Supporting information for

Visible-Light Photocatalyzed Radical Dipolar Annulations for Diastereoselective Synthesis of Pyrrolo[2,1-a]isoquinoline-fused Benzosulfolanes Skeletons

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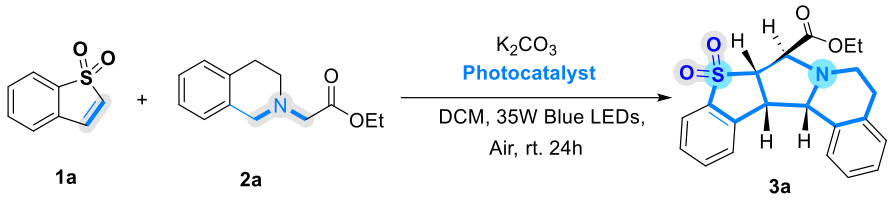
1. General information

All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-AV (400 MHz and 100 MHz, respectively) instrument internally referenced to $SiMe_4$, chloroform or dimethyl sulfoxide signals. Chemical shifts are referenced to solvent residual peak (0 ppm ^{1} H for tetramethylsilane, 77.00 ppm ^{13}C for $CDCl_3$). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br (broad singlet). Coupling constants (*J*) were reported in Hertz (Hz). All the high resolution mass spectra were obtained on a Thermo LTQ mass spectrometer (quadrupole). Flash chromatographic separations were performed on Merck 60 (200-300) mesh silica gel. For light apparatus: All the commercially available LEDs (HIPAR30, luminousflux is not less than 3200 lm) were purchased from Shenzhen Jing Feng Times LightingTechnology Co., Ltd as the reaction light source. All the photo-irradiated reactions were carried out in borosilicate glass vessel. The distance from the light source to the irradiation vessel is around 4-5 cm. Unless otherwise noted, all photocatalysts and other reagents were obtained from commercial suppliers and used without further purification. Photosyn-10 manufactured by Shanghai Quanhuan Technology Co., Ltd was used in this reaction for the reaction optimization. The Crystal structure determination a suitable crystal was selected and mounted on a Bruker D8 Quest SC-XRD.

2. Optimization of reaction conditions

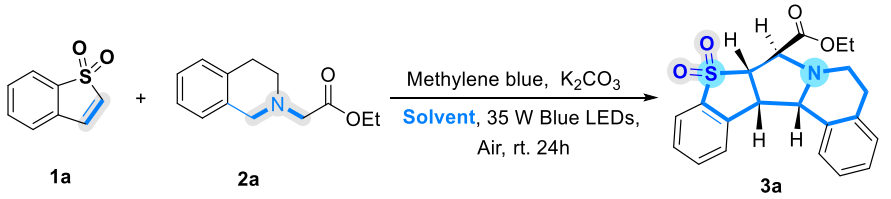
Table S1: Optimization of photocatalyst [a]



Entry	Photosensitizer	Yield [b] (%)	dr[c]
1	Eosin B	29	>20:1
2	Eosin Y	40	>20:1
3	**Methylene blue**	**48**	**>20:1**
4	$Acr^{+}MesClO_4^{-}$	21	>20:1
5	Rose Bengal	43	>20:1
6	Eosin Y Disodium Salt	36	>20:1
7	TiO_2	5	>20:1
8	$Co(bpy)_3(PF_6)_2$	trace	N.D. [d]
9	$Ru(bpy)_3Cl_2$	trace	N.D. [d]
10	-	N.R.	N.D. [d]

[a] Reactions were performed with **1a** (0.10 mmol), **2a** (0.10 mmol), and a catalyst (5 mol %), K_2CO_3(2.0eq), in the presence of DCM (1.0 mL) at room temperature under an air atmosphere for 24 h. [b] Isolated yield based on **1a**. [c] dr values determined by crude ^{1}HNMR analysis. [d] N.D. is not detected.

Table S2: Optimization of solvent [a]

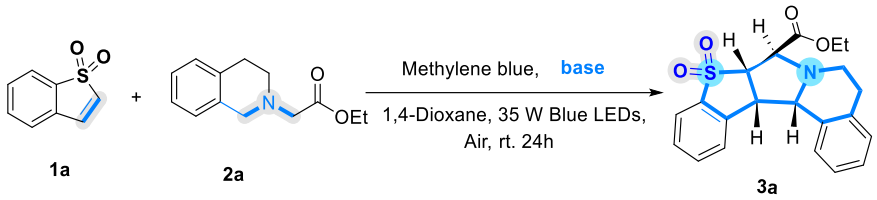


Entry	Solvent	Yield [b] (%)	dr[c]
1	CH_3CN	27	>20:1
2	DMSO	43	>20:1

3	$CHCl_3$	31	>20:1
4	CH_3OH	26	>20:1
5	NMP	5	N.D. [d]
6	Toluene	53	>20:1
7	Acetone	32	>20:1
8	**1,4-Dioxane**	**72**	**>20:1**
9	DCM	48	>20:1
10	THF	12	>20:1

[a] Reactions were performed with **1a** (0.10 mmol), **2a** (0.10 mmol), and a Methylene blue (5 mol %), K_2CO_3(2.0eq), in the presence of indicated solvent (1.0 mL) at room temperature under an air atmosphere for 24 h. [b] Isolated yield based on **1a**. [c] dr values determined by crude ^{1}HNMR analysis. [d] N.D. is not detected.

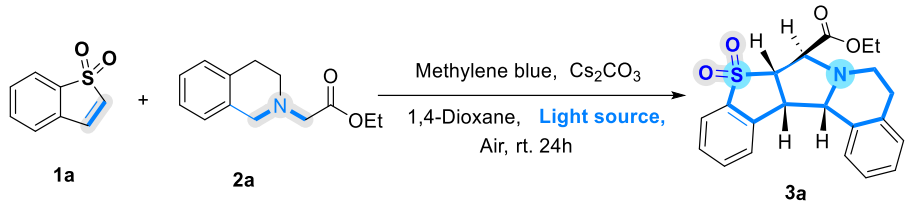
Table S3: Optimization of base [a]



Entry	Base	Yield [b] (%)
1	**-**	N.D. [d]
2	K_2CO_3	72
3	Na_2CO_3	48
4	**Cs_2CO_3**	**76**
5	$NaHCO_3$	44
6	NaOH	22
7	KOH	27
8	DABCO	5
9	DBU	8
10	DIPEA	10

[a] Reactions were performed with **1a** (0.10 mmol), **2a** (0.10 mmol), and a Methylene blue (5 mol %), Cs_2CO_3(2.0eq), in the presence of 1,4-Dioxane(1.0 mL) at room temperature under an air atmosphere for 24 h. [b] Isolated yield based on **1a**. [c] dr values determined by crude ^{1}HNMR analysis, and unless otherwise indicated, all the dr were >20:1. [d] N.D. is not detected.

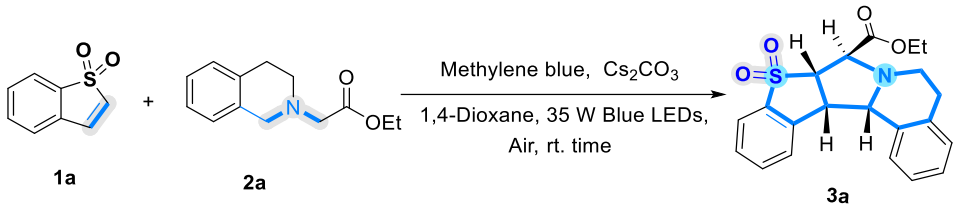
Table S4: Optimization of light source [a]



Entry	LED source	λ (nm)	Yield [b] (%)	dr[c]
1	36 W White	400-1050	46	>20:1
2	**35 W Blue**	**440-450**	**76**	>20:1
3	35W Red	620-640	trace	N.D. [d]
4	30 W Purple	395-420	35	>20:1
5	35 W Green	510-530	trace	N.D. [d]
6	5 W Blue	460-470	21	>20:1
7	12 W Blue	450-470	42	>20:1
8	18 W Blue	420-440	55	>20:1

[a] Reactions were performed with **1a** (0.10 mmol), **2a** (0.10 mmol), and a Methylene blue (5 mol %), Cs_2CO_3 (2.0eq), in the presence of 1,4-Dioxane (1.0 mL) at room temperature under an air atmosphere for 24 h. [b] Isolated yield based on **1a**. [c] dr values determined by crude ^{1}HNMR analysis. [d] N.D. is not detected.

Table S5: Optimization of others [a]



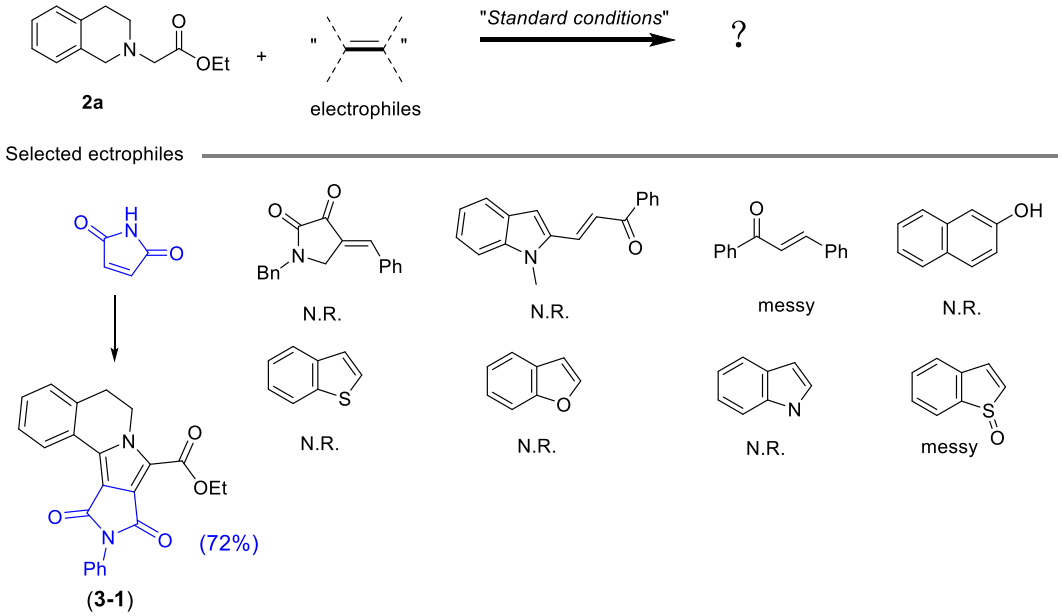
Entry	1a/2a	Atomsphere	Time(h)	Yield [b] (%)	dr[c]
1	1:1	air	24	76	>20:1
2	1:1.2	air	24	83	>20:1
3	1:1.5	air	24	83	>20:1
4	1.5:1 [d]	air	24	62[d]	>20:1

5	1.2:1 [d]	air	24	64[d]	>20:1
6	1:1.2	N_2	24	trace	N.D. [e]
7	1:1.2	O_2	24	61	>20:1
8	**1:1.2**	**air**	**36**	**87**	**>20:1**
9	1:1.2	air	48	82	>20:1

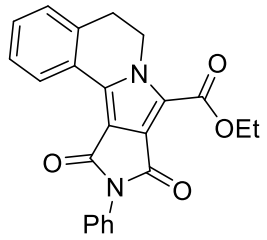
[a] Reactions were performed with **1a** (0.10 mmol), **2a** (x mmol), and a Methylene blue (5 mol %), Cs_2CO_3 (2.0 eq), in the presence of 1,4-dioxane (1.0 mL) at room temperature. [b] Isolated yield based on **1a**. [c] dr values determined by crude ^{1}HNMR analysis. [d] 0.1 mol **2a** was used and isolated yield based on **2a**. [e] N.D. is not detected.

Table S6: Investigation of other electrophiles for this reaction

To investigate the broader applicability of this method, some electrophiles beyond benzothiophene sulfone were selected and combined with **2a** as rection partner under the standard conditions were conducted. As shown in the follow, when *N*-Phenylmaleimide was used as a reaction partner, the [3+2] cyclized/dehydrogenation oxidation product **3-1** was obtained with 72% isolated yield. Other tested electrophiles were not suitable for this transformation.



Ethyl-9,11-dioxo-10-phenyl-5,9,10,11-tetrahydro-6H-pyrrolo[3',4':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate (3-1)



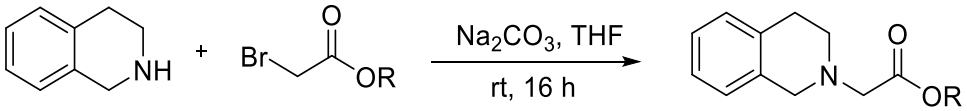
(3-1)

Known compound, A white solid, 72% yield, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, J = 7.5, 1.4 Hz, 1H), 7.51–7.46 (m, 2H), 7.43–7.36 (m, 5H), 7.29 (d, *J* = 6.8 Hz, 1H), 4.85–4.74 (m, 2H), 4.46- 4.39(m, 2H), 3.19 (t, *J* = 7.0 Hz, 2H), 1.47 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.36, 161.87, 159.93, 133.73, 132.82, 132.67, 130.59, 129.18, 128.26, 128.22, 128.06, 127.91, 127.41, 125.80, 125.46, 118.91, 116.48, 61.91, 43.71, 28.59, 14.50, 1.26. HRMS (ESI) *m/z* calcd for $C_{23}H_{18}N_2O_4$ $[M+H]^+$ 387.1345, found 387.1348.

3. Preparation of substrates

Substrates **2a-2k** were prepared according to the reported literature.[1]

1,2,3,4-tetrahydroisoquinoline (7.5 mmol), brominated esters (10 mmol) and Na_2CO_3 (5 mmol) were dissolved in THF (10 mL), the mixture was stirred at room temperature for 16 h. After the reaction was completed (monitored by TLC), Ethyl acetate and water were added. The aqueous layer was extracted twice with EtOAc. The combined organic layers were over $MgSO_4$, filtered and evaporated under reduced pressure. The residue is purified by flash chromatography (petroleum ether / ethyl acetate = 10/1) over silica gel to afford the desired products.

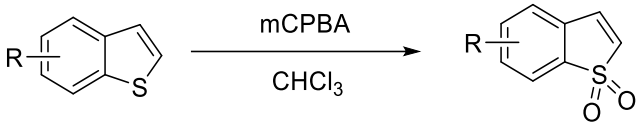


Scheme S1. synthesis of tetrahydroisoquinoline bromide ester

Substrates **1a-1j** were prepared according to the reported literature.[2]

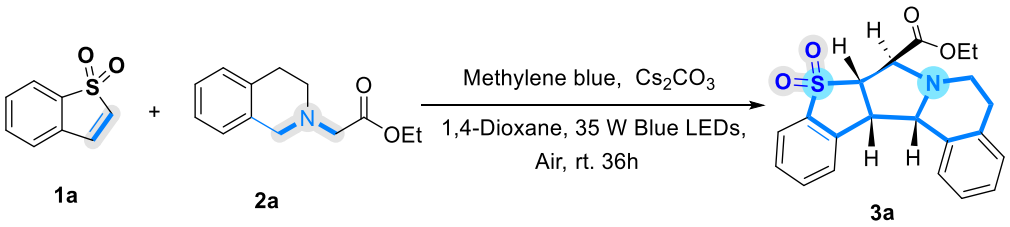
To a stirred solution of benzothiophene-d (0.3 g, 2.2 mmol, 1 equiv), in $CHCl_3$ (20

mL) was added mCPBA (0.95 g,5.5 mmol, 2.5 equiv) slowly at room temperature with vigorous stirring. Afterovernight stirring, saturated NaHCO, was added and the organic layer was extracted three times with DCM (10 mL). The solvent was dried with Na_2SO_4 and evaporated to dryness. The residue is purified by flash chromatography (petroleum ether / ethyl acetate = 8/1) over silica gel to afford the desired products.



Scheme S2 .The synthesis of benzothiophene sulfone derivatives

4. Typical procedure and characterization data for the products



To an over-dried reaction tube equipped with a magnetic stir bar was charged with tetrahydroisoquinoline compounds (**1a**, 0.1 mmol, 1.0 eq.), benzothiophene sulfone derivatives (**2a**, 0.12 mmol), Methylene blue (1.6 mg, 5 mol%), 1,4-dioxane (1.0 mL). The solution was stirred at room temperature with the irradiation of a 35 W Blue LEDs for 36 h. After the reaction was completed, the resulting mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether / ethyl acetate = 5/1) on silica gel to obtain the desired pure product.

In fact, two different types of photoreactors were used in this study, and the one on the left is mainly used for reaction condition screening, which can achieve multi-channel parallel screening of different light sources in Figure S1(left). The one on the right is the reaction that has finally been determined under 35W Blue LED light source. The photo of the reaction apparatus has been presented in Figure S1(right). The photochemical reaction set-up for irradiation of mixture with 35W Blue LEDs. The distance from the light source to the irradiation vessel is around 4-5 cm and the

homemade insulation attached to the apparatus and the sideward electric fan were used to maintain the reaction solution under irradiating with a 35W LED for 36 hours at 25-30ºC.

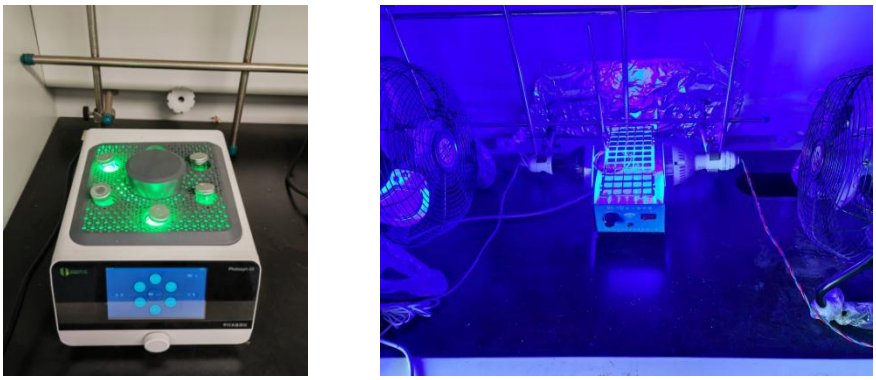
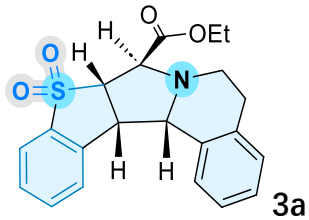


Figure S1. The photo photochemical reaction apparatus

Characterization data for the products

Ethyl -5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3a)



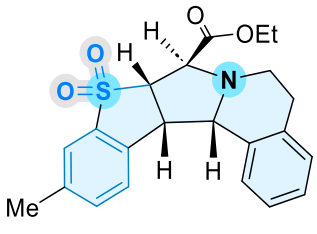
3a

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2 mg. 0.12 mmol, 1.2 eq.). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 33.3 mg, 87% yield of **3a** as white solid. m.p.: 151-153 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.8 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.32 (dt, J = 14.9, 7.5 Hz, 2H), 7.24 (dd, J = 13.5, 6.1 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H), 4.81 (d, J = 5.8 Hz, 1H), 4.63 – 4.53 (m, 2H), 4.43 (dd, J = 7.6, 2.2 Hz, 1H), 4.27 (q, J = 7.0 Hz, 2H), 2.89 – 2.72 (m, 2H), 2.69 – 2.60 (m, 1H), 2.55 – 2.45 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.77, 139.44, 137.38, 135.74, 133.02, 131.99, 129.34, 129.05, 127.74,

127.36, 127.26, 125.94, 121.60, 67.73, 65.50, 64.53, 61.84, 49.49, 45.89, 29.85, 14.30. HRMS (ESI) *m/z* calcd for $C_{21}H_{21}NO_4S$ $[M+H]^+$ 384.1270, found 384.1266.

Ethyl -11-methyl-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3b)

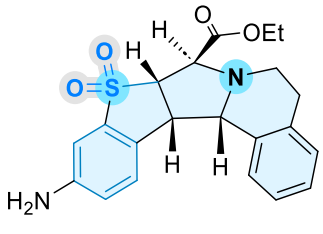


3b

The reaction was conducted with 6-methylbenzo[b]thiophene 1,1-dioxide (**1b**, 18 mg. 0.1 mmol). and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 15:1) to provide 34.9 mg, 88% yield of **3b** as white solid. m.p.: 144-145 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 9.0 Hz, 2H), 7.28 (dd, J = 12.8, 5.3 Hz, 1H), 7.23 (t, J = 7.3 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.94 (d, J = 8.1 Hz, 1H), 6.32 (d, J = 8.2 Hz, 1H), 4.77 (d, J = 5.9 Hz, 1H), 4.58 (d, J = 2.5 Hz, 1H), 4.51 (t, J = 6.8 Hz, 1H), 4.41 (dd, J = 7.6, 2.6 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 2.84 (dt, J = 10.9, 5.1 Hz, 1H), 2.80 – 2.73 (m, 1H), 2.69 – 2.62 (m, 1H), 2.55 – 2.47 (m, 1H), 2.29 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.87 , 139.54 , 139.42 , 135.75 , 134.55 , 134.22 , 132.18 , 129.29 , 127.75 , 127.25 , 126.90 , 125.87 , 121.47 , 67.83 , 65.91 , 64.50 , 61.78 , 49.22 , 45.92 , 29.90 , 20.95 , 14.28.HRMS (ESI) m/z calcd for $C_{22}H_{23}NO_4$ $[M+H]+$ 398.1426, found 398.1422.

Ethyl -11-amino-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3c)



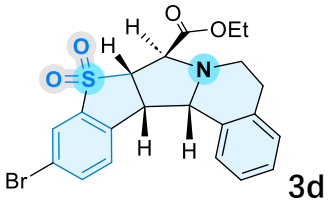
3c

The reaction was conducted with 6-aminobenzo[b]thiophene 1,1-dioxide (**1c**, 18.1

mg. 0.1 mmol) and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 31.8 mg, 80% yield of **3c** as white solid. m.p.: 144-146 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.5 Hz, 1H), 7.28 (d, J = 7.3 Hz, 1H), 7.22 (t, J = 7.0 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.84 (d, J = 2.3 Hz, 1H), 6.41 (dd, J = 8.5, 2.3 Hz, 1H), 6.16 (d, J = 8.5 Hz, 1H), 4.72 (d, J = 5.8 Hz, 1H), 4.58 (d, J = 2.6 Hz, 1H), 4.48 – 4.42 (m, 1H), 4.39 (dd, J = 7.6, 2.6 Hz, 1H), 4.30 – 4.21 (m, 2H), 3.82 (s, 2H), 2.88 – 2.75 (m, 2H), 2.72 – 2.64 (m, 1H), 2.53 (dt, J = 8.9, 6.0 Hz, 1H), 1.33 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.69 , 139.50 , 137.81 , 137.00 , 133.21, 132.98, 130.68, 129.27, 129.21, 129.03, 127.15, 126.25, 121.77, 67.45, 65.40, 64.07, 61.90, 49.24, 45.37, 29.83, 14.30.HRMS (ESI) m/z calcd for $C_{21}H_{22}N_2O_4S$[M-H]+ 397.1222, found 397.1228.

