

Enantioselective Synthesis of Tetrahydropyridines/Piperidines via Stepwise [4+2]/[2+2] Cyclizations†

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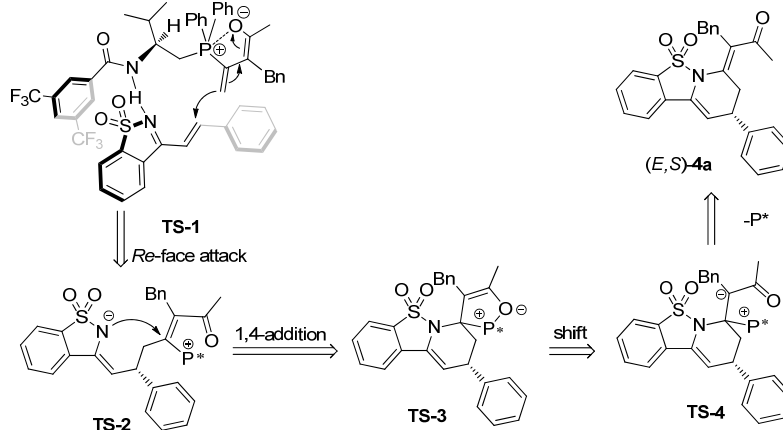
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(A) General Information:

All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated. ^1H and ^{13}C NMR spectra were recorded on a Agilent 400MR (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.1). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants were reported in Hertz (Hz). All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. For thin layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine, or ceric ammonium molybdate followed by heating on a hot plate. Flash chromatographic separations were performed on Merck 60 (0.040- 0.063 mm) mesh silica gel. Optical rotations were reported as follows: $[\alpha]_{\text{D}}^{\text{T}}$ (c: g/100 mL, in solvent). The enantiomeric excesses of products were determined by chiral-phase HPLC analysis, using a Daicel Chiralcel AD-H column (250 x 4.6 mm).

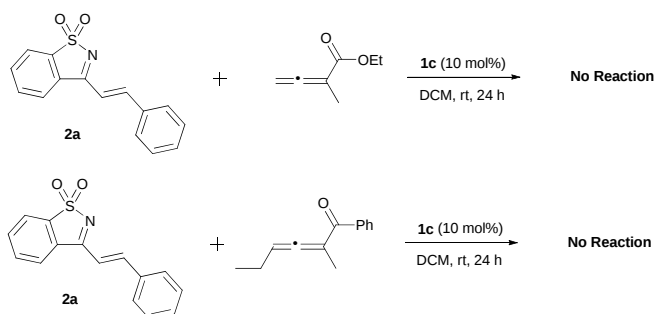
The 1-azadienes were prepared according to reported procedure.^[1] The allenones were prepared according to reported procedure.^[2] The phosphine catalysts were prepared by our previously reported procedures.^[3]

(B) Proposed transition state for phosphine-catalyzed [4+2]-annulation



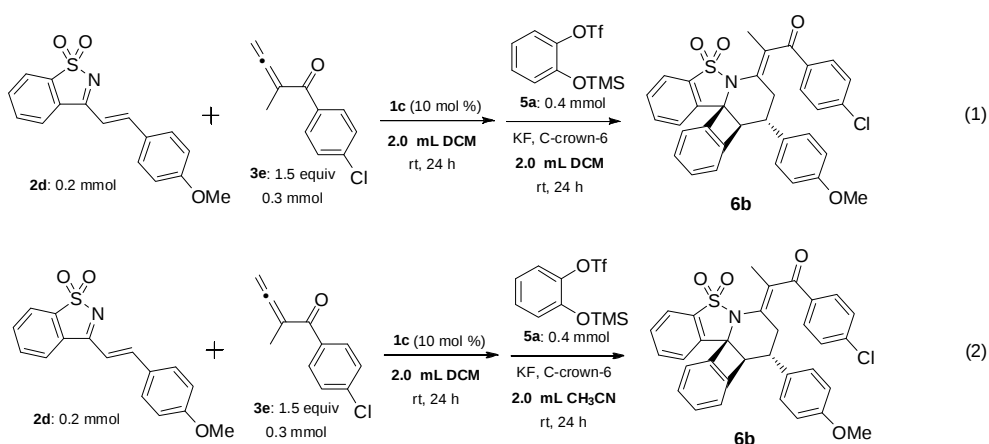
The intermolecular hydrogen bond was proposed to be formed between amide moiety of chiral phosphine and 1-azadiene substrate. The phosphonium dienolate intermediate, generated from the nucleophilic attack of the phosphine catalyst at the allenone (**TS-1**), attacked the *Re*-face of 1-azadiene to afford the [4+2]-annulation adduct **4a** with (*S*)-configuration. On the other hand, intramolecular aza 1,4-addition of **TS2** formed the **TS3**. The interaction between phosphonium and enolate may be crucial for formation of the *E*-isomer of the product **4a**.

(C) Other substrate participating reaction



When α -methyl-allenoates and γ -substituted allenones were used, no reaction took place under standard reaction conditions.

(D) One-pot [4+2]/[2+2] reaction



One-pot [4+2]/[2+2] reaction without purification: the reaction got only 10% yield of **6b** and 60% yield of [4+2]-cycloaddition product in DCM (eq 1). The yield of **6b** could be improved to 40%, when [2+2]-cycloaddition took place in CH₃CN (eq 2; removed the DCM after the [4+2]-cycloaddition).

(E) Representative procedure for [4+2] cycloaddition of allene ketones with 1-azadienes:

A dry reaction tube was charged with the phosphine **1c** (0.02 mmol), 1-azadiene (**2a**) (0.2 mmol), allene ketones (**3a**) (0.3 mmol). Then, DCM (2.0 mL) was added and the mixture was stirred at room temperature for 24 h. Separation by column chromatography on silica gel with hexane/ethyl acetate (10:1-6:1) afforded the desired [4+2] product **4a** in 61% yield and 99% *ee* with (*S*)-configuration.

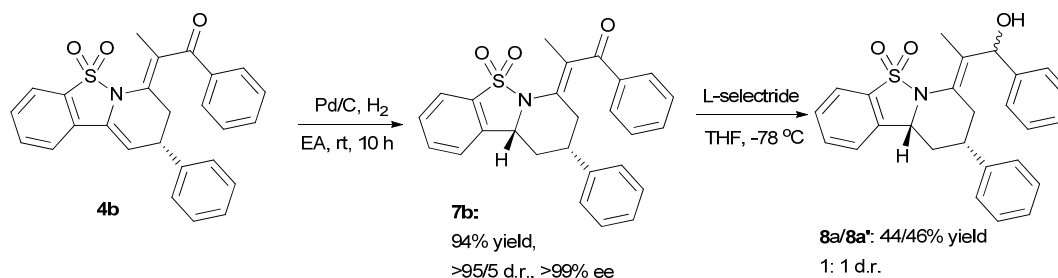
Scale-up synthesis of **4n**:

A dry reaction round-bottom flask was charged with the phosphine **1c** (0.35 mmol), 1-azadiene (**2a**) (3.50 mmol), allene ketones (**3e**) (5.20 mmol). Then, DCM (20.0 mL) was added and the mixture was stirred at room temperature for 48 h. Subsequently, the solvent was removed under vacuum and the crude residue was purified by column chromatography on silica gel with hexane/ethyl acetate (10:1-6:1) afforded the desired [4+2] product **4n** in 81% yield (1.30 g) and 98% *ee*.

(F) Representative procedure for [2+2] cycloaddition:

A dry reaction tube was charged with [4+2] product **4a** (0.1 mmol), 18-crown-6 (0.3 mmol), KF (0.3 mmol) and CH₃CN (1.0 mL). Then, 2-(trimethylsilyl)aryl triflate **5** (0.2 mmol) was added and the mixture was stirred at room temperature for 24 h. The reaction was quenched by H₂O (10.0 mL) and extracted with EA (10 mL * 3). The organic layer was dried with Na₂SO₄, and removed under vacuum. Subsequently, the crude residue was purified by flash column chromatography to afford the polycyclic piperidine **6a** in 58% yield and > 99% ee.

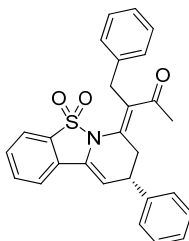
(G) Synthetic applications of **4b**:



a) To a stirred solution of **4b** (0.3 mmol) in anhydrous EA (15.0 mL) was added Pd/C (10 mol %). The reaction mixture was stirred overnight at room temperature under the H₂ atmosphere. After that, filtered the reaction mixture, and washed the solid with ethyl acetate (10.0 mL). Then, the filtrate was concentrated and the residue was purified directly by flash column chromatography (hexane/ethyl acetate = 10: 1- 6: 1) to get the product **7b** in 92% yield (81.4 mg), > 95: 5 d.r. and 99% ee.

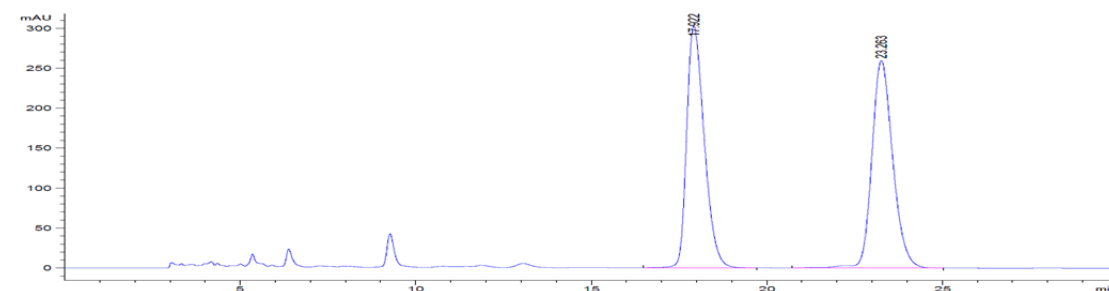
b) The stirred solution of **7b** (0.2 mmol) in anhydrous THF (10.0 mL) was cooled to -78 °C under the N₂ atmosphere. Then, *L*-selectride (0.3 mmol) was added to the mixture slowly. After that, the resulting mixture was stirred for 2 h at -78 °C until the reaction was finished. The reaction was quenched at -78 °C by H₂O (50.0 μL). The d.r. was determined to be 1:1 by NMR analysis of crude mixture after a short column chromatography. Finally, the diastereo-isomers **8a** (38.5 mg)/**8a'** (40.1 mg) were separated by column (petroleum ether: ethyl acetate = 12:1) in 44% and 46% yield, respectively.

(H) The analytical data for the products:

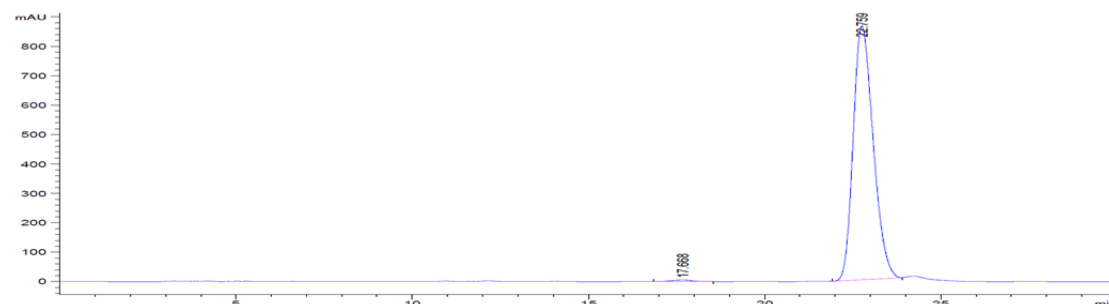


(*S,E*)-3-(5,5-dioxido-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)-4-phenylbutan-2-one (4a)

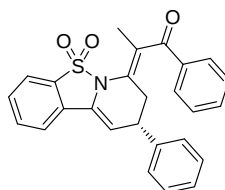
A white solid (53.3 mg), 61% yield, 99% *ee*. $[\alpha]_D^{20} = -31.22$ ($c = 0.41$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 22.76 min, t_R (minor) = 17.67 min. ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J = 7.8$ Hz, 1H), 7.68 (ddd, $J = 10.2, 8.6, 4.2$ Hz, 2H), 7.63 – 7.52 (m, 1H), 7.42 – 7.10 (m, 10H), 5.99 (d, $J = 5.2$ Hz, 1H), 4.38 (d, $J = 16.5$ Hz, 1H), 4.02 – 3.82 (m, 2H), 2.94 – 2.71 (m, 2H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 203.5, 142.0, 139.6, 137.7, 133.5, 132.2, 131.3, 130.9, 130.2, 128.9, 128.7, 128.5, 128.1, 127.3, 126.5, 121.3, 121.1, 106.9, 40.3, 37.0, 35.0, 30.0. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{23}\text{NNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 464.1291, found 464.1269.



	Retention Time (min)	Area (mAU*s)	% Area
1	17.922	1.05176e4	49.4689
2	23.263	1.07434e4	50.5311



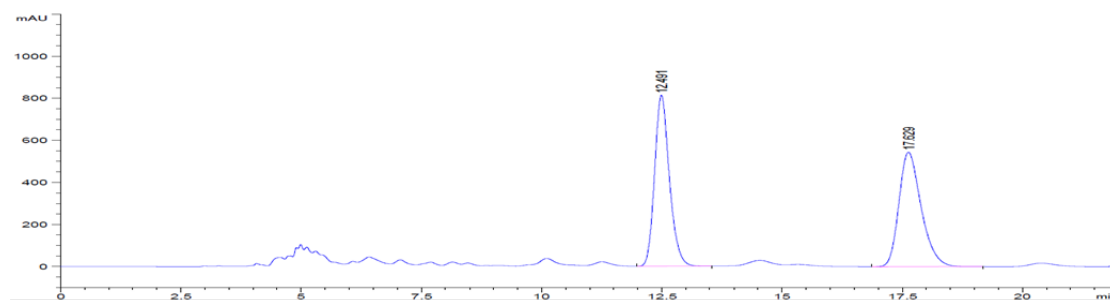
	Retention Time (min)	Area (mAU*s)	% Area
1	17.668	238.66943	0.6969
2	22.759	3.40088e4	99.3031



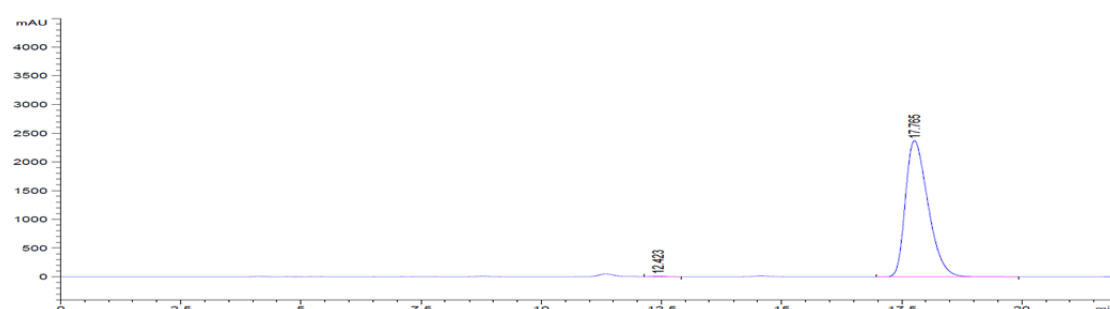
(*S,E*)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)-1-phenylpropan-1-one (4b)

A white solid (60.2 mg), 70% yield, > 99% *ee*. $[\alpha]_D^{20} = -77.59$ ($c = 0.29$ in EtOAc).

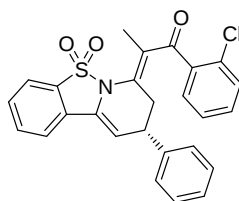
HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, λ = 254 nm, t_R (major) = 17.77 min, t_R (minor) = 12.42 min. ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 7.7 Hz, 2H), 7.86 (d, J = 7.7 Hz, 1H), 7.74 – 7.51 (m, 4H), 7.44 (t, J = 7.6 Hz, 2H), 7.35 – 7.18 (m, 3H), 7.10 (d, J = 6.8 Hz, 2H), 5.87 (d, J = 3.7 Hz, 1H), 3.75 (dt, J = 8.3, 4.2 Hz, 1H), 2.54 (dd, J = 12.8, 4.7 Hz, 1H), 2.32 (s, 3H) 2.28 (d, J = 18, 9.5 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 198.5, 142.1, 136.1, 133.8, 133.6, 132.6, 132.0, 131.8, 130.7, 130.2, 130.0, 129.6, 129.0, 128.8, 127.6, 127.3, 121.4, 121.0, 107.7, 40.0, 36.6, 18.9. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{21}\text{NNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 450.1134, found 450.1123.



	Retention Time (min)	Area (mAU*s)	% Area
1	12.491	1.73741e4	49.8291
2	17.629	1.74932e4	50.1709



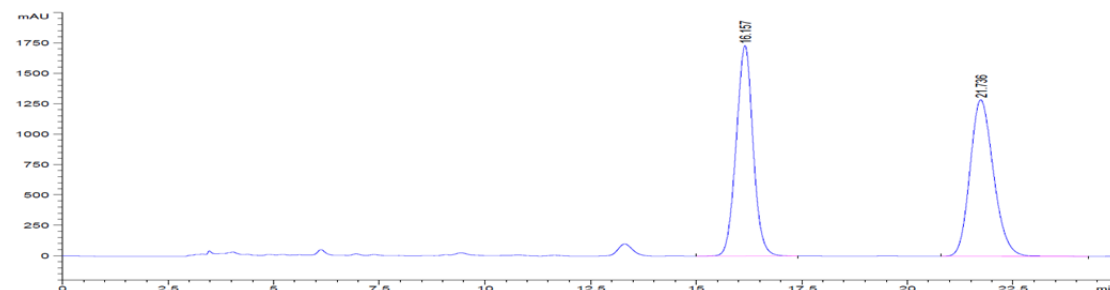
	Retention Time (min)	Area (mAU*s)	% Area
1	12.423	189.98885	0.2447
2	17.765	7.74479e4	99.7553



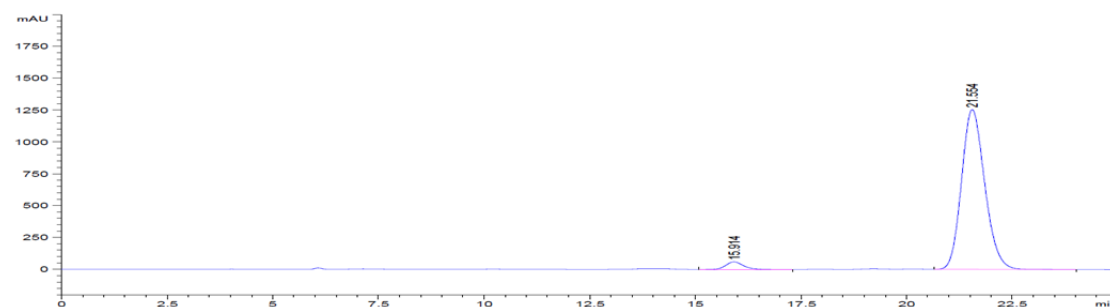
(*S,E*)-1-(2-chlorophenyl)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4c)

A white solid (67.1 mg), 73% yield, 93% *ee*. $[\alpha]_D^{20} = -66.44$ (c = 0.59 in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, λ = 254 nm, t_R (major) = 21.55 min, t_R (minor) = 15.94 min. ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, J = 7.8 Hz, 1H), 7.73 – 7.55 (m, 3H), 7.44 – 7.09 (m, 9H), 5.95 (d, J = 4.4 Hz,

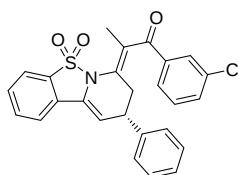
1H), 3.81 (dt, $J = 7.4, 4.8$ Hz, 1H), 2.79 (dd, $J = 12.9, 4.8$ Hz, 1H), 2.55 (dd, $J = 12.9, 7.3$ Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, cdCl_3) δ 197.1, 141.9, 138.1, 135.7, 133.6, 133.1, 132.8, 132.2, 132.1, 130.8, 130.4, 130.4, 130.2, 128.8, 127.7, 127.3, 127.1, 121.3, 121.1, 107.3, 39.6, 36.1, 18.7. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{20}\text{ClNNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 484.0745, found 484.0743.



	Retention Time (min)	Area (mAU*s)	% Area
1	16.157	4.82073e4	49.2669
2	21.736	4.96420e4	50.7331



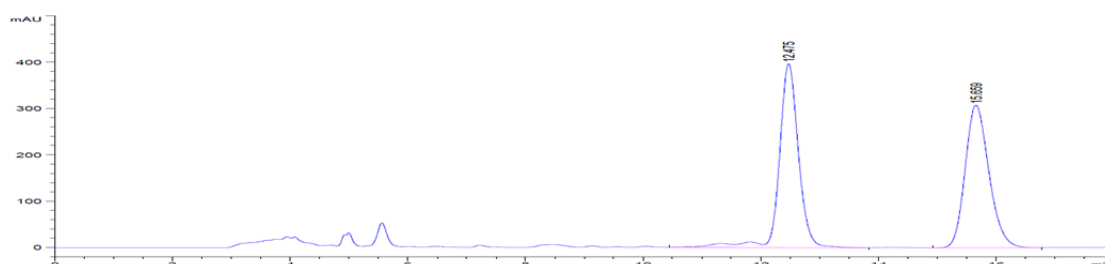
	Retention Time (min)	Area (mAU*s)	% Area
1	15.914	1709.19543	3.4446
2	21.554	4.79099e4	96.5554



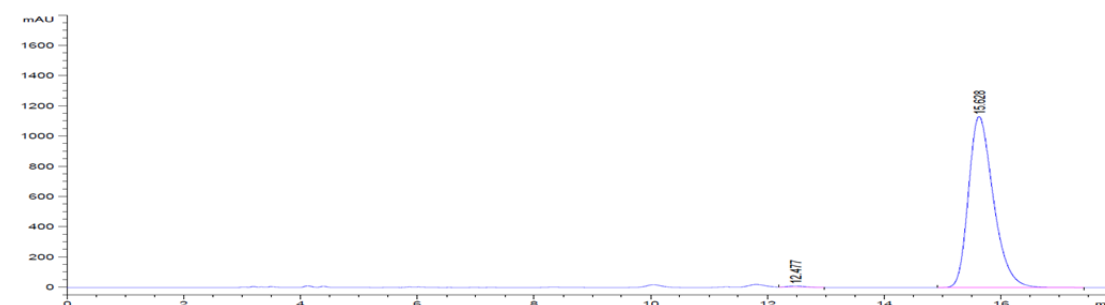
(S,E)-1-(3-chlorophenyl)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4d)

A white solid (67.2 mg), 73% yield, 99% ee. $[\alpha]_{\text{D}}^{20} = -77.14$ ($c = 0.56$ in EtOAc). HPLC (chiral AD-H column), n -hexane/ i -PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_{R} (major) = 15.63 min, t_{R} (minor) = 12.48 min. ^1H NMR (400 MHz, cdCl_3) δ 7.93 – 7.81 (m, 2H), 7.77 – 7.56 (m, 4H), 7.51 (ddd, $J = 8.0, 2.1, 1.0$ Hz, 1H), 7.36 (t, $J = 7.9$ Hz, 1H), 7.34 – 7.20 (m, 3H), 7.10 (dd, $J = 7.7, 1.5$ Hz, 2H), 5.90 (d, $J = 4.1$ Hz, 1H), 3.80 – 3.72 (m, 1H), 2.52 (dd, $J = 12.6, 5.0$ Hz, 1H), 2.31 (dd, $J = 10.6, 7.6$ Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, cdCl_3) δ 197.1, 141.9, 137.8, 135.3, 133.6,

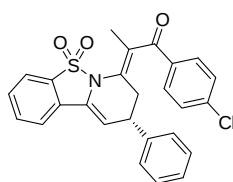
132.6, 131.9, 131.0, 131.0, 130.5, 130.4, 130.3, 129.1, 128.8, 128.0, 127.6, 127.4, 121.4, 121.1, 107.4, 39.8, 36.8, 18.9. ESI-HRMS: calcd for $C_{26}H_{20}ClNNaO_3S^+$ ($[M+Na]^+$) 484.0745, found 484.0743.



	Retention Time (min)	Area (mAU*s)	% Area
1	12.475	9035.37988	51.1530
2	15.659	8628.05664	48.8470



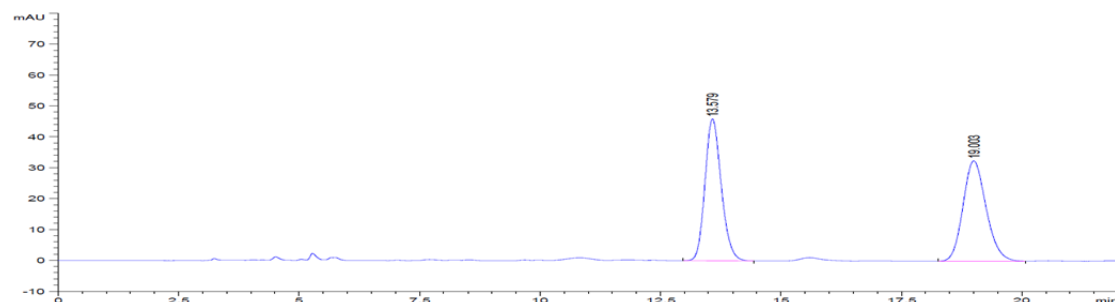
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1	12.477	158.78873	0.4714
2	15.628	3.35261e4	99.5286



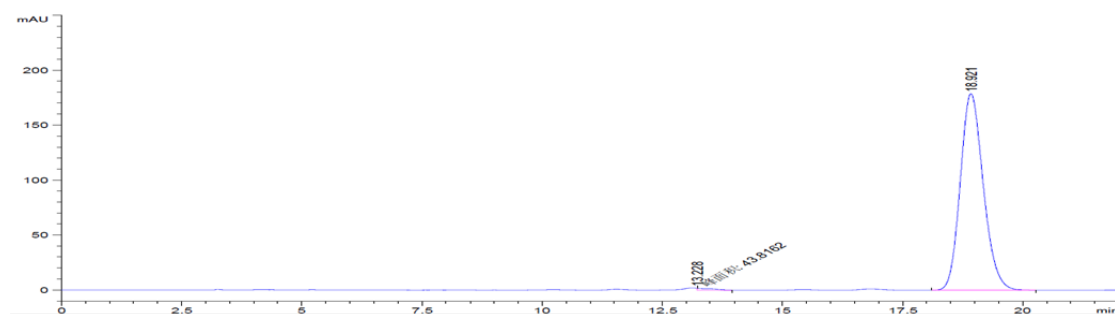
(S,E)-1-(4-chlorophenyl)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4e)

A white solid (64.9 mg), 70% yield, 99% *ee*. $[\alpha]_D^{20} = -66.33$ ($c = 0.3$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 18.92 min, t_R (minor) = 13.12 min. 1H NMR (400 MHz, $cdCl_3$) δ 7.87 (d, $J = 7.7$ Hz, 1H), 7.81 (d, $J = 8.4$ Hz, 2H), 7.75 – 7.58 (m, 3H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.33 – 7.03 (m, 5H), 5.88 (d, $J = 3.9$ Hz, 1H), 3.75 (dt, $J = 8.8, 4.4$ Hz, 1H), 2.51 (dd, $J = 12.9, 4.7$ Hz, 1H), 2.29 (s, 3H), 2.27 (dd, $J = 12.4, 8.0$ Hz, 1H). ^{13}C NMR (100 MHz, $cdCl_3$) δ 197.2, 142.0, 140.2, 134.6, 133.6, 132.6, 131.9, 131.2, 130.9, 130.6, 130.5, 130.3, 129.4, 128.8, 127.6, 127.4, 121.4, 121.1, 107.5, 39.9, 36.7,

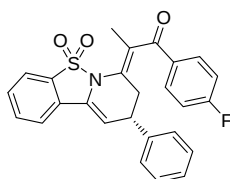
18.9. ESI-HRMS: calcd for $C_{26}H_{20}ClNNaO_3S^+$ ($[M+Na]^+$) 484.0745, found 484.0743.



	Retention Time (min)	Area (mAU*s)	% Area
1	13.579	1078.24084	49.9609
2	19.003	1079.92773	50.0391



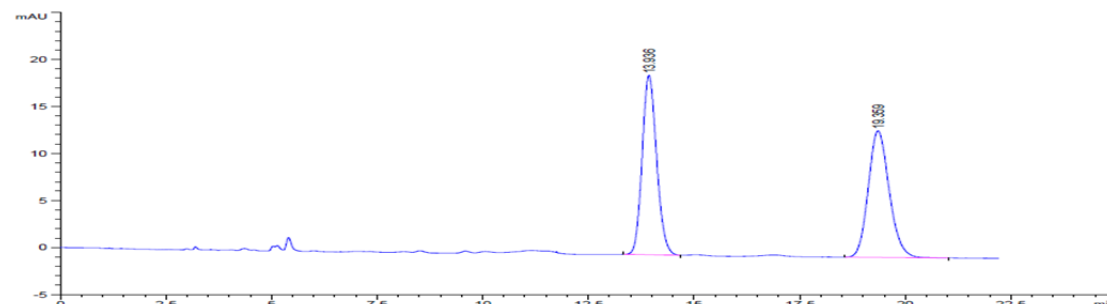
	Retention Time (min)	Area (mAU*s)	% Area
1	13.228	43.81617	0.7300
2	18.921	5958.31348	99.2700



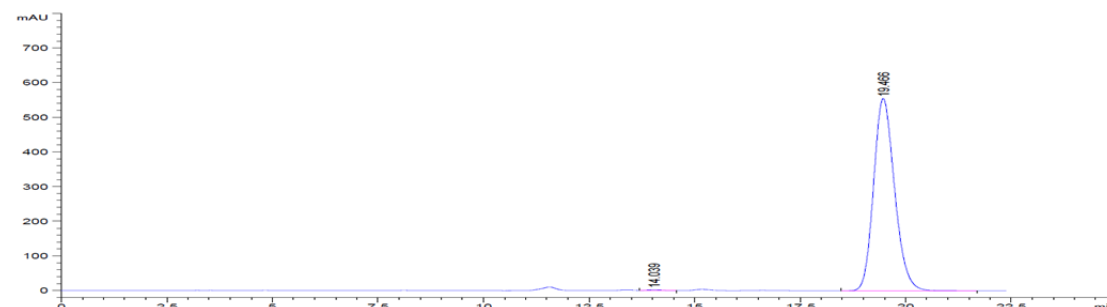
(S,E)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)-1-(4-fluorophenyl)propan-1-one (4f)

A white solid (61.1 mg), 69% yield, > 99% *ee*. $[\alpha]_D^{20} = -71.67$ ($c = 0.48$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 19.47 min, t_R (minor) = 14.04 min. 1H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.80 (m, 3H), 7.76 – 7.49 (m, 3H), 7.28–7.07 (m, 7H), 5.88 (d, $J = 3.5$ Hz, 1H), 3.80 – 3.68 (m, 1H), 2.52 (dd, $J = 12.4, 4.0$ Hz, 1H), 2.30 (s, 3H), 2.27 (dd, $J = 12.4, 8.0$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 167.4, 164.9, 142.1, 133.6, 132.6, 132.3, 132.3, 131.9, 131.4, 130.6, 130.2, 130.2, 128.8, 127.6, 127.4, 121.4, 121.1,

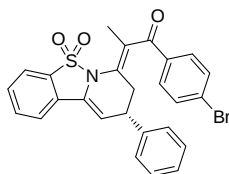
116.3, 116.1, 107.5, 39.9, 36.7, 18.9. ESI-HRMS: calcd for calcd for $C_{26}H_{20}FNNaO_3S^+$ ($[M+Na]^+$) 468.1040, found 468.1029.



	Retention Time (min)	Area (mAU*s)	% Area
1	13.936	454.90787	49.5397
2	19.359	463.36142	50.4603



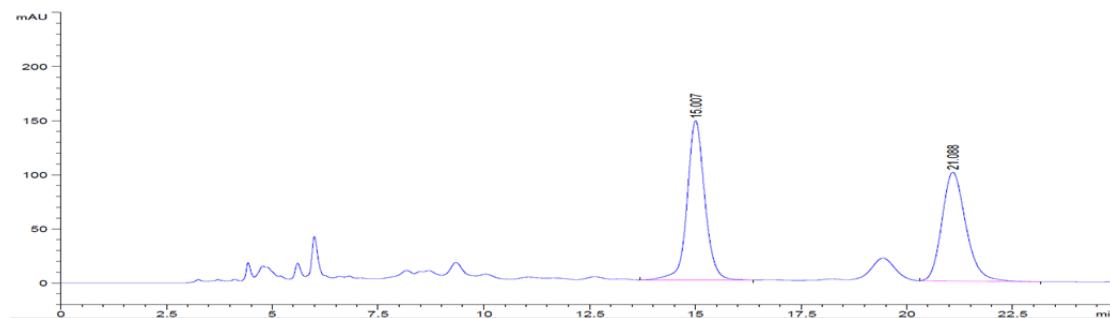
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1	14.039	44.33810	0.2314
2	19.466	1.91155e4	99.7686



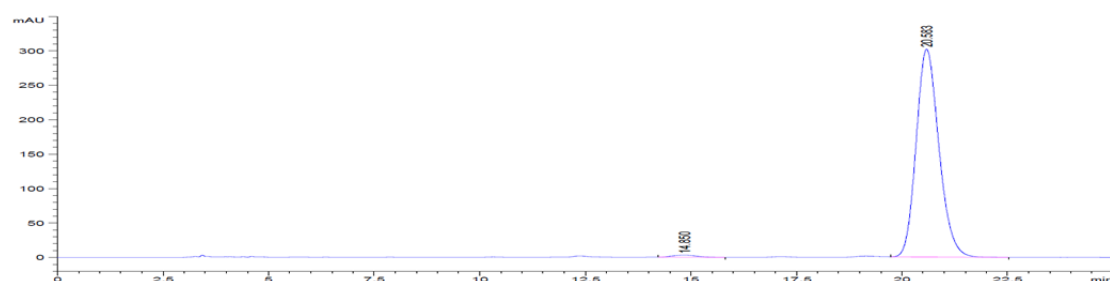
(S,E)-1-(4-bromophenyl)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4g)

A white solid (65.8 mg), 65% yield, 98% *ee*. $[\alpha]_D^{20} = -56.67$ ($c = 0.66$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 20.58 min, t_R (minor) = 14.85 min. 1H NMR (400 MHz, $cdCl_3$) δ 7.86 (d, $J = 7.6$ Hz, 1H), 7.81 – 7.50 (m, 7H), 7.27 (d, $J = 6.6$ Hz, 3H), 7.10 (d, $J = 6.5$ Hz, 2H), 5.88 (d, $J = 3.4$ Hz, 1H), 3.75 (s, 1H), 2.51 (dd, $J = 12.5, 4.1$ Hz, 1H), 2.29-2.25 (m, 4H). ^{13}C NMR (100 MHz, $cdCl_3$) δ 197.4, 142.0, 135.0, 133.6, 132.6, 132.3, 131.9, 131.2, 131.0, 130.6, 130.6, 130.3, 129.1, 128.8, 127.6, 127.4, 121.4, 121.1, 107.4, 39.9, 36.7, 18.9. ESI-HRMS: calcd for calcd for $C_{26}H_{20}BrNNaO_3S^+$

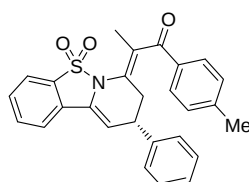
$([M+Na]^+)$ 528.0239, found 528.0224.



	Retention Time (min)	Area (mAU*s)	% Area
1	15.007	4285.72852	52.0160
2	21.088	3953.52588	47.9840

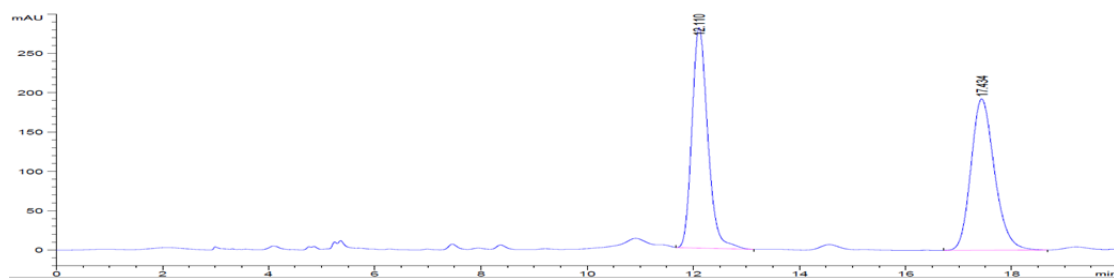


	Retention Time (min)	Area (mAU*s)	% Area
1	14.850	124.21114	1.0859
2	20.583	1.13142e4	98.9141

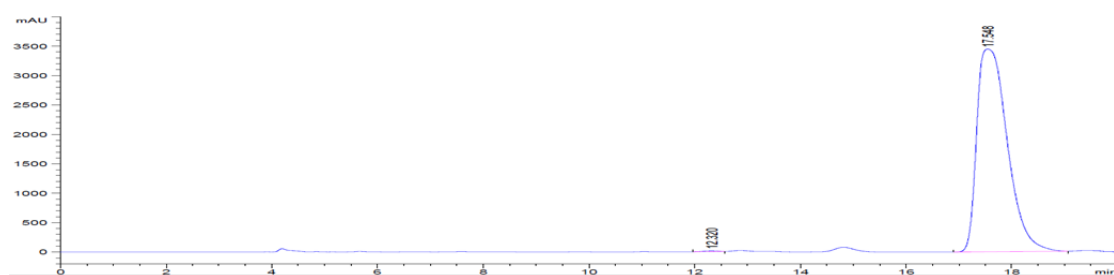


(*S,E*)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)-1-(*p*-tolyl)propan-1-one (4h)

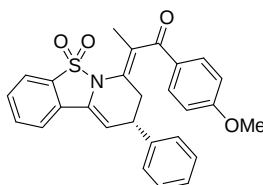
A white solid (62.2 mg), 70% yield, > 99% *ee*. $[\alpha]_D^{20} = -63.24$ ($c = 0.34$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 17.54 min, t_R (minor) = 12.32 min. ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, $J = 7.4$ Hz, 2H), 7.86 (d, $J = 7.7$ Hz, 1H), 7.68 (d, $J = 3.9$ Hz, 2H), 7.64 – 7.50 (m, 2H), 7.43 (t, $J = 7.7$ Hz, 2H), 7.08 (d, $J = 7.9$ Hz, 2H), 6.99 (d, $J = 8.0$ Hz, 2H), 5.86 (d, $J = 3.7$ Hz, 1H), 3.72 (dt, $J = 8.5, 4.3$ Hz, 1H), 2.53 (dd, $J = 12.9, 4.8$ Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 2.30 – 2.20 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 198.5, 139.1, 136.9, 136.1, 133.7, 133.5, 132.4, 131.9, 131.6, 130.7, 130.2, 130.1, 129.6, 129.4, 128.9, 127.4, 121.3, 121.0, 108.0, 39.6, 36.7, 21.1, 18.9. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{23}\text{NNaO}_3\text{S}^+$ ($[M+Na]^+$) 464.1291, found 464.1274.



	Retention Time (min)	Area (mAU*s)	% Area
1	12.110	5814.90381	49.5060
2	17.434	5930.94141	50.4940

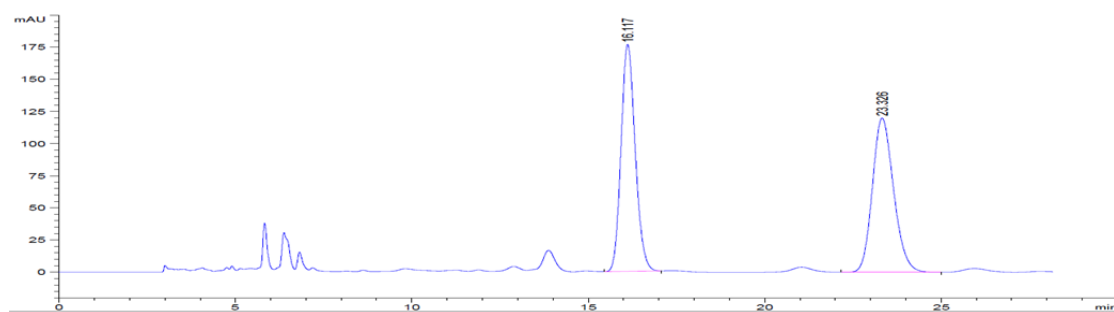


	Retention Time (min)	Area (mAU*s)	% Area
1	12.320	224.87375	0.1627
2	17.548	1.38022e5	99.8373

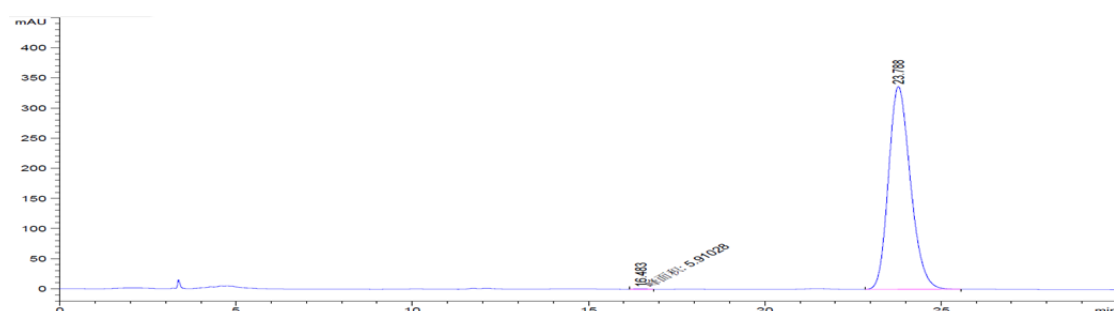


(S,E)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)-1-(4-methoxyphenyl)propan-1-one (4i)

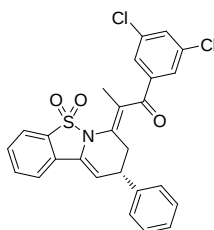
A white solid (42.1 mg), 46% yield, > 99% *ee*. $[\alpha]_D^{20} = -71.48$ ($c = 0.27$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 23.79 min, t_R (minor) = 16.48 min. ^1H NMR (400 MHz, CDCl_3) δ 7.94 (d, $J = 8.5$ Hz, 2H), 7.86 (d, $J = 7.6$ Hz, 1H), 7.78 – 7.46 (m, 3H), 7.43 – 7.18 (m, 3H), 7.11 (d, $J = 7.0$ Hz, 2H), 6.92 (d, $J = 8.5$ Hz, 2H), 5.85 (d, $J = 2.9$ Hz, 1H), 3.85 (s, 3H), 3.81 – 3.62 (m, 1H), 2.54 (dd, $J = 12.7, 4.3$ Hz, 1H), 2.31 (s, 3H), 2.24 (dd, $J = 12.0, 12.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.1, 164.2, 142.4, 133.5, 132.6, 132.1, 130.9, 130.2, 129.2, 129.2, 128.8, 127.6, 127.3, 121.4, 121.1, 114.3, 108.0, 55.7, 40.3, 36.6, 19.0. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{23}\text{NNaO}_4\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 480.1240, found 480.1219.



