

Supplementary information

Design, Synthesis and Evaluation of Clioquinol-Ebselen Hybrids as Multi-Target-Directed Ligands Against Alzheimer's Disease

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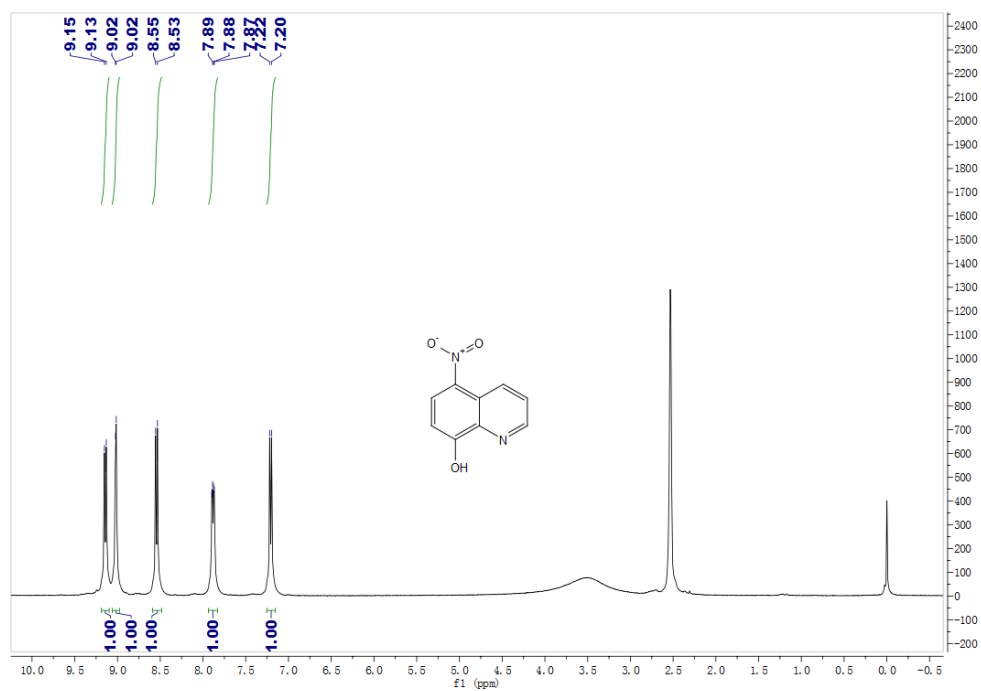
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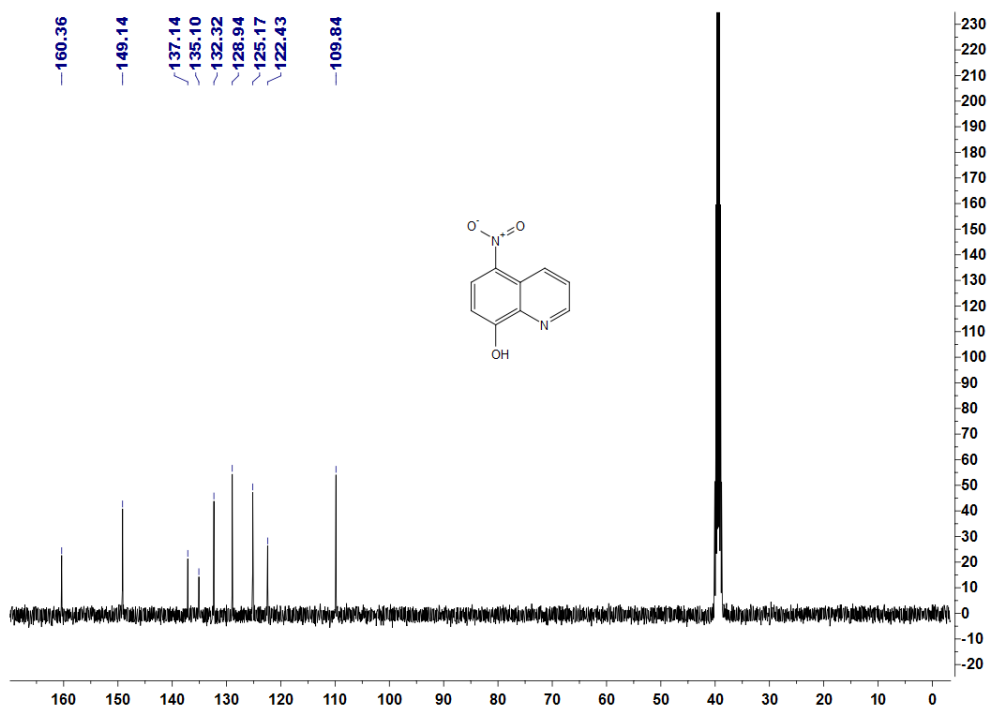
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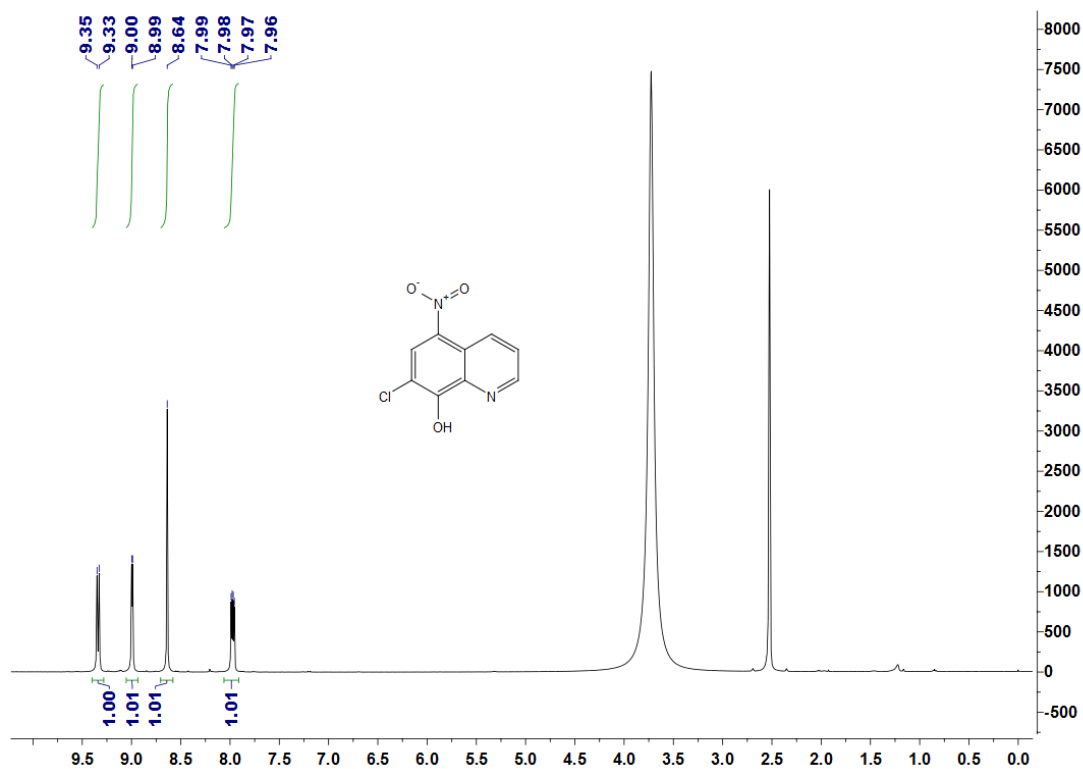
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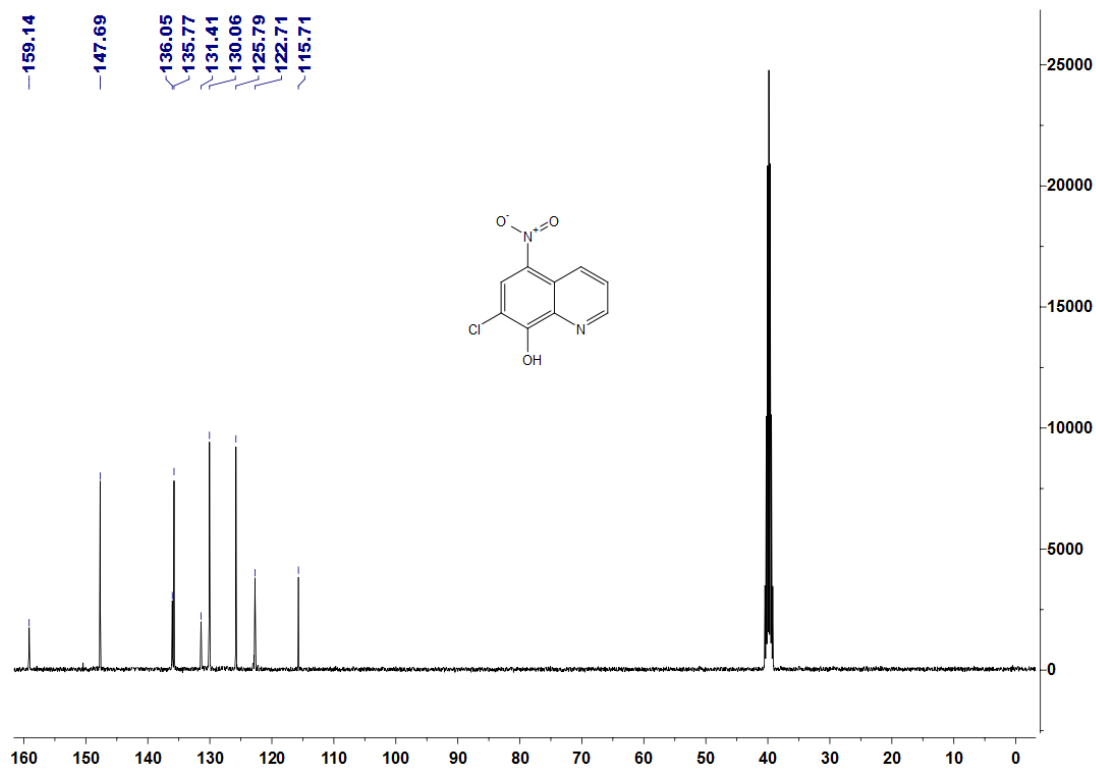
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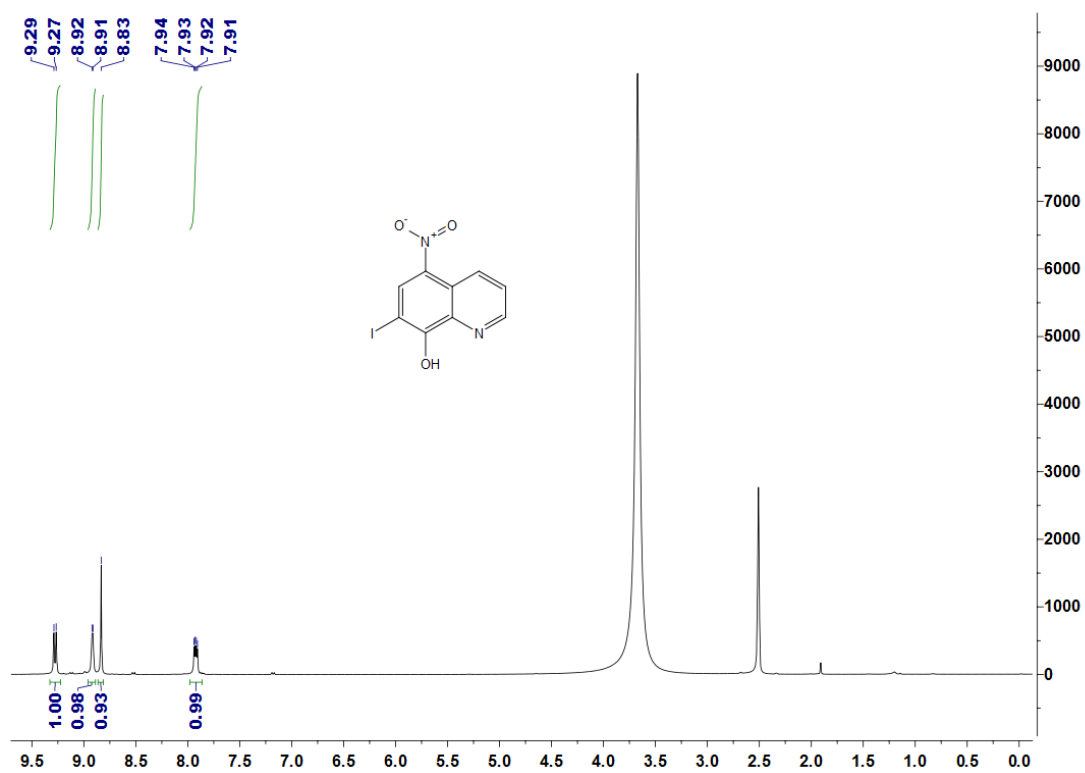
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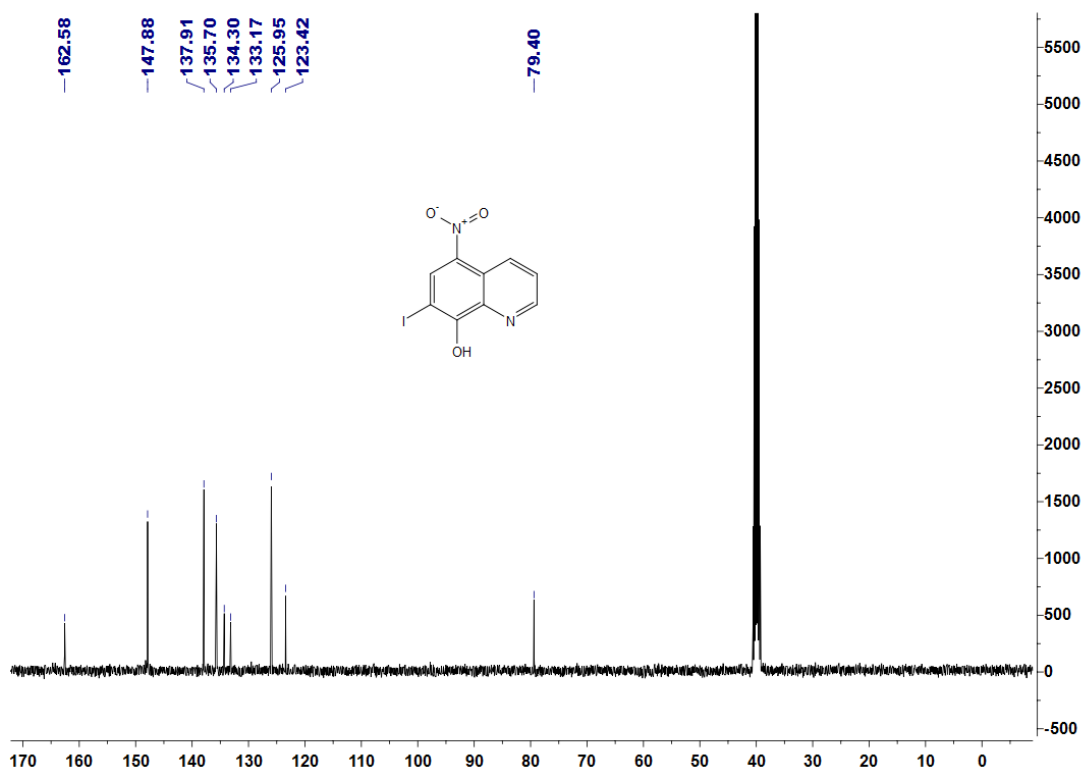
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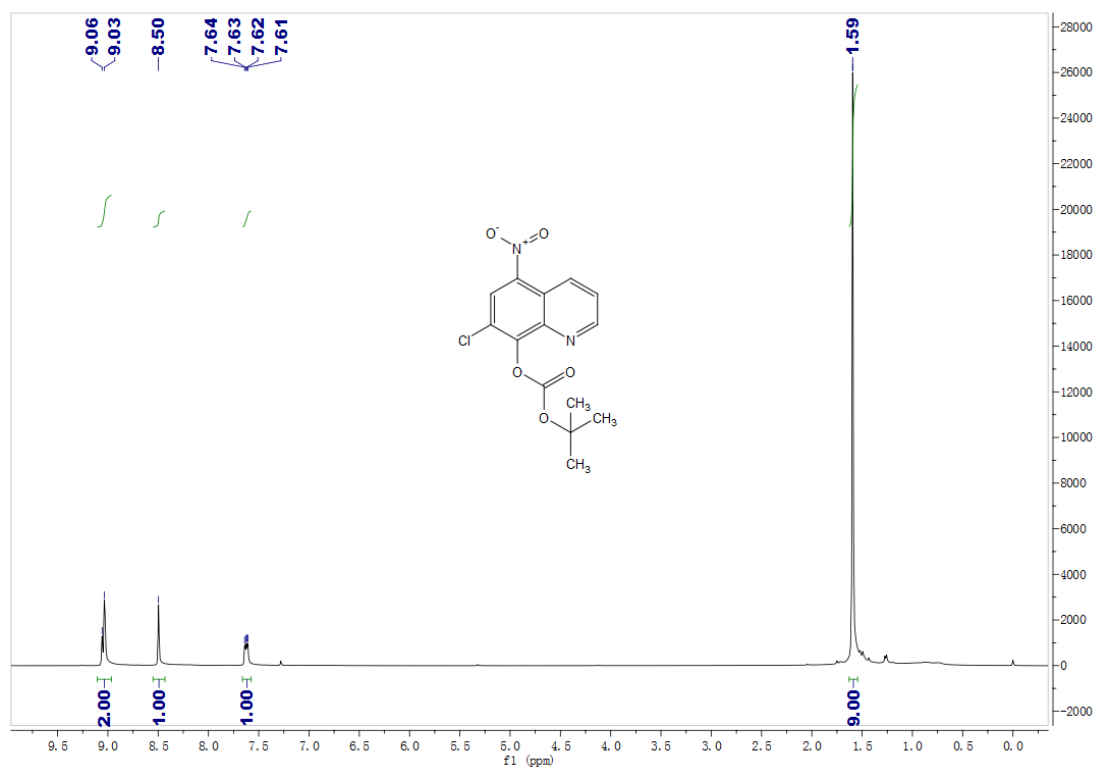
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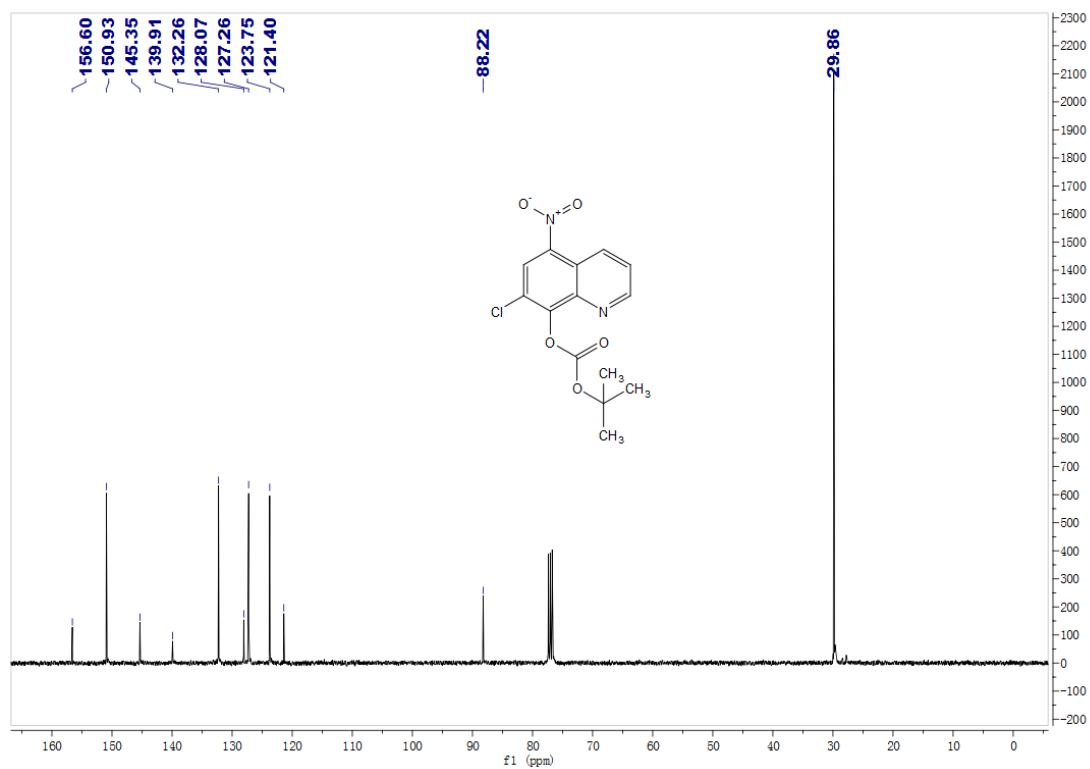
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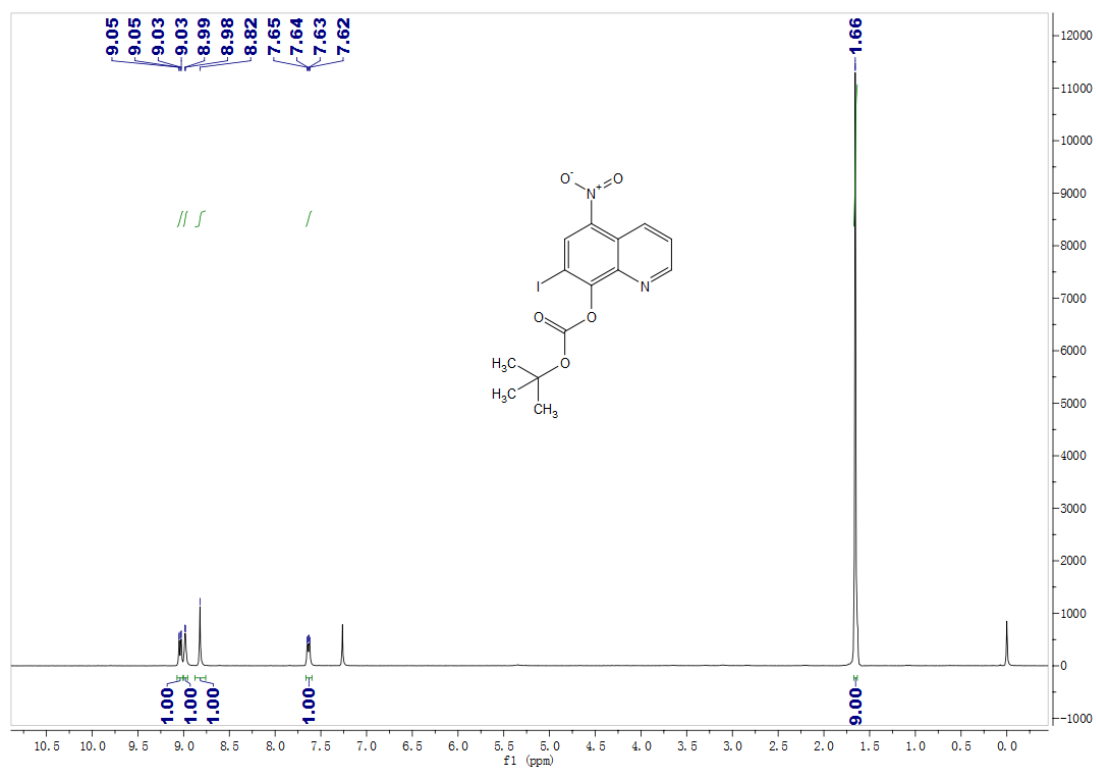
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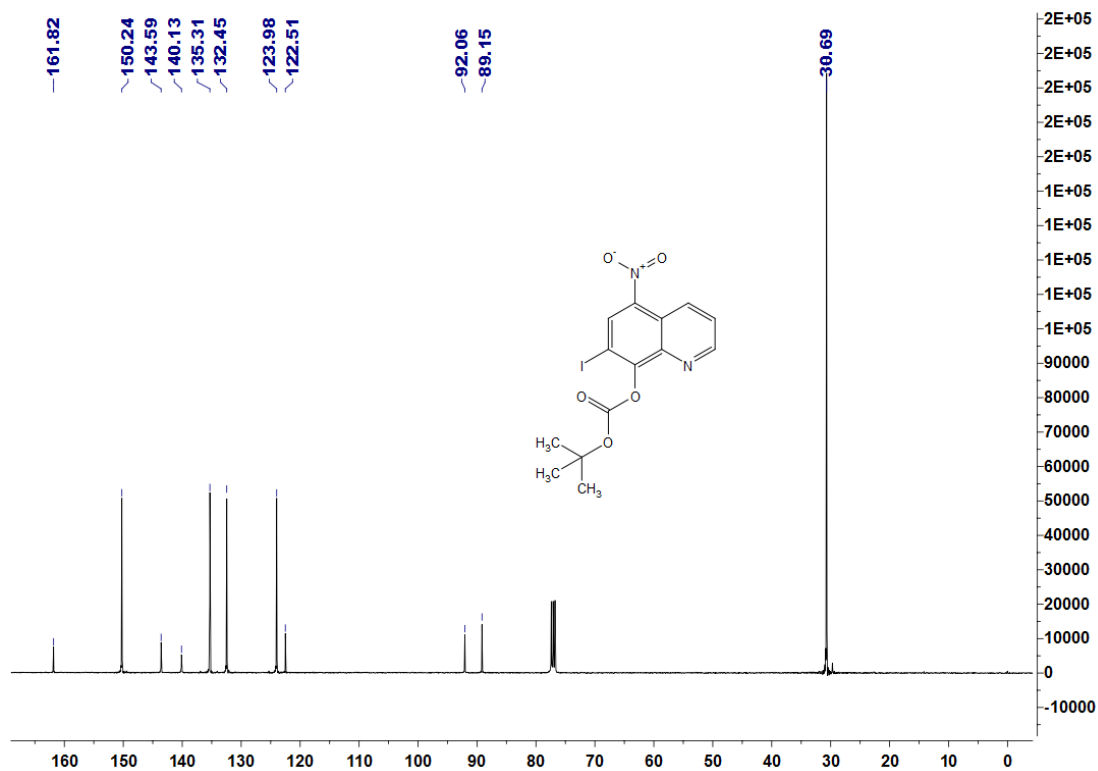
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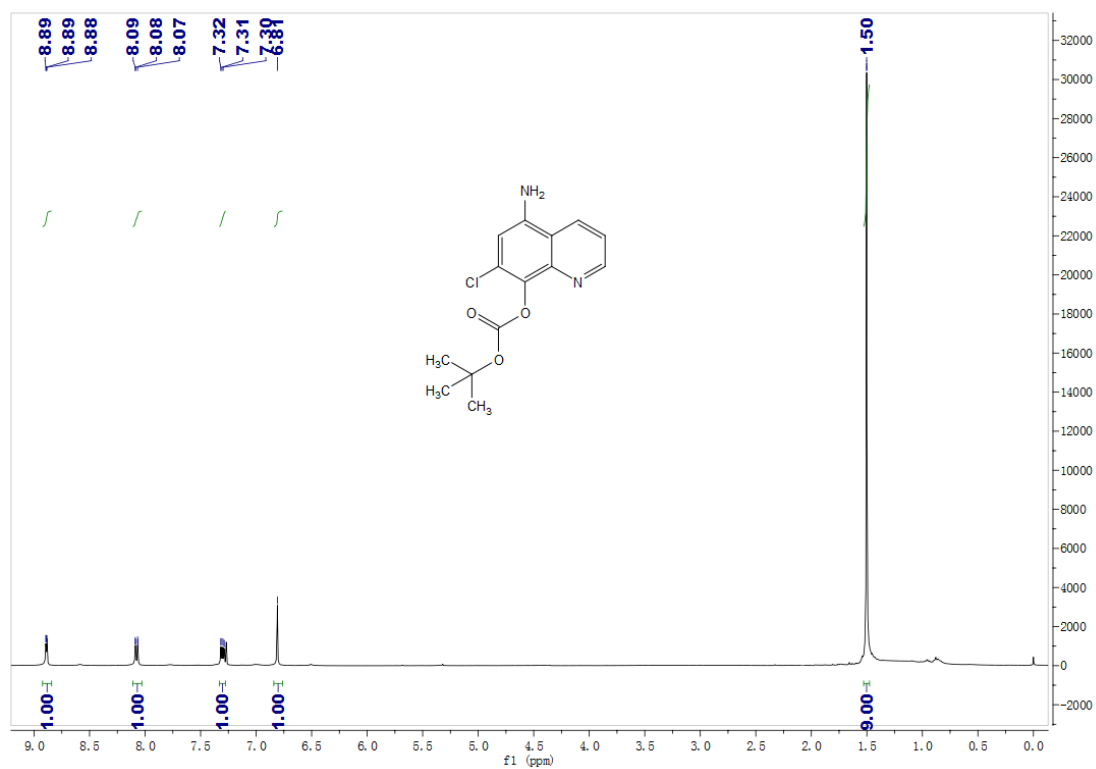
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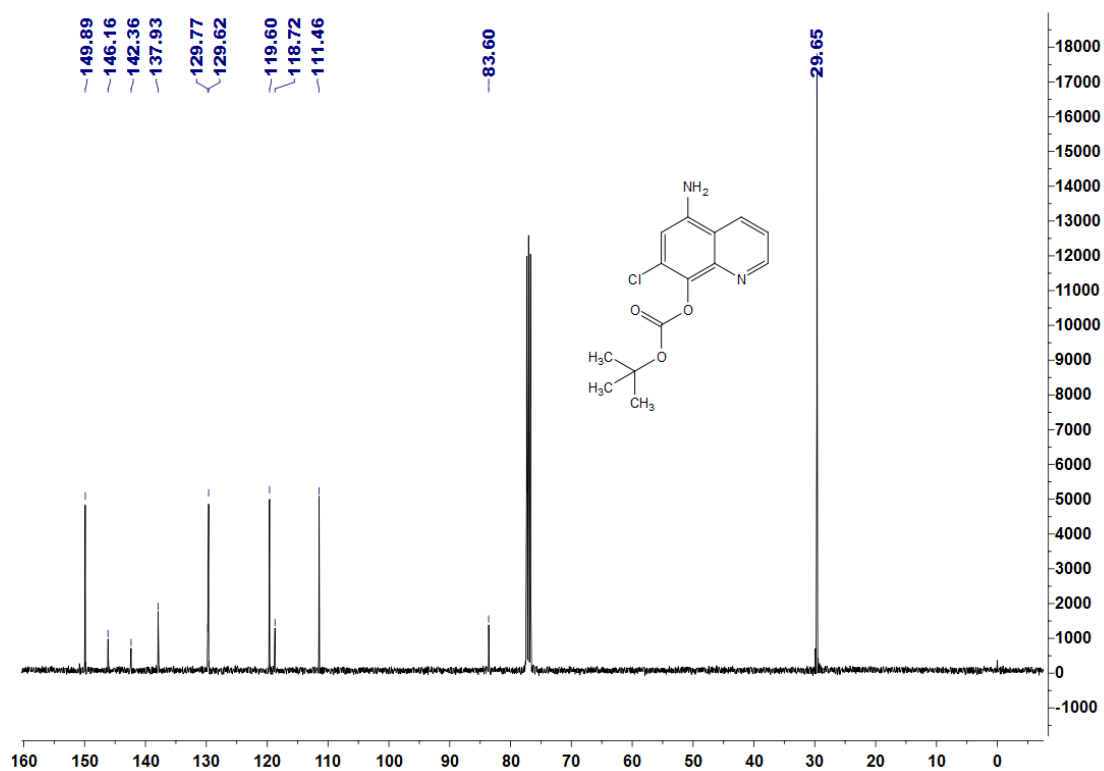
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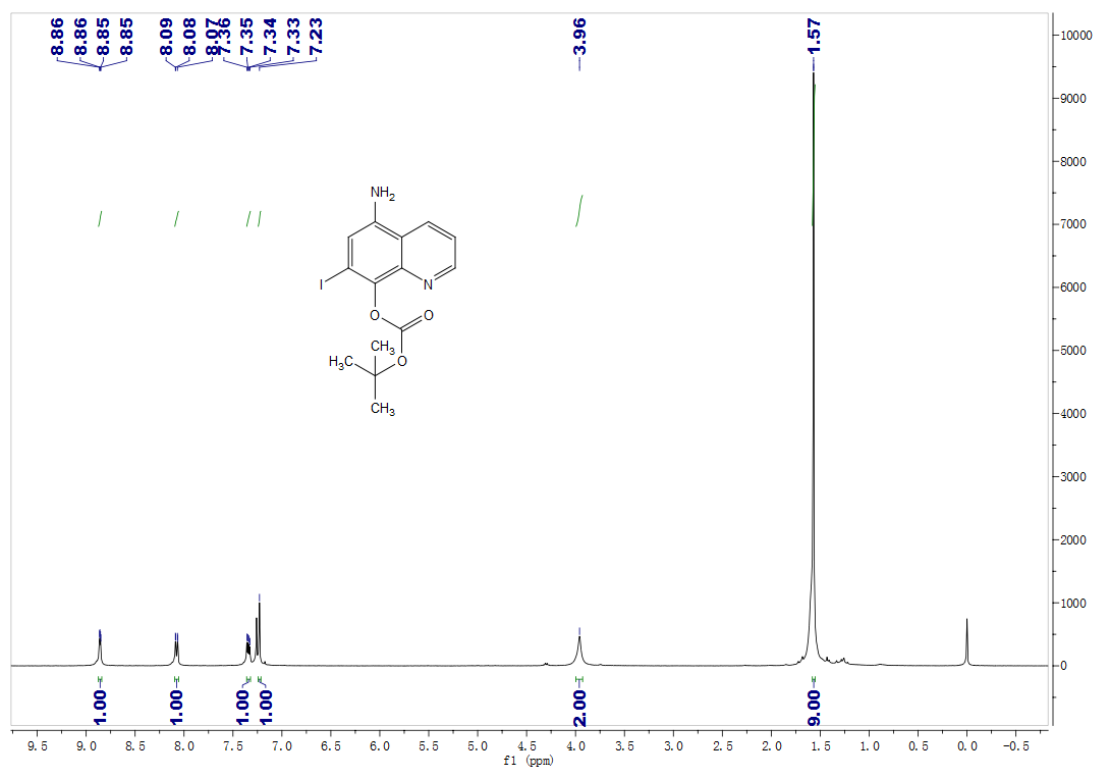
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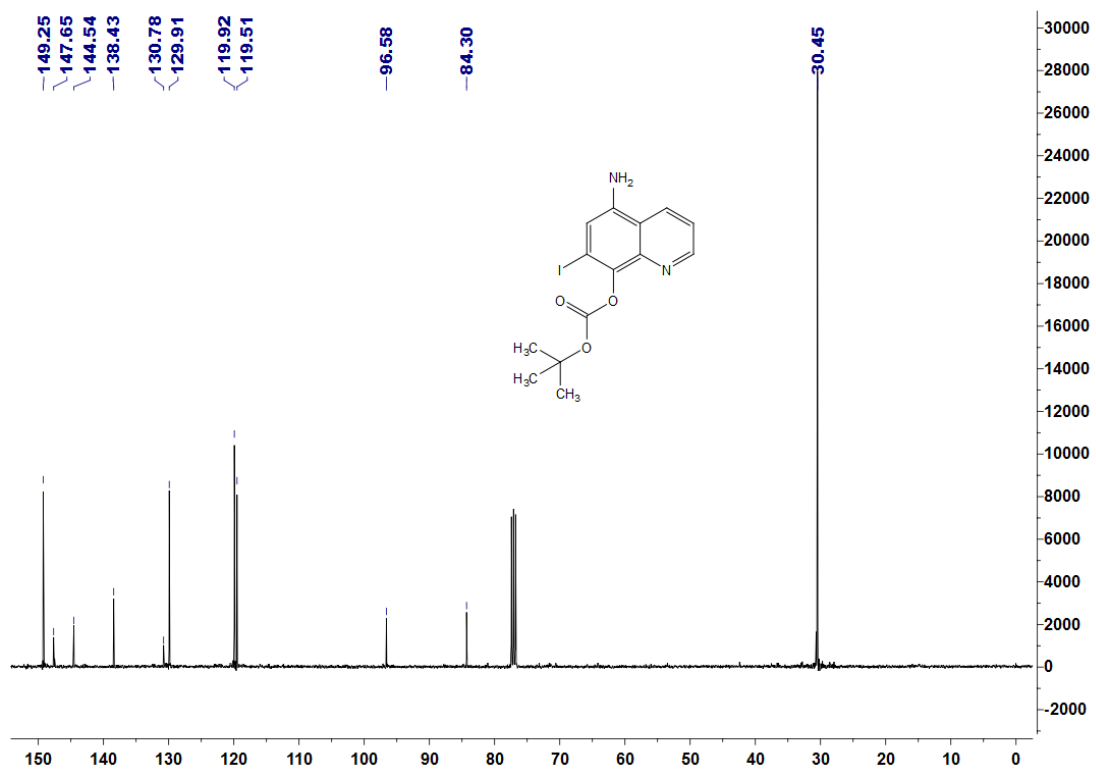
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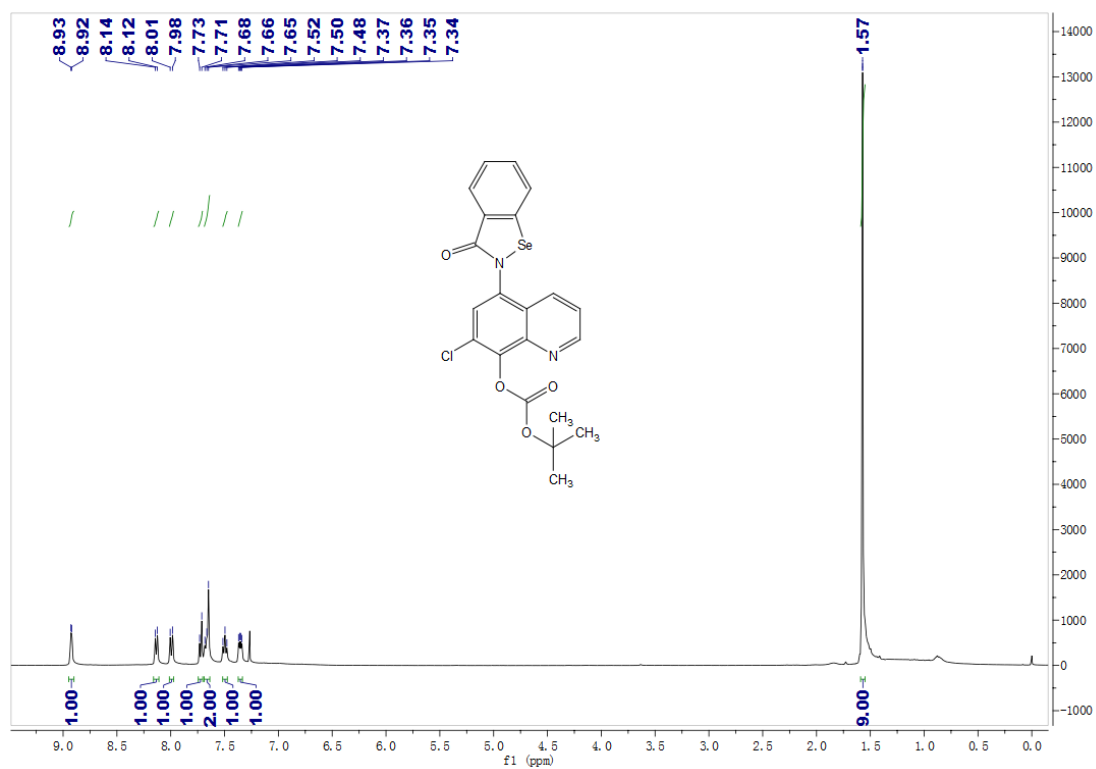
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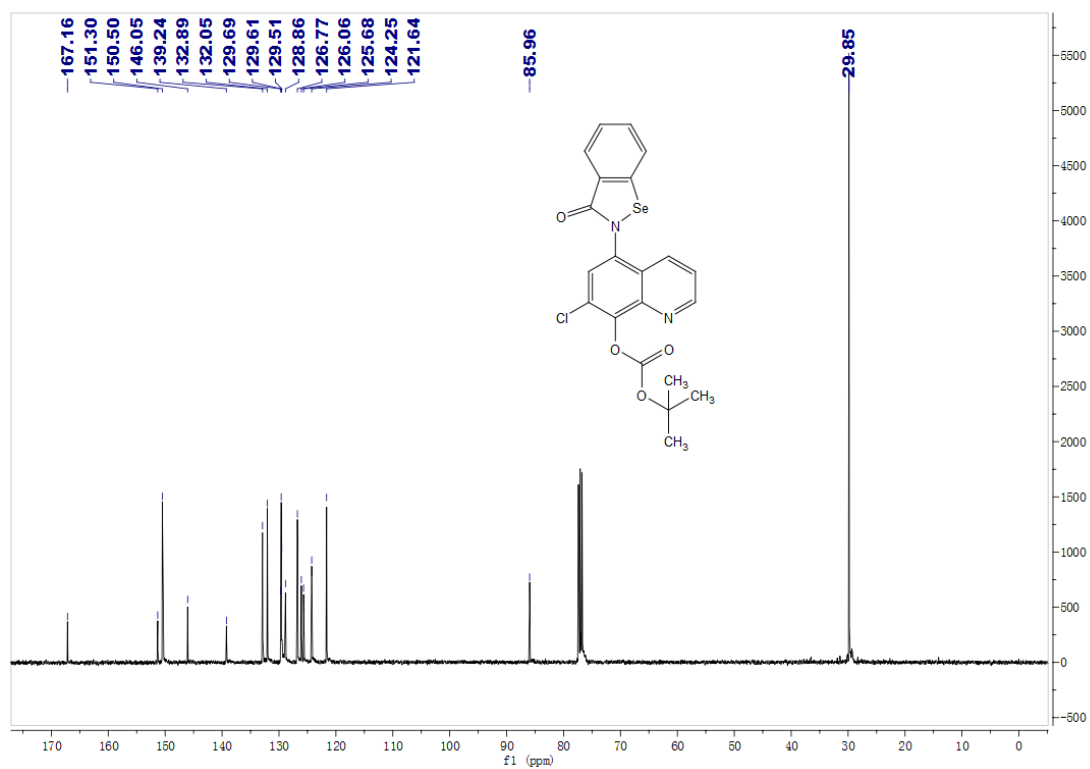
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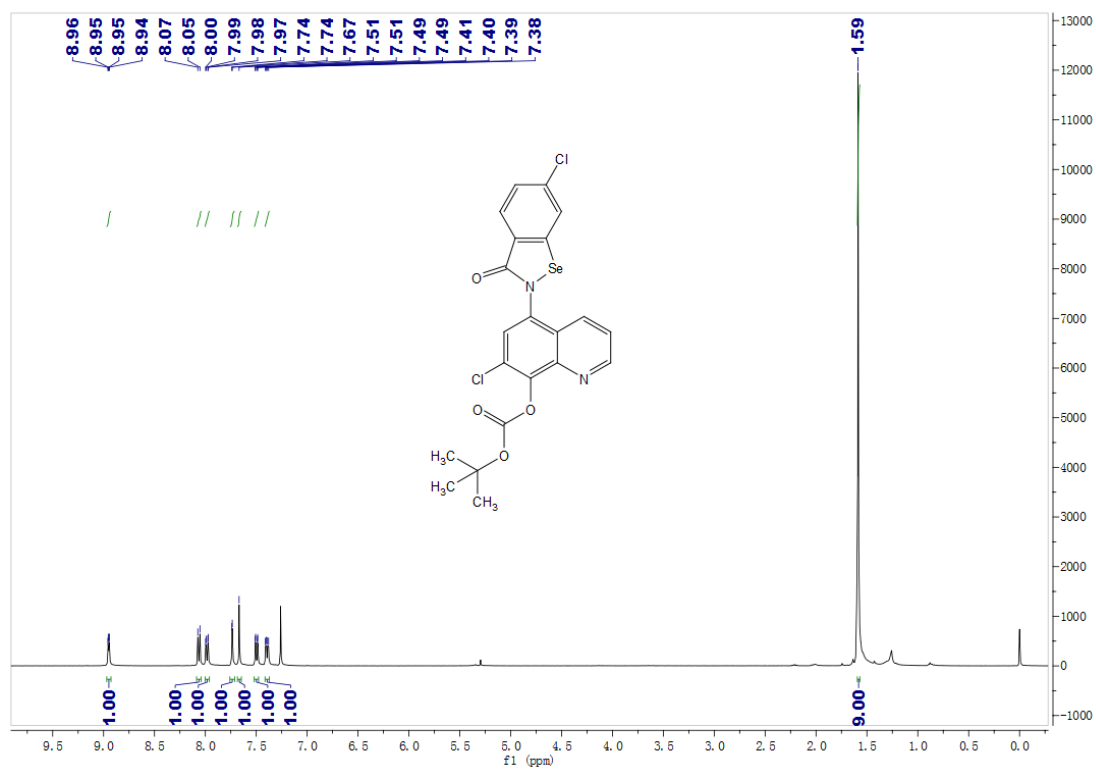
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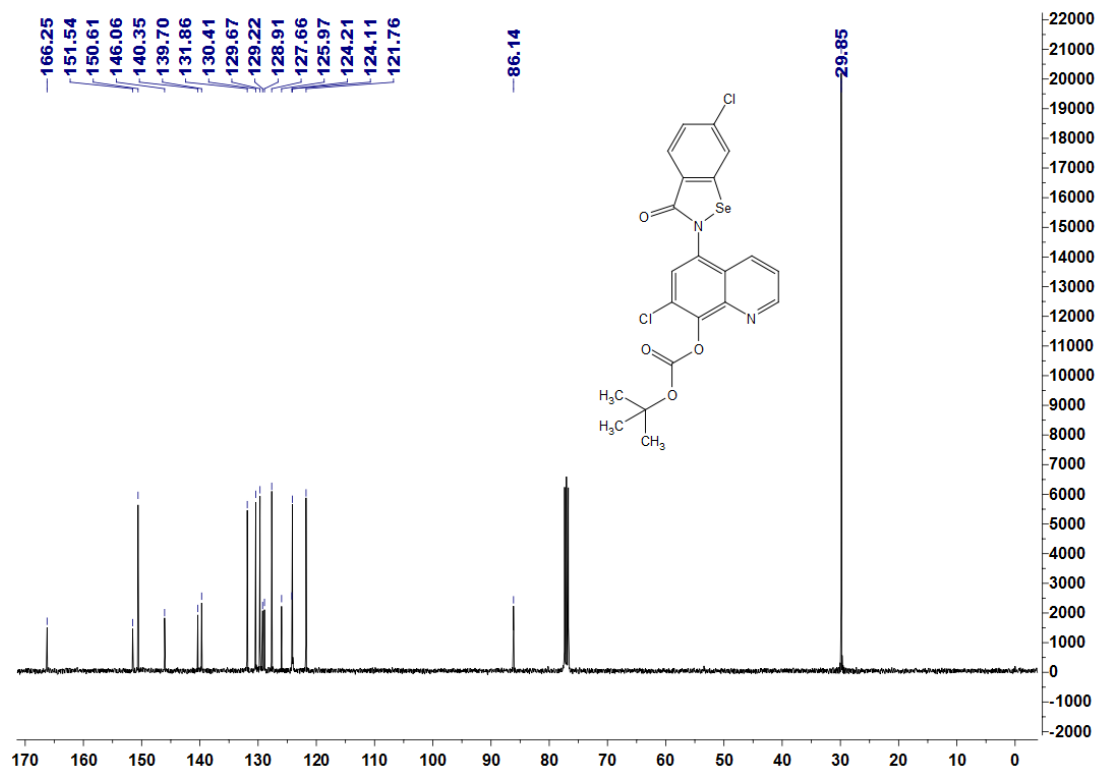
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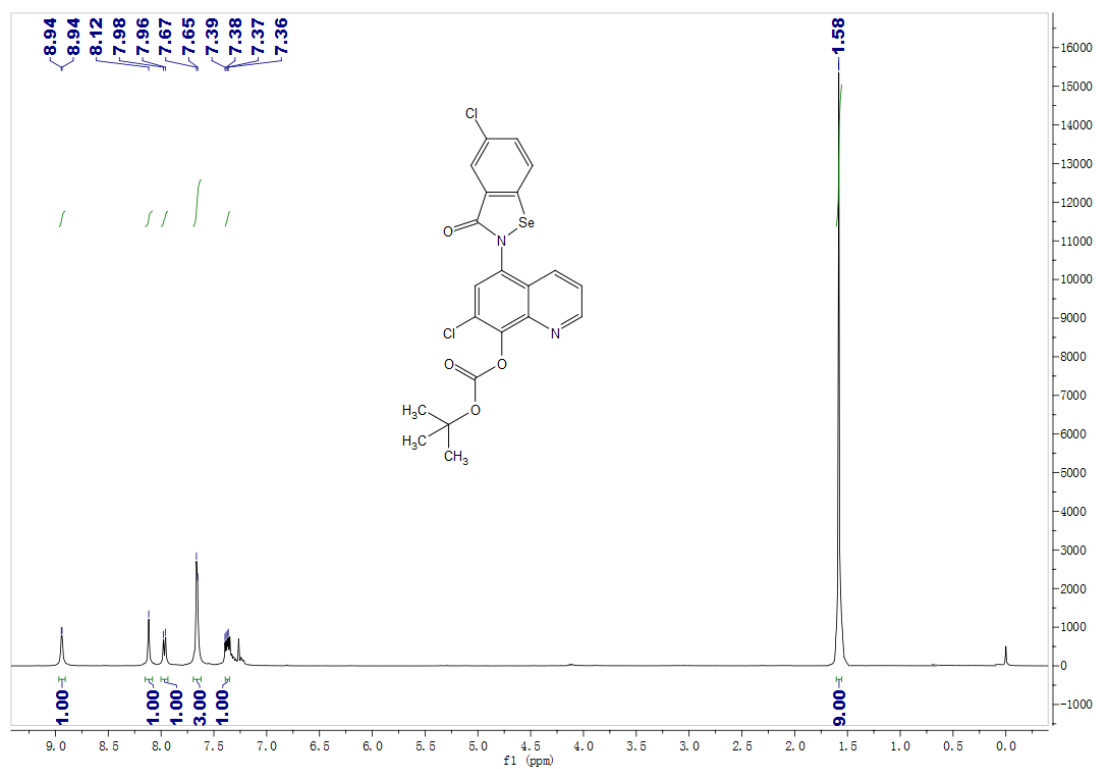
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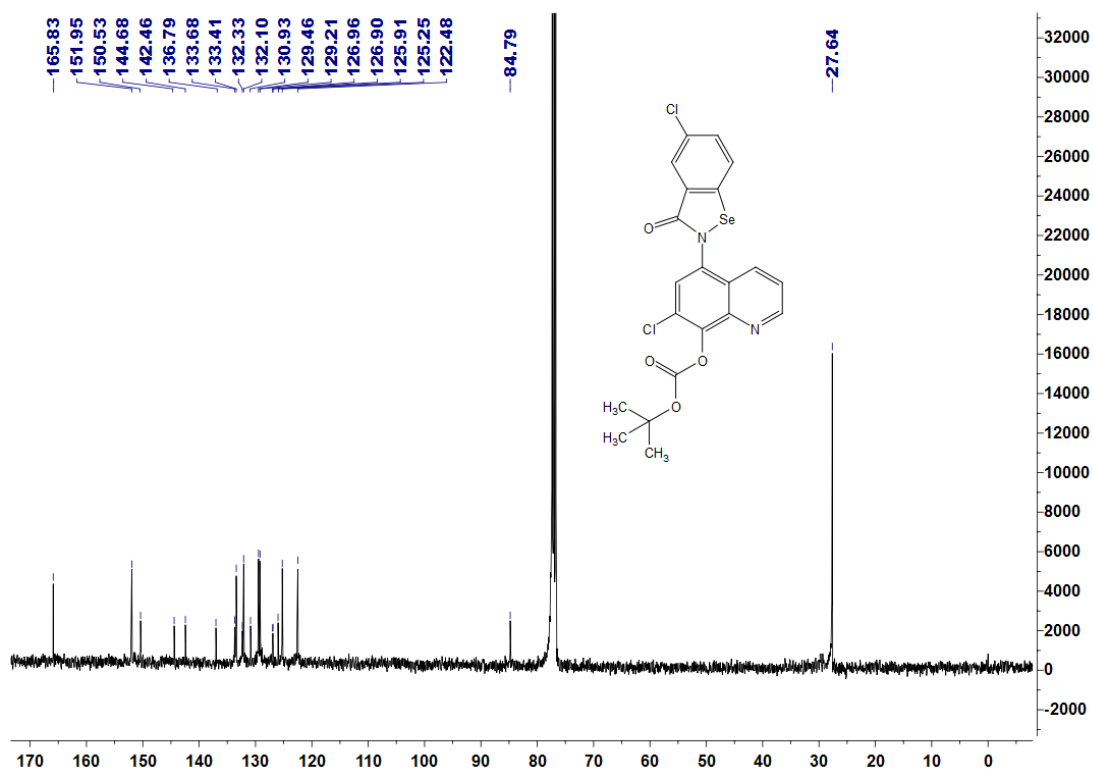
