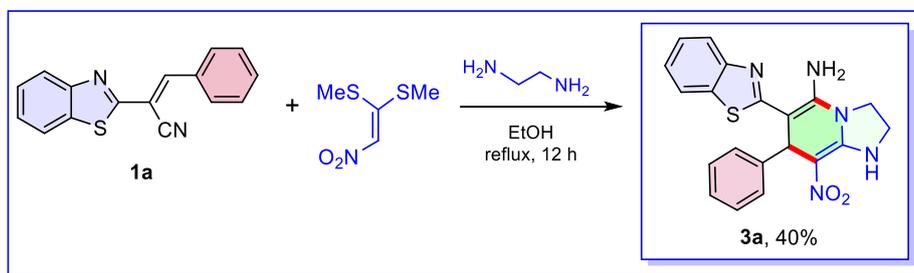
10. Gram-scale Synthesis



To an Oven dried 50 mL round-bottom flask equipped with magnetic stir bar, compound **1a** (1.0 g, 3.81 mmol, 1 equiv) and (2-nitromethylene)imidazolidine **2a** (0.5 g, 3.87 mmol, 1 equiv) were dissolved in ethanol (25 mL). The reaction mixture was then heated to reflux and stirred for 12 h. Upon completion of the reaction, the mixture was cooled to room temperature, leading to the formation of a precipitate. The solid product was collected by filtration, washed with cold ethanol, and dried to afford the compound **3a** as pure yellow solid in 85% yield.

11. One-pot Synthesis

Procedure for three-component one-pot reaction

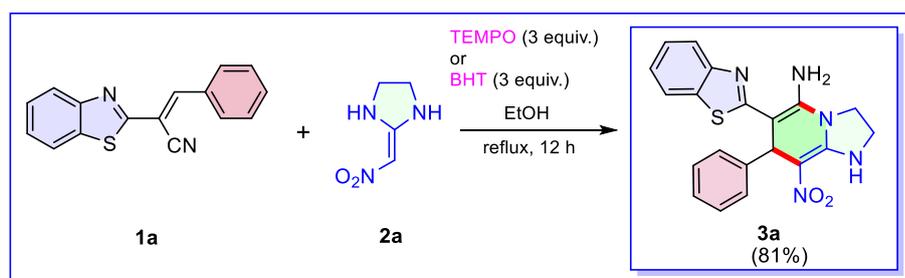


To an Oven dried 10 mL round-bottom flask equipped with magnetic stir bar, compound **1a** (62 mg, 0.25 mmol, 1 equiv) along with (2-nitroethene-1,1-diyl)bis(methylsulfane) (41mg, 0.25 mmol, 1 equiv), and ethylenediamine (15 mg, 0.25 mmol, 1 equiv) were dissolved in ethanol (2 mL) and reflux for 12 h. After completion of the reaction, the mixture was cooled

room temperature, resulting in the formation of a precipitate. The solid product was collected by filtration, washed with cold ethanol, and dried to afford the pure compound **3a** with yield of 40%.

12. Control Experiments:

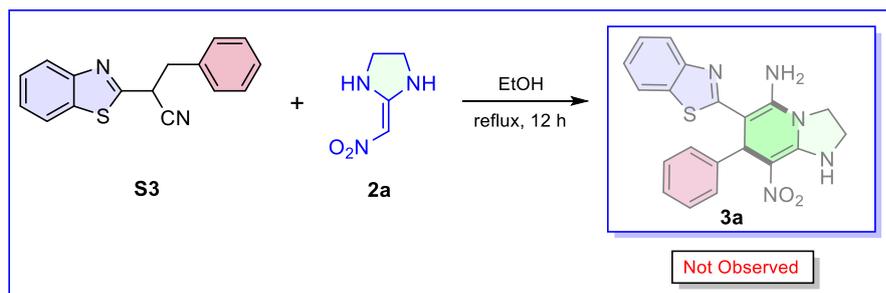
12.1. Radical trapping experiments



To a 10 mL round-bottom flask, compound **1a** (62 mg, 0.25 mmol, 1 equiv) and (2-nitromethylene)imidazolidine **2a** (32 mg, 0.25 mmol, 1 equiv) were added along with ethanol (2 mL). TEMPO (117.1 mg, 0.75 mmol, 3 equiv) /BHT (165.2 mg, 0.75 mmol, 3 equiv) was added and heated at reflux temperature for 12 h. Upon completion of the reaction, the mixture was allowed to cool to room temperature, resulting in the formation of a precipitate. The solid product was collected by filtration, washed with cold ethanol, and dried to afford 78 mg (81%) of pure **3a**.

The observation confirms that the reaction proceeds through radical-free pathway.

12.2. Reaction with 2-(Benzo[d]thiazol-2-yl)-3-phenylpropanenitrile



To a 10 mL round-bottom flask, compound **S3** (0.25 mmol, 1 equiv) and (2-nitromethylene)imidazolidine **2a** (0.25 mmol, 1 equiv) were added along with ethanol (2 mL) as the solvent. The reaction mixture is heated at reflux temperature for 12 h. After 12 h, no precipitate settled in the flask, and TLC observation confirms that both starting materials were unreacted and no product was obtained.

This observation confirms that product formation involves Michael addition in first step.

13. Calculation of Green Matrix

The following green matrix is evaluated for the synthesis of compound **3a**

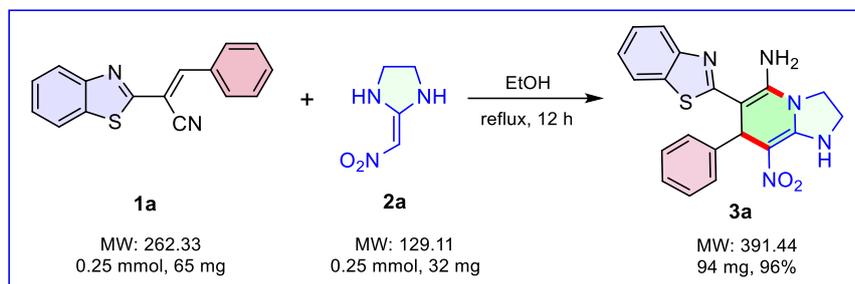


Table S6. Green matrix calculation

Catalyst/reagent	Oil bath	Yield	Atom economy
None	85 °C	96%	99%
Atom efficiency (%) = yield × atom economy/100 = 96 × 99/100 = 95.9%			
Total mass of starting materials (mg) = 65 mg (mass of reactant 1a) + 32 mg (mass of reactant 2a) + 1578.4 mg (solvent) = 1675.4 mg			
Total mass of product + recovered solvent = 93.86 mg + 1420 mg = 1513.86 mg			
Total mass of waste = 1675.4 – 1573.86 = 161.54 mg			
E- Factor (waste/ product) = 1.72 (around the amount of recovered solvent)			
Reaction mass efficiency (RME)(products/materials) = 93.86/(65+32) = 96.7% (yield)			
Process Mass Intensity (PMI)			
(Total mass of starting materials/product) = 1675.4–1420/93.86 = 2.72 (E-factor + 1)			

14. X-ray Crystallographic Analysis

X-Ray Crystallographic Data

Crystals of compounds **3d/3q/7a** were obtained by dissolving the compounds in an appropriate solvent. A suitable crystal was picked and placed on a glass fibre sheet using paraffin oil for mounting. The data were collected at 100 K on a Bruker Kappa (D8 QUEST) Apex-II CCD diffractometer by using graphite monochromated Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$). The crystal structure was solved by using Olex2 software and refined using least-squares minimization. The crystal structure details are deposited at the Cambridge Crystallographic Data Centre with the deposition number.

Compound **3d**

Crystals of compound **3d** were obtained by dissolving the compound in DMSO.

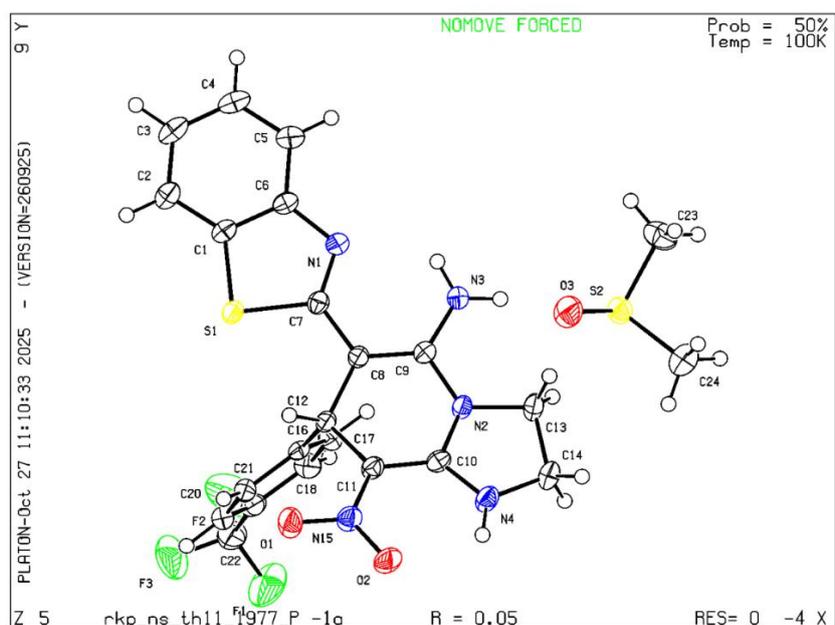


Figure S4: Structure refinement for **3d** (Thermal ellipsoids are shown at the 50% level).

Table S7. Crystal data and structure refinement for **3d**.

Compound	3d (CCDC: 2498191)
Empirical Formula	C ₂₁ H ₁₆ F ₃ N ₅ O ₂ S
Formula weight	537.58
Crystal system	triclinic
Space group	P -1
a (Å)	9.845 (4)
b (Å)	11.454 (4)
c (Å)	12.044 (4)
α (°)	94.609 (9)
β (°)	110.349 (9)
γ (°)	108.894 (9)
Volume (Å ³)	1175.9 (8)
Z	2
Crystal size, mm ³	0.144×0.045×0.044
Density (g/cm ³)	1.518
Absorption coefficient (mm ⁻¹)	0.288
Temp. (K)	100

Compound 3s

Crystals of compound **3s** were obtained by dissolving the compound in DMSO.

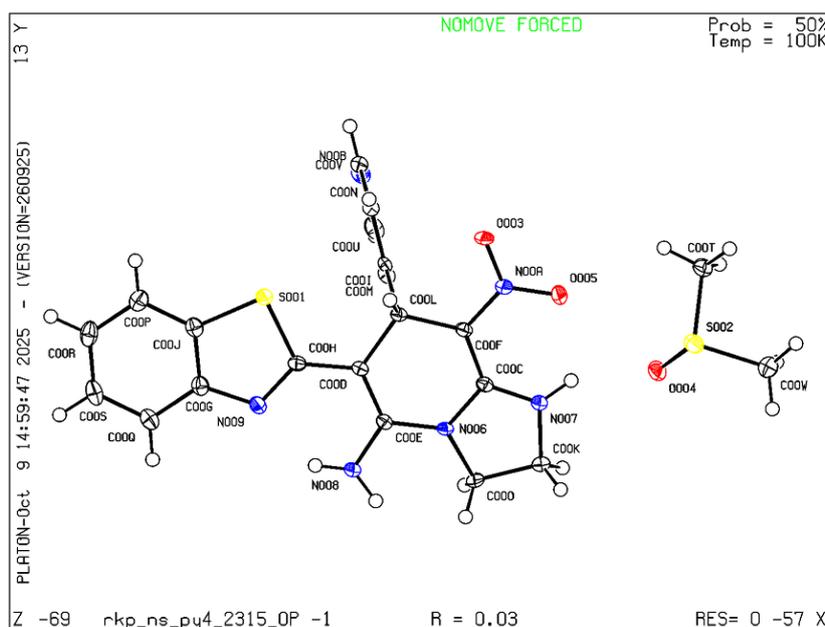


Figure S5. Structure refinement for **3s** (Thermal ellipsoids are shown at the 50% level).

Table S8. Crystal data and structure refinement for **3s**.

Compound	3s (CCDC: 2497628)
Empirical Formula	C ₁₉ H ₁₆ N ₆ O ₂ S
Formula weight	470.56
Crystal system	Triclinic
Space group	P - 1
a (Å)	8.725 (2)
b (Å)	9.713 (2)
c (Å)	13.679 (3)
α (°)	98.871 (9)
β (°)	93.284 (9)
γ (°)	110.537 (8)
Volume (Å ³)	1064.8 (4)
Z	2
Crystal size, mm ³	0.207×0.088×0.032
Density (g/cm ³)	1.468
Absorption coefficient (mm ⁻¹)	0.288
Temp. (K)	100

Compound 7a

Crystals of compound **7a** were obtained by dissolving the compound in DMSO.

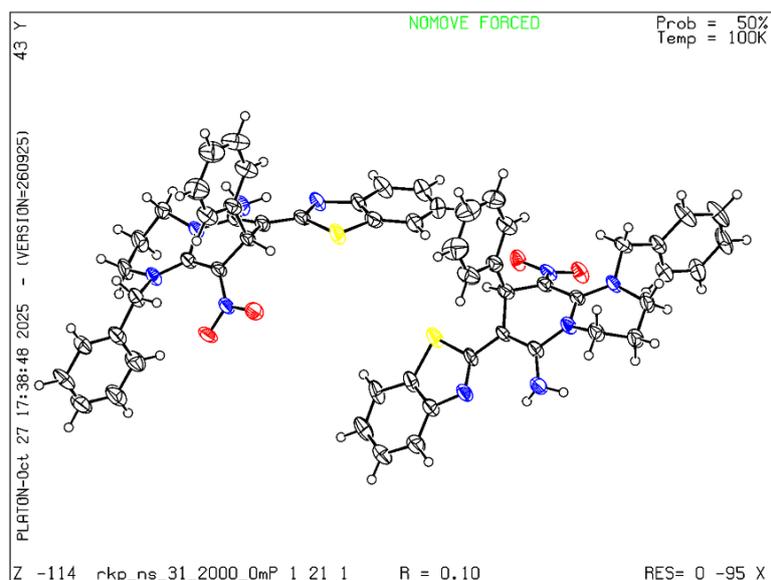
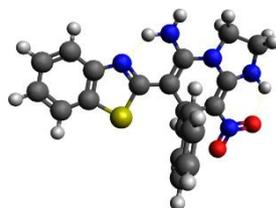


Figure S6: Structure refinement for **7a** (Thermal ellipsoids are shown at the 50% level).

Table S9. Crystal data and structure refinement for **7a**.

Compound	7a (CCDC: 2498289)
Empirical Formula	C ₂₈ H ₂₅ N ₅ O ₂ S
Formula weight	495.59
Crystal system	Monoclinic
Space group	P 21
a (Å)	8.499 (3)
b (Å)	15.707 (6)
c (Å)	18.184 (7)
α (°)	90
β (°)	90
γ (°)	90
Volume (Å ³)	2427.5 (16)
Z	4
Crystal size, mm ³	0.166×0.138×0.082
Density (g/cm ³)	1.356
Absorption coefficient (mm ⁻¹)	0.170
Temp. (K)	100

15. Optimised Structures and coordinated of optimised structure of Compounds 3a



3a

Figure S7. Optimised structures of the compounds **3a** obtained by DFT calculations in DCM solution.

XYZ Coordinates of 3a in S₀ optimized geometry

C	-0.49442758068261	-0.87603001080930	1.19053195926650
C	0.01039251466696	-0.98000866845326	-0.13363731221102
C	-0.10852820652312	0.12125995982109	-1.00065167572597
C	-0.71612115504190	1.28738501370483	-0.54043061544263
C	-1.21074269254216	1.37654245579009	0.77442748904301

C	-1.10388075887063	0.29540979529337	1.65163438275753
C	0.55693940453863	-3.03971057521783	0.56615010555404
H	0.27747811699465	0.04344174797260	-2.01955101531228
H	-0.81069585227297	2.14649335216681	-1.20987877714687
H	-1.68333135401038	2.30129828449335	1.11508341836414
H	-1.48540372601575	0.36374587751789	2.67304681555973
N	0.58251805680726	-2.19168172278688	-0.44257079998905
C	1.07366725011894	-4.38380789629186	0.55195305788880
C	1.03158631149961	-5.20649068685686	1.83601200307882
C	1.69254560564819	-4.87118994569418	-0.59106303180717
C	1.22457002276471	-6.67523544070827	1.53411686233413
C	1.85174220596562	-7.08312368784239	0.37922860983333
C	2.05565537557185	-4.72395056713274	2.87780713558086
C	3.37092624930035	-4.41977729916451	2.49618198009804
C	1.70055303610891	-4.60391014350661	4.22811083048632
C	4.31148587321465	-4.00255787609982	3.44069558951330
C	2.63886315929606	-4.18339482411310	5.17585580433361
H	0.68282845215581	-4.85160211121628	4.53606547494395
C	3.94683065816745	-3.88110938208587	4.78629954316503
H	5.33156589984454	-3.76512017159820	3.12549943272390
H	2.34456253703039	-4.09128373692117	6.22499227336548
N	2.22136944503510	-6.16501976152748	-0.59398657059825
N	2.16977773469900	-8.32434012961104	-0.05023394012393
C	2.66218286511094	-6.87663491534540	-1.79860969622764
C	2.98578687738738	-8.27974060408224	-1.24988264547880
H	1.84995534885289	-6.90133487430318	-2.54783346684886
H	3.54473999303767	-6.40043563500711	-2.25225052871846
H	2.71522123137696	-9.07515786997554	-1.96038274511973
H	4.06280399973553	-8.37783561305178	-1.01508956788829
H	2.09011686358385	-9.08372280529477	0.62344599652995

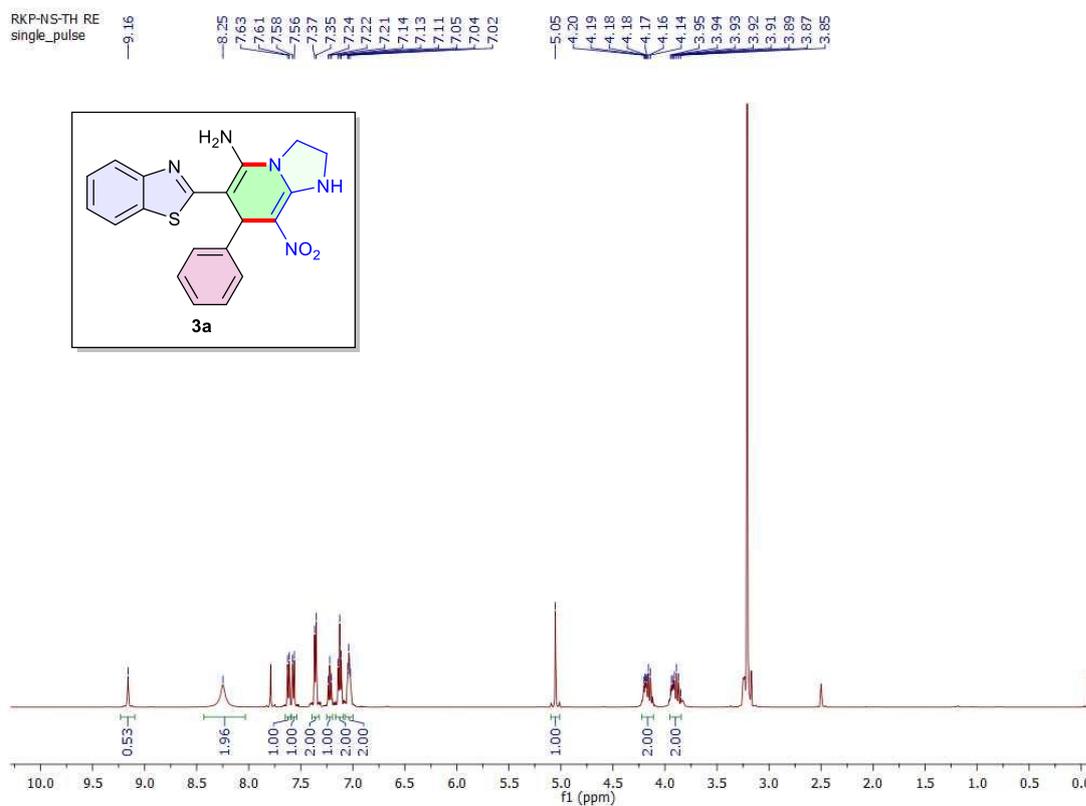
N	0.85018458164548	-7.62855781520954	2.50986962888668
O	1.12026771891946	-8.83128313411915	2.32278662815717
O	0.25582919321937	-7.23111257820921	3.51042154518889
N	1.78808232196534	-4.18282939027360	-1.75821197350758
H	1.45590095945506	-3.20761359601282	-1.69200807336294
H	2.49052218831018	-4.43086319041755	-2.44058637419944
S	-0.203347111169811	-2.37604348714251	2.04262763584459
H	3.65813461309156	-4.50005900882523	1.44426021520729
H	0.03237274508949	-5.10633569189139	2.29125243574577
H	4.67973121744778	-3.54995231996131	5.52713595625802

16. References

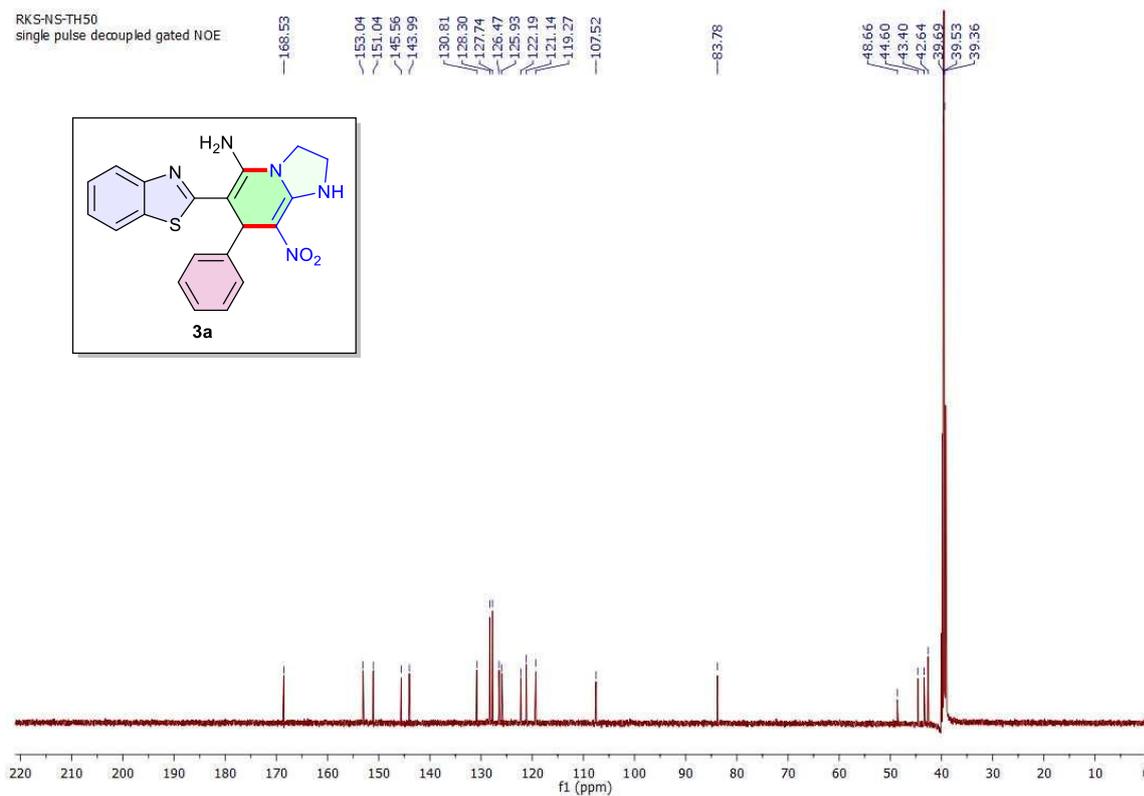
1. K. Wang, C. Chen, X. Liu, D. Li, T. Peng, X. Liu, D. Yang, L. Wang, *Org. Lett.* 2018, **20**, 5260–5263.
2. P. D. I. Torre, L. A. Saavedra, J. Caballero, J. Quiroga, J. H. Alzate-Morales, M. G. Cabrera, J. A. Trilleras, *Molecules* 2012, **17**, 12072–12085.
3. F. Yefeng, L. Song, C. Nanyang, S. Xusheng, X. Xiaoyong, L. Zhong; *Synlett* 2015, **26**, 393–403.
4. H. Nishiwaki, Y. Nakagawa, D. Y. Takeda, A. Okazawa, M. Akamatsu, H. Miyagawa, T. Ueno, K. Nishimura, *Pest Manage. Sci.* 2000, **56**, 875– 881.
5. X. Zhang, J. Chang, C. Chen, Q. Zhai, S. Li, X. Song, *Adv. Synth. Catal.* 2023, **365**, 3622.

17. Copies of NMR Spectra of Synthesized Compounds

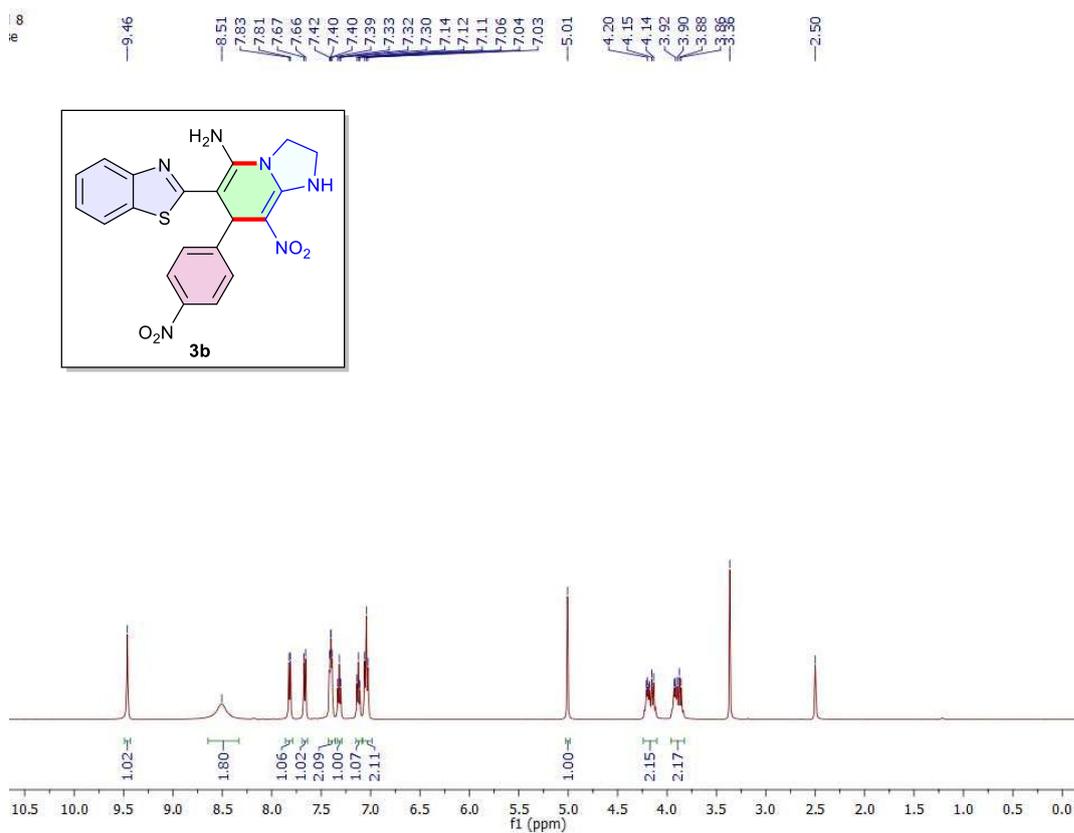
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3a**



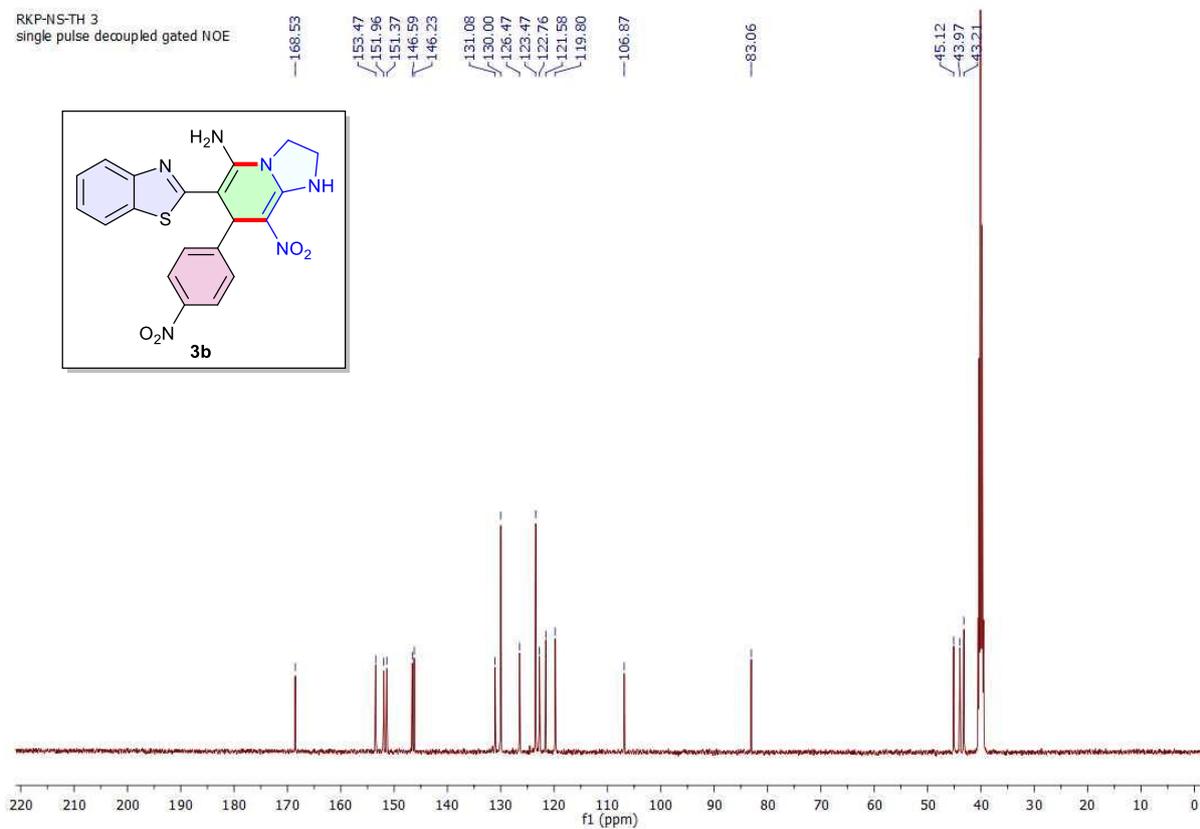
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3a**



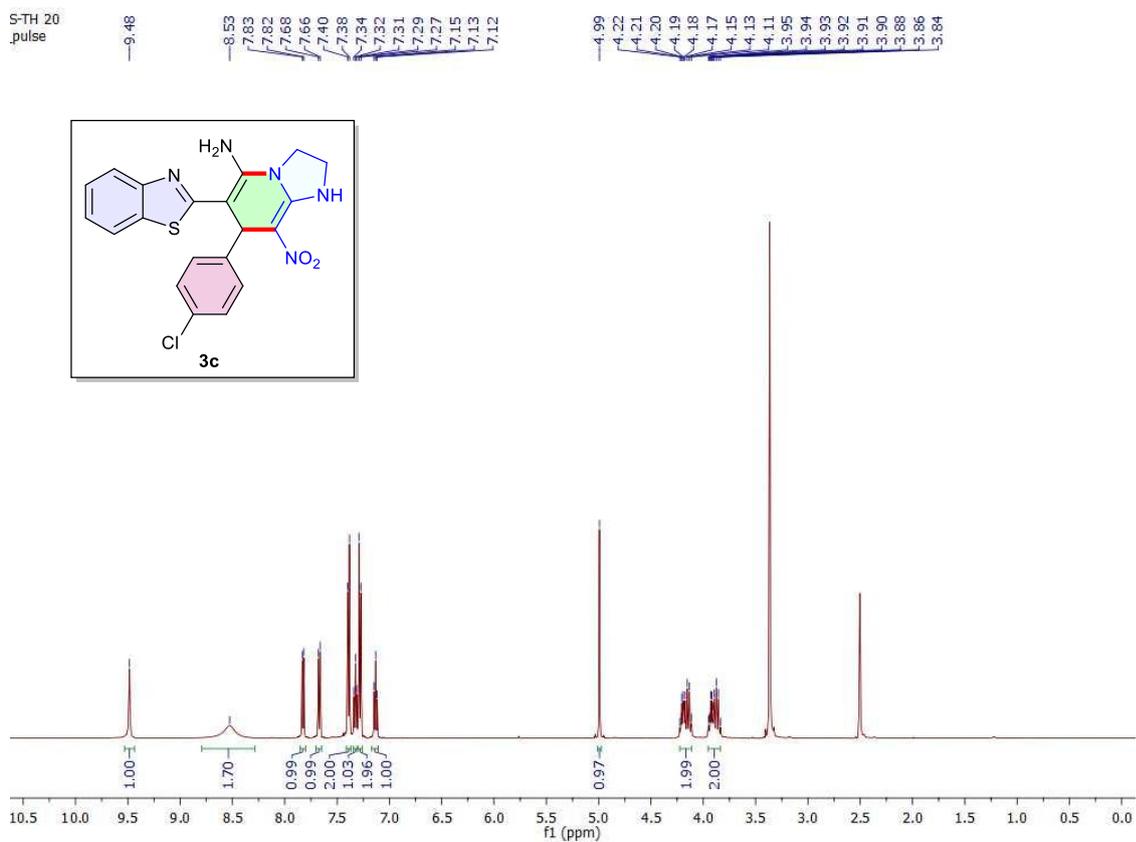
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3b**