	Retention Time (min)	Area (mAU*s)	% Area
1	16.117	4928.78076	49.5978
2	23.326	5008.70898	50.4022

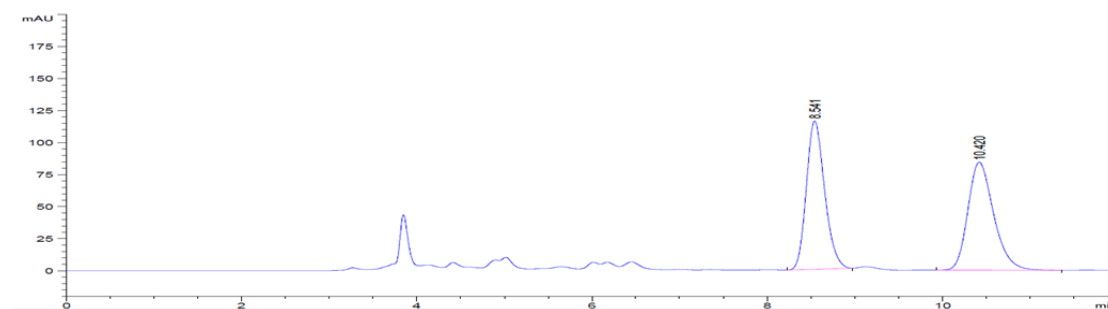


	Retention Time (min)	Area (mAU*s)	% Area
1	16.483	5.91028	0.0405
2	23.788	1.45868e4	99.9595

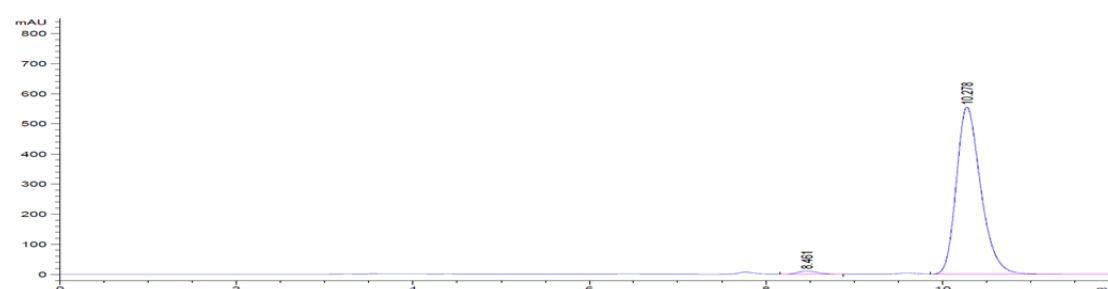


(S,E)-1-(3,5-dichlorophenyl)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4j)

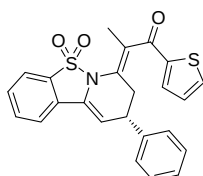
A white solid (64.9 mg), 65% yield, 97% *ee*. $[\alpha]_D^{20} = -50.94$ ($c = 0.64$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 10.28 min, t_R (minor) = 8.46 min. ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, $J = 7.8$ Hz, 1H), 7.71-7.68 (M, 4H), 7.62 (dq, $J = 8.2, 4.2$ Hz, 1H), 7.51 (t, $J = 1.9$ Hz, 1H), 7.33 – 7.24 (m, 3H), 7.10 (dd, $J = 7.7, 1.5$ Hz, 2H), 5.91 (d, $J = 4.3$ Hz, 1H), 3.76 (dt, $J = 9.1, 4.7$ Hz, 1H), 2.50 (dd, $J = 12.9, 4.8$ Hz, 1H), 2.44 – 2.24 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 195.7, 141.7, 138.8, 135.9, 133.7, 133.3, 132.7, 132.2, 131.8, 130.3, 130.1, 128.8, 127.8, 127.6, 127.5, 121.5, 121.1, 107.2, 39.6, 36.9, 18.9. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{NNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 518.0355, found 518.0333.



	Retention Time (min)	Area (mAU*s)	% Area
1	8.541	1677.68787	49.4359
2	10.420	1715.97485	50.5641

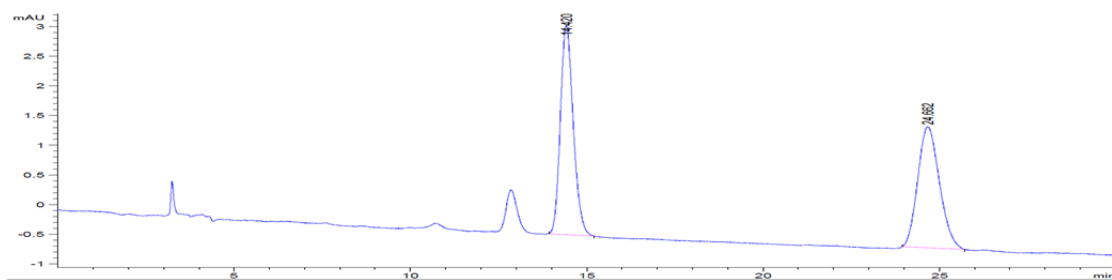


	Retention Time (min)	Area (mAU*s)	% Area
1	8.461	162.64943	1.5018
2	10.278	1.06675e4	98.4982

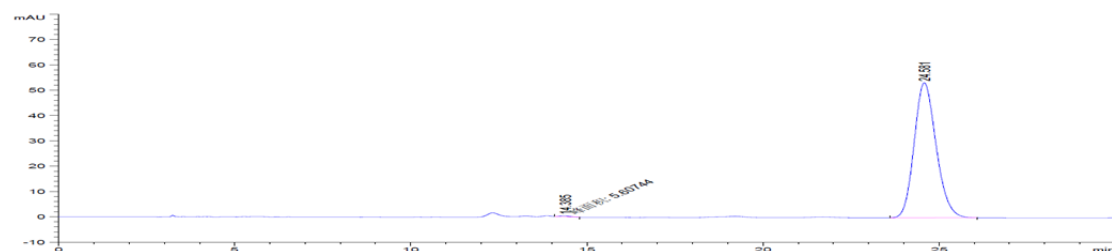


(S,E)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)-1-(thiophen-2-yl)propan-1-one (4k)

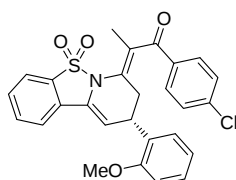
A light yellow solid (45.3 mg), 53% yield, > 99% *ee*. $[\alpha]_D^{20} = -75.11$ ($c = 0.45$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 24.58 min, t_R (minor) = 14.39 min. ^1H NMR (400 MHz, cdCl_3) δ 7.87 (d, $J = 7.7$ Hz, 1H), 7.76 (dd, $J = 3.8, 1.0$ Hz, 1H), 7.73 – 7.57 (m, 4H), 7.35 – 7.20 (m, 3H), 7.18 – 7.06 (m, 3H), 5.86 (d, $J = 3.6$ Hz, 1H), 3.77 (dt, $J = 8.5, 4.2$ Hz, 1H), 2.63 (dd, $J = 12.4, 4.6$ Hz, 1H), 2.34 (s, 3H), 2.31 (dd, $J = 7.4, 5.3$ Hz, 1H). ^{13}C NMR (100 MHz, cdCl_3) δ 190.7, 143.7, 142.2, 135.7, 135.7, 133.6, 132.5, 132.1, 132.0, 130.7, 130.2, 130.1, 128.9, 128.8, 127.6, 127.4, 121.4, 121.1, 107.9, 40.3, 37.1, 19.0. ESI-HRMS: calcd for $\text{C}_{24}\text{H}_{19}\text{NNaO}_3\text{S}_2^+$ ($[\text{M}+\text{Na}]^+$) 456.0699, found 456.0676.



	Retention Time (min)	Area (mAU*s)	% Area
1	14.420	89.39348	50.6528
2	24.662	87.08932	49.3472

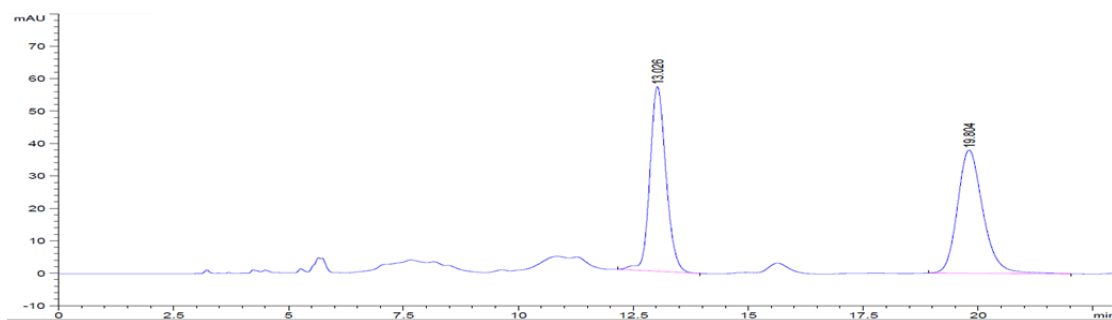


	Retention Time (min)	Area (mAU*s)	% Area
1	14.385	5.60744	0.2419
2	24.581	2312.25220	99.7581

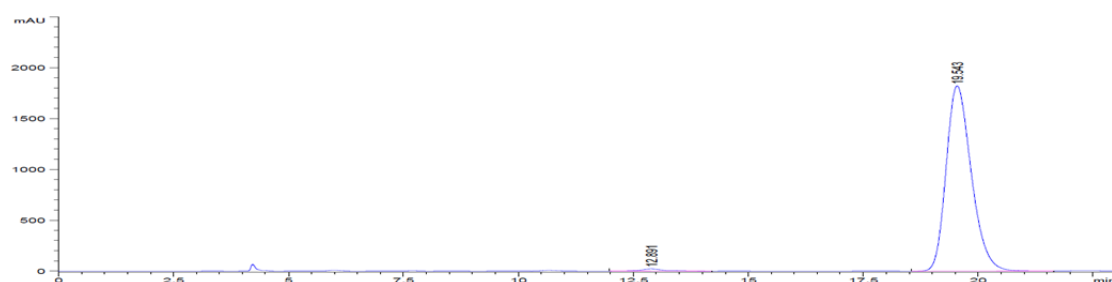


(*S,E*)-1-(4-chlorophenyl)-2-(9-(2-methoxyphenyl)-5,5-dioxido-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4l)

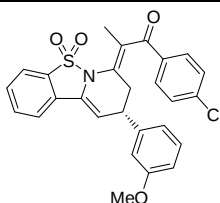
A white solid (63.0 mg), 64% yield, 98% *ee*. $[\alpha]_D^{20} = +8.04$ ($c = 0.56$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 19.54 min, t_R (minor) = 12.89 min. ^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, $J = 7.7$ Hz, 1H), 7.69 (dd, $J = 14.6, 8.0$ Hz, 4H), 7.59 (t, $J = 7.0$ Hz, 1H), 7.35 (d, $J = 8.4$ Hz, 2H), 7.23 (dd, $J = 12.3, 5.2$ Hz, 1H), 7.04 (d, $J = 6.6$ Hz, 1H), 6.91 (t, $J = 7.4$ Hz, 1H), 6.75 (d, $J = 8.2$ Hz, 1H), 5.90 (d, $J = 4.8$ Hz, 1H), 4.15 (dd, $J = 10.9, 5.2$ Hz, 1H), 3.64 (s, 3H), 2.43 (ddd, $J = 19.4, 13.0, 5.7$ Hz, 2H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.1, 156.3, 139.8, 134.6, 133.5, 132.9, 131.8, 131.1, 130.9, 130.8, 130.6, 130.1, 129.4, 129.2, 128.4, 128.3, 121.4, 121.0, 120.5, 110.6, 107.1, 55.2, 34.2, 33.0, 18.7. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{22}\text{ClNNaO}_4\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 514.0850, found 514.0837.



	Retention Time (min)	Area (mAU*s)	% Area
1	13.026	1388.84741	48.8023
2	19.804	1457.01501	51.1977

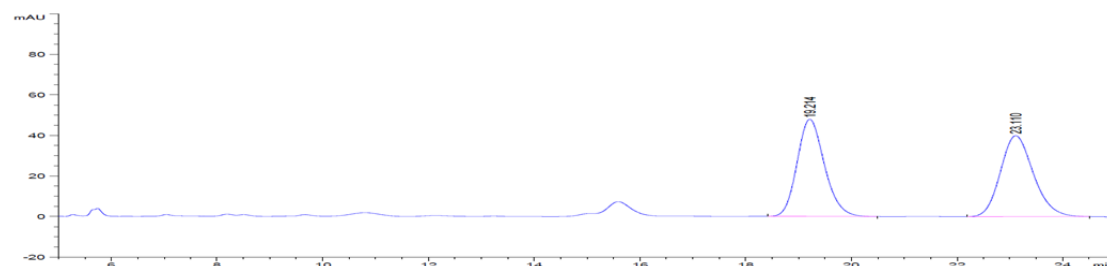


	Retention Time (min)	Area (mAU*s)	% Area
1	12.891	747.98285	1.0690
2	19.543	6.92194e4	98.9310

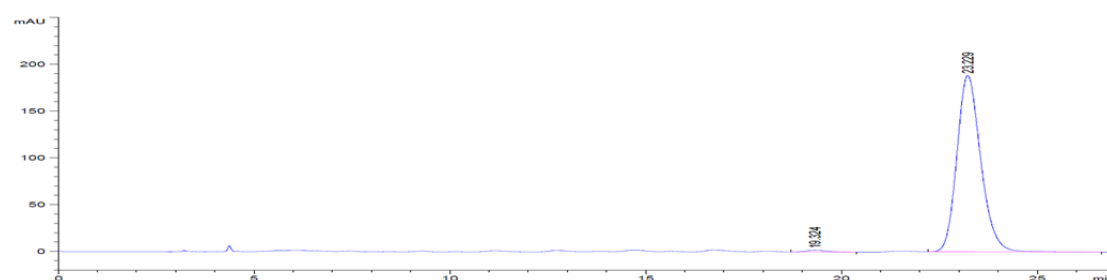


(S,E)-1-(4-chlorophenyl)-2-(9-(3-methoxyphenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4m)

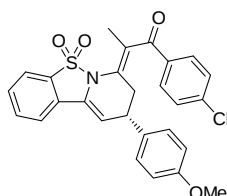
A white solid (50.0 mg), 51% yield, 98% *ee*. $[\alpha]_D^{20} = -62.95$ ($c = 0.44$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 23.23 min, t_R (minor) = 19.32 min. ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, $J = 7.7$ Hz, 1H), 7.81 (d, $J = 8.4$ Hz, 2H), 7.75 – 7.56 (m, 3H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.19 (t, $J = 7.9$ Hz, 1H), 6.78 (dd, $J = 8.1, 1.6$ Hz, 1H), 6.69 (d, $J = 7.5$ Hz, 1H), 6.62 (s, 1H), 5.87 (d, $J = 3.9$ Hz, 1H), 3.83 – 3.62 (m, 4H), 2.50 (dd, $J = 12.6, 4.7$ Hz, 1H), 2.29–2.26 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.2, 160.0, 143.6, 140.2, 134.5, 133.6, 132.6, 131.9, 131.2, 130.9, 130.5, 130.3, 129.8, 129.3, 121.4, 121.1, 119.9, 113.5, 112.5, 107.3, 55.3, 39.9, 36.6, 18.9, 12.2. ESI-HRMS: calcd for calcd for $\text{C}_{27}\text{H}_{22}\text{ClNNaO}_4\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 514.0850, found 514.0837.



	Retention Time (min)	Area (mAU*s)	% Area
1	19.214	1720.98511	49.8917
2	23.110	1728.45483	50.1083

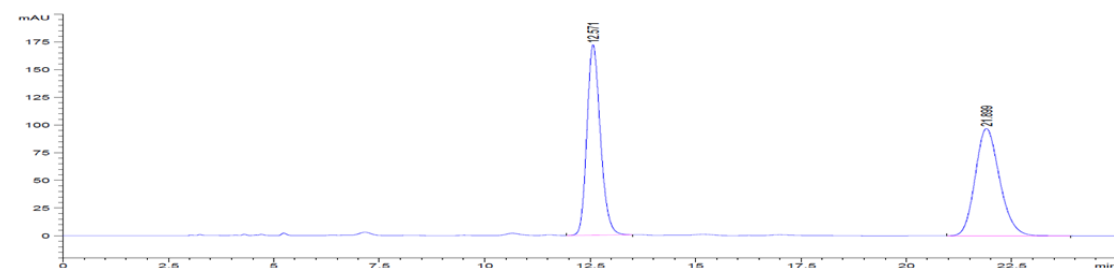


	Retention Time (min)	Area (mAU*s)	% Area
1	19.324	66.87785	0.8314
2	23.229	7976.97168	99.1686

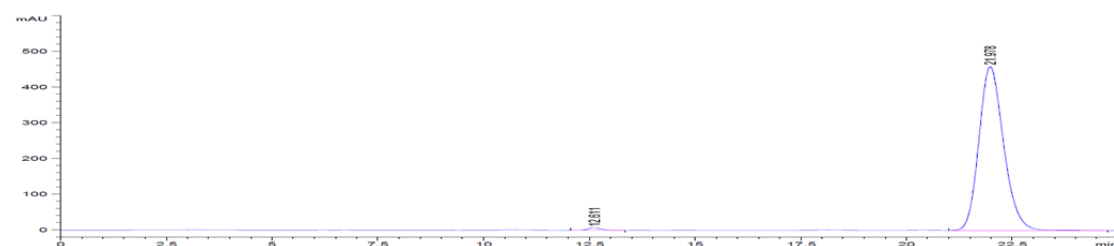


(S,E)-1-(4-chlorophenyl)-2-(9-(4-methoxyphenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4n)

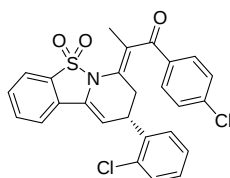
A white solid (90.5 mg), 92% yield, 98% *ee*. $[\alpha]_D^{20} = -85.45$ ($c = 0.66$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 21.98 min, t_R (minor) = 12.61 min. ^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, $J = 7.8$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.68 (d, $J = 4.0$ Hz, 2H), 7.60 (td, $J = 8.1, 4.5$ Hz, 1H), 7.36 (d, $J = 8.4$ Hz, 2H), 7.00 (d, $J = 8.6$ Hz, 2H), 6.78 (d, $J = 8.5$ Hz, 2H), 5.87 (d, $J = 4.2$ Hz, 1H), 3.77 (s, 3H), 3.70 (dt, $J = 8.9, 4.6$ Hz, 1H), 2.49 (dd, $J = 12.9, 4.8$ Hz, 1H), 2.28 (s, 3H), 2.27 (dd, $J = 12.0, 8.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.2, 158.8, 140.0, 134.5, 133.9, 133.6, 132.5, 131.9, 131.1, 130.9, 130.6, 130.6, 130.2, 129.2, 128.6, 121.4, 121.0, 114.1, 107.7, 55.3, 39.0, 36.9, 18.9. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{22}\text{ClNNaO}_4\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 514.0850, found 514.0837.



	Retention Time (min)	Area (mAU*s)	% Area
1	12.571	3816.11572	49.5366
2	21.899	3887.51904	50.4634

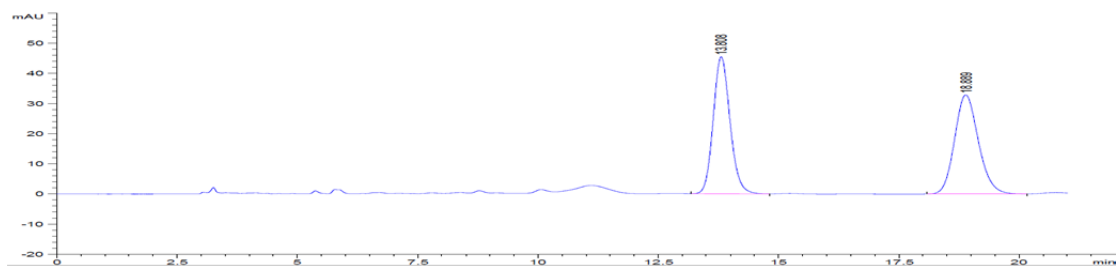


	Retention Time (min)	Area (mAU*s)	% Area
1	12.611	155.67668	0.8320
2	21.978	1.85547e4	99.1680

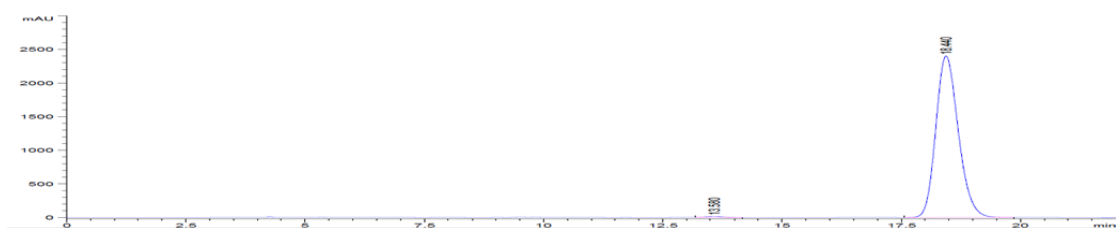


(*S,E*)-1-(4-chlorophenyl)-2-(9-(2-chlorophenyl)-5,5-dioxido-8,9-dihydro-7*H*-benz[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4o)

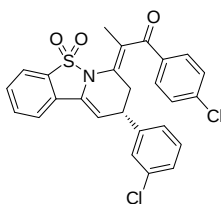
A white solid (32.1 mg), 32% yield, > 99% *ee*. $[\alpha]_D^{20} = -14.29$ ($c = 0.28$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 18.44 min, t_R (minor) = 13.58 min. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, $J = 7.8$ Hz, 1H), 7.79 (d, $J = 8.4$ Hz, 2H), 7.75 – 7.57 (m, 3H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.31 (dd, $J = 6.0, 3.2$ Hz, 1H), 7.24 – 7.17 (m, 2H), 7.16 – 7.06 (m, 1H), 5.87 (d, $J = 4.7$ Hz, 1H), 4.22 (dd, $J = 11.3, 5.0$ Hz, 1H), 2.51 (dd, $J = 13.0, 4.8$ Hz, 1H), 2.33 (dd, $J = 13.1, 6.8$ Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.8, 140.1, 138.6, 134.6, 133.7, 133.5, 131.9, 131.9, 130.8, 130.4, 129.9, 129.3, 128.9, 128.6, 127.0, 121.4, 121.1, 105.7, 36.4, 34.2, 18.7. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{NNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 518.0355, found 518.0332.



	Retention Time (min)	Area (mAU*s)	% Area
1	13.808	1102.52563	49.3531
2	18.889	1131.42773	50.6469

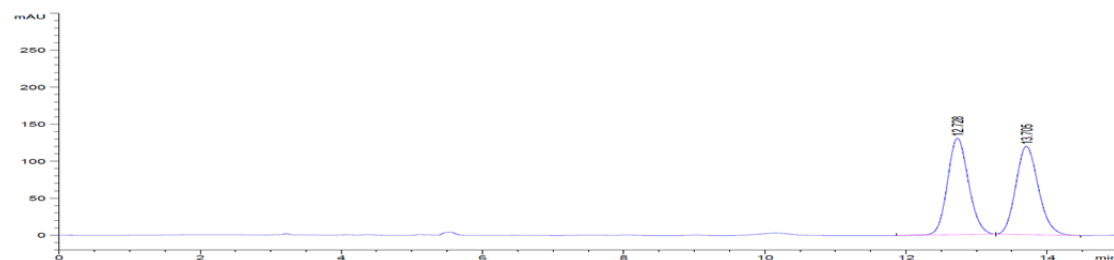


	Retention Time (min)	Area (mAU*s)	% Area
1	13.580	303.84811	0.3846
2	18.440	7.86989e4	99.6154

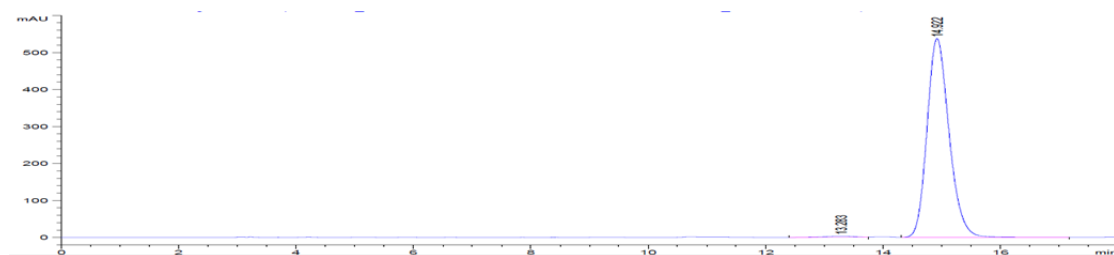


(S,E)-1-(4-chlorophenyl)-2-(9-(3-chlorophenyl)-5,5-dioxido-8,9-dihydro-7H-benz[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4p)

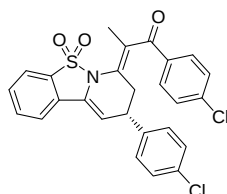
A white solid (49.4 mg), 49% yield, 99% *ee*. $[\alpha]_D^{20} = -76.90$ ($c = 0.40$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 14.92 min, t_R (minor) = 13.28 min. ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, $J = 7.7$ Hz, 1H), 7.82 (d, $J = 8.4$ Hz, 2H), 7.75 – 7.58 (m, 3H), 7.41 (d, $J = 8.5$ Hz, 2H), 7.25 – 7.15 (m, 2H), 7.07 (s, 1H), 6.98 (d, $J = 6.8$ Hz, 1H), 5.83 (d, $J = 4.1$ Hz, 1H), 3.78 – 3.68 (m, 1H), 2.50 (dd, $J = 12.8, 4.8$ Hz, 1H), 2.36 – 2.17 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.0, 144.1, 140.4, 134.7, 134.4, 133.7, 133.1, 132.0, 131.9, 130.9, 130.5, 130.1, 129.9, 129.4, 127.8, 127.6, 125.9, 121.5, 121.2, 106.3, 39.6, 36.4, 18.9. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{NNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 518.0355, found 518.0332.



	Retention Time (min)	Area (mAU*s)	% Area
1	12.728	2701.10181	50.4438
2	13.705	2653.57666	49.5562

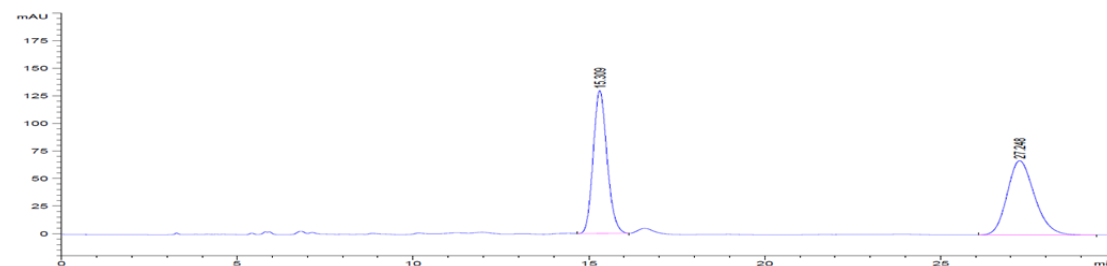


	Retention Time (min)	Area (mAU*s)	% Area
1	13.283	93.54295	0.6638
2	14.922	1.39991e4	99.3362

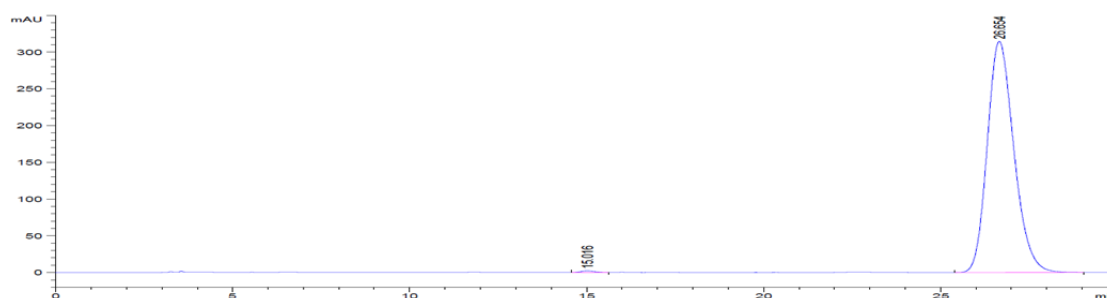


(*S,E*)-1-(4-chlorophenyl)-2-(9-(4-chlorophenyl)-5,5-dioxido-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4q)

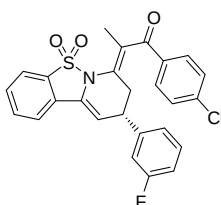
A white solid (65.6 mg), 66% yield, > 99% *ee*. $[\alpha]_{\text{D}}^{20} = -136.00$ ($c = 0.60$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_{R} (major) = 20.65 min, t_{R} (minor) = 15.02 min. ^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, $J = 7.7$ Hz, 1H), 7.75 (d, $J = 8.5$ Hz, 2H), 7.68 (t, $J = 6.1$ Hz, 2H), 7.62 (td, $J = 8.2, 4.4$ Hz, 1H), 7.39 (d, $J = 8.5$ Hz, 2H), 7.22 (d, $J = 8.4$ Hz, 2H), 7.02 (d, $J = 8.4$ Hz, 2H), 5.85 (d, $J = 4.4$ Hz, 1H), 3.73 (dt, $J = 9.3, 4.8$ Hz, 1H), 2.49 (dd, $J = 12.7, 4.9$ Hz, 1H), 2.28 (s, 3H), 2.49 (dd, $J = 9.6, 7.6$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.0, 140.4, 140.3, 134.4, 133.7, 133.2, 133.0, 131.9, 131.6, 130.8, 130.4, 130.0, 129.3, 129.0, 128.9, 121.4, 121.1, 106.4, 39.1, 36.5, 18.9. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{NNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 518.0355, found 518.0332.



	Retention Time (min)	Area (mAU*s)	% Area
1	15.309	3550.70630	49.5044
2	27.248	3621.80737	50.4956

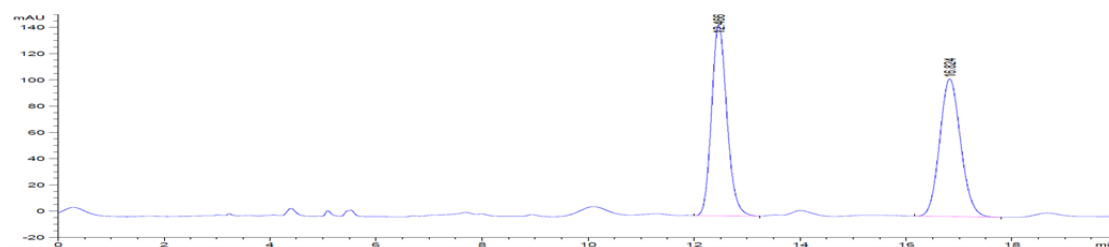


	Retention Time (min)	Area (mAU*s)	% Area
1	15.016	57.38476	0.3472
2	26.654	1.64682e4	99.6528

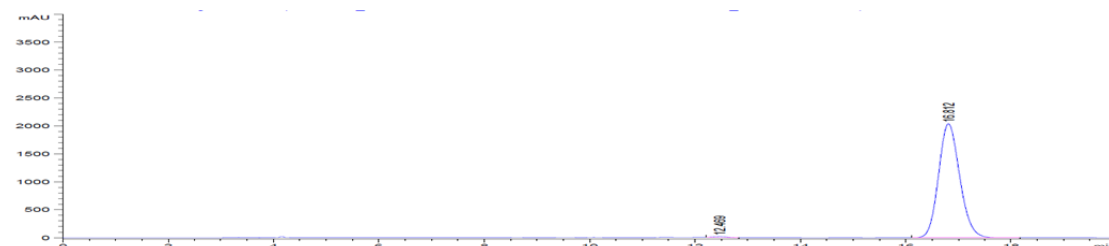


(S,E)-1-(4-chlorophenyl)-2-(9-(3-fluorophenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4r)

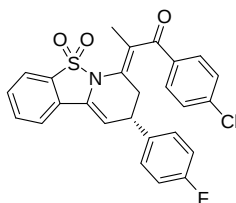
A white solid (34.9 mg), 36% yield, > 99% *ee*. $[\alpha]_D^{20} = -61.07$ ($c = 0.28$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 16.81 min, t_R (minor) = 12.50 min. ^1H NMR (400 MHz, CDCl_3) δ 7.85 (dd, $J = 12.8, 8.2$ Hz, 3H), 7.75 – 7.57 (m, 3H), 7.40 (d, $J = 8.4$ Hz, 2H), 7.25 – 7.15 (m, 1H), 7.02 – 6.84 (m, 2H), 6.80 (d, $J = 9.8$ Hz, 1H), 5.85 (d, $J = 4.1$ Hz, 1H), 3.75 (dd, $J = 7.4, 4.1$ Hz, 1H), 2.50 (dd, $J = 12.5, 4.5$ Hz, 1H), 2.40 – 2.15 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.0, 164.2, 161.8, 144.5, 144.5, 140.4, 134.5, 133.7, 133.0, 132.0, 131.7, 130.9, 130.4, 130.4, 130.3, 130.0, 129.4, 123.3, 123.3, 121.5, 121.1, 114.7, 114.5, 114.4, 114.2, 106.4, 39.6, 36.4, 18.9. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{19}\text{ClFNNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 502.0650, found 502.0640.



	Retention Time (min)	Area (mAU*s)	% Area
1	12.466	2930.14697	50.3593
2	16.824	2888.33521	49.6407

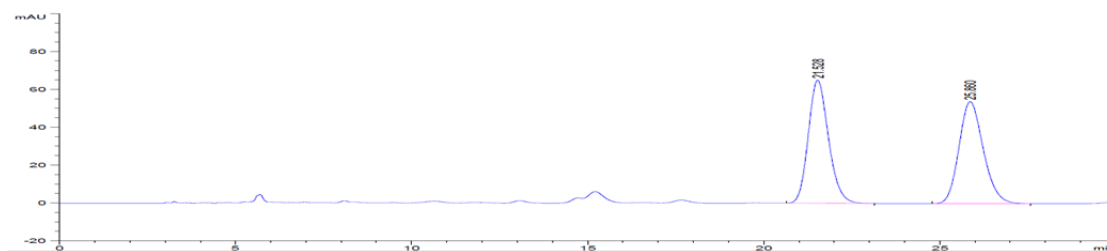


	Retention Time (min)	Area (mAU*s)	% Area
1	12.469	199.97885	0.3517
2	16.812	5.66683e4	99.6483

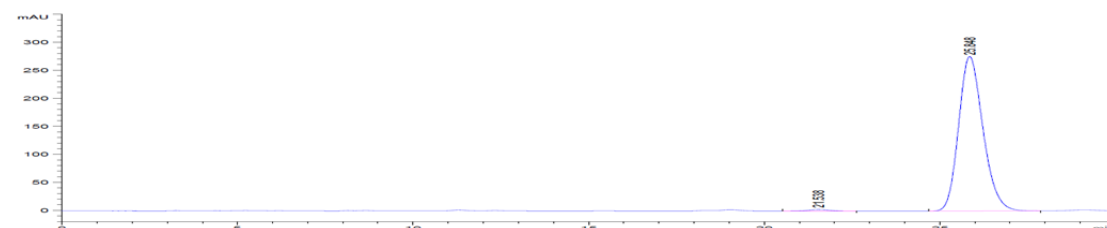


(S,E)-1-(4-chlorophenyl)-2-(9-(4-fluorophenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4s)

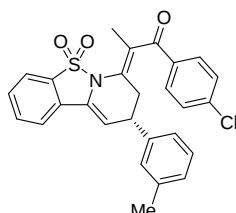
A white solid (70.3 mg), 73% yield, 98% *ee*. $[\alpha]_D^{20} = -70.95$ ($c = 0.42$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 25.85 min, t_R (minor) = 21.54 min. ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, $J = 7.7$ Hz, 1H), 7.81 (d, $J = 8.5$ Hz, 2H), 7.72 – 7.66 (m, 2H), 7.62 (td, $J = 8.3, 4.2$ Hz, 1H), 7.40 (d, $J = 8.5$ Hz, 2H), 7.09 – 7.02 (m, 2H), 6.95 (t, $J = 8.6$ Hz, 2H), 5.85 (d, $J = 4.3$ Hz, 1H), 3.74 (dt, $J = 12.0, 4.1$ Hz, 1H), 2.48 (dd, $J = 12.8, 4.8$ Hz, 1H), 2.28 (s, 3H), 2.24 (dd, $J = 10.6, 7.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.1, 163.3, 160.8, 140.3, 137.7, 137.6, 134.5, 133.7, 132.8, 132.0, 131.5, 130.9, 130.5, 130.4, 130.2, 129.4, 129.2, 129.1, 121.5, 121.1, 115.8, 115.5, 107.0, 39.1, 36.8, 18.9. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{19}\text{ClFNNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 502.0650, found 502.0640.



	Retention Time (min)	Area (mAU*s)	% Area
1	21.528	2597.41309	50.0758
2	25.860	2589.55371	49.9242

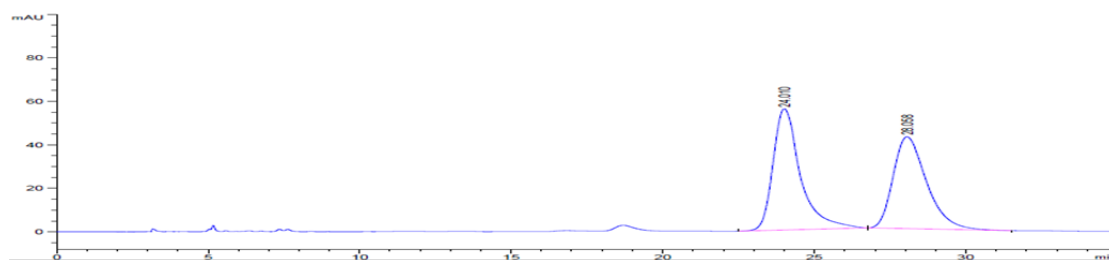


	Retention Time (min)	Area (mAU*s)	% Area
1	21.538	119.46928	0.8909
2	25.848	1.32905e4	99.1091

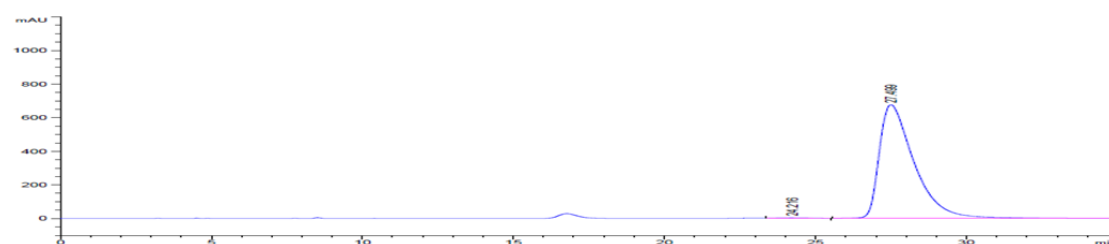


(S,E)-1-(4-chlorophenyl)-2-(5,5-dioxido-9-(m-tolyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4t)

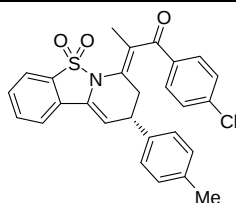
A white solid (70.0 mg), 74% yield, > 99% *ee*. $[\alpha]_D^{20} = -66.22$ ($c = 0.45$ in EtOAc). HPLC (chiral OD-H column), *n*-hexane/ *i*-PrOH = 95/5, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 27.50 min, t_R (minor) = 24.22 min. ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, $J = 7.7$ Hz, 1H), 7.81 (d, $J = 8.5$ Hz, 2H), 7.68 (d, $J = 4.0$ Hz, 2H), 7.62 (td, $J = 8.3, 4.3$ Hz, 1H), 7.39 (d, $J = 8.5$ Hz, 2H), 7.16 (t, $J = 7.5$ Hz, 1H), 7.05 (d, $J = 7.5$ Hz, 1H), 6.90 (d, $J = 9.0$ Hz, 1H), 6.87 (s, 1H), 5.86 (d, $J = 3.9$ Hz, 1H), 3.70 (dt, $J = 8.4, 4.4$ Hz, 1H), 2.49 (dd, $J = 12.5, 4.8$ Hz, 1H), 2.29 (s, 3H), 2.27 (s, 3H), 2.26 (dd, $J = 7.4, 6.4$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.3, 142.0, 140.2, 138.6, 134.5, 133.6, 132.5, 132.0, 131.1, 130.9, 130.7, 130.6, 130.2, 129.3, 128.7, 128.3, 128.1, 124.6, 121.4, 121.1, 107.7, 39.9, 36.7, 21.4, 18.9. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{22}\text{ClNNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 498.0901, found 498.0894.



	Retention Time (min)	Area (mAU*s)	% Area
1	24.010	3501.49438	51.9999
2	28.058	3232.15869	48.0001

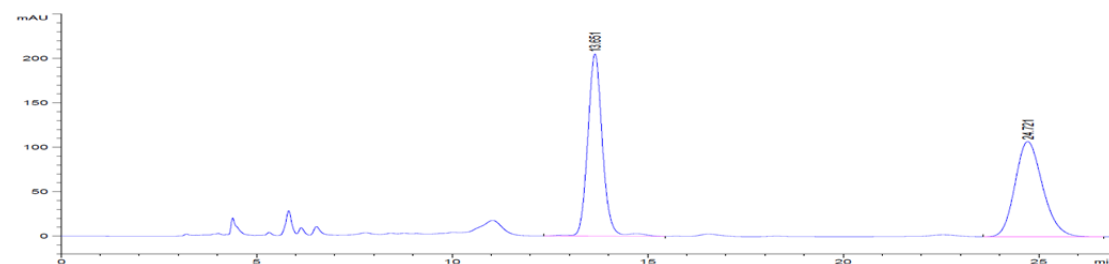


	Retention Time (min)	Area (mAU*s)	% Area
1	24.216	148.71239	0.2737
2	27.499	675.72760	99.7263



(*S,E*)-1-(4-chlorophenyl)-2-(5,5-dioxido-9-(*p*-tolyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4u)

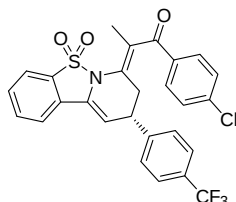
A white solid (81.3 mg), 85% yield, 99% *ee*. $[\alpha]_D^{20} = -89.83$ ($c = 0.59$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 24.70 min, t_R (minor) = 13.67 min. ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, $J = 7.7$ Hz, 1H), 7.80 (d, $J = 8.6$ Hz, 2H), 7.68 (d, $J = 4.0$ Hz, 2H), 7.61 (td, $J = 8.3, 4.3$ Hz, 1H), 7.37 (d, $J = 8.6$ Hz, 2H), 7.08 (d, $J = 7.9$ Hz, 2H), 6.99 (d, $J = 8.0$ Hz, 2H), 5.87 (d, $J = 4.0$ Hz, 1H), 3.71 (dt, $J = 8.8, 4.5$ Hz, 1H), 2.50 (dd, $J = 12.4, 4.5$ Hz, 1H), 2.32 (s, 3H), 2.31 (s, 3H), 2.28 (dd, $J = 9.8, 8.3$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.2, 140.1, 139.0, 137.0, 134.5, 133.6, 132.5, 131.9, 131.0, 130.9, 130.7, 130.6, 130.2, 129.5, 129.2, 127.5, 121.4, 121.0, 107.3, 39.5, 36.8, 21.1, 18.9. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{22}\text{ClNNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 498.0901, found 498.0894.



