Electronic Supplementary Information

Visible-light-driven C(sp^3)–H alkylation of heterobenzylic amines *via* electron donor–acceptor complexes

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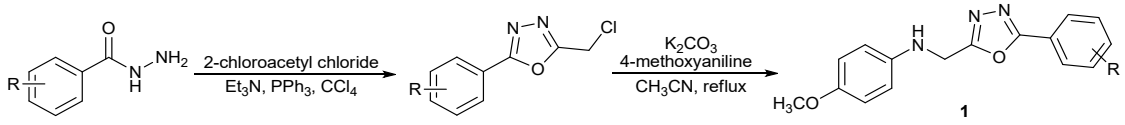
1. General information

All commercially available reagents were used without further purification unless otherwise stated. All solvents were purified and dried according to standard methods prior to use. 410-420 nm light source was bought in Xuzhou Aijia electronic technology, China. NMR spectra were recorded on a Bruker 300 M instrument spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standard unless otherwise stated. Data for ^1H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and dd = doublet of doublets coupling constant (s) in Hz, integration). Data for ^{13}C and ^{19}F NMR are reported in terms of chemical shift (δ, ppm). Reactions were monitored by thin layer chromatography (TLC) and column chromatography purifications were carried out using silica gel. Melting points were measured on a SCW X-4 and values are uncorrected. UV-Vis absorption spectra were recorded by using BIOMATE 3S UV-Visible Spectrophotometer. All new compounds were further characterized by high resolution mass spectra (HRMS) were obtained by quadrupole mass spectrometer with ESI ionization sources.

2. Substrates synthesis

General procedure for the synthesis of oxadiazoles amine[1]

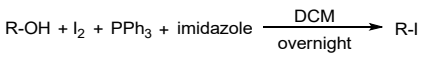


Step 1: In a two-neck round-bottom flask the appropriate aryl hidrazide (10 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (25 mL). After the Et_3N (20 mmol, 2.0 equiv) was added and stirred the reaction for 10 minutes, the temperature system was taken at 0 °C and the 2-choroacetyl chloride (15 mmol, 1.5 equiv) was slowly dripped in a flask. The mixture remained at ambient temperature for 4 h approximately, and the intermediate was obtained, without isolation. In the same flask, triphenylphosphine (15.7 mmol, 1.57 equiv), carbon tetra-chloride (50 mmol, 5.0 equiv) and triethylamine (15.7 mmol, 1.57 equiv) were added, followed by the mixture was heated at 40 °C for 12 h with stirring in an oil bath. Then the mixture was cooled to room temperature, poured into water (15 mL) and extracted with CH_2Cl_2 (3 x 15 mL). Combined organic layers were dried over Na_2SO_4, the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography to yield 1,3,4-oxadiazoles (about 63% yield).

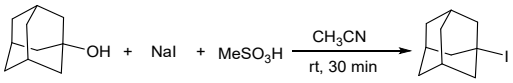
Step 2: To a solution of oxadiazoles (6.2 mmol, 1.0 equiv) in CH_3CN (13 mL) was added 4-methoxyaniline (9.3 mmol, 1.5 equiv). Then K_2CO_3 (15.5 mmol, 2.5 equiv) was added and the mixture was heated at 82 °C for 18 h with stirring in an oil bath. Subsequently, the mixture was cooled to room temperature. Diatomaceous earth suction filtration system, suction filtration to obtain the organic layer poured into water (15 mL) and extracted with CH_2Cl_2 (3 x 15 mL). Combined organic layers were

dried over Na_2SO_4, the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography to yield 1,3,4-oxadiazoles amine.

General procedure for the synthesis of alkyl iodide[2]



General protocol for the preparation of secondary and primary iodides: Iodine chips (12 mmol, 1.2 equiv) were added to a solution of Ph_3P (12 mmol, 1.2 equiv) and imidazole (12 mmol, 1.2 equiv) in dry CH_2Cl_2 (0.2 M) at 0 °C. The alcohol (10 mmol, 1.0 equiv, neat or a solution in CH_2Cl_2) was added dropwise to the reaction mixture at 0 °C. The mixture was allowed to warm to room temperature and stirred overnight. Next, the solvent was removed on a rotary evaporator. The residue was purified by silica gel column chromatography.

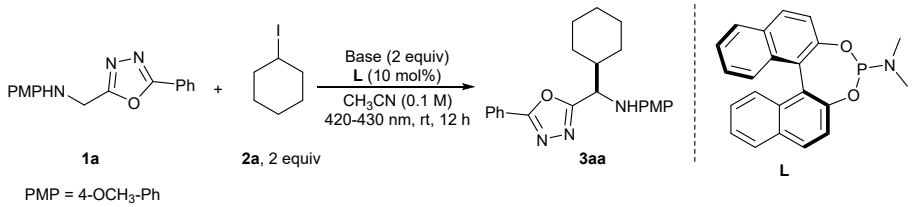


General protocol for the preparation of tertiary iodides: $MeSO_3H$ (20 mmol, 2.0 equiv) was added dropwise to a solution of NaI (20 mmol, 2.0 equiv) and the tertiary alcohol (10 mmol, 1 equiv), in MeCN (0.2 M in the tertiary alcohol) at 0 °C. The reaction mixture was allowed to warm up to room temperature and it was stirred for an additional 30 minutes. Next, the reaction mixture was diluted with Et_2O, washed with H_2O, $NaHCO_3$, $Na_2S_2O_3$, and brine, dried over anhydrous Na_2SO_4, and concentrated with rotatory evaporation. Further purification of the tertiary iodide would be done by distillation or column chromatography.

3. General procedure of C(sp^3)-H alkylation

3.1 Optimization of reaction conditions

Table S1 Base screening[a]



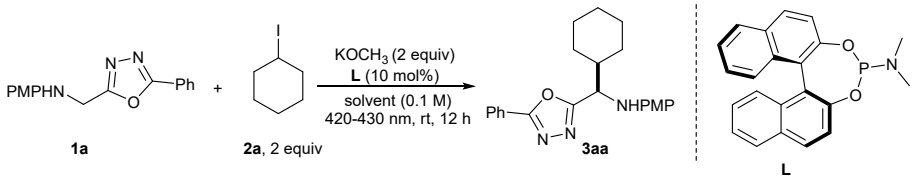
1a **2a**, 2 equiv **3aa** **L**

PMP = 4-OCH_3-Ph

entry	base	yield[b] (%)	entry	base	yield[b] (%)
1	TMG	17	10	Cs_2CO_3	24
2	Et_3N	trace	11	K_3PO_4	15
3	DIPEA	13	12	K_2HPO_4	N. D.
4	DBU	15	13	KH_2PO_4	N. D.
5	HMPA	N. D.	14	NaO^{t}Bu	30
6	DABCO	N. D.	15	NaOH	25
7	CsF	33	16	NaOAc	N. D.
8	***$KOCH_3$***	***36***	17	Na_2CO_3	N. D.
9	KF	N. D.	18	$NaHCO_3$	N. D.

[a] 0.05 mmol scale. [b] Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

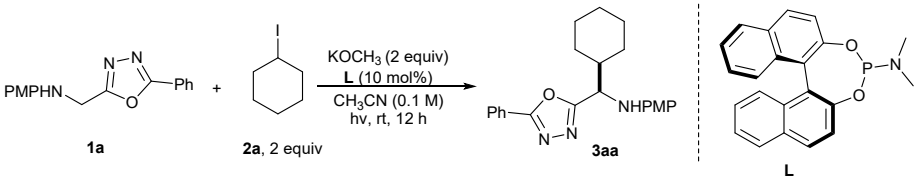
Table S2 Solvent screening[a]



entry	solvent	yield[b] (%)	entry	solvent	yield[b] (%)
1	Toluene	N. D.	12	DMPU	10
2	DCE	21	13	DCM	15
3	DMF	24	14	DMAc	29
4	***CH_3CN***	***36***	15	ethyl acetate	trace
5	THF	N. D.	16	CCl_4	N. D.
6	DMSO	30	17	HFIP	N. D.
7	CH_3CH_2OH	4	18	1,4-Dioxane	N. D.
8	CH_3OH	trace	19	1,3-Dioxolane	N. D.
9	$CHCl_3$	trace	20	*para*-xylene	N. D.
10	$(CH_3CH_2)O$	trace	21	2-ethoxyethanol	N. D.
11	Acetone	trace	22	1,2-Dimethoxyethane	N. D.

[a] 0.05 mmol scale. [b] Yield was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard.

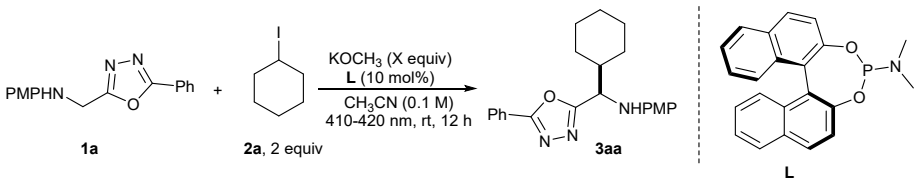
Table S3 Light source screening[a]



entry	light	yield[b] (%)	entry	light	yield[b] (%)
1	White LED	trace	***5***	***410-420 nm***	***38***
2	Green LED	N. D.	6	400-410 nm	29
3	Blue LED	10	7	395-400 nm	32
4	420-430 nm	36	8	380 nm	36

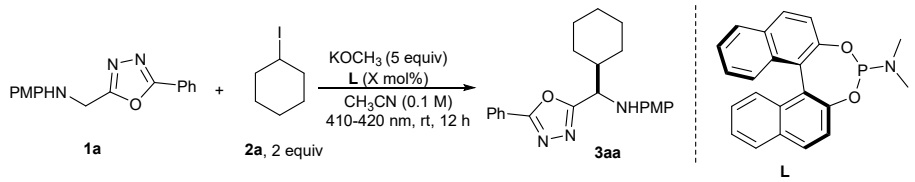
[a] 0.05 mmol scale. [b] Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Table S4 $KOCH_3$ loading screening[a]



entry	X	yield[b] (%)	entry	X	yield[b] (%)
1	0.5	trace	5	4.0	52
2	1.5	25	***6***	***5.0***	***57***
3	2.0	38	7	6.0	57
4	3.0	47	8	8.0	57

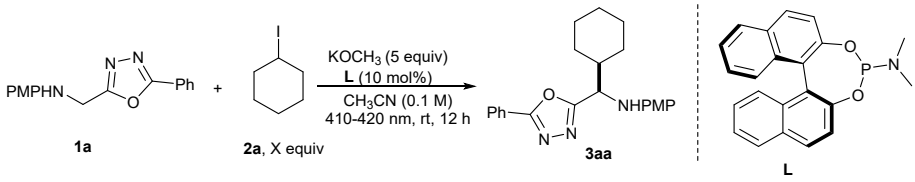
Table S5 L loading screening[a]



entry	X	yield[b] (%)	entry	X	yield[b] (%)
1	5	52	4	30	57
2	***10***	***57***	5	50	57
3	20	57			

[a] 0.05 mmol scale. [b] Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

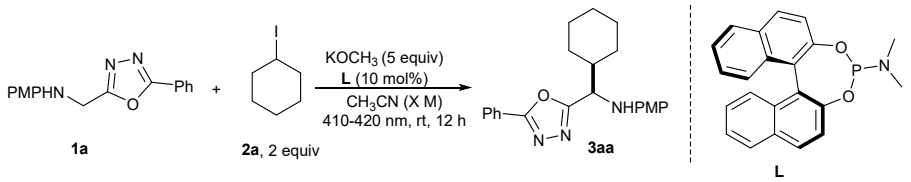
Table S6 Alkyl iodide loading screening [a]



entry	X	yield[b] (%)	entry	X	yield[b] (%)
1	1.5	33	***4***	***4.0***	***67***
2	2.0	57	5	5.0	67
3	3.0	60	6	6.0	57

[a] 0.05 mmol scale. [b] Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

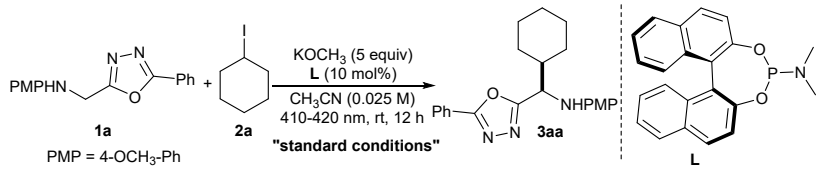
Table S7 Reaction concentration screening[a]

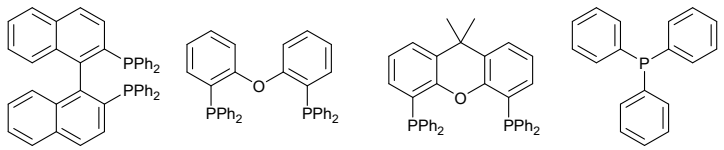


entry	X	yield[b] (%)	entry	X	yield[b] (%)
1	0.17	62	4	0.033	75
2	0.10	67	***5***	***0.025***	***85***
3	0.05	70			

[a] 0.05 mmol scale. [b] Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Table S8 Control experiments under standard reaction conditions[a]





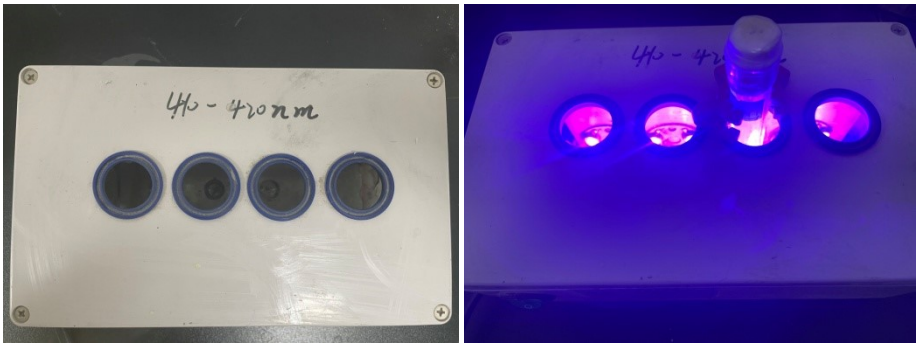
entry	change from the "standard conditions"	yield[b] (%)
1	**standard conditions**	**85**
2	without **L**	trace
3	without $KOCH_3$	N. D.
4	without **L** and $KOCH_3$	N. D.
5	without *hv*	N. D.
6	DIPEA instead of **L**	15
7	BINAP instead of **L**	30
8	DPEphos instead of **L**	46
9	Xantphos instead of **L**	53
10	PPh_3 instead of **L**	13
11	chlorocyclohexane instead of iodocyclohexane	N. D.
12	bromocyclohexane instead of iodocyclohexane	32
13	addition of TEMPO (3.0 equiv)	N. D.

[a] Conditions: **1a** (0.05 mmol), **2a** (0.2 mmol), **L** (10 mol%), base (0.25 mmol), solvent (2 mL), Ar, 12 h, rt, and under visible light (410-420 nm). [b] Yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

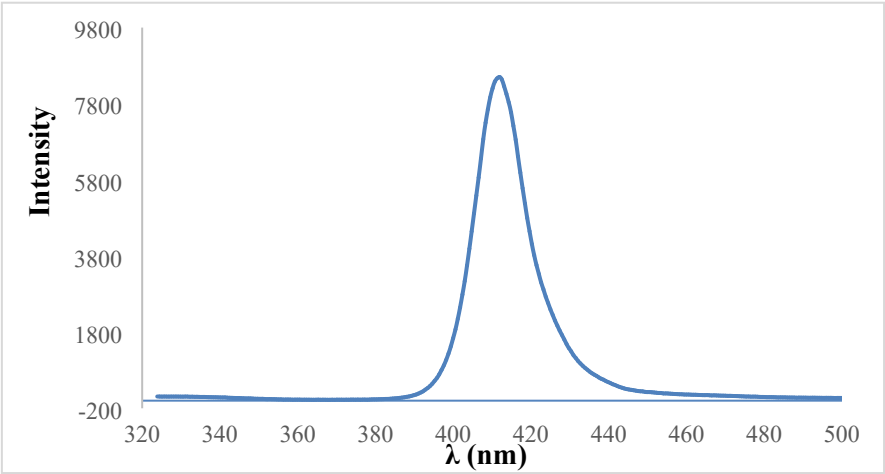
3.2 General procedure

General procedure: To an oven-dried 10 mL quartz test tube with a stirring bar was added derivative of 1,3,4-oxadiazoles amine (**1**, 0.1 mmol, 1.0 equiv), followed by the addition of (11b*S*)-*N*,*N*-dimethyldinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin-4-amine (**L**, 0.01 mmol, 0.1 equiv), iodoalkane (**2**, 0.4 mmol, 4.0 equiv) which added before air change if it is solid or injected after air change if it is liquid and $KOCH_3$ (0.5 mmol, 5.0 equiv). Then, air was withdrawn and backfilled with Ar (three times). CH_3CN (4 mL) was added. Thereafter, the test tube was transferred to a 410-420 nm light photoreactor, where it was irradiated for 12 h at room temperature. Then, the reaction was quenched with water (2 mL), extracted with ethyl acetate (3 x 10 mL), washed with brine (3 x 10 mL), dried over anhydrous sodium sulfate, concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate) to give the product **3**.

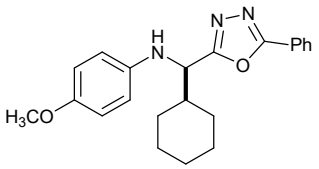
Reaction device diagram



We use a commercially available 24 W 410-420 nm purple LED lamp as the reaction light source. At ambient temperature, the sample is placed approximately 2 cm away from the lamp. The material of the irradiation vessel is quartz. We also measured the wavelength of the LED light by ourselves (recorded on an AVANTES® AvaSpec-ULS2048 spectrometer instrument). The result was shown as follow:

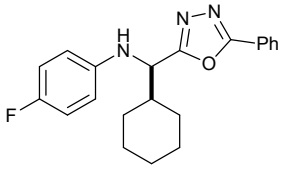


4. Characterization of products



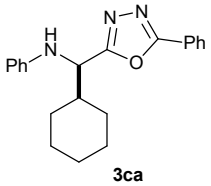
3aa

(*N*-(cyclohexyl(5-phenyl-1,3,4-oxadiazol-2-yl)methyl)-4-methoxyaniline (3aa): white solid, 59.6 mg, 82% yield. M. p. 150 - 155 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 15 Hz, 2H), 7.48 (d, *J* = 6.3 Hz, 3H), 6.71 (dd, *J* = 15.9 Hz, 9 Hz, 4H), 4.56 (t, *J* = 7.5 Hz, 1H), 3.95 (d, *J* = 9.3 Hz, 1H), 3.69 (s, 3H), 2.07 (d, *J* = 12 Hz, 1H), 1.99 – 1.94 (m, 1H), 1.82 – 1.74 (m, 2H), 1.68 (d, *J* = 9.9 Hz, 1H), 1.58 (d, *J* = 9.6 Hz, 1H), 1.31 – 1.21 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 164.7, 152.8, 140.5, 131.6, 128.9, 126.8, 123.8, 115.2, 114.8, 56.7, 55.6, 42.1, 29.6, 29.5, 26.0, 25.81, 25.75.
HRMS (ESI): $C_{22}H_{25}N_3NaO_2$ $[M+Na]^+$ calcd: 386.1844, found: 386.1838.



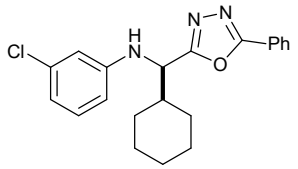
3ba

***N*-(cyclohexyl(5-phenyl-1,3,4-oxadiazol-2-yl)methyl)-4-fluoroaniline (3ba):** white solid, 51.3 mg, 73% yield. M. p. 155 - 157 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.2 Hz, 2H), 7.51 – 7.49 (m, 3H), 6.86 (t, *J* = 8.1 Hz, 2H), 6.68 – 6.64 (m, 2H), 4.56 (t, *J* = 8.1 Hz, 1H), 4.05 (d, *J* = 9.3 Hz, 1H), 2.06 (d, *J* = 10.8 Hz, 1H), 1.97 – 1.95 (m, 1H), 1.80 (t, *J* = 12 Hz, 2H), 1.65 (s, 1H), 1.58 (d, *J* = 10.5 Hz, 1H), 1.32 – 1.17 (m, 5H).
^{19}F NMR (282 MHz, $CDCl_3$): δ -126.34.
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 164.8, 142.8, 131.7, 129.0, 126.9, 123.8, 116.0, 115.7, 114.7, 56.4, 42.1, 29.6, 29.5, 26.1, 25.84, 25.79.
HRMS (ESI): $C_{21}H_{22}FN_3NaO$ $[M+Na]^+$ calcd: 374.1645, found: 374.1649.



3ca

***N*-(cyclohexyl(5-phenyl-1,3,4-oxadiazol-2-yl)methyl)aniline (3ca):** white solid, 46.7 mg, 70% yield. M. p. 185 - 190 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, *J* = 6.9 Hz, 2H), 7.50 – 7.48 (m, 3H), 7.16 (t, *J* = 7.5 Hz, 2H), 6.72 (d, *J* = 8.1 Hz, 3H), 4.65 (t, *J* = 7.8 Hz, 1H), 4.17 (d, *J* = 9 Hz, 1H), 2.07 (d, *J* = 12.3 Hz, 1H), 1.98 – 1.96 (m, 1H), 1.79 (t, *J* = 12.3 Hz, 2H), 1.69 (d, *J* = 9.9 Hz, 1H), 1.58 (d, *J* = 10.8 Hz, 1H), 1.32 – 1.12 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.8, 164.8, 146.5, 131.6, 129.4, 129.0, 126.9, 123.8, 118.6, 113.5, 55.5, 42.1, 29.7, 29.5, 26.1, 25.84, 25.78.
HRMS (ESI): $C_{21}H_{23}N_3NaO$ $[M+Na]^+$ calcd: 356.1739, found: 356.1735.



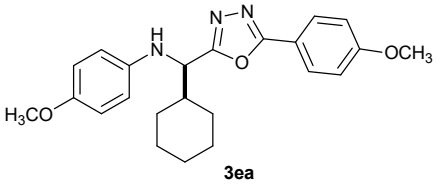
3da

3-chloro-*N*-(cyclohexyl(5-phenyl-1,3,4-oxadiazol-2-yl)methyl)aniline (3da): white solid, 52.1 mg, 71% yield. M. p. 195 - 200 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, *J* = 7.5 Hz, 2H), 7.52 – 7.49 (m, 3H), 7.06 (t, *J* = 7.8 Hz, 1H), 6.70 – 6.68 (m, 2H), 6.59 (d, *J* = 8.1 Hz, 1H), 4.61 (t, *J* = 8.1 Hz, 1H), 4.24 (d, *J* = 9 Hz, 1H), 2.05 – 1.96 (m, 2H), 1.84 – 1.75 (m, 2H), 1.70 (d, *J* = 9.9 Hz, 1H), 1.67 (s, 1H), 1.32 – 1.15 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 147.6, 135.1, 131.8, 130.4, 129.0, 126.9, 123.7, 118.6, 113.4, 111.6, 55.4, 42.1, 29.6, 29.5, 26.0, 25.81, 25.75.

HRMS (ESI): $C_{21}H_{23}ClN_3O$ $[M+H]^+$ calcd: 368.1530, found: 368.1527.



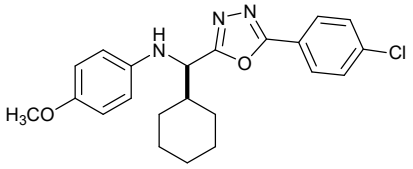
3ea

***N*-(cyclohexyl(5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl)methyl)-4-methoxyanili ne (3ea):** white solid, 62.9 mg, 80% yield. M. p. 128 - 133 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.71 (dd, *J* = 17.1 Hz, 8.7 Hz, 4H), 4.49 (d, *J* = 6.9 Hz, 1H), 3.94 (s, 1H), 3.86 (s, 3H), 3.70 (s, 3H), 2.07 (d, *J* = 12.3 Hz, 1H), 1.95 – 1.92 (m, 1H), 1.78 (t, *J* = 12 Hz, 2H), 1.68 (d, *J* = 9.3 Hz, 1H), 1.58 (d, *J* = 10.5 Hz, 1H), 1.31 – 1.15 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 164.6, 162.2, 152.8, 140.6, 128.6, 116.4, 115.2, 114.8, 114.3, 56.7, 55.6, 55.4, 42.1, 29.6, 29.5, 26.1, 25.9, 25.8.

HRMS (ESI): $C_{23}H_{27}N_3NaO_3$ $[M+Na]^+$ calcd: 416.1950, found: 416.1951.



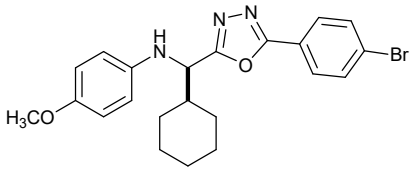
3fa

***N*-((5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl)(cyclohexyl)methyl)-4-methoxyanilin e (3fa):** white solid, 59.7 mg, 75% yield. M. p. 179 - 183 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 6.71 (dd, *J* = 19.8 Hz, 8.7 Hz, 4H), 4.55 (t, *J* = 7.2 Hz, 1H), 3.90 (d, *J* = 7.8 Hz, 1H), 3.70 (s, 3H), 2.06 (d, *J* = 12.3 Hz, 1H), 1.95 – 1.93 (m, 1H), 1.83 – 1.75 (m, 2H), 1.68 (s, 1H), 1.24 (d, *J* = 7.5 Hz, 1H), 1.66 – 1.15 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 167.3, 164.0, 152.9, 140.4, 137.9, 129.3, 128.1, 122.3, 115.2, 114.9, 56.8, 55.6, 42.2, 29.64, 29.55, 26.1, 25.9, 25.8.

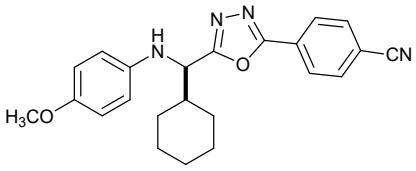
HRMS (ESI): $C_{22}H_{24}ClN_3NaO_2$ $[M+Na]^+$ calcd: 420.1455, found: 420.1444.



3ga

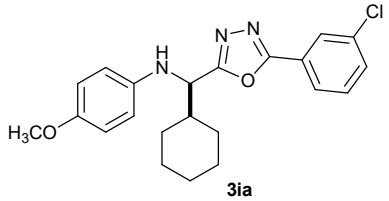
***N*-((5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl)(cyclohexyl)methyl)-4-methoxyanilin**

e (3ga): white solid, 69.9 mg, 79% yield. M. p. 180 - 185 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.1 Hz, 2H), 6.71 (dd, *J* = 20.1 Hz, 8.7 Hz, 4H), 4.55 (s, 1H), 3.90 (s, 1H), 3.70 (s, 3H), 2.06 (d, *J* = 10.8 Hz, 1H), 1.93 (s, 1H), 1.79 – 1.68 (m, 3H), 1.57 (d, *J* = 9.3 Hz, 1H), 1.23 (s, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.3, 164.0, 152.9, 140.4, 132.3, 128.3, 126.3, 122.8, 115.2, 114.9, 56.8, 55.6, 42.2, 29.6, 29.5, 26.1, 25.84, 25.79.
HRMS (ESI): $C_{22}H_{25}BrN_3O_2$ $[M+H]^+$ calcd: 442.1130, found: 442.1125.



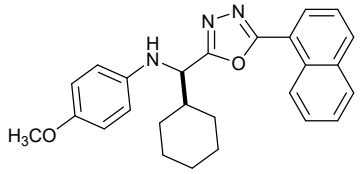
3ha

4-(5-(cyclohexyl((4-methoxyphenyl)amino)methyl)-1,3,4-oxadiazol-2-yl)benzonitrile (3ha): white solid, 66.0 mg, 85% yield. M. p. 150 - 154 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.1 Hz, 2H), 7.78 (d, *J* = 8.1 Hz, 2H), 6.71 (dd, *J* = 21 Hz, 8.7 Hz, 4H), 4.57 (s, 1H), 3.92 (s, 1H), 3.70 (s, 3H), 2.07 (d, *J* = 11.7 Hz, 1H), 1.97 – 1.94 (m, 1H), 1.80 (t, *J* = 12 Hz, 2H), 1.72 – 1.69 (m, 1H), 1.57 (d, *J* = 10.5 Hz, 1H), 1.32 – 1.16 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 168.1, 163.3, 153.0, 140.3, 132.8, 127.7, 127.3, 117.9, 115.14, 115.06, 114.9, 56.9, 55.6, 42.2, 29.63, 29.57, 26.0, 25.81, 25.77.
HRMS (ESI): $C_{23}H_{24}N_4NaO_2$ $[M+Na]^+$ calcd: 411.1797, found: 411.1795.



3ia

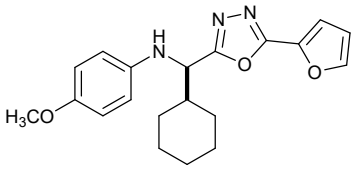
***N*-((5-(3-chlorophenyl)-1,3,4-oxadiazol-2-yl)(cyclohexyl)methyl)-4-methoxyanilin e (3ia):** white solid, 62.1 mg, 78% yield. M. p. 120 - 124 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.50 – 7.39 (m, 2H), 6.71 (dd, *J* = 19.2 Hz, 7.8 Hz, 4H), 4.55 (t, *J* = 7.2 Hz, 1H), 3.90 (d, *J* = 7.5 Hz, 1H), 3.71 (s, 3H), 2.07 (d, *J* = 12.3 Hz, 1H), 1.95 (d, *J* = 7.2 Hz, 1H), 1.83 – 1.75 (m, 2H), 1.68 (s, 1H), 1.56 (d, *J* = 10.5 Hz, 1H), 1.32 – 1.16 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.5, 163.6, 152.9, 140.4, 135.1, 131.6, 130.3, 126.8, 125.5, 125.0, 115.2, 114.9, 56.8, 55.6, 42.2, 29.7, 29.6, 26.1, 25.84, 25.79.
HRMS (ESI): $C_{22}H_{24}ClN_3NaO_2$ $[M+Na]^+$ calcd: 420.1455, found: 420.1450.



