Supporting Information

HFIP-Mediated Cascade Aminomethylation and Intramolecular Cyclization of Allenamides with *N,O*-Acetals to Access Tetrahydro-β-carboline Derivatives

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1. General Information:

Unless otherwise noted, all the reactions were performed using oven-dried Schlenk tubes under nitrogen. The reactions were monitored by Merck silica gel 60 F_{254} precoated plates (0.25 mm) visualizing under UV light (254 nm) or I_2 staining. The temperature mentioned for any reaction is corresponding to the oil bath temperature. Column chromatography was performed using silica gel 60-120 Å or 100-200 Å mesh of Merck Company. The room temperature recorded in our laboratory is around 25-30 ^{o}C.

2. Analytical Methods:

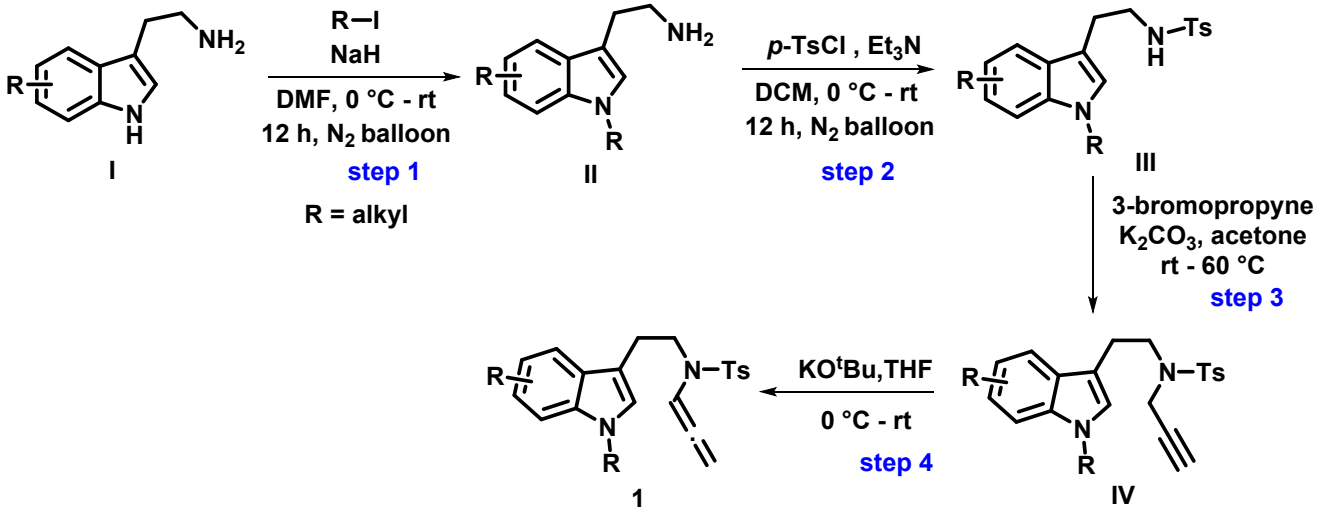
^{1}H, ^{13}C, and ^{19}F nuclear magnetic resonance spectra were recorded on Bruker Avance III 400 MHz spectrometer at 25 °C. NMRs of the products were measured in $CDCl_3$. The chemical shifts in ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR spectra are reported in parts per million (ppm) and are referenced to the residual solvent signal as the internal standard; ^{1}H NMR spectra ($CDCl_3$: δ 7.26 ppm or TMS: δ 0.00 ppm) and ^{13}C ($CDCl_3$: δ 77.16). The coupling constant (J) was reported in Hertz (Hz). Splitting patterns are denoted as "s" for singlet; "d" for doublet; "t" for triplet; "q" for quartet; "sext" for sextet; "sept" for septet; "m" for multiplet, "br" for broad; "dt" for doublet of triplets; "td" for triplet of doublets. ESI-HRMS were recorded on AGILENT 6520 Q-TOF spectrometer.

3. Materials:

All the commercially available reagents, starting materials and solvents were purchased from Sigma-Aldrich, Alfa Aesar, Merck, Spectrochem, Avra Synthesis and Glr Innovations Pvt. Ltd., and are used directly as received without any further purification. Solvent HFIP was purchased from Spectrochem. The starting materials are prepared according to the previously reported methods.

4. Preparation of Starting materials:

4.1. Preparation of Allenamides: [1]



General Procedure A for Allenamides 1:

Step 1: Procedure for alkylation:

To a solution of tryptamine **I** (1.00 equiv) in DMF under N_2 balloon at rt was added NaH (60% dispersion in mineral oil, 3.5 equiv) slowly, with vigorous stirring, and the stirring was continued at rt. After 30 minutes, the solution was cooled to 0 °C in an ice bath, and the appropriate alkyl halide (1.1 equiv) was added dropwise by syringe over three minutes. Stirring was continued at 0 °C for 30 minutes, and the reaction was allowed to warm to rt, and the stirring was continued for 12 hours. After the reaction was complete, the mixture was quenched with H_2O, the quenched mixture was extracted three times with ethylacetate, and dried over anhyd. Na_2SO_4. The filtrate was concentrated under reduced pressure and used for the next step without purification.

Step 2: Procedure for tosylation:

To a solution of *N*-alkyltryptamine **II** (1.00 equiv) in CH_2Cl_2 under N_2 balloon was added Et_3N (1.50 equiv). The solution was cooled to 0 °C in an ice bath and *p*-toluenesulfonyl chloride (1.01 equiv) was added in one portion. The solution was stirred for 15 minutes, then the ice bath was removed and allowed to warm up to ambient temperature (20 to 25 °C) and stirred for an additional 5 hours. The reaction was then quenched with 1 N aq. HCl (equal volume to CH_2Cl_2 was used) and the organic layer was separated and washed with another portion of 1N aq. HCl. The combined aqueous layers were then combined and back extracted with CH_2Cl_2, then the organic layers are combined, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The resulting crude residue was purified by flash chromatography to afford *N*-tosyltryptamine **III**.

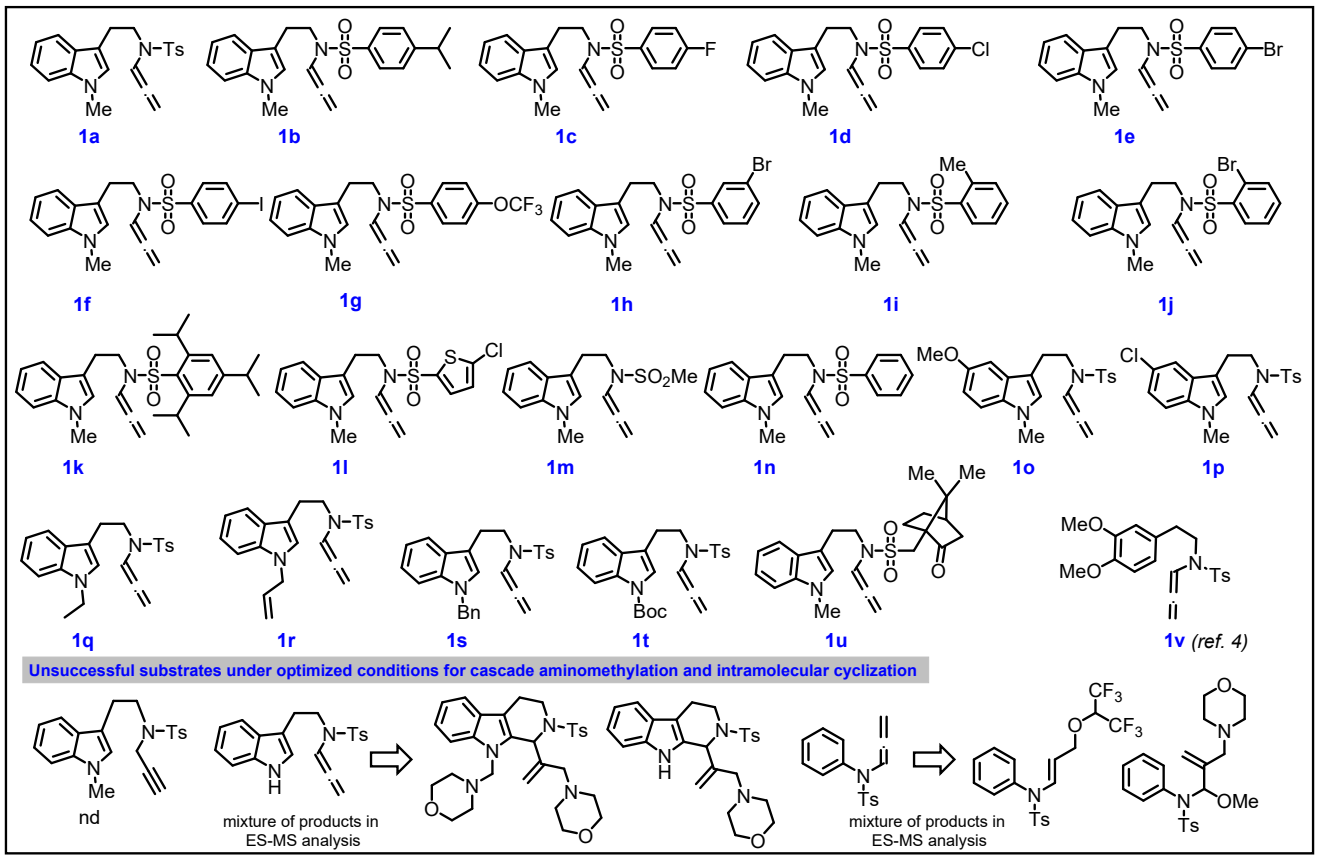
Step 3: Procedure for propargylamides:

To a solution of the crude *N*-tosyltryptamine product **III** (1.00 equiv) in acetone, K_2CO_3 (2.0 equiv) and 3-bromopropyne (1.5 equiv.) were added. Then the mixture was stirred in an oil bath at 60 °C for overnight. After the reaction was complete, the mixture was quenched with H_2O, and the quenched mixture was extracted three times with ethylacetate and dried over anhyd. Na_2SO_4. The filtrate was concentrated under reduced pressure and purified by flash column chromatography to give the propargylamide **IV**.

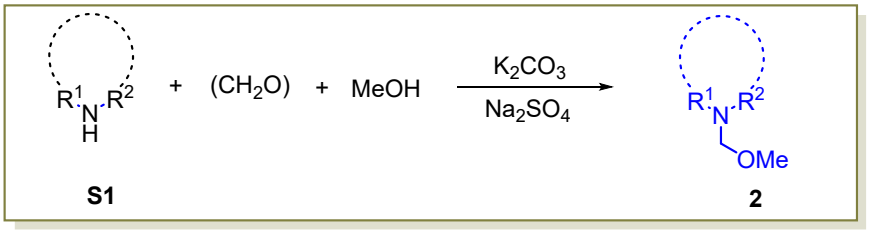
Step 4: Procedure for allenation reaction:

To a solution of propargylamide **IV** (1.0 equiv) in THF was added ^{t}BuOK (0.8 equiv) at 0 °C. The reaction was stirred at room temperature for 1 h before being concentrated under reduced pressure. Subsequently, the residue was suspended in DCM and then filtered through Celite. The filtrate was concentrated under reduced pressure and the crude residue was purified by flash column chromatography to give the allenamide **1.**

Table S1: Allenamides employed in the reaction

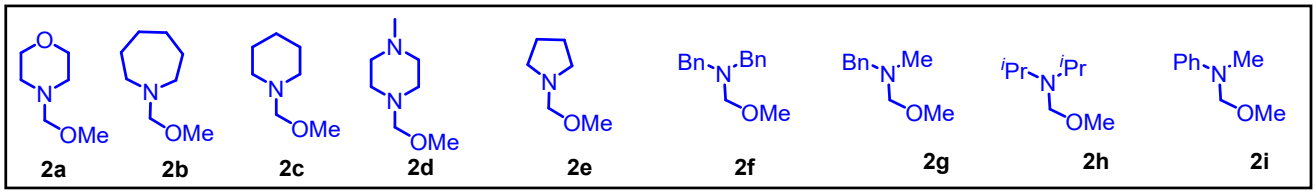


4.2. General Procedure B for N,O-acetals 2: Prepared according to the literature procedures.[2]



To a solution of amine **S1** (20 mmol) in MeOH (20 mL) was added paraformaldehyde (50 mmol), K_2CO_3 (40 mmol) and Na_2SO_4 (40 mmol) sequentially. The mixture was stirred at rt for 12 h, then filtered and washed with CH_2Cl_2 (20 mL X 3), the filtrate was concentrated under vacuum to give a mixture of oil and solid (paraformaldehyde). The mixture was dissolved in Et_2O (50 mL), filtered through a pad of Celite and anhydrous Na_2SO_4, washed with Et_2O (10 mL X 3). The combined filtrates were concentrated to about 20 mL, filtered through a pad of Celite and anhydrous Na_2SO_4 again, washed with Et_2O (10 mL X 3) and concentrated give N,O-acetals **2**, which was pure enough and used directly.

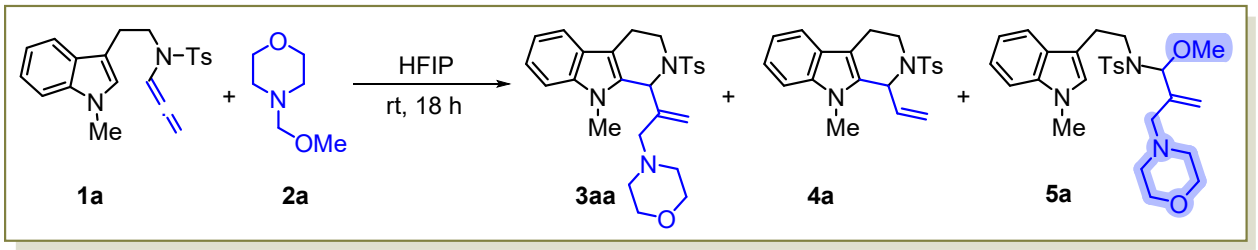
Table S2: N,O acetals employed in the reaction



4.3. General Procedure C for the synthesis of 3aa-3ta, and 3ab-3ai:

An oven-dried Schlenk/Seal tube was charged with **N,O-acetals 2** (1.5 equiv) in **HFIP** (3 mL), and then **allenamide 1** (0.3 mmol, 1.0 equiv) was added to the reaction mixture. The reaction was stirred at **room temperature (rt)** for **18 h**, and the solvent was evaporated under reduced pressure. The reaction mixture was purified by flash chromatography (EtOAc in Hexane) on silica gel (100-200 mesh), to give the corresponding product **3**.

4.4 Optimization of the reaction conditions:[a]

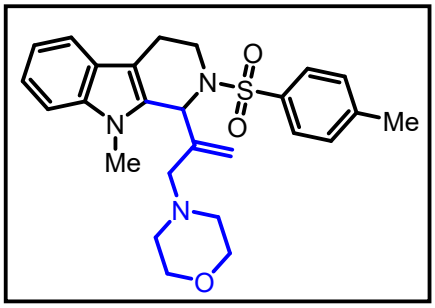


S.N.	Solvent /Additives	Temp °C	Time h	3aa	4a	5a
1	HFIP	80	18 h	60	32	nd
2	MeOH	80	18 h	nd	nd	nd
3	^{i}PrOH	80	18 h	nd	nd	nd
4	TFE	80	18 h	64	25	nd
5	HFIP	50	18 h	(74)	(20)	nd
6	**HFIP**	**rt**	**18 h**	**(75)**	**(18)**	nd
7	HFIP	rt	5 h	61	22	nd
8	HFIP	rt	10 h	67	18	nd
9	HFIP and NaOAc (30 mol%)	rt	18 h	(77)	(16)	nd
10	HFIP and NaOAc (50 mol%)	rt	18 h	51	10	nd
11	DCM (0.12 M): HFIP (5.0 equiv) and NaOAc (30 mol%)	rt	18 h	70	22	nd
12	pTSA (5.0 equiv) in DCM	rt	18 h	trace	55	nd
13	AcOH	rt	18 h	35	51	nd
14	TFA	rt	18 h	nd	nd	nd
15	TfOH (5.0 equiv) in DCM	rt	18 h	nd	nd	nd
16	HFIP under N_2	rt	18 h	(70)	(20)	nd
17	CPA (10 mol%) in cyclohexane (1 mL)	60	24 h	22	trace	nd
18	$CuCl_2$ (10mol%) in DCM	rt	24 h	68	trace	trace

[a]**Reaction conditions: 1a** (0.027 mmol, 1.0 equiv), **2a** (1.5 equiv) in HFIP (1 mL) at rt for 18 h. ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard. nd = not detected. Isolated yields on parentheses using **1a** (0.3 mmol, 1.0 equiv), **2a** (1.5 equiv) in HFIP (3 mL). CPA = (R)-(−)-1,1′-Binaphthalene-2,2′-diyl hydrogen phosphate.

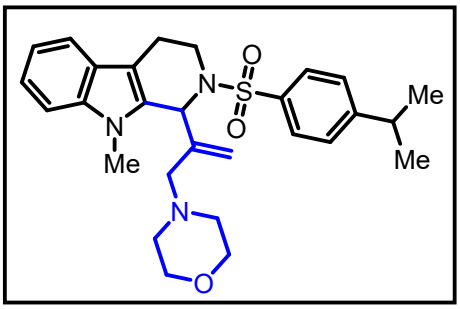
5. Characterization data of isolated products

4-(2-(9-methyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3aa):



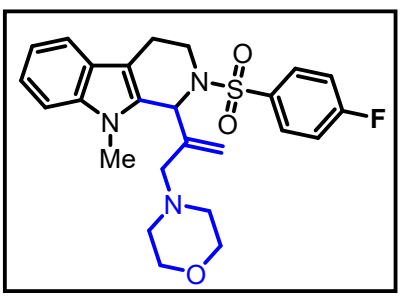
Prepared according to the general procedure **C** from **1a** (110 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3aa** as a white solid (105 mg, 75% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 163-165 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.22 (m, 1H), 7.16 (td, *J* = 6.9, 1.0 Hz, 1H), 7.04 – 7.00 (m, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 5.91 (s, 1H), 5.19 (s, 1H), 4.50 (s, 1H), 4.00 (dd, *J* = 14.8, 5.9 Hz, 1H), 3.83 – 3.70 (m, 4H), 3.51 (s, 3H), 3.44 – 3.36 (m, 1H), 2.81 (d, *J* = 13.3 Hz, 1H), 2.67 – 2.56 (m, 4H), 2.48 – 2.32 (m, 3H), 2.17 (s, 3H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 143.4, 137.8, 137.1, 131.7, 129.3, 126.8, 126.4, 121.6, 119.0, 118.9, 118.2, 108.8, 108.2, 67.4, 61.0, 53.8, 53.5, 38.6, 29.3, 21.4, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{32}N_3O_3S$ 466.2159; found 466.2159.

4-(2-(2-((4-isopropylphenyl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ba):



Prepared according to the general procedure **C** from **1b** (118 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ba** as a brown liquid (91 mg, 61% yield). Reaction time: 18 h. Reaction temperature: room temperature. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.56 (d, *J* = 8.2 Hz, 2H), 7.22 – 7.19 (m, 2H), 7.14 (t, *J* = 8.2 Hz, 1H), 6.98 (t, *J* = 8.2 Hz, 3H), 5.88 (s, 1H), 5.20 (s, 1H), 4.53 (s, 1H), 4.02 (dd, *J* = 14.8, 5.3 Hz, 1H), 3.80 – 3.73 (m, 4H), 3.51 (s, 3H), 3.44 – 3.36 (m, 1H), 2.82 (d, *J* = 13.2 Hz, 1H), 2.72 – 2.63 (m, 2H), 2.55 (brs, 2H), 2.46 – 2.37 (m, 2H), 2.04 (s, 1H), 1.27 – 1.23 (m, 2H), 0.99 – 0.97 (m, 5H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 154.1, 143.3, 137.7, 137.0, 131.6, 127.0, 126.6, 126.4, 121.6, 119.0, 118.1, 108.7, 108.1, 67.4, 61.0, 53.8, 53.6, 38.7, 34.0, 29.2, 23.6, 23.4, 19.4. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{36}N_3O_3S$ 494.2472; found 494.2472.

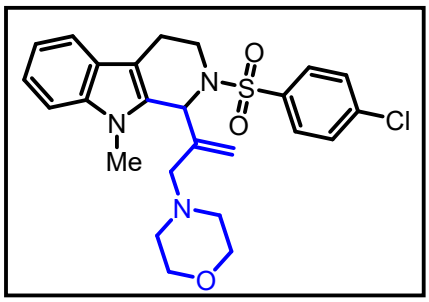
4-(2-(2-((4-fluorophenyl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ca):



Prepared according to the general procedure **C** from **1c** (112 mg, 0.3 mmol). Flash column chromatography (25% EtOAc in Hexane) afforded the desired product **3ca** as a white solid (93 mg, 66% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 145-146 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.70 – 7.66 (m, 2H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 7.1 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.87 (t, *J* = 8.5 Hz, 2H), 5.95 (s, 1H), 5.21 (s, 1H), 4.51 (s,

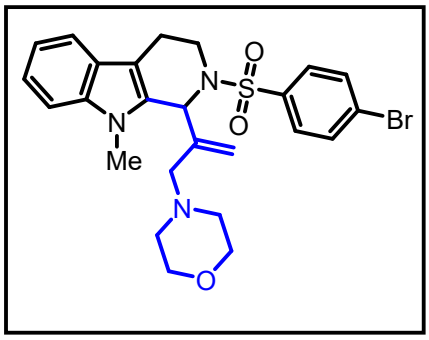
1H), 4.01 (dd, *J* = 14.9, 6.0 Hz, 1H), 3.83 – 3.71 (m, 4H), 3.52 (s, 3H), 3.47 – 3.39 (m, 1H), 2.82 (d, *J* = 13.3 Hz, 1H), 2.74 – 2.57 (m, 4H), 2.51 – 2.27 (m, 3H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 164.9 (d, *J* = 255.0 Hz), 143.2, 137.1, 136.9 (d, *J* = 3.0 Hz), 131.5, 129.6, 129.5, 126.3, 121.9, 119.2 (d, *J* = 6.2 Hz), 118.2, 116.1, 115.9 (d, *J* = 22.4 Hz), 108.9, 108.1, 67.4, 61.0, 53.9, 53.7, 38.7, 29.4, 19.5. **^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$):** δ -105.4. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{29}FN_3O_3S$ 470.1908; found 470.1908.

4-(2-(2-((4-chlorophenyl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3da):



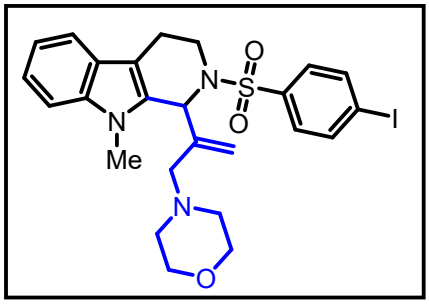
Prepared according to the general procedure **C** from **1d** (116 mg, 0.3 mmol). Flash column chromatography (25% EtOAc in Hexane) afforded the desired product **3da** as a white solid (99 mg, 68% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 155-157 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.60 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 4.6 Hz, 1H), 7.21 – 7.16 (m, 3H), 7.05 (t, *J* = 7.3 Hz, 1H), 5.93 (s, 1H), 5.21 (s, 1H), 4.52 (s, 1H), 4.00 (dd, *J* = 14.9, 6.1 Hz, 1H), 3.83 – 3.70 (m, 4H), 3.52 (s, 3H), 3.48 – 3.39 (m, 1H), 2.81 (d, *J* = 13.2 Hz, 1H), 2.75 – 2.51 (m, 5H), 2.48 – 2.29 (m, 2H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 143.2, 139.4, 139.1, 137.2, 131.5, 129.0, 128.3, 126.3, 121.9, 119.3, 118.3, 108.9, 108.2, 67.4, 61.0, 53.9, 53.8, 38.7, 29.4, 19.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{29}ClN_3O_3S$ 486.1613; found 486.1614.

4-(2-(2-((4-bromophenyl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ea):



Prepared according to the general procedure **C** from **1e** (129 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ea** as a white solid (115 mg, 72% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 145-147 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.53 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 5.3 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 5.93 (s, 1H), 5.21 (s, 1H), 4.52 (s, 1H), 4.00 (dd, *J* = 14.8, 6.1 Hz, 1H), 3.83 – 3.71 (m, 4H), 3.52 (s, 3H), 3.48 – 3.39 (m, 1H), 2.81 (d, *J* = 13.2 Hz, 1H), 2.67 – 2.51 (m, 5H), 2.48 – 2.29 (m, 2H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 143.1, 139.9, 137.2, 132.0, 131.5, 128.4, 127.6, 126.3, 121.9, 119.3, 118.3, 108.9, 108.2, 67.4, 61.0, 53.9, 53.8, 38.7, 29.4, 19.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{29}BrN_3O_3S$ 530.1108; found 530.1106.

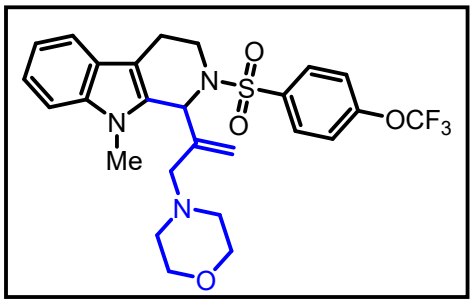
4-(2-(2-((4-iodophenyl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3fa):



Prepared according to the general procedure **C** from **1f** (143 mg, 0.3 mmol). Flash column chromatography (25% EtOAc in Hexane) afforded the desired product **3fa** as a white solid (121 mg, 70% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 198-200 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.55 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 3.3 Hz, 1H), 7.22 – 7.18 (m, 1H), 7.08 – 7.04 (m, 1H), 5.91 (s, 1H), 5.21 (s, 1H), 4.52 (s, 1H), 3.99 (dd, *J* = 14.9, 6.2 Hz, 1H), 3.82 – 3.70 (m, 4H), 3.52 (s, 3H), 3.47 – 3.38 (m, 1H), 2.80 (d, *J* = 13.3 Hz, 1H), 2.57 – 2.50 (m, 5H), 2.48 –

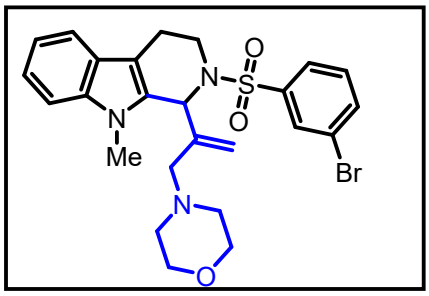
2.30 (m, 2H). **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$):** δ 143.1, 140.5, 137.9, 137.1, 131.5, 128.2, 126.3, 122.0, 119.3, 118.3, 108.9, 108.2, 99.9, 67.4, 61.0, 53.9, 53.8, 38.7, 29.4, 19.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{29}IN_3O_3S$ 578.0969; found 578.0966.

4-(2-(9-methyl-2-((4-(trifluoromethoxy)phenyl)sulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ga):



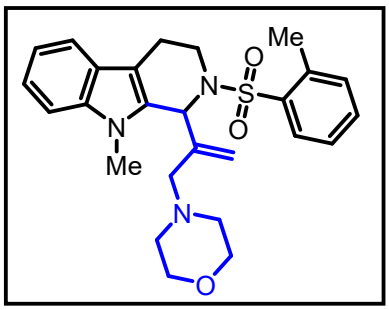
Prepared according to the general procedure **C** from **1g** (130 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ga** as a white solid (78 mg, 48% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 158-160 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.71 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 5.3 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 7.20 – 7.16 (m, 1H), 7.05 – 6.99 (m, 3H), 5.94 (s, 1H), 5.22 (s, 1H), 4.54 (s, 1H), 4.01 (dd, *J* = 14.9, 6.3 Hz, 1H), 3.83 – 3.71 (m, 4H), 3.52 (s, 3H), 3.48 – 3.44 (m, 1H), 2.82 (d, *J* = 13.3 Hz, 1H), 2.76 – 2.51 (m, 5H), 2.48 – 2.27 (m, 2H). **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 152.0, 143.1, 139.1, 137.1, 131.4, 129.0, 126.2, 122.0, 120.6, 119.4, 119.3, 118.2, 108.8, 108.1, 67.4, 61.0, 53.9, 53.8, 38.8, 29.3, 19.5. **$^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$):** δ -57.9. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{29}F_3N_3O_4S$ 536.1825; found 536.1826.

4-(2-(2-((3-bromophenyl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ha):



Prepared according to the general procedure **C** from **1h** (129 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ha** as a white solid (115 mg, 72% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 128-130 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.80 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.25 – 7.23 (m, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.04 – 7.00 (m, 2H), 5.92 (s, 1H), 5.23 (s, 1H), 4.56 (s, 1H), 4.04 (dd, *J* = 14.9, 6.2 Hz, 1H), 3.84 – 3.73 (m, 4H), 3.54 (s, 3H), 3.50 – 3.47 (m, 1H), 2.82 (d, *J* = 13.2 Hz, 1H), 2.72 – 2.51 (m, 5H), 2.48 – 2.36 (m, 2H). **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$):** δ 143.1, 142.4, 137.2, 135.4, 131.3, 130.2, 130.0, 126.3, 125.1, 122.4, 121.9, 119.5, 119.2, 118.2, 108.9, 108.0, 67.5, 61.0, 53.9, 38.9, 29.3, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{29}BrN_3O_3S$ 530.1108; found 530.1111.

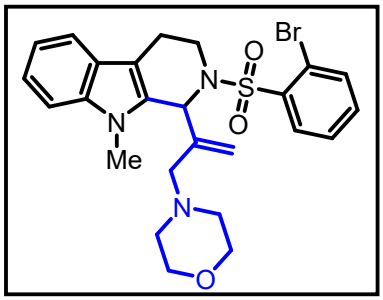
4-(2-(9-methyl-2-(o-tolylsulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ia):



Prepared according to the general procedure **C** from **1i** (110 mg, 0.3 mmol). Flash column chromatography (20% EtOAc in Hexane) afforded the desired product **3ia** as a white solid (88 mg, 63% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 158-160 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.00 (d, *J* = 7.9 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.28 – 7.25 (m, 2H), 7.22 (t, *J* = 6.6 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.3 Hz, 1H), 5.79 (s, 1H), 5.19 (s, 1H), 4.54 (s, 1H), 3.98 (dd, *J* = 14.9, 5.2 Hz, 1H), 3.72 – 3.62 (m, 4H), 3.52 (s, 3H), 3.48 – 3.39 (m, 1H), 3.15 (d, *J* = 13.2 Hz, 1H), 2.67 (d, *J* = 13.2 Hz, 1H), 2.59 – 2.51 (m, 4H), 2.46 (s, 3H), 2.24 – 2.18 (m, 2H). **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$):** δ 143.2, 139.0, 137.8, 137.2,

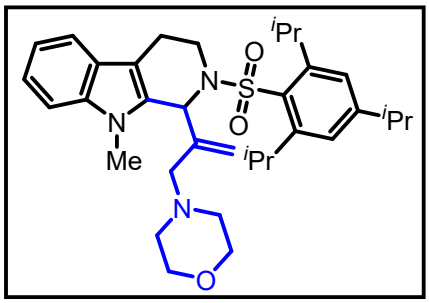
132.8, 132.7, 132.2, 130.0, 126.5, 126.2, 121.7, 119.6, 119.2, 118.4, 109.0, 108.8, 67.3, 61.1, 53.8, 53.3, 38.7, 29.4, 20.6, 20.3. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{32}N_3O_3S$ 466.2159; found 466.2156.

4-(2-(2-((2-bromophenyl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ja):



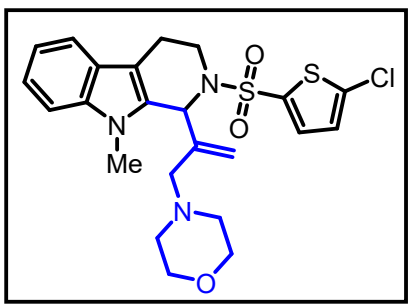
Prepared according to the general procedure **C** from **1j** (129 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ja** as a pale white solid (110 mg, 69% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 172-175 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.19 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.55 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.29 – 7.25 (m, 2H), 7.22 – 7.18 (m, 1H), 7.08 – 7.05 (m, 1H), 5.97 (s, 1H), 5.21 (s, 1H), 4.54 (s, 1H), 4.12 (dd, *J* = 14.6, 5.5 Hz, 1H), 3.73 – 3.61 (m, 4H), 3.52 (s, 3H), 3.48 – 3.43 (m, 1H), 3.22 (d, *J* = 13.2 Hz, 1H), 2.73 (d, *J* = 13.4 Hz, 1H), 2.62 – 2.52 (m, 4H), 2.26 – 2.23 (m, 2H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 143.2, 140.5, 137.2, 135.7, 133.5, 132.4, 132.1, 127.7, 126.5, 121.6, 120.3, 119.7, 119.1, 118.3, 109.0, 108.5, 67.4, 61.1, 54.2, 53.8, 39.4, 29.4, 20.7. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{29}BrN_3O_3S$ 530.1108; found 530.1110.

4-(2-(9-methyl-2-((2,4,6-triisopropylphenyl)sulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ka):



Prepared according to the general procedure **C** from **1k** (144 mg, 0.3 mmol). Flash column chromatography (15% EtOAc in Hexane) afforded the desired product **3ka** as a white solid (102 mg, 59% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 196-198 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.49 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.22 – 7.18 (m, 3H), 7.11 – 7.07 (m, 1H), 5.43 (s, 1H), 5.11 (s, 1H), 4.58 (s, 1H), 4.19 – 4.08 (m, 3H), 3.63 – 3.52 (m, 4H), 3.51 (s, 3H), 3.43 – 3.40 (m, 1H), 3.07 – 2.99 (m, 1H), 2.92 – 2.85 (m, 1H), 2.78 – 2.71 (m, 2H), 2.45 – 2.39 (m, 3H), 1.79 – 1.75 (m, 2H), 1.35 (d, *J* = 6.7 Hz, 6H), 1.23 (d, *J* = 6.9 Hz, 6H), 1.16 (d, *J* = 6.7 Hz, 6H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 153.3, 151.6, 142.6, 137.3, 132.7, 132.1, 126.8, 124.2, 121.6, 120.8, 119.2, 118.5, 109.2, 108.9, 67.0, 61.6, 53.6, 52.8, 38.2, 34.3, 29.8, 29.1, 25.5, 24.8, 23.8, 23.7, 21.3. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{34}H_{48}N_3O_3S$ 578.3411; found 578.3414.

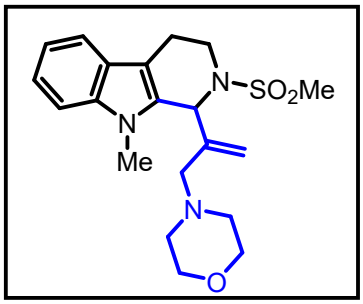
4-(2-(2-((5-chlorothiophen-2-yl)sulfonyl)-9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3la):



Prepared according to the general procedure **C** from **1l** (118 mg, 0.3 mmol). Flash column chromatography (25% EtOAc in Hexane) afforded the desired product **3la** as a colorless liquid (96 mg, 65% yield). Reaction time: 18 h. Reaction temperature: room temperature. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.37 (d, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 7.22 – 7.19 (m, 1H), 7.15 (d, *J* = 3.8 Hz, 1H), 7.08 (d, *J* = 7.3 Hz, 1H), 6.62 (d, *J* = 4.0 Hz, 1H), 5.88 (s, 1H), 5.23 (s, 1H), 4.55 (s, 1H), 4.09 (dd, *J* = 14.8, 5.8 Hz, 1H), 3.80 – 3.74 (m, 4H), 3.53 (s, 3H), 3.49 – 3.46 (m, 1H), 2.82 (d, *J*

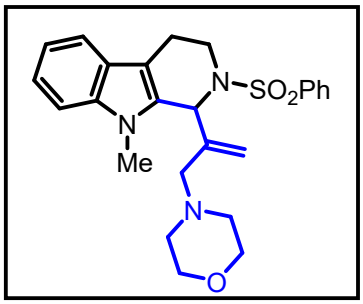
= 13.2 Hz, 1H), 2.71 – 2.55 (m, 7H). **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 143.0, 139.4, 137.2, 131.2, 130.9, 126.6, 126.3, 121.9, 119.5, 119.3, 118.3, 109.0, 108.3, 67.4, 60.9, 53.9, 53.8, 39.2, 29.4, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{27}ClN_3O_3S_2$ 492.1177; found 492.1173.