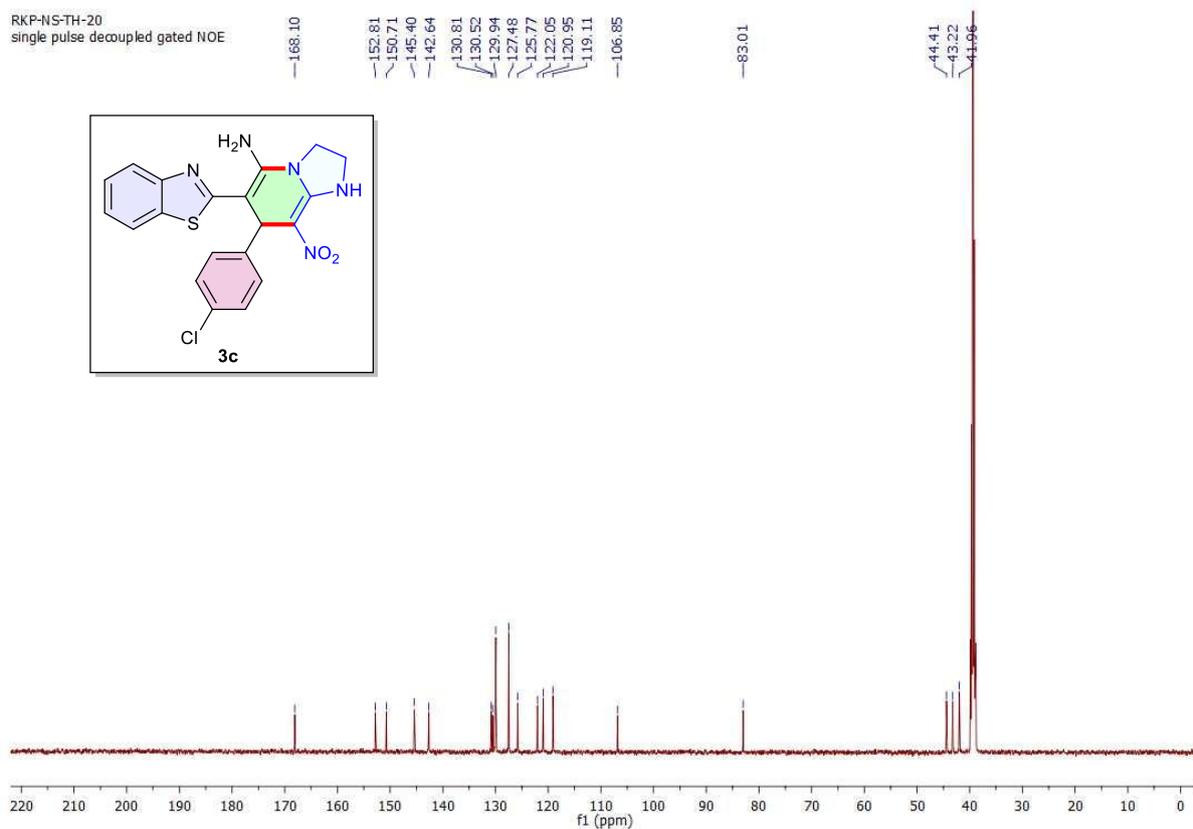
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3b**



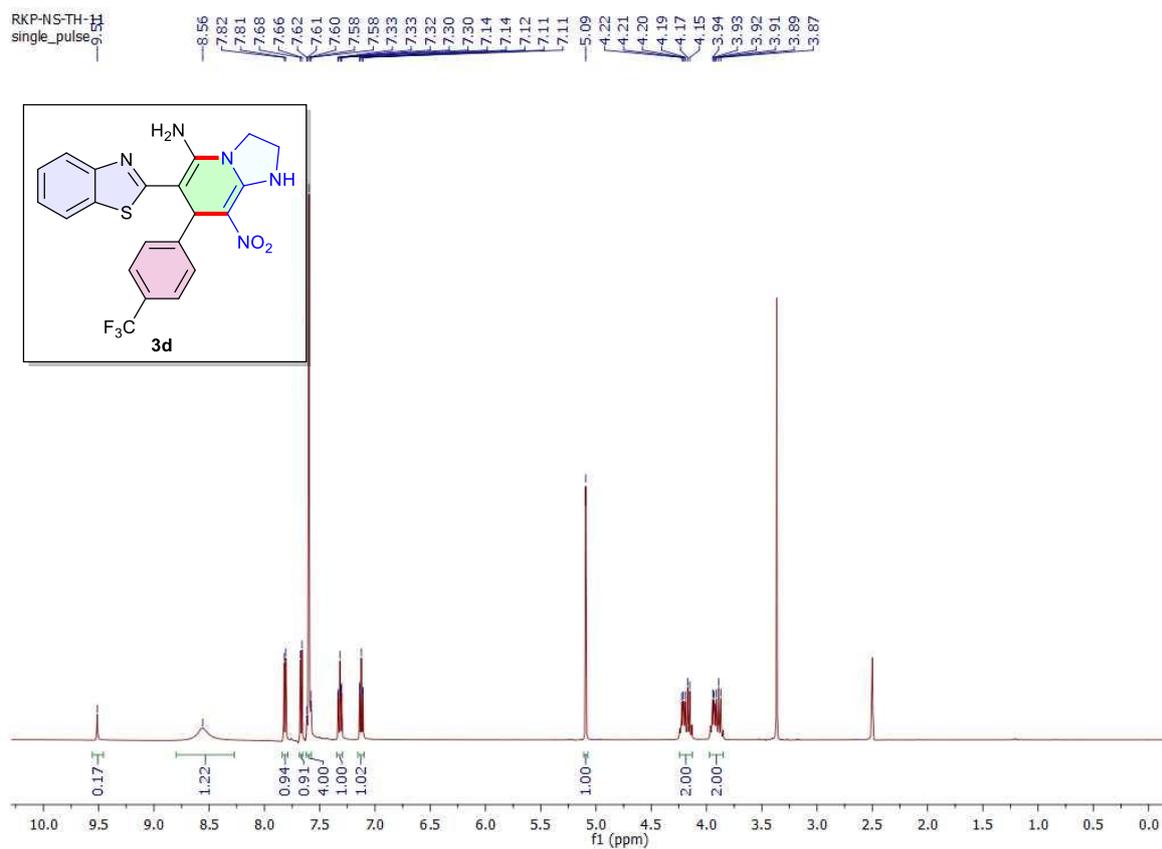
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3c**



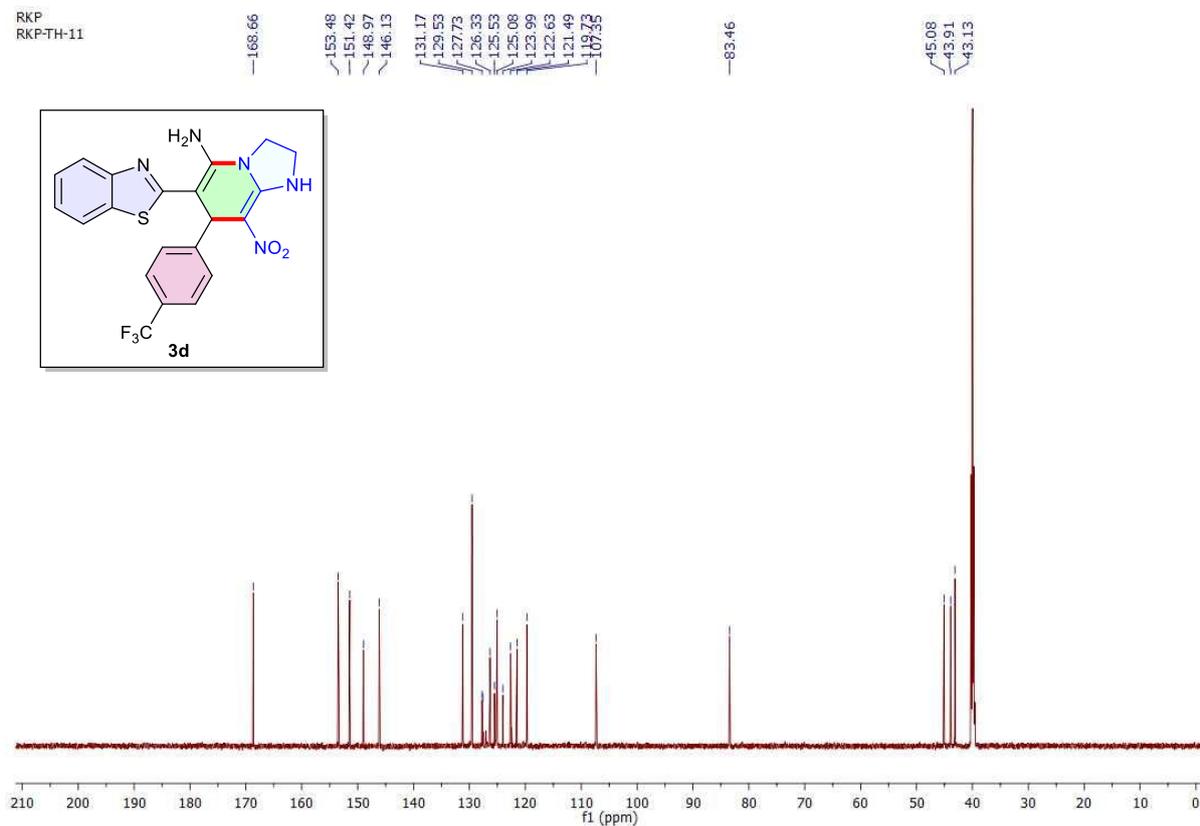
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3c**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3d**

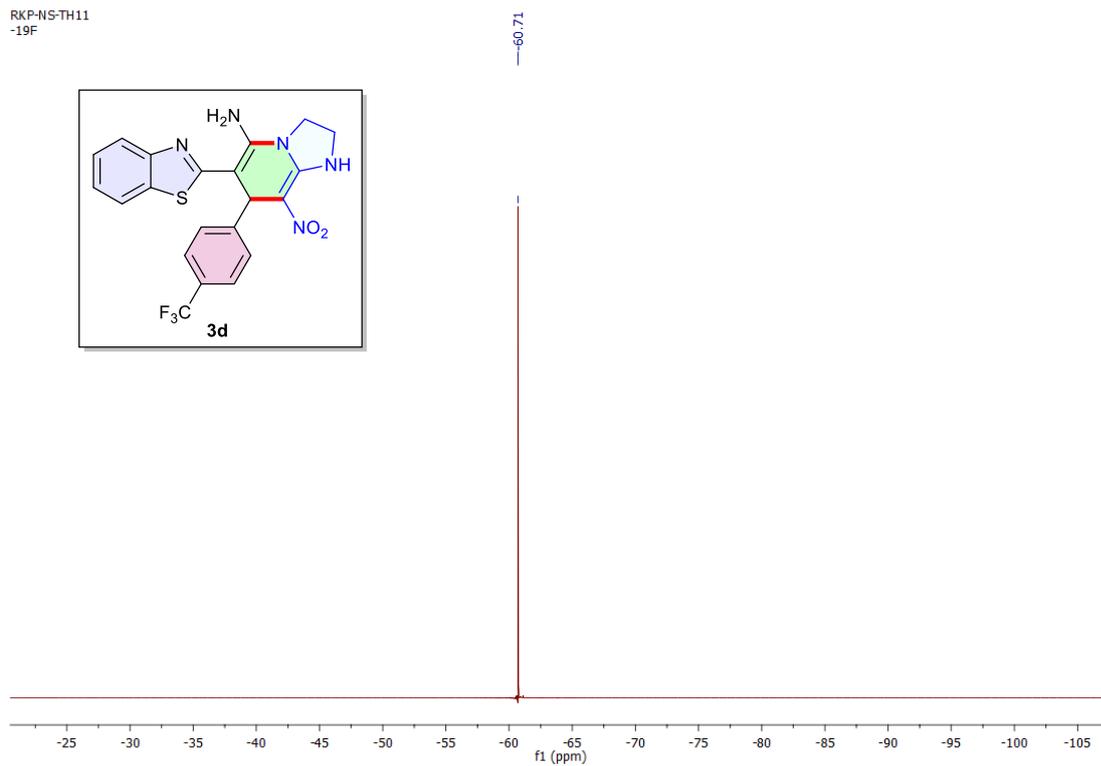


^{13}C { ^1H } NMR (126 MHz, $\text{DMSO-}d_6$) of **3d**

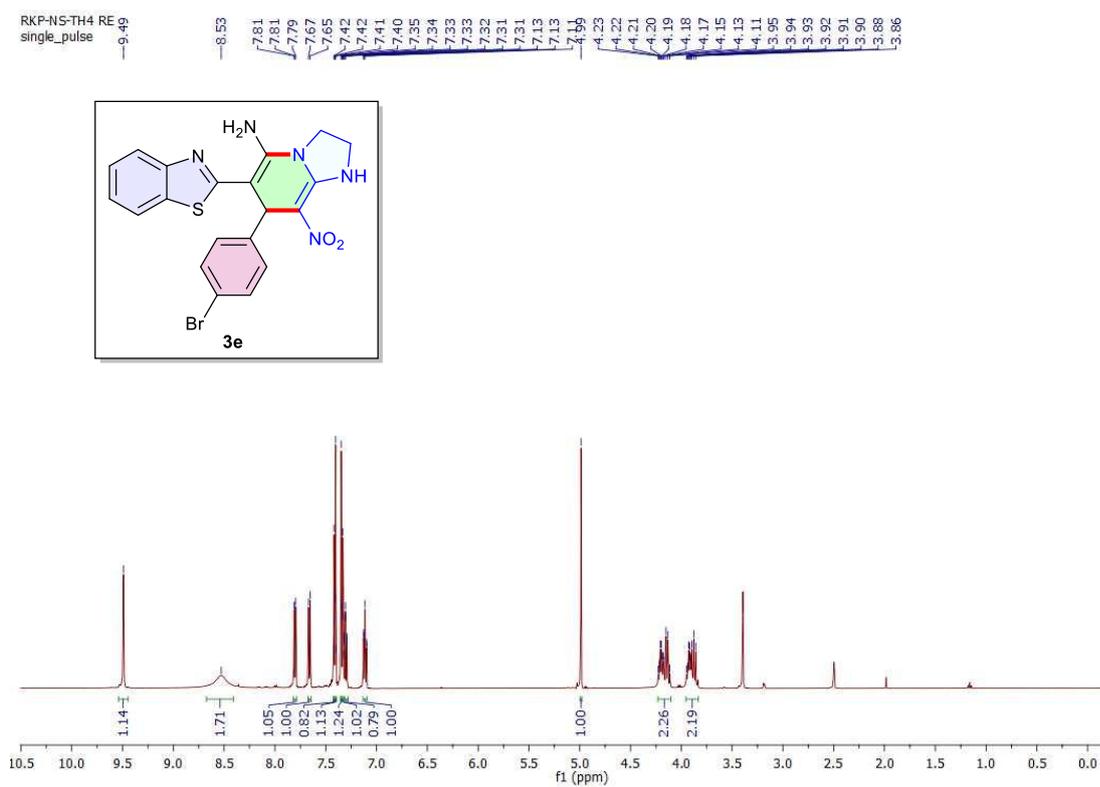


$^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, $\text{DMSO-}d_6$) of **3d**

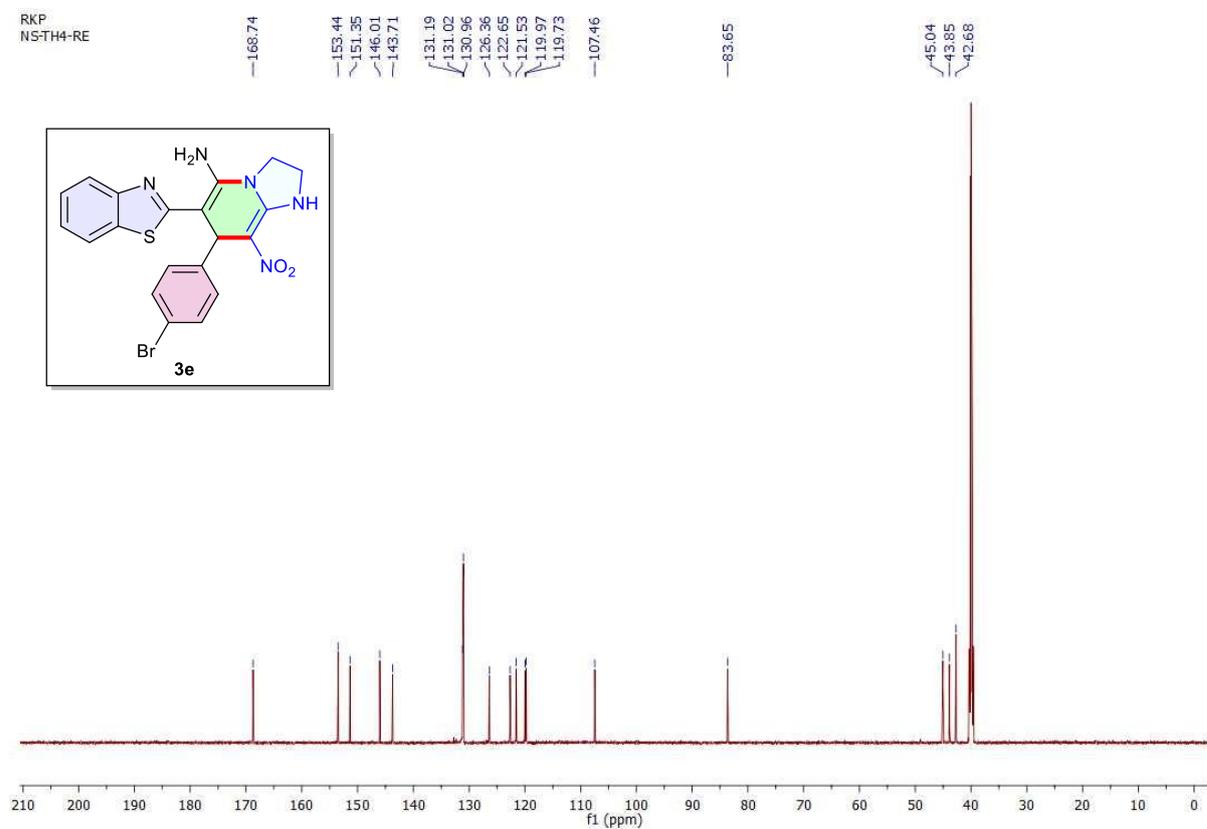
RKP-NS-TH11
-19F



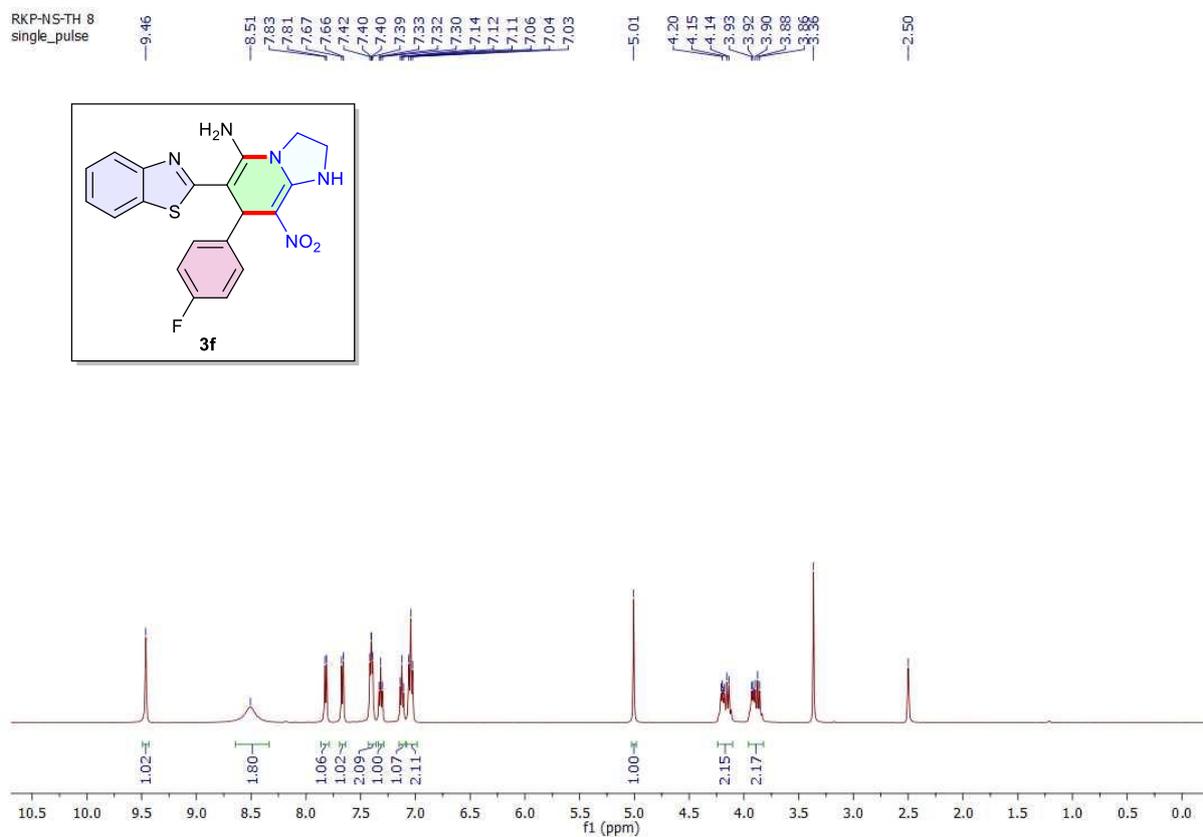
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3e**



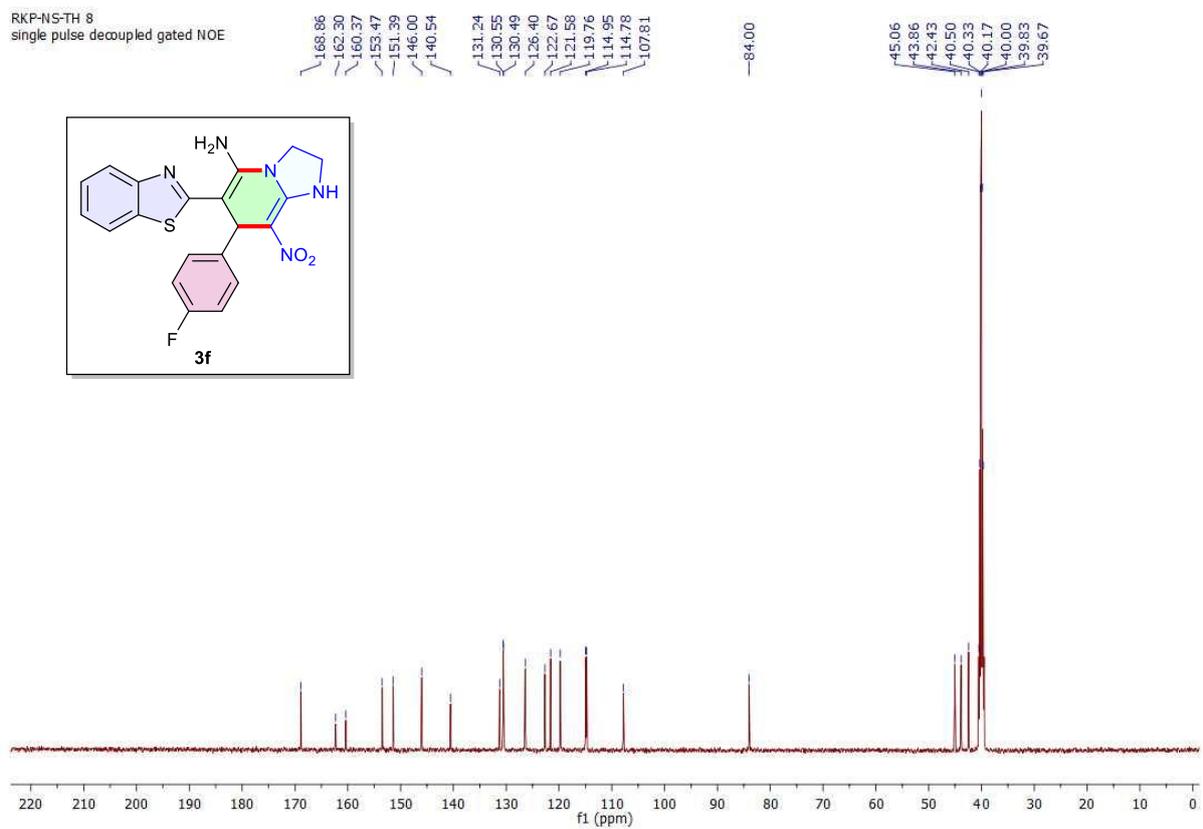
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3e**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3f**

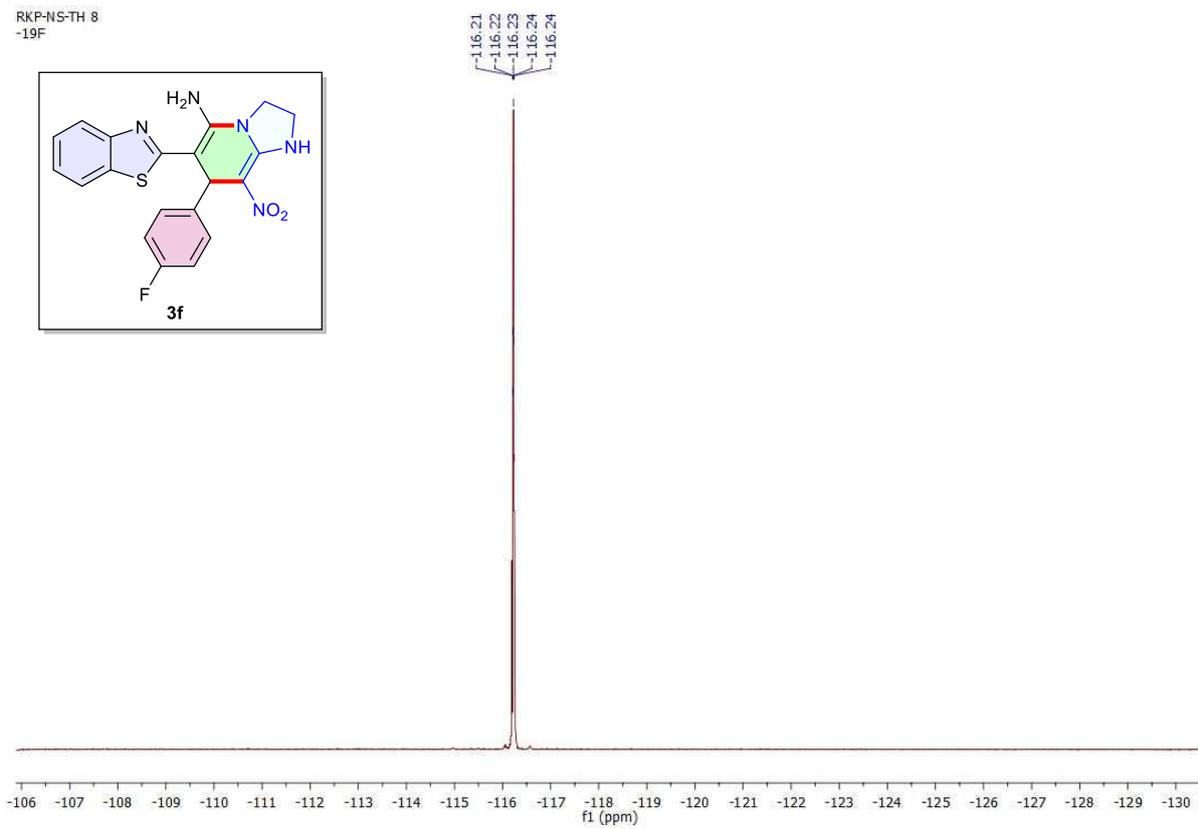
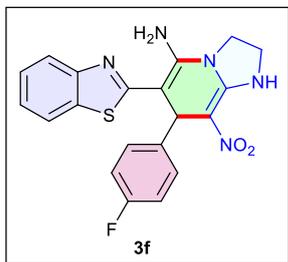


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3f**



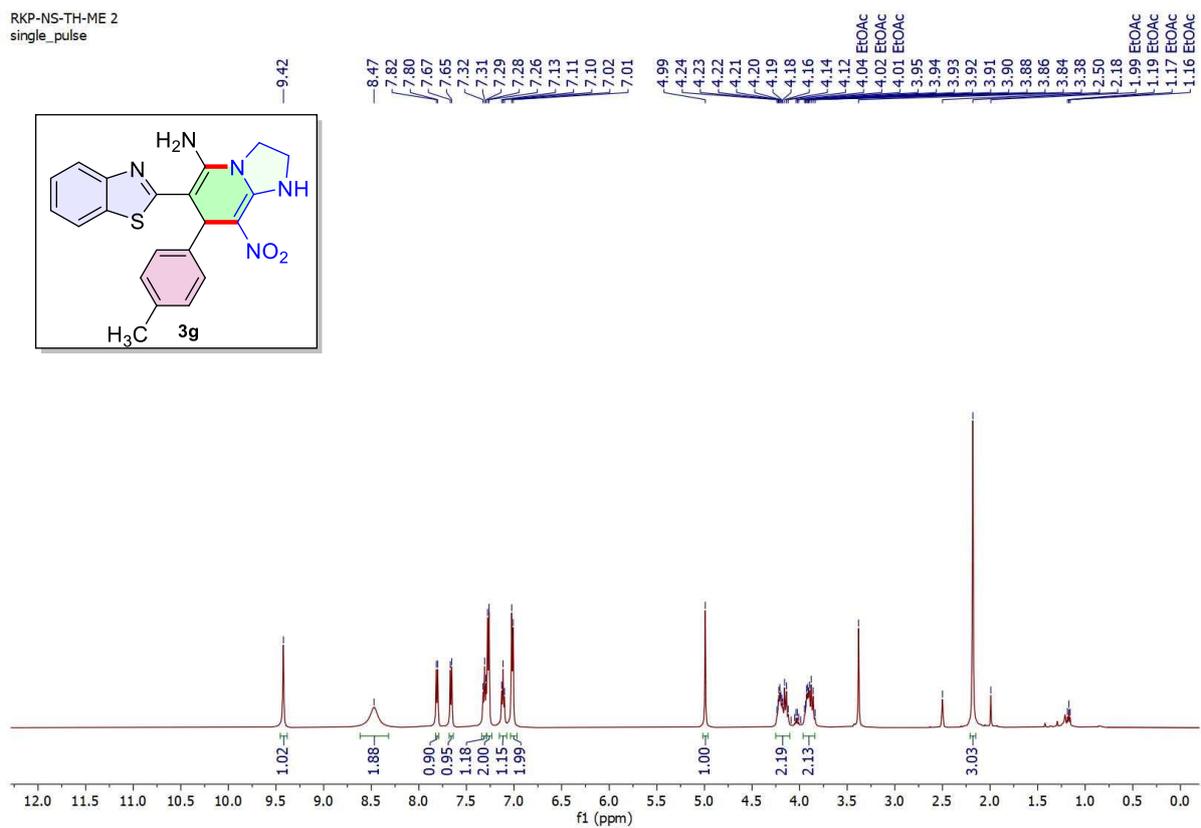
^{19}F NMR (126 MHz, $\text{DMSO-}d_6$) of **3f**