3ja

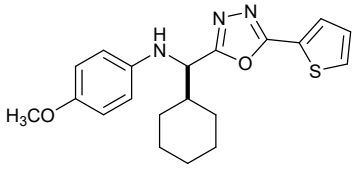
***N*-(cyclohexyl(5-(naphthalen-1-yl)-1,3,4-oxadiazol-2-yl)methyl)-4-methoxyaniline (3ja):** white solid, 66.2 mg, 80% yield. M. p. 105 - 108 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.05 (d, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 7.2 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.65 – 7.51 (m, 3H), 6.75 (dd, *J* = 11.7 Hz, 9.3 Hz, 4H), 4.63 (t, *J* = 6.9 Hz, 1H), 3.97 (d, *J* = 7.8 Hz, 1H), 3.70 (s, 3H), 2.10 (d, *J* = 11.7 Hz, 1H), 2.01 (d, *J* = 6.6 Hz, 1H), 1.80 – 1.77 (m, 2H), 1.72 – 1.67 (m, 2H), 1.34 – 1.17 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 164.7, 152.9, 140.6, 133.7, 132.5, 129.9, 128.6, 128.3, 128.0, 126.6, 126.1, 124.7, 120.5, 115.3, 114.9, 56.8, 55.6, 42.2, 29.7, 29.6, 26.1, 25.9, 25.8.
HRMS (ESI): $C_{26}H_{27}N_3NaO_2$ $[M+Na]^+$ calcd: 436.2001, found: 436.1994.



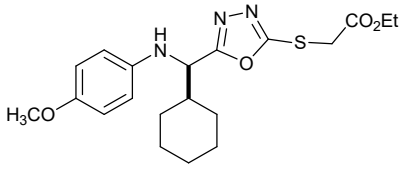
3ka

***N*-(cyclohexyl(5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)methyl)-4-methoxyaniline (3ka):** white solid, 57.3 mg, 81% yield. M. p. 138 - 142 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.13 (d, *J* = 3 Hz, 1H), 6.70 (dd, *J* = 21.6 Hz, 8.4 Hz, 4H), 6.57 (d, *J* = 1.5 Hz, 1H), 4.54 (t, *J* = 7.5 Hz, 1H), 3.90 (t, *J* = 7.2 Hz, 1H), 3.71 (s, 3H), 2.07 (d, *J* = 12.6 Hz, 1H), 1.94 – 1.92 (m, 1H), 1.82 – 1.74 (m, 2H), 1.70 – 1.67 (m, 1H), 1.54 (d, *J* = 10.8 Hz, 1H), 1.31 – 1.14 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.4, 157.6, 152.9, 145.5, 140.4, 139.4, 115.1, 114.9, 114.0, 112.1, 56.6, 55.7, 42.1, 29.7, 29.6, 26.1, 25.83, 25.77.
HRMS (ESI): $C_{20}H_{23}N_3NaO_3$ $[M+Na]^+$ calcd: 376.1637, found: 376.1633.



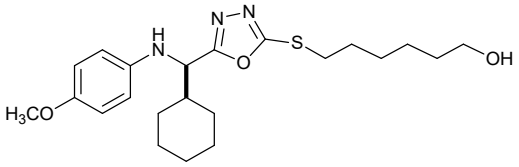
3la

***N*-(cyclohexyl(5-(thiophen-2-yl)-1,3,4-oxadiazol-2-yl)methyl)-4-methoxyaniline (3la):** white solid, 61.3 mg, 83% yield. M. p. 137 - 141 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, *J* = 3.3 Hz, 1H), 7.52 (d, *J* = 4.8 Hz, 1H), 7.14 (t, *J* = 3.9 Hz, 1H), 6.71 (dd, *J* = 19.8 Hz, 8.7 Hz, 4H), 4.53 (s, 1H), 3.89 (s, 1H), 3.71 (s, 3H), 2.07 (d, *J* = 11.4 Hz, 1H), 1.94 – 1.92 (m, 1H), 1.83 – 1.75 (m, 2H), 1.71 – 1.64 (m, 1H), 1.57 (d, *J* = 10.8 Hz, 1H), 1.31 – 1.15 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 161.0, 152.9, 140.5, 130.0, 129.7, 128.0, 125.2, 115.2, 114.9, 56.7, 55.7, 42.1, 29.7, 29.6, 26.1, 25.9, 25.8.
HRMS (ESI): $C_{20}H_{23}N_3NaO_2S$ $[M+Na]^+$ calcd: 392.1409, found: 392.1407.



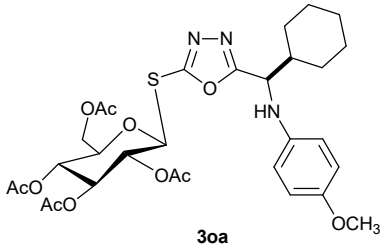
3ma

ethyl-2-((5-(cyclohexyl((4-methoxyphenyl)amino)methyl)-1,3,4-oxadiazol-2-yl)thio)acetate (3ma): yellow oil, 62.4 mg, 77% yield.
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.74 (d, *J* = 7.8 Hz, 2H), 6.63 (d, *J* = 7.8 Hz, 2H), 4.44 (s, 1H), 4.21 (dd, *J* = 14.1 Hz, 6.9 Hz, 2H), 4.01 (s, 2H), 3.79 (s, 1H), 3.72 (s, 3H), 2.01 (d, *J* = 11.7 Hz, 1H), 1.82 – 1.70 (m, 3H), 1.67 (s, 1H), 1.50 (d, *J* = 12 Hz, 1H), 1.28 – 1.10 (m, 8H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 168.4, 167.4, 163.0, 152.9, 140.3, 115.1, 114.9, 62.3, 56.7, 55.7, 42.0, 34.3, 29.6, 29.5, 26.0, 25.80, 25.76, 14.0.
HRMS (ESI): $C_{20}H_{27}N_3NaO_4S$ $[M+Na]^+$ calcd: 428.1620, found: 428.1624.



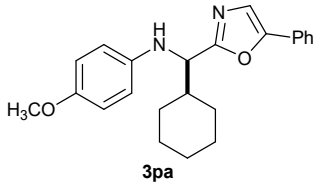
3na

6-((5-(cyclohexyl((4-methoxyphenyl)amino)methyl)-1,3,4-oxadiazol-2-yl)thio)hexan-1-ol (3na): yellow oil, 52.9 mg, 63% yield.
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.74 (d, *J* = 7.5 Hz, 2H), 6.64 (d, *J* = 7.5 Hz, 2H), 4.44 (t, *J* = 6.9 Hz, 1H), 3.80 (d, *J* = 8.7 Hz, 1H), 3.72 (s, 3H), 3.15 (s, 2H), 3.18 (t, *J* = 7.2 Hz, 2H), 2.02 (d, *J* = 12.3 Hz, 1H), 1.78 – 1.73 (m, 7H), 1.56 – 1.53 (m, 3H), 1.47 – 1.41 (m, 4H), 1.25 – 1.11 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.9, 164.5, 152.9, 140.5, 115.2, 114.9, 62.7, 56.7, 55.7, 42.0, 32.5, 29.6, 29.5, 29.1, 28.3, 26.1, 25.84, 25.79, 25.1.
HRMS (ESI): $C_{22}H_{33}N_3NaO_3S$ $[M+Na]^+$ calcd: 442.2140, found: 442.2145.



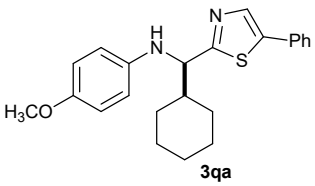
3oa

(2*R*,3*R*,5*R*,6*S*)-2-(acetoxymethyl)-6-((5-((*R*)-cyclohexyl((4-methoxyphenyl)amino)methyl)-1,3,4-oxadiazol-2-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (3oa): yellow solid, 92.3 mg, 71% yield. M. p. 122 - 125 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.75 (d, *J* = 8.4 Hz, 2H), 6.64 (d, *J* = 8.7 Hz, 2H), 5.38 (t, *J* = 10.5 Hz, 1H), 5.27 (t, *J* = 9 Hz, 1H), 5.18 – 5.08 (m, 2H), 4.47 (s, 1H), 4.30 – 4.22 (m, 1H), 4.05 (d, *J* = 12.3 Hz, 1H), 3.83 – 3.76 (m, 2H), 3.72 (s, 3H), 2.05 – 2.02 (m, 13H), 1.82 – 1.75 (m, 3H), 1.68 (s, 1H), 1.52 (d, *J* = 11.4 Hz, 1H), 1.26 – 1.12 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.0, 169.4, 169.3, 169.1, 153.0, 152.9, 140.2, 115.1, 115.0, 114.8, 83.2, 73.53, 73.46, 69.6, 69.5, 67.6, 61.3, 55.6, 41.9, 29.6, 29.5, 26.0, 25.7, 20.6, 20.5.
HRMS (ESI): $C_{30}H_{40}N_3O_{11}S$ $[M+H]^+$ calcd: 650.2384, found: 650.2366.



3pa

***N*-(cyclohexyl(5-phenyloxazol-2-yl)methyl)-4-methoxyaniline (3pa):** white solid, 58.0 mg, 80% yield. M. p. 160 - 165 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (d, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 2H), 7.33 – 7.28 (m, 1H), 7.23 (s, 1H), 6.70 (dd, *J* = 22.5 Hz, 8.4 Hz, 4H), 4.38 (t, *J* = 6.6 Hz, 1H), 3.99 (d, *J* = 7.5 Hz, 1H), 3.70 (s, 3H), 2.03 (d, *J* = 11.7 Hz, 1H), 1.90 (s, 1H), 1.81 – 1.66 (m, 3H), 1.55 (d, *J* = 11.1 Hz, 1H), 1.30 – 1.10 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 152.5, 151.0, 141.3, 128.8, 128.3, 128.0, 124.1, 121.6, 115.1, 114.7, 58.5, 55.7, 42.9, 29.8, 29.5, 26.2, 26.01, 25.96.
HRMS (ESI): $C_{23}H_{26}N_2NaO_2$ $[M+Na]^+$ calcd: 385.1892, found: 385.1895.



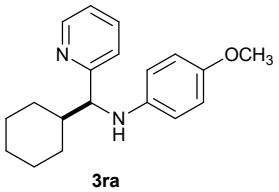
3qa

***N*-(cyclohexyl(5-phenylthiazol-2-yl)methyl)-4-methoxyaniline (3qa):** yellow solid, 57.5 mg, 76% yield. M. p. 107 - 110 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 6.6 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 2H), 6.60 (d, *J* = 7.8 Hz, 2H), 4.44 (s, 1H), 4.07 (s, 1H), 3.71 (s, 3H), 1.91 – 1.88 (m, 2H), 1.78 (s, 2H), 1.70 – 1.64 (m, 2H), 1.30 – 1.19 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 175.4, 152.5, 141.3, 138.8, 137.8, 131.6, 128.9, 127.9, 126.5, 114.8, 114.6, 62.8, 55.6, 44.4, 29.9, 28.9, 26.23, 26.15.

HRMS (ESI): $C_{23}H_{27}N_2OS$ $[M+H]^+$ calcd: 379.1844, found: 379.1836.



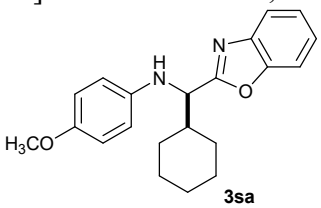
3ra

***N*-(cyclohexyl(pyridin-2-yl)methyl)-4-methoxyaniline (3ra):** yellow oil, 41.5 mg, 70% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.58 (d, *J* = 4.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 5.7 Hz, 1H), 6.68 (d, *J* = 8.7 Hz, 2H), 6.51 (d, *J* = 8.1 Hz, 2H), 4.27 (s, 1H), 4.19 (d, *J* = 6 Hz, 1H), 3.68 (s, 3H), 1.86 (d, *J* = 11.1 Hz, 2H), 1.77 – 1.67 (m, 3H), 1.49 (d, *J* = 12.6 Hz, 1H), 1.25 – 1.07 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 162.3, 151.8, 149.2, 142.1, 136.0, 122.2, 121.8, 114.7, 114.6, 65.3, 55.7, 43.8, 30.3, 29.1, 26.3.

HRMS (ESI): $C_{19}H_{25}N_2O$ $[M+H]^+$ calcd: 297.1967, found: 297.1958.



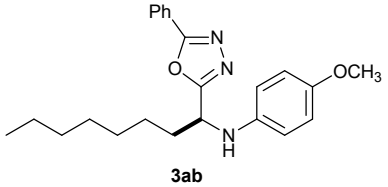
3sa

***N*-(benzo[d]oxazol-2-yl(cyclohexyl)methyl)-4-methoxyaniline (3sa):** yellow solid, 43.7 mg, 65% yield. M. p. 105 - 110 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 – 7.66 (m, 1H), 7.50 – 7.47 (m, 1H), 7.31 – 7.26 (m, 2H), 6.70 (dd, *J* = 15 Hz, 9 Hz, 4H), 4.48 (d, *J* = 5.4 Hz, 1H), 4.06 (s, 1H), 3.69 (s, 3H), 2.06 (d, *J* = 12.3 Hz, 1H), 1.98 – 1.96 (m, 1H), 1.81 –1.65 (m, 3H), 1.53 (d, *J* = 9.6 Hz, 1H), 1.26 – 1.17 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 152.6, 150.6, 141.0, 140.8, 124.7, 124.2, 119.9, 115.0, 114.8, 110.6, 59.0, 55.6, 42.7, 29.8, 29.6, 26.2, 26.0, 25.9.

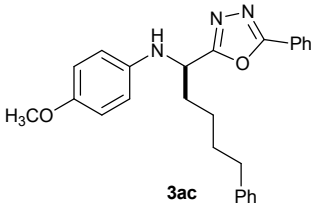
HRMS (ESI): $C_{21}H_{25}N_2O_2$ $[M+H]^+$ calcd: 337.1916, found: 337.1904.



3ab

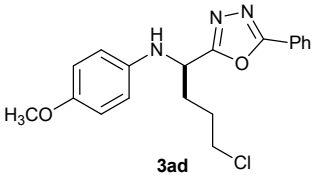
4-methoxy-*N*-(1-(5-phenyl-1,3,4-oxadiazol-2-yl)octyl)aniline (3ab): white solid, 49.3 mg, 65% yield. M. p. 96 - 100 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 6.9 Hz, 2H), 7.52 – 7.46 (m, 3H), 6.73 (dd, *J* = 17.1 Hz, 8.7 Hz, 4H), 4.75 (s, 1H), 3.85 (s, 1H), 3.71 (s, 3H), 2.02 (dd, *J* = 14.1 Hz, 6.9 Hz, 2H), 1.35 – 1.26 (m, 10H), 0.86 (t, *J* = 5.4 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.6, 164.8, 153.0, 140.1, 131.7, 129.0, 126.9, 123.8, 115.2, 114.9, 55.6, 51.4, 34.5, 31.7, 29.1, 29.0, 25.8, 22.6, 14.0.
HRMS (ESI): $C_{23}H_{30}N_3O_2$ $[M+H]^+$ calcd: 380.2338, found: 380.2323.



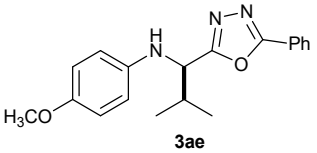
3ac

4-methoxy-*N*-(5-phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)pentyl)aniline (3ac): white solid, 57.9 mg, 70% yield. M. p. 100 - 105 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.55 – 7.48 (m, 3H), 7.28 – 7.23 (m, 2H), 7.16 (t, *J* = 7.2 Hz, 3H), 6.72 (dd, *J* = 20.4 Hz, 8.7 Hz, 4H), 4.75 (t, *J* = 6.6 Hz, 1H), 3.89 (s, 1H), 3.71 (s, 3H), 2.62 (t, *J* = 7.2 Hz, 2H), 2.05 (dd, *J* = 14.7 Hz, 7.2 Hz, 2H), 1.72 – 1.43 (m, 4H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.5, 164.8, 153.0, 142.0, 140.0, 131.7, 129.0, 128.32, 128.30, 126.9, 125.8, 123.8, 115.3, 114.9, 55.6, 51.4, 35.6, 34.3, 30.9, 25.4.
HRMS (ESI): $C_{26}H_{28}N_3O_2$ $[M+H]^+$ calcd: 414.2182, found: 414.2171.



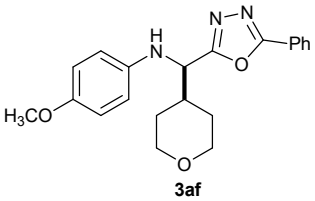
3ad

***N*-(4-chloro-1-(5-phenyl-1,3,4-oxadiazol-2-yl)butyl)-4-methoxyaniline (3ad):** yellow oil, 36.5 mg, 51% yield.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.50 – 7.47 (m, 3H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 5.07 (d, *J* = 6.9 Hz, 1H), 3.73 – 3.68 (m, 5H), 3.38 (dd, *J* = 15 Hz, 8.1 Hz, 1H), 2.45 – 2.32 (m, 3H), 2.21 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 168.1, 164.9, 151.8, 141.2, 131.6, 128.9, 126.9, 123.8, 114.9, 113.3, 55.8, 54.8, 49.0, 31.8, 24.2.
HRMS (ESI): $C_{19}H_{21}ClN_3O_2$ $[M+H]^+$ calcd: 358.1322, found: 358.1319.



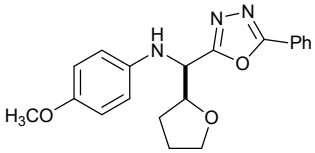
3ae

4-methoxy-*N*-(2-methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propyl)aniline (3ae): white solid, 53.7 mg, 83% yield. M. p. 143 - 147 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 6.6 Hz, 2H), 7.49 – 7.47 (m, 3H), 6.73 (dd, *J* = 13.8 Hz, 7.5 Hz, 4H), 4.53 (t, *J* = 8.1 Hz, 1H), 3.94 (d, *J* = 8.7 Hz, 1H), 3.70 (s, 3H), 2.33 – 2.24 (m, 1H), 1.16 (d, *J* = 6.6 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 164.7, 152.9, 140.4, 131.6, 128.9, 126.8, 123.8, 115.3, 114.8, 57.5, 55.6, 23.6, 19.1, 19.0.
HRMS (ESI): $C_{19}H_{22}N_3O_2$ $[M+H]^+$ calcd: 324.1712, found: 324.1705.



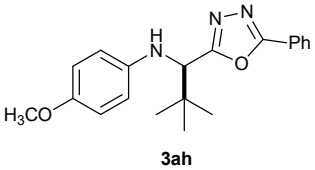
3af

4-methoxy-*N*-((5-phenyl-1,3,4-oxadiazol-2-yl)(tetrahydro-2H-pyran-4-yl)methyl) aniline (3af): white solid, 60.7 mg, 83% yield. M. p. 170 - 173 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.5 Hz, 2H), 7.51 – 7.49 (m, 3H), 6.73 (dd, *J* = 16.5 Hz, 8.7 Hz, 4H), 4.58 (t, *J* = 7.2 Hz, 1H), 4.07 – 3.97 (m, 2H), 3.88 (d, *J* = 9.3 Hz, 1H), 3.71 (s, 3H), 3.41 (dd, *J* = 24 Hz, 12 Hz, 2H), 2.12 – 2.18 (m, 1H), 2.00 (d, *J* = 12.6 Hz, 1H), 1.63 – 1.55 (m, 2H), 1.45 (d, *J* = 13.2 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.4, 164.9, 153.2, 140.1, 131.8, 129.0, 126.9, 123.7, 115.5, 115.0, 67.6, 67.4, 56.6, 55.7, 39.6, 29.8, 29.5.
HRMS (ESI): $C_{21}H_{23}N_3NaO_3$ $[M+Na]^+$ calcd: 388.1637, found: 388.1634.



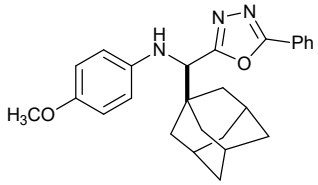
3ag

4-methoxy-*N*-((5-phenyl-1,3,4-oxadiazol-2-yl)(tetrahydrofuran-2-yl)methyl)anilin e (3ag): yellow solid, 59.7 mg, 85% yield, 1:1 d.r. M. p. 95 - 100 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.2 Hz, 2H), 7.49 – 7.26 (m, 3H), 6.77 – 6.70 (m, 4H), 5.00 – 4.90 (m, 1H), 4.60 – 4.50 (m, 1H), 4.15 – 3.94 (m, 1H), 3.91 – 3.86 (m, 1H), 3.80 – 3.74 (m, 1H), 3.71 (s, 3H), 2.31 – 2.19 (m, 1H), 2.04 (s, 1H), 1.91 – 1.84 (m, 2H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 167.8, 167.7, 152.9, 152.8, 140.4, 131.6, 128.9, 126.9, 126.8, 123.8, 115.2, 114.8, 68.1, 67.9, 55.6, 50.5, 49.7, 39.8, 39.6, 31.9, 31.5, 25.5, 25.4.
HRMS (ESI): $C_{20}H_{21}N_3NaO_3$ $[M+Na]^+$ calcd: 374.1478, found: 374.1475.



3ah

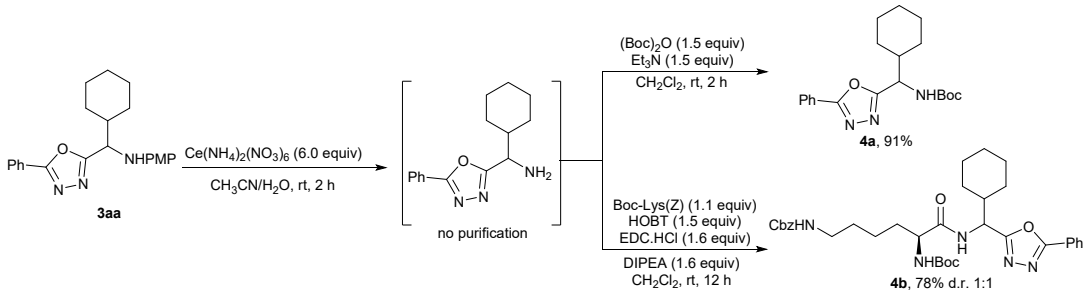
***N*-(2,2-dimethyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propyl)-4-methoxyaniline (3ah):** white solid, 53.9 mg, 80% yield. M. p. 189 -193 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.2 Hz, 2H), 7.49 – 7.47 (m, 3H), 6.71 (dd, *J* = 11.7 Hz, 9.6 Hz, 4H), 4.48 (d, *J* = 9.9 Hz, 1H), 3.98 (d, *J* = 10.2 Hz, 1H), 3.70 (s, 3H), 1.15 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.8, 164.6, 153.0, 140.7, 131.6, 129.0, 126.8, 123.8, 115.6, 114.8, 60.9, 55.6, 35.2, 26.6.
HRMS (ESI): $C_{20}H_{24}N_3O_2$ $[M+H]^+$ calcd: 338.1869, found: 338.1866.



3ai

***N*-((1*s*,3*s*)-adamantan-1-yl(5-phenyl-1,3,4-oxadiazol-2-yl)methyl)-4-methoxyanil ine (3ai):** white solid, 54.8 mg, 66% yield. M. p. 145 -150 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 – 7.99 (m, 2H), 7.51 – 7.48 (m, 3H), 6.73 (dd, *J* = 9.3 Hz, 3 Hz, 4H), 4.34 (s, 1H), 4.02 (s, 1H), 3.70 (s, 3H), 2.05 (s, 3H), 1.90 (d, *J* = 12.3 Hz, 3H), 1.76 – 1.57 (m, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 164.6, 152.9, 140.9, 131.6, 129.0, 126.8, 123.9, 115.6, 114.8, 61.7, 55.6, 38.9, 37.0, 36.7, 28.2.
HRMS (ESI): $C_{26}H_{30}N_3O_2$ $[M+H]^+$ calcd: 416.2338, found: 416.2329.

5. Synthetic applications

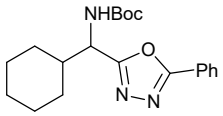


Step 1: A mixture of **3aa** (0.44 mmol, 159.8 mg) and $Ce(NH_4)_2(NO_3)_6$ (cerium ammonium, 2.82 mmol, 1.54 g) in 5:2 solution of H_2O/CH_3CN (3.0 mL) was stirred at 0 °C for 2 h. The mixture was modulated to alkalescence with saturated aqueous sodium carbonate. Then the mixture was extracted by CH_2Cl_2 for three times, washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was not purified and was directly used for the next steps. (crude yield 91%)

Synthesis of 4a: The residue (0.2 mmol, 51.4 mg) was dissolved in 4 mL CH_2Cl_2. Di-tert-butyl dicarbonate (0.3 mmol, 65.5 mg) and Et_3N (0.3 mmol, 30.4 mg) were then added dropwise. The mixture was allowed to stir for 2.5 h at room temperature. 20 mL CH_2Cl_2 was added and the mixture was washed with H_2O (20 mL) and brine (20 mL). The resulting solution was dried over Na_2SO_4 and evaporated in vacuo. The product **4a** was purified by silica gel column chromatography using hexane-EtOAc as eluents.

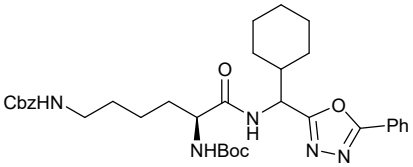
Synthesis of 4b: The residue (0.2 mmol, 51.4 mg) was dissolved in 0.5 mL CH_2Cl_2, followed the 1-hydroxybenzotriazole (HOBT 0.3 mmol, 37.0 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl 0.32 mmol, 61.3 mg), (*S*)-6-(((benzyloxy)carbonyl)amino)-2-((tert-butoxycarbonyl)amino)hexanoic acid (0.22 mmol, 83.7 mg) and DIPEA (0.32 mmol, 37.8 mg) were added. The mixture was stirred for 12 h. After completion of the reaction monitored by TLC, water (2 mL) was added to quench the reaction and concentrated under reduced pressure. The resultant residue was dissolved with ethyl acetate (10 mL), washed with 1M HCl (5 mL), and brine (5 mL x 2). The combined organic layers were dried over with Na_2SO_4, filtered and concentrated under reduced

pressure to afford the crude residue. The **4b** was purified by silica gel column chromatography using hexane-EtOAc as eluents.



4a

tert-butyl (cyclohexyl(5-phenyl-1,3,4-oxadiazol-2-yl)methyl)carbamate (4a): white solid, 65.0 mg, 91% yield. M. p. 175 -179 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.2 Hz, 2H), 7.53 – 7.51 (m, 3H), 5.22 (d, *J* = 8.7 Hz, 1H), 4.97 (t, *J* = 6 Hz, 1H), 1.89 (s, 1H), 1.78 (d, *J* = 8.7 Hz, 3H), 1.67 (d, *J* = 11.1 Hz, 2H), 1.45 (s, 9H), 1.26 – 1.13 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 164.8, 155.3, 131.7, 129.0, 126.9, 123.7, 80.3, 52.1, 42.0, 29.3, 28.3, 25.9, 25.8.
HRMS (ESI): $C_{20}H_{27}N_3NaO_3$ $[M+Na]^+$ calcd: 380.1950, found: 380.1954.

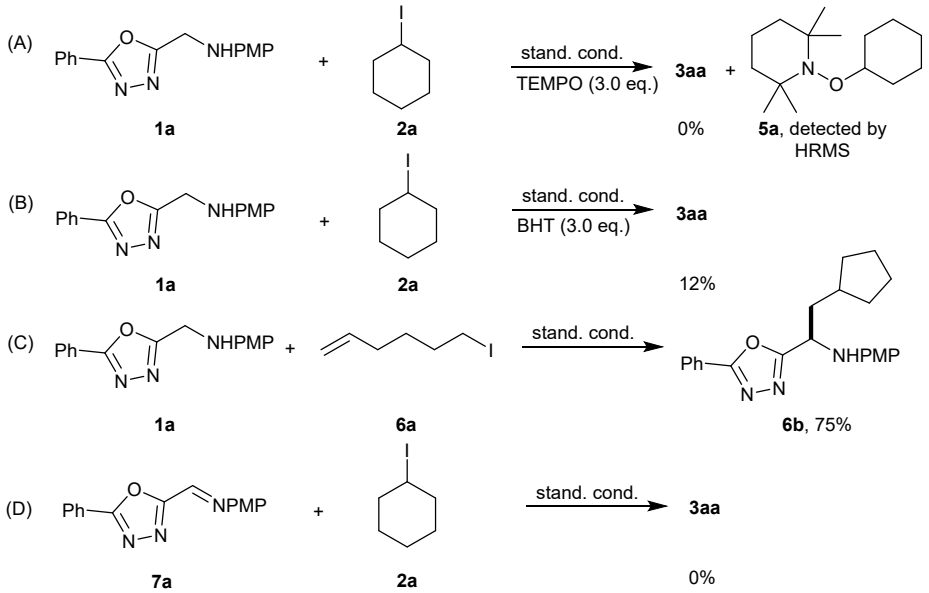


4b

benzyl tert-butyl ((5*S*)-6-((cyclohexyl(5-phenyl-1,3,4-oxadiazol-2-yl)methyl)amino)-6-oxohexane-1,5-diyl)dicarbamate (4b): yellow oil, 96.6 mg, 78% yield. 1:1 d.r.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (d, *J* = 6.9 Hz, 2H), 7.51 – 7.49 (m, 3H), 7.34 (s, 5H), 7.15 – 7.03 (m, 1H), 5.28 (t, *J* = 7.5 Hz, 1H), 5.18 (d, *J* = 6.9 Hz, 1H), 5.09 (d, *J* = 5.7 Hz, 2H), 4.98 – 4.92 (m, 1H), 4.13 (s, 1H), 3.19 (s, 2H) 1.94 – 1.74 (m, 6H), 1.66 (d, *J* = 11.4 Hz, 2H), 1.51 (d, *J* = 5.7 Hz, 2H), 1.43 (s, 11H), 1.26 – 1.14 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 165.7, 164.8, 156.6, 155.9, 136.6, 131.8, 129.0, 128.0, 126.9, 123.6, 122.3, 80.2, 66.5, 54.2, 53.4, 50.4, 41.6, 40.3, 31.3, 29.6, 29.2, 28.3, 25.8, 25.7, 22.5.
HRMS (ESI): $C_{34}H_{45}N_5NaO_6$ $[M+Na]^+$ calcd: 642.3268, found: 642.3262.

