

Supplementary Information

Title:

Novel Thiazolylketenyl Quinazolinones and Analogues as Potential Anti-MRSA Agents and Allosteric Modulator for PBP2a

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1. Antibacterial activity

Table S1 Antibacterial data (MIC, $\mu\text{g/mL}$) for thiazolylketenyl quinazolinone **4** against MRSA and *S. aureus*.

Comps	MRSA	<i>S. a.</i>	<i>S. a.</i>	<i>S. a.</i>	<i>S. a.</i>
	43300	26003	26001	12600	6538
4	1	8	4	1	2
Norfloxacin	4	1	4	2	4

Table S2 Minimum bactericidal concentration (MBC, $\mu\text{g/mL}$) of active compound **4** against MRSA.

Bacteria	Compound	MIC	MBC	MBC/MIC	Effect
MRSA	4	0.5	8	16	Bacteriostatic

2. Hemolytic activity

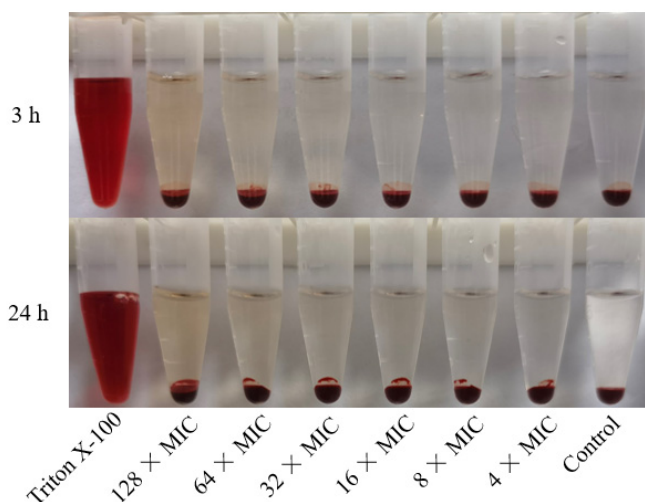


Figure S1 Images of RBC processed with compound **4** at different times.

3. ADMET study

The radar plot bears six axes for six important properties for oral bioavailability: saturation (INSATU), size (SIZE), polarity (POLAR), solubility (INSOLU), lipophilicity (LIPO) and flexibility (FLEX). **Figure S2** showed that compound **4** almost fall in the pink area and reference drug norfloxacin was completely in this area, which revealed that candidate compound **4** had good drug-likeness and bioavailability profile.

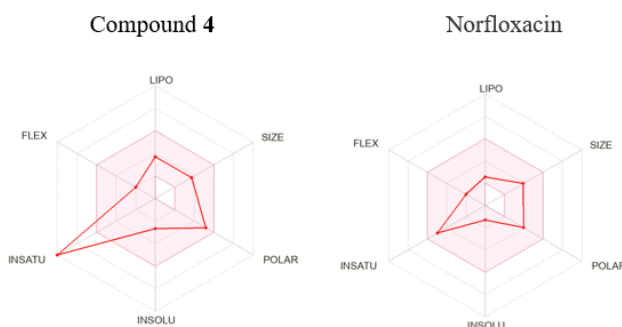


Figure S2 Bioavailability radar charts from swiss ADME web tool for compound **4** and norfloxacin.

4. Interactions of 7 with calf thymus DNA

Equation (1) is utilized to calculate the binding constant (K). Where A^0 and A are the absorbance of DNA in the absence and presence of compound **4** at 260 nm, ξ_C and ξ_{D-C} represent the absorption coefficients of compound **4** and compound **4**-DNA complex respectively (**Figure S3**).

$$\frac{A^0}{A - A^0} = \frac{\xi_C}{\xi_{D-C} - \xi_C} + \frac{\xi_C}{\xi_{D-C} - \xi_C} \times \frac{1}{K[Q]} \quad (1)$$