	Retention Time (min)	Area (mAU*s)	% Area
1	13.651	5368.32178	50.4721
2	24.721	5267.89990	49.5279

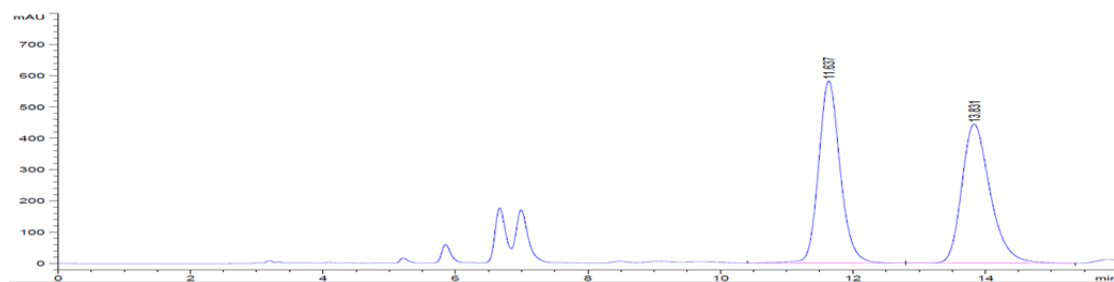


	Retention Time (min)	Area (mAU*s)	% Area
1	13.674	296.24078	0.7048
2	24.701	4.17365e4	99.2952

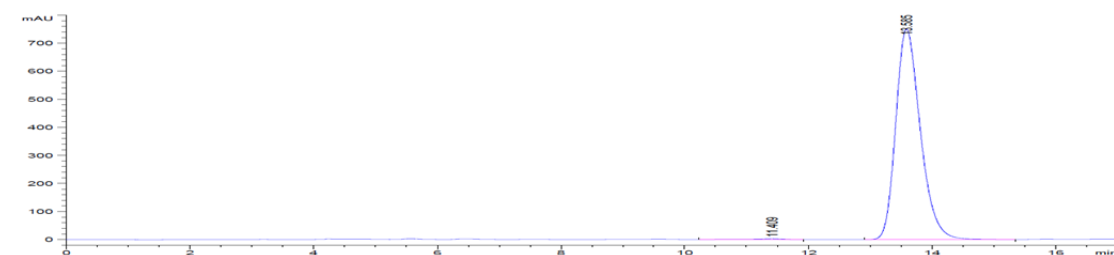


(S,E)-1-(4-chlorophenyl)-2-(5,5-dioxido-9-(4-(trifluoromethyl)phenyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4v)

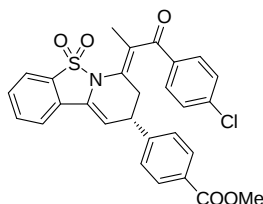
A white solid (45.0 mg), 43% yield, 99% *ee*. $[\alpha]_D^{20} = -85.00$ ($c = 0.36$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 13.59 min, t_R (minor) = 11.41 min. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, $J = 7.7$ Hz, 1H), 7.84 – 7.76 (m, 2H), 7.74 – 7.67 (m, 2H), 7.64 (ddd, $J = 8.3, 6.5, 4.1$ Hz, 1H), 7.53 (d, $J = 8.1$ Hz, 2H), 7.44 – 7.35 (m, 2H), 7.23 (d, $J = 8.1$ Hz, 2H), 5.85 (d, $J = 4.2$ Hz, 1H), 3.81 (dt, $J = 8.4, 4.4$ Hz, 1H), 2.53 (dd, $J = 12.7, 5.1$ Hz, 1H), 2.30 (dd, $J = 10.1, 4.6$ Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.0, 146.1, 140.5, 134.3, 133.8, 133.2, 132.0, 131.7, 130.9, 130.5, 130.4, 129.9, 129.4, 128.1, 125.8, 125.8, 121.5, 121.1, 106.0, 39.7, 36.3, 18.9. ESI-HRMS: calcd for $\text{C}_{27}\text{H}_{19}\text{ClF}_3\text{NNaO}_3\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 552.0618, found 552.0602.



	Retention Time (min)	Area (mAU*s)	% Area
1	11.637	1.31785e4	49.8778
2	13.831	1.32430e4	50.1222

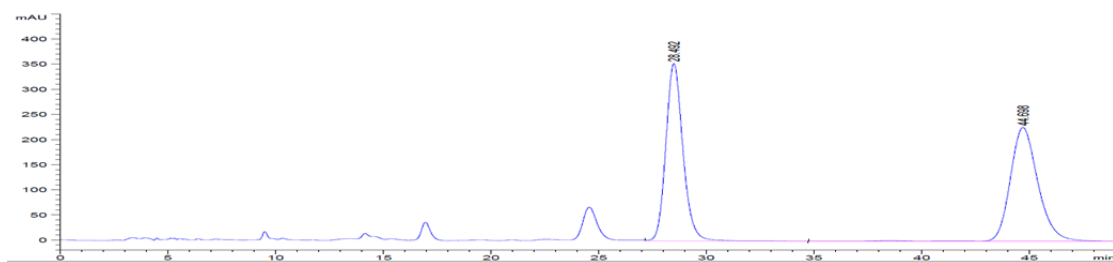


	Retention Time (min)	Area (mAU*s)	% Area
1	11.409	113.65214	0.5461
2	13.585	2.06961e4	99.4539

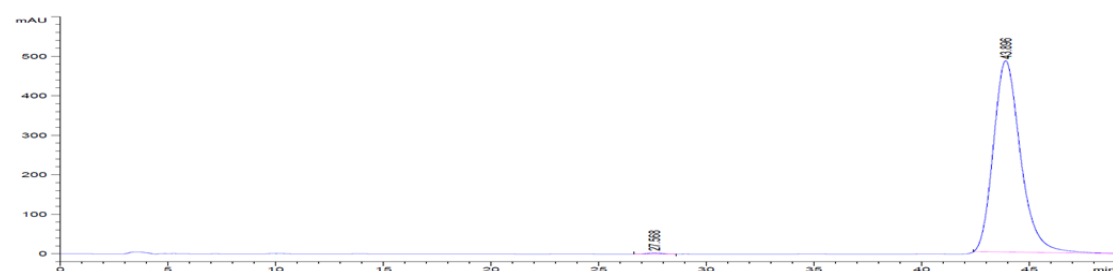


(S,E)-methyl 4-(7-(1-(4-chlorophenyl)-1-oxopropan-2-ylidene)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-9-yl)benzoate (4w)

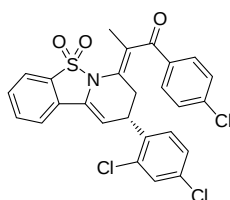
A white solid (52.1 mg), 50% yield, > 99% *ee*. $[\alpha]_D^{20} = -70.32$ ($c = 0.63$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 43.90 min, t_R (minor) = 27.57 min. ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, $J = 8.1$ Hz, 2H), 7.86 (d, $J = 7.7$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.73 – 7.57 (m, 3H), 7.36 (d, $J = 8.4$ Hz, 2H), 7.16 (d, $J = 8.1$ Hz, 2H), 5.86 (d, $J = 4.3$ Hz, 1H), 3.91 (d, $J = 10.9$ Hz, 3H), 3.81 (dt, $J = 9.3, 4.8$ Hz, 1H), 2.51 (dd, $J = 12.7, 4.7$ Hz, 1H), 2.30 (dd, $J = 10.6, 7.5$ Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.9, 166.8, 147.1, 140.3, 134.3, 133.7, 133.2, 132.0, 131.8, 130.9, 130.4, 130.1, 129.9, 129.3, 127.7, 121.5, 121.1, 106.0, 52.3, 39.8, 36.3, 18.9. ESI-HRMS: calcd for $\text{C}_{28}\text{H}_{22}\text{ClNNaO}_5\text{S}^+$ ($[\text{M}+\text{Na}]^+$) 542.0799, found 542.0789.



	Retention Time (min)	Area (mAU*s)	% Area
1	28.492	1.95611e4	49.1010
2	44.698	2.02774e4	50.8990

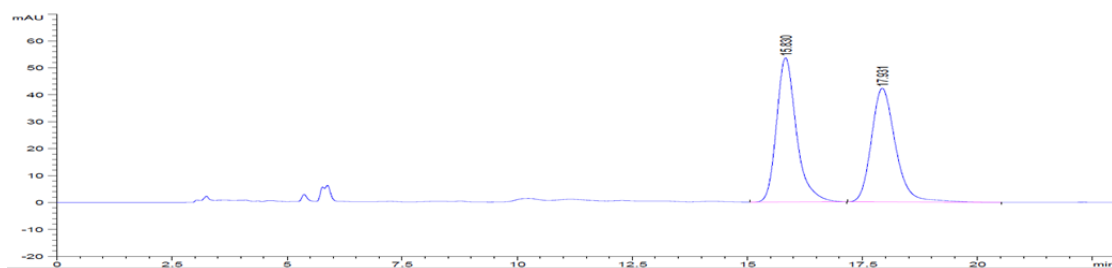


	Retention Time (min)	Area (mAU*s)	% Area
1	27.568	134.38991	0.3162
2	43.896	4.23625e4	99.6838

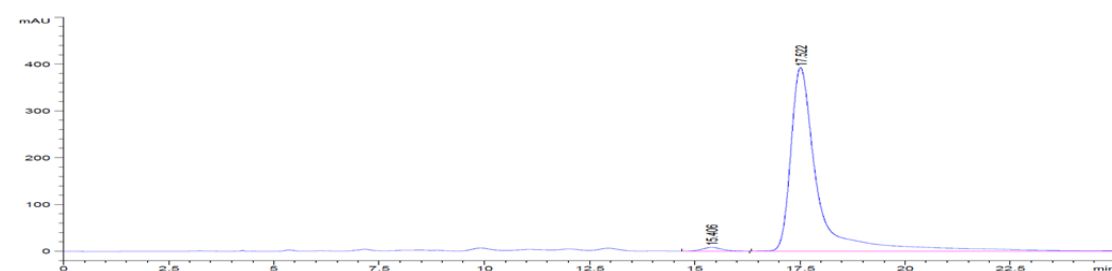


(*S,E*)-1-(4-chlorophenyl)-2-(9-(2,4-dichlorophenyl)-5,5-dioxido-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4x)

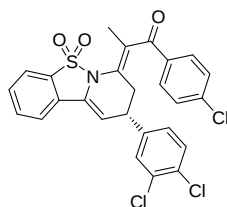
A white solid (65.2 mg), 61% yield, 97% *ee*. $[\alpha]_{\text{D}}^{20} = -150.92$ ($c = 0.65$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_{R} (major) = 17.52 min, t_{R} (minor) = 15.41 min. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, $J = 7.6$ Hz, 1H), 7.78 (d, $J = 8.4$ Hz, 2H), 7.71 (d, $J = 3.6$ Hz, 2H), 7.67 – 7.58 (m, 1H), 7.41 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.17 (d, $J = 1.6$ Hz, 1H), 6.94 (d, $J = 8.0$ Hz, 1H), 5.81 (d, $J = 4.4$ Hz, 1H), 3.72 (dt, $J = 9.2, 4.8$ Hz, 1H), 2.50 (dd, $J = 12.8, 4.8$ Hz, 1H), 2.37 – 2.15 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.9, 142.2, 140.5, 134.2, 133.8, 133.4, 132.9, 132.2, 132.0, 131.5, 130.9, 130.7, 130.6, 130.3, 129.6, 129.5, 129.4, 127.1, 121.5, 121.2, 105.4, 39.0, 36.2, 18.9. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{18}\text{Cl}_3\text{NNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 551.9965, found 551.9957.



	Retention Time (min)	Area (mAU*s)	% Area
1	15.830	1612.82092	51.2231
2	17.931	1535.79907	48.7769

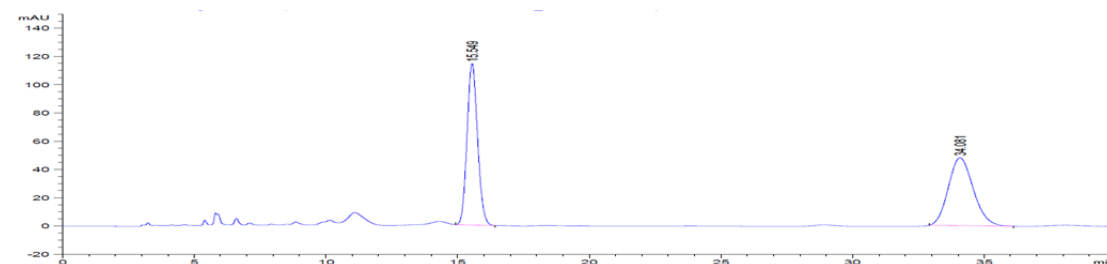


	Retention Time (min)	Area (mAU*s)	% Area
1	15.406	256.28461	1.4553
2	17.522	1.73546e4	98.5447

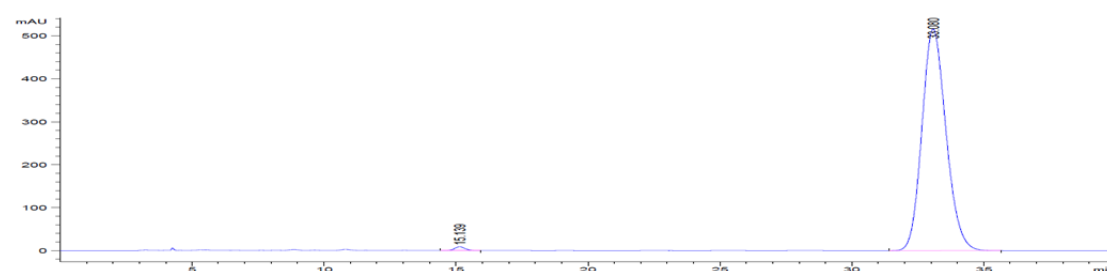


(*S,E*)-1-(4-chlorophenyl)-2-(9-(3,4-dichlorophenyl)-5,5-dioxido-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4y)

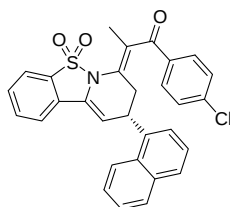
A white solid (34.0 mg), 32% yield, 99% *ee*. $[\alpha]_D^{20} = -41.98$ ($c = 0.37$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 33.08 min, t_R (minor) = 15.14 min. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, $J = 7.7$ Hz, 1H), 7.76-7.63 (m, 5H), 7.40 (d, $J = 8.3$ Hz, 2H), 7.29 (s, 1H), 7.20 (d, $J = 8.0$ Hz, 1H), 7.06 (d, $J = 8.3$ Hz, 1H), 5.83 (d, $J = 4.8$ Hz, 1H), 4.15 (dd, $J = 10.2, 5.0$ Hz, 1H), 2.49 (dd, $J = 13.0, 4.5$ Hz, 1H), 2.33 (dd, $J = 13.0, 6.1$ Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.7, 140.3, 137.2, 134.4, 134.2, 133.9, 133.8, 133.7, 132.2, 132.0, 130.8, 130.6, 130.2, 129.9, 129.7, 129.4, 127.2, 121.5, 121.1, 104.9, 35.9, 33.9, 18.7. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{18}\text{Cl}_3\text{NNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 551.9965, found 551.9957.



	Retention Time (min)	Area (mAU*s)	% Area
1	15.549	3178.78345	50.1497
2	34.081	3159.80078	49.8503

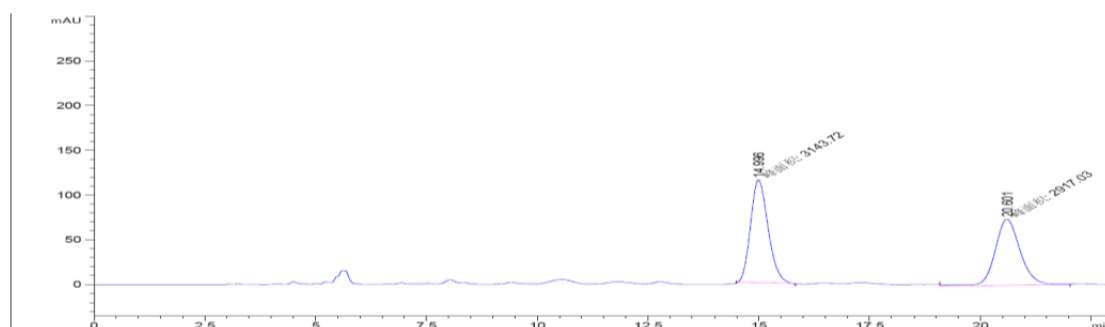


	Retention Time (min)	Area (mAU*s)	% Area
1	15.139	248.94138	0.7538
2	33.080	3.27764e4	99.2462

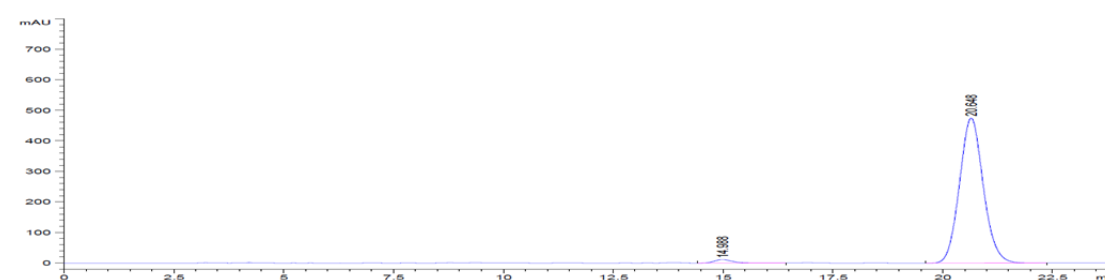


(*S,E*)-1-(4-chlorophenyl)-2-(9-(naphthalen-1-yl)-5,5-dioxido-8,9-dihydro-7*H*-benz o[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4z)

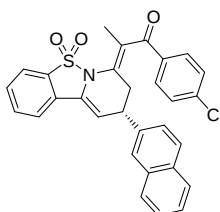
A white solid (41.2 mg), 40% yield, 96% *ee*. $[\alpha]_{\text{D}}^{20} = +110.77$ ($c = 0.26$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_{R} (major) = 20.65 min, t_{R} (minor) = 16.99 min. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, $J = 7.7$ Hz, 1H), 7.87 – 7.65 (m, 5H), 7.66 – 7.57 (m, 3H), 7.50 – 7.37 (m, 3H), 7.32 – 7.23 (m, 3H), 6.01 (d, $J = 4.2$ Hz, 1H), 4.55 (dt, $J = 7.0, 4.8$ Hz, 1H), 2.69 (dd, $J = 13.0, 4.8$ Hz, 1H), 2.48 (dd, $J = 12.2, 7.8$ Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.1, 140.1, 137.2, 134.2, 134.1, 133.6, 133.1, 132.0, 131.4, 130.9, 130.6, 130.6, 130.3, 130.3, 129.2, 128.1, 126.6, 125.9, 125.4, 124.8, 122.4, 121.5, 121.1, 107.4, 35.6, 35.2, 18.7. ESI-HRMS: calcd for $\text{C}_{30}\text{H}_{22}\text{ClNNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 534.0901, found 534.0897.



	Retention Time (min)	Area (mAU*s)	% Area
1	14.995	3143.72046	51.8702
2	20.601	2917.03003	48.1298

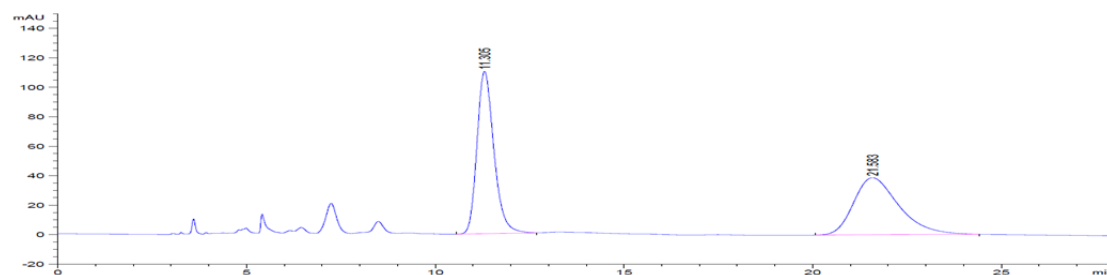


	Retention Time (min)	Area (mAU*s)	% Area
1	14.988	329.64178	1.8082
2	20.648	1.79008e4	98.1918

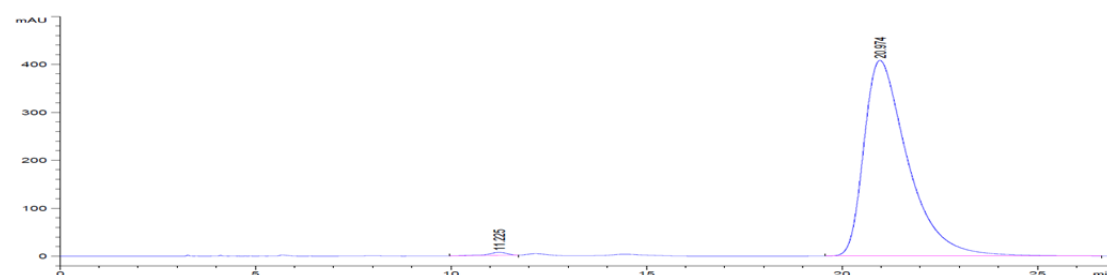


(S,E)-1-(4-chlorophenyl)-2-(9-(naphthalen-2-yl)-5,5-dioxido-8,9-dihydro-7H-benzothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4ba)

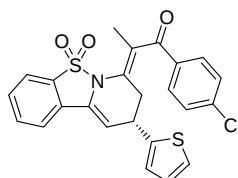
A white solid (83.3 mg), 81% yield, > 99% *ee*. $[\alpha]_D^{20} = -166.27$ ($c = 0.59$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 70/30, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 20.97 min, t_R (minor) = 11.23 min. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, $J = 7.8$ Hz, 1H), 7.81–7.46 (m, 9H), 7.53 – 7.43 (m, 2H), 7.17 (dd, $J = 8.5, 1.6$ Hz, 1H), 7.08 (d, $J = 8.5$ Hz, 2H), 5.98 (d, $J = 4.4$ Hz, 1H), 3.91 (dt, $J = 7.0, 4.8$ Hz, 1H), 2.62 (dd, $J = 13.0, 4.9$ Hz, 1H), 2.46 (dd, $J = 13.0, 7.2$ Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.1, 139.9, 139.3, 134.2, 133.6, 133.4, 132.9, 132.7, 132.0, 131.6, 130.7, 130.6, 130.4, 130.3, 129.0, 128.6, 127.8, 127.7, 126.5, 126.3, 126.1, 125.8, 121.4, 121.1, 106.9, 39.8, 36.4, 18.9. ESI-HRMS: calcd for $\text{C}_{30}\text{H}_{22}\text{ClNNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 534.0901, found 534.0897.



	Retention Time (min)	Area (mAU*s)	% Area
1	11.305	3436.88940	51.6316
2	21.583	3219.66821	48.3684

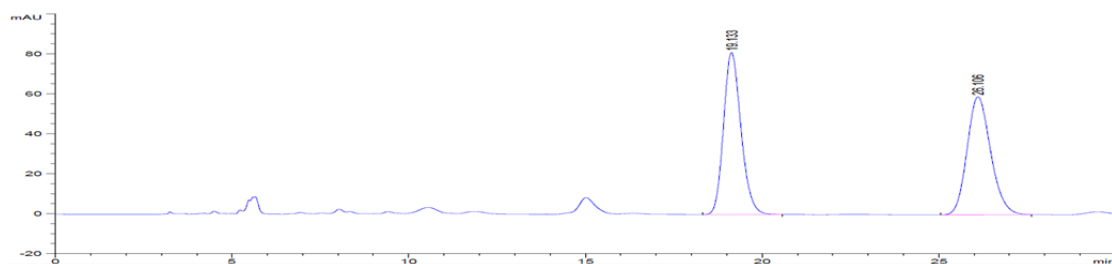


	Retention Time (min)	Area (mAU*s)	% Area
1	11.225	213.80417	0.6698
2	20.974	3.17090e4	99.3302

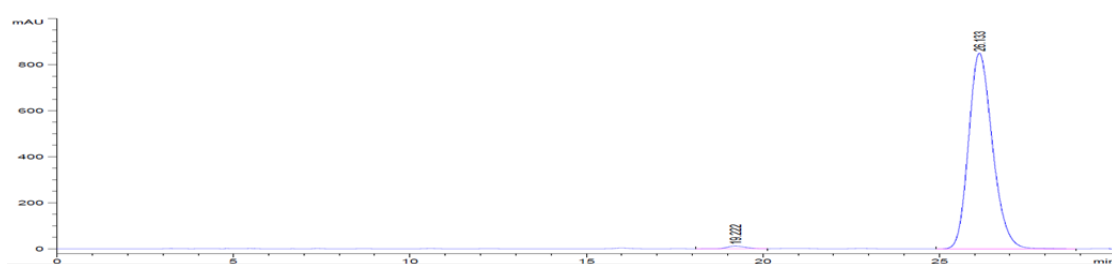


(*S,E*)-1-(4-chlorophenyl)-2-(5,5-dioxido-9-(thiophen-2-yl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)propan-1-one (4bb)

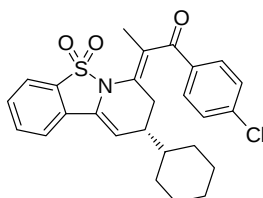
A white solid (80.2 mg), 86% yield, 98% *ee*. $[\alpha]_D^{20} = -55.93$ ($c = 0.59$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 26.13 min, t_R (minor) = 19.22 min. ^1H NMR (400 MHz, CDCl_3) δ 7.92 – 7.78 (m, 3H), 7.69 (d, $J = 4.1$ Hz, 2H), 7.62 (dq, $J = 8.2, 4.2$ Hz, 1H), 7.49 – 7.39 (m, 2H), 7.18 (dd, $J = 5.1, 1.1$ Hz, 1H), 6.93 (dd, $J = 5.1, 3.5$ Hz, 1H), 6.78 (d, $J = 3.4$ Hz, 1H), 5.92 (d, $J = 4.6$ Hz, 1H), 4.05 (dt, $J = 6.8, 4.7$ Hz, 1H), 2.55 (dd, $J = 12.9, 4.8$ Hz, 1H), 2.38 (dd, $J = 12.9, 7.1$ Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.0, 145.0, 140.2, 134.6, 133.7, 132.4, 132.0, 131.9, 130.9, 130.4, 130.1, 129.3, 127.0, 124.9, 124.5, 121.4, 121.2, 106.6, 36.9, 34.9, 19.0. ESI-HRMS: calcd for calcd for $\text{C}_{24}\text{H}_{18}\text{ClNNaO}_3\text{S}_2^+$ ($[\text{M} + \text{Na}]^+$) 490.0309, found 490.0306.



	Retention Time (min)	Area (mAU*s)	% Area
1	19.133	2784.80420	50.3976
2	26.106	2740.86792	49.6024

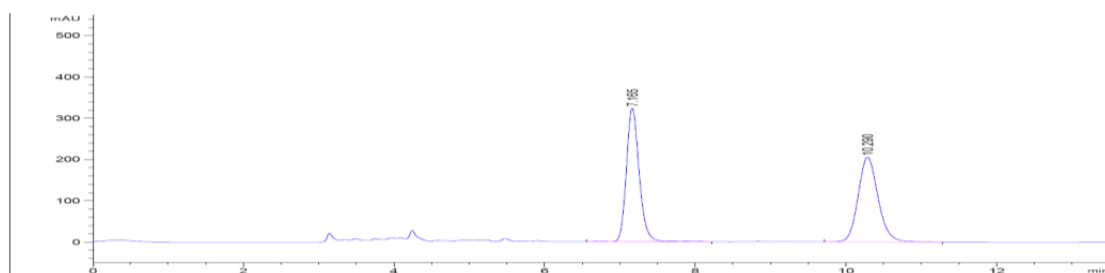


	Retention Time (min)	Area (mAU*s)	% Area
1	19.222	433.95984	1.0710
2	26.133	4.00835e4	98.9290

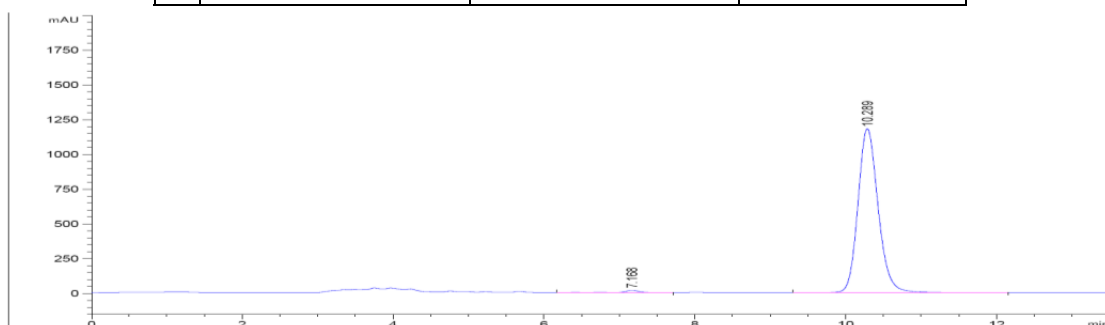


(R,E)-1-(4-chlorophenyl)-2-(9-cyclohexyl-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)propan-1-one (4bc)

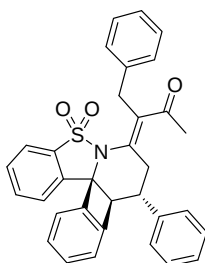
A white solid (29.1 mg), 61% yield, 98% *ee*. $[\alpha]_D^{20} = -14.3$ ($c = 0.63$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 10.29 min, t_R (minor) = 7.17 min. ^1H NMR (400 MHz, CDCl_3) δ 8.04 (d, $J = 8.0$ Hz, 2H), 7.82 (d, $J = 8.0$ Hz, 1H), 7.66 (d, $J = 3.2$ Hz, 2H), 7.56 (dd, $J = 10.0, 5.6$ Hz, 1H), 7.49 (d, $J = 8.0$ Hz, 2H), 5.79 (d, $J = 4.0$ Hz, 1H), 2.31 (s, 3H), 2.26 – 2.19 (m, 1H), 2.17 – 2.05 (m, 2H), 1.74 – 1.54 (m, 5H), 1.23 – 1.10 (m, 3H), 0.98 – 0.84 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.8, 140.4, 135.1, 133.5, 131.9, 131.8, 131.2, 130.9, 123.0, 129.9, 129.5, 121.4, 120.9, 108.1, 41.3, 39.6, 31.3, 30.6, 30.5, 26.5, 26.4, 26.3, 19.1. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{26}\text{ClNNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 490.1214, found 490.1217.



	Retention Time (min)	Area (mAU*s)	% Area
1	7.165	3844.90698	50.4658
2	10.290	3773.92651	49.5342

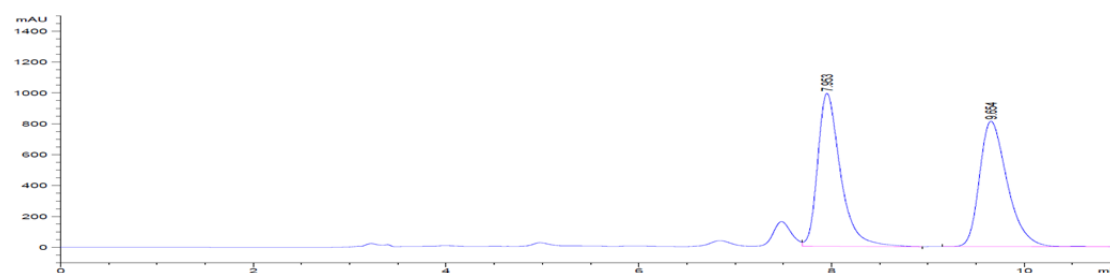


	Retention Time (min)	Area (mAU*s)	% Area
1	7.168	210.29852	0.9508
2	10.289	2.19078e4	99.0492

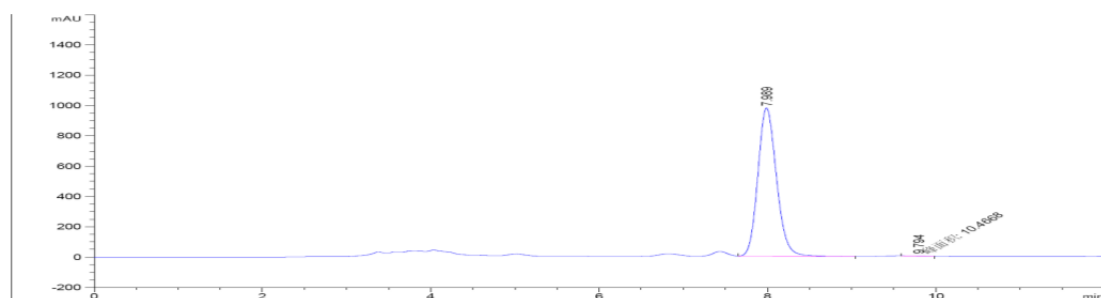


(E)-3-((9S,9aS,13bS)-5,5-dioxido-9-phenyl-9,9a-dihydrobenzo[3,4]cyclobuta[1,2-b]benzo[4,5]isothiazolo[2,3-a]pyridin-7(8H)-ylidene)-4-phenylbutan-2-one (6a)

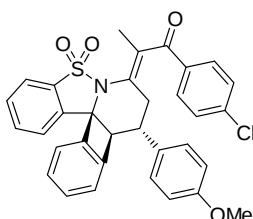
A white solid (60.2 mg), 58% yield, > 99% *ee*. $[\alpha]_{\text{D}}^{20} = +106.43$ ($c = 0.28$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 70/30, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_{R} (major) = 7.97 min, t_{R} (minor) = 9.68 min. ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, $J = 6.8$ Hz, 1H), 7.56 (dd, $J = 16.0, 7.6$ Hz, 2H), 7.47 – 7.41 (m, 1H), 7.38 – 7.24 (m, 7H), 7.14 (s, 3H), 7.09 – 6.90 (m, 3H), 6.88 (d, $J = 6.8$ Hz, 1H), 4.57 (d, $J = 16.0$ Hz, 1H), 3.91 (dd, $J = 23.2, 11.6$ Hz, 2H), 3.40 – 3.27 (m, 1H), 2.82 (d, $J = 12.8$ Hz, 1H), 2.55 (t, $J = 13.2$ Hz, 1H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 203.6, 147.0, 145.9, 144.3, 143.4, 140.8, 137.7, 134.6, 134.0, 133.4, 130.9, 129.9, 129.3, 130.0, 128.9, 128.6, 127.2, 127.2, 126.5, 123.7, 122.4, 122.0, 121.3, 71.4, 59.6, 48.9, 35.8, 32.5, 30.9. ESI-HRMS: calcd for $\text{C}_{33}\text{H}_{27}\text{NNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 540.1604, found 540.1598.



	Retention Time (min)	Area (mAU*s)	% Area
1	7.953	1.63275e4	50.1741
2	9.654	1.62142e4	49.8259

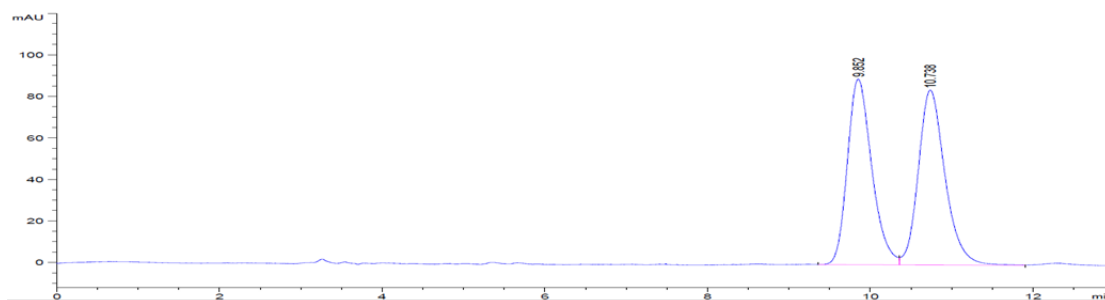


	Retention Time (min)	Area (mAU*s)	% Area
1	7.989	1.50471e4	99.9305
2	9.794	10.46683	0.0695

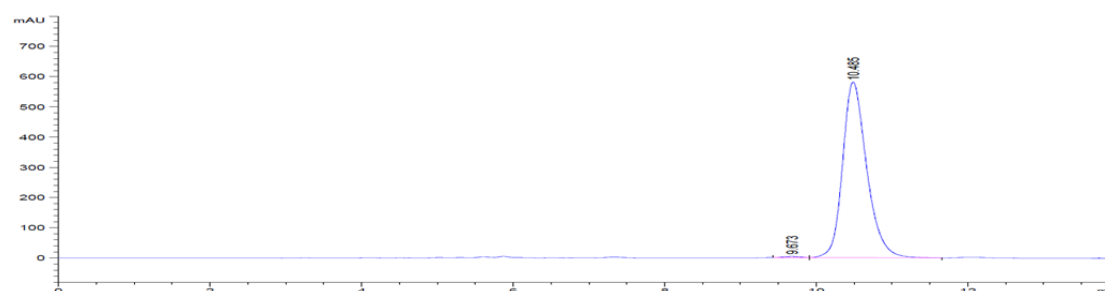


(E)-1-(4-chlorophenyl)-2-((9S,9aS,13bS)-9-(4-methoxyphenyl)-5,5-dioxido-9,9a-dihydrobenzo[3,4]cyclobuta[1,2-b]benzo[4,5]isothiazolo[2,3-a]pyridin-7(8H)-ylidenepropan-1-one (6b)

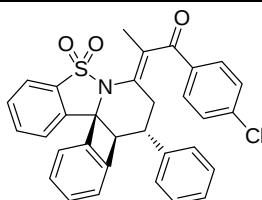
A white solid (78.1 mg), 69% yield, 99% *ee*. $[\alpha]_D^{20} = +107.7$ ($c = 0.74$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 70/30, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 10.49 min, t_R (minor) = 9.67 min. ^1H NMR (400 MHz, CDCl_3) δ 8.09 (d, $J = 8.4$ Hz, 2H), 7.90 (d, $J = 7.6$ Hz, 1H), 7.59 – 7.49 (m, 2H), 7.45 – 7.33 (m, 4H), 7.18 (t, $J = 7.0$ Hz, 2H), 7.04 (d, $J = 8.5$ Hz, 2H), 6.91 (d, $J = 7.4$ Hz, 1H), 6.82 (d, $J = 8.5$ Hz, 2H), 3.83 (d, $J = 8.9$ Hz, 1H), 3.76 (s, 3H), 3.10 – 3.04 (m, 1H), 2.31 (s, 3H), 2.25 – 2.14 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 193.0, 154.0, 141.8, 141.4, 136.4, 135.7, 131.0, 130.6, 129.4, 129.1, 128.8, 128.1, 126.6, 125.8, 124.8, 124.6, 123.2, 118.8, 117.3, 117.1, 116.3, 109.6, 64.7, 55.4, 50.5, 42.3, 13.5. ESI-HRMS: calcd for $\text{C}_{33}\text{H}_{27}\text{ClNO}_4\text{S}^+$ ($[\text{M} + \text{H}]^+$) 568.1344, 568.1338.



	Retention Time (min)	Area (mAU*s)	% Area
1	9.852	1862.63989	49.1599
2	10.738	1926.29822	50.8401

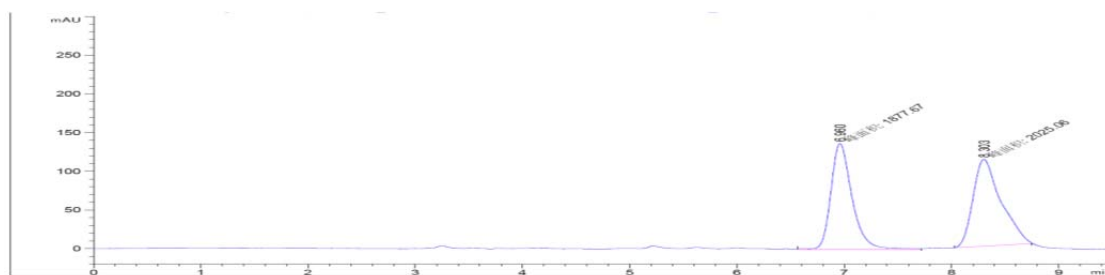


	Retention Time (min)	Area (mAU*s)	% Area
1	9.673	53.97691	0.4185
2	10.485	1.28431e4	99.5815

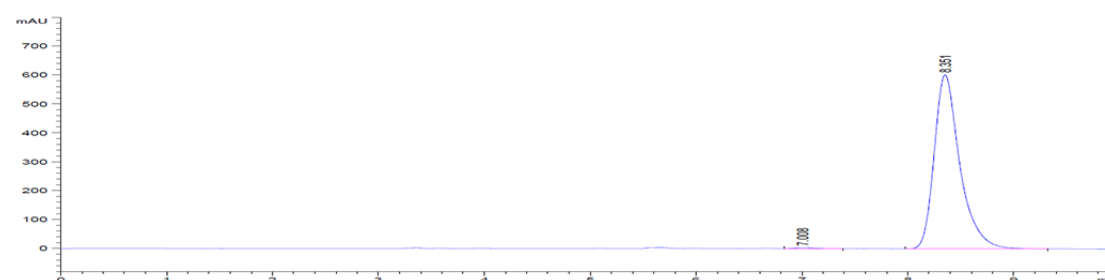


(*E*)-1-(4-chlorophenyl)-2-((9*S*,9*aS*,13*bS*)-5,5-dioxido-9-phenyl-9,9*a*-dihydrobenzo[3,4]cyclobuta[1,2-*b*]benzo[4,5]isothiazolo[2,3-*a*]pyridin-7(8*H*)-ylidene)propan-1-one (6c)

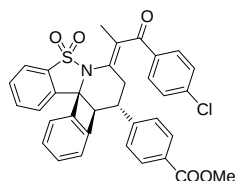
A white solid (73.2 mg), 68% isolate yield, 99% *ee*. $[\alpha]_{\text{D}}^{20} = +81.43$ ($c = 0.14$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 70/30, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_{R} (major) = 8.35 min, t_{R} (minor) = 7.01 min. ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.4$ Hz, 2H), 7.91 (d, $J = 7.5$ Hz, 1H), 7.64 – 7.49 (m, 2H), 7.49 – 7.06 (m, 11H), 6.91 (d, $J = 7.4$ Hz, 1H), 3.87 (d, $J = 8.8$ Hz, 1H), 3.23 – 3.07 (m, 1H), 2.32 (s, 3H), 2.30 – 2.17 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.8, 146.7, 146.2, 143.8, 141.2, 140.6, 135.7, 134.2, 134.0, 133.7, 132.8, 131.5, 130.7, 129.8, 129.5, 129.4, 129.1, 127.3, 127.1, 123.7, 122.2, 122.0, 121.2, 77.5, 69.6, 60.0, 47.8, 33.5, 18.3. ESI-HRMS: calcd for $\text{C}_{32}\text{H}_{24}\text{ClNNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 560.1058, found 560.1068.



	Retention Time (min)	Area (mAU*s)	% Area
1	6.960	1877.66919	48.1117
2	8.303	2025.05969	51.8883

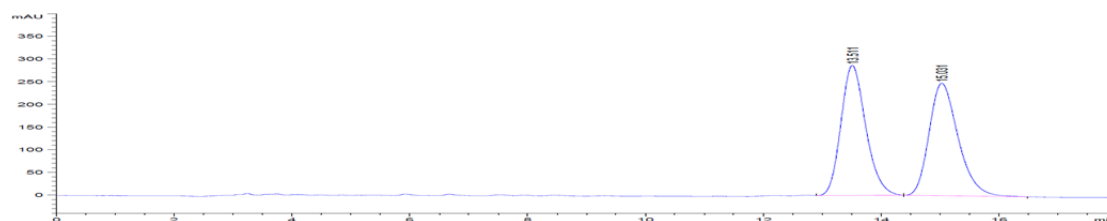


	Retention Time (min)	Area (mAU*s)	% Area
1	7.008	43.08905	0.4242
2	8.351	1.01144e4	99.5758

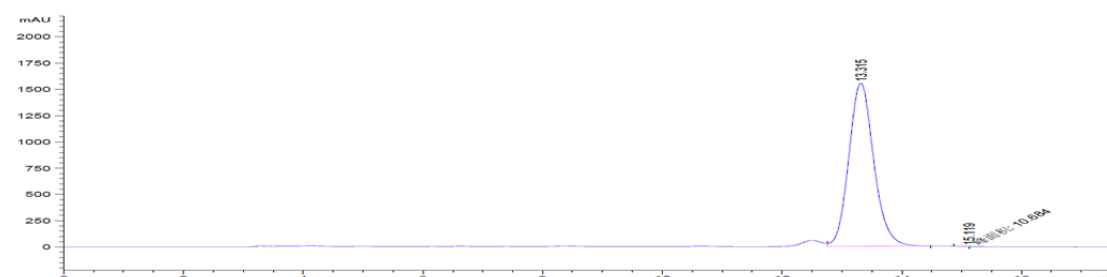


methyl 4-((9S,9aS,13bS,E)-7-(1-(4-chlorophenyl)-1-oxopropan-2-ylidene)-5,5-dioxido-7,8,9,9a-tetrahydrobenzo[3,4]cyclobuta[1,2-b]benzo[4,5]isothiazolo[2,3-a]pyridin-9-yl)benzoate (6d)

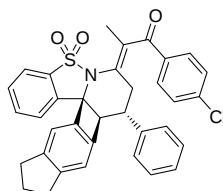
A white solid (86.4 mg), 72% yield, > 99% *ee*. $[\alpha]_D^{20} = +99.83$ ($c = 0.60$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 13.32 min, t_R (minor) = 15.12 min. ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, $J = 7.4$ Hz, 1H), 7.55 (dt, $J = 15.9, 6.9$ Hz, 2H), 7.44 (t, $J = 7.5$ Hz, 1H), 7.37 – 7.25 (m, 7H), 7.15 (dd, $J = 5.0, 1.6$ Hz, 3H), 7.02 – 6.96 (m, 3H), 6.89 (d, $J = 7.5$ Hz, 1H), 4.58 (d, $J = 16.0$ Hz, 1H), 3.91 (dd, $J = 23.3, 12.1$ Hz, 2H), 3.37 – 3.31 (m, 1H), 2.82 (dd, $J = 12.8, 3.7$ Hz, 1H), 2.56 (t, $J = 13.3$ Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 203.7, 147.0, 146.0, 144.3, 143.4, 140.8, 137.7, 134.6, 134.0, 133.5, 130.9, 129.9, 129.4, 129.1, 129.0, 128.6, 127.3, 127.2, 126.6, 123.8, 122.5, 122.0, 121.4, 71.4, 59.7, 49.0, 35.9, 32.6, 30.9. ESI-HRMS: calcd for $\text{C}_{34}\text{H}_{27}\text{ClNO}_5\text{S}^+$ ($[\text{M} + \text{H}]^+$) 596.1293, found 596.1301. calcd for $\text{C}_{34}\text{H}_{26}\text{ClNNaO}_5\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 618.1112, found 618.1115.



