Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Tandem Copper (Cu) Catalyzed *N*-Arylation–Vinylogous Nitroaldol Condensation of 3,5-Disubstituted 4-Nitropyrazoles

Owk Obulesu,[a,b] Jagadeesh Babu Nanubolu,[c] and Surisetti Suresh[a,b]*

[a.] *Organic and Biomolecular Chemistry Division, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, 500007, India. E-mail: surisetti@iict.res.in*

[b.] *Academy of Scientific and Innovative Research (AcSIR), CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, 500007, India.*

[c.] *Center for X-ray Crystallography, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, 500007, India.*

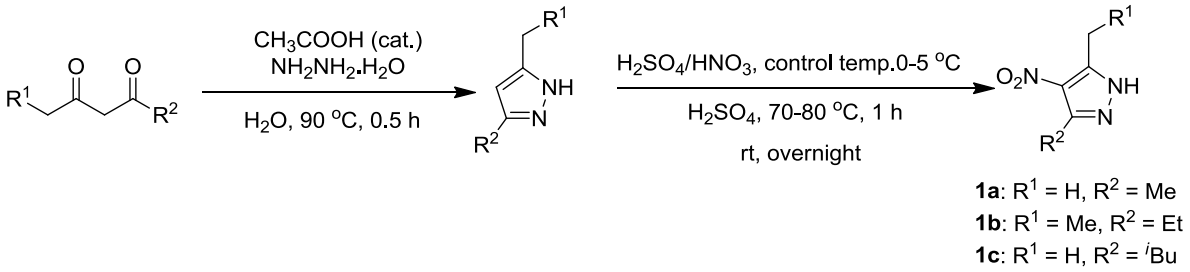
Contents:

1. General

Reactions were carried out in oven dried reaction flasks or screw-cap vials. Solvents and reagents were transferred by oven-dried syringes at ambient temperature. Analytical thin layer chromatography (TLC) was performed on Merck glass or aluminium sheets pre-coated with silica gel 60 F_{254} by using UV as a visualizing agent (or) a 0.5% aqueous potassium permanganate solution—heat (or) iodine as developing agents. Solvents were removed under reduced pressure. Column chromatography was performed using silica gel (60-120 or 100-200 or 230-400 mesh). The elution was assisted by applying pressure with an air pump. Melting points reported in this work are uncorrected and were determined using a Superfit capillary point apparatus. The IR spectra were recorded on a Bruker FT-IR spectrophotometer by dissolving the sample in chloroform. IR (KBr) spectra were recorded on a Thermo Nicolet NEXUS 670 FT-IR instrument. ^{1}HNMR spectra were recorded on 300 and 500 MHz spectrometers in appropriate solvents and chemical shifts are referenced to TMS via residual solvent signals. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. ^{13}C NMR spectra were recorded on 75 and 125 MHz spectrometers. The mass spectral analyses were carried out using Electrospray Ionization (ESI) techniques. Mass spectra were obtained on a Shimadzu LCMS-2020 mass spectrometer and high resolution mass spectra (HRMS) were recorded on a Thermo Scientific Exactive™ Orbitrap Mass Spectrometer or QSTAR XL Hybrid MS/MS mass spectrometer. X-ray data for compounds **3a** and **5a** were collected at room temperature using the Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method. All reactions were performed using freshly distilled and dried solvents wherever it was necessary. All solvents were distilled using standard procedures. Unless otherwise noted, starting materials, catalysts, ligands and reagents were obtained from commercial suppliers (Aldrich, Alfa Aesar, and TCI) and those were used without further purification.

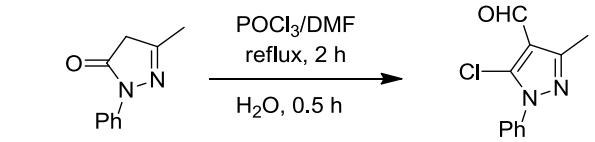
2. Synthesis of pyrazoles 1a-c and *ortho*-halo heteroaryl aldehydes 4a-d

3,5-Dialkyl 4-nitropyrazoles: Pyrazoles **1a-c** were prepared by following literature reports.[1]



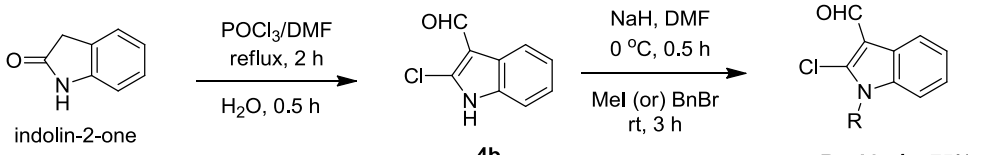
1a: R^1 = H, R^2 = Me
1b: R^1 = Me, R^2 = Et
1c: R^1 = H, R^2 = ^{i}Bu

***ortho*-Halo heteroaryl aldehydes 4a-d**: 5-Chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde **4d** was prepared according to the reported procedure.[2] 2-Chloro-1*H*-indole-3-carbaldehyde **4b** was prepared using the same procedure as for **4d** except indolin-2-one was used instead of 3-methyl-1-phenyl-1H- pyrazol-5(4*H*)-one. The compound **4b** was subjected to alkylation using MeI and BnBr in order to obtain *ortho*-halo heteroaryl aldehydes **4a** and **4c**, respectively.



3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one

4d
78%



indolin-2-one

4b
74%

R = Me **4a**, 75%
R = Bn, **4c**, 67%

References:

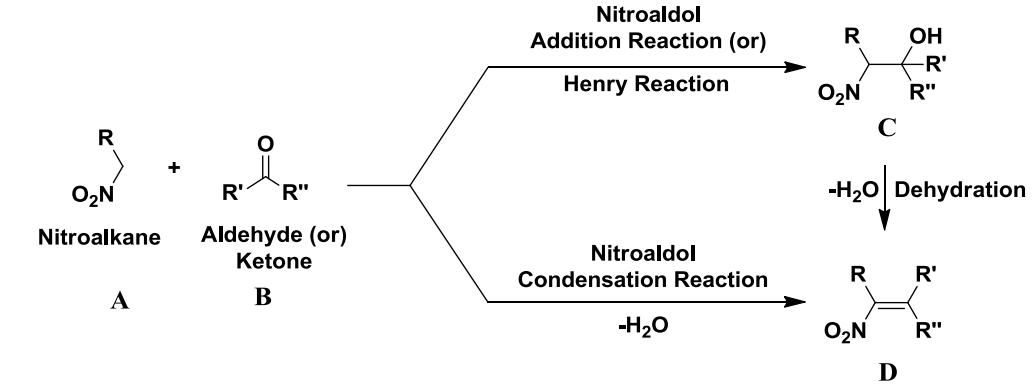
1. S. M Hecht and U. Jordis, US Patent 4282361, 1981.

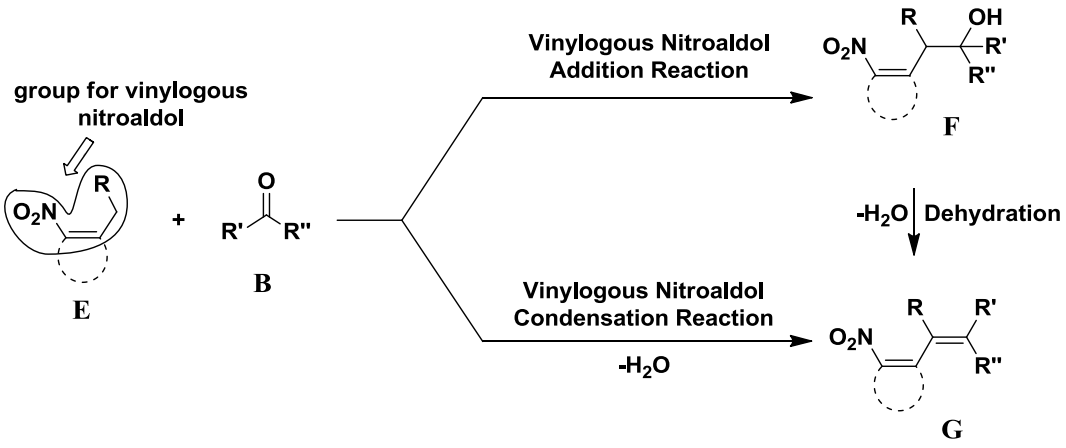
2. B. Datterl, N. Tröstner, D. Kucharski and W. Holzer, *Molecules,* 2010, **15**, 6106.

3. The Vinylogous Nitroaldol Condensation

Nitroaldol addition reaction is essentially the addition of nitroalkanes bearing α-hydrogen(s) **A** to aldehydes or ketones **B** to give the corresponding β-nitroalcohols **C**. Nitroaldol condensation[3,4] reaction is the reaction of nitroalkanes bearing α-hydrogens **A** and aldehydes or ketones **B** to give the corresponding β-nitroalkenes **D** by the elimination of water.

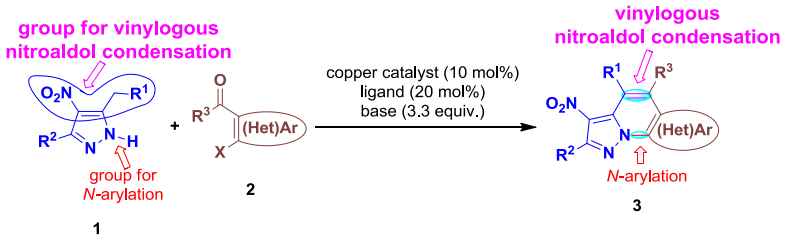
The vinylogous nitroaldol[5] condensation reaction is the reaction of nitroalkenes **E**, bearing a γ-methyl or methylene group, and aldehydes or ketones **B** to give the corresponding condensation products **G** by the elimination of water.





The present work:

In the present work, we have demonstrated a new tandem process involving copper catalysed *N*-arylation—***vinylogous nitroaldol condensation*** between 3,5-dialkylsubstituted 4-nitropyrazoles **1** and *ortho*-halo substituted (hetero)aryl aldehydes or ketones **2**. In this tandem process, the *vinylogous nitroaldol condensation* takes place between 5-methyl (or methylene group), which is activated by the conjugation of 4-nitro group, of **1** and aldehyde or ketone group of **2** (see Scheme below).



References:

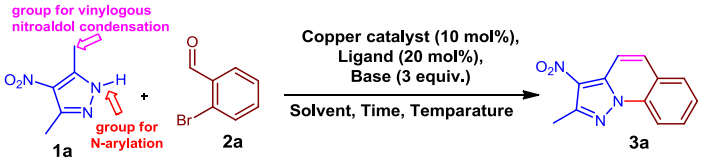
3. According to IUPAC condensation reactions is defined as "*a (usually stepwise) reaction in which two or more reactants (or remote reactive sites within the same molecular entity) yield a single main product with accompanying formation of water or of some other small molecule, e.g. ammonia, ethanol, acetic acid, hydrogen sulfide.*" *IUPAC. Compendium of Chemical Terminology*, 2nd ed. (the "Gold Book"). Compiled by A. D. McNaught and A. Wilkinson. Blackwell Scientific Publications, Oxford (1997). XML on-line corrected version: http://goldbook.iupac.org (2006-) created by M. Nic, J. Jirat, B. Kosata; updates compiled by A. Jenkins. ISBN 0-9678550-9-8. doi:10.1351/goldbook.

4. Articles on nitroaldol condensation: (a) S. Huh, H.-T. Chen, J. W. Wiench, M. Pruski and V. S.-Y. Lin, *J. Am. Chem. Soc.,* 2004, **126**, 1010; (b) A. Anan, K. K. Sharma and T. Asefa, *J. Mol. Catal. A, 2008,* **288**, 1; (c) T. M. Suzuki, T. Nakamura, K. Fukumoto, M. Yamamoto, Y. Akimoto and K. Yano, *J. Mol. Catal. A, 2008,* **280**, 224; (d) R. Ballini, M. Noè, A. Perosa and M. Selva, *J. Org. Chem.,* 2008, **73**, 8520; (e) L. Karadeniz and S. T. Astley, *Res. Chem. Intermed.,* 2013, **39**, 3407.

5. For vinylogous nitroaldol addition reaction see: (a) M. F. A. Adamo and S. Suresh, *Tetrahedron,* 2009, **65**, 990; (b) T. C. Judd and R. M. Williams, *Org. Lett.,* 2002, **4**, 3711; (c) S. Murata, Y. Tsubone, R. Kawai, D. Eguchi and H. Tomioka, *J. Phys. Org. Chem.,* 2005, **18**, 9.

4. Optimization Survey

Optimization conditions for the tandem Cu catalysed *N*-arylation—vinylogous nitroaldol condensation process



Entry	Copper Catalyst	Ligand	Base	Solvent	Time (h)	Temp (°C)	Yield %[a]
1	CuI	Ethylenediamine	K_2CO_3	DMSO	48	120	40
2	CuI	*N,N′*-Dimethylethylenediamine	K_2CO_3	DMSO	48	120	37
3	CuI	*N,N,N′,N′*-tetramethyl-ethylenediamine	K_2CO_3	DMSO	48	120	48
4	CuI	*o*-Phenylenediamine	K_2CO_3	DMSO	48	120	9
5	CuI	*trans*-1,2-diaminocyclohexane	K_2CO_3	DMSO	48	120	Trace
6	CuI	*trans*-N^1,N^2-dibenzylcyclohexane-1,2-diamine	K_2CO_3	DMSO	48	120	54
7	CuI	(L)-Proline	K_2CO_3	DMSO	48	120	33
8	CuI	BINOL	K_2CO_3	DMSO	48	120	17
9	CuI	1,3-Bis(2,4,6-trimethyl-phenyl)imidazolium chloride	K_2CO_3	DMSO	48	120	21 (39)[b]
10	**CuI**	**Neocuproine**	**K_2CO_3**	**DMSO**	**48**	**120**	**91 (84)[c]**
11	CuI	1,10-Phenonthroline	K_2CO_3	DMSO	48	120	26
12	CuI	Neocuproine	K_2CO_3	DMSO	24	120	57
13	CuI	Neocuproine	K_2CO_3	DMSO	24	150	76
14	CuBr	Neocuproine	K_2CO_3	DMSO	48	120	18
15	$Cu(OAc)_2$	Neocuproine	K_2CO_3	DMSO	48	120	29
16	$CuCl_2$	Neocuproine	K_2CO_3	DMSO	48	120	8
17	$Cu(OTf)_2$	Neocuproine	K_2CO_3	DMSO	48	120	29
18	CuI	Neocuproine	Cs_2CO_3	DMSO	48	120	31
19	CuI	Neocuproine	Na_2CO_3	DMSO	48	120	45
20	CuI	Neocuproine	$NaHCO_3$	DMSO	48	120	85
21	CuI	Neocuproine	NaH	DMSO	48	120	8
22	CuI	Neocuproine	KOH	DMSO	48	120	Trace
23	CuI	Neocuproine	K_3PO_4	DMSO	48	120	22
24	CuI	Neocuproine	KO^tBu	DMSO	48	120	13
25	CuI	Neocuproine	K_2CO_3	DMF	48	120	53
26	CuI	Neocuproine	K_2CO_3	Toluene	48	120	19
27	CuI	Neocuproine	K_2CO_3	1,4-dioxane	48	120	17
28	CuI	Neocuproine	K_2CO_3	CH_3CN	48	120	44
29	CuI	Neocuproine	K_2CO_3	NMP	48	120	53
30	CuI	—	K_2CO_3	DMSO	48	120	23
31	-	—	K_2CO_3	DMSO	48	120	19
32	CuI	Neocuproine	—	DMSO	48	120	NR[d]

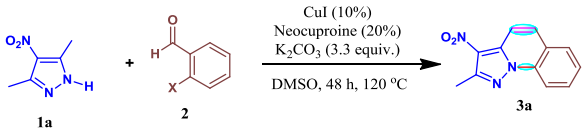
[a]Yields are for isolated products; Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), CuI (0.05 mmol), ligand (0.1 mmol), base (1.65 mmol), solvent (2 mL).

[b]Reaction was conducted in the presence of 40 mol% ligand;

[c]Reaction was carried out in gram scale (10 mmol with respect to 3,5-dimethyl-4-nitropyrazole **1a**)

[d]NR: no reaction

Scope of the 'X' Group in the Tandem Copper Catalyzed *N*-arylation–Vinylogous Nitroaldol Process



1a 2 3a

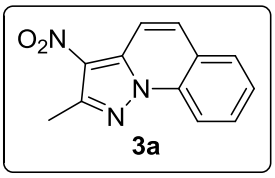
Entry	X in **2**	Yield of Product **3a**[a]
1	Br	91
2	Cl	17
3	I	49
4	OTs	trace
5	OTf	trace
6	$B(OH)_2$	—
7	BF_3K	—

[a]Yields are for isolated products; Reaction conditions: **1a** (0.5 mmol), **2** (0.5 mmol), CuI (0.05 mmol), neocuproine (0.1 mmol), K_2CO_3 (1.65 mmol), DMSO (2 mL).

5. General procedure for the synthesis of 3a-n

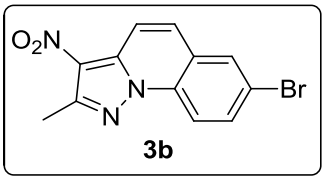
General procedure for the synthesis of pyrazolo[1,5-*a*]quinoline derivatives 3a-n:- 3,5-Dialkyl-4-nitro-1*H*-pyrazole **1a-c** (0.5 mmol), CuI (9.5 mg, 0.05 mmol), K_2CO_3 (227 mg, 1.65 mmol), neocuprione (21 mg, 0.1 mmol) and dimethyl sulfoxide (2 mL) were added into a 10 mL screw cap vial. The reaction mixture was stirred at room temperature for 30 min, followed by the addition of *o*-halo aryl aldehyde **2a-h** (0.5 mmol). The reaction mixture was stirred at 120 ^{o}C for 48 h. The reaction mixture was cooled to room temperature, diluted with water, extracted with ethyl acetate (2 x 20 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in vacuo to afford a crude residue. The residue was purified by flash column chromatography (hexane/EtOAc) on silica gel to obtain pyrazolo[1,5-*a*]quinoline derivatives **3a-n**.

6. Spectroscopic data of 3a-l



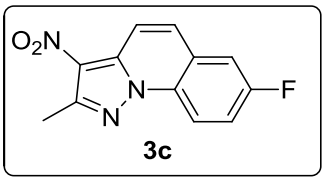
3a

2-Methyl-3-nitropyrazolo[1,5-*a*]quinoline 3a:- yellow solid, 103 mg, 91%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 192-194 ^{o}C; **IR** ($CHCl_3$) 742, 1214, 1431, 1515, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.85 (s, 3H), 7.60-7.63 (m, 1H), 7.81-7.84 (m, 1H), 7.90-7.94 (m, 2H), 8.26 (d, *J* = 9.5 Hz, 1H), 8.64 (d, *J* = 8.5 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.7, 115.6, 116.1, 123.9, 126.4, 128.7, 131.2, 131.3, 133.2, 133.4, 135.7, 149.9; **MS** (ESI) m/z 228 $[M+H]^+$ 250 $[M+Na]^+$; **HRMS** (ESI, m/z): calcd for $C_{12}H_{10}N_3O_2$ $[M+H]^+$ 228.07635, found 228.07675.



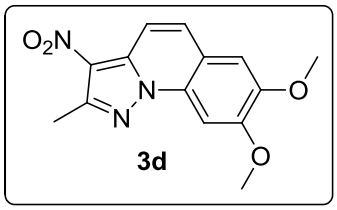
3b

7-Bromo-2-methyl-3-nitropyrazolo[1,5-*a*]quinoline 3b:- light green solid, 109 mg, 71%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 3:97); **MP** 220-222 ^{o}C; **IR** ($CHCl_3$) 668, 771, 1463, 1514, 2921, 3015 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.84 (s, 3H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.89-7.90 (dd,J_1 = 2.0 Hz, J_2 = 9 0 Hz, 1H), 8.06 (d, *J* = 2.0 Hz, 1H), 8.29 (d, *J* = 9.5 Hz, 1H), 8.52 (d, *J* = 9.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.6, 116.9, 117.9, 119.9, 125.2, 125.8, 129.9, 130.8, 132.2, 134.3, 135.5, 150.2; **MS** (ESI) m/z 305 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{12}H_9O_2N_3Br$ $[M+H]^+$ 305.9799, found 305.98784.



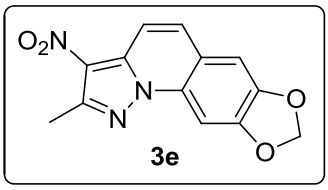
3c

7-Fluoro-2-methyl-3-nitropyrazolo[1,5-a]quinoline 3c:- yellow solid 29 mg, 24%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 180-182 ^{o}C; **IR** ($CHCl_3$) 742, 1214, 1531, 1693, 3019 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.84 (s, 3H), 7.54-7.61 (m, 2H), 7.86 (d, *J* = 9.0 Hz, 1H), 8.30 (d, *J* =9.0 Hz, 1H), 8.62-8.67 (m, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.6, 113.1, 113.2, 116.9, 118.4 (9.0 Hz), 120.0 (25.2 Hz), 125.0, 130.0, 130.3, 149.9; **MS** (ESI) m/z 246 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{12}H_9O_2N_3F$ $[M+H]^+$ 246.06757, found 246.06005.



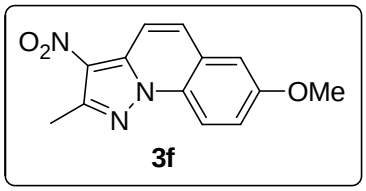
3d

7,8-Dimethoxy-2-methyl-3-nitropyrazolo[1,5-*a*]quinoline 3d:- yellow solid, 36 mg, 25%, R_f = 0.3 (EtOAc/hexane, 50:50) Column Chromatography (EtOAc/hexane, 25:75); **MP** 232-234 ^{o}C; **IR** ($CHCl_3$) 772, 1218, 1514, 2852, 2922 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.84 (s, 3H), 4.04 (s, 3H), 4.15 (s, 3H), 7.21 (s, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 8.02 (s, 1H), 8.16 (d, *J* = 9.3 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.7, 56.3, 56.7, 97.2, 107.6, 113.6, 118.4, 129.1, 130.3, 131.6, 135.2, 149.0, 150.0, 153.3; **MS** (ESI) m/z 288 **[**M+H]$^{+}$; **HRMS** (ESI, m/z): calcd for $C_{14}H_{14}O_4N_3$ [M+H]$^{+}$ 288.09061, found 288.09722.



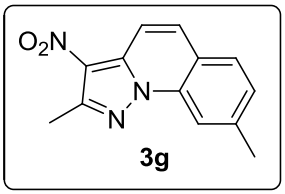
3e

2-Methyl-3-nitro-[1,3]dioxolo[4,5-*g*]pyrazolo[1,5-*a*]quinoline 3e:- yellow solid, 26 mg, 19%, R_f = 0.5 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 212-214 ^{o}C; **IR** ($CHCl_3$) 752, 1215, 1467, 1514, 2852, 2921 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.82 (s, 3H), 6.19 (s, 2H), 7.19 (s, 1H), 7.79 (d, *J* = 9.3 Hz, 1H), 8.03 (s, 1H), 8.14 (d, *J* = 9.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.7, 95.9, 102.5, 105.2, 113.6, 119.8, 130.6, 135.4, 147.4, 150.1, 151.6; **MS** (ESI) m/z 272 **[**M+H]$^{+}$; **HRMS** (ESI, m/z): calcd for $C_{13}H_{10}O_4N_3$ [M+H]$^{+}$ 272.05931, found 272.06648.



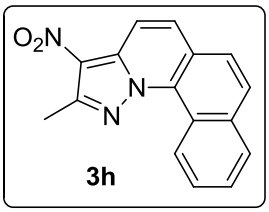
3f

7-Methoxy-2-methyl-3-nitropyrazolo[1,5-a]quinoline 3f:- yellow solid 23 mg, 18%, R_f = 0.3 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 198-200 ^{o}C; **IR** ($CHCl_3$) 741, 1215, 1420, 1516, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.82 (s, 3H), 3.96 (s, 3H), 7.23 (d, *J* = 2.5 Hz, 1H), 7.42 (dd, J_1 = 2.5 Hz, J_2 = 9.5 Hz, 1H), 7.84 (d, *J* = 9.5 Hz, 1H), 8.22 (d, *J* = 9.5 Hz, 1H), 8.52 (d, *J* = 9.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.6, 55.8, 108.5, 116.1, 117.6, 121.5, 125.2, 128.3, 130.7, 134.7, 149.7, 157.9; **MS** (ESI) m/z 258 [M+H]$^{+}$ **HRMS** (ESI, m/z): calcd for $C_{13}H_{12}O_3N_3$ [M+H]$^{+}$ 258.08732, found 258.08783.



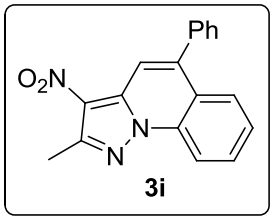
3g

2,8-Dimethyl-3-nitropyrazolo[1,5-*a*]quinoline 3g:- yellow solid, 59 mg, 49%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 198-200 ^oC; **IR** ($CHCl_3$) 772, 1219, 1499, 1510, 2852, 2922 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.63 (s, 3H), 2.83 (s, 3H), 7.42 (d, *J* =8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 8.17 (d, *J* =9.5 Hz, 1H), 8.42 (s, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.7, 22.2, 114.5, 115.6, 121.8, 128.1, 128.4, 131.2, 133.3, 135.8, 142.5, 149.8; **MS** (ESI) m/z 242 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{13}H_{12}O_2N_3$ $[M+H]^+$ 242.08513 found 242.09259.



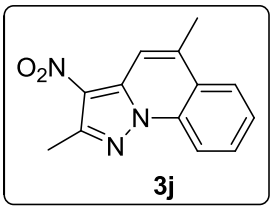
3h

2-Methyl-3-nitrobenzo[*h*]pyrazolo[1,5-*a*]quinoline 3h:- yellow solid, 62 mg, 45%, R_f = 0.5 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 222-224 ^oC; **IR** ($CHCl_3$) 772, 1218, 1511, 2852, 2921 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.98 (s, 3H), 7.80-7.90 (m, 3H), 7.98 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 8.53 (d, *J* = 9.0 Hz, 1H), 10.71 (d, *J* = 8.5 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.9, 115.7, 123.1, 124.0, 125.4, 127.7, 128.1, 128.3, 128.5, 128.6, 130.2, 131.8, 134.9, 137.7, 149.6; **MS** (ESI) m/z 278 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{16}H_{12}O_2N_3$ $[M+H]^+$ 278.09240, found 278.09254.



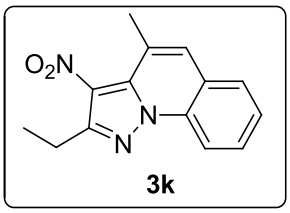
3i

2-Methyl-3-nitro-5-phenylpyrazolo[1,5-*a*]quinoline 3i:- white solid, 62 mg, 41%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 220-222 ^oC; **IR** ($CHCl_3$) 772, 1219, 1498, 1677 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.87(s, 3H), 7.53-7.58 (m, 6H), 7.81-7.85 (m, IH), 7.91 (d, *J* = 8.5 Hz, 1H), 8.22 (s, 1H), 8.73 (d, *J* = 8.5 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.8, 115.5, 116.3, 123.3, 126.2, 127.7, 128.8, 128.9, 129.6, 131.1, 133.5, 135.2, 137.4, 144.2, 150.1; **MS** (ESI) m/z 304 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{14}O_2N_3$ $[M+H]^+$ 304.10078, found 304.10847.



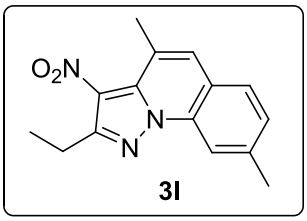
3j

2,5-Dimethyl-3-nitropyrazolo[1,5-*a*]quinoline 3j:- white solid, 43 mg, 36%, R_f = 0.7 (EtOAc/hexane, 0.5:9.5) Column Chromatography (EtOAc/hexane, 2:98); **MP** 208-210 ^{o}C; **IR** ($CHCl_3$) 772, 1219, 1515, 1709, 3019 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.77 (s, 3H), 2.82 (s, 3H), 7.61-7.64 (m, 1H), 7.79-7.85 (m, 1H), 8.01 (d, *J* = 8.1 Hz, 1H), 8.12 (s, 1H), 8.65 (d, *J* = 8.4 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.7, 19.6, 115.0, 116.3, 124.1, 124.8, 125.3, 126.2, 130.9, 132.9, 135.4, 139.8, 149.8; **MS** (ESI) m/z 242 $[M+H]^+$ **HRMS** (ESI, m/z): calcd for $C_{13}H_{12}O_2N_3$ $[M+H]^+$ 242.09240, found 242.09266.