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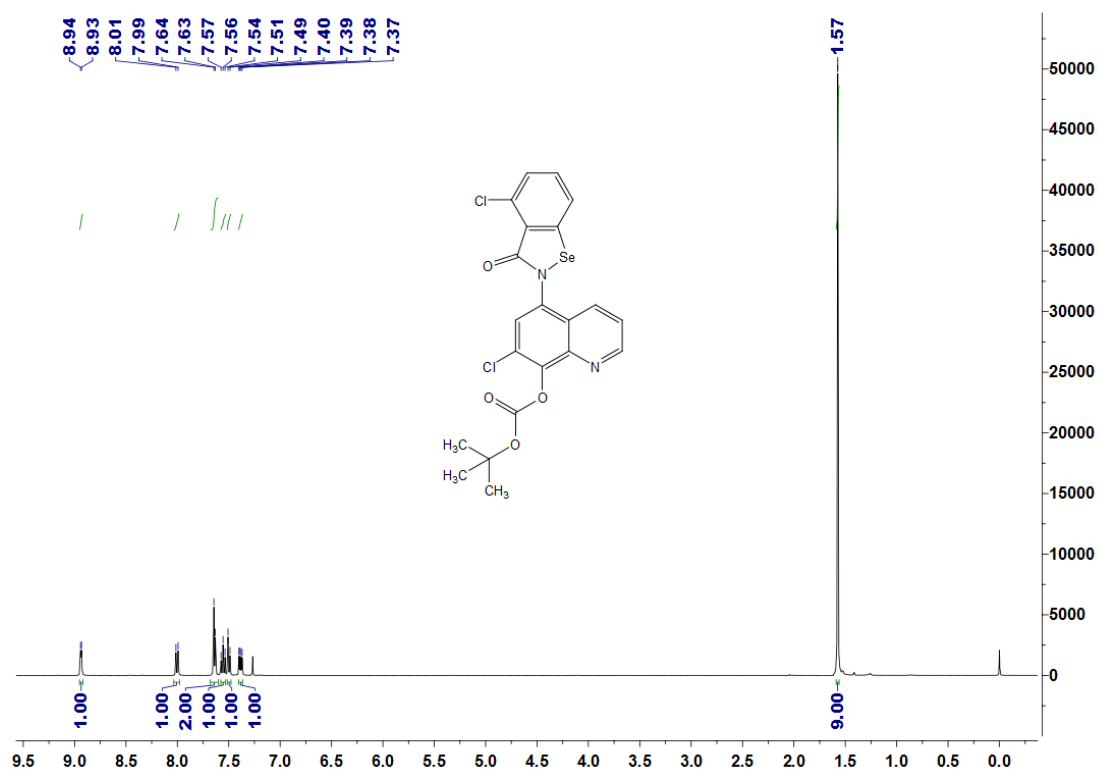
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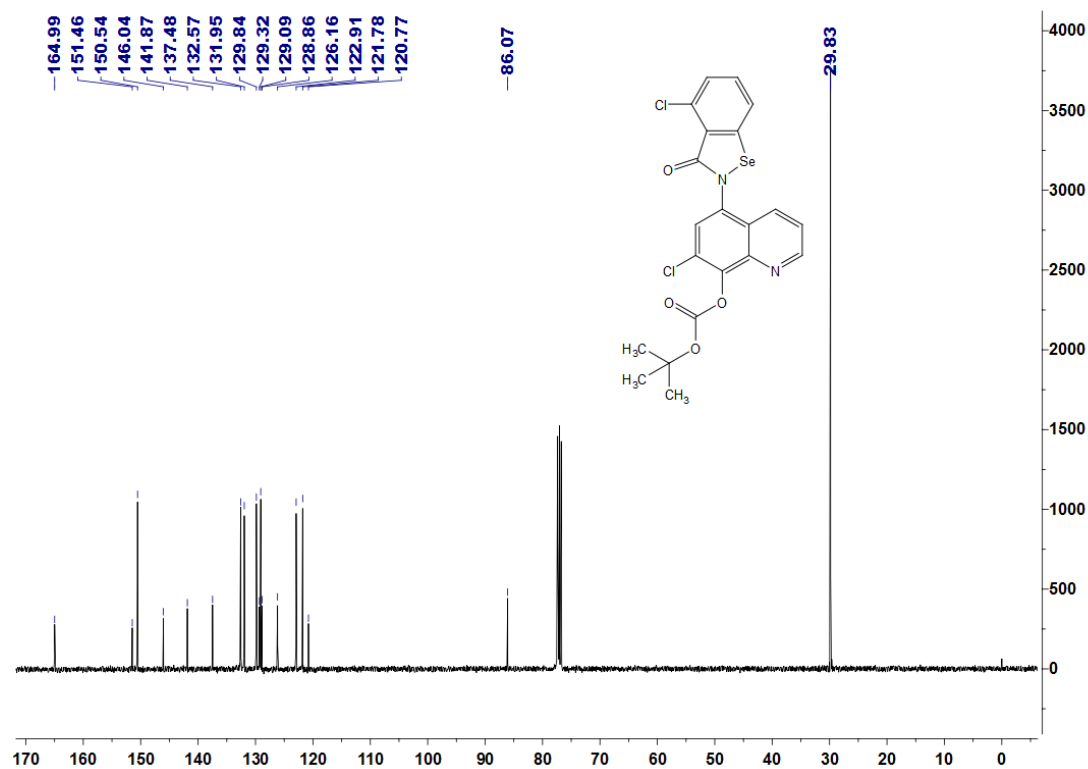
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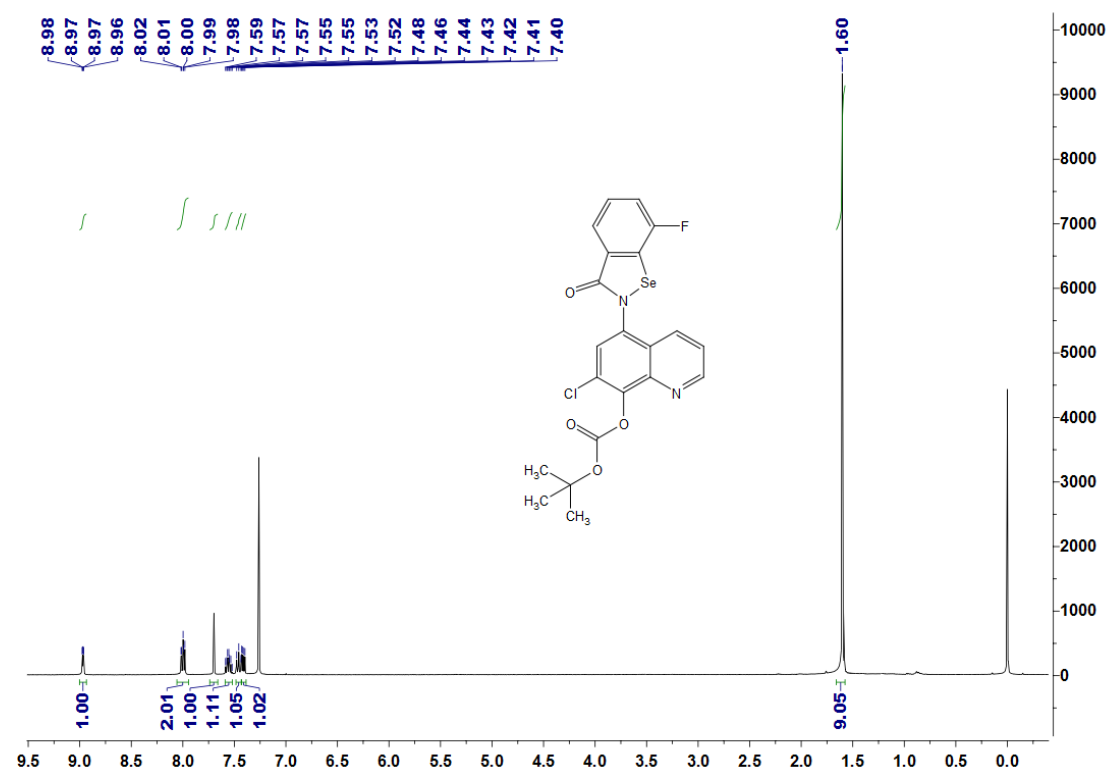
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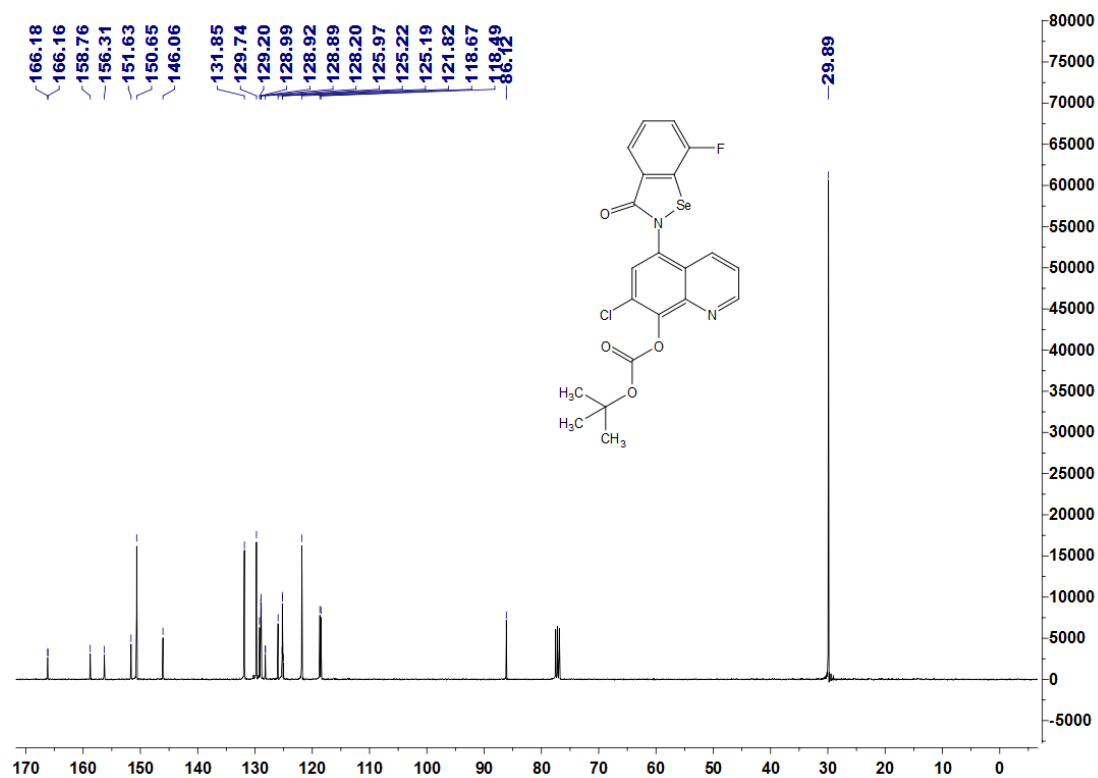
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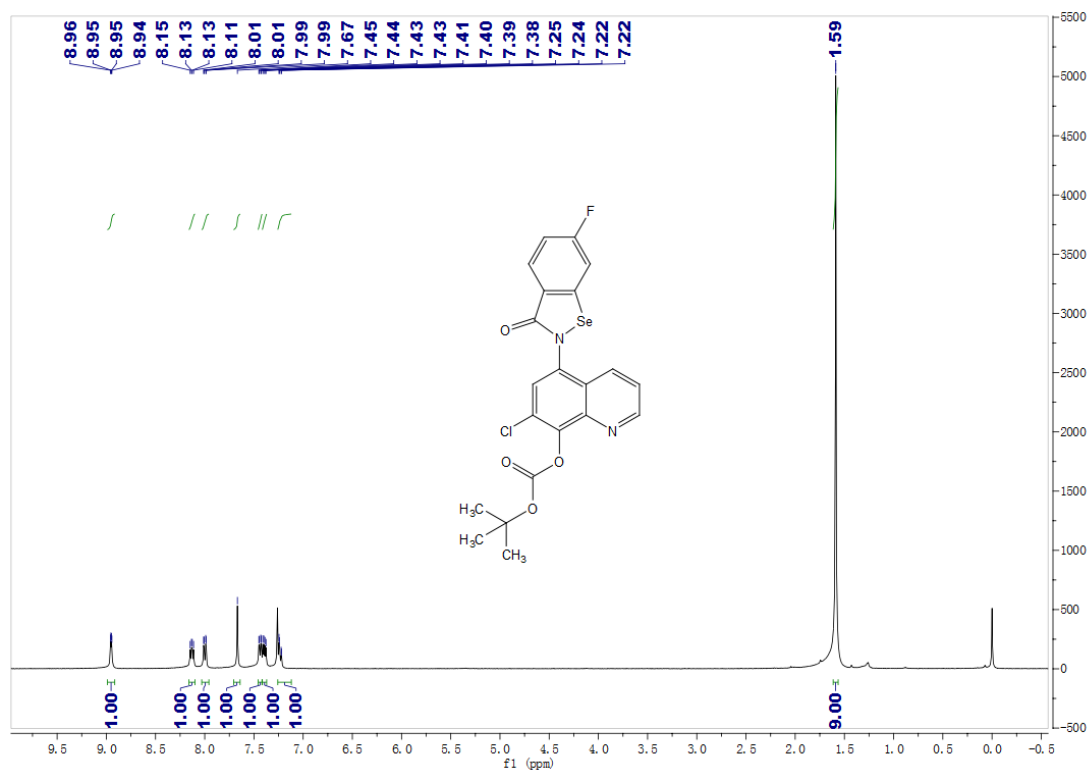
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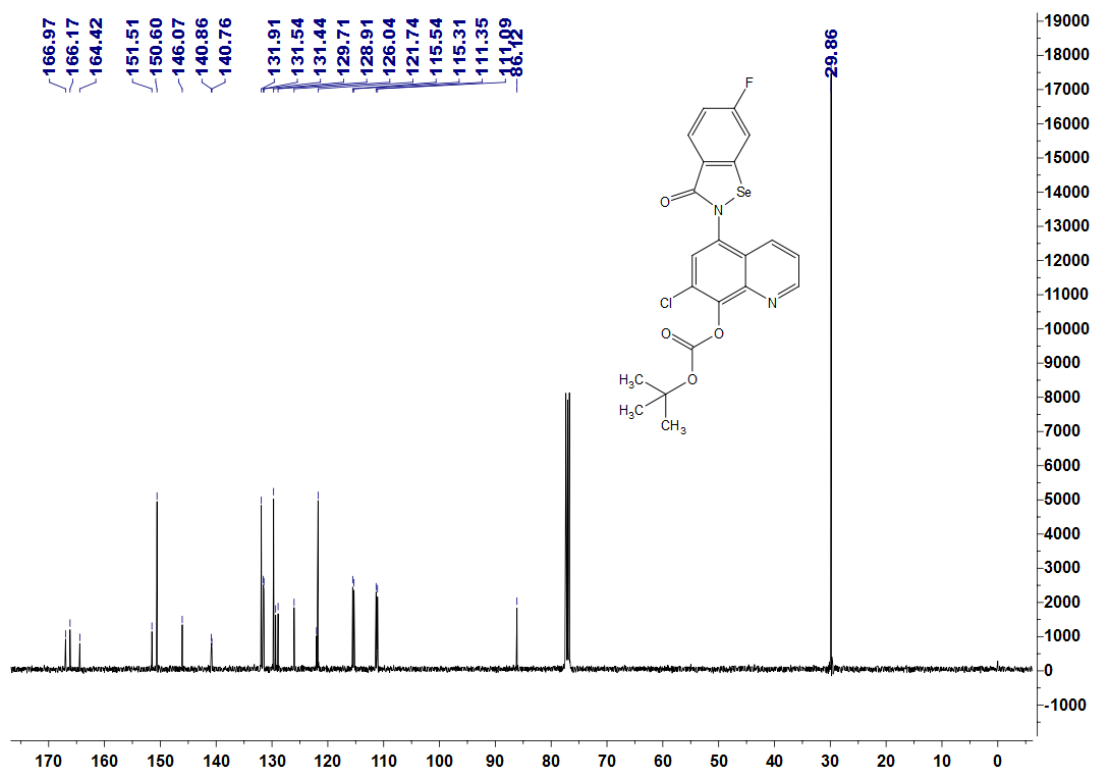
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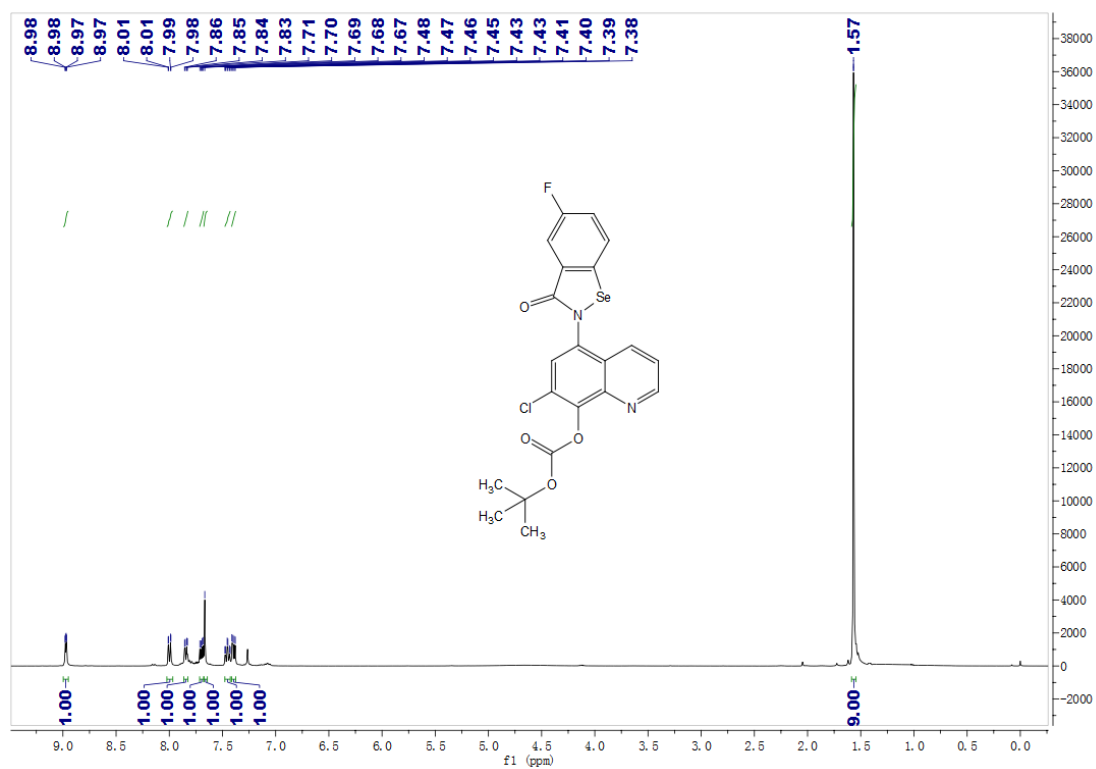
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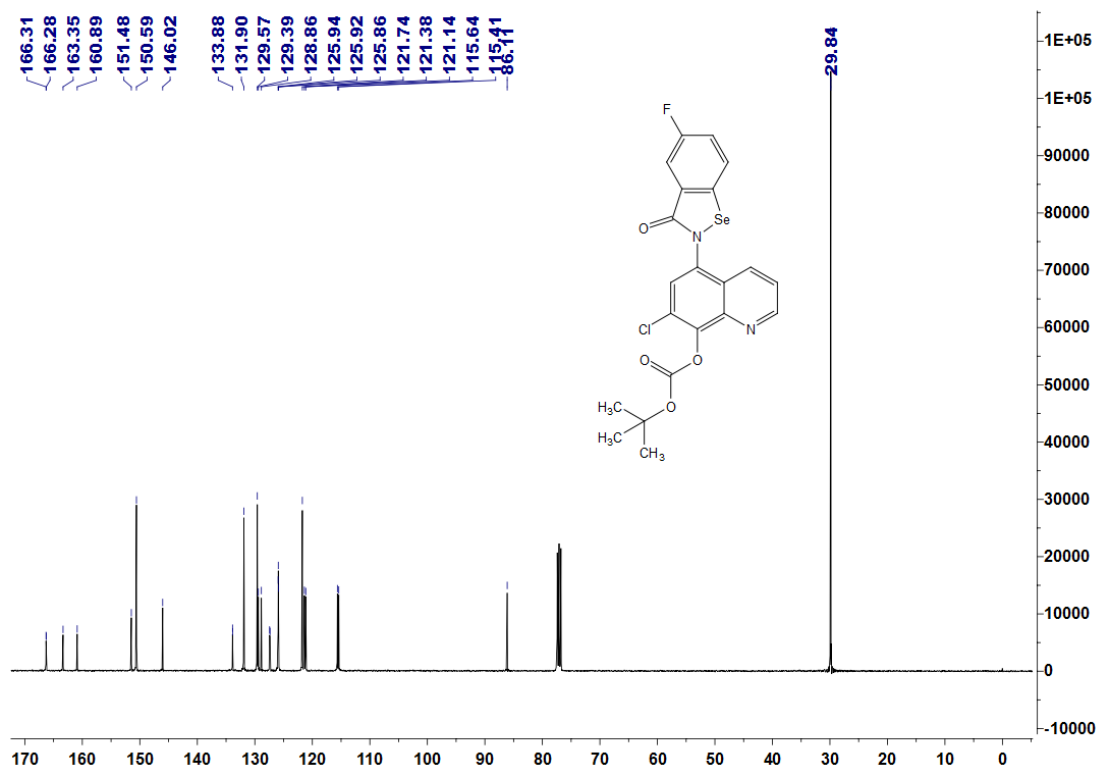
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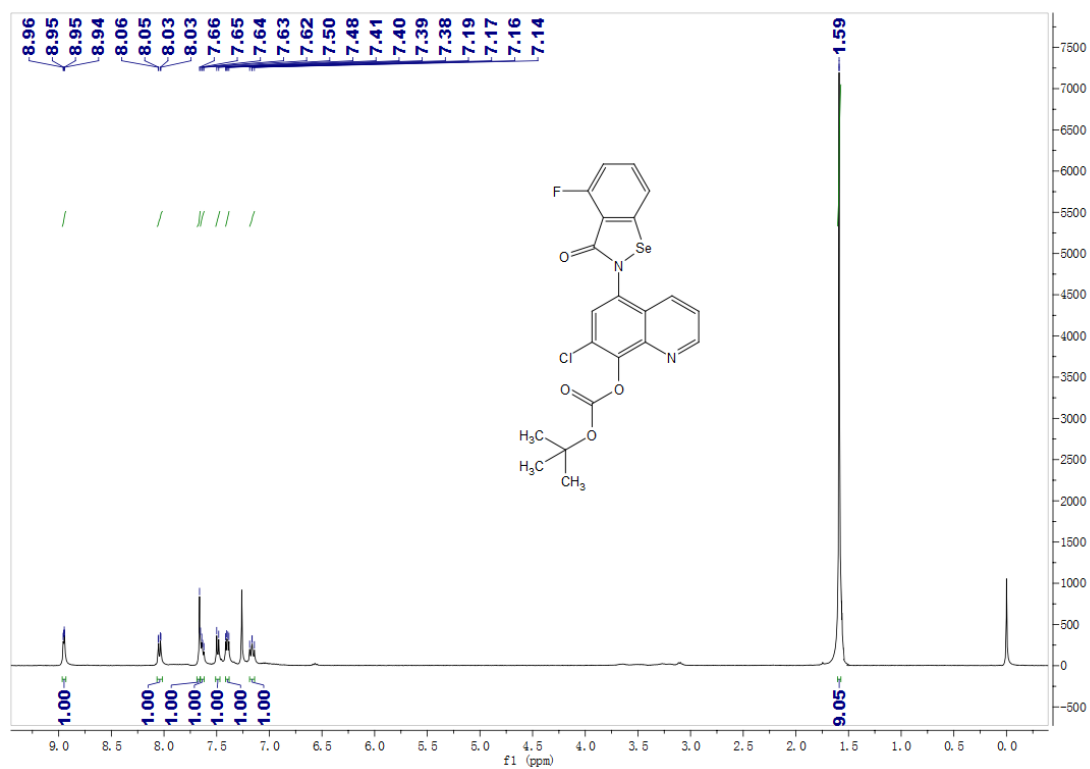
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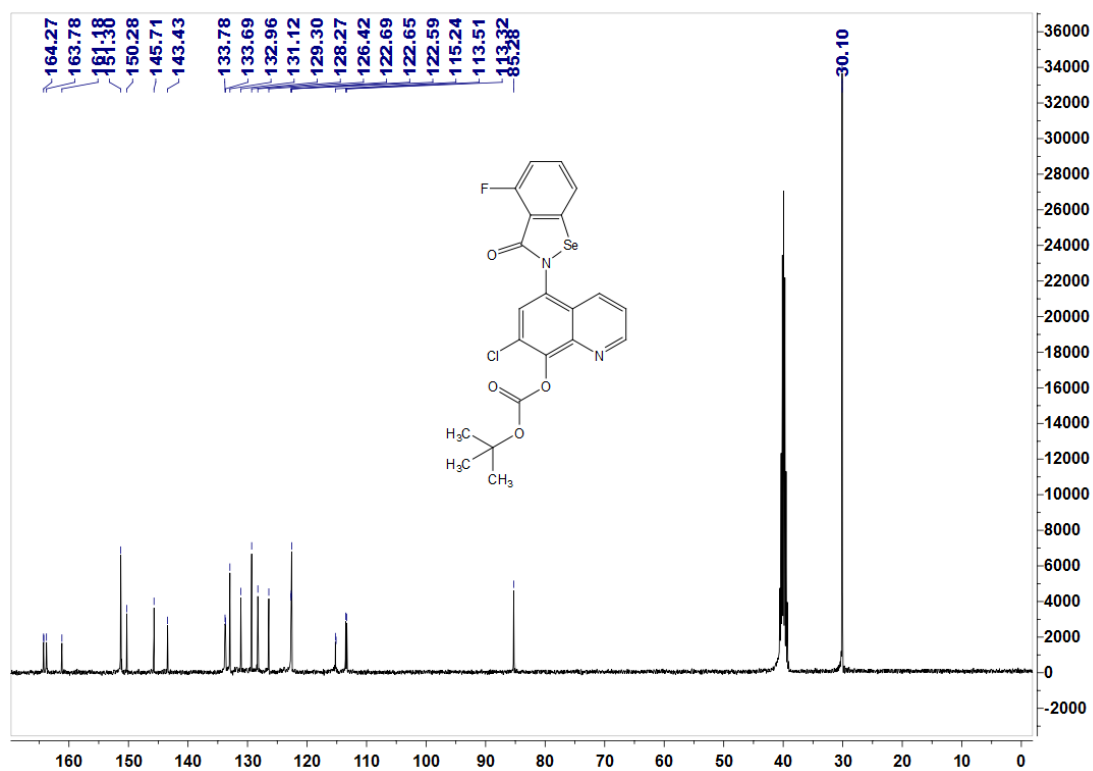
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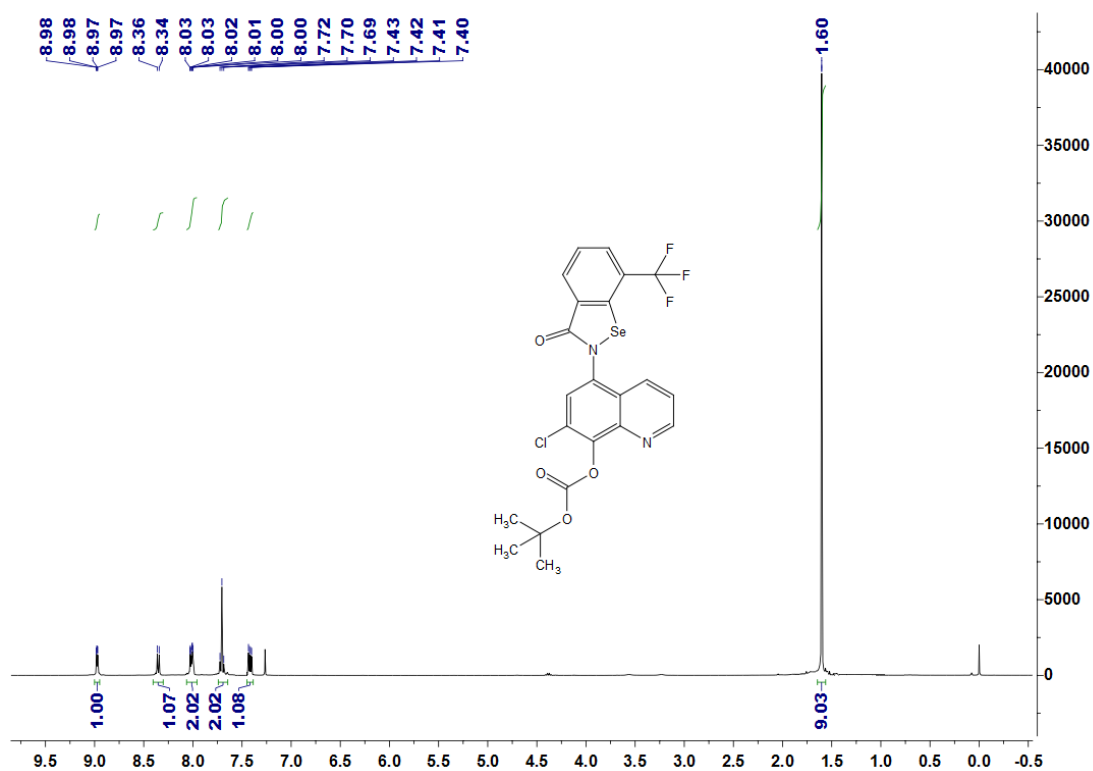
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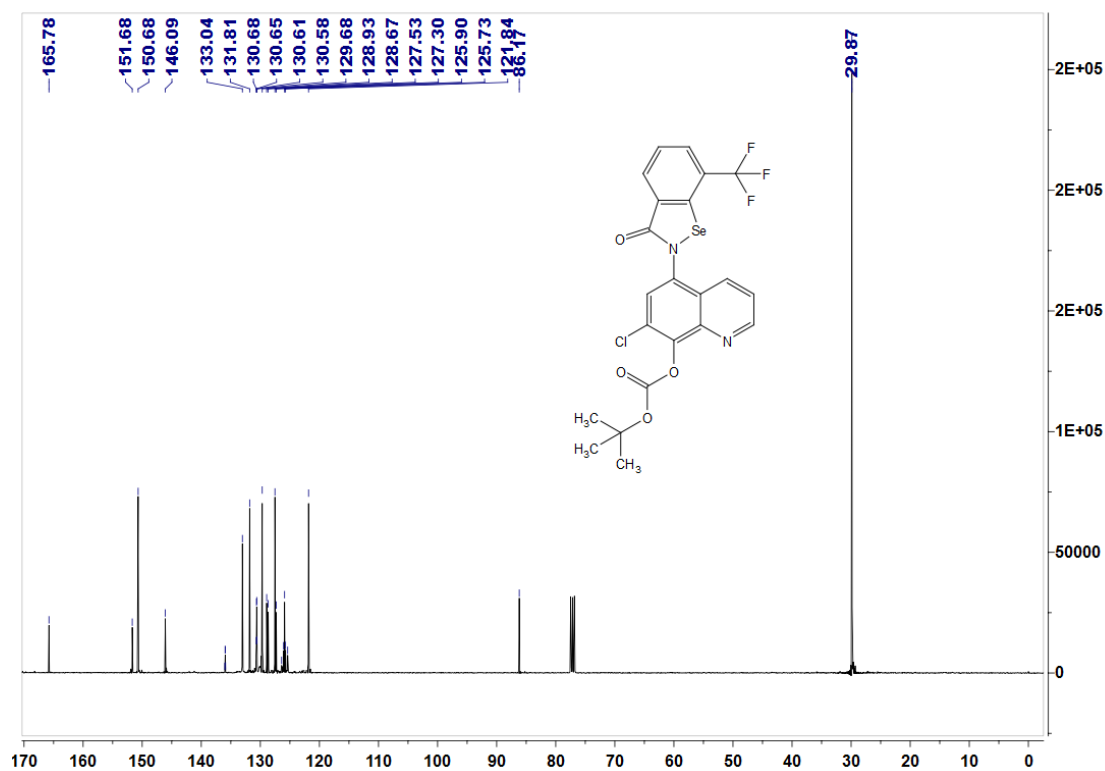
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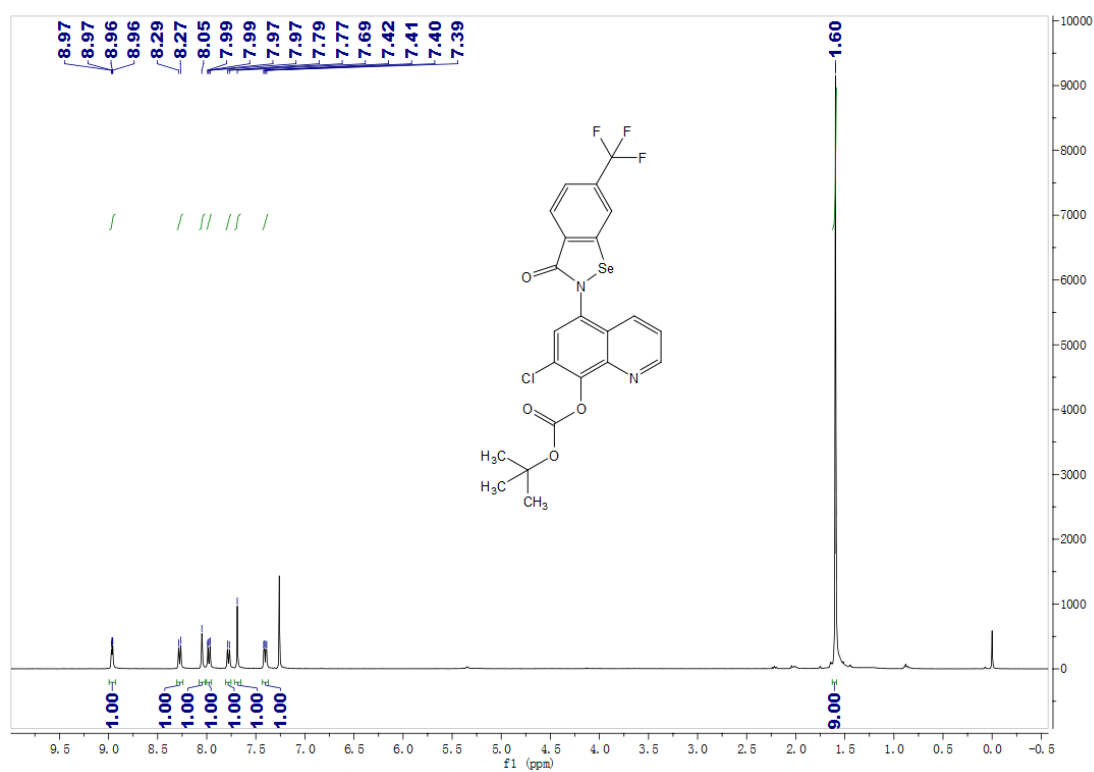
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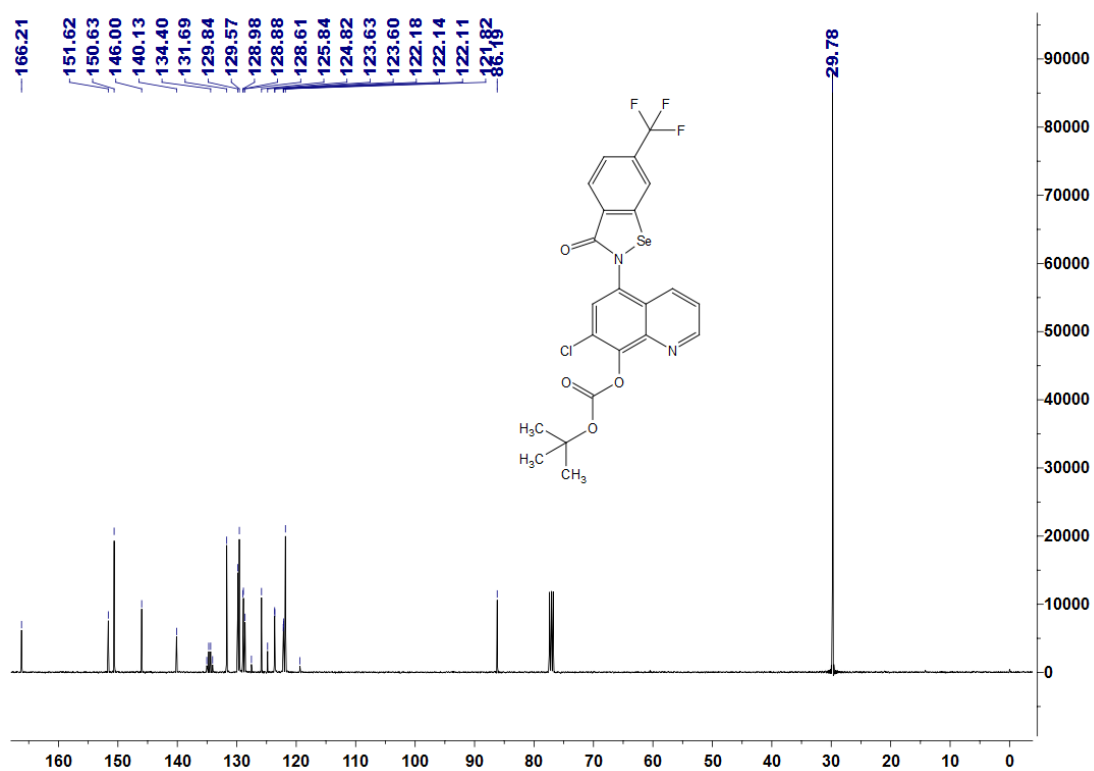
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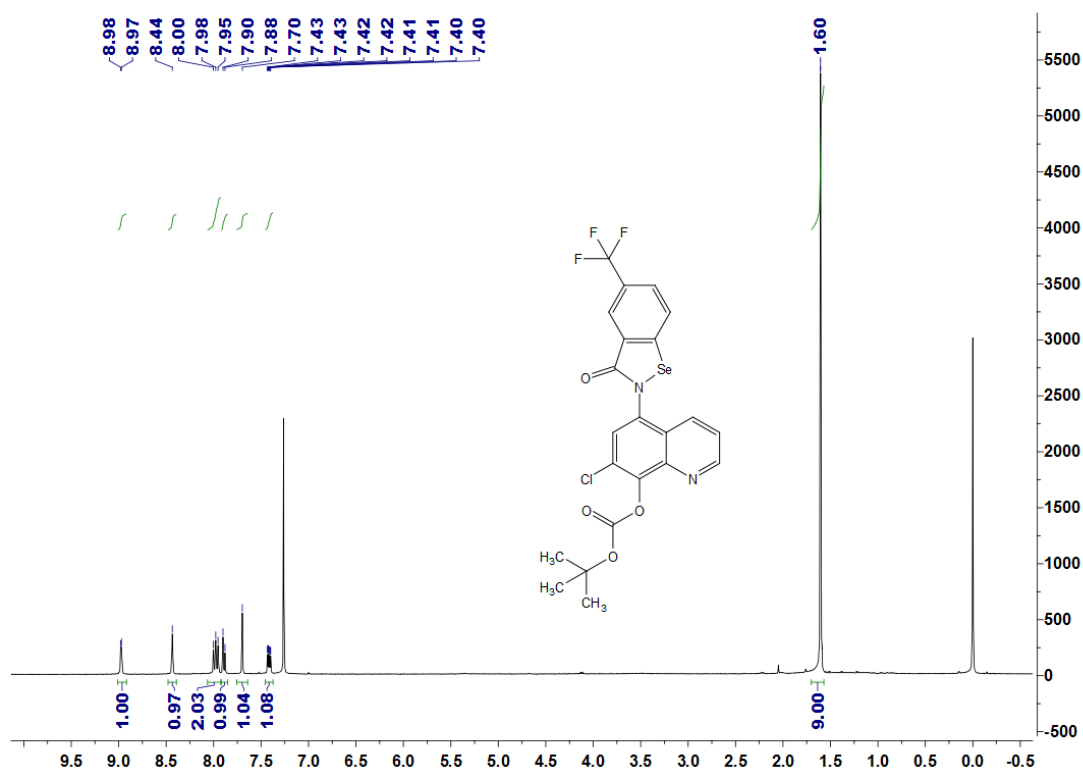
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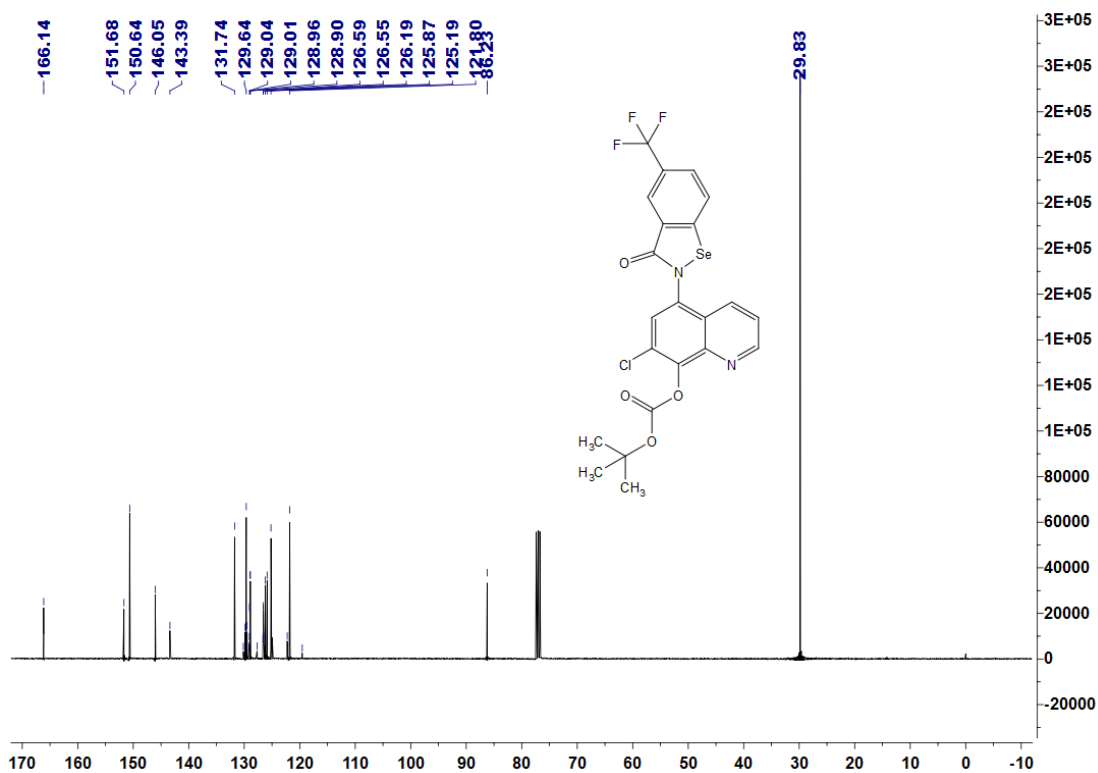
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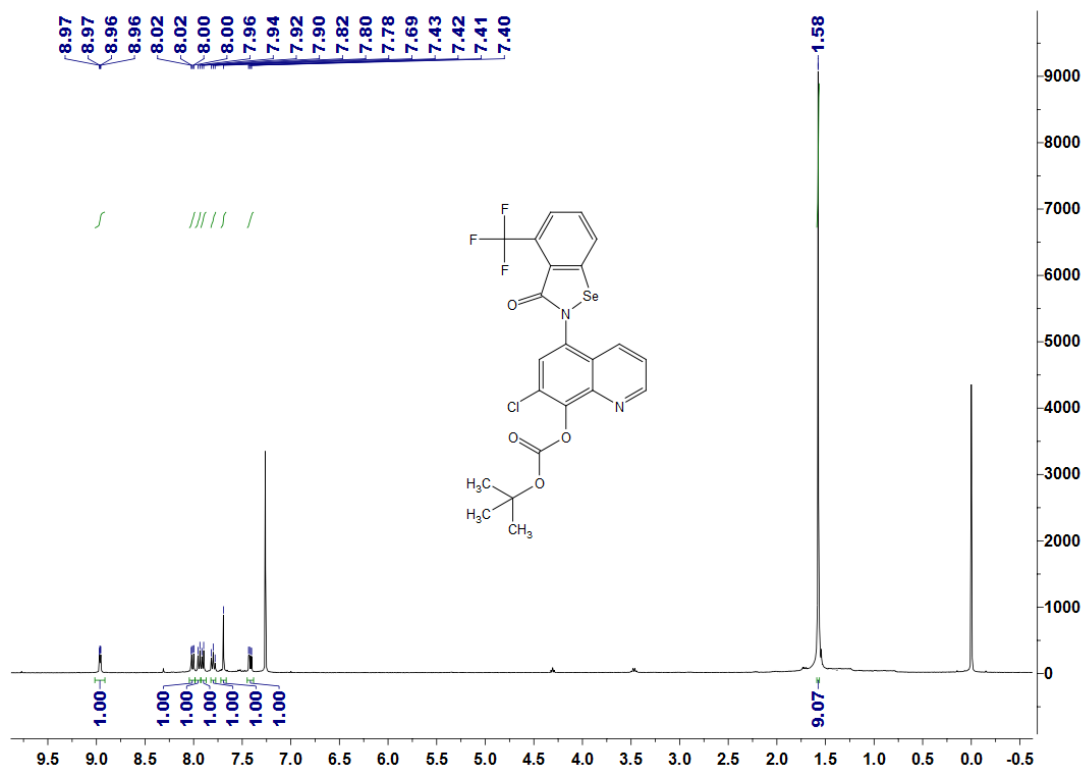
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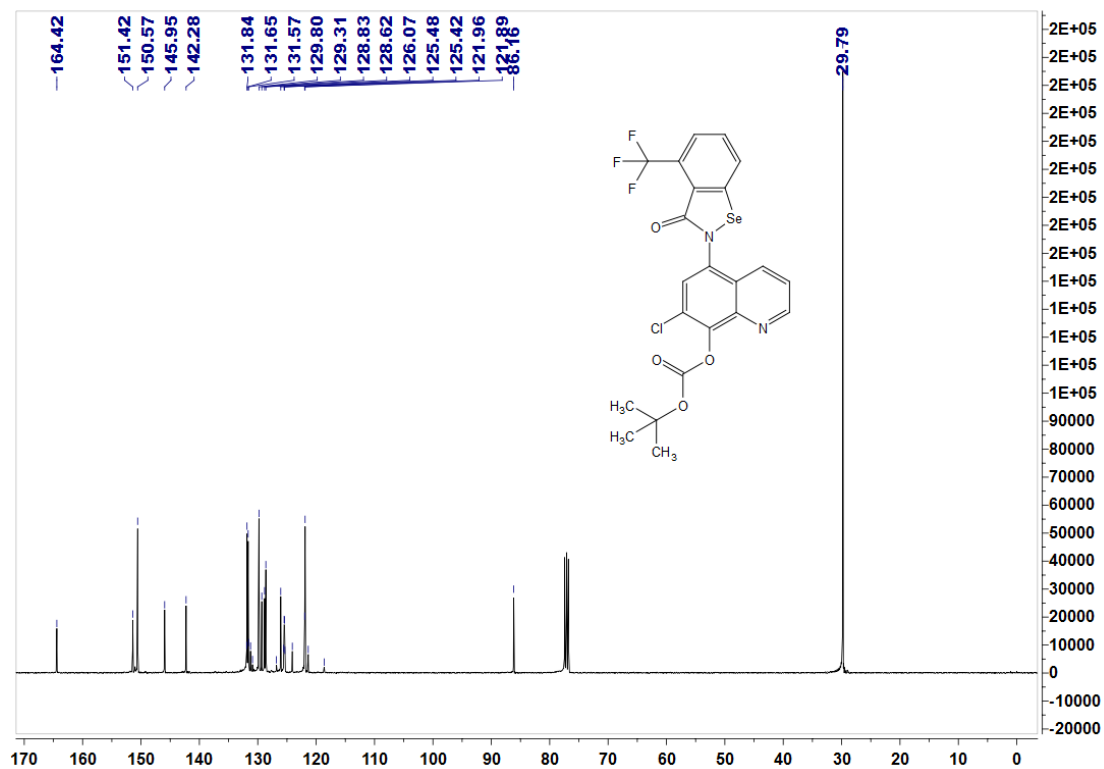
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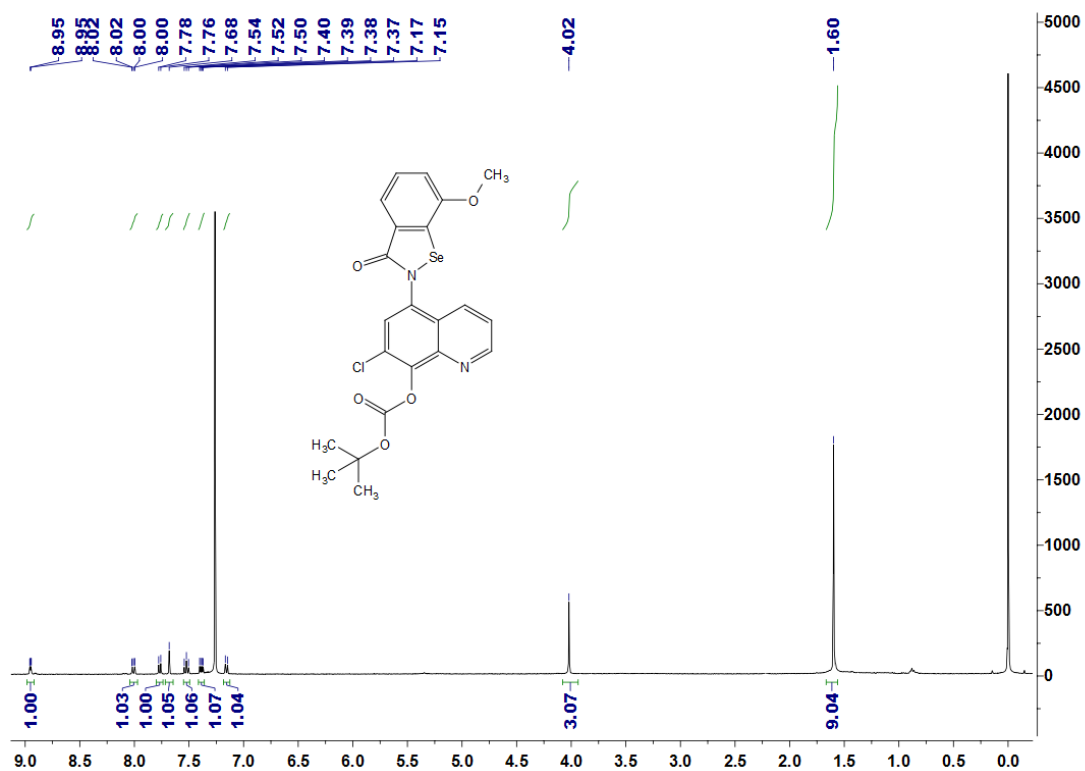
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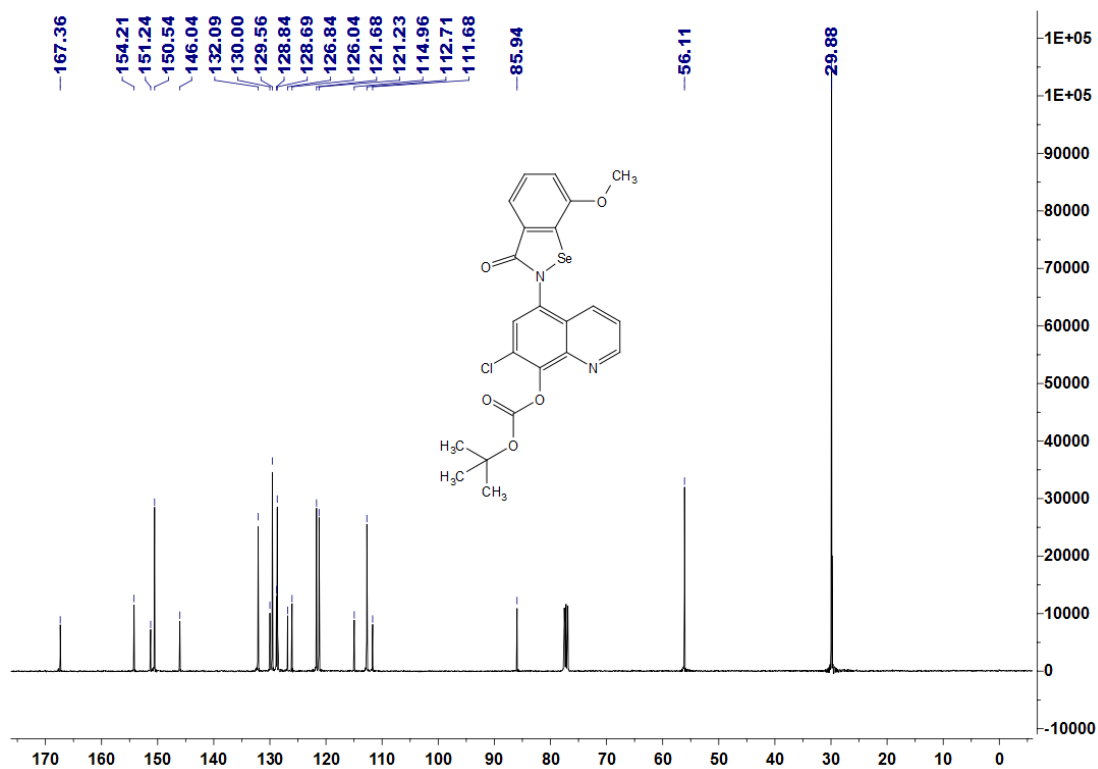
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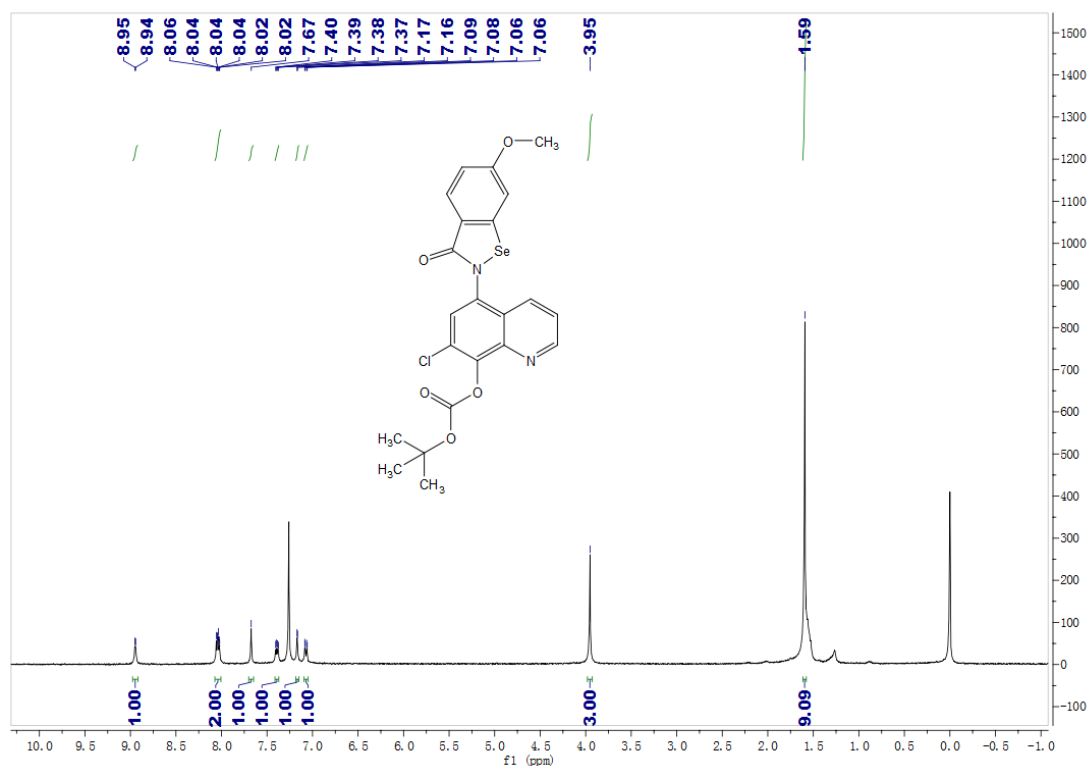
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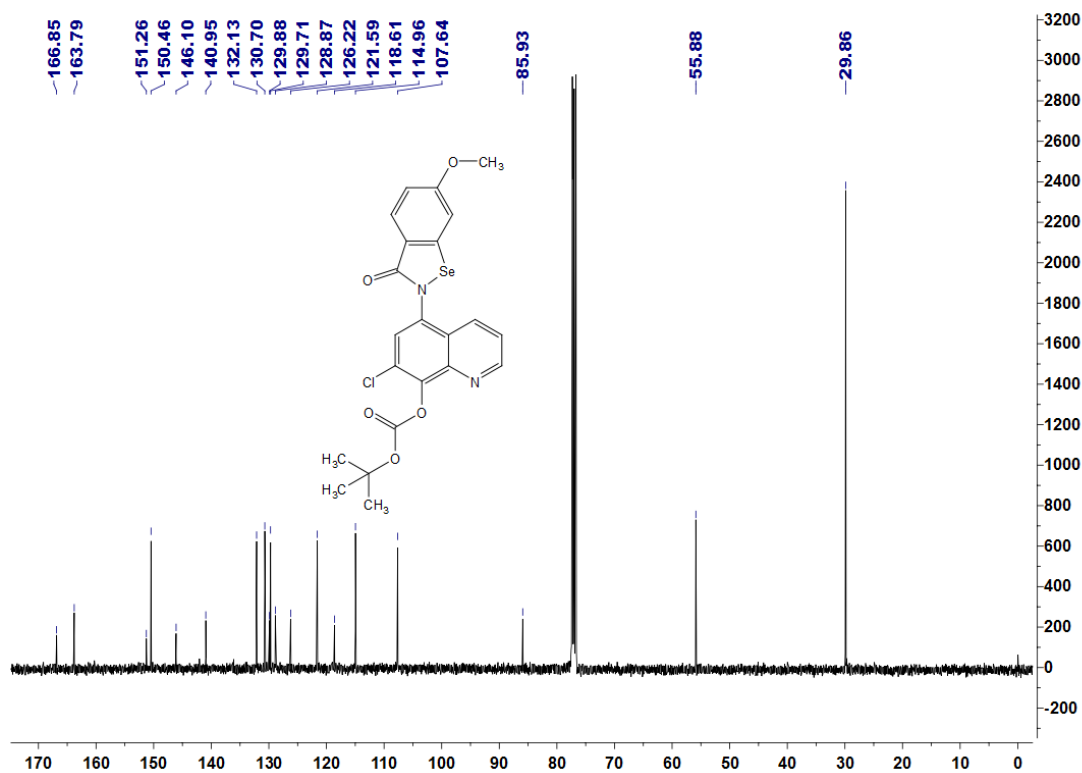
