Visible Light-Promoted Cascade Synthesis of Pyrazolidinones via *N*-Aryl Glycine and Azomethine Imines

Contents:

1. General

1.1. Materials and methods: All reactions were performed in oven-dried glassware; reactions are magnetically stirred and monitored by analytical thin layer chromatography (TLC). TLC was performed on Merk silica gel 60 $F_{254,}$ a UV lamp was used as a visualizing agent, Iodine, 5% aqueous potassium permanganate solution as a developing agent, followed by heating. Purification of products was carried out by column chromatography by using silica 60-120, mesh silica and distilled hexane, ethyl acetate, Chloroform, and Methanol were used as eluents, and concentration under reduced pressure was performed by rotary evaporator at 40-45 ^{o}C, at appropriate pressure. The yields were given to the purified products.

Solvents and reagents: All the reagents are purchased from commercial suppliers from Sigma-Aldrich, Alfa Aesar, and TCI, used without further purification; the ruthenium and iridium catalysts were prepared based on the reported procedure.[1] The solvents are distilled according to the traditional methods, and distilled solvents are used to purify the products.

1.2.Chromatography and Instrumentation

NMR spectroscopy: NMR data were recorded on an AVANCE 500, AVANCE 400, and AVANCE 300 MHz for ^{1}H NMR. Chemical shifts are reported in ppm, with the solvent resonance employed as the internal standard for TMS via residual solvent as $CDCl_3$. Peaks are reported as s = singlet, d = doublet, t = triplet, q = quartet, m = multiples, br = broad signal, *J* = coupling constant in Hz. ^{13}C NMR spectra were recorded with H-decoupling on ANANCE 125, AVANCE 100, and AVANCE 75 MHz spectrometer and are reported in ppm with solvent resonance employed as the internal standard as TMS via residual solvent as $CDCl_3$.[1]

IR spectroscopy: Infrared spectroscopy was performed neat on a BRUKER FT-IR spectrophotometer in chloroform, IR on KBr pellet spectra were recorded on a Thermo Nicolet-NEXUS 670 FT-IR instrument.

MASS spectrometry: Mass spectrometric analyses were performed using ESI techniques, and mass spectra were obtained on a SHIMADZU LCMS-2020 mass spectrometer. High-Resolution Mass Spectra data were obtained on a Thermo scientific Executiv^{e} Orbitrap mass spectrometer or Q STAR XL Hybrid MS/MS.

Melting points: Melting points (MP) were determined using a Super Fit capillary point apparatus. MPs are uncorrected.

Photochemical Equipment and Setup: The ThalesNano photoredox reactor was employed, featuring a built-in blue LED light source (emission: 435-445 nm) positioned at a 5-10 cm distance. The reactor's temperature was precisely controlled at ~30 °C using a thermocouple feedback system, and the integrated Amplifier Pump ensured accurate circulation of the reaction mixture.

X-ray Crystallography: X-ray data for compound **3e** was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-III detector.

The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [2]. The structure was solved using the intrinsic phasing method [3], refined with the SHELXL [3] program, and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All C-bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms].

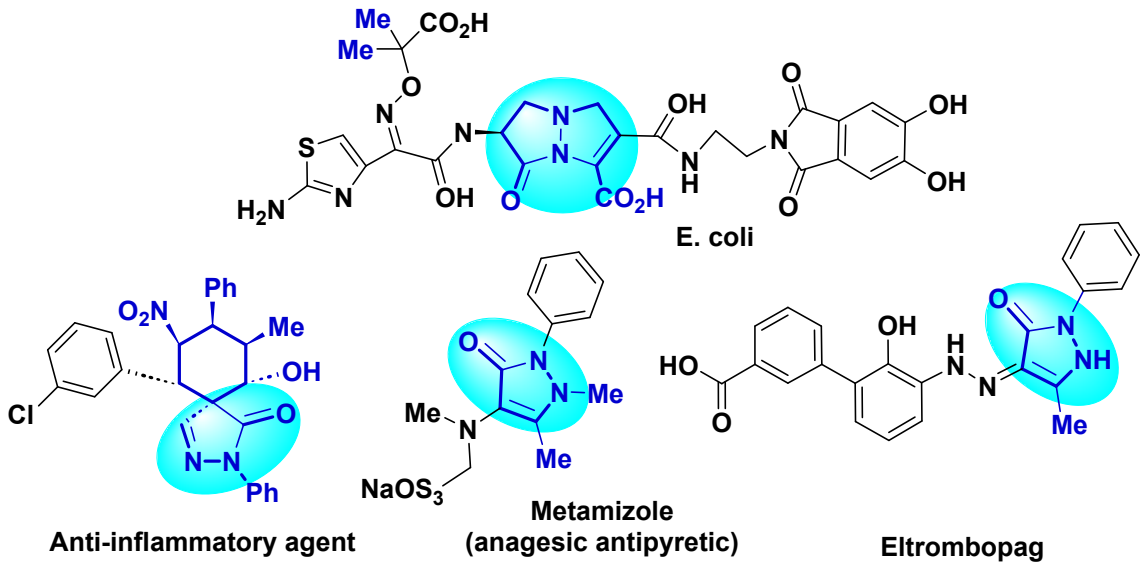


Fig. S1 Biologically valuable pyrazolidinone derivatives highlighting their significance in medicinal chemistry.

2. Experimental Set-up

Reactor: ThalesNano photoredox reactor

Light Source: Blue LED light (emission: 435-445 nm)

Irradiation Distance: 5-10 cm

Temperature Control: Temperature: ~30 °C

Control System: Thermocouple feedback system

Heating Method: Precise temperature control using the ThalesNano reactor's built-in temperature control system

Circulation: Pump: Amplifier Pump

Circulation Control: Precise control over reaction mixture circulation using the ThalesNano reactor's integrated pump system

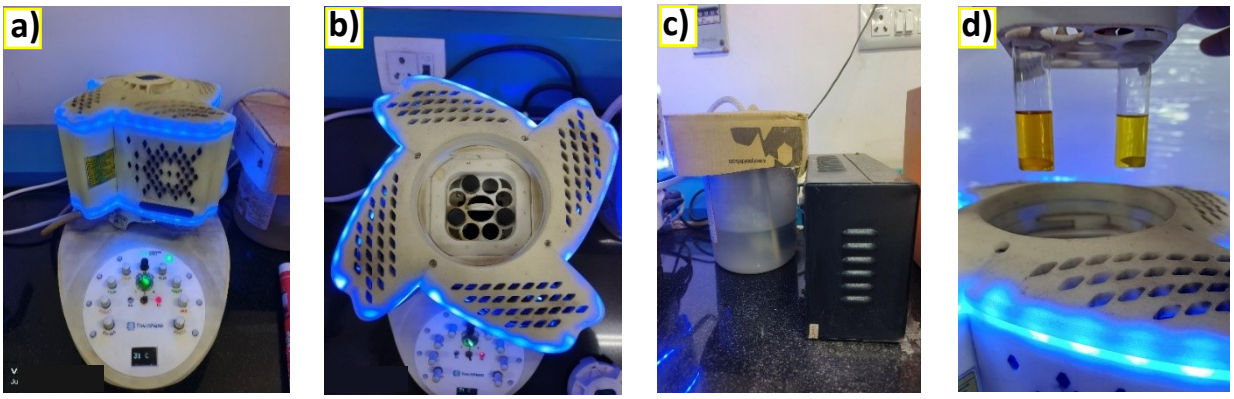
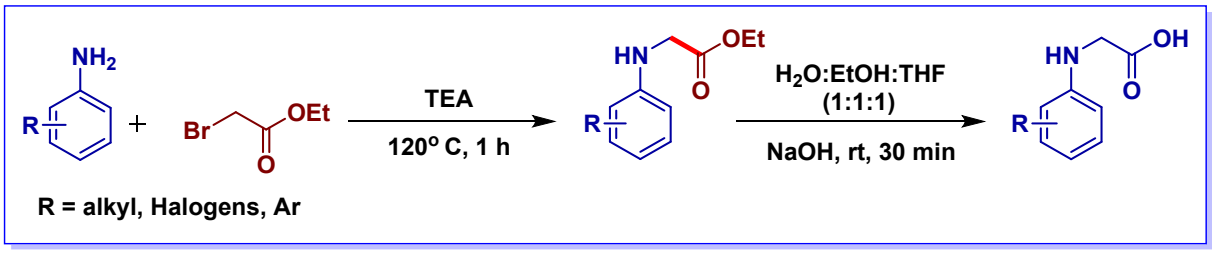


Figure S1. *Experimental set-up for the photocatalyzed reactions. a) Schlenk's tubes containing the reaction mixture. b) LED irradiation source positioned at a distance of 5-10cm from the Schlenk's tubes inside the ThalesNano photo redox reactor. c) Temperature control system with thermocouple feedback and Amplifier Pump providing precise control over reaction mixture circulation. d) Two vials containing solvents and substrates are placed in the reactor to ensure uniform photocatalysis.*

3. Synthesis of *N*-Phenylglycine derivatives

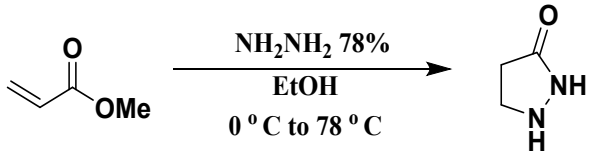
In a clean, dry round bottom flask, aniline (7.1 mmol) and ethyl bromoacetate (8.3 mmol) were taken in triethylamine (15 mL), and it was added dropwise within 2h. The reaction mixture was allowed to warm to 1 h at 120°C. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The ester derivatives were obtained by flash chromatography on silica gel. In order to obtain the desired *N-phenyl glycine derivative, in a clean 100 ml round bottom flask, a mixture of ester derivatives was mixed with an equal amount ratio of H_2O, THF, EtOH (1:1:1),* and NaOH was added. The reaction mixture was stirred for up to 30 min and cooled. Then, a small amount of ice water is filtered to give the *N*-penylglycine derivative as a white solid. The spectral data was in good agreement with the reported literature.[4]



Scheme S1. *N-Phenyl glycine was used as the starting material during the scope study.*

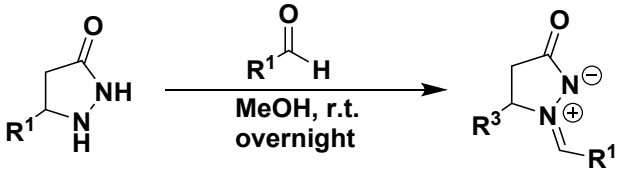
4. Synthesis of Azomethine Imine derivatives

Pyrazolidin-3-one:



Pyrazolidin-3-one (S1) was prepared following the reported experimental procedure with slight modifications. In a flame-dried round bottom flask, a solution of hydrazine monohydrate 78% (1.0 equiv) in absolute ethanol (4 M) was cooled to 0 °C using an ice bath. Methyl acrylate (1.0 equiv) was slowly added, and the solution was stirred at 0 °C for 30 min and then was heated to reflux using an oil bath until the reaction was completed judging by TLC analysis. The solution was concentrated under a vacuum to yield the crude pyrrolidine-3-one as a clear or yellow oil. The pyrazolidin-3-one was used immediately in the next step without purification.

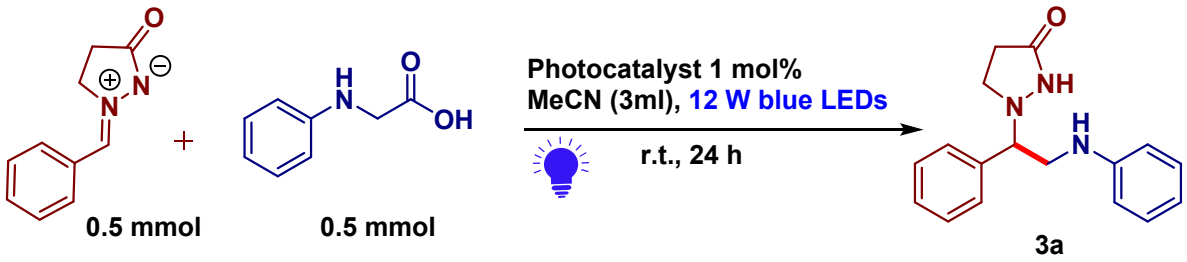
Synthesis of azomethine imines:



Azomethine imines were prepared following the reported experimental procedure with slight modifications: The crude pyrazolidinone S1 (1.0 equiv) obtained in the previous step and the corresponding aldehydes (1.2 equiv) were dissolved in anhydrous MeOH (1 M). The mixture was stirred at room temperature overnight and then concentrated under vacuum to remove the solvent. Et_2O was added to precipitate the product (if the precipitation does not occur, it can be promoted by adding a few drops of hexanes followed by cooling in the freezer). The resulting solid was collected by filtration, washed with Et_2O, and dried to yield the final product. For substrates that could not precipitate, the reaction crudes were purified by column chromatography using DCM/ MeOH (10:1) as eluent.

5. Optimization survey

3.1 General experimental procedure for optimization: In a clean, dry Schlenk tube, X mol% of Iridium catalyst, (0.5 mmol, 1.0 equiv) of *N*-phenylglycine **1a** and (0.5 mmol, 1.0 equiv) of azomethine imine **2a** were taken and degassed with N_2, followed by the addition of 3 ml of degassed solvent and placed the Schlenk tube under blue LED, stir the reaction mixture at mentioned time. The reaction mixture was diluted with ethyl acetate (2 x 20 mL) and washed with water (2 x 20 mL) followed by brine. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure to afford a crude residue. The crude was subjected to silica gel column chromatography by using EtOAc/ hexane (80:20) or DCM/ MeOH (20:1) as eluent to obtain pyrazolidinones **3a.**



General Procedure for the Synthesis of Compounds 3a-3w (GP): In a clean, dry Schlenk tube, 1 mol% of Iridium catalyst, (0.5 mmol, 1.0 equiv) of *N*-phenylglycine **1a** and (0.5 mmol, 1.0 equiv) of azomethine imine **2a** were taken and degassed with N_2, followed by the addition of 3 ml of degassed solvent and placed the Schlenk tube under blue LED, stir the reaction mixture at mentioned time. The reaction mixture was diluted with ethyl acetate (2 x 20 mL) and washed with water (2 x 20 mL), followed by brine. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure to afford a crude residue. The crude was subjected to silica gel column chromatography by using EtOAc/ hexane (80:20) or DCM/ MeOH (20:1) as eluent to obtain pyrazolidinnones **3a** with **83%** yield.

Electrochemical Properties and Oxidation Potential Prediction of Screened Photocatalysts

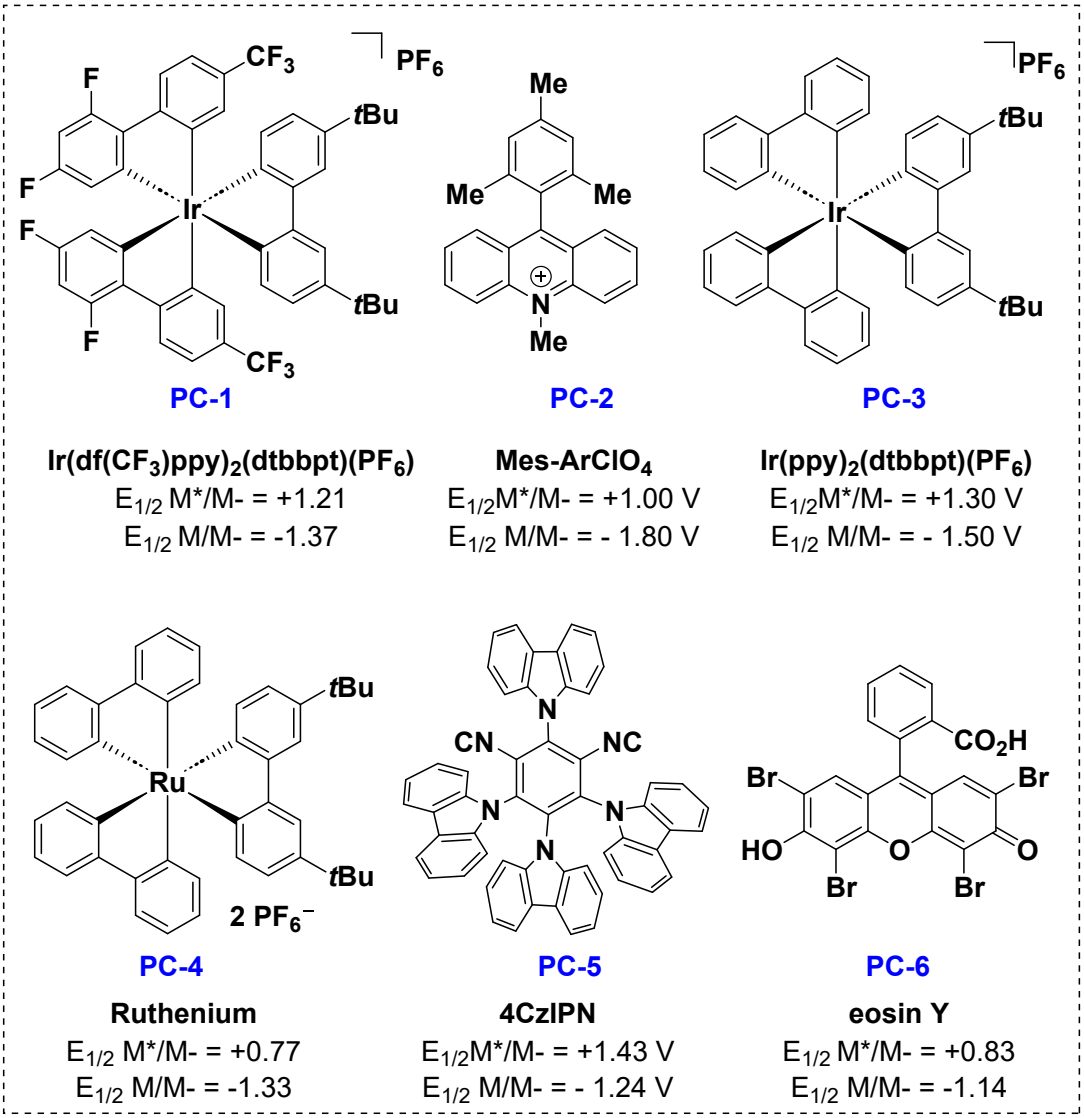
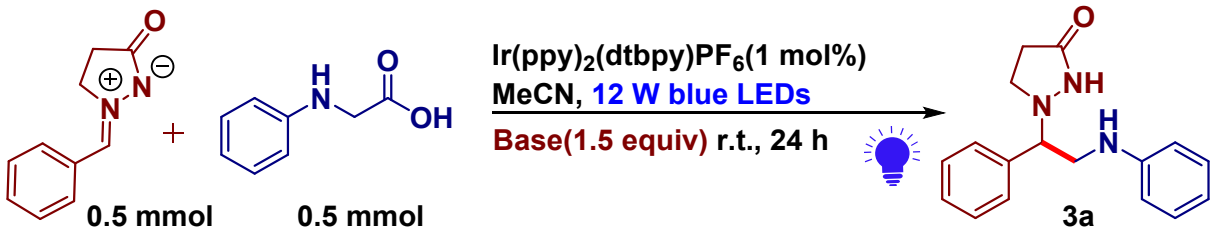


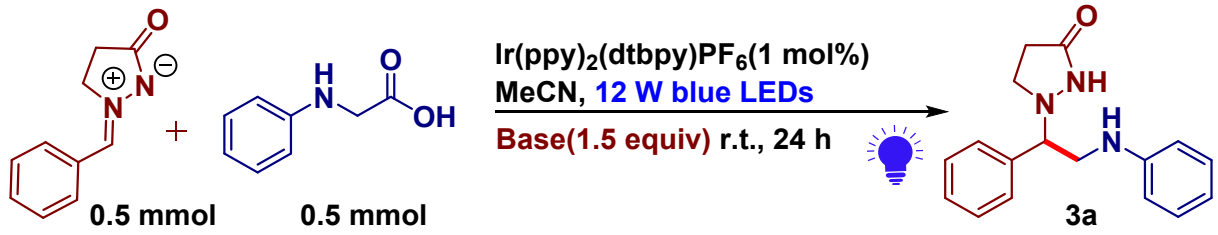
Figure S2. *The photocatalysts utilized in this study*

Table S1. Screening of photocatalyst



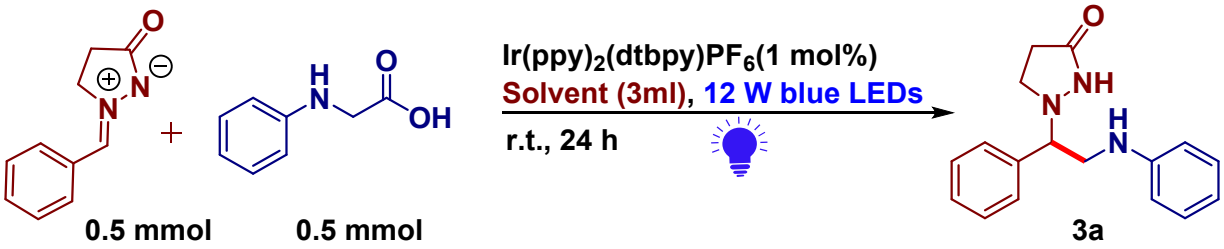
Entry	PC (mol%)	Solvent	Base	T (h)	Yield of 3a(%) & 3b
1	**$Ir(ppy)_2(dtbpy)PF_6$(1 mol%)**	MeCN		24	83
2	$Ru(bpy)_3PF_6$ (1 mol%)	MeCN		24	58
3	$Ir(df(CF_3)ppy)_2(dtbbpt)(PF_6)$	MeCN		24	48
4	Mes-Acr^+ (1 mol%)	MeCN		24	nr
5	4CzIPN	MeCN		24	nr
6	Eosin Y	MeCN		24	nr
7	4CzIPN	MeCN		24	64

Table S2. Screening of Base



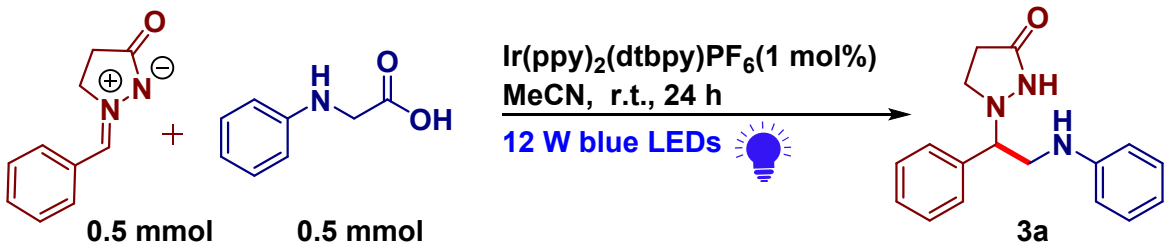
Entry	Base	3a (%)
1	K_2CO_3	74
2	CS_2CO_3	66
3	-	83

Table S3. Screening of Solvent



Entry	Solvent	3a (%)
1	MeCN	83
2	MeOH	81
3	DMF	67
4	DCE	61

Table S4. Screening of Irradiation Light and Photocatalysts for Optimized Photocatalytic Performance



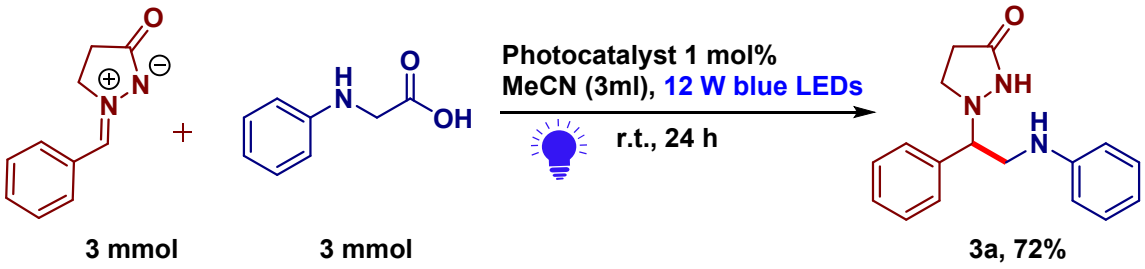
Entry	PC (mol%)	Light Source	Solvent	Base	Yield of 3a (%)
1	**PC-1**	12 W blue LED	MeCN	K_2CO_3	48 %
2	**PC-2**	12 W blue LED	MeCN	K_2CO_3	-
3	**PC-3**	12 W blue LED	MeCN	K_2CO_3	71%
4	**PC-4**	12W blue LED	MeCN	K_2CO_3	-
5	**PC-5**	12 W blue LED	MeCN	K_2CO_3	-
6	**PC-3**	**12 W blue LED**	**MeCN**	-	**83%**
7	**PC-3**	36 W blue LED	MeCN	-	48%
8	**PC-3**	8 W blue LED	MeCN	-	21%

Reaction conditions: 1a (0.5 mmol), 2a (0.5 mmol), photocatalyst (1 mol %), in MeCN (3 mL). c Isolated yield. Under blue-LED irradiation.

6. Experimental Procedure for the Large-Scale Synthesis of 3a

To assess the synthetic usefulness of the α-benzylation reaction, a larger-scale reaction was performed using substrates 1a and 2a. A dried Schlenk tube (borosilicate glass) equipped with a stir bar was charged with azomethine imine (2a, 3 mmol, 1.0 equiv), *N*-phenyl glycine (1a, 3 mmol, 1.0 equiv), and $[Ir(dtbbpy)(ppy)_2]PF_6$ photocatalyst (0.03 mmol, 1 mol%). Acetonitrile (5 mL) was added, and the Schlenk tube was sealed with a PTFE/silicon septum and connected to a vacuum line. The solution was degassed three times via the freeze-pump-thaw procedure and stirred under irradiation from a 12W blue LED (435–445 nm), with the temperature maintained at approximately 30 °C using a fan.

After the reaction (monitored by TLC), the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (230–400 mesh) using a DCM/MeOH (20:1) mixture as eluent, yielding compound 3a as a colorless solid in 72% yield (2.16 mmol, 542 mg).

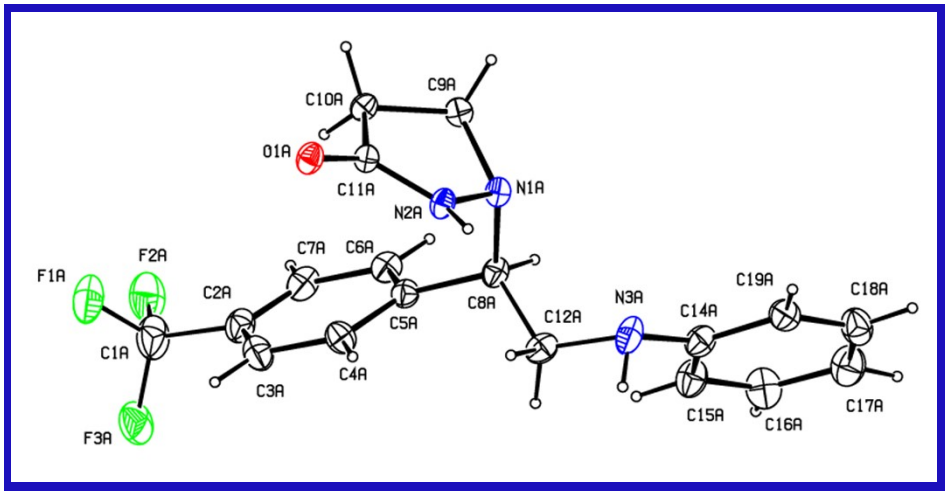


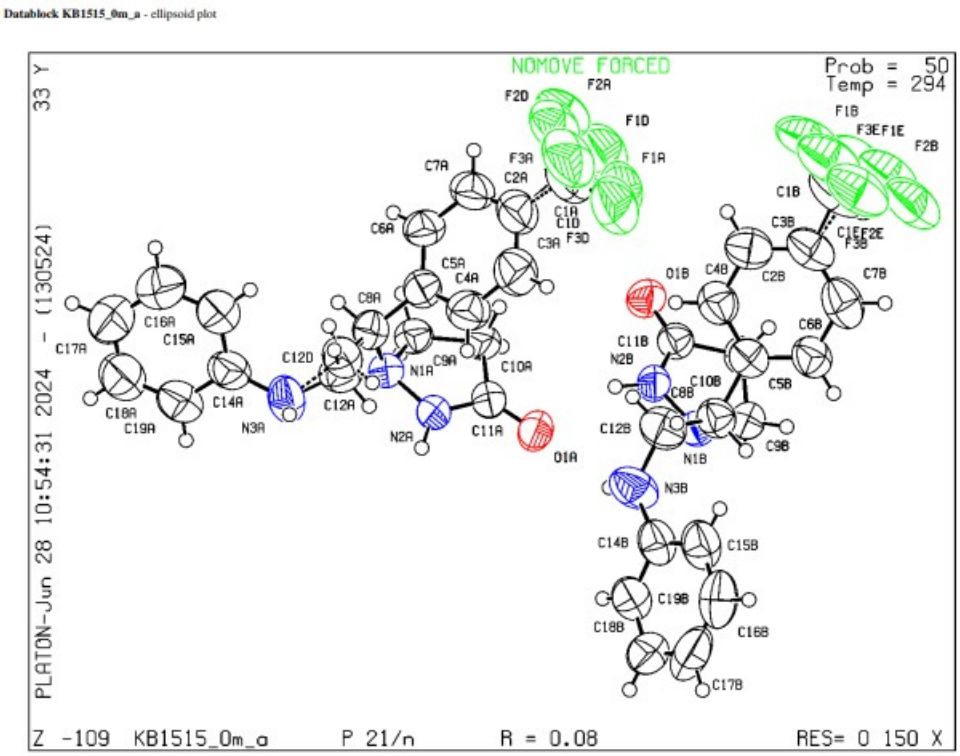
7. X-ray Crystallography

X-ray data for the compound was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 Å) and a PHOTON-III detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs.[1] The structure was solved using the intrinsic phasing method,[2] further refined with the SHELX [2] program, and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. The N-H were located in the different Fourier maps, and its positions and isotropic displacement parameters were refined. All C-bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms].