Ethyl -11-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3d)



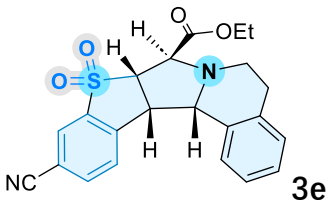
3d

The reaction was conducted with 6-bromobenzo[b]thiophene 1,1-dioxide (**1d**, 24.3 mg. 0.1 mmol), methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 37.8 mg, 82% yield of **3d** as white solid. m.p.: 144-145 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 1.8 Hz, 1H), 7.40 (d, J = 7.4 Hz, 1H), 7.30 (t, J = 7.2 Hz, 2H), 7.24 (dd, J = 4.5, 2.5 Hz, 1H), 7.10 (d, J = 7.5 Hz, 1H), 6.33 (d, J = 8.5 Hz, 1H), 4.83 (d, J = 4.6 Hz, 1H), 4.59 (d, J = 2.2 Hz, 1H), 4.53 – 4.47 (m, 1H), 4.45 (dd, J = 7.5, 2.2 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.94 – 2.87 (m, 1H), 2.85 – 2.76 (m, 1H), 2.74 – 2.66 (m, 1H), 2.62 – 2.51 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H).^{13}C

NMR (100 MHz, $CDCl_3$) δ 170.30, 141.28, 136.18, 136.08, 135.69, 131.47, 129.55, 128.67, 127.60, 127.57, 126.12, 124.62, 123.01, 67.37, 65.75, 64.30, 62.07, 48.97, 45.81, 29.66, 14.29.HRMS (ESI) m/z calcd for $C_{21}H_{20}BrNO_4S$ [M+H]+ 462.0375, found 462.0370.

Ethyl -11-cyano-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3e)

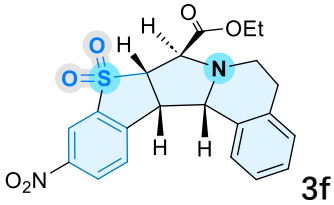


3e

The reaction was conducted with benzo[b]thiophene-6-carbonitrile 1,1-dioxide (**1e**, 19.1 mg. 0.1 mmol) and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 31 mg, 76% yield of **3e** as white solid. m.p.: 144-145 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 7.4 Hz, 1H), 7.37 (t, J = 7.3 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 6.74 (s, 1H), 4.80 (d, J = 5.4 Hz, 1H), 4.60 – 4.51 (m, 2H), 4.48 (d, J = 7.4 Hz, 1H), 4.28 (q, J = 7.0 Hz, 2H), 2.91 – 2.84 (m, 1H), 2.79 – 2.66 (m, 2H), 2.59 – 2.49 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.26, 143.61, 138.41, 135.89, 132.47, 131.39, 131.16, 129.82, 128.04, 127.28, 126.36, 122.51, 116.98, 116.67, 67.03, 65.27, 64.17, 62.02, 49.08, 45.34, 29.90, 14.32.HRMS (ESI) m/z calcd for $C_{22}H_{20}N_2O_4S$ [M+H]+ 409.1222, found 409.1219.

Ethyl -11-nitro-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3f)

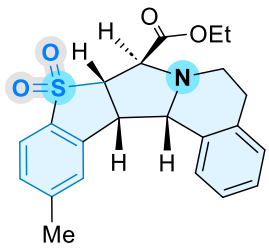


3f

The reaction was conducted with 6-nitrobenzo[b]thiophene 1,1-dioxide (**1f**, 21 mg. 0.1 mmol) and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**,26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 36.8 mg, 86% yield of **3f** as white solid. m.p.: 148-150 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 1.9 Hz, 1H), 7.98 (dd, J = 8.7, 2.1 Hz, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.29 (d, J = 7.4 Hz, 1H), 7.11 (d, J = 7.5 Hz, 1H), 6.69 (d, J = 8.7 Hz, 1H), 4.83 (d, J = 5.7 Hz, 1H), 4.63 – 4.57 (m, 2H), 4.54 (dd, J = 7.5, 2.3 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.91 – 2.84 (m, 1H), 2.73 (dq, J = 10.5, 5.7 Hz, 2H), 2.58 – 2.51 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 170.23, 148.17, 143.88, 141.50, 135.96, 131.36, 129.78, 128.40, 127.81, 127.45, 127.38, 126.23, 117.44, 66.97, 65.97, 64.44, 62.04, 49.32, 45.39, 29.91, 14.32.HRMS (ESI) m/z calcd for $C_{21}H_{20}N_2O_6S$[M+H]+ 429.1120, found429.1114.

Ethyl -12-methyl-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3g)



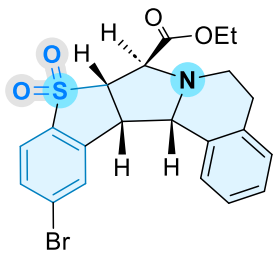
3g

The reaction was conducted with 5-methylbenzo[b]thiophene 1,1-dioxide (**1g**, 18 mg. 0.1 mmol) and with methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 30.9 mg, 78% yield of **3g** as white solid. m.p.: 144-146 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 7.23 (d, J = 7.2 Hz, 1H), 7.14 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 6.17 (s, 1H), 4.80 (d, J = 6.0 Hz, 1H), 4.59 (d, J = 2.5 Hz, 1H), 4.53 – 4.45 (m, 1H), 4.41 (dd, J = 7.7, 2.6 Hz, 1H), 4.27 (qd, J = 7.1, 1.1 Hz, 2H), 2.88 – 2.74 (m,

2H), 2.63 – 2.54 (m, 1H), 2.48 (dt, J = 9.4, 6.2 Hz, 1H), 2.02 (s, 3H), 1.34 (t, J = 7.1 Hz,3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.95, 143.82, 137.67, 136.59, 135.78, 132.13, 129.94, 129.17, 127.85, 127.84, 127.29, 125.80, 121.24, 68.17, 66.01, 64.63, 61.82, 49.64, 46.07, 29.85, 21.58, 14.29. HRMS (ESI) m/z calcd for $C_{22}H_{23}NO_4$ [M+H]+ 398.1426, found 398.1422.

Ethyl -12-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3h)

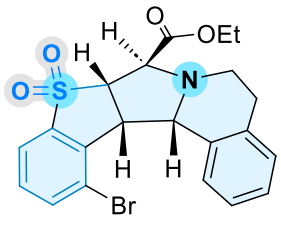


3h

The reaction was conducted with 5-bromobenzo[b]thiophene 1,1-dioxide (**1h**, 24.3 mg. 0.1 mmol) and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 35.0 mg, 76% yield of **3h** as white solid. m.p.: 147-149℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (q, J = 8.3 Hz,2H), 7.41 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.13 (d, J = 7.6 Hz, 1H), 6.56 (s, 1H), 4.79 (d, J = 5.9 Hz, 1H), 4.58 (d, J = 2.3 Hz, 1H), 4.52 – 4.47 (m, 1H), 4.43 (dd, J = 7.7, 2.3 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 2.90 – 2.83 (m, 1H), 2.83 – 2.74 (m, 1H), 2.69 – 2.61 (m, 1H), 2.59 – 2.50 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.61, 139.39, 138.48, 135.81, 132.34, 131.50, 130.73, 129.51, 127.83, 127.69, 127.49, 126.09, 122.71, 67.68, 65.78, 64.41, 61.93, 49.28, 45.77, 29.87, 14.30. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrNO_4S$ $[M+H]^+$ 462.0375, found 462.0369.

Ethyl-13-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3i)

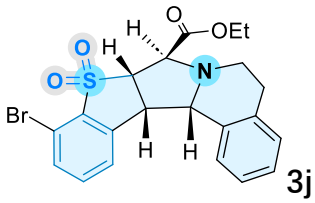


3i

The reaction was conducted with 4-bromobenzo[b]thiophene 1,1-dioxide (**1i**, 24.3 mg. 0.1 mmol) and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 35 mg, 76% yield of **3i** as white solid. m.p.: 144-145 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 2H), 7.42 (t, J = 8.1 Hz, 2H), 7.31 – 7.25 (m, 1H), 7.22 (t, J = 7.3 Hz, 1H), 7.15 (d, J = 7.5 Hz, 1H), 5.20 (d, J = 7.5 Hz, 1H), 4.71 – 4.64 (m, 2H), 4.15 – 4.09 (m, 1H), 3.90 – 3.82 (m, 2H), 3.15 (dd, J = 9.9, 4.5 Hz, 1H), 3.09 – 3.00 (m, 2H), 2.96 (dd, J = 11.1, 5.8 Hz, 1H), 0.94 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.52 , 142.69, 136.65, 135.46, 134.97, 133.39, 131.49, 128.76, 127.18, 126.89, 126.68, 122.27, 120.87, 68.79, 68.58, 62.17, 60.95, 48.73, 46.59, 29.09, 13.83. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrNO_4S$ $[M+H]^+$ 462.0375, found 462.0368.

Ethyl -10-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3j)



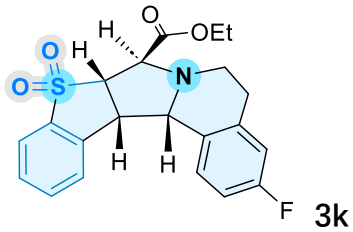
3j

The reaction was conducted with 7-bromobenzo[b]thiophene 1,1-dioxide (**1j**, 24.3 mg. 0.1 mmol) and methyl ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**, 26.2mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 35.4 mg, 77% yield of **3j** as white solid. m.p.: 149-151 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.8 Hz, 1H), 7.41 (d, J = 7.5 Hz, 1H),

7.30 (t, J = 7.4 Hz, 1H), 7.23 (d, J = 7.3 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 6.98 (t, J = 7.9 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H), 4.80 (s, 1H), 4.66 (s, 1H), 4.49 (s, 2H), 4.28 (q, J = 7.1 Hz, 2H), 2.94 – 2.84 (m, 1H), 2.84 – 2.76 (m, 1H), 2.75 – 2.68 (m, 1H), 2.60 – 2.50 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.49 , 140.58 , 138.53, 135.78, 133.72, 133.30, 131.63, 129.46, 127.73, 127.51, 126.16, 126.00, 116.28, 67.75, 66.29, 64.54, 61.98, 48.26, 45.88, 29.78, 14.30. HRMS (ESI) m/z calcd for $C_{21}H_{20}BrNO_4S$ [M+H]+ 462.0375, found 462.0371.

Ethyl -3-fluoro-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3k)

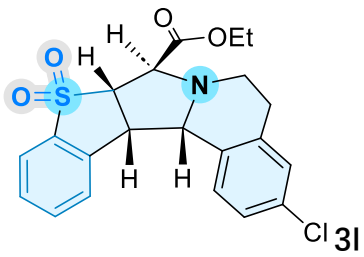


3k

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(6-fluoro-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2b**, 28.4 mg. 0.12 mmol,). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 26.8 mg, 67% yield of **3k** as white solid. m.p.: 152-154 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.03 (t, *J* = 8.3 Hz, 1H), 6.79 (d, *J* = 9.1 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 4.77 (d, *J* = 5.9 Hz, 1H), 4.60 (s, 1H), 4.54 (t, *J* = 6.8 Hz, 1H), 4.42 (dd, *J* = 7.7, 0.8 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.87 – 2.81 (m, 1H), 2.80 – 2.72 (m, 1H), 2.66 – 2.58 (m, 1H), 2.49 (dt, *J* = 15.9, 5.0 Hz, 1H), 1.34 (td, *J* = 7.1, 1.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.73, 162.97, 160.51, 139.47, 138.18 (d, *J* = 7.7 Hz), 137.12, 133.12, 129.29, 129.19, 127.82 (d, *J* = 3.3 Hz), 127.16, 121.76, 115.71 (d, *J* = 20.9 Hz), 113.45 (d, *J* = 22.2 Hz), 67.64, 65.48, 64.06, 61.91, 49.50, 45.46, 30.00, 14.29.HRMS (ESI) m/z calcd for $C_{21}H_{20}FNO_4S$ $[M+H]^+$ 402.1175, found 402.1166.

Ethyl-3-chloro-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3l)

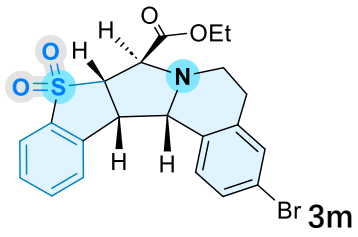


3l

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(6-chloro-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2c**, 30.3mg. 0.12 mmol). The crude mixture was purified by flash column lchromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 32.9 mg, 79% yield of **3l** as white solid. m.p.: 136-138 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.3 Hz, 1H), 7.29 (d, J = 7.2 Hz, 1H), 7.22 (d, *J* = 7.3 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 1H), 6.85 (d, J = 2.2 Hz, 1H), 6.43 (dd, J = 8.5, 2.2 Hz, 1H), 6.15 (d, J = 8.6 Hz, 1H), 4.84 (s, 1H), 4.60 (d, J = 2.4 Hz, 1H), 4.50 (s, 1H), 4.42 (d, J = 5.0 Hz, 1H), 4.29 (dd, J = 14.1, 7.0 Hz, 2H), 2.93 (s, 2H), 2.72 (t, J = 11.5 Hz, 1H), 2.56 (dd, J = 16.7, 5.5 Hz, 1H), 1.35 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.69, 139.50, 137.82 , 137.01, 133.21, 132.98, 130.69, 129.27, 129.21, 129.03, 127.15, 126.25, 121.77, 67.45, 65.40, 64.07, 61.90, 49.24, 45.37, 29.84 , 14.30. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}ClNO4S$ $[M+H]^+$ 418.0880, found 418.0873.

Ethyl-3-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3m)

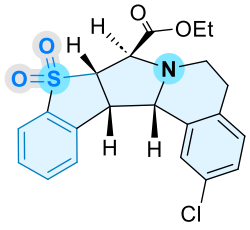


3m

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(6-bromo-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2d**, 33.4mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 33.6 mg, 73% yield of **3m** as white solid. m.p.: 142-144 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.8 Hz, 1H), 7.45 (dd, J = 8.2, 1.6 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 8.2 Hz, 1H), 7.26 – 7.18 (m, 2H), 6.52 (d, J = 8.0 Hz, 1H), 4.73 (d, J = 5.9 Hz, 1H), 4.60 (d, J = 2.5 Hz, 1H), 4.54 (t, J = 6.8 Hz, 1H), 4.40 (dd, J = 7.7, 2.5 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 2.84 (ddd, J = 10.8, 6.2, 4.5 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.68 – 2.60 (m, 1H), 2.54 – 2.45 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.67, 139.48, 138.17, 136.98, 133.25, 132.25, 131.21, 129.31, 129.23, 129.10, 127.15, 121.77, 121.07, 67.41, 65.38, 64.10, 61.91, 49.14, 45.34, 29.77, 14.30. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrNO_4S$ $[M+H]^+$ 462.0375, found 462.0380.

Ethyl-2-chloro-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3n)



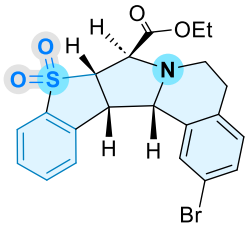
3n

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(7-chloro-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2e**, 30.3mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 30 mg, 72% yield of **3n** as white solid. m.p.: 146-148℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.7 Hz, 1H), 7.42 (d, J = 1.7 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.28 – 7.20 (m, 2H), 7.02 (d, J = 8.3 Hz, 1H), 6.54 (d, J = 8.0 Hz, 1H), 4.77 (d, J = 5.9 Hz, 1H), 4.60 (d, J = 2.6 Hz, 1H), 4.57 (t, J = 6.9 Hz, 1H), 4.42 (dd, J = 7.7, 2.6 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 2.89 – 2.83 (m, 1H), 2.70 (dtd, J = 14.7, 11.3, 6.7 Hz, 2H), 2.53 – 2.43 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.48, 139.48, 136.82, 134.25, 133.82, 133.24, 131.60, 130.77, 129.29, 127.60, 127.47, 127.19, 121.80, 67.36, 65.33, 64.15, 61.98, 49.22, 45.58, 29.26, 14.28. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}ClNO4S$ $[M+H]^+$ 418.0880, found 418.0876.

Ethyl-2-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrro

lo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3o)

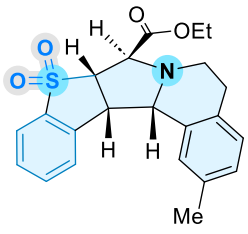


3o

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(7-bromo-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2f**, 33.4mg. 0.12 mmol, 1.2 eq). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 36.8 mg, 80% yield of **3o** as white solid. m.p.: 136-138 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.8 Hz, 1H), 7.58 (s, 1H), 7.38 (t, J = 9.4 Hz, 2H), 7.29 – 7.19 (m, 1H), 6.96 (d, J = 8.2 Hz, 1H), 6.53 (d, J = 7.7 Hz, 1H), 4.76 (d, J = 4.7 Hz, 1H), 4.63 – 4.51 (m, 2H), 4.45 – 4.37 (m, 1H), 4.27 (q, J = 7.1 Hz, 2H), 2.91 – 2.79 (m, 1H), 2.77 – 2.60 (m, 2H), 2.56 – 2.39 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.56, 139.48, 136.86, 134.82, 134.37, 134.29, 133.25, 131.06, 130.45, 129.27, 127.20, 121.79, 119.38, 67.37, 65.37, 64.05, 61.94, 49.26, 45.47, 29.39, 14.29. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrNO_4S$ $[M+H]^+$ 462.0375, found 462.0369.

Ethyl-2-methyl-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide (3p)

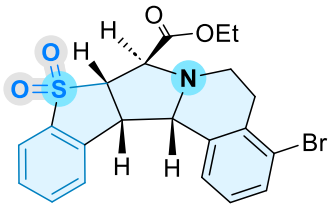


3p

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(7-methyl-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2g**, 28.4mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 36.9 mg, 93% yield of **3p** as white solid. m.p.: 132-134 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.8 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.19 (dd, J = 18.0, 10.3 Hz, 2H), 7.06 (d, J = 7.8 Hz, 1H), 6.97 (d, J = 7.8 Hz, 1H), 6.45 (d, J = 8.0 Hz, 1H), 4.79 (s, 1H), 4.57 (dd, J = 11.2, 4.5 Hz, 2H), 4.44 (dd, J = 7.6, 2.7 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.92 – 2.81 (m, 1H), 2.76 (dd, J = 15.2, 6.6 Hz, 1H), 2.67 – 2.58 (m, 1H), 2.51 – 2.46 (m, 1H), 2.41 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.85, 139.44, 137.58, 135.41, 133.03, 132.71, 131.86, 129.17, 129.00, 128.24, 128.05, 127.26, 121.59, 67.76, 65.53, 64.52, 61.79, 49.49, 46.04, 29.47, 21.20, 14.31.HRMS (ESI) *m/z* calcd for $C_{22}H_{23}NO_4S$ $[M+H]^+$ 398.1426, found 398.1417.

Ethyl-4-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3q)

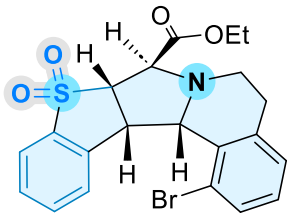


3q

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(5-bromo-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2h**, 35.6 mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 34.5 mg, 75% yield of **3q** as white solid. m.p.: 135-137℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 7.9 Hz, 1H), 7.39 (dd, J = 13.7, 7.3 Hz, 2H), 7.20 (td, J = 7.8, 3.3 Hz, 2H), 6.49 (d, J = 8.0 Hz, 1H), 4.84 (d, J = 5.3 Hz, 1H), 4.64 – 4.55 (m, 2H), 4.46 – 4.38 (m, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.96 – 2.75 (m, 2H), 2.66 (dd, J = 13.9, 8.1 Hz, 1H), 2.56 (dt, J = 16.6, 5.0 Hz, 1H), 1.35 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.42, 139.36, 136.90, 135.52, 134.25, 133.32, 131.60, 129.36, 127.17, 127.08, 126.97, 125.86, 121.88, 67.47 , 65.43, 64.50, 62.06, 49.36, 45.73, 30.55, 14.28.HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrNO_4S$ $[M+H]^+$ 462.0375, found 462.0370.

Ethyl -1-bromo-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3r)

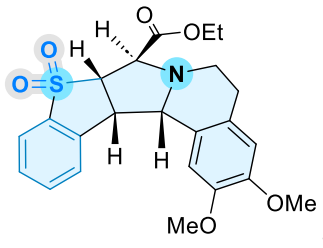


3r

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(8-bromo-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2i**, 35.6 mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 32.7 mg, 71% yield of **3r** as white solid. m.p.: 147-149℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.62 (m, 1H), 7.57 – 7.52 (m, 1H), 7.35 (dd, J = 9.1, 5.8 Hz, 1H), 7.21 – 7.10 (m, 2H), 7.05 – 6.99 (m, 1H), 6.44 – 6.40 (m, 1H), 5.20 (s, 1H), 4.78 (d, J = 5.6 Hz, 1H), 4.68 (s, 1H), 4.47 (dd, J = 5.7, 2.5 Hz, 1H), 4.35 – 4.25 (m, 2H), 2.84 (dd, J = 10.6, 4.8 Hz, 2H), 2.56 – 2.40 (m, 2H), 1.35 (ddd, J = 7.1, 5.8, 3.0 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.65, 138.95, 138.93, 137.37, 133.29 , 131.93, 130.71, 129.09, 128.89, 128.47, 126.95, 123.53, 121.72, 68.37, 65.83, 65.30, 62.04, 47.68, 46.17, 30.44, 14.27. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrNO_4S$ $[M+H]^+$ 462.0375, found 462.0369.

Ethyl -2,3-dimethoxy-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3s)



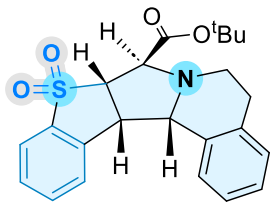
3s

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and tert-butyl ethyl 2-(6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2j**, 33.4 mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 10:1) to provide 32.3 mg, 73%

yield of **3s** as white solid. m.p.: 142-144 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.8 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 6.86 (s, 1H), 6.55 (d, J = 7.6 Hz, 2H), 4.76 (s, 1H), 4.63 – 4.51 (m, 2H), 4.46 – 4.39 (m, 1H), 4.28 (dd, J = 14.0, 6.9 Hz, 2H), 3.93 (s, 3H), 3.88 (s, 3H), 2.83 (d, J = 4.6 Hz, 1H), 2.80 – 2.69 (m, 1H), 2.59 (s, 1H), 2.46 – 2.36 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.77, 148.39, 147.56, 139.37, 137.36, 133.18, 129.12, 128.10, 127.24, 121.72, 111.53, 109.98, 67.75, 65.58 , 64.29, 61.95, 56.21, 55.84, 49.54, 46.17, 33.71, 29.31, 14.29. HRMS (ESI) *m/z* calcd for $C_{23}H_{25}NO_6S$ $[M+H]^+$ 444.1481, found 444.1473.