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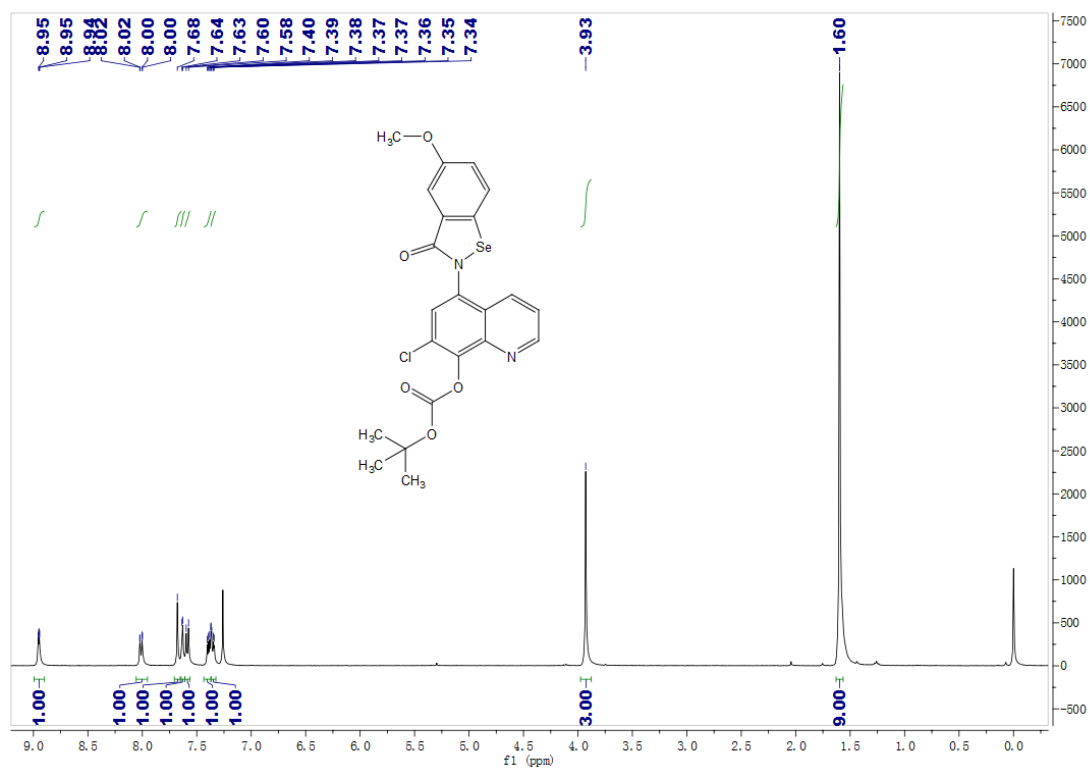
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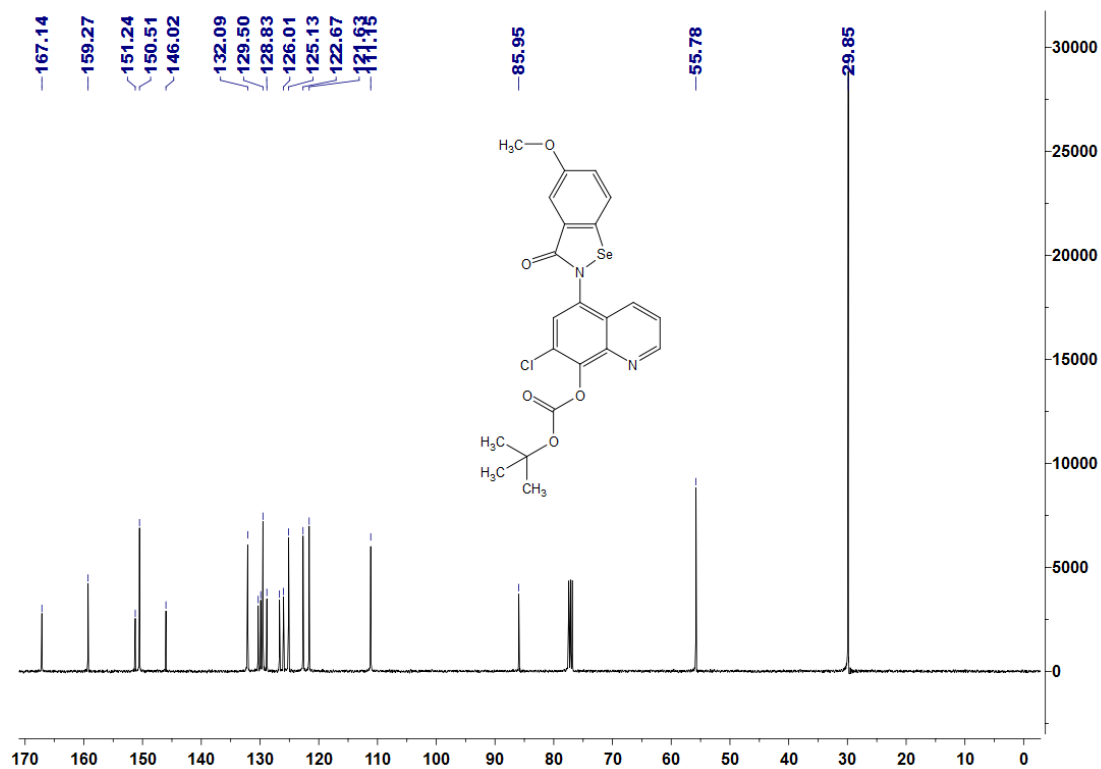
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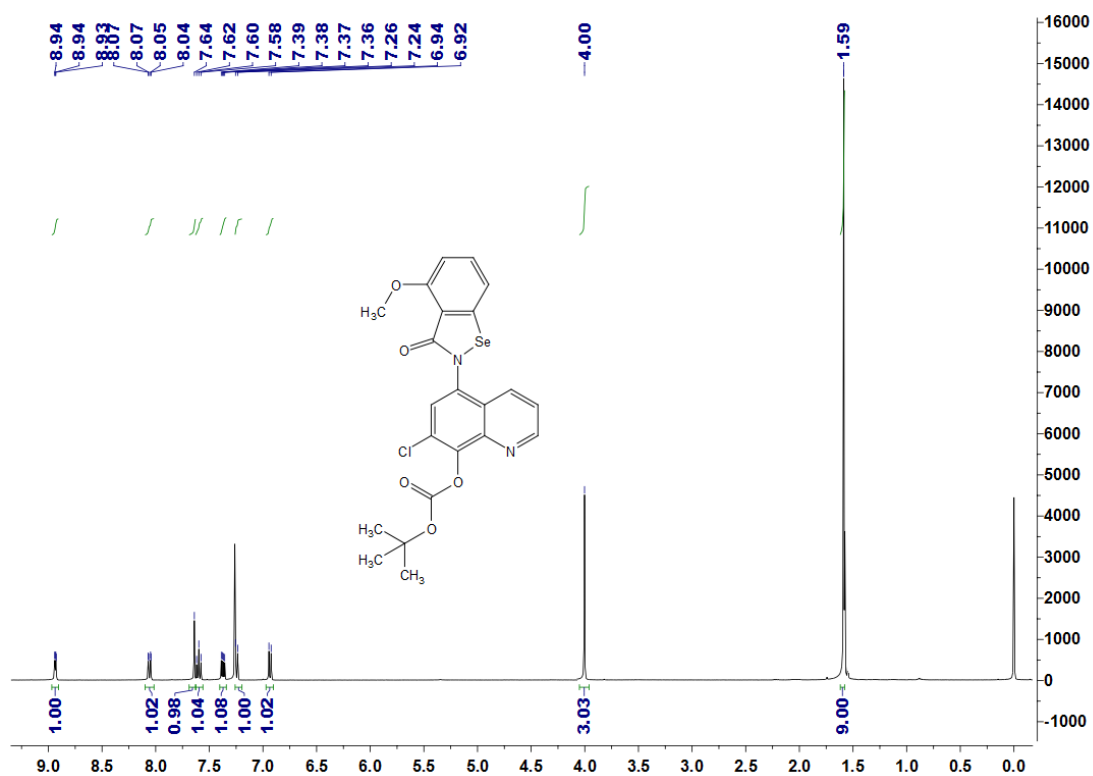
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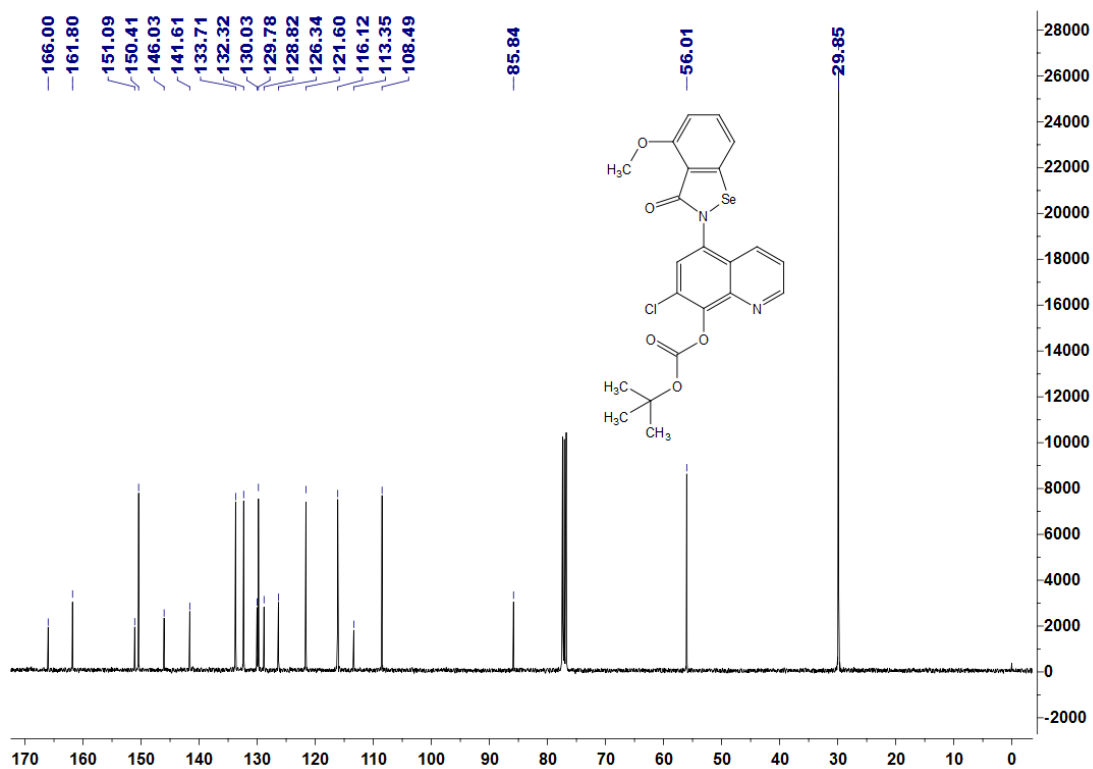
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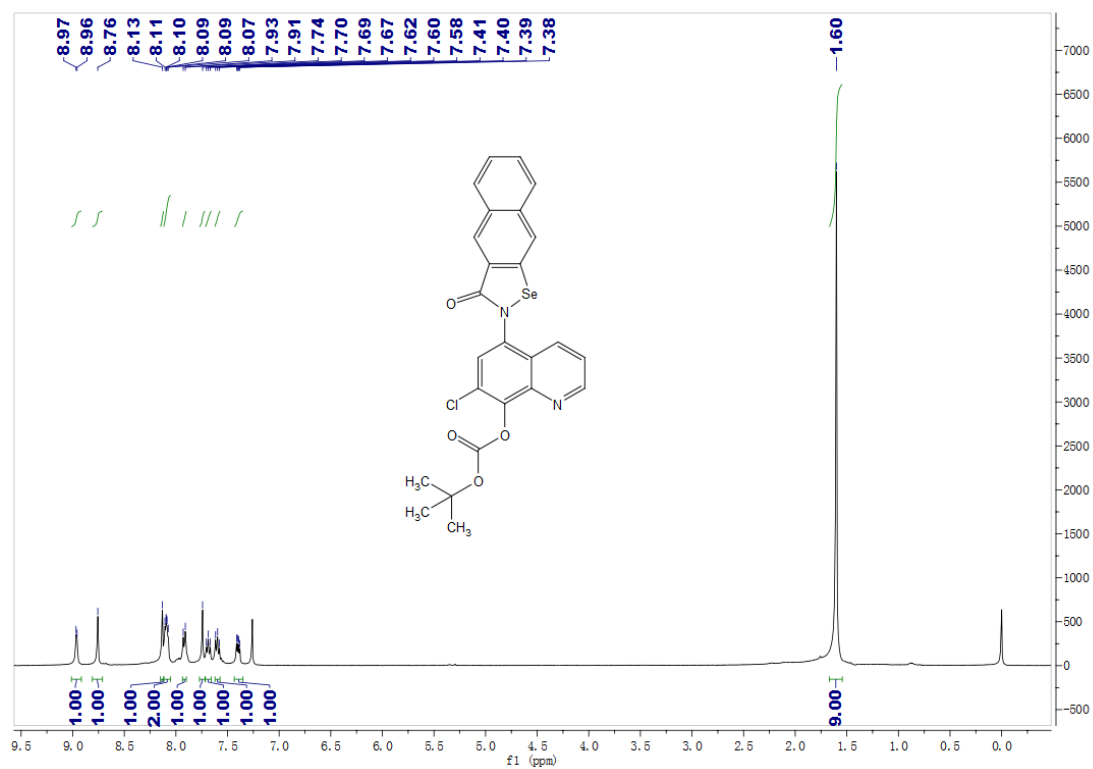
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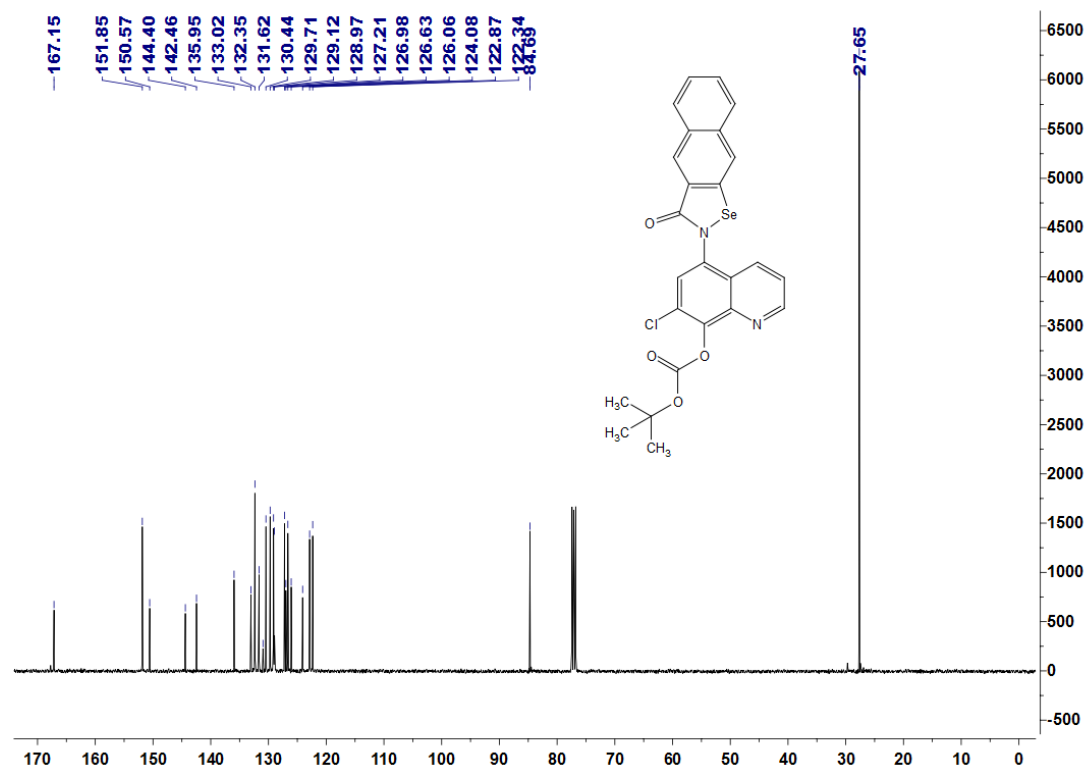
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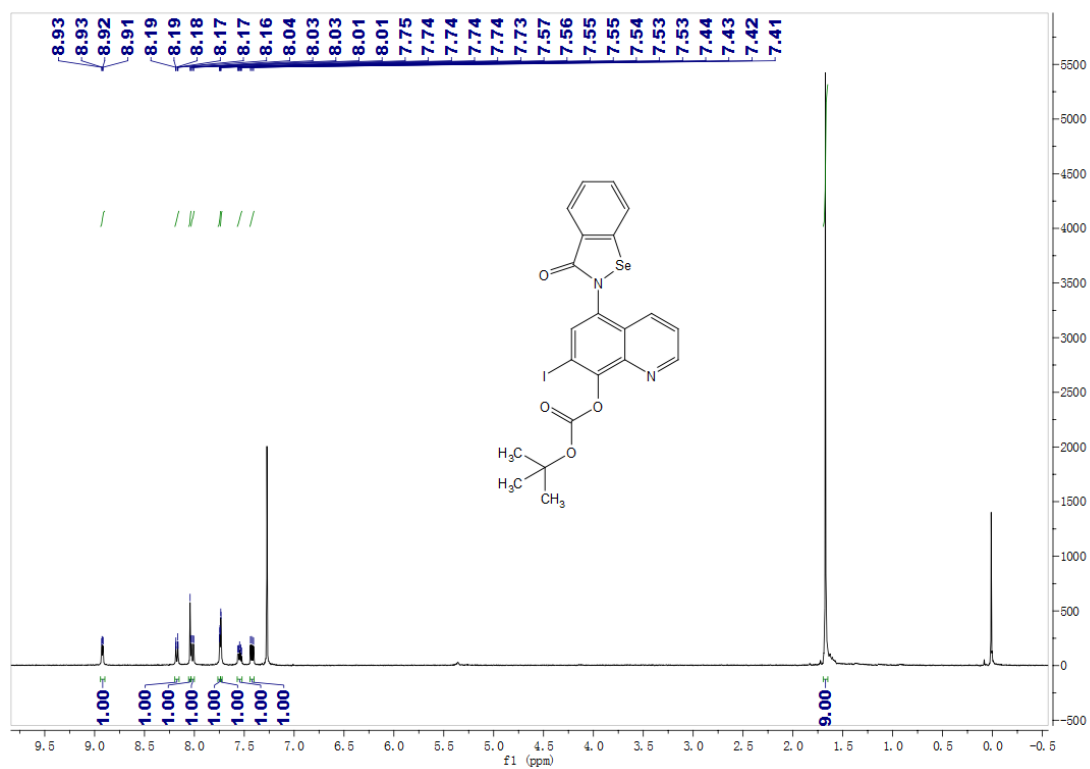
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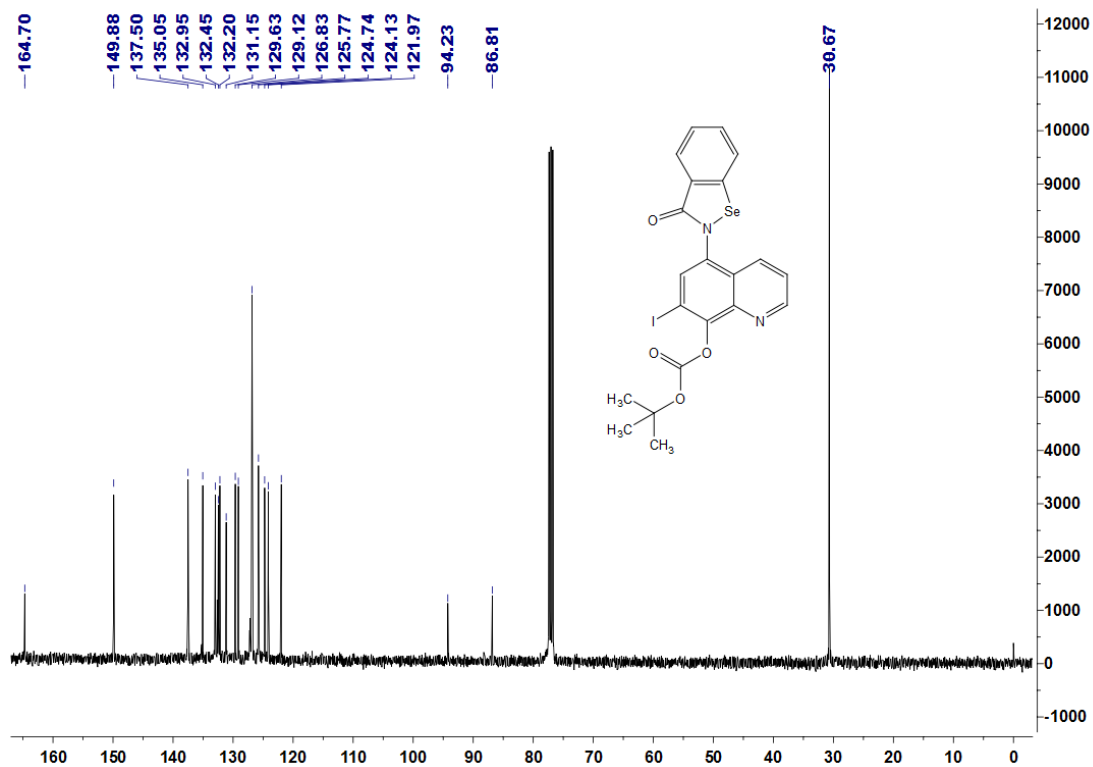
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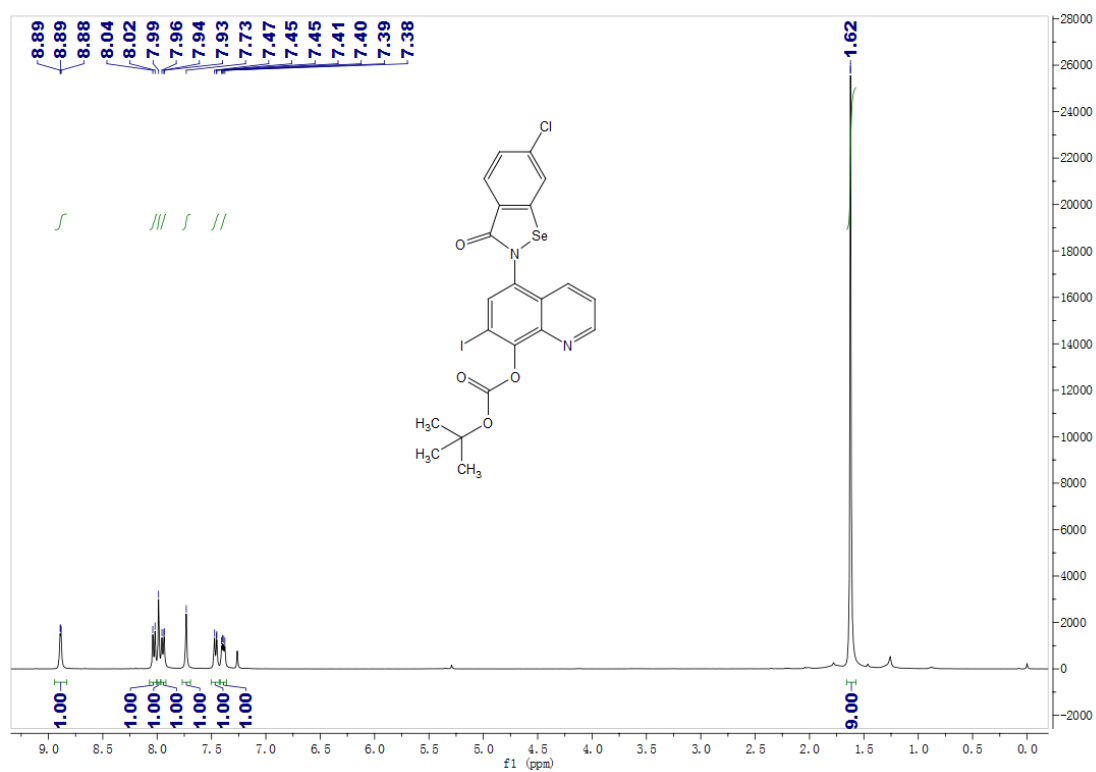
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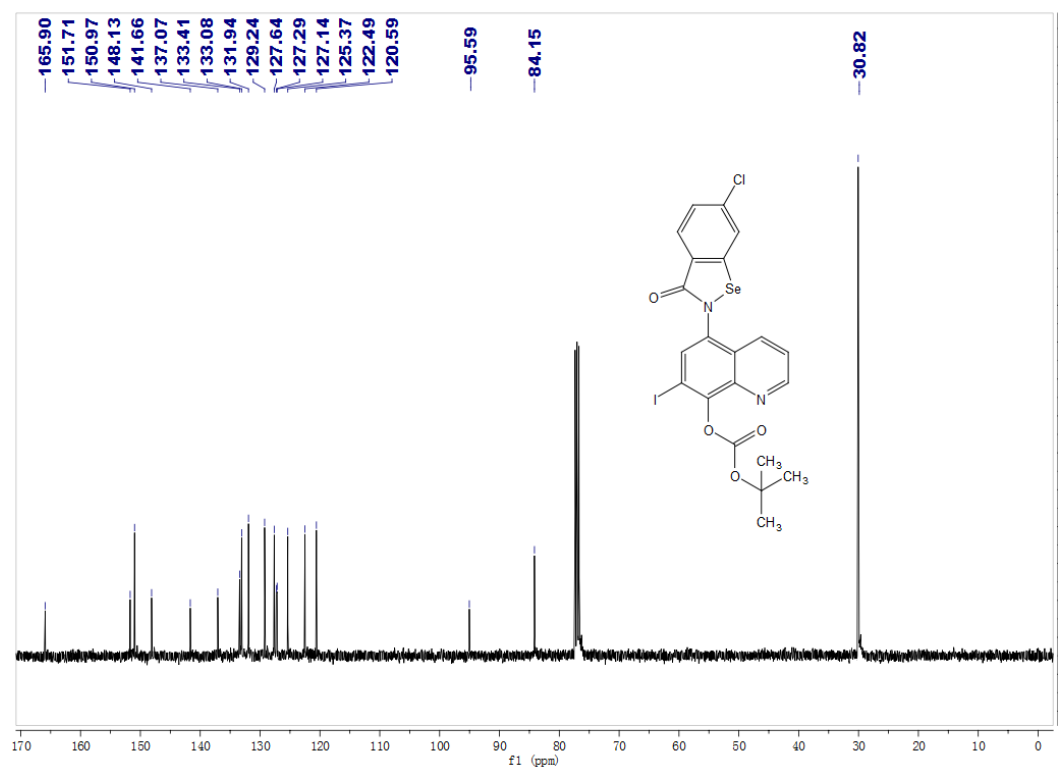
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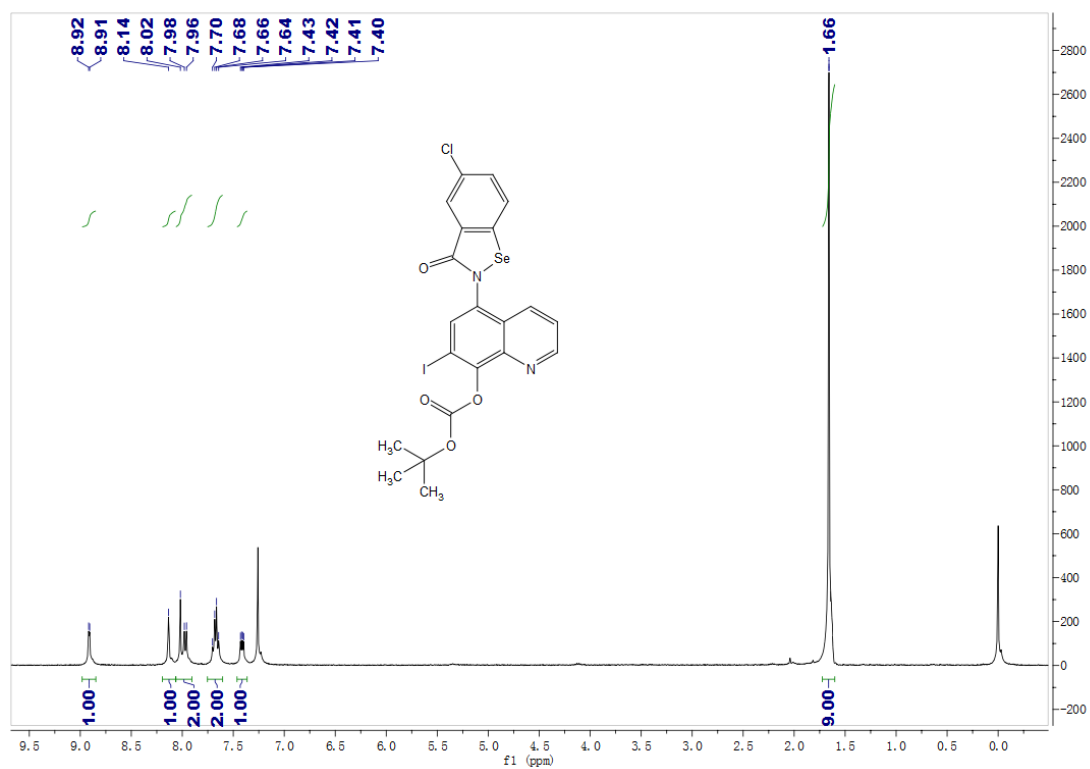
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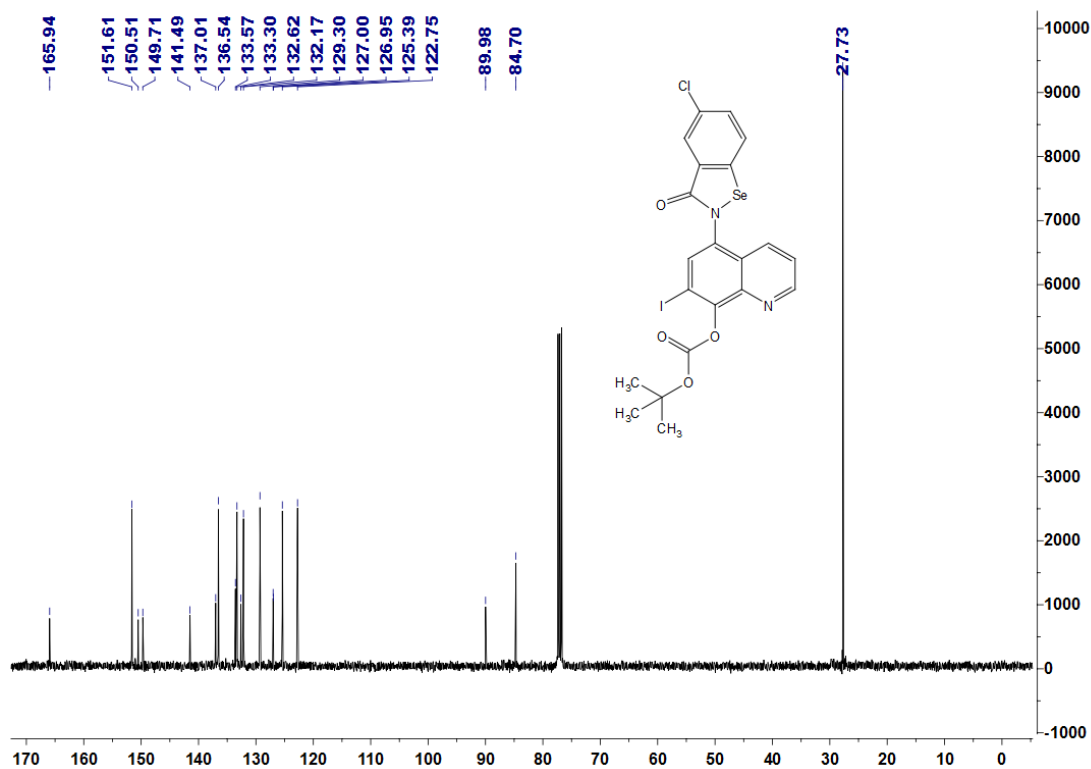
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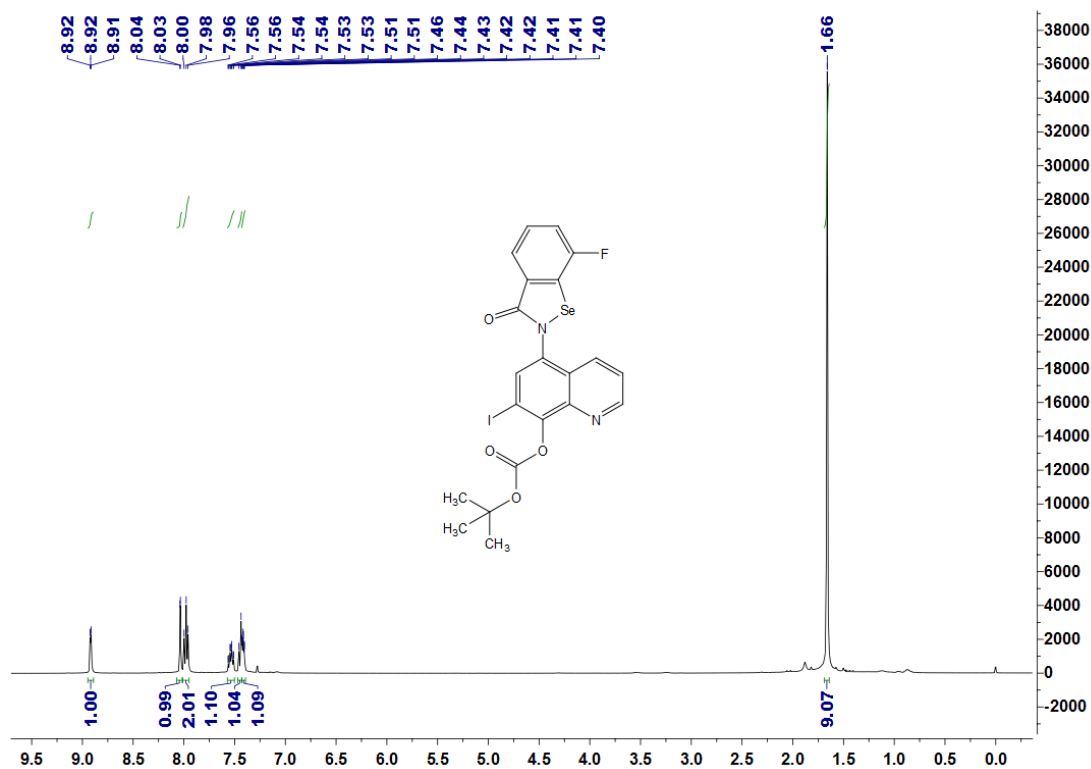
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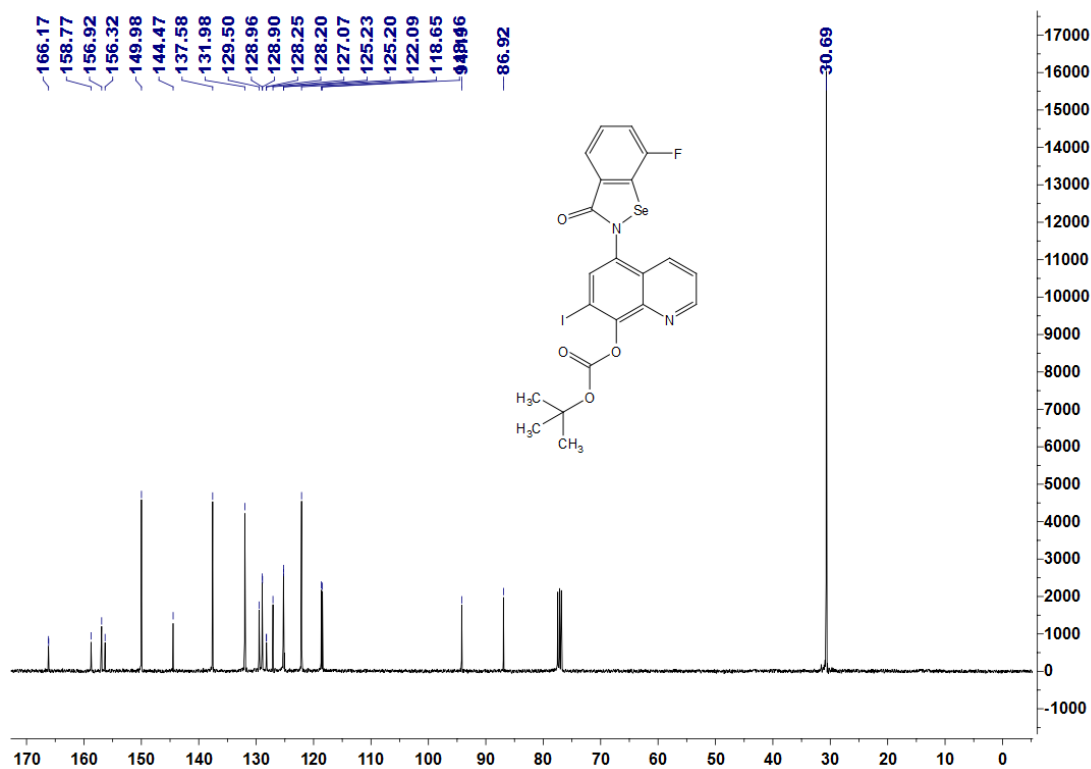
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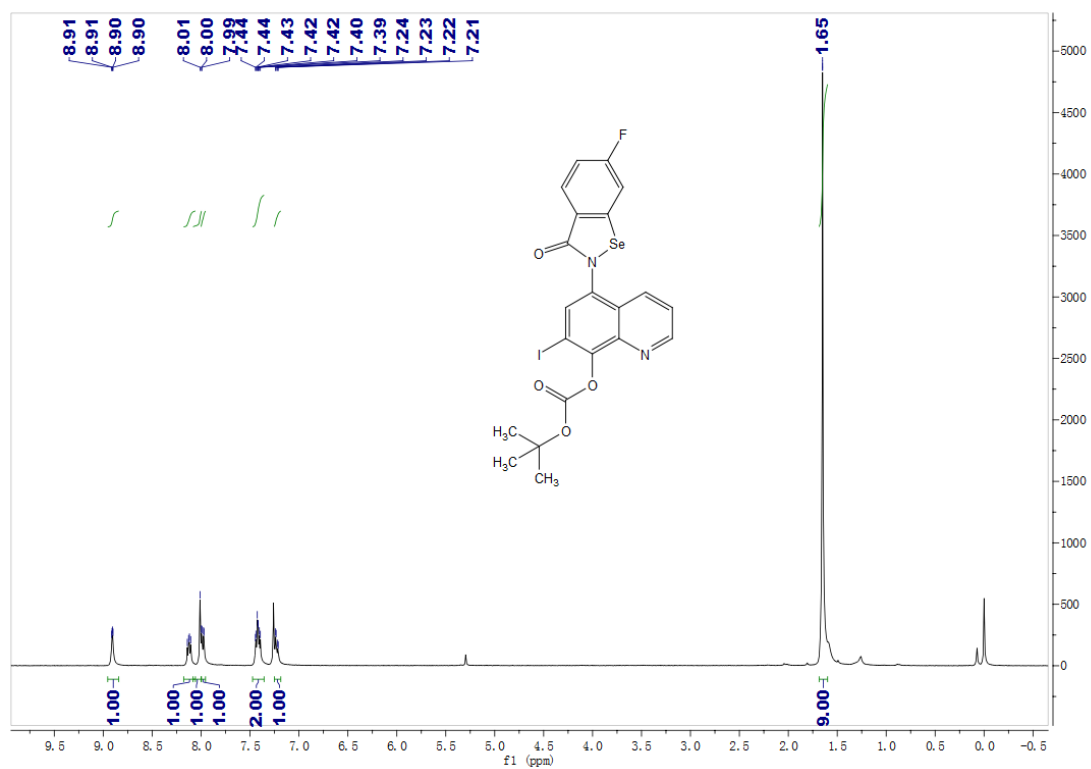
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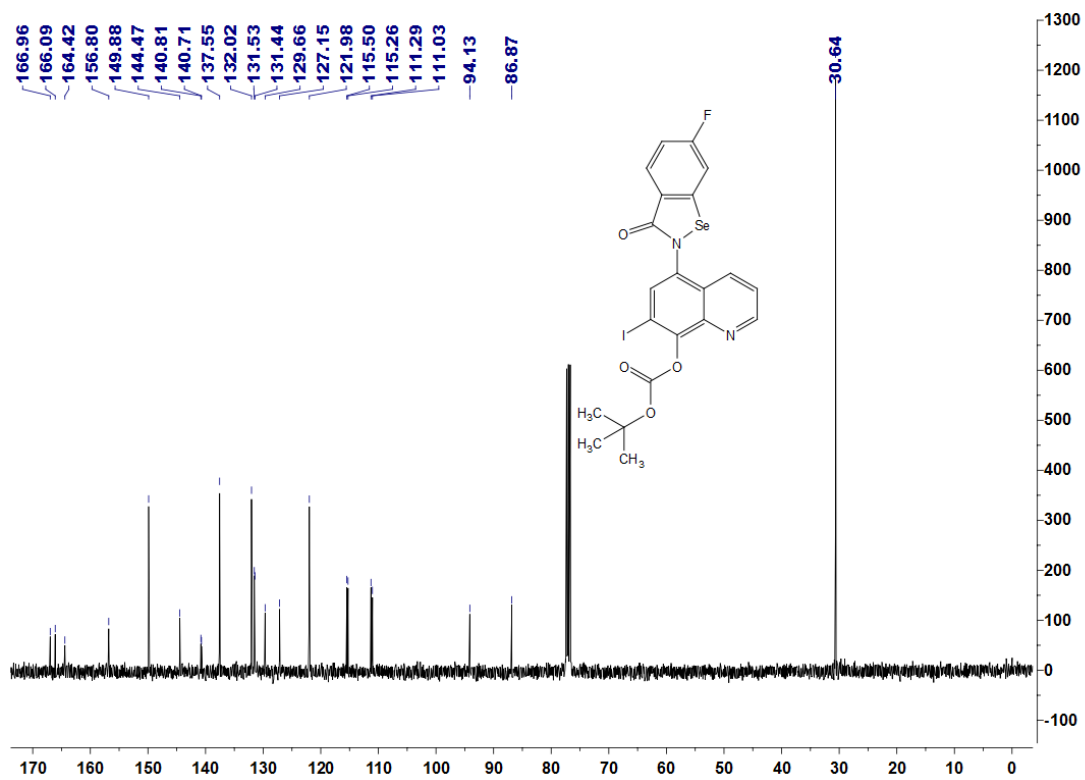
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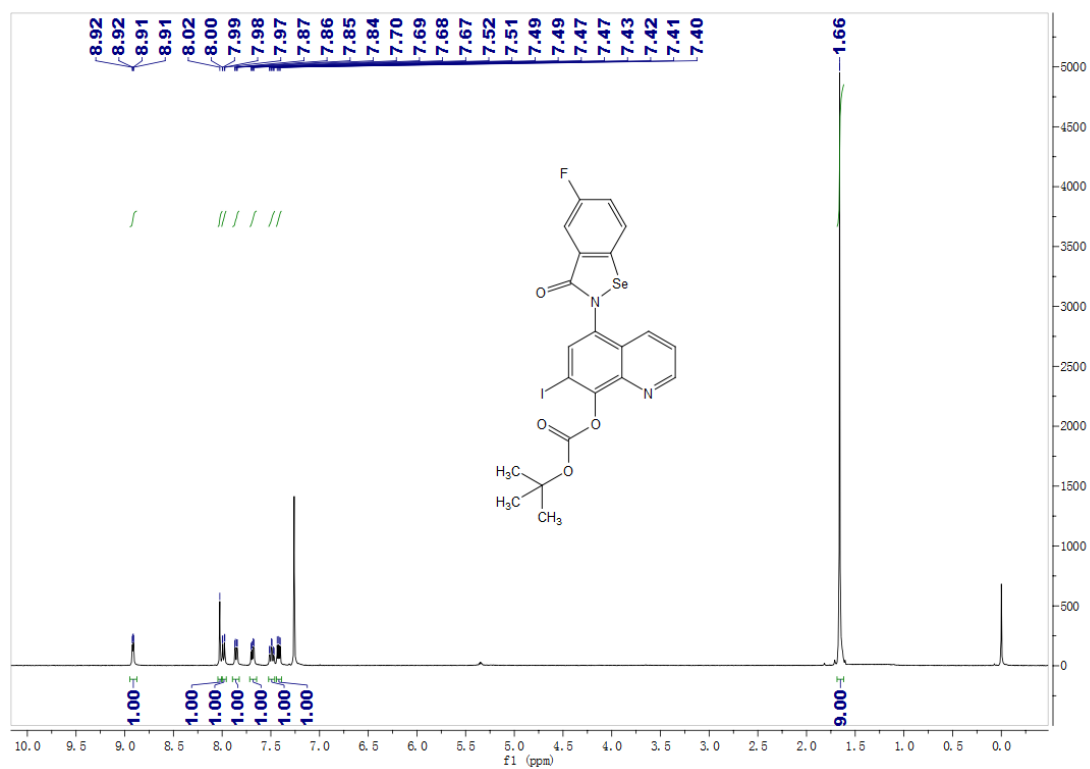
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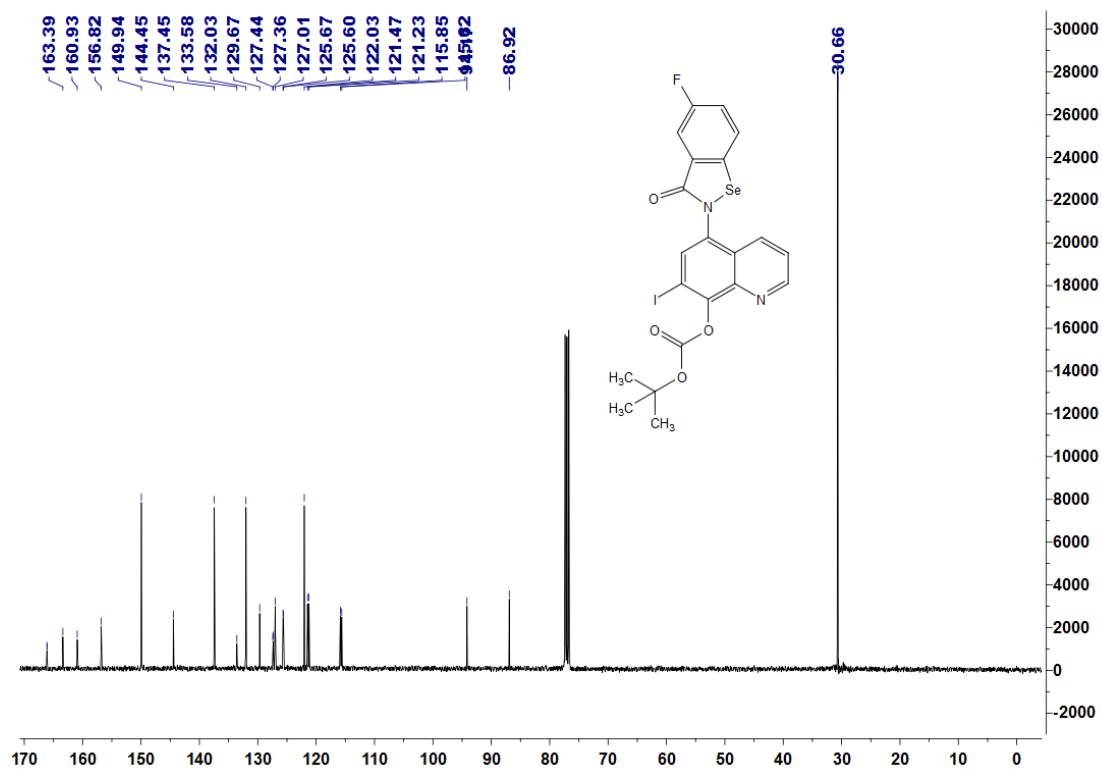
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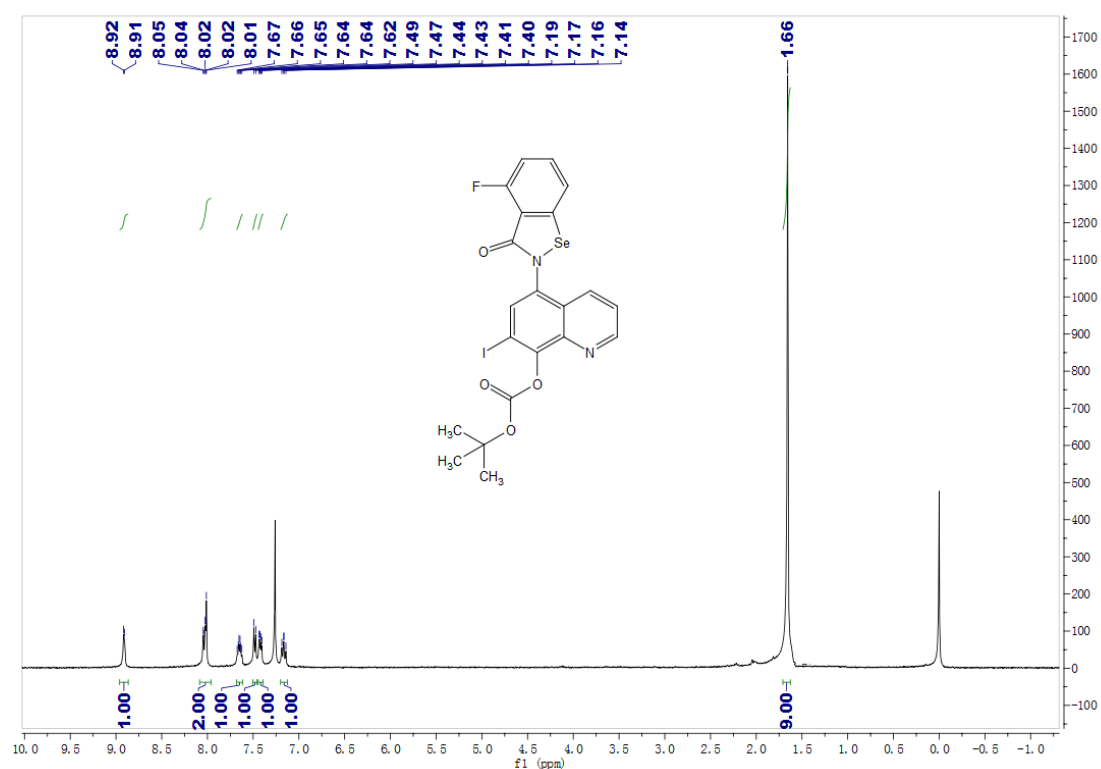
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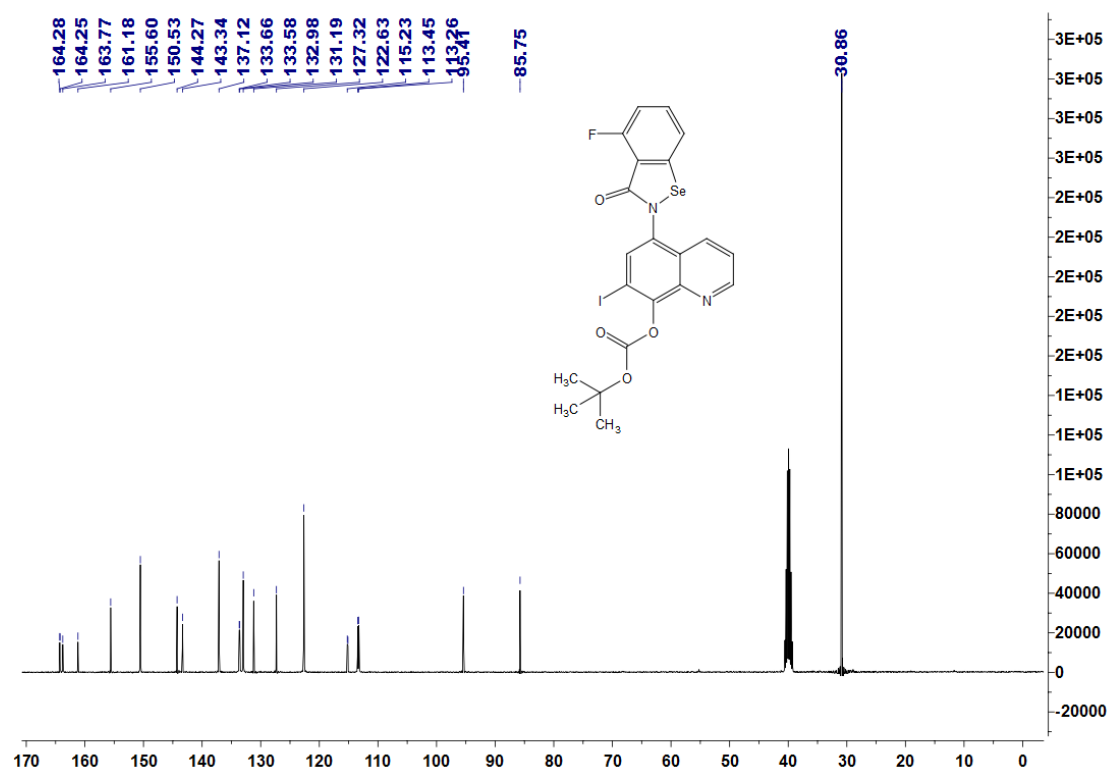
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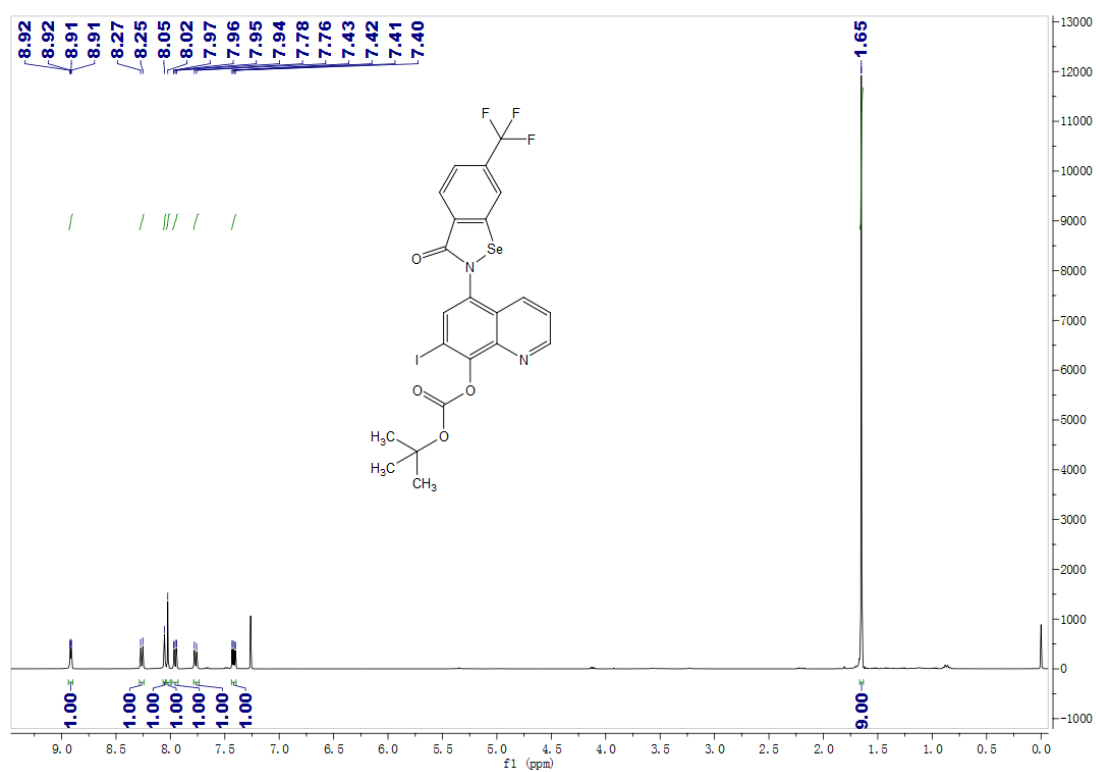
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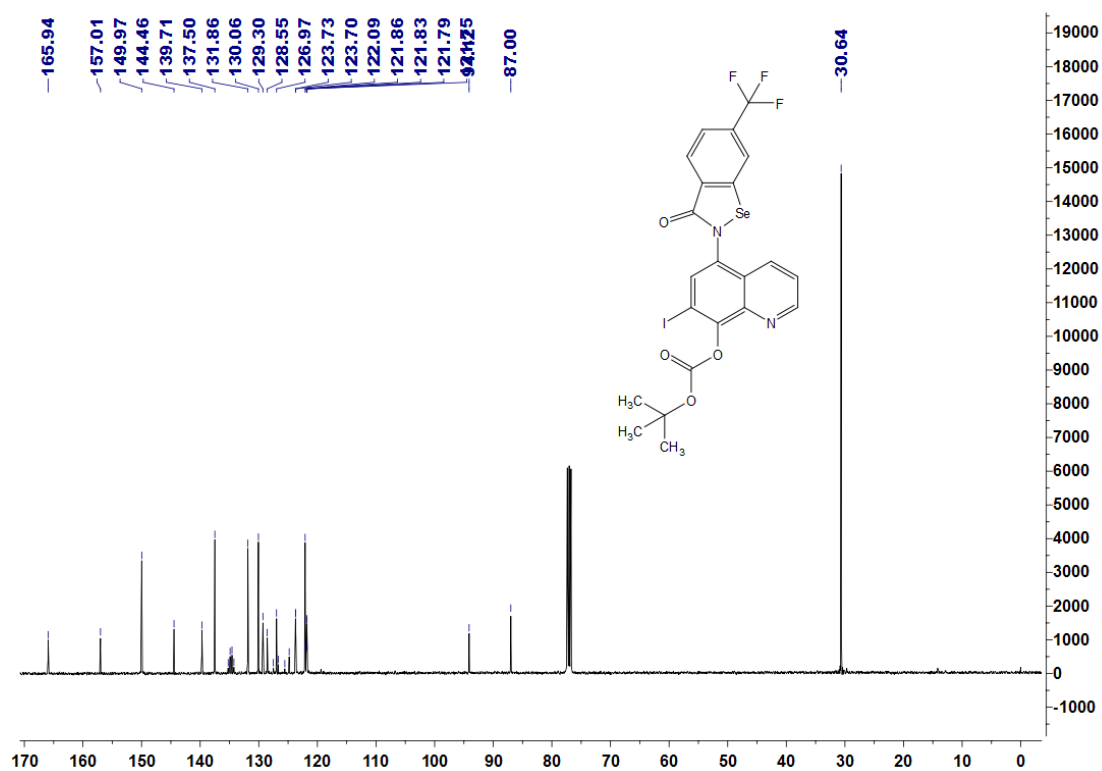