6. The mechanistic studies

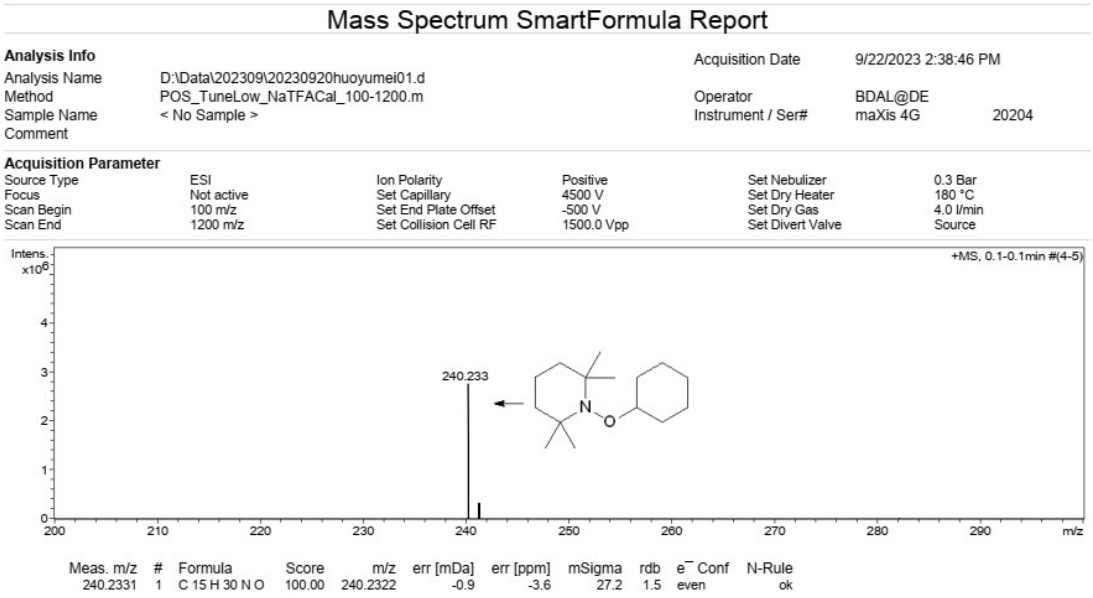
6.1 Control experiments



NOTE: To an oven-dried 10 mL quartz test tube with a stirring bar was added **1a** (0.1 mmol, 28.4 mg), **L** (0.01 mmol, 3.6 mg), $KOCH_3$ (0.5 mmol, 35.1 mg) and TEMPO (0.3 mmol, 46.9 mg). Then, air was withdrawn and backfilled with Ar (three times). CH_3CN (4 mL) and iodocyclohexane **2a** (0.4 mmol, 33.6 mg) were added and the mixture were transferred to a violet LED photoreactor (410-420 nm), where it was irradiated for 12 h. Then, the reaction was quenched with water (3 mL), extracted with ethyl acetate, washed with brine, dried over anhydrous sodium sulfate, concentrated in vacuo, and the yields of **3aa** were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. In the presence of TEMPO, the reaction was completely suppressed and the yield of **3aa** was 0%, and the radical trapping intermediate **5a** detected by HRMS (A), which revealed the involvement of a radical intermediate during the reaction process. Addition of BHT led to a dramatic decrease of the yield (B, 12%). To ensure the radical pathway, We also conducted a radical clock experiment using 6-iodohex-1-ene (**6a**) as the reaction partner. The ring-closing product **6b** was obtained (C)

Furthermore, we synthesized (*E*)-4-methoxy-*N*-((5-phenyl-1,3,4-oxadiazol-2-yl)me thylene)aniline (**7a**) was used instead of 4-methoxy-*N*-((5-phenyl-1,3,4-oxadiazol-2-yl)methyl)aniline (**1a**), no **3aa** was detected, which indicated that **7a** was not formed as the intermediate for this transformation (D).

***N*-(2-cyclopentyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)ethyl)-4-methoxyaniline (6b):** white solid, 27.3 mg, 75% yield. M. p. 116 - 120 ^{o}C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 6.9 Hz, 2H), 7.50 – 7.47 (m, 3H), 6.73 (dd, *J* = 14.7 Hz, 8.1 Hz, 4H), 4.78 (d, *J* = 5.4 Hz, 1H), 3.84 (s, 1H), 3.71 (s, 3H), 2.05 (t, *J* = 6.3 Hz, 2H), 1.92 – 1.90 (m, 2H), 1.77 – 1.72 (m, 1H), 1.63 – 1.51 (m, 4H), 1.26 – 1.15 (m, 2H).**^{13}C NMR** (75 MHz, $CDCl_3$): δ 167.7, 164.8, 152.9, 140.1, 131.6, 129.0, 126.9, 123.9, 115.2, 114.9, 55.6, 50.9, 40.8, 36.7, 32.7, 32.5, 25.0, 24.9. **HRMS (ESI)**: $C_{22}H_{25}N_3NaO_2$ $[M+Na]^+$ calcd: 386.1844, found: 386.1841.



6.2 UV-Vis absorption

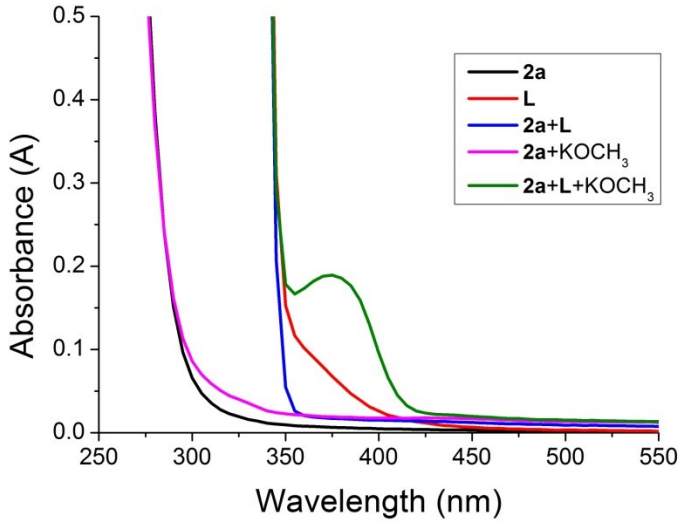
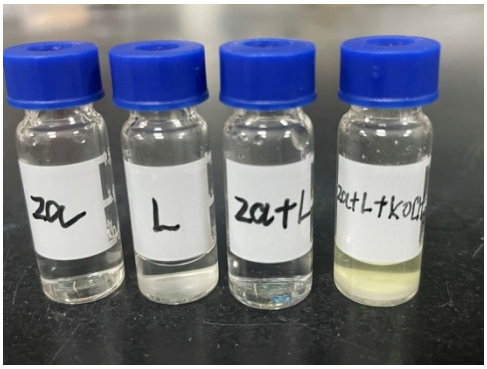


Figure S1. UV-Vis absorption spectra of substrate **2a** (1×10^{-3} M), **L** (1×10^{-3} M), [**2a**+**L**] (1×10^{-3} M), [**2a**+$KOCH_3$] (1×10^{-3} M) and [**2a**+**L**+$KOCH_3$] (1×10^{-3} M) in CH_3CN.



NOTE: In the UV-Vis absorption studies, Combined [**2a**+**L**+$KOCH_3$], respectively, in CH_3CN the optical absorption spectrum showed a bathochromic shift to the visible

spectral region, diagnostic of an EDA complex. And at this concentration, a solution containing this EDA complex is visibly yellow color.

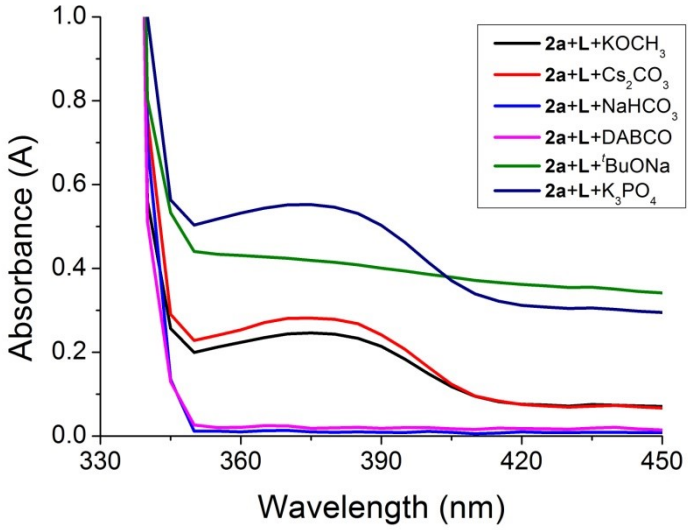
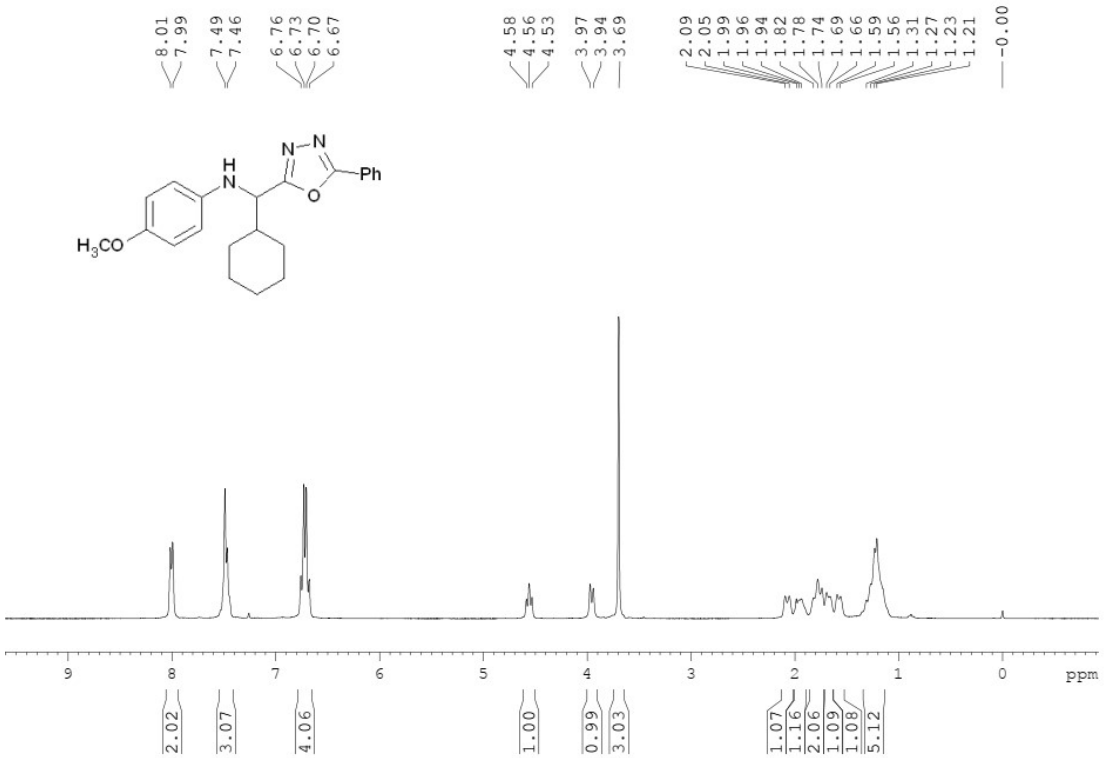


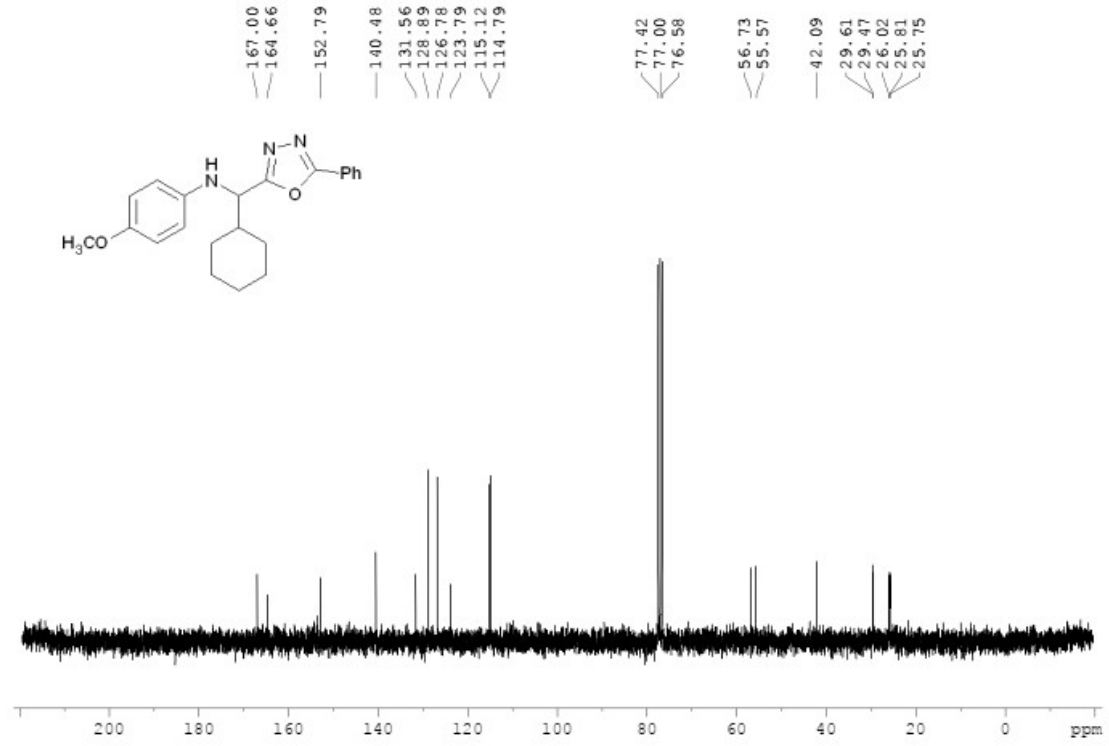
Figure S2. UV-Vis absorption spectra of substrate [**2a**+**L**+$KOCH_3$] (1×10^{-3} M), [**2a**+**L**+Cs_2CO_3] (1×10^{-3} M), [**2a**+**L**+$NaHCO_3$] (1×10^{-3} M), [**2a**+**L**+DABCO] (1×10^{-3} M), [**2a**+**L**+^{t}BuONa] (1×10^{-3} M) and [**2a**+**L**+K_3PO_4] (1×10^{-3} M) in CH_3CN.

NOTE: We found that the absorption was significantly different with the addition of different bases, and it is worth noting that the addition of bases that did not promote the reaction, such as $NaHCO_3$ and DABCO, did not change the absorption. Based on these experimental results, we hypothesized that the base might play two roles in the reaction transformations process: (1) promoting the formation of EDA complexes between iodoalkanes and organophosphine; (2) providing basic conditions to facilitate the deprotonation of heterocyclic amines.

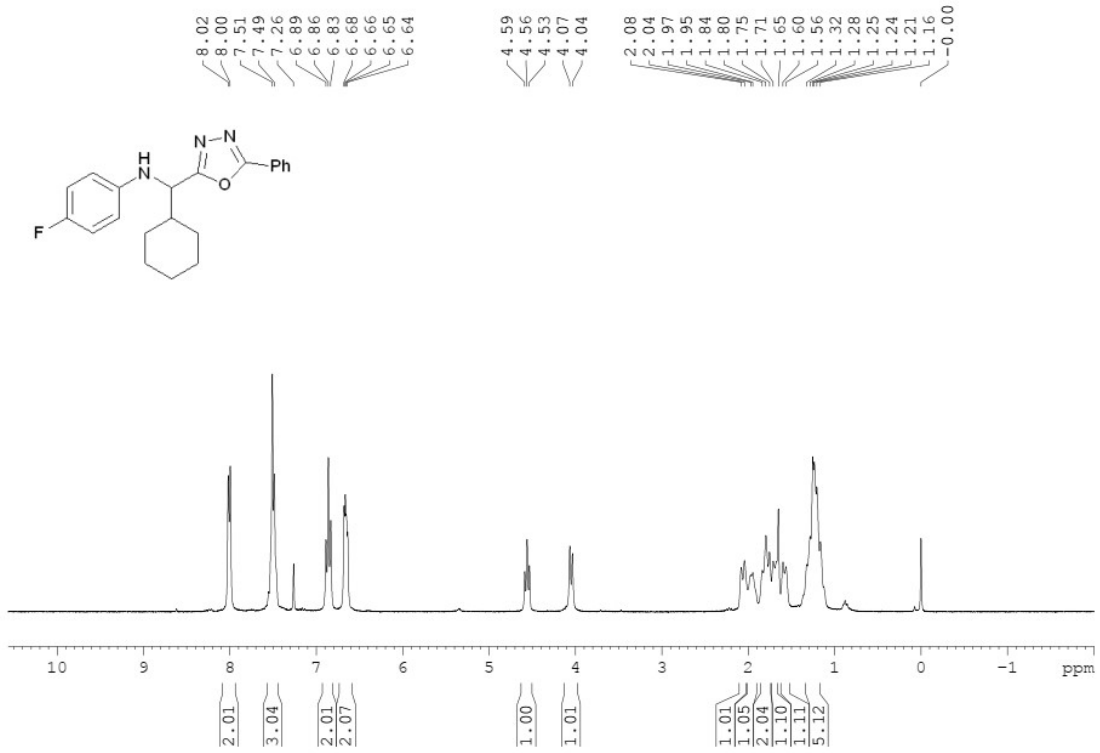
7. NMR spectra



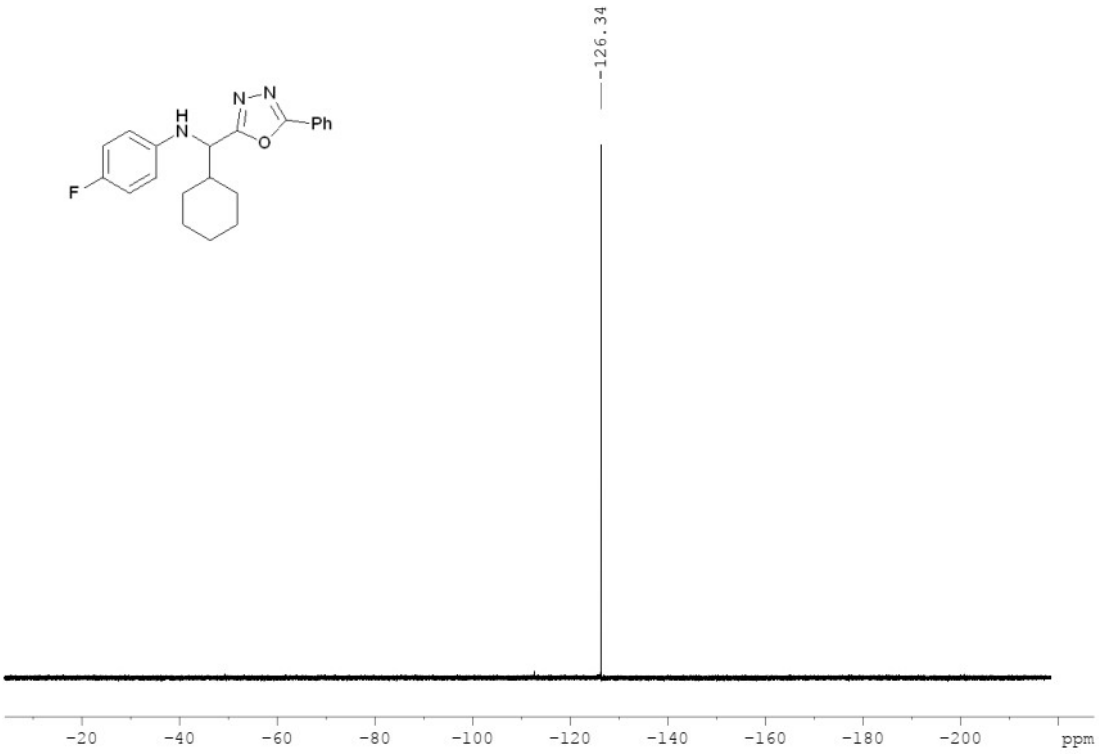
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3aa**.



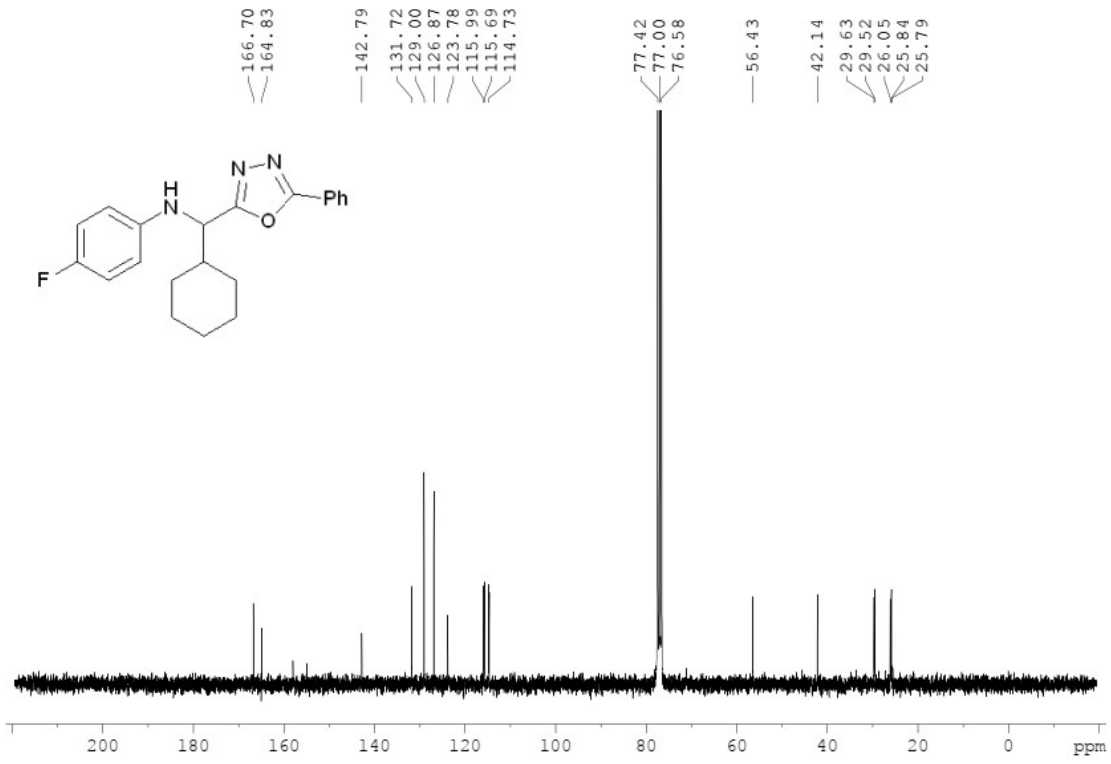
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3aa**.



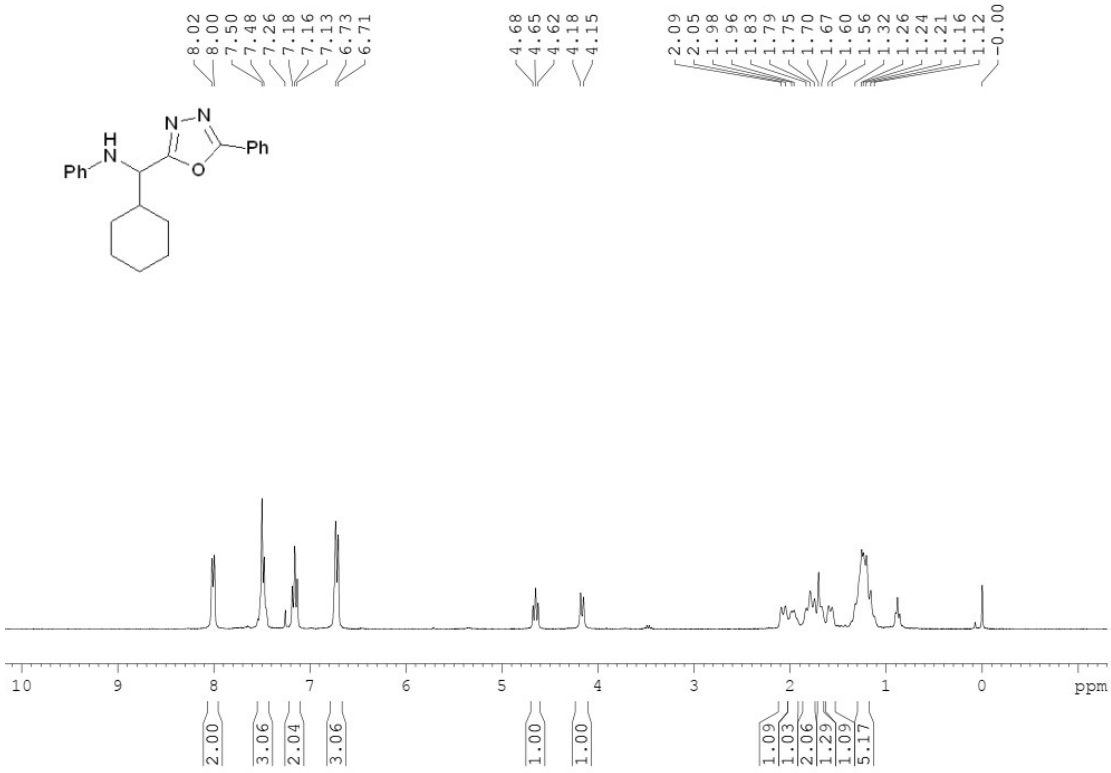
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ba**.



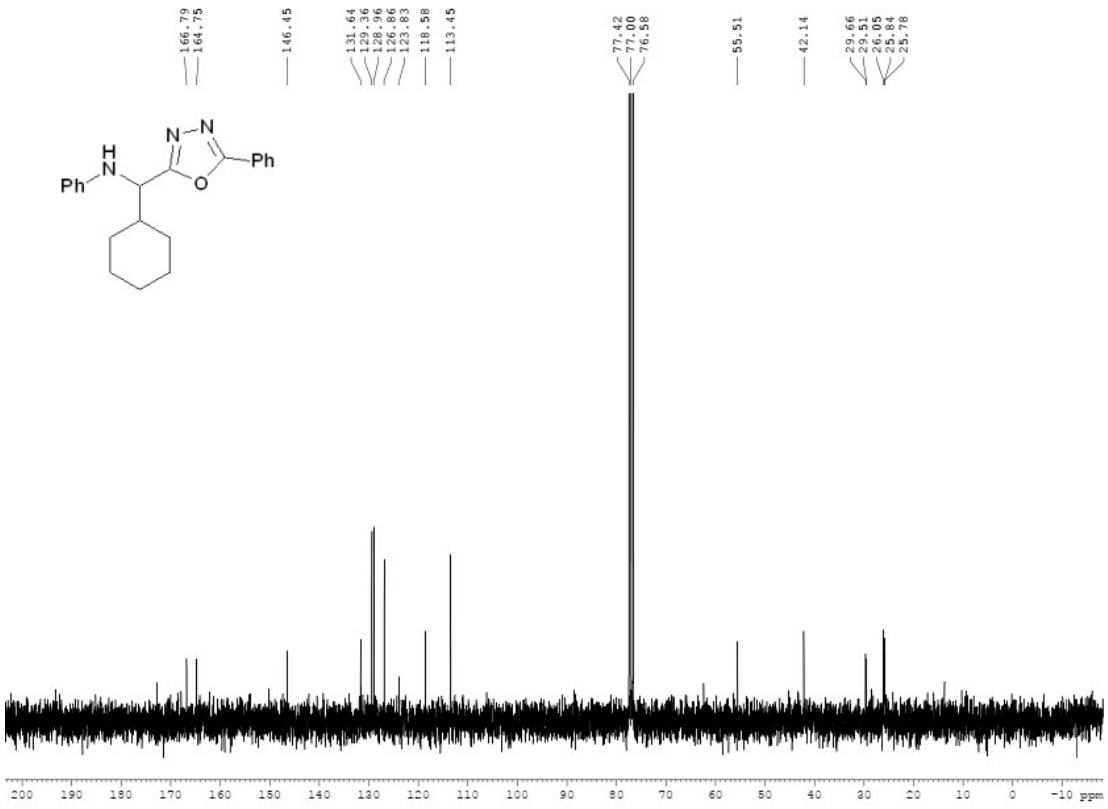
^{19}F NMR (282 MHz, $CDCl_3$)spectrum of compound **3ba**



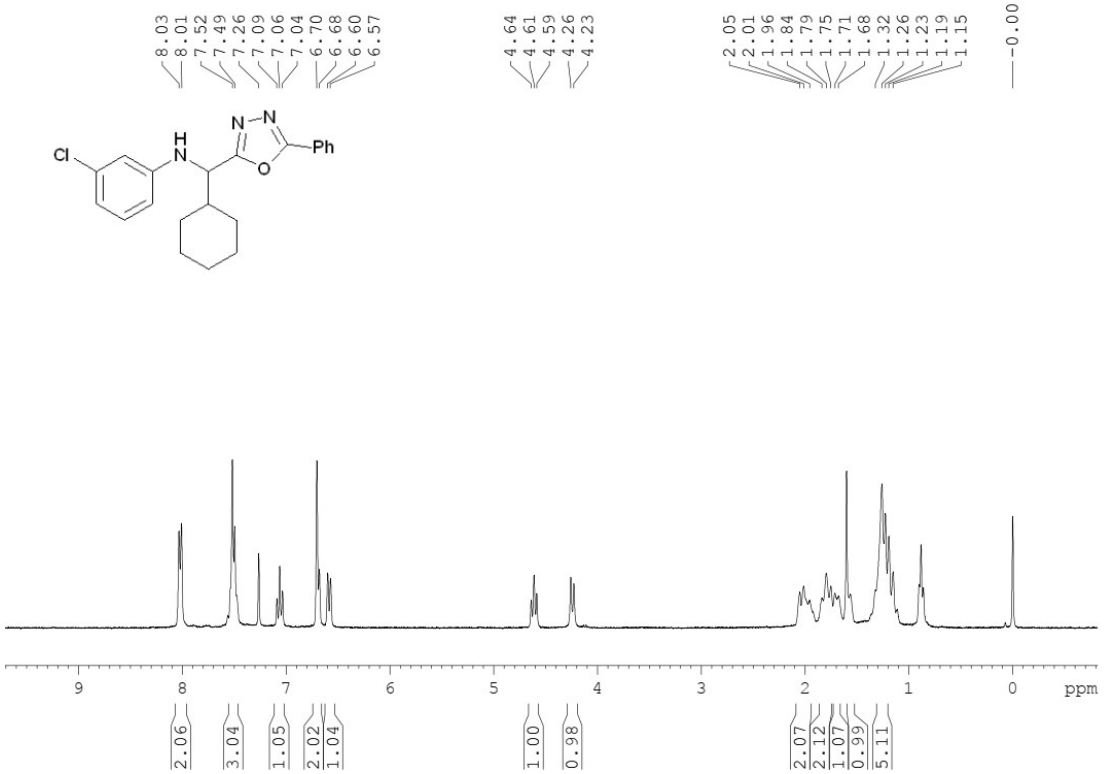
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ba**.