	Retention Time (min)	Area (mAU*s)	% Area
1	13.511	8394.97070	49.7090
2	15.031	8493.24707	50.2910

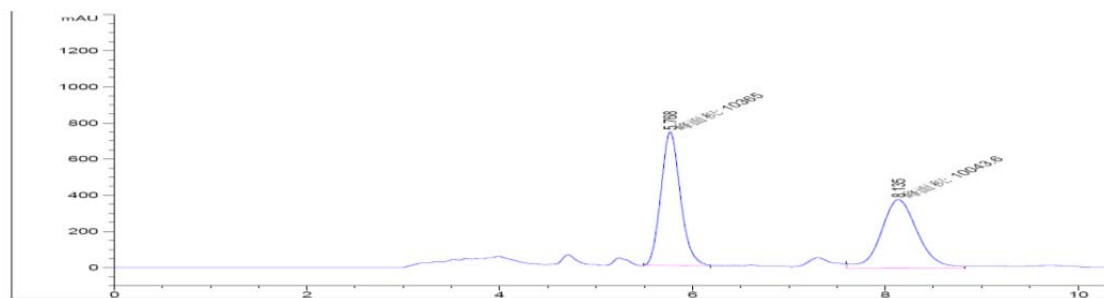


	Retention Time (min)	Area (mAU*s)	% Area
1	13.315	4.49559e4	99.9762
2	15.119	10.68405	0.0238

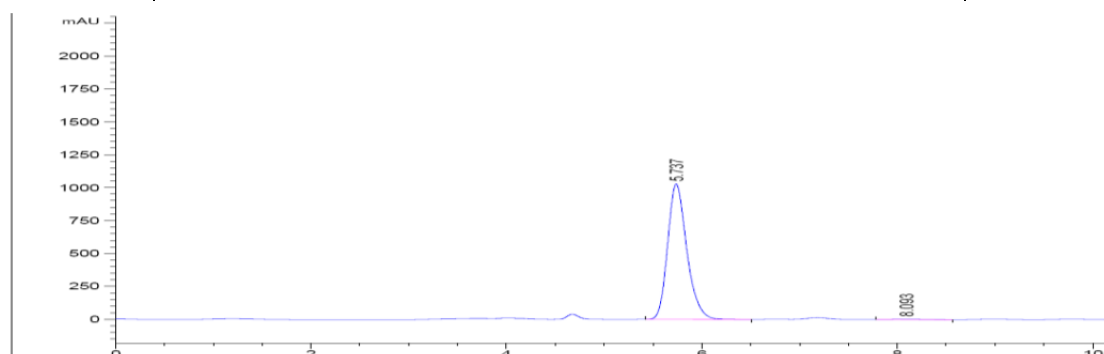


(E)-1-(4-chlorophenyl)-2-((9S,9aS,14bS)-5,5-dioxido-9-phenyl-8,9,9a,11,12,13-hexahydro-7H-benzo[4,5]isothiazolo[2,3-a]indeno[5',6':3,4]cyclobuta[1,2-b]pyridin-7-ylidene)propan-1-one (6e)

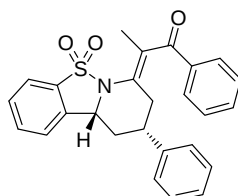
A white solid (63.0 mg), 55% isolate yield, 99% *ee*. $[\alpha]_D^{20} = +123.21$ ($c = 0.0028$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 70/30, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 6.82 min, t_R (minor) = 11.02 min. ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.2$ Hz, 2H), 7.89 (d, $J = 7.2$ Hz, 1H), 7.54 (td, $J = 13.6, 7.2$ Hz, 2H), 7.44 (d, $J = 8.4$ Hz, 2H), 7.29 (t, $J = 7.2$ Hz, 2H), 7.22 (t, $J = 7.2$ Hz, 1H), 7.12 (d, $J = 7.2$ Hz, 2H), 7.04 (d, $J = 6.0$ Hz, 2H), 6.95 (d, $J = 7.2$ Hz, 1H), 3.77 (d, $J = 8.8$ Hz, 1H), 3.15 – 3.07 (m, 1H), 2.98 – 2.80 (m, 4H), 2.31 (s, 3H), 2.28 – 2.18 (m, 2H), 2.16 – 2.06 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.9, 146.9, 145.5, 144.2, 144.0, 143.8, 141.7, 140.6, 135.4, 134.3, 133.9, 133.8, 133.0, 131.5, 129.6, 129.4, 129.1, 127.2, 127.2, 123.8, 121.1, 118.2, 118.1, 68.9, 58.9, 48.1, 33.6, 33.4, 33.2, 25.5, 18.4. ESI-HRMS: calcd for $\text{C}_{35}\text{H}_{29}\text{ClNO}_3\text{S}^+$ ($[\text{M} + \text{H}]^+$) 578.1551, found 578.1557. calcd for $\text{C}_{35}\text{H}_{28}\text{ClNNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 600.1371, found 600.1376.



	Retention Time (min)	Area (mAU*s)	% Area
1	5.768	1.03650e4	50.7873
2	8.135	1.00436e4	49.2127

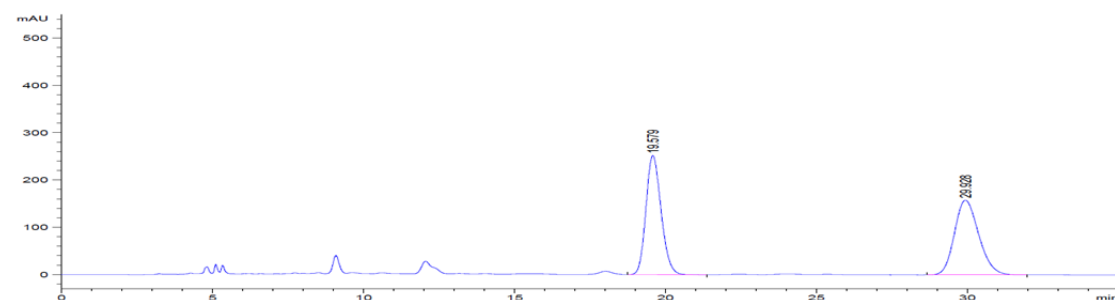


	Retention Time (min)	Area (mAU*s)	% Area
1	5.737	1027.70496	99.5769
2	8.093	2.91014	0.4231

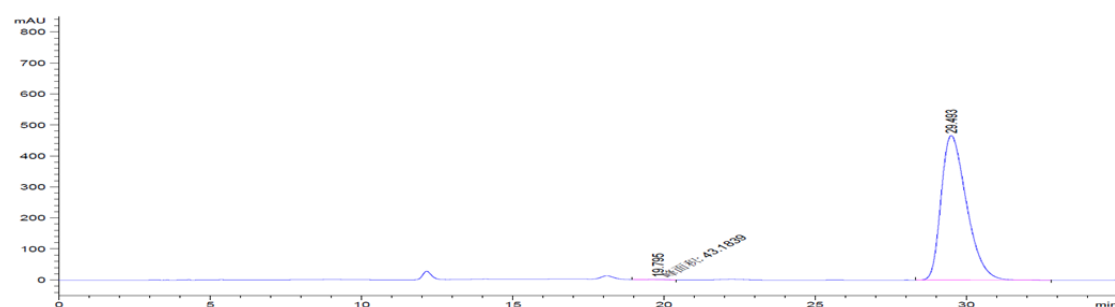


(*E*)-2-((9*R*,10*aR*)-5,5-dioxido-9-phenyl-8,9,10,10*a*-tetrahydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-ylidene)-1-phenylpropan-1-one (7b)

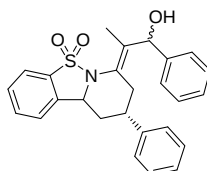
A white solid (81.4 mg), 94% yield, > 99% *ee*. $[\alpha]_D^{20} = -46.88$ ($c = 0.38$ in EtOAc). HPLC (chiral AD-H column), *n*-hexane/ *i*-PrOH = 75/25, flow rate 1.0 mL/min, $\lambda = 254$ nm, t_R (major) = 29.49 min, t_R (minor) = 19.80 min. ^1H NMR (400 MHz, CDCl_3) δ 8.09 (d, $J = 7.6$ Hz, 2H), 7.91 (d, $J = 7.6$ Hz, 1H), 7.66 (t, $J = 7.2$ Hz, 1H), 7.60 (t, $J = 7.6$ Hz, 2H), 7.51 (t, $J = 7.6$ Hz, 2H), 7.42 (d, $J = 7.6$ Hz, 1H), 7.22 (t, $J = 7.2$ Hz, 2H), 7.18 – 7.12 (m, 1H), 7.08 (d, $J = 7.3$ Hz, 2H), 4.75 (dd, $J = 12.0, 3.3$ Hz, 1H), 3.11 – 3.00 (m, 1H), 2.45 – 2.16 (m, 6H), 1.94 – 1.81 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 199.1, 143.6, 138.4, 137.7, 135.4, 134.2, 134.0, 133.2, 130.5, 129.8, 129.6, 129.2, 128.7, 127.0, 126.7, 124.1, 121.9, 60.5, 42.0, 39.7, 36.7, 18.0. ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{23}\text{ClNNaO}_3\text{S}^+$ ($[\text{M} + \text{Na}]^+$) 452.1291, found 452.1283.



	Retention Time (min)	Area (mAU*s)	% Area
1	19.579	8786.63965	49.9538
2	29.928	9902.90918	50.0462



	Retention Time (min)	Area (mAU*s)	% Area
1	19.795	43.18388	0.1586
2	29.493	2.71813e4	99.8414



(9*R,E*)-7-(1-hydroxy-1-phenylpropan-2-ylidene)-9-phenyl-8,9,10,10a-tetrahydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide

8a Up spot: colorless oil (38.5 mg), 44% yield. $[\alpha]_D^{20} = -67.50$ ($c = 0.40$ in EtOAc). ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, $J = 7.6$ Hz, 1H), 7.62 (t, $J = 7.4$ Hz, 1H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.49 – 7.15 (m, 10H), 5.90 (s, 1H), 4.64 (dd, $J = 12.0, 3.5$ Hz, 1H), 3.07 (d, $J = 13.3$ Hz, 1H), 2.97 (t, $J = 12.6$ Hz, 1H), 2.63 (t, $J = 12.9$ Hz, 1H), 2.32 (d, $J = 13.0$ Hz, 2H), 1.94 (q, $J = 12.6$ Hz, 1H), 1.93 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 144.1, 141.6, 141.0, 138.6, 134.5, 133.0, 129.5, 128.9, 128.6, 128.2, 127.5, 127.2, 126.8, 125.8, 123.9, 122.0, 71.7, 60.8, 43.1, 39.9, 34.8, 13.6.

8a' Down spot: colorless oil (40.1 mg), 46% yield. $[\alpha]_D^{20} = +29.13$ ($c = 0.23$ in EtOAc). ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, $J = 7.6$ Hz, 1H), 7.61 (t, $J = 7.5$ Hz, 1H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.45 (d, $J = 7.8$ Hz, 2H), 7.37 (t, $J = 7.8$ Hz, 2H), 7.34 – 7.16 (m, 5H), 5.87 (s, 1H), 4.67 (dd, $J = 12.0, 3.6$ Hz, 1H), 3.13 (d, $J = 13.6$ Hz, 1H), 3.06 (td, $J = 12.6, 3.0$ Hz, 1H), 2.65 – 2.50 (m, 1H), 2.29 (d, $J = 13.3$ Hz, 1H), 2.21 (s, 1H), 1.92 (q, $J = 12.6$ Hz, 1H), 1.90 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 144.3,

141.8, 139.9, 138.7, 134.5, 133.0, 129.5, 129.0, 128.9, 128.7, 127.6, 127.1, 126.9, 125.7, 123.9, 121.9, 71.9, 60.7, 43.0, 39.8, 33.9, 13.9. ESI-HRMS: calcd for $C_{26}H_{25}NNaO_3S^+$ ($[M + Na]^+$) 454.1447, found 454.1442.

(I) X-ray crystallographic structures of **4a** and **6b**:

X-Ray Crystallographic Analysis of **4a** (CCDC 1515830)

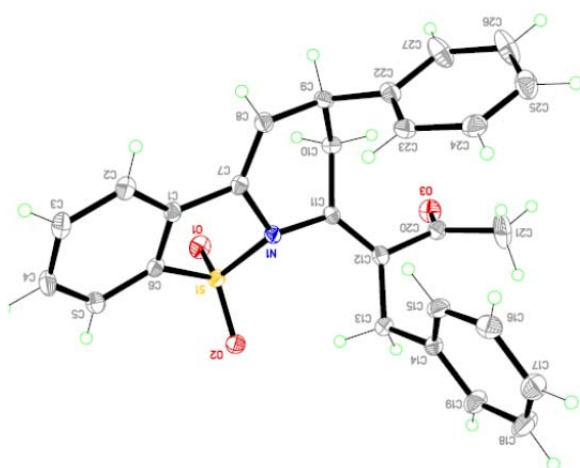


Figure 1. X-ray structure of (*S*)-**4a** (30% probability factor for the thermal ellipsoids).

Table S1. Crystal data and structure refinement for **4a**.

Empirical formula	$C_{29}H_{26}O_7$
Formula weight	486.50
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P 2(1)
Unit cell dimensions	$a = 11.2281(5)$ Å $\alpha = 90^\circ$ $b = 9.6521(5)$ Å $\beta = 101.793(2)^\circ$ $c = 24.3706(11)$ Å $\gamma = 90^\circ$
Volume	$2585.4(2)$ Å ³
Z	4
Density (calculated)	1.250 Mg/m ³
Absorption coefficient	0.735 mm ⁻¹
F(000)	1024
Crystal size	0.275 x 0.255 x 0.180 mm ³
Theta range for data collection	3.705 to 74.439°
Index ranges	$-13 \leq h \leq 12$, $-12 \leq k \leq 11$, $-30 \leq l \leq 29$
Reflections collected	30162
Independent reflections	10058 [$R(\text{int}) = 0.0342$]

Completeness to theta = 67.679° 98.1 %
 Refinement method Full-matrix least-squares on F²
 Data / restraints / parameters 10058 / 1 / 656
 Goodness-of-fit on F² 1.042
 Final R indices [I > 2sigma(I)] R1 = 0.0405, wR2 = 0.0987
 R indices (all data) R1 = 0.0441, wR2 = 0.1011
 Absolute structure parameter -0.03(17)*
 Largest diff. peak and hole 0.274 and -0.218 e.Å⁻³

X-Ray Crystallographic Analysis of **6b** (CCDC 1515831)

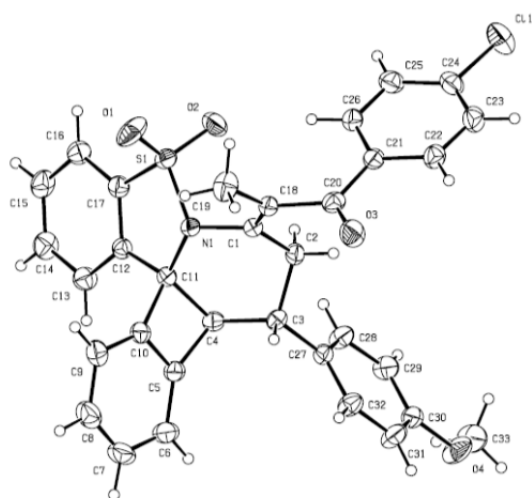


Figure 2. X-ray structure of **6b** (30% probability factor for the thermal ellipsoids).

Table 1. Crystal data and structure refinement for **6b**.

Identification code F570
 Empirical formula C₂₄ H₂₀ O₅ S
 Formula weight 420.46
 Temperature 100(2) K
 Wavelength 0.71073 Å
 Crystal system Monoclinic
 Space group P2₁
 Unit cell dimensions a = 5.4465(3) Å □ = 90°.
 b = 12.4107(7) Å □ = 92.621(2)°.
 c = 14.8394(9) Å □ = 90°.
 Volume 1002.02(10) Å³
 Z 2
 Density (calculated) 1.394 Mg/m³
 Absorption coefficient 0.196 mm⁻¹
 F(000) 440
 Crystal size 0.332 x 0.323 x 0.279 mm³
 Theta range for data collection 2.140 to 36.313°.

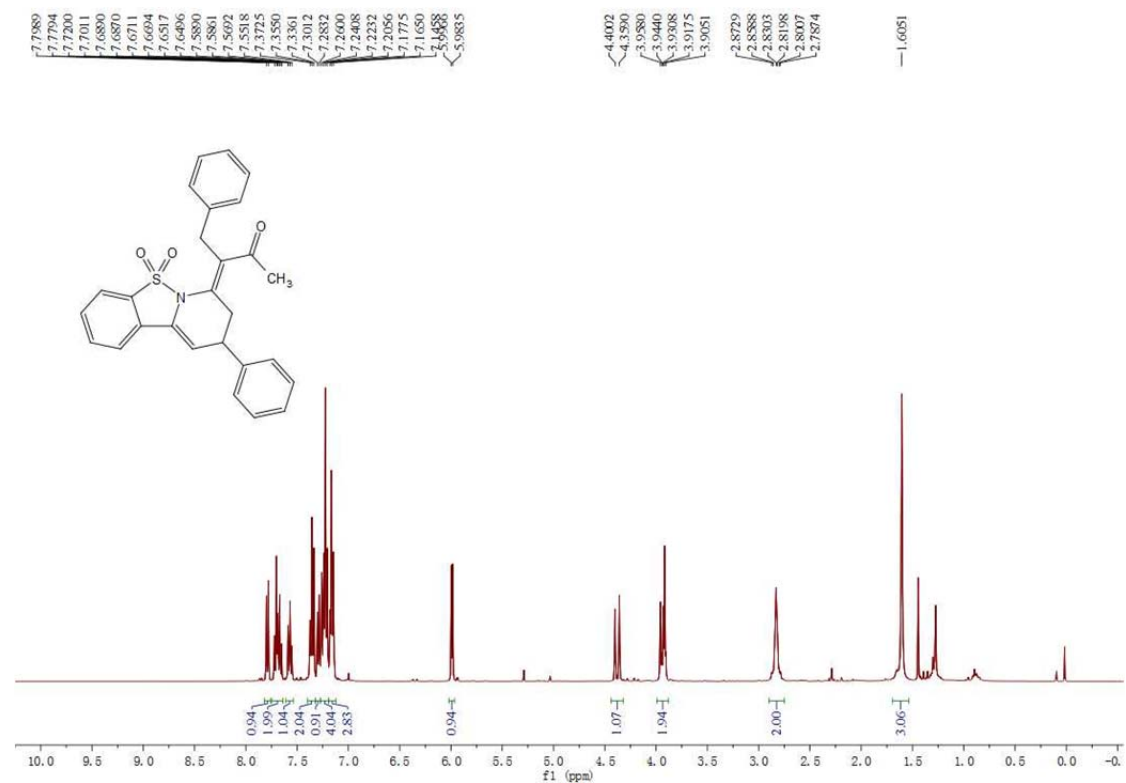
Index ranges $-9 \leq h \leq 9$, $-20 \leq k \leq 20$, $-24 \leq l \leq 24$
 Reflections collected 46026
 Independent reflections 9671 [$R(\text{int}) = 0.0348$]
 Completeness to $\theta = 25.242^\circ$ 99.9 %
 Absorption correction Semi-empirical from equivalents
 Max. and min. transmission 0.7471 and 0.7188
 Refinement method Full-matrix least-squares on F^2
 Data / restraints / parameters 9671 / 1 / 273
 Goodness-of-fit on F^2 1.059
 Final R indices [$I > 2\sigma(I)$] $R_1 = 0.0358$, $wR_2 = 0.0870$
 R indices (all data) $R_1 = 0.0479$, $wR_2 = 0.0920$
 Absolute structure parameter 0.019(14)
 Extinction coefficient n/a
 Largest diff. peak and hole 0.340 and -0.268 e. $\text{\AA}^{-3}$

(J) References:

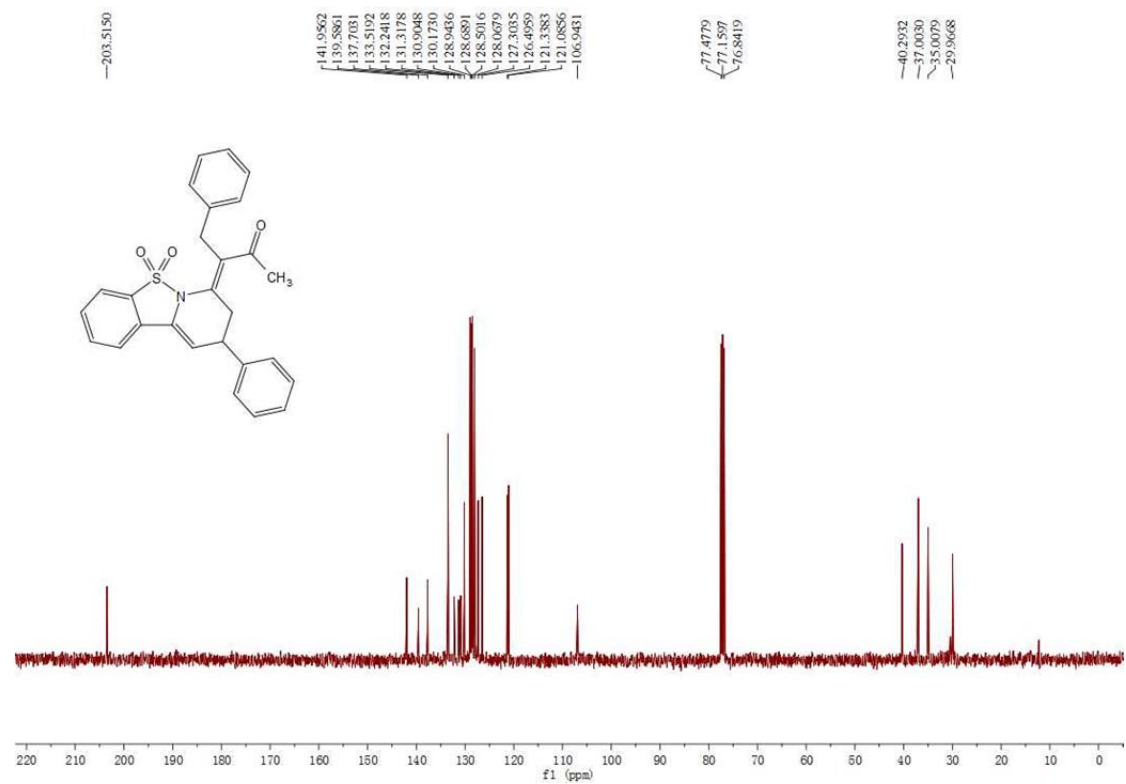
- [1] a) X. Feng, Z. Zhou, C. Ma, X. Yin, R. Li, L. Dong, Y.-C. Chen, *Angew. Chem. Int. Ed.* **2013**, 52, 14173; b) X. Yin, Y. Zheng, X. Feng, K. Jiang, X.-Z. Wei, N. Gao, Y.-C. Chen, *Angew. Chem., Int. Ed.* **2014**, 53, 6245; c) X.-L. He, Y.-C. Xiao, W. Du, Y.-C. Chen, *Chem. - Eur. J.* **2015**, 21, 3443.
 [2] a) J. Li, W. Kong, Y. Yu, C. Fu, S. Ma, *J. Org. Chem.* **2009**, 74, 8733; b) S. Ma, S. Yu, S. Yin, *J. Org. Chem.* **2003**, 68, 8996.
 [3] a) X. Han, Y. Wang, F. Zhong, Y. Lu, *J. Am. Chem. Soc.* **2011**, 133, 1726; b) X. Han, F. Zhong, Y. Wang, Y. Lu, *Angew. Chem. Int. Ed.* **2012**, 51, 767; c) F. Zhong, X. Han, Y. Wang, Y. Lu, *Chem. Sci.* **2012**, 3, 1231; d) F. Zhong, X. Han, Y. Wang, Y. Lu, *Angew. Chem. Int. Ed.* **2011**, 50, 7837; e) F. Zhong, J. Luo, G. - Y. Chen, X. Dou, Y. Lu, *J. Am. Chem. Soc.* **2012**, 134, 10222; f) F. Zhong, X. Dou, X. Han, W. Yao, Q. Zhu, Y. Meng, Y. Lu, *Angew. Chem. Int. Ed.* **2013**, 52, 943.

(K) NMR spectra

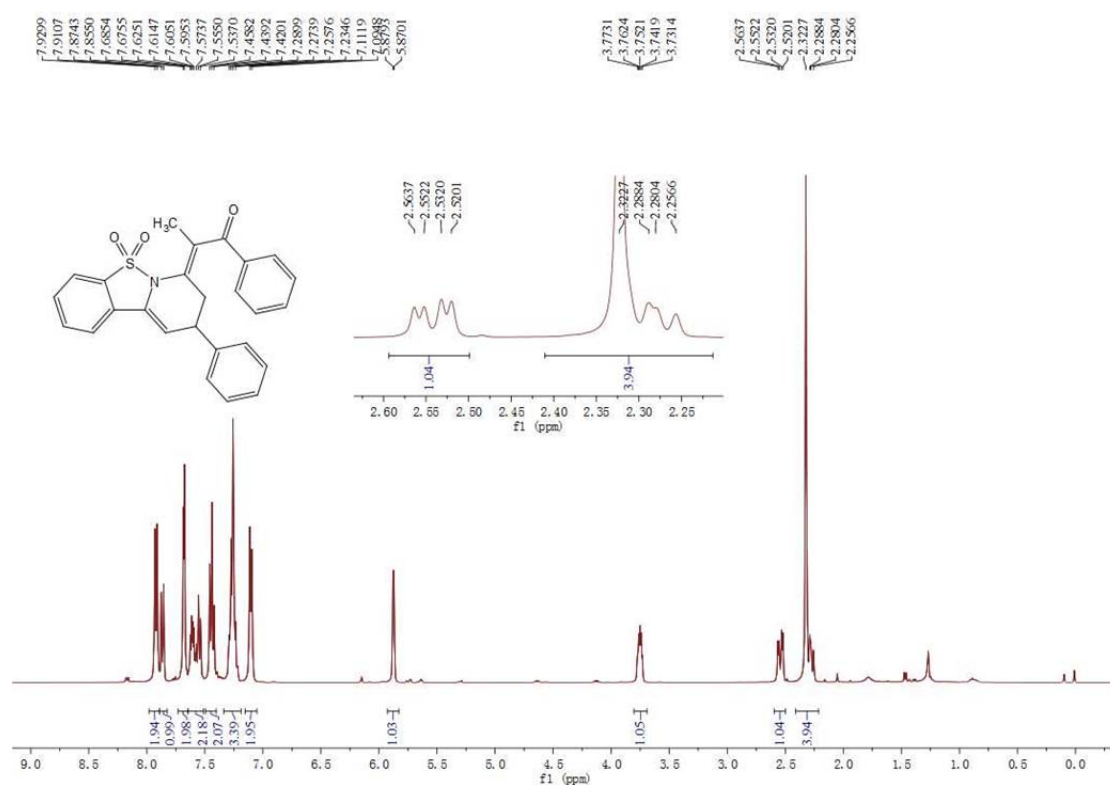
4a



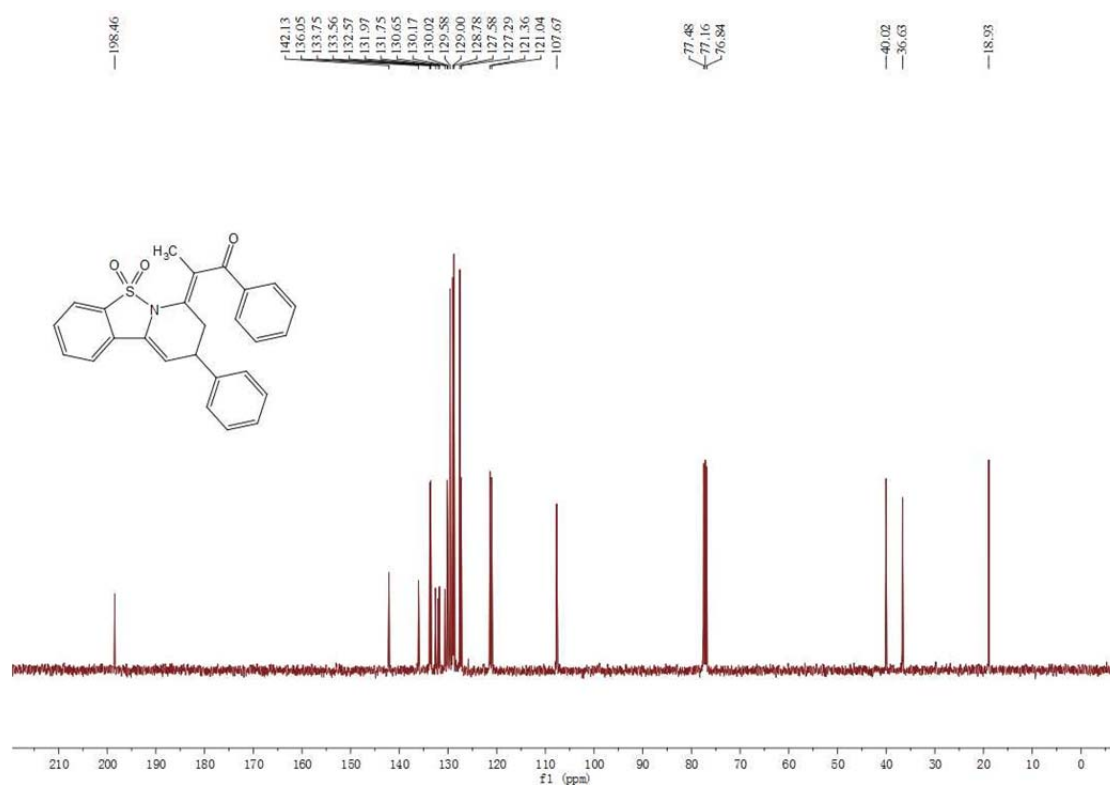
4a



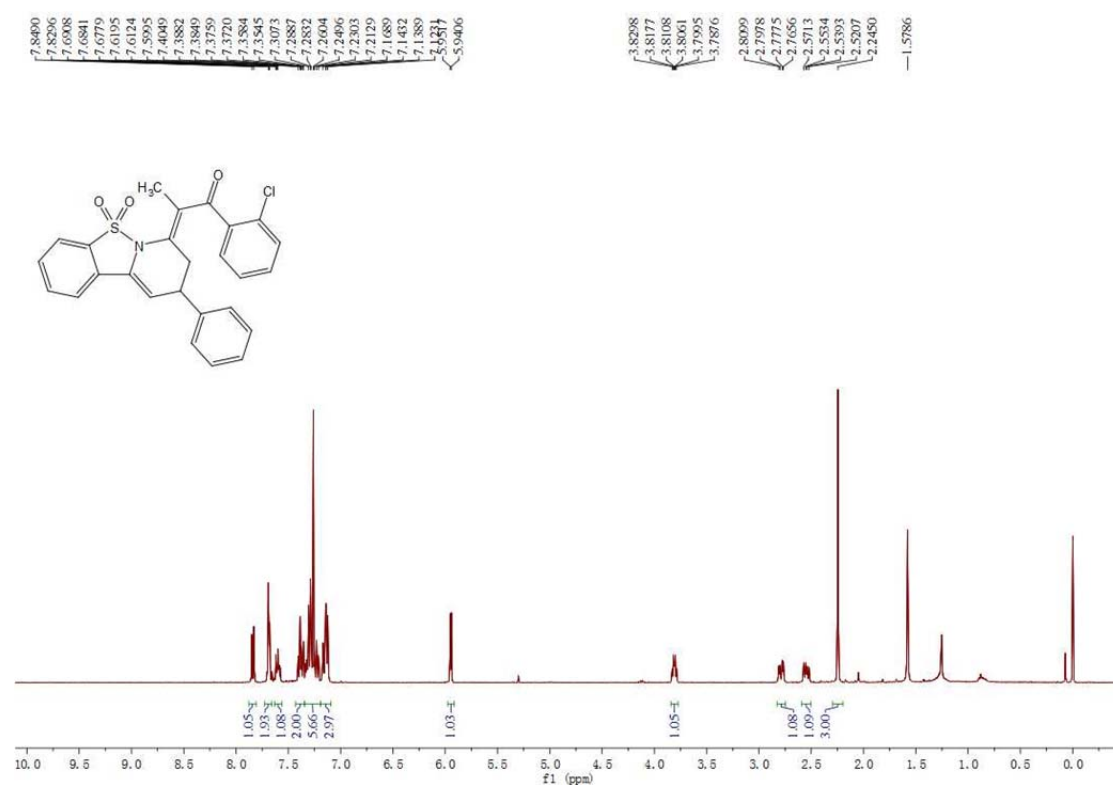
4b



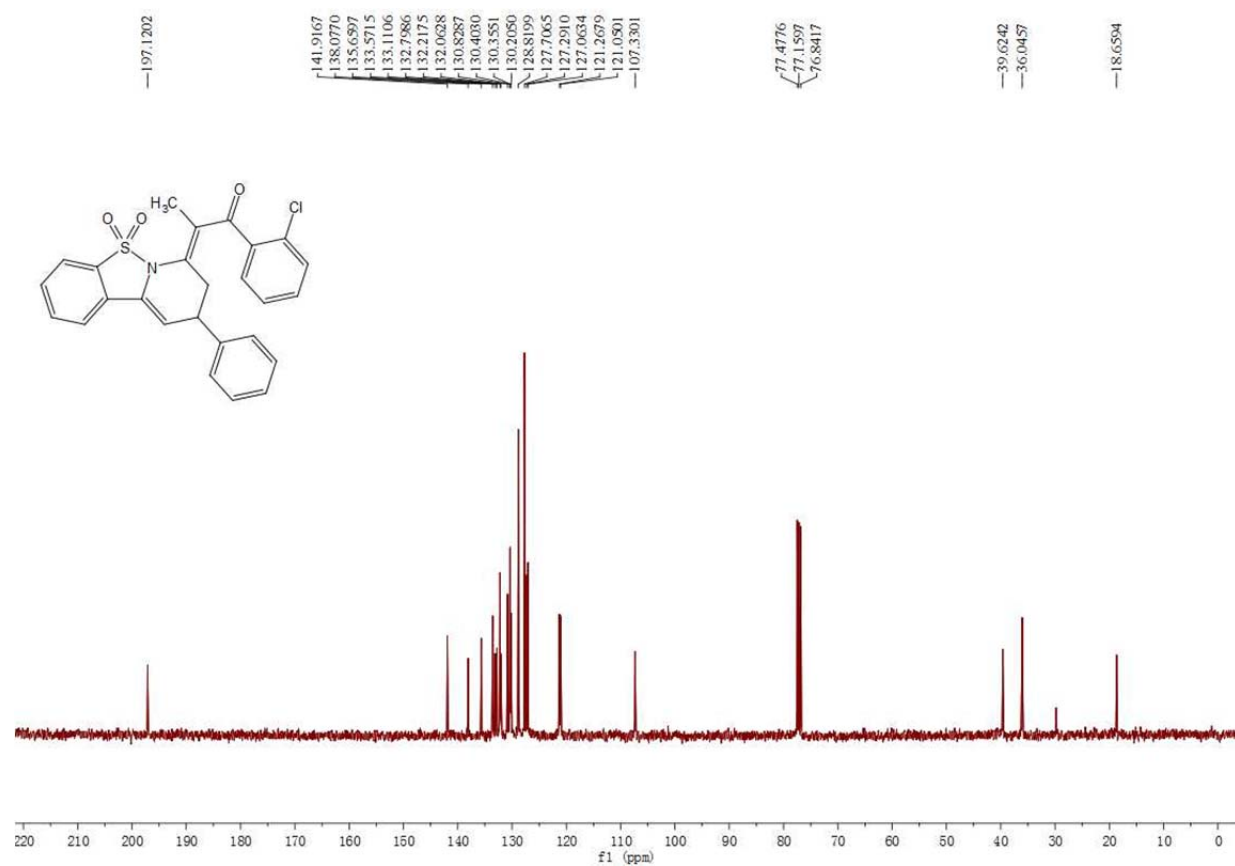
4b



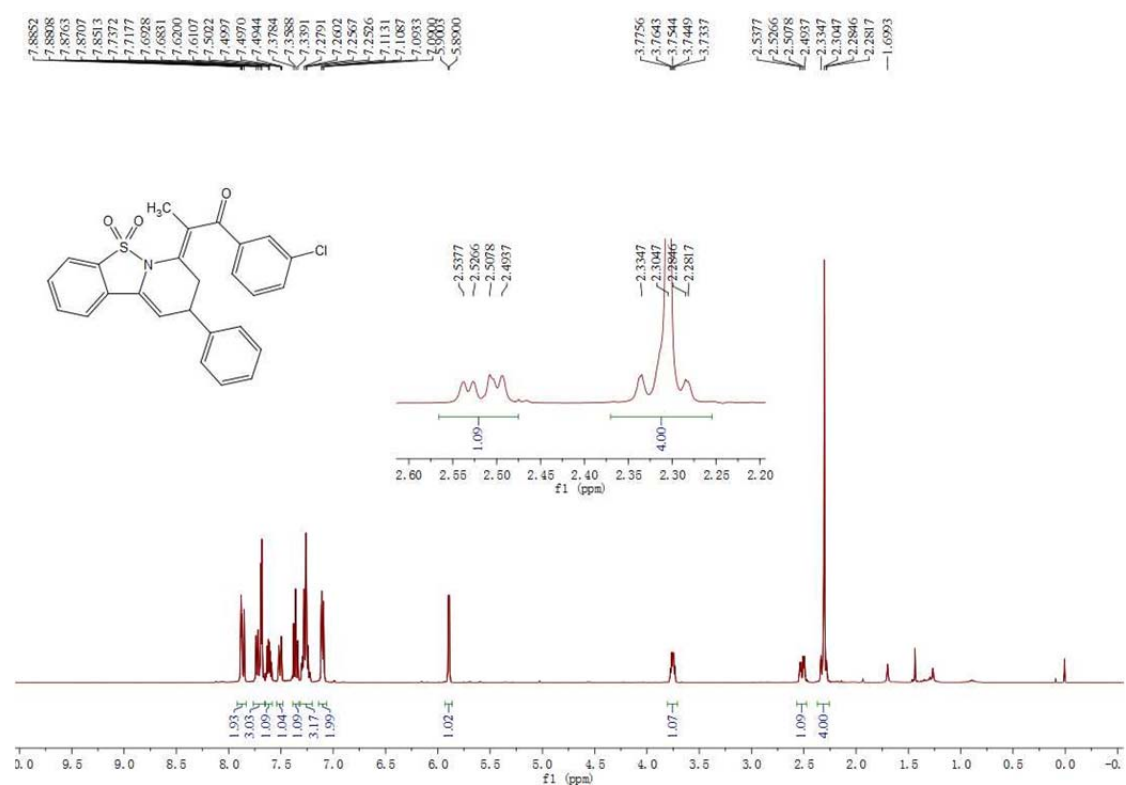
4c



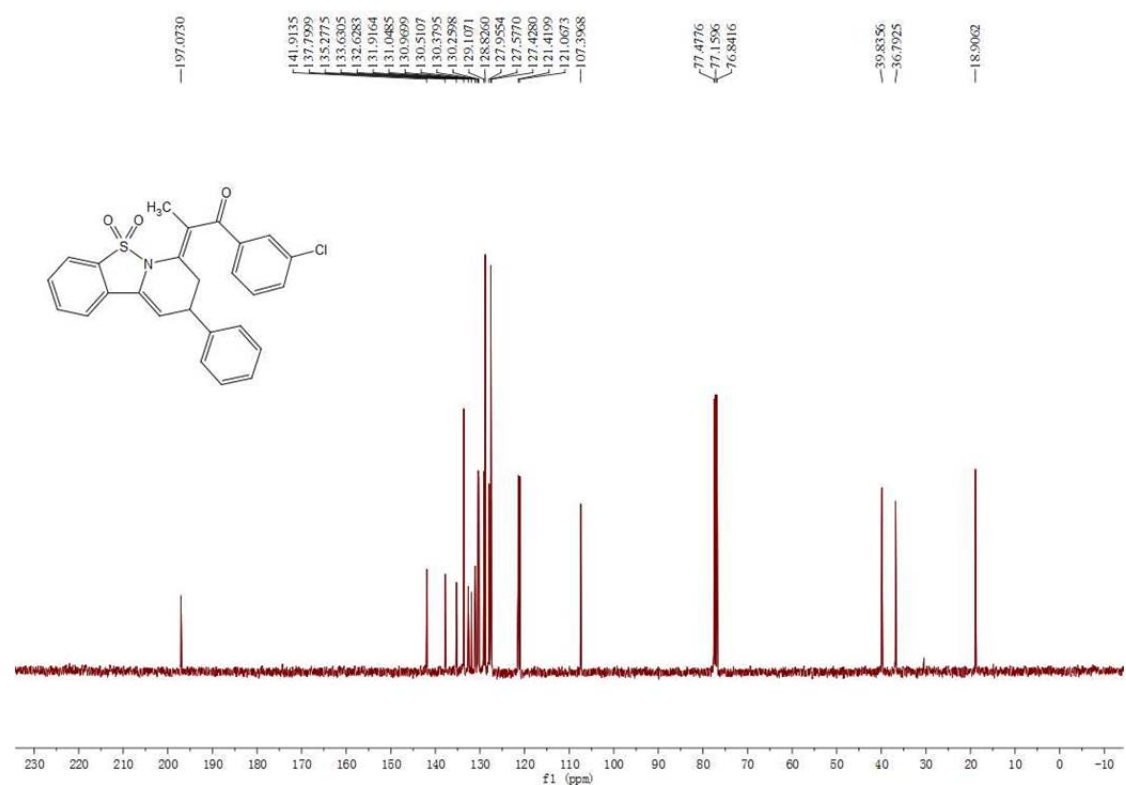
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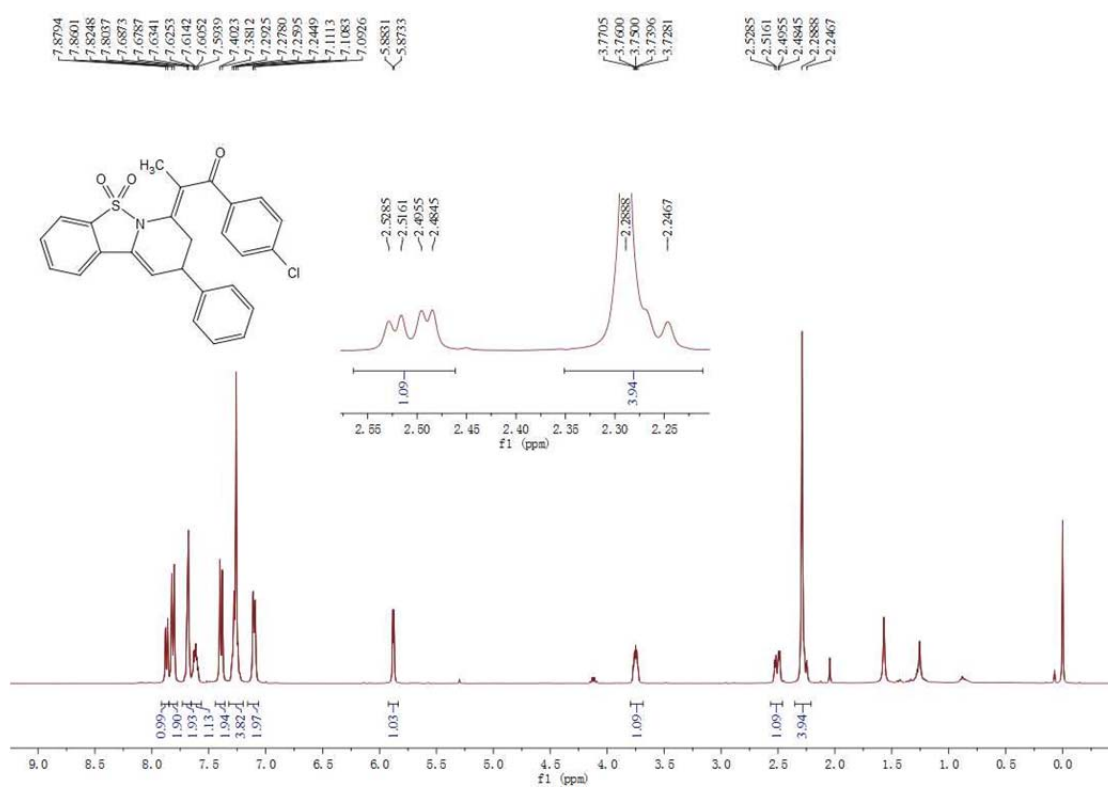
4d