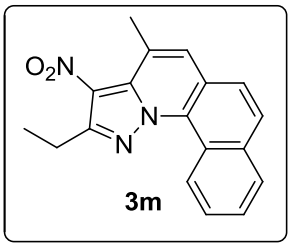
3k

2-Ethyl-4-methyl-3-nitropyrazolo[1,5-*a*]quinoline 3k:- yellow solid, 73 mg, 57%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 196-198 ^{o}C; **IR** ($CHCl_3$) 743, 1214, 1420, 1531, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.44 (t, *J* = 7.5 Hz, 3H), 2.76 (s, 3H), 3.17 (q, *J* = 7.5 Hz, 2H), 7.53-7.56 (m, 1H), 7.59 (s, 1H), 7.71.7.74 (m, 1H), 7.77 (d, *J* =8.0 Hz, 1H), 8.62 (d, *J* =8.5 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 12.4, 21.5, 21.9, 116.2, 123.6, 125.8, 126.2, 127.1, 127.5, 130.0, 130.5, 132.5, 134.9, 154.4; **MS** (ESI) m/z 256 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{14}H_{14}O_2N_3$ $[M+H]^+$ 256.10805 found, 256.10807.



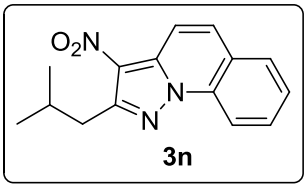
3l

2-Ethyl-4,8-dimethyl-3-nitropyrazolo[1,5-*a*]quinoline 3l:- yellow solid, 69 mg, 51%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 176-178 ^{o}C; **IR** ($CHCl_3$) 743, 1214, 1420, 1531, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.45 (t, *J* = 7.5 Hz 3H), 2.60 (s, 3H), 2.73 (s, 3H), 3.17 (q, *J* = 7.5 Hz, 2H), 7.35-7.37 (m, 1H), 7.54 (s, 1H), 7.65 (d, *J* =8.0 Hz, 1H), 8.42 (s, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 12.6, 21.4, 21.9, 22.1, 115.7, 121.5, 124.6, 127.3, 127.9, 130.5, 132.5, 135.1, 141.0, 154.4; **MS** (ESI) m/z 270 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{15}H_{16}O_2N_3$ $[M+H]^+$ 270.12374, found 270.12370.



3m

2-Ethyl-4-methyl-3-nitrobenzo[*h*]pyrazolo[1,5-*a*]quinoline 3m:- yellow solid, 64 mg, 42%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 228-230 ^{o}C; **IR** ($CHCl_3$) 753, 1411, 1645, 2824, 2946, 3329 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.58-1.60 (m, 3H), 2.83 (s, 3H), 3.31 (q, *J* = 7.5 Hz, 2H), 7.74-7.78 (m, 3H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 10.69 (d, *J* = 8.5 Hz, 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$) δ = 12.2, 21.2, 22.0, 122.6, 124.0, 124.7, 125.8, 127.5, 127.8, 127.9, 128.1, 128.6, 131.7, 134.5, 136.6, 153.7; **MS** (ESI) m/z 306 $[M+H]^+$ **HRMS** (ESI, m/z): calcd for $C_{18}H_{16}O_2N_3$ $[M+H]^+$ 306.12370, found 306.12278.



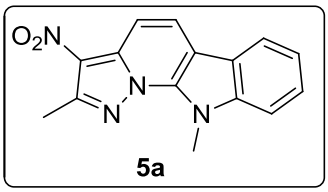
3n

2-Isobutyl-3-nitropyrazolo[1,5-a]quinoline 3n:- light yellow solid, 65 mg, 48%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 178-180 ^{o}C; **IR** ($CHCl_3$) 770, 1214, 2853, 2922, 3019 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 1.05 (d, *J* = 6.0 Hz, 6H), 2.25-2.34 (m, 1H), 3.13 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.89-7.94 (m, 2H), 8.28 (d, *J* = 9.3 Hz, 1H), 8.67 (d, *J* = 8.4 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ =22.6, 27.7, 36.8, 115.8, 116.2, 124.0, 126.4, 128.6, 131.2, 133.3, 152.8; **MS** (ESI) m/z 270 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{15}H_{16}O_2N_3$ $[M+H]^+$ 270.12370, found 270.12320.

7. General procedure for the synthesis of 5a-k

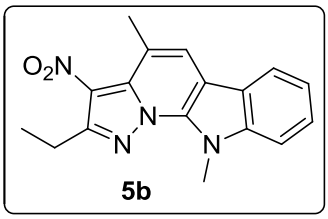
General procedure for the synthesis of heteroaryl-fused pyrazolo[1,5-*a*]quinoline derivatives 5a-k:- 3,5-Dialkyl-4-nitro-1*H*-pyrazole **1a-c** (0.5 mmol), CuI (9.5 mg, 0.05 mmol), K_2CO_3 (227 mg, 1.65 mmol), neocuproine (21 mg, 0.1 mmol) and dimethyl sulfoxide (2 mL), were added into a 10 mL screw cap vial. The reaction mixture was stirred at room temperature for 30 min, followed by the addition of *o*-halo heteroaryl aldehyde **4a-d** (0.5 mmol). The reaction mixture was stirred at 120 ^{o}C for 48 h. The reaction mixture was cooled to room temperature, diluted with water, extracted with ethyl acetate (2 x 20 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in vacuo to afford a crude residue. The residue was purified by flash column chromatography (hexane/EtOAc) on silica gel to obtain heteroaryl-fused pyrazolo[1,5-*a*]quinoline derivatives **5a-k**.

8. Spectroscopic data of 5a-k



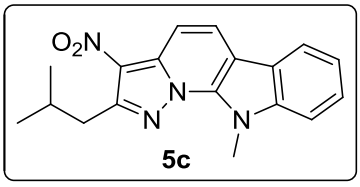
5a

2,10-Dimethyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5a:- yellow solid, 116 mg 83%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 258-260 ^oC; **IR** ($CHCl_3$) 772, 1219, 1507, 1626, 1644, 2920 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.85 (s, 3H), 4.59 (s, 3H), 7.43-7.40 (m, 1H), 7.54-7.58 (m, 2H), 8.05 (d, *J* = 7.5 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 8.26 (d, *J* = 9.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ =15.0, 32.6, 107.7, 109.9, 119.9, 121.3, 122.0, 125.5, 125.9, 134.7, 137.6, 138.4, 151.4; **MS** (ESI) m/z 281 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{15}H_{13}O_2N_4$ $[M+H]^+$ 281.10330, found 281.10323.



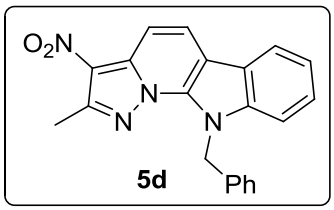
5b

2-Ethyl-4,10-dimethyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5b:- yellow solid, 119 mg 77%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 186-188 ^oC; **IR** ($CHCl_3$) 771, 1215, 1514, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.46 (t, *J* = 7.5 Hz, 3H), 2.79 (s, 3H), 3.19 (q, *J* = 7.5 Hz, 2H), 4.57 (s, 3H), 7.36-7.39 (m, 1H), 7.52-7.54 (m, 2H), 7.96 (s, 1H), 8.02 (d, *J* = 7.5 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 12.1, 21.2, 22.2, 32.6, 109.2, 109.8, 117.7, 119.8, 121.1, 121.5, 125.5, 126.2, 133.6, 136.5, 138.4, 155.9; **MS** (ESI) m/z 309 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{17}O_2N_4$ $[M+H]^+$309.13460, found 309.13350.

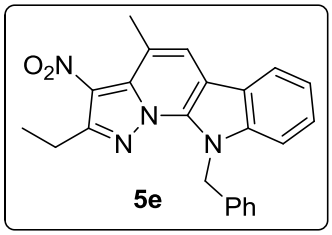


5c

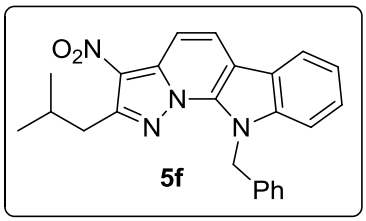
2-Isobutyl-10-methyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5c:- yellow solid, 118 mg, 73%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 182-184 ^oC; **IR** ($CHCl_3$) 771, 1216, 1530, 2853, 2925, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.08 (d, *J* = 6.5 Hz, 6H), 2.31-2.39 (m, 1H), 3.16 (d, *J* = 7.0 Hz, 2H), 4.60 (s, 3H), 7.40-7.43 (m, 1H), 7.56 (d, *J* = 4.0 Hz, 2H), 8.06-8.08 (m, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 8.28 (d, *J* = 9.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 22.7, 27.5, 32.6, 37.1, 107.9, 109.9, 110.1, 120.0, 121.1, 121.4, 121.9, 125.5, 125.8, 134.8, 137.9, 138.3, 154.2; **MS** (ESI) m/z 323 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{19}O_2N_4$ $[M+H]^+$ 323.15025, found 323.15094.



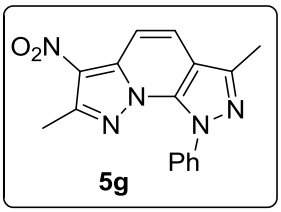
10-Benzyl-2-methyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5d:- yellow solid, 94 mg, 53%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 210-212 ^oC; **IR** ($CHCl_3$) 742, 1213, 1408, 1519, 1626, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.81 (s, 3H), 6.40 (s, 2H), 7.21-7.25 (m, 3H), 7.27-7.29 (m, 2H), 7.38-7.42 (m, 1H) 7.46-7.49 (m, 1H), 7.50-7.52 (m, 1H), 8.07 (d, *J* = 7.5 Hz, 1H), 8.15 (d, *J* = 9.0 Hz, 1H), 8.30 (d, *J* = 9.0 Hz, 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$) δ = 15.0, 48.8, 108.1, 110.3, 110.9, 112.0, 120.0, 121.6, 122.3, 125.4, 126.0, 126.9, 127.7, 128.8, 134.2, 136.8, 137.8, 151.5; **MS** (ESI) m/z 357 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{21}H_{17}O_2N_4$ $[M+H]^+$ 357.13460, found 357.13426.



10-Benzyl-2-ethyl-4-methyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5e:- yellow solid, 88 mg, 46%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 208-210 ^oC; **IR** ($CHCl_3$) 742, 1214, 1517, 3019 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 1.37 (t, *J* = 7.2 Hz, 3H), 2.81 (s, 3H), 3.16 (q, *J* = 7.6 Hz, 2H), 6.36 (s, 2H), 7.18-7.22 (m, 2H), 7.22-7.24 (m, 2H), 7.24-7.26 (m, 1H), 7.35-7.39 (m, 1H), 7.44-7.48 (m, 1H), 7.51-7.54 (m, 1H), 7.99 (s, 1H), 8.03 (d, *J* = 8.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 12.0, 21.2, 22.2, 48.8, 109.5, 110.7, 118.2, 119.9, 121.4, 121.7, 125.7, 126.1, 126.9, 127.6, 128.7, 133.2, 136.5, 137.4, 138.1, 155.9; **MS** (ESI) m/z 385 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{23}H_{21}O_2N_4$ $[M+H]^+$ 385.16590, found 385.16571.

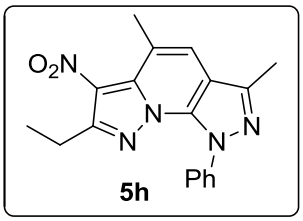


10-Benzyl-2-isobutyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5f:- yellow solid, 87 mg 44%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 206-208 ^oC; **IR** ($CHCl_3$) 771, 1216, 1464, 1713, 2912, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 0.97 (d, *J* = 6.5 Hz, 6H), 2.22-2.30 (m, 1H), 3.10 (d, *J* = 7.0 Hz, 2H), 6.38 (s, 2H), 7.20-7.25 (m, 5H), 7.39-7.42 (m, 1H), 7.47-7.51 (m, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 9.0 Hz, 1H), 8.32 (d, *J* = 9.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 22.6, 27.3, 37.1, 48.9, 108.6, 110.4, 110.7, 199.9, 121.9, 122.0, 125.4, 126.0, 126.9, 127.7, 128.7, 137.0, 137.9, 154.3; **MS** (ESI) m/z 399 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{24}H_{23}O_2N_4$ $[M+H]^+$ 399.18155, found 399.18233.



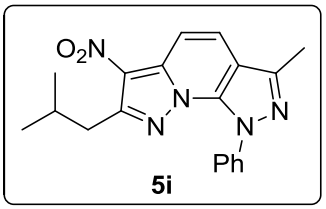
5g

3,7-Dimethyl-6-nitro-1-phenyl-1*H*-dipyrazolo[1,5-a:4',3'-*e*]pyridine 5g:- white solid, 100 mg 65%, R_f = 0.6 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 240-242 ^{o}C; **IR** ($CHCl_3$) 771, 1596, 1622, 2921, cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.67 (s, 6H), 7.48-7.57 (m, 3H), 7.60-7.67 (m, 2H), 7.90 (d, *J* = 8.7 Hz, 1H), 8.11 (d, *J* = 9.6 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 12.3, 14.9, 110.5, 113.1, 125.0, 126.7, 128.4, 128.6, 134.3, 138.0, 138.3, 145.4, 150.7; **MS** (ESI) m/z 308 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{16}H_{14}O_2N_5$ $[M+H]^+$ 308.11420, found 308.11421.



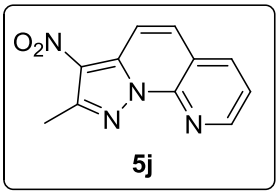
5h

7-Ethyl-3,5-dimethyl-6-nitro-1-phenyl-1H-dipyrazolo[1,5-a:4',3'-*e*]pyridine 5h:- yellow solid, 105 mg 63%, R_f = 0.6 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 178-180 ^{o}C; **IR** ($CHCl_3$) 772, 1219, 1484, 1743, 2923 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 1.19 (t, *J* = 7.5 Hz, 3H), 2.63 (s, 3H), 2.72 (s, 3H), 3.00 (q, *J* = 7.5 Hz, 2H), 7.46-7.53 (m, 3H), 7.56 (s, 1H), 7.60-7.63 (m, 2H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 11.3, 12.2, 21.1, 21.7, 112.2, 120.5, 124.5, 126.9, 128.1, 128.3, 133.5, 136.6, 138.6, 144.4, 154.9; **MS** (ESI) m/z 336 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{18}O_2N_5$ $[M+H]^+$ 336.14550, found 336.14562.



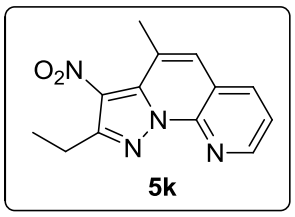
5i

7-Isobutyl-3-methyl-6-nitro-1-phenyl-1*H*-dipyrazolo[1,5-a:4',3'-*e*]pyridine 5i:- yellow solid, 89 mg, 51%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 180-182 ^{o}C; **IR** ($CHCl_3$) 771, 1215, 1505, 2852, 2955 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 0.95 (d, *J* = 6.6 Hz, 6H), 2.04-2.16 (m, 1H), 2.68 (s, 3H), 2.96 (d, *J* = 6.9 Hz, 2H), 7.47-7.54 (m, 3H), 7.60-7.66 (m, 2H), 7.90 (d, *J* = 9.3 Hz, 1H), 8.11 (d, *J* = 9.3 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 12.2, 22.5, 26.9, 36.8, 110.6, 112.9, 124.9, 126.8, 128.3, 128.6, 138.0, 138.3, 145.3, 153.3; **MS** (ESI) m/z 350 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{19}H_{20}O_2N_5$ $[M+H]^+$ 350.16115, found 350.16241.



5j

2-Methyl-3-nitropyrazolo[1,5-*a*][1,8]naphthyridine 5j:- light yellow solid, 65 mg 57%, R_f = 0.4 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 240-242 ^{o}C; **IR** ($CHCl_3$) 774, 1214, 1406, 1516,3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.93 (s, 3H), 7.66-7.70 (m, 1H), 7.93 (d, *J* = 9.5 Hz, 1H), 8.33 (dd, J_1 =8.0 Hz, J_2 =80 Hz, 1H), 8.36 (d, *J* = 9.5 Hz, 1H), 9.04 (s, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.7, 117.0, 118.9, 122.7, 130.2, 137.6, 137.7, 143.2, 151.0, 152.1; **MS** (ESI) m/z 229 $[M+H]^+$ **HRMS** (ESI, m/z): calcd for $C_{11}H_9O_2N_4$ $[M+H]^+$ 229.07200, found 229.07190.

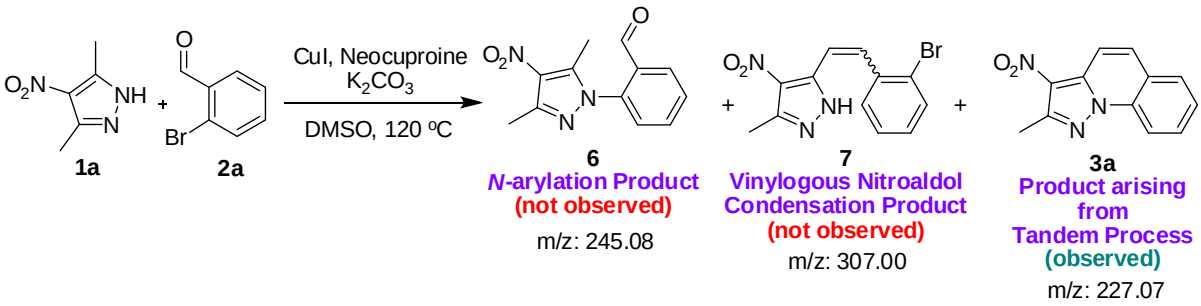


5k

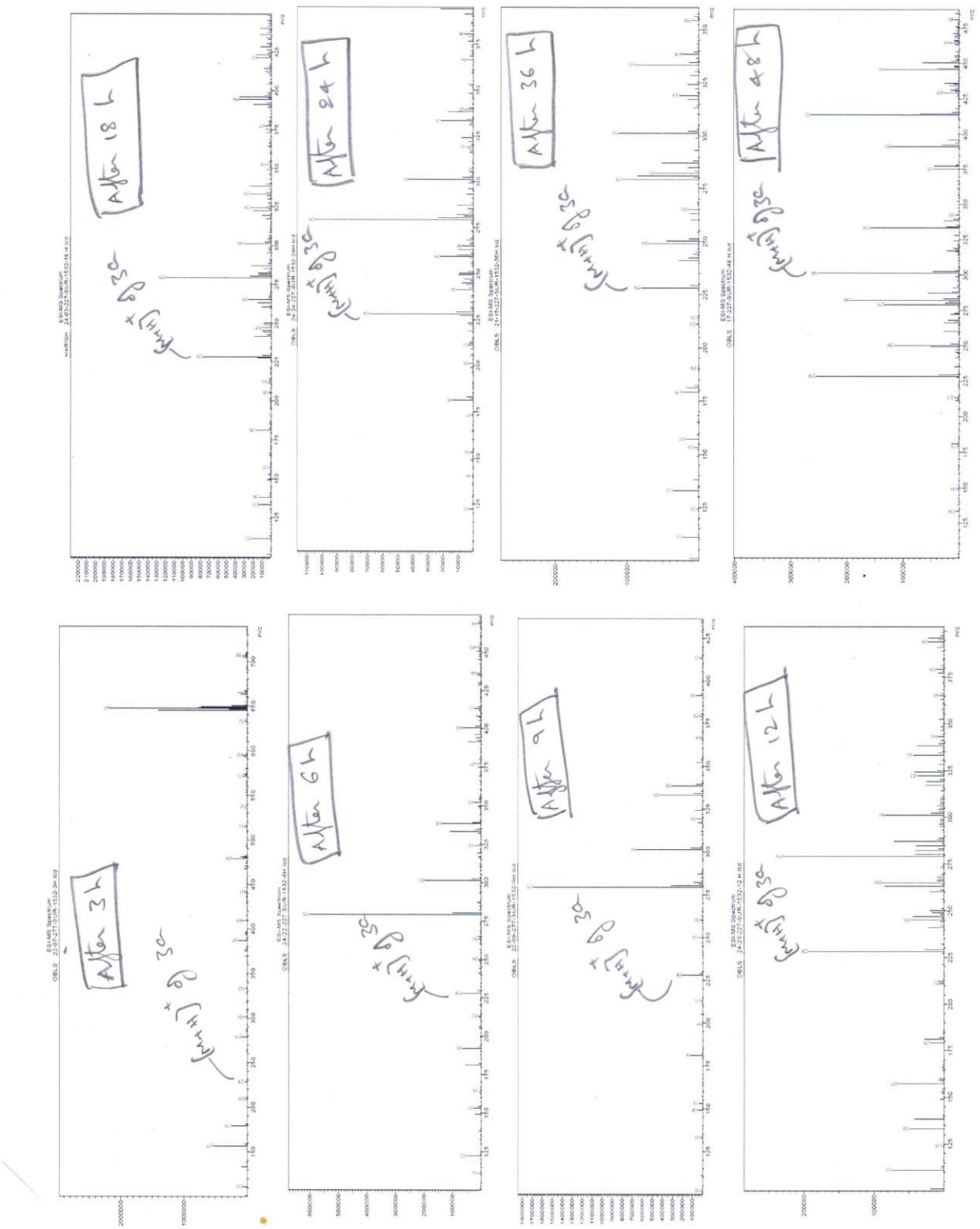
2-Ethyl-4-methyl-3-nitropyrazolo[1,5-*a*][1,8]naphthyridine 5k:- yellow solid, 64 mg, 50%, R_f = 0.6 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); **MP** 230-232 ^{o}C; **IR** ($CHCl_3$) 741, 1214, 1432, 1514, 3019 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.43 (t, *J* = 7.5 Hz, 3H), 2.76 (s, 3H), 3.21 (q, *J* = 7.0 Hz, 2H), 7.53 (s, 1H), 7.55-7.59 (m, 1H), 8.16 (d, J_1 =8.0 Hz, 1H), 8.92 (m, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 13.1, 21.2, 21.7, 118.5, 122.5, 127.4, 128.2, 128.9, 136.4, 142.4, 151.0, 155.4; **MS** (ESI) m/z 257 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{13}H_{13}O_2N_4$ $[M+H]^+$ 257.10330, found 257.10302.

9. Control Experiments

Reaction of 3,5-dimethyl-4-nitropyrazole **1a** and 2-bromobenzaldehyde **2a**.

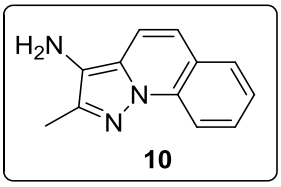


ESI-MS traces for the reaction of **1a** and **2a** at different reaction times.



10. Synthesis and Spectroscopic data of 10

Reduction of nitro group[6] of 2-methyl-3-nitropyrazolo[1,5-*a*]quinoline 3a: Compound **3a** (113 mg, 0.5 mmol) was suspended in water (10 mL) and added a 3.5 M KOH (10 mL) solution. To this mixture, solid $SnCl_2 \cdot 2H_2O$ (0.5 g, 2 mmol) was then added portion-wise. The reaction mixture was stirred at 100 ^oC and monitored by TLC. After 0.5 h, the compound **3a** disappeared (by TLC). The reaction mixture was cooled to room temperature and insoluble material was filtered. The filtrate was extracted with chloroform (2 x 20 mL) and the organic phase was washed with brine (5 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated to get the product, 2-methylpyrazolo[1,5-a]quinolin-3-amine **10** without any further purification.



10

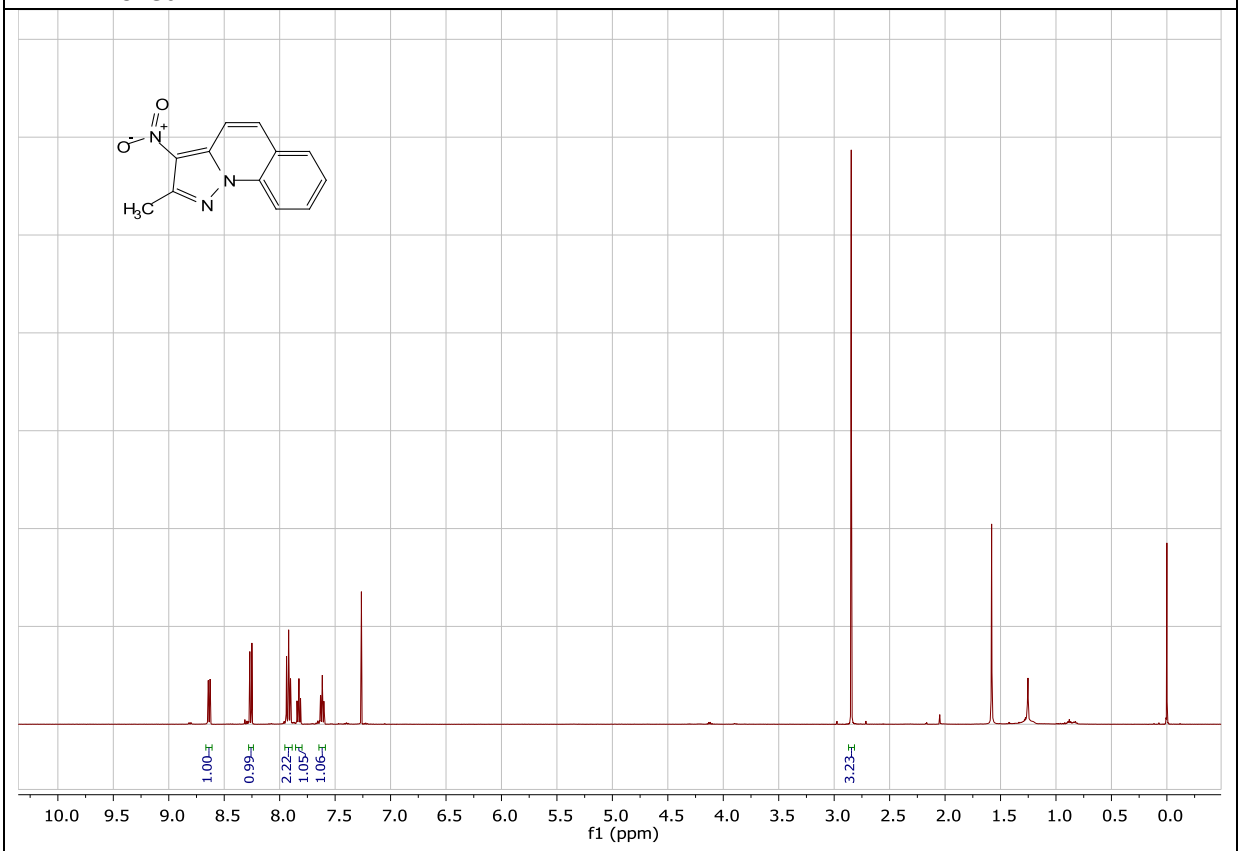
2-Methylpyrazolo[1,5-*a*]quinolin-3-amine 10:- yellow solid, 66 mg, 67%, R_f = 0.3 (EtOAc/hexane, 50:50) Column Chromatography (EtOAc/hexane, 40:60); **MP** 164-166 ^oC; **IR** (KBr) 764, 1218, 2853, 2923, 3423 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.47 (s, 3H), 7.18-7.22 (m, 1H), 7.23-7.25 (m, 1H), 7.31-7.35 (m, 1H), 7.55-7.60 (m, 1H), 7.64-7.67 (m, 1H), 8.40 (d, J_1 = 8.0 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$) δ = 14.7, 115.7, 116.0, 123.9, 126.4, 128.7, 131.2, 131.3, 133.4, 135.8, 149.9; **MS** (ESI) m/z 198 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{12}H_{12}N_3$ $[M+H]^+$ 198.10257, found 198.10239.

References:

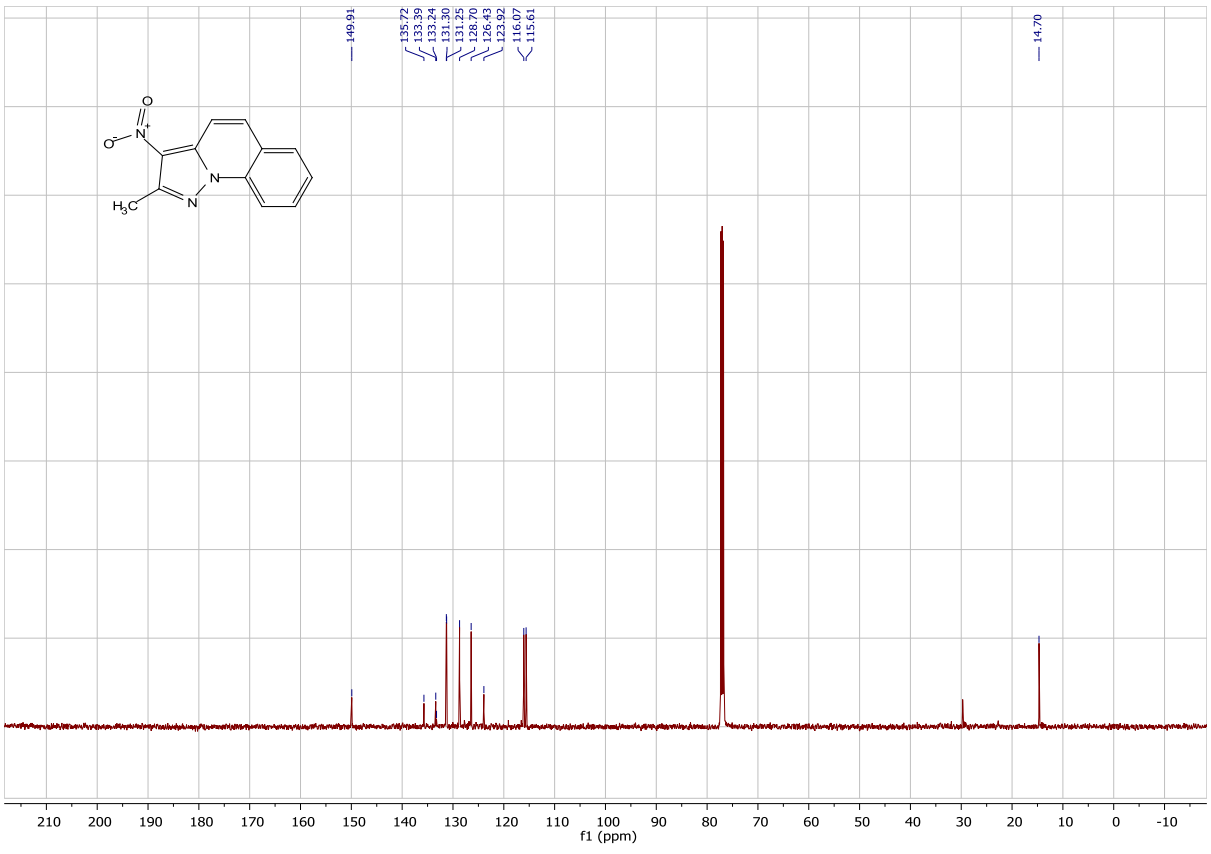
6. E. V. Govor, A. B. Lysenko, D. Quinonero, E. B. Rusanov, A. N. Chernega, J. Moellmer, R. Staudt, H. Krautscheid, A. Fronterab and K. V. Domasevitch, *Chem. Commun*., 2011, **47**, 1764.