4-(2-(9-methyl-2-(methylsulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ma):



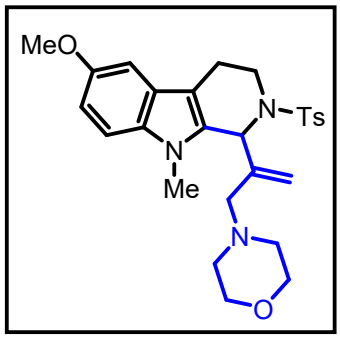
Prepared according to the general procedure **C** from **1m** (87 mg, 0.3 mmol). Flash column chromatography (30 % EtOAc in Hexane) afforded the desired product **3ma** as a white solid (56 mg, 58% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 195-197 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.52 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.3 Hz, 1H), 5.71 (s, 1H), 5.21 (s, 1H), 4.53 (s, 1H), 4.09 (dd, *J* = 14.9, 6.1 Hz, 1H), 3.80 – 3.69 (m, 4H), 3.54 (s, 3H), 3.49 – 3.44 (m, 1H), 3.04 – 2.96 (m, 1H), 2.82 – 2.77 (m, 3H), 2.74 (s, 3H), 2.66 – 2.55 (m, 4H). **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$):** δ 143.2, 137.3, 131.8, 126.5, 122.2, 119.5, 119.0, 118.5, 109.2, 108.1, 67.4, 60.8, 53.9, 53.2, 40.1, 38.6, 29.5, 20.2. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{28}N_3O_3S$ 390.1846; found 390.1843.

4-(2-(9-methyl-2-(phenylsulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3na):



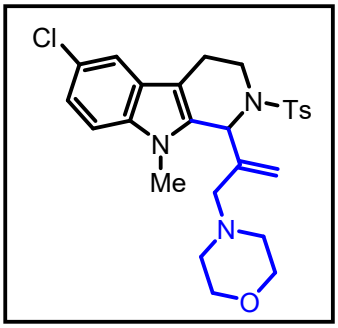
Prepared according to the general procedure **C** from **1n** (106 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3na** as a white solid (88 mg, 65% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 135-137 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.69 (d, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 7.6 Hz, 2H), 7.19 – 7.15 (m, 1H), 7.02 (t, *J* = 7.3 Hz, 1H), 5.94 (s, 1H), 5.20 (s, 1H), 4.51 (s, 1H), 4.03 (dd, *J* = 14.8, 6.0 Hz, 1H), 3.83 – 3.71 (m, 4H), 3.51 (s, 3H), 3.46 – 3.38 (m, 1H), 2.82 (d, *J* = 13.3 Hz, 1H), 2.67 – 2.47 (m, 5H), 2.44 – 2.28 (m, 2H). **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 143.3, 140.8, 137.1, 132.5, 131.7, 128.7, 126.9, 126.4, 121.7, 119.1, 118.2, 108.8, 108.3, 67.5, 61.0, 53.9, 53.6, 38.7, 29.3, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{30}N_3O_3S$ 452.2002; found 452.2003.

4-(2-(6-methoxy-9-methyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3oa):



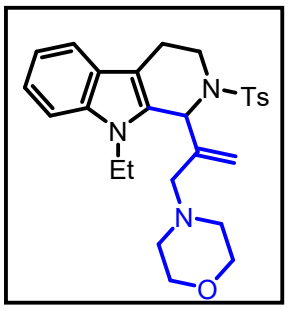
Prepared according to the general procedure **C** from **1o** (119 mg, 0.3 mmol). Flash column chromatography (35 % EtOAc in Hexane) afforded the desired product **3oa** as a white solid (89 mg, 60% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 150-152 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 1H), 6.99 (d, *J* = 7.9 Hz, 2H), 6.83 (dd, *J* = 8.7, 1.9 Hz, 1H), 6.72 (s, 1H), 5.88 (s, 1H), 5.19 (s, 1H), 4.51 (s, 1H), 4.00 (dd, *J* = 14.7, 5.4 Hz, 1H), 3.81 (s, 3H), 3.74 – 3.66 (m, 4H), 3.48 (s, 3H), 3.43 – 3.35 (m, 1H), 2.80 (d, *J* = 13.3 Hz, 1H), 2.63 – 2.54 (m, 4H), 2.45 – 2.29 (m, 3H), 2.20 (s, 3H). **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$):** δ 153.9, 143.3, 137.7, 132.4, 132.4, 129.3, 127.5, 126.9, 126.7, 118.9, 111.3, 109.5, 107.8, 100.5, 67.4, 61.0, 56.1, 53.8, 53.6, 38.7, 29.4, 21.4, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{34}N_3O_4S$ 496.2265; found 496.2268.

4-(2-(6-chloro-9-methyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3pa):



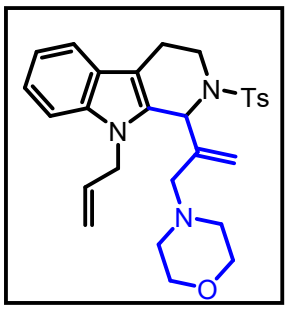
Prepared according to the general procedure **C** from **1p** (120 mg, 0.3 mmol). Flash column chromatography (30 % EtOAc in Hexane) afforded the desired product **3pa** as a white solid (83 mg, 55% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 150-152 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 1.2 Hz, 1H), 7.15 – 7.09 (m, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 5.90 (s, 1H), 5.20 (s, 1H), 4.47 (s, 1H), 4.00 (dd, *J* = 14.9, 5.8 Hz, 1H), 3.81 – 3.69 (m, 4H), 3.50 (s, 3H), 3.42 – 3.34 (m, 1H), 2.81 (d, *J* = 13.3 Hz, 1H), 2.65 – 2.55 (m, 4H), 2.41 – 2.25 (m, 3H), 2.20 (s, 3H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 143.6, 143.2, 137.6, 135.5, 133.3, 129.3, 127.4, 126.9, 124.9, 121.8, 119.0, 117.7, 109.8, 108.0, 67.4, 61.0, 53.9, 53.5, 38.5, 29.5, 21.4, 19.3. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{31}ClN_3O_3S$ 500.1769; found 500.1771.

4-(2-(9-ethyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3qa):



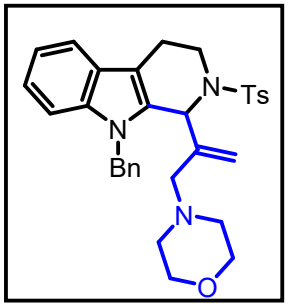
Prepared according to the general procedure **C** from **1q** (114 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3qa** as a light yellow liquid (88 mg, 59% yield). Reaction time: 18 h. Reaction temperature: room temperature. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.27 – 7.24 (m, 2H), 7.15 (t, *J* = 7.4, Hz, 1H), 7.03 – 6.95 (m, 3H), 5.91 (s, 1H), 5.17 (s, 1H), 4.55 (s, 1H), 4.06 – 3.88 (m, 3H), 3.81 – 3.74 (m, 4H), 3.54 (d, *J* = 13.1 Hz, 1H), 3.46 – 3.38 (m, 1H), 2.79 (d, *J* = 13.1 Hz, 1H), 2.64 – 2.58 (m, 4H), 2.48 – 2.34 (m, 2H), 2.17 (s, 3H), 1.32 (t, *J* = 7.1, Hz, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 143.6, 143.4, 137.7, 135.9, 131.0, 129.3, 126.8, 126.7, 121.5, 118.9, 118.3, 109.1, 108.3, 67.5, 60.9, 53.9, 53.4, 38.5, 37.7, 31.7, 21.4, 19.5, 15.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{34}N_3O_3S$ 480.2315; found 480.2308.

4-(2-(9-allyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3ra):



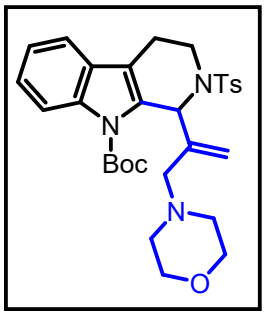
Prepared according to the general procedure **C** from **1r** (118 mg, 0.3 mmol). Flash column chromatography (25% EtOAc in Hexane) afforded the desired product **3ra** as a white solid (91 mg, 62% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 157-159 °C. **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.04 – 6.98 (m, 3H), 5.86 – 5.83 (m, 2H), 5.18 (d, *J* = 10.3 Hz, 1H), 5.15 (s, 1H), 4.96 (d, *J* = 17.1 Hz, 1H), 4.60 (d, *J* = 16.1 Hz, 1H), 4.54 (s, 1H), 4.44 (dd, *J* = 16.9, 4.9 Hz, 1H), 4.07 (dd, *J* = 14.8, 5.7 Hz, 1H), 3.79 – 3.74 (m, 4H), 3.55 (d, *J* = 13.0 Hz, 1H), 3.45 – 3.39 (m, 1H), 2.78 (d, *J* = 13.0 Hz, 1H), 2.65 – 2.57 (m, 4H), 2.49 – 2.45 (m, 1H), 2.40 – 2.33 (m, 1H), 2.21 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 143.6, 143.4, 137.9, 136.6, 133.5, 131.4, 129.4, 127.0, 126.6, 121.7, 119.1, 118.8, 118.3, 117.0, 109.6, 108.8, 67.5, 61.0, 53.9, 53.4, 45.3, 38.6, 21.5, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{34}N_3O_3S$ 492.2315; found 492.2300.

4-(2-(9-benzyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (3sa):



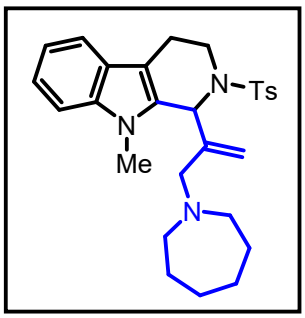
Prepared according to the general procedure **C** from **1s** (133 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3sa** as a yellow solid (86 mg, 53% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 90-92 °C. **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 7.32 – 7.29 (m, 6H), 7.20 (d, *J* = 8.1 Hz, 1H), 7.14 – 7.11 (m, 3H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 2H), 5.83 (s, 1H), 5.26 (d, *J* = 16.5 Hz, 1H), 5.16 (s, 1H), 4.98 (d, *J* = 16.5 Hz, 1H), 4.57 (s, 1H), 4.07 (dd, *J* = 15.3, 5.9 Hz, 1H), 3.71 (brs, 4H), 3.51 (d, *J* = 13.1 Hz, 1H), 3.46 – 3.39 (m, 1H), 2.75 (d, *J* = 13.1 Hz, 1H), 2.60 – 2.50 (m, 4H), 2.48 – 2.33 (m, 2H), 2.21 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 143.4, 143.2, 137.9, 137.7, 136.8, 131.6, 129.4, 128.9, 127.8, 126.9, 126.8, 126.7, 122.0, 119.2, 119.0, 118.4, 109.8, 109.2, 67.4, 61.1, 54.0, 53.7, 46.6, 38.5, 21.5, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{36}N_3O_3S$ 542.2472; found 542.2449.

tert-butyl-1-(3-morpholinoprop-1-en-2-yl)-2-tosyl-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-9-carboxylate (3ta):



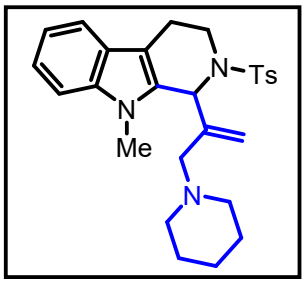
Prepared according to the general procedure **C** from **1t** (91 mg, 0.2 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ta** as a white solid (40 mg, 36% yield). Reaction time: 18 h. Reaction temperature: room temperature. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.98 – 7.92 (m, 3H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 5.81 (q, *J* = 3.3 Hz, 1H), 5.65 (brs, 1H), 5.08 (s, 1H), 4.89 (s, 1H), 4.53 (s, 1H), 4.36 (d, *J* = 18.7 Hz, 1H), 3.94 (d, *J* = 18.6 Hz, 1H), 3.63 (t, *J* = 4.6 Hz, 4H), 2.87 (d, *J* = 13.7 Hz, 1H), 2.66 (d, *J* = 13.8 Hz, 1H), 2.45 (s, 3H), 2.34 – 2.45 (m, 4H), 1.64 (s, 9H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 152.3, 143.6, 133.8, 130.0, 129.9, 127.2, 123.1, 120.4, 116.0, 110.9, 82.2, 67.1, 62.3, 61.1, 53.7, 43.1, 28.6, 21.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{38}N_3O_5S$ 552.2527; found 552.2508.

1-(3-(azepan-1-yl)prop-1-en-2-yl)-9-methyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (3ab):



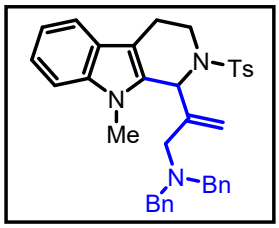
Prepared according to the general procedure **C** from **1a** (110 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ab** as a white solid (75 mg, 52% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 148-150 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.56 (d, *J* = 8.2 Hz, 2H), 7.27 – 7.22 (m, 2H), 7.16 (td, *J* = 7.0, 1.0 Hz, 1H), 7.03 – 6.99 (m, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 5.89 (s, 1H), 5.19 (s, 1H), 4.45 (s, 1H), 3.99 (dd, *J* = 14.4, 5.3 Hz, 1H), 3.53 (s, 3H), 3.49 – 3.37 (m, 2H), 3.03 (d, *J* = 13.7 Hz, 1H), 2.79 – 2.69 (m, 4H), 2.48 – 2.37 (m, 3H), 2.17 (s, 3H), 1.74 – 1.65 (m, 7H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 145.2, 143.3, 137.9, 137.1, 132.2, 129.2, 127.0, 126.5, 121.5, 118.9, 118.1, 108.8, 108.2, 60.8, 56.3, 53.6, 38.7, 29.8, 29.5, 28.5, 27.2, 21.4, 19.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{36}N_3O_2S$ 478.2523; found 478.2525.

9-methyl-1-(3-(piperidin-1-yl)prop-1-en-2-yl)-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (3ac):



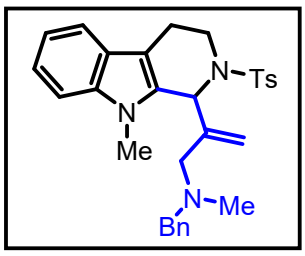
Prepared according to the general procedure **C** from **1a** (110 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **3ac** as a white solid (76 mg, 55% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 152-154 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.28 – 7.22 (m, 2H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.03 – 6.97 (m, 3H), 5.89 (s, 1H), 5.16 (s, 1H), 4.47 (s, 1H), 3.99 (dd, *J* = 14.9, 5.4 Hz, 1H), 3.52 (s, 3H), 3.45 – 3.37 (m, 2H), 2.75 (d, *J* = 13.4 Hz, 1H), 2.56 – 2.36 (m, 6H), 2.18 (s, 3H), 1.67 – 1.47 (m, 6H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 144.2, 143.3, 137.9, 137.1, 132.2, 129.3, 127.0, 126.5, 121.5, 118.9, 118.3, 118.2, 108.8, 108.1, 61.4, 54.9, 53.6, 38.7, 31.7, 29.3, 26.4, 24.7, 22.8, 21.4, 19.6, 14.2. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{34}N_3O_2S$ 464.2366; found 464.2356.

N,N-dibenzyl-2-(9-methyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)prop-2-en-1-amine (3af):



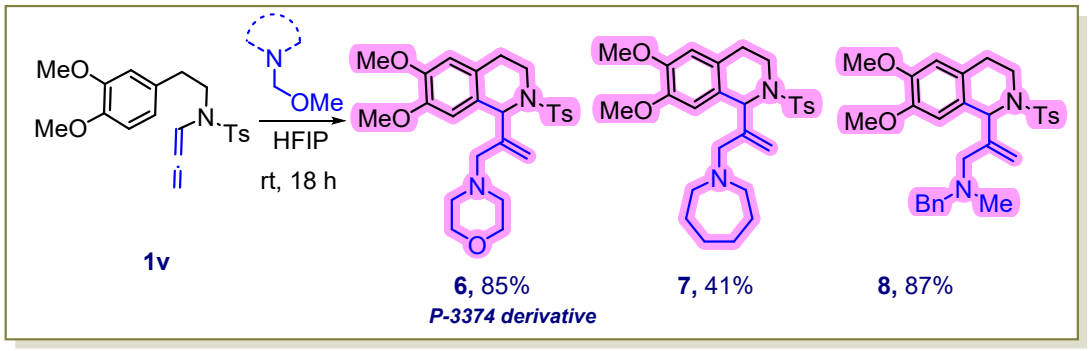
Prepared according to the general procedure **C** from **1a** (110 mg, 0.3 mmol). Flash column chromatography (8% EtOAc in Hexane) afforded the desired product **3af** as a white solid (104 mg, 61% yield). Reaction time: 24 h. Reaction temperature: room temperature. Melting point: 142-144 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.52 (d, *J* = 6.8 Hz, 2H), 7.39 (d, *J* = 6.9 Hz, 4H), 7.34 – 7.31 (m, 4H), 7.24 (d, *J* = 8.6 Hz, 3H), 7.20 – 7.13 (m, 2H), 7.02 – 6.99 (m, 1H), 6.94 (d, *J* = 7.7 Hz, 2H), 5.67 (s, 1H), 5.64 (s, 1H), 4.57 (s, 1H), 3.95 (d, *J* = 13.8 Hz, 1H), 3.78 (d, *J* = 13.9 Hz, 2H), 3.60 (d, *J* = 13.9 Hz, 2H), 3.48 (t, *J* = 15.4 Hz, 1H), 3.39 (s, 3H), 3.36 – 3.20 (m, 2H), 2.41 (d, *J* = 6.6 Hz, 2H), 2.15 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 144.6, 143.4, 139.1, 137.7, 137.1, 131.7, 129.2, 128.8, 128.4, 127.0, 126.9, 126.4, 121.6, 119.0, 118.2, 117.9, 108.8, 108.2, 57.7, 56.3, 54.7, 38.8, 29.5, 21.4, 19.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{36}H_{38}N_3O_2S$ 576.2679; found 576.2660.

N-benzyl-N-methyl-2-(9-methyl-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)prop-2-en-1-amine (3ag):

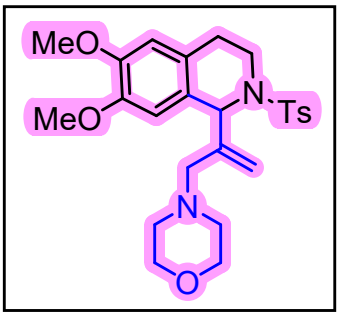


Prepared according to the general procedure **C** from **1a** (110 mg, 0.3 mmol). Flash column chromatography (15% EtOAc in Hexane) afforded the desired product **3ag** as a colorless liquid (110 mg, 73% yield). Reaction time: 18 h. Reaction temperature: room temperature. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.3 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 5.95 (s, 1H), 5.32 (s, 1H), 4.53 (s, 1H), 4.04 – 4.00 (m, 1H), 3.66 (s, 2H), 3.61 (d, *J* = 13.5 Hz, 1H), 3.48 (s, 3H), 3.44 – 3.38 (m, 1H), 2.93 (d, *J* = 13.6 Hz, 1H), 2.49 – 2.43 (m, 2H), 2.21 (s, 3H), 2.17 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 144.6, 143.3, 139.5, 137.8, 137.1, 132.0, 129.3, 129.0, 128.4, 127.0, 126.5, 121.6, 119.0, 118.7, 118.2, 108.8, 108.3, 62.3, 60.6, 53.8, 41.8, 38.7, 29.5, 21.4, 19.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{34}N_3O_2S$ 500.2366; found 500.2367.

a) Acess to tetrahydroquinoline derivatives via aminomethylative cyclization

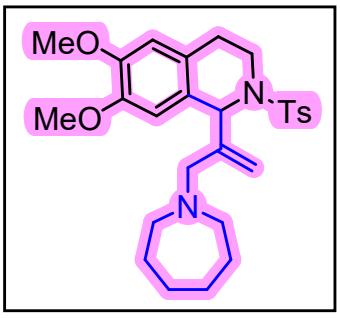


Synthesis of 4-(2-(6,7-dimethoxy-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)allyl)morpholine (6):[4]



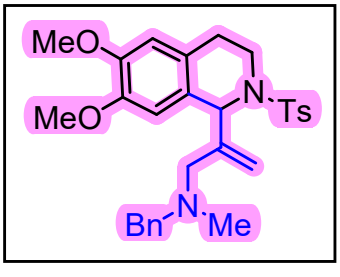
Prepared according to the general procedure **C** from **1v** (112 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **6** as a White solid (121 mg, 85% yield). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 109-111 °C. **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.28 (s, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 6.61 – 6.59 (m, 2H), 6.04 (s, 1H), 5.79 (s, 1H), 5.41 (s, 1H), 5.18 – 5.13 (m, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.71 – 3.62 (m, 4H), 3.41 – 3.34 (m, 1H), 3.23 – 3.17 (m, 1H), 2.92 – 2.86 (m, 1H), 2.79 – 2.73 (m, 1H), 2.49 (s, 1H), 2.41 (s, 3H), 2.37 – 2.28 (m, 2H), 1.97 – 1.94 (m, 2H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 149.1, 147.9, 144.1, 139.8, 137.8, 131.4, 129.9, 127.5, 120.7, 120.1, 112.2, 111.5, 87.9, 67.0, 61.2, 56.1, 56.0, 53.4, 45.9, 36.6, 21.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{33}N_2O_5S$ 473.2105; found 473.2109.

Synthesis of 1-(3-(azepan-1-yl)prop-1-en-2-yl)-6,7-dimethoxy-2-tosyl-1,2,3,4-tetrahydroisoquinoline (7):



Prepared according to the general procedure **C** from **1v** (112 mg, 0.3 mmol). Flash column chromatography (30% EtOAc in Hexane) afforded the desired product **7** as a White solid (60 mg, 41% yield). Reaction time: 18 h. Reaction temperature: room temperature. **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 8.6 Hz, 1H), 6.59 (s, 2H), 6.11 (s, 1H), 5.74 (s, 1H), 5.39 (s, 1H), 5.14 – 5.11 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.33 – 3.27 (m, 1H), 3.21 – 3.14 (m, 1H), 2.87 – 2.87 (m, 1H), 2.77 – 2.72 (m, 1H), 2.67 (d, *J* = 13.0 Hz, 1H), 2.57 (d, *J* = 12.9 Hz, 1H), 2.49 – 2.46 (m, 2H), 2.41 (s, 3H), 2.23 – 2.21 (m, 2H), 1.60 – 1.57 (m, 7H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 149.1, 147.8, 144.0, 137.6, 131.5, 129.8, 127.6, 120.7, 119.0, 112.1, 111.5, 88.3, 61.3, 56.0, 56.0, 55.5, 45.8, 36.4, 28.2, 26.8, 21.6. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{37}N_2O_4S$ 485.2469; found 485.2474.

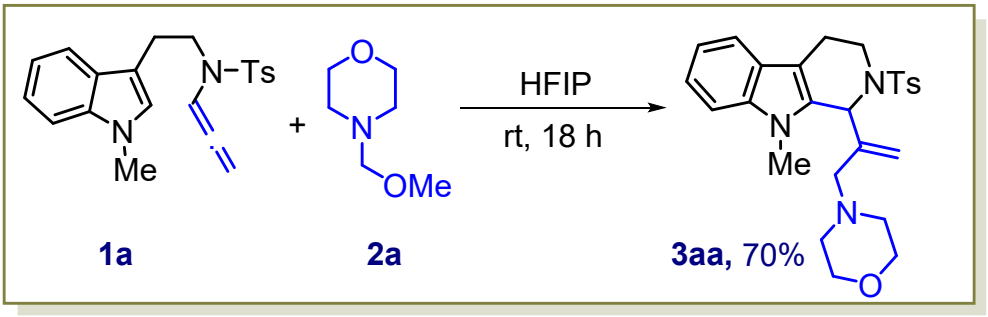
Synthesis of N-benzyl-2-(6,7-dimethoxy-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-N-methylprop-2-en-1-amine (8):



Prepared according to the general procedure **C** from **1v** (112 mg, 0.3 mmol). Flash column chromatography (10% EtOAc in Hexane) afforded the desired product **8** as a colorless liquid (132 mg, 87% yield). Reaction time: 18 h. Reaction temperature: room temperature. **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.34 – 7.31 (m, 2H), 7.29 – 7.24 (m, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 1H), 6.61 (s, 2H), 6.22 (s, 1H), 5.82 (s, 1H), 5.50 (s,

1H), 5.24 – 5.22 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.45 (d, *J* = 13.4 Hz, 1H), 3.40 – 3.34 (m, 1H), 3.25 – 3.19 (m, 1H), 3.12 (d, *J* = 13.4 Hz, 1H), 2.86 – 2.78 (m, 1H), 2.67 – 2.57 (m, 2H), 2.32 (s, 3H), 1.90 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 149.1, 147.8, 144.0, 140.9, 138.6, 137.5, 131.4, 129.9, 128.5, 127.5, 127.1, 120.7, 119.4, 112.1, 111.5, 88.3, 61.4, 60.9, 56.0, 55.9, 45.8, 41.5, 36.4, 21.5. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{35}N_2O_4S$ 507.2312; found 507.2320.

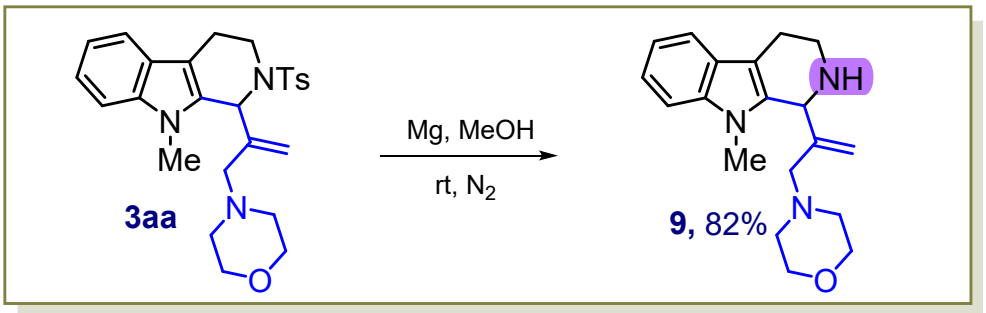
6. Gram scale synthesis of 3aa



An oven-dried Schlenk/Seal tube was charged with with N,O-acetal **2a** (535 mg, 1.5 equiv) in **HFIP** (15 mL), and then allenamide **1a** (1.0 g, 2.72 mmol, 1.0 equiv) was added to the reaction mixture. The reaction was stirred at room temperature for 18 h, and the solvent was evaporated under reduced pressure. The reaction mixture was purified by flash chromatography (EtOAc in Hexane) on silica gel (100-200 mesh) to give **3aa** as a white solid (890 mg, 70% yield).

7. Synthetic transformations

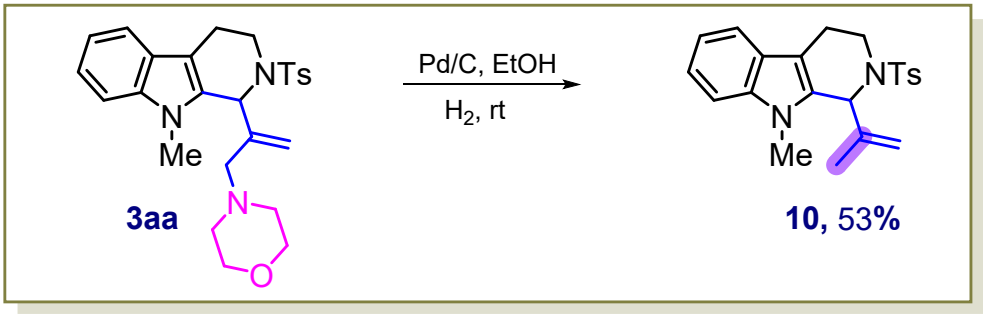
(b) (i) Synthesis of 4-(2-(9-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)allyl)morpholine (9):[3]



An oven dried Schlenk tube was charged with **3aa** (93 mg, 0.2 mmol), Mg turnings (267 mg, 11 mmol, 55.0 equiv) and MeOH (4.0 mL) under nitrogen. The reaction mixture was ultrasonicated for 5 minutes, and then stirred at room temperature for overnight. The white suspension was treated with Et_3N and filtered through a short pad of Celite, washed with Et_2O and MeOH. The filtrate was concentrated in vacuum and the residue was purified by flash column chromatography eluted with 5% MeOH in EtOAc and Et_3N to give the desired product **9** (51 mg, 82% yield) as a pale yellow liquid. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.55 (d, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 5.23 (s, 1H), 4.75 (s, 1H), 4.69 (s, 1H), 3.76 (brs, 4H), 3.49 (s, 3H), 3.26 (dd, *J* = 12.8 Hz, 1H), 3.11 – 3.09 (m, 2H), 3.01 (d, *J* = 12.9 Hz, 1H), 2.88 – 2.73 (m, 3H), 2.57 – 2.51 (m, 4H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 143.7, 137.0, 134.8, 126.9, 121.2, 118.9, 118.8, 118.2, 109.3, 108.8, 67.2, 63.5, 54.7, 54.0, 38.8, 29.5, 22.6. **HRMS** (ESI-TOF) m/z: [M +

H]$^+$ Calcd for $C_{19}H_{26}N_3O$ 312.2076; found 312.2068.

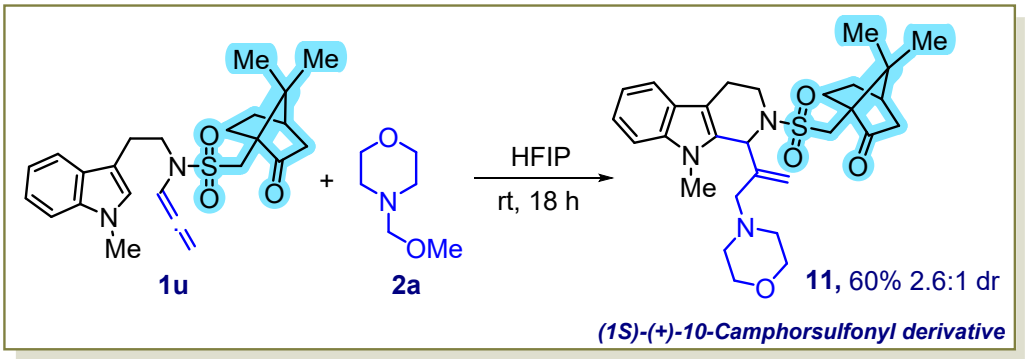
(b)(ii) Synthesis of 9-methyl-1-(prop-1-en-2-yl)-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (10):[3]



An oven dried Schlenk tube was charged with **3aa** (93 mg, 0.2 mmol) in EtOH (4 mL), and was added 10% Pd-C (0.4 equiv), and the mixture was stirred at room temperature for 48 h under H_2 atmosphere (H_2 balloon). The catalyst was removed by filtration through Celite pad, and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (eluted with 10% EtOAc in hexane) furnishing **10** (40 mg, 53 % yield) as a white solid. Melting point: 152-154 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 4.0 Hz, 1H), 7.19 – 7.15 (m, 1H), 7.04 – 6.97 (m, 3H), 5.51 (s, 1H), 5.09 (s, 1H), 4.37 (s, 1H), 3.99 (dd, *J* = 14.9, 5.8 Hz, 1H), 3.54 (s, 3H), 3.41 – 3.33 (m, 1H), 2.48 – 2.33 (m, 2H), 2.18 (s, 3H), 2.01 (s, 3H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 143.3, 142.9, 137.8, 137.1, 132.0, 129.3, 126.9, 126.4, 121.6, 119.0, 118.3, 117.1, 108.8, 107.9, 56.9, 38.8, 29.6, 21.4, 20.8, 19.7. **HRMS** (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{25}N_2O_2S$ 381.1631; found 381.1631.

8. Derivatives of biologically important molecules

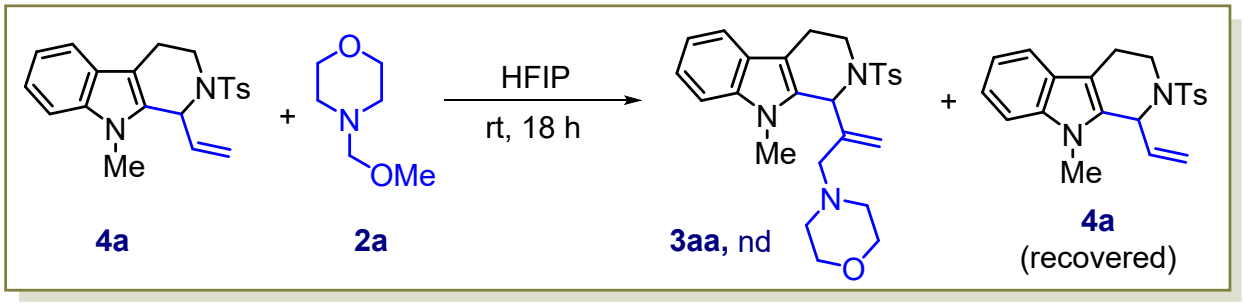
c) Synthesis of (1R,4R)-7,7-dimethyl-1-(((9-methyl-1-(3-morpholinoprop-1-en-2-yl)-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)sulfonyl)methyl)bicyclo[2.2.1]heptan-2-one (11):



Prepared according to the general procedure **C** from **1u** (127 mg, 0.3 mmol). Flash column chromatography (35% EtOAc in Hexane) afforded the desired product **11** as a white solid (94 mg, 60% yield, 2.6:1 dr). Reaction time: 18 h. Reaction temperature: room temperature. Melting point: 168-170 °C. **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 7.52 (t, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.22 (d, *J* =7.1 Hz, 1H), 7.12 (q, *J* = 6.7 Hz, 1H), 5.78 (d, *J* = 47.1 Hz, 1H), 5.21 (s, 1H), 4.52 (s, 1H), 4.14 – 4.06 (m, 1H), 3.77 – 3.72 (m, 4H), 3.57 (d, *J* = 16.9 Hz, 3H), 3.51 – 3.43 (m, 2H), 3.27 (dd, *J* =56.4 Hz, 14.5 Hz, 1H), 3.15 – 2.95 (m, 1H), 2.84 – 2.79 (m, 2H), 2.73 (t, *J* = 13.0 Hz, 1H), 2.62 – 2.55 (m, 4H), 2.44 – 2.28 (m, 2H), 2.04 – 1.99 (m, 2H), 1.89 (q, *J* = 9.4 Hz,

1H), 1.75 –1.67 (m, 1H), 1.40 – 1.26 (m, 2H), 1.05 (d, *J* = 8.3 Hz, 3H), 0.75 (s , 1H), 0.65 (s, 1H). **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):** δ 214.7, 143.3, 137.3, 132.1, 126.6, 121.9, 119.4, 119.0, 118.6, 118.4, 109.0, 108.0, 67.4, 61.0, 58.7, 53.9, 53.2, 49.6, 47.7, 43.1, 42.6, 38.6, 29.5, 26.9, 26.1, 25.4, 20.8, 20.1, 19.9. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{40}N_3O_4S$ 526.2740; found 526.2715.