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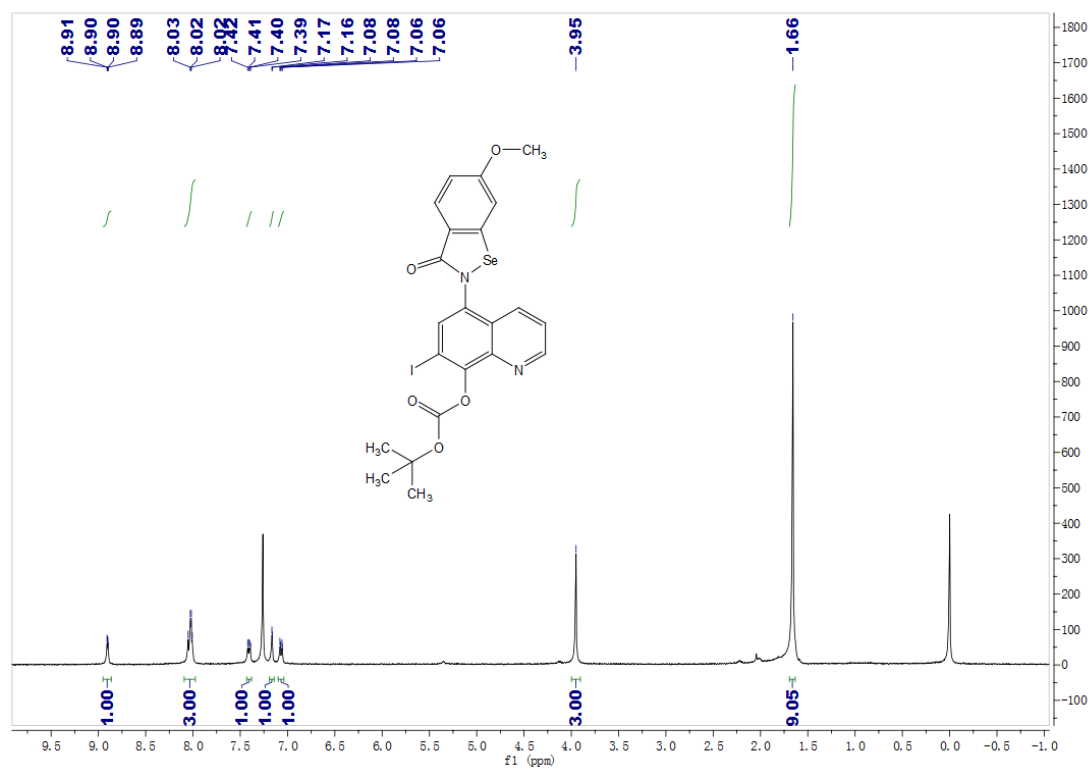
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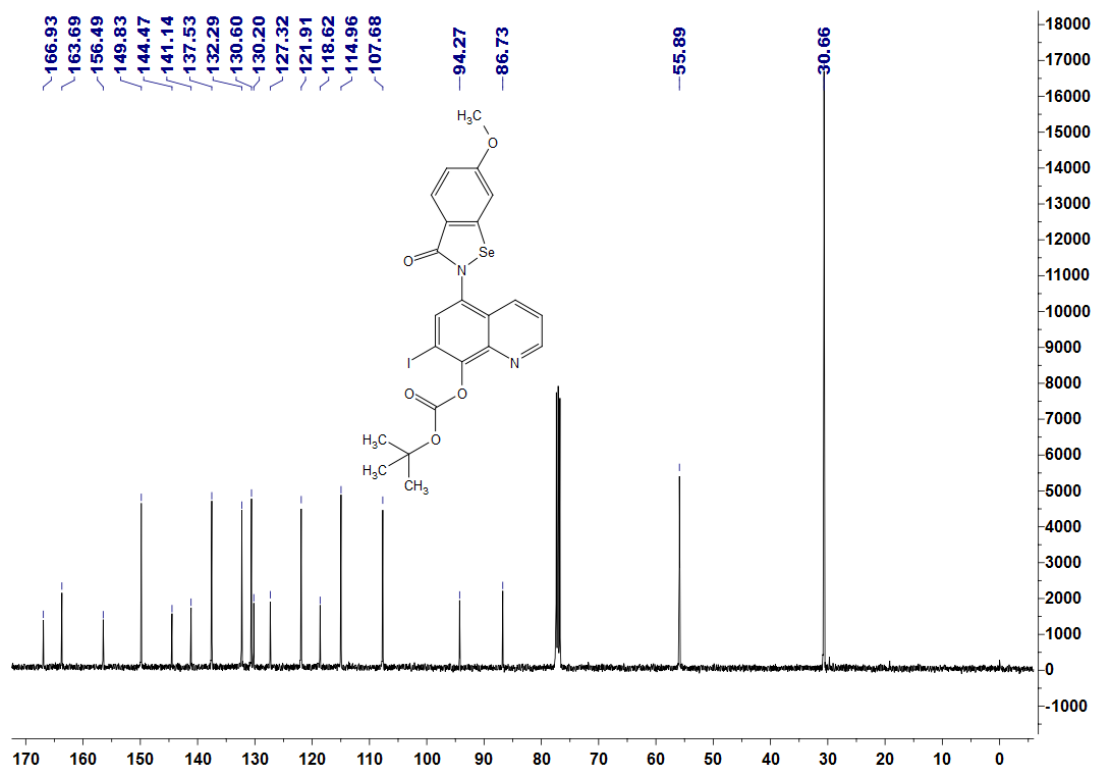
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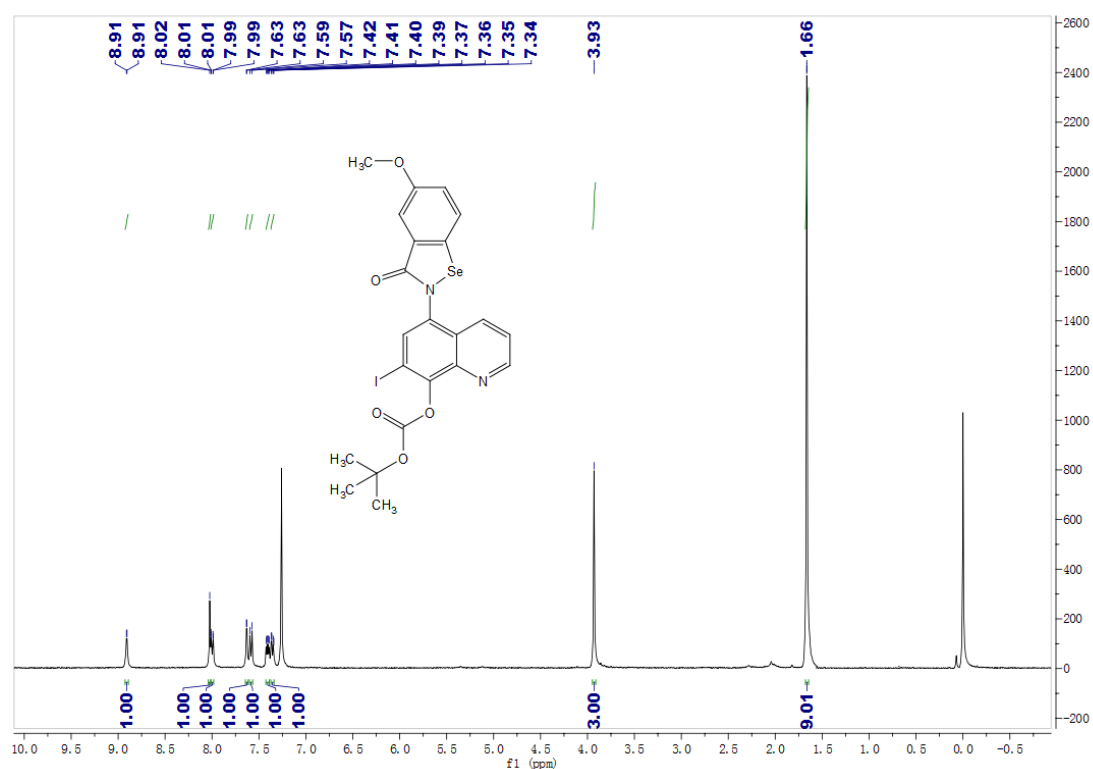
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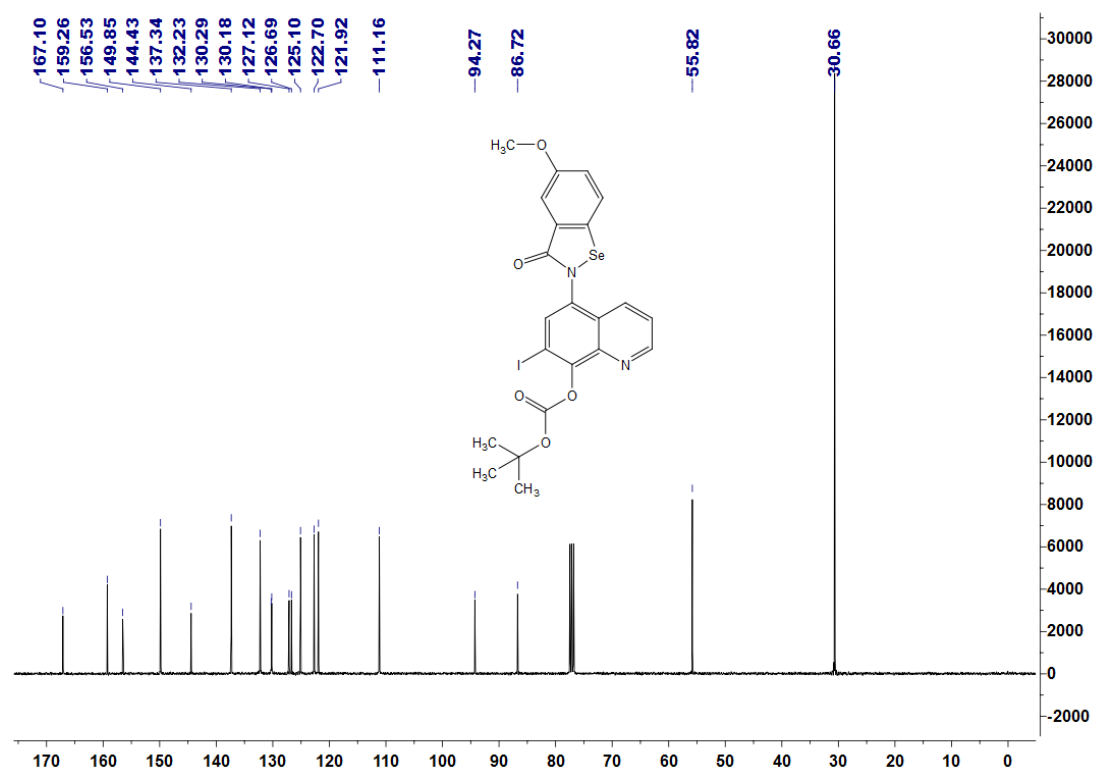
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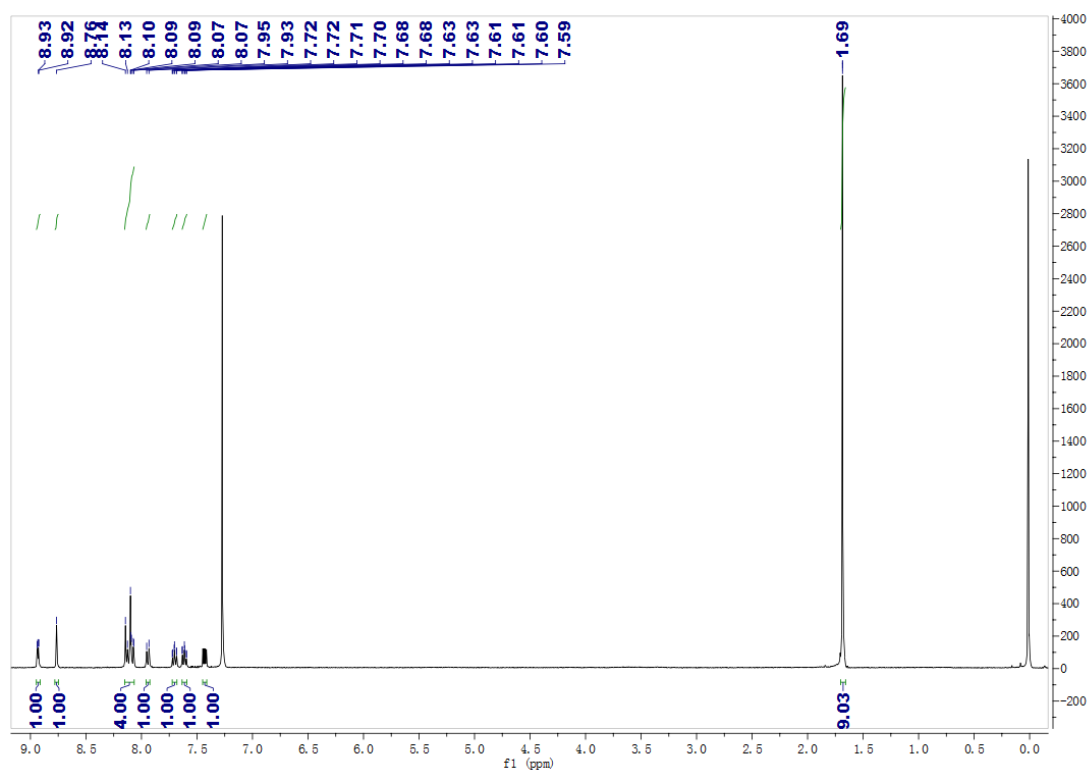
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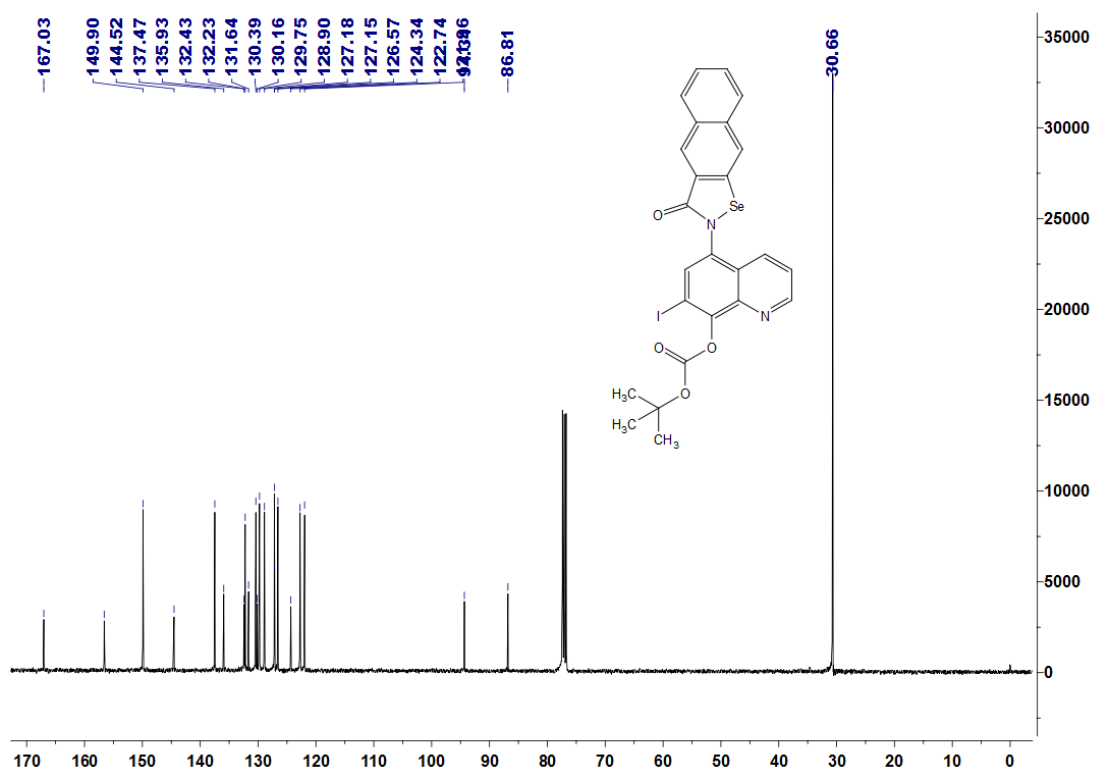
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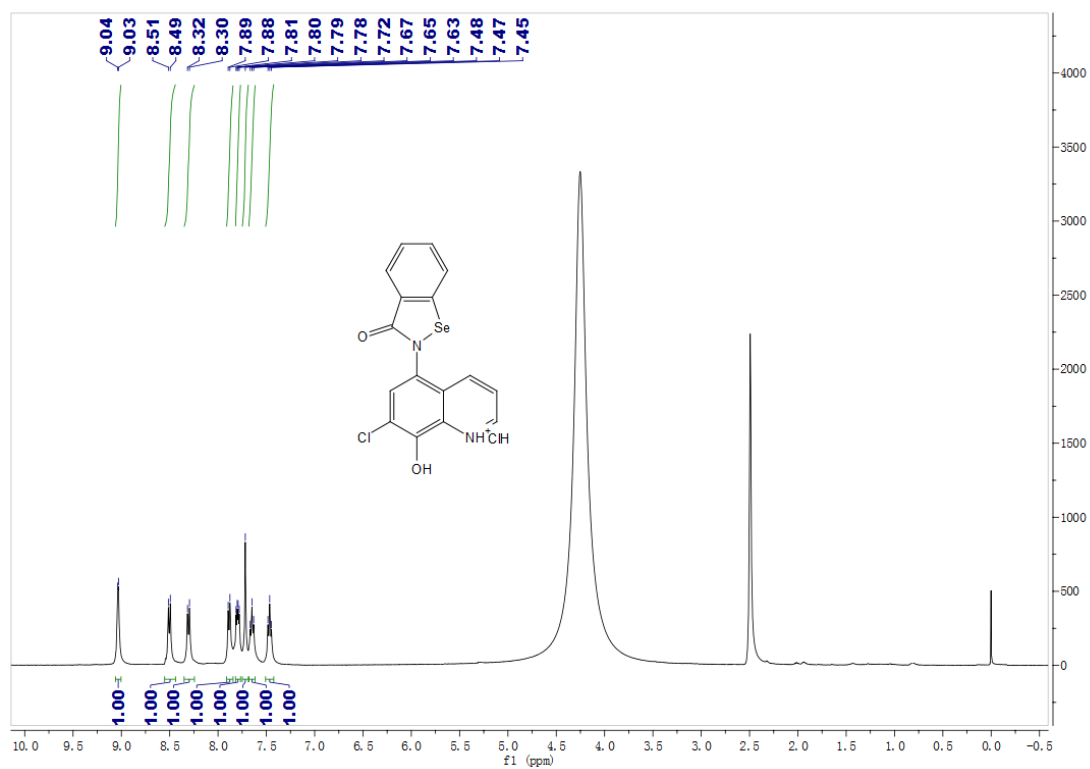
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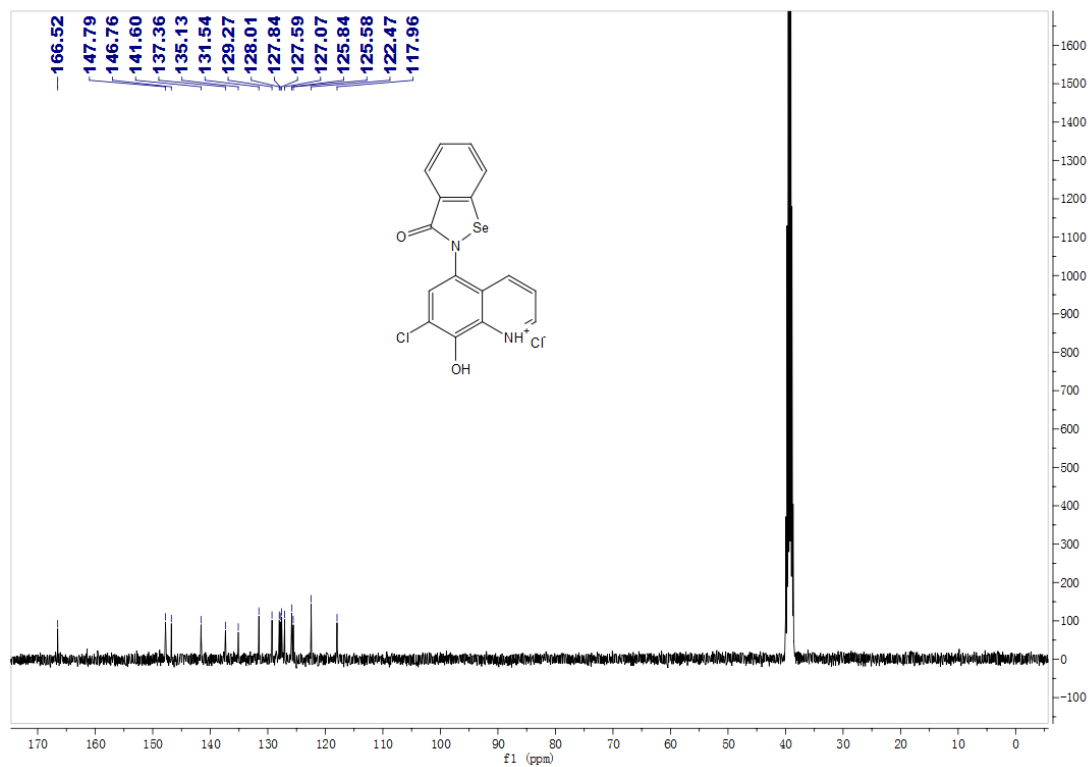
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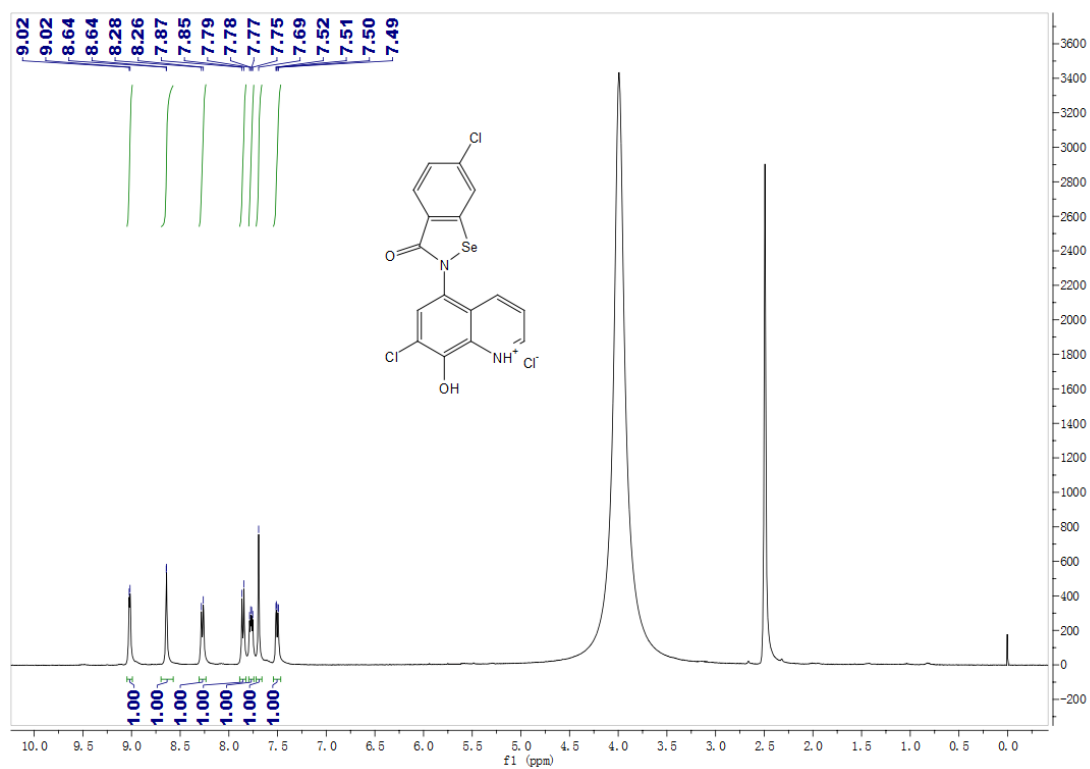
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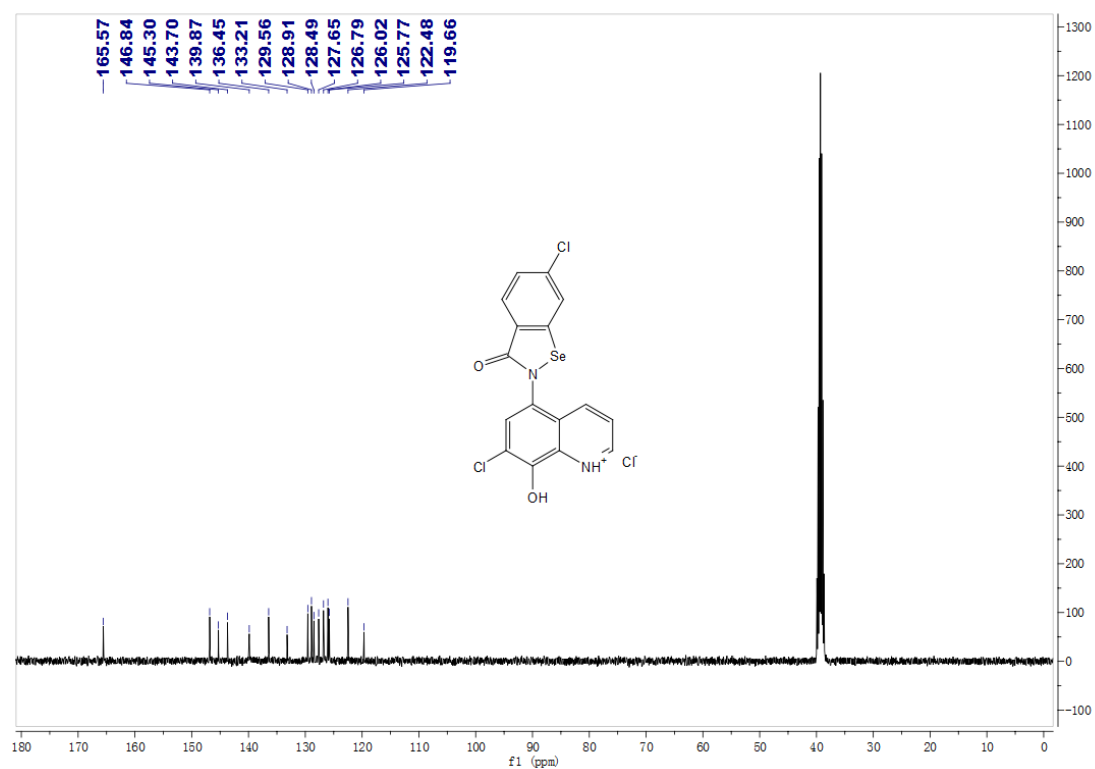
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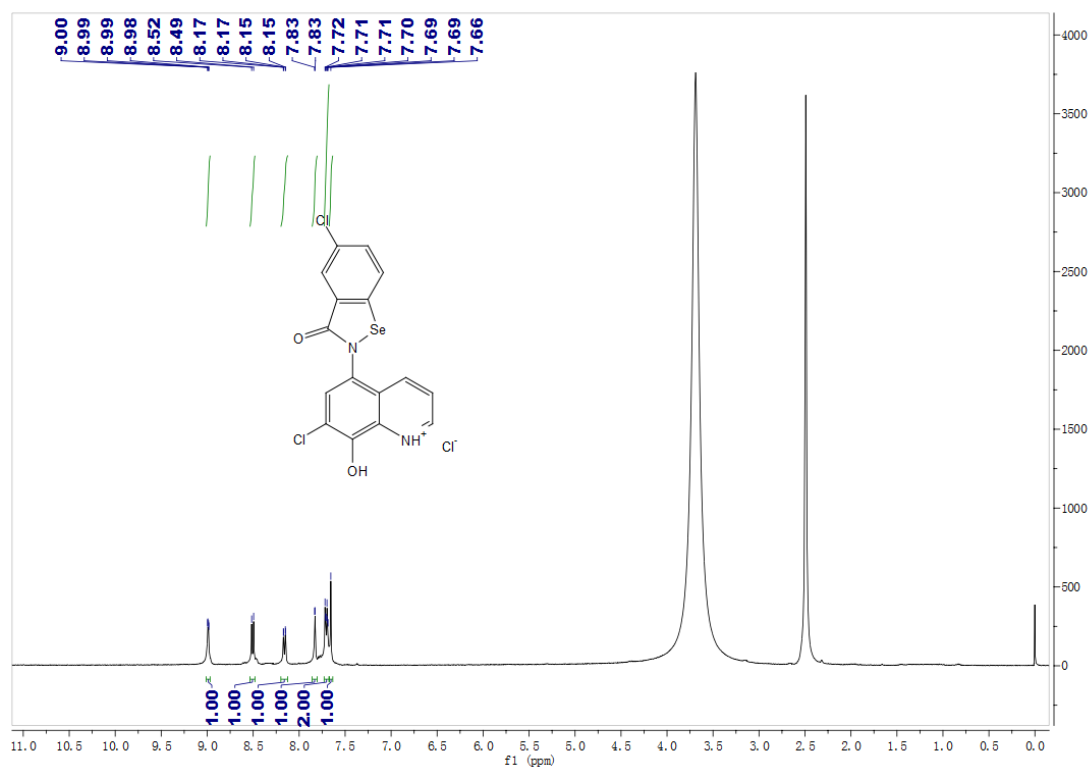
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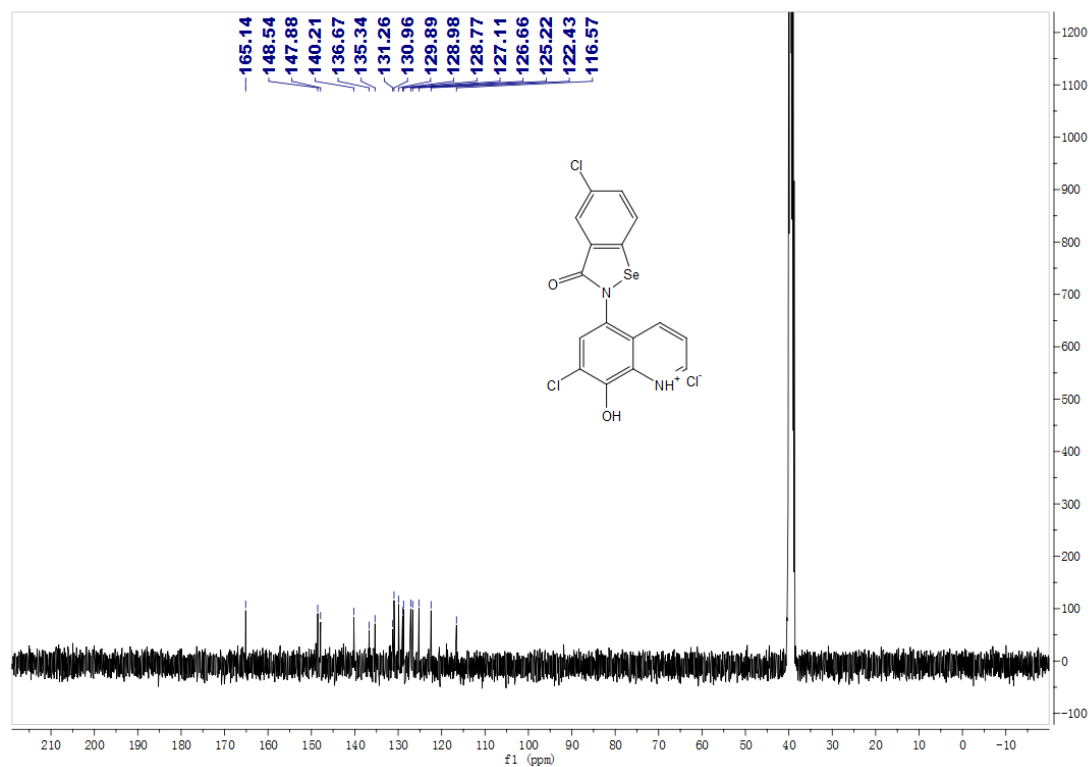
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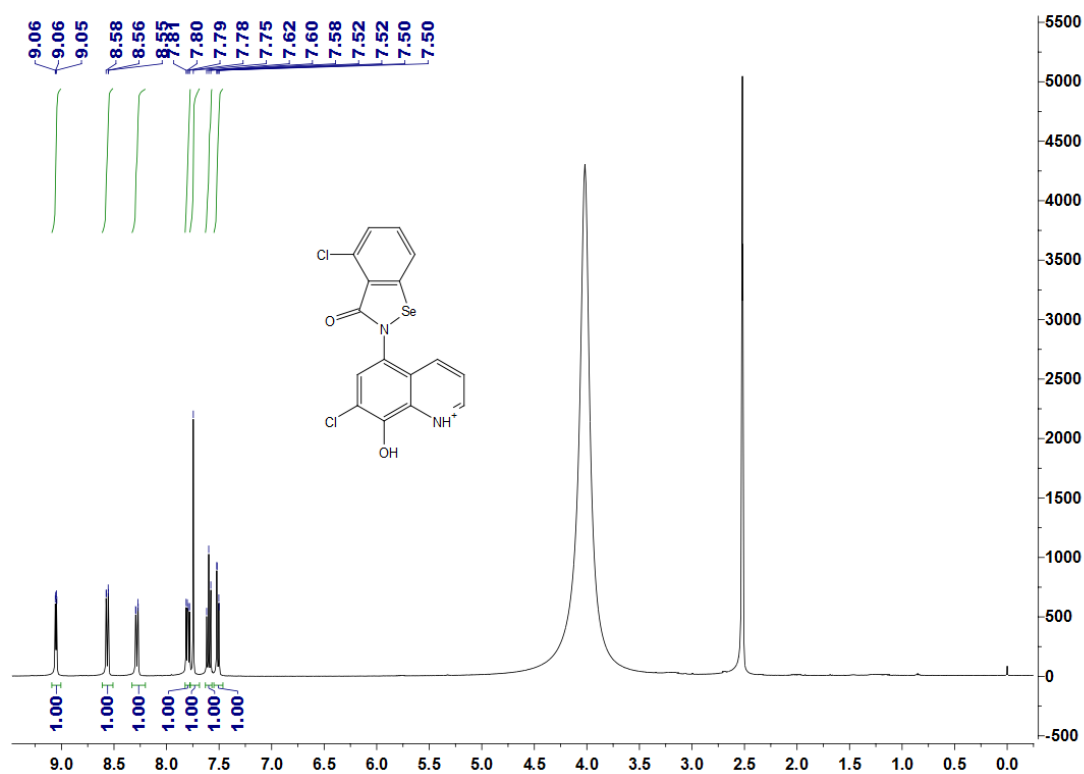
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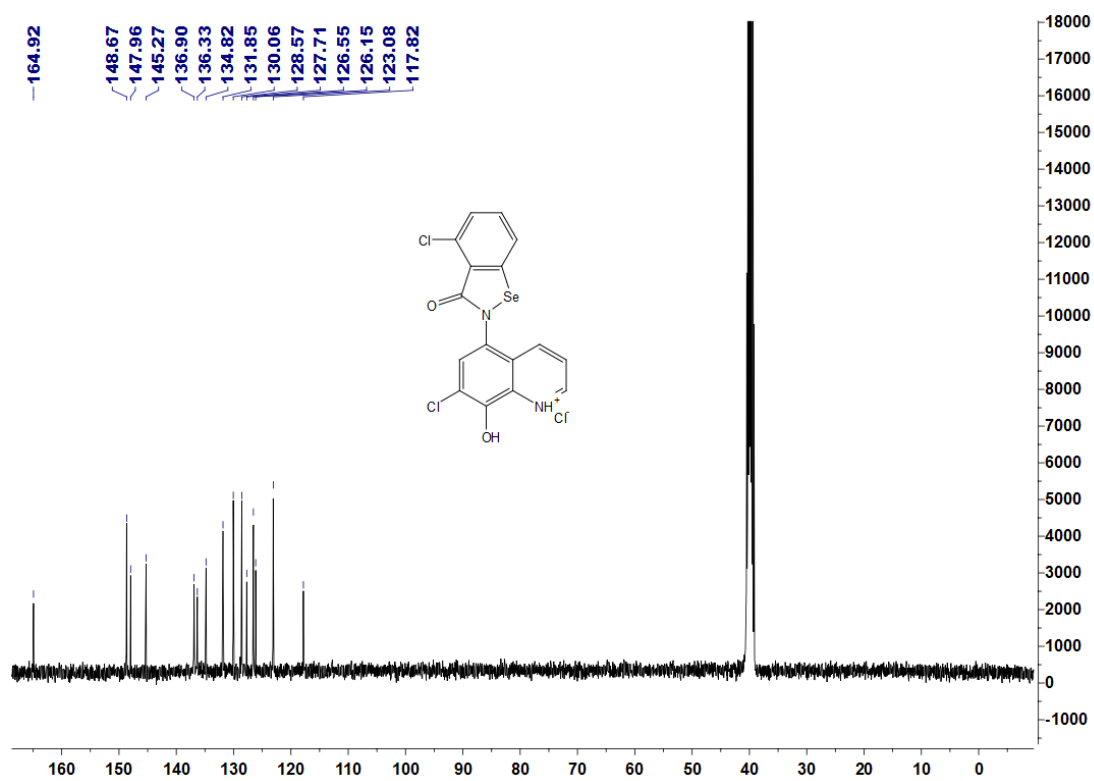
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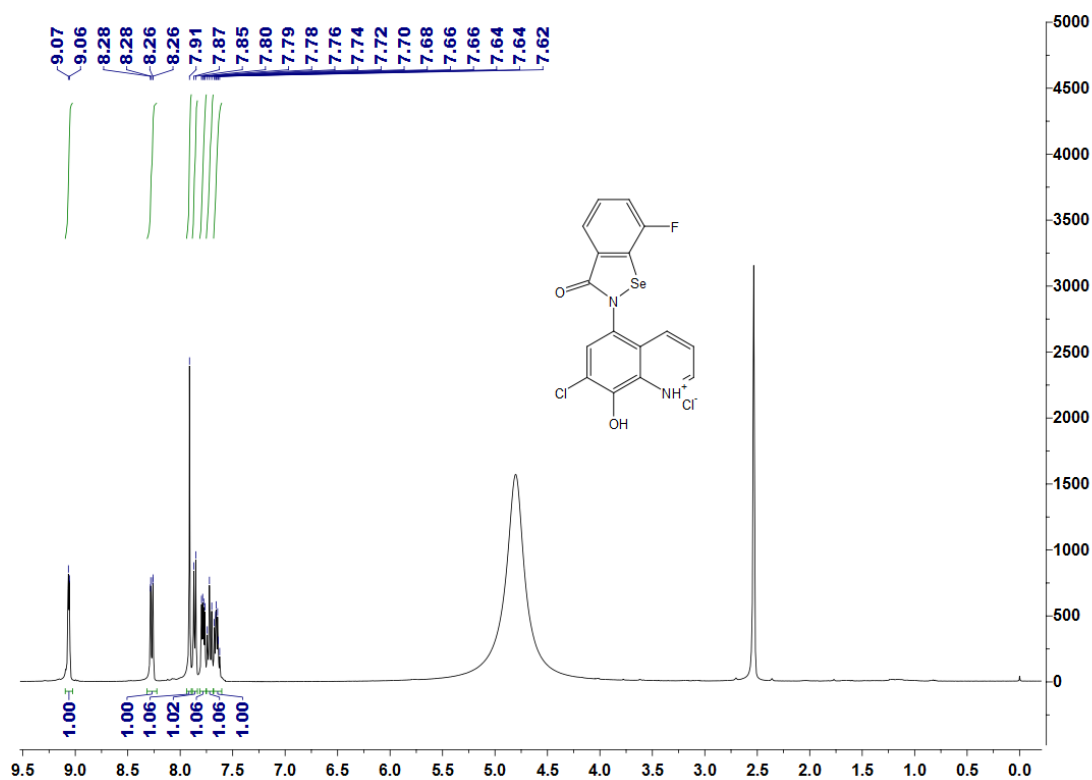
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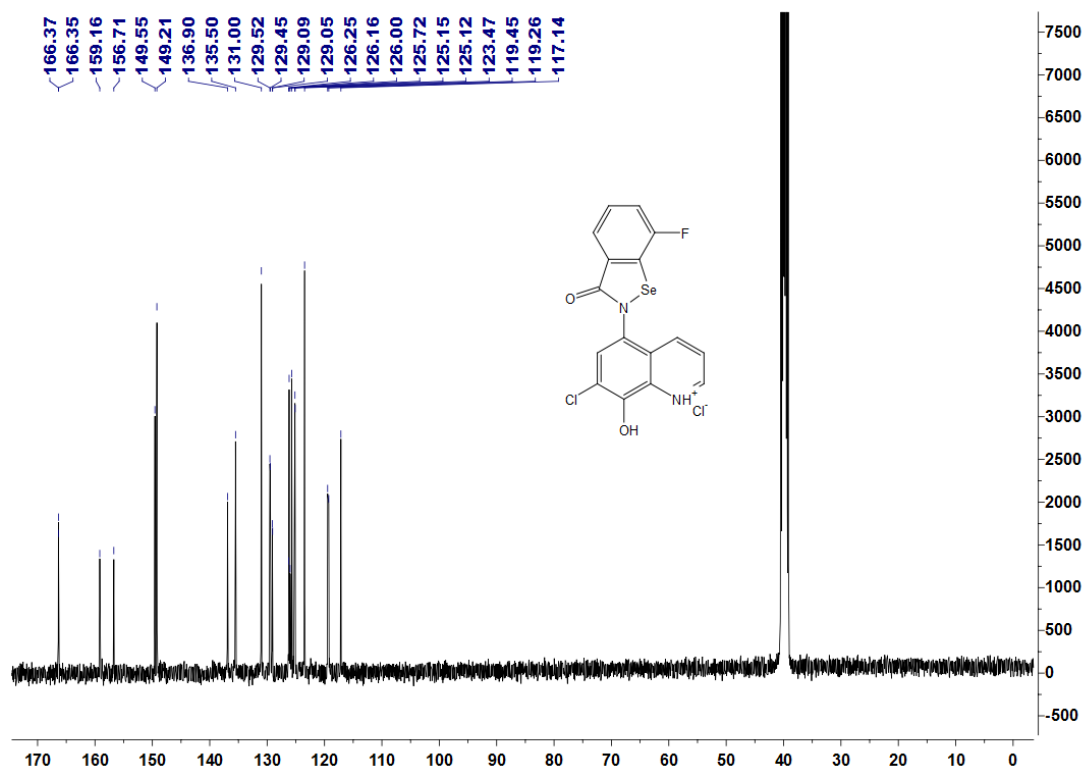
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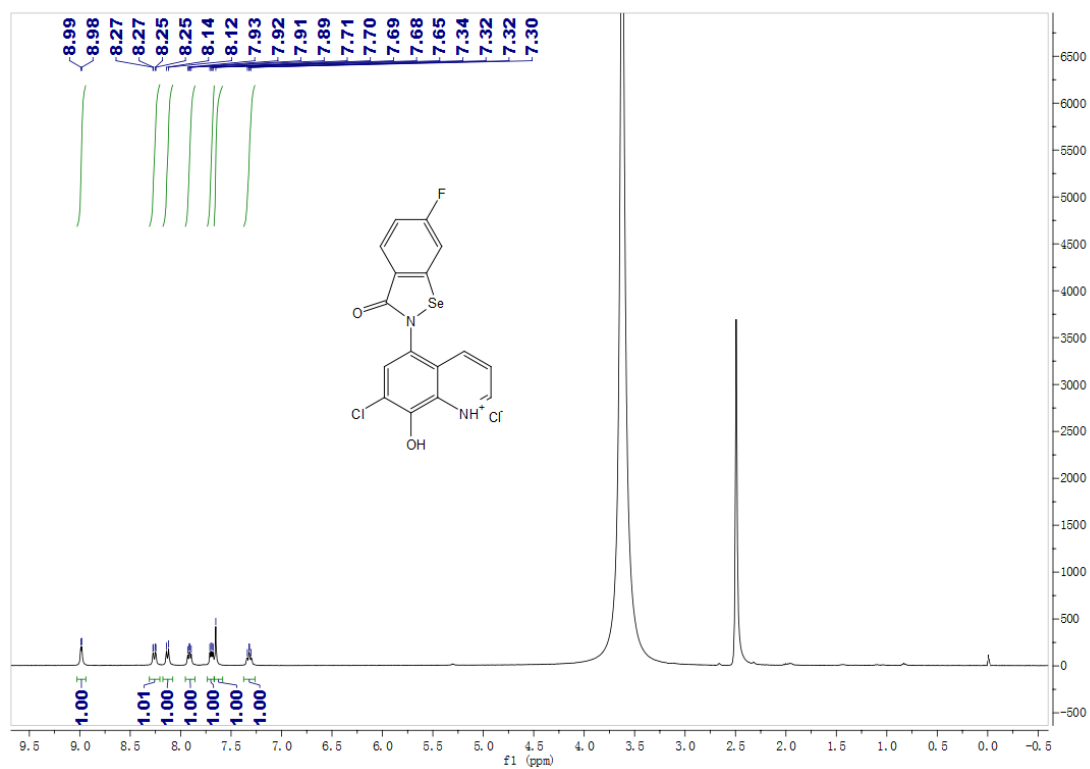
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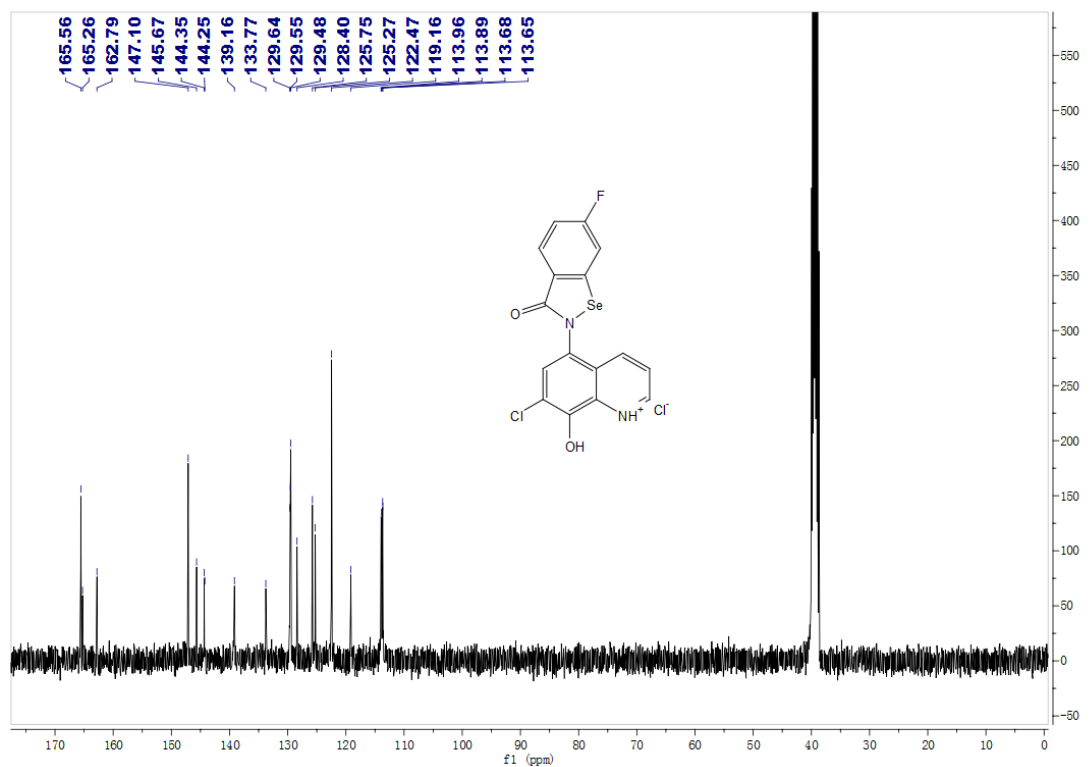
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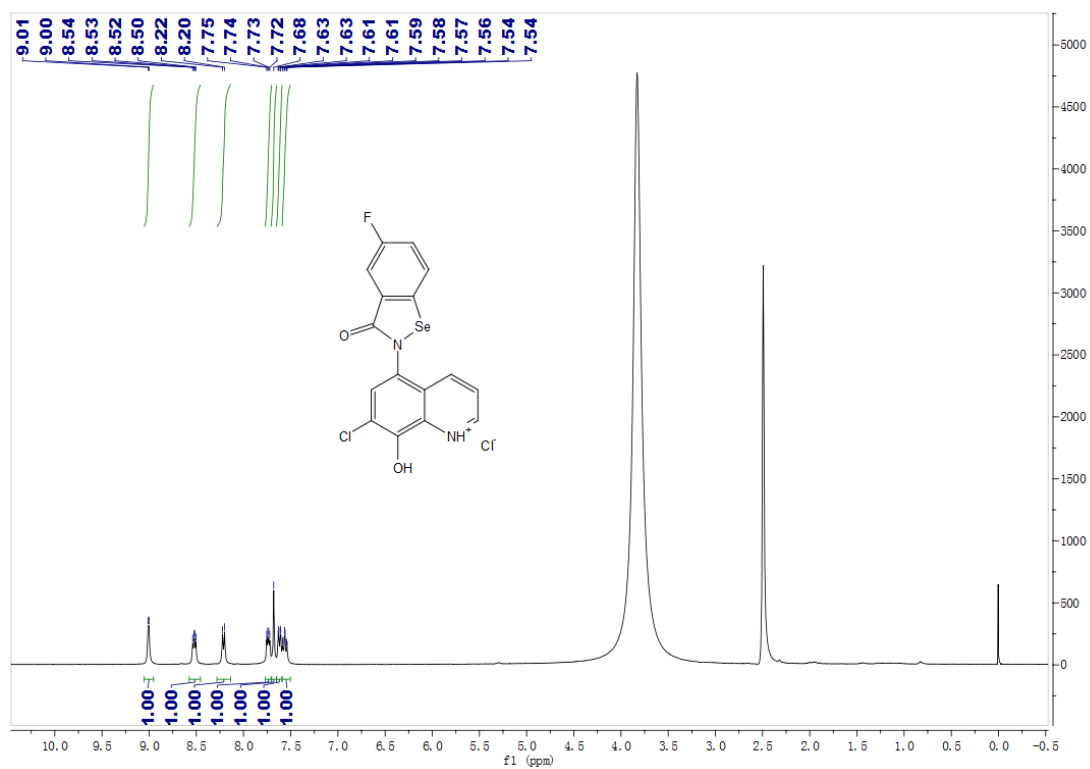
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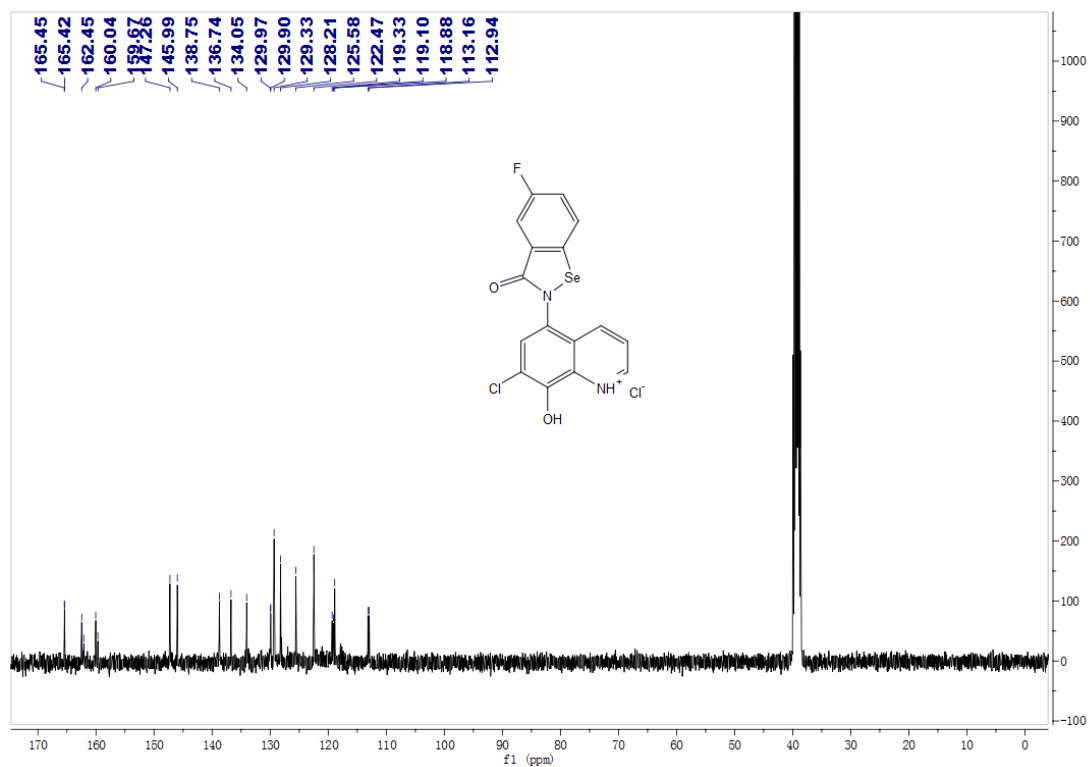
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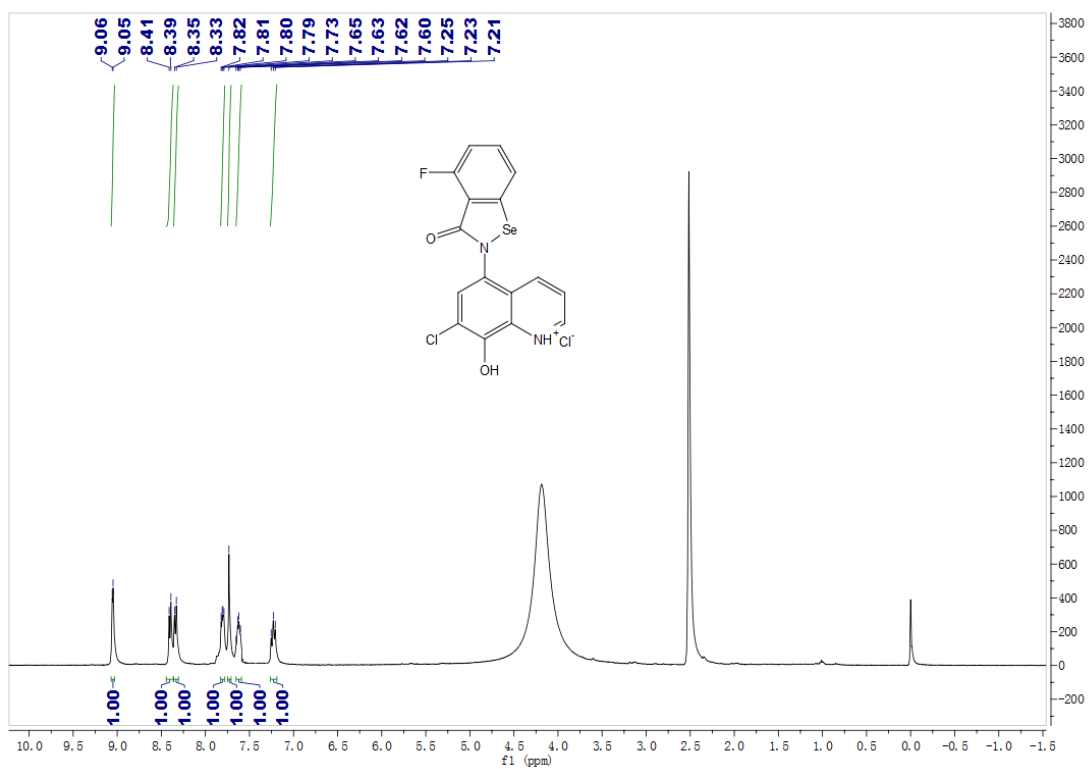
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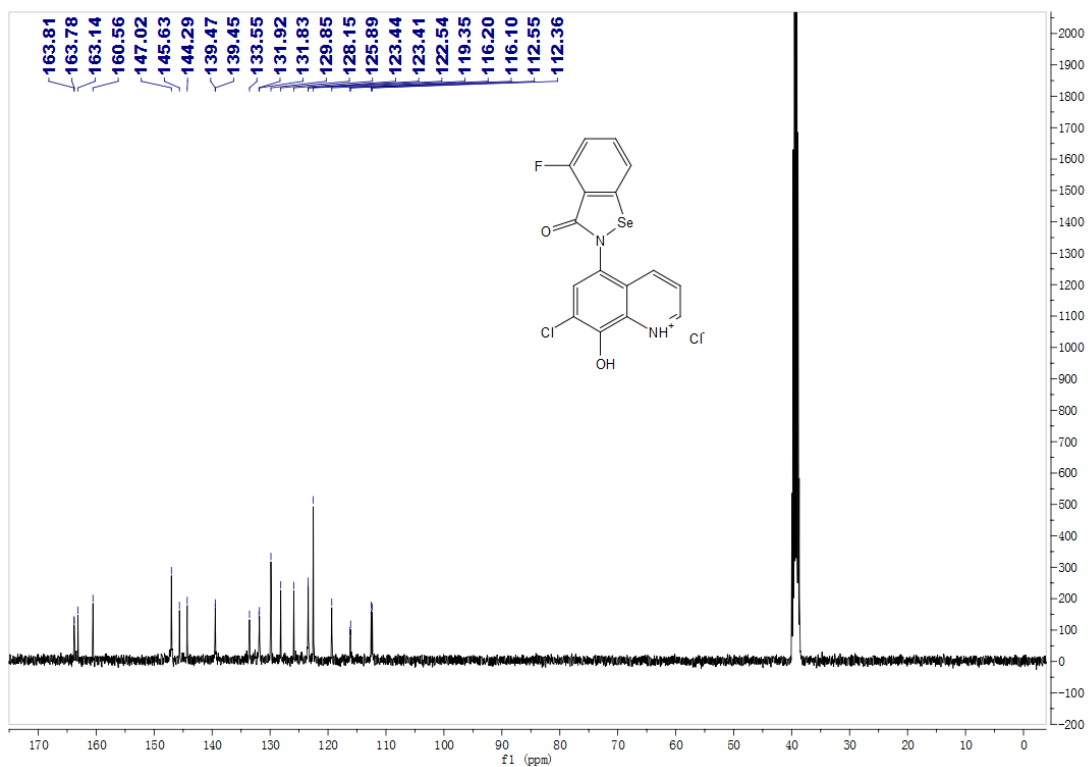
10g•HCl-¹³C