11. Copies of ^{1}H and ^{13}C NMR spectra of products 3a-n, 5a-k and 10

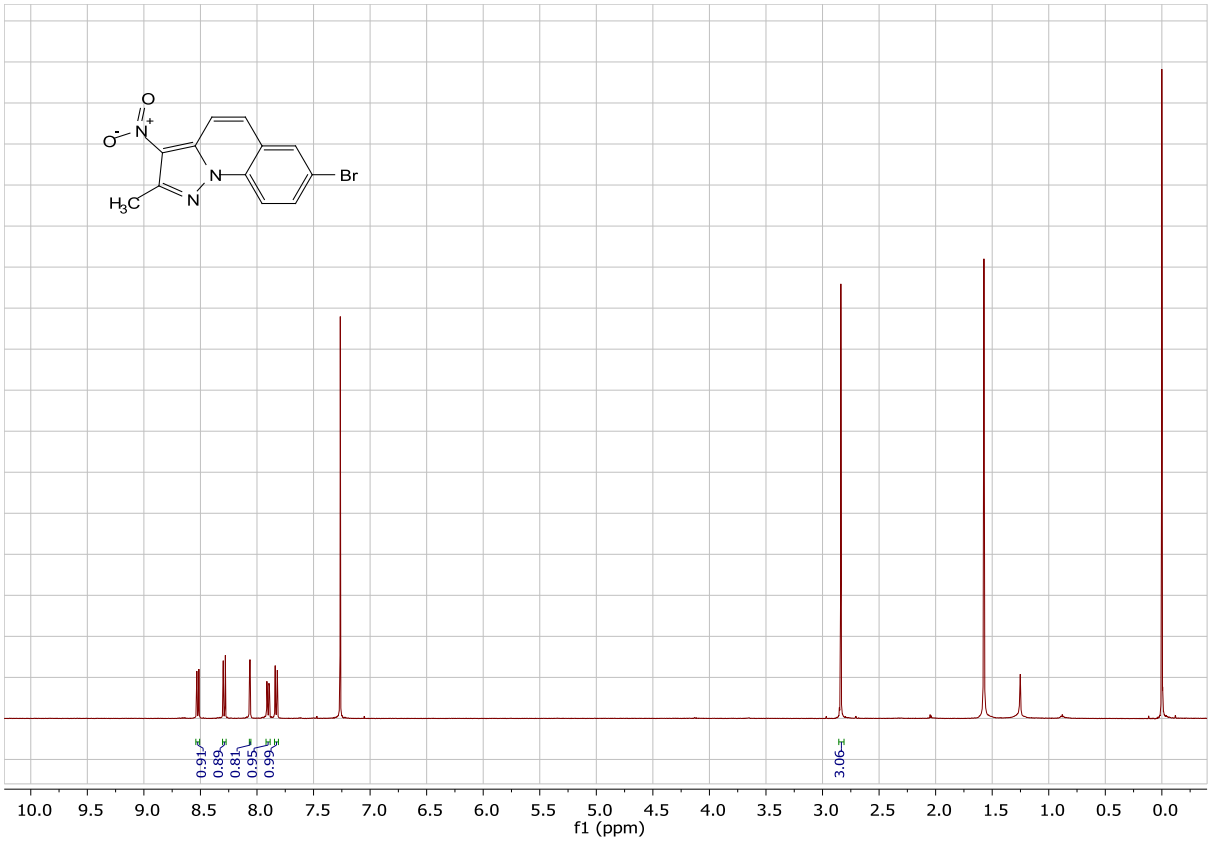
^{1}H NMR of **3a**



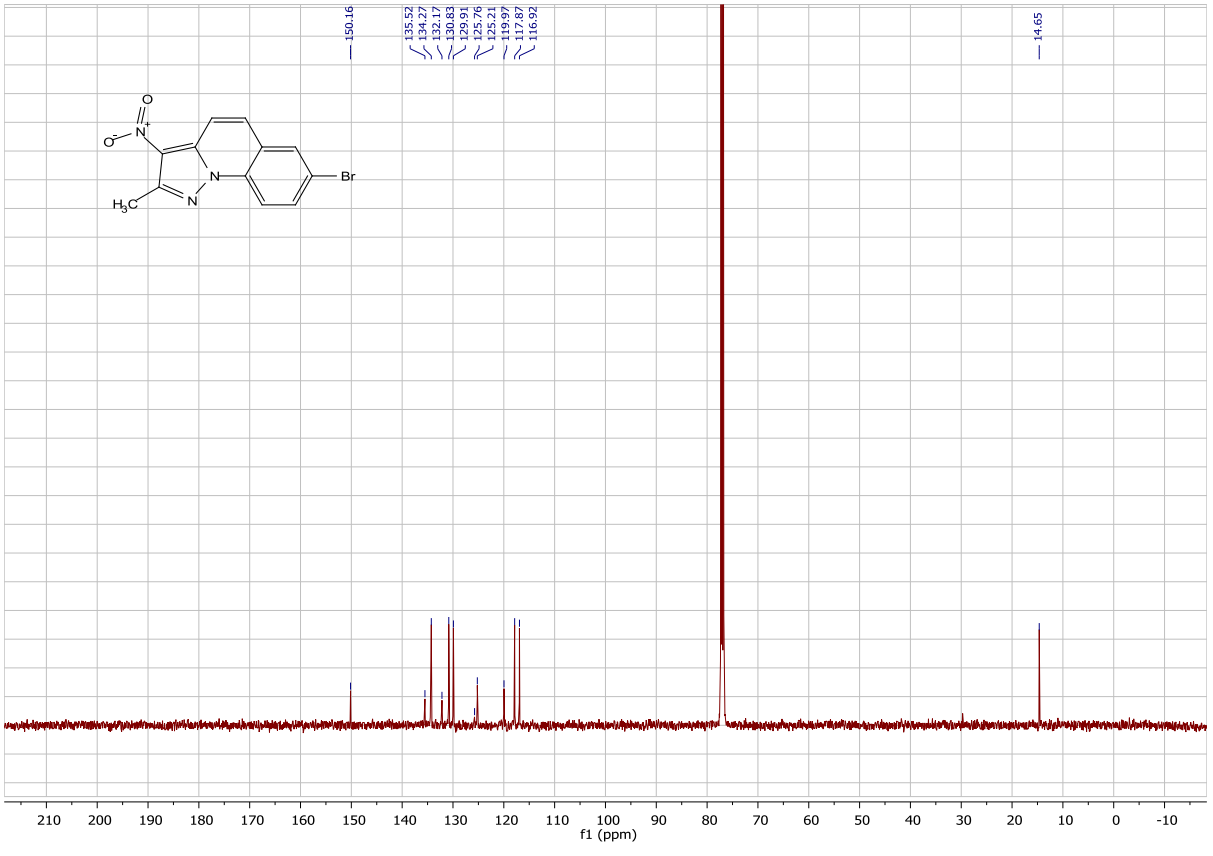
^{13}C NMR of **3a**



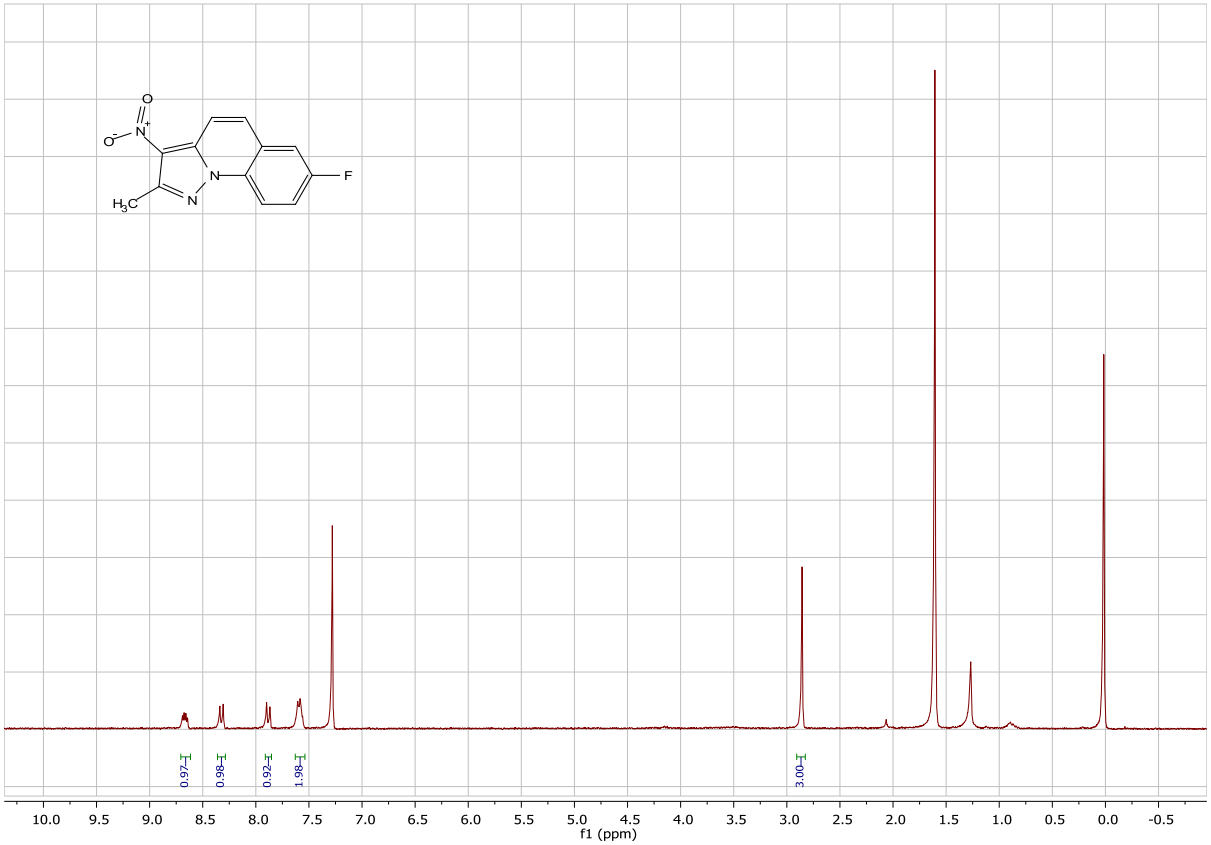
^{1}H NMR of **3b**



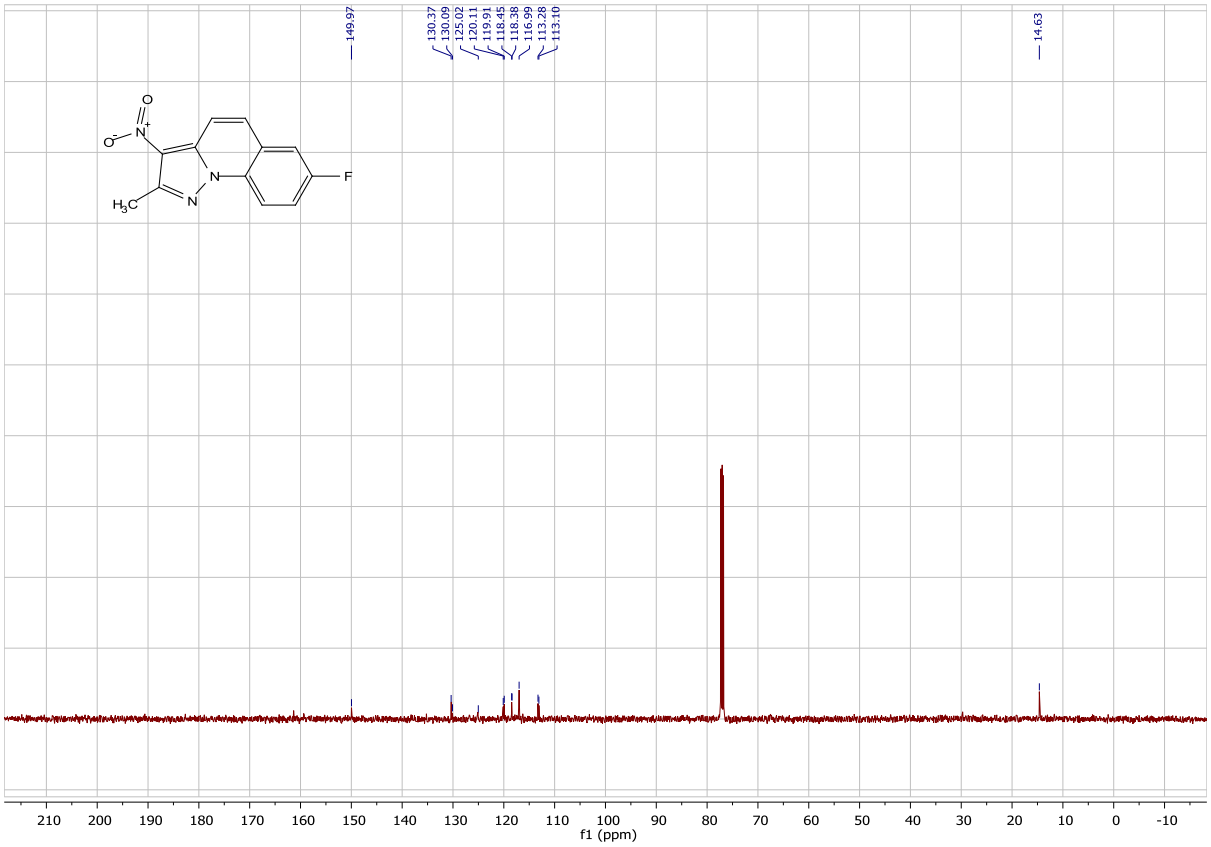
^{13}C NMR of **3b**



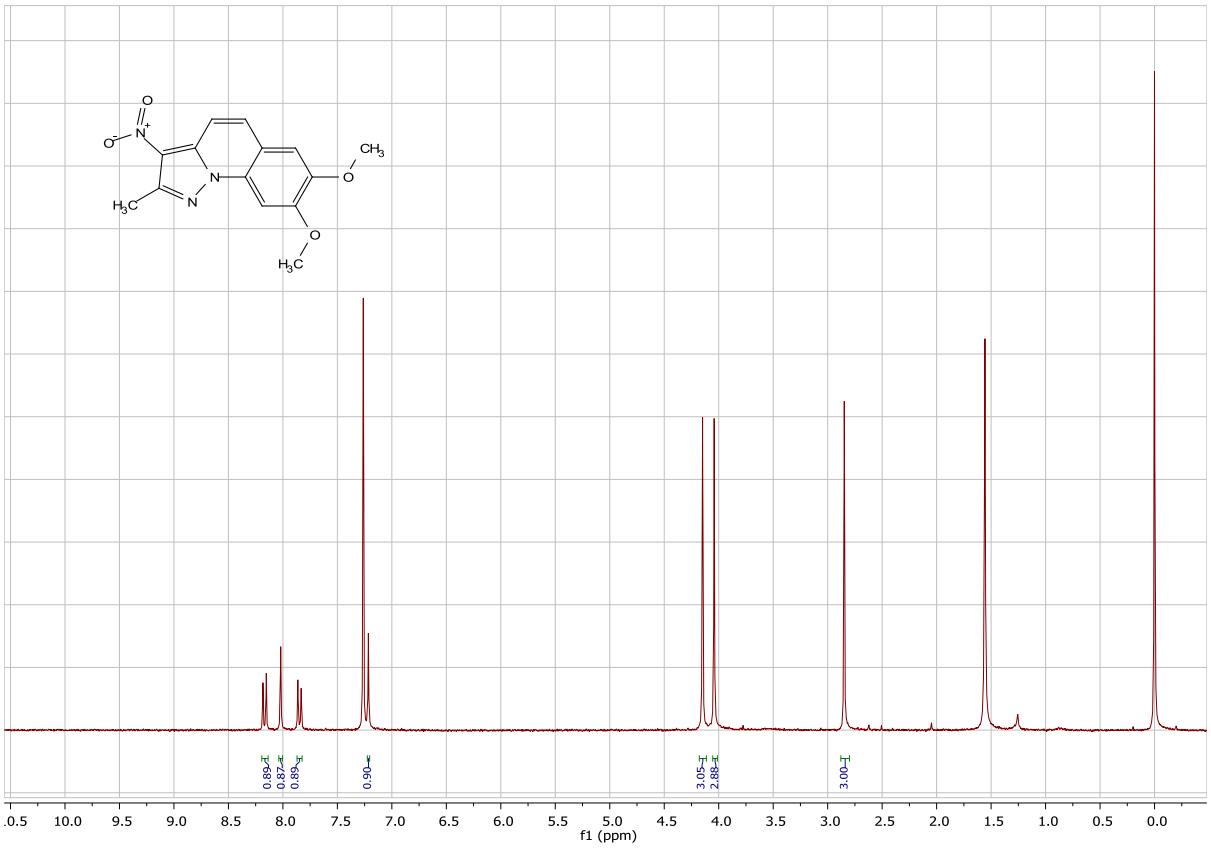
^{1}H NMR of **3c**



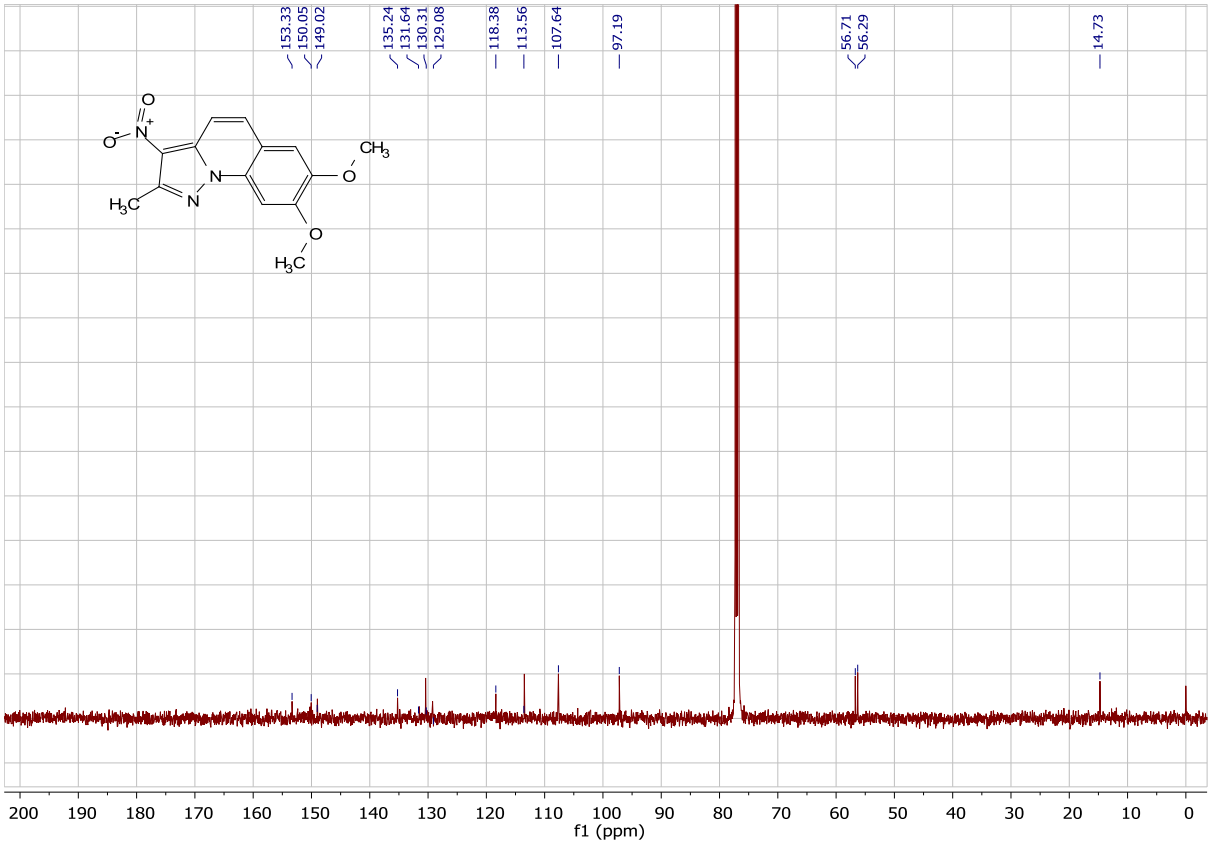
^{13}C NMR of **3c**



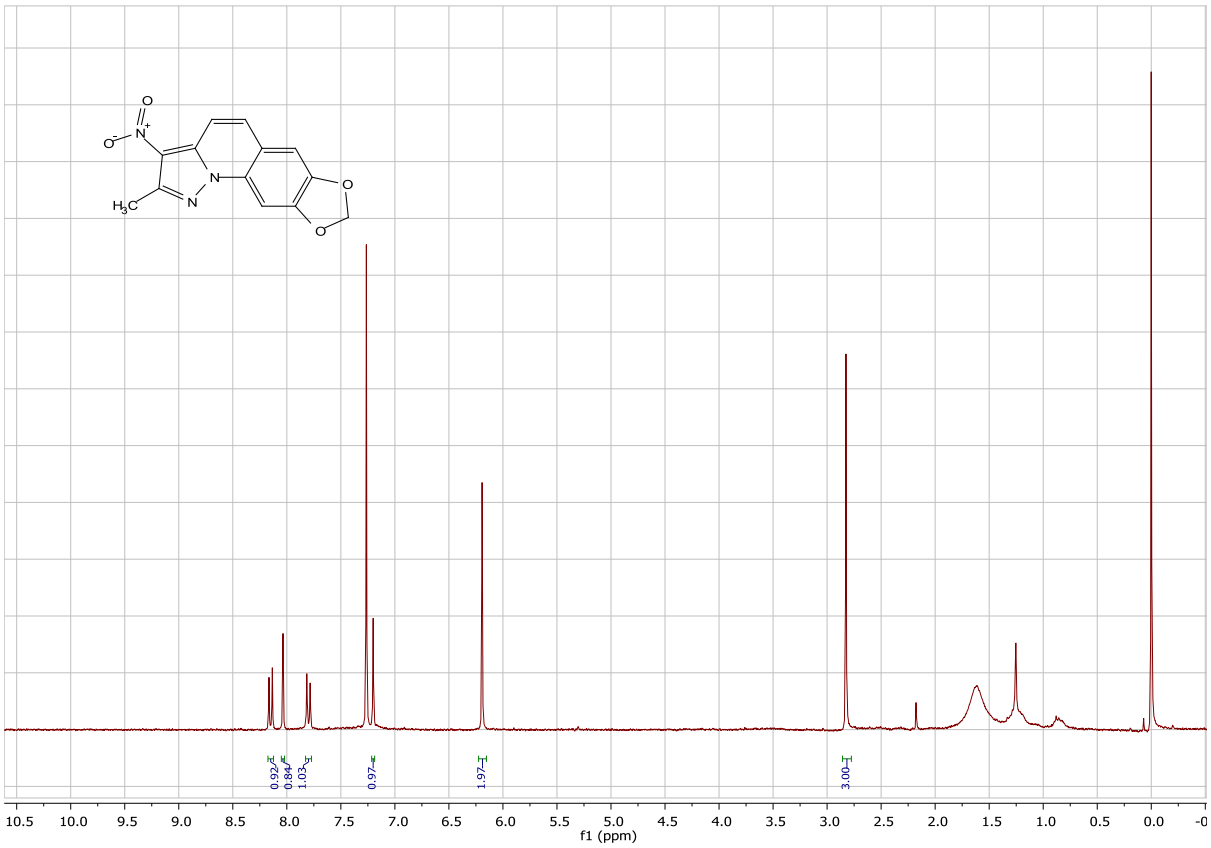
^{1}H NMR of **3d**



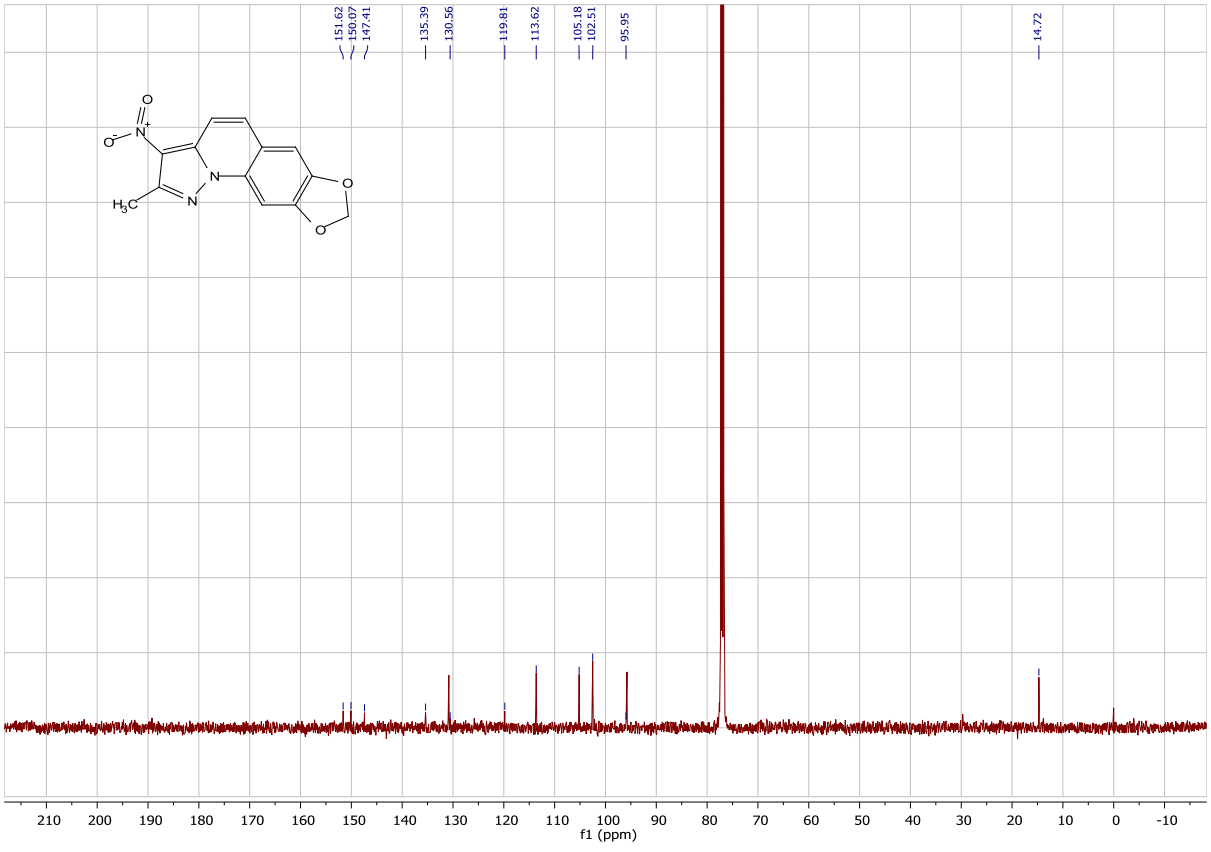
^{13}C NMR of **3d**



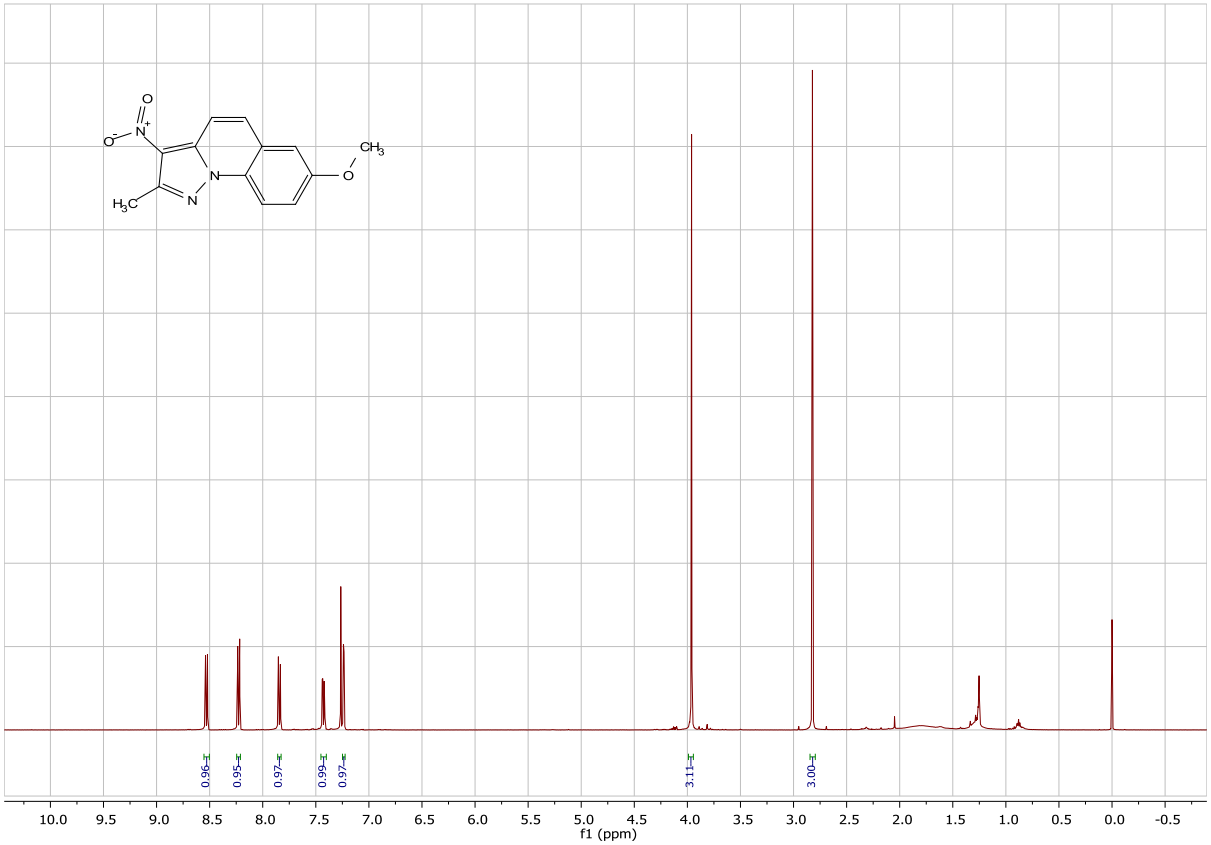
^{1}H NMR of **3e**



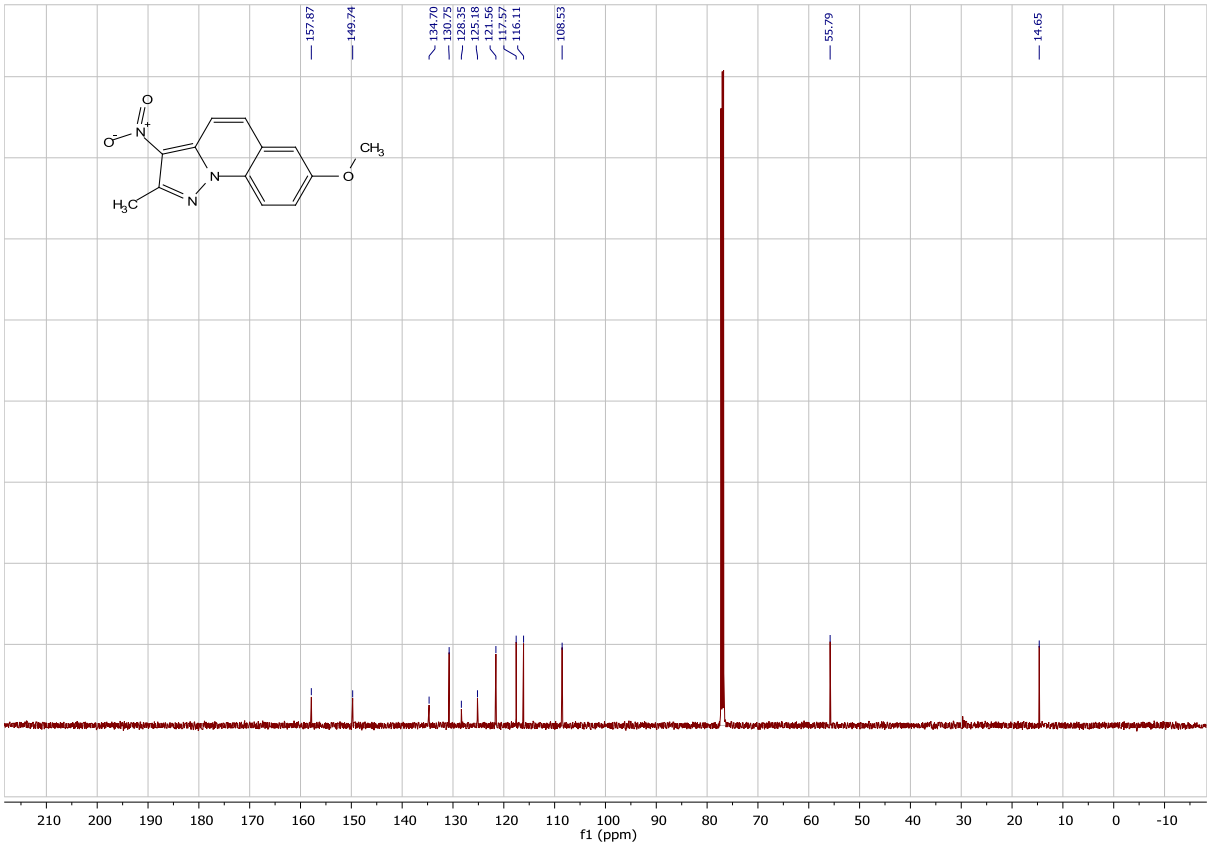
^{13}C NMR of **3e**



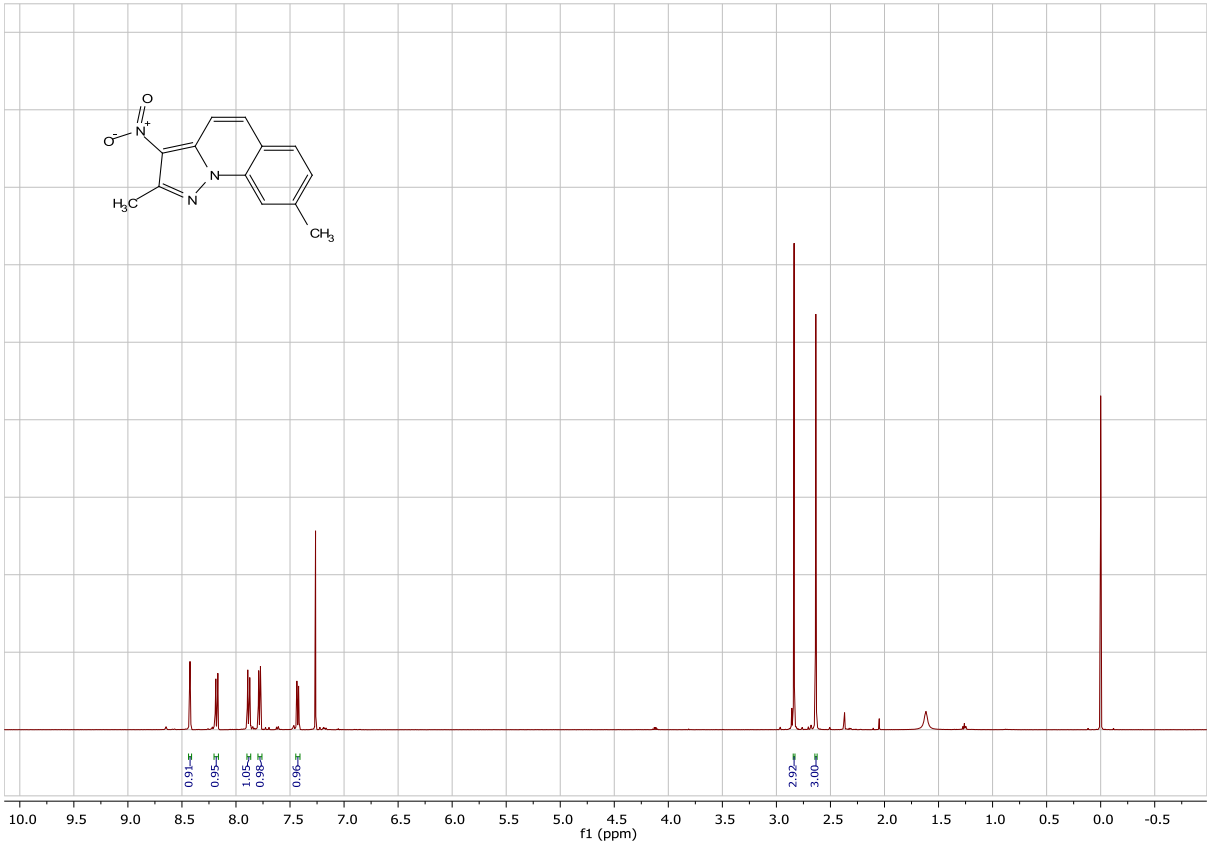
^{1}H NMR of **3f**



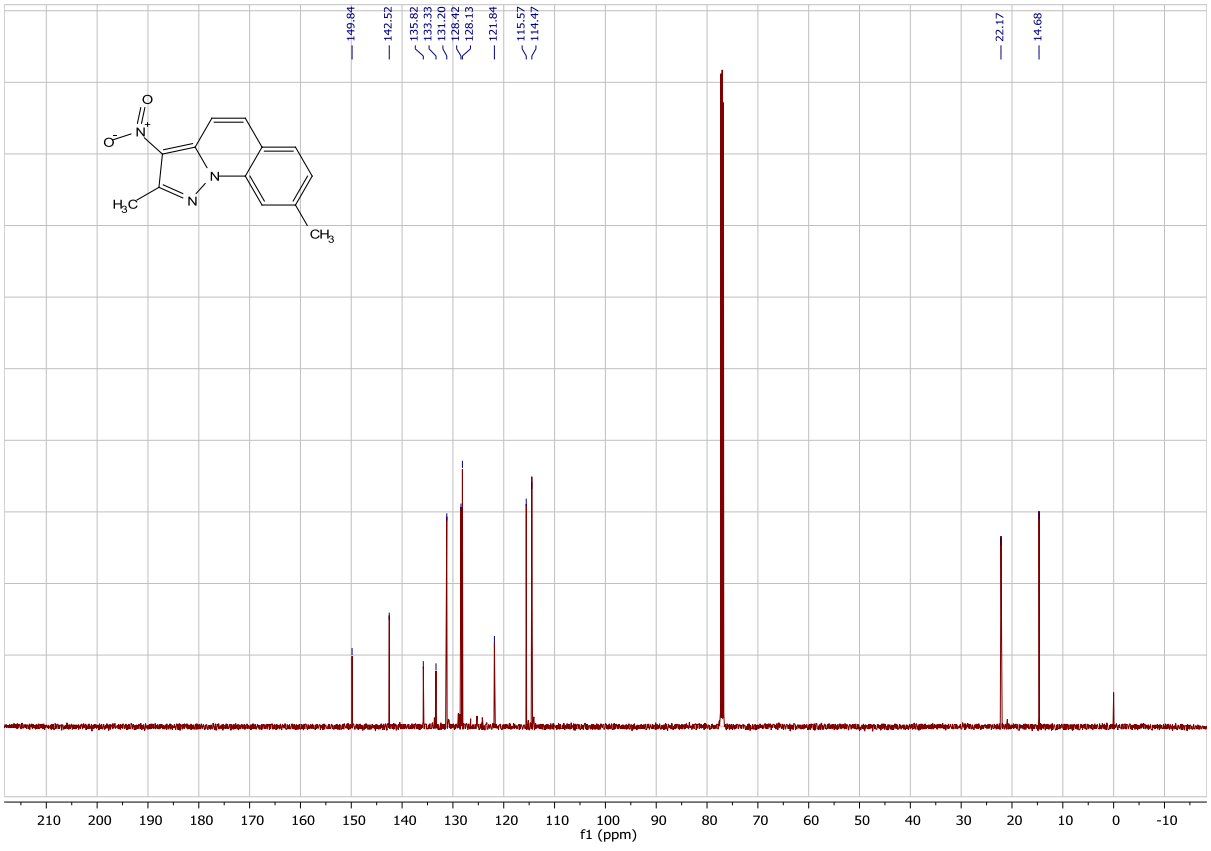
^{13}C NMR of **3f**



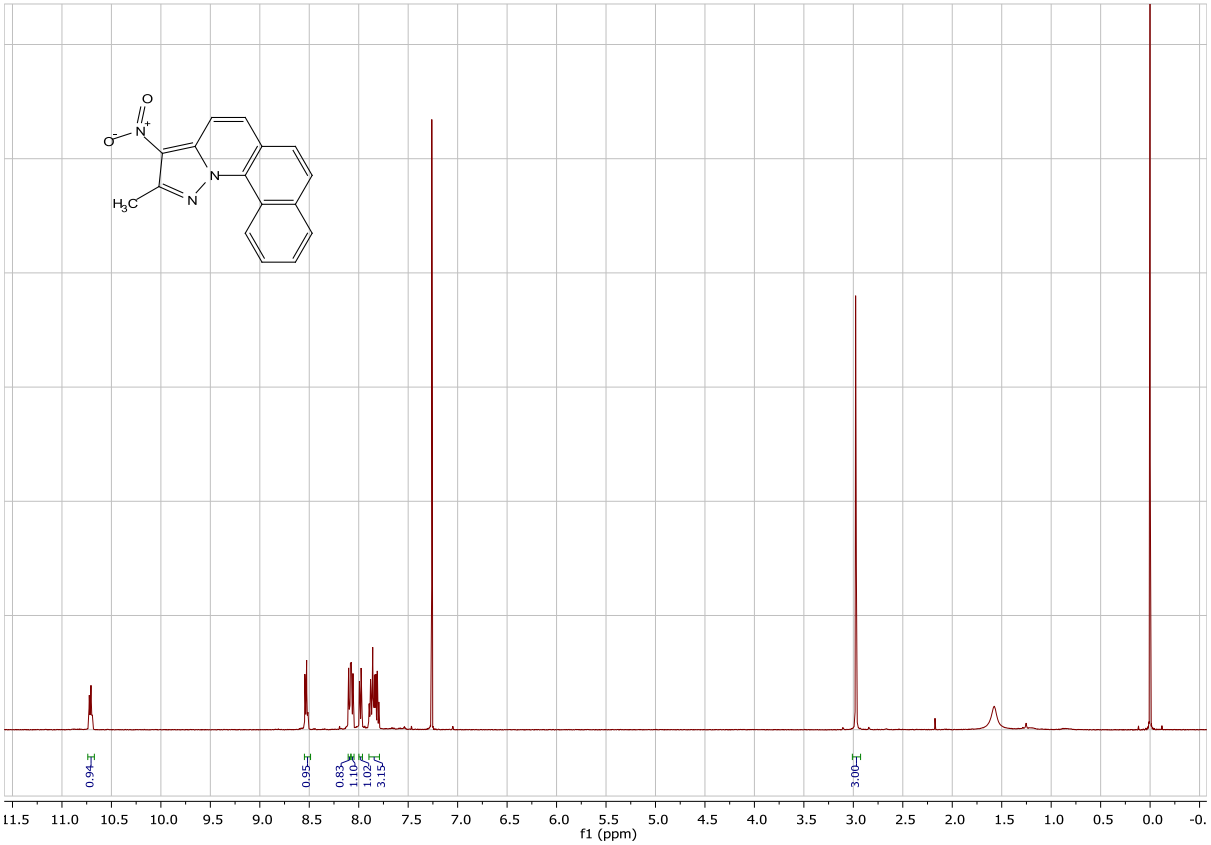
^{1}H NMR of **3g**



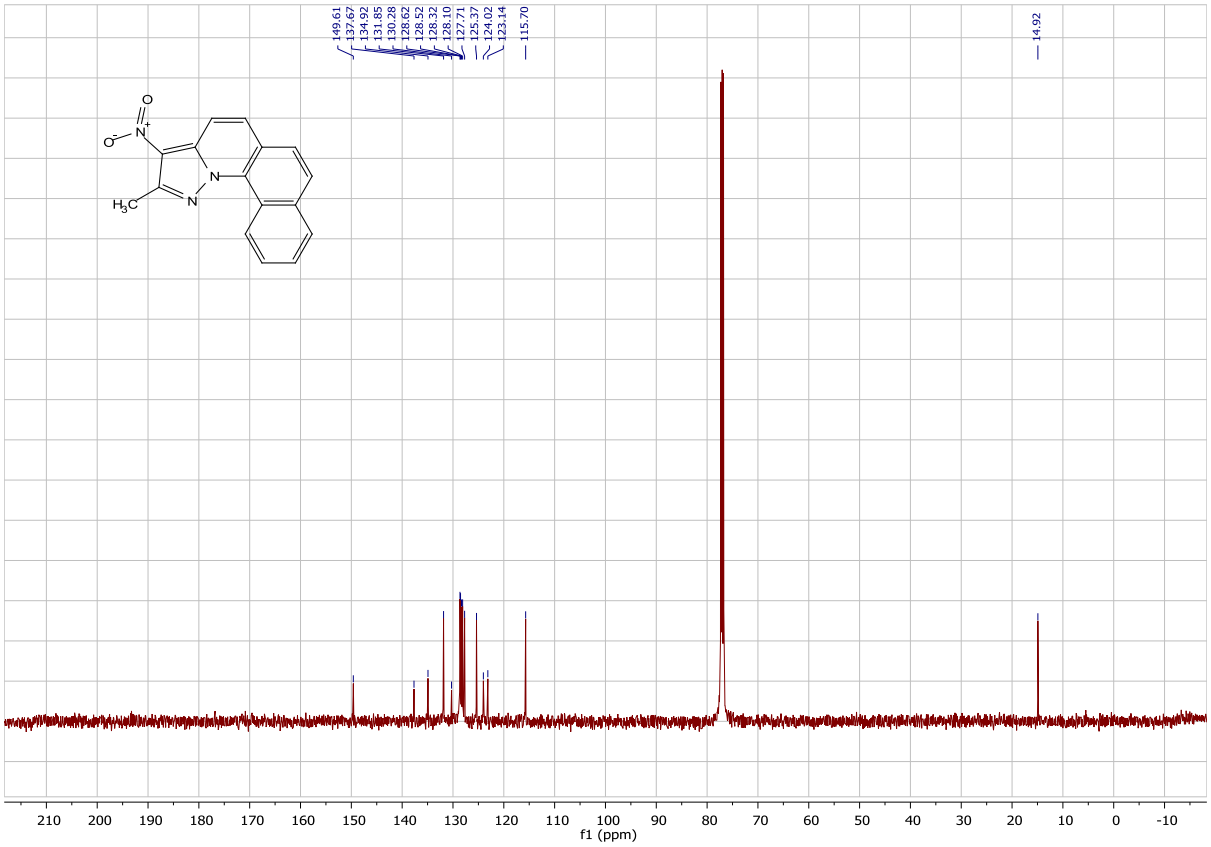
^{13}C NMR of **3g**



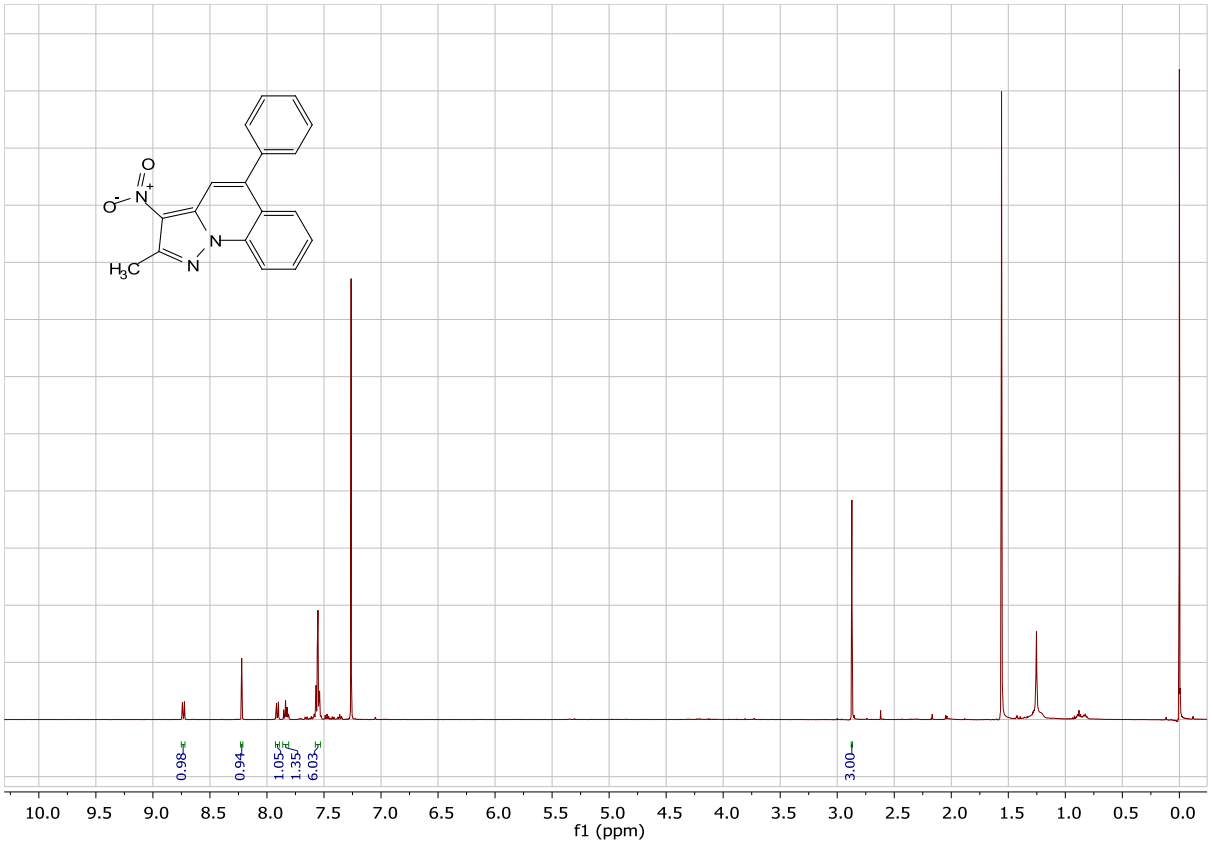
^{1}H NMR of **3h**



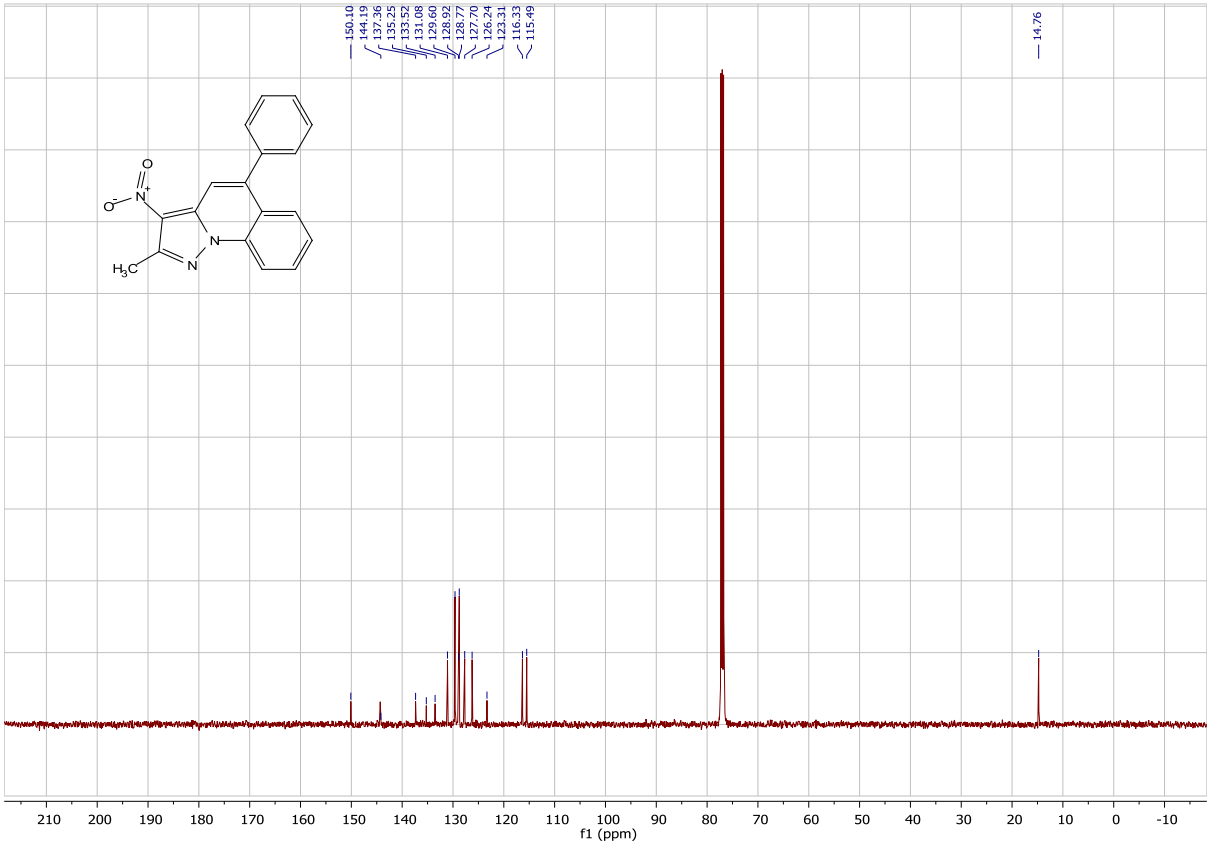
