

Supplementary Information

¹⁵N-Insertion into indoles and indenenes for isotopically pure quinazolines and isoquinolines

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1. General methods

NMR spectra were recorded with tetramethylsilane as the internal standard. ^1H NMR spectra were recorded at 400 MHz or 500 MHz, ^{13}C NMR spectra were recorded at 100 MHz or 125 MHz (Bruker Avance), and ^{15}N NMR spectra were recorded at 50 MHz (Bruker Avance). ^1H NMR chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) with the solvent signal as the internal standard (CDCl_3 at 7.26 ppm, $(\text{CD}_3)_2\text{SO}$ at 2.50 ppm). ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard (CDCl_3 at 77.00 ppm, $(\text{CD}_3)_2\text{SO}$ at 39.52 ppm). Data are given as: s (singlet), d (doublet), t (triplet), q (quartet), dd (double of doublet), br (broad) or m (multiplets), coupling constants (Hz) and integration. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. High resolution mass spectra were obtained with the Q-TOF-Premier mass spectrometer. Reactions were monitored by TLC and visualized with ultraviolet light. IR spectra were recorded on a Thermo Fisher Nicolet Avatar 360 FTIR spectrometer on a KBr beam splitter. All the solvents were used directly without any purification.

The photochemical reaction was conducted at room temperature under visible light irradiation by a blue LED. A Photosyn-YL 6-position Photo-Reaction-System (Shanghai Quanhuan Technology Co., Ltd.) was employed, equipped with six 12 W blue LEDs emitting at 455-460 nm. The reaction vessel consisted of a borosilicate-glass test tube positioned 5 mm from the light source; no optical filter was used.

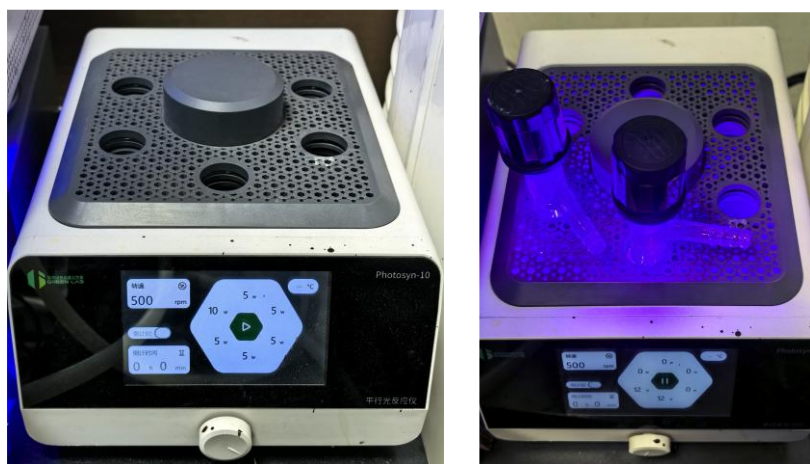
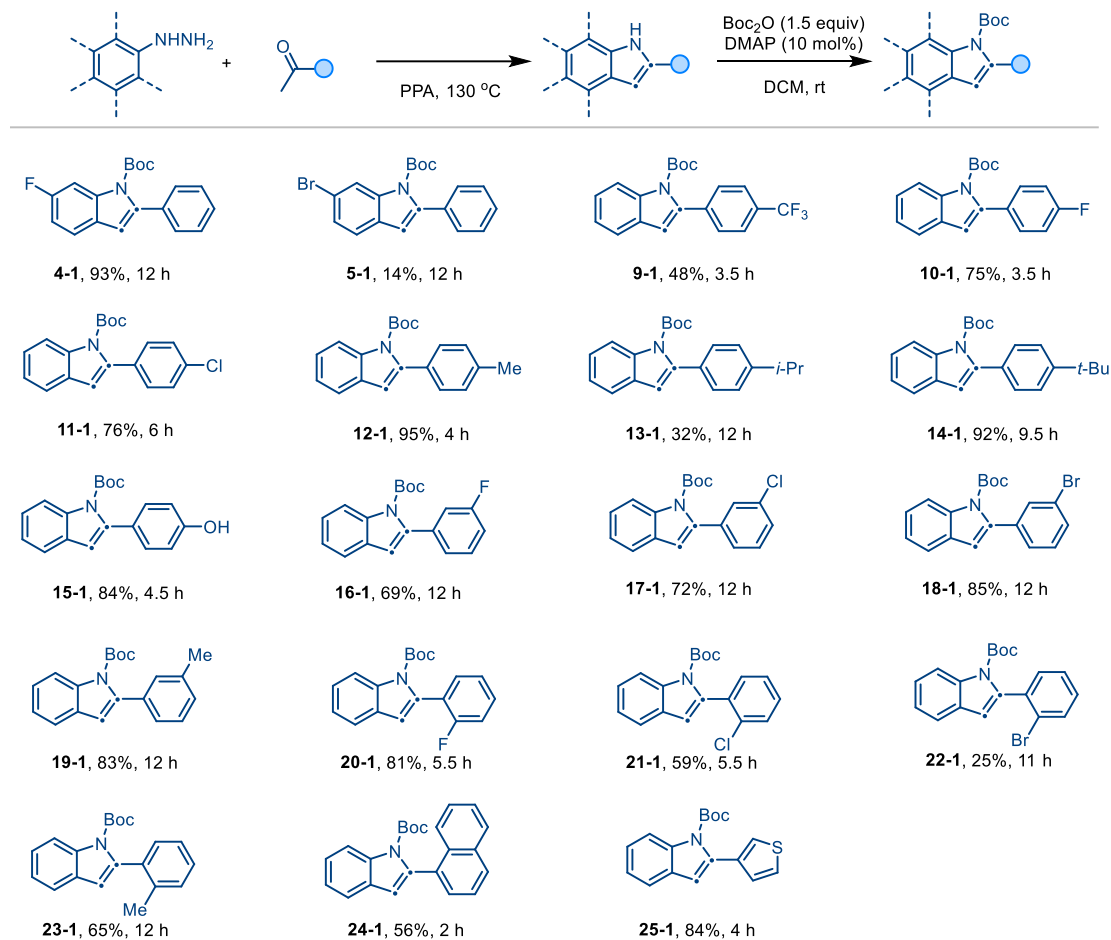


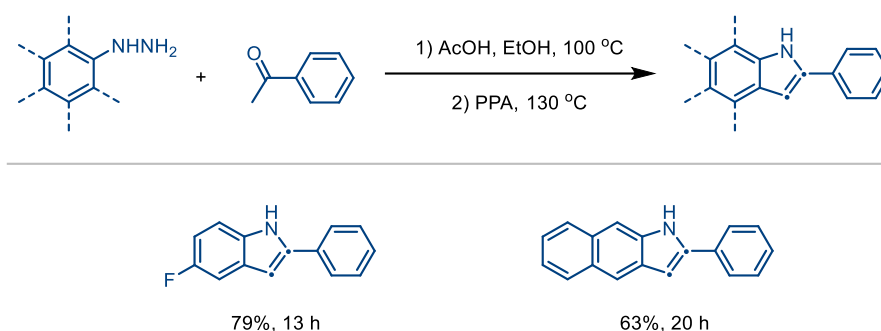
Figure S1. The photoreaction set-up.

2. Preparation of starting materials

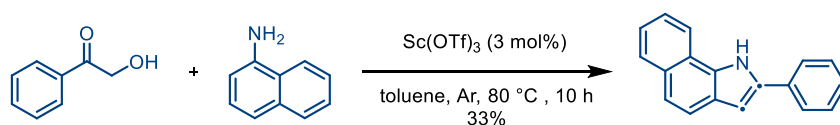
2.1 Preparation of indoles



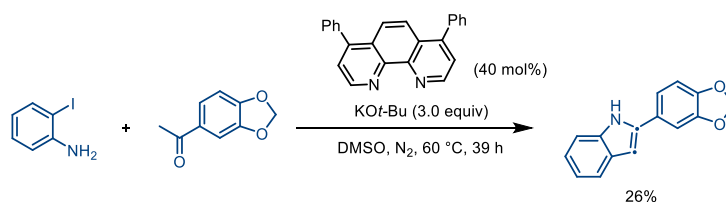
The above *N*-Boc indoles were synthesized according to literature reports.¹ Into a 50 mL round-bottom flask was added acetophenone (1.0 equiv), phenylhydrazine (1.2 equiv), and polyphosphoric acid (PPA, 10.0 mL). The reaction was heated to 130 °C with stirring until completion monitored by TLC. After cooling to room temperature, H₂O was added and the reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure, and purified by column chromatography to give the indoles. The above-obtained indoles were dissolved in dichloromethane, and DMAP (10 mol%) and Boc₂O (1.5 equiv) were then added. The reaction was stirred at room temperature until complete conversion of indoles monitored by TLC analysis. Then, the mixture was concentrated in vacuo and purified by column chromatography.



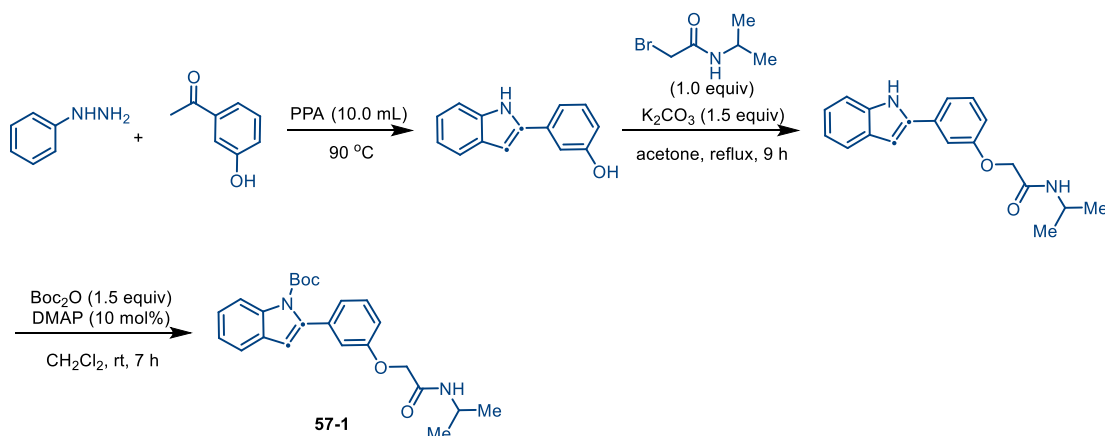
The above indoles were synthesized according to literature report.² Into a 50 mL round-bottom flask was added acetophenone (1.0 equiv), substituted phenylhydrazine (1.2 equiv), AcOH (2.0 equiv) and EtOH (20 mL). The reaction was heated to 100 °C with stirring until completion monitored by TLC. After cooling to room temperature, the mixture was concentrated under reduced pressure. PPA (10 mL) was added and the mixture was heated to 130 °C and stirred for 4 h. After cooling to room temperature, H₂O was added and the reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure, and purified by column chromatography to give the desired indoles.



This indole was synthesized according to literature report.³ To a 50 mL Schlenk tube charged with a magnetic stir bar were added 2-hydroxy-1-phenylethan-1-one (2.72 g, 20.0 mmol, 1.0 equiv), 1-naphthylamine (2.86 g, 20.0 mmol, 1.0 equiv), Sc(OTf)₃ (3 mol%), and toluene (20.0 mL). The reaction mixture was degasified by sparging with argon for 15 minutes. The reaction was heated to 80 °C and stirred for 10 h. The reaction mixture was cooled to room temperature, concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10:1 to 5:1) to afford the product as a yellow solid (1.63 g, 33%).



This indole was synthesized according to literature report.⁴ To an oven-dried 50 mL round-bottom flask charged with a magnetic stir bar were added 2-iodoaniline (1.31 g, 6.0 mmol, 1.0 equiv), *KOt*-Bu (2.02 g, 18.0 mmol, 3.0 equiv), bathophenanthroline (0.80 g, 2.4 mmol, 0.4 equiv) and DMSO (20 mL). The flask was cooled to 0 °C in an ice-water bath, evacuated and backfilled with nitrogen (three cycles). 1-(Benzo[*d*][1,3]dioxol-5-yl)ethan-1-one (1.97 g, 12.0 mmol, 2.0 equiv) was then added via syringe, and the resulting mixture was stirred at 60 °C for 39 h. Then, the mixture was cooled to room temperature. The reaction was quenched with sat. aq. NH_4Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, concentrated in vacuo, and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10:1 to 5:1) to afford the desired indole as a white solid (0.74 g, 26%).



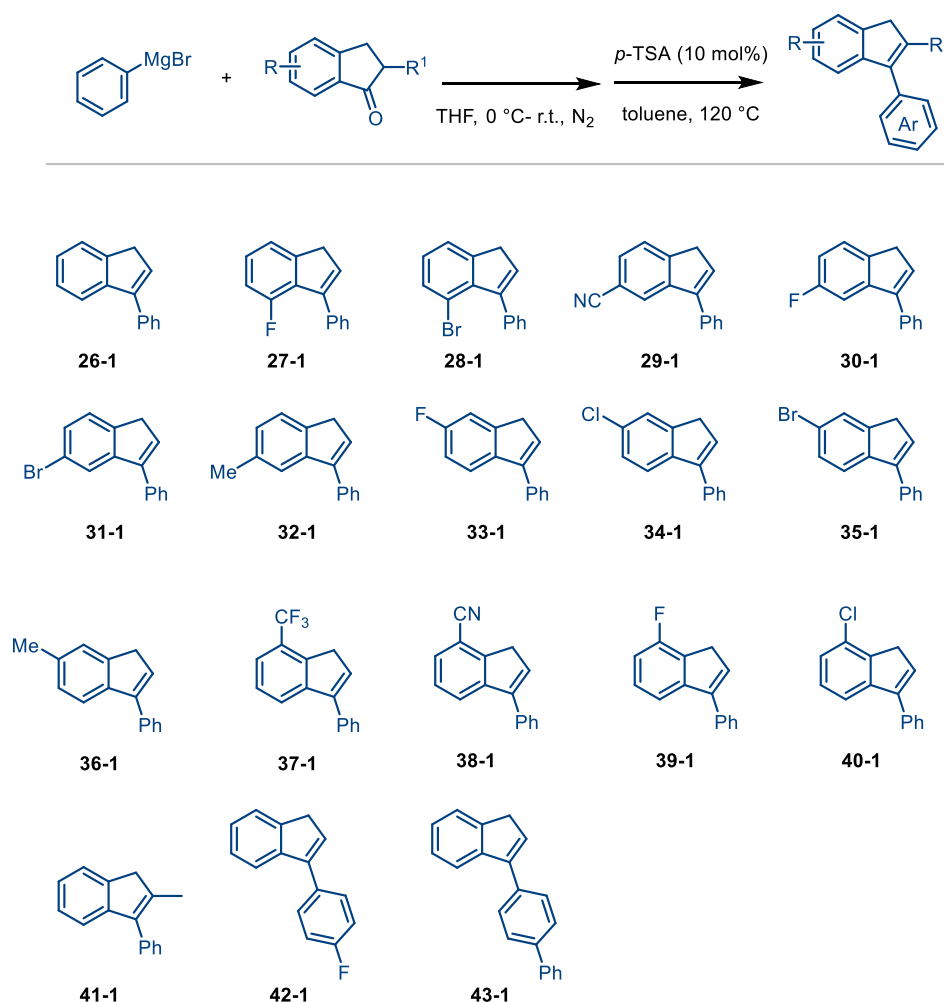
57-1 was synthesized according to literature reports.^{2,5} Into a 50 mL round-bottom flask was added 3-hydroxyacetophenone (0.68 g, 5.0 mmol), phenylhydrazine (0.81 g, 7.5 mmol), and polyphosphoric acid (PPA, 10.0 mL). The reaction was heated to 90 °C with stirring for 30 min. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure to give the crude product (0.48 g, 46%). The residue was directly used in the next step without further purification.

To the solution of the above-obtained product in acetone (10 mL) was added 2-bromo-*N*-isopropylacetamide (0.41 g, 2.3 mmol, 1.0 equiv) and K_2CO_3 (0.48 g, 3.4 mmol, 1.5 equiv). The reaction was heated to reflux for 9 h. After cooling to room temperature, the

solvent was removed under reduced pressure and the residue was purified by silica-gel column chromatography using petroleum ether/ethyl acetate as the eluent to produce the *O*-alkylated indole (0.53 g, 75%) as a yellow solid.

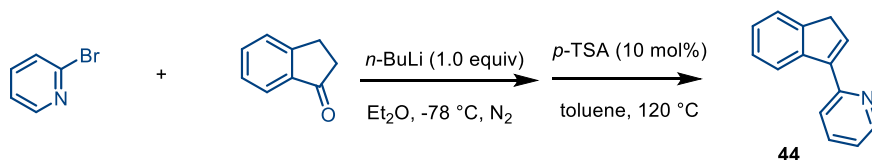
To a 50 mL round-bottom flask equipped with a magnetic stir bar were added the above-obtained *O*-alkylated indole (0.53 g), DMAP (0.02 g), and Boc_2O (0.56 g), followed by anhydrous DCM (10 mL). The resulting mixture was stirred at room temperature for 7 h. The reaction mixture was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1:1) to afford **57-1** (0.70 g, 98% yield) as a yellow solid.

2.2 Preparation of indenenes

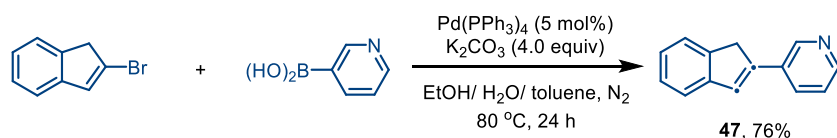


The synthesis of **26-1** was synthesized according to literature report.⁶ To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added 2,3-dihydro-1*H*-inden-1-one (3.96 g, 30.0 mmol, 1.0 equiv), and anhydrous tetrahydrofuran

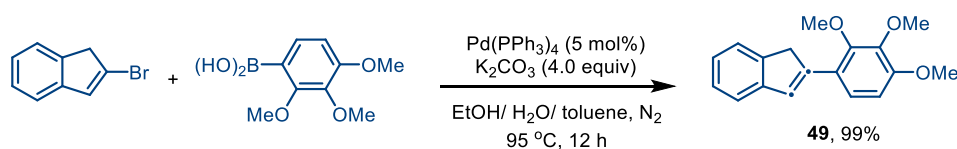
(THF, 30 mL). The flask was cooled to 0 °C in an ice-water bath, evacuated and backfilled with nitrogen (three cycles). Phenylmagnesium bromide (1.0 M in THF, 45.0 mL, 45.0 mmol, 1.5 equiv) was then added dropwise via syringe, and the resulting mixture was stirred at 0 °C for 30 min, then allowed to warm to room temperature with additional stirring for 3 h. The reaction was quenched with sat. aq. NH₄Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was dissolved in toluene (20 mL), and *p*-toluenesulfonic acid (*p*-TSA, 0.57 g, 3.0 mmol, 0.1 equiv) was added. The reaction was heated to 120 °C and stirred for 5 h. After cooling to room temperature, the mixture was concentrated in vacuo and purified by silica gel column chromatography (petroleum ether as the eluent) to afford **26-1** as a yellow oil (3.80 g, 66%). The remaining indenenes listed in the above scheme were prepared in an analogous manner.



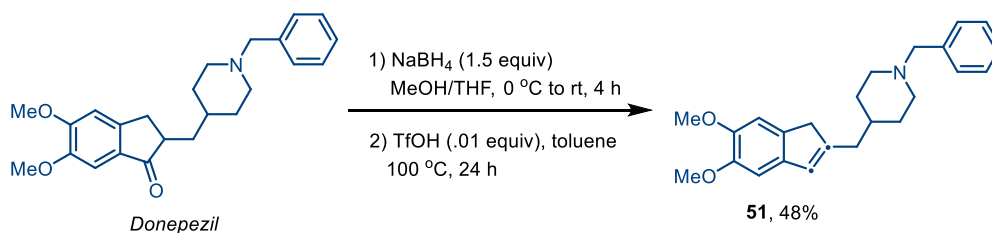
To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added 2,3-dihydro-1*H*-inden-1-one (3.96 g, 30.0 mmol, 1.0 equiv), 2-bromopyridine (4.74 g, 30.0 mmol, 1.0 equiv), and anhydrous ether (30 mL). The flask was cooled to -78 °C, evacuated and backfilled with nitrogen (three cycles). *n*-BuLi (2.5 M in THF, 12.0 mL, 30.0 mmol, 1.0 equiv) was then added dropwise via syringe, and the resulting mixture was stirred at -78 °C for 1 h. The reaction was quenched with sat. aq. NH₄Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was dissolved in toluene (20 mL), and *p*-toluenesulfonic acid (*p*-TSA, 0.57 g, 3 mmol, 0.1 equiv) was added. The reaction was heated to 120 °C and stirred for 7 h. After cooling to room temperature, the mixture was concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20:1 as the eluent) to afford **44** as a yellow solid (2.26 g, 39%).



This compound was prepared according to literature procedures.⁷ To a 50 mL Schlenk tube charged with a magnetic stir bar were added 2-bromo-1*H*-indene (1.00 g, 5.13 mmol, 1.0 equiv), pyridin-3-ylboronic acid (0.94 g, 7.68 mmol, 1.5 equiv), Pd(PPh₃)₄ (5 mol%), K₂CO₃ (2.83 g, 20.5 mmol, 4.0 equiv). Then, a combined solvents of EtOH (1.5 mL), H₂O (3.0 mL) and toluene (6.0 mL) were added. The reaction mixture was degasified by sparging with nitrogen for 15 minutes. The reaction was heated to 80 °C and stirred for 24 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (30.0 mL), and washed with H₂O (3 x 30.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 25:1 as the eluent) to afford **47** as a white solid (751.2 mg, 76%).



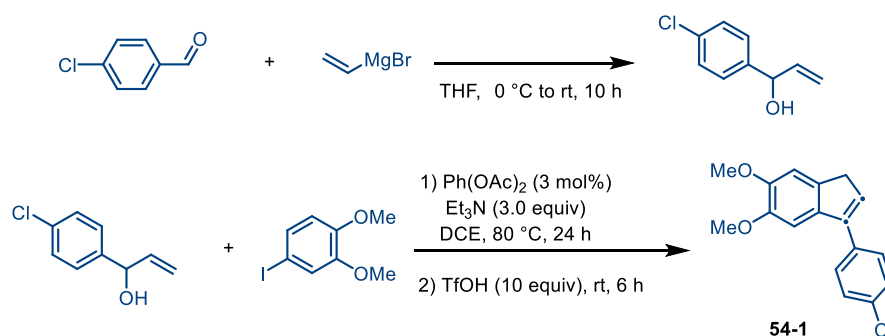
This compound was prepared according to literature procedures.⁸ To a 50 mL Schlenk tube charged with a magnetic stir bar were added 2-bromo-1*H*-indene (487.7 mg, 2.5 mmol, 1.0 equiv), (2,3,4-trimethoxyphenyl)boronic acid (0.80 g, 3.75 mmol, 1.5 equiv), Pd(PPh₃)₄ (5 mol%), K₂CO₃ (1.38 g, 10.0 mmol, 4.0 equiv). Then, a combined solvents of EtOH (1.5 mL), H₂O (3.0 mL) and toluene (5.0 mL) were added. The reaction mixture was degasified by sparging with nitrogen for 15 minutes. The reaction was heated to 95 °C and stirred for 12 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (30.0 mL), and washed with H₂O (3 x 30.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 15:1 as the eluent) to afford **49** as a white solid (698.2 mg, 99%).



The synthesis of **59-1** was synthesized according to literature report.⁹ To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added *Donepezil* (2.00 g,

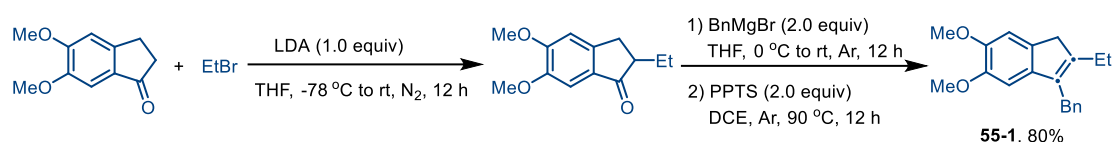
5.3 mmol, 1.0 equiv), anhydrous tetrahydrofuran (THF, 3 mL), and MeOH (6 mL). The flask was cooled to 0 °C in an ice-water bath. NaBH₄ (298.6 mg, 7.9 mmol, 1.5 equiv) was then added slowly, and the resulting mixture was warmed to room temperature with stirring for 4 h. The reaction was quenched with sat. aq. NH₄Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo to give the crude product.

The residue was dissolved in toluene (10 mL), and TfOH (100.2 mg, 0.53 mmol) was added. The reaction was heated to 100 °C and stirred for 24 h. The reaction mixture was cooled to room temperature, diluted with dichloromethane (30.0 mL), and washed with sat. Na₂CO₃ solution (30.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 25:1 as the eluent) to afford the dehydrated product as a white solid (878.9 mg, 48%).



The synthesis of **54-1** was synthesized according to literature reports.¹⁰ To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added *p*-chlorobenzaldehyde (1.41 g, 10.0 mmol, 1.0 equiv), and anhydrous tetrahydrofuran (THF, 15 mL). The flask was cooled to 0 °C in an ice-water bath, evacuated and backfilled with nitrogen (three cycles). Vinylmagnesium bromide (1.0 M in THF, 12.0 mL, 12.0 mmol, 1.2 equiv) was then added dropwise via syringe, and the resulting mixture was stirred at 0 °C for 2 h, then allowed to warm to room temperature with additional stirring for 8 h. The reaction was quenched with sat. aq. NH₄Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20:1 as the eluent) to afford the intermediate as a yellow oil (1.15 g, 68%).

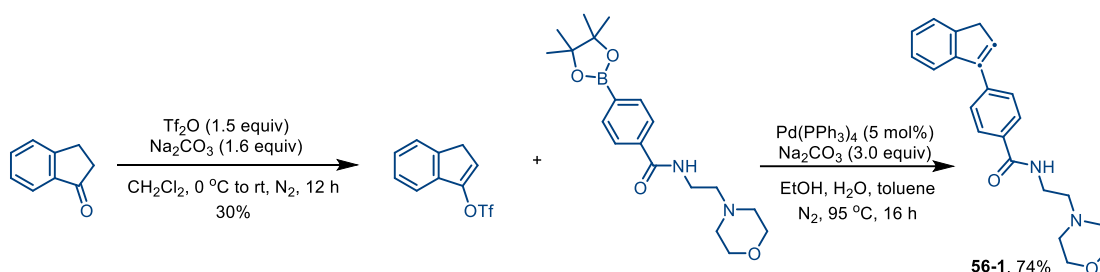
To a 50 mL Schlenk tube charged with a magnetic stir bar were added the above-obtained product (84.3 mg, 0.5 mmol, 1.0 equiv), 4-iodo-1,2-dimethoxybenzene (132.0 mg, 0.5 mmol, 1.0 equiv), Pd(OAc)₂ (3 mol%), Et₃N (151.8 mg, 1.5 mmol, 3.0 equiv). Then, DCE (2.0 mL) was added. The reaction was heated to 80 °C and stirred for 24 h. The reaction mixture was cooled to room temperature. Then, TfOH (0.75 g, 5 mmol, 10.0 equiv) was added. The reaction was stirred at room temperature for 12 h. Upon completion, the mixture was concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20:1 as the eluent) to afford **54-1** as a yellow oil (35.6 mg, 25%).



The synthesis of **55-1** was synthesized according to literature report. To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added 5,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (3.84 g, 20.0 mmol, 1.0 equiv), and anhydrous tetrahydrofuran (THF, 15 mL). The flask was cooled to -78 °C in an ice-water bath, evacuated and backfilled with nitrogen (three cycles). LDA (2.0 M in THF, 10.0 mL, 20.0 mmol, 1.0 equiv) was then added dropwise via syringe, and the resulting mixture was stirred at 0 °C for 2 h, then bromoethane (2.18 g, 20.0 mmol, 1.0 equiv) was added via syringe. The reaction was allowed to warm to room temperature with additional stirring for 10 h. The reaction was quenched with sat. aq. NH₄Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20:1 as the eluent) to afford the intermediate as a white solid (0.93 g, 21%).

To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added 2-ethyl-5,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (330.4 mg, 1.5 mmol, 1.0 equiv), and anhydrous tetrahydrofuran (THF, 15 mL). The flask was cooled to 0 °C in an ice-water bath, evacuated and backfilled with argon (three cycles). Benzylmagnesium bromide (1.0 M in THF, 3.0 mL, 3.0 mmol, 2.0 equiv) was then added dropwise via syringe. The reaction was allowed to warm to room temperature with stirring for 12 h. The reaction was quenched with

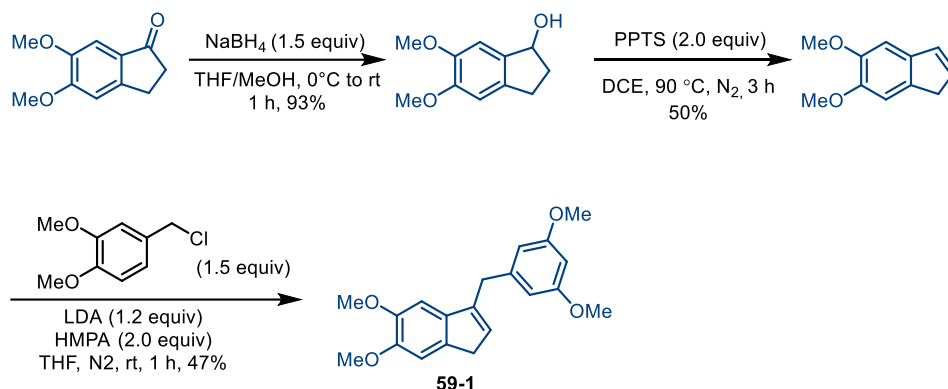
sat. aq. NH_4Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, concentrated in vacuo. The residue was dissolved in 1,2-dichloroethane (4 mL), and PPTS (753.9 mg, 3.0 mmol, 2.0 equiv) was added. The reaction mixture was degasified by sparging with argon for 15 minutes. The reaction was heated to 90 °C and stirred for 12 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (5.0 mL), and washed with sat. Na_2CO_3 solution (5.0 mL). The organic layer was dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1 as the eluent) to afford the dehydrated product as a yellow oil (353.3 mg, 80%).



This compound was prepared according to literature procedures.¹² To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added 2,3-dihydro-1*H*-inden-1-one (2.64 g, 20.0 mmol, 1.0 equiv), Na_2CO_3 (3.39 g, 32.0 mmol, 1.6 equiv) and dichloromethane (15 mL). The flask was cooled to -0 °C in an ice-water bath, evacuated and backfilled with nitrogen (three cycles). Triflic anhydride (8.46 g, 30.0 mmol, 1.5 equiv) was then added dropwise via syringe. The reaction was allowed to warm to room temperature with stirring for 12 h. The reaction was quenched with sat. aq. NH_4Cl (50 mL), extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10:1 as the eluent) to afford 1*H*-inden-3-yl trifluoromethanesulfonate as a brown oil (1.61 g, 30%).

To a 50 mL Schlenk tube charged with a magnetic stir bar were added trifluoromethanesulfonate (554.9 mg, 2.1 mmol, 1.0 equiv), *N*-(2-morpholinoethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (1.00 g, 2.80 mmol, 1.3 equiv), $\text{Pd}(\text{PPh}_3)_4$ (5 mol%), Na_2CO_3 (667.7 mg, 6.30 mmol, 3.0 equiv). Then, a combined solvents of EtOH (4.0 mL), H_2O (4.0 mL) and toluene (5.0 mL) were added.

The reaction mixture was degasified by sparging with nitrogen for 15 minutes. The reaction was heated to 95 °C and stirred for 16 h. The reaction mixture was cooled to room temperature, diluted with dichloromethane (10.0 mL), and washed with H₂O (3 x 30.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo and purified by silica gel column chromatography (ethyl acetate as the eluent) to afford **56-1** as a gray solid (542.8 mg, 74%).



The synthesis of **59-1** was synthesized according to literature report.¹³ To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added 5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (10.00 g, 52.0 mmol, 1.0 equiv), anhydrous tetrahydrofuran (THF, 20 mL), and MeOH (40 mL). The flask was cooled to 0 °C in an ice-water bath. NaBH₄ (2.95 mg, 78.0 mmol, 1.5 equiv) was then added slowly, and the resulting mixture was warmed to room temperature with stirring for 1 h. The reaction was quenched with sat. aq. NH₄Cl (50 mL), extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo to give the crude product (9.33 g, 93%).

The residue (1.94 g, ca. 10.0 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (40 mL), and PPTS (5.03 g, 20.0 mmol, 2.0 equiv) was added. The reaction mixture was degasified by sparging with nitrogen for 15 minutes. The reaction was heated to 90 °C and stirred for 3 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (30.0 mL), and washed with sat. Na₂CO₃ solution (30.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10:1 as the eluent) to afford the dehydrated product as a white solid (879.0 mg, 50%).

To an oven-dried 100 mL round-bottom flask charged with a magnetic stir bar were added LDA (1.8 mL, 2.0 M in THF, 3.6 mmol, 1.2 equiv) under a nitrogen atmosphere at -78 °C. A solution of the above-obtained product (528.6 mg, 3.0 mmol, 1.0 equiv) and HMPA (1.08 g, 6.0 mmol, 2.0 equiv) (dissolved in anhydrous THF, 10 mL) was added dropwise via syringe, and the mixture was stirred for 5 min. Subsequently, a solution of 4-(chloromethyl)-1,2-dimethoxybenzene (839.7 mg, 4.5 mmol, 1.3 equiv) in anhydrous THF (5 mL) was added. The reaction mixture was stirred at room temperature for 1 h under nitrogen, and the progress was monitored by TLC. Upon completion, the reaction was quenched with sat. aq. Na₂CO₃ (20 mL), extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to afford **59-1** as a white solid (460.9 mg, 47% yield).

3. Optimization studies

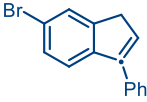
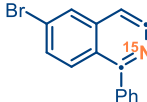
Table S1. Optimization of conditions for the editing of indole **1** into **2**^a

entry	N source	Yield (%) ^b
1	NH ₄ OAc (5.0 equiv)	95
2	NH ₃ •H ₂ O (25%, 2 mL)	95
3	NH ₄ Cl (5.0 equiv) + NaOAc (10.0 equiv)	99
4	NH ₄ Cl (4.0 equiv) + NaOAc (8.0 equiv)	98
5	NH ₄ Cl (3.0 equiv) + NaOAc (6.0 equiv)	97
6	NH ₄ Cl (2.0 equiv) + NaOAc (4.0 equiv)	83
7	NH ₄ Cl (1.0 equiv) + NaOAc (2.0 equiv)	23
8	¹⁵ NH ₄ Cl (3.0 equiv) + NaOAc (6.0 equiv)	94

^a Reaction conditions: **1** (88.0 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), blue LEDs (455-460 nm, 12 W) in TFE (2.0 mL) under air at room temperature for 5 h.

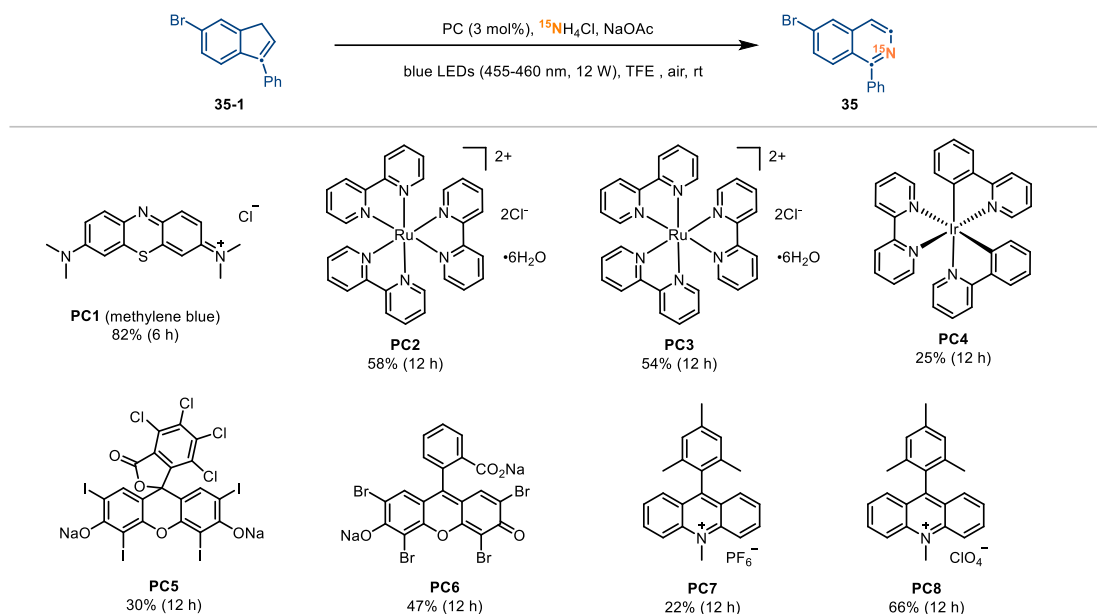
Then, trifluoroacetic acid (TFA, 67.0 μ L, 0.90 mmol, 3.0 equiv) was added with stirring for 6 h at room temperature. Finally, specified N source was added with stirring for 13 h at 70 $^{\circ}$ C. ^b Isolated yields obtained by column chromatography.

Table S2. Optimization of solvents for the editing of indene **35-1** into **35**^a

 35-1 $\xrightarrow[\text{blue LEDs (455-460 nm, 12 W), solvent, air, rt}]{\text{methylene blue (3 mol\%), } ^{15}\text{NH}_4\text{Cl, NaOAc}}$  35			
entry	solvent	Time (h)	Yield (%) ^b
1	TFE	6	82
2	HFIP	12	51
3	EtOH	6	31
4	THF	12	9
5	CH ₃ CN	12	16
6	DCE	12	19
7	CH ₃ CO ₂ Et	12	14
8	DMF	12	trace
9	DMSO	12	trace
10	acetone	12	trace

^a Reaction conditions: **35-1** (81.3 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), ¹⁵NH₄Cl (97.4 mg, 0.90 mmol, 3.0 equiv), NaOAc (147.7 mg, 1.80 mmol, 6.0 equiv), blue LEDs (455-460 nm, 12 W) in specified solvent (2.0 mL) under air at room temperature. ^b Isolated yields obtained by column chromatography. TFE = 2,2,2-trifluoroethanol; HFIP = hexafluoroisopropanol; DCE = 1,2-dichloroethane.

Table S3. Optimization of photocatalysts for the editing of indene **35-1** into **35**



Reaction conditions: **35-1** (81.3 mg, 0.30 mmol), photocatalyst (0.009 mmol), $^{15}\text{NH}_4\text{Cl}$ (97.4 mg, 0.90 mmol, 3.0 equiv), NaOAc (147.7 mg, 1.80 mmol, 6.0 equiv), blue LEDs (455-460 nm, 12 W) in TFE (2.0 mL) under air at room temperature. Isolated yields obtained by column chromatography.

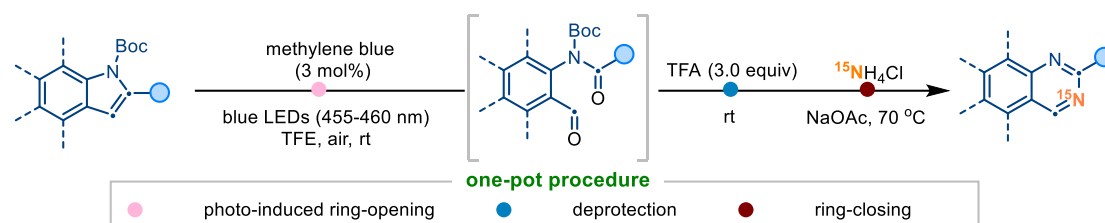
Table S4. Optimization of wavelengths for the editing of indene **35-1** into **35**^a

Reaction scheme showing the conversion of **35-1** to **35** using methylene blue (3 mol%), $^{15}\text{NH}_4\text{Cl}$, NaOAc, and blue LEDs (12 W) in TFE, air, rt.

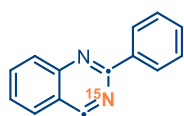
entry	Wavelength (nm)	Time (h)	Yield (%) ^b
1	420-425	6	69
2	430-435	6	77
3	455-460	6	82

^a Reaction conditions: **35-1** (81.3 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), $^{15}\text{NH}_4\text{Cl}$ (97.4 mg, 0.90 mmol, 3.0 equiv), NaOAc (147.7 mg, 1.80 mmol, 6.0 equiv), blue LEDs (12 W) in TFE (2.0 mL) under air at room temperature. ^b Isolated yields obtained by column chromatography.

4. General procedure for the skeletal editing of indoles

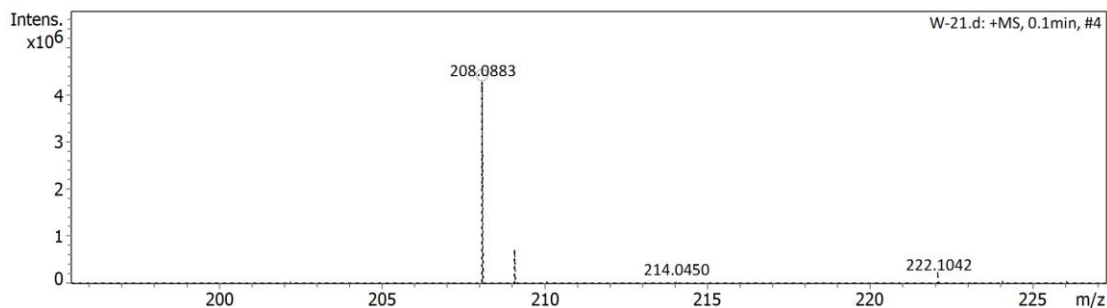


General procedure: Into a 25 mL Schlenk tube was sequentially added the indole (0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), and 2,2,2-trifluoroethanol (TFE, 2.0 mL). The reaction was stirred at room temperature under irradiation with visible light (455-460 nm, 12 W) until the complete consumption of the starting material as monitored by TLC. The light source was then removed, and trifluoroacetic acid (TFA, 67.0 μL , 0.90 mmol, 3.0 equiv) was added. The reaction was stirred at room temperature until full conversion of the intermediate. $^{15}\text{NH}_4\text{Cl}$ (97.4 mg, 0.90 mmol, 3.0 equiv) and NaOAc (147.7 mg, 1.80 mmol, 6.0 equiv) were added, and the reaction mixture was heated to 70 °C with stirring until complete conversion. The reaction was concentrated in vacuo and the residue was purified by silica-gel column chromatography using petroleum ether/ethyl acetate as the eluent to produce compounds **2-25**.

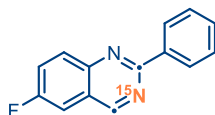


2-Phenylquinazoline-3- ^{15}N (**2**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 58.5 mg, 94% yield; reaction time = 24 h; mp 102.2-103.6 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.46 (d, J = 12.0 Hz, 1H), 8.63 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 2H), 8.09 (d, J = 8.0 Hz, 1H), 7.90 (t, J = 8.0 Hz, 2H), 7.61-7.49 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.0 (d, J = 3.0 Hz), 160.4, 150.7 (d, J = 3.0 Hz), 138.0 (d, J = 9.0 Hz), 134.1, 130.6, 128.6, 128.5 (d, J = 2.0 Hz), 127.2, 127.1, 123.5 (d, J = 1.0 Hz), one carbon missing in the aromatic region; ^{15}N NMR (50 MHz, CDCl_3) δ 287.3 (d, J = 11.0 Hz). IR (KBr) ν 3067, 2926, 1607, 1573, 1237, 793 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{11}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 208.0887, found: 208.0883, >99% ^{15}N incorporation determined by HRMS.

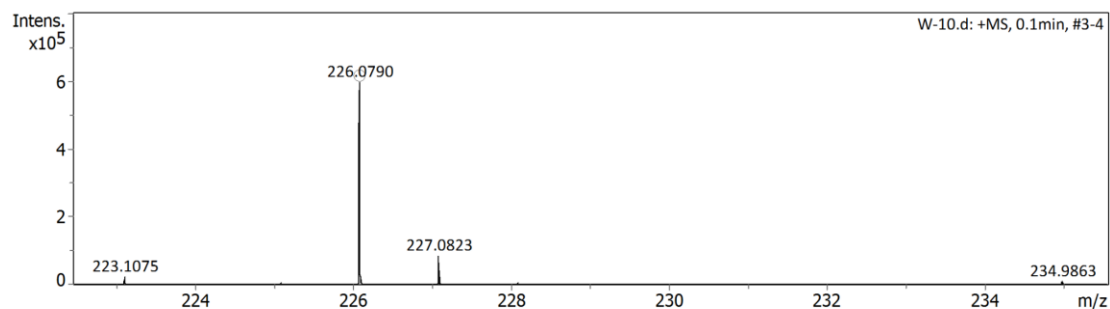


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
208.0883	1	C14H10N ¹⁵ N	208.0887	C14H11N ¹⁵ N	M+H	1.9	5.2	100.00	11.0	even	-

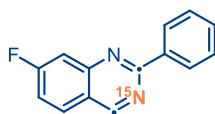


6-Fluoro-2-phenylquinazoline-3-¹⁵N (3)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 66.9 mg, 99% yield; reaction time = 36 h; mp 146.7-147.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.39 (d, *J* = 12.0 Hz, 1H), 8.59 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 2H), 8.08 (dd, *J*₁ = 12.0 Hz, *J*₂ = 8.0 Hz, 1H), 7.68-7.62 (m, 1H), 7.55-7.49 (m, 4H); ¹³C NMR (125 MHz, CDCl₃) δ 160.6 (t, *J* = 2.0 Hz), 160.3 (d, *J* = 199.0 Hz), 159.7 (d, *J* = 5.0 Hz), 147.8 (d, *J* = 2.0 Hz), 137.6 (d, *J* = 8.0 Hz), 131.3 (d, *J* = 7.0 Hz), 130.7, 128.6, 128.4 (d, *J* = 22.0 Hz), 124.4 (d, *J* = 21.0 Hz), 123.8 (d, *J* = 7.0 Hz), 110.1 (d, *J* = 18.0 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -110.6; ¹⁵N NMR (50 MHz, CDCl₃) δ 289.6 (d, *J* = 11.0 Hz). IR (KBr) ν 2379, 1582, 1552, 1376, 705 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀FN¹⁵N [M+H]⁺: 226.0793, found: 226.0790, >99% ¹⁵N incorporation determined by HRMS.

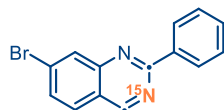
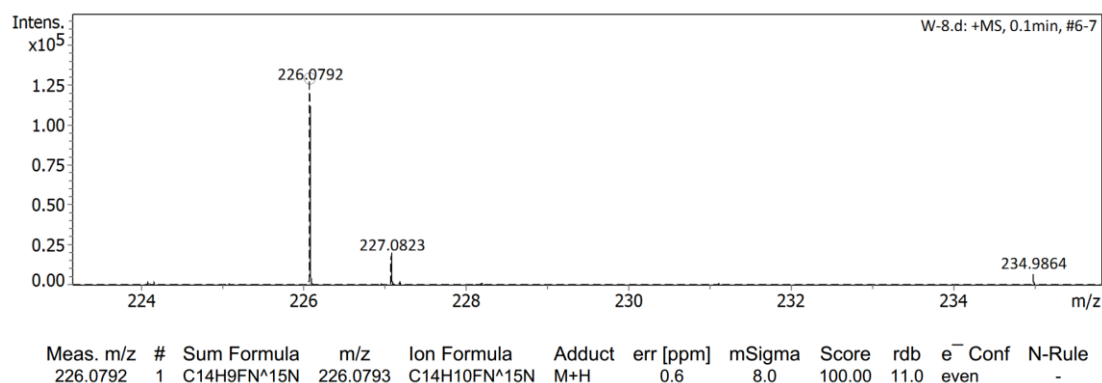


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
226.0790	1	C14H9FN ¹⁵ N	226.0793	C14H10FN ¹⁵ N	M+H	1.2	7.0	100.00	11.0	even	-



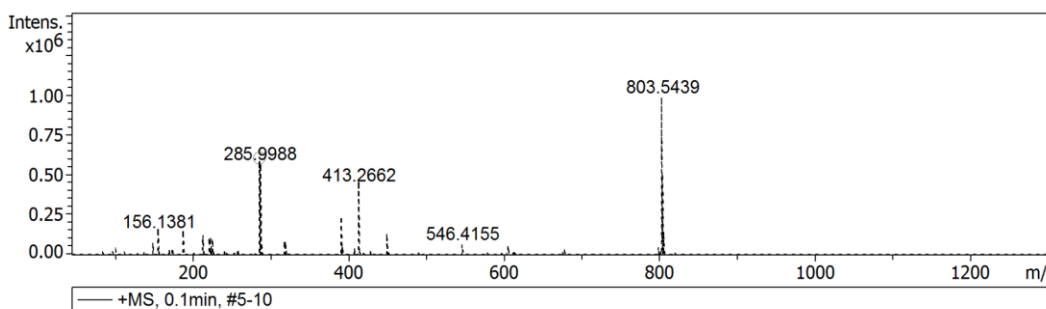
7-Fluoro-2-phenylquinazoline-3-¹⁵N (4)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 66.9 mg, 99% yield; reaction time = 24 h; mp 85.8-86.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.41 (d, *J* = 12.0 Hz, 1H), 8.62-8.60 (m, 2H), 7.94-7.90 (m, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.54-7.53 (m, 3H), 7.37 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 165.9 (d, *J* = 203.0 Hz), 161.8 (d, *J* = 2.0 Hz), 159.9, 152.4 (dd, *J*₁ = 12.0 Hz, *J*₂ = 2.0 Hz), 137.6 (d, *J* = 7.0 Hz), 130.9, 129.7 (d, *J* = 8.0 Hz), 128.6 (d, *J* = 2.0 Hz), 128.6, 120.8, 117.9 (d, *J* = 22.0 Hz), 123.4 (d, *J* = 17.0 Hz); ¹⁹F NMR (470 MHz, CDCl₃) δ -106.2 (d, *J* = 7.5 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 284.5 (d, *J* = 11.0 Hz). IR (KBr) ν 3059, 1621, 1587, 1405, 698 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀FN¹⁵N [M+H]⁺: 226.0793, found: 226.0792, >99% ¹⁵N incorporation determined by HRMS.

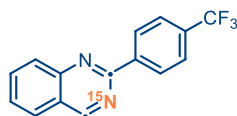


7-Bromo-2-phenylquinazoline-3-¹⁵N (5)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 79.1 mg, 92% yield; reaction time = 24 h; mp 97.5-98.5 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.45 (d, *J* = 12.0 Hz, 1H), 8.63 (d, *J* = 8.0 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.90 (t, *J* = 8.0 Hz, 2H), 7.61-7.53 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 161.0 (d, *J* = 3.0 Hz), 160.4, 150.7 (d, *J* = 2.0 Hz), 138.0 (d, *J* = 7.0 Hz), 134.1, 130.6, 128.6, 128.5 (d, *J* = 1.0 Hz), 127.2, 127.1, 123.5 (d, *J* = 1.0 Hz), one carbon missing in the aromatic region; ¹⁵N NMR (50 MHz, CDCl₃) δ 287.2 (d, *J* = 11.0 Hz). IR (KBr) ν 3062, 2380, 1614, 1553, 1373, 779 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀BrN¹⁵N [M+H]⁺: 285.9992, found: 285.9988, >99% ¹⁵N incorporation determined by HRMS.

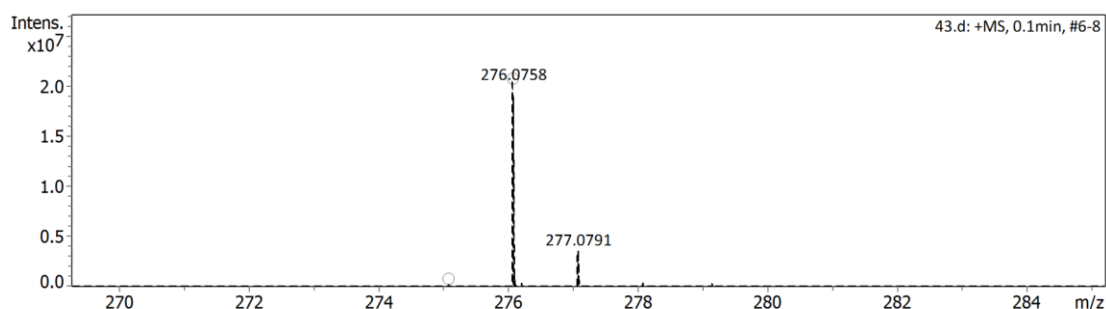


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
285.9988	1	C ₁₄ H ₉ BrN ¹⁵ N	285.9992	C ₁₄ H ₁₀ BrN ¹⁵ N	M+H	1.4	11.6	100.00	13.0	even		-

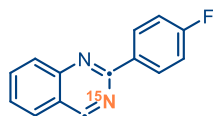


2-(4-(Trifluoromethyl)phenyl)quinazoline-3-¹⁵N (6)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 80.5 mg, 98% yield; reaction time = 24 h; mp 146.8-147.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.45 (d, *J* = 12.0 Hz, 1H), 8.72 (d, *J* = 8.0 Hz, 2H), 8.09 (d, *J* = 12.0 Hz, 1H), 7.93-7.90 (m, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.63 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.5, 159.5, 150.6 (d, *J* = 3.0 Hz), 141.2 (d, *J* = 8.0 Hz), 134.3, 132.0 (q, *J* = 32.0 Hz), 128.7 (d, *J* = 2.0 Hz), 128.7, 127.8, 127.1, 125.4 (q, *J* = 4.0 Hz), 123.7 (d, *J* = 2.0 Hz), 122.8; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.6; ¹⁵N NMR (50 MHz, CDCl₃) δ 287.3 (d, *J* = 11.0 Hz). IR (KBr) ν 3656, 2383, 1551, 1325, 858 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₀F₃N¹⁵N [M+H]⁺: 276.0761, found: 276.0758, >99% ¹⁵N incorporation determined by HRMS.



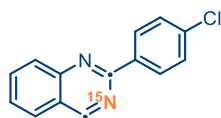
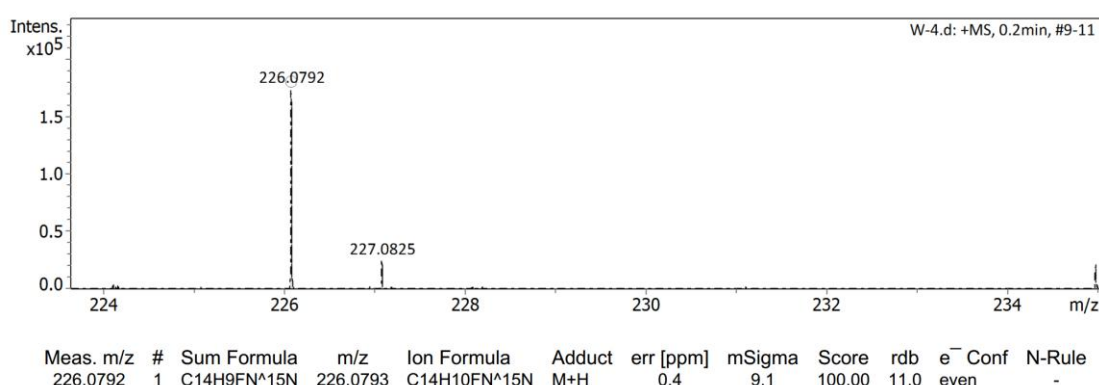
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
275.0791	1	C ₁₅ H ₉ F ₃ N ₂	275.0791	C ₁₅ H ₁₀ F ₃ N ₂	M+H	-0.2	753.3	100.00	11.0	even		ok
276.0758	1	C ₁₅ H ₉ F ₃ N ¹⁵ N	276.0761	C ₁₅ H ₁₀ F ₃ N ¹⁵ N	M+H	0.9	6.2	100.00	11.0	even		-



2-(4-Fluorophenyl)quinazoline-3-¹⁵N (7)

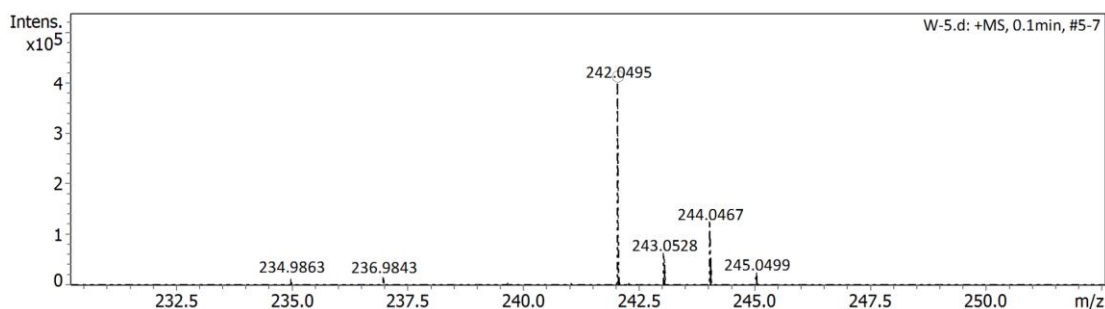
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to

10:1); 55.5 mg, 82% yield; reaction time = 24 h; mp 131.3-132.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.41 (d, *J* = 12.0 Hz, 1H), 8.62 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.89-7.86 (m, 2H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 164.6 (d, *J* = 249.0 Hz), 160.4, 159.9 (d, *J* = 3.0 Hz), 150.6 (d, *J* = 3.0 Hz), 134.2 (d, *J* = 3.0 Hz), 134.1, 130.6 (dd, *J*₁ = 8.0 Hz, *J*₂ = 2.0 Hz), 128.5, 127.1 (d, *J* = 13.0 Hz), 123.4 (d, *J* = 2.0 Hz), 115.6, 115.3; ¹⁹F NMR (376 MHz, CDCl₃) δ -110.5; ¹⁵N NMR (50 MHz, CDCl₃) δ 286.5 (d, *J* = 11.0 Hz). IR (KBr) ν 3066, 1599, 1558, 1509, 1402, 1220, 763 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀FN¹⁵N [M+H]⁺: 226.0793, found: 226.0792, >99% ¹⁵N incorporation determined by HRMS.

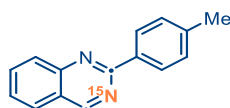


2-(4-Chlorophenyl)quinazoline-3-¹⁵N (**8**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 59.8 mg, 83% yield; reaction time = 24 h; mp 135.3-135.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.41 (d, *J* = 8.0 Hz, 1H), 8.55 (d, *J* = 8.0 Hz, 2H), 8.04 (d, *J* = 12.0 Hz, 1H), 7.90-7.87 (m, 2H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 160.5, 159.6 (d, *J* = 3.0 Hz), 150.6 (d, *J* = 3.0 Hz), 139.8 (d, *J* = 10.0 Hz), 134.5 (d, *J* = 47.0 Hz), 130.5, 129.8, 128.6 (d, *J* = 4.0 Hz), 127.6, 127.1 (d, *J* = 1.0 Hz), 126.6 (d, *J* = 2.0 Hz), 123.7 (d, *J* = 2.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 286.6 (d, *J* = 11.0 Hz). IR (KBr) ν 3056, 2380, 1581, 1403, 1085, 760 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀ClN¹⁵N [M+H]⁺: 242.0497, found: 242.0495, >99% ¹⁵N incorporation determined by HRMS.

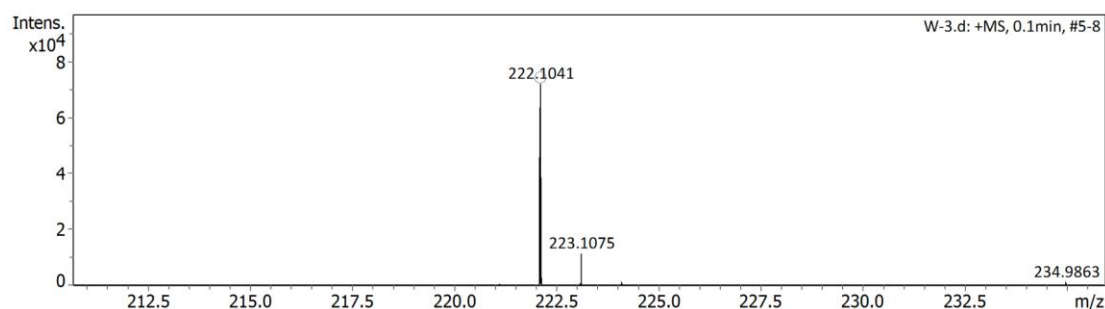


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
242.0495	1	C ₁₄ H ₉ CIN ¹⁵ N	242.0497	C ₁₄ H ₁₀ CIN ¹⁵ N	M+H	0.8	19.1	100.00	14.0	even		-

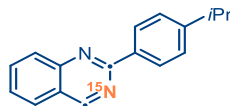


2-(p-Tolyl)quinazoline-3-¹⁵N (**9**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 61.2 mg, 92% yield; reaction time = 24 h; mp 103.7-104.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.43 (dd, *J*₁ = 12.0 Hz, *J*₂ = 4.0 Hz, 1H), 8.53 (d, *J* = 12.0 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.90-7.87 (m, 2H), 7.59-7.54 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.0 (d, *J* = 3.0 Hz), 160.3, 150.7 (d, *J* = 2.0 Hz), 140.8, 135.3, 135.2, 133.9, 129.3, 128.5, 127.0, 126.9, 123.4 (d, *J* = 1.0 Hz), 21.5; ¹⁵N NMR (50 MHz, CDCl₃) δ 286.9 (d, *J* = 11.0 Hz). IR (KBr) ν 3061, 1613, 1584, 1555, 1401, 1374, 757 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₃N¹⁵N [M+H]⁺: 222.1044, found: 222.1041, >99% ¹⁵N incorporation determined by HRMS.



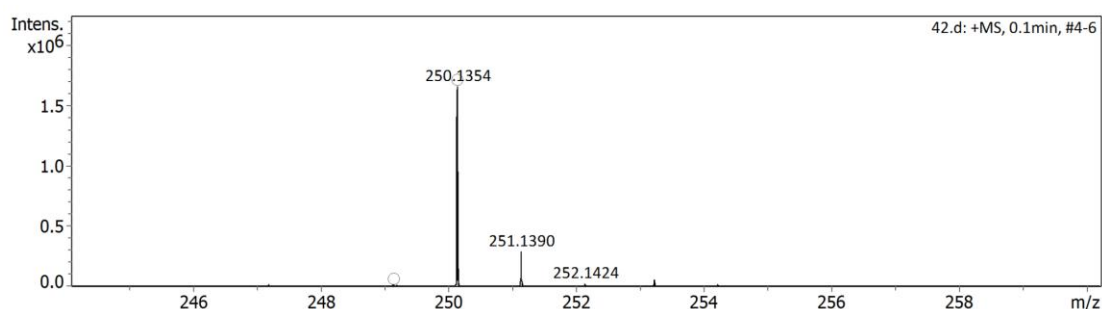
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
222.1041	1	C ₁₅ H ₁₂ N ¹⁵ N	222.1044	C ₁₅ H ₁₃ N ¹⁵ N	M+H	1.0	4.2	100.00	11.0	even		-



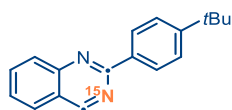
2-(4-Isopropylphenyl)quinazoline-3-¹⁵N (**10**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 68.7 mg, 92% yield; reaction time = 24 h; mp 57.0-57.7 °C; ¹H NMR (400 MHz, CDCl₃)

δ 9.45 (d, J = 12.0 Hz, 1H), 8.54 (d, J = 8.0 Hz, 2H), 8.07 (d, J = 8.0 Hz, 1H), 7.91-7.86 (m, 2H), 7.58 (t, J = 8.0 Hz, 1H), 7.40 (d, J = 8.0 Hz, 2H), 3.04-2.97 (m, 1H), 1.32 (d, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.1 (d, J = 3.0 Hz), 160.4, 151.7, 150.7 (d, J = 2.0 Hz), 135.7 (d, J = 9.0 Hz), 134.0, 128.6 (d, J = 2.0 Hz), 128.5, 127.0 (d, J = 1.0 Hz), 127.0, 126.7, 123.4 (d, J = 2.0 Hz), 34.1, 23.9; ^{15}N NMR (50 MHz, CDCl_3) δ 287.1 (d, J = 11.0 Hz). IR (KBr) ν 2956, 1614, 1581, 1403, 1022, 801 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{17}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 250.1357, found: 250.1354, >99% ^{15}N incorporation determined by HRMS.

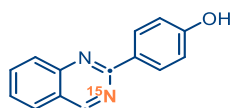
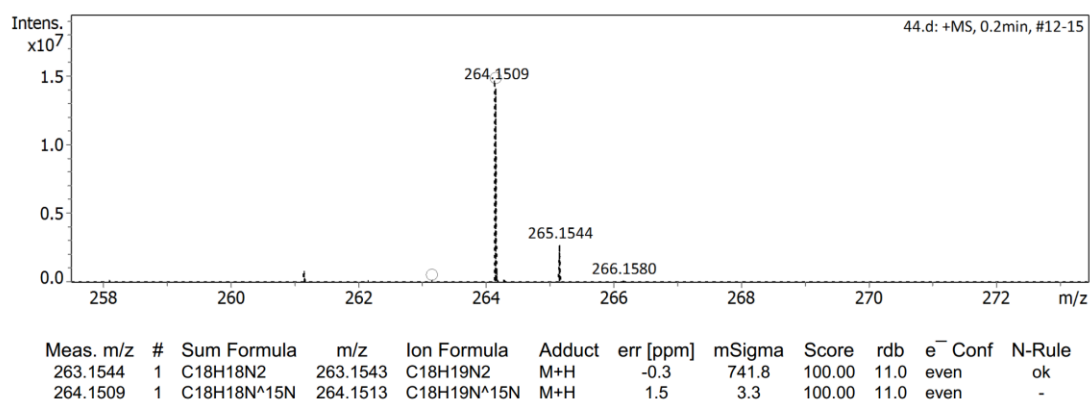


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
249.1387	1	C ₁₇ H ₁₆ N ₂	249.1386	C ₁₇ H ₁₇ N ₂	M+H	-0.4	744.3	100.00	11.0	even	ok
250.1354	1	C ₁₇ H ₁₆ N ¹⁵ N	250.1357	C ₁₇ H ₁₇ N ¹⁵ N	M+H	0.9	8.1	100.00	11.0	even	-



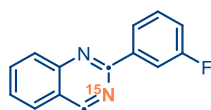
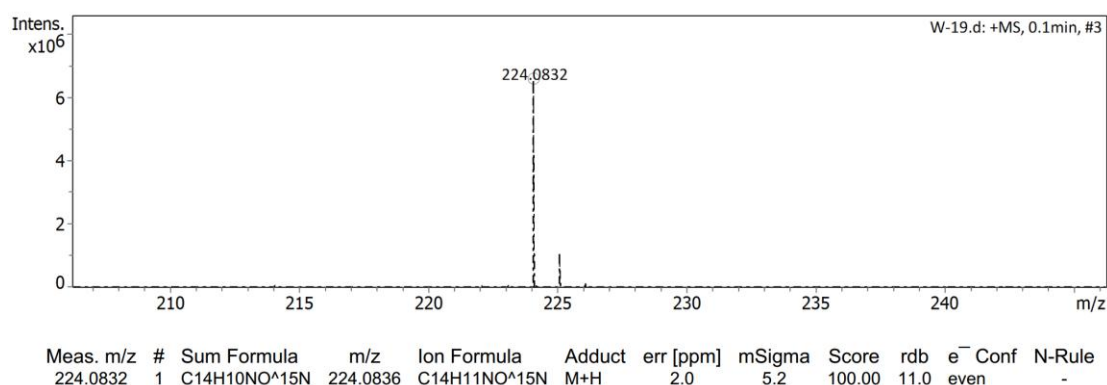
2-(4-(*tert*-Butyl)phenyl)quinazoline-3- ^{15}N (**11**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 72.6 mg, 92% yield; reaction time = 24 h; mp 85.1-86.2 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.46 (d, J = 12.0 Hz, 1H), 8.54 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 8.0 Hz, 1H), 7.93-7.88 (m, 2H), 7.61 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 12.0 Hz, 2H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 161.1, 160.4, 153.9, 150.8, 135.3 (d, J = 7.0 Hz), 134.0, 128.6, 128.3 (d, J = 2.0 Hz), 127.1, 127.0, 125.6, 123.5 (d, J = 1.0 Hz), 34.9, 31.3; ^{15}N NMR (50 MHz, CDCl_3) δ 287.2 (d, J = 11.0 Hz). IR (KBr) ν 3059, 2960, 1578, 1552, 1403, 767 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{19}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 264.1513, found: 264.1509, >99% ^{15}N incorporation determined by HRMS.



4-((Quinazolin-2-yl-3-¹⁵N)phenol (**12**))

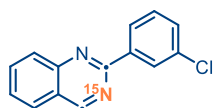
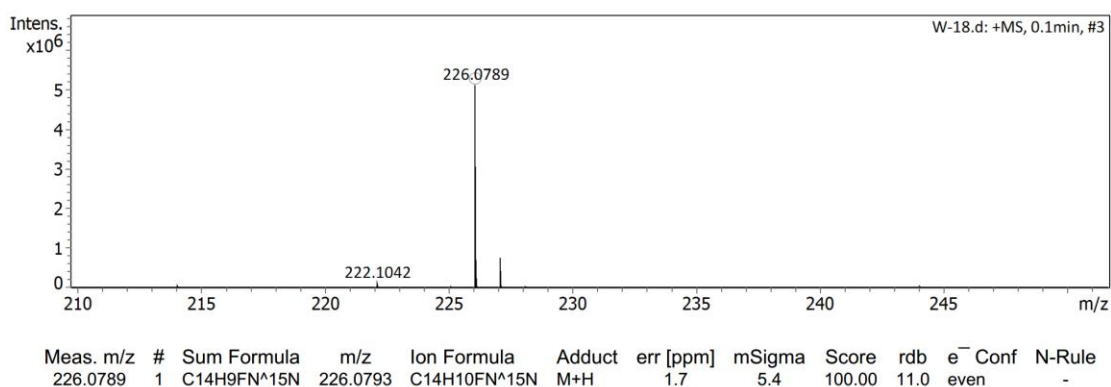
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 50.4 mg, 75% yield; reaction time = 36 h; mp 226.7–227.3 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.01 (s, 1H), 9.62 (d, *J* = 12.0 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 2H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 2H), 7.69–7.65 (m, 1H), 6.93 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 161.1, 160.2, 160.0 (d, *J* = 3.0 Hz), 150.0 (d, *J* = 2.0 Hz), 134.6, 130.0 (d, *J* = 2.0 Hz), 128.4 (d, *J* = 8.0 Hz), 127.8, 127.6, 127.0, 122.9 (d, *J* = 2.0 Hz), 115.5; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 287.3 (d, *J* = 11.0 Hz). IR (KBr) ν 3065, 2680, 1606, 1573, 1377, 764 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₁NO¹⁵N [M+H]⁺: 224.0836, found: 224.0832, >99% ¹⁵N incorporation determined by HRMS.



2-(3-Fluorophenyl)quinazoline-3-¹⁵N (**13**)

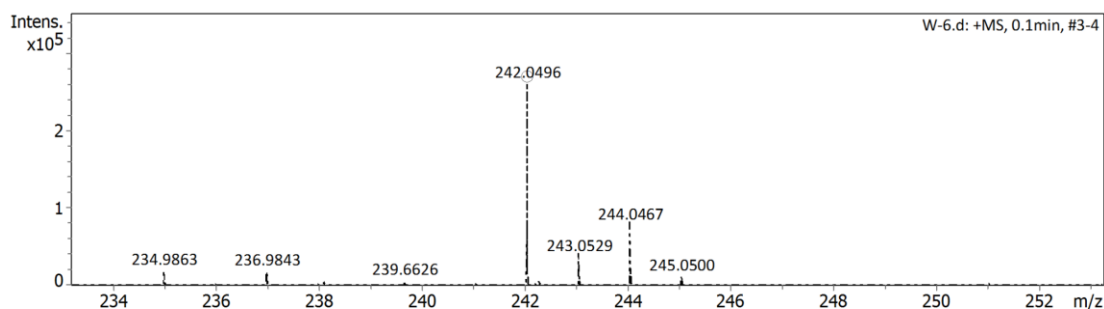
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to

10:1); 66.9 mg, 99% yield; reaction time = 24 h; mp 97.4-98.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.45 (d, *J* = 12.0 Hz, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.91 (t, *J* = 8.0 Hz, 2H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.49 (q, *J* = 8.0 Hz, 1H), 7.22-7.18 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 163.2 (d, *J* = 243.0 Hz), 160.4, 159.7, 150.6, 140.4 (t, *J* = 7.0 Hz), 134.2, 130.0 (d, *J* = 8.0 Hz), 128.6, 127.5, 127.1, 124.1 (t, *J* = 2.0 Hz), 123.7 (d, *J* = 8.0 Hz), 117.4 (d, *J* = 21.0 Hz), 115.3 (dd, *J*₁ = 23.0 Hz, *J*₂ = 2.0 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -113.2; ¹⁵N NMR (50 MHz, CDCl₃) δ 287.1 (d, *J* = 11.0 Hz). IR (KBr) ν 3066, 2380, 1556, 782 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀FN¹⁵N [M+H]⁺: 226.0793, found: 224.0789, >99% ¹⁵N incorporation determined by HRMS.

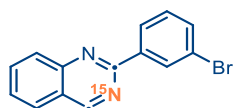


2-(3-Chlorophenyl)quinazoline-3-¹⁵N (**14**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 69.4 mg, 96% yield; reaction time = 24 h; mp 147.0-147.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.43 (d, *J* = 12.0 Hz, 1H), 8.62 (s, 1H), 8.50 (d, *J* = 4.0 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.90 (t, *J* = 8.0 Hz, 2H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 4.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 160.5, 159.6 (d, *J* = 2.0 Hz), 150.6 (d, *J* = 2.0 Hz), 139.8 (d, *J* = 7.0 Hz), 134.7, 134.2, 130.5, 129.8, 128.6, 128.6, 127.6, 127.1, 126.6 (d, *J* = 2.0 Hz), 123.7 (d, *J* = 1.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 286.9 (d, *J* = 11.0 Hz). IR (KBr) ν 3067, 1549, 1401, 783 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀ClN¹⁵N [M+H]⁺: 242.0497, found: 242.0496, >99% ¹⁵N incorporation determined by HRMS.

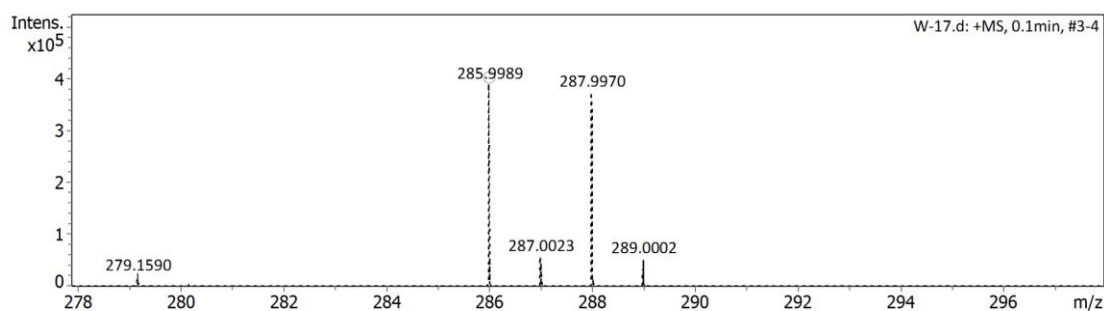


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
242.0496	1	C ₁₄ H ₉ CIN ¹⁵ N	242.0497	C ₁₄ H ₁₀ CIN ¹⁵ N	M+H	0.6	17.9	100.00	14.0	even	-	-

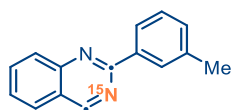


2-(3-Bromophenyl)quinazoline-3-¹⁵N (**15**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 54.9 mg, 64% yield; reaction time = 24 h; mp 155.5-156.1 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.44 (d, *J* = 8.0 Hz, 1H), 8.78 (s, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.91 (t, *J* = 8.0 Hz, 2H), 7.62 (t, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 160.5, 159.4 (d, *J* = 2.0 Hz), 150.5 (d, *J* = 2.0 Hz), 140.0 (d, *J* = 7.0 Hz), 134.3, 133.4, 131.5 (d, *J* = 2.0 Hz), 130.1, 128.6, 127.6, 127.1, 127.0 (d, *J* = 2.0 Hz), 123.6 (d, *J* = 1.0 Hz), 122.9; ¹⁵N NMR (50 MHz, CDCl₃) δ 286.8 (d, *J* = 11.0 Hz). IR (KBr) ν 3062, 1618, 1547, 1399, 741 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀BrN¹⁵N [M+H]⁺: 285.9992, found: 285.9989, >99% ¹⁵N incorporation determined by HRMS.



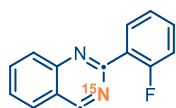
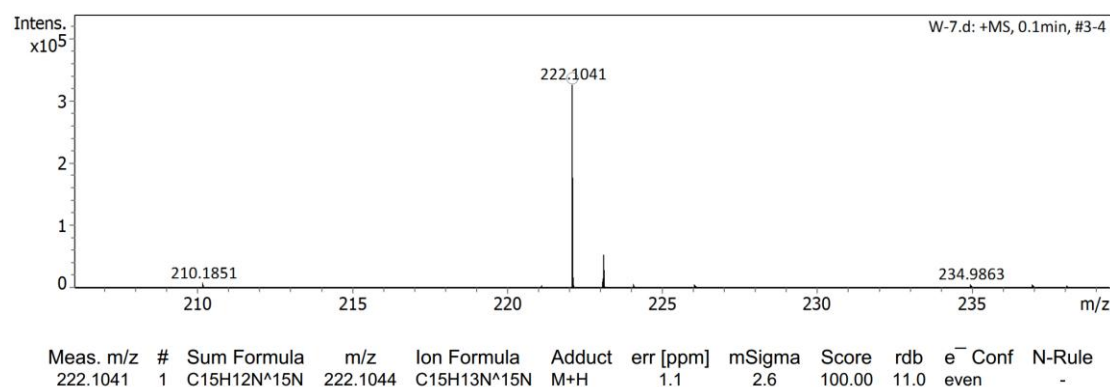
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
285.9989	1	C ₁₄ H ₉ BrN ¹⁵ N	285.9992	C ₁₄ H ₁₀ BrN ¹⁵ N	M+H	1.3	12.2	100.00	13.0	even	-	-



2-(*m*-Tolyl)quinazoline-3-¹⁵N (**16**)

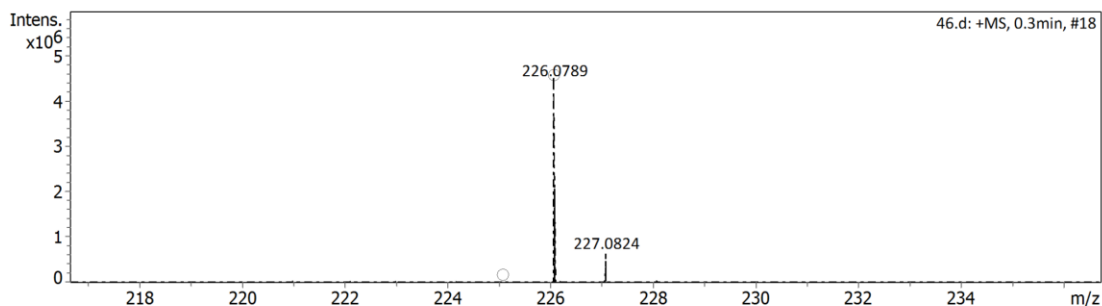
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to

10:1); 63.3 mg, 95% yield; reaction time = 24 h; mp 96.6-97.5 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.45 (d, J = 12.0 Hz, 1H), 8.43 (d, J = 12.0 Hz, 2H), 8.09 (d, J = 8.0 Hz, 1H), 7.89 (t, J = 8.0 Hz, 2H), 7.59 (t, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.1 (d, J = 3.0 Hz), 160.4, 150.7 (d, J = 3.0 Hz), 138.2, 137.9 (d, J = 9.0 Hz), 134.0, 131.4, 129.0 (d, J = 2.0 Hz), 128.5, 127.1, 127.0 (d, J = 1.0 Hz), 125.7 (d, J = 3.0 Hz), 123.5 (d, J = 1.0 Hz), one carbon missing in the aromatic region, 21.5; ^{15}N NMR (50 MHz, CDCl_3) δ 287.2 (d, J = 11.0 Hz). IR (KBr) ν 3050, 2915, 1614, 1556, 1399, 783 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{13}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 222.1044, found: 222.1041, >99% ^{15}N incorporation determined by HRMS.

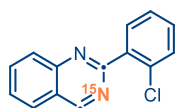


2-(2-Fluorophenyl)quinazoline-3- ^{15}N (**17**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 46.1 mg, 68% yield; reaction time = 24 h; mp 82.4-83.5 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.57 (d, J = 12.0 Hz, 1H), 8.19 (dd, J_1 = 16.0 Hz, J_2 = 8.0 Hz, 2H), 8.02-7.97 (m, 2H), 7.72 (t, J = 8.0 Hz, 1H), 7.54-7.49 (m, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.5, 160.4, 160.0, 150.6, 134.3, 132.1 (t, J = 2.0 Hz), 130.6 (d, J = 9.0 Hz), 128.7, 127.9, 127.0 (d, J = 1.0 Hz), 124.2 (d, J = 4.0 Hz), 123.2 (d, J = 2.0 Hz), 117.0, 116.7; ^{19}F NMR (376 MHz, CDCl_3) δ -115.1 (d, J = 3.8 Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 292.8 (dd, J_1 = 11.0 Hz, J_2 = 6.0 Hz). IR (KBr) ν 3072, 1582, 1549, 774 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{10}\text{FN}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 226.0793, found: 224.0789, >99% ^{15}N incorporation determined by HRMS.

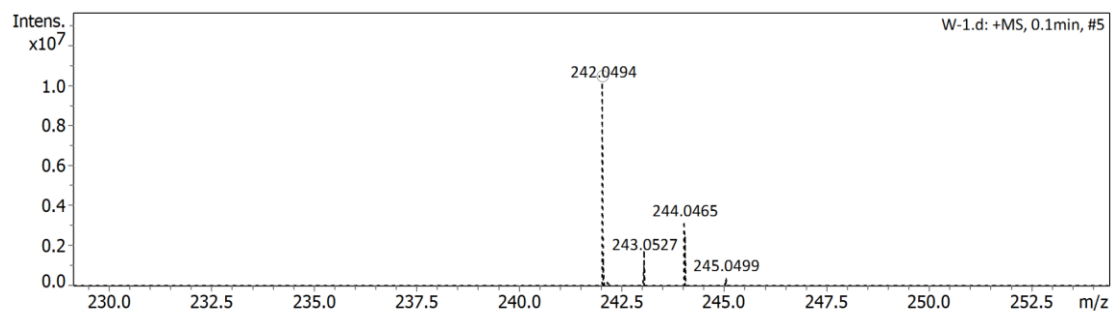


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdB	e ⁻	Conf	N-Rule
225.0822	1	C ₁₄ H ₉ FN ₂	225.0823	C ₁₄ H ₁₀ FN ₂	M+H	0.0	755.3	100.00	11.0	even		ok
226.0789	1	C ₁₄ H ₉ FN ¹⁵ N	226.0793	C ₁₄ H ₁₀ FN ¹⁵ N	M+H	1.8	8.0	100.00	11.0	even		-

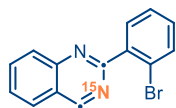


2-(2-Chlorophenyl)quinazoline-3-¹⁵N (**18**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 39.9 mg, 55% yield; reaction time = 24 h; mp 67.0-67.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.53 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.97 (dd, *J*₁ = 16.0 Hz, *J*₂ = 8.0 Hz, 2H), 7.83 (t, *J* = 8.0 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 4.0 Hz, 1H), 7.41 (d, *J* = 4.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 161.9, 160.2, 150.3 (d, *J* = 3.0 Hz), 138.2, 134.4, 132.8, 131.7, 130.5, 130.3, 128.6, 128.0, 127.1, 126.9, 123.2 (d, *J* = 2.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 294.0 (d, *J* = 11.0 Hz). IR (KBr) ν 3059, 1573, 1551, 760 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀ClN¹⁵N [M+H]⁺: 242.0497, found: 242.0494, >99% ¹⁵N incorporation determined by HRMS.



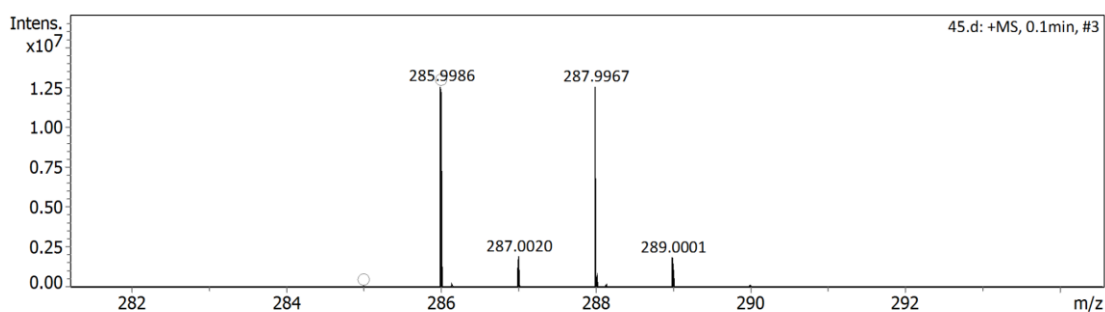
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdB	e ⁻	Conf	N-Rule
242.0494	1	C ₁₄ H ₉ BrN ¹⁵ N	242.0497	C ₁₄ H ₁₀ BrN ¹⁵ N	M+H	1.5	8.2	100.00	14.0	even		-



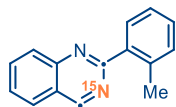
2-(2-Bromophenyl)quinazoline-3-¹⁵N (**19**)

Yellow oil obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 42.0 mg, 49% yield; reaction time = 24 h; ¹H NMR (400 MHz, CDCl₃) δ 9.53 (d, *J* = 12.0

Hz, 1H), 8.13 (d, $J = 8.0$ Hz, 1H), 7.98 (d, $J = 12.0$ Hz, 1H), 7.94 (d, $J = 8.0$ Hz, 1H), 7.78 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 7.74-7.67 (m, 2H), 7.45 (t, $J = 8.0$ Hz, 1H), 7.32 (t, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.7 (d, $J = 3.0$ Hz), 160.2, 150.2 (d, $J = 3.0$ Hz), 140.1 (d, $J = 9.0$ Hz), 134.4, 133.6, 131.6, 130.4, 128.6, 128.0, 127.4, 127.1, 123.2, 121.9; ^{15}N NMR (50 MHz, CDCl_3) δ 293.9 (d, $J = 11.0$ Hz). IR (KBr) ν 3058, 2924, 1618, 1556, 1372, 764 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{10}\text{BrN}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 285.9992, found: 285.9986, >99% ^{15}N incorporation determined by HRMS.

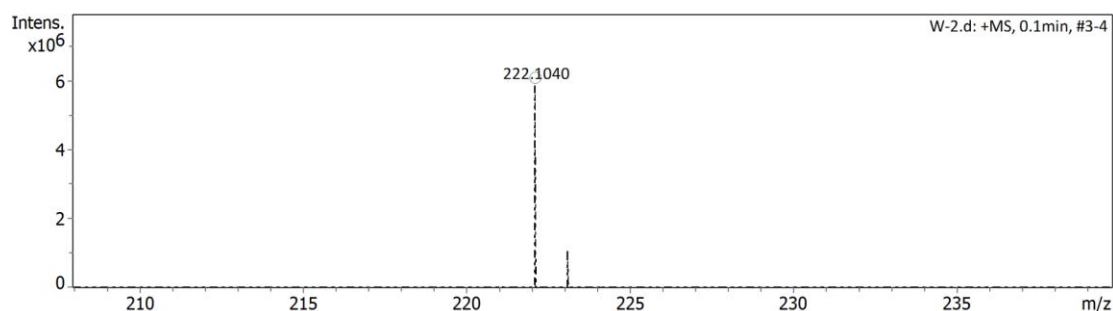


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
285.0021	1	C14H9BrN2	285.0022	C14H10BrN2	M+H	0.3	789.4	100.00	13.0	even	ok	
285.9986	1	C14H9BrN ¹⁵ N	285.9992	C14H10BrN ¹⁵ N	M+H	2.1	7.4	100.00	13.0	even	-	

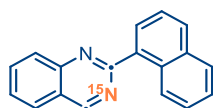


2-(o-Tolyl)quinazoline-3- ^{15}N (**20**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 47.7 mg, 72% yield; reaction time = 24 h; mp 43.0-43.5 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.48 (d, $J = 12.0$ Hz, 1H), 8.09 (d, $J = 8.0$ Hz, 1H), 7.94-7.89 (m, 3H), 7.63 (t, $J = 8.0$ Hz, 1H), 7.38-7.35 (m, 3H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.9 (d, $J = 3.0$ Hz), 160.0, 150.2 (d, $J = 3.0$ Hz), 138.5 (d, $J = 8.0$ Hz), 137.3, 134.0, 131.2, 130.6 (d, $J = 1.0$ Hz), 129.2, 128.4, 127.4, 127.0, 125.9, 122.7 (d, $J = 1.0$ Hz), 21.0; ^{15}N NMR (50 MHz, CDCl_3) δ 294.8 (d, $J = 11.0$ Hz). IR (KBr) ν 3061, 2923, 1555, 1374, 767 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{13}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 222.1044, found: 222.1040, >99% ^{15}N incorporation determined by HRMS.

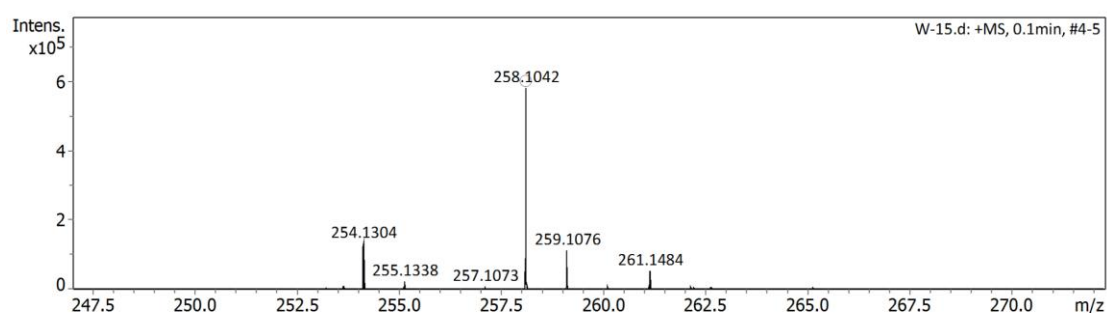


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
222.1040	1	C ₁₅ H ₁₂ N ¹⁵ N	222.1044	C ₁₅ H ₁₃ N ¹⁵ N	M+H	1.7	3.4	100.00	11.0	even	-

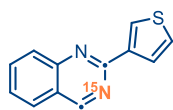


2-(Naphthalen-1-yl)quinazoline-3-¹⁵N (**21**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 39.6 mg, 51% yield; reaction time = 72 h; mp 120.9-121.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.60 (d, *J* = 12.0 Hz, 1H), 8.70 (d, *J* = 8.0 Hz, 1H), 8.17 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 2H), 8.04-7.93 (m, 4H), 7.71 (t, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.58-7.52 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 163.4 (d, *J* = 3.0 Hz), 160.4, 150.5 (d, *J* = 2.0 Hz), 136.2 (d, *J* = 7.0 Hz), 134.3, 134.2, 131.2, 130.4, 129.6 (d, *J* = 1.0 Hz), 128.6, 128.5, 127.7, 127.1, 126.8, 125.9, 125.3, 123.1, one carbon missing in the aromatic region; ¹⁵N NMR (50 MHz, CDCl₃) δ 295.1 (d, *J* = 11.0 Hz). IR (KBr) ν 3045, 1620, 1555, 1373, 760 cm⁻¹. HRMS (ESI) calcd for C₁₈H₁₃N¹⁵N [M+H]⁺: 258.1044, found: 258.1042, >99% ¹⁵N incorporation determined by HRMS.



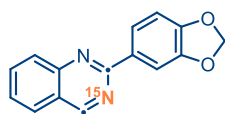
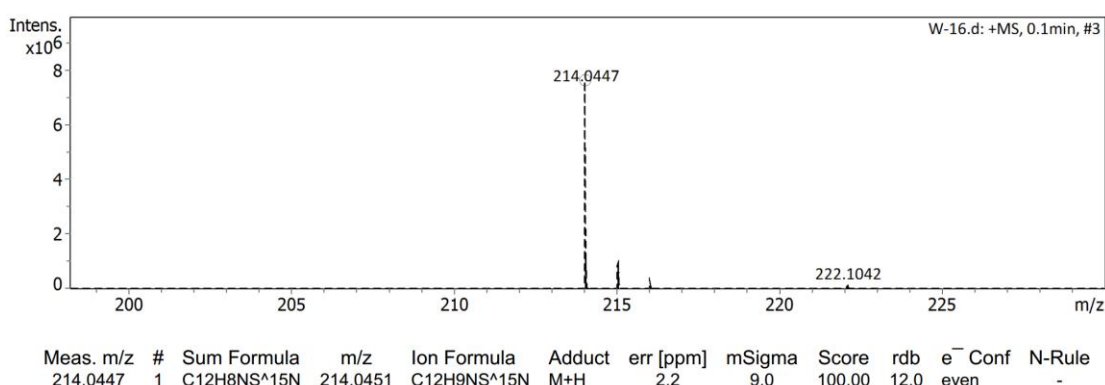
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
258.1042	1	C ₁₈ H ₁₂ N ¹⁵ N	258.1044	C ₁₈ H ₁₃ N ¹⁵ N	M+H	0.8	3.2	100.00	14.0	even	-



2-(Thiophen-3-yl)quinazoline-3-¹⁵N (**22**)

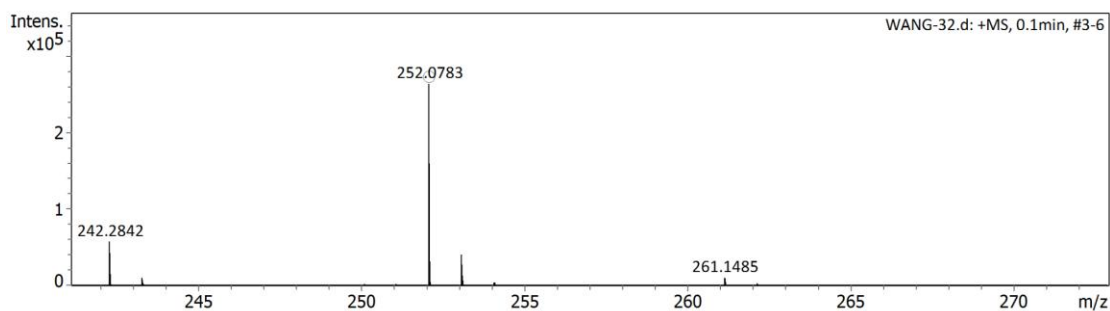
Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to

10:1); 59.9 mg, 94% yield; reaction time = 60 h; mp 107.5-108.5 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.38 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 1H), 8.44 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 1H), 8.06-8.01 (m, 2H), 7.89-7.85 (m, 2H), 7.59-7.55 (m, 1H), 7.42 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.4, 158.1 (d, *J* = 3.0 Hz), 150.6 (d, *J* = 3.0 Hz), 142.0 (d, *J* = 9.0 Hz), 134.1, 128.3, 128.2 (d, *J* = 2.0 Hz), 127.6 (d, *J* = 2.0 Hz), 127.1, 127.0, 126.0, 123.3 (d, *J* = 1.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 287.8 (d, *J* = 11.0 Hz). IR (KBr) ν 3113, 2957, 1613, 1560, 1370, 786 cm⁻¹. HRMS (ESI) calcd for C₁₂H₉NS¹⁵N [M+H]⁺: 214.0451, found: 214.0447, >99% ¹⁵N incorporation determined by HRMS.

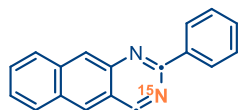


2-(Benzo[d][1,3]dioxol-5-yl)quinazoline-3-¹⁵N (**23**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 56.0 mg, 74% yield; reaction time = 36 h; mp 133.3-134.1 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.41 (d, *J* = 8.0 Hz, 1H), 8.23 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 1H), 8.12 (d, *J* = 4.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.91-7.87 (m, 2H), 7.60-7.56 (m, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 6.06 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 160.5 (d, *J* = 3.0 Hz), 160.3, 150.7 (d, *J* = 3.0 Hz), 149.9, 148.2, 134.1, 132.6, 128.4, 127.1, 126.9, 123.5 (d, *J* = 3.0 Hz), 123.4 (d, *J* = 2.0 Hz), 108.7 (d, *J* = 3.0 Hz), 108.3, 101.4; ¹⁵N NMR (50 MHz, CDCl₃) δ 286.3 (d, *J* = 11.0 Hz). IR (KBr) ν 3394, 2921, 1559, 1457, 1253, 1037, 792 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₁NO₂¹⁵N [M+H]⁺: 252.0785, found: 252.0783, >99% ¹⁵N incorporation determined by HRMS.

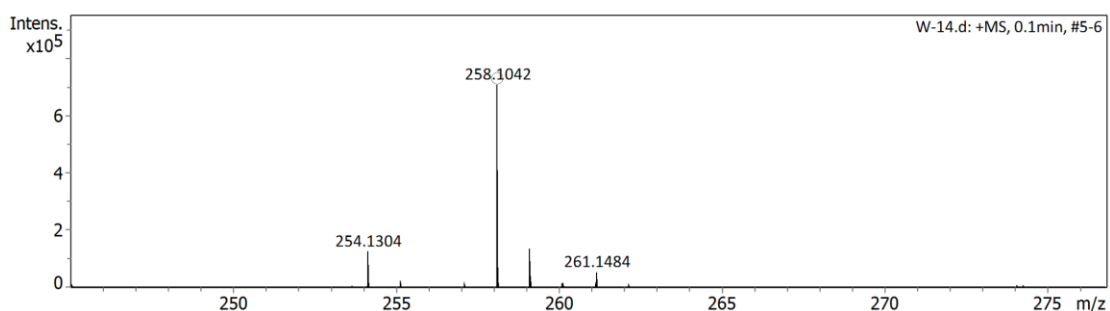


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
252.0783	1	C ₁₅ H ₁₀ NO ₂ ¹⁵ N	252.0785	C ₁₅ H ₁₁ NO ₂ ¹⁵ N	M+H	0.7	9.6	100.00	12.0	even	-	-

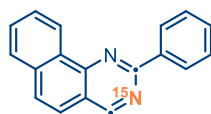


2-Phenylbenzo[*g*]quinazoline-3-¹⁵N (**24**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 10:1); 60.5 mg, 78% yield; reaction time = 48 h; mp 188.7-189.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.13 (d, *J* = 12.0 Hz, 1H), 8.71 (d, *J* = 8.0 Hz, 1H), 8.66 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 2H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.77 (t, *J* = 8.0 Hz, 1H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.59-7.51 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 161.9, 154.5, 152.2 (d, *J* = 3.0 Hz), 137.9 (d, *J* = 7.0 Hz), 135.7, 131.6, 130.6, 129.0, 128.6, 128.5, 128.4, 128.3, 127.8, 127.0, 121.7, 120.1 (d, *J* = 2.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 282.7 (d, *J* = 11.0 Hz). IR (KBr) ν 3053, 2381, 1565, 1407, 690 cm⁻¹. HRMS (ESI) calcd for C₁₈H₁₃N¹⁵N [M+H]⁺: 258.1044, found: 258.1042, >99% ¹⁵N incorporation determined by HRMS.



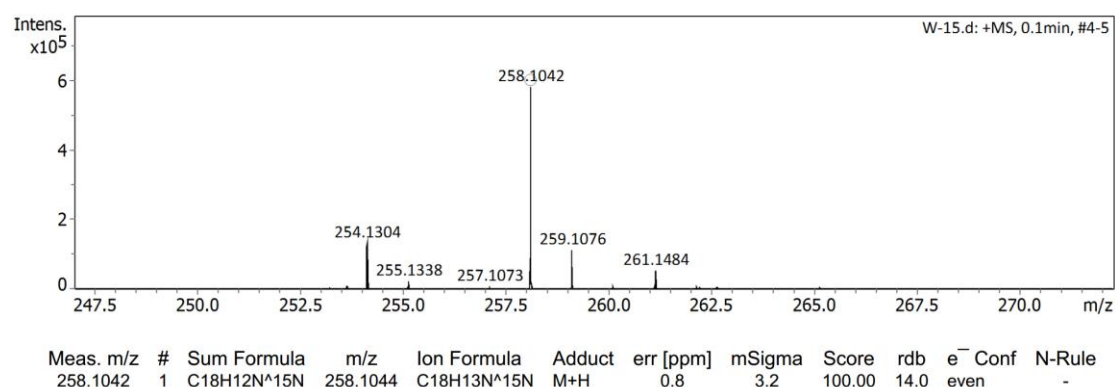
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
258.1042	1	C ₁₈ H ₁₂ N ¹⁵ N	258.1044	C ₁₈ H ₁₃ N ¹⁵ N	M+H	0.7	4.0	100.00	14.0	even	-	-



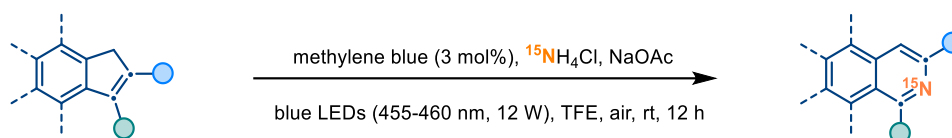
2-Phenylbenzo[*h*]quinazoline-3-¹⁵N (**25**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to

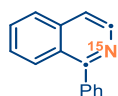
10:1); 49.0 mg, 63% yield; reaction time = 48 h; mp 143.5-144.2 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.43 (s, 1H), 8.37 (d, J = 12.0 Hz, 1H), 8.77 (d, J = 8.0 Hz, 2H), 7.91 (s, 1H), 7.83-7.80 (m, 3H), 7.70 (d, J = 8.0 Hz, 1H), 7.59-7.57 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 161.0 (d, J = 2.0 Hz), 158.6, 150.7 (d, J = 3.0 Hz), 138.2 (d, J = 7.0 Hz), 135.5, 130.5, 130.3, 130.1, 128.6, 128.5 (d, J = 1.0 Hz), 128.4, 128.0, 127.4, 124.9, 122.9, 121.4 (d, J = 1.0 Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 284.0 (d, J = 11.0 Hz). IR (KBr) ν 3043, 2923, 1555, 1401, 804, 748 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{13}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 258.1044, found: 258.1042, >99% ^{15}N incorporation determined by HRMS.



5. General procedure for the skeletal editing of indenenes



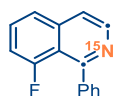
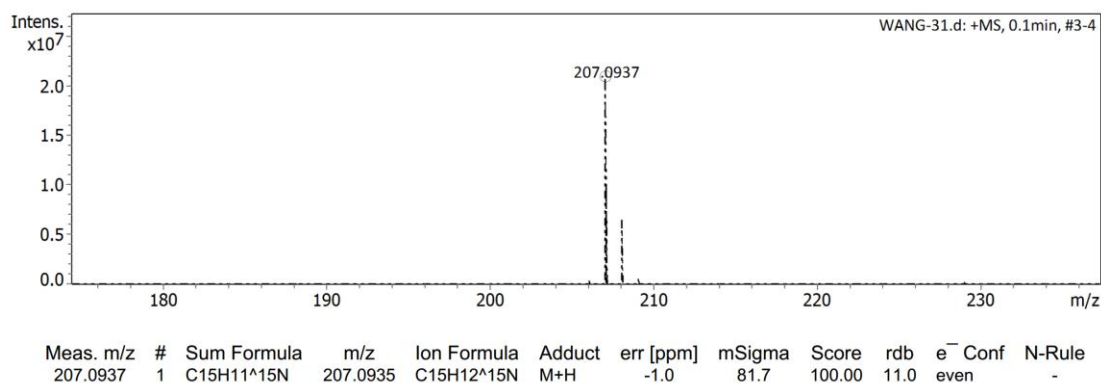
General procedure: Into a 25 mL Schlenk tube was sequentially added the indene (0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), $^{15}\text{NH}_4\text{Cl}$ (97.4 mg, 0.90 mmol, 3.0 equiv), NaOAc (147.7 mg, 1.80 mmol, 6.0 equiv) and 2,2,2-trifluoroethanol (TFE, 2.0 mL). The reaction was stirred at room temperature under air with visible light irradiation (455-460 nm, 12 W). Upon completion of the reaction as monitored by TLC, the mixture was concentrated in vacuo, and the residue was purified by silica-gel column chromatography using petroleum ether/ethyl acetate as the eluent to produce compounds **26-52**.



1-Phenylisoquinoline- ^{15}N (**26**)

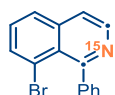
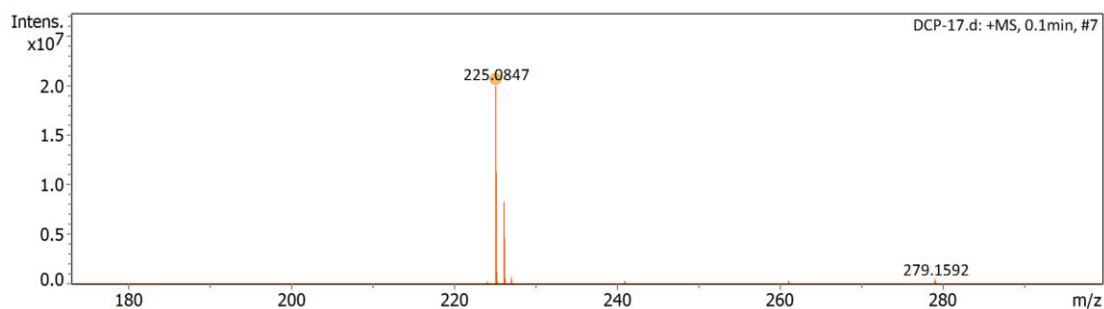
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to

10:1); 41.7 mg, 67% yield; reaction time = 6 h; mp 88.9-89.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.61 (dd, *J*₁ = 12.0 Hz, *J*₂ = 8.0 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.72-7.63 (m, 4H), 7.55-7.48 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 160.6 (d, *J* = 2.0 Hz), 142.1, 139.5 (d, *J* = 7.0 Hz), 136.7 (d, *J* = 2.0 Hz), 129.9, 129.8 (d, *J* = 1.0 Hz), 128.5, 128.3, 127.5, 127.1, 126.9, 126.6 (d, *J* = 2.0 Hz), 119.8 (d, *J* = 2.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 305.9 (d, *J* = 11.0 Hz). IR (KBr) ν 3048, 1544, 1383, 761 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₂¹⁵N [M+H]⁺: 207.0935, found: 207.0937, >99% ¹⁵N incorporation determined by HRMS.



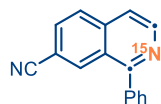
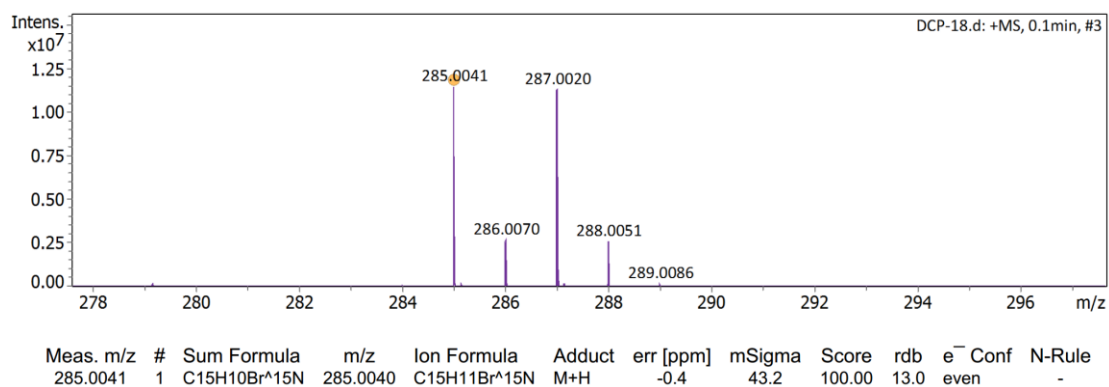
8-Fluoro-1-phenylisoquinoline-¹⁵N (**27**)

Light yellow oil obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 49.5 mg, 74% yield; reaction time = 12 h; ¹H NMR (400 MHz, CDCl₃) δ 8.63 (dd, *J*₁ = 12.0 Hz, *J*₂ = 8.0 Hz, 1H), 7.64-7.54 (m, 5H), 7.50-7.43 (m, 3H), 7.18-7.13 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 158.4 (d, *J* = 258.0 Hz), 157.3 (dd, *J*₁ = 4.0 Hz, *J*₂ = 2.0 Hz), 142.3, 142.0 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz), 138.6 (t, *J* = 2.0 Hz), 130.3 (d, *J* = 9.0 Hz), 128.5 (dd, *J*₁ = 4.0 Hz, *J*₂ = 2.0 Hz), 128.0, 127.4, 122.9 (d, *J* = 4.0 Hz), 119.0 (t, *J* = 2.0 Hz), 116.9 (dd, *J*₁ = 13.0 Hz, *J*₂ = 2.0 Hz), 112.4 (d, *J* = 22.0 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -102.74; ¹⁵N NMR (50 MHz, CDCl₃) δ 312.6 (d, *J* = 11.0 Hz). IR (KBr) ν 3058, 1629, 1553, 1348, 1234, 777 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₁F¹⁵N [M+H]⁺: 225.0840, found: 225.0847, >99% ¹⁵N incorporation determined by HRMS.



8-Bromo-1-phenylisoquinoline-¹⁵N (**28**)

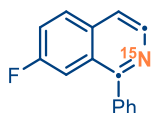
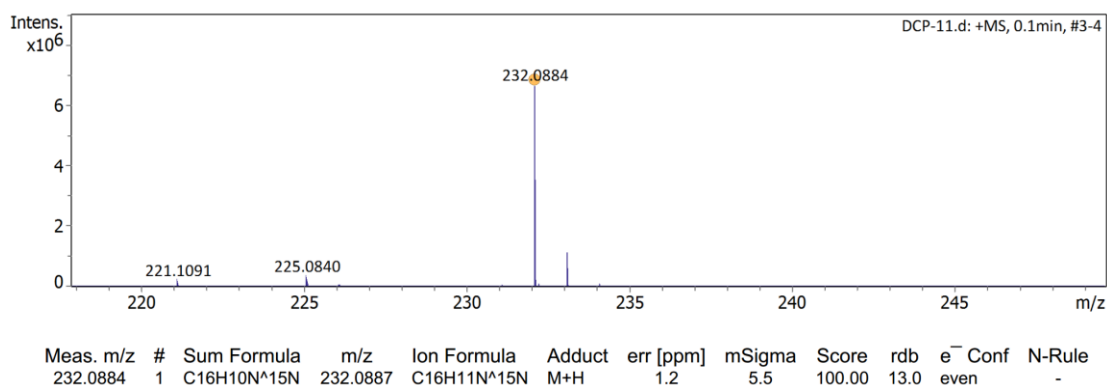
Light yellow oil obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 63.1 mg, 74% yield; reaction time = 6 h; ¹H NMR (400 MHz, CDCl₃) δ 8.57 (dd, *J*₁ = 16.0 Hz, *J*₂ = 4.0 Hz, 1H), 7.82 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.58 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 1H), 7.47-7.39 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 160.0, 141.6 (d, *J* = 7.0 Hz), 141.3, 138.9 (d, *J* = 1.0 Hz), 134.3, 129.9, 129.4 (d, *J* = 1.0 Hz), 127.9, 127.6, 127.0, 125.1 (d, *J* = 2.0 Hz), 120.5, 119.7 (d, *J* = 3.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 314.3 (d, *J* = 11.0 Hz). IR (KBr) ν 3059, 1525, 1348, 767 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₁Br¹⁵N [M+H]⁺: 285.0040, found: 285.0041, >99% ¹⁵N incorporation determined by HRMS.



1-Phenylisoquinoline-¹⁵N-7-carbonitrile (**29**)

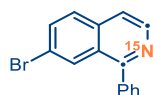
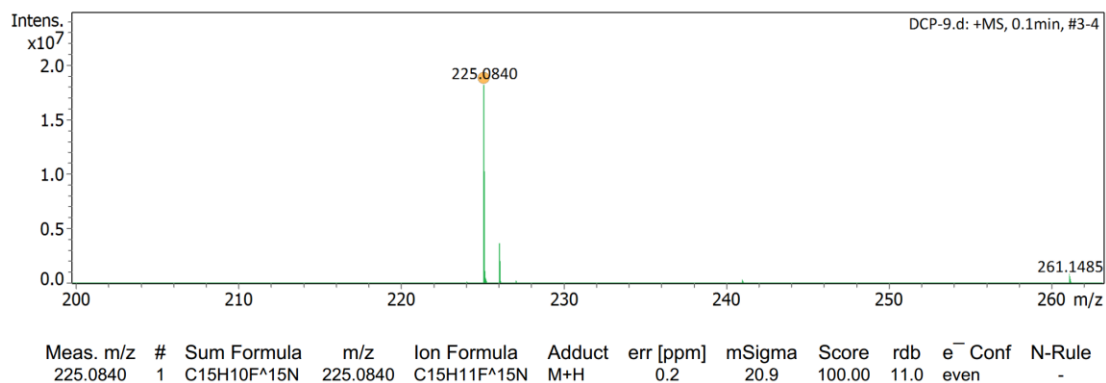
Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 52.6 mg, 76% yield; reaction time = 12 h; mp 131.7-132.4 °C; ¹H NMR (500 MHz,

CDCl₃) δ 8.76 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 8.50 (s, 1H), 7.98 (d, $J = 8.0$ Hz, 1H), 7.82 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 7.71 (d, $J = 4.0$ Hz, 1H), 7.68-7.65 (m, 2H), 7.60-7.55 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 161.4, 145.1, 138.1 (d, $J = 1.0$ Hz), 138.1, 134.2, 130.3, 129.9, 129.4, 128.7, 128.5, 125.6, 119.5 (d, $J = 2.0$ Hz), 118.5, 110.8; ¹⁵N NMR (50 MHz, CDCl₃) δ 311.9 (d, $J = 11.0$ Hz). IR (KBr) ν 3058, 2226, 1617, 1398, 767 cm⁻¹. HRMS (ESI) calcd for C₁₆H₁₁N¹⁵N [M+H]⁺: 232.0887, found: 232.0884, >99% ¹⁵N incorporation determined by HRMS.