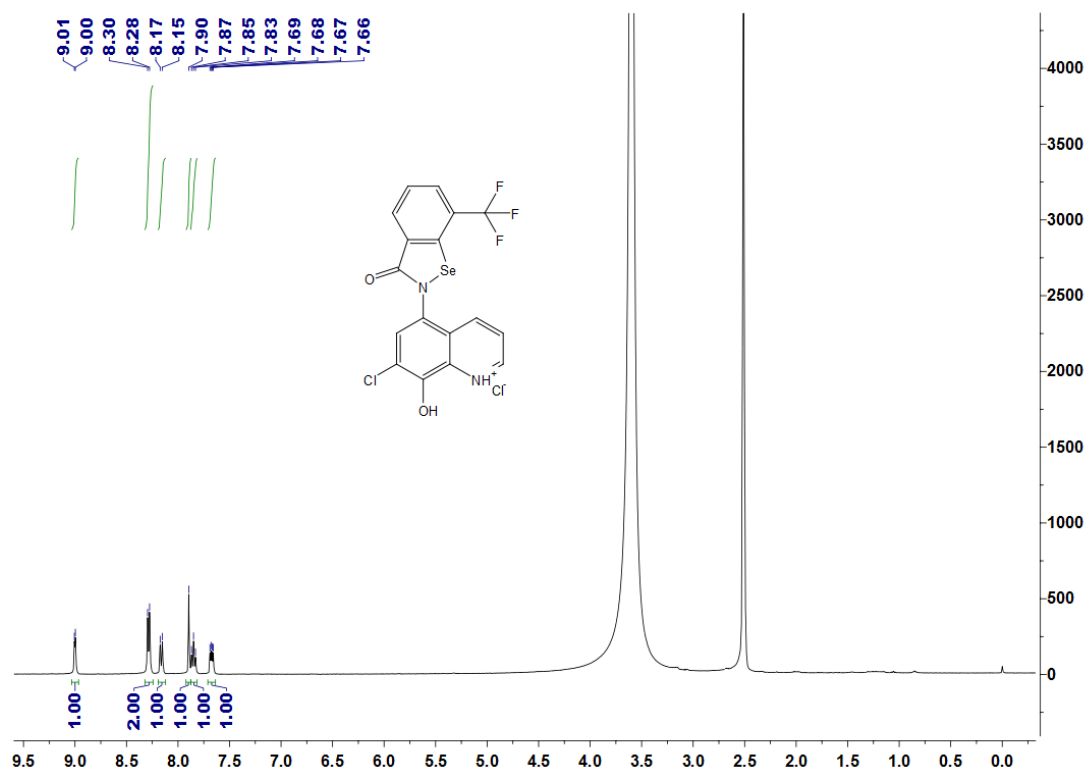
10h•HCl-¹H



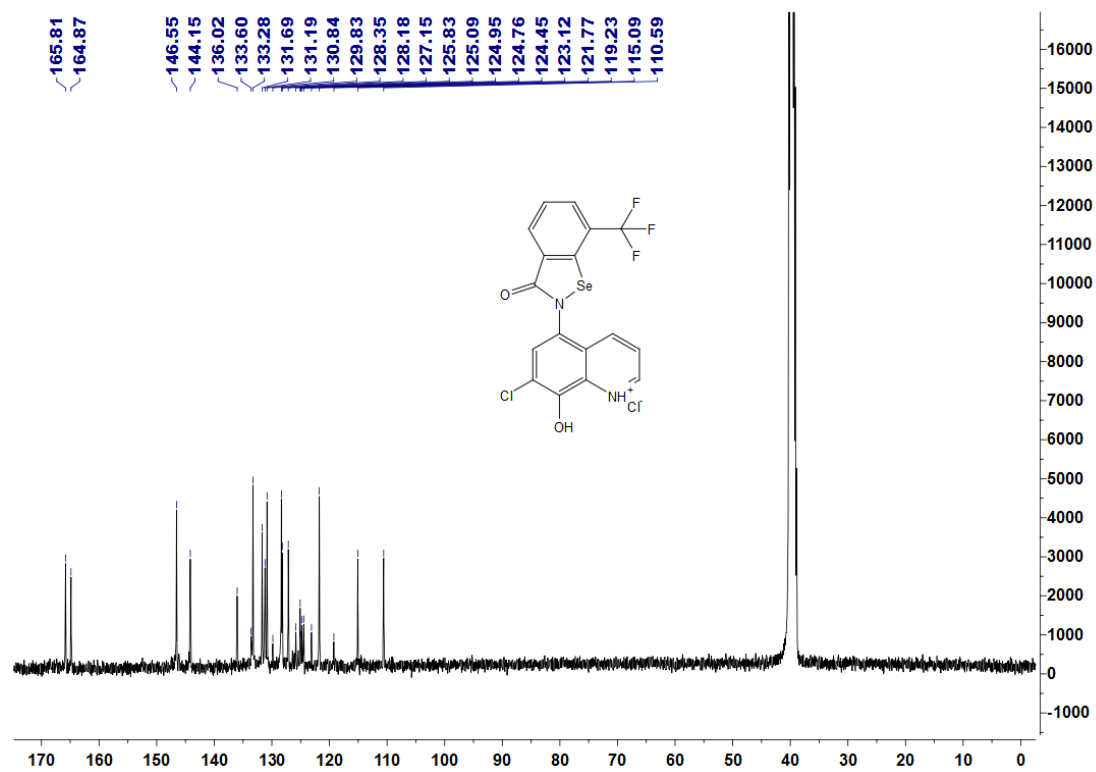
10h•HCl-¹³C



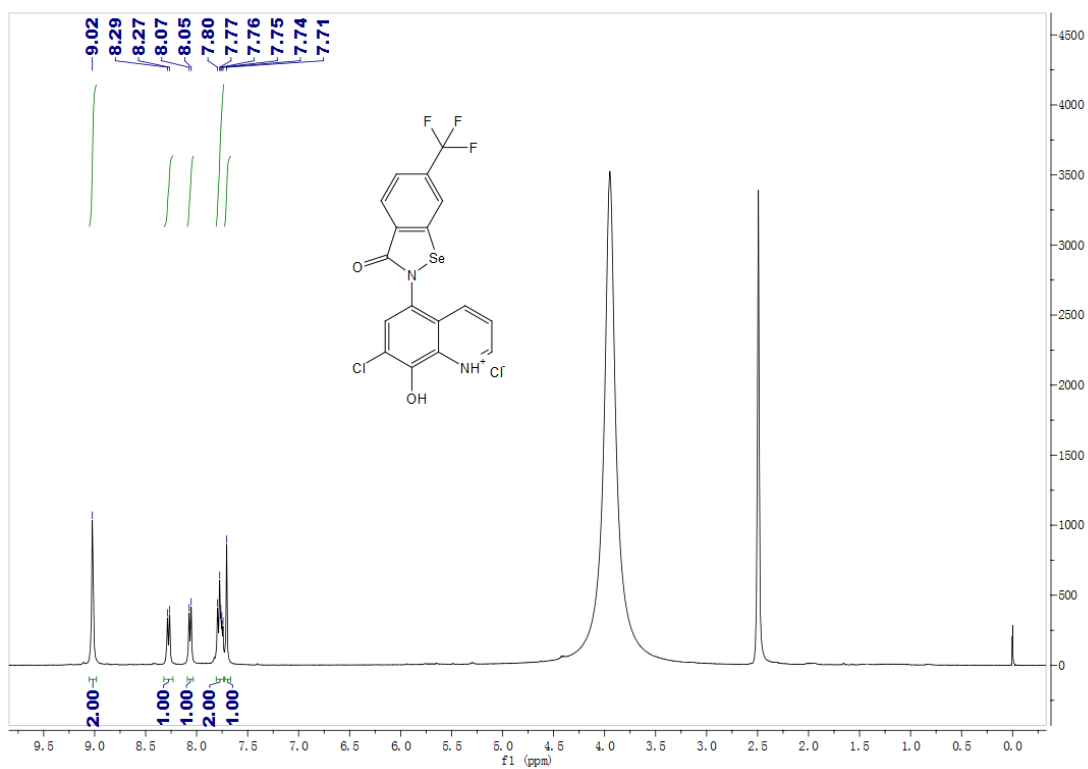
10i•HCl-¹H



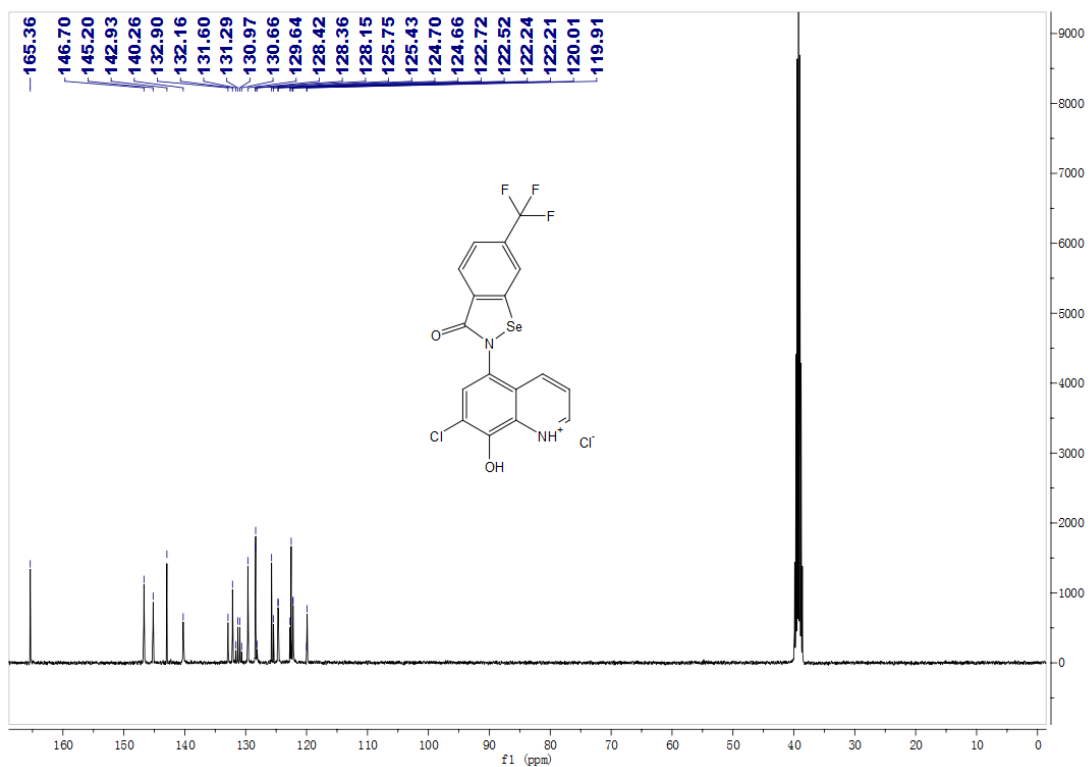
10i•HCl-¹³C



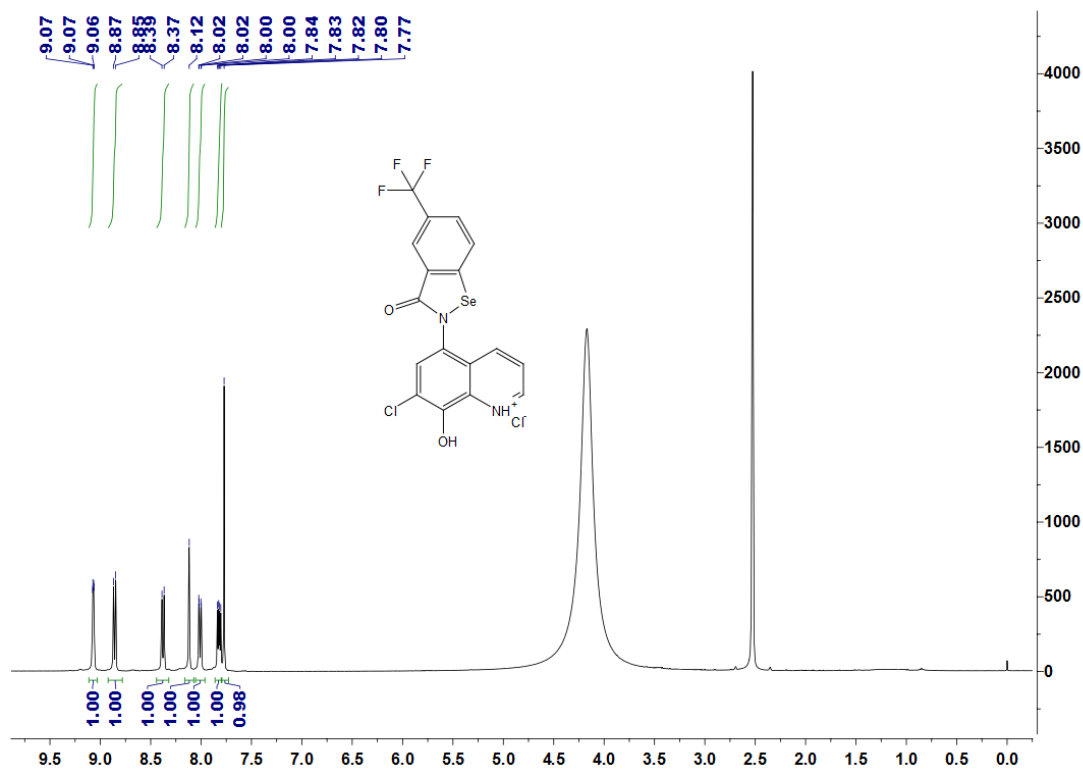
10j•HCl-¹H



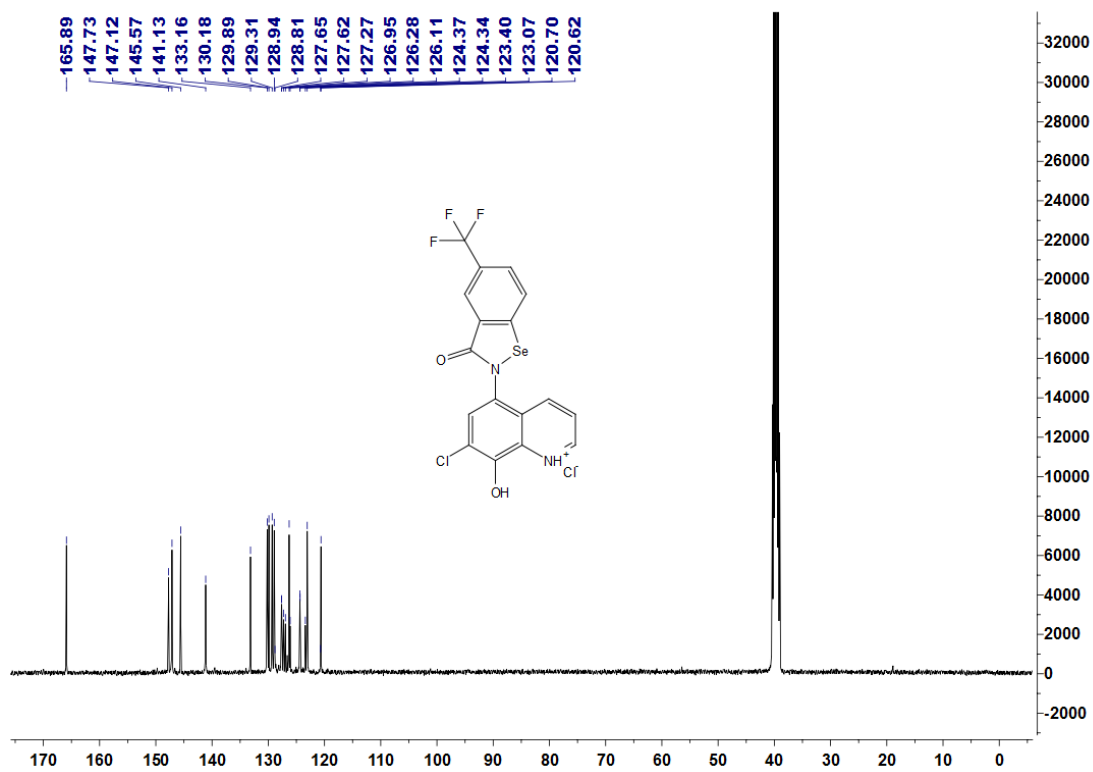
10j•HCl-¹³C



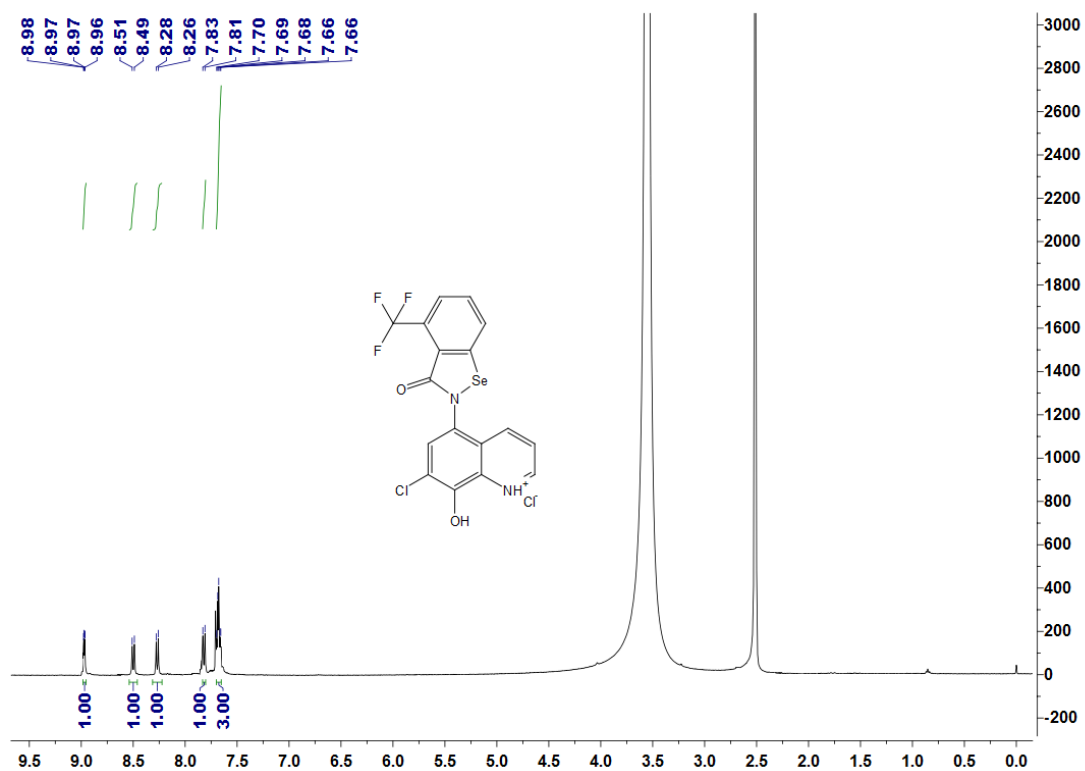
10k•HCl-¹H



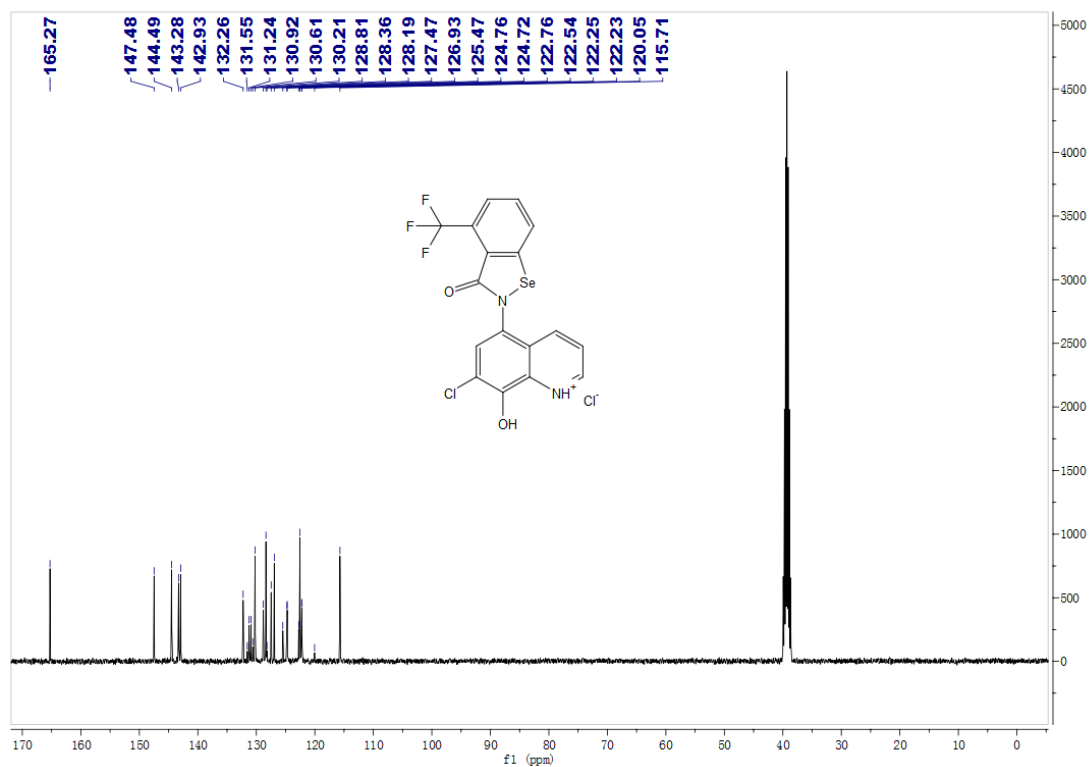
10k•HCl-¹³C



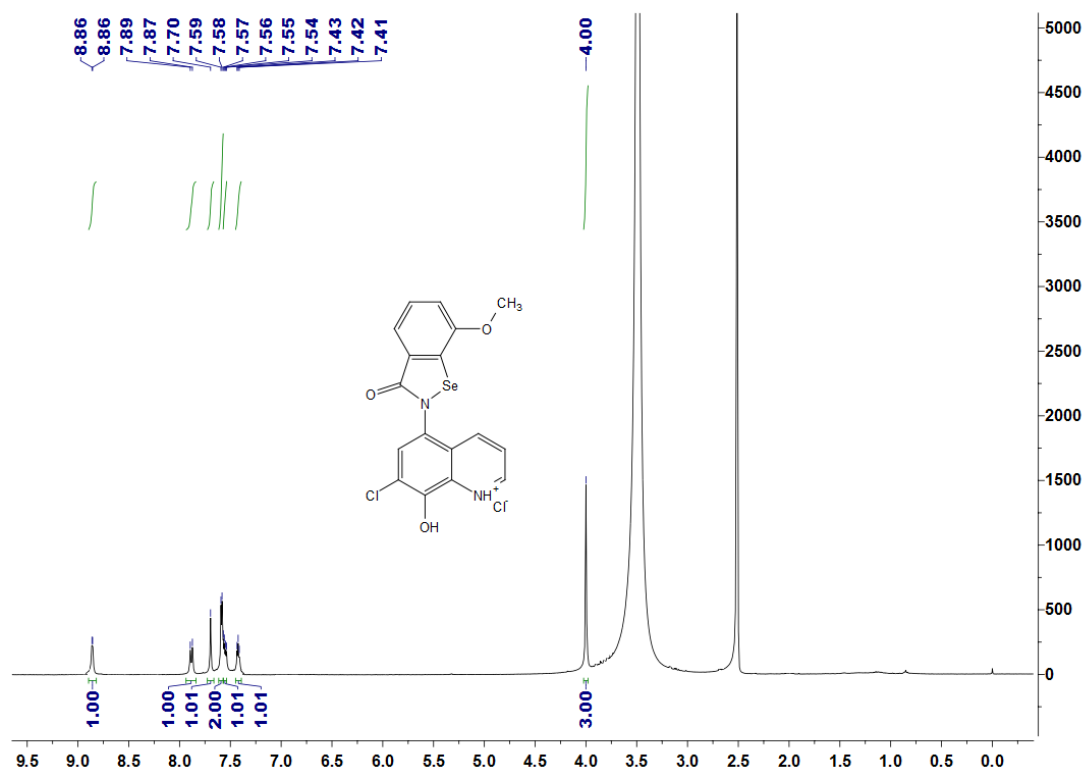
10l•HCl-¹H



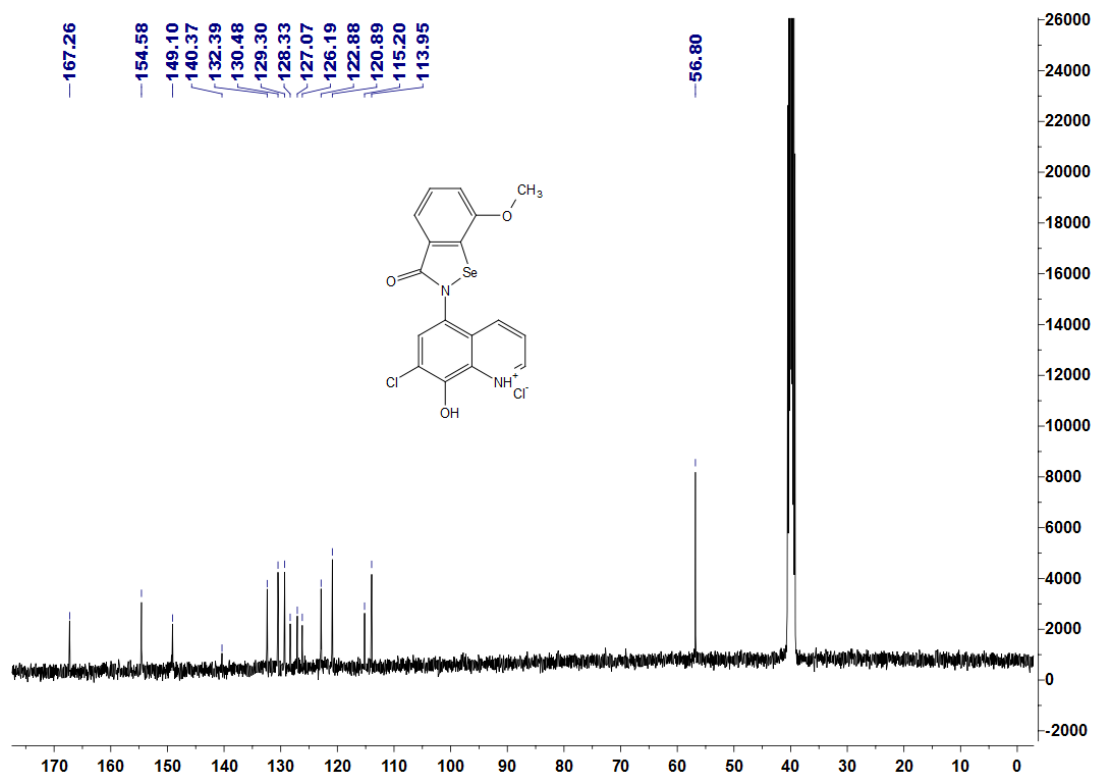
10l•HCl-¹³C



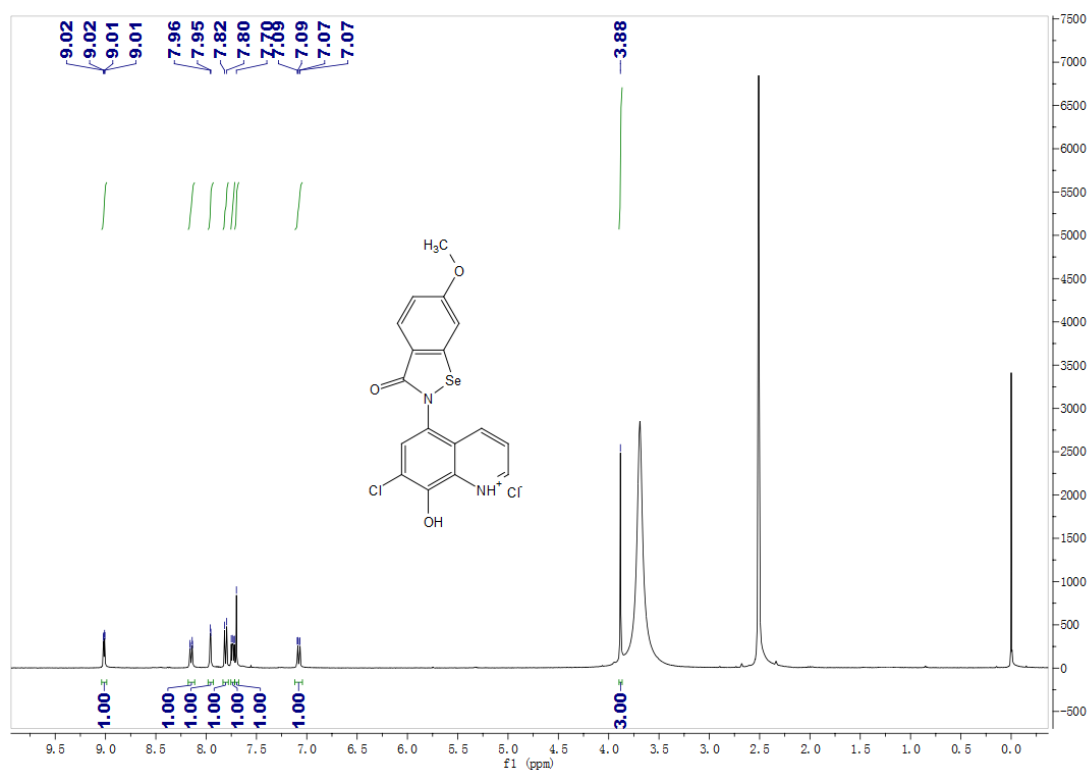
10m•HCl-¹H



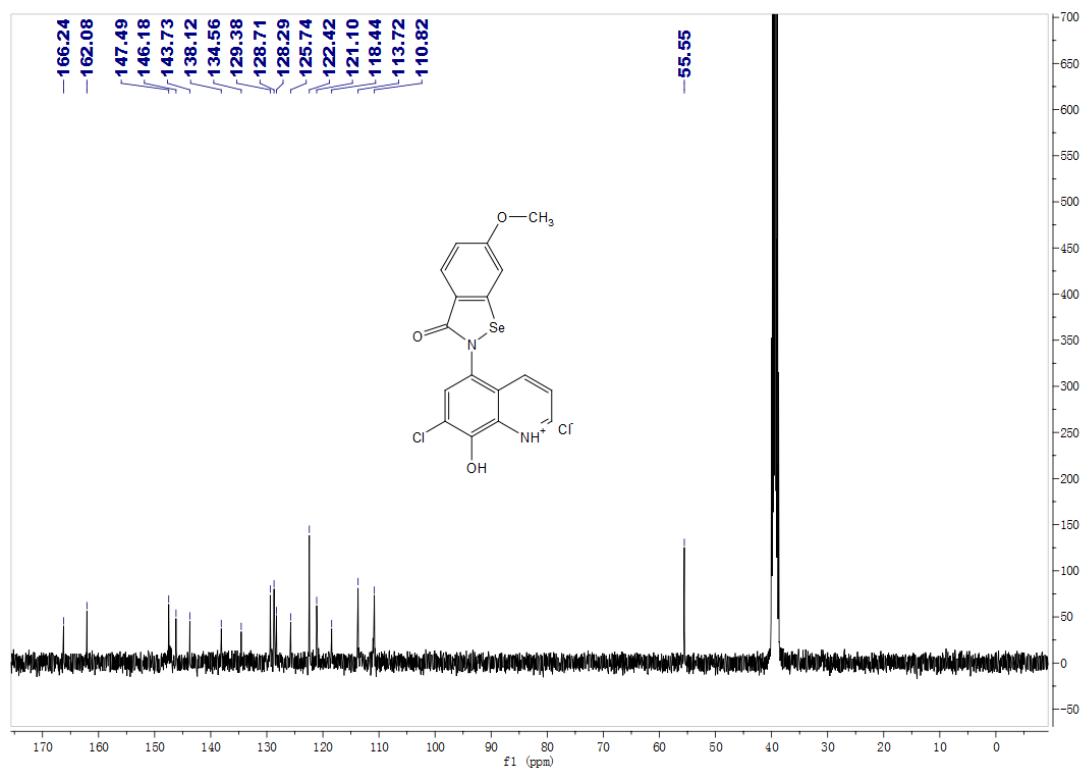
10m•HCl-¹³C



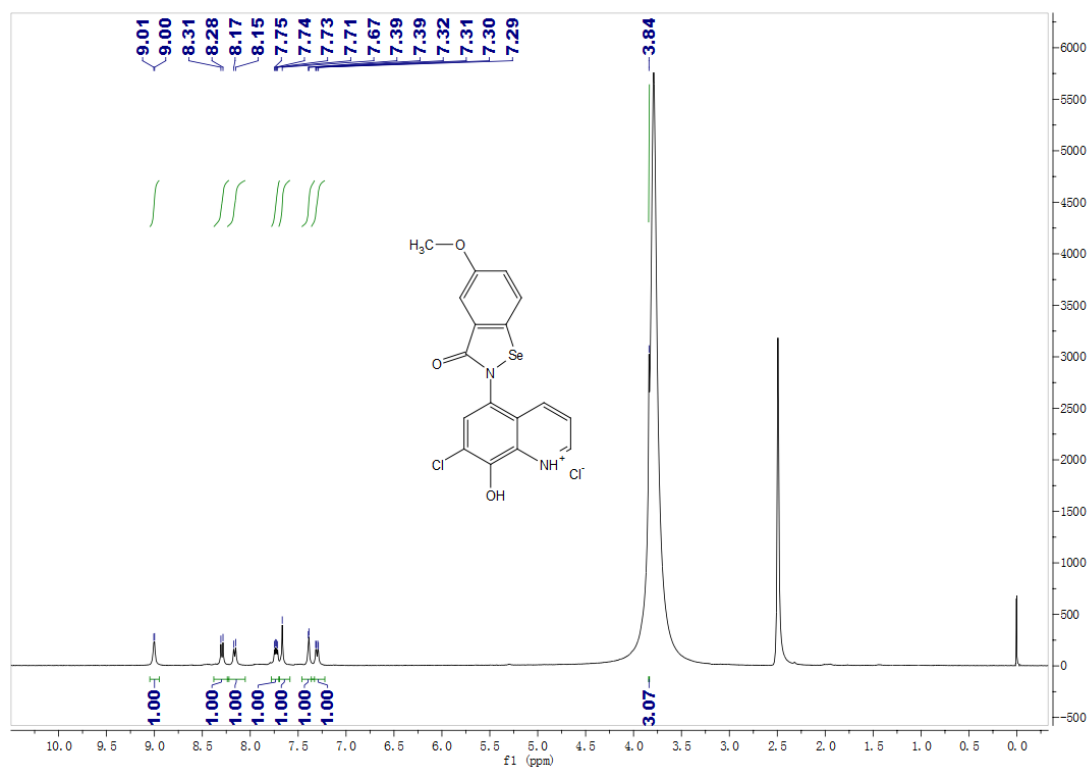
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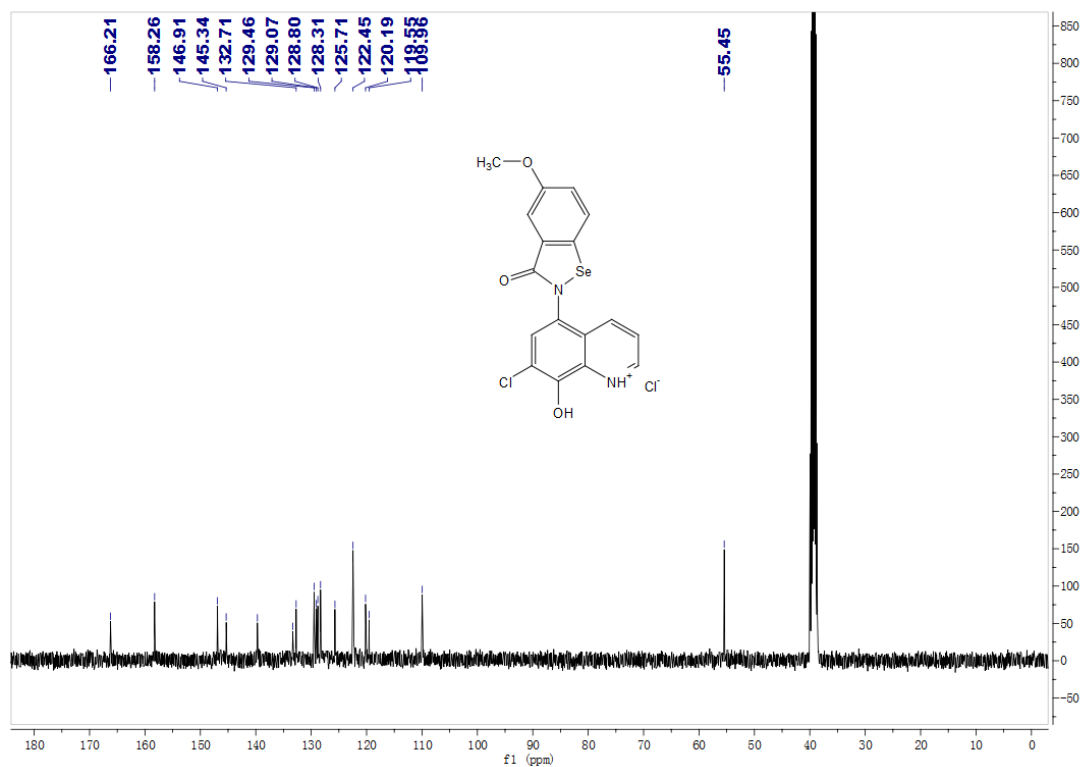
10n•HCl-¹³C