^{13}C NMR of **3h**



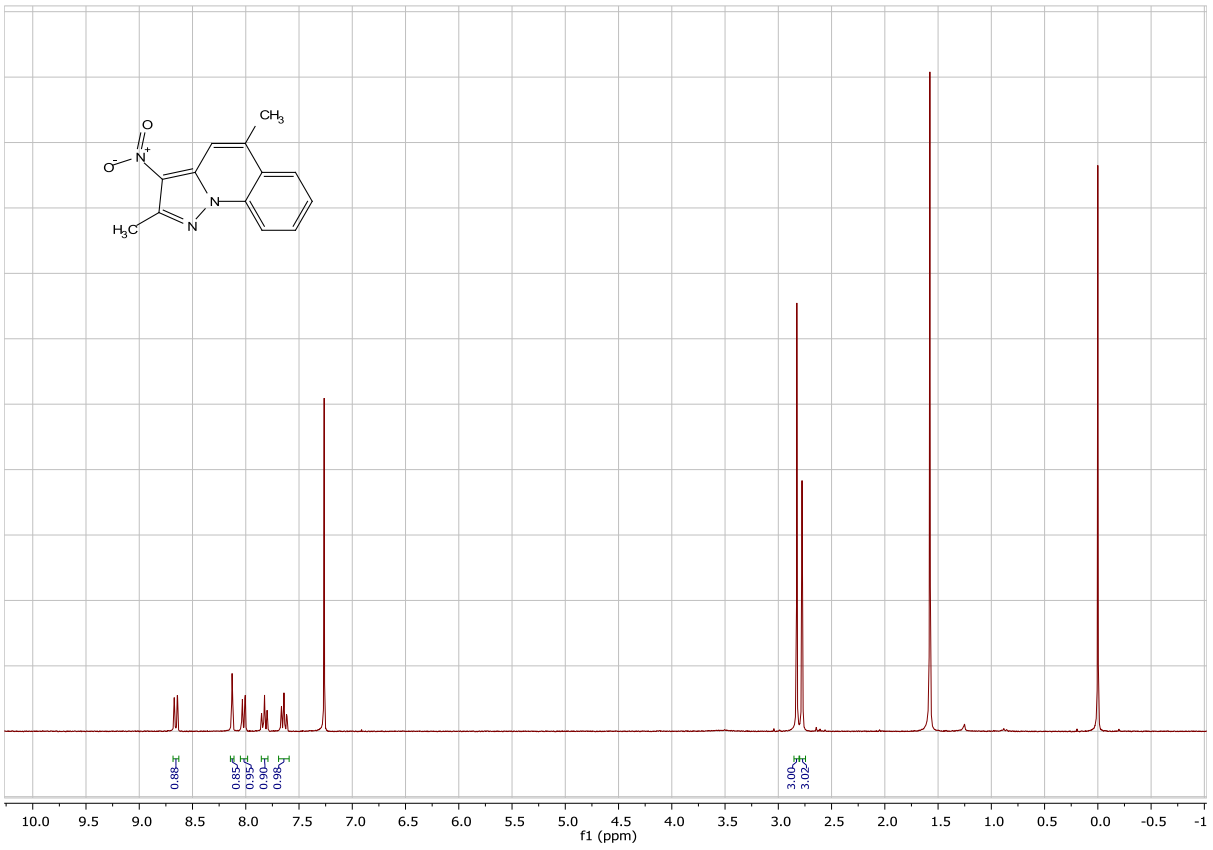
^{1}H NMR of **3i**



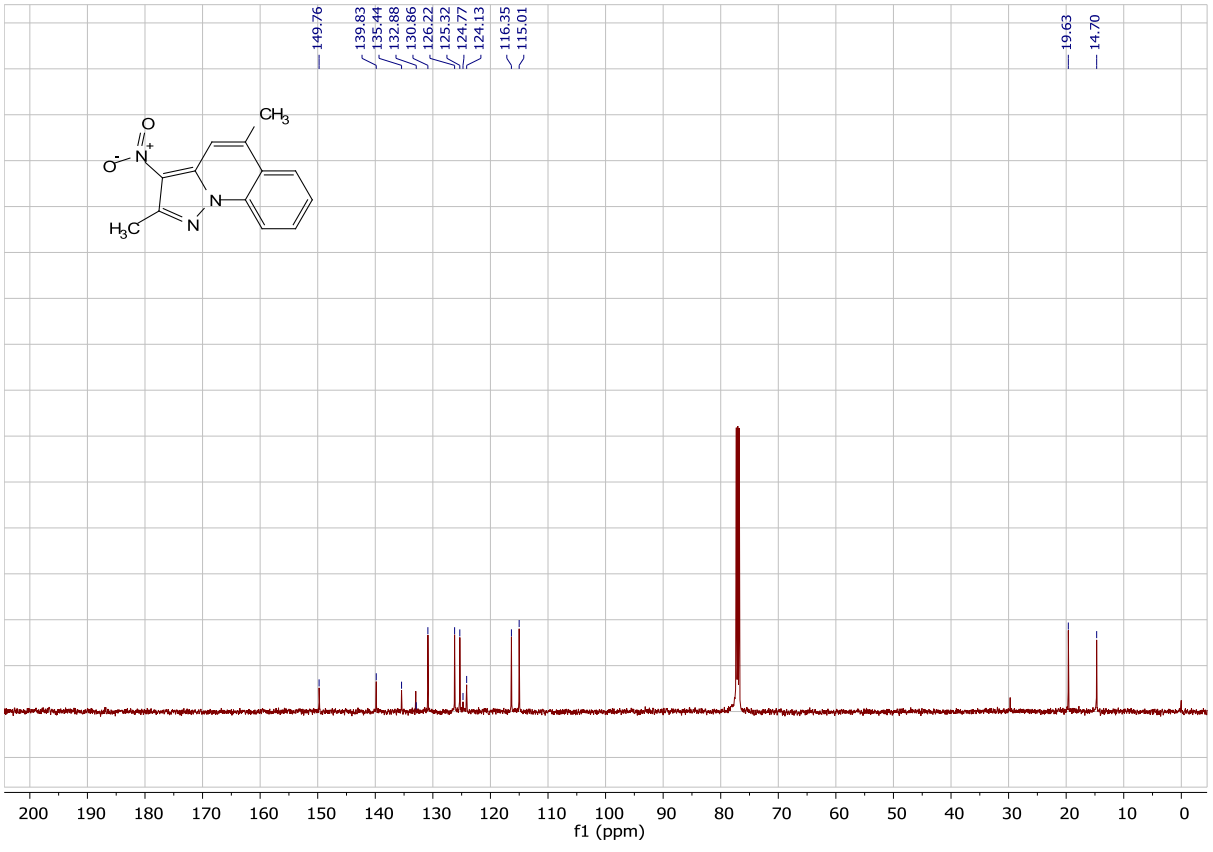
^{13}C NMR of **3i**



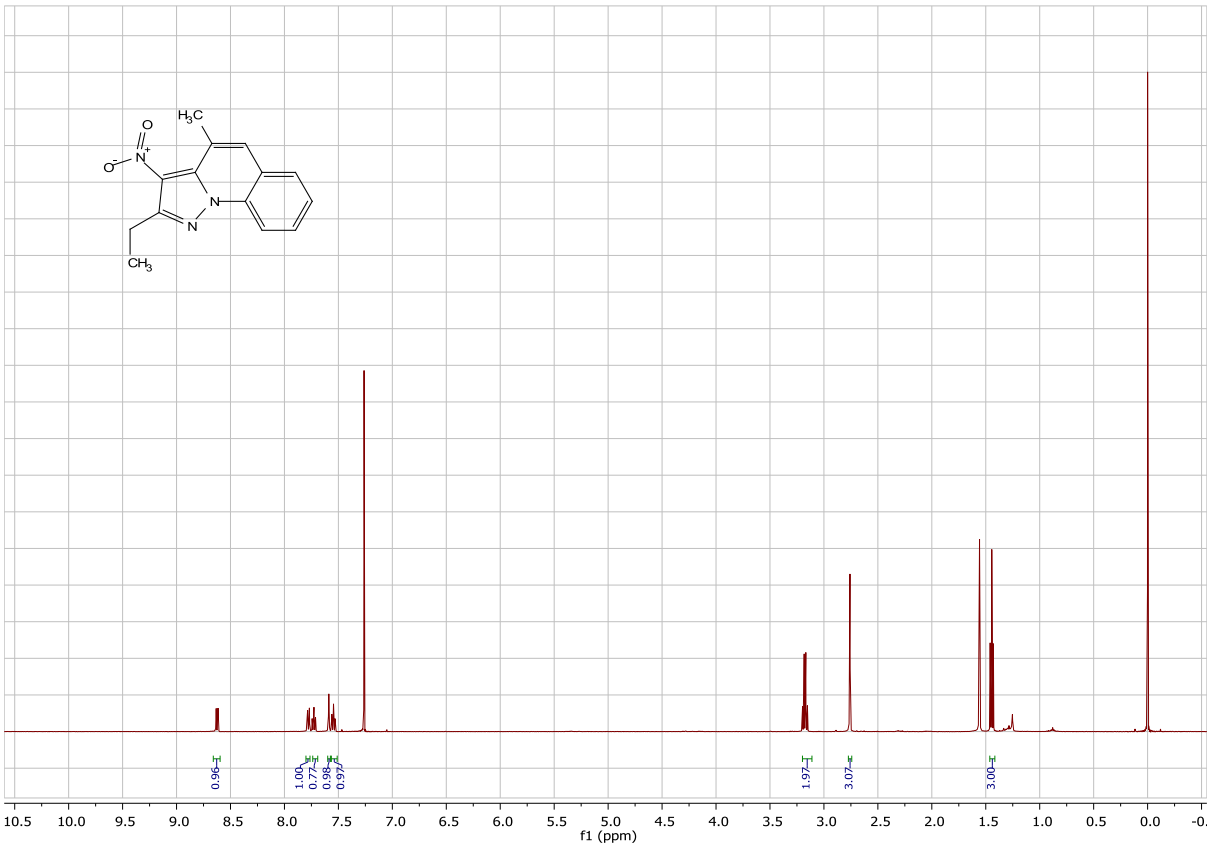
^{1}H NMR of **3j**



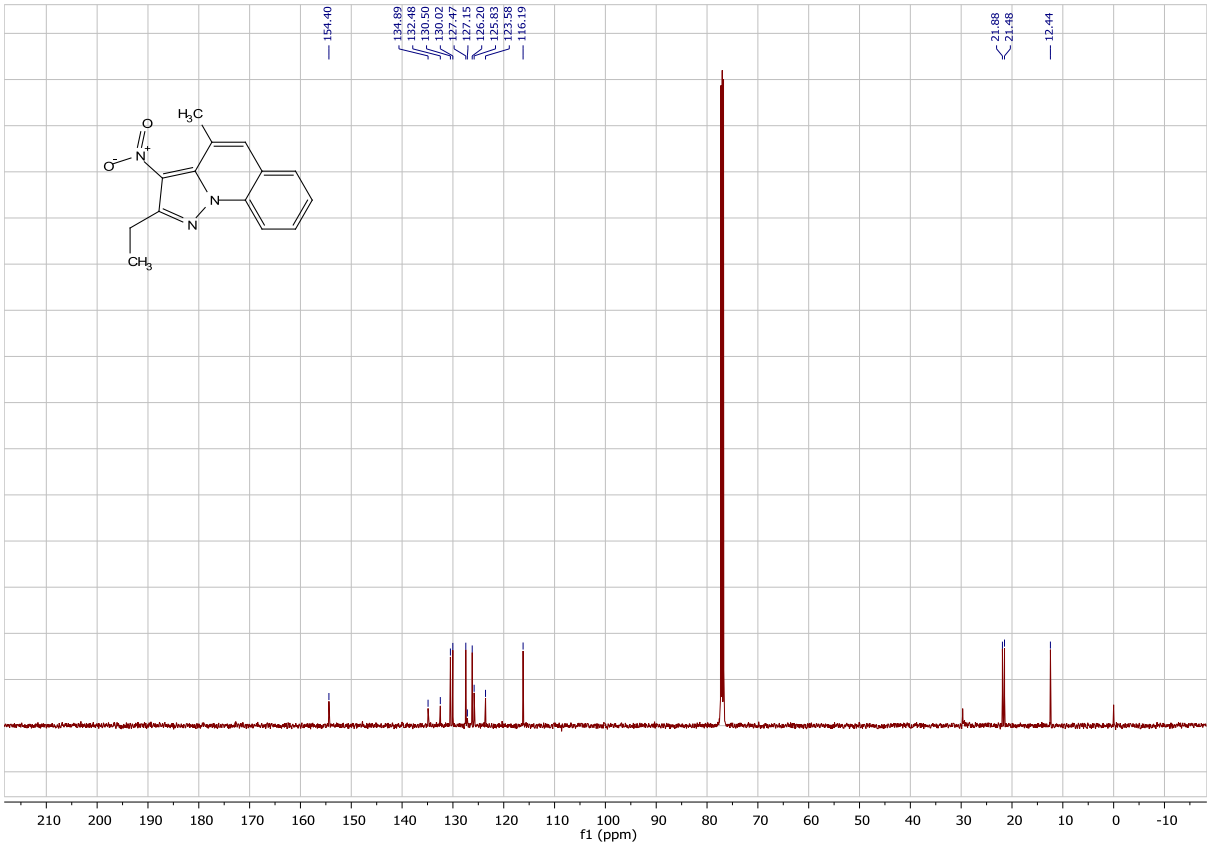
^{13}C NMR of **3j**



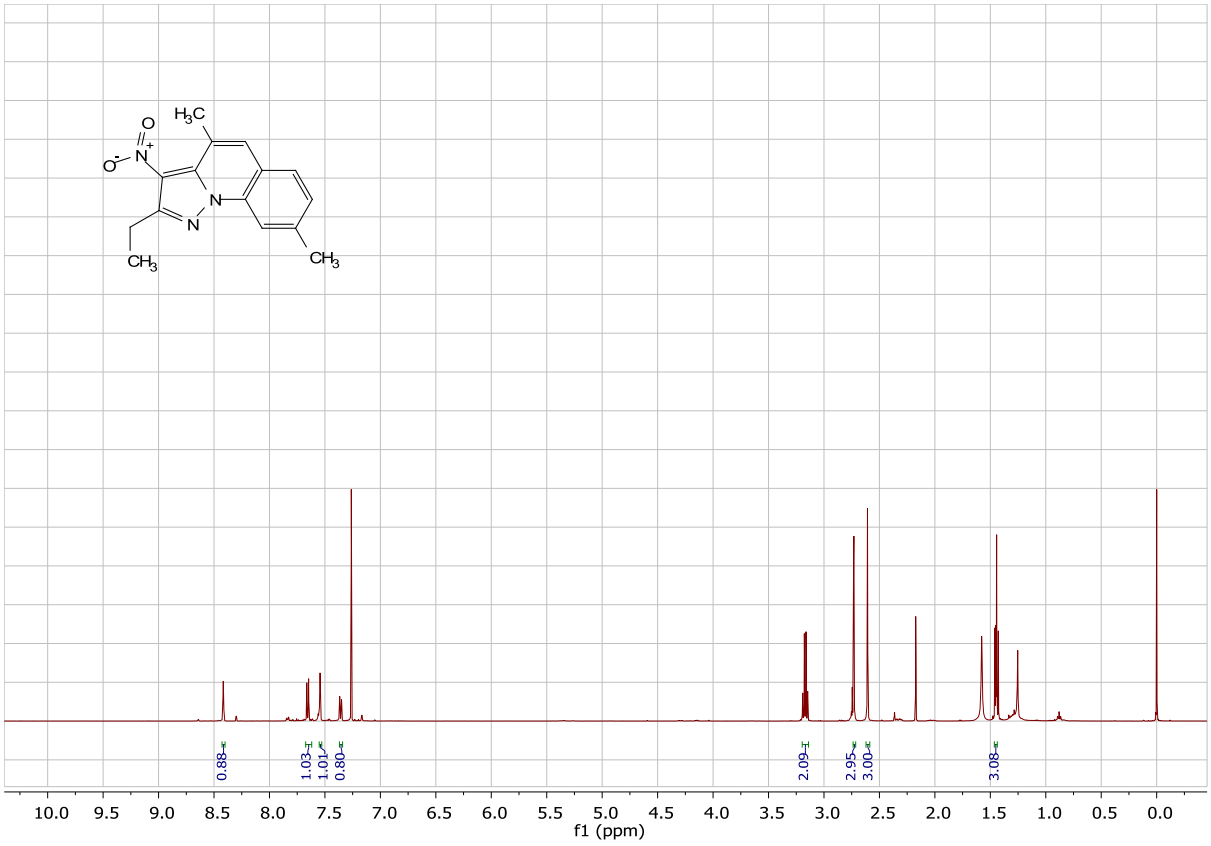
^{1}H NMR of **3k**



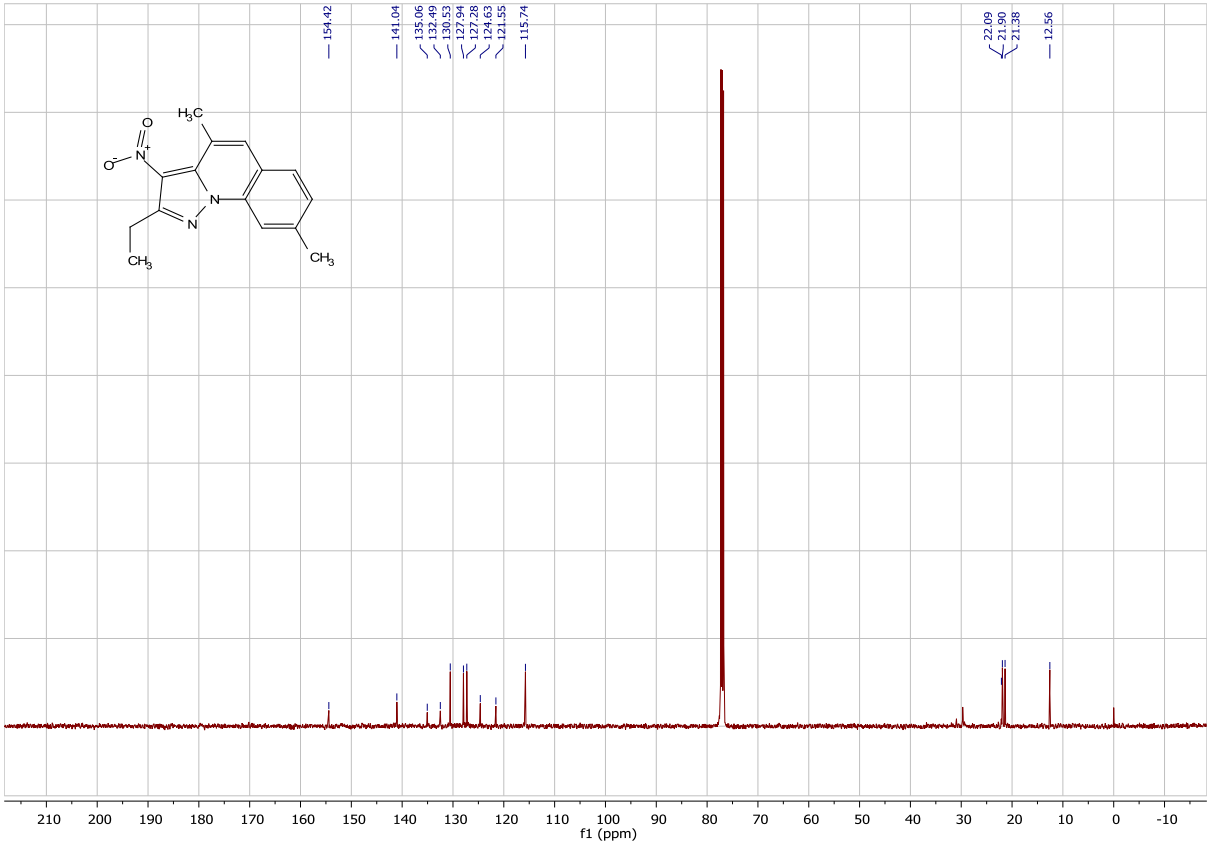
^{13}C NMR of **3k**



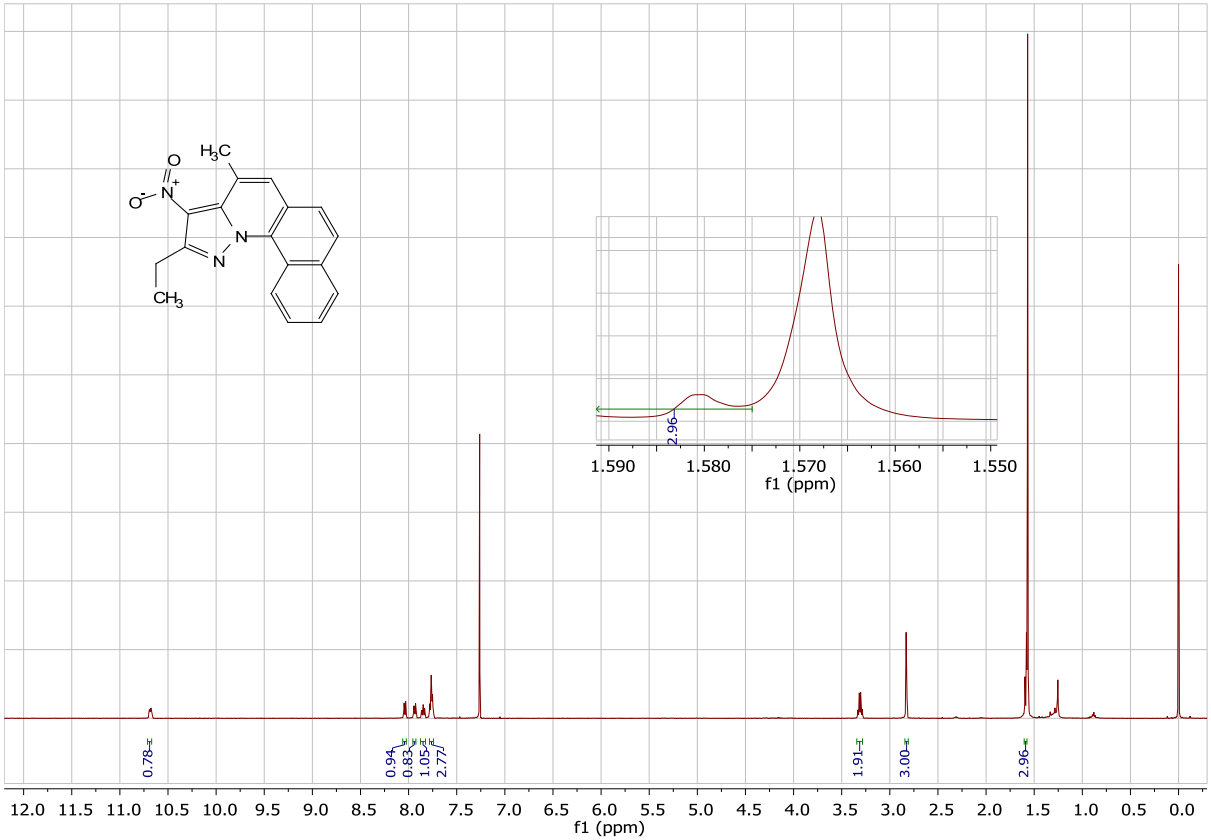
^{1}H NMR of **3l**



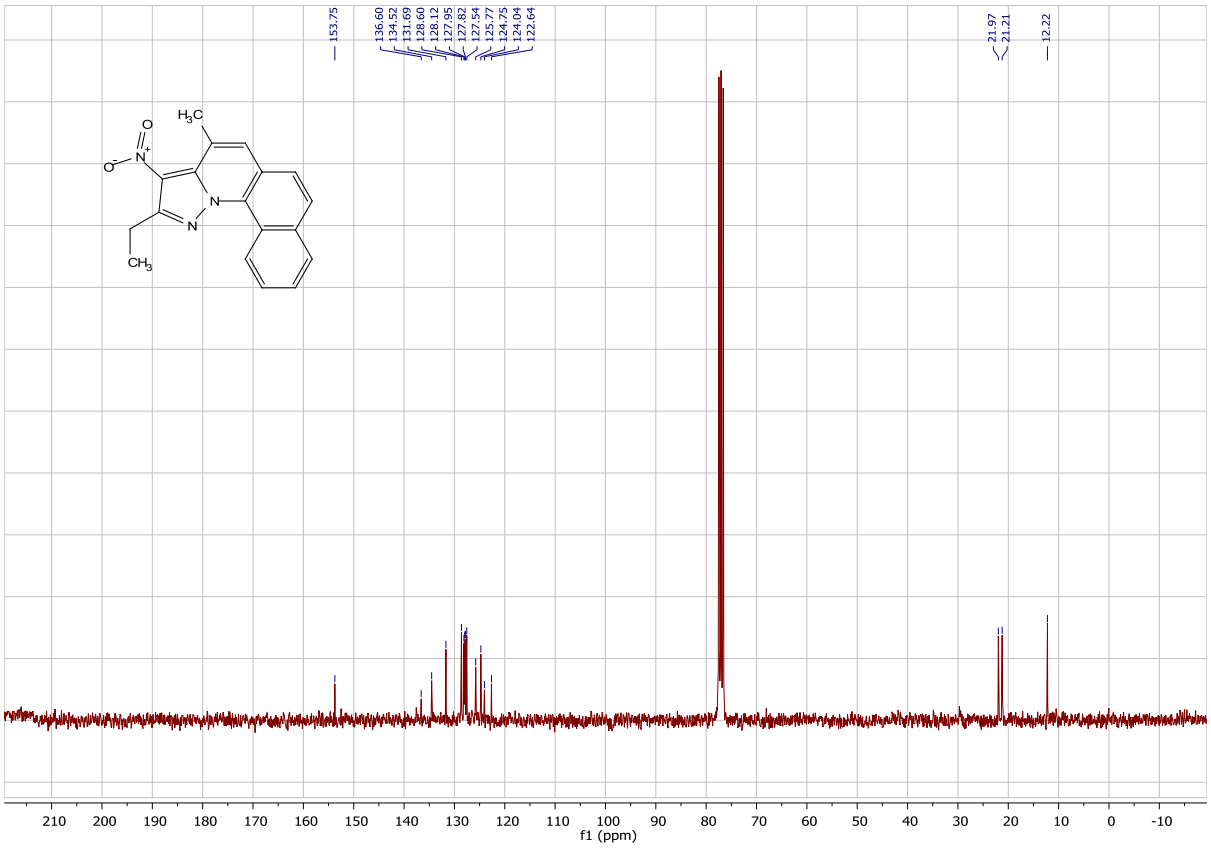
^{13}C NMR of **3l**



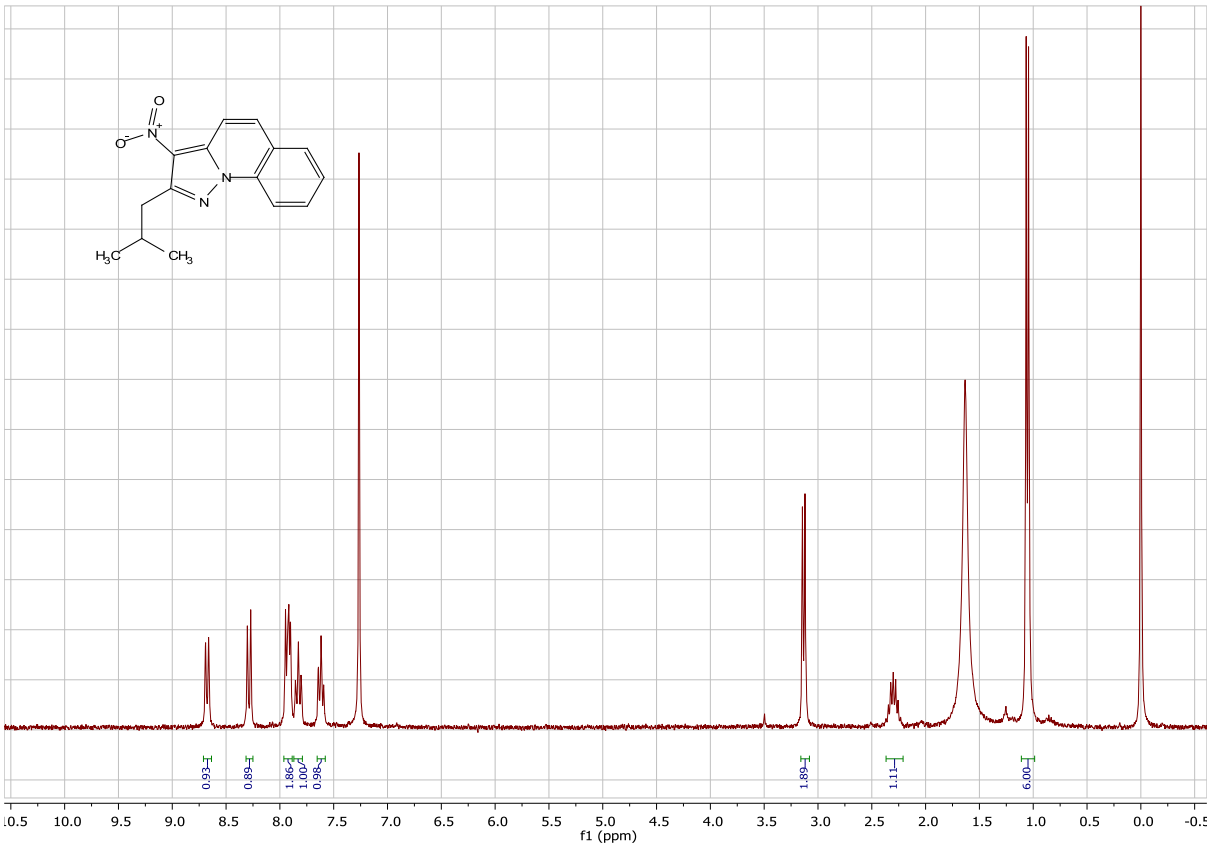
^{1}H NMR of **3m**



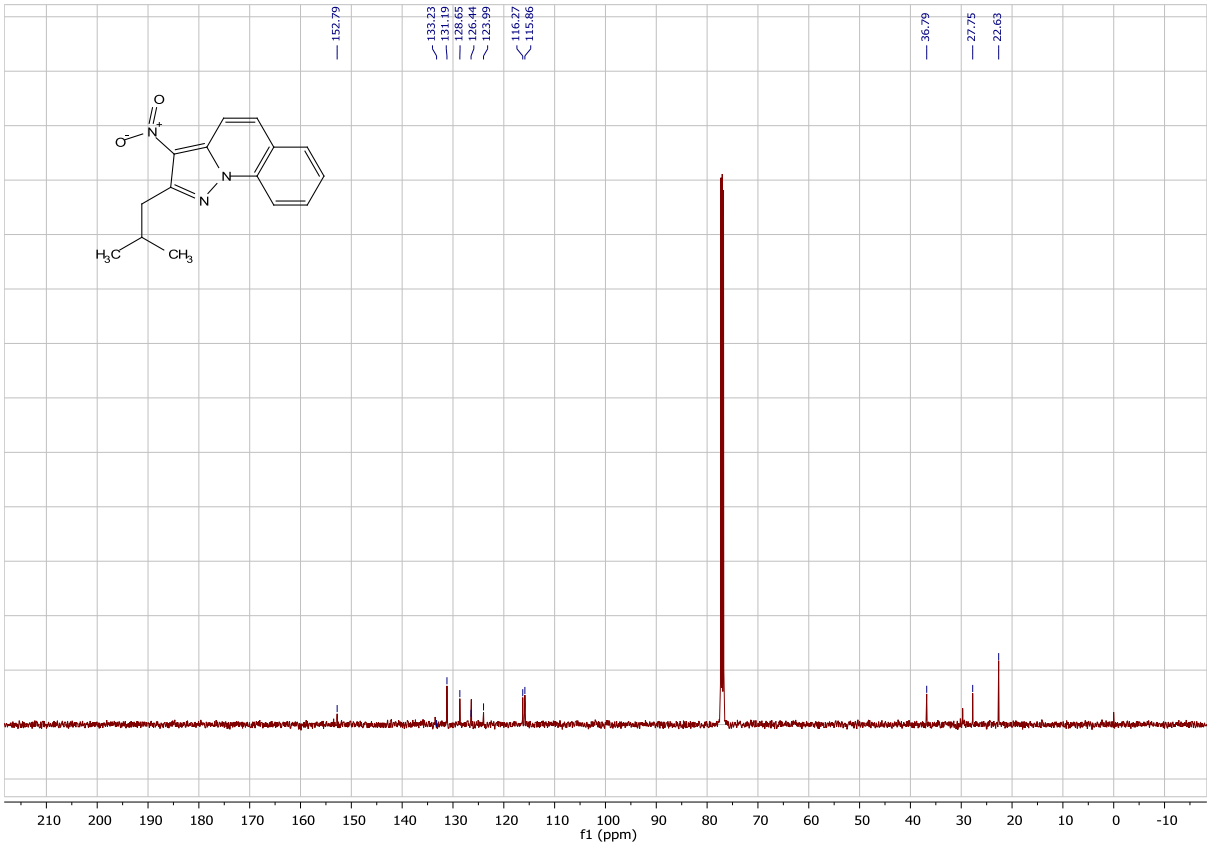
^{13}C NMR of **3m**



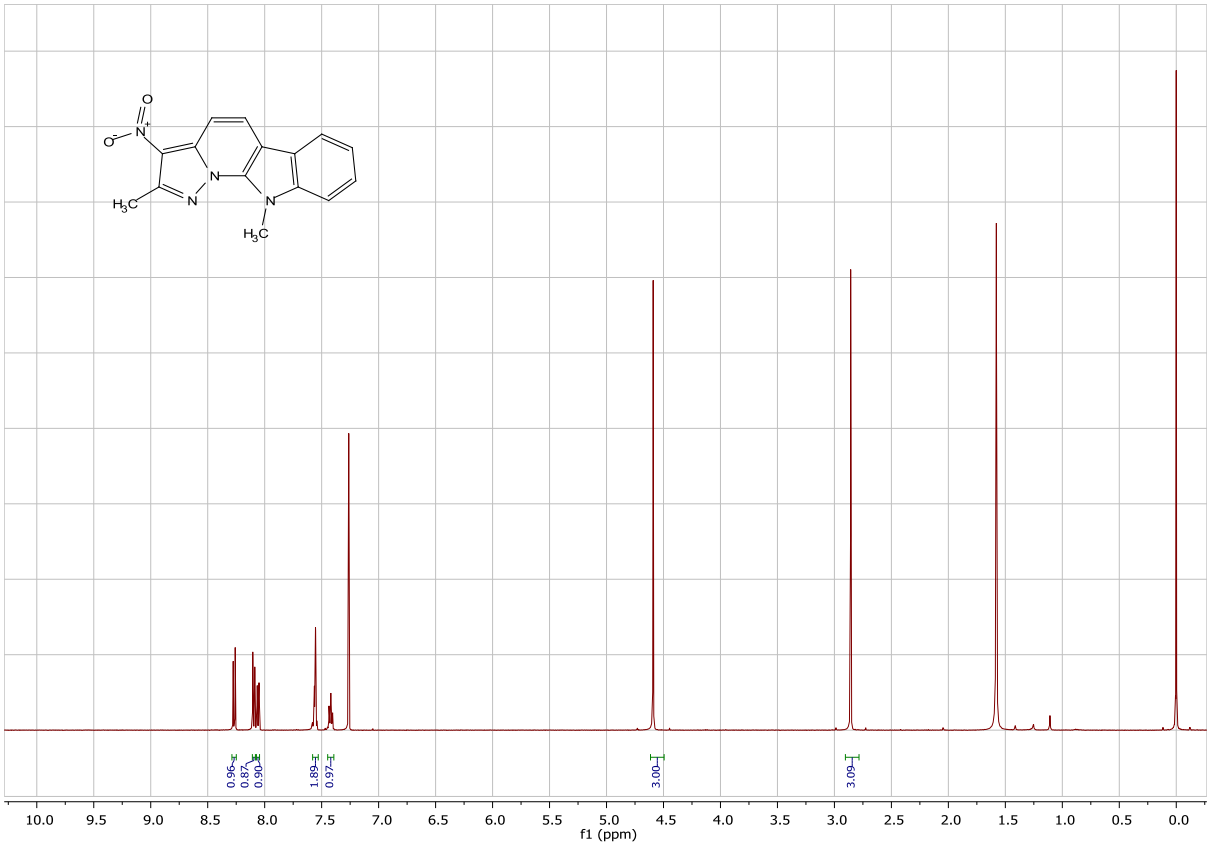
^{1}H NMR of **3n**



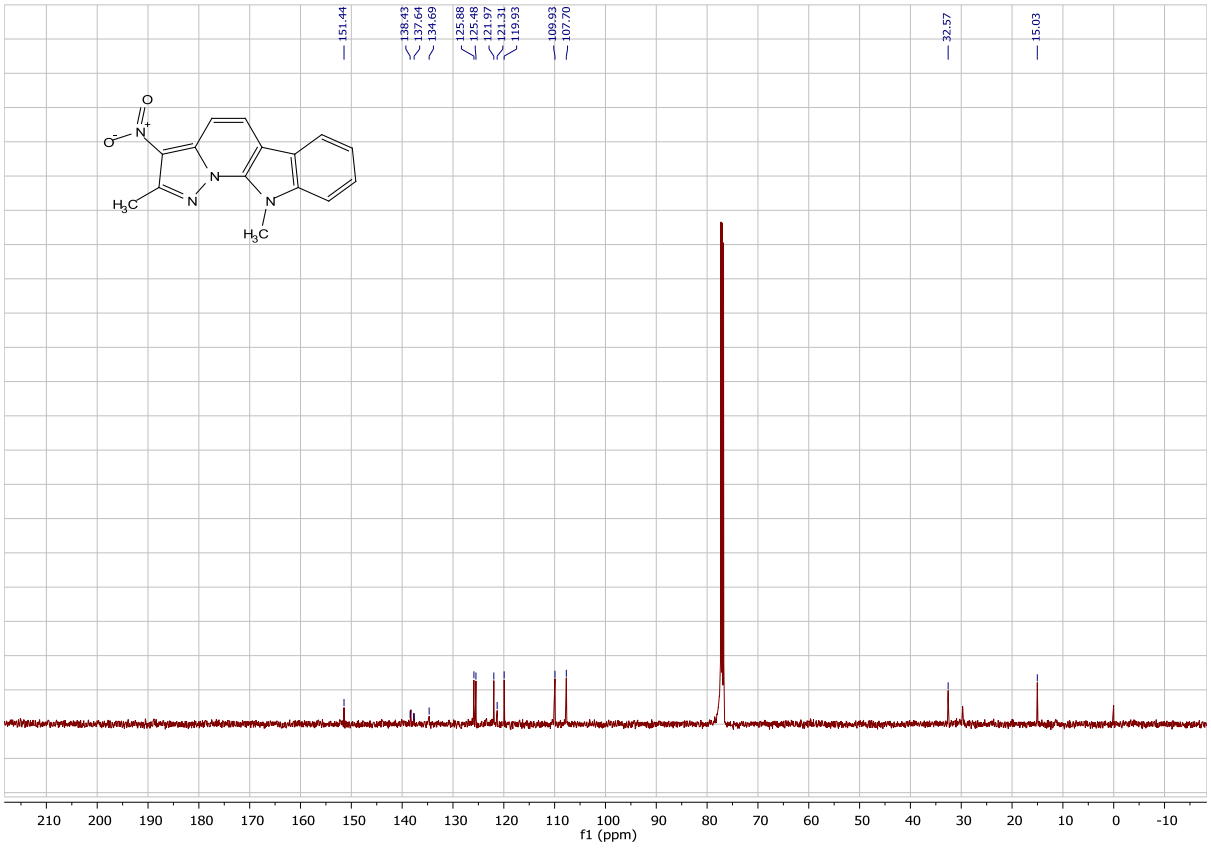
^{13}C NMR of **3n**



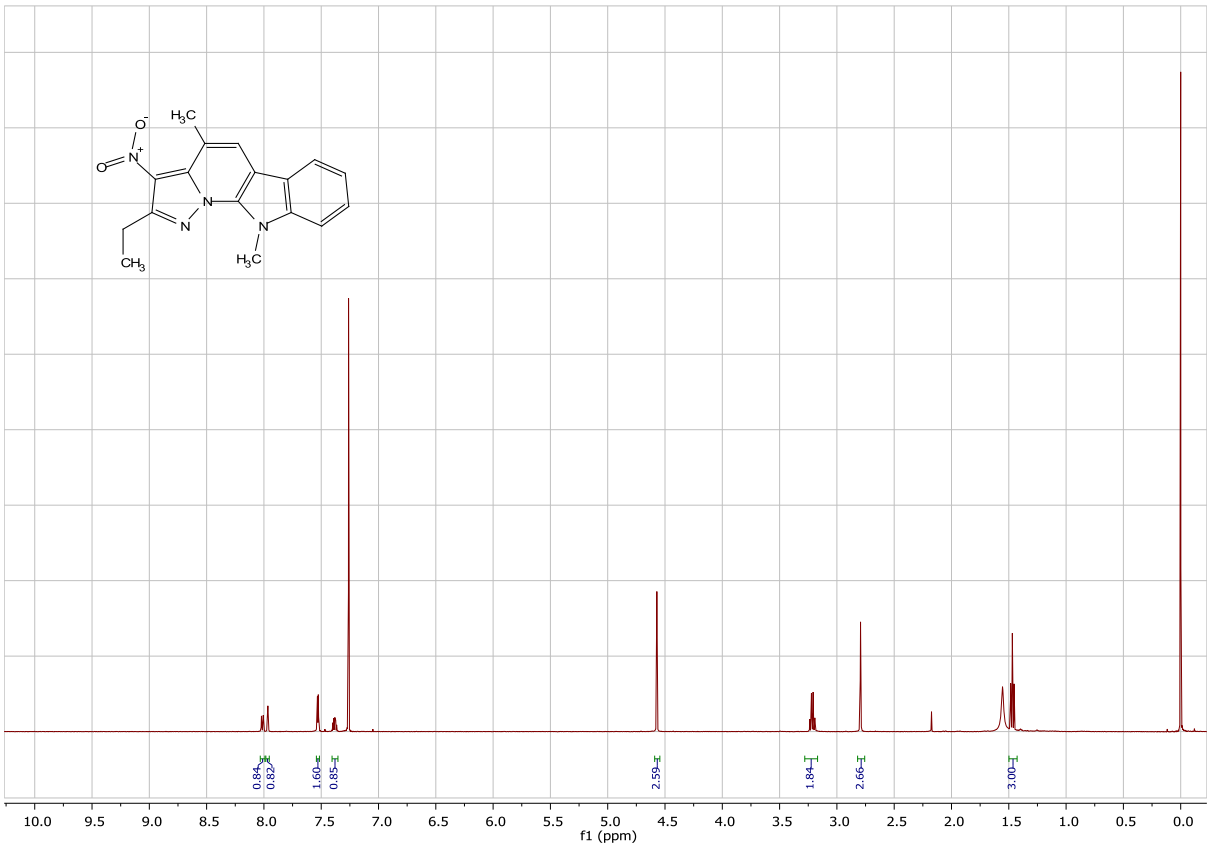
^{1}H NMR of **5a**



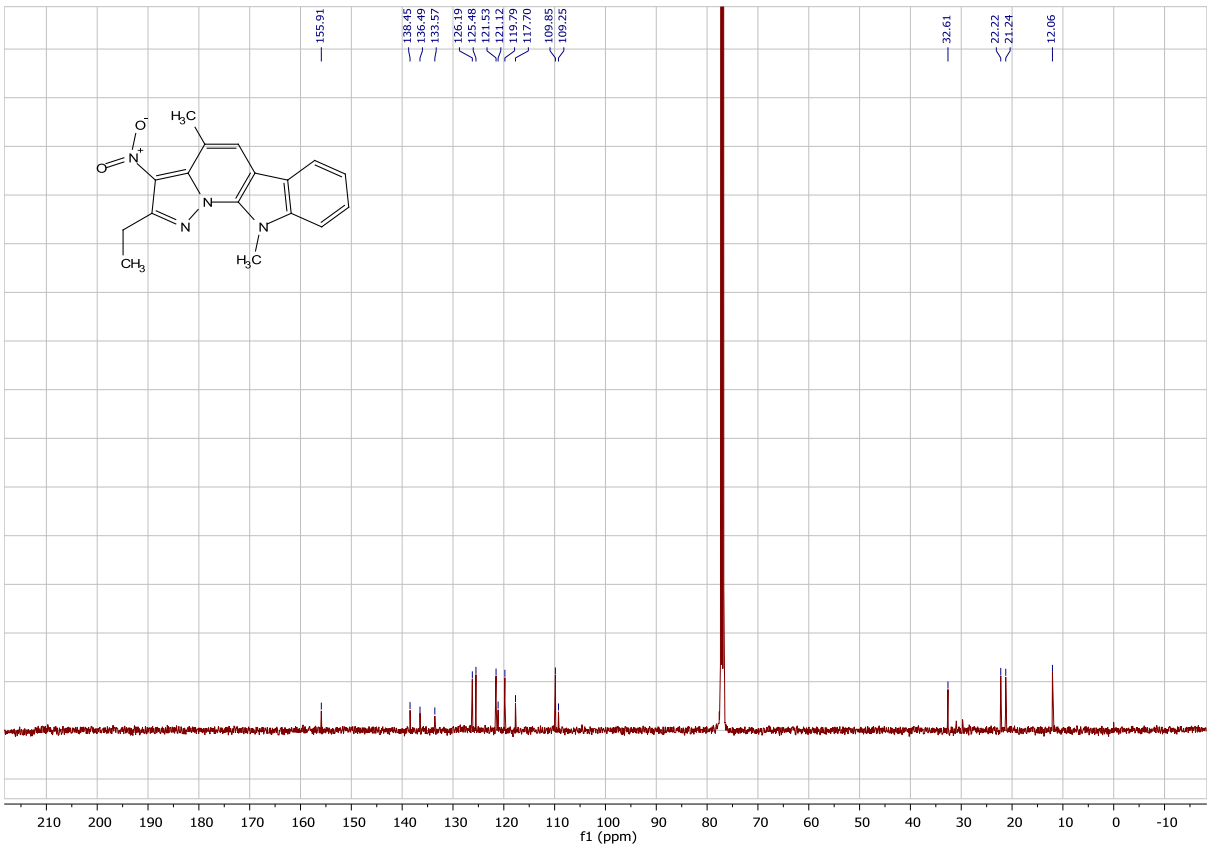
^{13}C NMR of **5a**



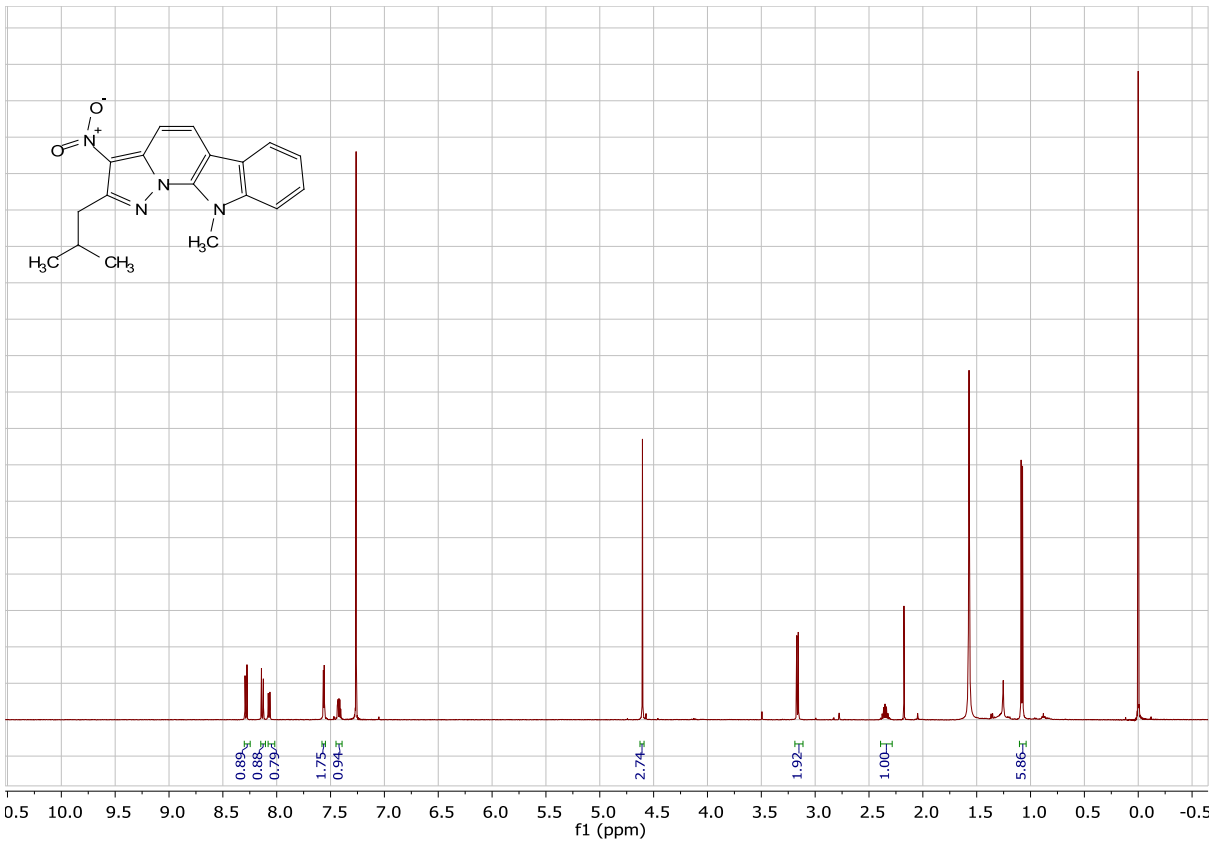
^{1}H NMR of **5b**



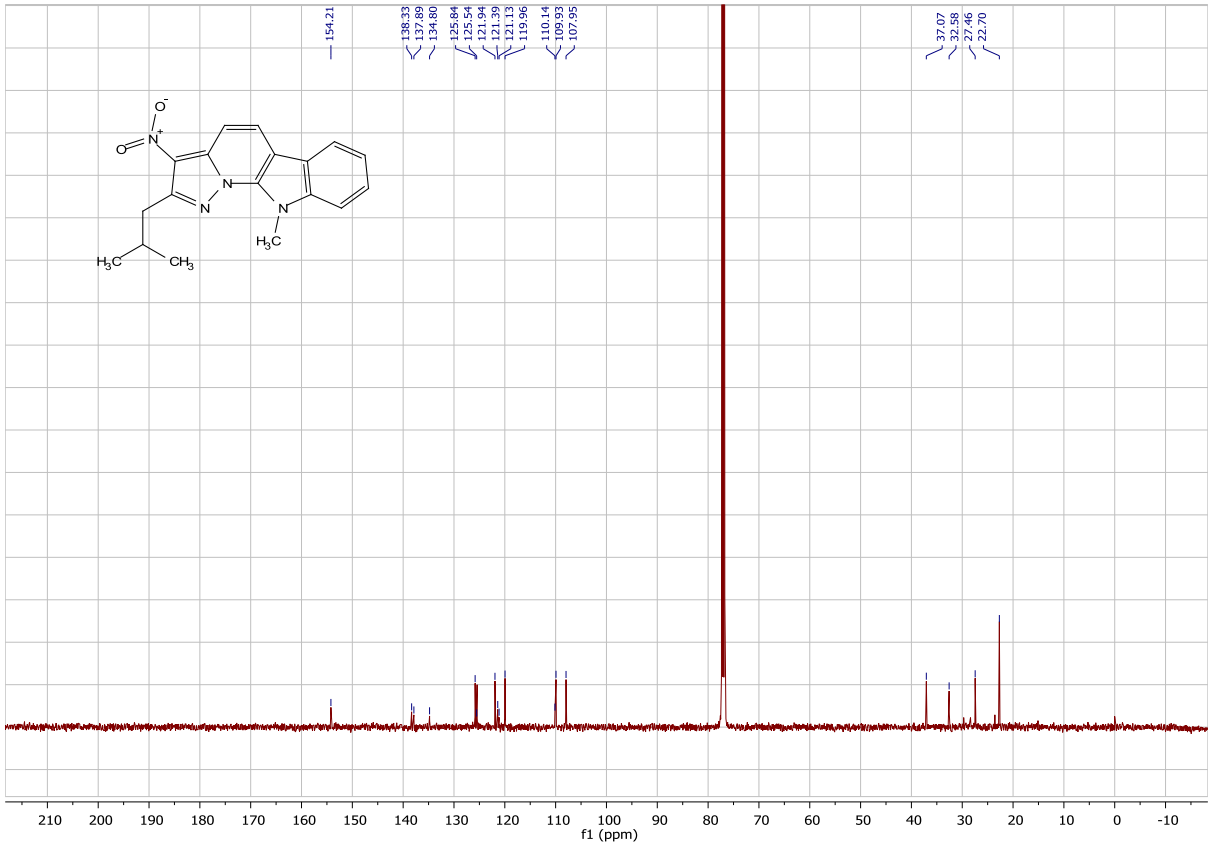
^{13}C NMR of **5b**



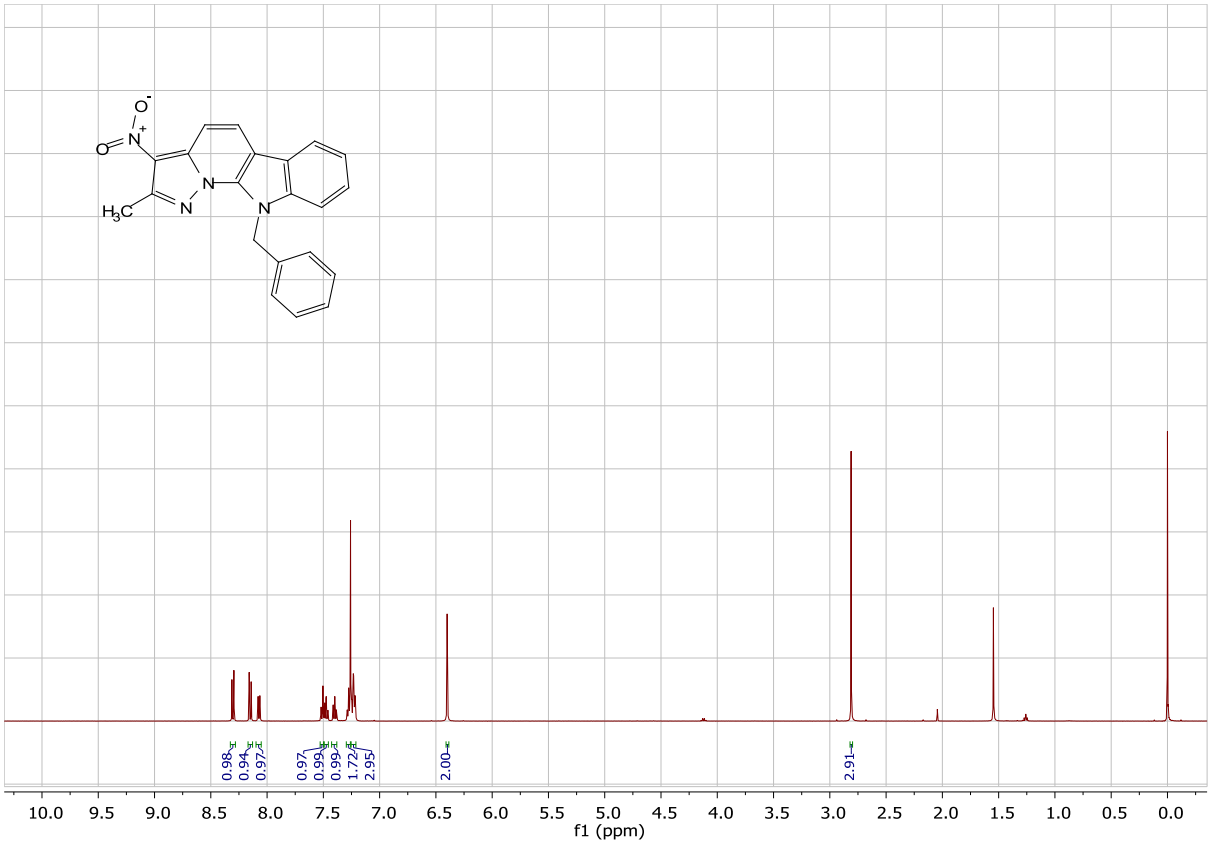