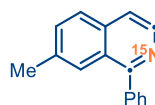
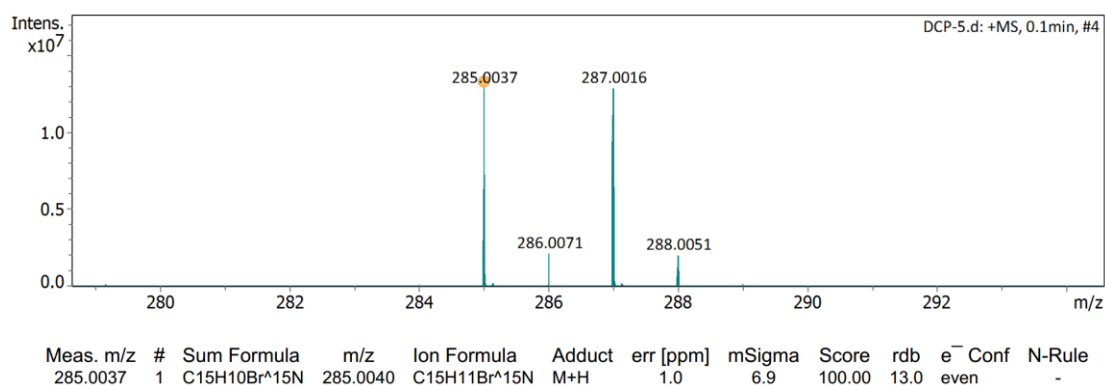
7-Fluoro-1-phenylisoquinoline-¹⁵N (**30**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 45.3 mg, 67% yield; reaction time = 12 h; mp 37.2-38.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.46-8.41 (m, 1H), 7.69-7.65 (m, 1H), 7.58-7.51 (m, 3H), 7.43-7.42 (m, 1H), 7.40-7.31 (m, 3H), 7.29-7.24 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.6 (d, $J = 247.0$ Hz), 159.8 (d, $J = 3.0$ Hz), 141.5 (d, $J = 2.0$ Hz), 138.9 (d, $J = 8.0$ Hz), 133.6, 129.5 (d, $J = 2.0$ Hz), 129.4, 128.6, 128.3, 127.1 (d, $J = 8.0$ Hz), 120.4 (d, $J = 25.0$ Hz), 119.4 (t, $J = 2.0$ Hz), 110.6 (d, $J = 22.0$ Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -110.46; ¹⁵N NMR (50 MHz, CDCl₃) δ 309.3 (d, $J = 11.0$ Hz). IR (KBr) ν 3058, 1584, 1500, 1191, 760 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₁F¹⁵N [M+H]⁺: 225.0840, found: 225.0840, >99% ¹⁵N incorporation determined by HRMS.



7-Bromo-1-phenylisoquinoline-¹⁵N (**31**)

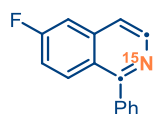
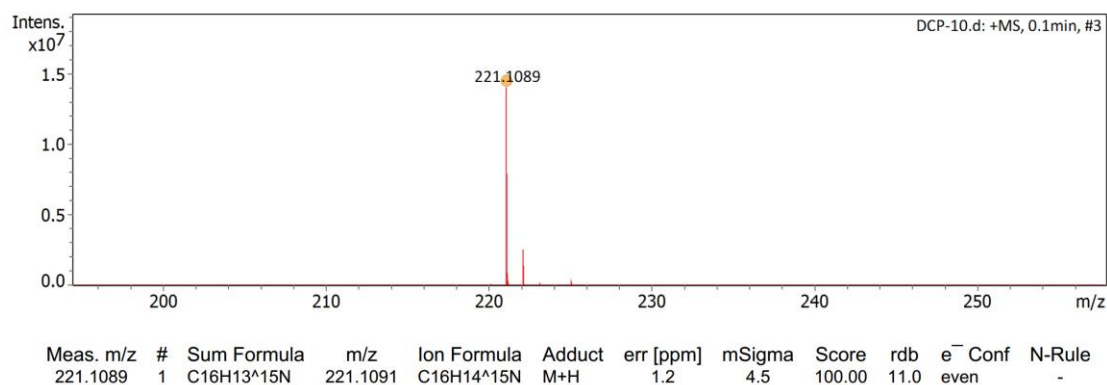
Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 57.9 mg, 68% yield; reaction time = 12 h; mp 84.5-85.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.63 (dd, *J*₁ = 12.0 Hz, *J*₂ = 4.0 Hz, 1H), 8.25 (s, 1H), 7.74 (d, *J* = 4.0 Hz, 2H), 7.68-7.66 (m, 2H), 7.61-7.59 (m, 1H), 7.57-7.49 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.6 (d, *J* = 2.0 Hz), 142.5, 138.7 (d, *J* = 8.0 Hz), 135.1 (d, *J* = 2.0 Hz), 133.4, 129.7 (d, *J* = 1.0 Hz), 129.5, 128.8, 128.6, 128.5, 127.4 (d, *J* = 2.0 Hz), 120.9, 119.4 (d, *J* = 2.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 309.4 (d, *J* = 11.0 Hz). IR (KBr) ν 3055, 1579, 1393, 756 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₁Br¹⁵N [M+H]⁺: 285.0040, found: 285.0037, >99% ¹⁵N incorporation determined by HRMS.



7-Methyl-1-phenylisoquinoline-¹⁵N (**32**)

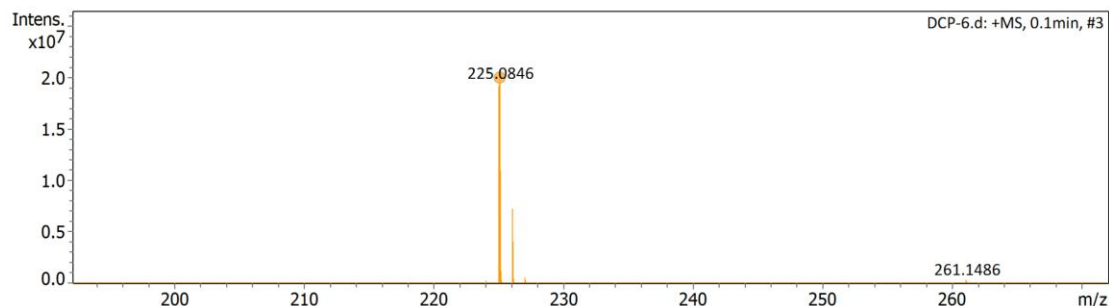
Light yellow oil obtained by column chromatography (petroleum ether/ethyl acetate = 30:1

to 10:1); 43.2 mg, 65% yield; reaction time = 12 h; ^1H NMR (400 MHz, CDCl_3) δ 8.55 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 7.86 (s, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.71-7.69 (m, 2H), 7.60 (d, $J = 8.0$ Hz, 1H), 7.57-7.48 (m, 4H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.9 (d, $J = 2.0$ Hz), 141.3, 139.6 (d, $J = 7.0$ Hz), 137.1, 135.0 (d, $J = 2.0$ Hz), 132.2, 129.8 (d, $J = 2.0$ Hz), 128.4, 128.3, 126.8 (d, $J = 2.0$ Hz), 126.7, 126.1, 119.7 (d, $J = 2.0$ Hz), 21.9; ^{15}N NMR (50 MHz, CDCl_3) δ 305.9 (d, $J = 11.0$ Hz). IR (KBr) ν 3051, 2920, 1585, 1399, 761 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 221.1091, found: 221.1089, >99% ^{15}N incorporation determined by HRMS.

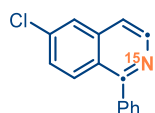


6-Fluoro-1-phenylisoquinoline- ^{15}N (**33**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 46.1 mg, 69% yield; reaction time = 12 h; mp 84.0-84.8 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 8.60-8.56 (m, 1H), 8.11-8.06 (m, 1H), 7.65 (d, $J = 8.0$ Hz, 2H), 7.56-7.41 (m, 5H), 7.27-7.20 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.7 (d, $J = 251.0$ Hz), 160.5, 143.0, 139.1 (d, $J = 7.0$ Hz), 138.3 (dd, $J_1 = 10.0$, $J_2 = 2.0$, Hz), 130.7 (d, $J = 10.0$ Hz), 129.6 (d, $J = 1.0$ Hz), 128.6, 128.3, 123.7, 119.3 (dd, $J_1 = 5.0$, $J_2 = 2.0$, Hz), 117.3 (d, $J = 25.0$ Hz), 111.0 (d, $J = 21.0$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ -107.88 (t, $J = 3.8$ Hz, 1F); ^{15}N NMR (50 MHz, CDCl_3) δ 304.4 (d, $J = 11.0$ Hz). IR (KBr) ν 3052, 1620, 1453, 763 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{11}\text{F}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 225.0840, found: 225.0846, >99% ^{15}N incorporation determined by HRMS.

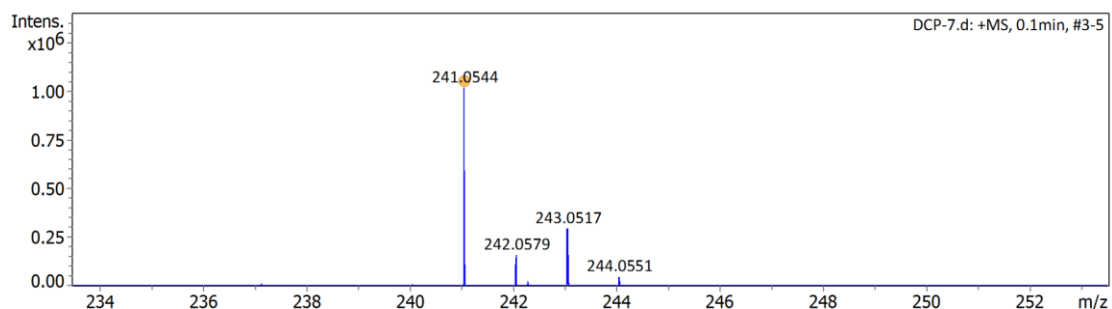


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
225.0846	1	C ₁₅ H ₁₀ F ¹⁵ N	225.0840	C ₁₅ H ₁₁ F ¹⁵ N	M+H	-2.3	121.7	100.00	11.0	even	-

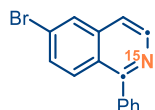


6-Chloro-1-phenylisoquinoline-¹⁵N (**34**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 50.3 mg, 70% yield; reaction time = 12 h; mp 108.3-108.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.62-8.58 (m, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.82 (s, 1H), 7.65 (d, *J* = 4.0 Hz, 2H), 7.54-7.47 (m, 4H), 7.44-7.42 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.6 (d, *J* = 2.0 Hz), 143.2, 138.9 (d, *J* = 7.0 Hz), 137.5 (d, *J* = 2.0 Hz), 136.1, 129.7 (d, *J* = 1.0 Hz), 129.3, 128.7, 128.3, 128.0, 125.6, 124.7 (d, *J* = 2.0 Hz), 118.8 (d, *J* = 2.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 307.3 (d, *J* = 11.0 Hz). IR (KBr) ν 3058, 1611, 1539, 1073, 753 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₁Cl¹⁵N [M+H]⁺: 241.0545, found: 241.0544, >99% ¹⁵N incorporation determined by HRMS.



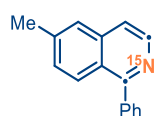
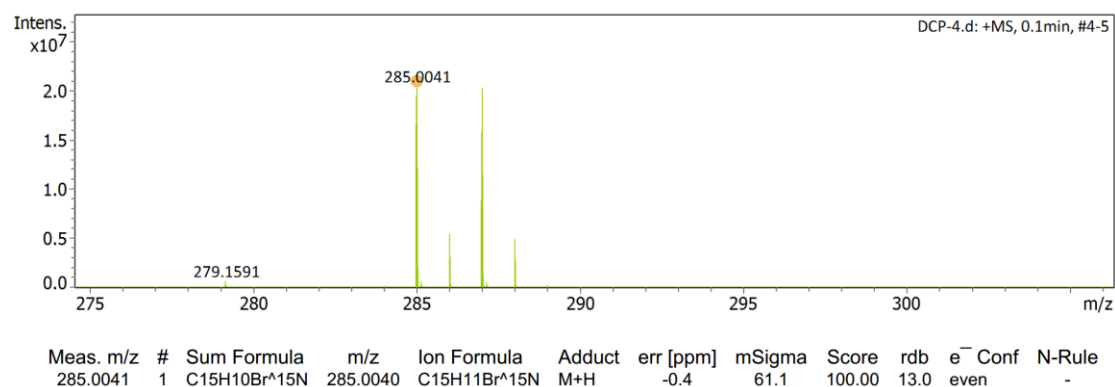
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
241.0544	1	C ₁₅ H ₁₀ Cl ¹⁵ N	241.0545	C ₁₅ H ₁₁ Cl ¹⁵ N	M+H	0.2	21.7	100.00	14.0	even	-



6-Bromo-1-phenylisoquinoline-¹⁵N (**35**)

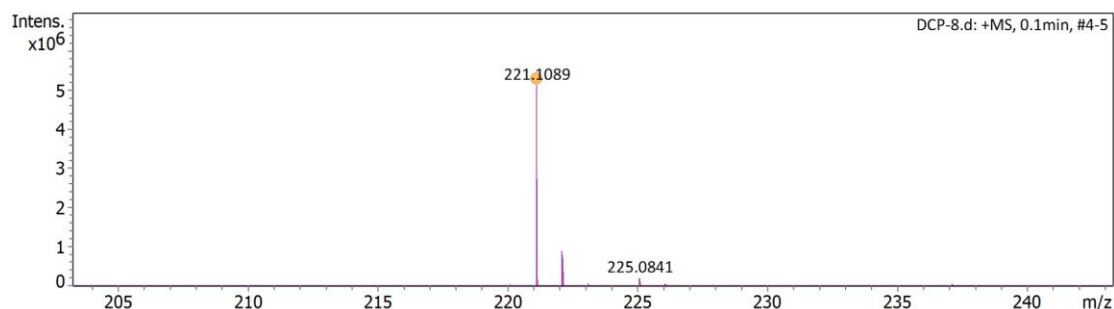
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 69.8 mg, 82% yield; reaction time = 6 h; mp 108.5-109.3 °C; ¹H NMR (400 MHz, CDCl₃)

δ 8.59 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 7.97 (s, 1H), 7.92 (d, $J = 8.0$ Hz, 1H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.54-7.47 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.5 (d, $J = 2.0$ Hz), 143.1, 138.8 (d, $J = 8.0$ Hz), 137.7 (d, $J = 2.0$ Hz), 130.4, 129.6 (d, $J = 1.0$ Hz), 129.1, 128.8, 128.7, 128.3, 124.8 (d, $J = 2.0$ Hz), 124.6, 118.6 (d, $J = 2.0$ Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 307.6 (d, $J = 11.0$ Hz). IR (KBr) ν 3056, 1555, 1481, 1372, 765 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{11}\text{Br}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 285.0040, found: 285.0041, >99% ^{15}N incorporation determined by HRMS.



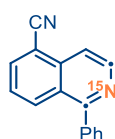
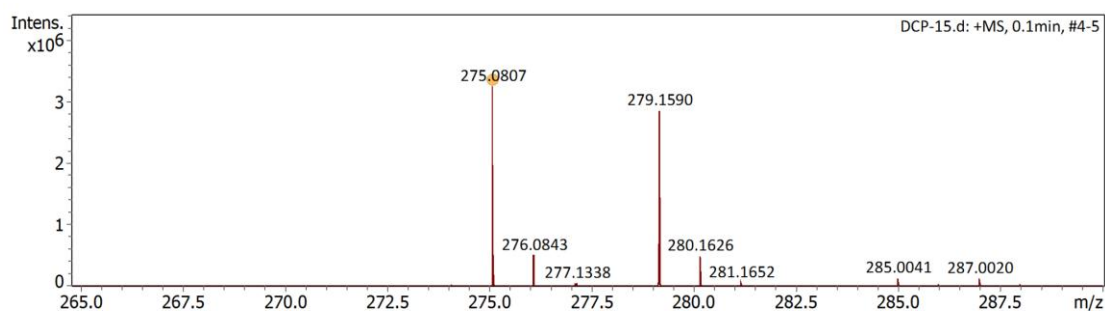
6-Methyl-1-phenylisoquinoline- ^{15}N (**36**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 36.2 mg, 55% yield; reaction time = 12 h; mp 102.4-102.8 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 8.56 (dd, $J_1 = 12.0$ Hz, $J_2 = 4.0$ Hz, 1H), 7.99 (d, $J = 8.0$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 2H), 7.64 (s, 1H), 7.56-7.47 (m, 4H), 7.36 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.3 (d, $J = 2.0$ Hz), 142.2, 140.3, 139.6 (d, $J = 8.0$ Hz), 137.1 (d, $J = 2.0$ Hz), 129.8 (d, $J = 1.0$ Hz), 129.4, 128.5, 128.3, 127.4, 125.8, 125.1, 119.4 (d, $J = 2.0$ Hz), 21.8; ^{15}N NMR (50 MHz, CDCl_3) δ 303.3 (d, $J = 11.0$ Hz). IR (KBr) ν 3049, 2375, 1628, 1550, 1382, 763 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 221.1091, found: 221.1089, >99% ^{15}N incorporation determined by HRMS.



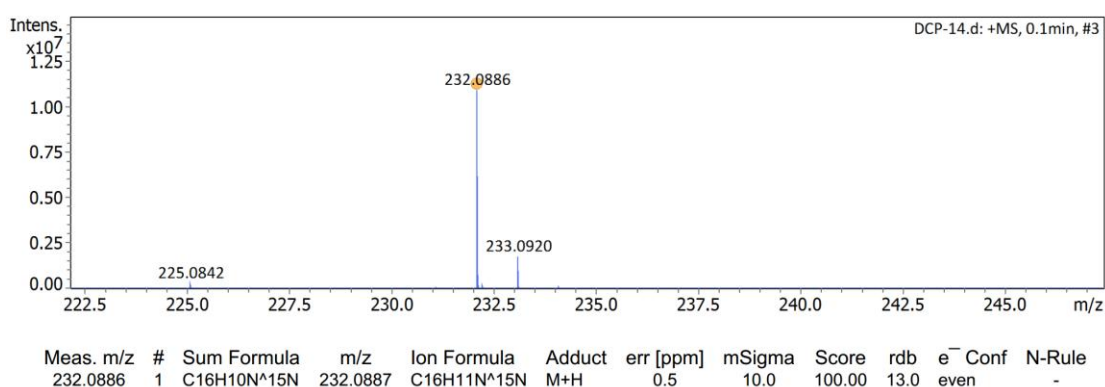
1-Phenyl-5-(trifluoromethyl)isoquinoline-¹⁵N (**37**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 47.0 mg, 57% yield; reaction time = 6 h; mp 131.5-131.8 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.76-8.71 (m, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 8.06-8.04 (m, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.67-7.65 (m, 2H), 7.56-7.49 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 161.5 (d, *J* = 2.0 Hz), 143.6, 139.0 (d, *J* = 7.0 Hz), 132.8, 132.2, 129.9 (d, *J* = 1.0 Hz), 128.9, 128.5-128.3 (m, 1C), 126.8 (d, *J* = 2.0 Hz), 125.8, 125.5, 125.4, 122.8, 115.9 (t, *J* = 2.0 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -59.99; ¹⁵N NMR (50 MHz, CDCl₃) δ 309.3 (d, *J* = 11.0 Hz). IR (KBr) ν 3077, 1549, 1311, 1131, 767 cm⁻¹. HRMS (ESI) calcd for C₁₆H₁₁F₃¹⁵N [M+H]⁺: 275.0808, found: 275.0807, >99% ¹⁵N incorporation determined by HRMS.



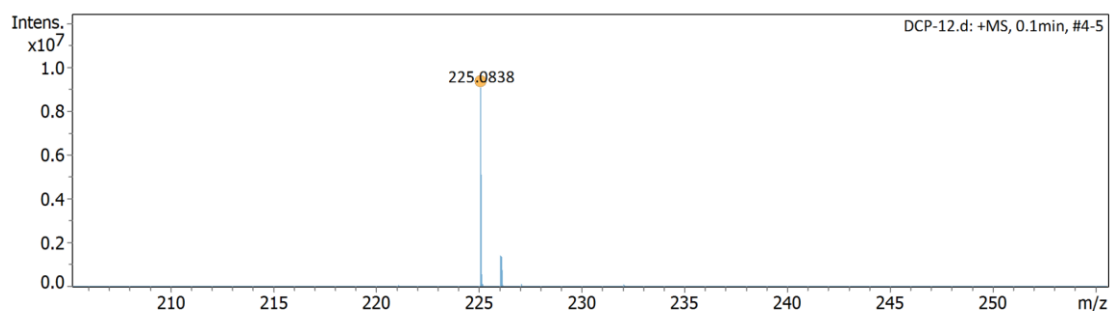
1-Phenylisoquinoline-¹⁵N-5-carbonitrile (**38**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 41.7 mg, 60% yield; reaction time = 6 h; mp 131.5-132.6 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.78-8.73 (m, 1H), 8.34-8.31 (m, 1H), 8.08-8.06 (m, 1H), 7.97-7.96 (m, 1H), 7.64-7.62 (m, 2H), 7.59-7.48 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.3 (d, $J = 2.0$ Hz), 144.4, 138.2 (d, $J = 7.0$ Hz), 136.1, 132.8, 129.8, 129.7, 129.0, 128.4, 126.2, 125.8 (d, $J = 2.0$ Hz), 116.6, 116.5, 109.6; ^{15}N NMR (50 MHz, CDCl_3) δ 312.0 (d, $J = 11.0$ Hz). IR (KBr) ν 3040, 2223, 1578, 1551, 1345, 764 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{11}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 232.0887, found: 232.0886, >99% ^{15}N incorporation determined by HRMS.



5-Fluoro-1-phenylisoquinoline- ^{15}N (**39**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 56.6 mg, 84% yield; reaction time = 12 h; mp 66.1-67.3 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.67 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 7.90-7.87 (m, 2H), 7.69 (s, 1H), 7.68 (s, 1H), 7.55-7.48 (m, 3H), 7.46-7.40 (m, 1H), 7.33 (t, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.2 (d, $J = 3.0$ Hz), 157.7 (d, $J = 252.0$ Hz), 142.4, 139.1 (d, $J = 8.0$ Hz), 129.7 (d, $J = 2.0$ Hz), 128.7, 128.3, 127.6 (dd, $J_1 = 5.0$ Hz, $J_2 = 2.0$ Hz), 127.4 (dd, $J_1 = 17.0$ Hz, $J_2 = 2.0$ Hz), 126.6 (d, $J = 8.0$ Hz), 123.3 (d, $J = 4.0$ Hz), 113.3 (d, $J = 19.0$ Hz), 112.3 (dd, $J_1 = 4.0$ Hz, $J_2 = 2.0$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ -122.41; ^{15}N NMR (50 MHz, CDCl_3) δ 309.2 (d, $J = 11.0$ Hz). IR (KBr) ν 3051, 1585, 1490, 1412, 1233, 759 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{11}\text{F}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 225.0840, found: 225.0838, >99% ^{15}N incorporation determined by HRMS.

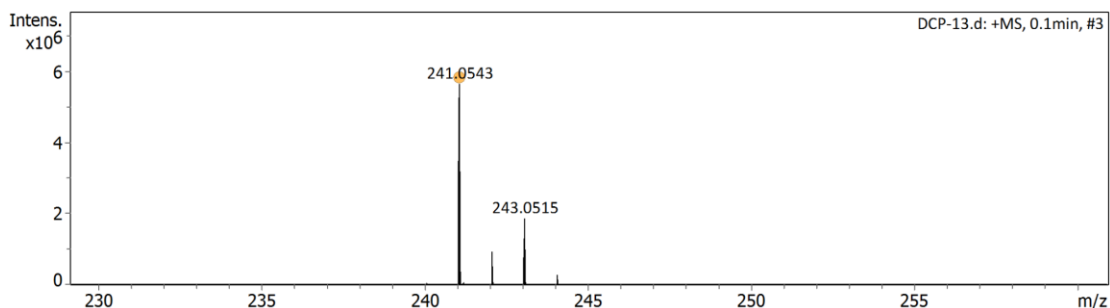


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdB	e ⁻ Conf	N-Rule
225.0838	1	C ₁₅ H ₁₀ F ¹⁵ N	225.0840	C ₁₅ H ₁₁ F ¹⁵ N	M+H	1.0	3.7	100.00	11.0	even	-

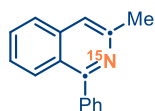


5-Chloro-1-phenylisoquinoline-¹⁵N (**40**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 46.3 mg, 64% yield; reaction time = 12 h; mp 41.2-42.1 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.56-8.52 (m, 1H), 7.85 (s, 2H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.37-7.35 (m, 3H), 7.23-7.21 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.7 (d, *J* = 2.0 Hz), 143.0, 139.9 (d, *J* = 7.0 Hz), 134.4 (d, *J* = 2.0 Hz), 131.1, 129.7 (d, *J* = 1.0 Hz), 129.7, 128.6, 128.2, 127.4 (d, *J* = 2.0 Hz), 126.6, 126.5, 115.9 (d, *J* = 2.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 308.9 (d, *J* = 11.0 Hz). IR (KBr) ν 3051, 1571, 1339, 757 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₁Cl¹⁵N [M+H]⁺: 241.0545, found: 241.0543, >99% ¹⁵N incorporation determined by HRMS.



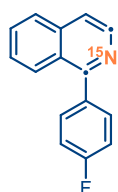
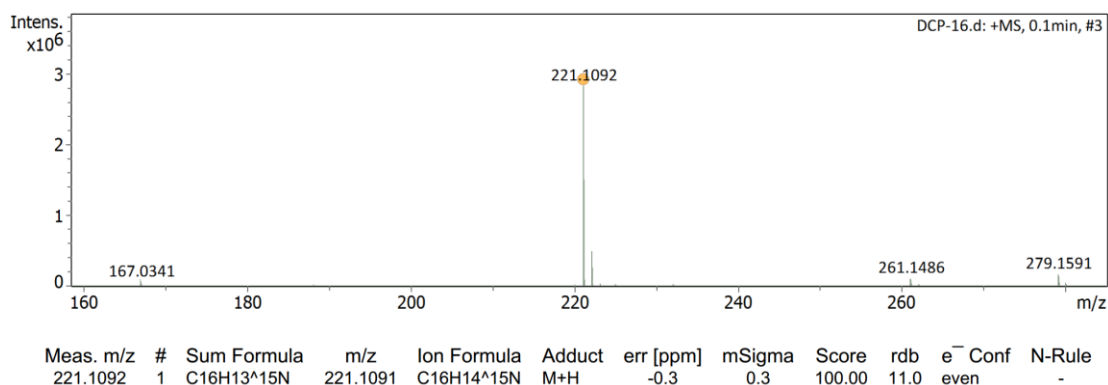
Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdB	e ⁻ Conf	N-Rule
241.0543	1	C ₁₅ H ₁₀ Cl ¹⁵ N	241.0545	C ₁₅ H ₁₁ Cl ¹⁵ N	M+H	0.8	2.1	100.00	14.0	even	-



3-Methyl-1-phenylisoquinoline-¹⁵N (**41**)

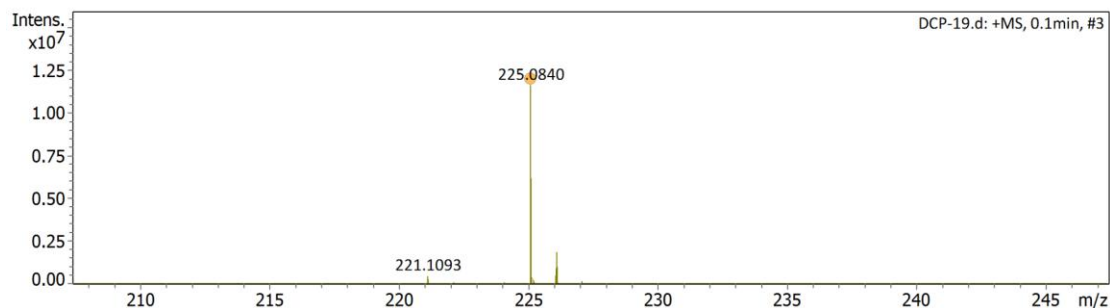
Light yellow oil obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 45.4 mg, 69% yield; reaction time = 12 h; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, *J* =

8.0 Hz, 1H), 7.69-7.64 (m, 3H), 7.53 (t, $J = 8.0$ Hz, 1H), 7.49-7.33 (m, 5H), 2.71 (d, $J = 4.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.9 (d, $J = 3.0$ Hz), 150.5, 139.4 (d, $J = 7.0$ Hz), 137.2 (d, $J = 1.0$ Hz), 129.6 (d, $J = 1.0$ Hz), 129.6, 128.2, 128.1, 127.2, 126.1, 125.9, 124.6 (d, $J = 2.0$ Hz), 117.7 (d, $J = 2.0$ Hz), 24.2 (d, $J = 10.0$ Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 310.9. IR (KBr) ν 3065, 2920, 1620, 1551, 1351, 763 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 221.1091, found: 221.1092, >99% ^{15}N incorporation determined by HRMS.

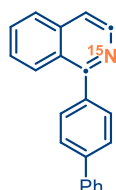


1-(4-Fluorophenyl)isoquinoline- ^{15}N (**42**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 49.0 mg, 73% yield; reaction time = 6 h; mp 79.0-79.9 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.61 (dd, $J_1 = 8.0$ Hz, $J_2 = 4.0$ Hz, 1H), 8.08 (d, $J = 8.0$ Hz, 1H), 7.89 (s, 1H), 7.71-7.65 (m, 4H), 7.55 (d, $J = 4.0$ Hz, 1H), 7.26-7.22 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.9 (d, $J = 246.0$ Hz), 159.3 (d, $J = 2.0$ Hz), 142.0, 136.7 (d, $J = 2.0$ Hz), 135.5 (dd, $J_1 = 7.0$ Hz, $J_2 = 3.0$ Hz), 131.6 (dd, $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz), 129.9, 127.2, 127.1, 126.9, 126.4 (d, $J = 2.0$ Hz), 119.9 (d, $J = 2.0$ Hz), 115.2 (d, $J = 21.0$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ -113.0 (d, $J = 3.8$ Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 306.7 (d, $J = 11.0$ Hz). IR (KBr) ν 3058, 1602, 1508, 1221, 759 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{11}\text{F}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 225.0840, found: 225.0840, >99% ^{15}N incorporation determined by HRMS.

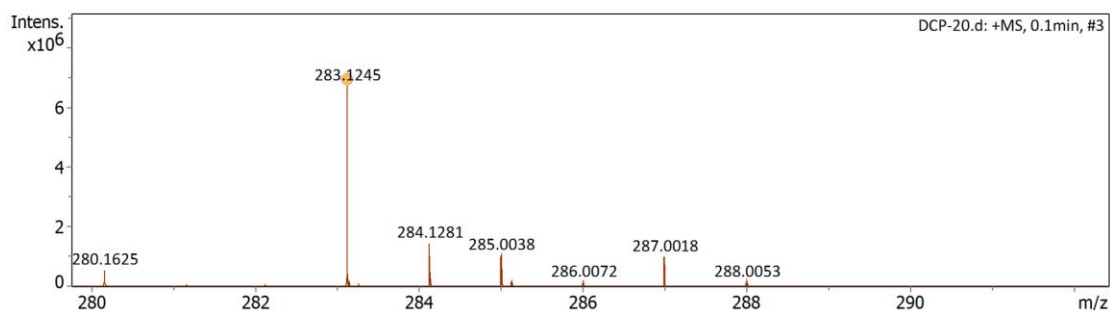


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
225.0840	1	C15H10F ¹⁵ N	225.0840	C15H11F ¹⁵ N	M+H	0.3	2.1	100.00	11.0	even	-

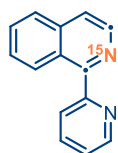


1-([1,1'-Biphenyl]-4-yl)isoquinoline-¹⁵N (**43**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 61.8 mg, 73% yield; reaction time = 12 h; mp 178.9-179.5 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.65 (dd, *J*₁ = 12.0 Hz, *J*₂ = 8.0 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.81 (q, *J* = 8.0 Hz, 4H), 7.72-7.66 (m, 4H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.2 (d, *J* = 2.0 Hz), 142.2, 141.3, 140.6, 138.4 (d, *J* = 7.0 Hz), 136.8 (d, *J* = 2.0 Hz), 130.3, 130.3, 129.9, 128.8, 127.5, 127.1, 127.0, 126.9, 126.6 (d, *J* = 2.0 Hz), 119.8 (d, *J* = 2.0 Hz), one carbon missing in the aromatic region; ¹⁵N NMR (50 MHz, CDCl₃) δ 306.5 (d, *J* = 11.0 Hz). IR (KBr) ν 3050, 1540, 1485, 1381, 764 cm⁻¹. HRMS (ESI) calcd for C₂₁H₁₆¹⁵N [M+H]⁺: 283.1248, found: 283.1245, >99% ¹⁵N incorporation determined by HRMS.

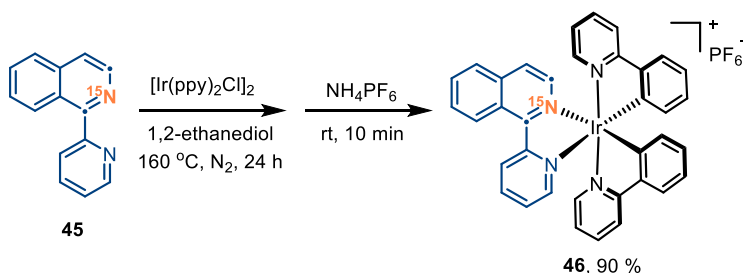
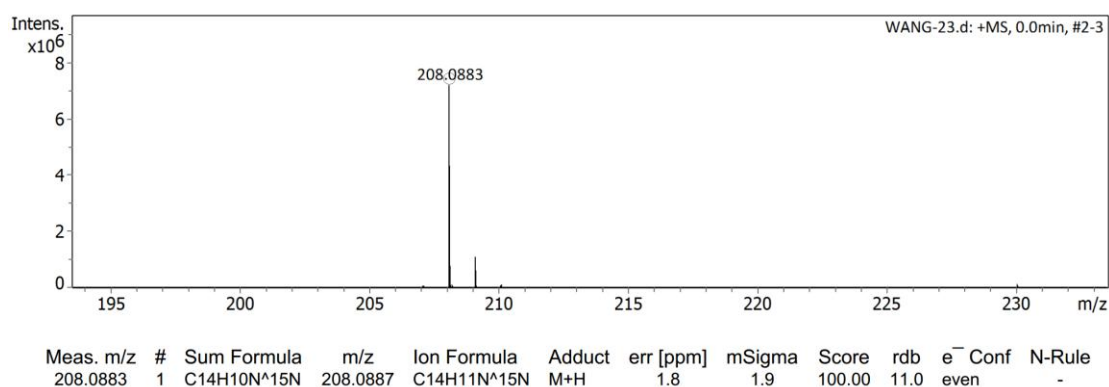


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
283.1245	1	C21H15 ¹⁵ N	283.1248	C21H16 ¹⁵ N	M+H	0.8	6.0	100.00	15.0	even	-



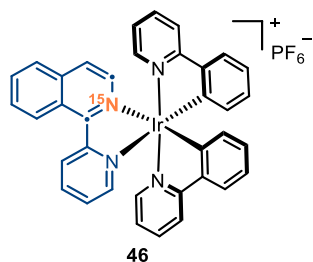
1-(Pyridin-2-yl)isoquinoline-¹⁵N (**45**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1 to 10:1); 53.4 mg, 86% yield; reaction time = 12 h; mp 64.7-65.9 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.77 (d, *J* = 4.0 Hz, 1H), 8.66-8.60 (m, 2H), 8.07-8.03 (m, 3H), 7.94 (d, *J* = 4.0 Hz, 1H), 7.80 (t, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 158.2 (d, *J* = 8.0 Hz), 157.5, 148.6, 141.8, 137.1 (d, *J* = 2.0 Hz), 136.9, 130.1, 127.7, 127.6, 126.9, 126.6, 125.2, 123.2, 121.2; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 305.5 (d, *J* = 9.0 Hz). IR (KBr) ν 3055, 1582, 1545, 745 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₁N¹⁵N [M+H]⁺: 208.0887, found: 208.0883, >99% ¹⁵N incorporation determined by HRMS.

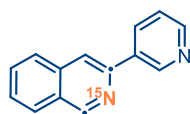
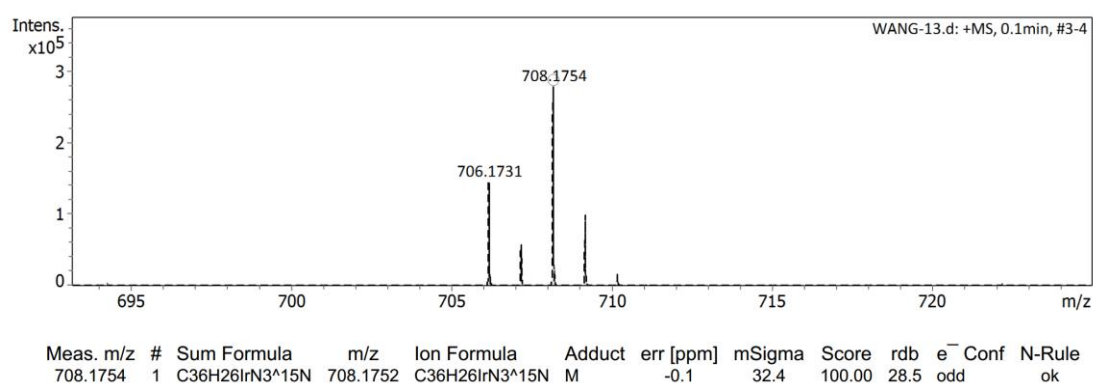


General procedure: To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **45** (32.6 mg, 0.156 mmol, 2.1 equiv.) and [Ir(ppy)₂Cl]₂ (80.4 mg, 0.075 mmol, 1.0 equiv.) at room temperature. 1,2-Ethanediol (2.0 mL) was subsequently added, and the reaction mixture was degasified by sparging with nitrogen for 15 minutes. The reaction mixture was stirred at 160 °C for 24 h. After cooling to room temperature, NH₄PF₆ (200.0 mg) in H₂O (2.0 mL) was added, and the resulting mixture was stirred for 10 min. Then, the crude mixture was concentrated under reduced pressure and purified by

silica gel column chromatography (200–300 mesh size, using ethyl acetate as eluent) to afford compound **46** (90%, 115.3 mg).



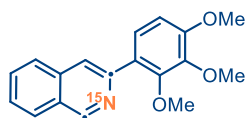
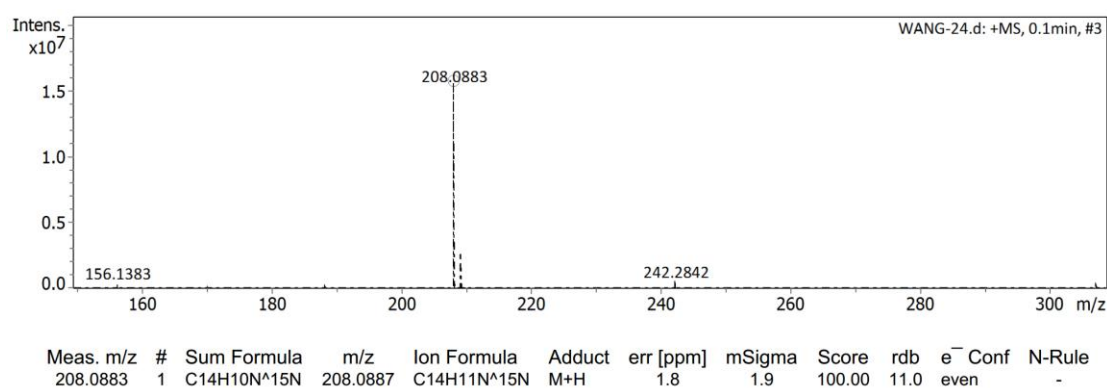
Grey solid obtained by column chromatography (ethyl acetate as the eluent); 115.3 mg, 90% yield; reaction time = 24 h; mp 196.2–197.2 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.86 (d, J = 8.0 Hz, 1H), 8.77 (d, J = 8.0 Hz, 1H), 8.19 (t, J = 8.0 Hz, 1H), 8.06 (d, J = 4.0 Hz, 1H), 7.96–7.80 (m, 6H), 7.76–7.64 (m, 6H), 7.54 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.02–6.98 (m, 3H), 6.94–6.87 (m, 3H), 6.29 (t, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.5, 167.3, 156.6 (d, J = 9.0 Hz), 155.9 (d, J = 4.0 Hz), 151.0, 149.9, 149.8, 149.7, 148.9, 148.6, 143.5, 143.4, 141.1, 141.0, 139.4, 138.2, 138.1, 137.1 (d, J = 4.0 Hz), 132.6, 131.8, 131.6, 131.1, 130.7, 130.2 (d, J = 2.0 Hz), 128.1 (d, J = 2.0 Hz), 127.5 (d, J = 2.0 Hz), 126.3, 126.2, 126.1, 124.8, 124.7, 123.6, 123.2, 122.6 (d, J = 2.0 Hz), 119.7, 119.4; ^{15}N NMR (50 MHz, CDCl_3) δ 244.8 (q, J = 3.0 Hz); ^{19}F NMR (376 MHz, CDCl_3) δ -73.21 (d, J = 710.6 Hz); ^{31}P NMR (162 MHz, CDCl_3) δ -131.3 to -157.7 (m, 1P). IR (KBr) ν 3050, 1476, 841 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{36}\text{H}_{26}\text{IrN}_3^{15}\text{N}$ $[\text{M}-\text{PF}_6]^+$: 708.1752, found: 708.1754, >99% ^{15}N incorporation determined by HRMS.



3-(Pyridin-3-yl)isoquinoline- ^{15}N (**48**)

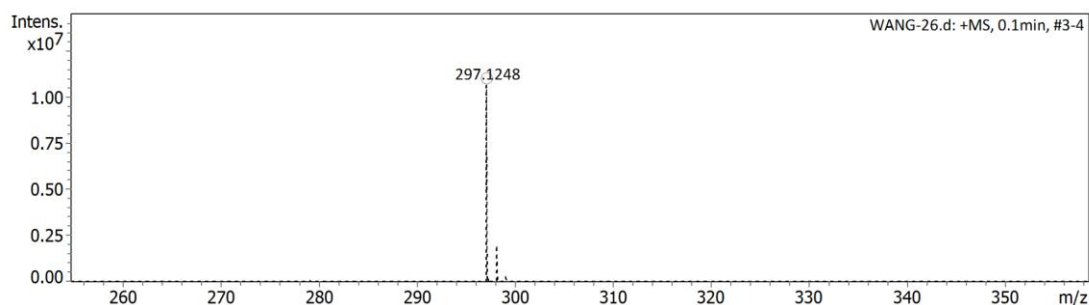
Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate =

30:1 to 10:1); 48.7 mg, 78% yield; reaction time = 12 h; mp 87.7-88.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.25 (s, 2H), 8.58 (s, 1H), 8.34 (s, 1H), 7.97-7.75 (m, 3H), 7.62-7.51 (m, 2H), 7.34 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 152.4, 148.9, 147.9, 147.8 (d, *J* = 2.0 Hz), 136.0, 134.7 (dd, *J*₁ = 7.0 Hz, *J*₂ = 2.0 Hz), 134.0, 130.5, 127.6, 127.3, 127.2, 126.6, 123.3, 116.5; ¹⁵N NMR (50 MHz, CDCl₃) δ 302.9 (d, *J* = 11.0 Hz). IR (KBr) ν 3050, 1584, 1485, 1439, 749 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₁N¹⁵N [M+H]⁺: 208.0887, found: 208.0883, >99% ¹⁵N incorporation determined by HRMS.

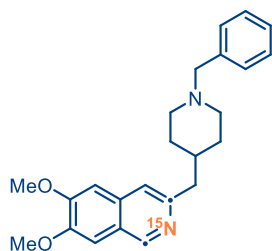


3-(2,3,4-Trimethoxyphenyl)isoquinoline-¹⁵N (50)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 3:1); 72.0 mg, 81% yield; reaction time = 12 h; mp 96.5-97.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.32 (d, *J* = 12.0 Hz, 1H), 8.21 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.70-7.65 (m, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H), 3.78 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 153.8, 152.1, 151.8 (d, *J* = 1.0 Hz), 148.9, 142.5, 136.4, 130.2, 127.3 (d, *J* = 1.0 Hz), 127.2 (d, *J* = 1.0 Hz), 127.0 (d, *J* = 7.5 Hz), 126.9, 126.8, 125.5 (d, *J* = 2.5 Hz), 120.1 (d, *J* = 1.0 Hz), 107.7, 61.1, 61.0, 56.0; ¹⁵N NMR (50 MHz, CDCl₃) δ 307.2 (d, *J* = 11.0 Hz). IR (KBr) ν 2970, 2937, 1599, 1286, 1110, 1078, 760 cm⁻¹. HRMS (ESI) calcd for C₁₈H₁₈O₃¹⁵N [M+H]⁺: 297.1252, found: 297.1248, >99% ¹⁵N incorporation determined by HRMS.

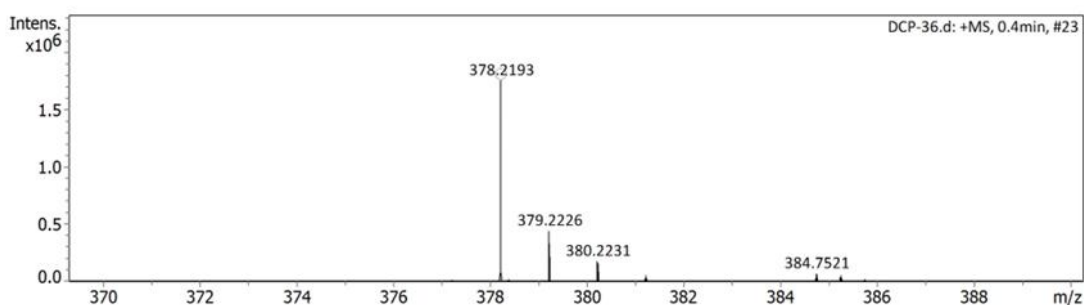


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
297.1248	1	C ₁₈ H ₁₇ O ₃ ¹⁵ N	297.1252	C ₁₈ H ₁₈ O ₃ ¹⁵ N	M+H	1.2	6.1	100.00	11.0	even		-



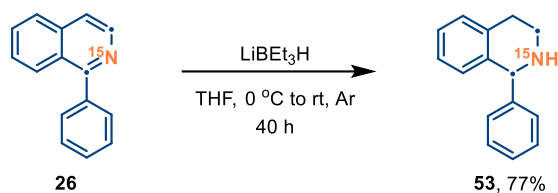
3-((1-Benzylpiperidin-4-yl)methyl)-6,7-dimethoxyisoquinoline-¹⁵N (**52**)

Light yellow solid obtained by column chromatography (dichloromethane/methanol = 50:1 to 20:1); 80.6 mg, 71% yield; reaction time = 12 h; mp 127.9-128.3 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.08 (d, *J* = 8.0 Hz, 1H), 7.43-7.38 (m, 7H), 7.09 (s, 1H), 4.11 (s, 6H), 3.72 (s, 2H), 3.08 (s, 2H), 2.89 (s, 2H), 2.19 (s, 2H), 2.03 (s, 1H), 1.76 (s, 2H), 1.61 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 153.1, 152.2, 149.8, 149.5, 133.0 (d, *J* = 2.0 Hz), 129.6, 128.3, 127.5, 122.9, 118.1, 105.1, 104.2, one carbon missing in the aromatic region, 62.8, 56.0, 56.0, 53.5, 44.7 (d, *J* = 8.0 Hz), 36.0, 31.4; ¹⁵N NMR (50 MHz, CDCl₃) δ 298.1 (d, *J* = 11.0 Hz). IR (KBr) ν 2919, 2803, 1501, 1245, 1146, 738 cm⁻¹. HRMS (ESI) calcd for C₂₄H₂₉NO₂¹⁵N [M+H]⁺: 378.2194, found: 378.2192, >99% ¹⁵N incorporation determined by HRMS.

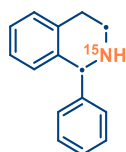


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
378.2193	1	C ₂₄ H ₂₈ NO ₂ ¹⁵ N	378.2194	C ₂₄ H ₂₉ NO ₂ ¹⁵ N	M+H	0.4	36.4	100.00	12.0	even		-

6. Late-stage assembly of drugs and bioactive natural products

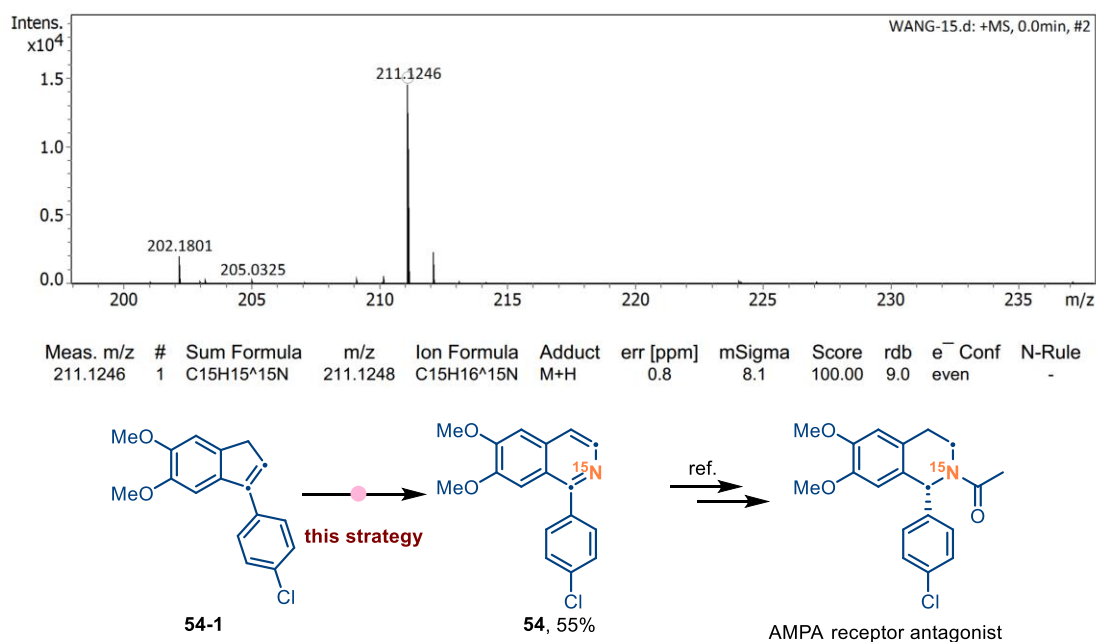


General procedure: To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **26** (41.2 mg, 0.20 mmol) and THF (0.3 mL). The reaction mixture was degasified by sparging with argon for 15 minutes. After cooling to 0 °C, LiBEt₃H (1.0 M in THF, 2.0 mL) was added via syringe. The reaction mixture was allowed to warm to room temperature and stirred for 40 h. The reaction was then quenched with MeOH (1.0 mL) and stirred for an additional 10 min. The mixture was concentrated under reduced pressure, and the residue was partitioned between water (5.0 mL) and EtOAc. The organic layer was dried over Na₂SO₄, concentrated, and purified by silica gel column chromatography to afford compound **53** as a white solid (77%, 32.3 mg).

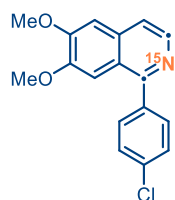


1-Phenyl-1,2,3,4-tetrahydroisoquinoline-¹⁵N (53**)**

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1); 32.3 mg, 77% yield; reaction time = 40 h; mp 89.4-89.9 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.32-7.29 (m, 2H), 7.26-7.23 (m, 3H), 7.12-7.07 (m, 2H), 6.99 (t, *J* = 5.0 Hz, 1H), 6.62 (d, *J* = 10.0 Hz, 1H), 4.97 (s, 1H), 3.12-3.07 (m, 1H), 2.94-2.87 (m, 2H), 2.73-2.70 (m, 1H), one hydrogen for ¹⁵N-H was missing; ¹³C NMR (125 MHz, DMSO-*d*₆) δ 145.4 (d, *J* = 2.0 Hz), 138.9, 135.5, 128.9, 128.1, 127.6, 126.9, 125.9, 125.3, 61.2 (d, *J* = 4.0 Hz), 41.7 (d, *J* = 4.0 Hz), 29.3, one carbon in aromatic region was missing; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 46.6. IR (KBr) ν 3433, 3250, 2792, 1489, 743 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₆¹⁵N [M+H]⁺: 211.1248, found: 211.1246, >99% ¹⁵N incorporation determined by HRMS.

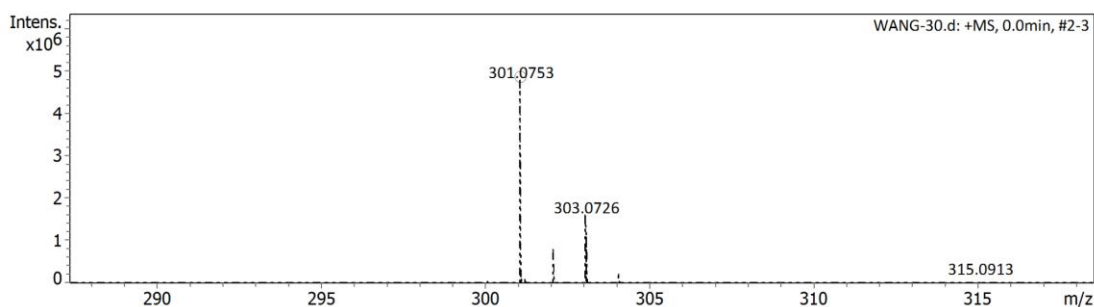


General procedure: To an oven-dried 25 mL Schlenk tube equipped with a magnetic stir bar were added indene **54-1** (86.0 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), ¹⁵NH₄Cl (48.7 mg, 0.90 mol), NaOAc (147.7 mg, 1.80 mmol), and TFE (2.0 mL). The mixture was irradiated with a 12 W blue LED lamp ($\lambda_{\text{max}} = 455\text{-}460\text{ nm}$) in air at room temperature for 24 h. The reaction mixture was then concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford compound **54** as a white solid (55%, 49.2 mg).

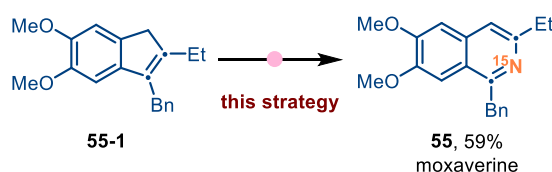


1-(4-Chlorophenyl)-6,7-dimethoxyisoquinoline-¹⁵N (**54**)

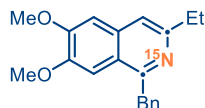
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1); 49.2 mg, 55% yield; reaction time = 24 h; mp 134.1-134.7 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.49-8.45 (m, 1H), 7.66 (d, $J = 8.0\text{ Hz}$, 2H), 7.51 (d, $J = 8.0\text{ Hz}$, 3H), 7.30 (s, 1H), 7.14 (s, 1H), 4.05 (s, 3H), 3.88 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 156.9, 152.8, 150.2, 141.3, 138.4 (d, $J = 8.0\text{ Hz}$), 134.5, 133.8, 131.0, 130.9, 128.7, 122.4, 119.1, 105.0, 56.1, 55.9; ¹⁵N NMR (50 MHz, CDCl₃) δ 299.9 (d, $J = 11.0\text{ Hz}$). IR (KBr) ν 2945, 1625, 1508, 1483, 1230, 1118 cm⁻¹. HRMS (ESI) calcd for C₁₇H₁₅ClO₂¹⁵N [M+H]⁺: 301.0756, found: 301.0753, >99% ¹⁵N incorporation determined by HRMS.



Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
301.0753	1	C17H14ClO2 ¹⁵ N	301.0756	C17H15ClO2 ¹⁵ N	M+H	1.0	10.7	100.00	14.0	even	-	-

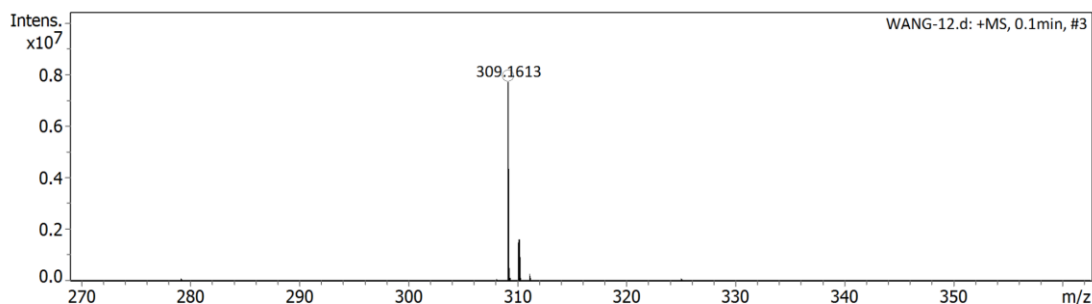


General procedure: To an oven-dried 25 mL Schlenk tube equipped with a magnetic stir bar were added indene **55-1** (58.9 mg, 0.20 mmol), methylene blue (1.9 mg, 0.006 mmol), $^{15}\text{NH}_4\text{Cl}$ (64.9 mg, 1.20 mol), NaOAc (98.4 mg, 1.20 mmol), and TFE (2.0 mL). The mixture was irradiated with a 12 W blue LED lamp ($\lambda_{\text{max}} = 455\text{-}460\text{ nm}$) in air at room temperature for 17 h. The reaction mixture was then concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford compound **55** as a colorless oil (59%, 36.3 mg).

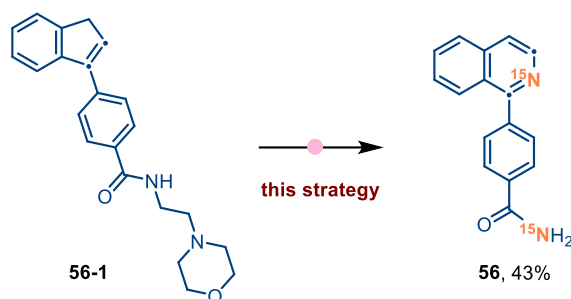


1-Benzyl-3-ethyl-6,7-dimethoxyisoquinoline- ^{15}N (**55**)

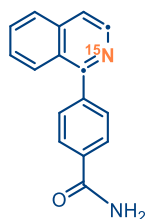
Colorless oil obtained by column chromatography (petroleum ether/ethyl acetate = 3:1); 36.3 mg, 59% yield; reaction time = 17 h; ^1H NMR (400 MHz, CDCl_3) δ 7.19-7.13 (m, 6H), 7.06 (t, $J = 8.0\text{ Hz}$, 1H), 6.89 (s, 1H), 4.51 (d, $J = 4.0\text{ Hz}$, 2H), 3.88 (s, 3H), 3.74 (s, 3H), 2.90-2.85 (m, 2H), 1.31 (t, $J = 8.0\text{ Hz}$, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.9 (d, $J = 2.5\text{ Hz}$), 154.6, 152.3, 149.0, 139.7, 134.2, 128.4, 128.4, 126.1, 120.9 (d, $J = 2.5\text{ Hz}$), 115.4 (d, $J = 2.5\text{ Hz}$), 104.8, 104.2, 55.8, 55.7, 42.6 (d, $J = 8.8\text{ Hz}$), 30.8 (d, $J = 8.8\text{ Hz}$), 14.2; ^{15}N NMR (50 MHz, CDCl_3) δ 302.1. IR (KBr) ν 2961, 1507, 1423, 1242, 1162, 759 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{22}\text{O}_2^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 309.1615, found: 309.1613, >99% ^{15}N incorporation determined by HRMS.



Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
309.1613	1	C ₂₀ H ₂₁ O ₂ ¹⁵ N	309.1615	C ₂₀ H ₂₂ O ₂ ¹⁵ N	M+H	0.8	5.1	100.00	11.0	even		-



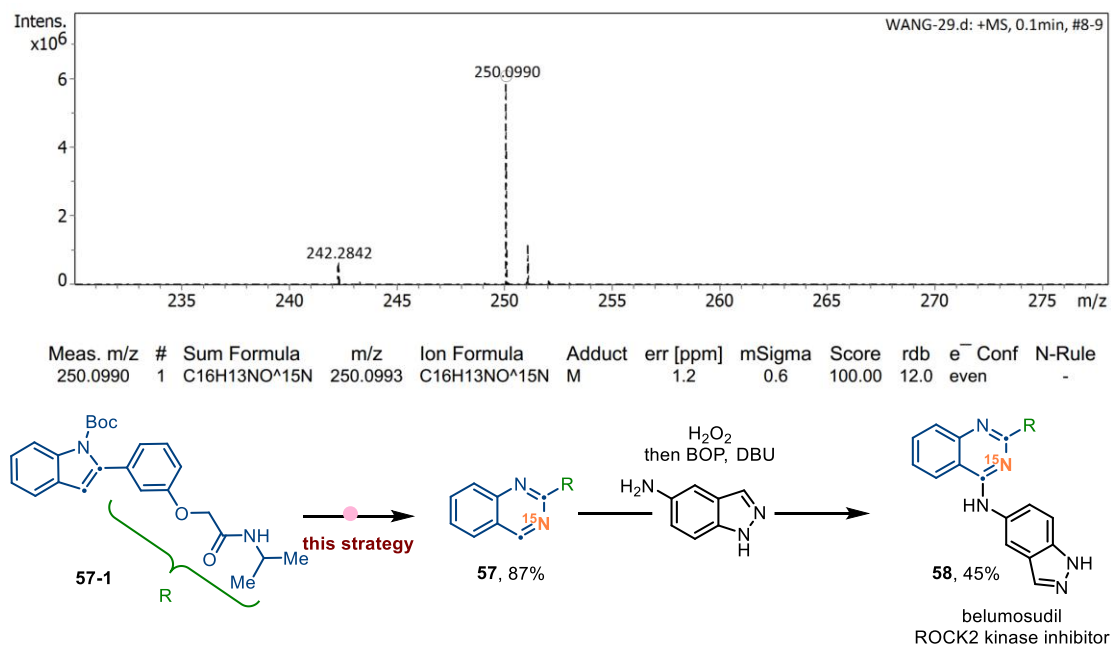
General procedure: To an oven-dried 25 mL Schlenk tube equipped with a magnetic stir bar were added indene **56-1** (104.5 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), ¹⁵NH₄Cl (81.1 mg, 1.50 mol), NaOAc (246.1 mg, 3.0 mmol), and TFE (2.0 mL). The mixture was irradiated with a 12 W blue LED lamp ($\lambda_{\text{max}} = 455\text{-}460\text{ nm}$) in air at room temperature for 17 h. The reaction mixture was then concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford compound **56** as a light yellow solid (43%, 32.3 mg).



4-(Isoquinolin-1-yl-¹⁵N)benzamide-¹⁵N (**56**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1 to 5:1); 32.3 mg, 43% yield; reaction time = 72 h; mp 226.9-227.4 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.61 (dd, $J_1 = 12.0\text{ Hz}$, $J_2 = 4.0\text{ Hz}$, 1H), 8.13 (br, 1H), 8.07 (t, $J = 8.0\text{ Hz}$, 3H), 8.00 (d, $J = 8.0\text{ Hz}$, 1H), 7.90 (d, $J = 8.0\text{ Hz}$, 1H), 7.82 (t, $J = 8.0\text{ Hz}$, 1H), 7.75 (d, $J = 8.0\text{ Hz}$, 2H), 7.67 (t, $J = 8.0\text{ Hz}$, 1H), 7.50 (br, 1H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 167.6, 159.0, 142.1, 141.8 (d, $J = 7.5\text{ Hz}$), 136.4, 134.3, 130.5, 129.8, 128.0, 127.5, 127.3, 126.6, 125.8, 120.4; ¹⁵N NMR (50

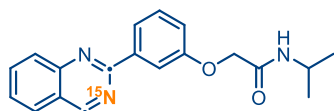
MHz, DMSO-*d*₆) δ 309.7 (d, *J* = 11.0 Hz). IR (KBr) ν 3351, 3178, 1666, 1620, 1390 cm⁻¹. HRMS (ESI) calcd for C₁₆H₁₃NO¹⁵N [M+H]⁺: 250.0993, found: 250.0990, >99% ¹⁵N incorporation determined by HRMS.



General procedure for the formation of 57: To an oven-dried 25 mL Schlenk tube equipped with a magnetic stir bar were added indole **57-1** (122.6 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), and TFE (2.0 mL). The mixture was irradiated with a 12 W blue LED lamp (λ_{max} = 455-460 nm) under air at room temperature for 12 h. Upon completion, the light source was removed, and TFA (67.0 μ L, 0.90 mmol) was added. The resulting mixture was stirred at room temperature for 2 h. ¹⁵NH₄Cl (81.1 mg, 1.50 mol) and NaOAc (246.1 mg, 3.0 mmol) were subsequently added, and the reaction was stirred at 70 °C for 10 h. After cooling to rt, the mixture was concentrated and purified by silica gel column chromatography to give compound **57** as a white solid (87%, 84.2 mg).

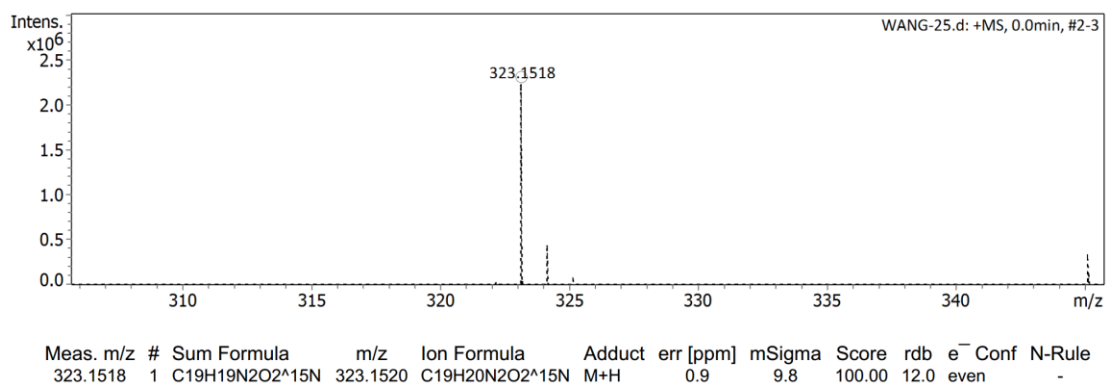
General procedure for the formation of 58 (step 1): To an oven-dried 25 mL round-bottom flask equipped with a magnetic stir bar were added indole **57** (360.4 mg, 1.20 mmol), aqueous H₂O₂ (326.0 mg, 2.88 mmol, 2.4 equiv), and AcOH (5.0 mL). The mixture was degassed by sparging with oxygen for 15 min. The reaction mixture was then heated to 55 °C with stirring for 10 h. The reaction mixture was cooled to room temperature, diluted with dichloromethane (5.0 mL), and washed with sat. K₂CO₃ solution (5.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure.

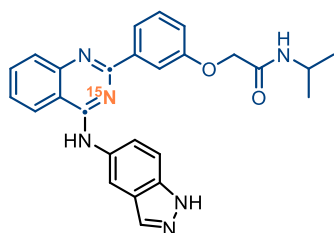
The residue was directly used in the next step without further purification. (**Step 2**): To a 10 mL Schlenk tube charged with a magnetic stir bar were added above-obtained product (33.8 mg, 0.10 mmol, 1.0 equiv), bis(2-oxooxazolidin-3-yl)phosphinic chloride (BOP-Cl, 66.4 mg, 0.15 mmol, 1.5 equiv), DBU (30.4 mg, 0.20 mmol, 2.0 equiv) and DMF (2.0 mL). The mixture was degassed by sparging with oxygen for 15 min. The reaction mixture was stirred at room temperature for 30 min. Then, 1*H*-indazol-5-amine (20.0 mg, 0.15 mmol, 1.5 equiv) was added and the reaction mixture was heated to 100 °C with stirring for 24 h. After cooling to room temperature, the mixture was diluted with water (5.0 mL) and extracted with dichloromethane. The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **58** as a yellow solid (20.7 mg, 45%).



N-isopropyl-2-(3-(quinazolin-2-yl-3-¹⁵N)phenoxy)acetamide (**57**)

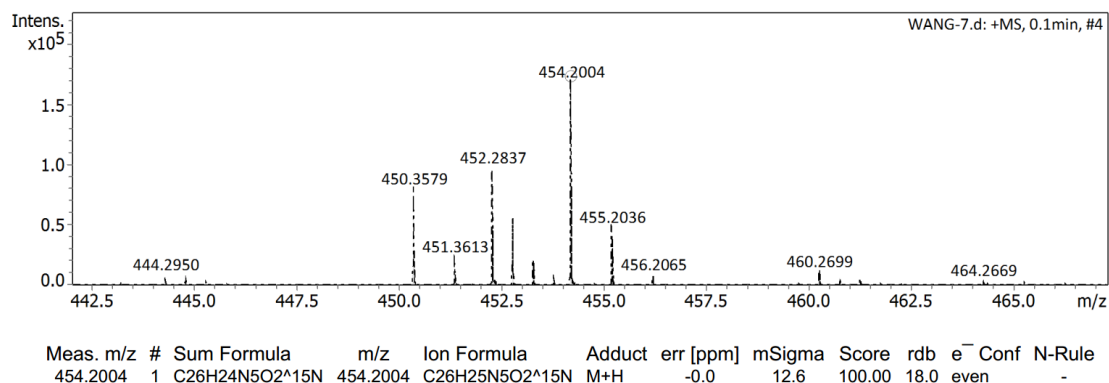
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 3:1); 84.2 mg, 87% yield; reaction time = 24 h; mp 67.4-68.1 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.41 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.20 (s, 1H), 8.04 (d, *J* = 4.0 Hz, 1H), 7.87 (s, 2H), 7.58 (s, 1H), 7.44 (s, 1H), 7.04 (d, *J* = 4.0 Hz, 1H), 6.53 (s, 1H), 4.57 (s, 2H), 4.21-4.20 (m, 1H), 1.21 (s, 3H), 1.20 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.1, 160.3, 160.1, 157.5, 150.5, 139.7 (d, *J* = 9.0 Hz), 134.1, 129.8, 128.5, 127.3, 127.0, 123.5 (d, *J* = 1.0 Hz), 122.2 (d, *J* = 2.0 Hz), 116.7, 114.6 (d, *J* = 2.0 Hz), 67.3, 41.0, 22.6; ¹⁵N NMR (50 MHz, CDCl₃) δ 287.0 (d, *J* = 11.0 Hz). IR (KBr) ν 3311, 2927, 1649, 1537, 1286, 1063 cm⁻¹. HRMS (ESI) calcd for C₁₉H₂₀N₂O₂¹⁵N [M+H]⁺: 323.1520, found: 323.1518, >99% ¹⁵N incorporation determined by HRMS.

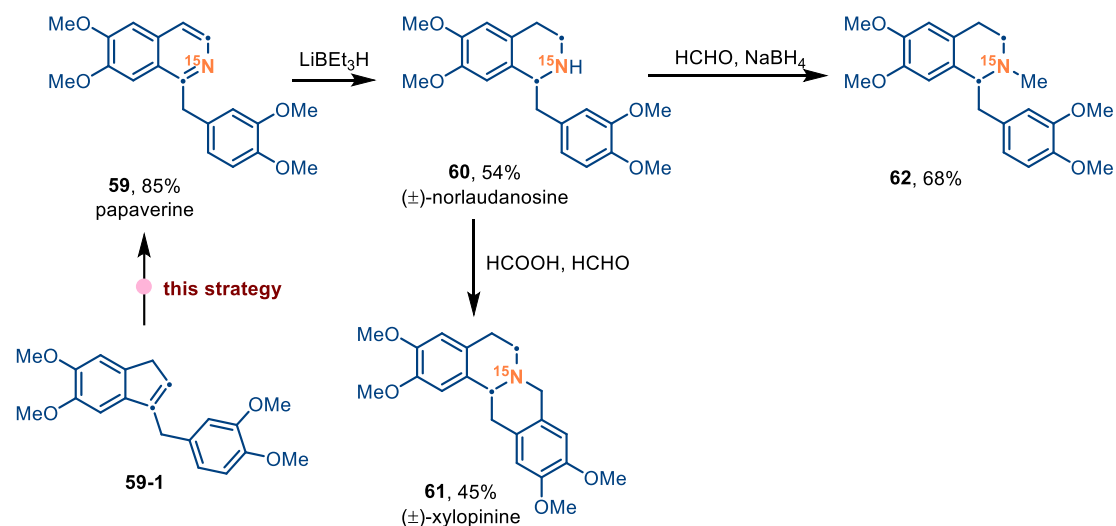




2-(3-(4-((1*H*-Indazol-5-yl)amino)quinazolin-2-yl-3-¹⁵N)phenoxy)-*N*-isopropylacetamide
(58)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 1:1 to 0:1); 20.7 mg, 45% yield; reaction time = 34 h; mp 227.3-227.5 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.12 (s, 1H), 9.97 (s, 1H), 8.58 (d, *J* = 8.0 Hz, 1H), 8.31 (s, 1H), 8.16 (s, 1H), 8.05-8.02 (m, 2H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.85-7.83 (m, 3H), 7.66-7.59 (m, 2H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 4.52 (s, 2H), 4.03-3.94 (m, 1H), 1.11 (d, *J* = 4.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 166.6, 158.9, 158.2 (d, *J* = 8.0 Hz), 158.0, 150.4, 140.1, 140.0, 137.4, 133.6, 133.2, 132.1, 129.5, 128.1, 126.0, 123.7, 123.1, 122.9, 121.0, 116.7, 114.1, 113.5, 109.9, 67.1, 40.0, 22.3; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 225.3 (d, *J* = 4.5 Hz). IR (KBr) ν 3366, 3134, 1669, 1565, 1394, 767 cm⁻¹. HRMS (ESI) calcd for C₂₆H₂₅N₅O₂¹⁵N [M+H]⁺: 454.2004, found: 454.2004, >99% ¹⁵N incorporation determined by HRMS.





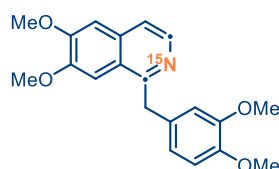
General procedure for the preparation of **59:** To an oven-dried 25 mL Schlenk tube equipped with a magnetic stir bar were added indene **59-1** (102.1 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), $^{15}\text{NH}_4\text{Cl}$ (48.7 mg, 0.90 mol), NaOAc (147.7 mg, 1.80 mmol), and TFE (2.0 mL). The mixture was irradiated with a 12 W blue LED lamp ($\lambda_{\text{max}} = 455\text{-}460\text{ nm}$) under air at room temperature for 24 h. The reaction mixture was then concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford compound **59** as a white solid (85%, 86.4 mg).

General procedure for the formation of **60:** To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **59** (34.4 mg, 0.10 mmol) and THF (0.50 mL). The reaction mixture was degasified by sparging with argon for 15 minutes. After cooling to 0 °C, LiEt_3H (1.0 M in THF, 1.0 mL) was added via syringe. The reaction mixture was allowed to warm to room temperature and stirred for 48 h. The reaction was then quenched with MeOH (1.0 mL) and stirred for an additional 10 min. The mixture was concentrated under reduced pressure, and the residue was partitioned between water (2.0 mL) and EtOAc. The organic layer was dried over Na_2SO_4 , concentrated, and purified by silica gel column chromatography to afford compound **60** as a yellow oil (54%, 18.4 mg).

General procedure for the formation of **61:** To a 10 mL reaction tube charged with a magnetic stir bar were added compound **60** (34.4 mg, 0.10 mmol), formalin (37% aqueous solution, 0.60 mL), and formic acid (0.90 mL). The reaction mixture was stirred at 90 °C for 5 h. The reaction was then quenched with saturated aqueous K_2CO_3 (3.0 mL) and extracted with dichloromethane. The combined organic layer was dried over anhydrous Na_2SO_4 ,

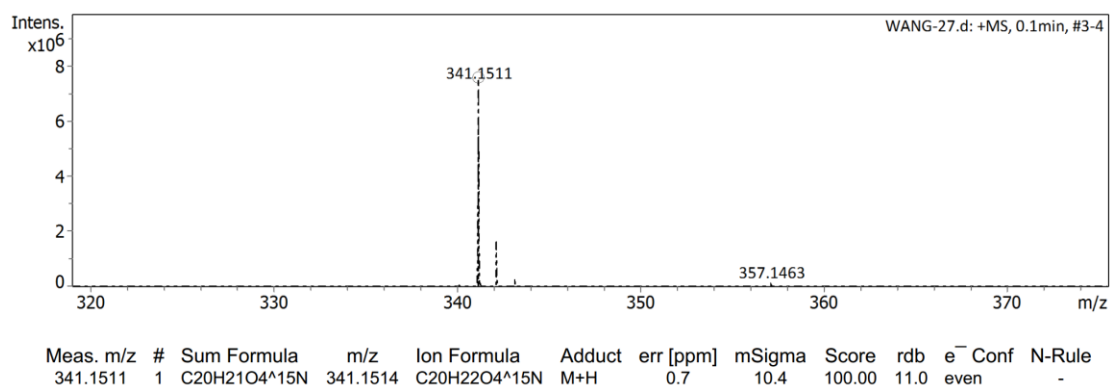
concentrated under reduced pressure, and purified by silica gel column chromatography to afford compound **61** as a white solid (45%, 15.9 mg).

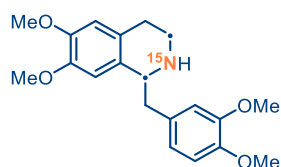
General procedure for the formation of 62: To a 10 mL reaction tube charged with a magnetic stir bar were added compound **60** (34.4 mg, 0.10 mmol), formalin (37% aqueous solution, 0.30 mL), and MeOH (0.90 mL). The reaction mixture was stirred at room temperature for 5 h. Then, NaBH₄ (37.8 mg, 1.0 mmol) was added and the reaction was stirred for additional 24 h. The reaction was then quenched with saturated aqueous K₂CO₃ (3.0 mL) and extracted with dichloromethane. The combined organic layer was dried over anhydrous Na₂SO₄, concentrated under reduced pressure, and purified by silica gel column chromatography to afford compound **62** as a white solid (68%, 24.3 mg).



1-(3,4-Dimethoxybenzyl)-6,7-dimethoxyisoquinoline-¹⁵N (**59**)

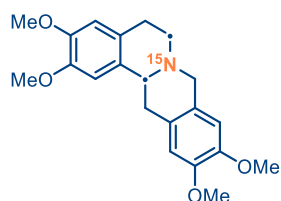
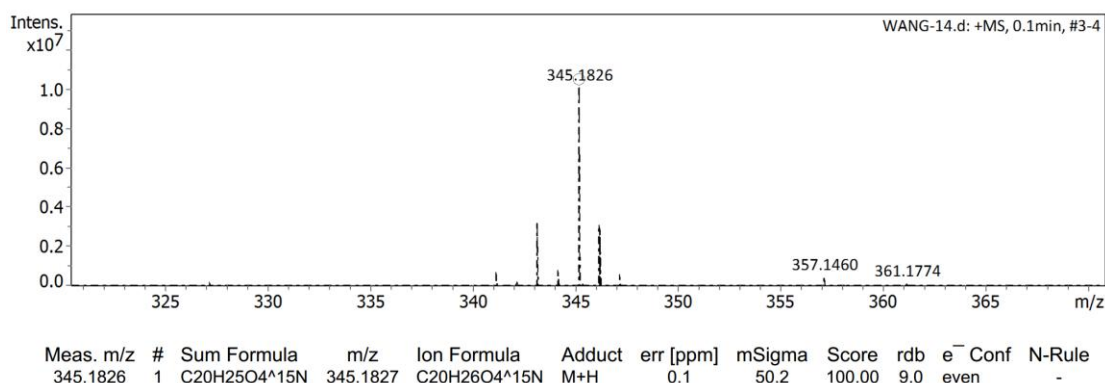
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 1:1); 86.4 mg, 85% yield; reaction time = 24 h; mp 135.7-136.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.27 (dd, *J*₁ = 12.0 Hz, *J*₂ = 4.0 Hz, 1H), 7.35 (dd, *J*₁ = 8.0 Hz, *J*₂ = 4.0 Hz, 1H), 7.17 (s, 1H), 6.96 (s, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 6.67 (d, *J* = 8.0 Hz, 1H), 4.45 (d, *J* = 4.0 Hz, 2H), 3.91 (s, 3H), 3.82 (s, 3H), 3.73 (s, 3H), 3.68 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.6, 152.6, 149.9, 149.1, 147.6, 140.6, 132.1, 122.9, 120.5, 118.8, 111.9, 111.2, 105.3, 104.2, 100.0, 56.0, 55.9, 55.8, 55.8, 42.0 (d, *J* = 8.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 297.3. IR (KBr) ν 3011, 2959, 1511, 1264, 1234, 1153, 1033 cm⁻¹. HRMS (ESI) calcd for C₂₀H₂₂O₄¹⁵N [M+H]⁺: 341.1514, found: 341.1511, >99% ¹⁵N incorporation determined by HRMS.





1-(3,4-Dimethoxybenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-¹⁵N (**6o**)

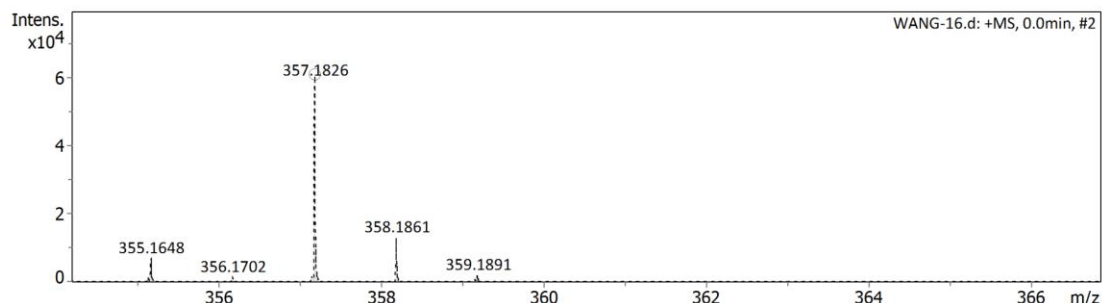
Yellow oil obtained by column chromatography (dichloromethane/methanol = 30:1); 18.4 mg, 54% yield; reaction time = 48 h; ¹H NMR (400 MHz, CDCl₃) δ 6.79 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.72 (s, 1H), 6.62 (s, 1H), 6.56 (s, 1H), 4.12-4.09 (m, 1H), 3.83-3.79 (m, 12H), 3.19-3.11 (m, 2H), 2.90-2.81 (m, 2H), 2.75-2.63 (m, 2H), 2.19 (br, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 148.7, 147.4, 147.2, 146.8, 131.2, 130.1, 127.1 (d, *J* = 1.3 Hz), 121.2, 112.2, 111.6, 111.1, 109.2, 56.6 (d, *J* = 4.0 Hz), 55.8, 55.7, 55.7, 55.6, 42.0, 40.7 (d, *J* = 4.0 Hz), 29.3; ¹⁵N NMR (50 MHz, CDCl₃) δ 39.8. IR (KBr) ν 3451, 2936, 2607, 1516, 1265, 1026 cm⁻¹. HRMS (ESI) calcd for C₂₀H₂₆O₄¹⁵N [M+H]⁺: 345.1827, found: 345.1826, >99% ¹⁵N incorporation determined by HRMS.



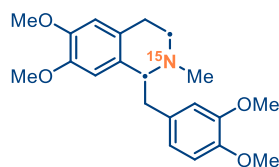
2,3,10,11-Tetramethoxy-5,8,13,13a-tetrahydro-6H-isoquinolino[3,2-a]isoquinoline-7-¹⁵N (**61**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 1:1); 15.9 mg, 45% yield; reaction time = 5 h; mp 141.3-142.7 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.74 (s, 1H), 6.66 (s, 1H), 6.62 (s, 1H), 6.58 (s, 1H), 4.03-3.78 (m, 13H), 3.68 (d, *J* = 16.0 Hz, 1H), 3.59 (d, *J* = 8.0 Hz, 1H), 3.27-3.23 (m, 1H), 3.17-3.14 (m, 2H), 2.87-2.80 (m, 1H), 2.69-2.59 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 147.6, 147.4, 147.4, 147.3, 129.8, 126.7, 126.3, 126.3, 111.3, 111.2, 108.9, 108.4, 59.5 (d, *J* = 2.5 Hz), 58.2 (d, *J* = 4.0 Hz), 56.0, 55.9, 55.9, 55.8, 51.3 (d, *J* = 4.0 Hz),

36.4, 29.0 (d, $J = 1.3$ Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 50.1 (t, $J = 5.0$ Hz). IR (KBr) ν 2934, 2836, 1514, 1258, 1138 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{26}\text{O}_4^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 357.1827, found: 357.1826, >99% ^{15}N incorporation determined by HRMS.

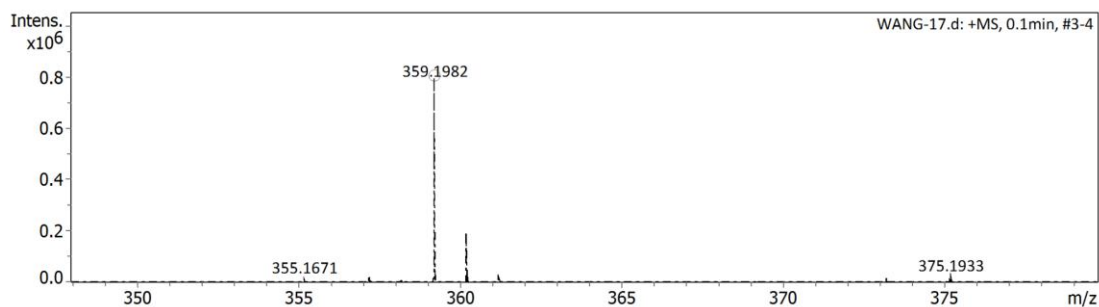


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
357.1826	1	C ₂₁ H ₂₅ O ₄ ¹⁵ N	357.1827	C ₂₁ H ₂₆ O ₄ ¹⁵ N	M+H	0.1	5.6	100.00	10.0	even	-	-



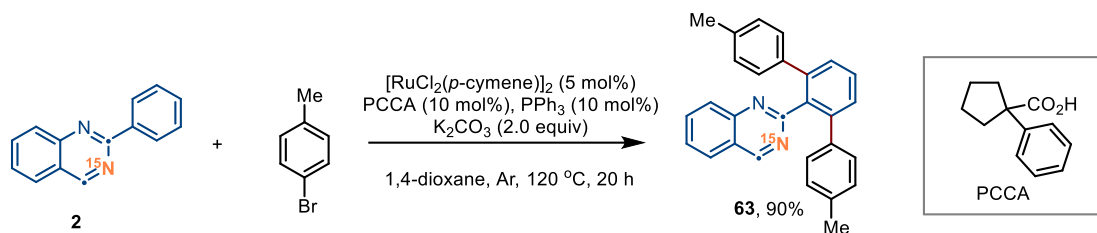
1-(3,4-Dimethoxybenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline- ^{15}N (**62**)

White solid obtained by column chromatography (dichloromethane/methanol = 30:1); 24.3 mg, 68% yield; reaction time = 28 h; mp 83.1-83.9 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 6.79 (d, $J = 8.0$ Hz, 1H), 6.71 (s, 1H), 6.64-6.61 (m, 2H), 6.35 (s, 1H), 3.69 (s, 6H), 3.64 (s, 3H), 3.53 (s, 3H), 3.08-2.97 (m, 3H), 2.80-2.61 (m, 4H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6$) δ 148.2, 147.0, 146.4, 121.8, 113.5, 111.6, 111.5, 111.4, 63.9 (d, $J = 4.0$ Hz), 55.5, 55.4, 55.4, 55.3, 46.5, 42.3, 24.8, four carbons in the aromatic region and one carbon in the aliphatic region were missing due to the limited solubility; ^{15}N NMR (50 MHz, $\text{DMSO}-d_6$) δ 30.2. IR (KBr) ν 2932, 1518, 1400, 762 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{28}\text{O}_4^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 359.1983, found: 359.1982, >99% ^{15}N incorporation determined by HRMS.

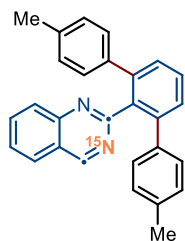


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
359.1982	1	C ₂₁ H ₂₇ O ₄ ¹⁵ N	359.1983	C ₂₁ H ₂₈ O ₄ ¹⁵ N	M+H	0.3	3.4	100.00	9.0	even	-	-

7. Chemical transformations

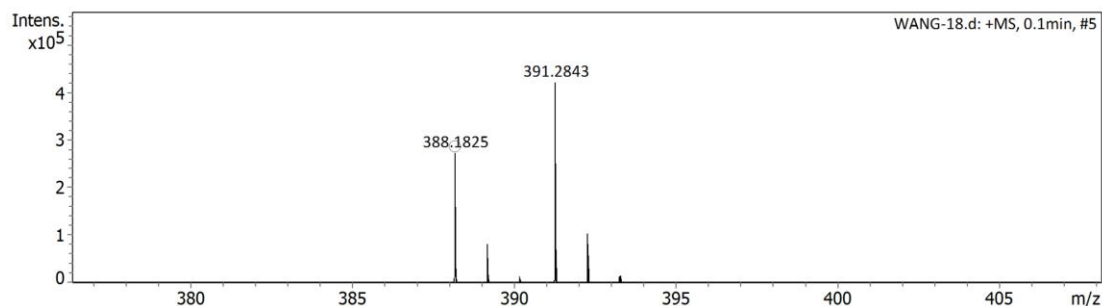


General procedure: To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **2** (103.1 mg, 0.50 mmol), *p*-bromotoluene (265.6 mg, 1.50 mmol, 3.0 equiv), $[\text{RuCl}_2(\text{p-cymene})]_2$ (15.0 mg, 0.025 mmol), 1-phenylcyclopentanecarboxylic acid (PCCA, 10.0 mg, 0.05 mmol), PPh_3 (13.0 mg, 0.05 mmol) and K_2CO_3 (138.2 mg, 1.0 mmol, 2.0 equiv). The mixture was suspended in 1,4-dioxane (2.0 mL) and degassed by sparging with argon for 15 min. The reaction mixture was then heated to 120 °C with stirring for 20 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. Purification of the residue by silica gel column chromatography afforded compound **63** as a grey solid (90%, 174.9 mg).

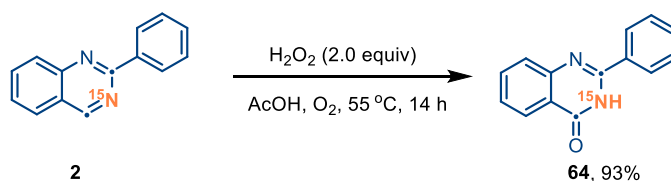


2-(4,4''-Dimethyl-[1,1':3',1''-terphenyl]-2'-yl)quinazoline-3- ^{15}N (**63**)

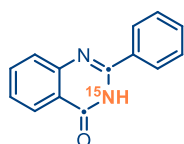
Grey solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1); 174.9 mg, 90% yield; reaction time = 20 h; mp 165.3-165.8 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.13 (d, J = 12.0 Hz, 1H), 7.80-7.75 (m, 3H), 7.57-7.53 (m, 2H), 7.47 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.0 Hz, 4H), 6.88 (d, J = 8.0 Hz, 4H), 2.18 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 164.2 (d, J = 4.0 Hz), 159.1, 149.4 (d, J = 3.0 Hz), 141.6, 138.4, 137.6 (d, J = 8.0 Hz), 135.8, 133.7, 129.3, 129.0, 128.6, 128.4, 128.2, 127.4, 126.9, 122.1 (d, J = 2.0 Hz), two carbons missing in the aromatic region, 20.9; ^{15}N NMR (50 MHz, CDCl_3) δ 299.9 (d, J = 11.0 Hz). IR (KBr) ν 3060, 3022, 2921, 2219, 1622, 1558, 1367, 761 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{23}\text{N}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 388.1826, found: 388.1825, >99% ^{15}N incorporation determined by HRMS.



Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻ Conf	N-Rule
388.1825	1	C ₂₈ H ₂₂ N ⁺ ¹⁵ N	388.1826	C ₂₈ H ₂₃ N ⁺ ¹⁵ N	M+H	0.3	5.1	100.00	19.0	even	-

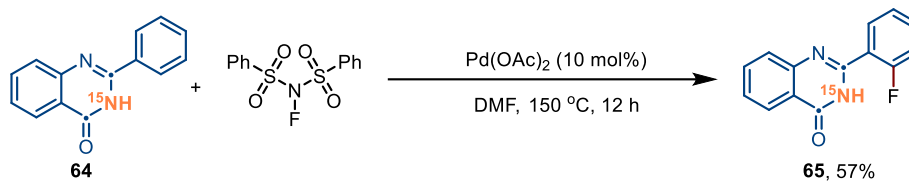


General procedure: To a 25 mL Schlenk tube charged with a magnetic stir bar were added compound **2** (300.0 mg, 1.45 mmol), aqueous H₂O₂ (265.6 mg, 2.90 mmol, 2.0 equiv), and AcOH (5.0 mL). The mixture was degassed by sparging with oxygen for 15 min. The reaction mixture was then heated to 55 °C with stirring for 14 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (5.0 mL), and washed with sat. K₂CO₃ solution (5.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was recrystallized from EtOAc to afford compound **64** as a white solid (299.4 mg, 93%).

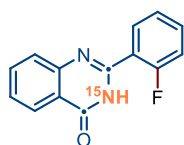


2-Phenylquinazolin-4(3H)-one-3-¹⁵N (**64**)

White solid obtained by recrystallization; 299.4 mg, 93% yield; reaction time = 14 h; mp 214.5–215.3 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.21 (d, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.58–7.50 (m, 3H), 7.47 (d, *J* = 8.0 Hz, 1H), one hydrogen for ¹⁵N-H was missing; ¹³C NMR (100 MHz, DMSO-*d*₆) δ 163.3 (d, *J* = 10.0 Hz), 153.3 (d, *J* = 8.0 Hz), 149.0, 134.2, 133.6 (d, *J* = 4.0 Hz), 131.1, 128.5, 127.8, 127.3, 126.2, 125.9, 121.1 (d, *J* = 5.0 Hz); ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 167.0. IR (KBr) ν 3444, 3071, 1669, 771 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₁NO¹⁵N [M+H]⁺: 224.0836, found: 224.0834, >99% ¹⁵N incorporation determined by HRMS.

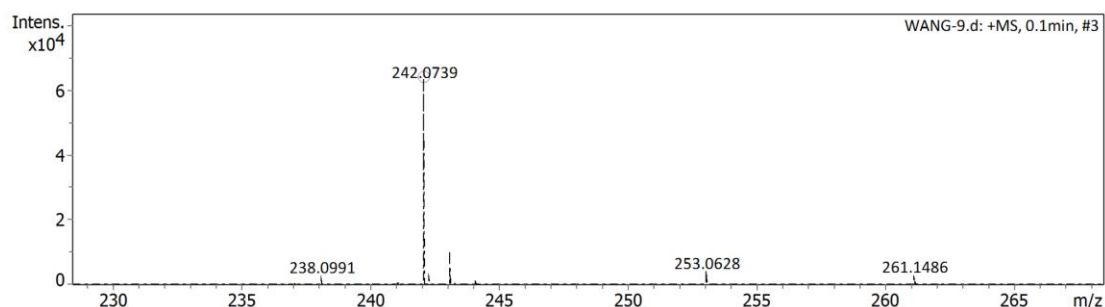


General procedure: To a 25 mL Schlenk tube charged with a magnetic stir bar were added compound **64** (20.0 mg, 0.09 mmol, 1.0 equiv), NFSI (85.1 mg, 0.27 mmol, 3.0 equiv), Pd(OAc)₂ (2.0 mg, 0.009 mmol) and DMF (2.0 mL). The reaction mixture was heated to 150 °C with stirring for 12 h. The reaction mixture was cooled to room temperature, diluted with dichloromethane (5.0 mL), and washed with sat. K₂CO₃ solution (5.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford compound **65** as a white solid (12.3 mg, 57%).

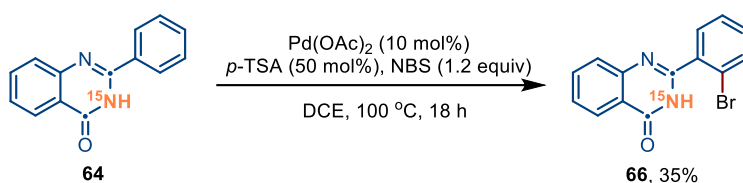


2-(2-Fluorophenyl)quinazolin-4(3*H*)-one-3-¹⁵N (**65**)

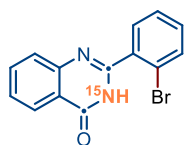
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1); 12.3 mg, 57% yield; reaction time = 12 h; mp 103.1–104.0 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.59 (d, *J* = 92.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 4.0 Hz, 1H), 7.78 (t, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.65–7.53 (m, 2H), 7.38 (q, *J* = 8.0 Hz, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 161.5 (d, *J* = 12.0 Hz), 159.6 (d, *J* = 248.0 Hz), 149.9 (d, *J* = 9.0 Hz), 148.7, 134.7, 132.9 (d, *J* = 7.5 Hz), 131.1, 128.2 (d, *J* = 106.0 Hz), 127.5, 127.1, 125.9, 124.6 (d, *J* = 2.5 Hz), 121.1 (d, *J* = 6.3 Hz), 116.2 (d, *J* = 21.3 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -114.7; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 164.9 (d, *J* = 89.0 Hz). IR (KBr) ν 3079, 1676, 1612, 1024, 997, 764 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀FN¹⁵O [M+H]⁺: 242.0742, found: 242.0739, >99% ¹⁵N incorporation determined by HRMS.



Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
242.0739	1	C14H9FNO ¹⁵ N	242.0742	C14H10FNO ¹⁵ N	M+H	1.1	8.6	100.00	11.0	even		-

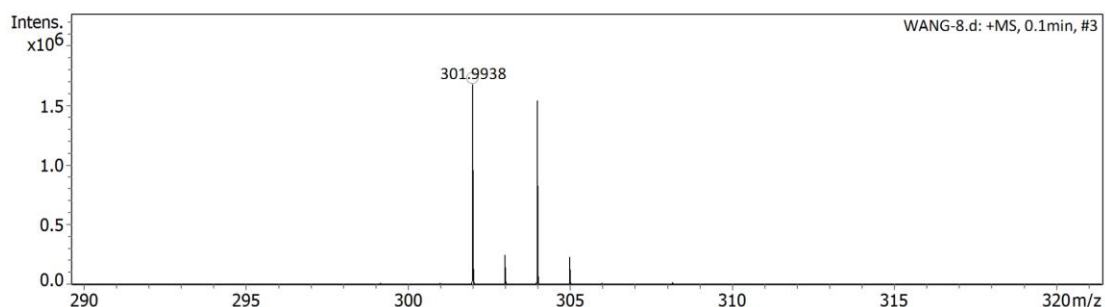


General procedure: To a 25 mL Schlenk tube charged with a magnetic stir bar were added compound **64** (44.7 mg, 0.20 mmol, 1.0 equiv), NBS (28.3 mg, 0.24 mmol, 1.2 equiv), Pd(OAc)₂ (4.5 mg, 0.02 mmol), *p*-TSA (11.7 mg, 0.10 mmol) and DCE (2.0 mL). The reaction mixture was heated to 100 °C with stirring for 18 h. The reaction mixture was cooled to room temperature, concentrated under reduced pressure, and purified by silica gel column chromatography to afford compound **66** as a white solid (21.1 mg, 35%).

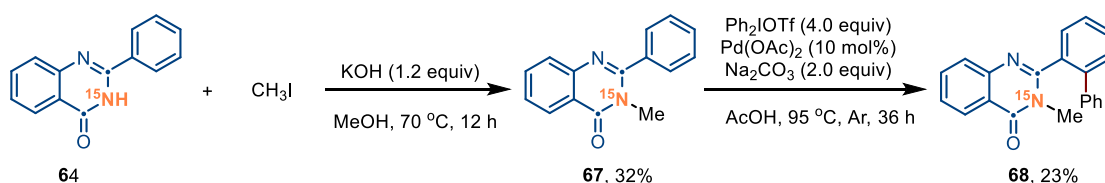


2-(2-Bromophenyl)quinazolin-4(3*H*)-one-3-¹⁵N (**66**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1); 21.1 mg, 35% yield; reaction time = 18 h; mp 126.1-126.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.70 (d, *J* = 90.0 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 4.0 Hz, 2H), 7.71 (t, *J* = 8.0 Hz, 2H), 7.55-7.46 (m, 2H), 7.39 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 162.4 (d, *J* = 12.0 Hz), 152.1 (d, *J* = 10.0 Hz), 148.9, 134.9, 134.9, 133.7, 132.0, 131.2, 127.9, 127.9, 127.4, 126.5, 121.0 (d, *J* = 6.0 Hz), 120.9; ¹⁵N NMR (50 MHz, CDCl₃) δ 162.2 (d, *J* = 87.5 Hz). IR (KBr) ν 3125, 1666, 1603, 1308, 771 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀BrNO¹⁵N [M+H]⁺: 301.9941, found: 301.9938, >99% ¹⁵N incorporation determined by HRMS.

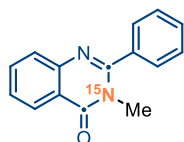


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
301.9938	1	C ₁₄ H ₉ BrNO ⁺ 15N	301.9941	C ₁₄ H ₁₀ BrNO ⁺ 15N	M+H	1.0	31.5	100.00	13.0	even		-



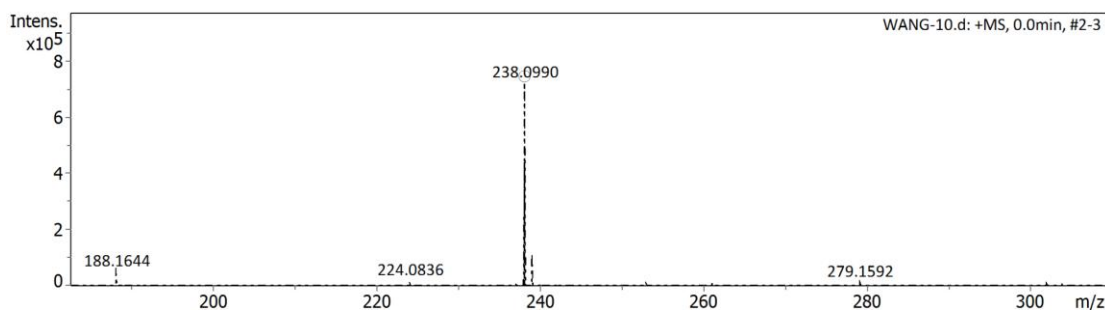
General procedure for the formation of 67: To a 25 mL round-bottom flask charged with a magnetic stir bar were added compound **64** (223.3 mg, 1.00 mmol, 1.0 equiv), KOH (67.3 mg, 1.20 mmol, 1.2 equiv), CH₃I (170.3 mg, 1.20 mmol, 1.2 equiv) and MeOH (10.0 mL). The reaction mixture was heated to 70 °C with stirring for 12 h. The reaction mixture was cooled to room temperature, concentrated under reduced pressure, and purified by silica gel column chromatography to afford compound **67** as a white solid (75.0 mg, 32%).

General procedure for the formation of 68: To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **67** (47.5 mg, 0.20 mmol), diphenyliodonium trifluoromethanesulfonate (344.2 mg, 0.80 mmol, 4.0 equiv), Pd(OAc)₂ (4.5 mg, 0.02 mmol), Na₂CO₃ (42.4 mg, 0.40 mmol, 2.0 equiv). The mixture was suspended in AcOH (1.0 mL) and degassed by sparging with argon for 15 min. The reaction mixture was then heated to 95 °C with stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with dichloromethane (5.0 mL), and washed with sat. K₂CO₃ solution (5.0 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford compound **68** as a white solid (14.2 mg, 23%).

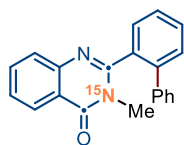


3-Methyl-2-phenylquinazolin-4(3*H*)-one-3-¹⁵N (**67**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1); 75.0 mg, 32% yield; reaction time = 12 h; mp 126.1-126.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.22 (d, *J* = 8.0 Hz, 1H), 7.66-7.63 (m, 2H), 7.48-7.36 (m, 6H), 3.40-3.39 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.5 (d, *J* = 10.0 Hz), 155.9 (d, *J* = 8.0 Hz), 147.1, 135.2 (d, *J* = 4.0 Hz), 134.1, 129.9, 128.7, 127.9, 127.3, 126.8, 126.5, 120.3 (d, *J* = 6.0 Hz), 34.1 (d, *J* = 10.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 158.1. IR (KBr) ν 3058, 2923, 1678, 1556, 1468, 766 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₃NO¹⁵N [M+H]⁺: 238.0993, found: 238.0990, >99% ¹⁵N incorporation determined by HRMS.

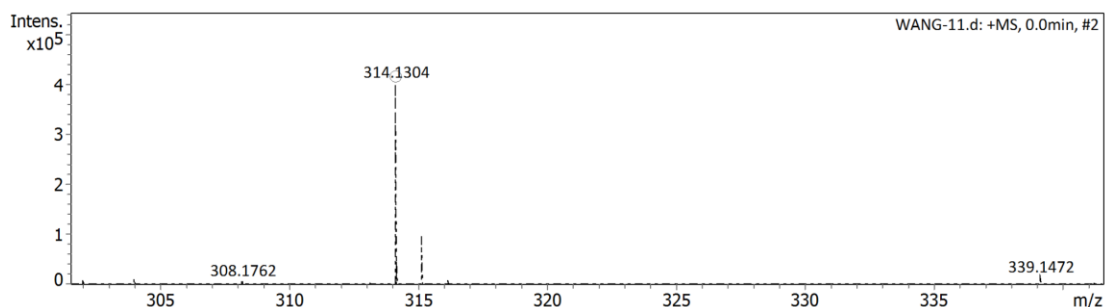


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
238.0990	1	C ₁₅ H ₁₂ NO ¹⁵ N	238.0993	C ₁₅ H ₁₃ NO ¹⁵ N	M+H	1.3	8.2	100.00	11.0	even		-

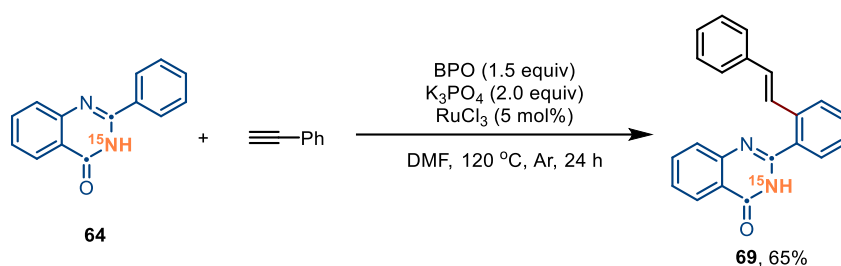


2-([1,1'-Biphenyl]-2-yl)-3-methylquinazolin-4(3*H*)-one-3-¹⁵N (**68**)

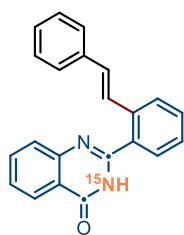
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1); 14.2 mg, 23% yield; reaction time = 36 h; mp 120.4-120.8 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.67 (dd, *J*₁ = 16.0 Hz, *J*₂ = 8.0 Hz, 3H), 7.60-7.53 (m, 3H), 7.28 (s, 5H), 2.92 (s, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 161.1 (d, *J* = 10.0 Hz), 155.9 (d, *J* = 10.0 Hz), 146.8, 139.4, 139.3, 134.5, 133.8 (d, *J* = 4.0 Hz), 130.4, 129.9, 129.4, 128.6, 128.3, 127.9, 127.8, 127.3, 127.1, 126.1, 119.9 (d, *J* = 6.0 Hz), 32.4 (d, *J* = 11.0 Hz); ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 161.2. IR (KBr) ν 3063, 2928, 1676, 1586, 772 cm⁻¹. HRMS (ESI) calcd for C₂₁H₁₇NO¹⁵N [M+H]⁺: 314.1306, found: 314.1304, >99% ¹⁵N incorporation determined by HRMS.



Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
314.1304	1	C21H16NO ⁺ 15N	314.1306	C21H17NO ⁺ 15N	M+H	0.6	6.9	100.00	15.0	even		-



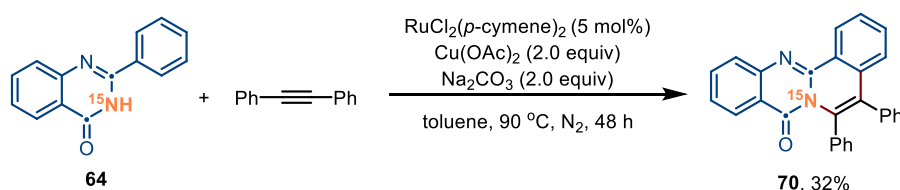
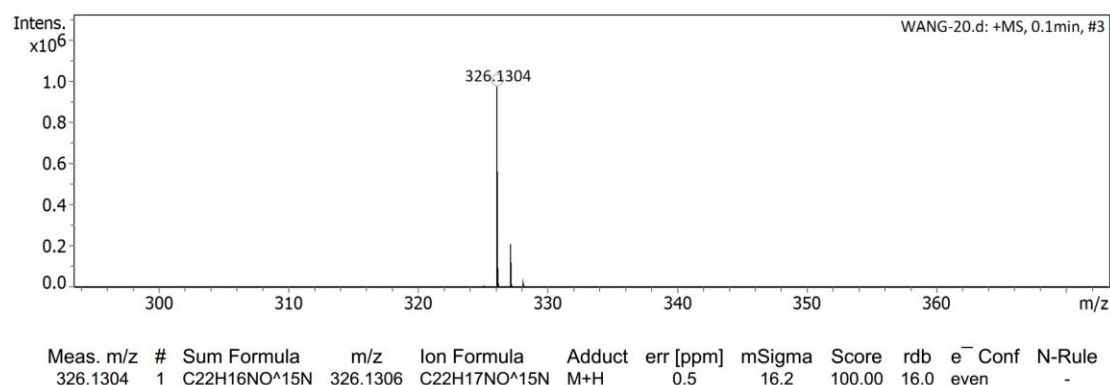
General procedure: To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **64** (44.6 mg, 0.20 mmol), phenylacetylene (81.7 mg, 0.80 mmol, 4.0 equiv), BPO (72.7 mg, 0.30 mmol), K₃PO₄ (84.9 mg, 0.40 mmol, 2.0 equiv), and RuCl₃ (2.3 mg, 0.01 mmol). The mixture was suspended in DMF (2.0 mL) and degassed by sparging with argon for 15 min. The reaction mixture was then heated to 120 °C with stirring for 24 h. After cooling to room temperature, the mixture was diluted with water (5.0 mL) and extracted with EtOAc. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **69** as a white solid (42.4 mg, 65%).



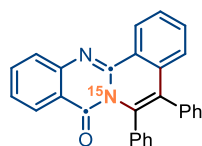
(E)-2-(2-Styrylphenyl)quinazolin-4(3H)-one-3-¹⁵N (69**)**

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1 to 3:1); 42.4 mg, 65% yield; reaction time = 24 h; mp 212.5–213.4 °C; ¹H NMR (500 MHz, CDCl₃) δ 10.87 (d, *J* = 90.0 Hz, 1H), 8.20 (d, *J* = 10.0 Hz, 1H), 7.74–7.70 (m, 3H), 7.59 (d, *J* = 5.0 Hz, 1H), 7.46–7.42 (m, 2H), 7.38–7.31 (m, 2H), 7.26 (d, *J* = 10.0 Hz, 2H), 7.16 (t, *J* = 5.0 Hz, 2H),

7.10 (t, $J = 10.0$ Hz, 1H), 6.98 (d, $J = 10.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.8 (d, $J = 10.0$ Hz), 152.8 (d, $J = 10.0$ Hz), 149.0, 136.8, 136.6, 134.9, 132.2 (d, $J = 4.0$ Hz), 132.2, 130.9, 129.5, 128.6, 128.0, 127.9, 127.8, 127.1, 126.9, 126.7, 126.4, 125.6, 120.7 (d, $J = 6.0$ Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 162.5 (d, $J = 90.5$ Hz). IR (KBr) ν 3436, 3056, 1677, 1607, 757 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{17}\text{NO}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 326.1306, found: 326.1304, >99% ^{15}N incorporation determined by HRMS.

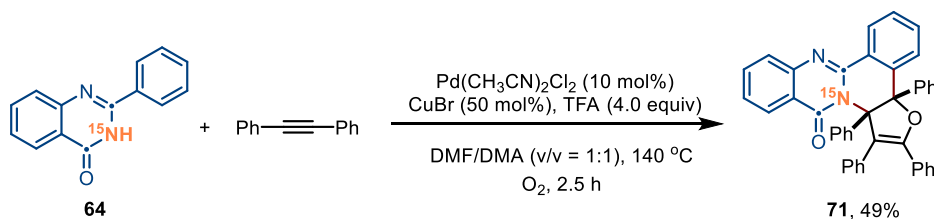
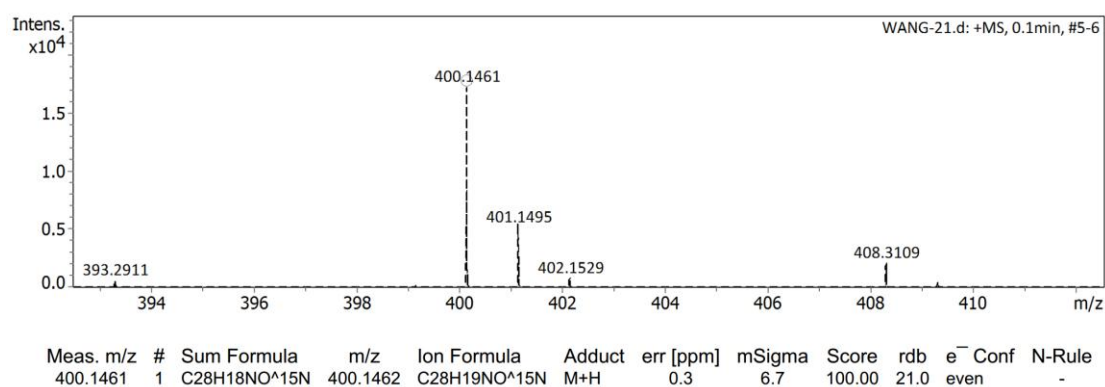


General procedure: To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **64** (44.6 mg, 0.20 mmol), diphenylacetylene (53.5 mg, 0.30 mmol, 1.5 equiv), $[\text{RuCl}_2(p\text{-cymene})_2]$ (6.1 mg, 0.01 mmol), $\text{Cu}(\text{OAc})_2$ (72.7 mg, 0.40 mmol, 2.0 equiv), and Na_2CO_3 (42.4 mg, 0.40 mmol, 2.0 equiv). The mixture was suspended in toluene (2.0 mL) and degassed by sparging with nitrogen for 15 min. The reaction mixture was then heated to 90 °C with stirring for 48 h. After cooling to room temperature, the mixture was diluted with water (5.0 mL) and extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **70** as a white solid (25.8 mg, 32%).