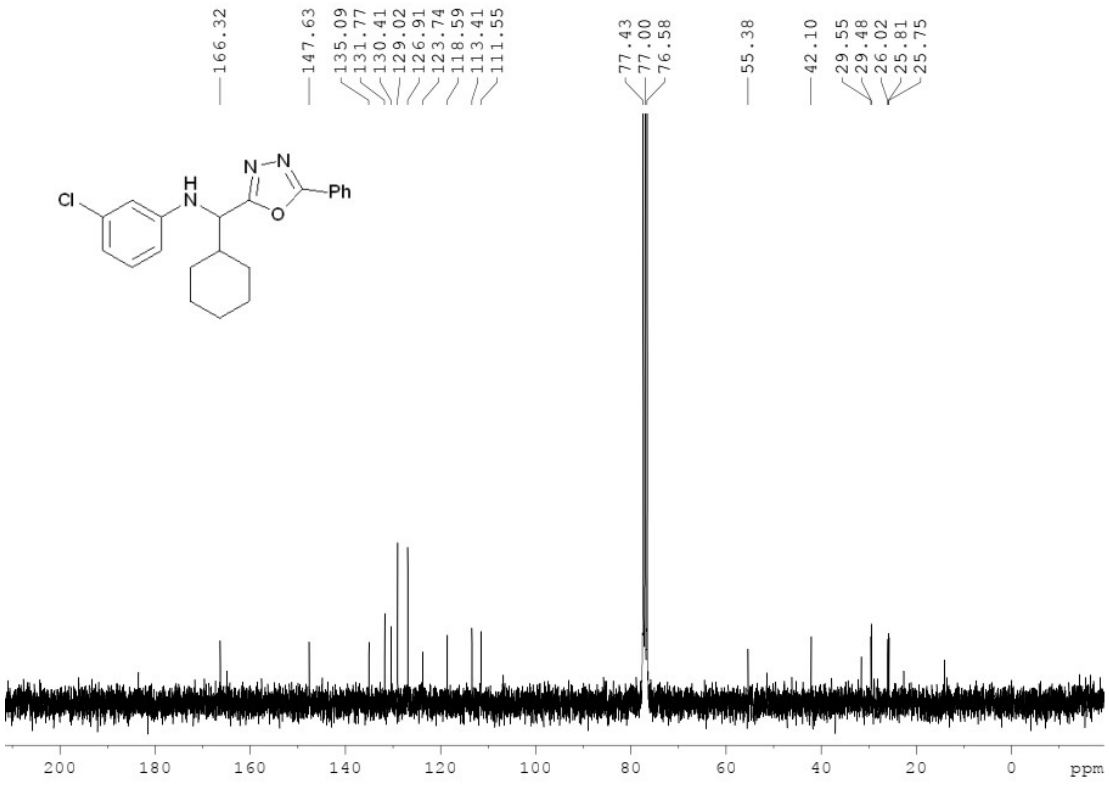
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ca**.



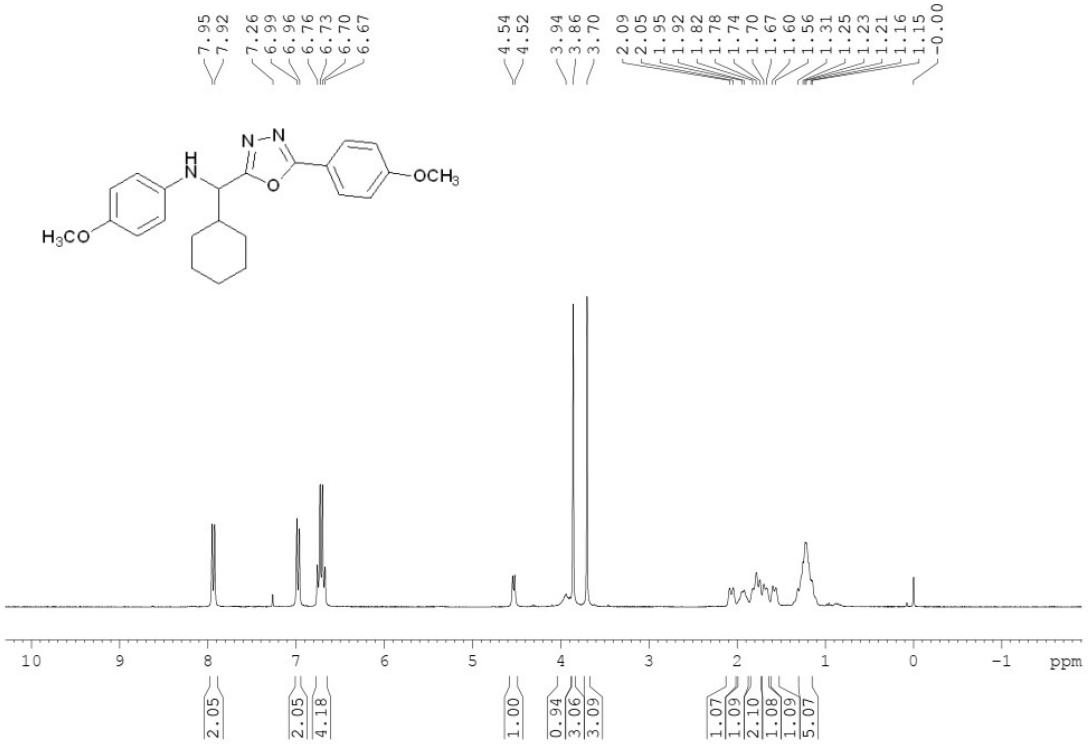
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ca**.



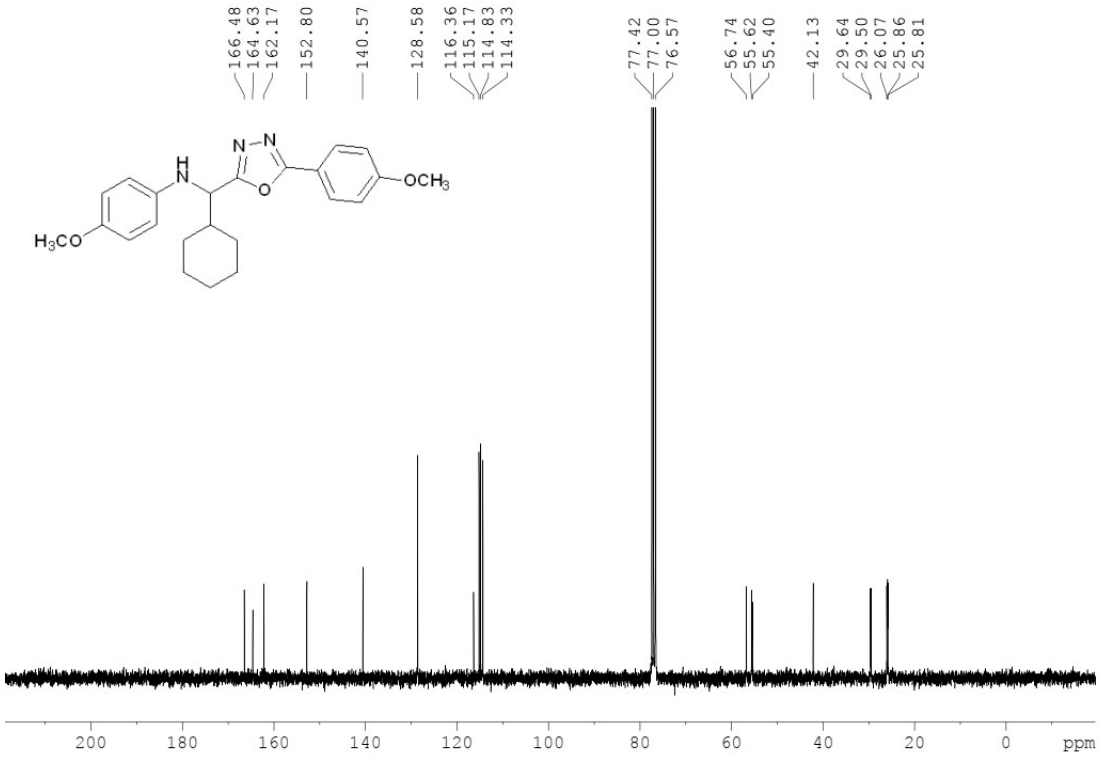
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3da**.



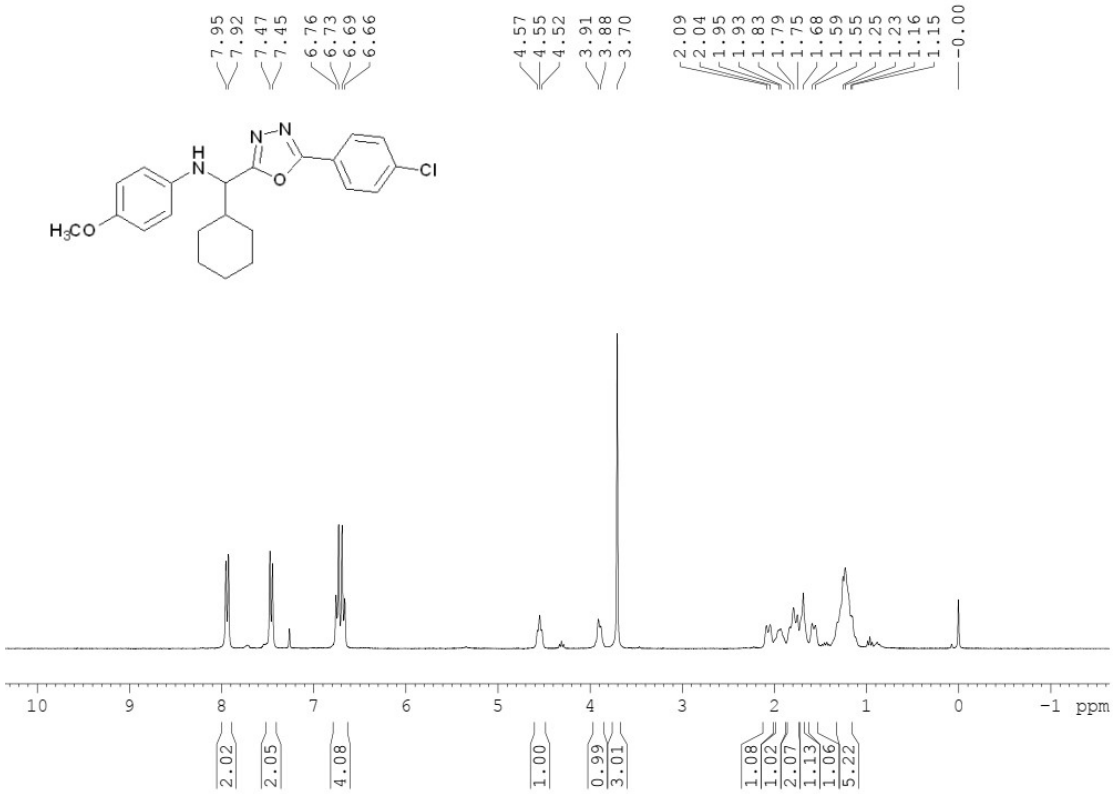
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3da**.



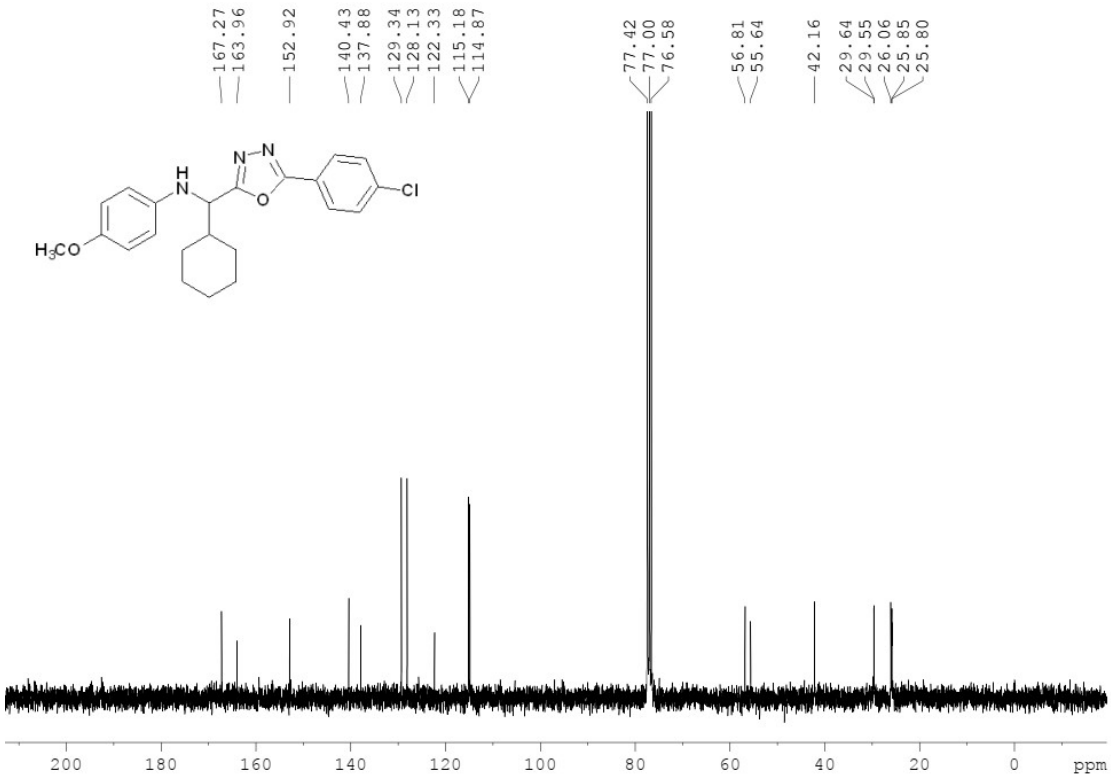
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ea**.



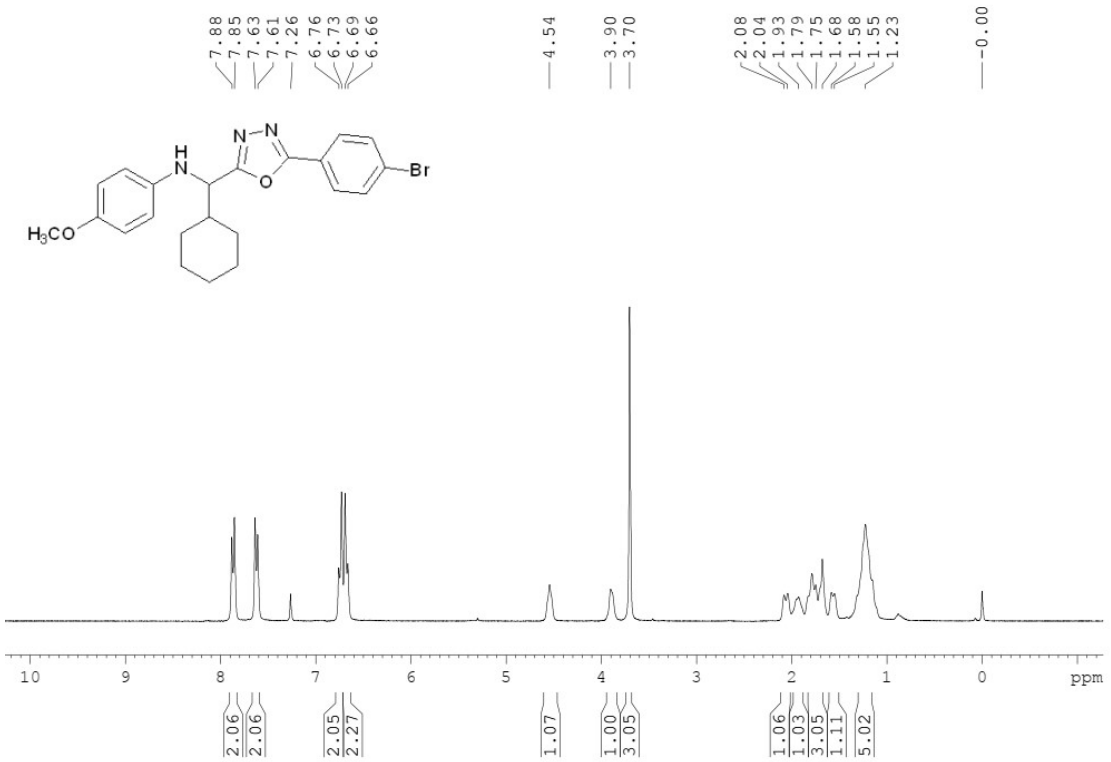
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ea**.



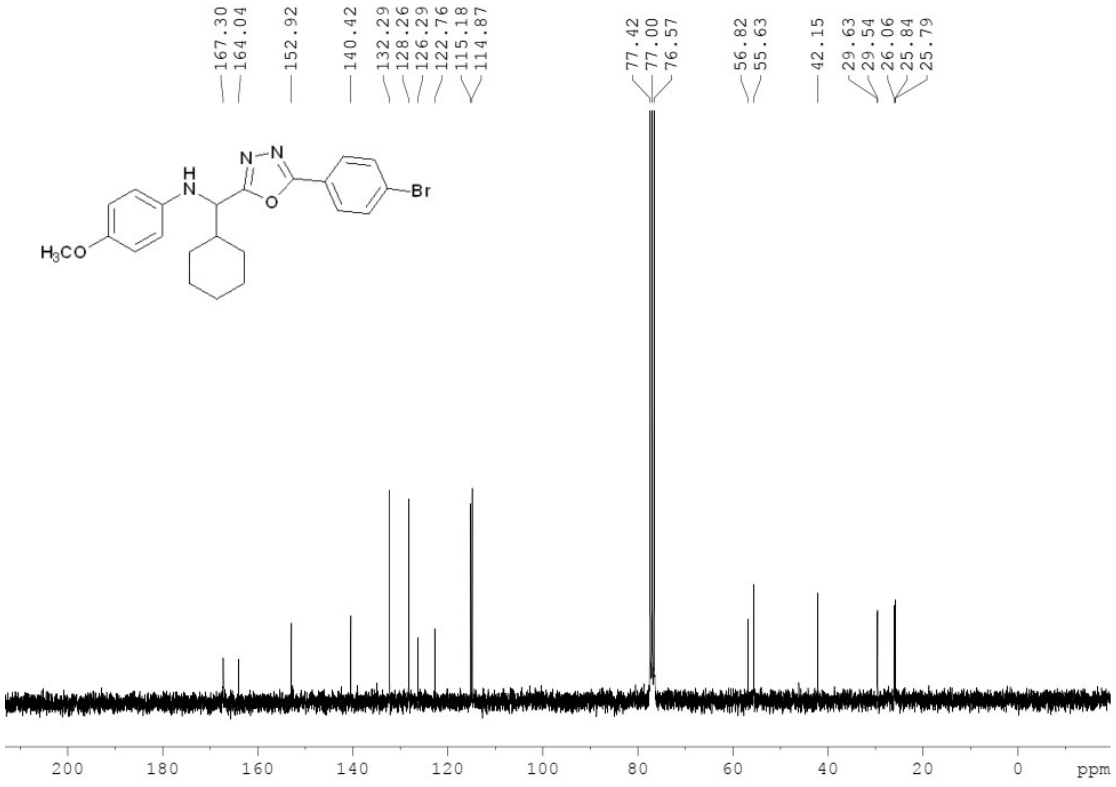
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3fa**.



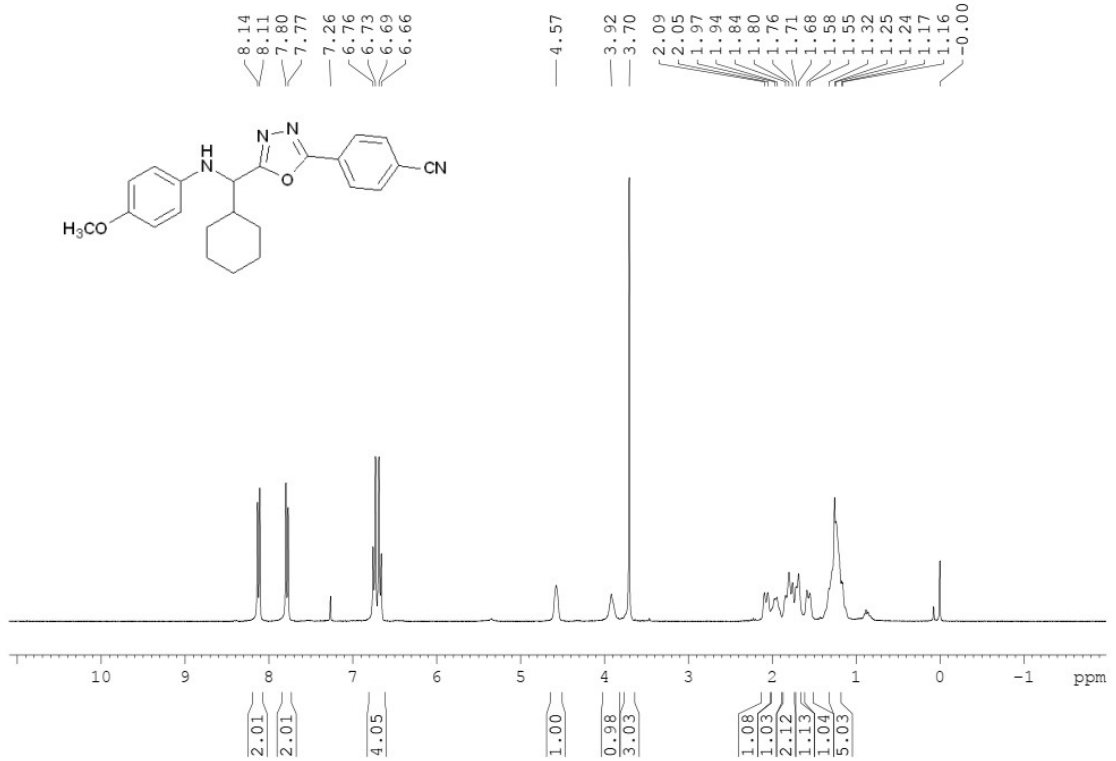
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3fa**.



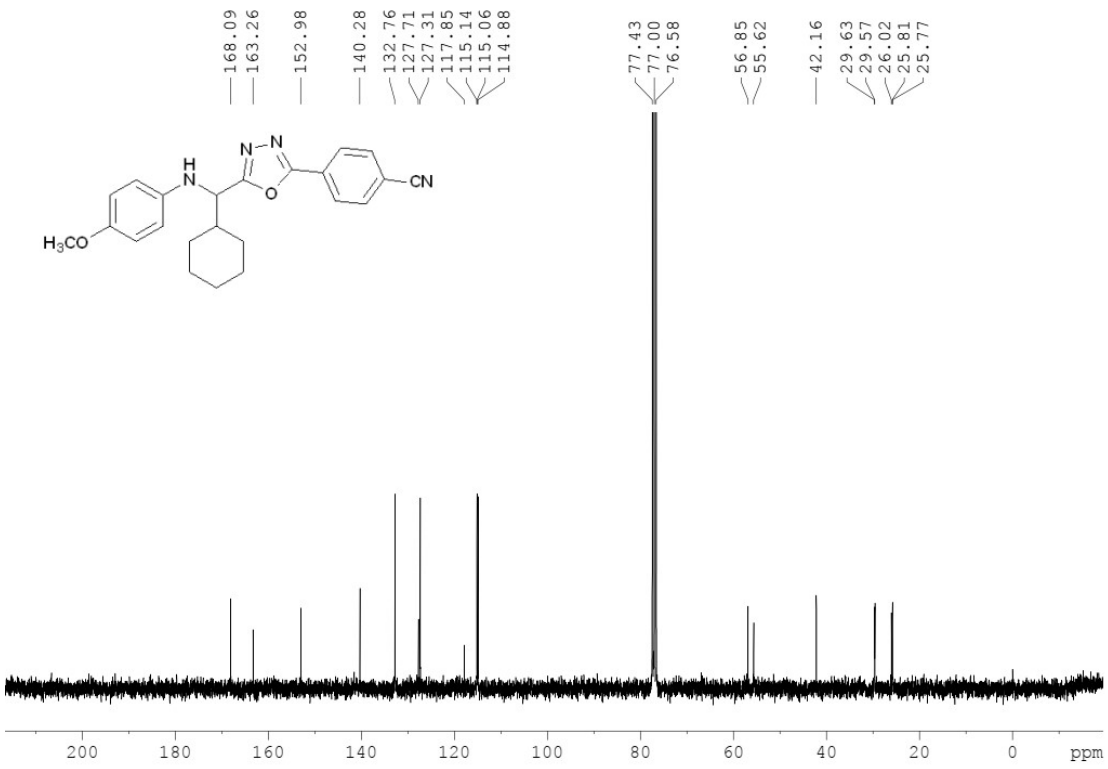
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ga**.



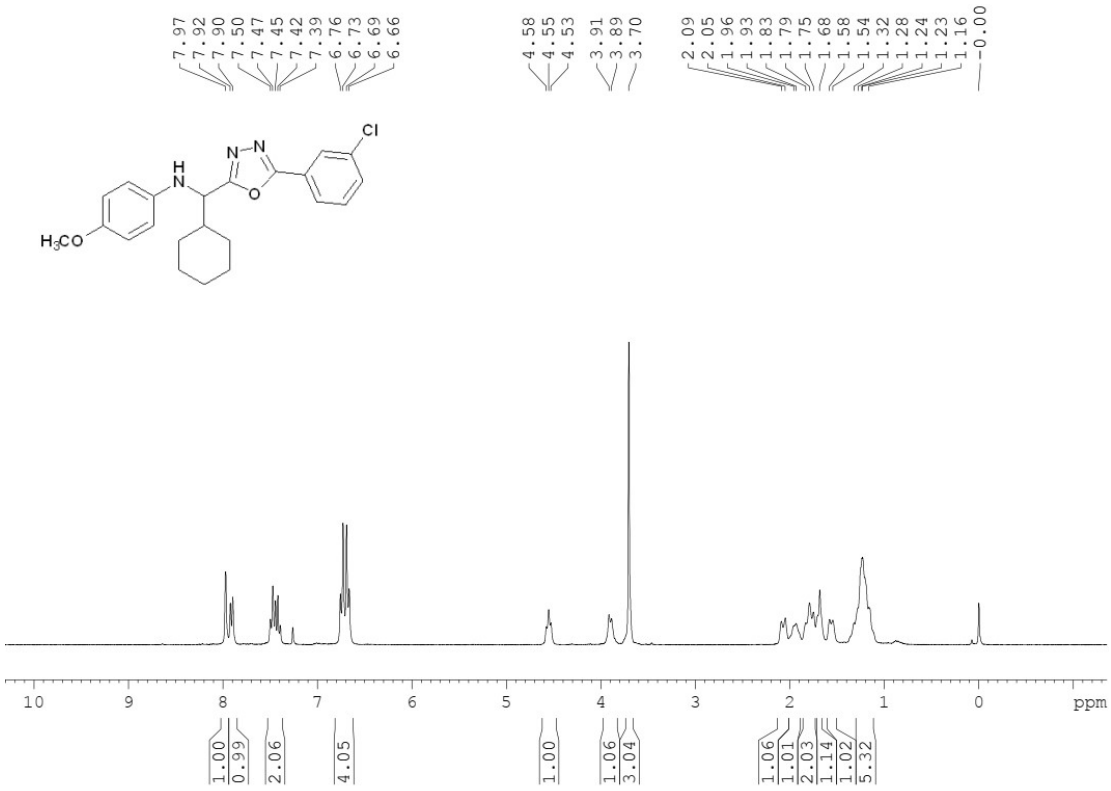
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ga**.