Eert-butyl -5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo [2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3t)



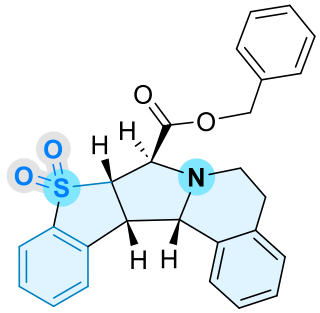
3t

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and methyl ethyl tert-butyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2k**, 28 mg. 0.12 mmol). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 29.6 mg, 72% yield of **3t** as white solid. m.p.: 163-165℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.61 (m, 1H), 7.43 (s, 1H), 7.37 – 7.27 (m, 2H), 7.24 (d, J = 2.7 Hz, 1H), 7.19 – 7.04 (m, 2H), 6.50 (d, J = 4.6 Hz, 1H), 4.82 (s, 1H), 4.52 (d, J = 22.1 Hz, 2H), 4.41 – 4.33 (m, 1H), 2.89 – 2.66 (m, 3H), 2.58 – 2.46 (m, 1H), 1.56 (dt, J = 31.5, 4.1 Hz, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ 169.69, 139.60, 137.33, 135.88, 132.96, 132.18, 129.37, 128.99, 127.72, 127.32, 127.28, 125.88, 121.54, 82.81, 67.88, 65.36, 64.33, 49.15, 45.67, 29.87, 28.15.HRMS (ESI) *m/z* calcd for $C_{23}H_{25}NO_4S$ $[M+H]^+$ 412.1583, found 412.1579.

Benzyl (8R,8aS,13bS,13cS)-5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,

4]pyrrolo[2,1-a]isoquinoline-8-carboxylate 9,9-dioxide(3u)

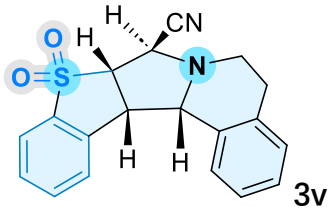


3u

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and benzyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2l**, 33.7 mg. 0.12 mmol, 1.2 eq). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 33.3 mg, 75% yield of **3u** as white solid. m.p.: 182-183℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.8 Hz, 1H), 7.46 – 7.27 (m, 8H), 7.23 (d, J = 7.2 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.45 (d, J = 8.0 Hz, 1H), 5.30 – 5.20 (m, 2H), 4.80 (d, J = 5.9 Hz, 1H), 4.65 (d, J = 2.6 Hz, 1H), 4.55 (t, J = 6.8 Hz, 1H), 4.43 (dd, J = 7.6, 2.6 Hz, 1H), 2.87 – 2.70 (m, 2H), 2.65 – 2.57 (m, 1H), 2.49 (dt, J = 15.7, 5.1 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.70, 139.44, 137.35, 135.79, 135.65, 135.26, 133.03, 132.00, 129.35, 129.05, 128.71, 128.63, 128.53, 128.37, 127.73, 127.36, 127.25, 125.94, 121.63, 67.77, 67.41, 65.47, 64.53, 49.53, 45.91, 29.92.HRMS (ESI) *m/z* calcd for $C_{26}H_{23}NO_4S$ $[M+H]^+$ 446.1426, found 446.1421.

5,6,8,8a,13b,13c-hexahydrobenzo[4',5']thieno[3',2':3,4]pyrrolo[2,1-a]isoquinoline -8-carbonitrile 9,9-dioxide(3v)



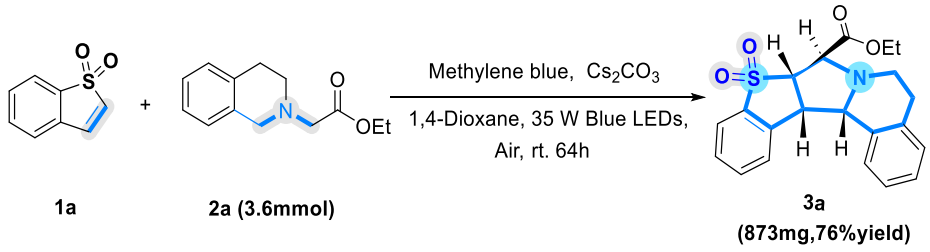
3v

The reaction was conducted with benzo[b]thiophene 1,1-dioxide (**1a**, 16.7 mg. 0.1 mmol) and 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetonitrile (**2m**, 20.6 mg. 0.12 mmol,

1.2 eq). The crude mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 20:1) to provide 15.4 mg, 46% yield of **3v** as white solid. m.p.: 176-177℃.

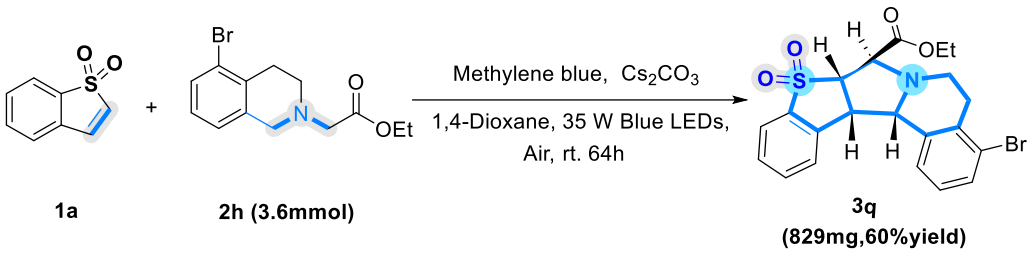
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.65 (dd, J = 7.3, 4.7 Hz, 2H), 7.38 – 7.27 (m, 3H), 7.19 (d, J = 6.9 Hz, 1H), 4.60 (t, J = 9.3 Hz, 1H), 4.26 (d, J = 8.3 Hz, 1H), 4.12 (dd, J = 9.9, 8.6 Hz, 1H), 3.51 – 3.42 (m, 2H), 3.24 (ddd, J = 16.9, 10.3, 6.9 Hz, 1H), 2.88 (ddd, J = 24.5, 15.3, 10.9 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 139.48, 134.69, 134.03, 133.73, 133.44, 130.96, 128.79, 127.81, 126.93, 126.37, 125.97, 122.55, 117.07, 66.17, 64.98, 59.18, 49.53, 47.11, 28.65.HRMS (ESI) *m/z* calcd for $C_{19}H_{16}N_2O_2S$ $[M+H]^+$ 337.1011, found 337.1007.

5. Scale up synthesis and manipulation of product.



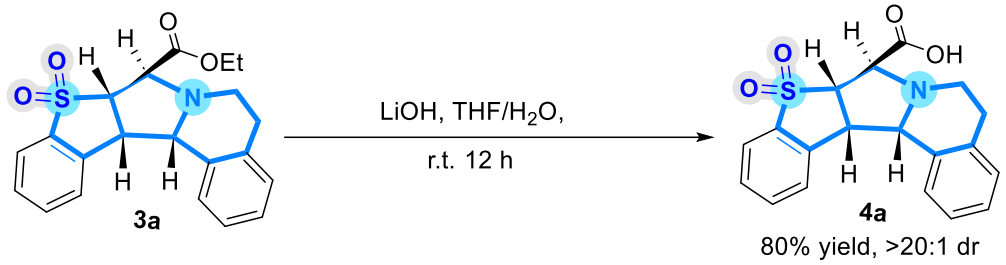
Scheme S3. Scale-up synthesis of **3a**

To a reaction tube equipped with a magnetic stir bar was charged with benzo[b]thiophene 1,1-dioxide (**1a**, 501 mg. 3mmol,.), ethyl 2-(3,4-dihydroisoquinolin -2(1H)-yl) acetate (**2a**, 788 mg, 3.6 mmol), Methylene blue, (48 mg, 5 mol%), Cs_2CO_3 (975 mg) and 1,4-Dioxane (40 mL). The solution was stirred at room temperature with the irradiation of a 35 W Blue LEDs for 64 h. After the reaction was completed, the resulting mixture purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 20:1 to 10:1, v/v) to obtain the **3a** pure product in 873 mg, 76% yield and >20:1 dr.



Scheme S4. Scale-up synthesis of **3q**

To a reaction tube equipped with a magnetic stir bar was charged with benzo[b]thiophene 1,1-dioxide (501 mg. 3mmol), tert-butyl ethyl 2-(5-bromo-3,4-dihydroisoquinolin-2(1H)-yl)acetate(1.069 g, 3.6mmol), Methylene blue, (48 mg, 5 mol%), Cs_2CO_3 (975mg) and 1,4-Dioxane (40 mL). The solution was stirred at room temperature with the irradiation of a 35 W Blue LEDs for 64 h. After the reaction was completed, the resulting mixture purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 30:1 to 20:1, v/v) to obtain the **3q** pure product in 829 mg, 60% yield and >20:1 dr.

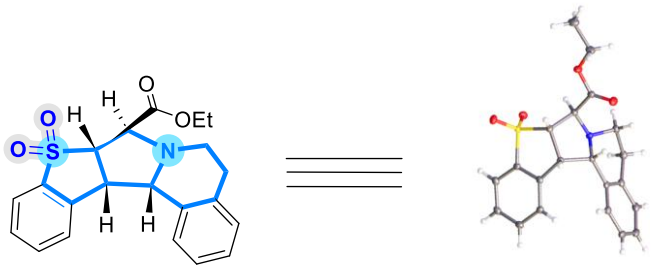


To a reaction tube equipped with a magnetic stir bar was charged with **3a** (383 mg, 1mmol), LiOH (72 mg, 3mmol), THF/H_2O (5:1, v/v). The solution was stirred at room temperature in air for 12 hours. After the reaction was completed, the resulting mixture purified by flash chromatography on silica gel (eluant: ethyl acetate) to obtain the **4a** pure product in 28.3 mg, 80% yield and >20:1 dr. Due to the poor solubility of the compound **4a**, we tried various deuterated reagents and finally obtained its hydrogen spectrum structure information using deuterated trifluoroacetic acid.

^{1}H NMR (400 MHz, CF_3COOD) δ 8.32 (d, J = 7.7 Hz, 1H), 8.05 (t, J = 7.8 Hz, 1H), 7.96 (s, 3H), 7.81 (t, J = 7.6 Hz, 1H), 7.67 (d, J = 5.4 Hz, 1H), 6.77 (d, J = 8.1 Hz, 1H), 6.25 (d, J = 7.7 Hz, 1H), 5.92 (s, 1H), 5.66 (d, J = 7.8 Hz, 1H), 5.51 (d, J = 5.0 Hz,

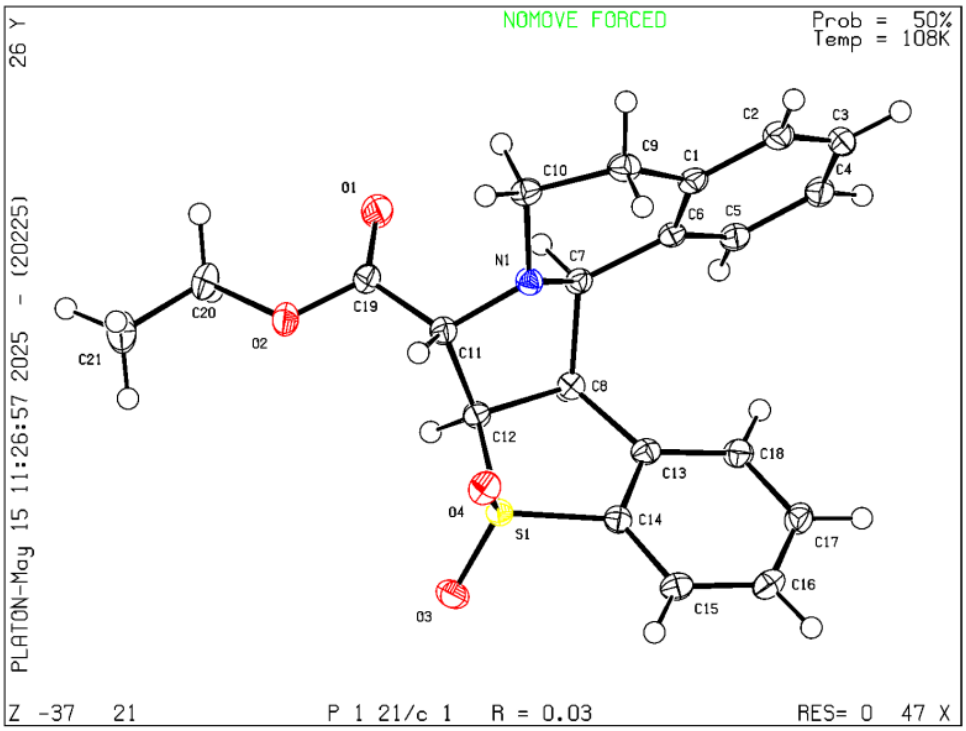
1H), 4.22 (s, 1H), 3.81 (s, 1H), 3.32 – 3.15 (m, 2H), 2.65 (s, 1H).HRMS (ESI) *m/z* calcd for $C_{19}H_{17}NO_4S$ $[M-H]^+$ 354.0800 found 354.0794.

6. Determination of the structure and configuration of products



3a

X-ray of **3a**(CCDC:2480959)



The ellipsoid contour 50 % probability levels in the caption for the image of the structure.

Figure S2. The x-ray of **3a**.

Method for crystal preparation: Dissolve 50 mg of the product **3a** in a 10 mL glass tube with Ethyl acetate/ Petroleum ether (v/v, 3/1), make the solution saturated at room temperature (25 °C), seal it with a parafilm, and then place it in a cool and dry place to

observe the precipitation rate of 3a. It takes about 3 days to get the crystal in granular form.

Single Crystal X-ray diffraction data were collected using a Bruker D8 Quest diffractometer (Mo Kα, λ= 0.71073 Å). Indexing was performed using APEX3 (Difference Vectors method). Data integration and reduction were performed using SaintPlus. Absorption correction was performed by multiscan method implemented in SADABS. Space groups were determined using XPREP implemented in APEX3. Structures were solved using SHELXT(direct methods) and refined using SHELXL-2017 (full-matrix least-squares on F^2) with anisotropic displacement contained in APEX3 program packages.

The X-ray crystal of **3a** was obtained (**Table *S7***). CCDC 2480959 contains the supplementary crystallographic data of the adduct **3a** for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

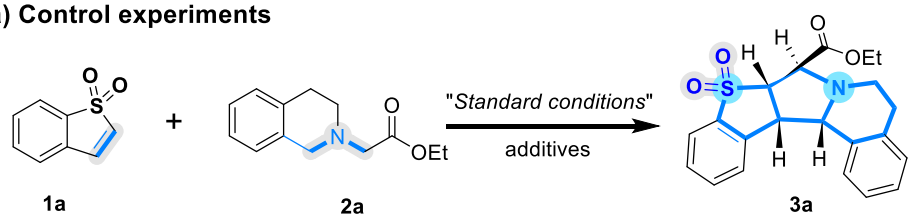
Table *S7* Crystal data and structure refinement for 3a.

Identification code	**3a**
Empirical formula	$C_{21}H_{21}NO_4S$
Formula weight	383.45
Temperature/K	108(13)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	14.37285(12)
b/Å	15.50755(14)
c/Å	8.02703(7)
α/°	90
β/°	96.2915(7)
γ/°	90
Volume/Å^3	1778.35(3)
Z	4
ρcalcg/cm^3	1.432
μ/mm^{-1}	1.858
F(000)	808.0

Crystal size/mm^3	0.14 × 0.12 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.416 to 130.092
Index ranges	$-12 \leq h \leq 16$, $-18 \leq k \leq 18$, $-9 \leq l \leq 9$
Reflections collected	13707
Independent reflections	2967 [R_{int} = 0.0164, R_{sigma} = 0.0112]
Data/restraints/parameters	2967/0/245
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2σ (I)]	R_1 = 0.0319, wR_2 = 0.0817
Final R indexes [all data]	R_1 = 0.0323, wR_2 = 0.0820
Largest diff. peak/hole / e $Å^{-3}$	0.38/-0.40

7. Mechanism studies and proposed mechanism

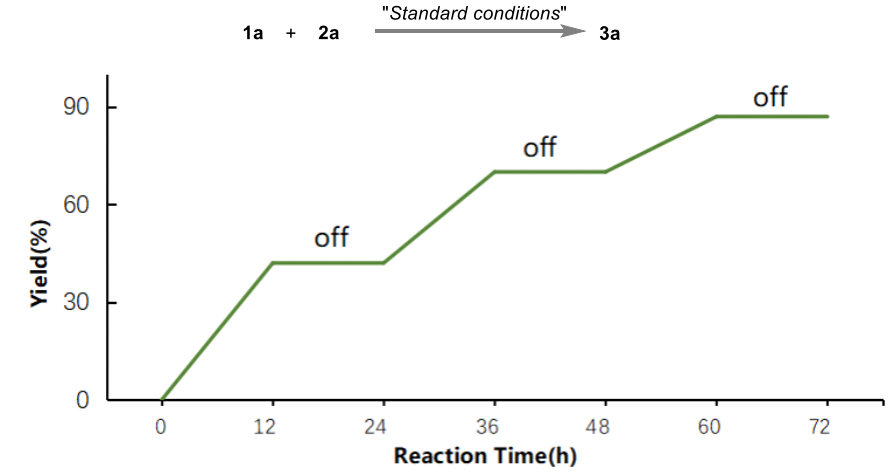
a) Control experiments



1a 2a 3a

entry	additive	results (**3a**)
1	no	87%
2	TEMPO (3.0 equiv)	N.R.
3	BHT (3.0 equiv)	trace
4	1,1-Diphenylethylene (3.0 equiv)	trace

b) Light on/off experiments



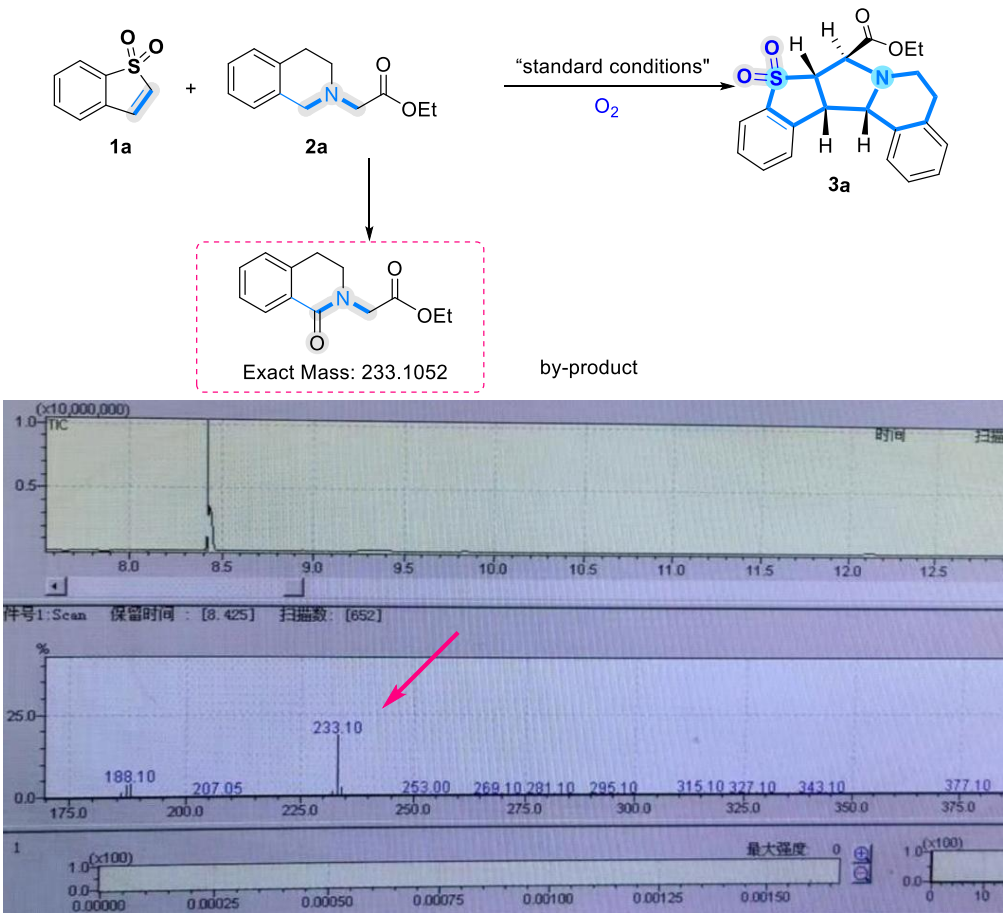
Scheme S5. Control experiments and Light on/off experiments

To gain further insight into the reaction mechanism, a series of control experiments were thoroughly conducted in **Scheme S5.** Firstly, the radical trapping experiments with radical quenchers were carried out. When When 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), butylated hydroxytoluene (BHT) and 1,1-diphenylethylene were added in this photo-redox catalytic system under standard conditions, the reaction was completely inhibited. These experimental results strongly indicated a typical radical process might be involved in this reaction. Additionally, the light on/off visible-light-irradiation experiments for this visible-Light catalytic system was carried out and the

result was shown in **Scheme S6**, which clearly supported that continuous visible light irradiation was an indispensable element for this transformation.

b) GC-MS analysis to understand the reaction process

Actually, the substrate 2a was produced the isoquinolinone by-product under the photocatalytic conditions, especially when the reaction is carried out under an oxygen atmosphere, it is detectable in the reaction system by GC-MS. We have attempted to separate and characterize its structure, but due to the small amount, we did not obtain its nuclear magnetic resonance (NMR) information**.**

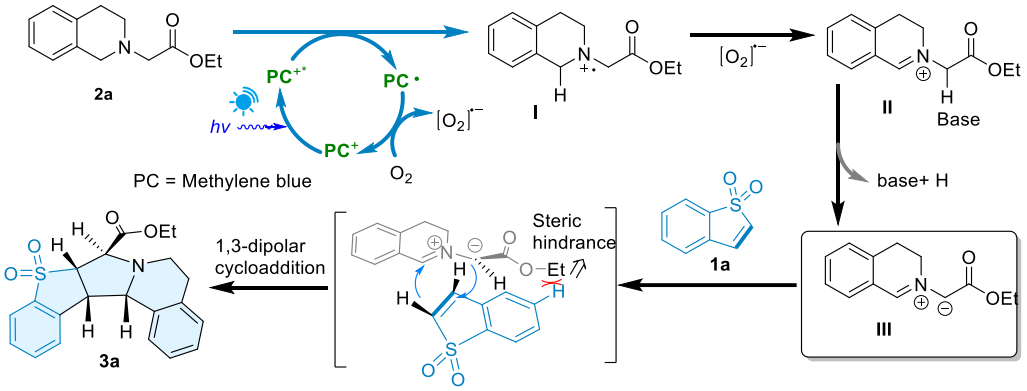


Scheme S6. GC-MS analysis to understand the reaction process

c) Proposed reaction mechanism

According to the observations of the above-mentioned mechanism experimental results and previous reports[3], a plausible mechanism for this photo-induced

stereoselective radical 1,3-dipolar cycloaddition was depicted in **Scheme S7**., Initially, we envisioned that the methylene blue (photocatalyst) was photoexcited to excited state from ground state under Blue LEDs light irradiation, then tetrahydroisoquinoline derivative (2a) generate the tetrahydroisoquinoline nitrogen cation radical (I) via single electron transfer. The radical was oxidized to generate the iminium ion intermediate II in the presence of superoxide radical anion which generated from the O2. Subsequently, the tetrahydroisoquinoline iminium ion intermediate II affords 1,3-dipole azomethine III in situ by a deprotonation process with base, which further undergoes 1,3-dipolar cycloaddition reaction to rapidly constructe pyrrolo[2,1-a]isoquinoline-fused benzosulfolane product (3a) with excellent diastereoselectivities, in which, the high diastereoselectivity of the final product was contributed to the steric effect between the two substrates.