RKP-NS-TH 8
-19F



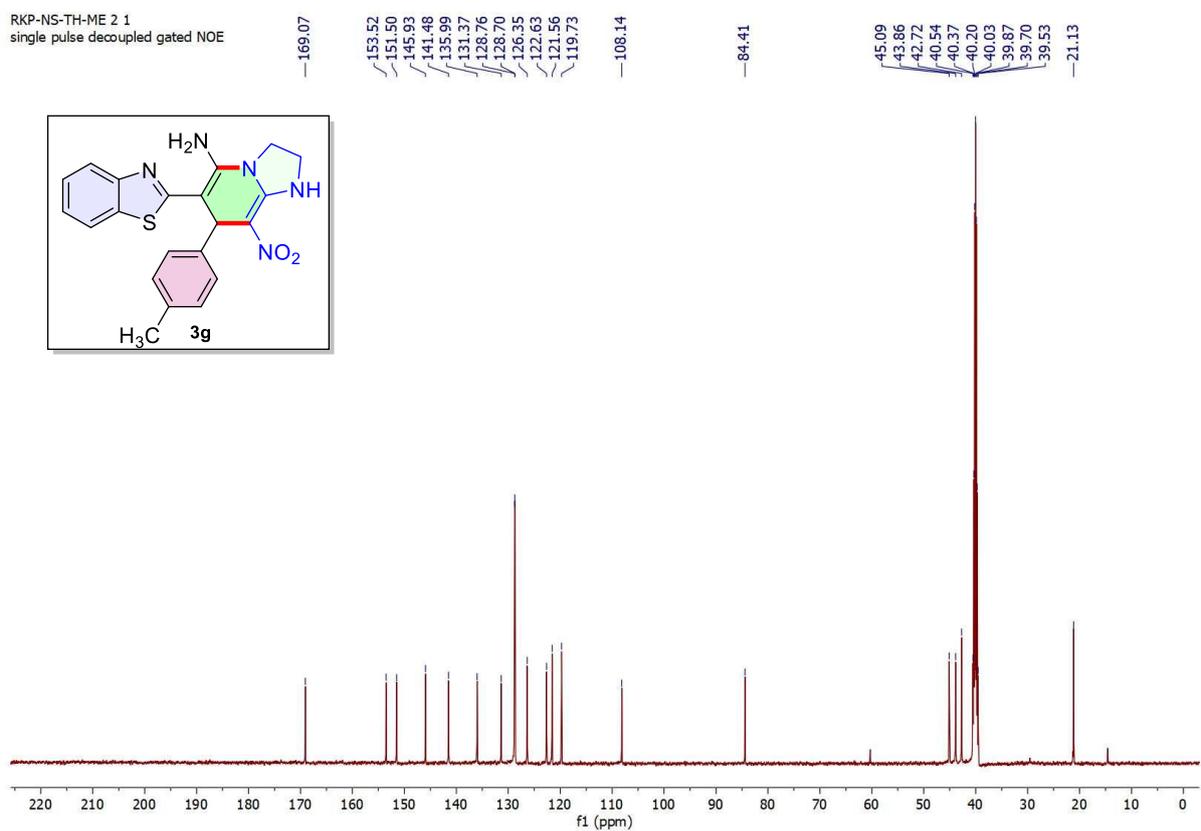
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3g**

RKP-NS-TH-ME 2
single_pulse



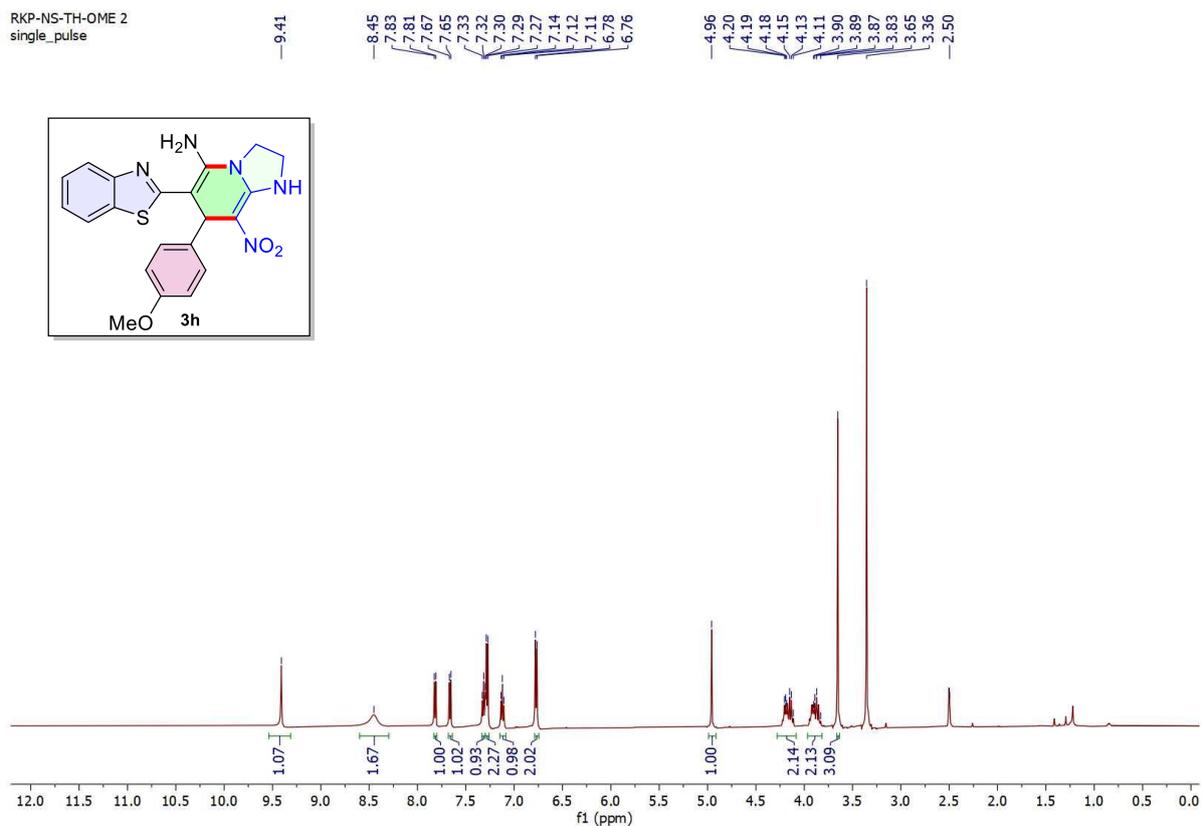
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3g**

RKP-NS-TH-ME 2 1
single pulse decoupled gated NOE



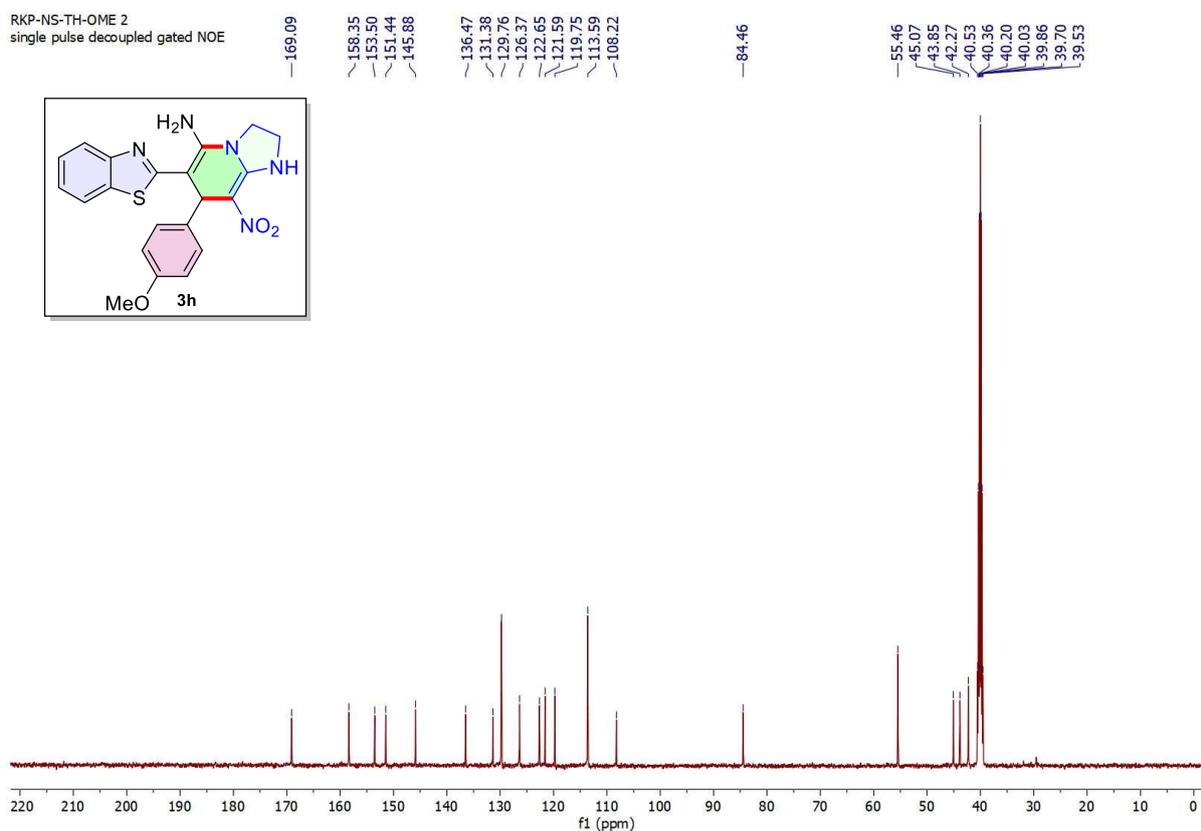
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3h**

RKP-NS-TH-OME 2
single_pulse

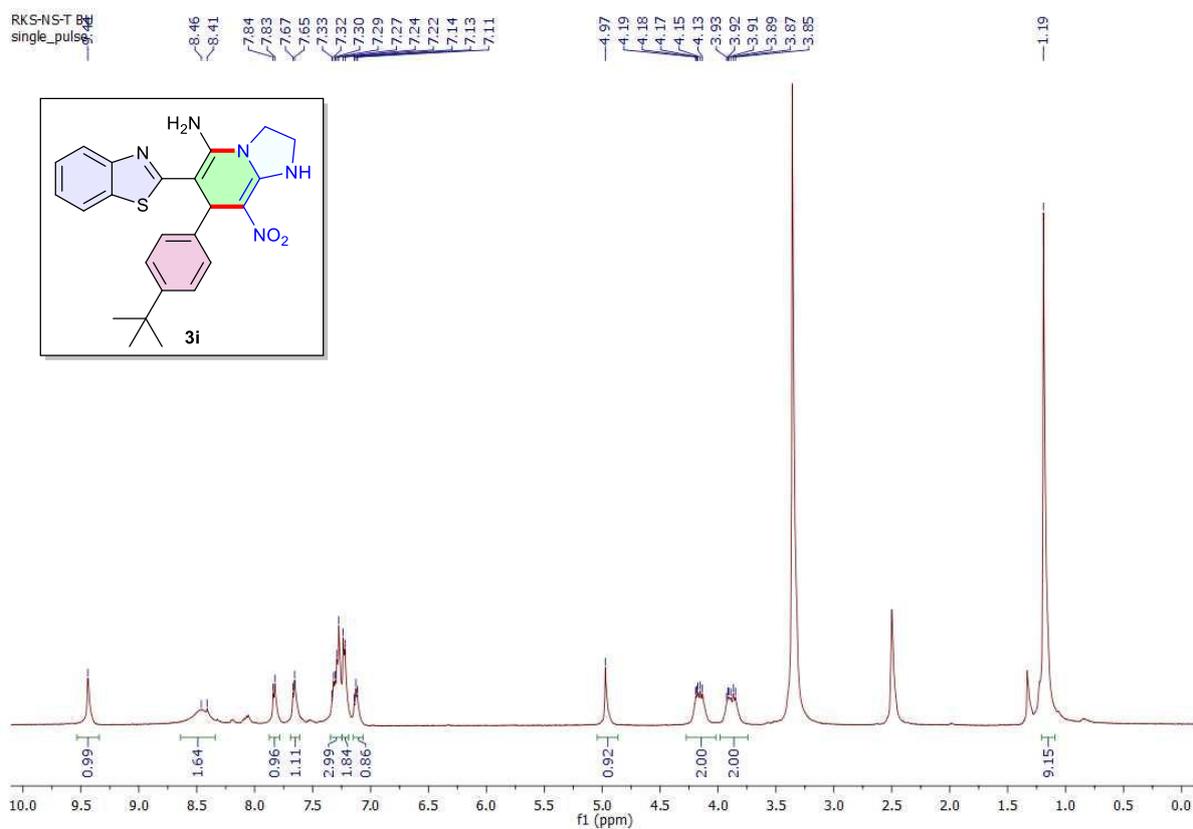


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3h**

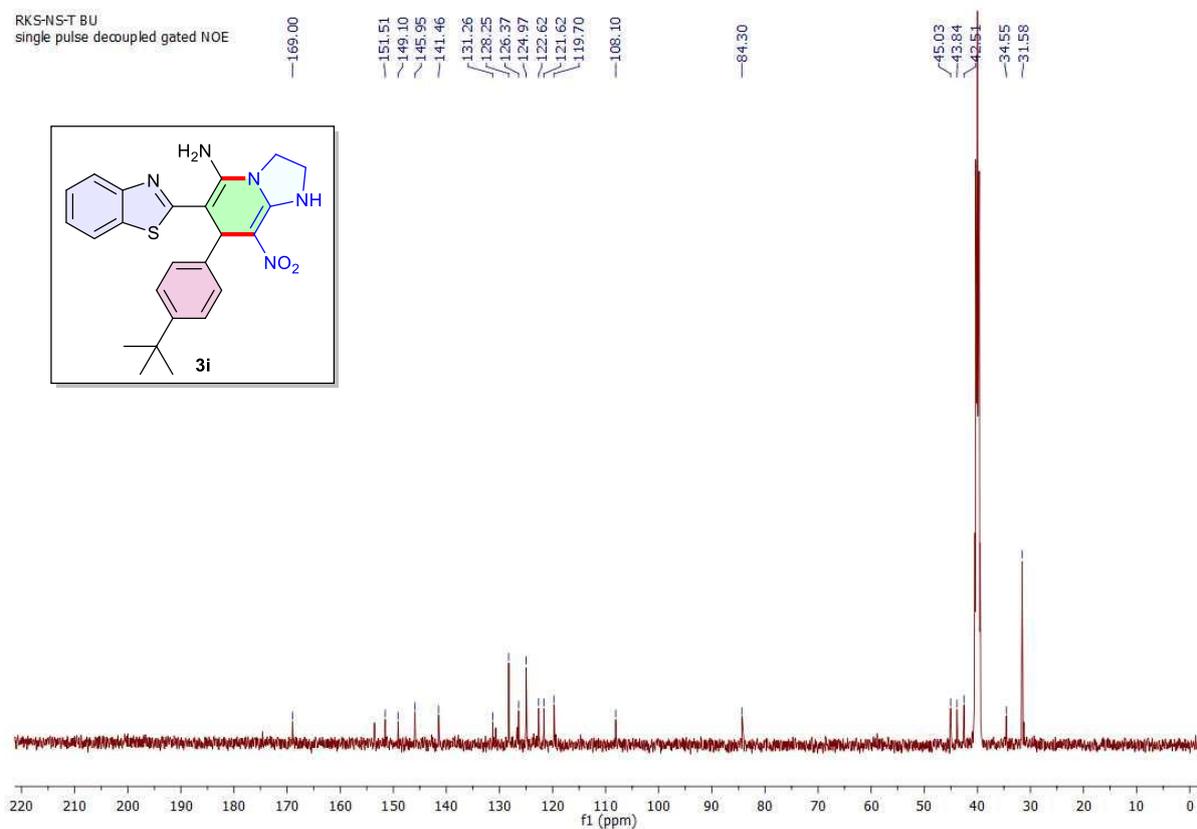
RKP-NS-TH-OME 2
single pulse decoupled gated NOE



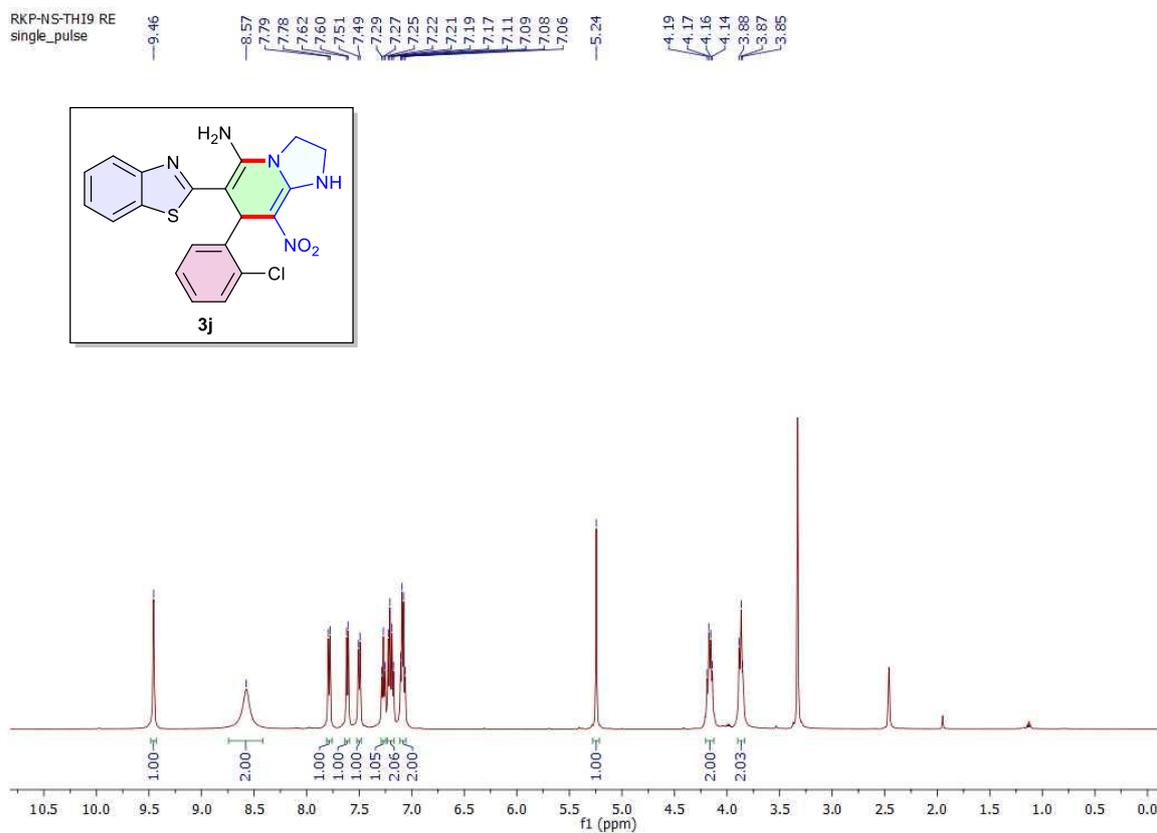
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3i**



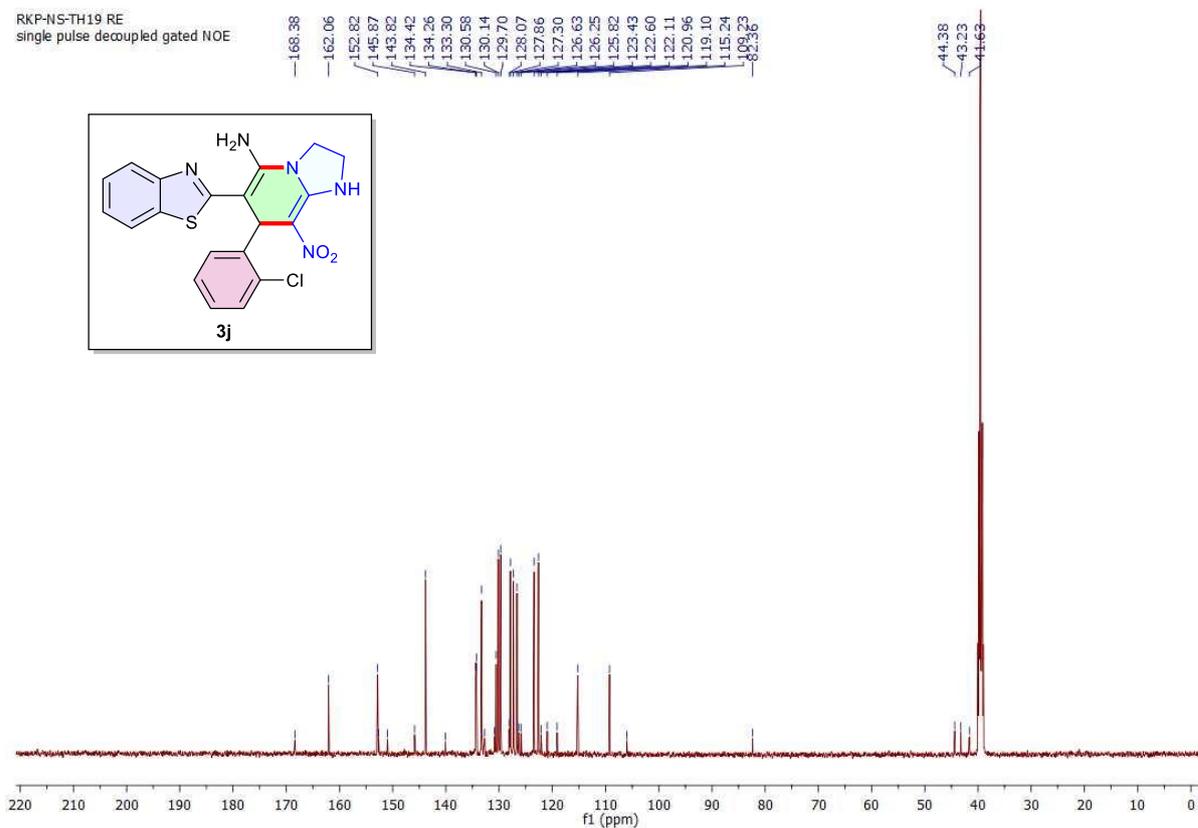
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3i**



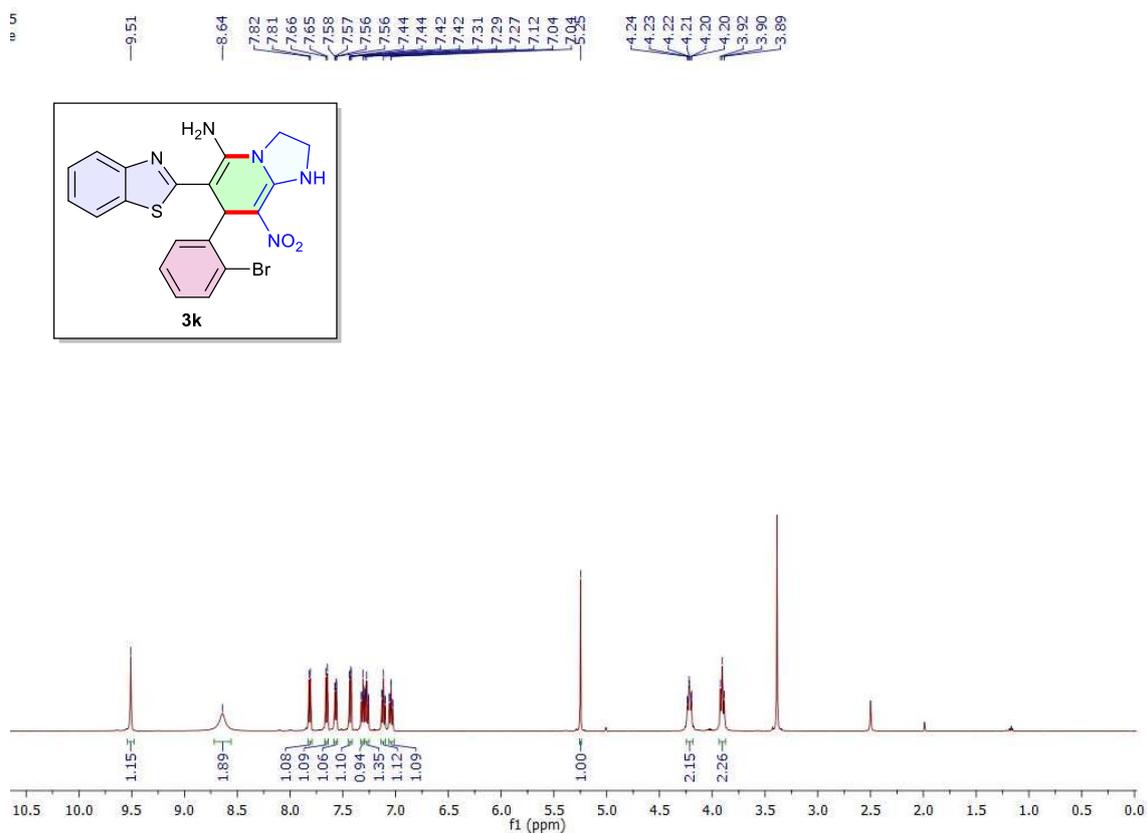
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3j**



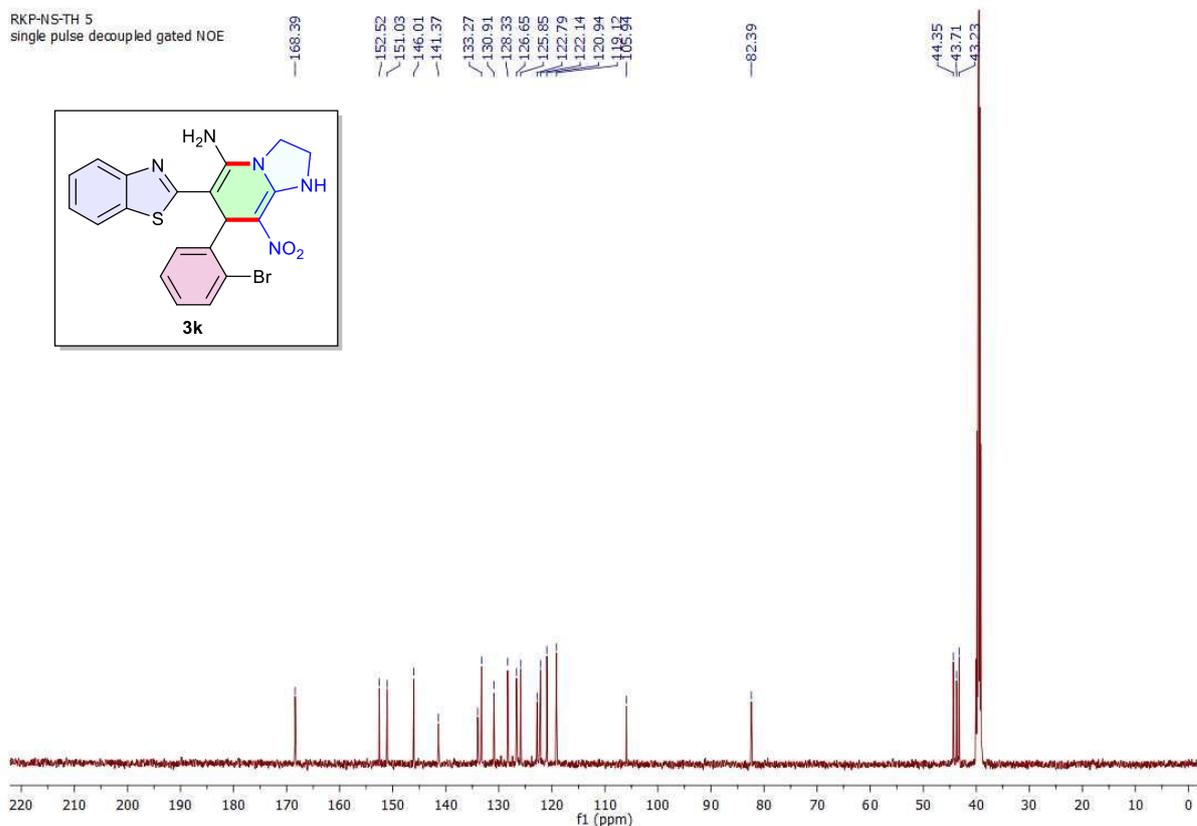
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3j**



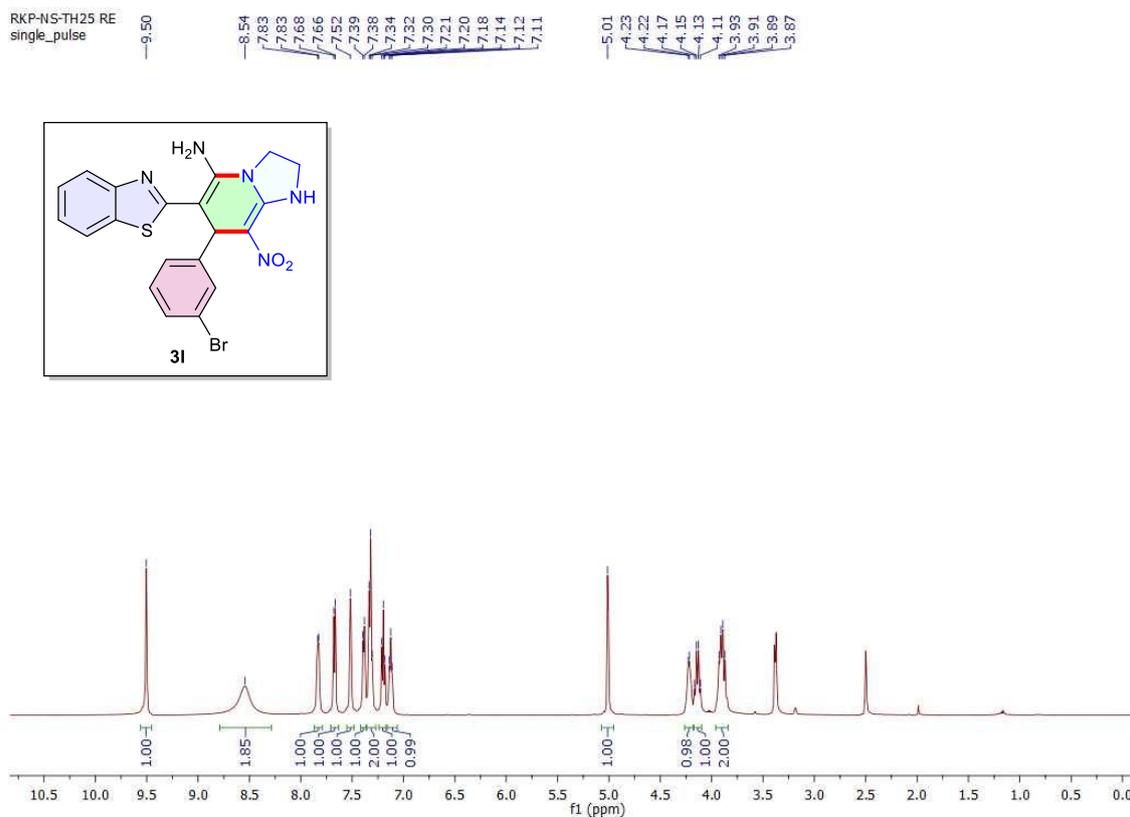
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3k**



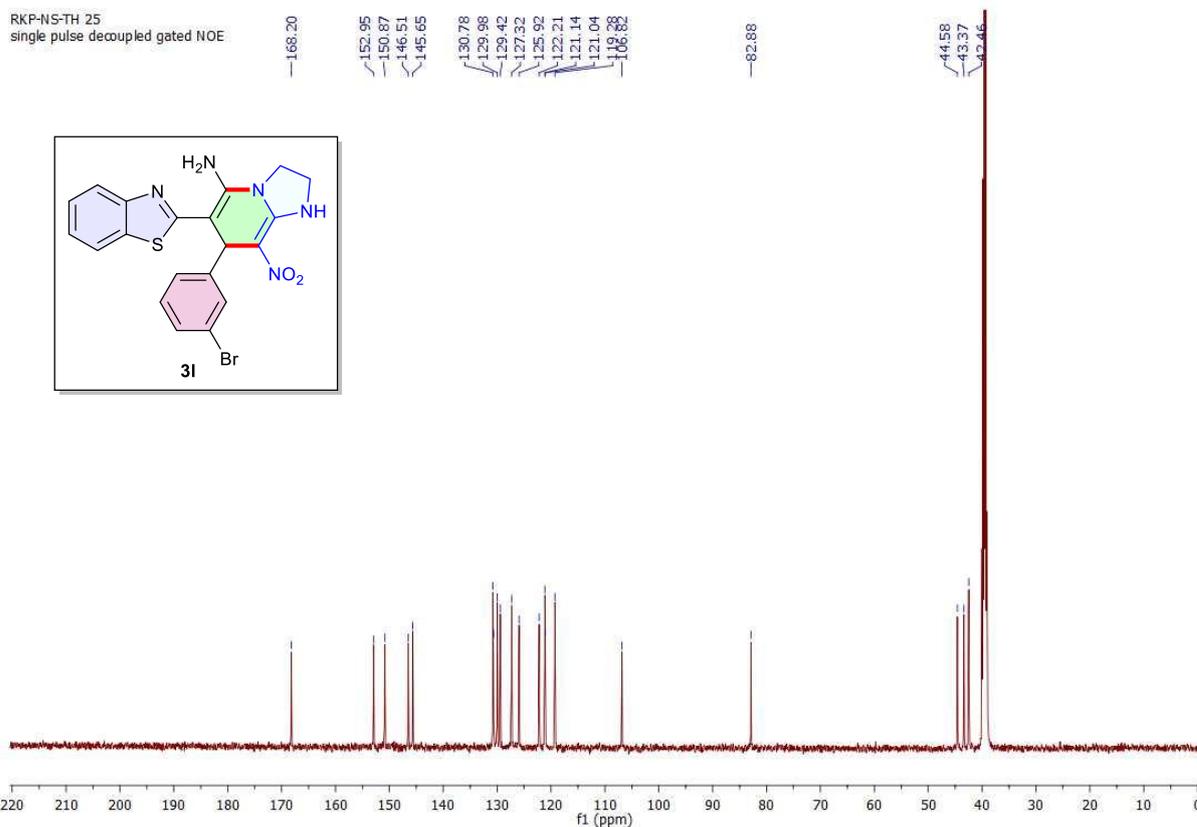
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3k**