^{1}H NMR of **5c**



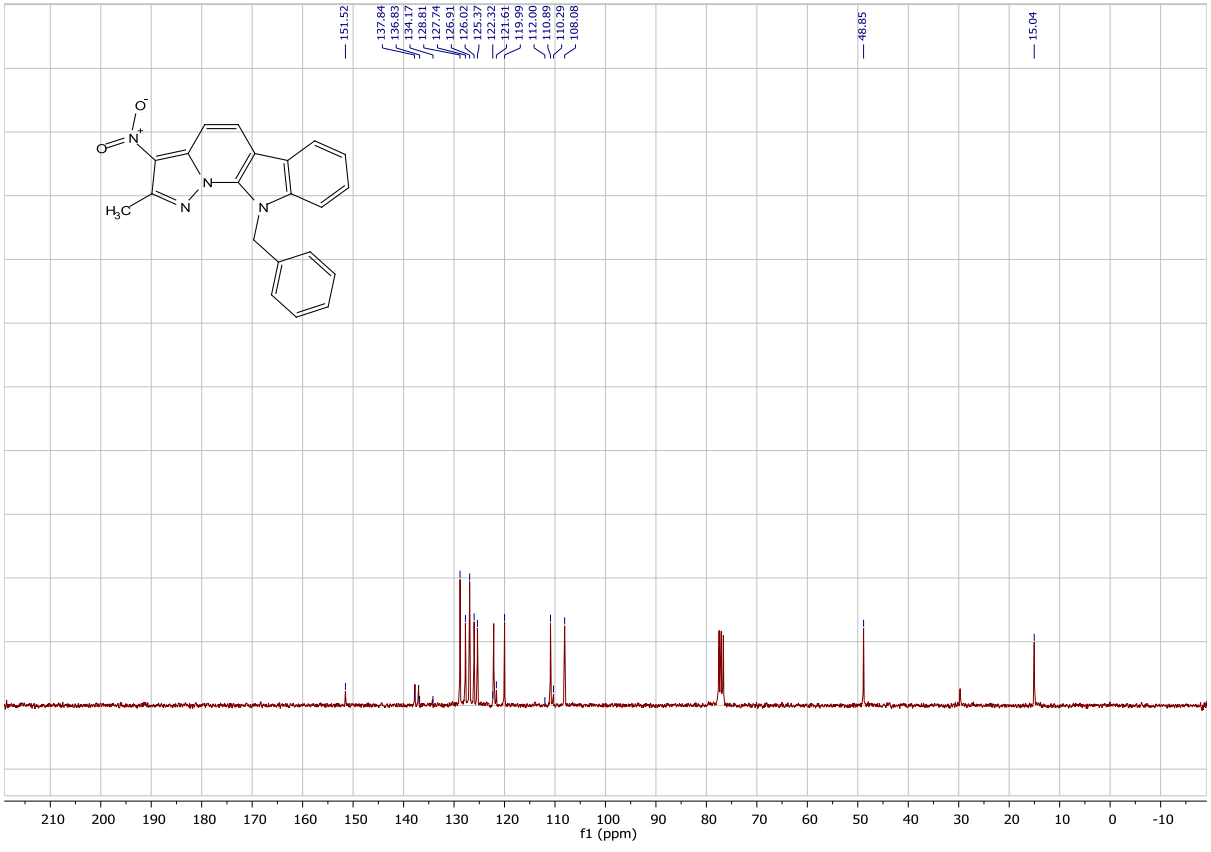
^{13}C NMR of **5c**



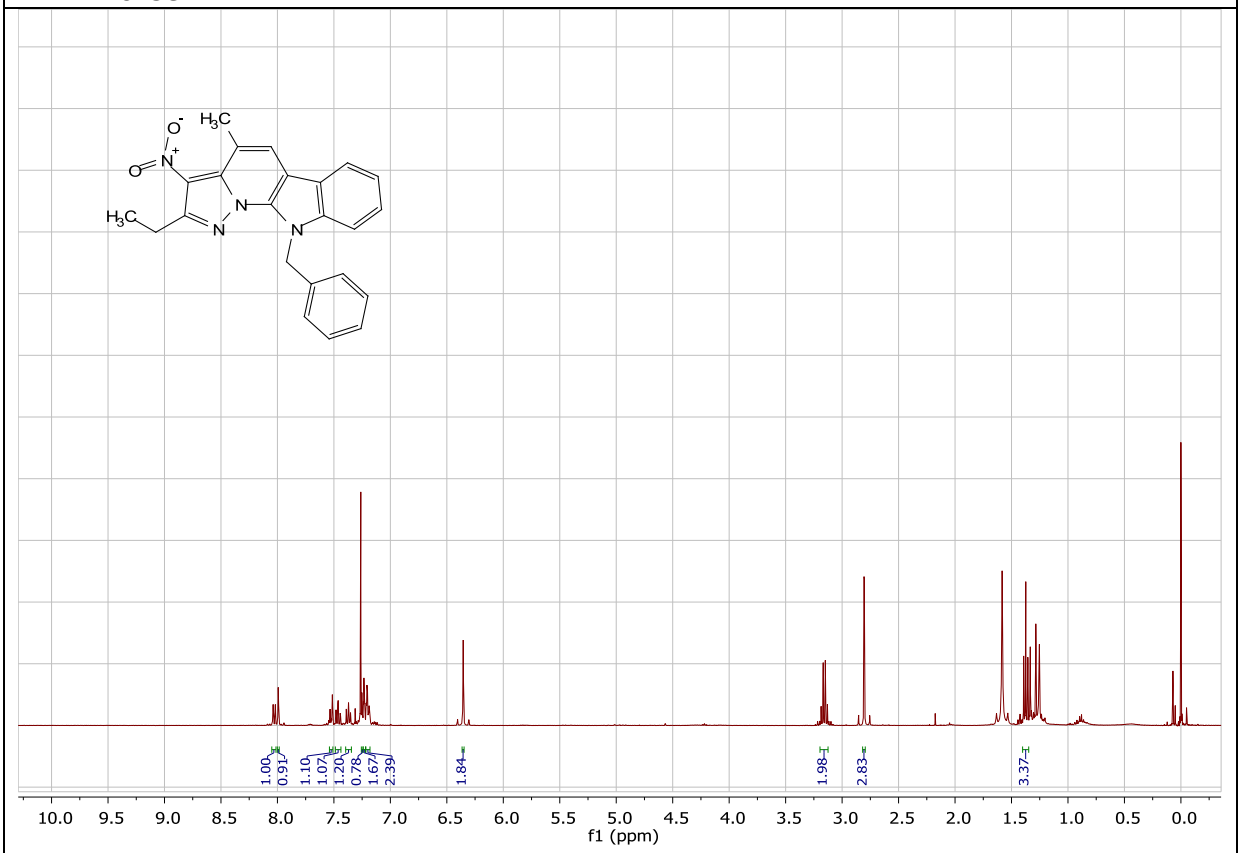
^{1}H NMR of **5d**



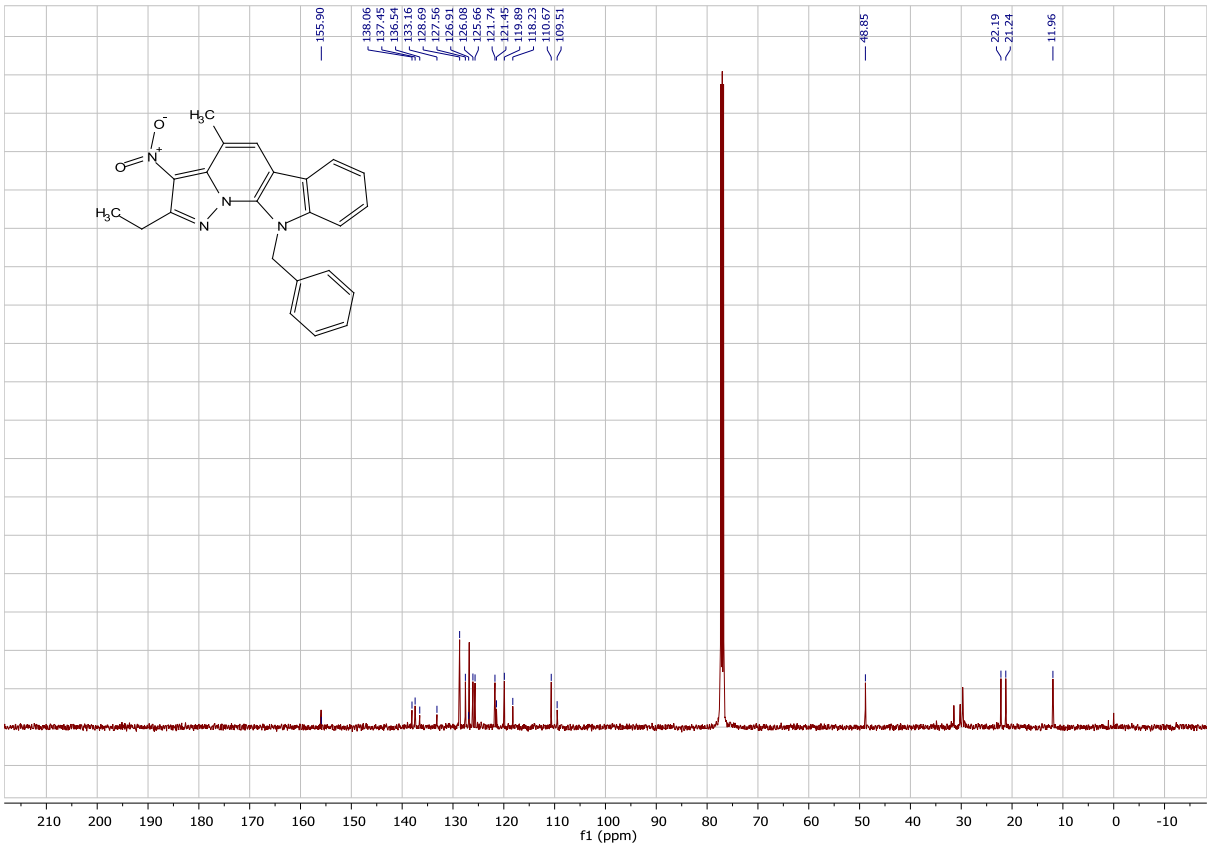
^{13}C NMR of **5e**



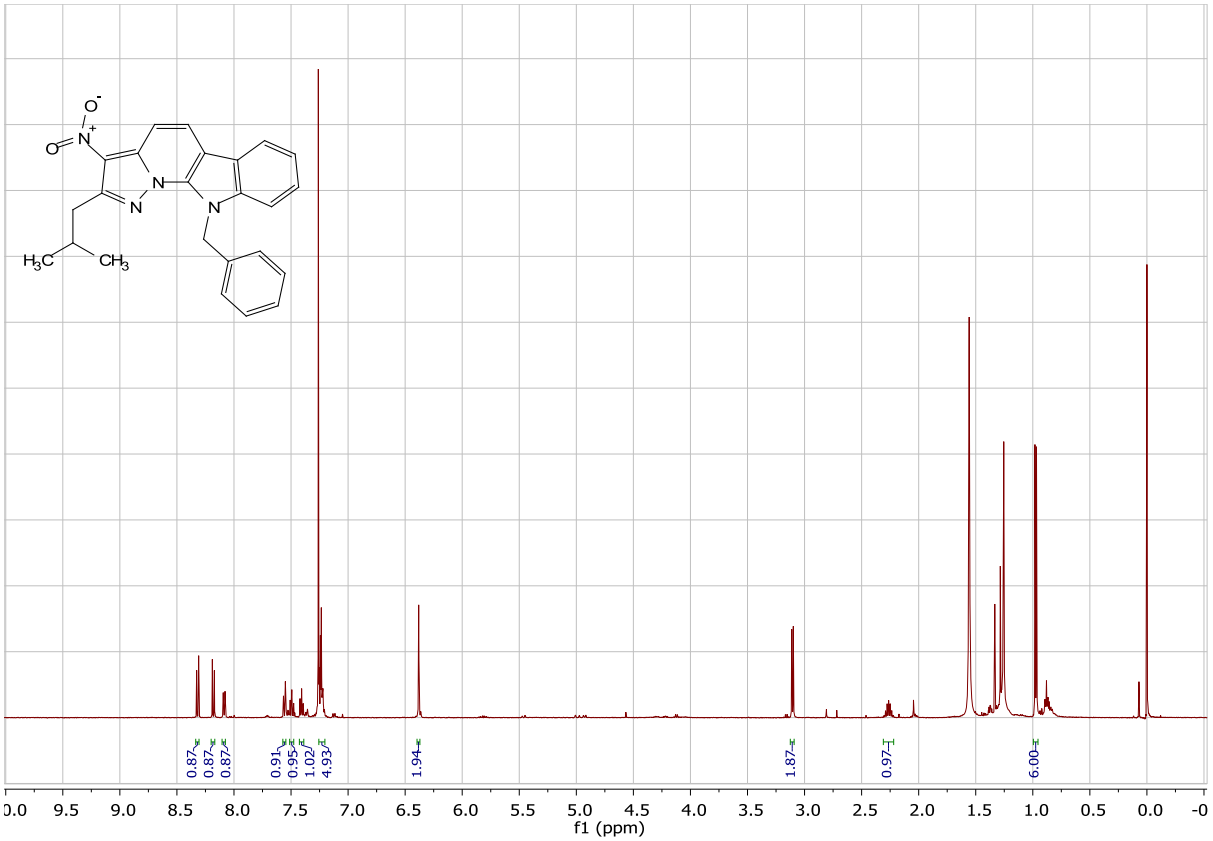
^{1}H NMR of **5e**



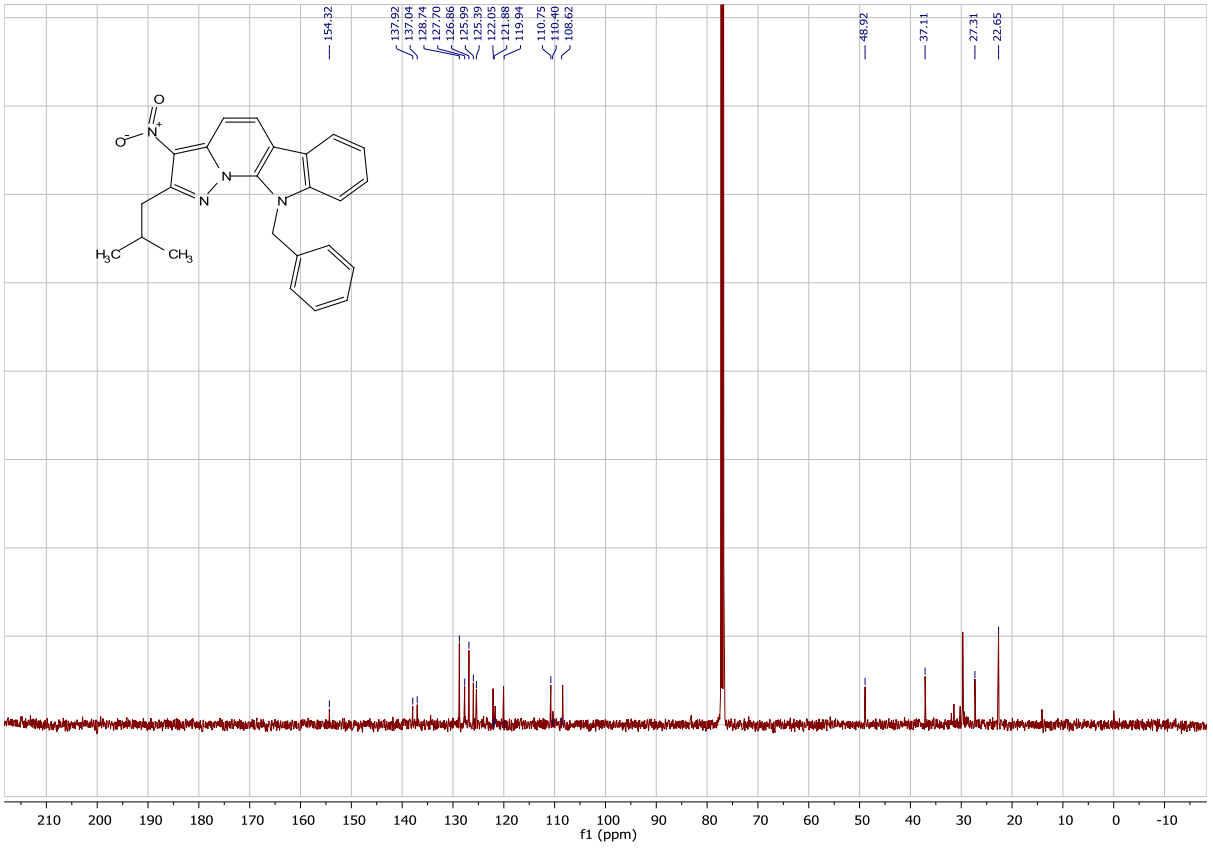
^{13}C NMR of **5e**



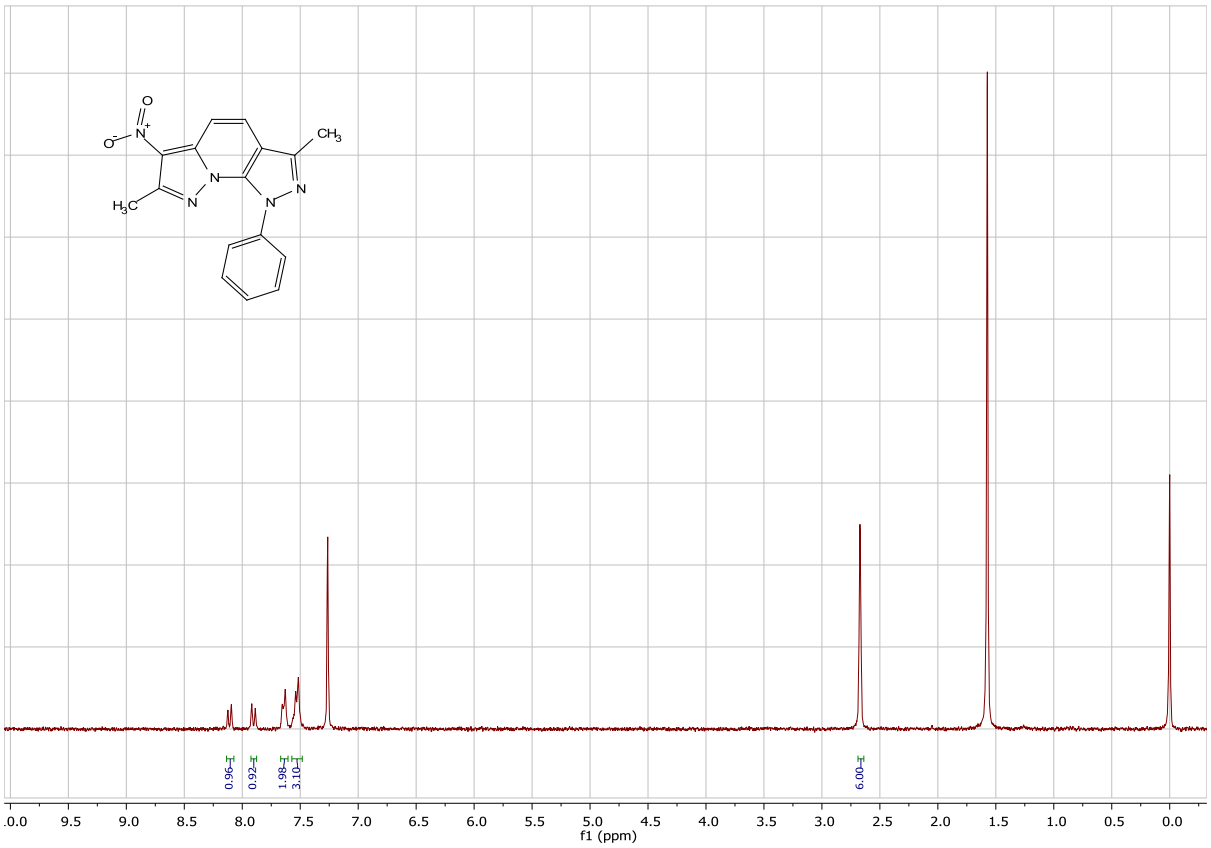
^{1}H NMR of **5f**



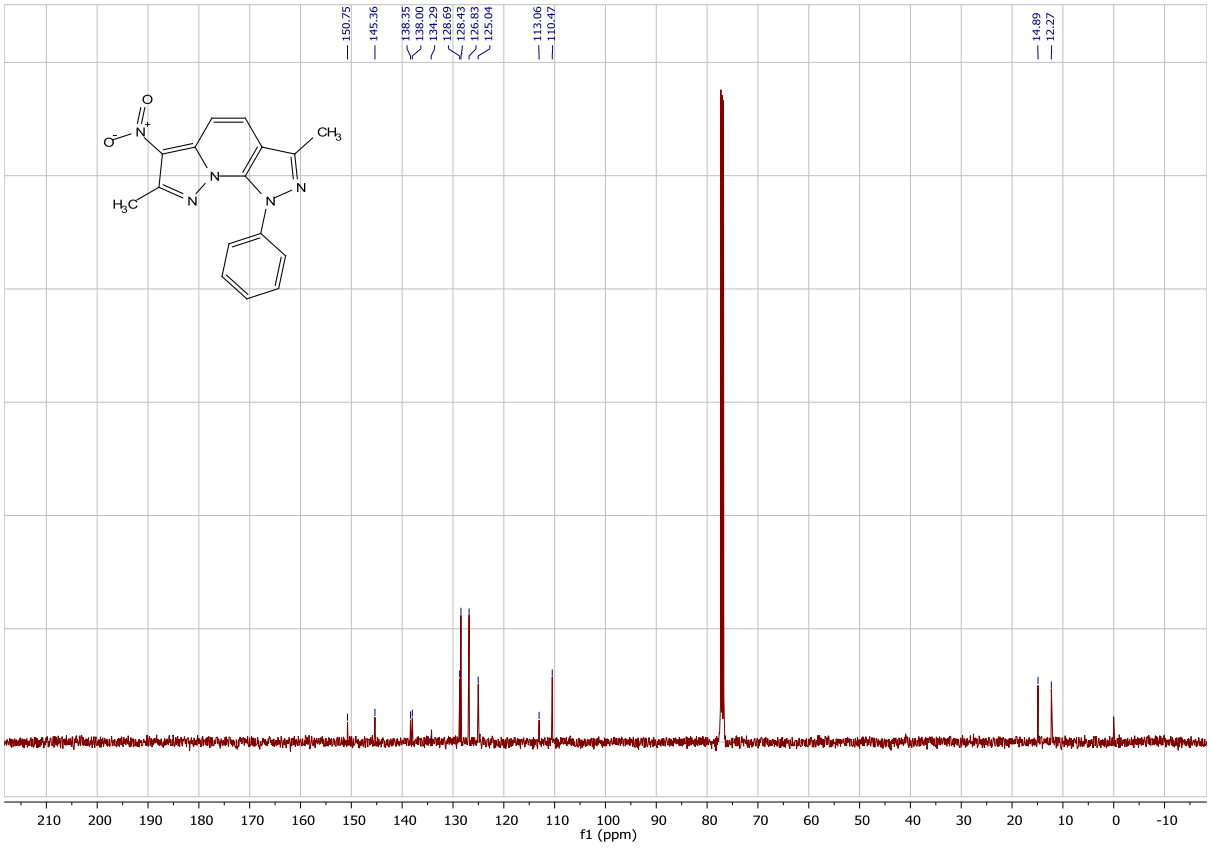
^{13}C NMR of **5f**



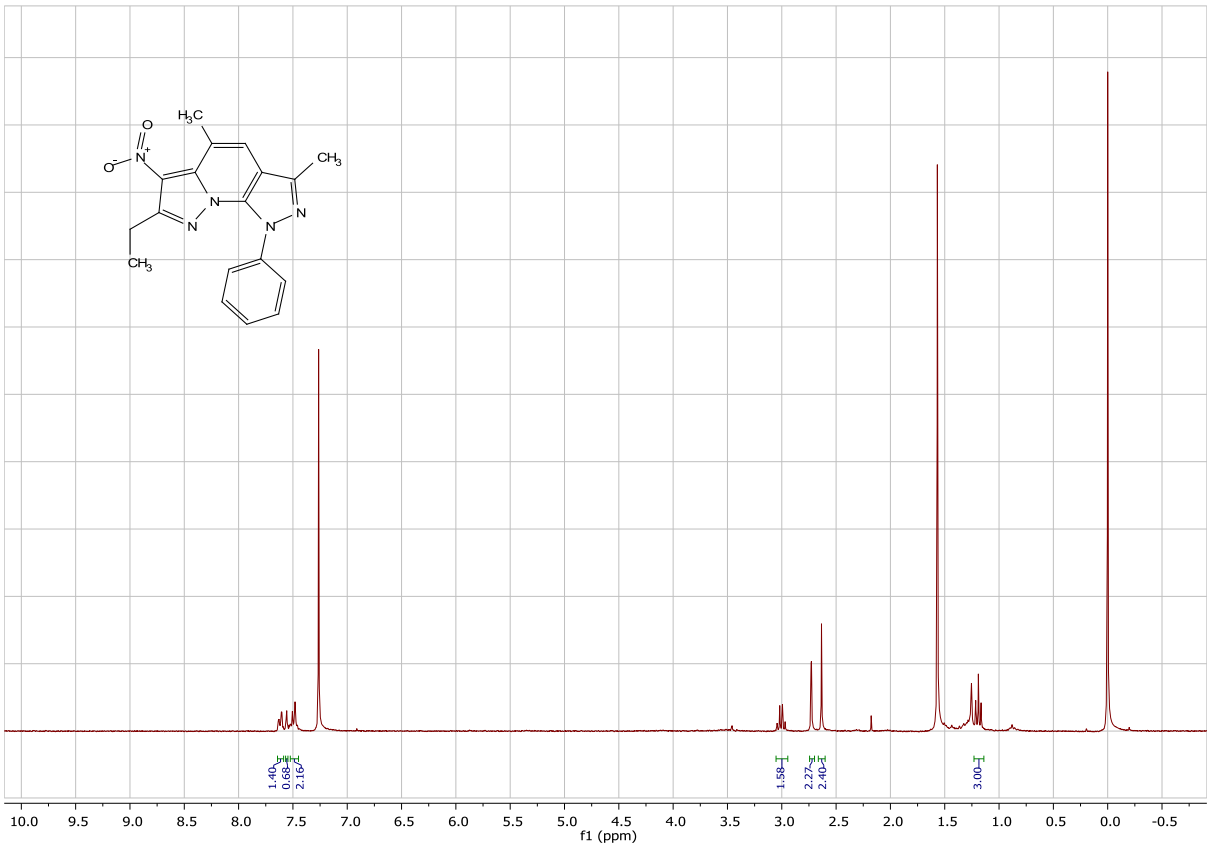
^{1}H NMR of **5g**



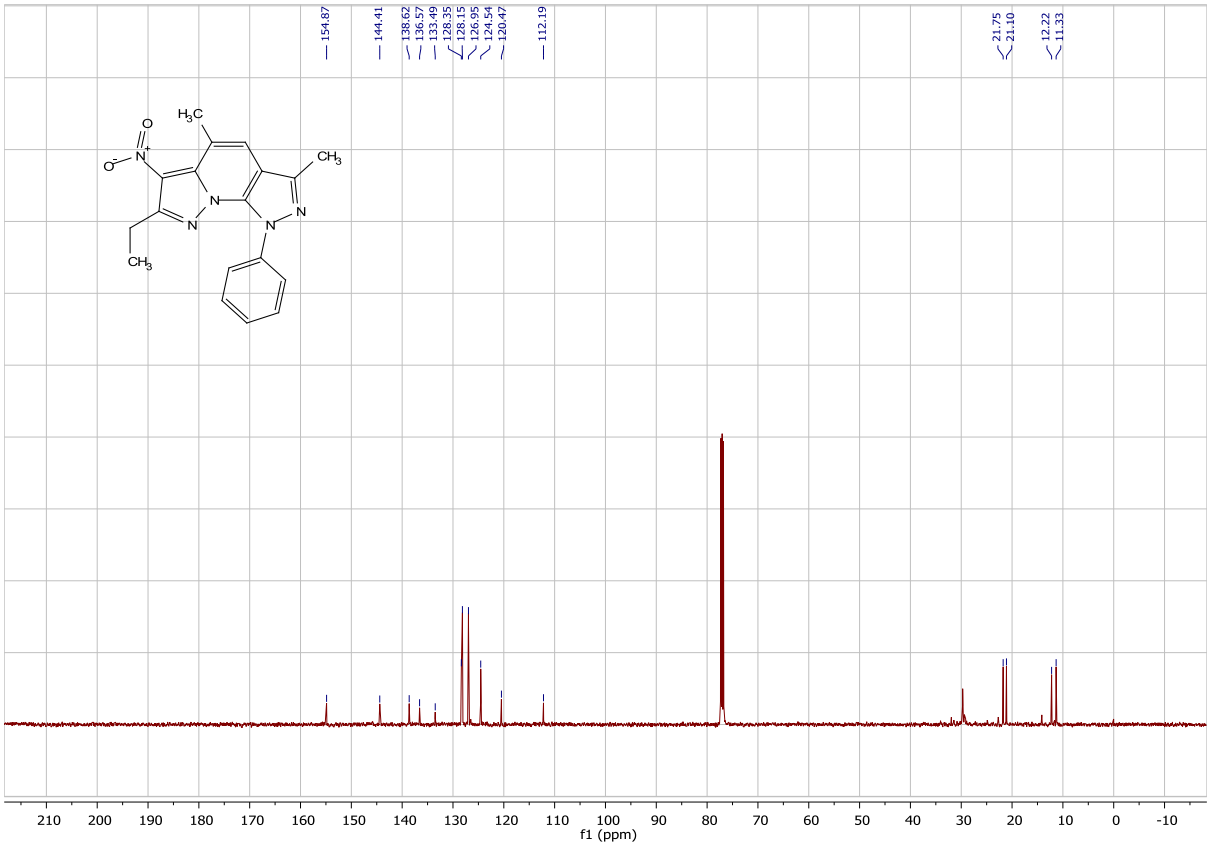
^{13}C NMR of **5g**



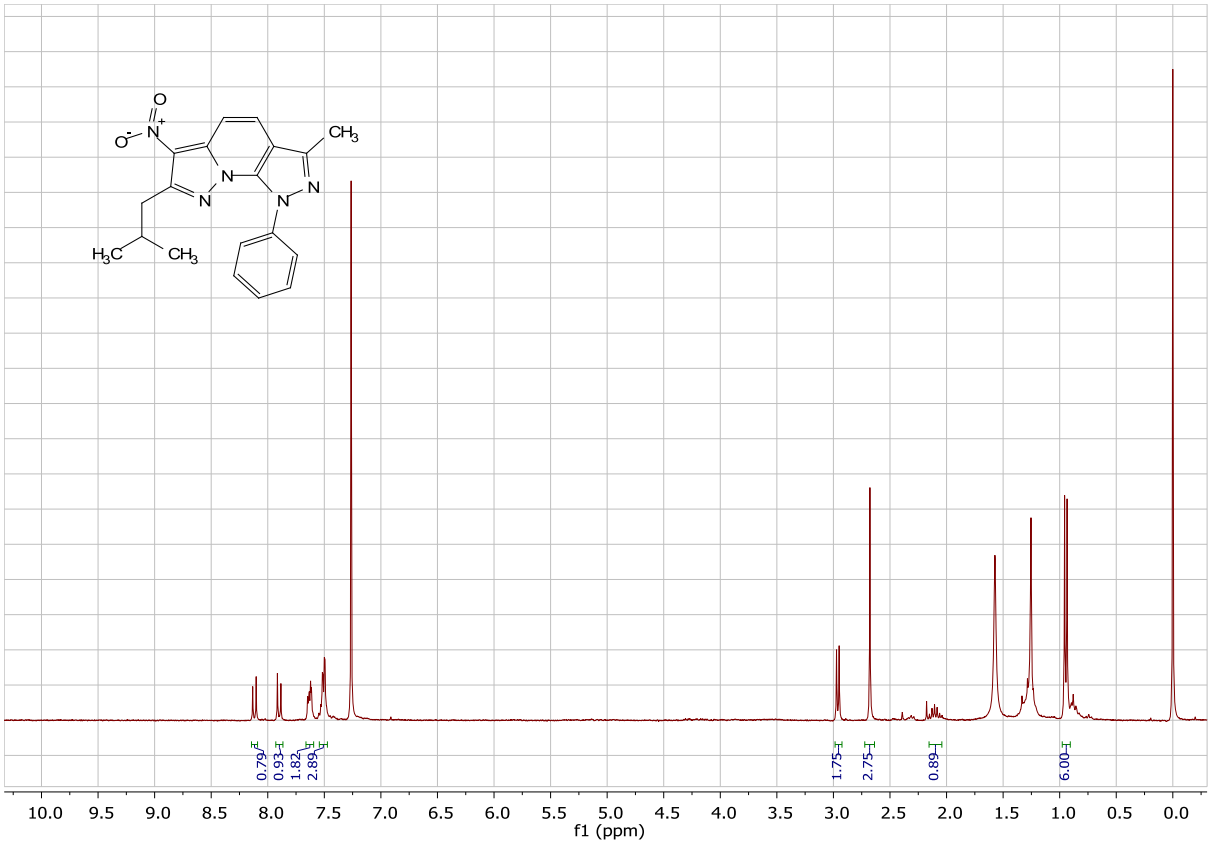
^{1}H NMR of **5h**



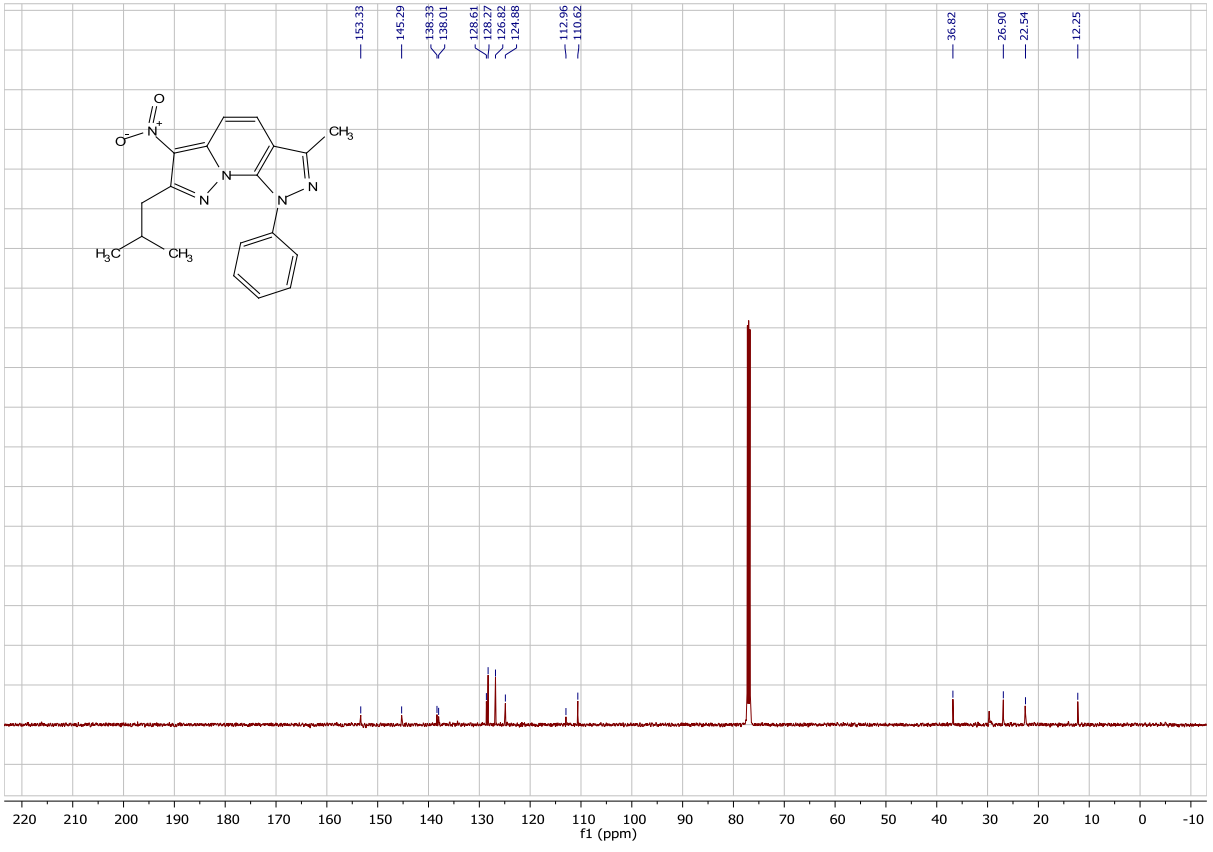
^{13}C NMR of **5h**



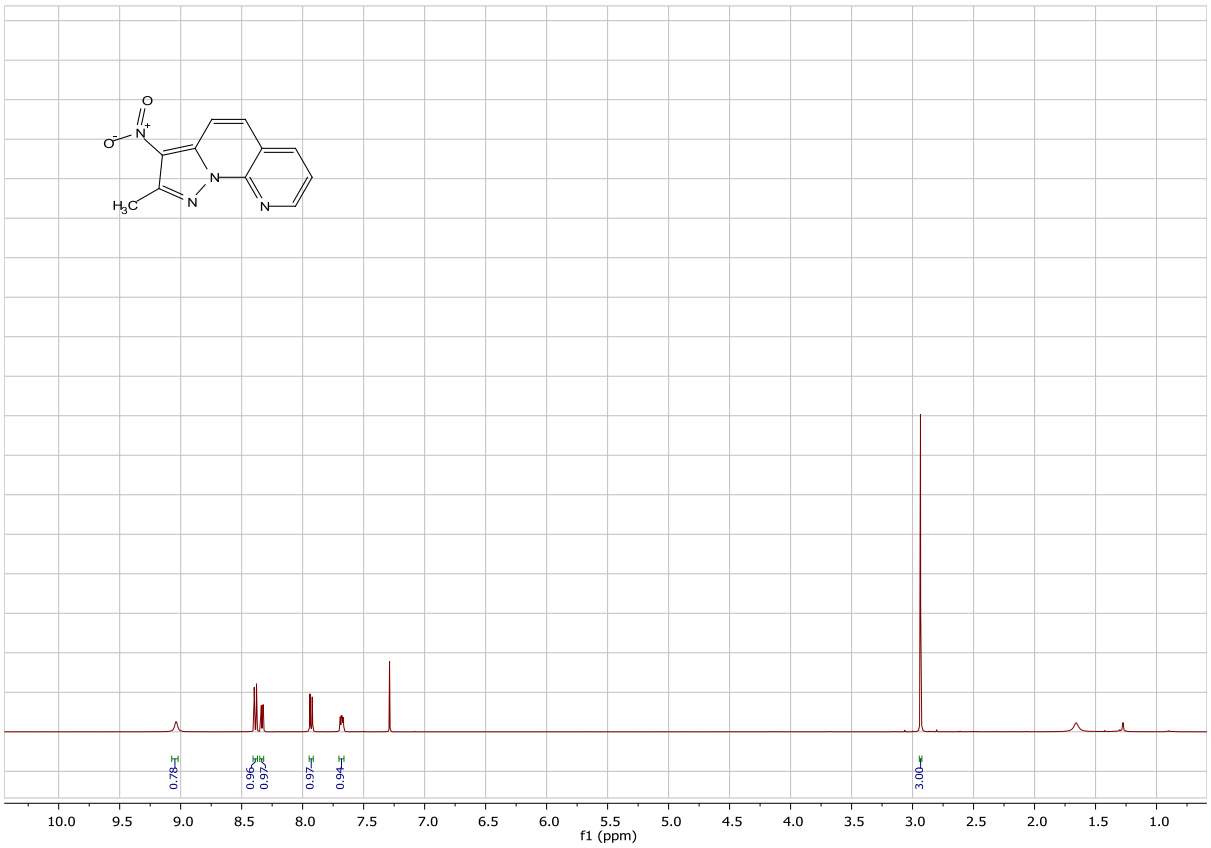
^{1}H NMR of **5i**



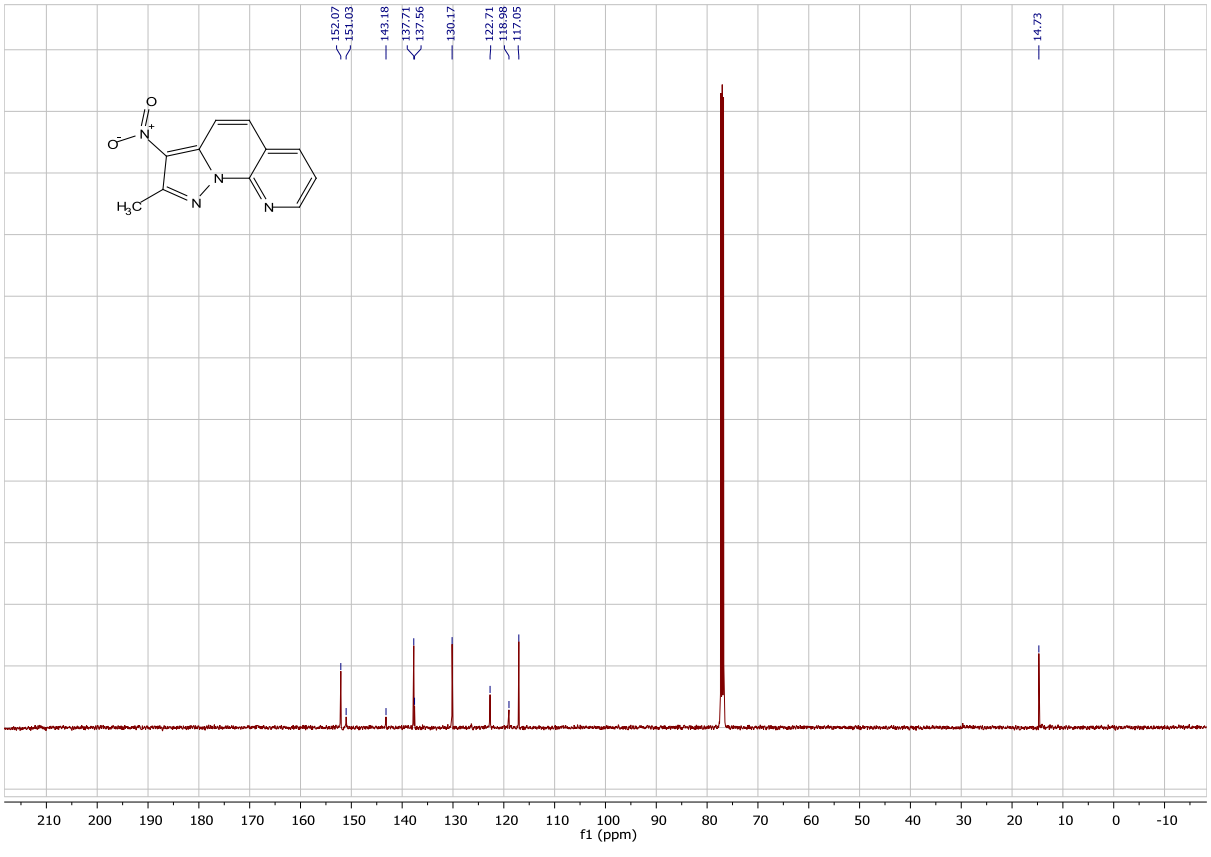
^{13}C NMR of **5i**



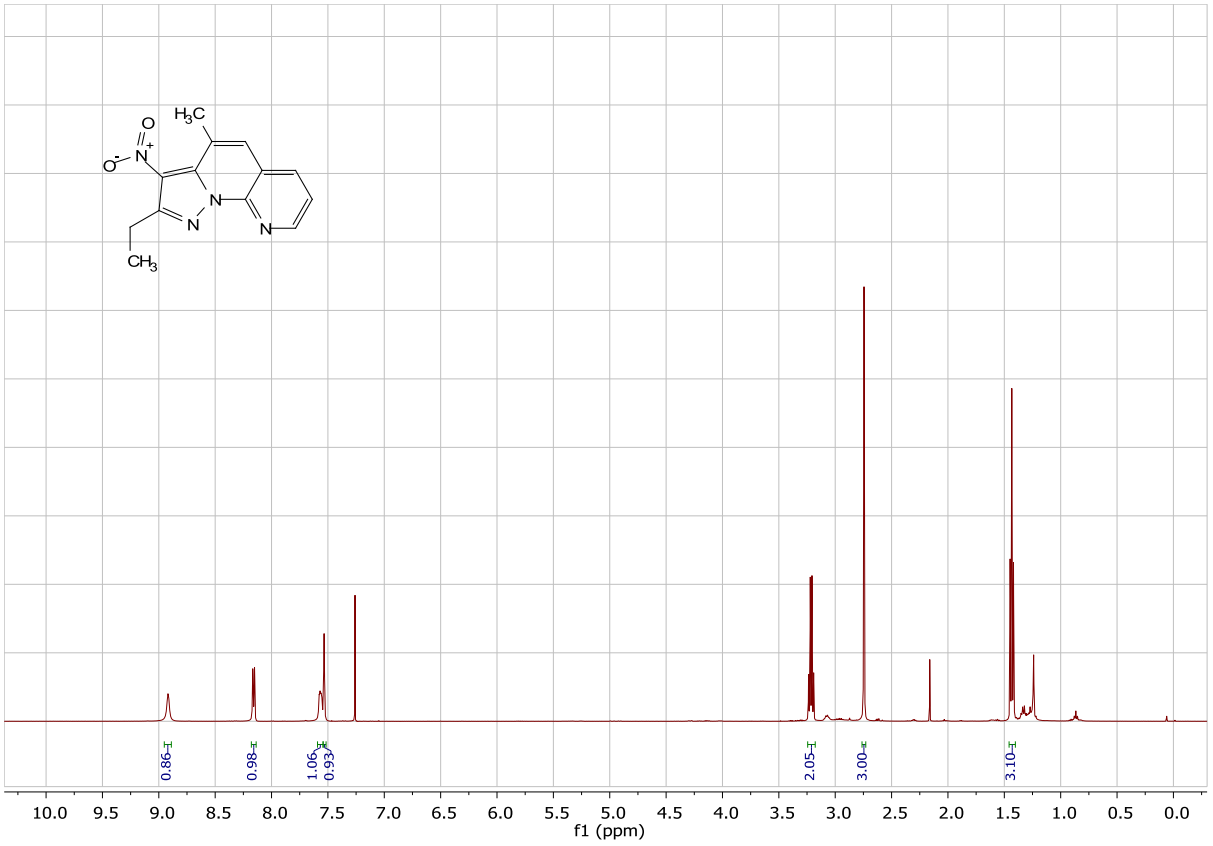
^{1}H NMR of **5j**



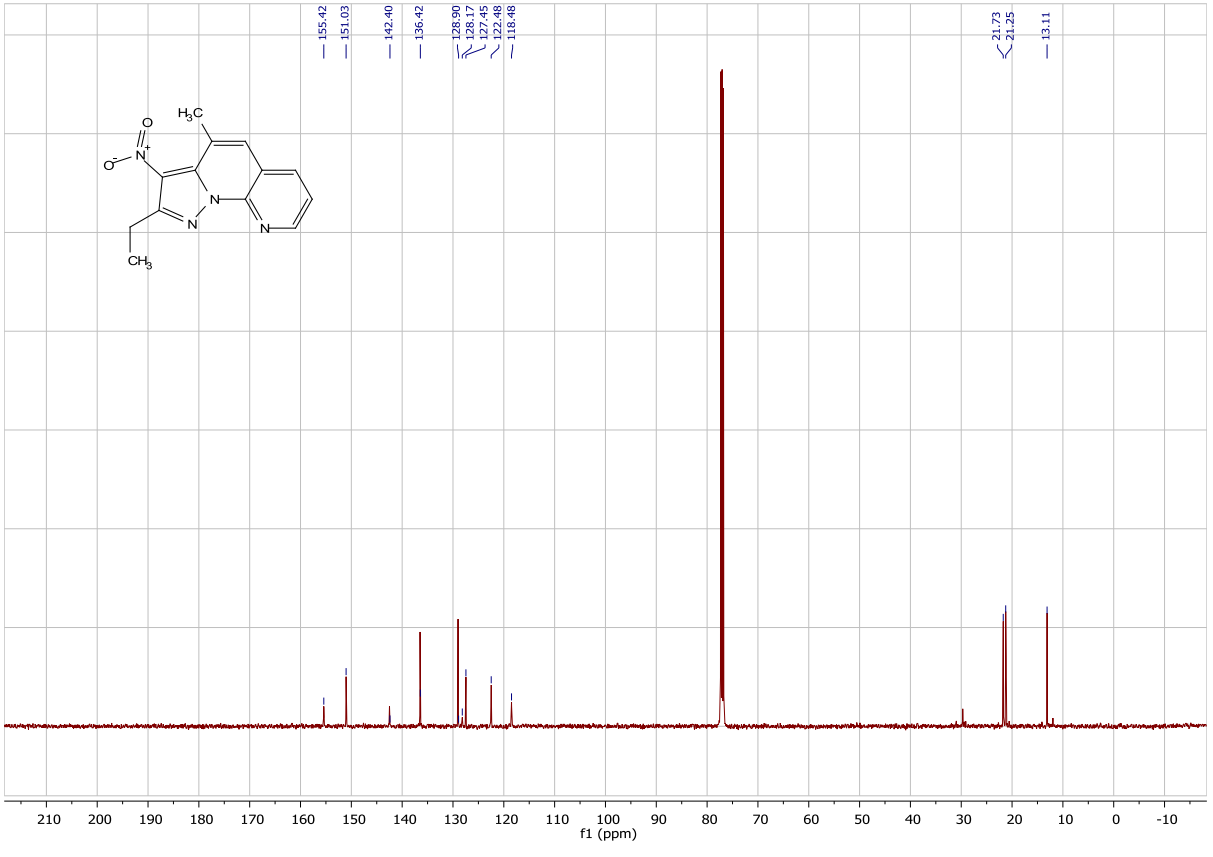
^{13}C NMR of **5j**



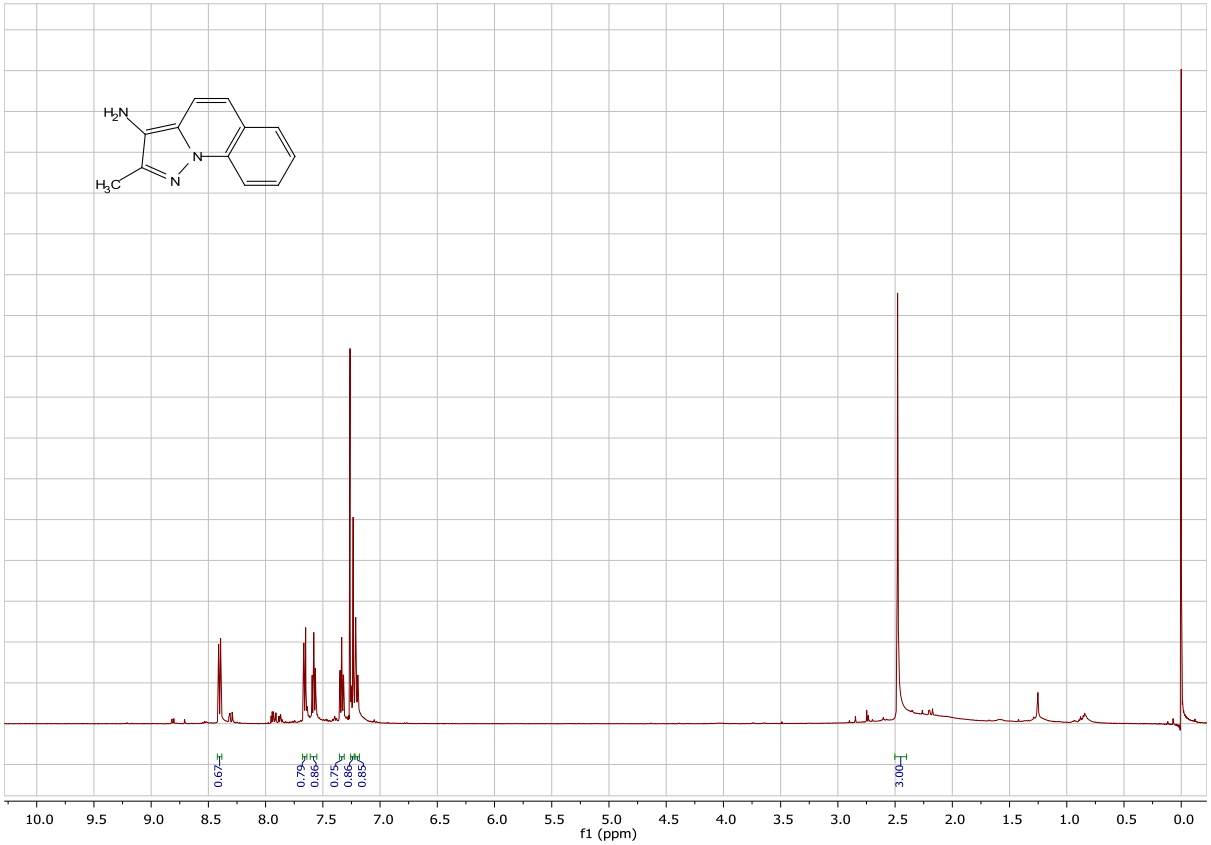
^{1}H NMR of **5k**