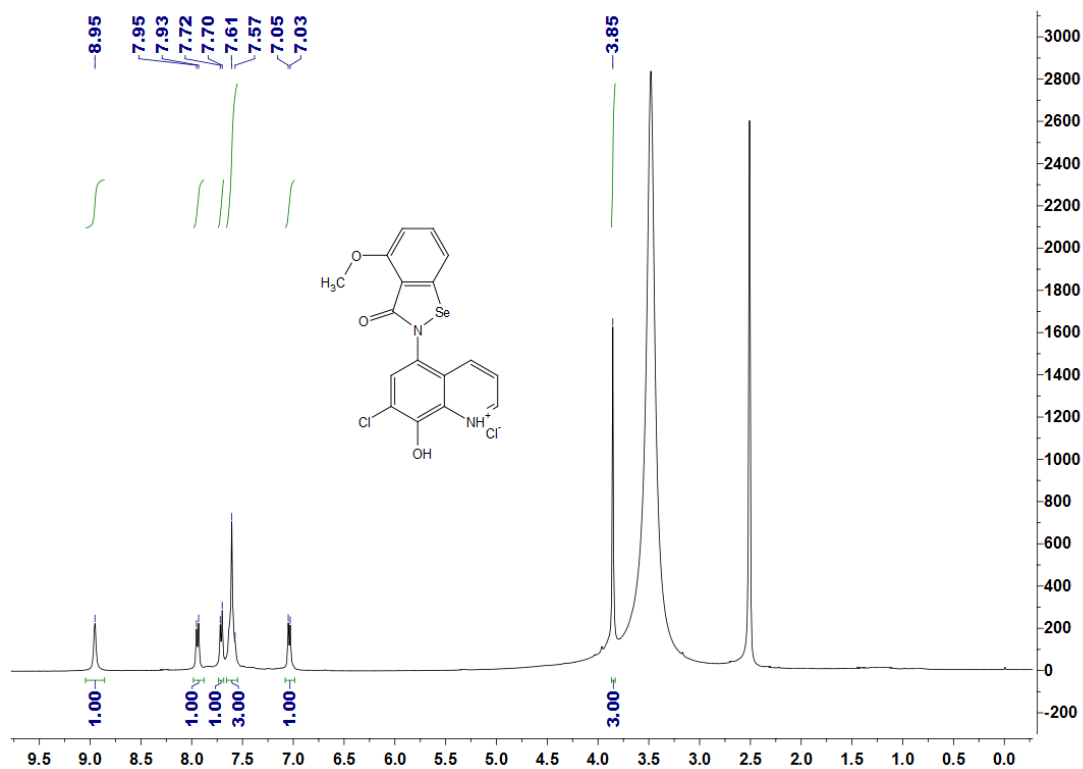
10o•HCl-¹H



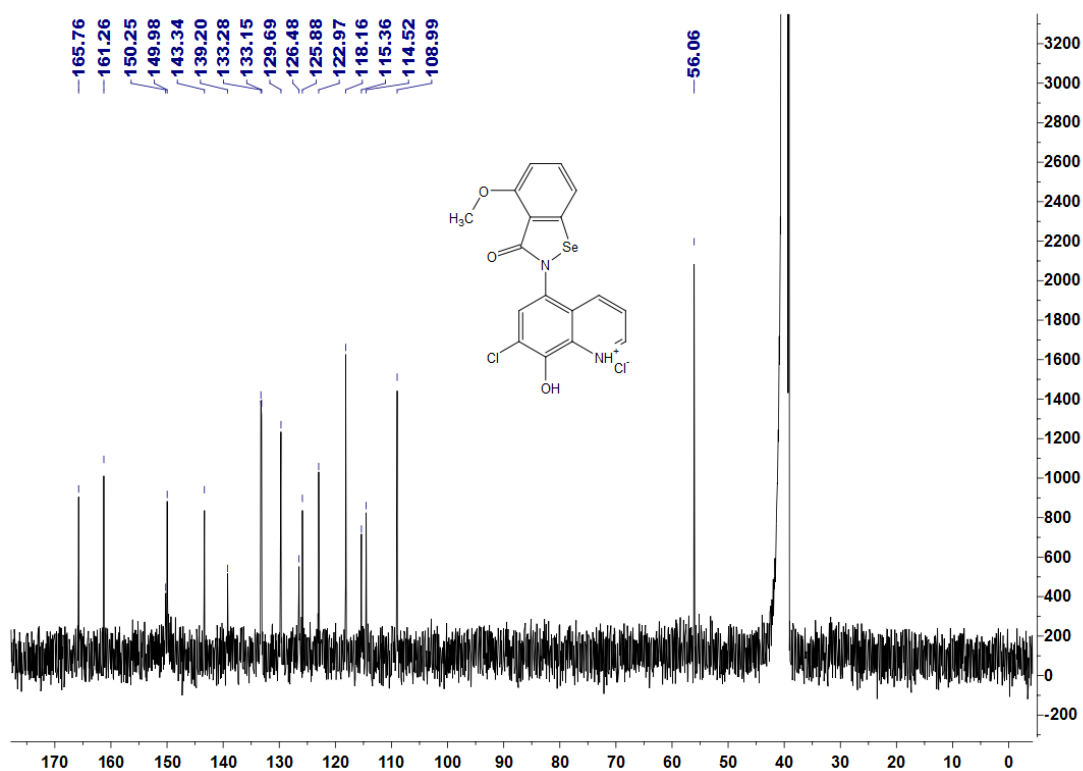
10o•HCl-¹³C



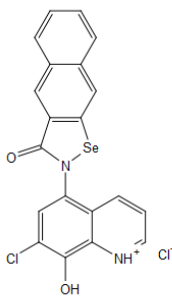
10p•HCl-¹H



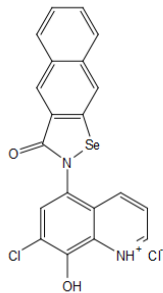
10p•HCl-¹³C

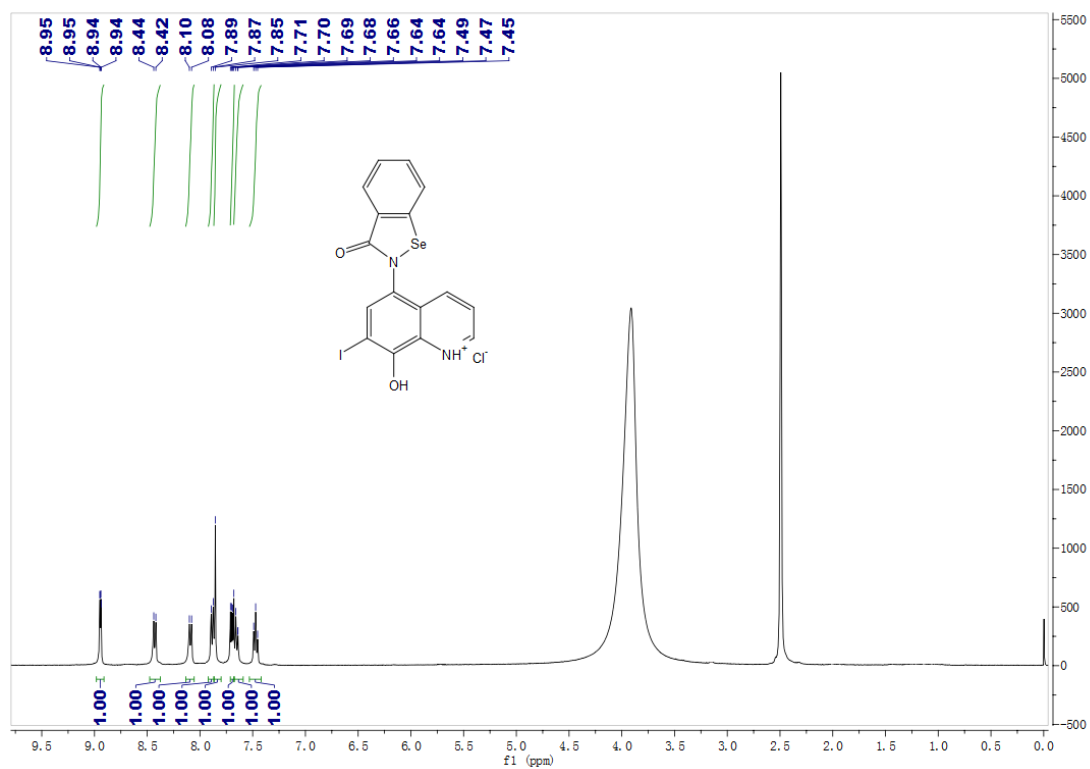


10q•HCl-¹H

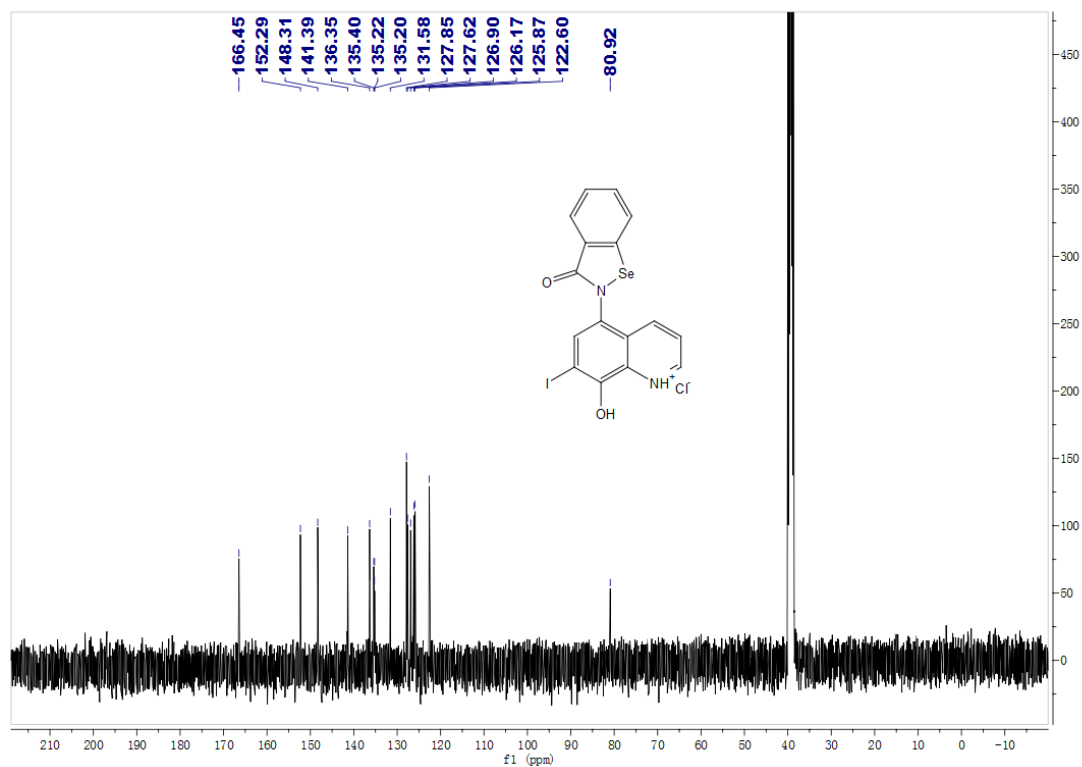


11a•HCl-¹H

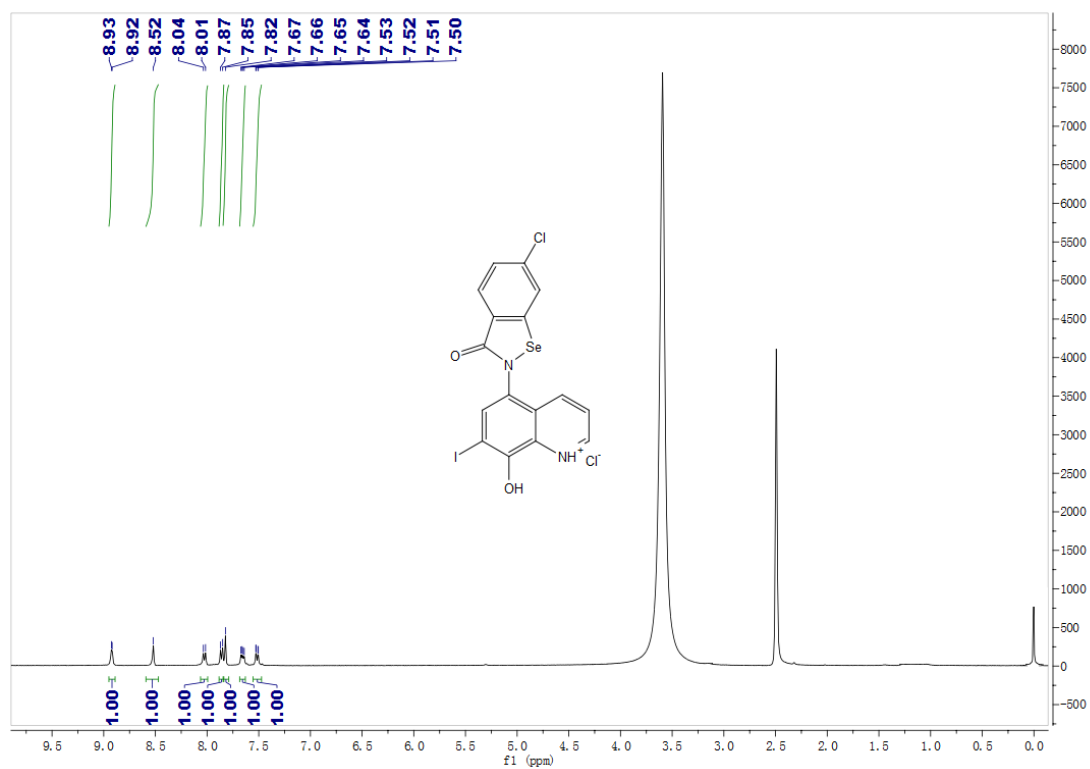




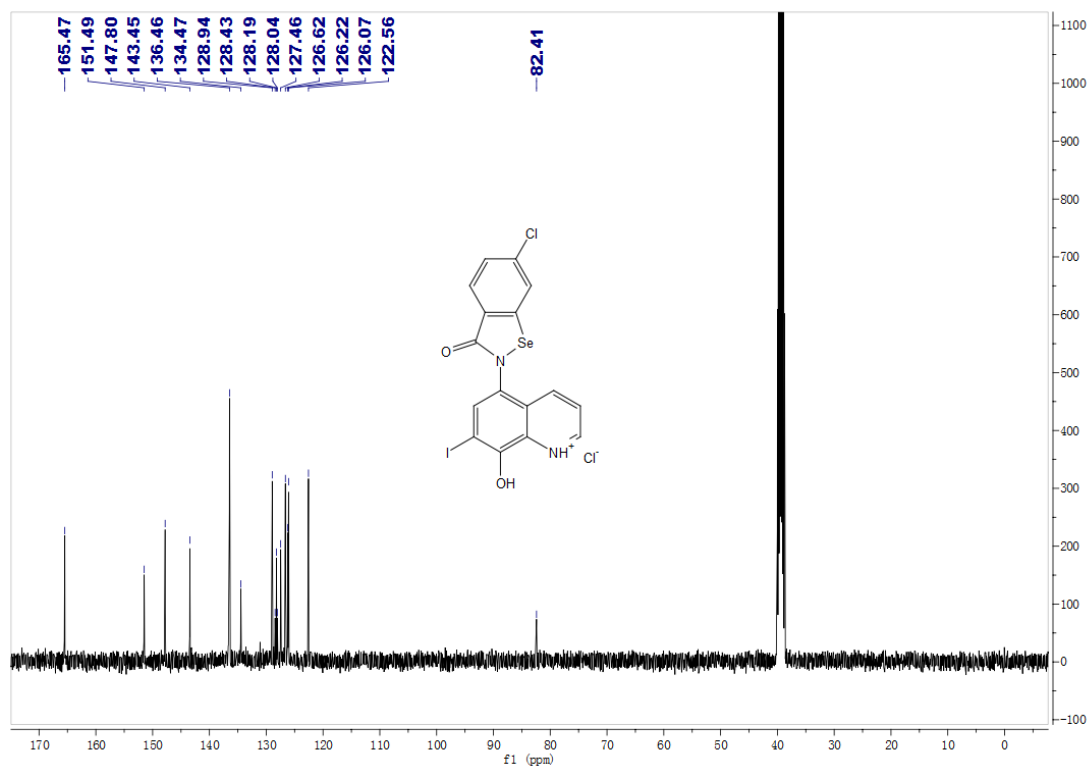
11a•HCl-¹³C



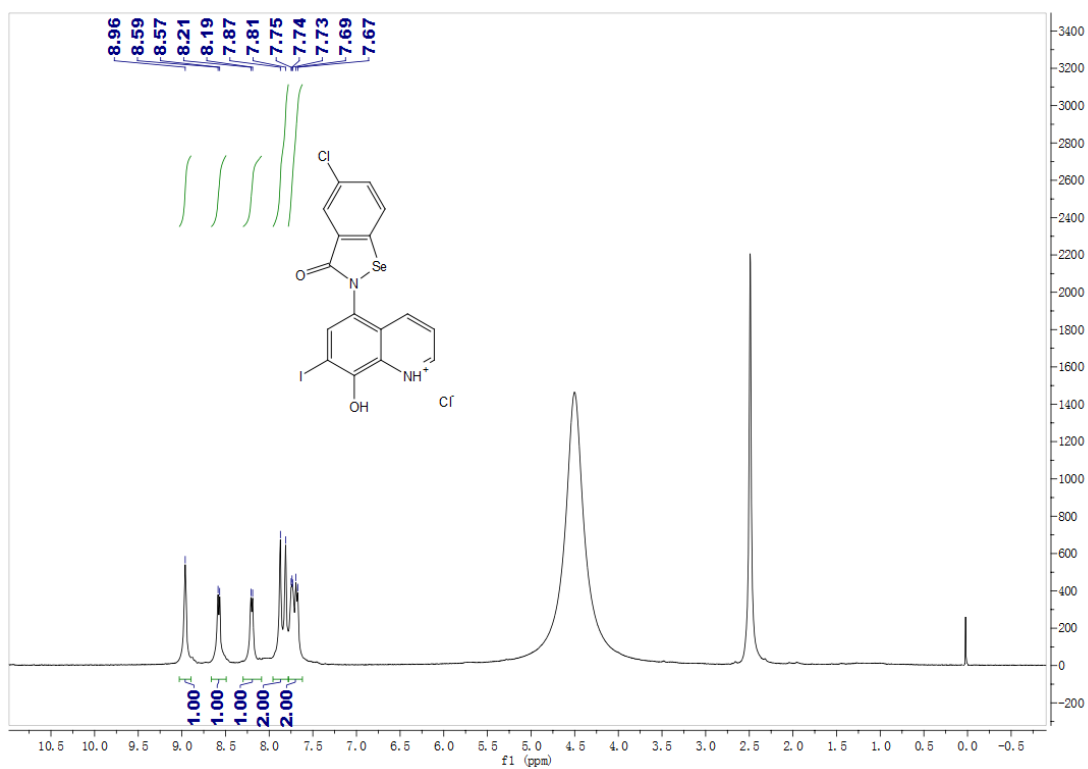
11b•HCl-¹H



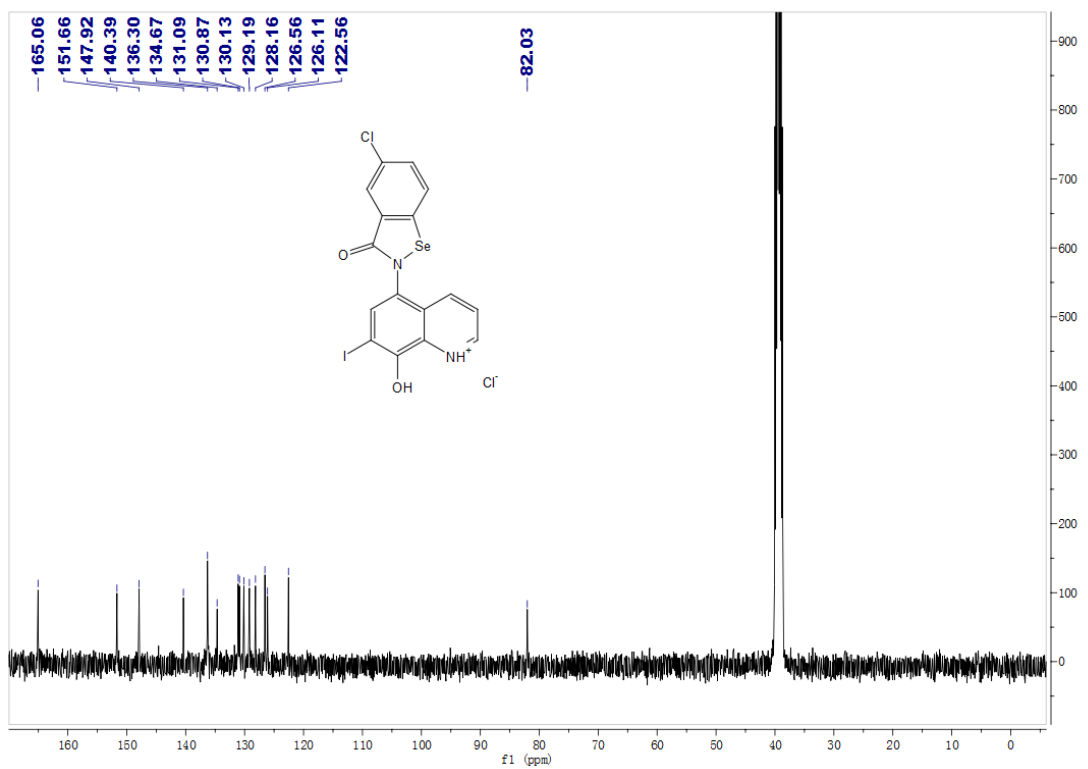
11b•HCl-¹³C



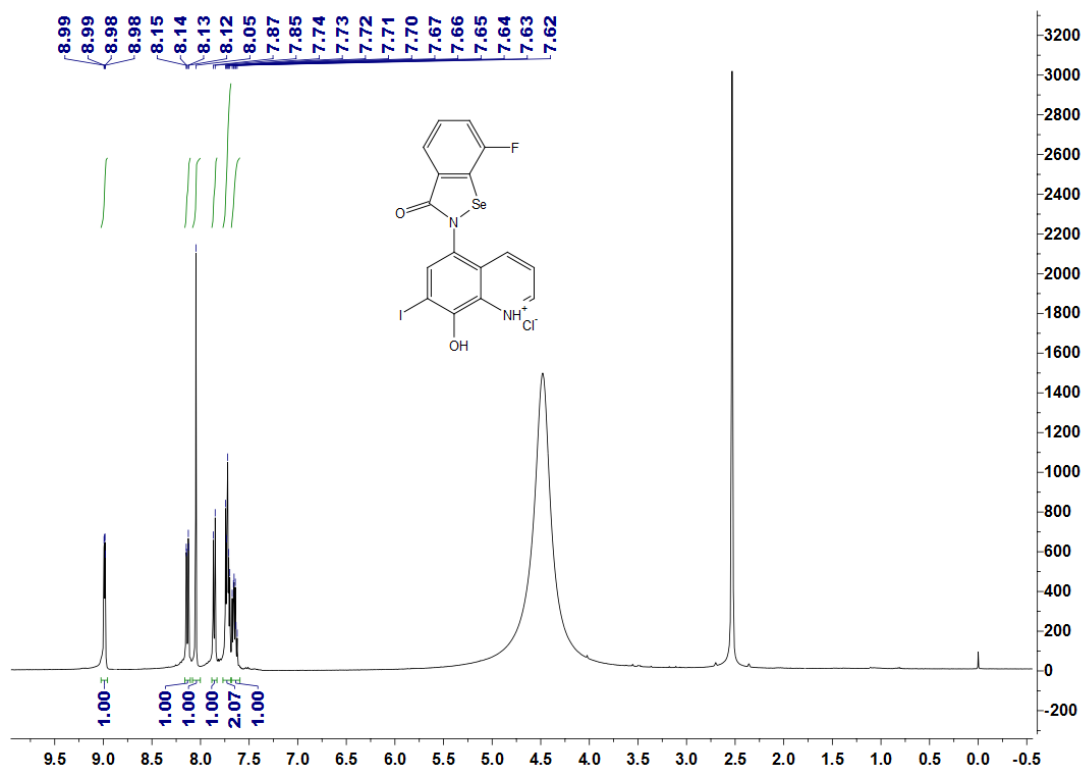
11c•HCl-¹H



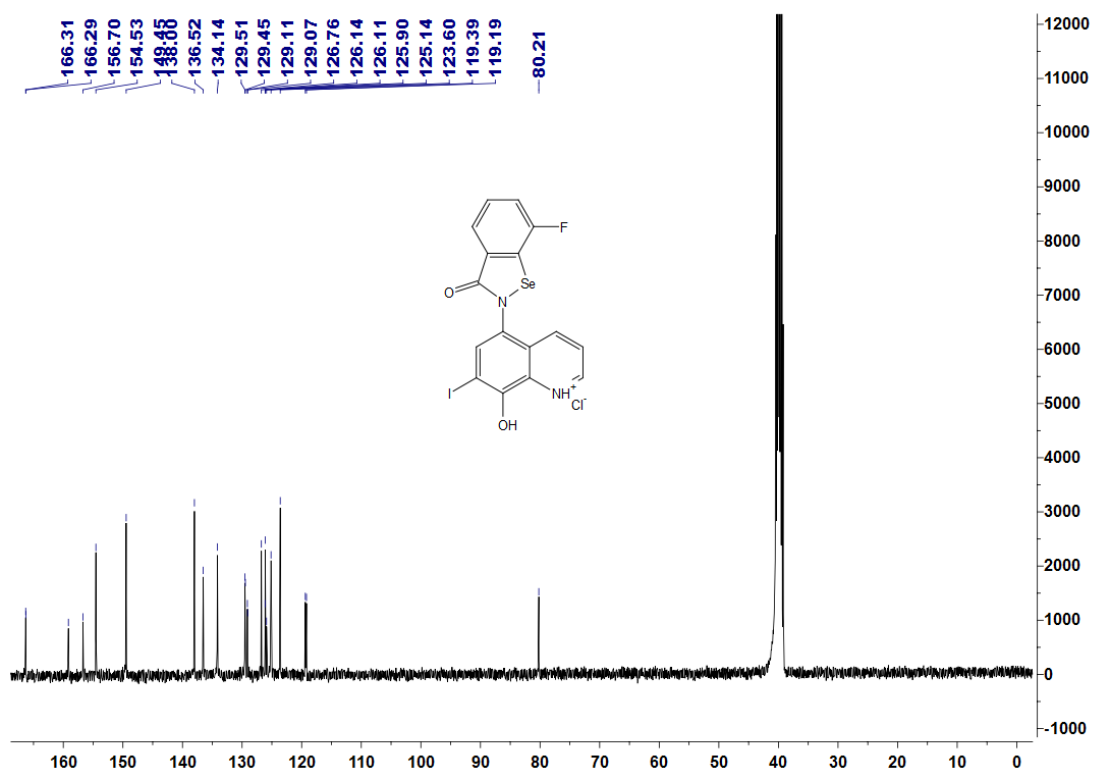
11c•HCl-¹³C



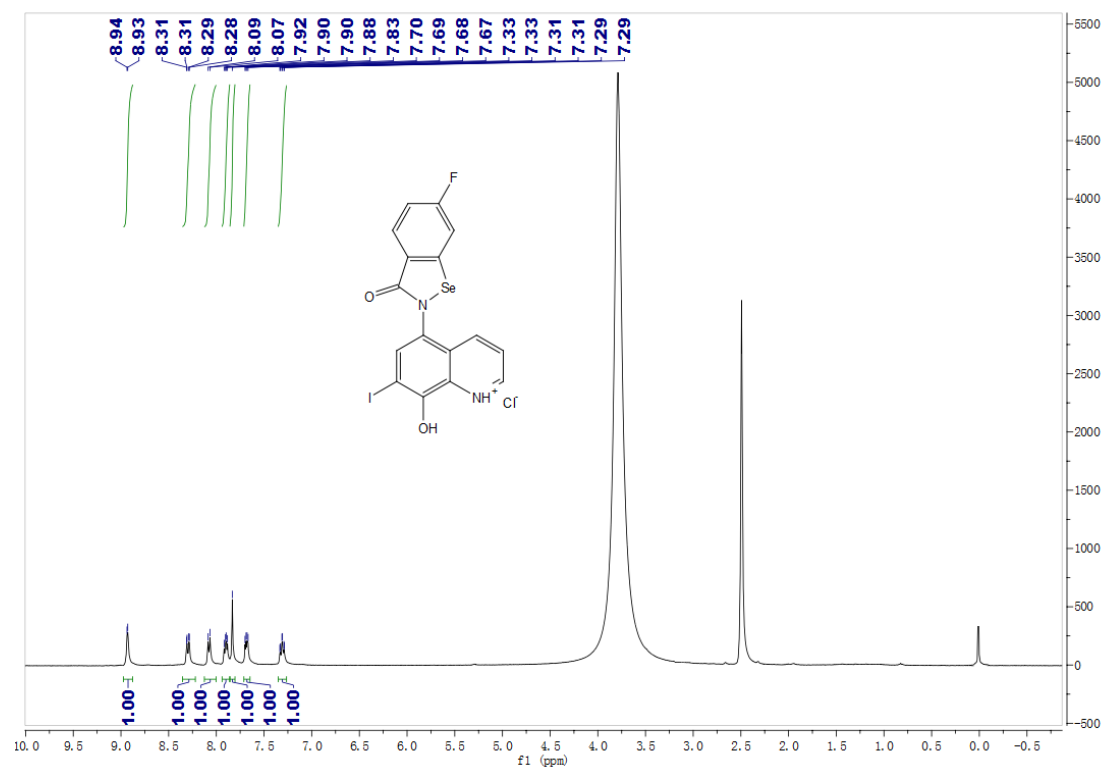
11e•HCl-¹H



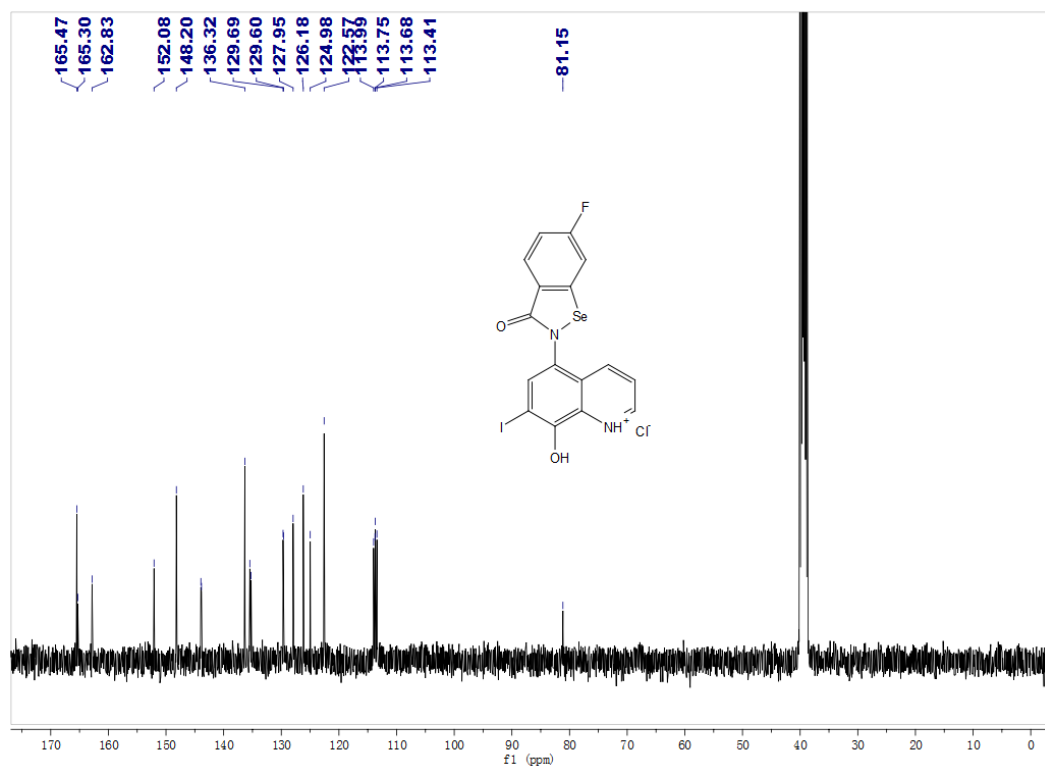
11e•HCl-¹³C



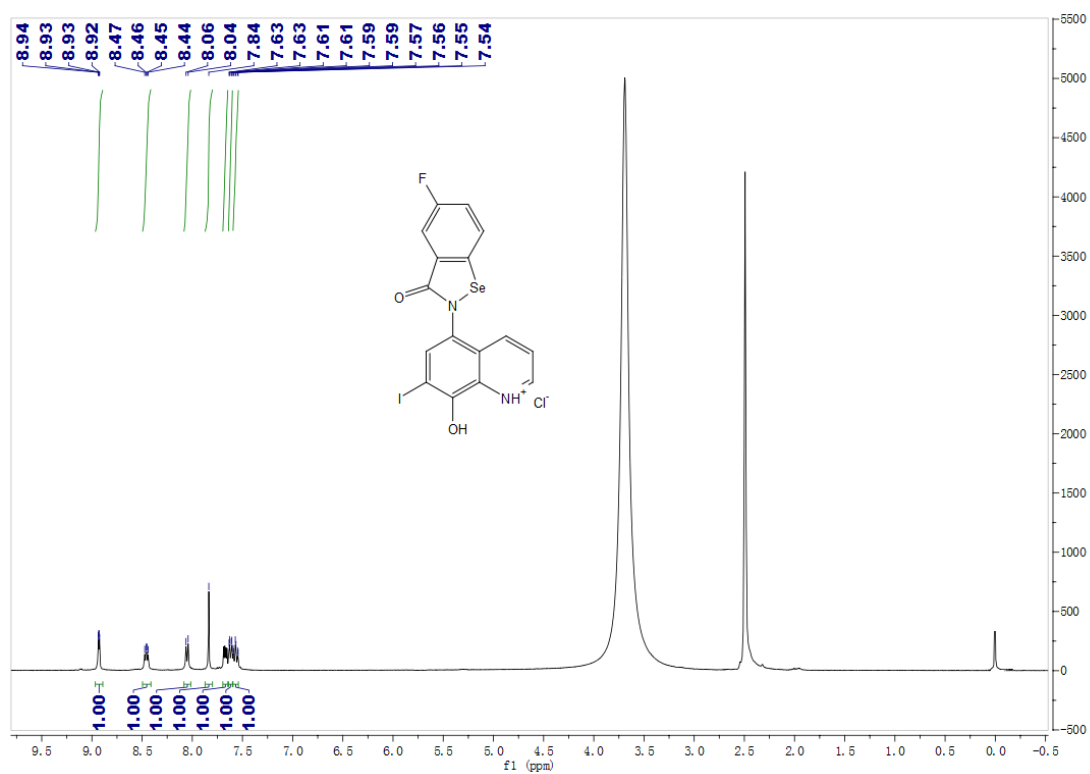
11f•HCl-¹H



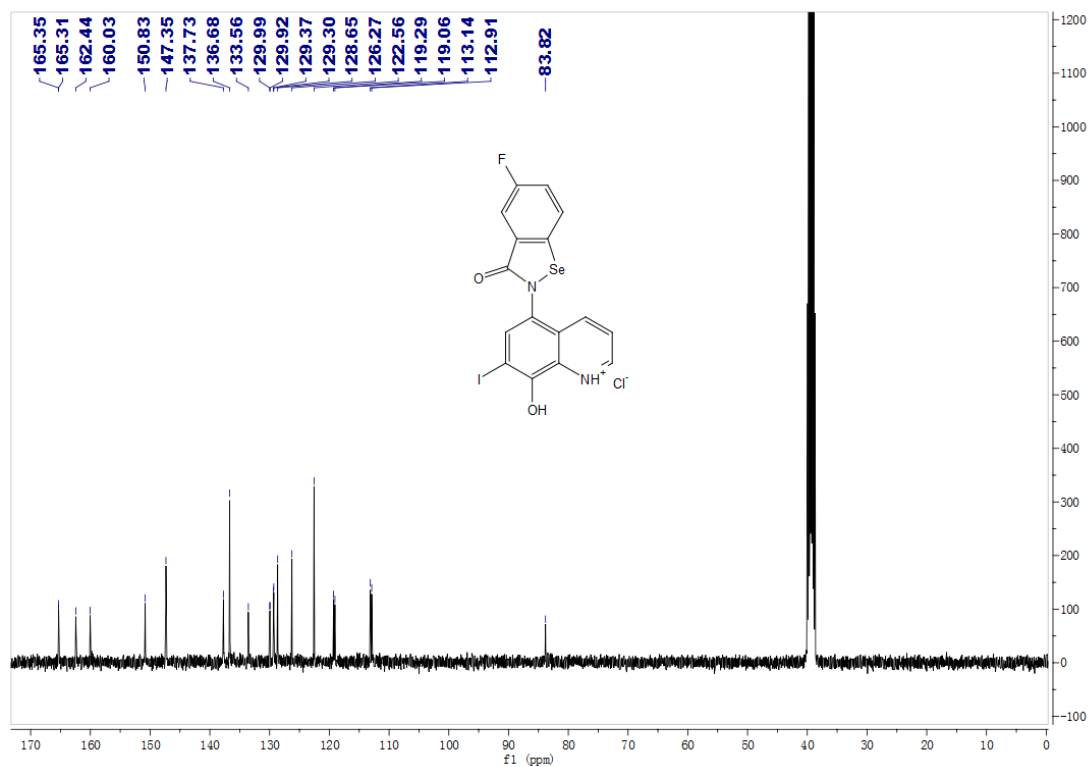
11f•HCl-¹³C



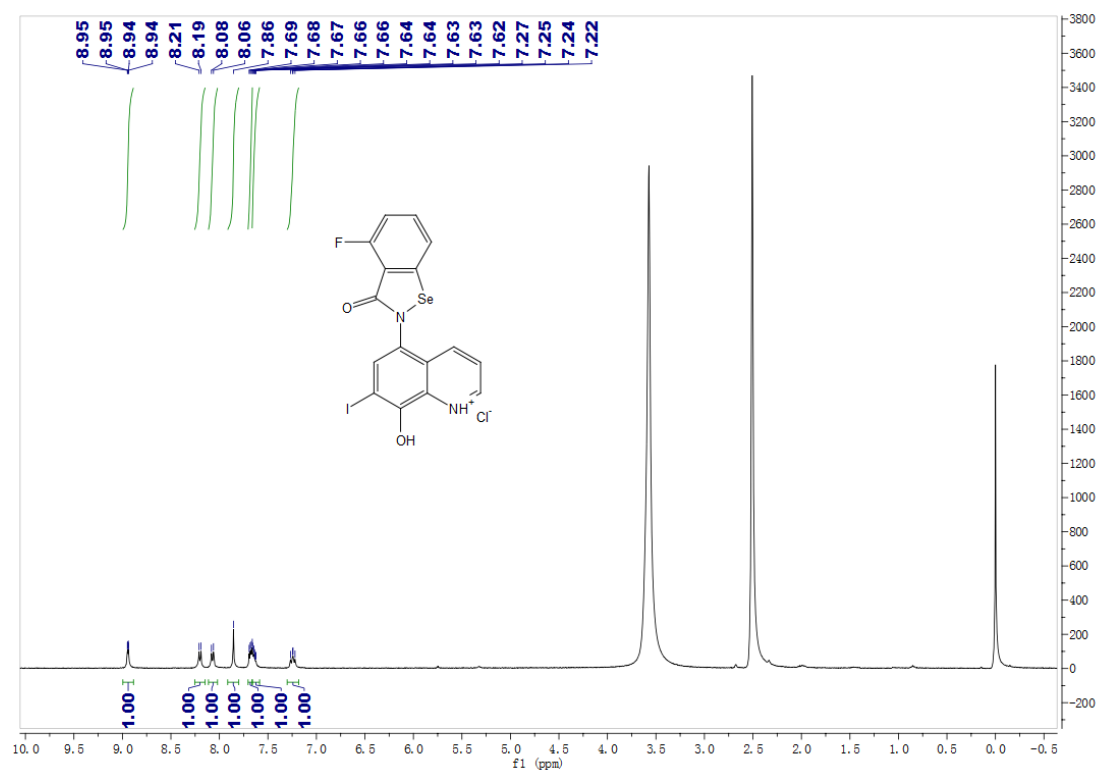
11g•HCl-¹H



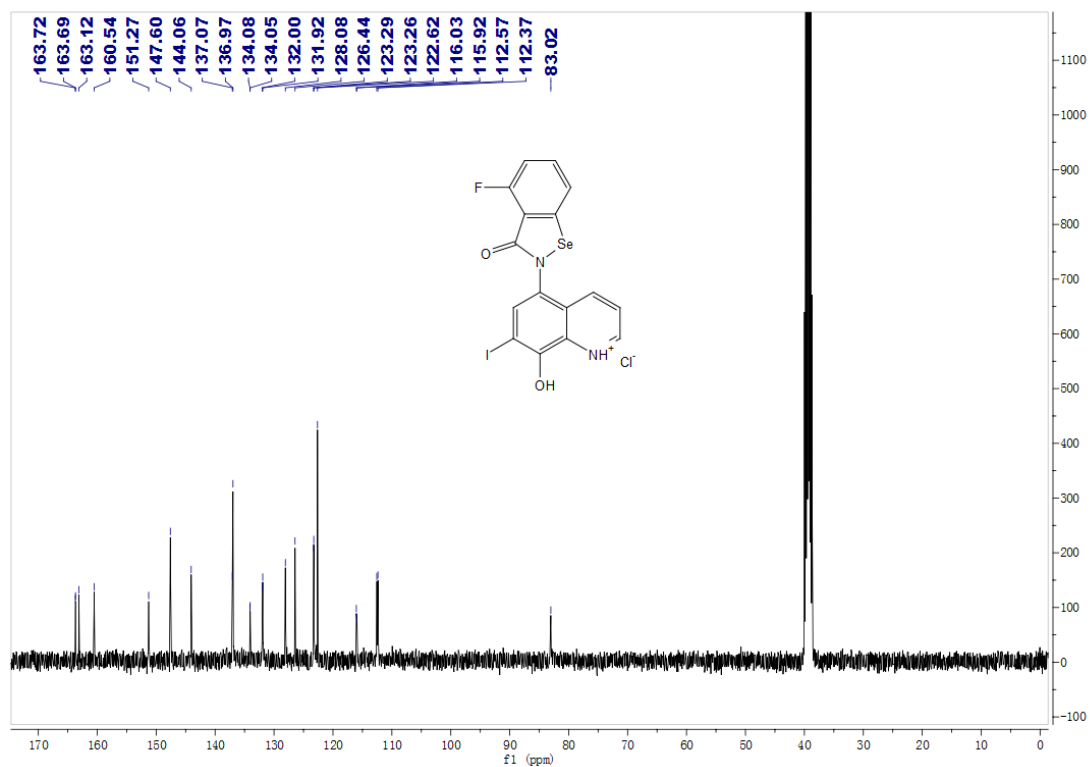
11g•HCl-¹³C



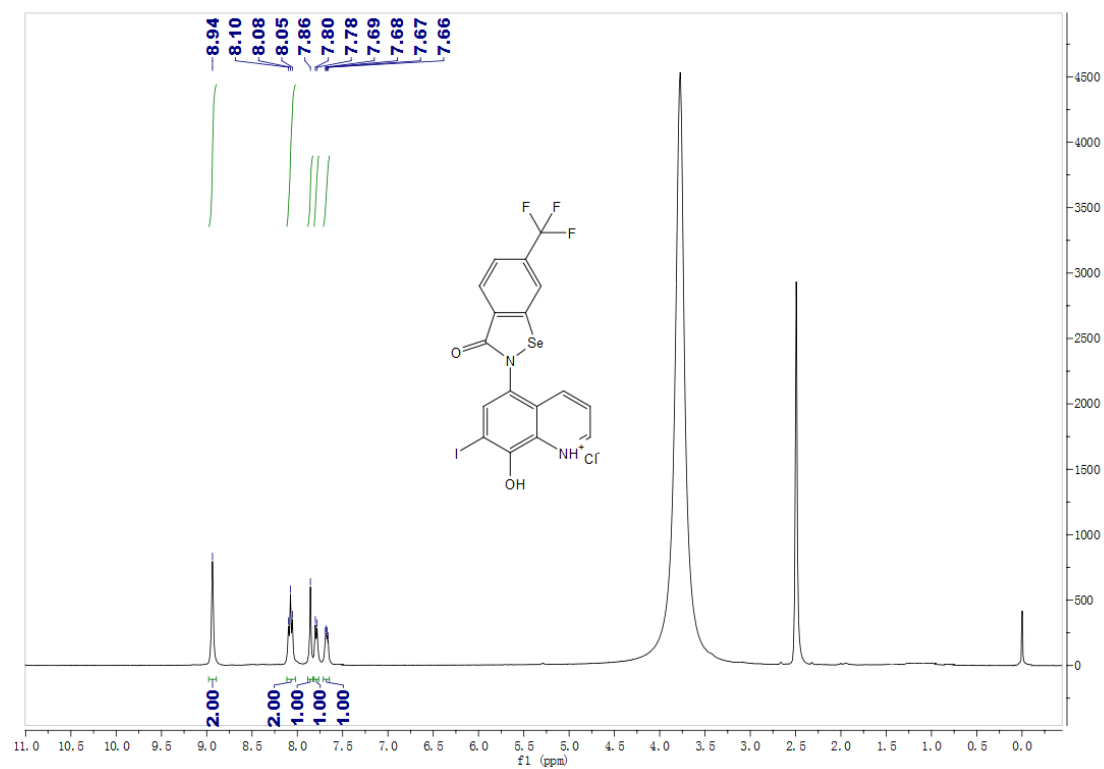
11h•HCl-¹H



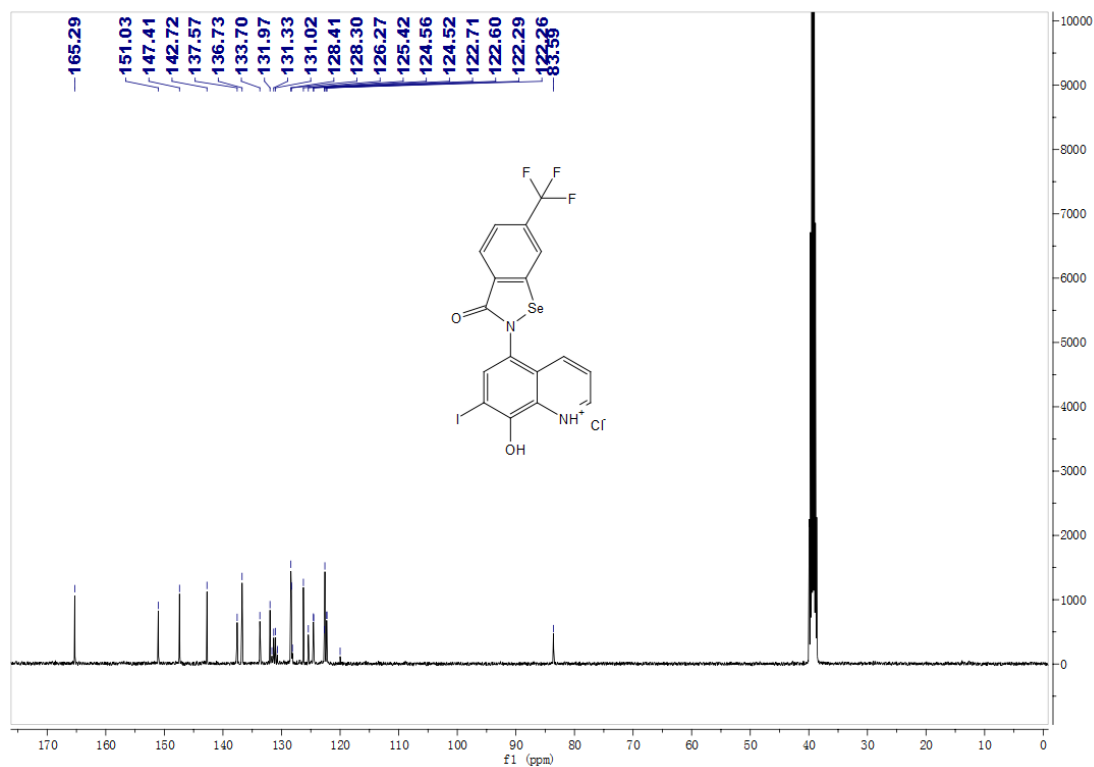
11h•HCl-¹³C



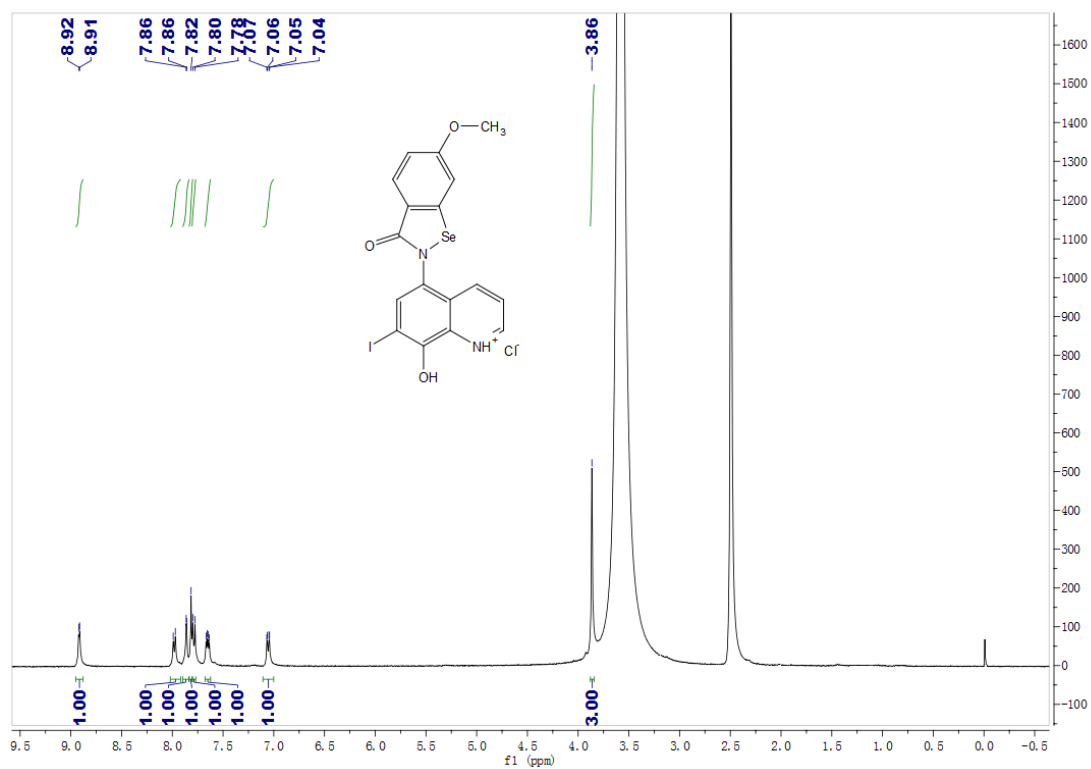
11j•HCl-¹H



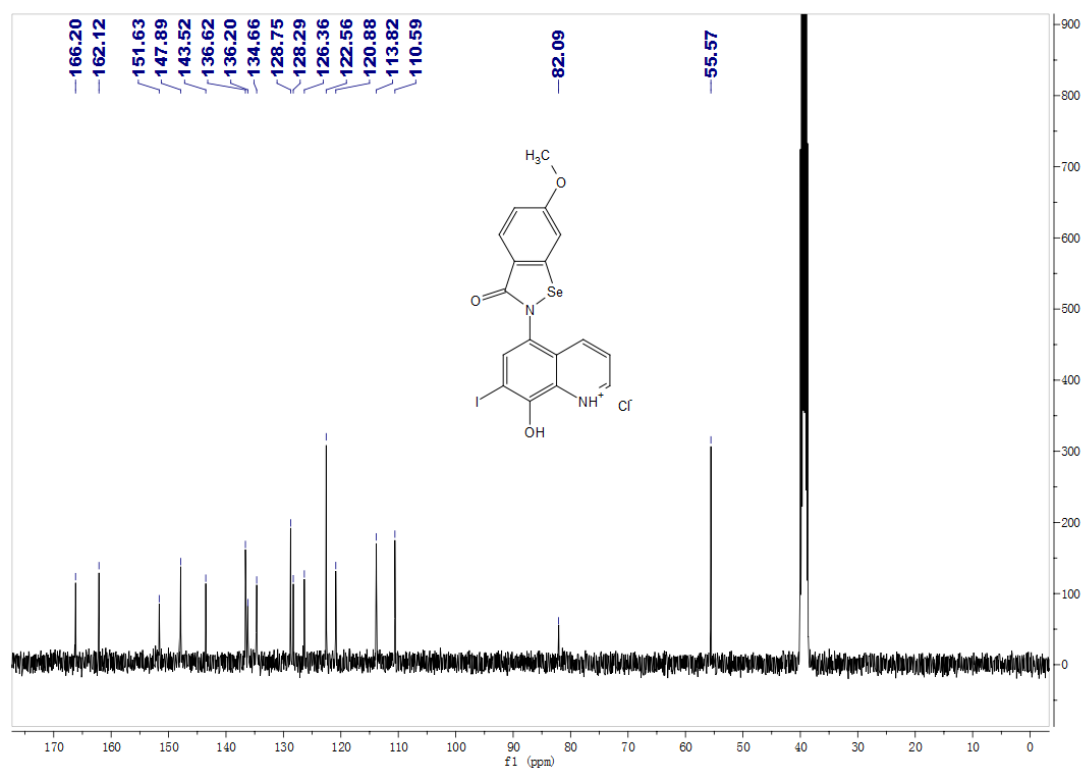
11j•HCl-¹³C



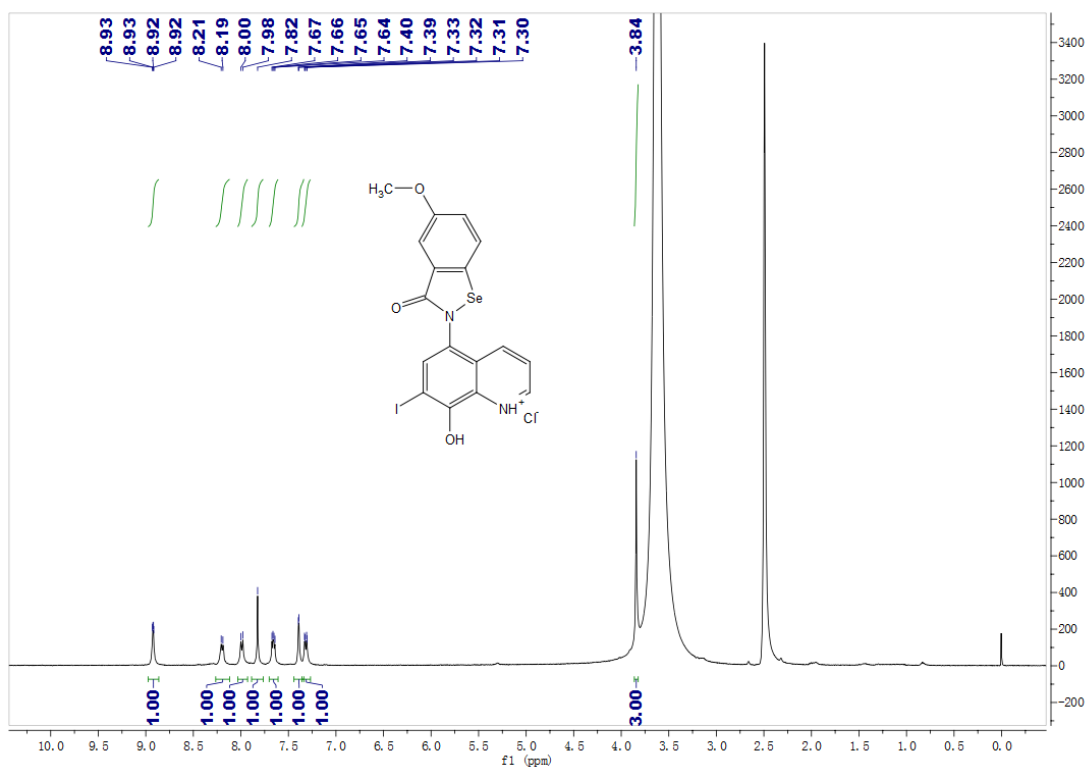
11n•HCl-¹H



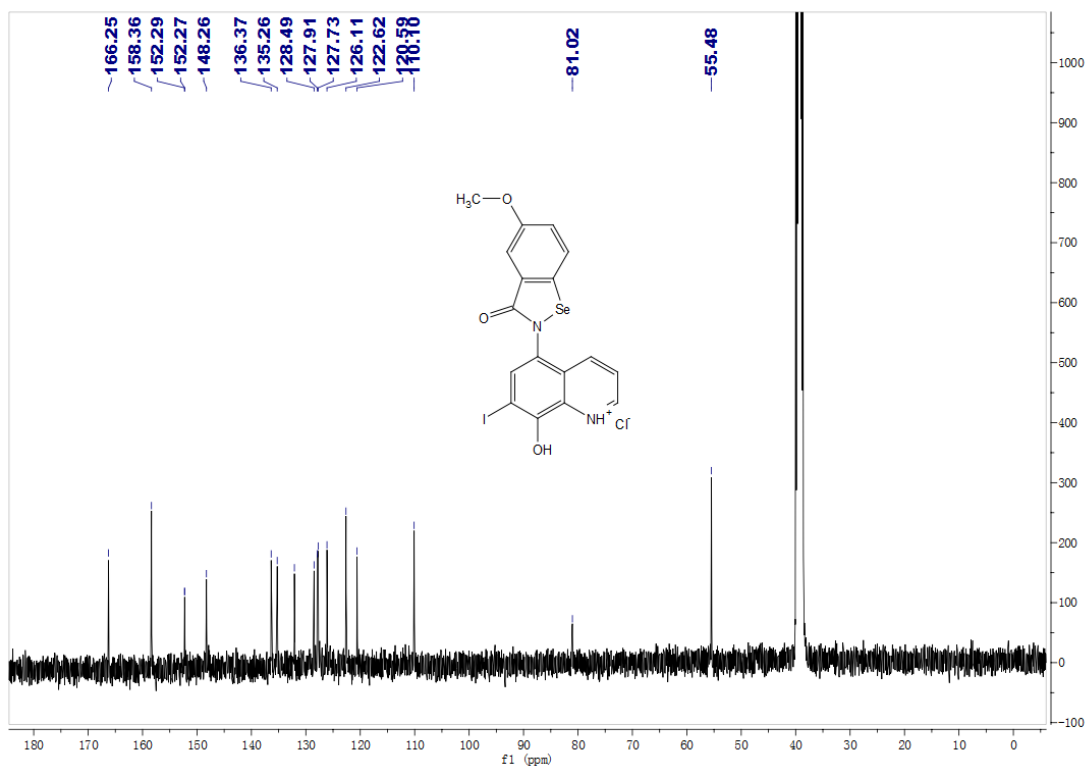
11n•HCl-¹³C



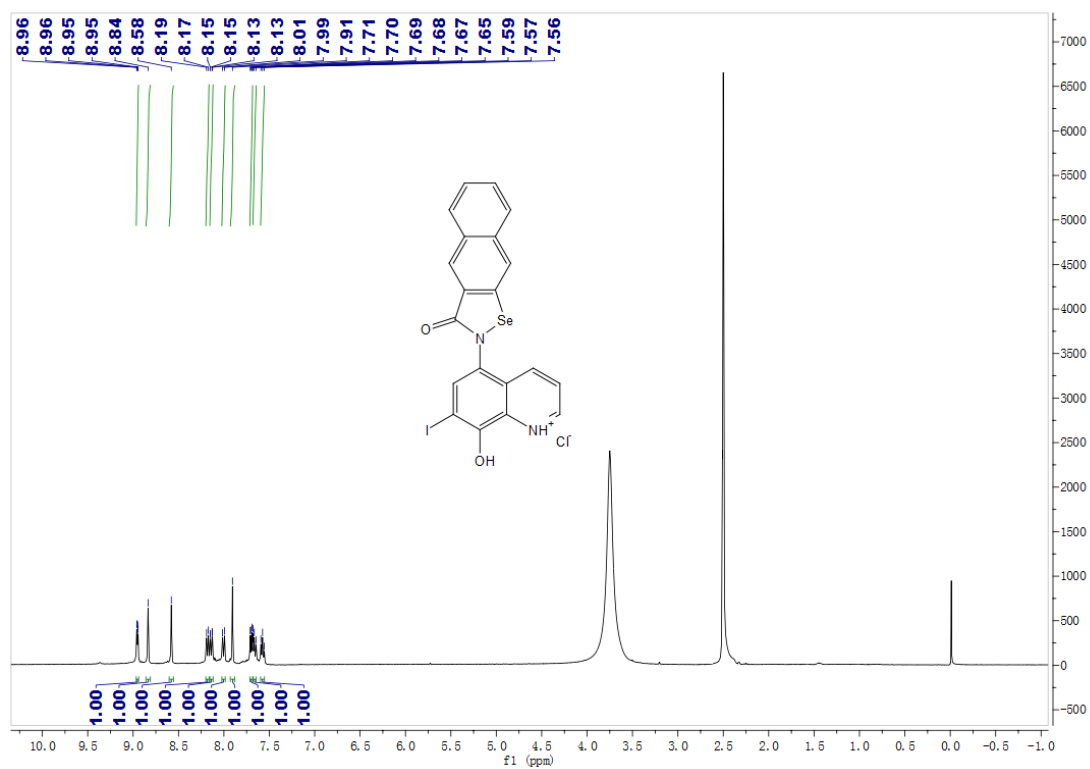
11o•HCl-¹H



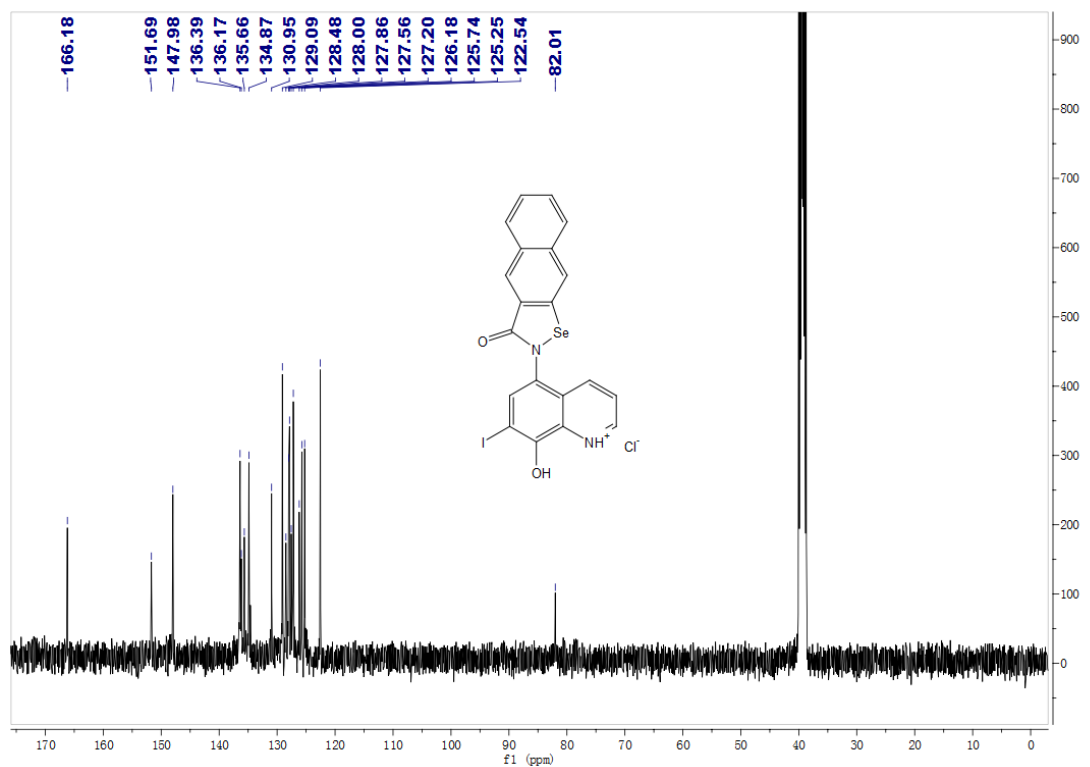
11o•HCl-¹³C



11q•HCl-¹H

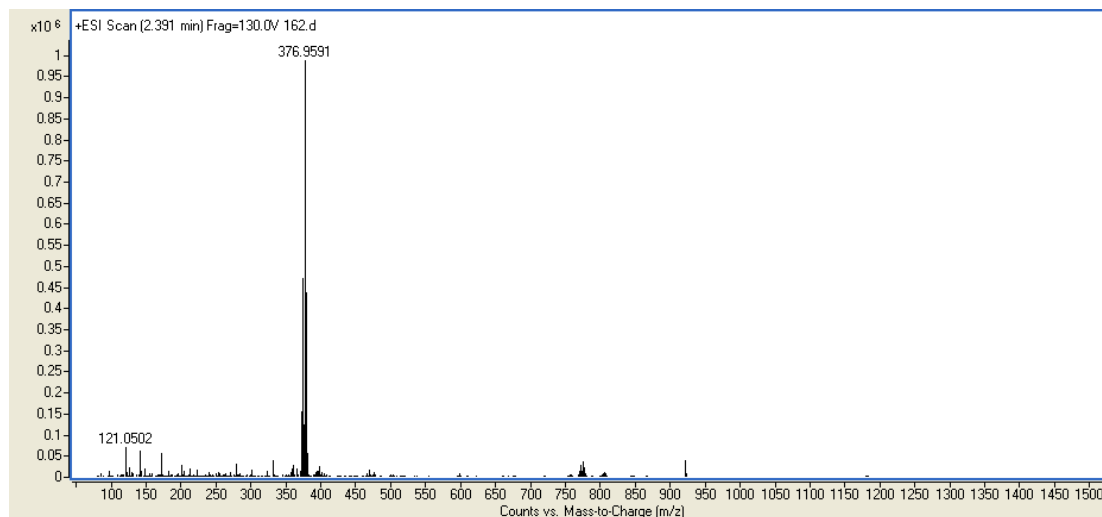


11q•HCl-¹³C

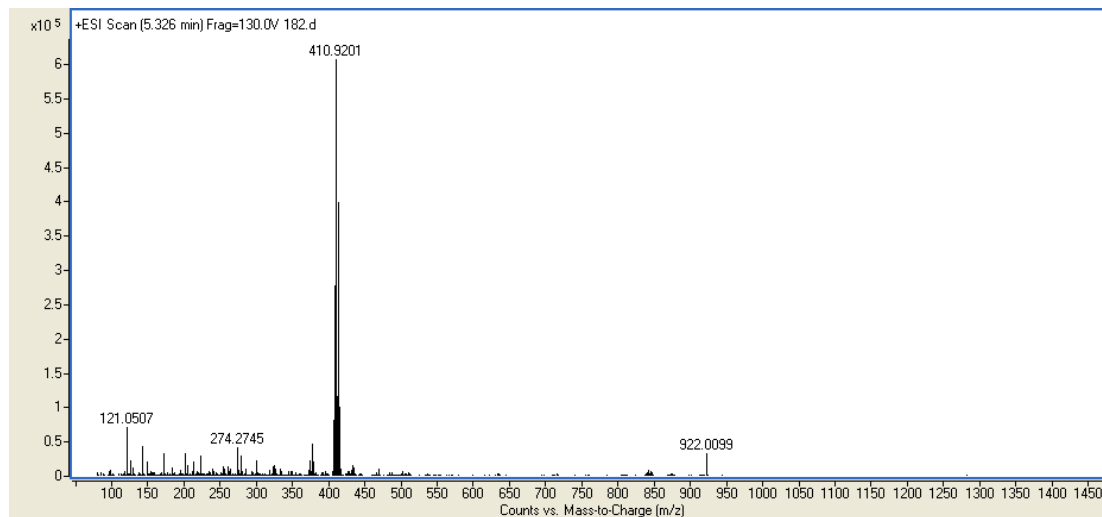


2. LC-HRMS Spectrum of the Target Compound

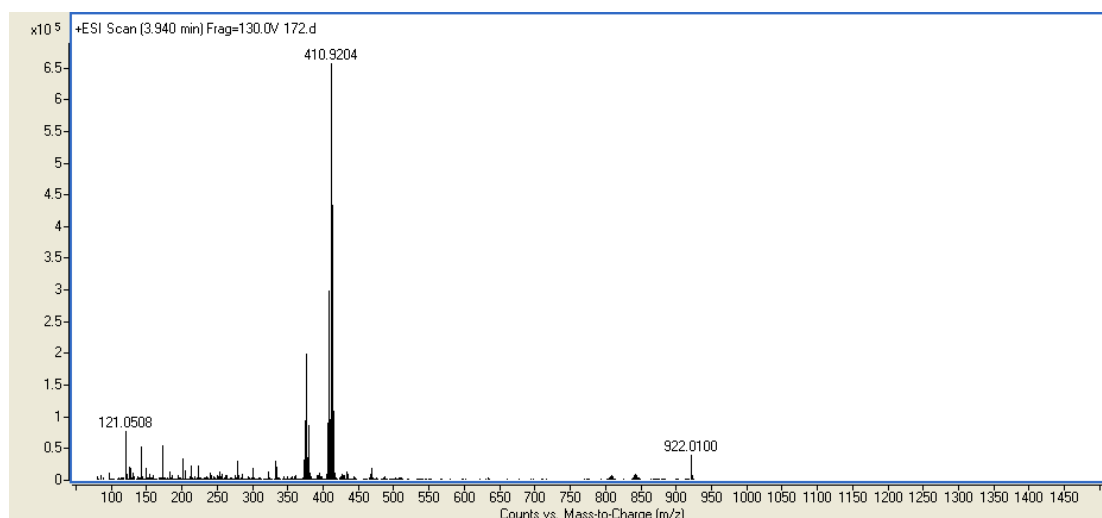
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10a	C ₁₆ H ₉ ClN ₂ O ₂ Se	C ₁₆ H ₁₀ ClN ₂ O ₂ Se	376.9591	376.9591	0



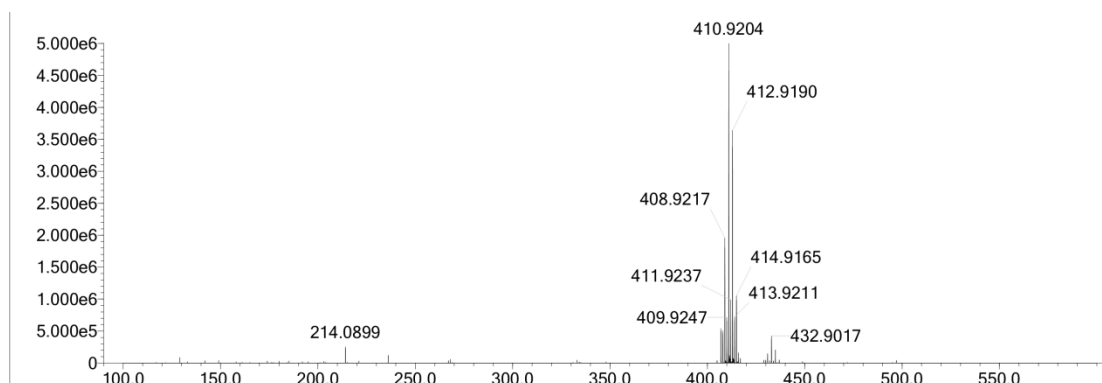
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10b	C ₁₆ H ₈ Cl ₂ N ₂ O ₂ Se	C ₁₆ H ₉ Cl ₂ N ₂ O ₂ Se	410.9201	410.9201	0



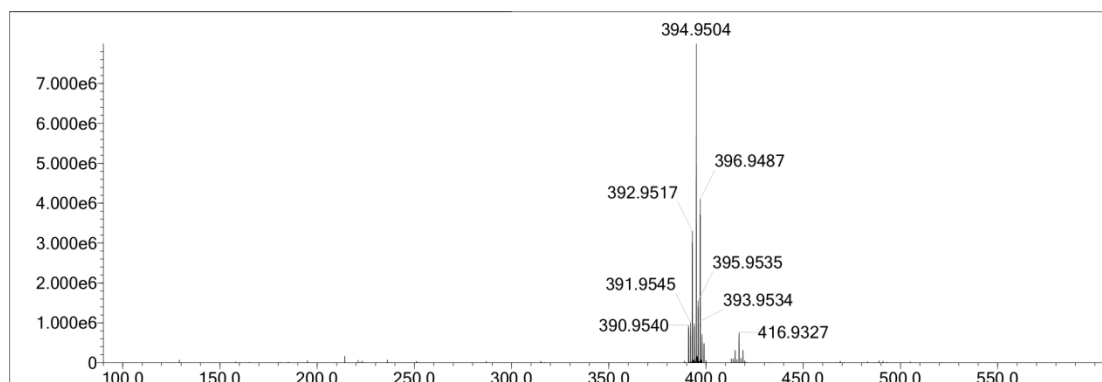
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10c	C ₁₆ H ₈ Cl ₂ N ₂ O ₂ Se	C ₁₆ H ₉ Cl ₂ N ₂ O ₂ Se	410.9204	410.9201	-0.73



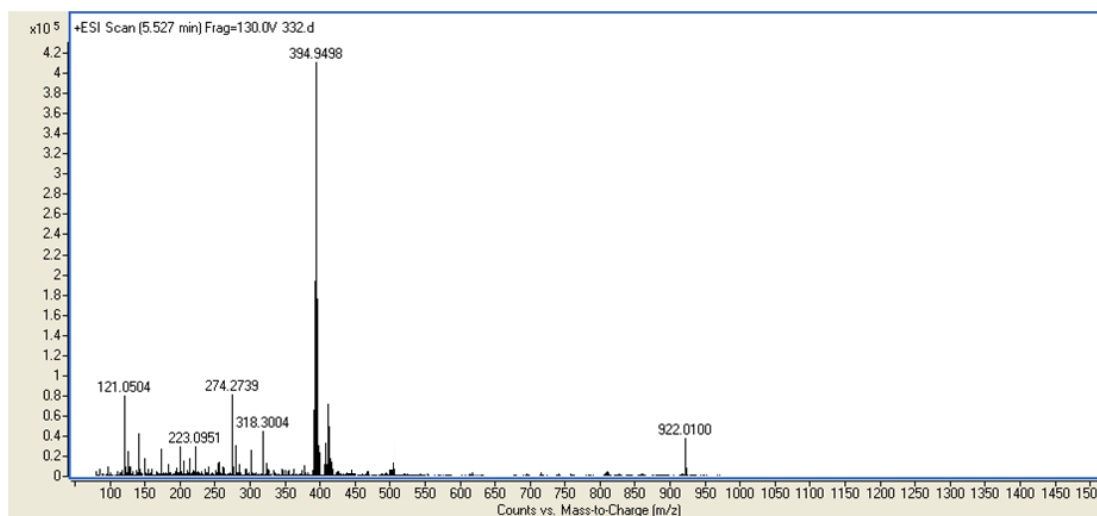
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10d	C ₁₆ H ₈ Cl ₂ N ₂ O ₂ Se	C ₁₆ H ₉ Cl ₂ N ₂ O ₂ Se	410.9204	410.9201	-0.73