Scheme S7. Proposed reaction mechanism

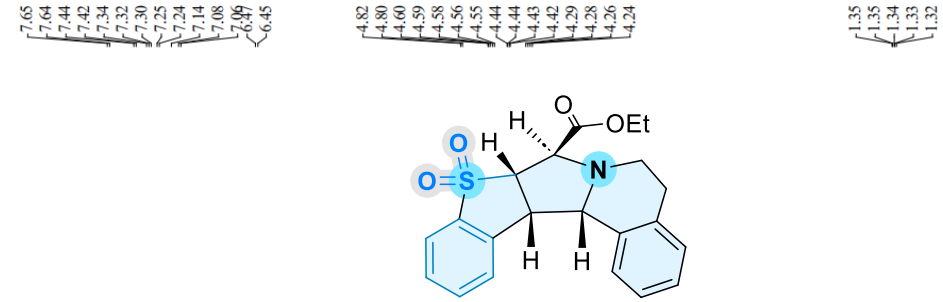
8. References

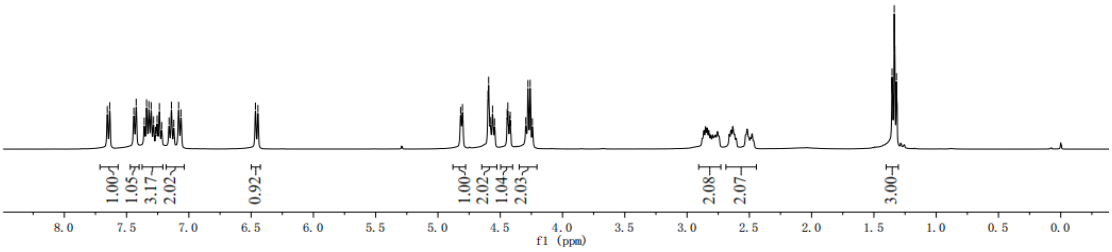
[1] L. Huang and J. Z. Zhao, *Chem. Commun.,* **2013**, 49, 3751.

[2] Subban Kathiravan and Ian A. Nicholls, *Org. Lett*. **2019**, 21, 9806−9811.

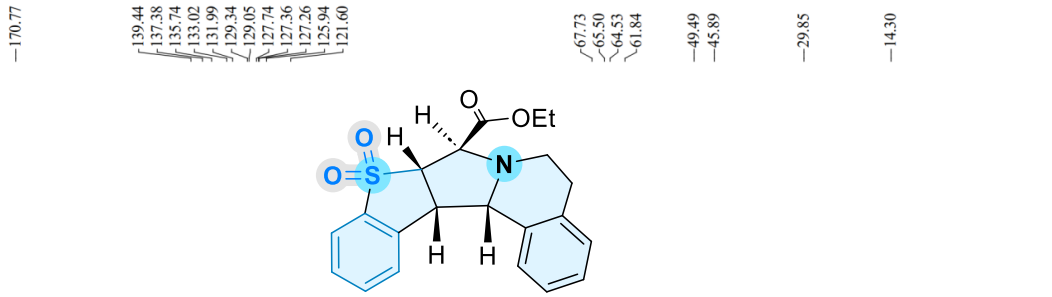
[3] (a) Y. Q. Zou, L. Q. Lu, L. Fu, N. J. Chang, J. Rong, J. R. Chen and W. J. Xiao, *Angew. Chem. Int. Ed*. **2011**, 50, 7171; (b) A. Fujiya, M. Tanaka, E. Yamaguchi and N. Tada, A. Itoh; *J. Org. Chem*. **2016**, 81, 7262.c. (b) Yi, Z.-Q.; Zhang, W.; Yi, B.; Liu, C.; Xie, Y.; Li, M.; Xiong, Y.; Wu, W.; Tan, J.-P. *Org. Lett*. **2025**, 27, 9, 2197–2202.

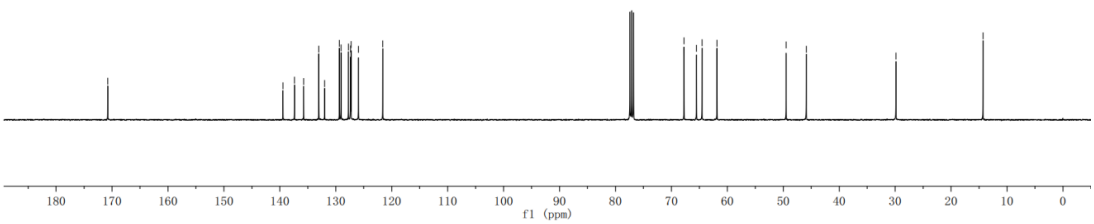
9. NMR spectra



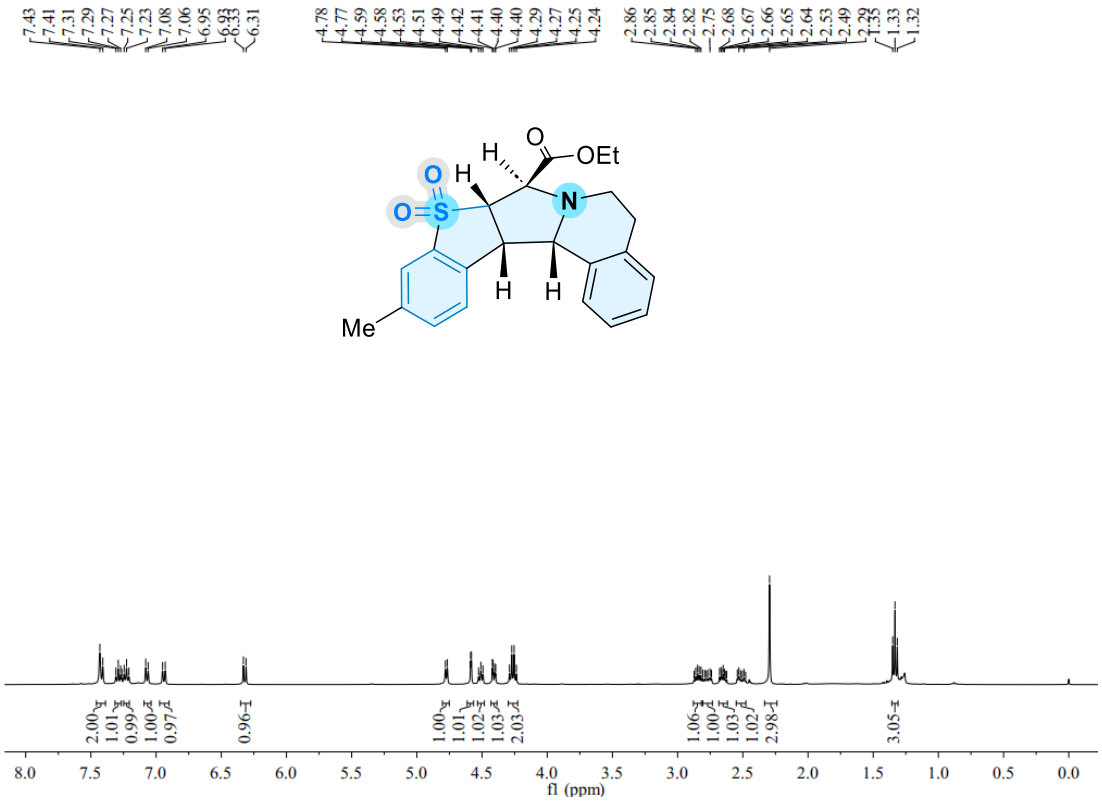


^{1}HNMR of **3a** ($CDCl_3$, 400MH_Z)

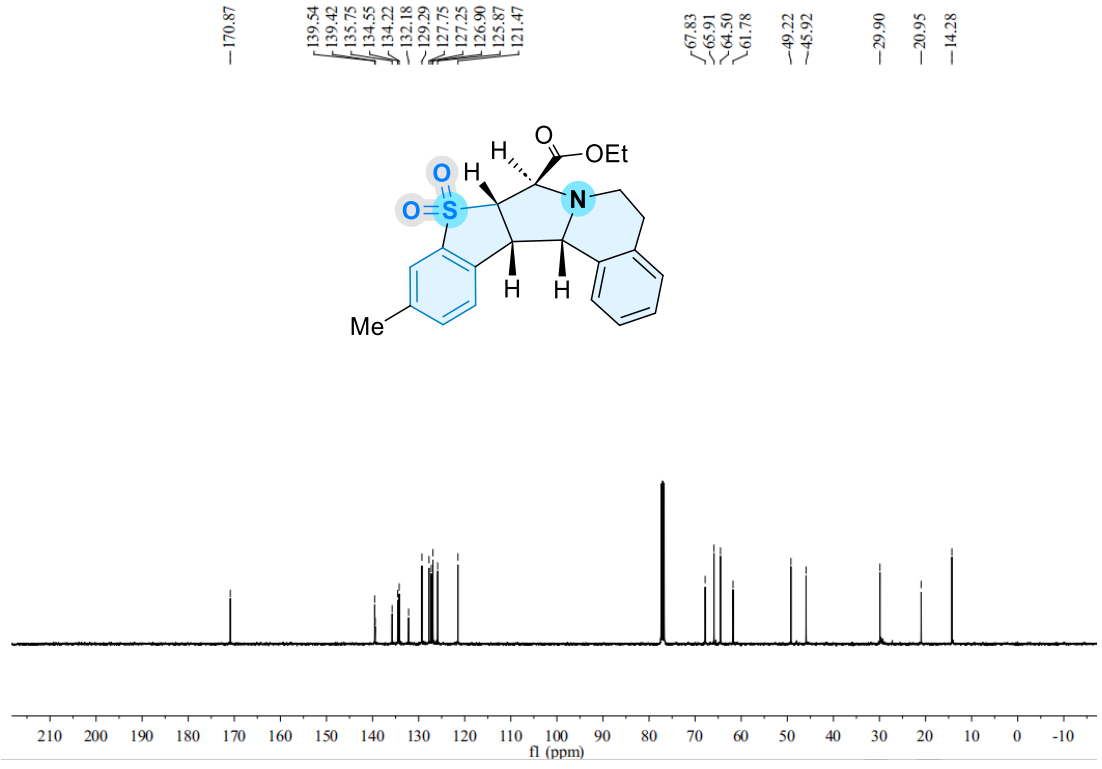




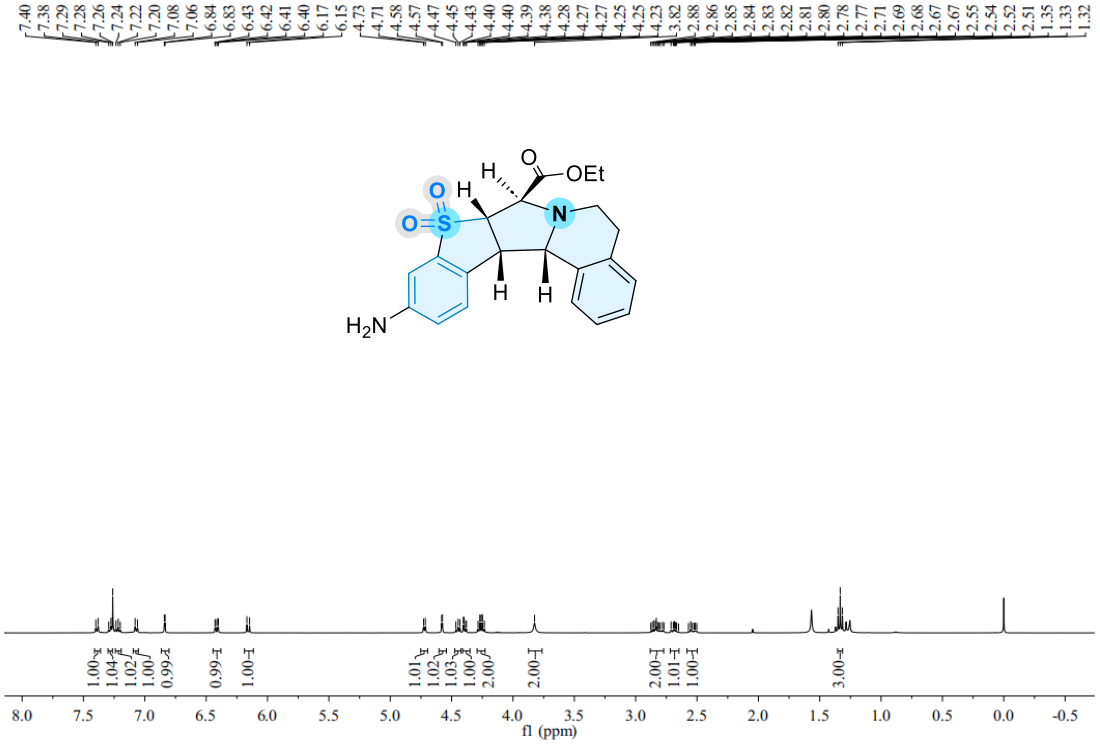
^{13}CNMR of **3a** ($CDCl_3$, 100MH_Z)



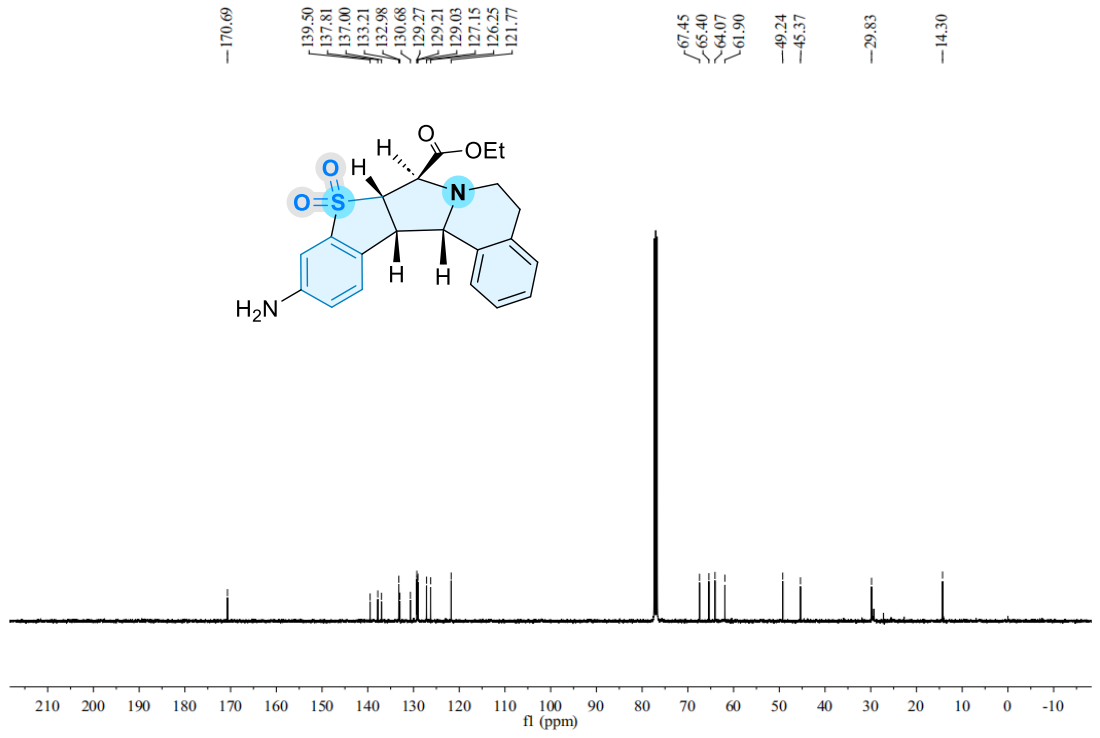
^{1}HNMR of **3b** ($CDCl_3$, 400MH_Z)



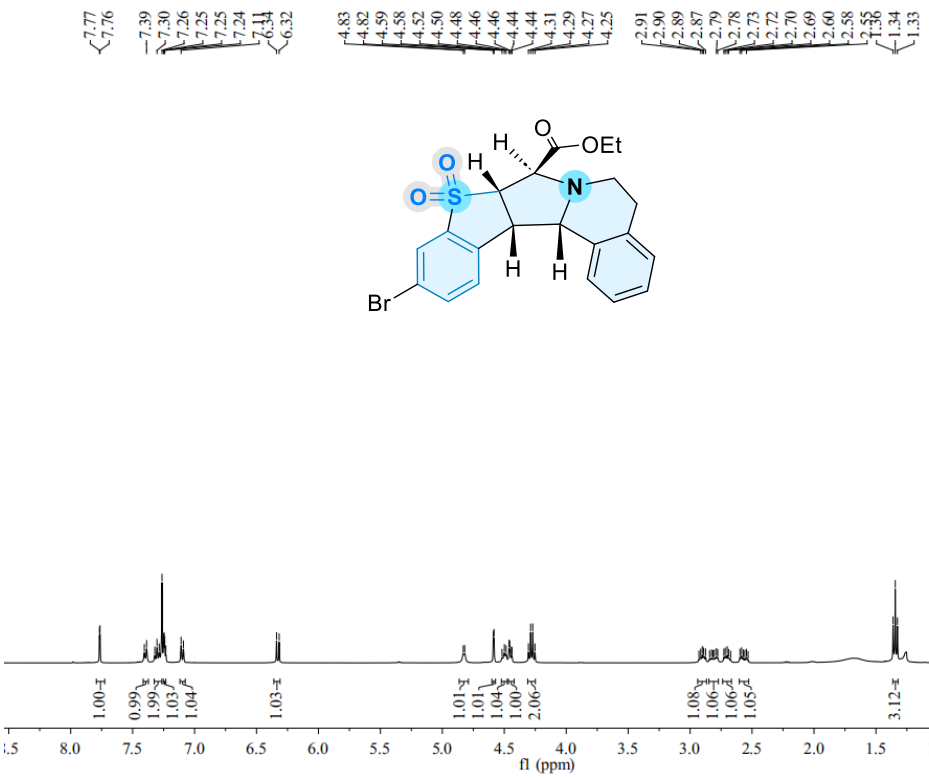
^{13}CMR of **3b** ($CDCl_3$, 100MH_Z)



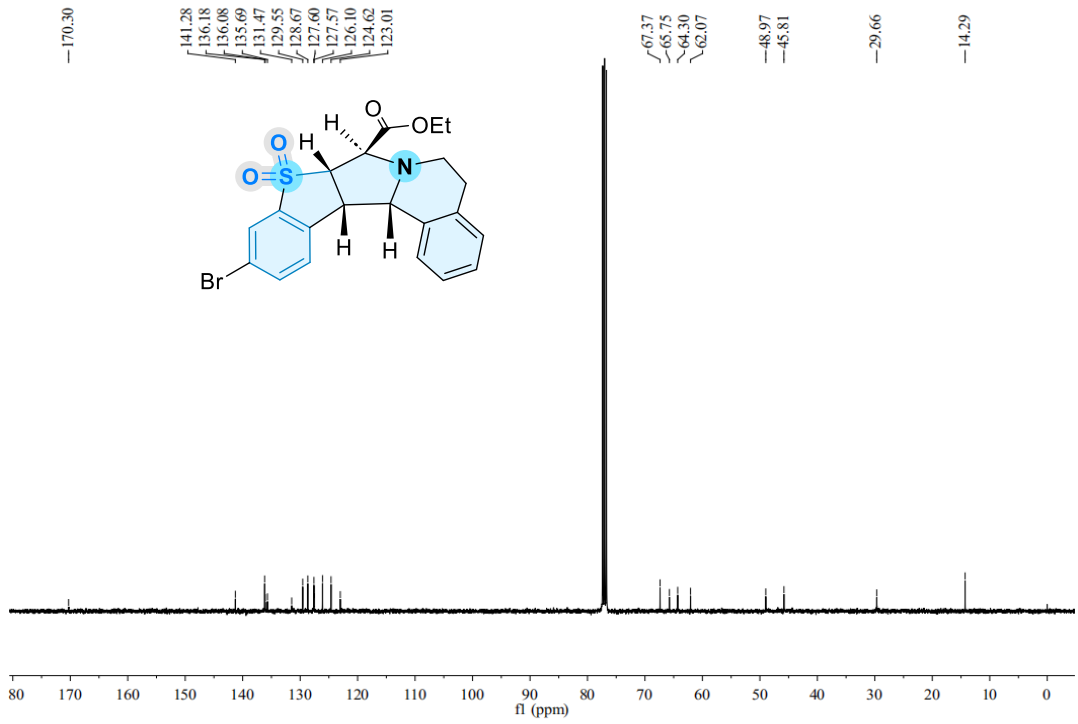
^{1}HNMR of **3c**($CDCl_3$, 400MHz)



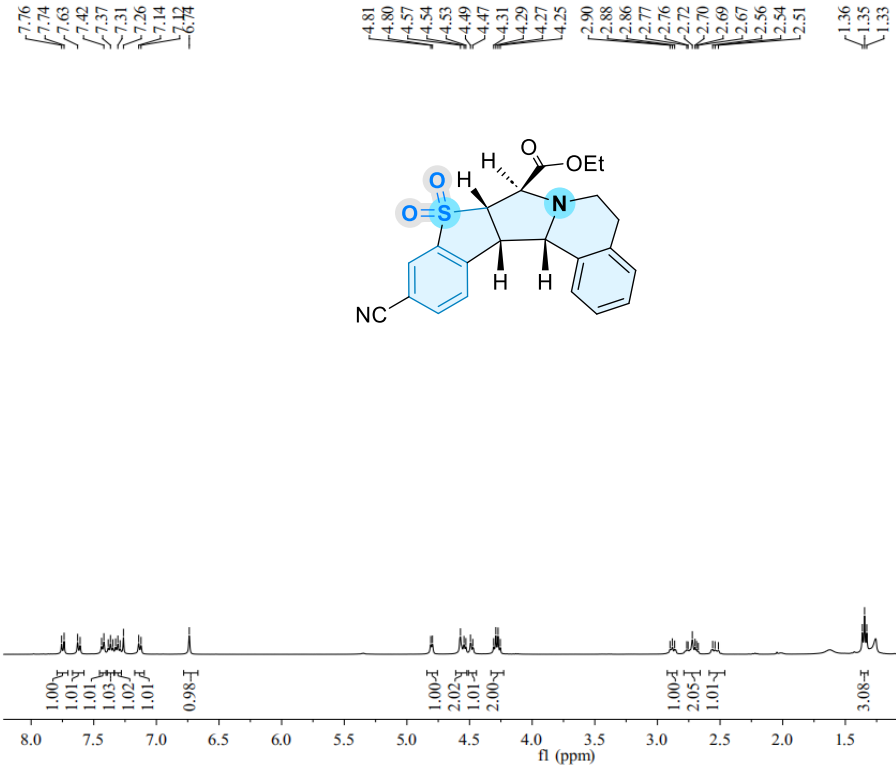
^{13}CNMR of **3c**($CDCl_3$, 100MHz)