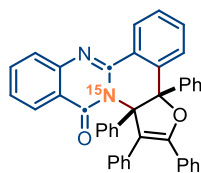
5,6-Diphenyl-8H-isoquinolino[1,2-b]quinazolin-8-one-7- ^{15}N (**70**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 100:1 to 30:1); 25.8 mg, 32% yield; reaction time = 48 h; mp 260.7-261.6 °C; ^1H NMR (500 MHz, CDCl_3) δ 9.05 (d, J = 10.0 Hz, 1H), 8.08 (dd, J_1 = 10.0 Hz, J_2 = 5.0 Hz, 1H), 7.81 (d, J = 10.0 Hz, 1H), 7.75-7.72 (m, 1H), 7.56-7.53 (m, 1H), 7.50-7.47 (m, 1H), 7.32 (t, J = 10.0 Hz, 1H), 7.21-7.15 (m, 3H), 7.11 (d, J = 10.0 Hz, 1H), 7.05-7.03 (m, 3H), 7.01-6.98 (m, 4H); ^{13}C NMR (125 MHz, CDCl_3) δ 161.5 (d, J = 7.5 Hz), 147.4 (d, J = 6.3 Hz), 146.8, 137.0, 135.5, 135.2 (d, J = 11.0 Hz), 134.4, 133.9, 132.0, 131.1, 128.5, 128.3, 128.0, 127.7, 127.2, 127.2, 127.2, 127.1, 127.1, 126.9, 126.8, 126.2, 125.6, 120.2 (d, J = 6.0 Hz); ^{15}N NMR (50 MHz, CDCl_3) δ 177.9. IR (KBr) ν 1698, 1547, 1488, 767 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{19}\text{NO}^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 400.1462, found: 400.1461, >99% ^{15}N incorporation determined by HRMS.



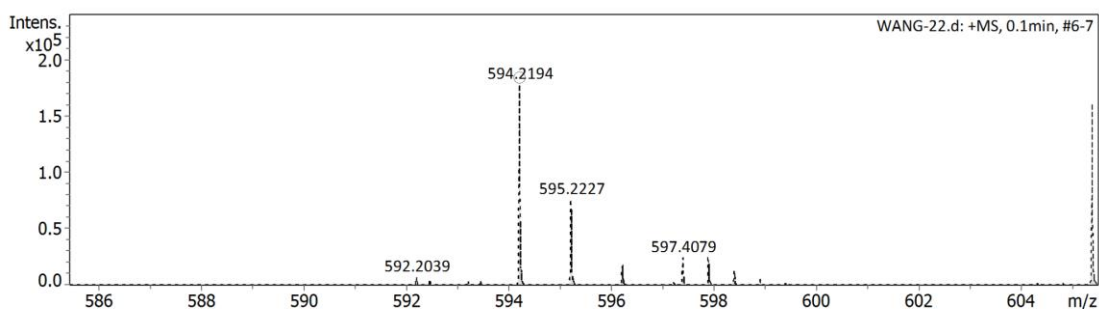
General procedure: To an oven-dried 25 mL Schlenk tube charged with a magnetic stir bar were added compound **64** (22.3 mg, 0.10 mmol), diphenylacetylene (53.5 mg, 0.30 mmol, 3.0 equiv), $\text{Pd}(\text{CH}_3\text{CN})_2\text{Cl}_2$ (2.6 mg, 0.01 mmol), CuBr (7.2 mg, 0.05 mmol), and TFA (45.6 mg, 0.40 mmol, 4.0 equiv). The mixture was dissolved in a combined solvent of DMF and DMA (v/v = 1:1, 1.0 mL) and degassed by sparging with oxygen for 15 min. The reaction mixture was then heated to 140 °C with stirring for 2.5 h. After cooling to room temperature, the mixture was diluted with water (5.0 mL) and extracted with EtOAc. The combined organic layers were washed with sat. aq. NaHCO_3 , dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to

afford compound **71** as a light yellow solid (29.0 mg, 49%).

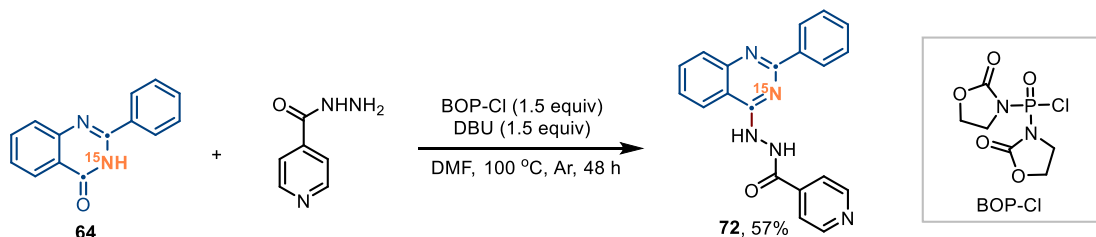


1,2,3a,14a-Tetraphenyl-3a,14a-dihydro-13H-furo[3',2':3,4]isoquinolino[1,2-b]quinazolin-13-one-14-¹⁵N (**71**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 50:1 to 20:1); 29.0 mg, 49% yield; reaction time = 2.5 h; mp 261.9-262.5 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.75 (dd, *J*₁ = 10.0 Hz, *J*₂ = 5.0 Hz, 1H), 7.98 (d, *J* = 5.0 Hz, 1H), 7.78 (d, *J* = 10.0 Hz, 1H), 7.73-7.67 (m, 3H), 7.60-7.53 (m, 2H), 7.50-7.49 (m, 2H), 7.41-7.38 (m, 1H), 7.29-7.27 (m, 1H), 7.24 (d, *J* = 10.0 Hz, 2H), 7.12-7.11 (m, 5H), 7.03-6.99 (m, 5H), 6.86-6.84 (m, 1H), 6.58-6.54 (m, 2H), 6.11 (d, *J* = 10.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 160.6 (d, *J* = 10.0 Hz), 151.7, 148.7 (d, *J* = 7.5 Hz), 146.5, 139.6, 139.4, 137.2, 134.0, 133.1, 132.6, 130.8, 130.2, 129.1, 129.0, 128.6 (d, *J* = 2.5 Hz), 128.3 (d, *J* = 6.0 Hz), 128.2, 128.1, 127.7, 127.6, 127.3, 127.2, 127.1, 126.9, 126.8 (d, *J* = 1.2 Hz), 126.5 (d, *J* = 6.3 Hz), 126.2 (d, *J* = 7.5 Hz), 126.1, 125.4, 122.3, 122.3, 116.6, 91.8, 81.6 (d, *J* = 9.0 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 158.0. IR (KBr) ν 3063, 2926, 1701, 1560, 766 cm⁻¹. HRMS (ESI) calcd for C₄₂H₂₉NO₂¹⁵N [M+H]⁺: 594.2194, found: 594.2194, >99% ¹⁵N incorporation determined by HRMS.

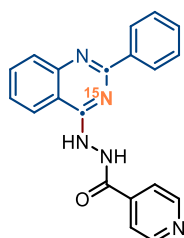


Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdb	e ⁻	Conf	N-Rule
594.2194	1	C42H28NO2 ¹⁵ N	594.2194	C42H29NO2 ¹⁵ N	M+H	-0.1	20.8	100.00	30.0	even		-



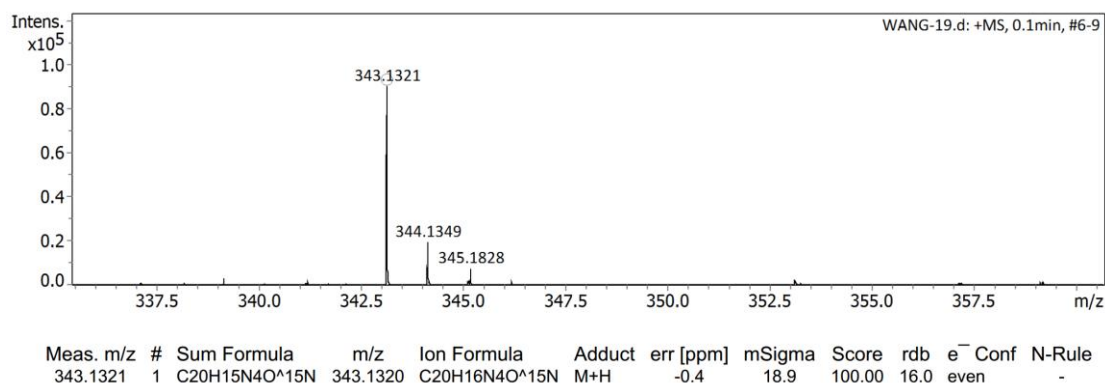
General procedure: To a 25 mL Schlenk tube charged with a magnetic stir bar were

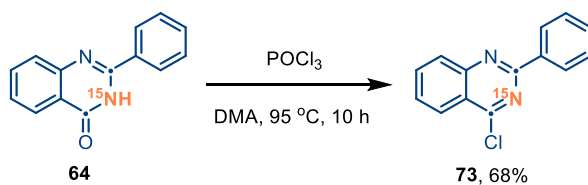
added compound **64** (60.0 mg, 0.23 mmol, 1.0 equiv), bis(2-oxooxazolidin-3-yl)phosphinic chloride (BOP-Cl, 92.2 mg, 0.36 mmol, 1.5 equiv), DBU (71.2 mg, 0.47 mmol, 2.0 equiv) and DMF (4.0 mL). The mixture was degassed by sparging with oxygen for 15 min. The reaction mixture was stirred at room temperature for 30 min. Then, isonicotinohydrazide (49.7 mg, 0.36 mmol, 1.5 equiv) was added and the reaction mixture was heated to 100 °C with stirring for 48 h. After cooling to room temperature, the mixture was diluted with water (5.0 mL) and extracted with dichloromethane. The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **72** as a yellow solid (45.6 mg, 57%).



N'-(2-Phenylquinazolin-4-yl-3-¹⁵N)isonicotinohydrazide (72)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 1:1); 45.6 mg, 57% yield; reaction time = 48 h; mp 230.5–231.3 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.06 (s, 1H), 10.51 (s, 1H), 8.87 (s, 2H), 8.36 (s, 3H), 7.91 (d, *J* = 16.0 Hz, 4H), 7.61 (s, 1H), 7.44 (s, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 165.2 (d, *J* = 7.5 Hz), 160.0, 159.1, 150.6, 150.2, 140.1, 138.0, 133.5, 130.4, 128.3, 128.1, 127.8, 126.1, 122.6 (d, *J* = 4.0 Hz), 121.4, 112.5; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 226.2. IR (KBr) ν 3479, 3413, 2923, 1659, 1600, 764 cm⁻¹. HRMS (ESI) calcd for C₂₀H₁₆N₄O¹⁵N [M+H]⁺: 343.1320, found: 343.1321, >99% ¹⁵N incorporation determined by HRMS.



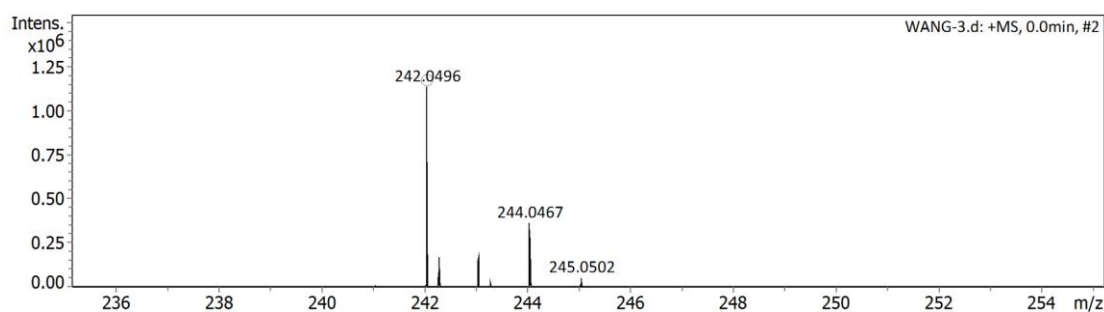


General procedure: To a 25 mL Schlenk tube charged with a magnetic stir bar were added compound **64** (200.0 mg, 0.9 mmol, 1.0 equiv) and POCl₃ (4.0 mL) at 0 °C. After stirring for 2 min, *N,N*-dimethylacetamide (DMA, 100.0 μL) was added dropwise. The reaction mixture was then heated to 95 °C and stirred for 10 h. After cooling to room temperature, the reaction was quenched with sat. aq. K₂CO₃ (5.0 mL), extracted with ethyl acetate (3 x 5.0 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **73** as a white solid (147.9 mg, 68%).

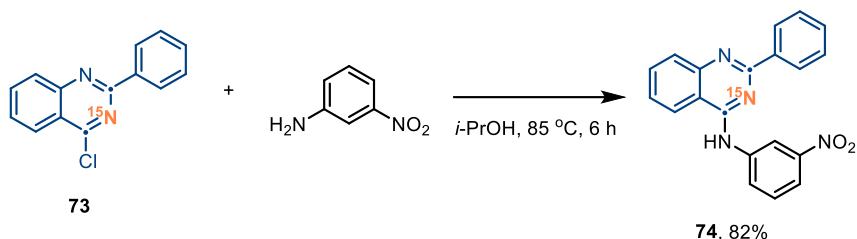


4-Chloro-2-phenylquinazoline-3-¹⁵N (**73**)

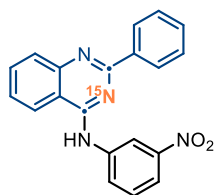
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1); 147.9 mg, 68% yield; reaction time = 10 h; mp 119.8-120.6 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.60-8.59 (m, 2H), 8.24 (d, *J* = 10.0 Hz, 1H), 8.09 (d, *J* = 5.0 Hz, 1H), 7.92 (t, *J* = 10.0 Hz, 1H), 7.65 (t, *J* = 10.0 Hz, 1H), 7.55-7.53 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 162.4 (d, *J* = 7.5 Hz), 160.0 (d, *J* = 2.5 Hz), 151.8 (d, *J* = 1.3 Hz), 136.6 (d, *J* = 8.8 Hz), 134.8, 131.1, 128.9, 128.7 (d, *J* = 2.5 Hz), 128.6, 128.2, 125.8, 122.4 (d, *J* = 2.5 Hz); ¹⁵N NMR (50 MHz, CDCl₃) δ 279.9. IR (KBr) ν 1551, 1478, 1311, 766 cm⁻¹. HRMS (ESI) calcd for C₁₄H₁₀ClN¹⁵N [M+H]⁺: 242.0497, found: 242.0496, >99% ¹⁵N incorporation determined by HRMS.



Meas. m/z	#	Sum Formula	m/z	Ion Formula	Adduct	err [ppm]	mSigma	Score	rdB	e ⁻	Conf	N-Rule
242.0496	1	C14H9ClN^15N	242.0497	C14H10ClN^15N	M+H	0.7	8.2	100.00	14.0	even	-	-

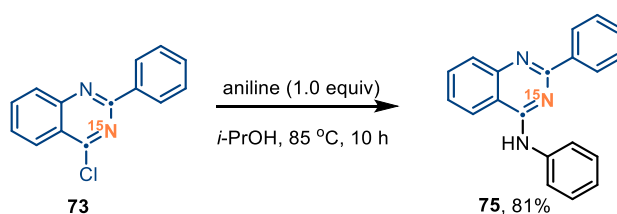
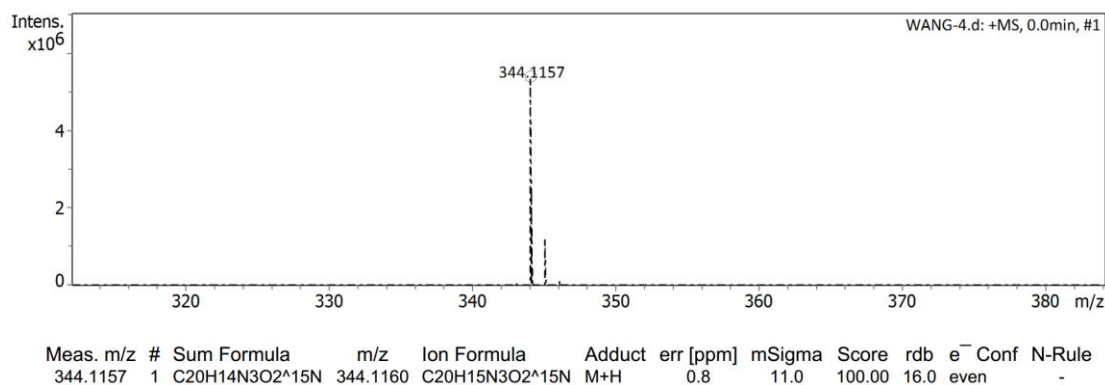


General procedure: To a 25 mL round-bottom flask charged with a magnetic stir bar were added compound **73** (50.0 mg, 0.21 mmol, 1.0 equiv), 3-nitroaniline (28.6 mg, 0.21 mmol, 1.0 equiv) and isopropanol (8.0 mL). The reaction mixture was then heated to 85 °C and stirred for 6 h. After cooling to room temperature, the reaction was quenched with sat. aq. K₂CO₃ (5.0 mL), extracted with ethyl acetate (3 x 5.0 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **74** as a light yellow solid (58.3 mg, 82%).

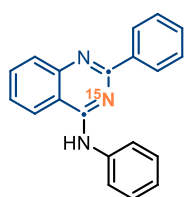


N-(3-Nitrophenyl)-2-phenylquinazolin-3-¹⁵N-4-amine (**74**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1); 58.3 mg, 82% yield; reaction time = 6 h; mp 236.1-237.0 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 10.27 (br, 1H), 9.34 (s, 1H), 8.60 (d, *J* = 5.0 Hz, 1H), 8.53 (d, *J* = 5.0 Hz, 2H), 8.31 (d, *J* = 10.0 Hz, 1H), 7.98 (d, *J* = 5.0 Hz, 1H), 7.90-7.87 (m, 2H), 7.71 (t, *J* = 10.0 Hz, 1H), 7.65-7.63 (m, 1H), 7.53-7.52 (m, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 158.8, 157.8 (d, *J* = 6.3 Hz), 150.6, 147.9, 141.2, 138.0 (d, *J* = 10.0 Hz), 133.5, 130.5, 129.7, 128.5, 128.2, 128.0, 127.5, 126.2, 123.1, 117.4, 115.7 (d, *J* = 4.0 Hz), 114.2; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 229.0. IR (KBr) ν 3411, 2926, 1629, 1526, 1345, 703 cm⁻¹. HRMS (ESI) calcd for C₂₀H₁₅N₃O₂¹⁵N [M+H]⁺: 344.1160, found: 344.1157, >99% ¹⁵N incorporation determined by HRMS.



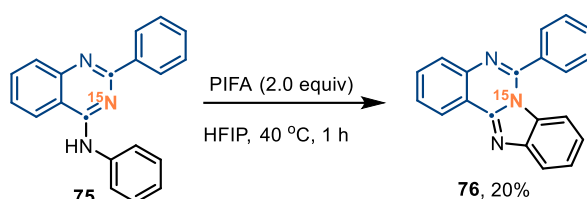
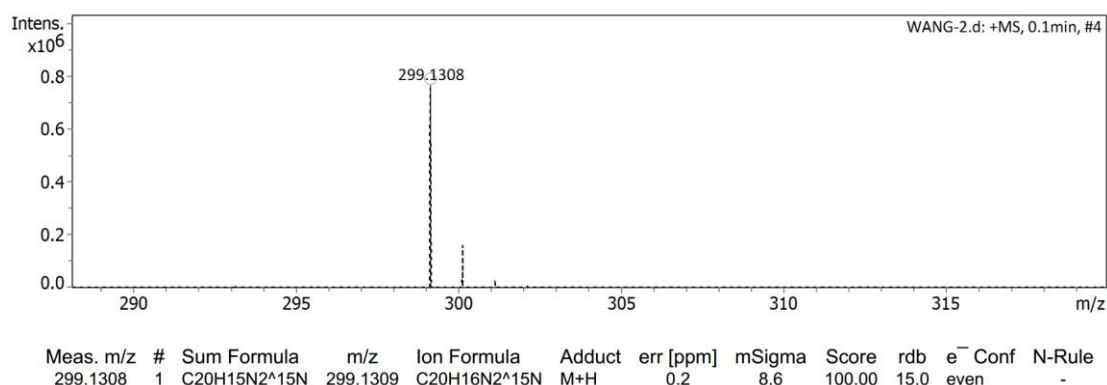
General procedure: To a 25 mL round-bottom flask charged with a magnetic stir bar were added compound **73** (40.0 mg, 0.17 mmol, 1.0 equiv), aniline (15.4 mg, 0.17 mmol, 1.0 equiv) and isopropanol (8.0 mL). The reaction mixture was then heated to 85 °C and stirred for 10 h. After cooling to room temperature, the reaction was quenched with sat. aq. K₂CO₃ (5.0 mL), extracted with ethyl acetate (3 x 5.0 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **75** as a light yellow solid (39.8 mg, 81%).



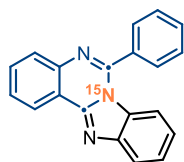
N,2-diphenylquinazolin-3-¹⁵N-4-amine (**75**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1); 39.8 mg, 81% yield; reaction time = 10 h; mp 150.1-150.9 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.91 (br, 1H), 8.60 (d, *J* = 10.0 Hz, 1H), 8.45 (d, *J* = 10.0 Hz, 2H), 7.98 (d, *J* = 5.0 Hz, 2H), 7.87 (d, *J* = 5.0 Hz, 2H), 7.63-7.60 (m, 1H), 7.52-7.46 (m, 5H), 7.18 (t, *J* = 5.0 Hz, 1H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 159.0 (d, *J* = 5.0 Hz), 157.1 (d, *J* = 2.5 Hz), 140.5, 136.9, 135.9, 133.4, 131.5, 129.3 (d, *J* = 2.5 Hz), 129.0, 128.7, 128.2, 126.5, 124.7, 124.7, 120.5, 112.7; ¹⁵N NMR (50 MHz, DMSO-*d*₆) δ 222.1 (d, *J* = 5.0 Hz). IR (KBr) ν 3280, 1561, 1512, 1357, 752 cm⁻¹. HRMS (ESI)

calcd for C₂₀H₁₆N₂¹⁵N [M+H]⁺: 299.1309, found: 299.1308, >99% ¹⁵N incorporation determined by HRMS.



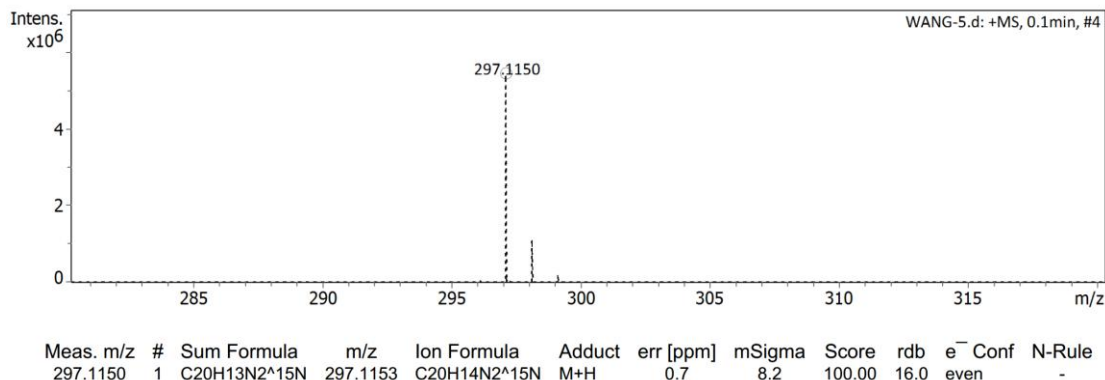
General procedure: To a 25 mL round-bottom flask charged with a magnetic stir bar were added compound **75** (150.1 mg, 0.50 mmol, 1.0 equiv), [bis(trifluoroacetoxy)iodo]benzene (PIFA, 430.0 mg, 1.00 mmol, 2.0 equiv) and hexafluoroisopropanol (HFIP, 3.0 mL). The reaction mixture was then heated to 40 °C and stirred for 1 h. After cooling to room temperature, the reaction was quenched with sat. aq. NaHCO₃ (5.0 mL), extracted with ethyl acetate (3 x 5.0 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford compound **76** as a yellow solid (30.2 mg, 20%).



6-Phenylbenzo[4,5]imidazo[1,2-c]quinazoline-7-¹⁵N (**76**)

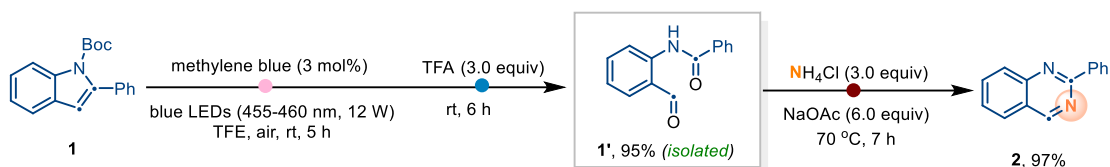
Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1 to 3:1); 30.2 mg, 20% yield; reaction time = 1 h; mp 242.1-242.8 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.79 (d, *J* = 4.0 Hz, 1H), 8.01 (t, *J* = 8.0 Hz, 2H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.75-7.65 (m, 6H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 148.4 (d, *J* = 9.0 Hz), 147.9 (d, *J* = 7.5 Hz), 142.4, 137.9, 134.2, 132.0, 131.0, 129.3, 129.1,

128.4, 128.3, 128.2, 125.7, 124.3, 122.7, 120.0, 118.3, 114.4; ^{15}N NMR (50 MHz, CDCl_3) δ 178.9. IR (KBr) ν 3442, 2370, 1627, 1441, 771 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{14}\text{N}_2^{15}\text{N}$ $[\text{M}+\text{H}]^+$: 297.1153, found: 297.1150, >99% ^{15}N incorporation determined by HRMS.

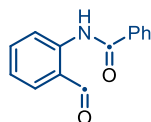


8 Mechanistic studies

8.1 Control experiment to trap the intermediate for indole 1 editing



Into a 25 mL Schlenk tube was sequentially added the indole **1** (88.0 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), and 2,2,2-trifluoroethanol (TFE, 2.0 mL). The reaction was stirred for 5 h at room temperature under irradiation with visible light (455-460 nm, 12 W). The light source was then removed, and trifluoroacetic acid (TFA, 67.0 μL , 0.90 mmol, 3.0 equiv) was added. The reaction was stirred at room temperature for 6 h. The reaction mixture was concentrated in vacuo, and the residue was purified by silica gel column chromatography to afford intermediate **1'** in 95% yield. Comprehensive ^1H and ^{13}C NMR analysis confirmed its structure. Treatment of **1'** with NH_4Cl and NaOAc under standard conditions furnished **2** in 97% yield, establishing **1'** as the key intermediate.



N-(2-Formylphenyl)benzamide (**1'**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1); 65.7 mg, 95% yield; reaction time = 12 h; ^1H NMR (400 MHz, CDCl_3) δ 12.09 (s, 1H), 10.00 (s,

1H), 8.97 (d, $J = 8.0$ Hz, 1H), 8.08 (d, $J = 8.0$ Hz, 2H), 7.74-7.66 (m, 2H), 7.60-7.52 (m, 3H), 7.27 (t, $J = 8.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 195.9, 166.1, 141.2, 136.4, 136.2, 134.2, 132.2, 128.8, 127.5, 123.0, 121.9, 119.9.

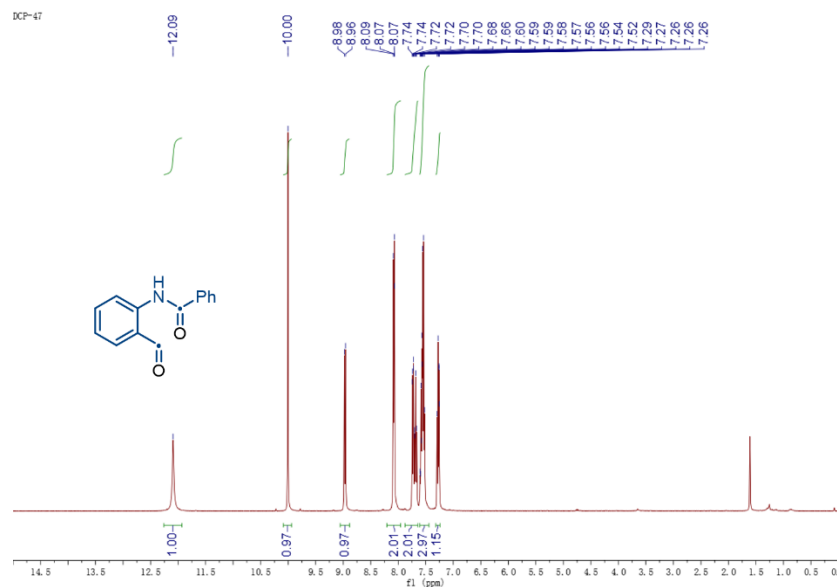


Figure S2. ^1H NMR spectrum of intermediate **1'**

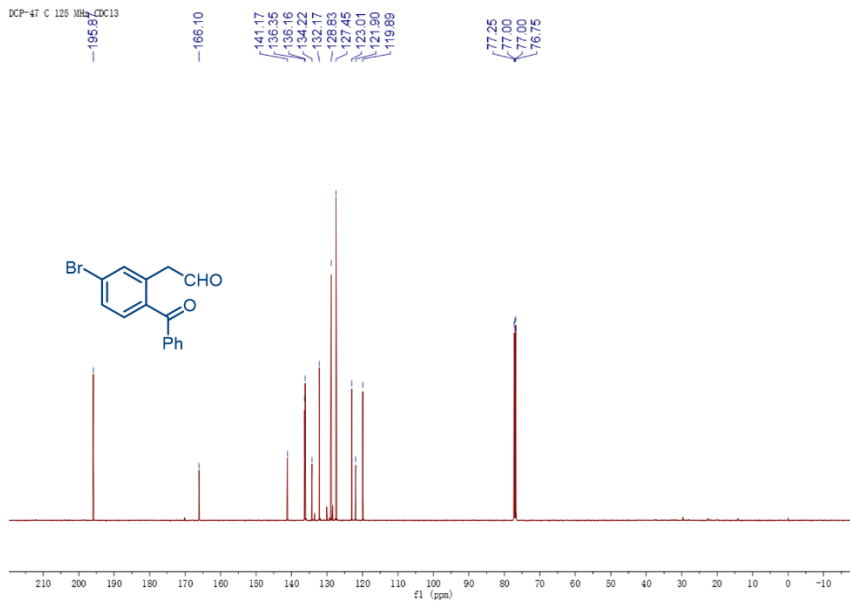
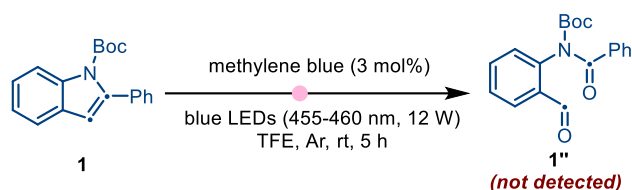


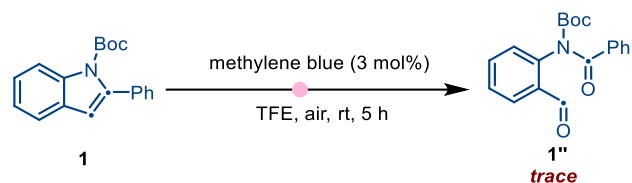
Figure S3. ^{13}C NMR spectrum of intermediate **1'**

8.2 Control experiments under argon atmosphere



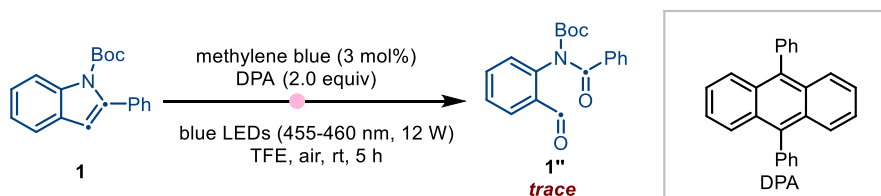
Into a 25 mL Schlenk tube was sequentially added the indole **1** (88.0 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), and 2,2,2-trifluoroethanol (TFE, 2.0 mL). The reaction mixture was degasified using argon for 15 minutes under constant purging and monitoring. Then, the reaction was stirred at room temperature under irradiation with visible light (455-460 nm, 12 W) for 5 h. The oxidative cleavage product **1''** was not detected in the mixture, indicating air atmosphere was essential.

8.3 Control experiments without blue LEDs irradiation



Into a 25 mL Schlenk tube was sequentially added the indole **1** (88.0 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), and 2,2,2-trifluoroethanol (TFE, 2.0 mL). Then, the reaction was stirred at room temperature under air atmosphere in dark for 5 h. Only trace amount of the oxidative cleavage product **1''** was detected in the mixture, indicating light irradiation was indispensable.

8.4 Control experiments with DPA as additive



Into a 25 mL Schlenk tube was sequentially added the indole **1** (88.0 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), 9,10-diphenylanthracene (DPA, 198.3 mg, 0.60 mmol, 2.0 equiv), and 2,2,2-trifluoroethanol (TFE, 2.0 mL). Then, the reaction was stirred at room temperature in air atmosphere under irradiation with visible light (455-460 nm, 12 W) for 5 h. Only trace amounts of product **1''** was produced, and the corresponding endoperoxide adducts ($^1\text{O}_2$ -DPA) was detected by HRMS, thus corroborating the intermediacy of singlet

oxygen in the photochemical cleavage.

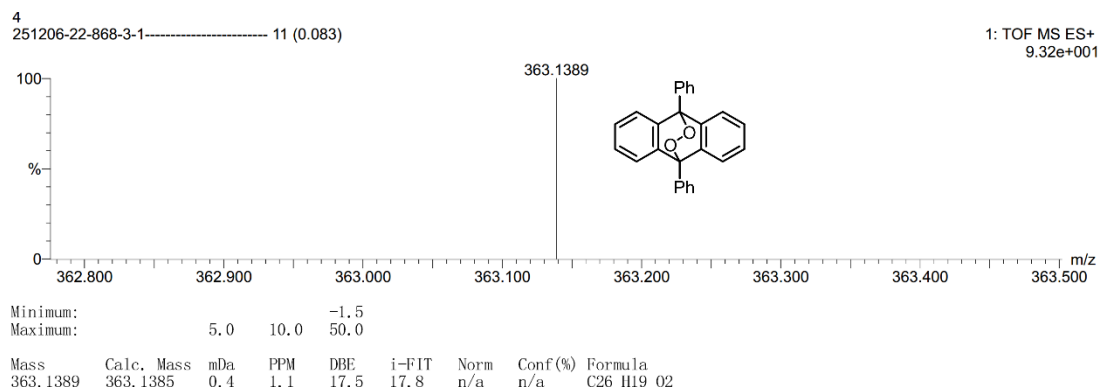
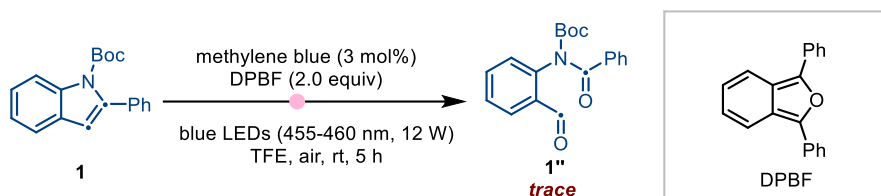


Figure S4. The HRMS spectrum of the crude mixture with DPA as an additive

8.5 Control experiments with DPBF as additive



Into a 25 mL Schlenk tube was sequentially added the indole **1** (88.0 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), 9,10-diphenylanthracene (DPBF, 162.2 mg, 0.60 mmol, 2.0 equiv), and 2,2,2-trifluoroethanol (TFE, 2.0 mL). Then, the reaction was stirred at room temperature in air atmosphere under irradiation with visible light (455-460 nm, 12 W) for 5 h. Only trace amounts of product **1''** was produced, and the corresponding endoperoxide adducts (¹O₂-DPBF) was detected by HRMS, thus corroborating the intermediacy of singlet oxygen in the photochemical cleavage.

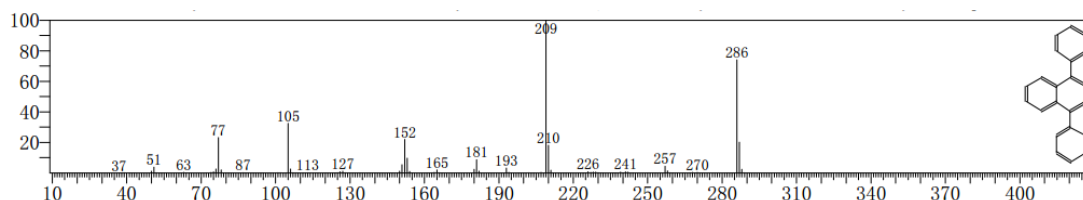
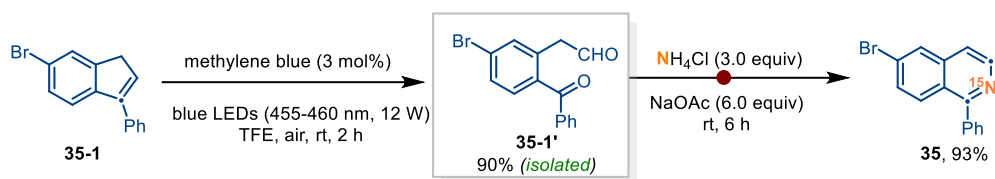
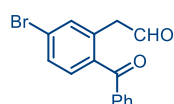


Figure S5. The HRMS spectrum of the crude mixture with DPBF as an additive

8.6 Control experiment to trap the intermediate for indene 35-1 editing



Into a 25 mL Schlenk tube was sequentially added the indene **35-1** (81.6 mg, 0.30 mmol), methylene blue (2.9 mg, 0.009 mmol), and 2,2,2-trifluoroethanol (TFE, 2.0 mL). The reaction was stirred for 2 h at room temperature under irradiation with visible light (455-460 nm, 12 W). The light source was then removed, and the reaction mixture was concentrated in vacuo, and the residue was purified by silica gel column chromatography to afford intermediate **35-1'** in 90% yield. Comprehensive ^1H and ^{13}C NMR analysis confirmed its structure. Treatment of **35-1'** with NH_4Cl and NaOAc under standard conditions furnished **35** in 93% yield, establishing **35-1'** as the key intermediate.



2-(2-Benzoyl-5-bromophenyl)acetaldehyde (**35-1'**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 30:1); 81.9 mg, 90% yield; reaction time = 2 h; ^1H NMR (400 MHz, CDCl_3) δ 9.76 (s, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.60 (t, J = 8.0 Hz, 1H), 7.51-7.45 (m, 4H), 7.33 (d, J = 8.0 Hz, 1H), 3.91 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 197.8, 196.8, 137.2, 136.7, 135.0, 134.9, 133.3, 131.8, 130.2, 129.9, 128.5, 125.8, 47.9.

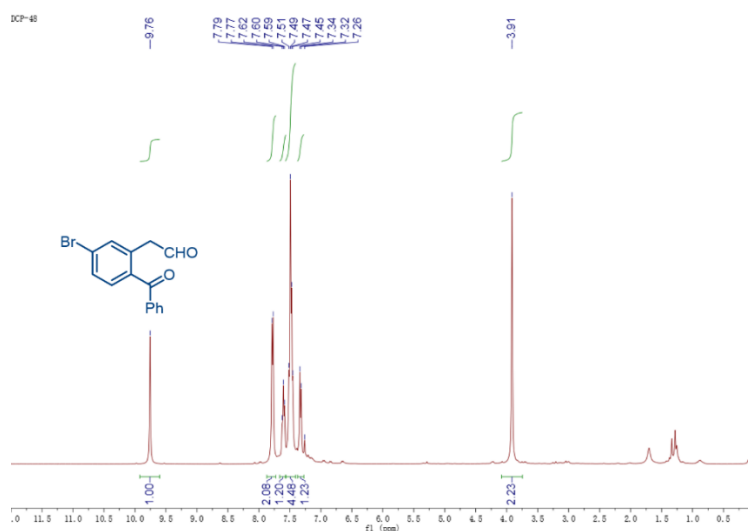


Figure S6. ^1H NMR spectrum of intermediate **35-1'**

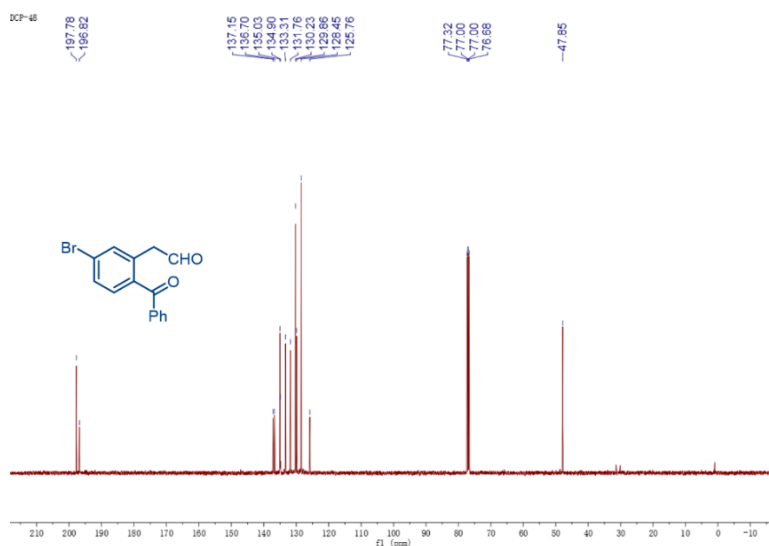


Figure S7. ¹³C NMR spectrum of intermediate **35-1'**

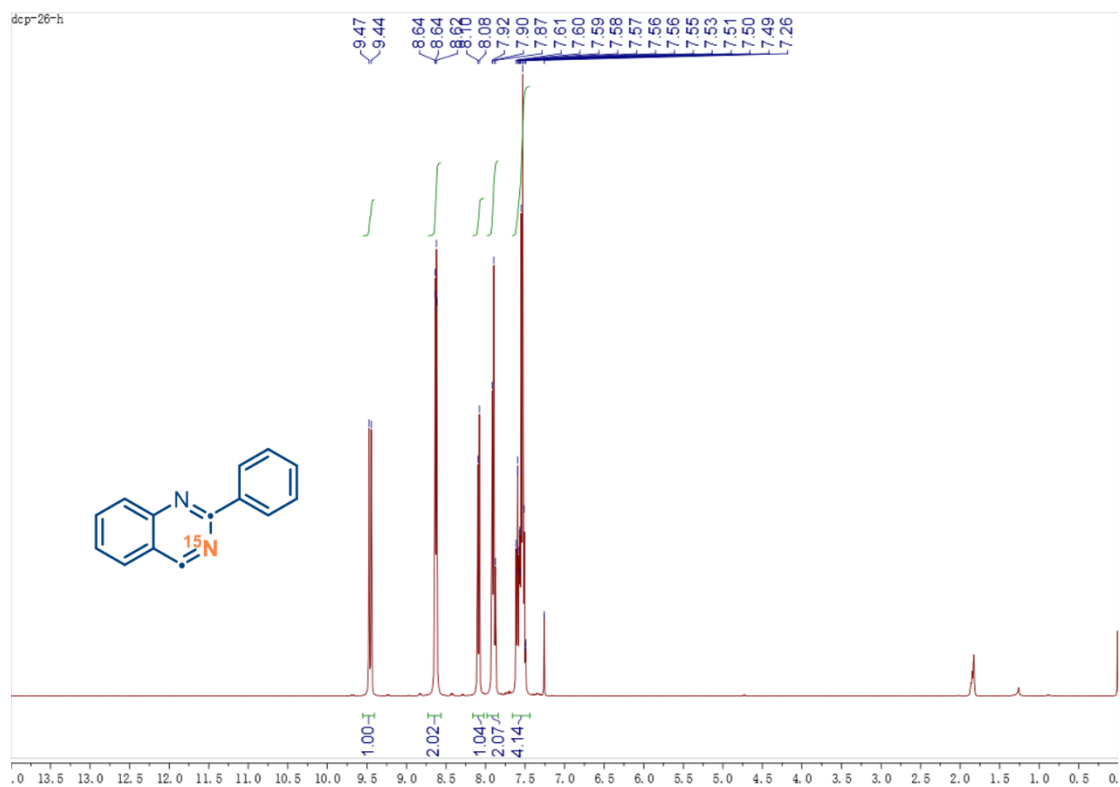
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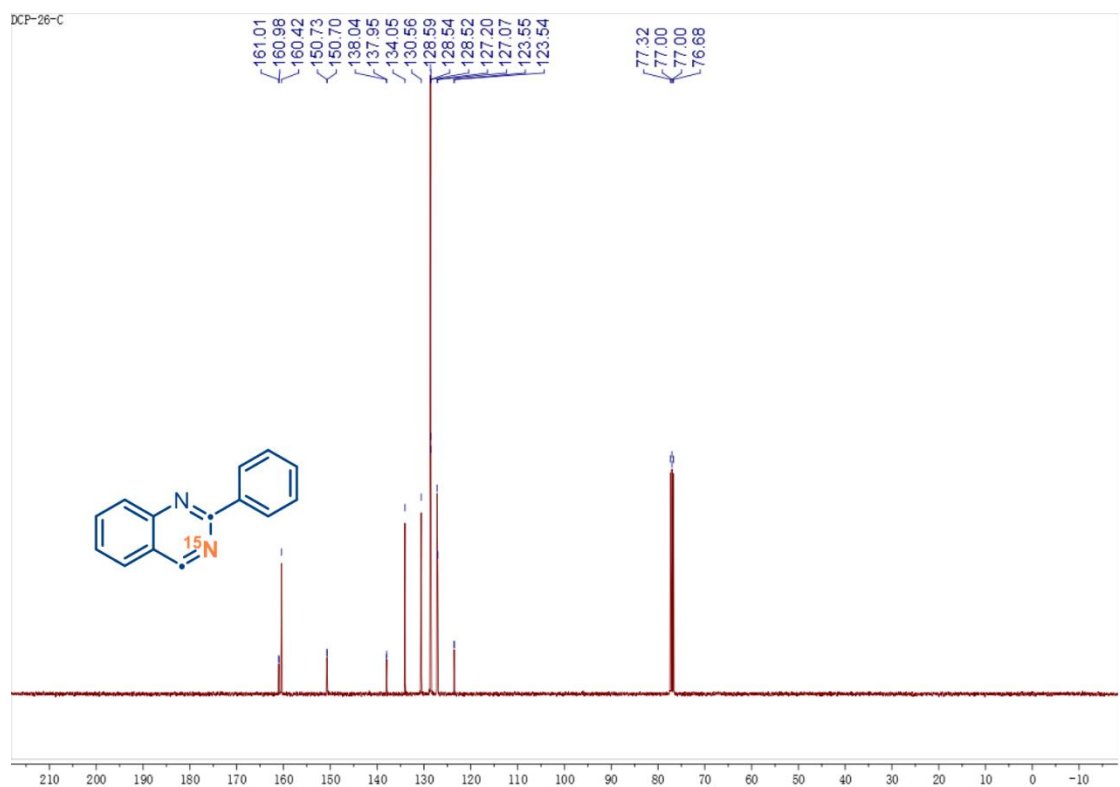
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10. NMR spectra

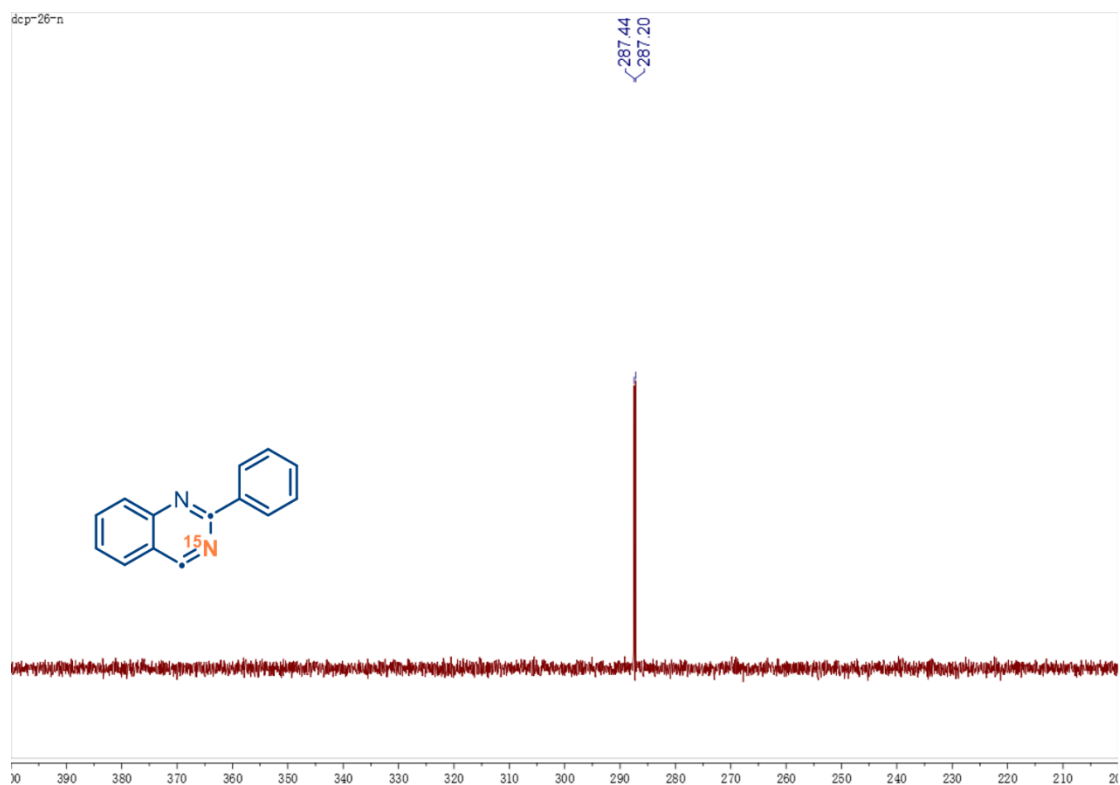
^1H NMR spectrum of **2** (400 MHz, CDCl_3)



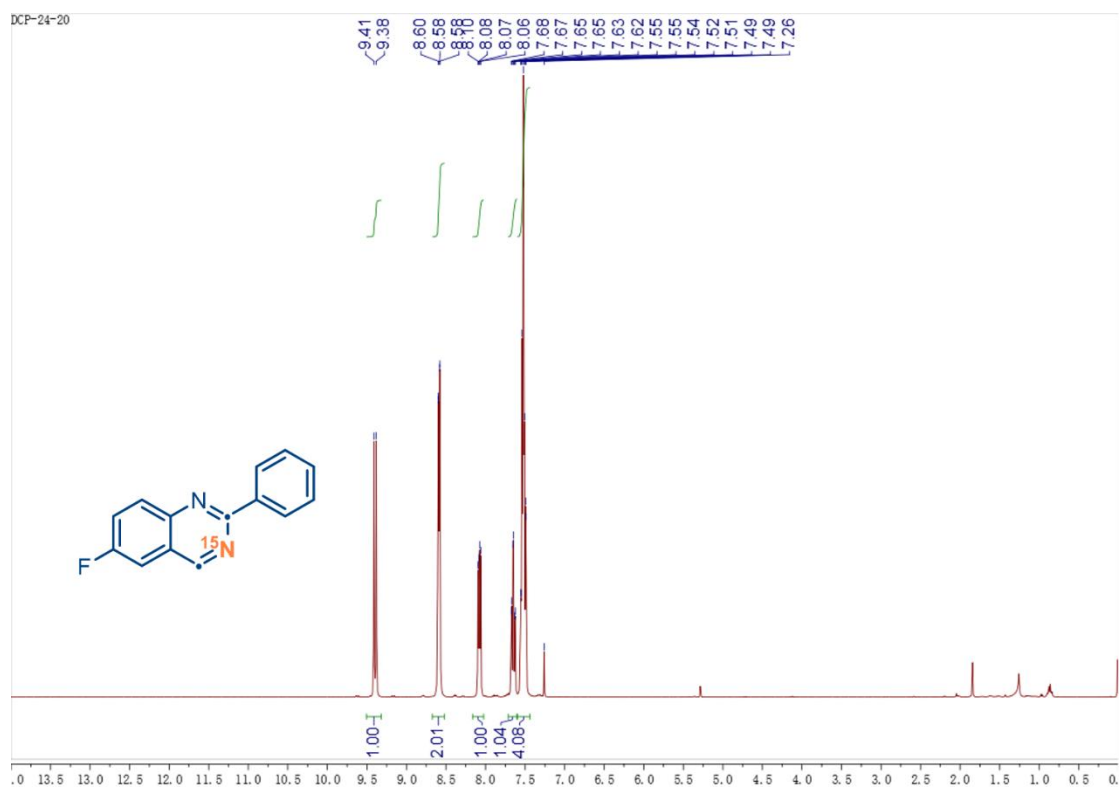
^{13}C NMR spectrum of **2** (100 MHz, CDCl_3)



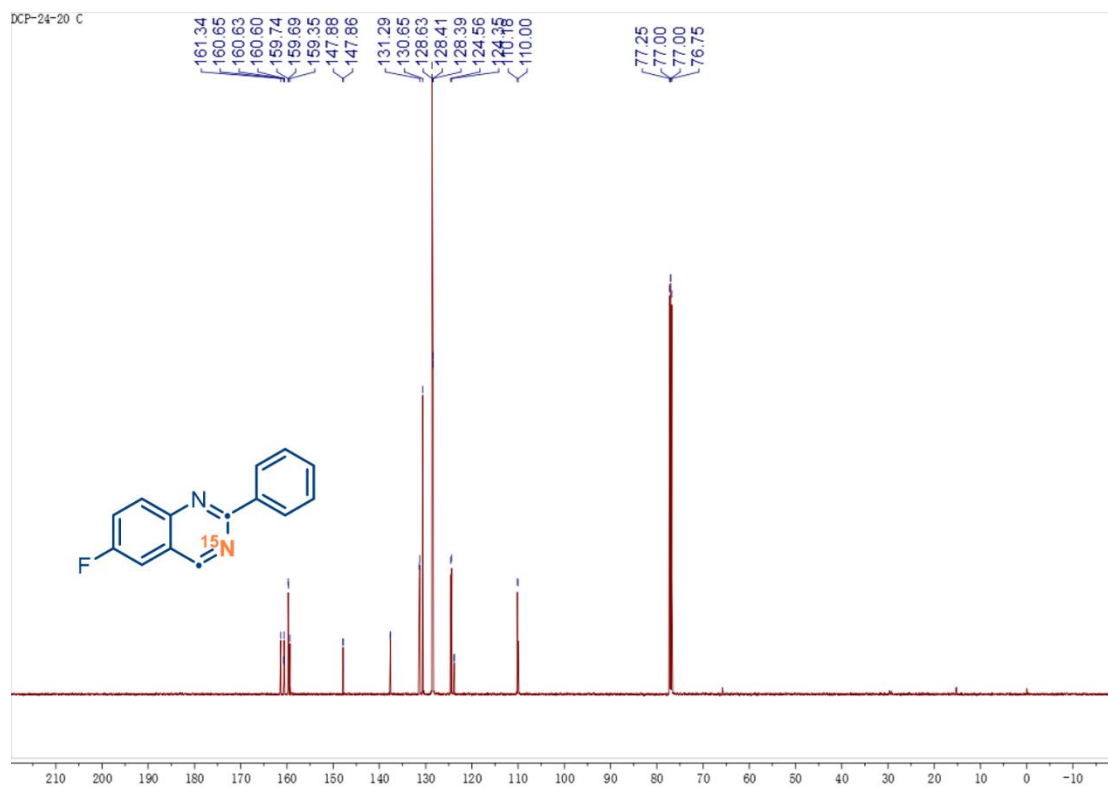
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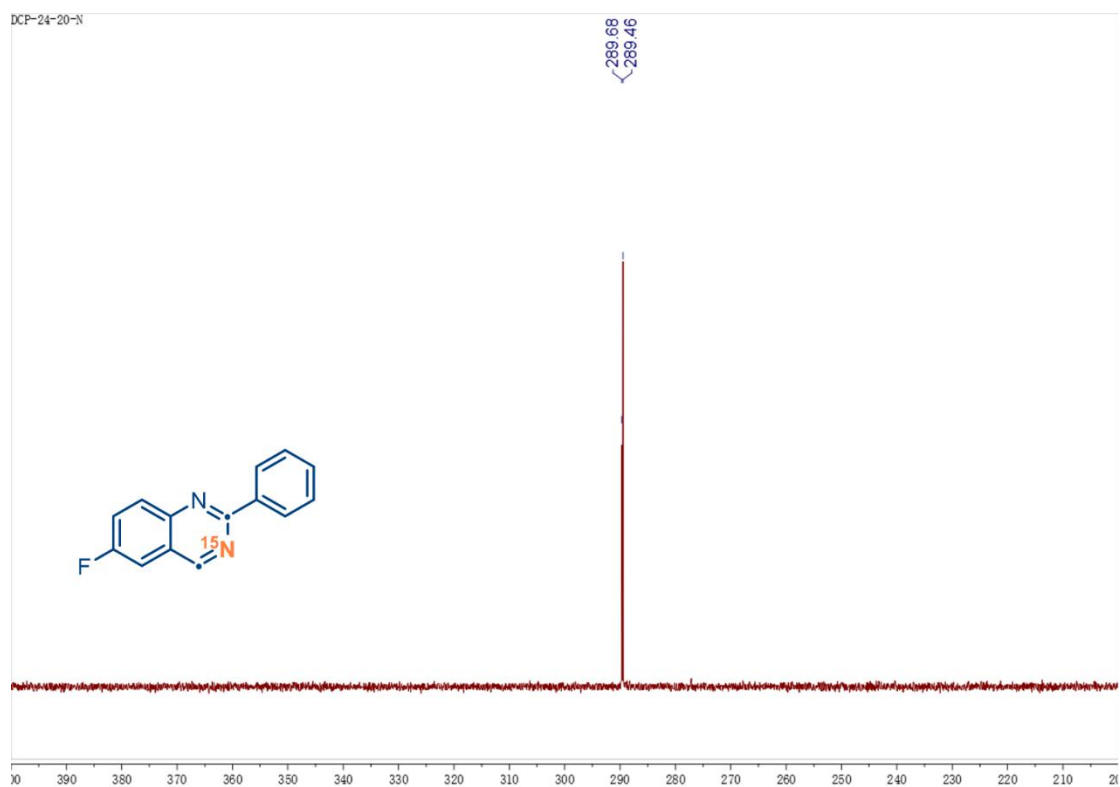
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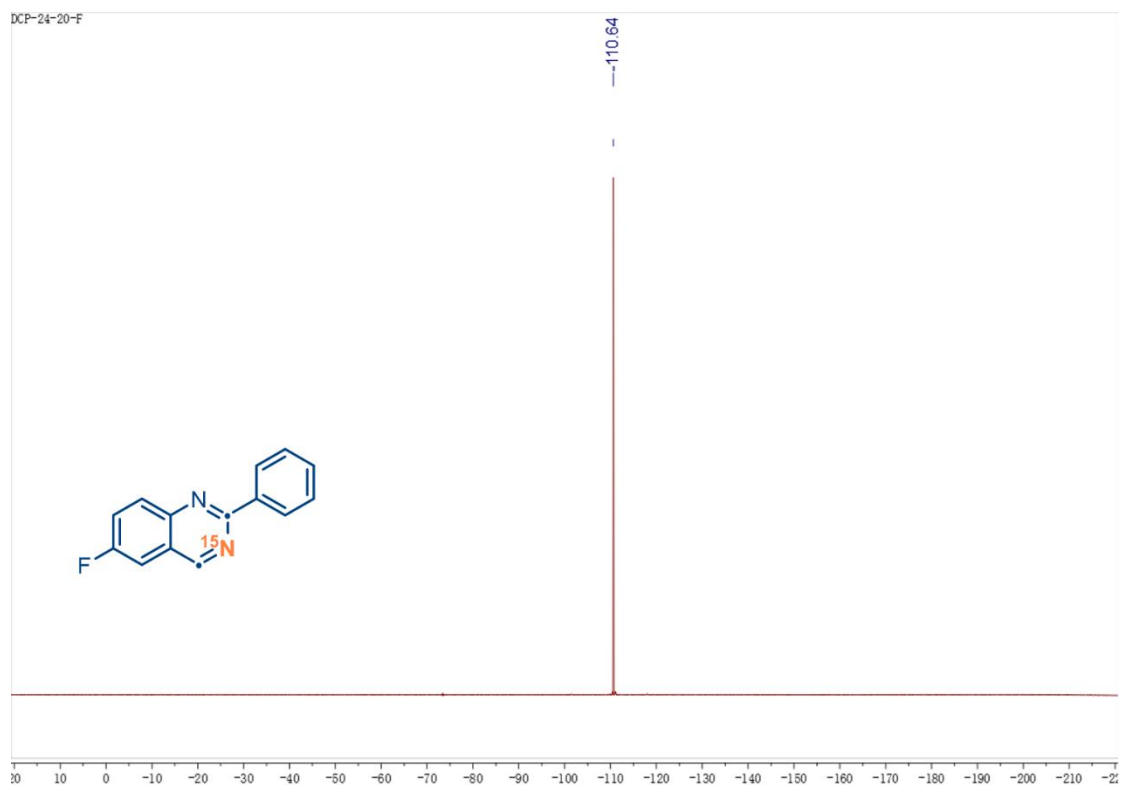
^{13}C NMR spectrum of **3** (125 MHz, CDCl_3)



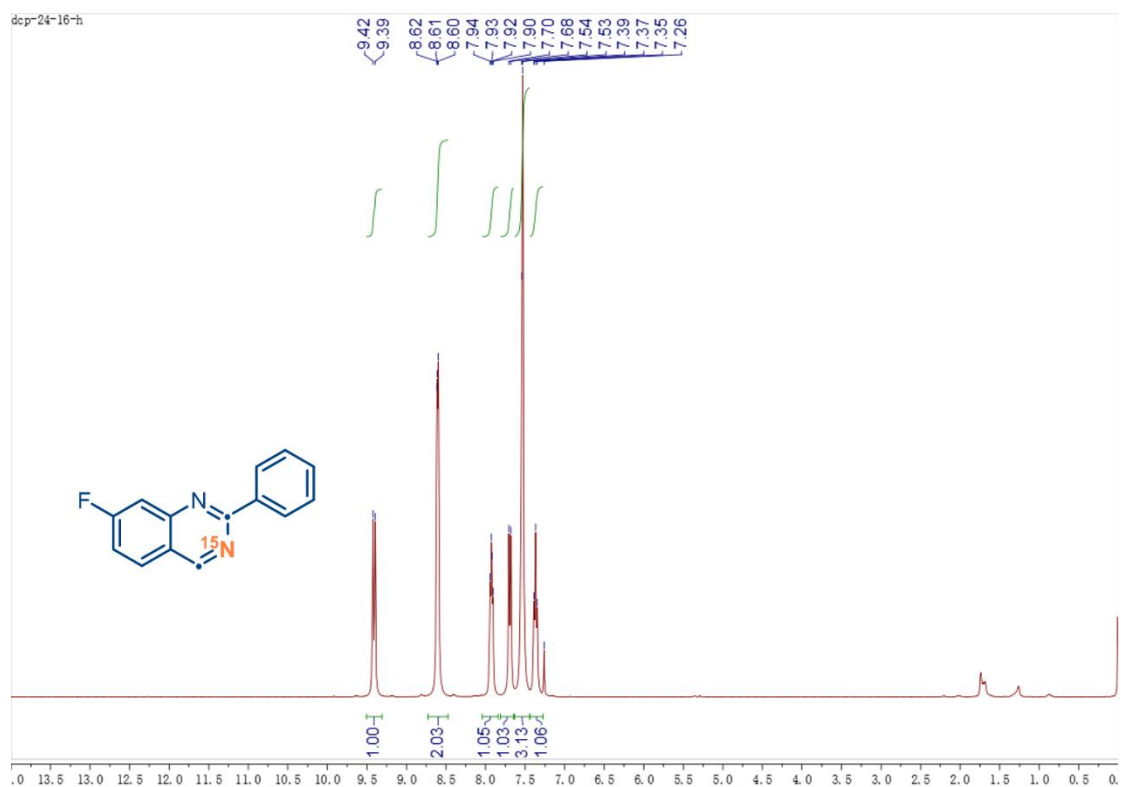
^{15}N NMR spectrum of **3** (50 MHz, CDCl_3)



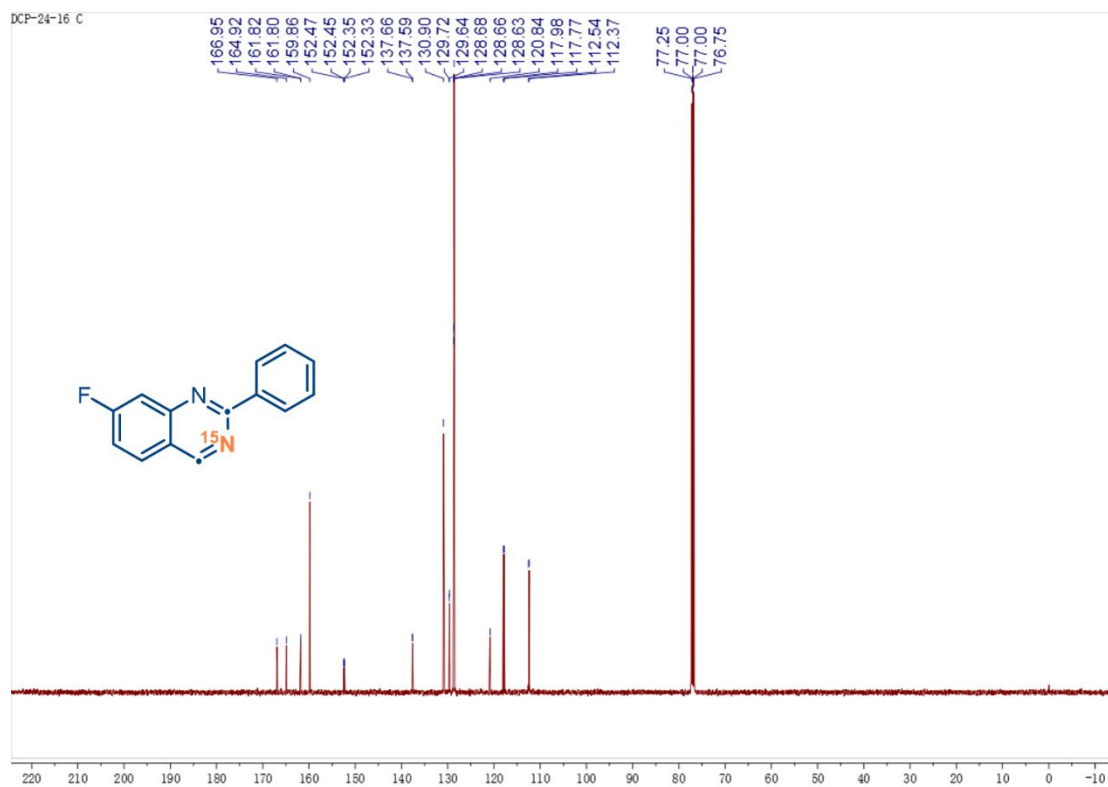
^{19}F NMR spectrum of **3** (376 MHz, CDCl_3)



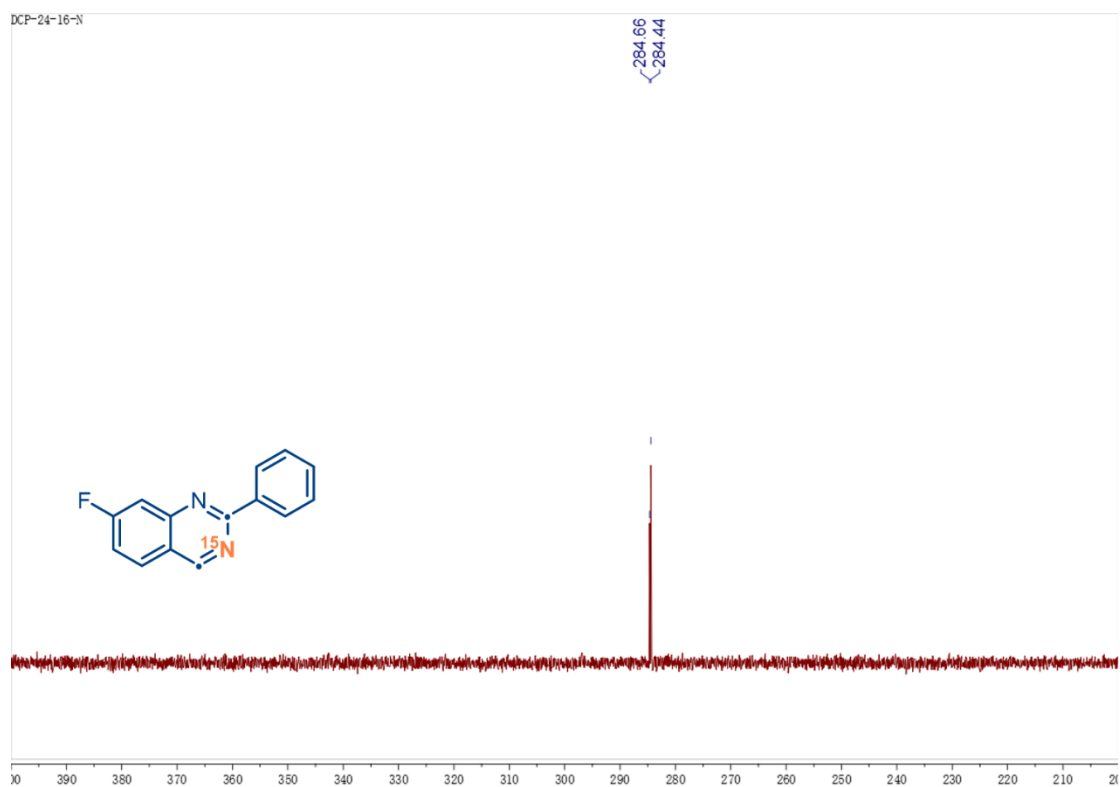
^1H NMR spectrum of **4** (400 MHz, CDCl_3)



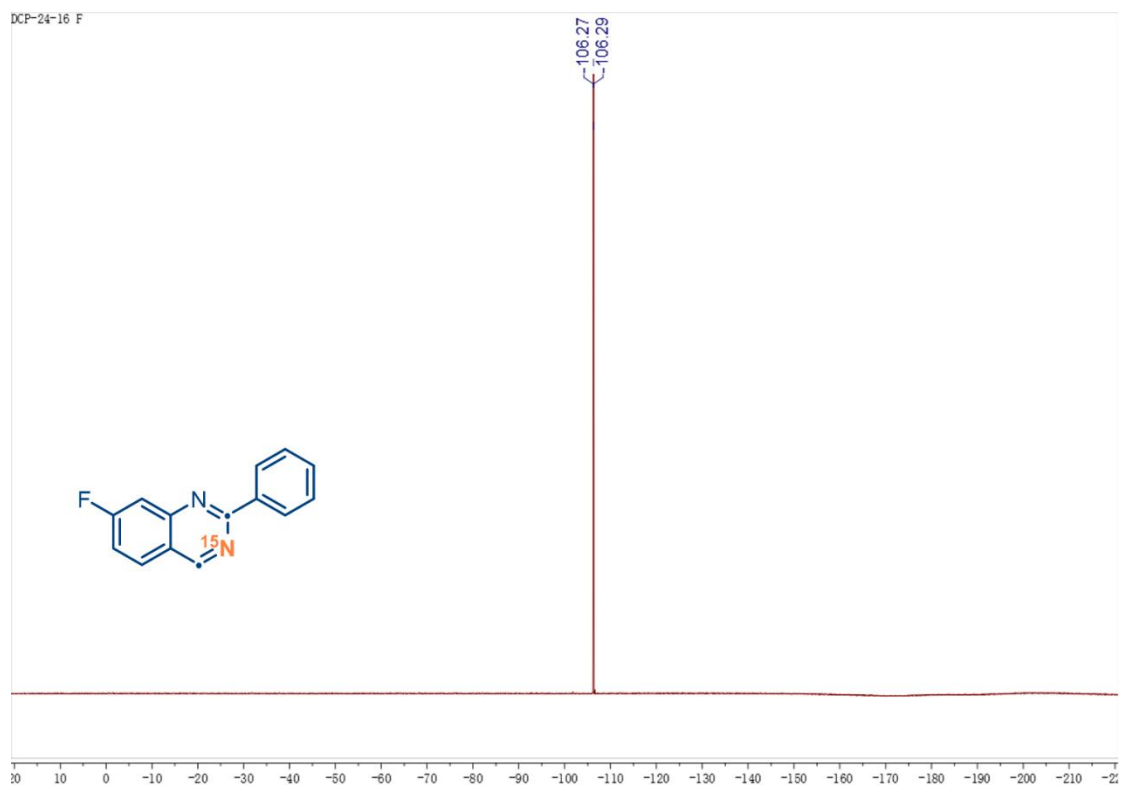
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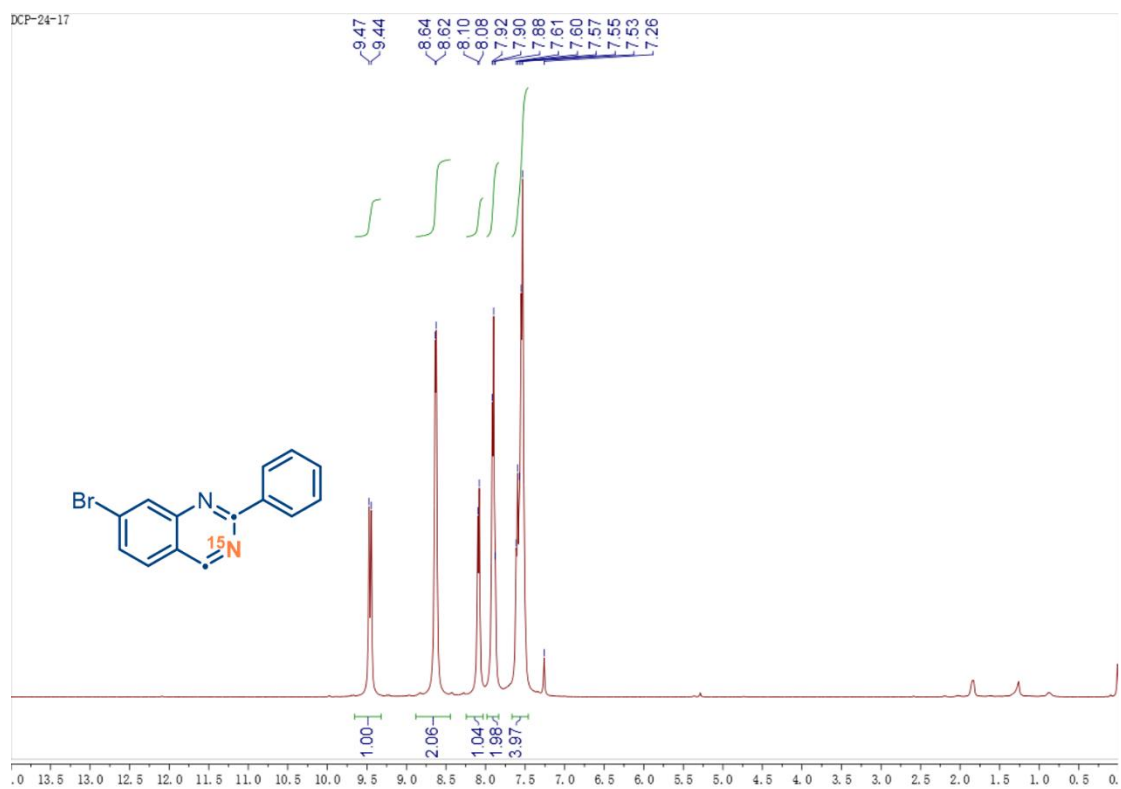
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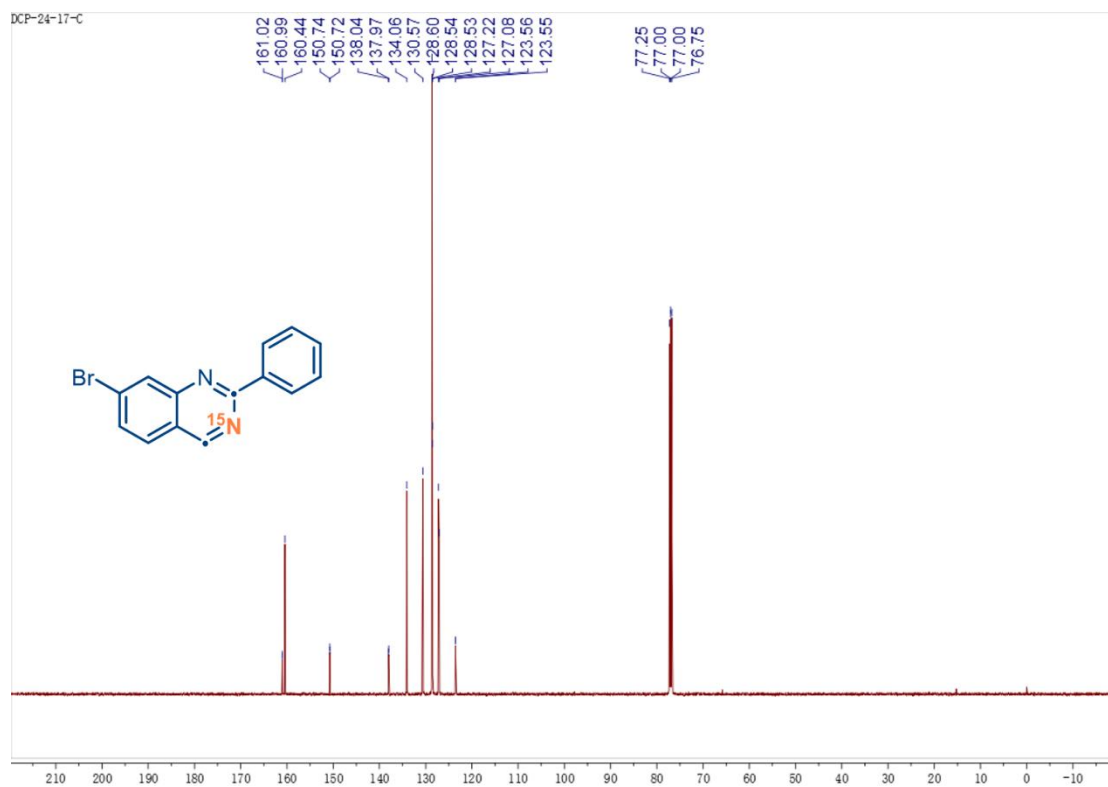
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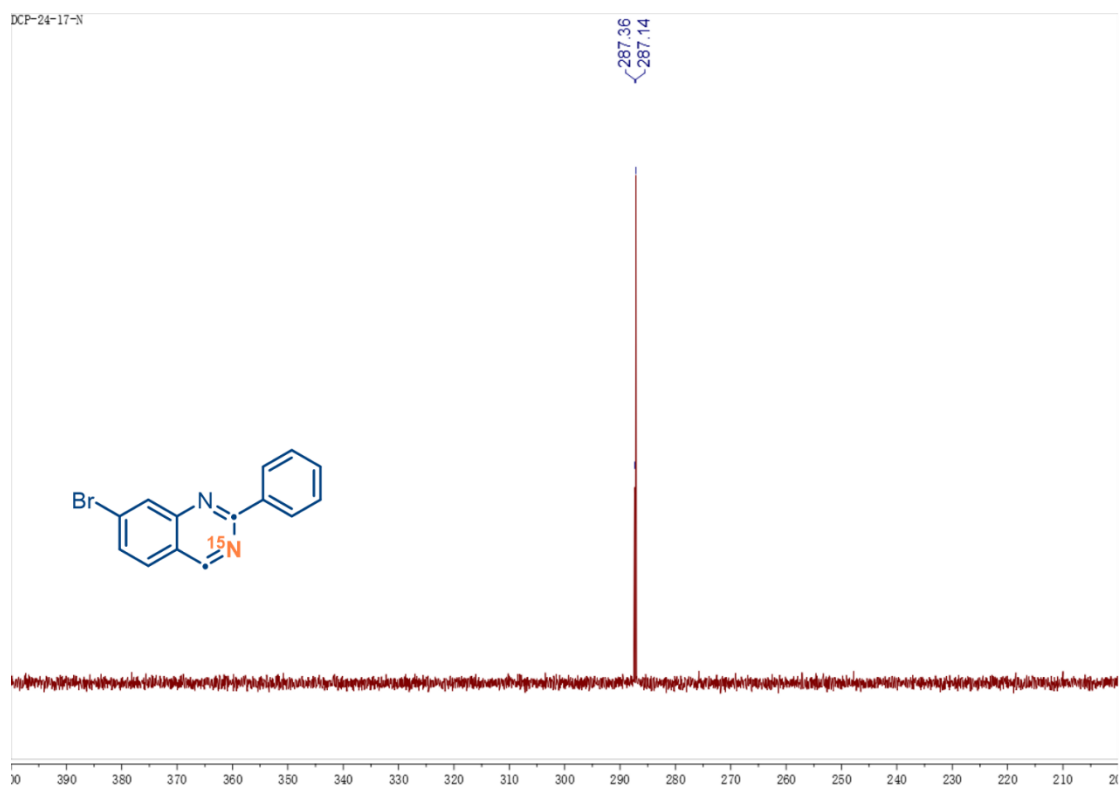
^1H NMR spectrum of **5** (400 MHz, CDCl_3)



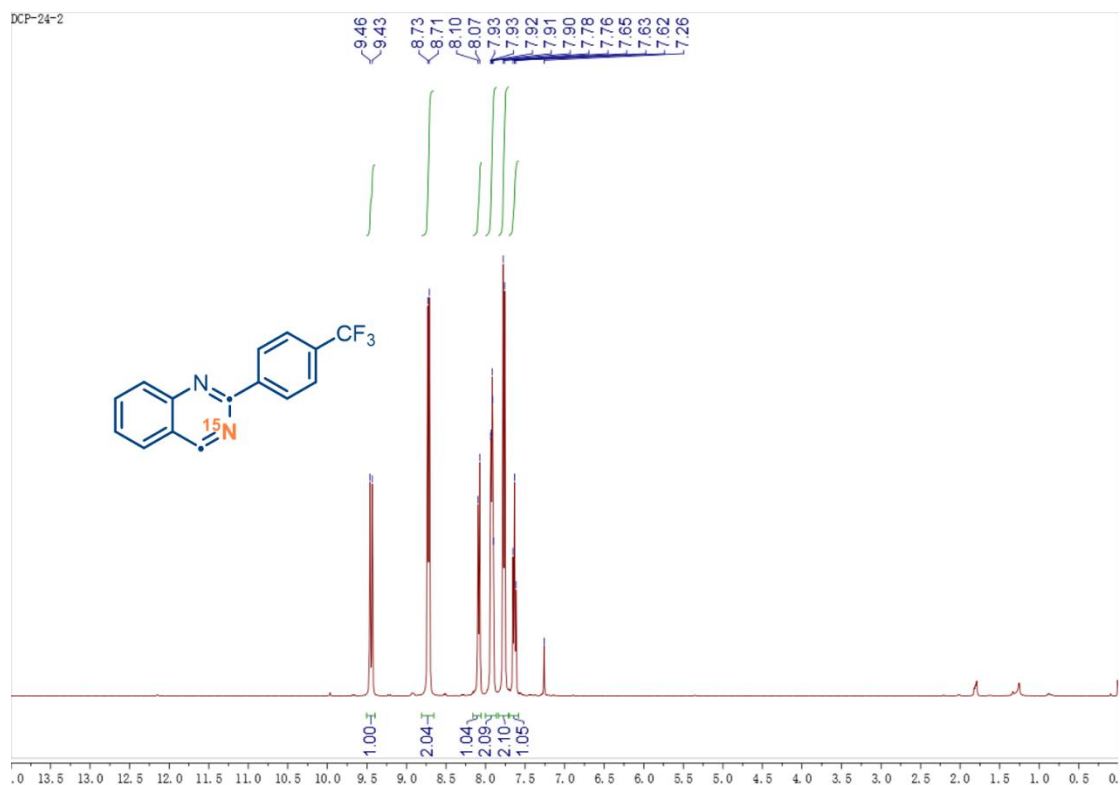
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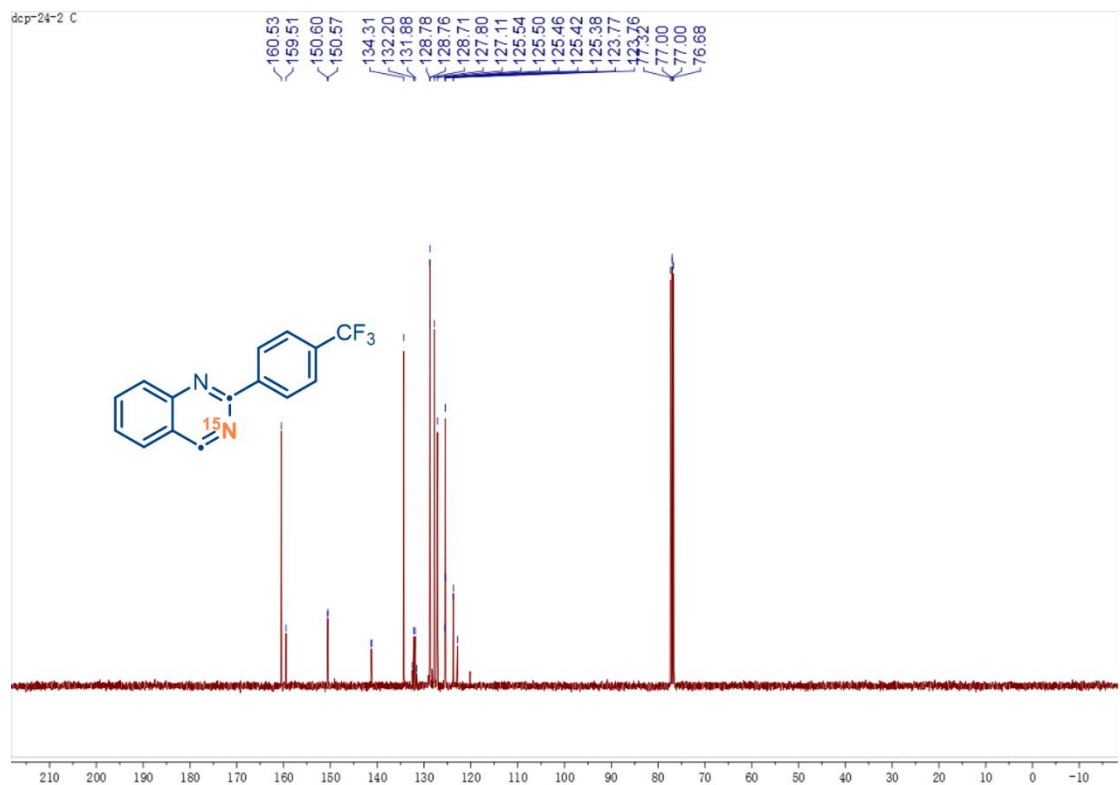
^{15}N NMR spectrum of **5** (50 MHz, CDCl_3)



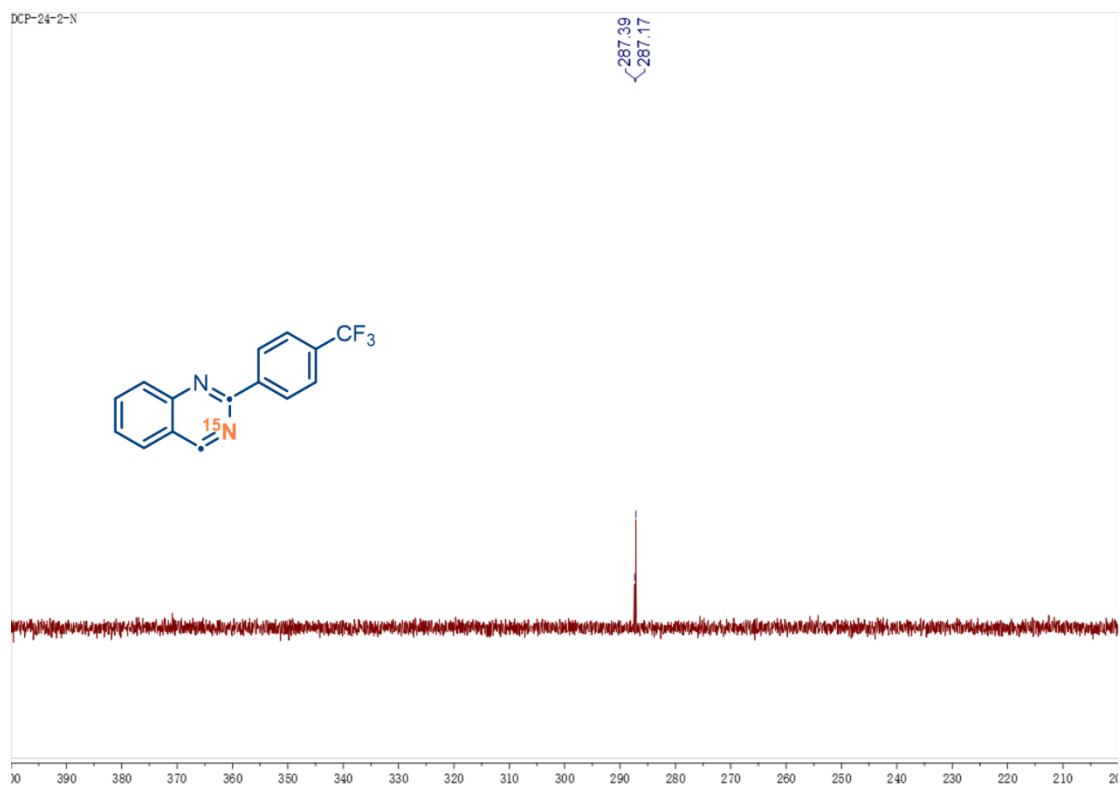
¹H NMR spectrum of **6** (400 MHz, CDCl₃)



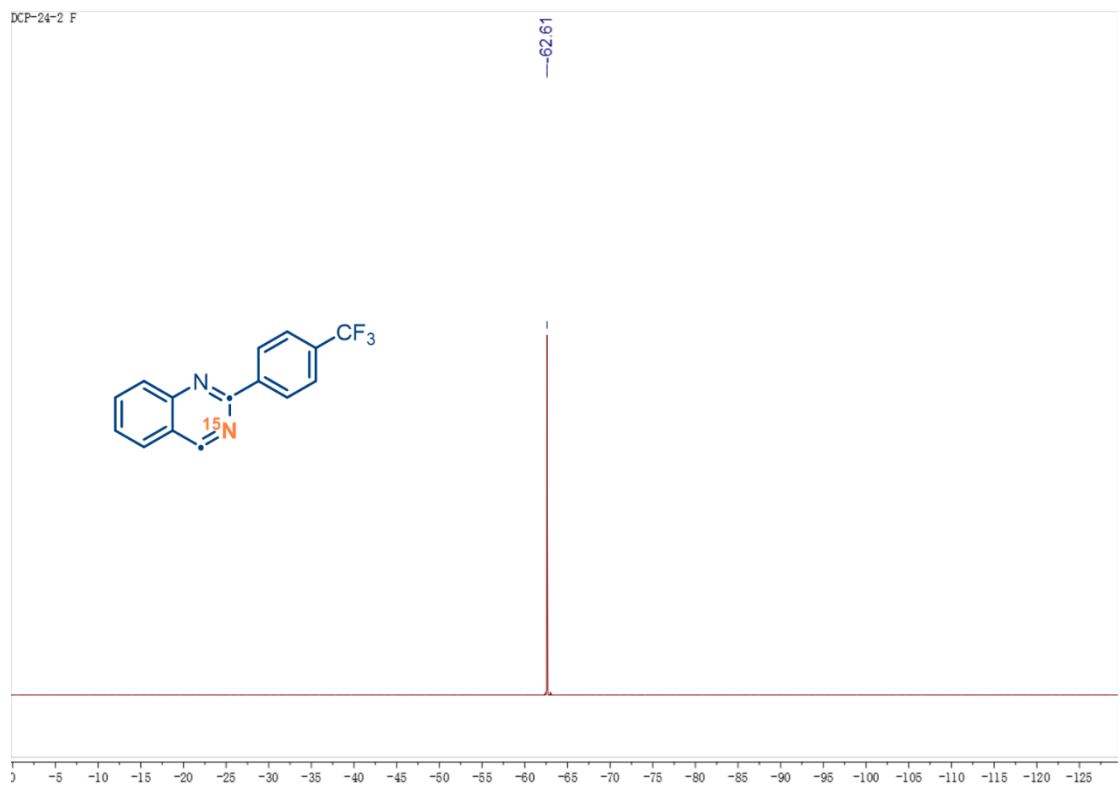
¹³C NMR spectrum of **6** (100 MHz, CDCl₃)



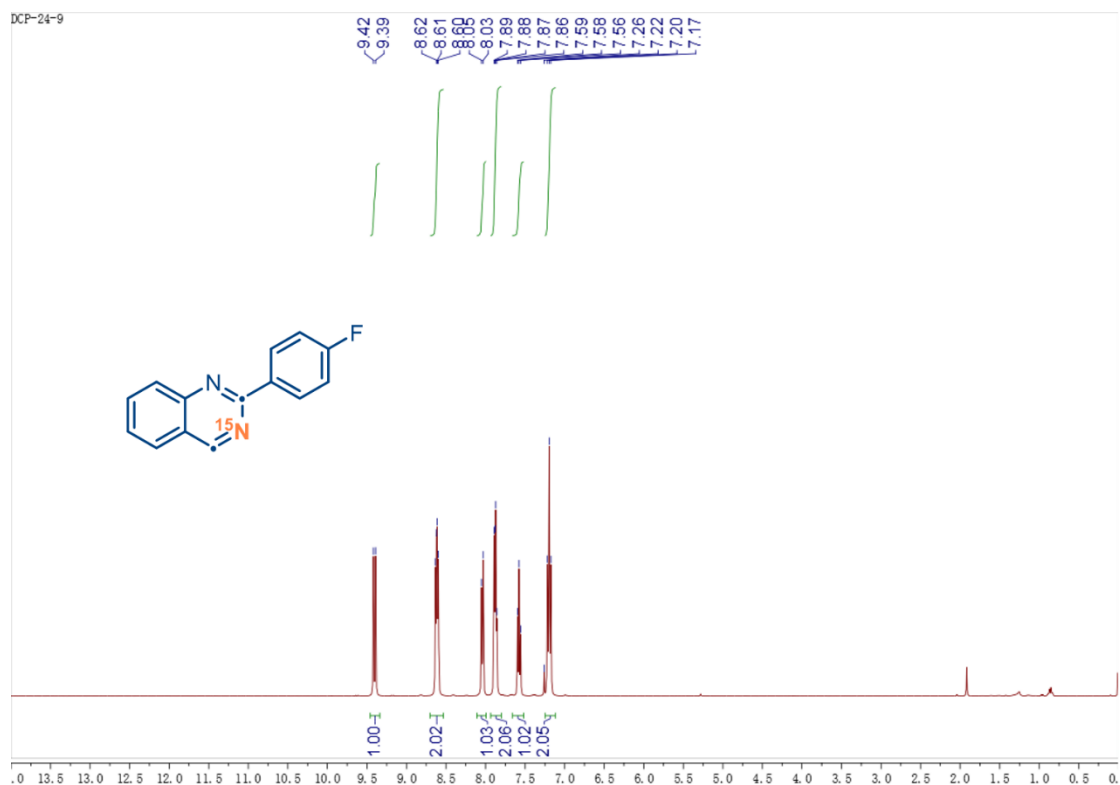
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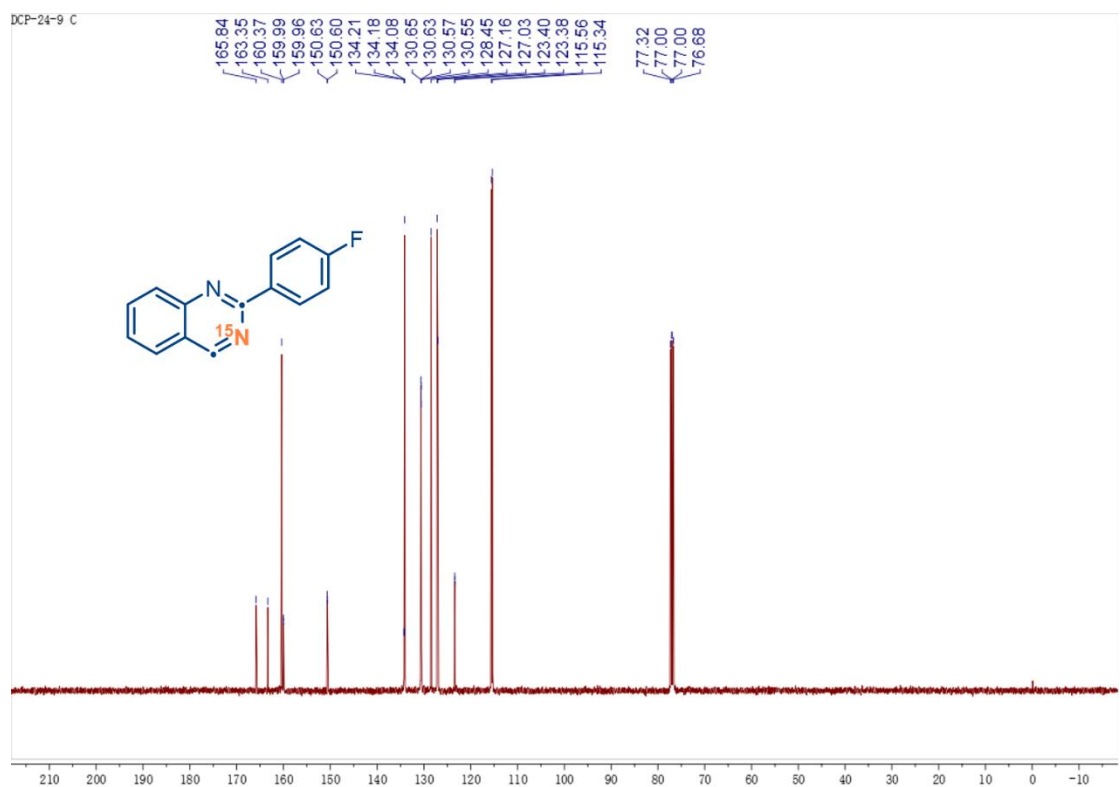
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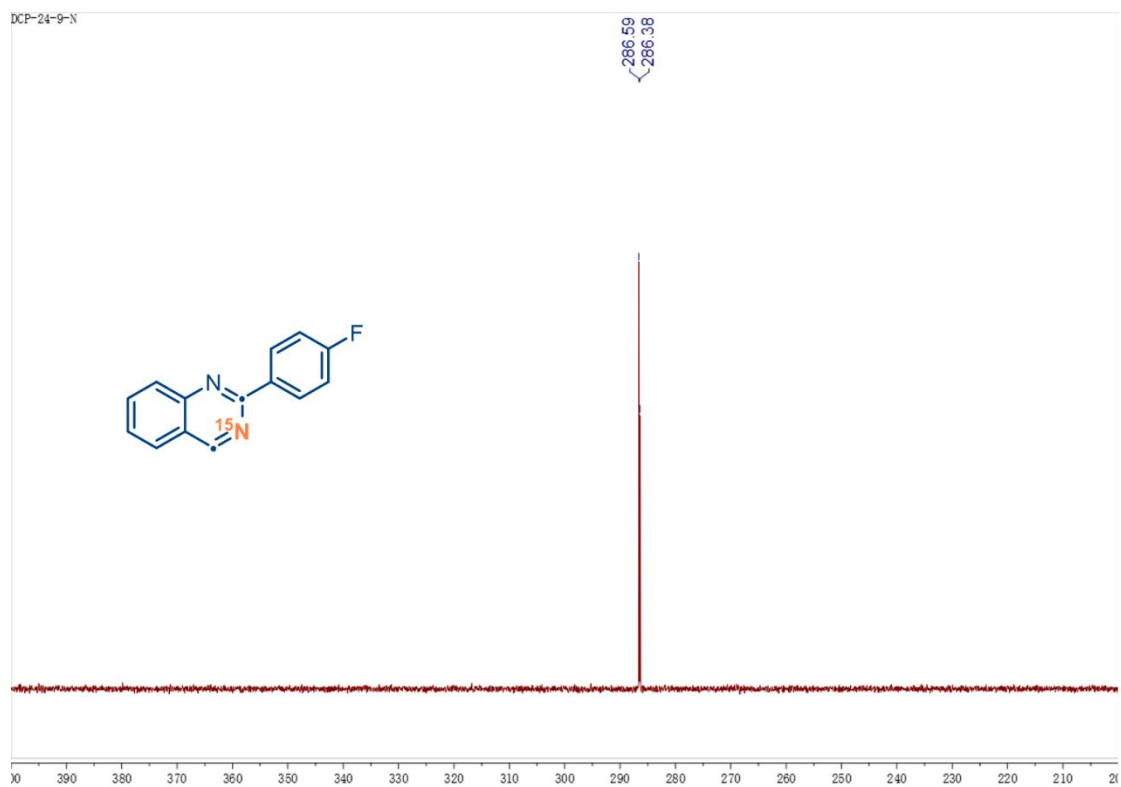
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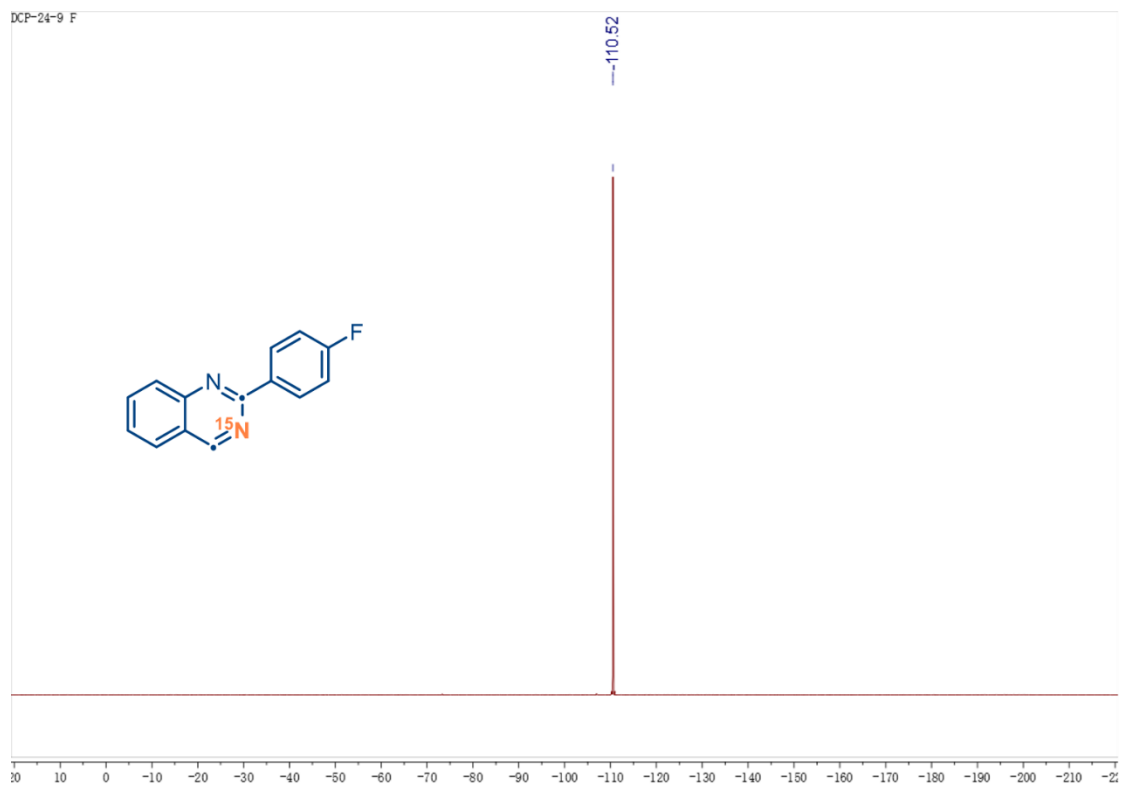
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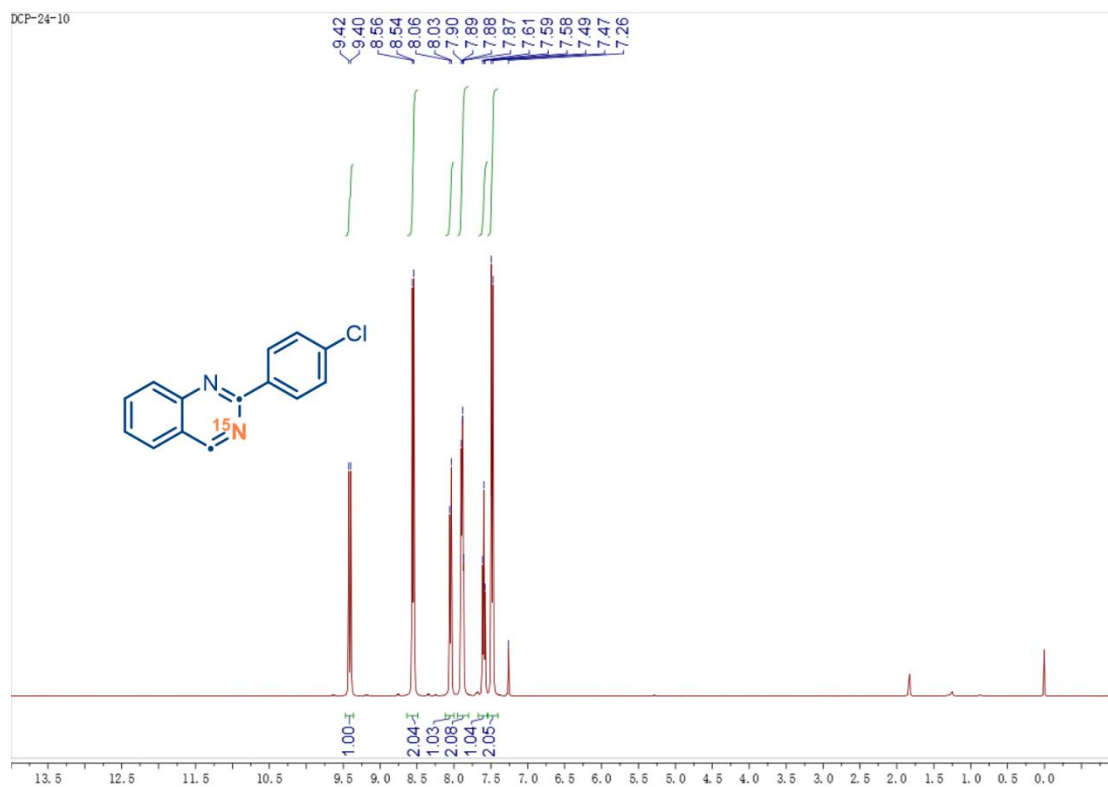
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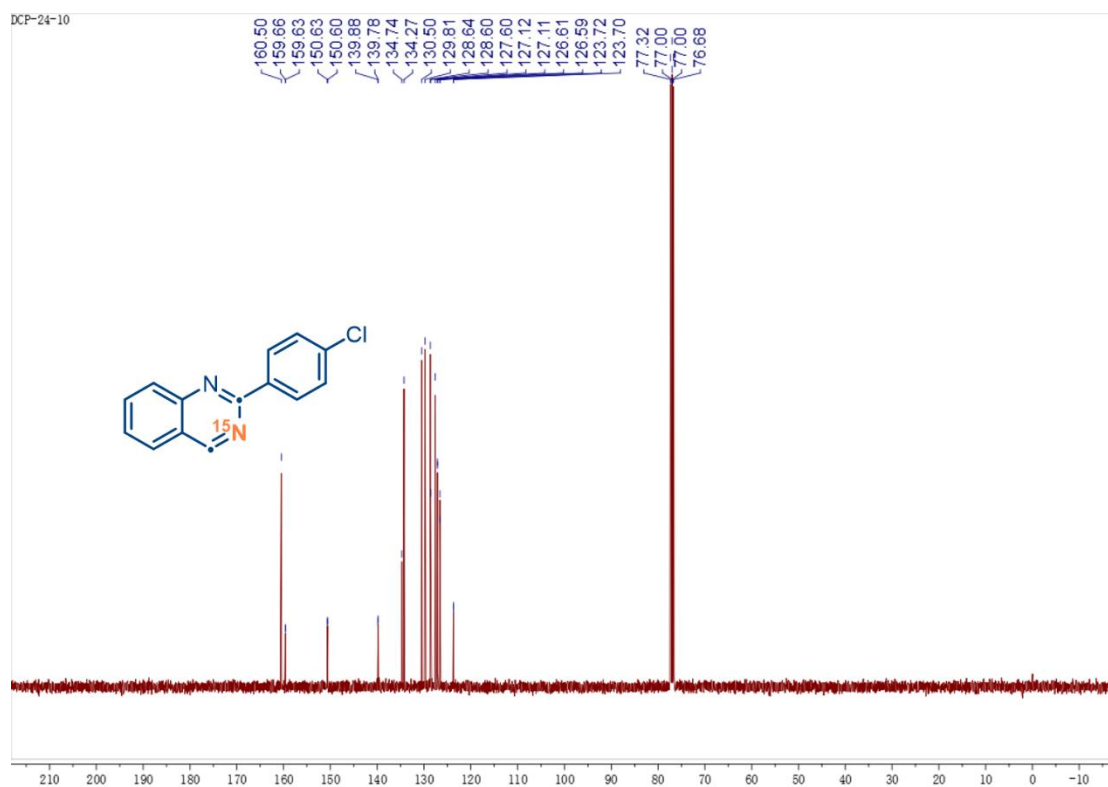
^{19}F NMR spectrum of **7** (376 MHz, CDCl_3)



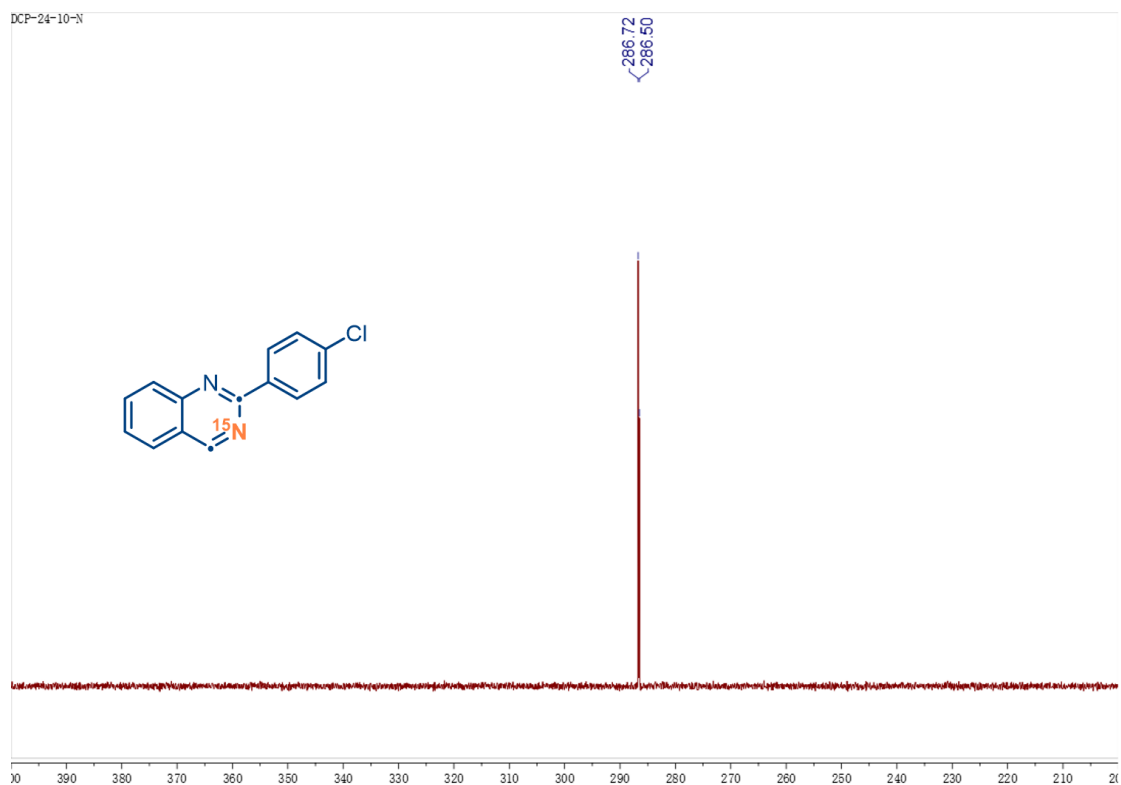
¹H NMR spectrum of **8** (400 MHz, CDCl₃)



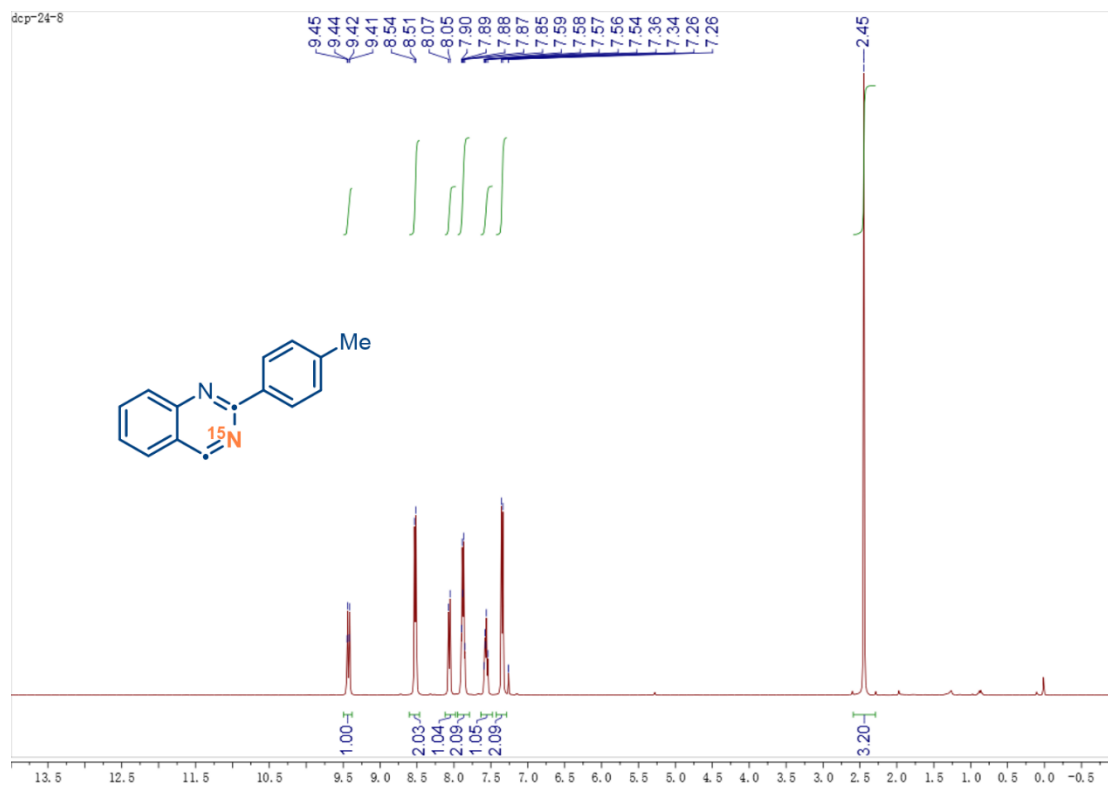
¹³C NMR spectrum of **8** (100 MHz, CDCl₃)