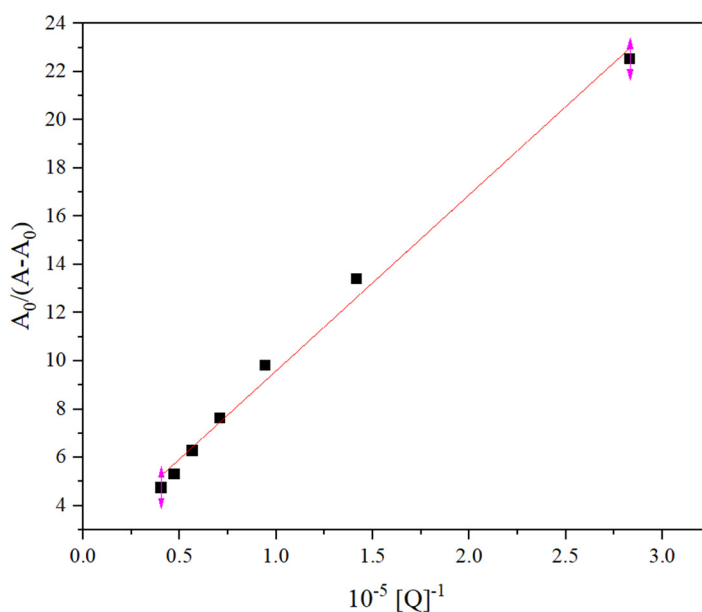
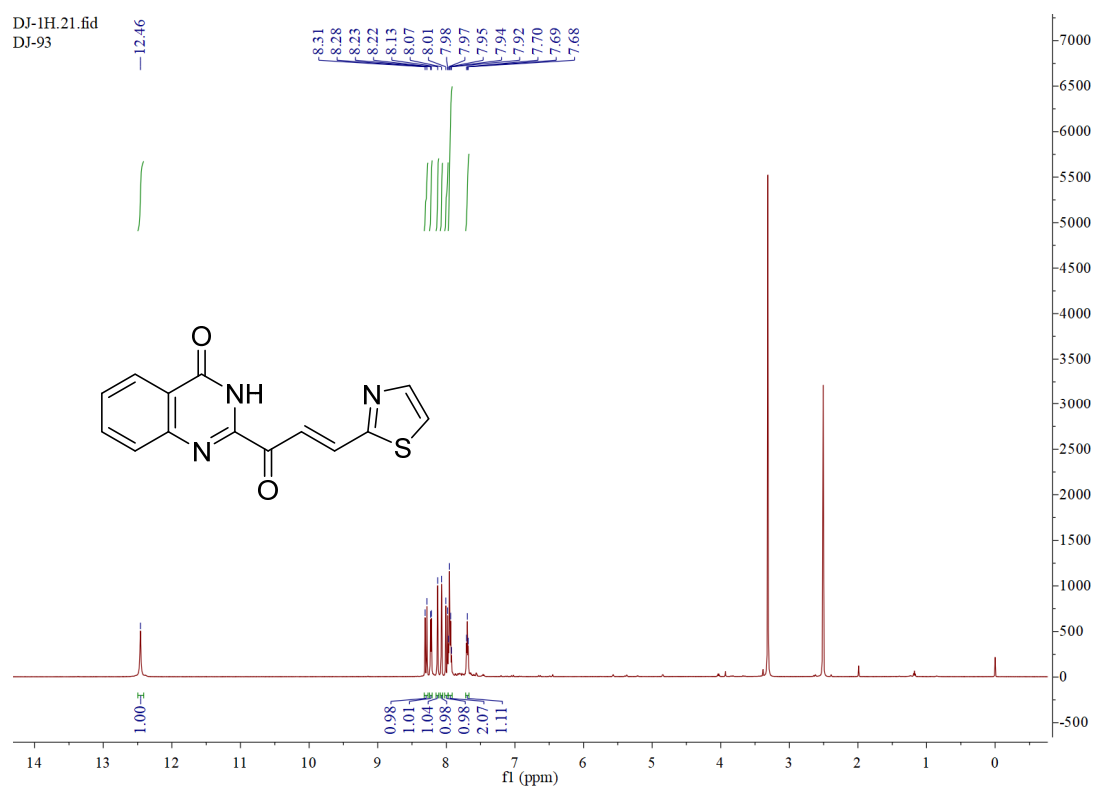


Figure S3 The plot of $A^0 / (A - A^0)$ versus $1/[$ compound **4**], yielding the binding constant, $K = 1.01 \times 10^5$ L/mol, $R = 0.996$, $SD = 0.039$ (R is the correlation coefficient. SD is standard deviation).

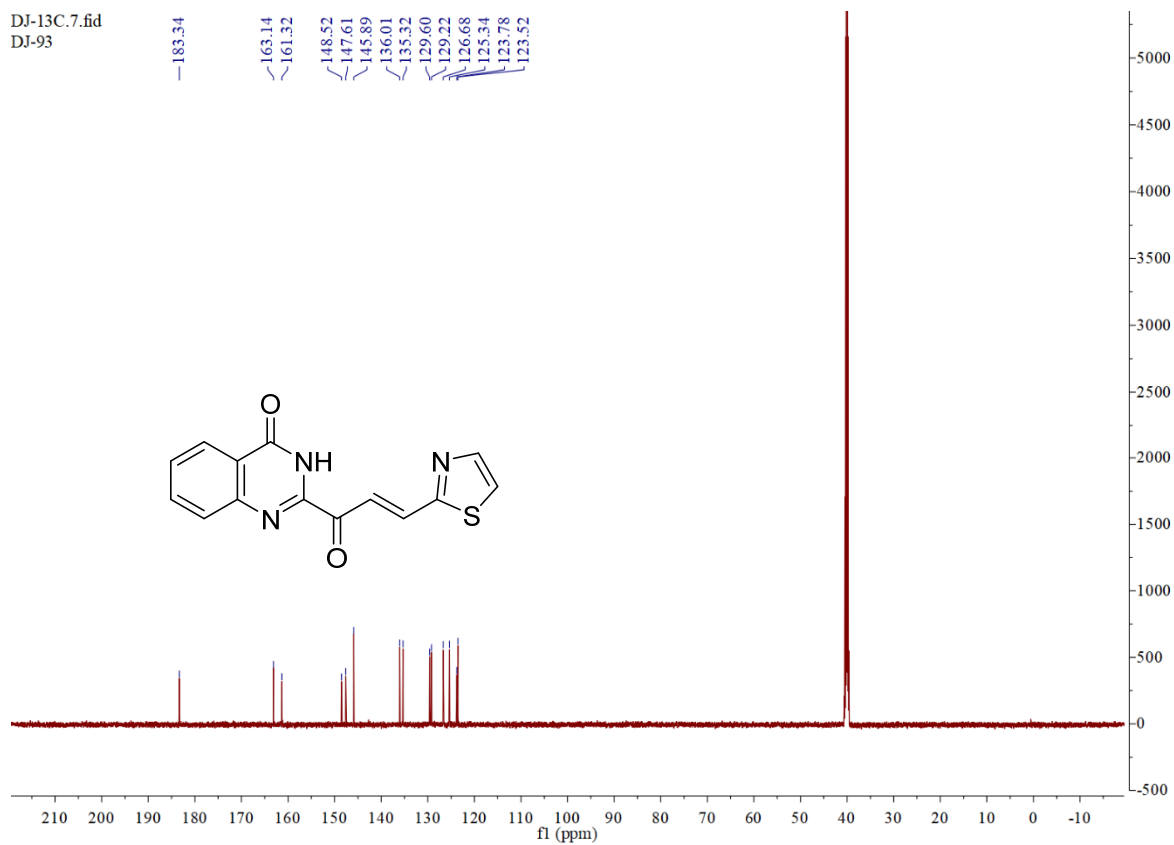
5. Characterizations of some representative compounds