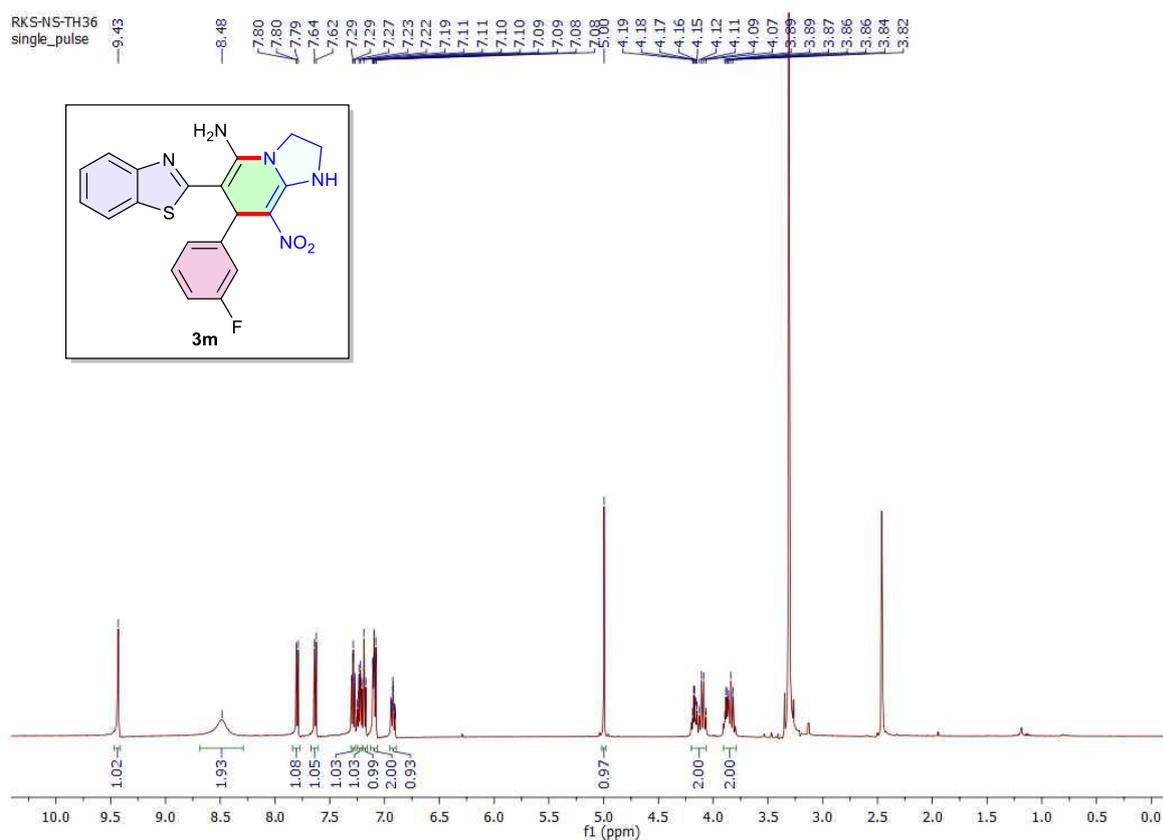
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **31**



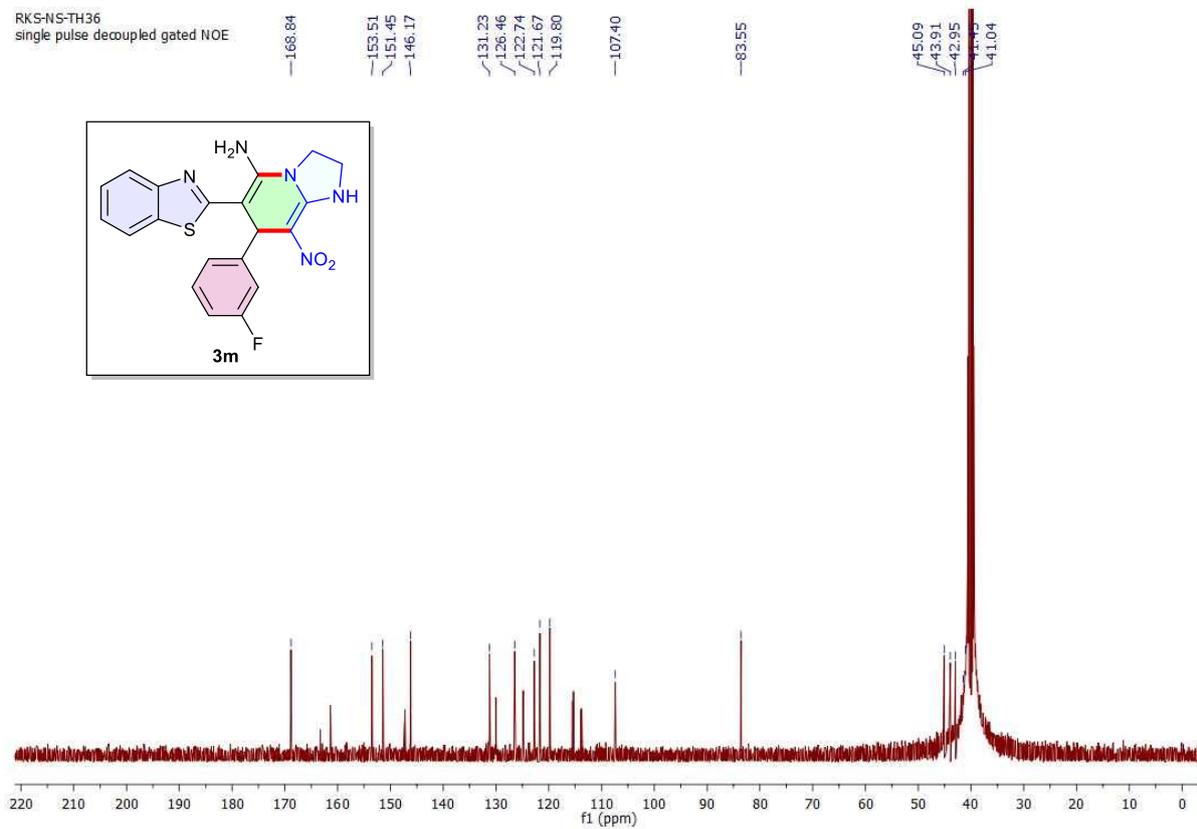
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **31**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3m**



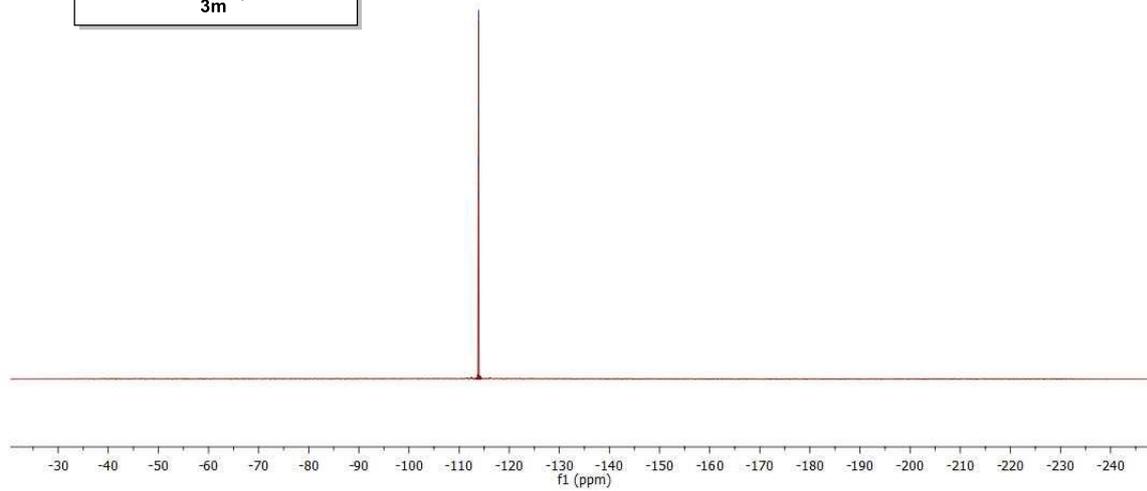
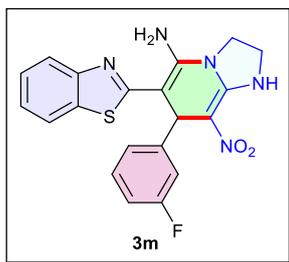
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3m**



$^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, $\text{DMSO-}d_6$) of **3m**

RKP-NS-TH36
-19F

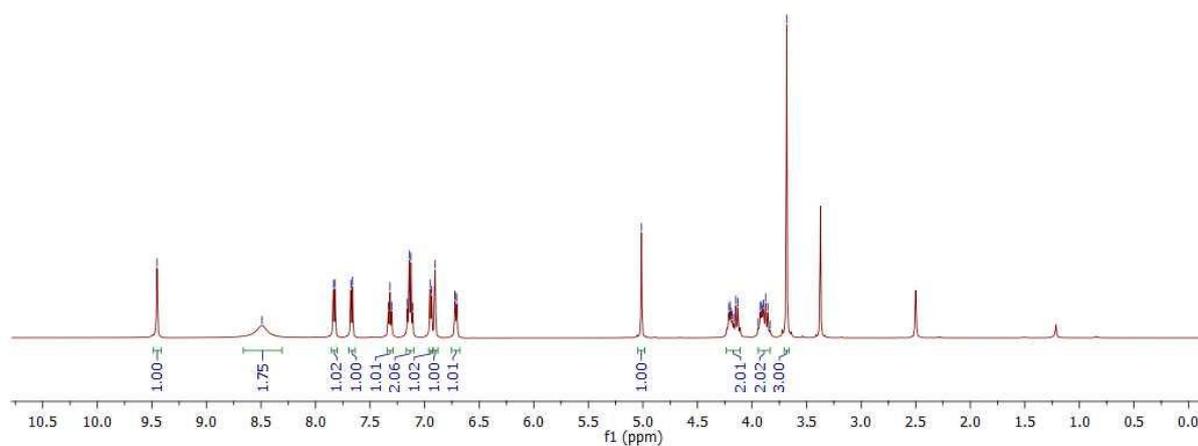
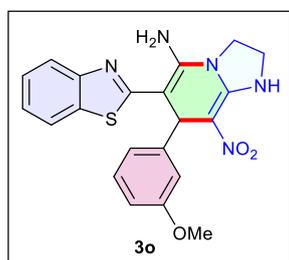
-113.86
-113.87
-113.88
-113.89
-113.91



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3o**

RKP-NS-TH-13
single_pulse

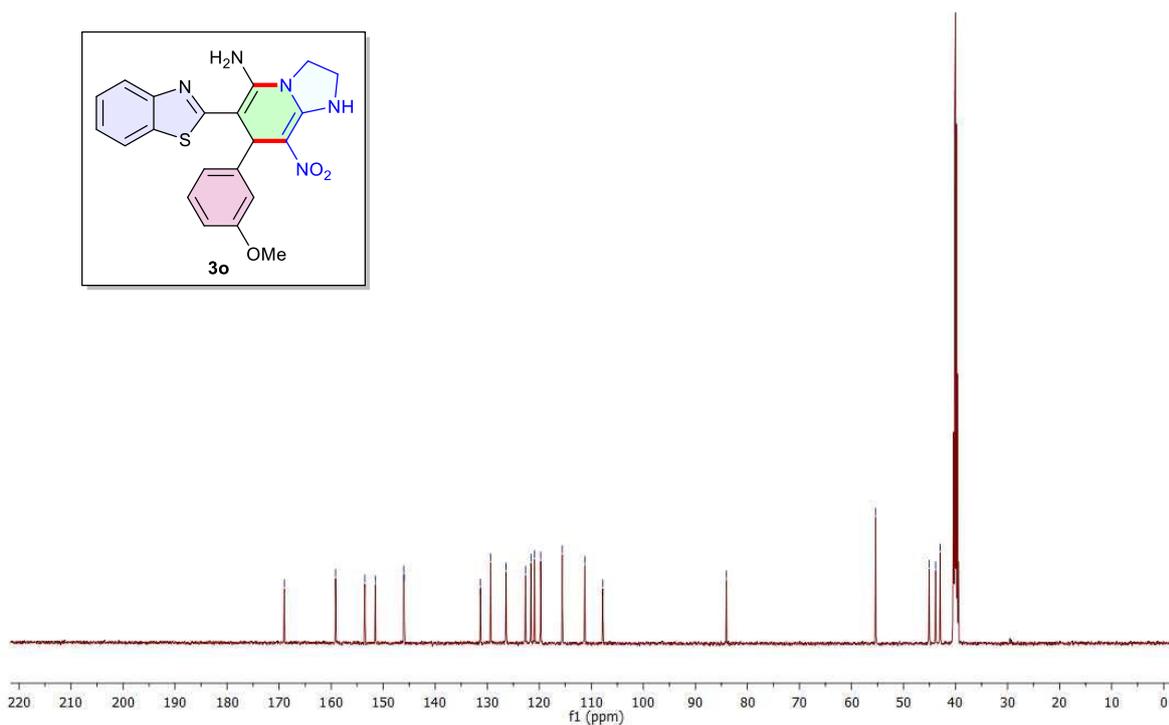
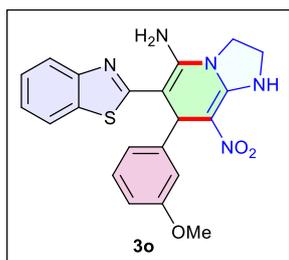
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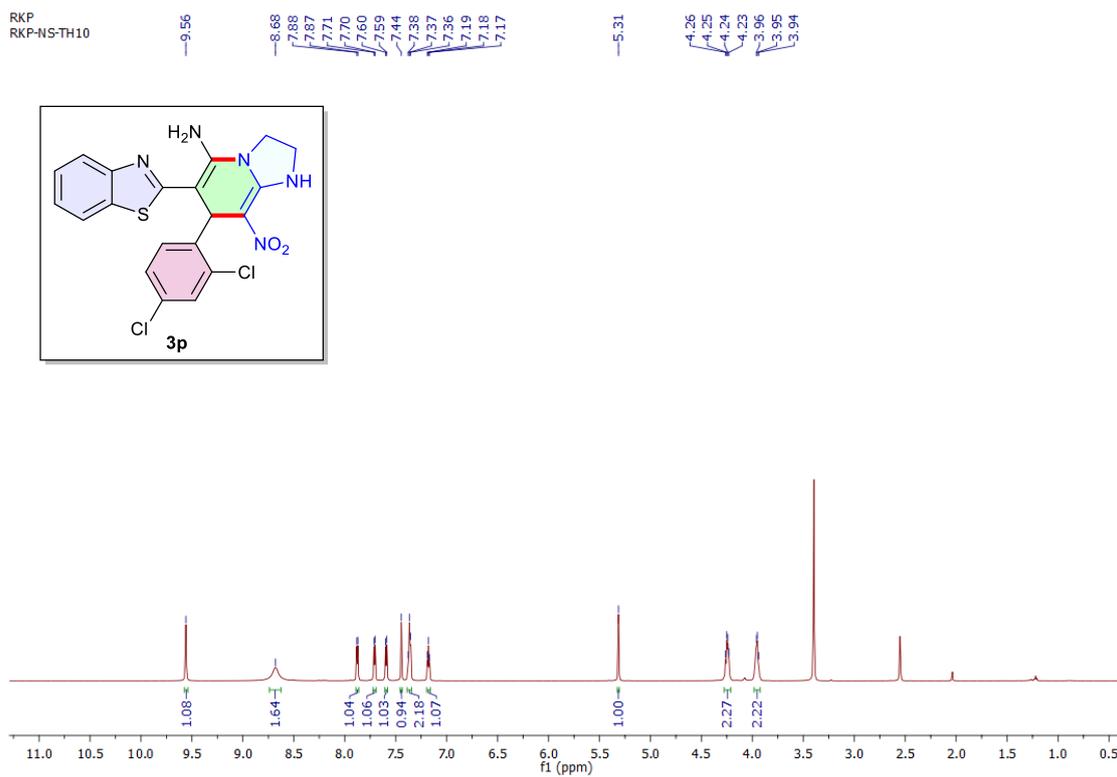
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3o**

RKP-NS-TH 13
single pulse decoupled gated NOE

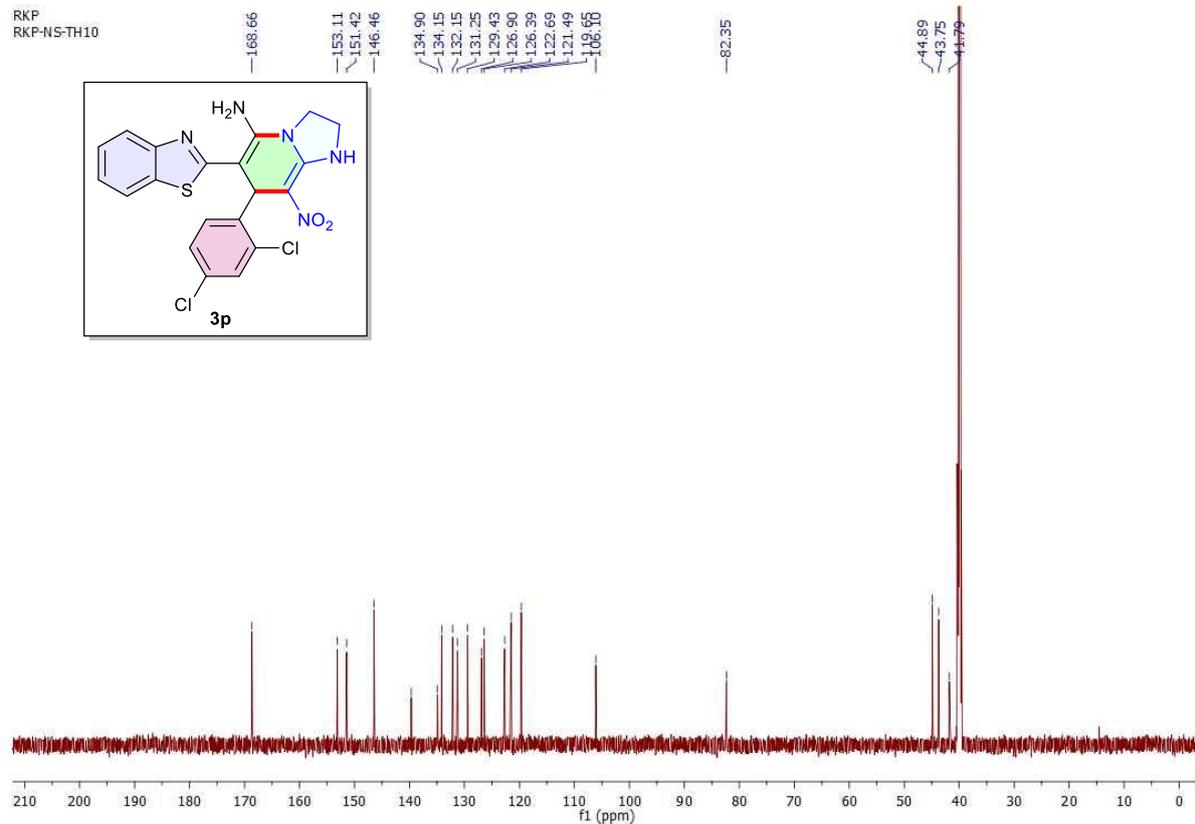
169.01, 159.16, 153.51, 151.52, 146.05, 145.94, 131.32, 129.33, 126.37, 122.65, 121.60, 120.89, 119.73, 115.68, 111.25, 107.78, 84.02, 55.35, 45.06, 43.84, 42.95



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3p**



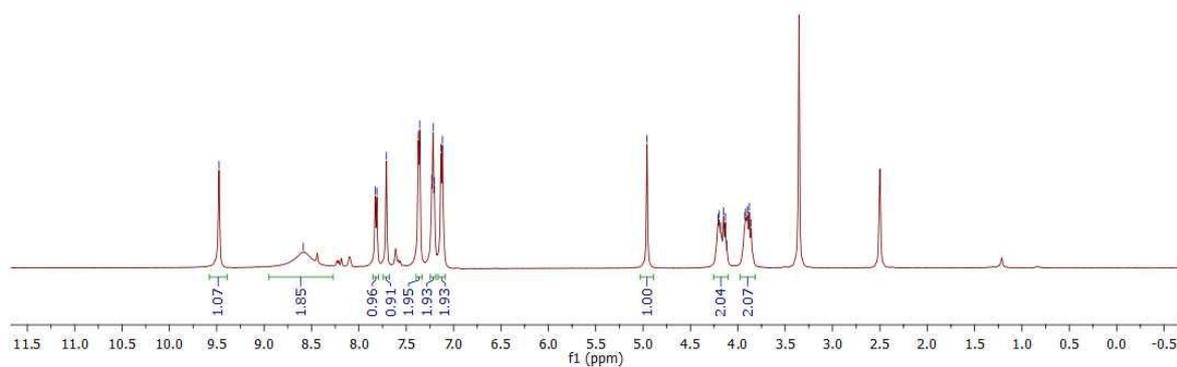
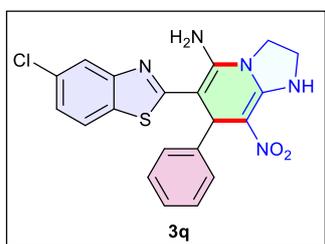
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3p**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3q**

RKP-NS-BN CL
single_pulse

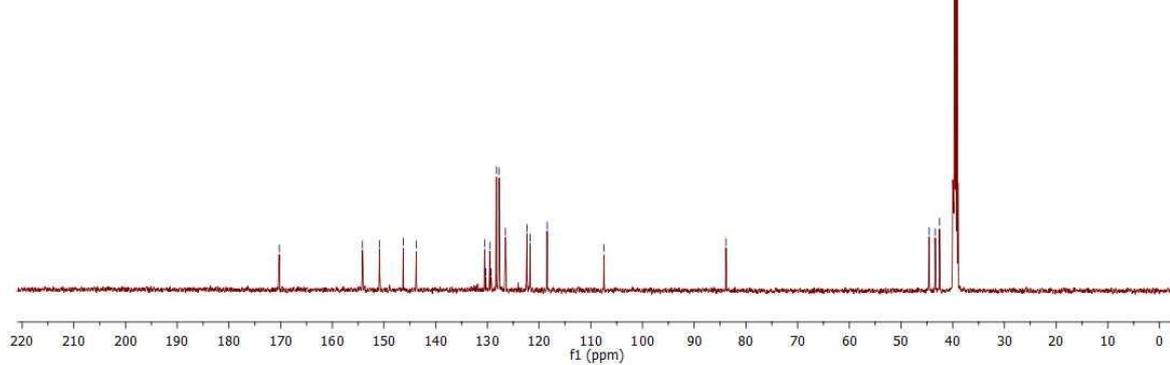
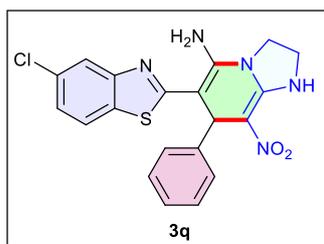
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$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3q**

RKP-NS-BN CL
single_pulse decoupled gated NOE

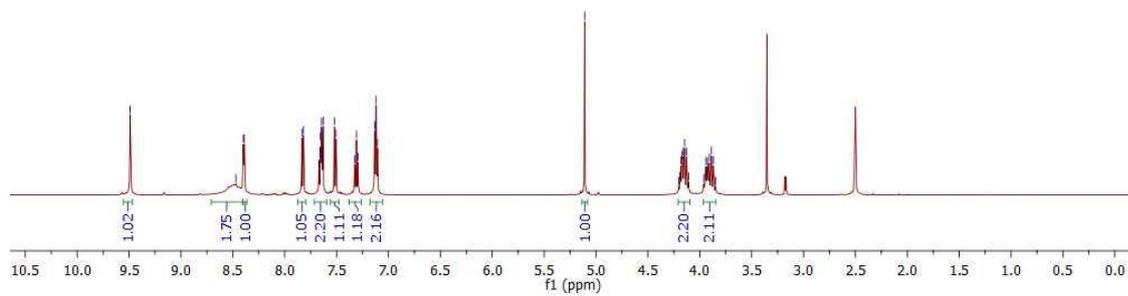
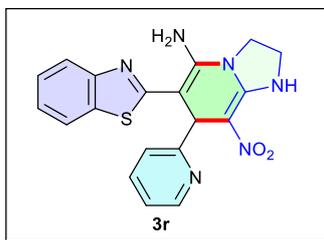
170.25, 154.17, 150.85, 146.27, 143.73, 130.55, 130.31, 129.53, 128.27, 127.73, 126.49, 122.34, 121.74, 118.45, 107.43, 83.86, 44.59, 43.38, 42.55



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3r**

VS-PY 1
_pulse

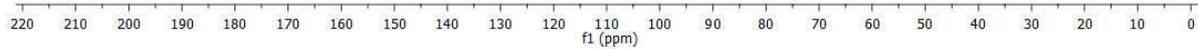
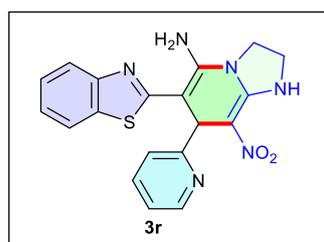
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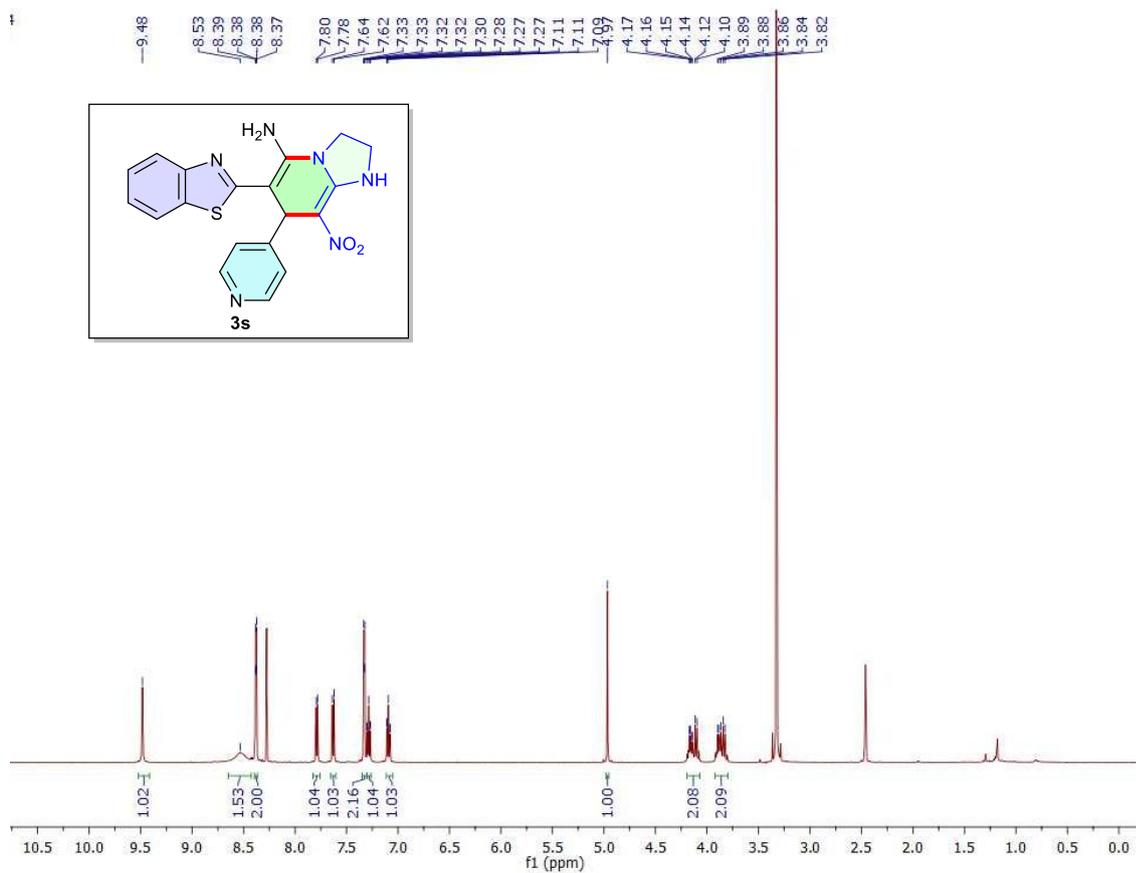
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3r**

RKP-NS-PY1
single pulse decoupled gated NOE

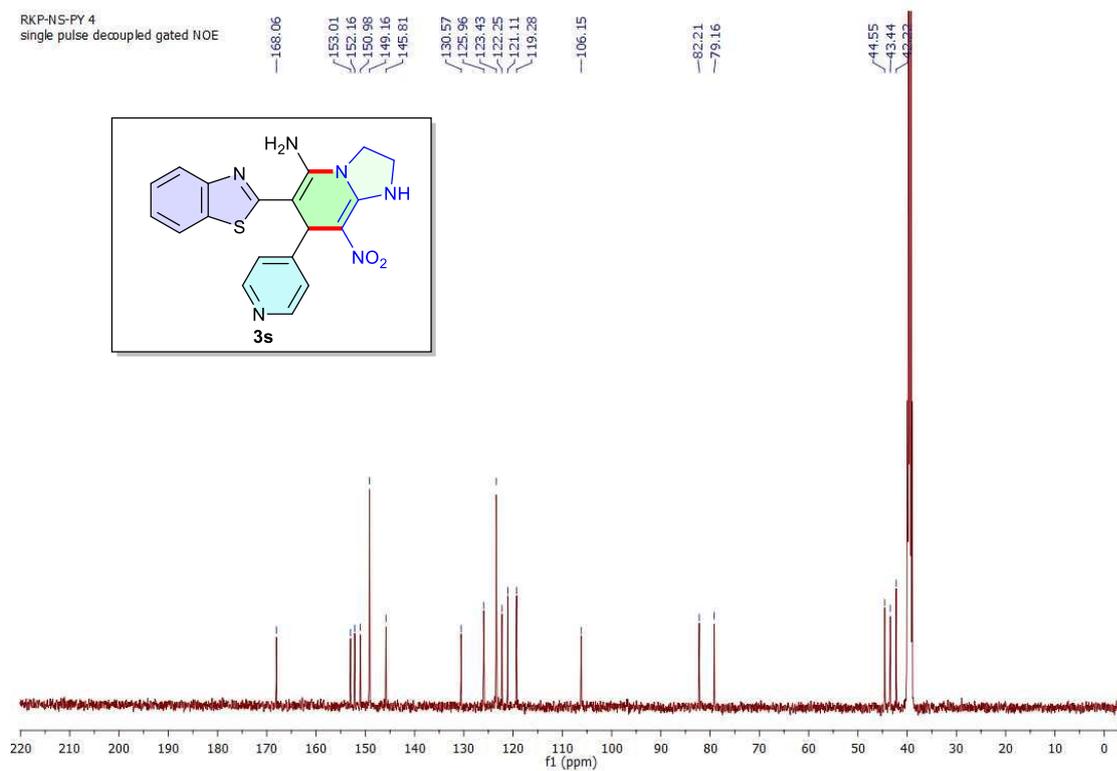
168.81, 162.06, 153.59, 152.08, 149.83, 146.49, 135.78, 131.08, 126.38, 124.47, 122.54, 122.30, 121.53, 119.59, 107.14, 83.67, 45.53, 45.03, 43.79



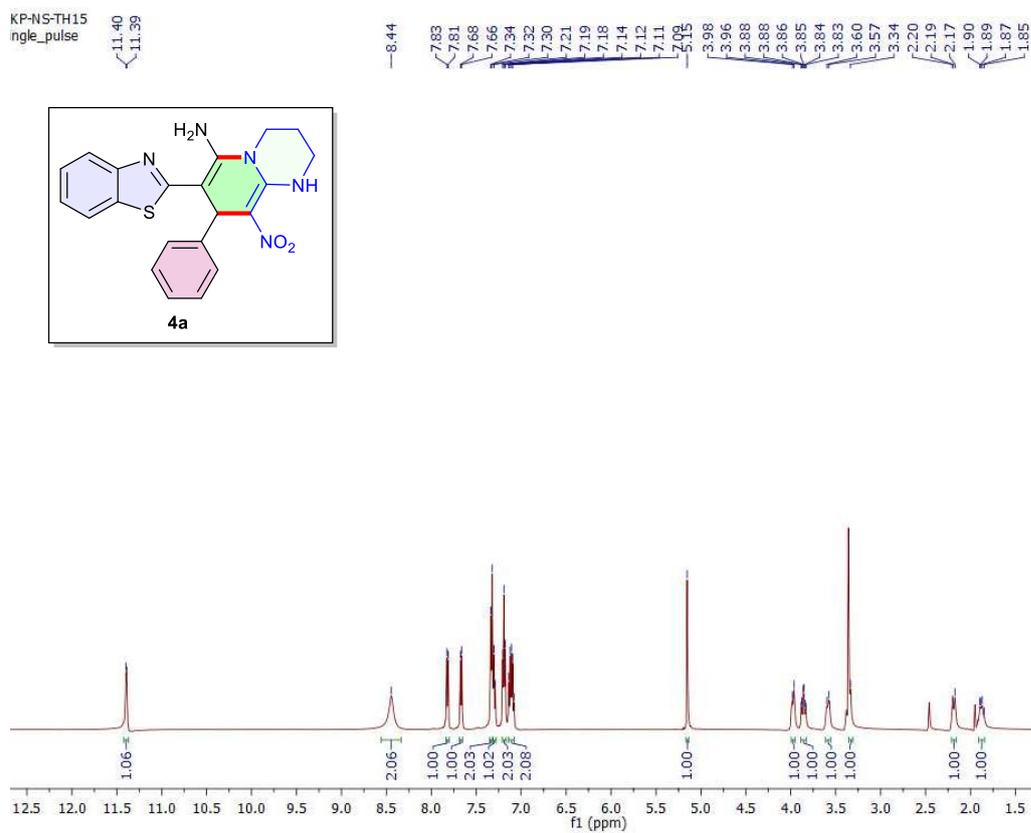
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **3s**