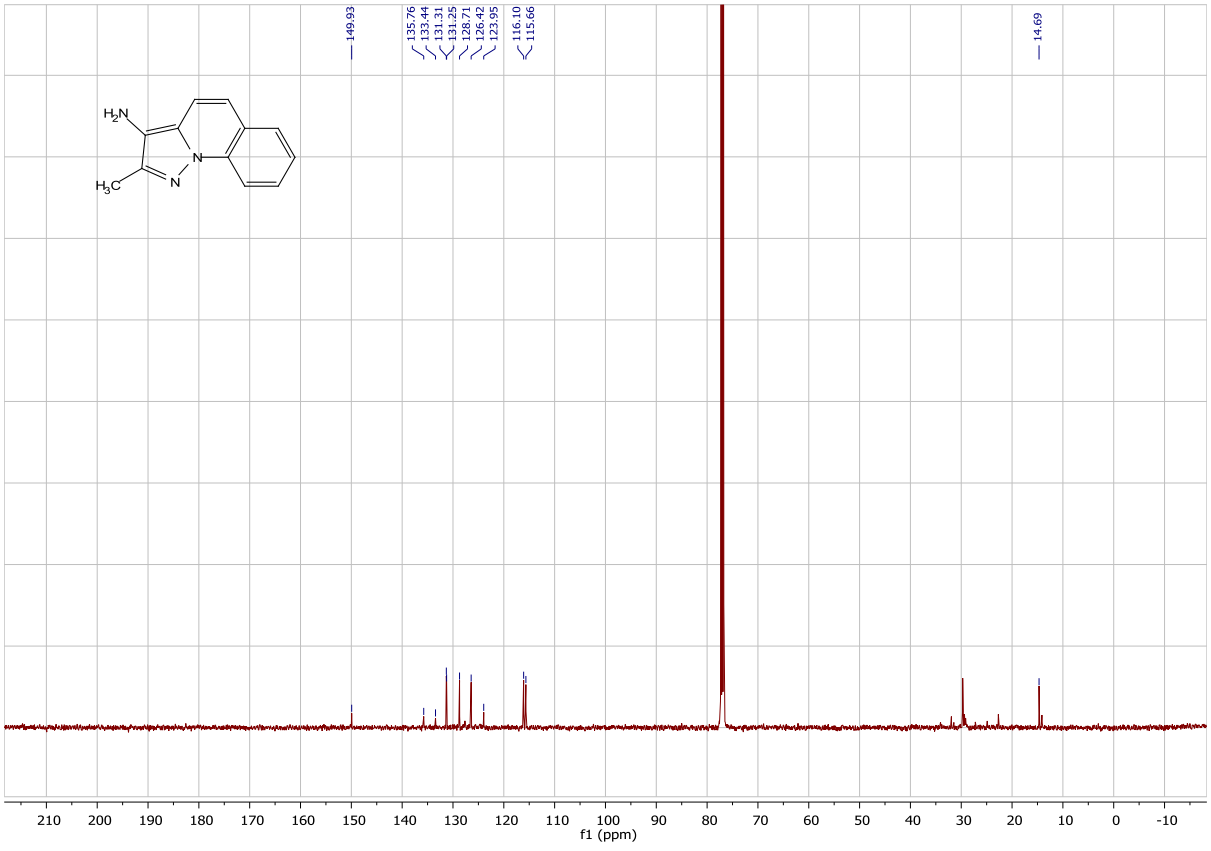
^{13}C NMR of **5k**



^{1}H NMR of **10**



^{13}C NMR of **10**



12. X-ray crystallography data of 3a and 5a

Crystallographic data of 3a

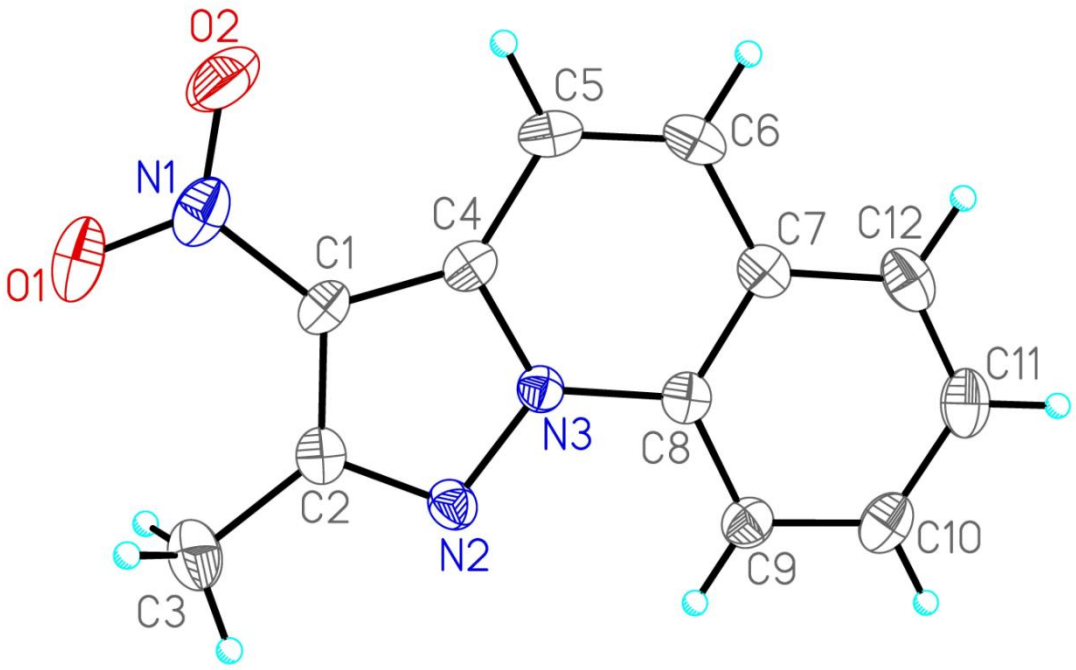


Figure caption: ORTEP diagram of **3a** compound with the atom-numbering. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius.

Crystal data for **3a**: $C_{12}H_9N_3O_2$, M = 227.22, Pale Yellow Needle, 0.48 x 0.15 x 0.06 mm^3, orthorhombic, space group *Pbca* (No. 61), a = 7.4947(11), b = 13.0618(18), c = 21.098(3) Å, V = 2065.4(5) $Å^3$, Z = 8, D_c = 1.461 g/cm^3, F_{000} = 944, CCD area detector, MoKα radiation, λ = 0.71073 Å, T = 293(2)K, $2\vartheta_{max}$ = 49.9º, 18250 reflections collected, 1809 unique (R_{int} = 0.0403), Final *GooF* = 1.399, *R1* = 0.0840, *wR2* = 0.1622, *R* indices based on 1709 reflections with I >2σ(I) (refinement on F^2), 155 parameters, μ = 0.104 mm^{-1}. We deposited the Crystallographic Information File (CIF) of AV39 at the Cambridge Crystallographic Data Centre (CCDC) and obtained a unique depository number, CCDC 1052135. The