Supporting Information

Reagent-Assisted Regio-Divergent Cyclization Synthesis of Pyrazole

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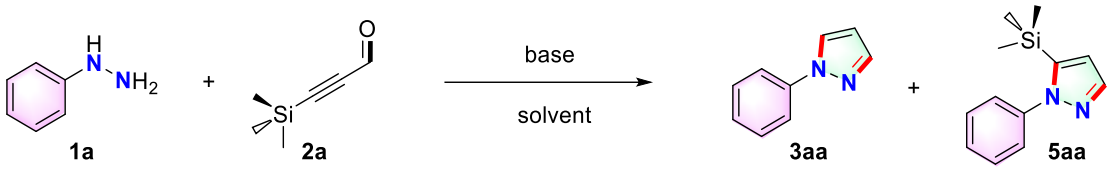
Contents

1. General

Experimental: All reactions and manipulations with air sensitive compounds being present were performed under dry nitrogen (N_2 5.0), using Schlenk and glove box techniques. Deuterated solvents were bought from Cambridge Isotope Laboratories, distilled accordingly, and stored over molecular sieves (3 Å). Other chemicals were purchased from commercial vendors and used without further purification. NMR spectra were collected on a Varian INOVA 300 and 400 MHz spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvent signal. Coupling constants (J) are given in Hz (coupling patterns: s: singlet, s br: broad singlet, d: doublet, t: triplet, q: quartet, m: multiplet). GC analyses were carried out using an Agilent Technologies 6890N system equipped with a Machinery-Nagel (MN) Optima 5 HT column (30 m, 320 µm, 0.25 µm) or an Agilent Technologies 6850 system equipped with a MN Optima 17 column (30 m, 320 µm, 0.25 µm). GC/MS analyses were carried out on an Agilent 7890A/MSD 5975C system equipped with a HP-5MS column (30 m, 320 µm, 0.25 µm). High resolution mass spectra (HRMS) were recorded on Bruker MicroTOF-QII mass (ESI). MN silica gel 60 (0.040 – 0.063 mm particle size) was used for flash column chromatography.

2. Screening of reaction parameters



In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, base, solvent, phenyl hydrazine (**1a**) and 3-(trimethylsilyl)propiolaldehyde (**2a**). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (design temperature) for design time. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 40:1) on silica gel to give the product **3aa** and **5aa** in the reported yields.

Entry	Parameter
Table S1	The difference of solvent screening
Table S2	The difference of co-solvent screening
Table S3	The difference of base screening
Table S4	Screening the loading of ^{t}BuOK
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Table S6	Reaction time screening
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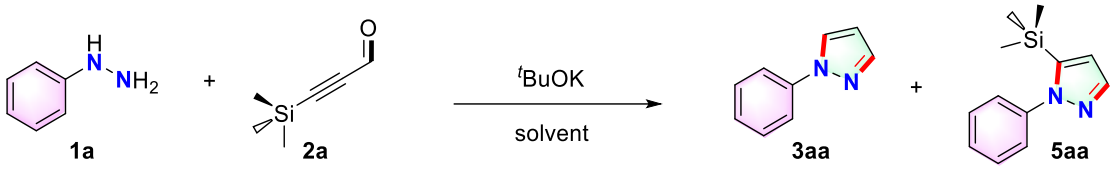
Table S8	The atmosphere screening
Table S9	The additive screening

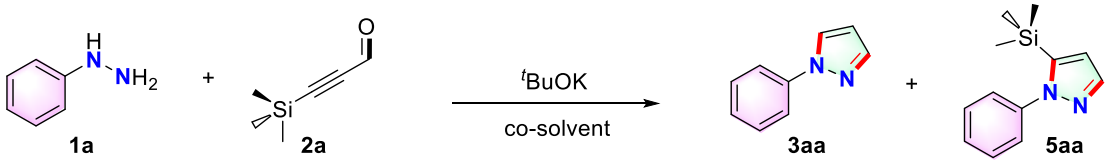
Table S1. The difference of solvent screening [a]



Entry	Solvent (2.0 mL)	**3aa** (%)	**5aa** (%)
1	DMAc	41	<5
2	DMSO	30	<5
3	DMF	37	<5
4	NMP	44	<5
5	CH_3CN	57	<5
6	CH_2Cl_2	45	<5
7	EA	35	<5
8	TFA	0	0
9	**^{t}BuOH**	**>95**	**<5**
10	isopropanol	67	12
11	ethanol	48	8
12	methanol	17	<5
13	toluene	39	<5
14	1,4-dioxane	73	0
15	THF	77	0
16	H_2O	21	0

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), ^{t}BuOK (1.1 mmol), solvent (2.0 mL), 60 °C, 6 h. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

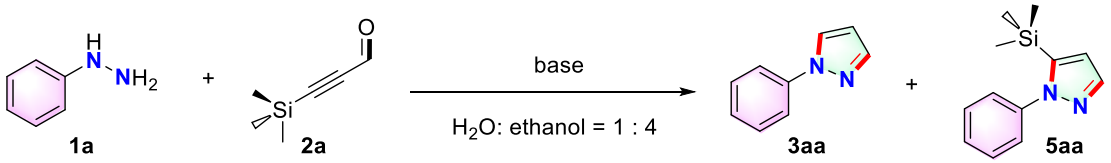
Table S2. The difference of co-solvent screening [a]



Entry	Co-solvent (2.0 mL)	**3aa** (%)	**5aa** (%)
1	H_2O: CH_3CN = 1: 4	68	<5
2	H_2O: ^{t}BuOH = 1: 4	43	<5
3	H_2O: isopropanol = 1: 4	38	<5
4	H_2O: methanol = 1: 4	35	<5
5	H_2O: DMSO = 1: 4	14	<5
6	H_2O: DMF = 1: 4	37	<5
7	H_2O: toluene = 1: 4	52	0
8	H_2O: NMP = 1: 4	14	0
9	H_2O: DMA = 1: 4	32	<5
10	H_2O: ethanol = 1: 1	63	12
11	H_2O: ethanol = 1: 2	78	<5
12	H_2O: ethanol = 1: 3	81	<5
13	**H_2O: ethanol = 1: 4**	**>95**	**<5**
14	H_2O: ethanol = 2: 1	57	<5
15	H_2O: ethanol = 3: 1	61	<5
16	H_2O: ethanol = 4: 1	60	<5

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), ^{t}BuOK (1.1 mmol), co-solvent = x: y (v/v, 2.0 mL), 60 °C, 6 h. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

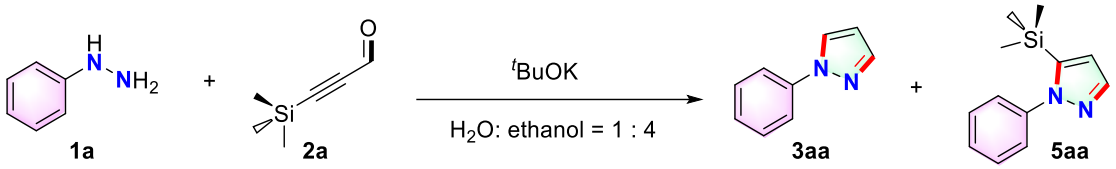
Table S3. The difference of base screening [a]



Entry	base	**3aa** (%)	**5aa** (%)
1	^{t}BuOLi	n.d.	<5
2	**^{t}BuOK**	**>95**	**<5**
3	^{t}BuONa	33	<5
4	LiOH	0	0
5	NaH	44	<5
6	Na_2CO_3	<5	12
7	K_2CO_3	0	<5
8	$KHCO_3$	0	0
9	Cs_2CO_3	35	0
10	NaOH	53	12
11	KOH	86	<5
12	Pyridine	0	0
13	Et_3N	0	0
14	DBU	0	0
15	TEMDA	0	0

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), base (1.1 mmol), H_2O: ethanol = 1: 4 (v/v, 2.0 mL), 60 °C, 6 h. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

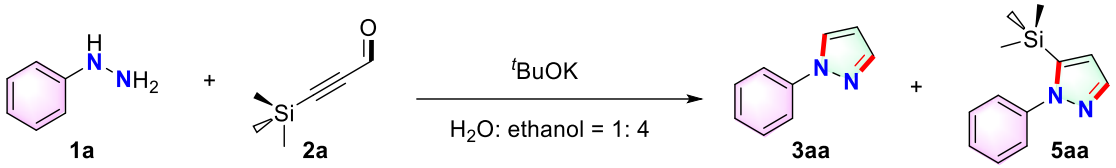
Table S4. Screening the loading of ^{t}BuOK [a]



Entry	^{t}BuOK (mmol)	**3aa** (%)	**5aa** (%)
1	0	0	>95
2	0.2	22	73
3	0.4	29	64
4	0.6	36	47
5	0.8	47	42
6	1.0	78	12
7	**1.1**	**>95**	**<5**
8	1.2	93	0
9	1.3	90	0
10	1.5	86	0
11	2.0	80	0
12	3.0	76	0

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), ^{t}BuOK (x mmol), H_2O: ethanol = 1:4 (v/v, 2.0 mL), 60 °C, 6 h. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

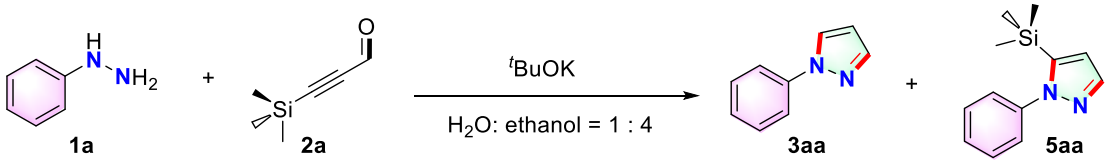
Table S5. Reaction temperature screening [a]



Entry	T (°C)	**3aa** (%)	**5aa** (%)
1	25	25	0
2	30	30	<5
3	40	59	0
4	50	90	0
5	**60**	**>95**	**<5**
6	80	>95	0
7	100	>95	0

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), ^{t}BuOK (1.1 mmol), H_2O: ethanol = 1:4 (v/v, 2.0 mL), T, 6 h. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

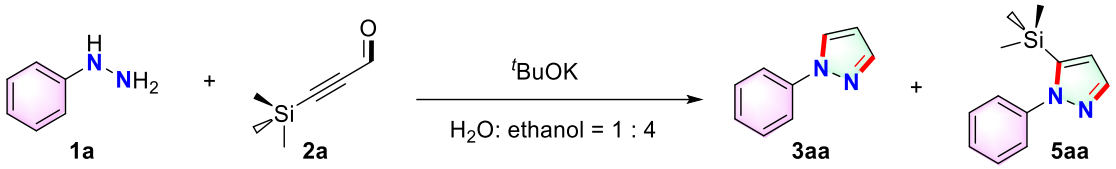
Table S6. Reaction time screening [a]



Entry	^{t}BuOK (mmol)	**3aa** (%)	**5aa** (%)
1	1	54	0
2	2	67	<5
3	4	85	<5
4	**6**	**>95**	**<5**
5	8	>95	<5

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), ^{t}BuOK (1.1 mmol), H_2O: ethanol = 1:4 (v/v, 2.0 mL), 60 °C, t. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

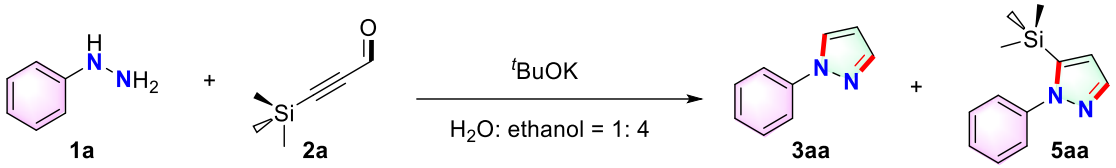
Table S7. The ratio of 1a:2a screening [a]



Entry	**1a** (mmol)	**2a** (mmol)	**3aa** (%)	**5aa** (%)
1	0.4	0.4	81	0
2	**0.4**	**0.5**	**>95**	**<5**
3	0.4	0.6	>95	0
4	0.4	0.7	>95	0
5	0.5	0.4	81	<5
6	0.6	0.4	74	<5
7	0.7	0.4	66	<5

[a] Reaction conditions: **1a** (x mmol), **2a** (y mmol), ^{t}BuOK (1.1 mmol), H_2O: ethanol = 1:4 (v/v, 2.0 mL), 60 ºC, 6 h. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

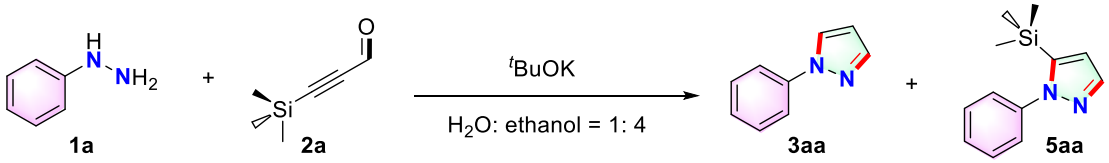
Table S8. The atmosphere screening [a]



Entry	atmosphere	**3aa** (%)	**5aa** (%)
1	air	92	<5
2	O_2	0	0
3	**N_2**	**>95**	**<5**
4	Ar	>95	0

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), ^{t}BuOK (1.1 mmol), H_2O: ethanol = 1:4 (v/v, 2.0 mL), 60 ºC, 6 h. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

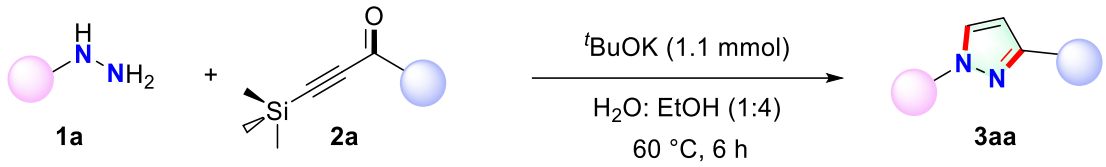
Table S9. The additive screening [a]



Entry	additive (mmol)	**3aa** (%)	**5aa** (%)
1	$FeCl_2$ (0.04)	6	<5
2	$PdCl_2(COD)$ (0.04)	5	<5
3	$PdBr_2$ (0.04)	7	<5
4	$NiCl_2(BINP)$ (0.4)	27	<5
5	$CoCl_2(PPh_3)_2$ (0.4)	1	<5
6	CuBr (0.4)	22	<5
7	CuI (0.4)	17	<5
8	$NiBr_2$ (0.4)	11	<5
9	$CrCl_3$ (0.4)	29	<5
10	CuCN (0.4)	19	<5
11	$(^nBu)_4NF$ (0.6)	15	<5
12	$(^nBu)_4NCl$ (0.6)	3	<5
13	$(^nBu)_4NBr$ (0.6)	8	<5
14	$(^nBu)_4NI$ (0.6)	15	<5
15	$(^nBu)_4NBF_4$ (0.6)	6	<5
16	$(^nBu)_4NPF_6$ (0.6)	6	<5
17	$(^nBu)_4NHSO_4$ (0.6)	2	<5

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.5 mmol), ^{t}BuOK (1.1 mmol), H_2O: ethanol = 1:4 (v/v, 2.0 mL), 60 °C, 6 h, additive. Yields of **3aa** and **5aa** were determined *via* GC with *n*-dodecane as the internal standard.

3. General Procedure for the products



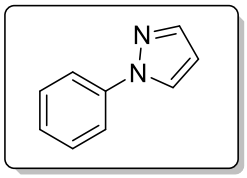
In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, ^{t}BuOK (1.1 mmol), hydrazine (**1**, 0.4 mmol), aldehyde (**2**, 0.5 mmol), and H_2O: ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 6 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (petroleum ether / ethyl acetate = 40:1) on silica gel to give the products in the reported yields.

4. The source of starting material

All the compounds used as starting material (include hydrazines **1**, aldehyde **2**) were purchased from Aldrich, Acros, Energy, or Aladdin. They were used as received and without further purification.

5. Characterization Data

1-phenyl-1H-pyrazole (3aa)[1]



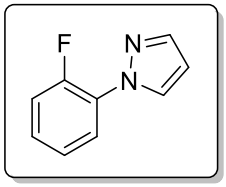
The title compound was prepared according to the general procedure and purified by column chromatography to give the white solid 53.0 mg, 92% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) 7.86 – 7.81 (m, 1H), 7.73 – 7.63 (m, 3H), 7.42 – 7.28 (m, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.41 – 6.33 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 139.8, 129.0, 126.3, 126.0, 118.7, 107.3.

HRMS (ESI) calcd. for $C_9H_9N_2$ $[M+H]^+$: 145.0766, found: 145.0768.

1-(2-fluorophenyl)-1H-pyrazole (3ab)[2]



The title compound was prepared according to the general procedure and purified by column chromatography to give the yellow oil 58.3 mg, 90% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

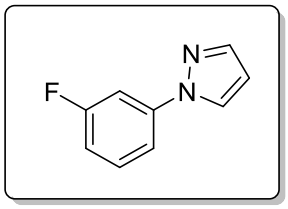
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (t, *J* = 2.8 Hz, 1H), 7.94 – 7.88 (m, 1H), 7.75 (d, *J* = 1.8 Hz, 1H), 7.36 – 7.18 (m, 3H), 6.49 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 152.3, 140.9, 130.8 (d, *J* = 10.3 Hz), 127.7 (d, *J* = 7.8 Hz), 125.0 (d, *J* = 3.7 Hz), 124.4, 116.9 (d, *J* = 20.6 Hz), 107.5 (d, *J* = 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -125.17.

HRMS (ESI) calcd. for $C_9H_8FN_2$ $[M+H]^+$: 163.0672, found: 163.0675.

1-(3-fluorophenyl)-1H-pyrazole (3ac)[1]



The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 60.3 mg, 93% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

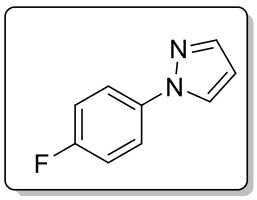
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.73 (s, 1H), 7.54 – 7.36 (m, 3H), 6.98 (t, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 64.5, 162.1, 141.6 (d, *J* = 12.7 Hz), 130.8 (d, *J* = 9.2 Hz), 126.8, 114.3 (d, *J* = 3.1 Hz), 113.2 (d, *J* = 21.3 Hz), 108.1, 106.9 (d, *J* = 26.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -110.97.

HRMS (ESI) calcd. for $C_9H_8FN_2$ $[M+H]^+$: 163.0672, found: 163.0673.

1-(4-fluorophenyl)-1H-pyrazole (3ad)[1]



The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 61.6 mg, 95% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

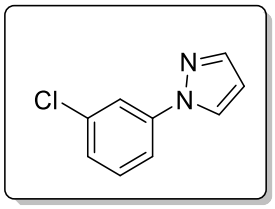
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 2.4 Hz, 1H), 7.71 (d, *J* = 1.6 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.20 – 7.09 (m, 2H), 6.46 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 159.9, 141.2, 136.6, 136.6, 126.9, 121.0 (d, *J* = 8.2 Hz), 116.2 (d, *J* = 22.9 Hz), 107.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -116.03.

HRMS (ESI) calcd. for $C_9H_8FN_2$ $[M+H]^+$: 163.0672, found: 163.0676.

1-(3-chlorophenyl)-1H-pyrazole (3ae)[1]



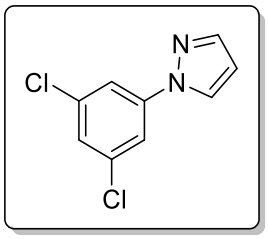
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 64.8 mg, 91% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 2.4 Hz, 1H), 7.81 – 7.70 (m, 2H), 7.63 – 7.55 (m, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.32 – 7.23 (m, 1H), 6.48 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 135.3, 130.5, 126.8, 126.4, 119.5, 117.0, 108.1.

HRMS (ESI) calcd. for $C_9H_8ClN_2$ $[M+H]^+$: 179.0376, found: 179.0377.

1-(3,5-dichlorophenyl)-1H-pyrazole (3af)



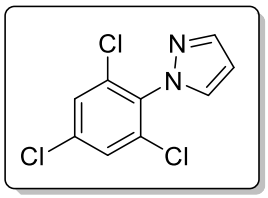
The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 81.9 mg, 86% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.4 Hz, 1H), 7.72 (d, *J* = 1.6 Hz, 1H), 7.62 (d, *J* = 2.0 Hz, 2H), 7.25 (t, *J* = 1.6 Hz, 1H), 6.50 – 6.45 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 141.5, 135.9, 126.8, 126.2, 117.4, 108.6.

HRMS (ESI) calcd. for $C_9H_7Cl_2N_2$ $[M+H]^+$: 212.9986, found: 212.9988.

1-(2,4,6-trichlorophenyl)-1H-pyrazole (3ag)



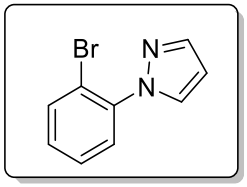
The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 92.4 mg, 80% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.47 (s, 2H), 6.51 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 135.9, 135.3, 135.3, 131.6, 128.7, 107.0.

HRMS (ESI) calcd. for $C_9H_6Cl_3N_2$ $[M+H]^+$: 246.9597, found: 246.9599.

1-(2-bromophenyl)-1H-pyrazole (3ah)[3]



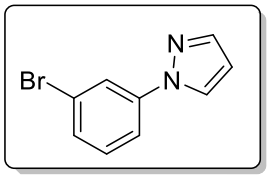
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 57.6 mg, 88% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.4 Hz, 1H), 7.74 (d, *J* = 1.6 Hz, 1H), 7.69 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.30 – 7.25 (m, 1H), 6.46 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 139.9, 133.7, 131.3, 129.6, 128.3, 128.2, 118.6, 106.5.

HRMS (ESI) calcd. for $C_9H_8BrN_2$ $[M+H]^+$: 222.9871, found: 222.9872.

1-(3-bromophenyl)-1H-pyrazole (3ai)[4]



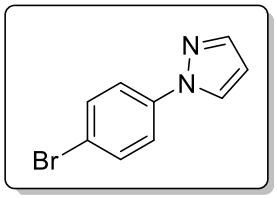
The title compound was prepared according to the general procedure and purified by column chromatography to give the yellow oil 81.3 mg, 92% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (q, *J* = 2.4 Hz, 2H), 7.72 (d, *J* = 1.6 Hz, 1H), 7.63 – 7.58 (m, 1H), 7.42 – 7.37 (m, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 6.47 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 141.1, 130.7, 129.3, 126.7, 123.1, 122.3, 117.4, 108.1.

HRMS (ESI) calcd. for $C_9H_8BrN_2$ $[M+H]^+$: 222.9871, found: 222.9873.

1-(4-bromophenyl)-1H-pyrazole (3aj)[1]



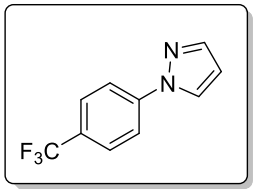
The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 83.1 mg, 94% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 2.4 Hz, 1H), 7.72 (d, *J* = 1.6 Hz, 1H), 7.65 – 7.52 (m, 4H), 6.47 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 139.2, 132.5, 126.7, 120.6, 119.6, 108.1.

HRMS (ESI) calcd. for $C_9H_8BrN_2$ $[M+H]^+$: 222.9871, found: 222.9871.

1-(4-(trifluoromethyl)phenyl)-1H-pyrazole (3ak)[1]



The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 78.9 mg, 93% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

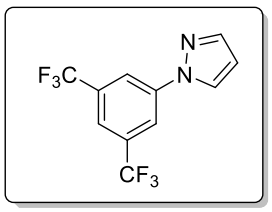
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 2.4 Hz, 1H), 7.85 – 7.71 (m, 5H), 6.51 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 142.0, 128.8, 128.8, 128.4, 128.1, 128.0, 127.8, 126.8, 126.8, 126.8, 126.8, 126.7, 124.0 (d, *J* = 270.0 Hz), 118.8, 108.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.28.

HRMS (ESI) calcd. for $C_{10}H_8F_3N_2$ $[M+H]^+$: 213.0640, found: 213.0642.

1-(3,5-bis(trifluoromethyl)phenyl)-1H-pyrazole (3al)



The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 98.6 mg, 88% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 20:1).

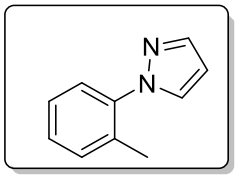
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 1.6 Hz, 2H), 8.03 (d, *J* = 2.8 Hz, 1H), 7.88 – 7.71 (m, 2H), 6.56 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5, 141.1, 133.1 (q, *J* = 34.0 Hz), 123.0 (d, *J* = 272.0 Hz), 119.7, 119.6, 119.5, 119.5, 118.8 (dd, *J* = 13.0, 9.0 Hz), 109.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.08.

HRMS (ESI) calcd. for $C_{11}H_7F_6N_2$ $[M+H]^+$: 281.0513, found: 281.0515.

1-(o-tolyl)-1H-pyrazole (3am)[5]



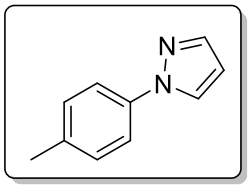
The title compound was prepared according to the general procedure and purified by column chromatography to give the yellow oil 54.4 mg, 86% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 2.0 Hz, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 7.36 – 7.27 (m, 4H), 6.44 (t, *J* = 2.0 Hz, 1H), 2.25 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 140.0, 133.8, 131.3, 130.5, 128.4, 126.6, 126.2, 106.2, 18.1.

HRMS (ESI) calcd. for $C_{10}H_{11}N_2$ $[M+H]^+$: 159.0922, found: 159.0925.

1-(p-tolyl)-1H-pyrazole (3an)[5]



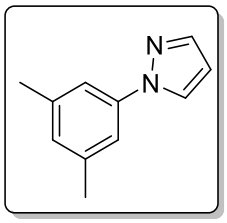
The title compound was prepared according to the general procedure and purified by column chromatography to give the yellow oil 55.6 mg, 88% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.4 Hz, 1H), 7.71 (d, *J* = 1.6 Hz, 1H), 7.63 – 7.49 (m, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.44 (t, *J* = 2.0 Hz, 1H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 138.0, 136.3, 130.0, 126.7, 119.2, 107.3, 20.9.

HRMS (ESI) calcd. for $C_{10}H_{11}N_2$ $[M+H]^+$: 159.0922, found: 159.0923.

1-(3,5-dimethylphenyl)-1H-pyrazole (3ao)[1]



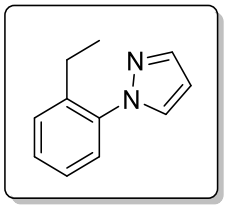
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 56.4 mg, 82% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.32 (d, *J* = 1.6 Hz, 2H), 6.93 (d, *J* = 1.2 Hz, 1H), 6.45 (d, *J* = 2.0 Hz, 1H), 2.38 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 140.2, 139.3, 128.2, 126.8, 117.1, 107.3, 21.4.

HRMS (ESI) calcd. for $C_{11}H_{13}N_2$ $[M+H]^+$: 173.1079, found: 173.1080.

1-(2-ethylphenyl)-1H-pyrazole (3ap)[6]



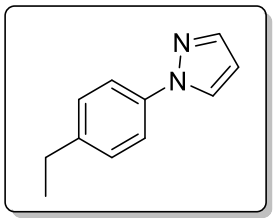
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 53.7 mg, 78% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.59 (s, 1H), 7.40 – 7.26 (m, 4H), 6.50 – 6.40 (m, 1H), 2.62 – 2.54 (m, 2H), 1.52 – 0.96 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 140.2, 139.6, 130.8, 129.6, 128.8, 126.6, 126.5, 106.1, 24.4, 14.8.

HRMS (ESI) calcd. for $C_{11}H_{13}N_2$ $[M+H]^+$: 173.1079, found: 173.1081.

1-(4-ethylphenyl)-1H-pyrazole (3aq)[7]



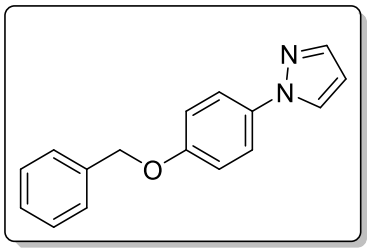
The title compound was prepared according to the general procedure and purified by column chromatography to give the yellow oil 54.4 mg, 79% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 2.4 Hz, 1H), 7.71 (d, *J* = 1.6 Hz, 1H), 7.64 – 7.54 (m, 2H), 7.27 (d, *J* = 9.2 Hz, 2H), 6.45 (t, *J* = 2.4 Hz, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 140.8, 138.2, 128.8, 126.7, 119.3, 107.3, 28.4, 15.6.

HRMS (ESI) calcd. for $C_{11}H_{13}N_2$ $[M+H]^+$: 173.1079, found: 173.1082.

1-(4-(benzyloxy)phenyl)-1H-pyrazole (3ar)



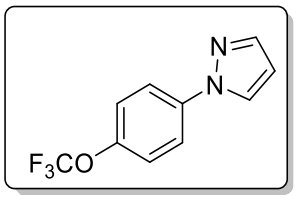
The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 75.0 mg, 75% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.64 – 7.56 (m, 2H), 7.49 – 7.29 (m, 5H), 7.09 – 6.94 (m, 2H), 6.44 (t, *J* = 2.0 Hz, 1H), 5.10 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 140.7, 136.7, 134.2, 128.7, 128.1, 127.5, 126.8, 120.9, 115.5, 107.2, 70.4.

HRMS (ESI) calcd. for $C_{16}H_{15}N_2O$ $[M+H]^+$: 251.1184, found: 251.1186.

1-(4-(trifluoromethoxy)phenyl)-1H-pyrazole (3as)



The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 71.1 mg, 78% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

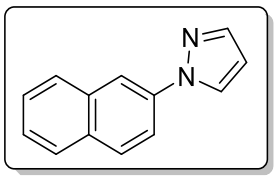
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 2.4 Hz, 1H), 7.78 – 7.63 (m, 3H), 7.31 (d, *J* = 8.8 Hz, 2H), 6.49 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3 (d, *J* = 2.0 Hz), 141.5, 138.8, 126.8, 122.2, 120.5 (d, *J* = 256.0 Hz), 120.4, 108.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -58.08.

HRMS (ESI) calcd. for $C_{10}H_8F_3N_2O$ $[M+H]^+$: 229.0589, found: 229.0591.

1-(naphthalen-2-yl)-1H-pyrazole (3at)[8]



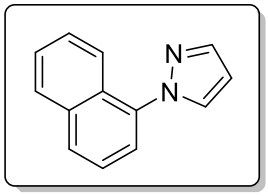
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 59.8 mg, 77% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 2.0 Hz, 1H), 8.05 (d, *J* = 2.4 Hz, 1H), 7.96 – 7.84 (m, 4H), 7.80 (d, *J* = 1.6 Hz, 1H), 7.55 – 7.45 (m, 2H), 6.52 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 137.6, 133.6, 131.8, 129.5, 127.9, 127.8, 127.0, 125.9, 118.5, 116.3, 107.8.

HRMS (ESI) calcd. for $C_{13}H_{11}N_2$ $[M+H]^+$: 195.0922, found: 195.0925.

1-(naphthalen-1-yl)-1H-pyrazole (3au)[1]



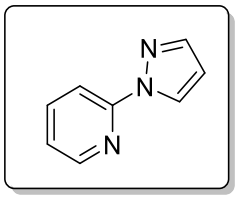
The title compound was prepared according to the general procedure and purified by column chromatography to give the yellow oil 59.8 mg, 77% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.89 (m, 2H), 7.87 – 7.76 (m, 3H), 7.58 – 7.47 (m, 4H), 6.55 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 137.4, 134.3, 131.6, 129.2, 128.9, 128.1, 127.2, 126.7, 125.1, 123.3, 123.2, 106.5.

HRMS (ESI) calcd. for $C_{13}H_{11}N_2$ $[M+H]^+$: 195.0922, found: 195.0926.

2-(1H-pyrazol-1-yl)pyridine (3av)[9]



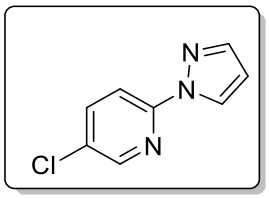
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 46.4 mg, 80% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 20:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 2.8 Hz, 1H), 8.47 – 8.34 (m, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.83 – 7.77 (m, 1H), 7.74 (d, *J* = 1.6 Hz, 1H), 7.22 – 7.14 (m, 1H), 6.51 – 6.41 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 148.1, 142.1, 138.7, 127.0, 121.4, 112.5, 107.8.

HRMS (ESI) calcd. for $C_8H_8N_3$ $[M+H]^+$: 146.0718, found: 146.0722.

5-chloro-2-(1H-pyrazol-1-yl)pyridine (3aw)[10]



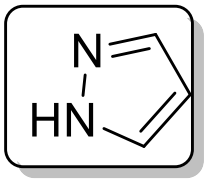
The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 61.6 mg, 86% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) 8.50 (d, *J* = 2.4 Hz, 1H), 8.34 (d, *J* = 2.4 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.79 – 7.67 (m, 2H), 6.48 – 6.44 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) 149.9, 146.7, 142.4, 138.4, 129.0, 127.1, 113.3, 108.2.

HRMS (ESI) calcd. for $C_8H_7ClN_3$ $[M+H]^+$: 180.0329, found: 180.0330.

1H-pyrazole (3ax)[11]



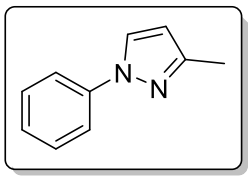
The Yield of **3ax** was determined via GC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.28 (s, 1H), 7.64 (d, *J* = 2.0 Hz, 2H), 6.36 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7, 105.0.

HRMS (ESI) calcd. for $C_3H_5N_2$ $[M+H]^+$: 69.0453, found: 69.0455.

3-methyl-1-phenyl-1H-pyrazole (4aa)[1]



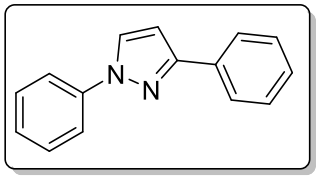
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 51.8 mg, 82% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 2.4 Hz, 1H), 7.71 – 7.60 (m, 2H), 7.49 – 7.35 (m, 2H), 7.25 – 7.17 (m, 1H), 6.23 (d, *J* = 2.4 Hz, 1H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.5, 140.2, 129.4, 127.3, 125.9, 118.8, 107.5, 13.7.

HRMS (ESI) calcd. for $C_{10}H_{11}N_2$ $[M+H]^+$: 159.0922, found: 159.0925.

1,3-diphenyl-1H-pyrazole (4ab)[12]



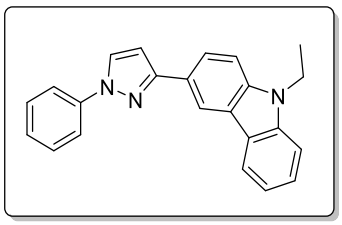
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 71.3 mg, 81% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 40:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.85 (m, 3H), 7.83 – 7.71 (m, 2H), 7.47 – 7.38 (m, 4H), 7.36 – 7.29 (m, 1H), 7.29 – 7.23 (m, 1H), 6.74 (d, *J* = 2.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9, 140.1, 133.0, 129.4, 128.7, 128.5, 128.1, 126.4, 125.9, 119.1, 105.0.

HRMS (ESI) calcd. for $C_{15}H_{13}N_2$ $[M+H]^+$: 221.1079, found: 221.1082.

9-ethyl-3-(1-phenyl-1H-pyrazol-3-yl)-9H-carbazole (4ac)



The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid 121.3 mg, 90% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 20:1).

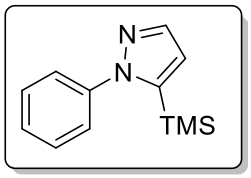
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 1.6 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 8.09 – 8.03 (m, 1H), 7.95 (d, *J* = 2.4 Hz, 1H), 7.87 – 7.77 (m, 2H), 7.51 – 7.29 (m, 6H), 7.25 – 7.17 (m, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.44 (t, *J* = 7.2 Hz,

3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 140.4, 140.2, 139.8, 129.5, 128.6, 128.4, 128.2, 126.6, 125.9, 124.2, 123.3, 123.1, 120.8, 119.5, 119.1, 118.2, 108.6, 104.9, 37.7, 13.9.

HRMS (ESI) calcd. for $C_{23}H_{20}N_3$ $[M+H]^+$: 338.1657, found: 338.1658.

5-(tert-butyl)-1-phenyl-1H-pyrazole (5aa)



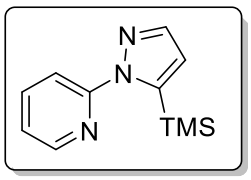
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 77.8 mg, 90% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 20:1).

^{1}H NMR (400 MHz, $CDCl_3$) 8.69 (s, 1H), 7.32 – 7.21 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.95 (t, *J* = 7.2 Hz, 1H), 6.42 (d, *J* = 3.2 Hz, 1H), 0.32 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 129.4, 121.2, 114.6, 113.3, 109.2, 94.6, -0.2.

HRMS (ESI) calcd. for $C_{12}H_{17}N_2Si$ $[M+H]^+$: 217.1161, found: 217.1163.

2-(5-(trimethylsilyl)-1H-pyrazol-1-yl)pyridine (5ab)



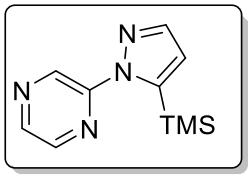
The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 67.7 mg, 78% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 20:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.19 – 8.14 (m, 1H), 7.62 – 7.56 (m, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 6.84 – 6.79 (m, 1H), 6.45 (s, 1H), 0.27 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 147.7, 138.2, 116.8, 116.8, 109.4, 108.0, 94.1, 0.3.

HRMS (ESI) calcd. for $C_{11}H_{16}N_3Si$ $[M+H]^+$: 218.1114, found: 218.1116.

2-(5-(trimethylsilyl)-1H-pyrazol-1-yl)pyrazine (5ac)



The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 65.4 mg, 75% yield. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate = 20:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.65 (d, *J* = 1.2 Hz, 1H), 8.18 – 8.01 (m, 2H), 6.54 (s, 1H), 0.28 (s, 9H).

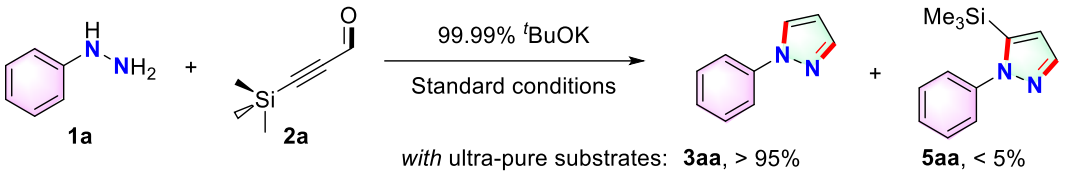
^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 141.6, 137.1, 132.4, 119.0, 110.5, 93.4, 0.4.

HRMS (ESI) calcd. for $C_{10}H_{15}N_4Si$ $[M+H]^+$: 219.1066, found: 219.1068.

6. Mechanism investigations

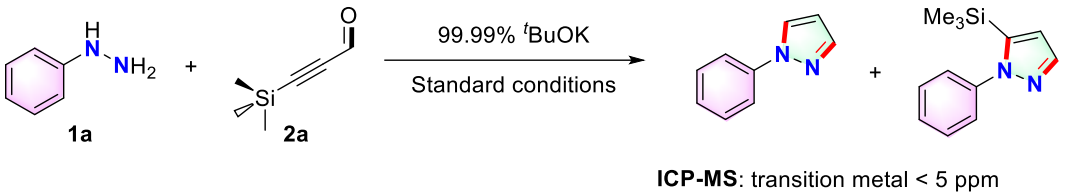
6.1 Control experiments

6.1.1



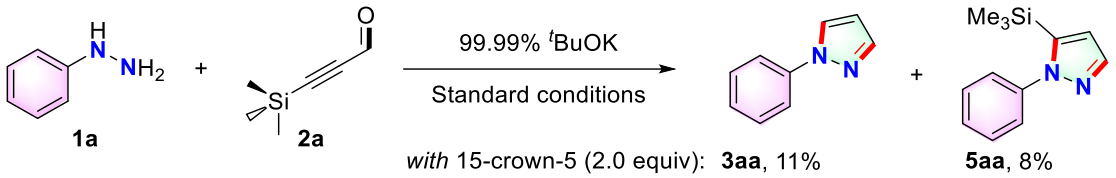
In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, 99.99% ^{t}BuOK (1.1 mmol), purified phenyl hydrazine (**1a**, 0.4 mmol), 3-(trimethylsilyl)propiolaldehyde (**2a**, 0.5 mmol), and H_2O: ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 6 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation.