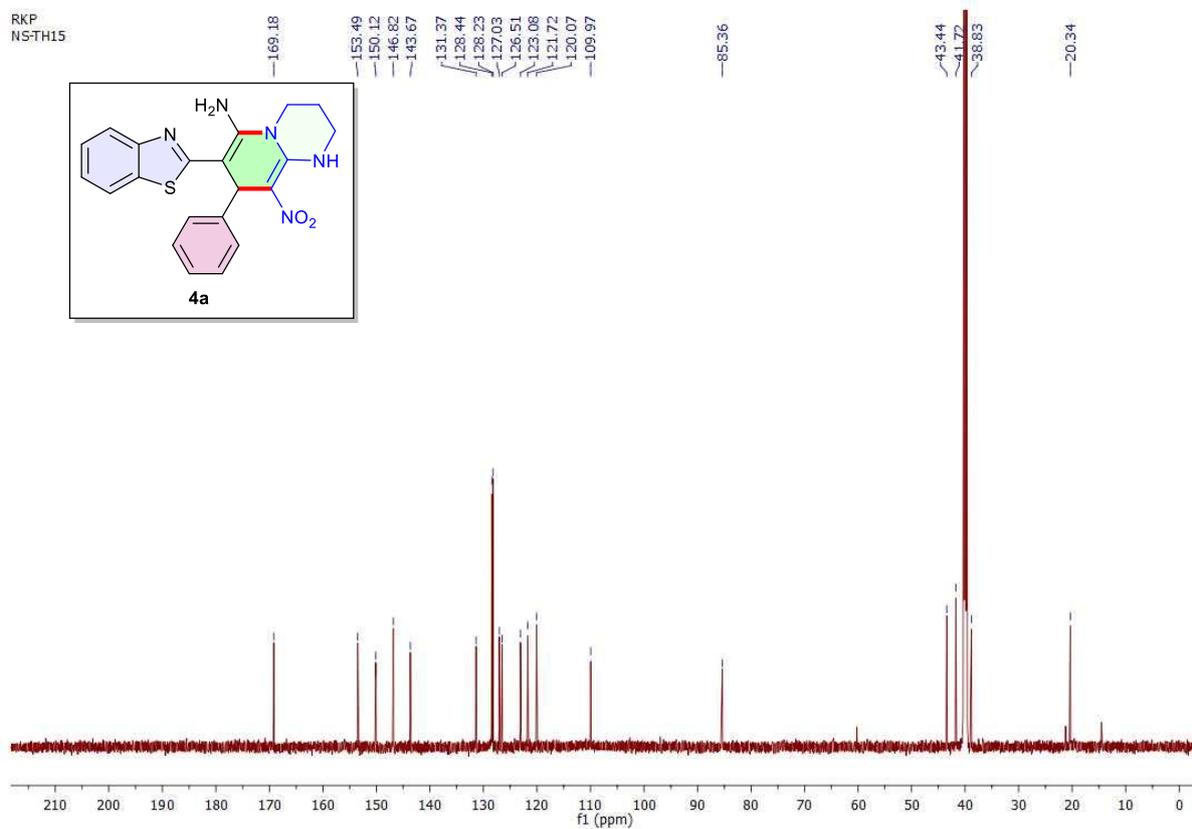
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **3s**



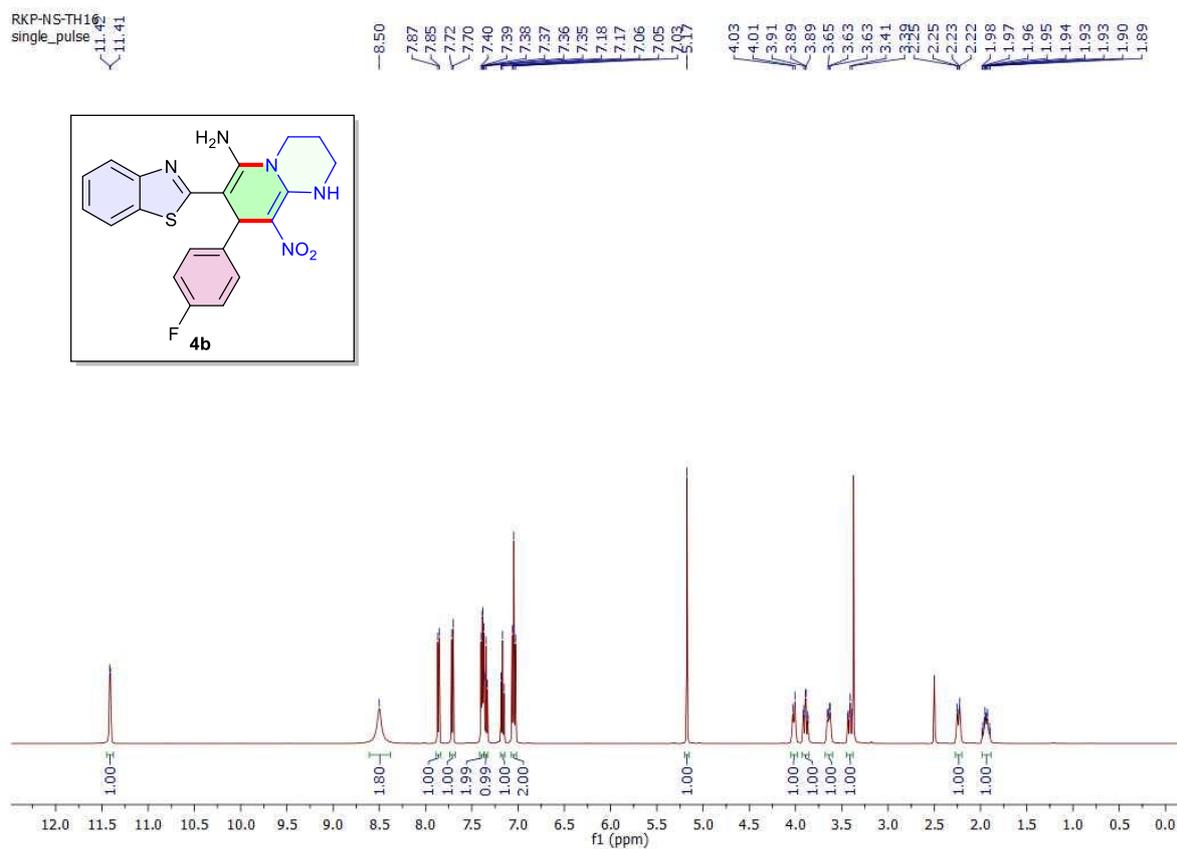
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4a**



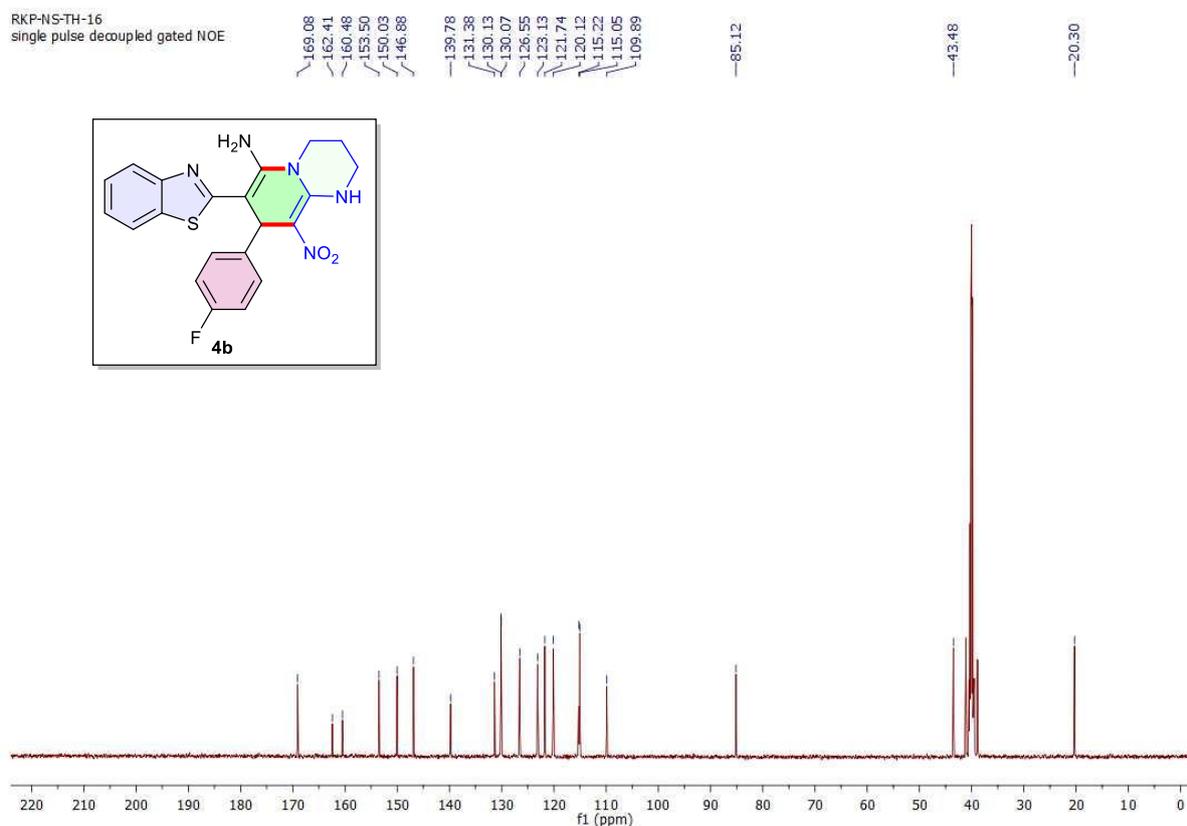
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4a**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4b**

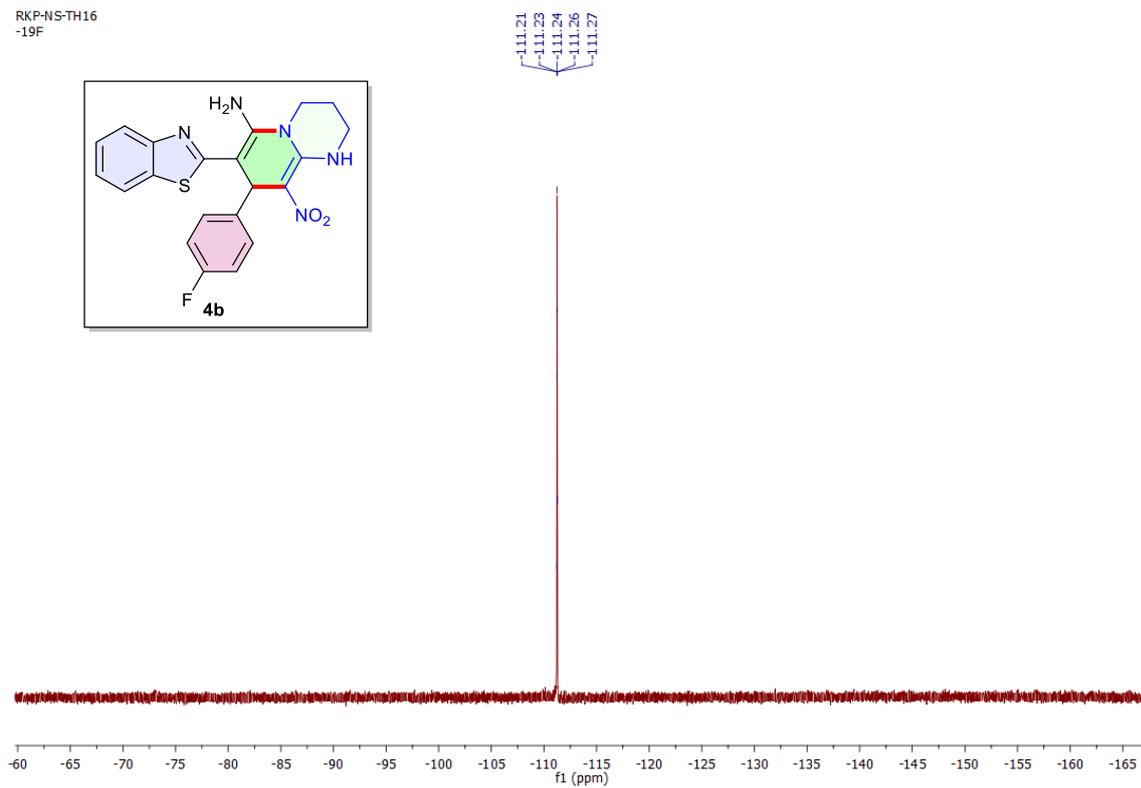
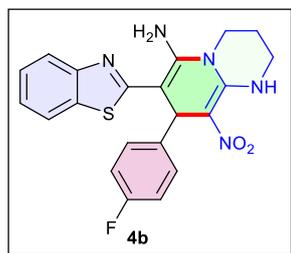


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4b**

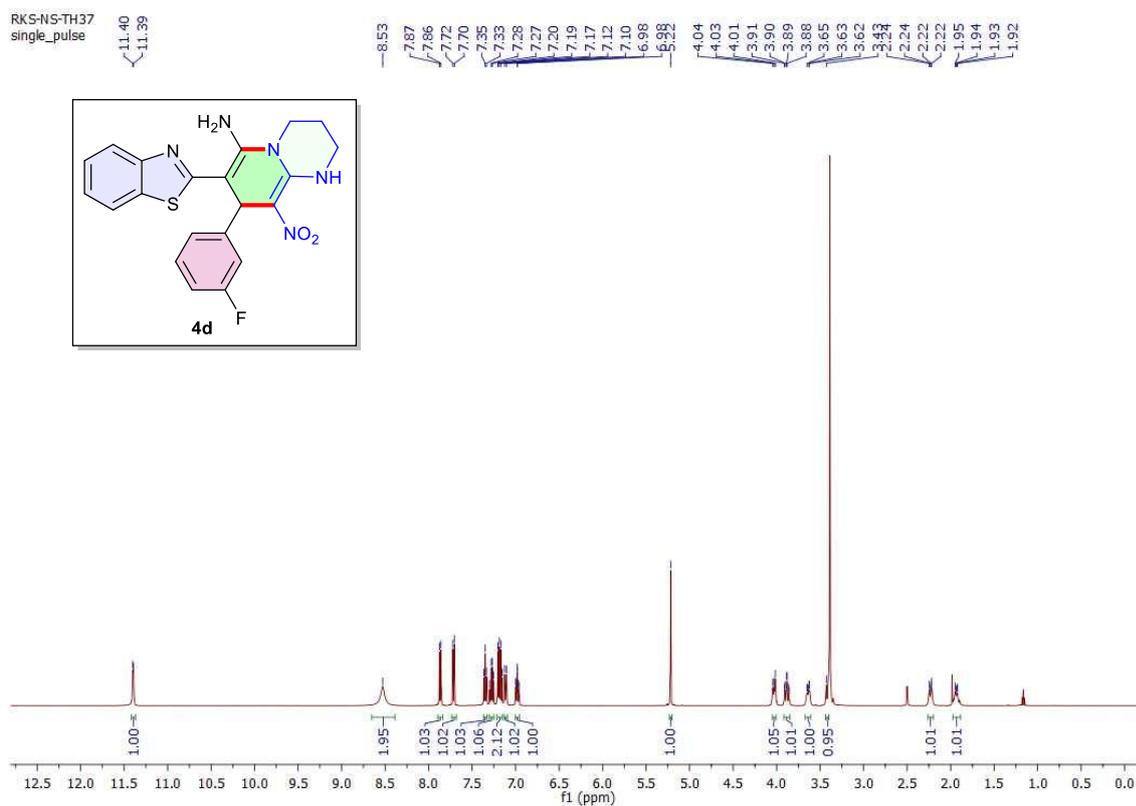


$^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, $\text{DMSO-}d_6$) of **4b**

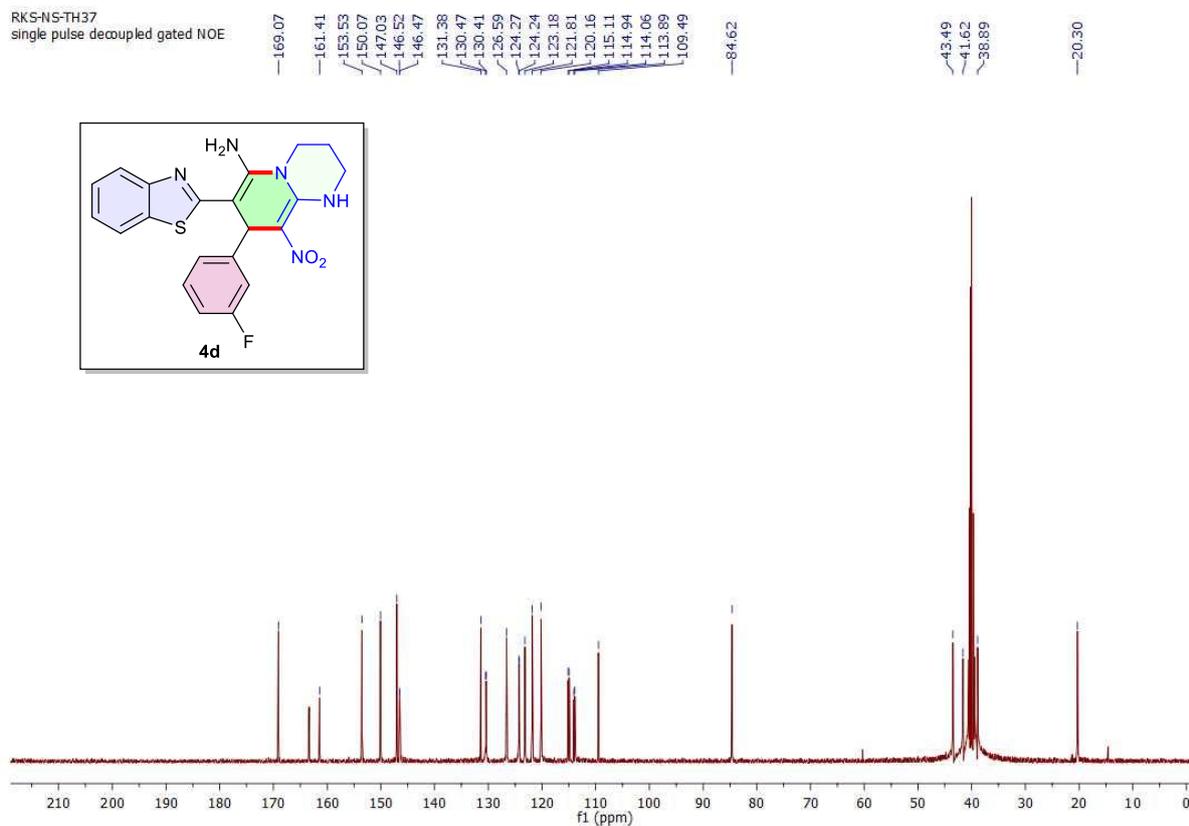
RKP-NS-TH16
-19F



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4d**

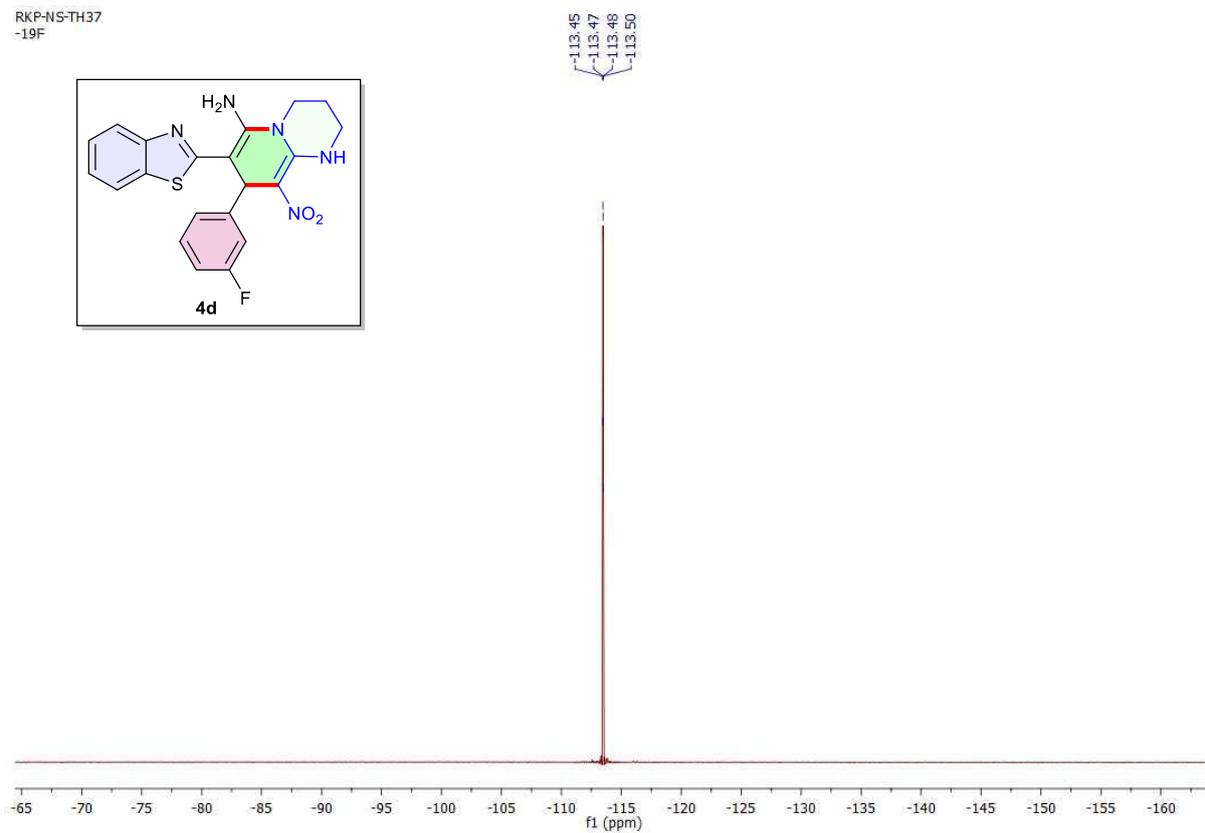
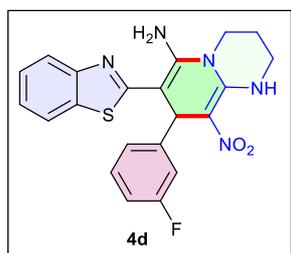


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4d**

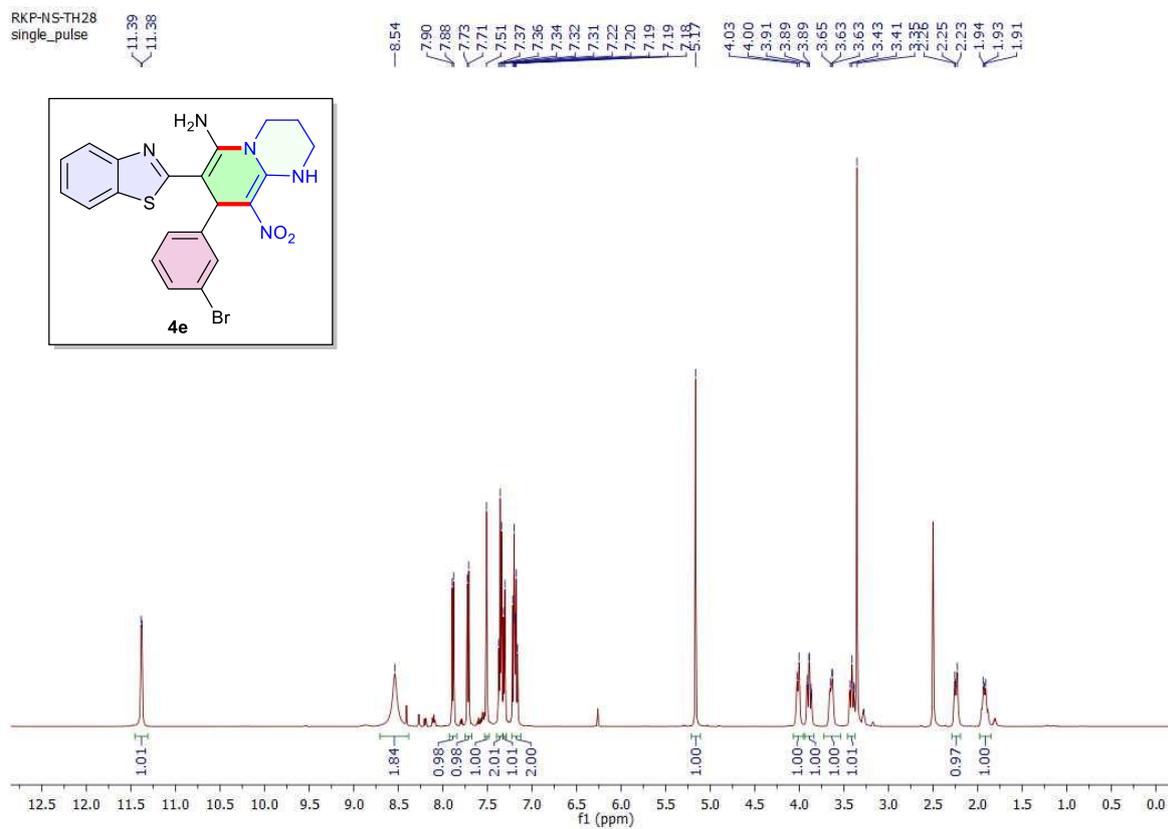


$^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, $\text{DMSO-}d_6$) of **4d**

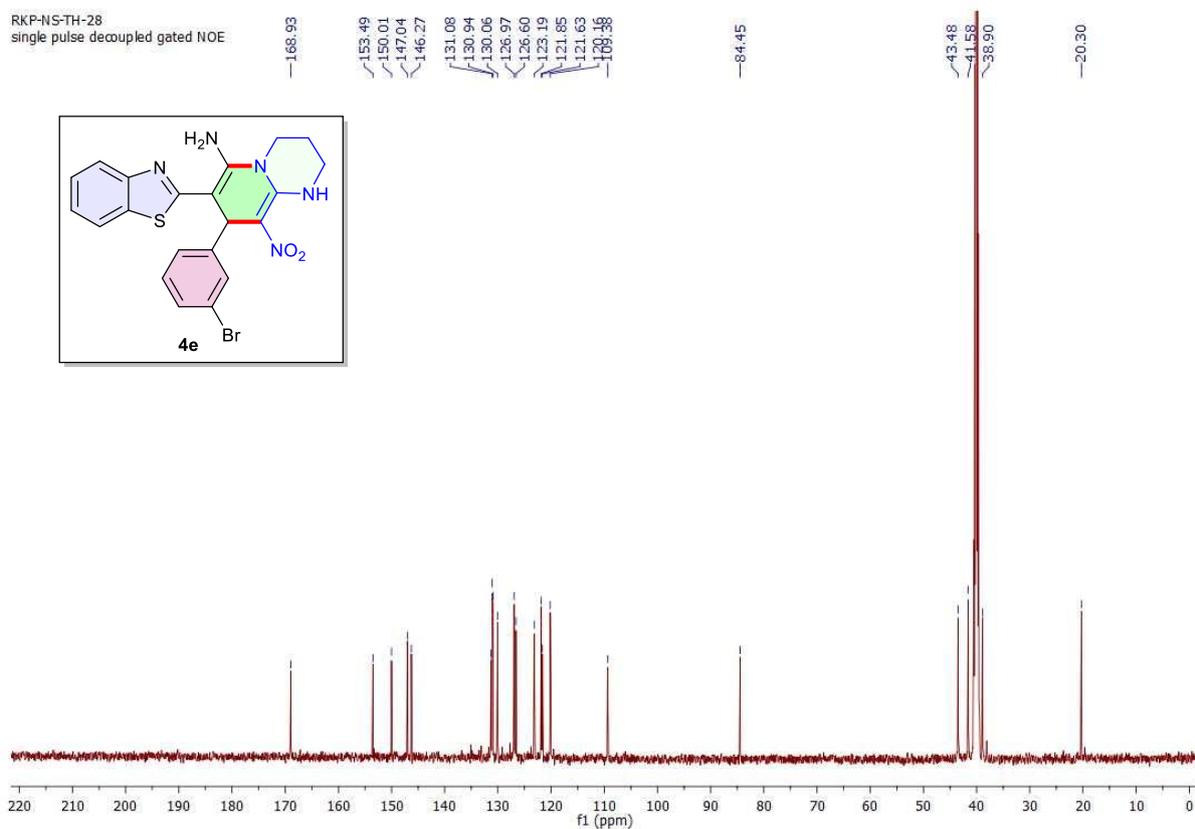
RKP-NS-TH37
-19F



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4e**

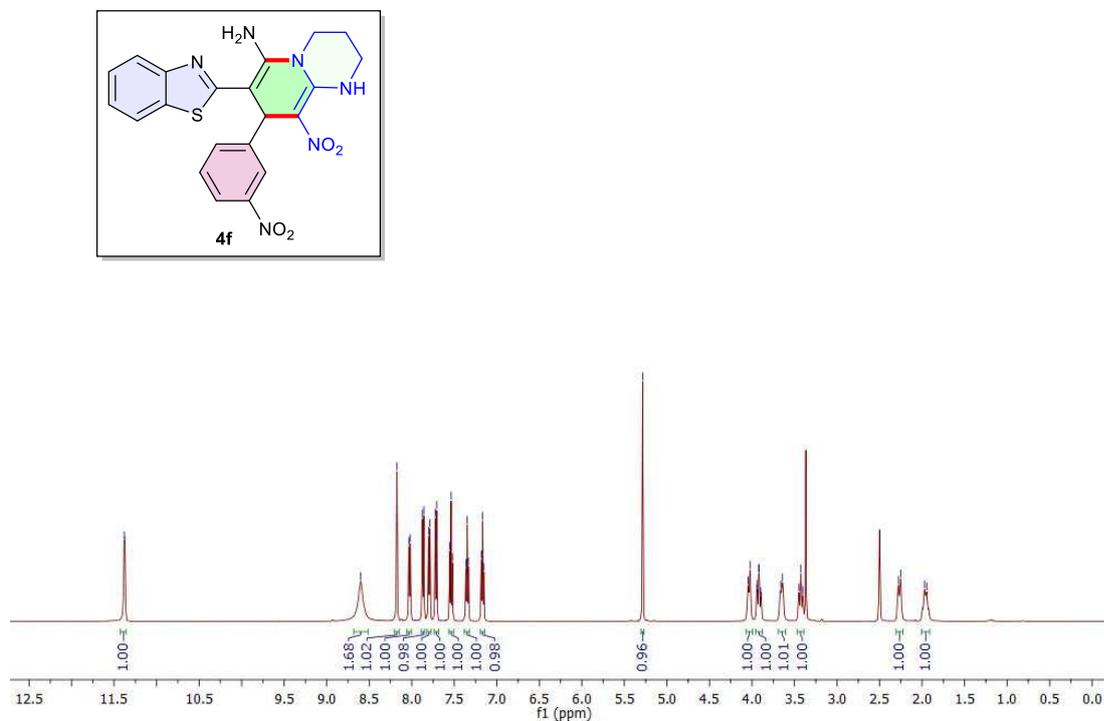


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4e**



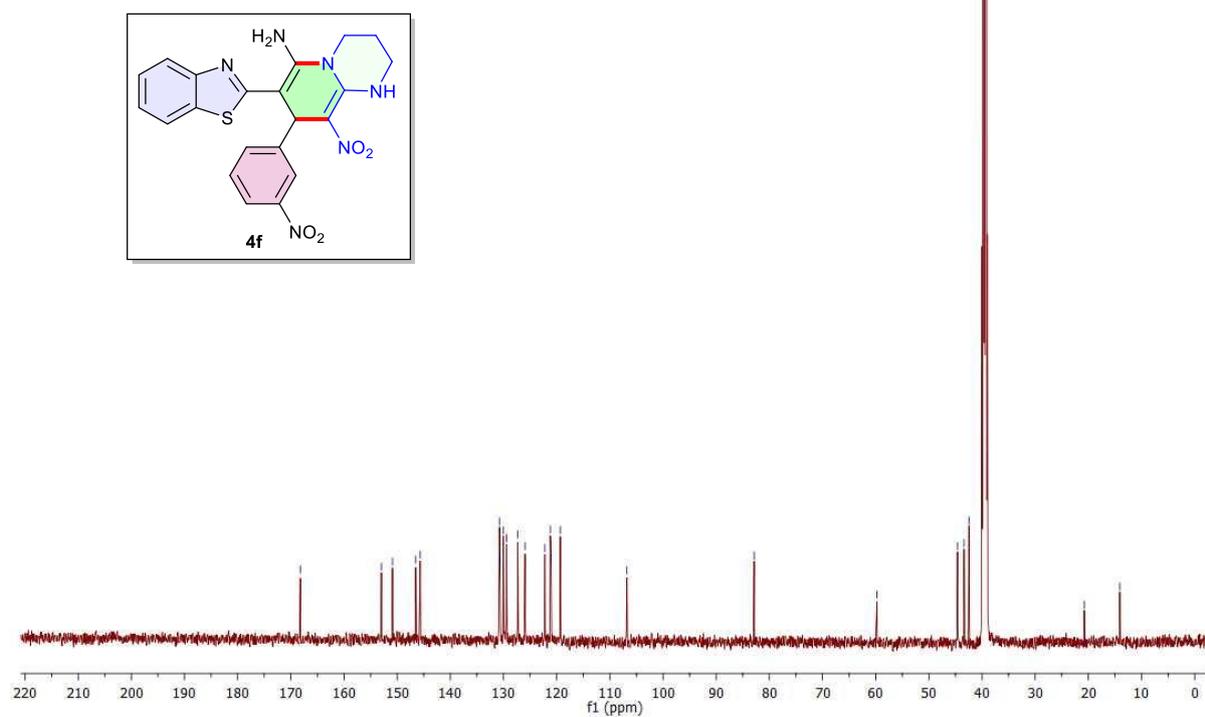
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4f**