Crystal structure determination of [KB1515_0m_a]

Crystal Data for $C_{18}H_{18}F_3N_3O$ (M =349.35 g/mol): monoclinic, space group P2 1 /n (no. 14), a = 15.854(7) Å, b = 8.493(4) Å, c = 26.645(11) Å, β = 101.786(5)°, V = 3512(3) Å 3 , Z = 8, T = 294.15 K, μ(MoKα) = 0.106 mm -1 , Dcalc = 1.321 g/cm 3 , 20441 reflections measured (2.766° ≤ 2Θ ≤ 49.996°), 6164 unique (R int = 0.0581, R sigma = 0.0763) which were used in all calculations. The final R 1 was 0.0763 (I > 2σ(I)), and wR 2 was 0.2698 (all data). **CCDC 2370668** deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/





1. Bruker (2016). APEX3, SAINT and SADABS. Bruker AXS, Inc., Madison, Wisconsin, USA.

2. Sheldrick G. M. (2015).ActaCrystallogr C71: 3-8.

Figure caption: ORTEP diagram of **3e** compound with the atom-numbering. Displacement ellipsoids are drawn at the 30% probability level, and H atoms are shown as small spheres of arbitrary radius.

7. Controlled experiments

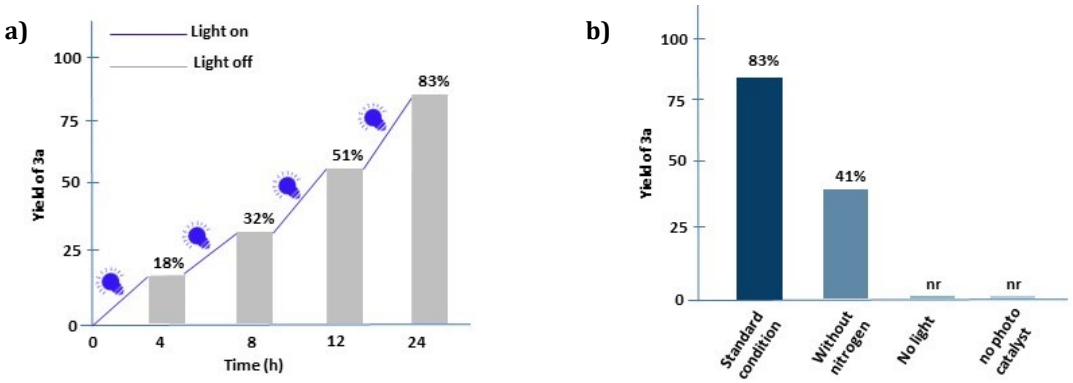
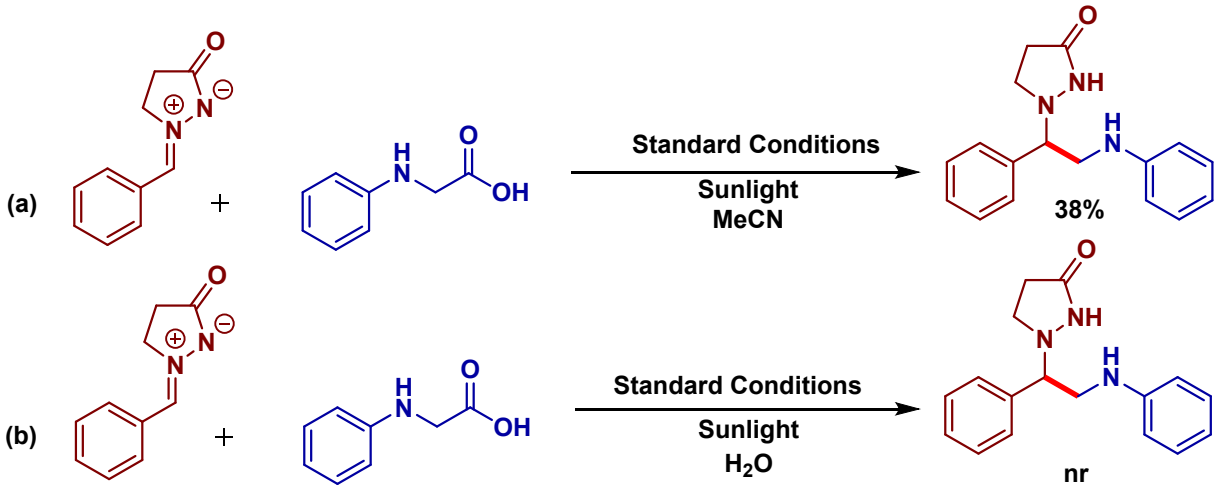


Figure S3. *a) Light on/off Experiment b) Control Experiment*

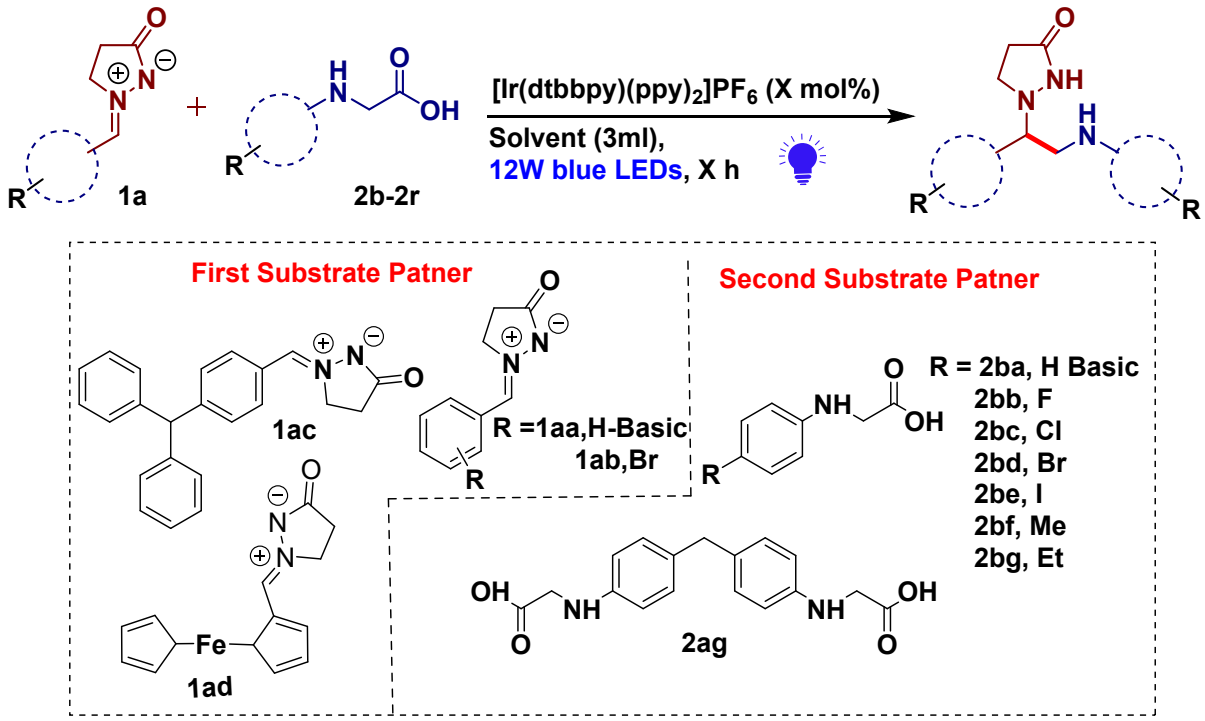
Experiments were conducted under standardized reaction conditions to establish the essential role of photoirradiation. The light source was turned on and off at regular intervals at 4-24 h. The results clearly demonstrated that continuous light exposure is required for the reaction to proceed (**Figure S4a**)

To emphasize the reaction mechanism, a control experiment was performed without nitrogen, light, and catalyst; these studies indicated that which could be important to enable the product (**Figure S4b)**



Scheme S2. Evaluation of Solvent Effects under Standard Conditions

Table S5. Optimization Attempts in Photoredox Catalysis: Summary of Conditions and Outcomes



Reaction Conditions and Outcomes

First Reactive Partner	Second Reactive Partner	Conditions	Outcome
1aa-Basic	2ba-Basic	Optimized Reaction Conditions	83%
1aa	***2bd***	***Optimized Reaction Conditions***	***99%***
1aa	2bx = F, Cl, I	50 °C, 1.5 mol% PC, ACN	Trace
1aa	2bx = F, Cl, I	50 °C, 2 mol% PC, MeOH	Trace
1aa	2bf, 2bg	i)Optimized Reaction Conditions ii) 50 °C, 2 mol% PC, CAN	No result
1aa	2ag	i)Optimized Reaction Conditions ii) 50 °C, 2 mol% PC, ACN	No result

Additional Reaction Conditions and Outcomes

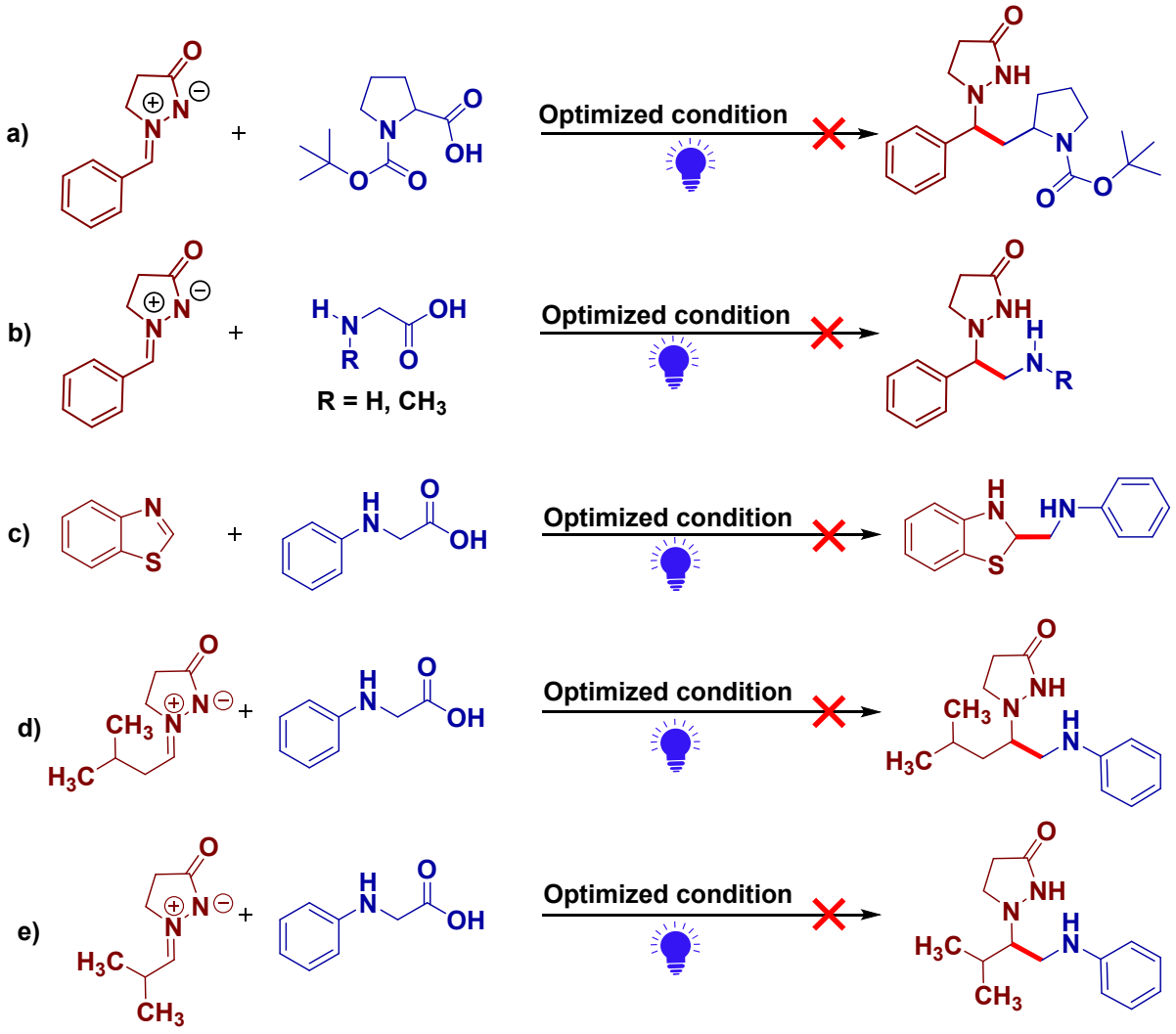
First Reactive Partner	Second Reactive Partner	Conditions	Outcome
1ab	2db	Optimized Reaction Condition	No result
1ab	2db	50 °C, 2 mol% PC, MeCN	No result
1ac	2ba	Optimized Reaction Conditions	No result
1ac	2ba	50 °C, 5 mol% PC, MeCN	No result

[a]Reaction conditions: 1a (1 equiv, 0.5 mmol), 2a (1 equiv, 0.5 mmol), photocatalyst (1 mol %), in MeCN (3 mL) and blue LED (435-445 nm),

Key:

- *PC: Photocatalyst*
- *ACN: Acetonitrile*
- *MeOH: Methanol*
- *MeCN: Acetonitrile*

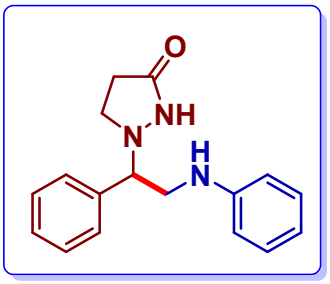
8. Unsuccessful experiments with other amino acids and imines



Scheme S3. *Attempts to react various amino acids with azomethine imines, and vice versa, were unsuccessful under the conditions tested*

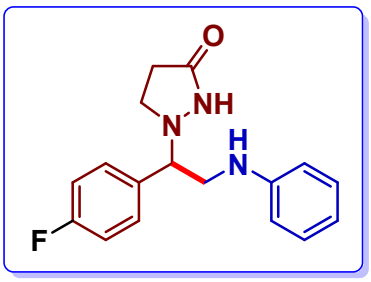
9. Spectroscopic data of 3a-3v&5

(R)-1-(1-phenyl-2-(phenylamino)ethyl)pyrazolidin-3-one (3a)



Colorless ; (120.0.mg, 83% yield); m.p. 123-124 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.27 (s, 1H), 7.32 (d, *J* = 1.9 Hz, 5H), 7.12 (t, *J* = 7.9 Hz, 2H), 6.67 (t, *J* = 7.3 Hz, 1H), 6.54 (d, *J* = 7.8 Hz, 2H), 3.83 (t, *J* = 6.4 Hz, 1H), 3.62 (dd, *J* = 13.1, 6.8 Hz, 1H), 3.33 (dd, *J* = 13.1, 6.1 Hz, 1H), 3.20 (s, 2H), 2.24 – 2.12 (m, 2H), 2.01 – 1.89 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.16, 147.87, 137.73, 129.36, 128.98, 128.65, 117.71, 113.28, 50.61, 47.22, 30.13. HRMS (ESI) calcd. For $C_{17}H_{20}N_3O$ (M^+ + H): 282.1606, found 282.1594; IR (neat cm-1): 3333, 2938, 2830, 2840,1672, 1499, 1115, 1021, 750, 750.

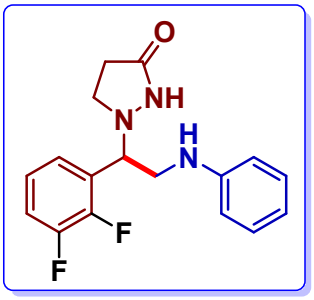
1-(1-(4-fluorophenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3b)



White solid; (150.0 mg, 99% yield); m.p. 135 – 136 °C; **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.97 (s, 1H), 7.33 (q, J = 8.6 Hz, 4H), 7.17 (dd, J = 8.5, 7.4 Hz, 2H), 6.77 – 6.70 (m, 1H), 6.58 (dd, J = 8.6, 0.9 Hz, 2H), 3.86 (t, J = 6.2 Hz, 1H), 3.59 (dd, J = 13.0, 6.3 Hz, 1H), 3.36 (d, J = 6.2 Hz, 1H), 3.32 – 3.24 (m, 2H), 2.35 (dt, J = 16.3, 8.0 Hz, 1H), 2.15 (dt, *J* = 16.6, 8.1 Hz, 1H).Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.51, 147.37, 136.34, 134.55, 129.70, 129.32 (d, J = 16.8 Hz), 118.20,

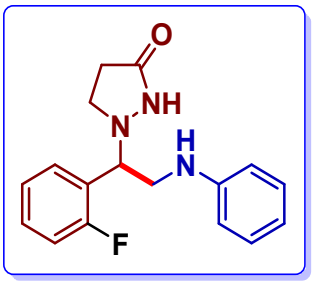
113.29, 69.78, 50.92, 47.61, 29.98. HRMS (ESI) calcd. For $C_{17}H_{19}FN_3O$ (M^+ + H):300.1512, found 300.1503; IR (neat cm-1): 2924, 1648, 1511, 1269, 1092, 828, 749.

1-(1-(2,3-difluorophenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3c)



White solid; (168.0 mg, 98% yield); m.p. 149 –150 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.44 (s, 1H), 7.36 – 7.30 (m, 2H), 7.19 – 7.13 (m, 2H), 7.10 – 7.04 (m, 2H), 6.72 (t, J = 7.3 Hz, 1H), 6.57 (dd, J = 8.5, 0.9 Hz, 2H), 3.86 (t, J = 6.3 Hz, 1H), 3.60 (dd, J = 13.0, 6.5 Hz, 1H), 3.36 – 3.31 (m, 1H), 3.31 – 3.21 (m, 2H), 2.30 (dt, J = 16.2, 8.0 Hz, 1H), 2.09 (dt, J = 16.5, 8.1 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.60, 164.03, 161.56, 147.47, 130.04 (d, J_{C-H} = 7.9 Hz), 129.38, 118.11, 115.99 (d, J_{C-F} = 21.3 Hz), 115.83–115.60, 113.28, 69.66, 50.79, 47.59, 30.02. HRMS (ESI) calcd. For $C_{17}H_{18}F_2N_3O$ (M^+ + H): 318.1414, found 318.1425; IR (neat cm-1): 3285, 2925, 1697, 1451, 1270, 1150, 833,749.

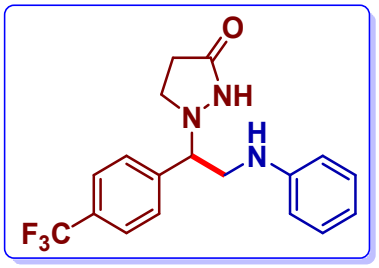
(R)-1-(1-(2-fluorophenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3d)



White solid; (154.0 mg, 99% yield); m.p. 130 – 138°C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36 – 7.30 (m, 2H), 7.19 – 7.13 (m, 2H), 7.10 – 7.04 (m, 2H), 6.75 – 6.70 (m, 1H), 6.58 (dt, J = 6.7, 1.5 Hz, 2H), 3.86 (t, J = 6.3 Hz, 1H), 3.59 (dd, J = 13.0, 6.5 Hz, 1H), 3.35 (d, J = 6.2 Hz, 1H), 3.28 (dd, J

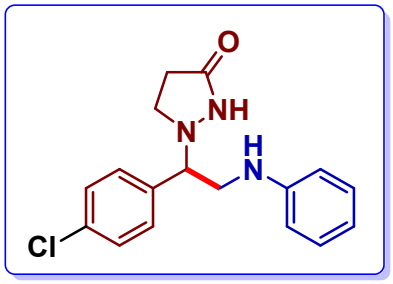
= 14.2, 6.3 Hz, 2H), 2.29 (ddd, J = 14.9, 13.1, 6.8 Hz, 2H), 2.20 – 2.04 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 175.60, 155.66, 147.73, 129.31, 127.12, 125.33, 122.98, **117.86, 113.28**, 103.46, 55.62, 51.07, 47.55, 30.24. HRMS (ESI) calcd. For $C_{17}H_{19}FN_3O$ (M^+ + H): 300.1508, found 300.1520; IR (neat cm-1): 3422, 3057, 2852, 1698, 1597, 1219, 1155, 1063, 832, 744.

(R)-1-(2-(phenylamino)-1-(4-(trifluoromethyl)phenyl)ethyl)pyrazolidin-3-one (3e)



White solid; (146.0 mg, 83% yield); m.p. 149 – 150 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 7.8 Hz, 2H), 7.17 (t, *J* = 7.6 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 7.8 Hz, 2H), 3.95 (t, *J* = 5.7 Hz, 1H), 3.63 (dd, *J* = 13.1, 5.9 Hz, 1H), 3.38 (dd, *J* = 13.2, 6.2 Hz, 1H), 3.29 (dd, *J* = 17.7, 9.3 Hz, 2H), 2.39 (dt, *J* = 16.2, 8.0 Hz, 1H), 2.25 – 2.13 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.66, 147.32, 142.22, 129.41, 128.77, 125.91 (d, *J* = 3.4 Hz), 118.18, 113.20, 70.05, 50.97, 47.66, 29.92. HRMS (ESI) calcd. For $C_{18}H_{19}F_3N_3O$ (M^+ + H): 350.1476, found 350.1468; IR (neat cm-1): 3564, 3352, 2925, 1699, 1647, 1320, 1111, 750.

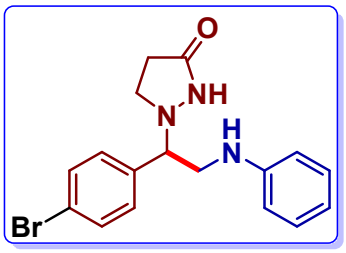
(R)-1-(1-(4-chlorophenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3f)



White solid; (162.0 mg, 99% yield); m.p. 148 – 149 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.02 (s, 1H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 15.9 Hz, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 9.3 Hz, 2H), 3.86 (d, *J* = 6.2 Hz, 1H), 3.59 (dd, *J* = 13.0, 6.3 Hz, 1H), 3.37 –

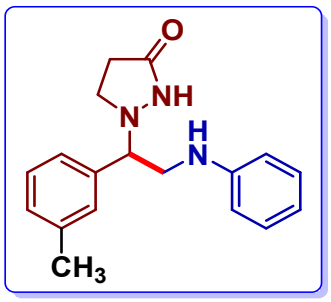
3.32 (m, 1H), 3.29 (d, J = 12.2 Hz, 2H), 2.34 (dt, J = 16.3, 8.0 Hz, 1H), 2.15 (dt, J = 16.5, 8.1 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 175.35, 147.36, 136.39, 134.57, 129.65, 129.33 (d, J = 19.2 Hz), 118.26, 113.28, 69.84, 51.00, 47.67, 29.95. HRMS (ESI) calcd. For $C_{17}H_{19}ClN_3O$ (M+ + H): 316.1217, found 316.1205; IR (neat cm-1): 3419, 2925, 1699, 1512, 1269, 1091, 751, 616.

1-(1-(4-bromophenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3g)



White solid; (167.0 mg, 99% yield); m.p. 149 – 150 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.94 (s, 1H), 7.54 – 7.48 (m, 2H), 7.26 – 7.22 (m, 2H), 7.19 – 7.14 (m, 2H), 6.74 (t, J = 7.3 Hz, 1H), 6.58 (dd, J = 8.5, 0.9 Hz, 2H), 3.85 (t, J = 6.2 Hz, 2H), 3.58 (dd, J = 13.0, 6.2 Hz, 1H), 3.37 – 3.32 (m, 1H), 3.32 – 3.22 (m, 2H), 2.35 (dt, J = 16.4, 8.0 Hz, 1H), 2.16 (dt, J = 16.4, 8.0 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.44 (s), 147.36, 136.92, 132.20, 130.00, 129.41, 122.68, 118.21, 113.26, 69.87, 50.97, 47.60, 29.96. HRMS (ESI) calcd. For $C_{17}H_{19}BrN_3O$ (M^+ + H): 360.0711, found 360.0699; IR (neat cm-1): 2924, 1699, 1511, 1269, 616, 828, 749.

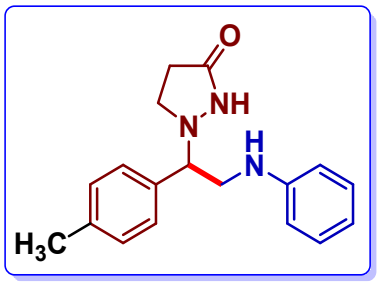
(R)-1-(2-(phenylamino)-1-(m-tolyl)ethyl)pyrazolidin-3-one (3h)



White solid; (113.0 mg, 81% yield); m.p. 138– 140°C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.98 (s, 1H), 7.27 – 7.21 (m, 1H), 7.15 (dd, J = 11.2, 4.6 Hz, 5H), 6.70 (t, J = 7.3 Hz, 1H), 6.56 (dd, J = 8.5, 0.9 Hz, 2H), 3.80 (t, J = 6.4 Hz, 1H), 3.61 (dd, J = 13.0, 6.6 Hz, 1H), 3.33 (dd, J = 12.9, 6.2

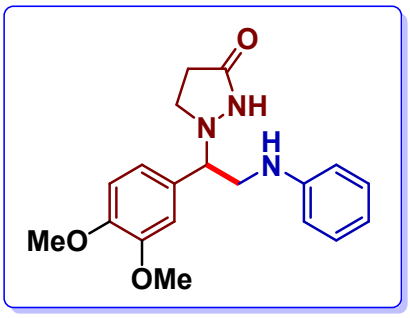
Hz, 1H), 3.23 (s, 2H), 2.35 (s, 3H), 2.24 (dd, *J* = 16.4, 8.1 Hz, 1H), 2.07 – 1.99 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.94, 147.81, 138.68, 137.68, 129.27 (d, *J* = 10.1 Hz), 128.86, 125.59, 117.77, 113.29, 70.38, 50.72, 47.37, 30.13, 21.54. HRMS (ESI) calcd. For $C_{18}H_{22}N_3O$ (M^+ + H): 296.1758, found 296.1751; IR (neat cm-1): 3326, 2941, 2830, 1677, 1597, 1450, 1021.

(R)-1-(2-(phenylamino)-1-(p-tolyl)ethyl)pyrazolidin-3-one (3i)



White solid; (146.0 mg, 99% yield); m.p. 140-150 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 (s, 1H), 7.23 (s, 2H), 7.20 – 7.14 (m, 4H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 2H), 3.83 (t, *J* = 6.4 Hz, 1H), 3.58 (dd, *J* = 12.7, 6.6 Hz, 1H), 3.36 (d, *J* = 6.3 Hz, 1H), 3.34 – 3.23 (m, 2H), 2.36 (s, 3H), 2.30 – 2.24 (m, 1H), 2.09 (dd, *J* = 16.6, 8.2 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 176.06, 159.08, 147.80, 136.82, 129.76, 129.38, 128.71, 128.15, 127.61, 70.13, 69.64, 50.53, 47.19, 22.80. HRMS (ESI) calcd. For $C_{18}H_{22}N_3O$ (M^+ + H): 296.1758, found 296.1751; IR (neat cm-1): 3415, 3052, 2919, 1700, 1509, 1270, 819, 747.

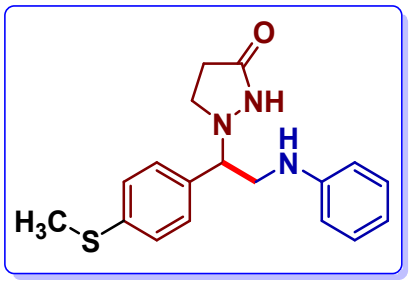
1-(1-(3,4-dimethoxyphenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3j)



White solid; (130.0 mg, 82% yield); m.p. 149 – 150 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.47 (s, 1H), 7.16 (dd, *J* = 8.3, 7.5 Hz, 2H), 6.90 – 6.83 (m, 3H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 7.7 Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.79 (t, *J* = 6.4 Hz, 1H), 3.62 (dd, *J* = 12.8, 6.3 Hz, 1H), 3.34

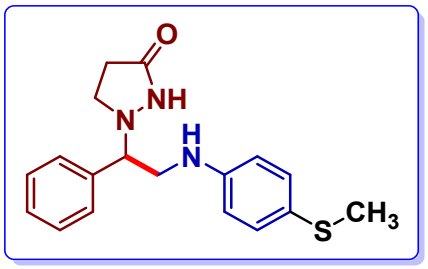
(d, *J* = 6.7 Hz, 1H), 3.26 (dd, *J* = 18.0, 10.0 Hz, 2H), 2.32 (dt, *J* = 16.4, 8.2 Hz, 1H), 2.17 – 2.08 (m, 1H). **^{13}C NMR (75 MHz, CDCl3)** δ 175.55, 149.33 (d, J = 9.4 Hz), 147.64, 130.06, 129.34, 120.92, 117.97, 113.31, 111.15 (d, J = 27.3 Hz), 110.96 – 110.54, 70.26, 56.00 (d, J = 6.6 Hz), 50.83, 47.49, 30.12. HRMS (ESI) calcd. For $C_{19}H_{24}N_3O_3$ (M^+ + H): 342.1812, found 342.1821; IR (neat cm-1): 3328, 2938, 2831, 1671, 1510, 1262, 1114, 1021, 753.