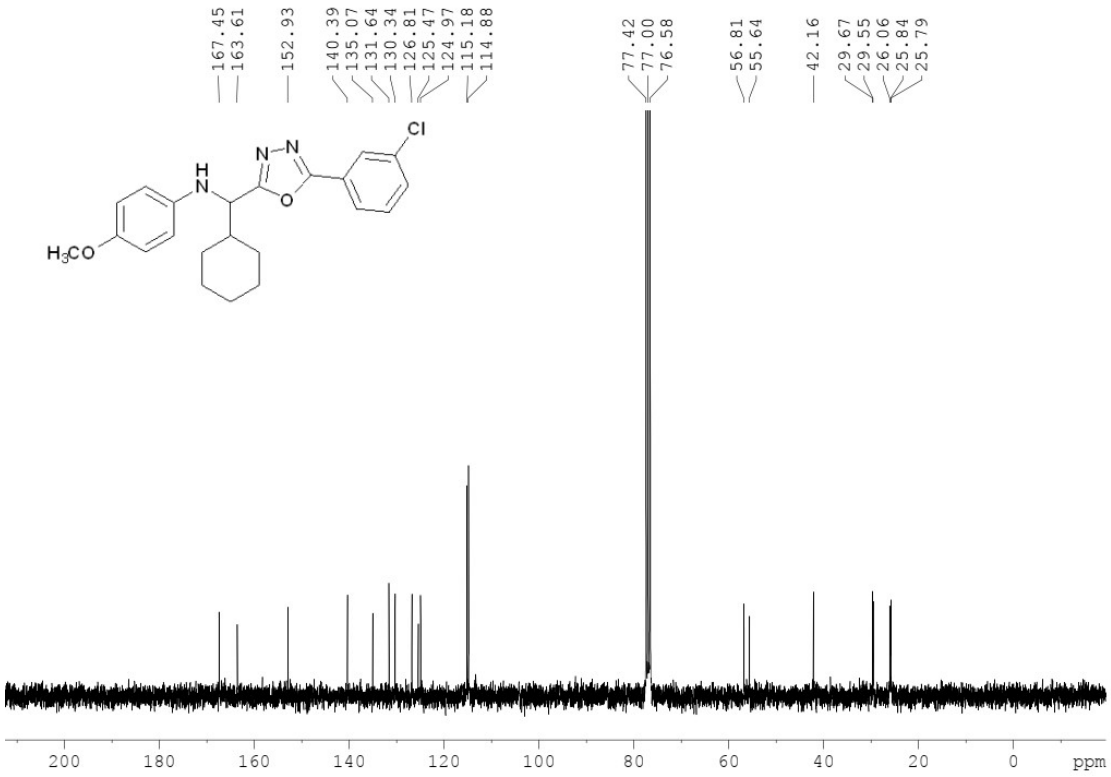
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ha**.



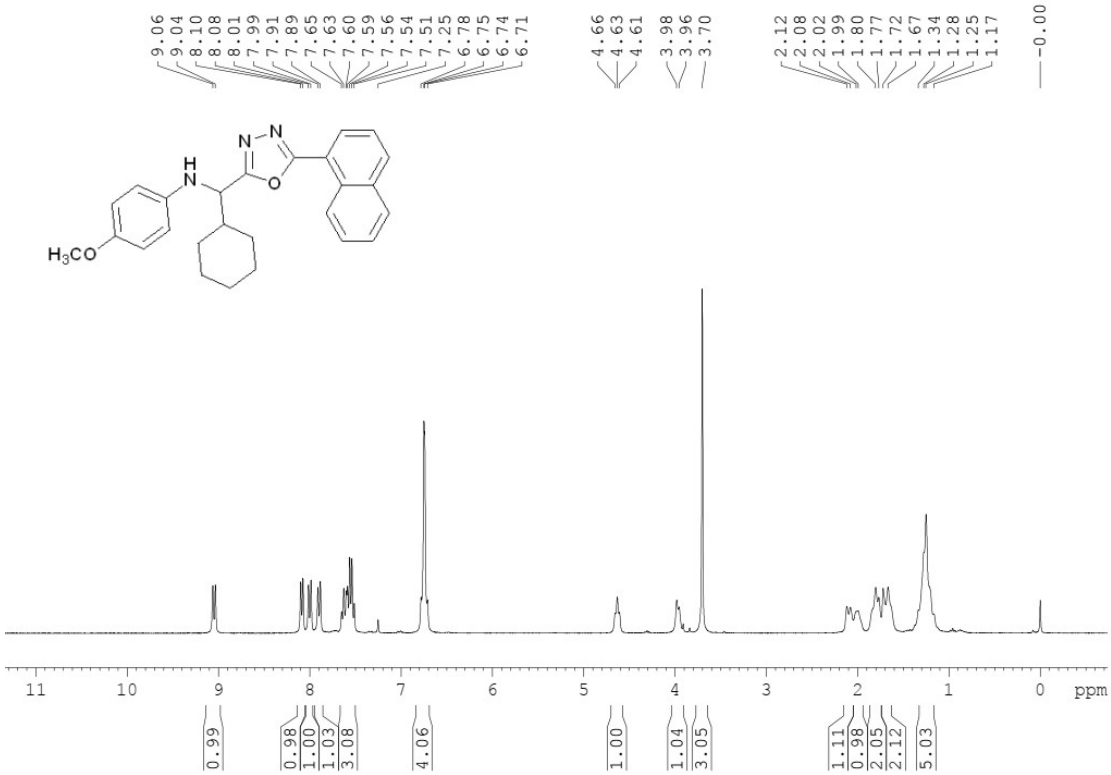
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ha**.



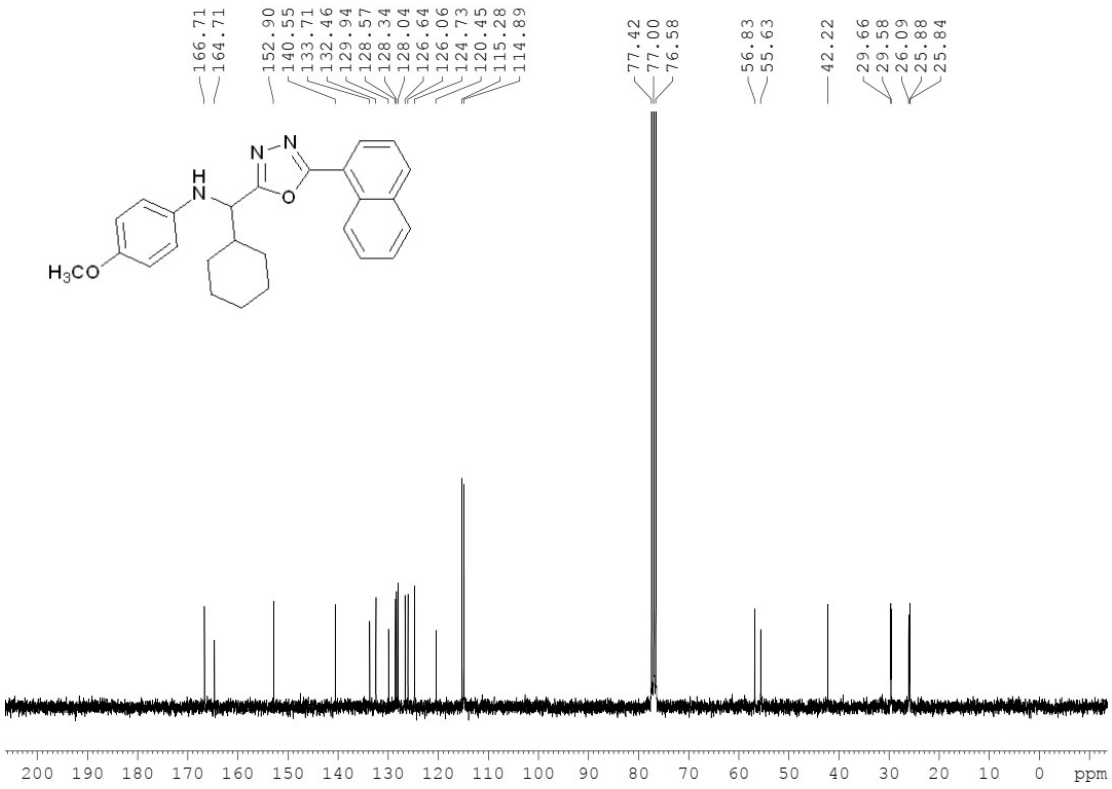
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ia**.



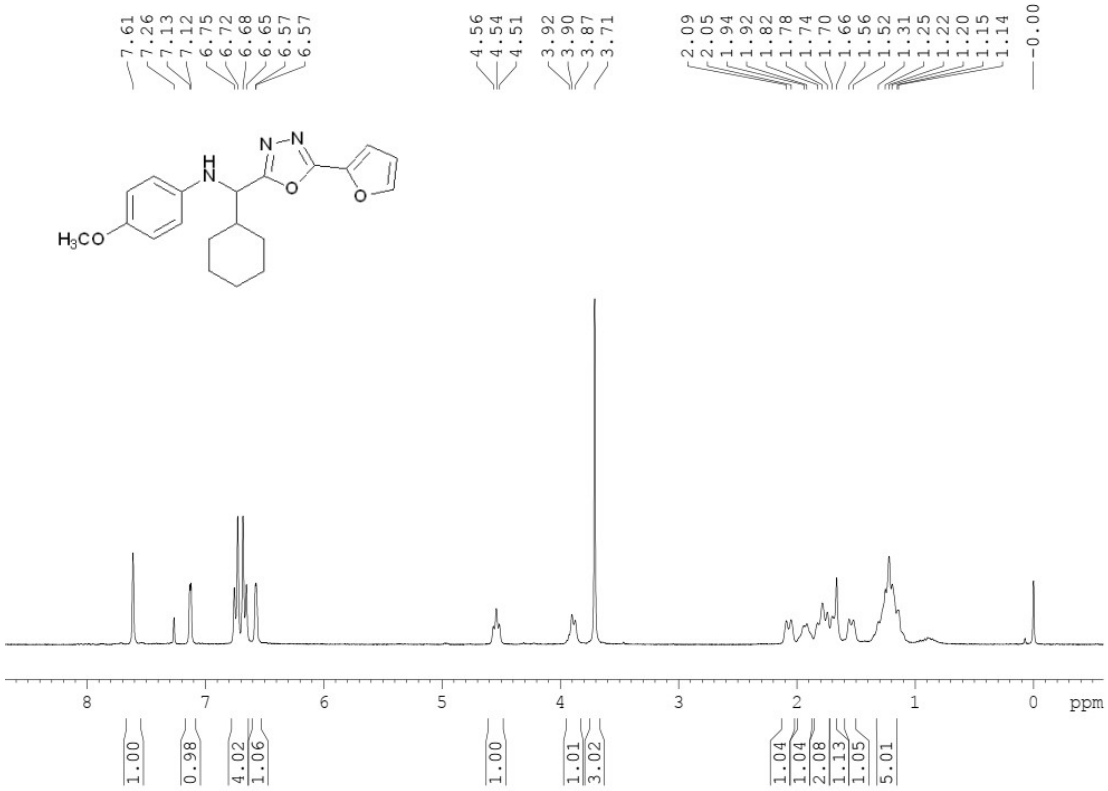
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ia**.



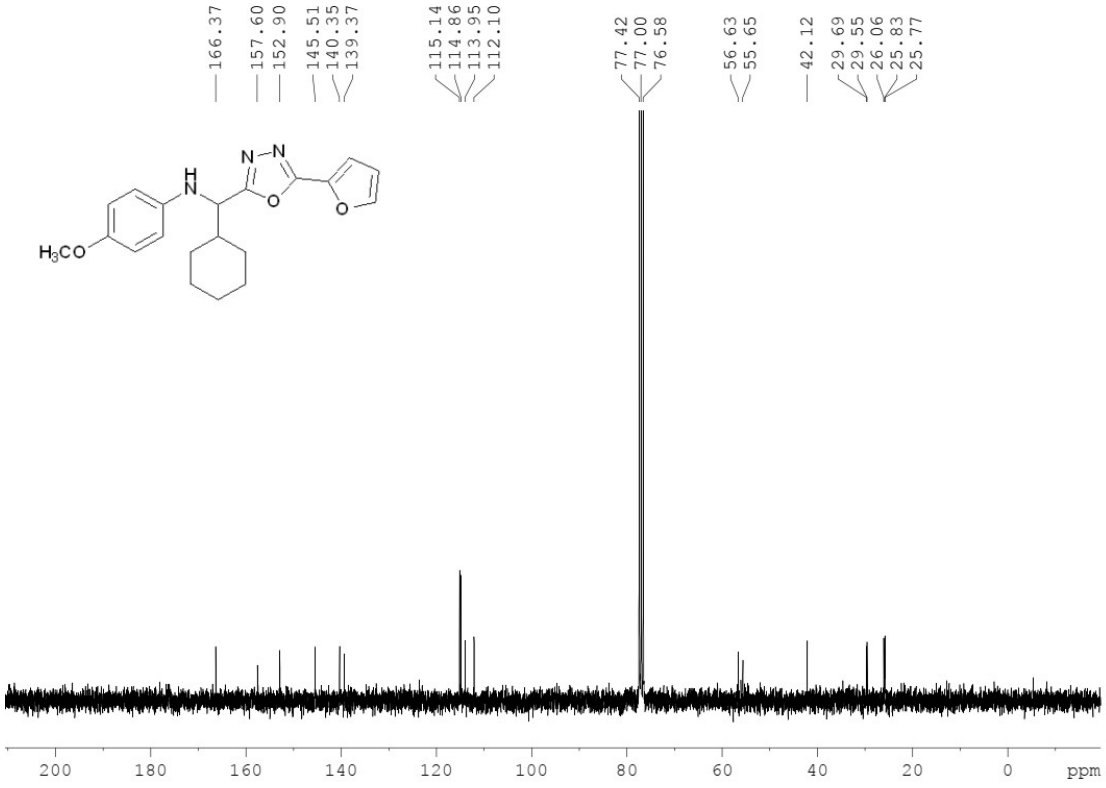
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ja**.



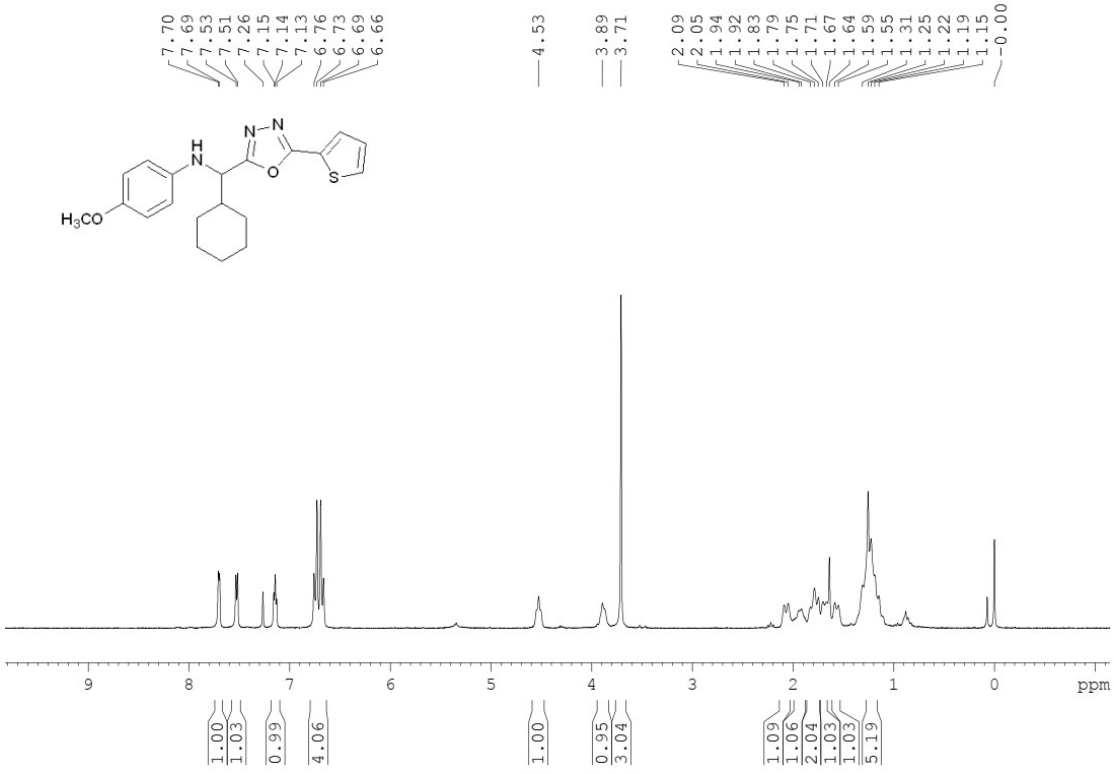
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ja**.



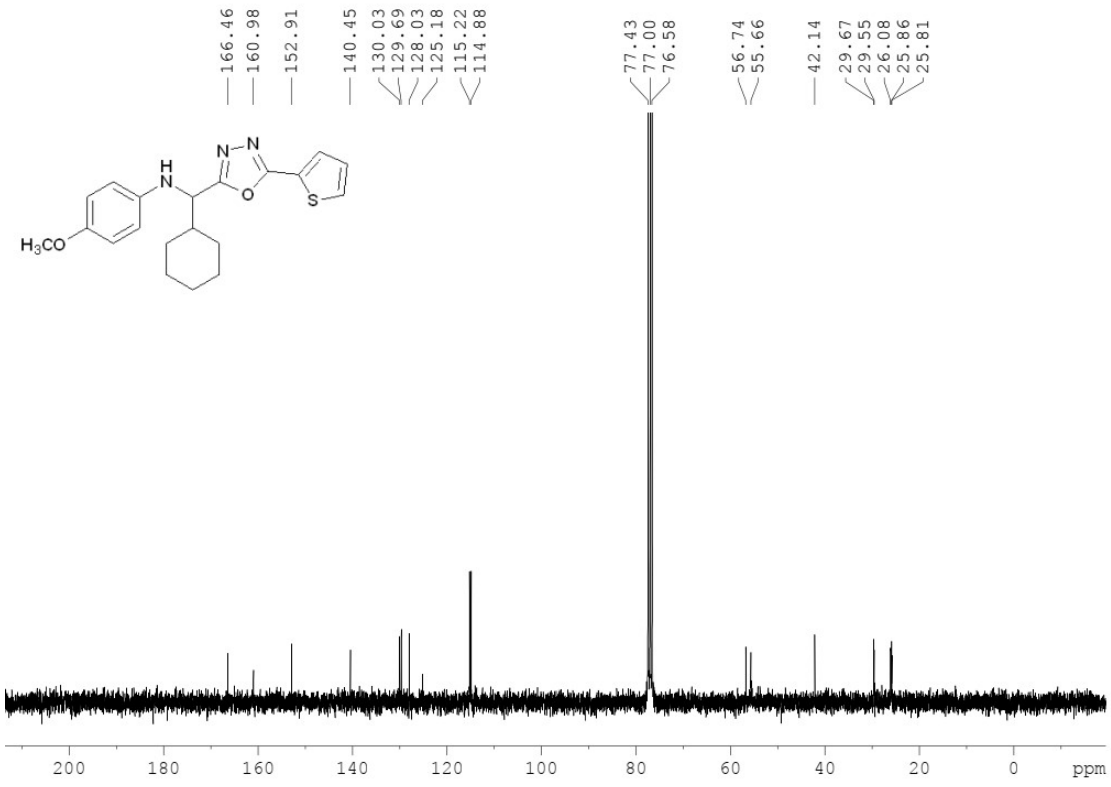
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ka**.



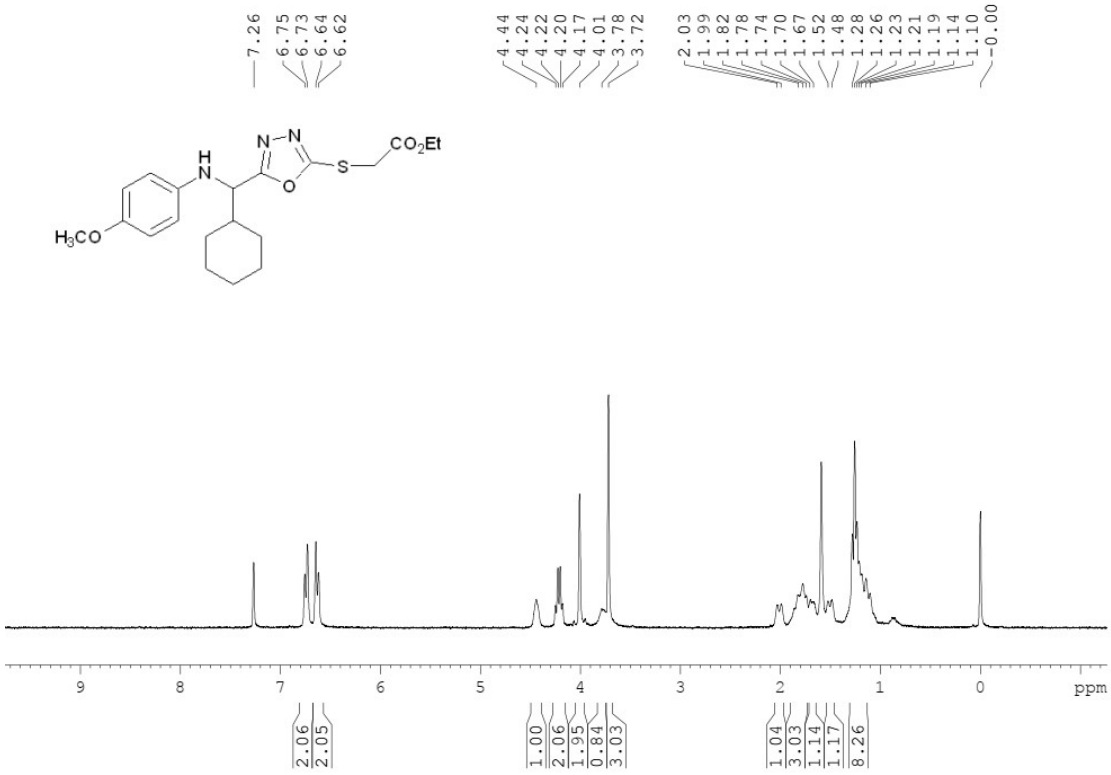
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ka**.



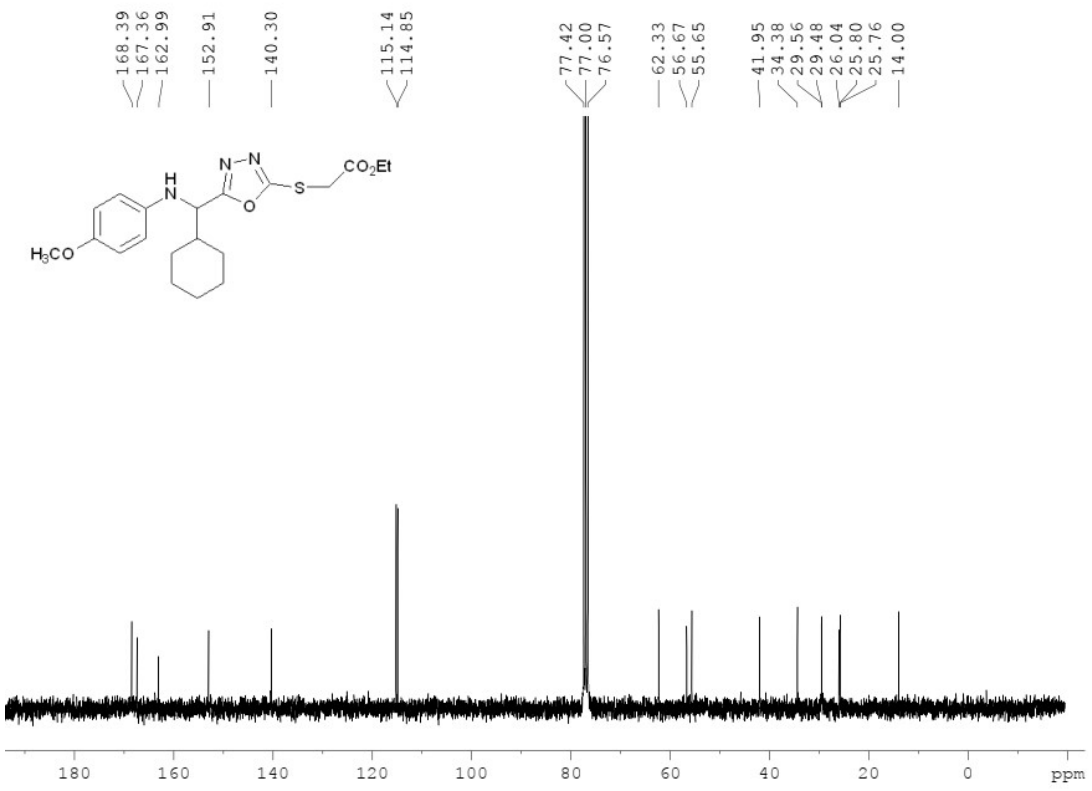
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3la**.



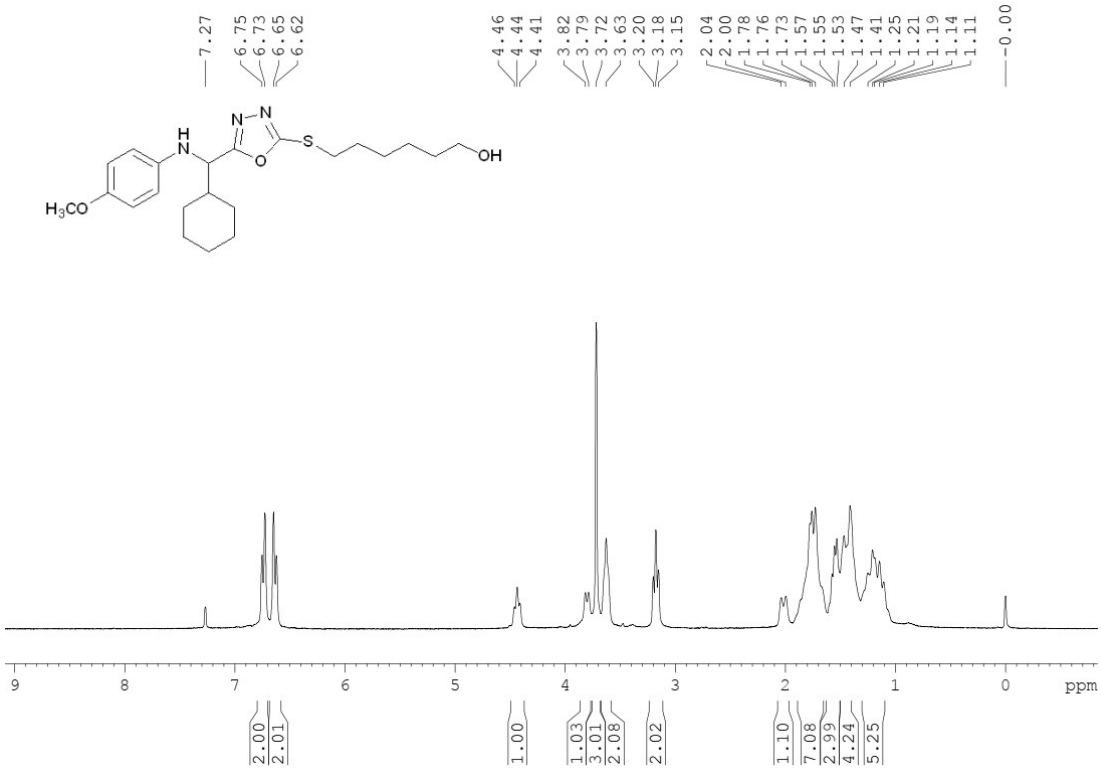
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3la**.



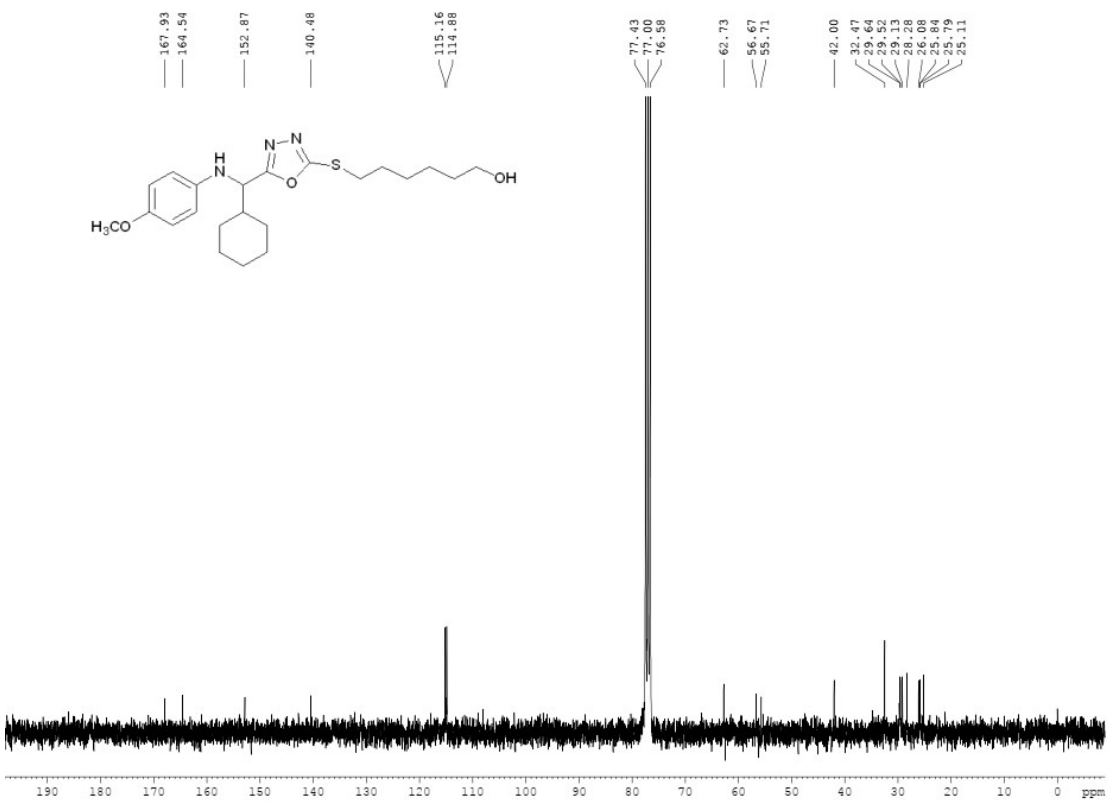
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ma**.