6.1.2



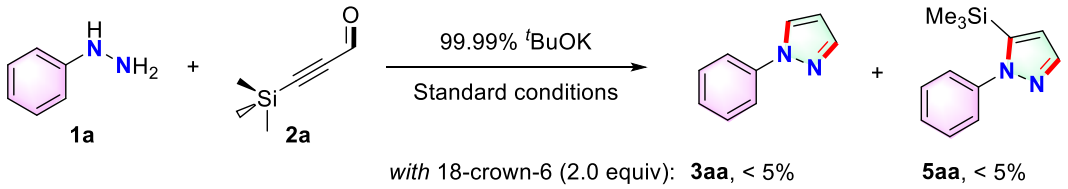
In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, 99.99% ^{t}BuOK (1.1 mmol), phenyl hydrazine (**1a**, 0.4 mmol), 3-(trimethylsilyl)propiolaldehyde (**2a**, 0.5 mmol), and H_2O:ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 6 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by ICP-MS to monitor product formation. Based on ICP-MS analysis, it was determined that the concentration of transition-metal species in the reaction mixture is undetectable, suggesting that this transformation does not rely on catalysis facilitated by transition metals.

6.1.3



In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, 99.99% ^{t}BuOK (1.1 mmol), phenyl hydrazine (**1a**, 0.4 mmol), 3-(trimethylsilyl)propiolaldehyde (**2a**, 0.5 mmol), 15-crown-5 (0.8 mmol, 163 μL) and H_2O:ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 6 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation.

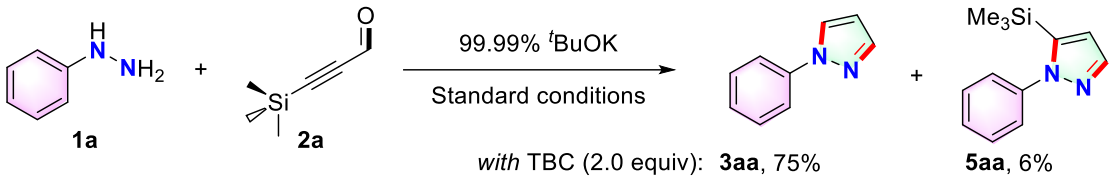
6.1.4



In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, ^{t}BuOK (1.1 mmol), phenyl hydrazine (**1a**, 0.4 mmol), 3-(trimethylsilyl)propiolaldehyde (**2a**, 0.5 mmol), 18-crown-6 (0.8 mmol, 211.46 mg) and H_2O:ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 6 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation.

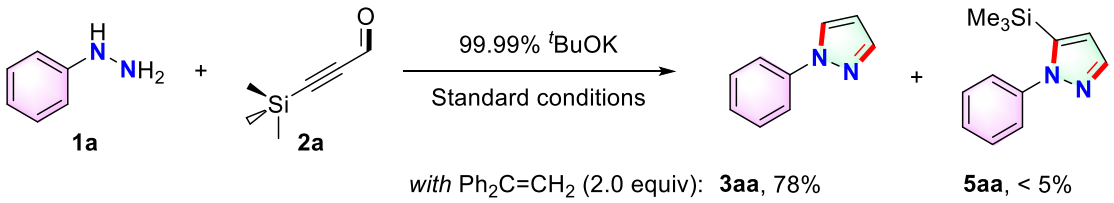
6.2 Radical trap experiments

6.2.1



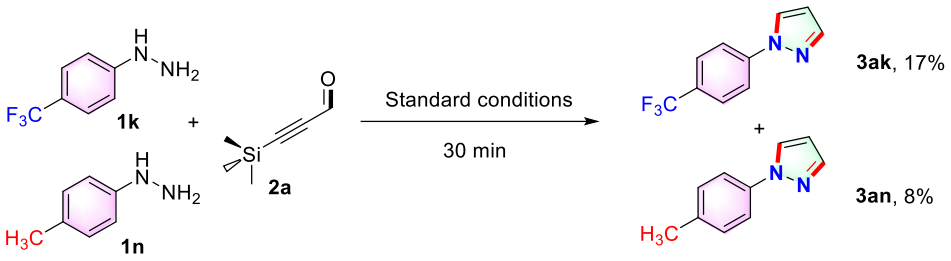
In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, ^{t}BuOK (1.1 mmol), phenyl hydrazine (**1a**, 0.4 mmol), 3-(trimethylsilyl)propiolaldehyde (**2a**, 0.5 mmol), TBC (0.8 mmol, 133.0 mg) and H_2O:ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 6 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation.

6.2.2



In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, 99.99% ^{t}BuOK (1.1 mmol), phenyl hydrazine (**1a**, 0.4 mmol), 3-(trimethylsilyl)propiolaldehyde (**2a**, 0.5 mmol), ethene-1,1-diyldibenzene (0.8 mmol, 146 μL) and H_2O:ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 6 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation.

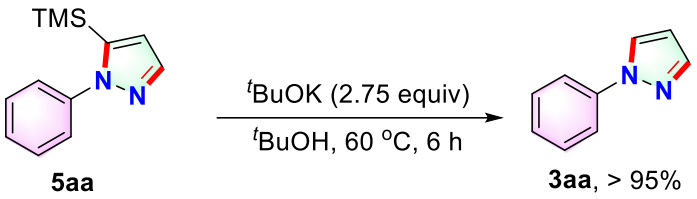
6.3 Competition experiment



In the nitrogen atmosphere, an oven-dried pressure tube (38 mL volume) was charged with a magnetic stirring bar, ^{t}BuOK (1.1 mmol, 123.4 mg), (4-(trifluoromethyl)phenyl)hydrazine (**1k**, 0.4 mmol), p-tolylhydrazine (**1n**, 0.4 mmol), 3-(trimethylsilyl)propiolaldehyde (**2a**, 0.5 mmol) and H_2O:ethanol = 1:4 (v/v, 2.0 mL). Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal bath (60 °C) for 0.5 hours. After the reaction was finished, the reaction was analyzed by TLC to monitor product formation. Then a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor the corresponding products formation.

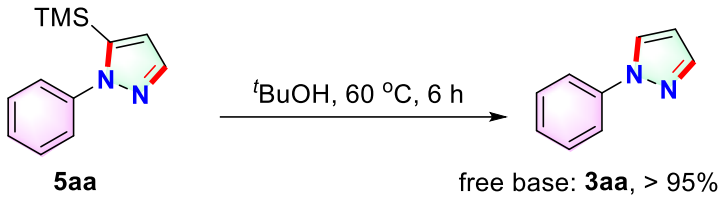
6.4 Intermediate experiments

6.4.1



In the nitrogen atmosphere, an oven-dried new pressure tube (38 mL volume) was charged with a magnetic stirring bar, **5aa** (0.4 mmol, 86.4 mg), ^{t}BuOK (1.1 mmol, 123.4 mg) and 2.0 mL of ^{t}BuOH were added in sequence under magnetic stirring. Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal sand bath (60 °C). After 6 hours the reaction was cooled, a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation.

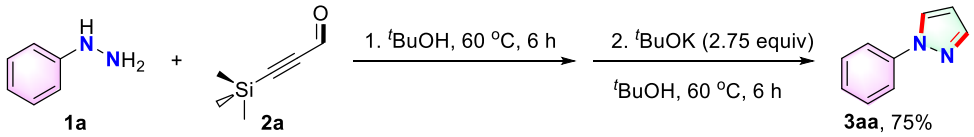
6.4.2



5aa free base: **3aa**, > 95%

In the nitrogen atmosphere, an oven-dried new pressure tube (38 mL volume) was charged with a magnetic stirring bar, **5aa** (0.4 mmol, 86.4 mg), and 2.0 mL of ^{t}BuOH were added in sequence under magnetic stirring. Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal sand bath (60 °C). After 6 hours the reaction was cooled, a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation.

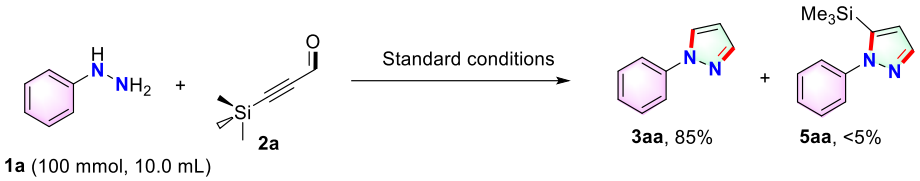
6.4.3 The cascade reaction



1a **2a** **3aa**, 75%

In the nitrogen atmosphere, an oven-dried new pressure tube (38 mL volume) was charged with a magnetic stirring bar, **1a** (0.4 mmol), **2a** (0.5 mmol) and ^{t}BuOH (2.0 mL) were added in sequence under magnetic stirring. Then the seal tube was closed tightly with a teflon cap, and immersed into a pre-heated metal sand bath (60 °C). After 6 hours the reaction was cooled, ^{t}BuOK (0.4 mmol) was added into the reaction mixture. Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal sand bath (60 °C). After 6 hours the reaction was cooled, a small aliquot of the organic phase was analyzed by GC and GC-MS to monitor product formation. Purification of the remainder by column chromatography on silica gel gave the corresponding product **3aa** (petroleum ether / ethyl acetate = 40:1) in the reported yield.

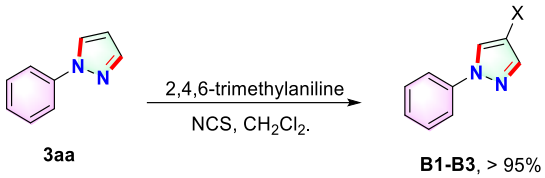
7. Gram-Scale Synthesis



In the nitrogen atmosphere, an oven-dried pressure tube (1000 mL volume) was charged with a magnetic stirring bar, ^{t}BuOK (275 mmol, 30.9 g), **1a** (100 mmol, 10.0 mL), **2a** (125 mmol, 18.5 mL) and H_2O: ethanol = 1:4 (v/v, 300.0 mL). Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath (60 °C) for 6 h. After completion of the reaction based on TLC monitoring, the reaction mixture was concentrated under vacuum. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 40:1 – 10:1) on silica gel to give the product as **3aa** a white solid in 85% yield (12.2 g).

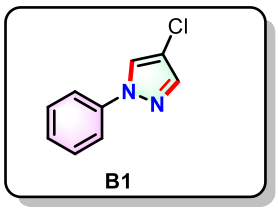
8. Further Transformation

8.1 Synthesis of B1 - B3 from hydrazone 3aa



In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, **3aa** (0.5 mmol, 72mg), 2,4,6 trimethylaniline (10 μmol, 1.4 μL), NXS (0.55 mmol) and CH_2Cl_2 (3.0 mL). Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated bath (-40 °C) for 18 h and then at 0 °C for 6 h. After completion of the reaction based on TLC monitoring, the reaction mixture was concentrated under vacuum. The residue was purified by column chromatography (hexane/ethyl acetate = 19:1) on silica gel to give the corresponding products, respectively.

4-chloro-1-phenyl-1H-pyrazole (B1)[13]



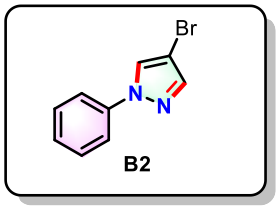
The title compound was prepared according to the general procedure and purified by column chromatography to give the white solid 88.1 mg, 99% yield. Purification by column chromatography on silica gel (hexane/ethyl acetate = 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.64 – 7.62 (m, 3H), 7.47 – 7.44 (m, 2H), 7.33 – 7.29 (m, 1H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 139.6, 129.7, 127.1, 124.9, 119.1, 112.5.

HRMS (ESI) calcd. for $C_9H_8ClN_2$ $[M+H]^+$: 179.0376, found: 179.0279.

4-bromo-1-phenyl-1H-pyrazole (B2)[13]



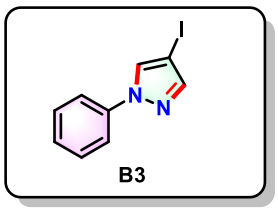
The title compound was prepared according to the general procedure and purified by column chromatography to give the white solid 109.4 mg, 99% yield. Purification by column chromatography on silica gel (hexane/ethyl acetate = 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.67 (s, 1H), 7.64 – 7.62 (m, 2H), 7.46 – 7.42 (m, 2H), 7.31 (tt, *J* = 7.2, 1.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 139.7, 129.6, 127.1, 119.1, 95.7.

HRMS (ESI) calcd. for $C_9H_8BrN_2$ $[M+H]^+$: 222.9871, found: 222.9874.

4-iodo-1-phenyl-1H-pyrazole (B3)[14]



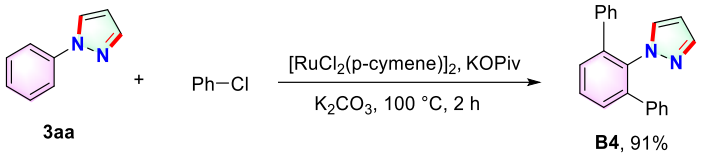
The title compound was prepared according to the general procedure and purified by column chromatography to give the white solid 131.8 mg, 98% yield. Purification by column chromatography on silica gel (hexane/ethyl acetate = 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.71 (s, 1H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 139.5, 131.3, 129.5, 127.0, 119.1, 58.8.

HRMS (ESI) calcd. for $C_9H_8IN_2$ $[M+H]^+$: 270.9732, found: 270.9735.

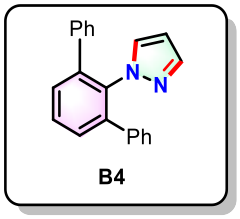
8.2 Synthesis of B4 from hydrazone 3aa



3aa **B4**, 91%

In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, 15.2 mg (0.025 mol, 5 mol%) of $[RuCl_2(p\text{-cymene})]_2$, 14.8 mg of KOPiv (0.1 mmol, 20 mol%) and 198 mg of K_2CO_3 (1.5 mmol, 3 equiv.). 2 mL of distilled water was added before addition of 72.0 mg of **3aa** (0.5 mmol) and 141 mg of chlorobenzenze (1.25 mmol, 2.5 equiv). Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 100 °C for 2 h. After completion of the reaction, the separated aqueous phase was extracted with EtOAc (2 × 5 mL). The combined organic layers were washed with H_2O (5.0 mL) and dried over $MgSO_4$ and concentrated in vacuum. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to give **B4** a white solid in 91% yield (142.0 g).

1-([1,1':3',1''-terphenyl]-2'-yl)-1H-pyrazole (B4)[15]



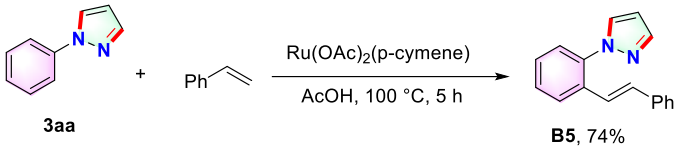
B4

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.4 Hz, *J* = 6.4 Hz, 1 H), 7.54 – 7.52 (m, 2H), 7.40 (d, *J* =1.6 Hz, 1H), 7.28 – 7.27 (m, 6H), 7.17 – 7.15 (m, 4H), 7.11 (d, *J* = 2.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 139.4, 138.8, 136.5, 132.4, 130.1, 129.1, 128.3, 128.1, 127.2, 106.1.

HRMS (ESI) calcd. for $C_{21}H_{17}N_2$ $[M+H]^+$: 297.1392, found: 297.1394.

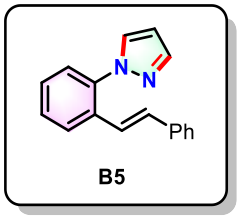
8.3 Synthesis of B5 from hydrazone 3aa



3aa **B5**, 74%

In the air atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, 9.9 mg (0.025 mmol, 5 mol%) of $Ru(OAc)_2$(p-cymene), 20 mg of $Cu(OAc)_2$•H_2O (0.1 mmol, 20 mol%), 72 mg (0.5 mmol, 1 equiv) of **3aa**, styrene (1.25 mmol, 2.5 equiv) and 1 mL of AcOH as solvent. Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 100 °C for 5 h. After completion of the reaction, the reaction mixture was cooled and added 10 mL of $NaHCO_3$ solution followed by the addition of 15 mL of ethyl acetate. The combined organic layers were washed with $NaHCO_3$ and dried over $MgSO_4$ and concentrated in vacuum. The residue was purified by column chromatography (petroleum ether/Et_2O = 4:1) on silica gel to give **B5** a white solid in 74% yield (91.0 mg).

(*E*)-1-(2-styrylphenyl)-1H-pyrazole (B5)[16]

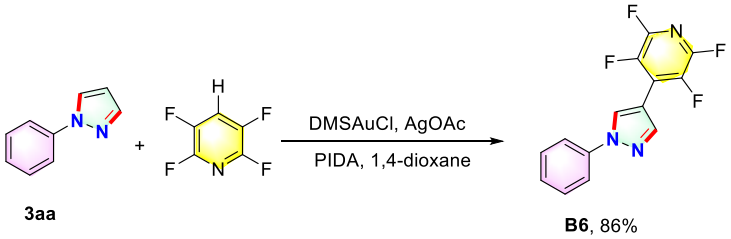


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 1.2 Hz, 1H), 7.71 (d, *J* = 2.0 Hz, 1H), 7.51 – 7.38 (m, 5H), 7.38 – 7.22 (m, 3H), 7.09 (d, *J* = 16.0 Hz, 1H), 6.96 (d, *J* = 16.0 Hz, 1H), 6.50 (t, *J* = 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 138.8, 137.0, 133.0, 131.5, 131.2, 128.6, 128.4, 128.1, 127.9, 126.7, 126.6, 126.3, 123.9, 106.6.

HRMS (ESI) calcd. for $C_{17}H_{15}N_2$ $[M+H]^+$: 247.1235, found: 247.1236.

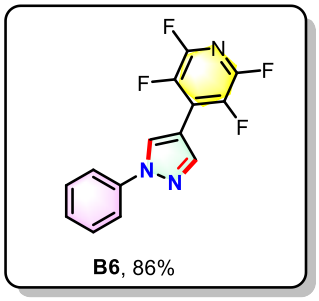
8.4 Synthesis of B6 from hydrazone 3aa



3aa **B6**, 86%

In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, DMSAuCl (0.025 mmol, 5 mol%), AgOAc (0.1 mmol, 20 mol%), and PIDA (0.75 mmol). Then a solution of **3aa** (0.5 mmol) and 2,3,5,6-tetrafluoropyridine (0.75 mmol) in 1,4-dioxane (5.0 mL) was added to the tube. Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 100 °C for 15 h. After completion of the reaction, the reaction mixture was cooled and added 5.0 mL of $NaHCO_3$ solution followed by the addition of 5.0 mL of ethyl acetate. The combined organic layers were washed with $NaHCO_3$ and dried over $MgSO_4$ and concentrated in vacuum. The residue was purified by column chromatography on silica gel to give **B6** a white solid in 86% yield (93.3 mg).

2,3,5,6-tetrafluoro-4-(1H-pyrazol-1-yl)pyridine (B6)[17]



B6, 86%

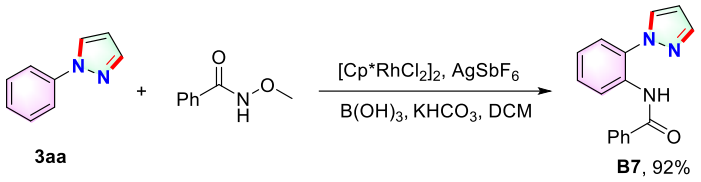
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.34 (t, *J* = 1.6 Hz, 1H), 7.80 – 7.77 (m, 2H), 7.57 – 7.53 (m, 2H), 7.44 – 7.40 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1 (dddd, *J* = 243.4, 16.8, 14.1, 2.8 Hz), 141.3 (t, *J* = 7.4 Hz), 139.2, 138.7 (dm, J = 259.6 Hz), 129.7, 128.3 (t, *J* = 7.6 Hz), 127.9, 125.0 – 124.7 (m), 119.7, 110.0 (t, *J* = 5.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -91.50 – -91.71 (m, 2F), -142.35 – -142.56 (m, 2F).

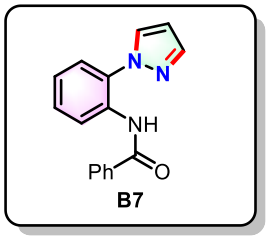
HRMS (ESI) calcd. for $C_{14}H_8F_4N_3$ $[M+H]^+$: 294.0654, found: 294.0657.

8.5 Synthesis of B7 from hydrazone 3aa



In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, *N*-Methoxybenzamide (6.7 mmol, 1.0 g), boric acid (0.34 mmol, 21.0 mg), potassium bicarbonate (6.7 mmol, 670.0 mg) and $[Cp^*RhCl_2]_2$ (0.34 mmol, 210.2 mg). Then silver hexafluoroantimonate (1.34 mmol, 460.5 mg), anhydrous DCM (13.5 mL) and 1-phenyl-1H-pyrazole **3aa** (6.7 mmol, 964.8 mg) was added to the tube. Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 90 °C for 24 h. When the reaction was finished, the residue was purified by column chromatography (petroleum ether / ethyl acetate = 10:1) on silica gel to give **B7** a white solid in 92% yield.

***N*-(2-(1H-pyrazol-1-yl)phenyl)benzamide (B7)[18]**

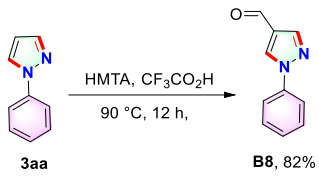


^{1}H NMR (400 MHz, $CDCl_3$) δ 11.32 (s, 1H), 8.71 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.96 – 7.93 (m, 2H), 7.87 – 7.85 (m, 2H), 7.56 – 7.46 (m, 3H), 7.43 – 7.36 (m, 2H), 7.19 (ddd, *J* = 8.0, 7.2, 1.2 Hz, 1H), 6.52 – 6.51 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 141.2, 134.9, 131.9, 131.9, 130.3, 129.2, 128.8, 128.2, 127.4, 124.1, 123.0, 122.3, 107.4.

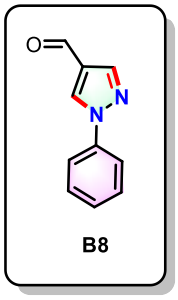
HRMS (ESI) calcd. for $C_{16}H_{14}N_3O$ $[M+H]^+$: 264.1137, found: 264.1136.

8.6 Synthesis of LQFM219 from hydrazone 3aa



In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, 1-phenyl-1H-pyrazole **3aa** (0.5 mmol, 72.0 mg), HMTA (1.0 mmol, 140.19 mg) and 2.0 mL of CF_3CO_2H. Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 90 °C for 12 h. After completion of the reaction based on TLC monitoring, the reaction mixture was concentrated under vacuum. The residue was purified by column chromatography (petroleum ether / ethyl acetate = 10:1) on silica gel to give **B8** a white solid in 82% yield (70.5 mg).

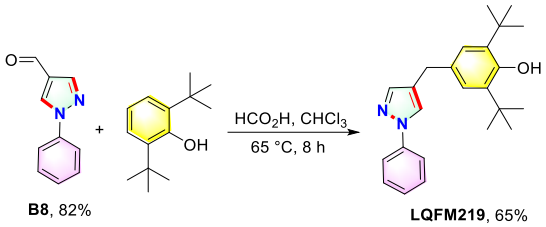
1-phenyl-1H-pyrazole-4-carbaldehyde (B8)[19]



^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.44 (s, 1H), 8.16 (s, 1H), 7.73 – 7.68 (m, 2H), 7.50 (dd, *J* = 8.4, 7.5 Hz, 2H), 7.40 – 7.37 (m, 1H).

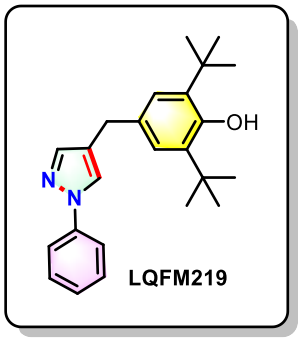
^{13}C NMR (100 MHz, $CDCl_3$) δ 184.2, 141.8, 139.2, 130.1, 129.8, 128.1, 125.8, 120.0.

HRMS (ESI) calcd. for $C_{10}H_9N_2O$ $[M+H]^+$: 173.0715, found: 173.0716.



In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, formic acid (3.0 mL), **3aa** (1.0 mmol, 172 mg), 2,6-di-tert-butylphenol (1.0 mmol, 206.0 mg), and 2.0 mL of $CHCl_3$. Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 65 °C for 8 h. After completion of the reaction, the reaction mixture was cooled and added 5.0 mL of H_2O solution followed by the addition of 5.0 mL of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuum. The residue was purified by column chromatography on silica gel to give **LQFM219** a white solid in 65% yield (235.3 mg).

2,6-di-tert-butyl-4-((1-phenyl-1H-pyrazol-4-yl)methyl)phenol (LQFM219)[19]

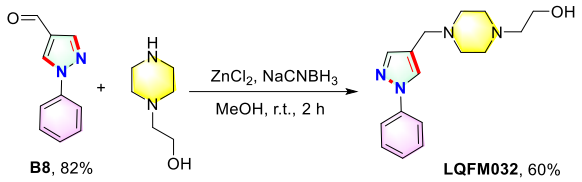


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 0.8 Hz, 1H), 7.65 (dd, J = 8.4 Hz, J = 1.2 Hz, 2H), 7.57 (s, 1H), 7.42 (ddd, J = 8.4 Hz, J = 7.2 Hz, J = 1.2 Hz, 2H), 7.24 (tt, J = 7.2 Hz, J = 1.2 Hz, 1H), 7.05 (s, 2H), 5.08 (s, 1H), 3.81 (s, 2H), 1.43 (s, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 141.3, 140.4, 136.1, 131.1, 129.4, 126.0, 125.4, 125.0, 123.8, 118.7, 34.6, 30.4.

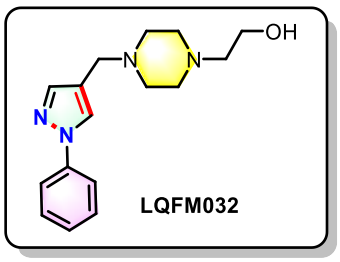
HRMS (ESI) calcd. for $C_{24}H_{31}N_2O$ $[M+H]^+$: 363.2436, found: 363.2438.

8.7 Synthesis of LQFM032 from hydrazone 3aa



In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, $ZnCl_2$ (0.5 mmol), **B8** (1.0 mmol, 172.1 mg), 1-(2- hydroxyethyl)piperazine (1.0 mmol, 130.11 mg), $NaBH_3CN$ (0.5 mmol, 31.42 mg) and 5 mL of MeOH. Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 25 °C for 2 h. In turn, MeOH was then evaporated and the residue was partitioned between water and CH_2Cl_2. The combined organic layers were dried with Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography (hexane / ethyl acetate = 10:1) on silica gel to give **LQFM032** the colorless oil in 60% yield (171.6 mg).

2-(4-((1-phenyl-1H-pyrazol-4-yl)methyl)piperazin-1-yl)ethan-1-ol (LQFM032)[20]

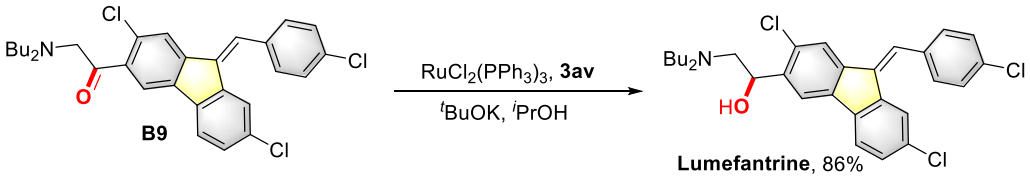


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.71 – 7.63 (m, 2H), 7.64 (s, 1H), 7.54 – 7.36 (m, 2H), 7.35 – 7.19 (m, 1H), 3.66 (t, *J* = 5.28, 2H), 3.54 (s, 2H), 2.98 (s, 1H), 2.77 – 2.57 (m, 8H), 2.62 (t, *J* = 5.28, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 129.4, 126.7, 126.4, 118.9, 118.8, 59.4, 57.6, 52.8, 52.3 40.0.

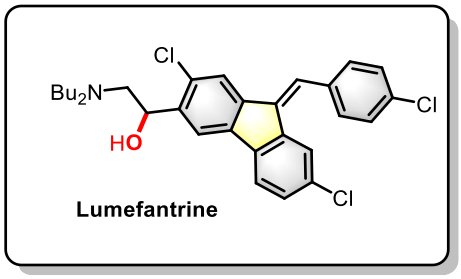
HRMS (ESI) calcd. for $C_{16}H_{23}N_4O$ $[M+H]^+$: 287.1872, found: 287.1876.

8.8 3av as ligand



In the nitrogen atmosphere, an oven-dried Schlenk Flask (38 mL volume) was charged with a magnetic stirring bar, ketone **B9** (0.5 mmol, 262.5 mg), ^{t}BuOK (0.6 mmol, 1.2 equiv, 67.3 mg), $RuCl_2(PPh_3)_3$ (0.005 mmol, 1 mol%), **3av** (0.006 mmol, 1.2 mol%, 0.87 mg) and ^{i}PrOH (5.0 mL). Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 120 °C for 6 h. After completion of the reaction, the reaction mixture was cooled and added 100 µL of half-saturated brine solution followed by the addition of 5.0 mL of CH_2Cl_2. The combined organic layers were extracted with ethyl acetate (5.0 mL) for four times and dried over $MgSO_4$ and concentrated in vacuum. The residue was purified by column chromatography on silica gel to give **Lumefantrine** a yellow solid in 86% yield (226.61 mg).

(*E*)-2-(dibutylamino)-1-(2,7-dichloro-9-(4-chlorobenzylidene)-9H-fluoren-3-yl)ethan-1-ol[21]

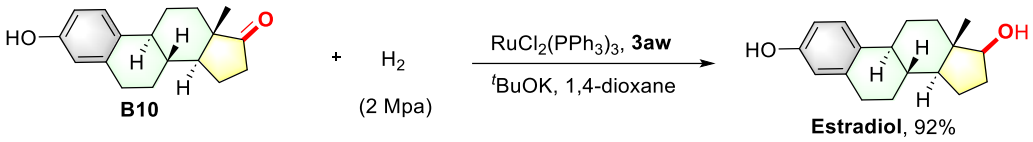


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 1.6 Hz, 1H), 7.68 (d, *J* = 1.6 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.52 – 7.39 (m, 5H), 7.33 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.36 (dd, *J* = 10.0, 3.2 Hz, 1H), 4.54 (s, 1H), 2.88 (dd, *J* = 13.2, 3.6 Hz, 1H), 2.79 – 2.59 (m, 2H), 2.59 – 2.38 (m, 3H), 1.54 – 1.45 (m, 4H), 1.43 – 1.30 (m, 4H), 0.96 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 139.8, 138.2, 136.4, 135.0, 135.0, 134.7, 134.2, 133.2, 132.9, 130.6, 129.1, 128.4, 127.7, 126.3, 123.9, 123.0, 120.7, 65.4, 59.9, 53.4, 29.1, 20.6, 14.1.

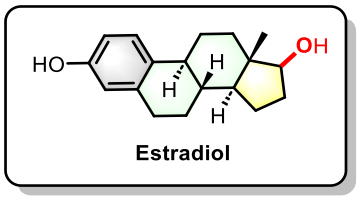
HRMS (ESI) calcd. for $C_{30}H_{33}Cl_3NO$ $[M+H]^+$: 528.1628, found: 528.1626.

8.9 3aw as ligand



In the nitrogen atmosphere, an oven-dried vial (10 mL volume) was charged with a magnetic stirring bar, $RuCl_2(PPh_3)_3$ (0.025 mmol, 1 mol%), **3aw** (0.003 mmol, 1.2 mol%, 0.54 mg) and 1,4-dioxane (2.0 mL). Then the seal tube was closed tightly with a teflon cap and immersed into a pre-heated metal bath at 25 °C for 10 minutes. Then, ^{t}BuOK (0.3 mol, 33.7 mg) and **B10** (0.25 mmol) were added into the vial, which was capped with a septum equipped with a syringe needle. The vials were placed in an alloy plate, which was then placed to the pre-dried autoclave. Once sealed, the autoclave was purged 3 times with hydrogen, then pressurized to 20 bar and heated at 110 °C for 16 h. After completion of the reaction, the reaction mixture was cooled to 0 °C and depressurized. The combined organic layers were extracted with ethyl acetate (1.5 mL) and concentrated in vacuum. The residue was purified by column chromatography on silica gel (pentane/ethyl ether = 20:1 – 5:1) to give **Estradiol** a light yellow solid in 92% yield (62.6 mg).

(8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diol[22]



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.50 (d, *J* = 8.4 Hz, 1H), 6.44 (s, 1H), 4.34 (d, *J* = 4.4 Hz, 1H), 3.65 – 3.49 (m, 1H), 2.84 – 2.59 (m, 2H), 2.35 – 2.17 (m, 1H), 2.15 – 1.95 (m, 2H), 1.88 – 1.63 (m, 3H), 1.56 (td, *J* = 11.2, 7.5 Hz, 1H), 1.47 – 1.11 (m, 6H), 0.61 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 137.6, 131.0, 126.6, 115.4, 113.2, 78.5, 47.7, 45.5, 43.9, 32.6, 32.0, 29.8, 28.4, 26.5, 24.4, 17.5.

HRMS (ESI) calcd. for $C_{18}H_{25}O_2$ $[M+H]^+$: 273.1855, found: 273.1857.

9. References

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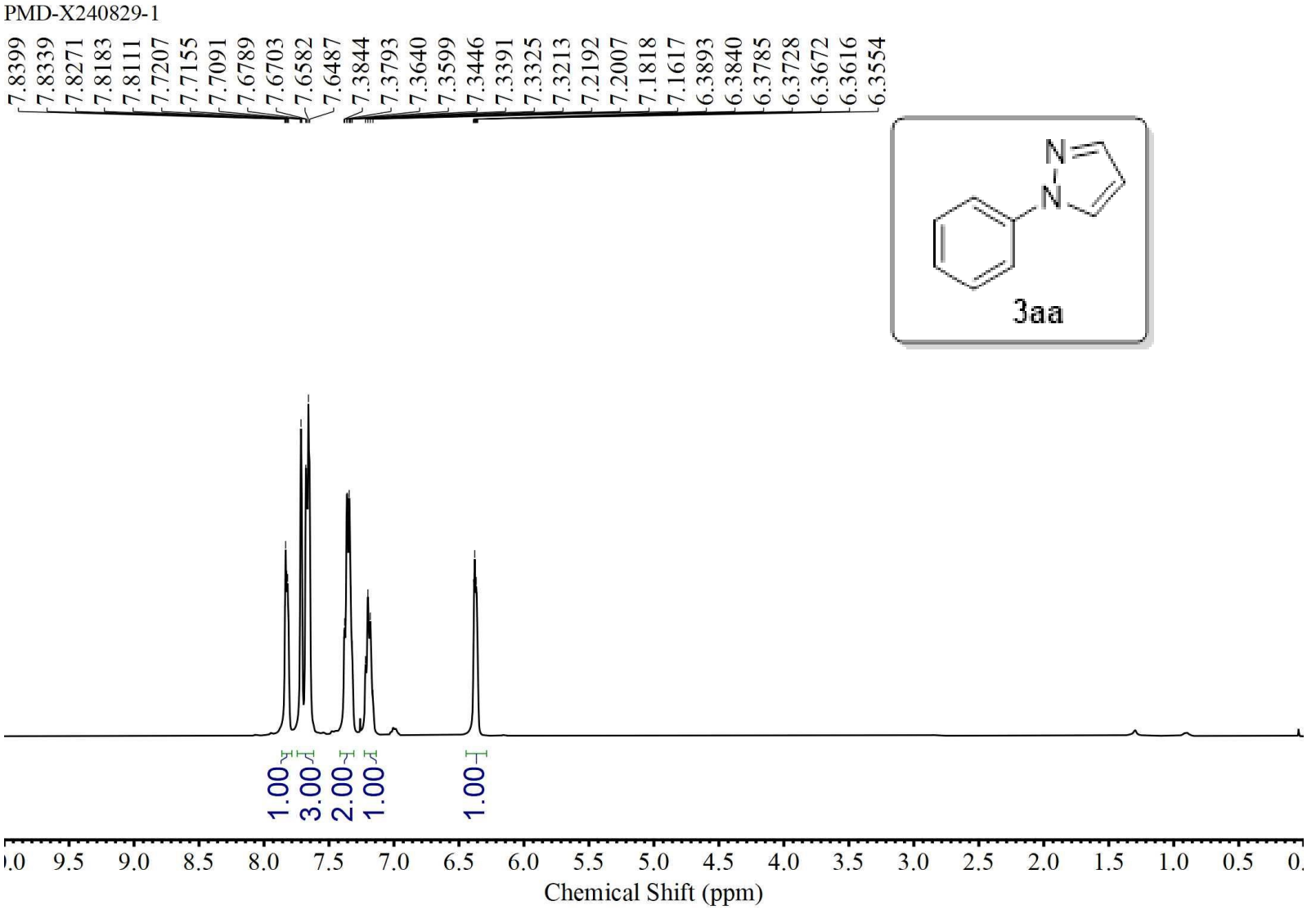
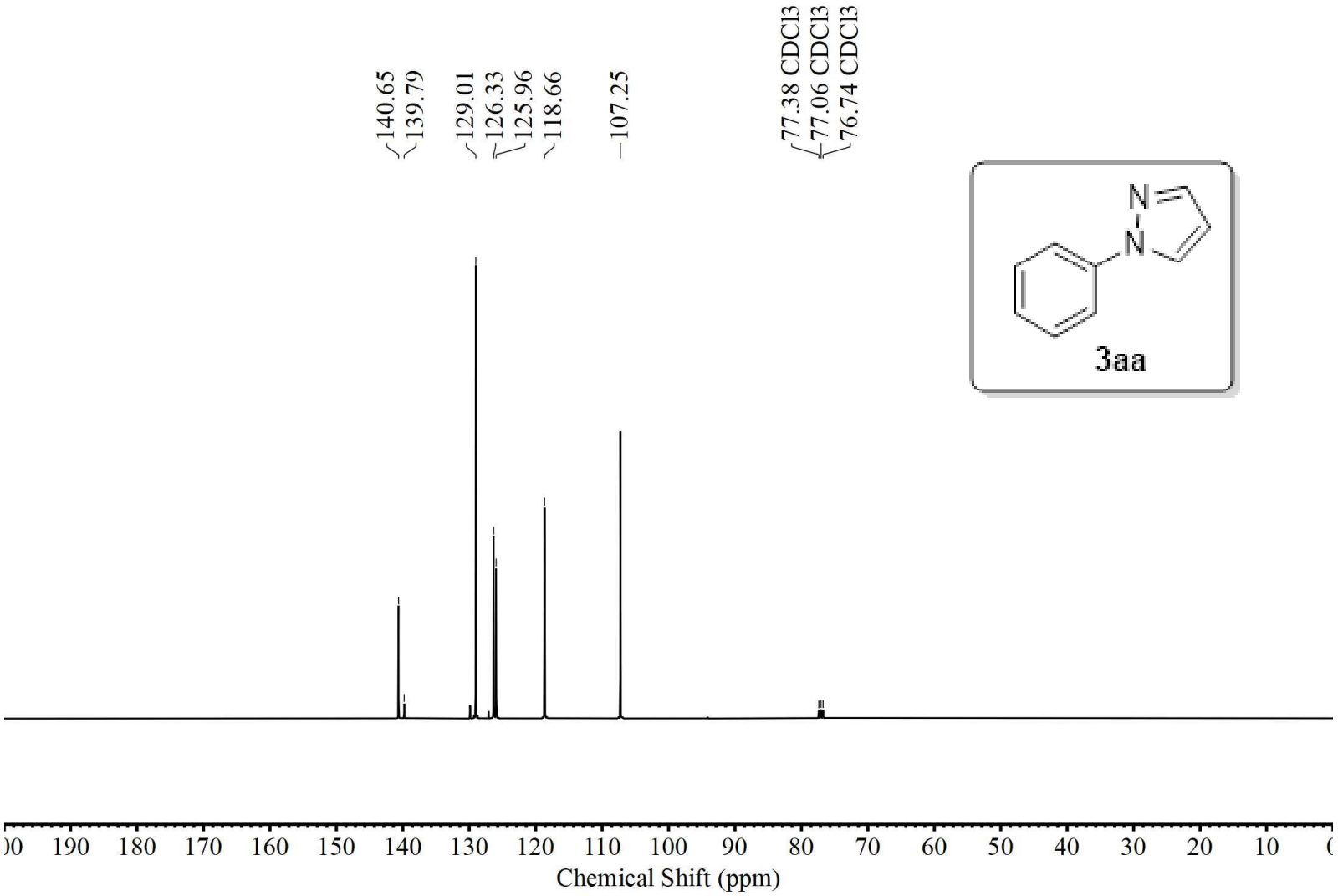
10. NMR Spectra