NS-TH-26
:pulse

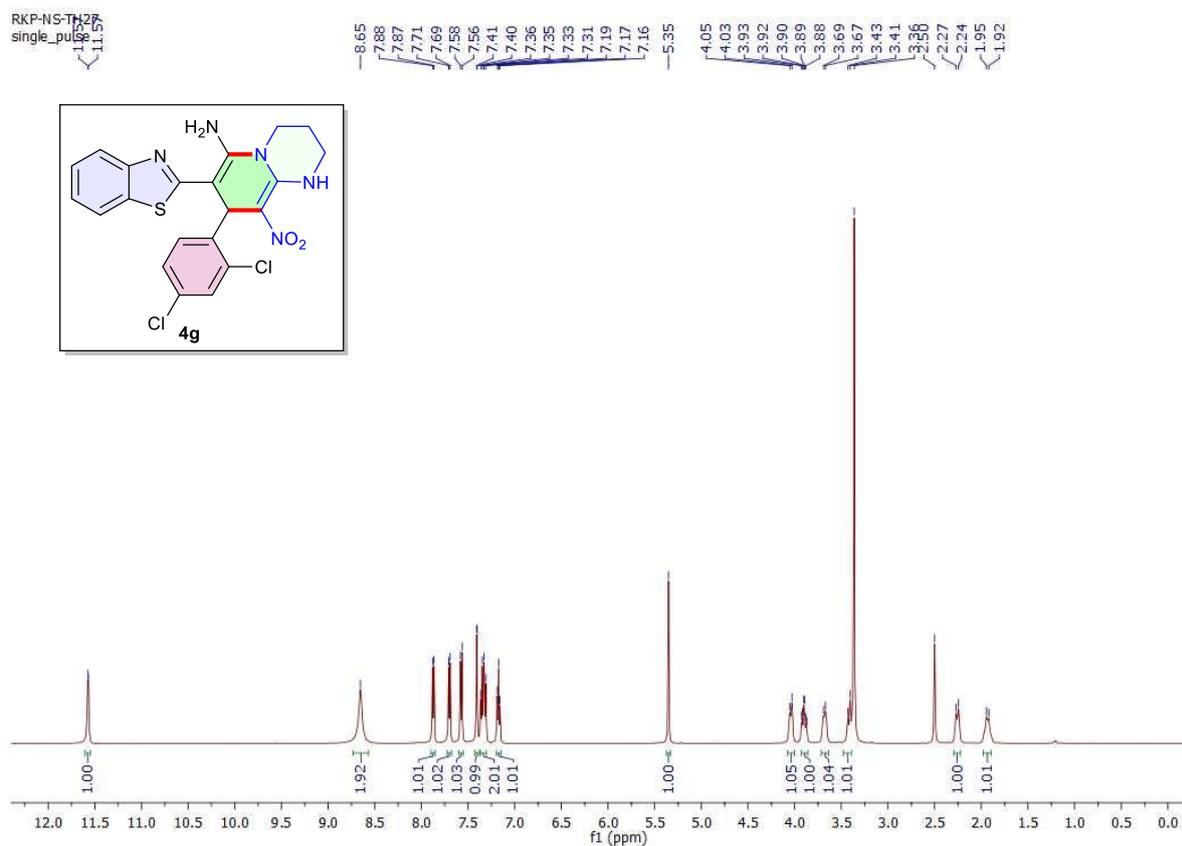


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4f**

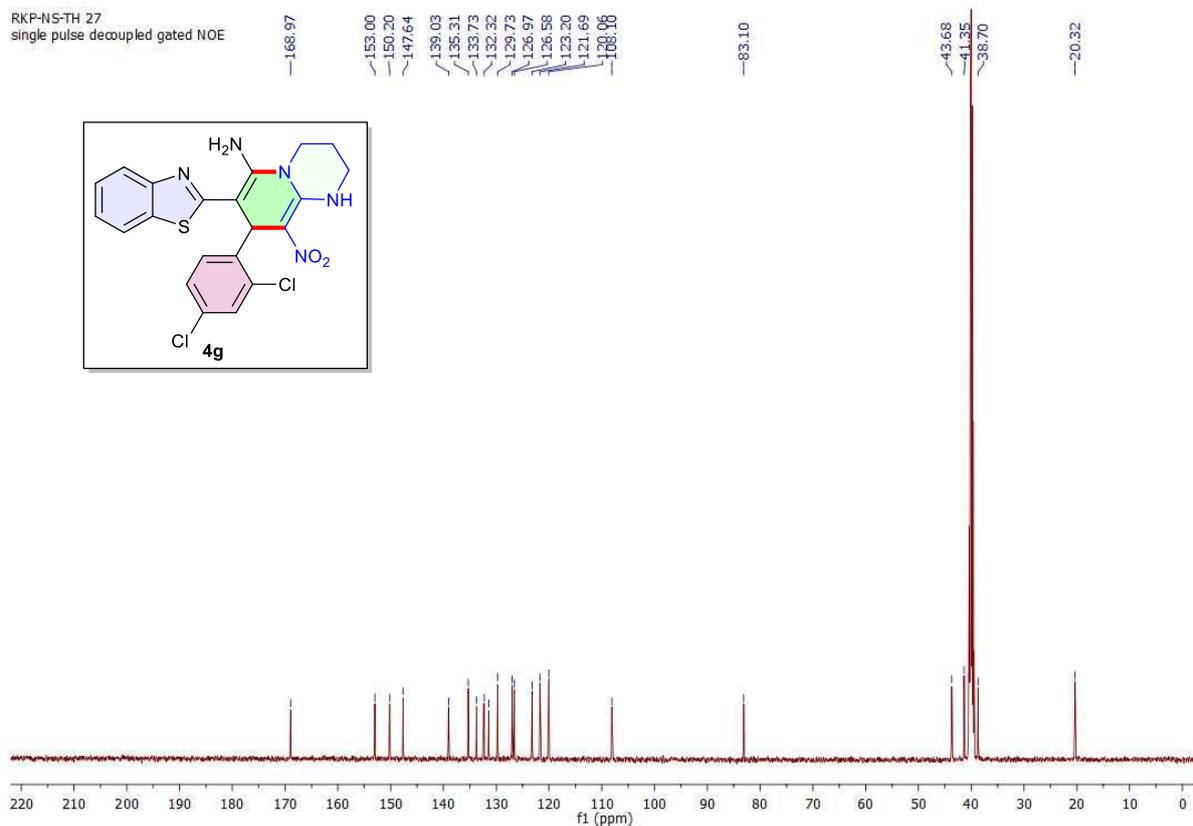
RKP-NS-TH-26
single pulse decoupled gated NOE



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4g**



$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4g**



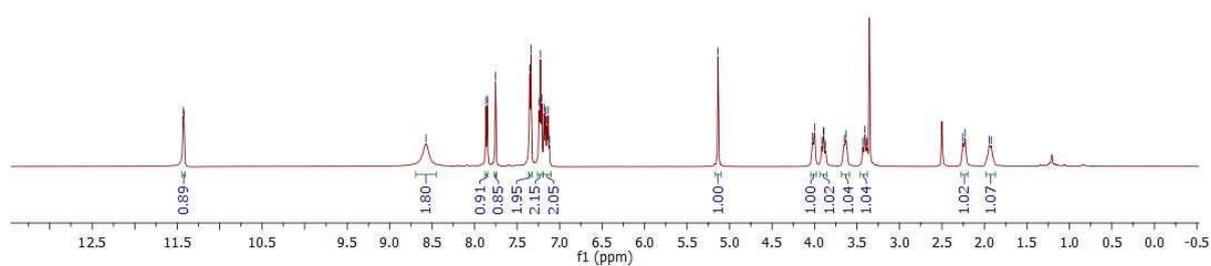
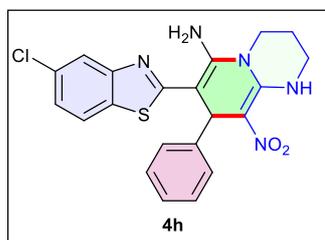
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4h**

RKP-NS-BN-CL 1
single_pulse

11.43
11.42

8.57
7.87
7.85
7.75
7.35
7.34
7.24
7.23
7.21
7.18
7.17
7.15
7.13
7.12

5.14
4.02
4.00
3.91
3.90
3.89
3.87
3.65
3.63
3.43
3.41
3.38
2.25
2.23
1.95
1.92



$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4h**

RKP-NS-BNCL 1
single pulse decoupled gated NOE

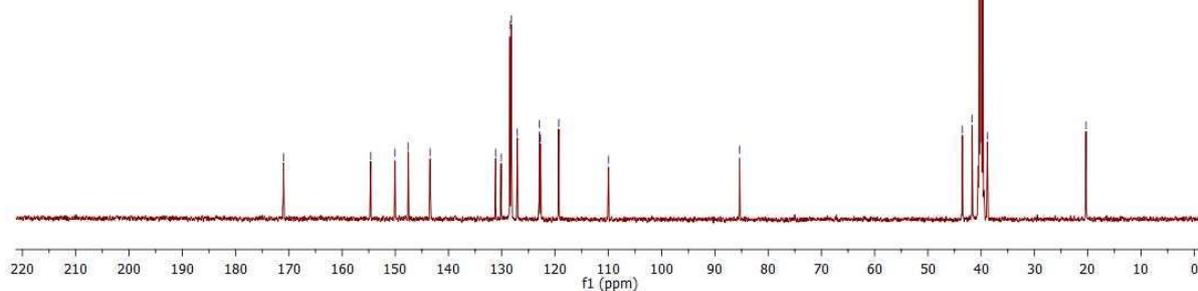
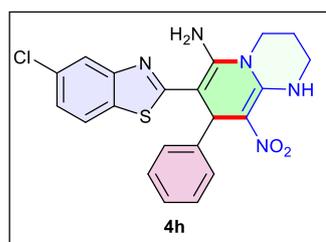
171.02

154.62
150.06
147.57
143.48
131.17
130.13
128.46
128.23
127.08
122.96
122.71
119.31
109.95

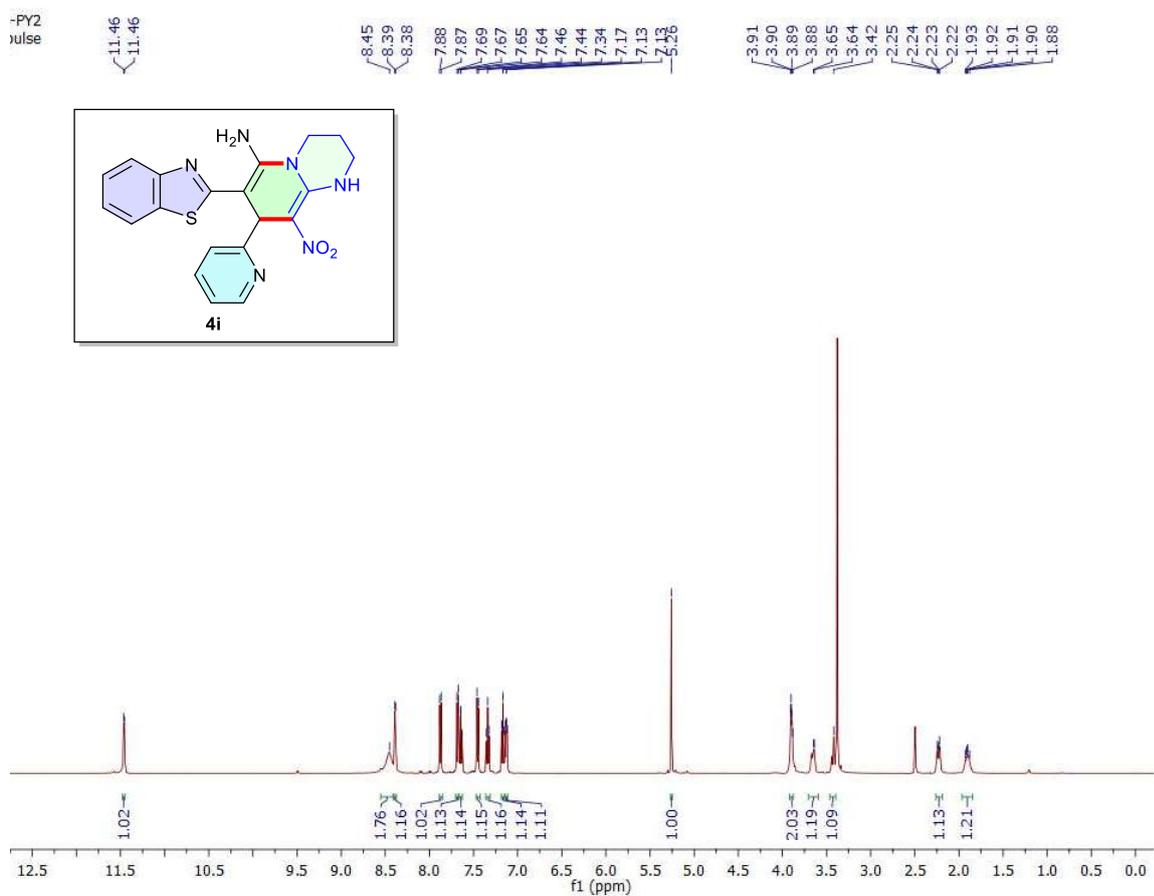
85.36

43.52
41.69
40.17
40.00
39.83
38.84

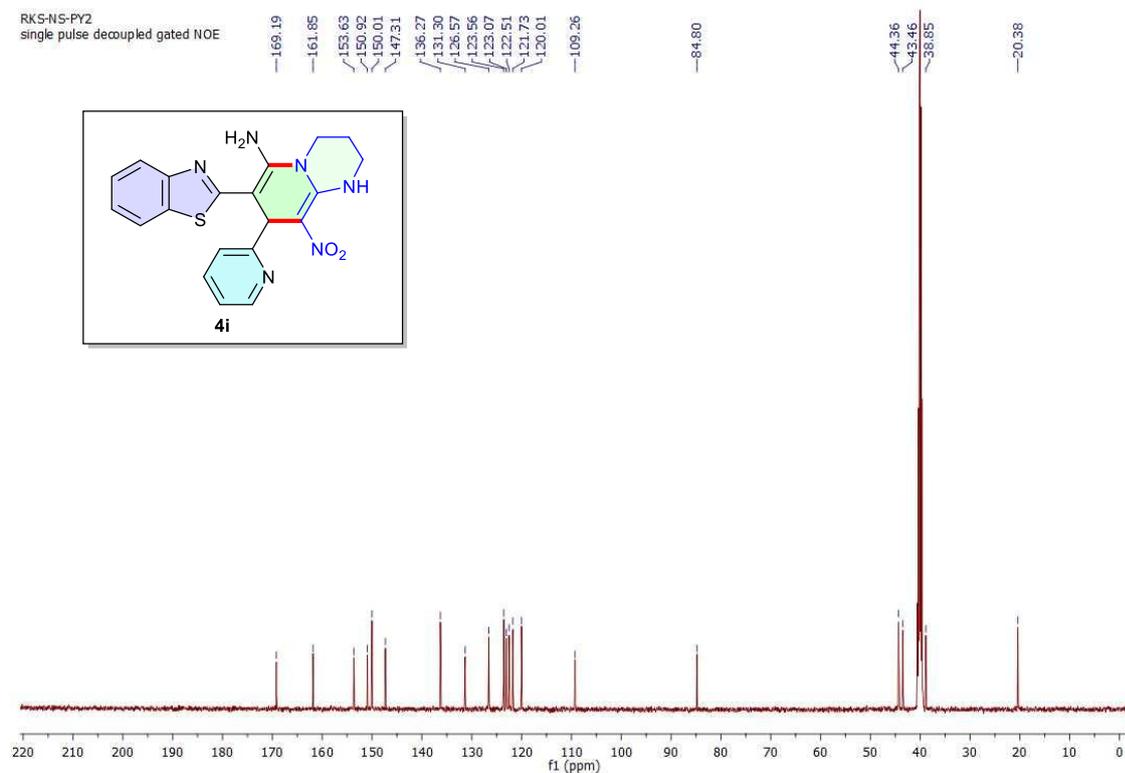
20.32



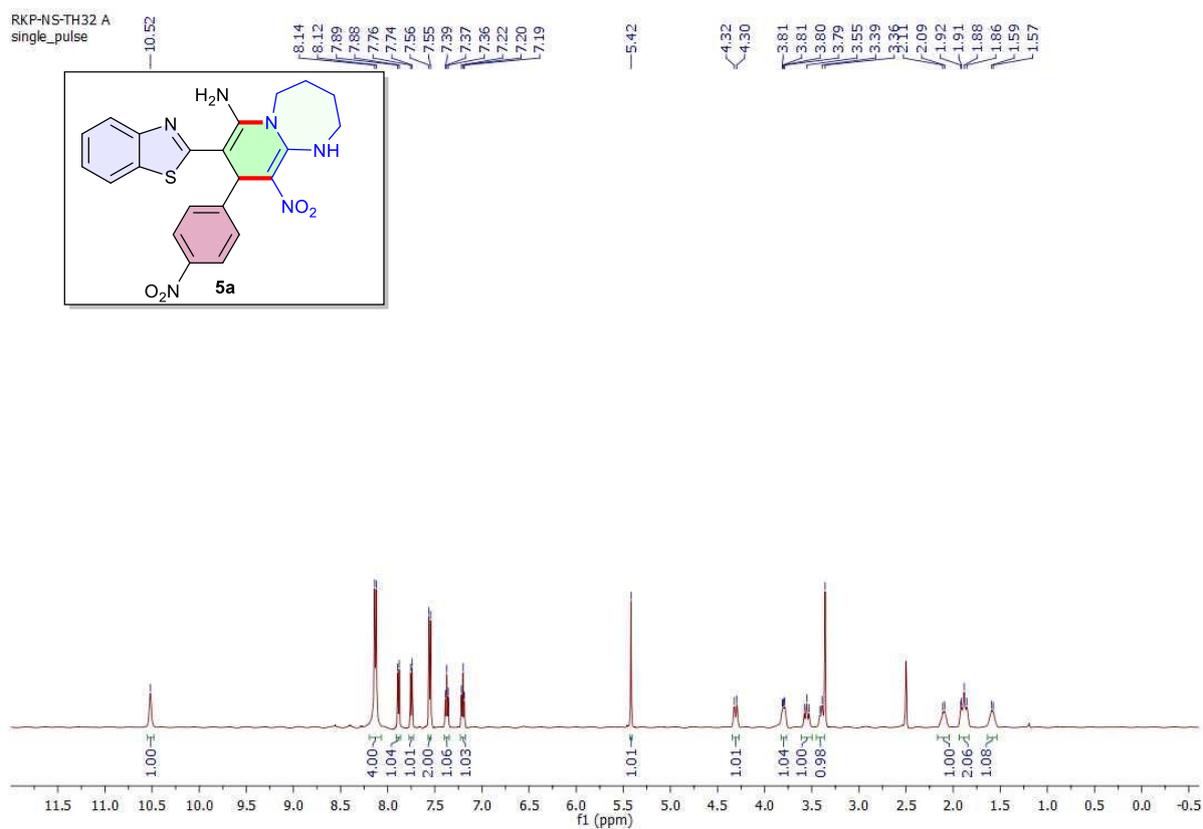
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4i**



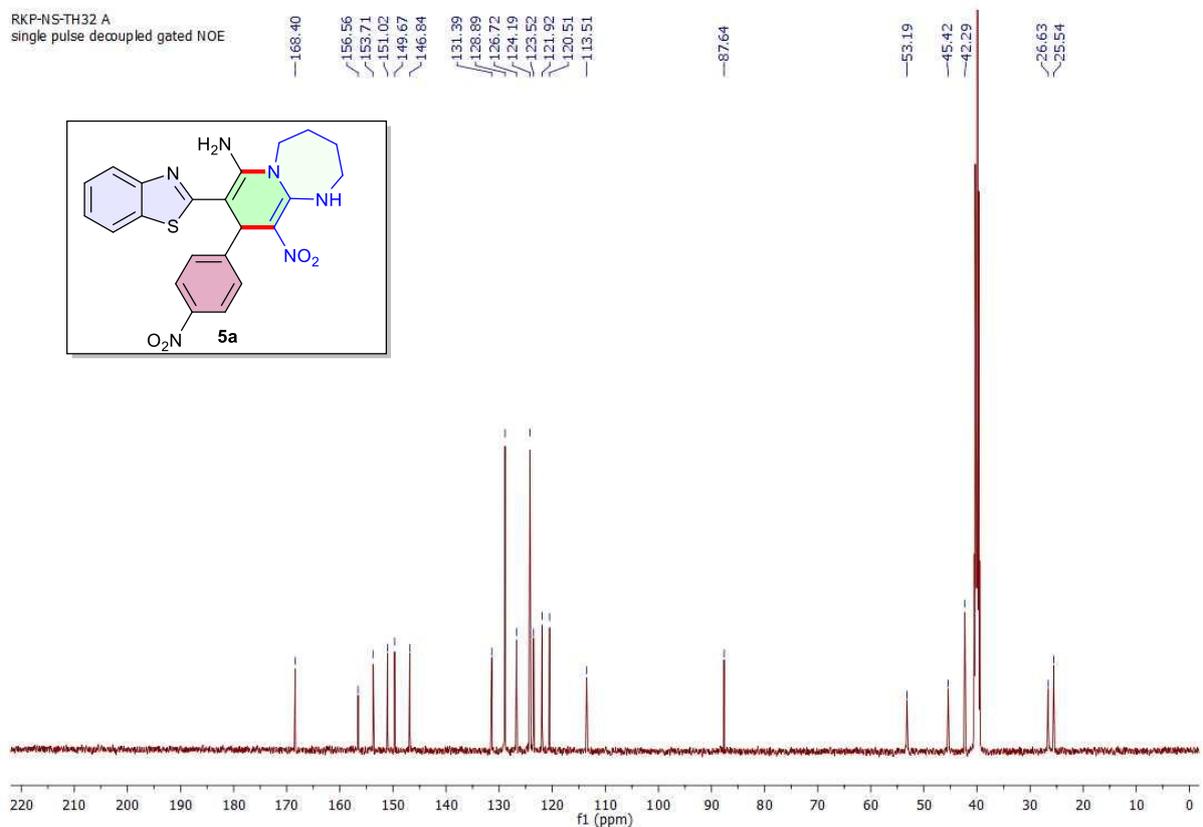
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **4i**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **5a**

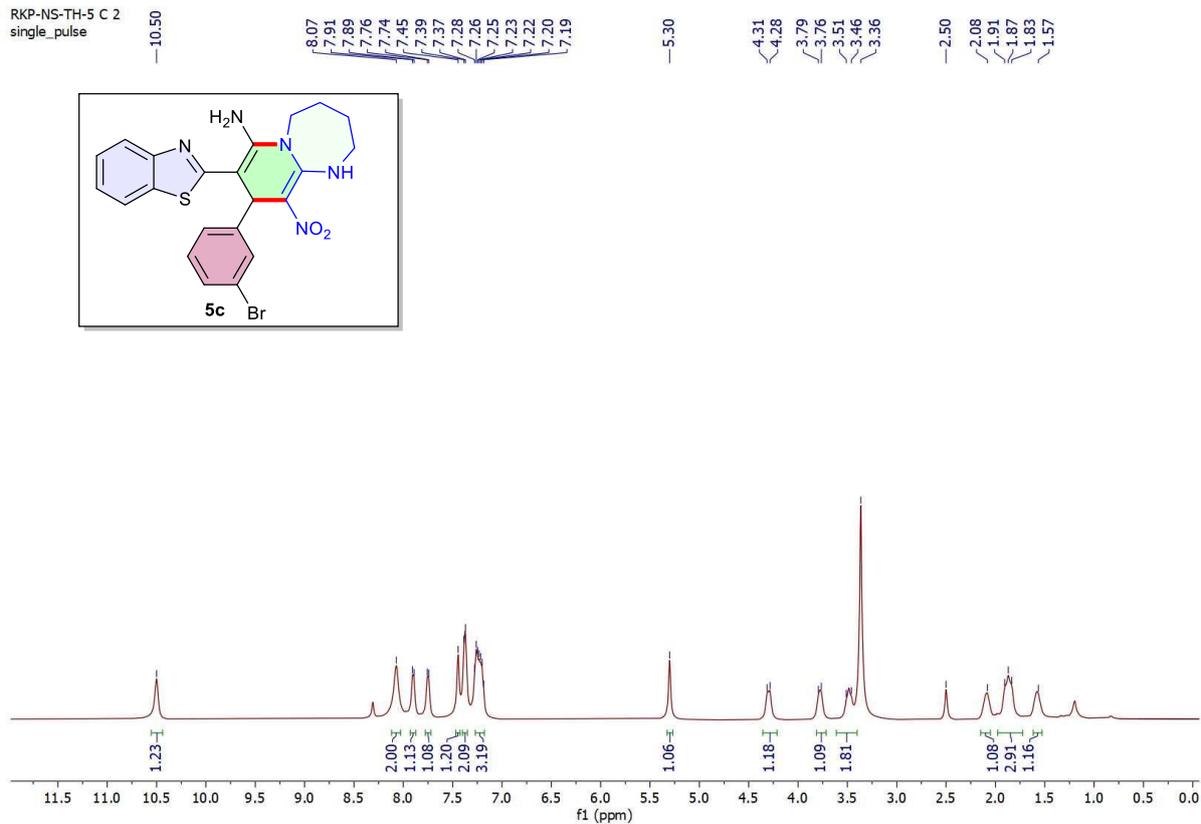
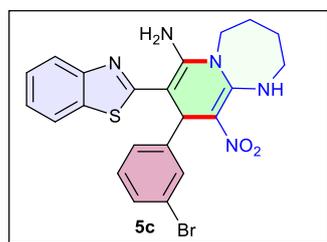


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **5a**



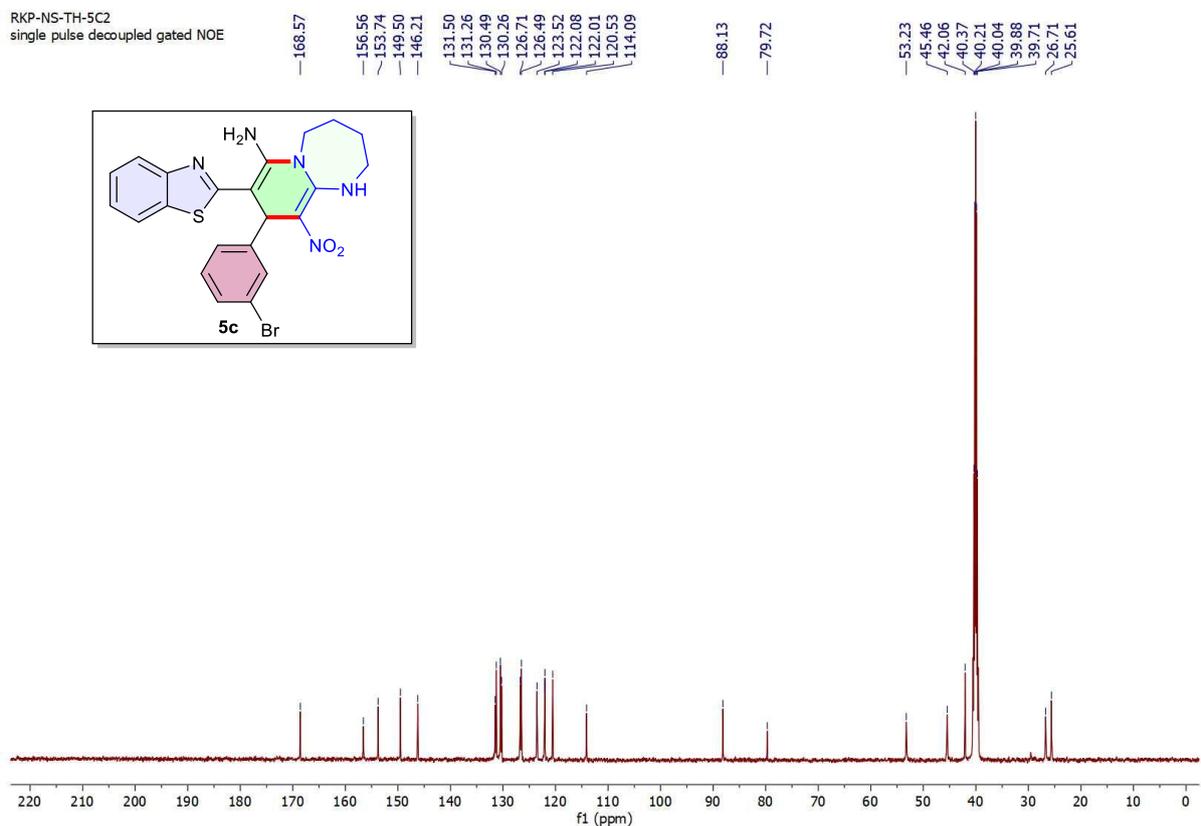
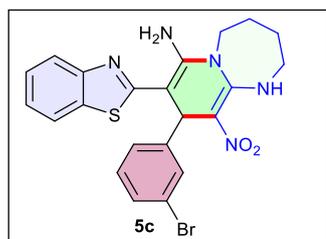
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **5c**