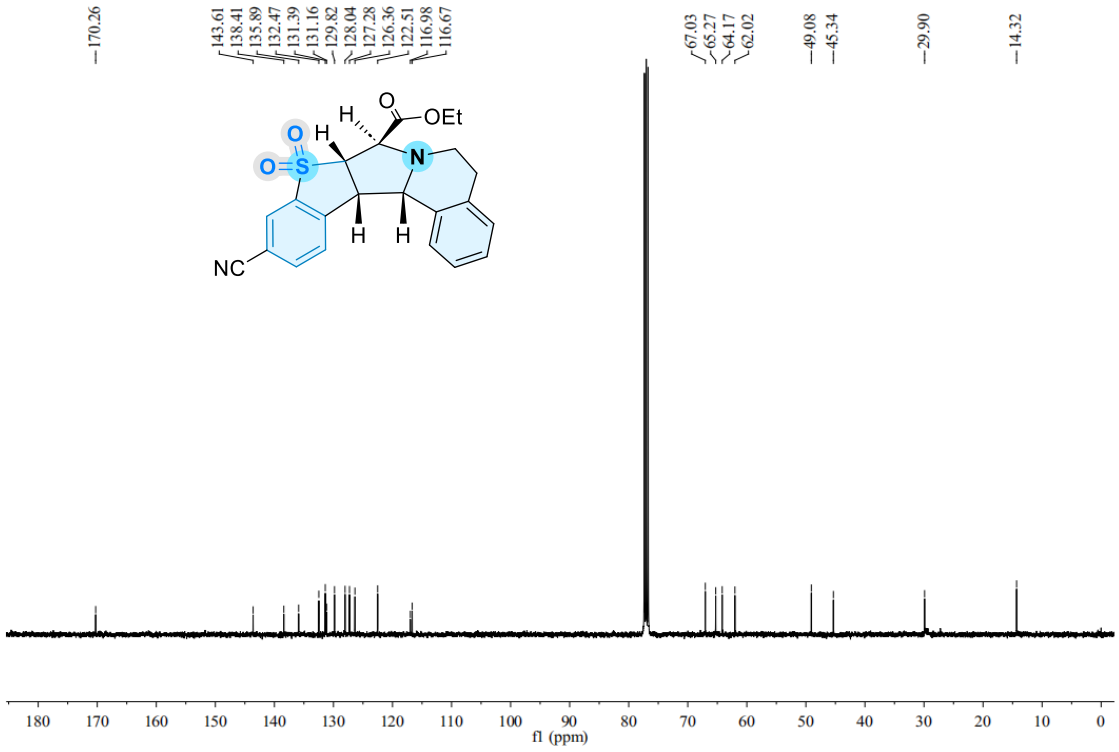
^{1}HNMR of **3d**($CDCl_3$, 400MH_Z)



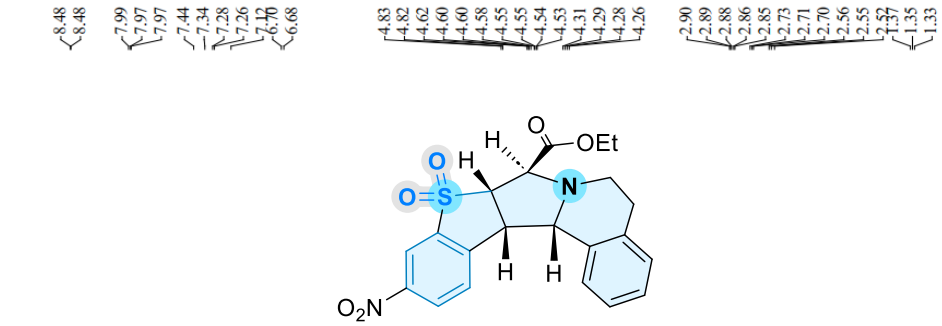
^{13}CNMR of **3d** ($CDCl_3$, 100MH_Z)



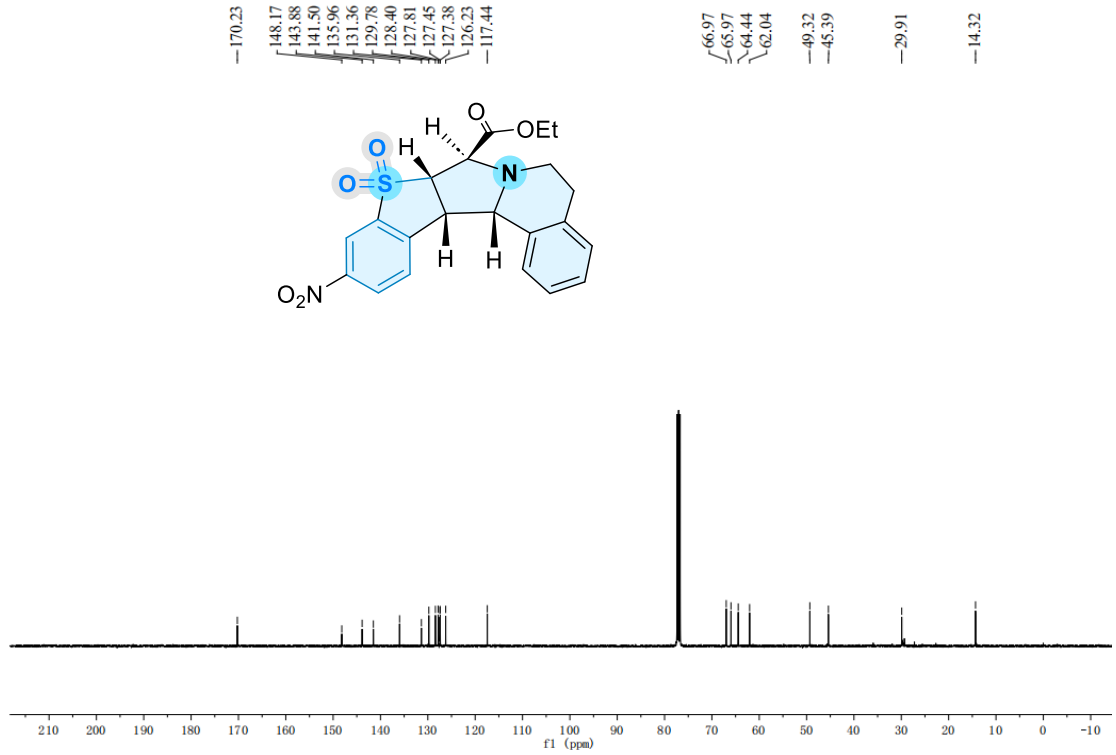
^{1}HNMR of **3e** ($CDCl_3$, 400MH_Z)



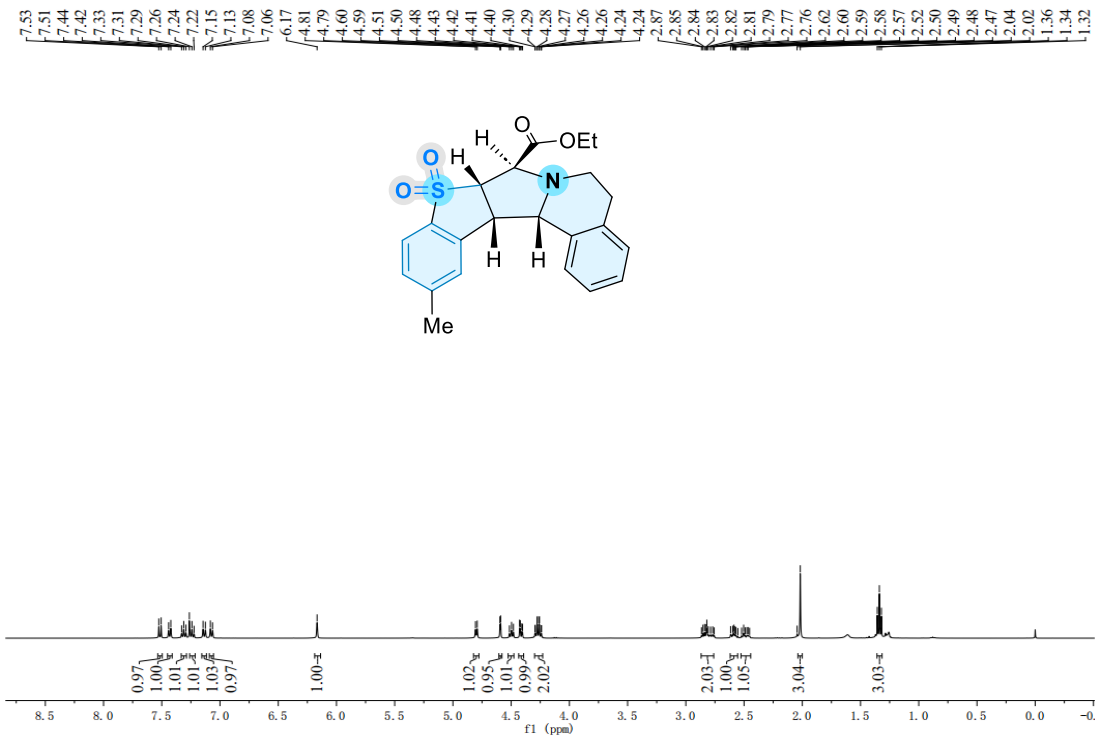
^{13}CNMR of **3e** ($CDCl_3$, 100MH_Z)



^{1}HNMR of **3f** ($CDCl_3$, 400MH_Z)



^{13}CNMR of **3f** ($CDCl_3$, 100MH_Z)



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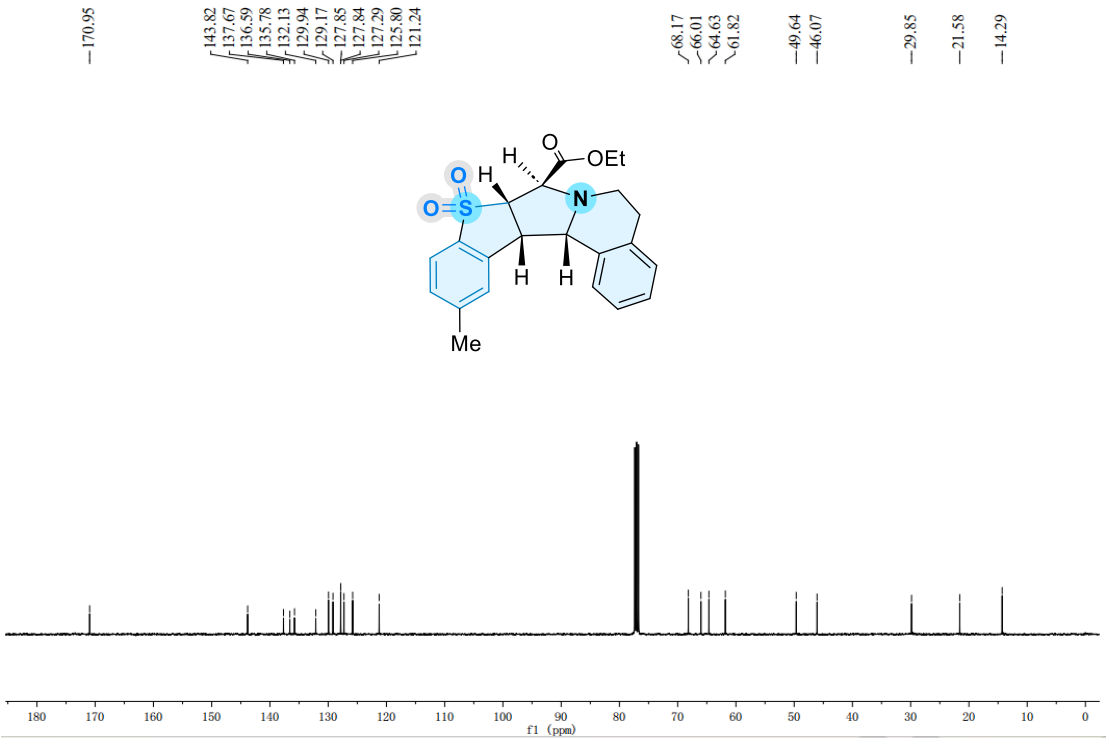
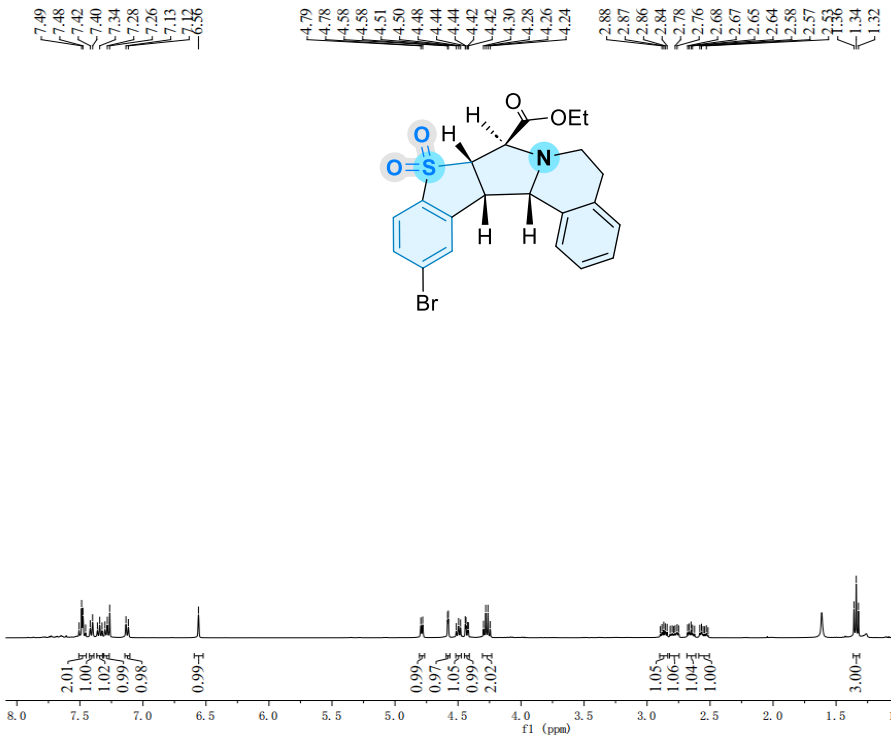


^{13}CNMR of **3g** ($CDCl_3$, 100MH_Z)



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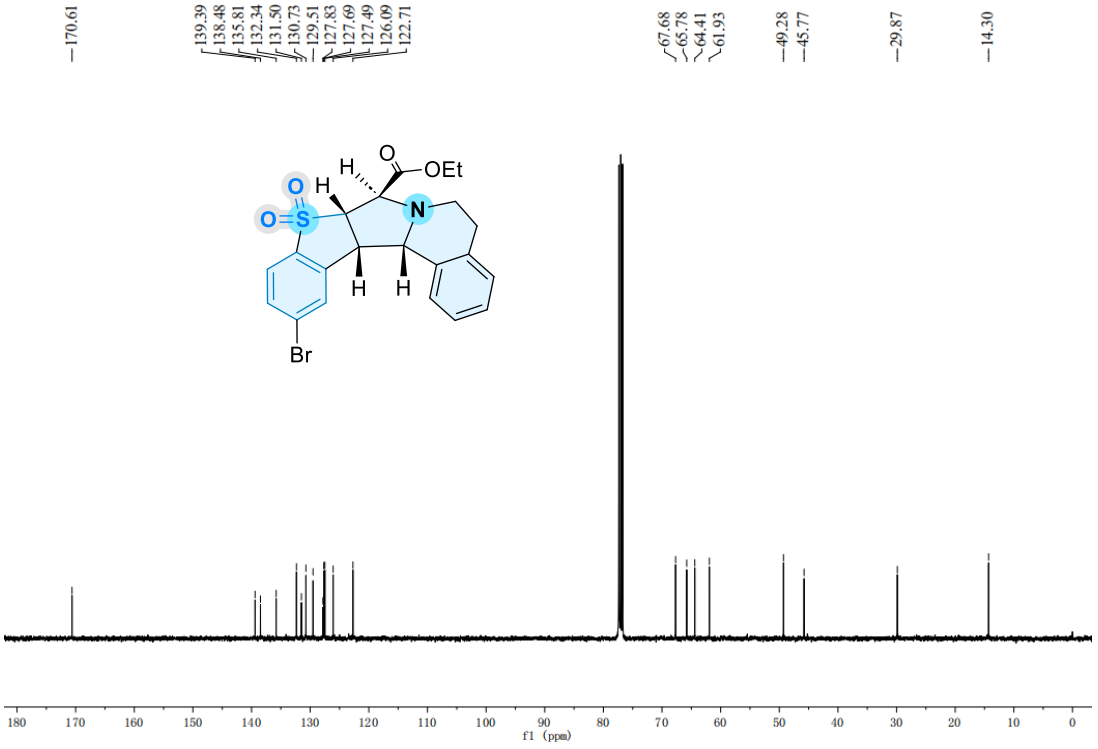
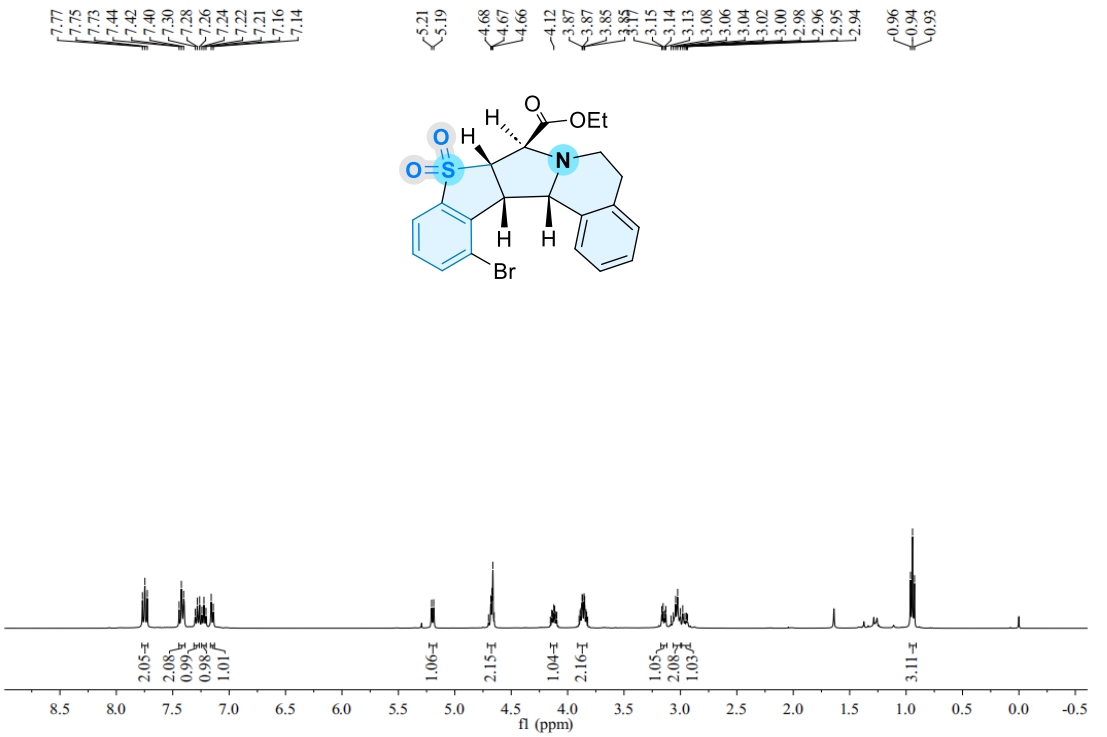
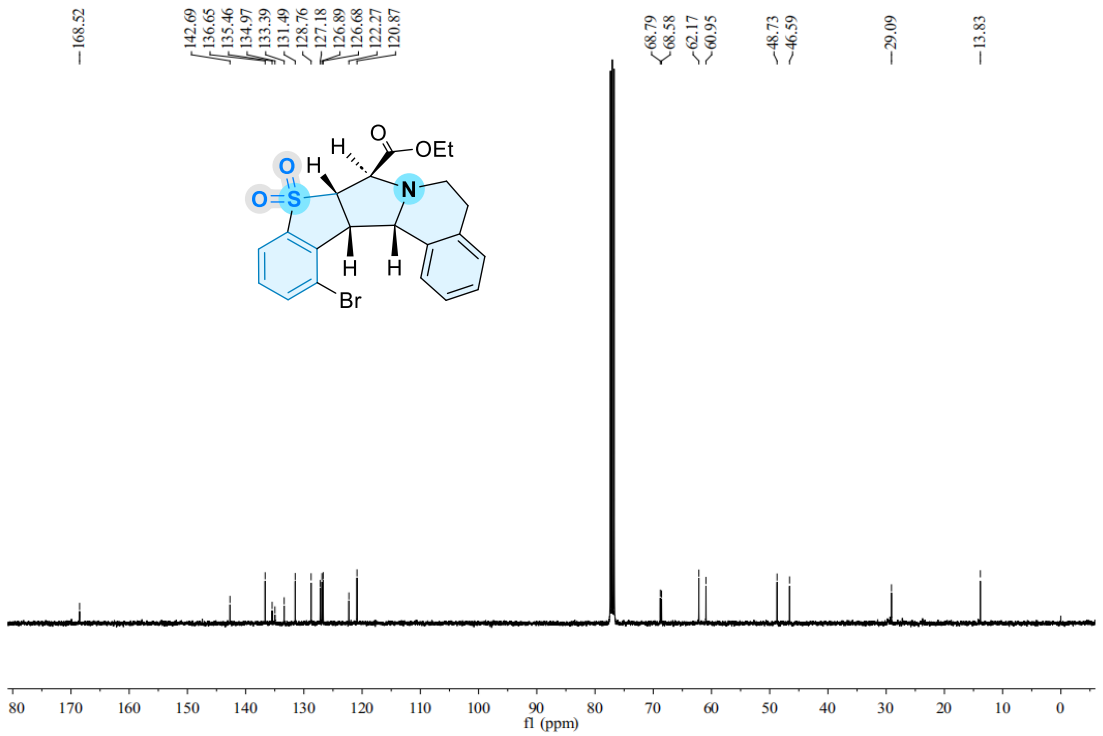


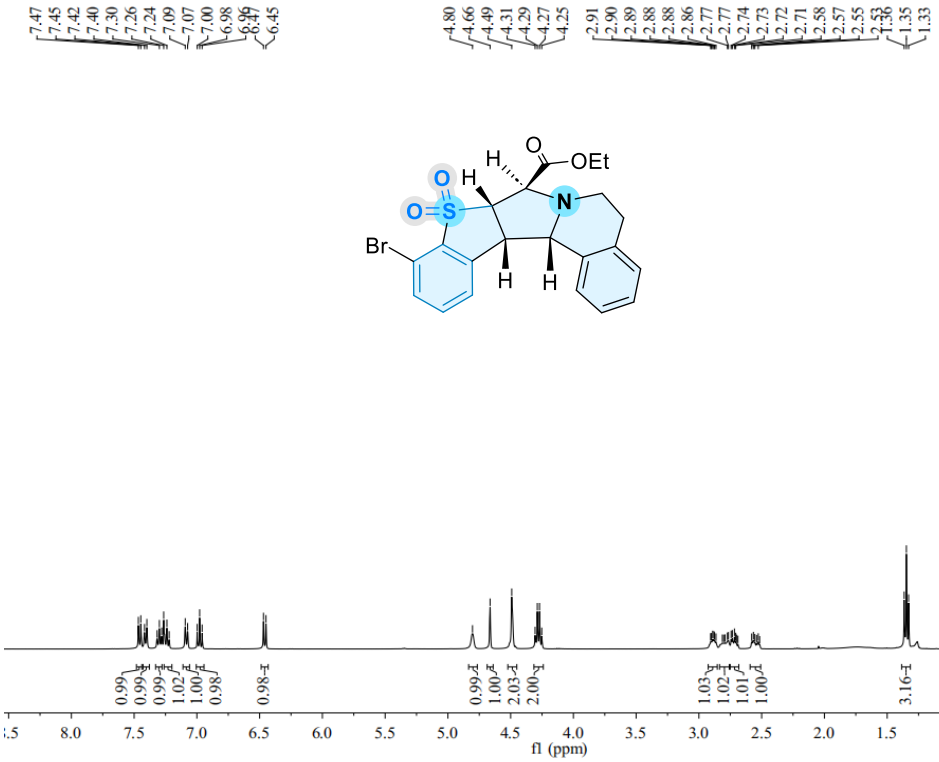
^{13}CNMR of **3h** ($CDCl_3$, 100MH_Z)