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

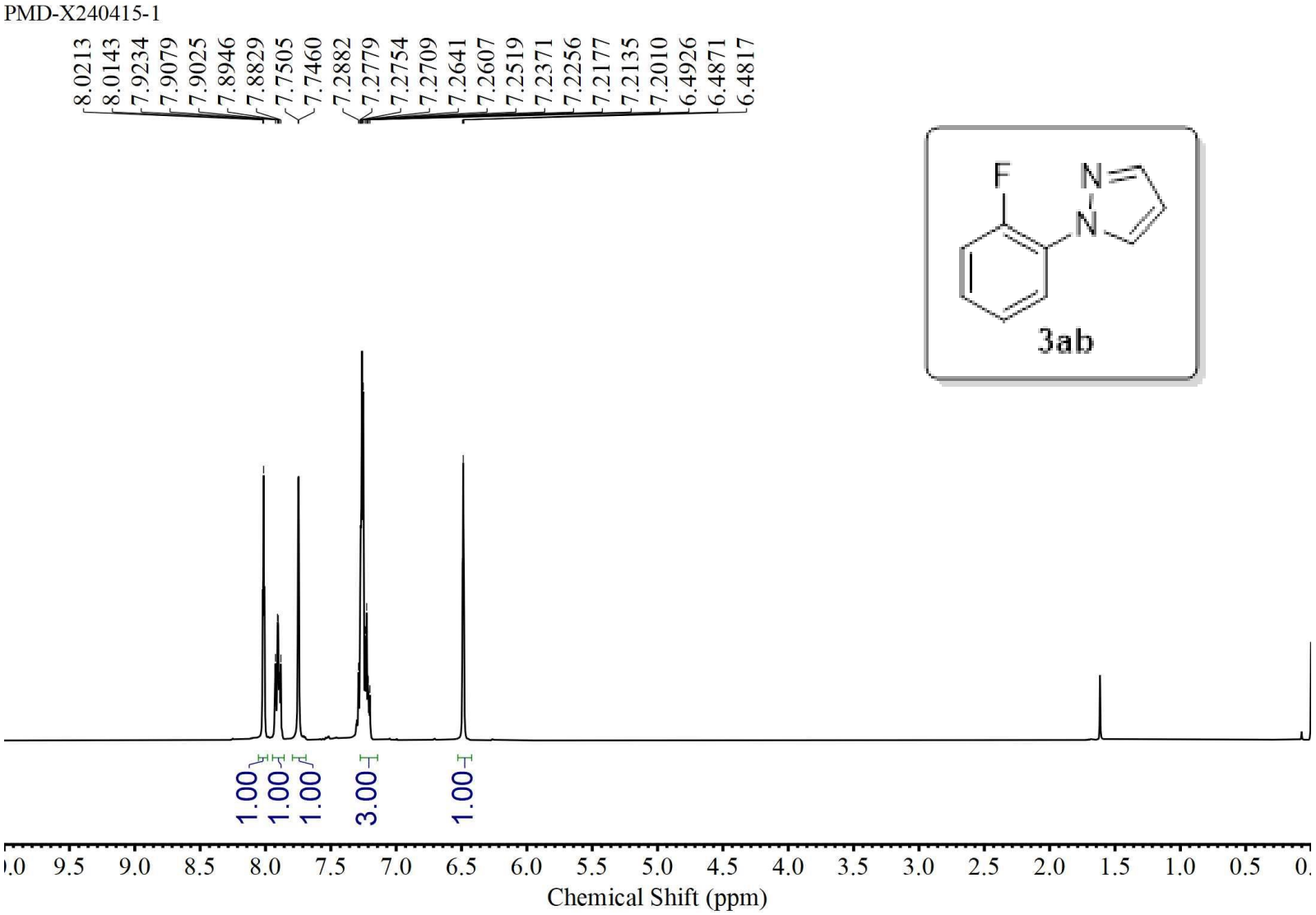


^{13}C NMR spectrum of 3aa (100 MHz, $CDCl_3$)

PMD-X240829-1

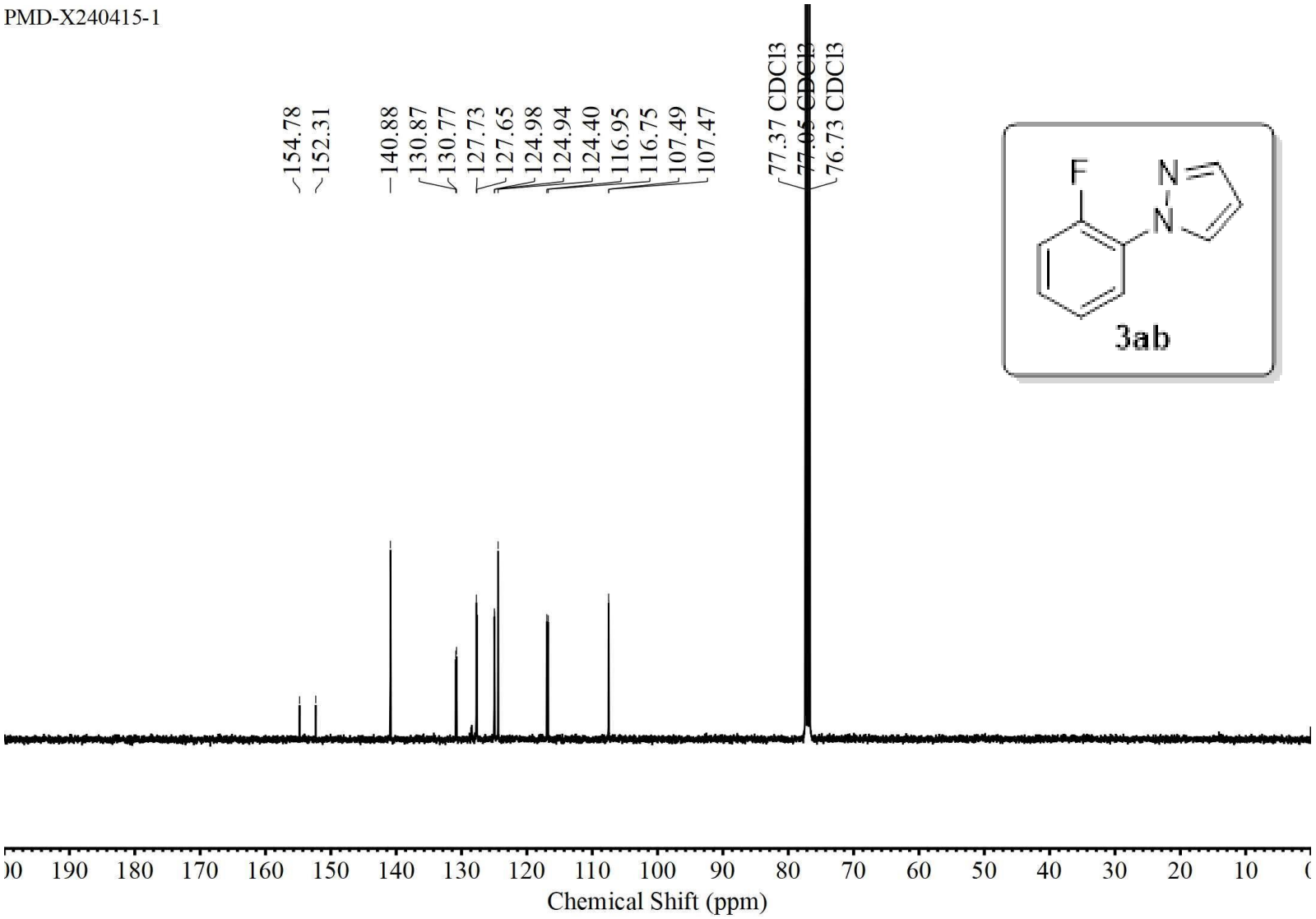


^{1}H NMR spectrum of 3ab (400 MHz, $CDCl_3$)



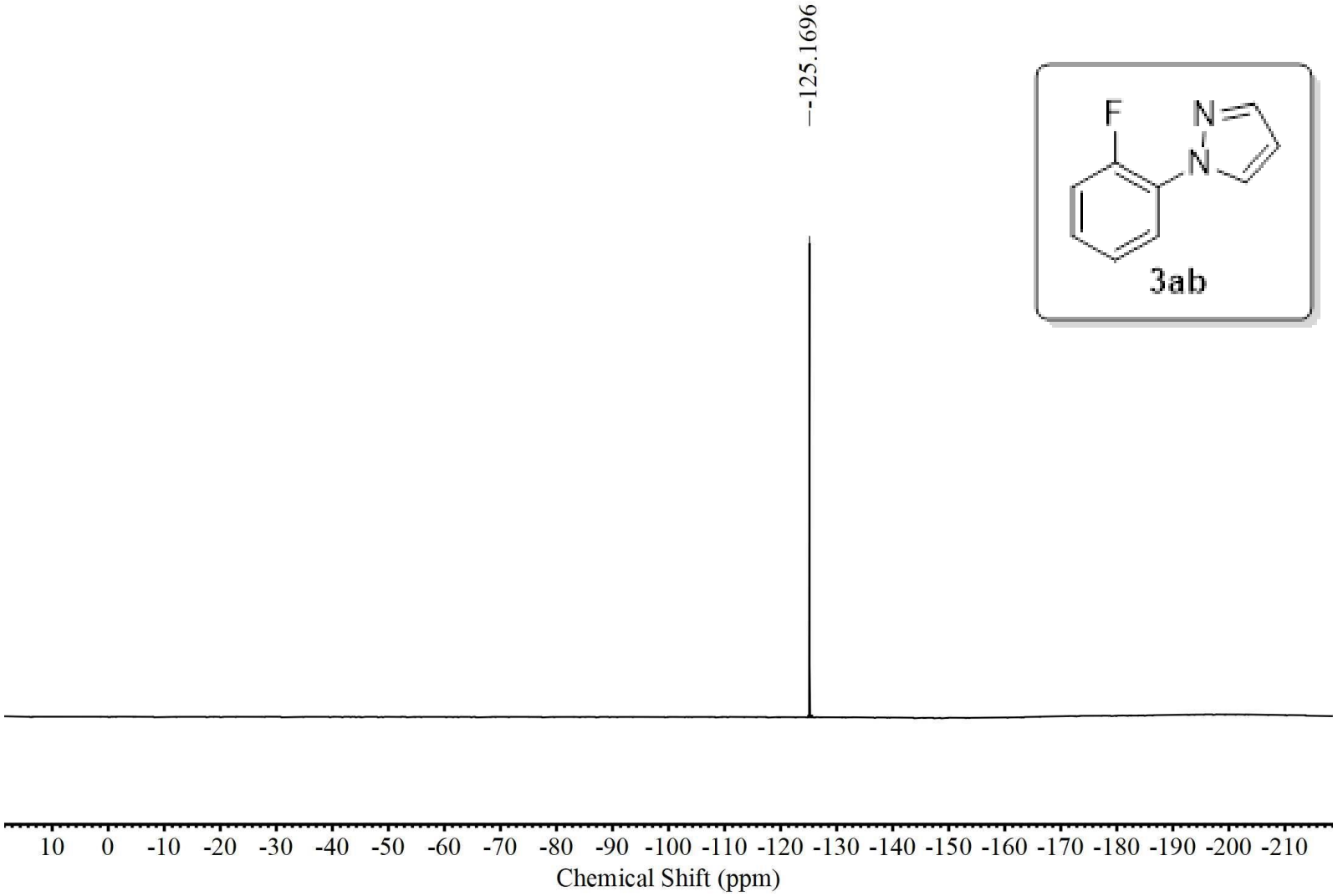
^{13}C NMR spectrum of 3ab (100 MHz, $CDCl_3$)

PMD-X240415-1

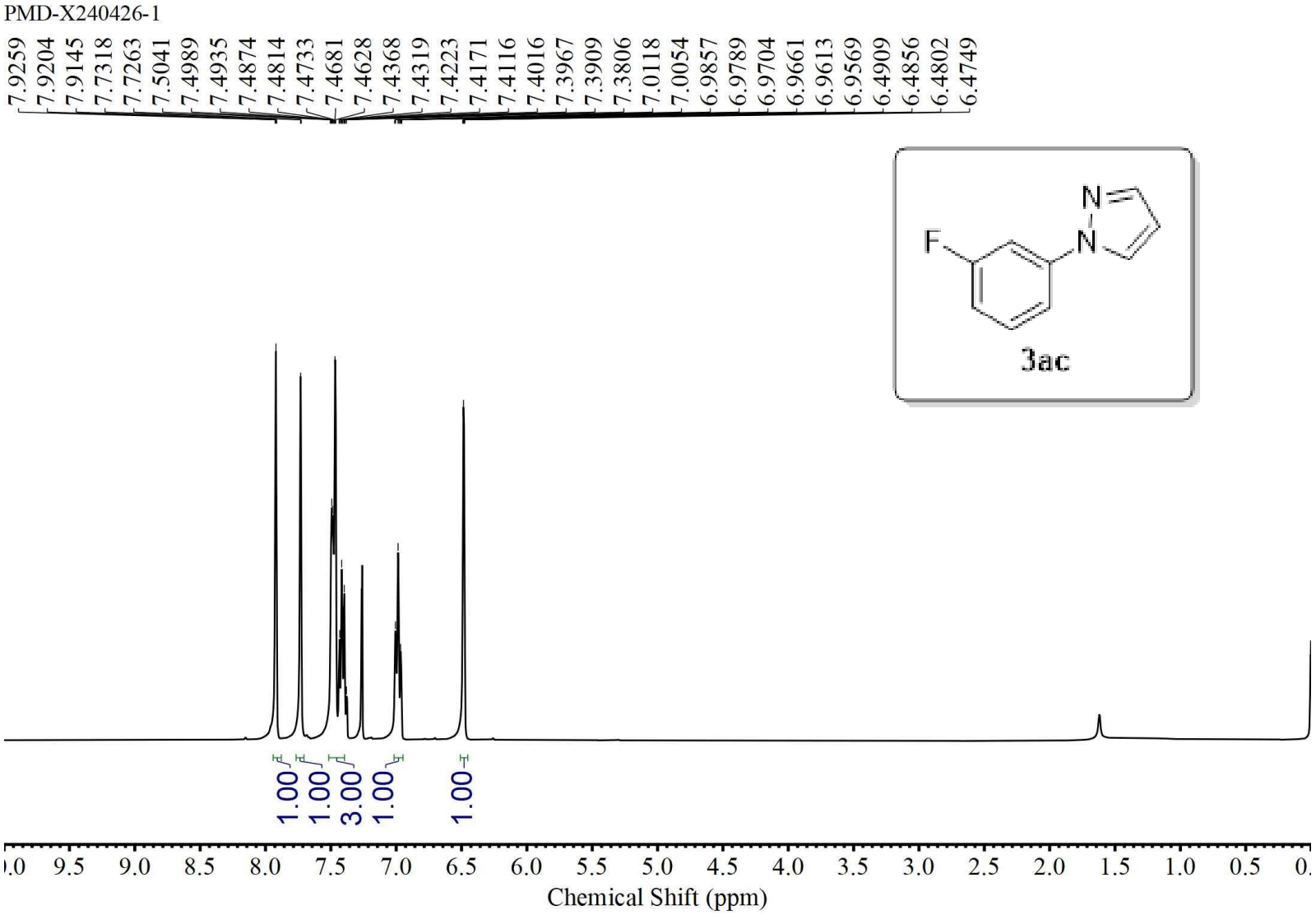


^{19}F NMR spectrum of 3ab (376 MHz, $CDCl_3$)

PMD-X240415-1

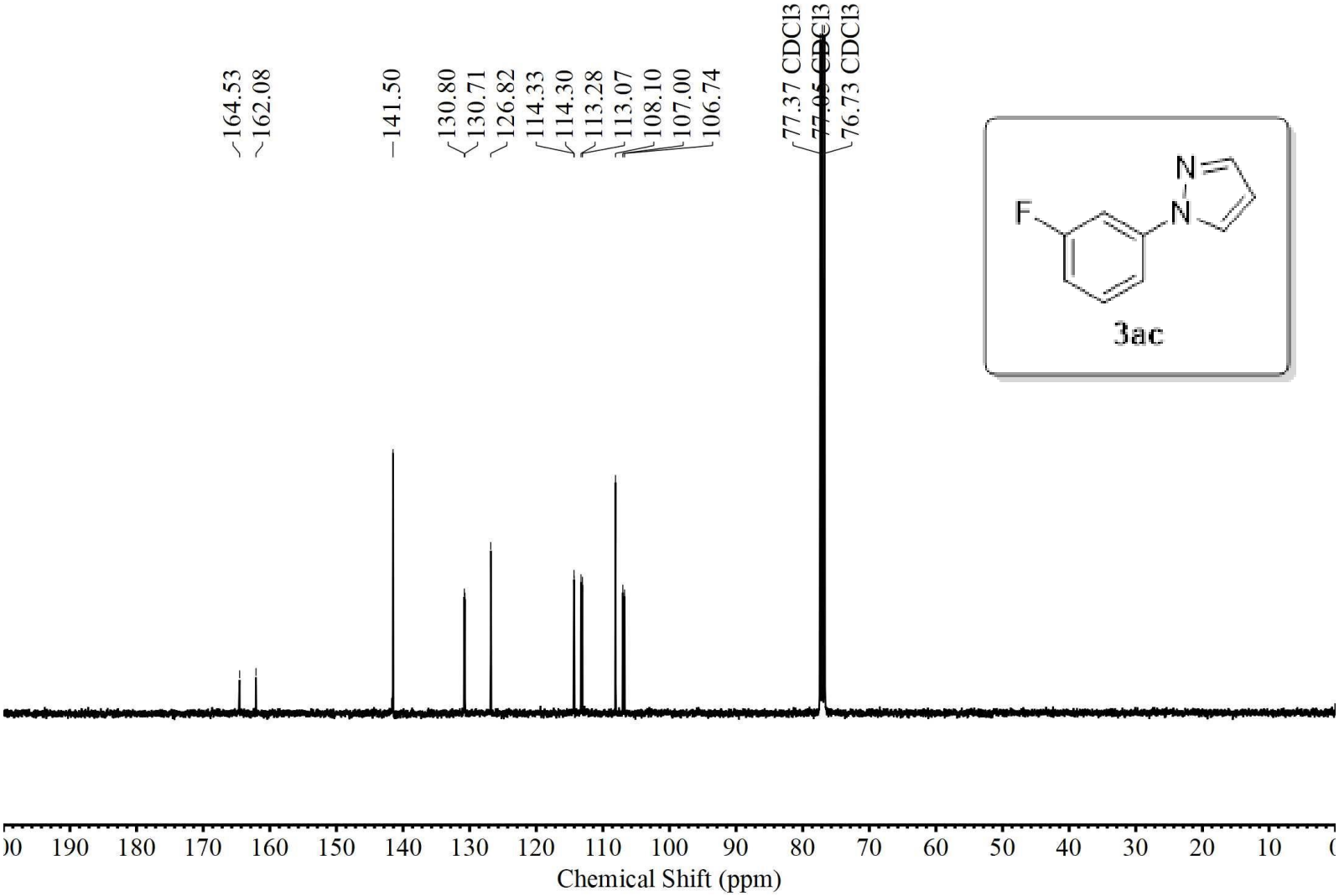


^{1}H NMR spectrum of 3ac (400 MHz, $CDCl_3$)



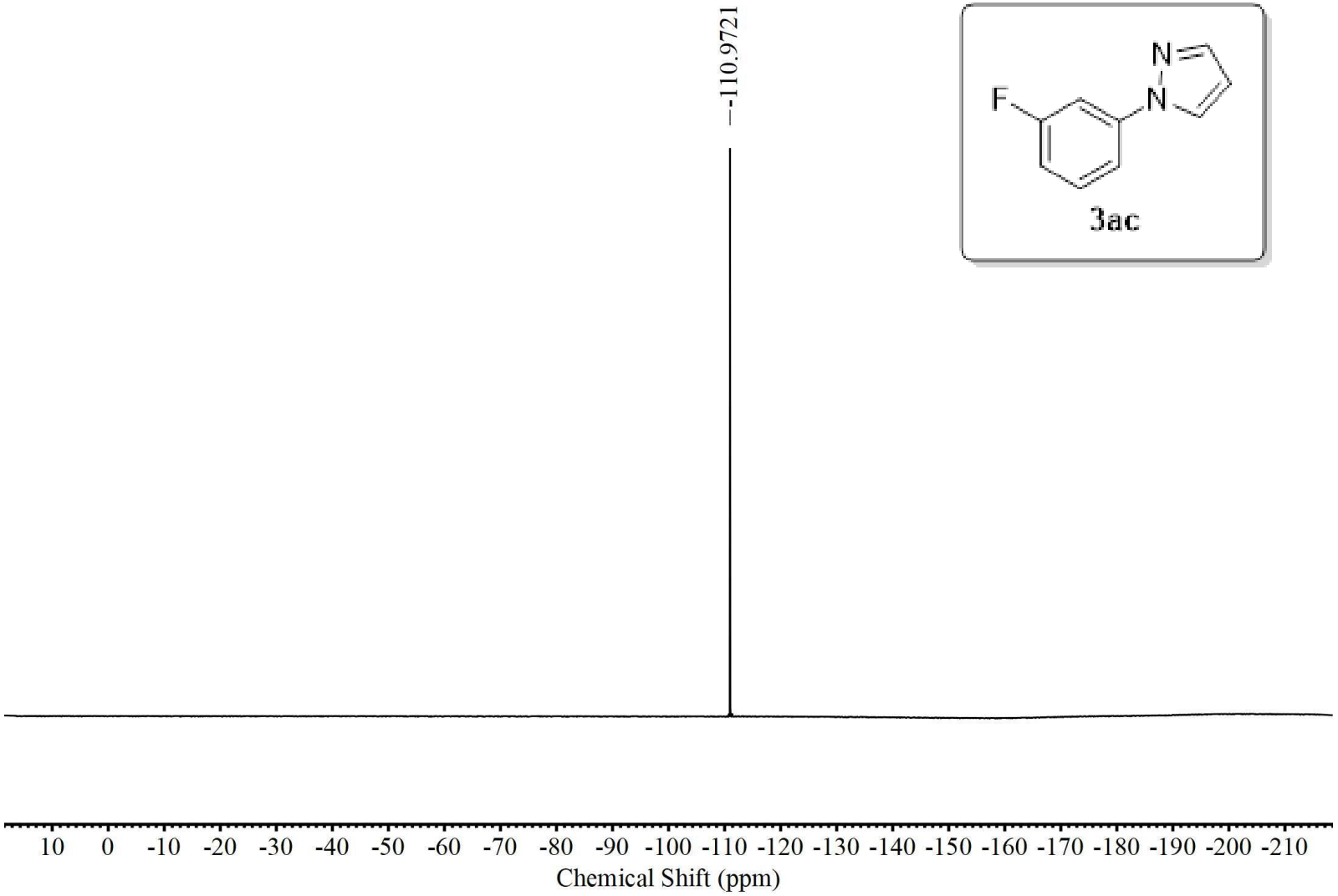
^{13}C NMR spectrum of 3ac (100 MHz, $CDCl_3$)

PMD-X240423-1

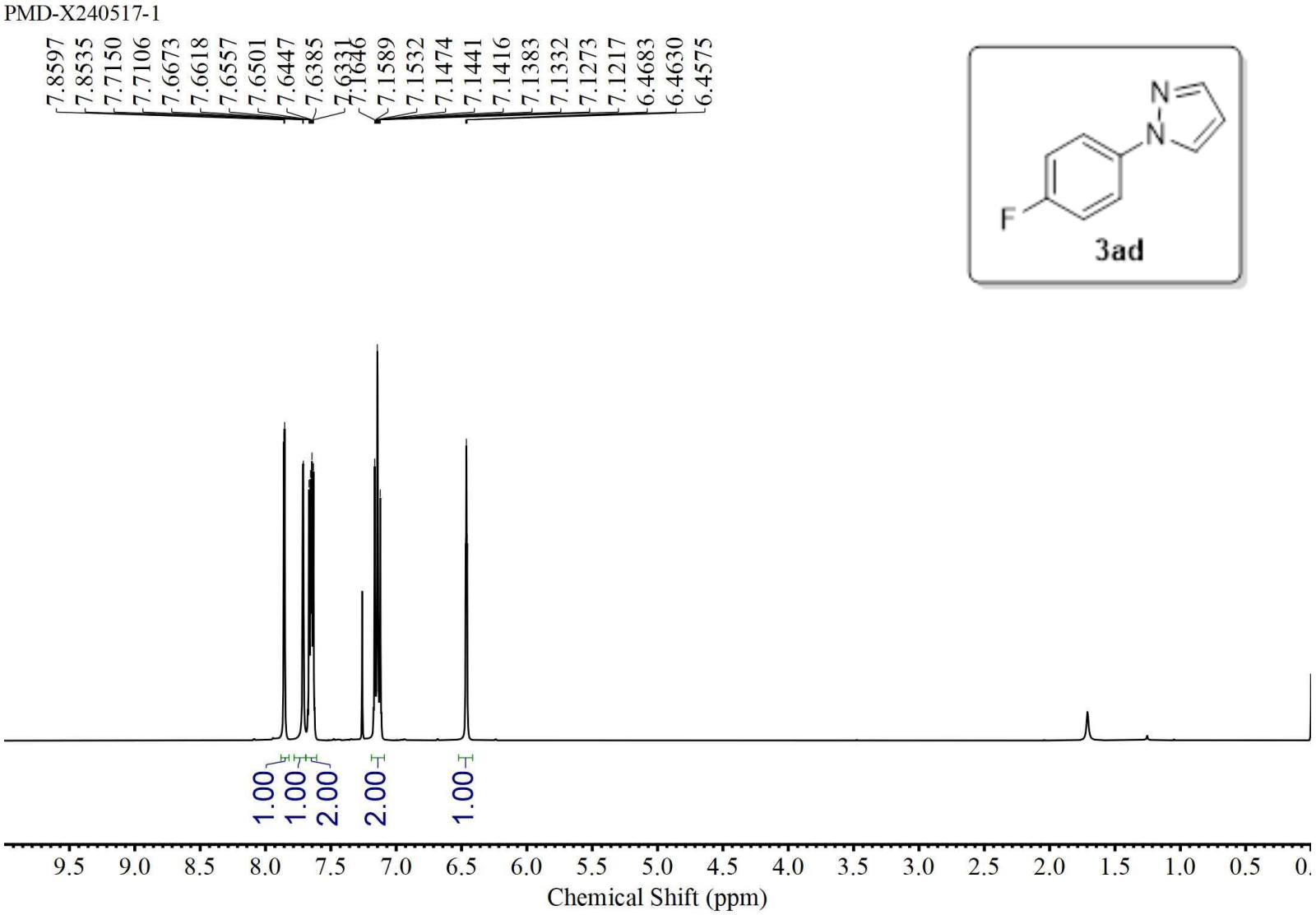


^{19}F NMR spectrum of 3ac (376 MHz, $CDCl_3$)

PMD-X240426-1

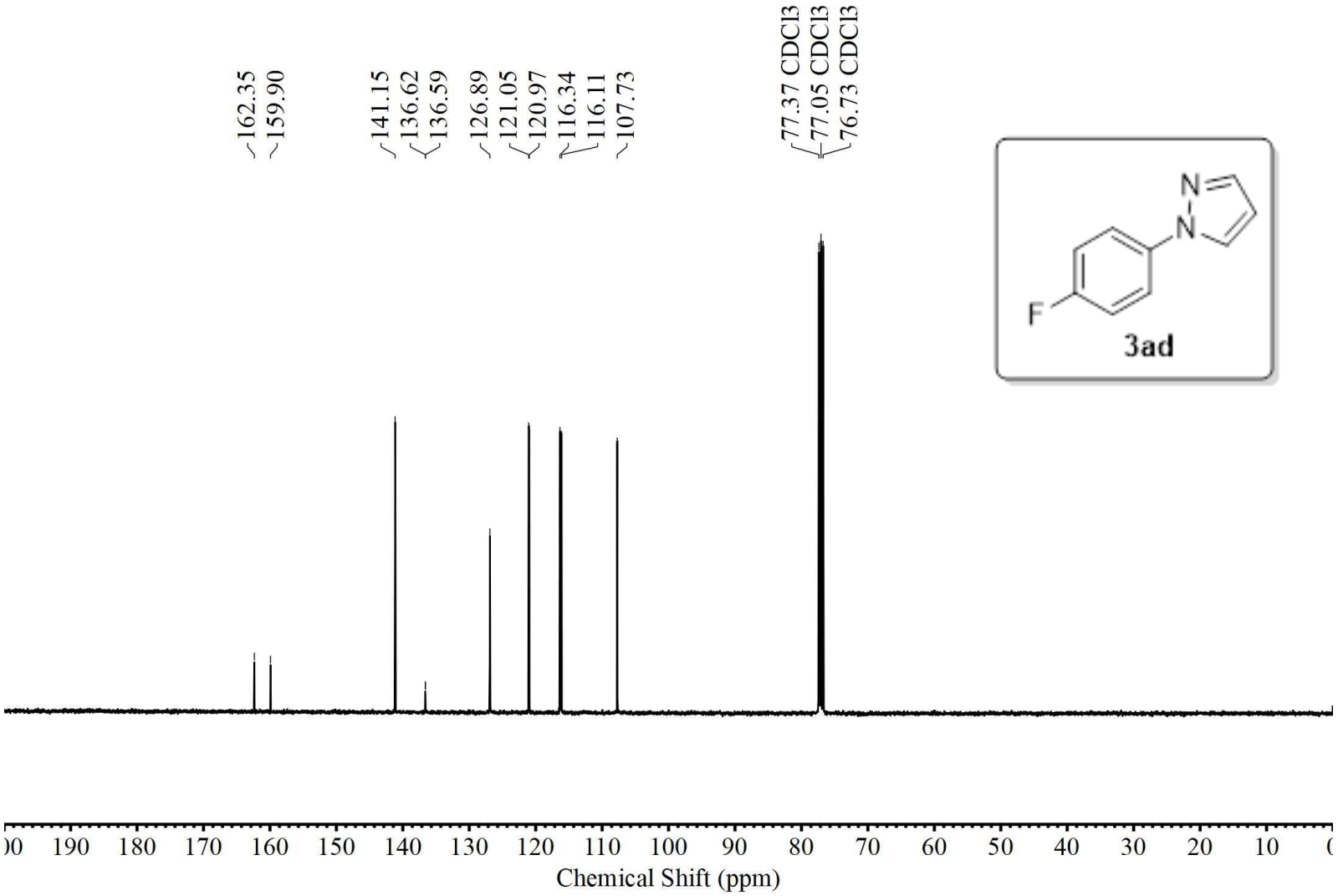


^{1}H NMR spectrum of 3ad (400 MHz, $CDCl_3$)



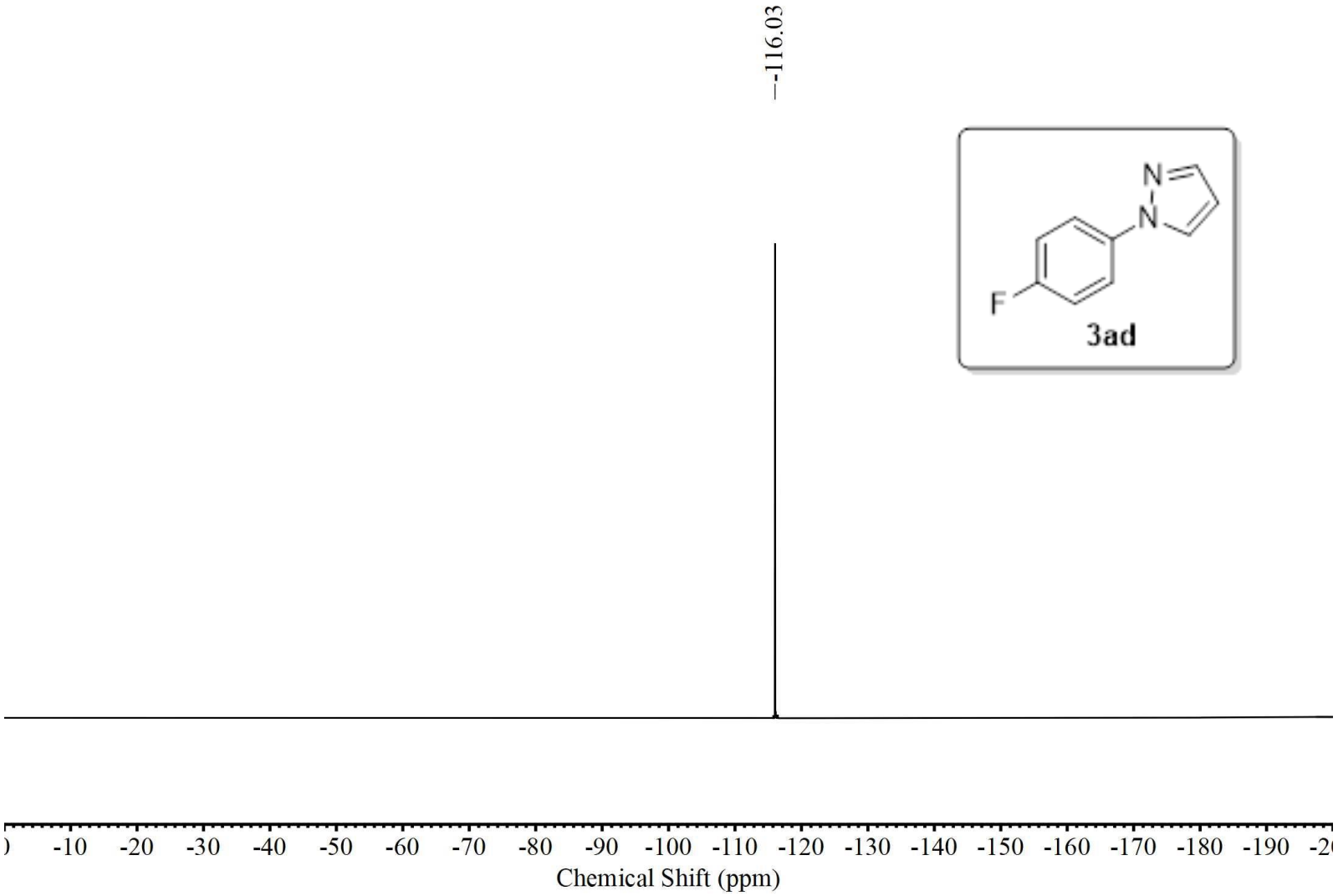
^{13}C NMR spectrum of 3ad (100 MHz, $CDCl_3$)

PMD-X240517-1

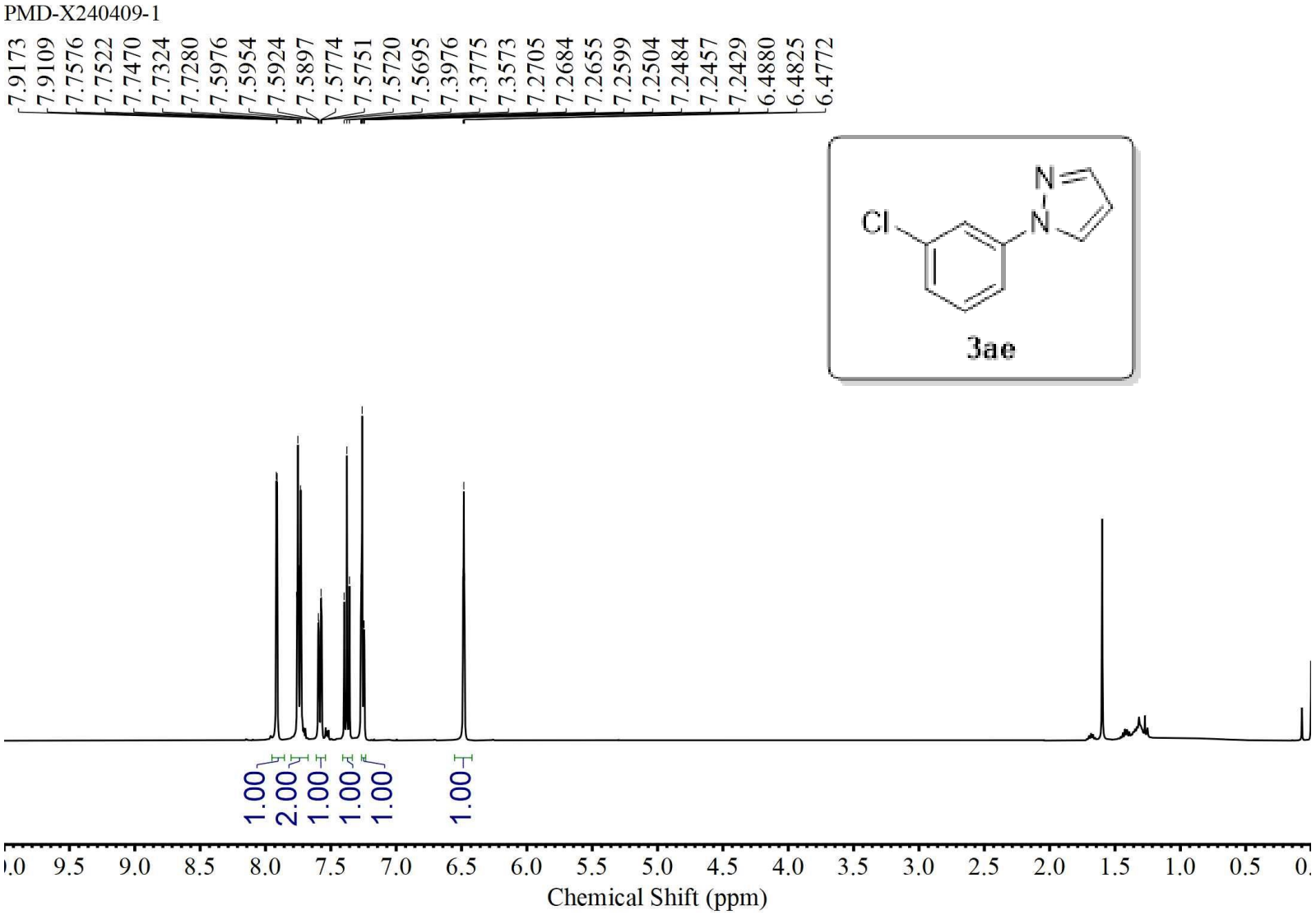


^{19}F NMR spectrum of 3ad (376 MHz, $CDCl_3$)