9. Control Experiment

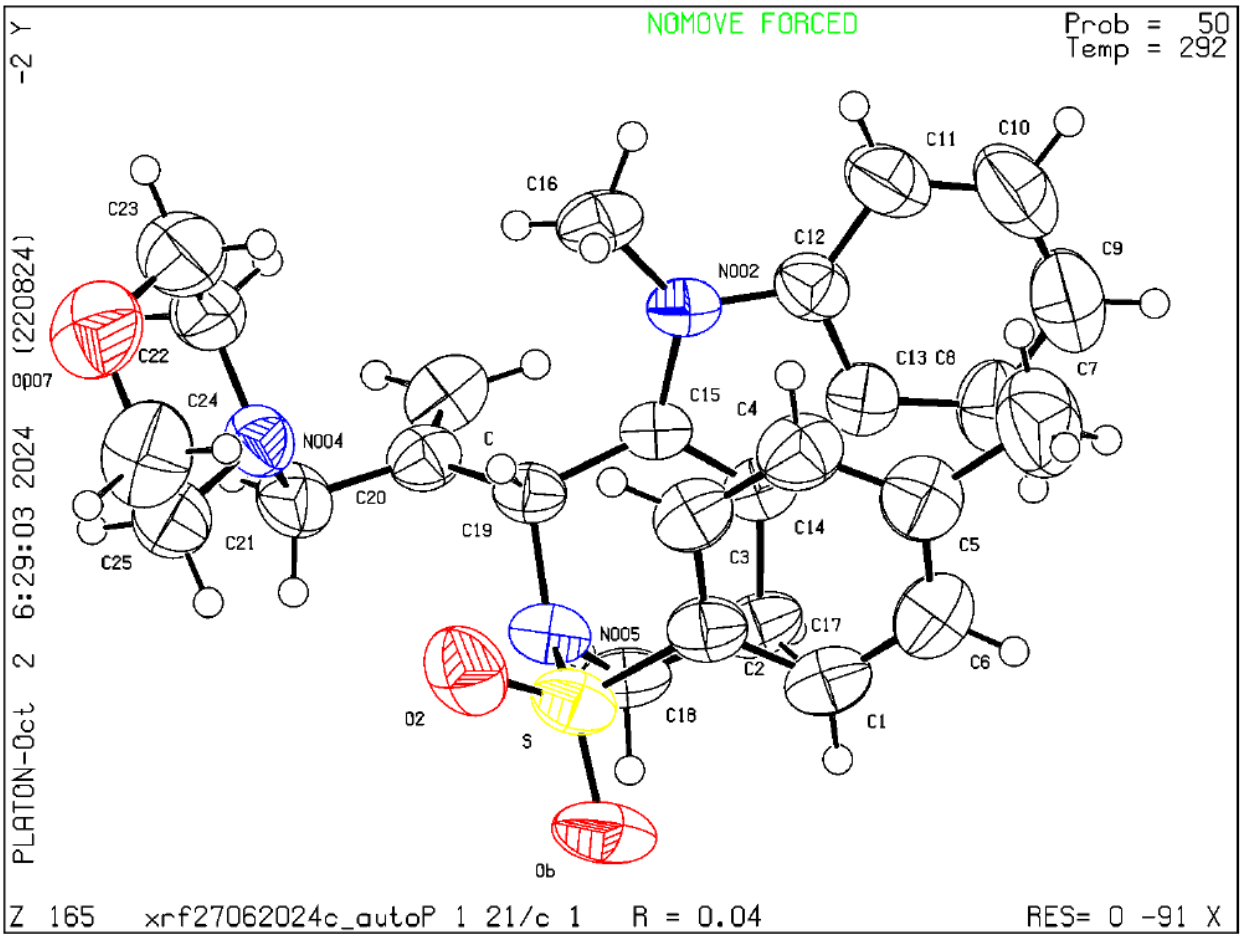


An oven-dried Schlenk tube was charged with N,O-acetal **2a** (1.5 equiv) in HFIP (3 mL), and then compound **4a** (0.3 mmol, 1.0 equiv) was added to the reaction mixture. The reaction was stirred at room temperature (rt) for 18 h. **3aa** was not detected and **4a** was recovered.

10. X-Ray Data Collection and Check CIF Report

Single crystal X-ray data for compound **3aa (CCDC 2390767)** was collected on the Rigaku XtaLAB Synergy-S single crystal X-ray diffractometer equipped with a HyPix-6000HE Hybrid Photon Counting (HPC)detector and dual Mo and Cu microfocus sealed X-ray source with kappa goiniometer at 293 (2) K. Data collection cell determination, and data reduction was performed using the CrysAlisPro[16] software. Structure solution and refinement were performed by using SHELX-97[17]. Refinement of coordinates and anisotropic thermal parameters of non-hydrogen atoms was carried out by the full-matrix least-squares method. The hydrogen atoms attached to carbon atoms were generated with idealized geometries and isotropically refined using a riding model.