^{1}HNMR of **3i** ($CDCl_3$, 400MH_Z)



^{13}CNMR of **3i** ($CDCl_3$, 100MH_Z)



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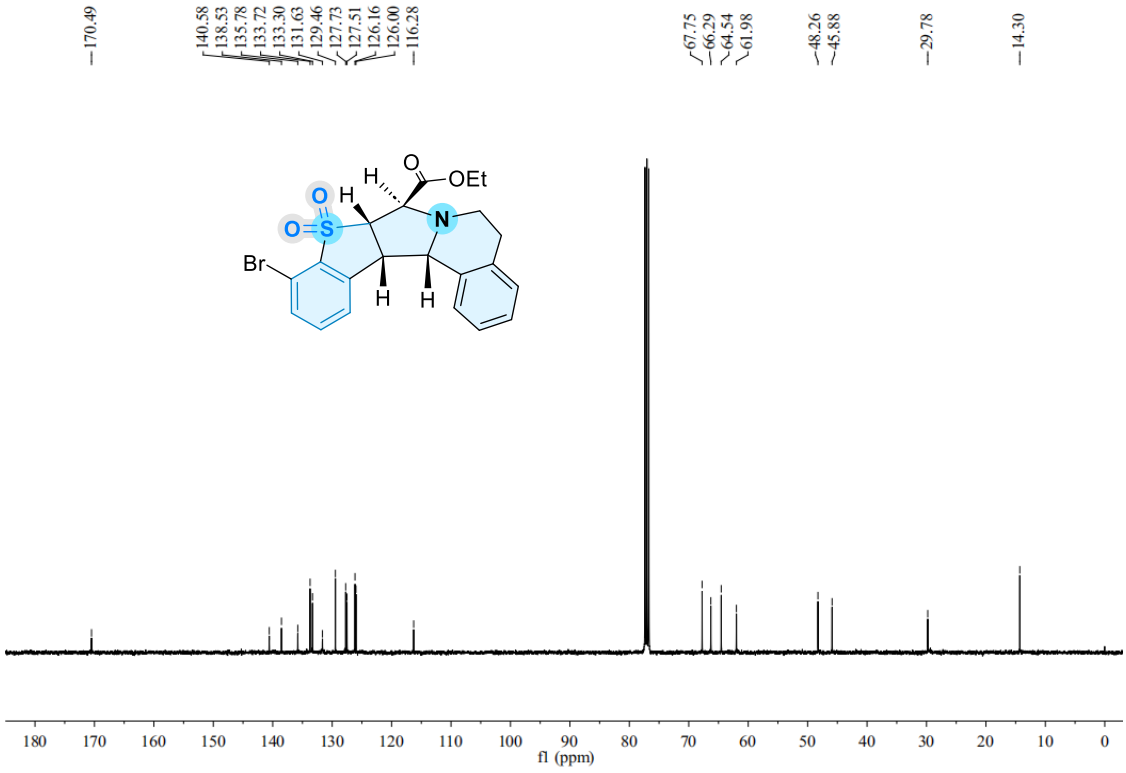

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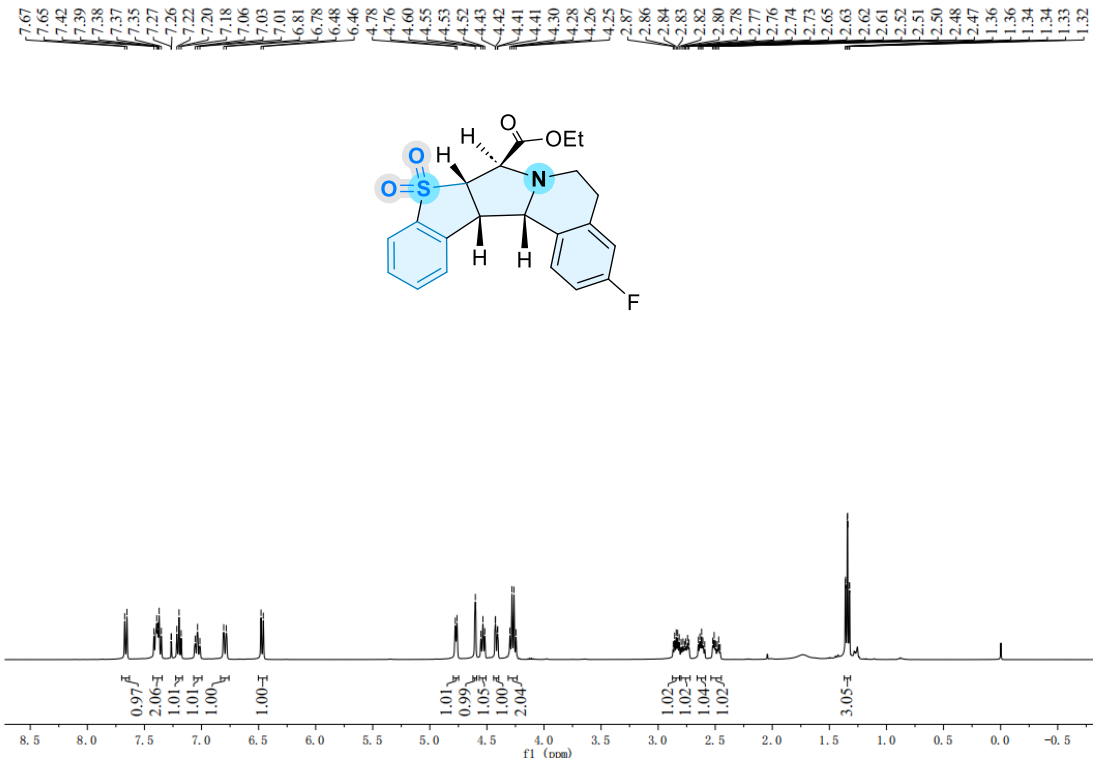

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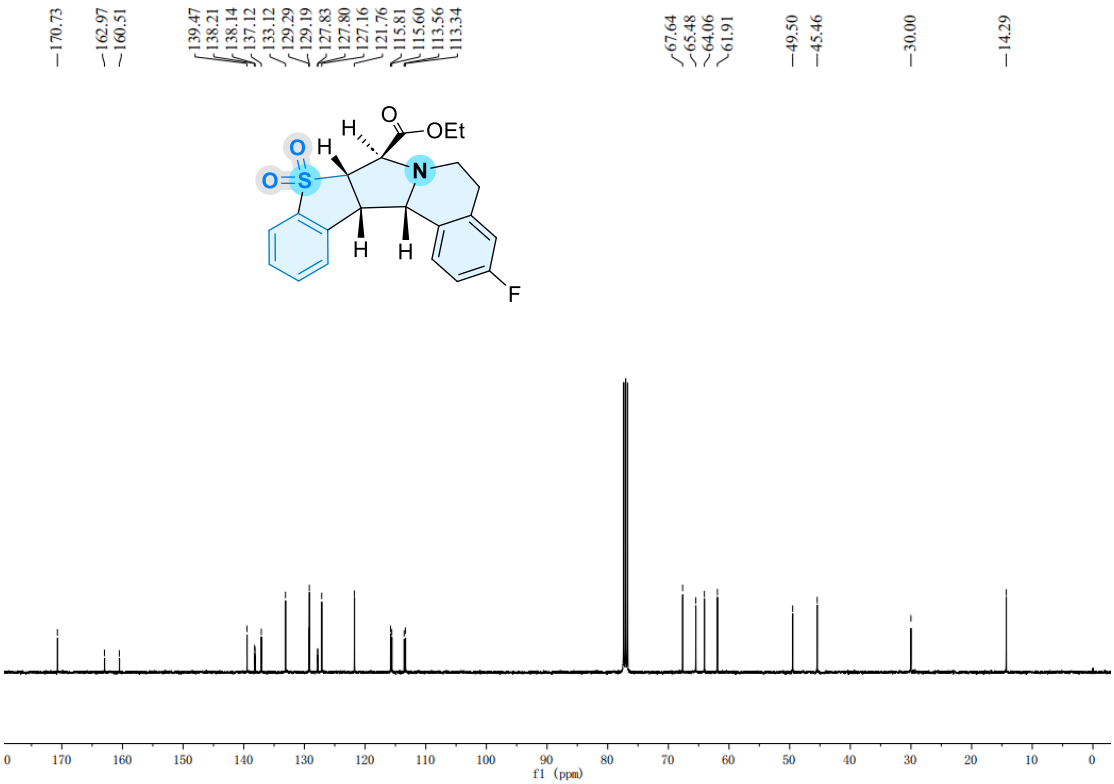

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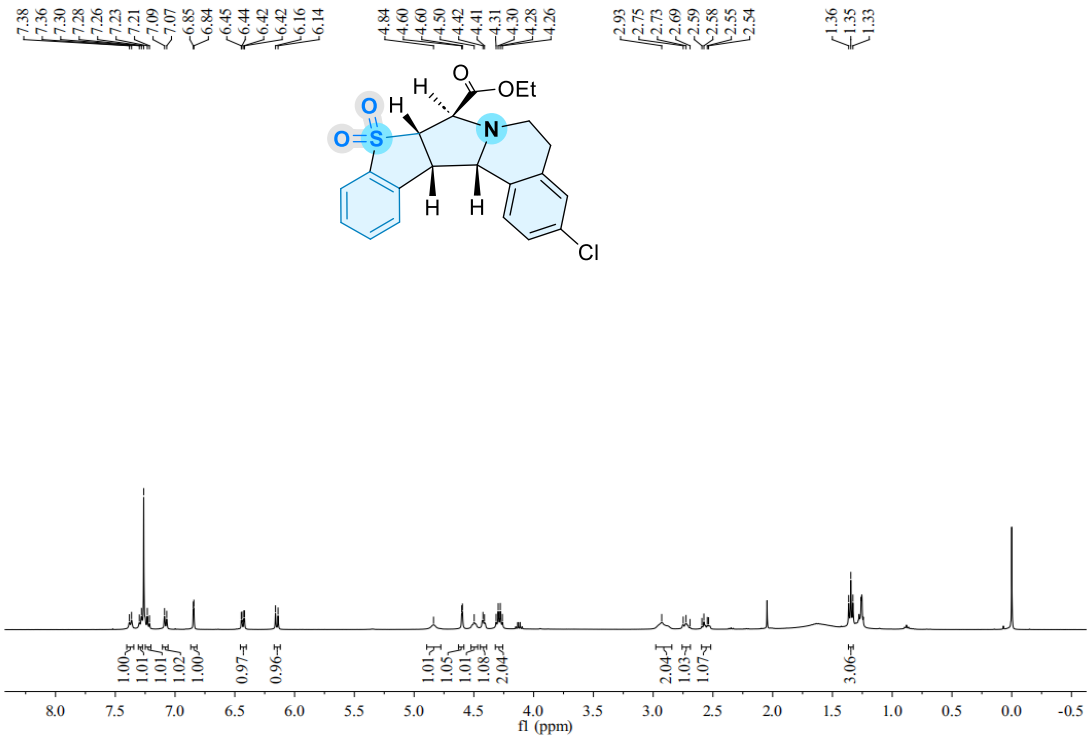

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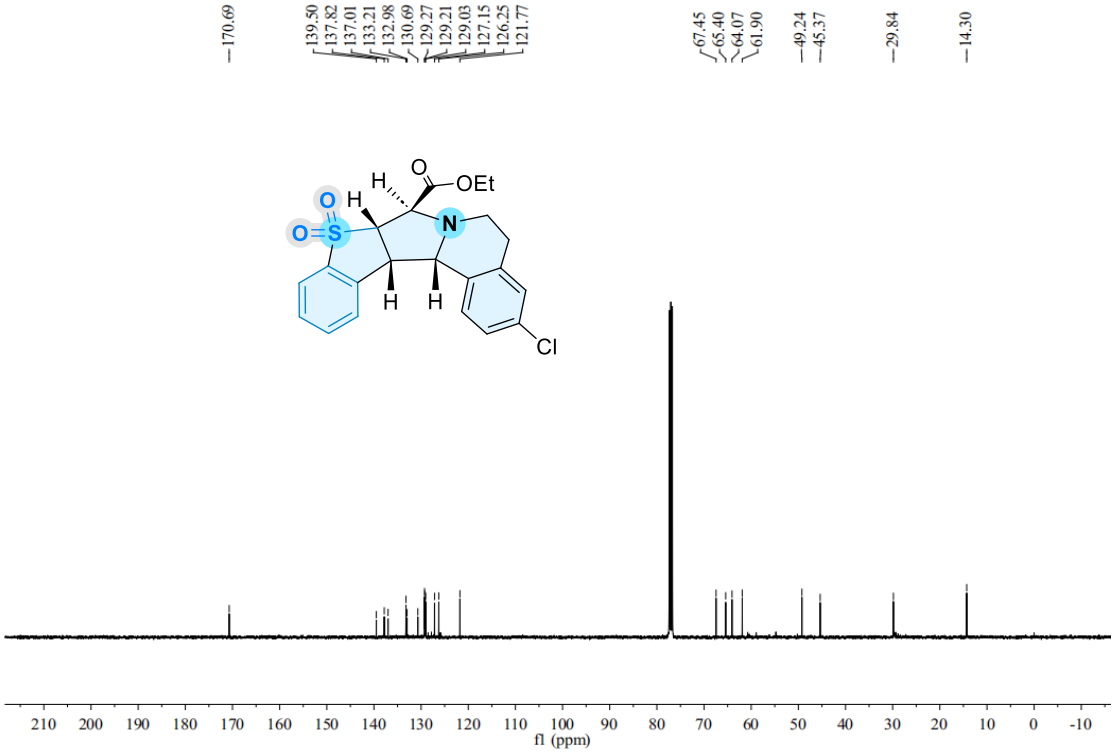

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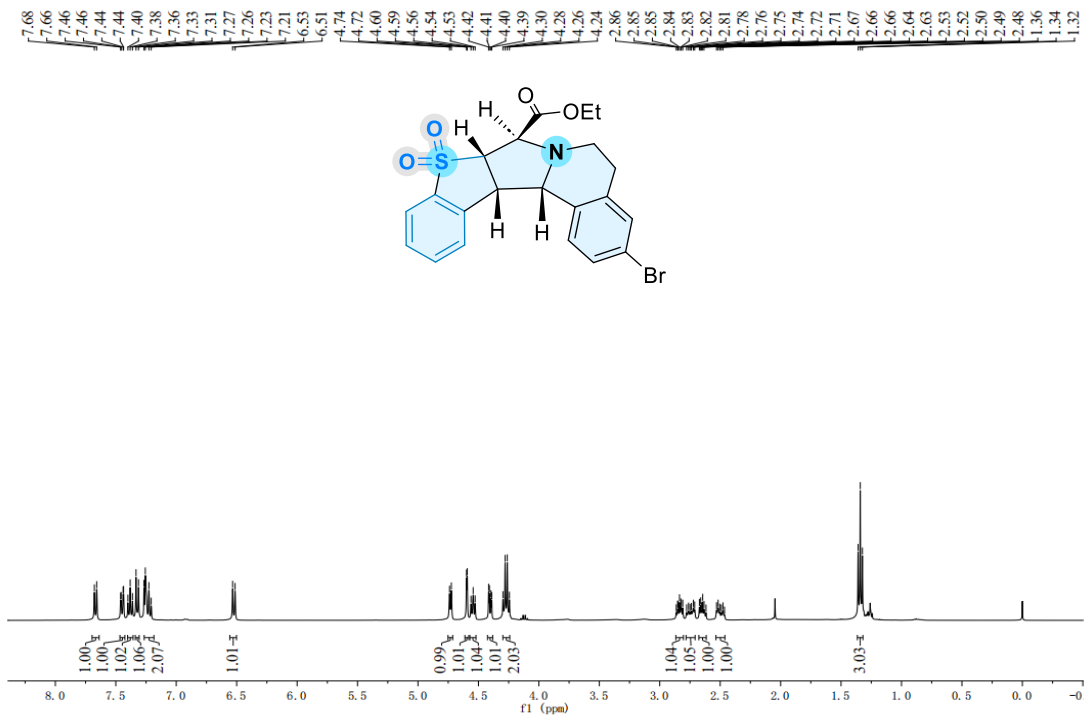
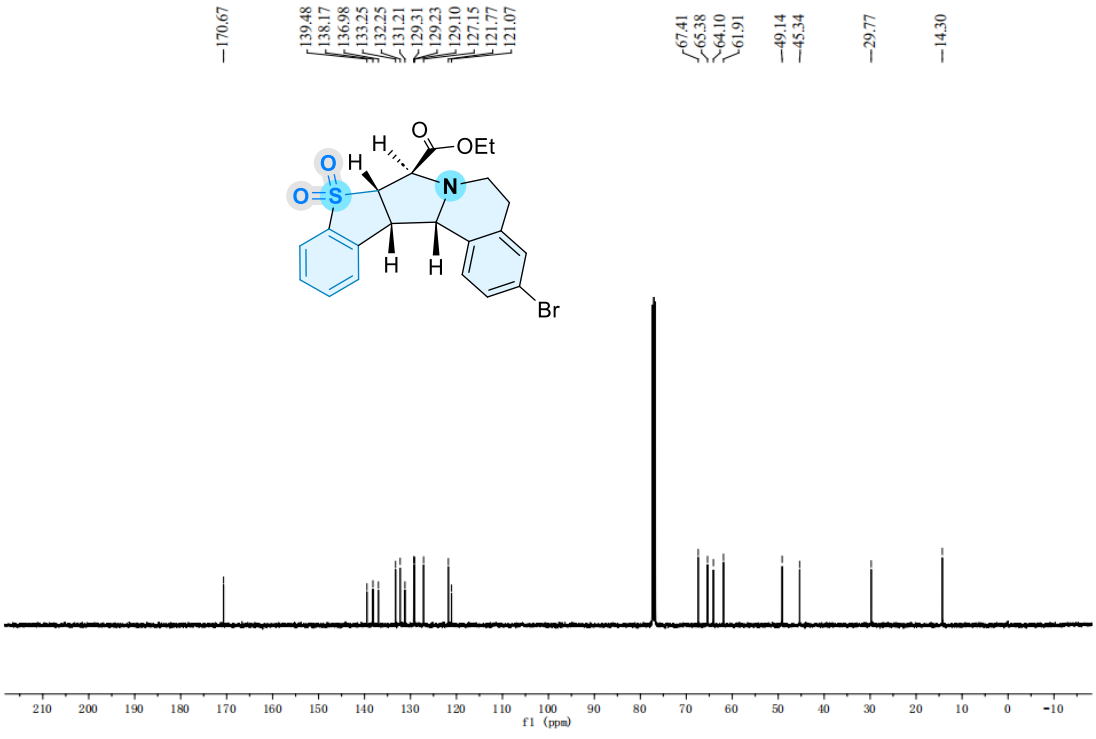


^{1}HNMR of **3m** ($CDCl_3$, 400MH_Z)



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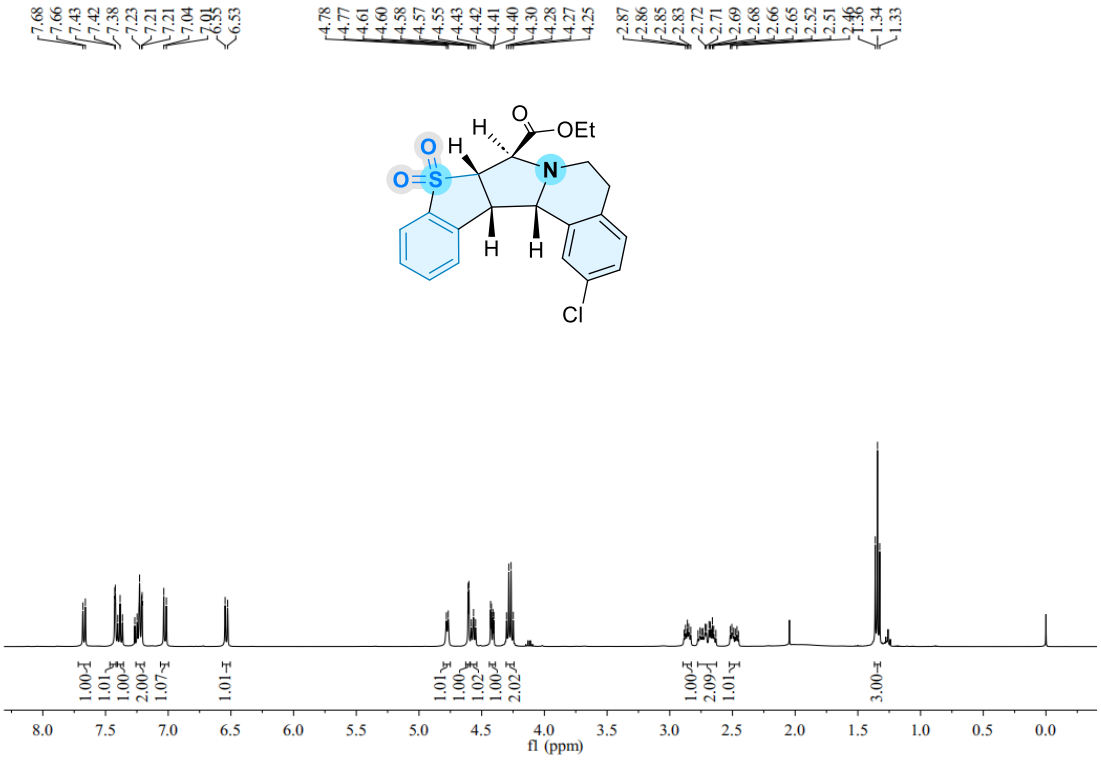

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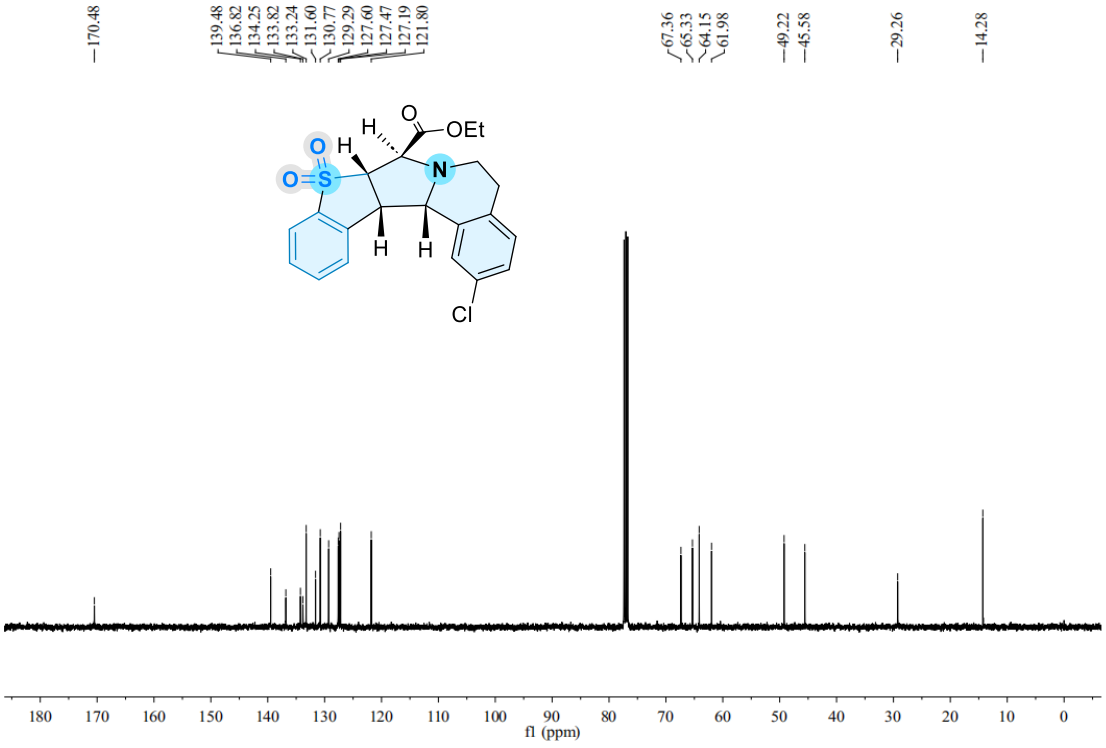