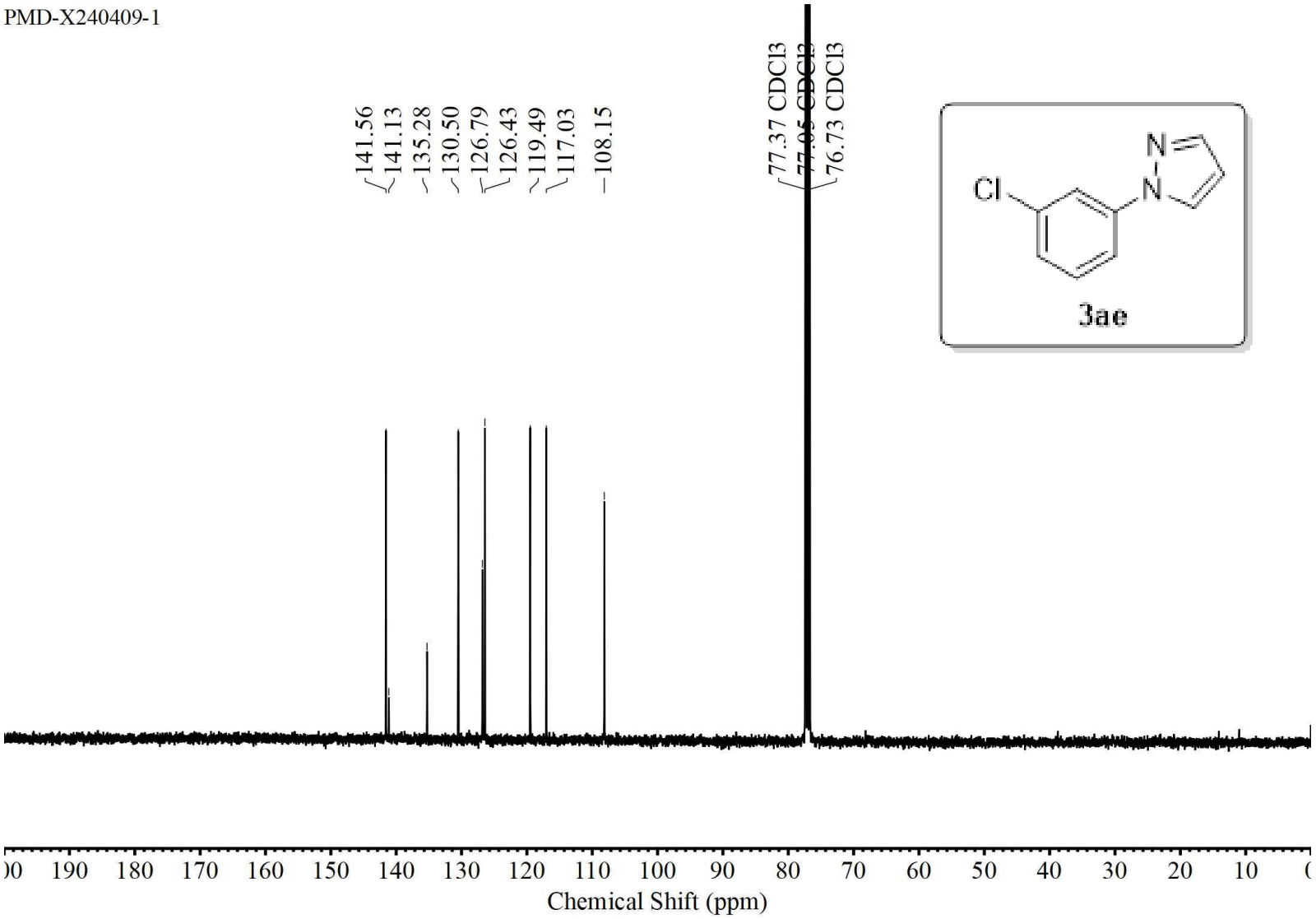
PMD-X240517-1



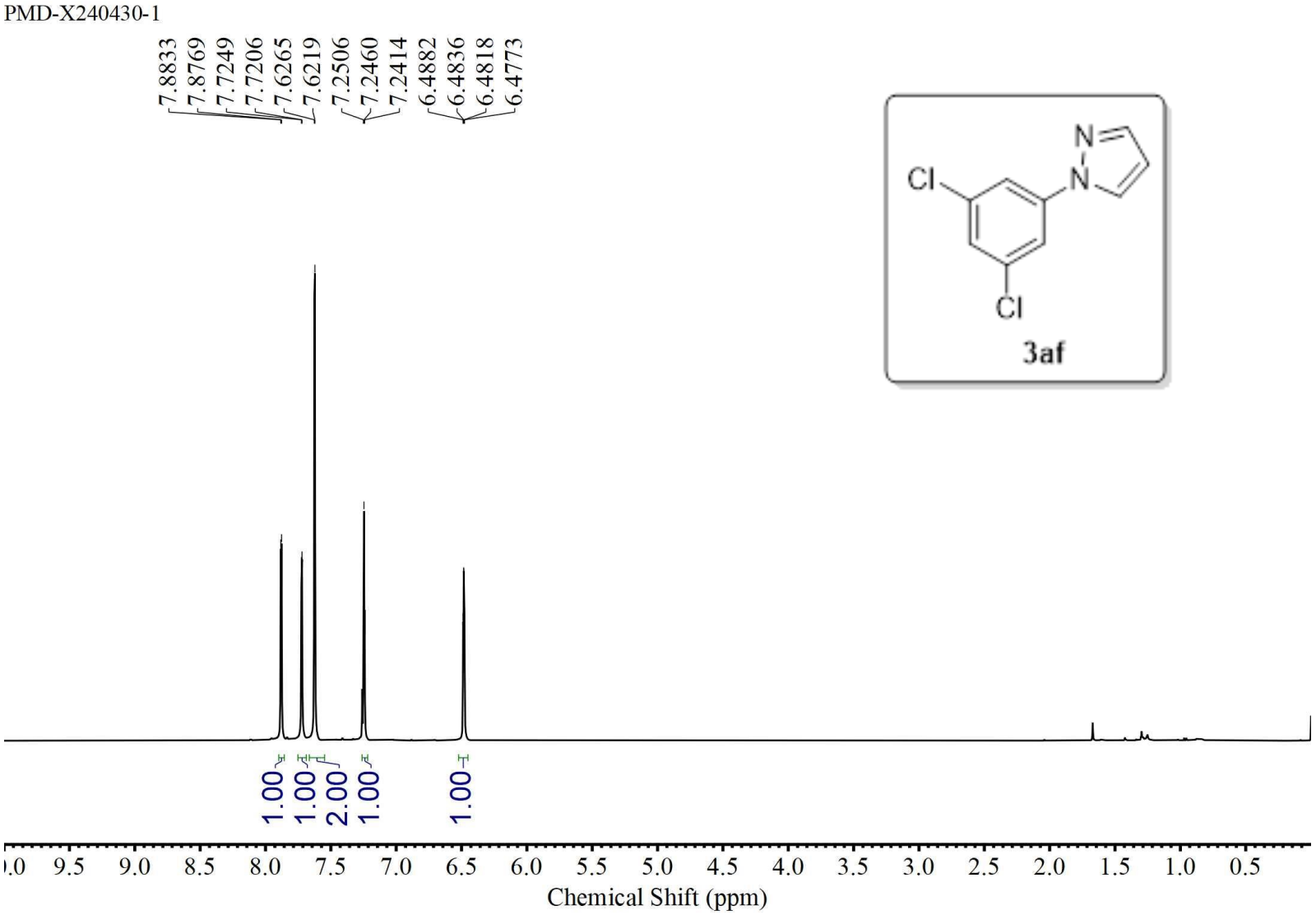
^{1}H NMR spectrum of 3ae (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of 3ae (100 MHz, $CDCl_3$)

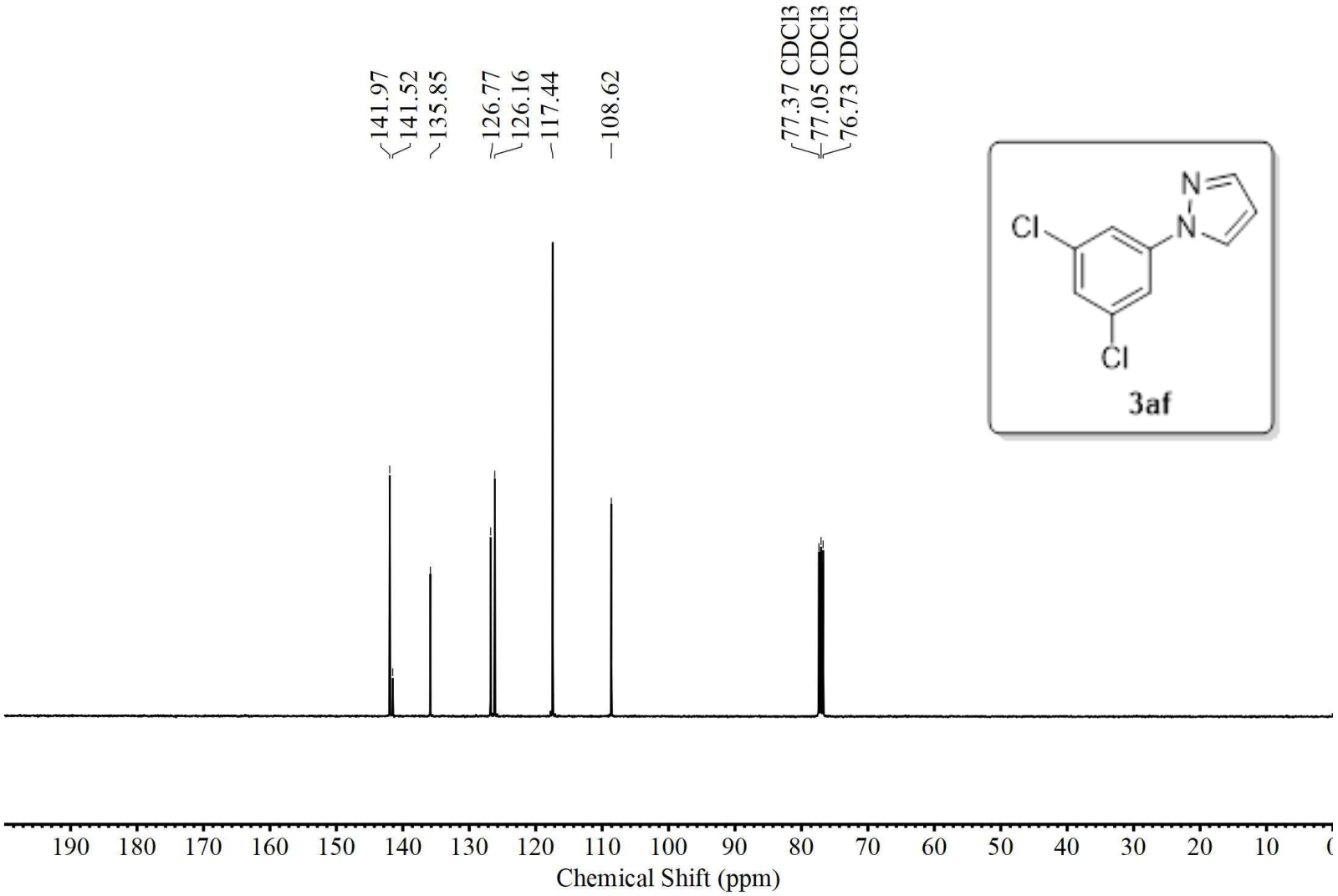


^{1}H NMR spectrum of 3af (400 MHz, $CDCl_3$)



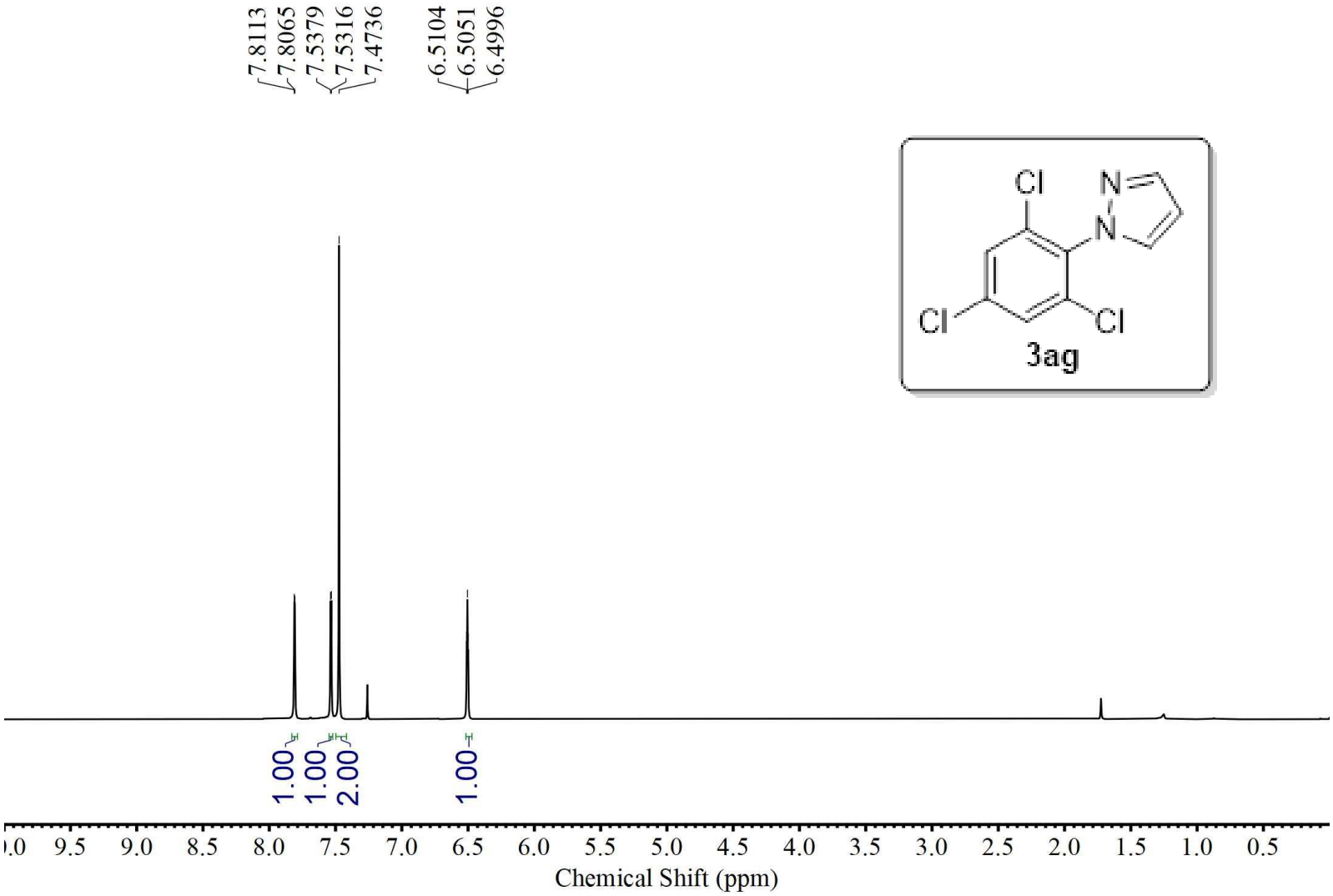
^{13}C NMR spectrum of 3af (100 MHz, $CDCl_3$)

PMD-X240430-1



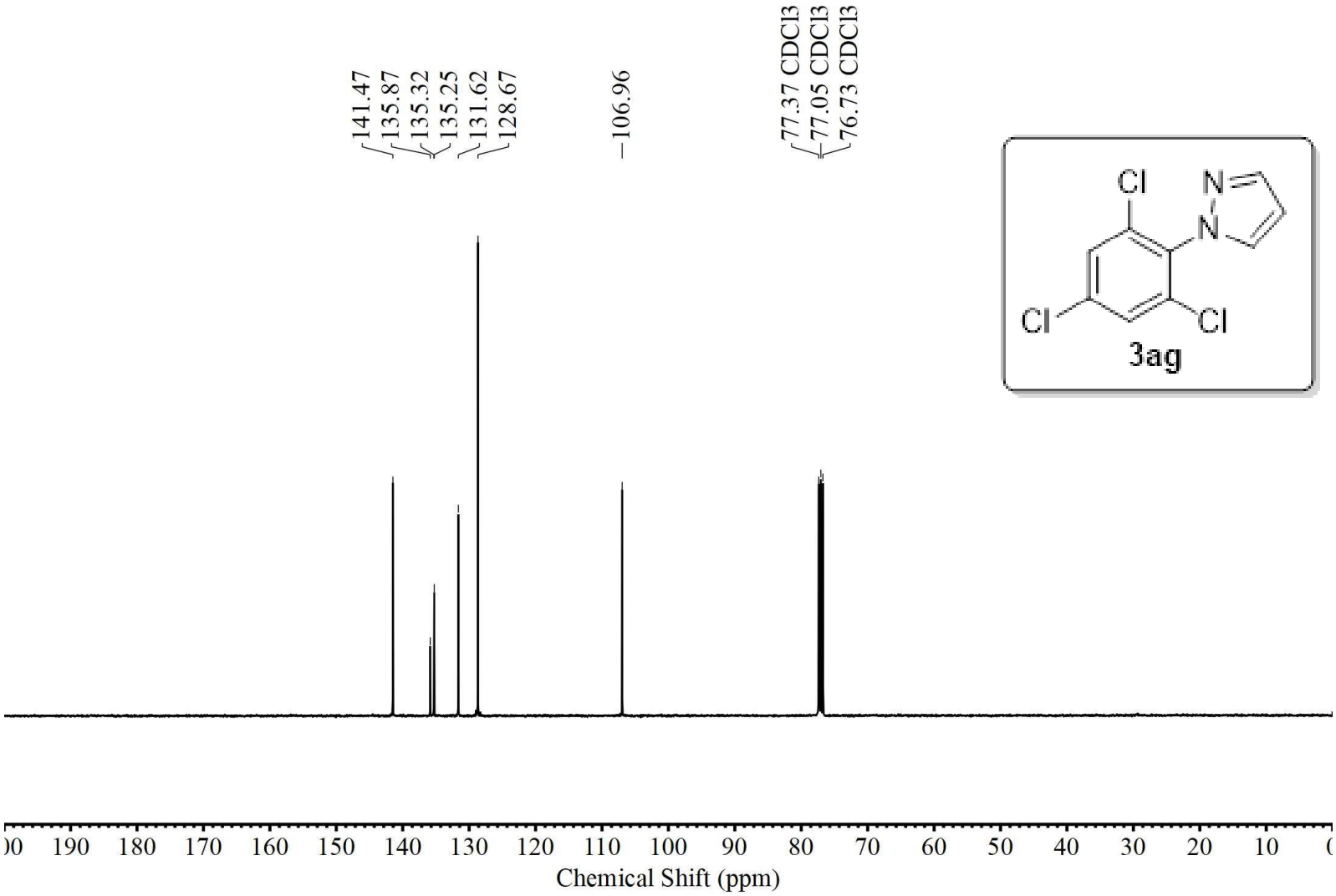
^{1}H NMR spectrum of 3ag (400 MHz, $CDCl_3$)

PMD-X240419-1

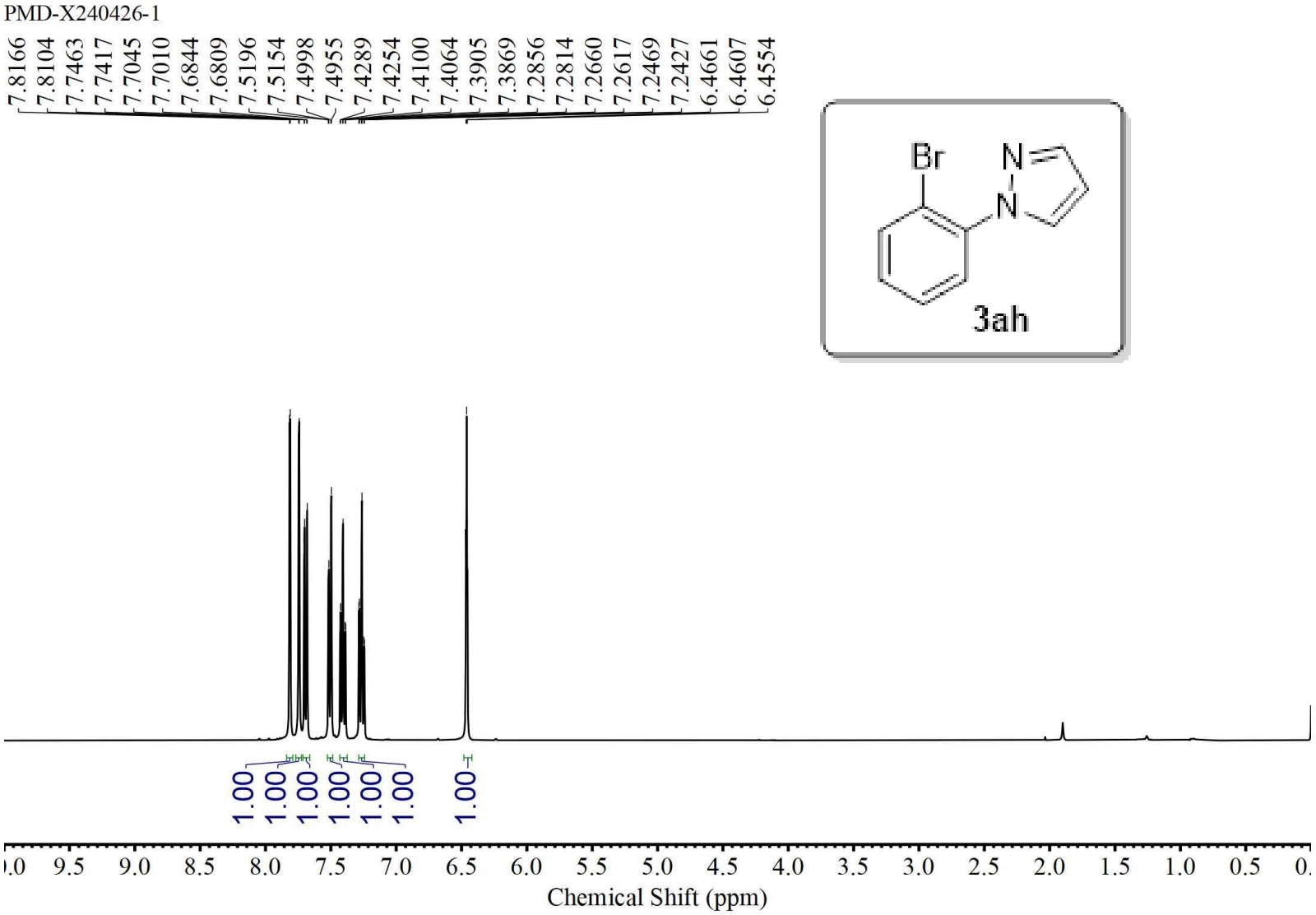


^{13}C NMR spectrum of 3ag (100 MHz, $CDCl_3$)

PMD-X240419-1

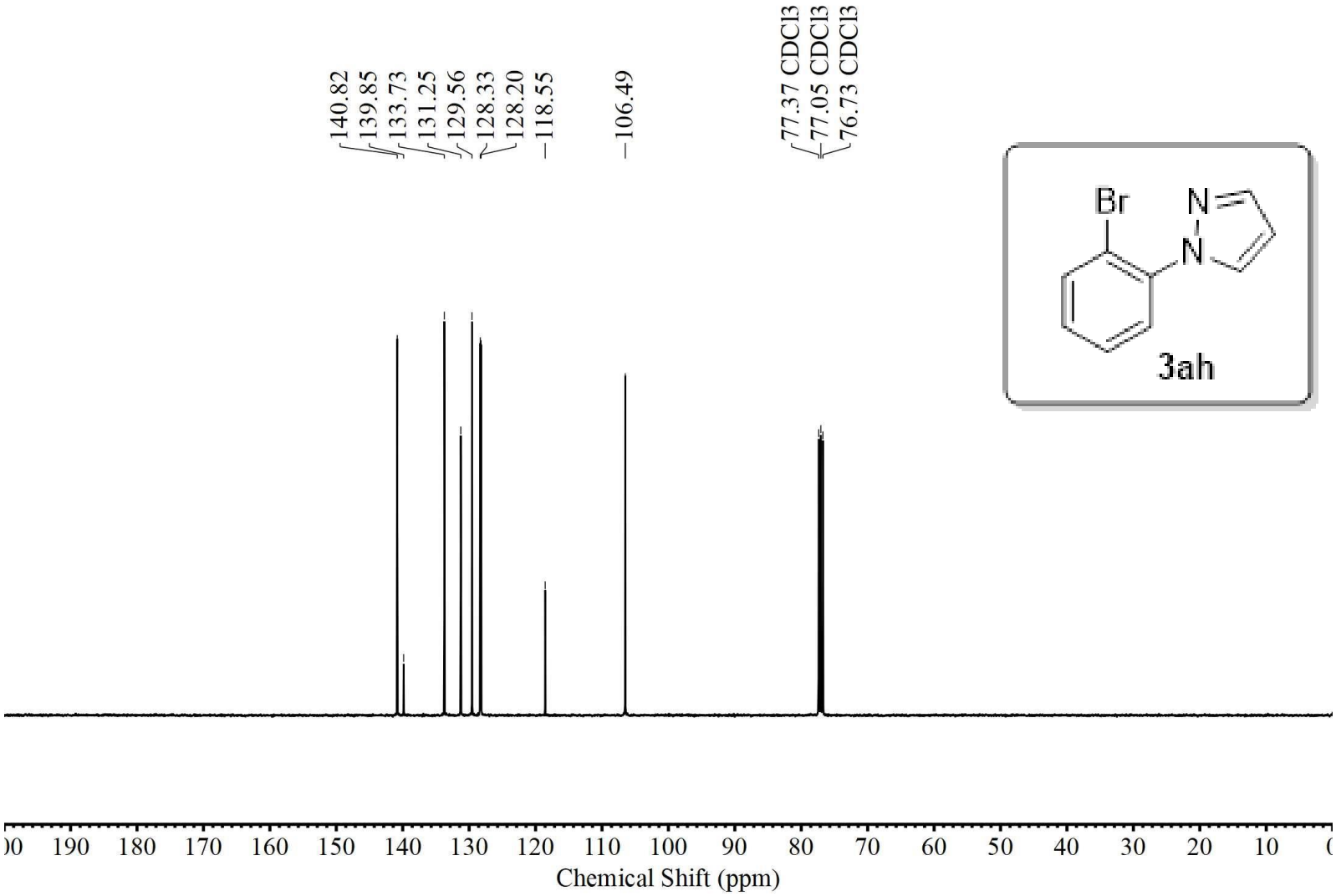


^{1}H NMR spectrum of 3ah (400 MHz, $CDCl_3$)

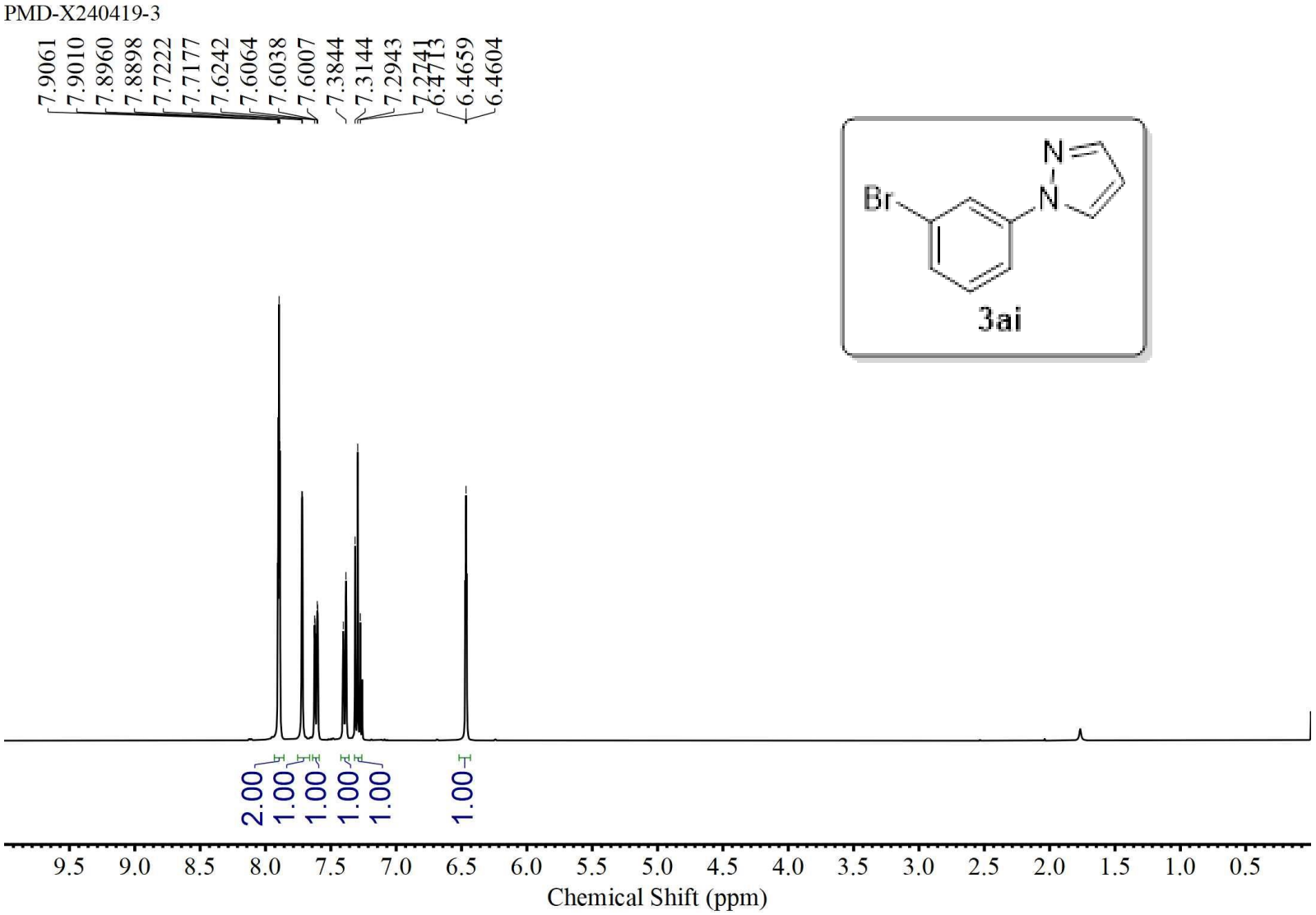


^{13}C NMR spectrum of 3ah (100 MHz, $CDCl_3$)

PMD-X240426-1

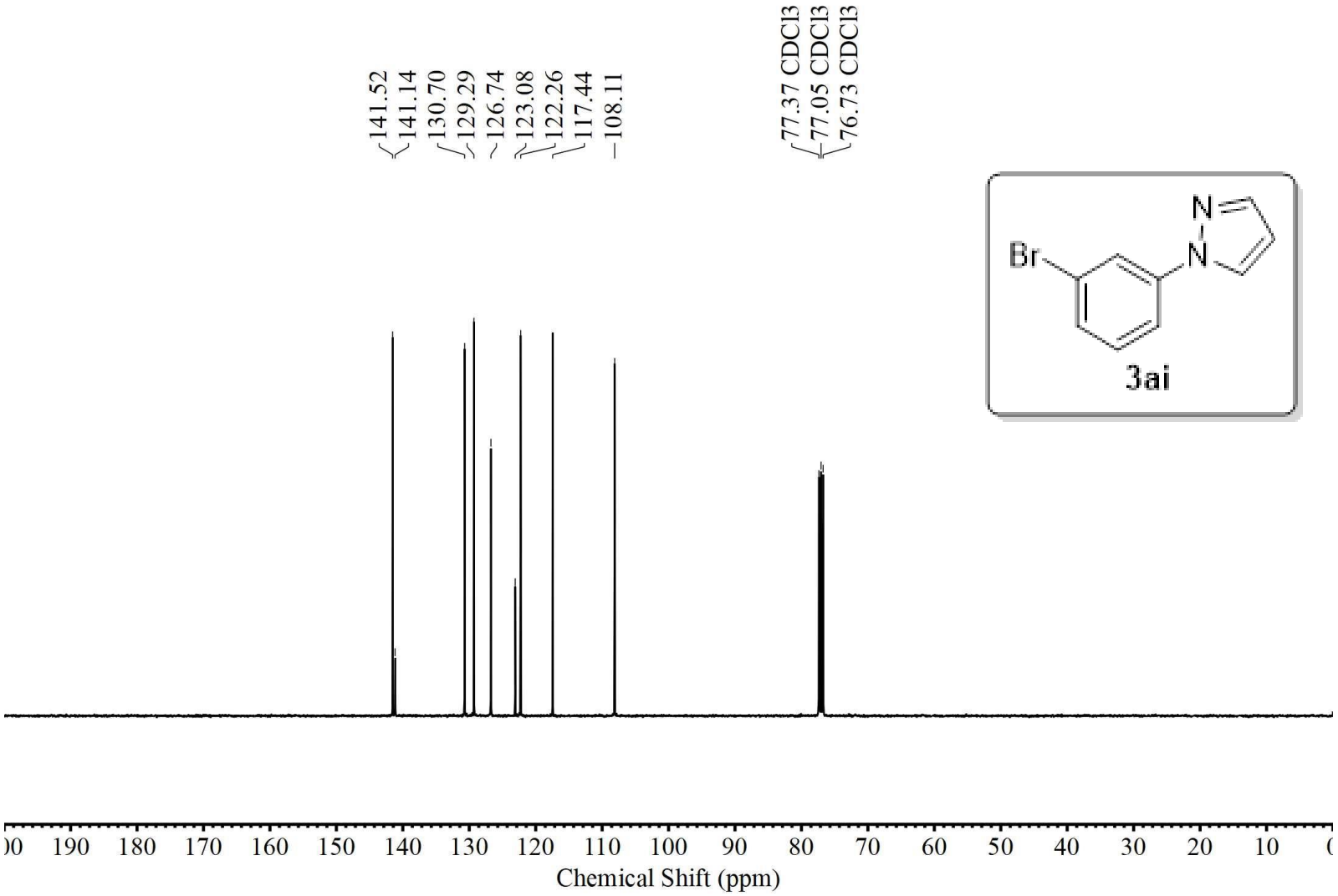


^{1}H NMR spectrum of 3ai (400 MHz, $CDCl_3$)

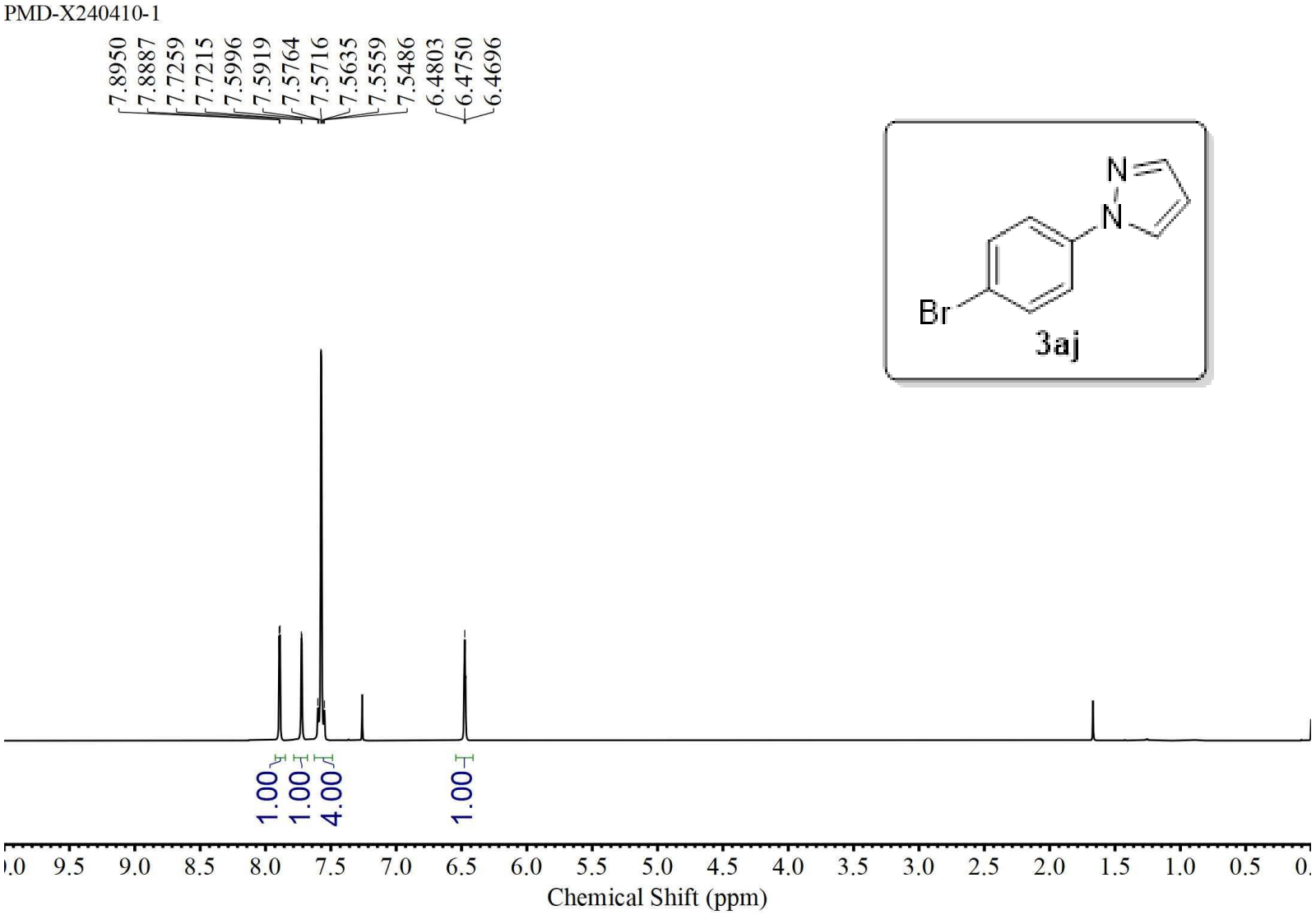


^{13}C NMR spectrum of 3ai (100 MHz, $CDCl_3$)

PMD-X240419-2

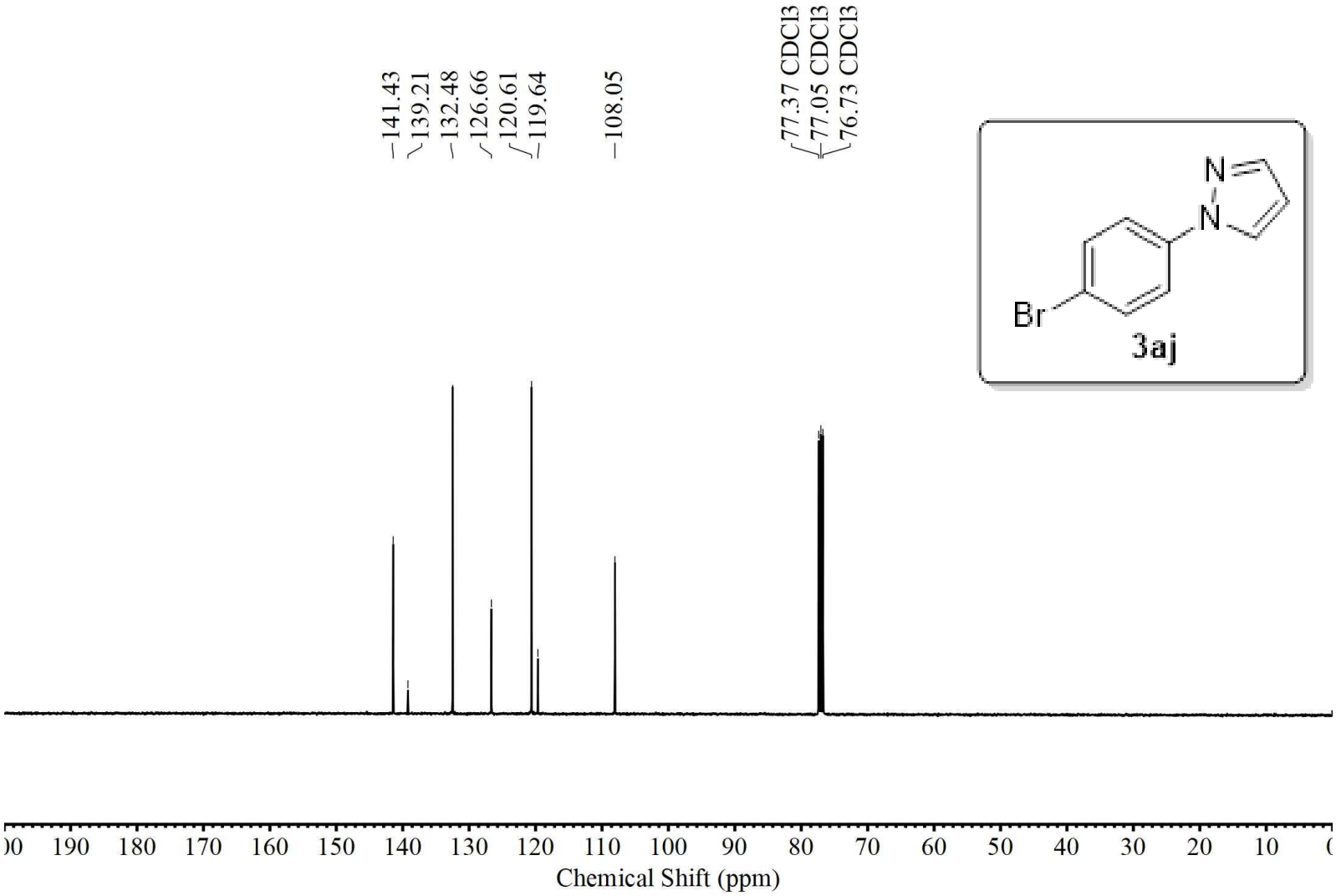


^{1}H NMR spectrum of 3aj (400 MHz, $CDCl_3$)