Datablock xrf27062024c_auto - ellipsoid plot



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) xrf27062024c_auto

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: xrf27062024c_auto

```
Bond precision:   C-C = 0.0027 A          Wavelength=1.54184

Cell:             a=12.6627(2)     b=15.3055(2)         c=12.8279(2)
                  alpha=90         beta=101.373(2)      gamma=90
Temperature:      292 K

                 Calculated                Reported
Volume           2437.34(7)                2437.34(6)
Space group      P 21/c                    P 1 21/c 1
Hall group       -P 2ybc                   -P 2ybc
Moiety formula   C26 H31 N3 O3 S           C26 H31 N3 O3 S
Sum formula      C26 H31 N3 O3 S           C26 H31 N3 O3 S
Mr               465.60                    465.60
Dx,g cm-3        1.269                     1.269
Z                4                         4
Mu (mm-1)        1.437                     1.437
F000             992.0                     992.0
F000'            996.02
h,k,lmax         16,19,16                  16,19,16
Nref             5216                      4961
Tmin,Tmax        0.886,0.917               0.612,1.000
Tmin'            0.818

Correction method= # Reported T Limits: Tmin=0.612 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.951          Theta(max)= 78.005

R(reflections)= 0.0432( 4136)                wR2(reflections)=
                                             0.1302( 4961)
S = 1.060                 Npar= 313
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11. References

1. (a) Mondal, A.; Chowdhury, C. *J. Org. Chem.* **2021**, *86*, 3, 3810–3825. (b) Chaudhary, D.; Kuram, M. R. *J. Org. Chem.* **2024**, *89*, 11783−11788. (c). Wang, Y.; Zhang, P.; Di, X.; Dai, Q.; Zhang, Z.-M.; Zhang, J. *Angew. Chem. Int. Ed.* **2017**, *56*, 15905–15909. (d). Zhao, L.-P.; Li, P.-J.; Wang, L.; Tang, Y. *Angew. Chem. Int. Ed.* **2022**, *134*, e202207360. (e). Pradhan, T. R.; Kim, H. W.; Park, J. K. *Angew. Chem. Int. Ed.* **2018**, *57*, 9930–9935. (f). Kumar, D.; Chaudhary, D.; Ishu, K.; Yadav, S.; Maurya, N. K.; Kant, R.; Kuram, M. R. ***Org. Biomol. Chem.*** **2022*, 20,*** 8610–8614. (g). Kumar, D.; Kuram, M. R. *Adv. Syn. Cat.* **2023**, *365*, 3935–3941.