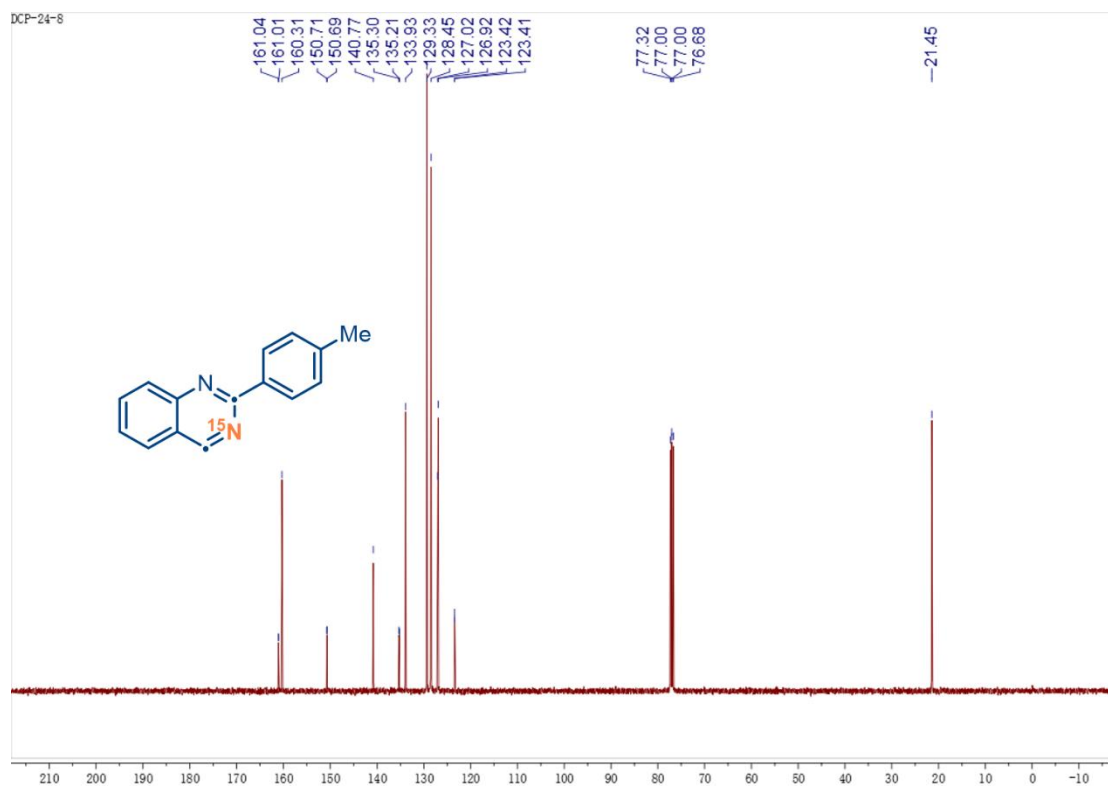
^{15}N NMR spectrum of **8** (50 MHz, CDCl_3)



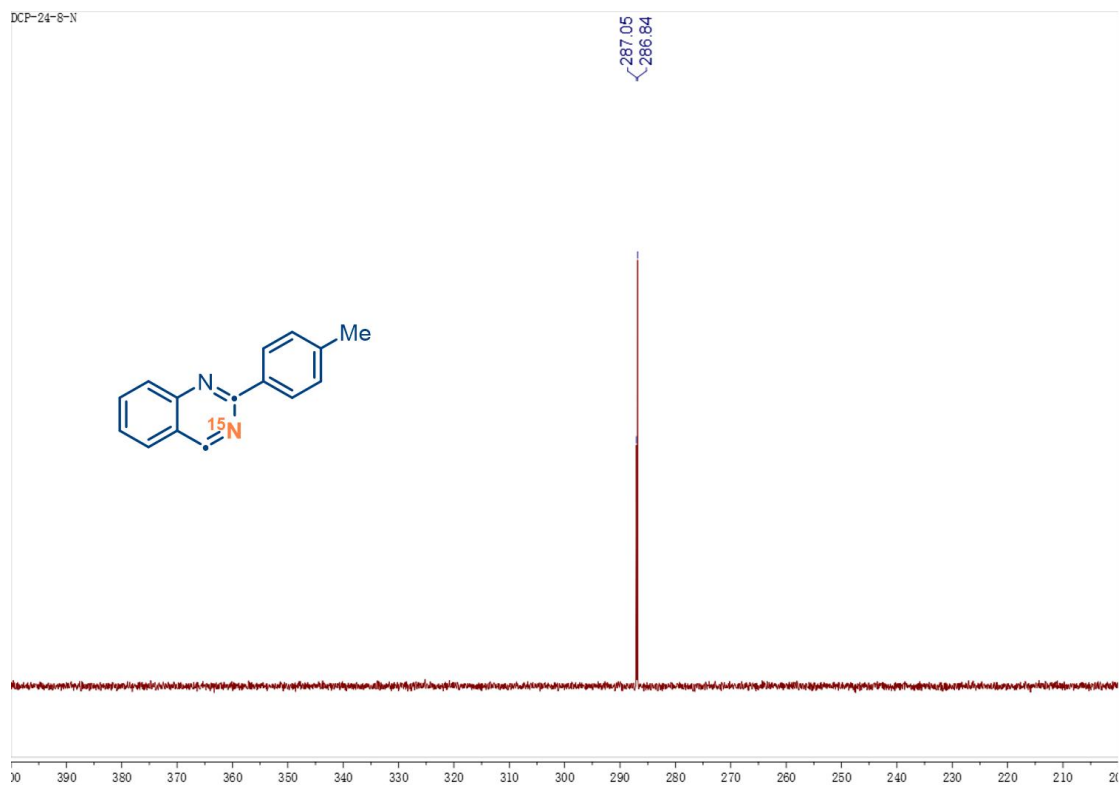
^1H NMR spectrum of **9** (400 MHz, CDCl_3)



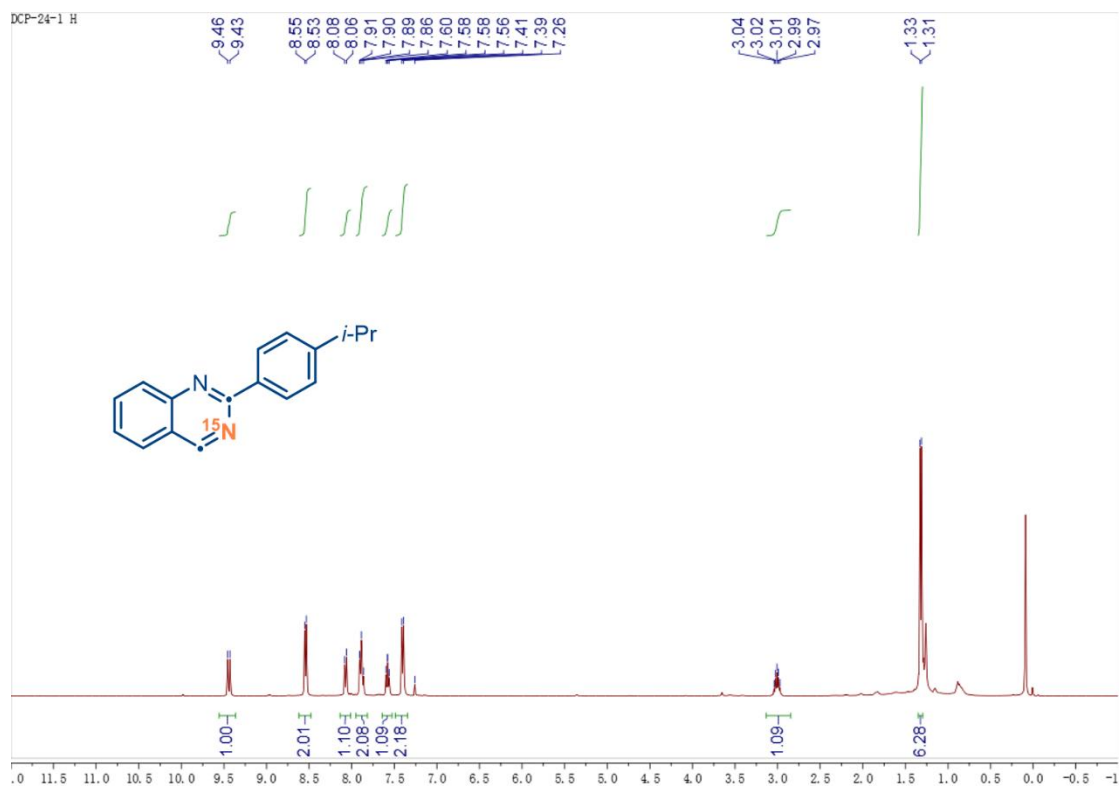
^{13}C NMR spectrum of **9** (100 MHz, CDCl_3)



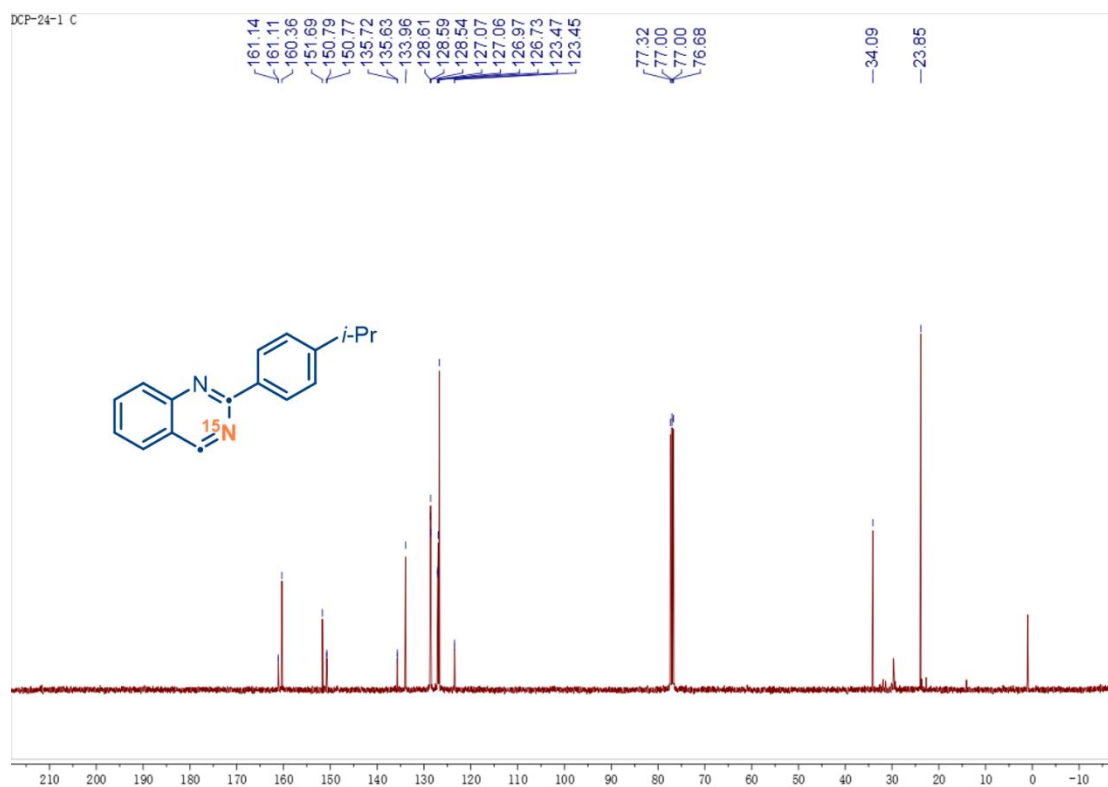
^{15}N NMR spectrum of **9** (50 MHz, CDCl_3)



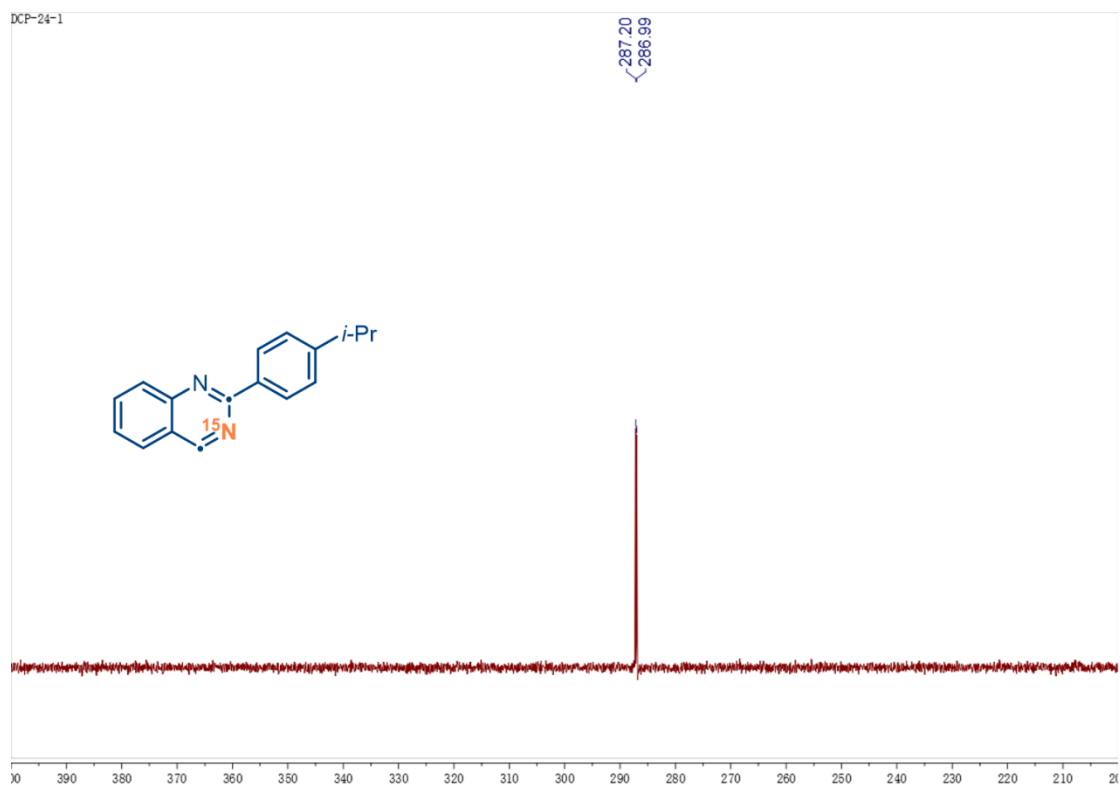
¹H NMR spectrum of **10** (400 MHz, CDCl₃)



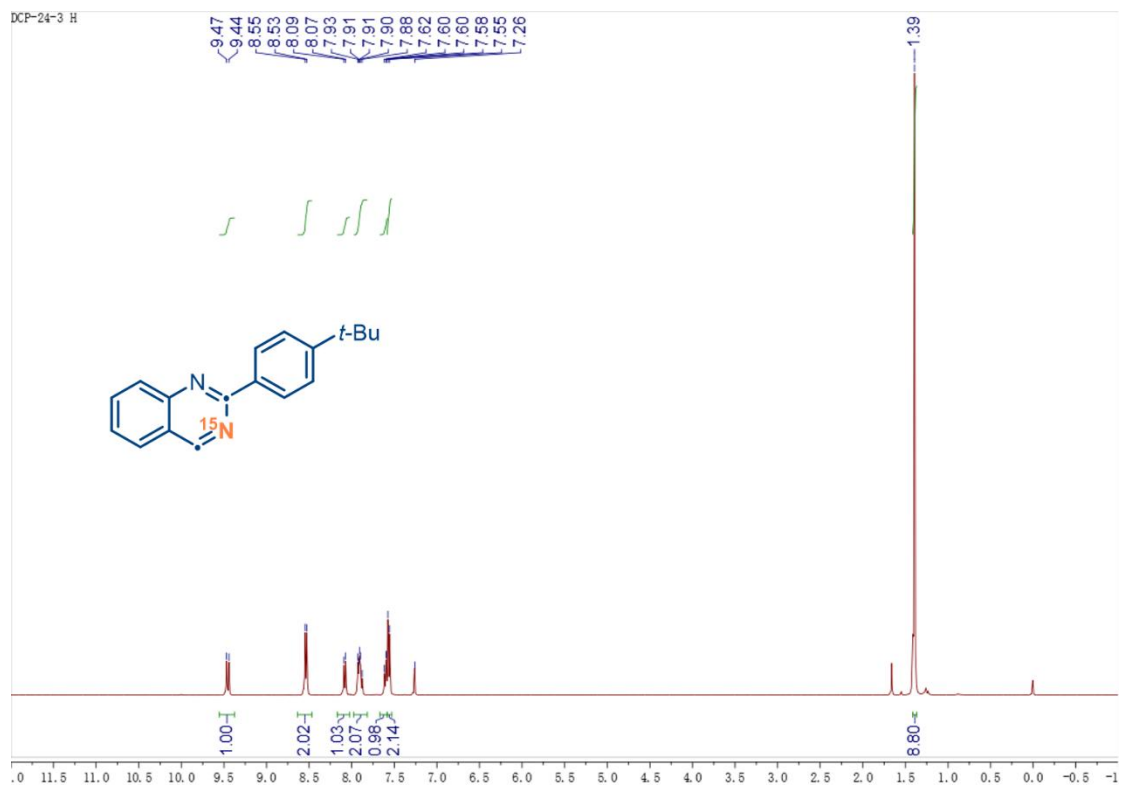
¹³C NMR spectrum of **10** (100 MHz, CDCl₃)



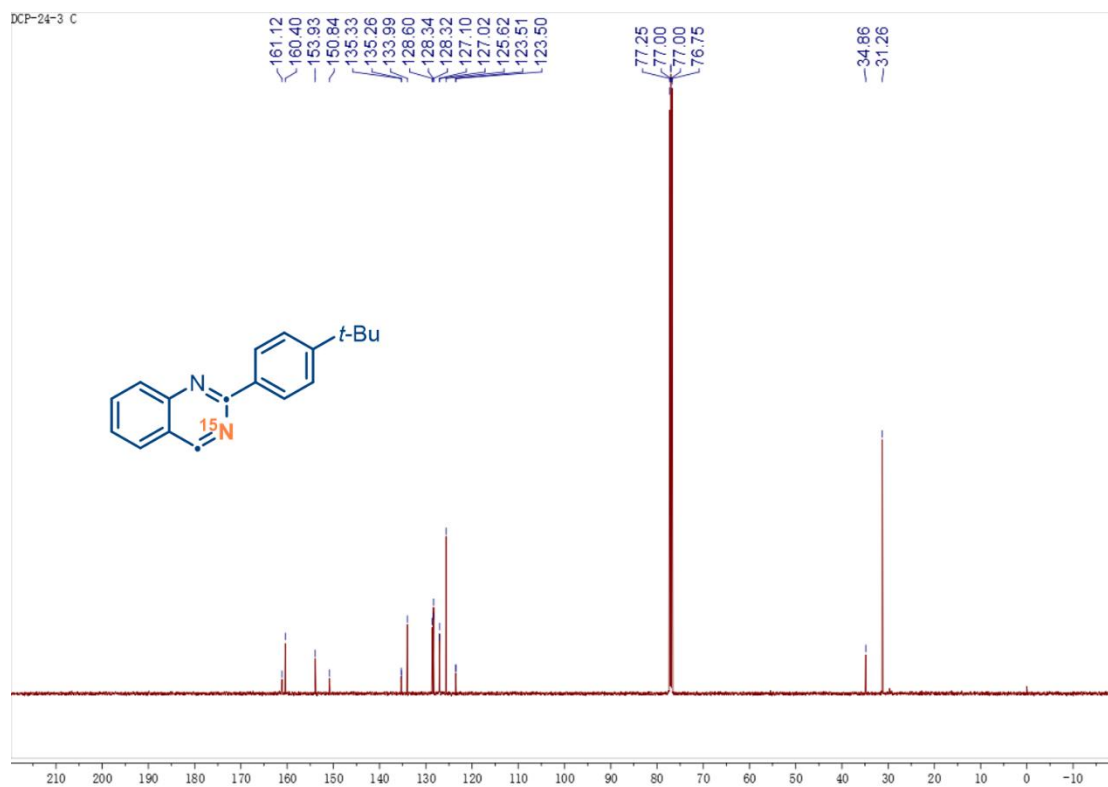
^{15}N NMR spectrum of **10** (50 MHz, CDCl_3)



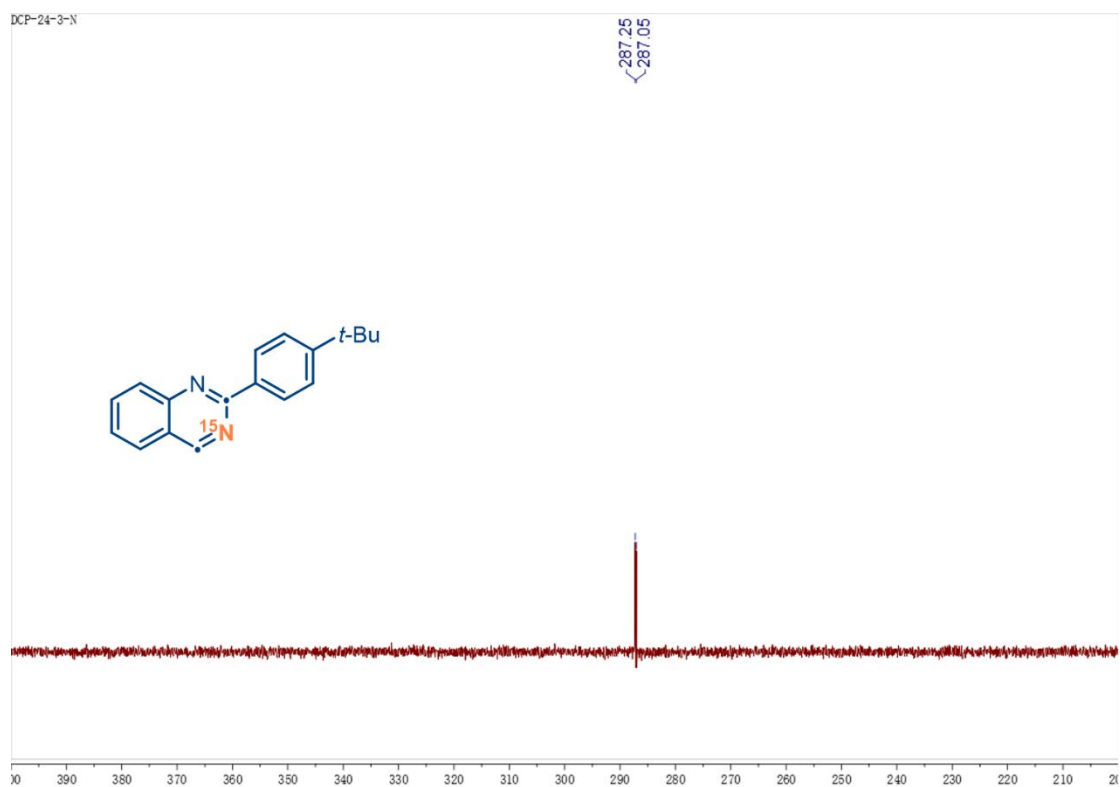
^1H NMR spectrum of **11** (400 MHz, CDCl_3)



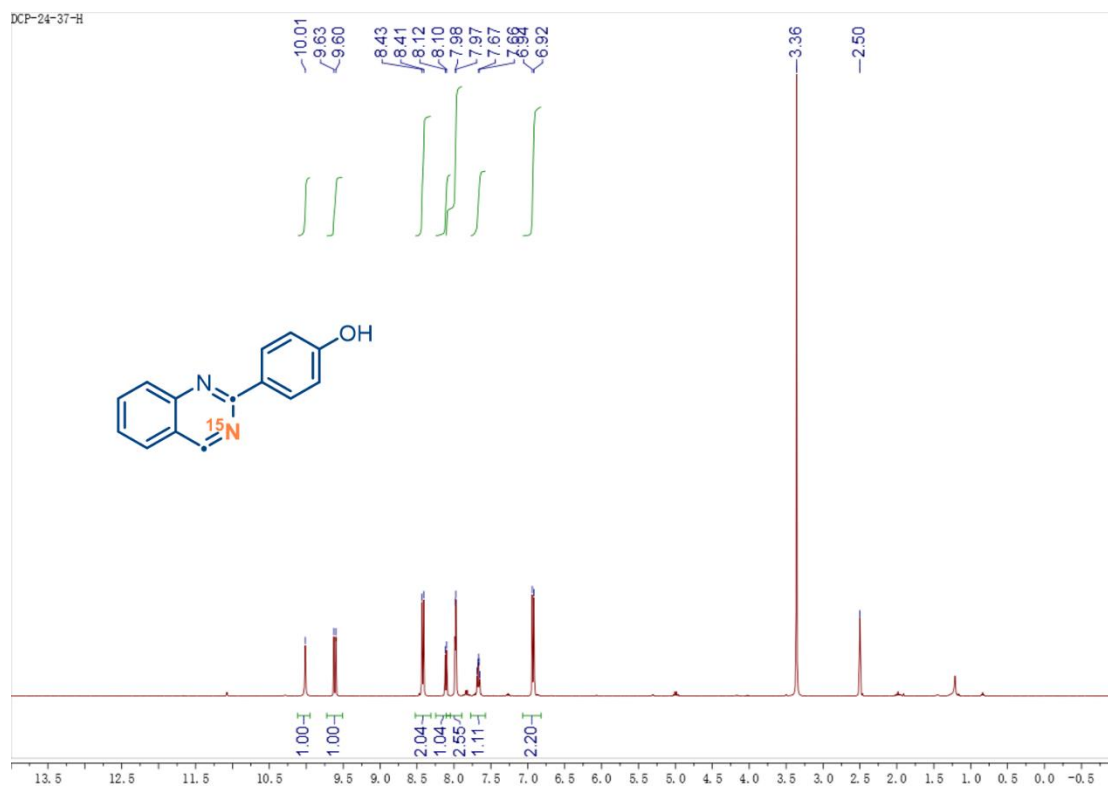
^{13}C NMR spectrum of **11** (125 MHz, CDCl_3)



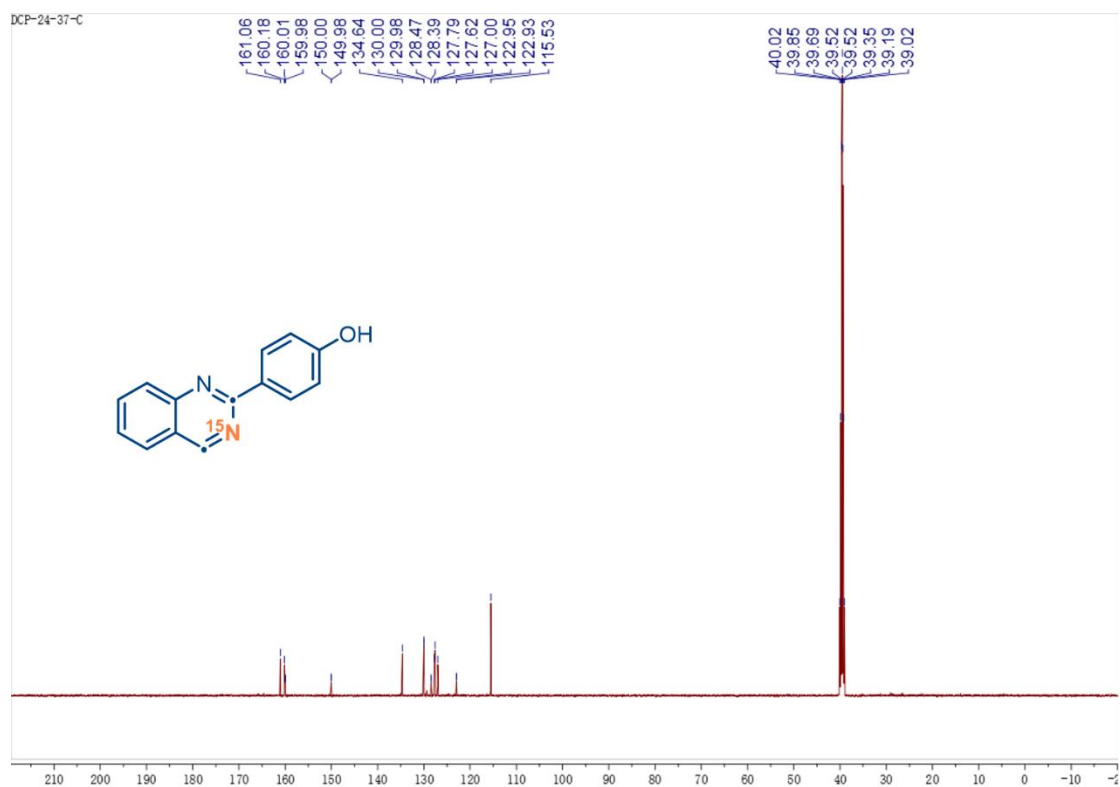
^{15}N NMR spectrum of **11** (50 MHz, CDCl_3)



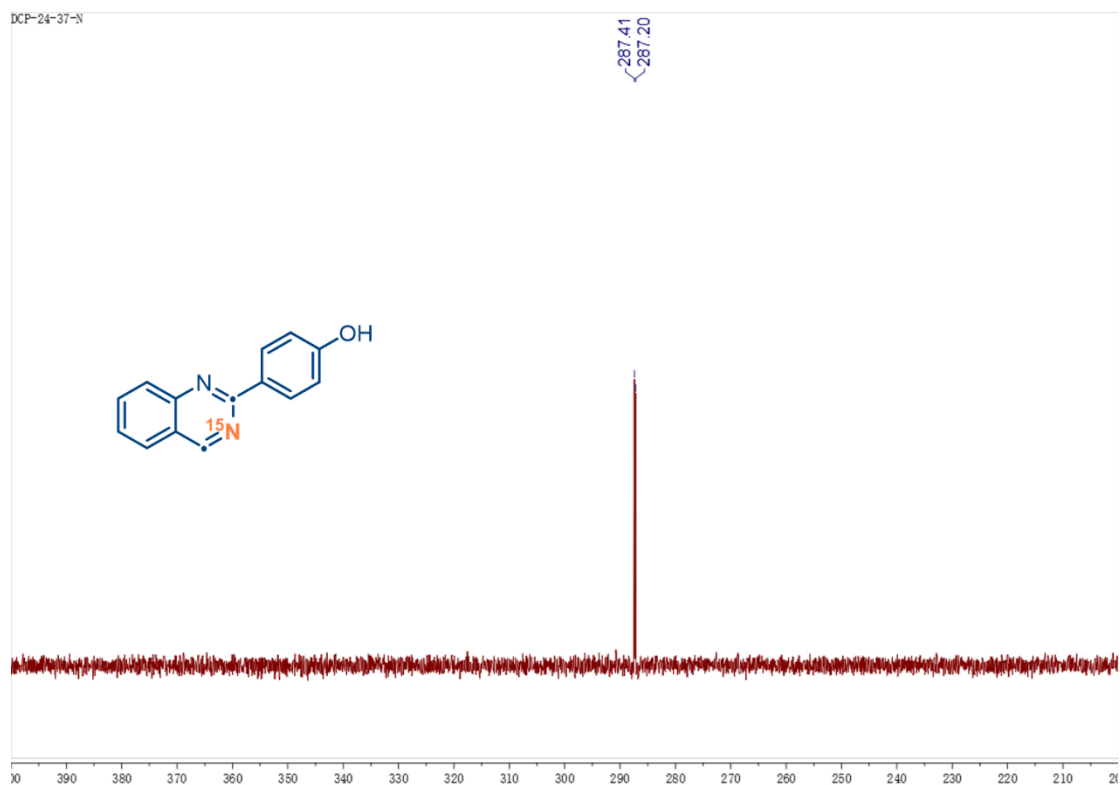
¹H NMR spectrum of **12** (400 MHz, DMSO-*d*₆)



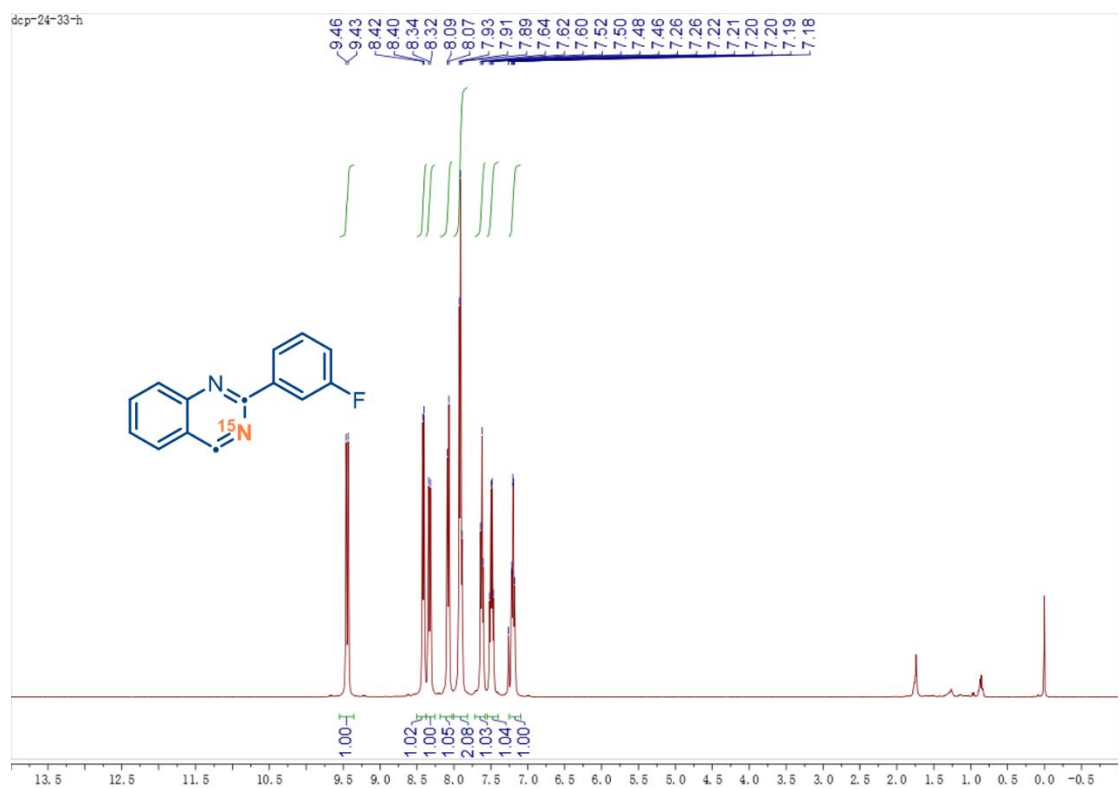
¹³C NMR spectrum of **12** (125 MHz, DMSO-*d*₆)



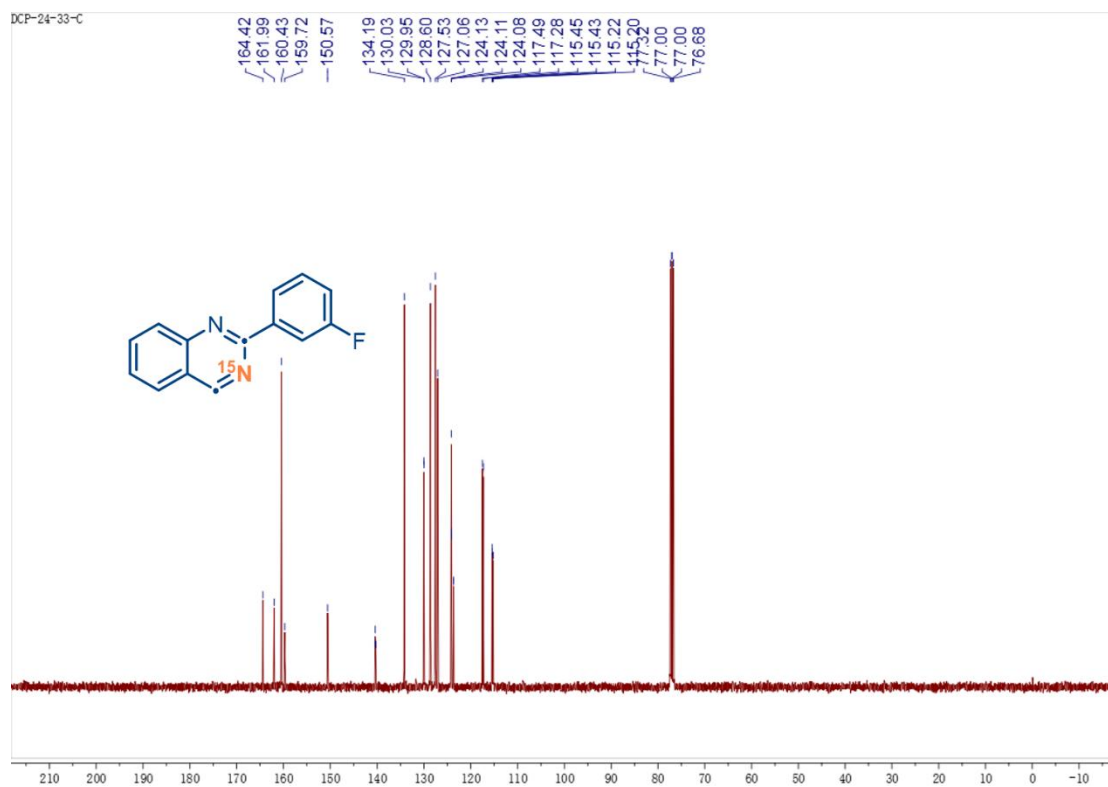
^{15}N NMR spectrum of **12** (50 MHz, $\text{DMSO}-d_6$)



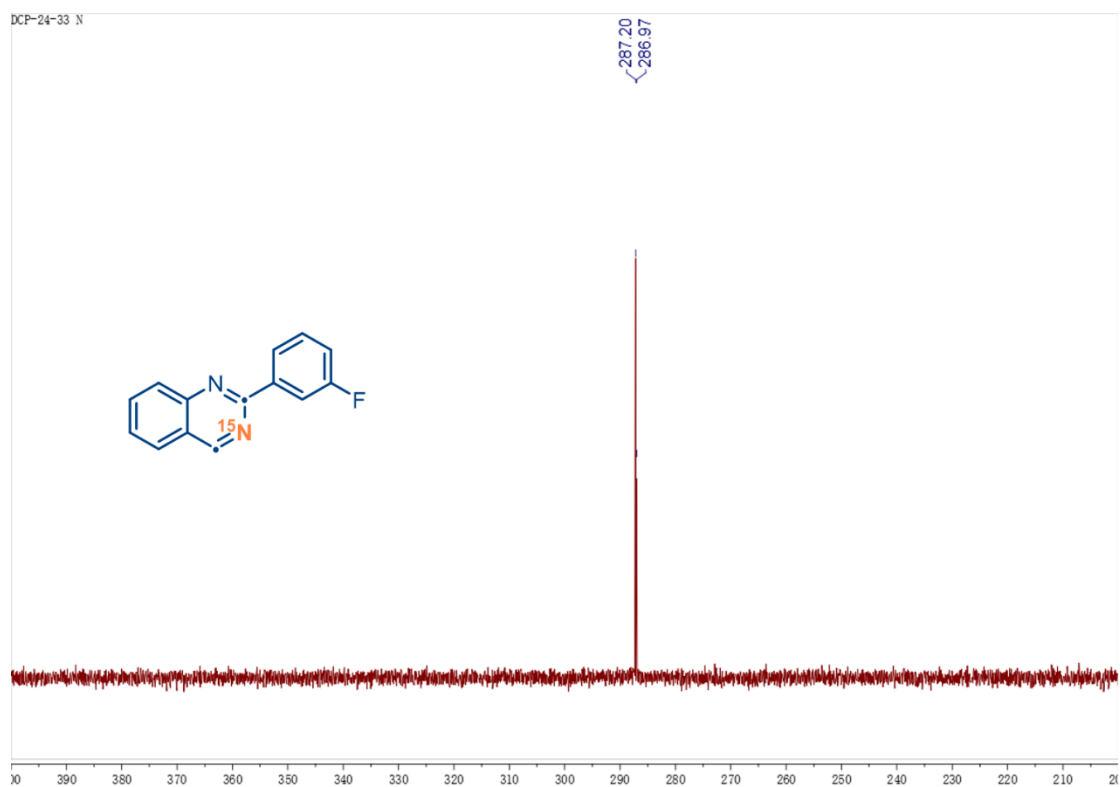
^1H NMR spectrum of **13** (400 MHz, CDCl_3)



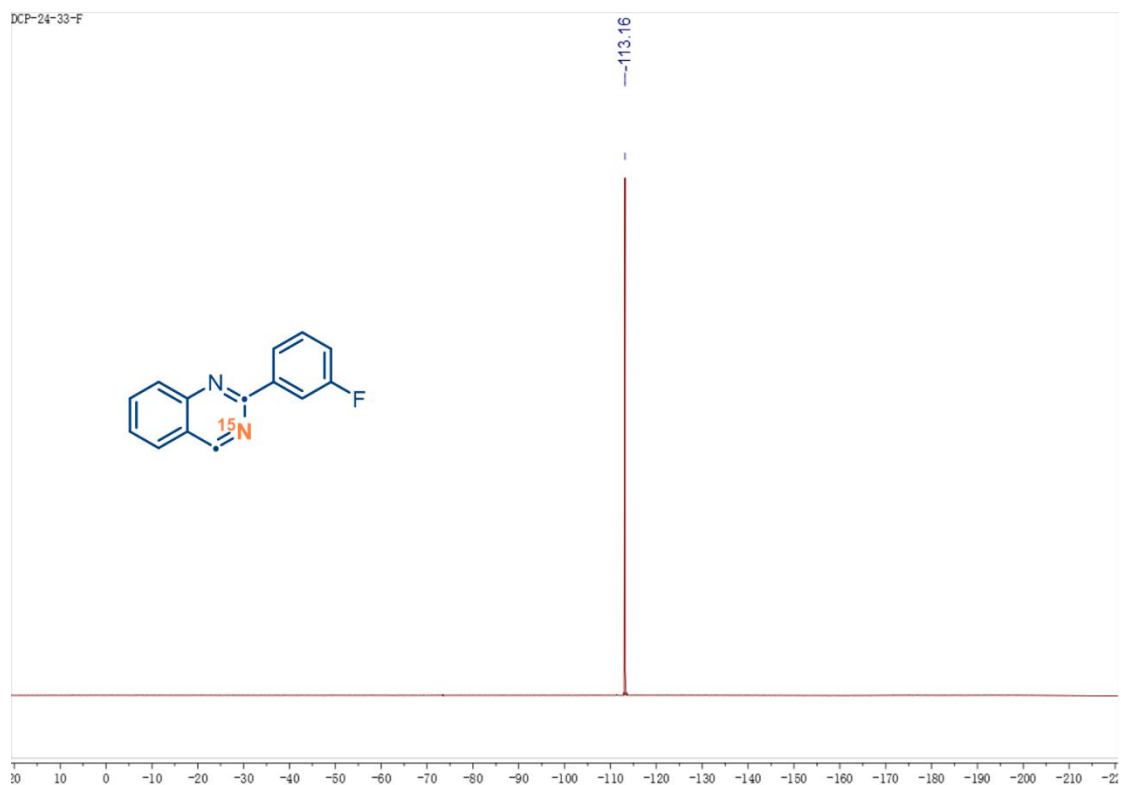
^{13}C NMR spectrum of **13** (100 MHz, CDCl_3)



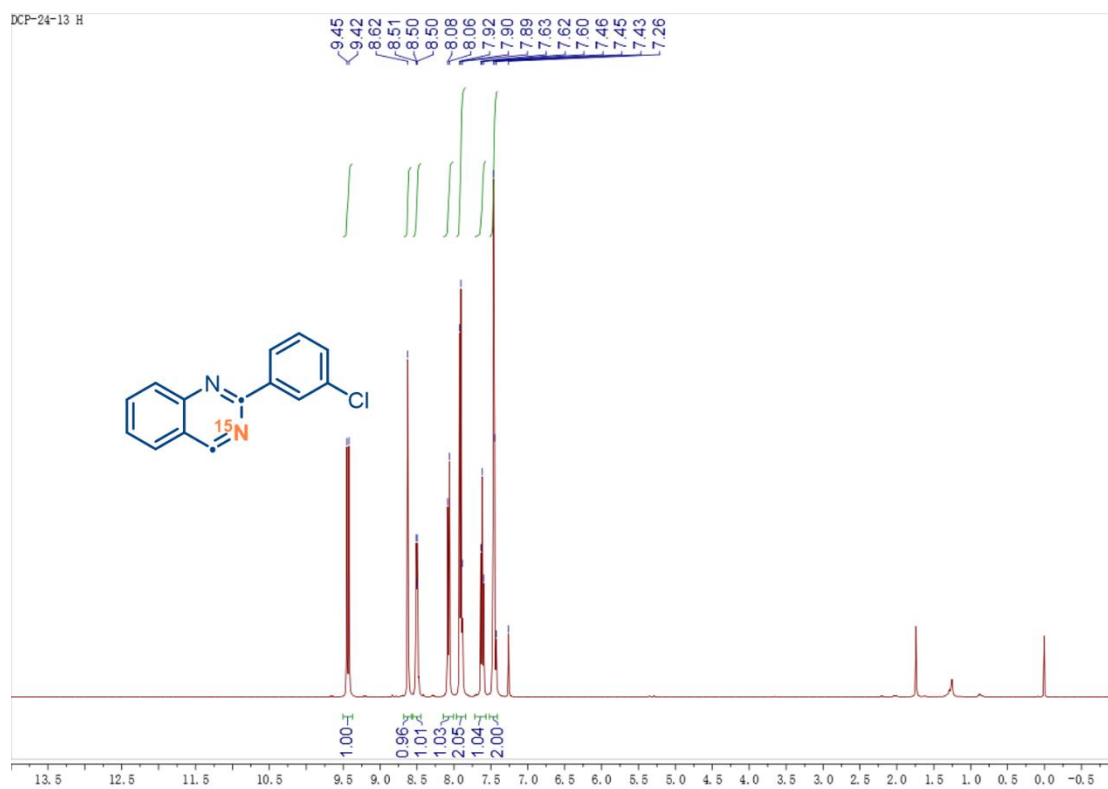
^{15}N NMR spectrum of **13** (50 MHz, CDCl_3)



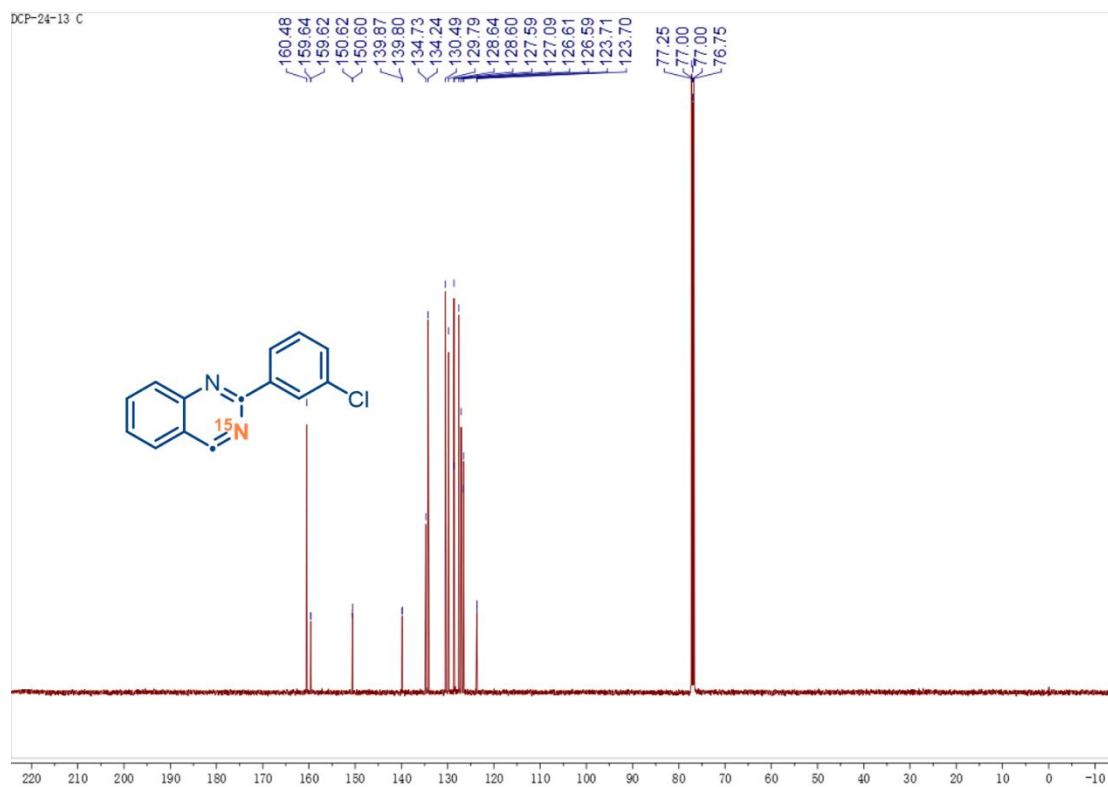
^{19}F NMR spectrum of **13** (376 MHz, CDCl_3)



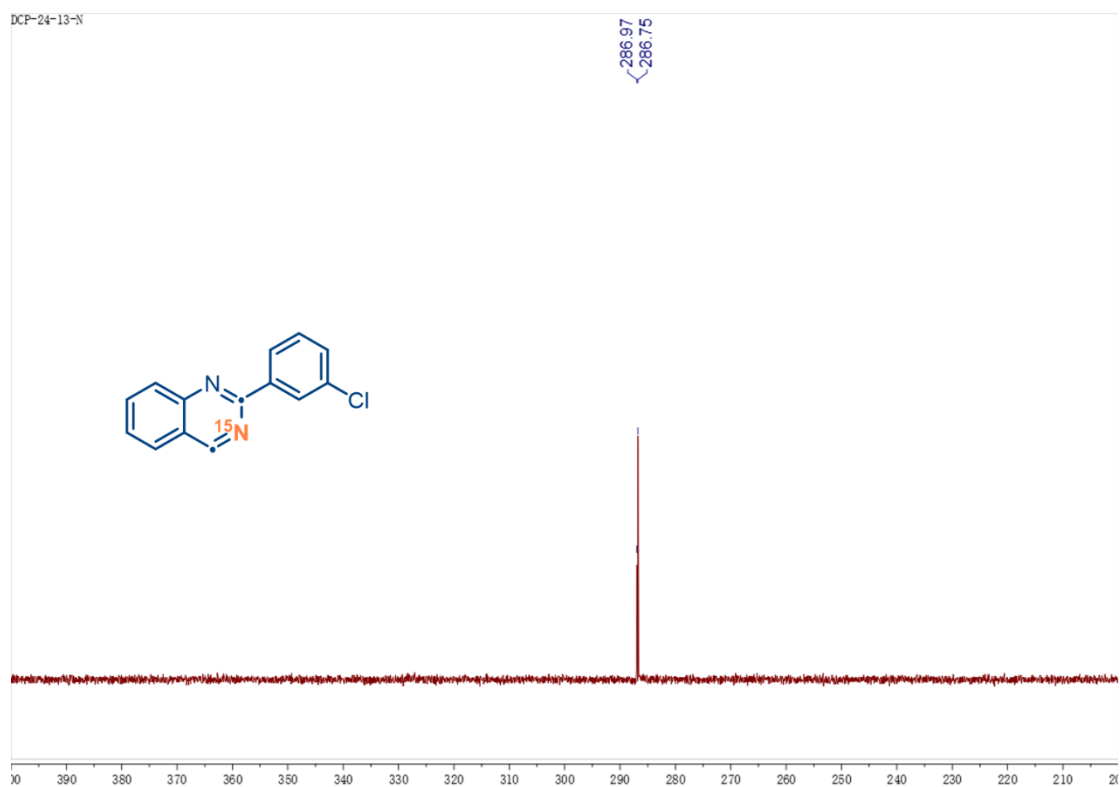
^1H NMR spectrum of **14** (400 MHz, CDCl_3)



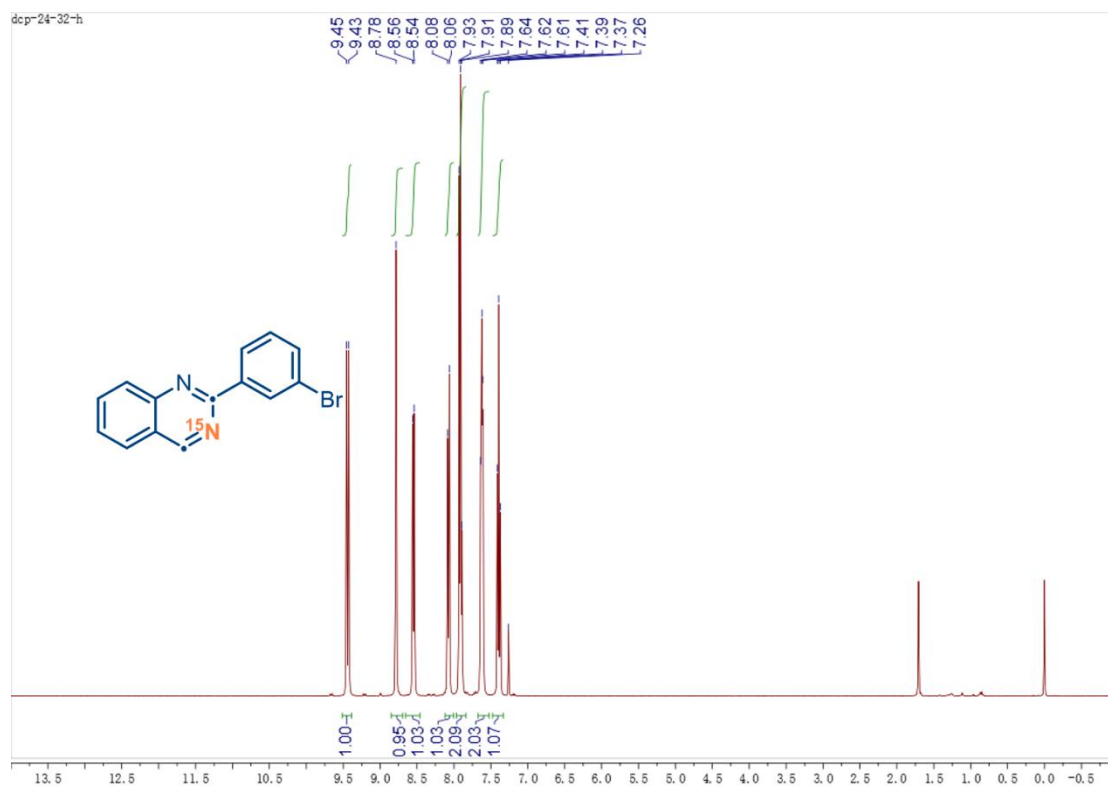
^{13}C NMR spectrum of **14** (125 MHz, CDCl_3)



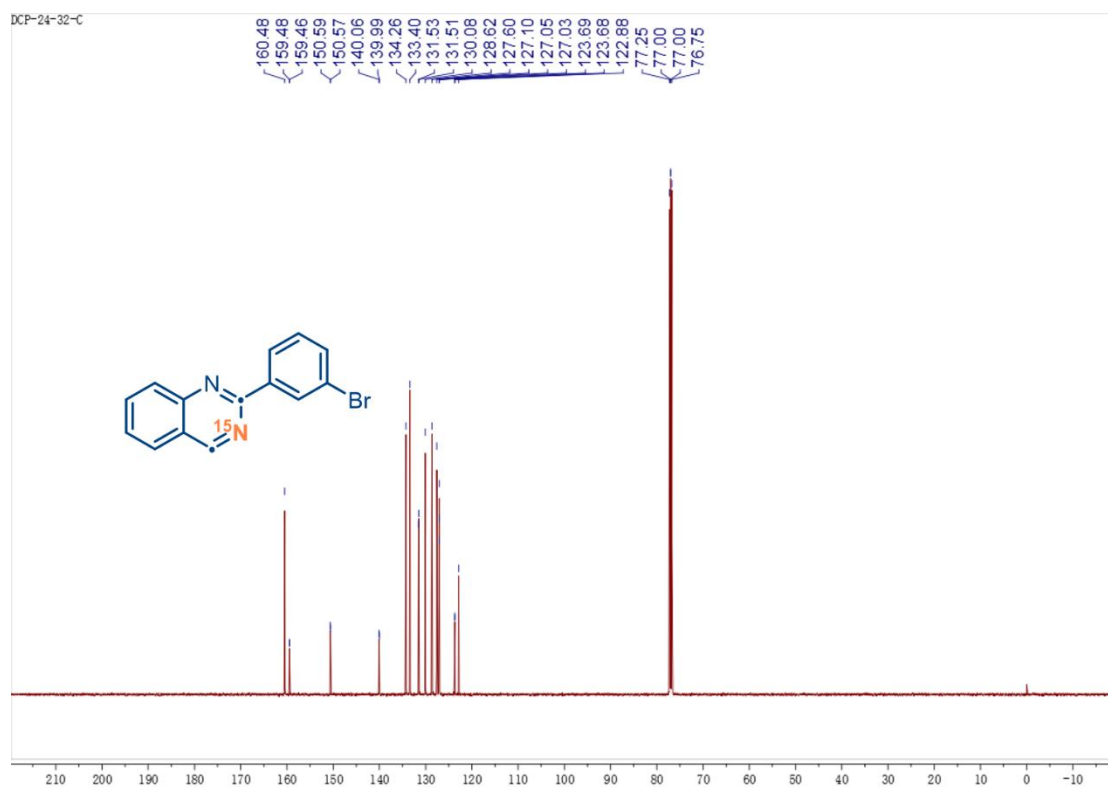
^{15}N NMR spectrum of **14** (50 MHz, CDCl_3)



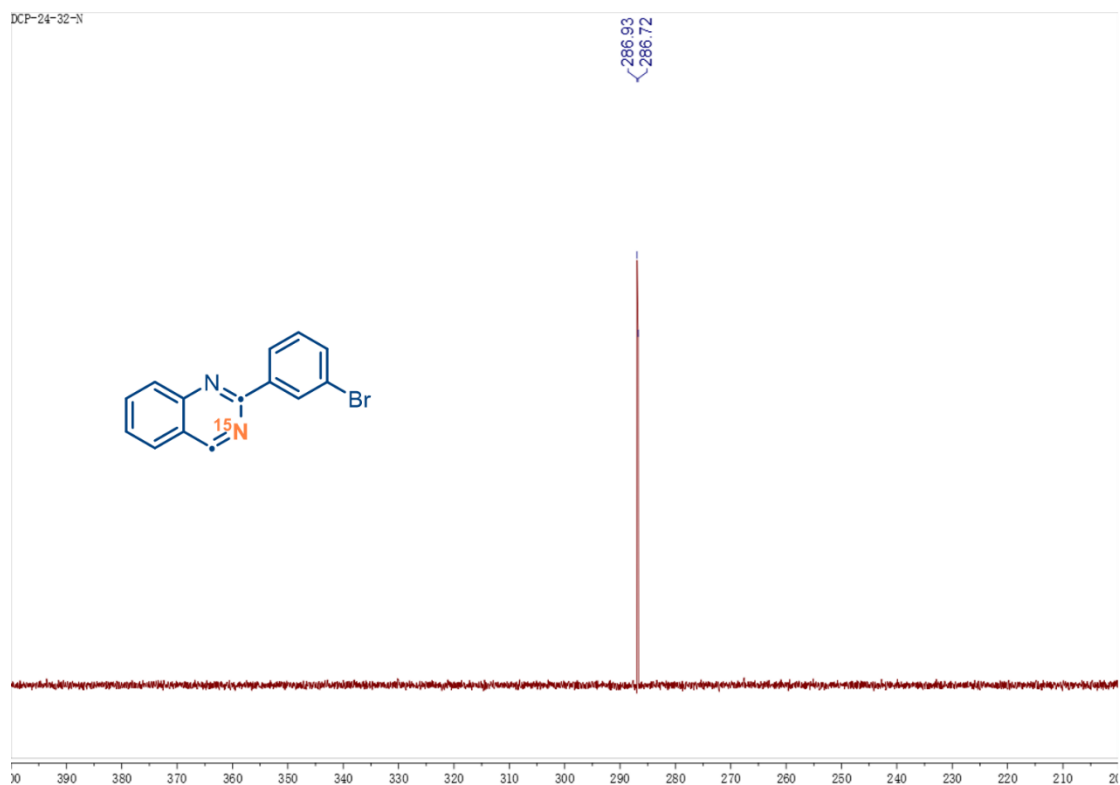
¹H NMR spectrum of **15** (400 MHz, CDCl₃)



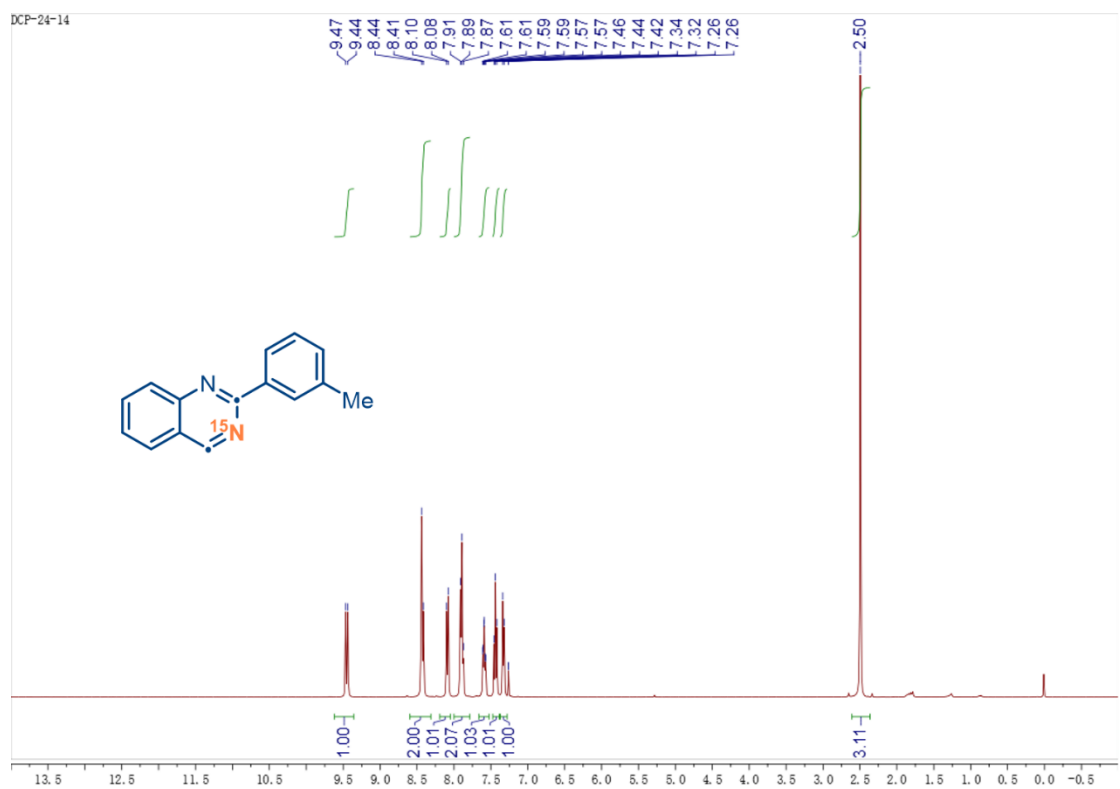
¹³C NMR spectrum of **15** (125 MHz, CDCl₃)



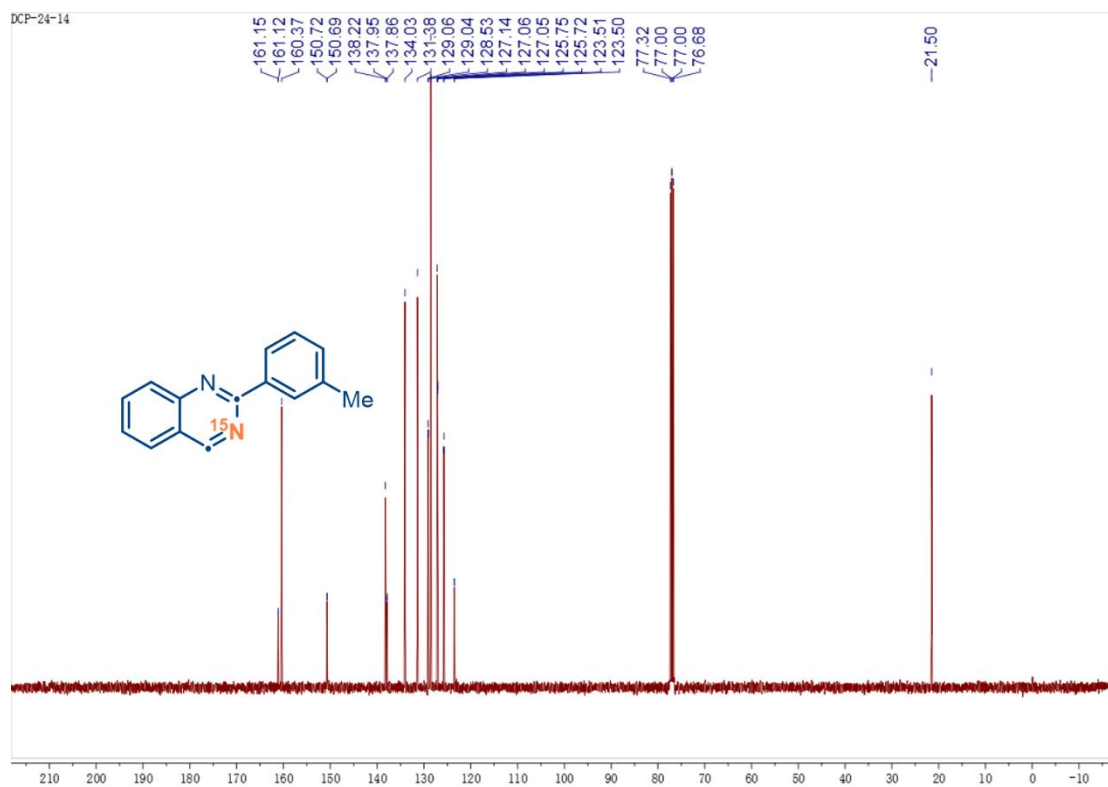
^{15}N NMR spectrum of **15** (50 MHz, CDCl_3)



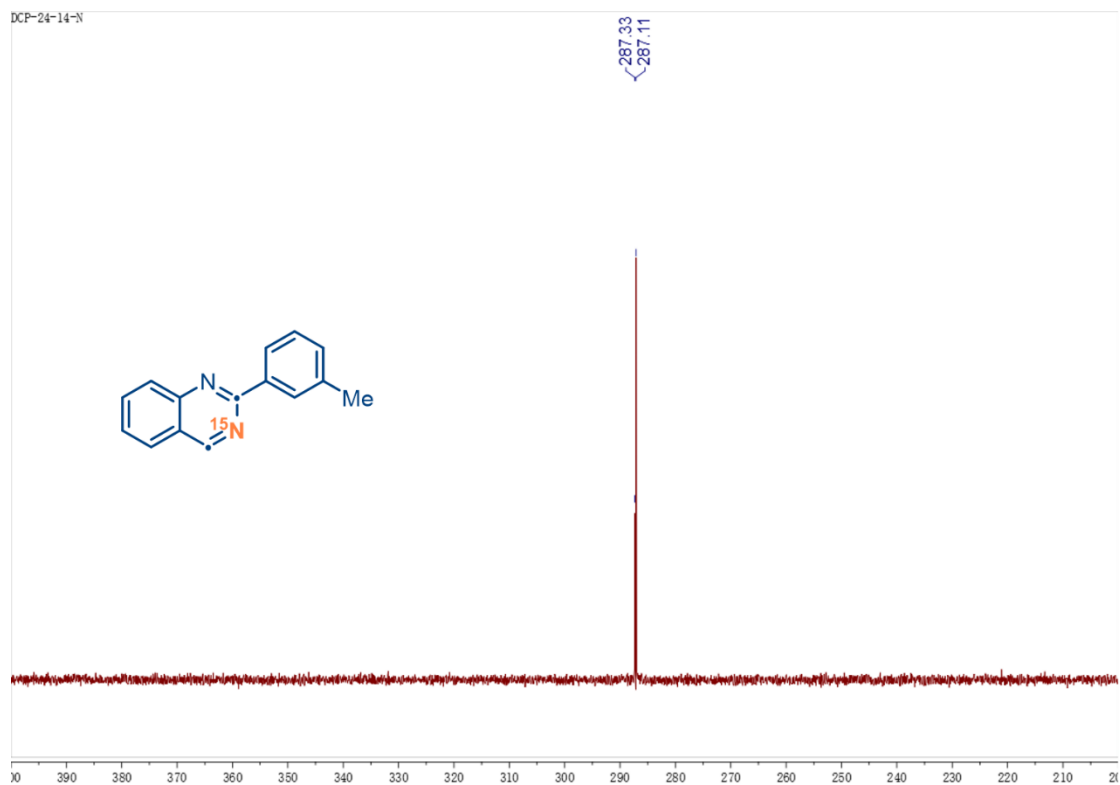
^1H NMR spectrum of **16** (400 MHz, CDCl_3)



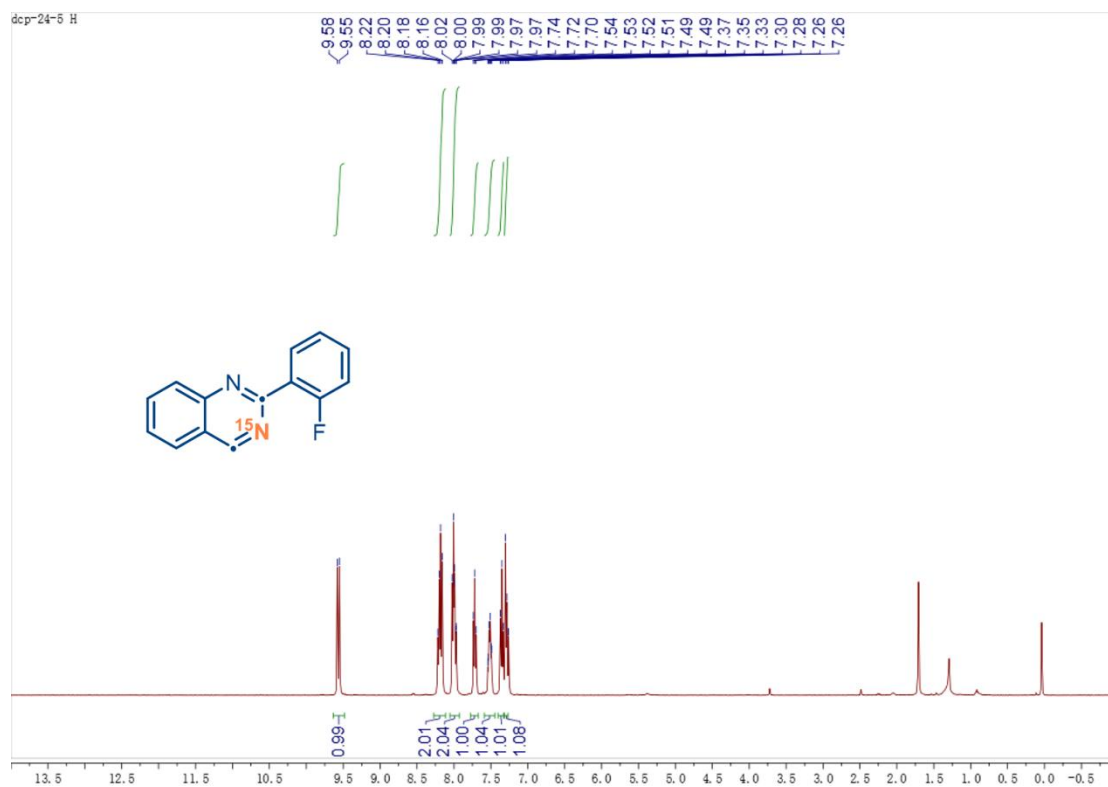
^{13}C NMR spectrum of **16** (100 MHz, CDCl_3)



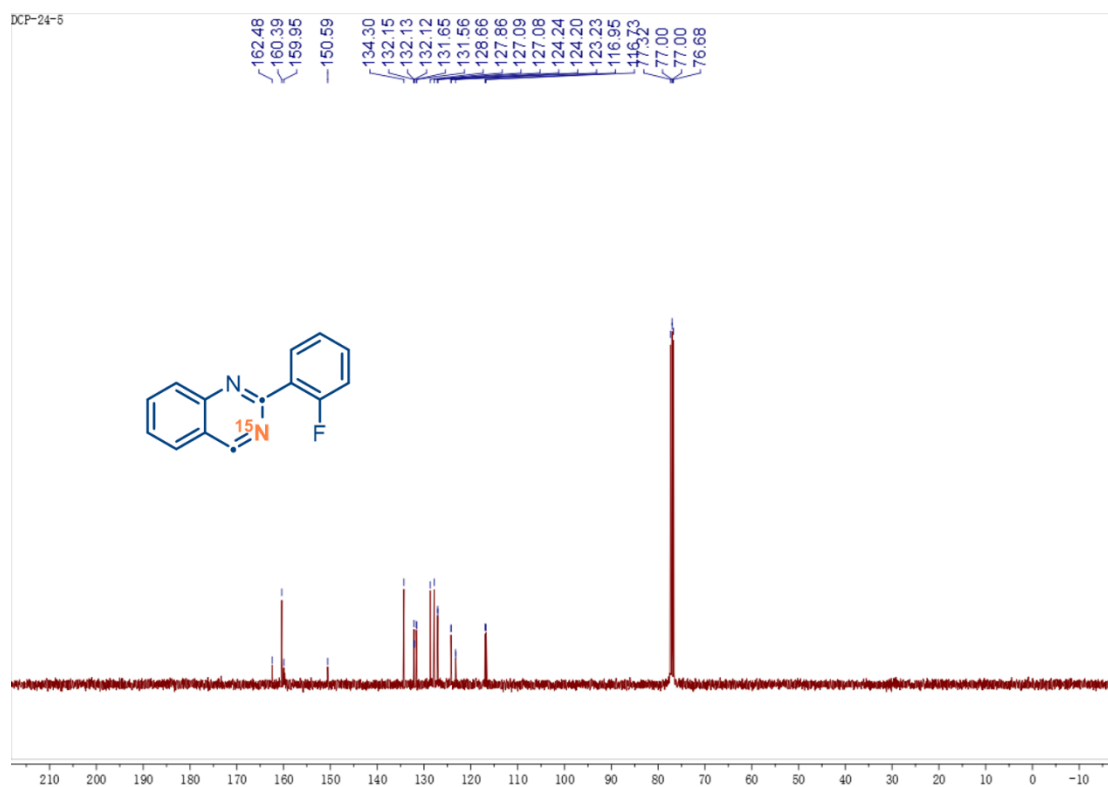
^{15}N NMR spectrum of **16** (50 MHz, CDCl_3)



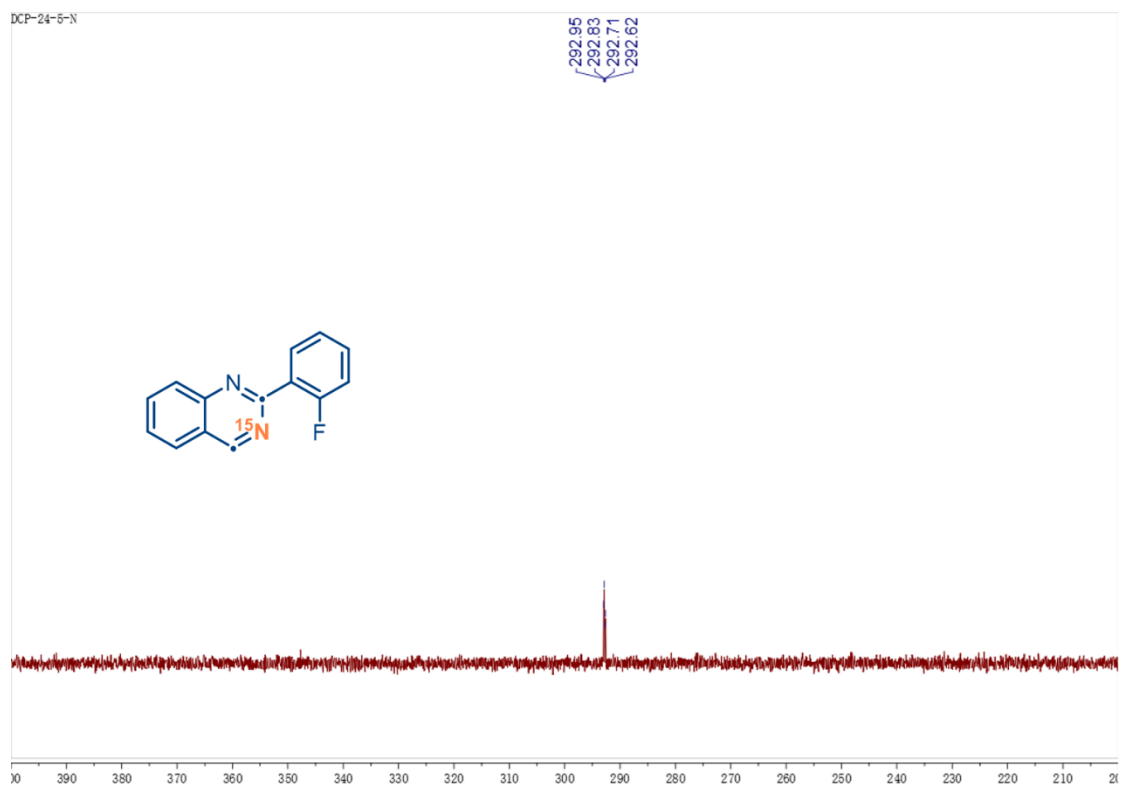
¹H NMR spectrum of **17** (400 MHz, CDCl₃)



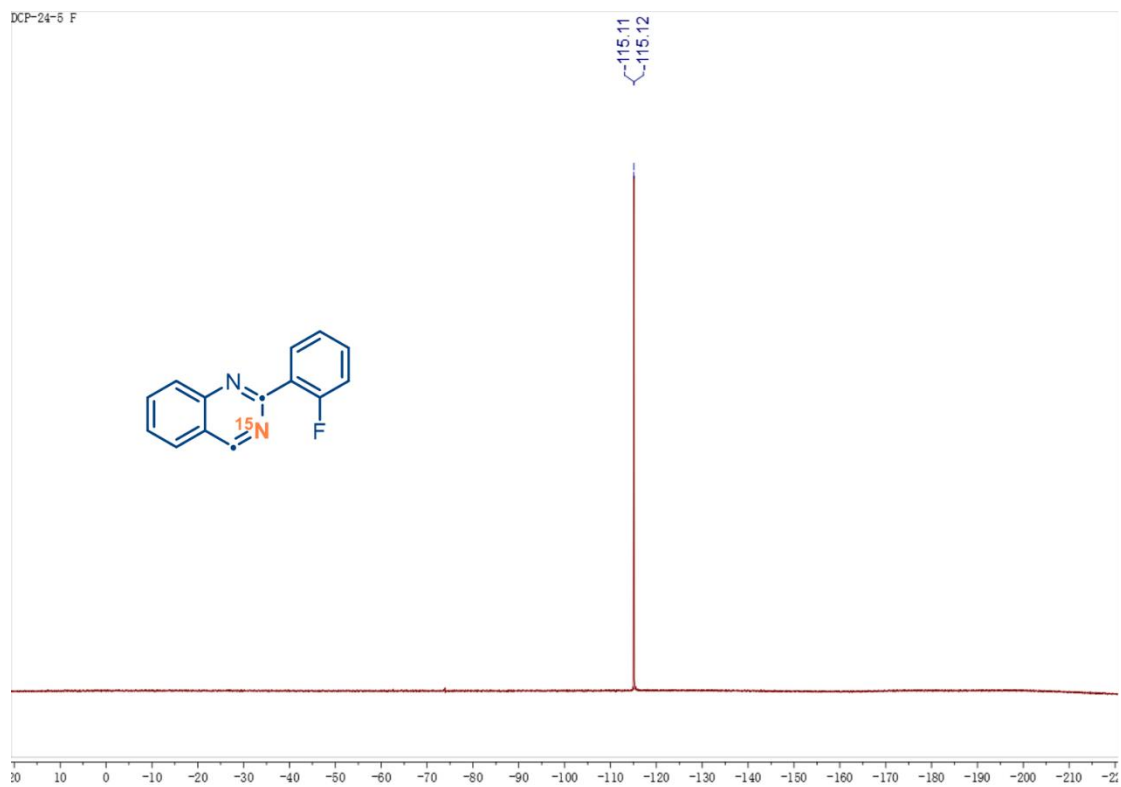
¹³C NMR spectrum of **17** (100 MHz, CDCl₃)



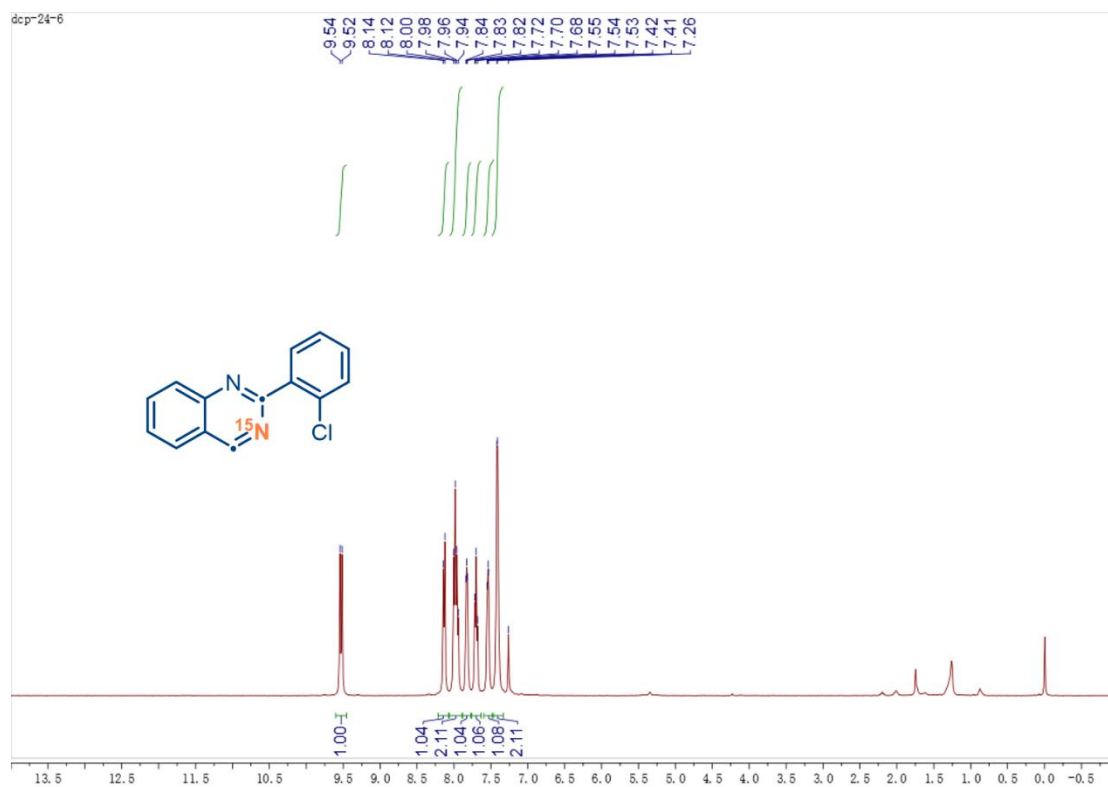
^{15}N NMR spectrum of **17** (50 MHz, CDCl_3)



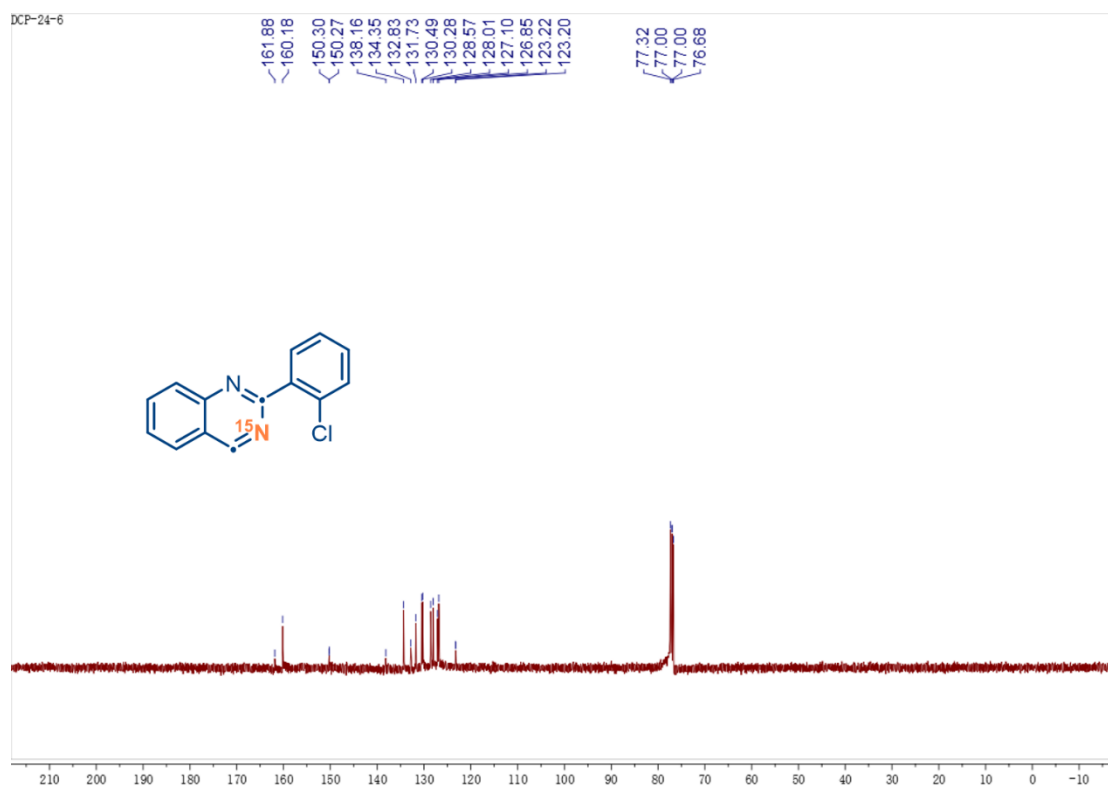
^{19}F NMR spectrum of **17** (376 MHz, CDCl_3)



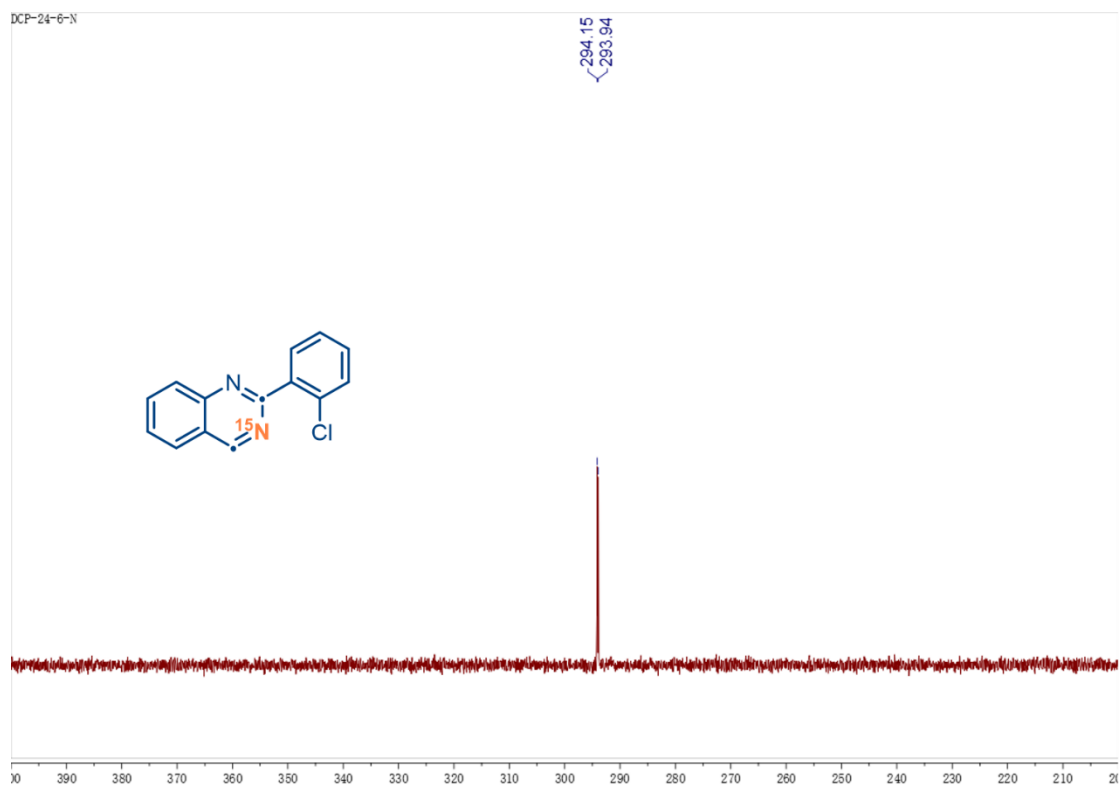
^1H NMR spectrum of **18** (400 MHz, CDCl_3)



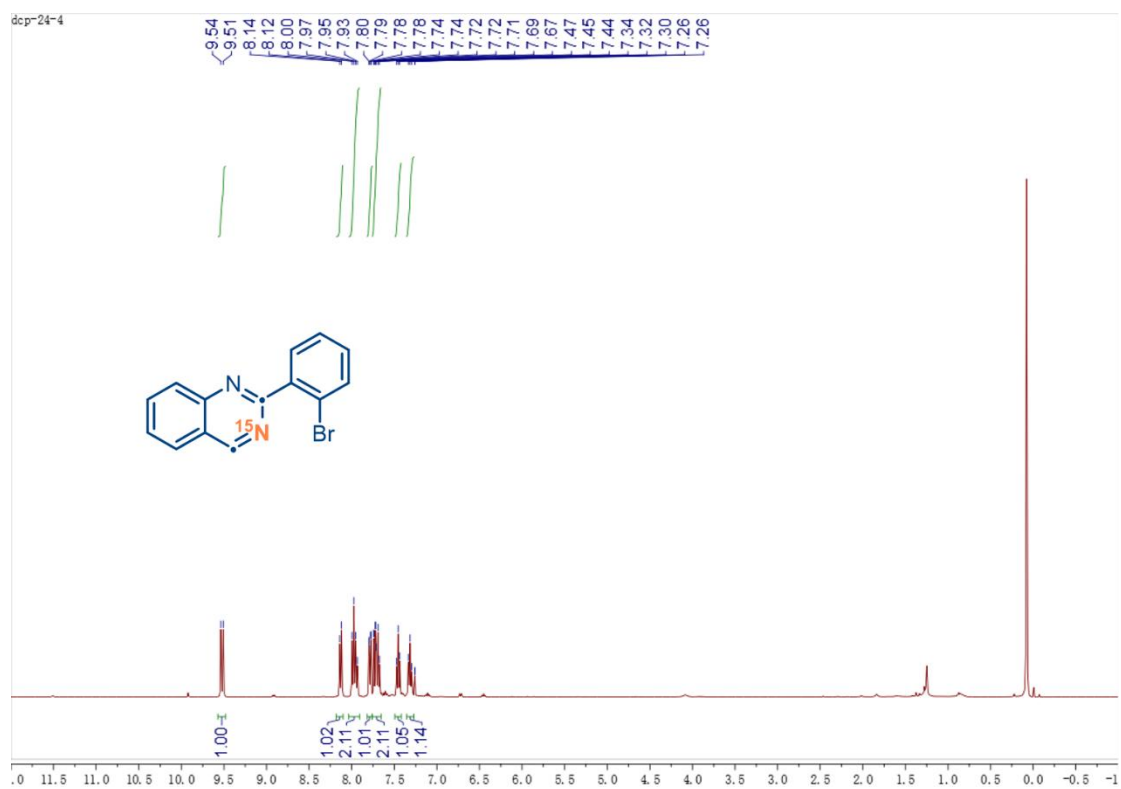
^{13}C NMR spectrum of **18** (100 MHz, CDCl_3)



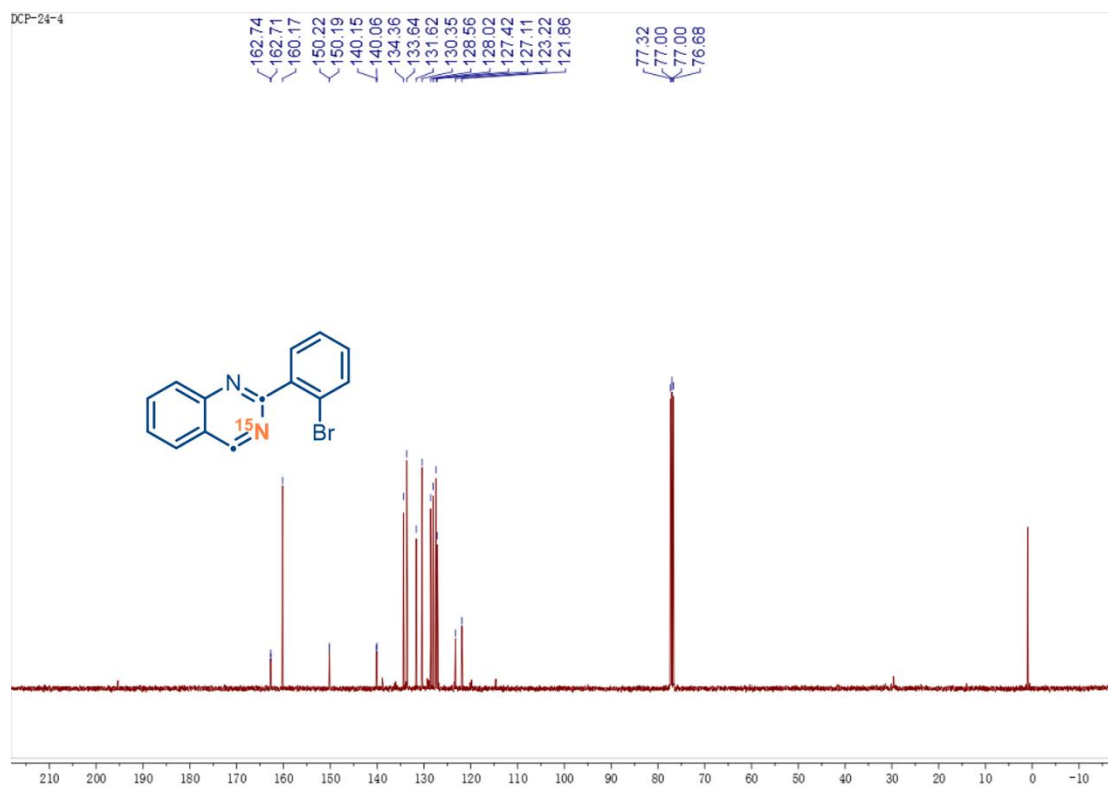
^{15}N NMR spectrum of **18** (50 MHz, CDCl_3)



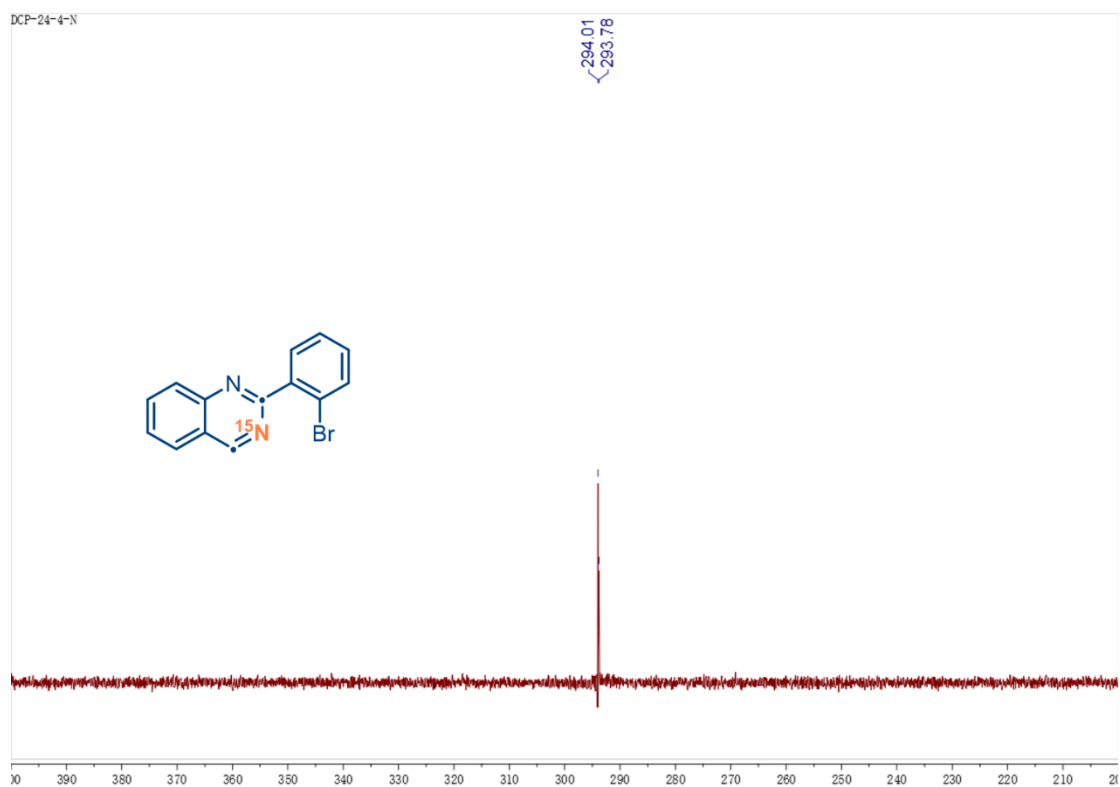
^1H NMR spectrum of **19** (400 MHz, CDCl_3)



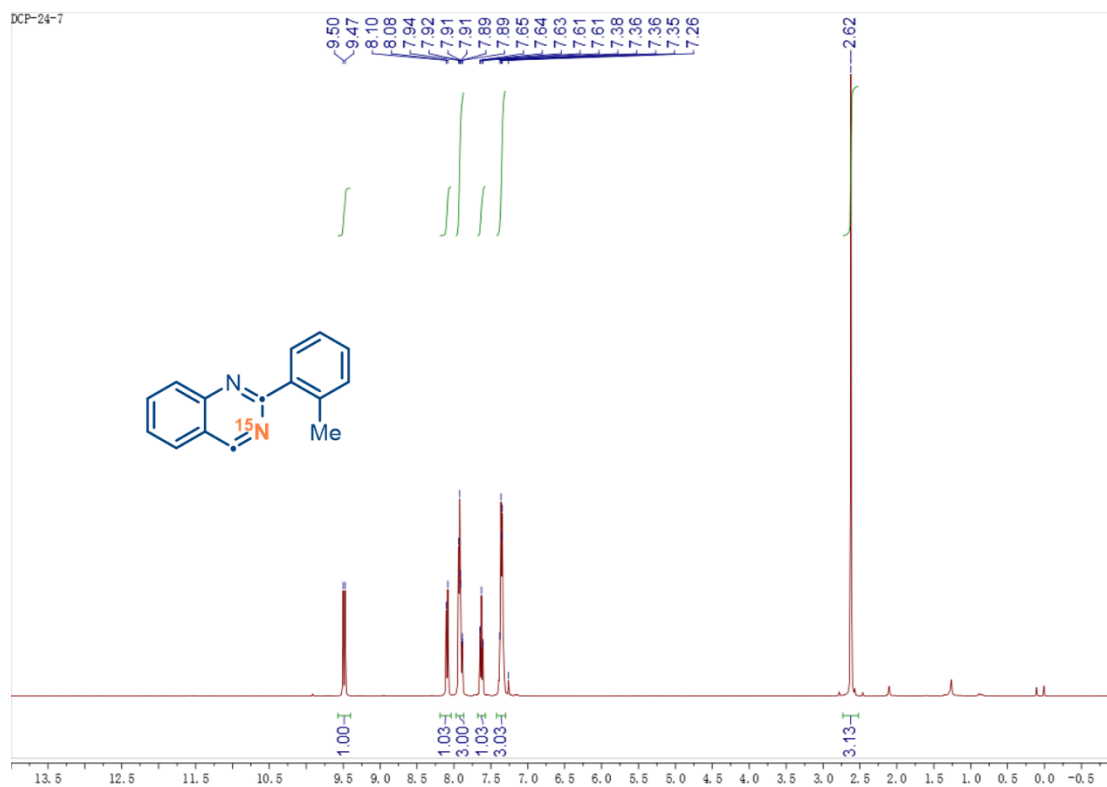
^{13}C NMR spectrum of **19** (100 MHz, CDCl_3)



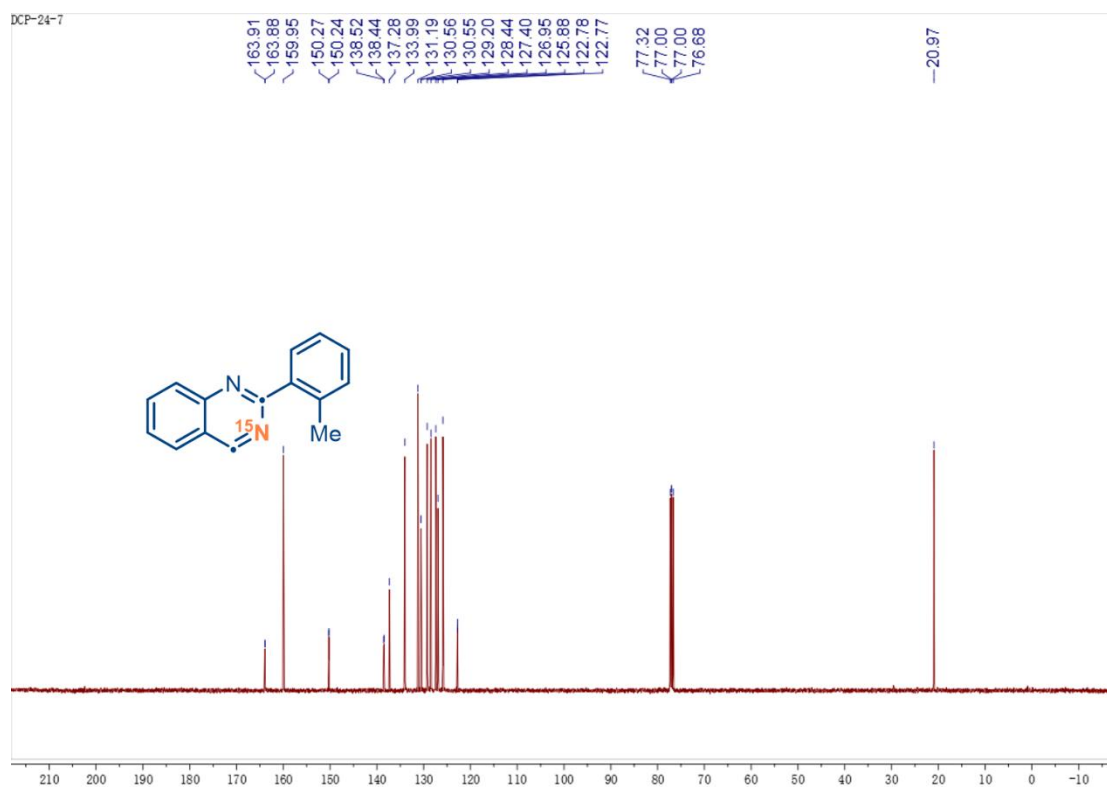
^{15}N NMR spectrum of **19** (50 MHz, CDCl_3)



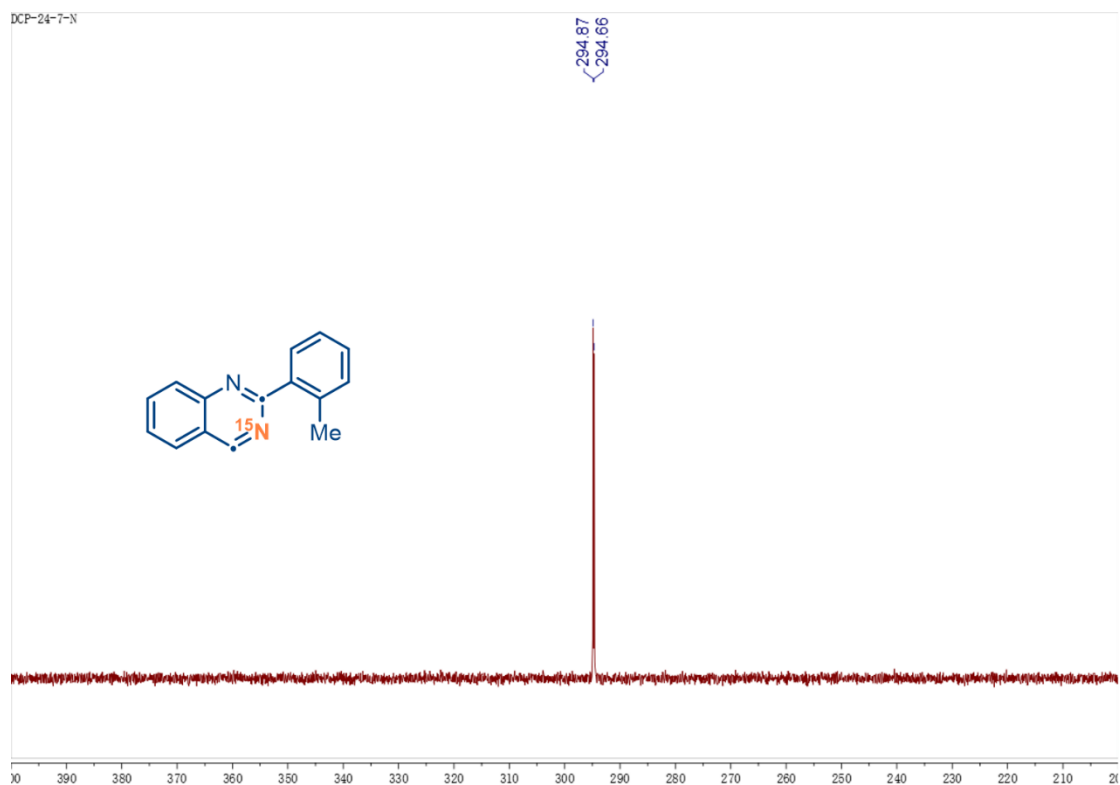
¹H NMR spectrum of **2o** (400 MHz, CDCl₃)



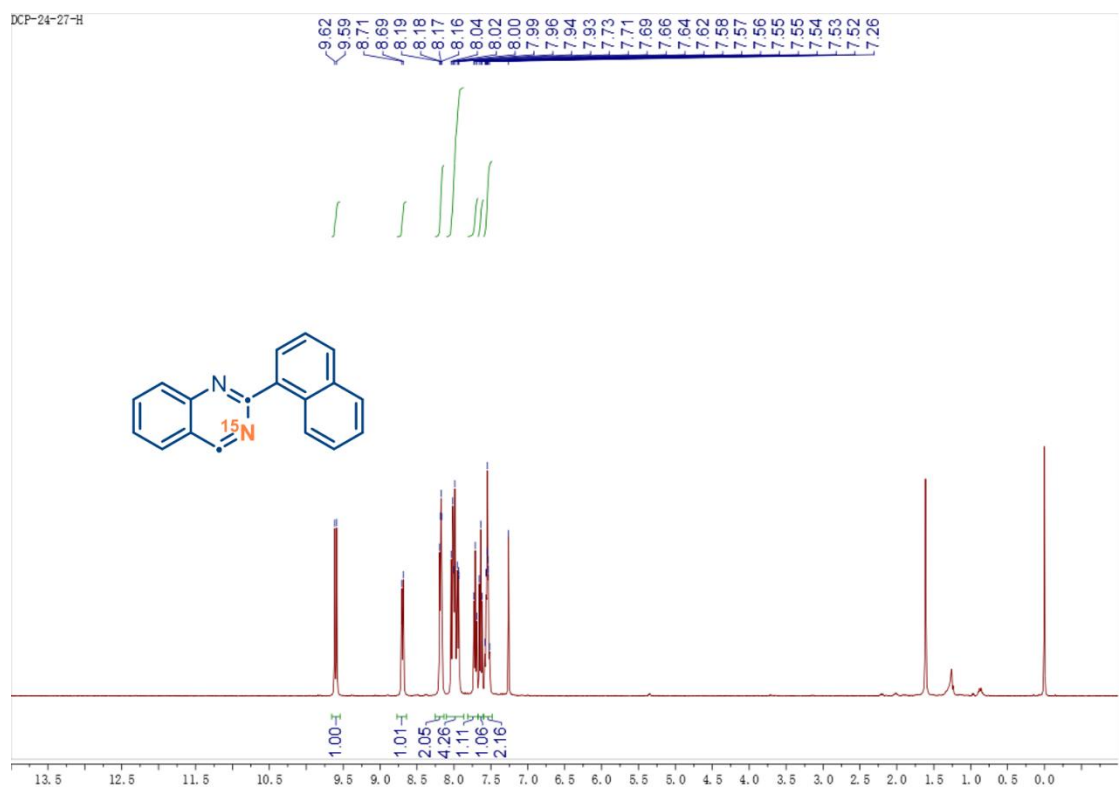
¹³C NMR spectrum of **2o** (100 MHz, CDCl₃)



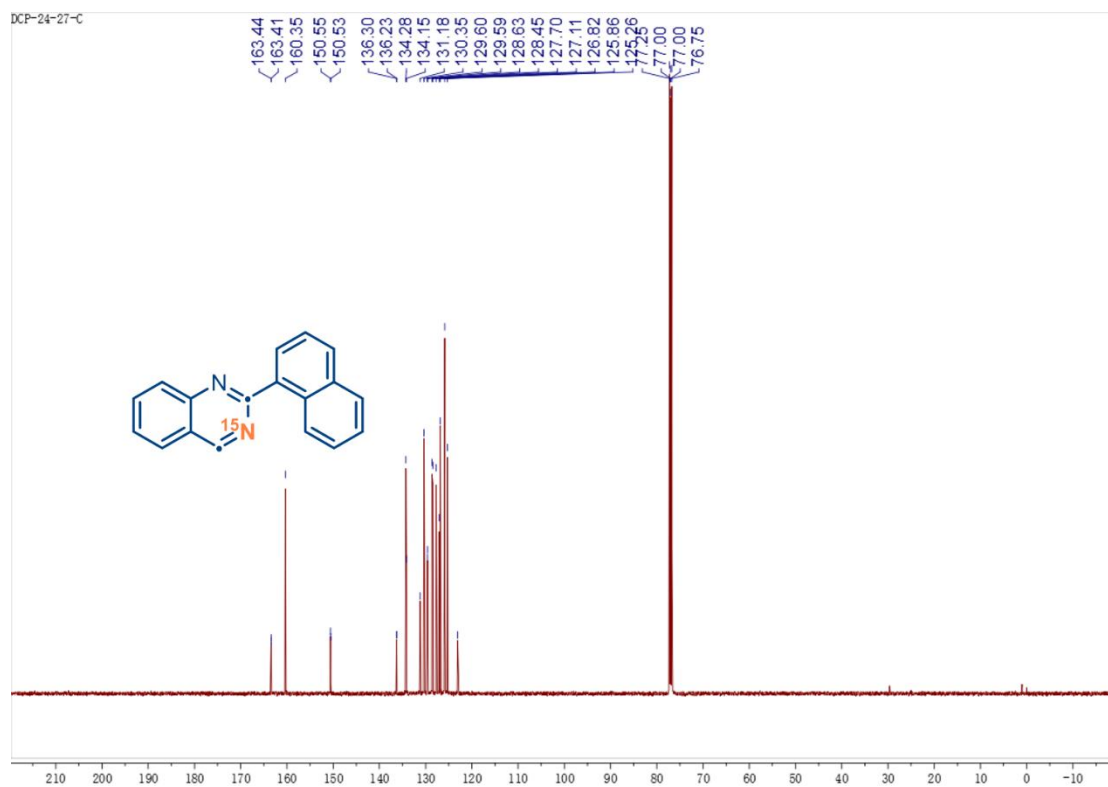
^{15}N NMR spectrum of **20** (50 MHz, CDCl_3)



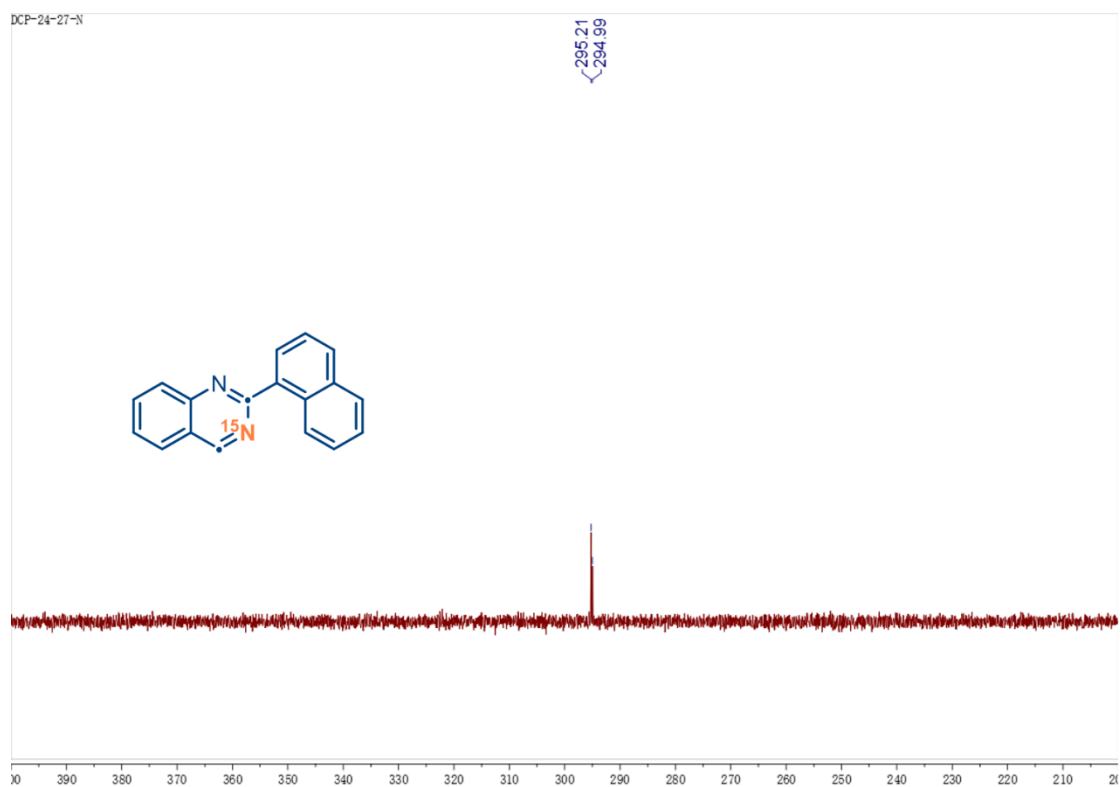
^1H NMR spectrum of **21** (400 MHz, CDCl_3)