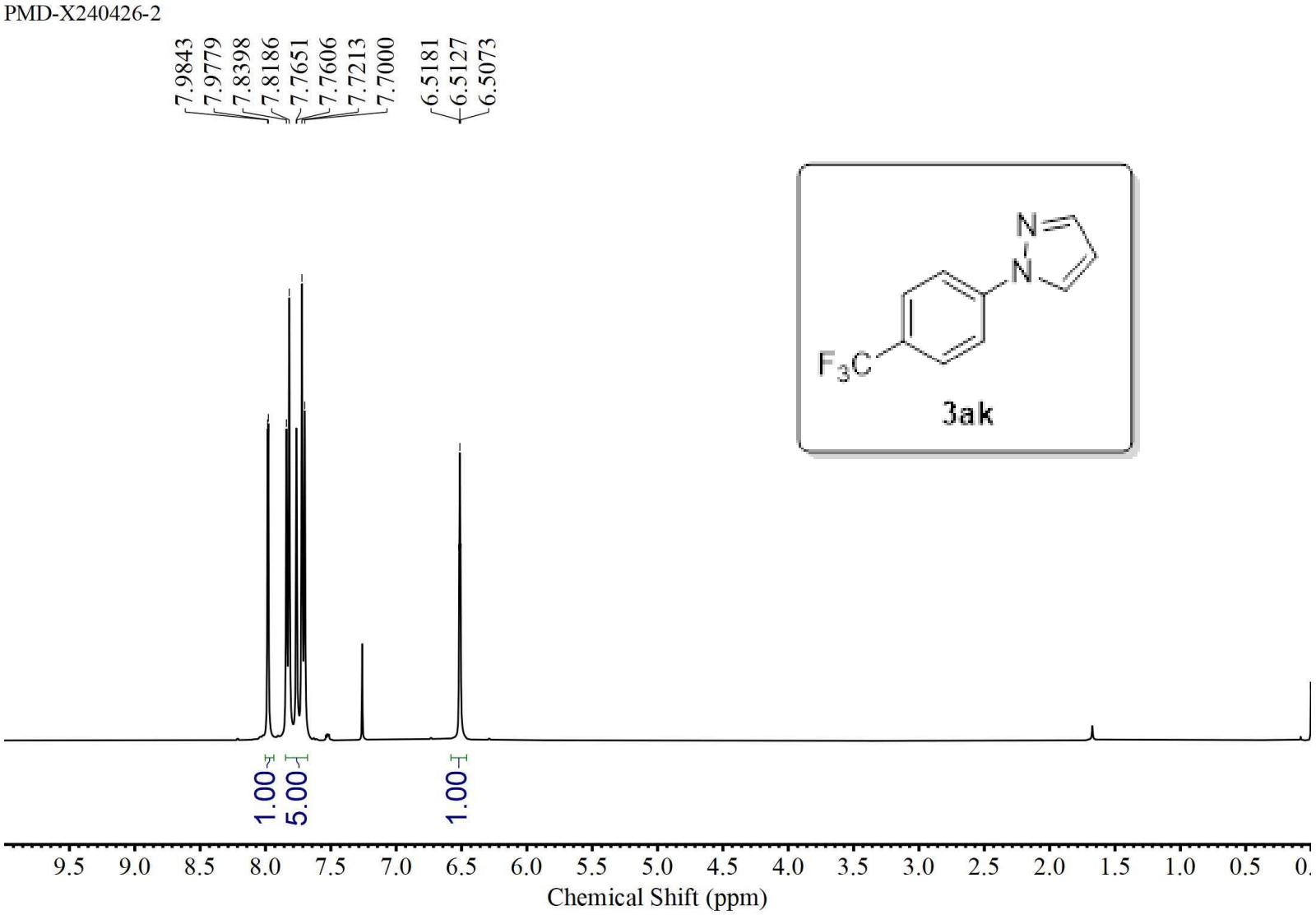


^{13}C NMR spectrum of 3aj (100 MHz, $CDCl_3$)

PMD-X240410-1

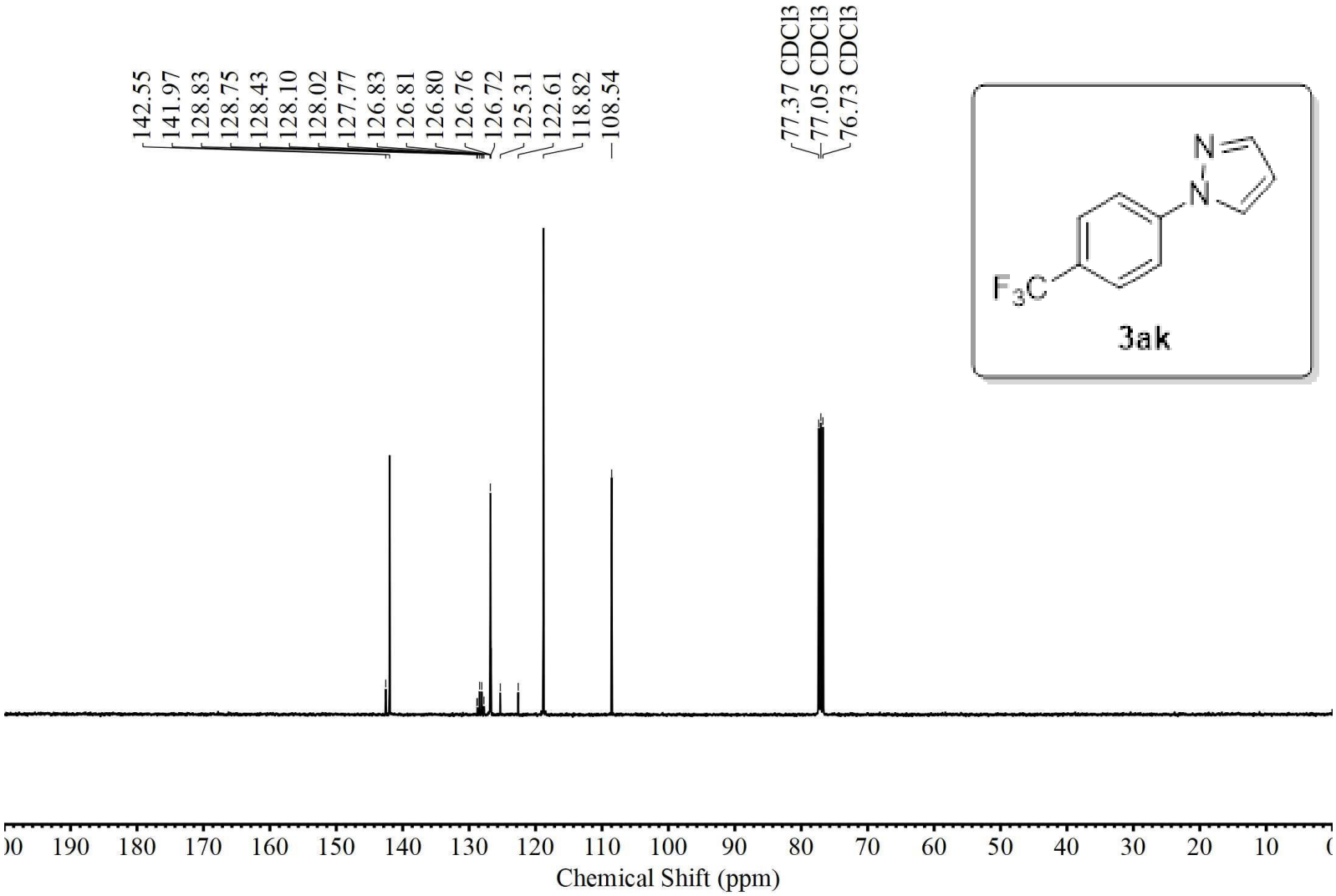


^{1}H NMR spectrum of 3ak (400 MHz, $CDCl_3$)



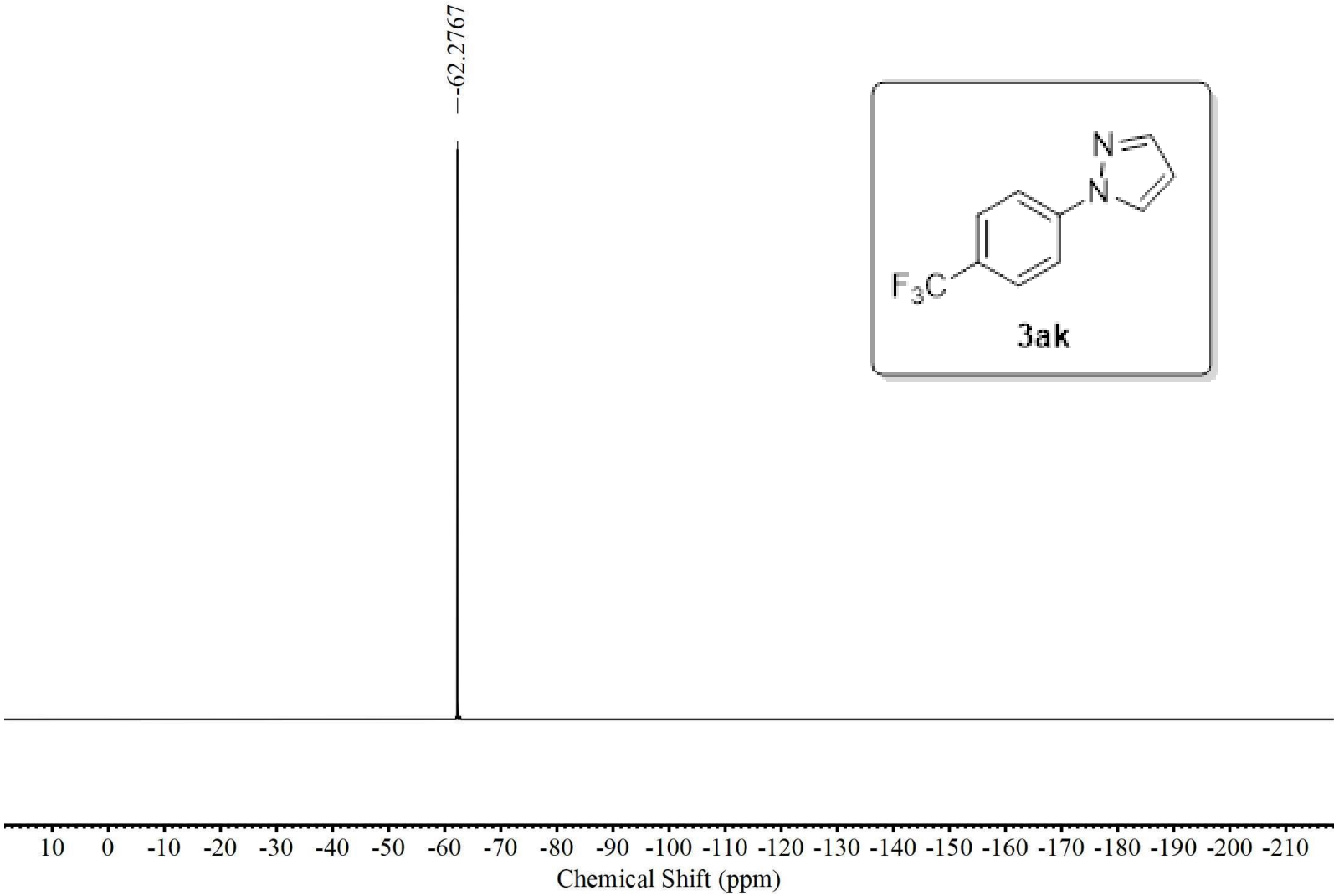
^{13}C NMR spectrum of 3ak (100 MHz, $CDCl_3$)

PMD-X240426-2

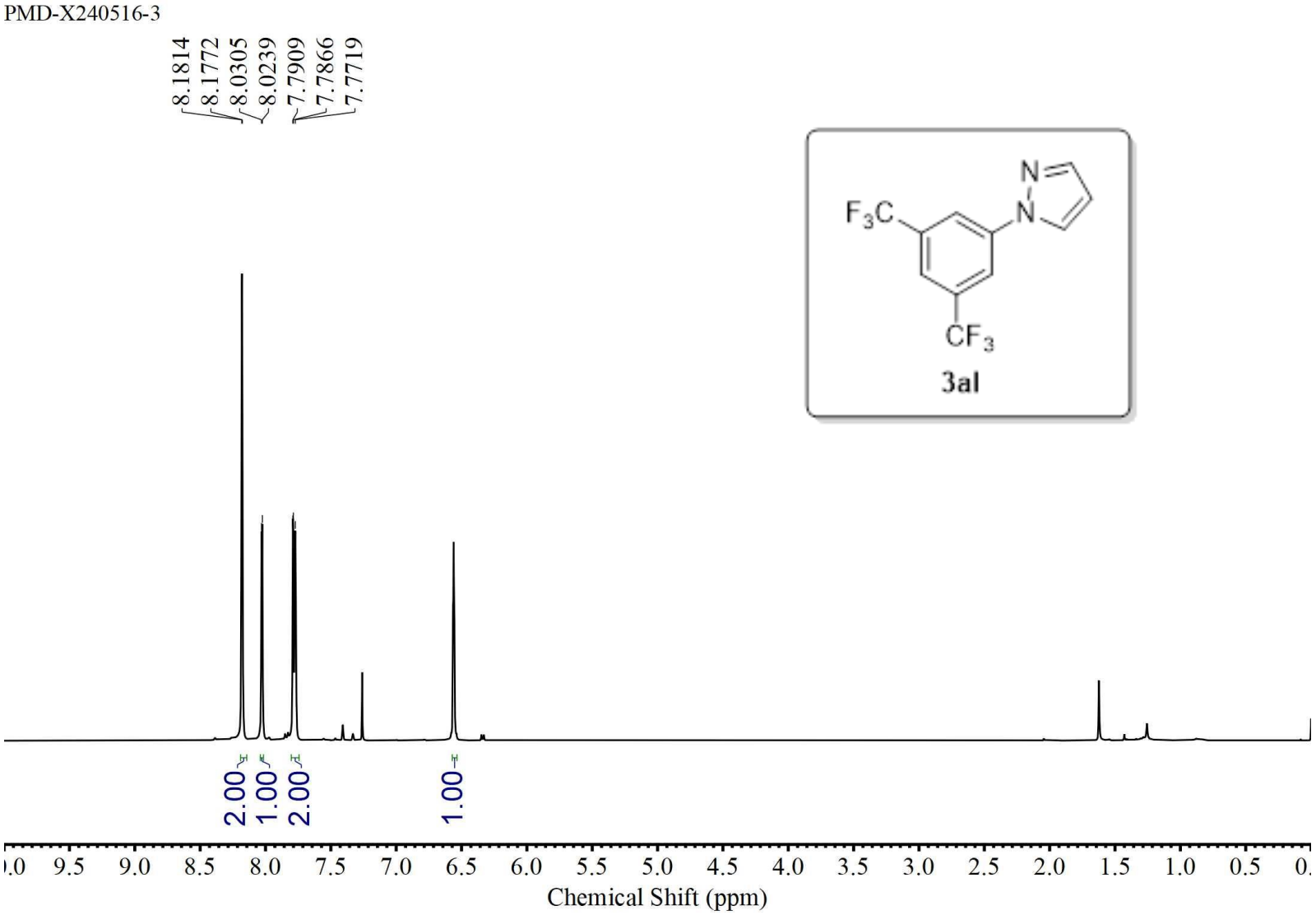


^{19}F NMR spectrum of 3ak (376 MHz, $CDCl_3$)

PMD-X240426-2

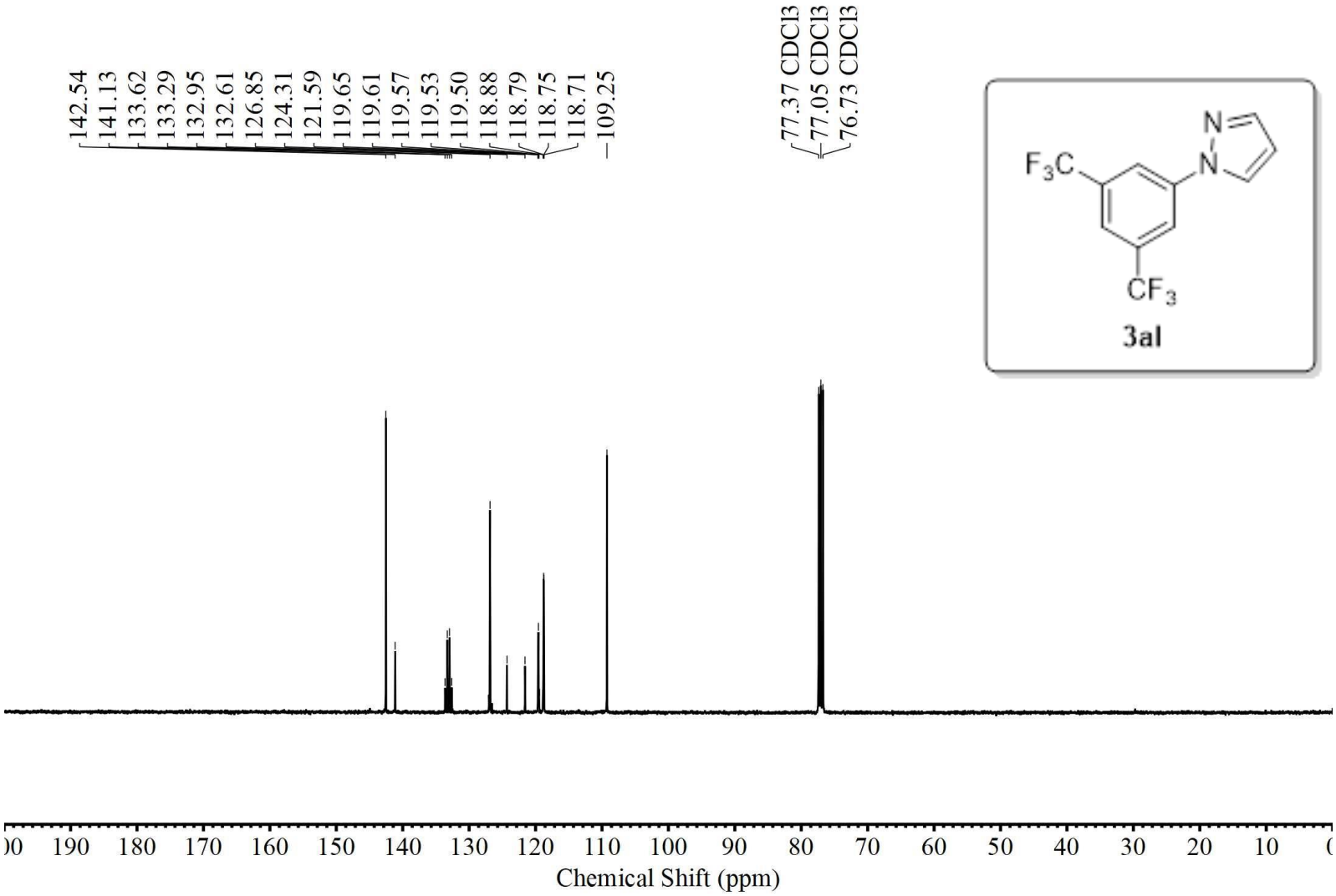


^{1}H NMR spectrum of 3al (400 MHz, $CDCl_3$)



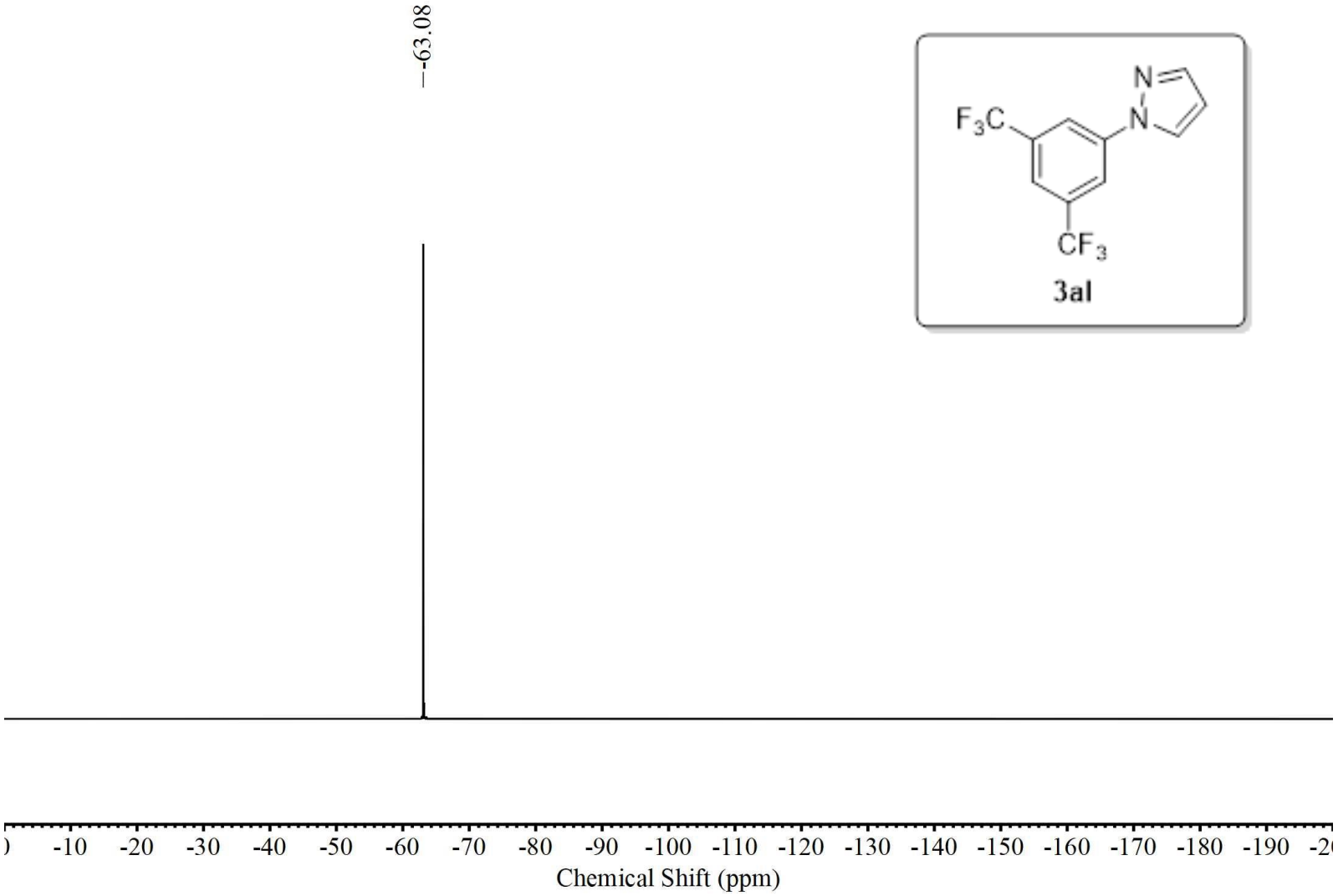
^{13}C NMR spectrum of 3al (100 MHz, $CDCl_3$)

PMD-X240516-3

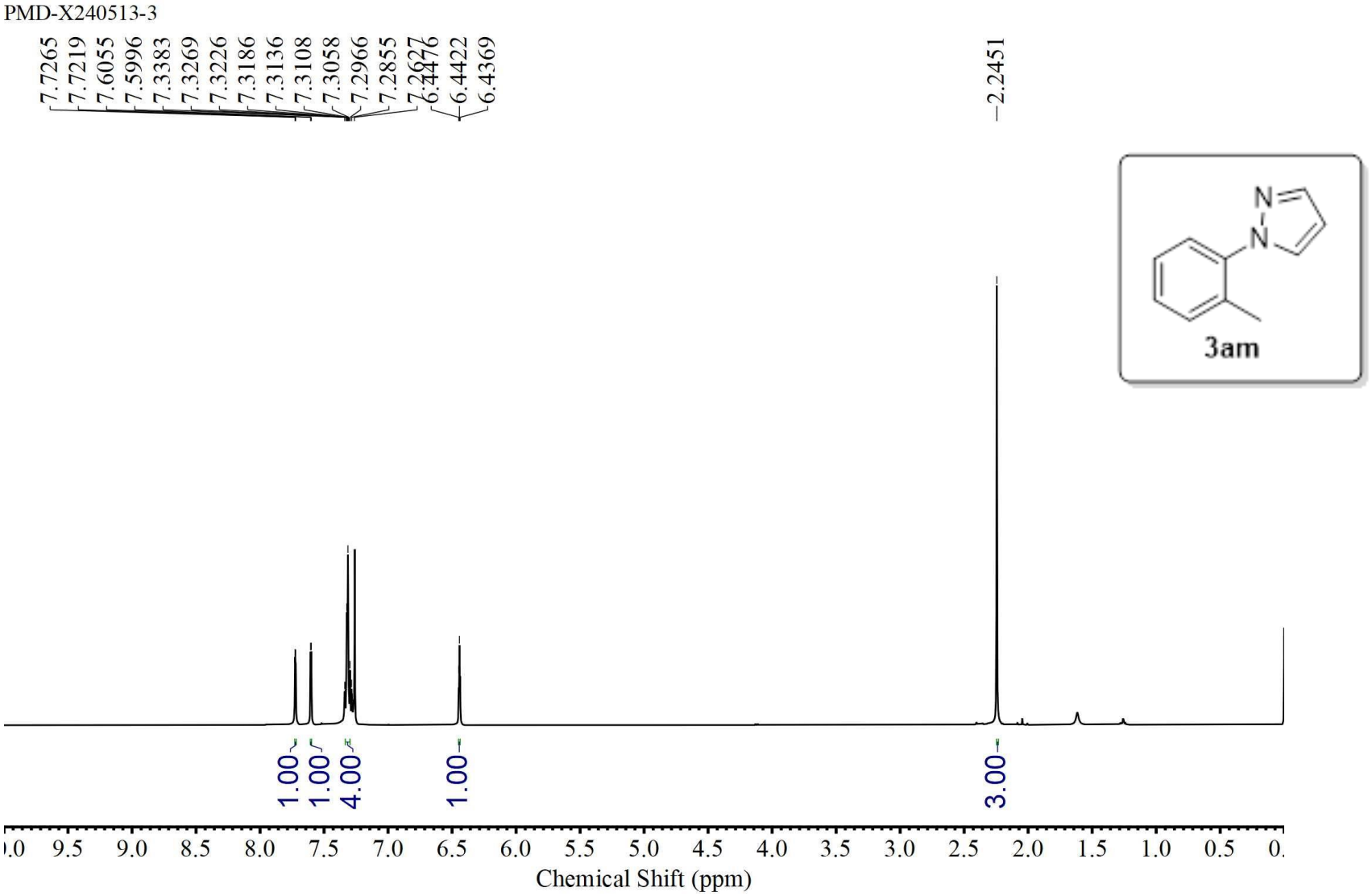


^{19}F NMR spectrum of 3al (376 MHz, $CDCl_3$)

PMD-X240516-3

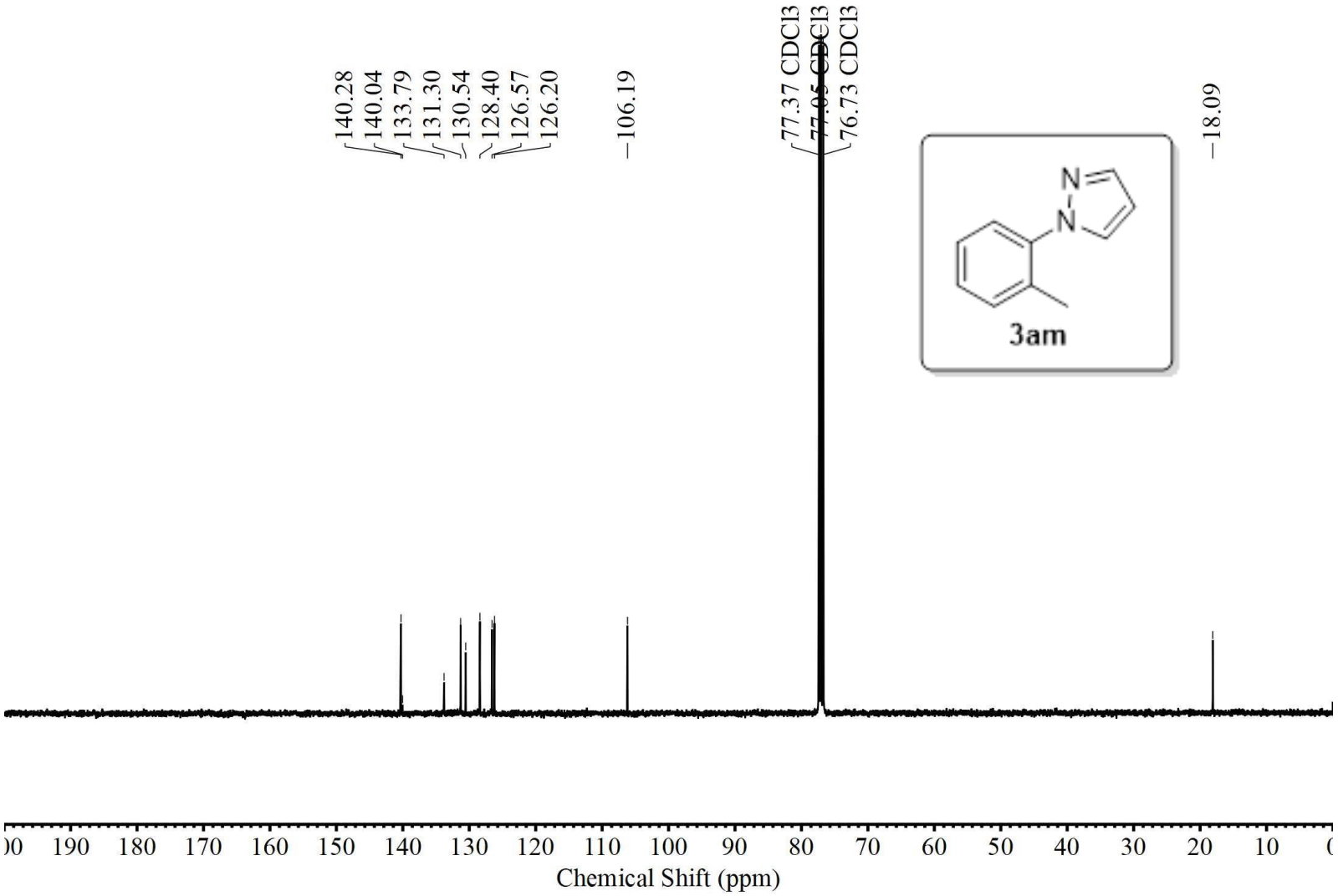


^{1}H NMR spectrum of 3am (400 MHz, $CDCl_3$)

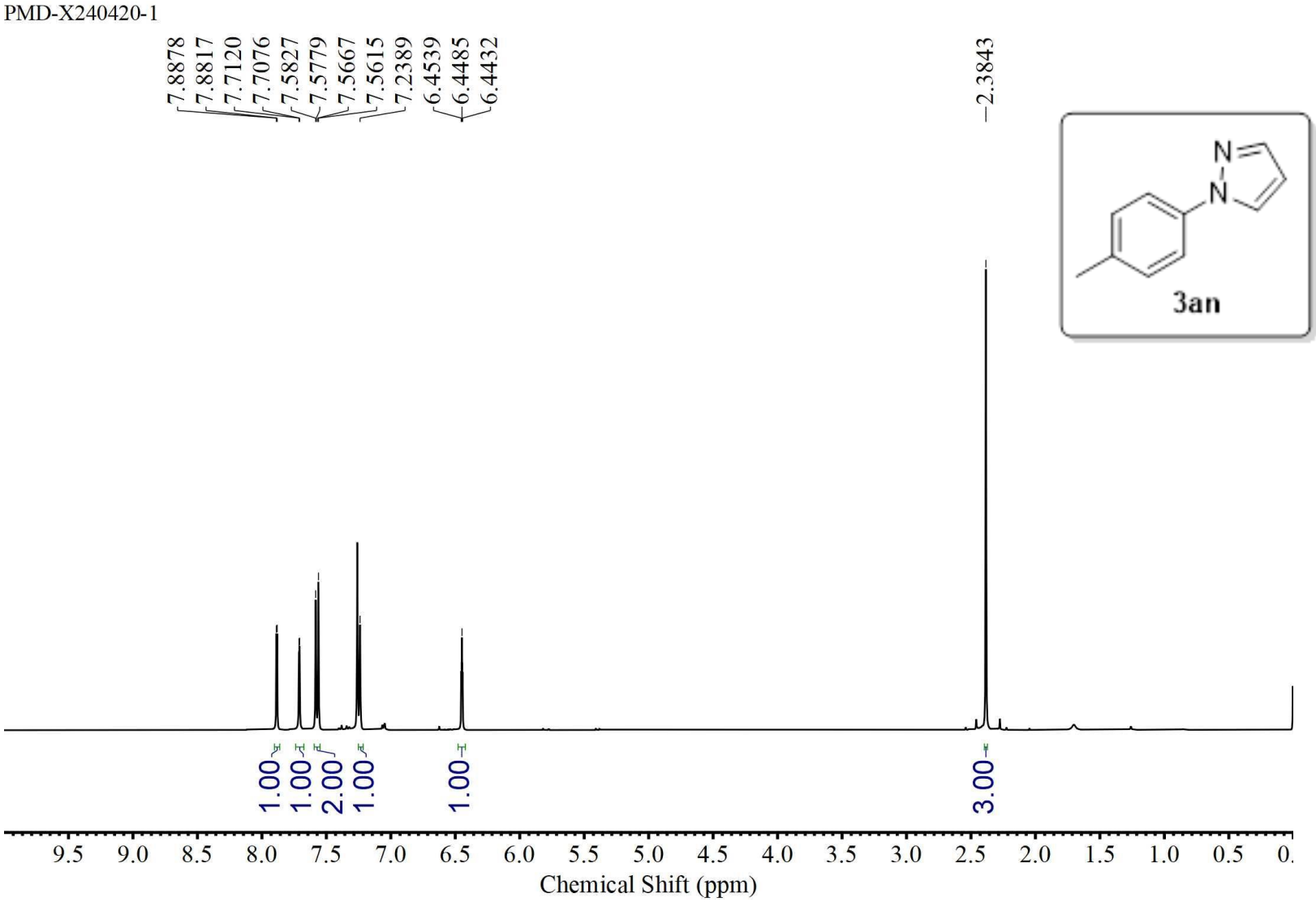


^{13}C NMR spectrum of 3am (100 MHz, $CDCl_3$)

PMD-X240513-3

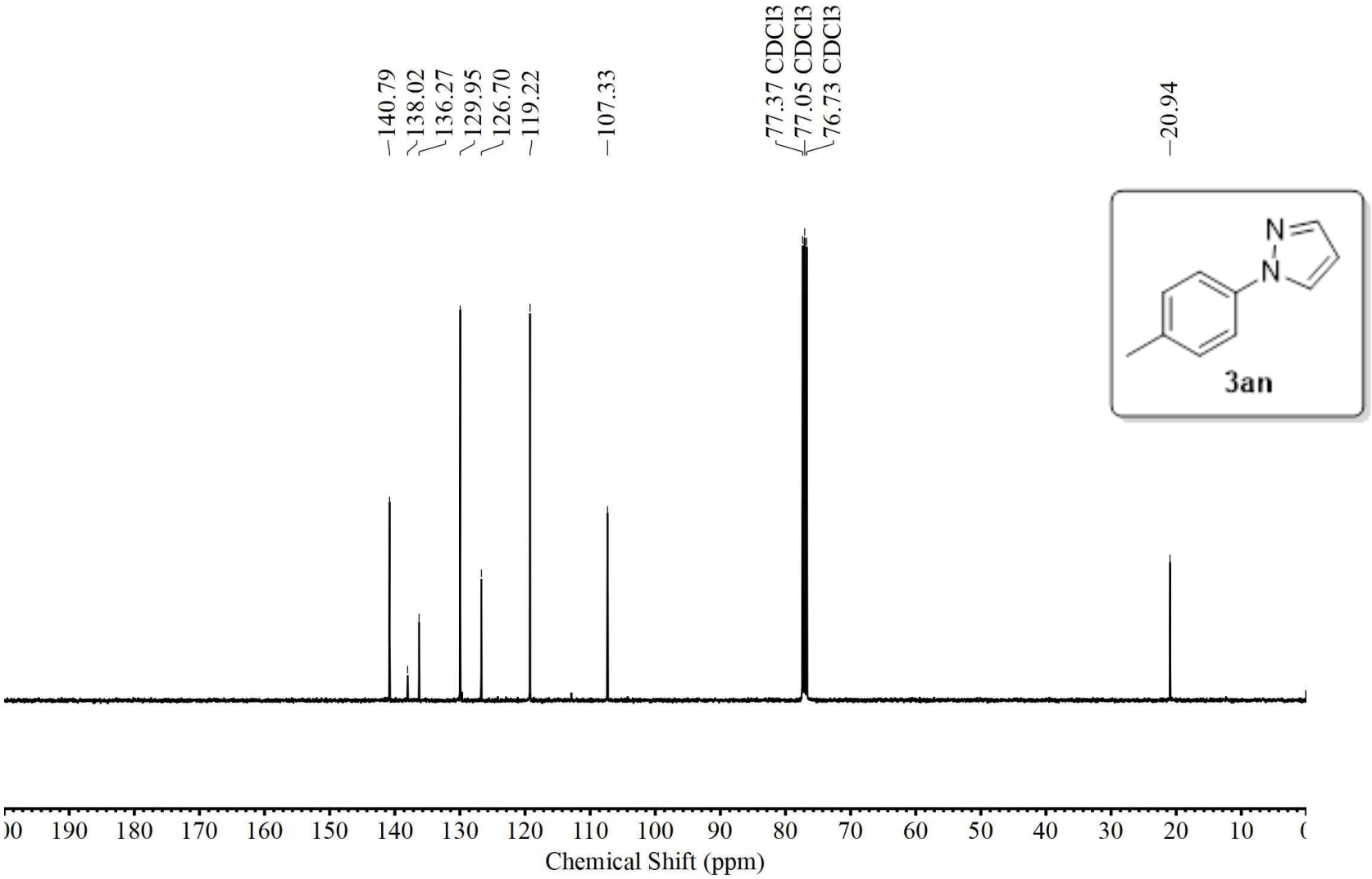


^{1}H NMR spectrum of 3an (400 MHz, $CDCl_3$)