2. (a) Y. Chi, E. P. English, W. C. Pomerantz, W. S. Horne, L. A. Joyce, L. R. Alexander, W. S. Fleming, E. A. Hopkins, S. H. Gellman, *J. Am. Chem. Soc.* **2007**, *129*, 6050. (b) A. Martinez-Cuezva, C. Lopez-Leonardo, D. Bautista, M. Alajarin, J. Berna, *J. Am. Chem. Soc.* **2016**, *138*, 8726. (c) Yu, J.; Chen, L.; Sun, J. *Org. Lett.* **2019**, *21*, 1664–1667. (d) Sakai, N.; Shimamura, K.; Ikeda, R.; Konakahara, T. *J. Org. Chem.* **2010**, *75*, 3923–3926.

3. Chaudhary, D.; Kuram, M. R. *J. Org. Chem.* **2024**, *89*, 11783−11788.

4. (a) Perego, L. A.; Blieck, R.; Groué, A.; Monnier, F.; Taillefer, M.; Ciofini, I.; Grimaud, L. *ACS Catal*. **2017**, *7*, 4253−4264. (b) Manoni, E.; Gualandi, A.; Mengozzi, L.; Bandini, M.; Cozzi,P. G. *RSC Adv.* **2015**, *5*, 10546−10550.

12. NMR Spectra

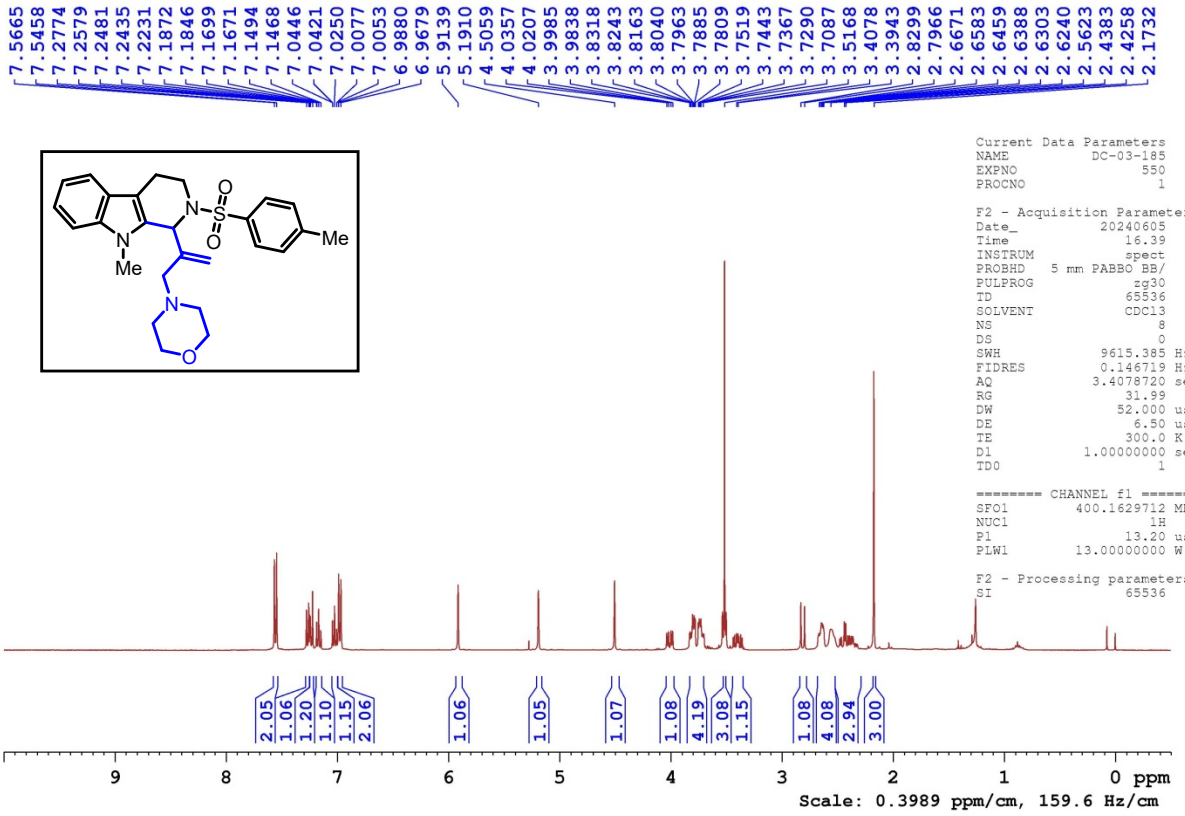

Figure S-1: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3aa**

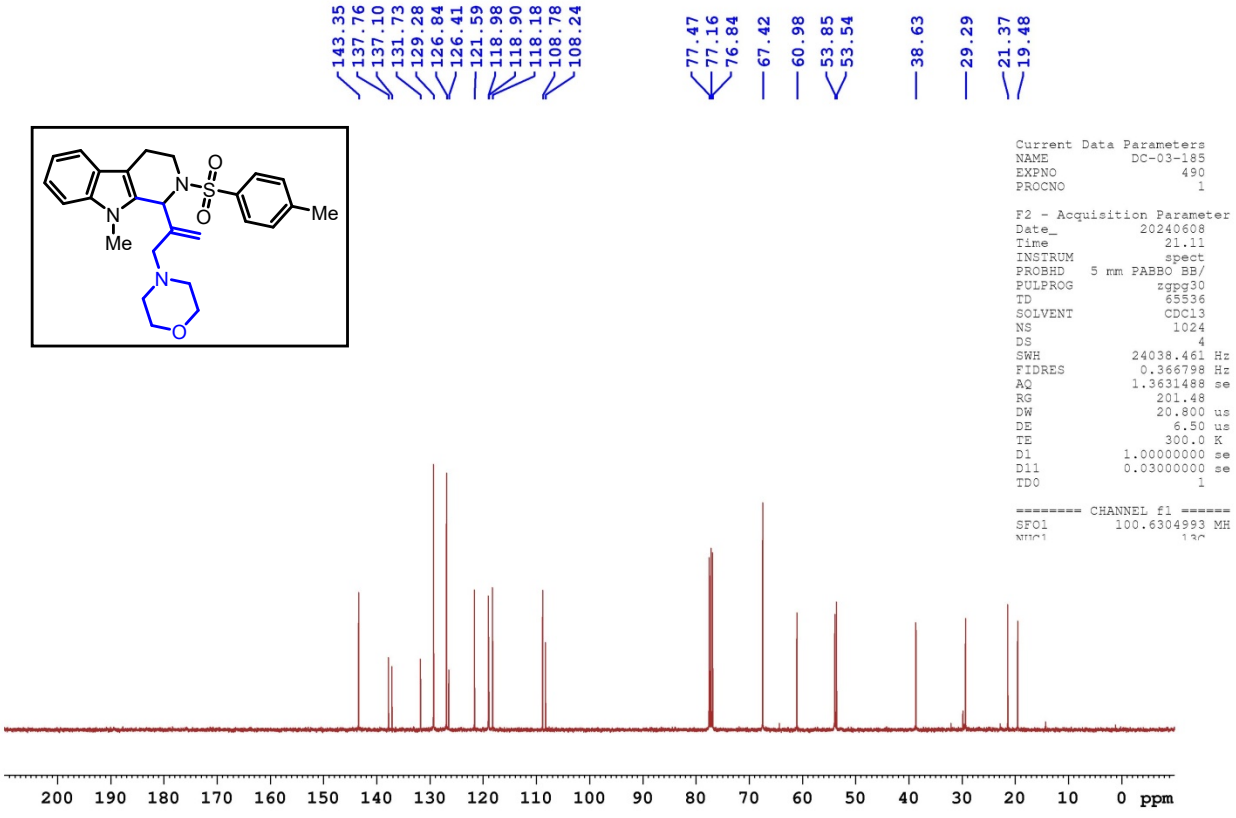

Figure S-2: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3aa**

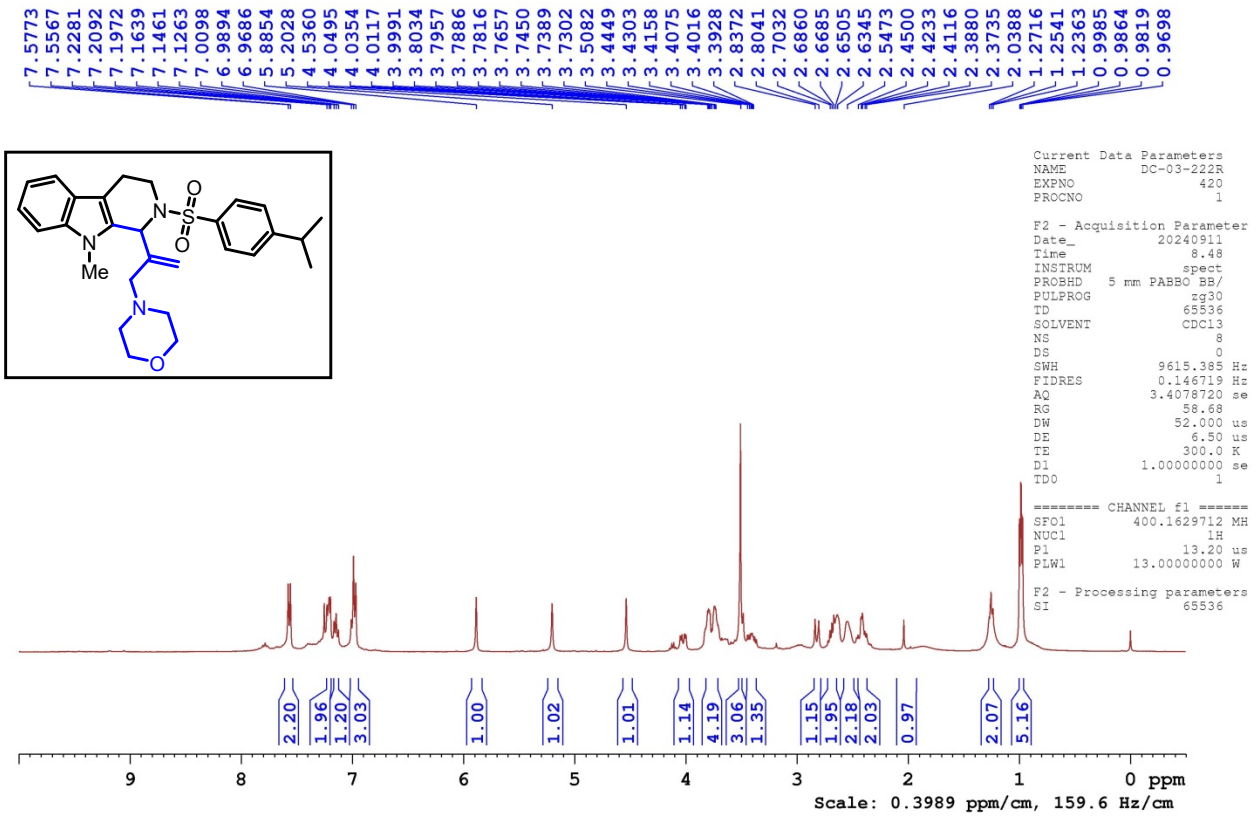

Figure S-3: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ba**

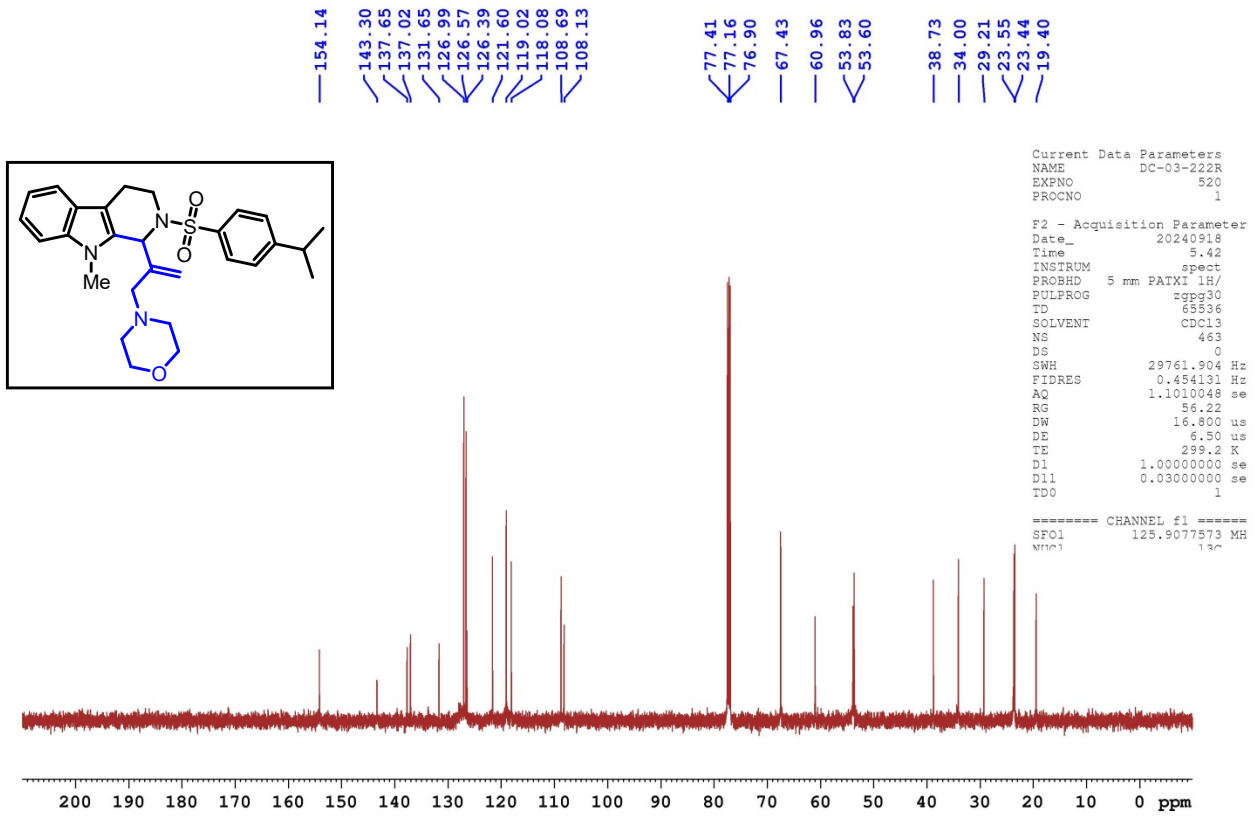

Figure S-4: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3ba**

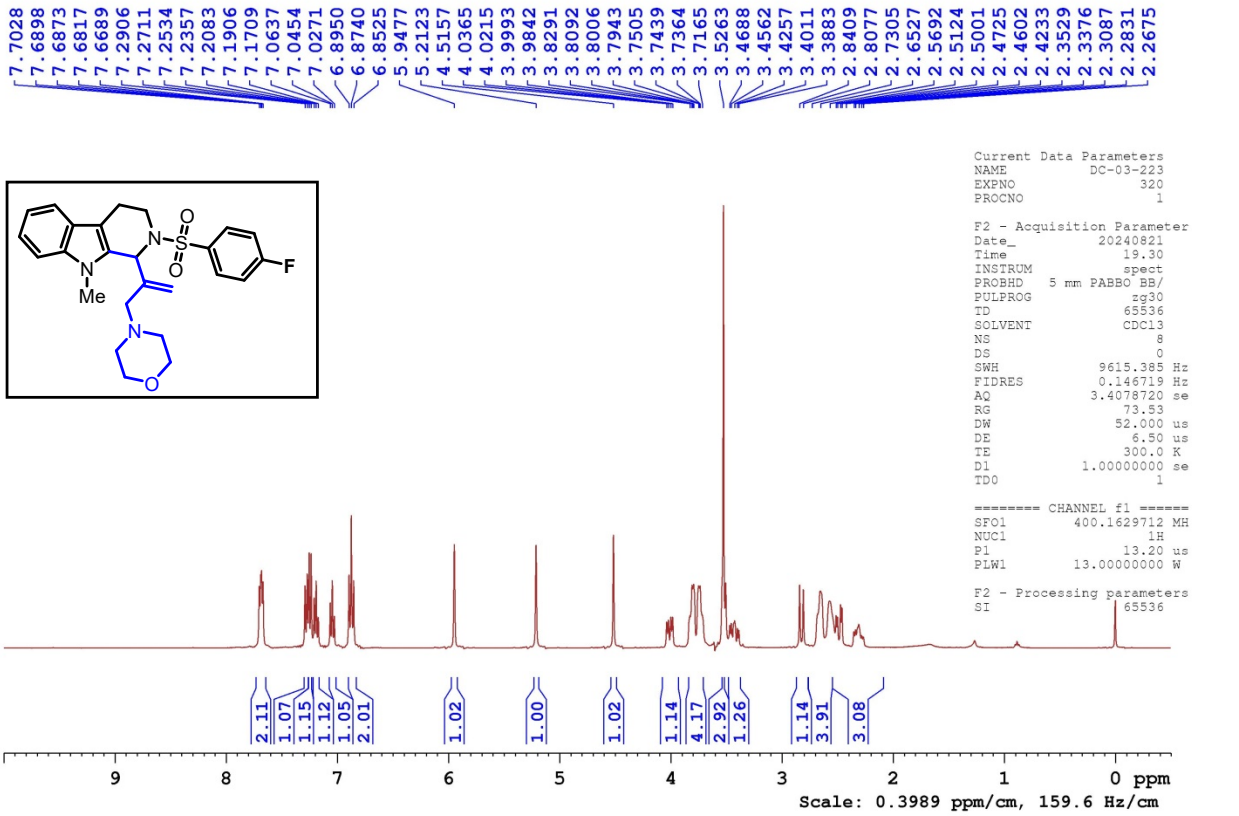

Figure S-5: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ca**

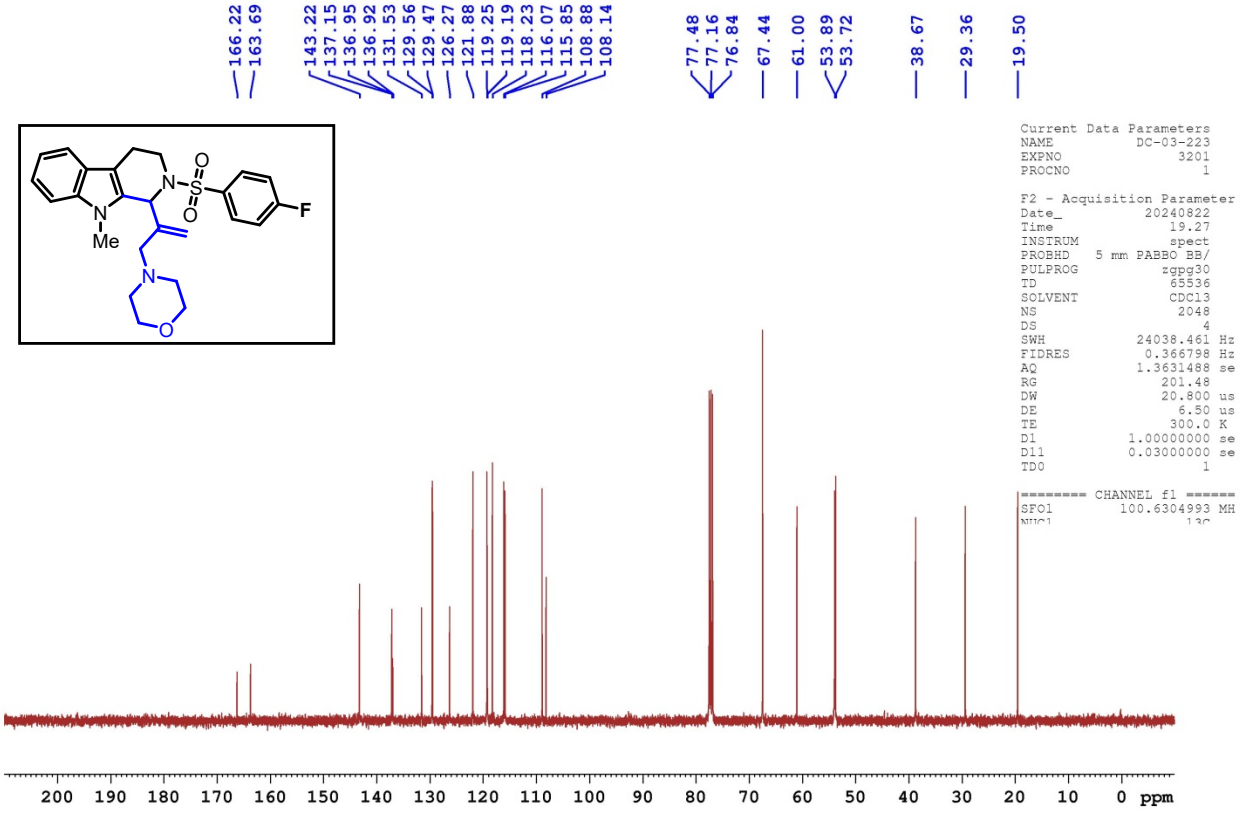

Figure S-6: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ca**

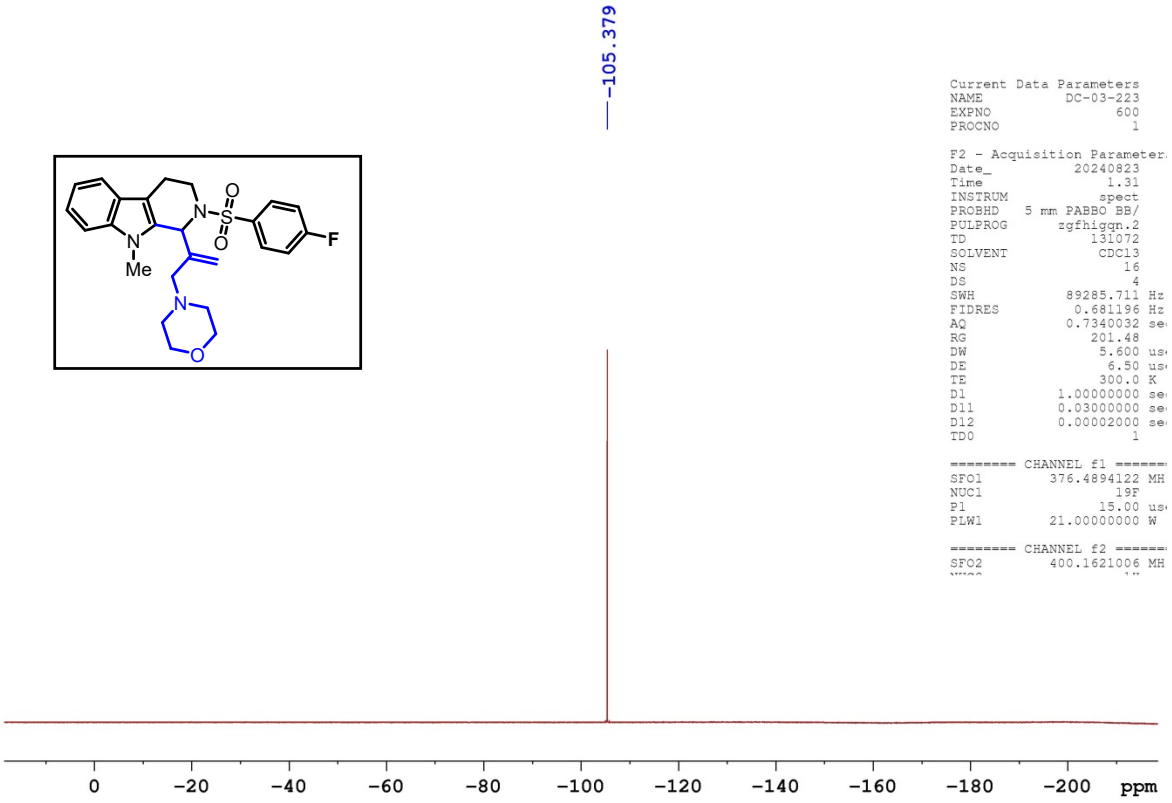

Figure S-7: ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound **3ca**

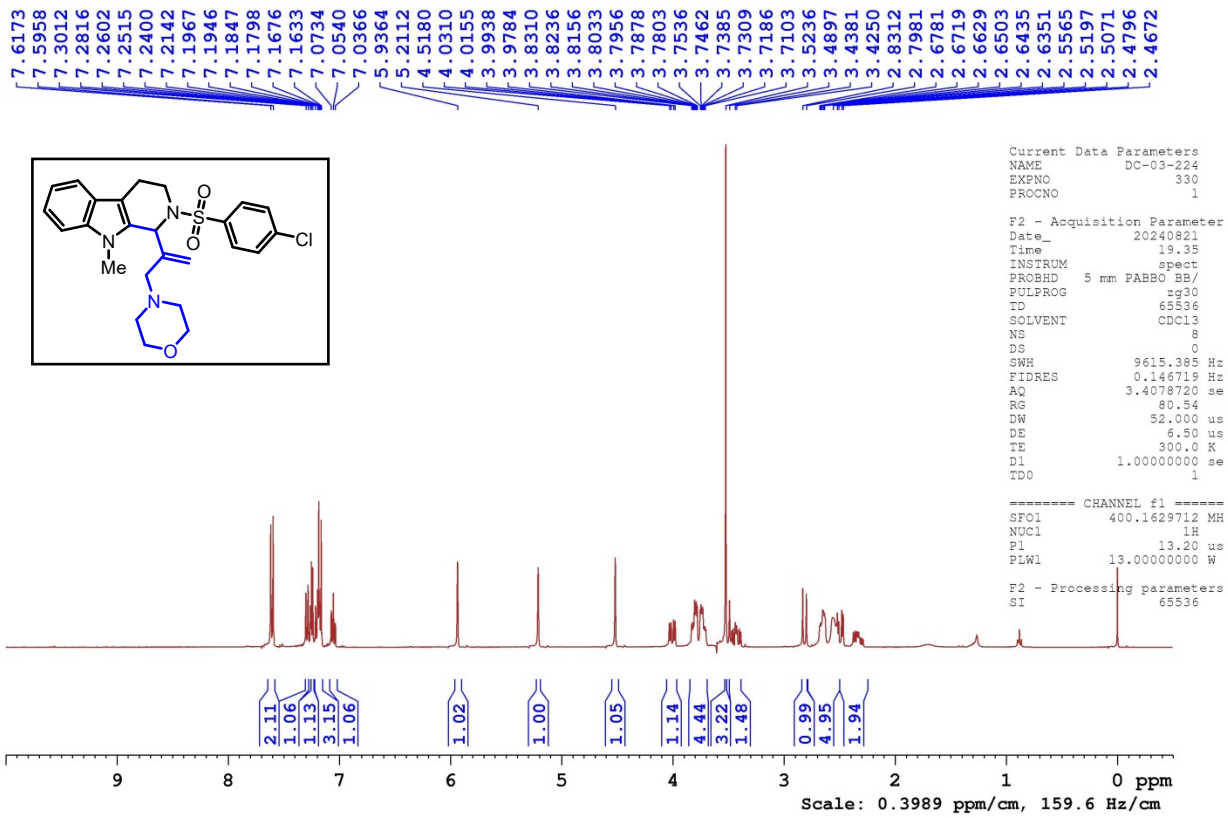

Figure S-8: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3da**

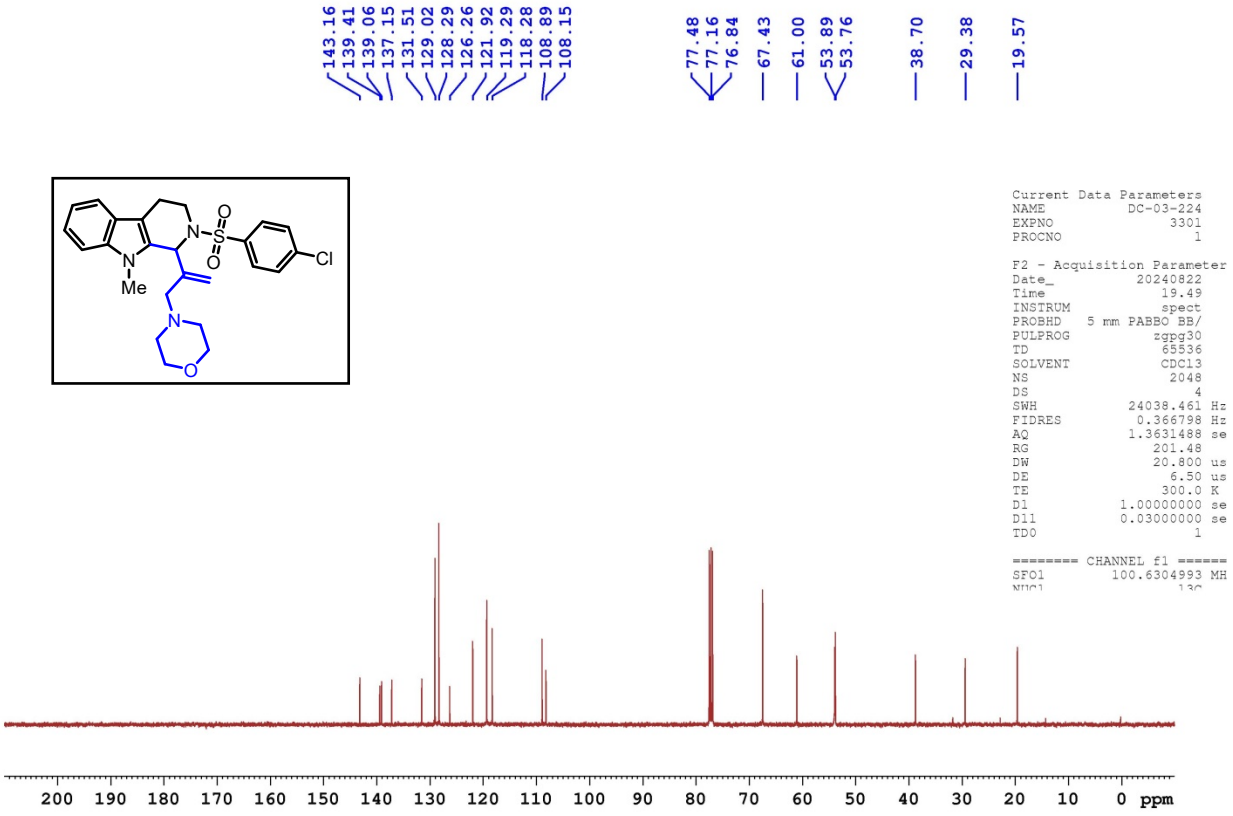

Figure S-9: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3da**

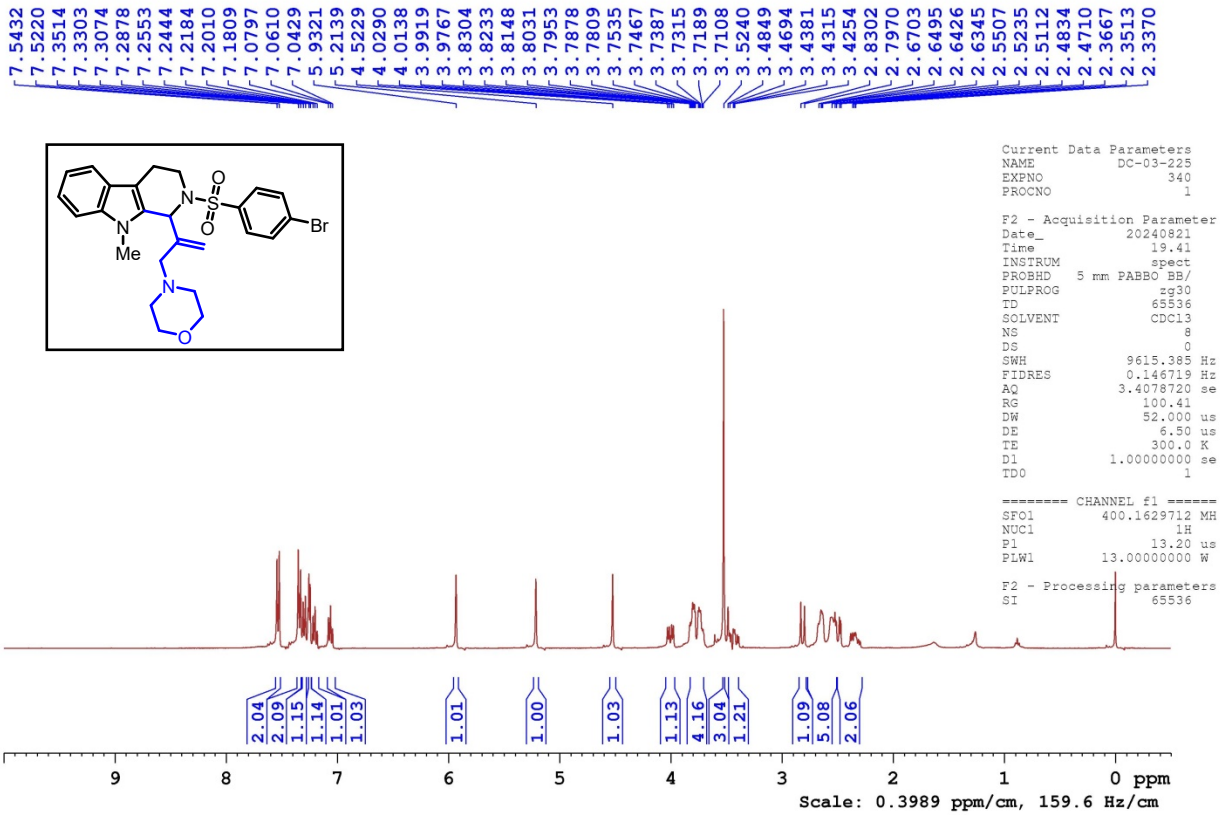