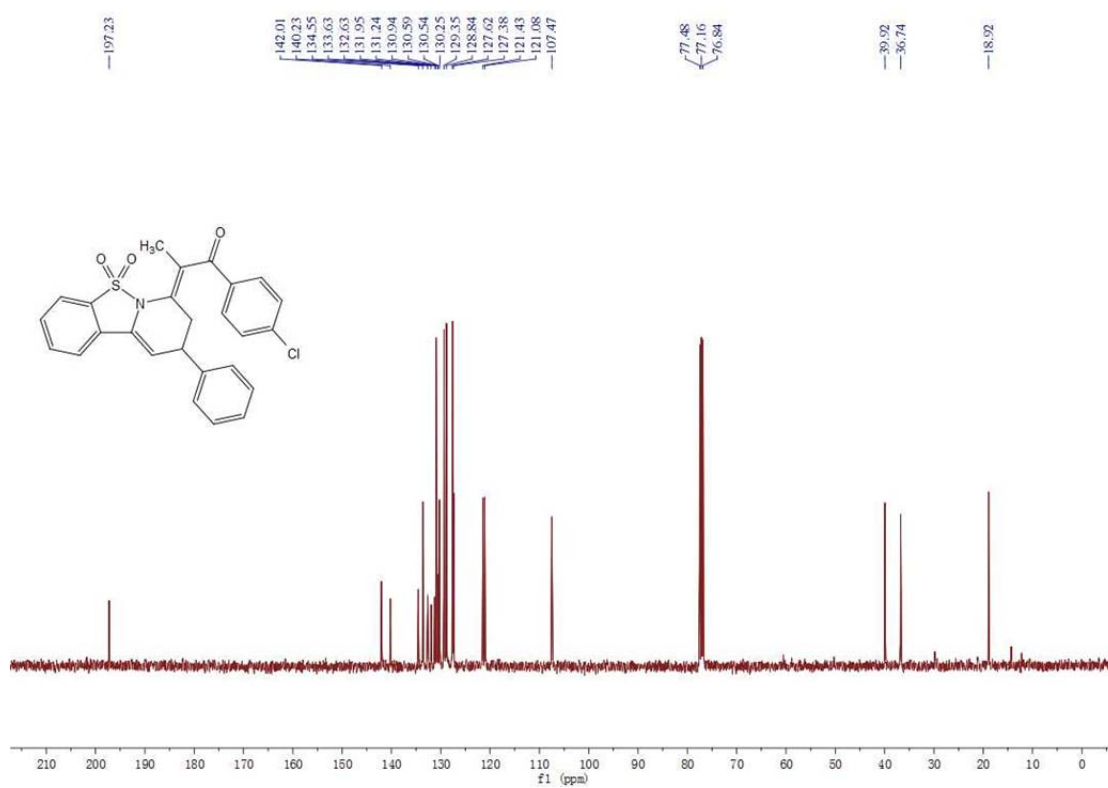
4d



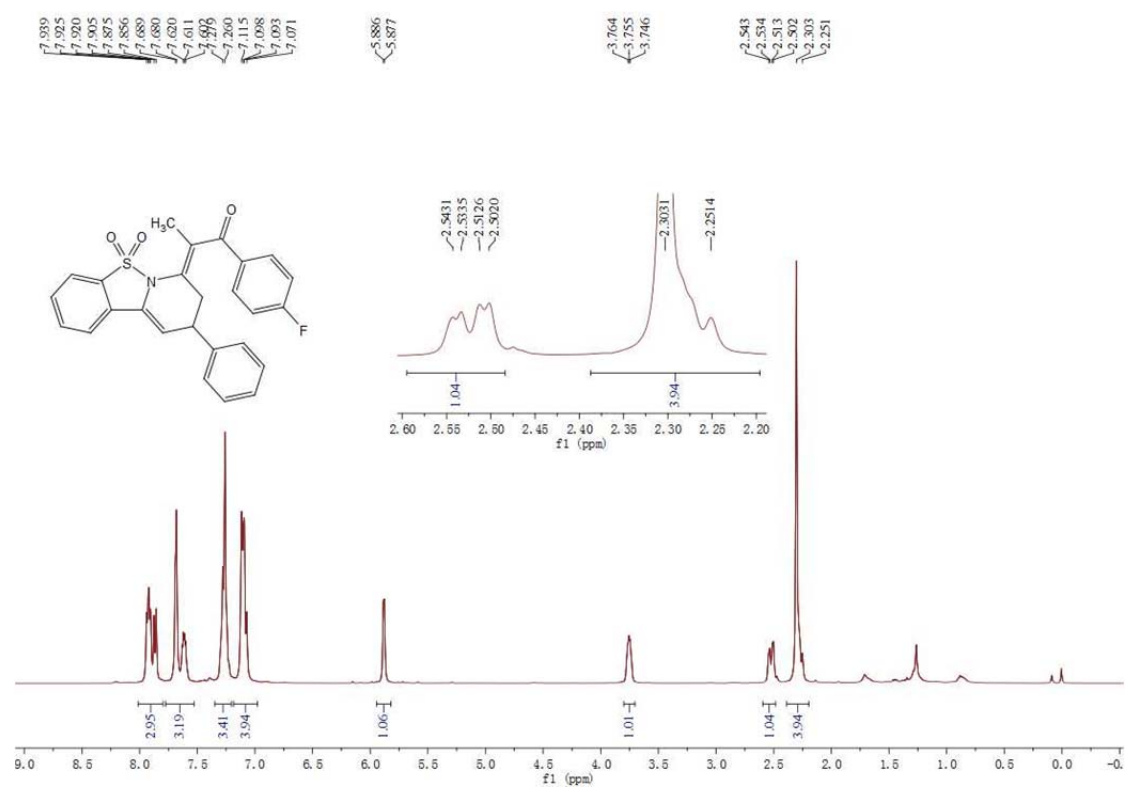
4e



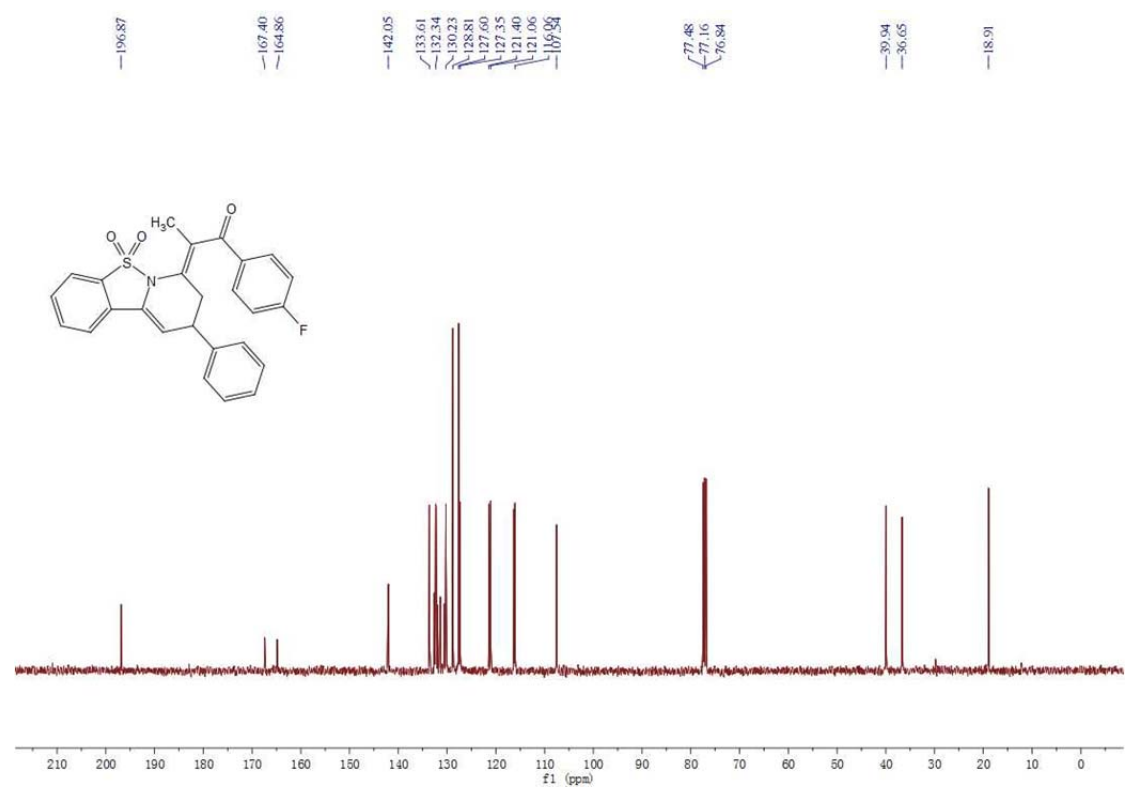
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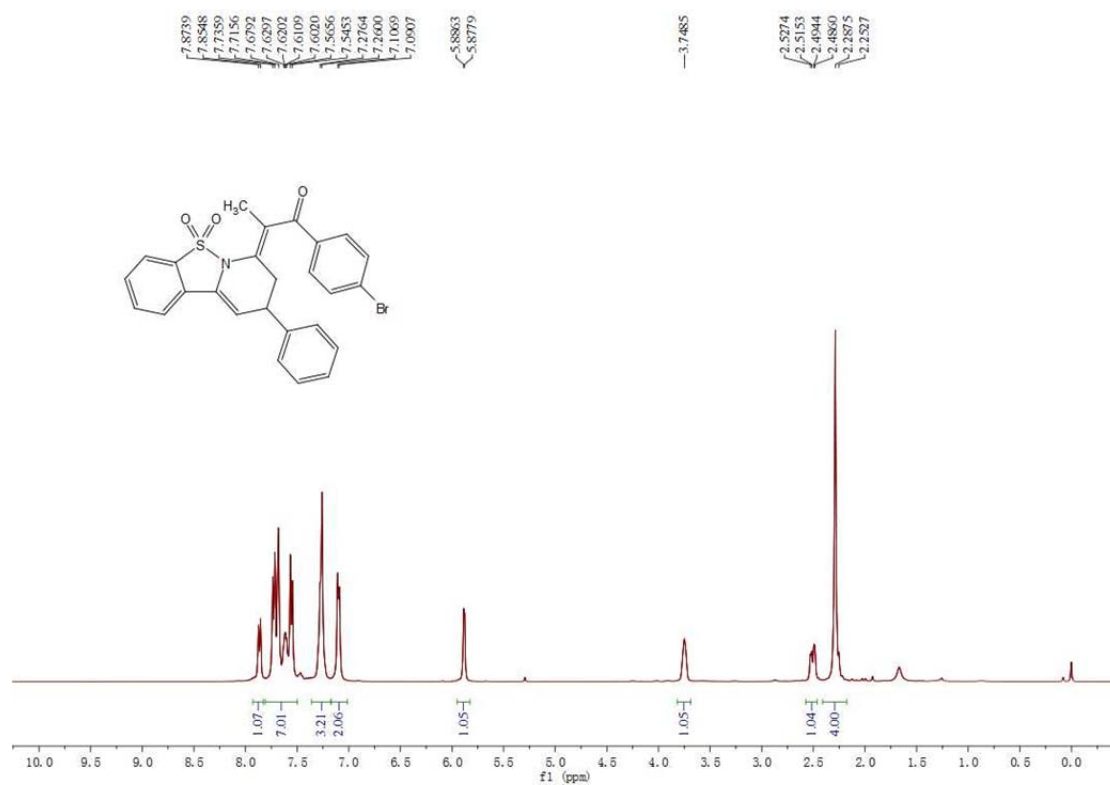
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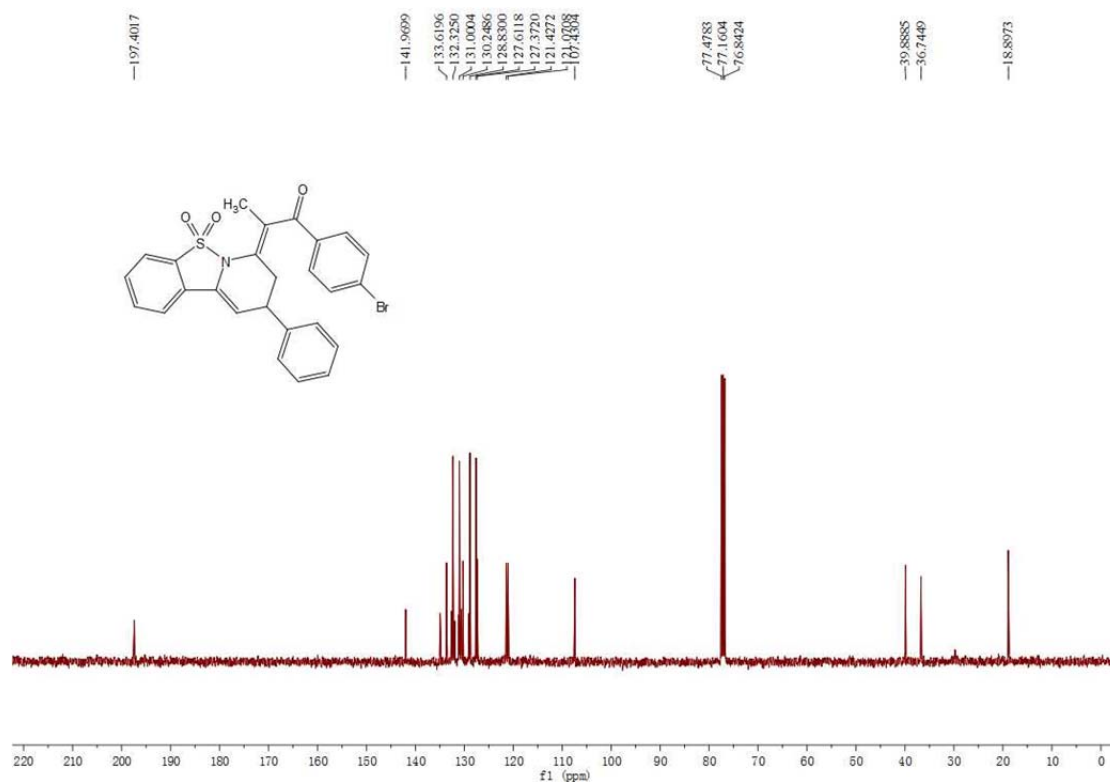
4f