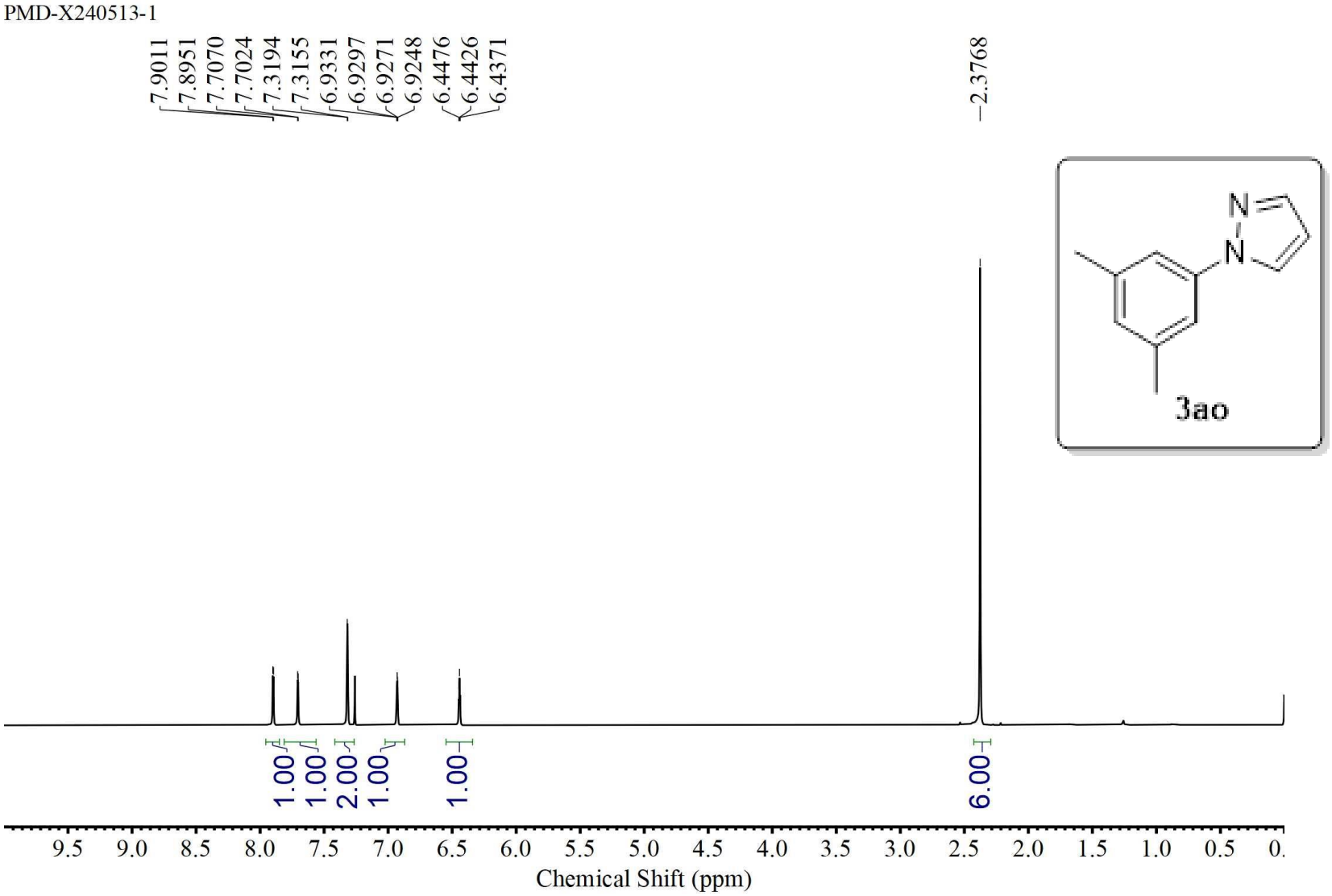


^{13}C NMR spectrum of 3an (100 MHz, $CDCl_3$)

PMD-X240420-1

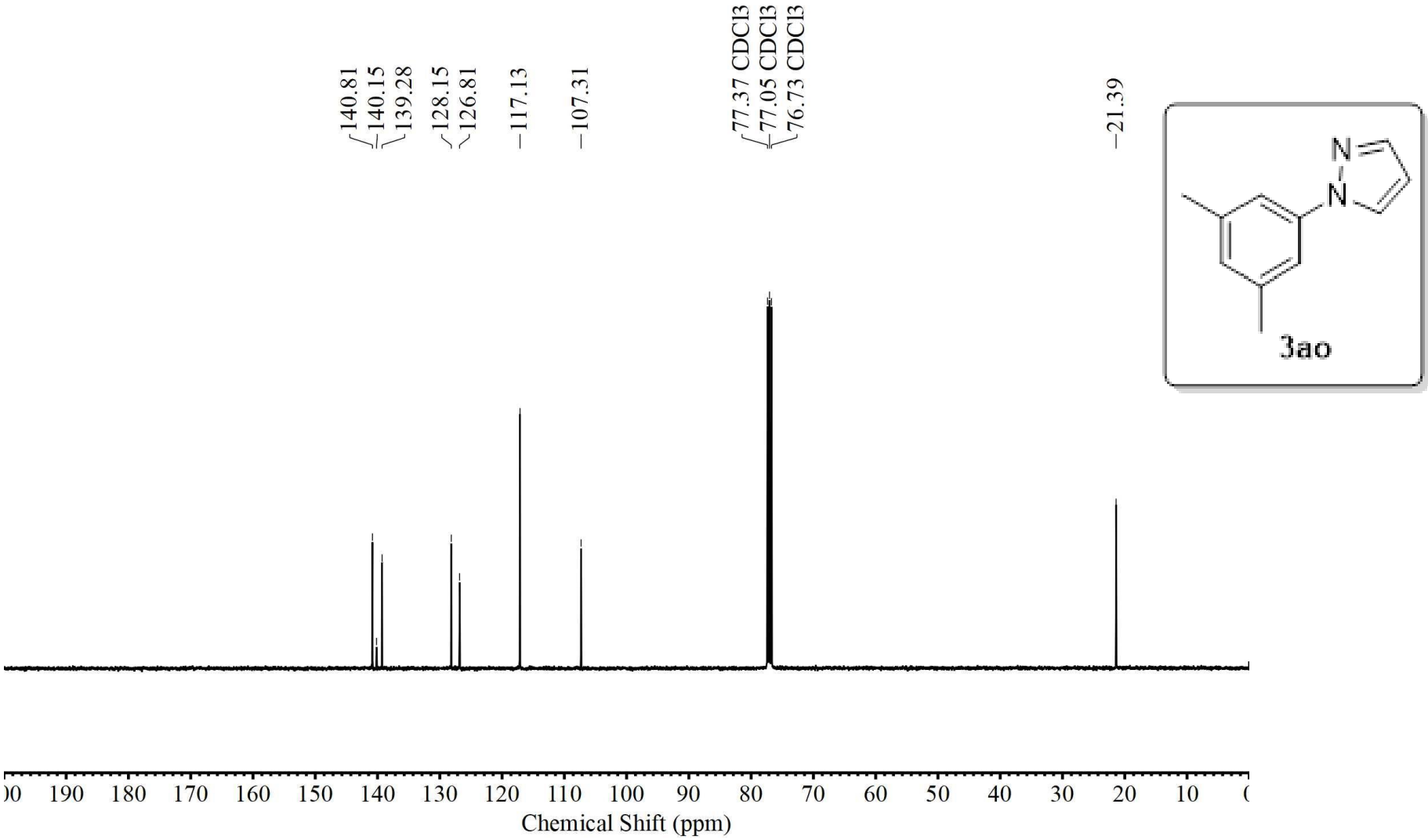


^{1}H NMR spectrum of 3ao (400 MHz, $CDCl_3$)

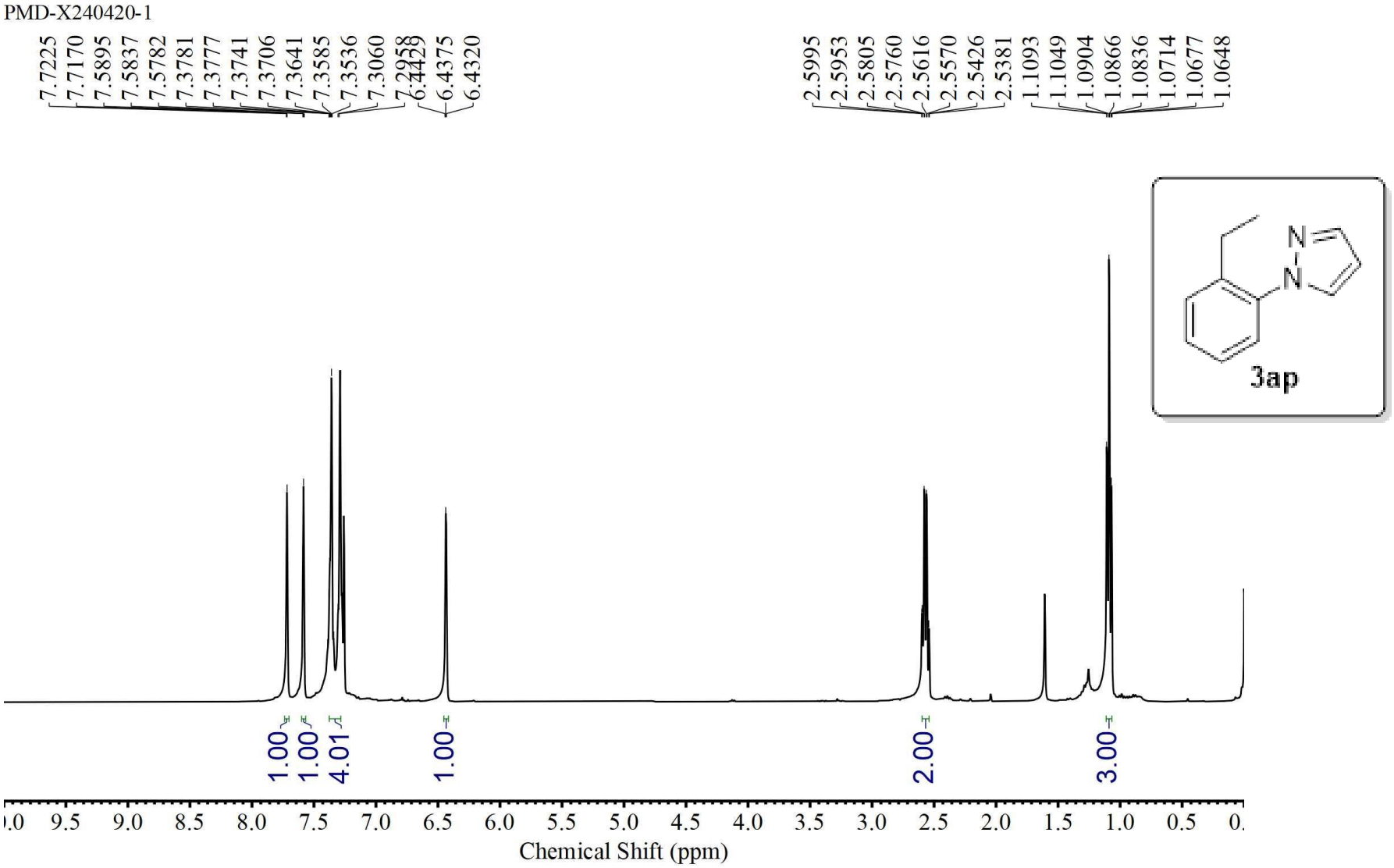


^{13}C NMR spectrum of 3ao (100 MHz, $CDCl_3$)

PMD-X240513-1

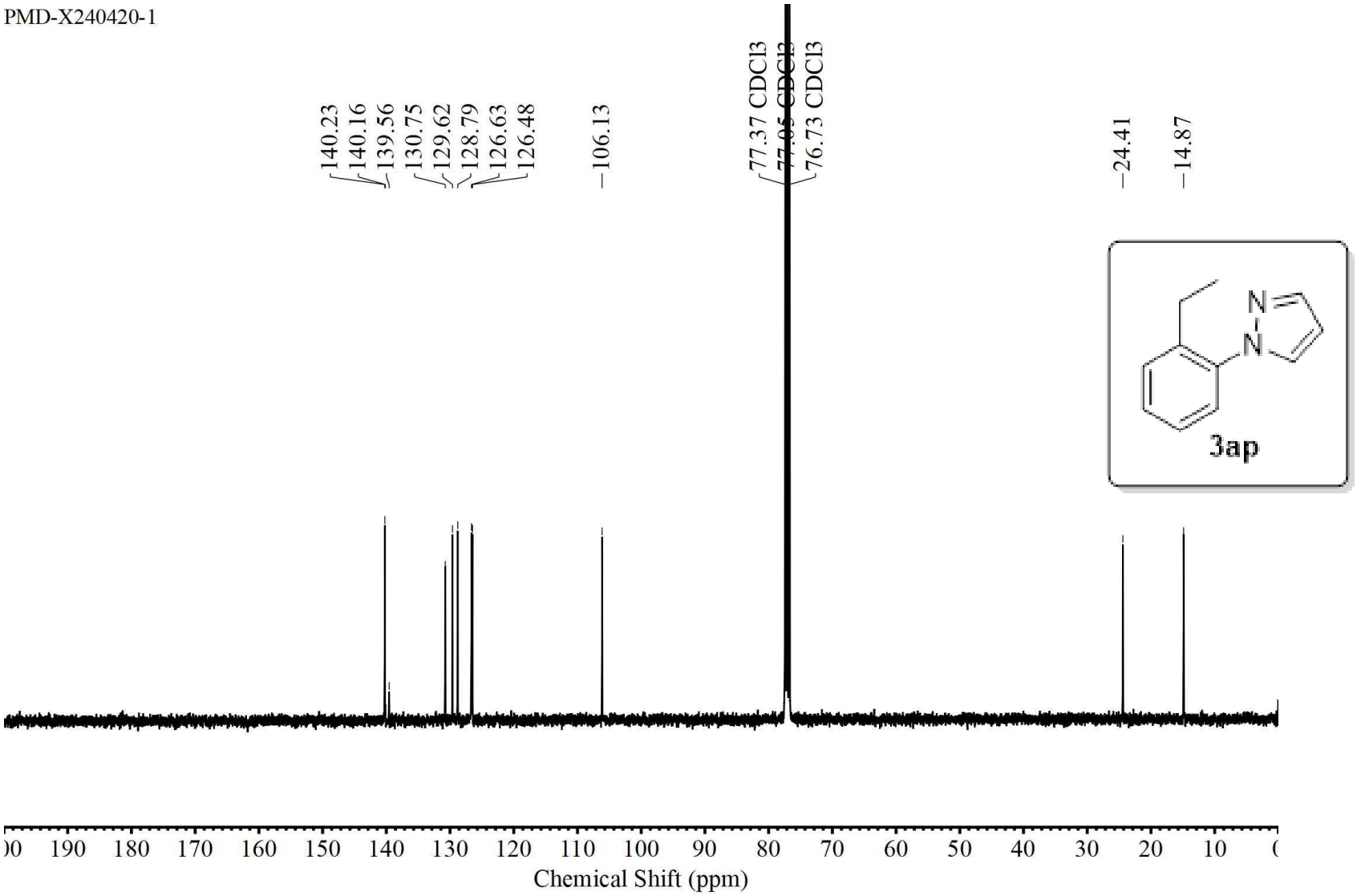


^{1}H NMR spectrum of 3ap (400 MHz, $CDCl_3$)

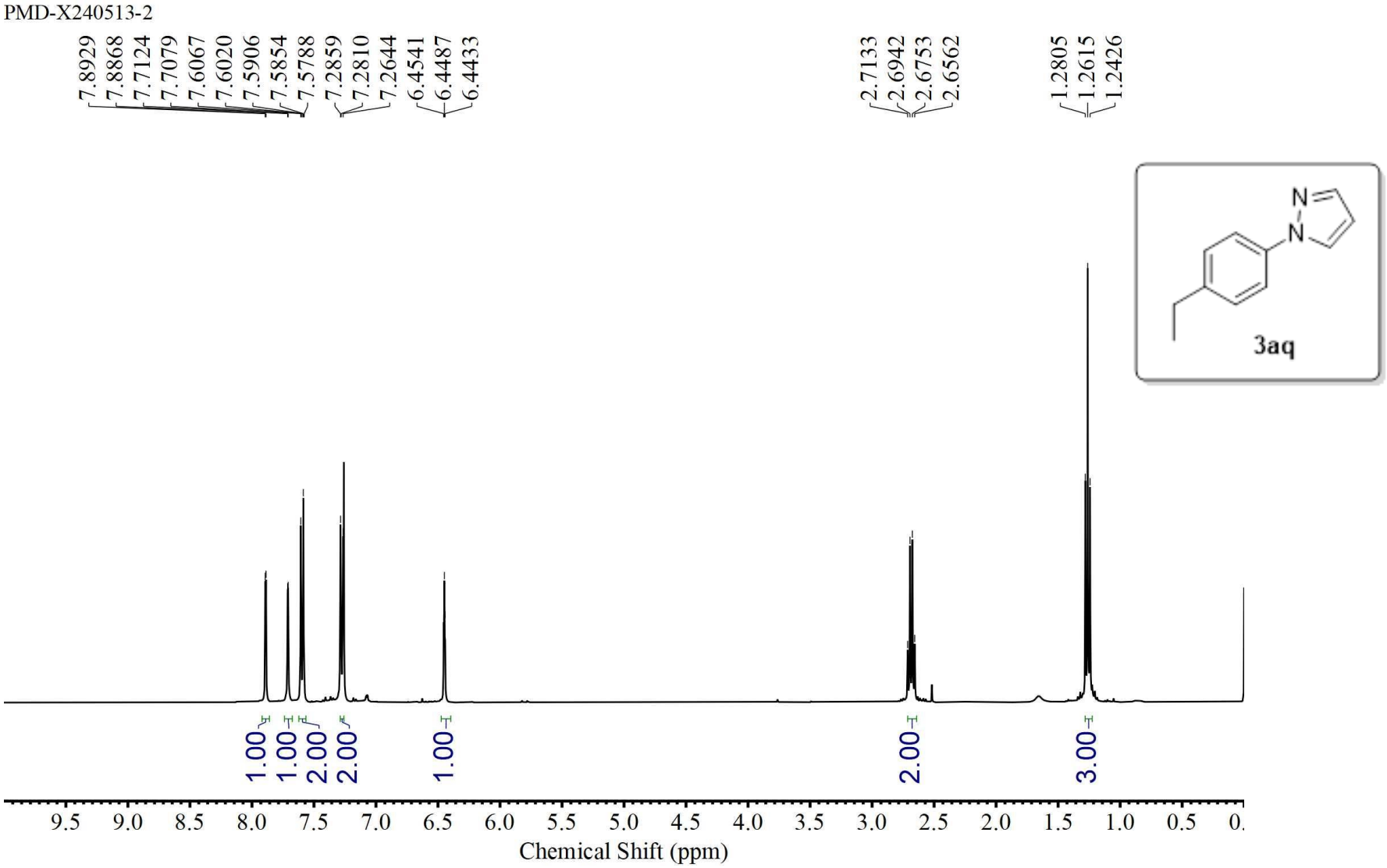


^{13}C NMR spectrum of 3ap (100 MHz, $CDCl_3$)

PMD-X240420-1

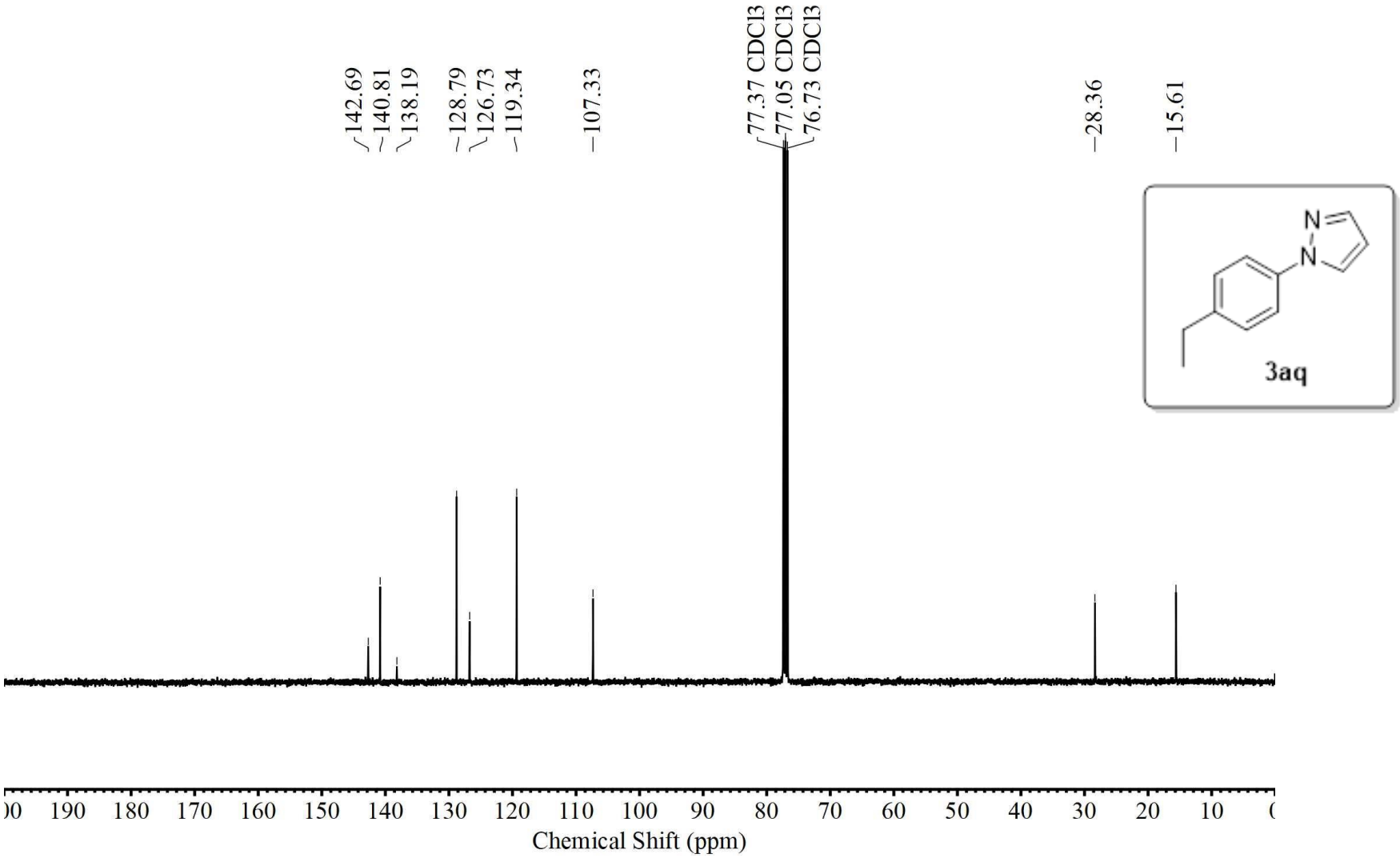


^{1}H NMR spectrum of 3aq (400 MHz, $CDCl_3$)

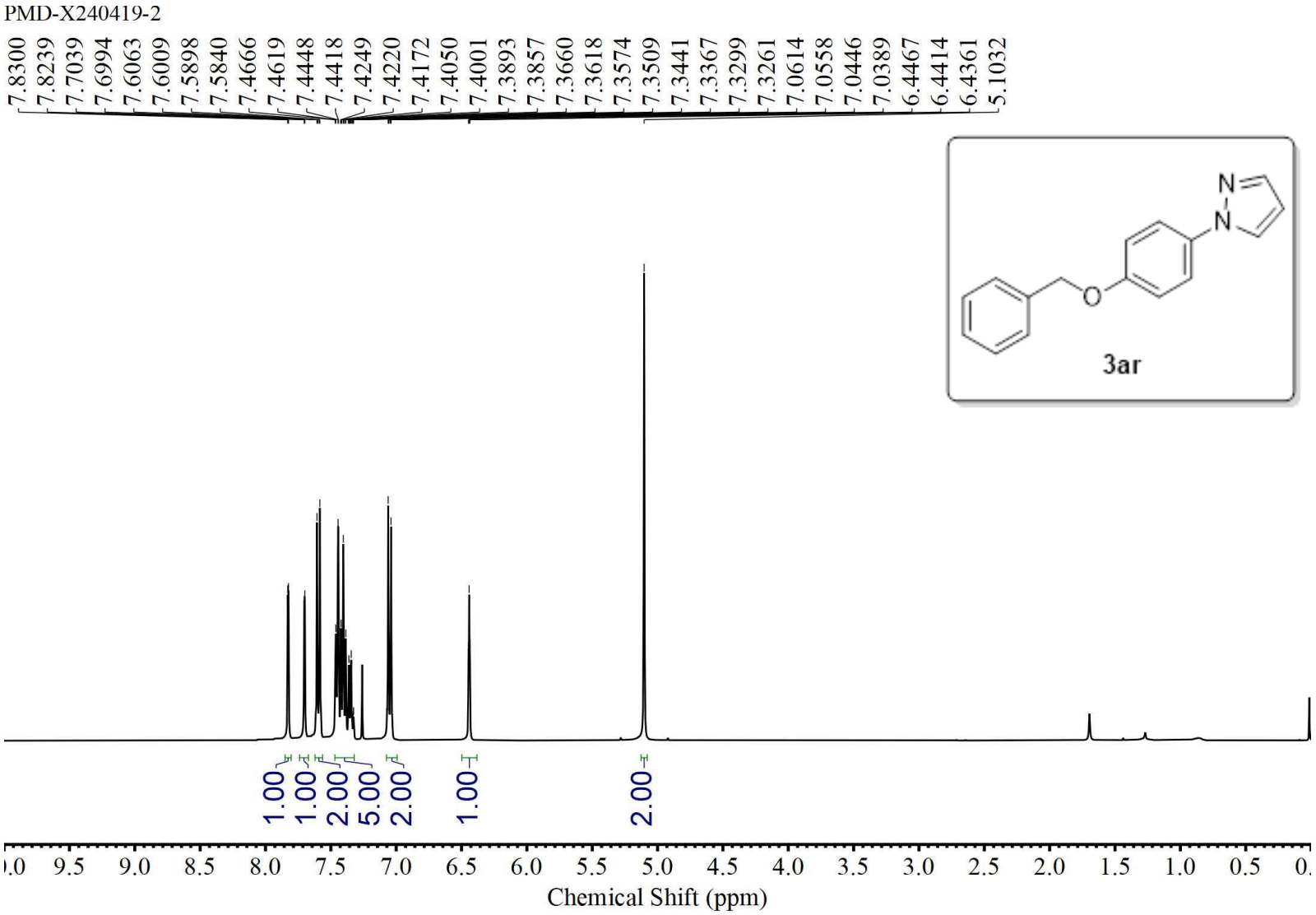


^{13}C NMR spectrum of 3aq (100 MHz, $CDCl_3$)

PMD-X240513-2

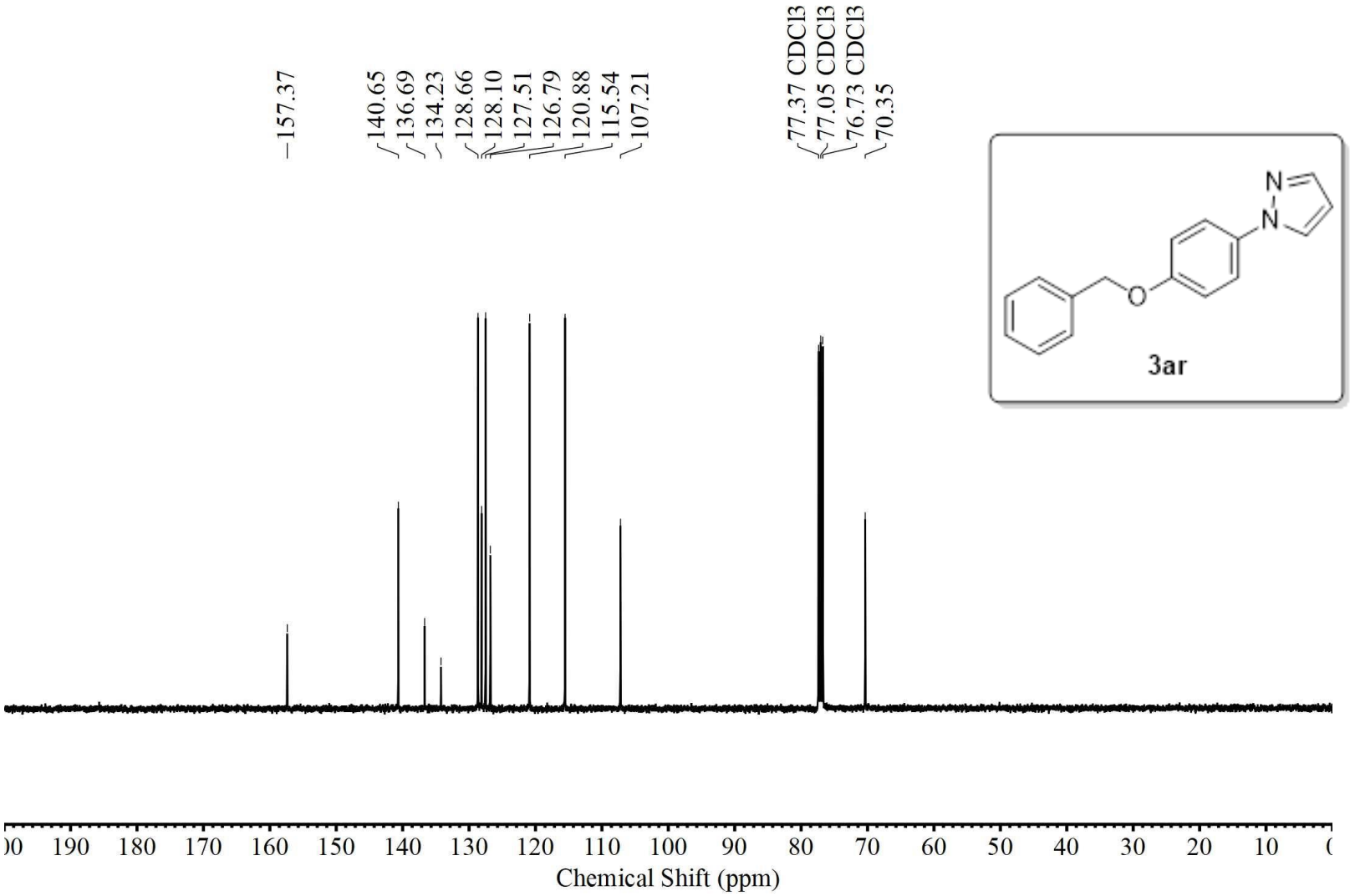


^{1}H NMR spectrum of 3ar (400 MHz, $CDCl_3$)

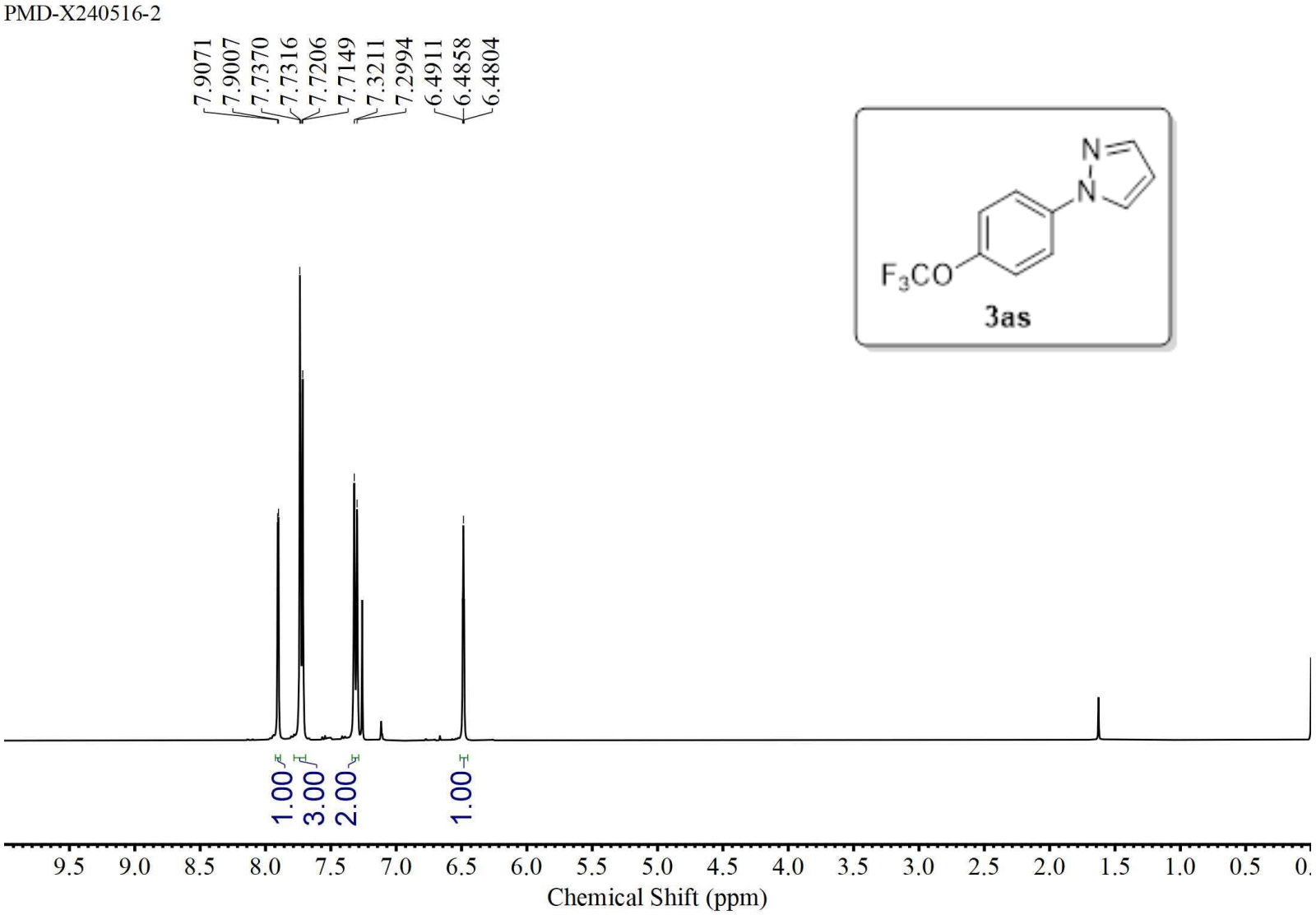


^{13}C NMR spectrum of 3ar (100 MHz, $CDCl_3$)

PMD-X240419-2

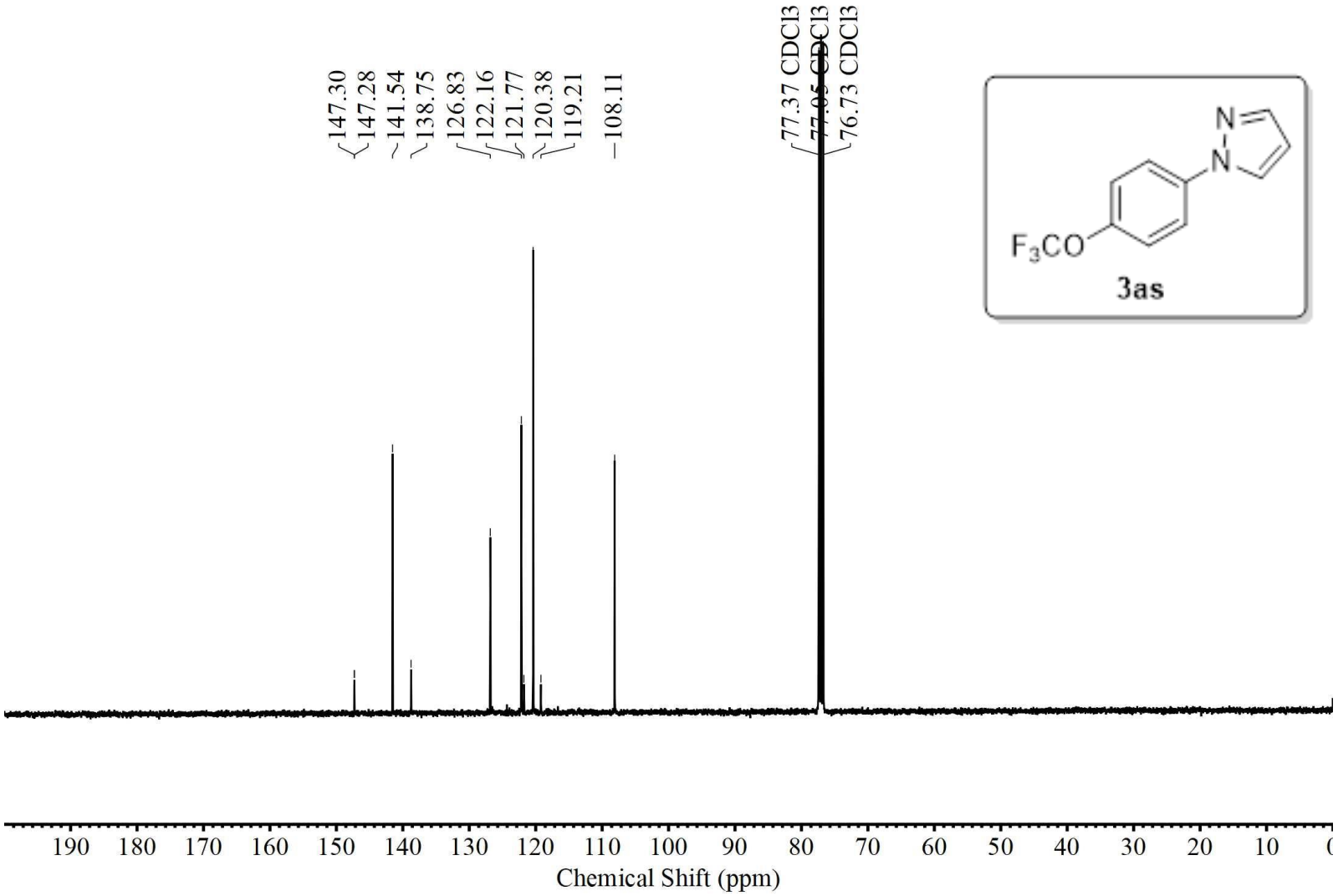


^{1}H NMR spectrum of 3as (400 MHz, $CDCl_3$)



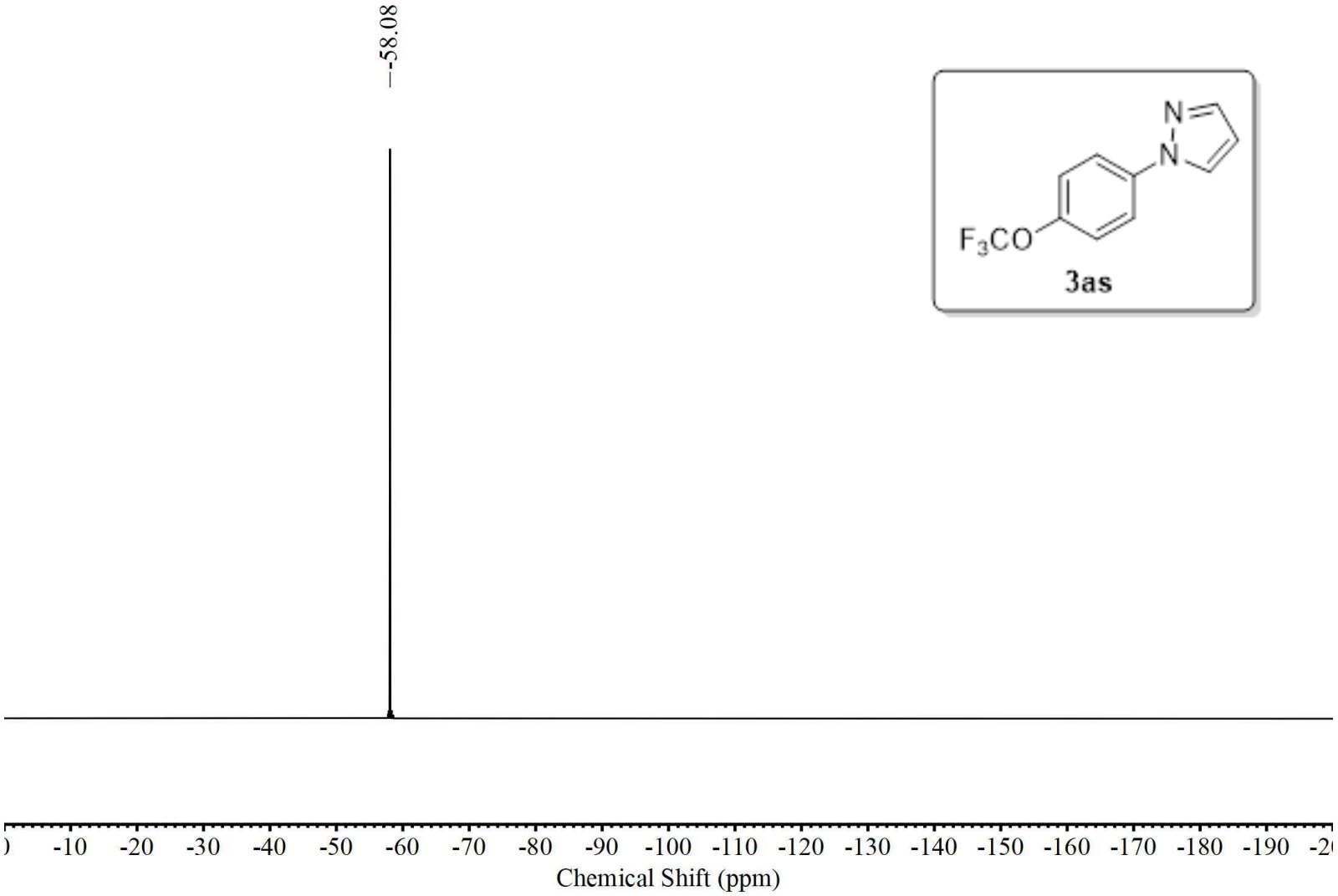
^{13}C NMR spectrum of 3as (100 MHz, $CDCl_3$)