(R)-1-(1-(4-(methylthio)phenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3k)



White solid; (165.0 mg, 96% yield); m.p. 150 – 152 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.60 (s, 1H), 7.28 – 7.21 (m, 4H), 7.15 (dd, *J* = 8.5, 7.4 Hz, 2H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.57 (dd, *J* = 8.5, 0.9 Hz, 2H), 3.82 (t, *J* = 6.4 Hz, 1H), 3.60 (dd, *J* = 13.0, 6.6 Hz, 1H), 3.36 – 3.31 (m, 1H), 3.27 (dd, *J* = 15.9, 7.8 Hz, 2H), 2.48 (s, 3H), 2.27 (dt, *J* = 16.1, 6.0 Hz, 1H), 2.07 (dt, *J* = 8.2, 5.8 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 175.63, 147.57, 139.28, 134.19, 129.36, 128.87, 126.71, 118.01, 113.28, 69.94, 50.79, 47.39, 30.06, 15.57. HRMS (ESI) calcd. For $C_{18}H_{22}N_3OS$ (M^+ + H): 328.2358, found 328.2325; IR (neat cm-1): 3352, 2853, 1675, 1456, 1274, 700, 816, 754.

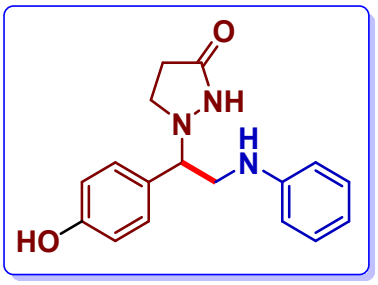
(R)-1-(2-((4-(methylthio)phenyl)amino)-1-phenylethyl)pyrazolidin-3-one (3l)



White solid; (128.0 mg, 74% yield); m.p. 145 – 148 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36 (d, *J* = 3.7 Hz, 5H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.58 (d, *J* = 8.6 Hz, 2H), 3.89 (t, *J* = 6.4 Hz, 1H), 3.67 – 3.62 (m, 1H), 3.39 – 3.34 (m, 1H), 3.30 (dd, *J* = 15.9, 7.5 Hz, 2H), 2.40 (s, 3H), 2.24 (dd, *J* = 16.4,

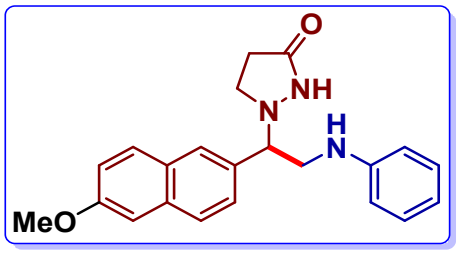
8.2 Hz, 1H), 2.07 – 2.00 (m, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 175.12, 145.71, 137.15, 131.10, 129.08, 128.81, 128.47, 125.84, 114.40, 70.19, 50.85, 47.75, 29.73, 18.80. HRMS (ESI) calcd. For $C_{18}H_{22}N_3OS$ (M^+ + H): 328.2358, found 328.2325; IR (neat cm-1): 3352, 2853, 1675, 1456, 1274, 700, 816, 754.

(R)-1-(1-(4-hydroxyphenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3m)



Colorless; (90.0 mg, 52% yield); m.p. 146 – 148 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 13.77 (s, 1H), 12.24 (s, 1H), 11.84 (d, *J* = 8.5 Hz, 2H), 11.79 (t, *J* = 7.9 Hz, 2H), 11.50 (d, *J* = 8.5 Hz, 2H), 11.32 (t, *J* = 7.3 Hz, 1H), 11.25 (d, *J* = 7.7 Hz, 2H), 8.48 (t, *J* = 6.6 Hz, 1H), 8.24 (dd, *J* = 12.8, 7.5 Hz, 1H), 7.95 (d, *J* = 6.9 Hz, 1H), 7.74 – 7.73 (m, 2H), 6.75 (d, *J* = 15.7 Hz, 1H), 6.50 (d, *J* = 26.2 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 180.34, 162.30, 152.91, 134.18 (d, *J* = 56.0 Hz), 121.89, 121.26, 120.53, 117.80, 74.07, 55.07, 51.63, 34.86. HRMS (ESI) calcd. For $C_{17}H_{20}N_3O_2$ (M^+ + H): 298.1551, found 298.1629; IR (neat cm-1): 3421, 3021, 1650, 1451, 1248, 1021, 761.

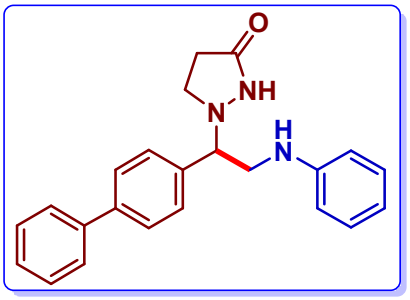
(R)-1-(1-(6-methoxynaphthalen-2-yl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3n)



White solid; (119.0 mg, 67% yield); m.p. 140-145 °C ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.36 (d, *J* = 7.7 Hz, 7H), 7.58 – 7.48 (m, 14H), 7.16 – 7.12 (m, 9H), 6.82 (d, *J* = 7.7 Hz, 4H), 6.71 (t, *J* = 7.3 Hz, 4H), 6.56 (d, *J* = 7.7 Hz, 9H), 4.02 (s, 19H), 3.69 (d, *J* = 19.1 Hz, 8H), 3.62 – 3.44 (m, 8H), 3.39 – 3.19 (m, 11H), 2.45 (dt, *J* = 15.2, 7.5 Hz, 5H), 2.26 – 2.16 (m, 4H). **^{13}C NMR (126 MHz,**

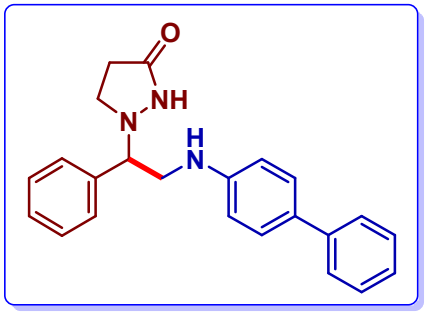
$CDCl_3$) δ 175.16, 169.22, 147.89, 135.37, 133.37, 129.49, 128.92 (d, *J* = 37.3 Hz), 127.88, 127.09, 126.48 (d, *J* = 18.8 Hz), 125.19, 120.48, 117.10, 113.38, 70.80, 68.78, 62.81, 50.27, 48.38, 30.18. HRMS (ESI) calcd. For $C_{22}H_{24}N_3O_2$ (M^+ + H): 362.1863, found 362.1860; IR (neat cm-1): 3379, 3055, 2924, 1671, 1460, 1161, 1087, 751, 818.

(R)-1-(1-([1,1'-biphenyl]-4-yl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3o)



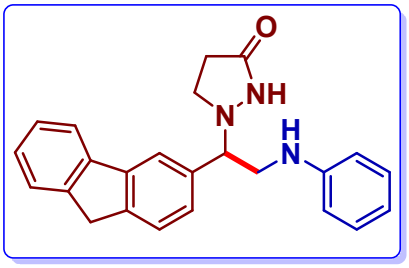
White solid; (114.0 mg, 96% yield); m.p. 150-152 °C ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.88 – 7.70 (m, 1H), 7.60 (t, *J* = 8.1 Hz, 4H), 7.46 (dd, *J* = 7.1, 1.6 Hz, 2H), 7.44 – 7.42 (m, 2H), 7.39 – 7.34 (m, 1H), 7.18 (dd, *J* = 8.5, 7.4 Hz, 2H), 6.76 – 6.71 (m, 1H), 6.62 (dd, *J* = 8.6, 1.0 Hz, 2H), 3.92 (t, *J* = 6.3 Hz, 1H), 3.64 (dd, *J* = 12.8, 6.4 Hz, 1H), 3.43 (d, *J* = 6.3 Hz, 1H), 3.41 – 3.30 (m, 2H), 2.35 (dt, *J* = 16.4, 8.1 Hz, 1H), 2.18 (dt, *J* = 21.7, 8.0 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.31, 147.53, 141.59, 140.32, 136.68, 129.38, 128.83 (d, *J* = 8.8 Hz), 128.07 – 127.07, 127.07 – 126.76, 118.13, 113.32, 70.23, 51.03, 47.62, 30.06. HRMS (ESI) calcd. For $C_{23}H_{24}N_3O$ (M^+ + H): 358.1914, found 358.1908; IR (neat cm-1): 3320, 3054, 2942, 2830, 1672, 1449, 1113, 1020, 752.

(R)-1-(2-([1,1'-biphenyl]-4-ylamino)-1-phenylethyl) pyrazolidin-3-one (3p)



White solid; (100.0 mg, 67% yield); m.p. 146-150 °C ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.24 (s, 1H), 7.56 – 7.52 (m, 2H), 7.42 (s, 1H), 7.40 (s, 1H), 7.38 – 7.35 (m, 5H), 7.33 (dd, *J* = 4.9, 3.7 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.95 (ddd, *J* = 7.6, 1.5, 0.9 Hz, 1H), 6.79 – 6.77 (m, 1H), 6.57 (ddd, *J* = 8.1, 2.3, 0.8 Hz, 1H), 3.88 (t, *J* = 6.3 Hz, 1H), 3.66 (dd, *J* = 12.8, 6.5 Hz, 1H), 3.42 (dd, *J* = 12.8, 6.2 Hz, 1H), 3.28 (t, *J* = 8.0 Hz, 2H), 2.27 (dt, *J* = 16.3, 8.0 Hz, 1H), 2.07 (dt, *J* = 16.5, 8.1 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.57, 148.01, 142.47, 141.57, 137.66, 129.71, 129.07, 128.66, 128.43, 127.17, 117.11, 112.19 (d, *J* = 5.5 Hz), 70.57, 50.86, 47.54, 29.74. HRMS (ESI) calcd. For $C_{23}H_{24}N_3O$ (M^+ + H): 358.1914, found 358.1910; IR (neat cm-1): 3320, 3054, 1675, 1450, 1115, 755.

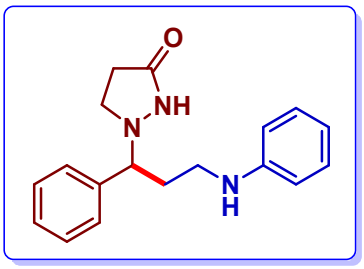
(R)-1-(1-(9H-fluoren-3-yl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3q)



White solid; (55.0 mg, 56% yield); m.p. 140 – 142 °C ; **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.28 (s, 1H), 7.78 (dd, *J* = 7.4, 2.4 Hz, 2H), 7.58 – 7.50 (m, 2H), 7.42 – 7.28 (m, 2H), 7.16 (dd, *J* = 8.4, 7.4 Hz, 2H), 6.72 (t, *J* = 7.3 Hz, 2H), 6.60 (d, *J* = 7.6 Hz, 2H), 3.94 (d, *J* = 6.4 Hz, 1H), 3.90 (s, 1H), 3.67 (dd, *J* = 12.8, 6.5 Hz, 1H), 3.43 (d, *J* = 6.4 Hz, 1H), 3.40 – 3.24 (m, 2H), 2.36 – 2.24 (m, 1H), 2.11 (dt, *J* = 16.6, 8.1 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.52, 147.64, 144.05, 143.39, 142.32, 141.02, 136.08, 129.37, 127.35, 127.06 (d, *J* = 21.9 Hz), 125.09 (d, *J* = 17.4 Hz), 120.20 (d, *J* = 19.2 Hz), 118.05, 113.34, 70.71, 50.96, 47.66, 36.96, 30.12. HRMS (ESI) calcd.

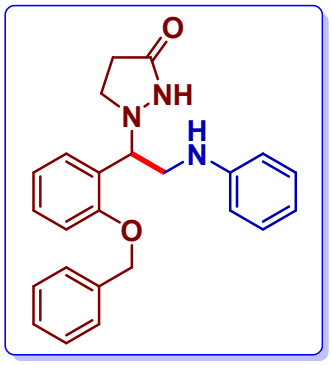
For $C_{24}H_{24}N_3O$ (M^+ + H): 370.1914, found 370.1906; IR (neat cm-1): 3374, 3051, 1684, 1504, 1260, 744, 836.

1-(1-phenyl-3-(phenylamino)propyl)pyrazolidin-3-one (3r)



White solid; (58.0 mg, 56% yield); m.p. 160 – 168 °C ; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.75 – 7.70 (m, 2H), 7.66 (s, 1H), 7.44 (s, 2H), 7.42 – 7.34 (m, 4H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.24 (s, 1H), 3.98 (s, 1H), 3.11 (ddd, *J* = 10.9, 9.4, 6.1 Hz, 2H), 2.82 (dt, *J* = 11.0, 8.7 Hz, 2H), 2.62 (ddd, *J* = 16.9, 9.0, 6.1 Hz, 2H), 2.50 – 2.40 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.69, 169.19, 146.17, 136.82, 132.20, 131.25, 130.23 (d, *J* = 26.0 Hz), 130.03, 129.55 (d, *J* = 27.3 Hz), 122.73, 117.78, 113.86, 69.75, 50.86, 48.24, 30.02. HRMS (ESI) calcd. For $C_{18}H_{21}N_3O$ (M^+ + H): 295.1680, found 295.1762; IR (neat cm-1): 3374, 3051, 1684, 1504, 1260, 744, 836.; IR (neat cm-1): 3372, 3053, 1687, 1508, 1264, 746, 836.

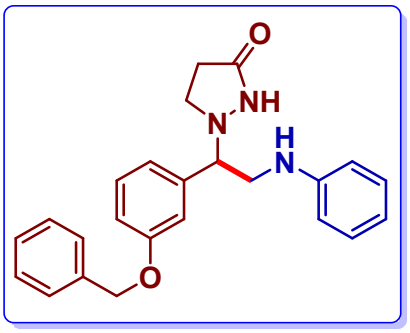
(R)-1-(1-(2-(benzyloxy) phenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3s)



White solid; (56.0 mg, 51% yield); m.p. 130-134 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.05 (s, 1H), 7.44 – 7.27 (m, 6H), 7.16 (t, *J* = 7.6 Hz, 2H), 7.00 – 6.90 (m, 3H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 2H), 5.06 (s, 2H), 3.81 (t, *J* = 5.9 Hz, 1H), 3.58 (dd, *J* = 12.7, 6.1 Hz, 1H), 3.37 –

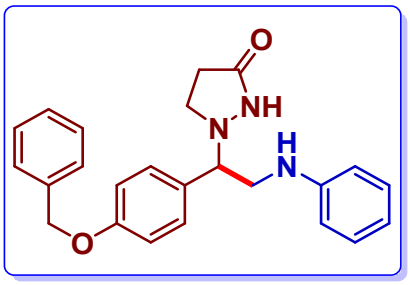
3.32 (m, 1H), 3.27 (dd, *J* = 18.3, 10.8 Hz, 2H), 2.32 (dt, *J* = 15.9, 7.8 Hz, 1H), 2.17 – 2.04 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.60, 159.14, 147.63, 139.37, 136.74, 130.08, 129.35, 128.67, 128.11, 127.62, 121.01, 117.95, 114.97 (d, *J* = 8.2 Hz), 113.29, 70.41, 70.11, 50.83, 47.47, 30.11. HRMS (ESI) calcd. For $C_{24}H_{26}N_3O_2$ (M^+ + H): 388.2029, found 388.2012; IR (neat cm-1): 3289, 3050, 2942, 1710, 1460, 1350, 1121, 741.

(R)-1-(1-(3-(benzyloxy)phenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3t)



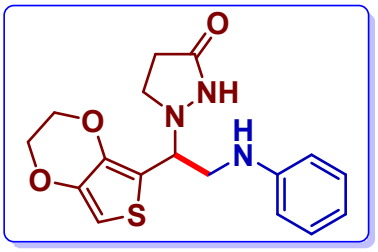
White solid; (58.0 mg, 59% yield); m.p. 150 – 154 °C ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.96 (s, 1H), 7.42 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.35 – 7.28 (m, 5H), 7.23 (td, *J* = 8.2, 1.7 Hz, 1H), 7.06 (dd, *J* = 8.4, 7.4 Hz, 2H), 6.96 (t, *J* = 7.3 Hz, 2H), 6.63 (t, *J* = 7.3 Hz, 1H), 6.52 (d, *J* = 7.7 Hz, 2H), 5.01 (t, *J* = 7.9 Hz, 2H), 4.64 (t, *J* = 6.3 Hz, 1H), 3.54 (dd, *J* = 13.0, 7.1 Hz, 1H), 3.35 – 3.24 (m, 2H), 3.18 (dd, *J* = 18.2, 9.0 Hz, 1H), 2.16 (dd, *J* = 15.6, 7.9 Hz, 1H), 1.95 (dt, *J* = 16.7, 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.52, 147.64, 144.05, 143.39, 142.32, 141.02, 136.08, 129.37, 127.35, 127.06 (d, *J* = 21.9 Hz), 125.09 (d, *J* = 17.4 Hz), 120.20 (d, *J* = 19.2 Hz), 118.05, 113.34, 70.71, 50.96, 36.96, 30.12. HRMS (ESI) calcd. For $C_{24}H_{26}N_3O_2$ (M^+ + H): 388.2029, found 388.2012; IR (neat cm-1): 3359, 3033, 2929, 2835, 1675, 1494, 1379, 1257, 1021.

1-(1-(4-(benzyloxy)phenyl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3u)



White solid; (65.0 mg, 67% yield); m.p. 130-140 °C; **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.41 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.31 (s, 1H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.13 (t, *J* = 7.9 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 2H), 4.99 (s, 2H), 3.79 (t, *J* = 6.6 Hz, 1H), 3.57 (dd, *J* = 12.9, 6.9 Hz, 1H), 3.36 – 3.27 (m, 1H), 3.28 – 3.12 (m, 2H), 2.31 – 2.02 (m, 2H), 2.06 – 1.89 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.28, 147.62, 138.55, 134.51, 129.74, 129.35, 128.27, 118.06, 113.31, 70.26, 50.92, 47.5, 30.07, 21.19. HRMS (ESI) calcd. For $C_{24}H_{26}N_3O_2$ (M^+ + H): 388.2029, found 388.2012; IR (neat cm-1): 3054, 2927, 2849, 1673, 1157, 743, 834.

(S)-1-(1-(2,3-dihydrothieno[3,4-b][1,4]dioxin-5-yl)-2-(phenylamino)ethyl)pyrazolidin-3-one (3v)



White solid; (60.0 mg, 63% yield); m.p. 160-164 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.30 – 7.26 (m, 2H), 6.95 (d, *J* = 7.9 Hz, 2H), 6.89 (t, *J* = 7.3 Hz, 1H), 6.27 (s, 1H), 6.10 (d, *J* = 6.0 Hz, 1H), 4.52 (t, *J* = 2.5 Hz, 1H), 4.26 – 4.16 (m, 4H), 3.82 (dd, *J* = 11.9, 3.1 Hz, 1H), 3.45 (dd, *J* = 12.0, 2.3 Hz, 2H), 3.27 (ddd, *J* = 11.7, 10.0, 3.9 Hz, 1H), 2.19 – 2.10 (m, 1H), 1.89 (dt, *J* = 16.6, 10.1 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 170.06, 146.91, 140.54, 139.80, 129.36, 120.43, 116.93, 111.19, 102.31, 64.86 (d, *J* = 14.1 Hz), 62.34, 55.34, 46.09, 30.45, 11.33. HRMS (ESI) calcd. For $C_{17}H_{20}N_3O_3S$ (M^+ + H): 346.1221, found 346.1220; IR (neat cm-1): 3300, 2931, 1681, 1600, 1512, 1250, 1023.

10. References

[1] H. E. Gottlieb, V. Kotlyar and A. Nudelman, *J. Org. Chem.,* 1997, **62**, 7512–7515.

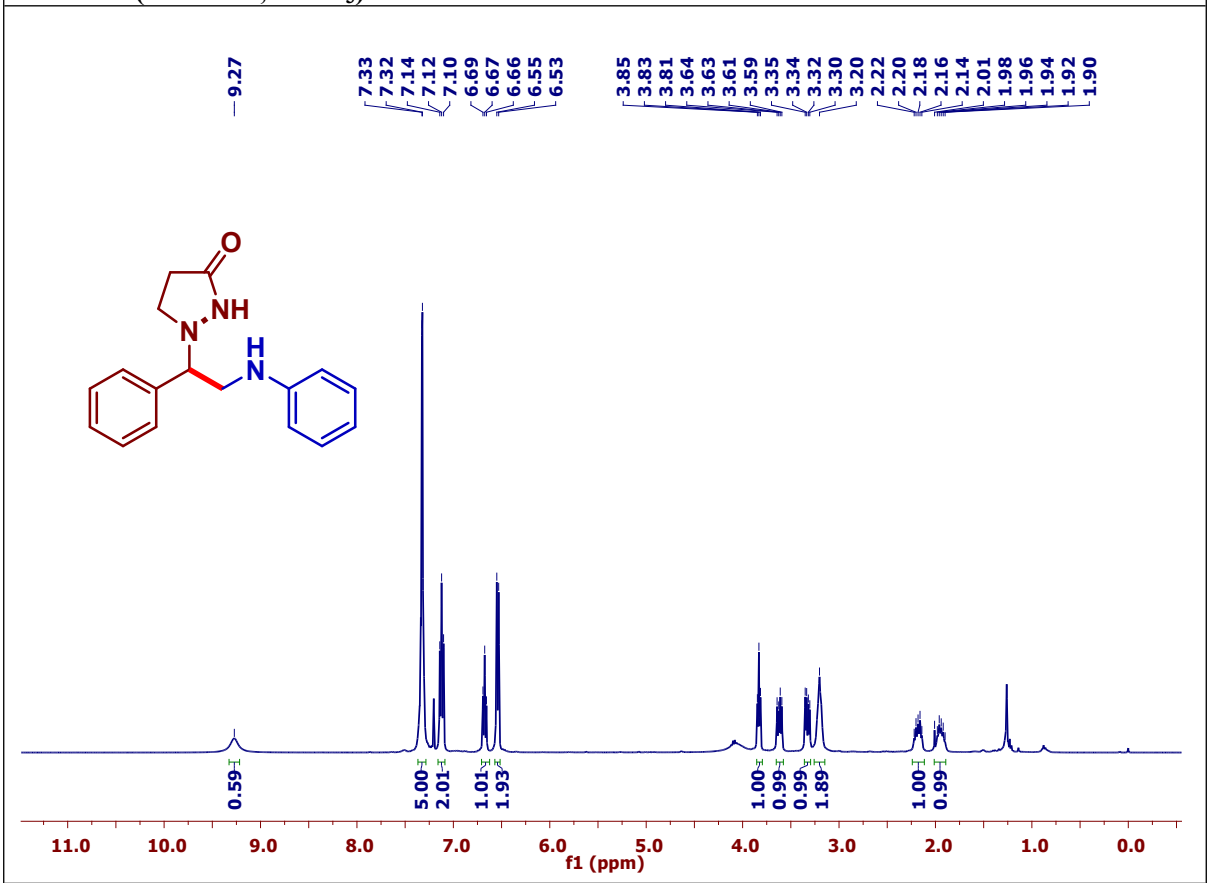
[2] Bruker (2016). APEX3, SAINT and SADABS. Bruker AXS, Inc., Madison, Wisconsin, USA.

[3] Sheldrick G. M. (2015).ActaCrystallogr C71: 3–8.

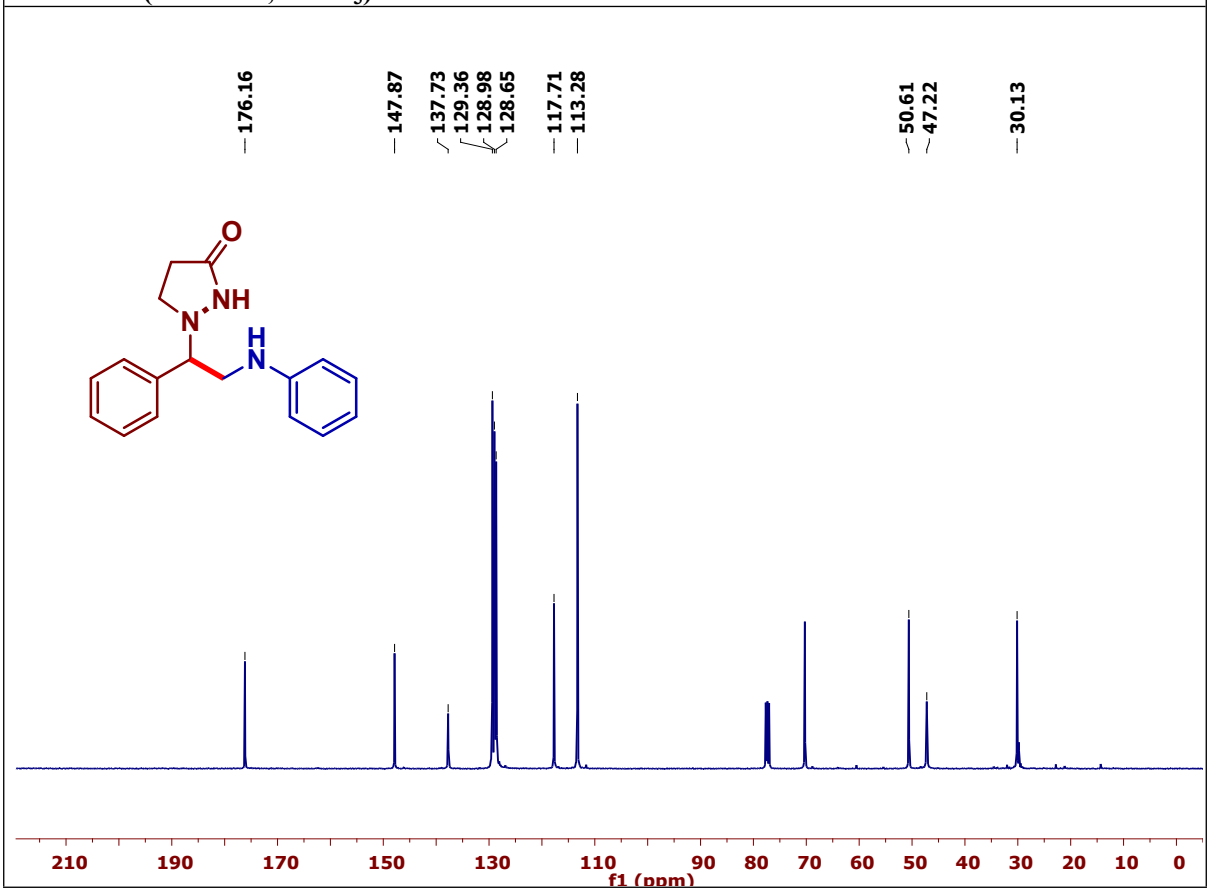
[4] Z. Yao, X. Wu, X. Zhang, Q. Xiong, S. Jianga, Z. Yu, *Org. Biomol. Chem.,* 2019, **17**, 6777–6781.