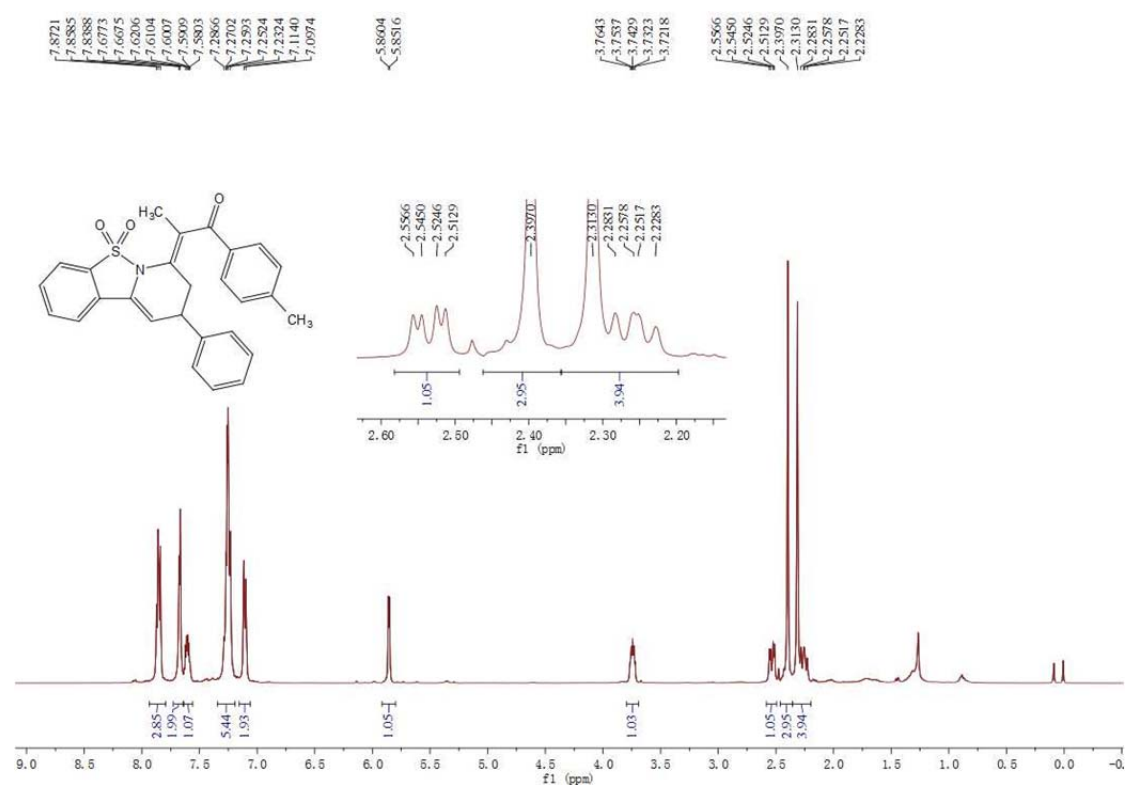
4g



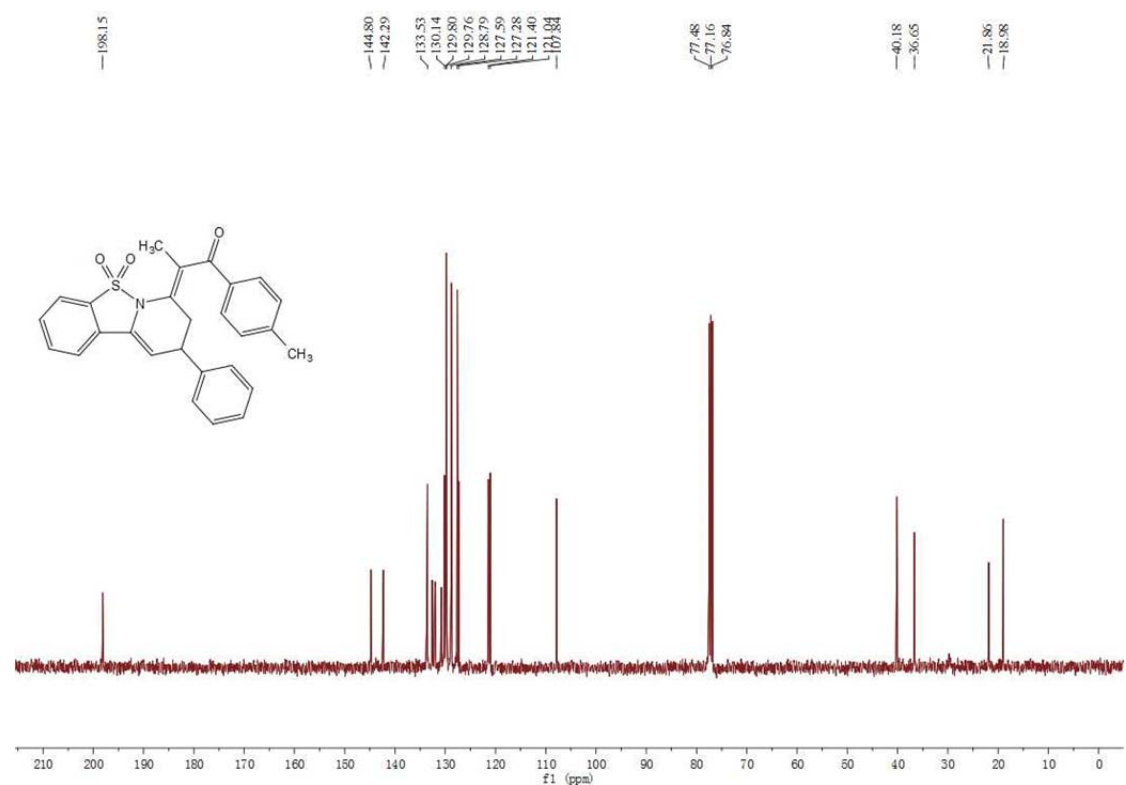
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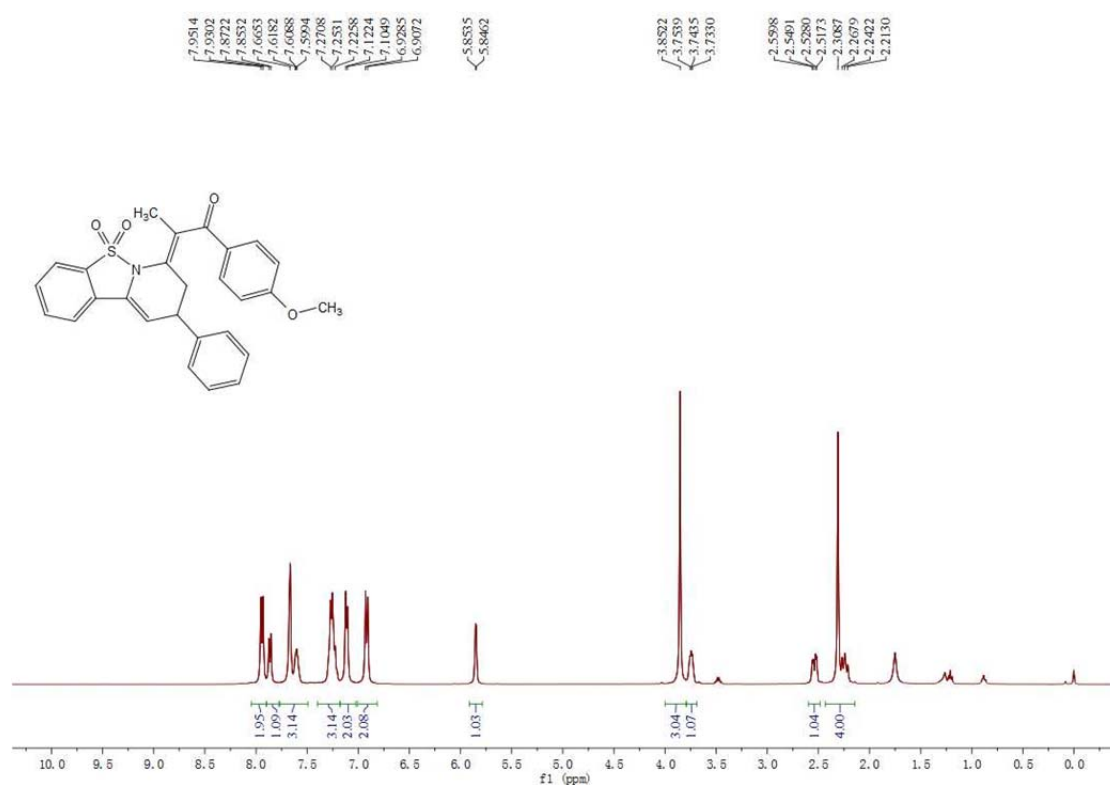
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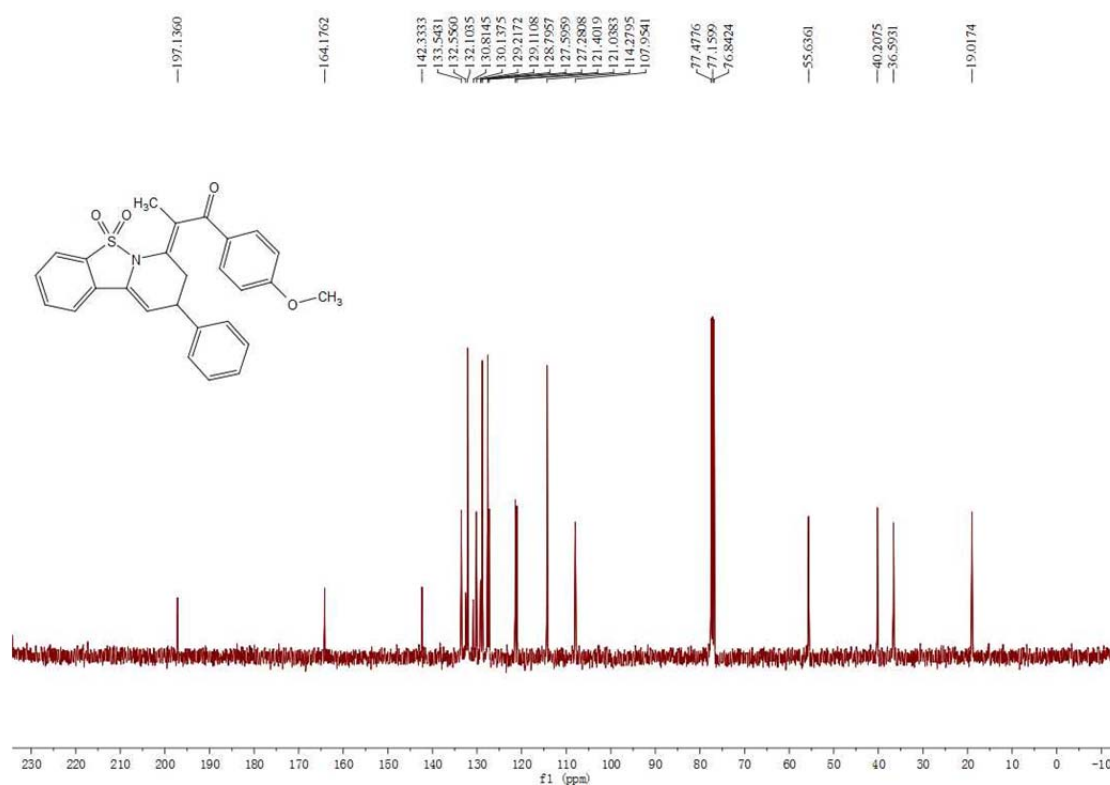
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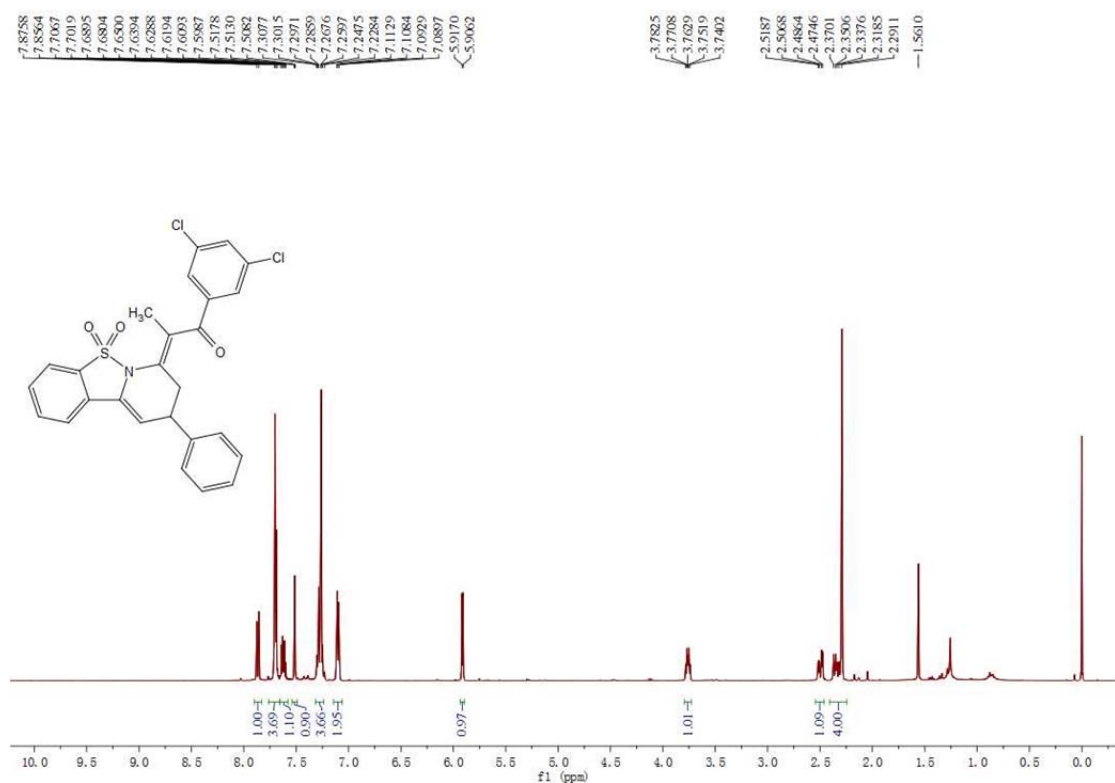
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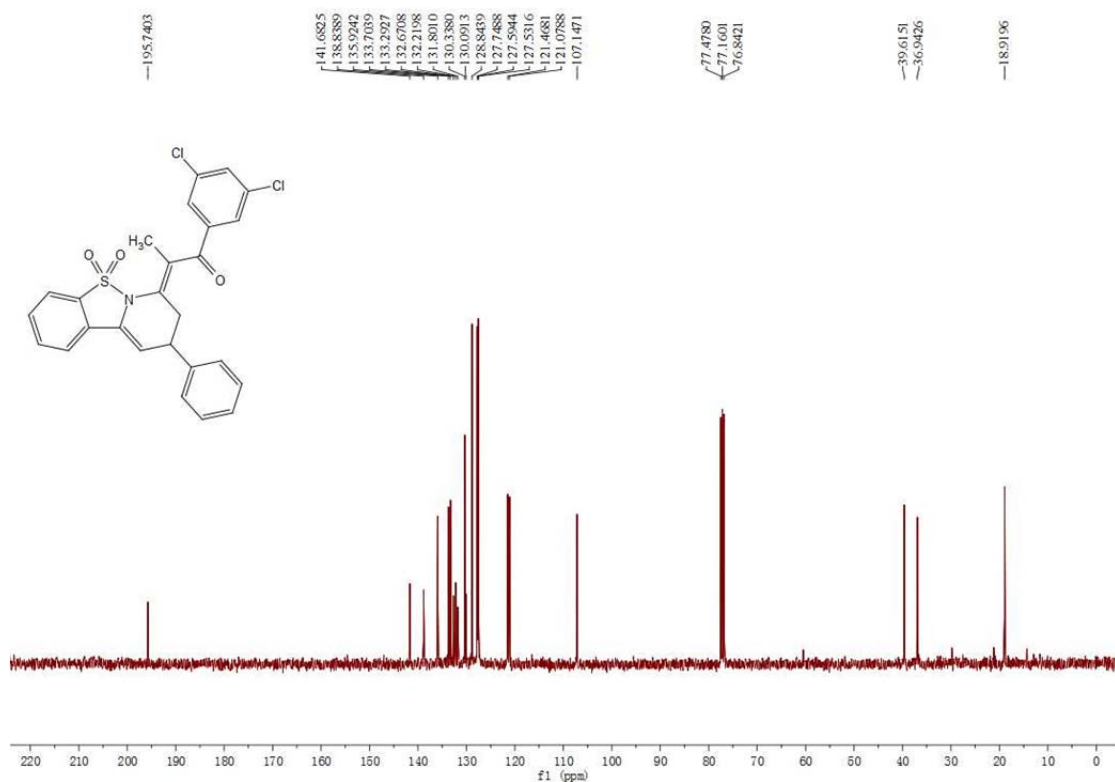
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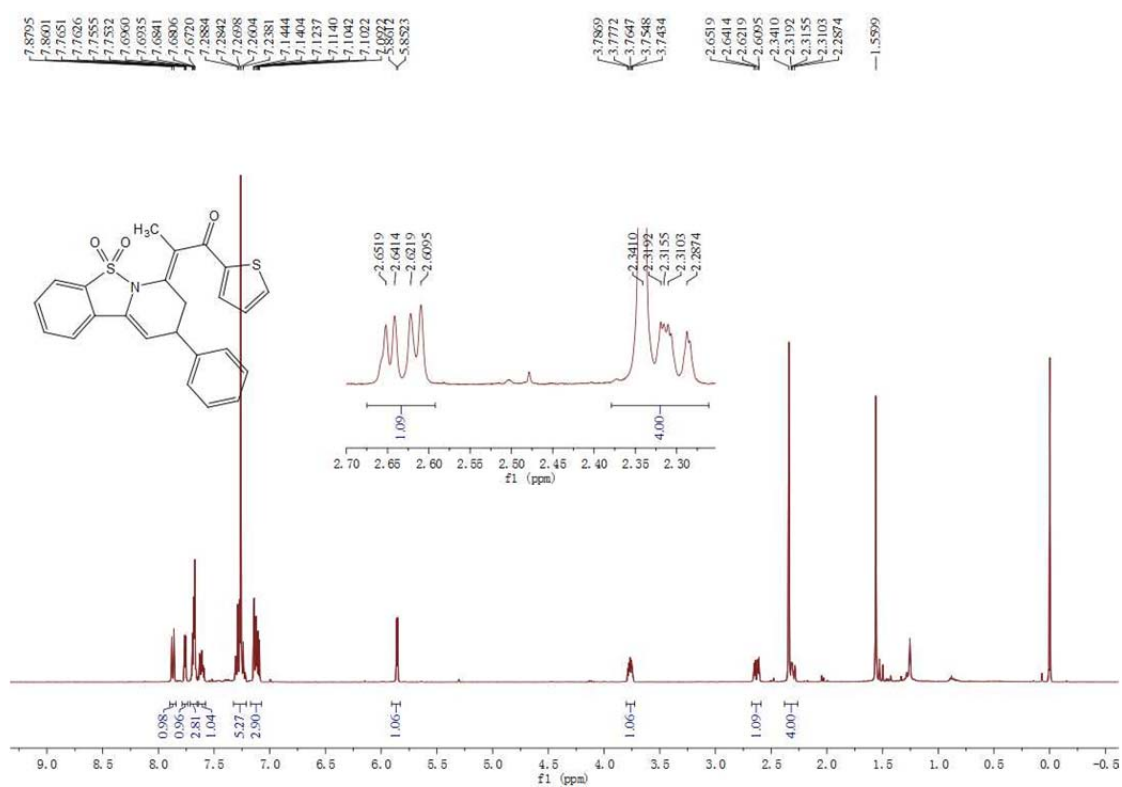
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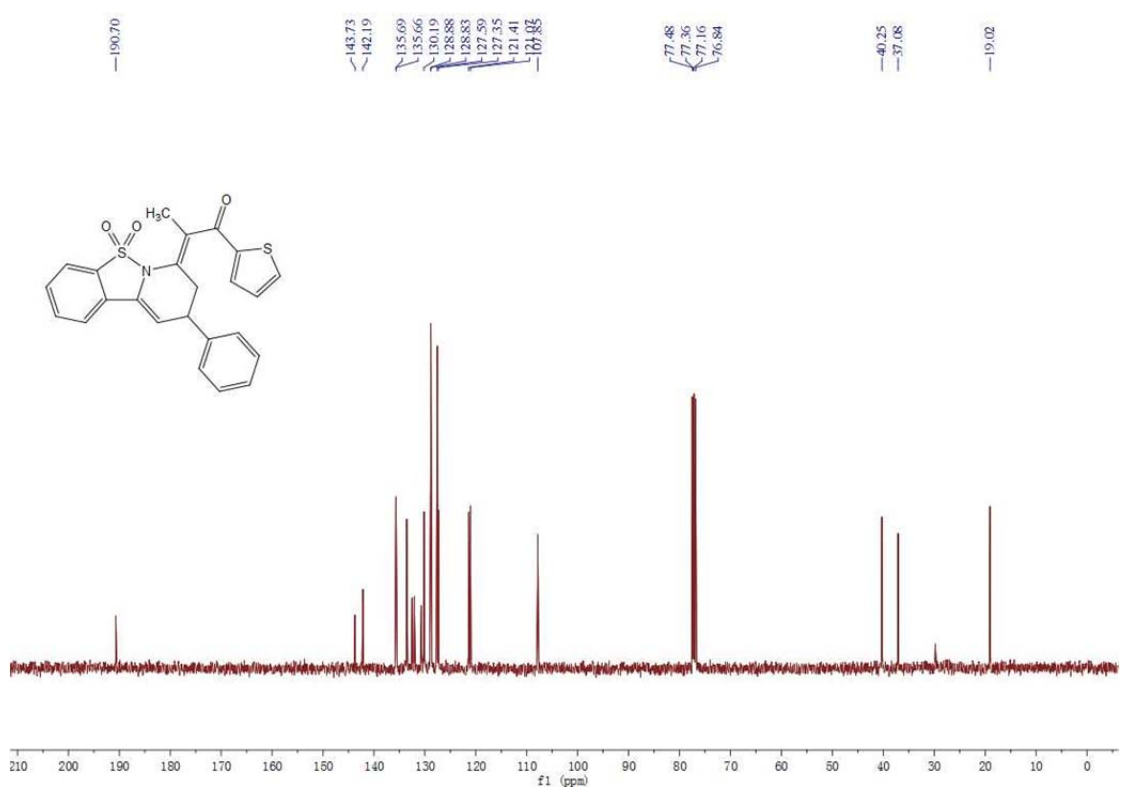
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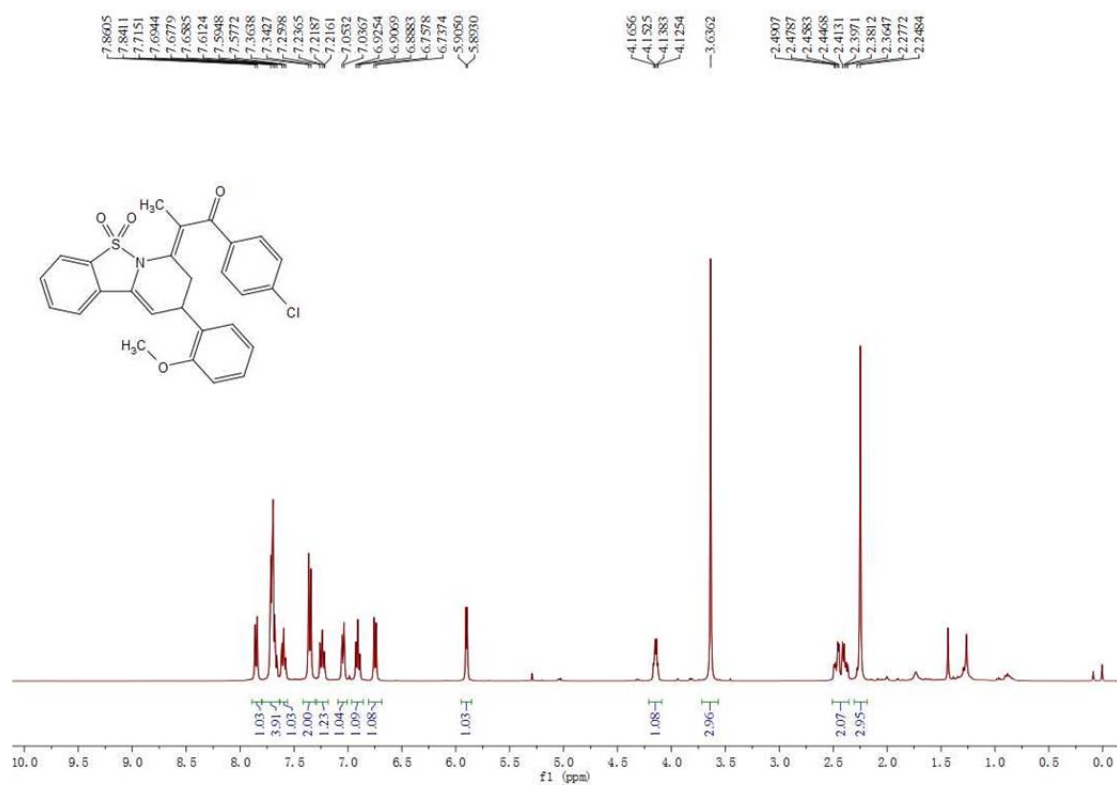
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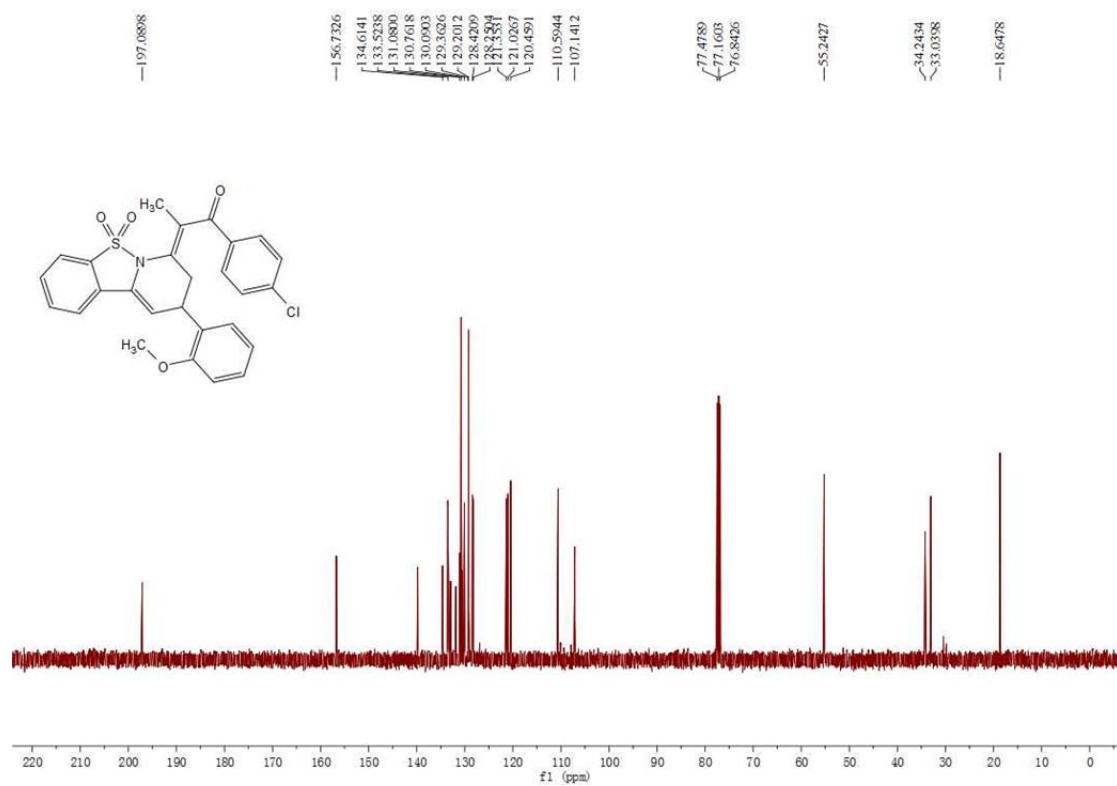
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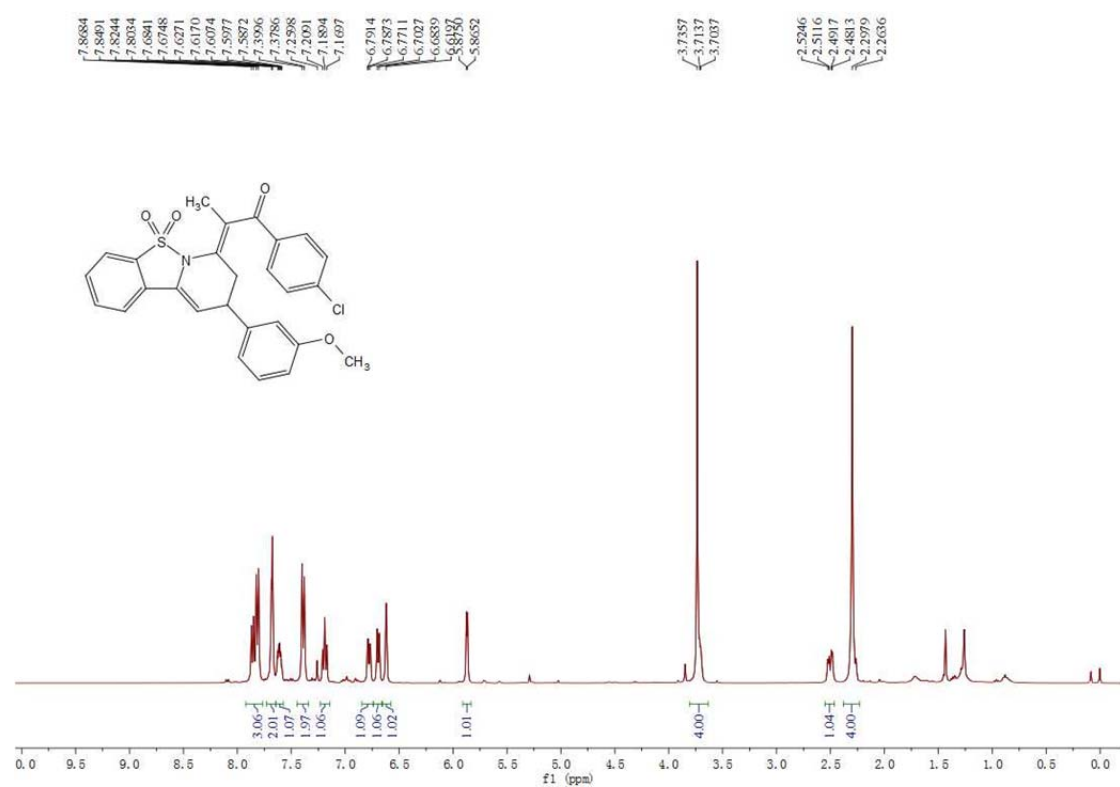
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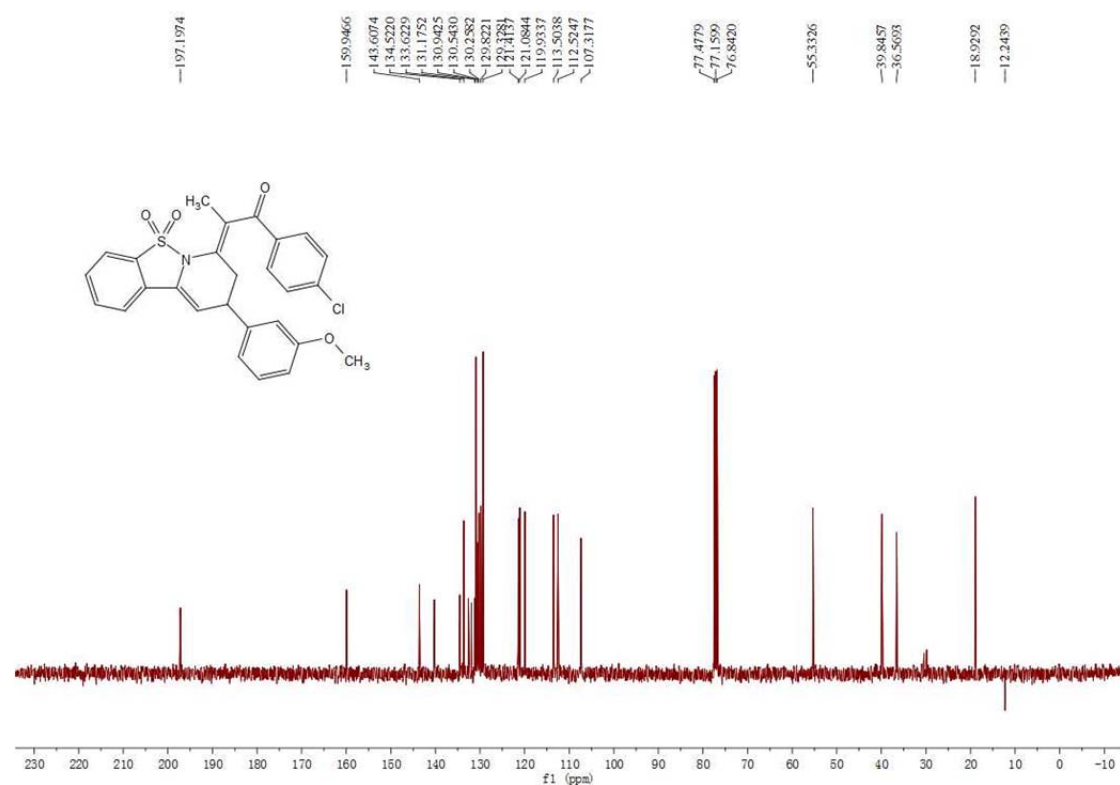
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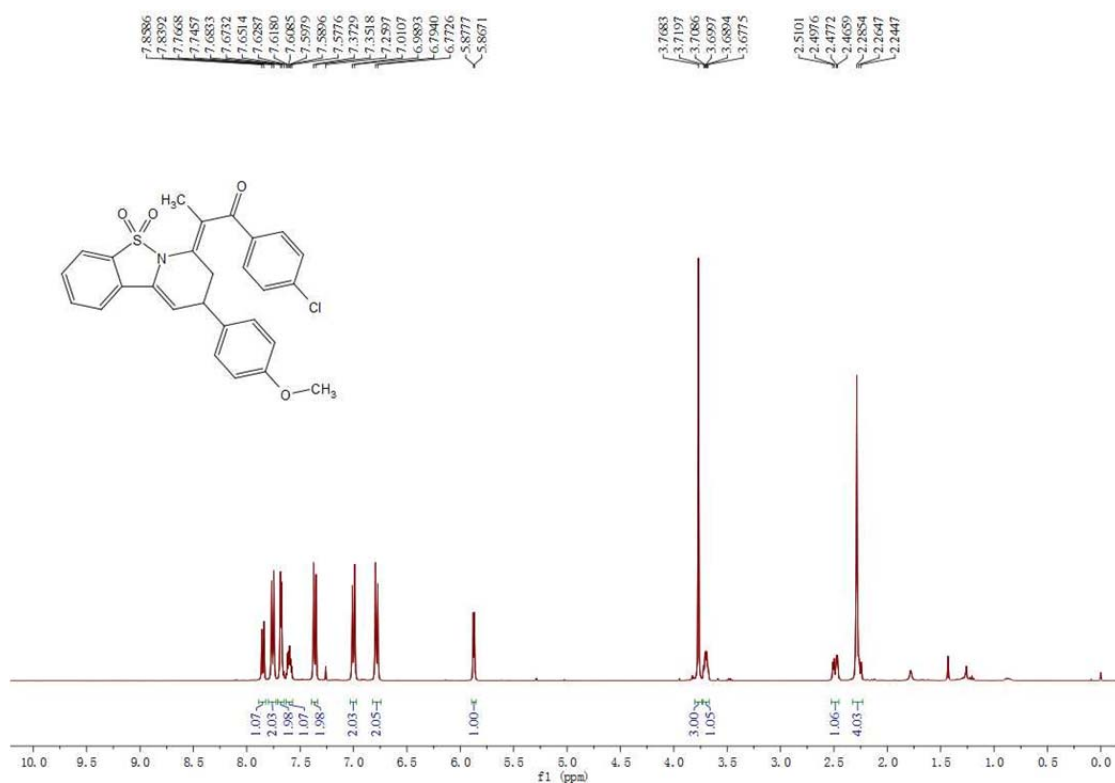
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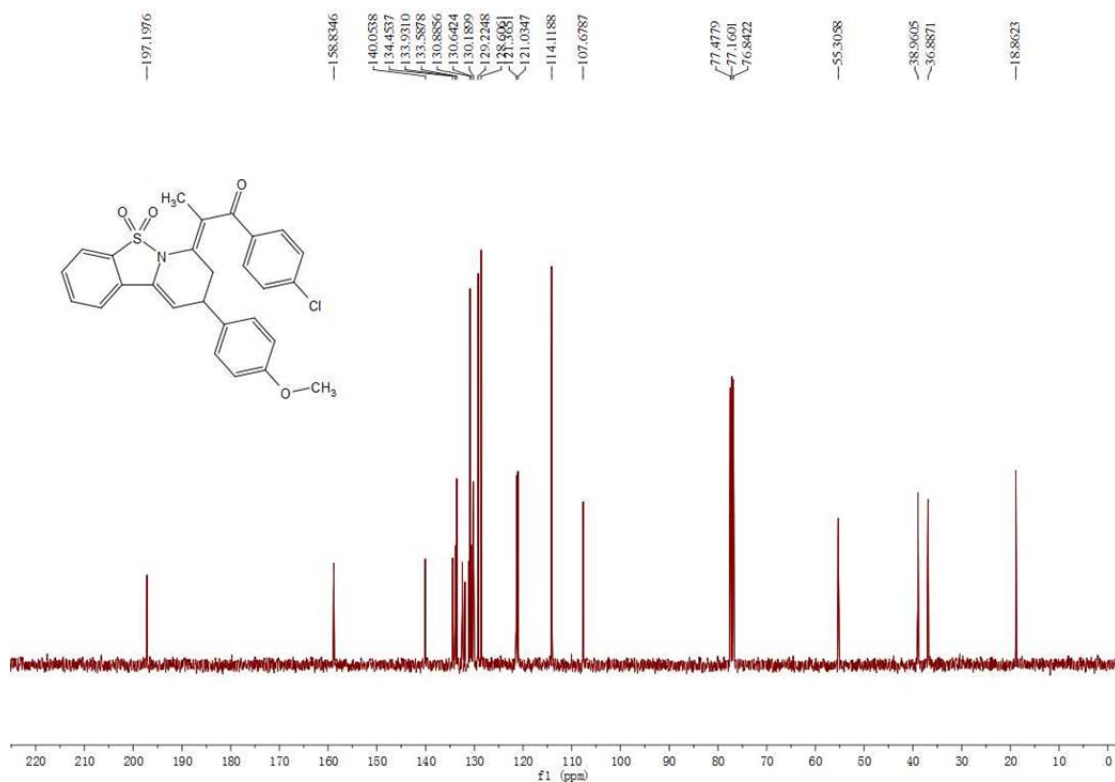
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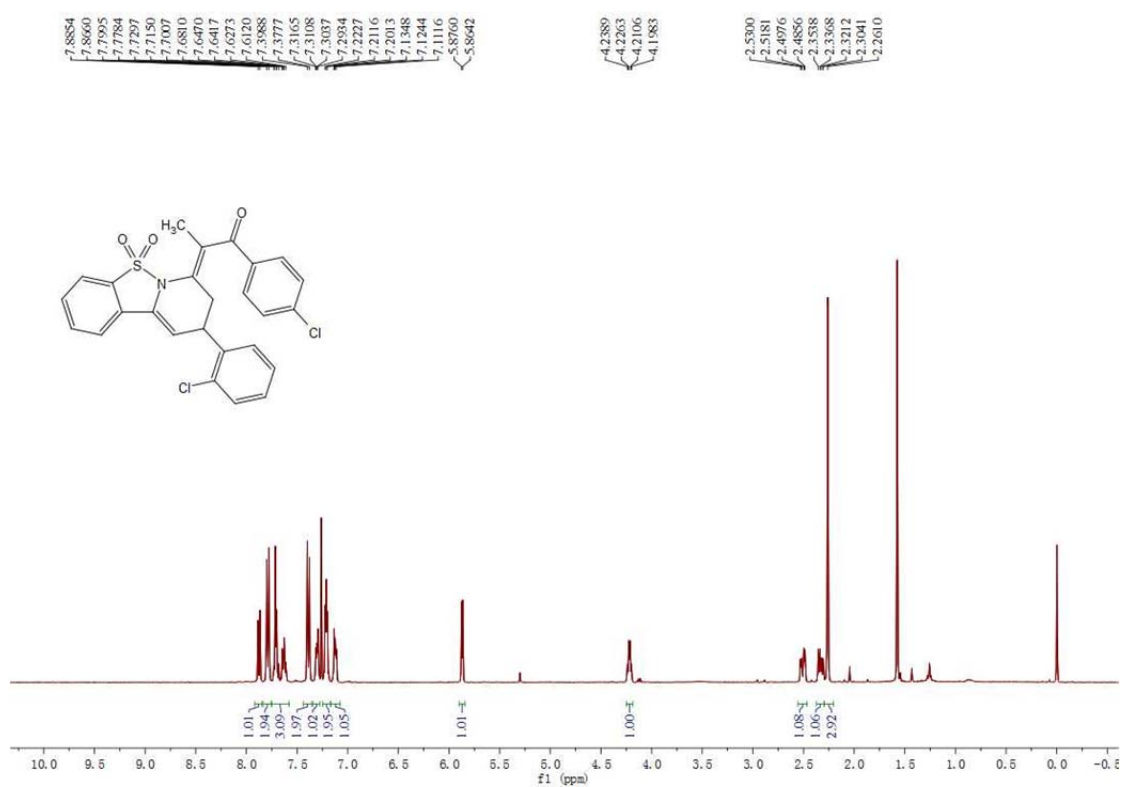
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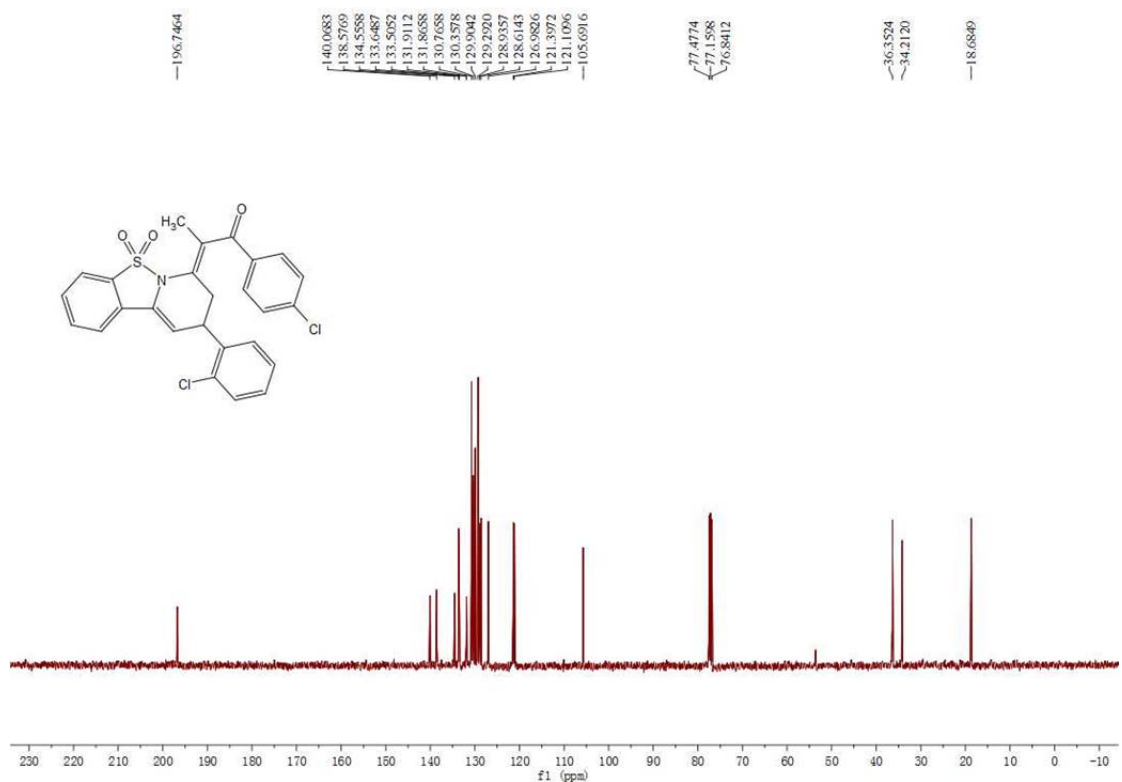
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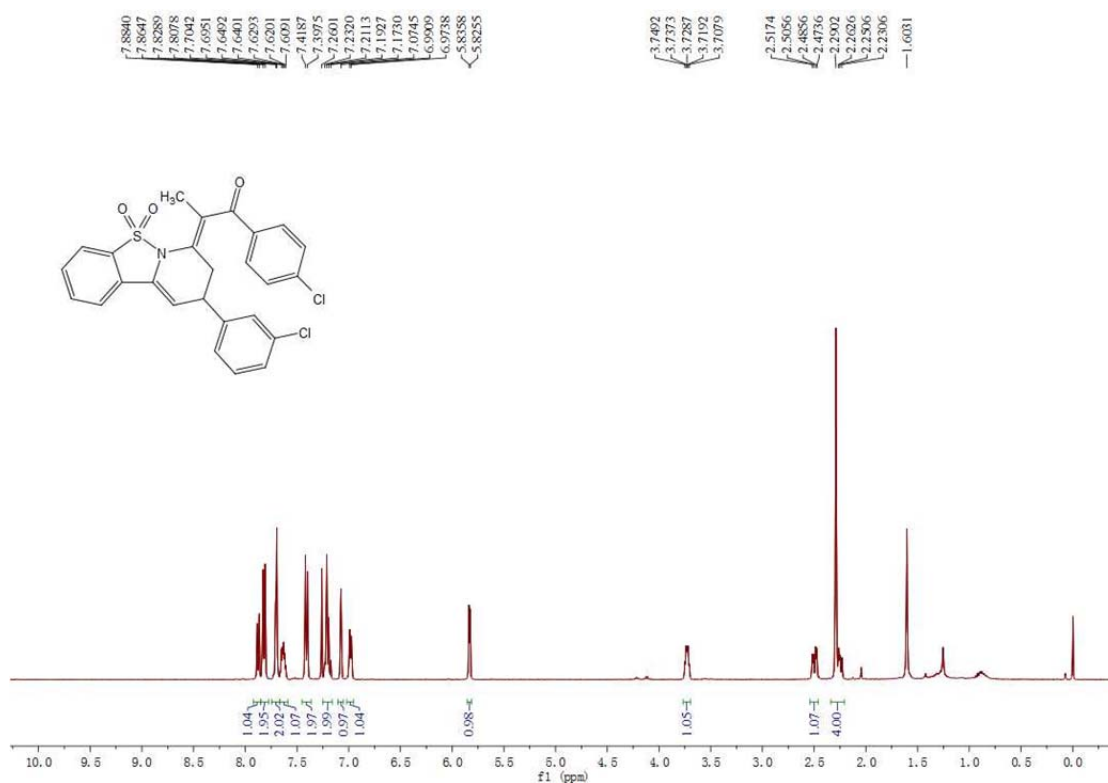
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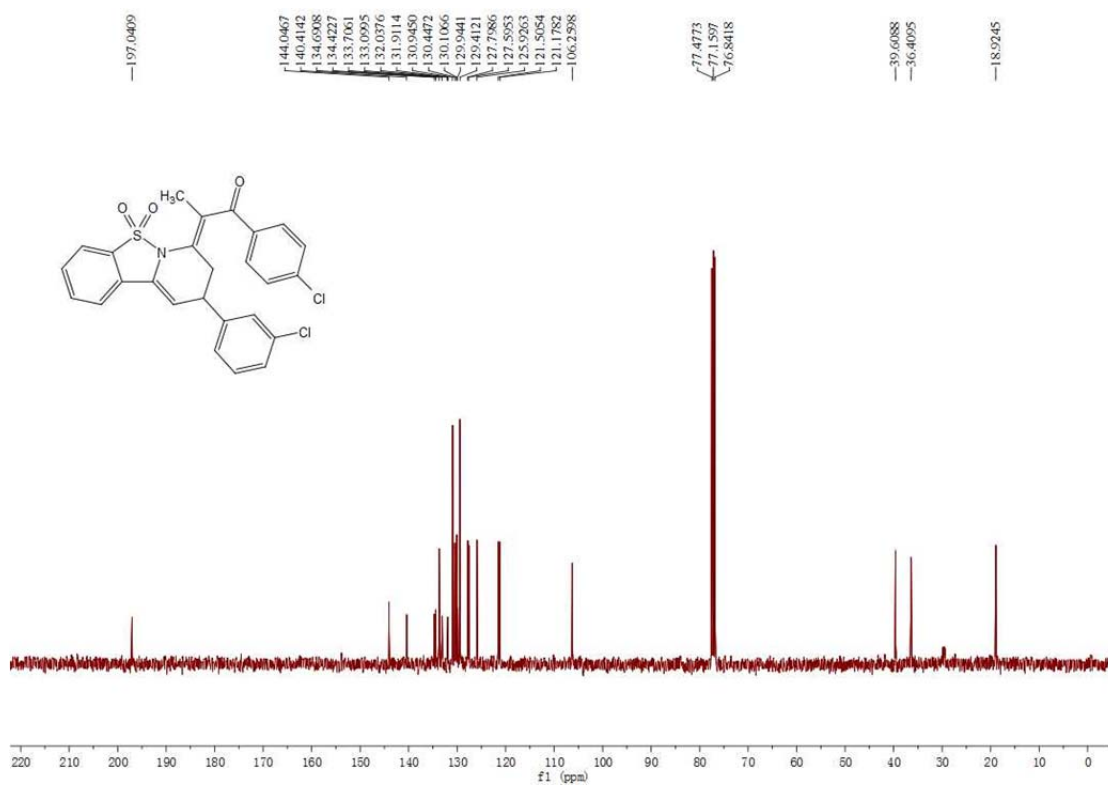
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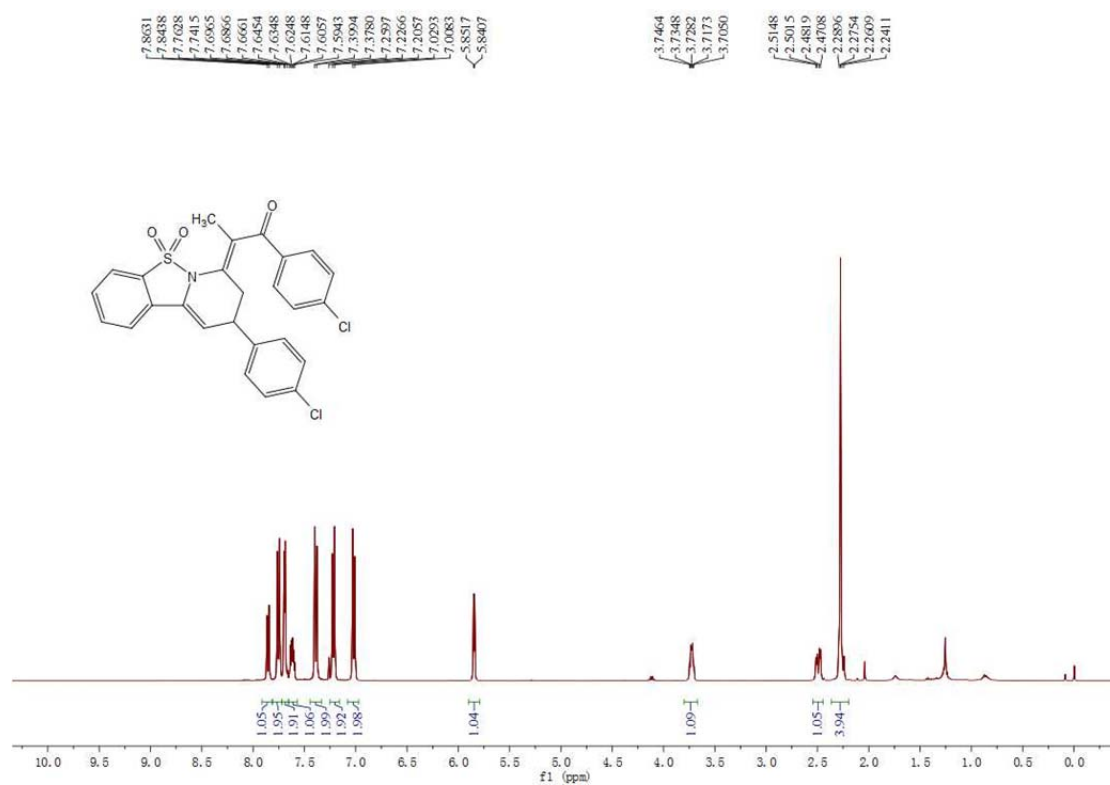
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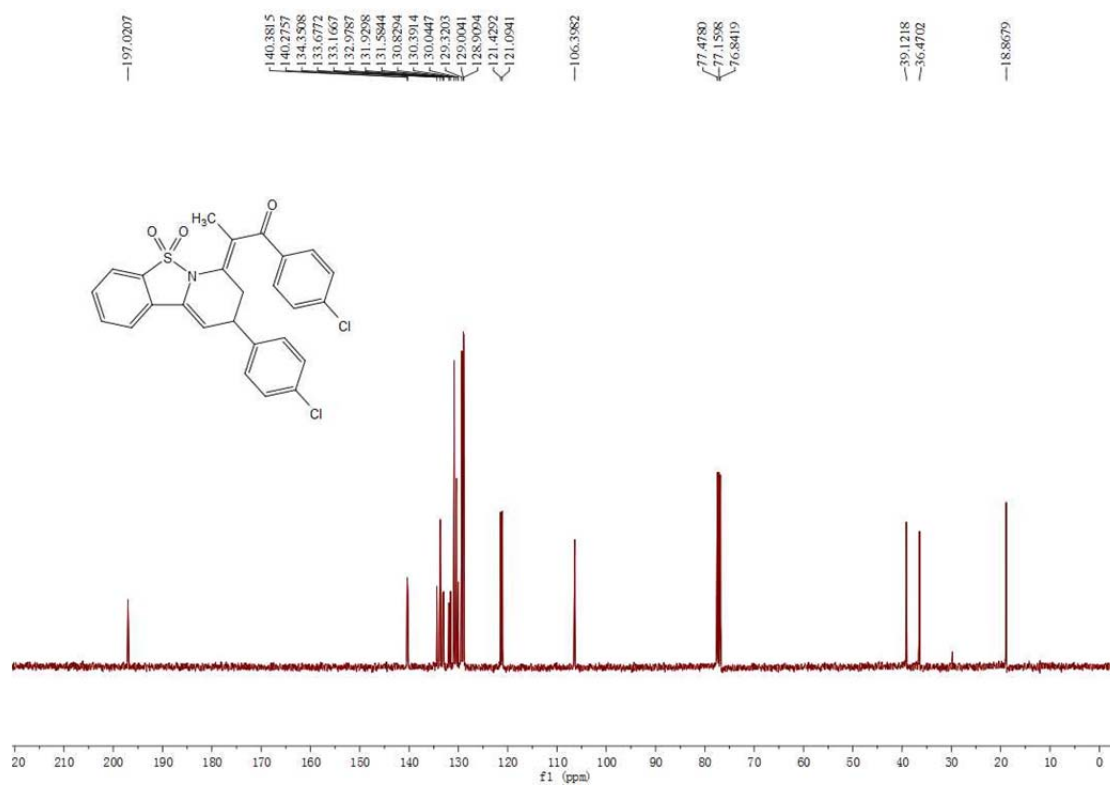