PMD-X240516-2

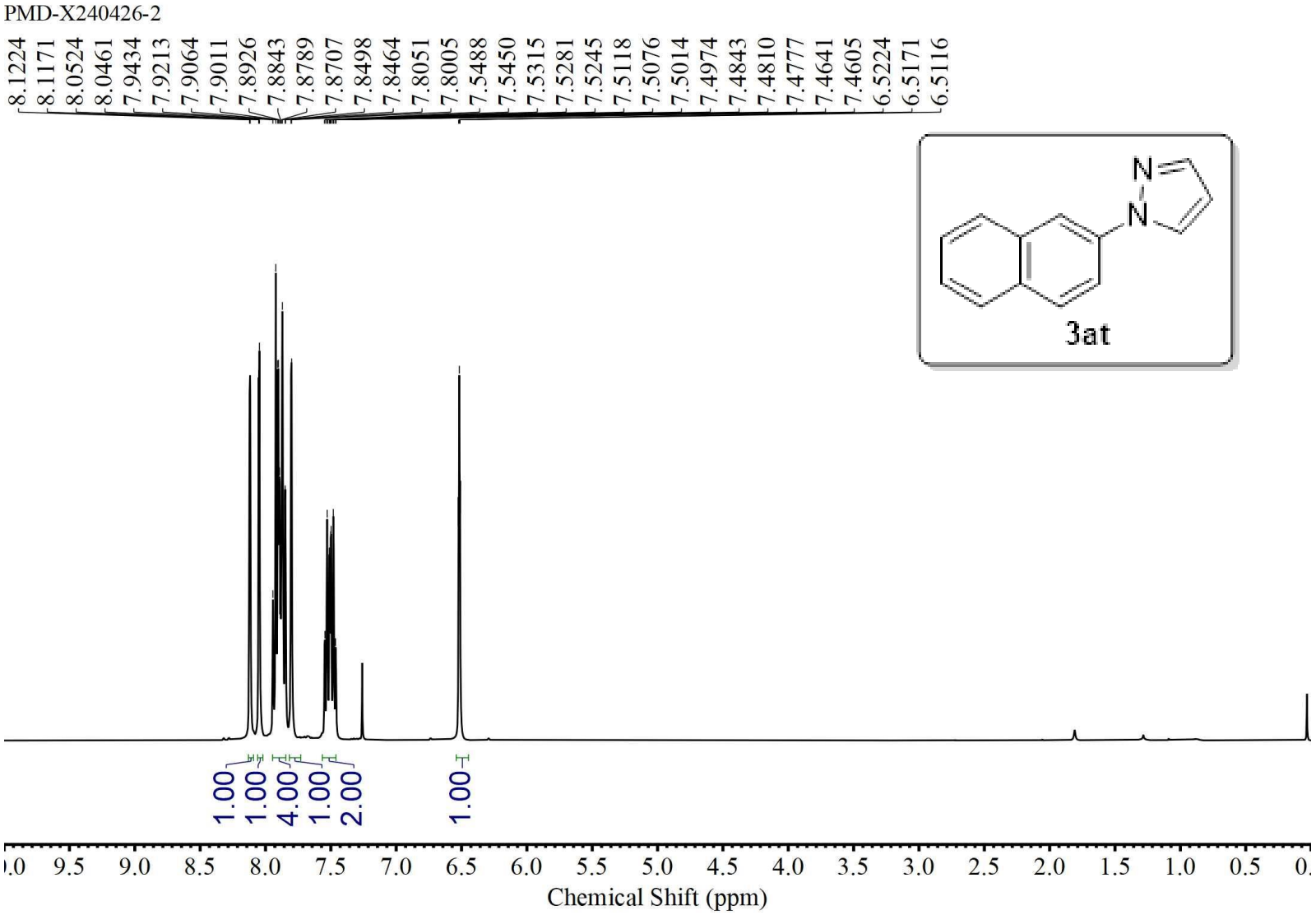


^{19}F NMR spectrum of 3as (376 MHz, $CDCl_3$)

PMD-X240516-2

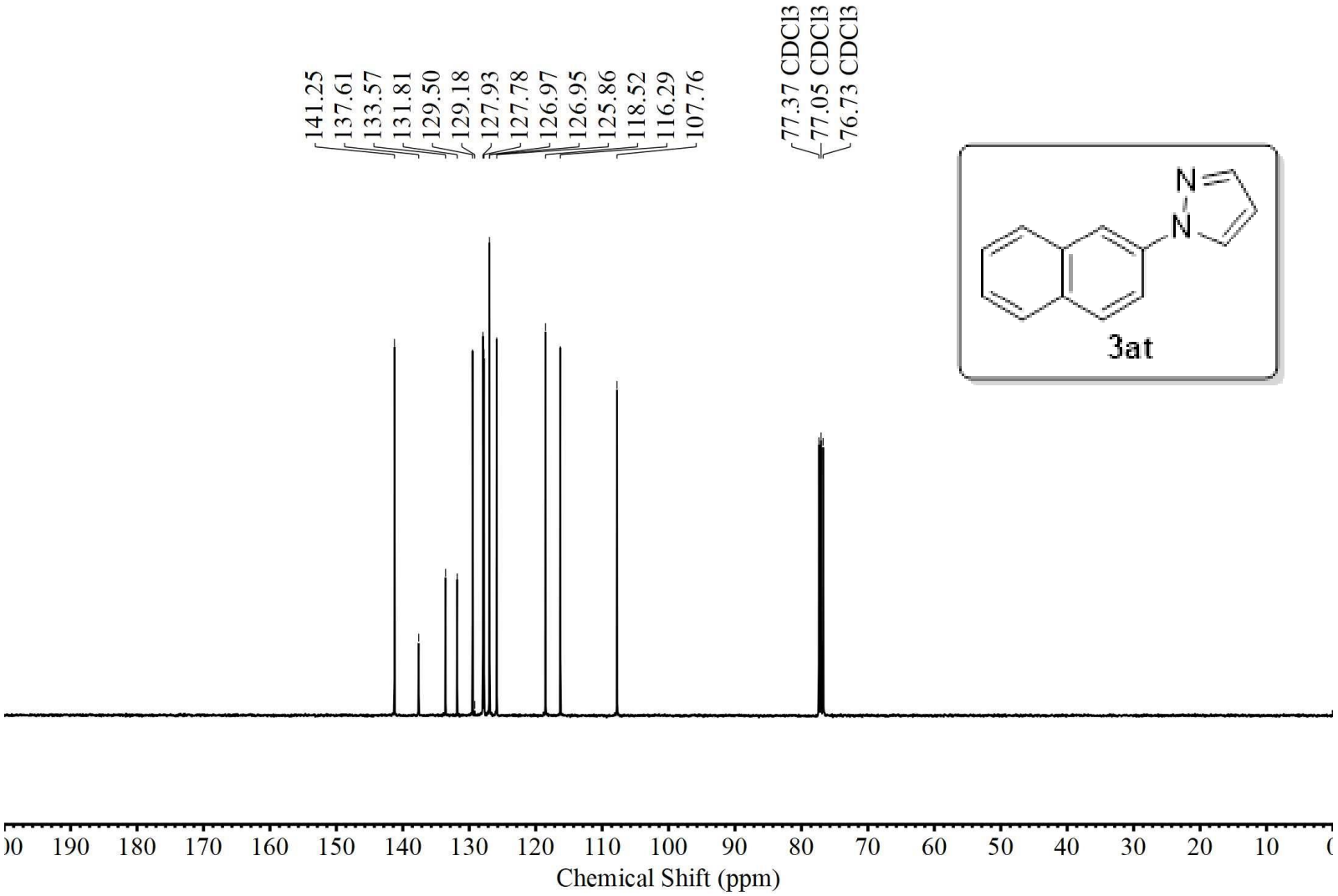


^{1}H NMR spectrum of 3at (400 MHz, $CDCl_3$)

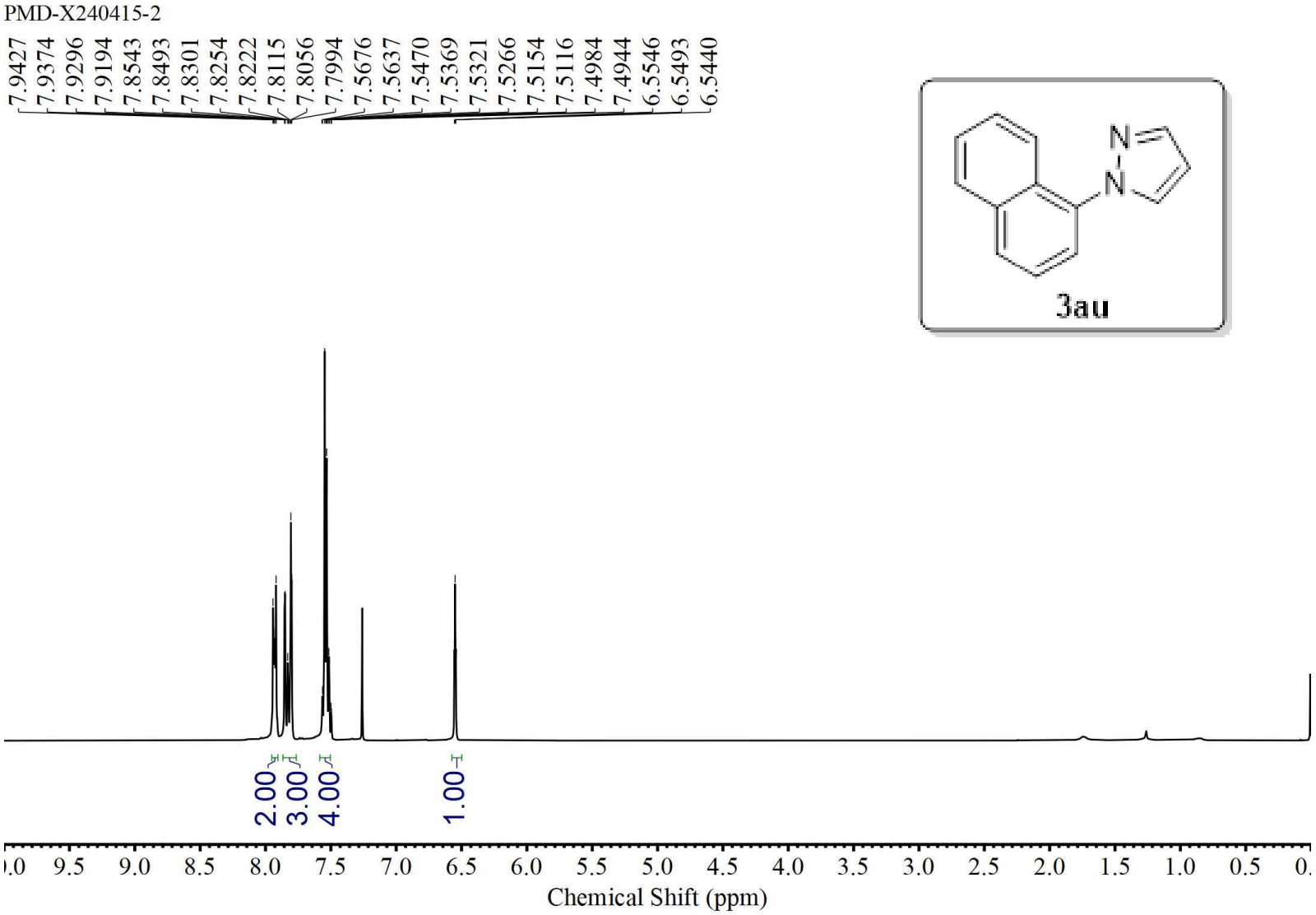


^{13}C NMR spectrum of 3at (100 MHz, $CDCl_3$)

PMD-X240516-1

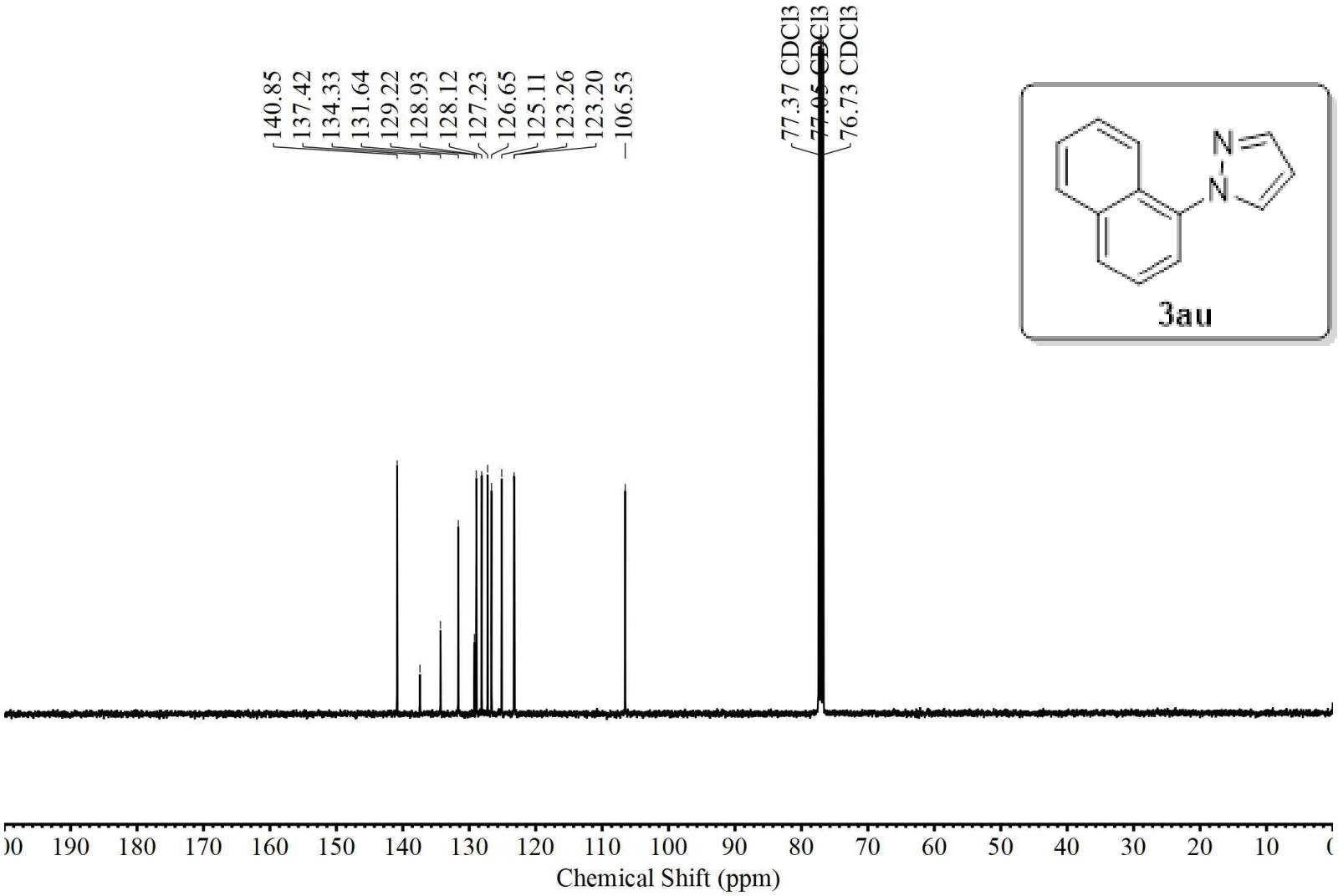


^{1}H NMR spectrum of 3au (400 MHz, $CDCl_3$)

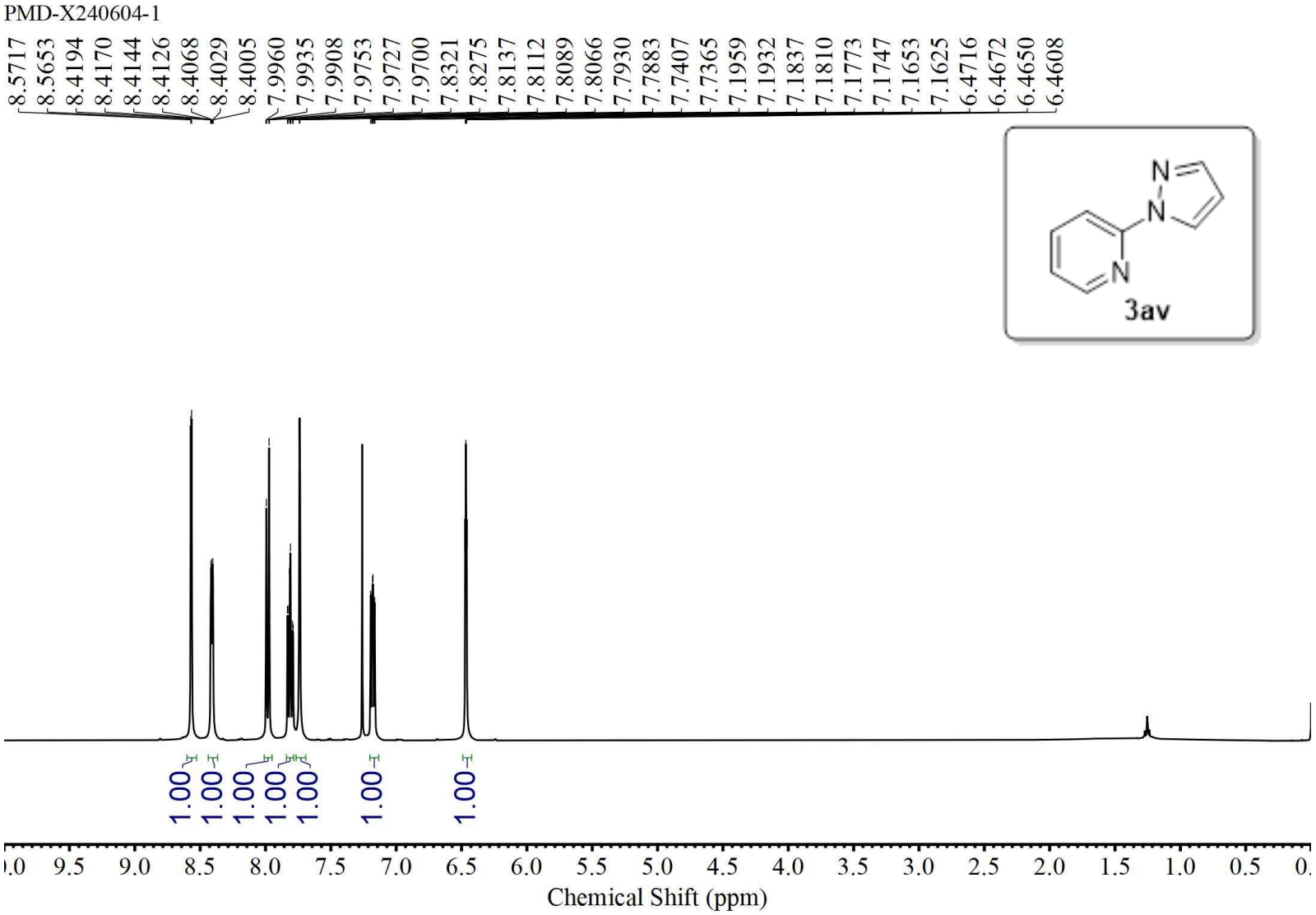


^{13}C NMR spectrum of 3au (100 MHz, $CDCl_3$)

PMD-X240415-2

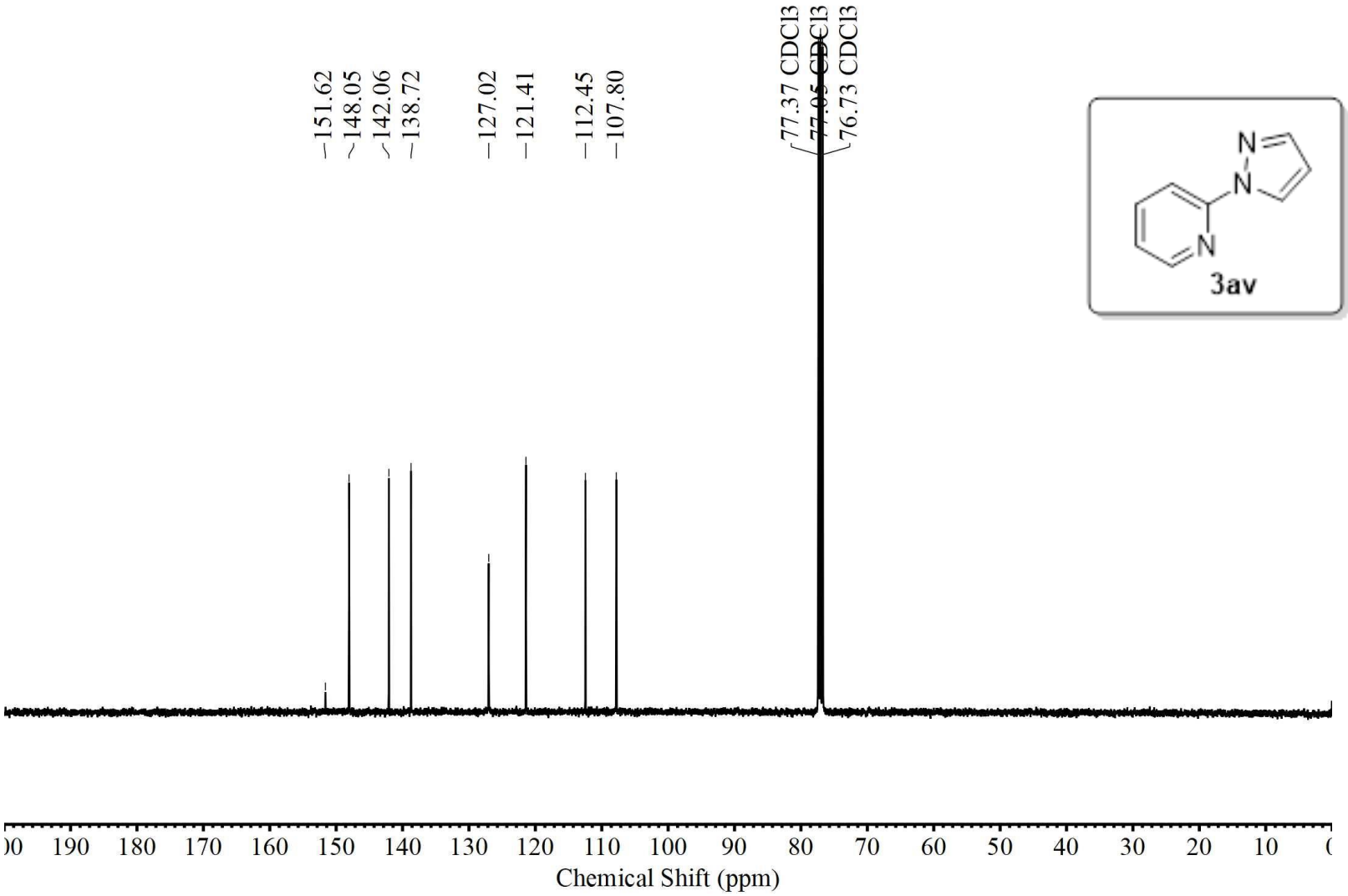


^{1}H NMR spectrum of 3av (400 MHz, $CDCl_3$)

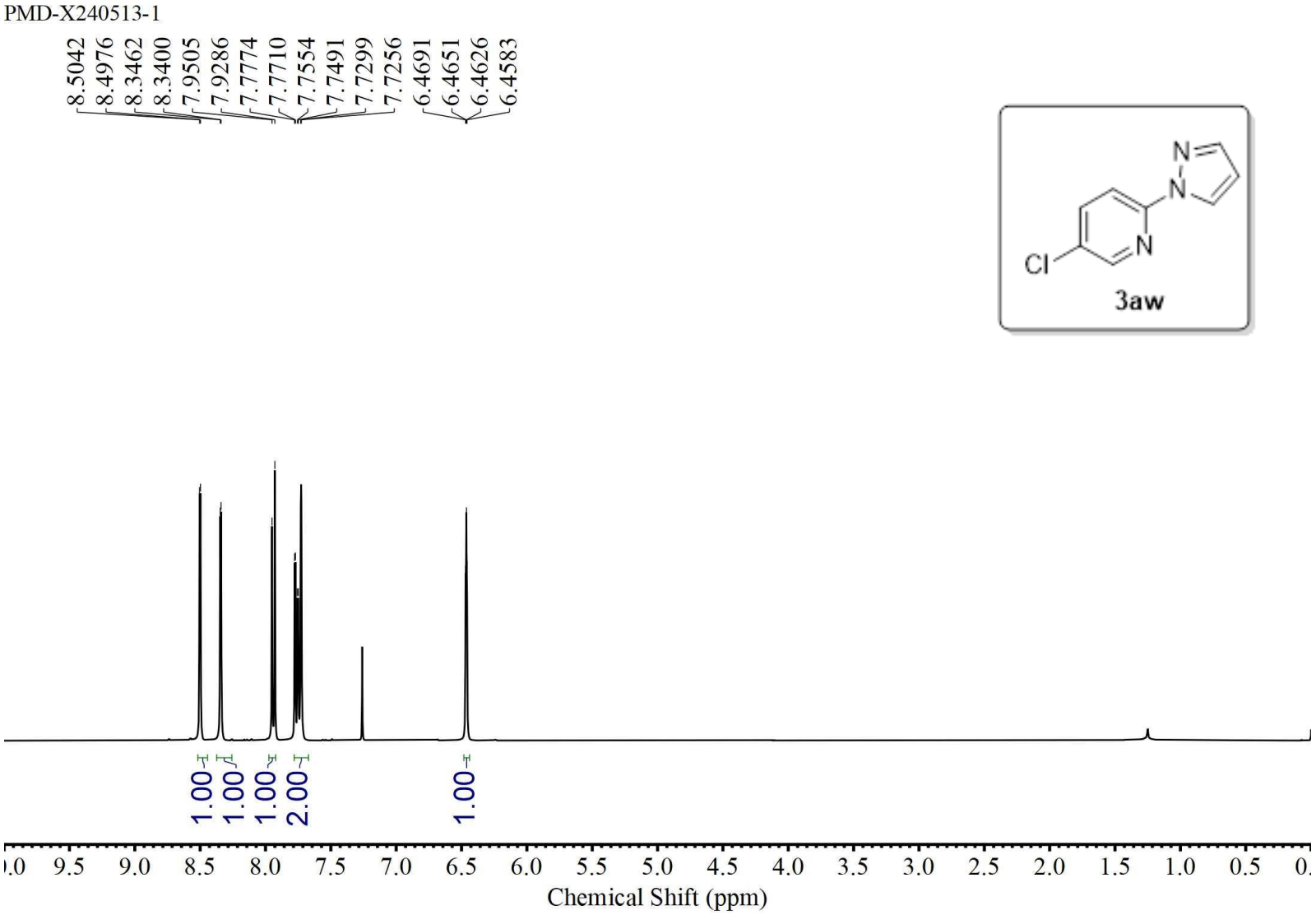


^{13}C NMR spectrum of 3av (100 MHz, $CDCl_3$)

PMD-X240604-1

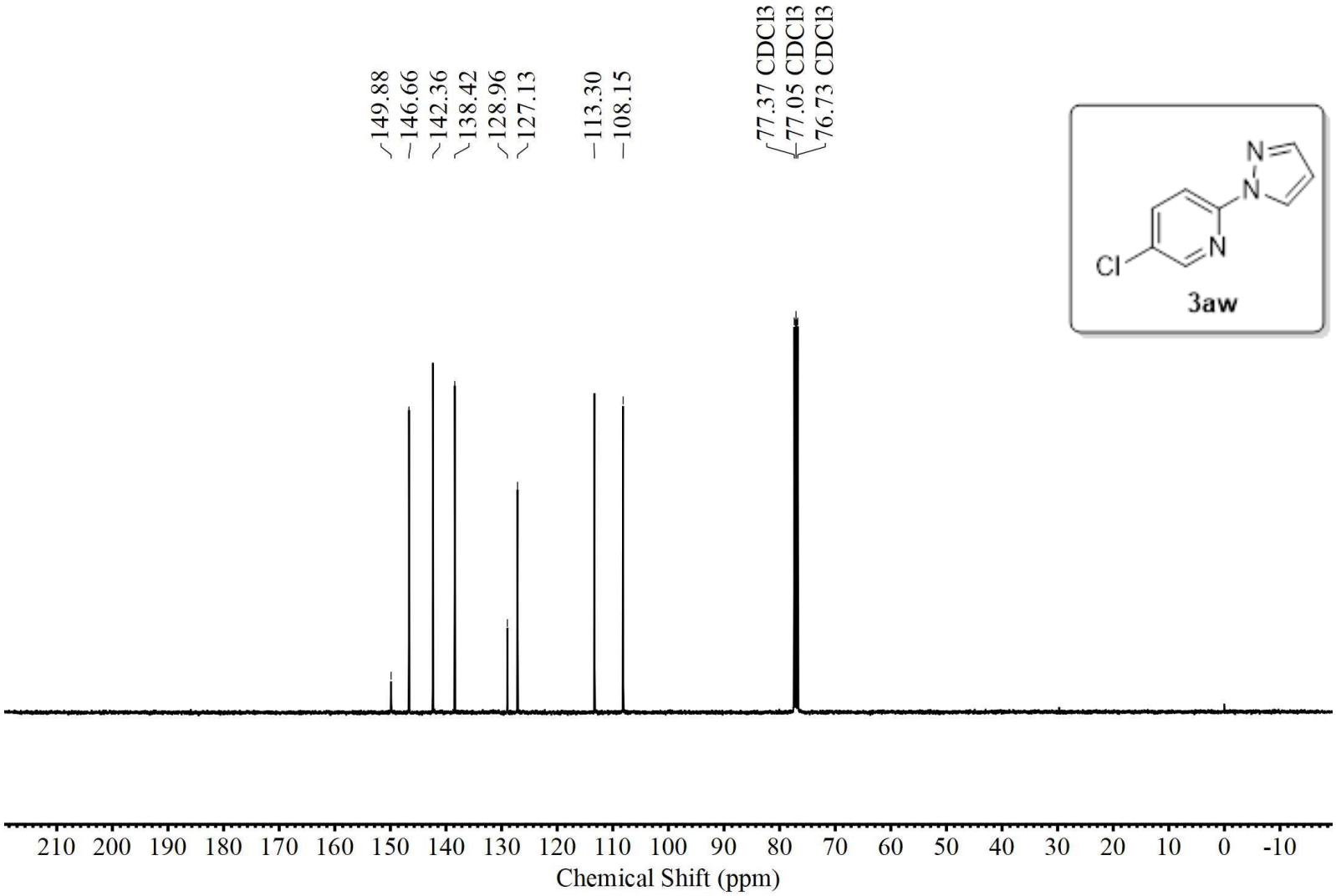


^{1}H NMR spectrum of 3aw (400 MHz, $CDCl_3$)

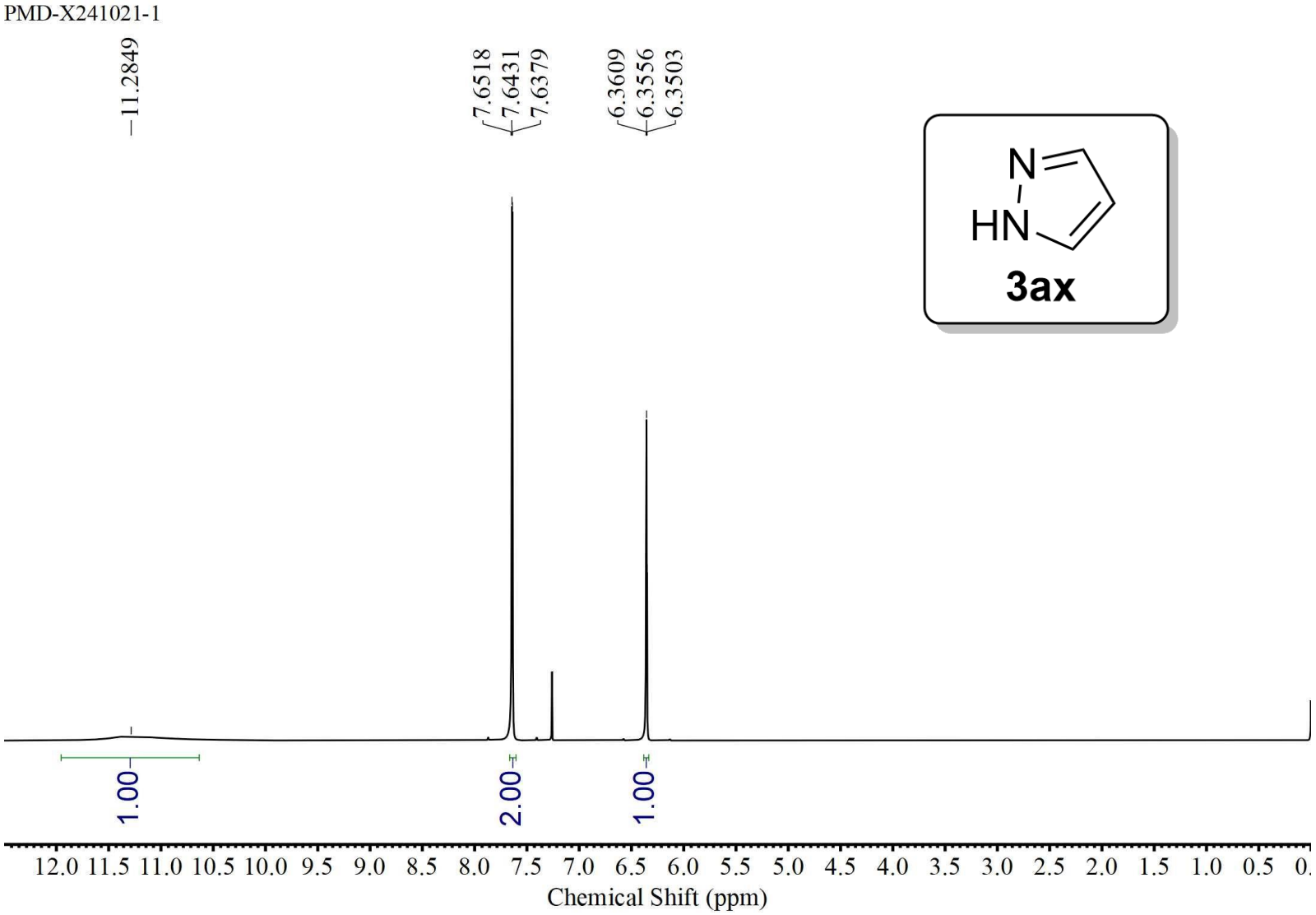


^{13}C NMR spectrum of 3aw (100 MHz, $CDCl_3$)

PMD-X240430-1

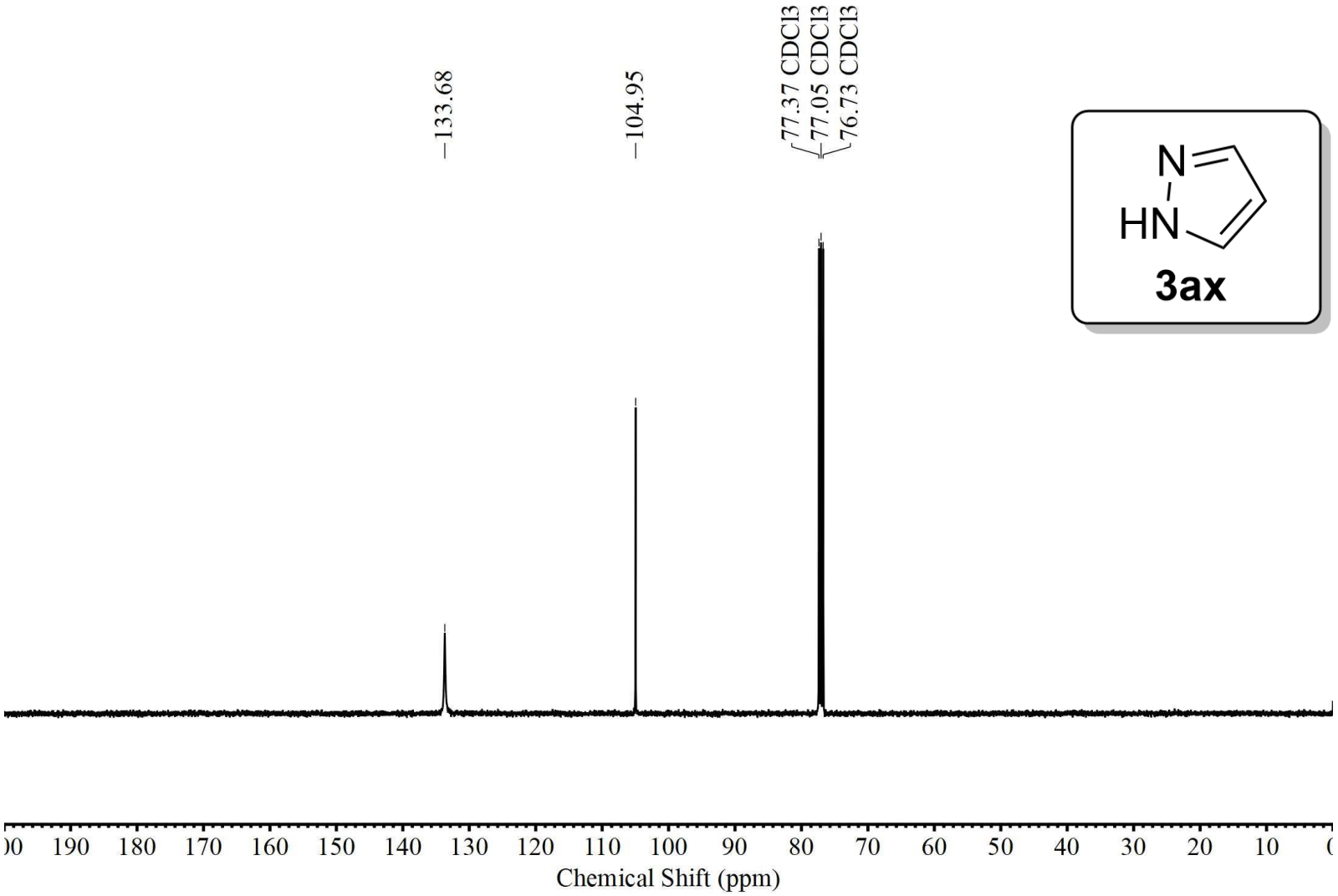


^{1}H NMR spectrum of 3ax (400 MHz, $CDCl_3$)