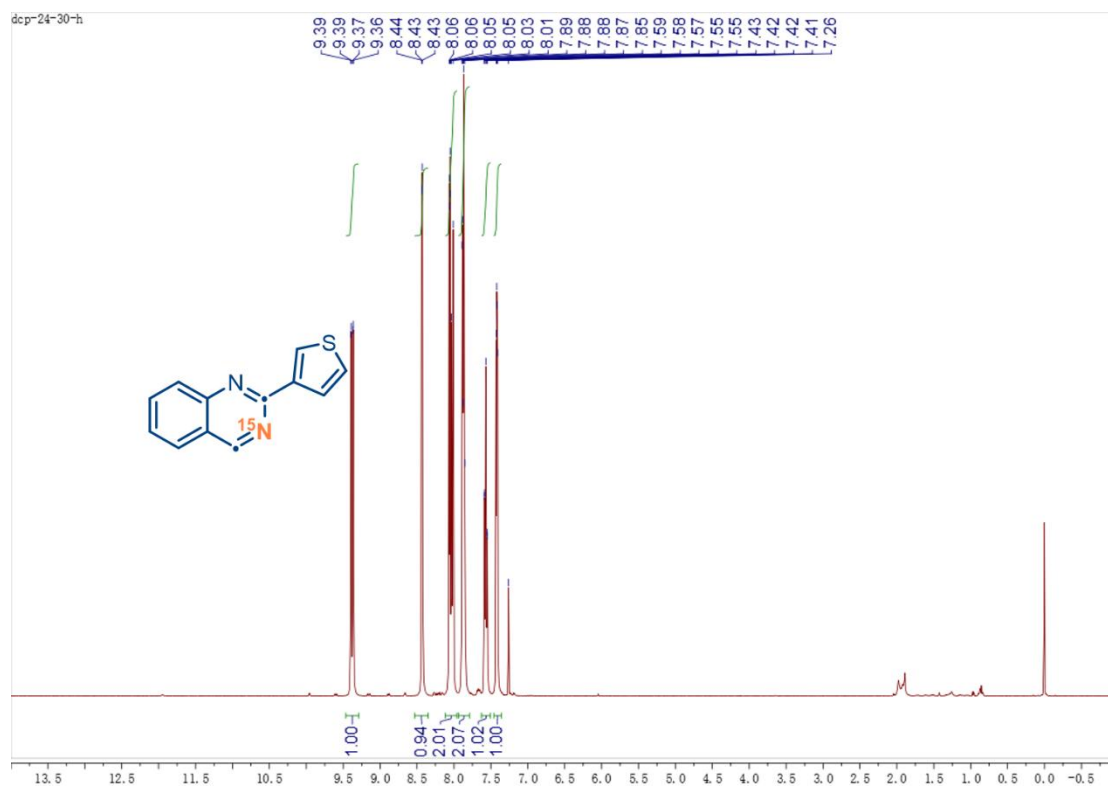
^{13}C NMR spectrum of **21** (125 MHz, CDCl_3)



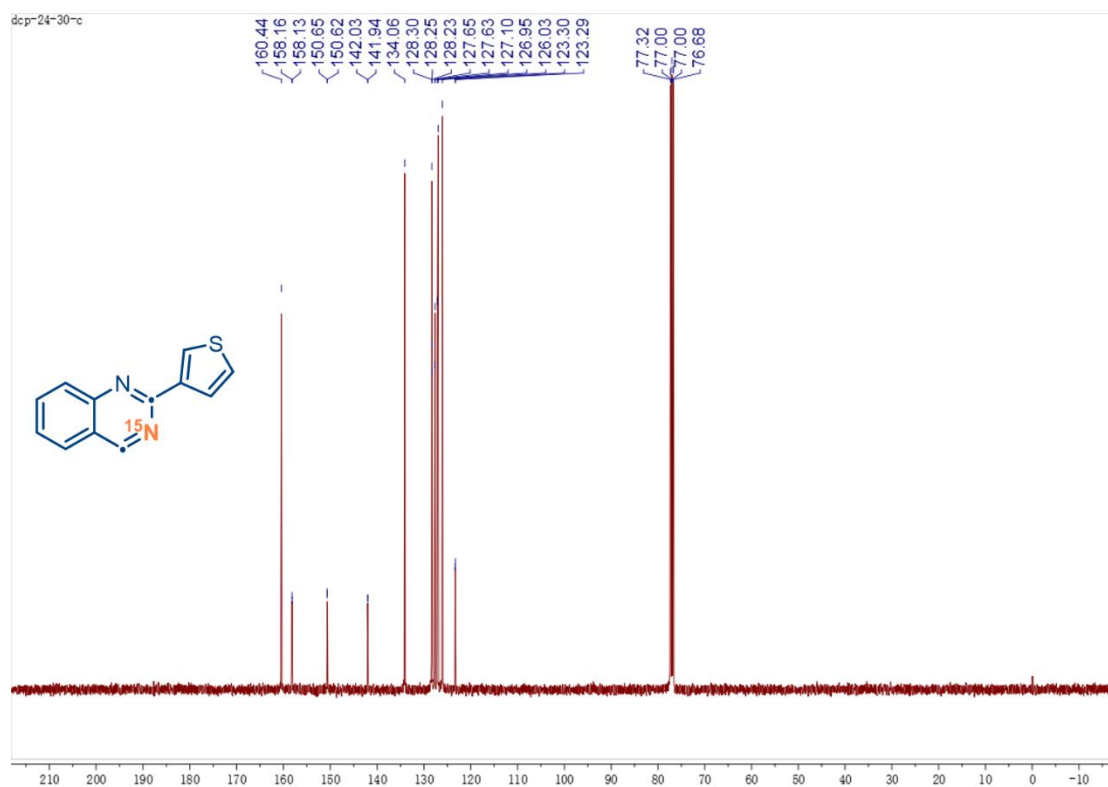
^{15}N NMR spectrum of **21** (50 MHz, CDCl_3)



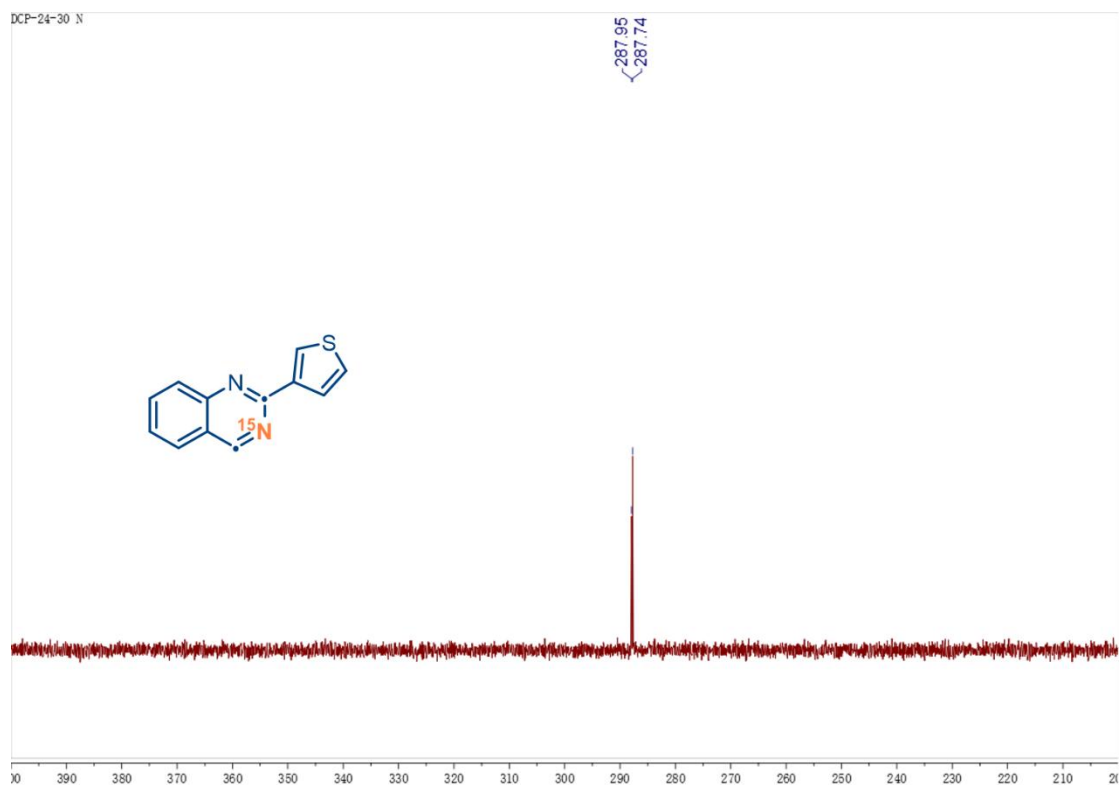
¹H NMR spectrum of **22** (400 MHz, CDCl₃)



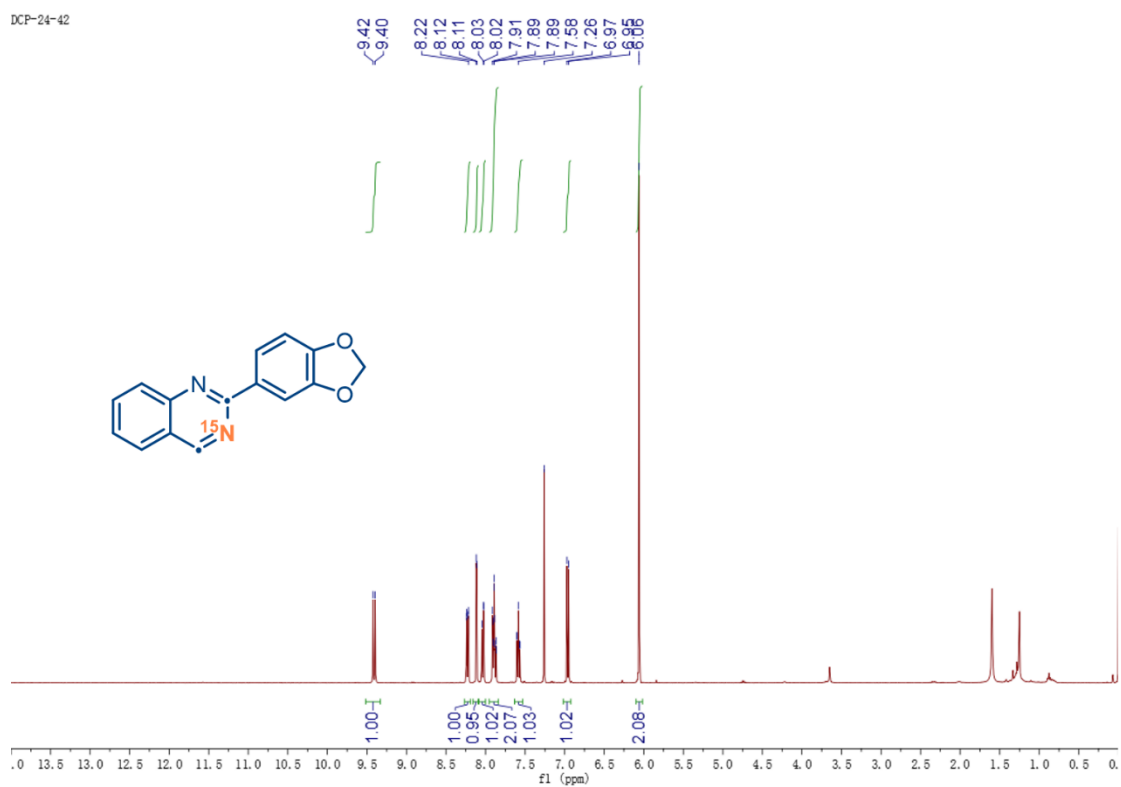
¹³C NMR spectrum of **22** (100 MHz, CDCl₃)



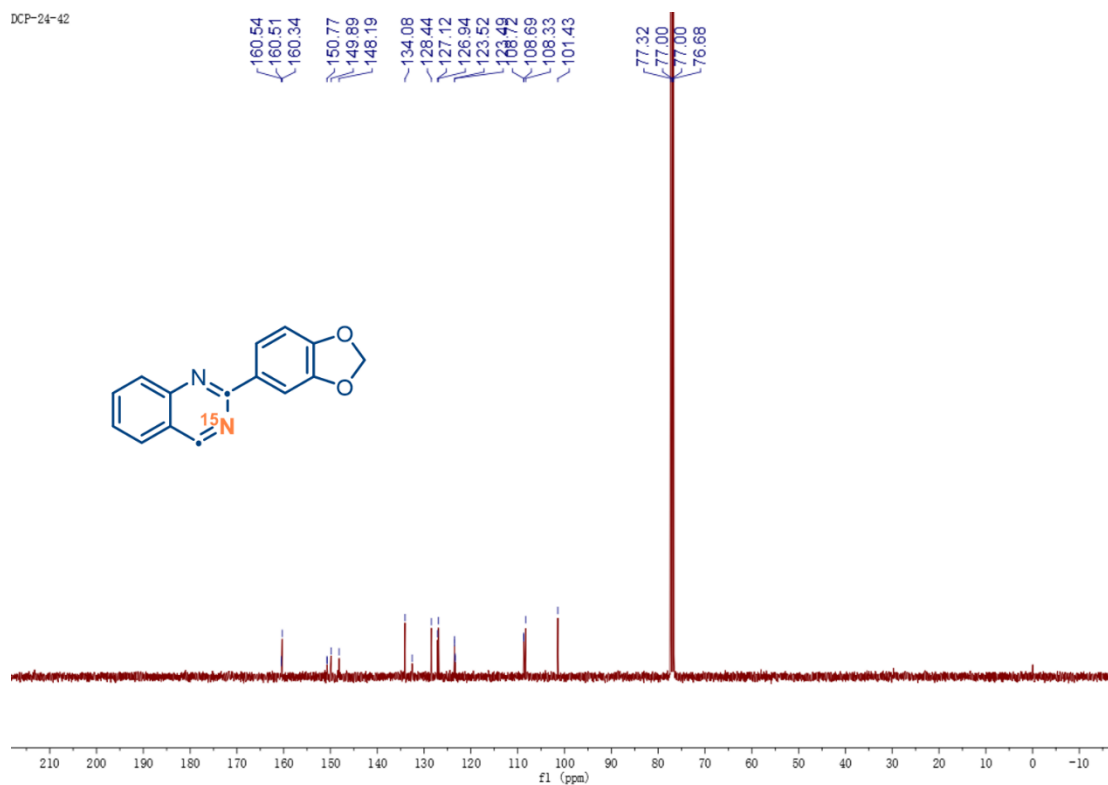
^{15}N NMR spectrum of **22** (50 MHz, CDCl_3)



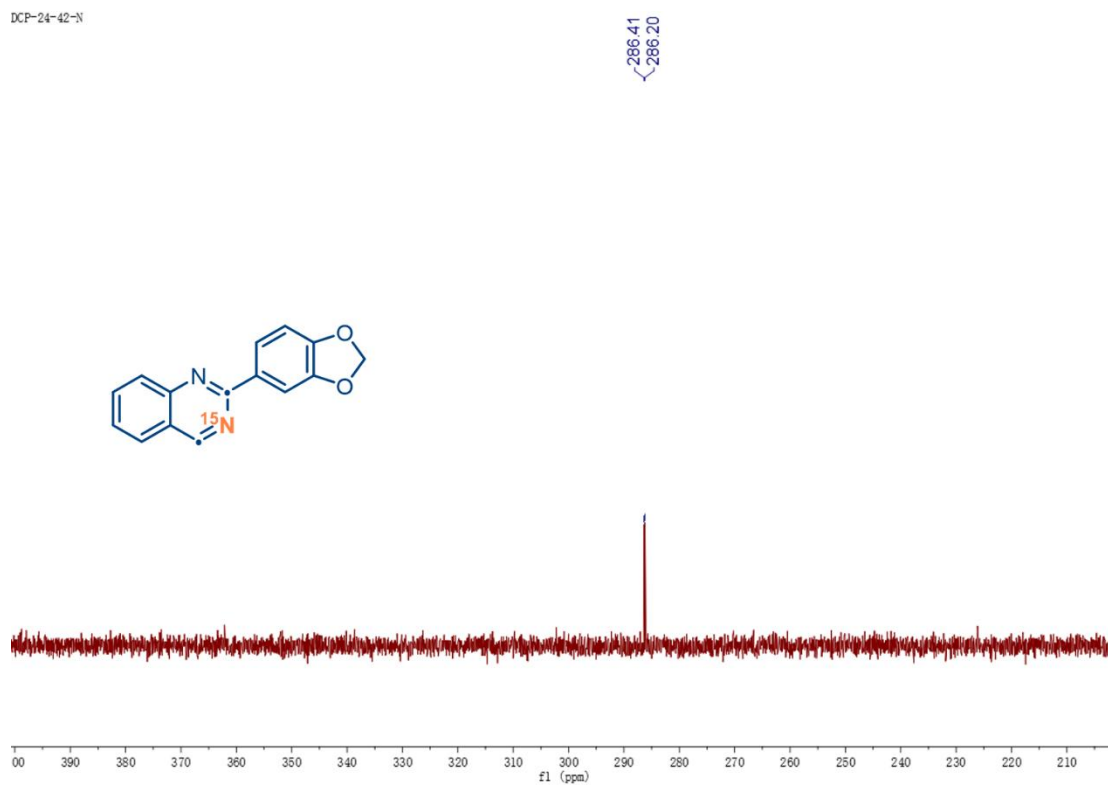
^1H NMR spectrum of **23** (400 MHz, CDCl_3)



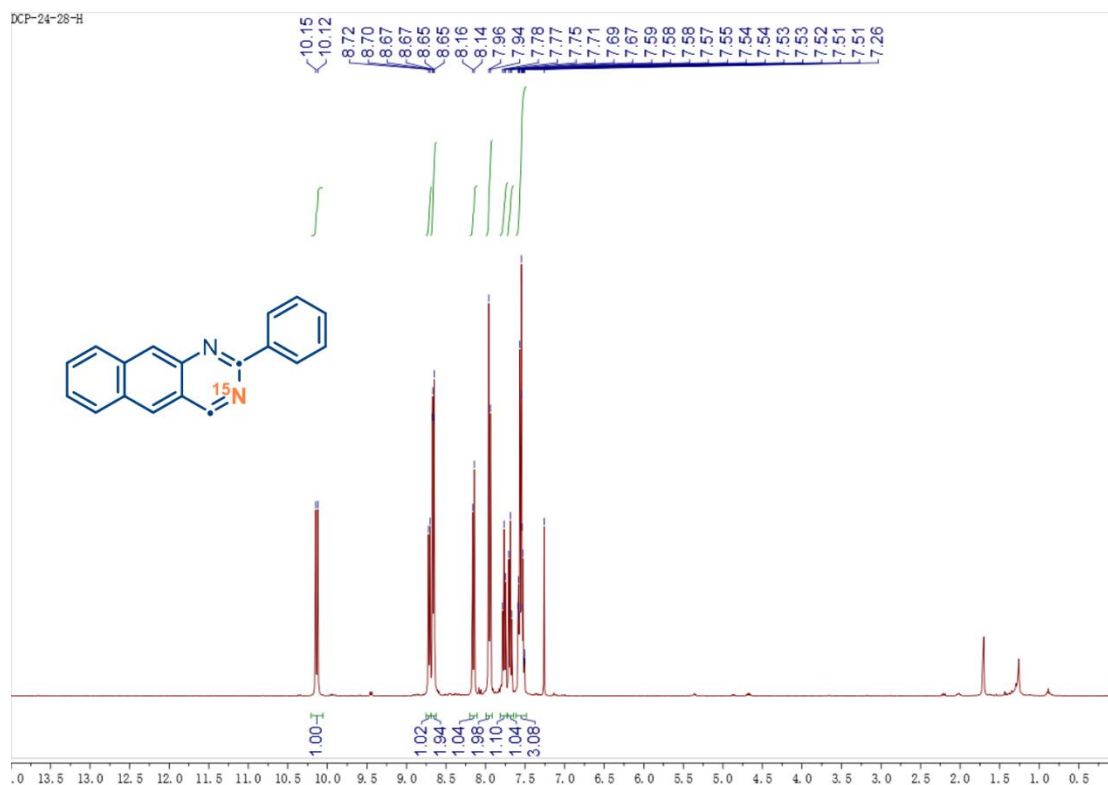
^{13}C NMR spectrum of **23** (100 MHz, CDCl_3)



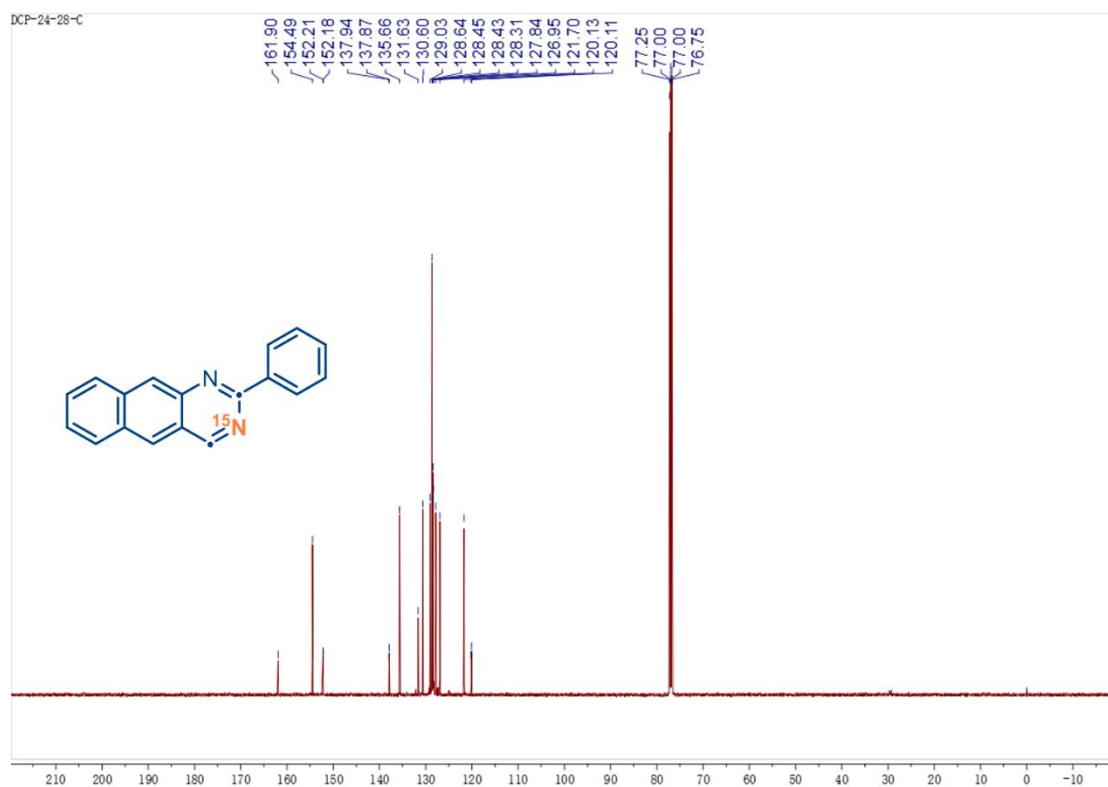
^{15}N NMR spectrum of **23** (50 MHz, CDCl_3)



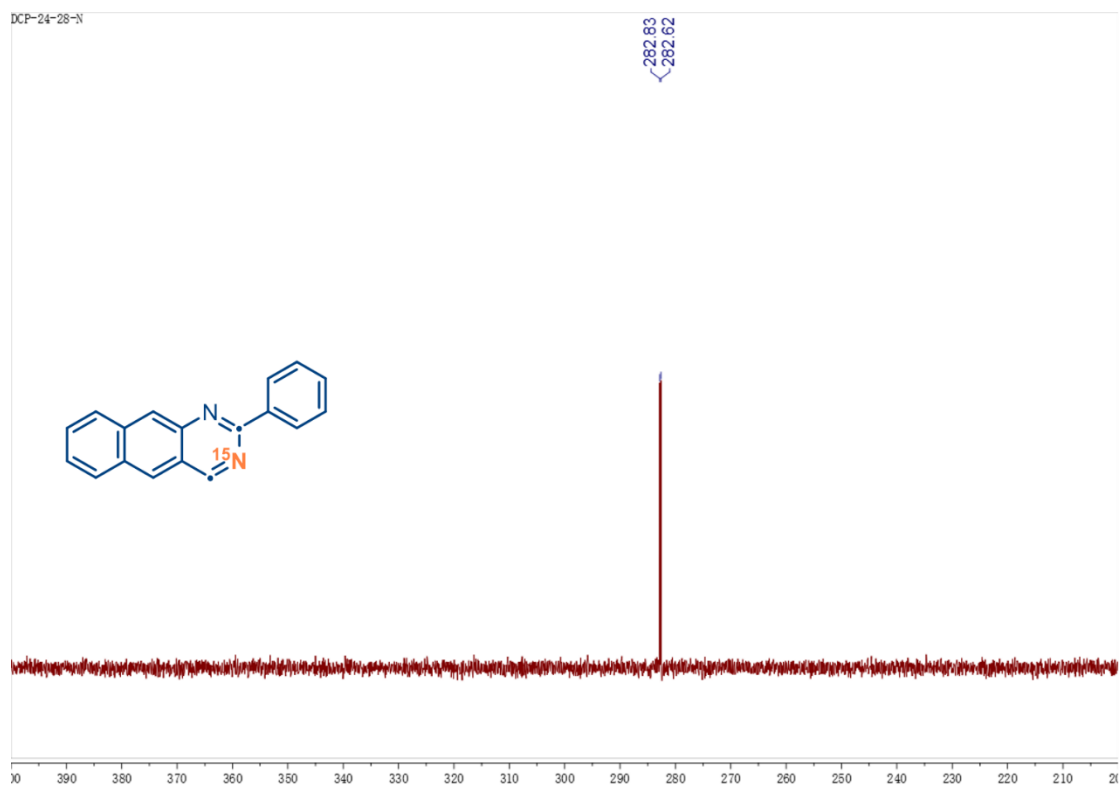
¹H NMR spectrum of **24** (400 MHz, CDCl₃)



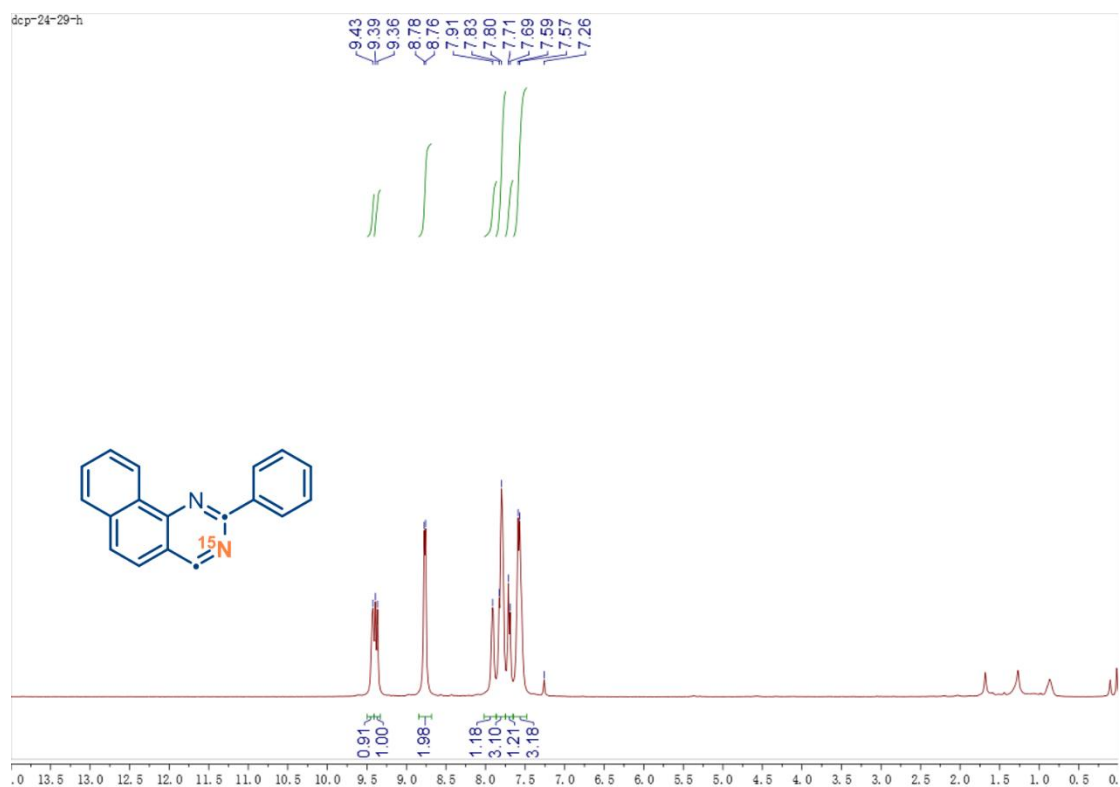
¹³C NMR spectrum of **24** (125 MHz, CDCl₃)



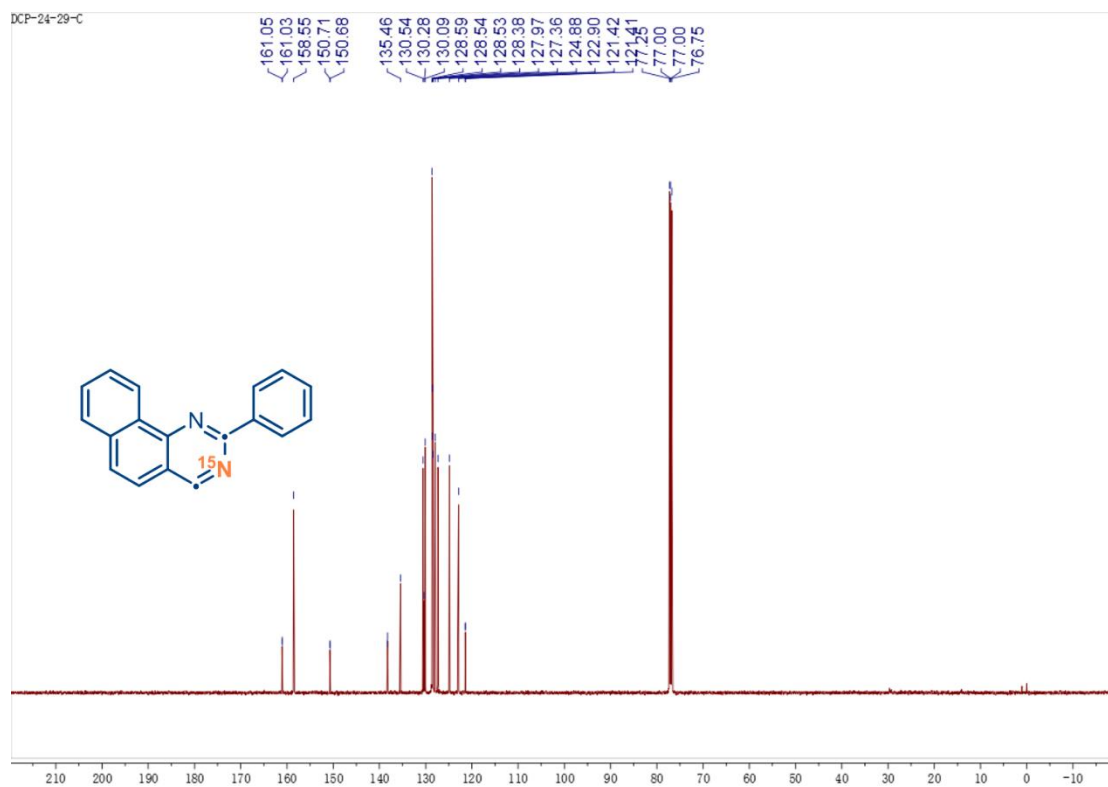
^{15}N NMR spectrum of **24** (50 MHz, CDCl_3)



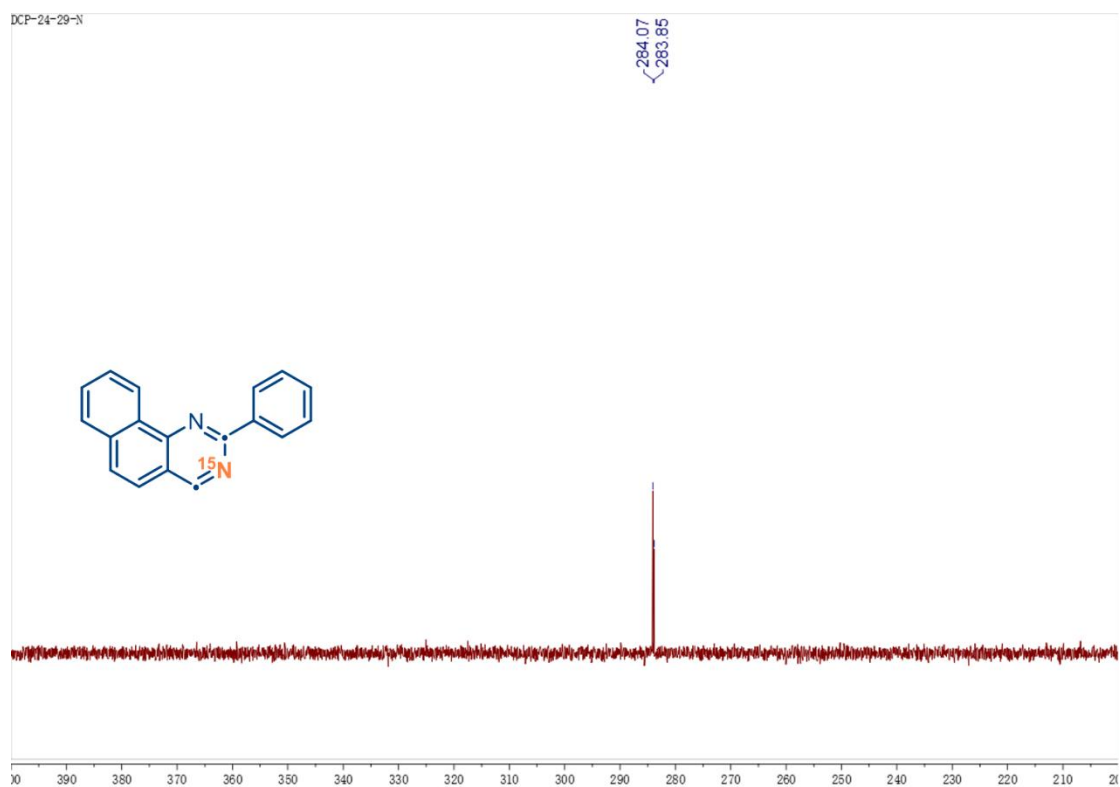
^1H NMR spectrum of **25** (400 MHz, CDCl_3)



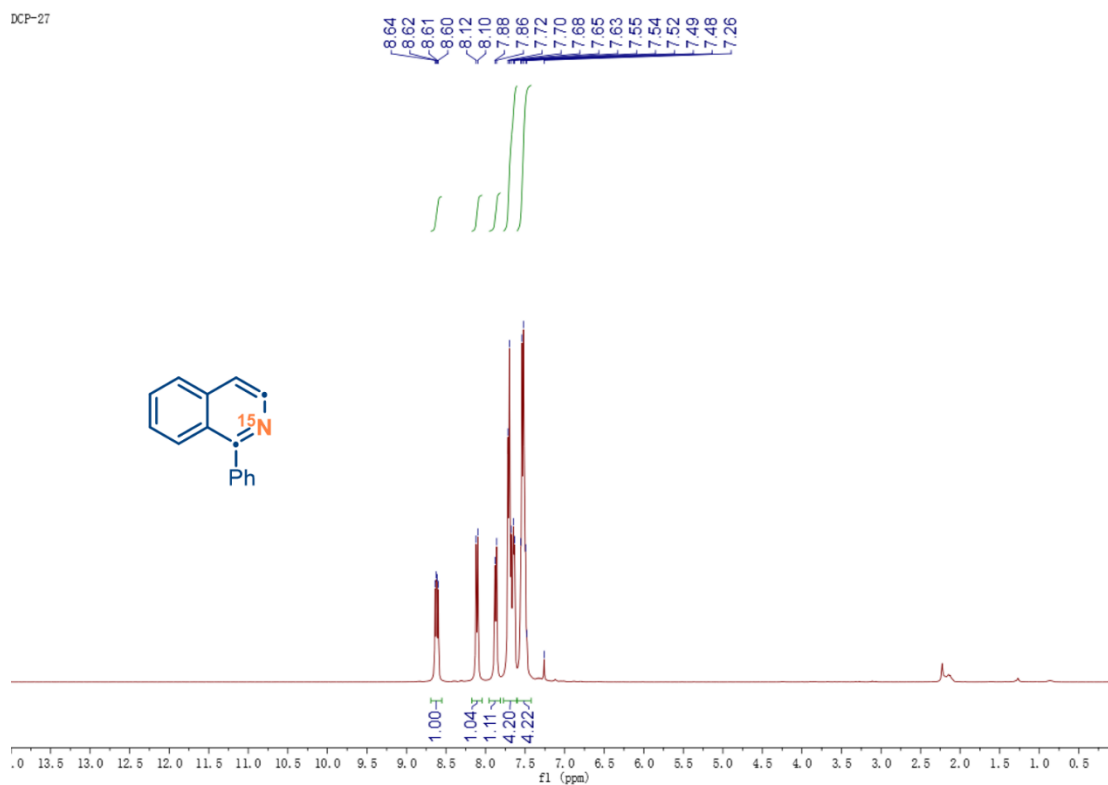
^{13}C NMR spectrum of **25** (125 MHz, CDCl_3)



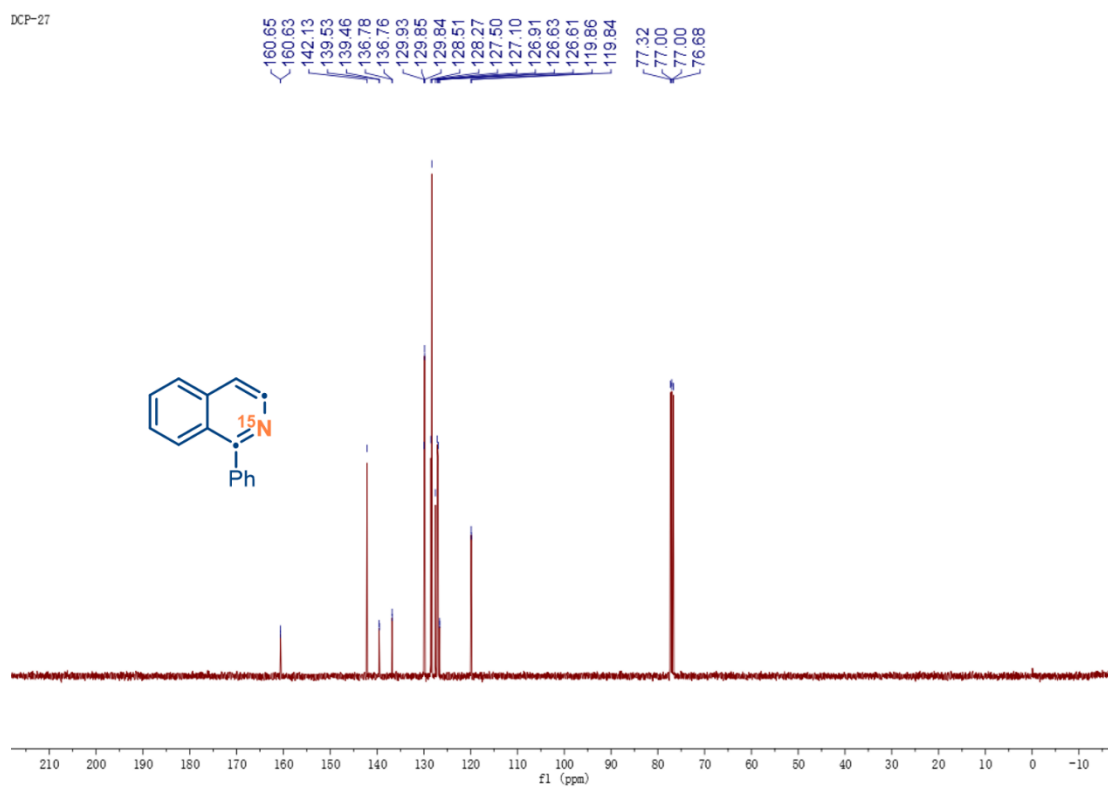
^{15}N NMR spectrum of **25** (50 MHz, CDCl_3)



¹H NMR spectrum of **26** (400 MHz, CDCl₃)

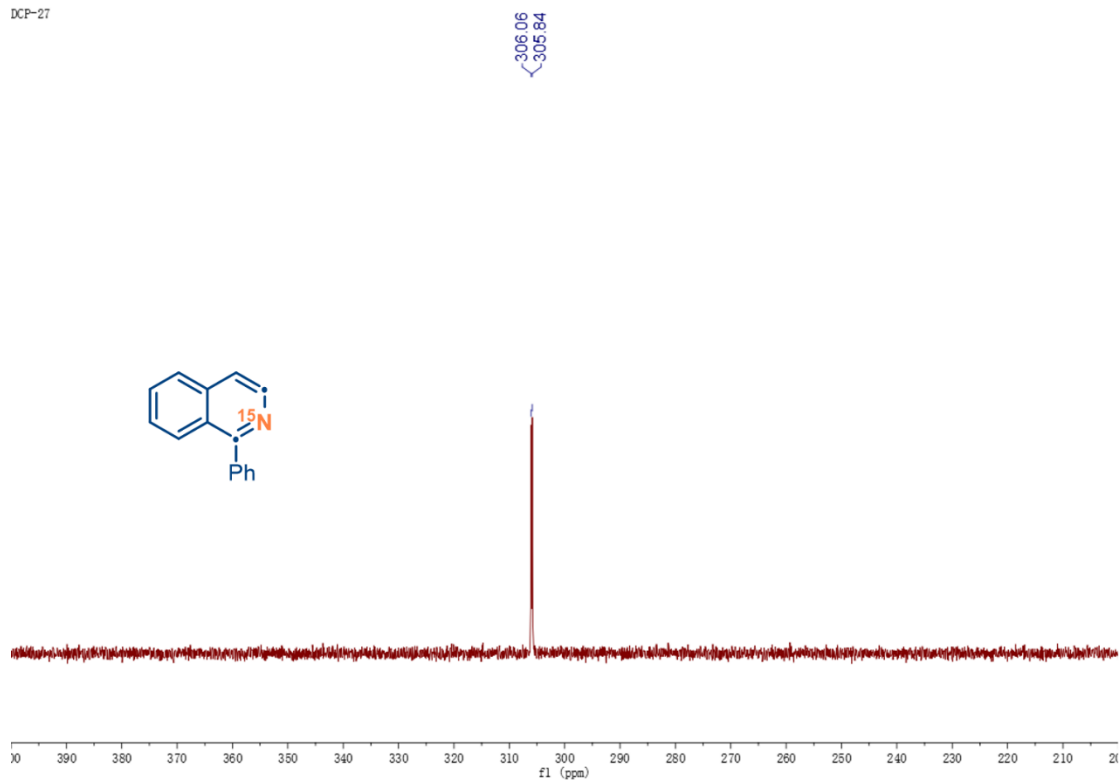


¹³C NMR spectrum of **26** (100 MHz, CDCl₃)



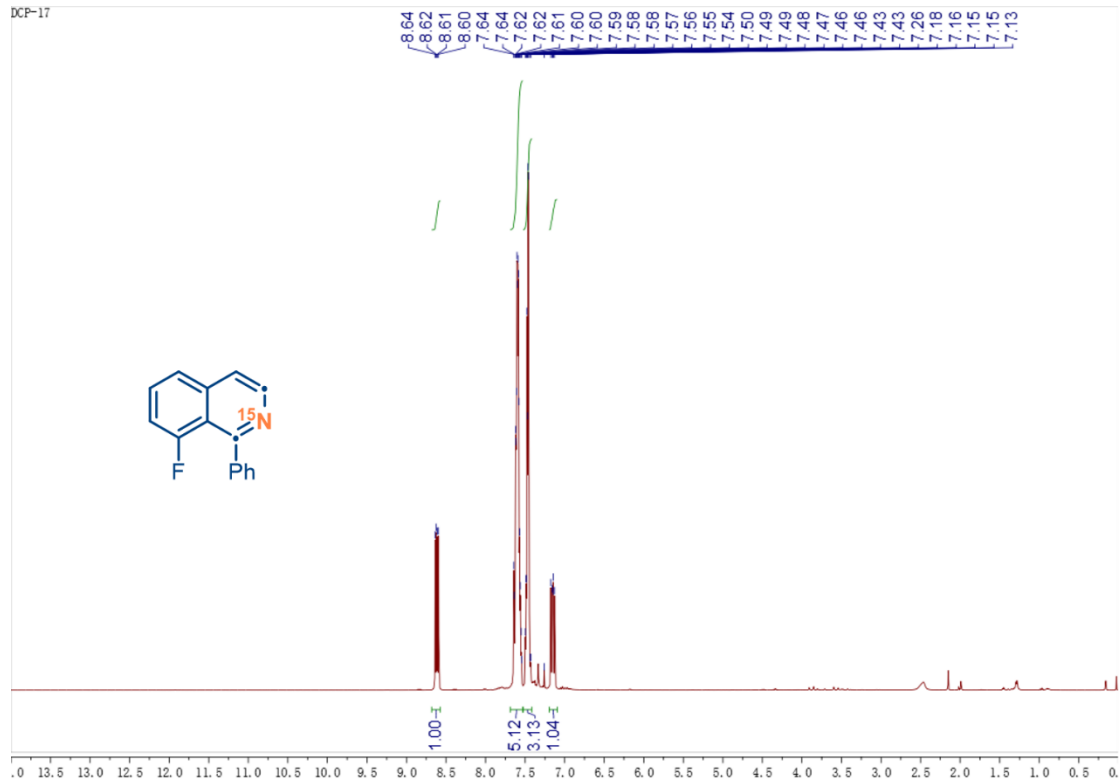
^{15}N NMR spectrum of **26** (50 MHz, CDCl_3)

DCP-27

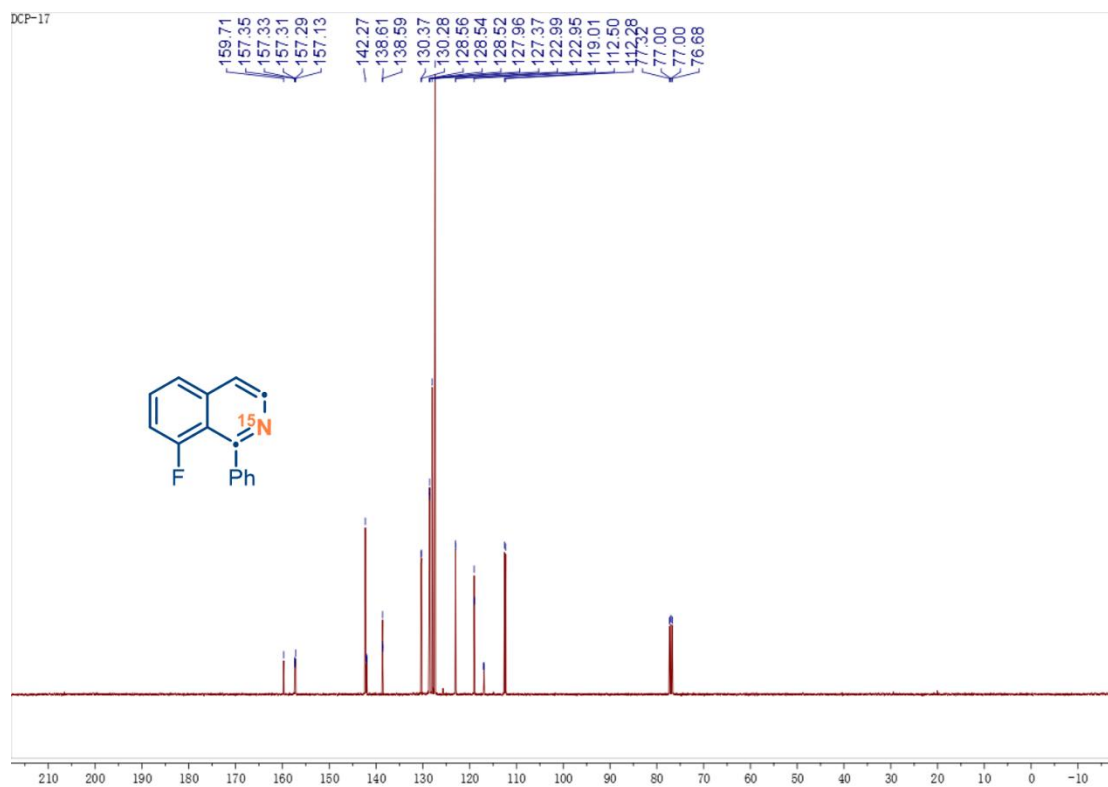


^1H NMR spectrum of **27** (400 MHz, CDCl_3)

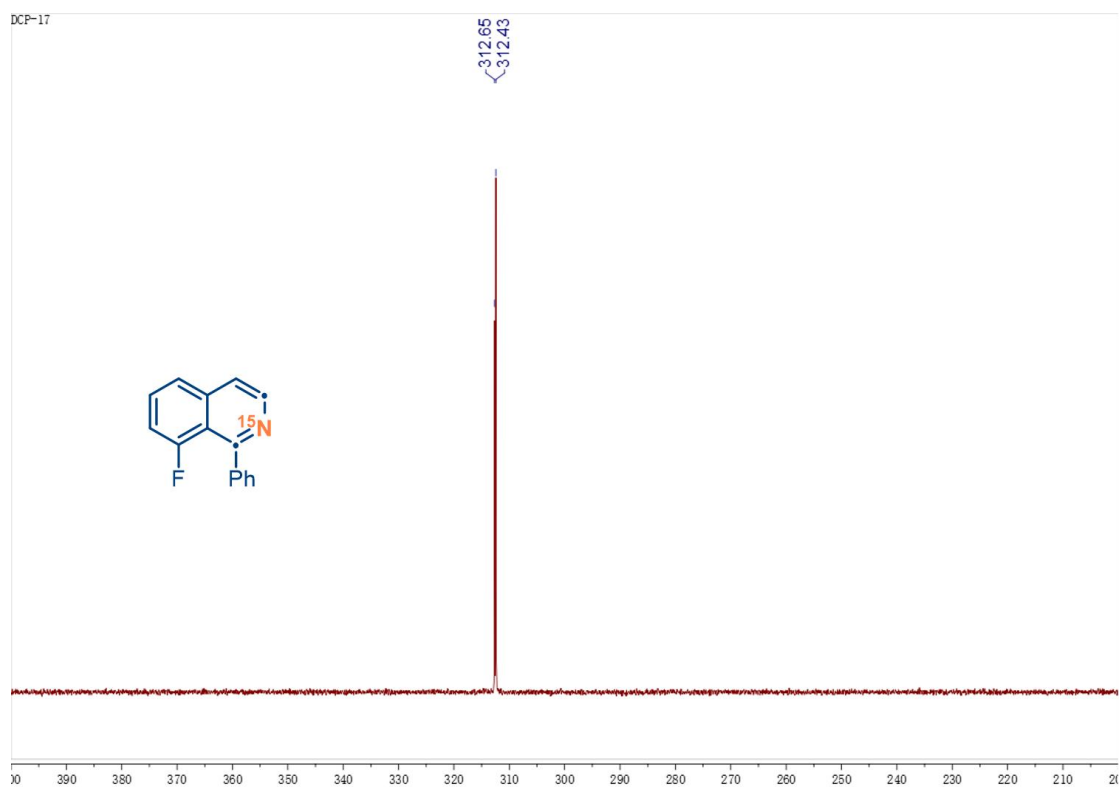
DCP-17



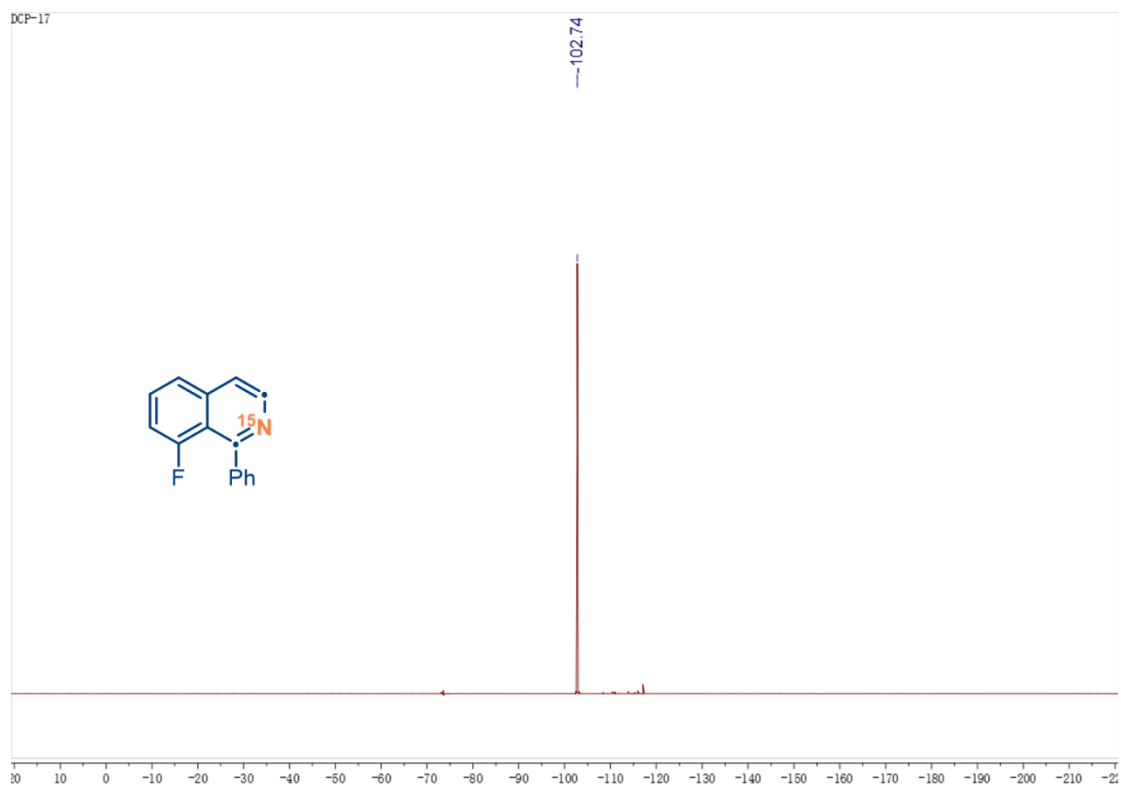
^{13}C NMR spectrum of **27** (100 MHz, CDCl_3)



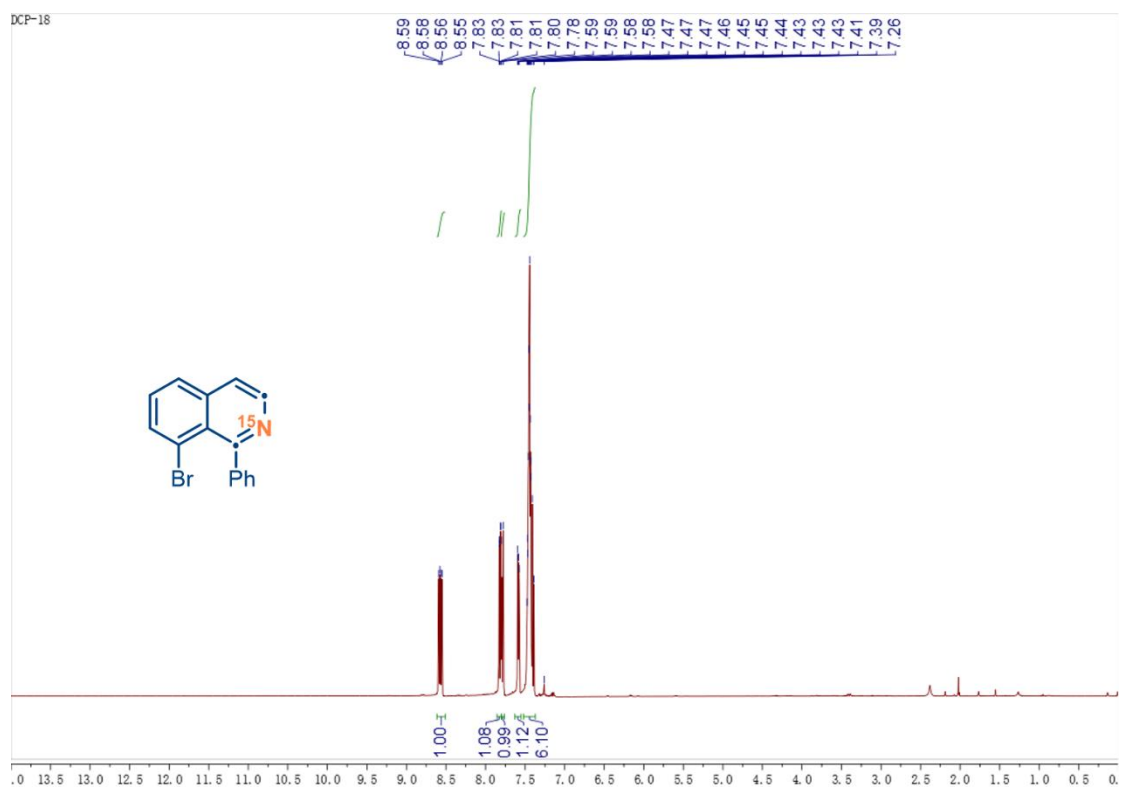
^{15}N NMR spectrum of **27** (50 MHz, CDCl_3)



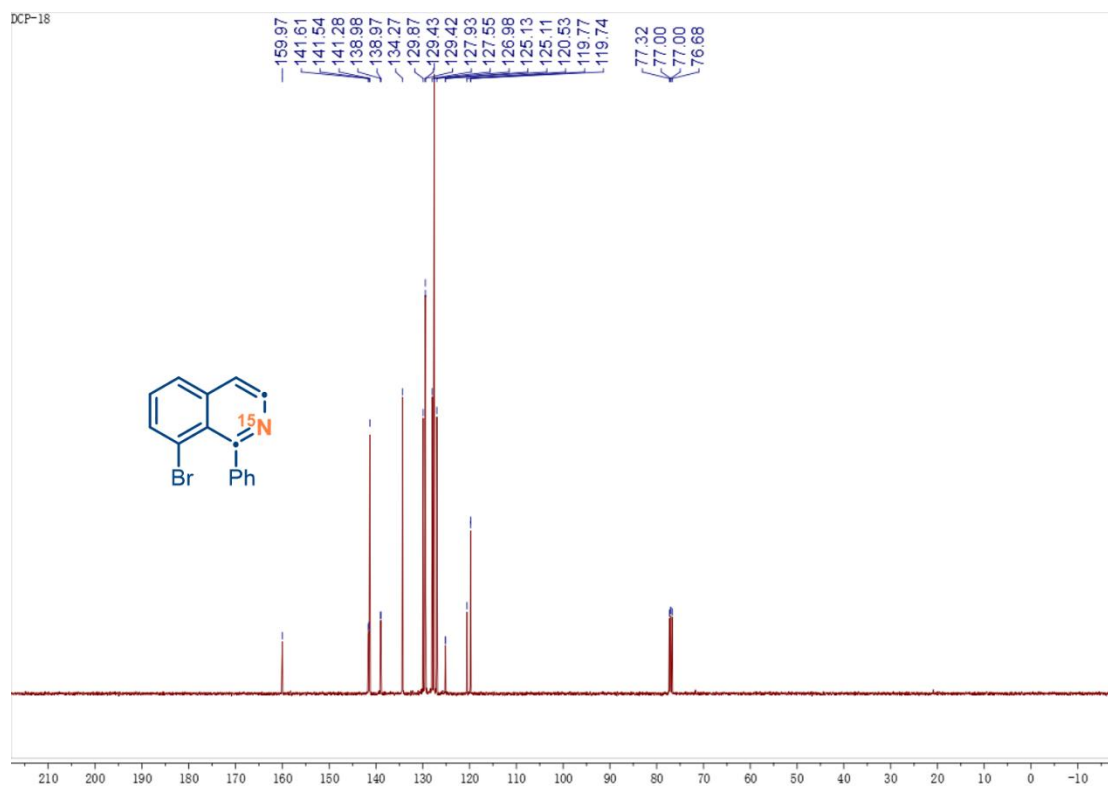
^{19}F NMR spectrum of **27** (376 MHz, CDCl_3)



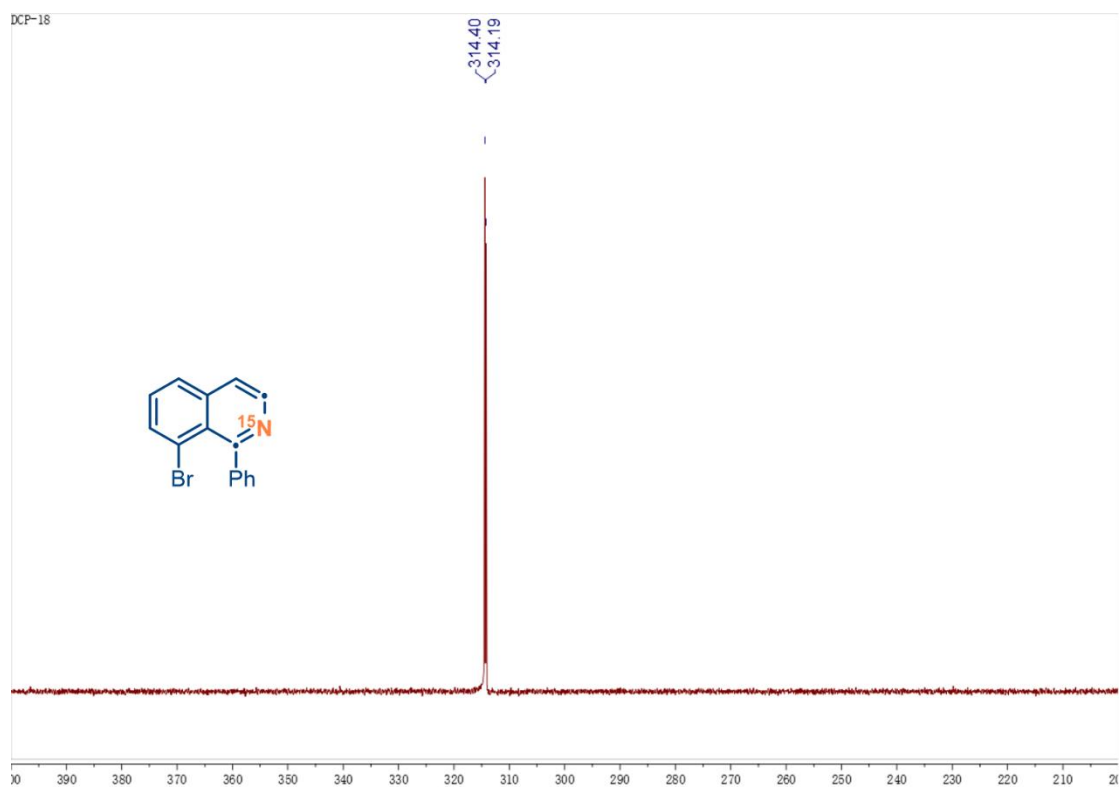
^1H NMR spectrum of **28** (400 MHz, CDCl_3)



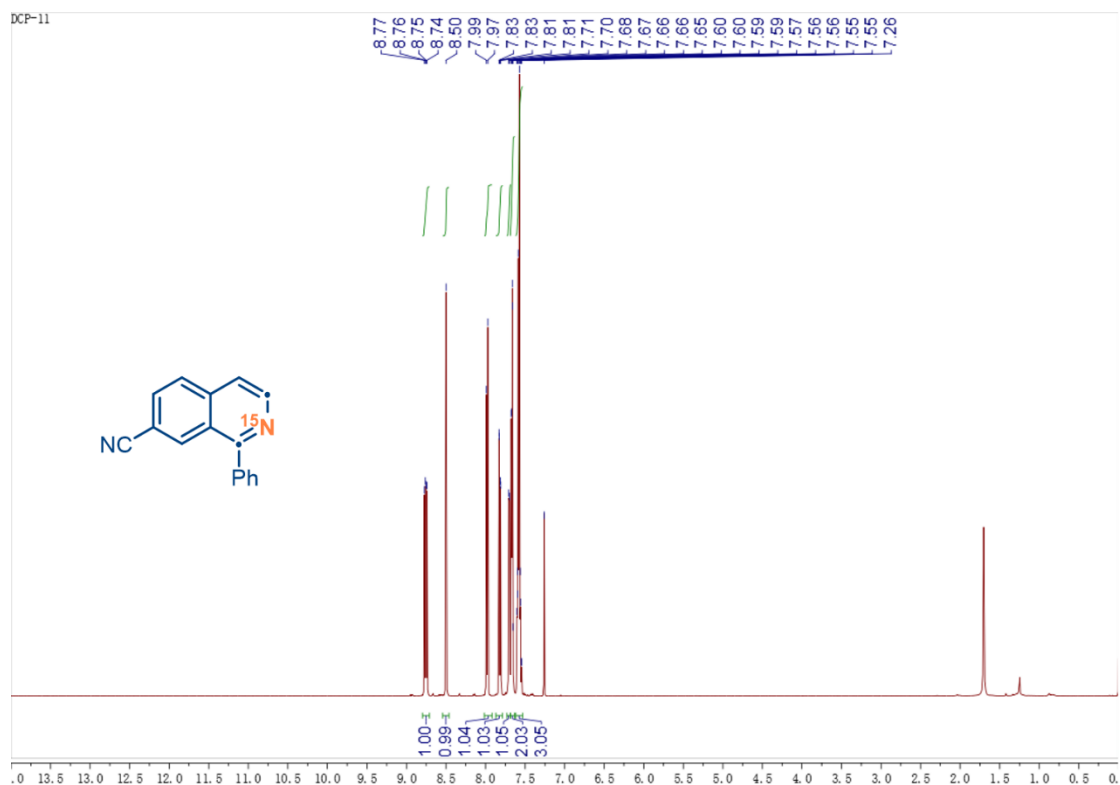
^{13}C NMR spectrum of **28** (100 MHz, CDCl_3)



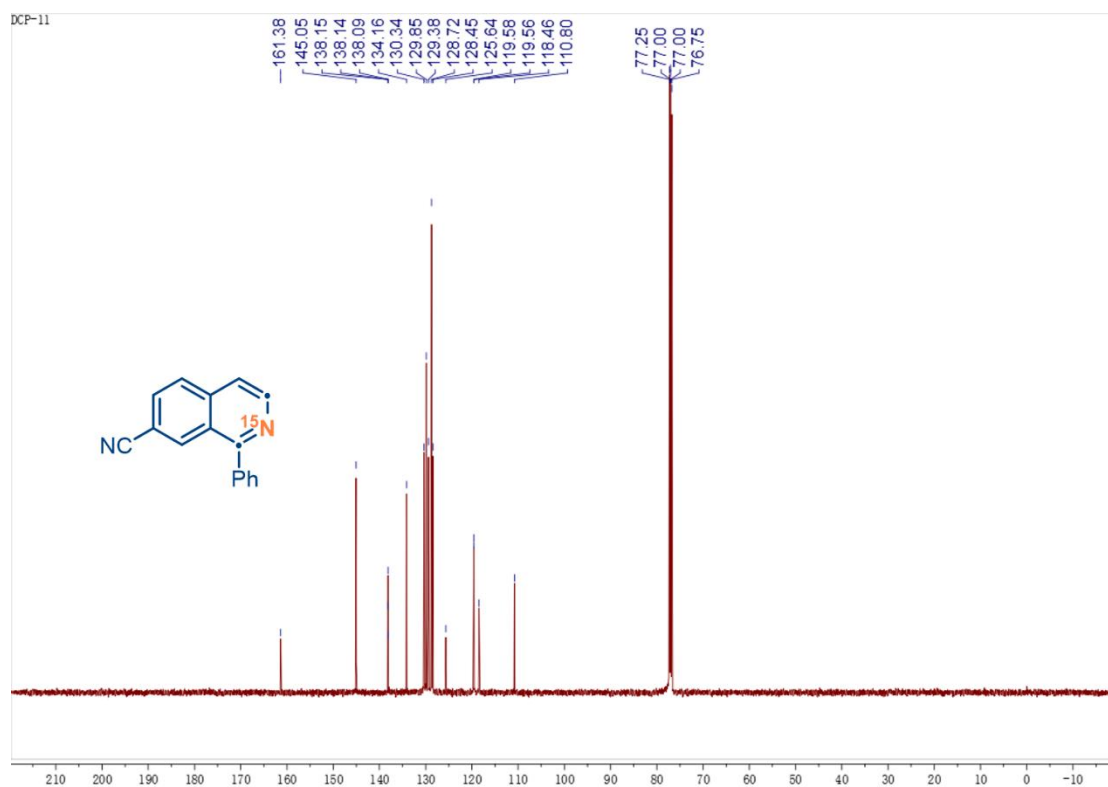
^{15}N NMR spectrum of **28** (50 MHz, CDCl_3)



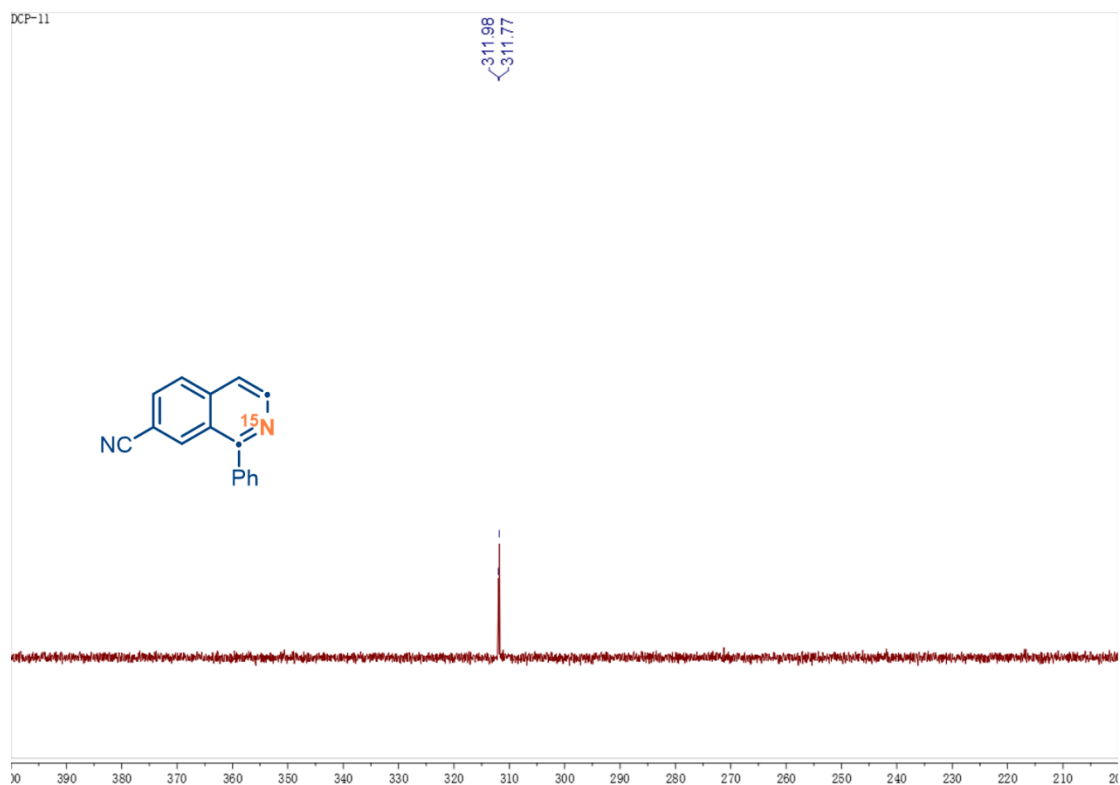
¹H NMR spectrum of **29** (500 MHz, CDCl₃)



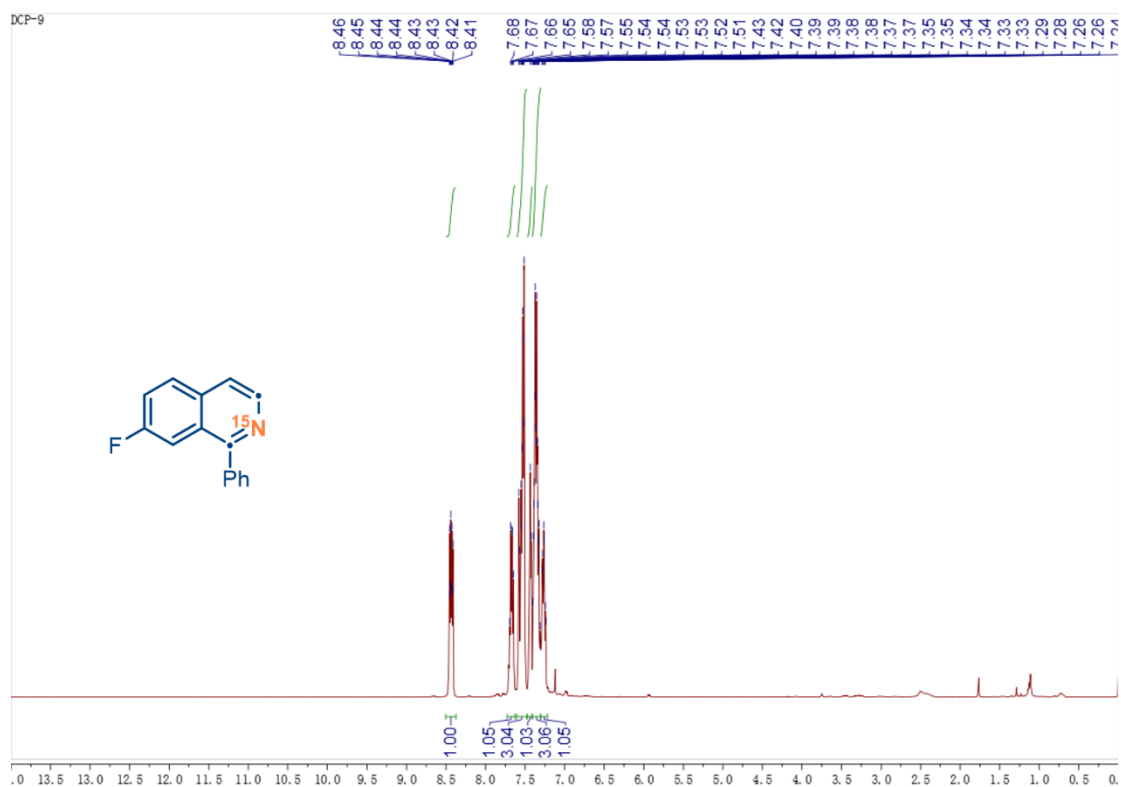
¹³C NMR spectrum of **29** (125 MHz, CDCl₃)



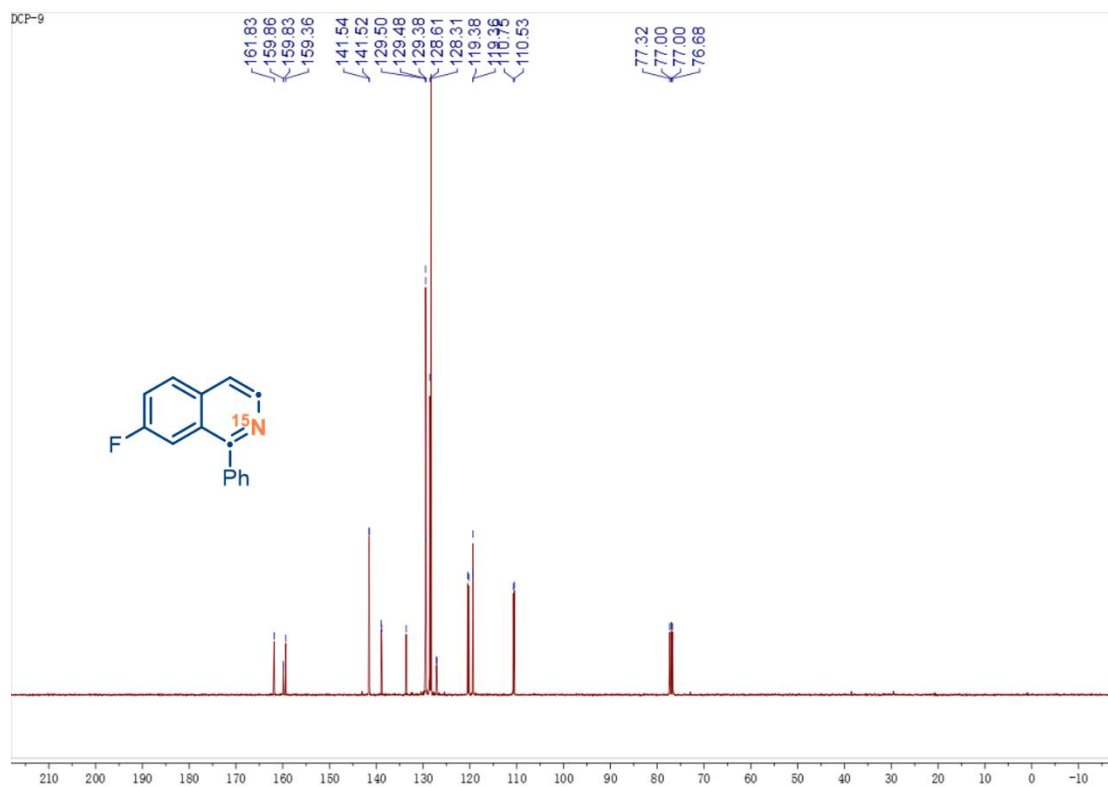
^{15}N NMR spectrum of **29** (50 MHz, CDCl_3)



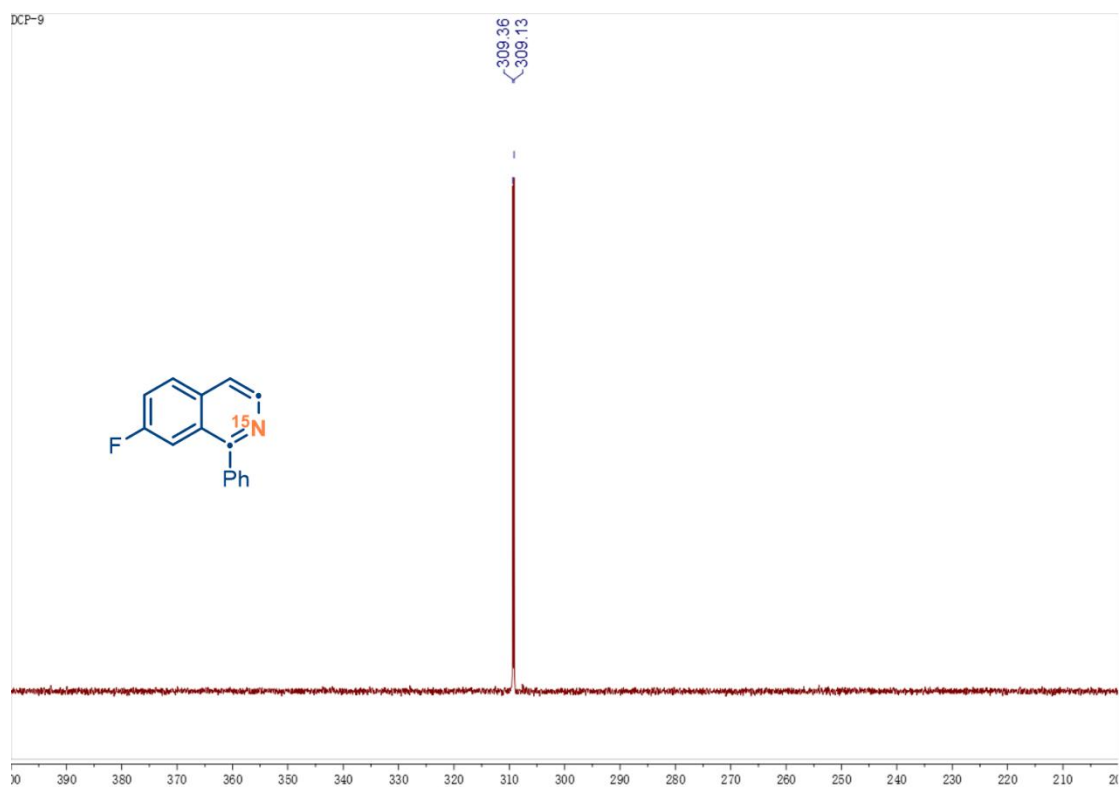
^1H NMR spectrum of **30** (400 MHz, CDCl_3)



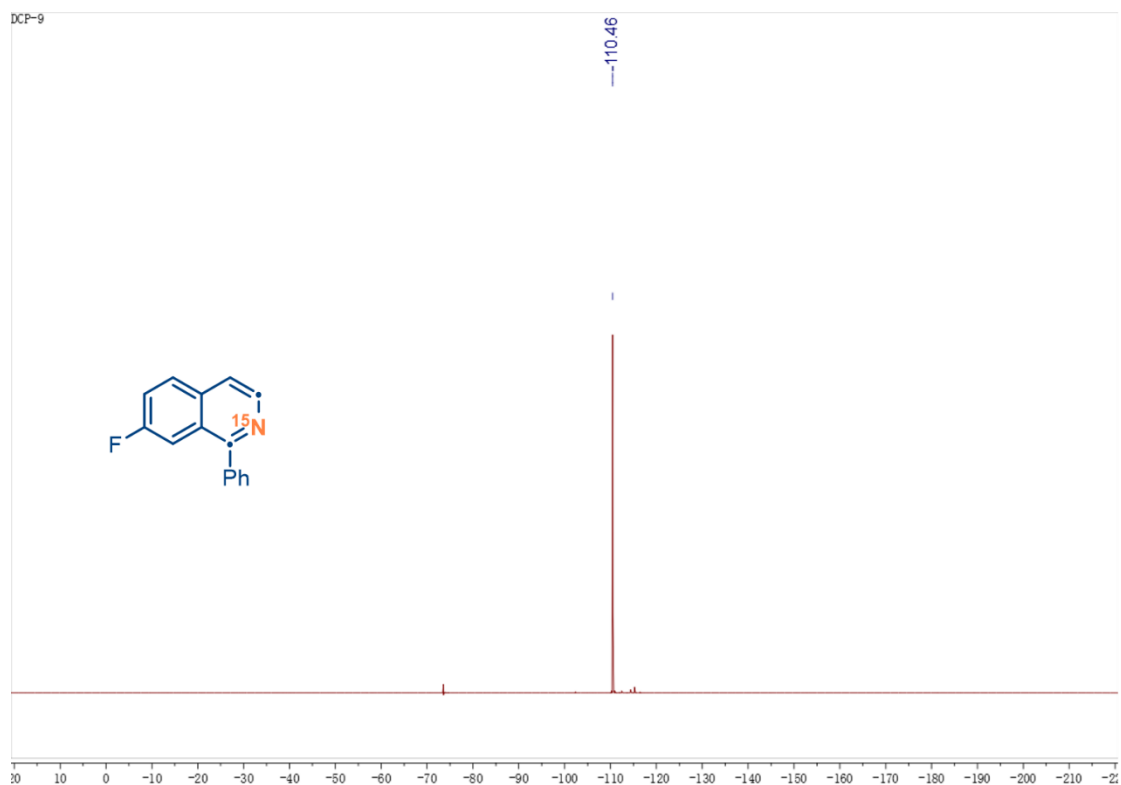
^{13}C NMR spectrum of **30** (100 MHz, CDCl_3)



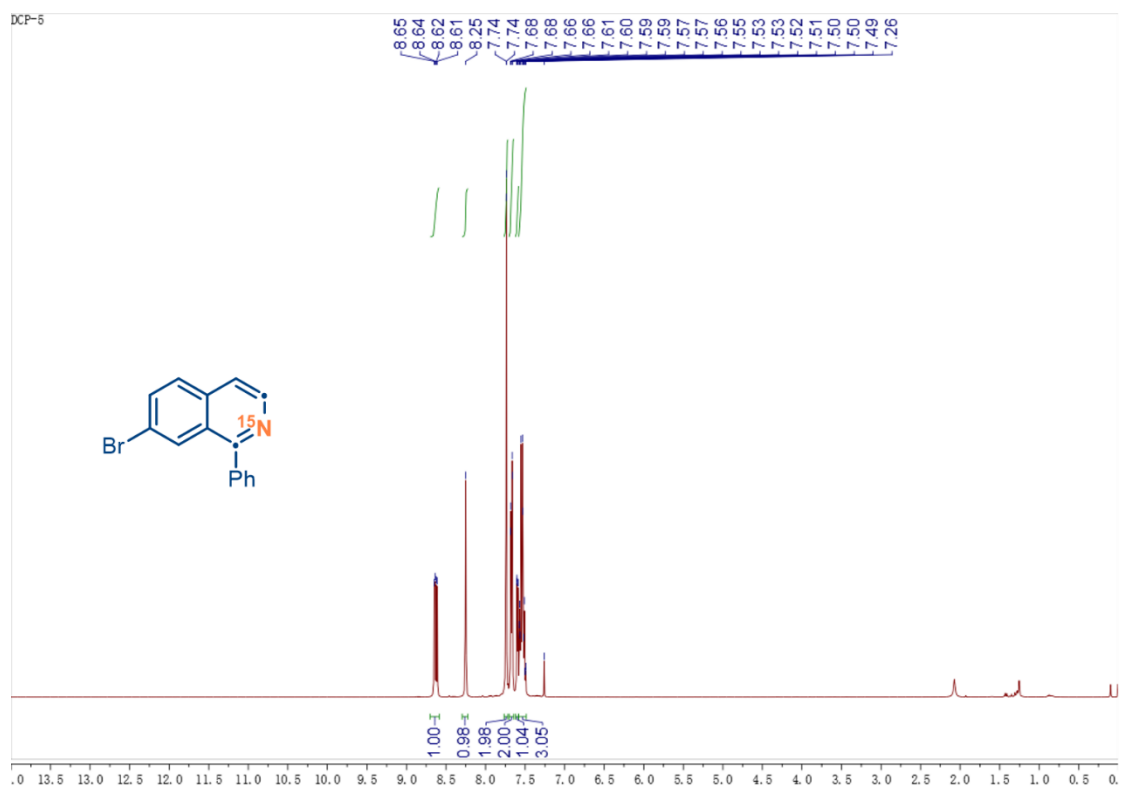
^{15}N NMR spectrum of **30** (50 MHz, CDCl_3)



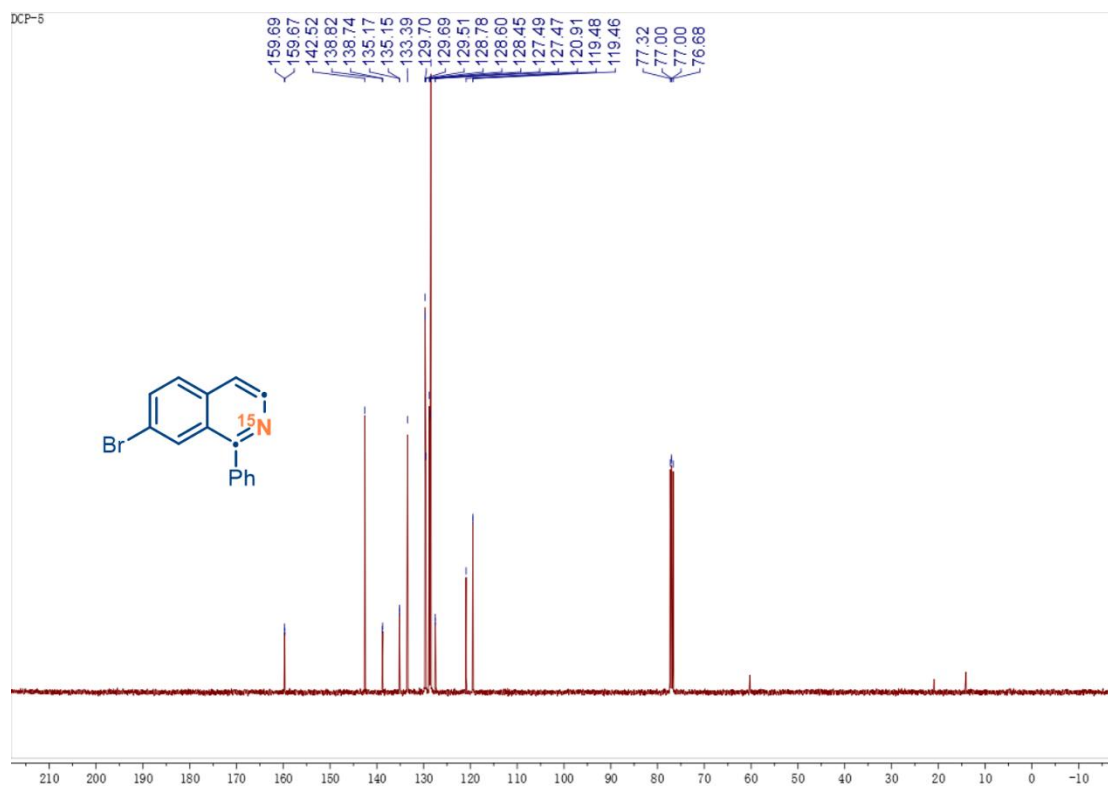
^{19}F NMR spectrum of **30** (376 MHz, CDCl_3)



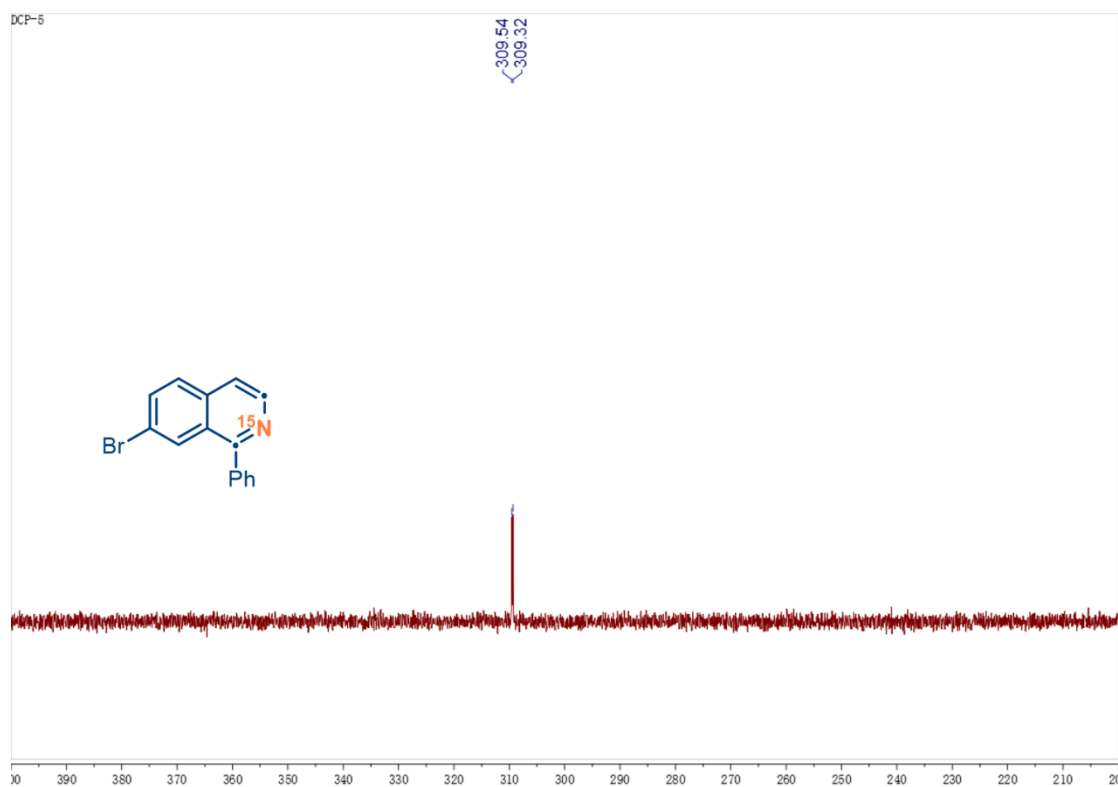
^1H NMR spectrum of **31** (400 MHz, CDCl_3)



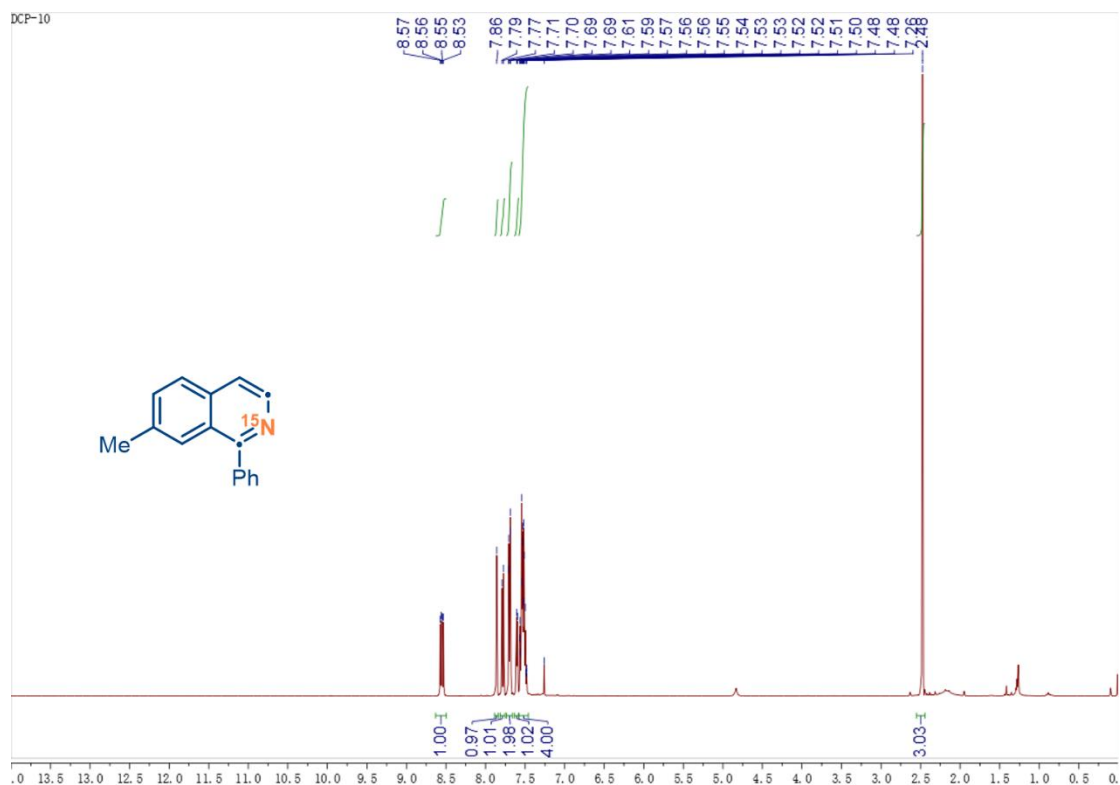
^{13}C NMR spectrum of **31** (100 MHz, CDCl_3)



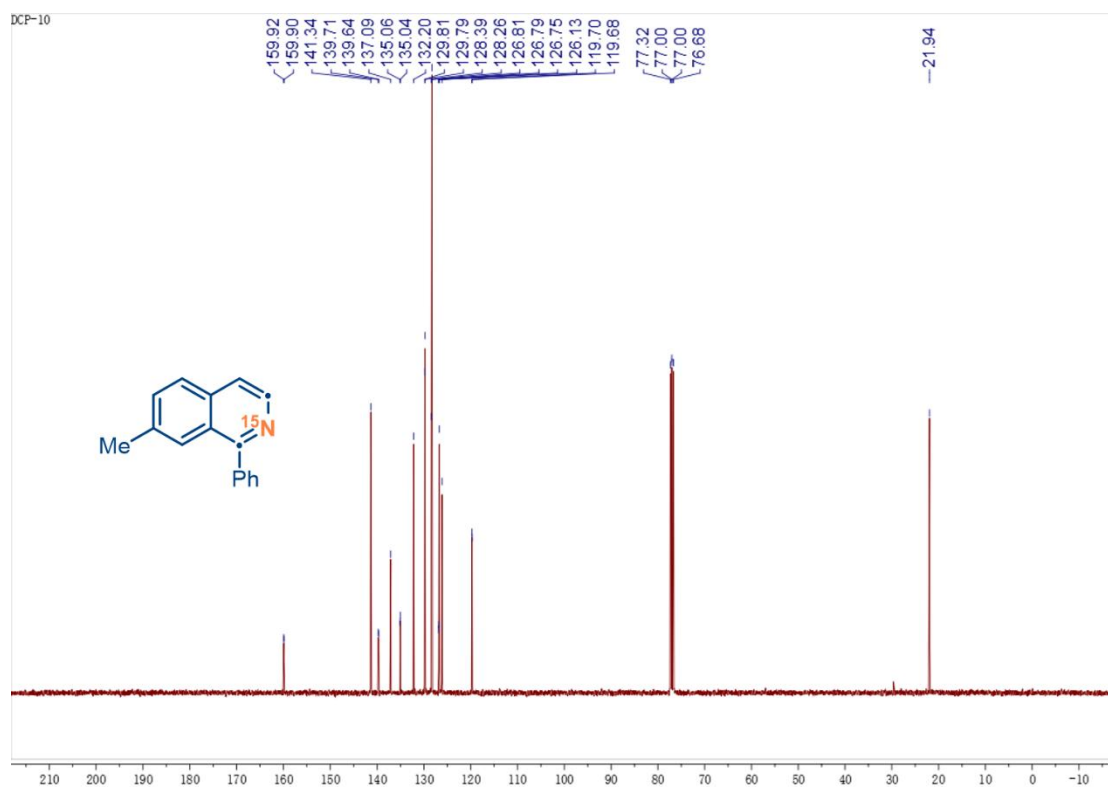
^{15}N NMR spectrum of **31** (50 MHz, CDCl_3)



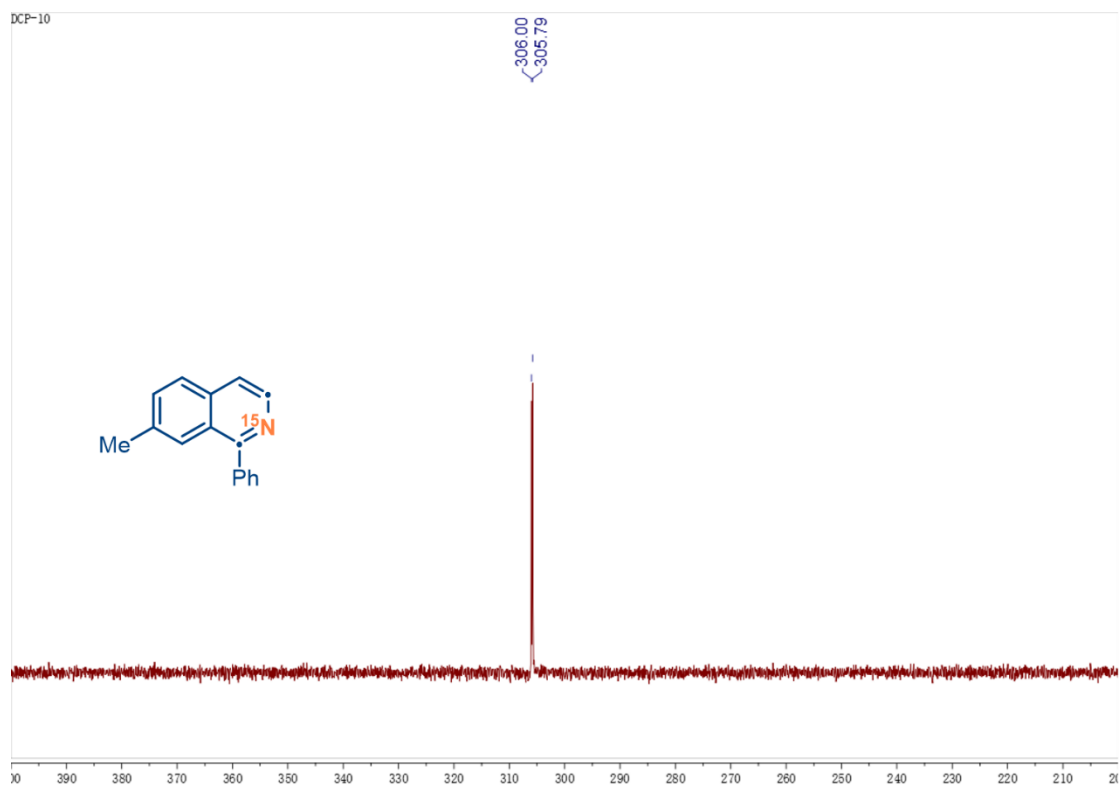
^1H NMR spectrum of **32** (400 MHz, CDCl_3)



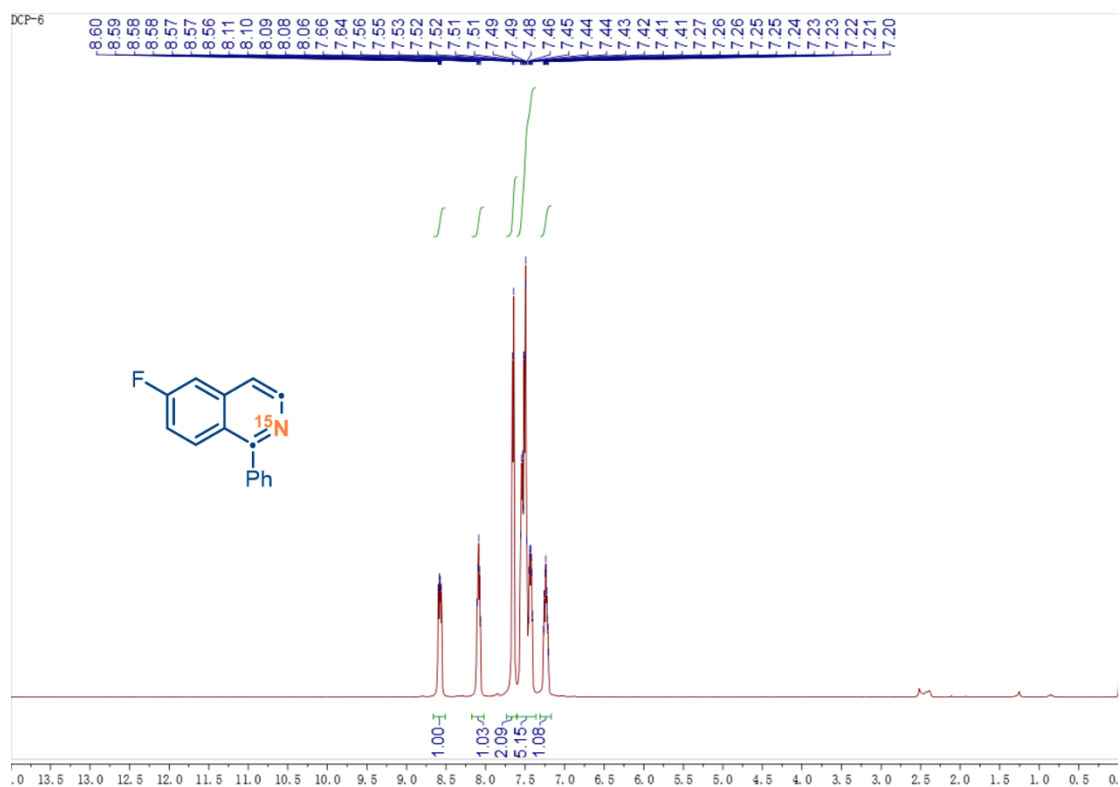
^{13}C NMR spectrum of **32** (100 MHz, CDCl_3)



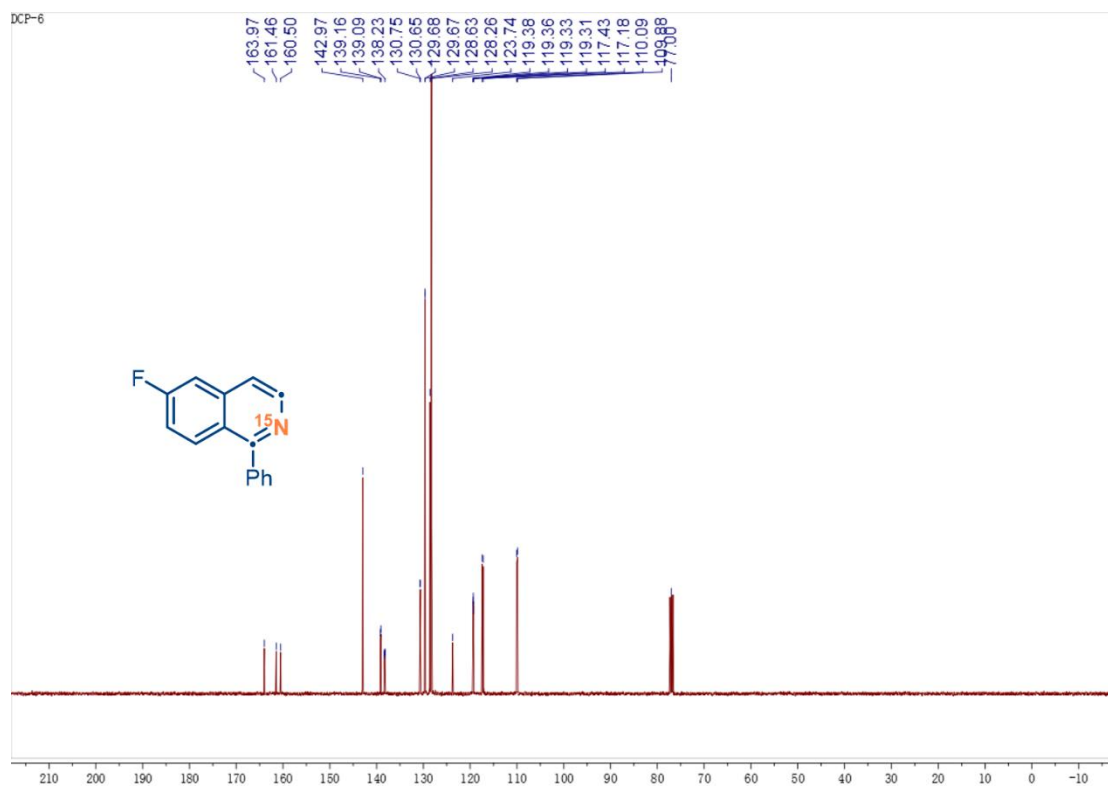
^{15}N NMR spectrum of **32** (50 MHz, CDCl_3)



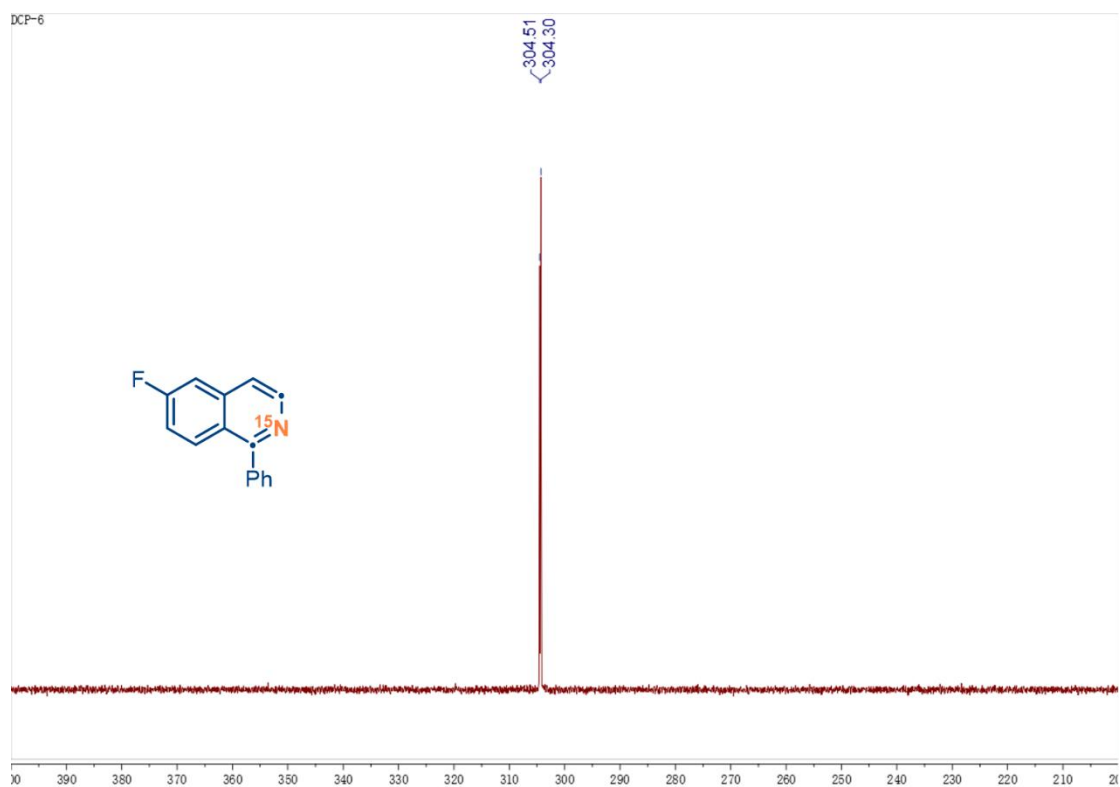
^1H NMR spectrum of **33** (400 MHz, CDCl_3)



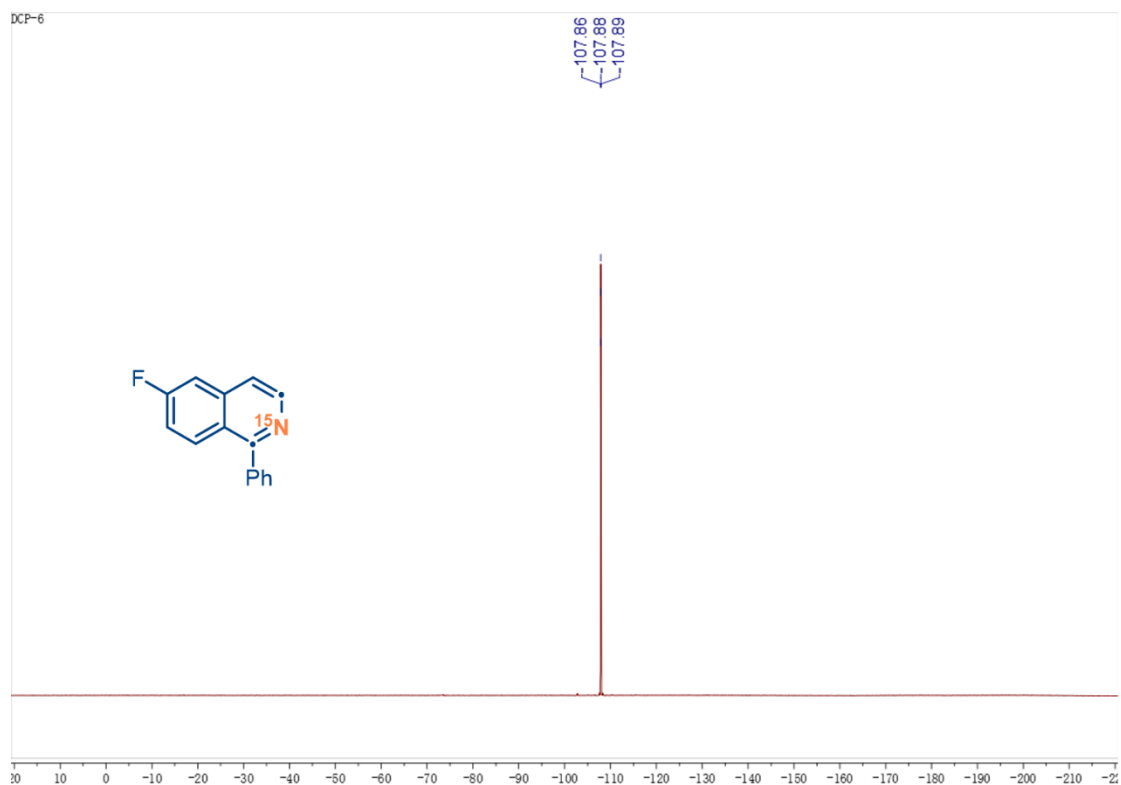
^{13}C NMR spectrum of **33** (100 MHz, CDCl_3)