Copies of ^{1}H and ^{13}C NMR spectra

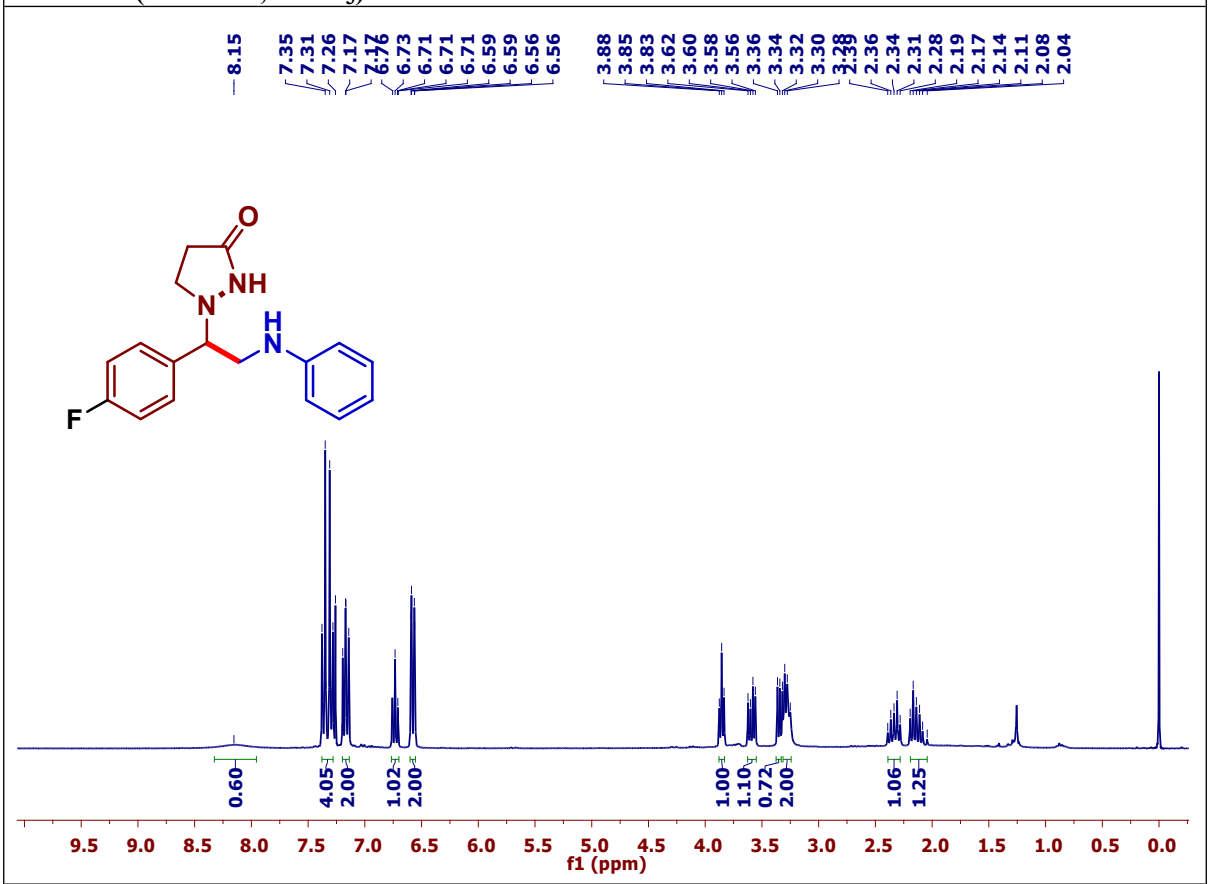
^{1}H NMR (400 MHz, $CDCl_3$) of 3a



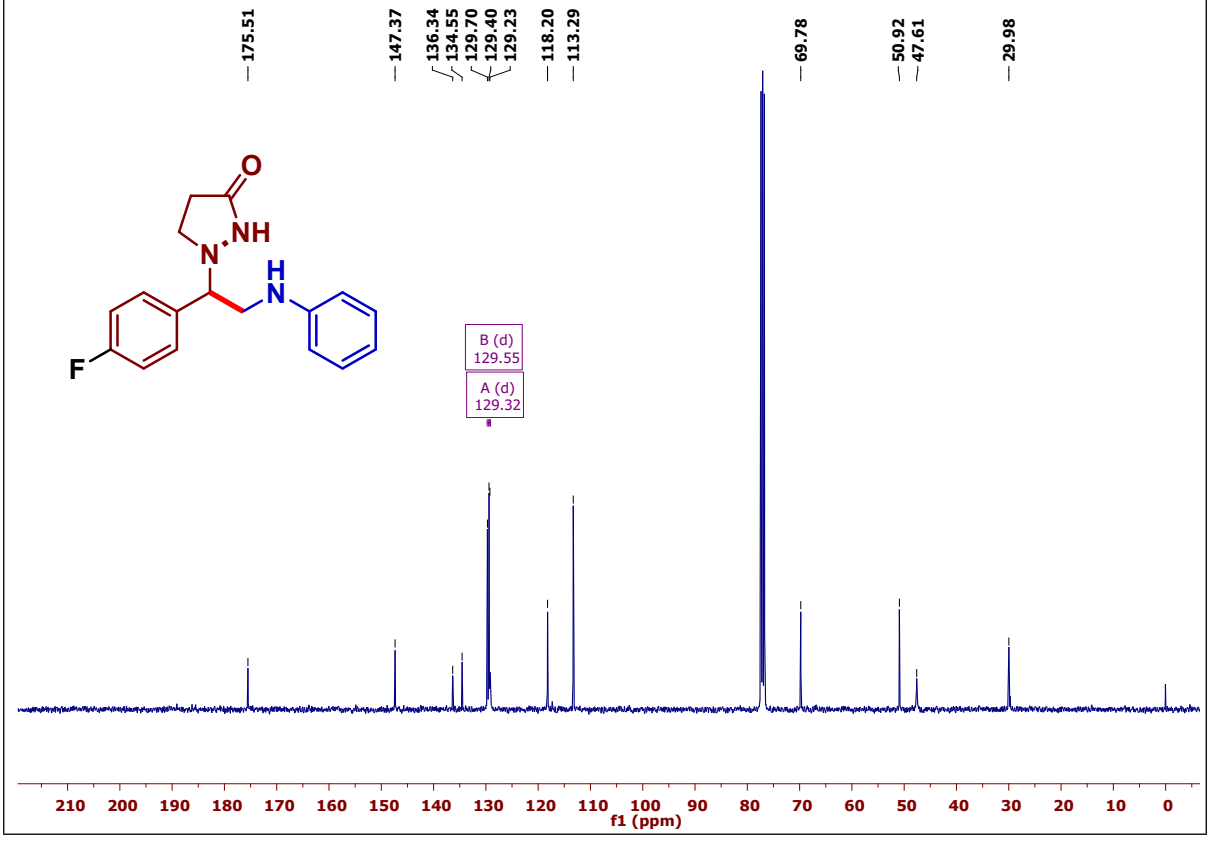
^{13}C NMR (101 MHz, $CDCl_3$) of 3a



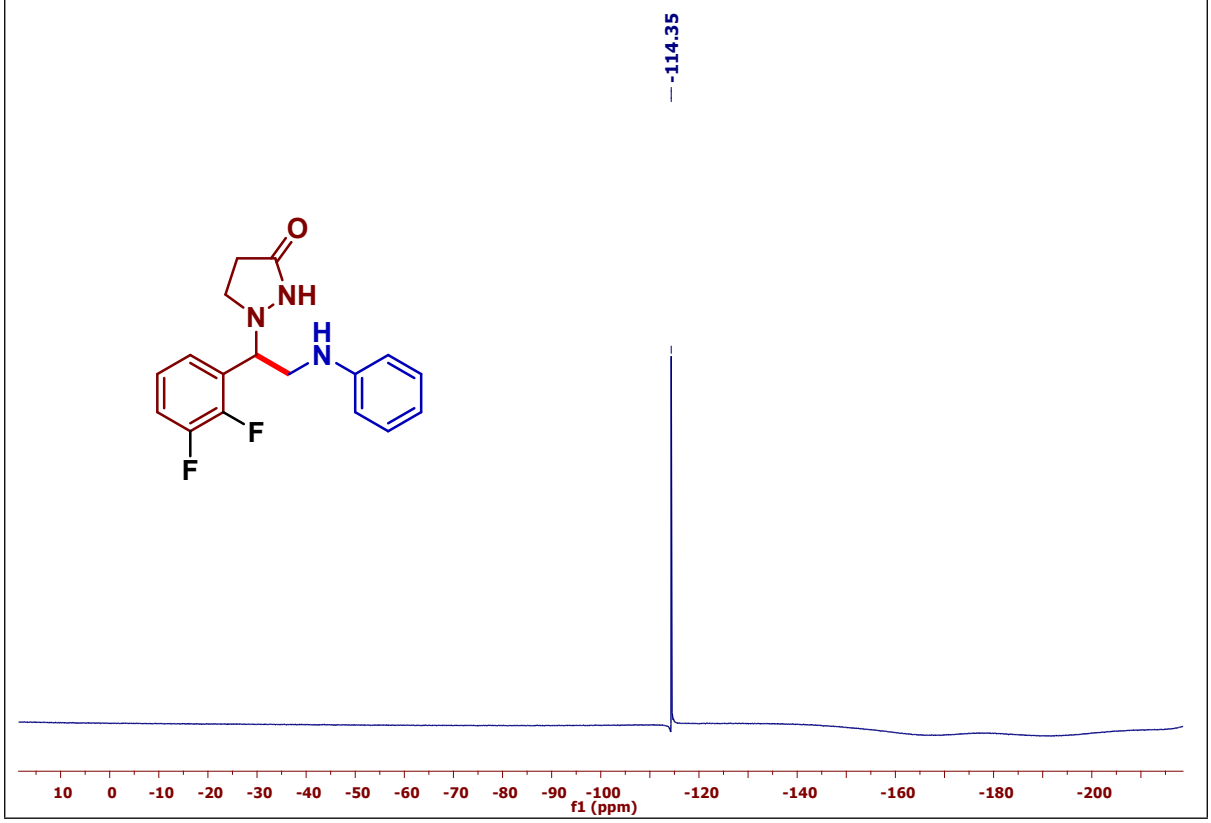
^{1}H NMR (400 MHz, $CDCl_3$) of 3b



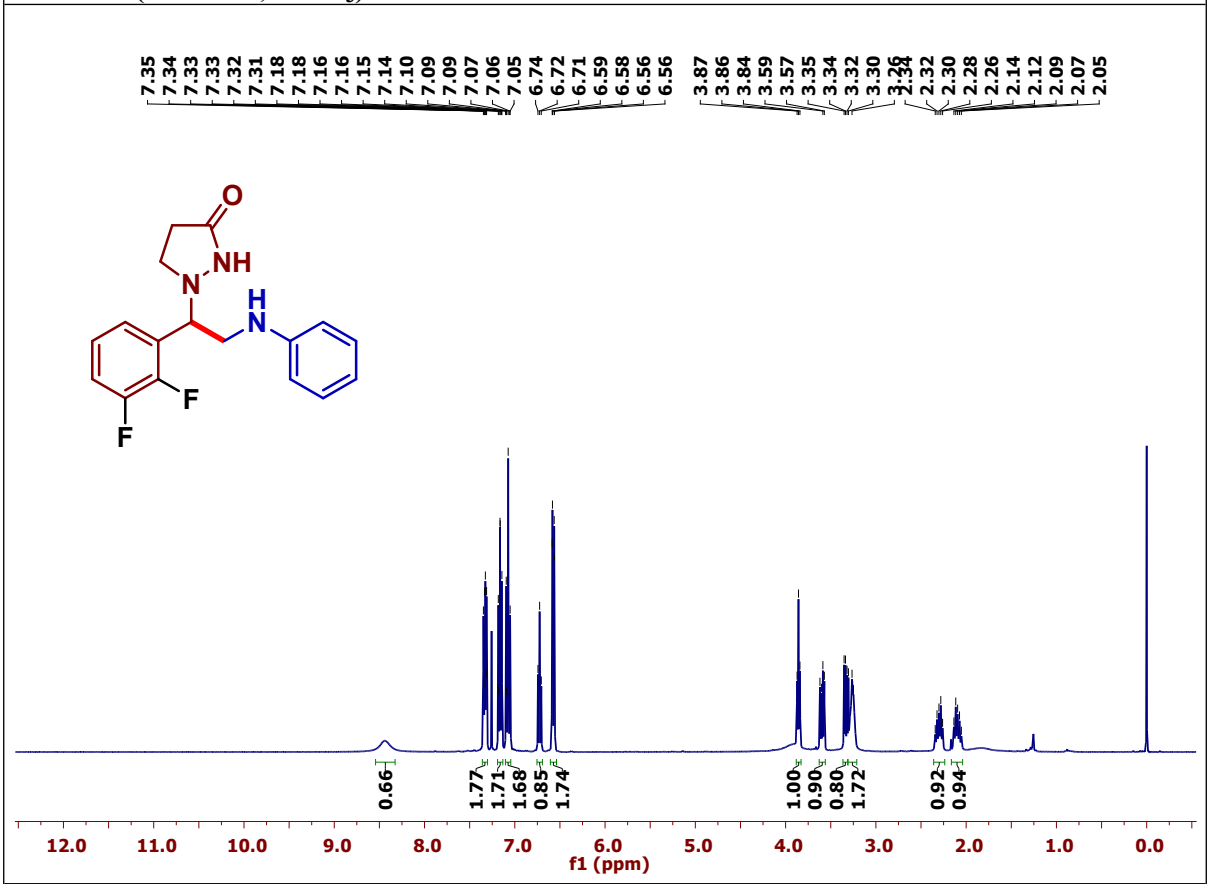
^{13}C NMR (101 MHz, $CDCl_3$) of 3b



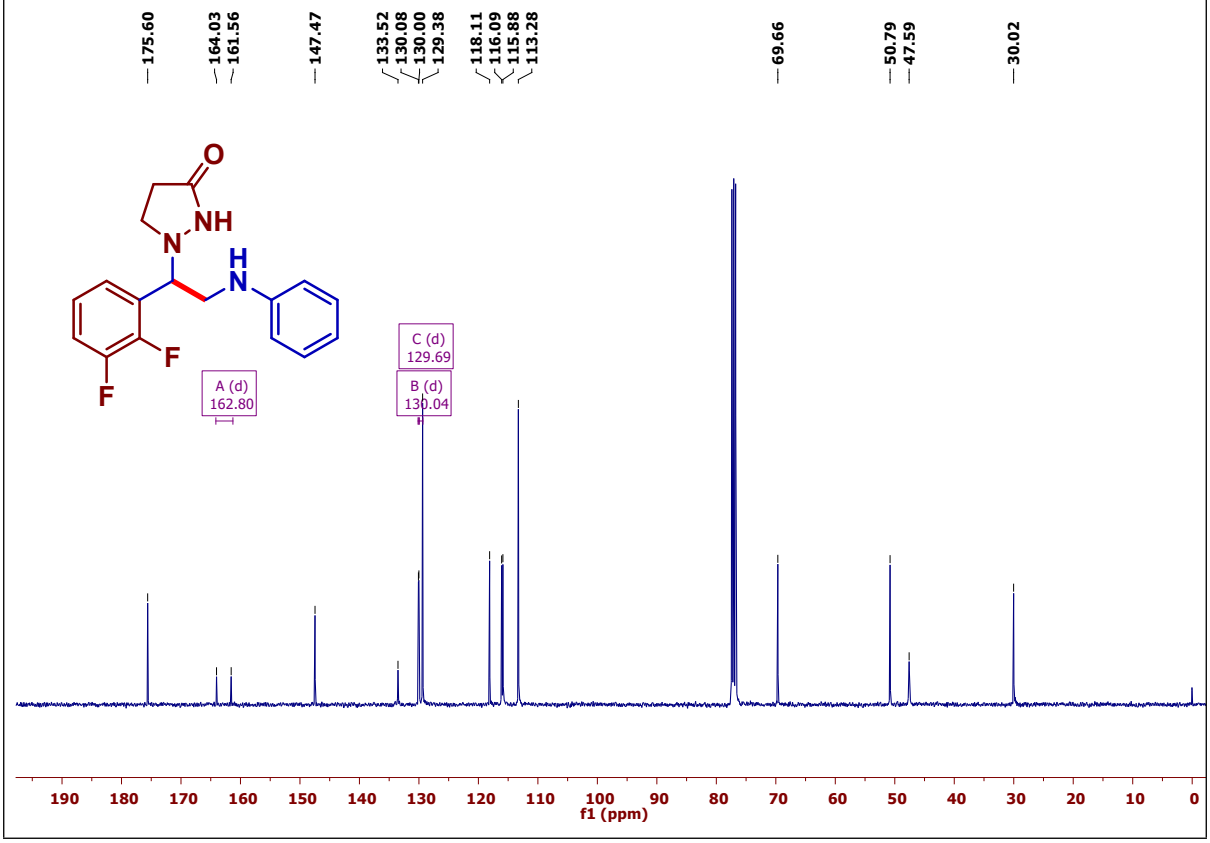
^{19F} NMR (400 MHz, $CDCl_3$) of 3b



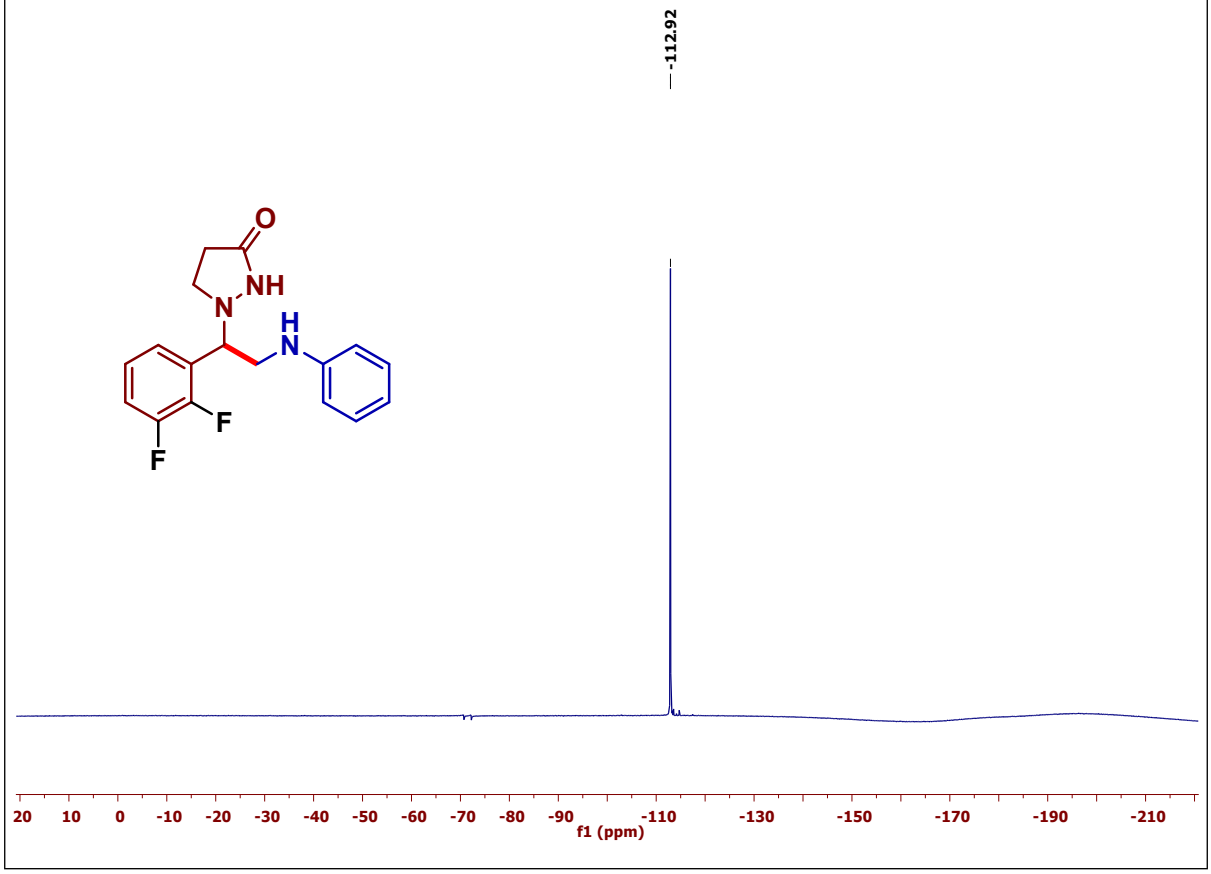
^{1}H NMR (400 MHz, $CDCl_3$) of 3c



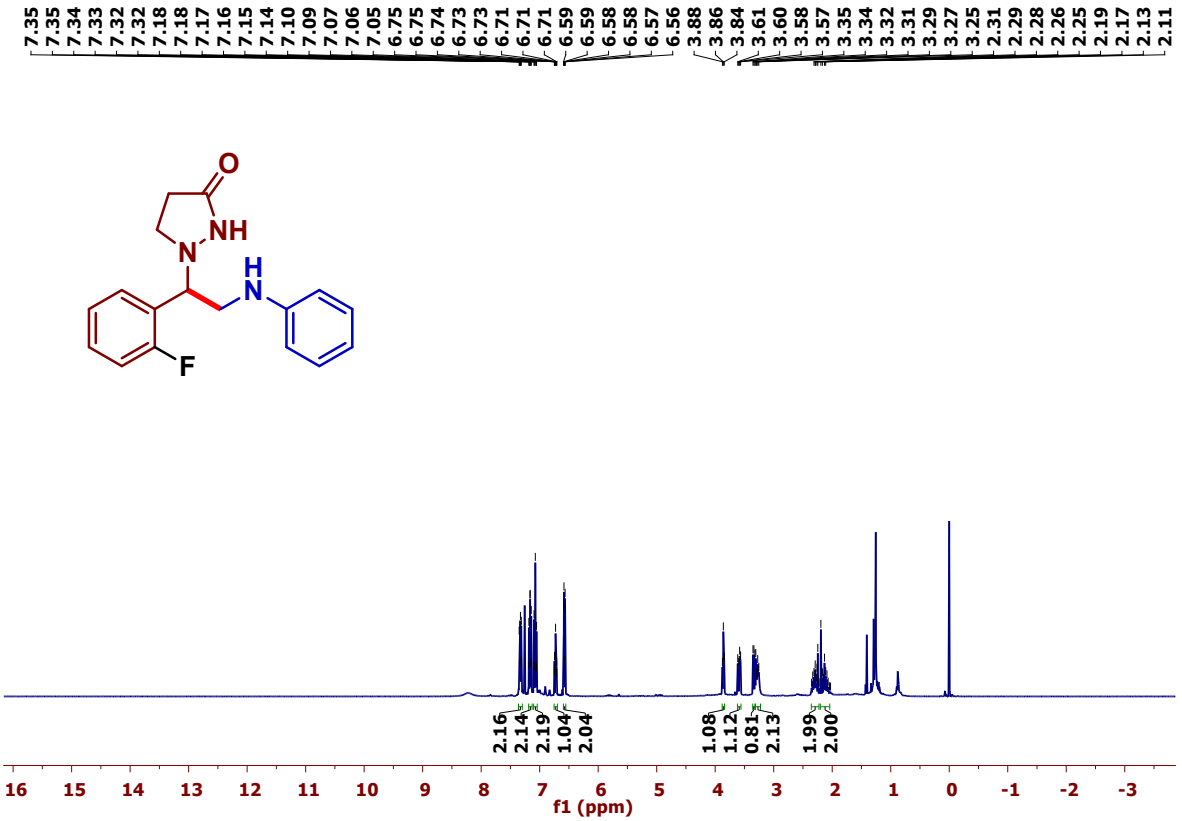
^{13}C NMR (101 MHz, $CDCl_3$) of 3c



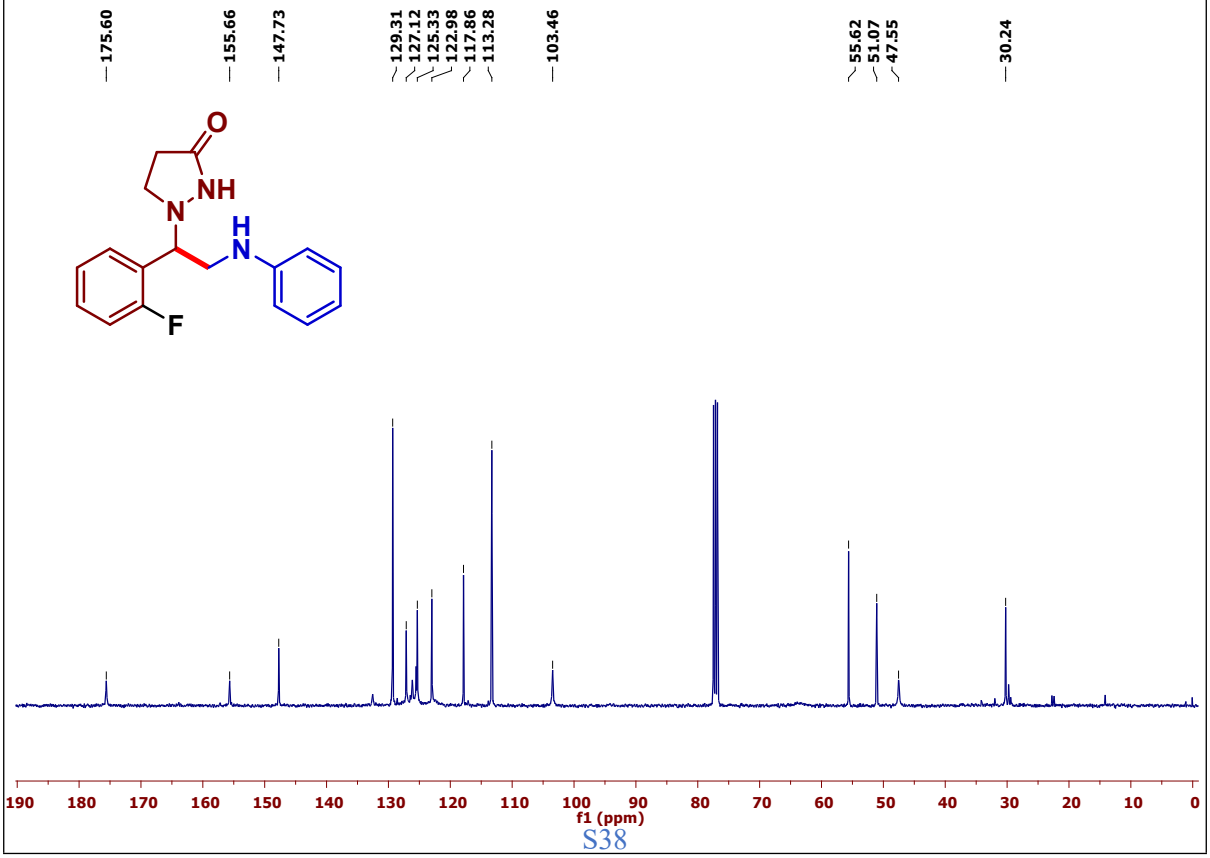
^{1}H NMR (400 MHz, $CDCl_3$) of 3c



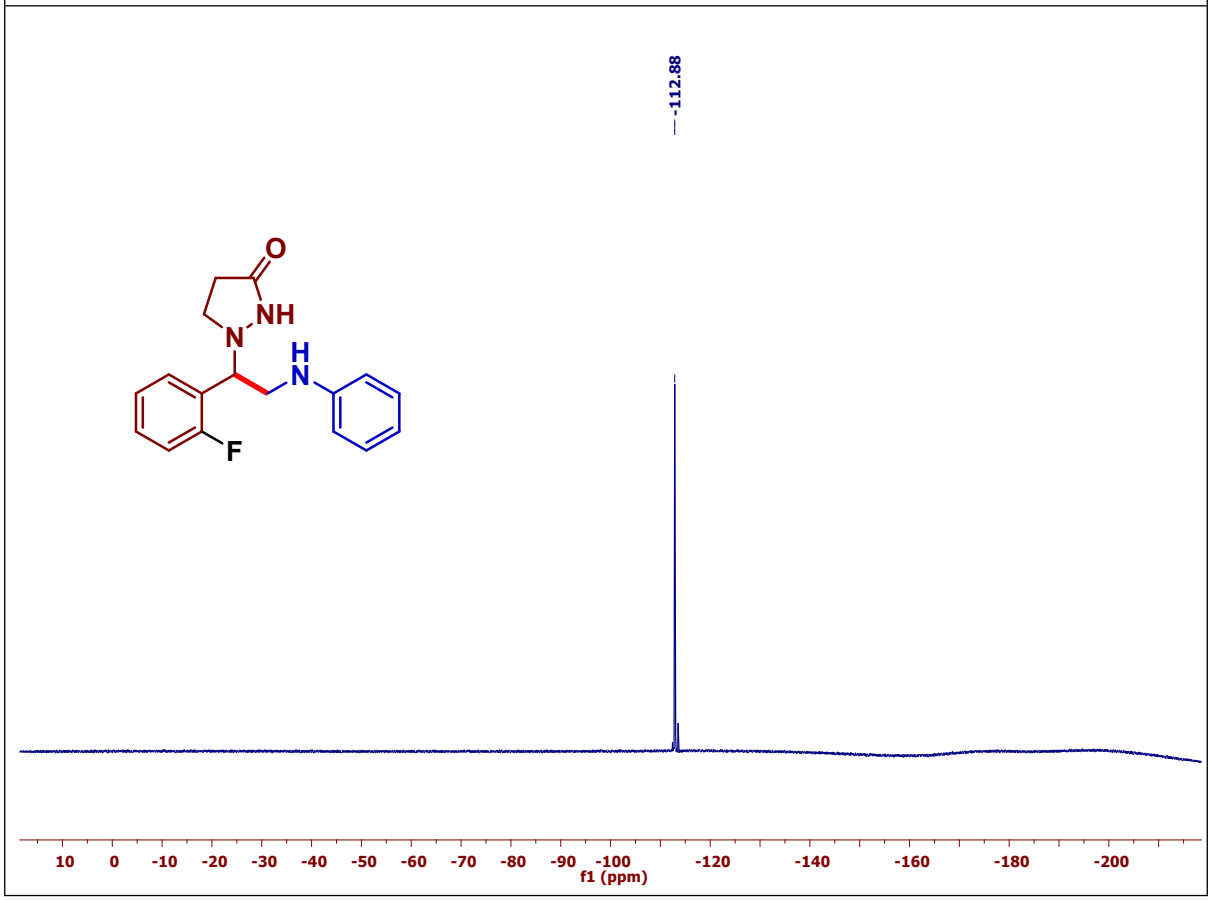
^{1}H NMR (400 MHz, $CDCl_3$) of 3d