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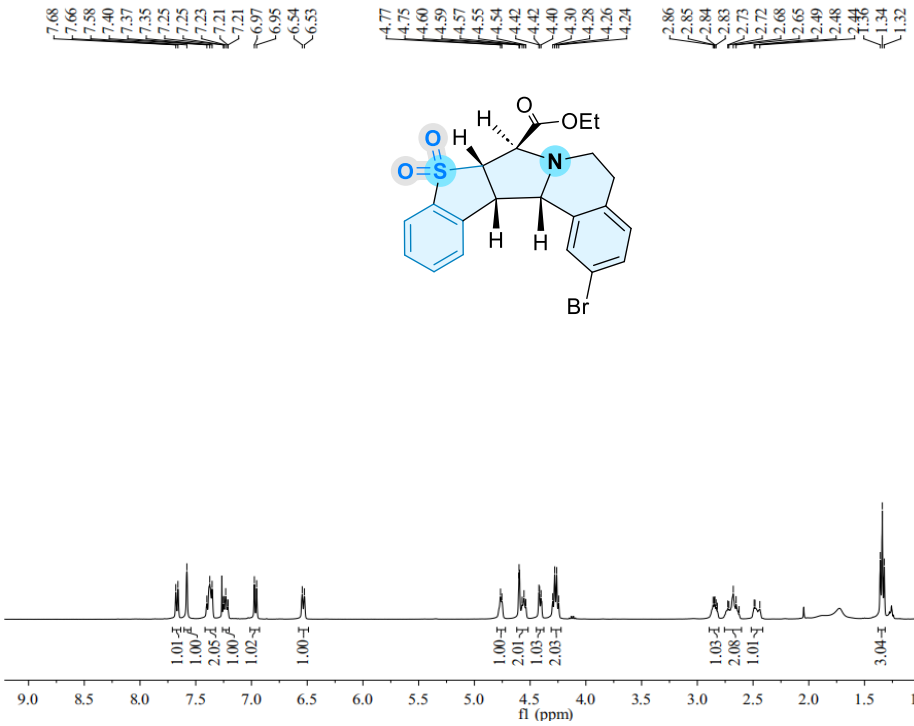
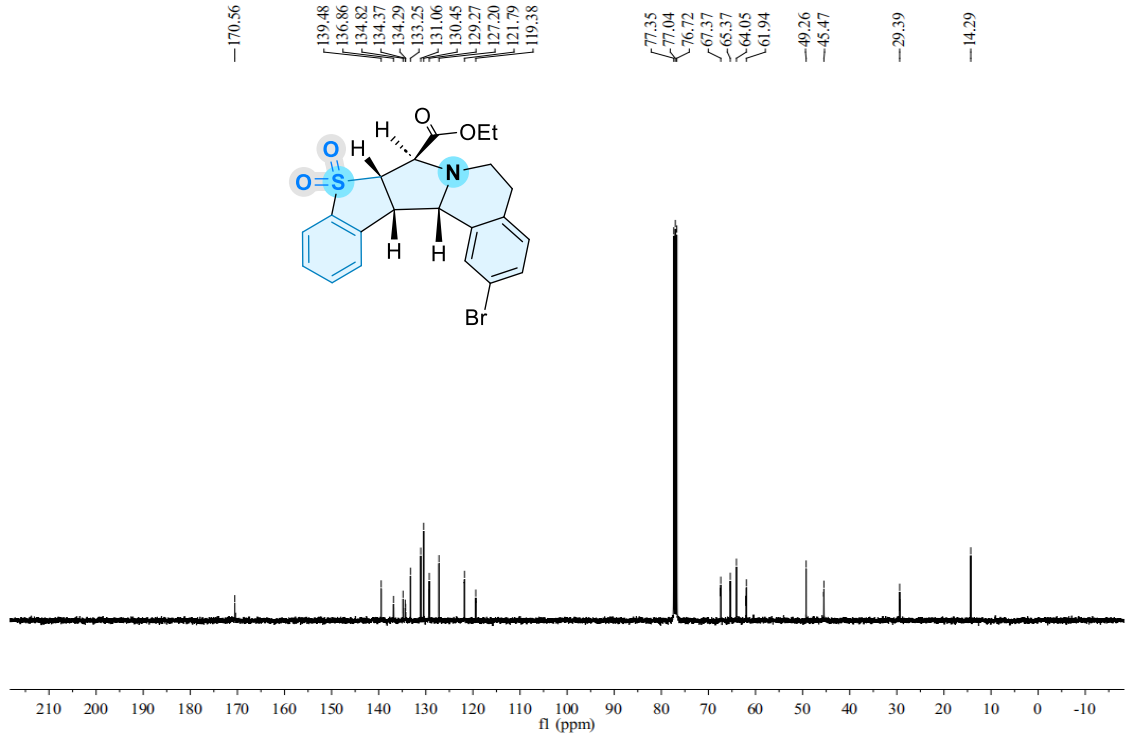
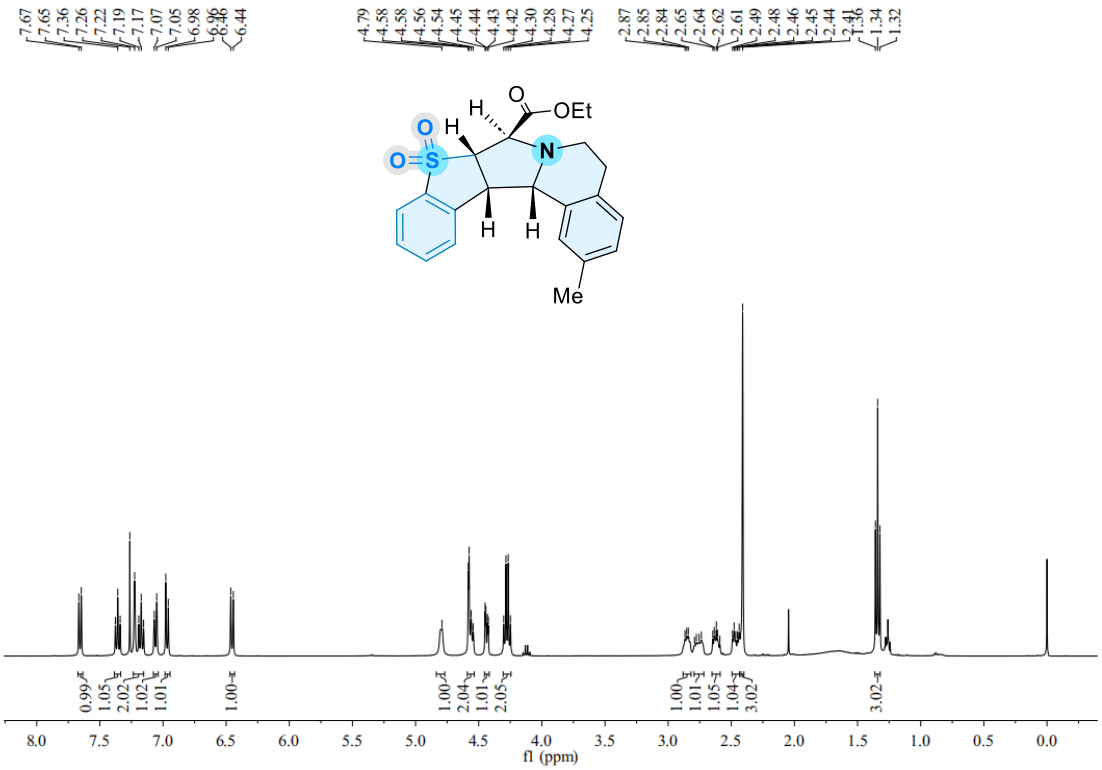


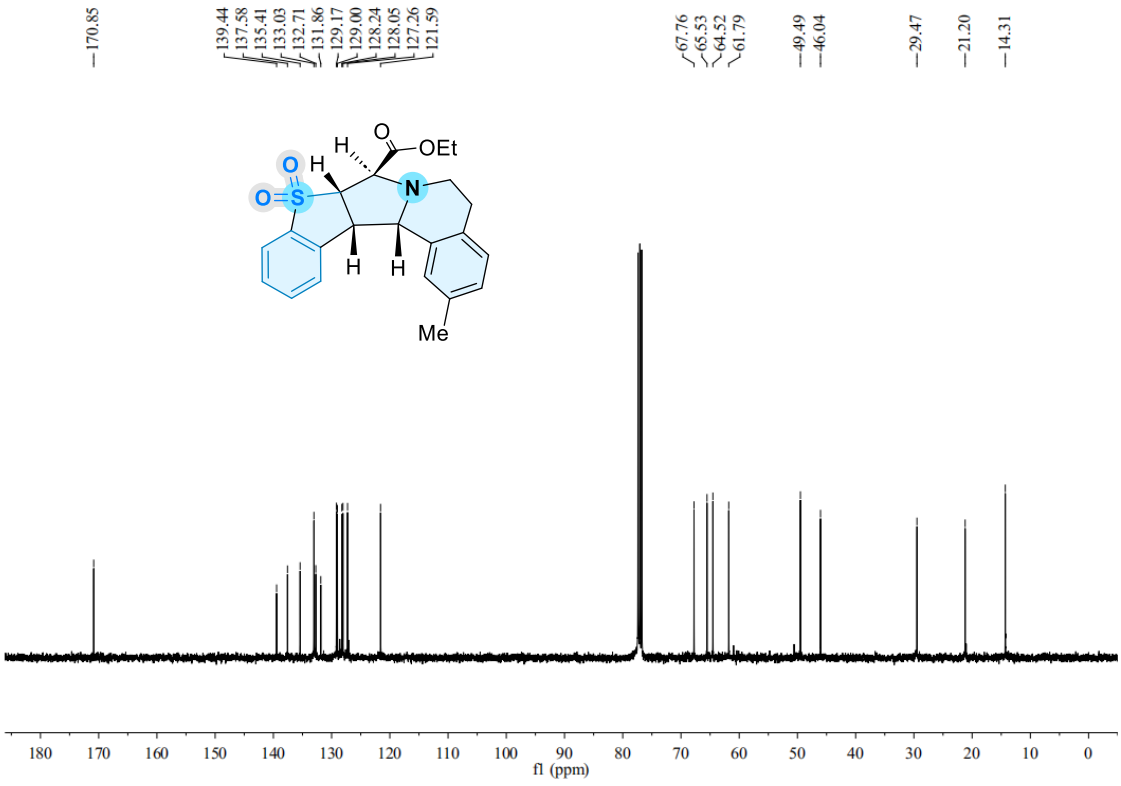
^{1}HNMR of **3o** ($CDCl_3$, 400MH_Z)



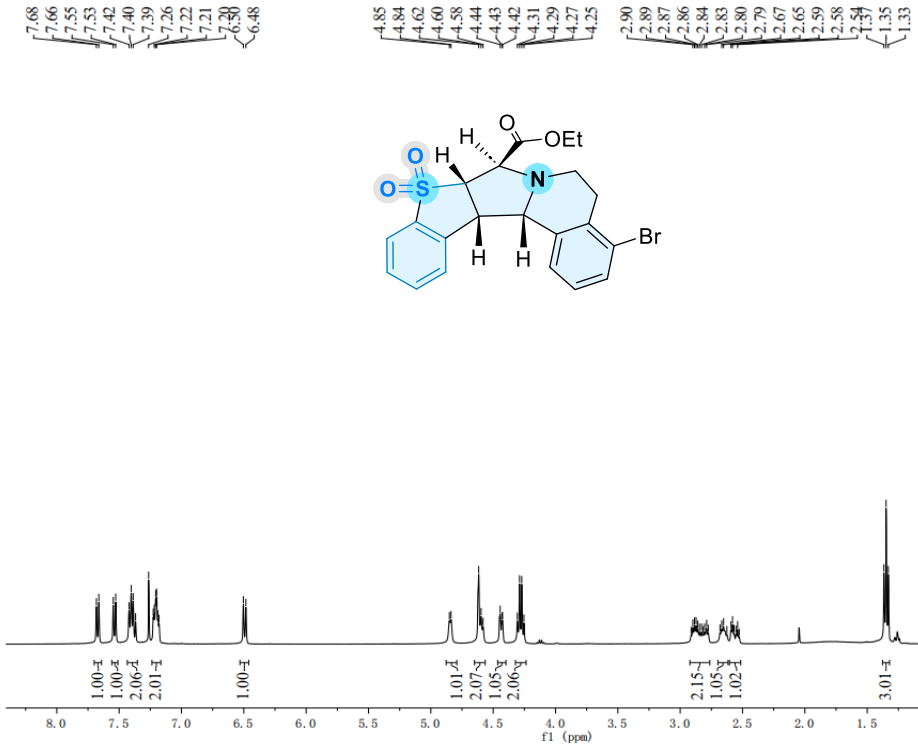
^{13}CNMR of **3o** ($CDCl_3$, 100MH_Z)



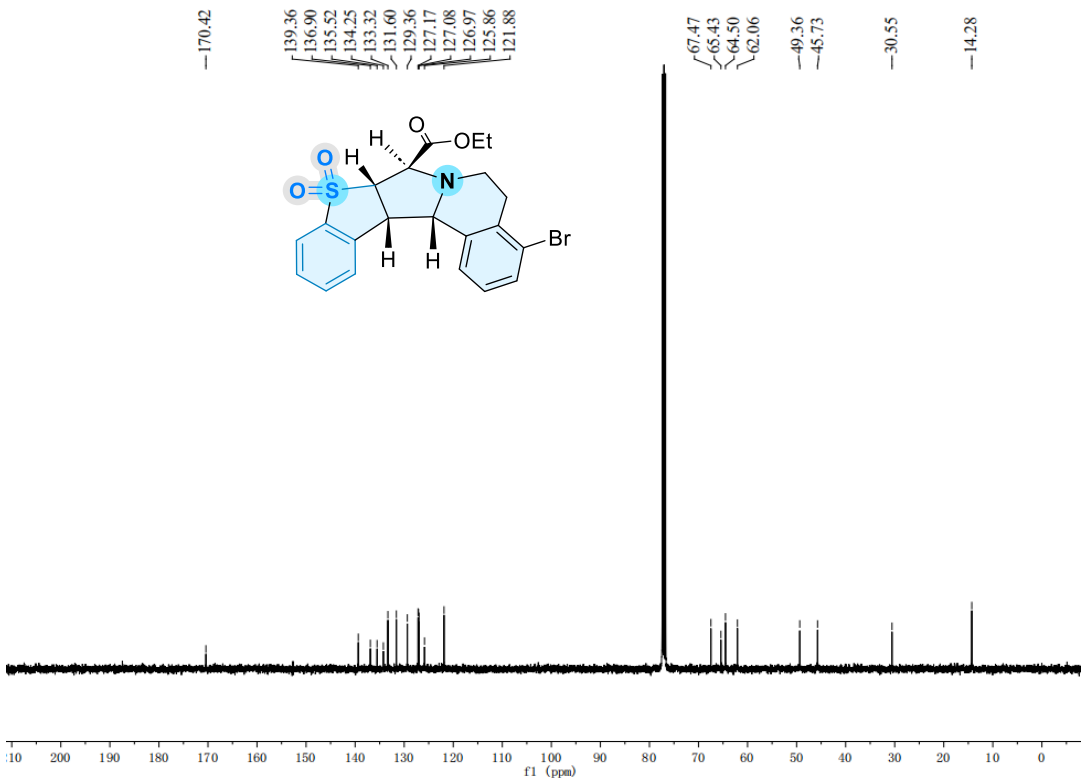
^{1}HNMR of **3p** ($CDCl_3$, 400MHz)



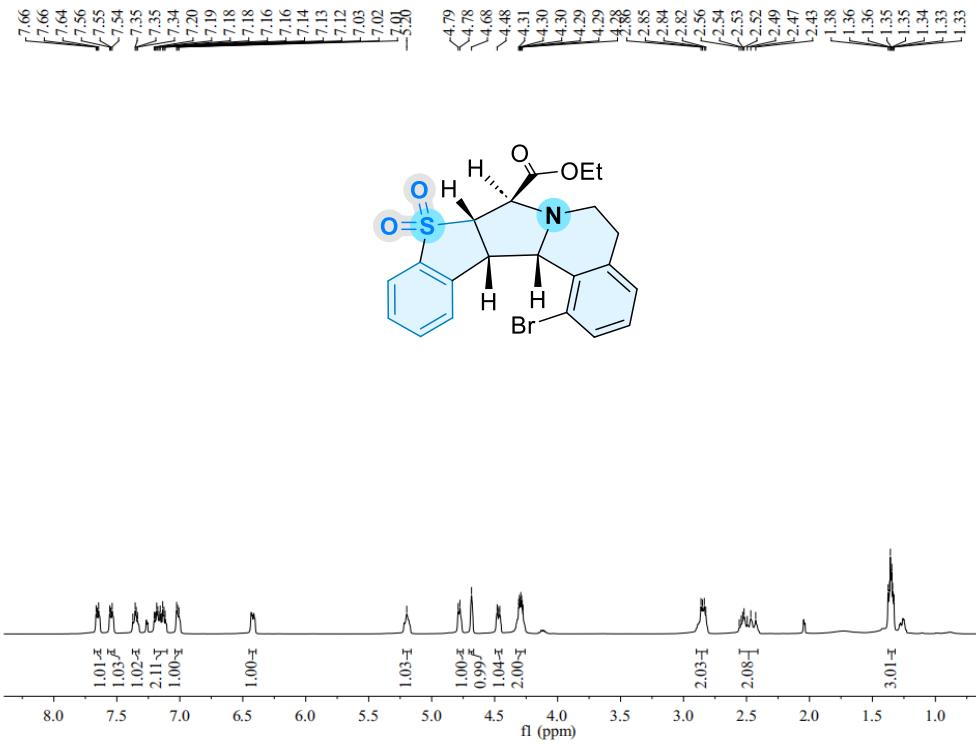
^{13}CNMR of **3p** ($CDCl_3$, 100MHz)



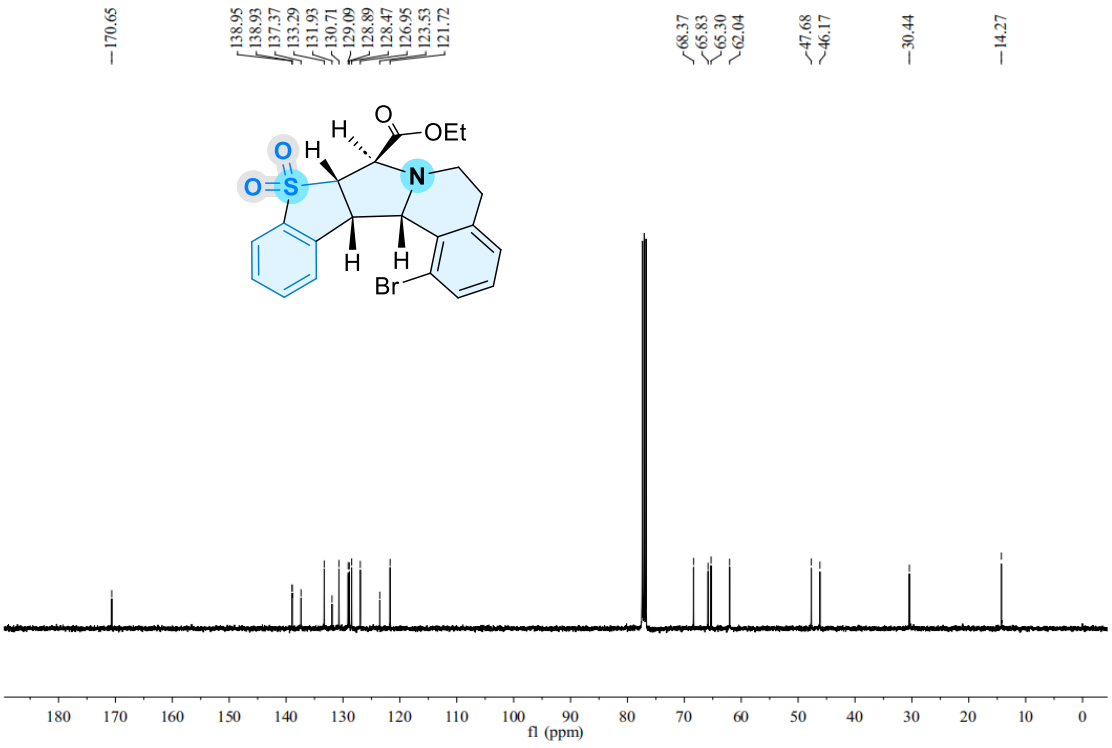
^{1}HNMR of **3q** ($CDCl_3$, 400MHz)



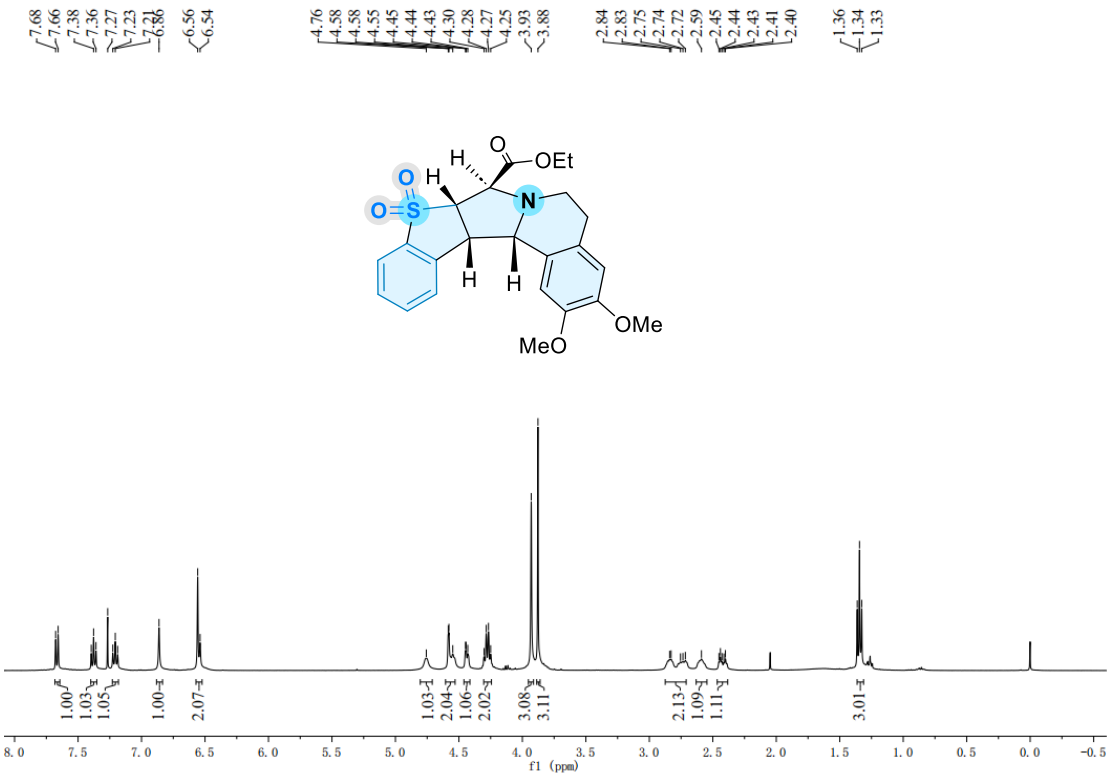
^{13}CNMR of **3q** ($CDCl_3$, 100MHz)