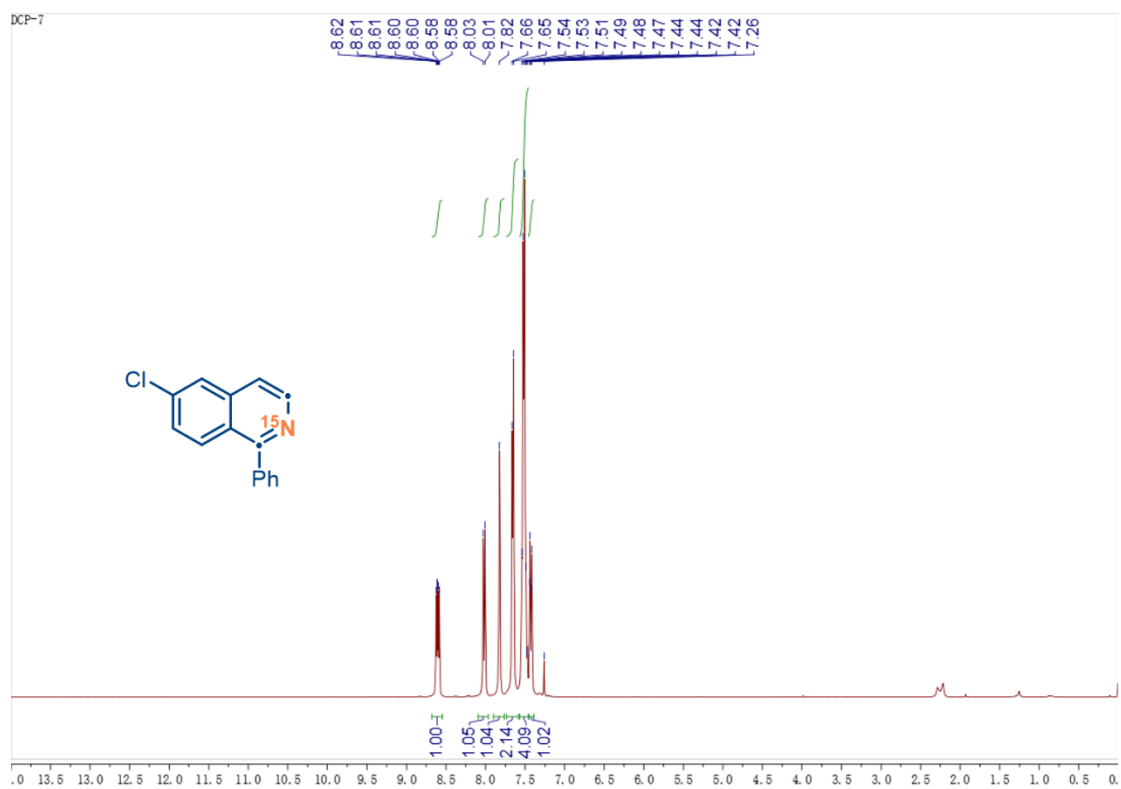
^{15}N NMR spectrum of **33** (50 MHz, CDCl_3)



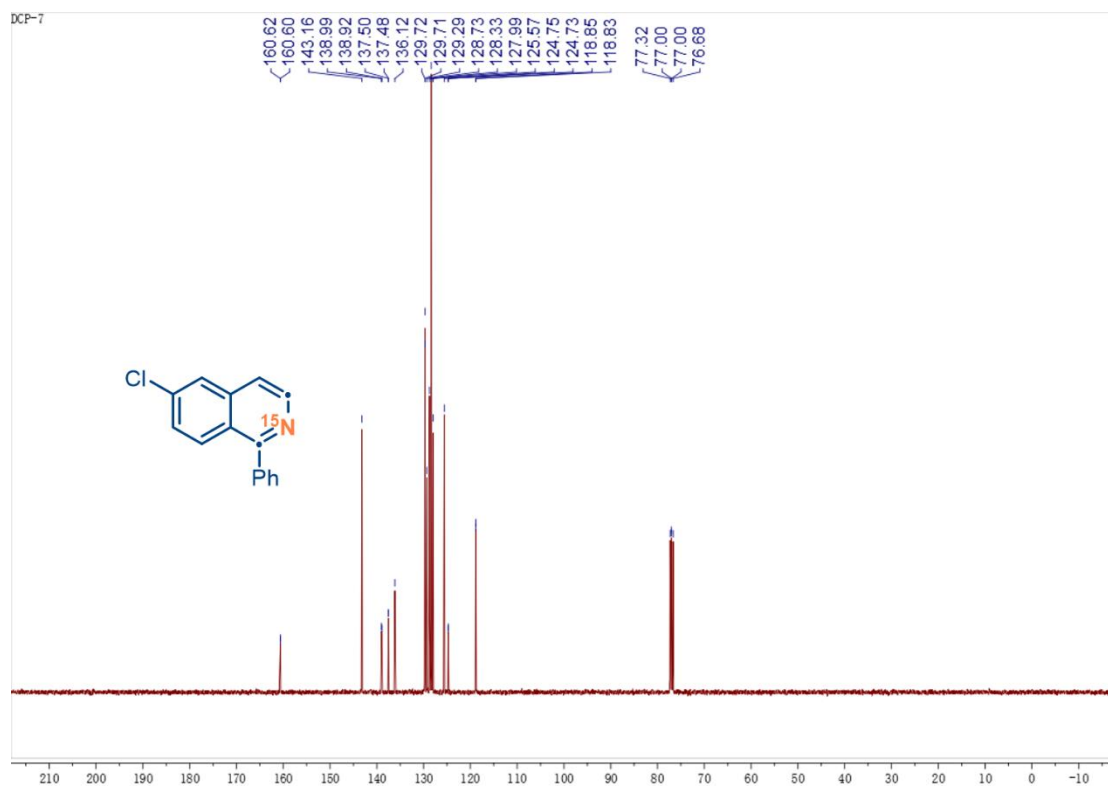
^{19}F NMR spectrum of **33** (376 MHz, CDCl_3)



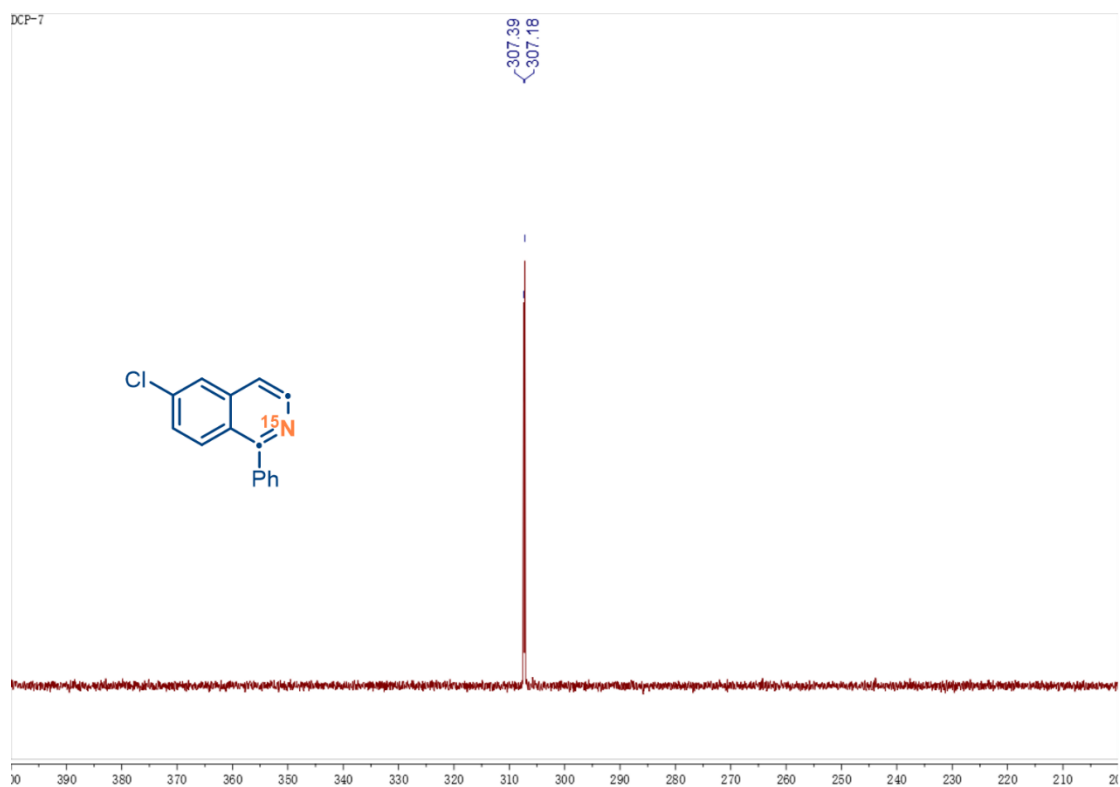
^1H NMR spectrum of **34** (400 MHz, CDCl_3)



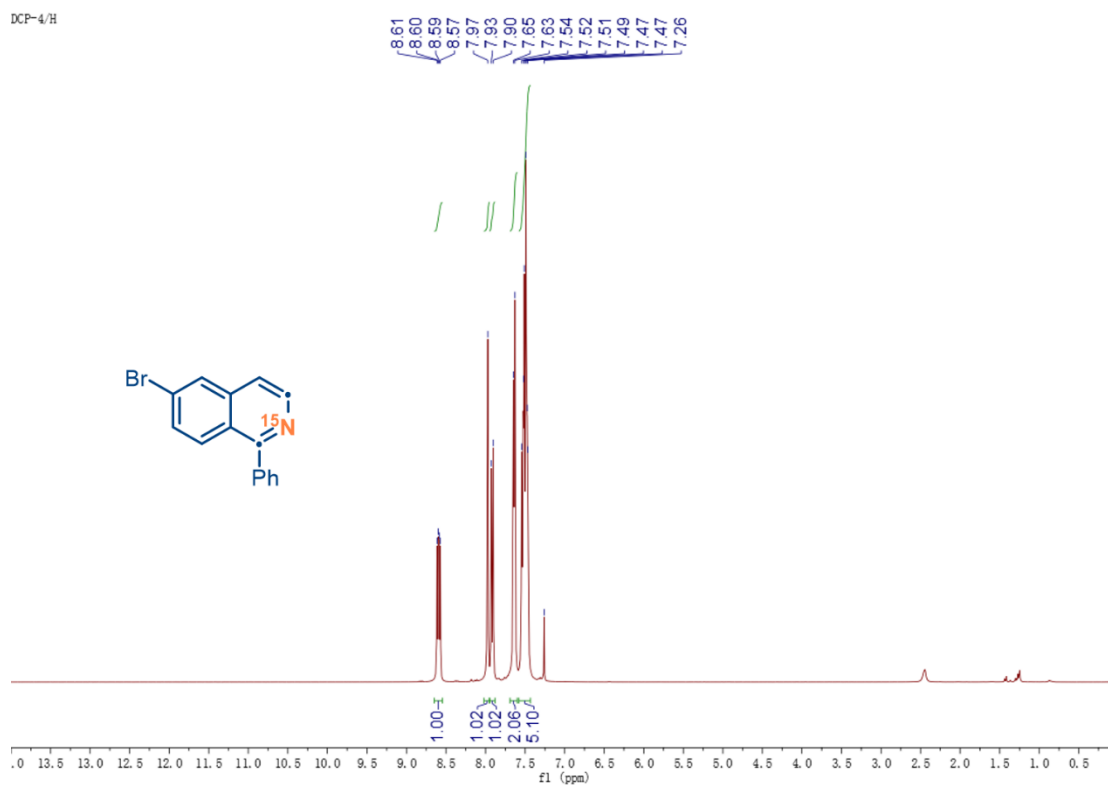
^{13}C NMR spectrum of **34** (100 MHz, CDCl_3)



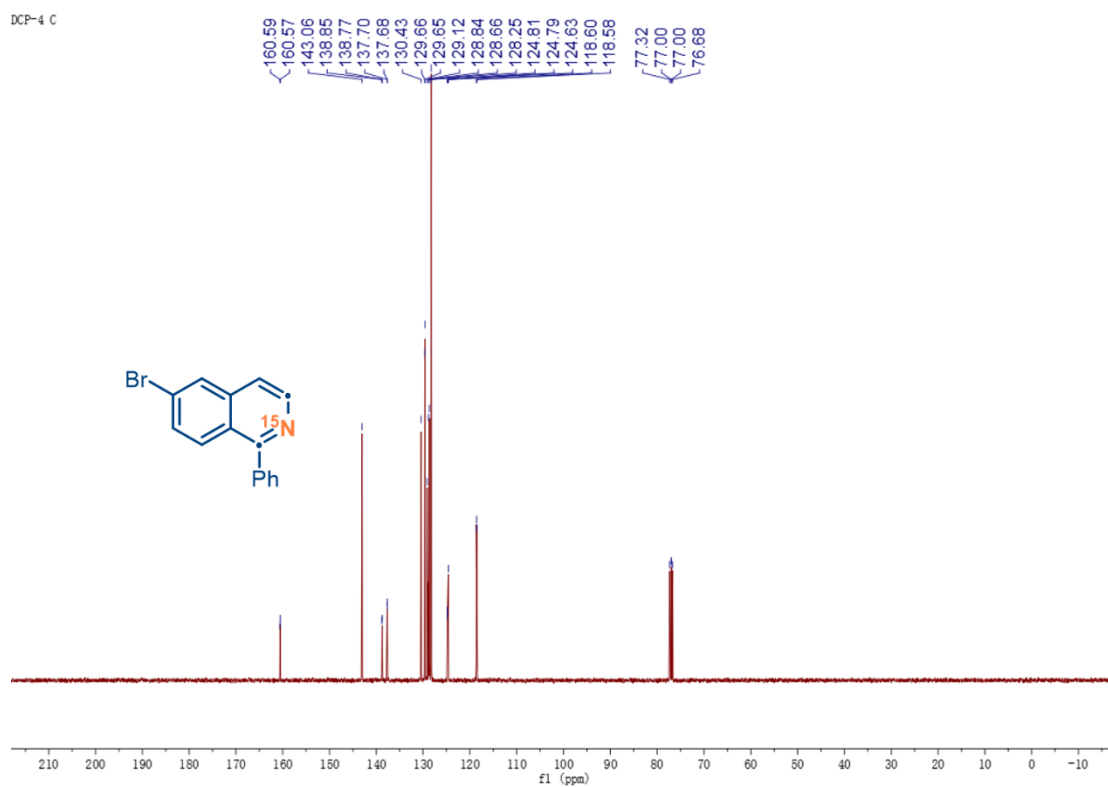
^{15}N NMR spectrum of **34** (50 MHz, CDCl_3)



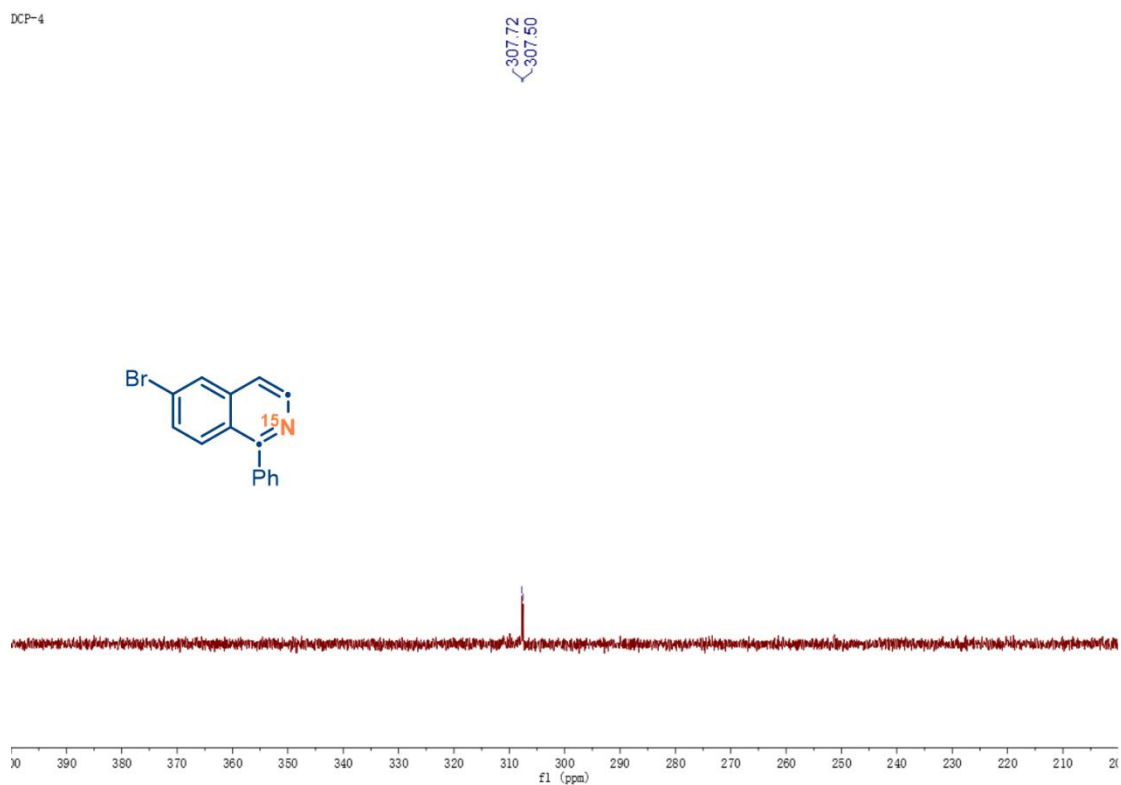
¹H NMR spectrum of **35** (400 MHz, CDCl₃)



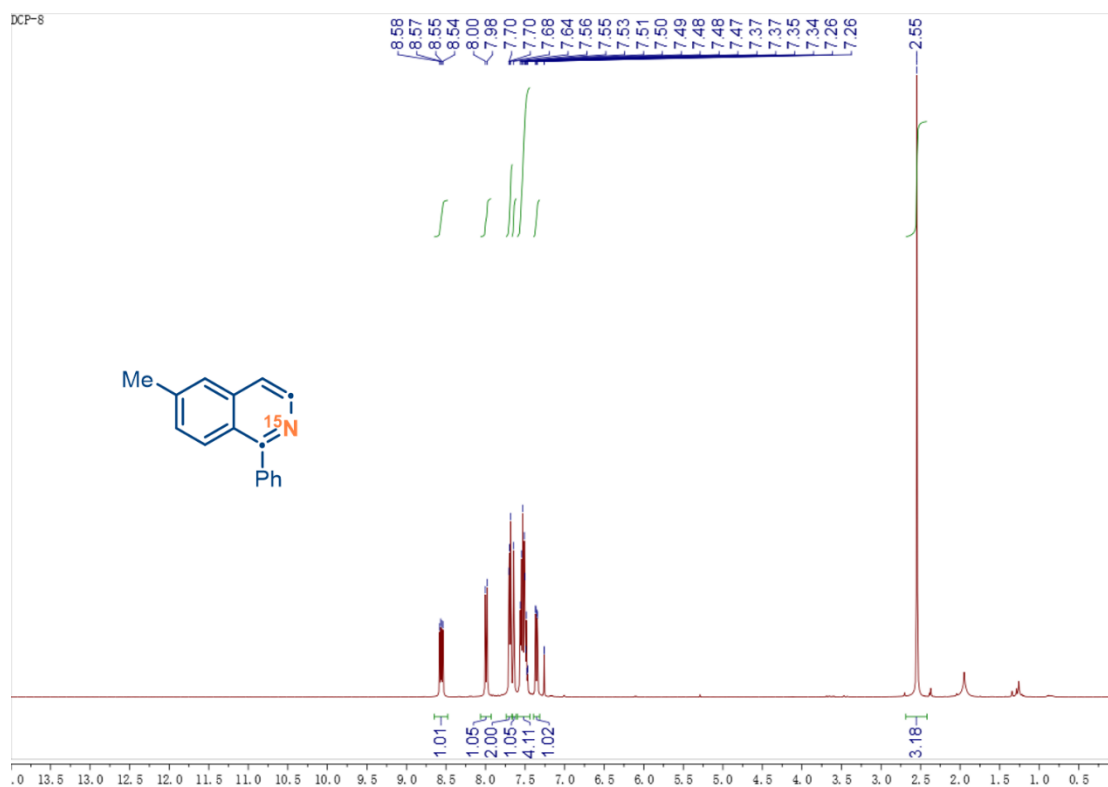
¹³C NMR spectrum of **35** (100 MHz, CDCl₃)



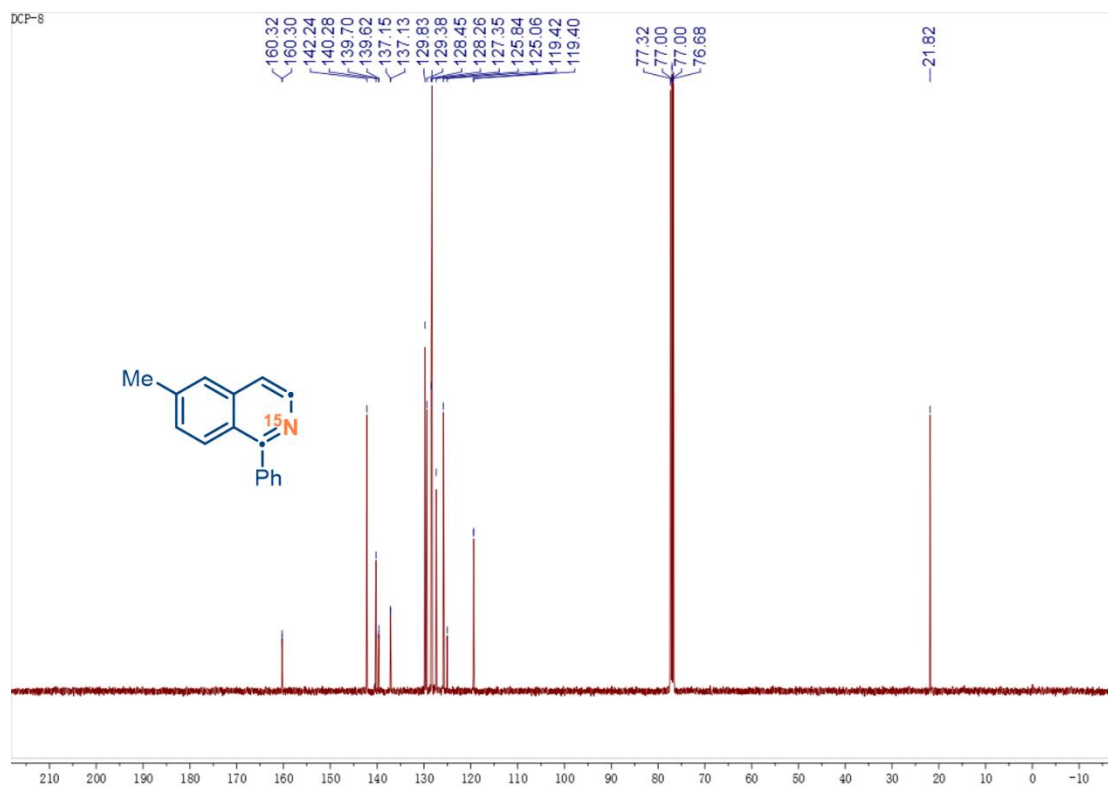
^{15}N NMR spectrum of **35** (50 MHz, CDCl_3)



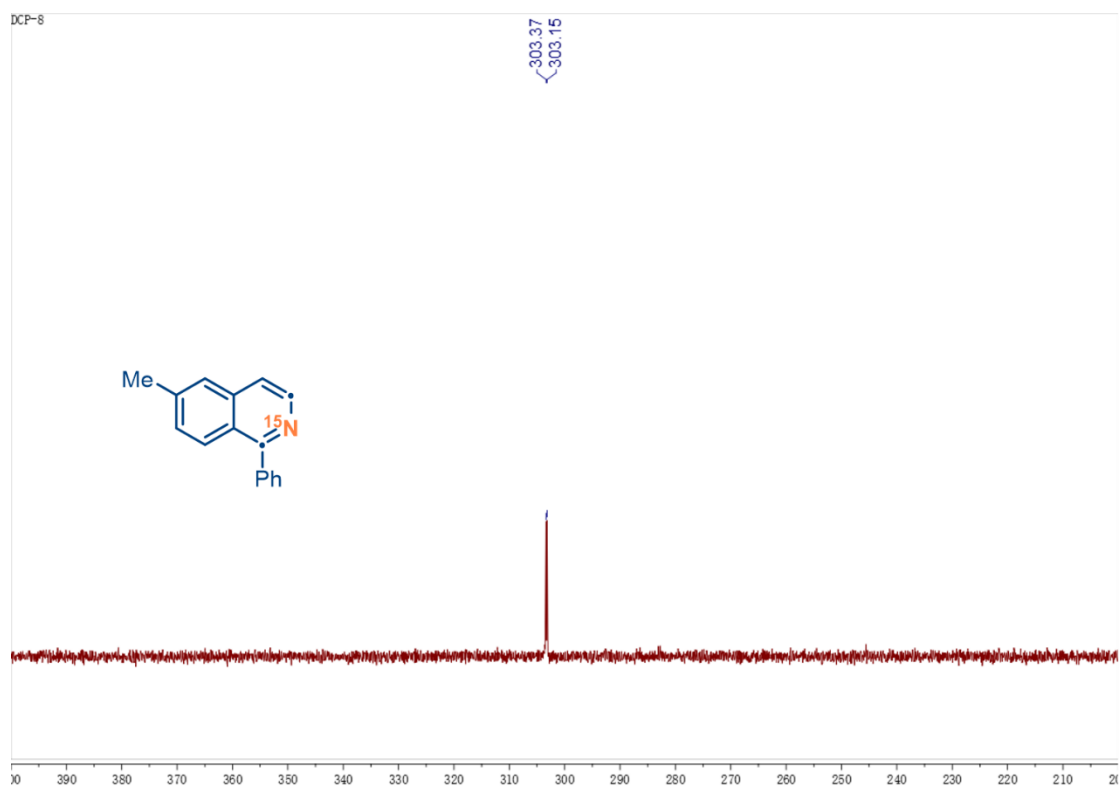
^1H NMR spectrum of **36** (400 MHz, CDCl_3)



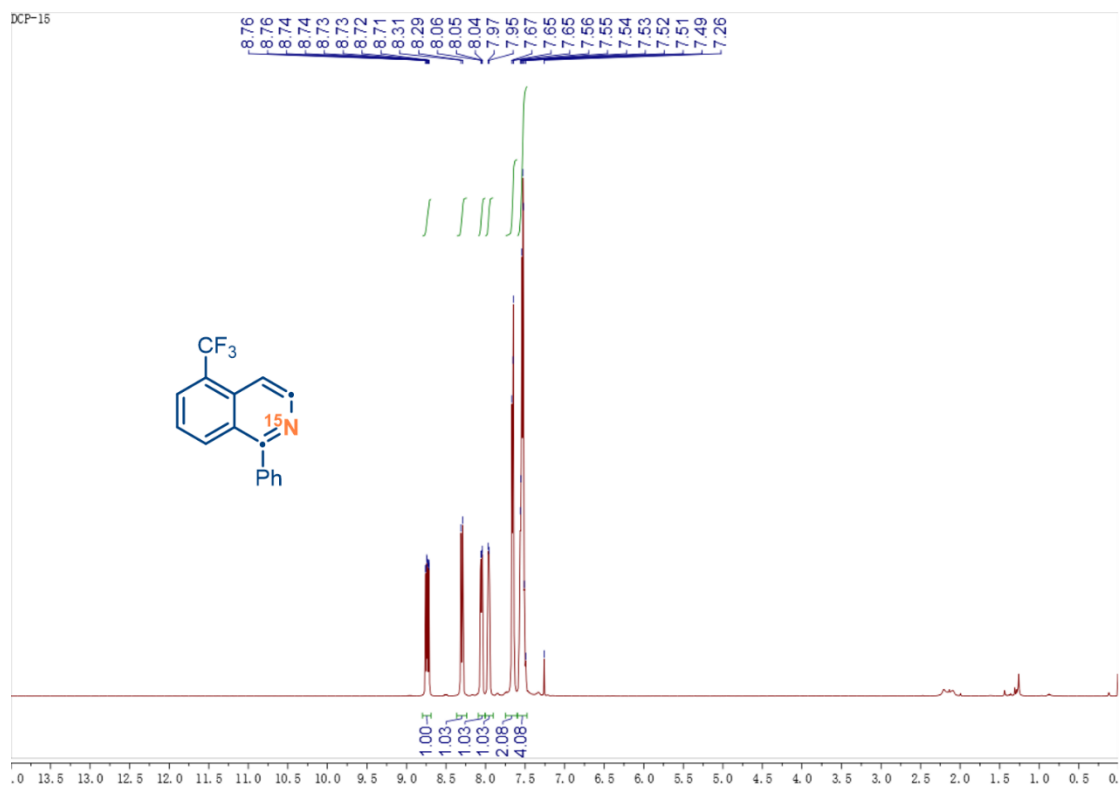
^{13}C NMR spectrum of **36** (100 MHz, CDCl_3)



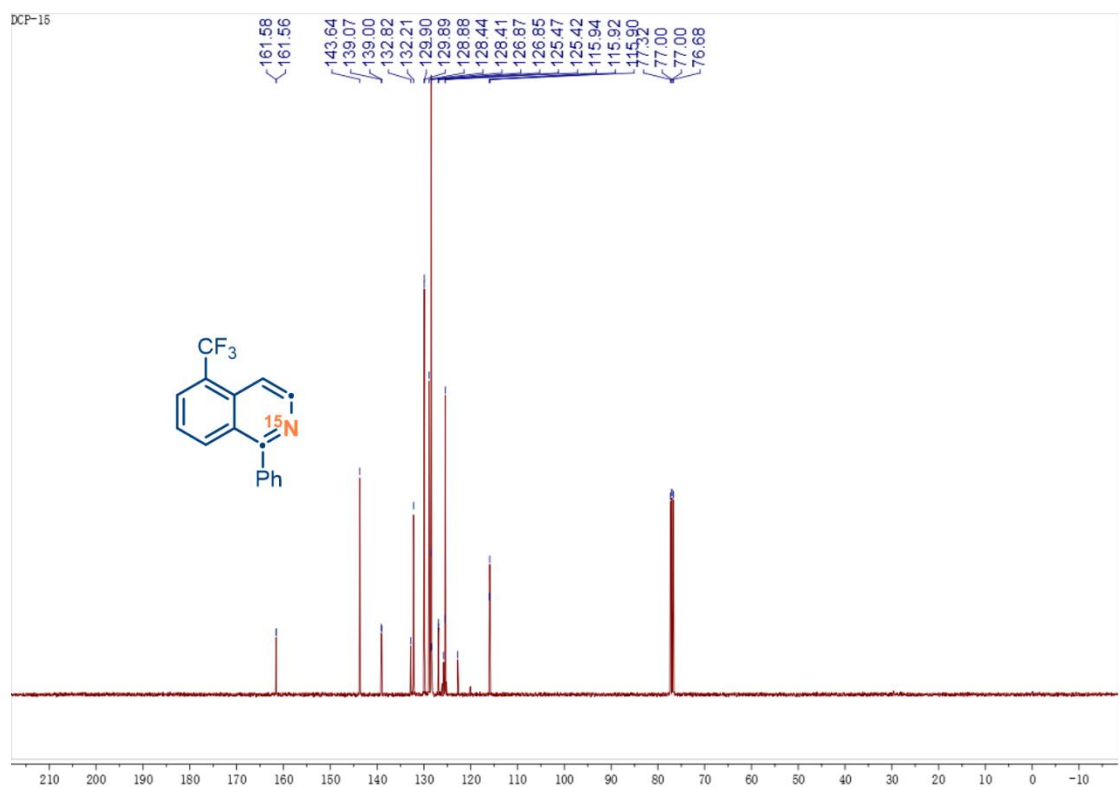
^{15}N NMR spectrum of **36** (50 MHz, CDCl_3)



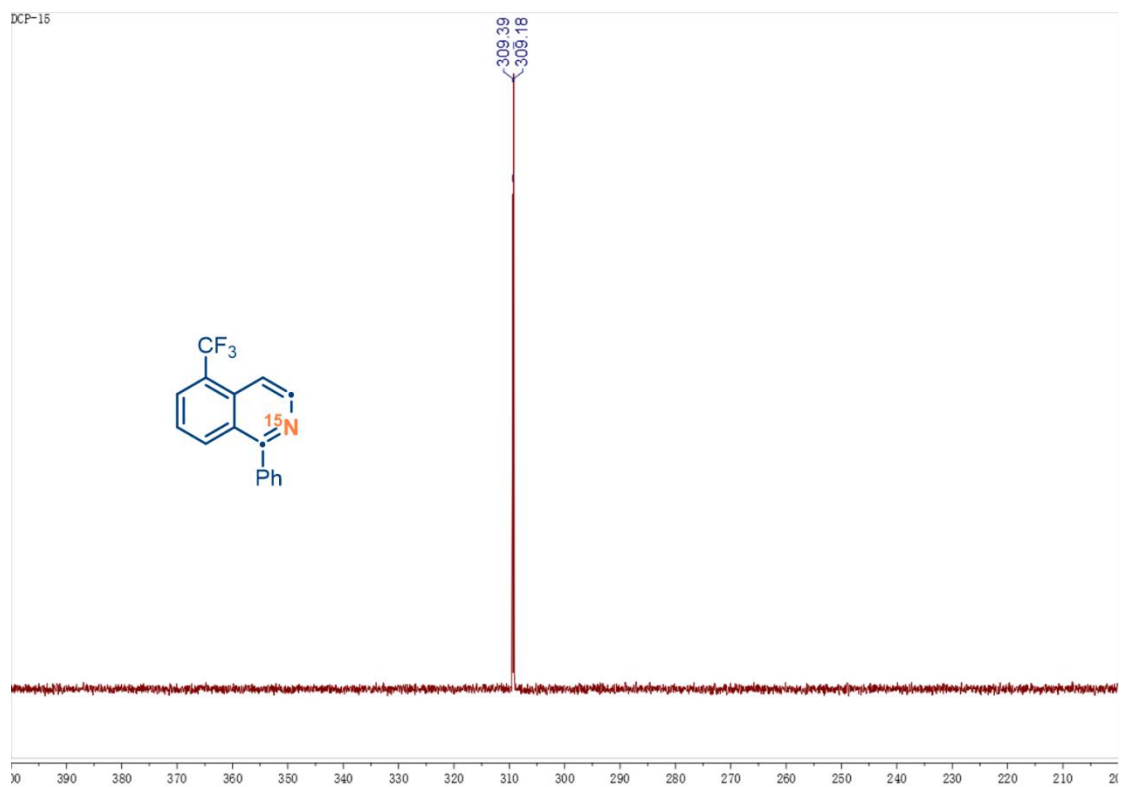
¹H NMR spectrum of **37** (400 MHz, CDCl₃)



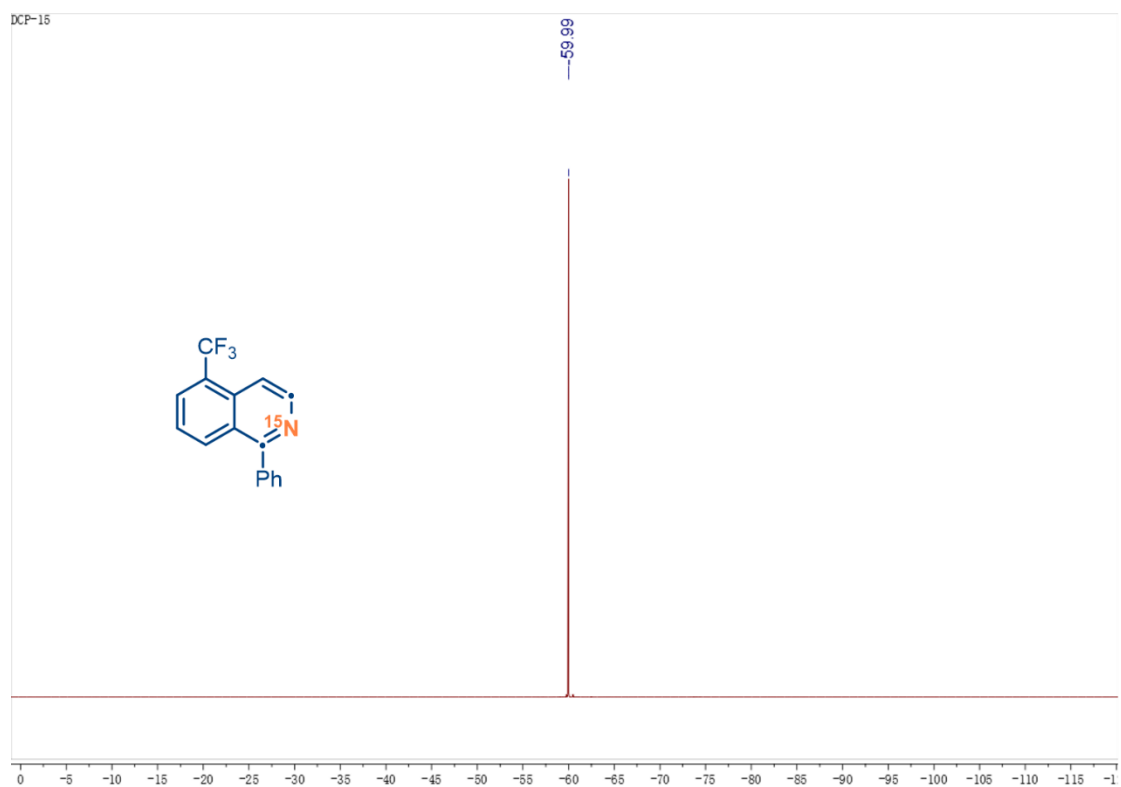
¹³C NMR spectrum of **37** (100 MHz, CDCl₃)



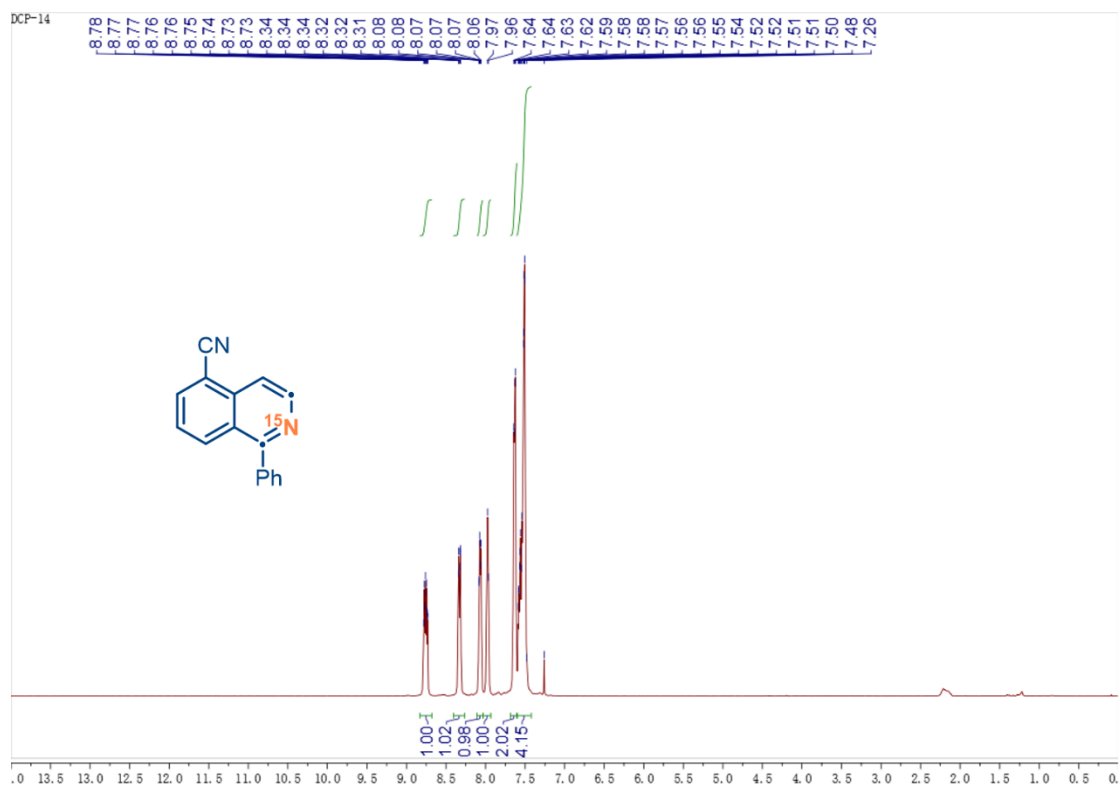
^{15}N NMR spectrum of **37** (50 MHz, CDCl_3)



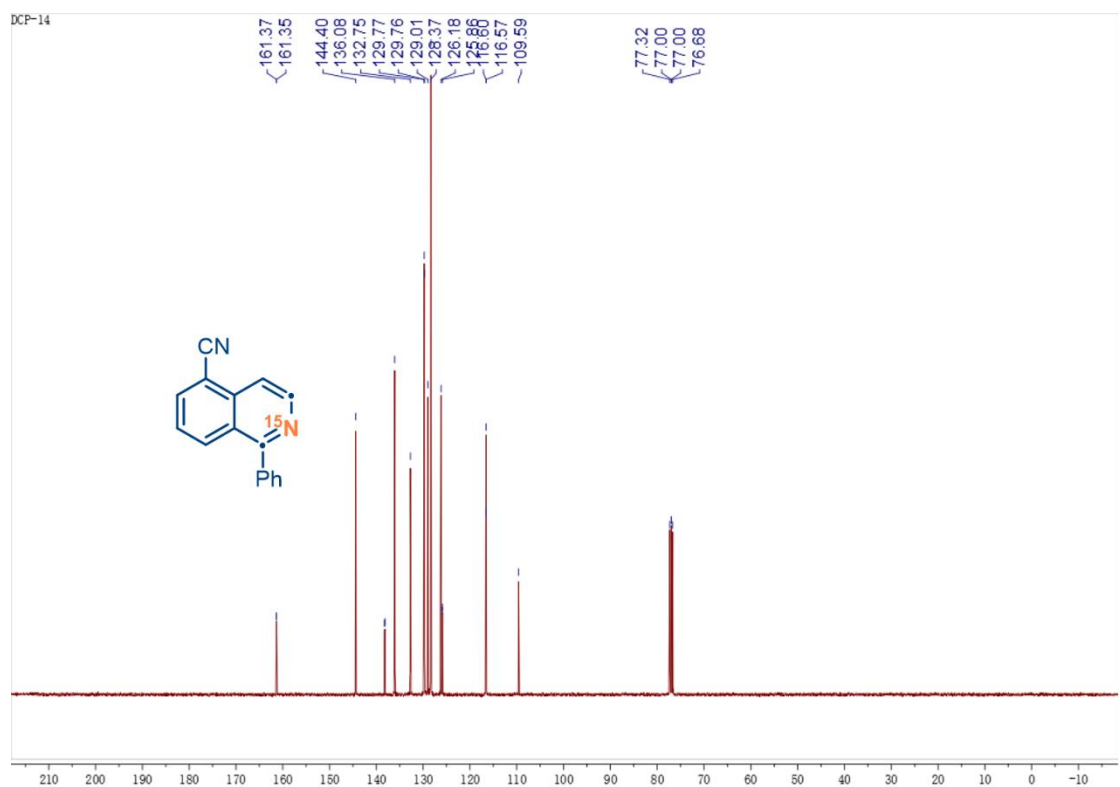
^{19}F NMR spectrum of **37** (376 MHz, CDCl_3)



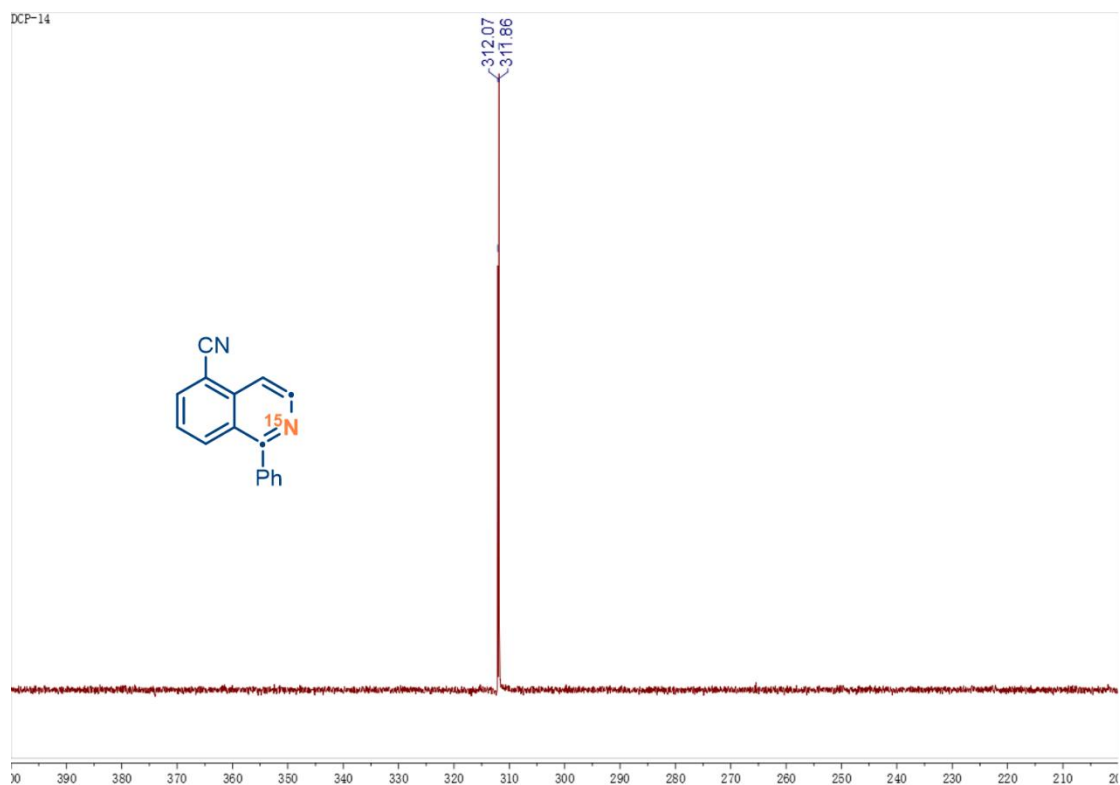
^1H NMR spectrum of **38** (400 MHz, CDCl_3)



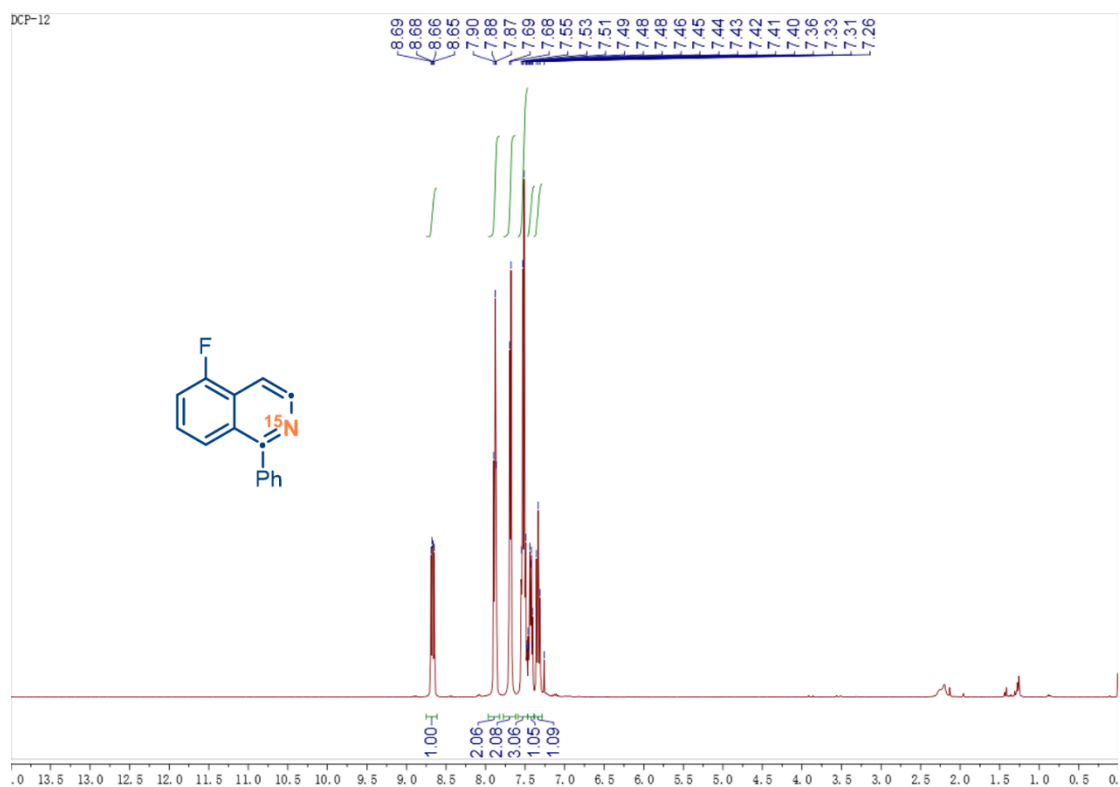
^{13}C NMR spectrum of **38** (100 MHz, CDCl_3)



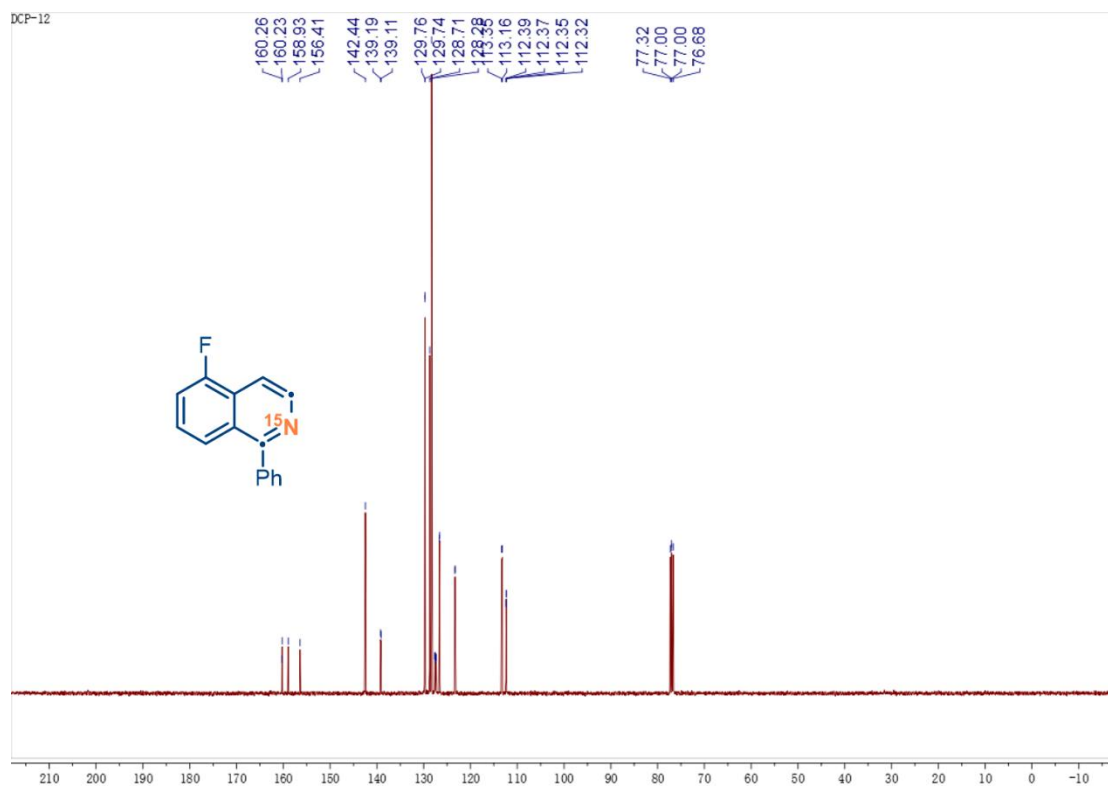
^{15}N NMR spectrum of **38** (50 MHz, CDCl_3)



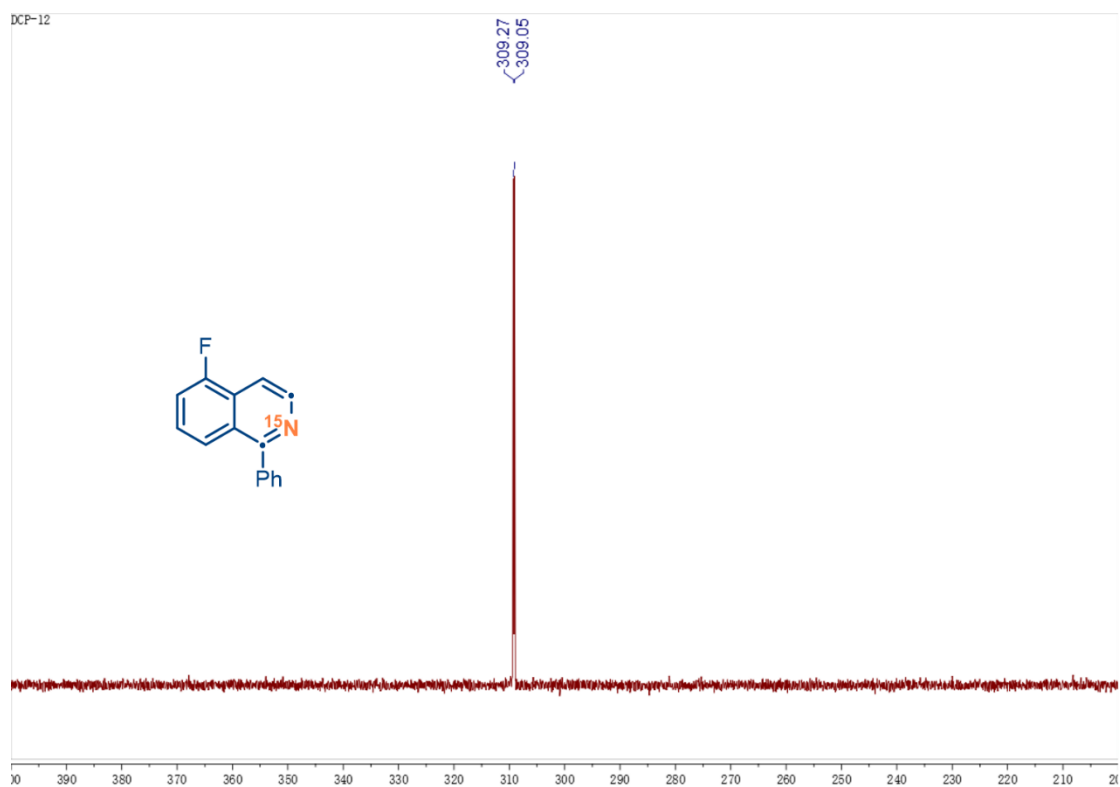
^1H NMR spectrum of **39** (400 MHz, CDCl_3)



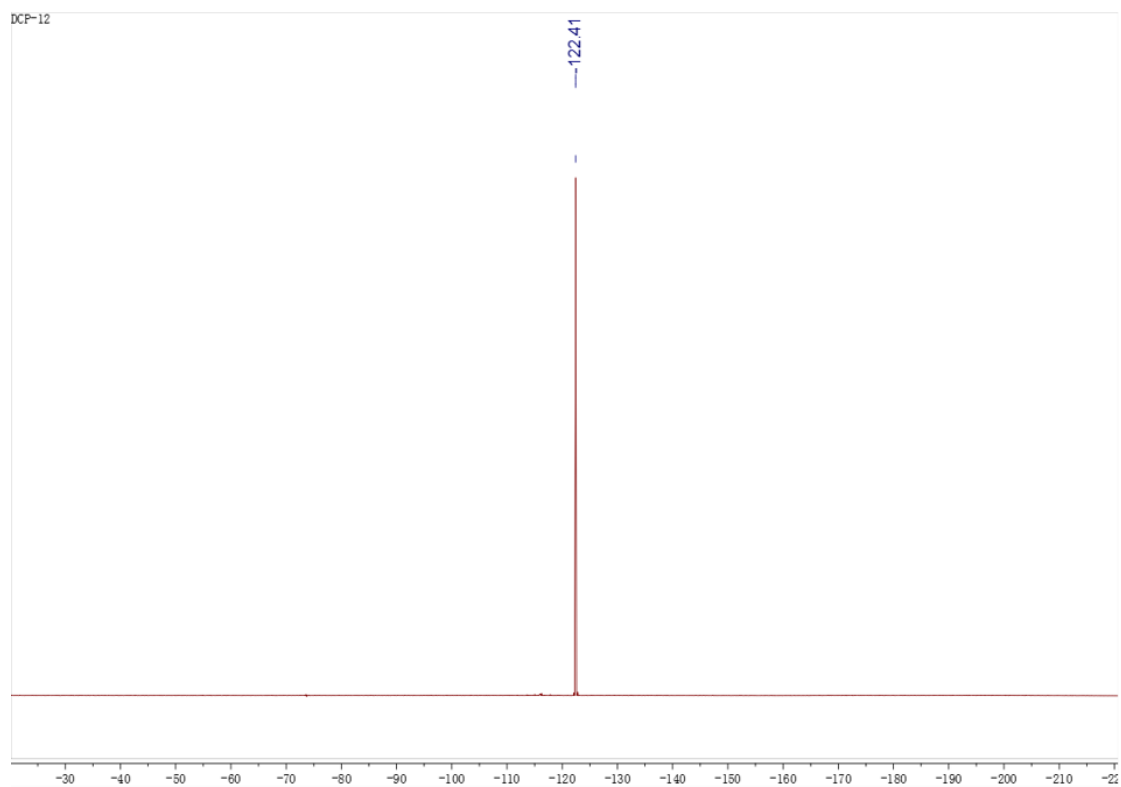
^{13}C NMR spectrum of **39** (100 MHz, CDCl_3)



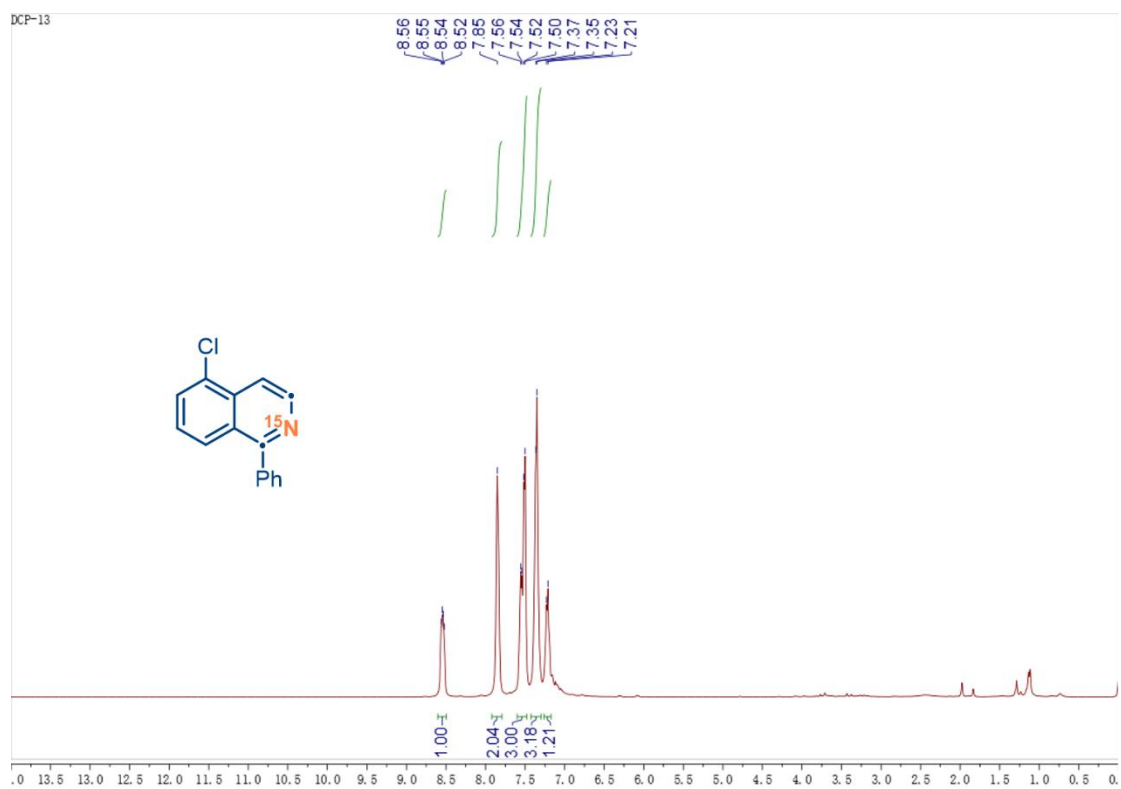
^{15}N NMR spectrum of **39** (50 MHz, CDCl_3)



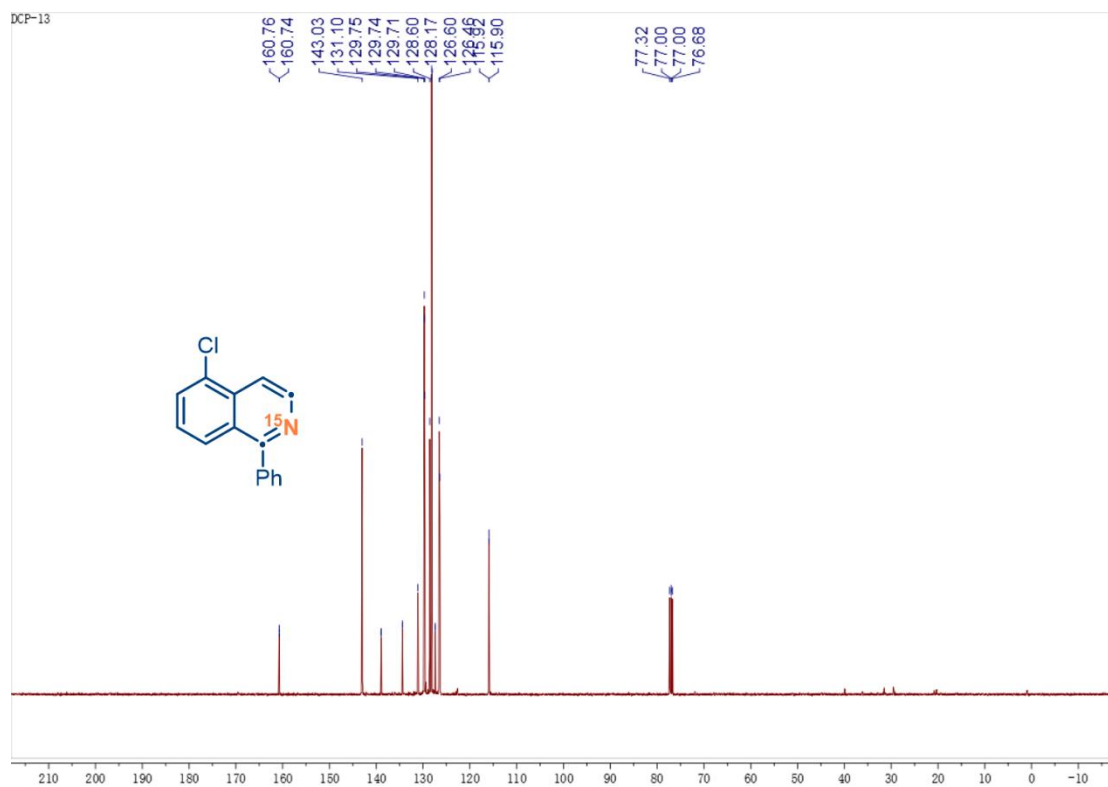
^{19}F NMR spectrum of **39** (376 MHz, CDCl_3)



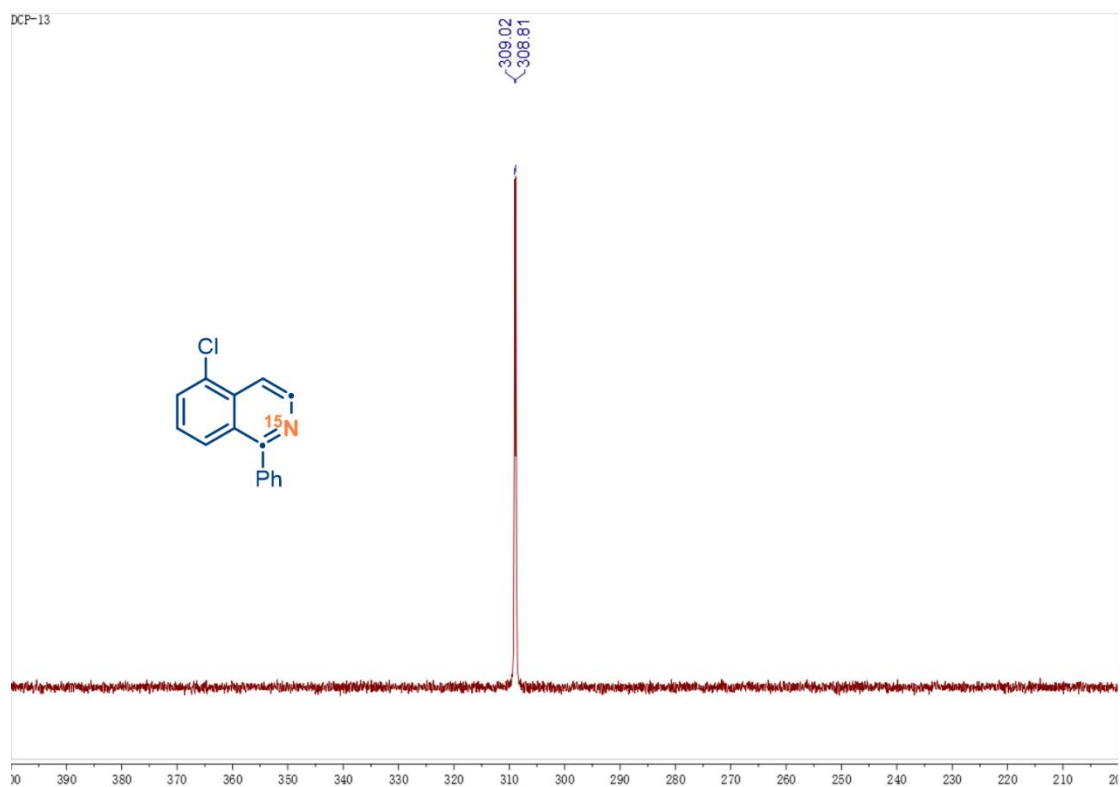
^1H NMR spectrum of **40** (400 MHz, CDCl_3)



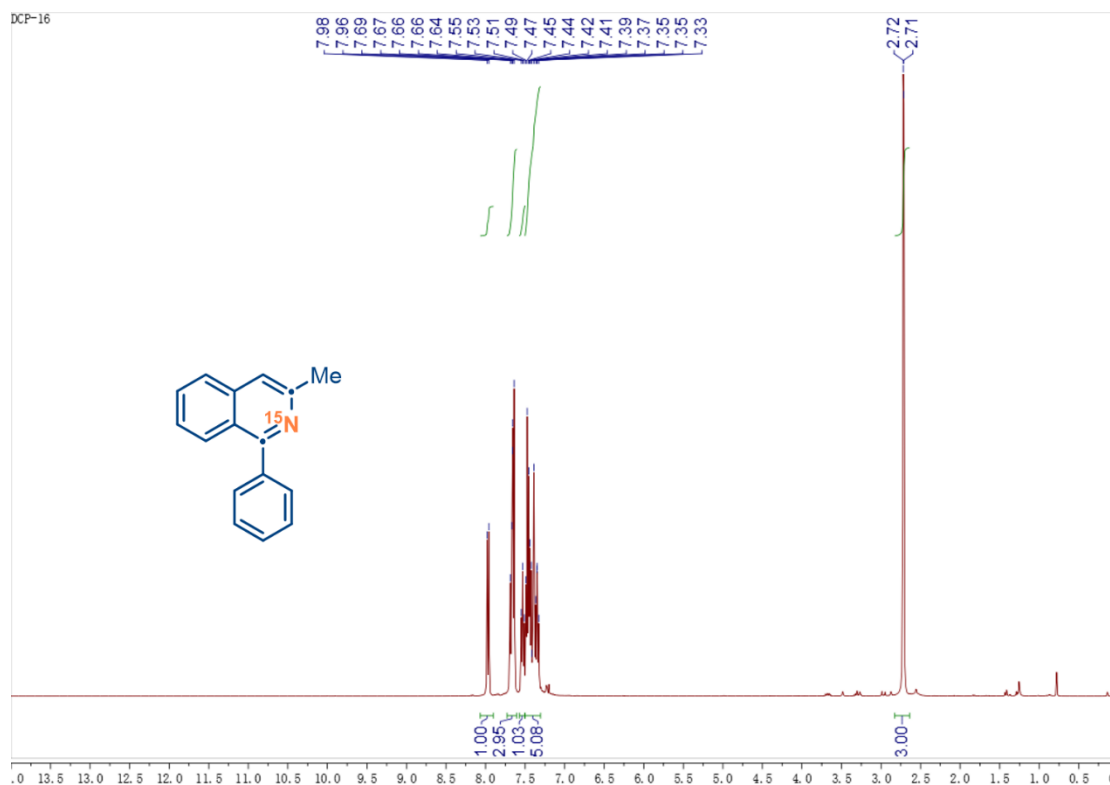
^{13}C NMR spectrum of **4o** (100 MHz, CDCl_3)



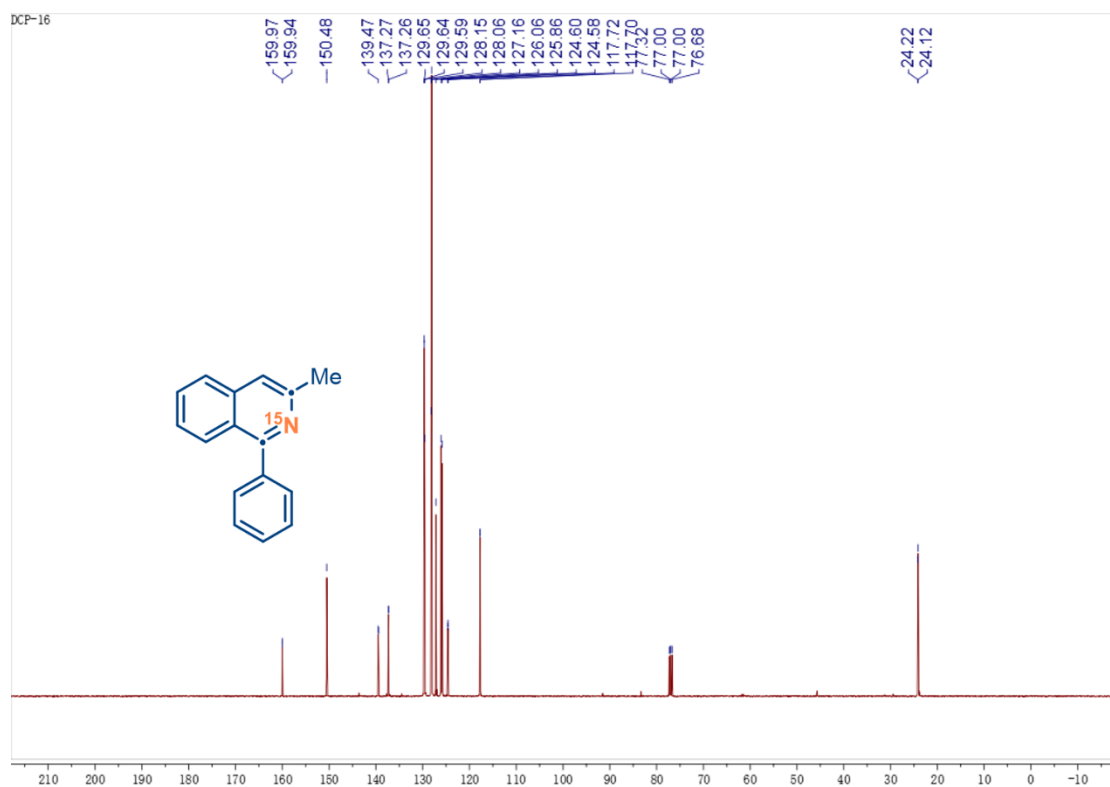
^{15}N NMR spectrum of **4o** (50 MHz, CDCl_3)



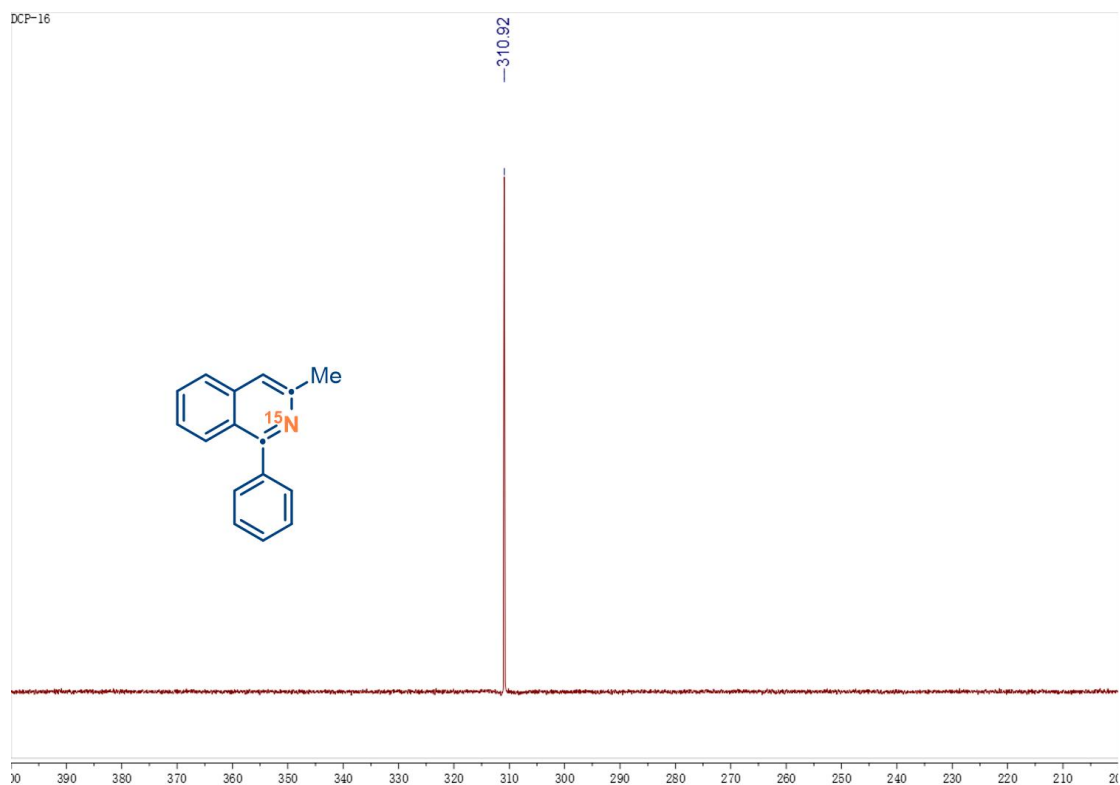
¹H NMR spectrum of **41** (400 MHz, CDCl₃)



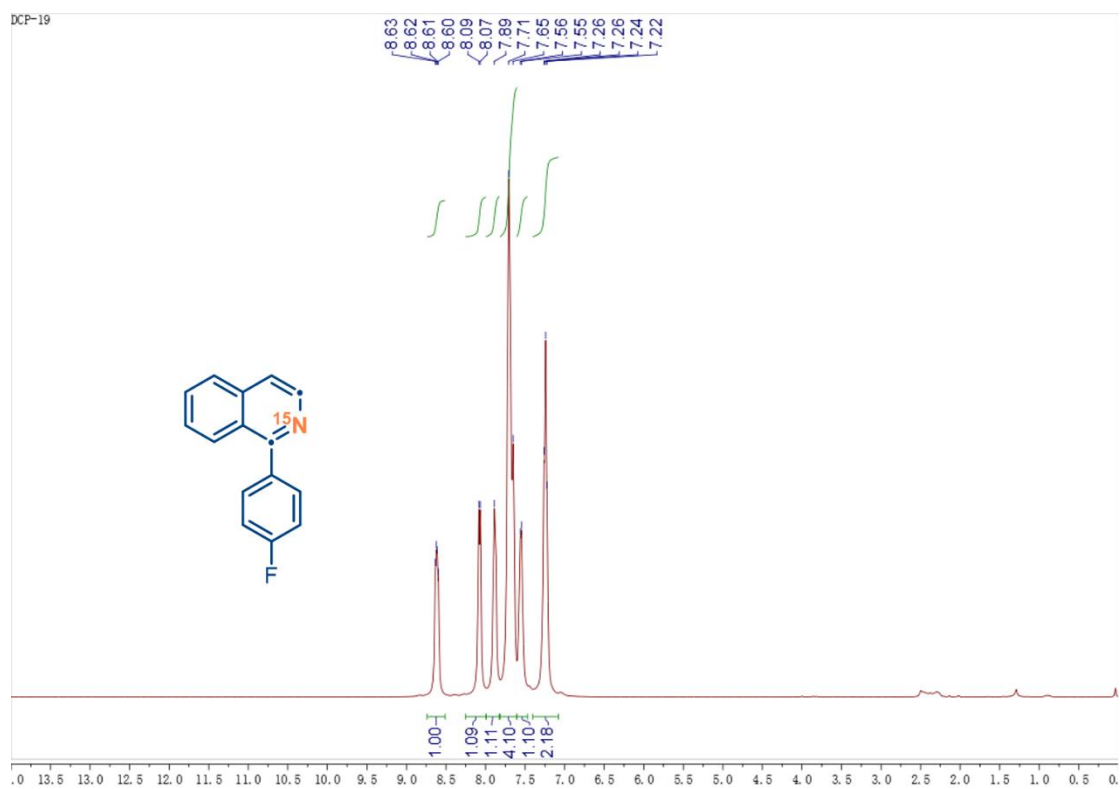
¹³C NMR spectrum of **41** (100 MHz, CDCl₃)



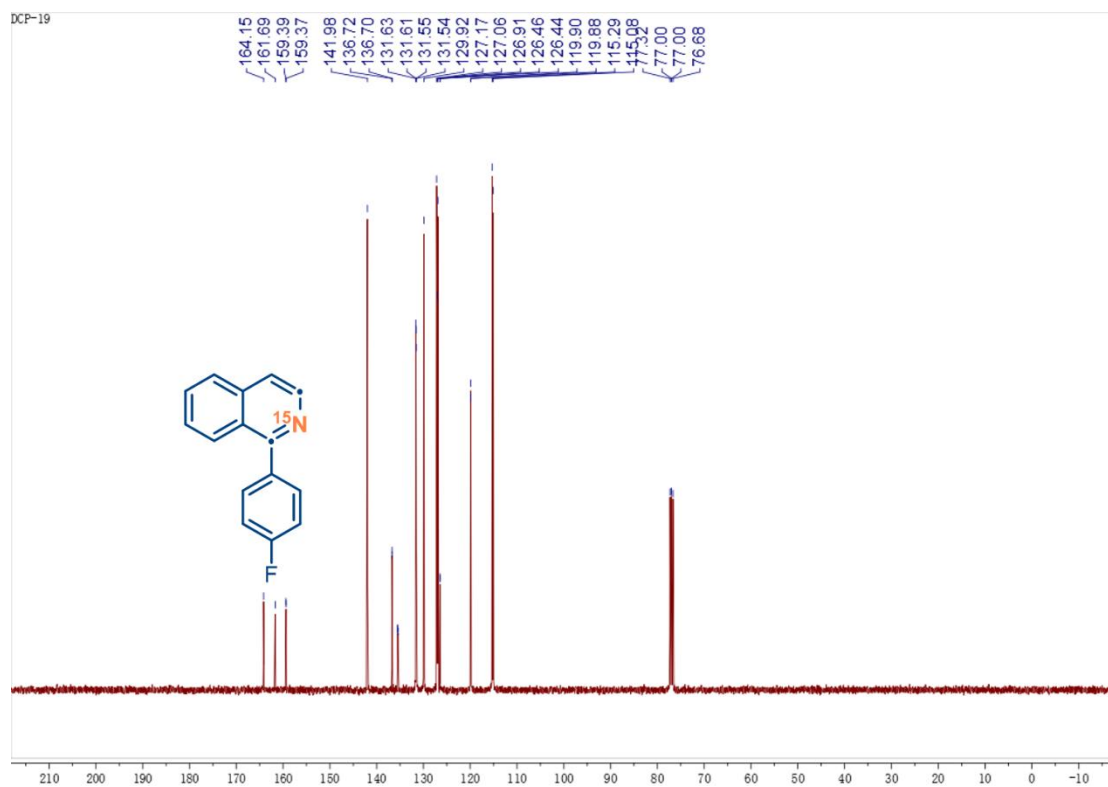
^{15}N NMR spectrum of **41** (50 MHz, CDCl_3)



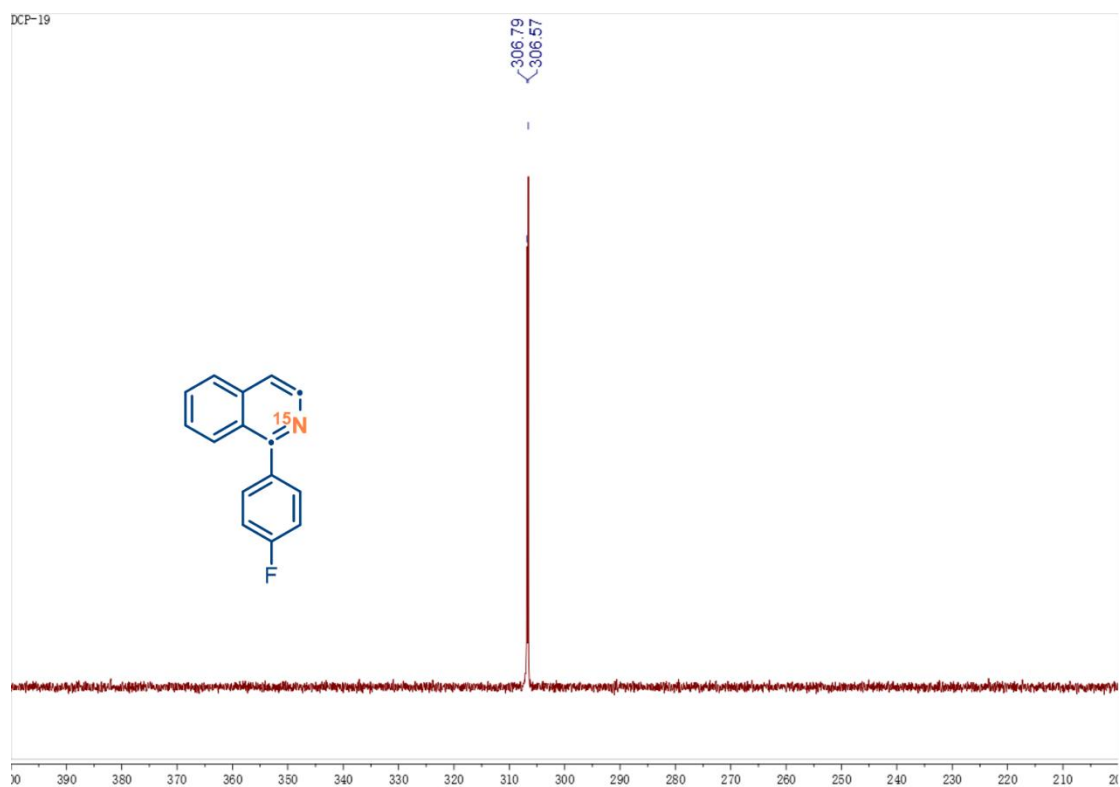
^1H NMR spectrum of **42** (400 MHz, CDCl_3)



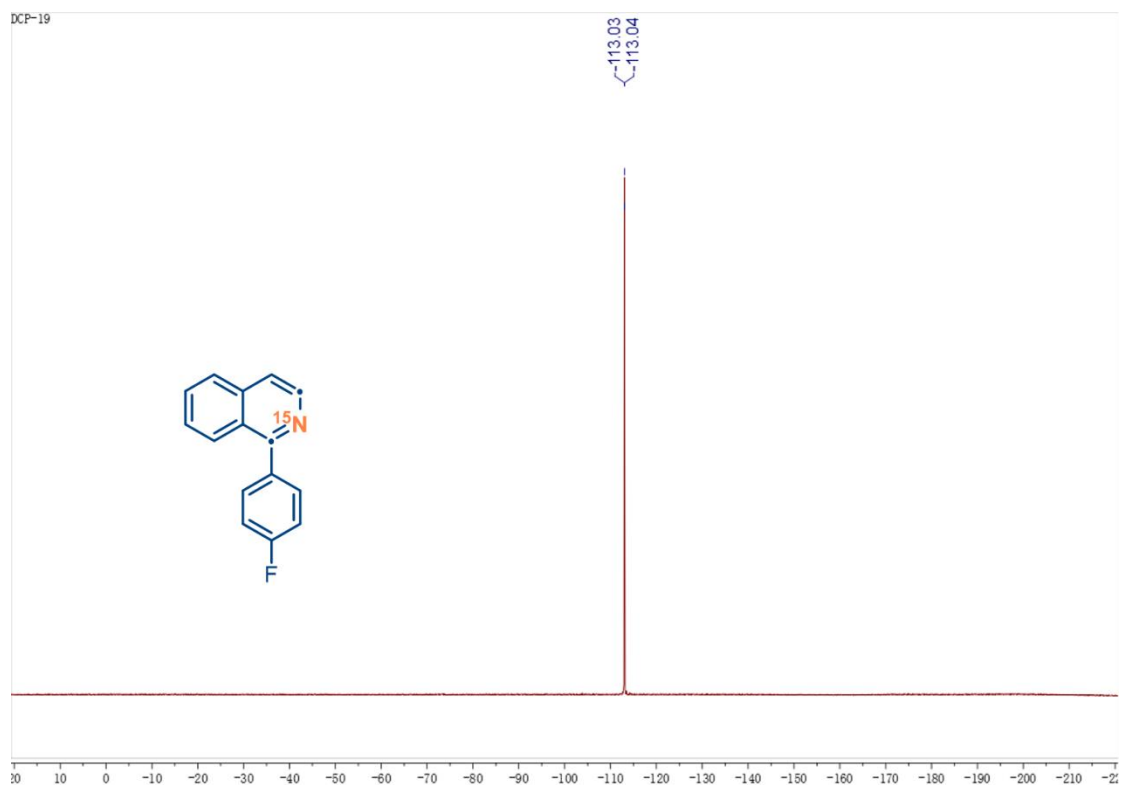
^{13}C NMR spectrum of **42** (100 MHz, CDCl_3)



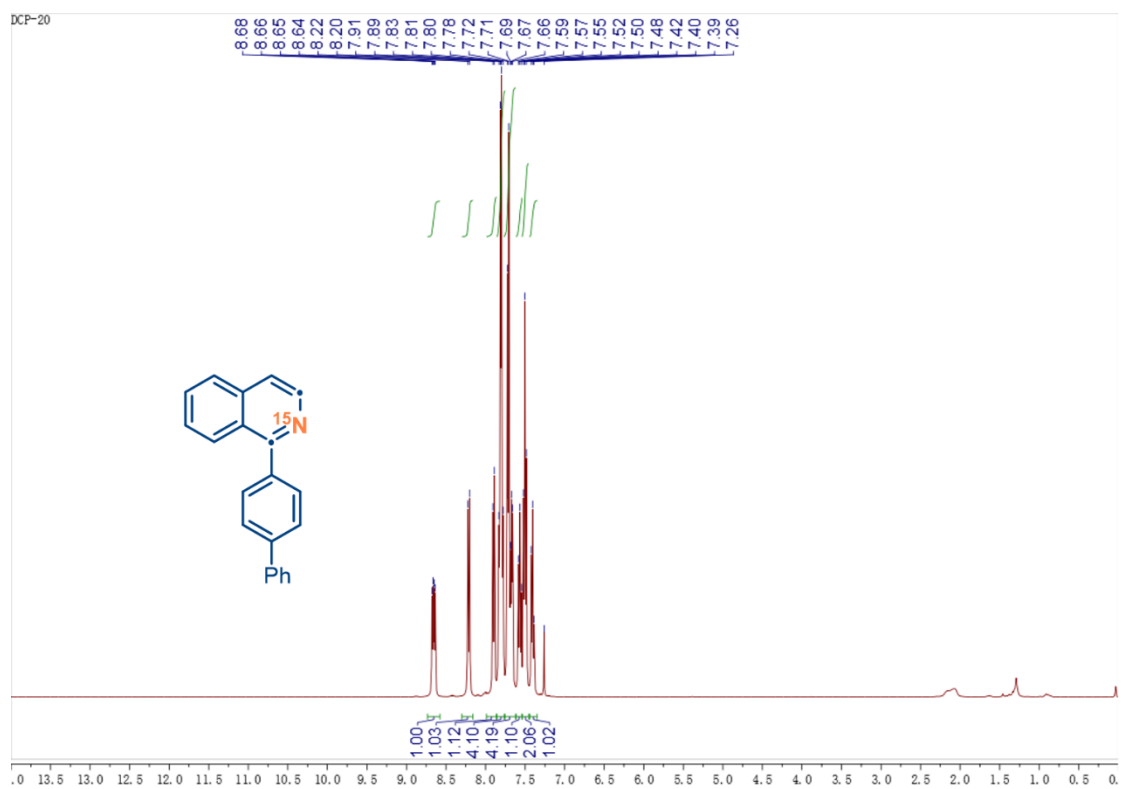
^{15}N NMR spectrum of **42** (50 MHz, CDCl_3)



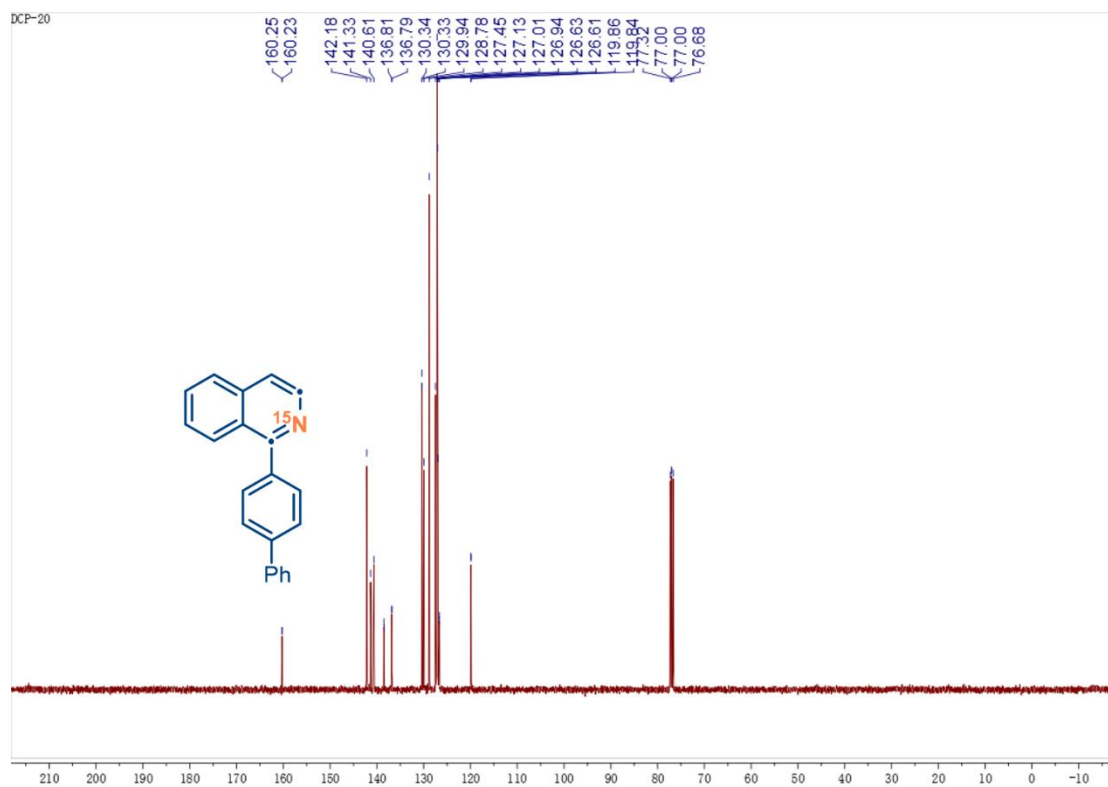
^{19}F NMR spectrum of **42** (376 MHz, CDCl_3)



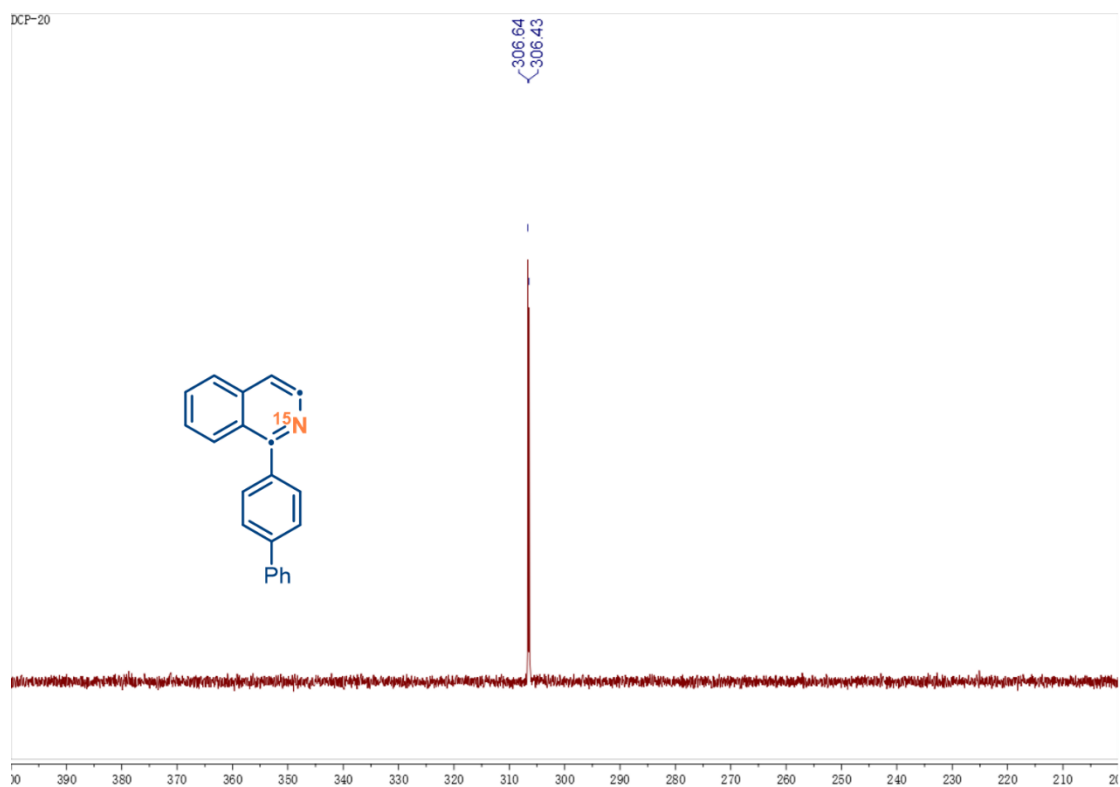
^1H NMR spectrum of **43** (400 MHz, CDCl_3)



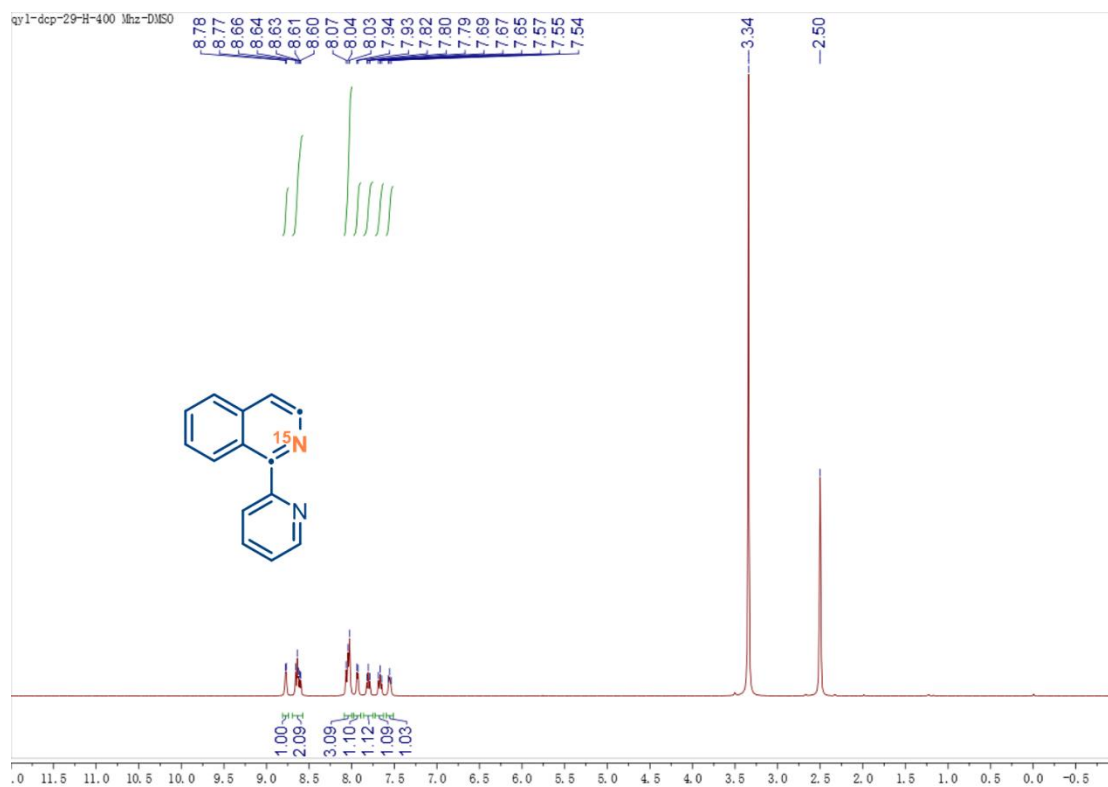
^{13}C NMR spectrum of **43** (100 MHz, CDCl_3)



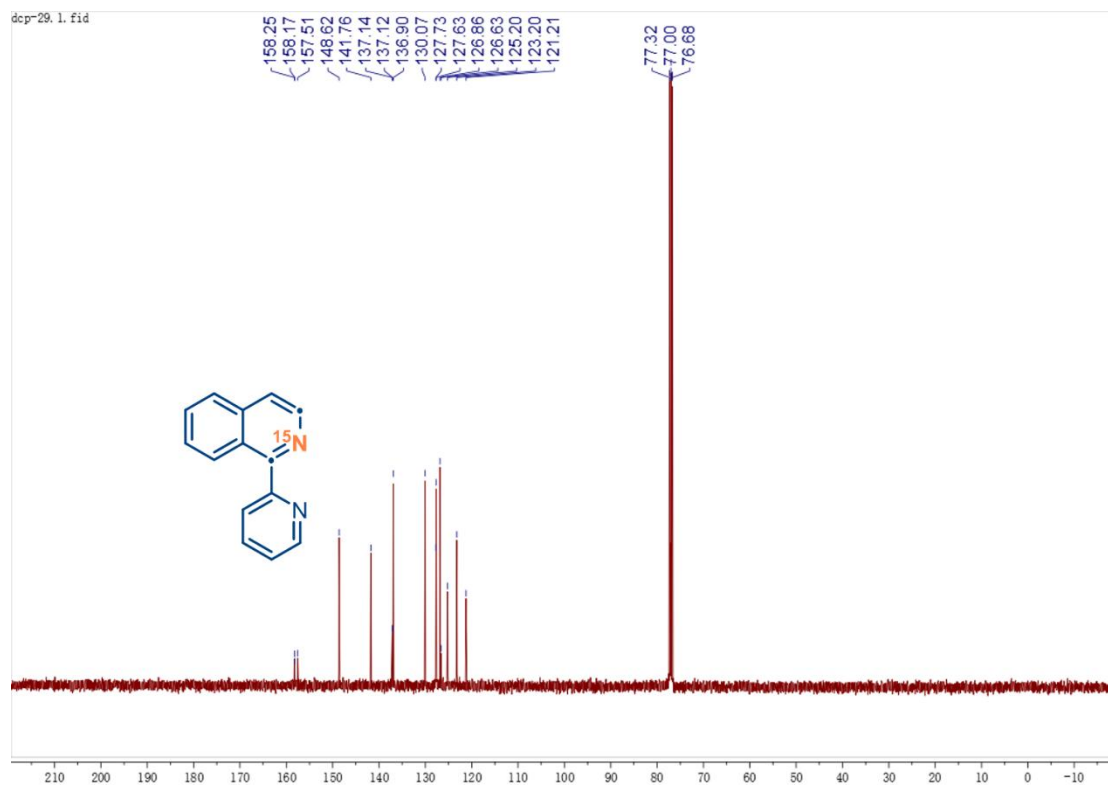
^{15}N NMR spectrum of **43** (50 MHz, CDCl_3)



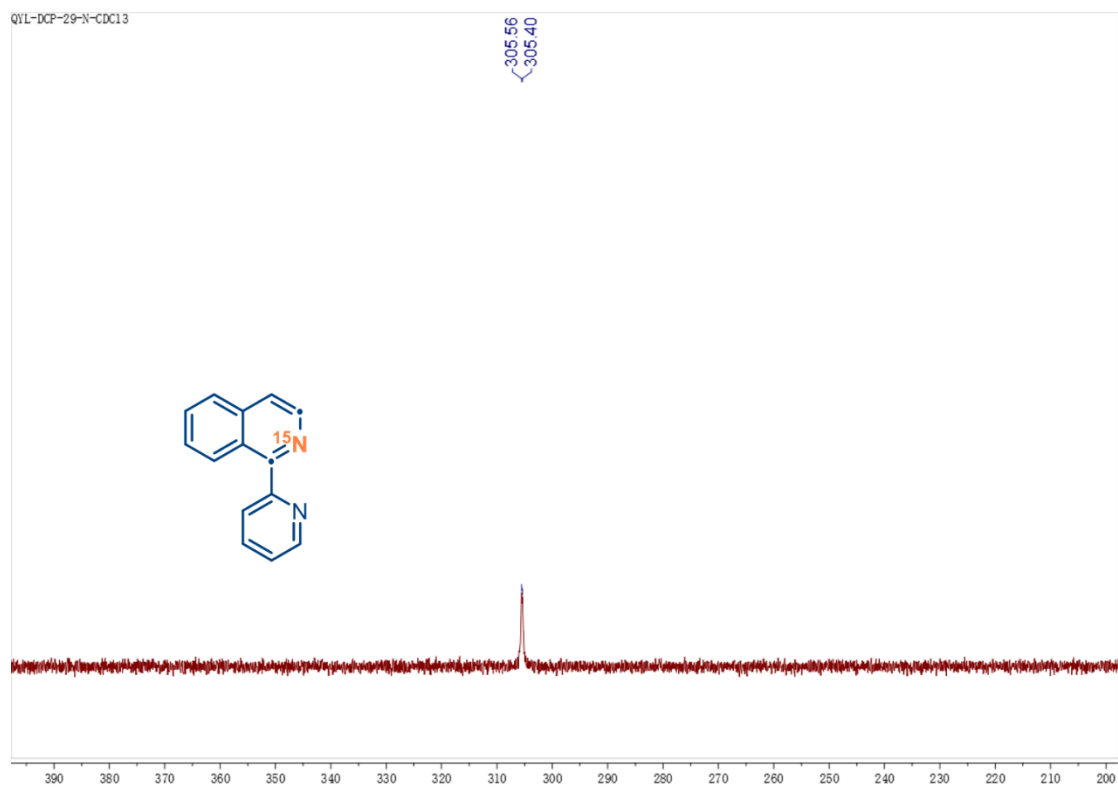
¹H NMR spectrum of **45** (400 MHz, DMSO-*d*₆)



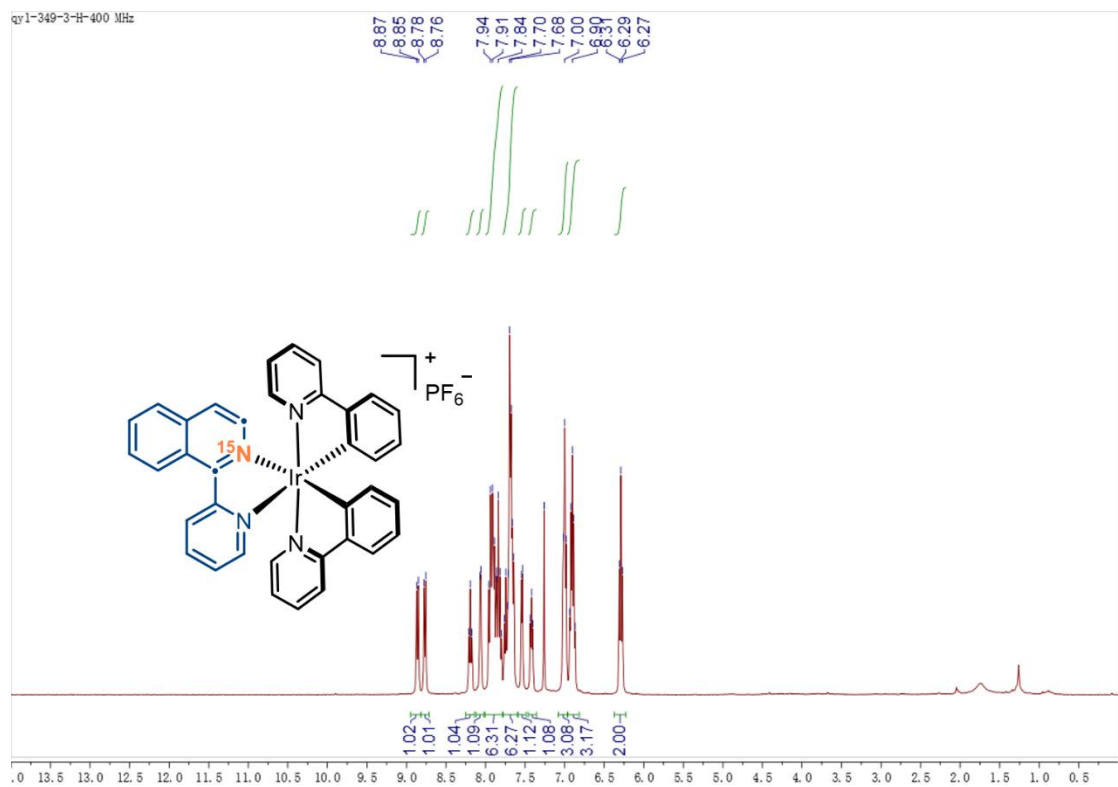
¹³C NMR spectrum of **45** (100 MHz, CDCl₃)



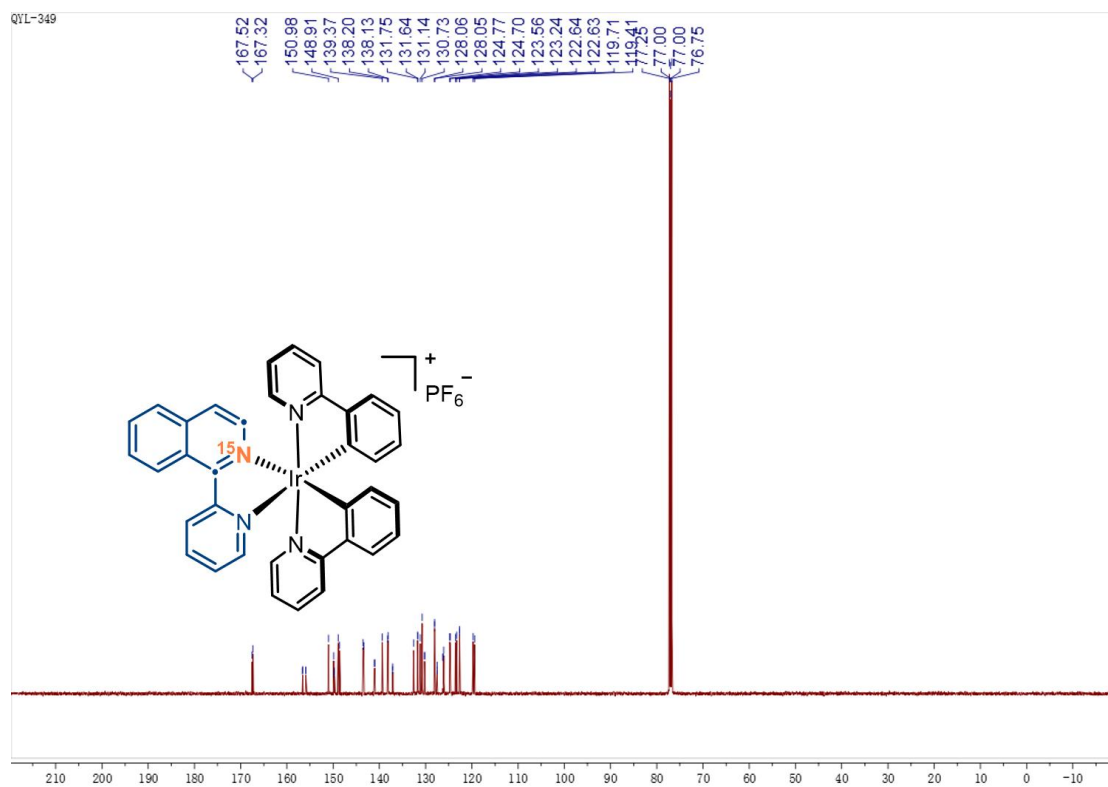
^{15}N NMR spectrum of **45** (50 MHz, CDCl_3)



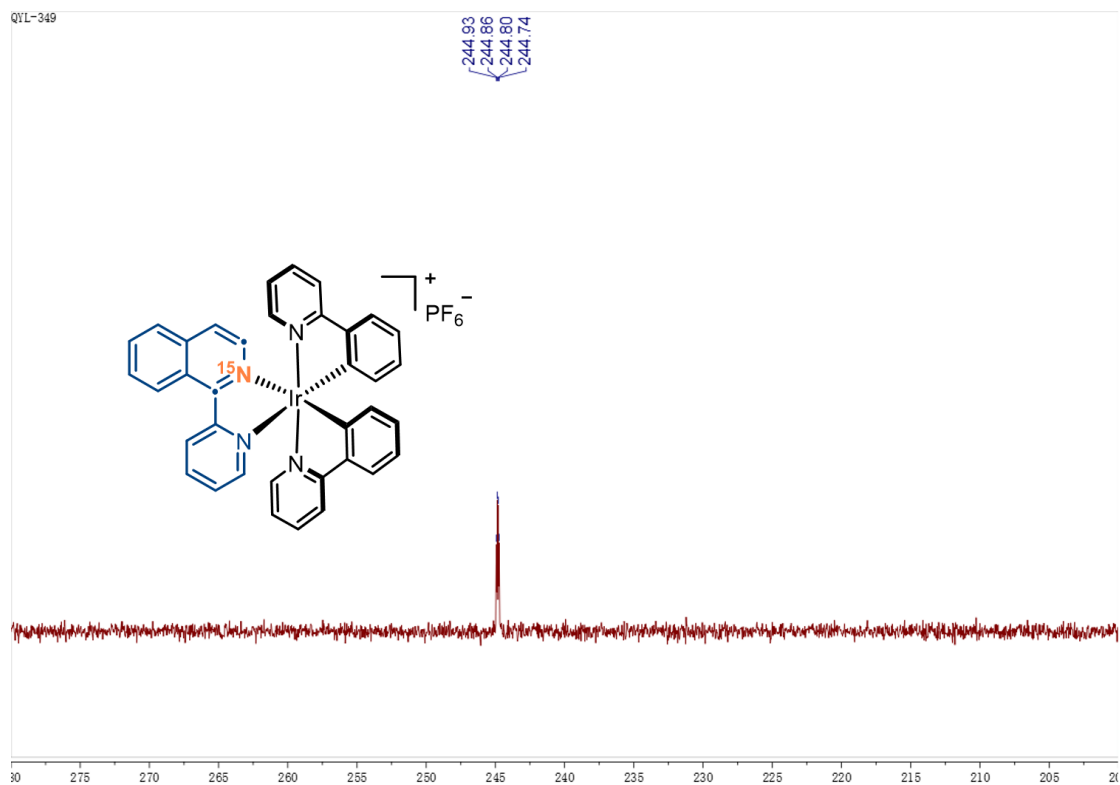
^1H NMR spectrum of **46** (400 MHz, CDCl_3)



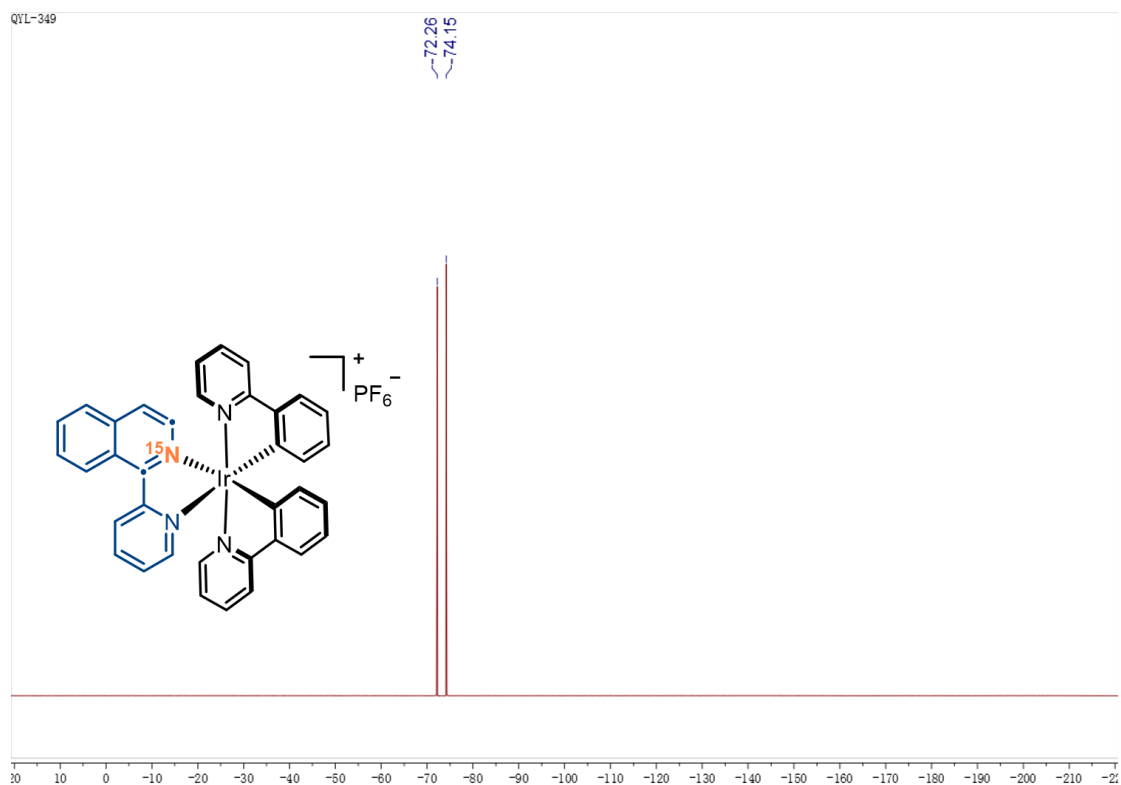
^{13}C NMR spectrum of **46** (125 MHz, CDCl_3)