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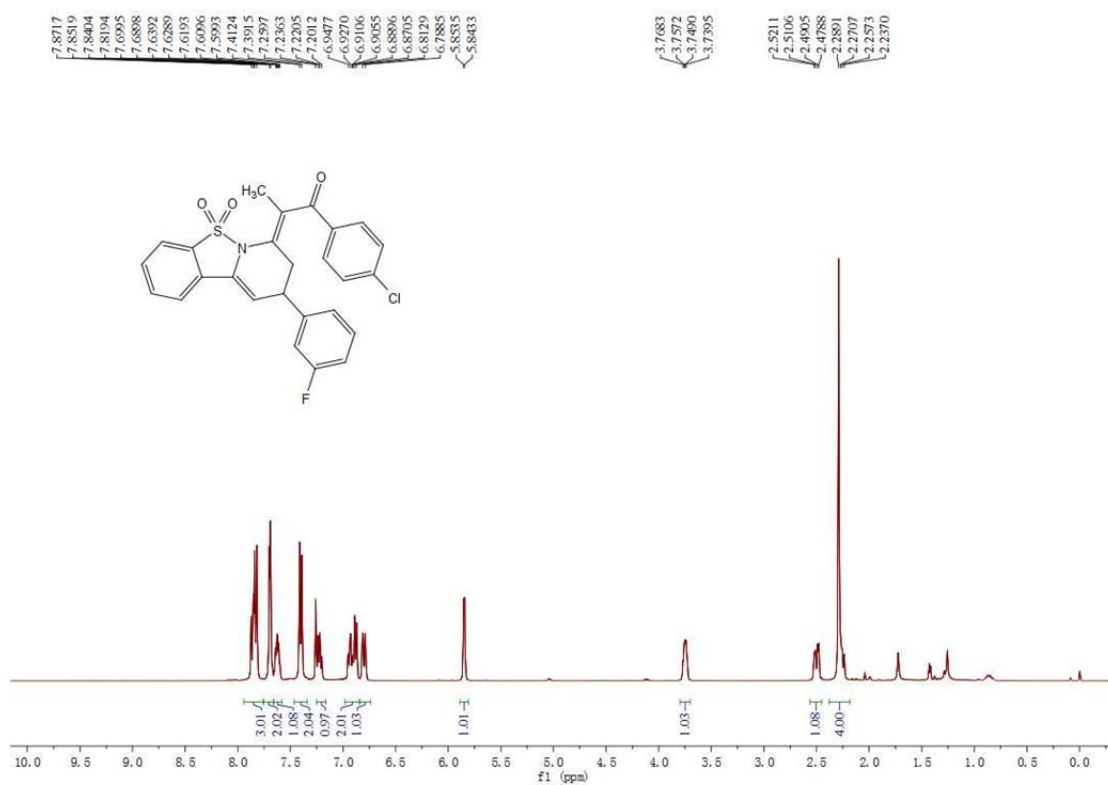
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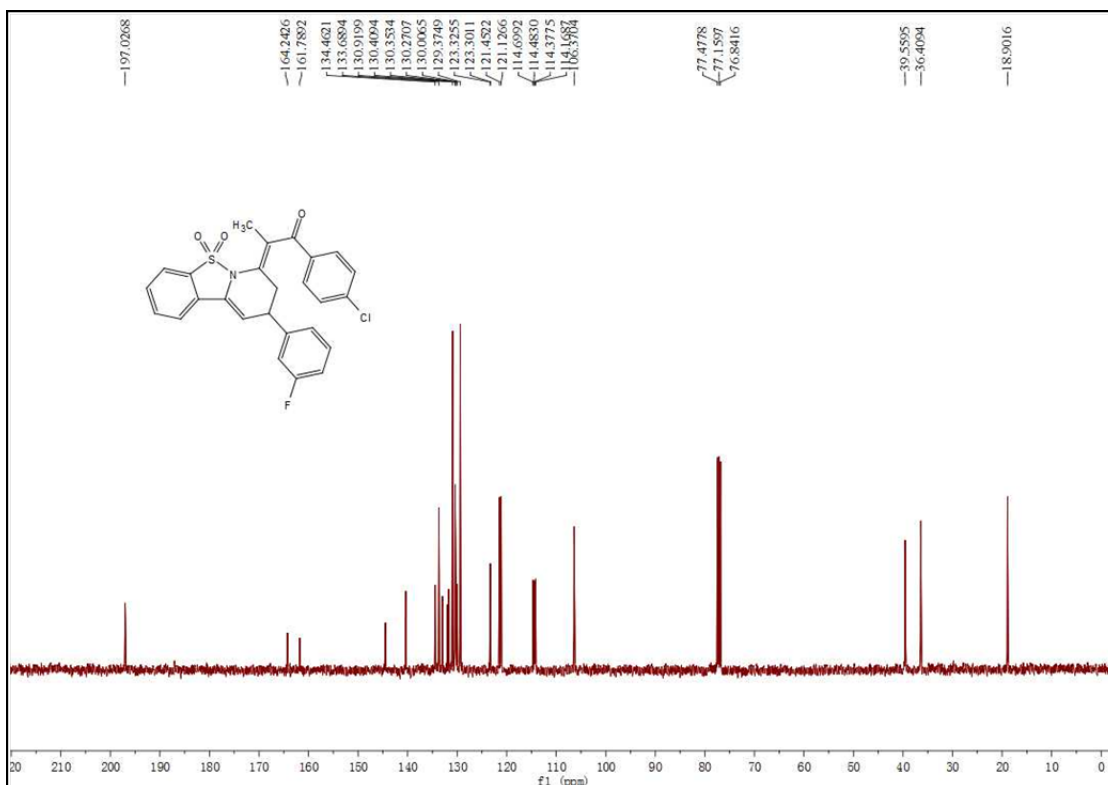
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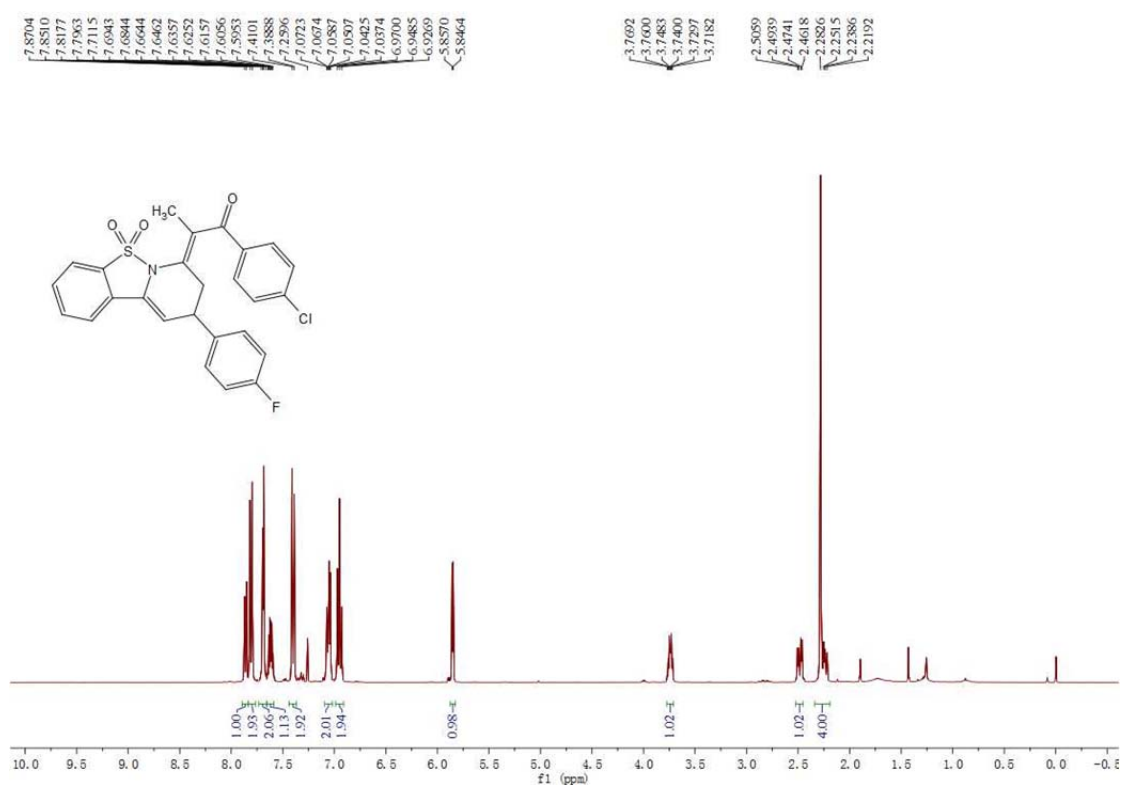
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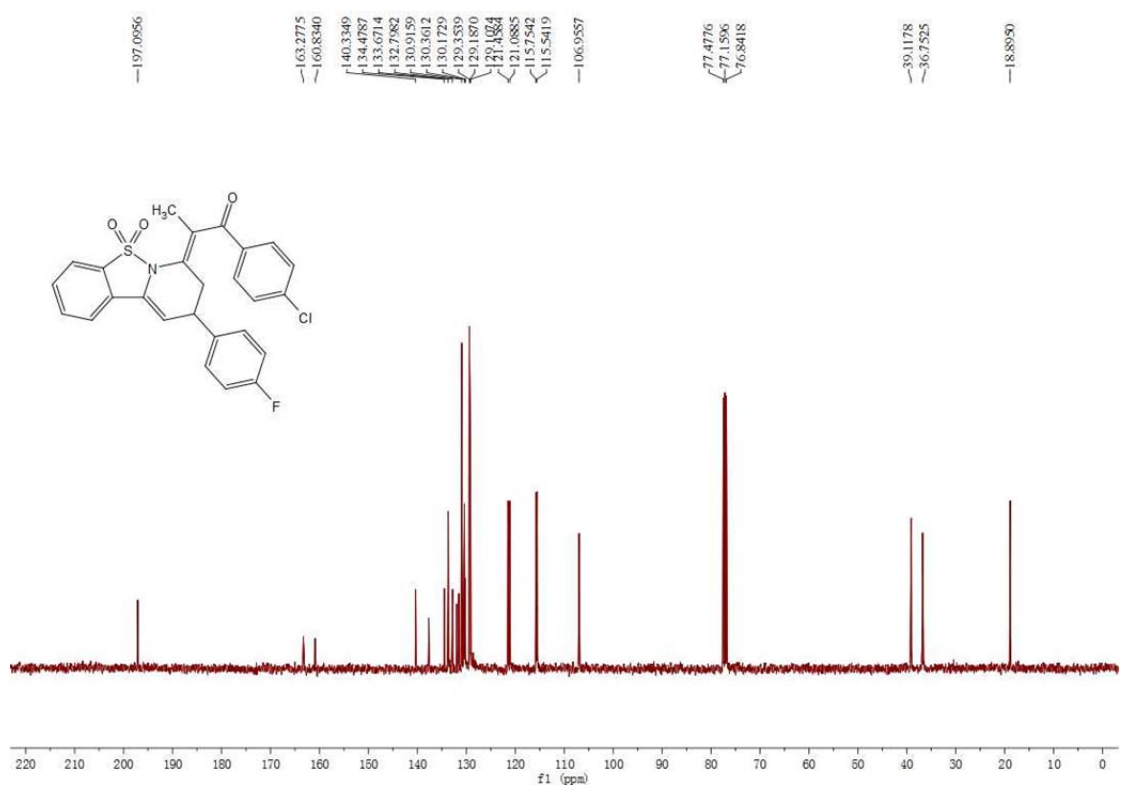
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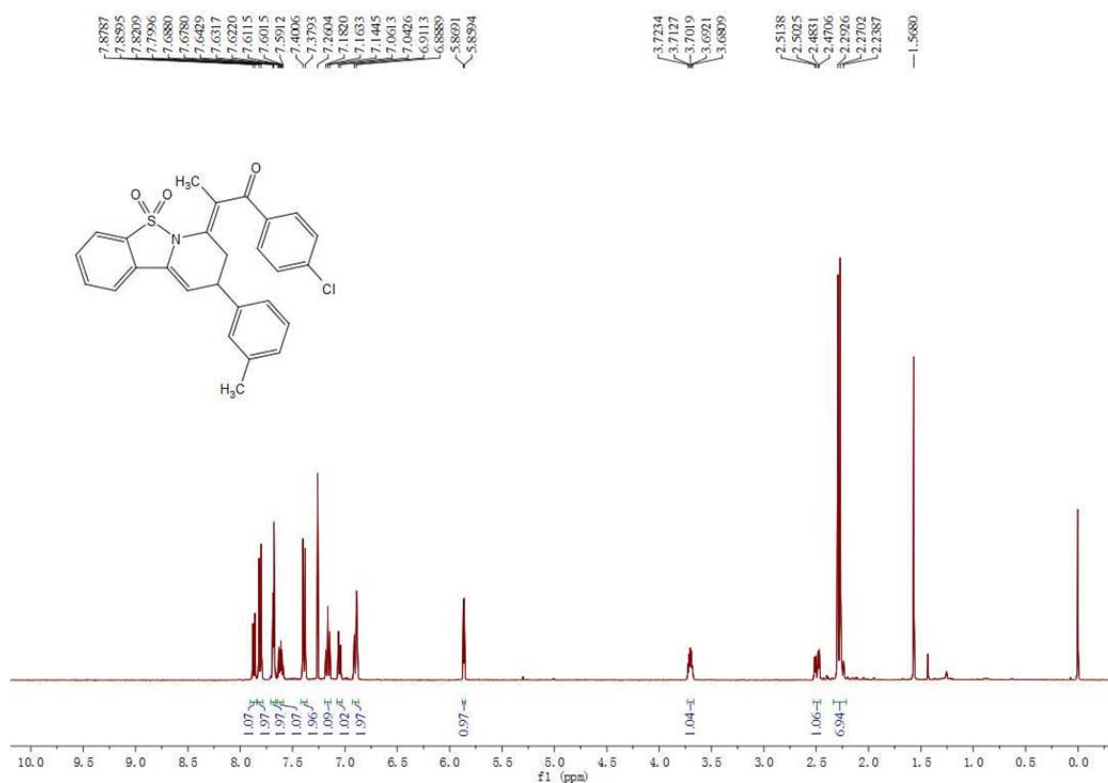
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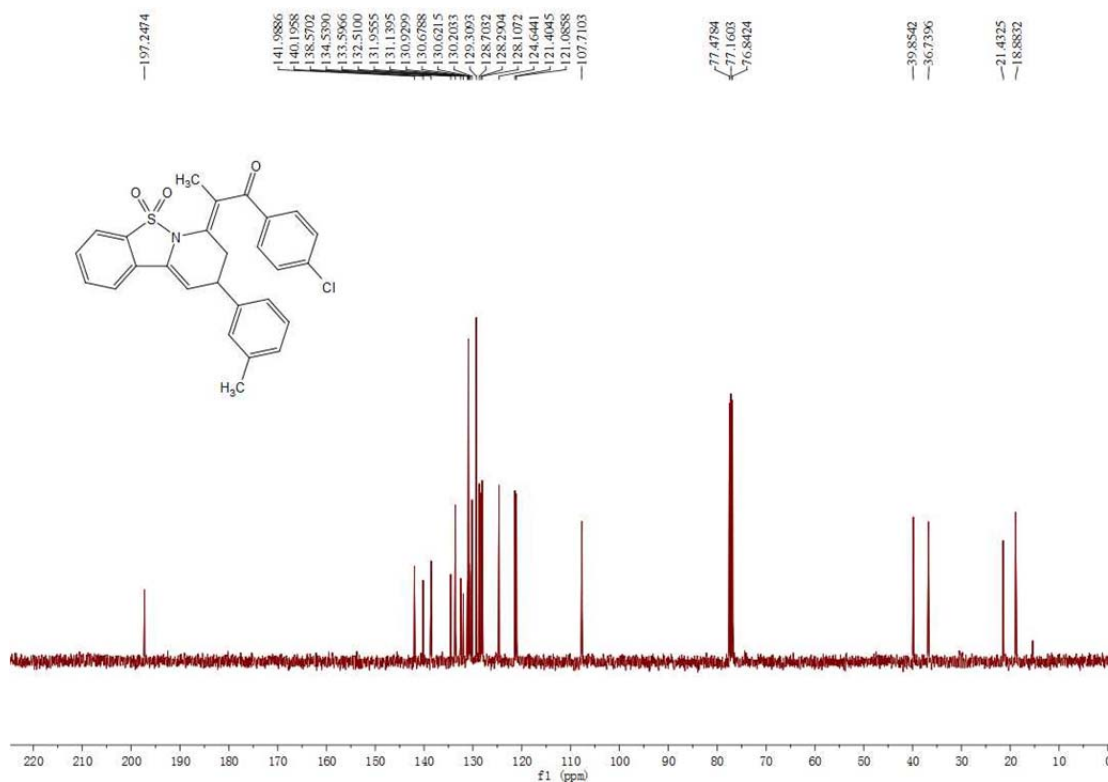
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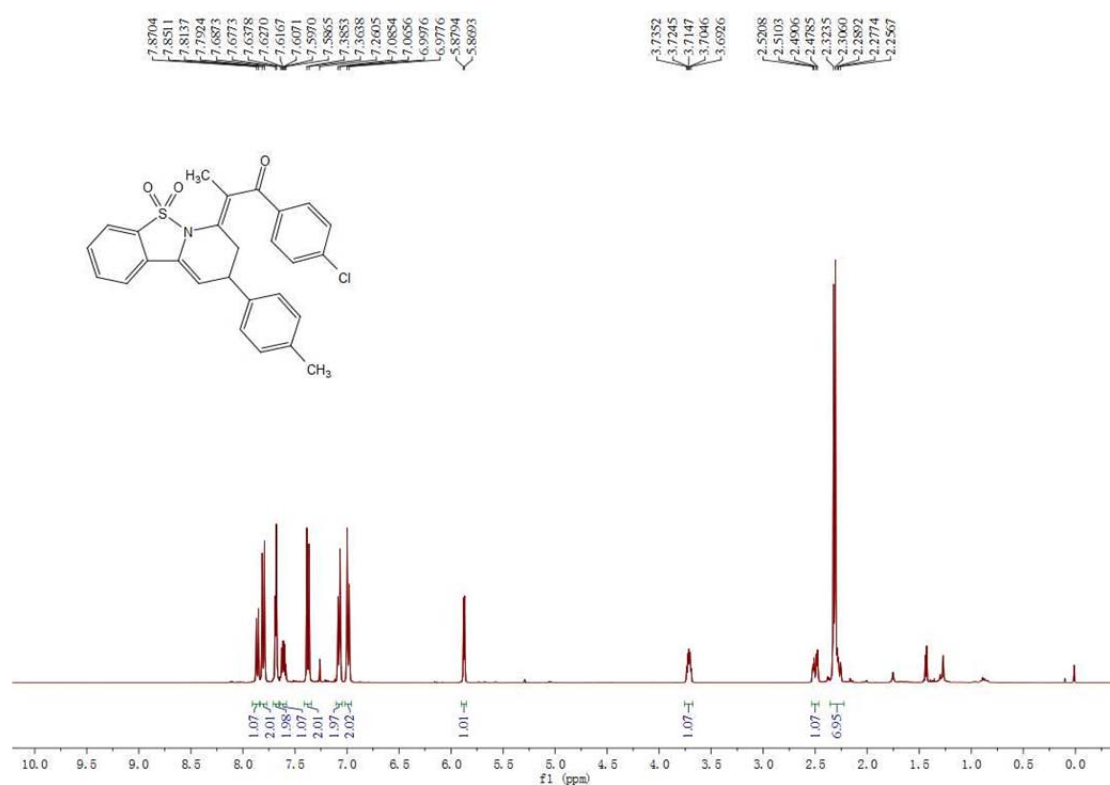
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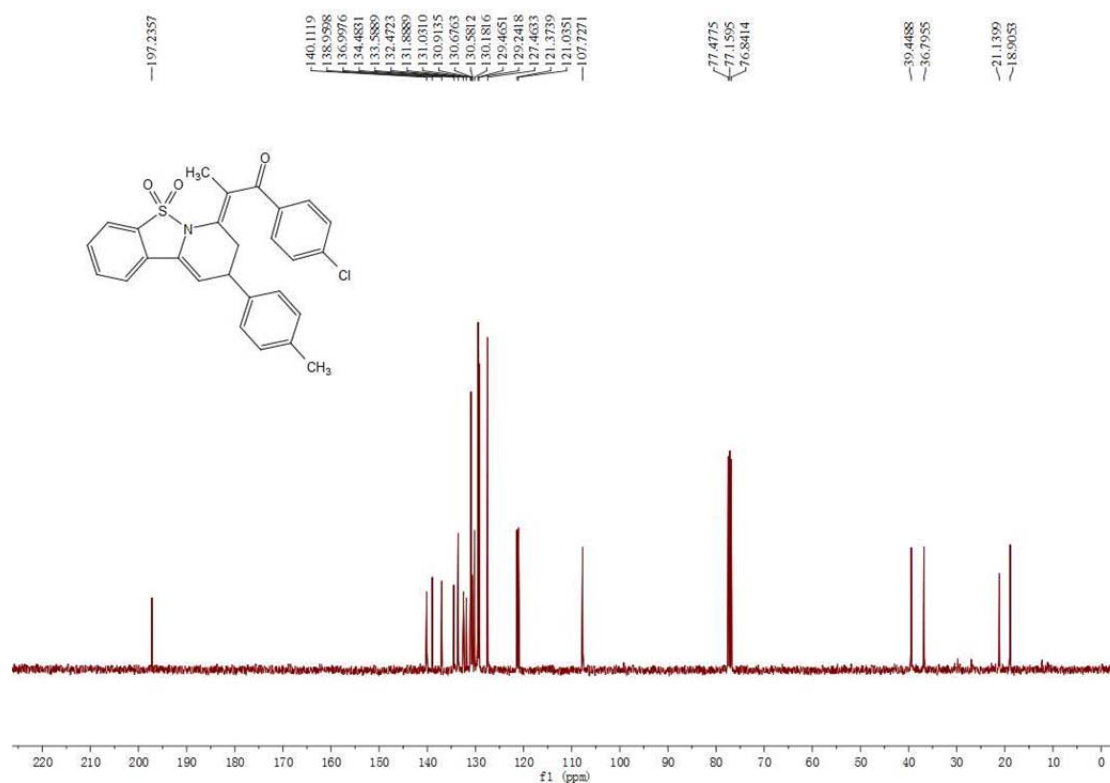
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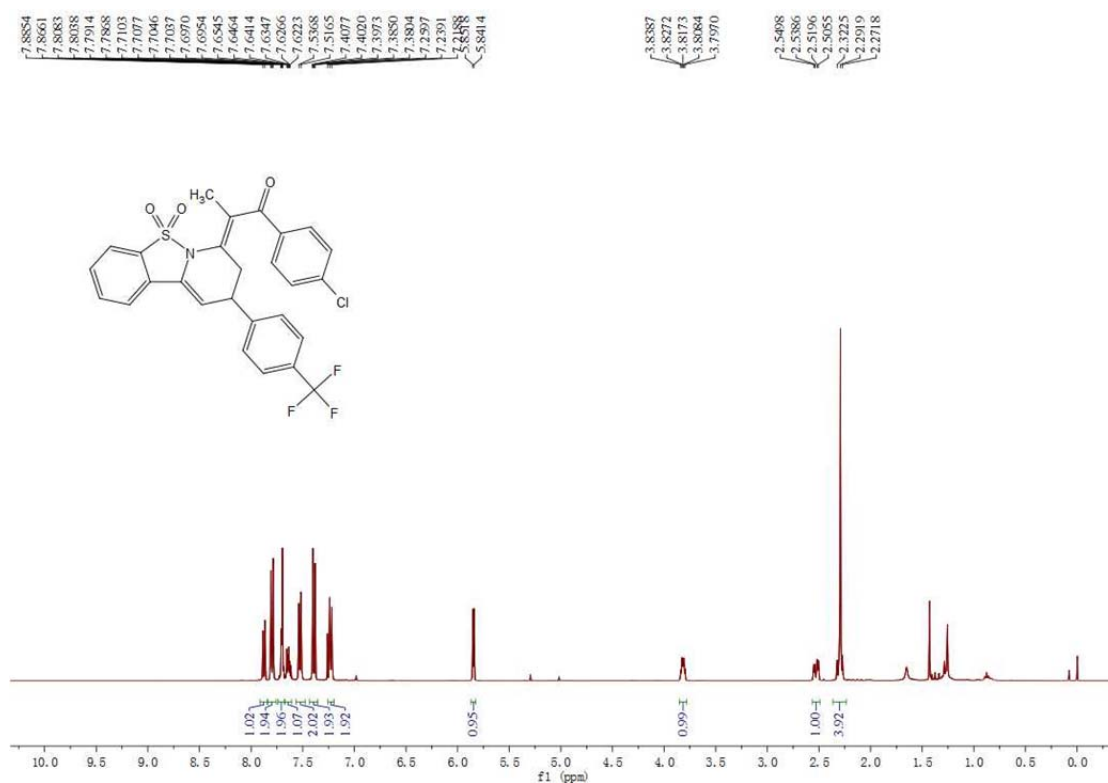
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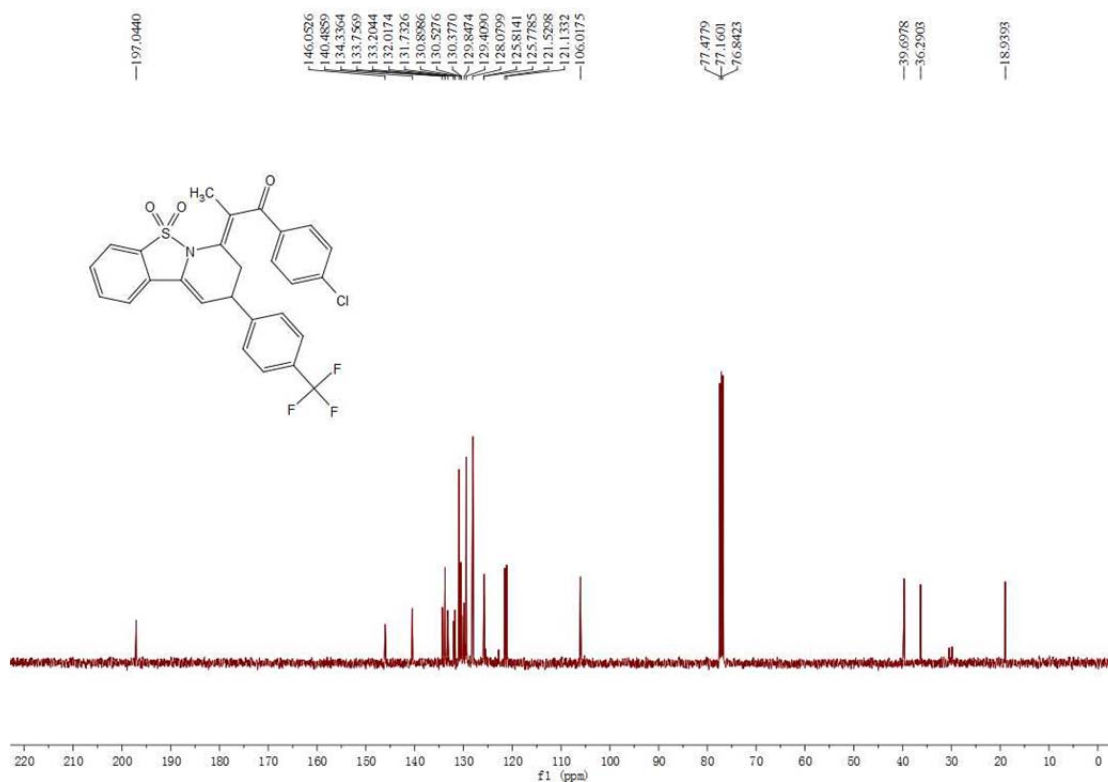
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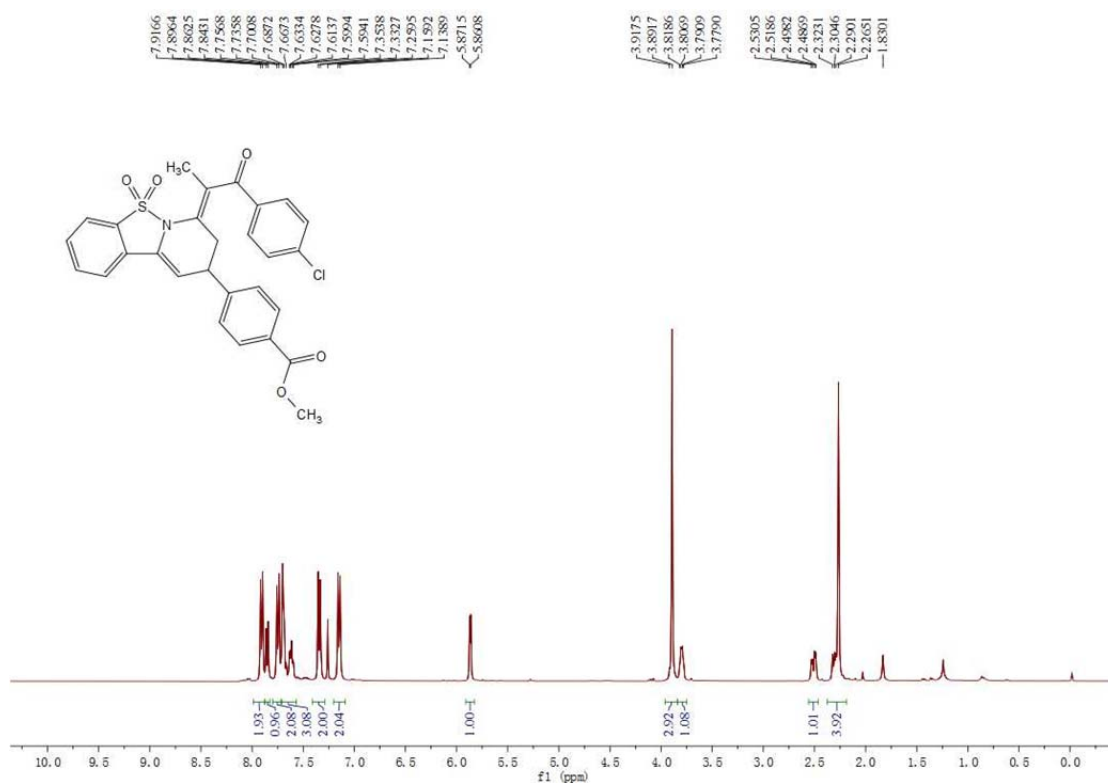
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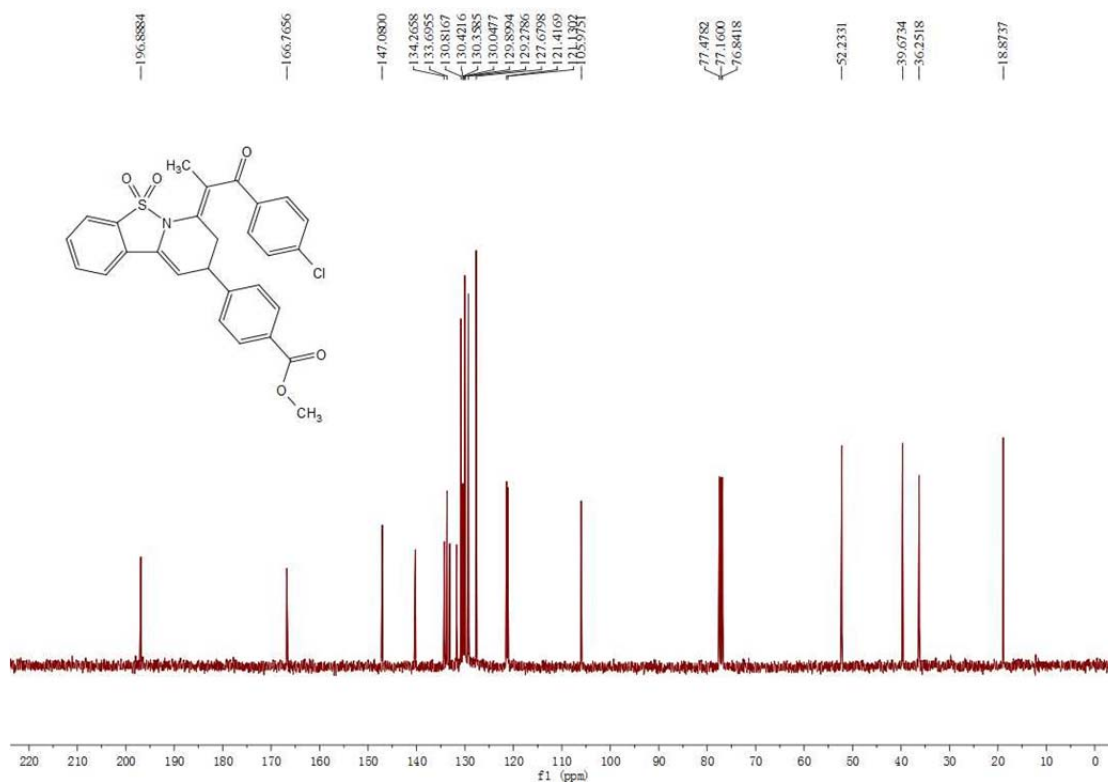
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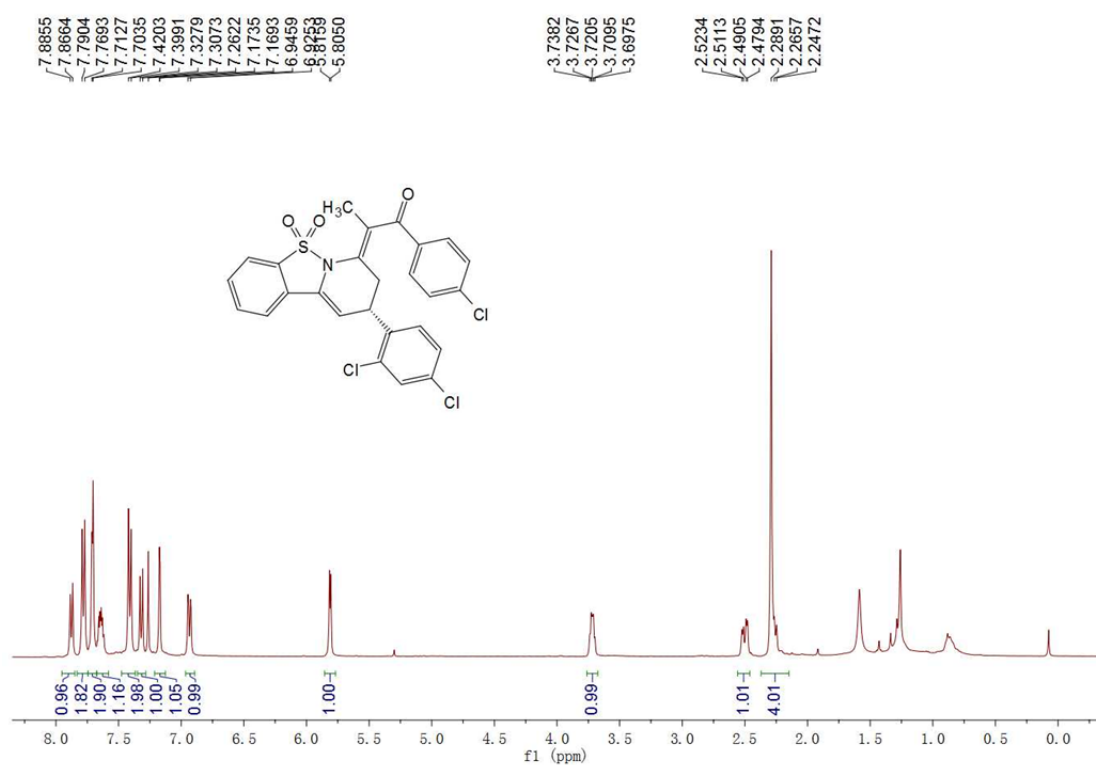
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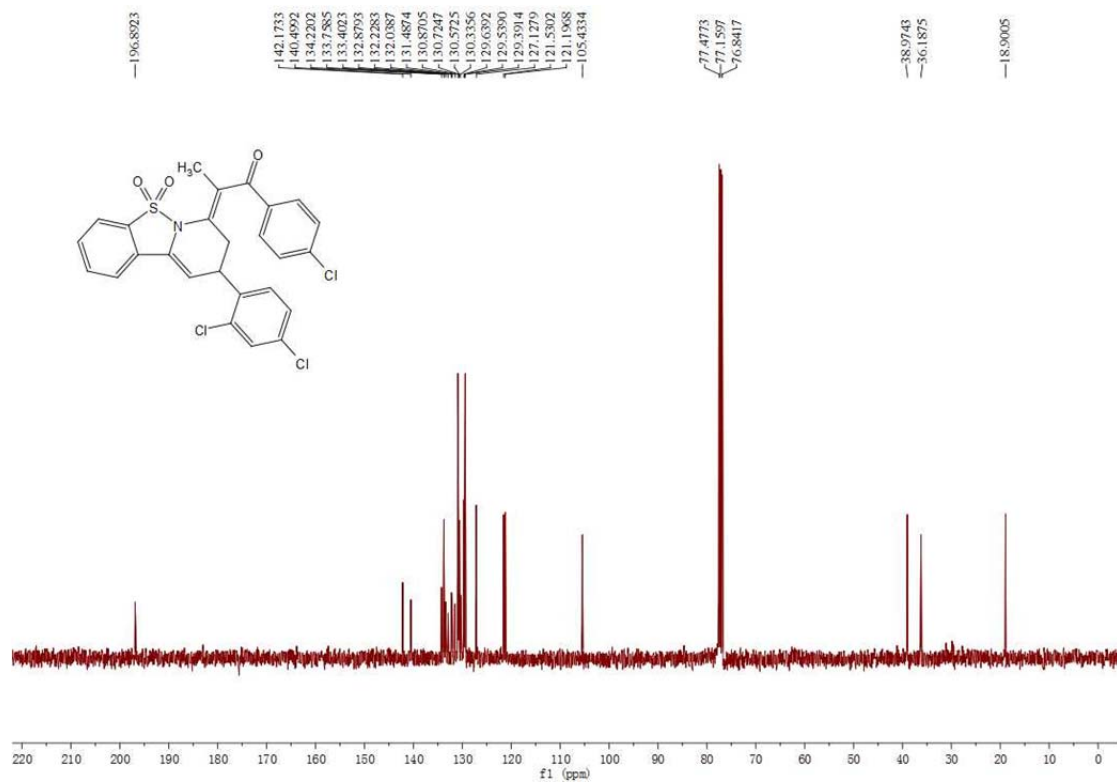
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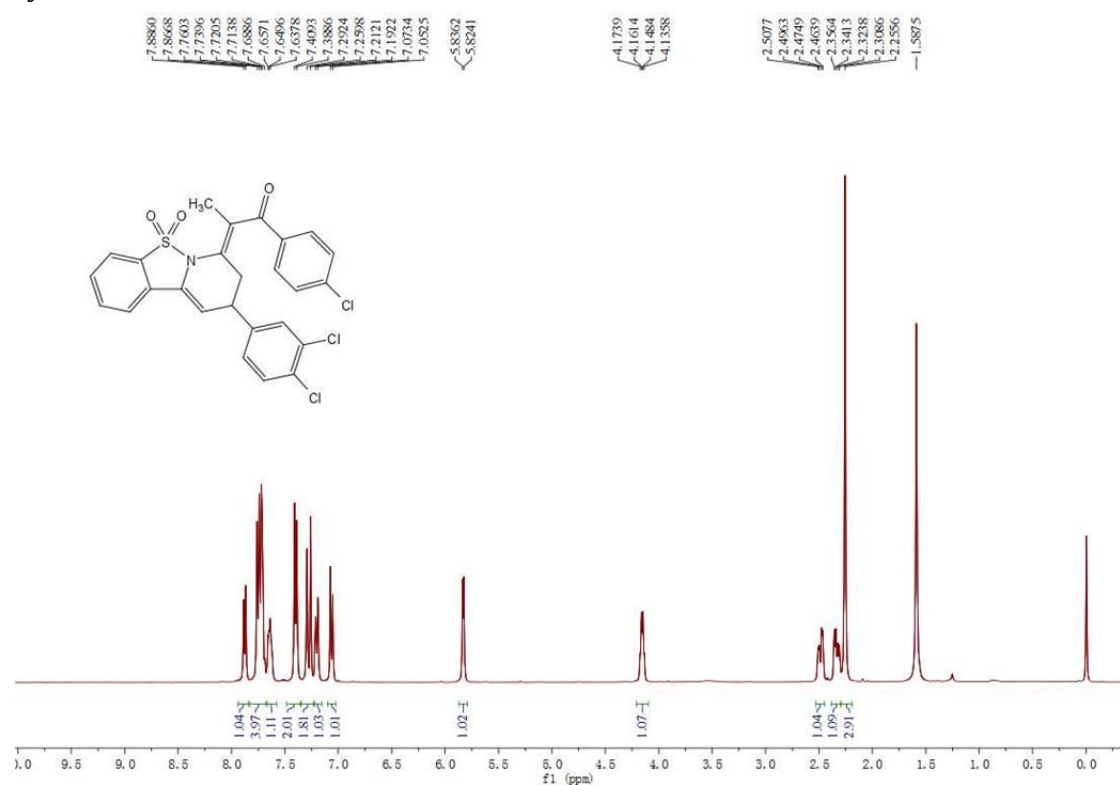
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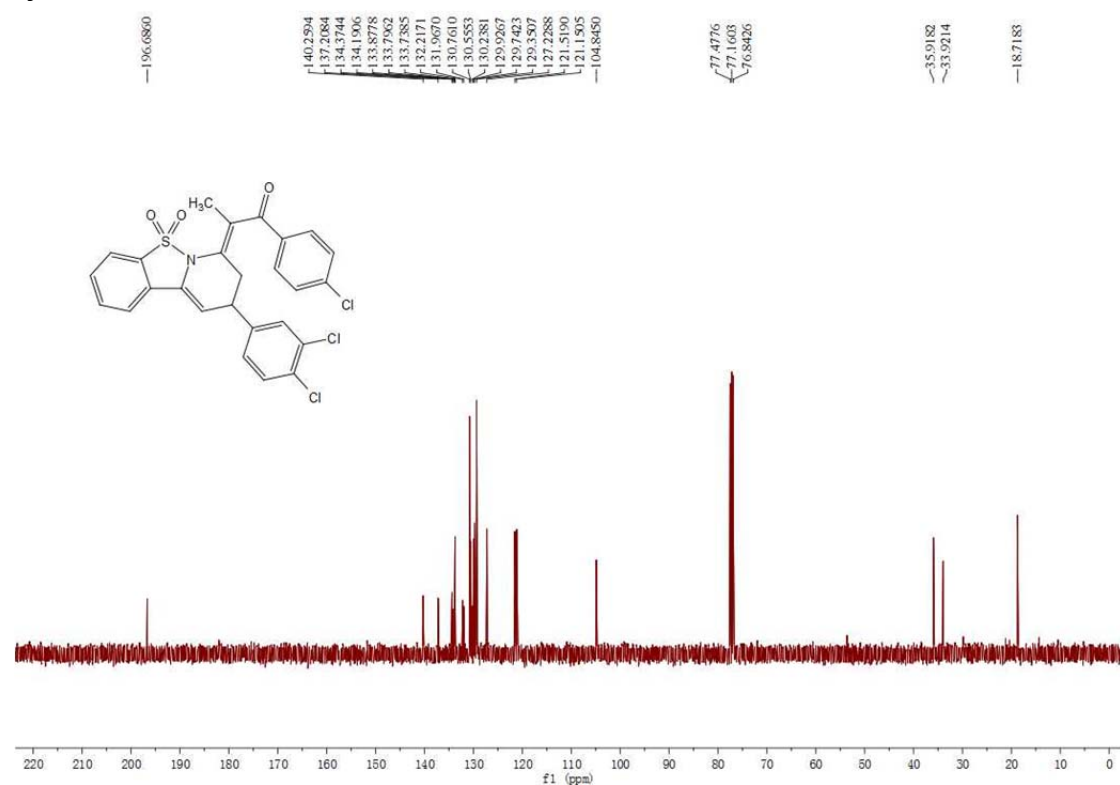
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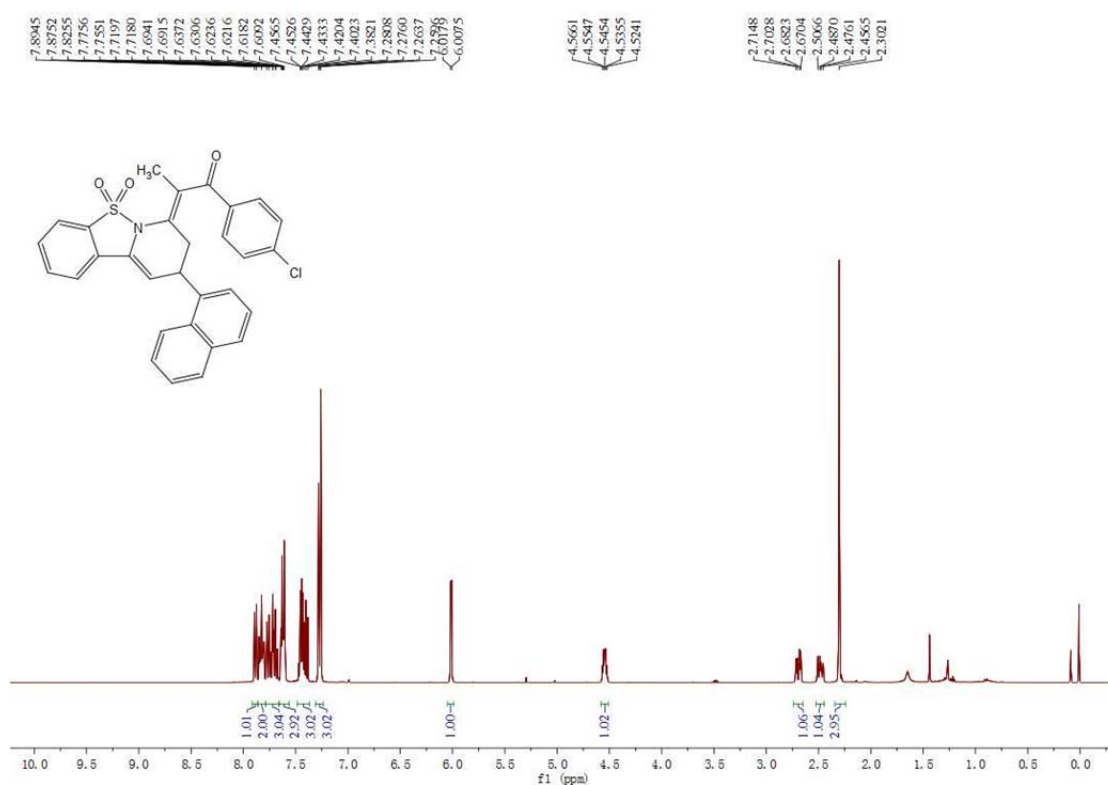
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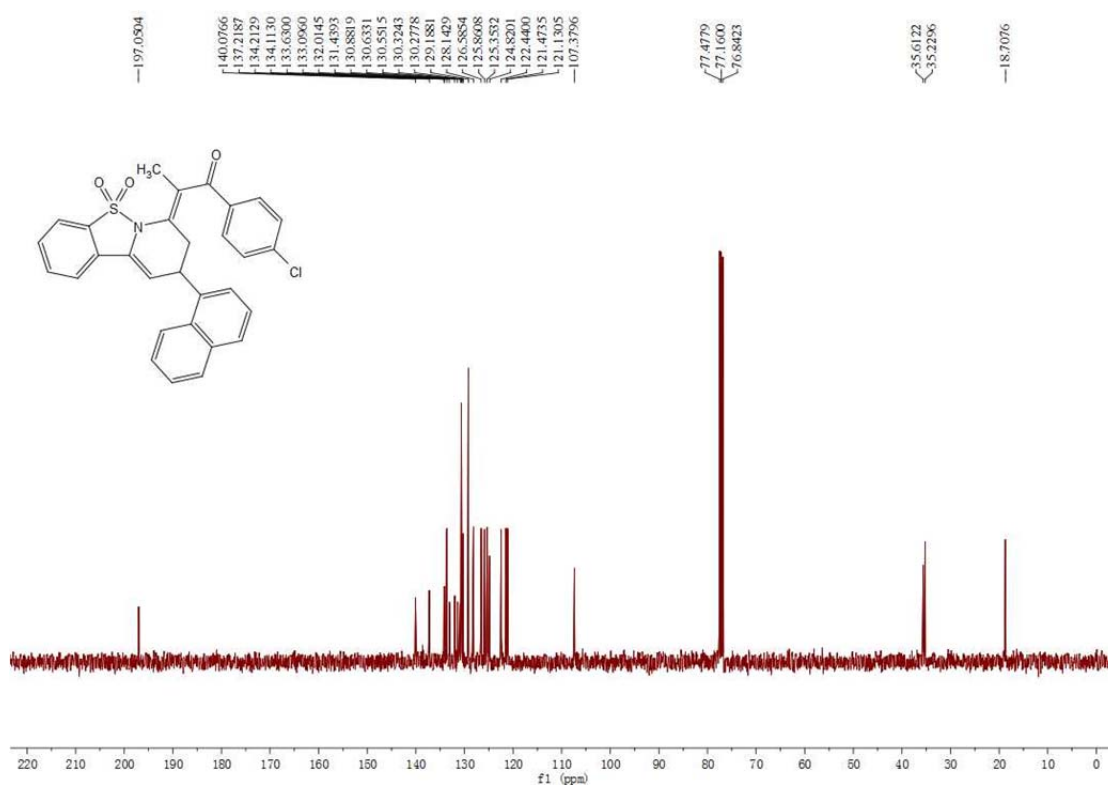
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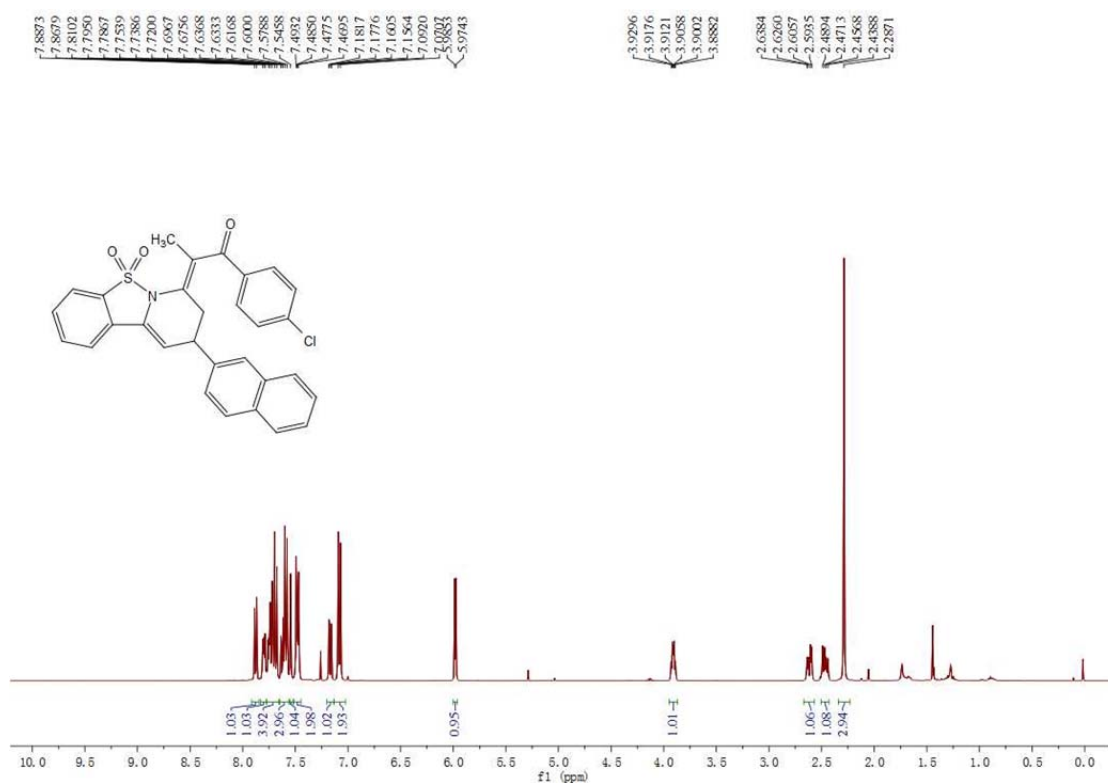