RKP-NS-TH-5 C 2
single_pulse

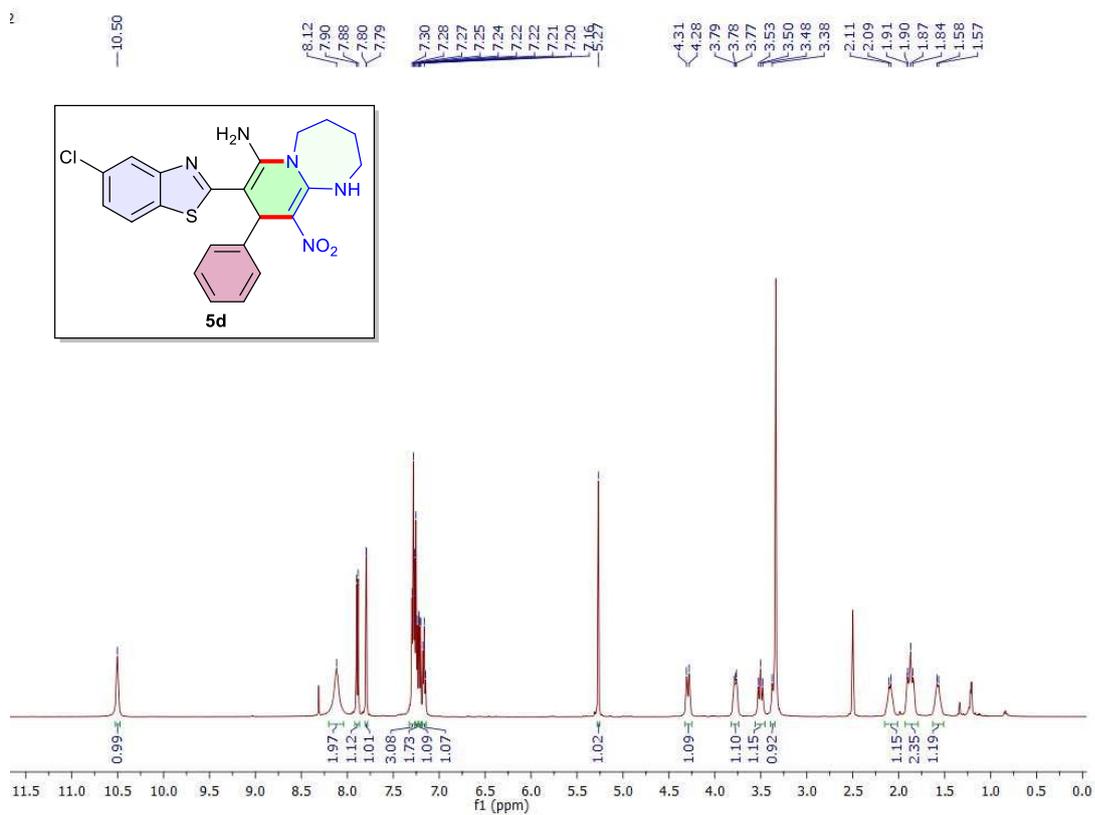


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **5c**

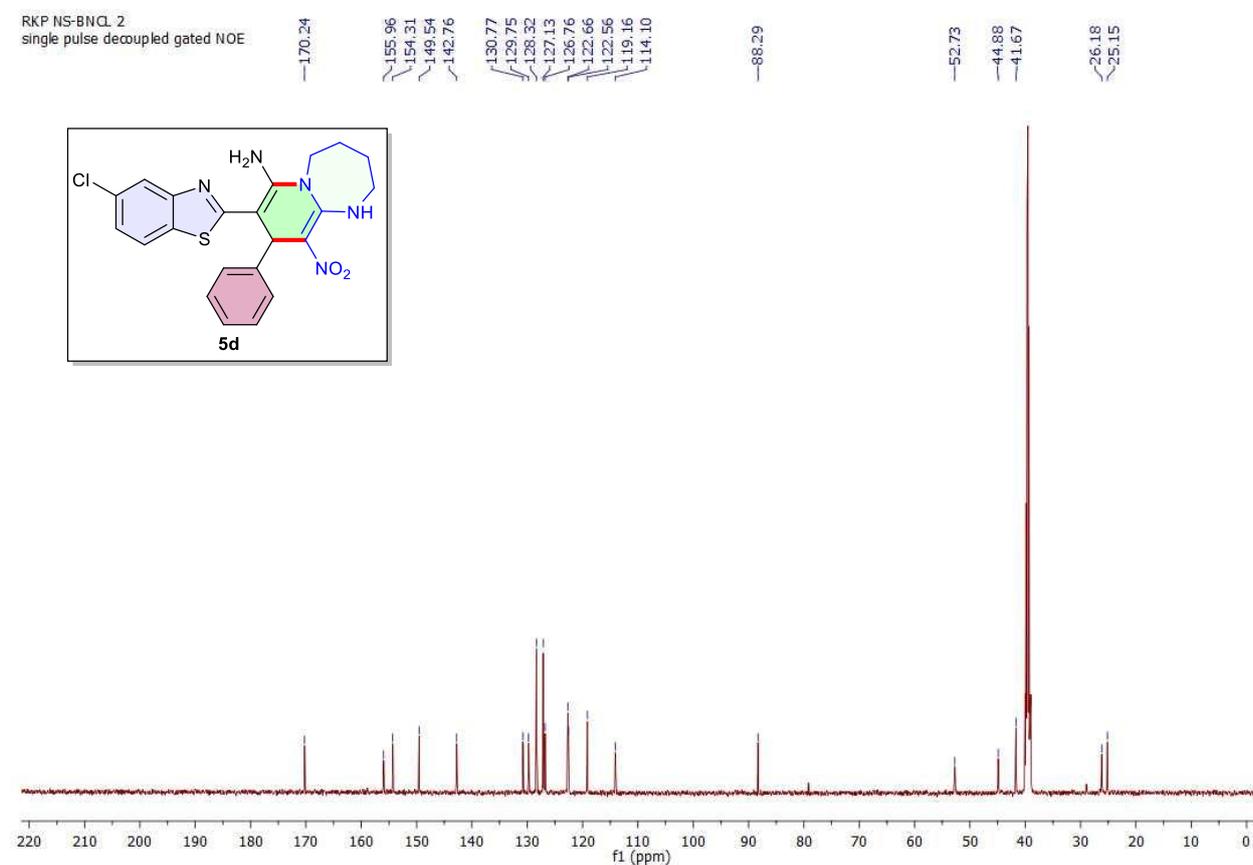
RKP-NS-TH-5C2
single_pulse decoupled gated NOE



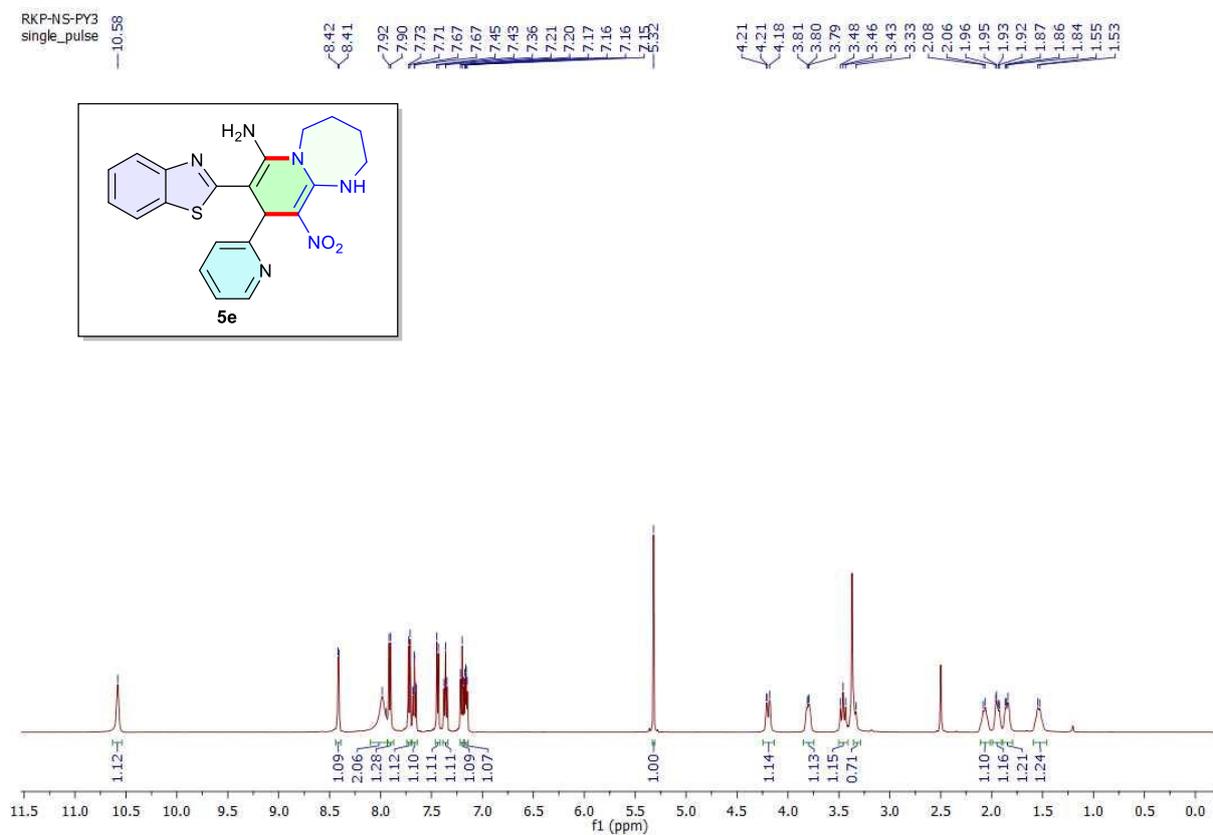
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **5d**



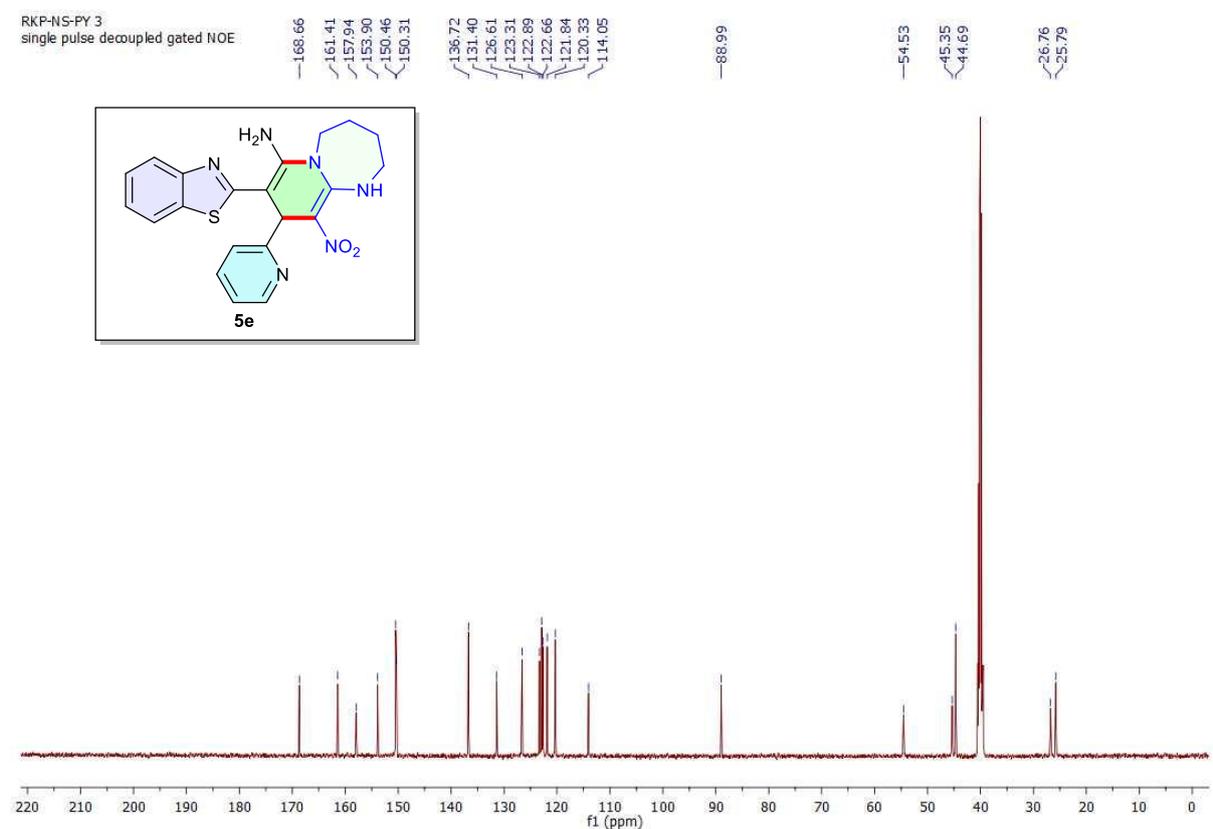
^{13}C $\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **5d**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **5e**

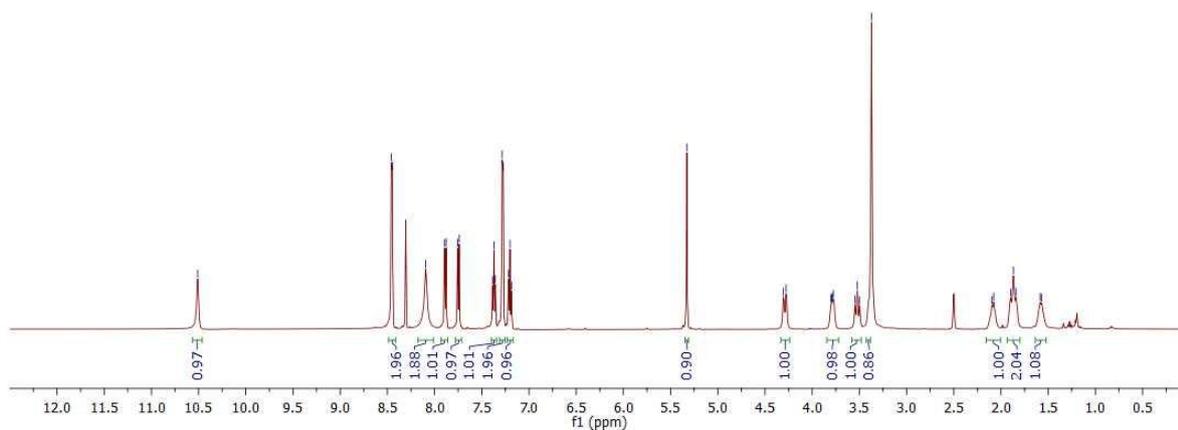
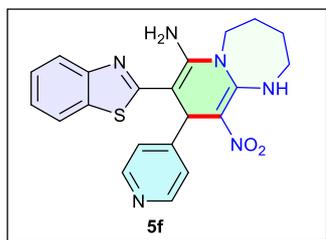


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **5e**



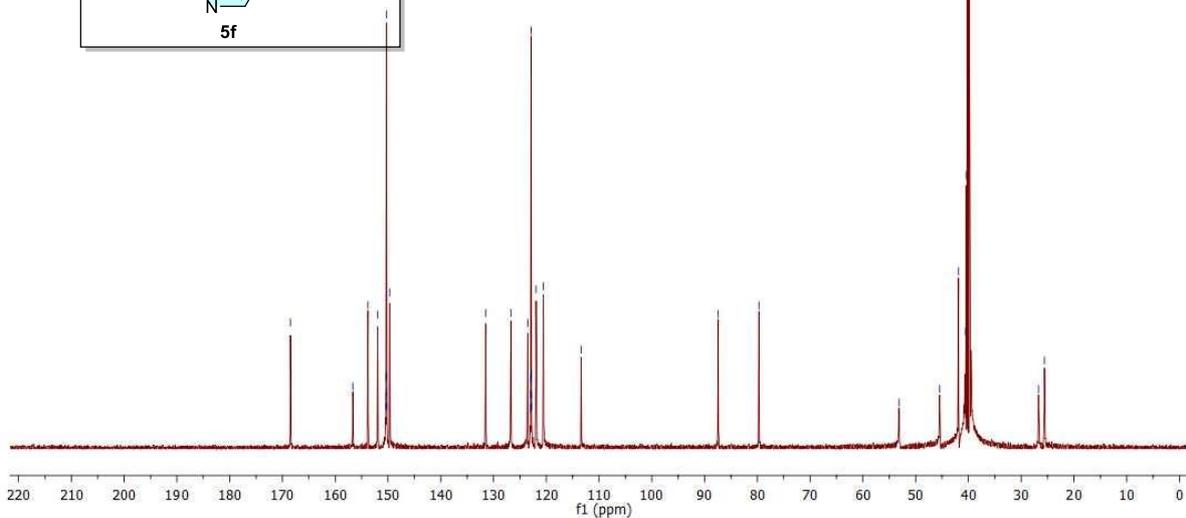
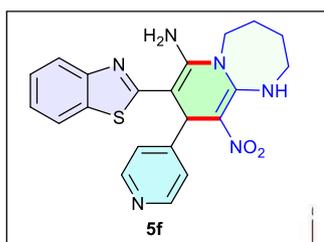
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **5f**

RKP-NS-PY 6
single_pulse



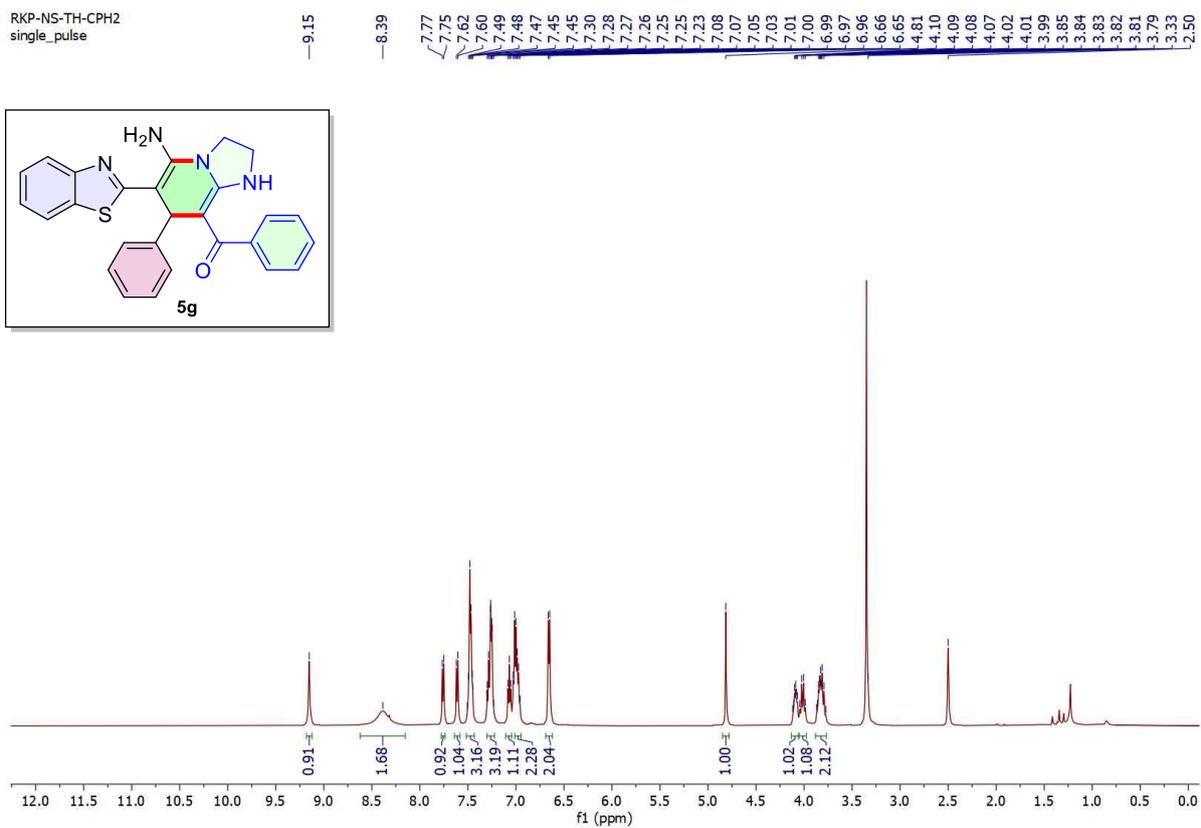
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **5f**

RKP-NS-PY 6
single pulse decoupled gated NOE



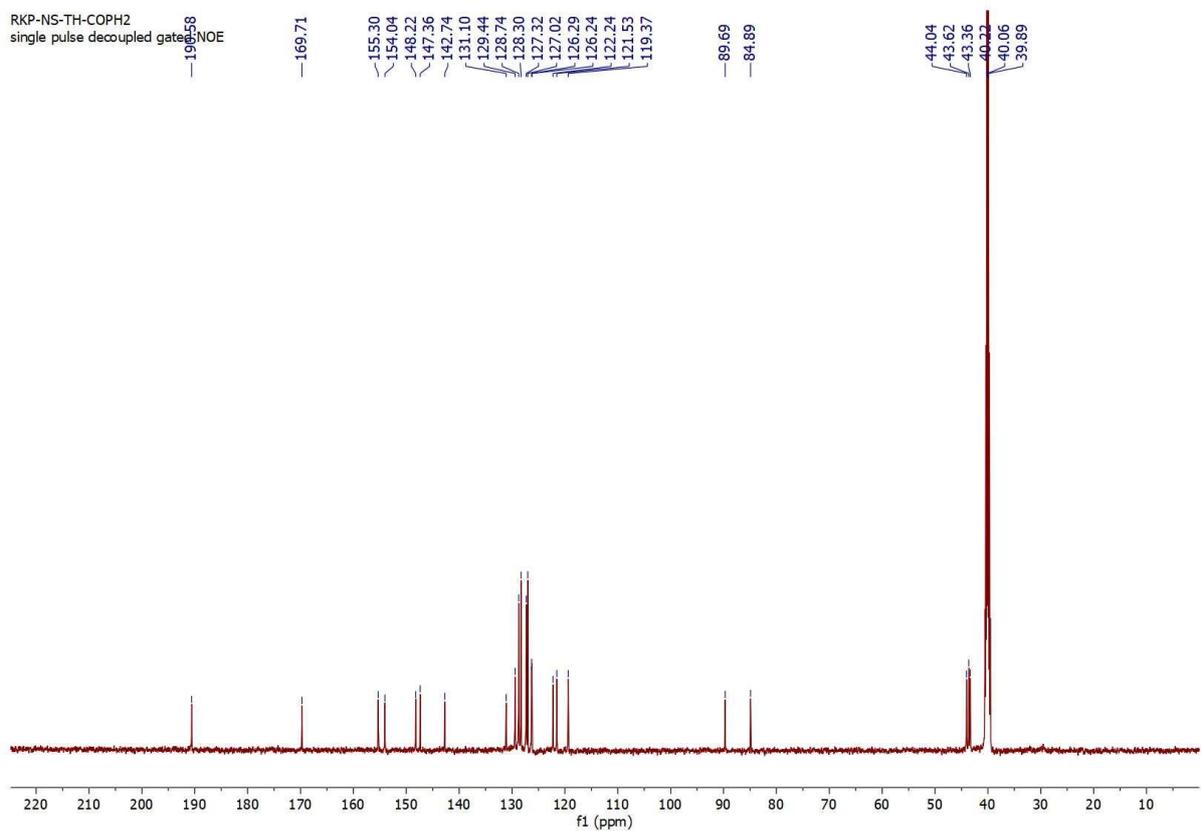
^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **5g**

RKP-NS-TH-CPH2
single_pulse

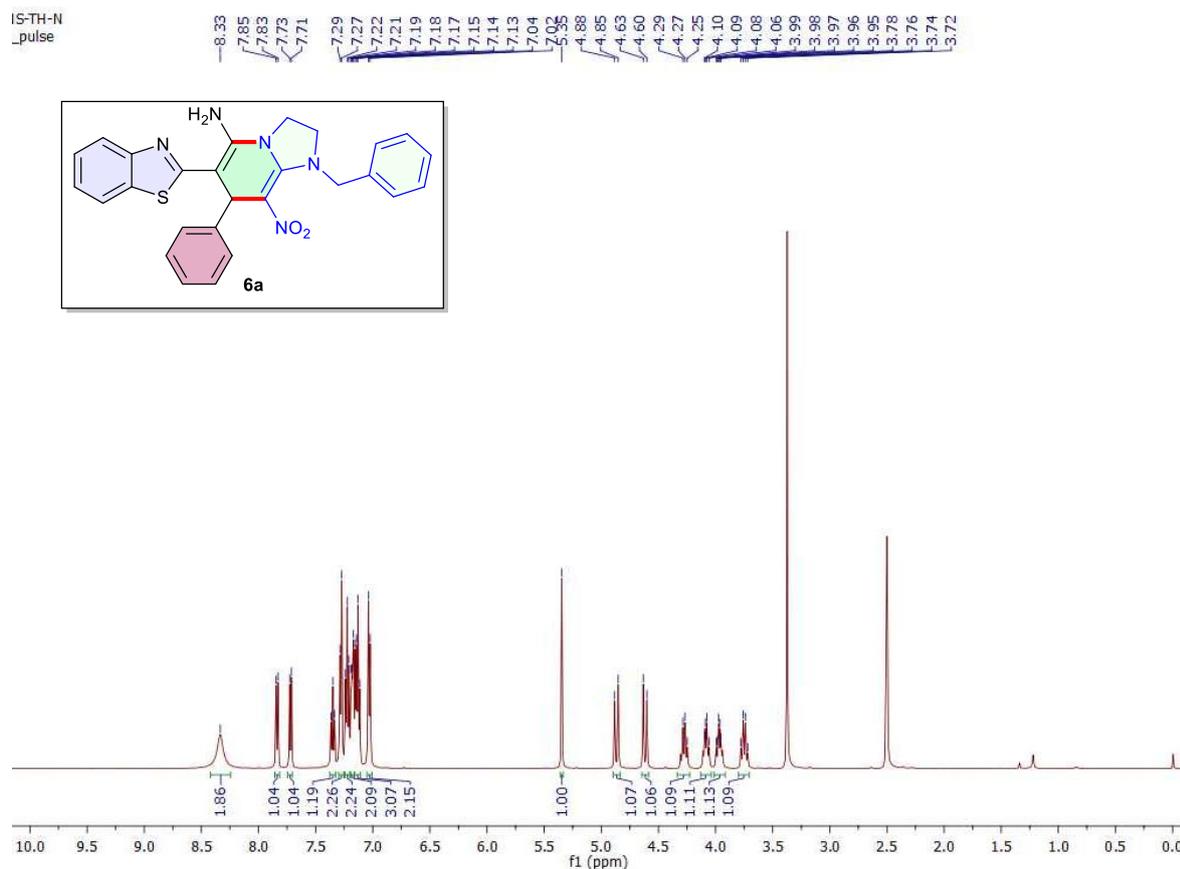


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **5g**

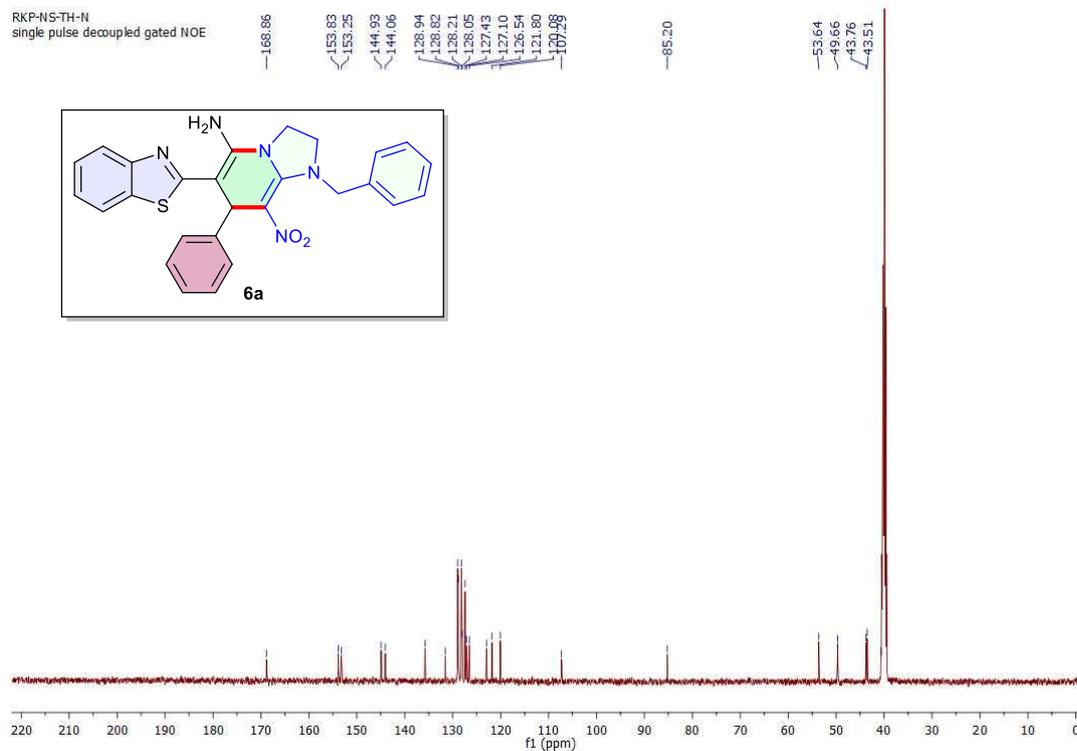
RKP-NS-TH-COPH2
single pulse decoupled gated NOE



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **6a**



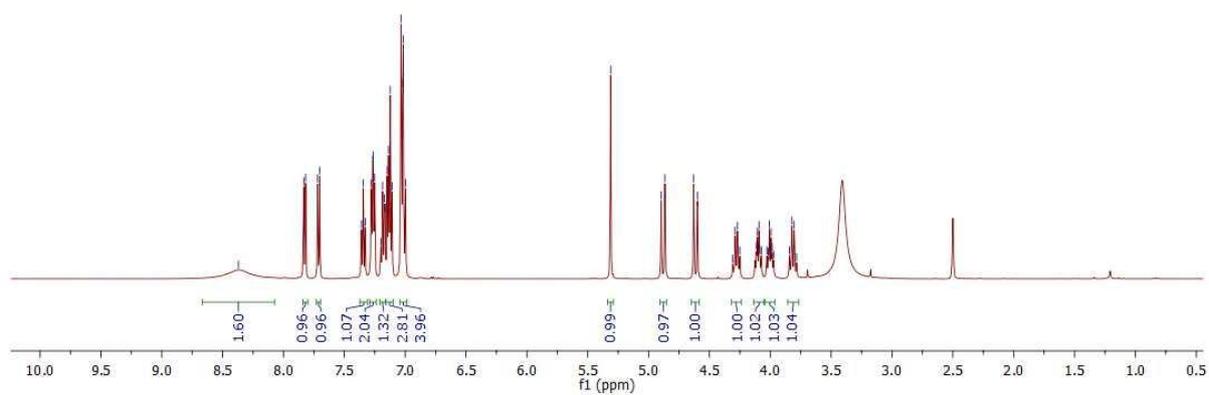
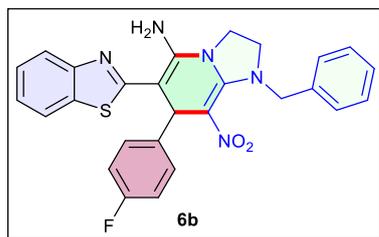
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **6a**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **6b**

RKP-NS-TH-21
single_pulse

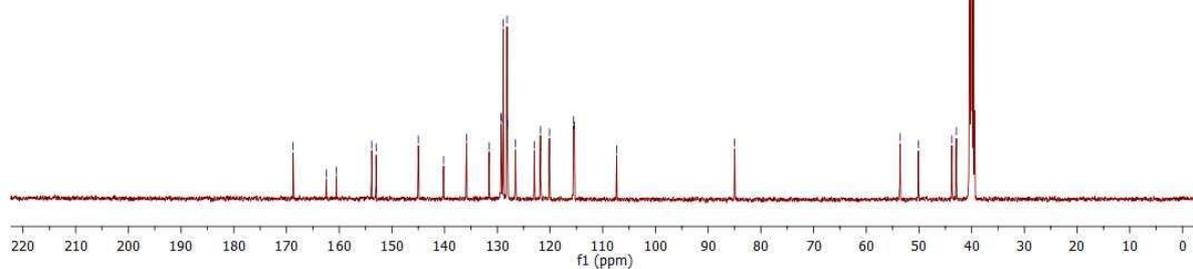
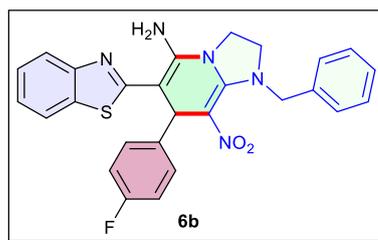
8.37, 7.83, 7.82, 7.72, 7.70, 7.34, 7.28, 7.27, 7.26, 7.25, 7.19, 7.15, 7.14, 7.12, 7.11, 7.03, 7.02, 7.01, 5.31, 4.90, 4.87, 4.63, 4.60, 4.31, 4.29, 4.27, 4.25, 4.11, 4.09, 4.07, 4.03, 4.02, 4.01, 3.99, 3.97, 3.84, 3.82, 3.80, 3.78



$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **6b**

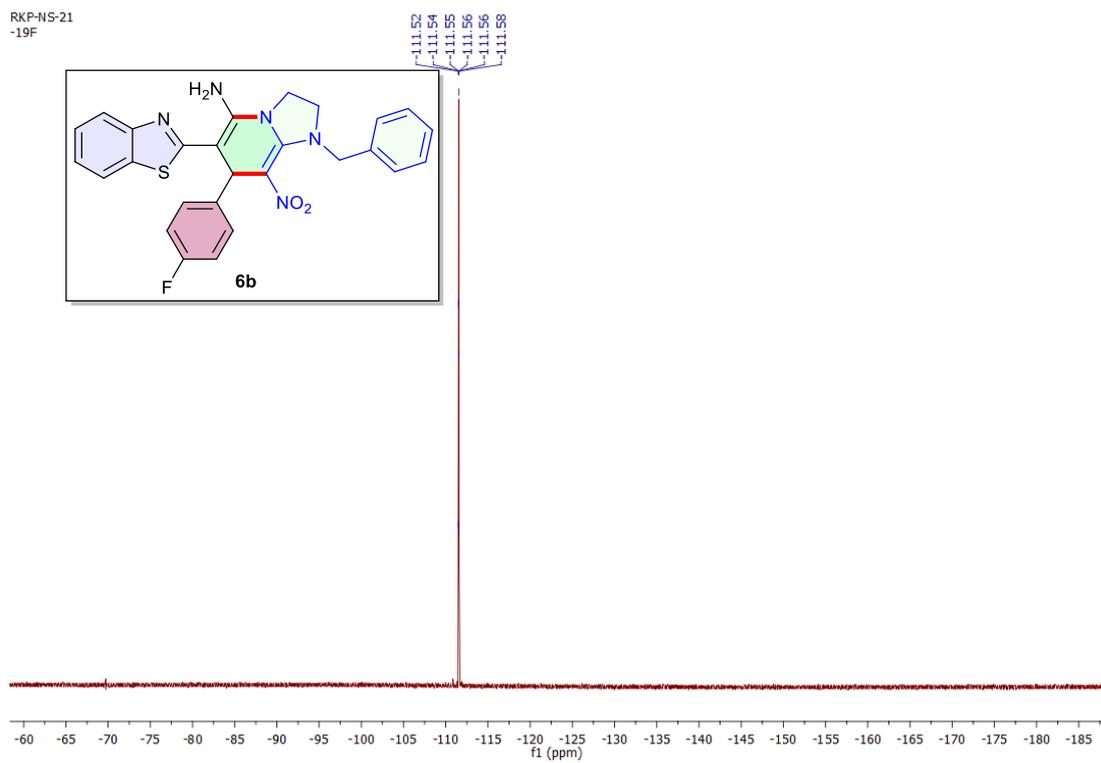
RKP-NS-21
single pulse decoupled gated NOE