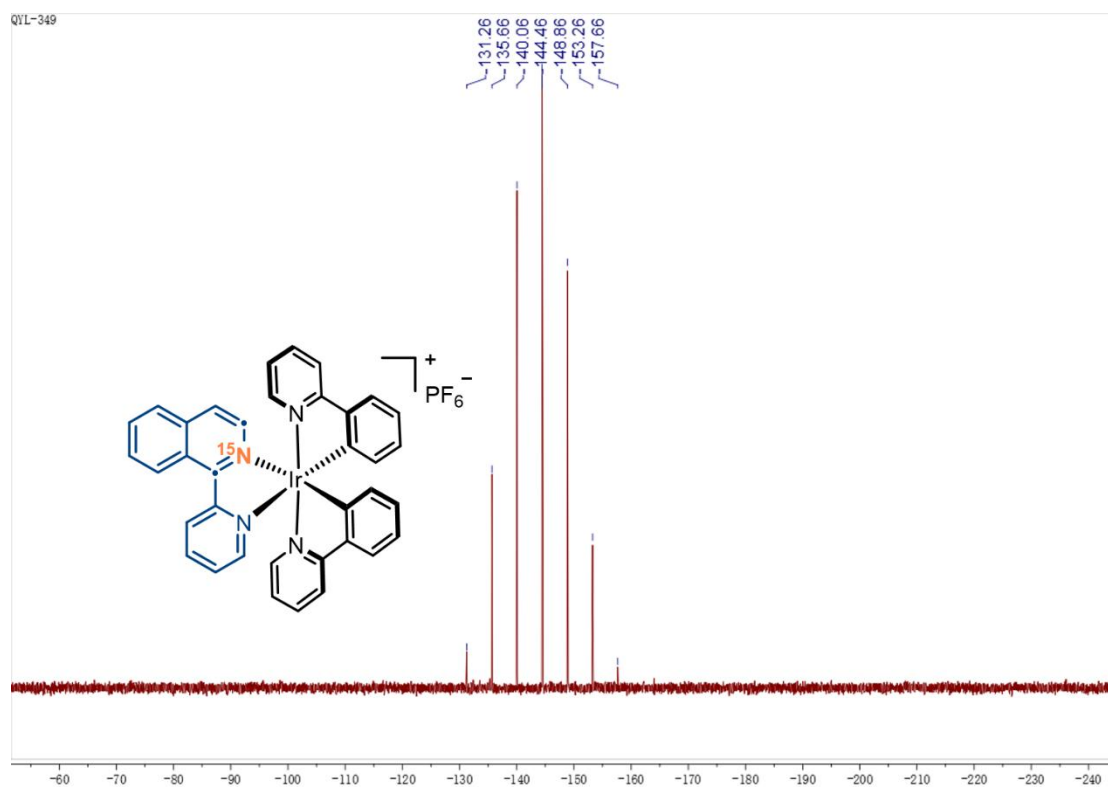
^{15}N NMR spectrum of **46** (50 MHz, CDCl_3)



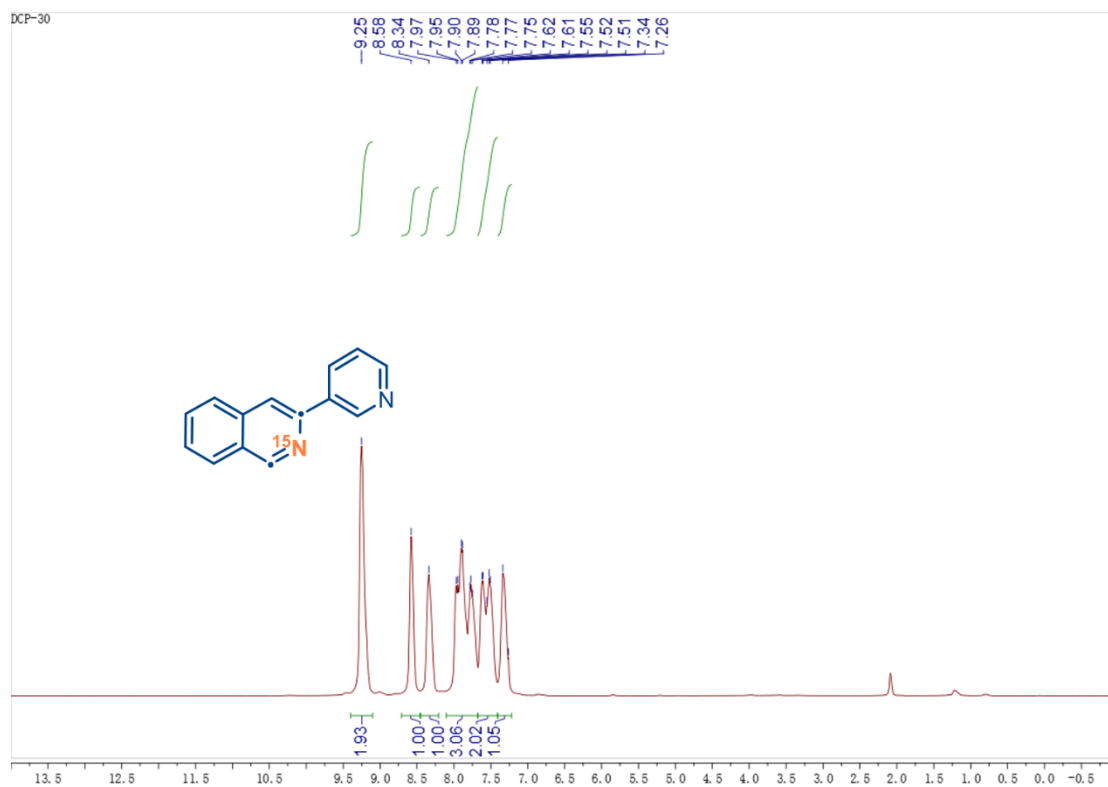
^{19}F NMR spectrum of **46** (376 MHz, CDCl_3)



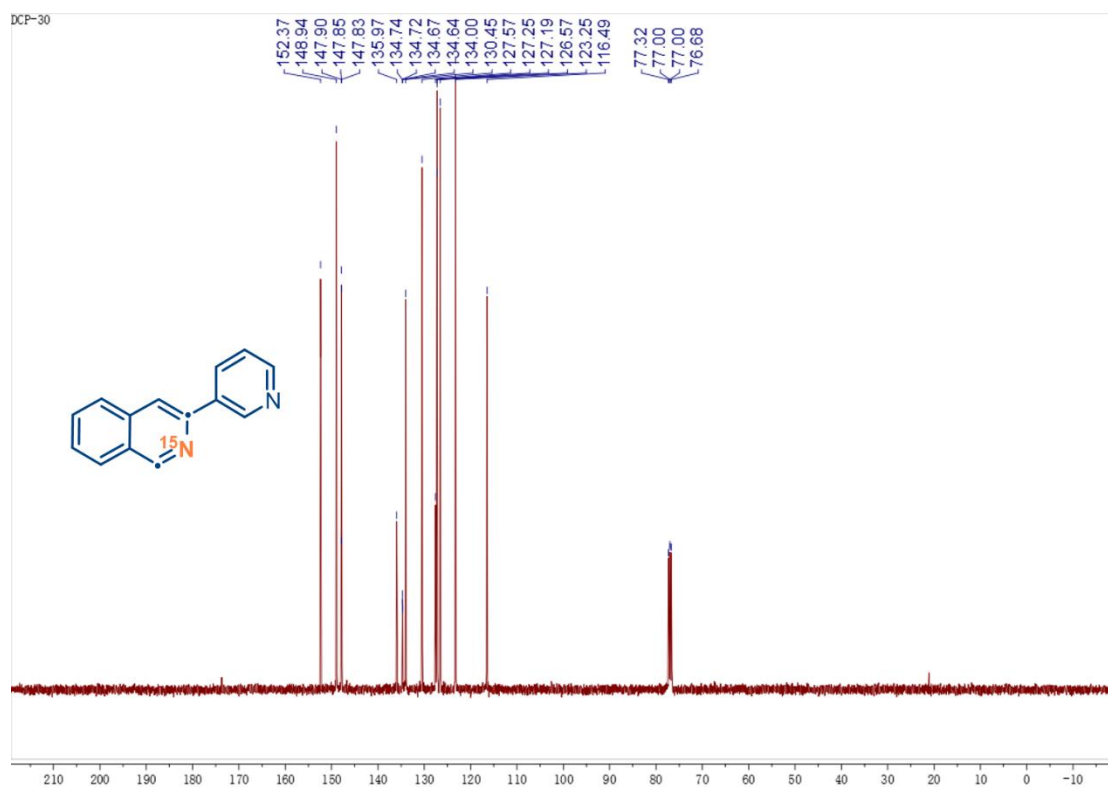
^{31}P NMR spectrum of **46** (162 MHz, CDCl_3)



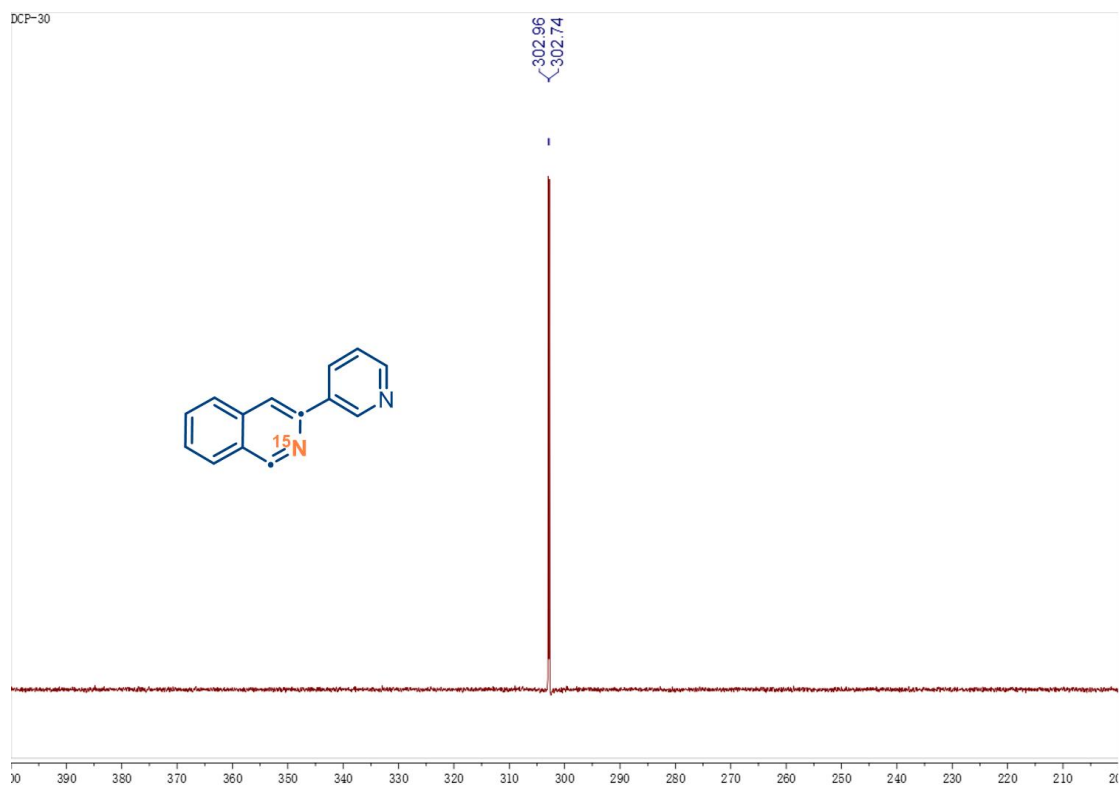
^1H NMR spectrum of **48** (400 MHz, CDCl_3)



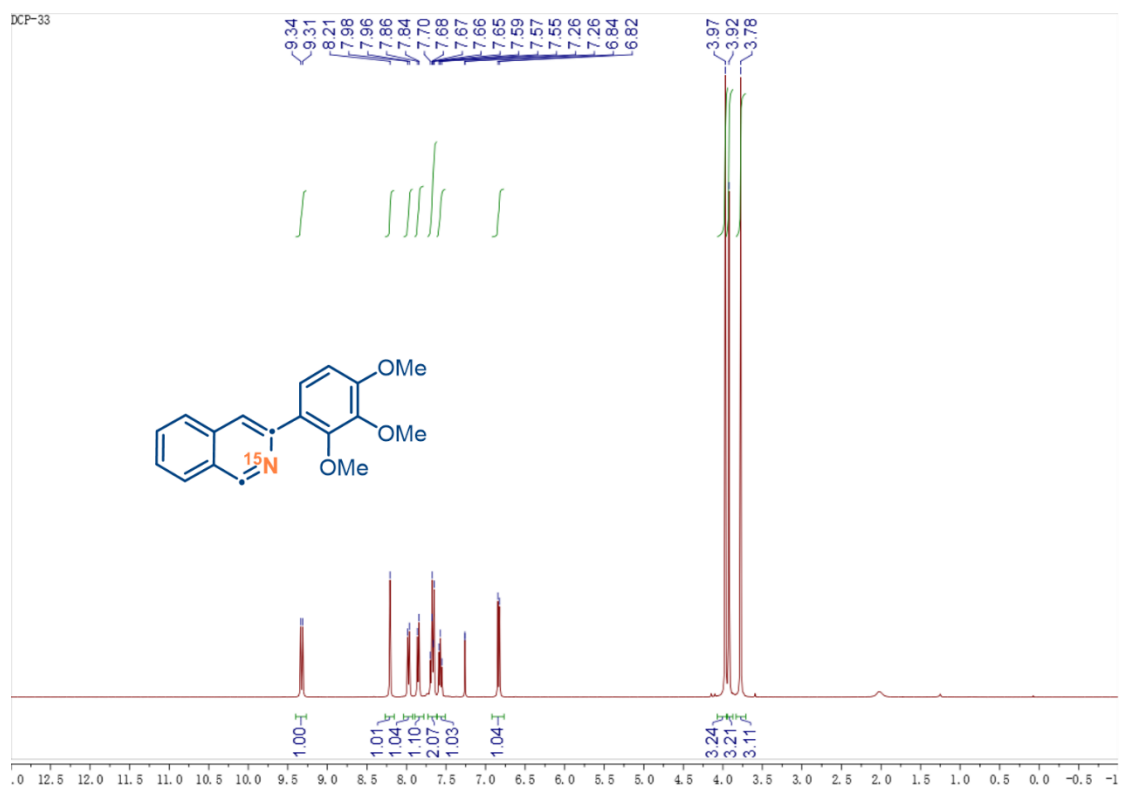
^{13}C NMR spectrum of **48** (100 MHz, CDCl_3)



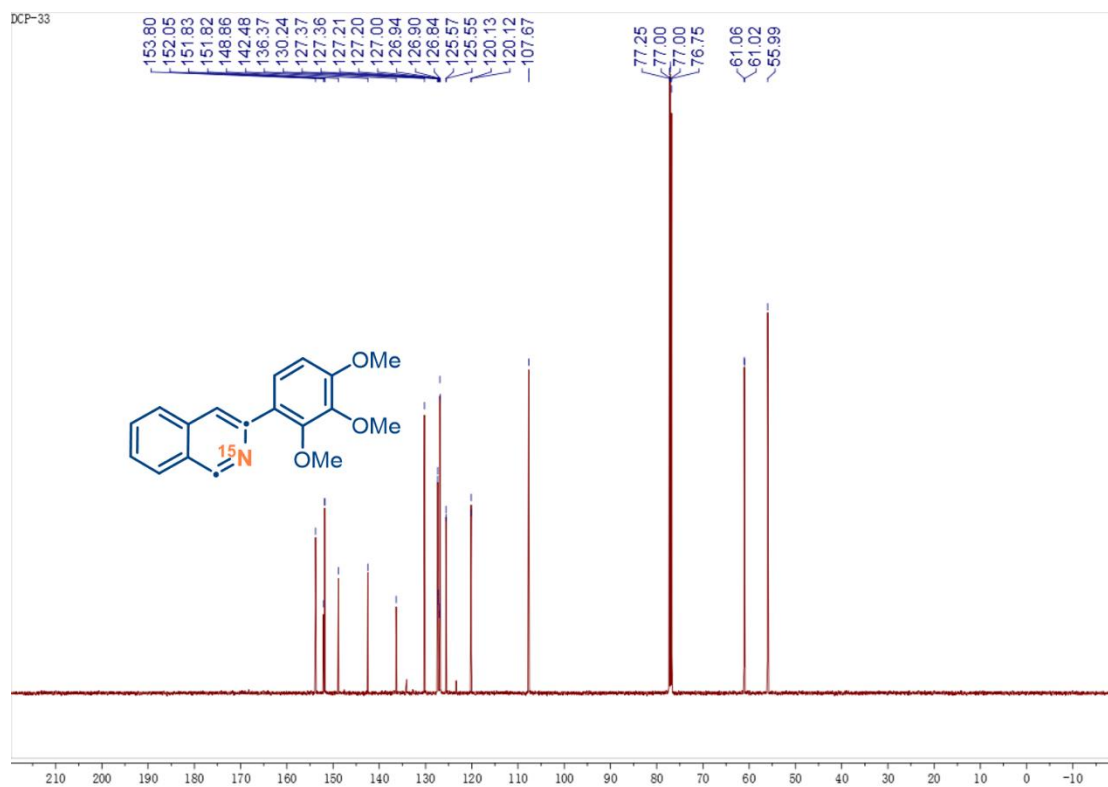
^{15}N NMR spectrum of **48** (50 MHz, CDCl_3)



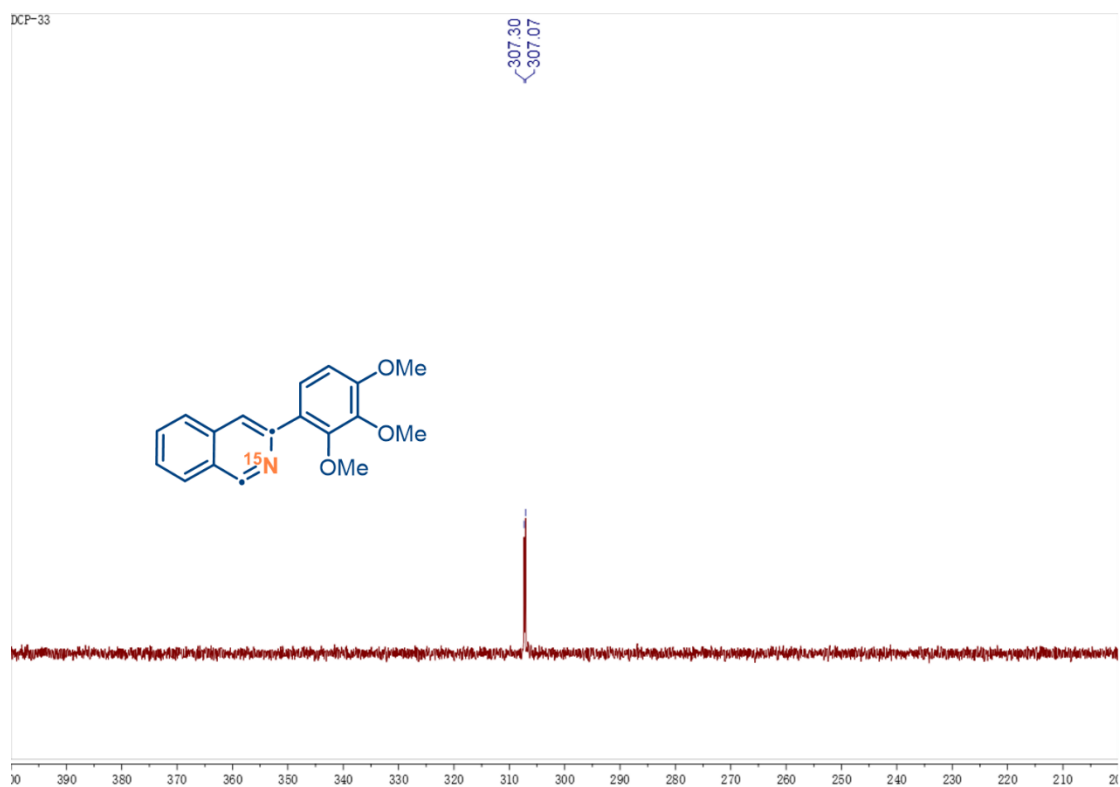
^1H NMR spectrum of **50** (400 MHz, CDCl_3)



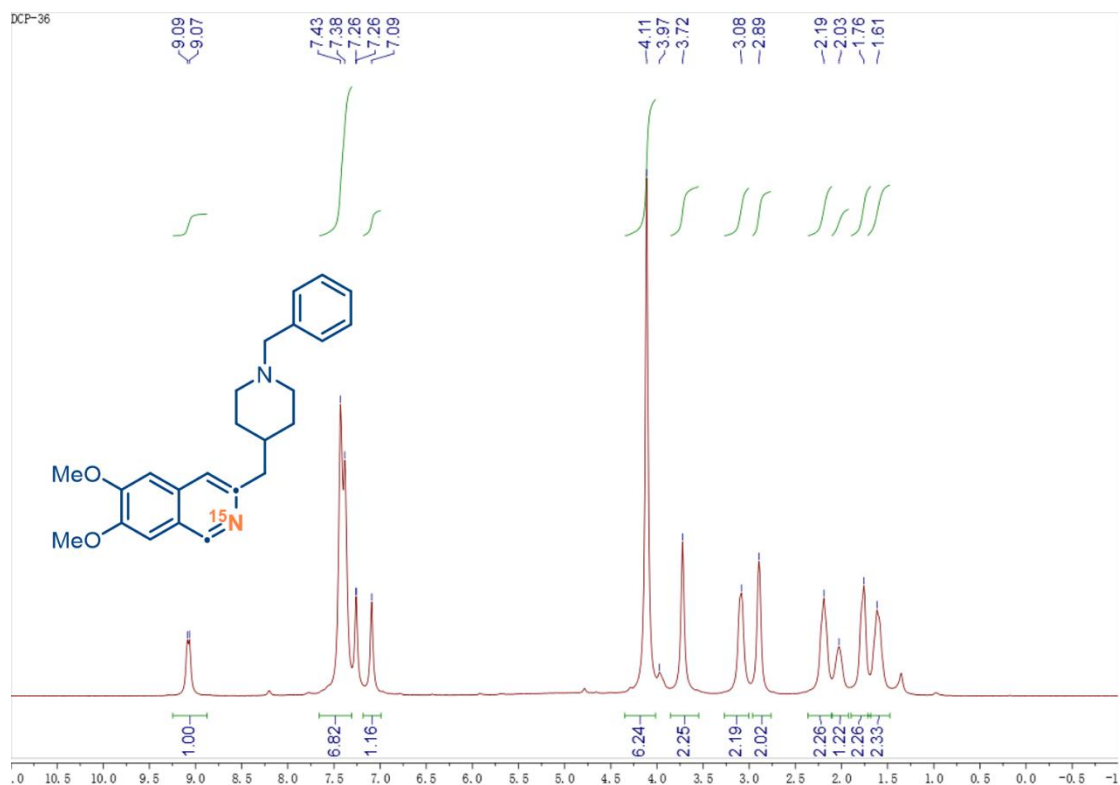
^{13}C NMR spectrum of **50** (125 MHz, CDCl_3)



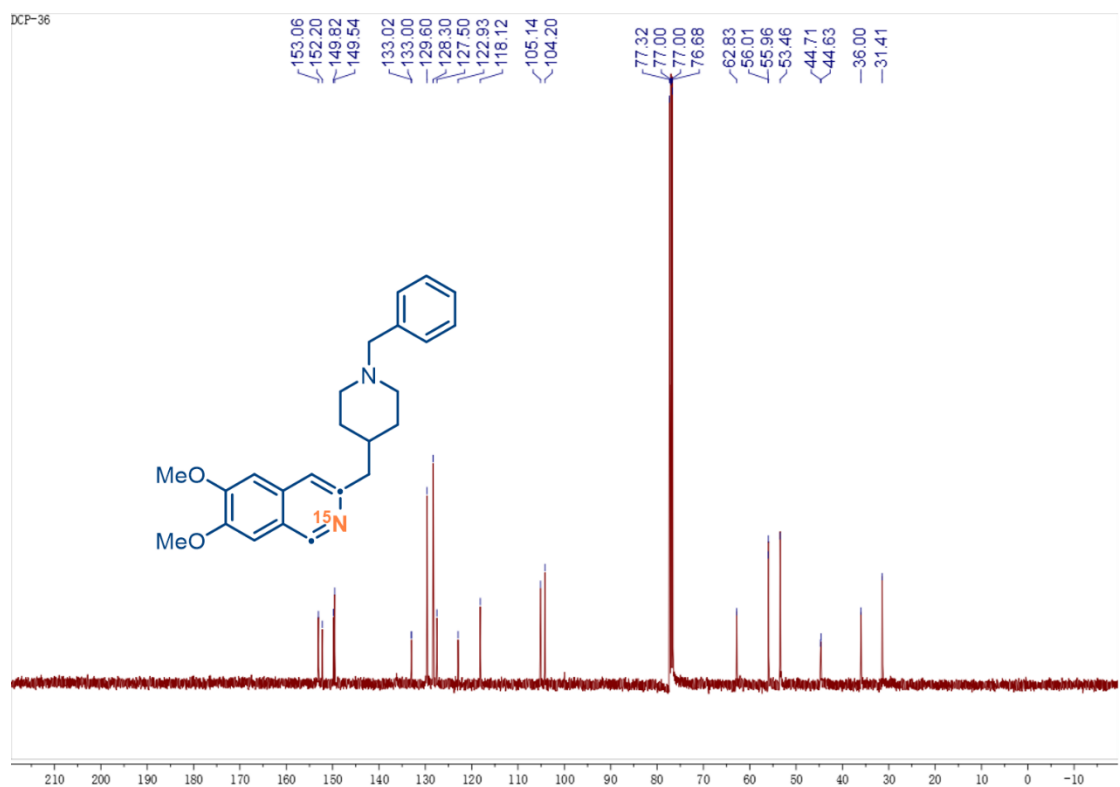
^{15}N NMR spectrum of **50** (50 MHz, CDCl_3)



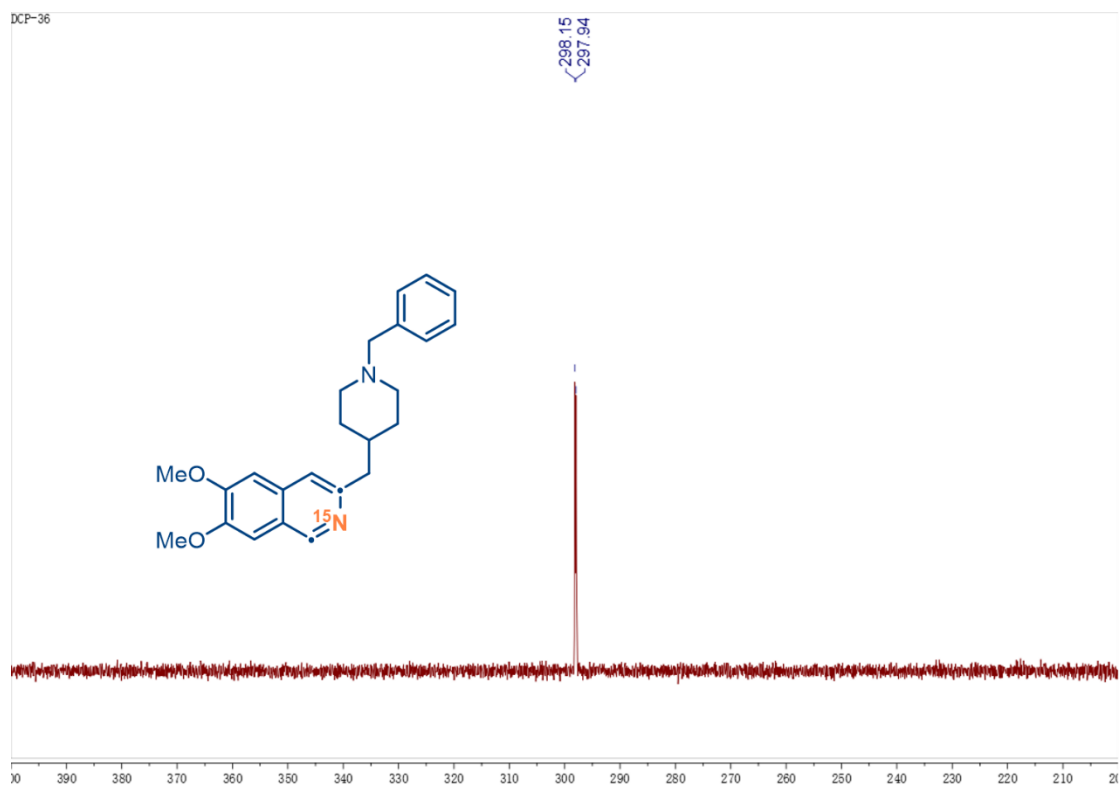
¹H NMR spectrum of **52** (400 MHz, CDCl₃)



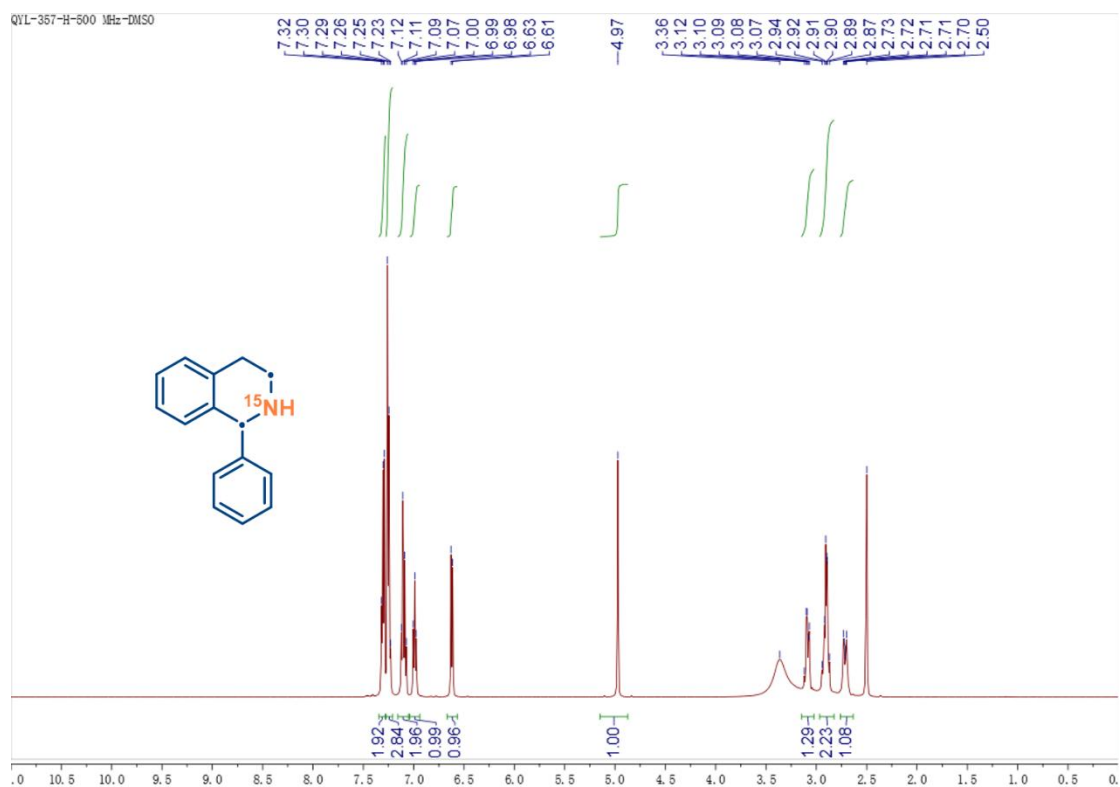
¹³C NMR spectrum of **52** (100 MHz, CDCl₃)



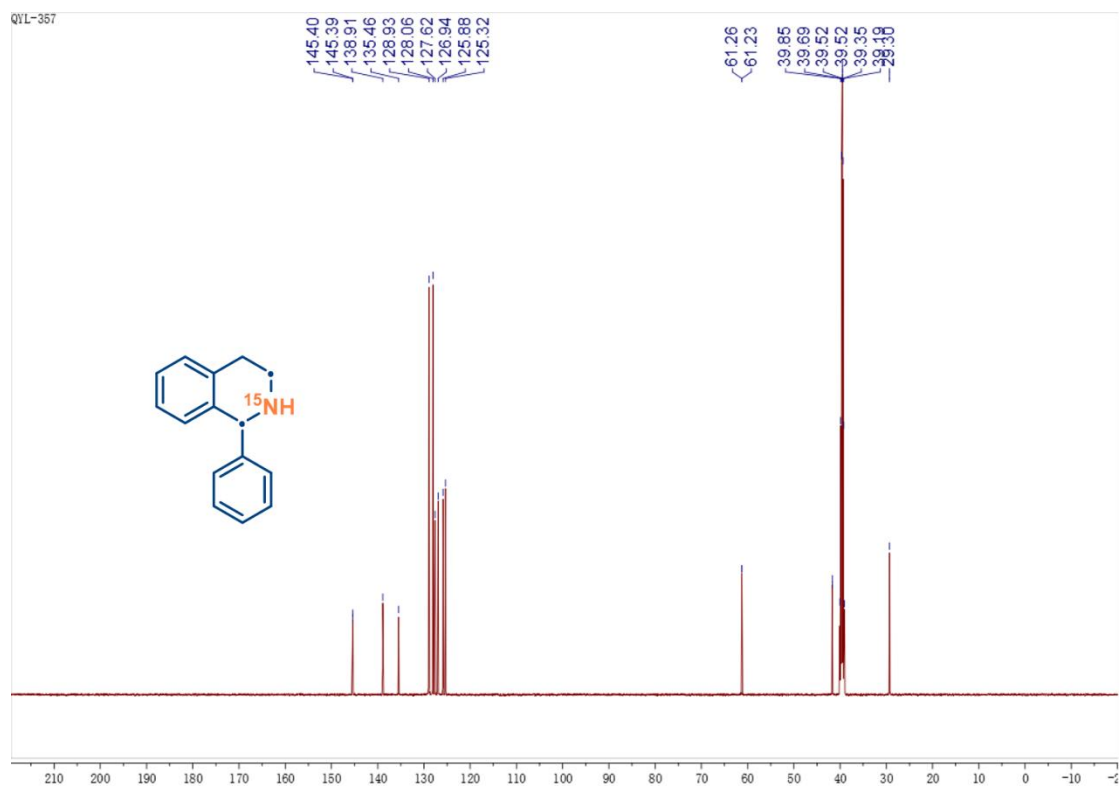
^{15}N NMR spectrum of **52** (50 MHz, CDCl_3)



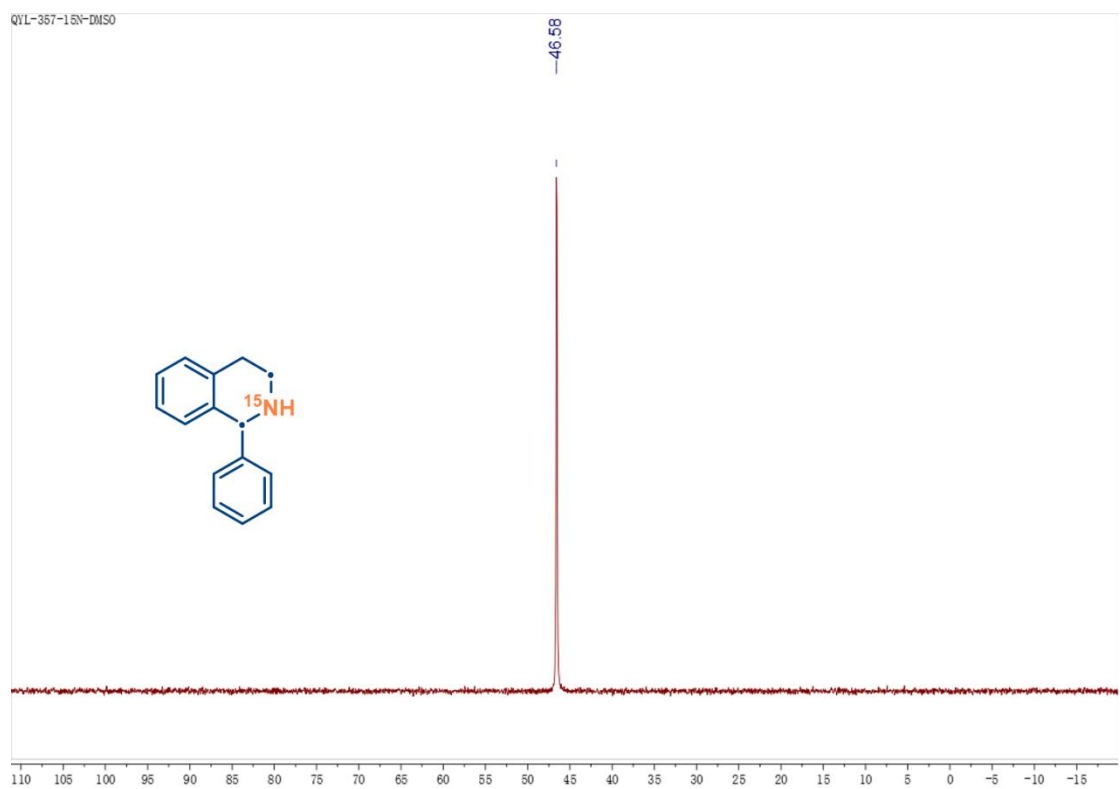
^1H NMR spectrum of **53** (500 MHz, $\text{DMSO}-d_6$)



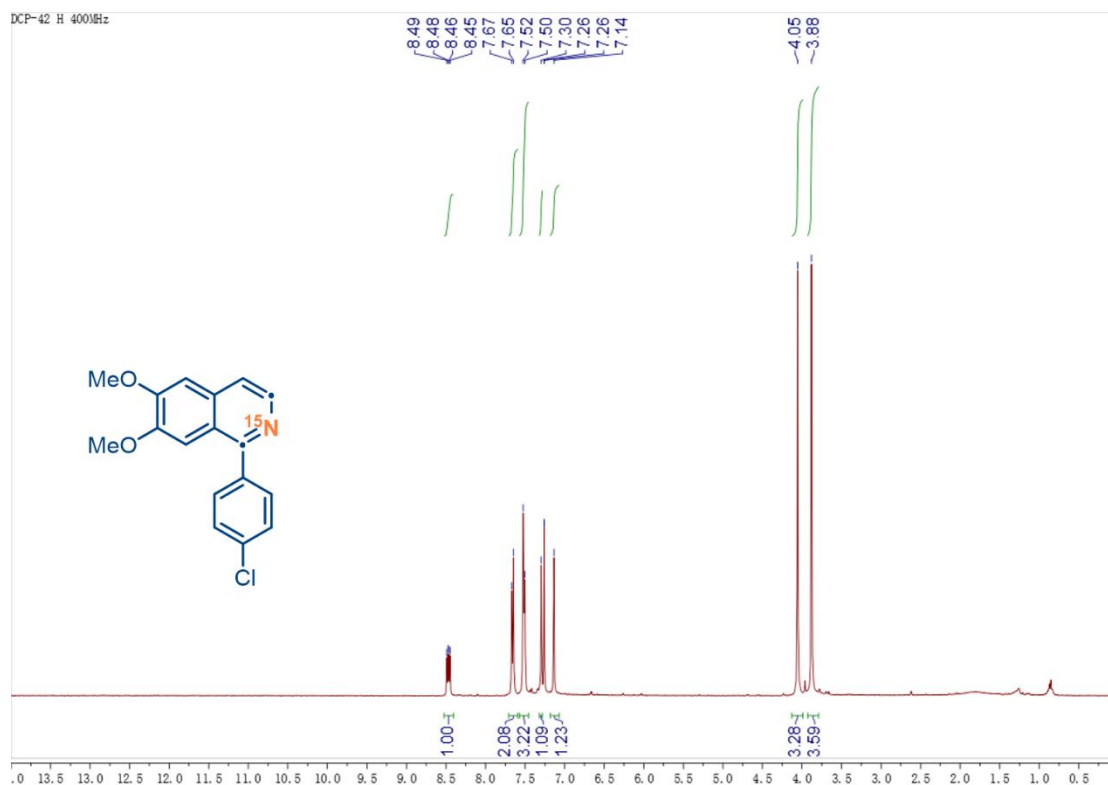
^{13}C NMR spectrum of **53** (125 MHz, DMSO- d_6)



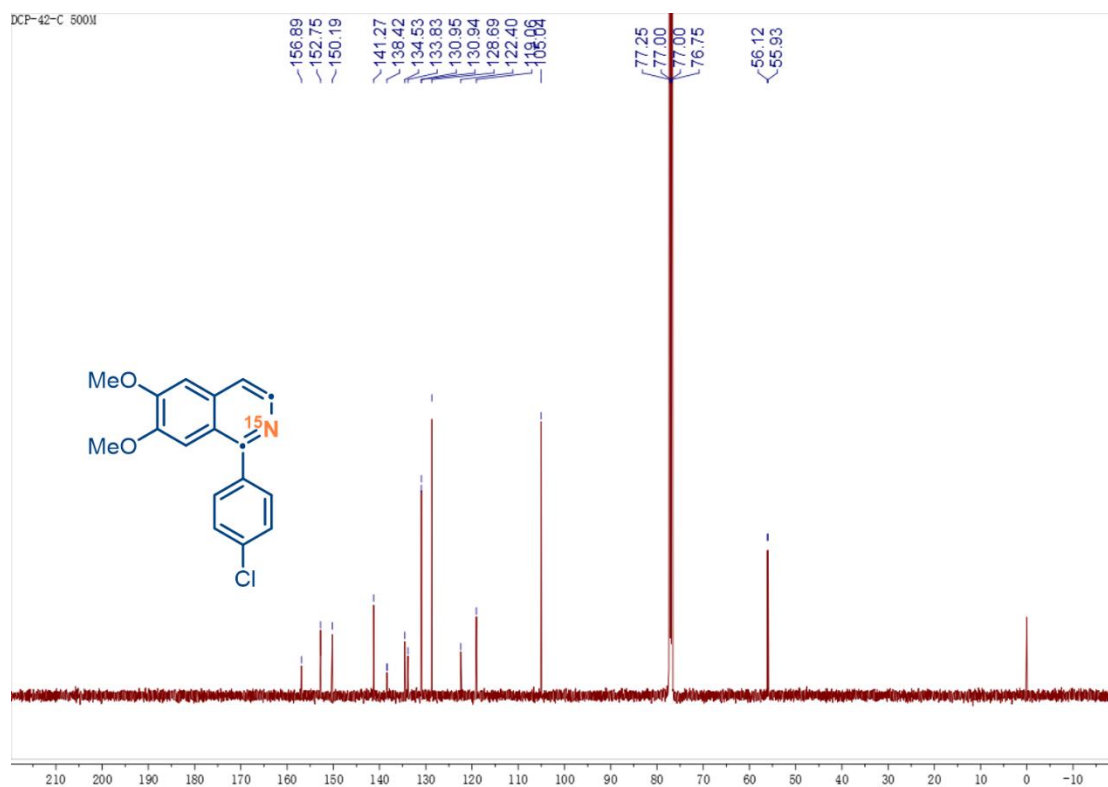
^{15}N NMR spectrum of **53** (50 MHz, DMSO- d_6)



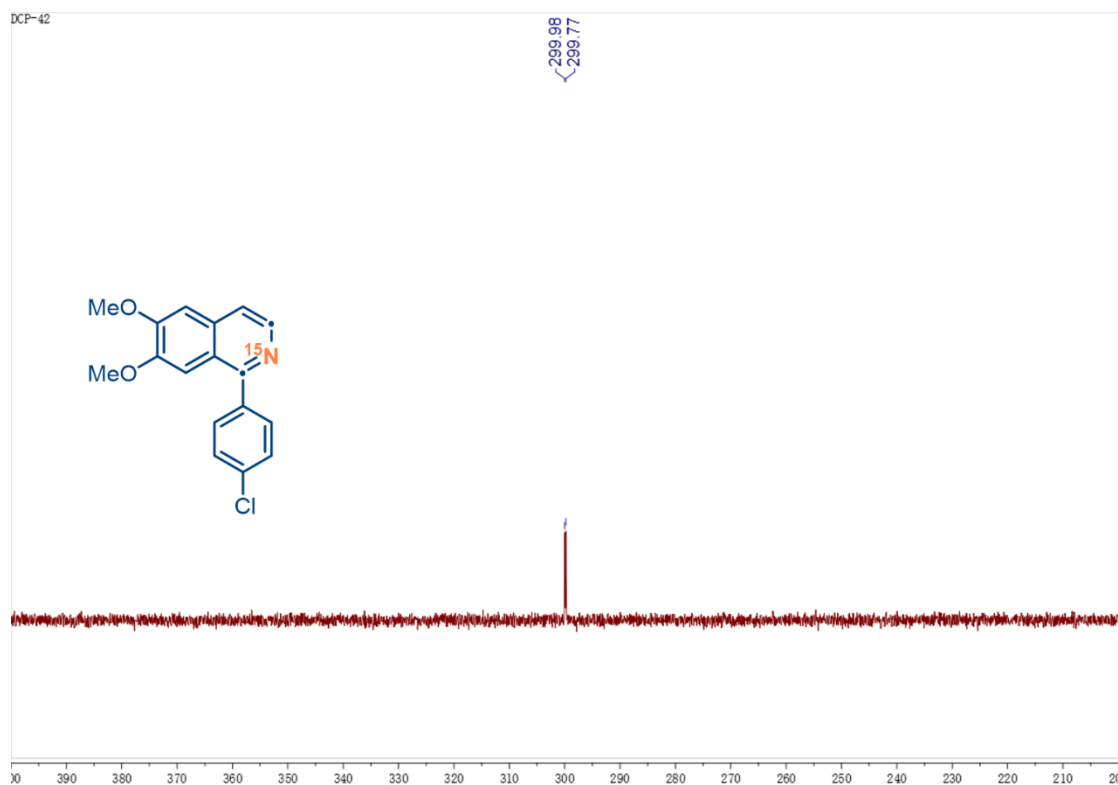
¹H NMR spectrum of **54** (400 MHz, CDCl₃)



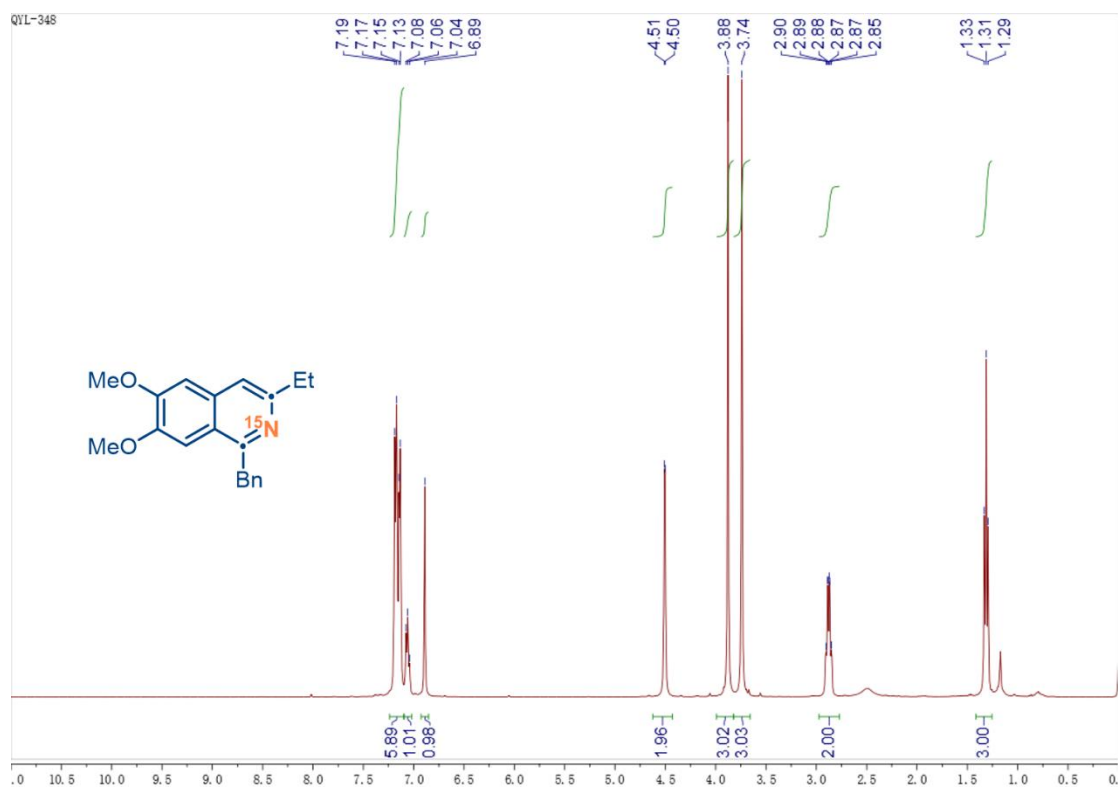
¹³C NMR spectrum of **54** (125 MHz, CDCl₃)



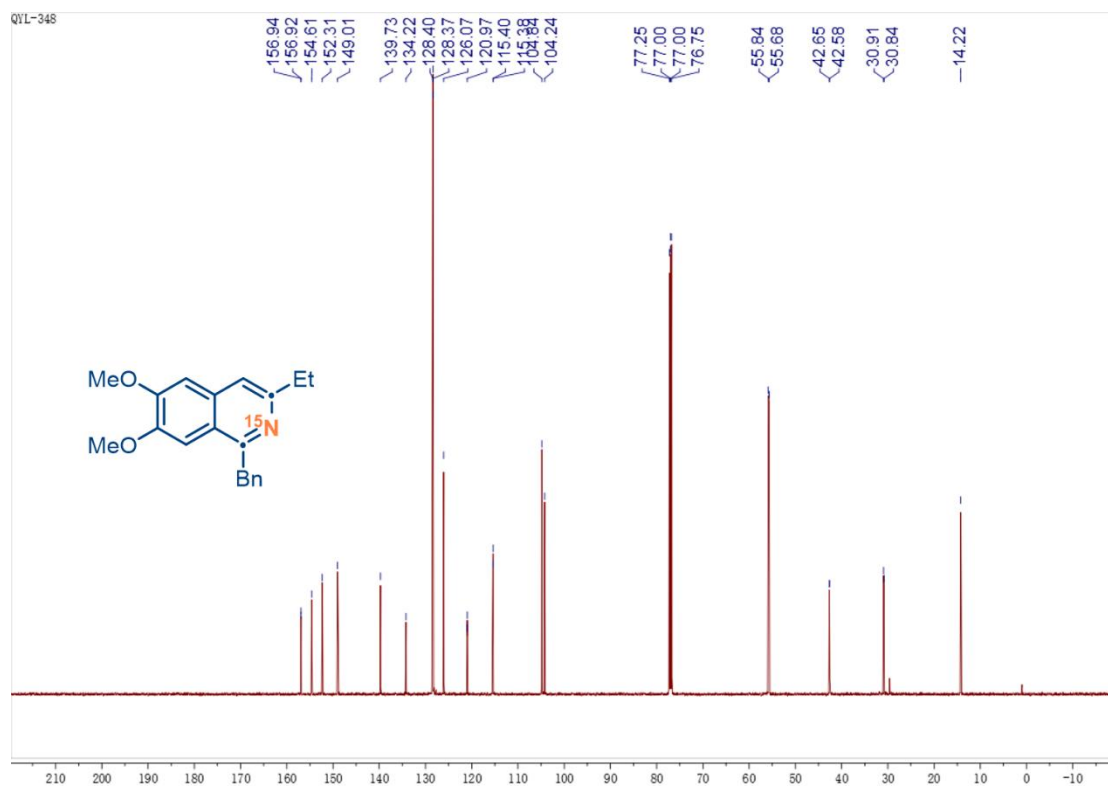
^{15}N NMR spectrum of **54** (50 MHz, CDCl_3)



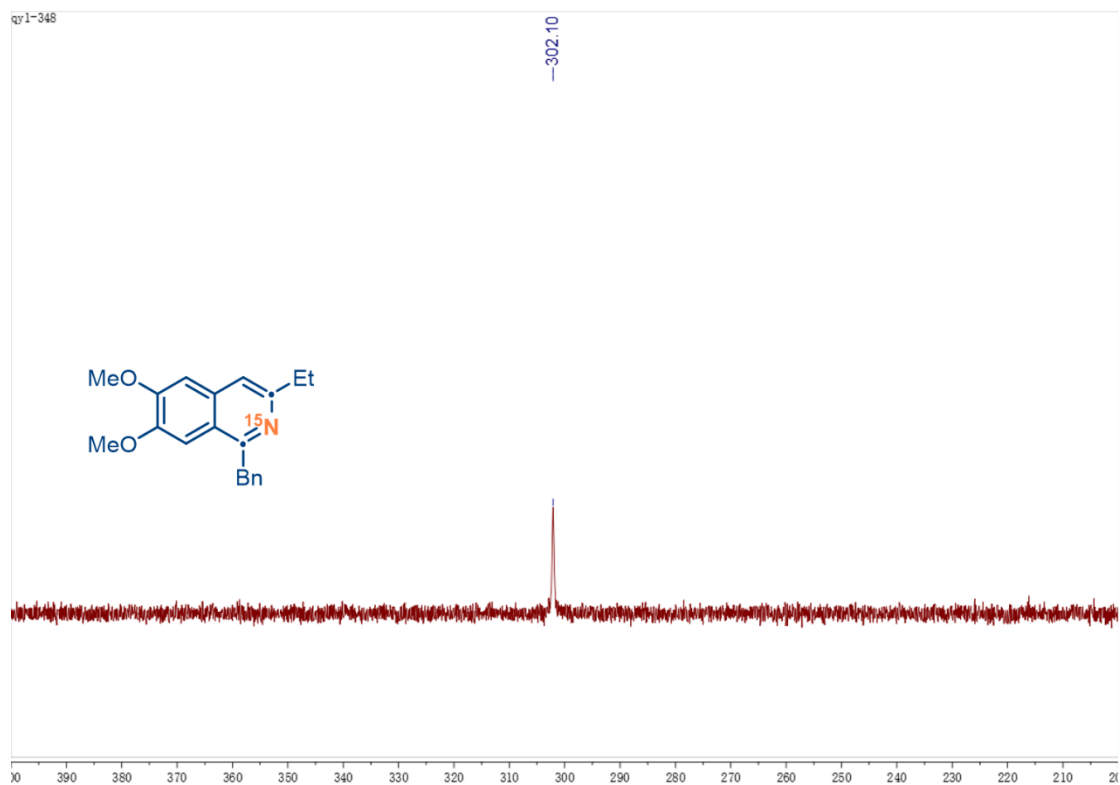
^1H NMR spectrum of **55** (400 MHz, CDCl_3)



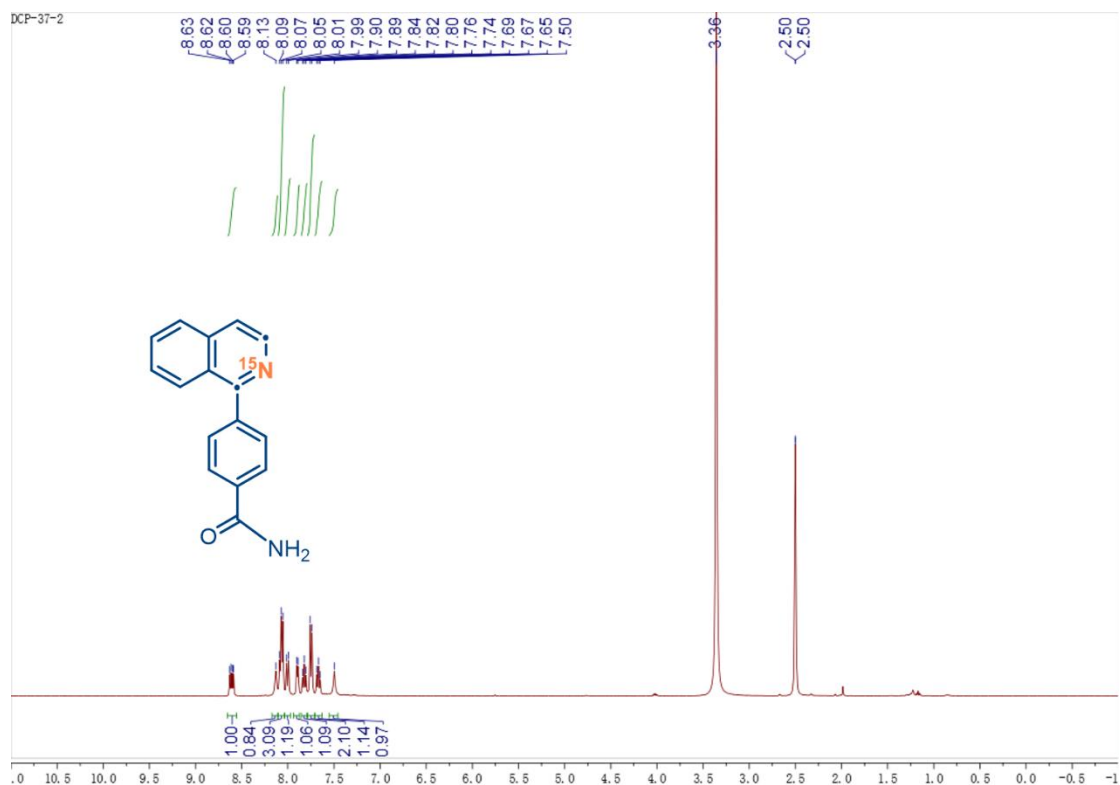
^{13}C NMR spectrum of **55** (125 MHz, CDCl_3)



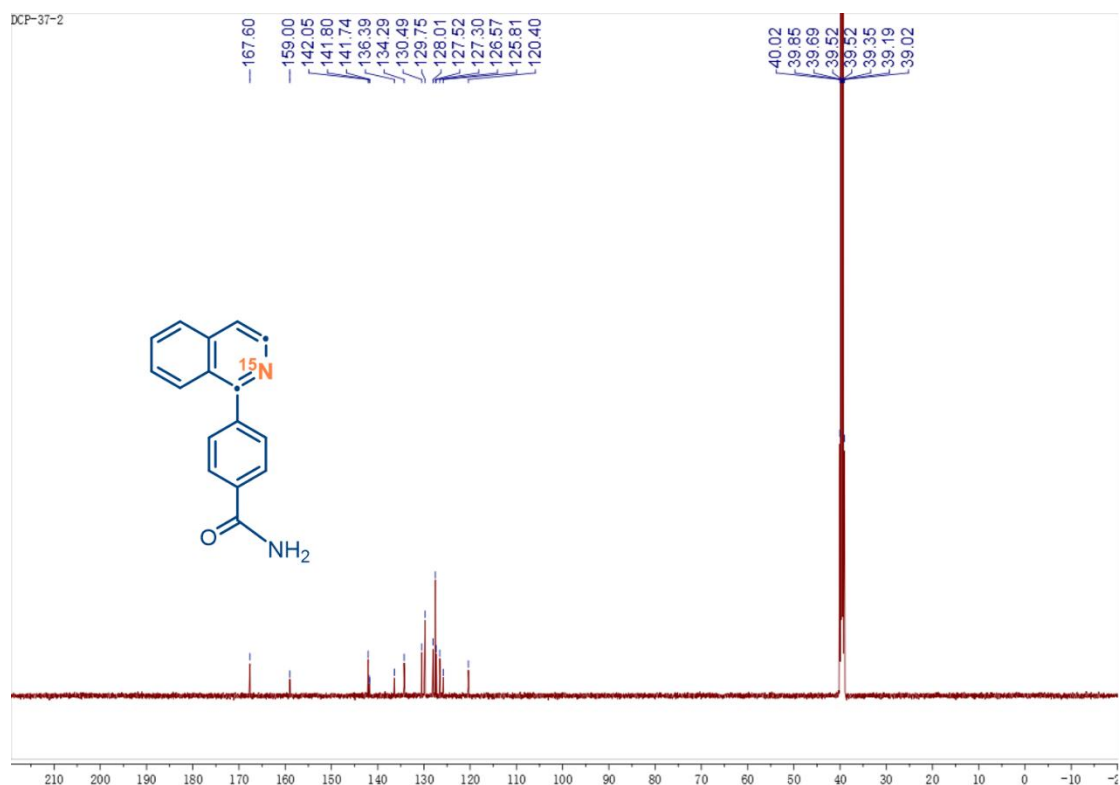
^{15}N NMR spectrum of **55** (50 MHz, CDCl_3)



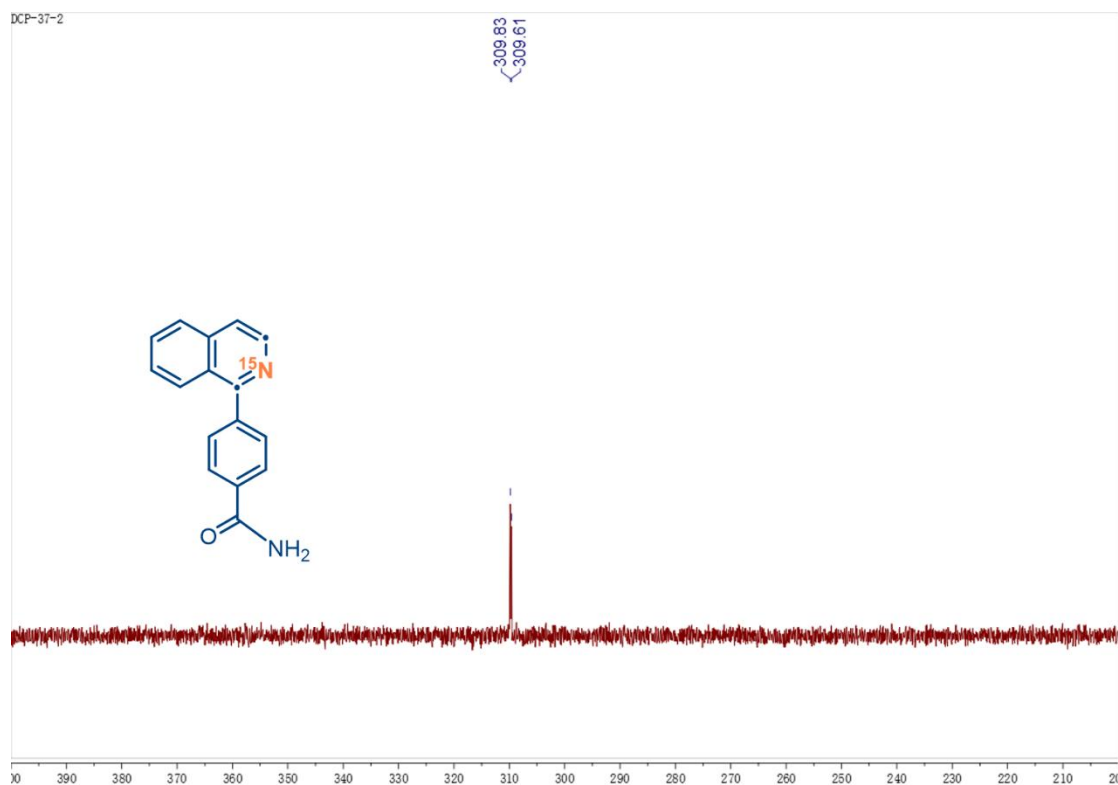
¹H NMR spectrum of **56** (400 MHz, DMSO-*d*₆)



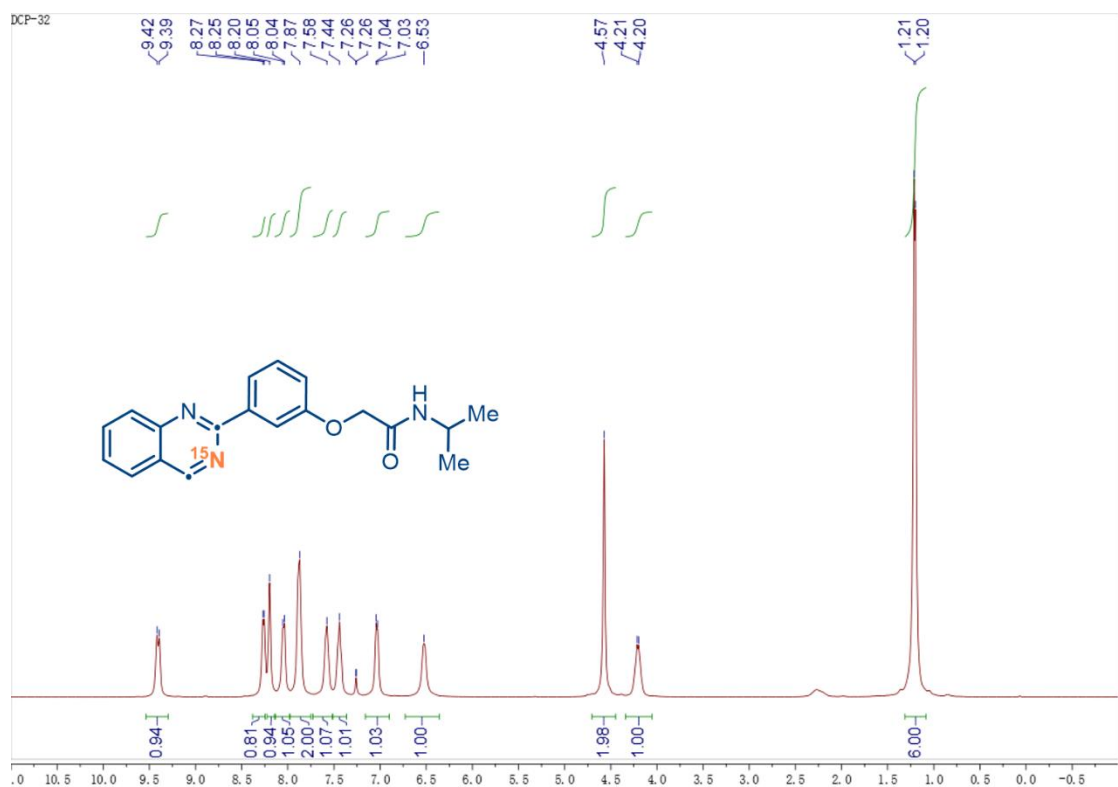
¹³C NMR spectrum of **56** (125 MHz, DMSO-*d*₆)



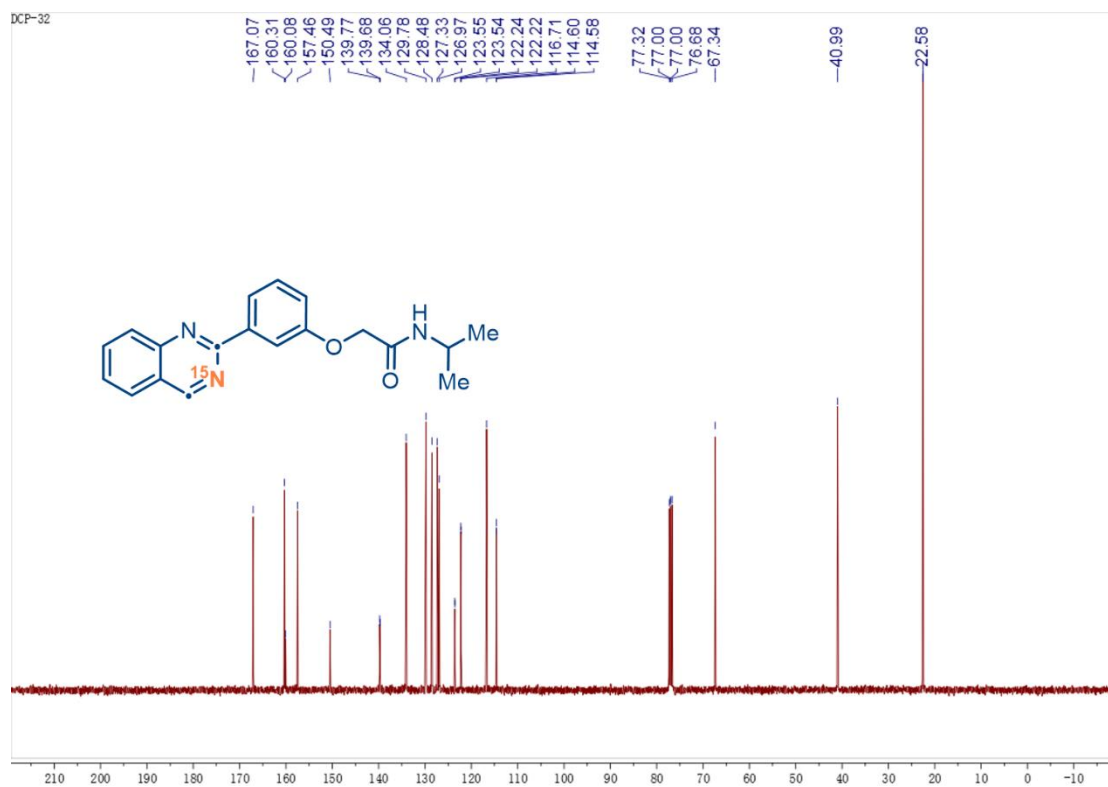
^{15}N NMR spectrum of **56** (50 MHz, $\text{DMSO}-d_6$)



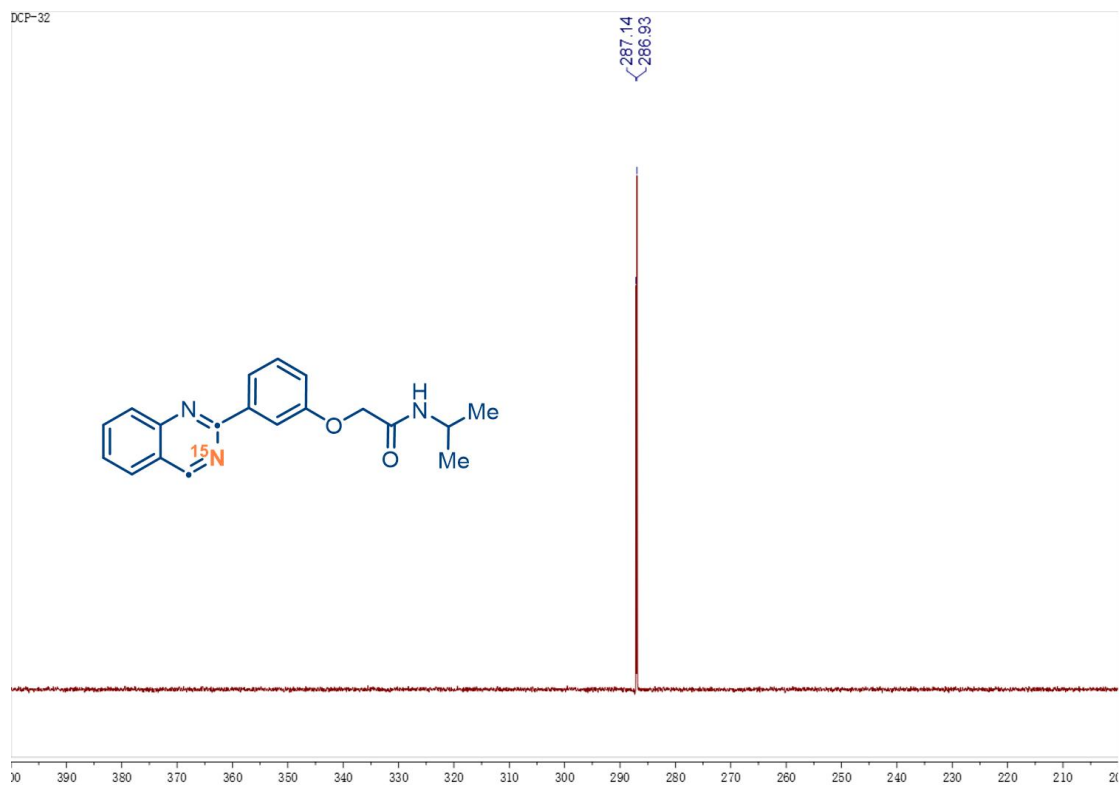
^1H NMR spectrum of **57** (400 MHz, CDCl_3)



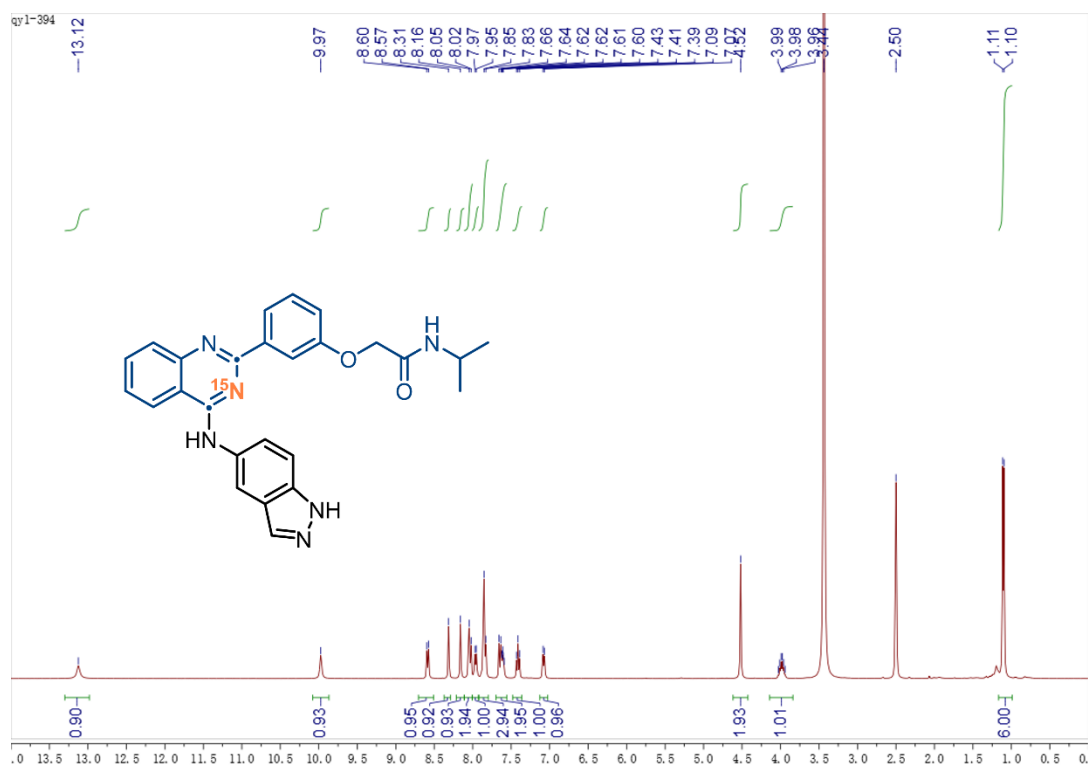
^{13}C NMR spectrum of **57** (100 MHz, CDCl_3)



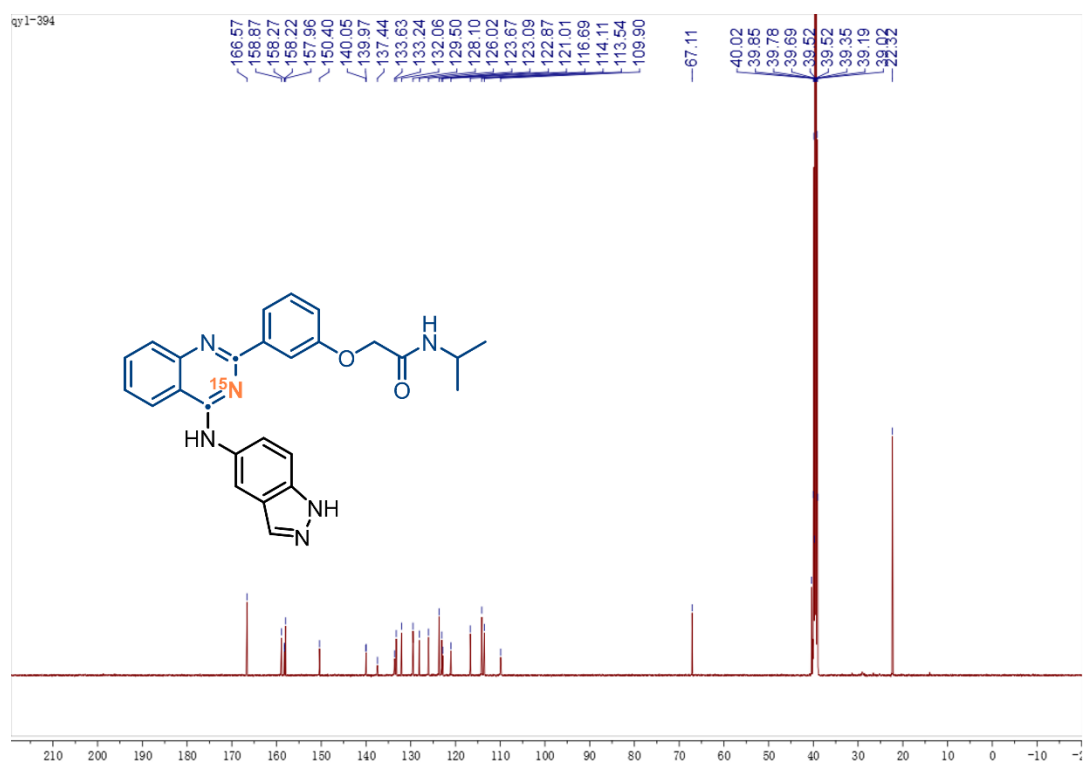
^{15}N NMR spectrum of **57** (50 MHz, CDCl_3)



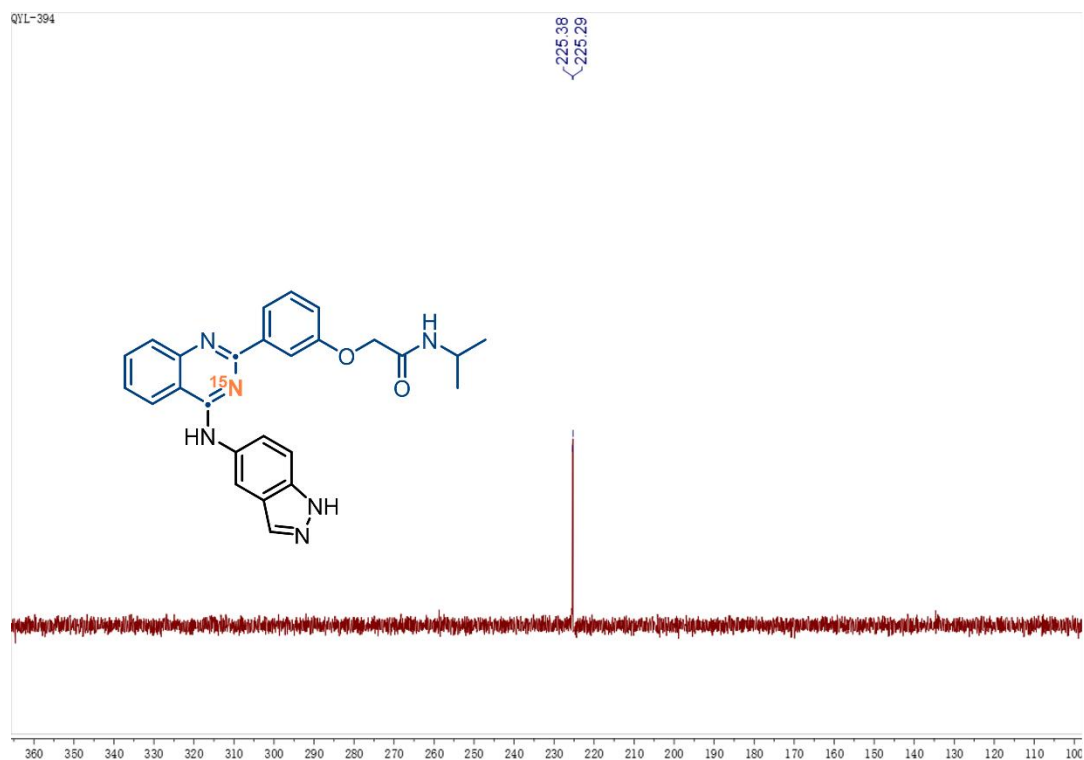
¹H NMR spectrum of **58** (400 MHz, DMSO-*d*₆)



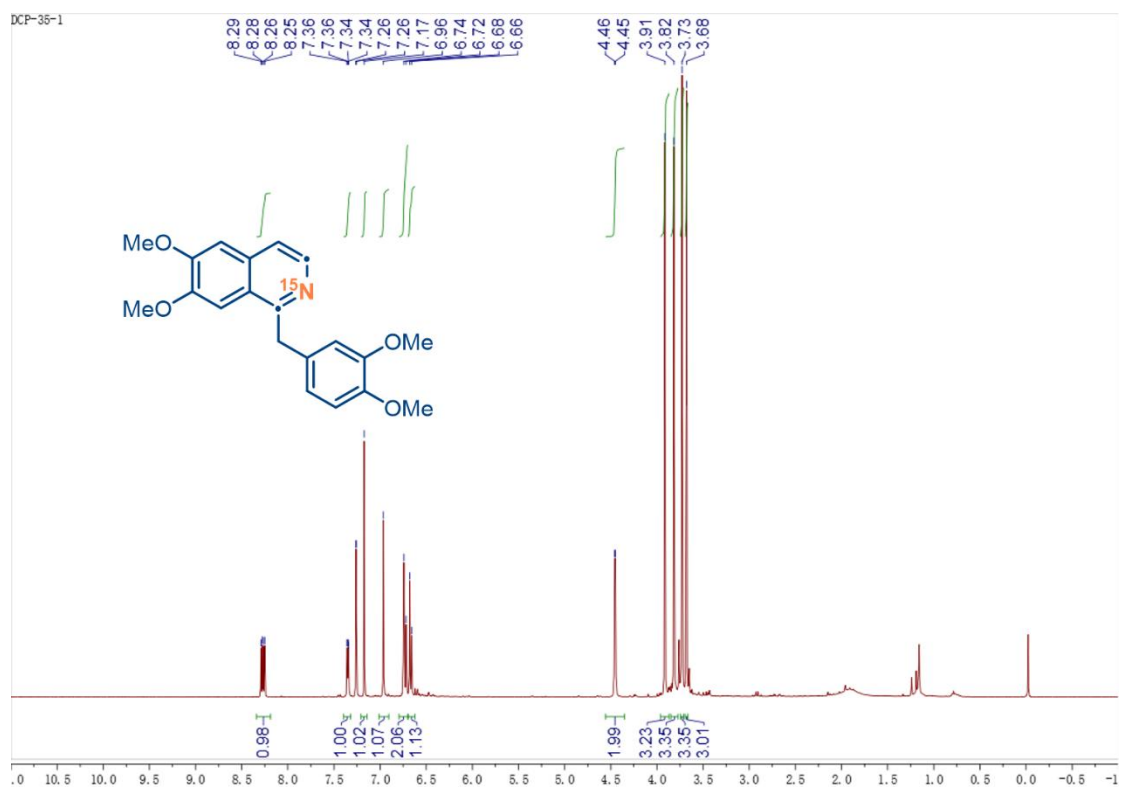
¹³C NMR spectrum of **58** (125 MHz, DMSO-*d*₆)



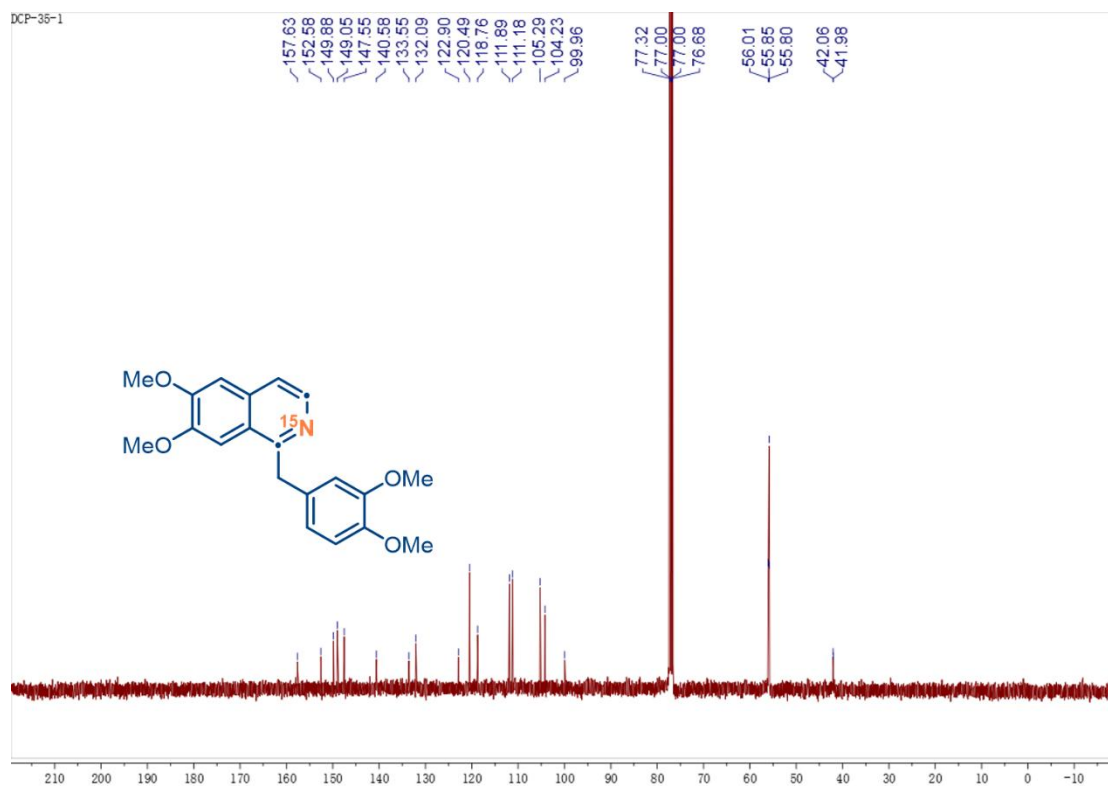
^{15}N NMR spectrum of **58** (50 MHz, $\text{DMSO}-d_6$)



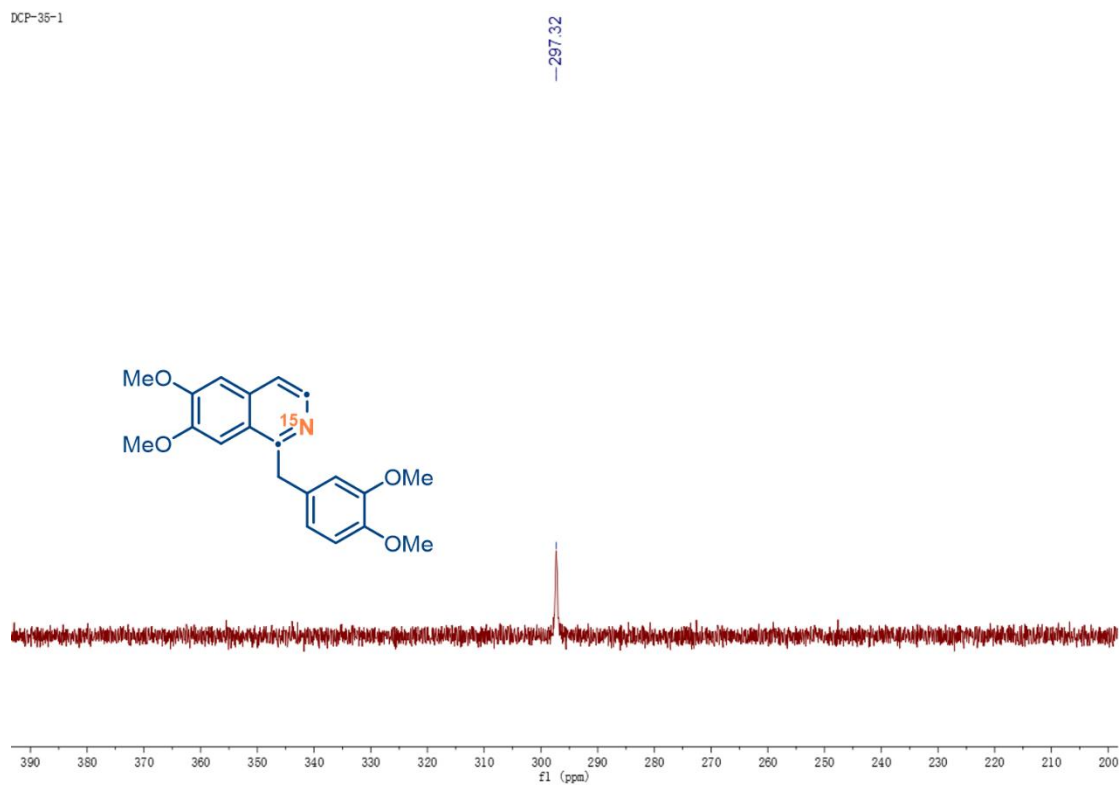
^1H NMR spectrum of **59** (400 MHz, CDCl_3)



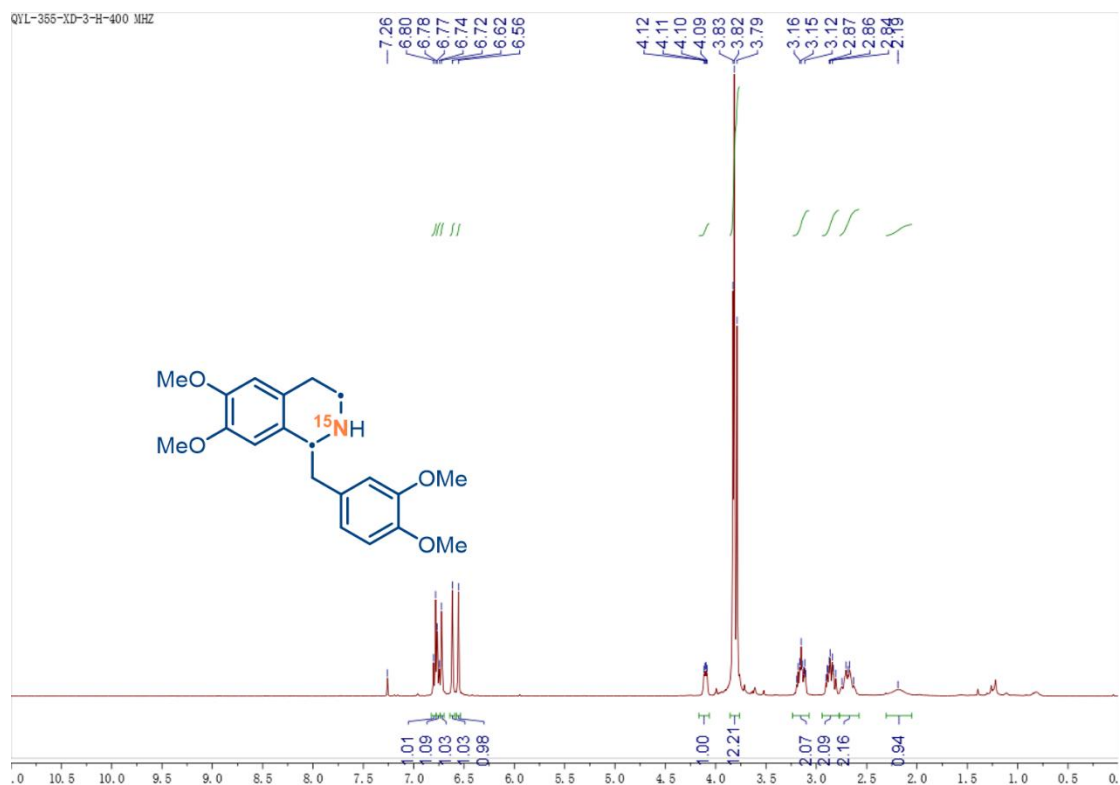
^{13}C NMR spectrum of **59** (100 MHz, CDCl_3)



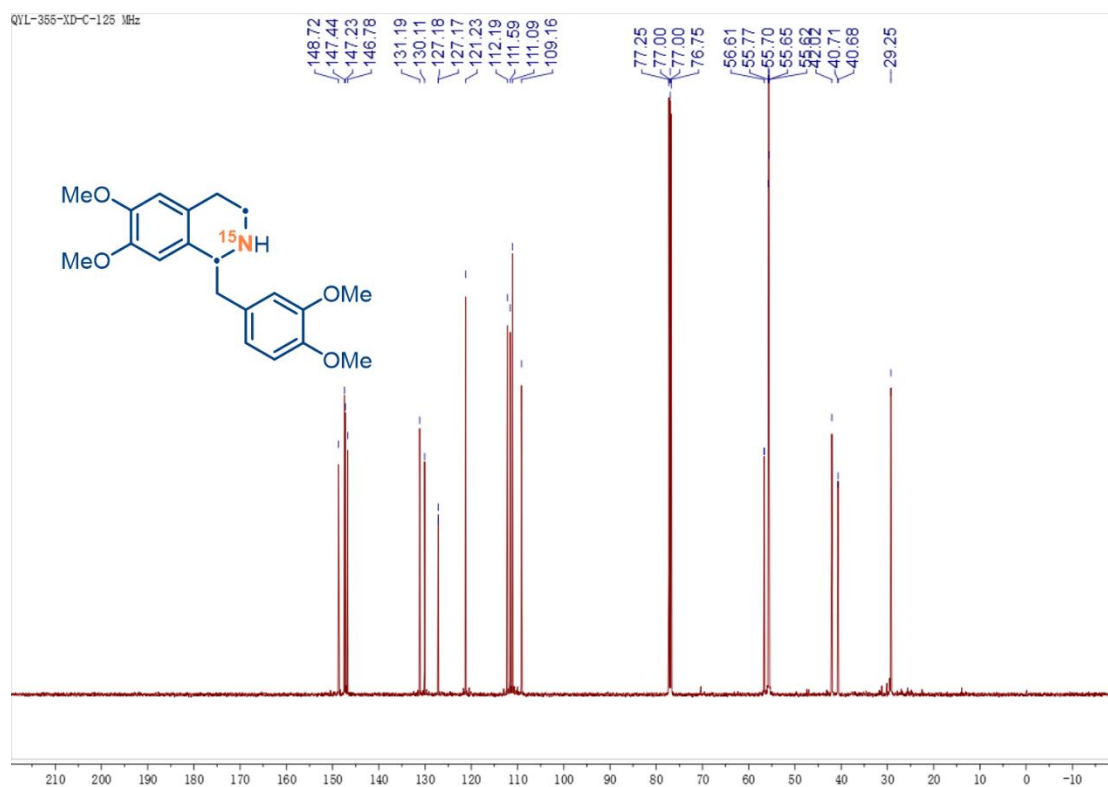
^{15}N NMR spectrum of **59** (50 MHz, CDCl_3)



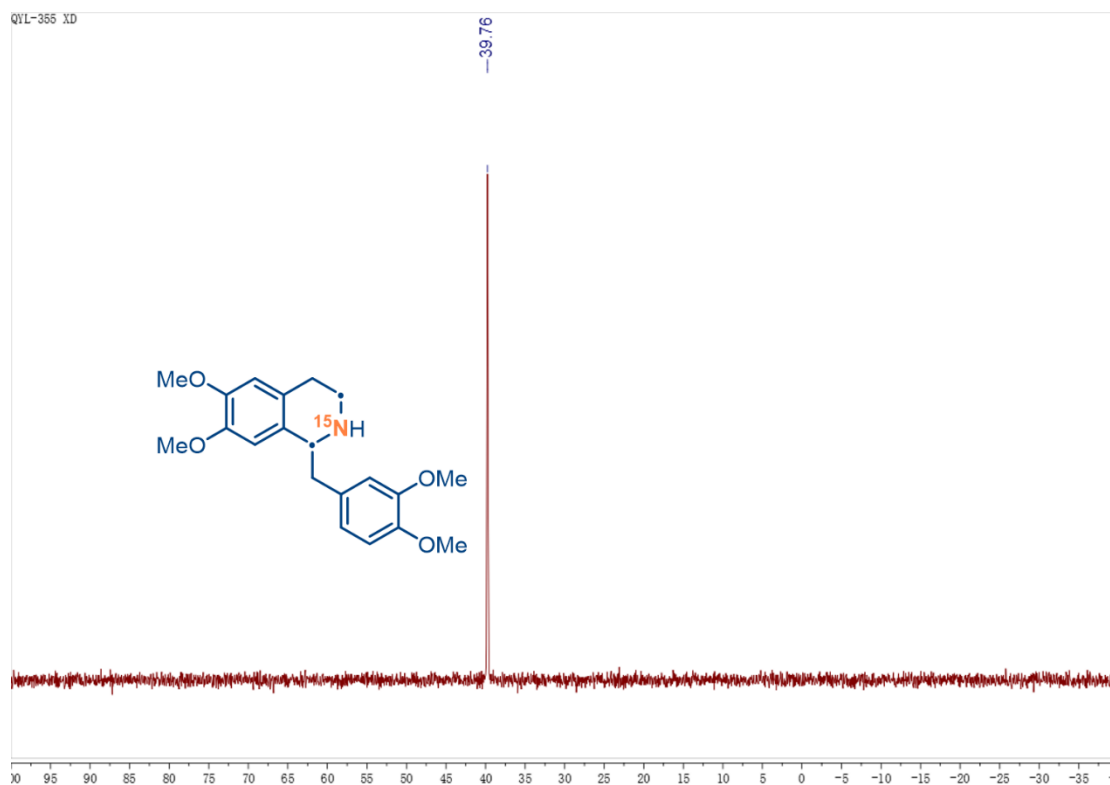
¹H NMR spectrum of **6o** (400 MHz, CDCl₃)



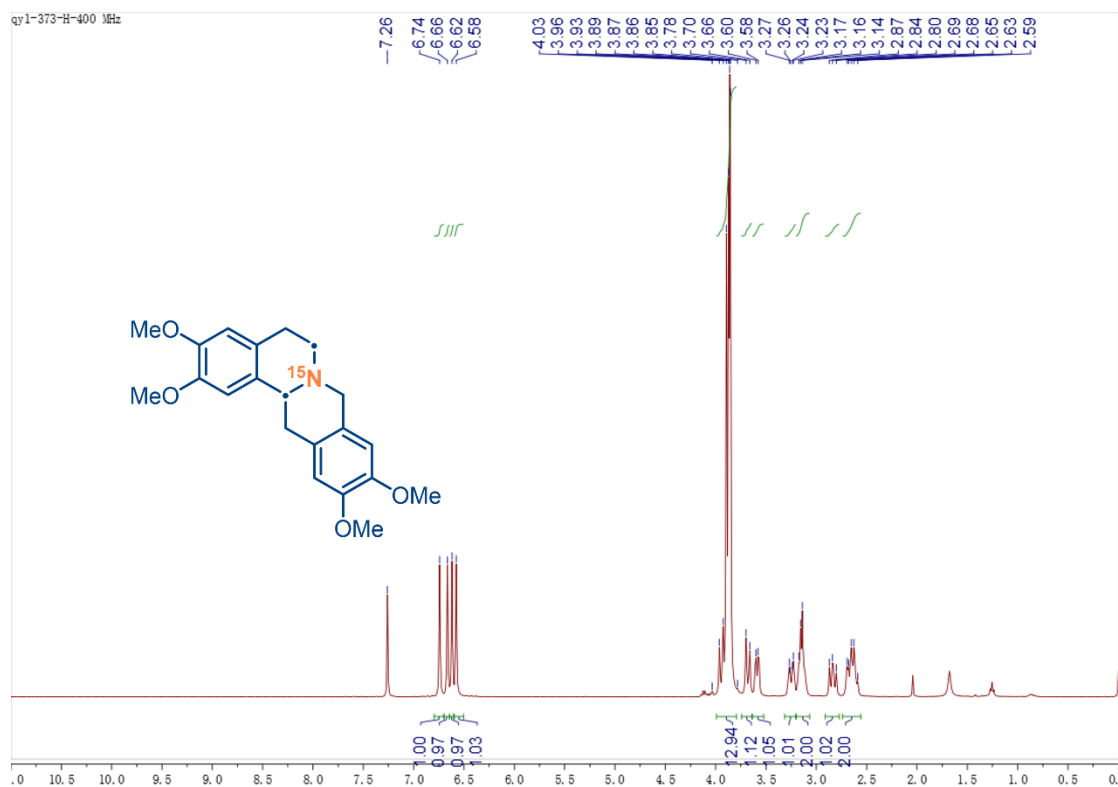
¹³C NMR spectrum of **6o** (125 MHz, CDCl₃)



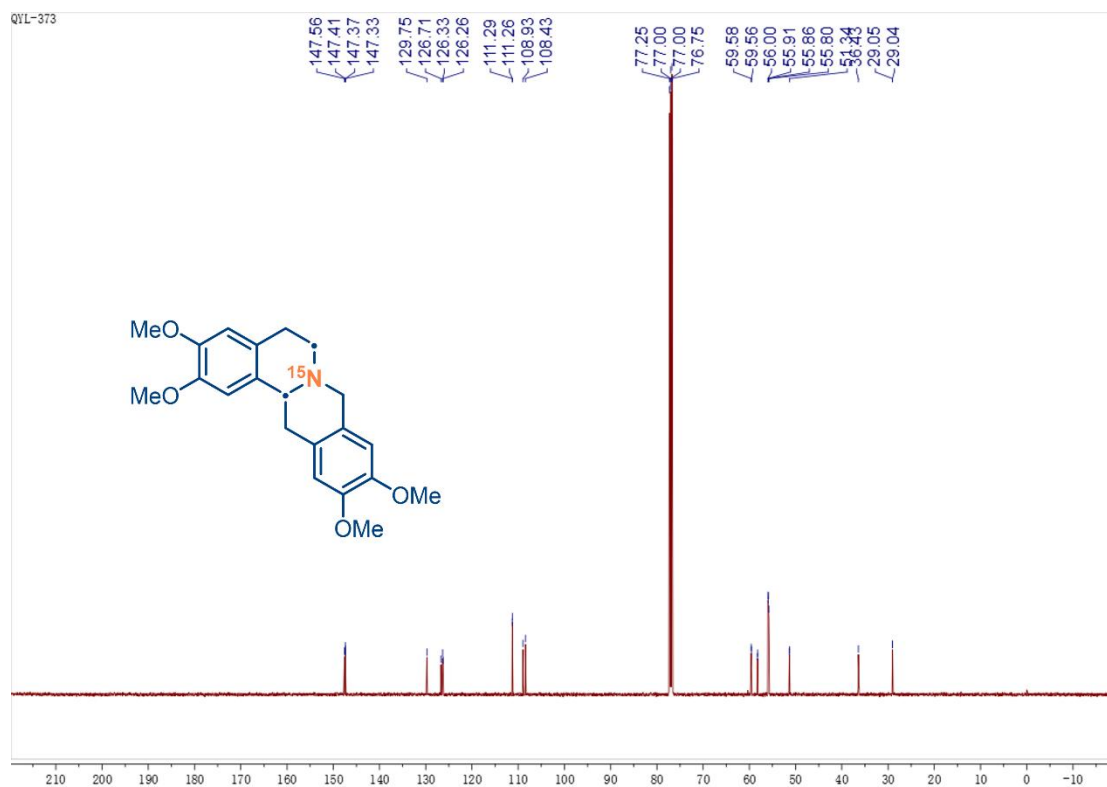
^{15}N NMR spectrum of **6o** (50 MHz, CDCl_3)



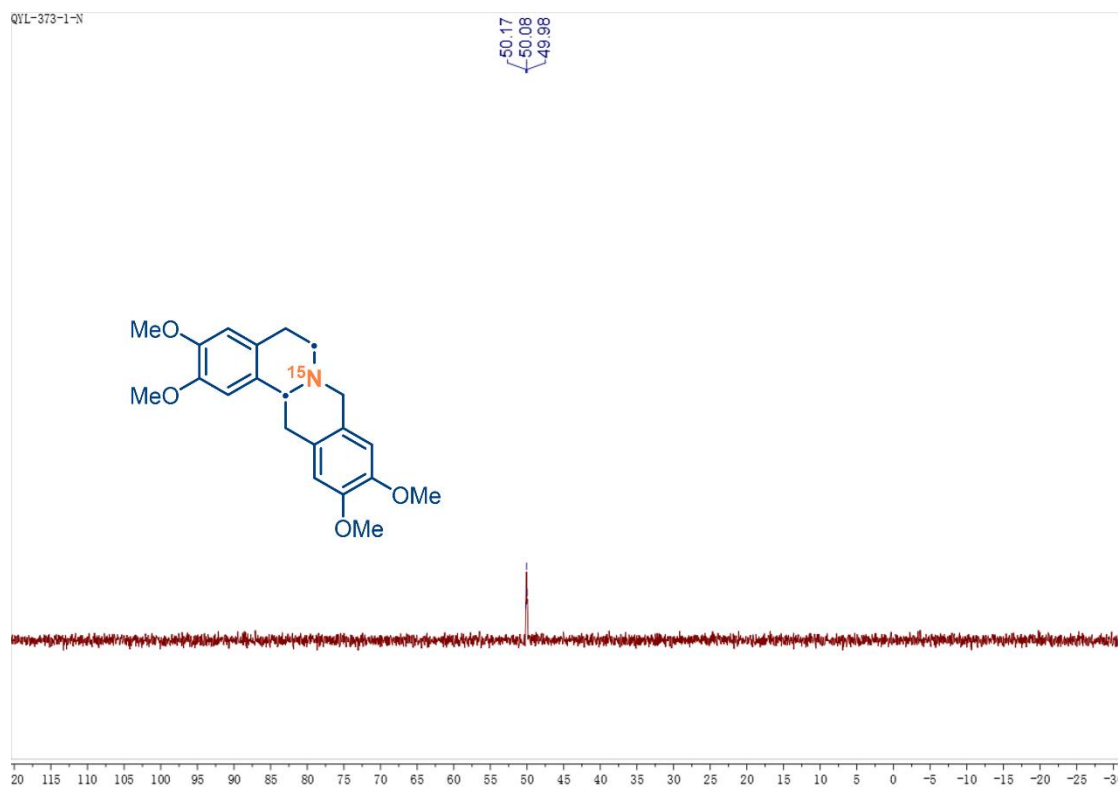
^1H NMR spectrum of **6i** (400 MHz, CDCl_3)



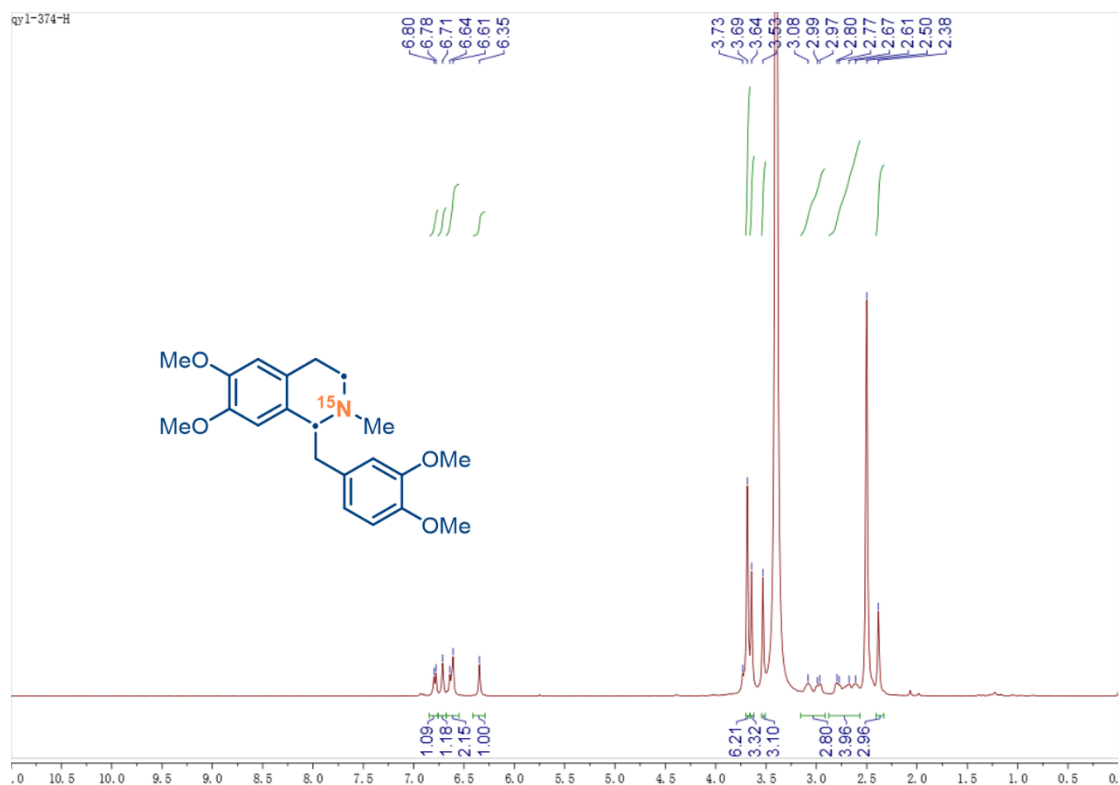
^{13}C NMR spectrum of **61** (125 MHz, CDCl_3)



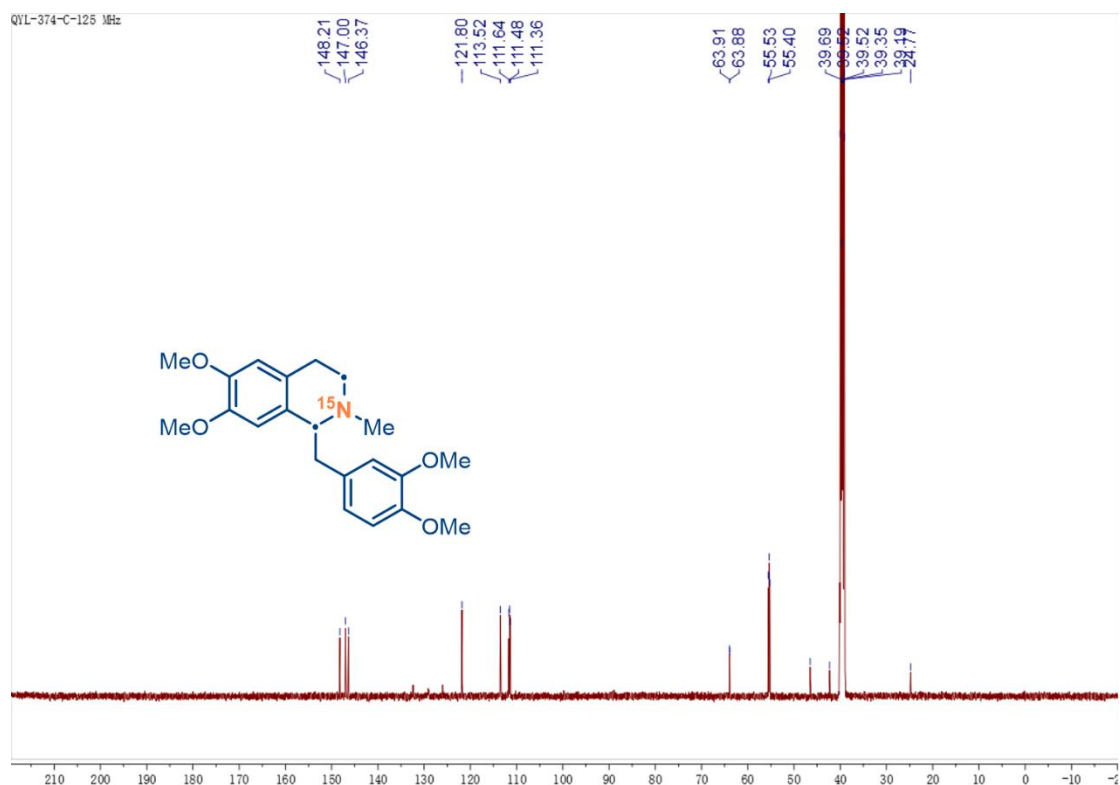
^{15}N NMR spectrum of **61** (50 MHz, CDCl_3)



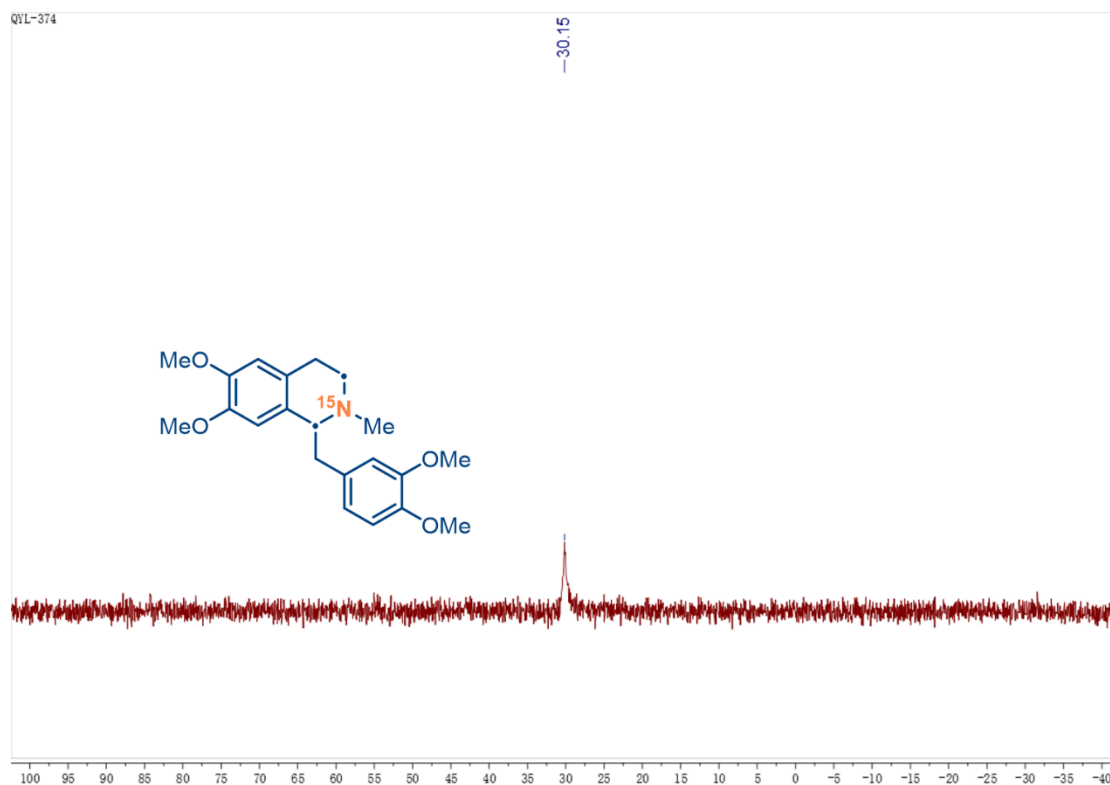
^1H NMR spectrum of **62** (400 MHz, $\text{DMSO}-d_6$)