Figure S-10: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ea**

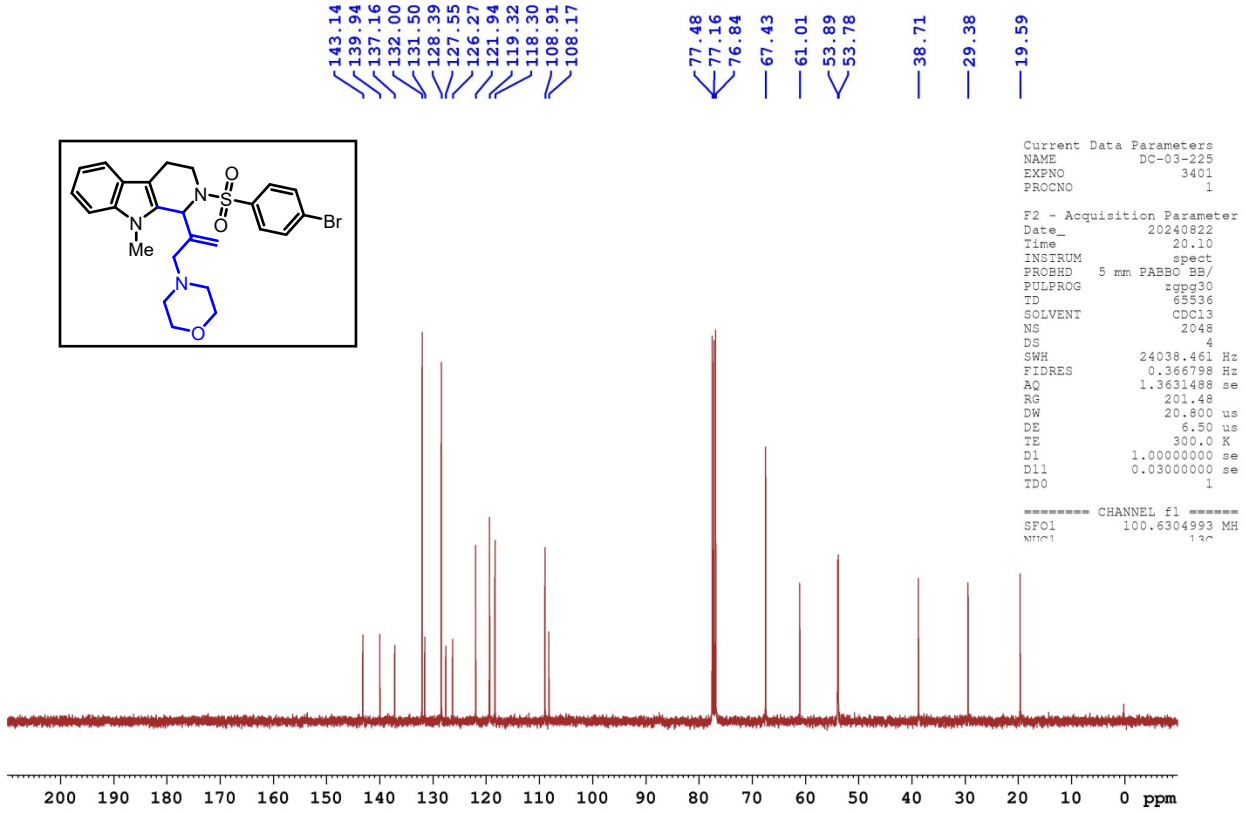

Figure S-11: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ea**

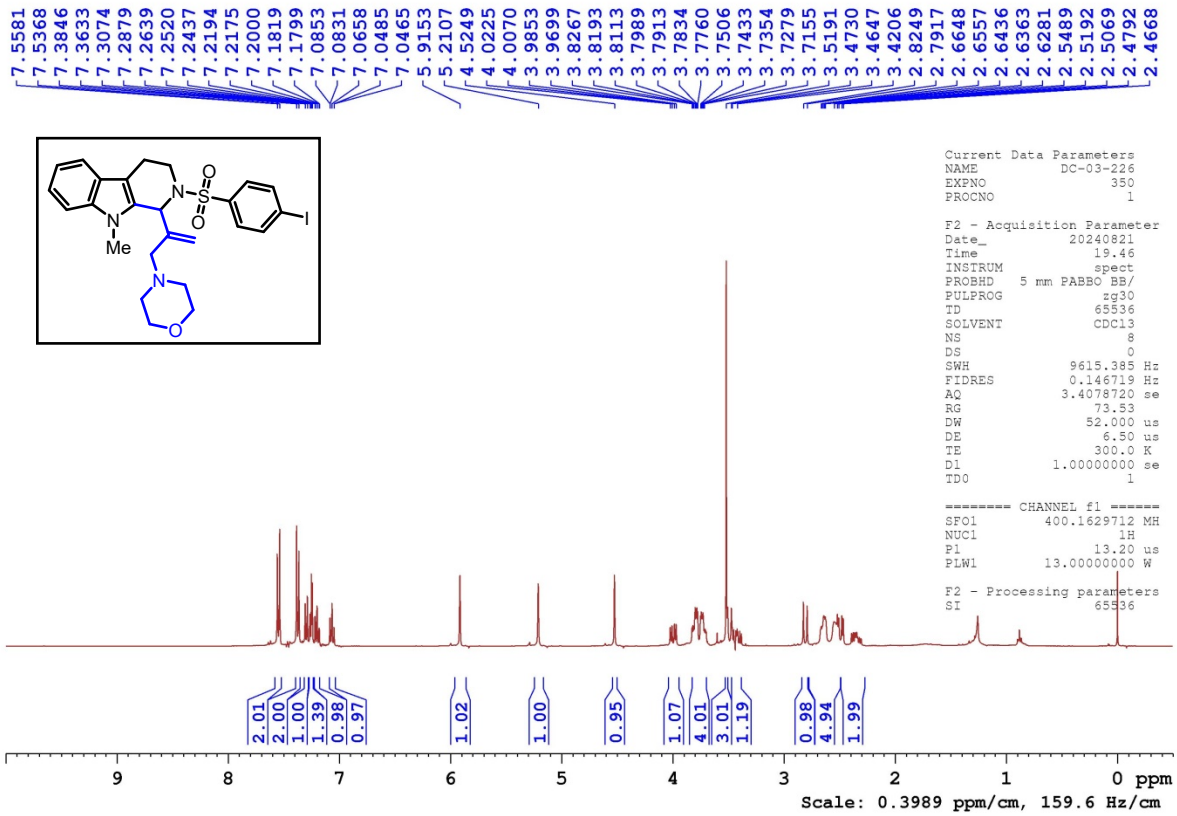

Figure S-12: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3fa**

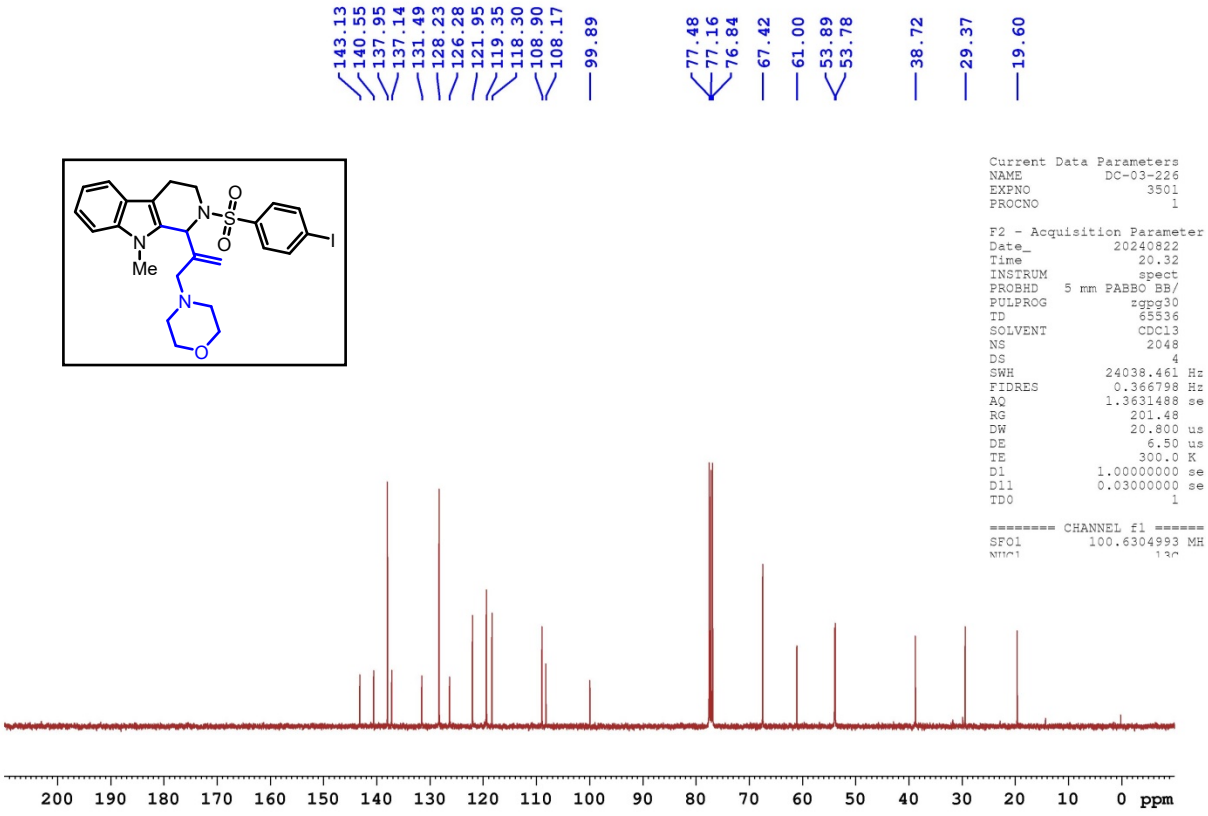

Figure S-13: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3fa**

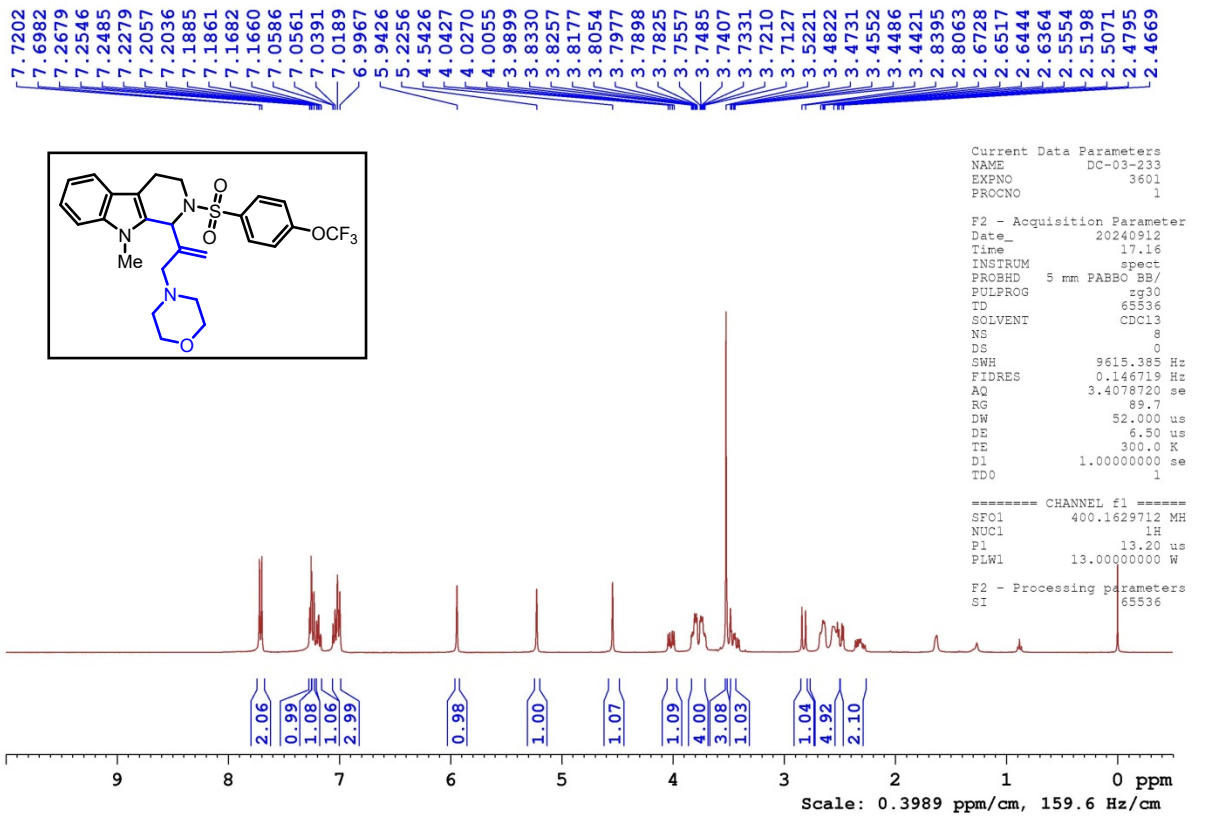

Figure S-14: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ga**

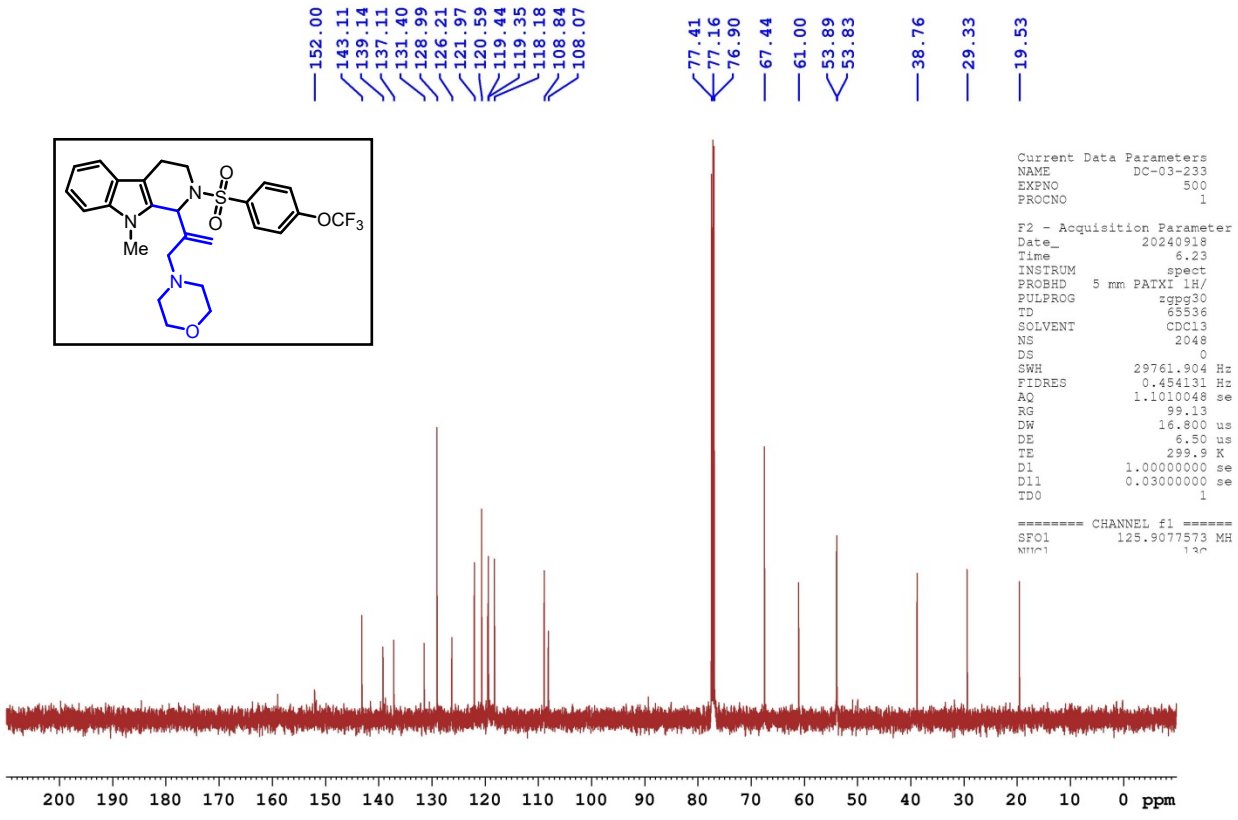

Figure S-15: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3ga**

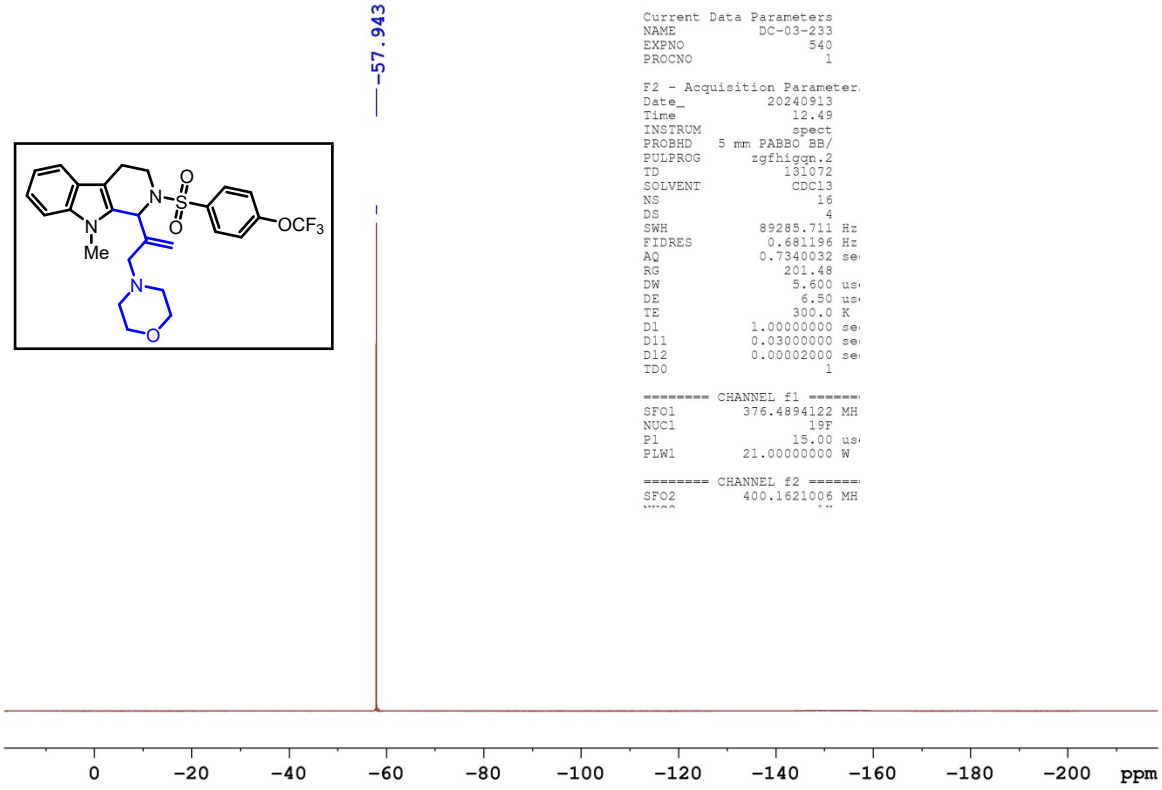

Figure S-16: ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound **3ga**

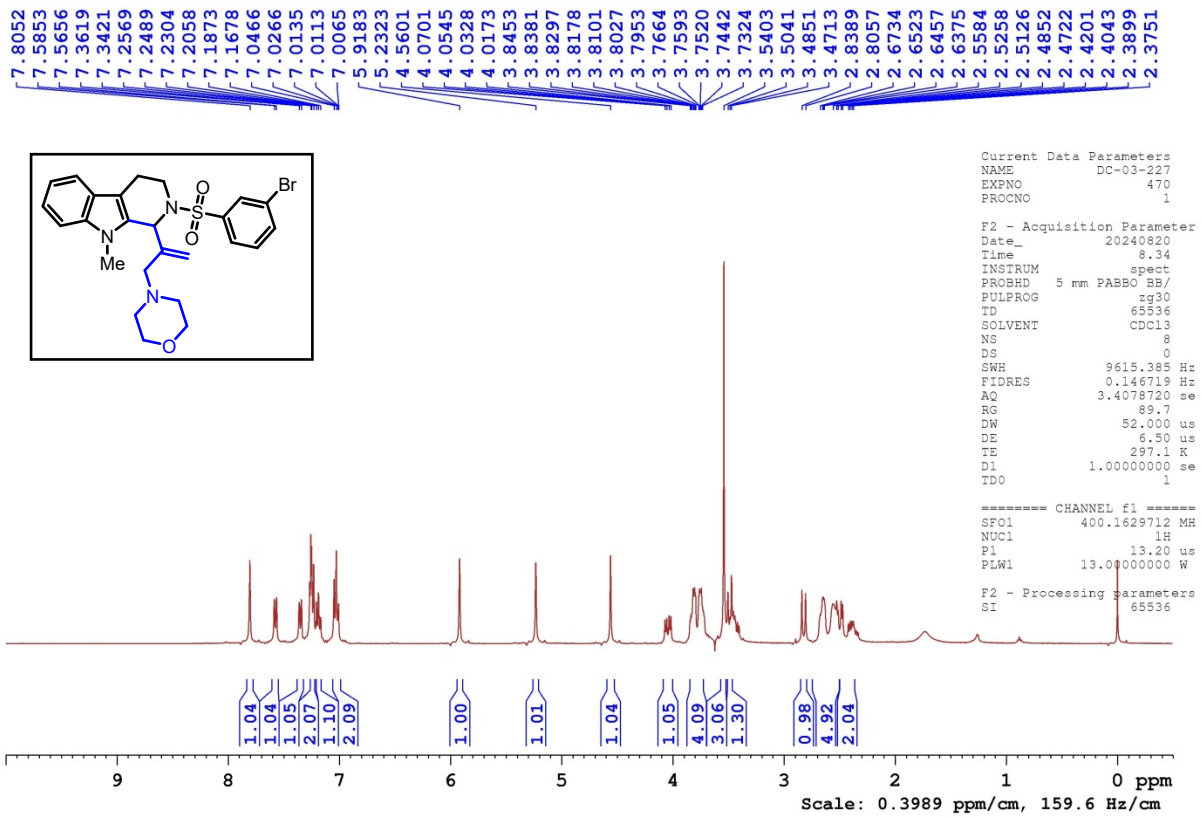

Figure S-17: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ha**

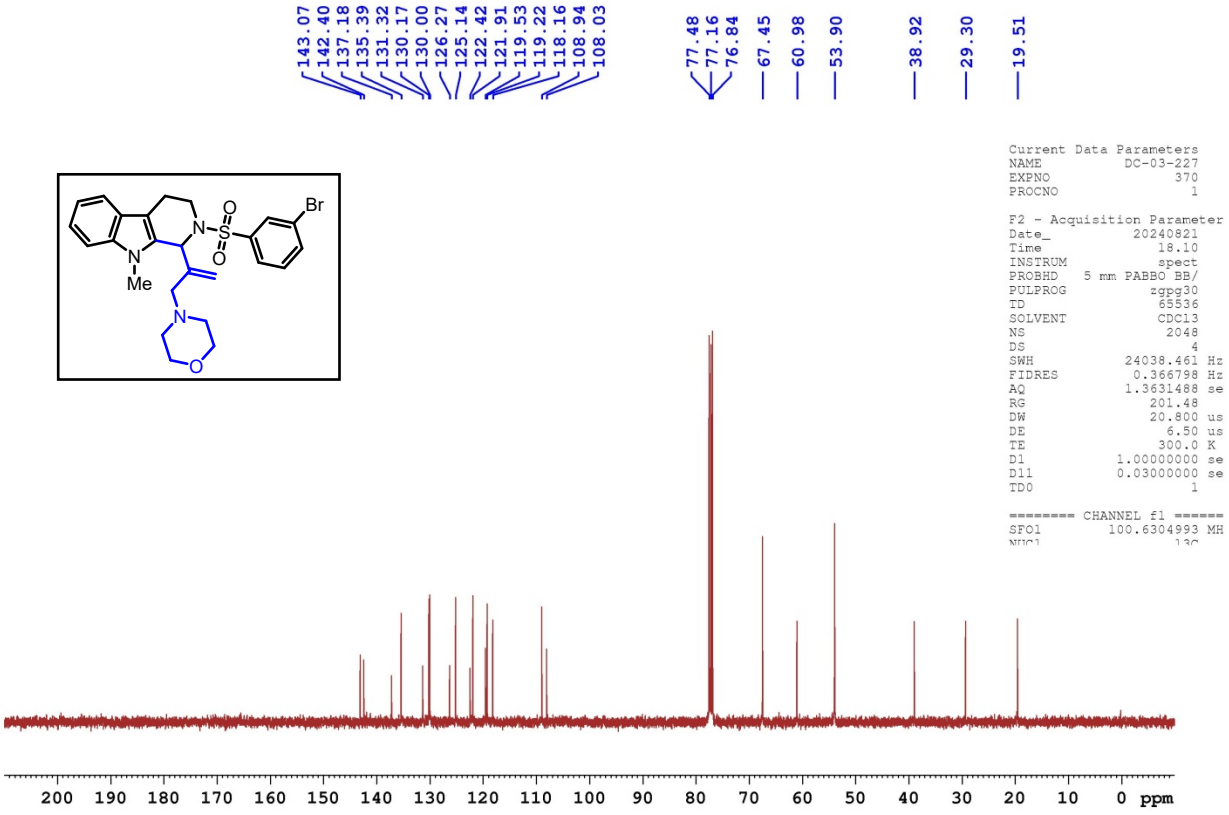

Figure S-18: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ha**

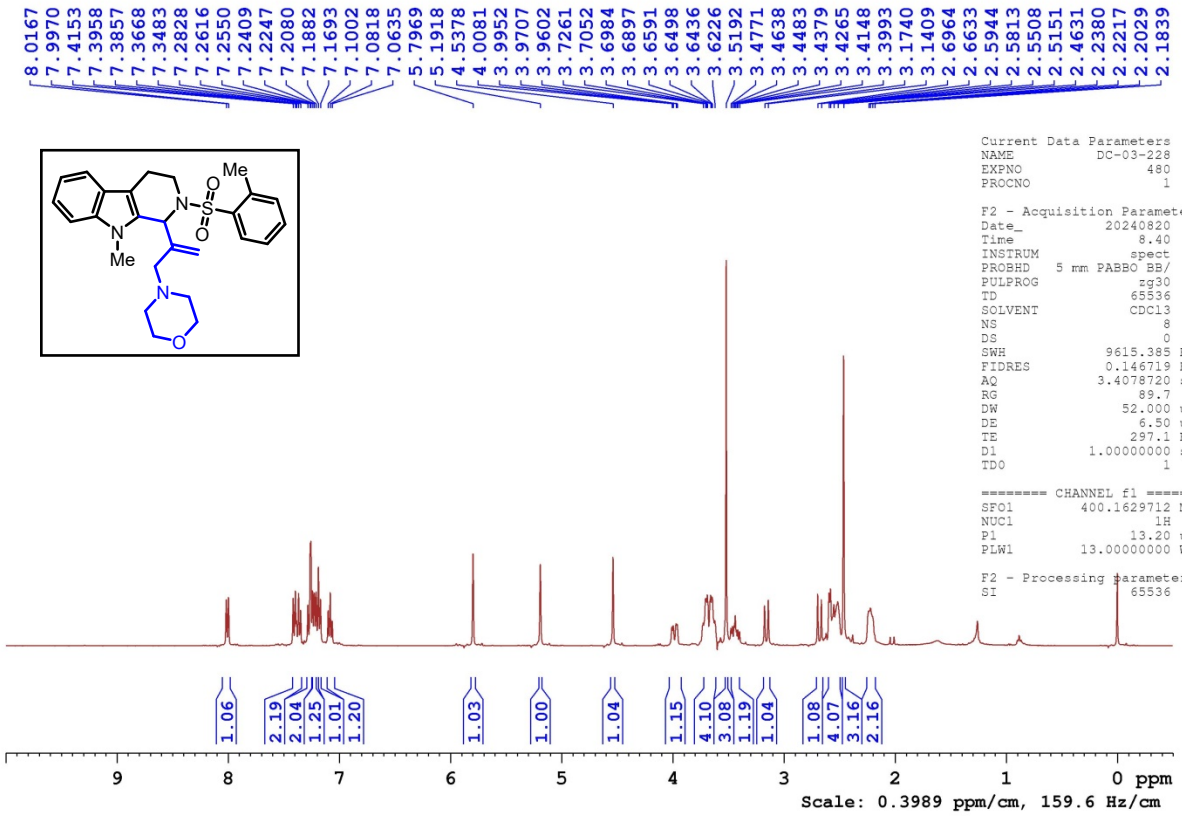

Figure S-19: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ia**

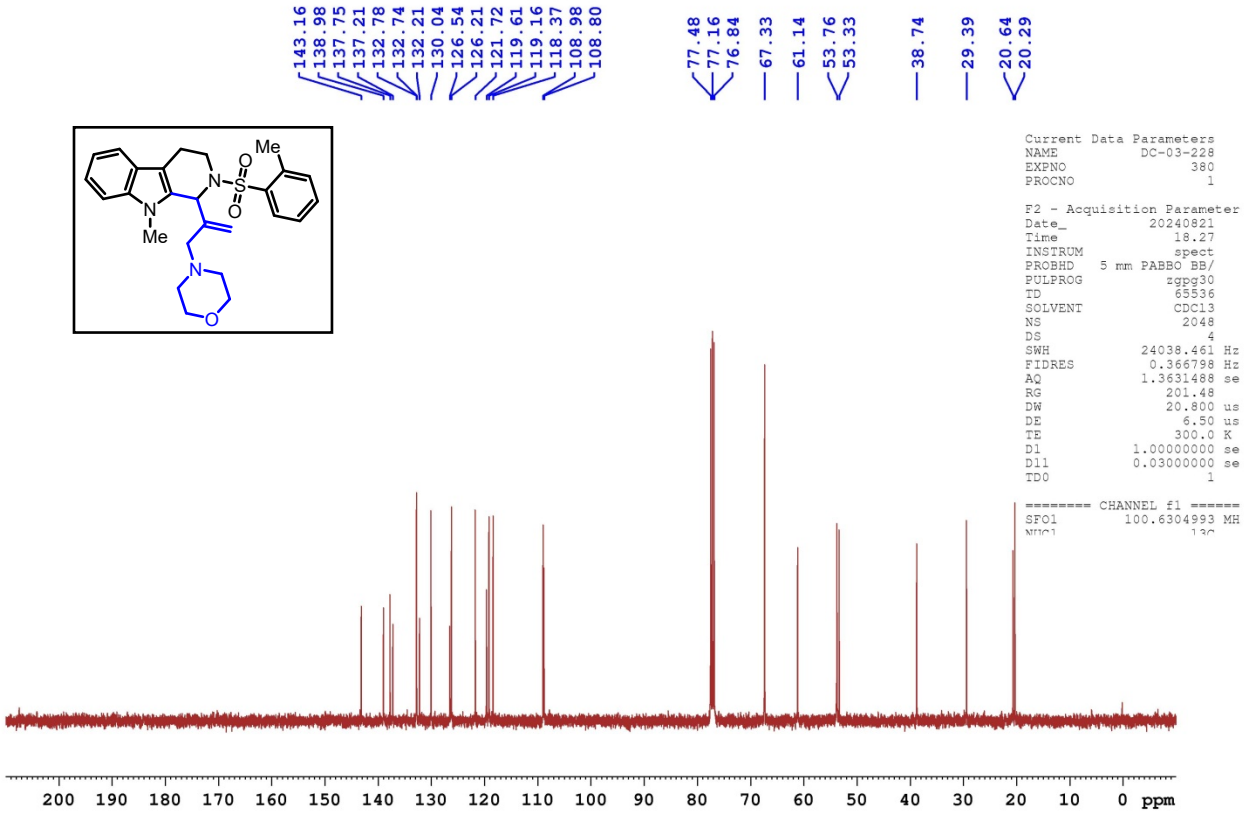

Figure S-20: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ia**

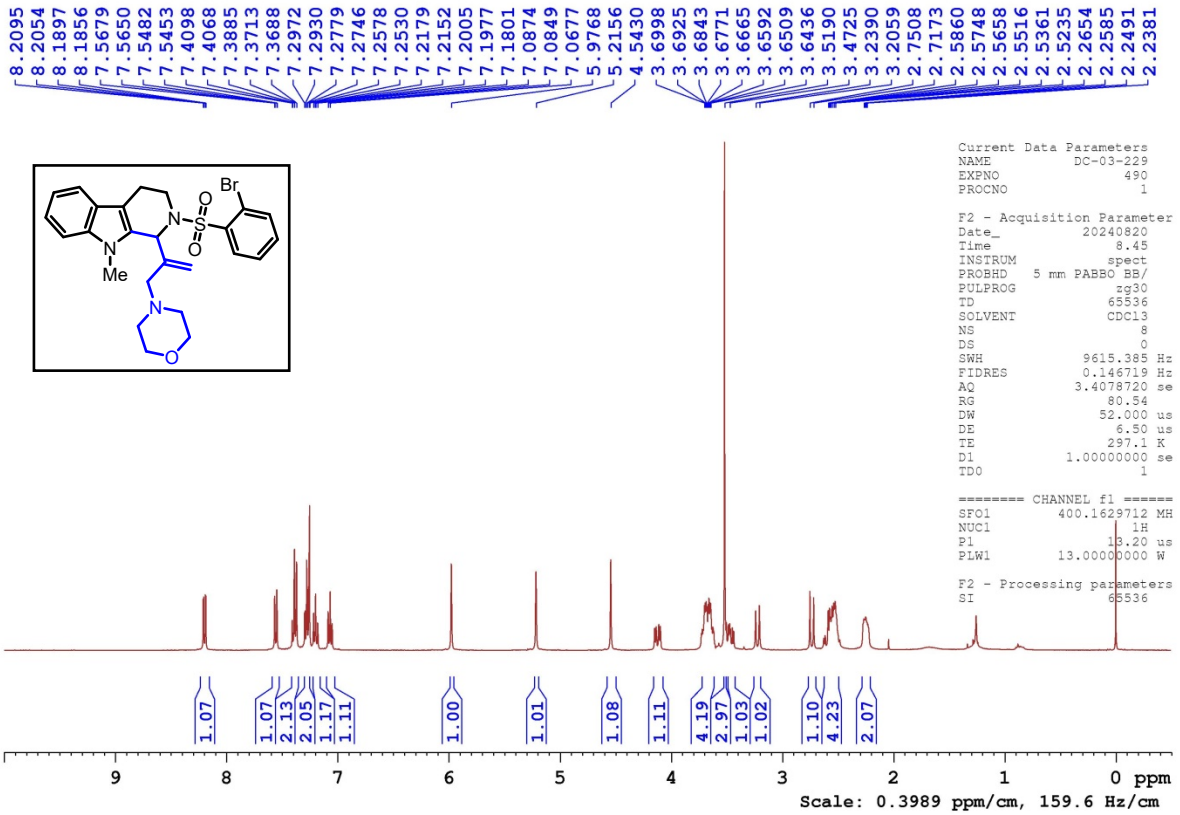

Figure S-21: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ja**

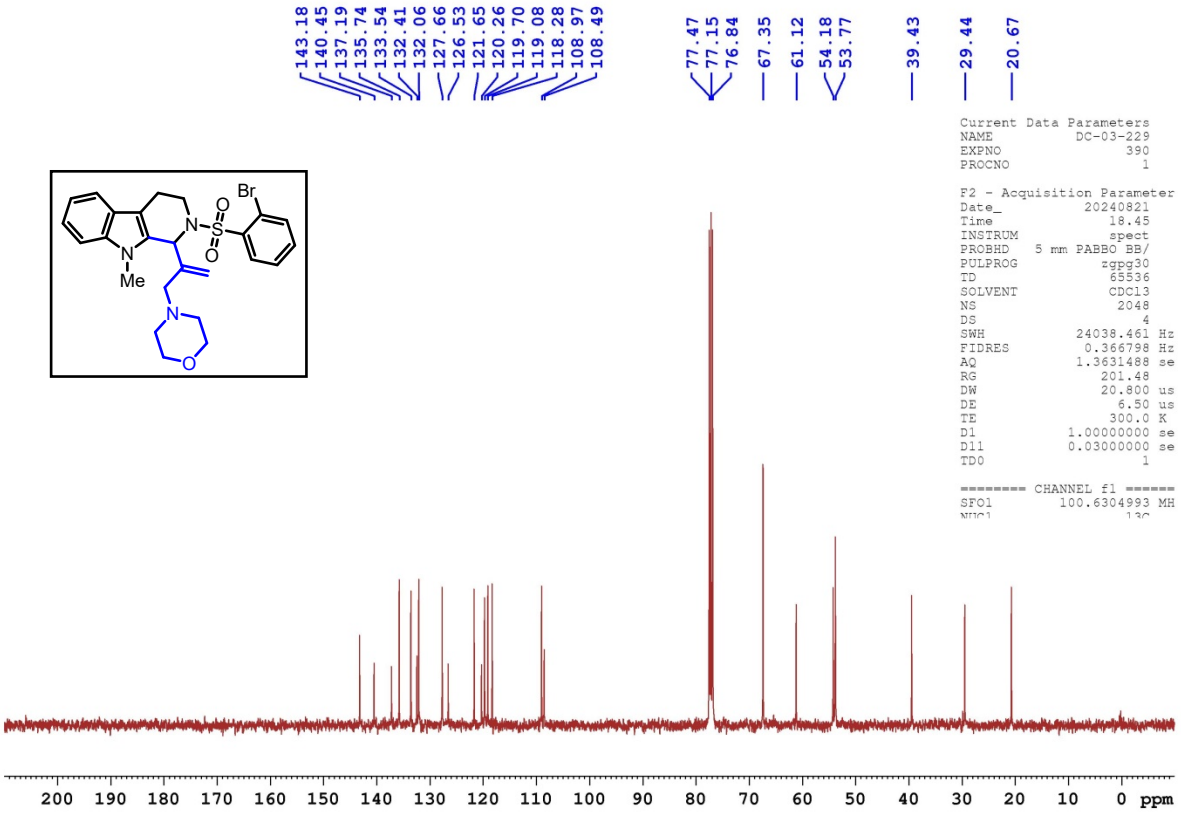

Figure S-22: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ja**

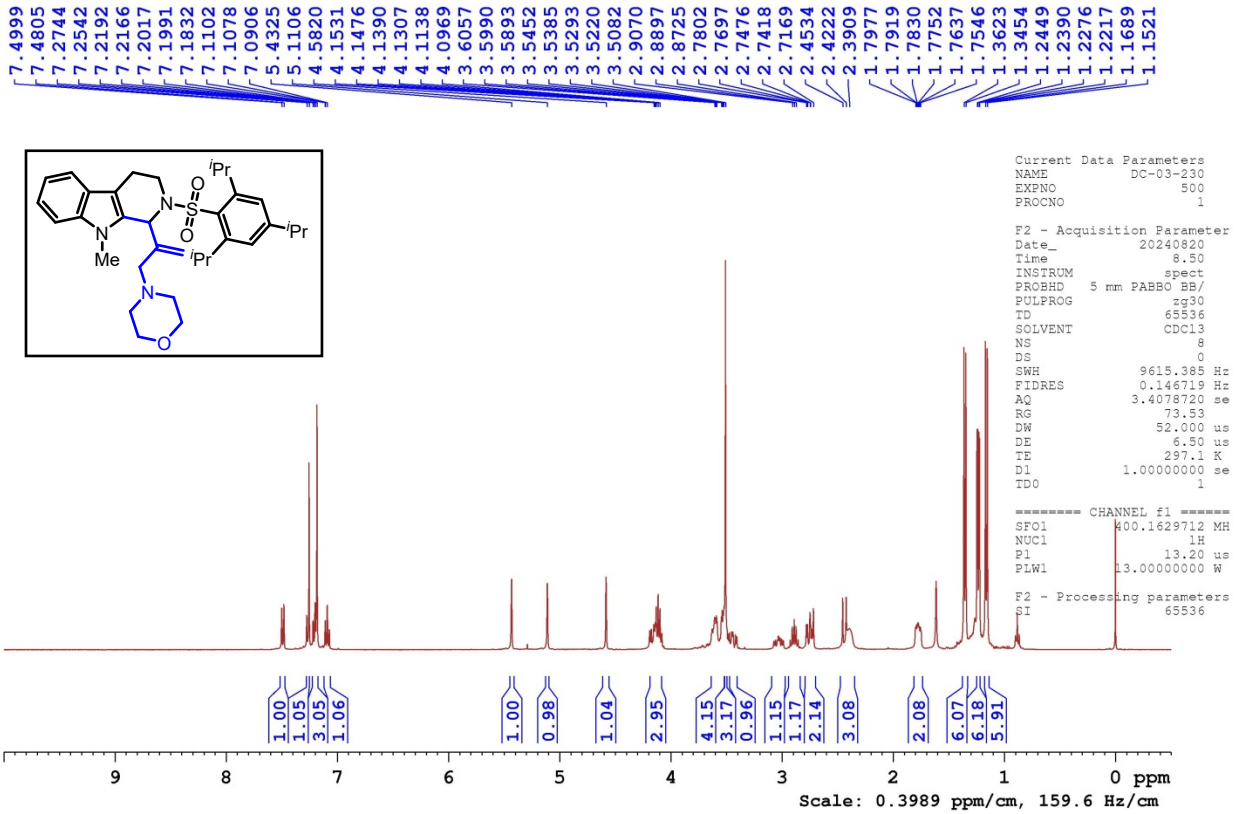

Figure S-23: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ka**

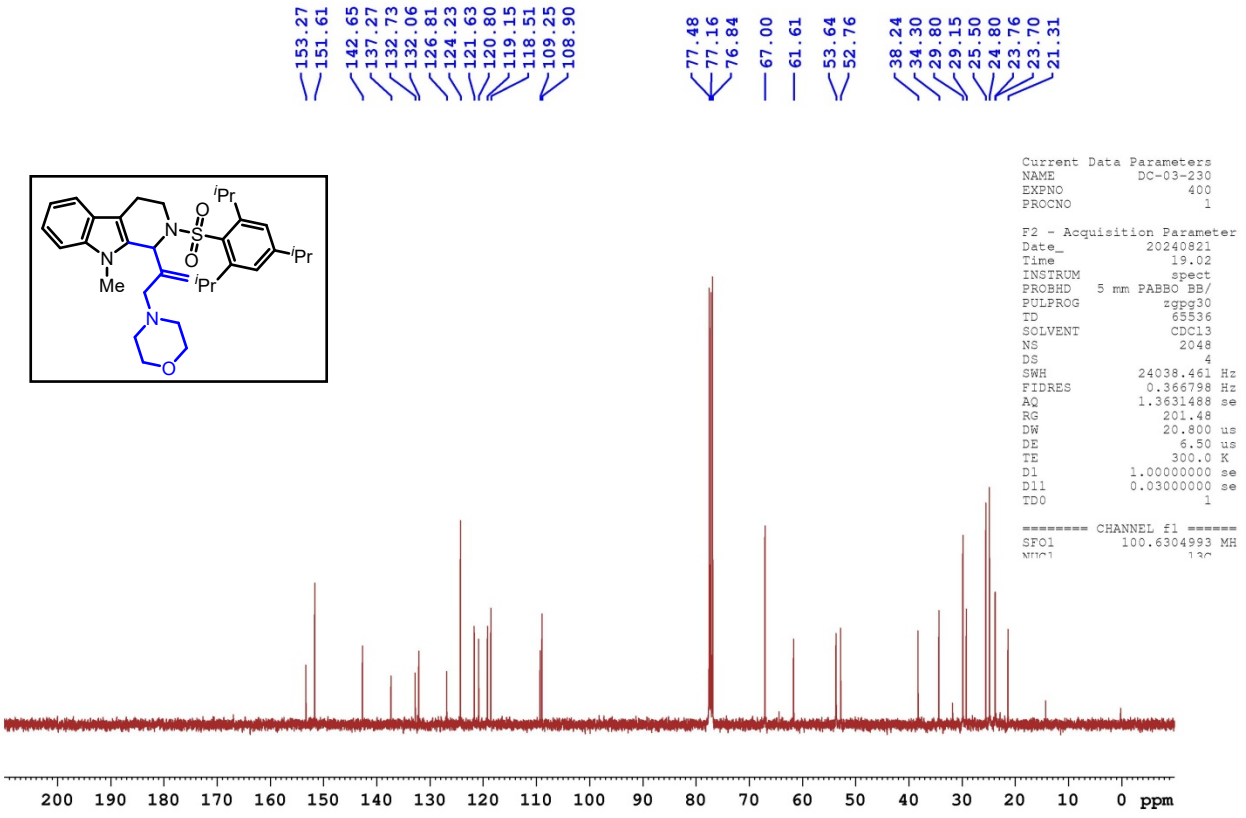

Figure S-24: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ka**

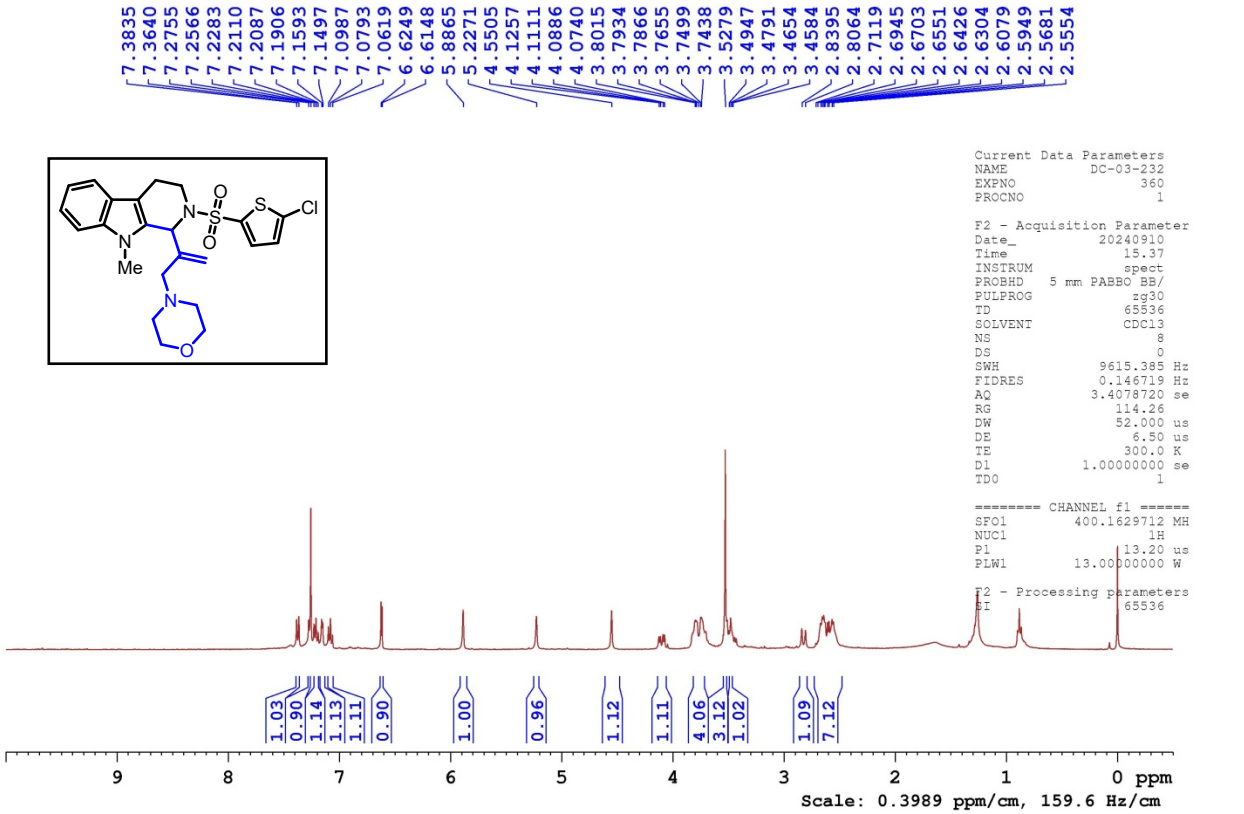

Figure S-25: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3la**

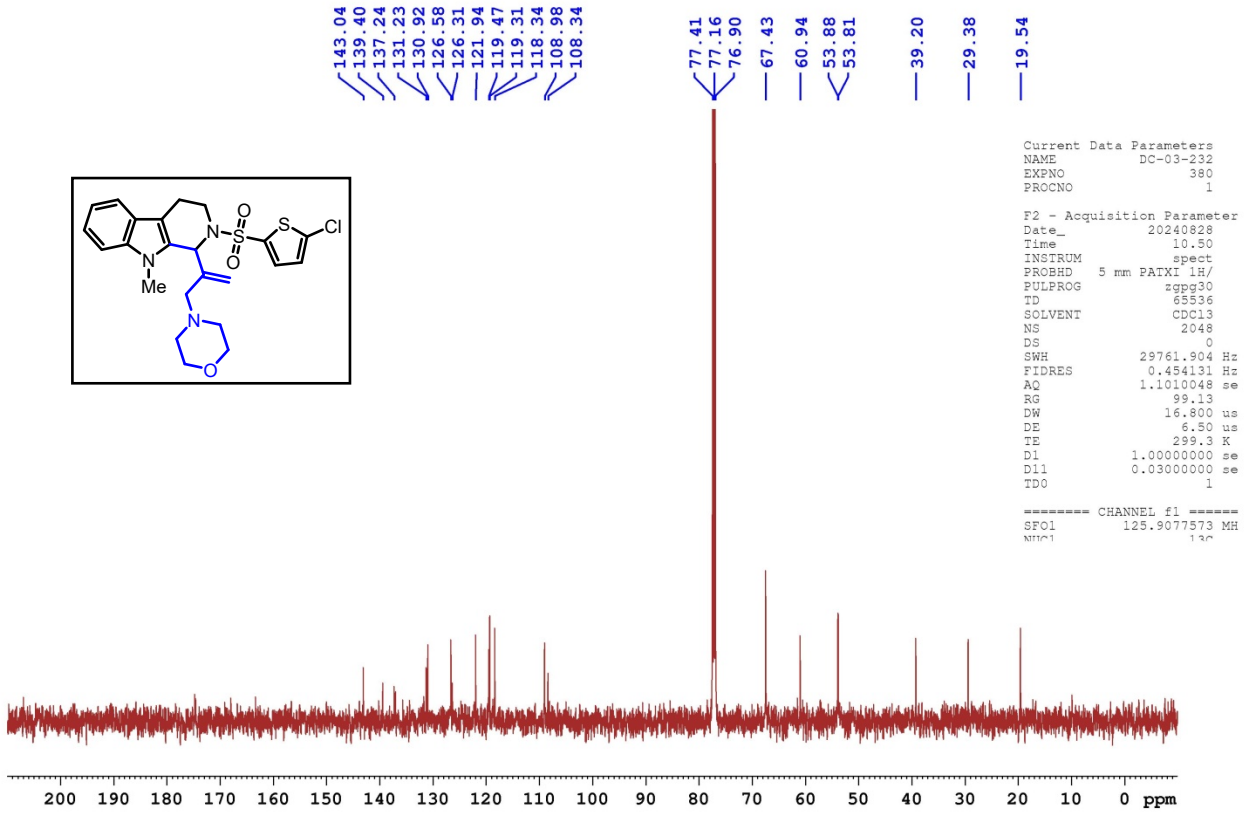

Figure S-26: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3la**

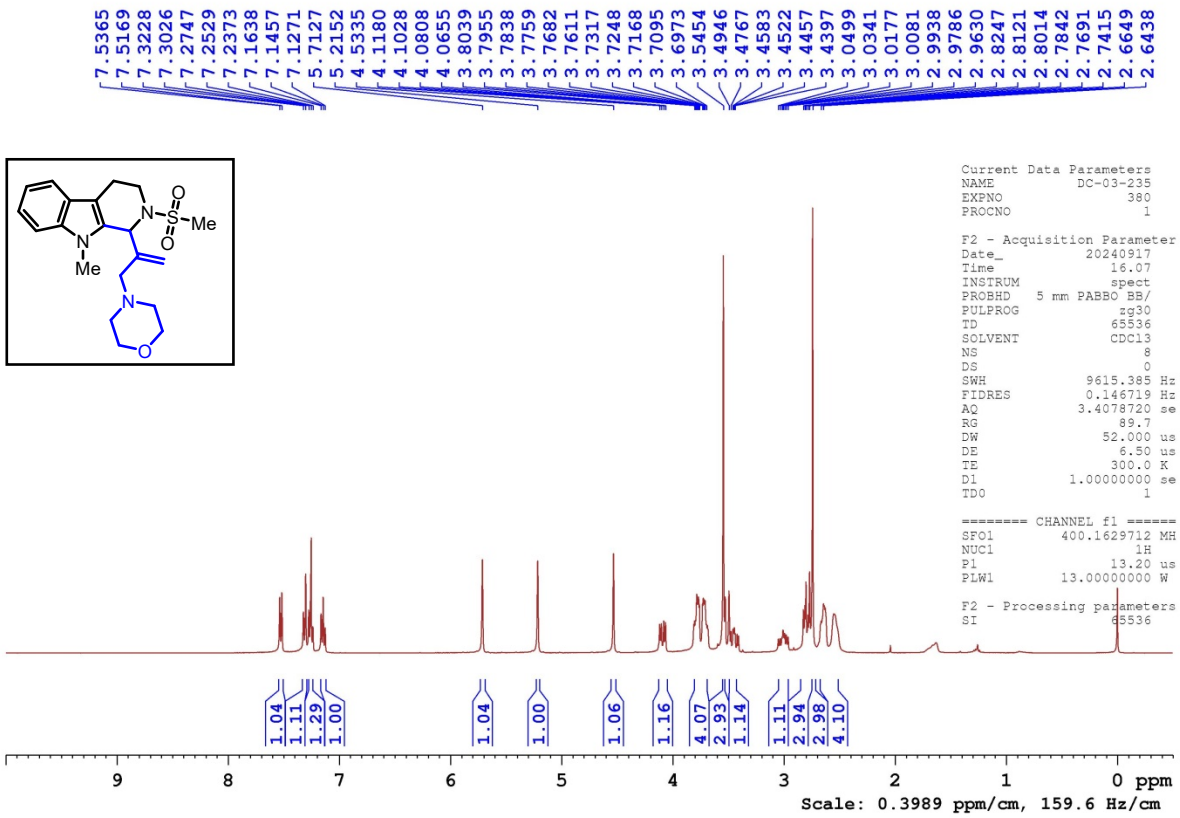

Figure S-27: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ma**

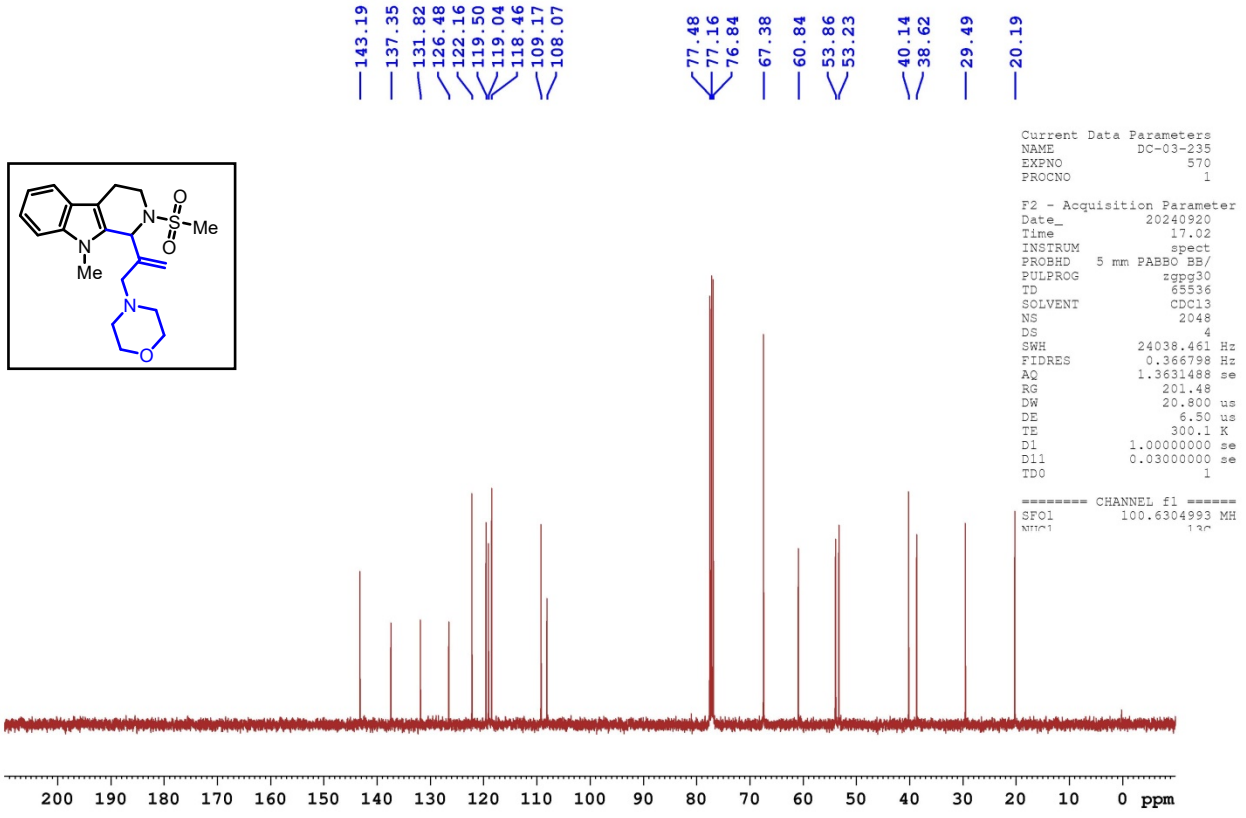