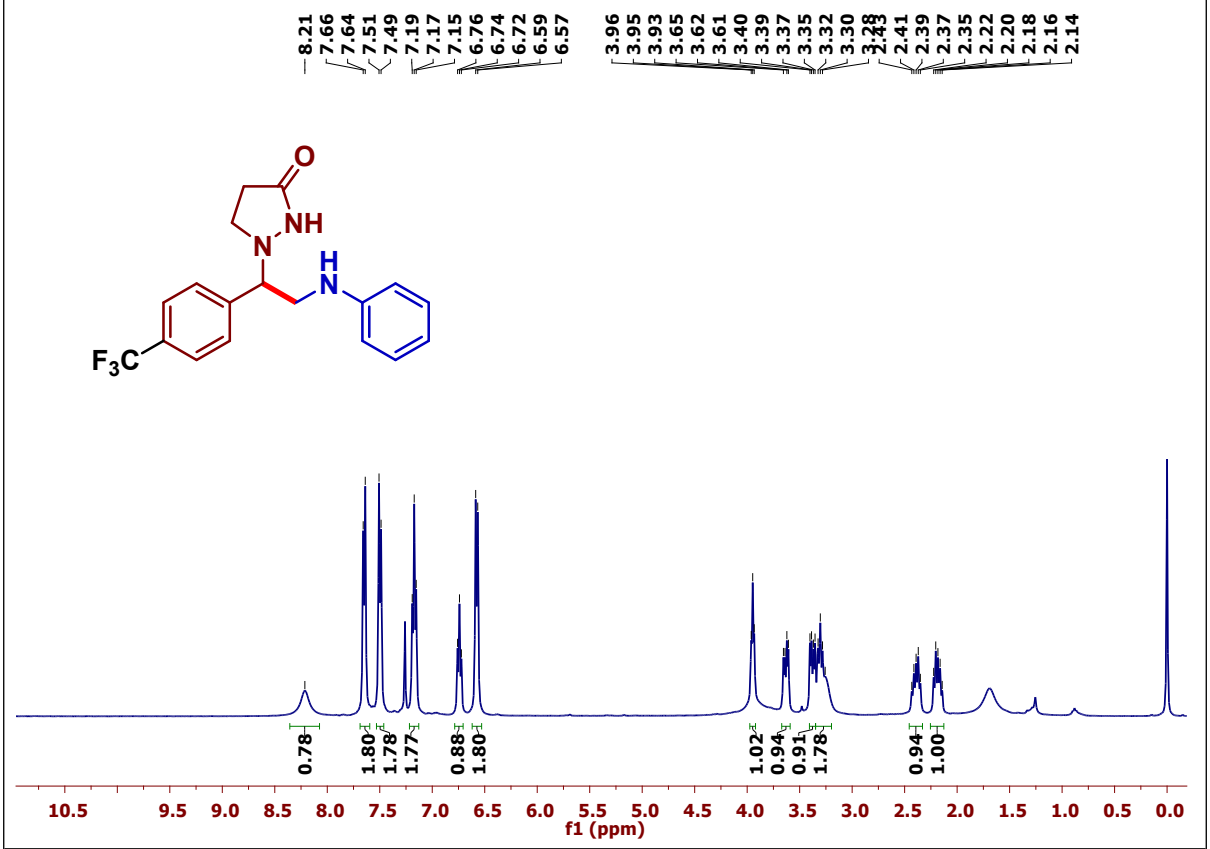
^{13}C NMR (101 MHz, $CDCl_3$) of 3d



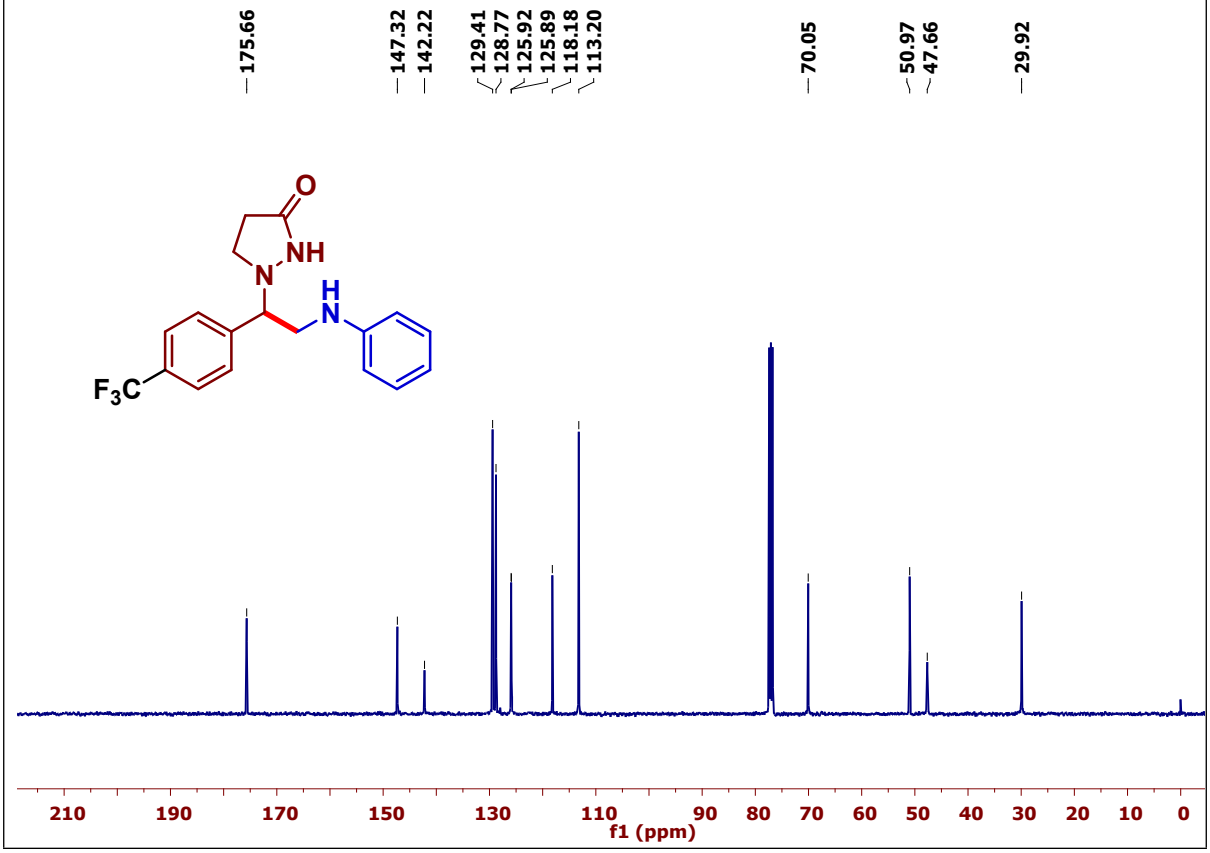
^{19}F NMR of 3d


-112.88
O
NH
N
H
N
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

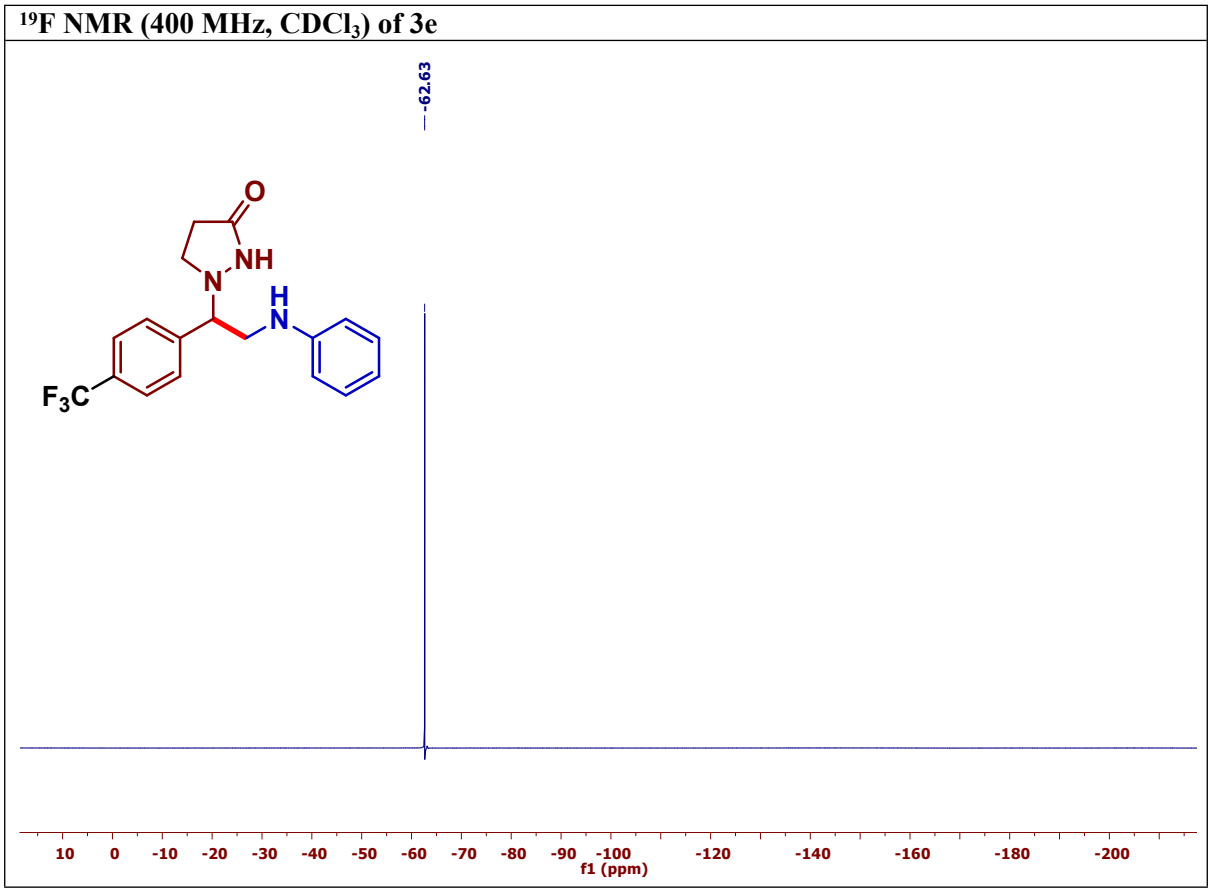
^{1}H NMR (400 MHz, $CDCl_3$) of 3e



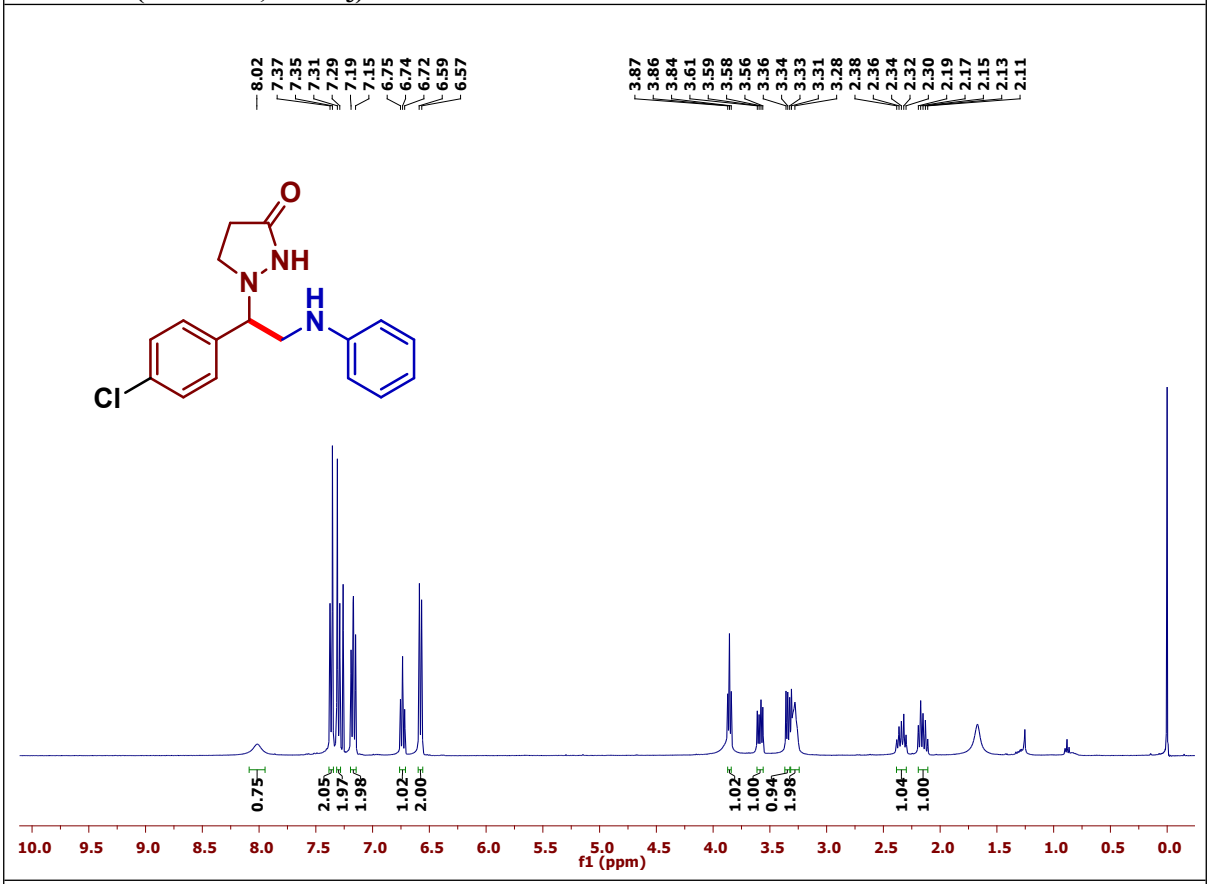
^{13}C NMR (101 MHz, $CDCl_3$) of 3e



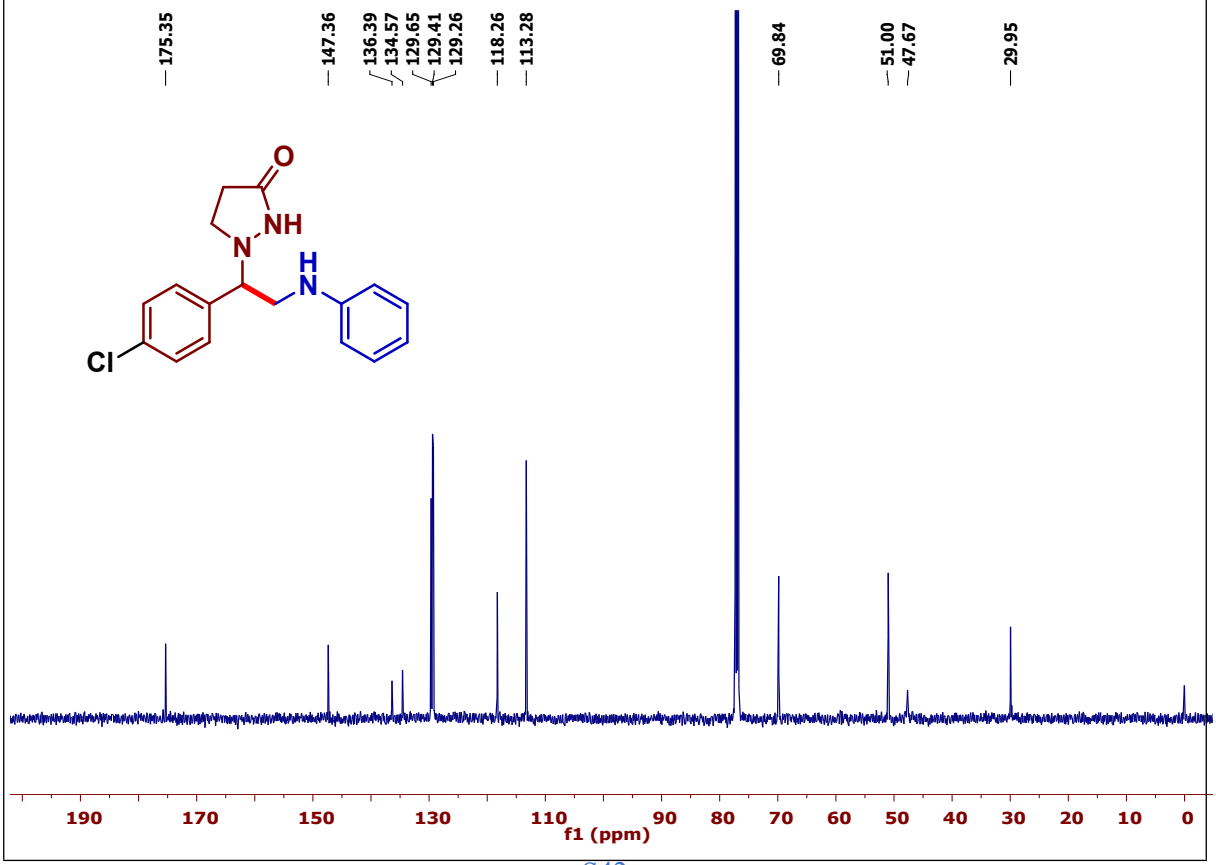
^{19}F NMR (400 MHz, $CDCl_3$) of 3e



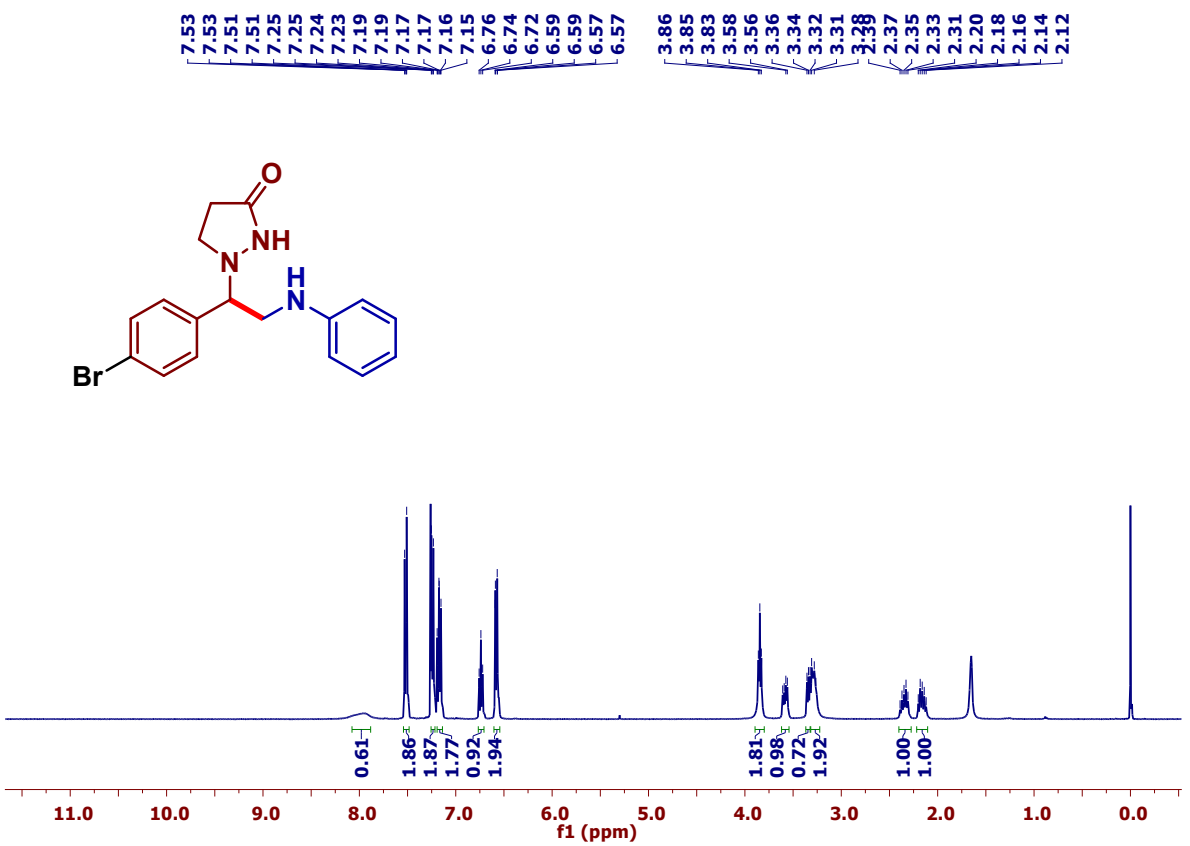
^{1}H NMR (400 MHz, $CDCl_3$) of 3f



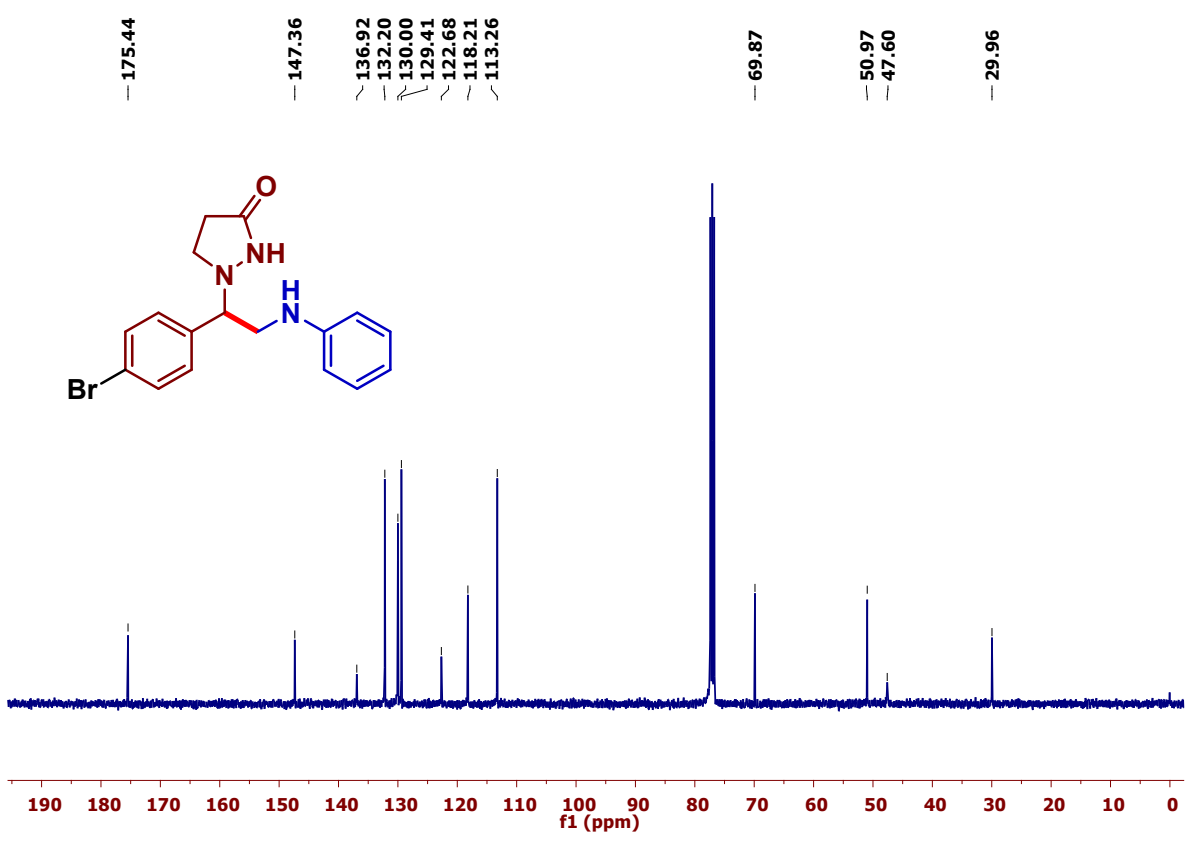
^{13}C NMR (126 MHz, $CDCl_3$) of 3f



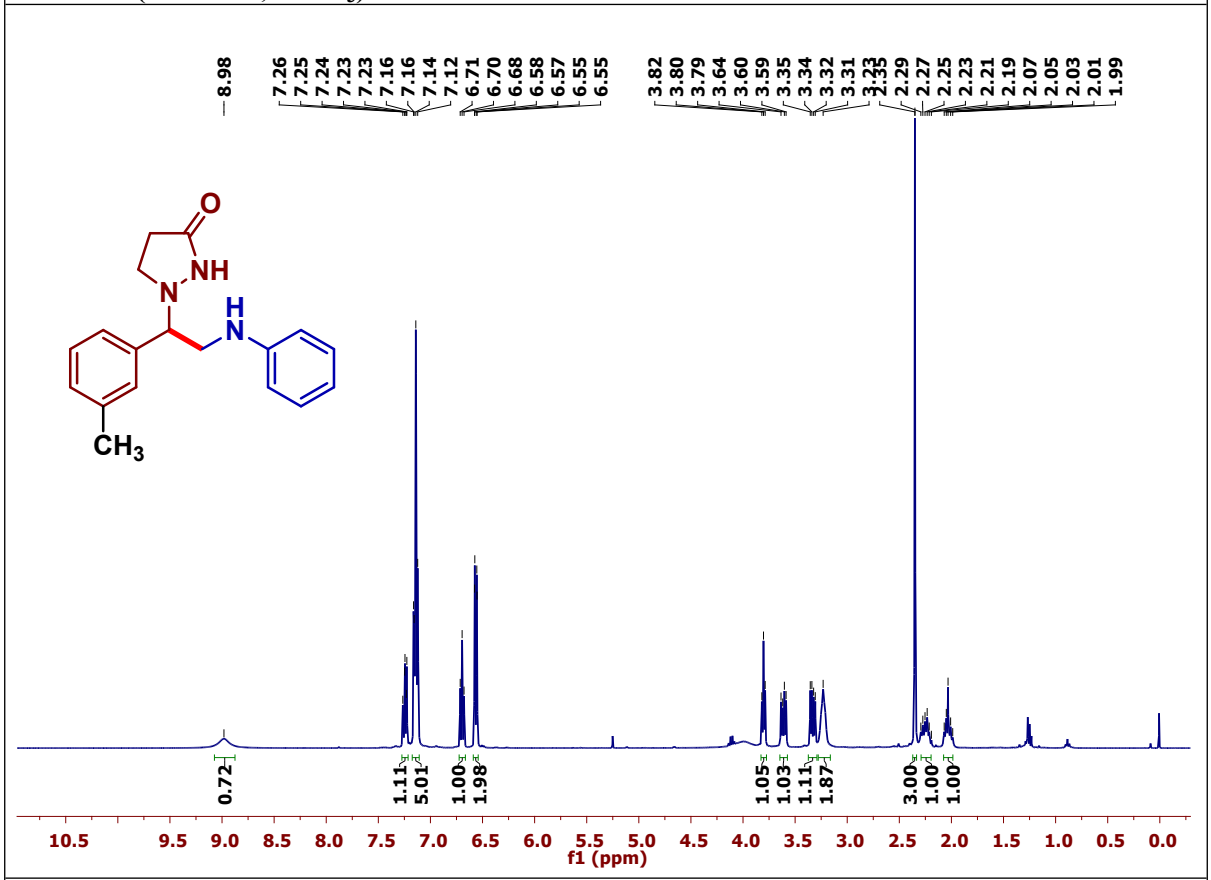
^{1}H NMR (400 MHz, $CDCl_3$) of 3g



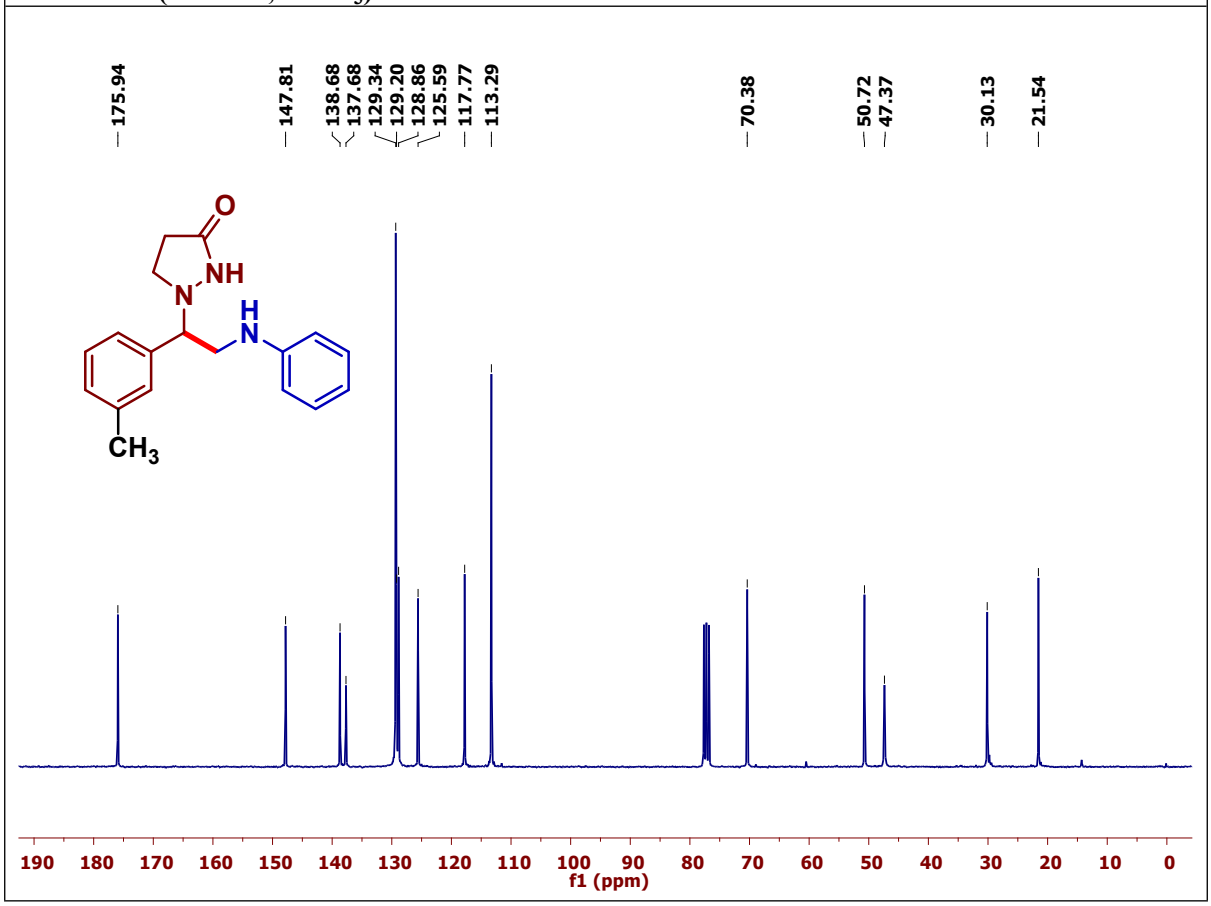
^{13}C NMR (101 MHz, $CDCl_3$) of 3g