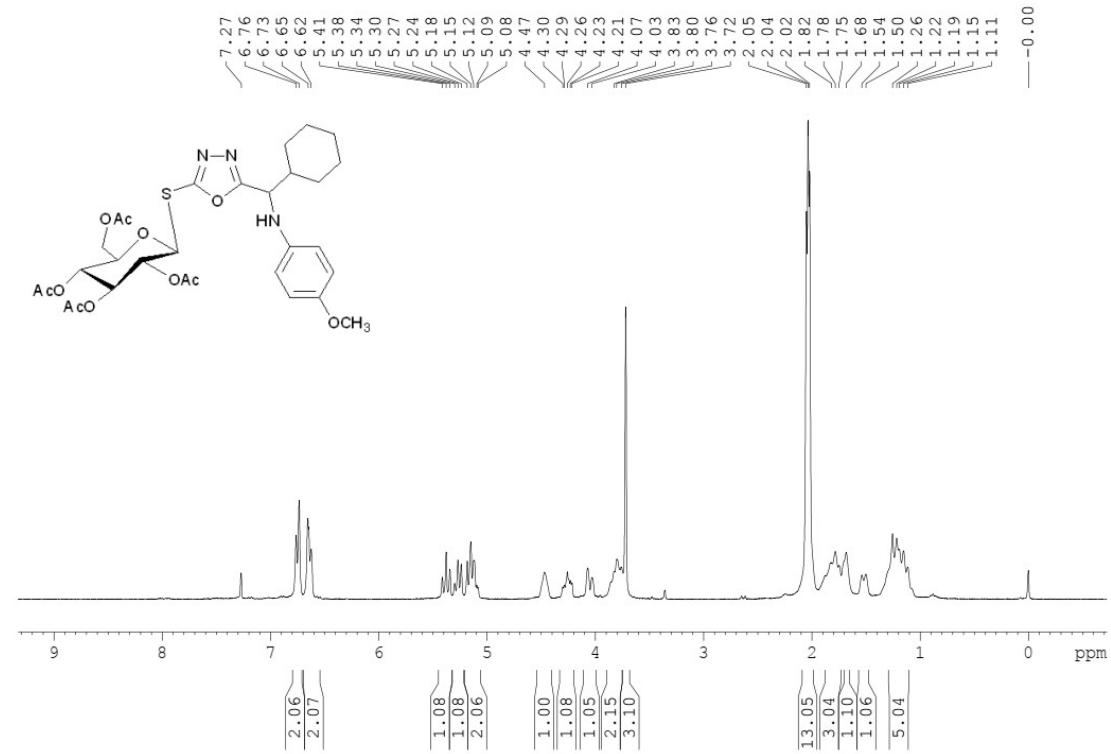
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ma**.



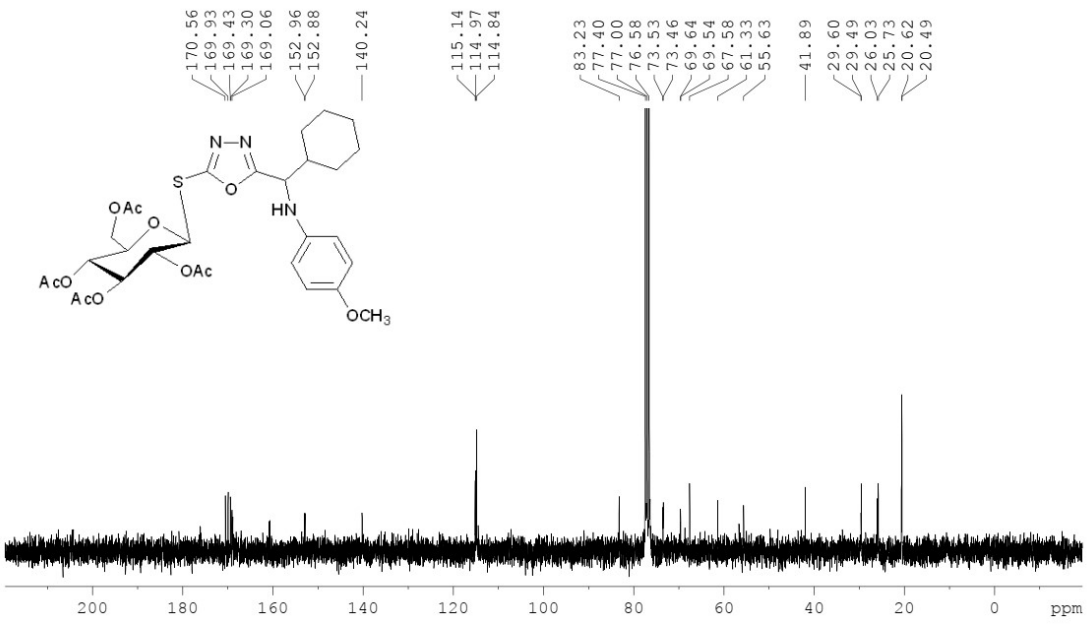
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3na**.



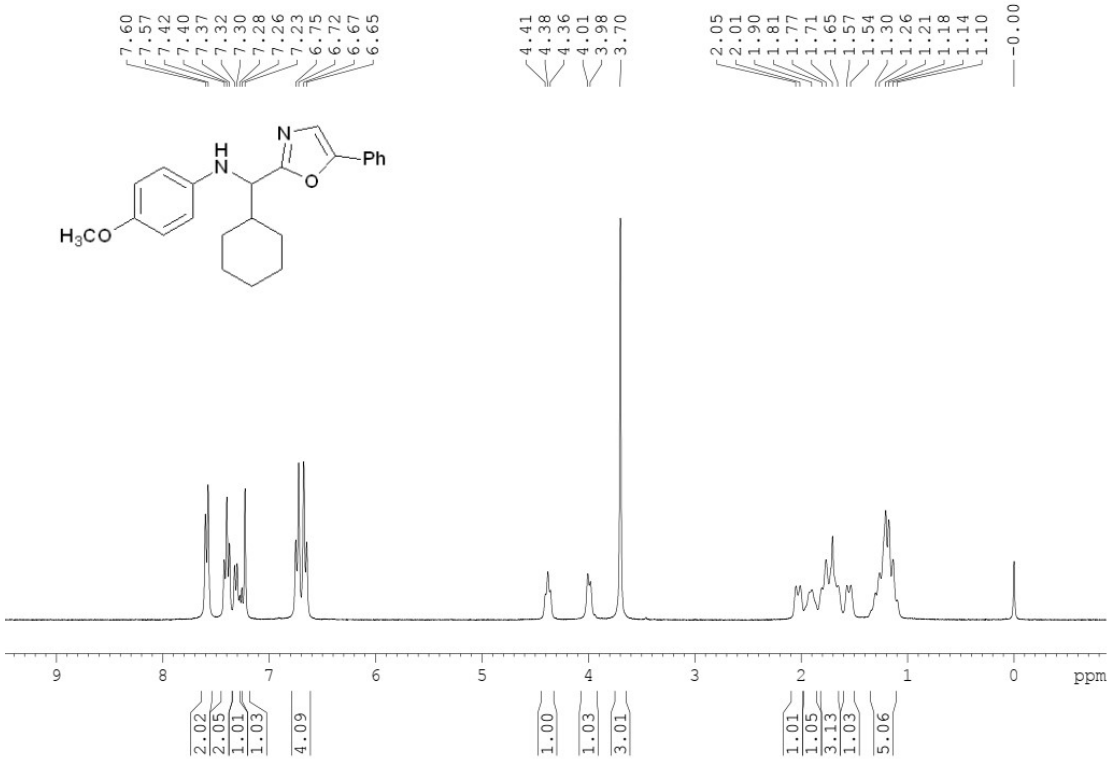
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3na**.



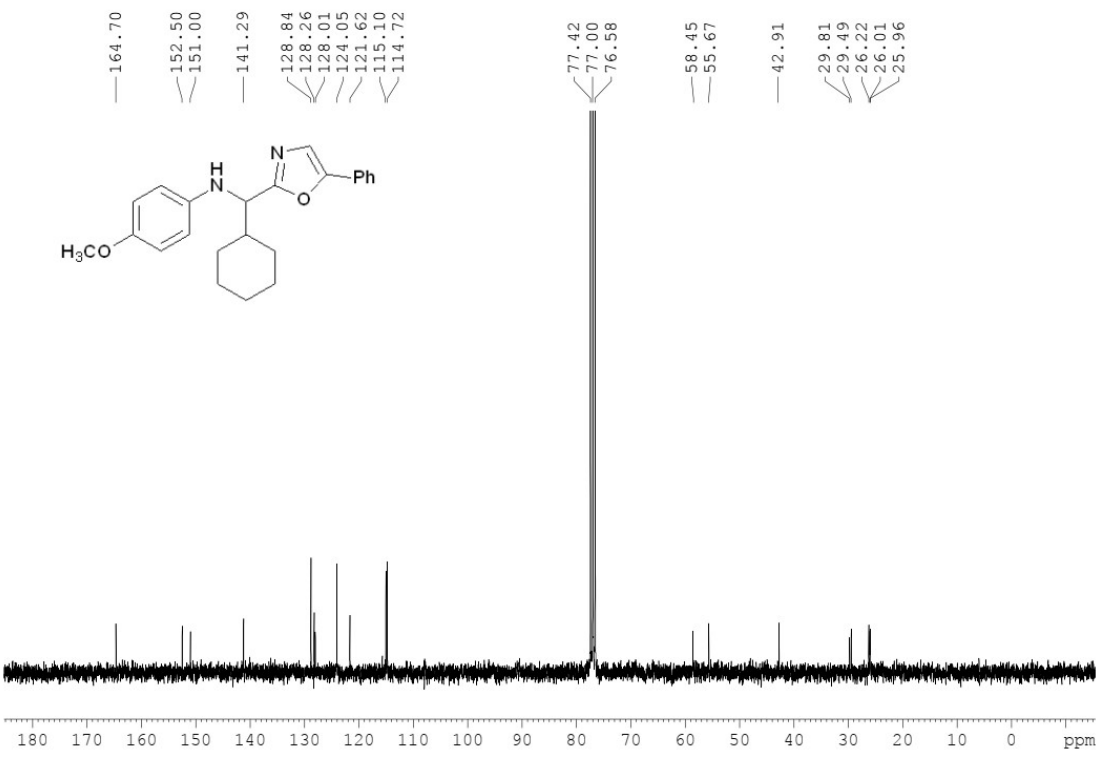
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3oa**.



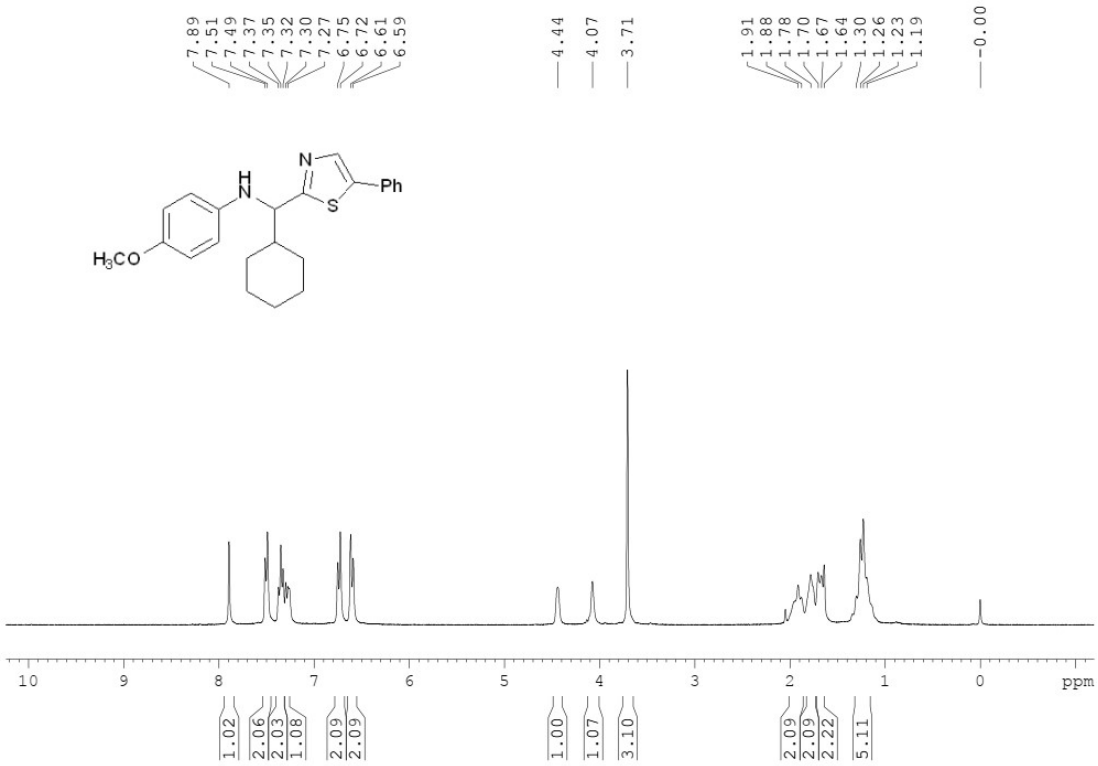
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3oa**.



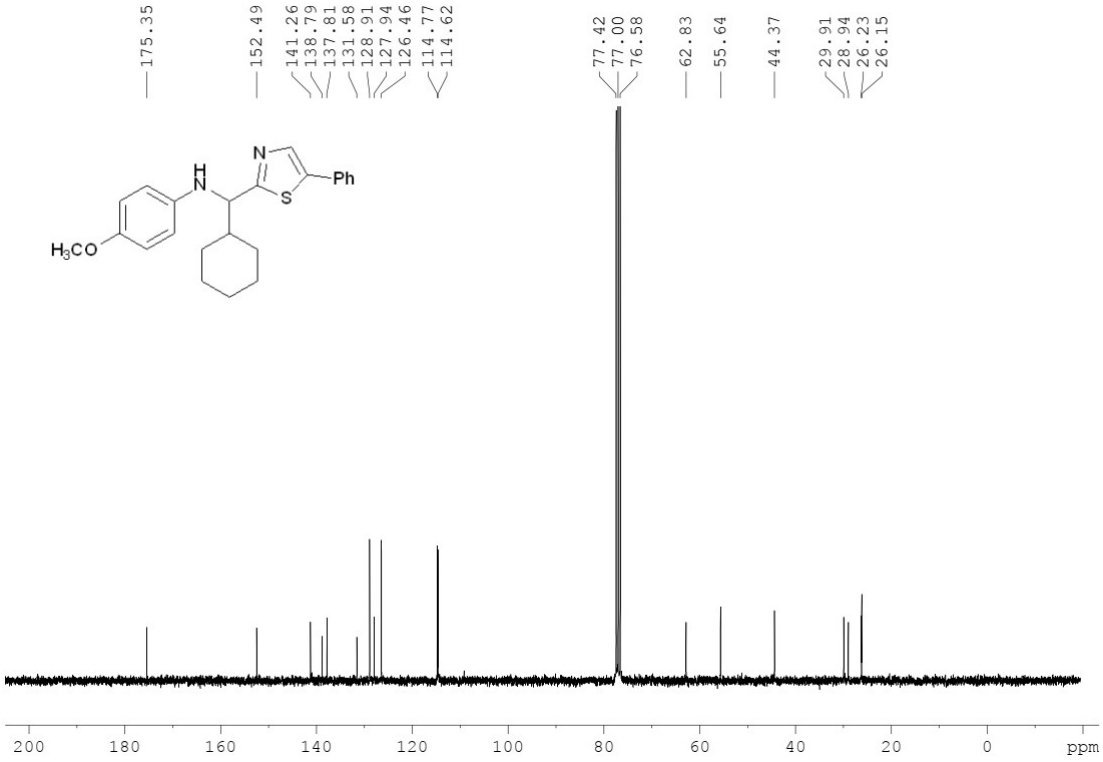
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3pa**.



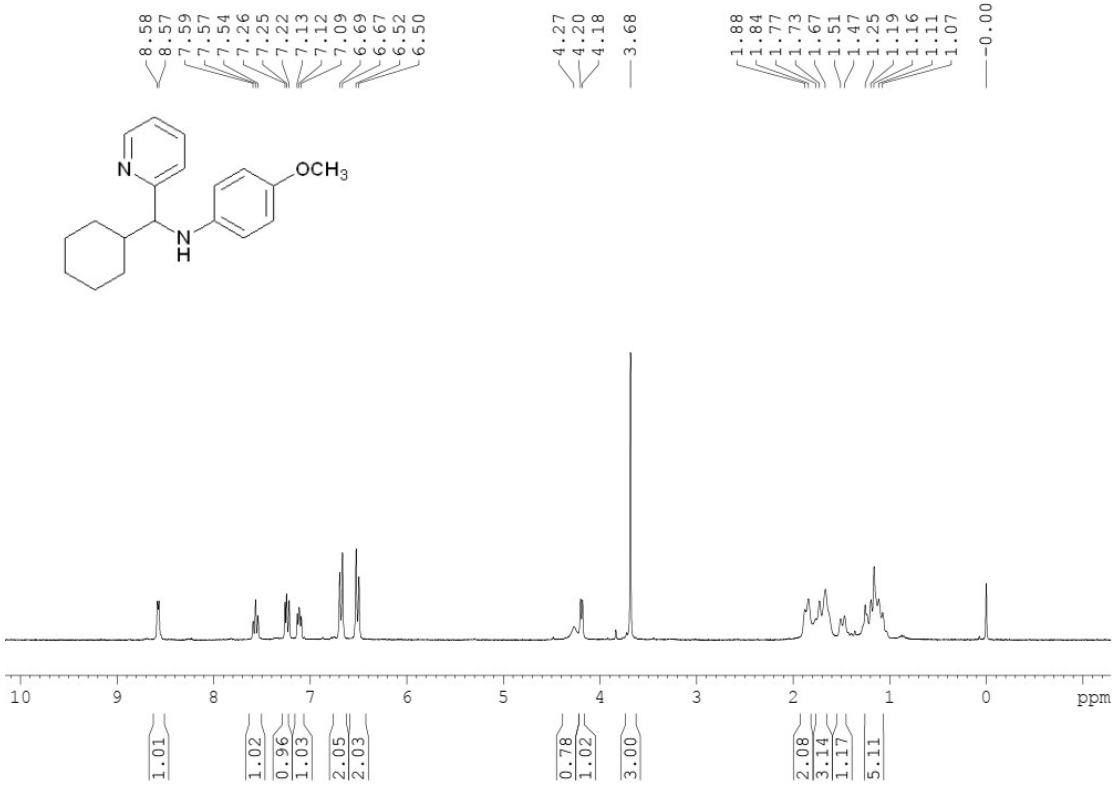
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3pa**.



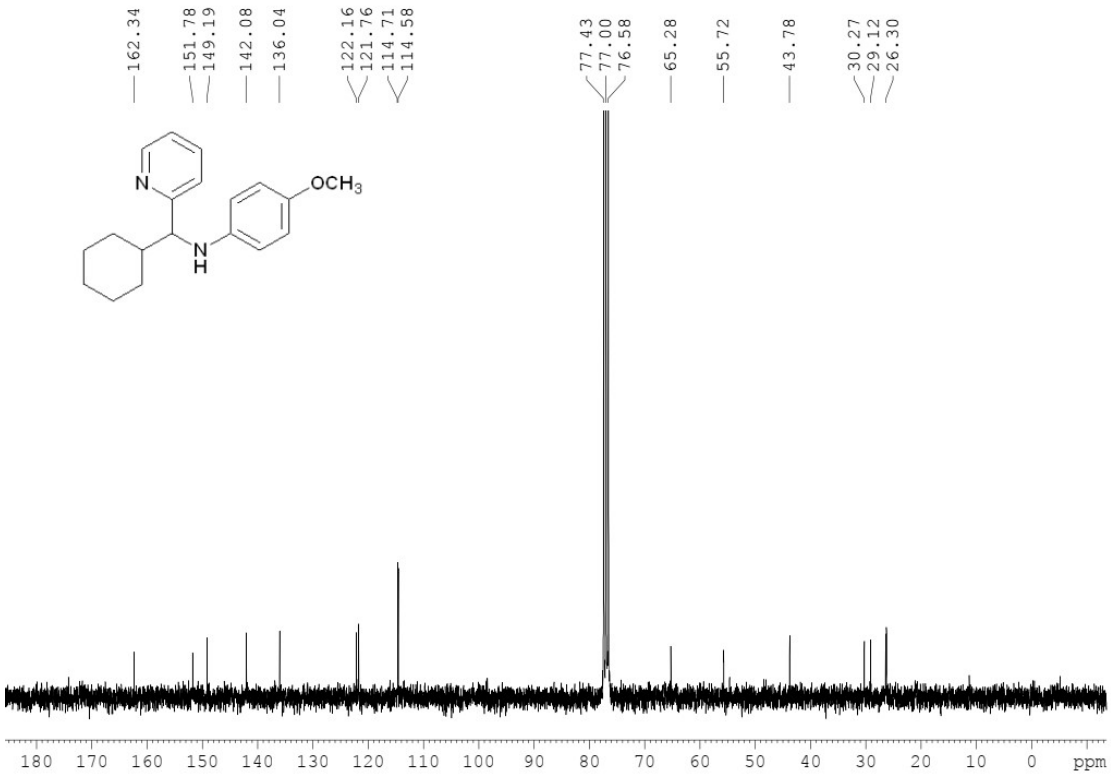
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3qa**.



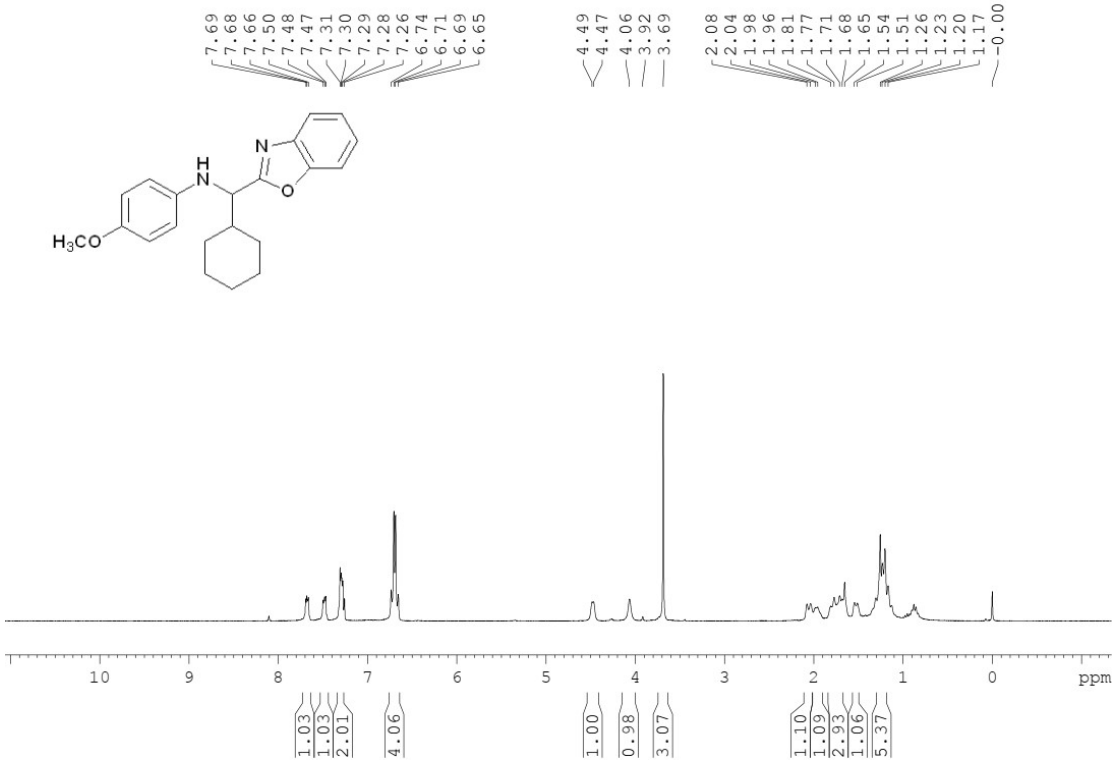
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3qa**.



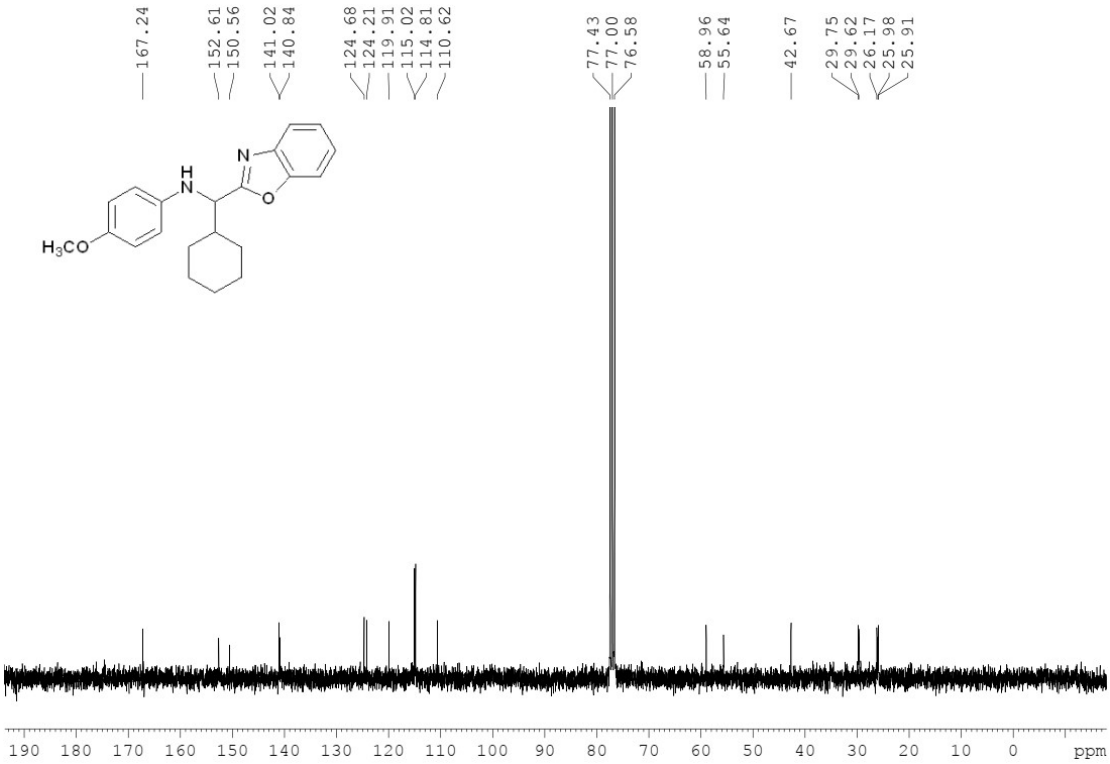
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ra**.



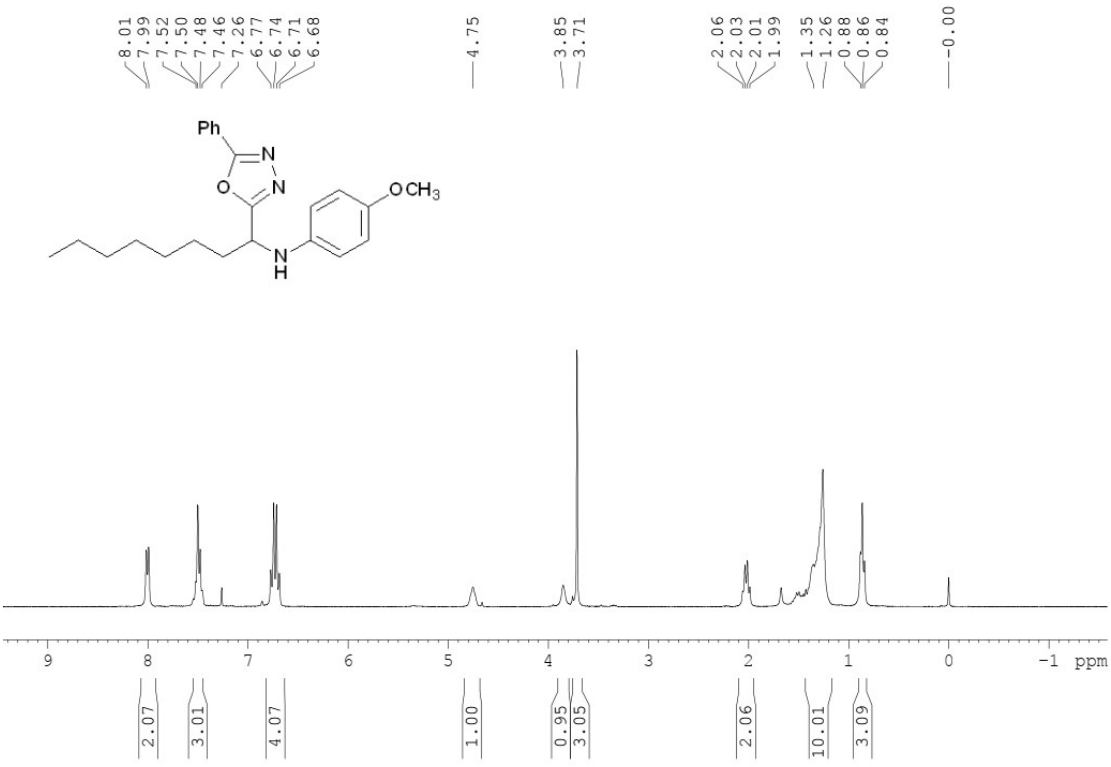
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ra**.