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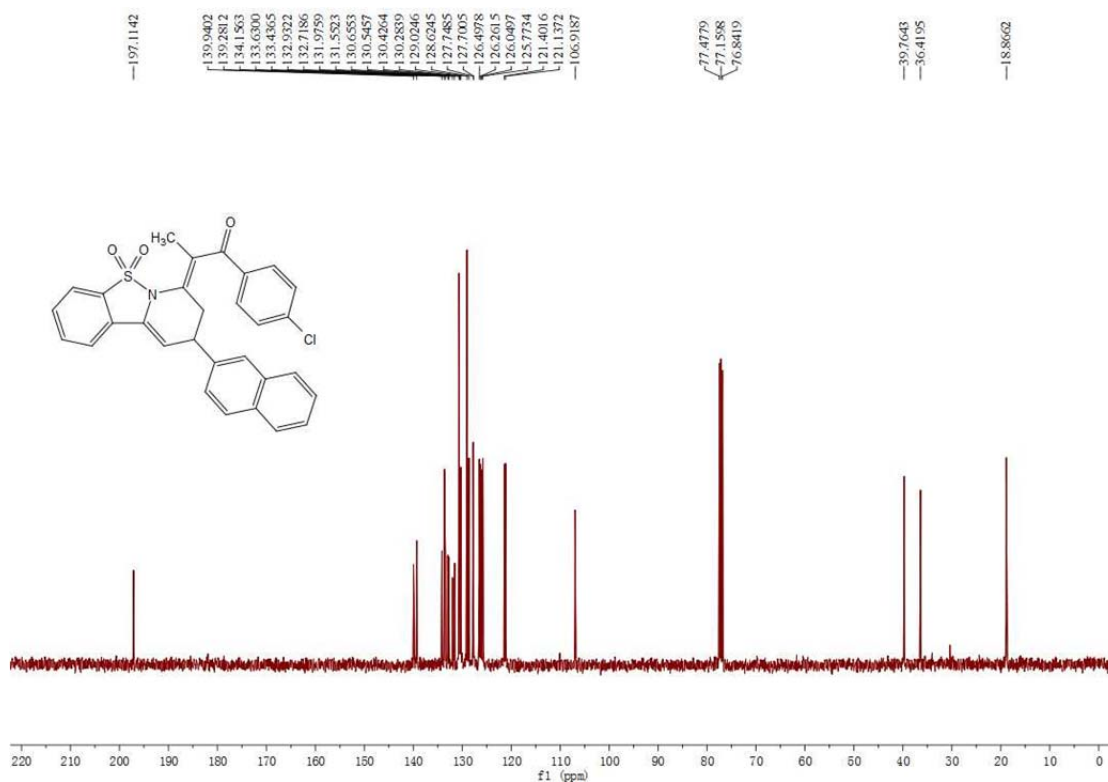
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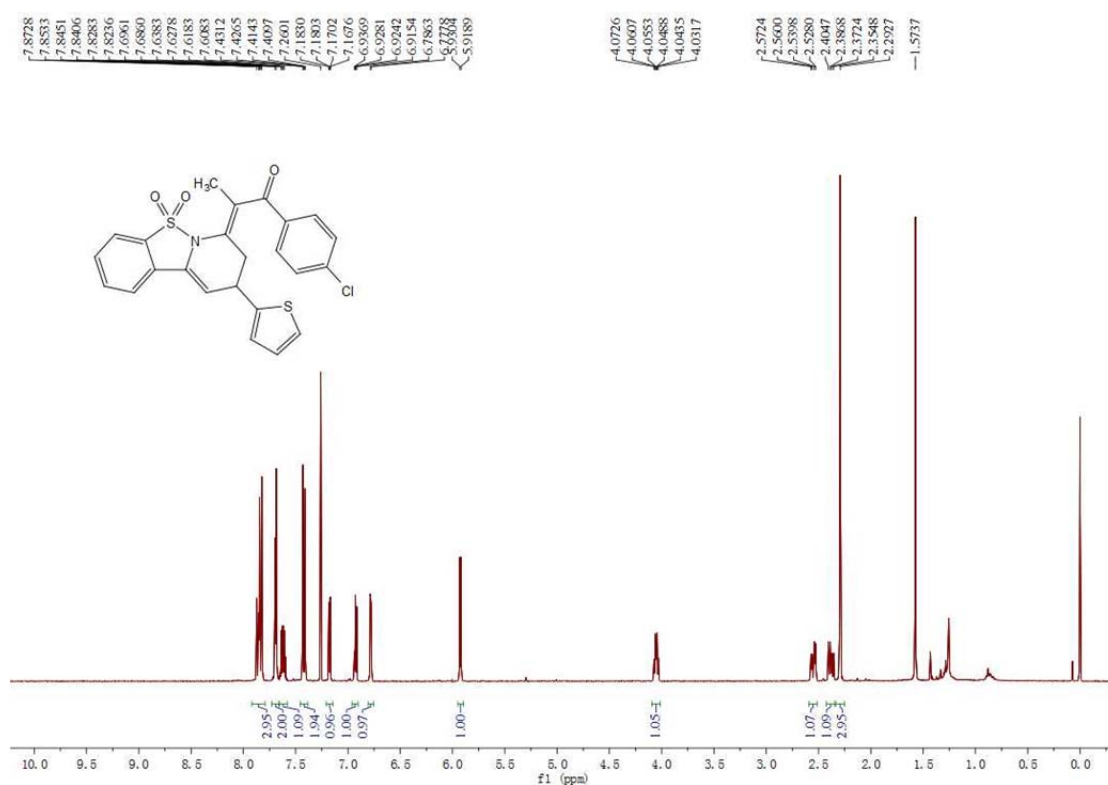
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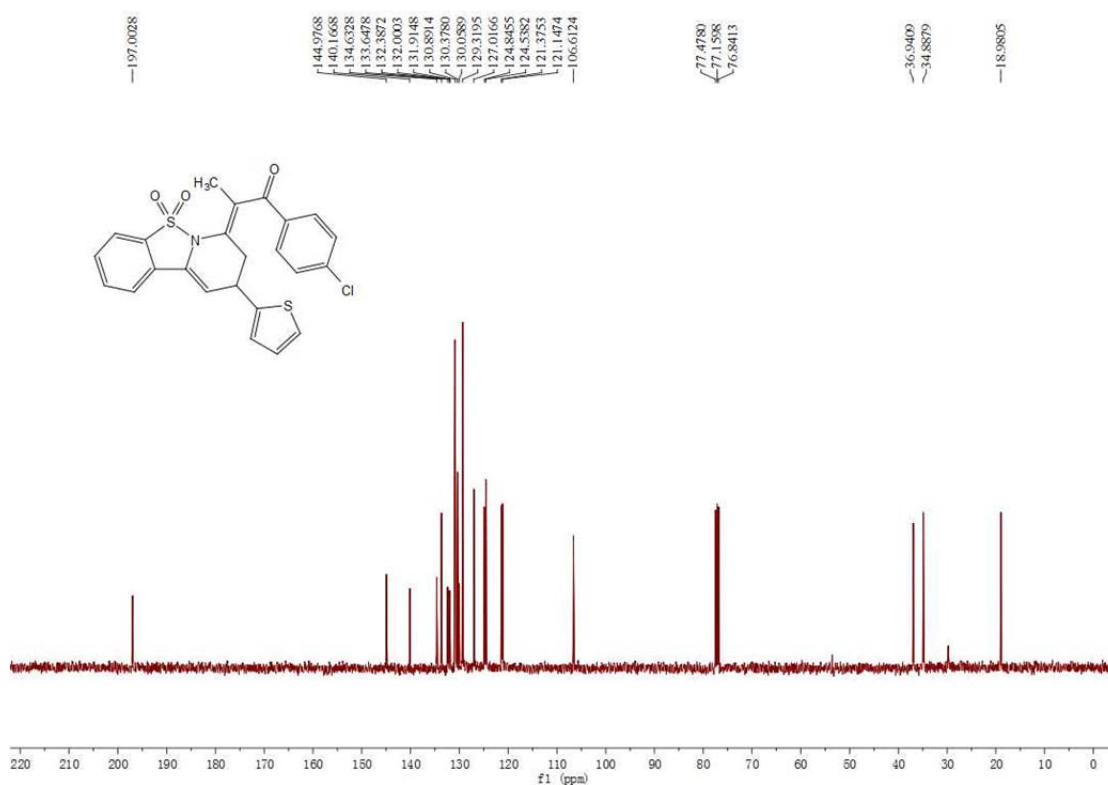
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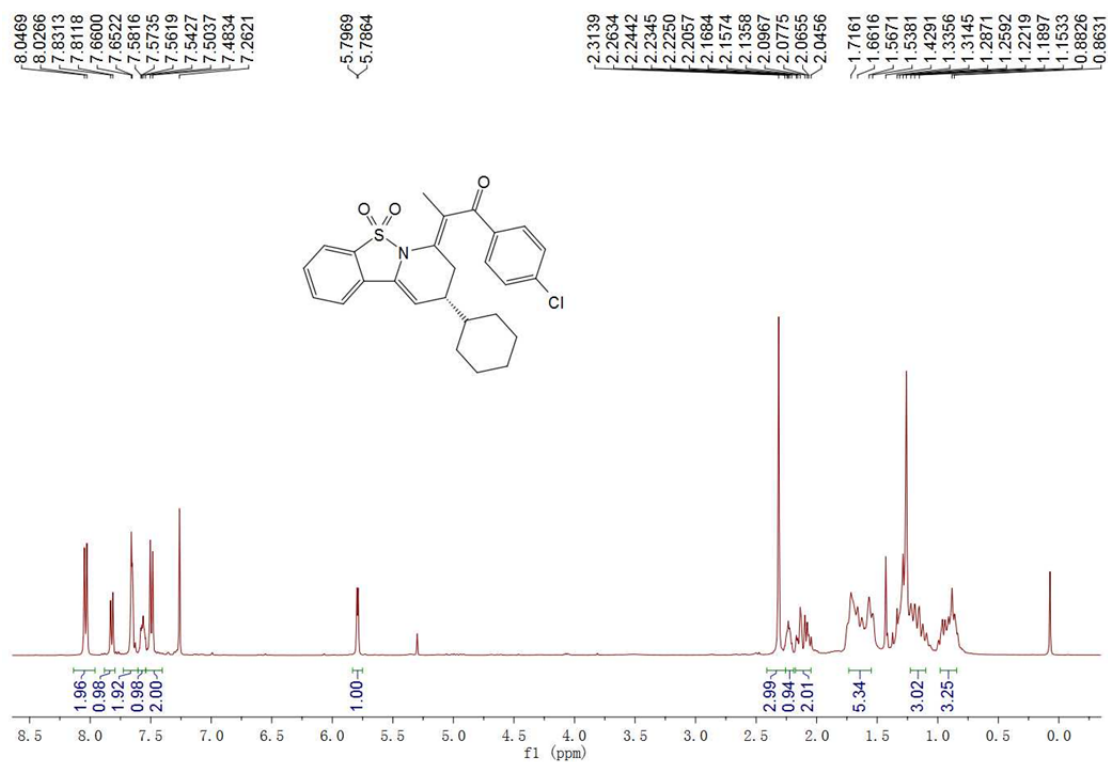
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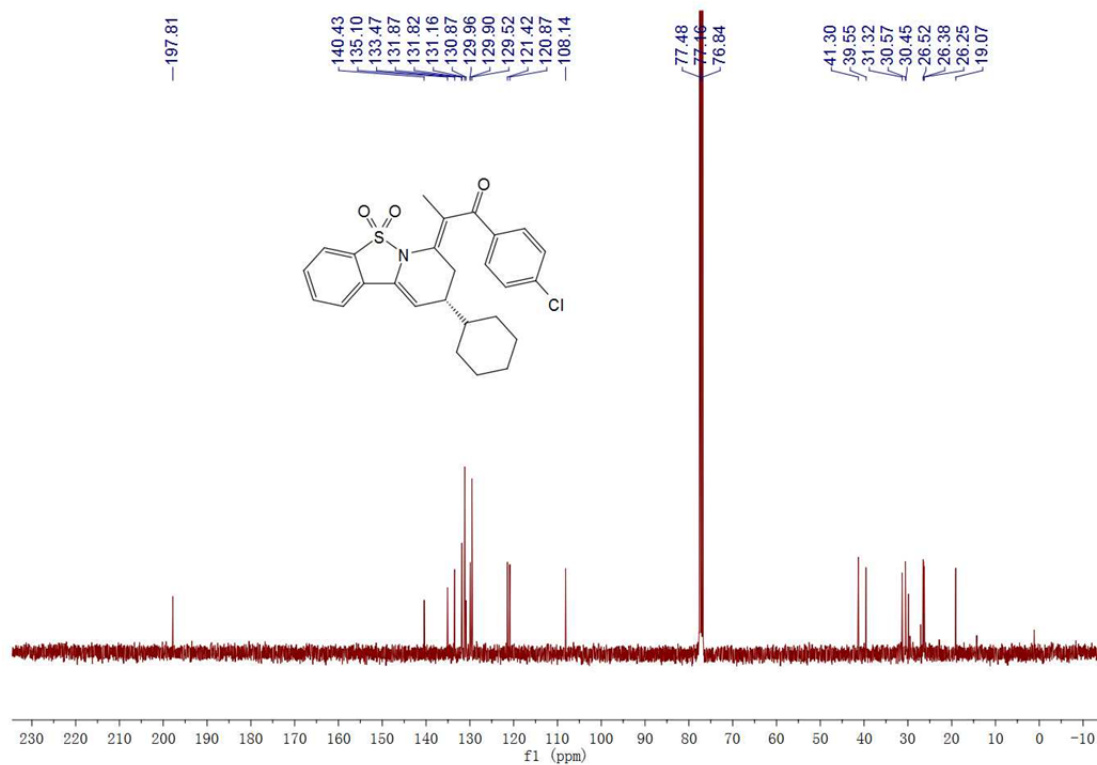
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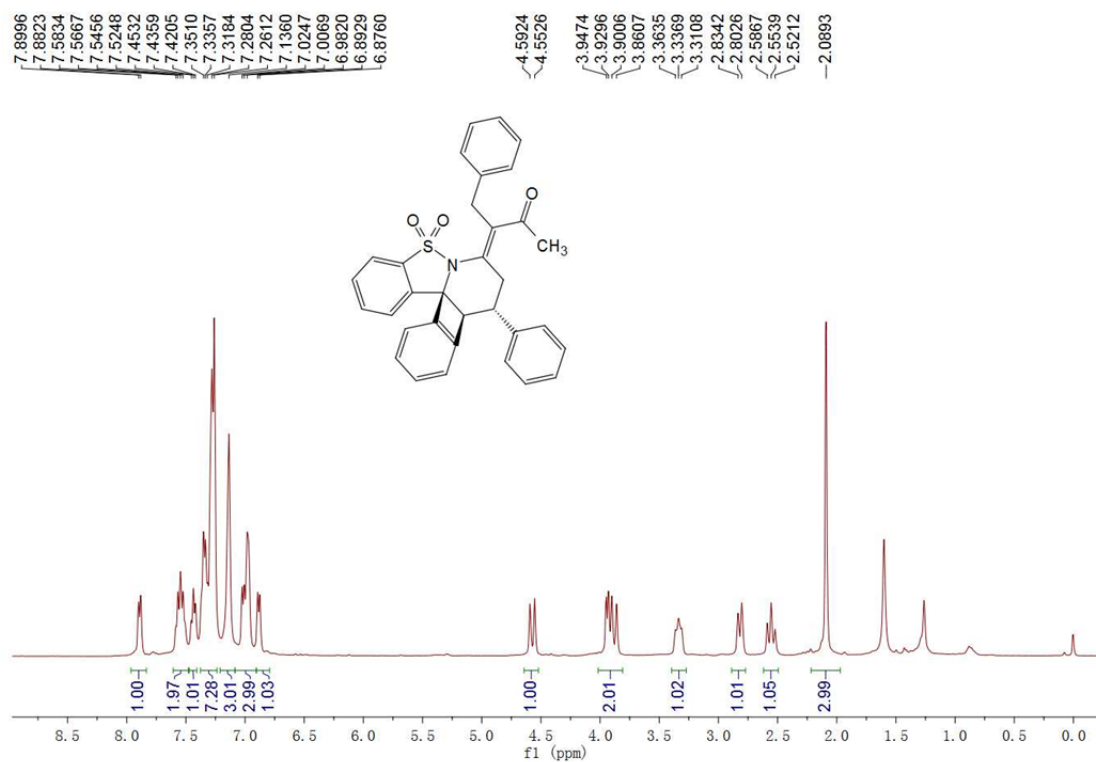
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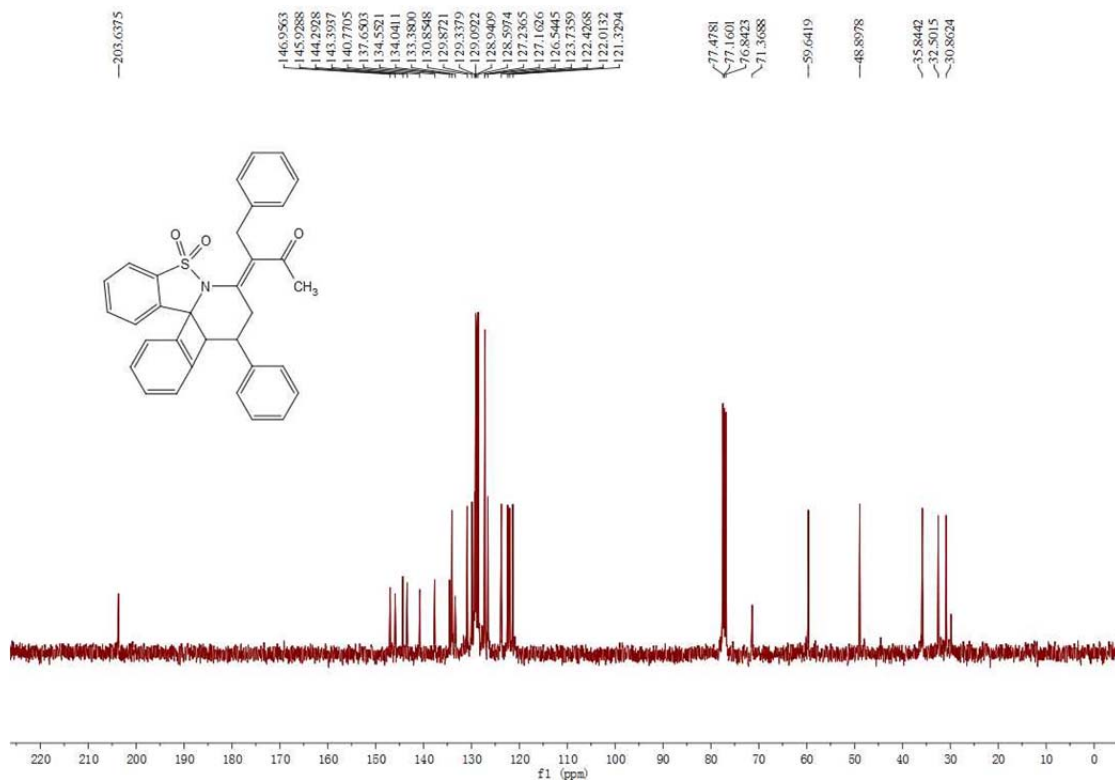
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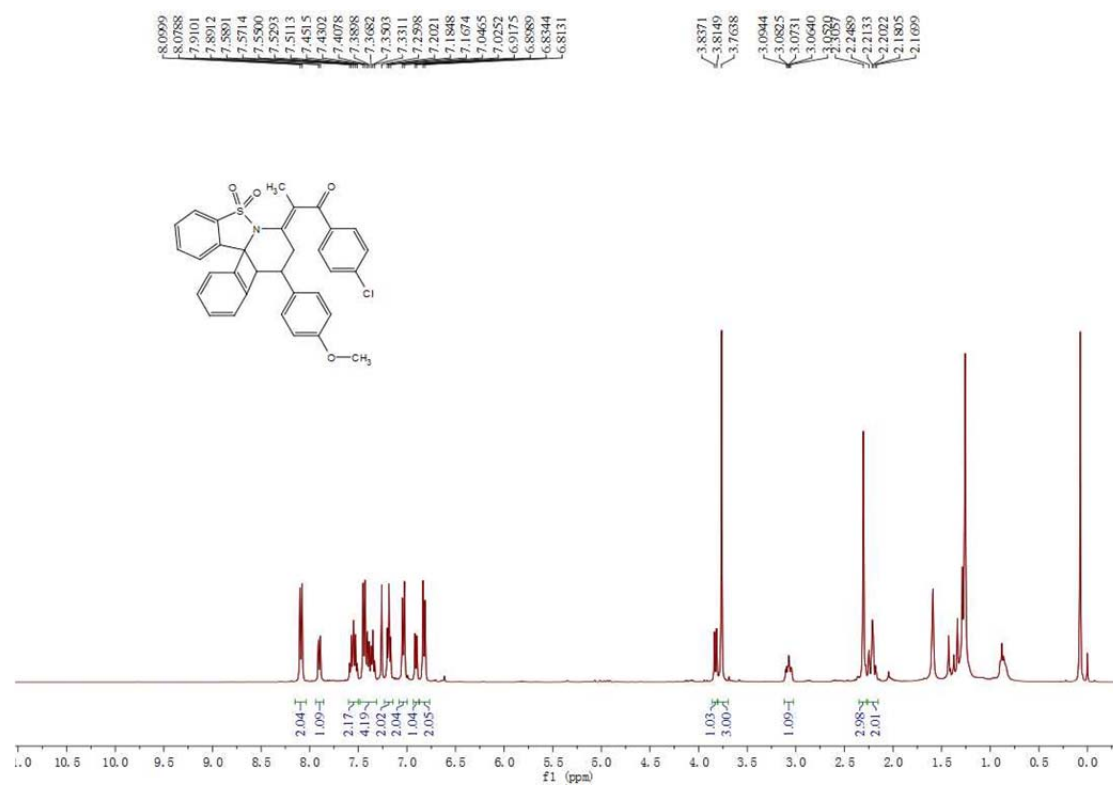
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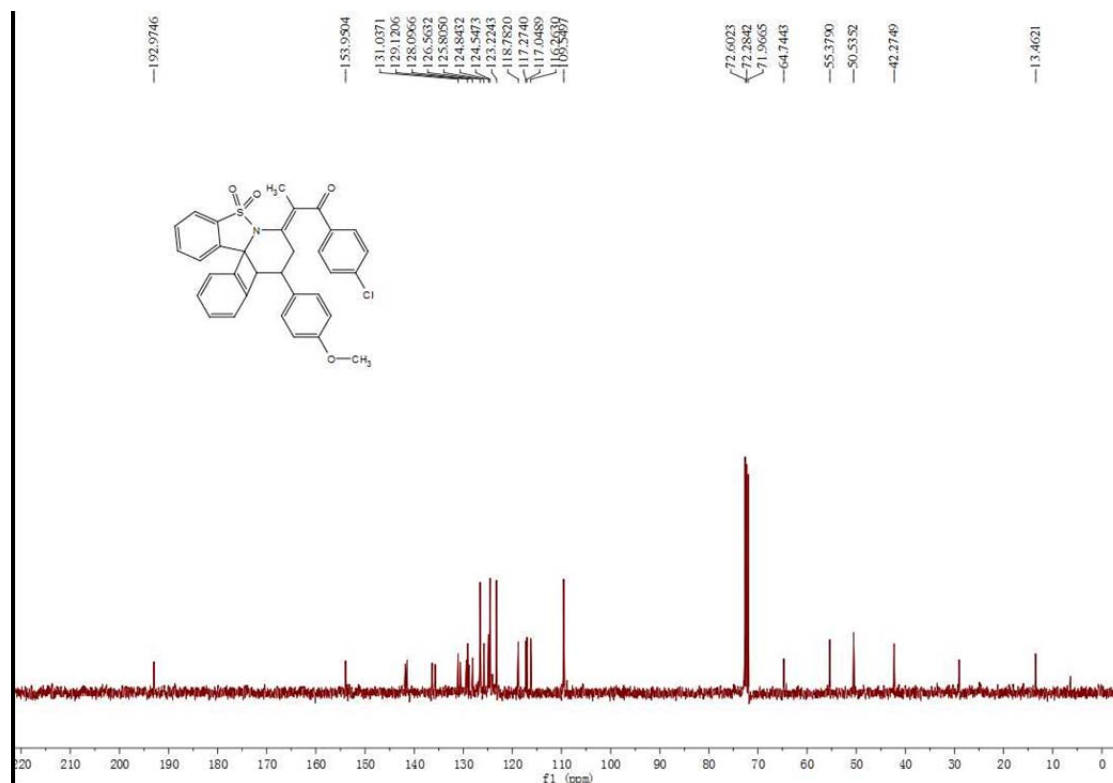
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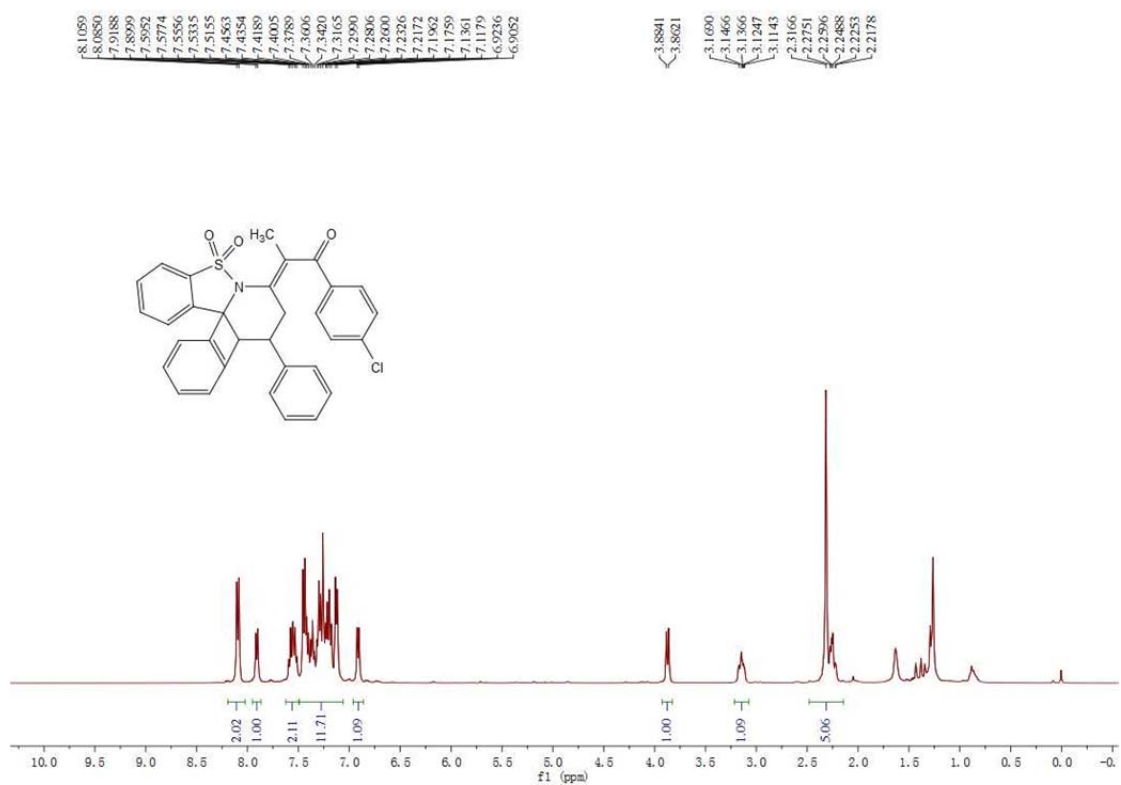
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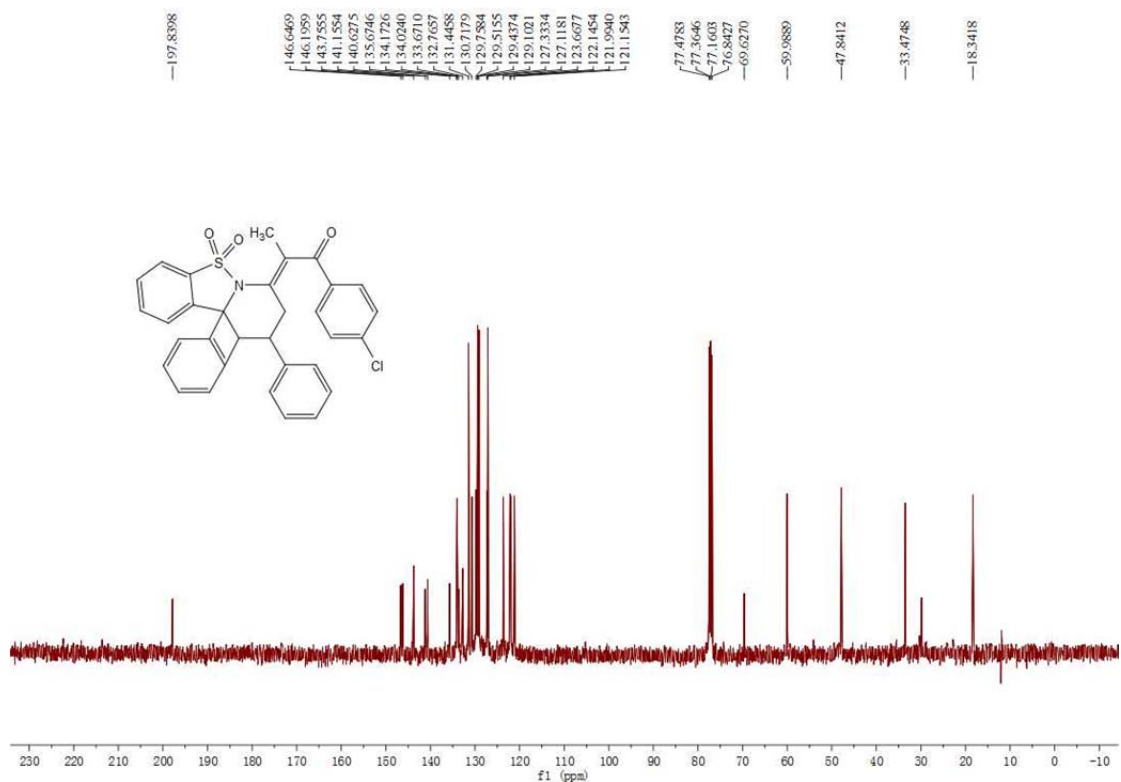
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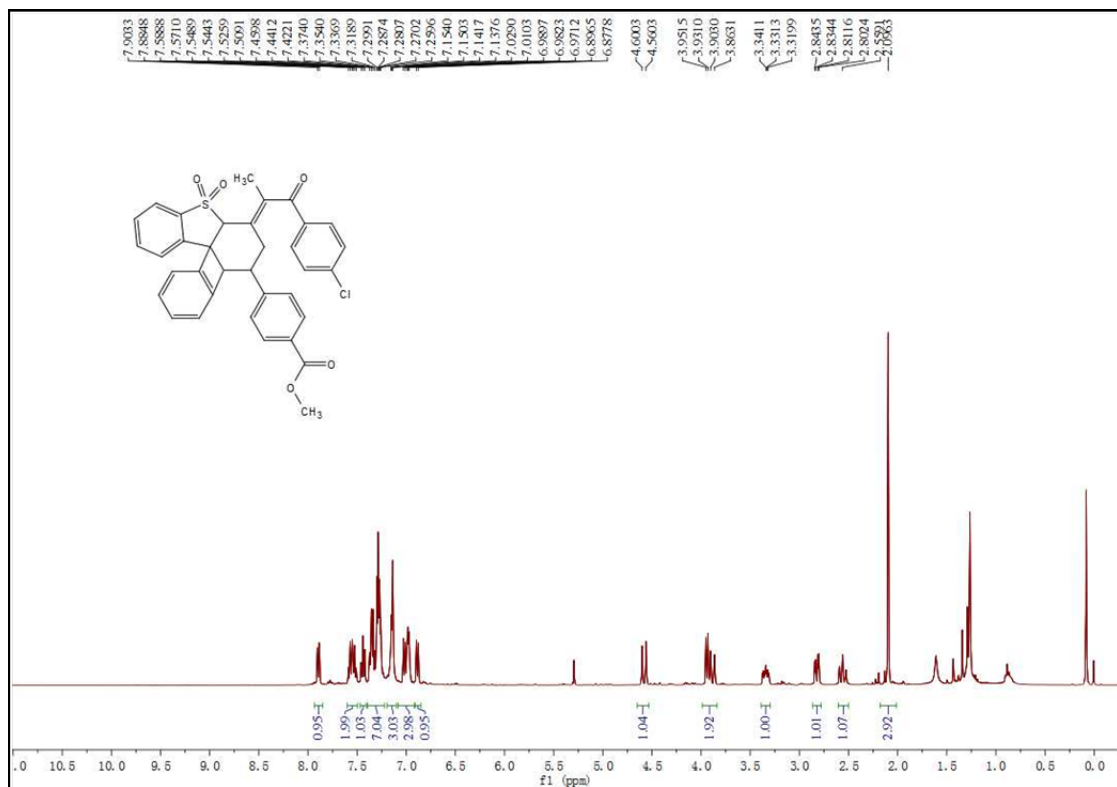
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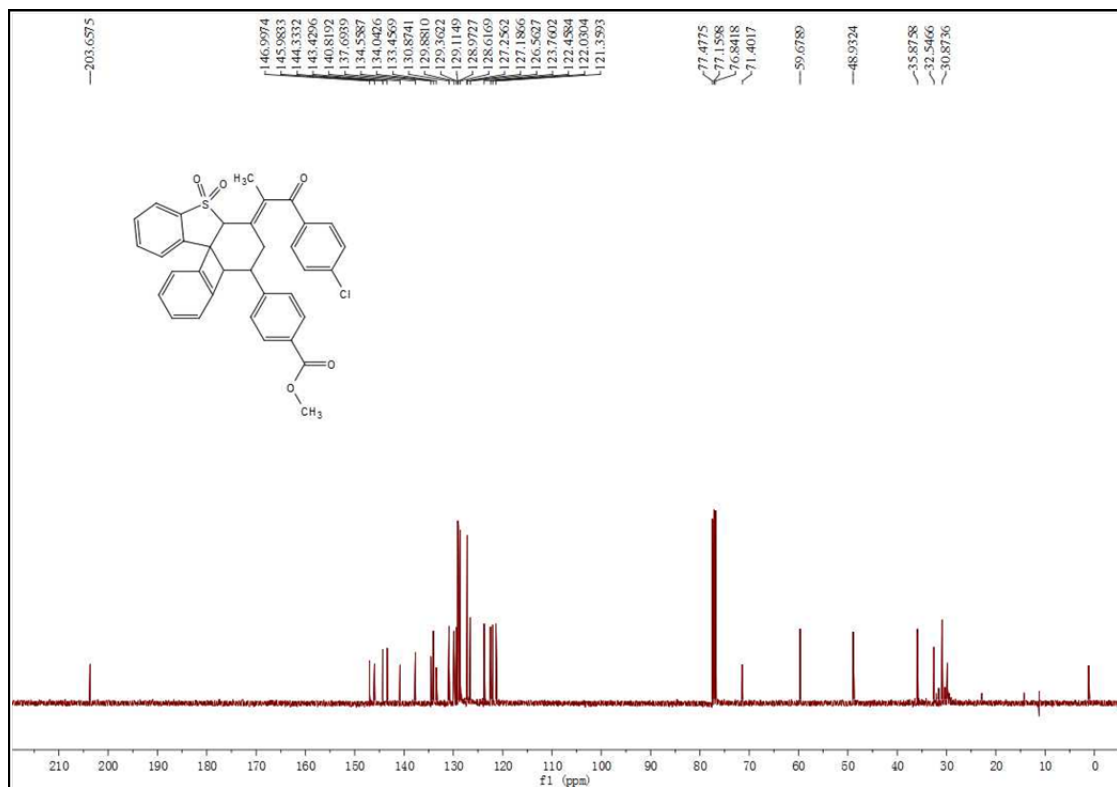
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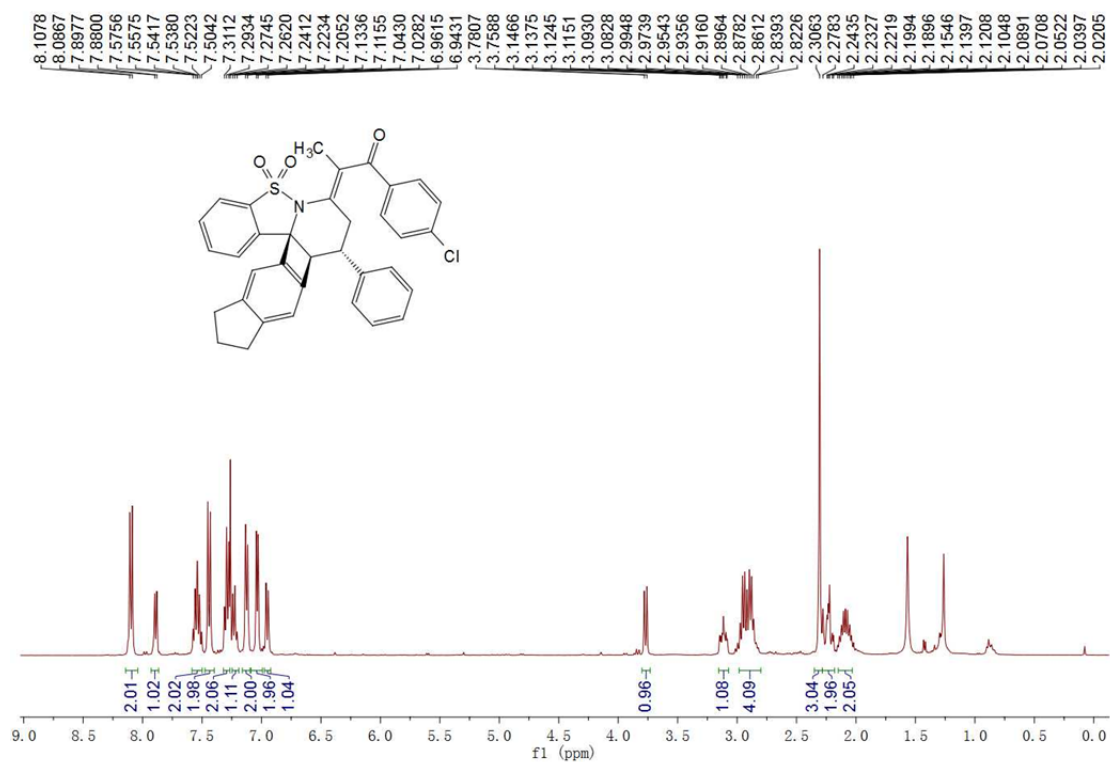
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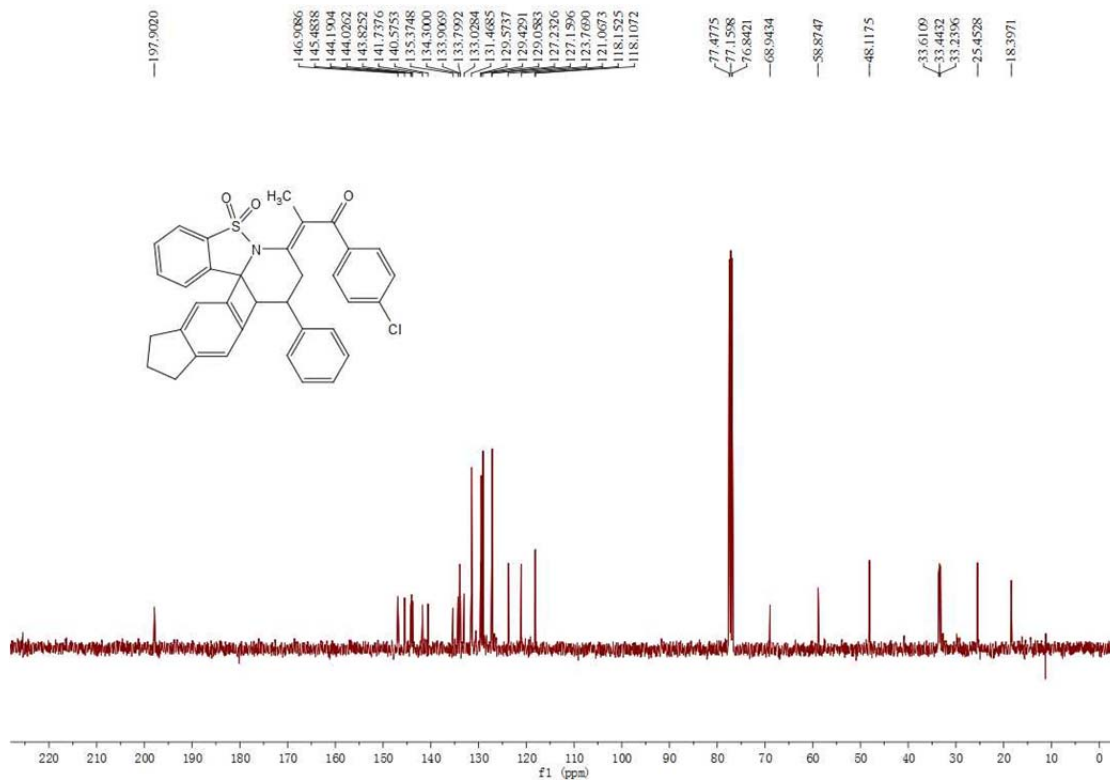
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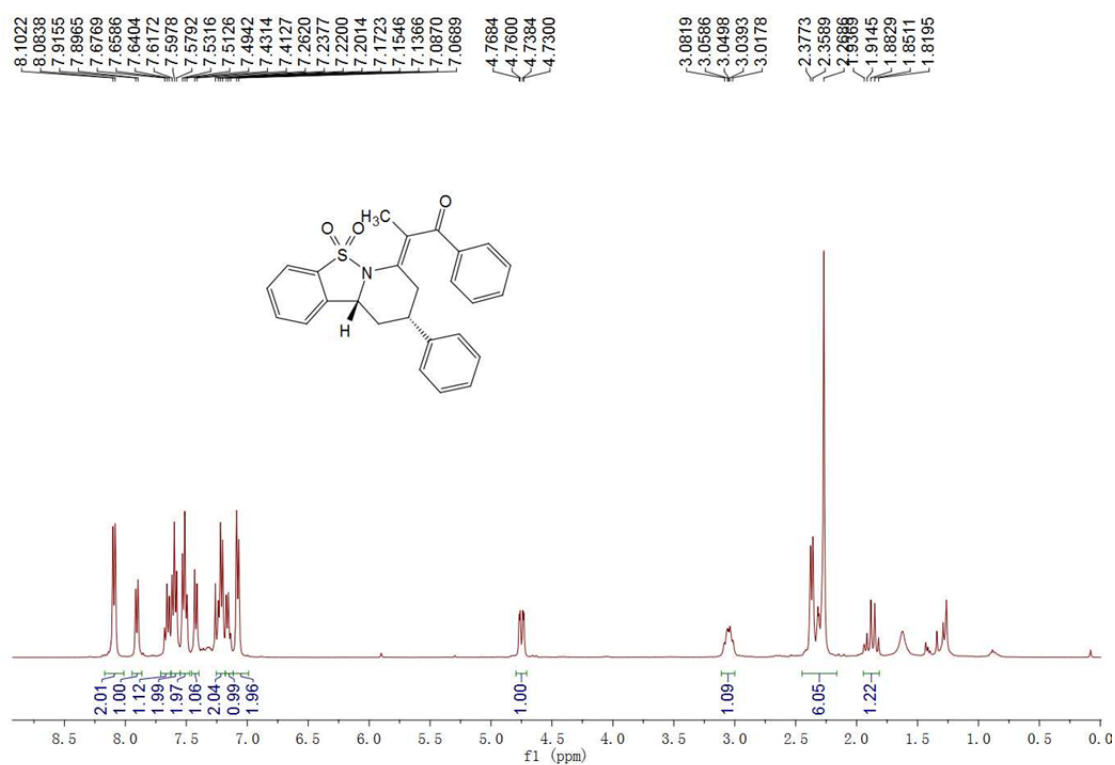
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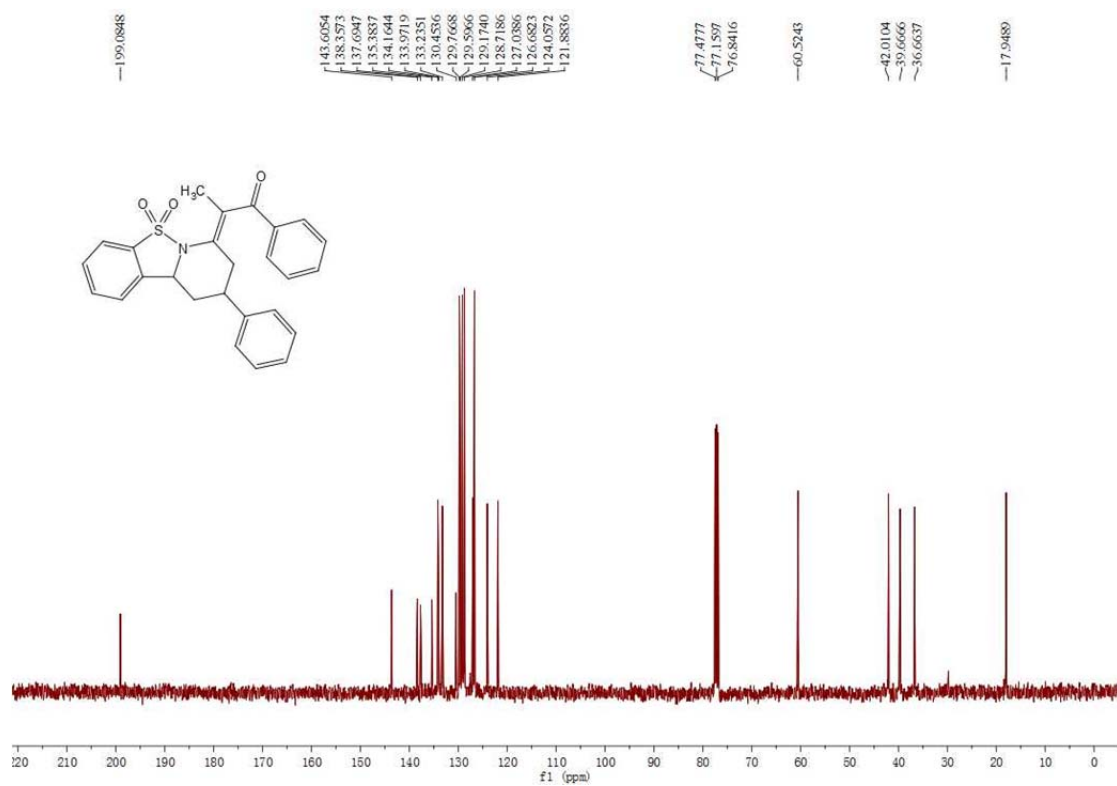
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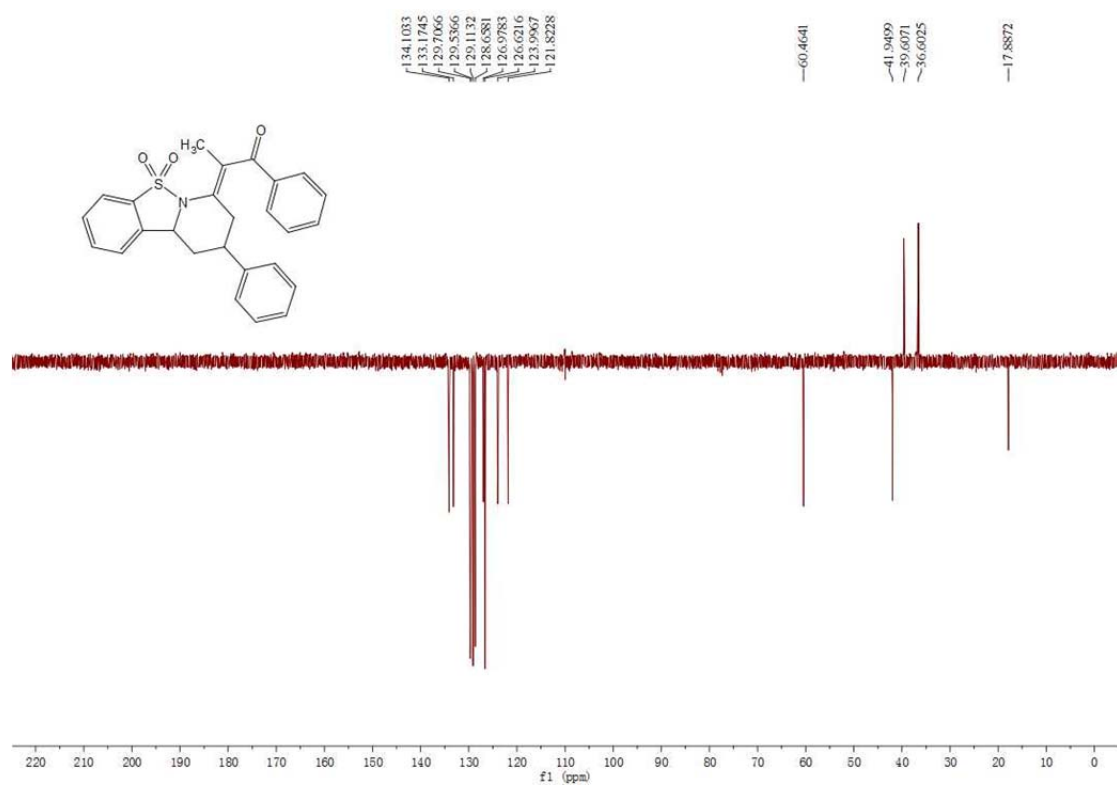
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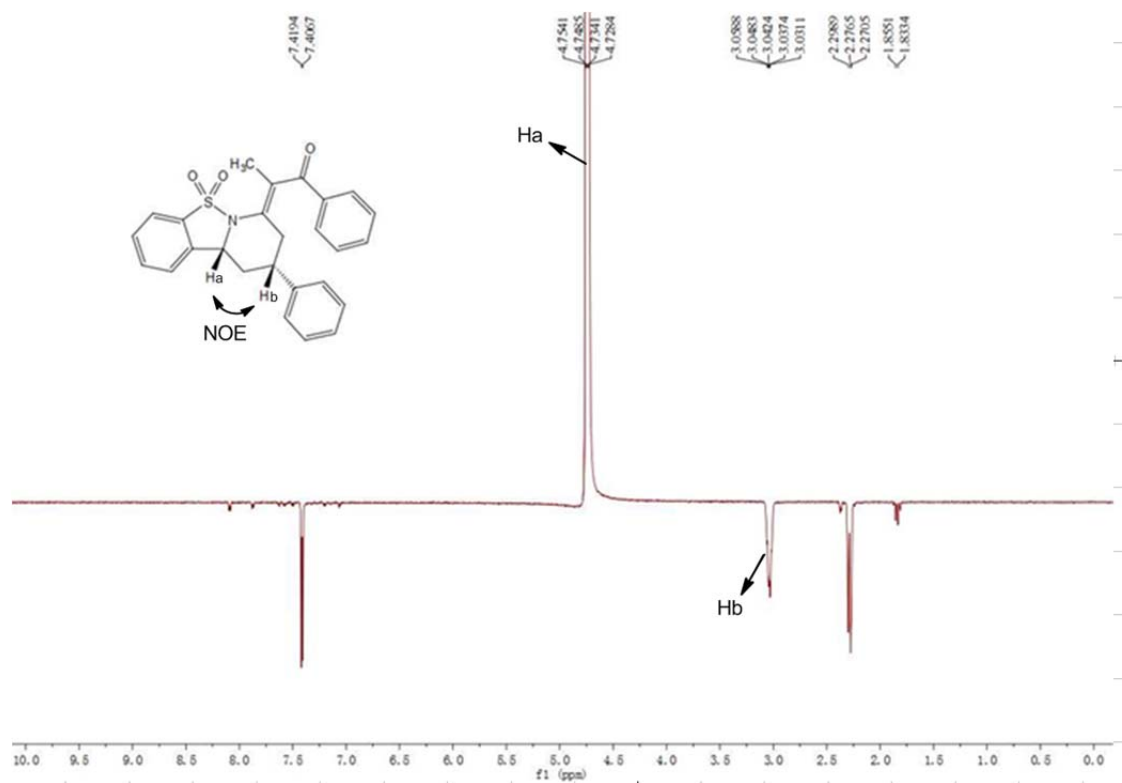
7b



7b



7b



7b