Figure S-28: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ma**

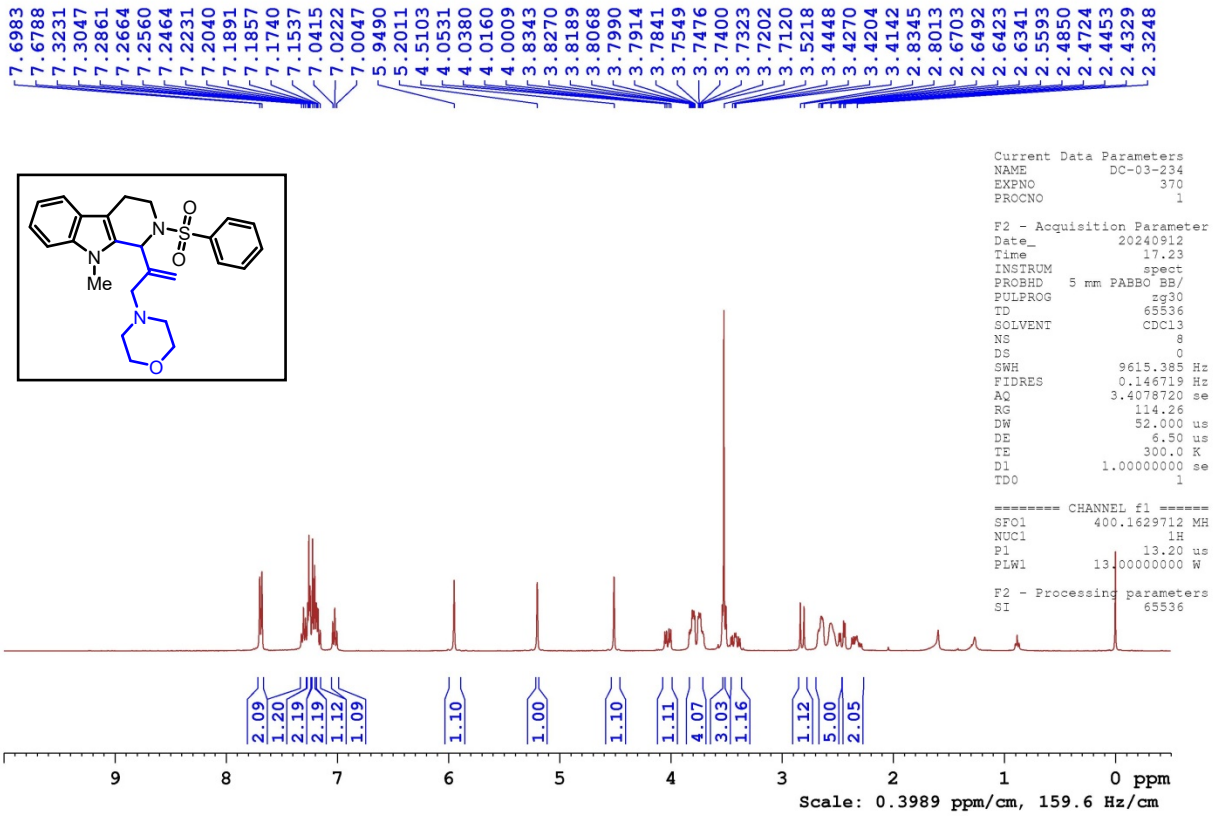

Figure S-29: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3na**

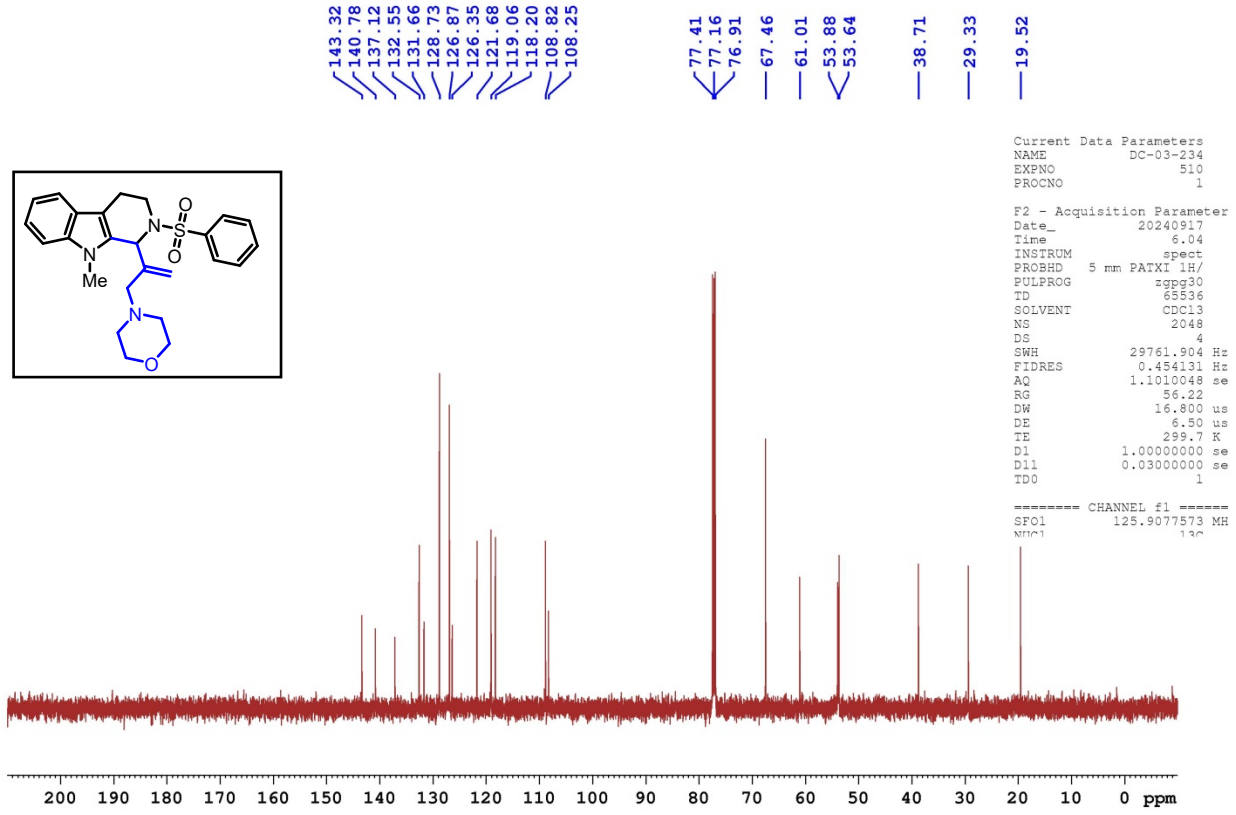

Figure S-30: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3na**

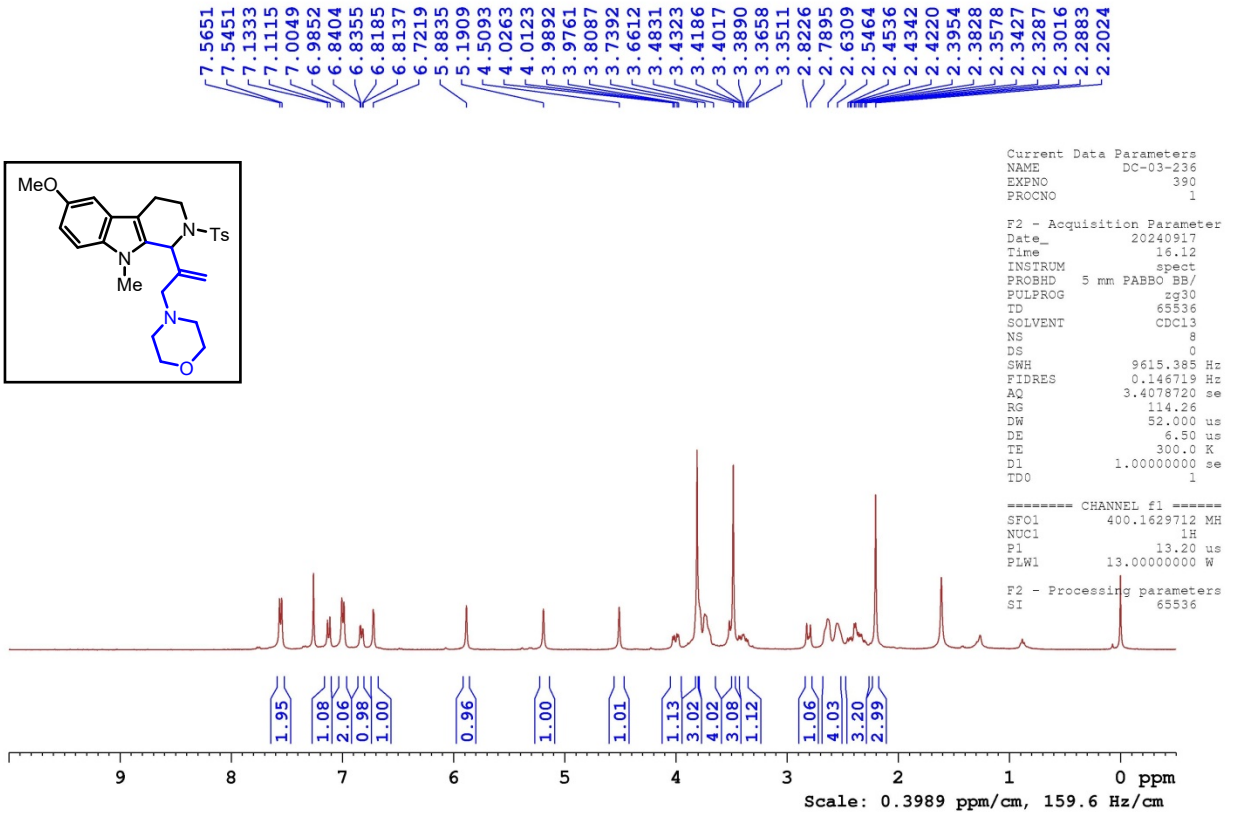

Figure S-31: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3oa**

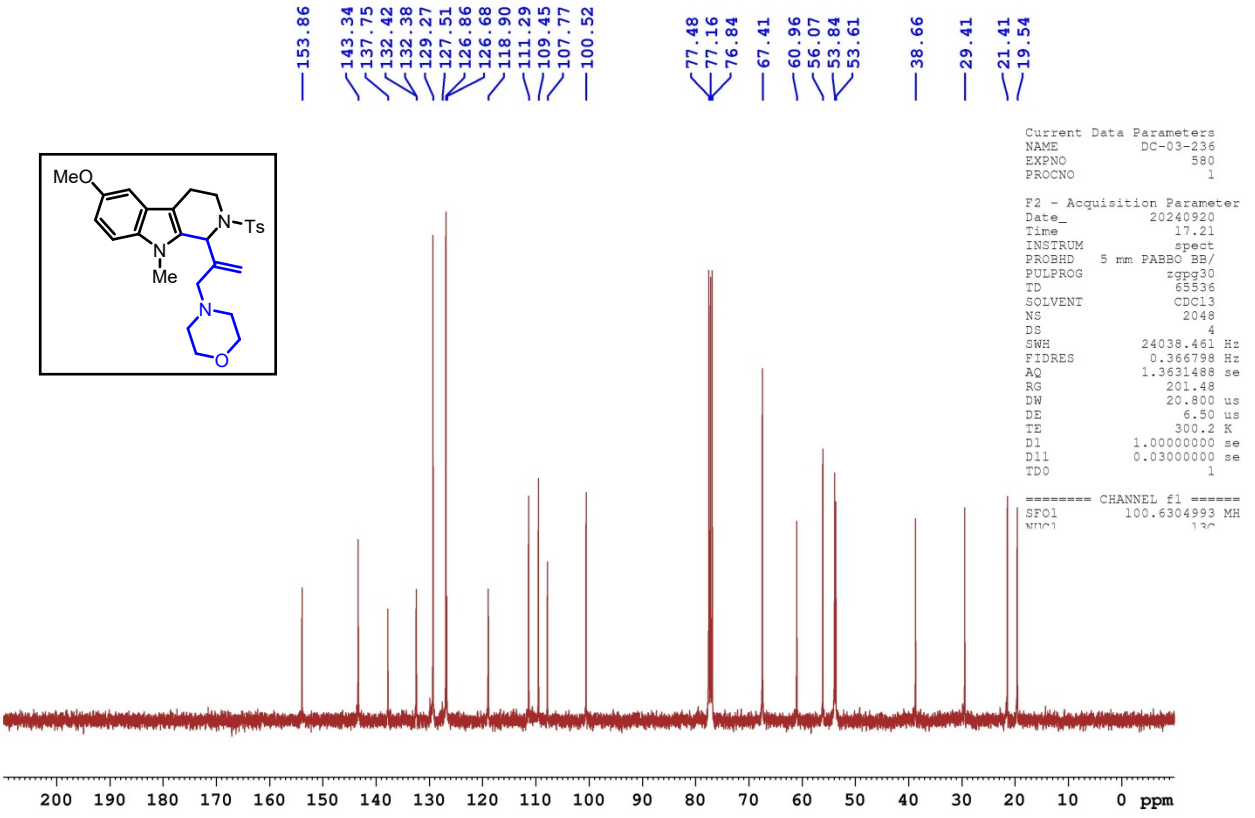

Figure S-32: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3oa**

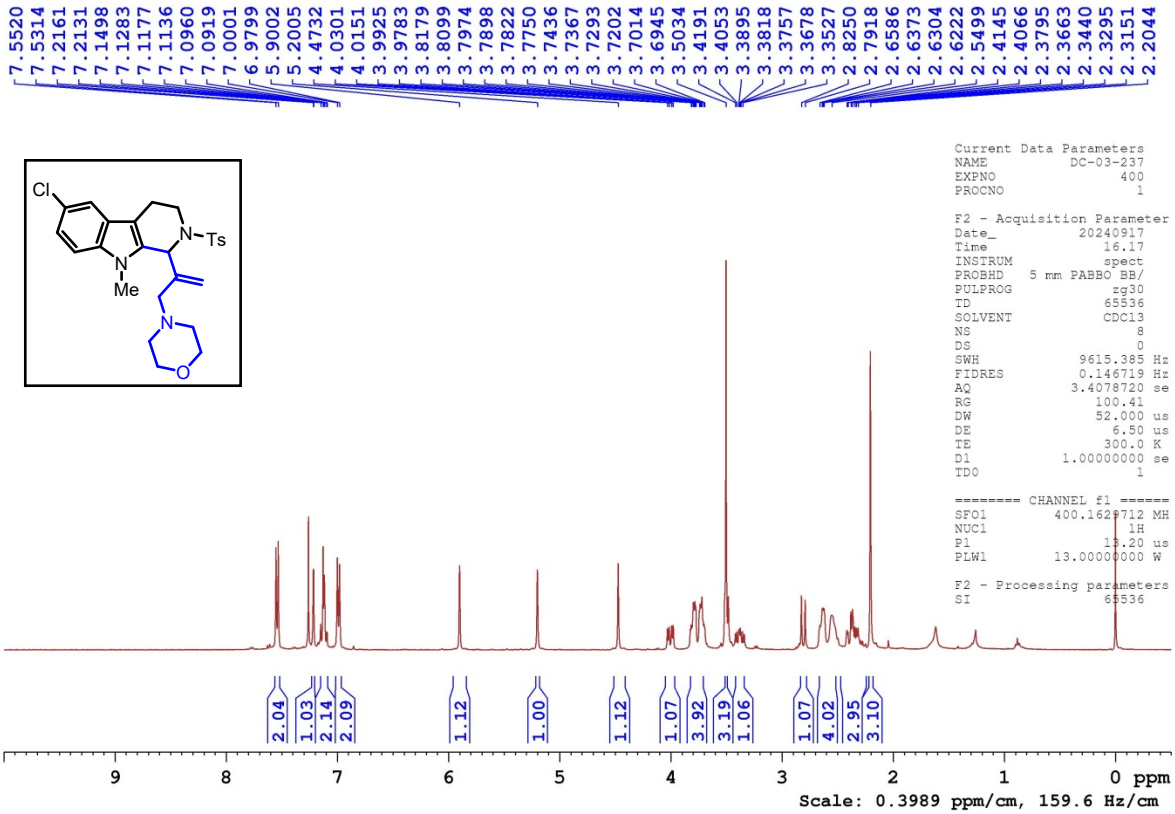

Figure S-33: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3pa**

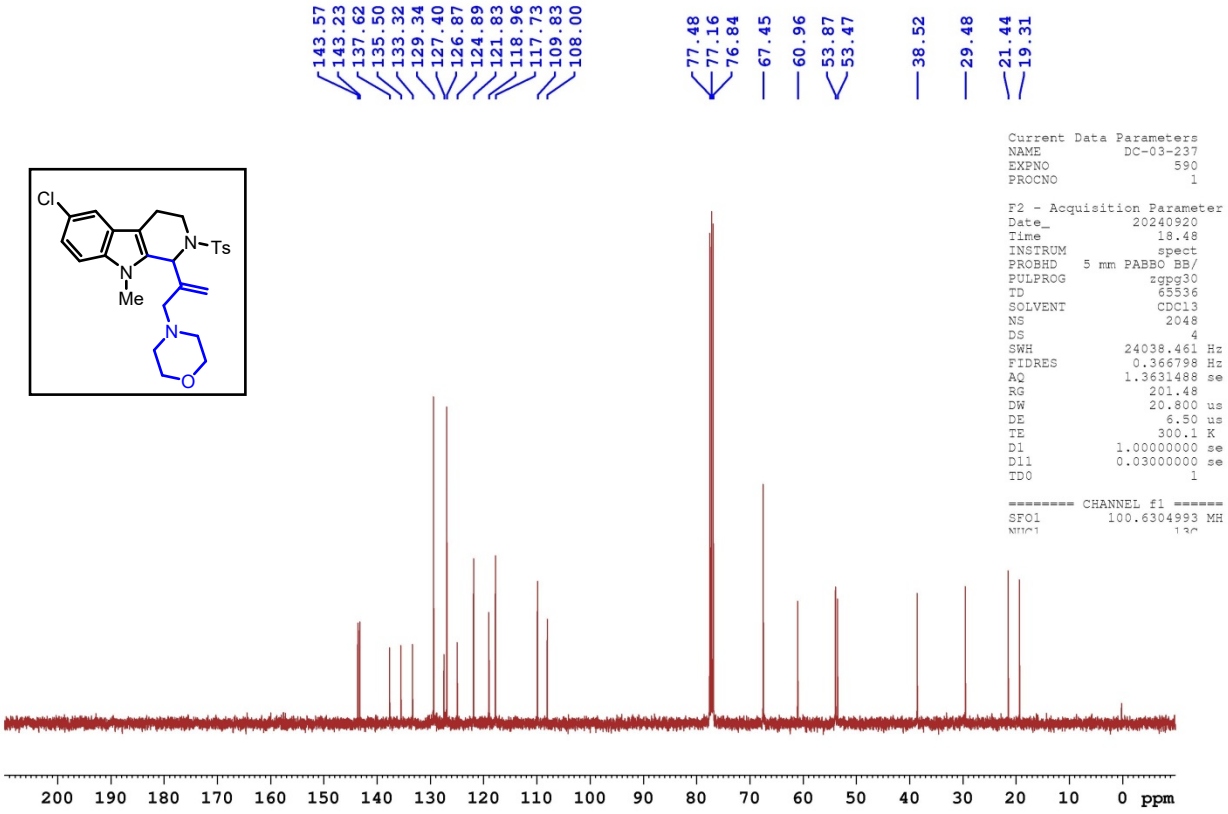

Figure S-34: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3pa**

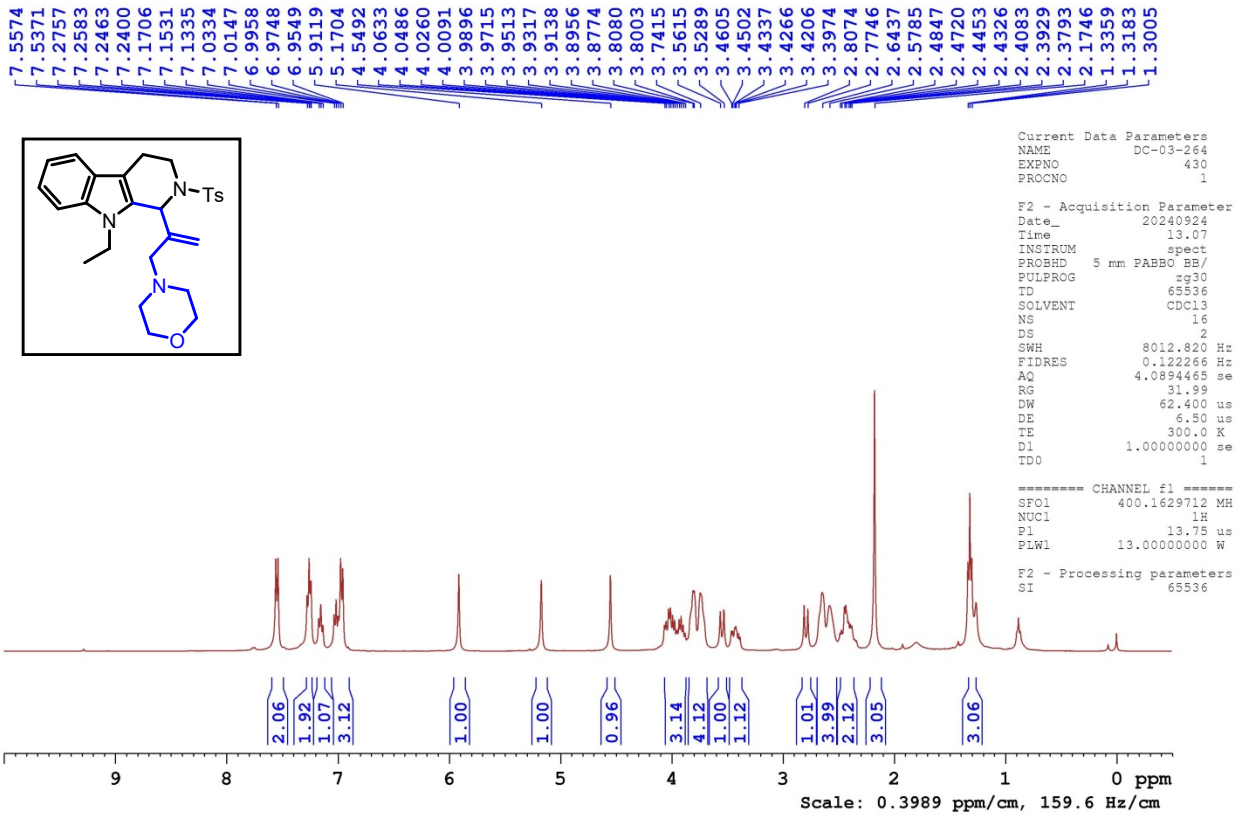

Figure S-35: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3qa**

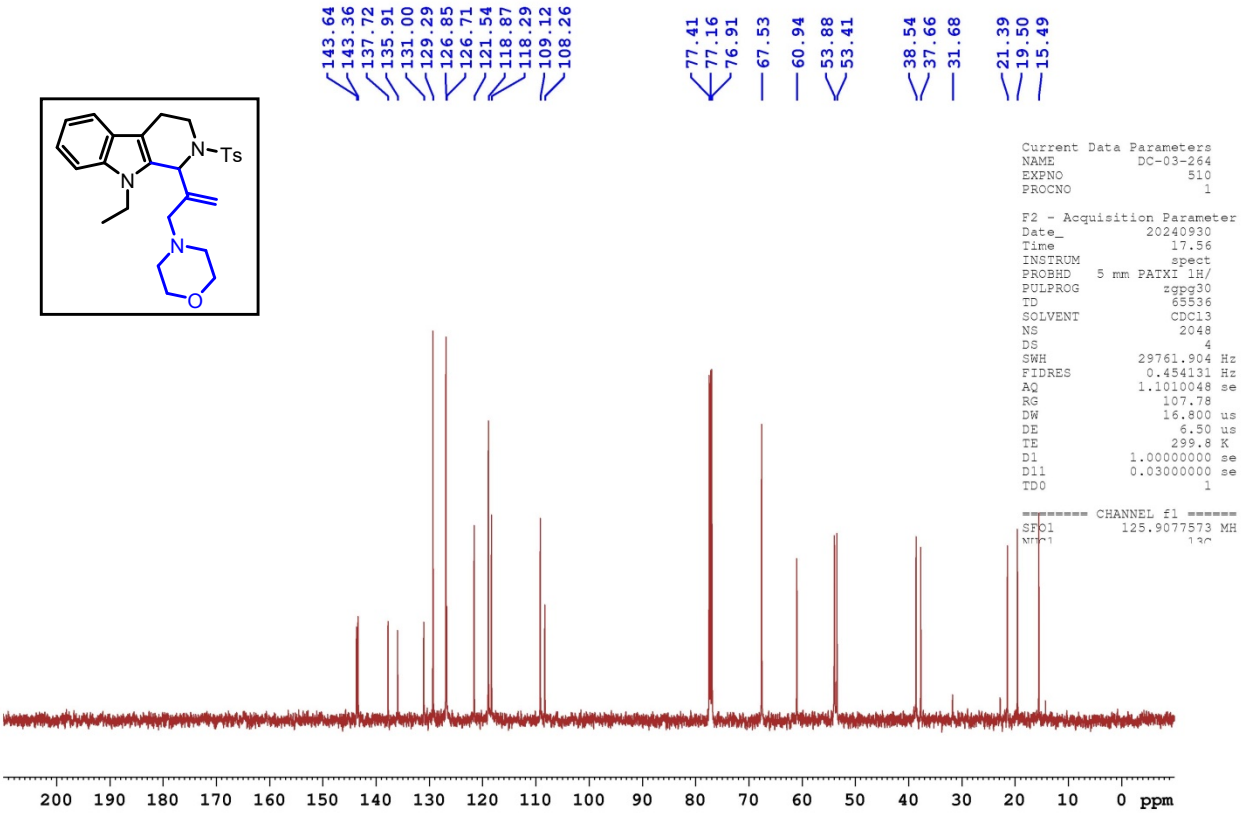

Figure S-36: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3qa**

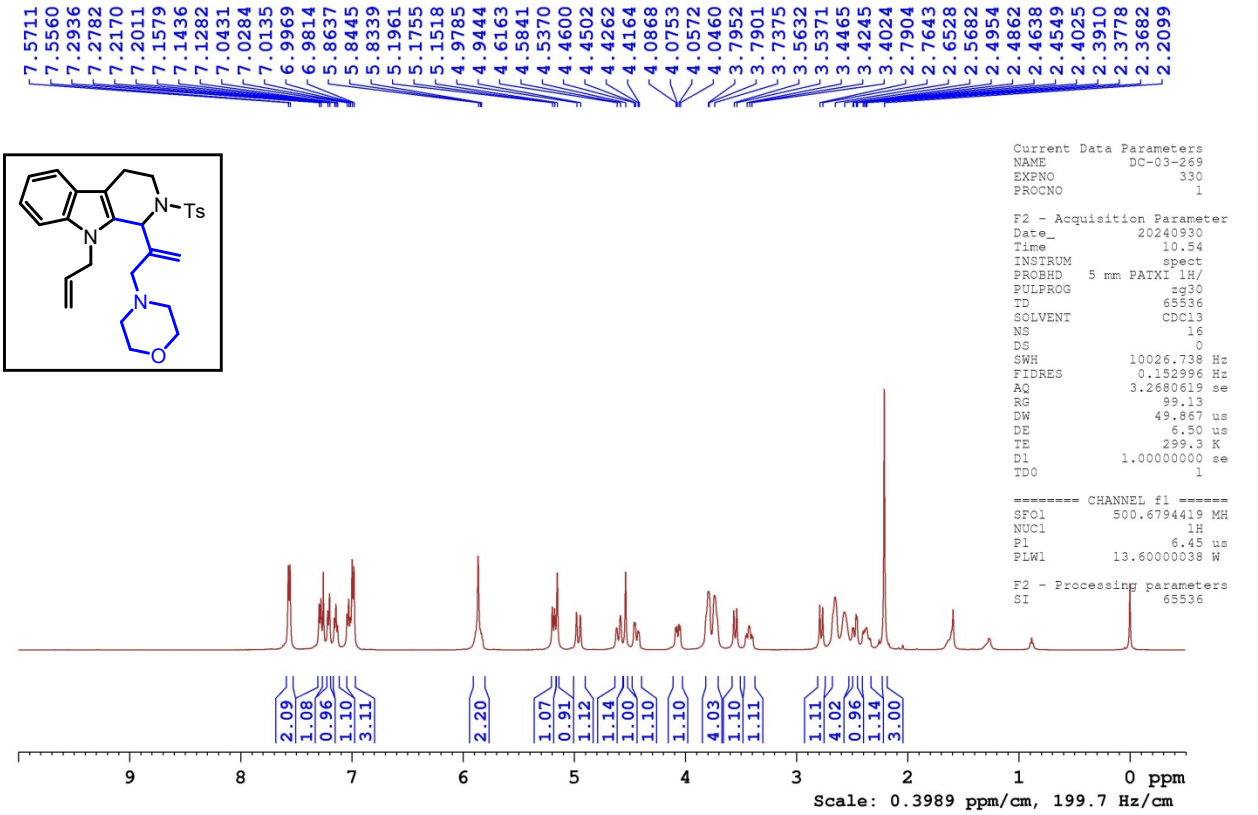

Figure S-37: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound **3ra**

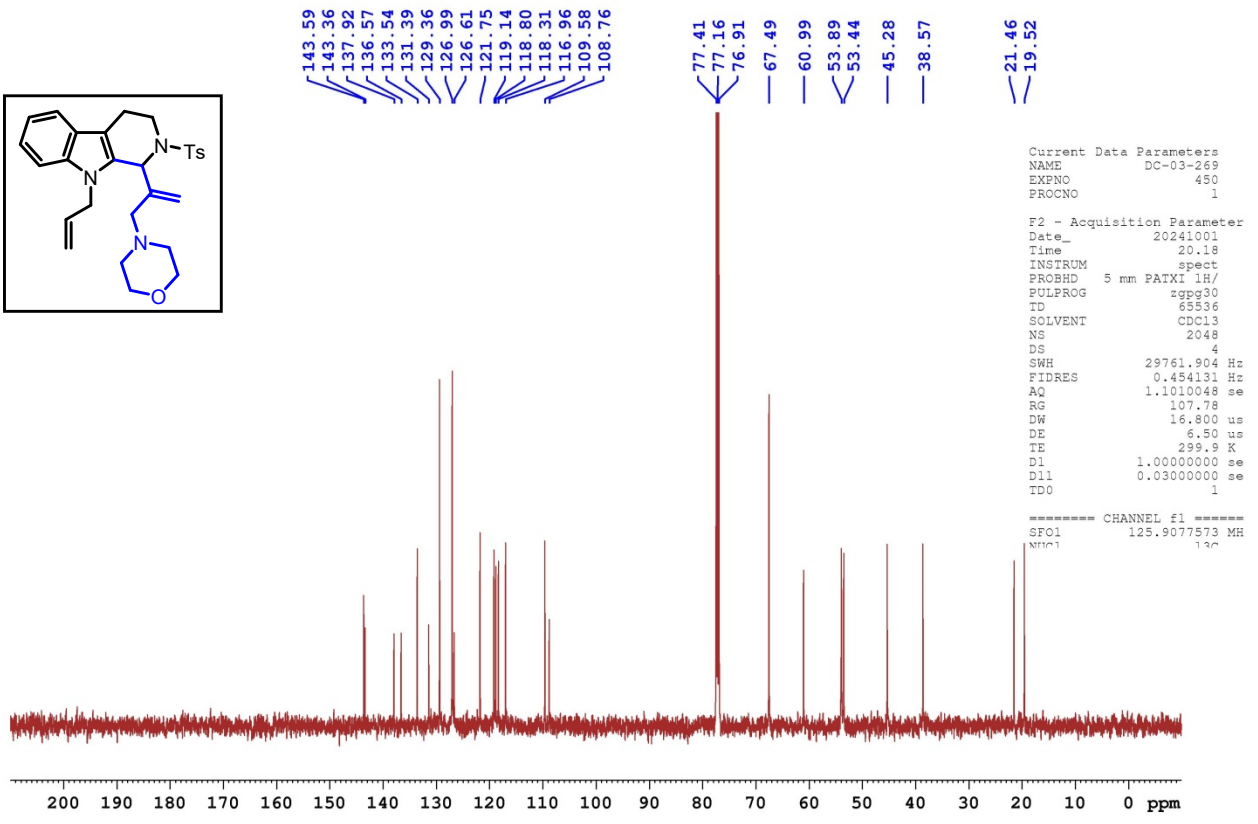

Figure S-38: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ra**

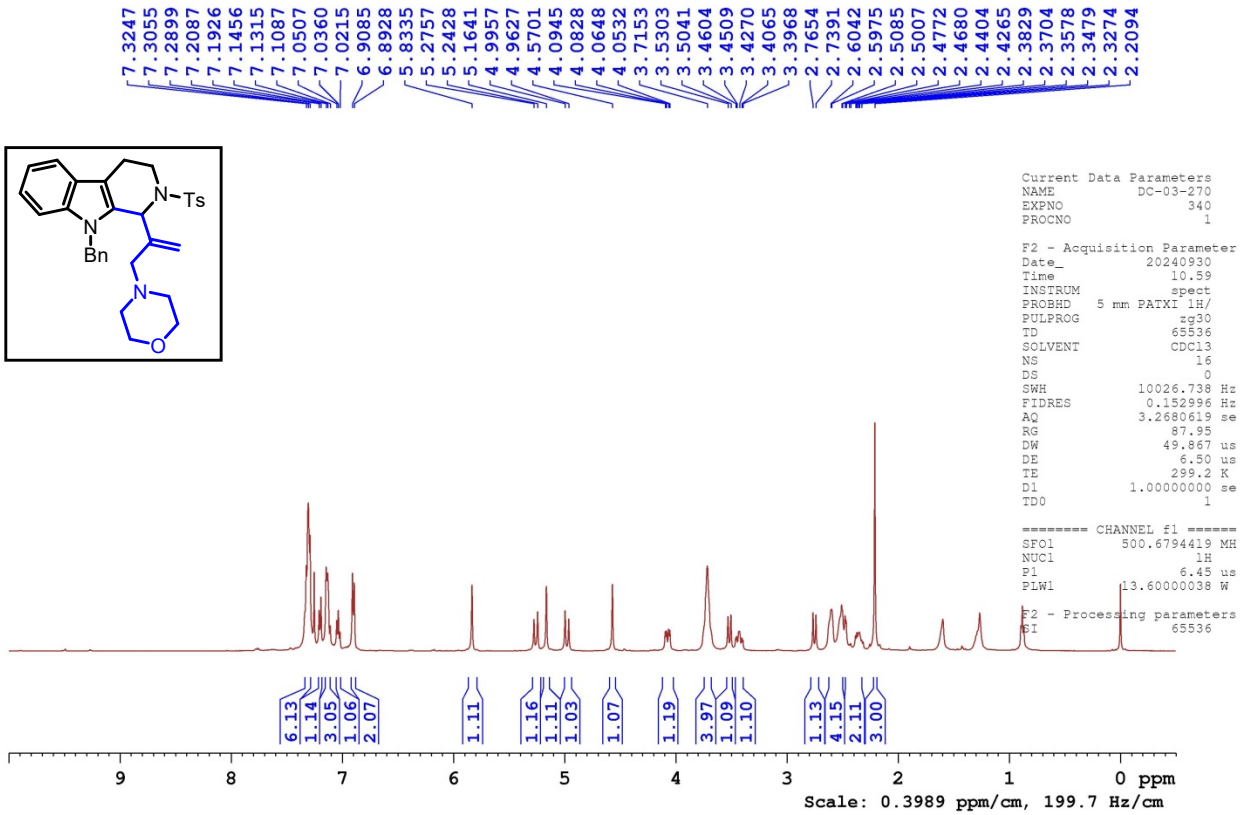

Figure S-39: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound **3sa**

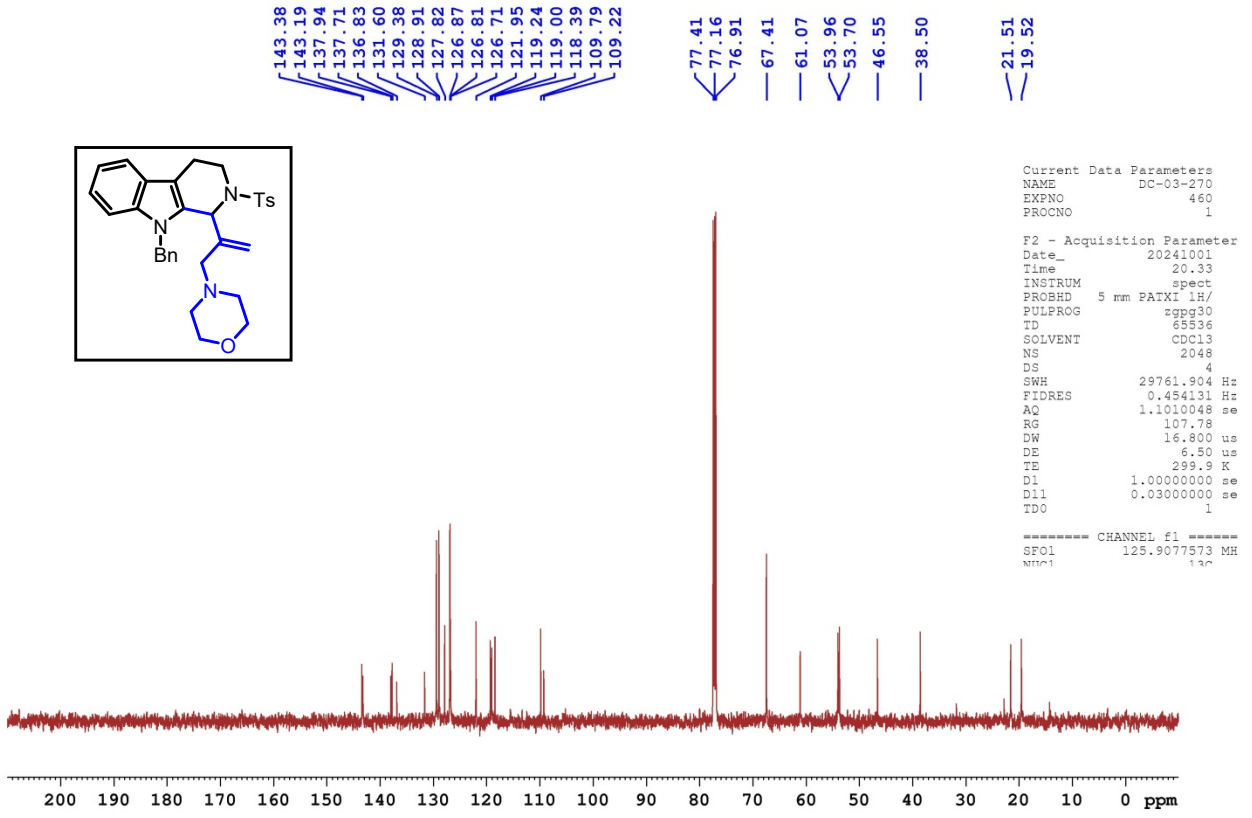

Figure S-40: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3sa**

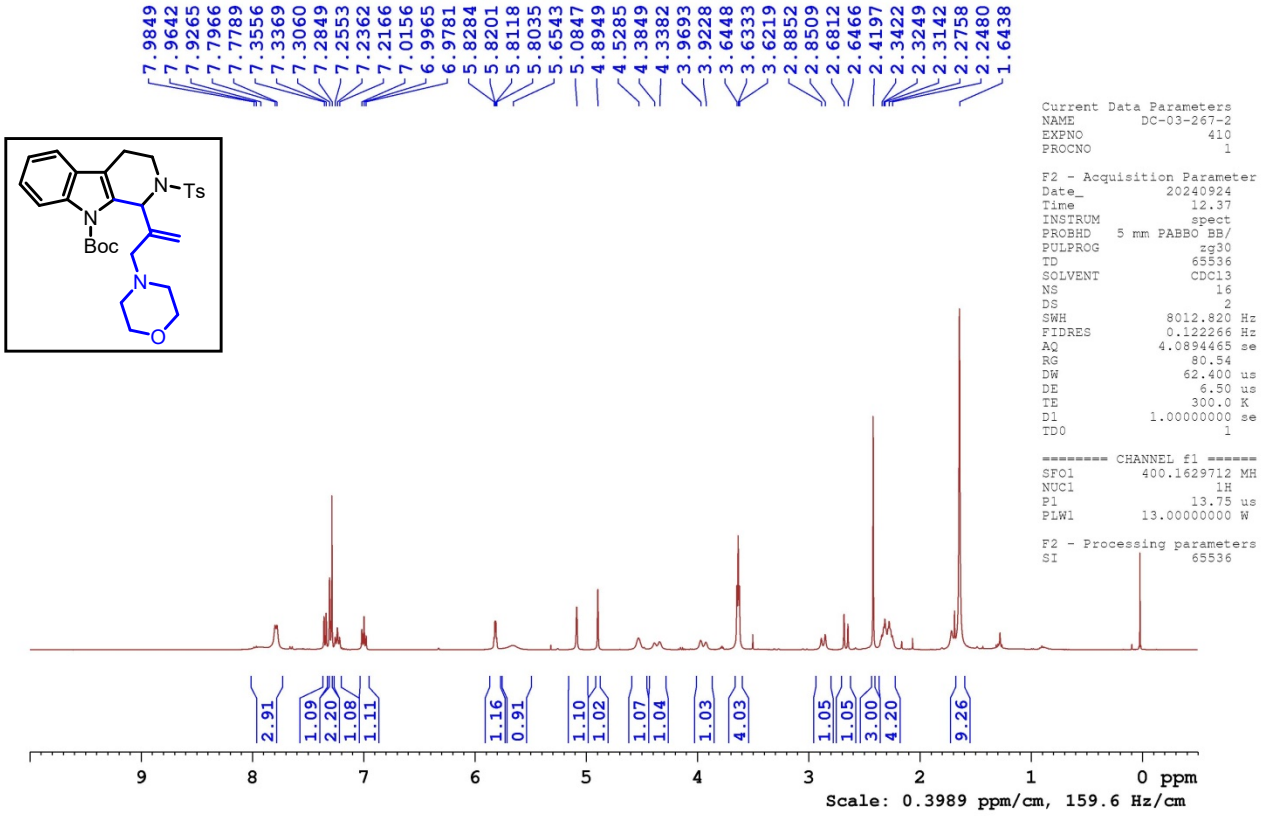

Figure S-41: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ta**

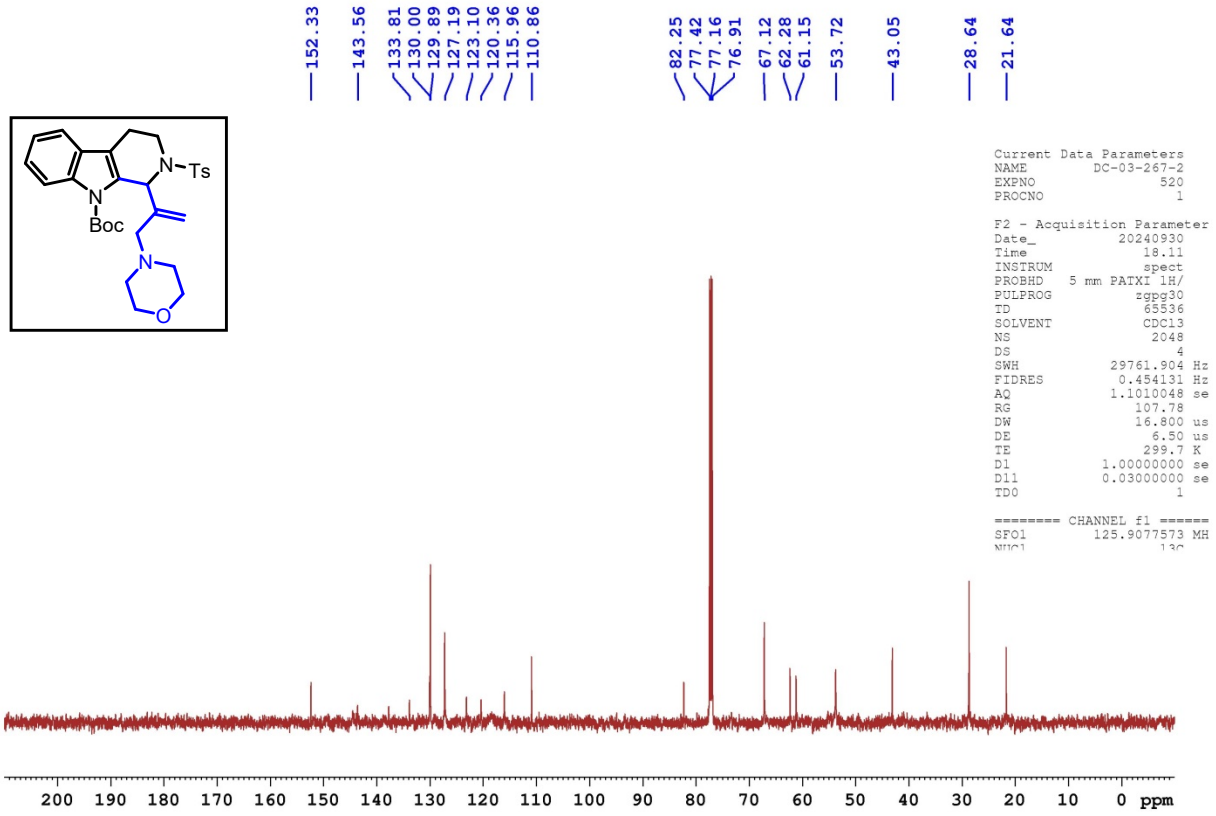

Figure S-42: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3ta**

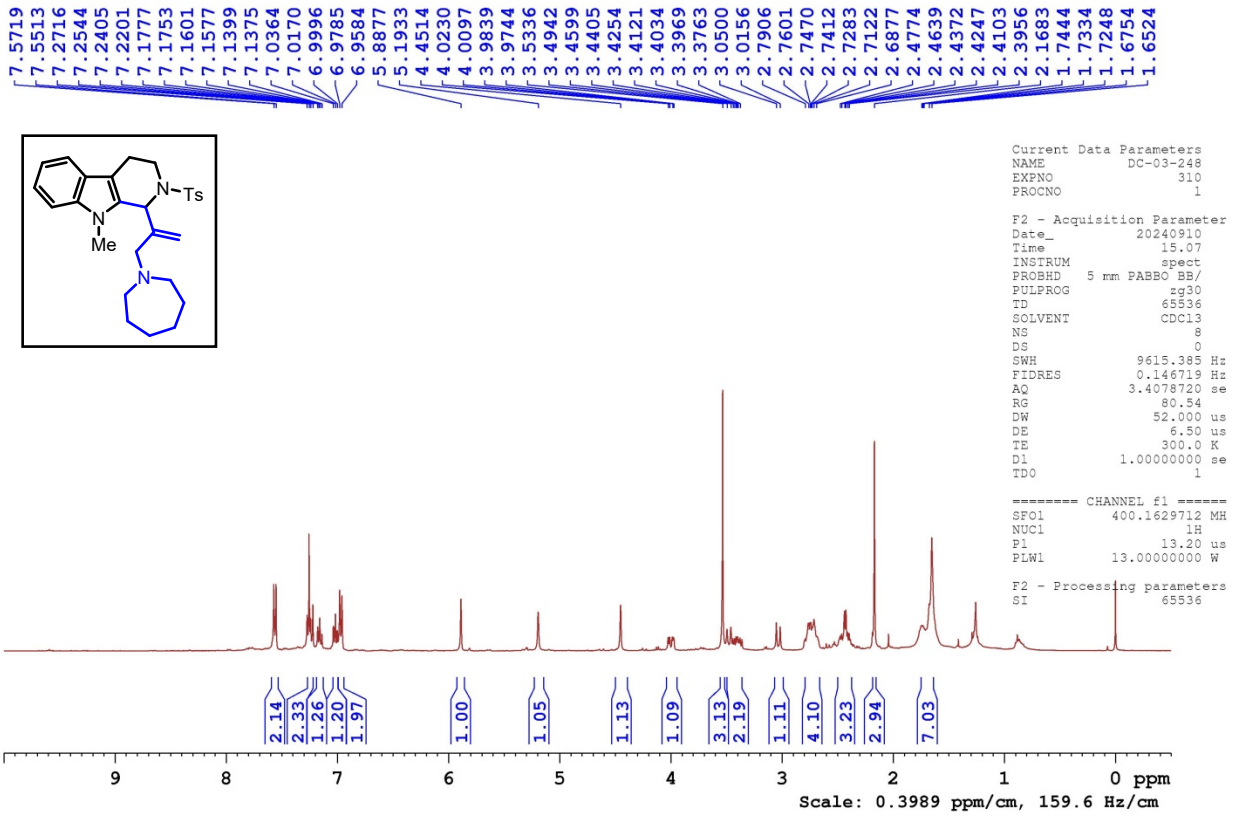

Figure S-43: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ab**

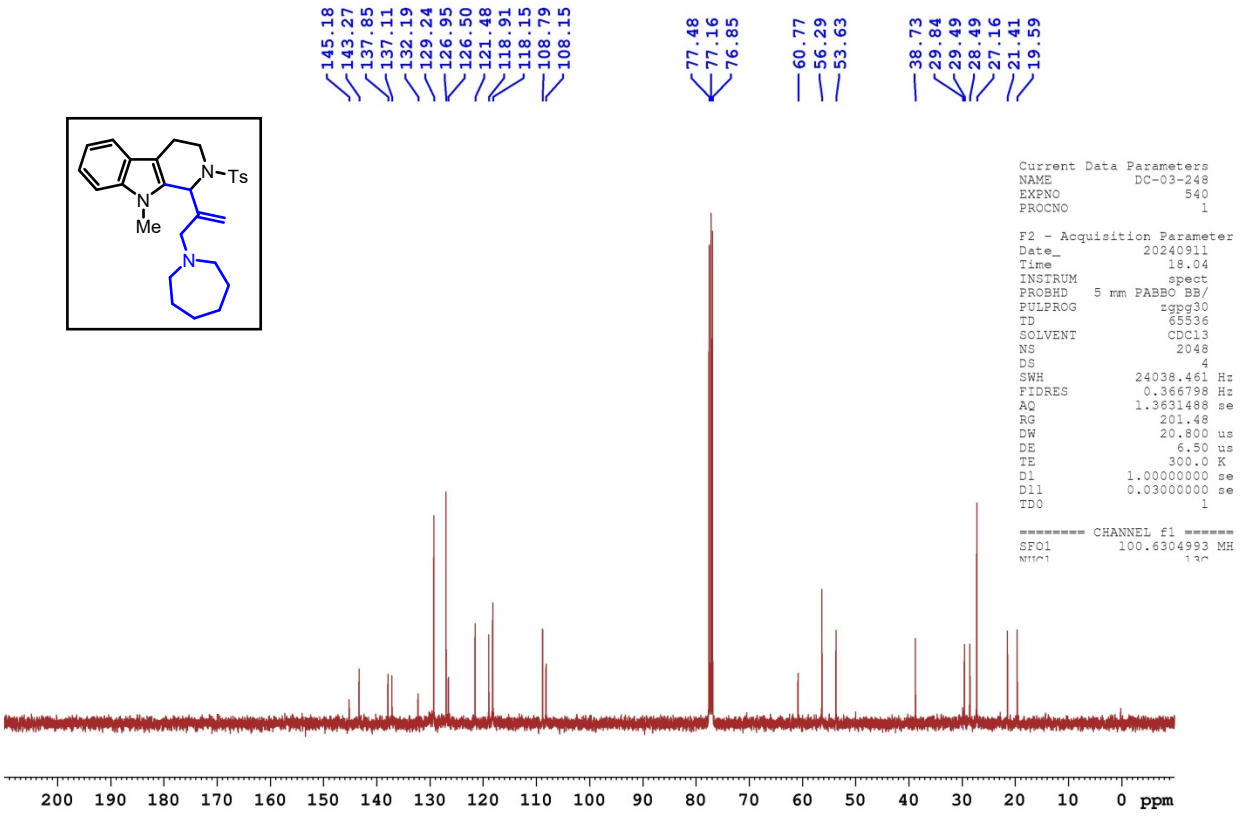

Figure S-44: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ab**

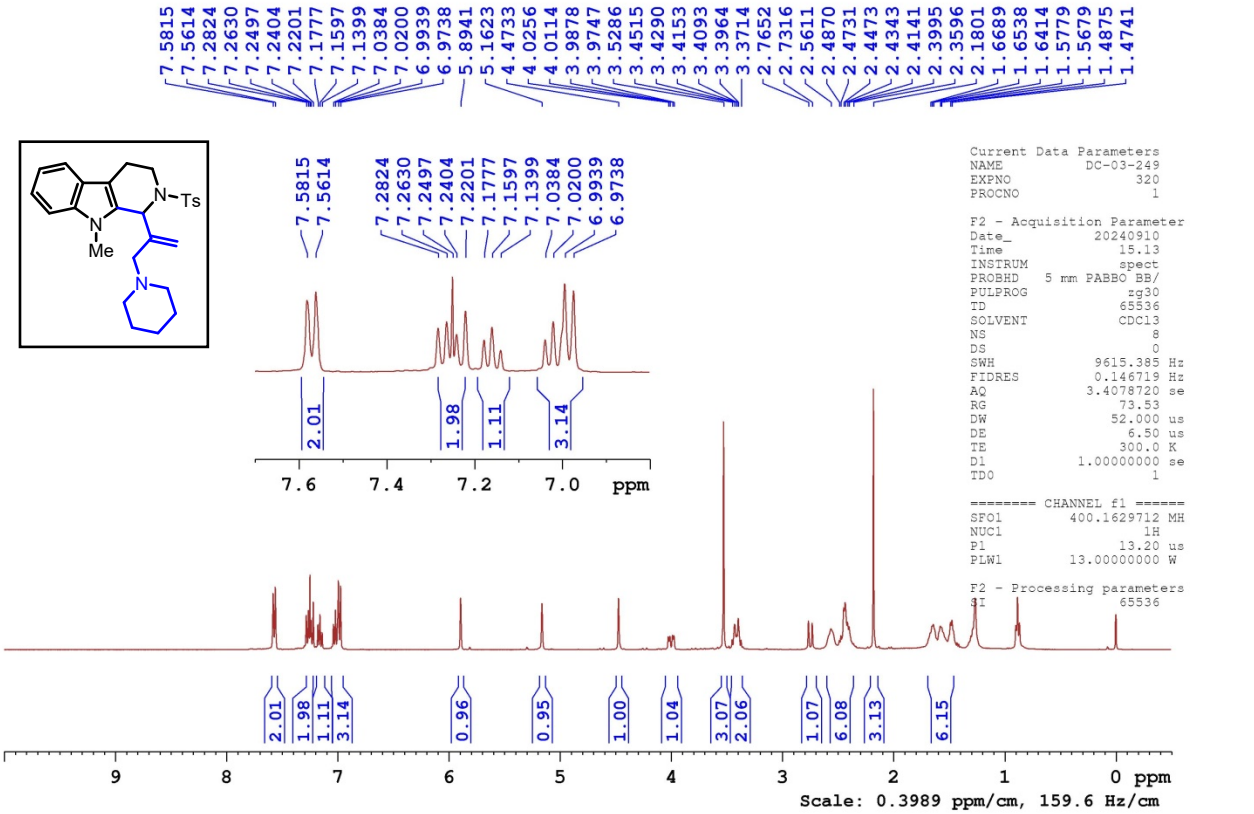

Figure S-45: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ac**

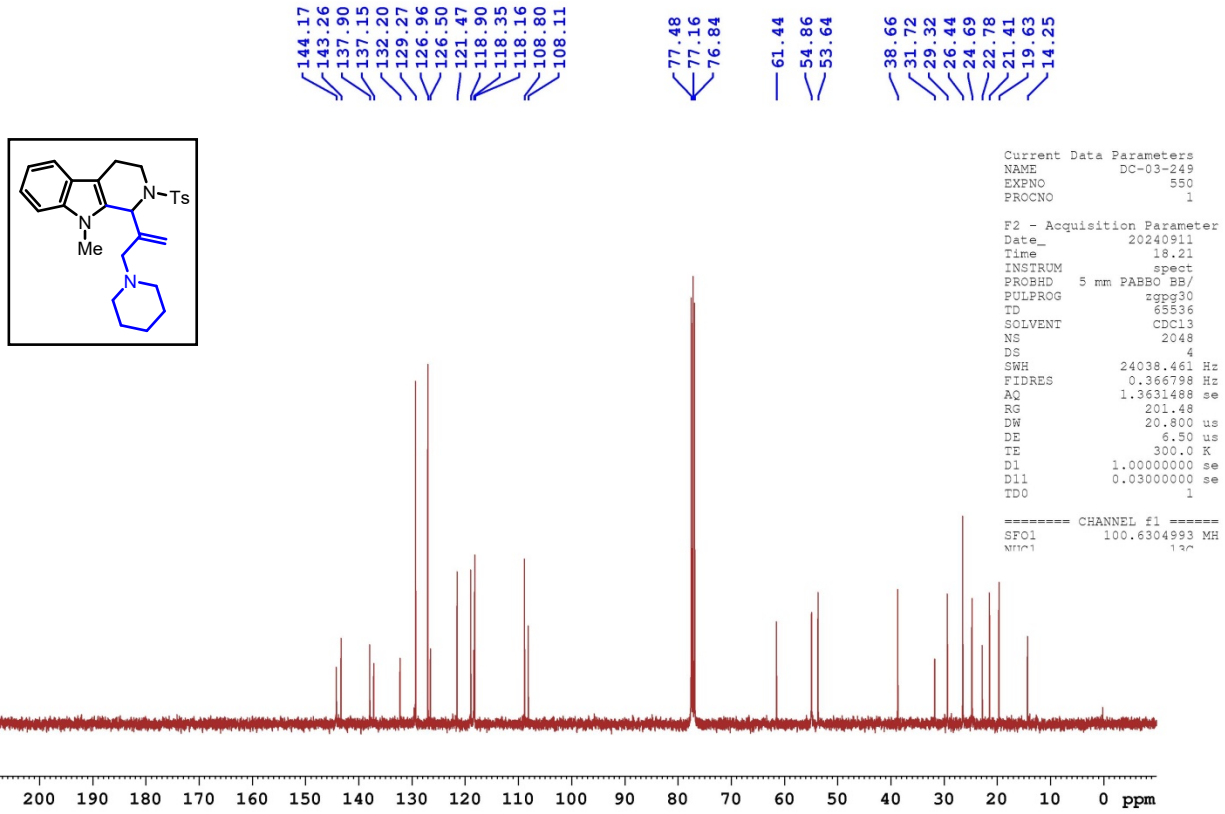