crystal data can be obtained free of charge at https://summary.ccdc.cam.ac.uk/structure-summary-form or by writing to the Cambridge Crystallographic Data Centre, Cambridge CB2 1EZ, UK, E-mail: deposit@ccdc.cam.ac.uk.

Data collection and Structure solution: X-ray data for **3a** compound were collected at room temperature using the Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα

radiation (λ=0.71073Å) with ω-scan method.[6] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 3157 reflections. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[7] and refinement was carried out by full-matrix least-squares technique using SHELXL97.[7] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms.

Crystallographic data of 5a

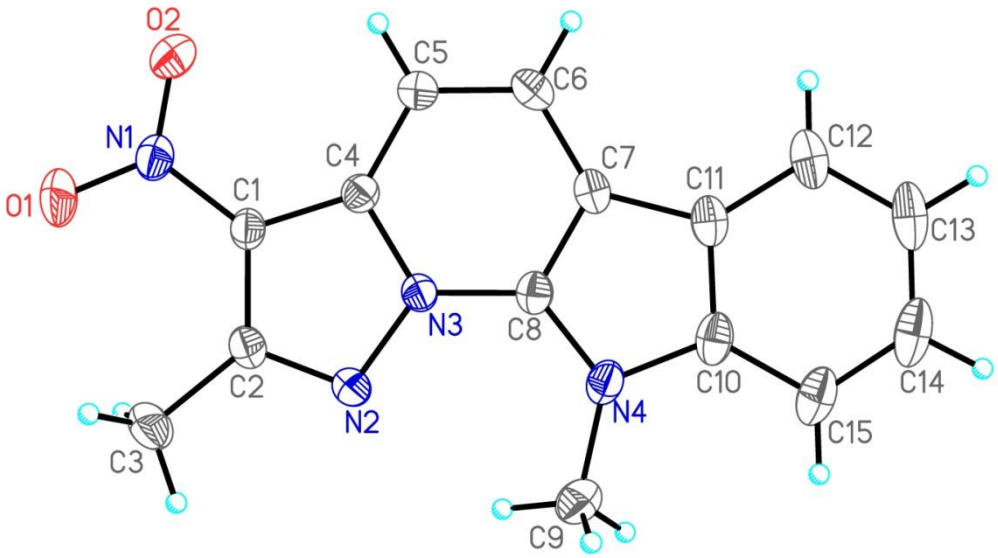


Figure caption: ORTEP diagram of **5a** compound with the atom-numbering. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius.

Crystal data for **5a**: $C_{15}H_{12}N_4O_2$, *M* = 280.29, brown needle, 0.43 x 0.18 x 0.09 mm^3, triclinic, space group $P\bar{1}$ (No. 2), a = 7.1508(10), b = 9.6154(14), c = 10.0654(14) Å, α = 82.965(2), β = 70.019(2), γ = 87.230(2)°, V = 645.50(16) Å^3, *Z* = 2, *Dc* = 1.442 g/cm^3, F_{000} = 292, CCD area detector, MoKα radiation, λ = 0.71073 Å, T = 293(2)K, $2\vartheta_{max}$ = 50.0º, 6234 reflections collected, 2269 unique (R_{int} = 0.0252), Final *GooF* = 1.155, R1 = 0.0568, wR2 = 0.1339, R indices based on 1968 reflections with I >2σ(I) (refinement on F^2), 192 parameters, μ = 0.100 mm^{-1}. CCDC 1057420 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Data collection and Structure solution: X-ray data for **5a** compound were collected at room temperature using the Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method.[1] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 2280 reflections. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL97.[2] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms.

References:

7. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
8. Sheldrick, G. M. SHELXS97 and SHELXL97, Programs for crystal structure solution and refinement; University of Gottingen: Germany, 1997.