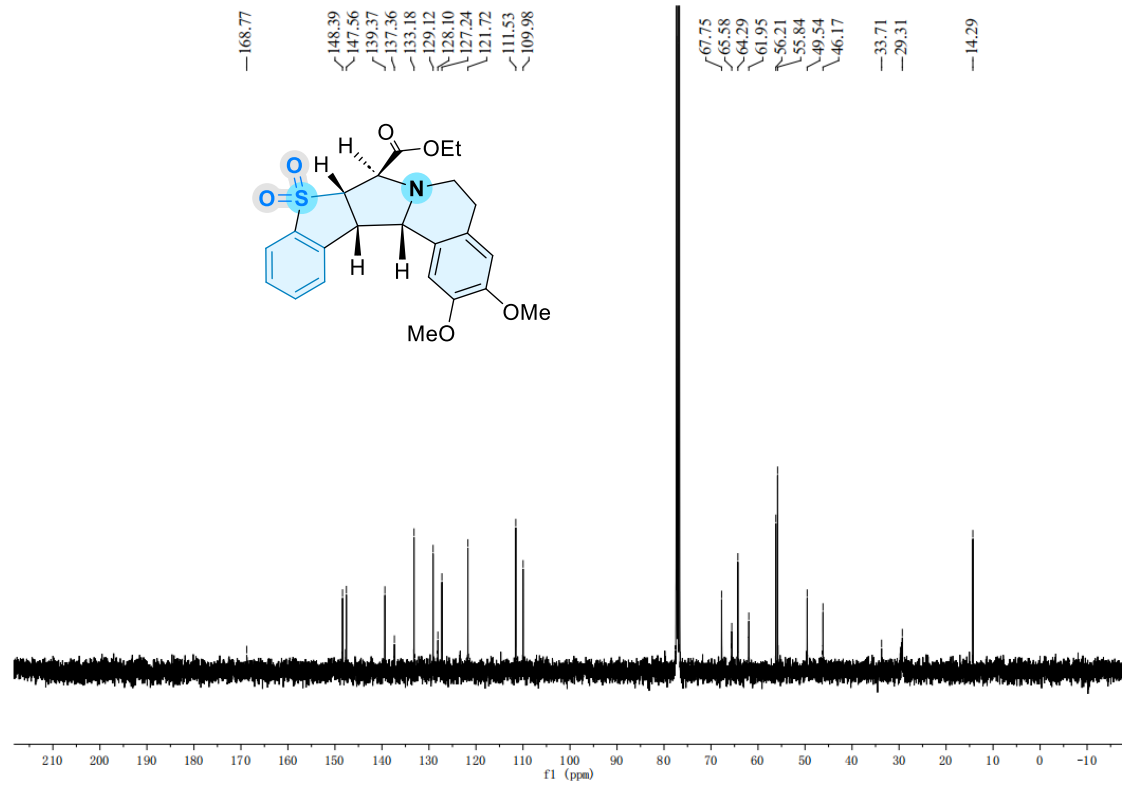
^{1}HNMR of **3r** ($CDCl_3$, 400MHz)



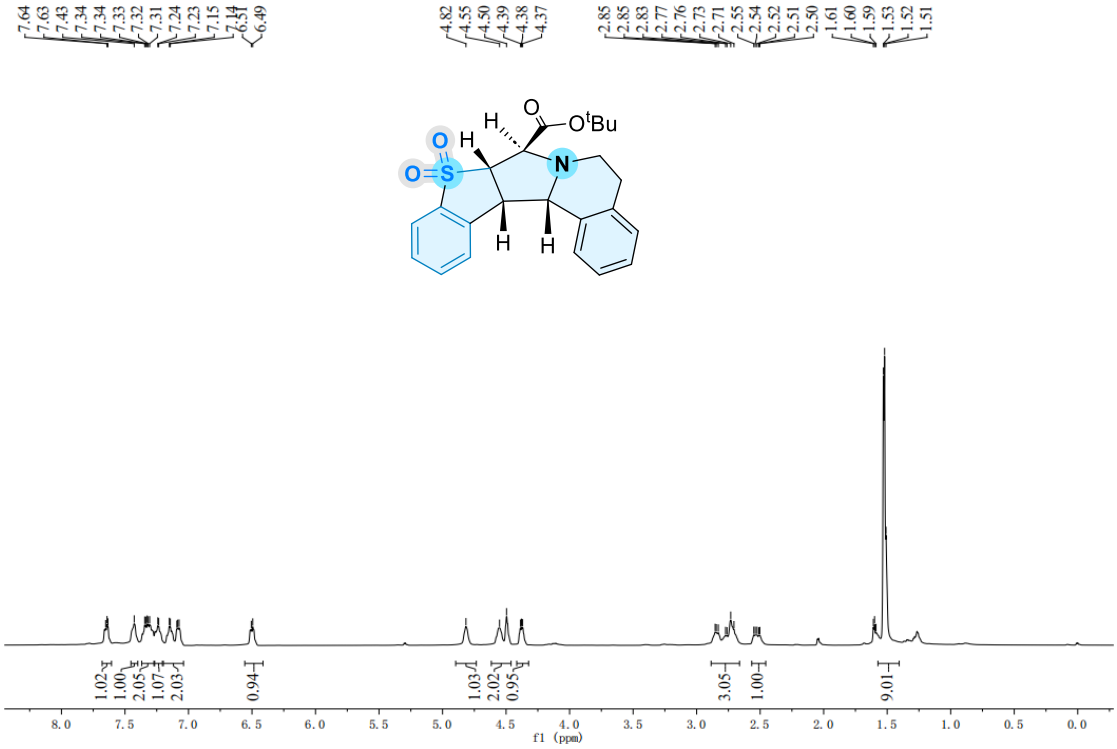
^{13}CNMR of **3r** ($CDCl_3$, 100MHz)



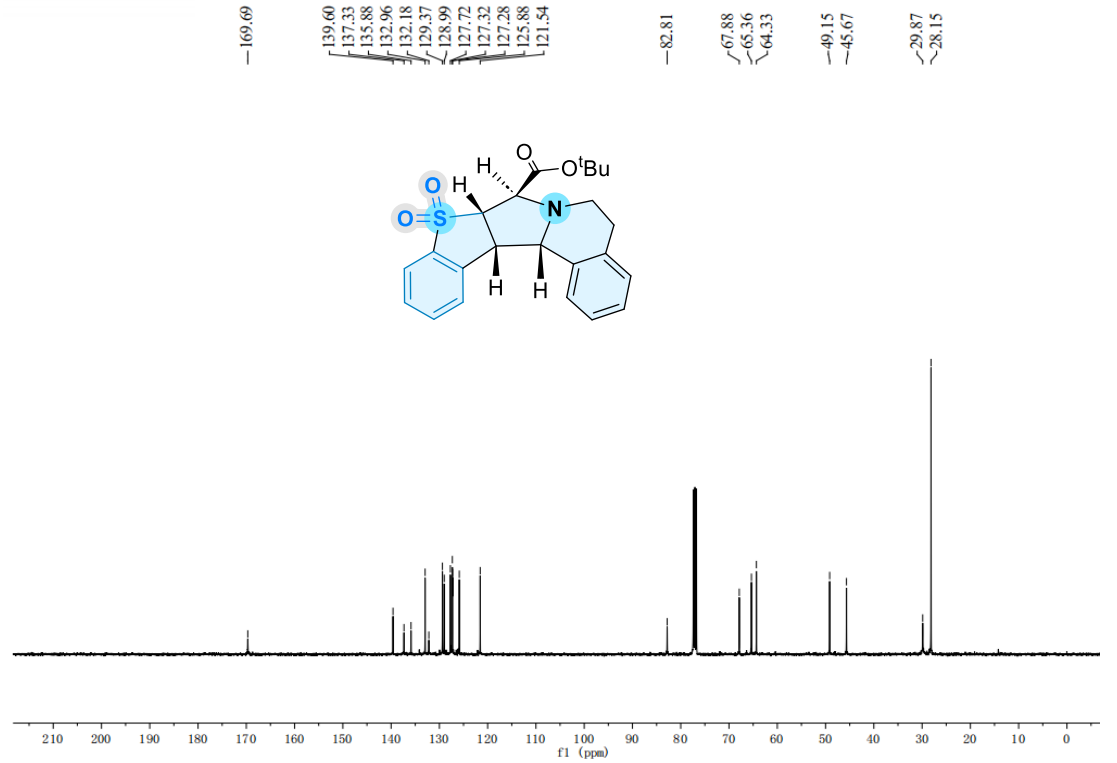
^{1}HNMR of **3s** ($CDCl_3$, 400MHz)



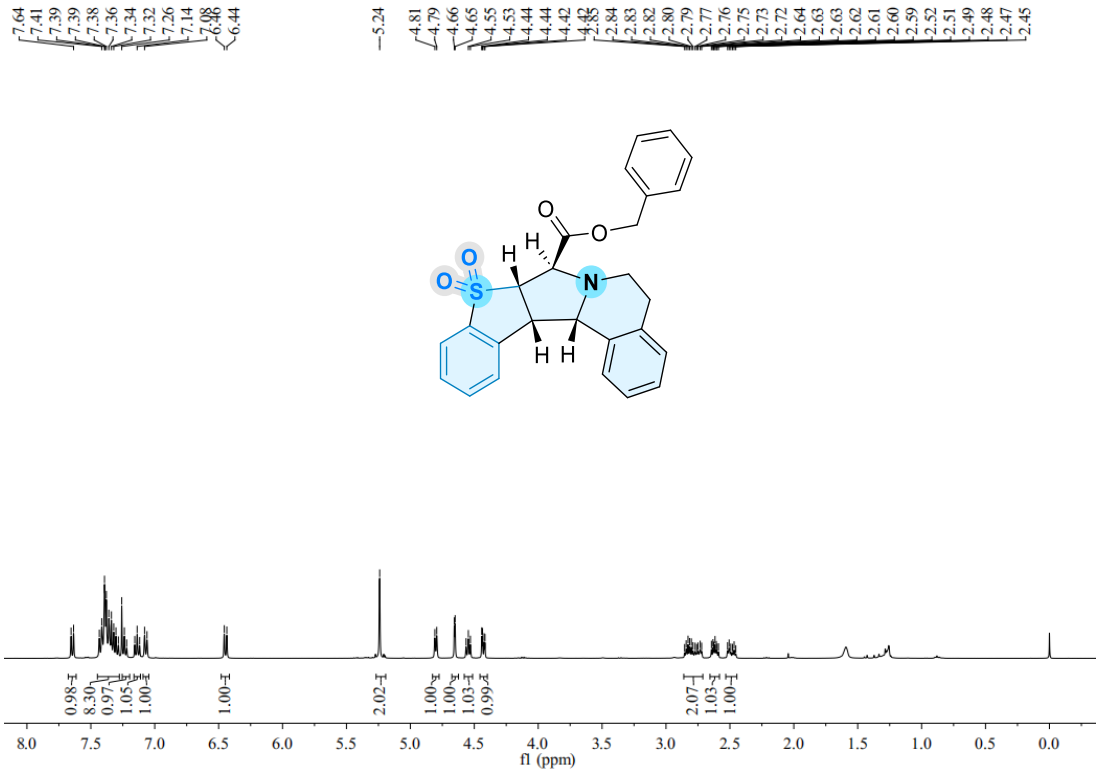
^{13}CNMR of **3s** ($CDCl_3$, 100MHz)



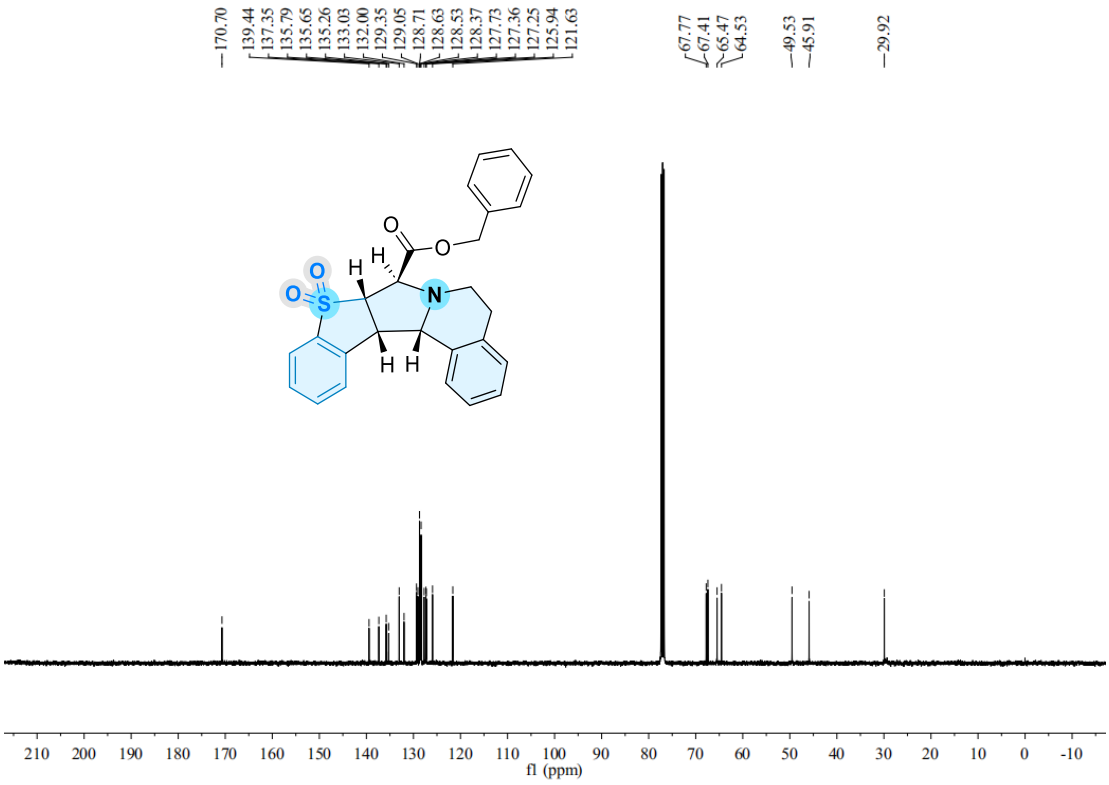
^{1}HNMR of **3t** ($CDCl_3$, 400MH_Z)



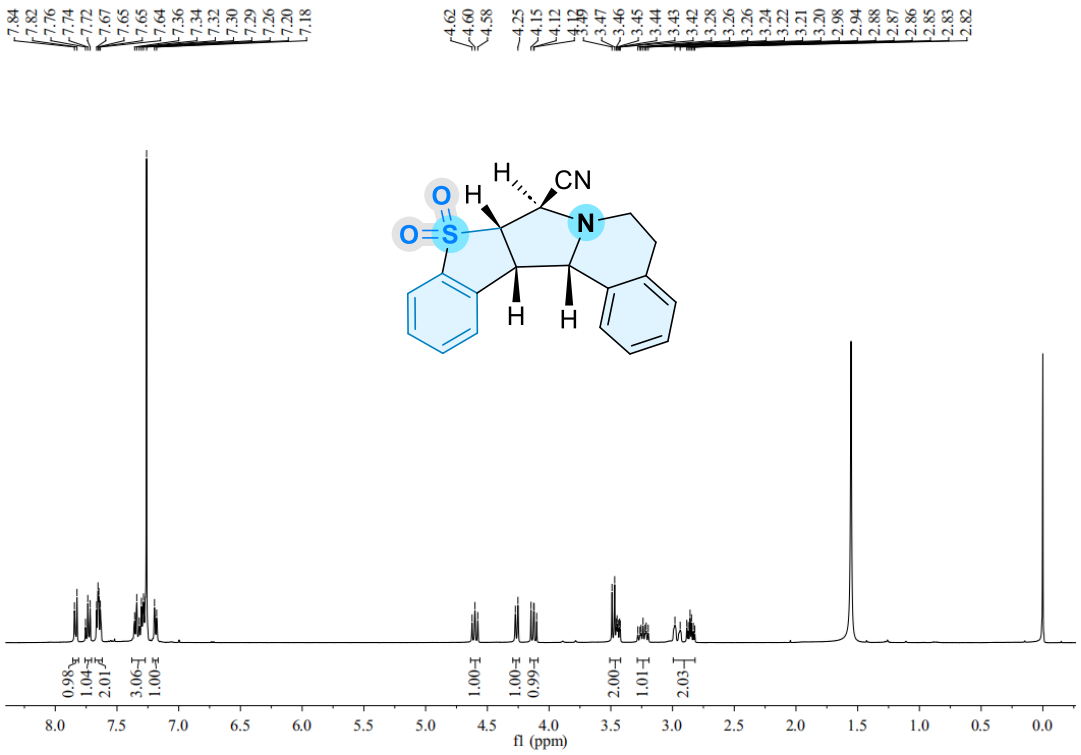
^{13}CNMR of **3t** ($CDCl_3$, 100MH_Z)



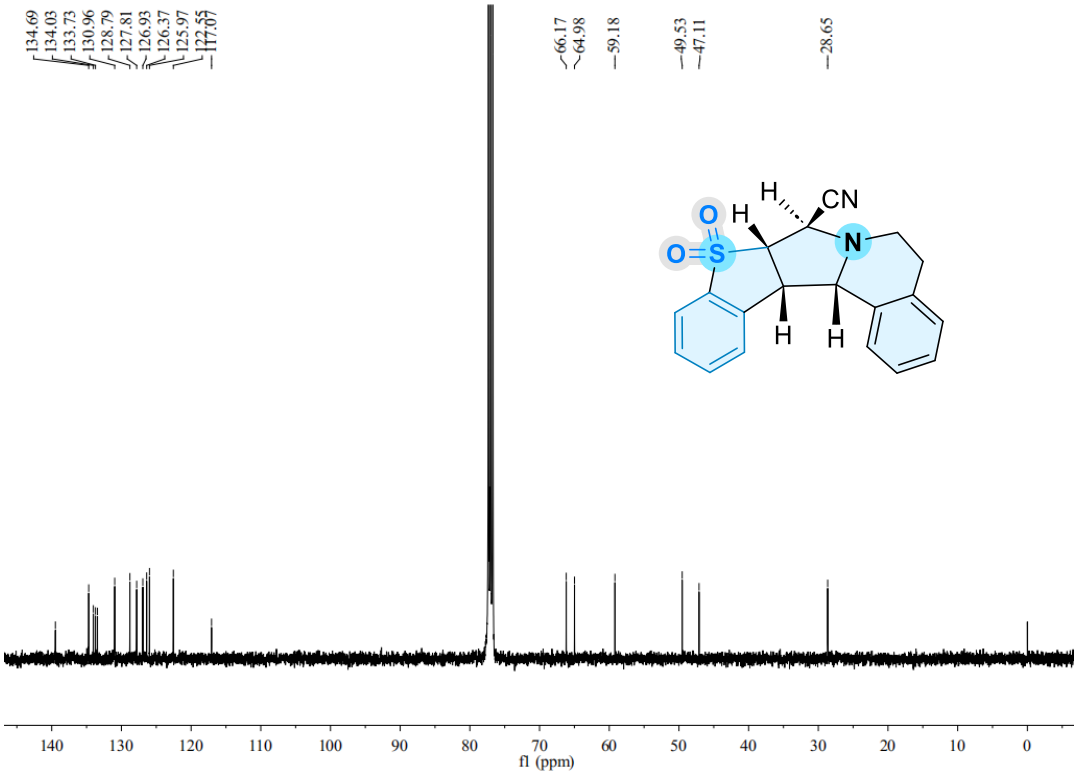
^{1}HNMR of **3u** ($CDCl_3$, 400MHz)



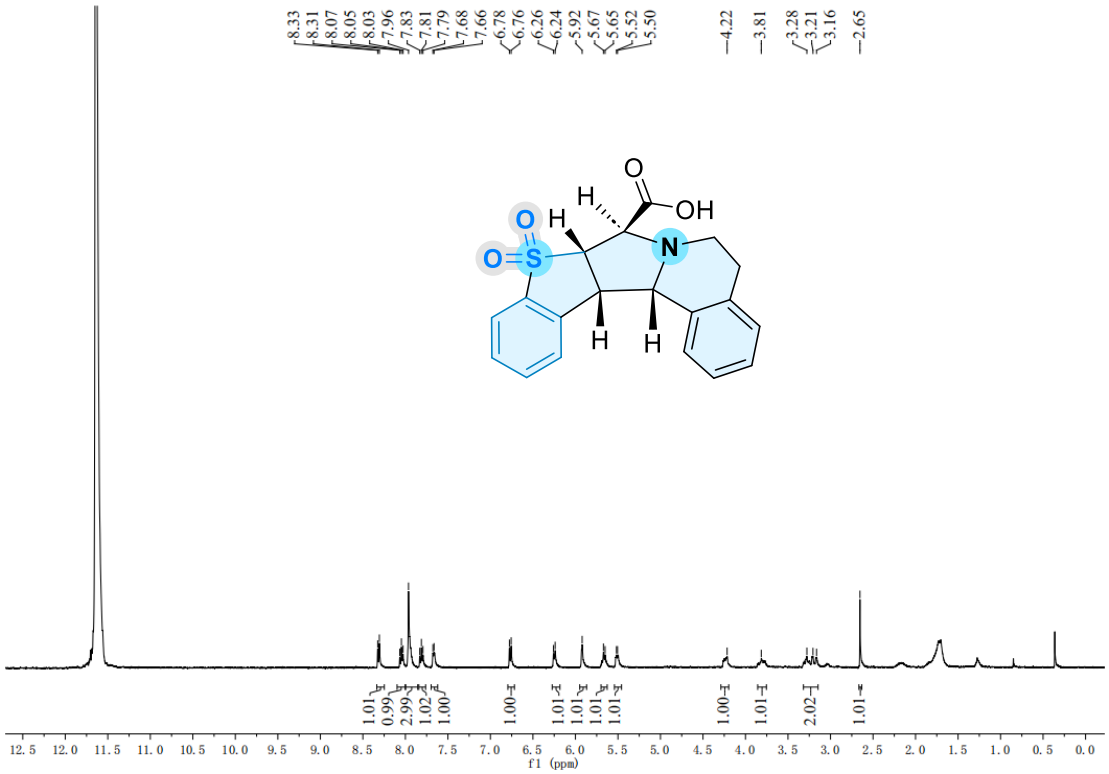
^{13}CNMR of **3u** ($CDCl_3$, 100MHz)



^{1}HNMR of **3v** ($CDCl_3$, 400MHZ)



^{13}CNMR of **3v** ($CDCl_3$, 100MHZ)



^{1}HNMR of **4a** (CF_3COOD, 400 MHz)