Figure S-46: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ac**

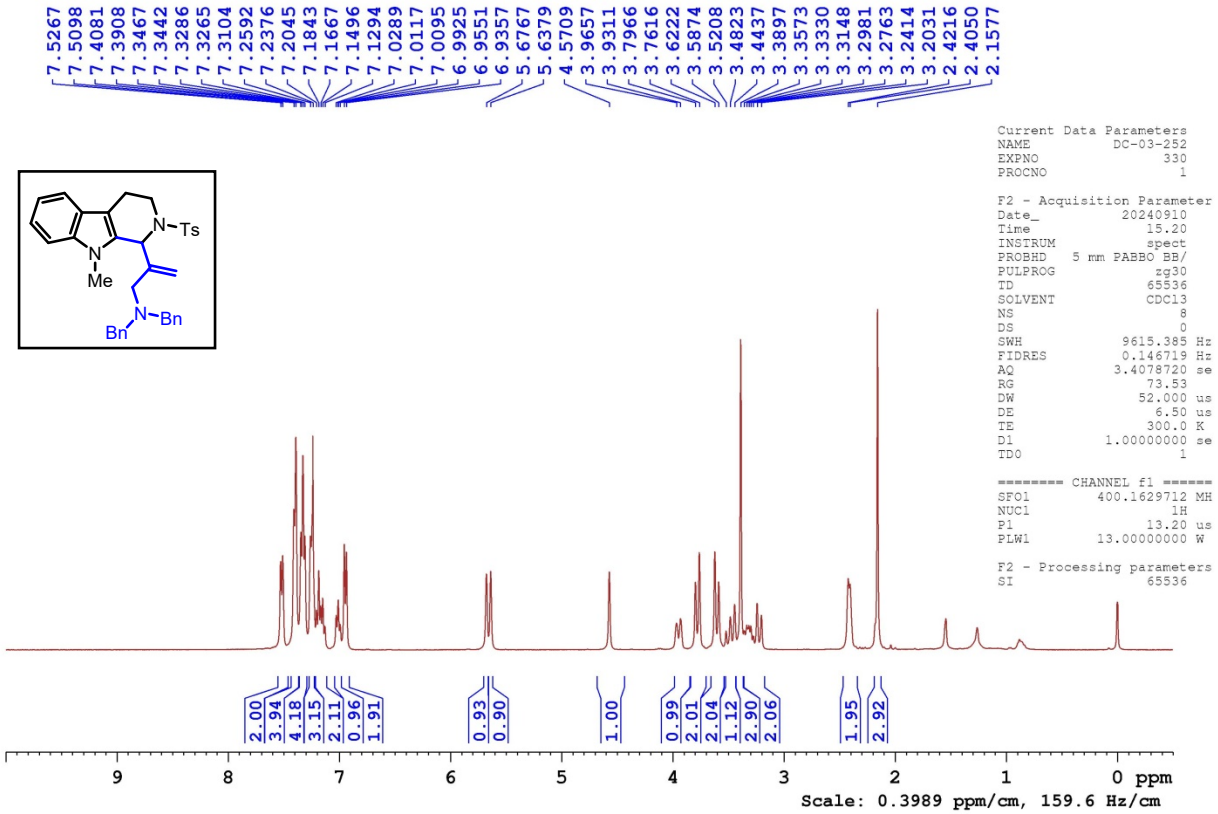

Figure S-47: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3af**

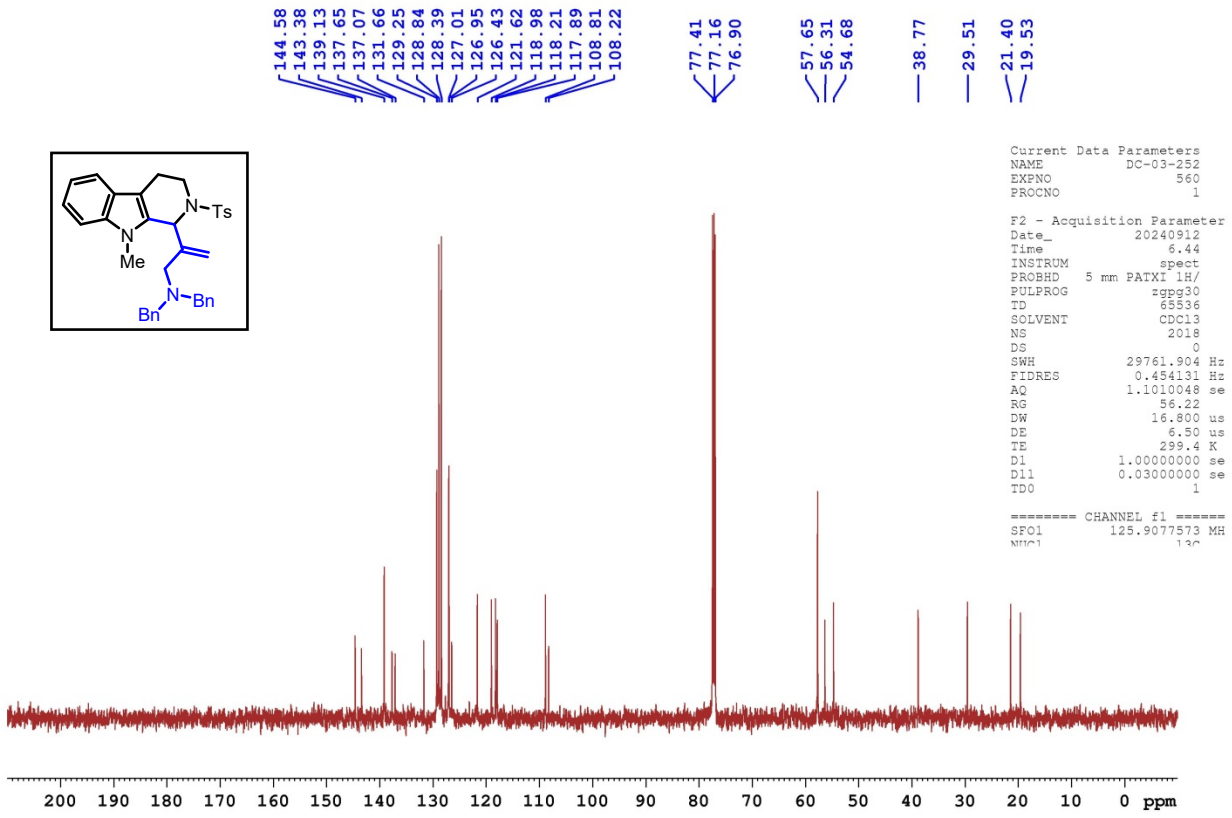

Figure S-48: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3af**

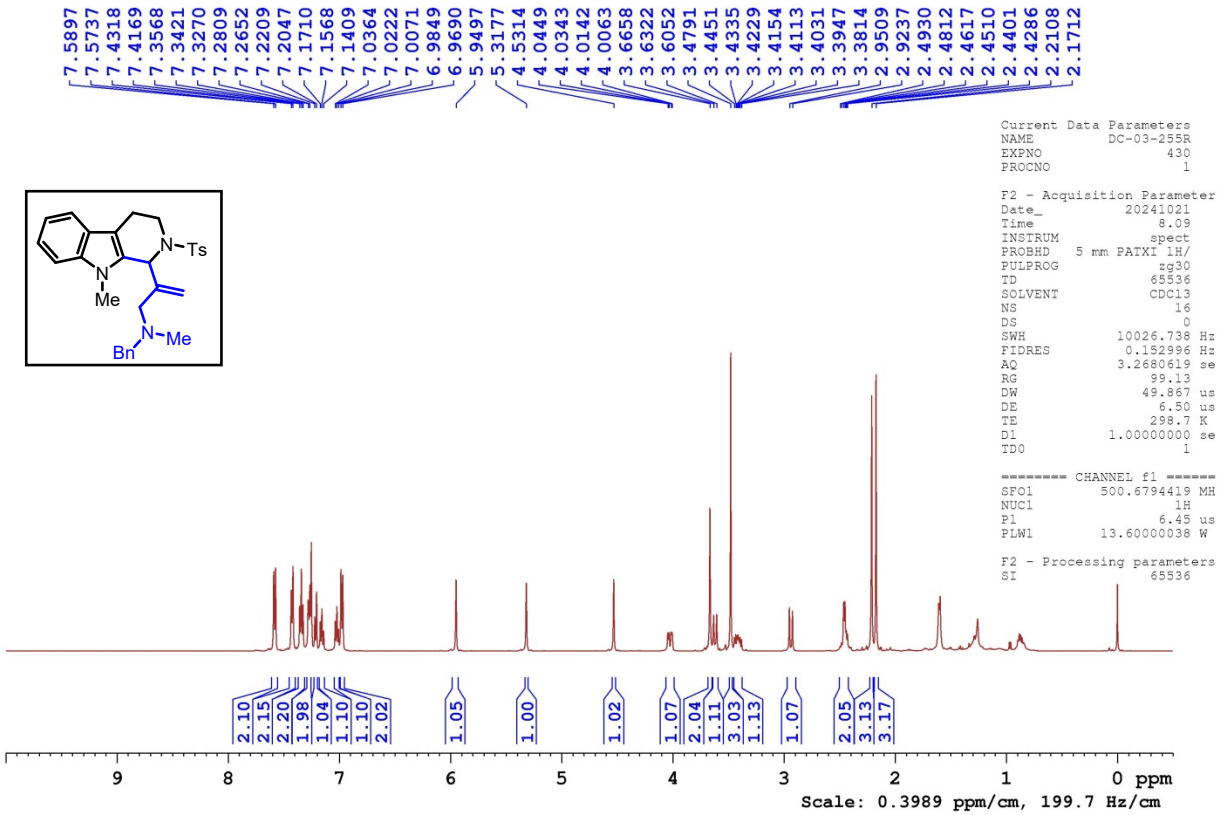

Figure S-49: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ag**

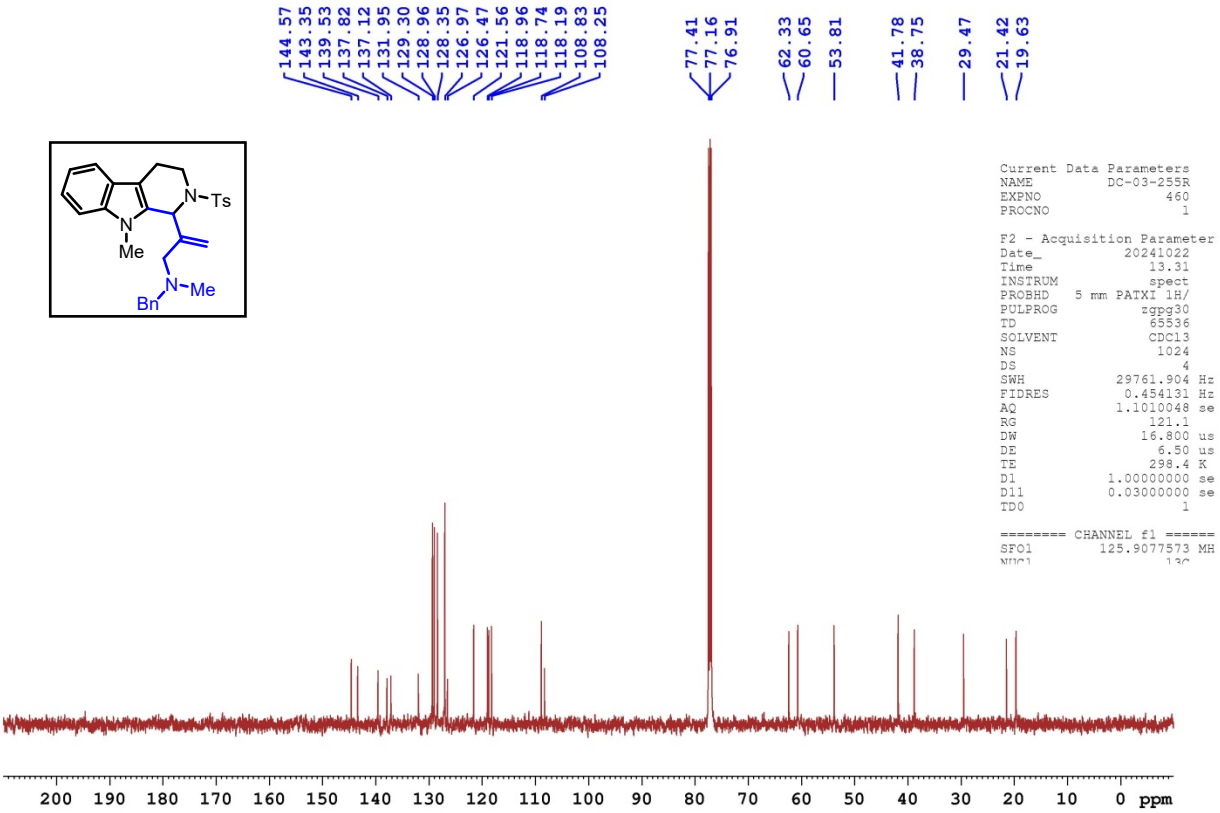

Figure S-50: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **3ag**

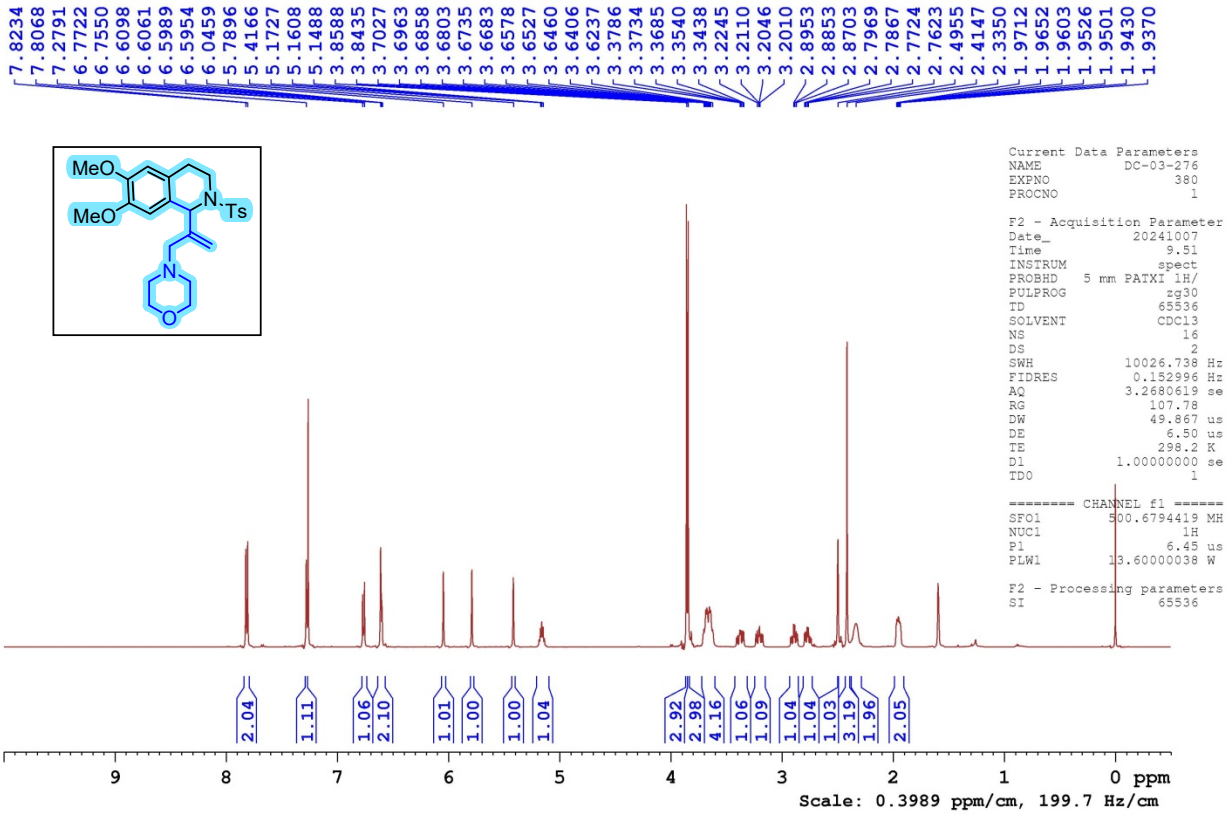

Figure S-51: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound **6**

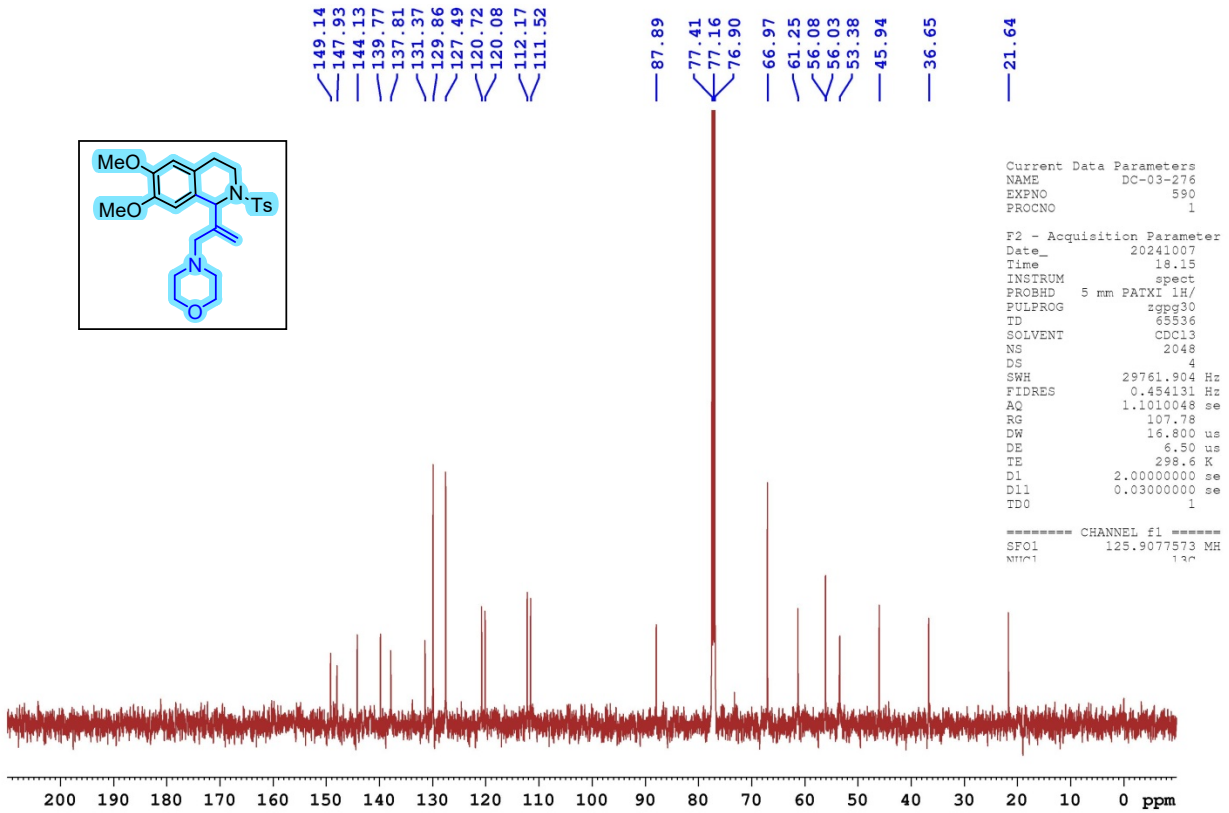

Figure S-52: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **6**

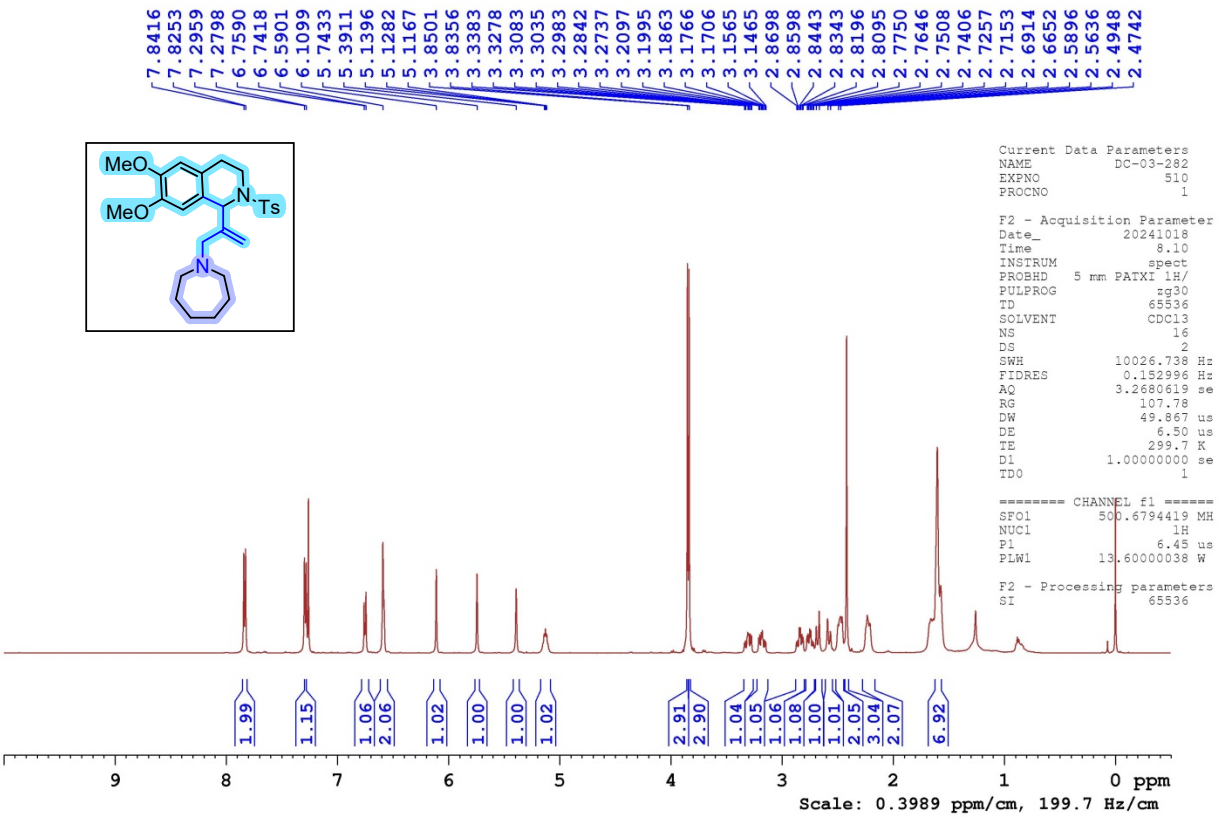

Figure S-53: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound **7**

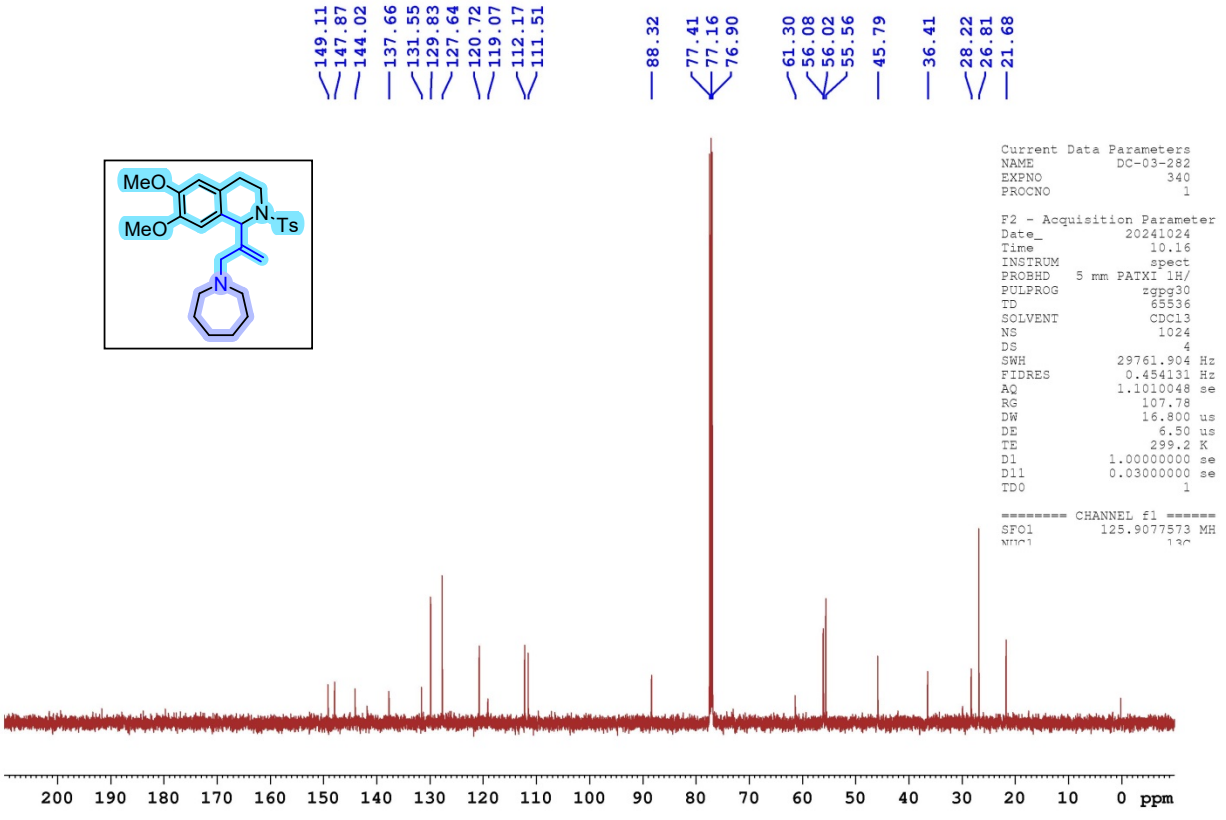

Figure S-54: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **7**

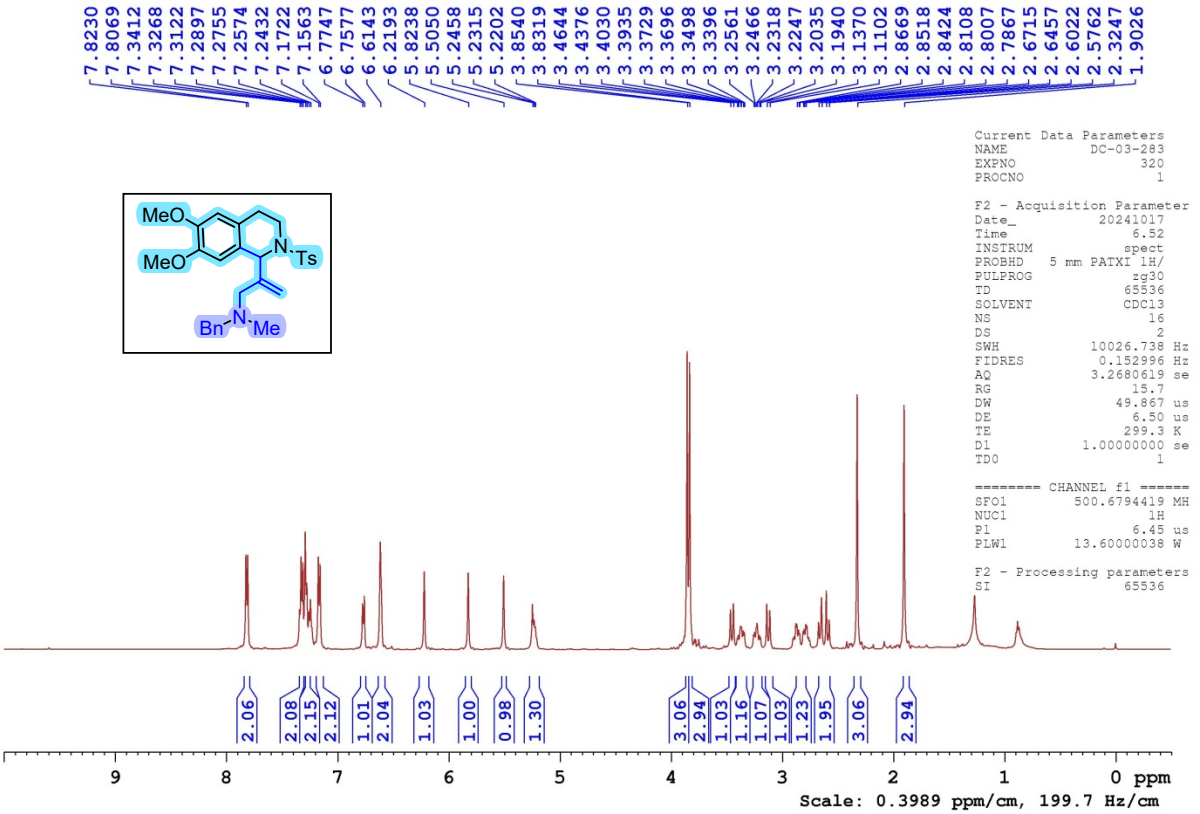

Figure S-55: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound **8**

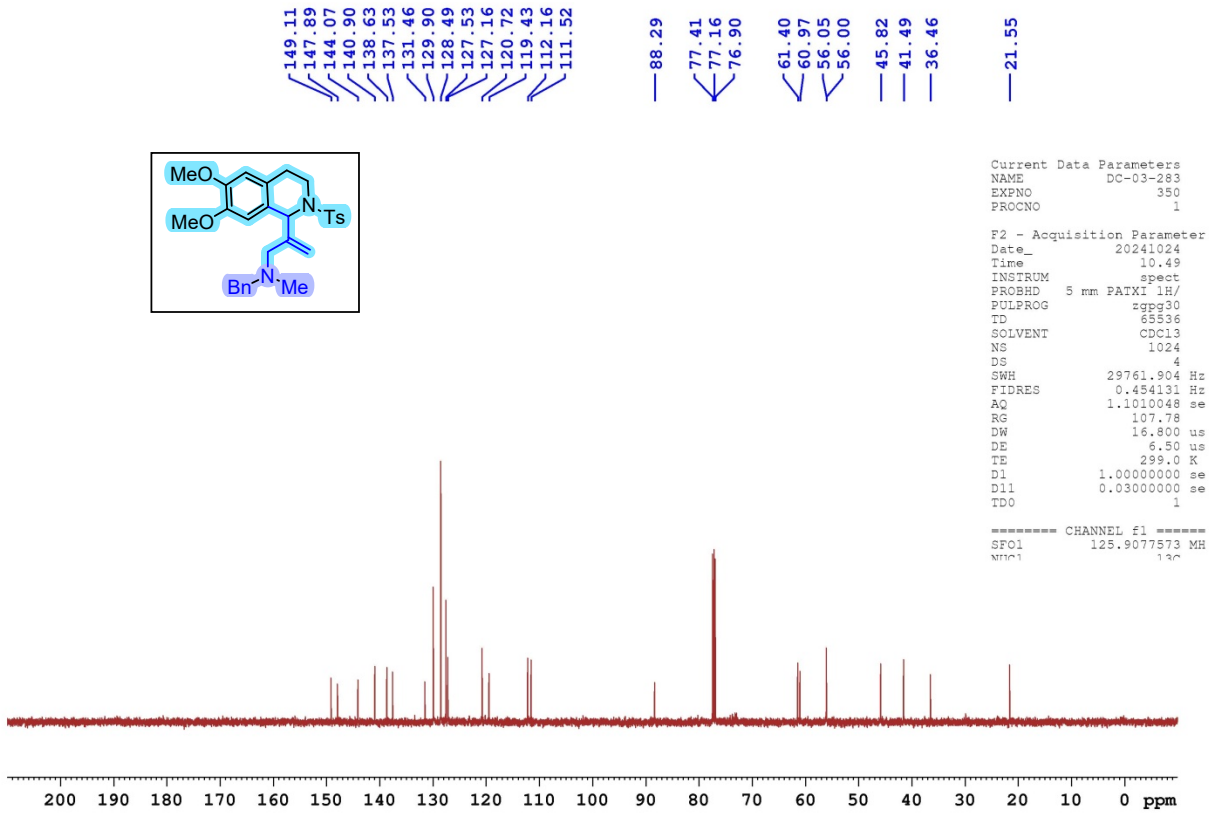

Figure S-56: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **8**

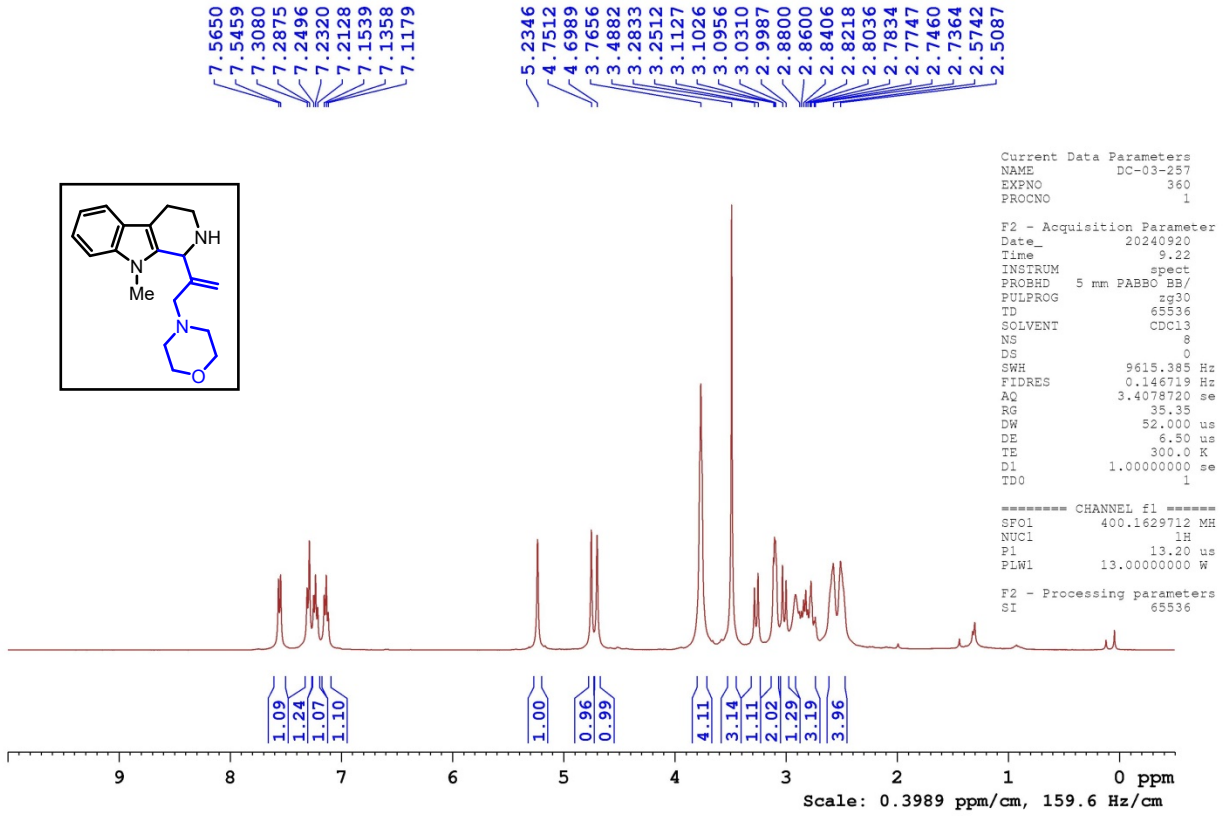

Figure S-57: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **9**

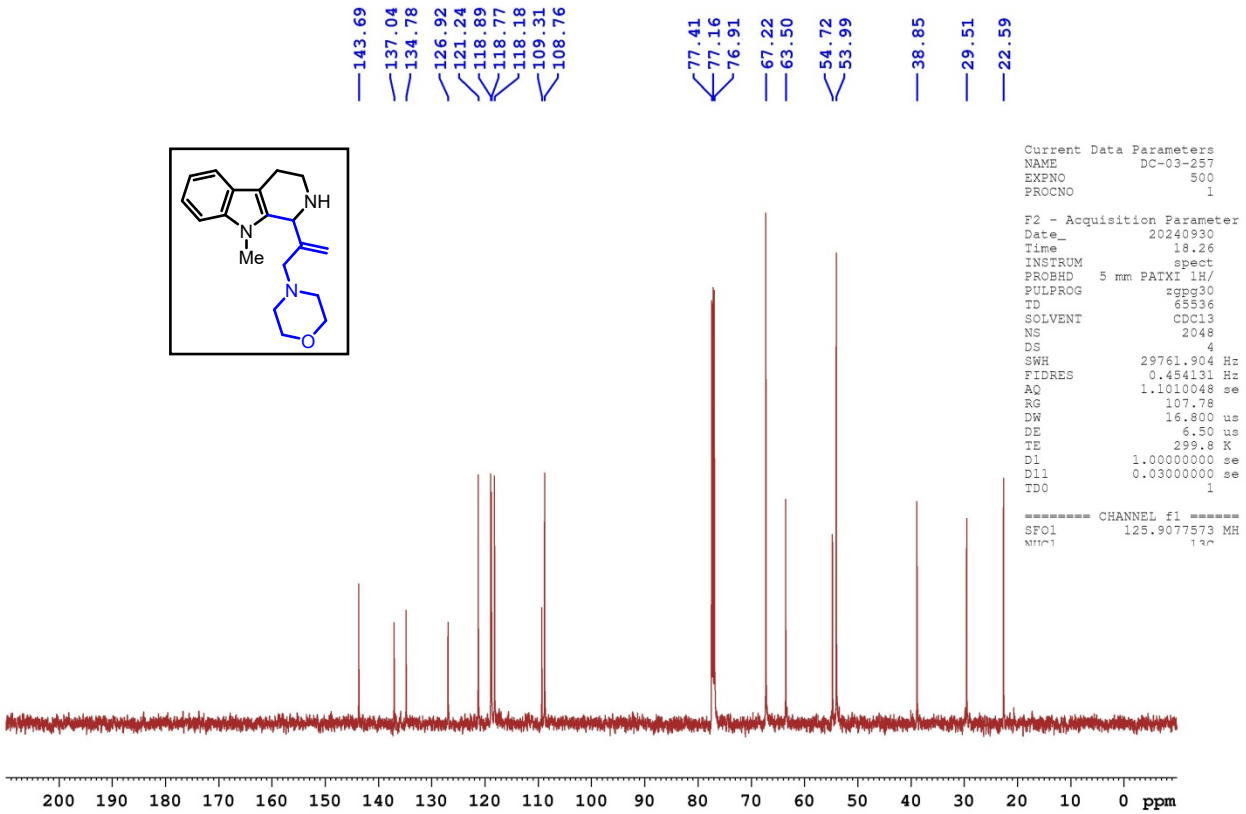

Figure S-58: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **9**

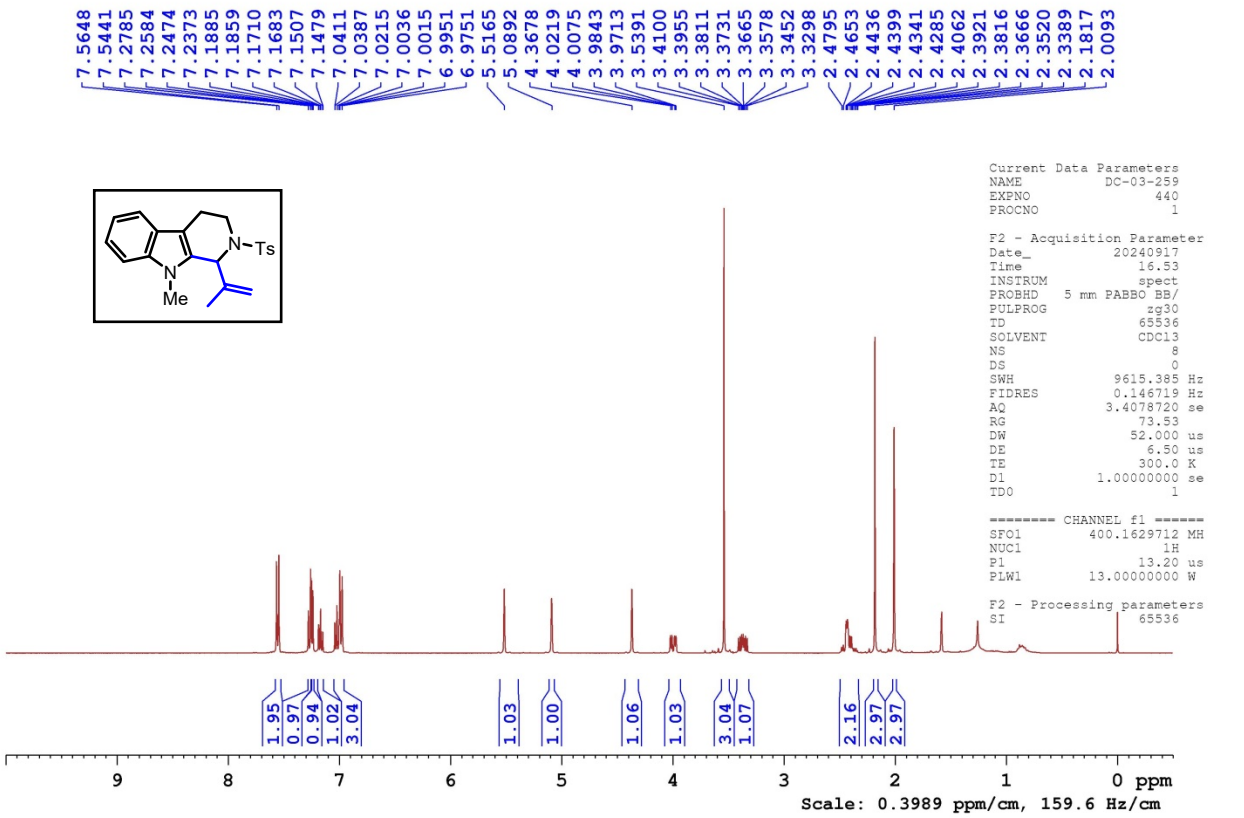

Figure S-59: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **10**

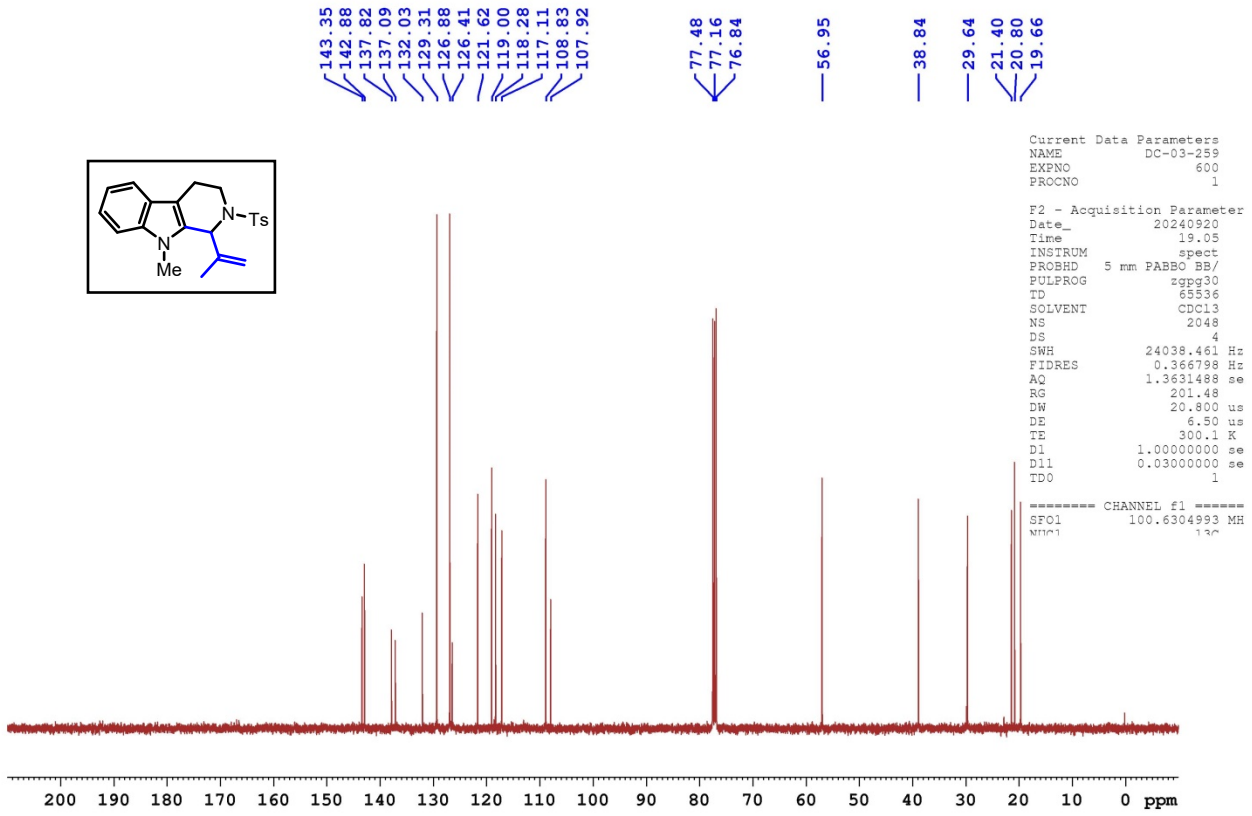

Figure S-60: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **10**

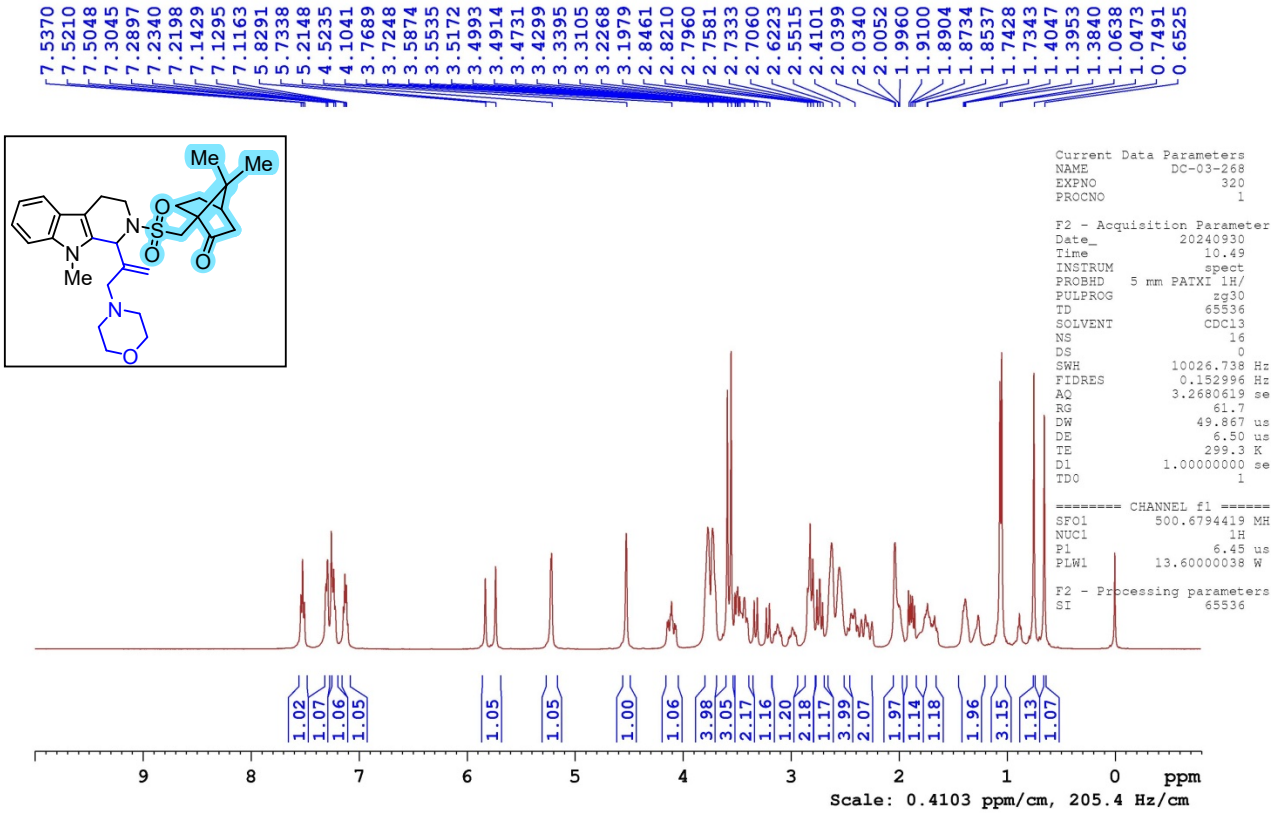

Figure S-61: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **11**

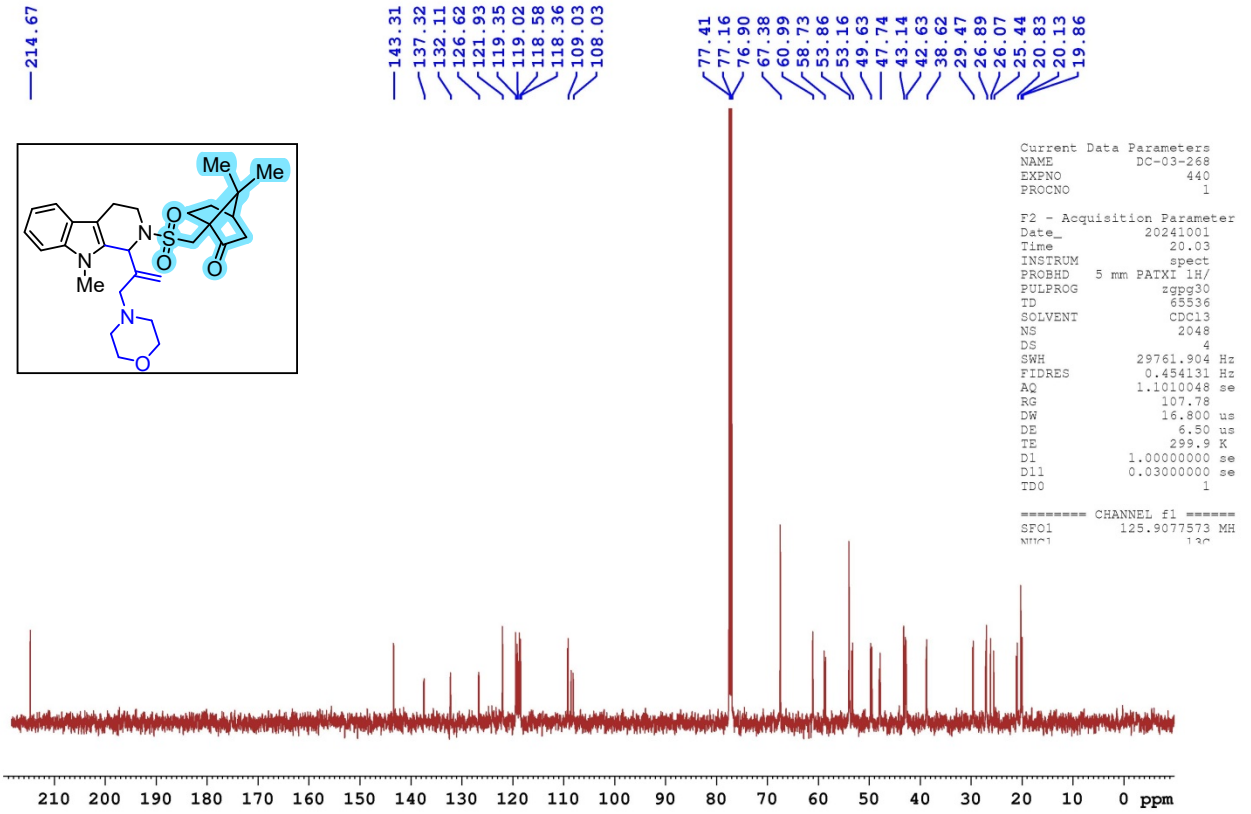

Figure S-62: $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) spectrum of compound **11**

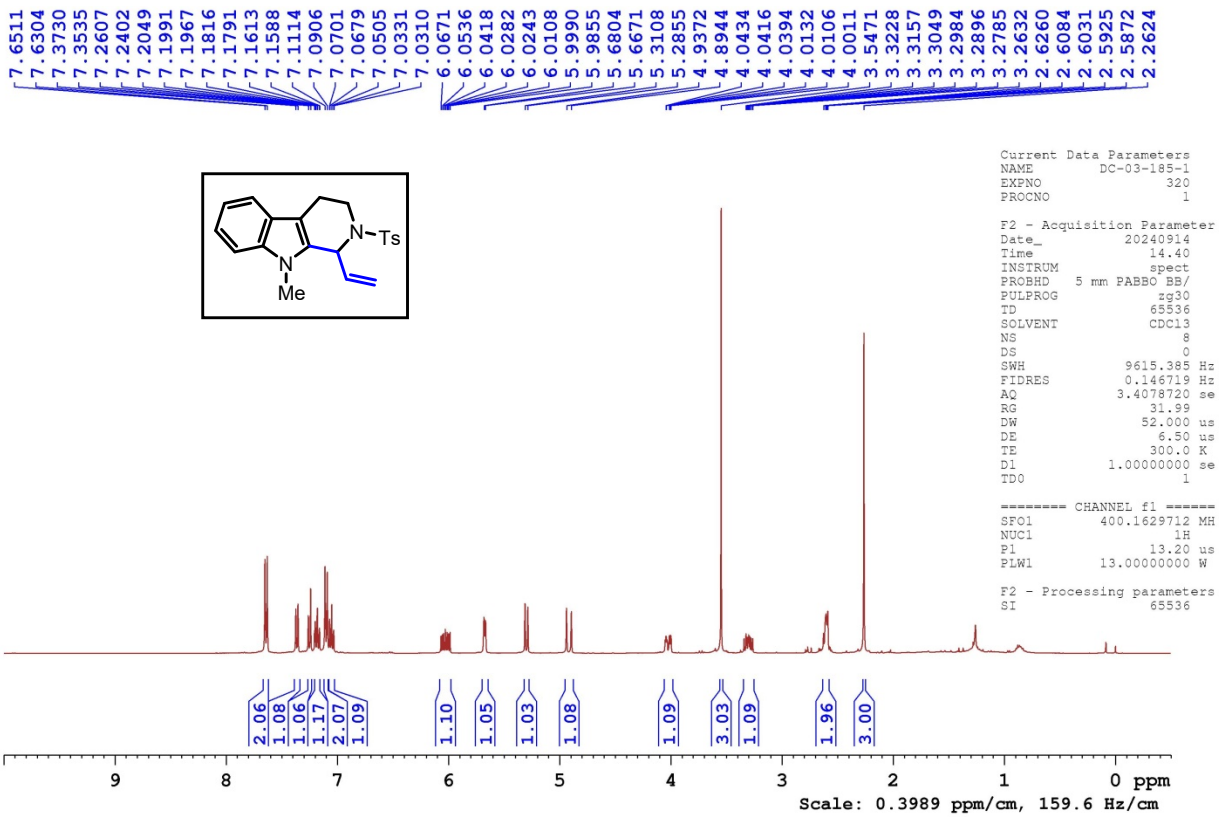

Figure S-63: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **4a**