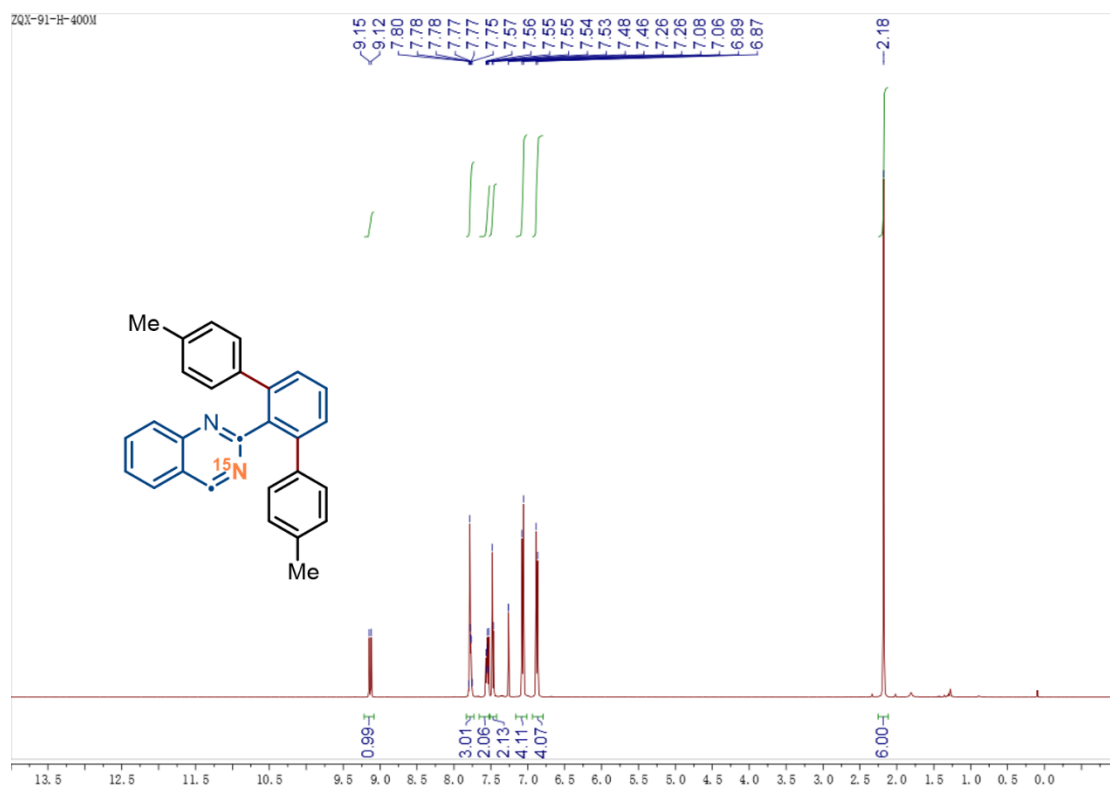
^{13}C NMR spectrum of **62** (125 MHz, $\text{DMSO}-d_6$)



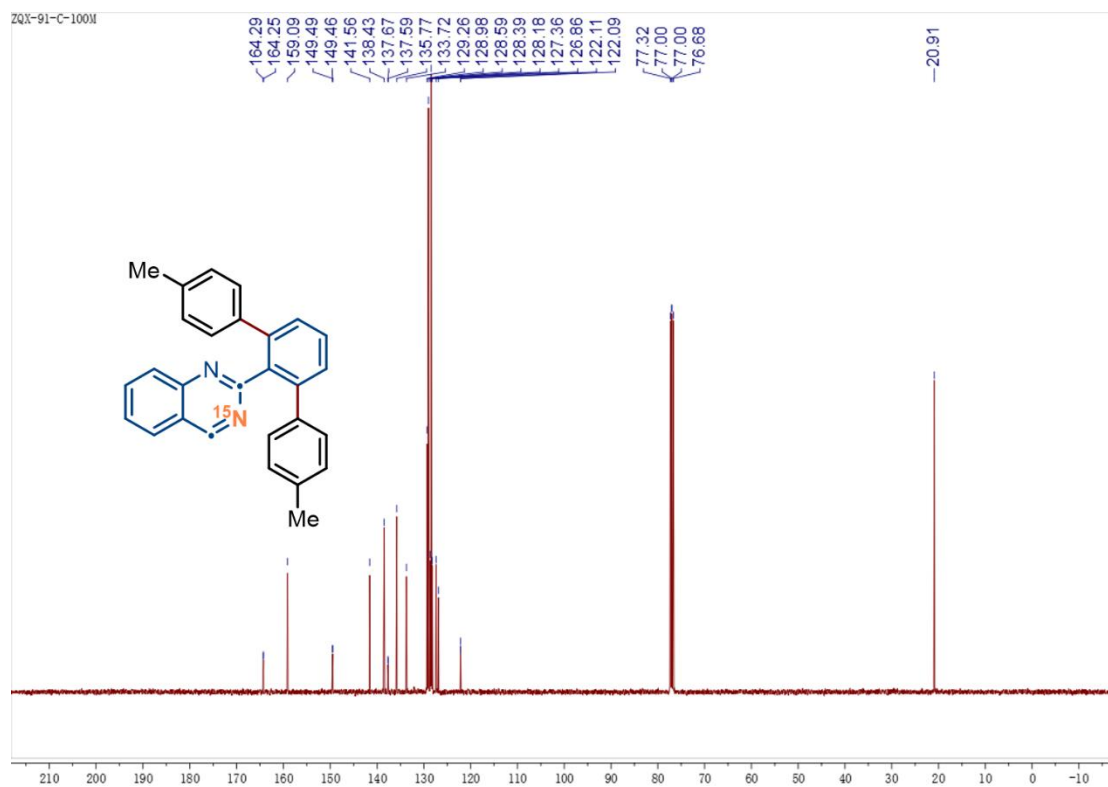
^{15}N NMR spectrum of **62** (50 MHz, $\text{DMSO}-d_6$)



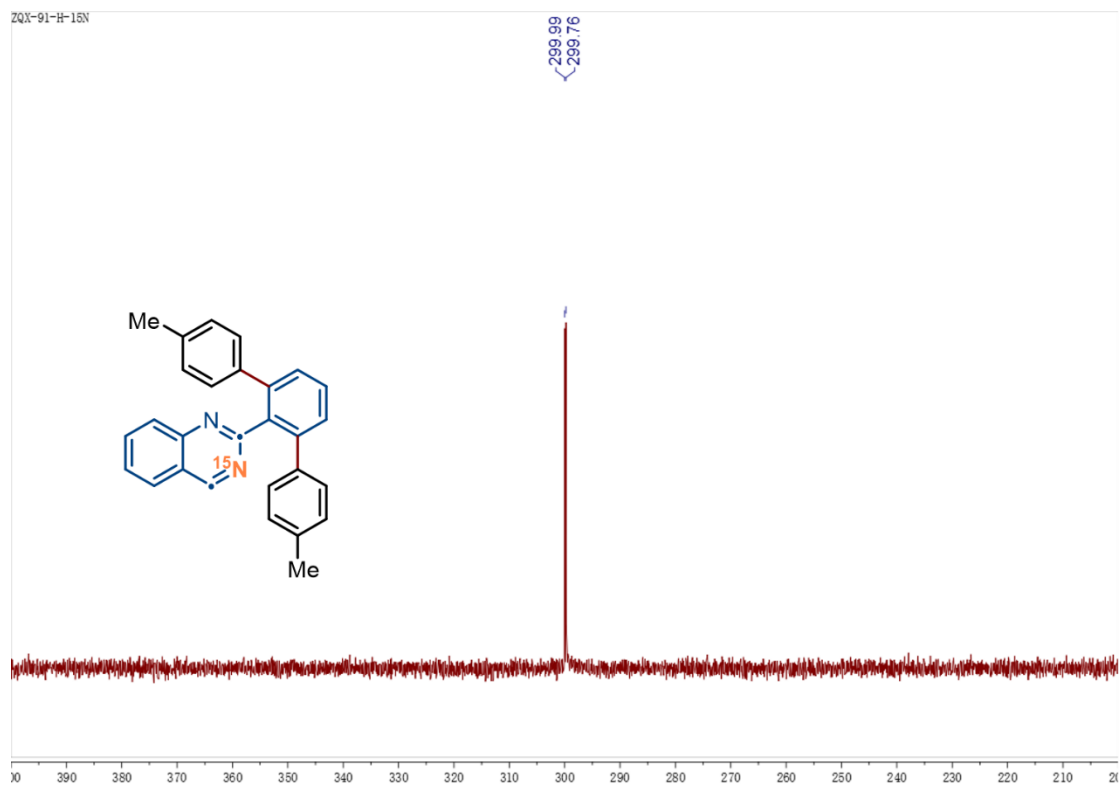
^1H NMR spectrum of **63** (400 MHz, CDCl_3)



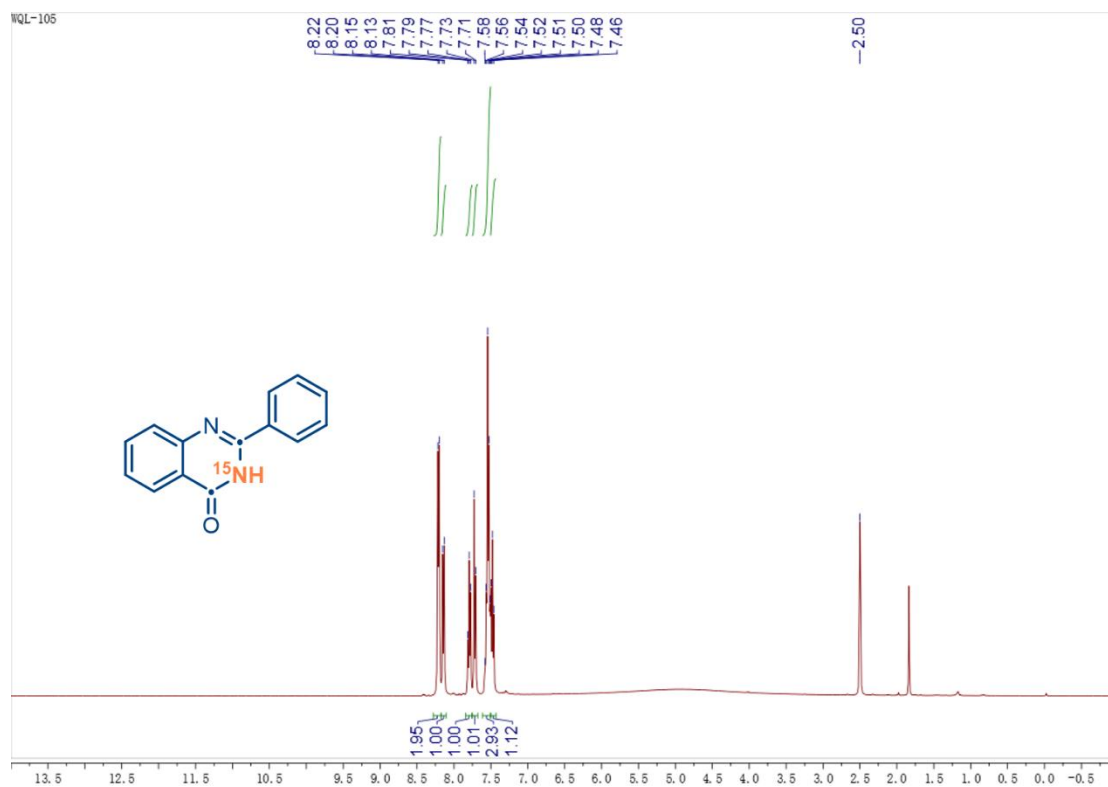
^{13}C NMR spectrum of **63** (100 MHz, CDCl_3)



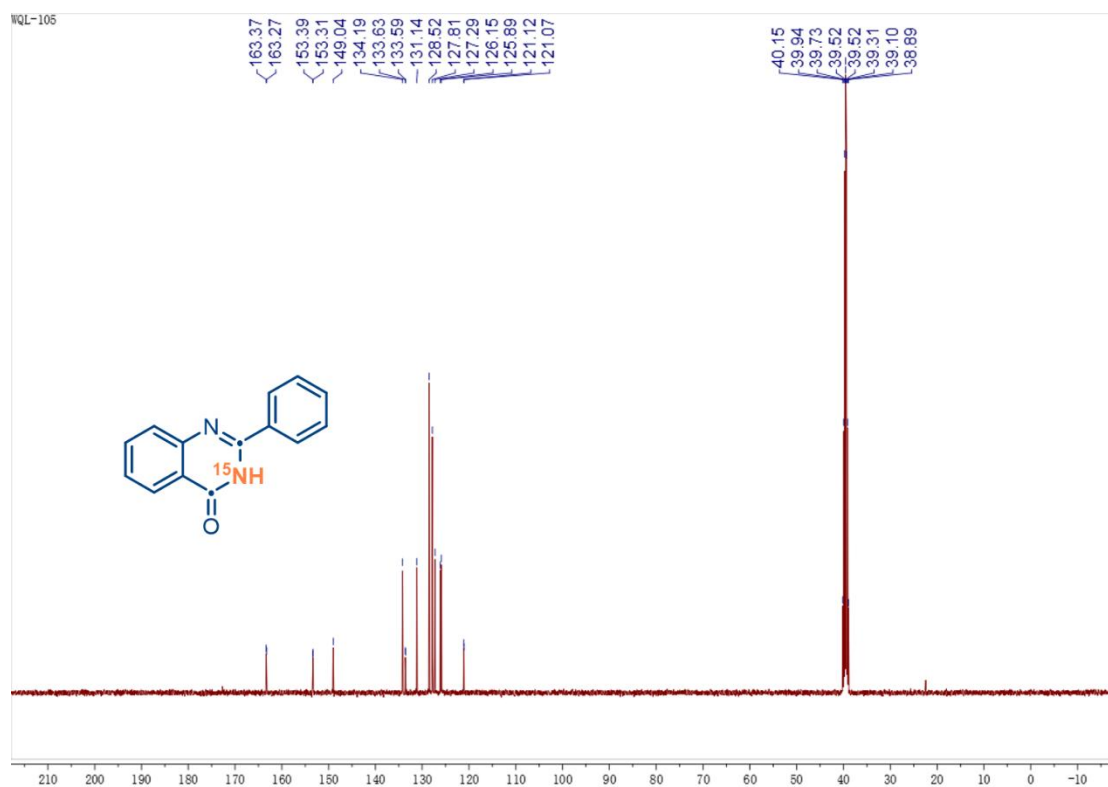
^{15}N NMR spectrum of **63** (50 MHz, CDCl_3)



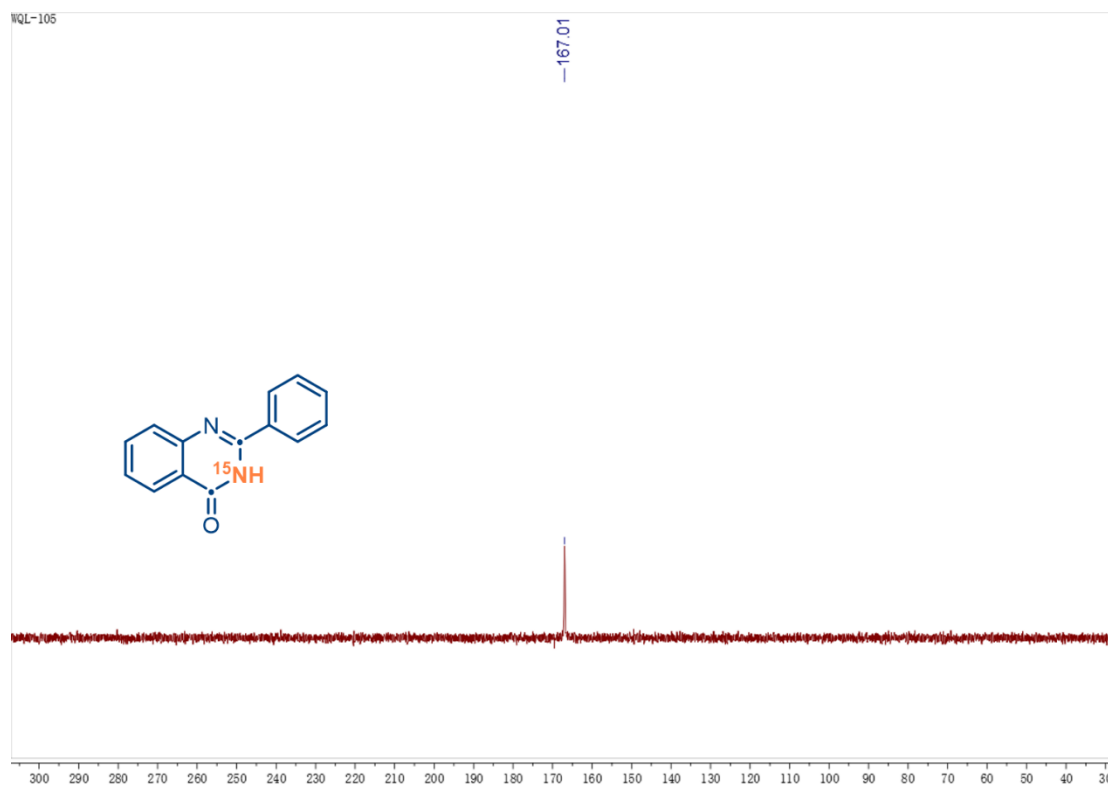
¹H NMR spectrum of **64** (400 MHz, DMSO-*d*₆)



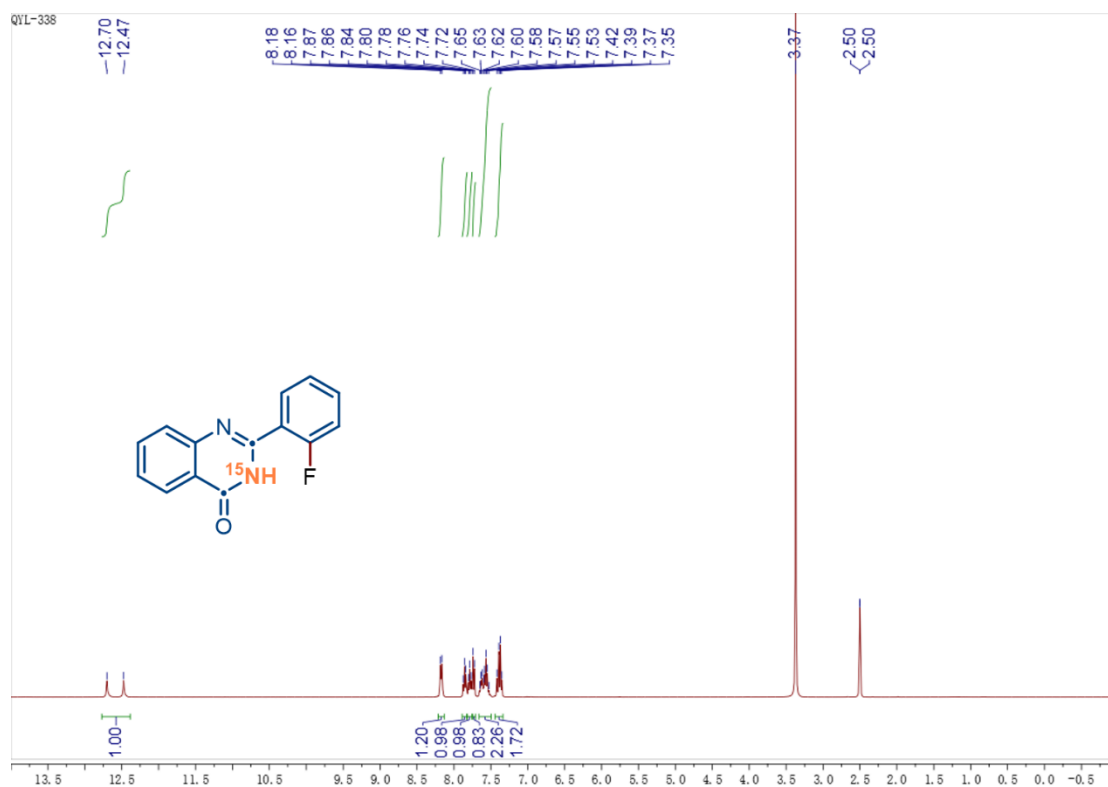
¹³C NMR spectrum of **64** (100 MHz, DMSO-*d*₆)



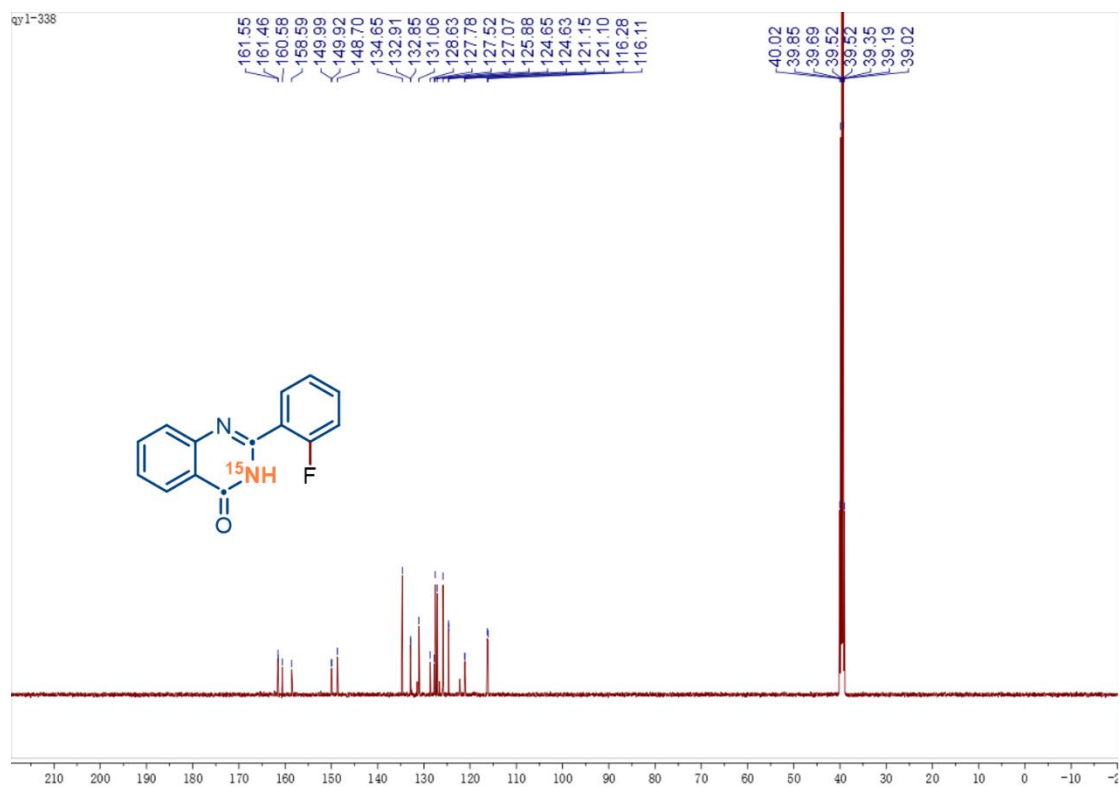
^{15}N NMR spectrum of **64** (50 MHz, $\text{DMSO}-d_6$)



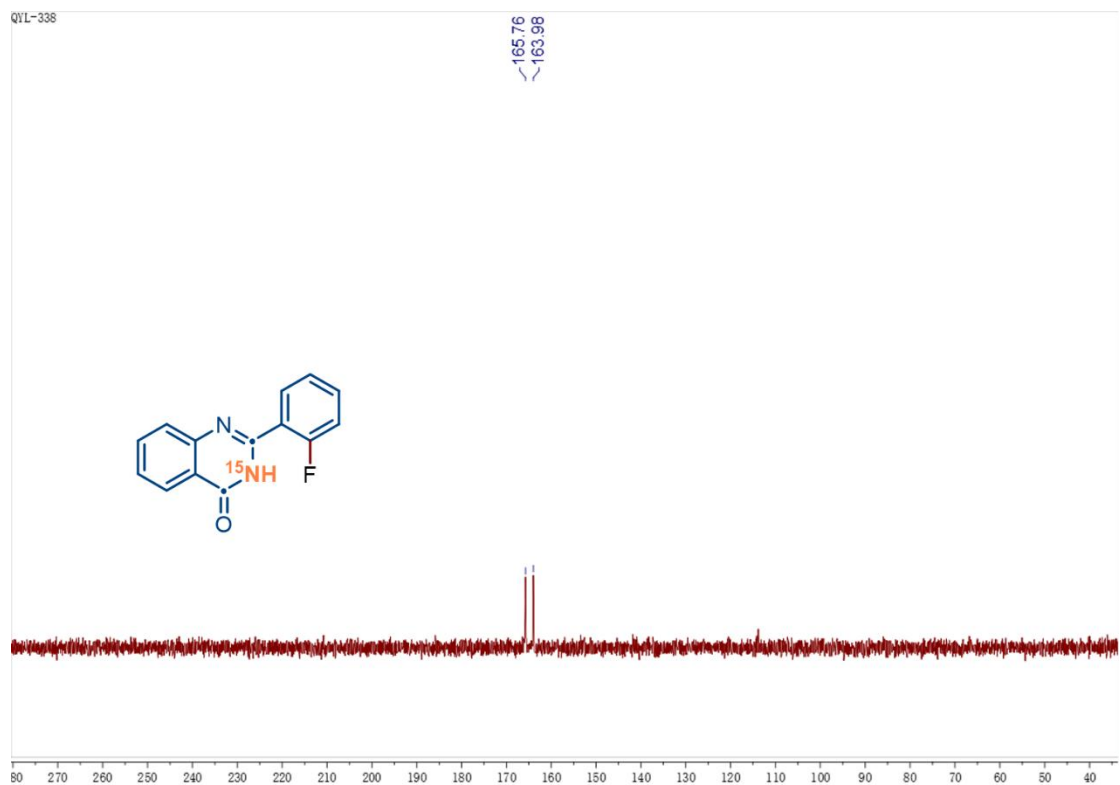
^1H NMR spectrum of **65** (400 MHz, $\text{DMSO}-d_6$)



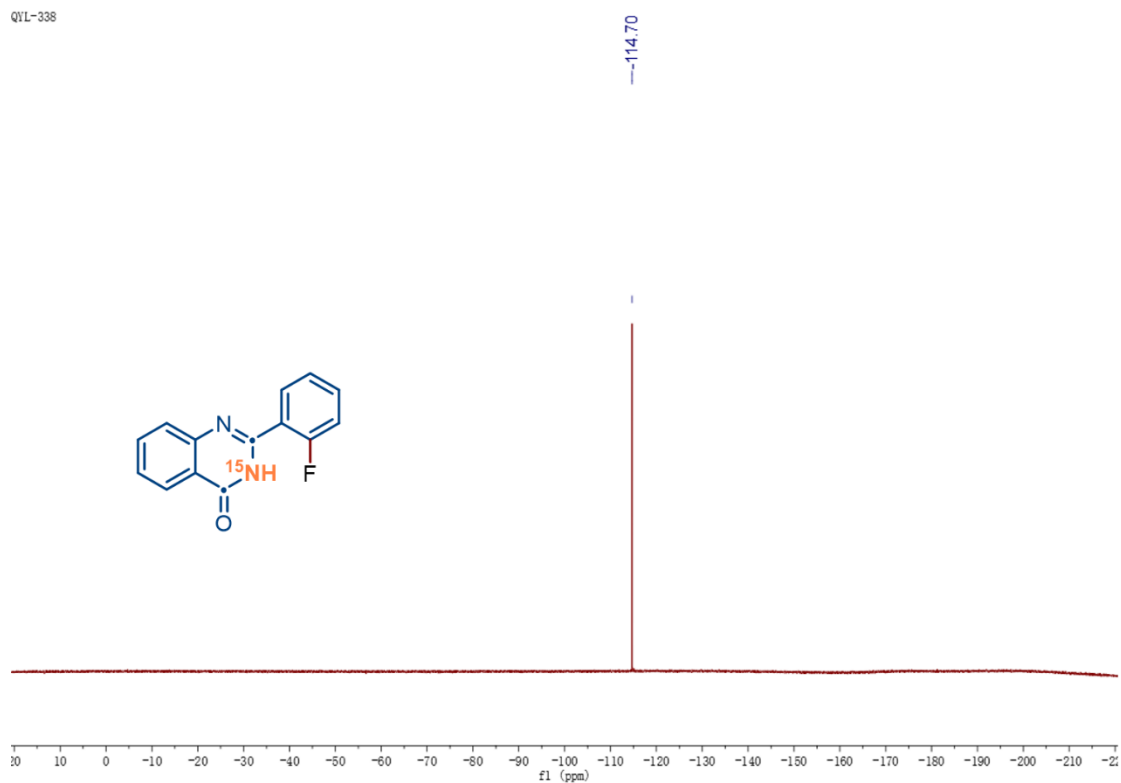
^{13}C NMR spectrum of **65** (125 MHz, DMSO- d_6)



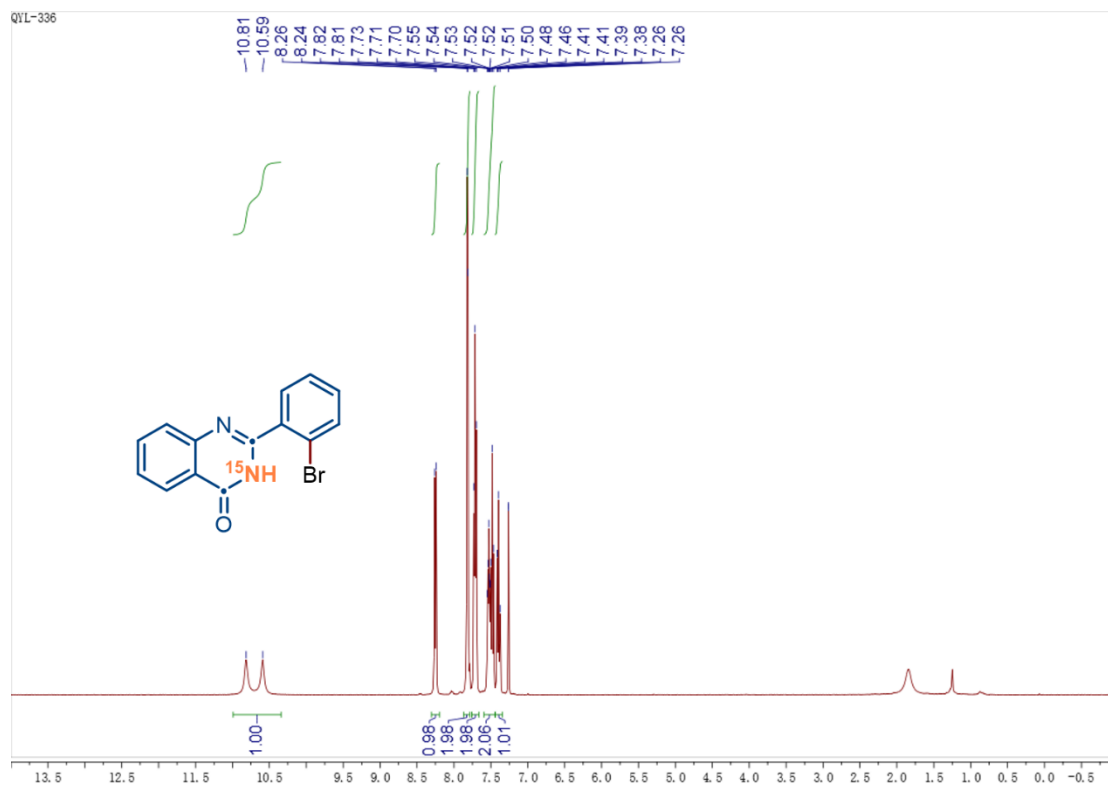
^{15}N NMR spectrum of **65** (50 MHz, DMSO- d_6)



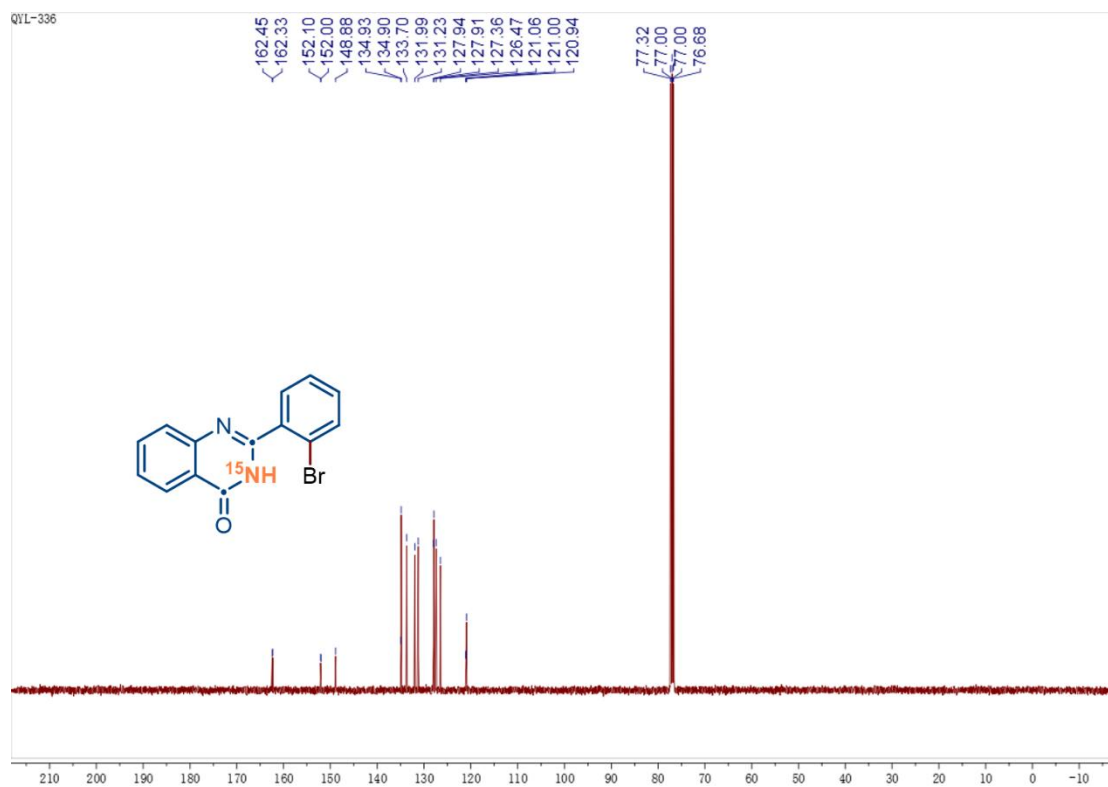
^{19}F NMR spectrum of **65** (376 MHz, $\text{DMSO-}d_6$)



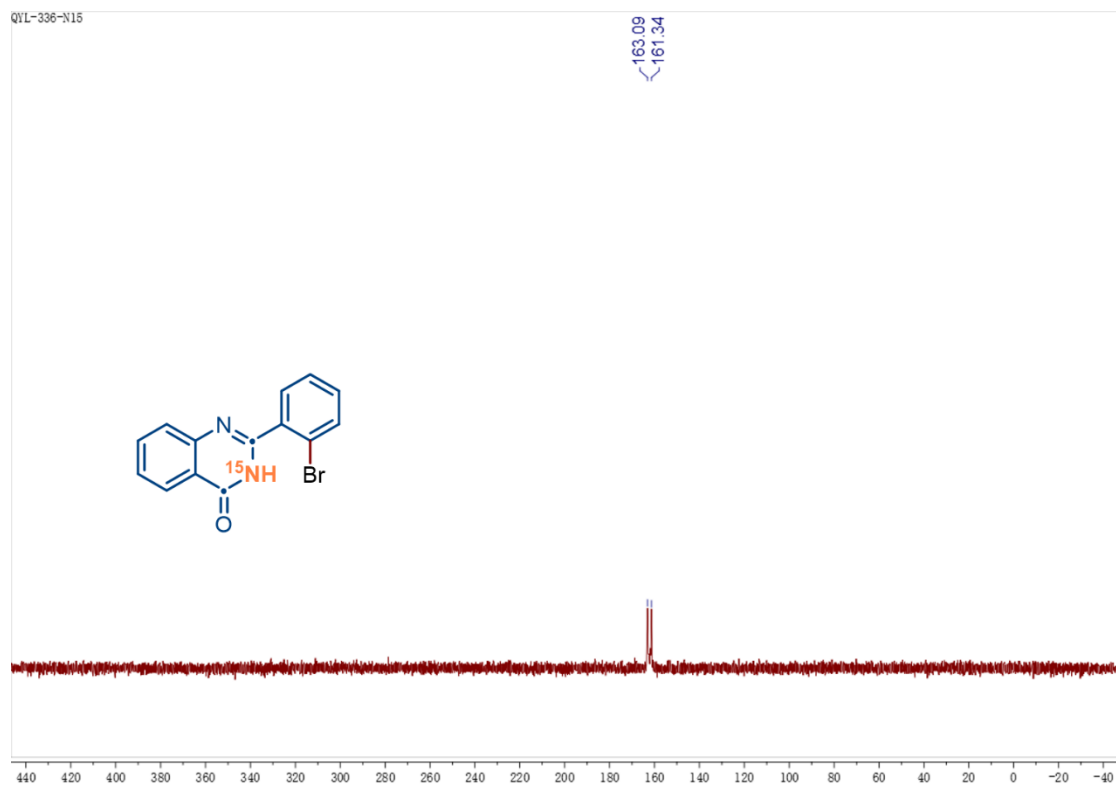
^1H NMR spectrum of **66** (400 MHz, CDCl_3)



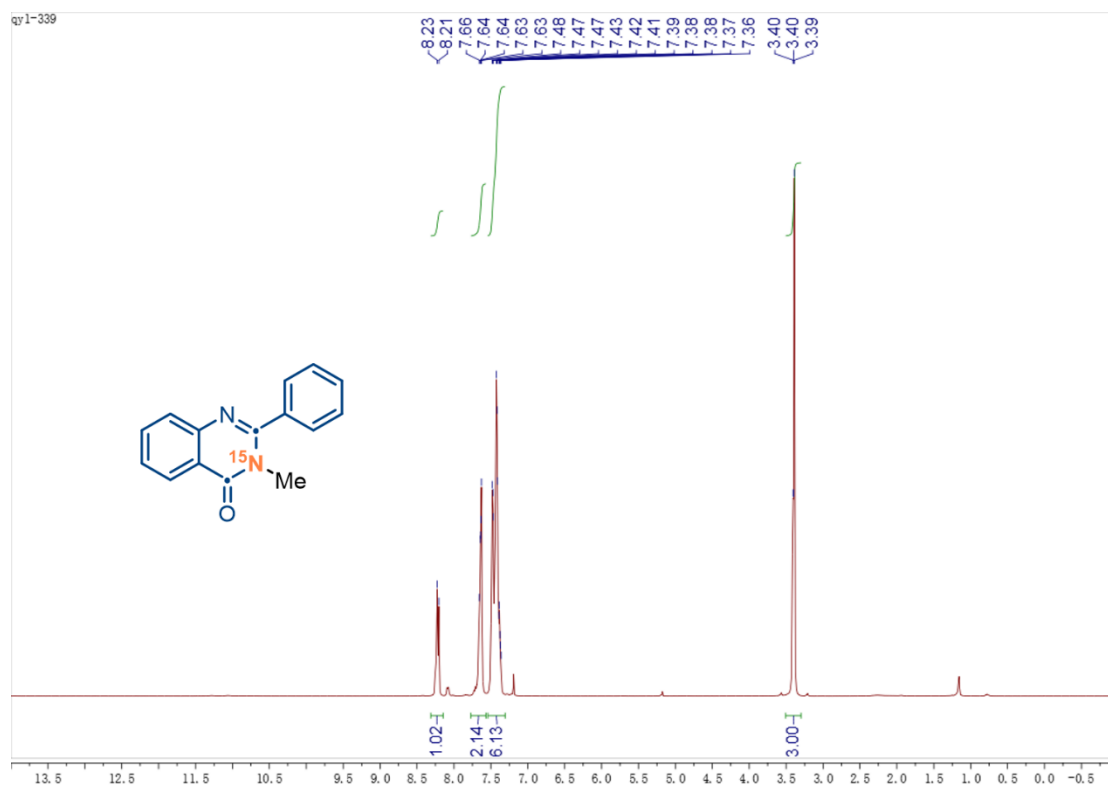
^{13}C NMR spectrum of **66** (100 MHz, CDCl_3)



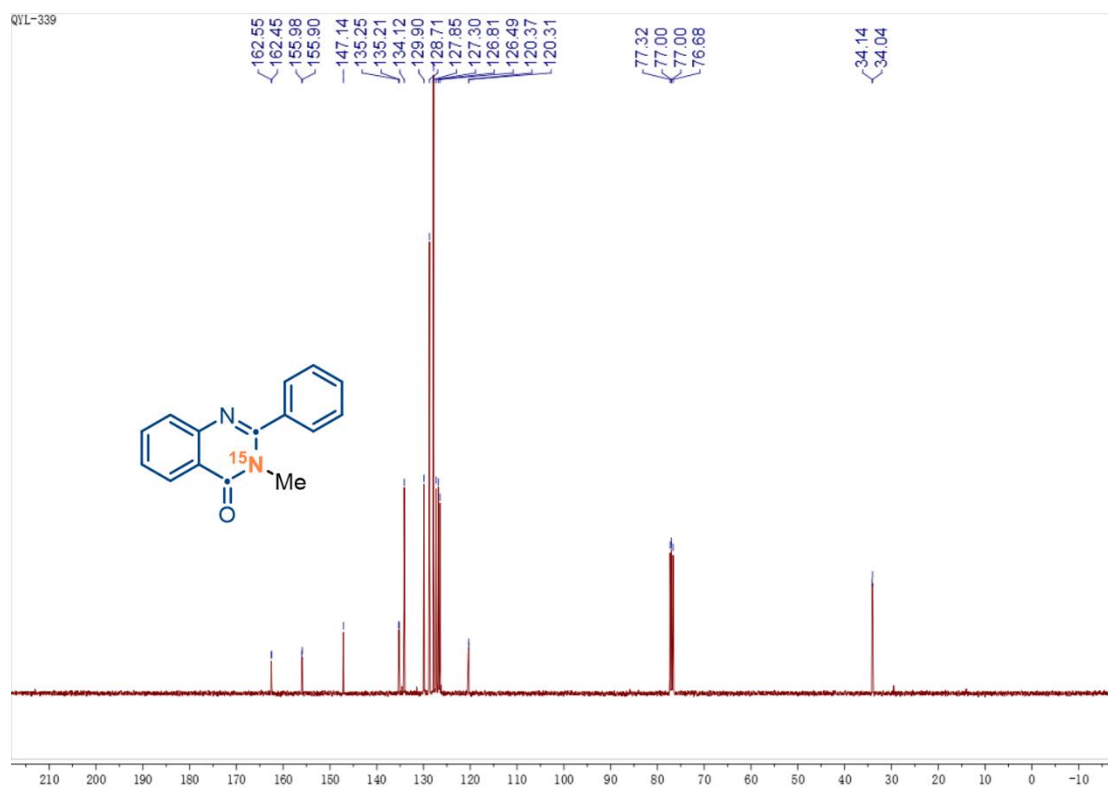
^{15}N NMR spectrum of **66** (50 MHz, CDCl_3)



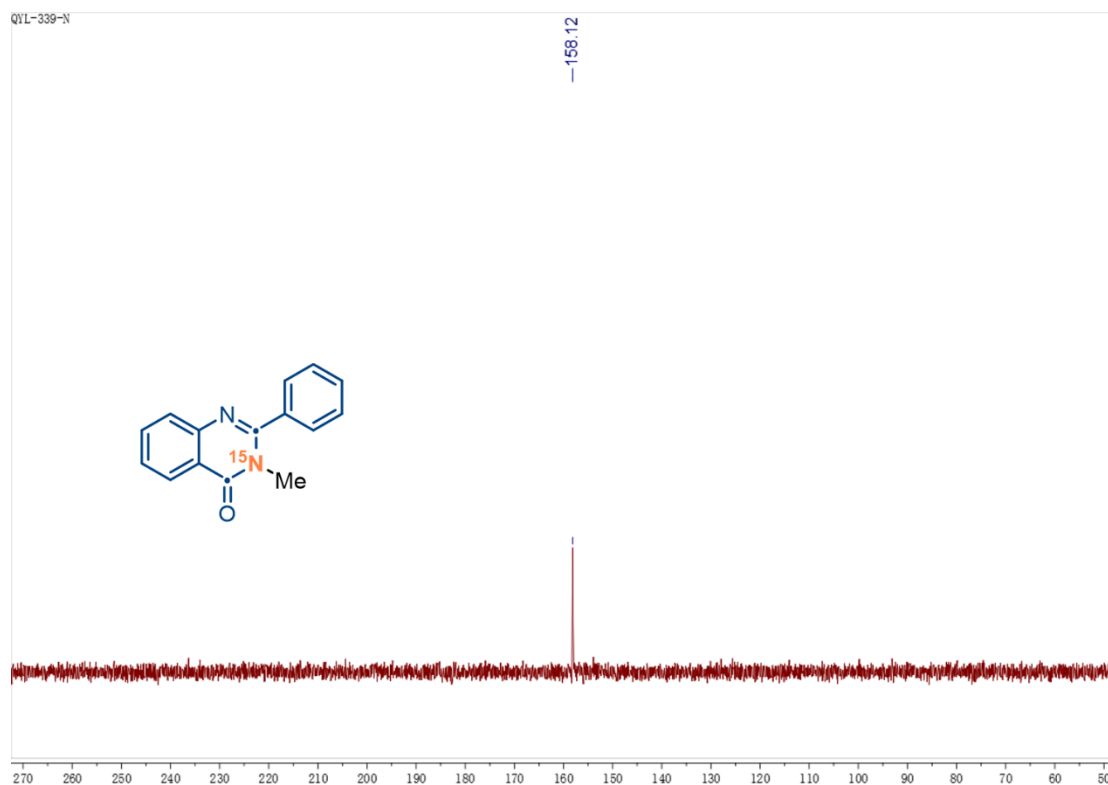
^1H NMR spectrum of **67** (400 MHz, CDCl_3)



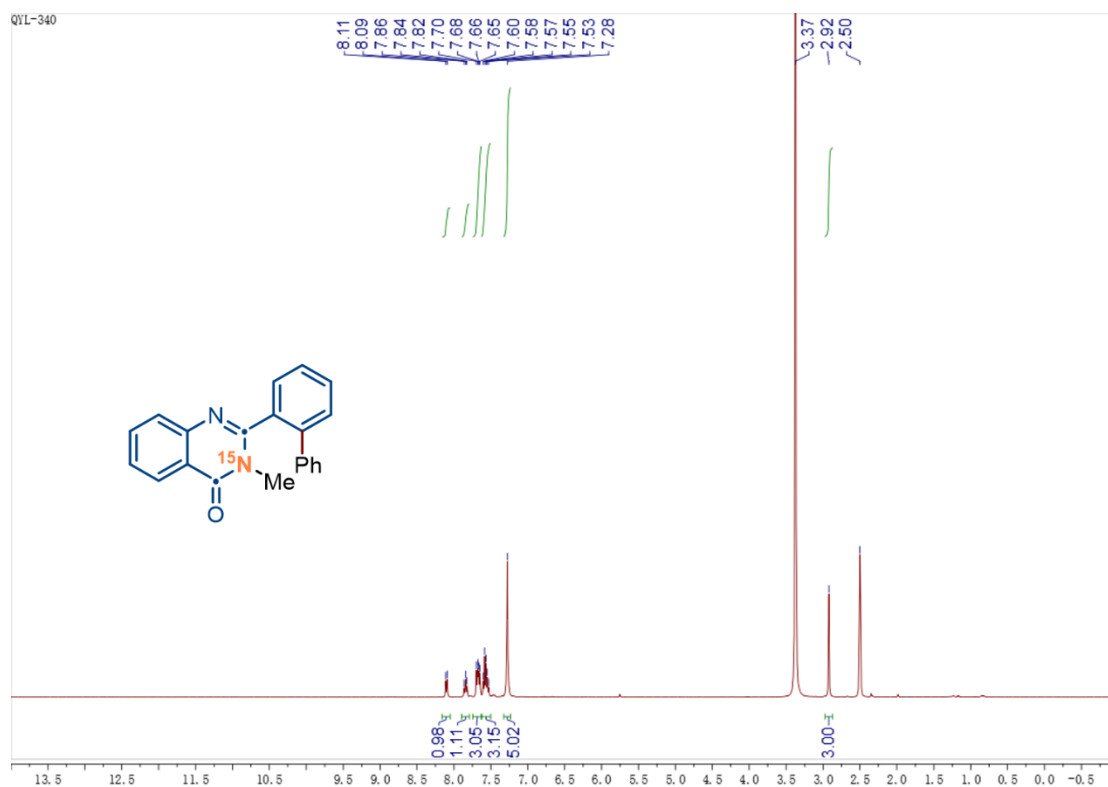
^{13}C NMR spectrum of **67** (100 MHz, CDCl_3)



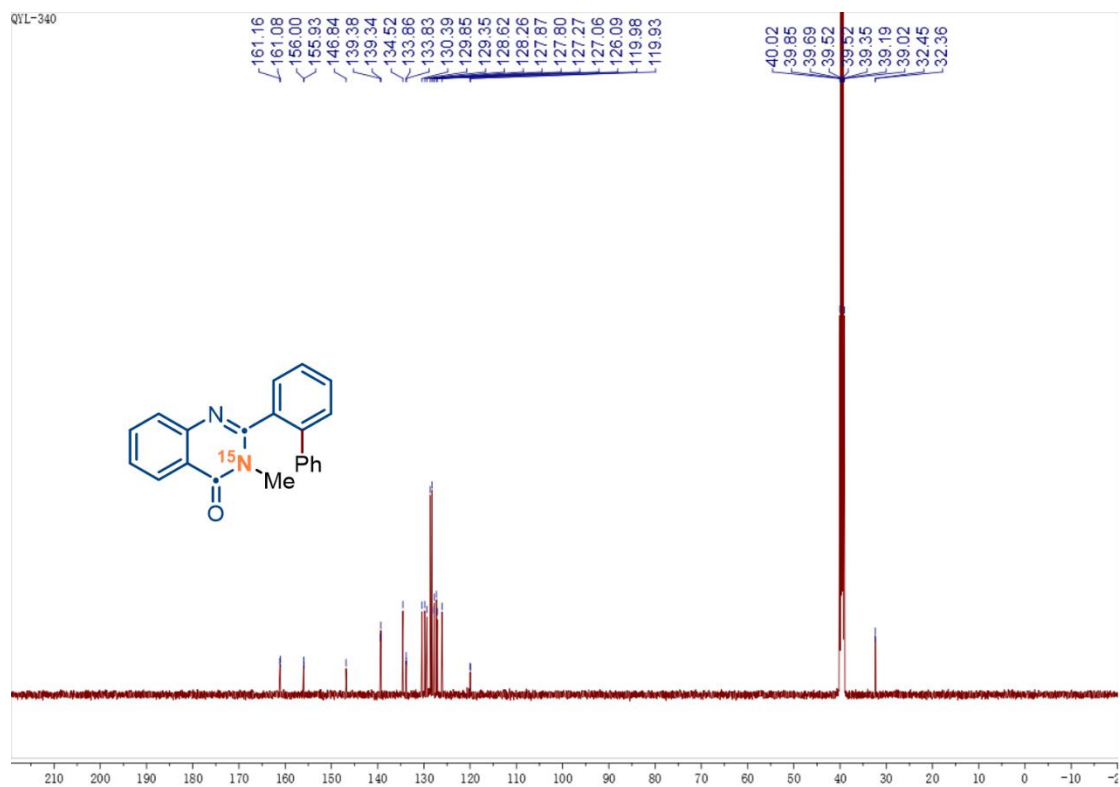
^{15}N NMR spectrum of **67** (50 MHz, CDCl_3)



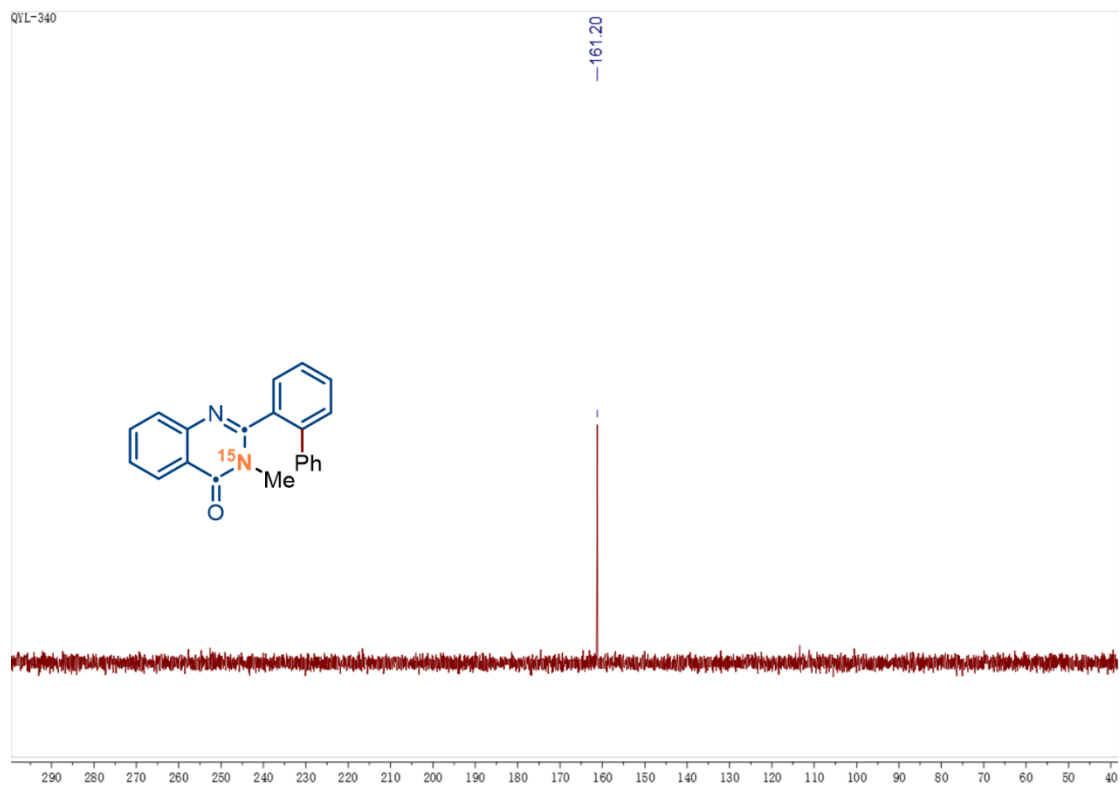
^1H NMR spectrum of **68** (400 MHz, $\text{DMSO}-d_6$)



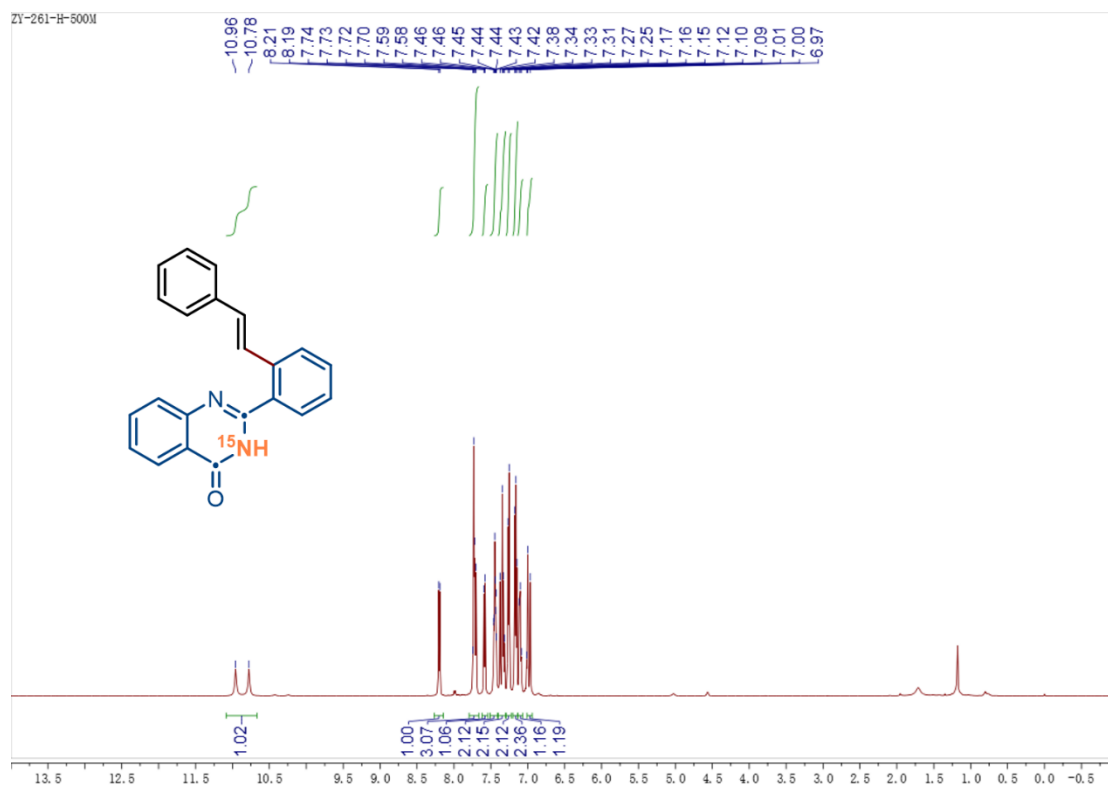
^{13}C NMR spectrum of **68** (125 MHz, $\text{DMSO}-d_6$)



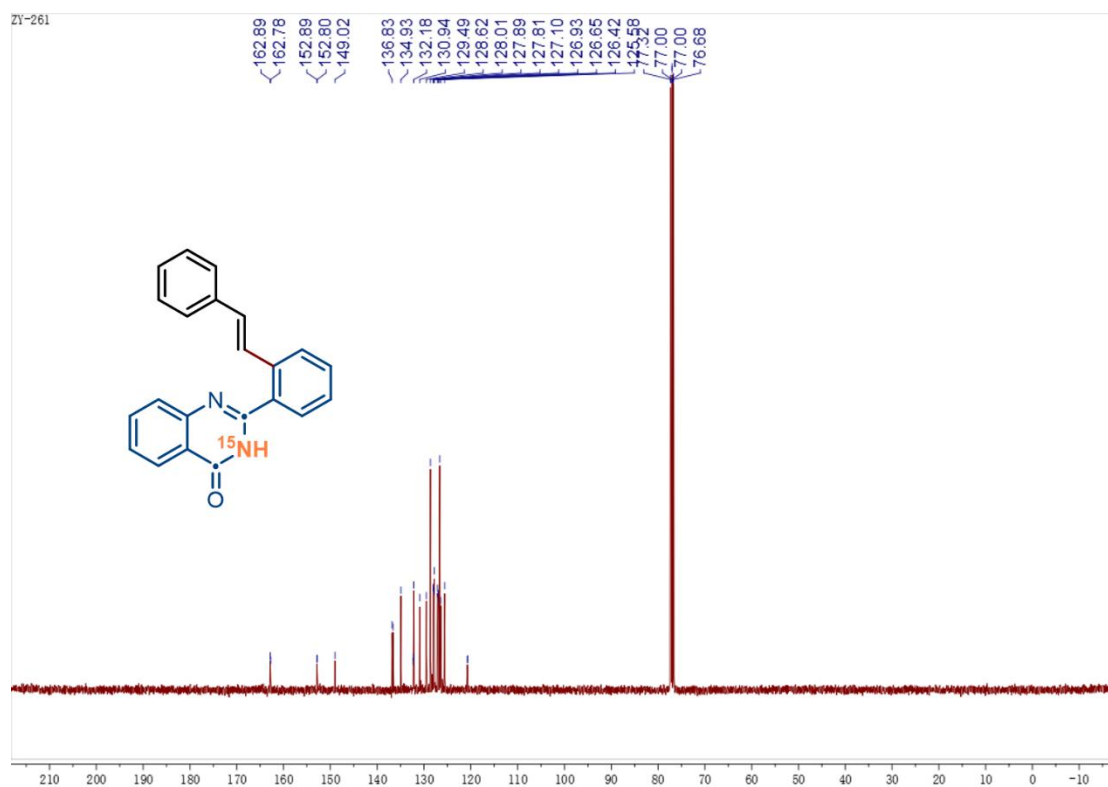
^{15}N NMR spectrum of **68** (50 MHz, $\text{DMSO}-d_6$)



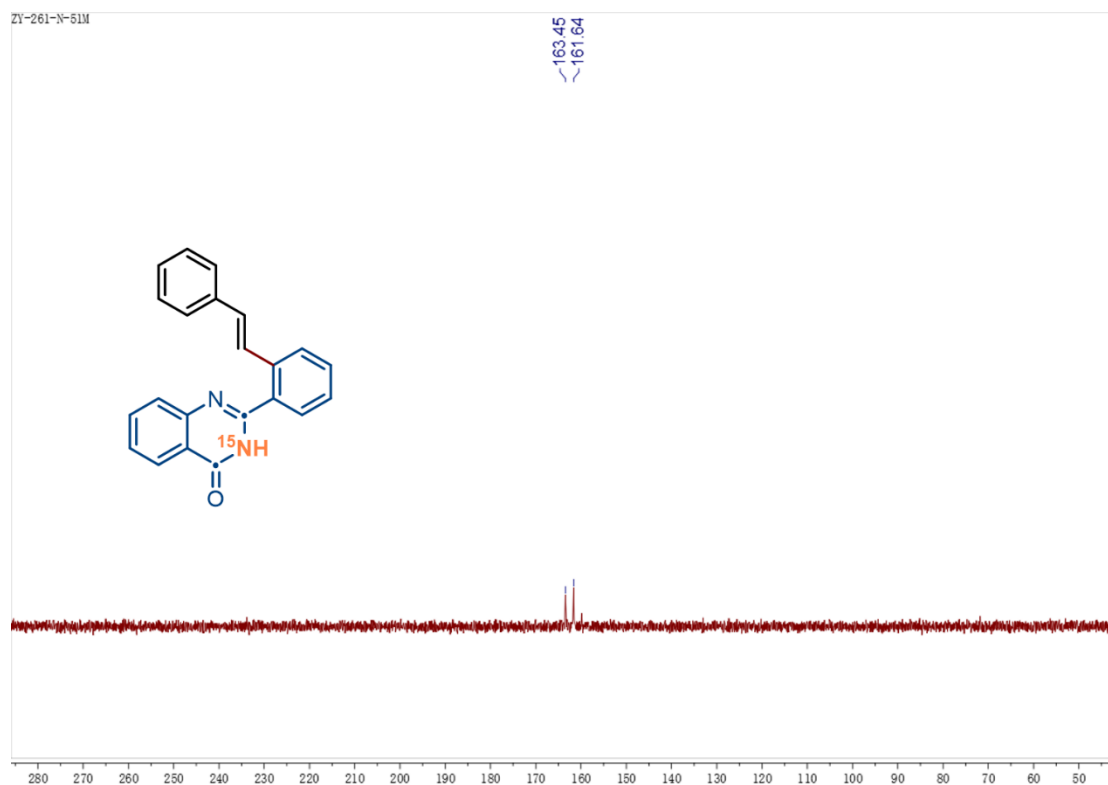
^1H NMR spectrum of **69** (500 MHz, CDCl_3)



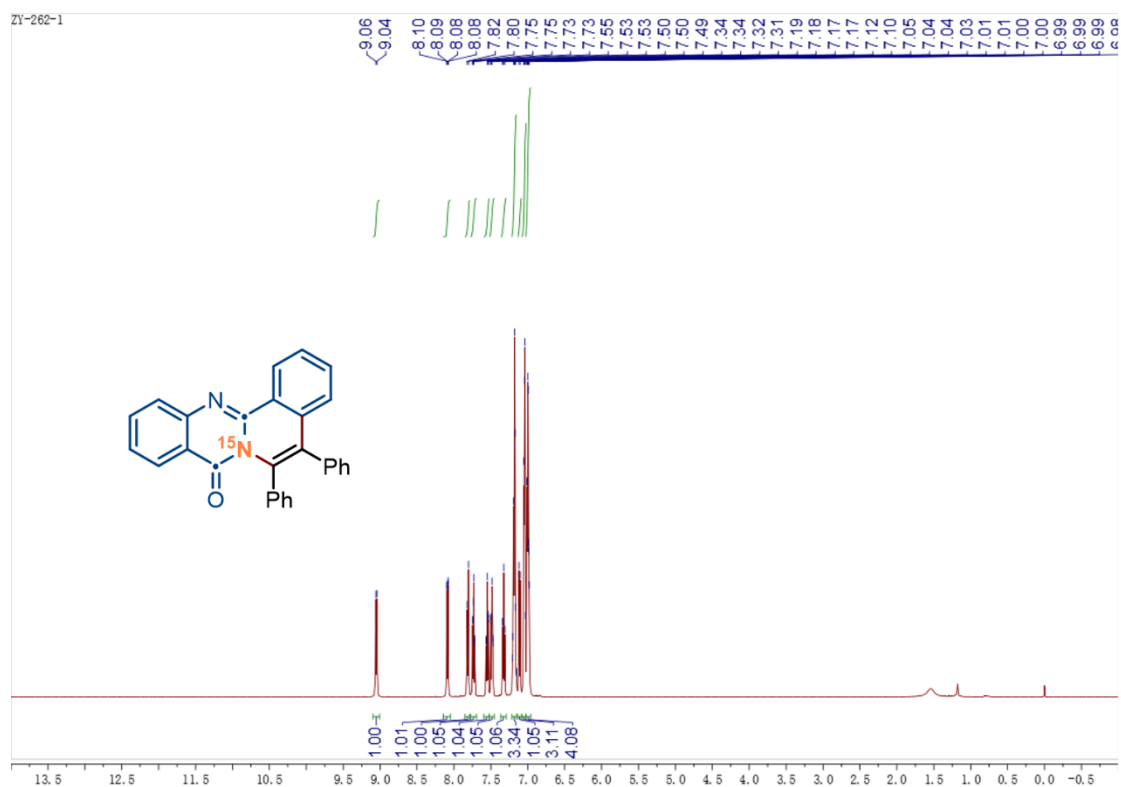
^{13}C NMR spectrum of **69** (100 MHz, CDCl_3)



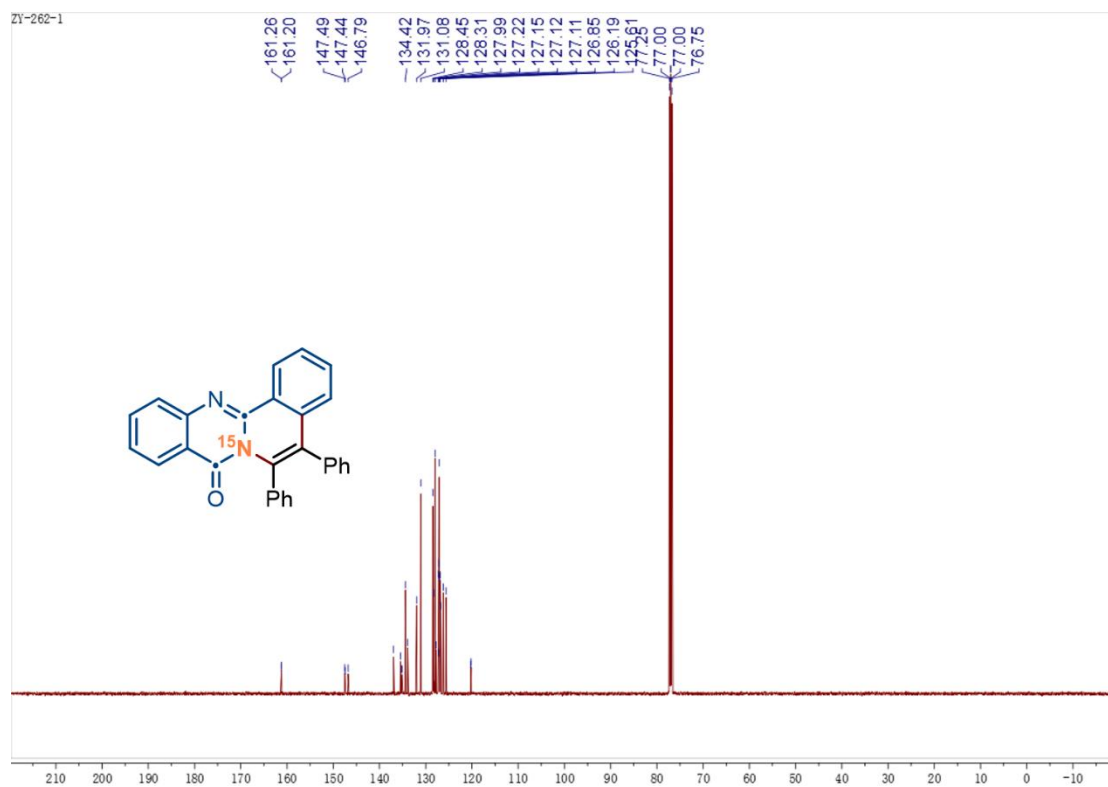
^{15}N NMR spectrum of **69** (50 MHz, CDCl_3)



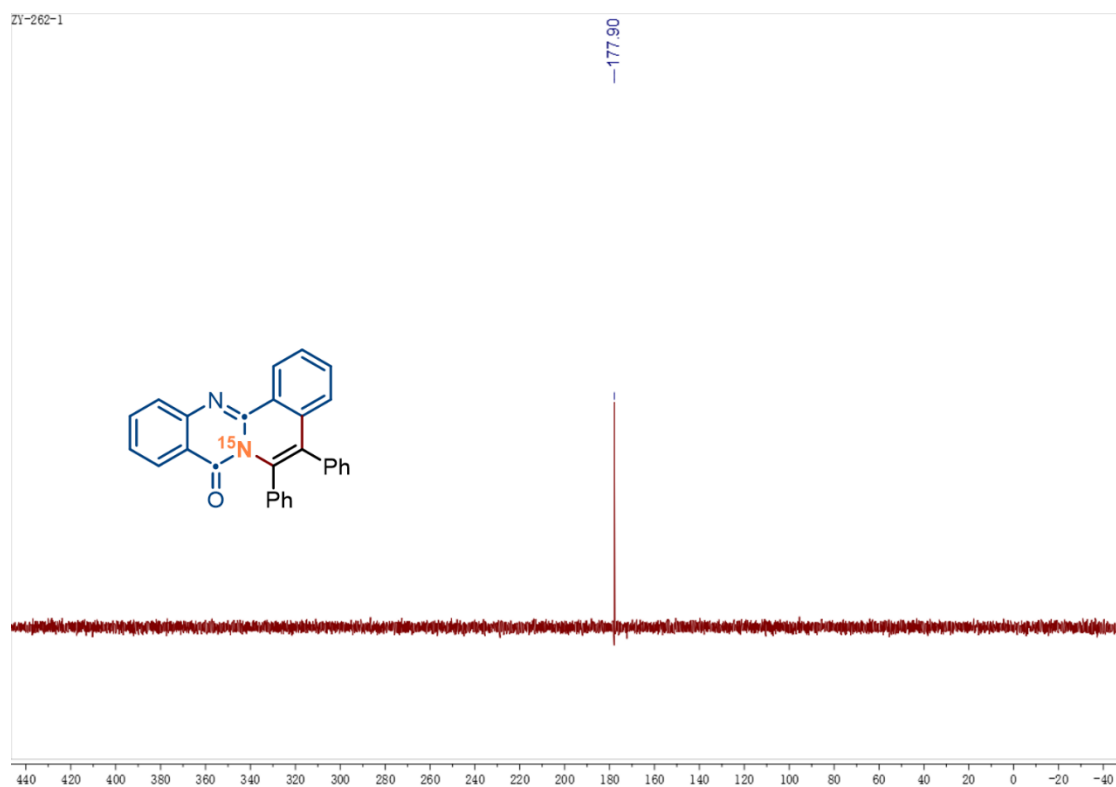
^1H NMR spectrum of **70** (500 MHz, CDCl_3)



^{13}C NMR spectrum of **70** (125 MHz, CDCl_3)



^{15}N NMR spectrum of **70** (50 MHz, CDCl_3)



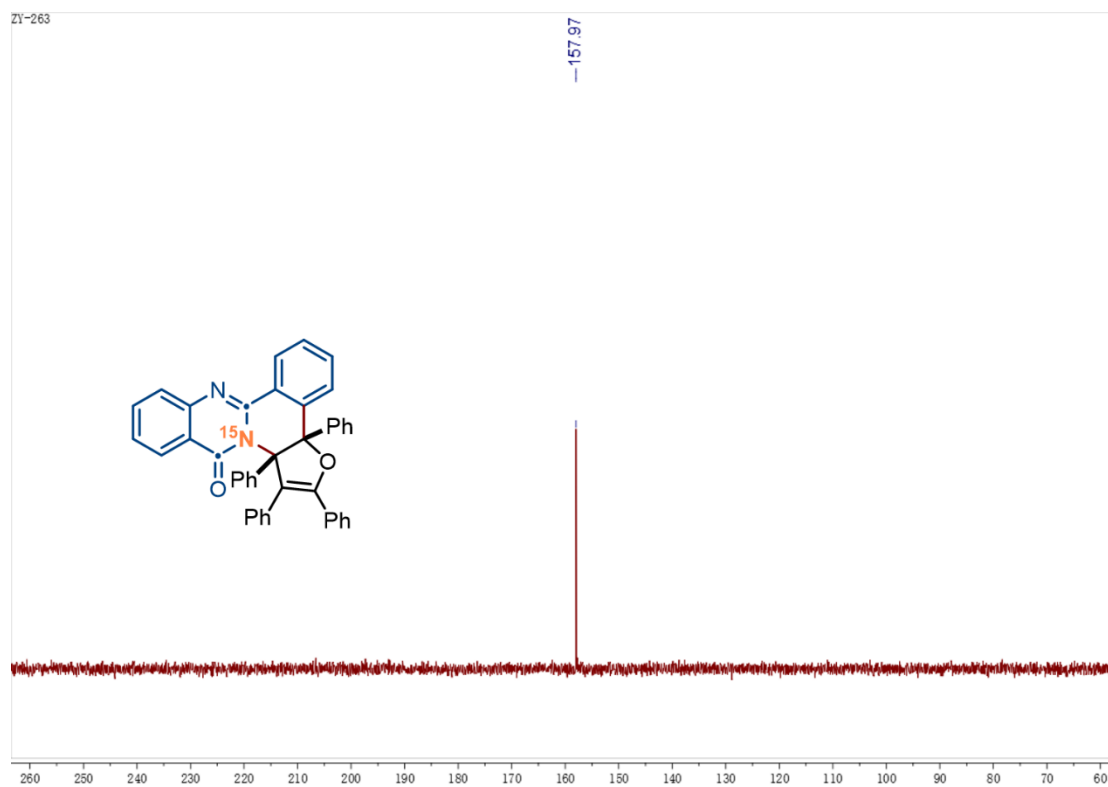
Z1-263-C-125M

Chemical structure of compound 1 is shown as an inset. The structure is a complex heterocycle featuring a benzimidazole core fused to a benzene ring, with a nitro group (NO₂) at the 2-position. The structure is labeled with ¹⁵N and Ph groups.

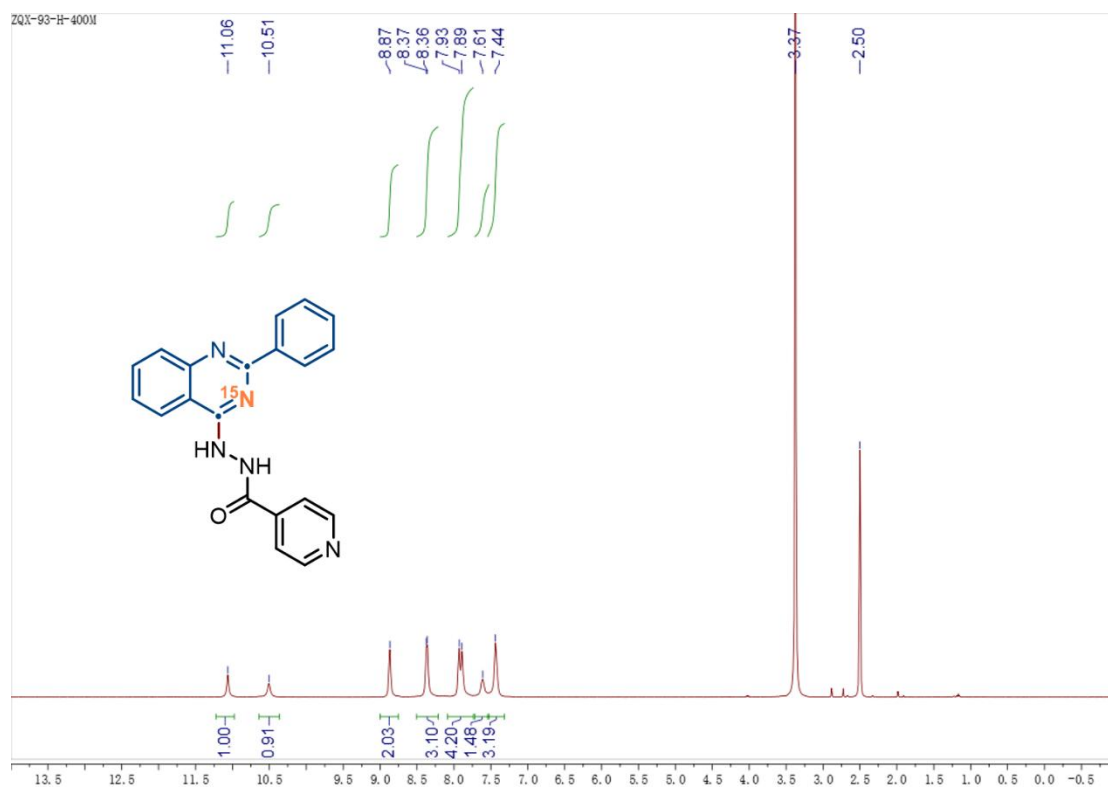
The ¹⁵N NMR spectrum shows a series of peaks in the aromatic region (120-160 ppm) and a solvent peak at 77.00 ppm. The x-axis is labeled from 210 to -10 ppm.

Peak list (ppm): 160.63, 160.56, 129.05, 128.95, 128.19, 128.12, 127.89, 127.62, 127.33, 127.16, 127.05, 126.84, 126.83, 126.52, 126.47, 126.27, 126.21, 81.62, 81.55, 77.25, 77.00, 76.75.

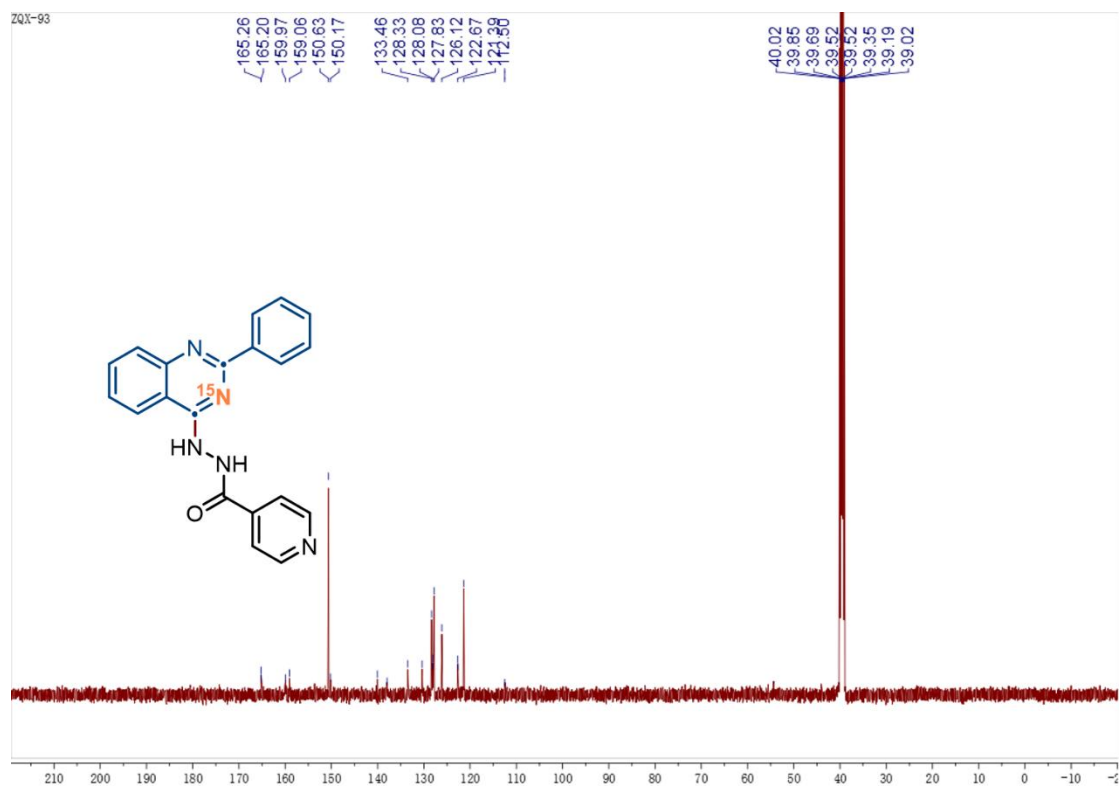
^{15}N NMR spectrum of **71** (50 MHz, CDCl_3)



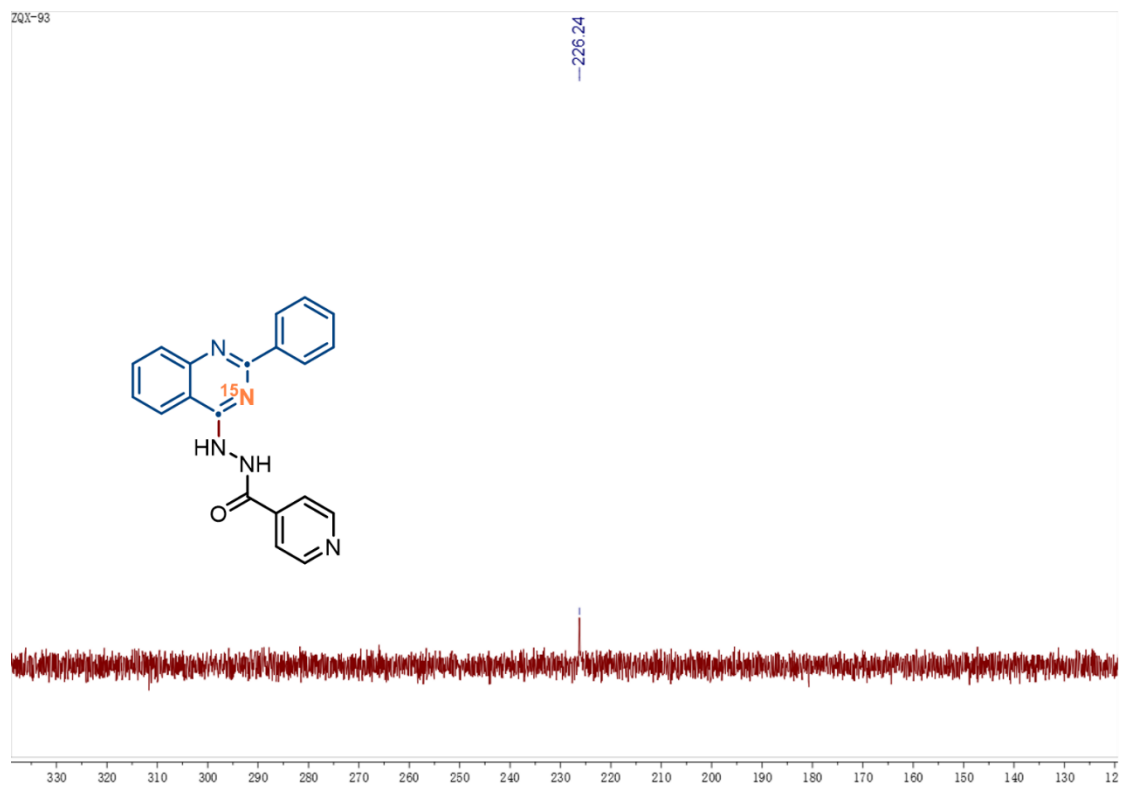
^1H NMR spectrum of **72** (400 MHz, $\text{DMSO}-d_6$)



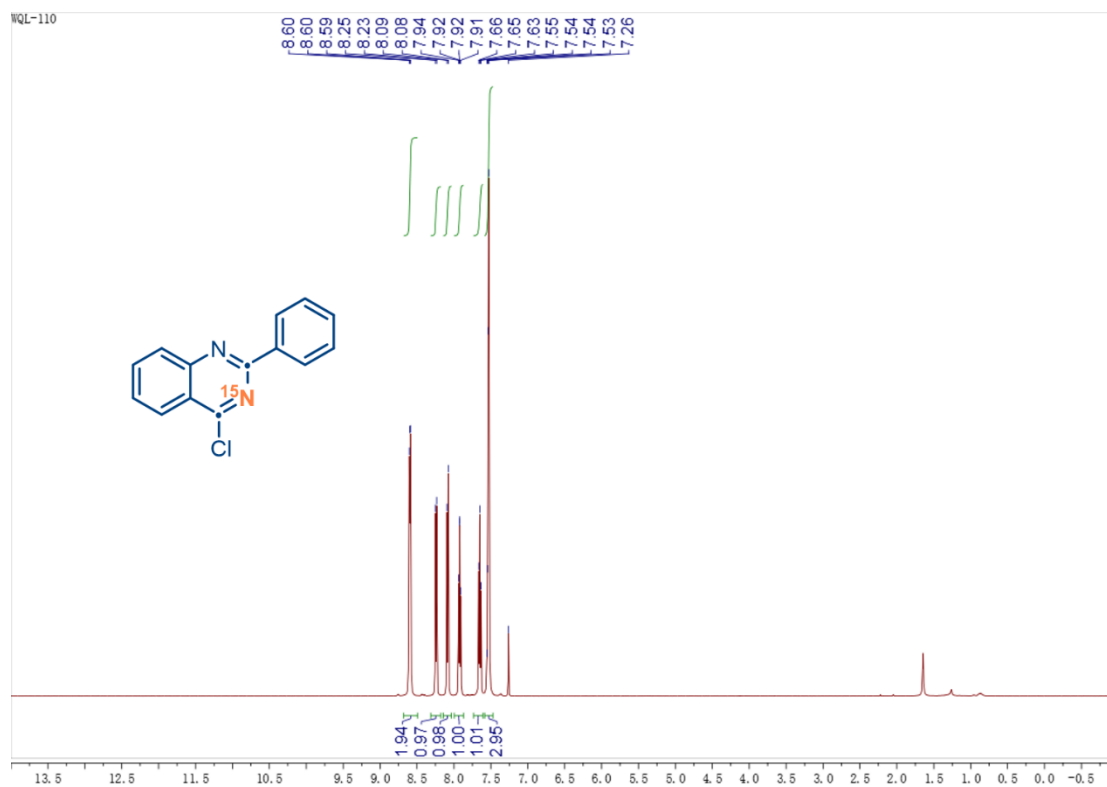
^{13}C NMR spectrum of **72** (125 MHz, $\text{DMSO}-d_6$)



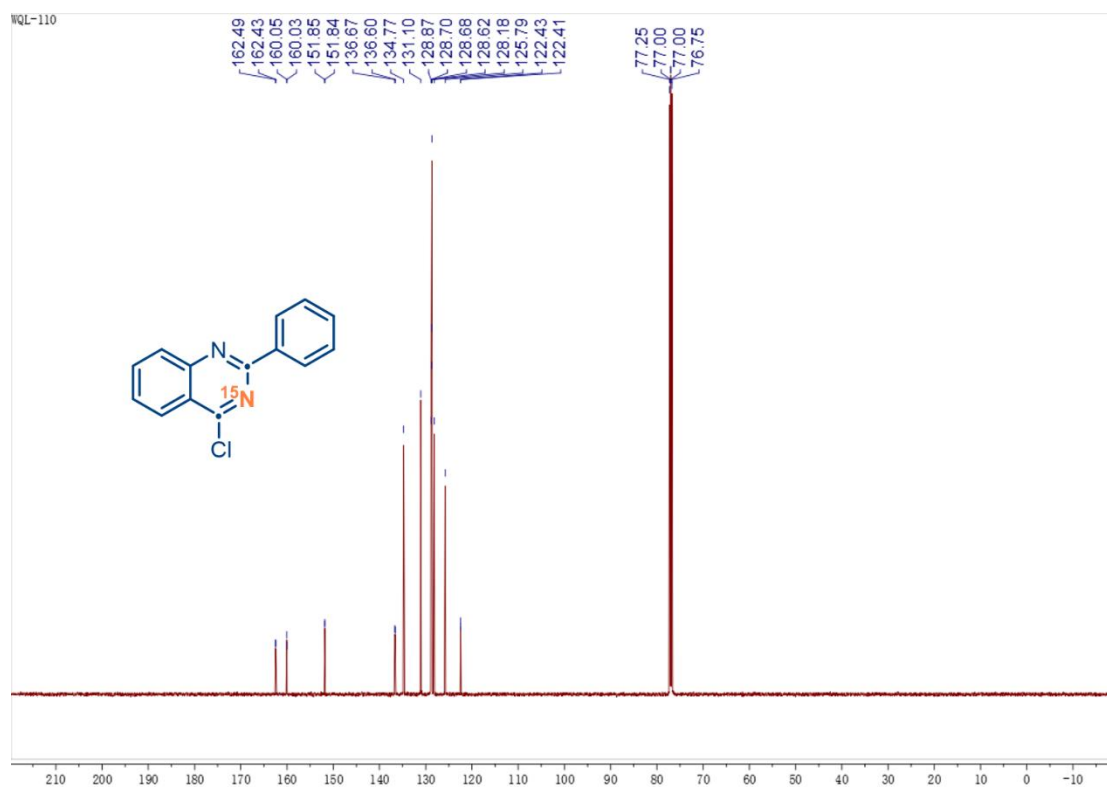
^{15}N NMR spectrum of **72** (50 MHz, $\text{DMSO}-d_6$)



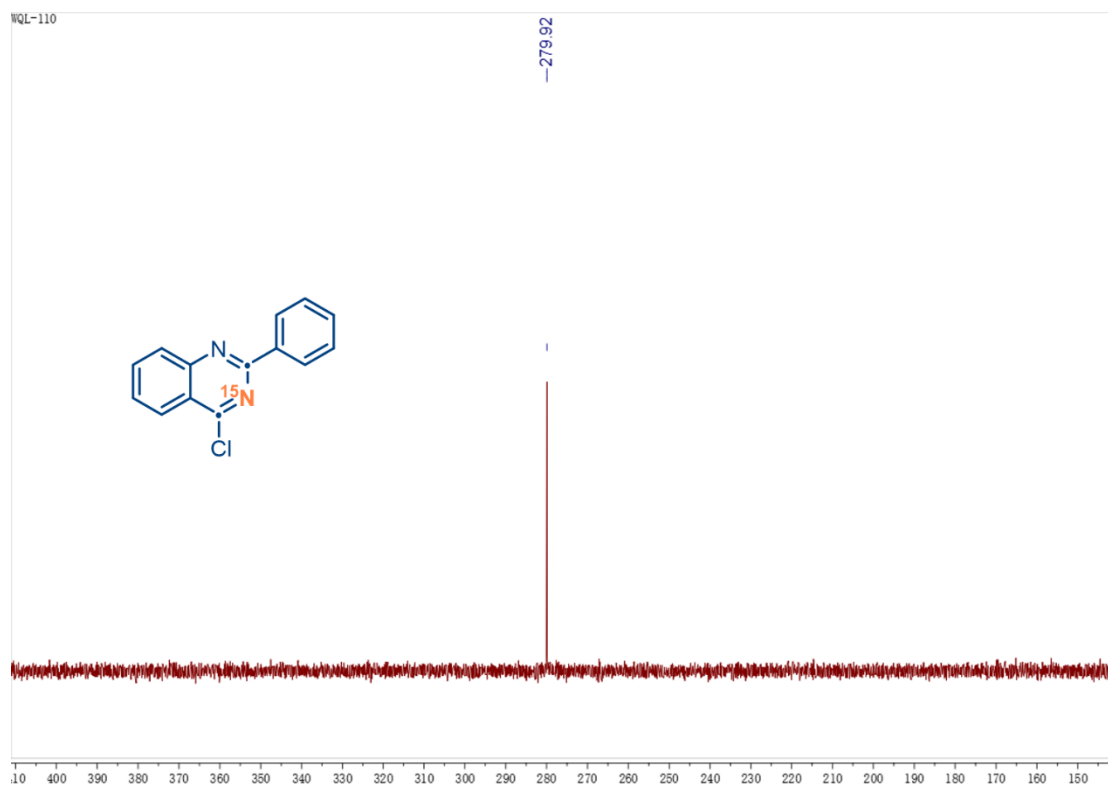
¹H NMR spectrum of **73** (500 MHz, CDCl₃)



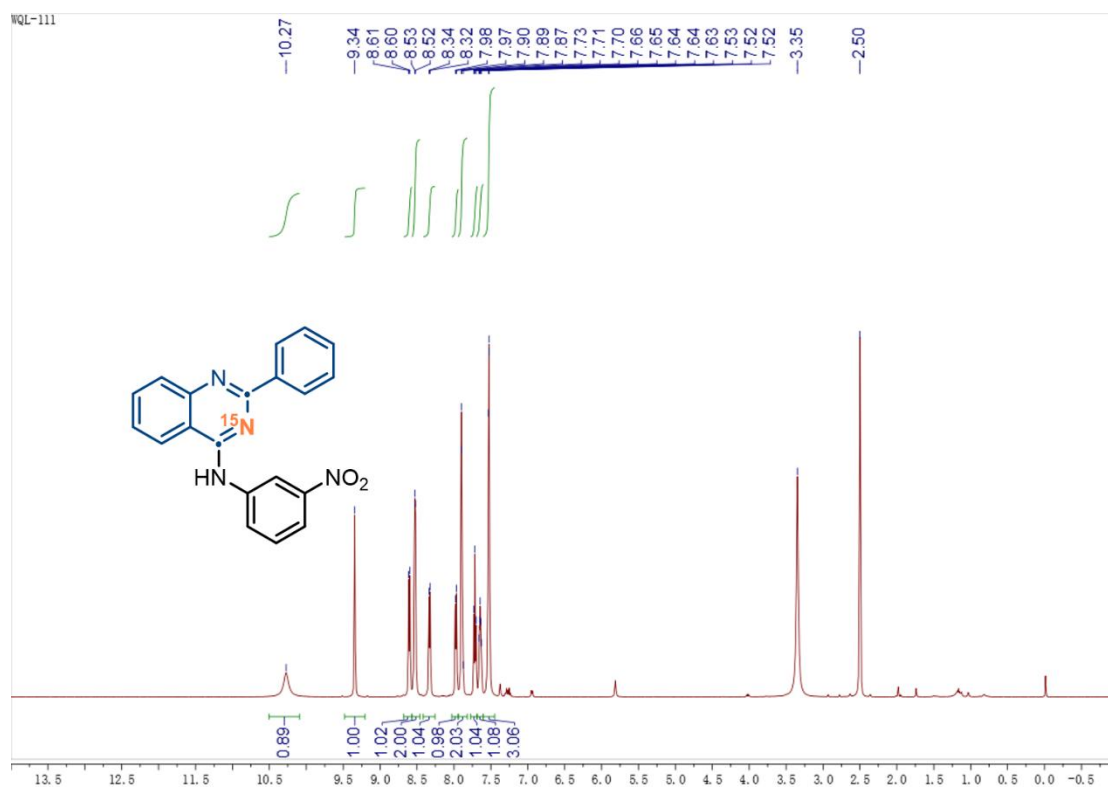
¹³C NMR spectrum of **73** (125 MHz, CDCl₃)



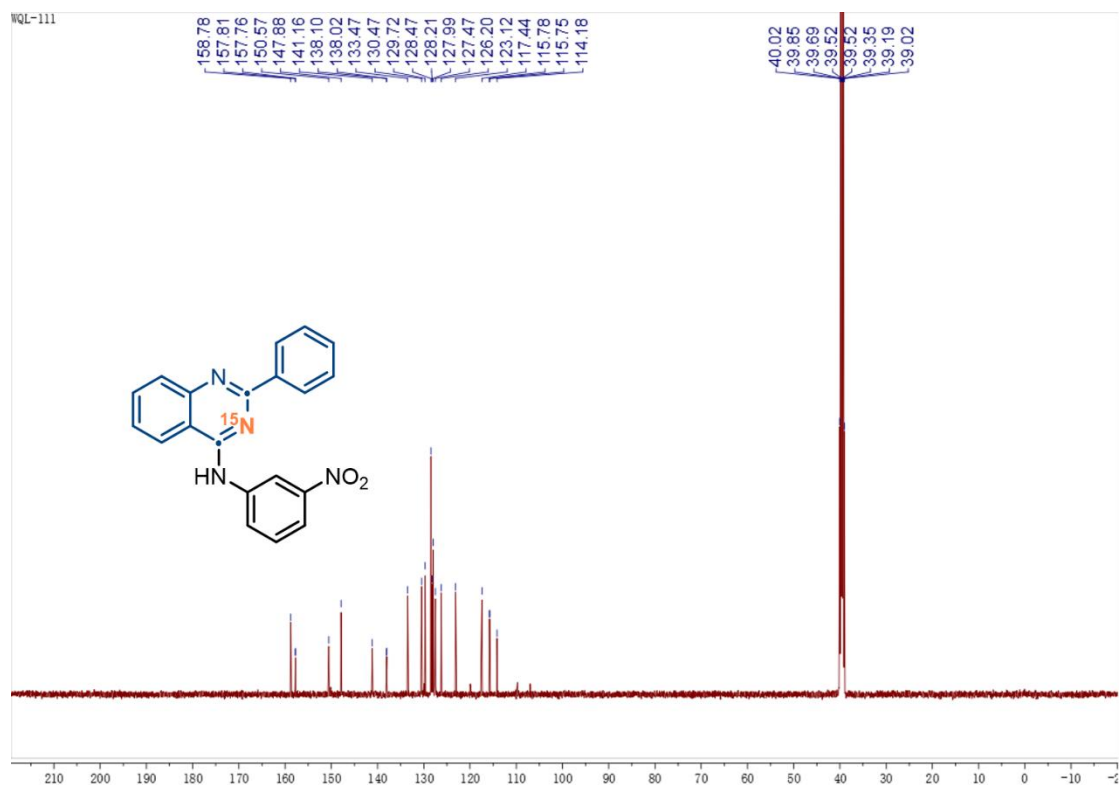
^{15}N NMR spectrum of **73** (50 MHz, CDCl_3)



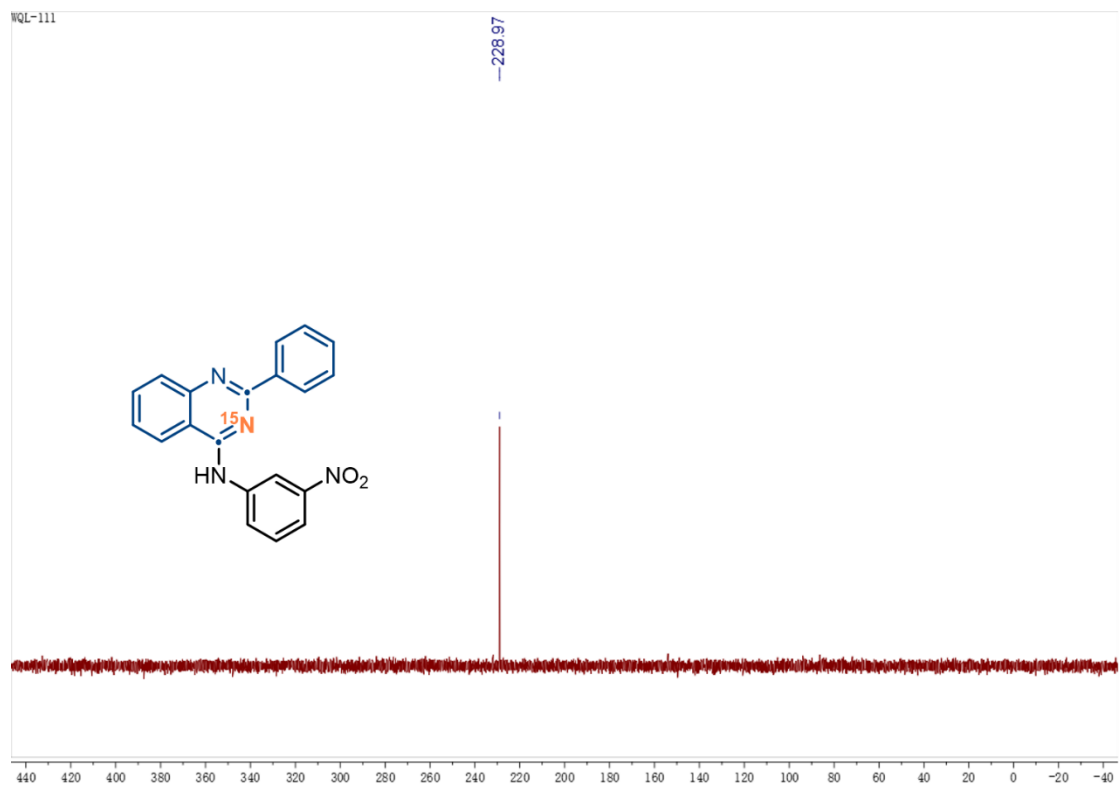
^1H NMR spectrum of **74** (500 MHz, $\text{DMSO}-d_6$)



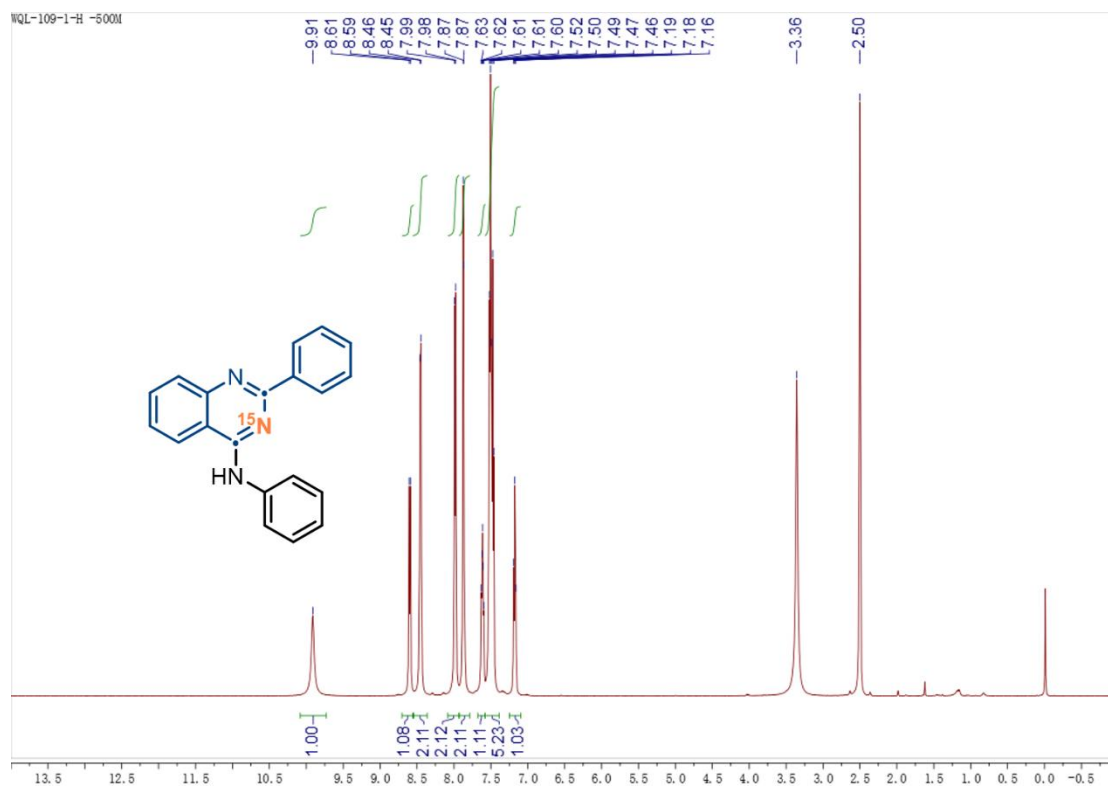
^{13}C NMR spectrum of **74** (125 MHz, $\text{DMSO}-d_6$)



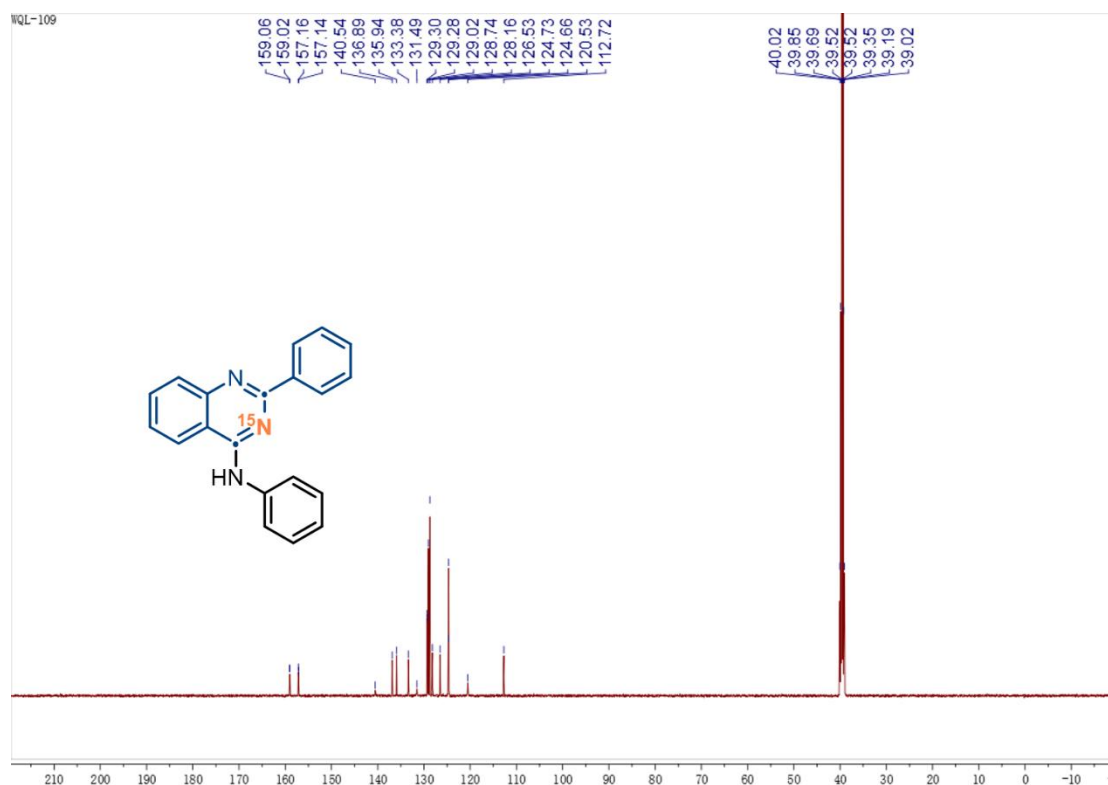
^{15}N NMR spectrum of **74** (50 MHz, $\text{DMSO}-d_6$)



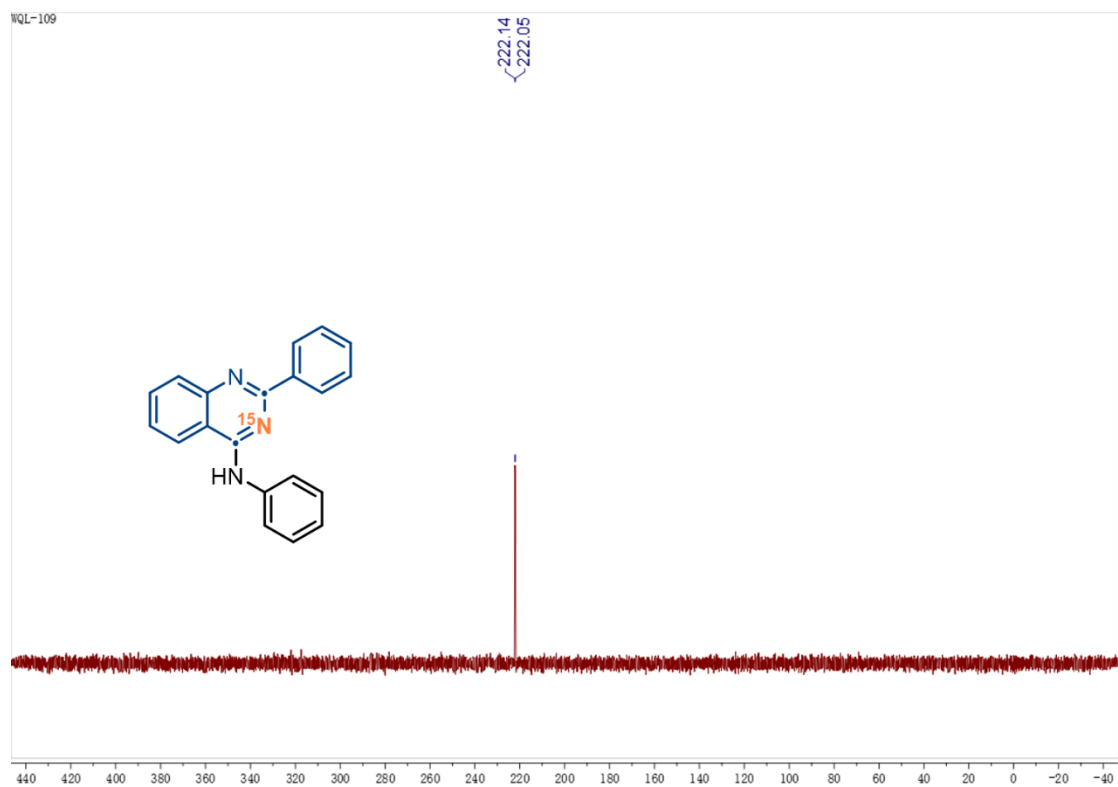
^1H NMR spectrum of **75** (500 MHz, $\text{DMSO}-d_6$)



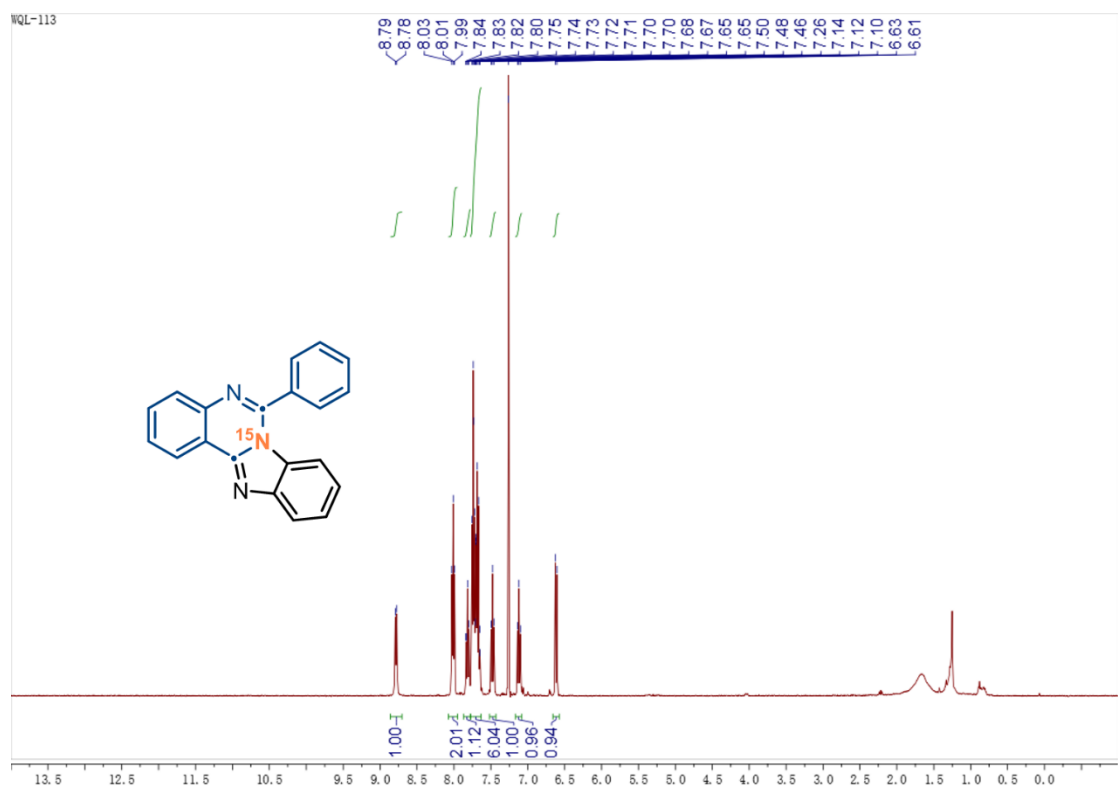
^{13}C NMR spectrum of **75** (125 MHz, $\text{DMSO}-d_6$)



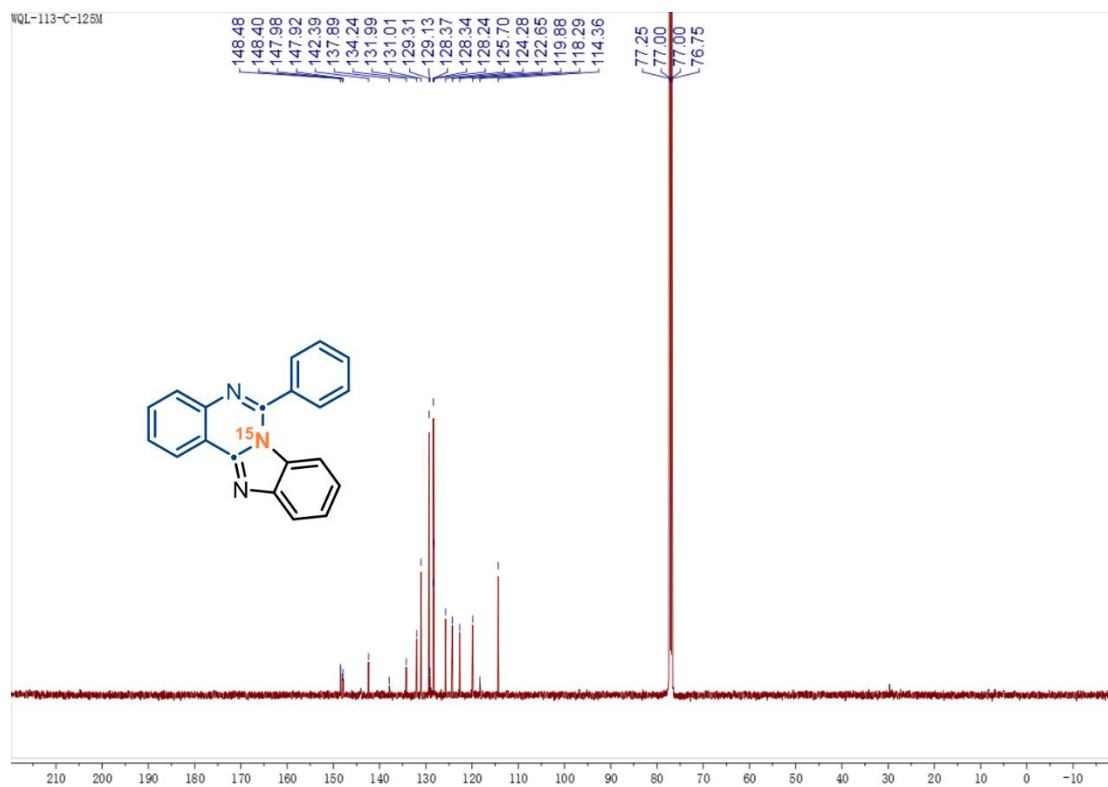
^{15}N NMR spectrum of **75** (50 MHz, $\text{DMSO-}d_6$)



^1H NMR spectrum of **76** (400 MHz, CDCl_3)



^{13}C NMR spectrum of **76** (125 MHz, CDCl_3)



^{15}N NMR spectrum of **76** (50 MHz, CDCl_3)