168.74, 162.45, 160.55, 153.85, 153.00, 145.00, 135.84, 129.28, 129.22, 128.90, 128.15, 126.58, 126.06, 121.81, 120.11, 115.54, 107.37, 84.97, 53.59, 50.10, 43.76, 42.90

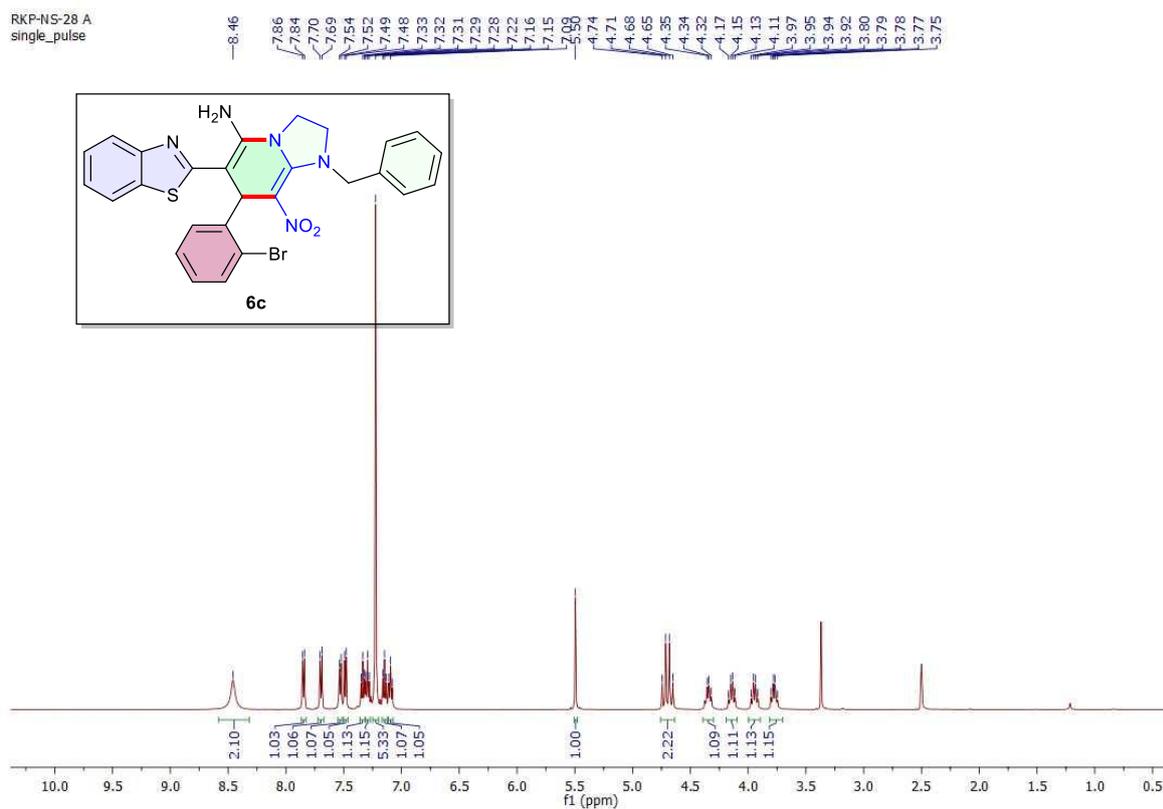


$^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, $\text{DMSO-}d_6$) of **6b**

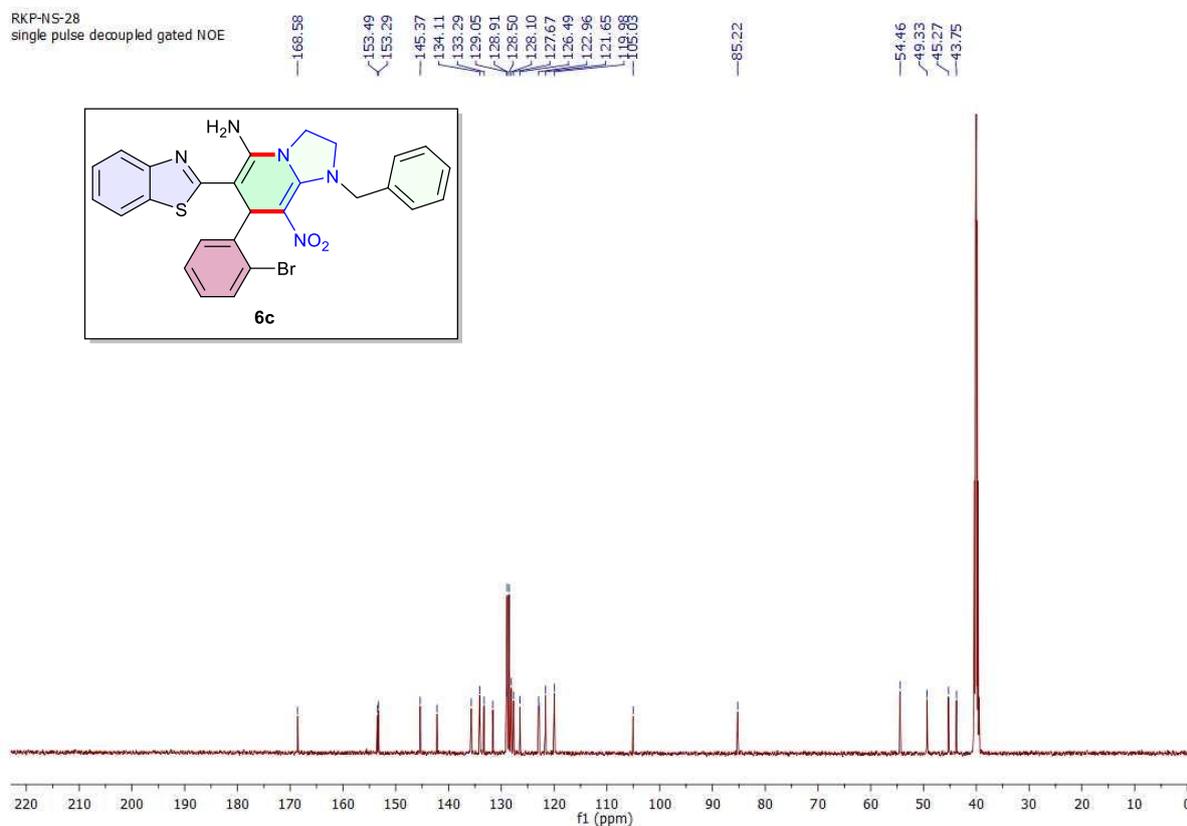
RKP-NS-21
-19F



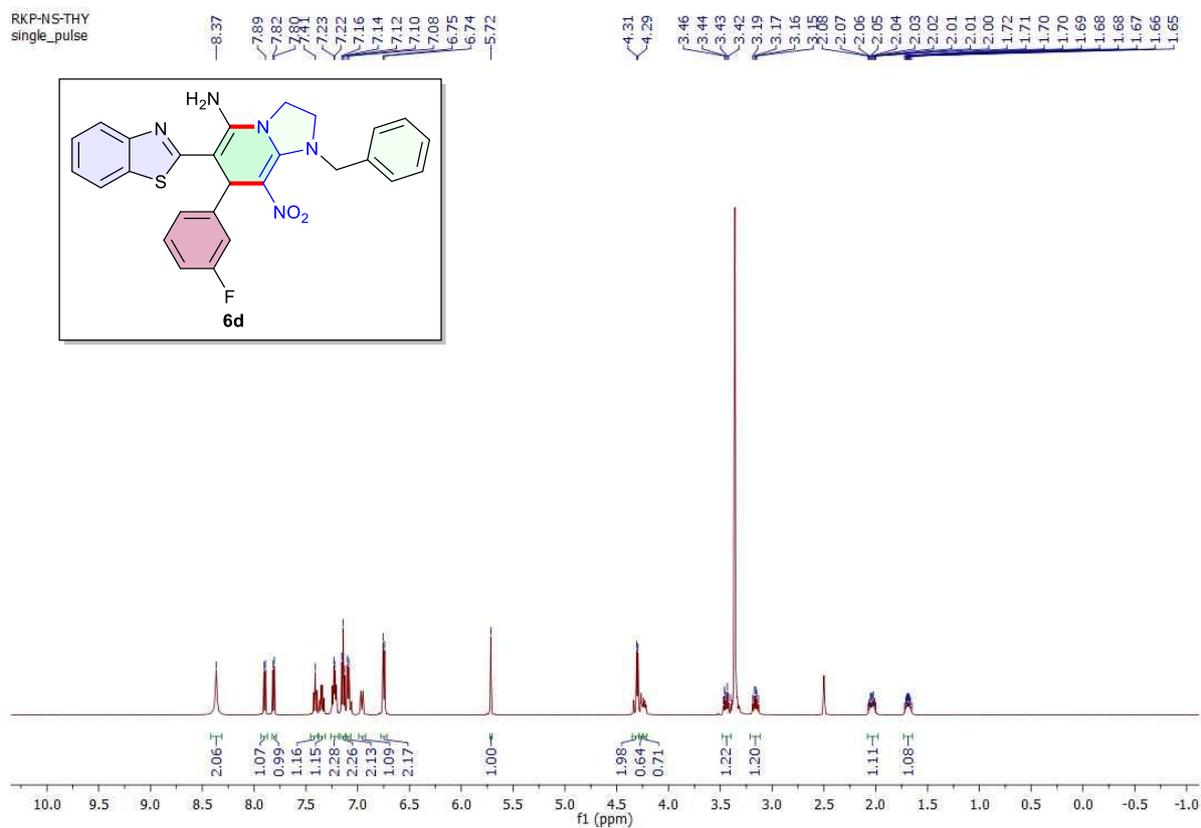
^1H NMR (500 MHz, $\text{DMSO-}d_6 + \text{CDCl}_3$) of **6c**



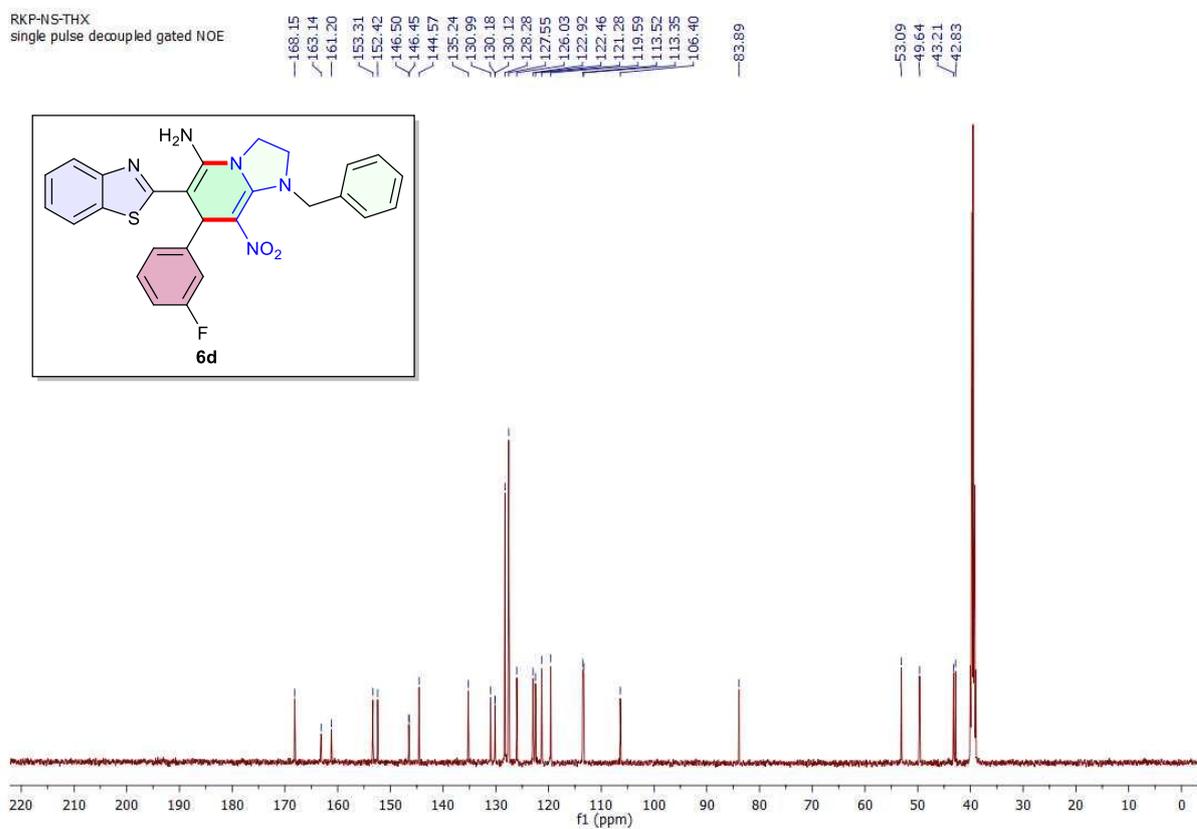
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **6c**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **6d**

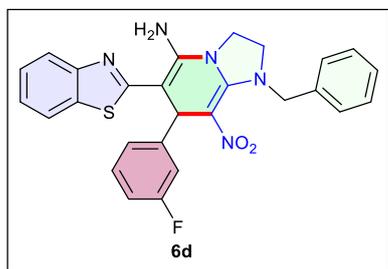


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **6d**

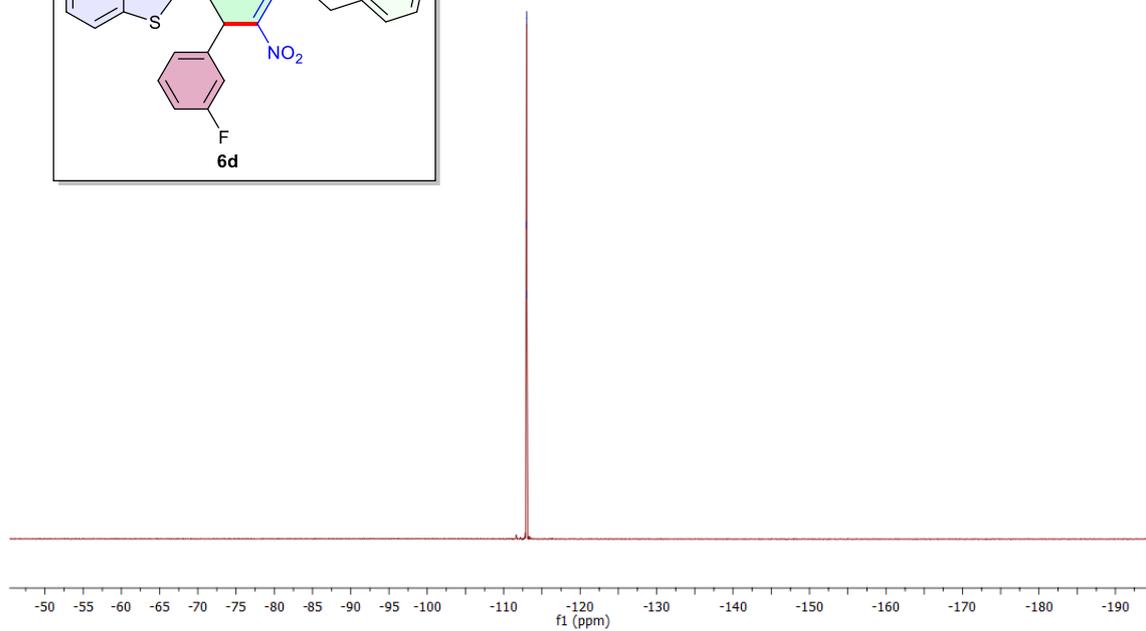


$^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, $\text{DMSO-}d_6$) of **6d**

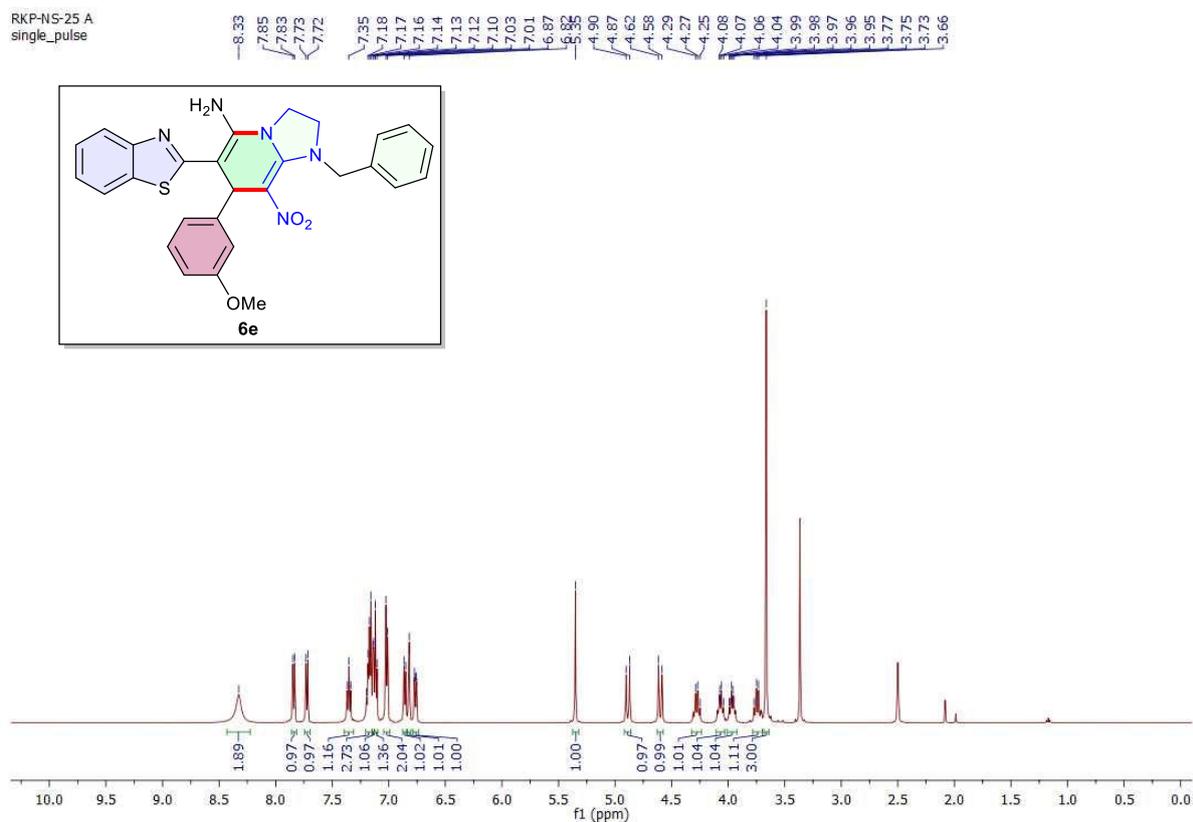
RKP-NS-THX
-19F



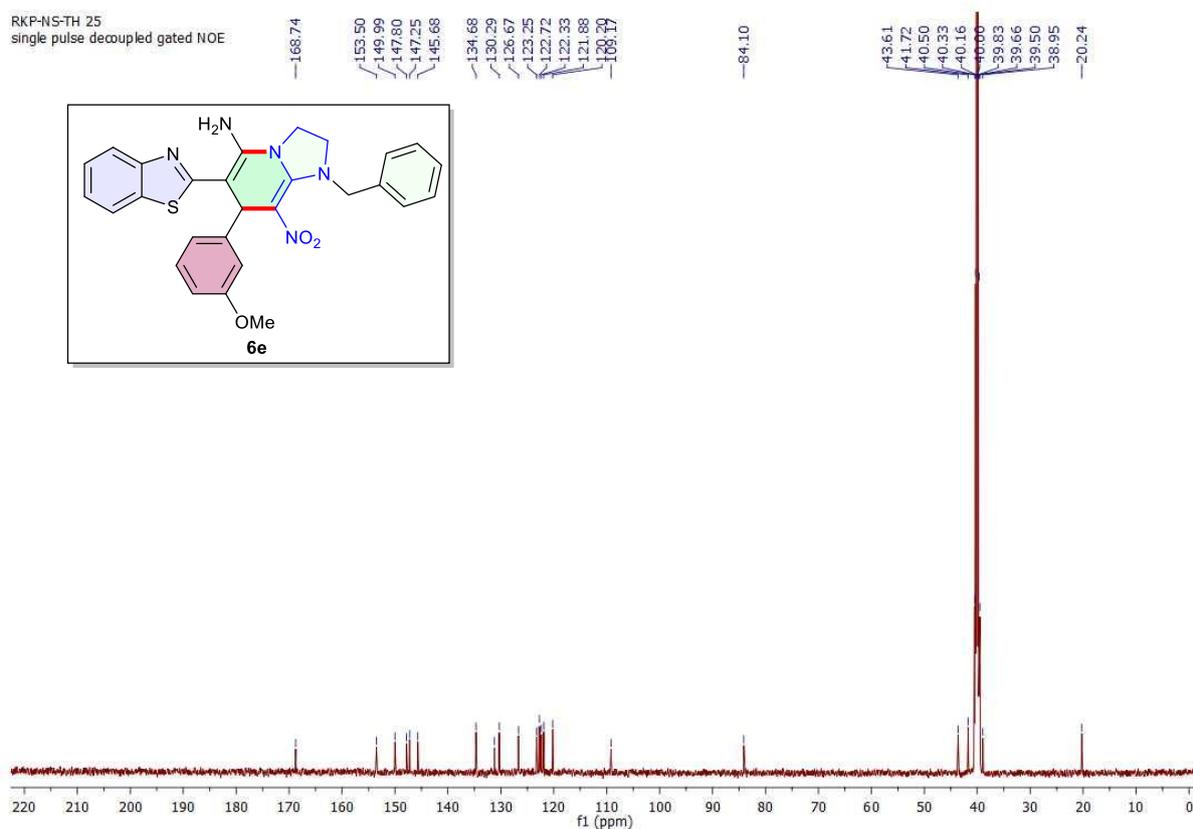
-112.98
-113.00
-113.01
-113.03



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **6e**



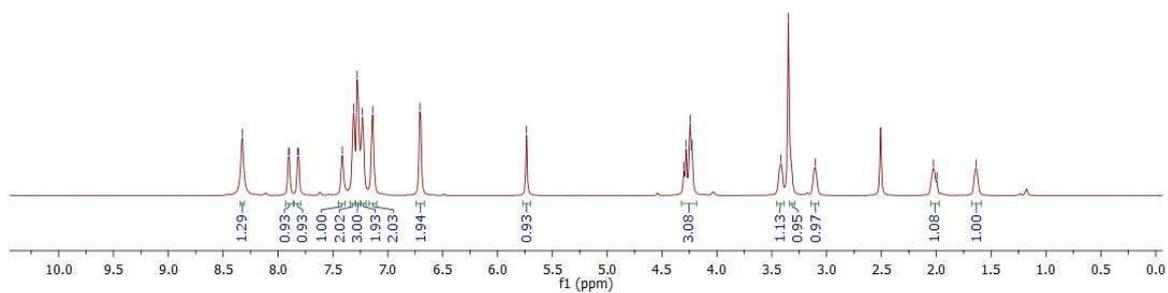
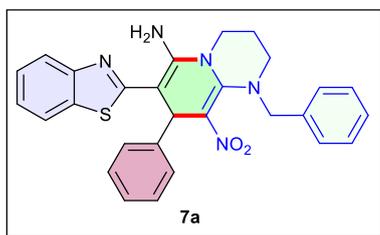
$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **6e**



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **7a**

From IIC
RKP-NS-31

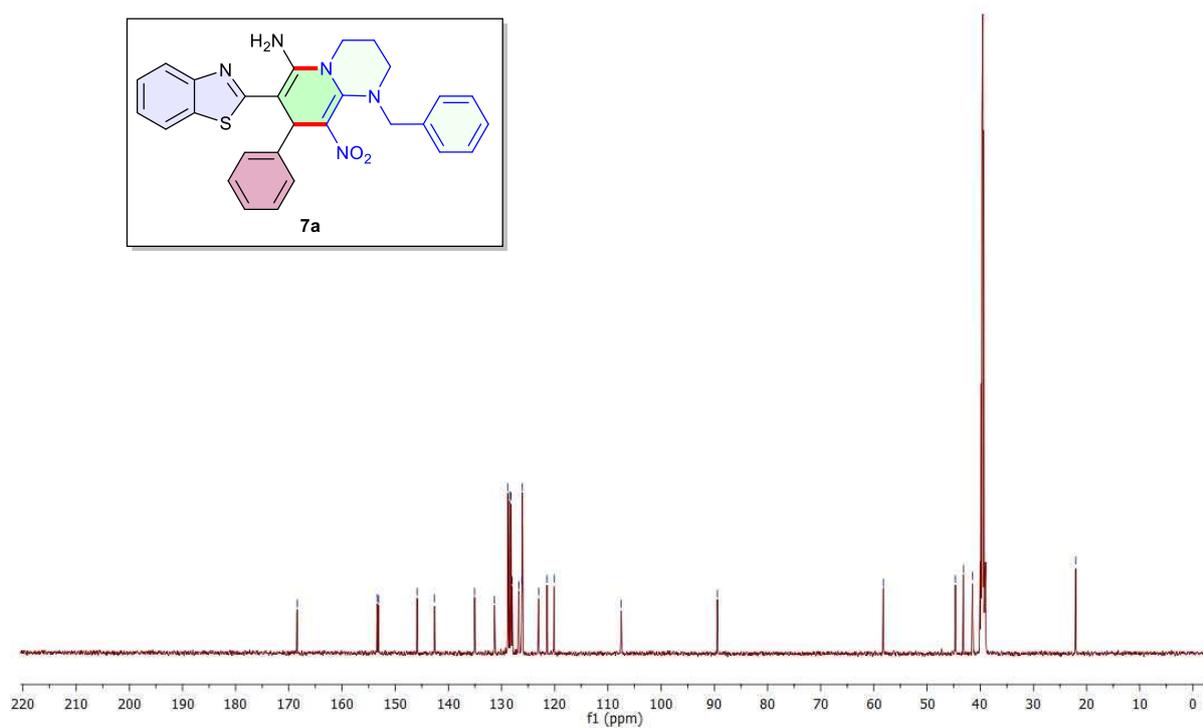
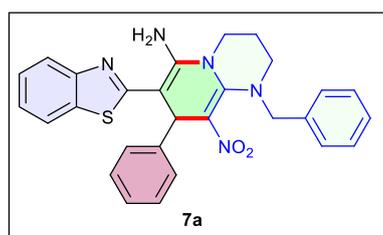
8.33, 7.90, 7.82, 7.81, 7.31, 7.28, 7.23, 7.14, 6.71, 5.74, 4.30, 4.28, 4.24, 4.23, 3.42, 3.35, 3.10, 2.03, 1.99, 1.64



$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **7a**

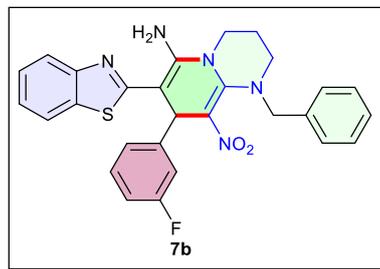
RKP-NS-31
single pulse decoupled gated NOE

168.43, 153.39, 153.15, 145.87, 142.61, 128.81, 128.52, 128.21, 128.01, 126.78, 126.19, 126.08, 121.46, 107.50, 89.42, 58.23, 44.68, 43.17, 41.45, 22.06

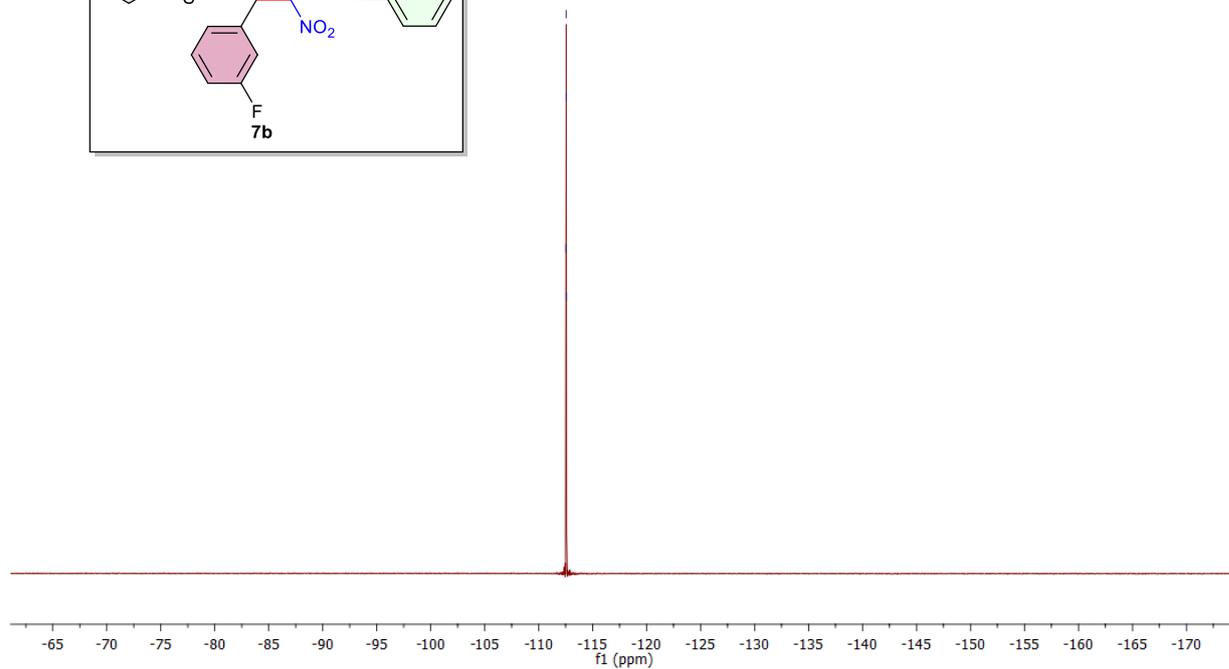


$^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, $\text{DMSO-}d_6$) of **7b**

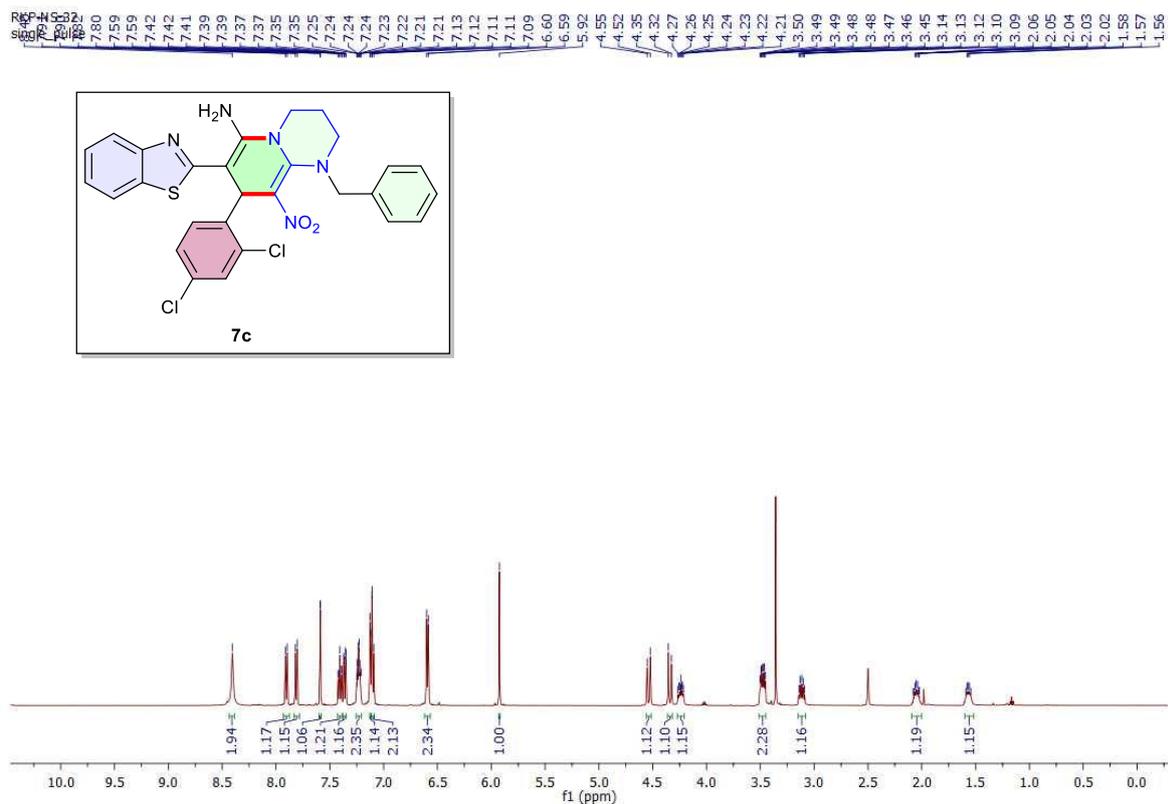
RKP-NS-THY
-19F



-112.52
-112.54
-112.56
-112.58



^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **7c**



$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) of **7c**