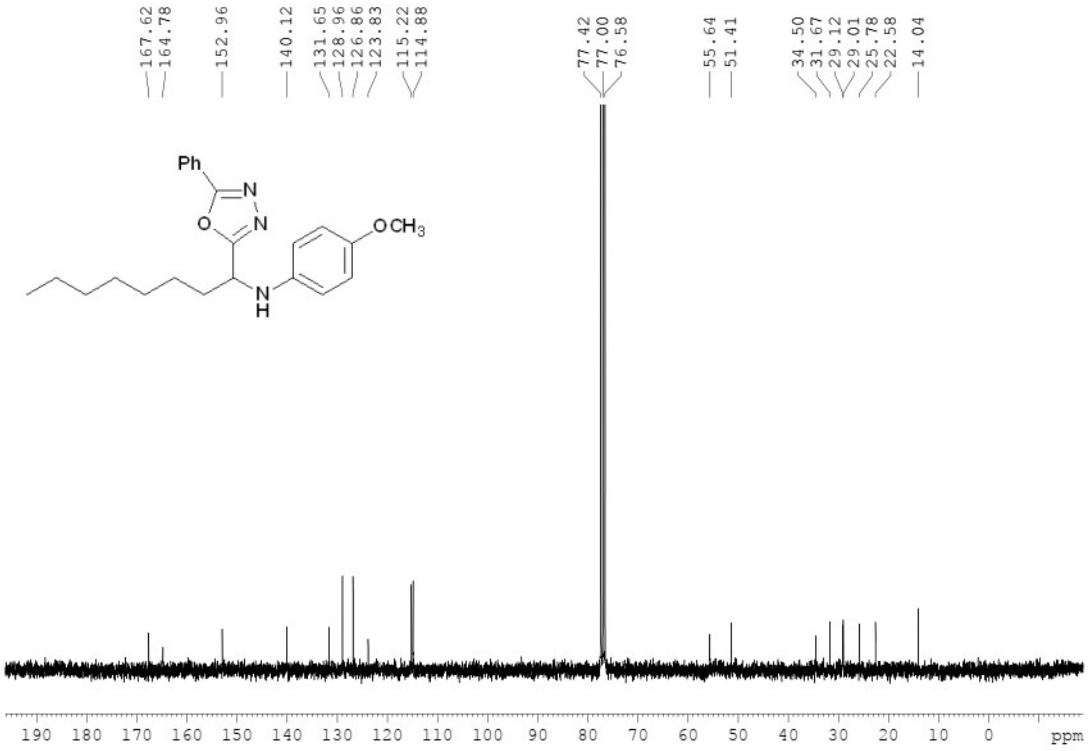
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3sa**.



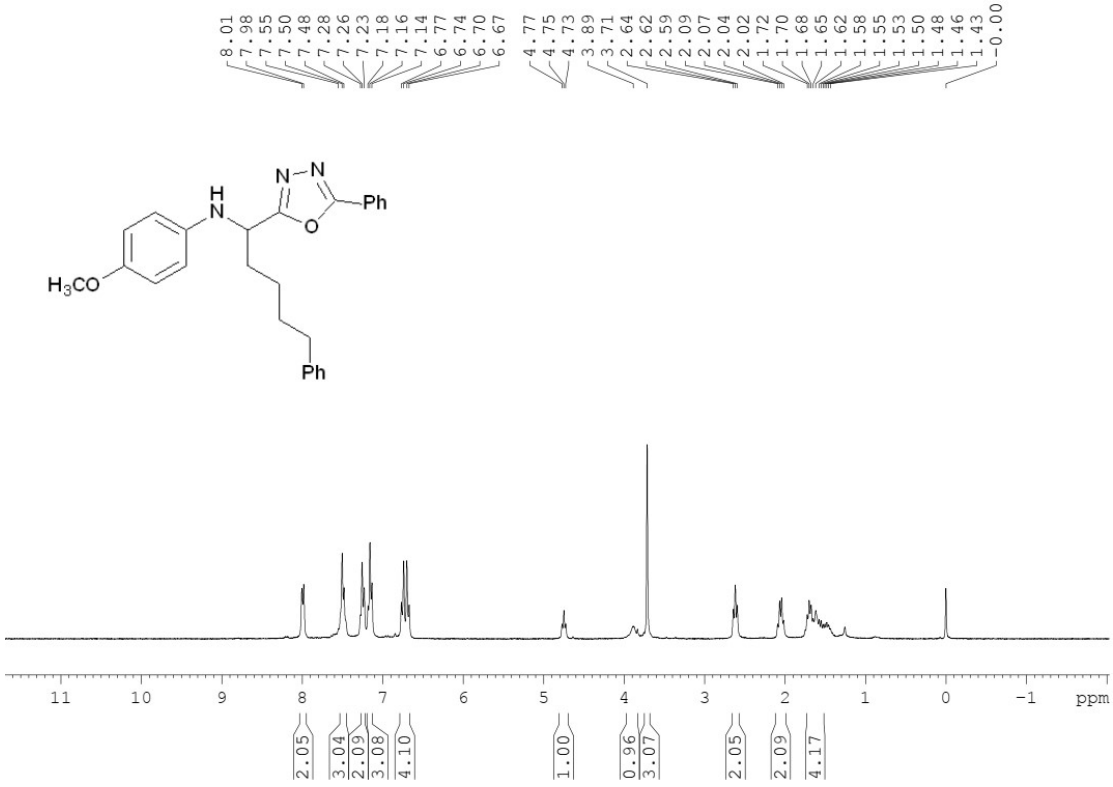
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3sa**.



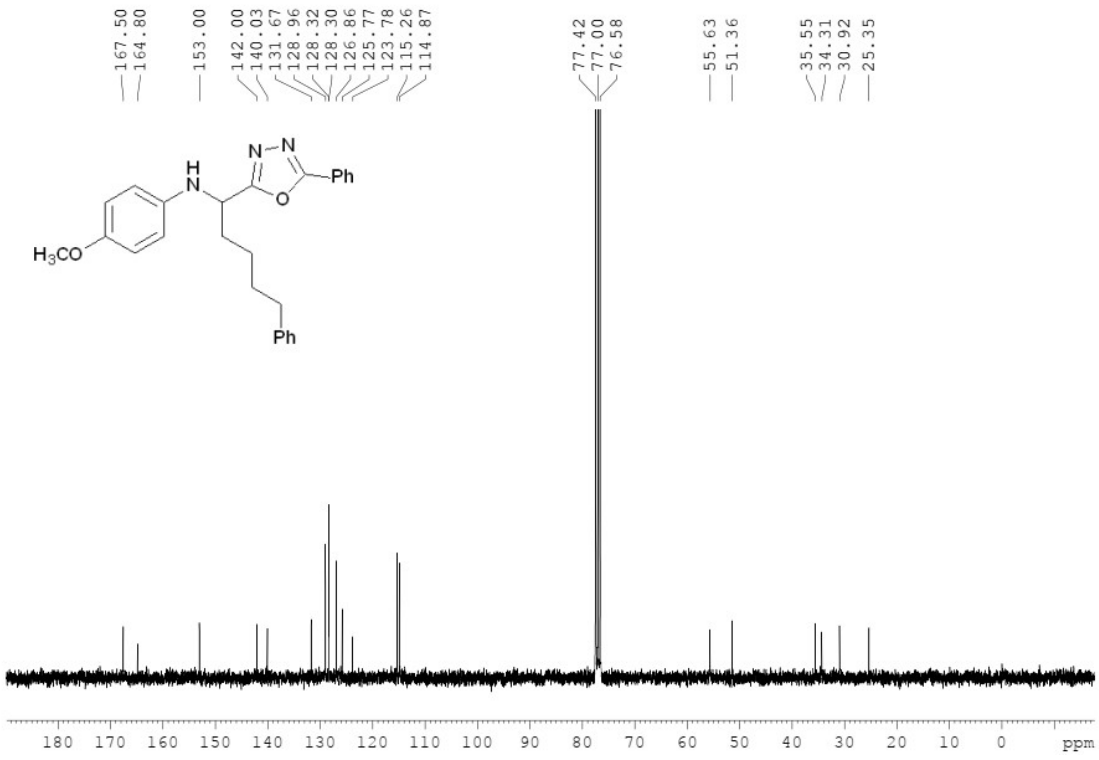
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ab**.



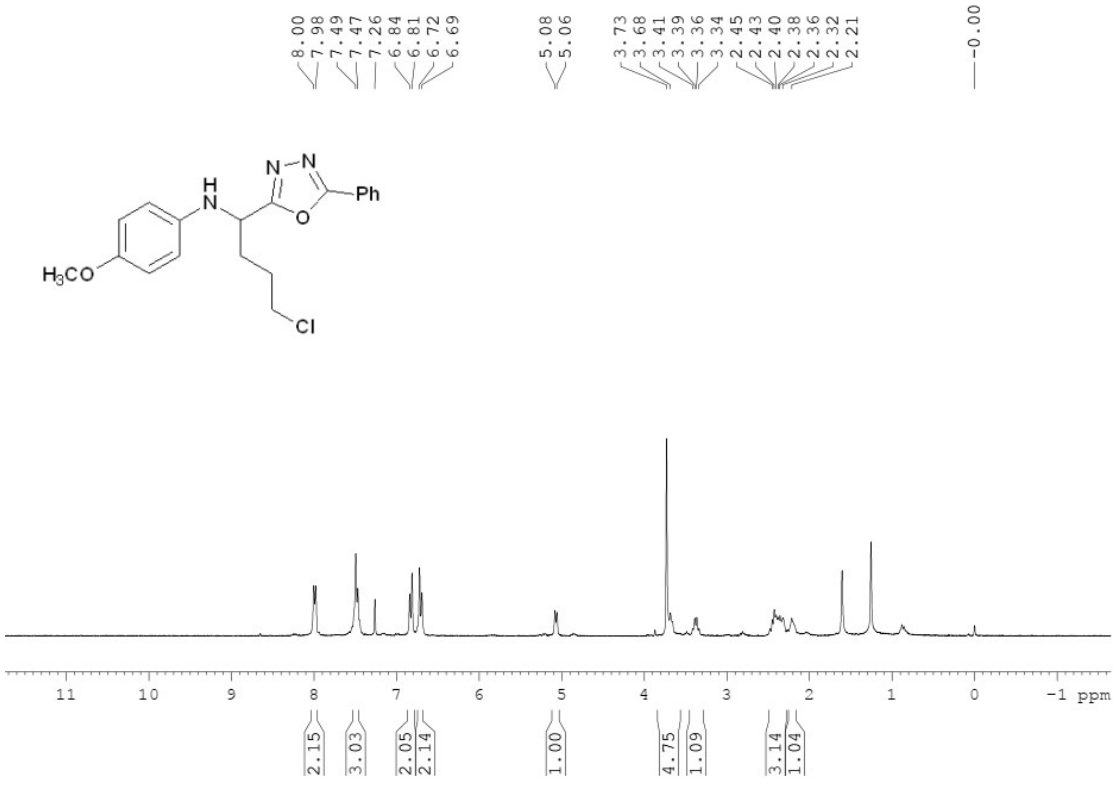
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ab**.



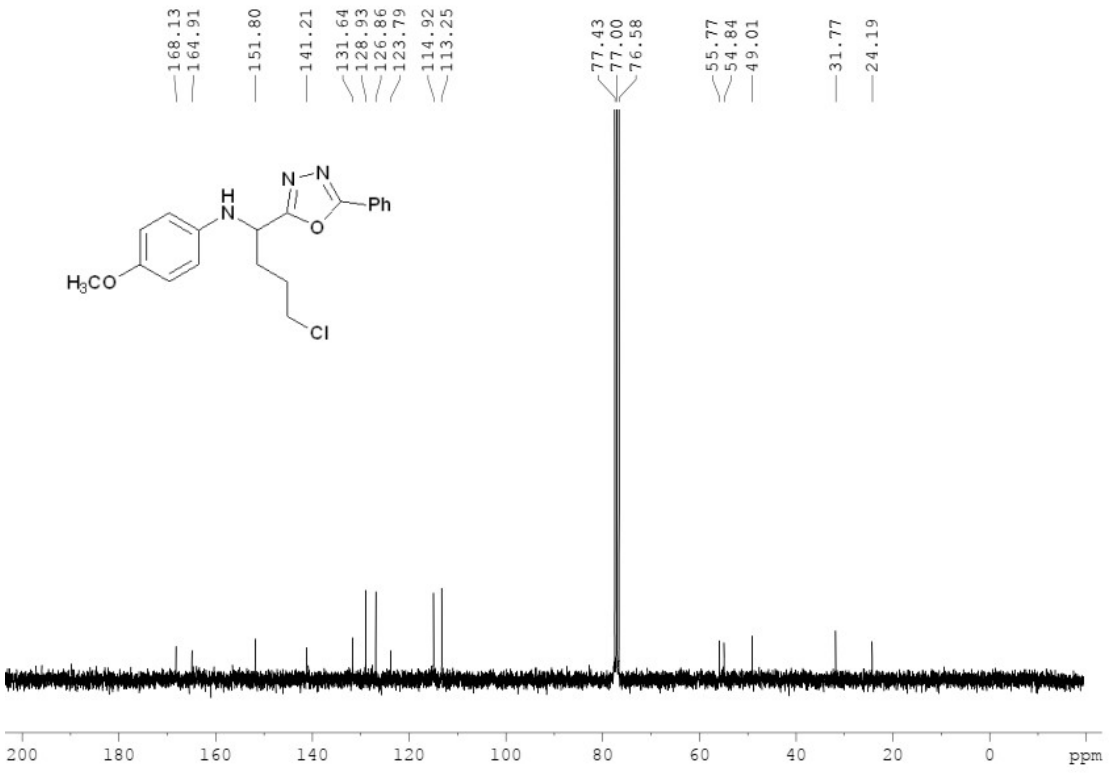
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ac**.



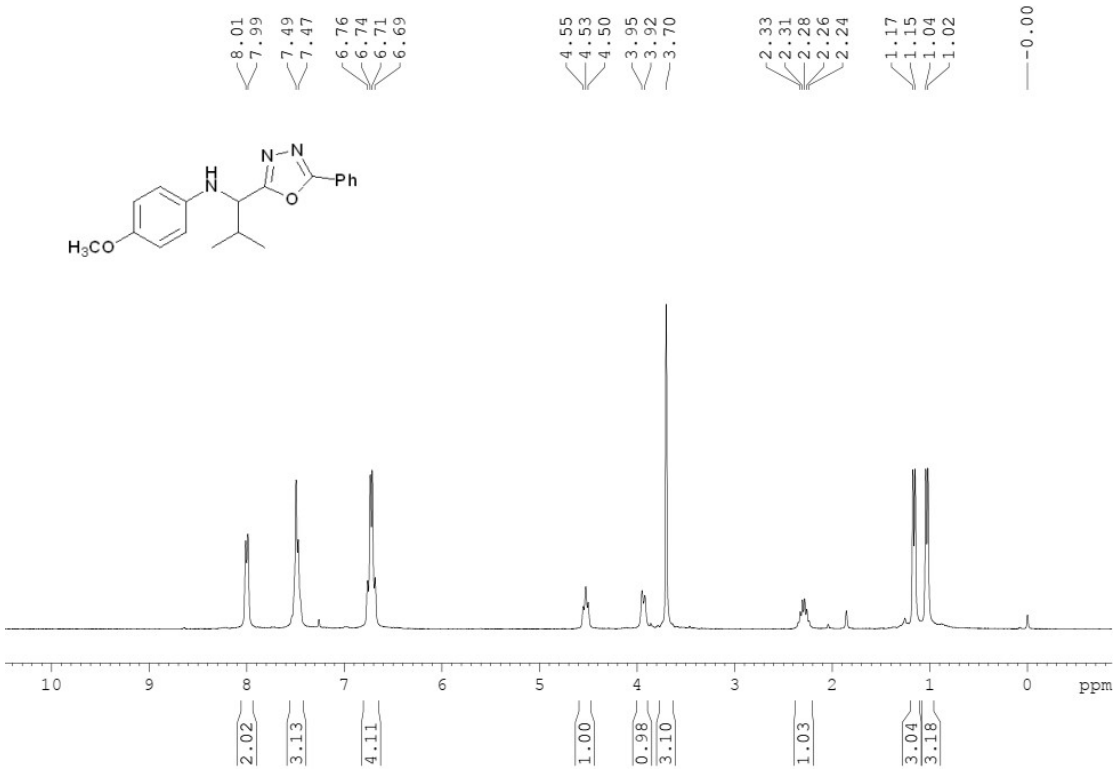
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ac**.



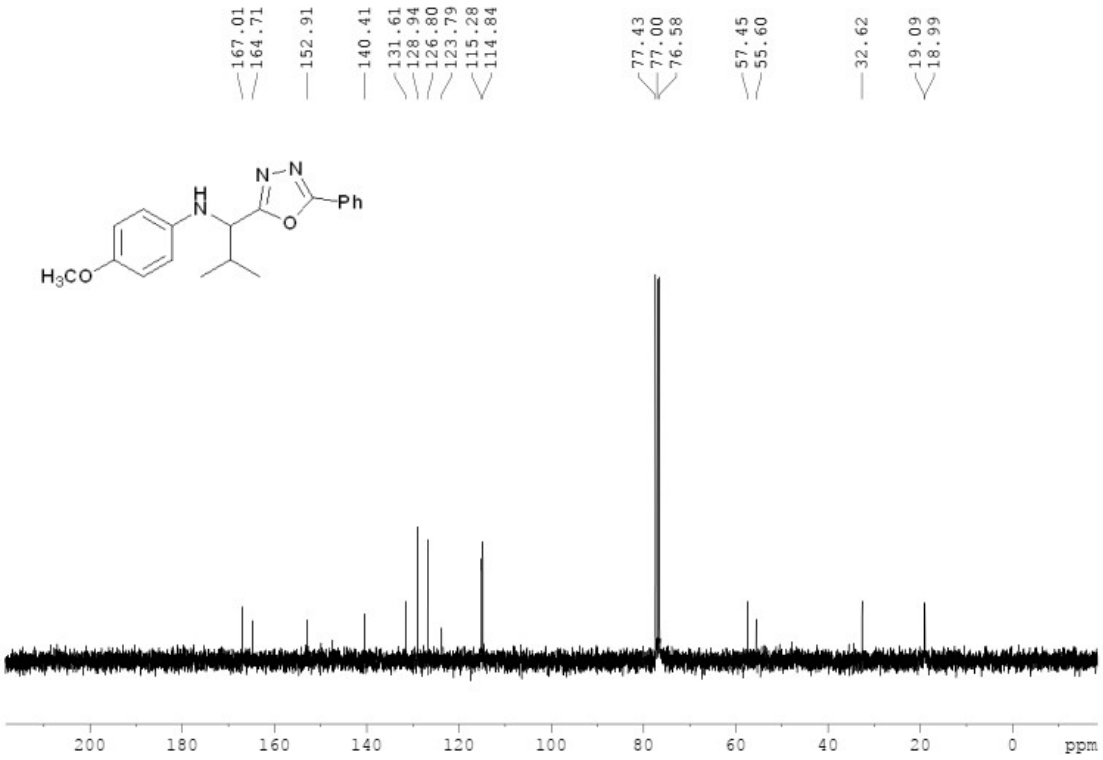
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ad**.



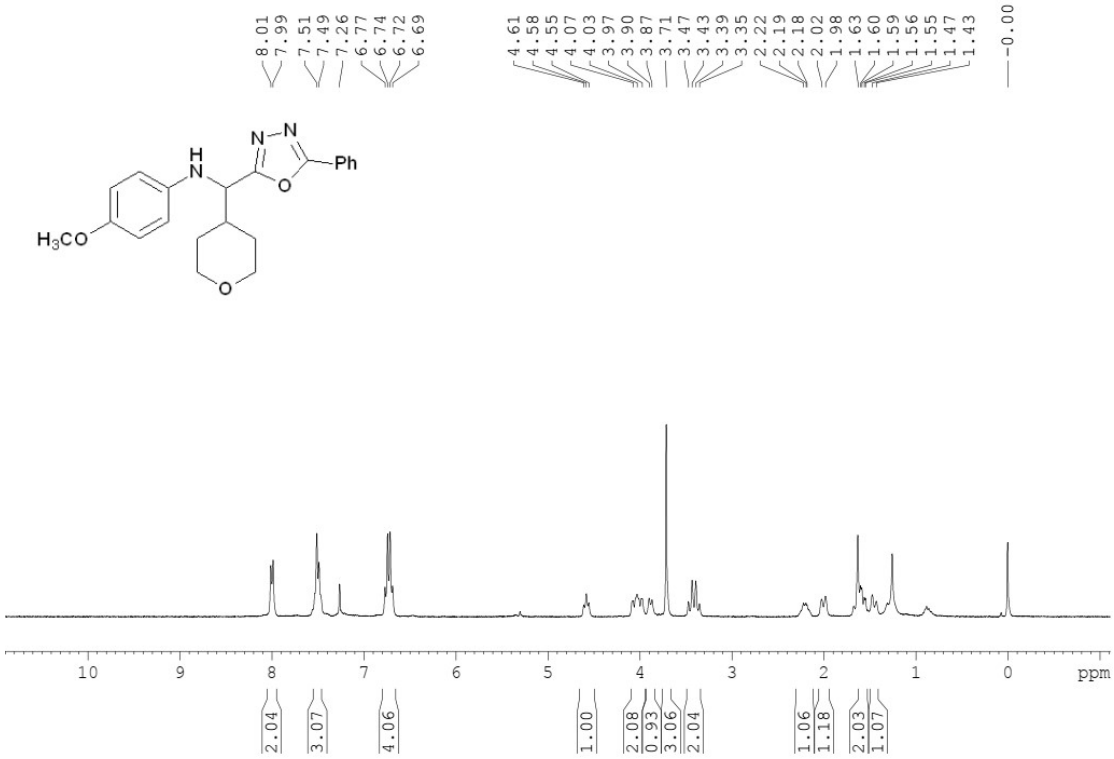
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ad**.



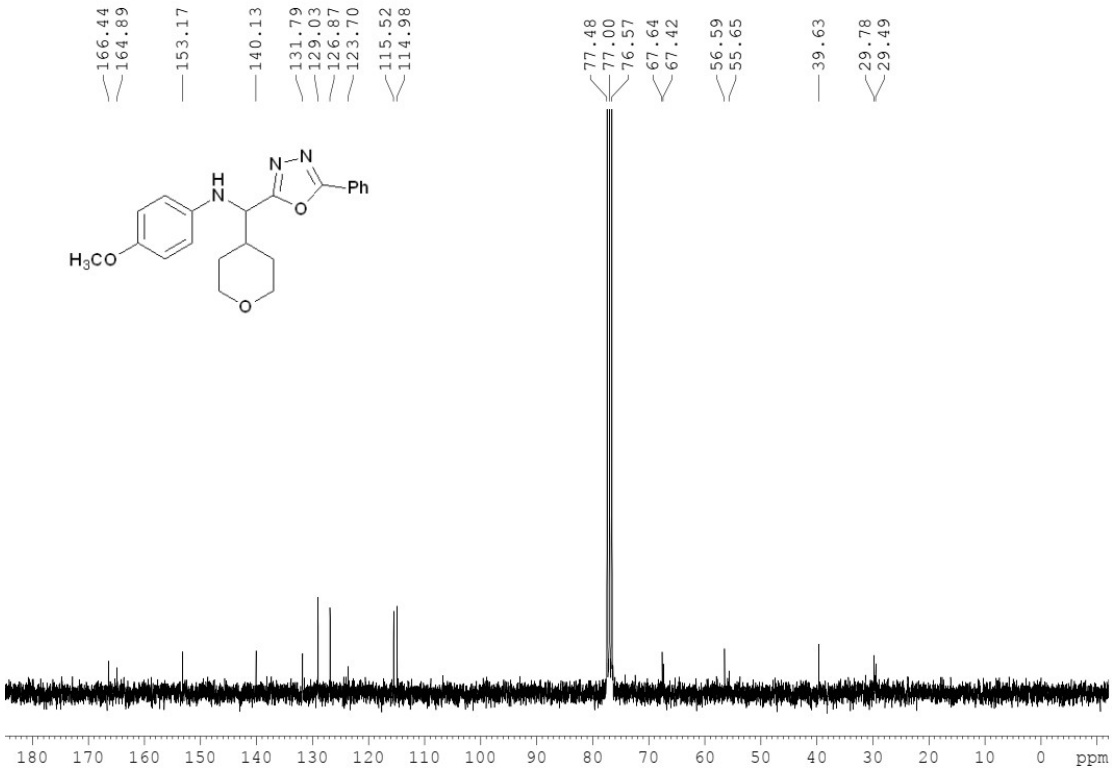
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ae**.



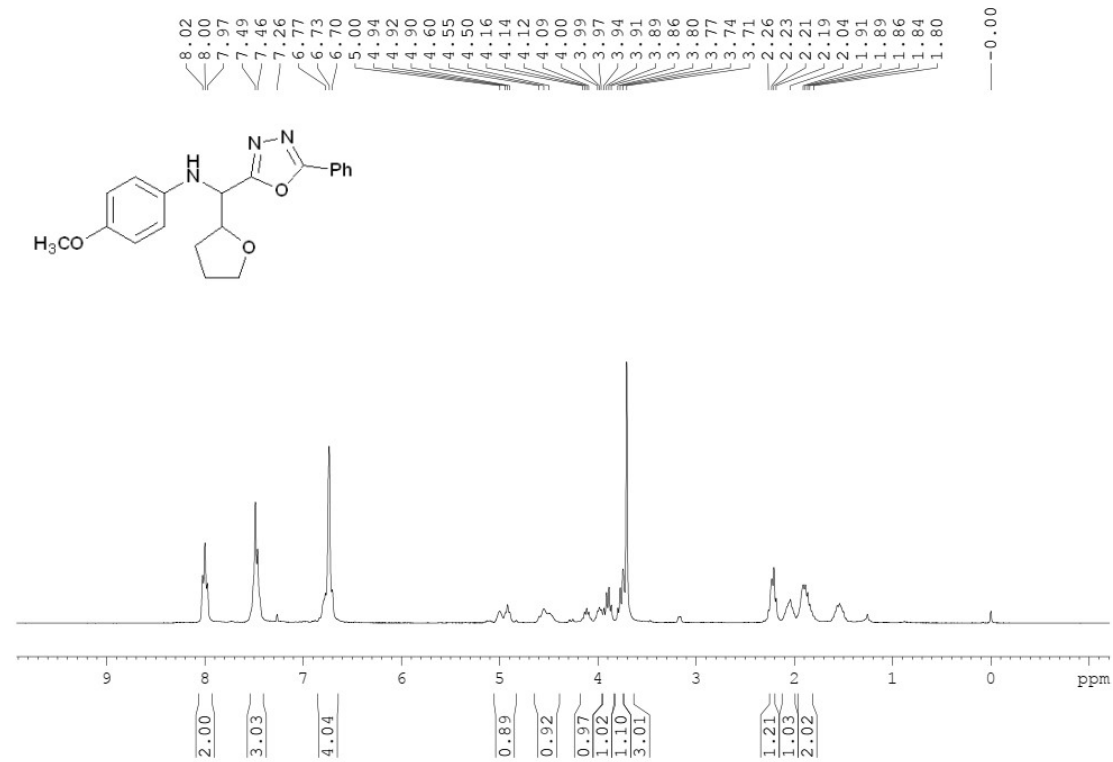
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ae**.