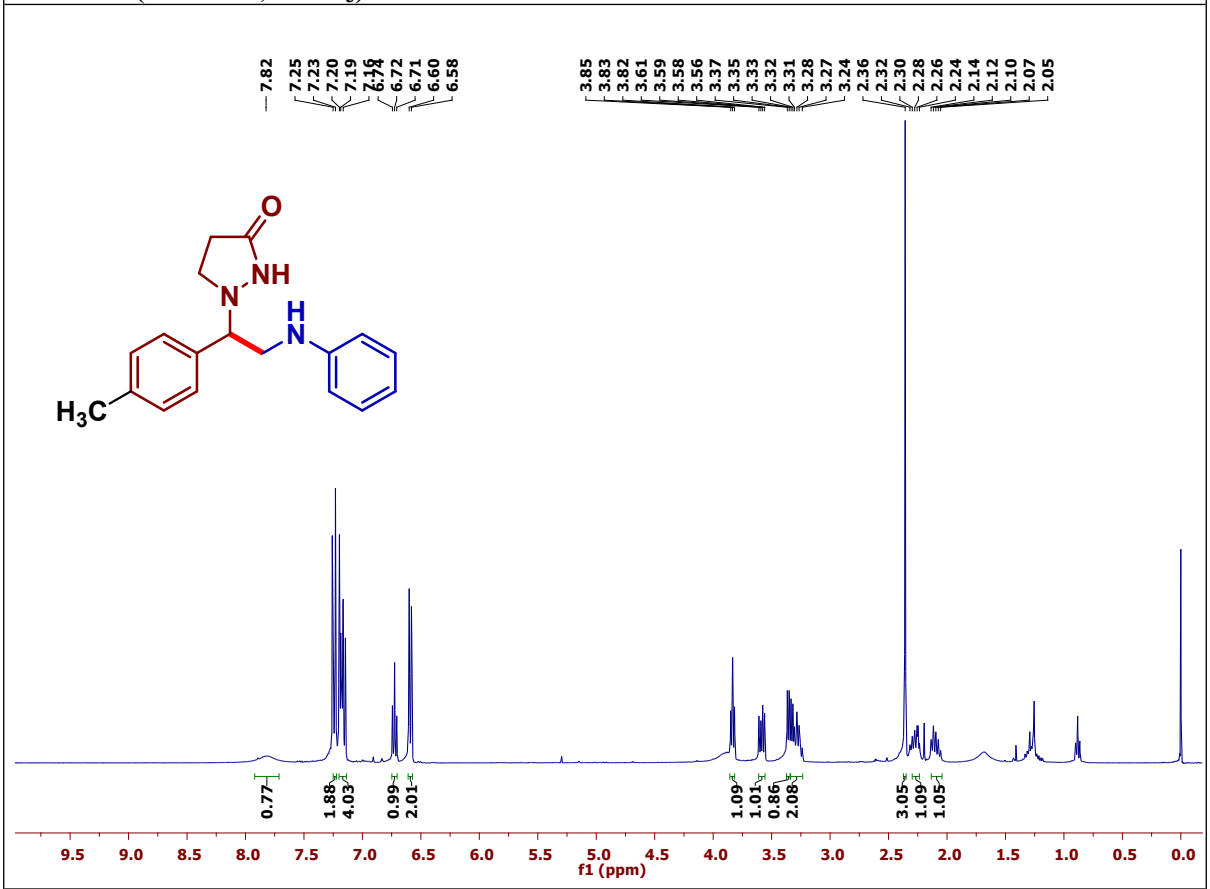
^{1}H NMR (400 MHz, $CDCl_3$) of 3h



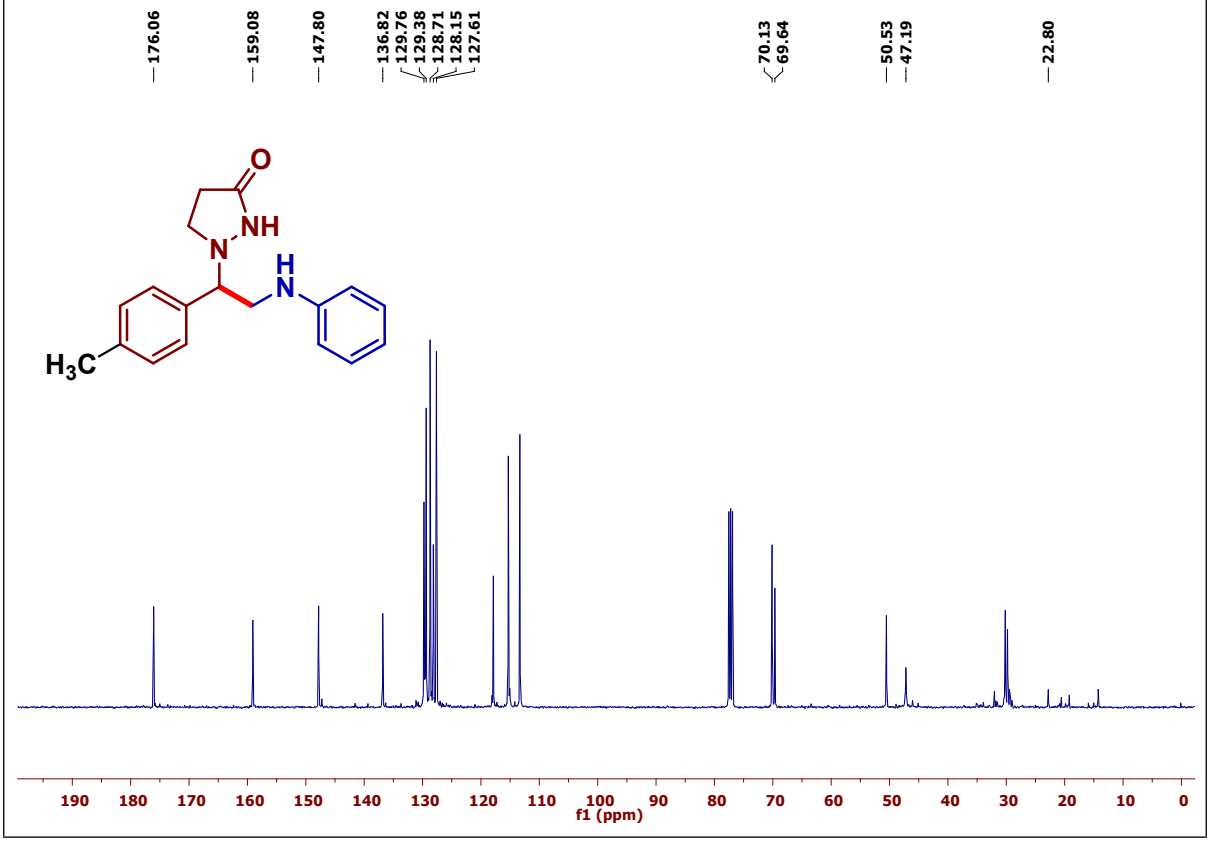
^{13}C NMR (75 MHz, $CDCl_3$) of 3h



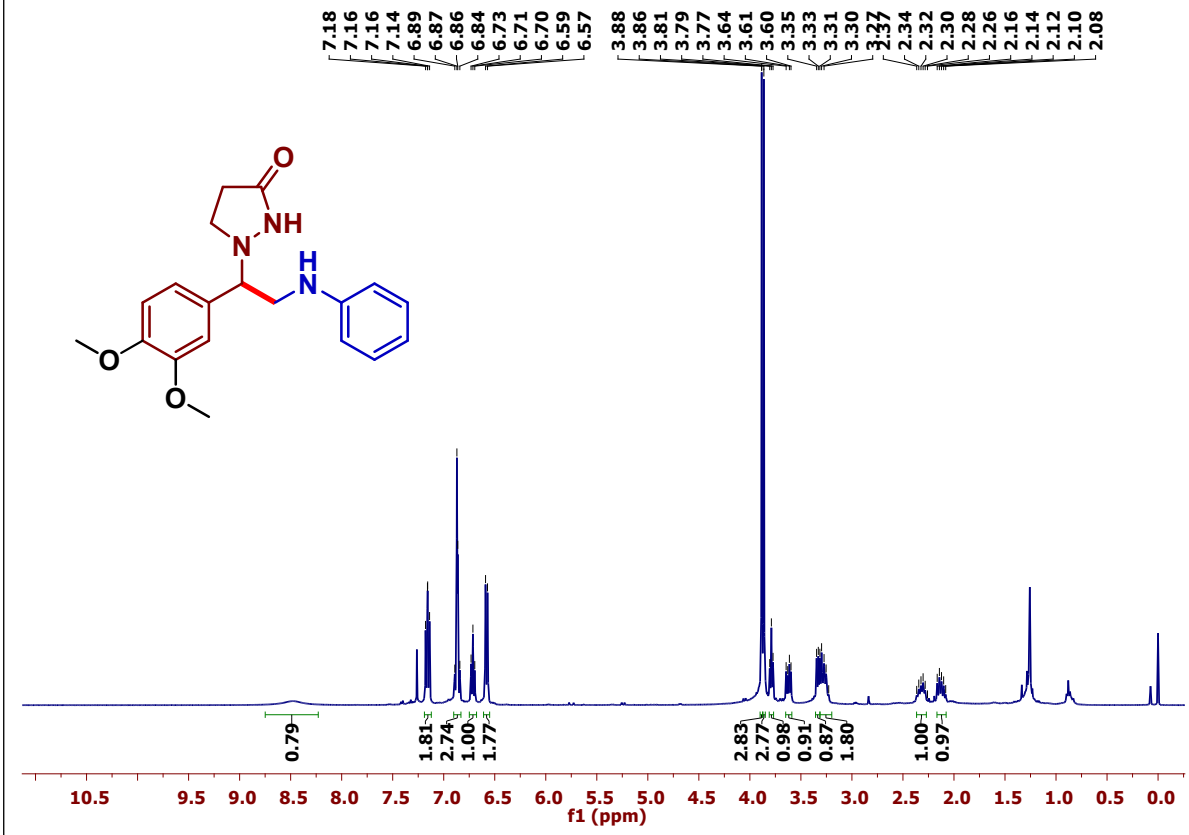
^{1}H NMR (400 MHz, $CDCl_3$) of 3i



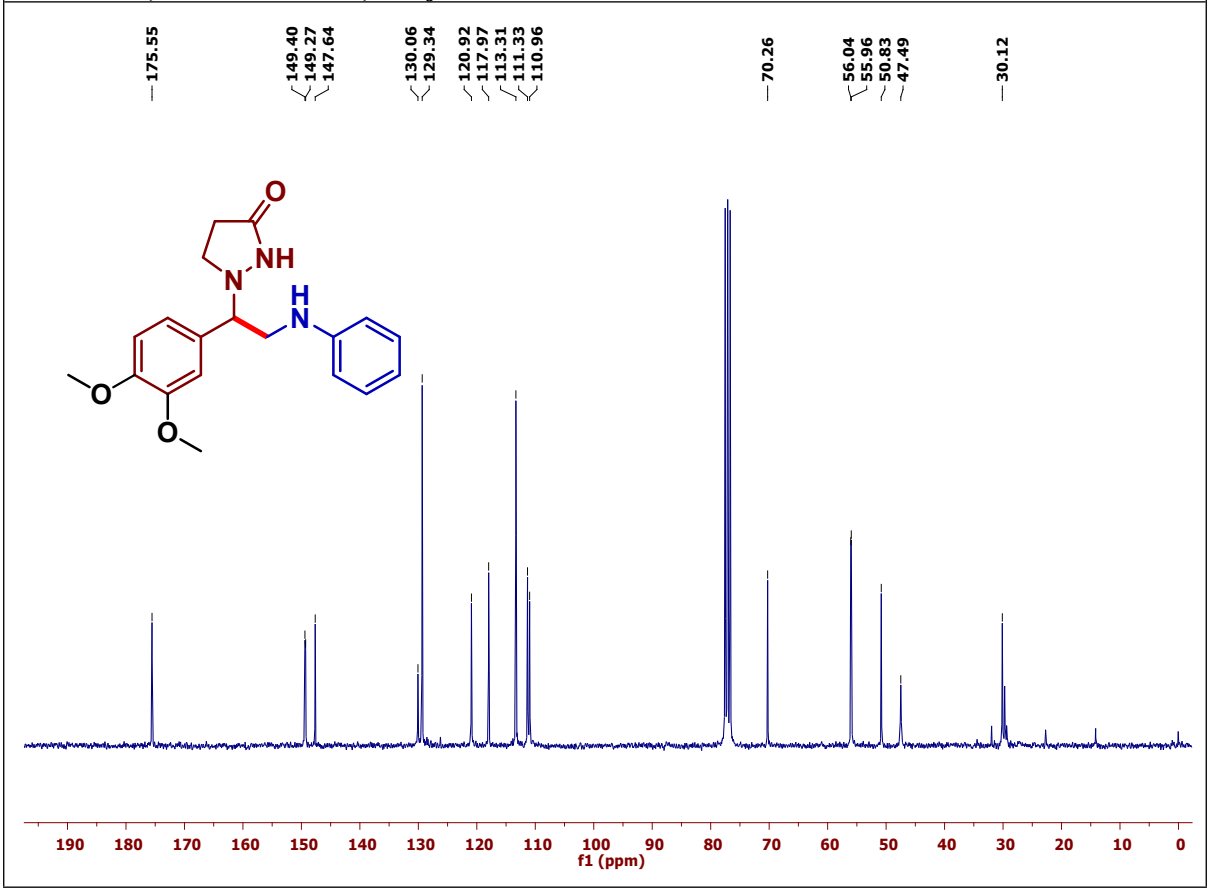
^{13}C NMR (101 MHz, $CDCl_3$) of 3i



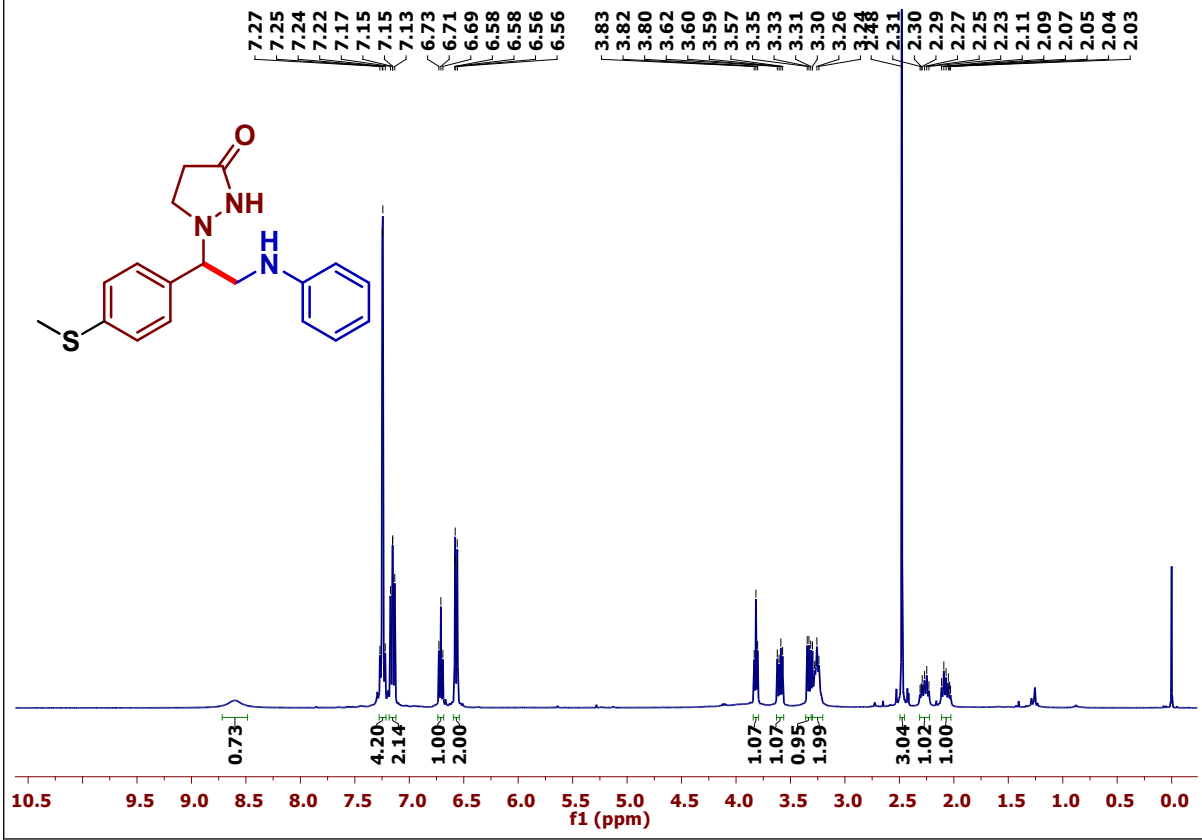
^{1}H NMR (400 MHz, $CDCl_3$) of 3j



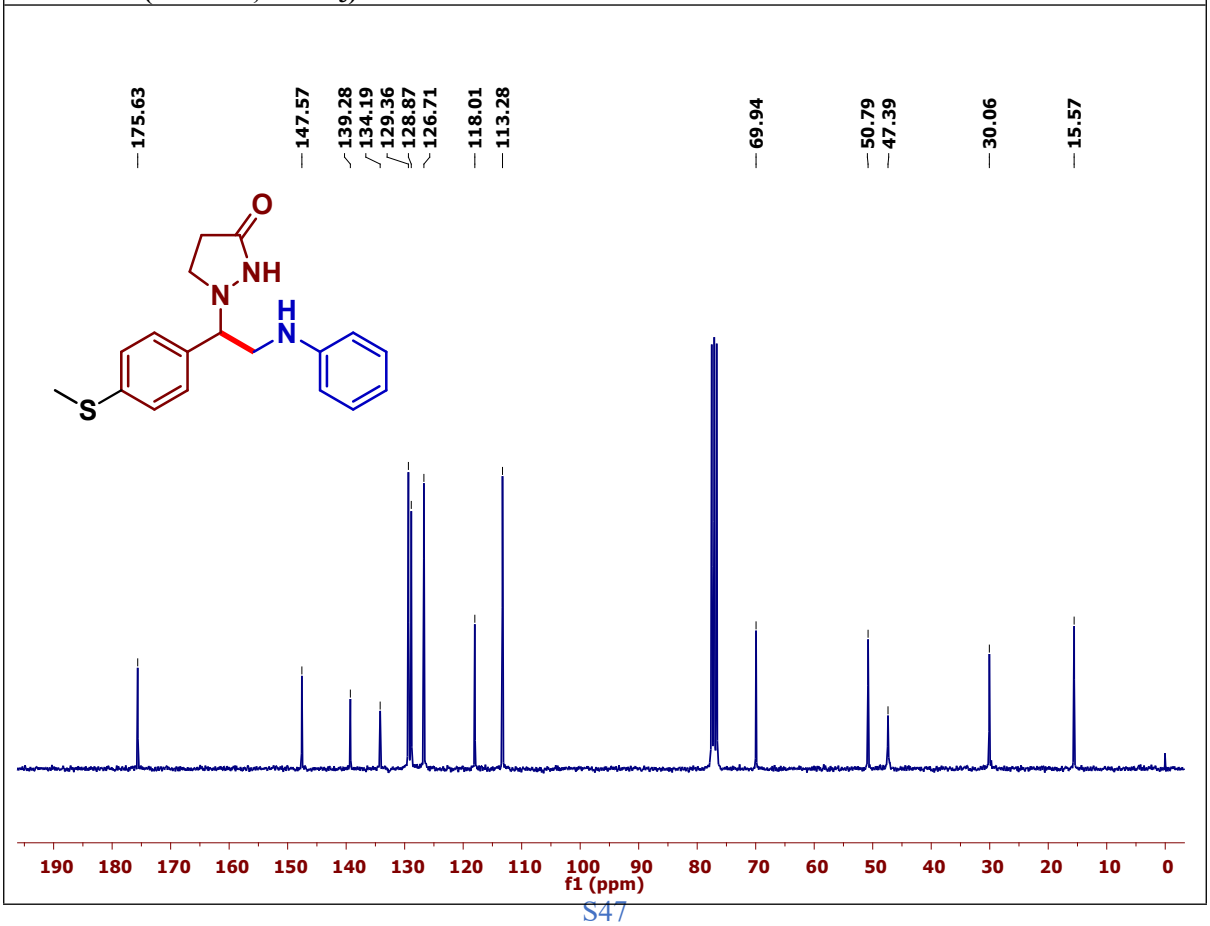
^{13}C NMR (101 MHz, $CDCl_3$) of 3j



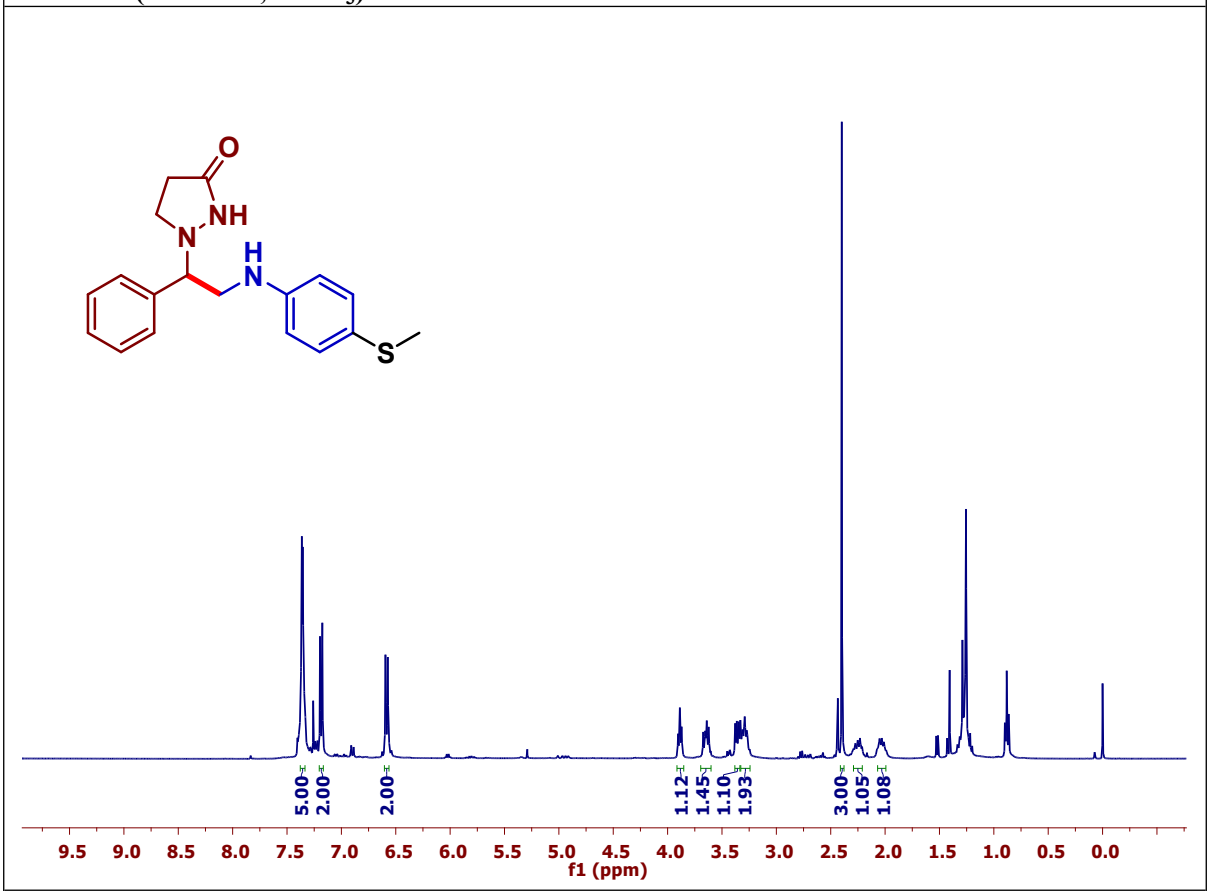
^{1}H NMR (400 MHz, $CDCl_3$) of 3k



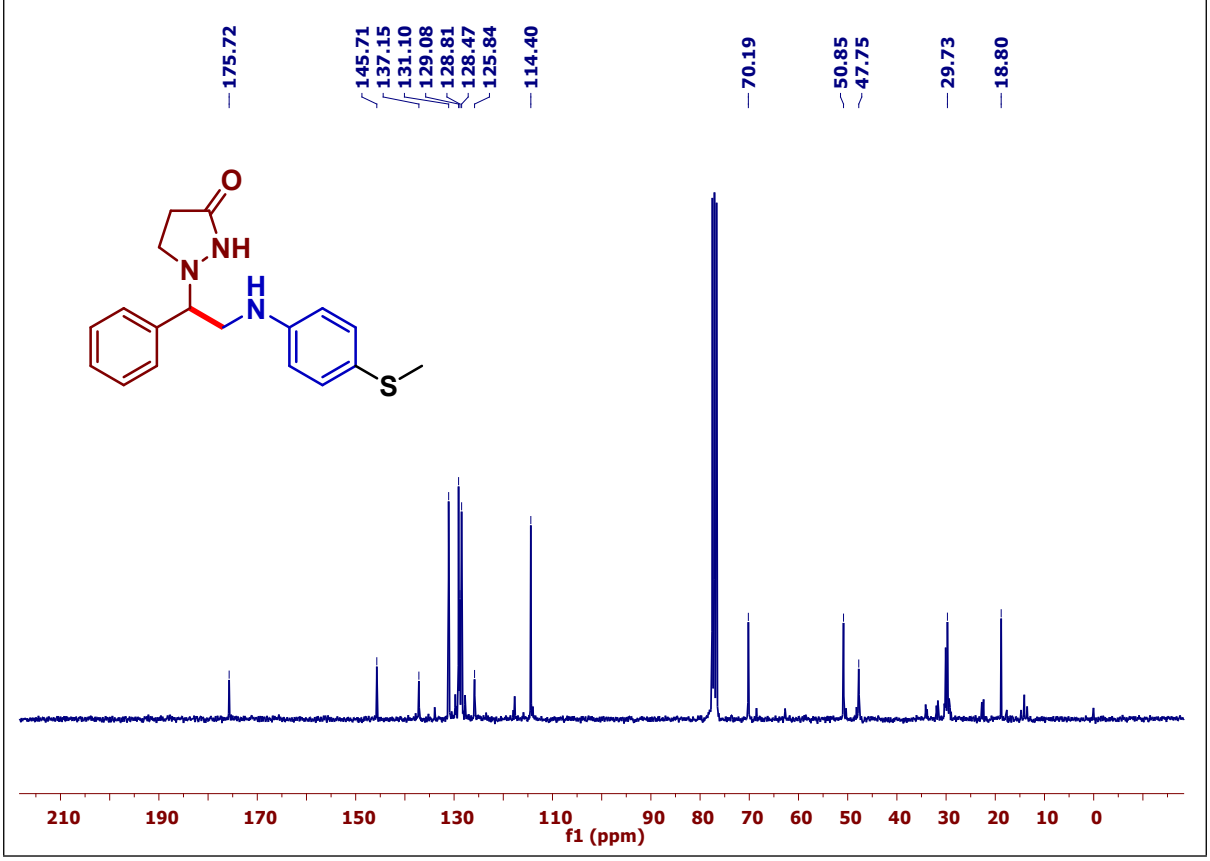
^{13}C NMR (75 MHz, $CDCl_3$) of 3k



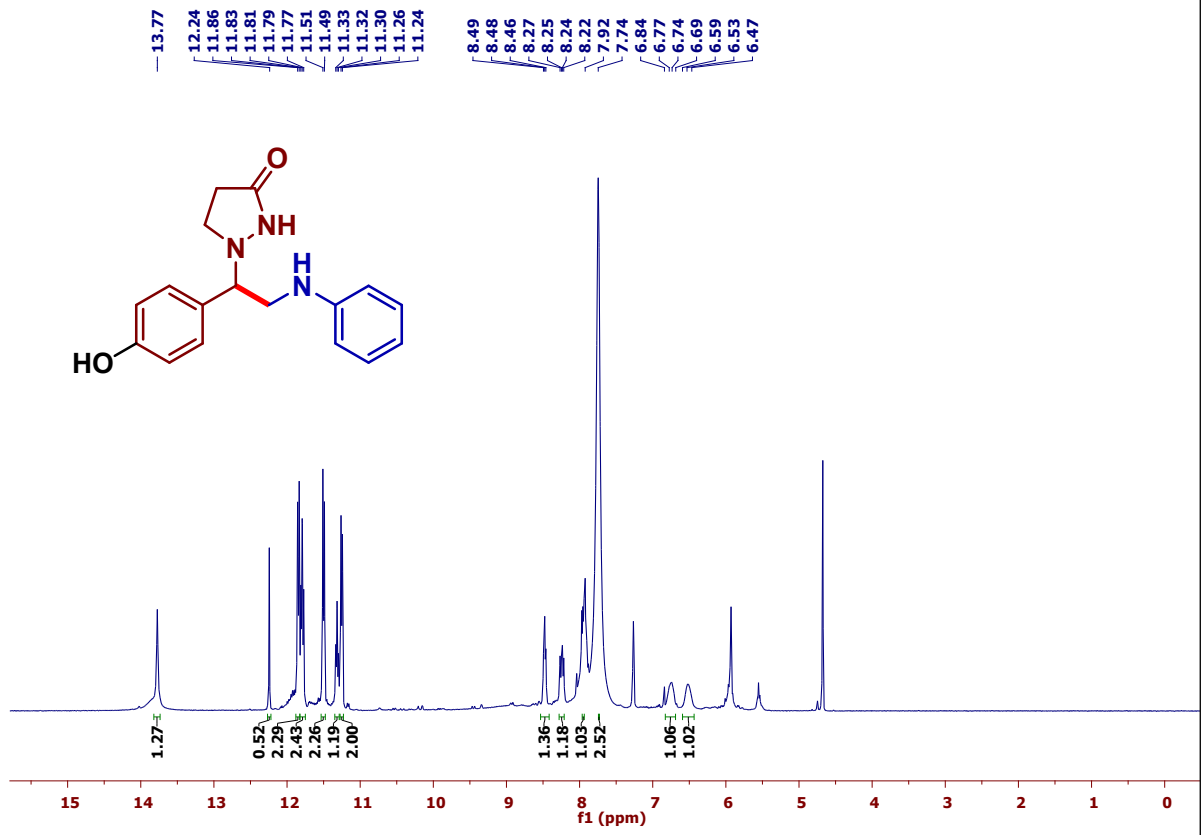
^{1}H NMR (400 MHz, $CDCl_3$) of 3l



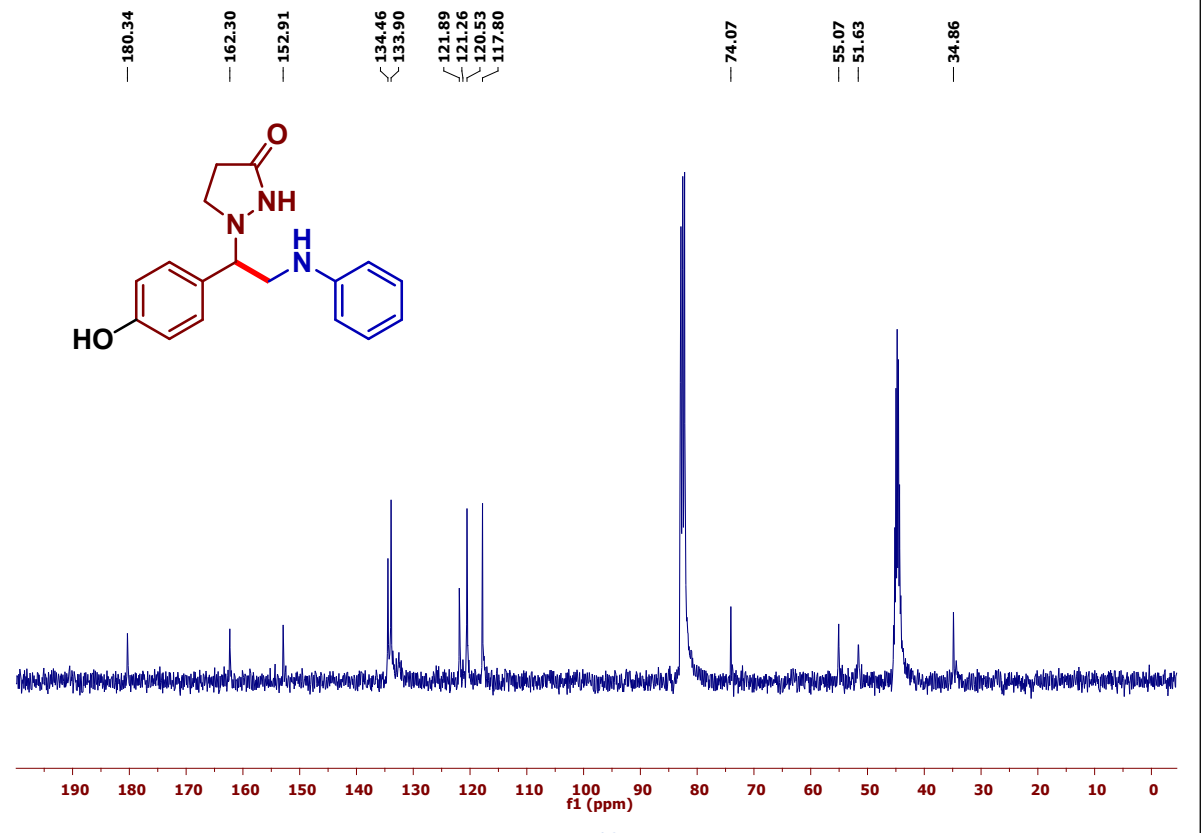