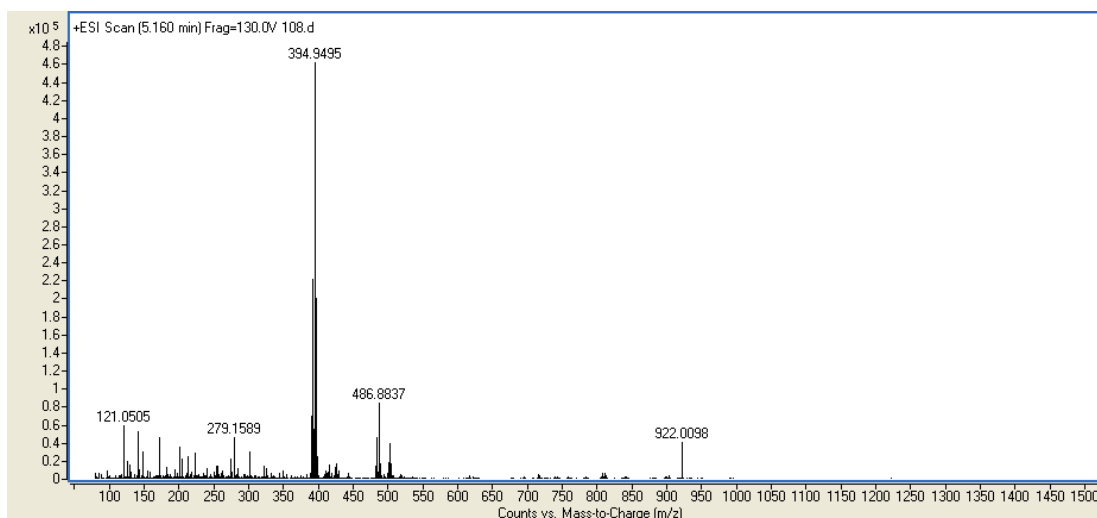
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10e	C ₁₆ H ₈ ClFN ₂ O ₂ Se	C ₁₆ H ₉ ClFN ₂ O ₂ Se	394.9504	394.9496	2.41



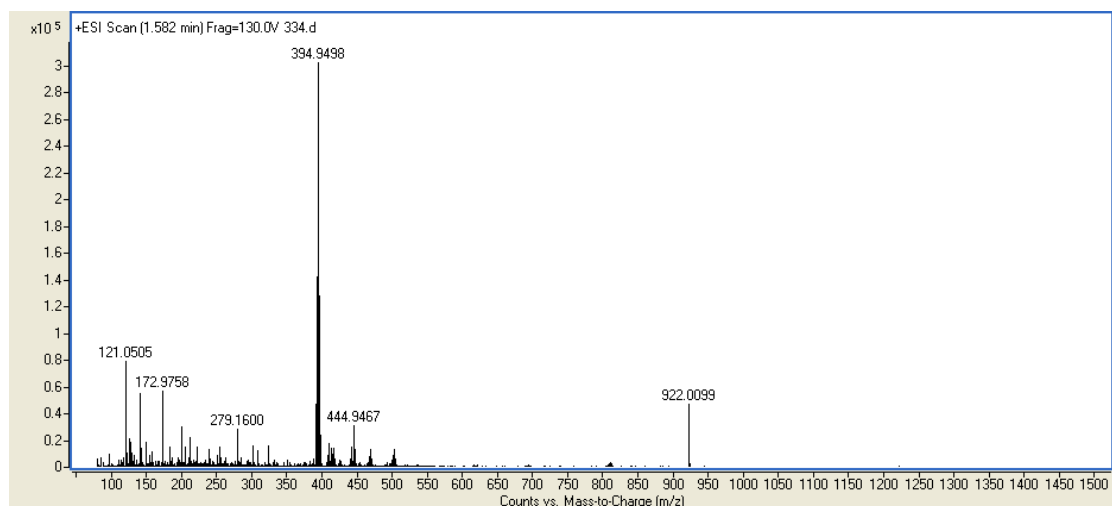
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10f	C ₁₆ H ₈ ClFN ₂ O ₂ Se	C ₁₆ H ₉ ClFN ₂ O ₂ Se	394.9498	394.9496	-0.51



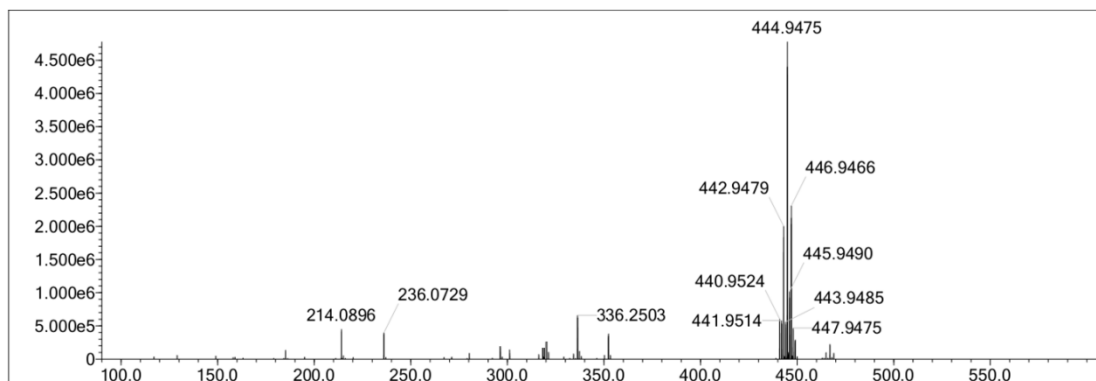
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10g	C ₁₆ H ₈ ClFN ₂ O ₂ Se	C ₁₆ H ₉ ClFN ₂ O ₂ Se	394.9495	394.9496	0.26



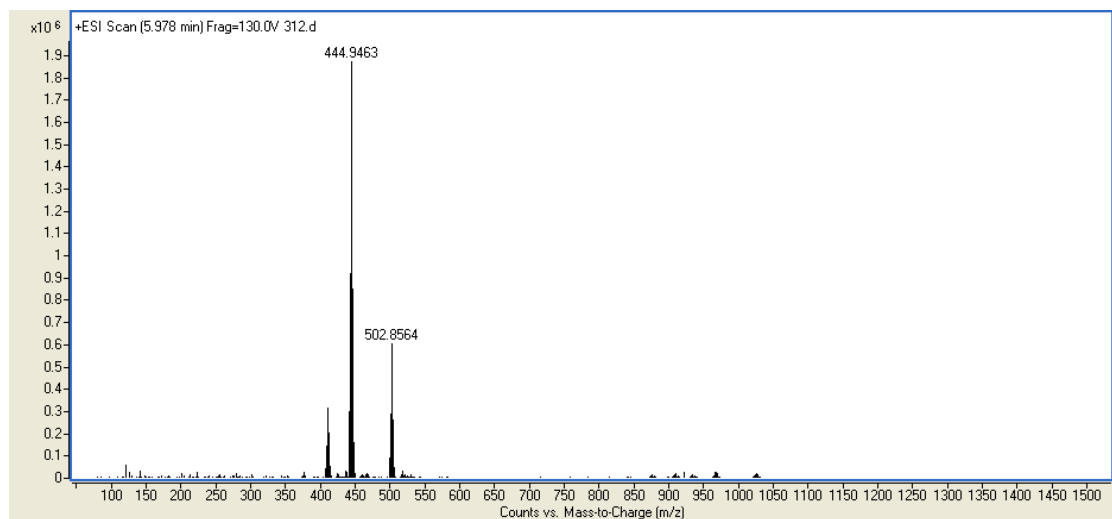
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10h	C ₁₆ H ₈ ClFN ₂ O ₂ Se	C ₁₆ H ₉ ClFN ₂ O ₂ Se	394.9498	394.9496	-0.51



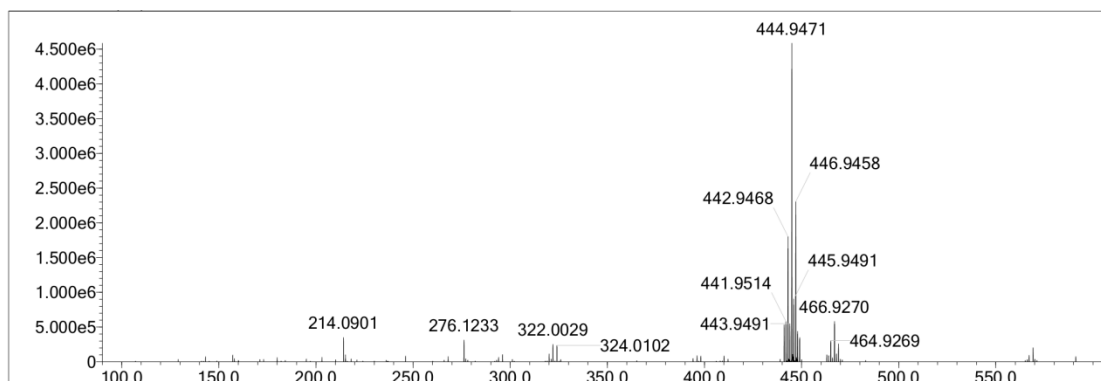
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10i	C ₁₇ H ₈ ClF ₃ N ₂ O ₂ Se	C ₁₇ H ₉ ClF ₃ N ₂ O ₂ Se	444.9475	444.9464	2.22



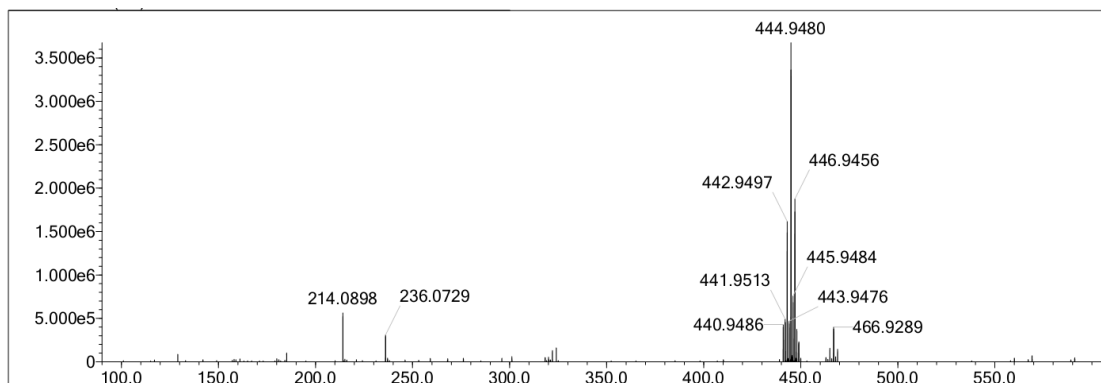
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10j	C ₁₇ H ₈ ClF ₃ N ₂ O ₂ Se	C ₁₇ H ₉ ClF ₃ N ₂ O ₂ Se	444.9463	444.9464	0.22



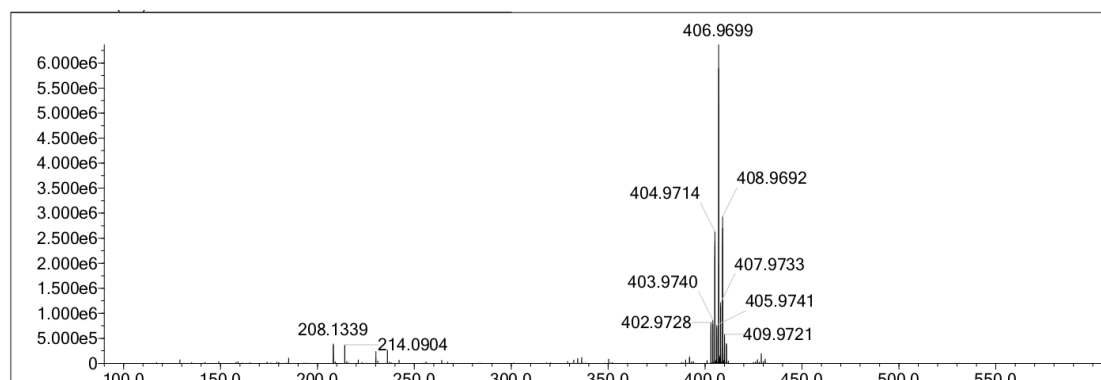
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10k	C ₁₇ H ₈ ClF ₃ N ₂ O ₂ Se	C ₁₇ H ₉ ClF ₃ N ₂ O ₂ Se	444.9471	444.9464	1.80



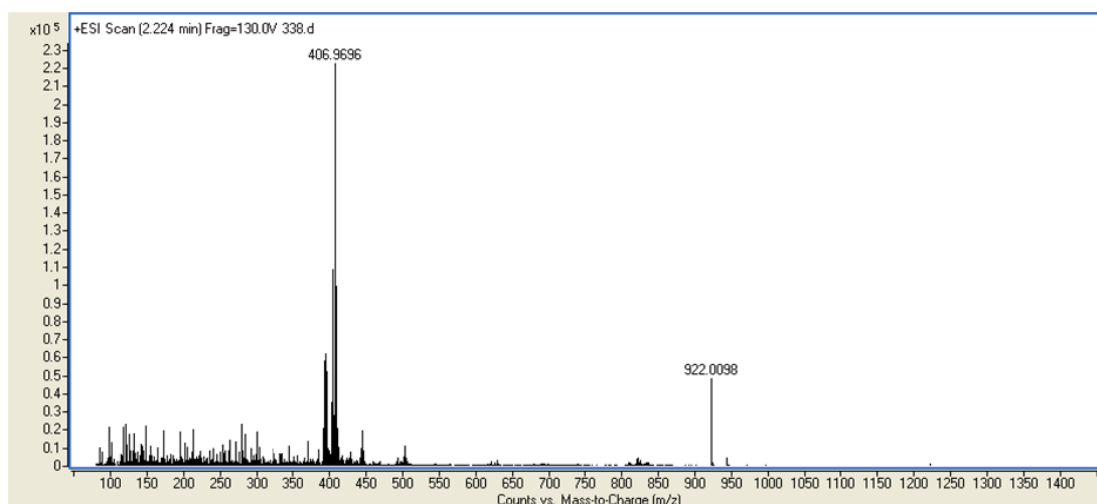
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10l	C ₁₇ H ₈ ClF ₃ N ₂ O ₂ Se	C ₁₇ H ₉ ClF ₃ N ₂ O ₂ Se	444.9480	444.9464	2.46



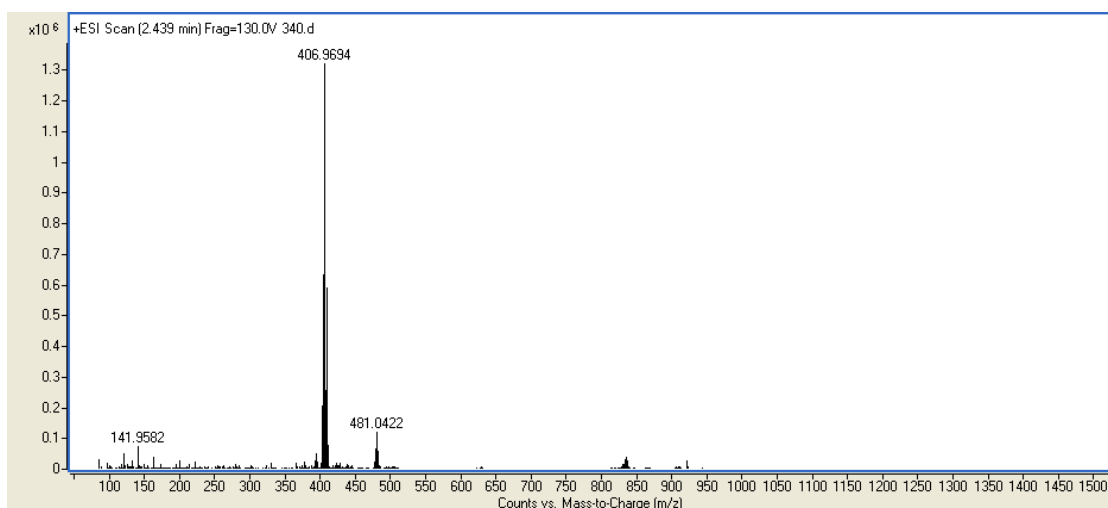
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10m	C ₁₇ H ₁₁ ClN ₂ O ₃ Se	C ₁₇ H ₁₂ ClN ₂ O ₃ Se	406.9699	406.9696	0.5



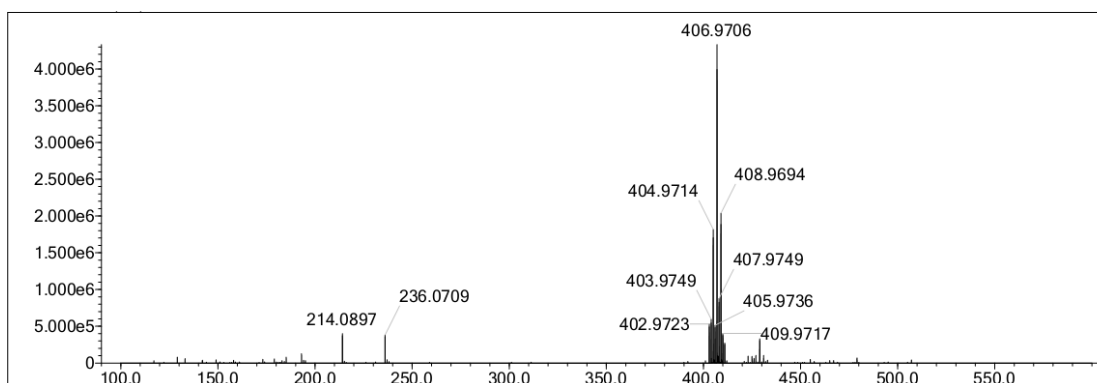
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10n	C ₁₇ H ₁₁ ClN ₂ O ₃ Se	C ₁₇ H ₁₂ ClN ₂ O ₃ Se	406.9696	406.9696	0



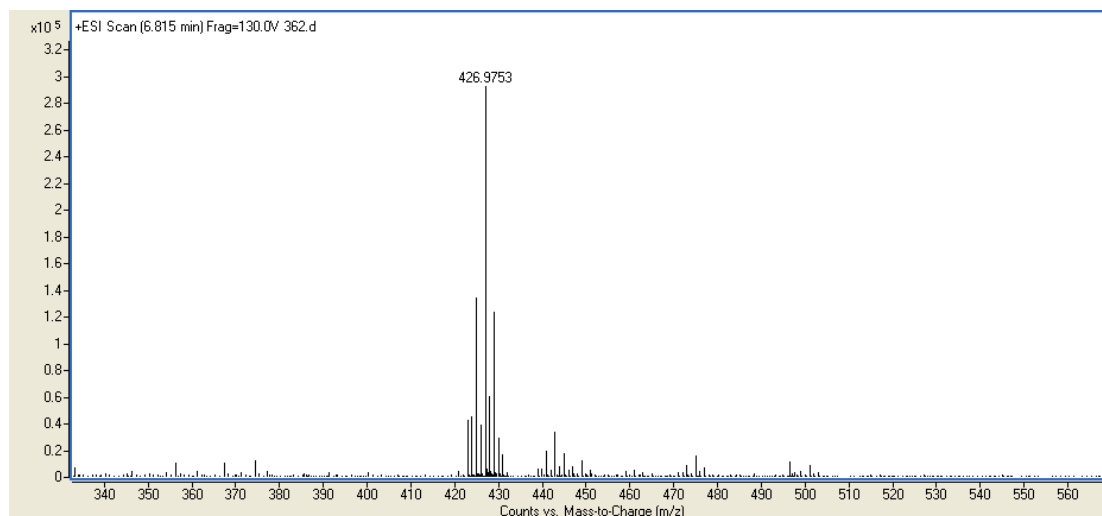
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10o	C ₁₇ H ₁₁ ClN ₂ O ₃ Se	C ₁₇ H ₁₂ ClN ₂ O ₃ Se	406.9694	406.9696	0.49



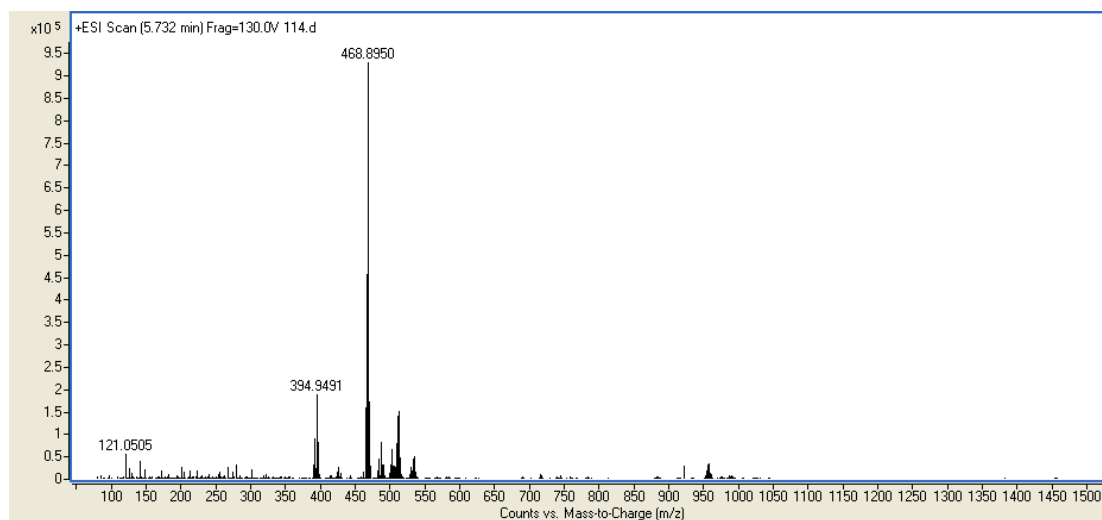
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10p	C ₁₇ H ₁₁ ClN ₂ O ₃ Se	C ₁₇ H ₁₂ ClN ₂ O ₃ Se	406.9706	406.9696	2.95



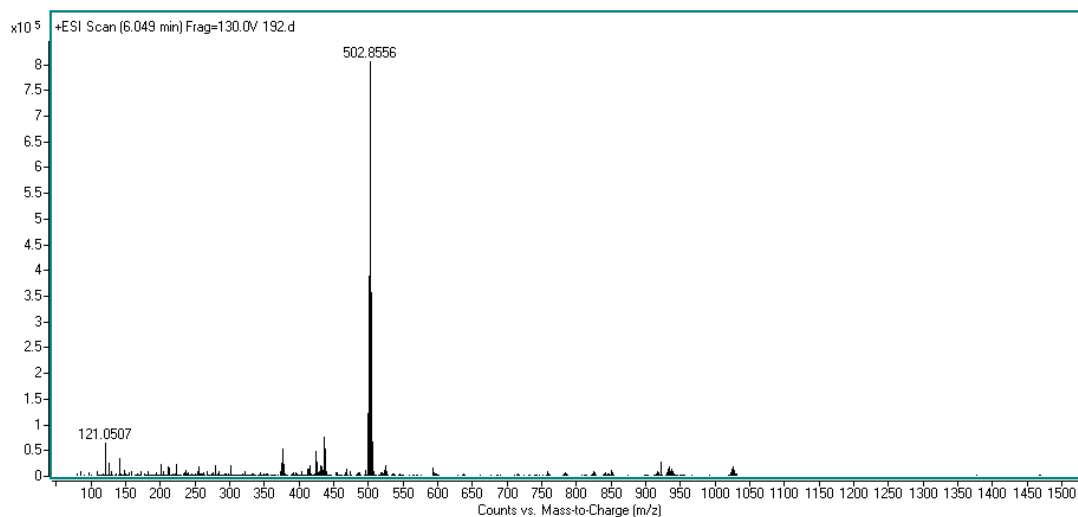
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
10q	C ₂₀ H ₁₁ ClN ₂ O ₂ Se	C ₂₀ H ₁₂ ClN ₂ O ₂ Se	426.9753	426.9747	-1.41



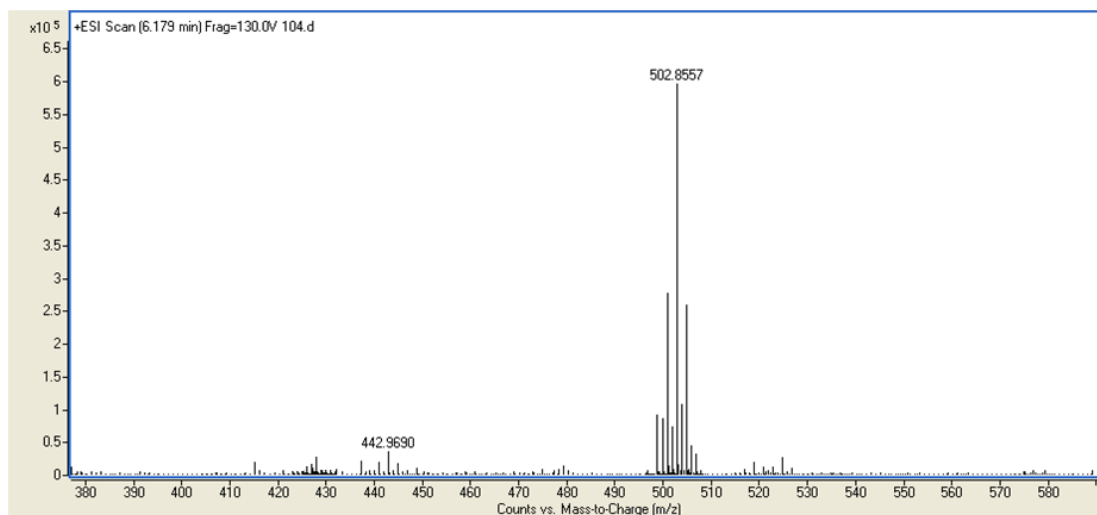
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11a	C ₁₆ H ₉ IN ₂ O ₂ Se	C ₁₆ H ₁₀ IN ₂ O ₂ Se	468.8950	468.8947	-0.64



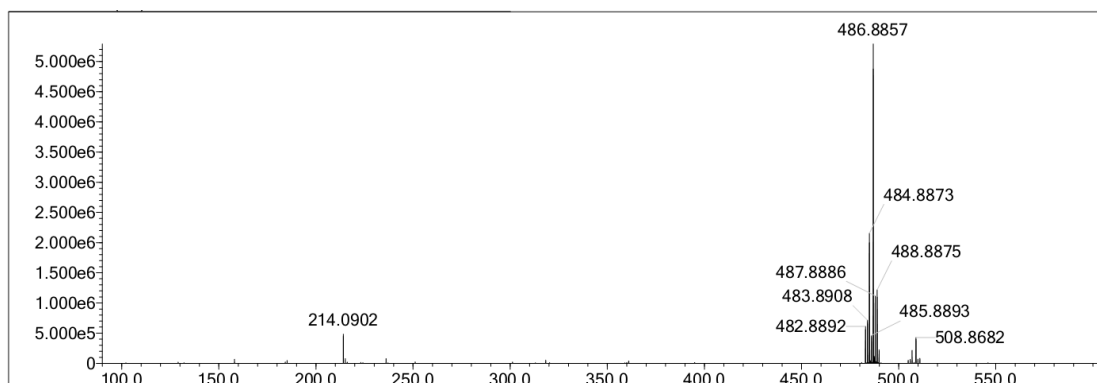
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11b	C ₁₆ H ₈ ClIN ₂ O ₂ Se	C ₁₆ H ₉ ClIN ₂ O ₂ Se	502.8556	502.8557	0.19



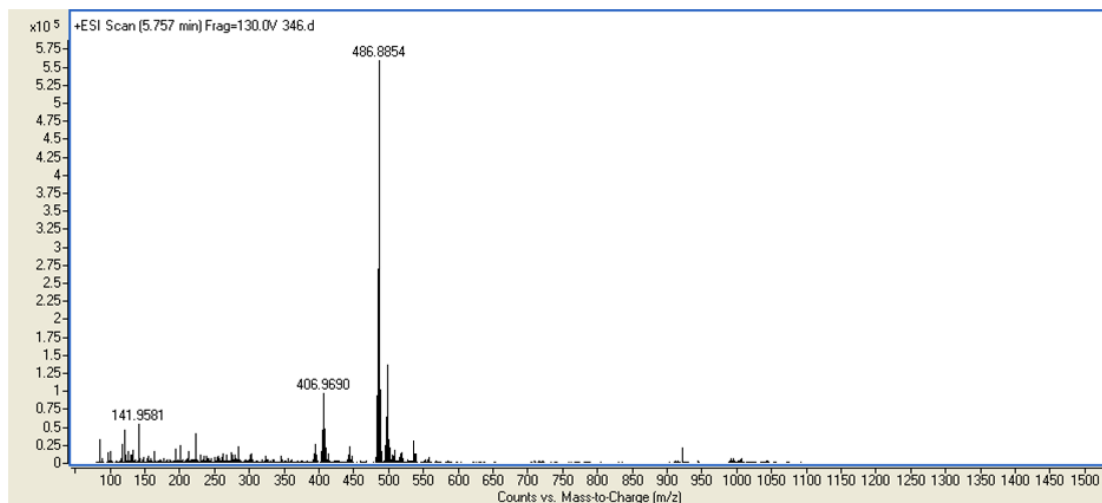
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11c	C ₁₆ H ₈ ClIN ₂ O ₂ Se	C ₁₆ H ₉ ClIN ₂ O ₂ Se	502.8557	502.8557	0



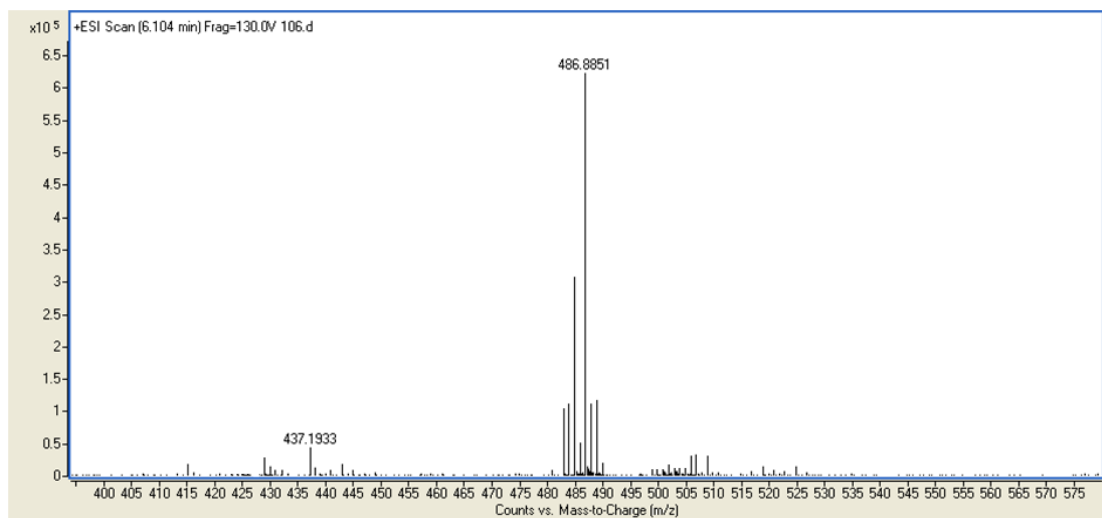
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11e	C ₁₆ H ₈ FIN ₂ O ₂ Se	C ₁₆ H ₉ FIN ₂ O ₂ Se	486.8857	486.8852	-0.81



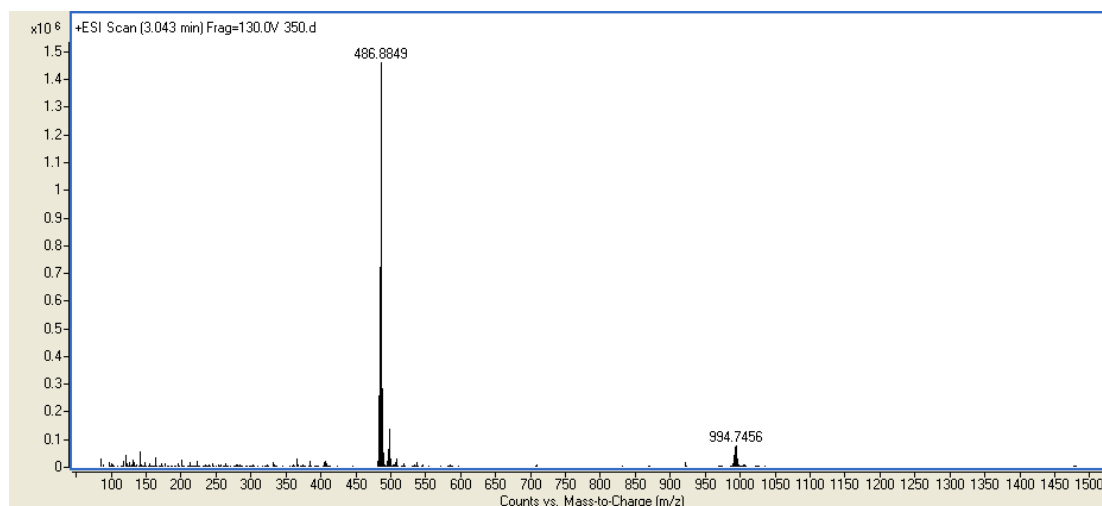
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11f	C ₁₆ H ₈ FIN ₂ O ₂ Se	C ₁₆ H ₉ FIN ₂ O ₂ Se	486.8854	486.8852	-0.41



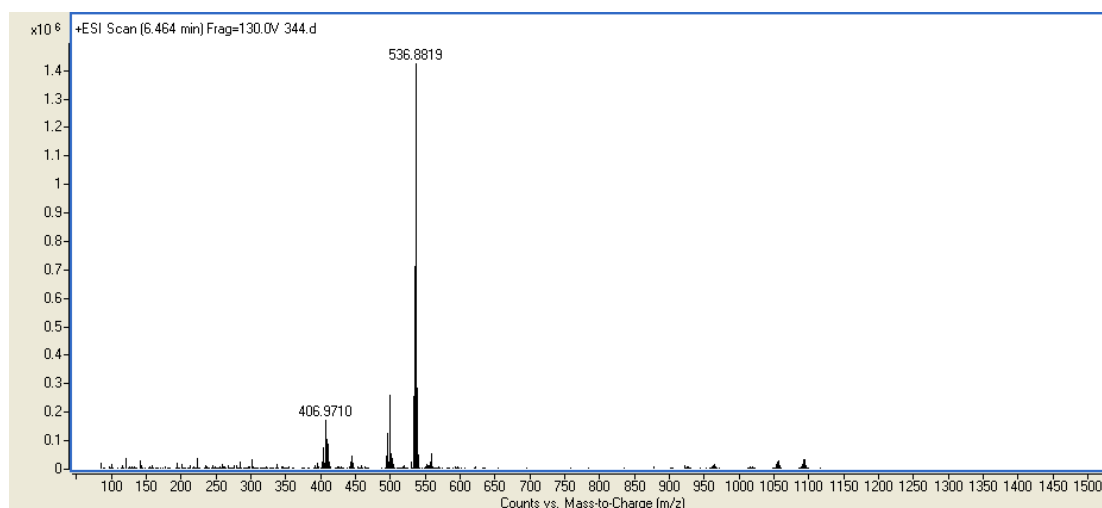
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11g	C ₁₆ H ₈ FIN ₂ O ₂ Se	C ₁₆ H ₉ FIN ₂ O ₂ Se	486.8851	486.8852	0.21



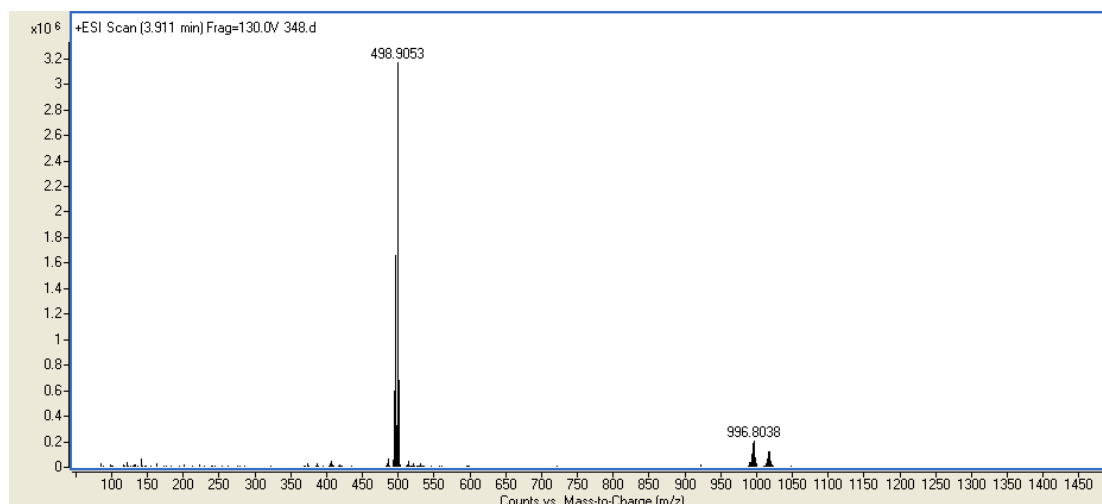
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11h	C ₁₆ H ₈ FIN ₂ O ₂ Se	C ₁₆ H ₉ FIN ₂ O ₂ Se	486.8849	486.8852	0.61



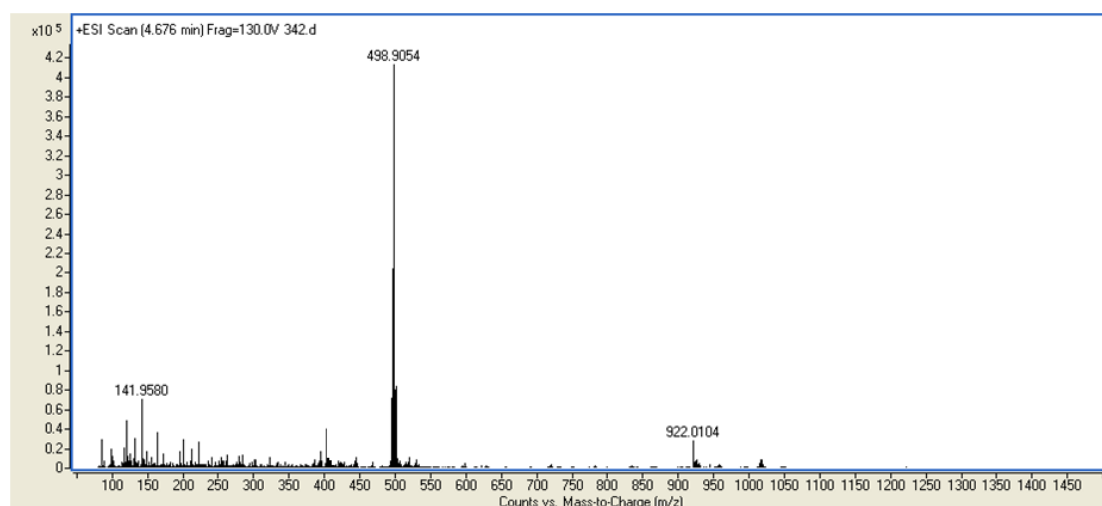
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11j	$C_{17}H_8F_3IN_2O_2Se$	$C_{17}H_8F_3IN_2O_2Se$	536.8819	536.8821	0.37



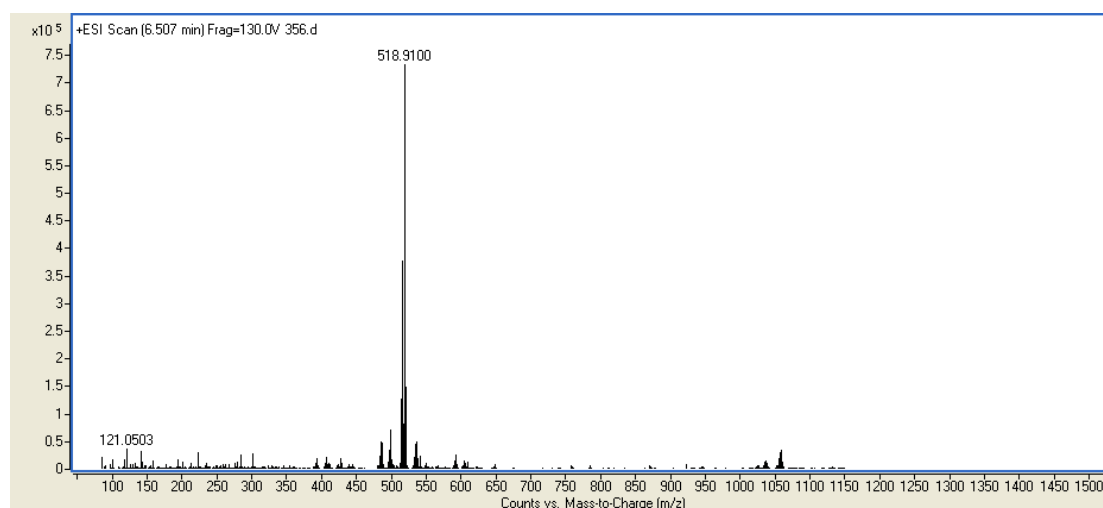
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11n	$C_{17}H_{11}IN_2O_3Se$	$C_{17}H_{12}IN_2O_3Se$	498.9053	498.9052	-0.2



Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11o	$C_{17}H_{11}IN_2O_3Se$	$C_{17}H_{12}IN_2O_3Se$	498.9054	498.9052	-0.4



Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
11q	$C_{20}H_{11}IN_2O_2Se$	$C_{20}H_{12}IN_2O_2Se$	518.9100	518.9103	0.58



3. Coupled Reductase Assay.

Procedure: Phosphate buffer solutions of pH 7.5, GSH, NADPH, GR were added into cuvette contained buffer solution. Finally, peroxide was added to initiate the reaction in a cuvette having mixture of all and immediately start the experiment for the control values in absence of any catalyst. For the test samples, solution was made in appropriate solvent and added into cuvette containing the mixture of buffer solution, GSH, NADPH and GR. Now, peroxide was added to initiate the reaction. Each of the measurement was carried out in triplicates. The initial reduction rate (5-10% consumption of NADPH) was expressed as μM of NADPH depleting per minute ($\mu\text{M}/\text{min}$) after the addition of peroxide. A plot of inverse of initial reaction rate v_0 inverse of GSH and peroxide concentration gave the catalytic parameters such as maximum velocities (V_{max}), Michaelis constants (K_m), catalytic constants (k_{cat}) and catalytic efficiencies (η) for the reduction of peroxide by GSH in presence of compound.

Initial reaction rate (v_0) = $\Delta A / 6.22 \times 1000$ ($\mu\text{M} \cdot \text{min}^{-1}$)

$$\frac{1}{v_0} = \frac{K_m}{V_{\text{max}}} \cdot \frac{1}{[S]} + \frac{1}{V_{\text{max}}}$$

$$k_{\text{cat}} = \frac{V_{\text{max}}}{[S]_0}$$

$$\eta = \frac{k_{\text{cat}}}{K_m}$$

$$\text{Slope} = \frac{K_m}{V_{\text{max}}}$$

$$\text{Intercept} = \frac{1}{V_{\text{max}}}$$

Where, ΔA = Difference in absorbance for one minute obtained from the initial 5-10%

of the NADPH consumption measured at 340 nm. It is obtained from the graph of absorbance in the first 10 s. The graphs are given as follows.

v_0 = Initial reaction rate

η = Catalytic efficiency

k_{cat} = Catalytic constant

K_m = Michaelis constant

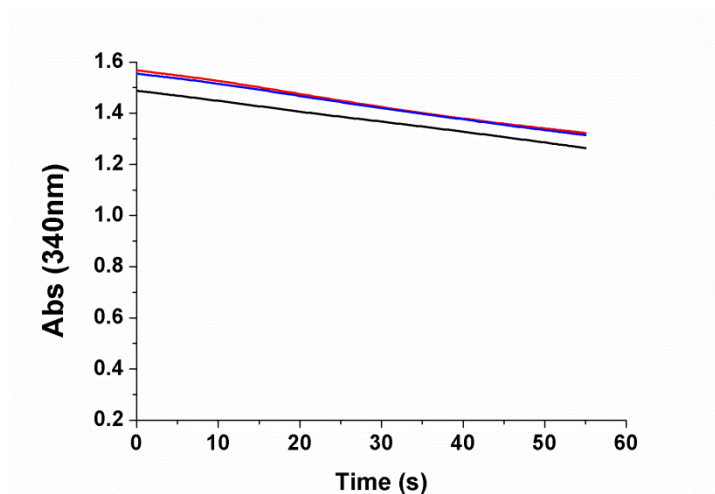
$[S]_0$ = The concentration of catalyst

	sample (μL)	control (μL)
PBS	140	150
GSH	20	20
NADPH	5	5
GR	5	5
Catalyst (in MeOH)	10	0
Peroxide	20	20

Total volume of the solution was taken 200 μL . GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), catalyst (80 μM) and peroxide (1.6 mM).

Table S1. Control values (in the absence of the catalyst) in the coupled reductase assay. Catalyzed reduction of H_2O_2 by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and H_2O_2 (1.6 mM), at pH 7.5.

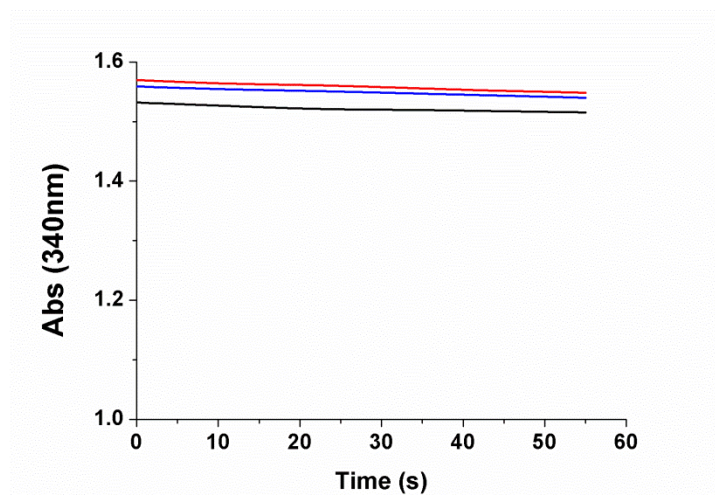
Control



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_o(\mu\text{M} \cdot \text{min}^{-1})$	$v_o(\mu\text{M} \cdot \text{min}^{-1})$
1	0.0392	0.235636	37.88366	37.21 ± 0.75
2	0.0387	0.232364	37.35750	
3	0.0377	0.226364	36.39287	

Table S2. Control values (in the absence of the catalyst) in the coupled reductase assay. Catalyzed reduction of *t*-BuOOH by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and *t*-BuOOH (1.6 mM), at pH 7.5.

Control

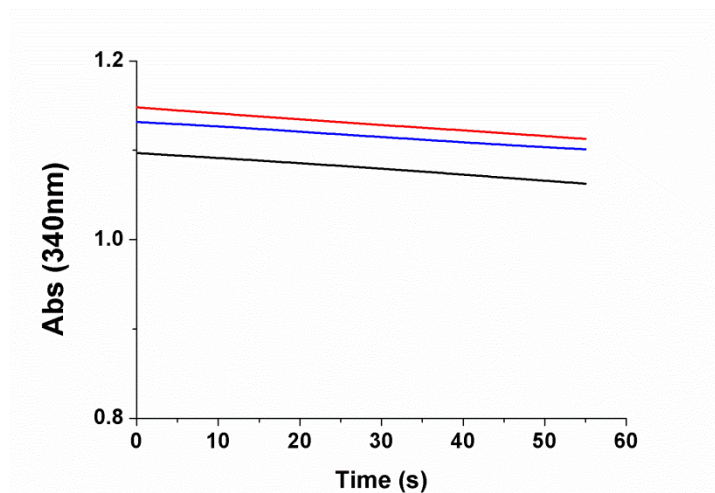


Sr. No.	ΔA	$\Delta A/\text{min}$	$v_o(\mu\text{M} \cdot \text{min}^{-1})$	$v_o(\mu\text{M} \cdot \text{min}^{-1})$
1	0.005091	0.030545	4.910845	5.05 ± 0.84
2	0.006182	0.037091	5.963169	
3	0.004455	0.026727	4.296989	

Table S3. Control values (in the absence of the catalyst) in the coupled reductase assay. Catalyzed reduction of Cum-OOH by GSH: GSH (2 mM), NADPH (0.4 mM),

GR (1.3 unit/mL), and Cum-OOH (1.6 mM), at pH 7.5.

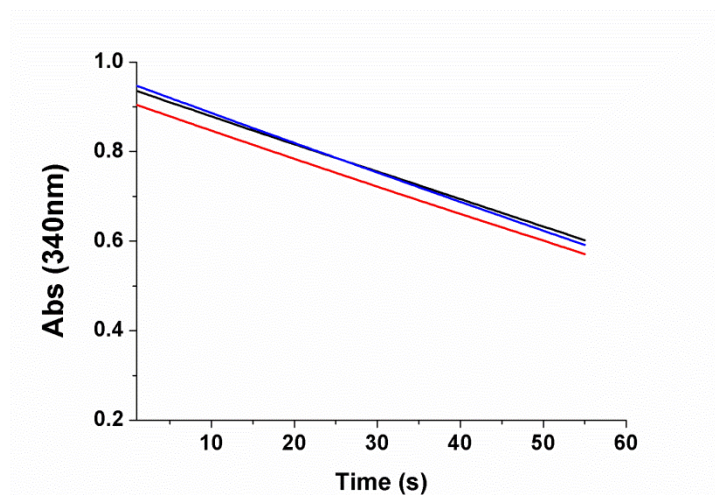
Control



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$
1	0.005273	0.031636	5.086232	5.34 ± 1.11
2	0.006818	0.040909	6.577024	
3	0.004545	0.027273	4.384683	

Table S4. Reduction rate (v_0) of ebselen in the coupled reductase assay. Catalyzed reduction of H_2O_2 by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and H_2O_2 (1.6 mM), at pH 7.5.

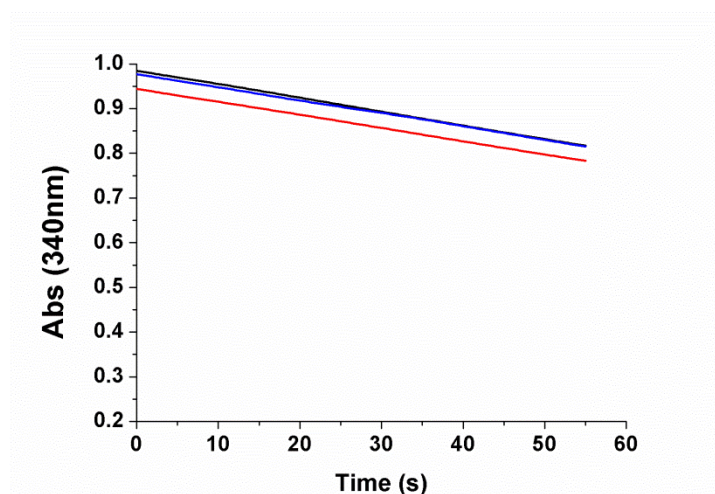
Ebselen



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$
1	0.131455	0.788727	126.8050	124.29 ± 3.41
2	0.124818	0.748909	120.4034	
3	0.130273	0.781636	125.6650	

Table S5. Reduction rate (v_0) of Ebselen in the coupled reductase assay. Catalyzed reduction of *t*-BuOOH by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and *t*-BuOOH (1.6 mM), at pH 7.5.

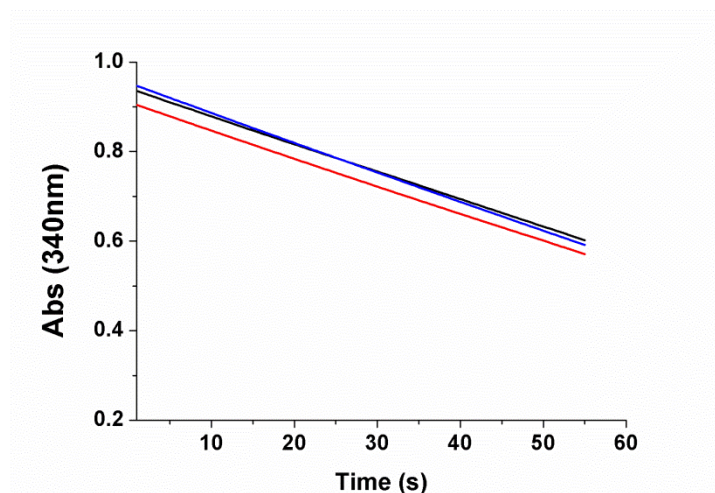
Ebselen



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$
1	0.028455	0.170727	27.44811	
2	0.028455	0.170727	27.44811	27.47 ± 0.05
3	0.028545	0.171273	27.53581	

Table S6. Reduction rate (v_0) of ebselen in the coupled reductase assay. Catalyzed reduction of Cum-OOH by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and Cum-OOH (1.6 mM), at pH 7.5.

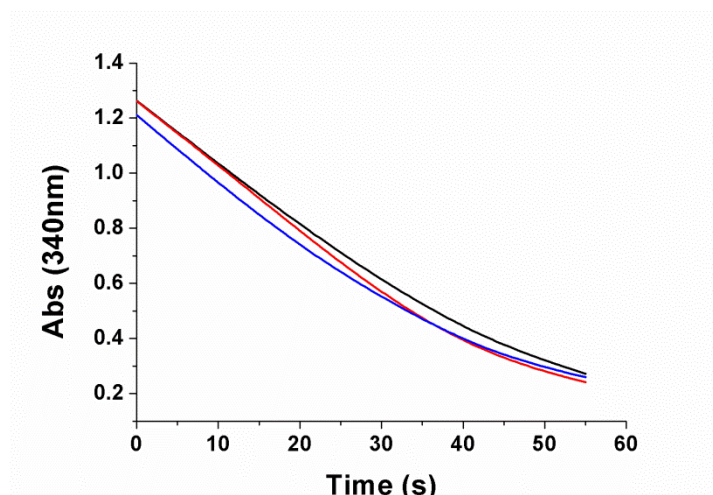
Ebselen



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$
1	0.063545	0.381273	61.29787	
2	0.063727	0.382364	61.47325	61.38 ± 0.08
3	0.063636	0.381818	61.38556	

Table S7. Reduction rate (v_0) of **10h** in the coupled reductase assay. Catalyzed reduction of H_2O_2 by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and H_2O_2 (1.6 mM), at pH 7.5.

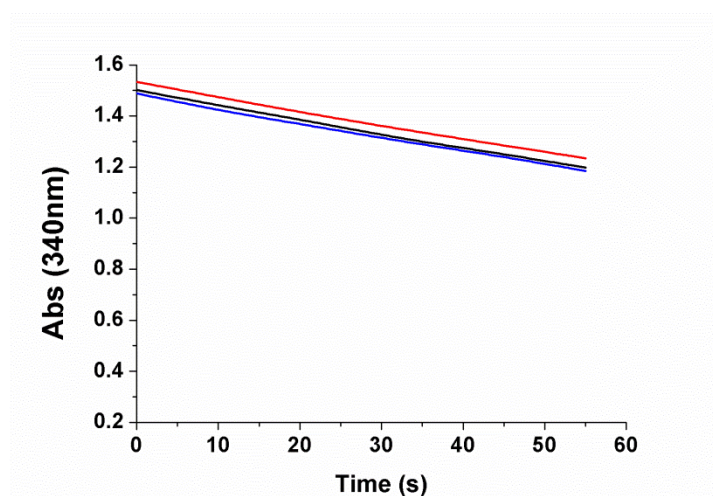
10h



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$
1	0.229182	1.375091	221.0757	
2	0.231818	1.390909	223.6188	228.00 $\pm$ 9.87
3	0.248091	1.488545	239.3160	

Table S8. Reduction rate (v_0) of **10h** in the coupled reductase assay. Catalyzed reduction of $t\text{-BuOOH}$ by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and $t\text{-BuOOH}$ (1.6 mM), at pH 7.5.

10h

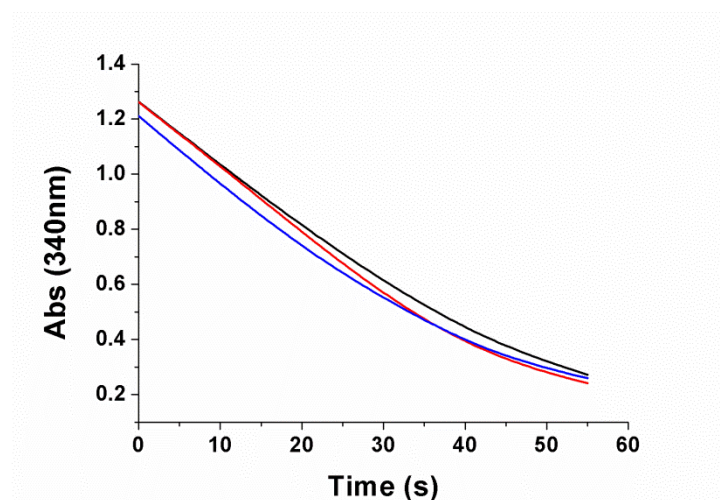


Sr. No.	ΔA	$\Delta A/\text{min}$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$
1	0.059727	0.358364	57.61473	55.07 $\pm$ 4.55

2	0.059909	0.359455	57.79012
3	0.051636	0.309818	49.81001

Table S9. Reduction rate (v_0) of **10h** in the coupled reductase assay. Catalyzed reduction of Cum-OOH by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and Cum-OOH (1.6 mM), at pH 7.5.