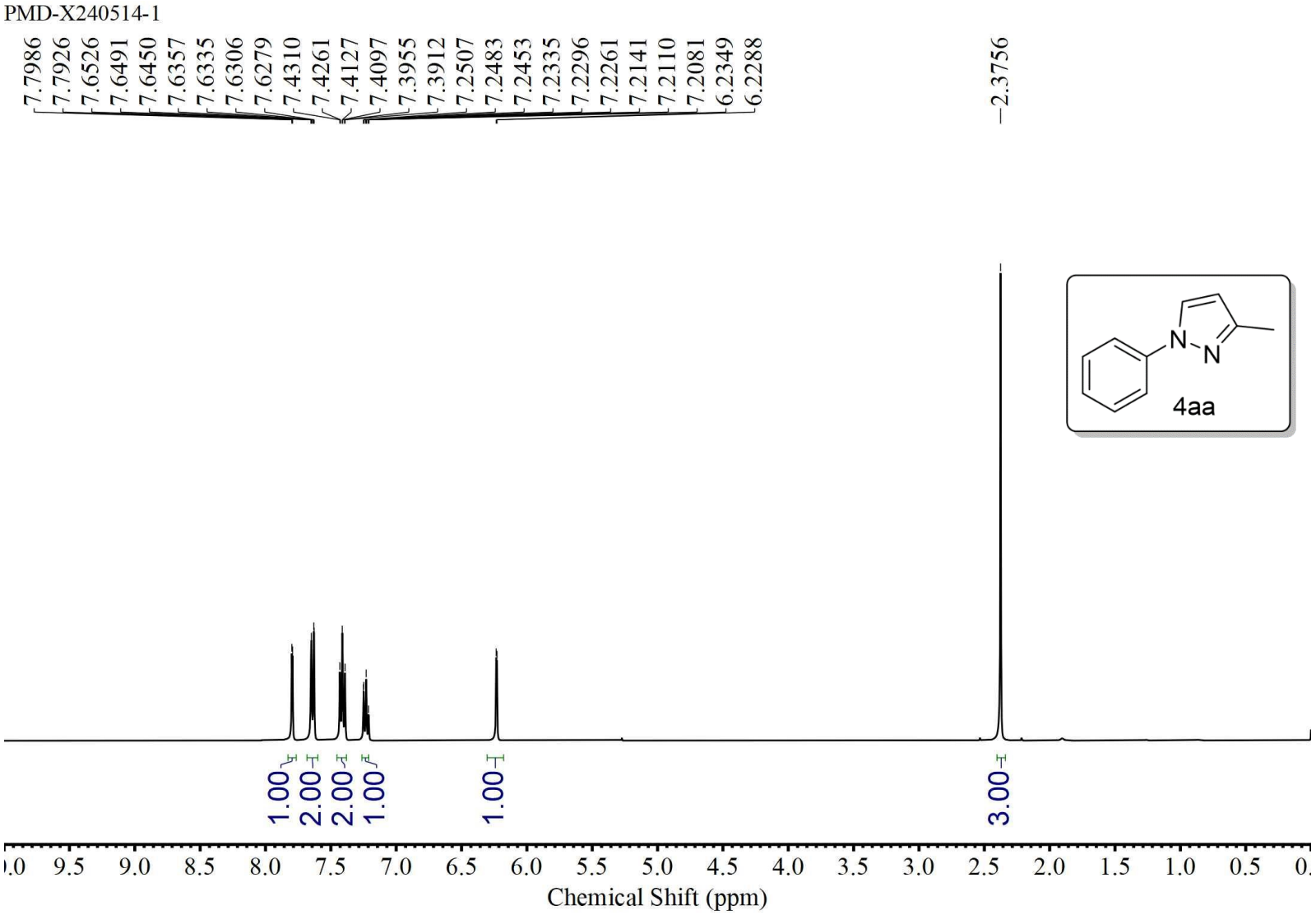


^{13}C NMR spectrum of 3ax (100 MHz, $CDCl_3$)

PMD-X241021-1

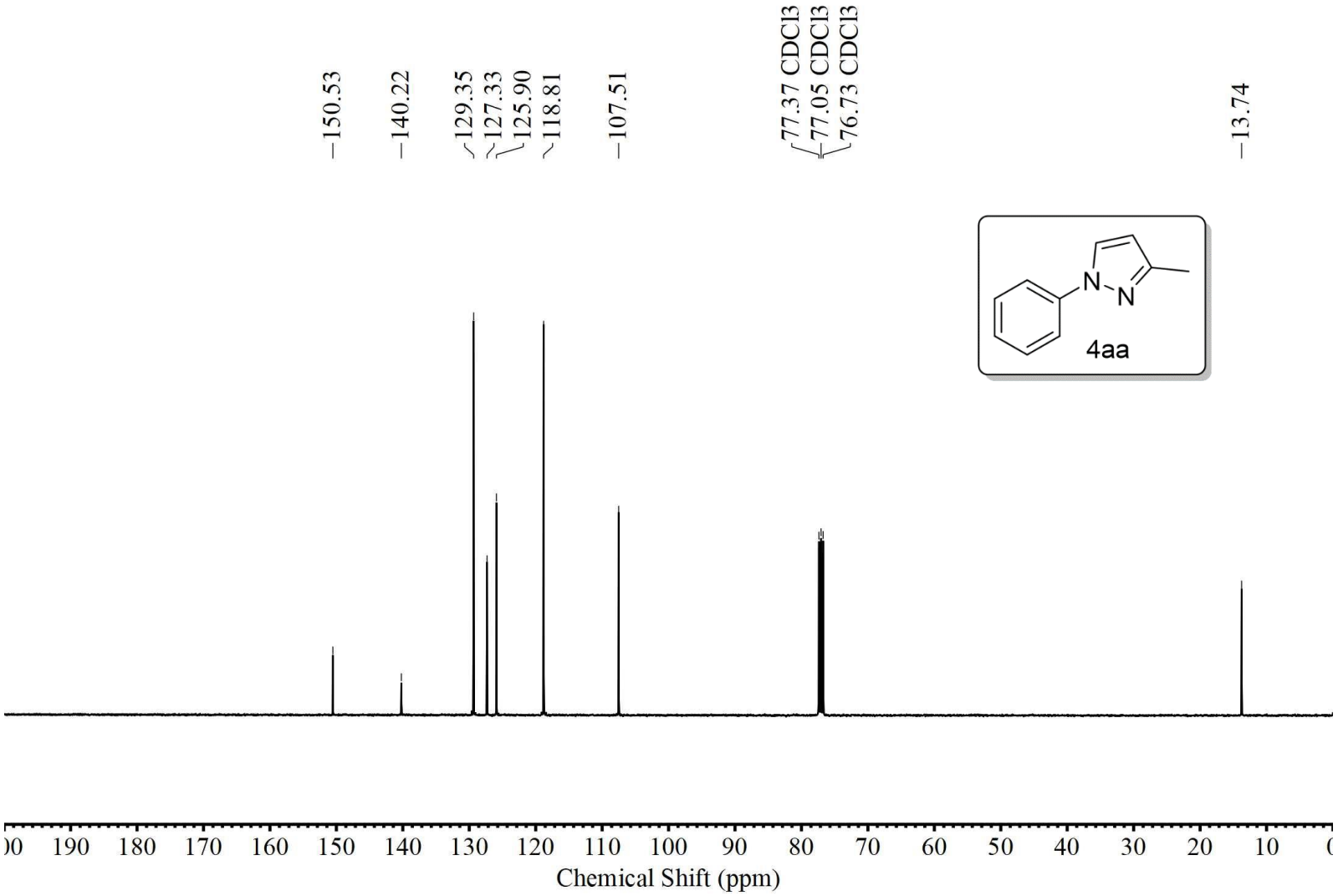


^{1}H NMR spectrum of 4aa (400 MHz, $CDCl_3$)

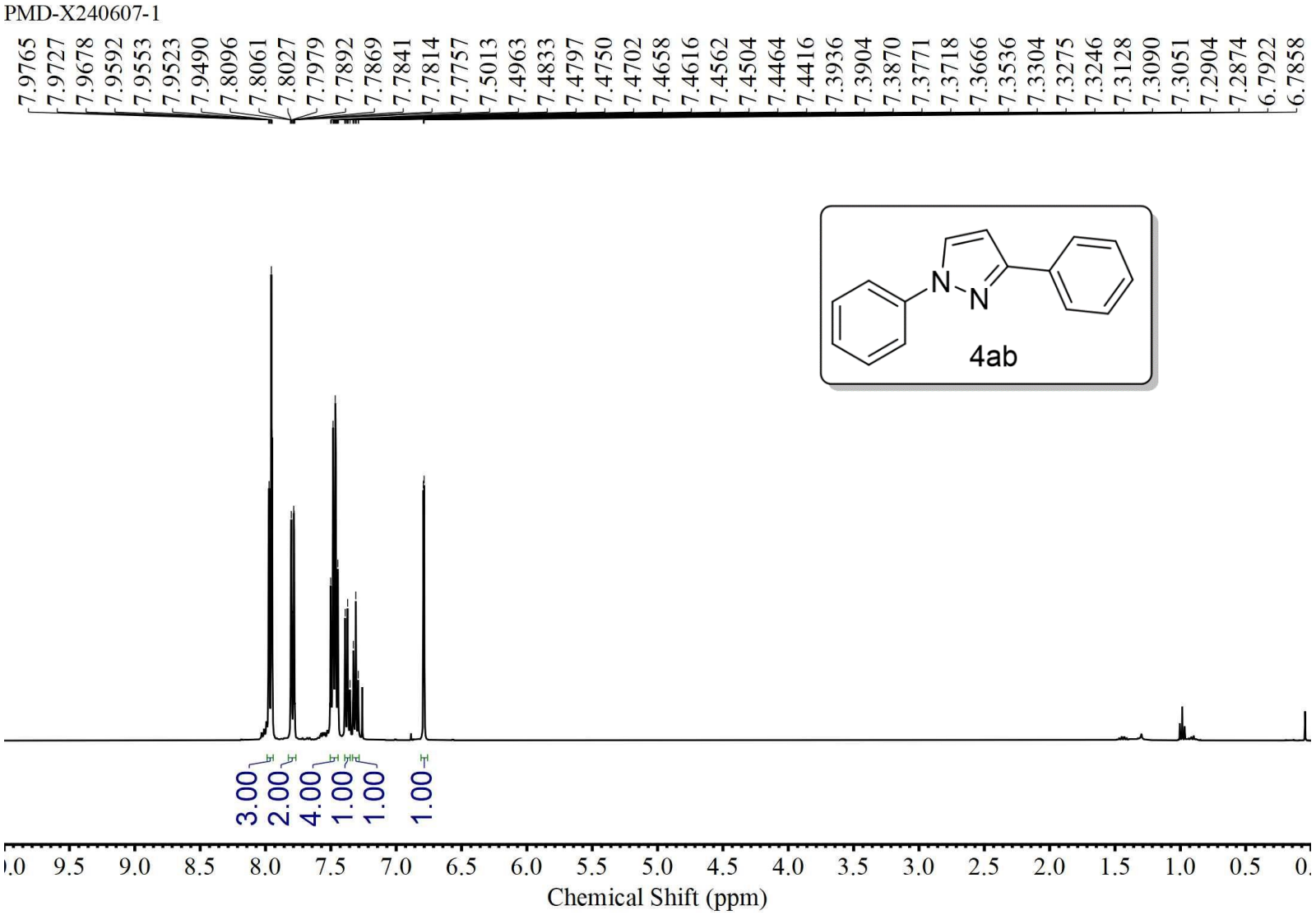


^{13}C NMR spectrum of 4aa (100 MHz, $CDCl_3$)

PMD-X240514-1

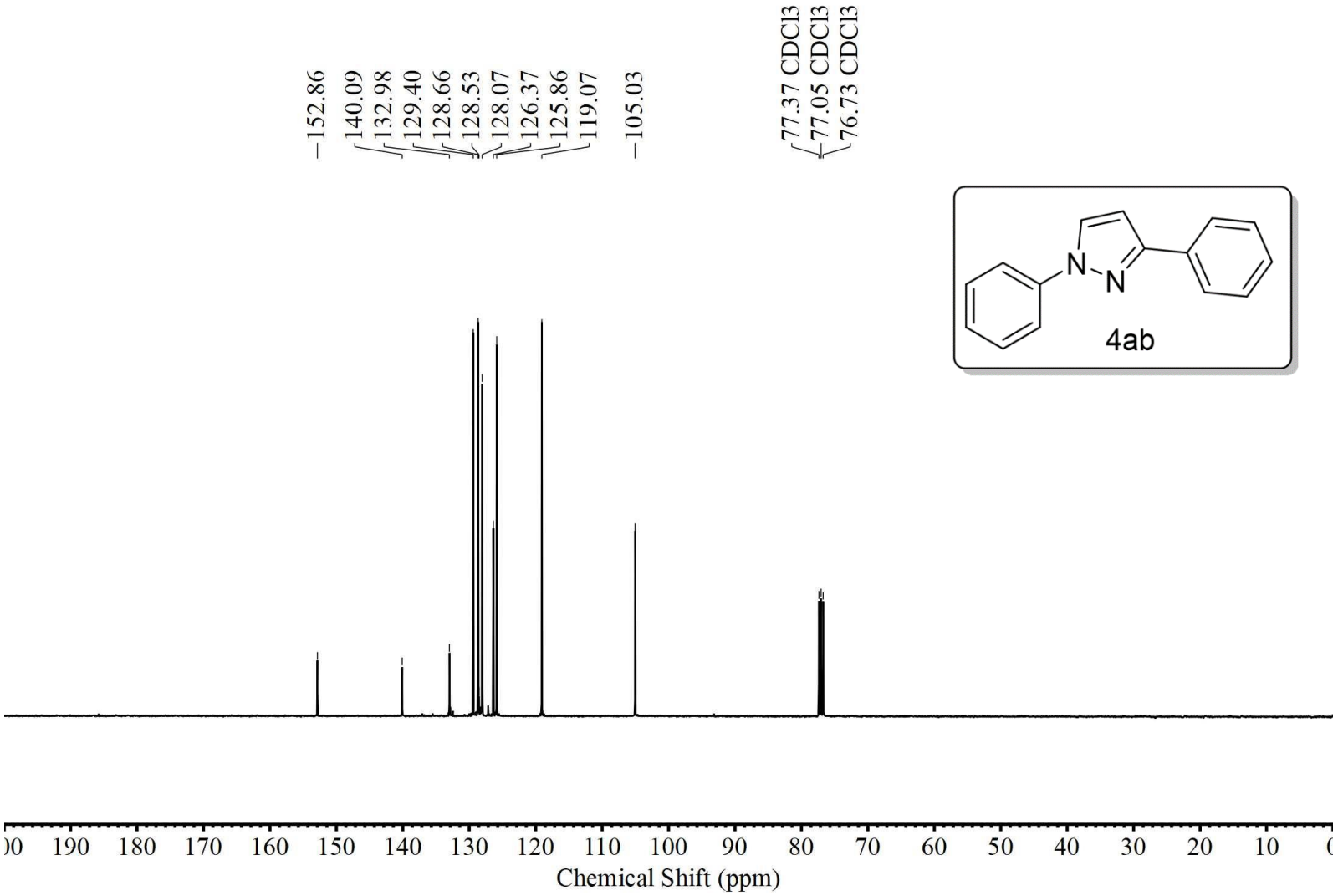


^{1}H NMR spectrum of 4ab (400 MHz, $CDCl_3$)

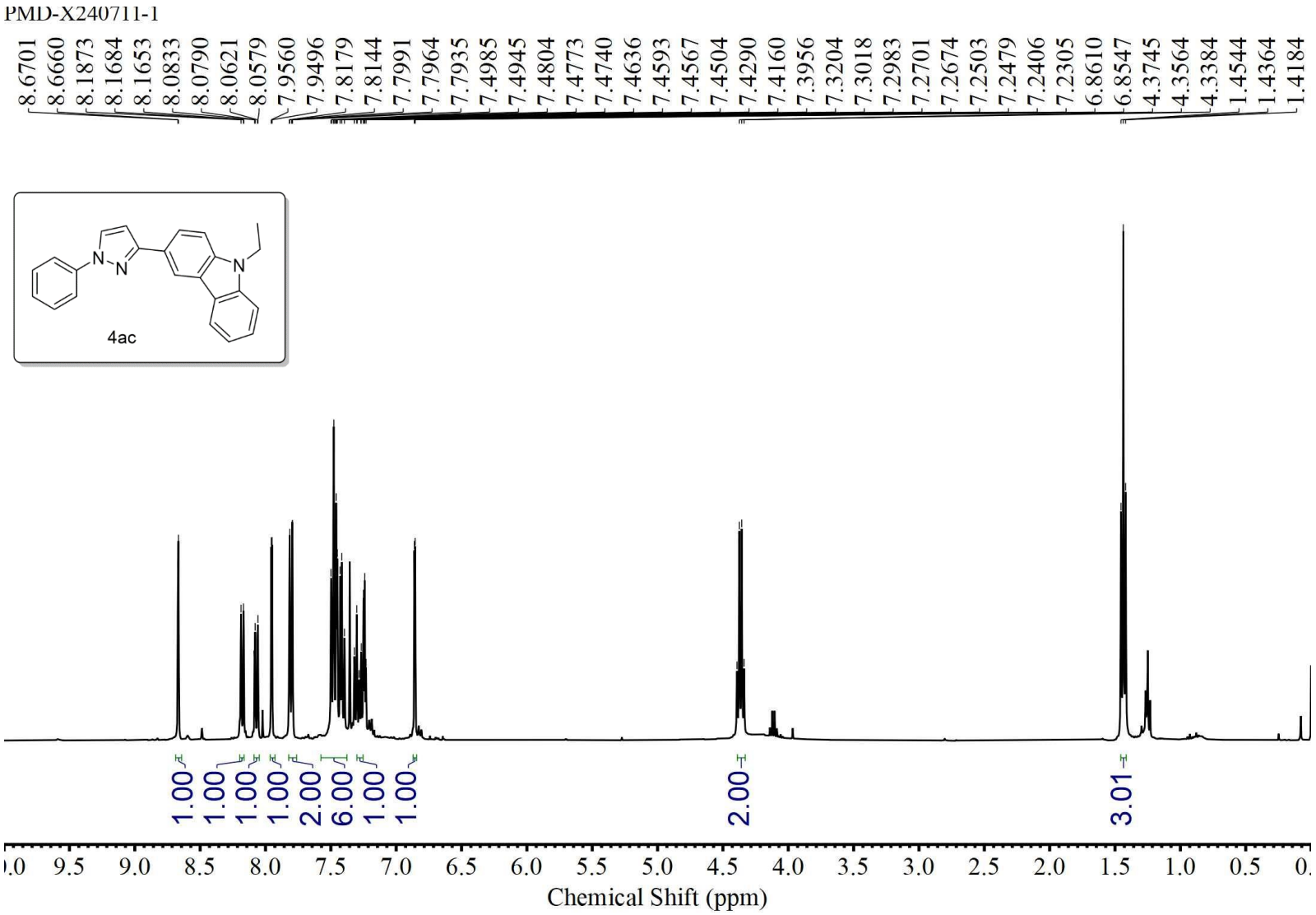


^{13}C NMR spectrum of 4ab (100 MHz, $CDCl_3$)

PMD-X240607-1

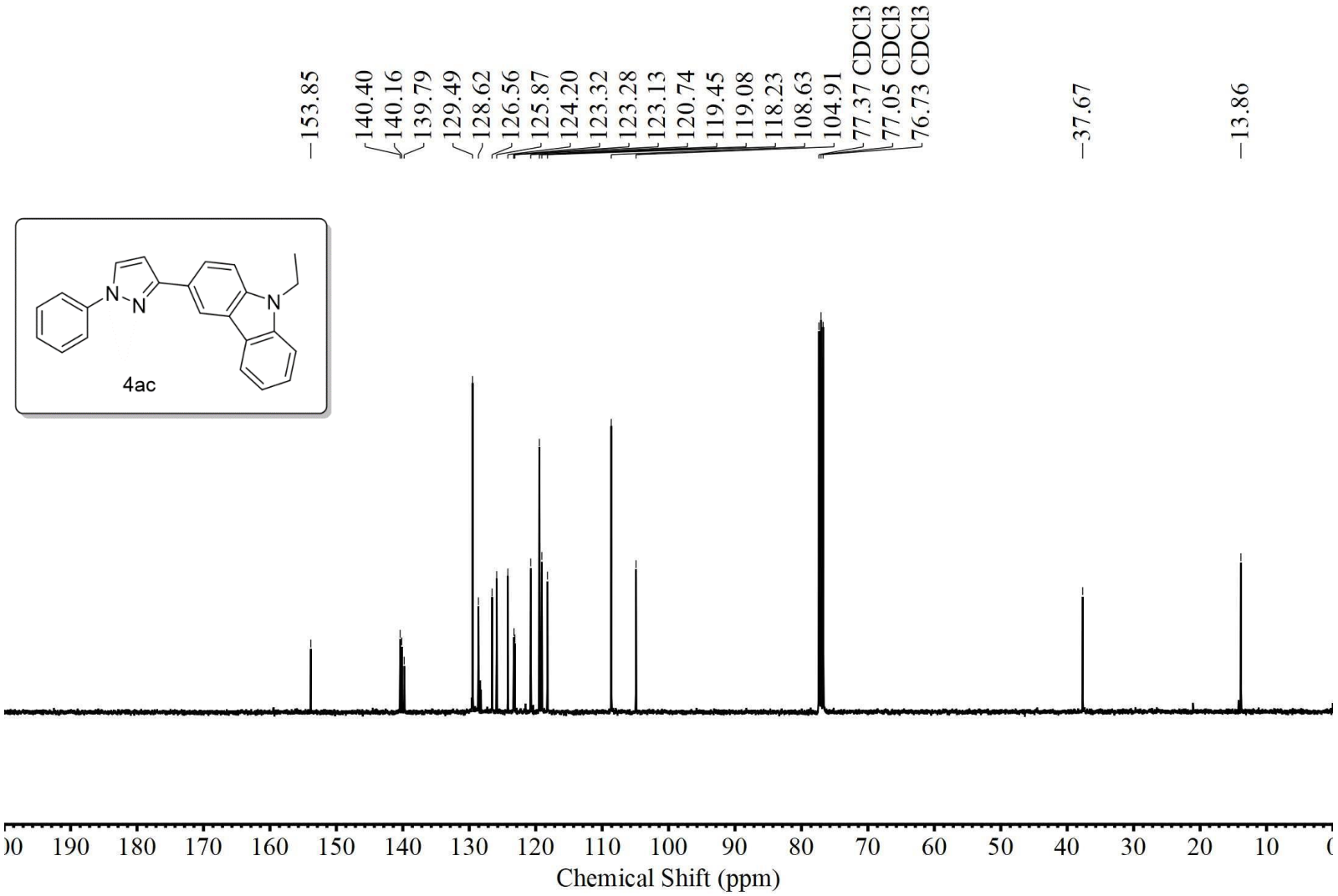


^{1}H NMR spectrum of 4ac (400 MHz, $CDCl_3$)

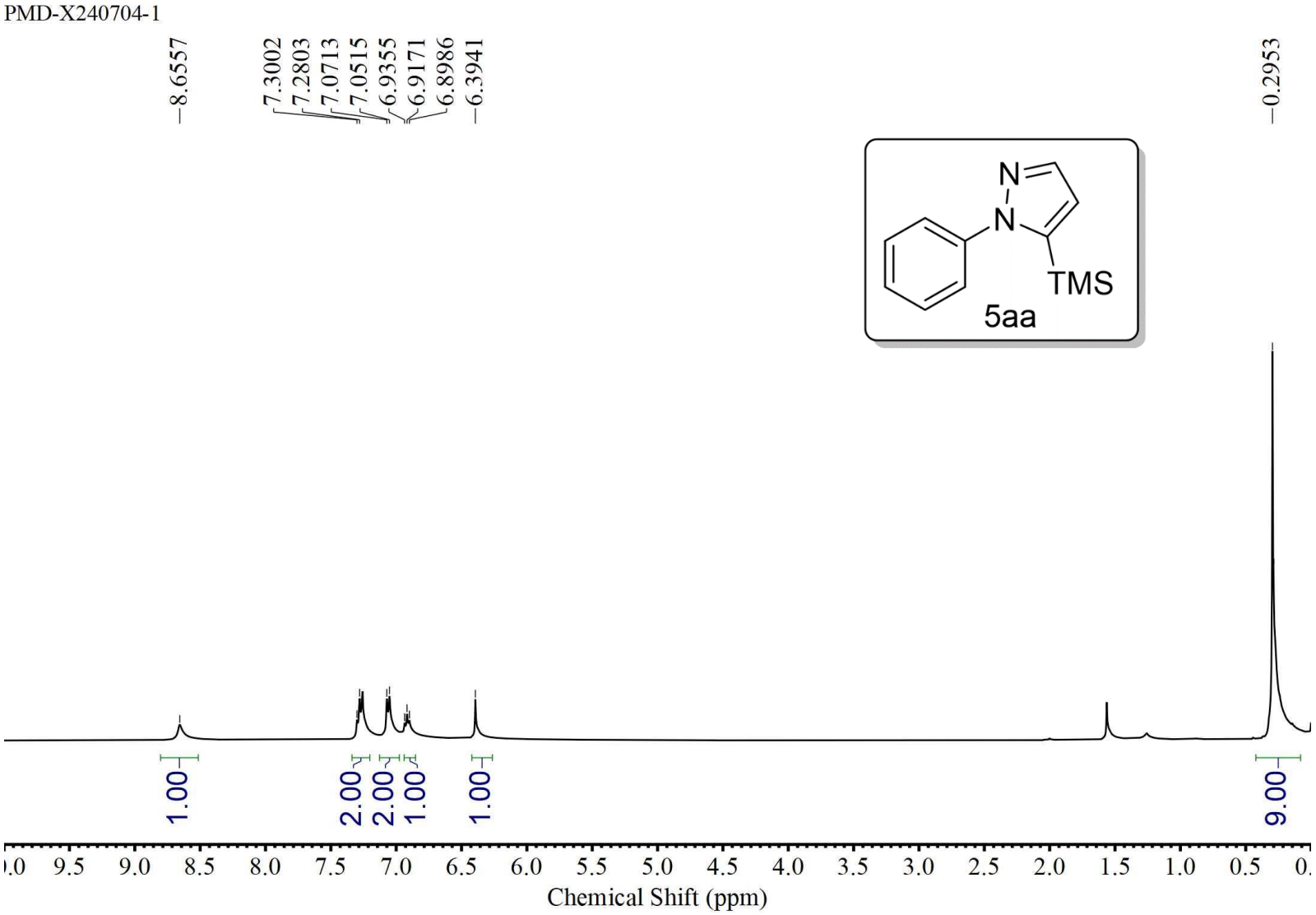


^{13}C NMR spectrum of 4ac (100 MHz, $CDCl_3$)

PMD-X240711-1

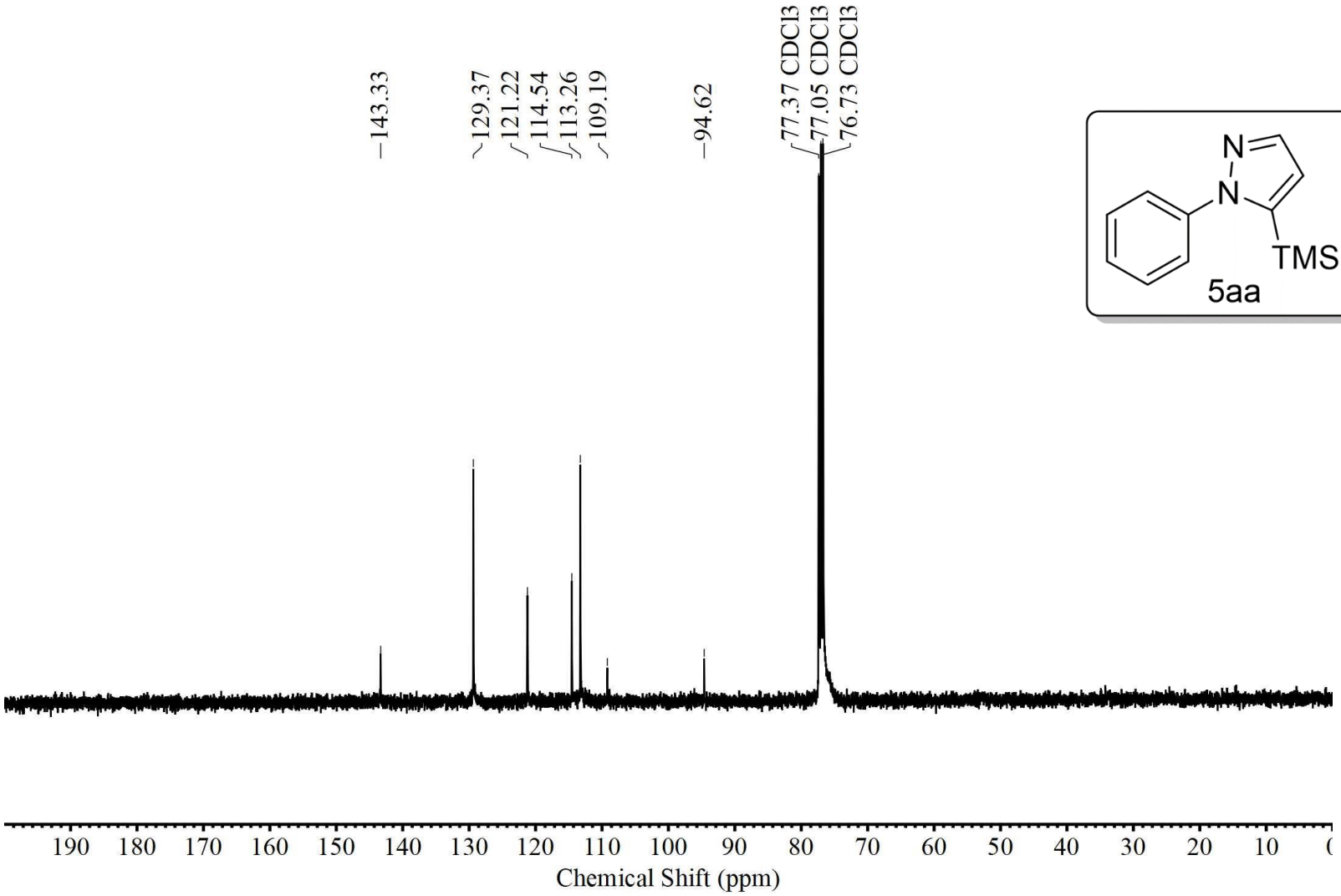


^{1}H NMR spectrum of 5aa (400 MHz, $CDCl_3$)

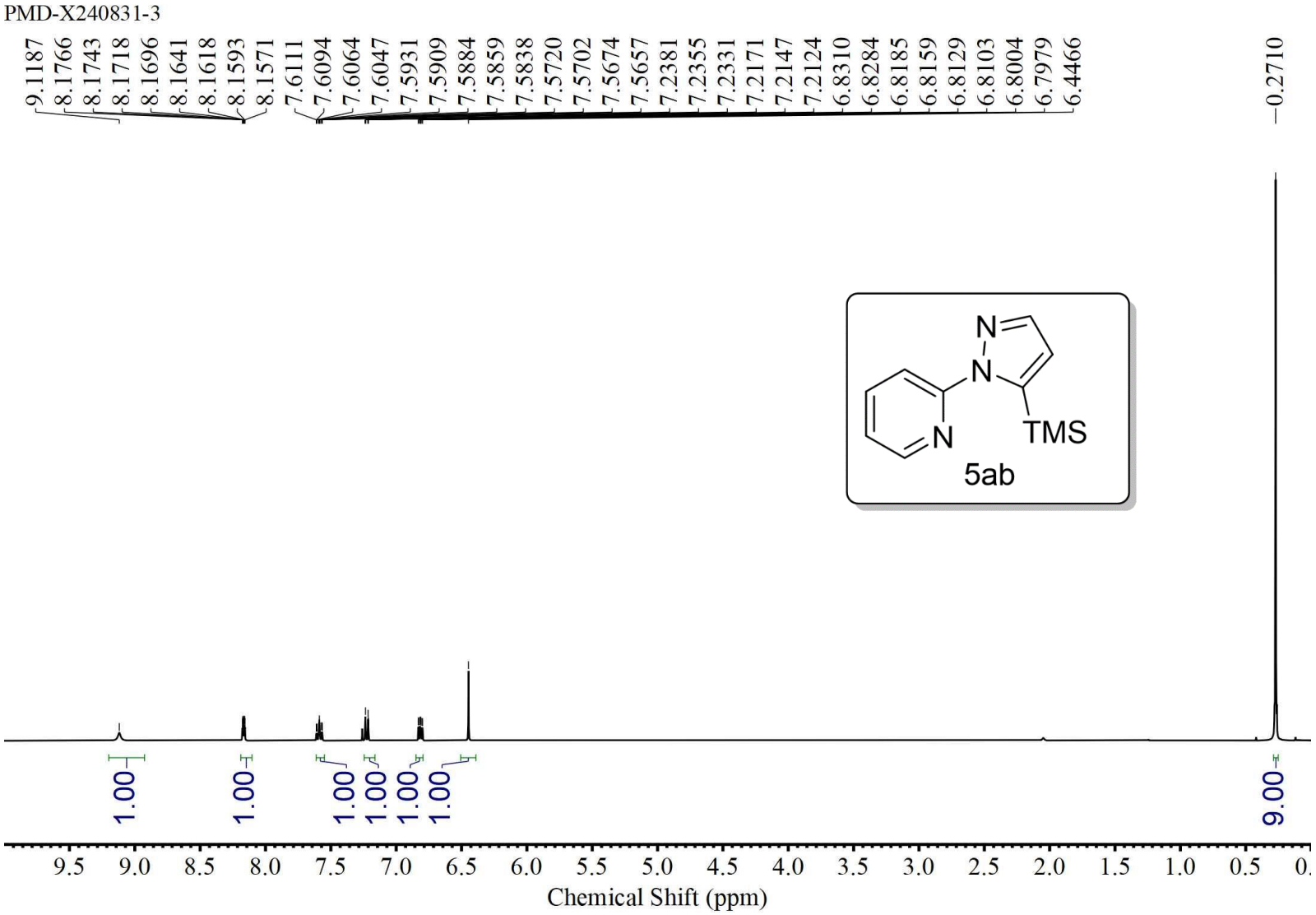


^{13}C NMR spectrum of 5aa (100 MHz, $CDCl_3$)

PMD-X240704-1

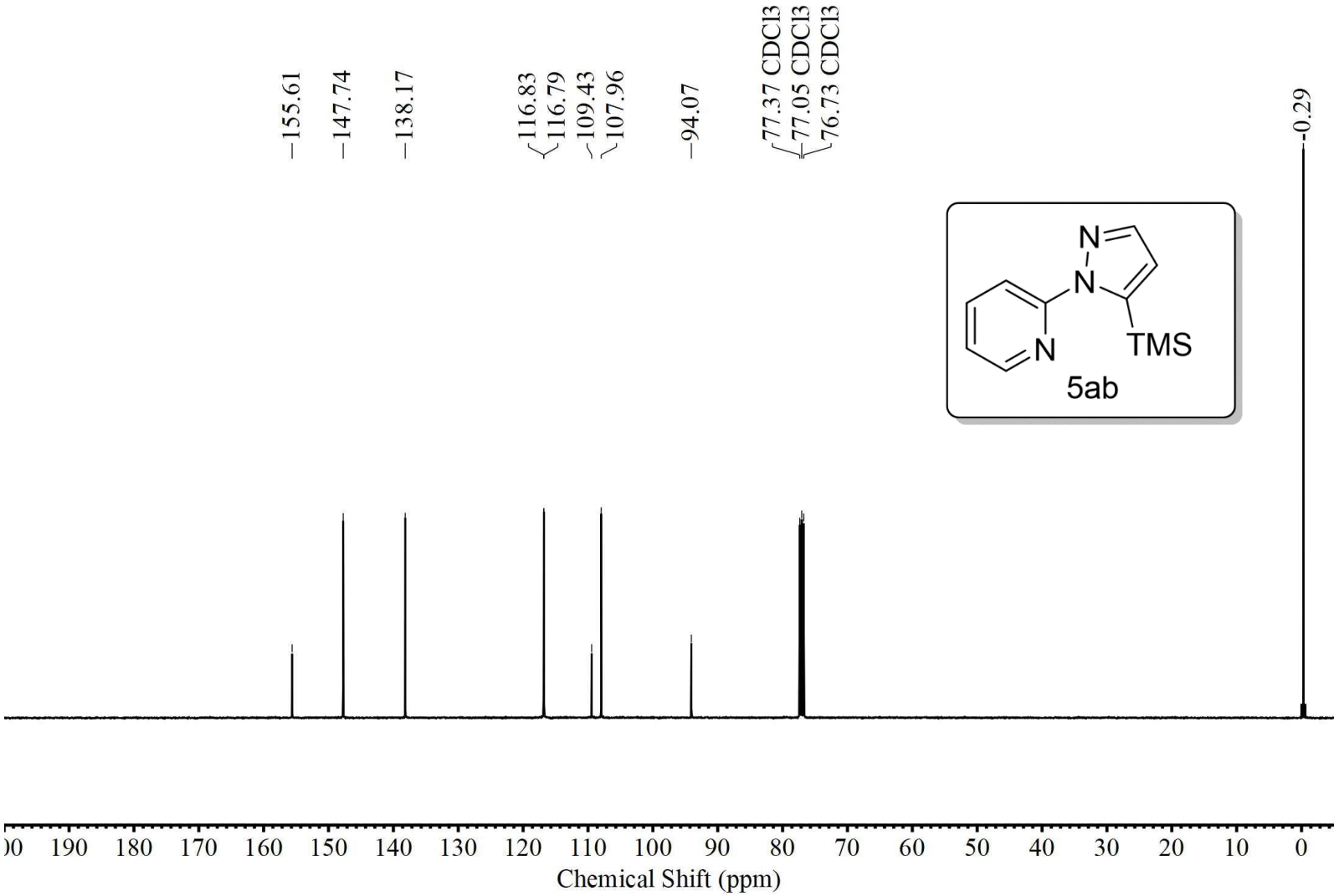


^{1}H NMR spectrum of 5ab (400 MHz, $CDCl_3$)

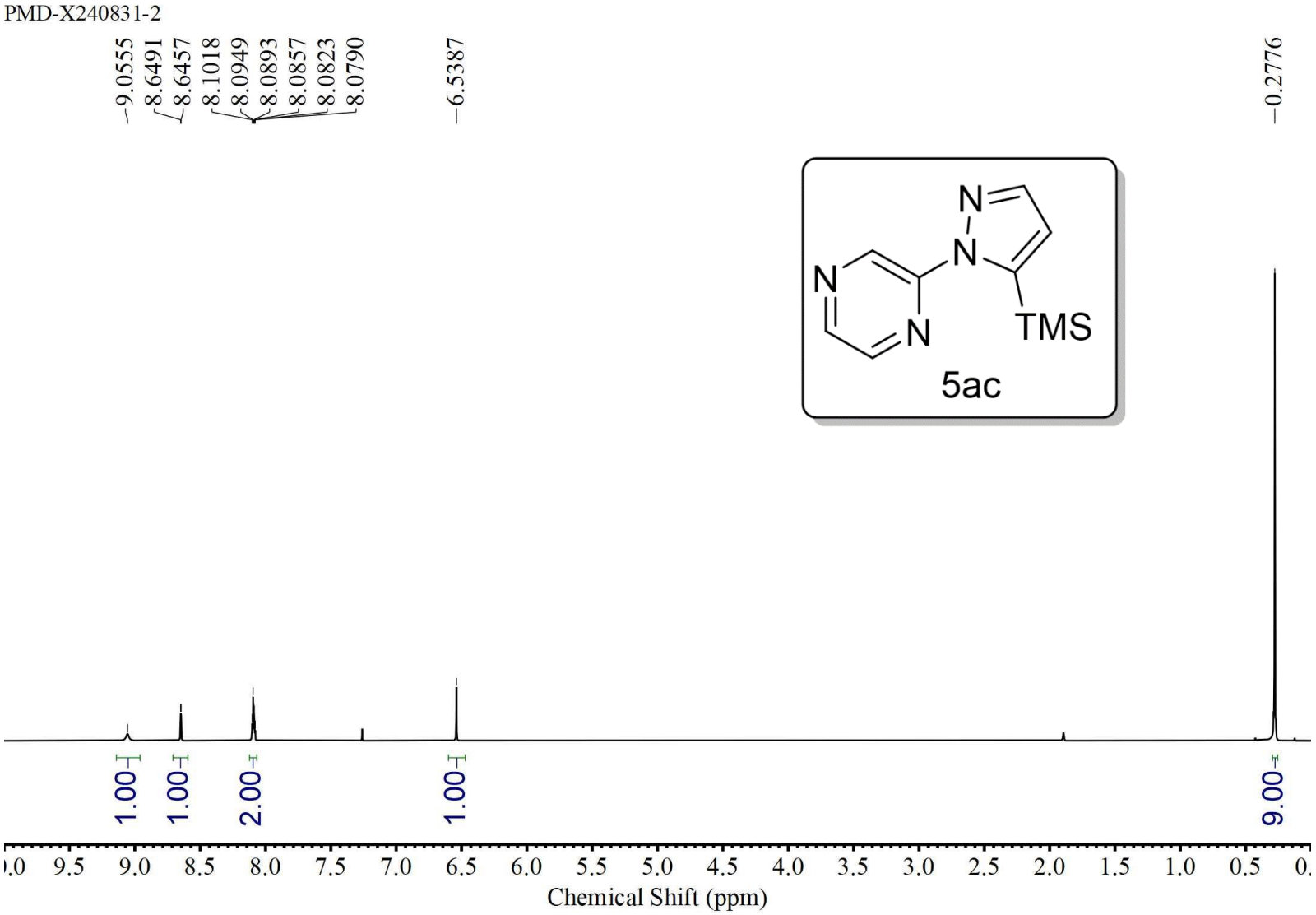


^{13}C NMR spectrum of 5ab (100 MHz, $CDCl_3$)

PMD-X240831-3



^{1}H NMR spectrum of 5ac (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of 5ac (100 MHz, $CDCl_3$)

PMD-X240831-2