^{13}C NMR (75 MHz, $CDCl_3$) of 3l



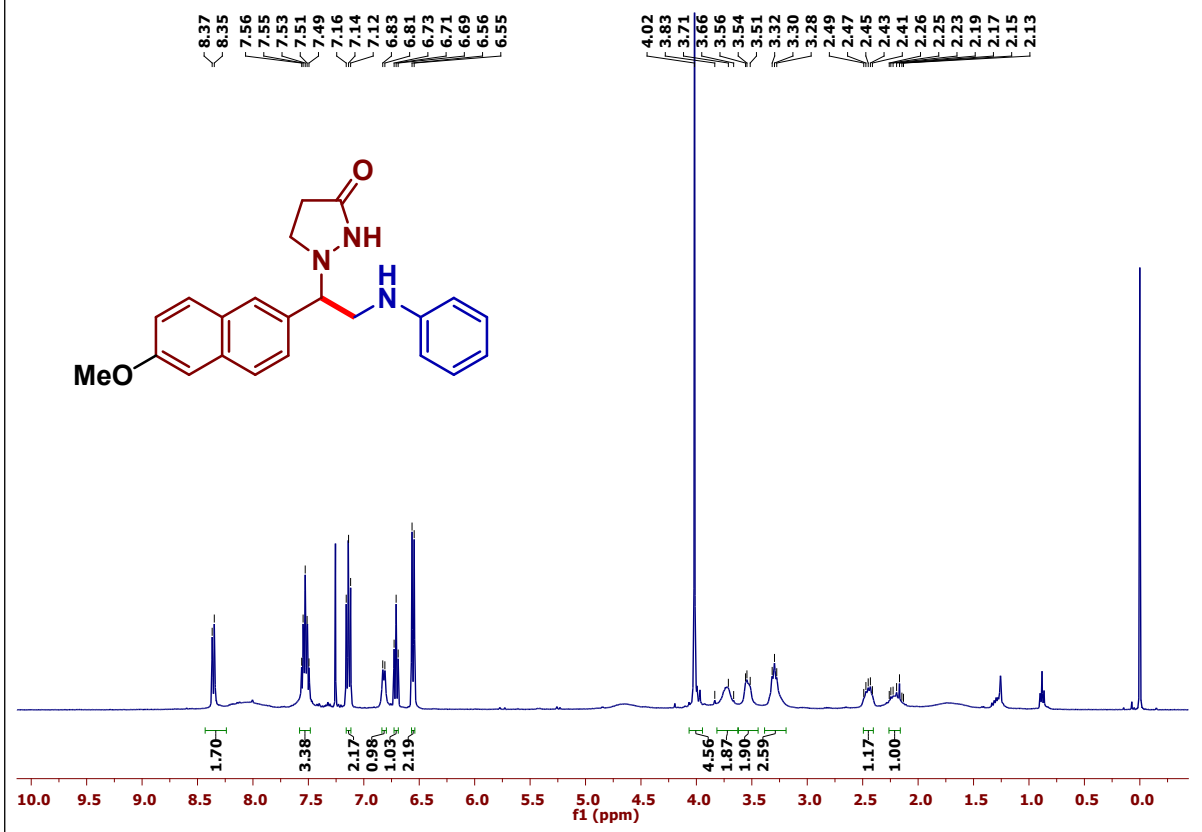
^{1}H NMR (400 MHz, $CDCl_3$) of 3m



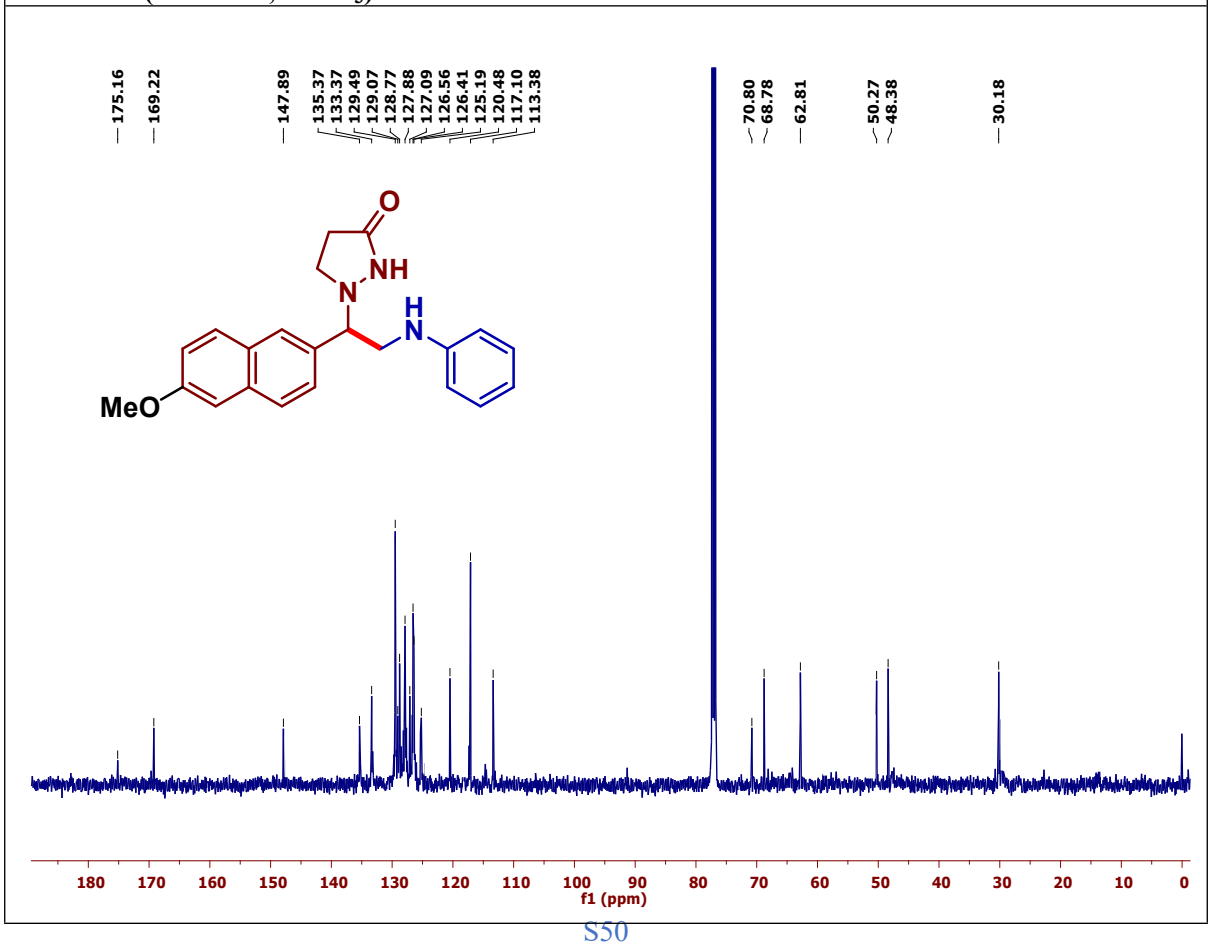
^{13}C NMR (101 MHz, $CDCl_3$) of 3m



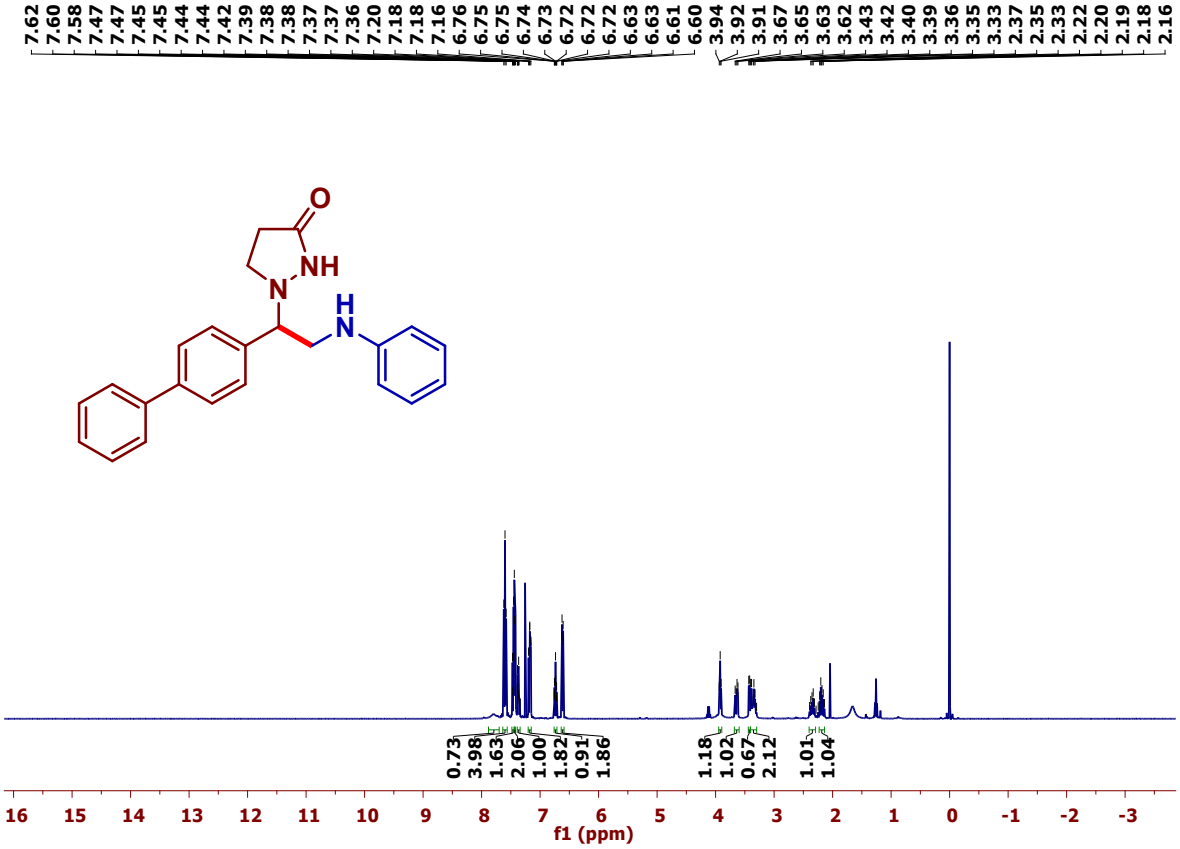
^{1}H NMR (400 MHz, $CDCl_3$) of 3n



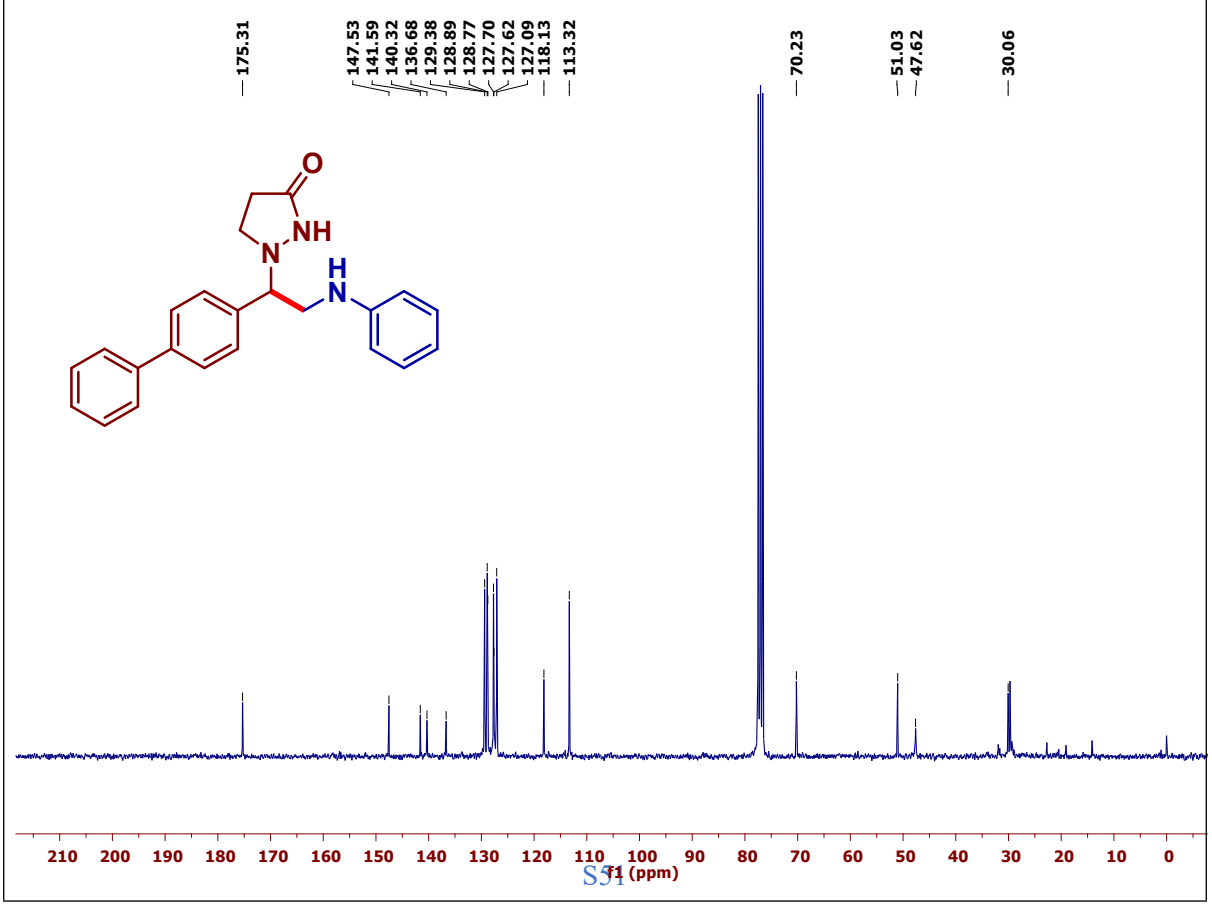
^{13}C NMR (126 MHz, $CDCl_3$) of 3n



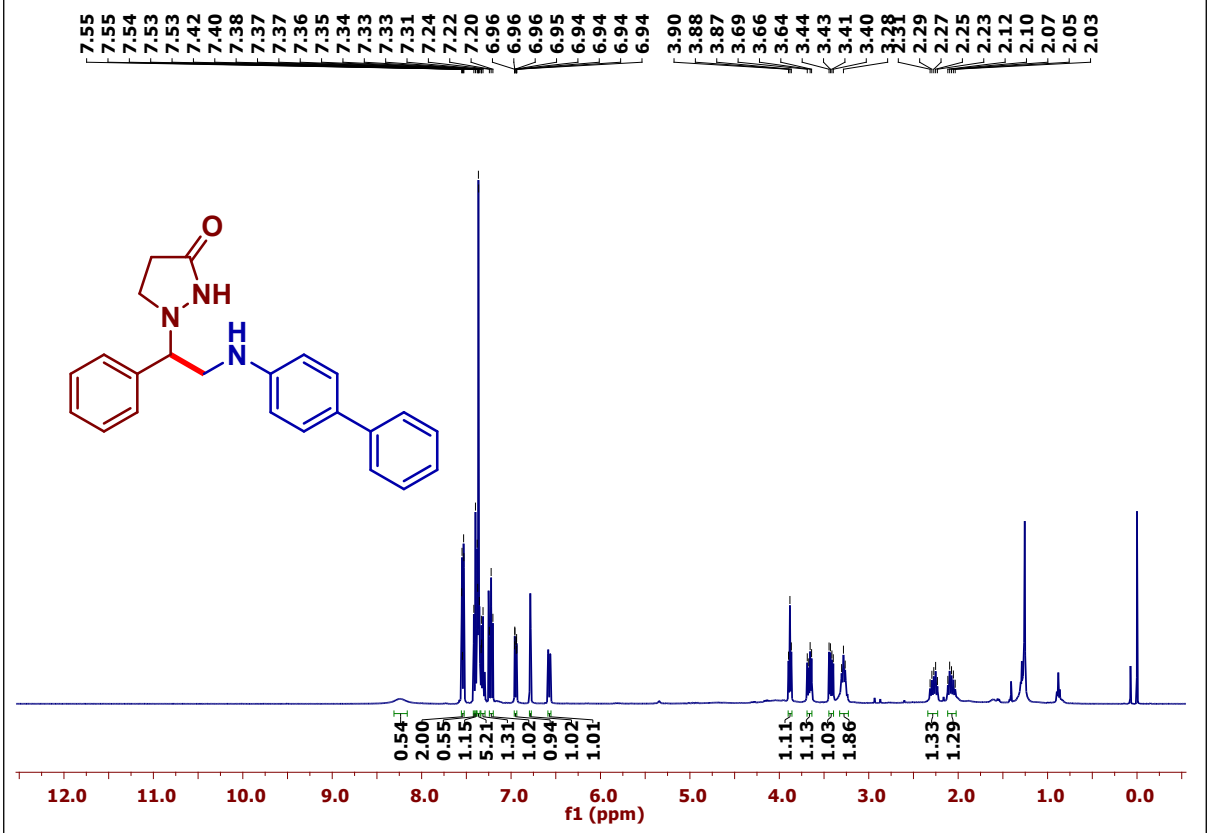
^{13}C NMR (75 MHz, $CDCl_3$) of 3o



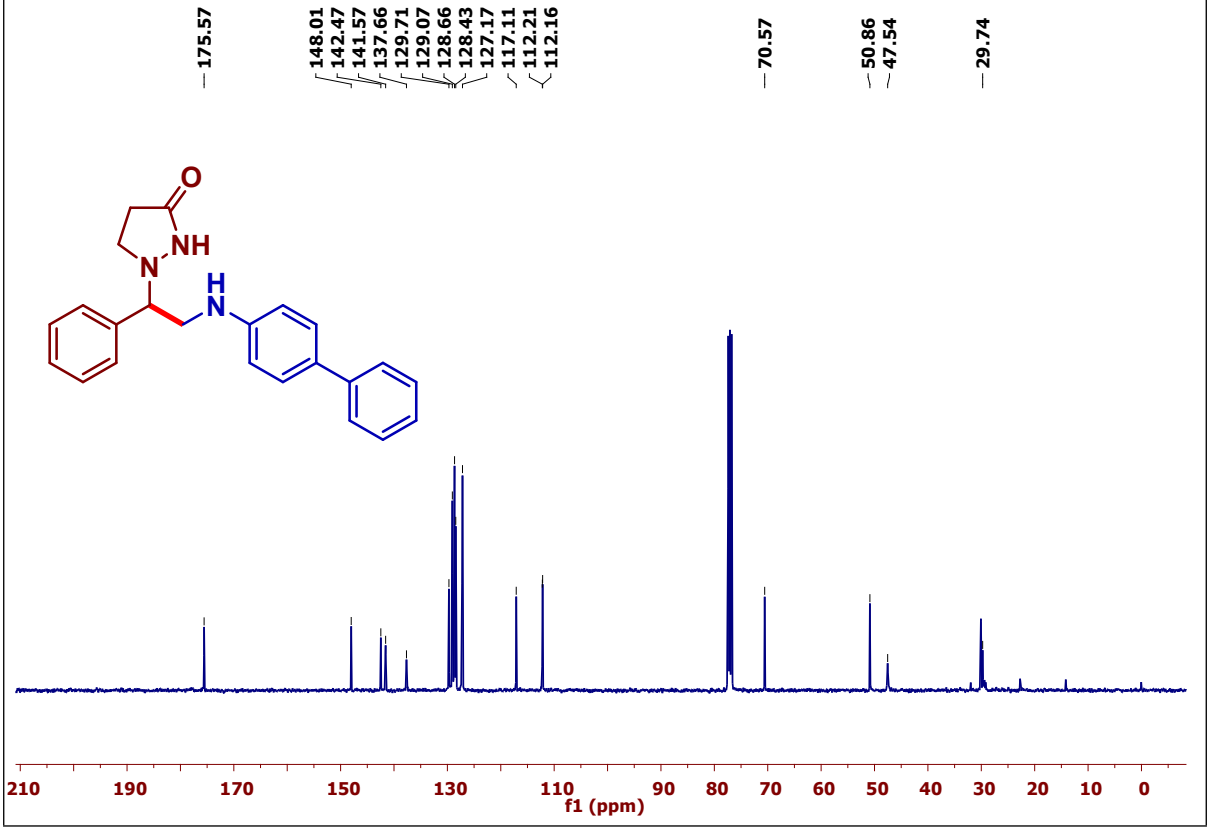
^{13}C NMR (75 MHz, $CDCl_3$) of 3o



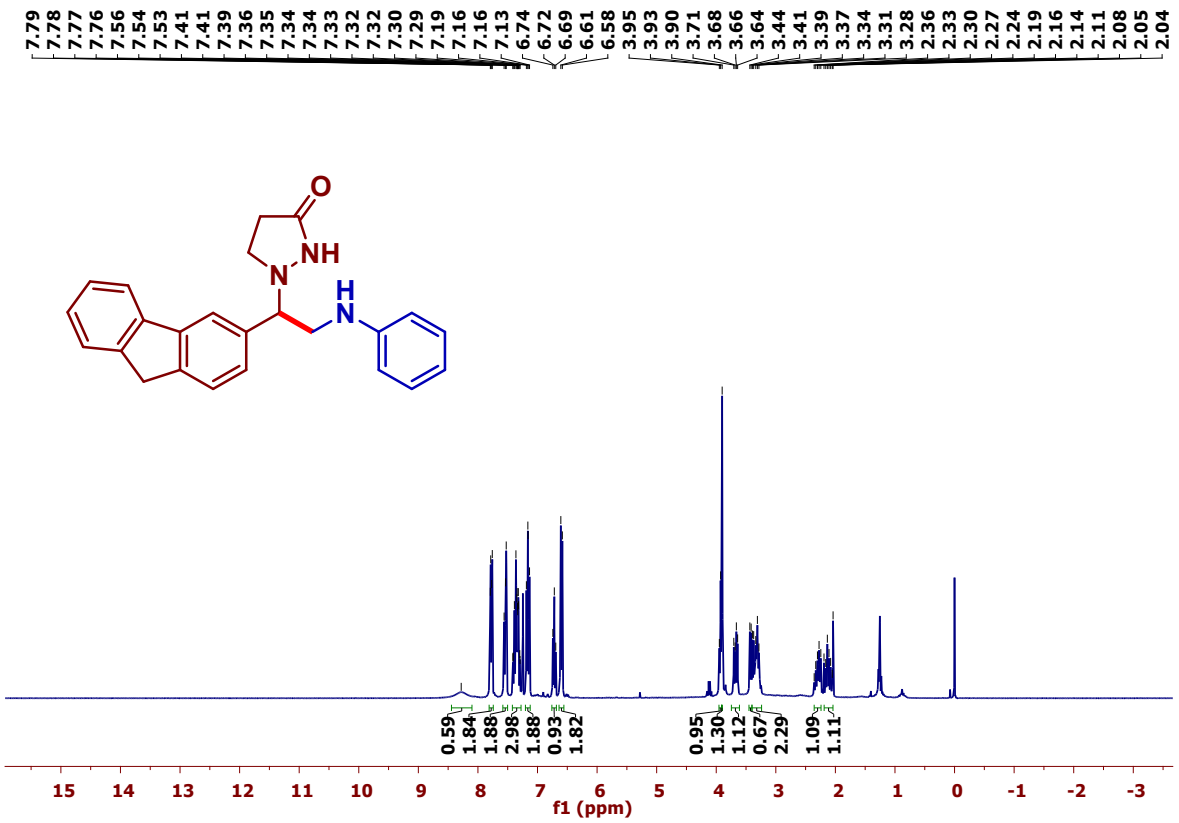
^{1}H NMR (400 MHz, $CDCl_3$) of 3p



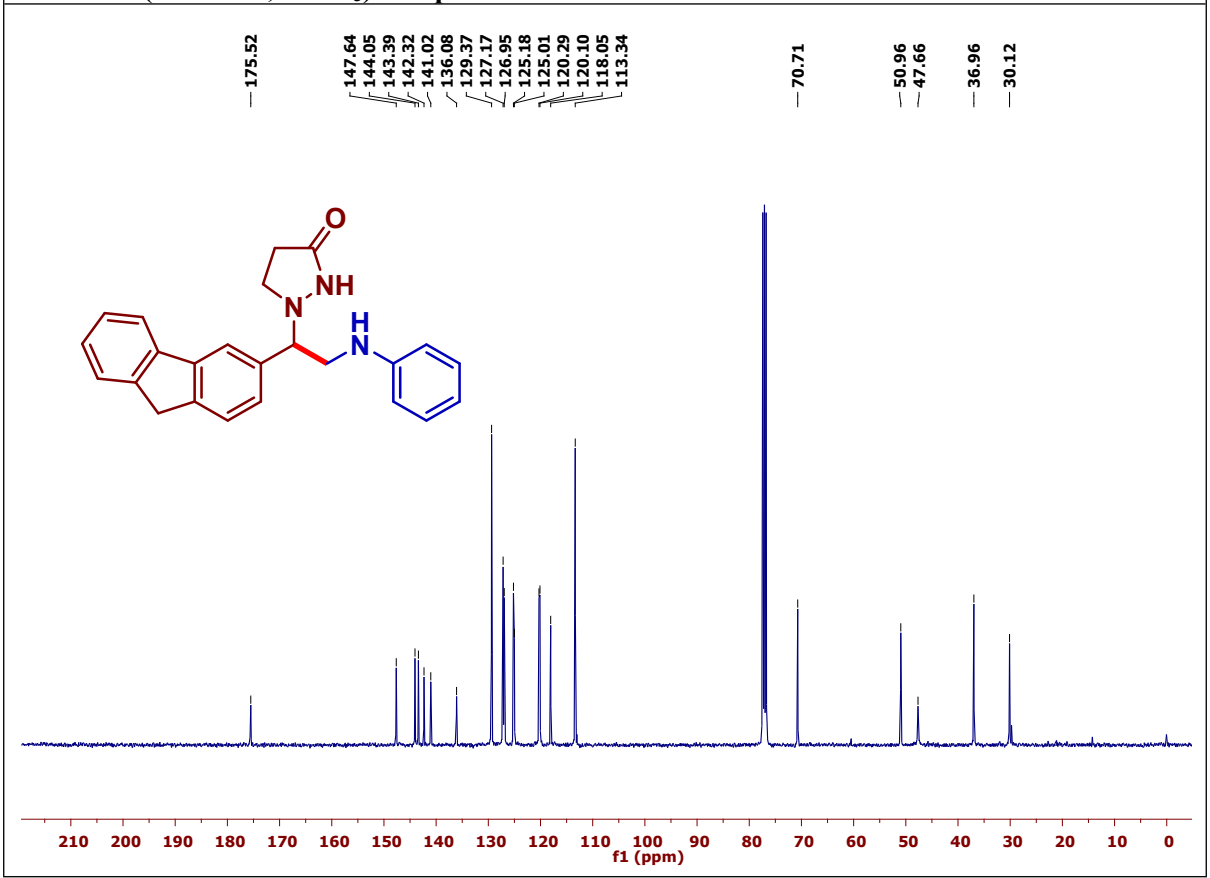
^{13}C NMR (101 MHz, $CDCl_3$) of 3p



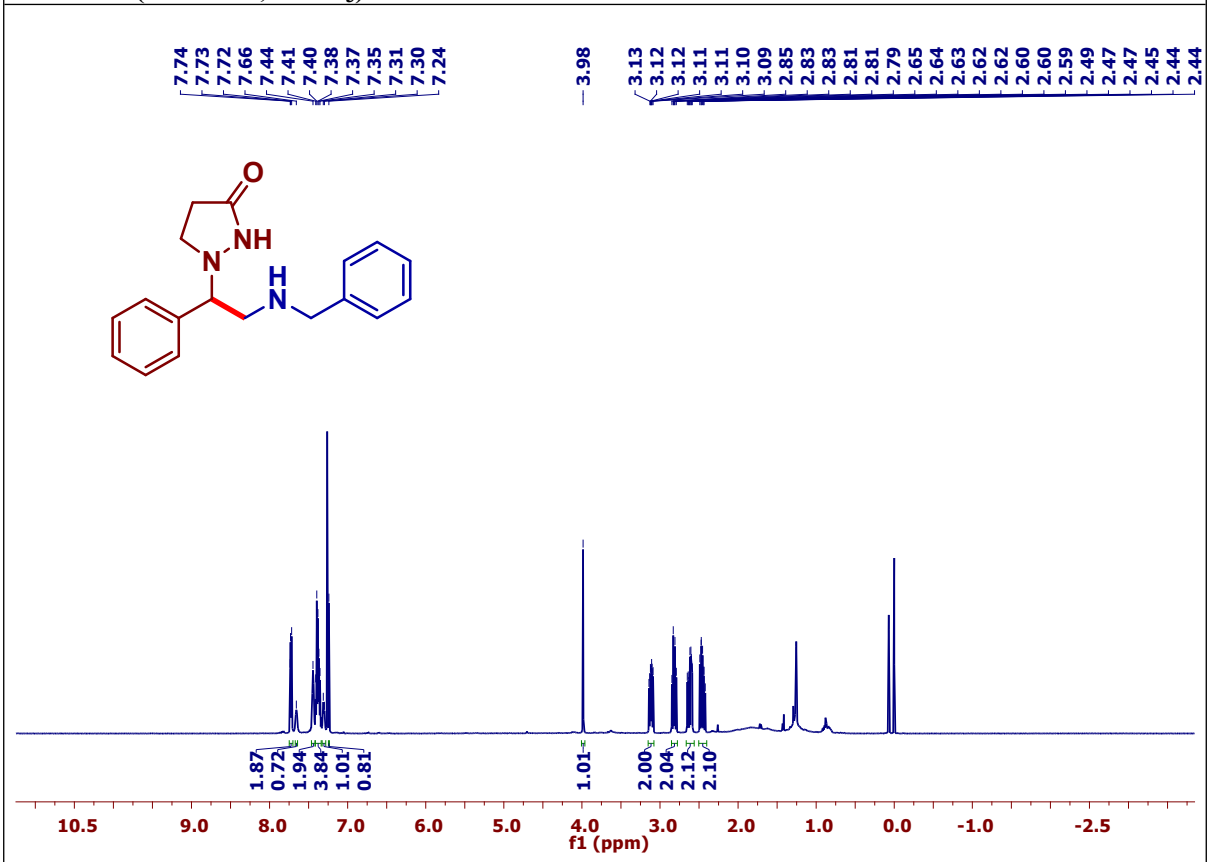
^{1}H NMR (300 MHz, $CDCl_3$) of 3q