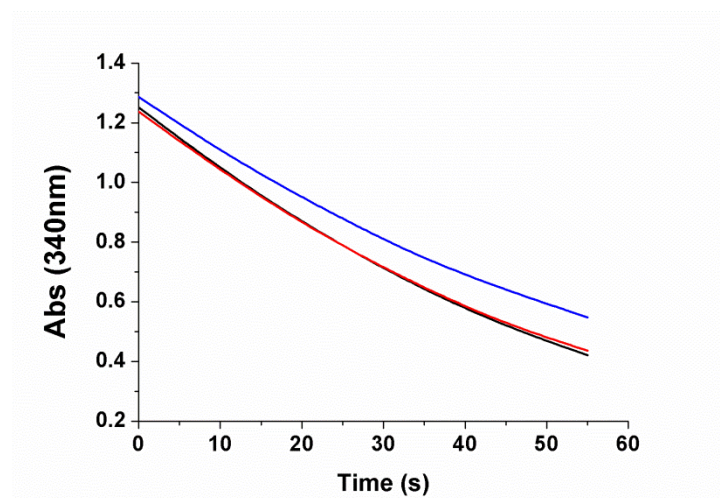
10h



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$	$v_0(\mu\text{M}\cdot\text{min}^{-1})$
1	0.176273	1.057636	170.038	
2	0.176455	1.058727	170.2134	172.11 $\pm$ 3.44
3	0.182545	1.095273	176.0889	

Table S10. Reduction rate (v_0) of **11h** in the coupled reductase assay. Catalyzed reduction of H_2O_2 by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and H_2O_2 (1.6 mM), at pH 7.5.

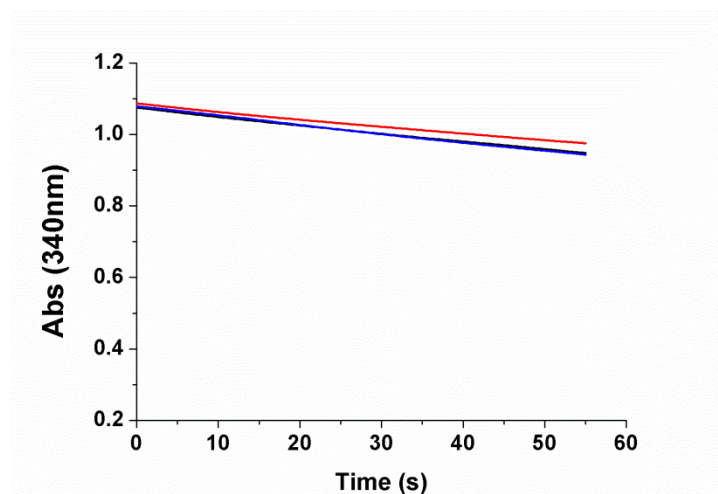
11h



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_o(\mu\text{M}\cdot\text{min}^{-1})$	$v_o(\mu\text{M}\cdot\text{min}^{-1})$
1	0.205455	1.232727	198.1877	193.65 ± 4.28
2	0.196636	1.179818	189.6814	
3	0.200162	1.200972	193.0823	

Table S11. Reduction rate (v_o) of **11h** in the coupled reductase assay. Catalyzed reduction of *t*-BuOOH by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and *t*-BuOOH (1.6 mM), at pH 7.5.

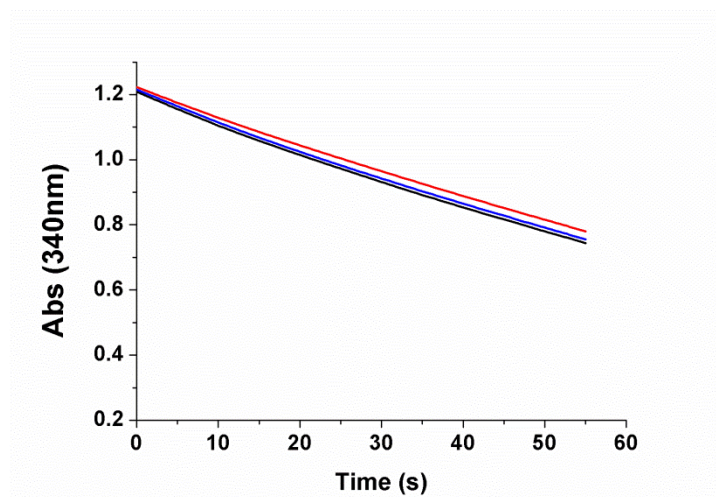
11h



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_o(\mu\text{M}\cdot\text{min}^{-1})$	$v_o(\mu\text{M}\cdot\text{min}^{-1})$
1	0.025091	0.150545	24.20345	24.68 ± 0.98
2	0.027091	0.162545	26.13271	
3	0.025091	0.150545	24.20345	

Table S12. Reduction rate (v_o) of **11h** in the coupled reductase assay. Catalyzed reduction of Cum-OOH by GSH: GSH (2 mM), NADPH (0.4 mM), GR (1.3 unit/mL), and Cum-OOH (1.6 mM), at pH 7.5.

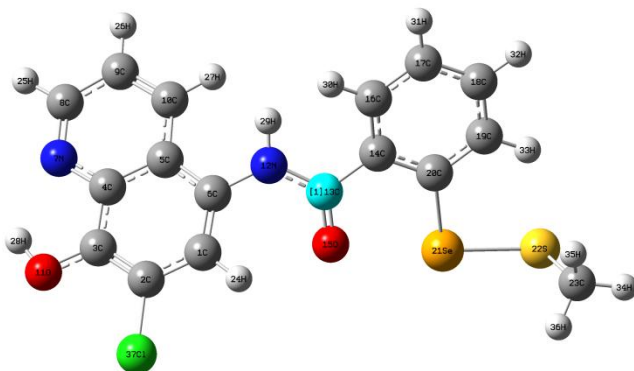
11h



Sr. No.	ΔA	$\Delta A/\text{min}$	$v_o(\mu\text{M} \cdot \text{min}^{-1})$	$v_o(\mu\text{M} \cdot \text{min}^{-1})$
1	0.106182	0.637091	102.4262	98.12 ± 5.14
2	0.095818	0.574909	92.42911	
3	0.103182	0.619091	99.5323	

4. Computation Studies

All calculations were performed by using the Gaussian 09 suite of quantum chemical programs. The computational models are fully optimized using DFT calculations at B3LYP/6-311+g(d,p) level of theory and characterized by frequency calculation. As glutathione was very flexible, the G group replaced with a Me group according to the reported method in literature.^{1, 2}

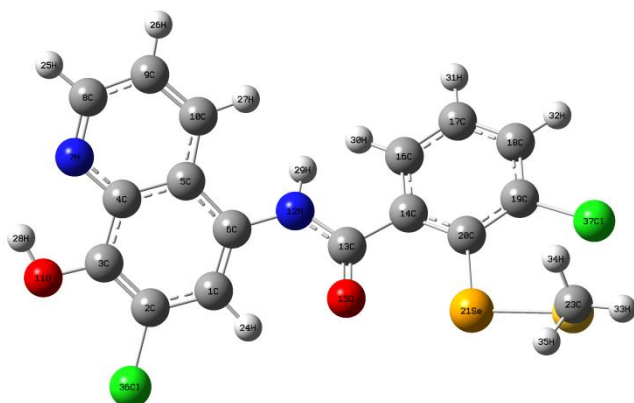


Selenenyl sulfides for 10a-S

Electronic Energy = -4175.8582389

C	-2.24228400	-1.04518600	0.71405900
C	-3.50686100	-1.64637700	0.55432700
C	-4.57635700	-0.94362200	0.04073000
C	-4.36726000	0.41065600	-0.35614300
C	-3.08470500	1.02115000	-0.23390700
C	-2.01945200	0.26299500	0.33981600
N	-5.45215700	1.04852000	-0.86472000
C	-5.31386700	2.29020200	-1.28002200
C	-4.08427800	2.98216000	-1.23397900
C	-2.97859000	2.34785500	-0.71643200
O	-5.79671800	-1.48754800	-0.10419100
N	-0.76611500	0.89125000	0.53623400
C	0.47110800	0.30693100	0.40796600
C	1.65831000	1.16234100	0.68623100
O	0.60897200	-0.86232600	0.05942100
C	1.56338000	2.37685200	1.38599400
C	2.67729600	3.17149800	1.61172900

C	3.91636500	2.75497500	1.12486900
C	4.03665600	1.54694800	0.44964900
C	2.92567900	0.72601800	0.23754300
Se	3.10692700	-1.00221000	-0.66041100
S	5.27886000	-0.95977600	-1.26273100
C	6.10697600	-1.71926700	0.19130600
H	-1.43812900	-1.63347700	1.12970800
H	-6.20062900	2.77390300	-1.67925700
H	-4.02081800	3.99425700	-1.61413200
H	-2.02470100	2.86298500	-0.70540600
H	-6.35431900	-0.78772000	-0.49115200
H	-0.78517500	1.87973500	0.72428200
H	0.61197600	2.69689900	1.79717900
H	2.58300500	4.09882100	2.16378100
H	4.79704500	3.36845400	1.27975400
H	5.00167500	1.23510200	0.06983500
H	7.16055500	-1.82088400	-0.07789400
H	6.01974600	-1.08419400	1.07281400
H	5.69183400	-2.70449900	0.39865100
Cl	-3.71777600	-3.30964600	1.04145000

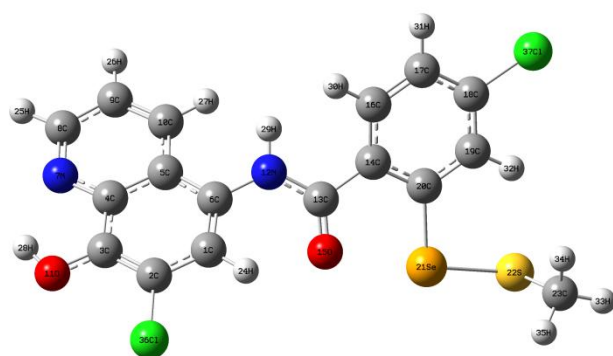


Selenenyl sulfides for 10b-S

Electronic Energy = -4635.4708367

C	-2.40941600	-1.37842000	-0.26004000
C	-3.78404600	-1.29409100	-0.56241900
C	-4.52773900	-0.18163700	-0.23444700
C	-3.87498800	0.88892900	0.44613900
C	-2.49202700	0.81076800	0.78315100
C	-1.75729000	-0.35216200	0.39250200
N	-4.65998100	1.95301200	0.75372900
C	-4.12314300	2.96211400	1.40719100
C	-2.77134100	2.98139700	1.81101100
C	-1.96448600	1.91086600	1.50054600

O	-5.83655200	-0.07190900	-0.52385000
N	-0.37257800	-0.39603700	0.68173000
C	0.42233600	-1.50940800	0.77722400
C	1.87569200	-1.22336300	1.10388100
O	0.02174100	-2.65634600	0.69862200
C	2.31891800	-1.68741900	2.34502400
C	3.64173400	-1.51147400	2.73057000
C	4.54130800	-0.88911600	1.87194700
C	4.10767100	-0.44458400	0.62620800
C	2.77117700	-0.59516900	0.21804600
Se	2.20099000	-0.10030900	-1.58116200
S	1.32226400	1.93493700	-1.24525000
C	2.76171900	3.07110400	-1.28130800
H	-1.86822100	-2.26841100	-0.54115100
H	-4.77664000	3.79885800	1.63684800
H	-2.38558900	3.82931100	2.36347000
H	-0.93016100	1.91378400	1.82318000
H	-6.10963100	0.79896000	-0.18116600
H	0.10978700	0.49233700	0.69992800
H	1.61822500	-2.19570500	2.99619900
H	3.98007500	-1.86648900	3.69694700
H	5.57747800	-0.75527400	2.15439500
H	2.34000300	4.07549100	-1.19719400
H	3.43309900	2.88541600	-0.44523000
H	3.29568000	2.97970900	-2.22551400
Cl	-4.54681800	-2.63178000	-1.38695700
Cl	5.31481600	0.29888000	-0.41274600

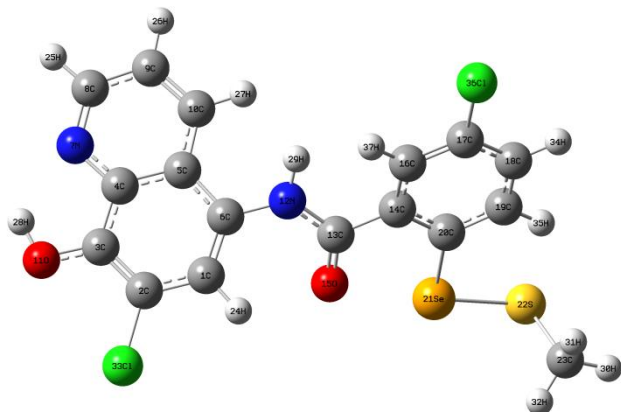


Selenenyl sulfides for 10c-S

Electronic Energy = -4635.4804995

C	2.72930900	-0.91187400	-0.82731500
C	4.05834400	-1.37557600	-0.76258200
C	5.05682800	-0.61324000	-0.19358700

C	4.70745100	0.65452000	0.36017100
C	3.36031900	1.12027900	0.33454800
C	2.37117300	0.31082600	-0.30085900
N	5.72861200	1.35420500	0.91681200
C	5.46333100	2.51687500	1.47469300
C	4.16186200	3.06094500	1.53262100
C	3.11927200	2.36340100	0.96784200
O	6.33516500	-1.02244800	-0.13699700
N	1.04687100	0.80400000	-0.40122500
C	-0.10722600	0.06586500	-0.29878900
C	-1.39566500	0.79128900	-0.47269000
O	-0.09585200	-1.13758200	-0.05593800
C	-1.47323300	2.05913300	-1.07008000
C	-2.67697100	2.73202300	-1.20842400
C	-3.83074100	2.11712200	-0.72743300
C	-3.79798200	0.85668300	-0.15079900
C	-2.58765700	0.17013500	-0.03449900
Se	-2.53671000	-1.63191900	0.72228800
S	-4.67467000	-1.89008100	1.38104100
C	-5.45777500	-2.64644900	-0.09968700
H	1.98465900	-1.53980200	-1.29297200
H	6.30171400	3.05342500	1.90926300
H	3.99600700	4.00971600	2.02779800
H	2.11286900	2.76088400	1.03499500
H	6.82204100	-0.30968800	0.31635000
H	0.94608400	1.80167500	-0.48799200
H	-0.58388600	2.52948600	-1.47487300
H	-2.72459900	3.70379400	-1.68103900
H	-4.71000600	0.40707400	0.22024400
H	-6.47982300	-2.89542600	0.19355900
H	-5.48319900	-1.94754900	-0.93543500
H	-4.93418900	-3.55662600	-0.38823600
Cl	4.44123000	-2.93774500	-1.44095700
Cl	-5.36779100	2.95248900	-0.87083800

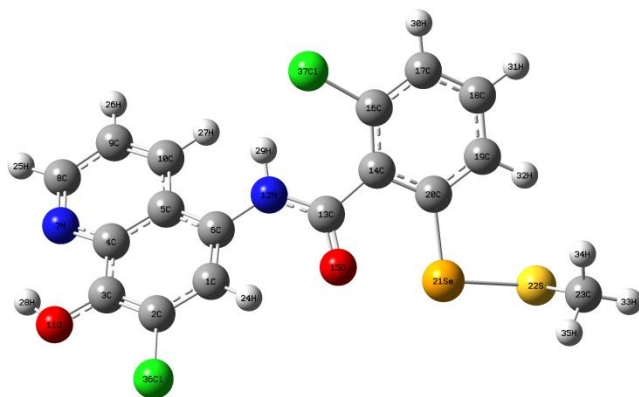


Selenenyl sulfides for 10d-S

Electronic Energy = -4635.4794496

C	2.52436100	-0.95717500	-0.91816000
C	3.84211100	-1.45608800	-0.90759000
C	4.84910900	-0.80570200	-0.22570100
C	4.52014400	0.37835800	0.49971900
C	3.18416900	0.87449000	0.52741700
C	2.18651800	0.18623100	-0.22629500
N	5.54917200	0.96778700	1.15976600
C	5.30218800	2.04585500	1.87397000
C	4.01239700	2.60697400	1.99547400
C	2.96199000	2.02097800	1.32788600
O	6.11742500	-1.24795900	-0.21557000
N	0.87356800	0.71777100	-0.26692000
C	-0.29515900	-0.00225400	-0.26763900
C	-1.56904200	0.77196200	-0.33291800
O	-0.31467600	-1.22693100	-0.19571000
C	-1.60452500	2.10228600	-0.77961600
C	-2.79840400	2.80314900	-0.80340500
C	-3.97901900	2.19916700	-0.37976000
C	-3.95393300	0.87652000	0.04128600
C	-2.76875200	0.13608500	0.05458000
Se	-2.75627200	-1.74121700	0.59756400
S	-4.87943500	-2.00634100	1.30069900
C	-5.73532400	-2.57013200	-0.22485100
H	1.77223400	-1.49494300	-1.47574800
H	6.14643100	2.49576800	2.38821700
H	3.86115900	3.48053800	2.61741800
H	1.96411000	2.42943500	1.44000100
H	6.61371900	-0.61759000	0.33851400
H	0.79371900	1.71988200	-0.21191100
H	-6.75263300	-2.82808500	0.07723000

H	-5.77124800	-1.78058300	-0.97529600
H	-5.24717800	-3.45302200	-0.63471700
Cl	4.20013000	-2.91398800	-1.79824500
H	-4.90900600	2.75376800	-0.38841500
H	-4.87147000	0.41015800	0.37837800
Cl	-2.82118100	4.46289600	-1.37938400
H	-0.71188800	2.59206800	-1.14841200

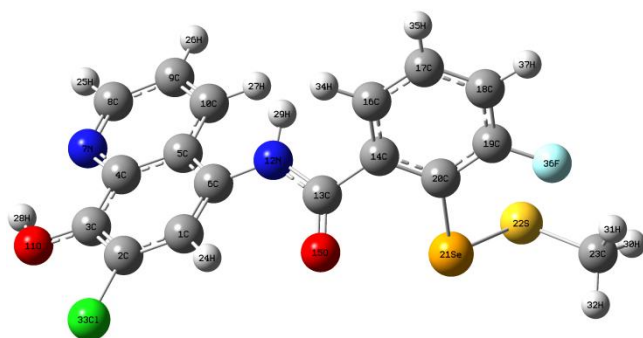


Selenenyl sulfides for 10e-S

Electronic Energy = -4635.4738404

C	2.23933600	-1.13149000	-0.75432500
C	3.50703100	-1.74416800	-0.68623500
C	4.56972000	-1.13232500	-0.05704600
C	4.35203400	0.13931200	0.55265000
C	3.07015200	0.76097800	0.51719400
C	2.00897700	0.10020600	-0.17698100
N	5.43131000	0.68683800	1.16723800
C	5.28798500	1.84638800	1.77408700
C	4.05905700	2.53841200	1.82431900
C	2.95907700	1.99582200	1.20085600
O	5.79118700	-1.68867400	0.00871400
N	0.76247000	0.76612100	-0.26548200
C	-0.46698300	0.19741700	-0.42111700
C	-1.67921400	1.08485100	-0.45534200
O	-0.62321300	-1.02188400	-0.45997800
C	-1.73479600	2.43094900	-0.87217100
C	-2.90176300	3.17936900	-0.83481700
C	-4.06625200	2.58754100	-0.35838800
C	-4.06406900	1.25916800	0.03807000
C	-2.89885100	0.49535500	-0.02494600
Se	-2.95420100	-1.39915400	0.48421500
S	-5.02647900	-1.56054200	1.36270700
C	-6.03167800	-2.05416800	-0.09468900

H	1.44084800	-1.64804000	-1.26341400
H	6.17025600	2.25913100	2.25468100
H	3.99110600	3.47900700	2.35676000
H	2.00814800	2.51272200	1.25632800
H	6.34216800	-1.05770400	0.50772800
H	0.79987600	1.77332400	-0.28867900
H	-2.89262400	4.20527300	-1.17727200
H	-4.98238700	3.16517600	-0.31090200
H	-4.97205000	0.80510200	0.41313900
H	-7.03601300	-2.25674800	0.28333100
H	-6.07883900	-1.25404500	-0.83334700
H	-5.62983100	-2.95802600	-0.55014000
Cl	3.72800500	-3.30588200	-1.43550800
Cl	-0.33112200	3.28863500	-1.54353400

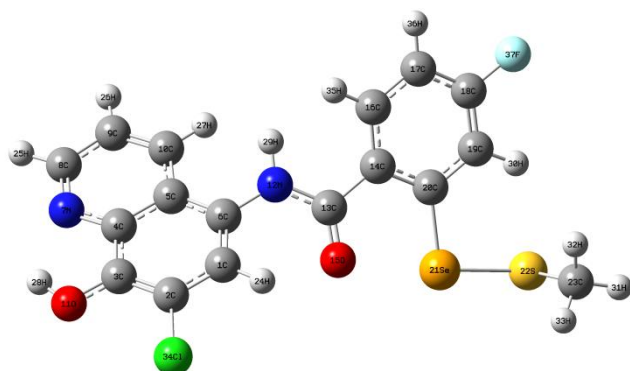


Selenenyl sulfides for 10f-S

Electronic Energy = - 4275.1193135

C	-2.63543600	-1.18935900	0.56887600
C	-3.96387000	-1.42958100	0.16342100
C	-4.77060100	-0.40975600	-0.29463300
C	-4.21891200	0.90359900	-0.37669400
C	-2.86694200	1.15688700	-0.00215500
C	-2.08522500	0.07341800	0.50265200
N	-5.05569000	1.86349700	-0.84654300
C	-4.59501200	3.08983200	-0.97784500
C	-3.26579100	3.44742900	-0.66506000
C	-2.40948300	2.48437900	-0.18335700
O	-6.04555200	-0.60875200	-0.67031800
N	-0.76552000	0.33416600	0.94342900
C	0.31376300	-0.51558300	0.86952400
C	1.58329300	0.04111700	1.45387300
O	0.26978800	-1.63497700	0.38887000
C	1.56958800	0.61156100	2.73080700

C	2.75117900	1.04222700	3.32860100
C	3.95736400	0.89264700	2.65463900
C	3.95506400	0.31759200	1.39251500
C	2.79521000	-0.10705700	0.74912400
Se	2.80011000	-0.88253800	-1.04128700
S	4.04869300	0.55951300	-2.21289000
C	5.71132000	-0.21241600	-2.26955200
H	-2.04369200	-2.01884000	0.92550700
H	-5.28929500	3.83530900	-1.35460900
H	-2.93143300	4.46621900	-0.81706100
H	-1.37985100	2.74755000	0.03049400
H	-6.37630300	0.26275700	-0.95594500
H	-0.57460800	1.26130600	1.28951100
H	6.30010800	0.42097400	-2.93747900
H	6.16688700	-0.22976700	-1.28264200
H	5.65567800	-1.21691100	-2.68634700
Cl	-4.59684100	-3.05331500	0.26789700
H	0.63471100	0.68437900	3.27477100
H	2.73530900	1.47409800	4.32187700
F	5.15187700	0.16230300	0.78461300
H	4.90059900	1.19723000	3.09112500



Selenenyl sulfides for 10g-S

Electronic Energy = -4275.1268711

C	2.47547100	-0.98397600	-0.78776200
C	3.77179300	-1.52512700	-0.67627500
C	4.80677400	-0.79948300	-0.12461300
C	4.52865600	0.51248600	0.36230300
C	3.21374000	1.05835900	0.28936200
C	2.18612200	0.28213400	-0.32591800
N	5.58240300	1.17411100	0.90467700
C	5.38098600	2.37620700	1.40250600
C	4.11502500	3.00112000	1.41062800

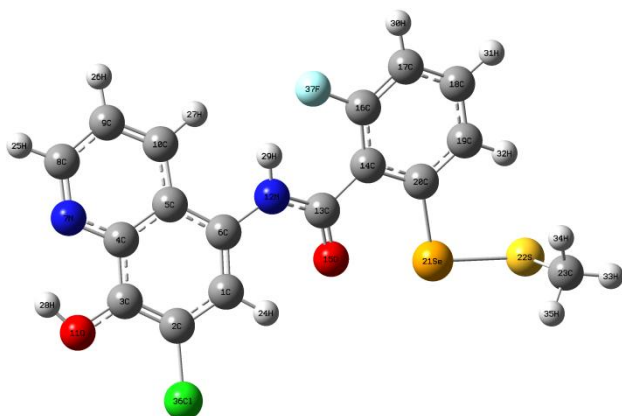
C	3.04030500	2.34268900	0.85928200
O	6.05586800	-1.28397500	-0.02439100
N	0.89675800	0.85050900	-0.47370400
C	-0.30237500	0.19288100	-0.33994200
C	-1.54241000	0.98316300	-0.56665500
O	-0.36536400	-0.99303300	-0.02727700
C	-1.53699300	2.22706400	-1.21860100
C	-2.69670300	2.96421300	-1.40113800
C	-3.87821000	2.42927400	-0.90659600
C	-3.94046400	1.20095200	-0.27778800
C	-2.77446400	0.45118700	-0.11699200
Se	-2.83733300	-1.31591700	0.71472500
S	-5.00215300	-1.42933900	1.32814000
C	-5.79162400	-2.19350000	-0.14511300
H	1.70050200	-1.58650900	-1.23745100
H	6.24412400	2.88055100	1.82708000
H	4.00060300	3.98090200	1.85764600
H	2.05949900	2.80371700	0.88811100
H	6.57929600	-0.58173700	0.40389800
H	0.86060900	1.84554000	-0.62017000
H	-4.89027900	0.83662600	0.09387100
H	-6.83281200	-2.37482700	0.12985600
H	-5.75768500	-1.52454600	-1.00480700
H	-5.31331400	-3.14094600	-0.38883600
Cl	4.06704600	-3.13878900	-1.27315900
H	-0.61641600	2.62530500	-1.63038600
H	-2.69827200	3.91731700	-1.91321700
F	-5.02042100	3.13494600	-1.05959600

Selenenyl sulfides for 10h-S

Electronic Energy = -4275.1248776

C	2.38573600	-1.00889000	-0.82539700
C	3.67732600	-1.56664200	-0.74550200

C	4.71362800	-0.89154200	-0.13547600
C	4.44187200	0.38376300	0.44410500
C	3.13202900	0.94457900	0.40235100
C	2.10296400	0.22285400	-0.27445300
N	5.49692400	0.99494900	1.04015300
C	5.30200200	2.15964500	1.62224100
C	4.04146500	2.79378700	1.66641800
C	2.96531300	2.18624200	1.06197400
O	5.95828000	-1.39170300	-0.06251700
N	0.81955600	0.81141200	-0.38805800
C	-0.38600400	0.15595900	-0.33942000
C	-1.61384600	0.98718400	-0.50152200
O	-0.47229200	-1.05318400	-0.15047200
C	-1.56904600	2.26984200	-1.07299100
C	-2.72640300	3.01232500	-1.17939600
C	-3.94595700	2.53004000	-0.72957900
C	-3.99681000	1.25458400	-0.18228800
C	-2.85216700	0.45844800	-0.07683600
Se	-2.95136300	-1.35896400	0.64225000
S	-5.09454300	-1.44262300	1.32749800
C	-5.96039300	-2.09855500	-0.15499300
H	1.60956900	-1.57105700	-1.32251400
H	6.16614000	2.62422300	2.08812600
H	3.93193000	3.74013400	2.18143400
H	1.98911000	2.65455800	1.11755700
H	6.48377300	-0.72623500	0.41877300
H	0.79038500	1.81680500	-0.42890900
H	-4.83590200	3.14114300	-0.81737300
H	-4.94152000	0.87069200	0.18222000
H	-6.99522000	-2.26897900	0.14973500
H	-5.93976400	-1.38264700	-0.97655700
H	-5.51828500	-3.04218800	-0.47103900
Cl	3.96465200	-3.13468000	-1.45653500
F	-2.66646100	4.24252300	-1.74407300
H	-0.65565100	2.68999400	-1.47633700

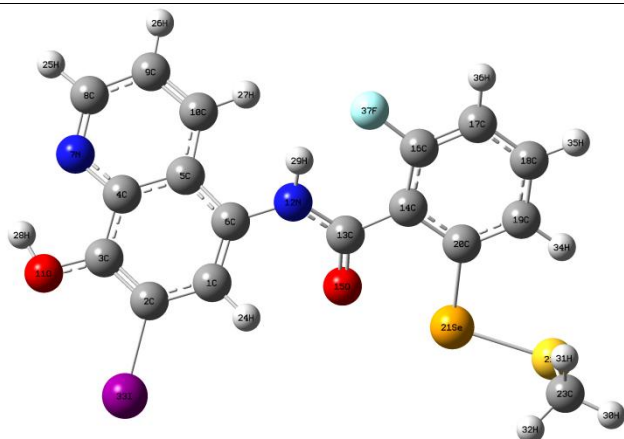


Selenenyl sulfides for 10i-S

Electronic Energy = 4275.1277383

C	-2.11585900	-1.25351000	0.20861400
C	-3.36557400	-1.90593700	0.18810600
C	-4.54521600	-1.20315000	0.07861000
C	-4.47458200	0.21734100	-0.03667400
C	-3.21997200	0.89426900	-0.04153700
C	-2.02373900	0.12029500	0.10457200
N	-5.66808600	0.85330000	-0.15219500
C	-5.67347800	2.16303600	-0.28548000
C	-4.49201000	2.93273600	-0.32412700
C	-3.27585900	2.29978700	-0.20519100
O	-5.74891600	-1.80122300	0.06907200
N	-0.79595600	0.81813600	0.16537900
C	0.45949100	0.32559800	-0.05460400
C	1.62739100	1.25372200	0.05093500
O	0.66395000	-0.85732200	-0.32900700
C	1.55619400	2.63586600	0.28194100
C	2.64673600	3.47304900	0.36104400
C	3.90940600	2.90841000	0.19778400
C	4.04676000	1.54721300	-0.03434300
C	2.93041000	0.71058900	-0.10756800
Se	3.16054800	-1.20389900	-0.44770100
S	5.41319500	-1.37821000	-0.46858500
C	5.80798600	-1.63263200	1.30750100
H	-1.22092500	-1.84763700	0.30087100
H	-6.64438800	2.64190900	-0.37364000
H	-4.55088100	4.00631200	-0.45364800
H	-2.36976400	2.89233200	-0.25643000
H	-6.39990200	-1.08139200	-0.02453400
H	-0.85178000	1.79581900	0.39776100
H	2.49797000	4.52968400	0.54069700

H	4.79077600	3.53741100	0.24699700
H	5.03195600	1.12122200	-0.17523900
H	6.88037600	-1.83282300	1.35658000
H	5.58142800	-0.74118500	1.89234300
H	5.26295100	-2.48832700	1.70352200
Cl	-3.40602300	-3.64683300	0.32003600
F	0.32936900	3.23277500	0.44144300

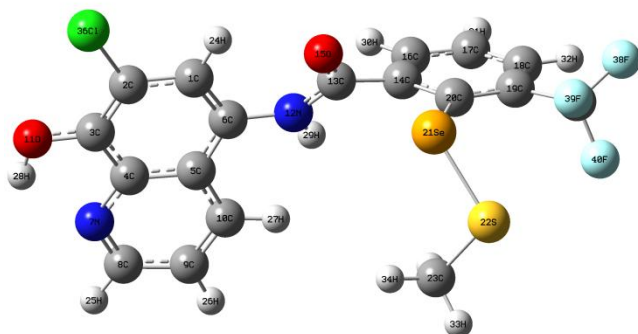


Selenenyl sulfides for 11i-S

Electronic Energy = -3826.2561684

C	-1.74989100	-0.27878500	0.33295800
C	-3.09315000	-0.67016400	0.15614000
C	-4.06326800	0.25185400	-0.16899400
C	-3.67789800	1.61642000	-0.34900200
C	-2.31843900	2.01599900	-0.20513800
C	-1.35378300	1.03154700	0.16419800
N	-4.67785500	2.47365100	-0.67758600
C	-4.37698000	3.73829300	-0.88579500
C	-3.06030800	4.23913700	-0.79482500
C	-2.03893800	3.38120100	-0.45807200
O	-5.35608100	-0.07858400	-0.32847000
N	-0.01401900	1.44702700	0.38132100
C	1.10733600	0.74761100	0.03152100
C	2.45211500	1.33312000	0.32198600
O	1.04335400	-0.35503200	-0.51098100
C	2.68861900	2.60389600	0.86689800
C	3.93886900	3.12725100	1.11322600
C	5.04391800	2.34190000	0.79417600
C	4.87520800	1.07630900	0.24995000
C	3.60049400	0.55672000	0.01173900
Se	3.39287300	-1.22964700	-0.76295000
S	5.54458200	-1.91360900	-0.88089200
C	5.81596600	-2.65345400	0.77781300

H	-1.01545900	-1.02404500	0.59925600
H	-5.20023000	4.39892500	-1.14480800
H	-2.86597700	5.28612700	-0.99802600
H	-1.02099500	3.75203700	-0.40710200
H	-5.82712400	0.74447500	-0.55793800
H	0.12066600	2.33839800	0.82997800
H	6.80513600	-3.11526400	0.75212400
H	5.79763200	-1.89415500	1.55968700
H	5.06993500	-3.41874600	0.98699900
I	-3.61856000	-2.70574000	0.42059000
H	5.74340700	0.48298400	-0.00849100
H	6.04447800	2.72406200	0.96717000
H	4.03104600	4.12004000	1.53641300
F	1.62620500	3.41179600	1.18498200

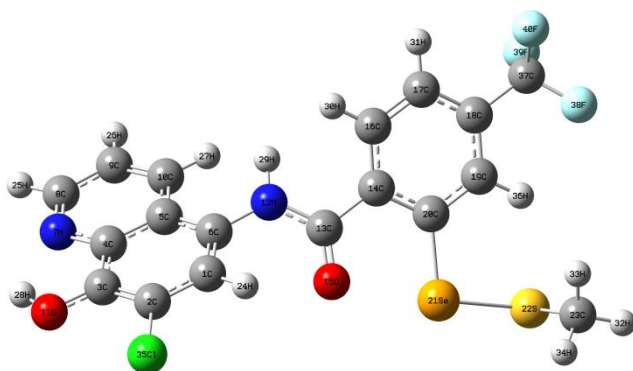


Selenenyl sulfides for 10j-S

Electronic Energy = -4512.9875081

C	-3.04159300	-1.34796700	0.18398700
C	-4.40626700	-1.45447300	-0.15360300
C	-5.23222200	-0.35140900	-0.17266600
C	-4.66577000	0.92057100	0.13816900
C	-3.28163600	1.05219800	0.45600400
C	-2.47536200	-0.12831000	0.49496800
N	-5.52473000	1.97053900	0.09378800
C	-5.06071500	3.17619200	0.34649400
C	-3.70536200	3.42673400	0.64909600
C	-2.82539400	2.37020700	0.69895500
O	-6.53881100	-0.43034300	-0.47725600
N	-1.11999700	-0.00284100	0.87979900
C	-0.08354600	-0.86885500	0.62410700
C	1.22545000	-0.46322600	1.25654100
O	-0.18928600	-1.89896900	-0.01819400
C	1.25298200	-0.25437500	2.63680300

C	2.45205600	0.01669200	3.28440800
C	3.62607000	0.04646200	2.54827900
C	3.62344500	-0.17704000	1.16495300
C	2.40934200	-0.40306400	0.48923000
Se	2.18208300	-0.66742100	-1.44992000
S	3.25360800	1.07825400	-2.34028800
C	1.97010900	2.38750400	-2.31637900
H	-2.43517000	-2.24039900	0.18739400
H	-5.77427400	3.99395700	0.30538100
H	-3.37080100	4.44092100	0.82872300
H	-1.77972200	2.56867000	0.90617000
H	-6.87957000	0.48140200	-0.42421000
H	-0.87093200	0.83456100	1.38128400
H	0.33406600	-0.33118500	3.20780700
H	2.47590700	0.17689800	4.35536300
H	4.56888200	0.22065700	3.04990700
H	2.41140700	3.24064500	-2.83750200
H	1.07286800	2.06702200	-2.84389700
H	1.73015900	2.67972400	-1.29430200
Cl	-5.05561000	-3.02775500	-0.53969600
C	5.00014500	-0.13815700	0.52086500
F	5.93265000	-0.63556300	1.37576100
F	5.10933800	-0.85282300	-0.60692300
F	5.38706200	1.13080100	0.24692300

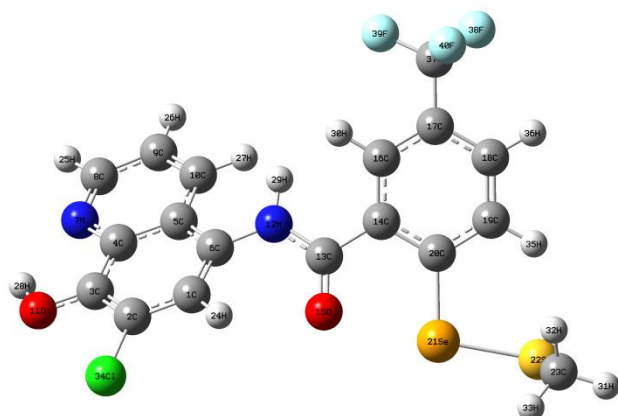


Selenenyl sulfides for 10k-S

Electronic Energy = -4513.0056451

C	3.19591900	-0.73731000	-0.98075400
C	4.56397100	-1.07262100	-0.94286000
C	5.47380100	-0.28944200	-0.26316200
C	4.99273300	0.86044900	0.43199700
C	3.60624700	1.19004800	0.43192600
C	2.71227900	0.37043500	-0.31897000

N	5.93198000	1.58403700	1.09231400
C	5.54382800	2.63681200	1.78114800
C	4.19311000	3.03740400	1.87502800
C	3.23250000	2.31533000	1.20565700
O	6.78560900	-0.57368400	-0.22794500
N	1.34364200	0.73526400	-0.39084500
C	0.27482500	-0.12331600	-0.32858300
C	-1.08431400	0.48290000	-0.44762100
O	0.40657900	-1.33098100	-0.16156000
C	-1.29152400	1.74301900	-1.03010900
C	-2.55570900	2.30189200	-1.11787900
C	-3.64118300	1.58944600	-0.60394900
C	-3.46419000	0.33175900	-0.04215000
C	-2.19548100	-0.25018200	0.02277600
Se	-1.95500900	-2.04882700	0.74687500
S	-4.01896100	-2.48016200	1.53177400
C	-4.82990300	-3.29015400	0.09522100
H	2.52251600	-1.37324500	-1.53649000
H	6.31861200	3.19662100	2.29677900
H	3.92692200	3.89663600	2.47812600
H	2.18991300	2.59841100	1.29527000
H	7.19407300	0.12266000	0.31889600
H	1.14039100	1.72135100	-0.41128800
H	-0.45895400	2.28729500	-1.46141700
H	-2.70038800	3.26633300	-1.58691400
H	-5.81458000	-3.60661500	0.44559800
H	-4.94996800	-2.59548200	-0.73560800
H	-4.26310800	-4.16333000	-0.22417400
Cl	5.11038500	-2.49362400	-1.79606100
H	-4.31523800	-0.20589800	0.35546900
C	-5.01252900	2.21463600	-0.63180400
F	-6.00060400	1.30038800	-0.55098700
F	-5.18708700	3.07518800	0.40230500
F	-5.21744200	2.92722000	-1.76387700

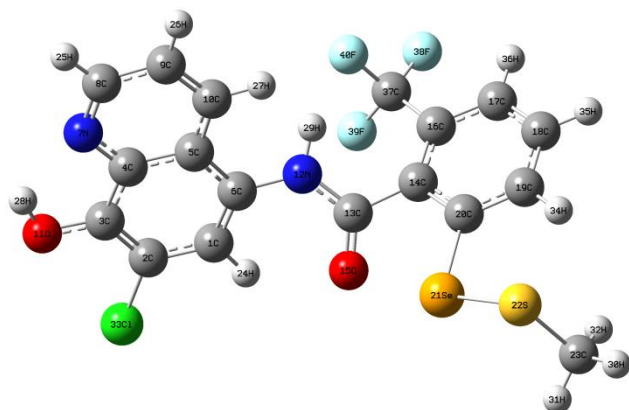


Selenenyl sulfides for 10I-S

Electronic Energy = - 4513.0068036

C	-2.80298700	-0.95209800	0.91809900
C	-4.16529000	-1.30763700	0.97693400
C	-5.12445700	-0.58628400	0.29745600
C	-4.70197800	0.52191400	-0.49626400
C	-3.32377800	0.87212700	-0.59299200
C	-2.37482200	0.11637800	0.15956300
N	-5.68868900	1.18627200	-1.14955200
C	-5.35897300	2.19929500	-1.92312100
C	-4.02360000	2.61532800	-2.11453500
C	-3.01499200	1.95223200	-1.45473700
O	-6.43103400	-0.89221400	0.35118100
N	-1.01414700	0.51178900	0.13003100
C	0.07803300	-0.31680000	0.16374700
C	1.42318600	0.32880600	0.14609900
O	-0.02126300	-1.54005100	0.18652000
C	1.60394000	1.68137900	0.46622100
C	2.85899200	2.26956100	0.41553700
C	3.96305300	1.50054900	0.03700000
C	3.80392000	0.15663200	-0.25805100
C	2.54825200	-0.45798400	-0.19007100
Se	2.34059700	-2.36226900	-0.55322900
S	4.42137100	-2.91173100	-1.22050900
C	5.22252900	-3.41335700	0.35545100
H	-2.09040000	-1.54083400	1.47593600
H	-6.17108600	2.71235600	-2.42987300
H	-3.80627000	3.44004500	-2.78189200
H	-1.98565900	2.24956000	-1.61992700
H	-6.88024600	-0.23934700	-0.21688000
H	-0.83914900	1.49534200	0.00588400
H	0.76726200	2.28811300	0.78864200

H	6.20568300	-3.80265200	0.08273300
H	5.34503300	-2.56407000	1.02739000
H	4.64842100	-4.19829200	0.84535400
Cl	-4.63880700	-2.67646500	1.95066200
H	4.66244900	-0.43026400	-0.55961400
H	4.94664700	1.95137200	-0.02259500
C	3.05129800	3.70883800	0.79984200
F	3.84144400	4.36496600	-0.08159800
F	1.88128300	4.38570600	0.86611500
F	3.64383900	3.83619800	2.01320400

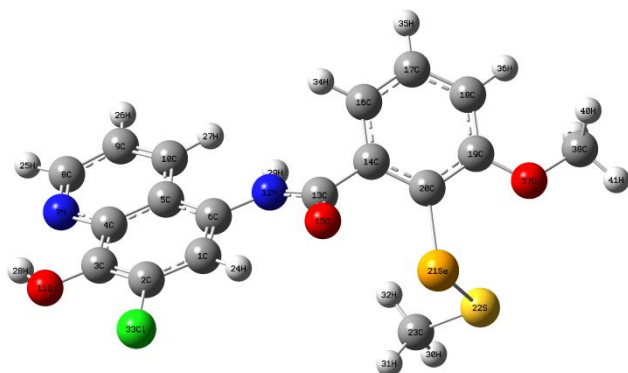


Selenenyl sulfides for 10m-S

Electronic Energy = -4512.9975058

C	-2.36194500	-0.79184700	-1.10260800
C	-3.67145300	-1.30993900	-1.16359800
C	-4.59694700	-1.04496700	-0.17748000
C	-4.19261200	-0.24099500	0.93015300
C	-2.86555600	0.27081400	1.02113600
C	-1.95256700	-0.00947700	-0.04268600
N	-5.14444000	-0.02141200	1.87230500
C	-4.82771800	0.69336600	2.93165400
C	-3.53885600	1.23014000	3.13606600
C	-2.56612400	1.01580500	2.18705700
O	-5.85438100	-1.51687700	-0.21817200
N	-0.65511800	0.55281600	0.02790400
C	0.47645400	0.10708900	-0.59126800
C	1.73844900	0.89570700	-0.32923800
O	0.53141300	-0.91873500	-1.25645500
C	1.87326700	2.29147300	-0.49186400
C	3.07944900	2.92727400	-0.20119600
C	4.16039500	2.18326600	0.25824800
C	4.05716000	0.80533000	0.38537400
C	2.86742100	0.15013500	0.06799200

Se	2.74095200	-1.80472700	0.16105700
S	4.55189600	-2.31225400	1.37649900
C	5.80616600	-2.68232500	0.08470600
H	-1.67400000	-1.02443000	-1.90034500
H	-5.61180200	0.85359300	3.66596900
H	-3.32596000	1.79501200	4.03514500
H	-1.56983400	1.40838100	2.35480800
H	-6.28654500	-1.18737600	0.59140400
H	-0.57175600	1.40481400	0.55979900
H	6.69618800	-3.01827700	0.62133200
H	5.45897000	-3.47974700	-0.57022000
H	6.04925500	-1.79611600	-0.50070100
Cl	-4.12282800	-2.29649000	-2.53151900
H	4.90121400	0.22974700	0.74384800
H	5.09394500	2.67877200	0.49800000
H	3.17309500	3.99447600	-0.34597100
C	0.74354000	3.15868400	-0.99986700
F	1.17363500	4.35764100	-1.43312400
F	0.06000100	2.59435700	-2.01390600
F	-0.17340200	3.42646300	-0.01264800

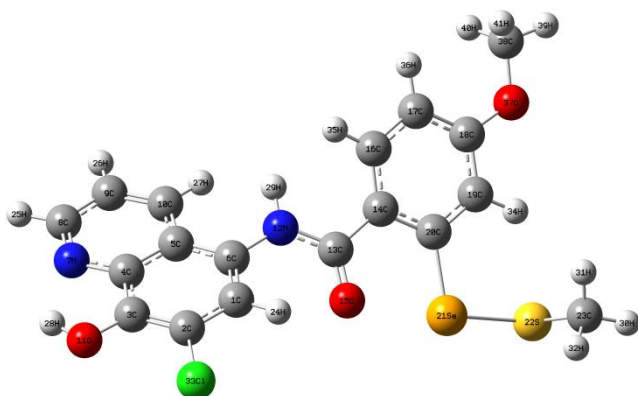


Selenenyl sulfides for 10n-S

Electronic Energy = - 4290.4061818

C	2.52792600	-0.98376900	-0.69270100
C	3.86905900	-1.40587800	-0.58460800
C	4.84038600	-0.59749700	-0.03713200
C	4.45901700	0.70150600	0.41163900
C	3.11149200	1.15622700	0.29472100
C	2.13521500	0.26877800	-0.26279500
N	5.45902500	1.45512200	0.93610100
C	5.18019200	2.67158200	1.35454200
C	3.88740600	3.23013600	1.27405700
C	2.86529600	2.47532000	0.74539800

O	6.12353300	-0.98302500	0.08454200
N	0.79778400	0.71455100	-0.34059800
C	-0.26611500	0.13638100	-0.99800100
C	-1.54047400	0.93559600	-0.90811900
O	-0.20317800	-0.90980400	-1.61995300
C	-1.52143200	2.28845700	-1.27556700
C	-2.70413800	3.01553400	-1.29868600
C	-3.91227200	2.40631300	-0.97264400
C	-3.94495800	1.05325700	-0.61627000
C	-2.74544100	0.30950900	-0.56002900
Se	-2.78139100	-1.56877500	-0.04211700
S	-3.78034200	-1.46438100	1.96323000
C	-2.35145700	-1.28316100	3.09961000
H	1.79964400	-1.65263600	-1.12364100
H	6.00234300	3.24703700	1.77009700
H	3.71298000	4.24140200	1.62007700
H	1.87798600	2.91744600	0.67122500
H	6.58784700	-0.22959300	0.49287000
H	0.56559700	1.53095100	0.20145700
H	-2.76981300	-1.31316900	4.10892300
H	-1.64546400	-2.10336600	2.97839100
H	-1.85124400	-0.32678500	2.94851100
Cl	4.29351600	-3.00140400	-1.15319200
H	-0.59143500	2.75235400	-1.58309000
H	-2.69520600	4.05888800	-1.59239000
H	-4.82658900	2.98221600	-1.01443700
O	-5.08606300	0.38933200	-0.32330900
C	-6.32567800	1.08737900	-0.33385200
H	-6.33183500	1.89830100	0.40163500
H	-6.55060300	1.48691900	-1.32818500
H	-7.07735200	0.34856400	-0.06301100



Selenenyl sulfides for 10o-S

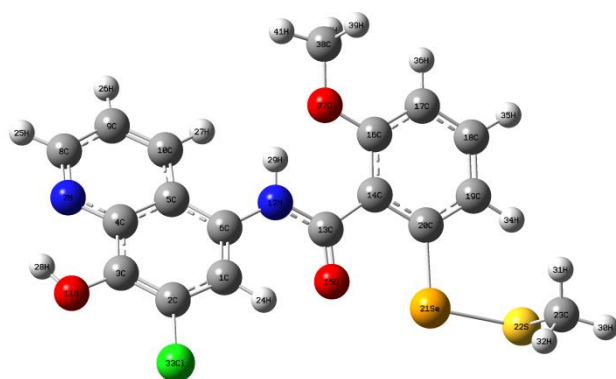
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C	2.70967100	-0.92707600	-0.78175300
C	4.04547700	-1.37537200	-0.75359000
C	5.05358900	-0.59939800	-0.22227200
C	4.70790200	0.66858000	0.33183400
C	3.35530100	1.12025600	0.34388200
C	2.35366300	0.29710200	-0.25556200
N	5.73813400	1.38338800	0.85205700
C	5.47793000	2.54723000	1.40978500
C	4.17332500	3.07793500	1.50425500
C	3.12160700	2.36504300	0.97631300
O	6.33833900	-0.99543700	-0.20169400
N	1.02619700	0.78095200	-0.32026900
C	-0.12760400	0.03382600	-0.23857500
C	-1.41558500	0.75643000	-0.37992300
O	-0.10360100	-1.17838400	-0.03922000
C	-1.50677100	2.05181000	-0.90446400
C	-2.71447800	2.72714300	-1.01604100
C	-3.88163400	2.08804900	-0.58115200
C	-3.81981800	0.78728200	-0.07429300
C	-2.61391200	0.10761200	0.01524600
Se	-2.55057300	-1.73260000	0.67824000
S	-4.69407300	-2.05018900	1.29373600
C	-5.45885300	-2.69993300	-0.24575800
H	1.95778600	-1.56718300	-1.21761000
H	6.32367600	3.09554000	1.81456400
H	4.01224900	4.02808600	1.99843100
H	2.11390100	2.75301500	1.07323800
H	6.83026700	-0.27398300	0.23163800
H	0.91755100	1.77999700	-0.36790700
H	-6.48090800	-2.98032300	0.01802000
H	-5.48424800	-1.93929700	-1.02590900
H	-4.92365300	-3.58025600	-0.59884300
Cl	4.42345300	-2.93987200	-1.43084800
H	-4.73900400	0.32214700	0.25940100
H	-0.61997600	2.55336000	-1.27710900
H	-2.73537100	3.72102700	-1.44014000
O	-5.12020200	2.64217100	-0.62365800
C	-5.26574200	3.96766300	-1.12295600
H	-6.32727200	4.19569500	-1.04834700
H	-4.69724700	4.68373400	-0.52075500
H	-4.95281500	4.03541500	-2.16999500



Electronic Energy = -4290.4137377

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H	-5.71616000	-1.87448700	-0.96664000
H	-5.17922300	-3.54474700	-0.63885200
Cl	4.28516100	-2.89769900	-1.71588900
H	-4.83599500	0.31690200	0.36732700
H	-4.91653100	2.64213400	-0.37015100
H	-0.71400700	2.57283900	-1.12208400
O	-2.72030600	4.04994200	-1.23639200
C	-3.92015900	4.81004000	-1.32214100
H	-4.38187700	4.94061800	-0.33761400
H	-3.62739700	5.78243800	-1.71400300
H	-4.63848900	4.34486800	-2.00541200



C	2.91327000	0.52777800	-0.12476800
Se	3.08501100	-1.38494800	-0.51515900
S	5.33517200	-1.60113100	-0.68767400
C	5.83502000	-1.90458500	1.05384600
H	-1.24444400	-1.93336700	0.62946300
H	-6.57803500	2.41138100	-1.01091600
H	-4.46923800	3.74146800	-1.17999700
H	-2.30760800	2.65442200	-0.68287000
H	-6.39010400	-1.23203600	-0.11883700
H	-0.83570600	1.67991900	0.38156200
H	6.90307700	-2.13141200	1.03297100
H	5.66711500	-1.02153900	1.67069800
H	5.29409700	-2.75534400	1.46619700
Cl	-3.43868400	-3.71778100	0.75669400
H	5.02677100	0.87418100	-0.26180000
H	4.86124000	3.28019200	0.24997400
H	2.67237700	4.32534300	0.66103800
O	0.33197700	3.04497600	0.59567600
C	0.22589700	4.41138400	0.99741200
H	0.77045700	4.58886800	1.92848300
H	0.59294500	5.08179100	0.21549900
H	-0.83599500	4.58868700	1.15933700

5. Tables of Results for the PAMPA

Table S13. Permeability ($P_e \times 10^{-6} \text{ cm s}^{-1}$) in the PAMPA-BBB assay for 13 commercial drugs, used in the Experiment Validation.

Commercial drugs	Bibl ^a	PBS : EtOH (70 : 30) ^b
testosterone	17	22.3 $\pm$ 1.4
verapamil	16	21.2 $\pm$ 1.9
desipramine	12	16.4 $\pm$ 1.2
progesterone	9.3	17.7 $\pm$ 1.2
promazine	8.8	14.3 $\pm$ 0.5
chlorpromazine	6.5	6.0 $\pm$ 0.3
clonidine	5.3	5.1 $\pm$ 0.3
piroxicam	2.5	0.24 $\pm$ 0.01
hydrocortisone	1.9	0.65 $\pm$ 0.01
lomefloxacin	1.1	0.37 $\pm$ 0.02
atenolol	0.8	0.78 $\pm$ 0.02
ofloxacin	0.8	0.37 $\pm$ 0.02
theophylline	0.1	0.26 $\pm$ 0.01

^a Taken from reference 3. ^b Data are the mean $\pm$ SD of three independent experiments

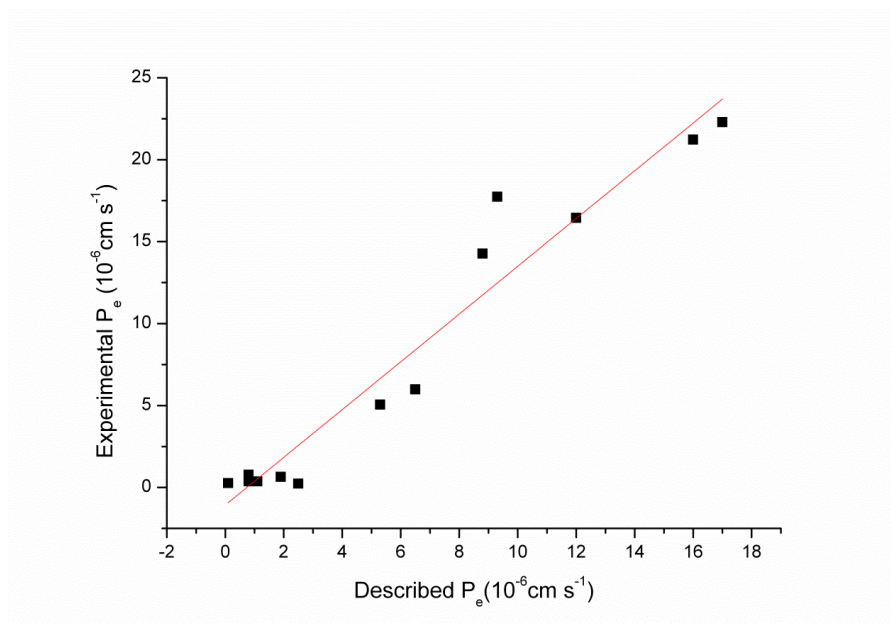


Figure S1. Lineal correlation between experimental and reported permeability of commercial drugs using the PAMPA-BBB assay. $P_e(\text{exp.}) = 1.4574P_e(\text{bibl.}) - 1.0773$ ($R^2 = 0.9427$)

Table S14. Ranges of Permeability of PAMPA-BBB Assays (P_e , $10^{-6} \text{ cm s}^{-1}$)

Compounds of high BBB permeation (CNS+)	$P_e > 4.7$
Compounds of uncertain BBB permeation (CNS±)	$4.7 > P_e > 1.8$
Compounds of low BBB permeation (CNS–)	$P_e < 1.8$

References

1. Sarma, B. K.; Mugesh, G. Glutathione peroxidase (GPx)-like antioxidant Activity of the organoselenium drug ebselen: unexpected complications with thiol exchange reactions. *J. Am. Chem. Soc.* 2005, **127**, 11477-11485.
2. Selvakumar, K.; Shah, P.; Singh, H. B.; Butcher, R. J. Synthesis, structure, and glutathione peroxidase-like activity of amino acid containing ebselen analogues and diaryl diselenides. *Chem. Eur. J.* 2011, **17**, 12741-12755.
3. Di, L.; Kerns, E. H.; Fan, K.; McConnell, O. J.; Carter, G. T. High throughput artificial membrane permeability assay for blood–brain barrier. *Eur. J. Med. Chem.* 2003, **38**, 223-232.