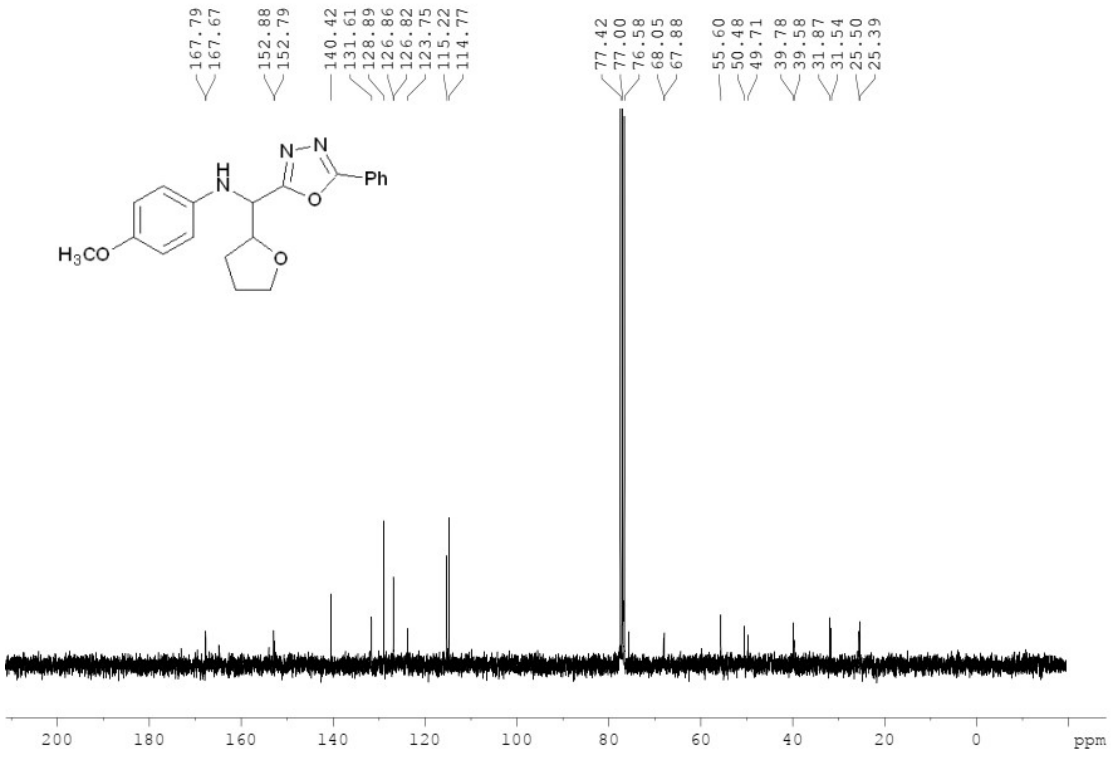
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3af**.



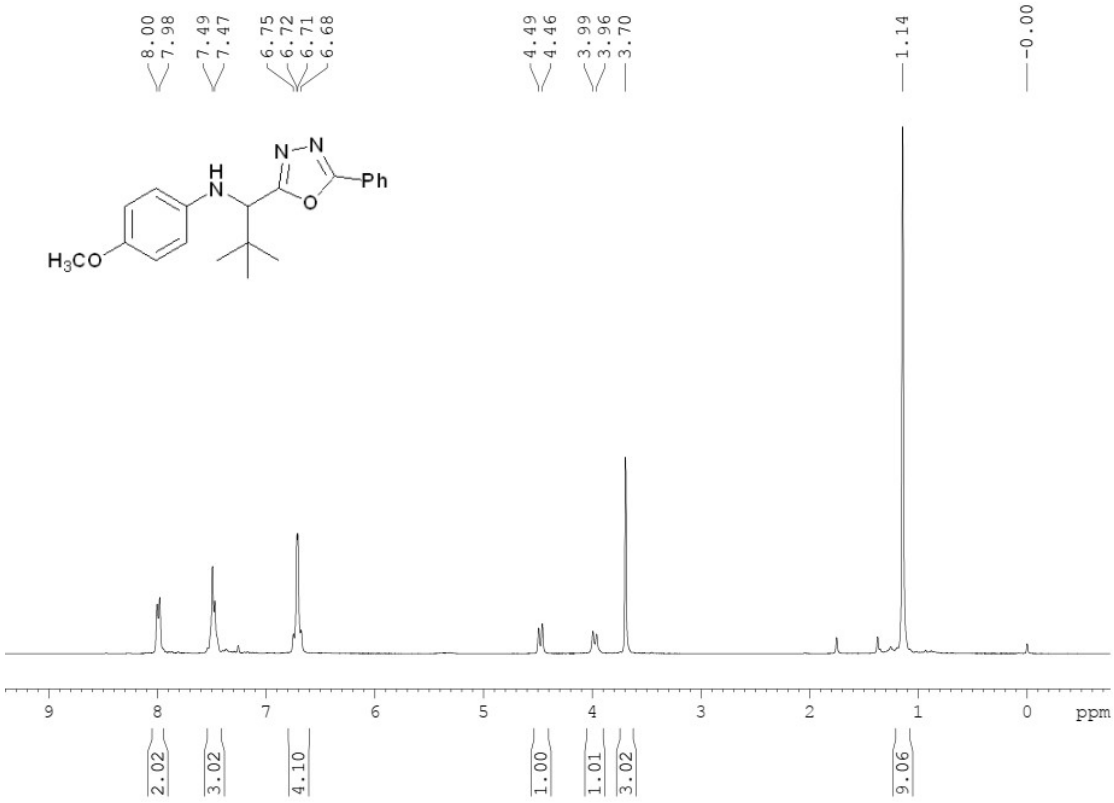
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3af**.



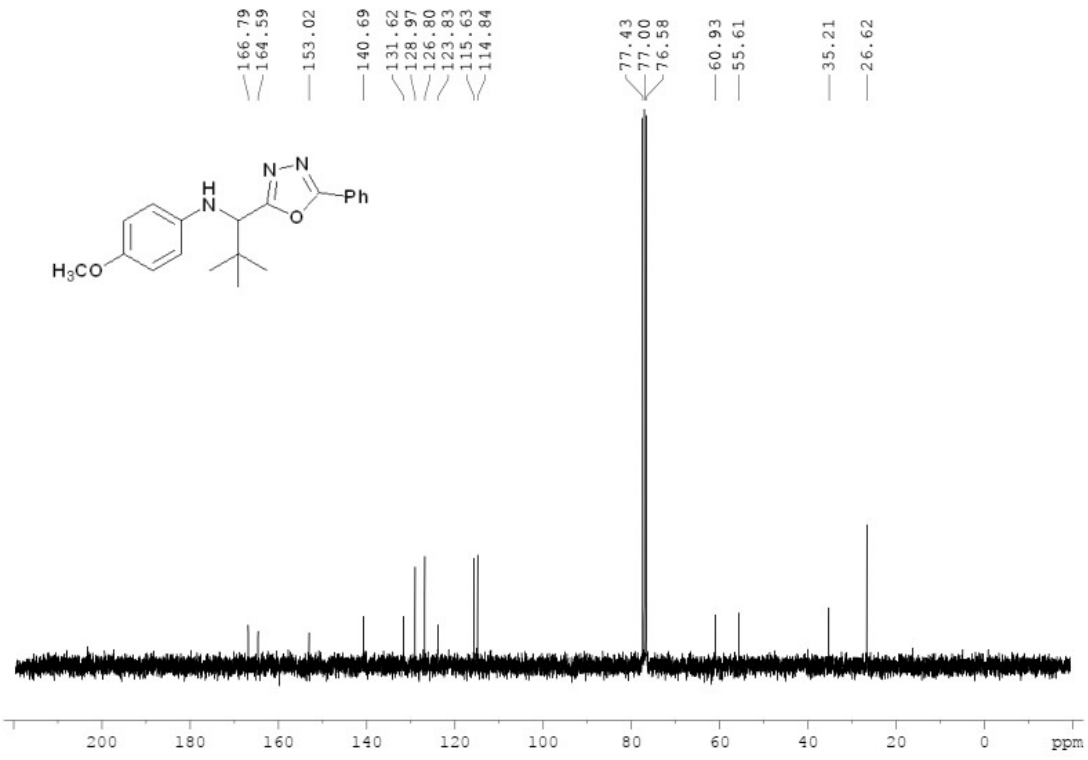
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ag**.



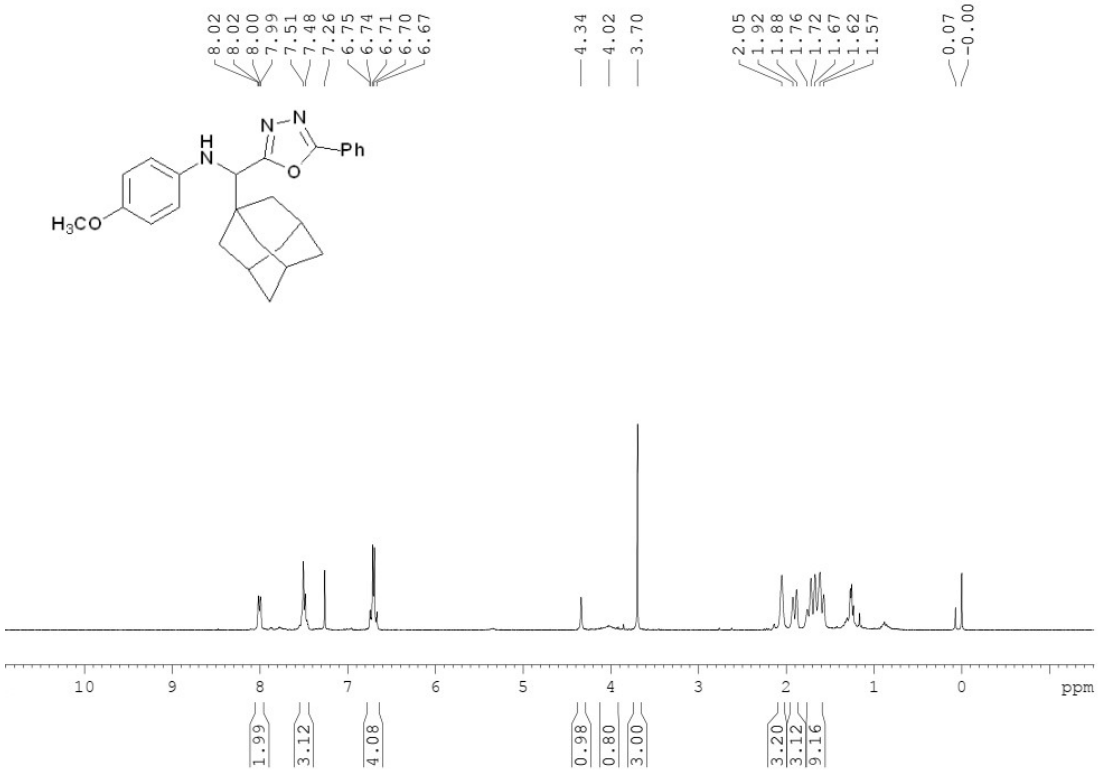
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ag**.



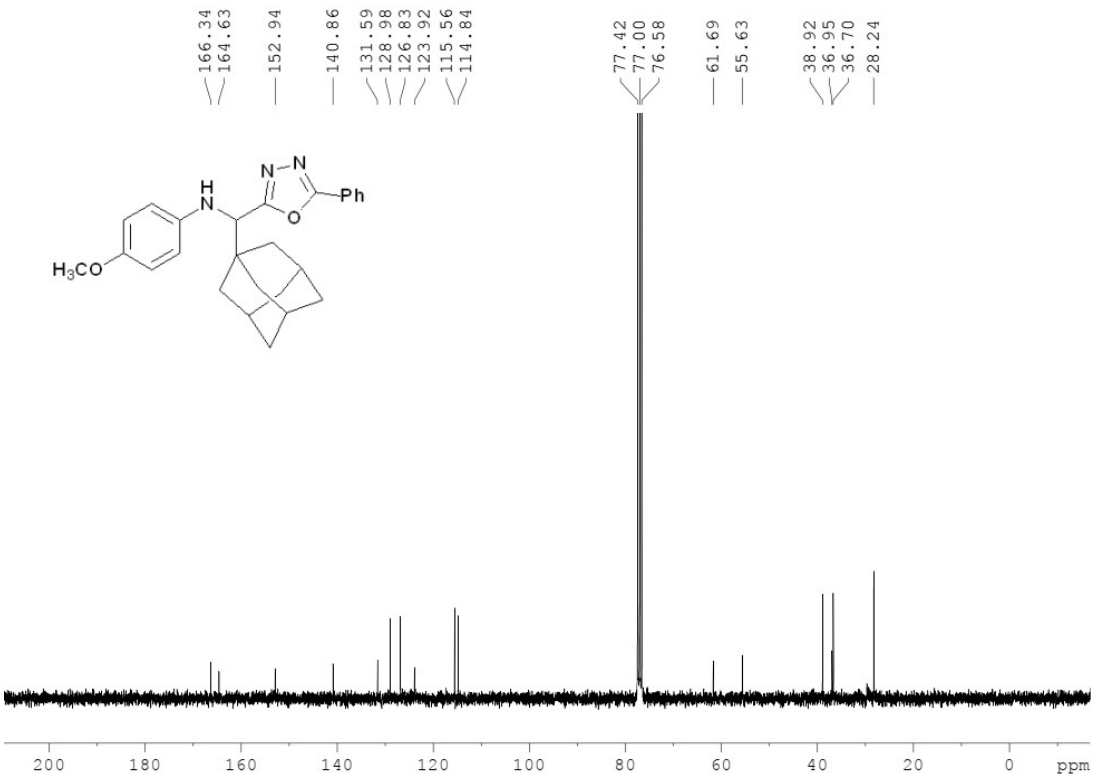
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ah**.



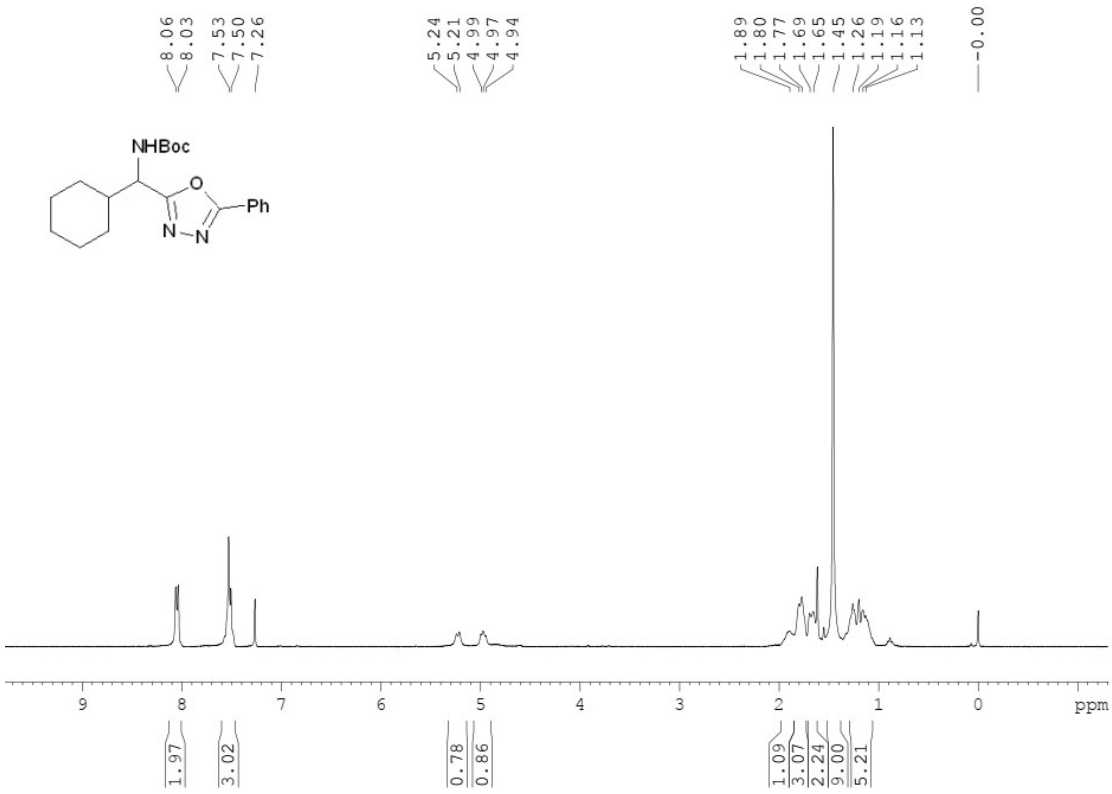
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ah**.



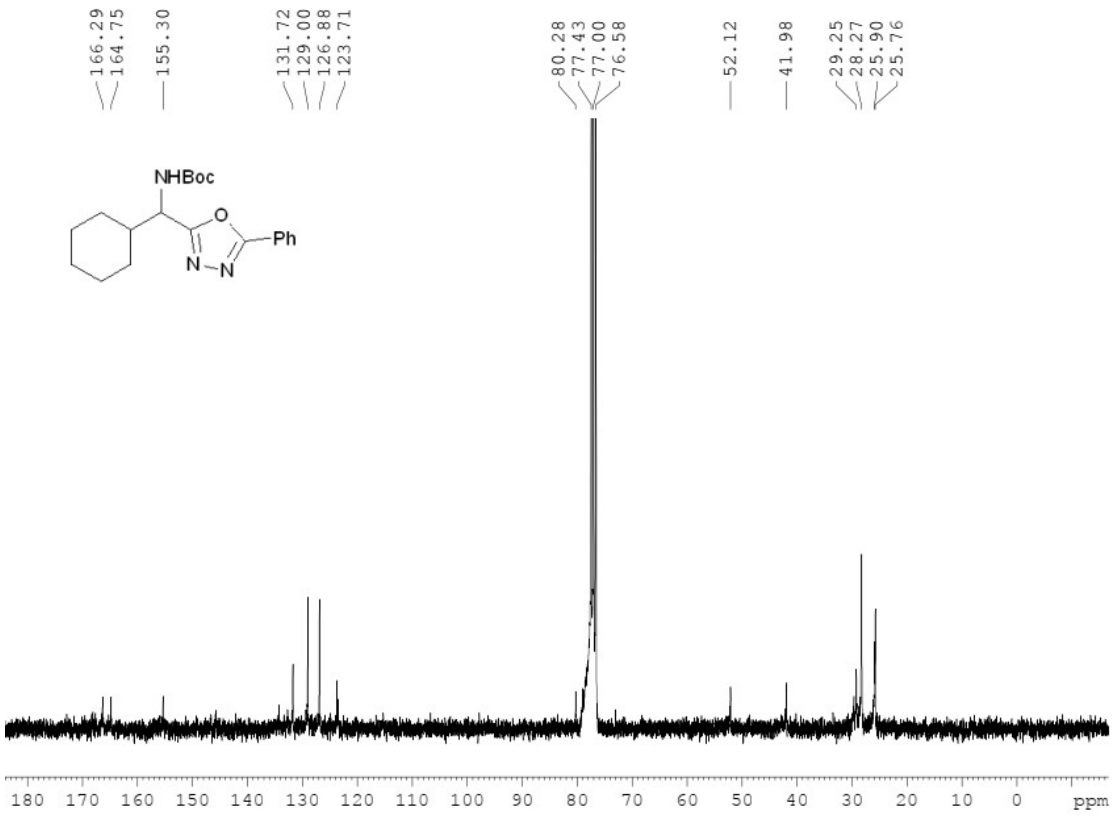
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **3ai**.



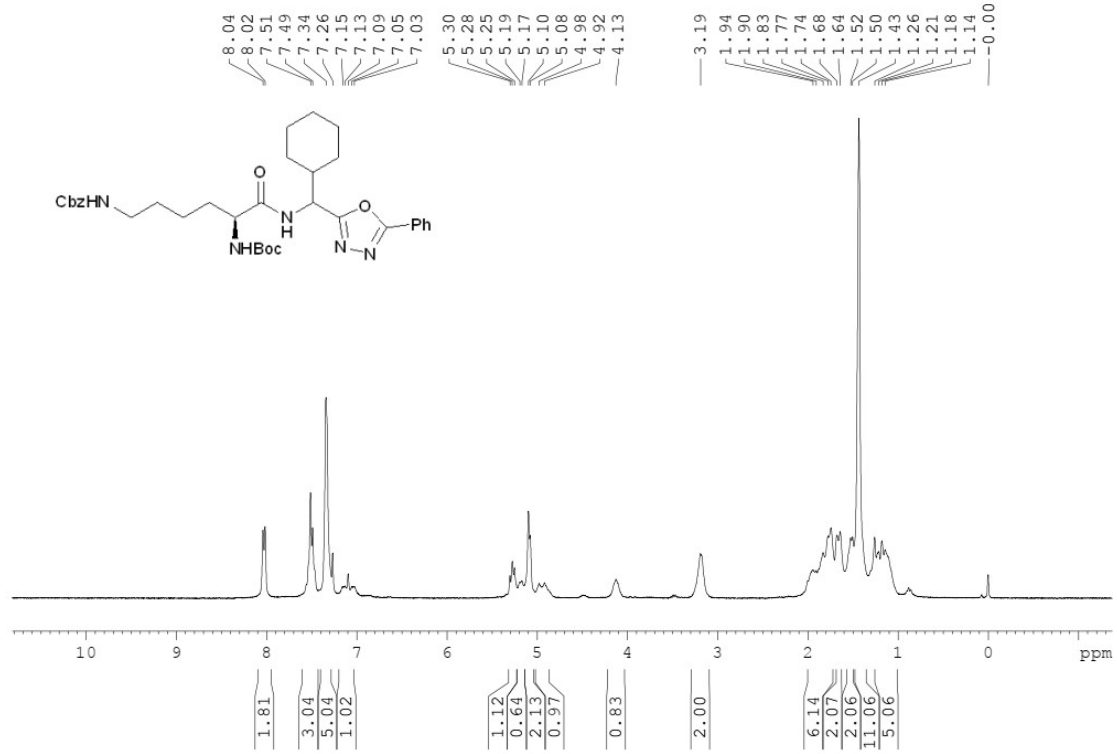
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **3ai**.



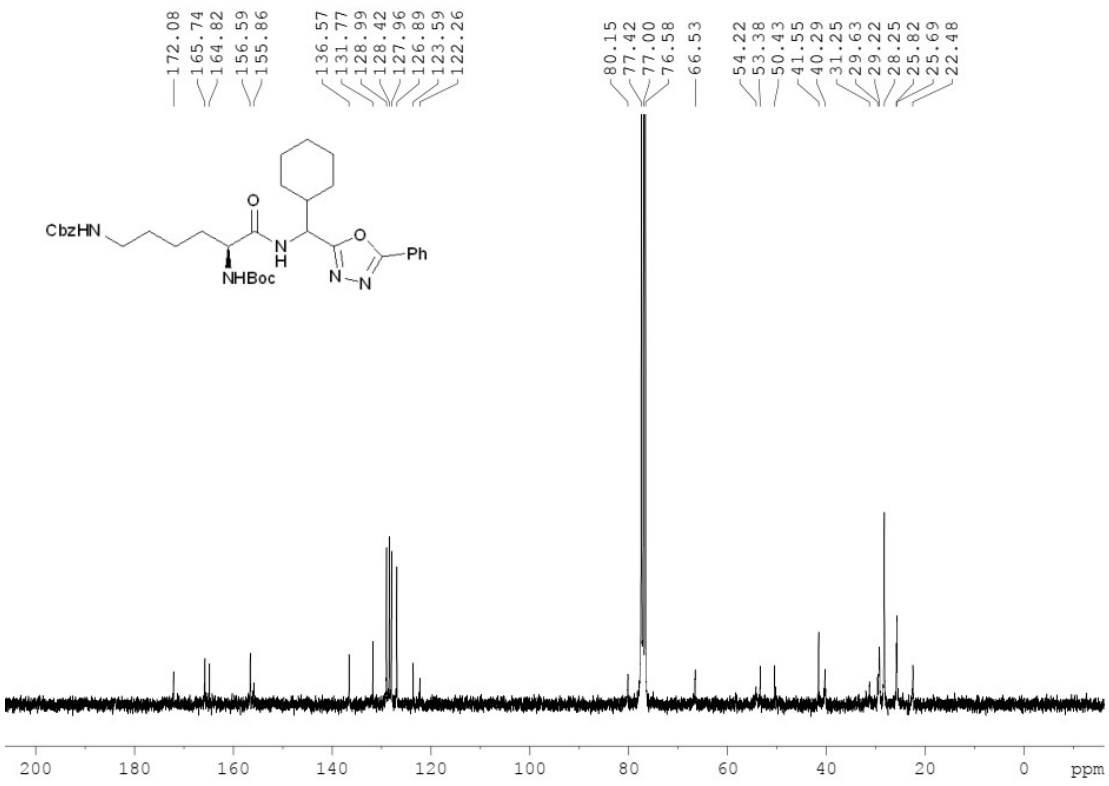
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **4a**.



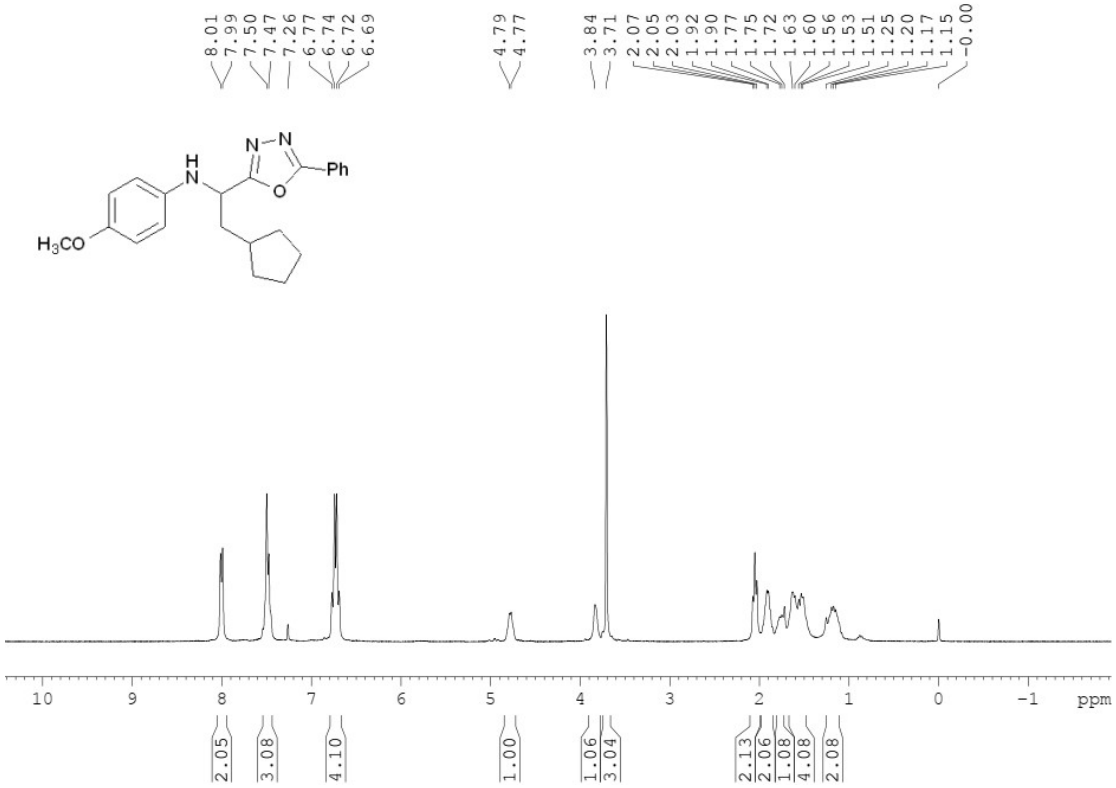
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **4a**.



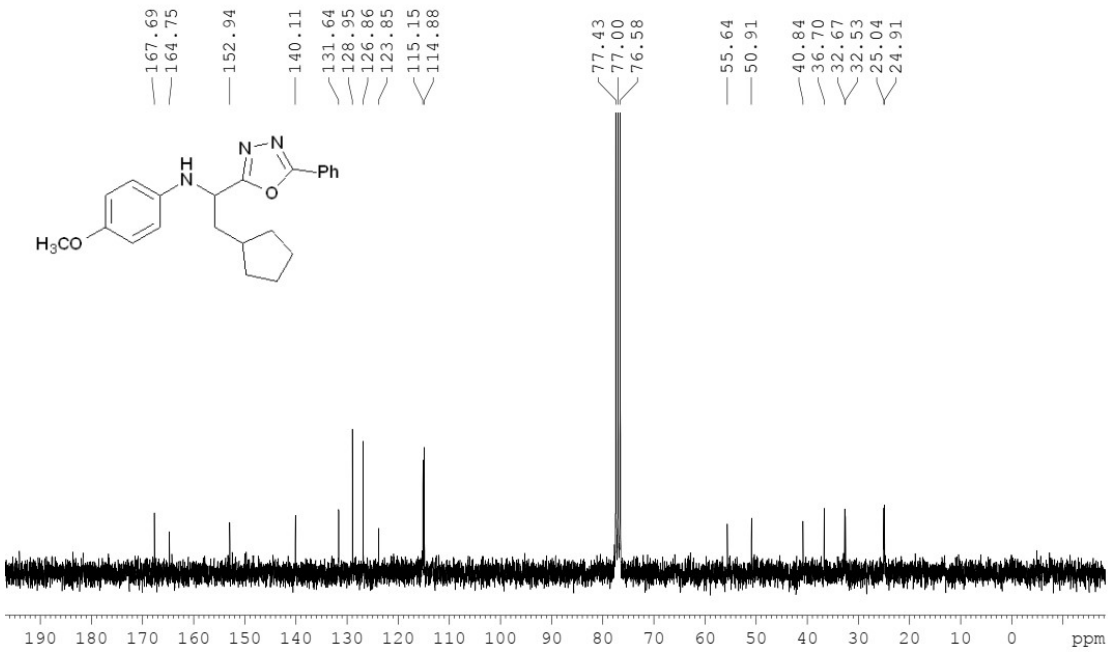
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **4b**.



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **4b**.



^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **6b**.



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of compound **6b**.

8. References

[1]. J. Leal, A. Sauer, J. Mayer, S. Stefanello, D. Gonçalves, F. Soares, B. Iglesias, D. Back, O .Rodrigues and L. Dornelles, Synthesis and Electrochemical and Antioxidant Properties of Chalcogenocyanate Oxadiazole and 5-Heteroarylchalcogenomethyl-1H-Tetrazole Derivatives, *New J. Chem.*, 2017, **41**, 5875-5883.

[2]. W. Liu, L. Li and C. J. Li, Empowering a Transition-Metal-Free Coupling between Alkyne and Alkyl Iodide with Light in Water, *Nat. Commun.*, 2015, **6**, 6526.