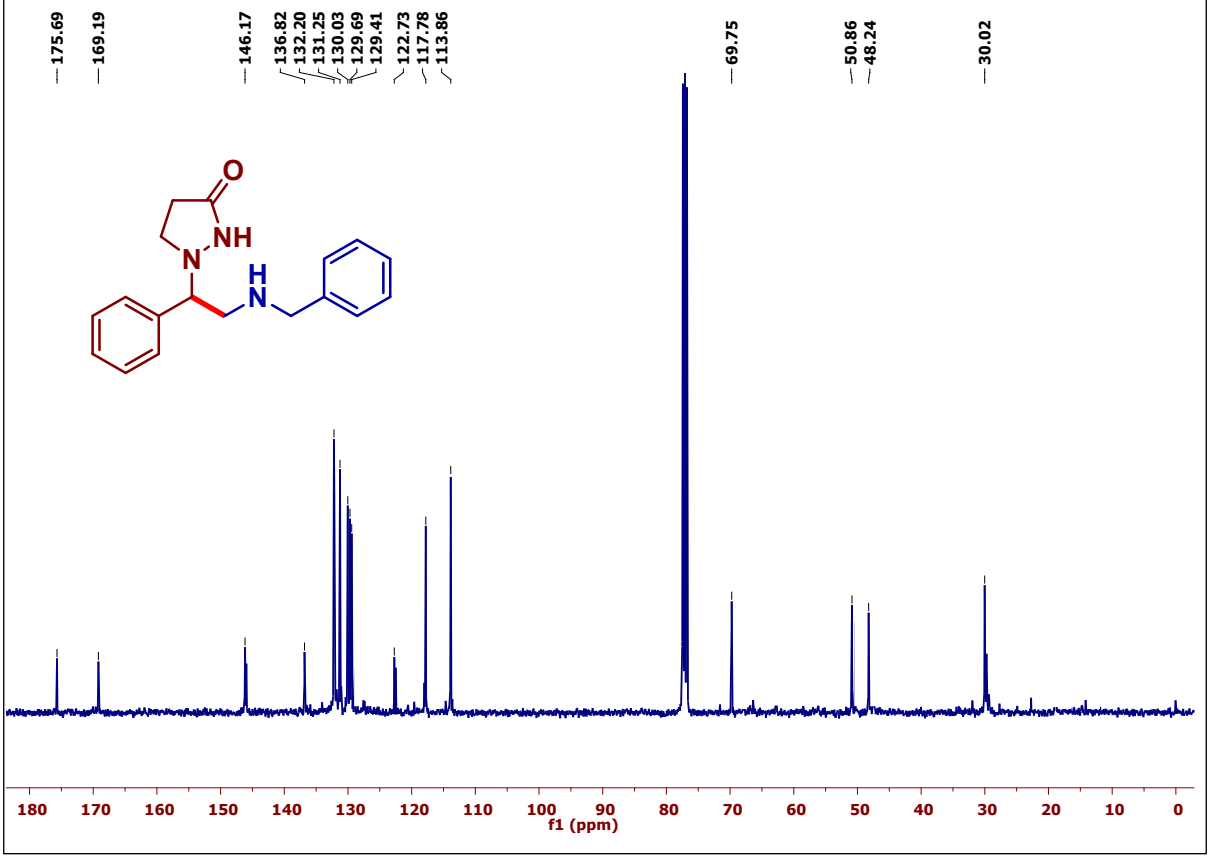
^{13}C NMR (101 MHz, $CDCl_3$) of 3q



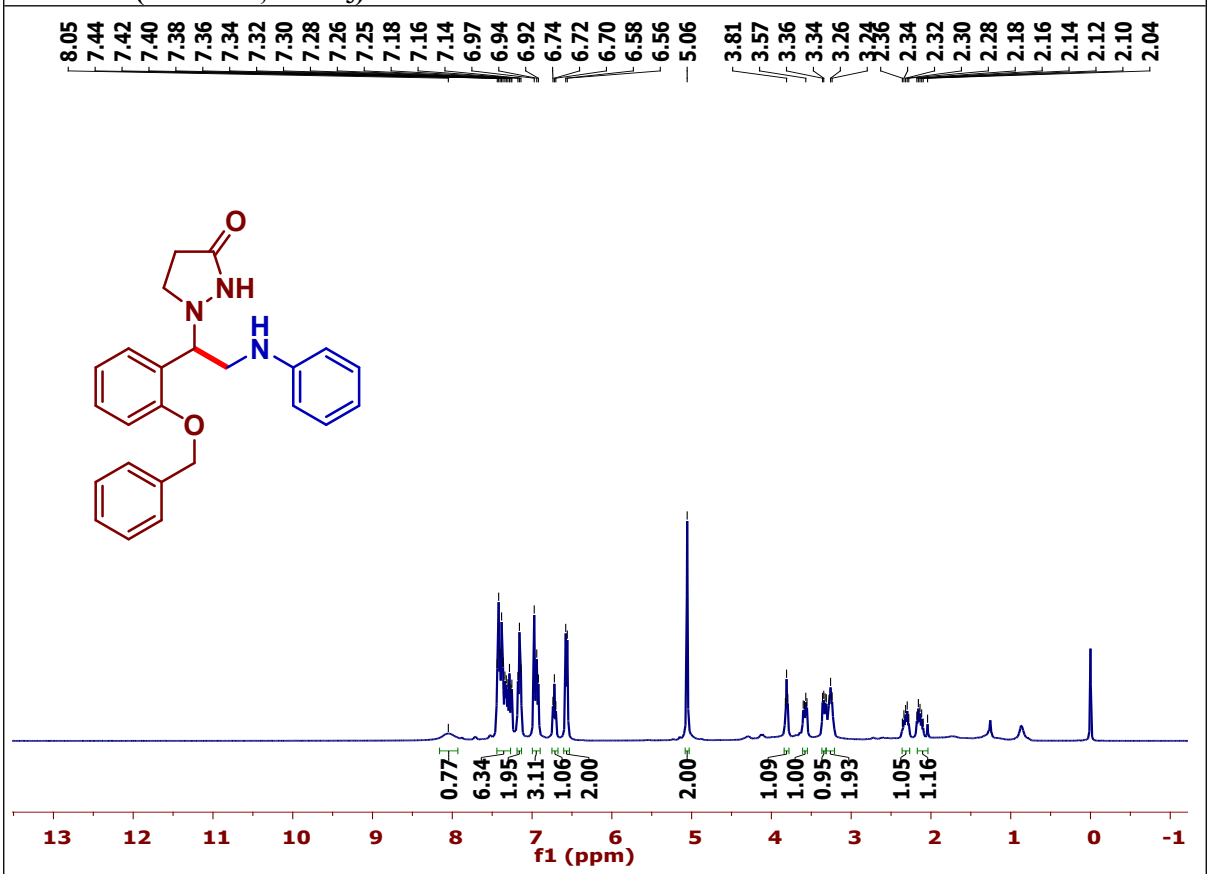
^{1}H NMR (500 MHz, $CDCl_3$) of 3r



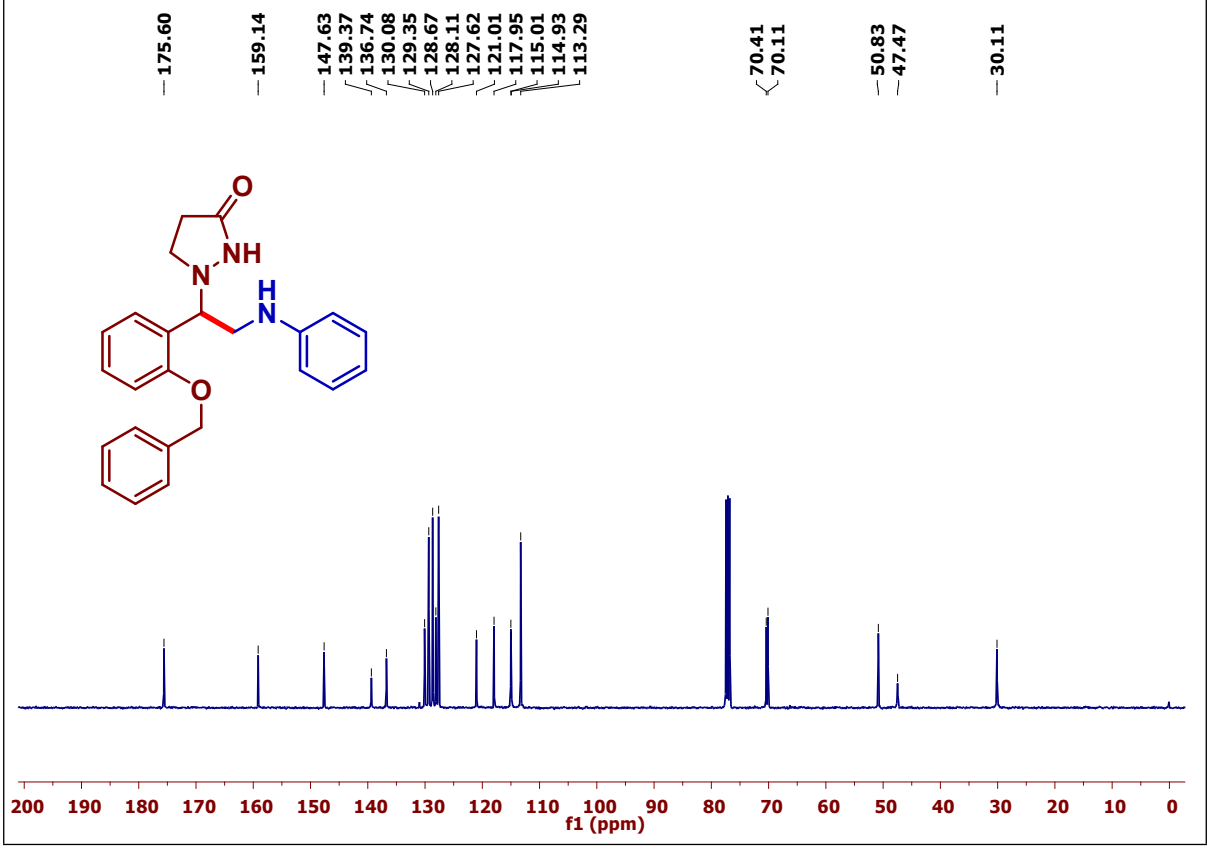
^{13}C NMR (101 MHz, $CDCl_3$) of 3r



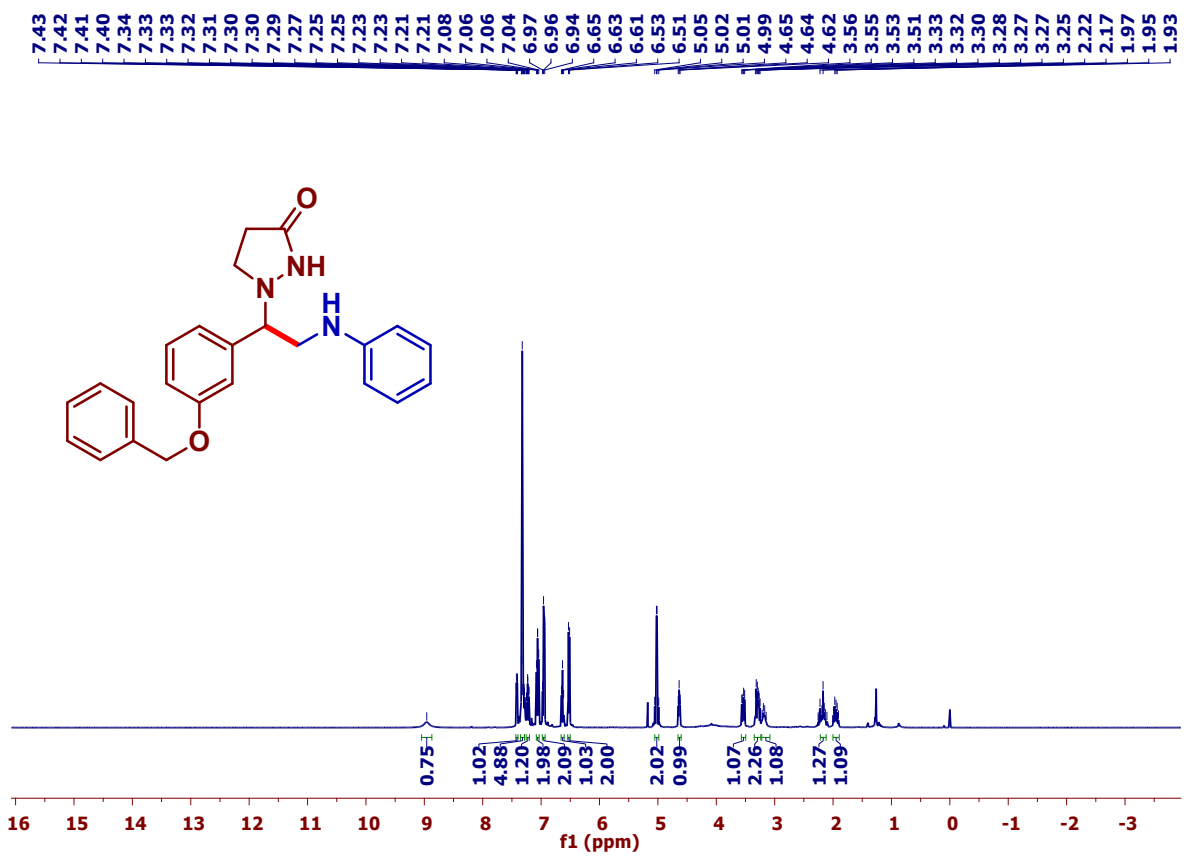
^{1}H NMR (400 MHz, $CDCl_3$) of 3s



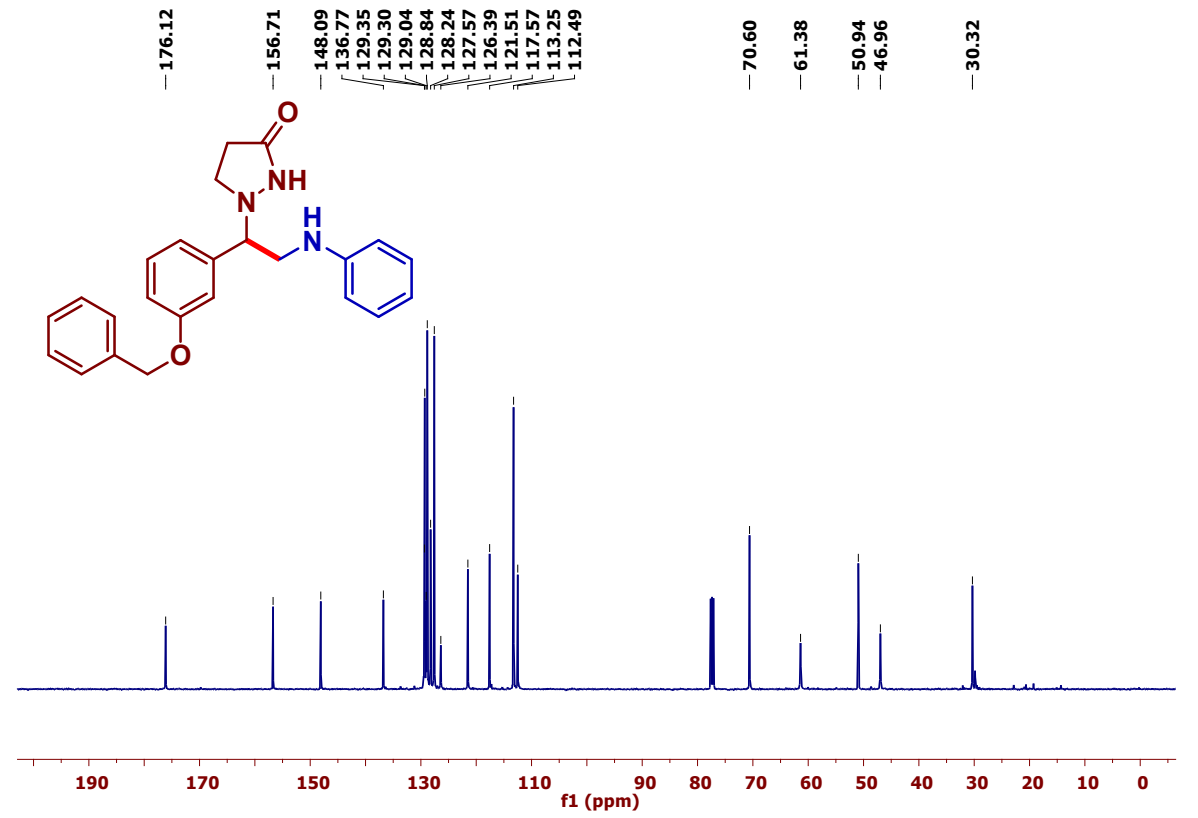
^{13}C NMR (101 MHz, $CDCl_3$) of 3s



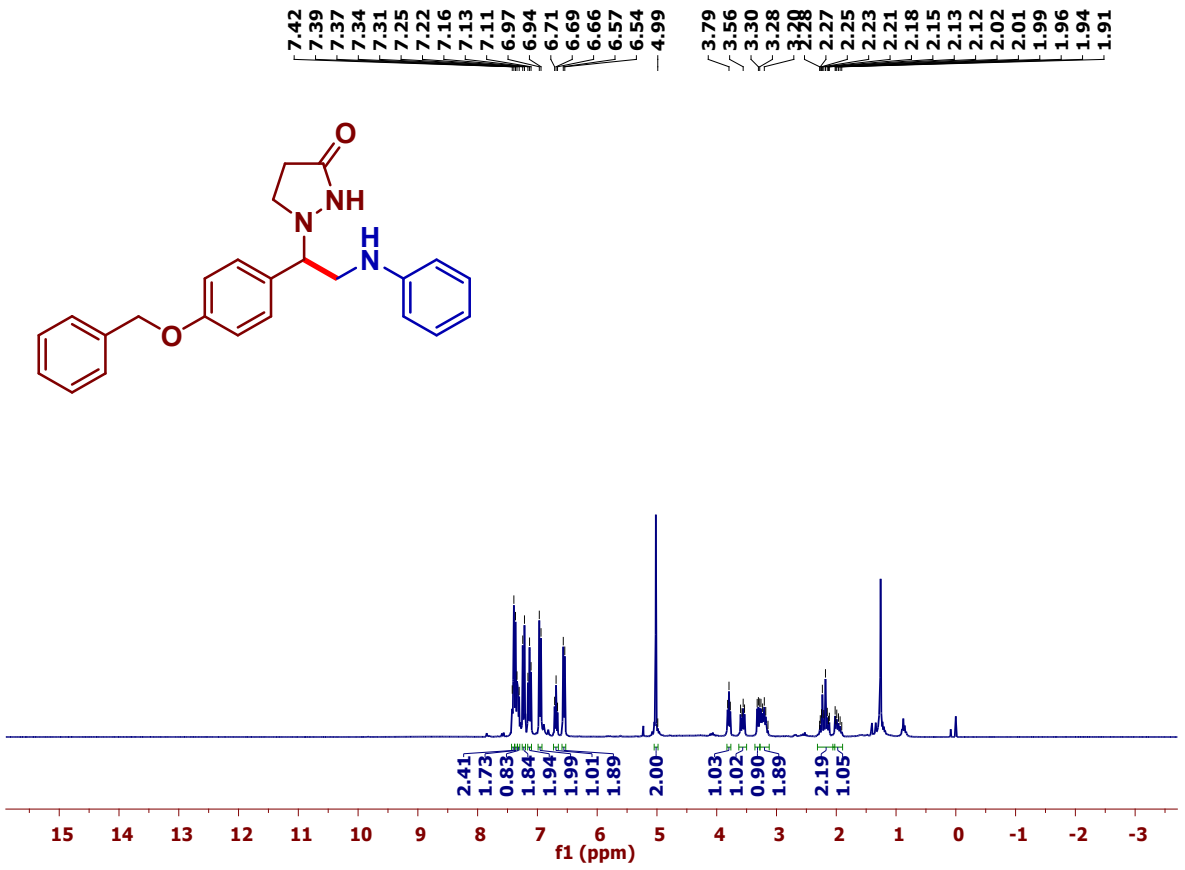
^{1}H NMR (300 MHz, $CDCl_3$) of 3t



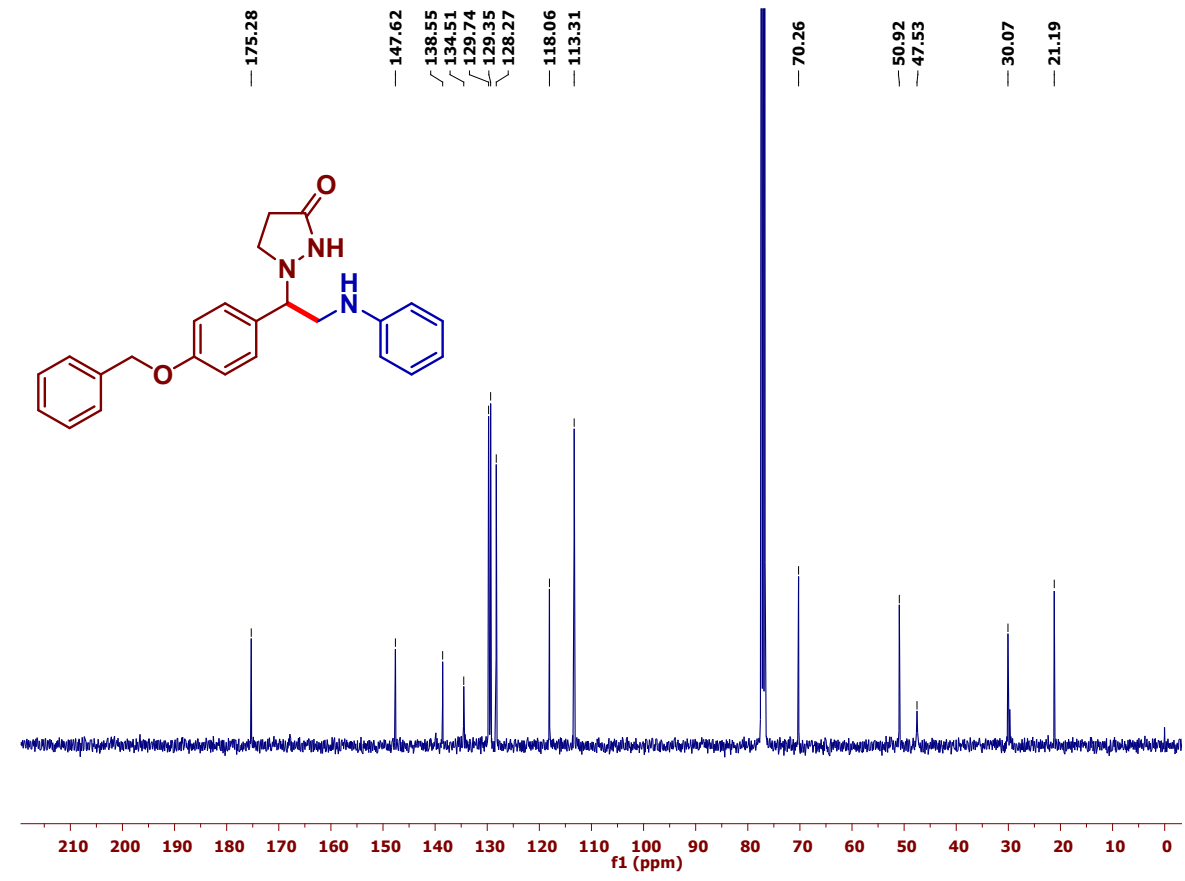
^{13}C NMR (101 MHz, $CDCl_3$) of 3t



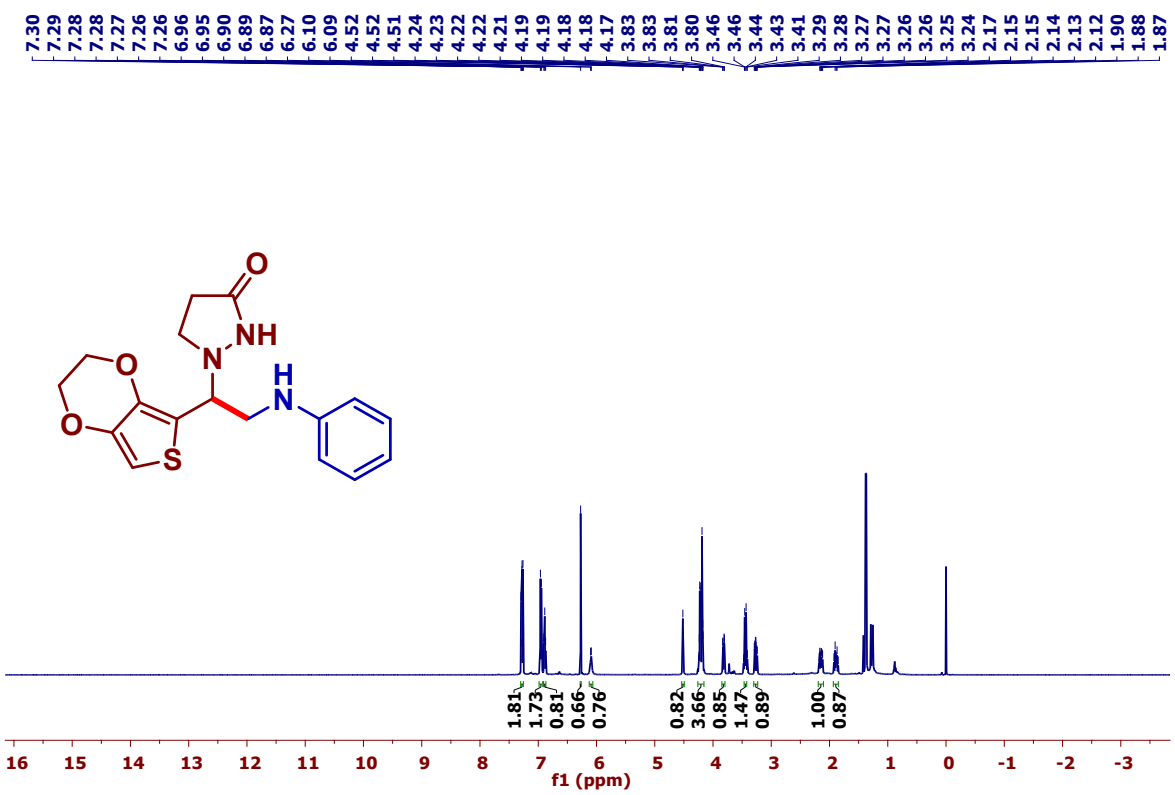
^{1}H NMR (300 MHz, $CDCl_3$) of 3u



^{13}C NMR (101 MHz, $CDCl_3$) of 3u



^{1}H NMR (500 MHz, $CDCl_3$) of 3v



^{13}C NMR (75 MHz, $CDCl_3$) of 3v