5.1 Spectra of compound 4

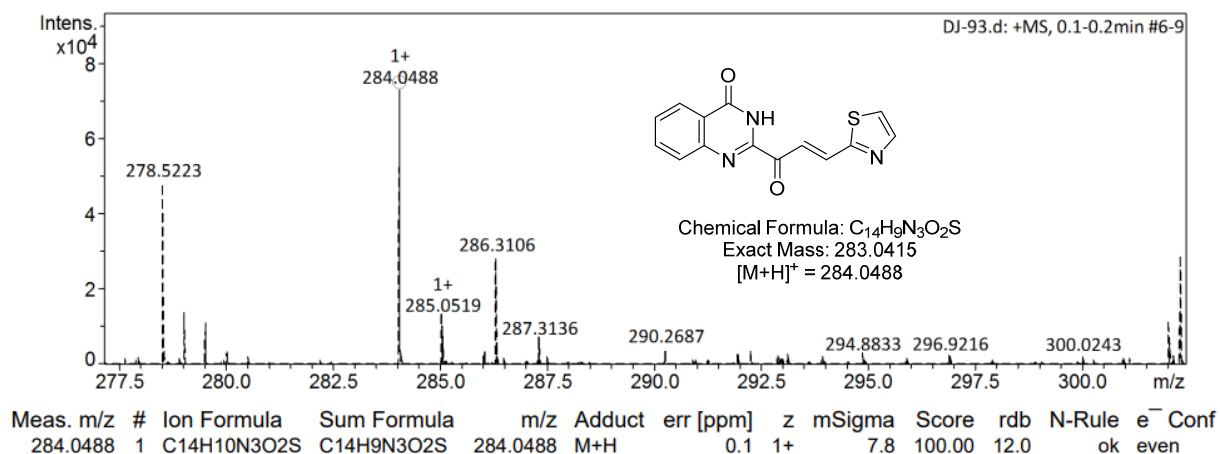
¹H NMR spectrum



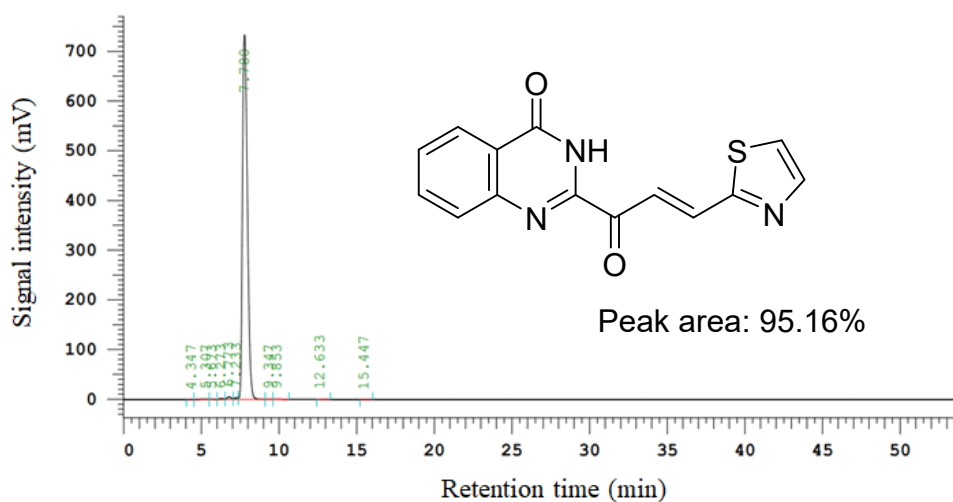
¹³C NMR spectrum



HRMS spectrum

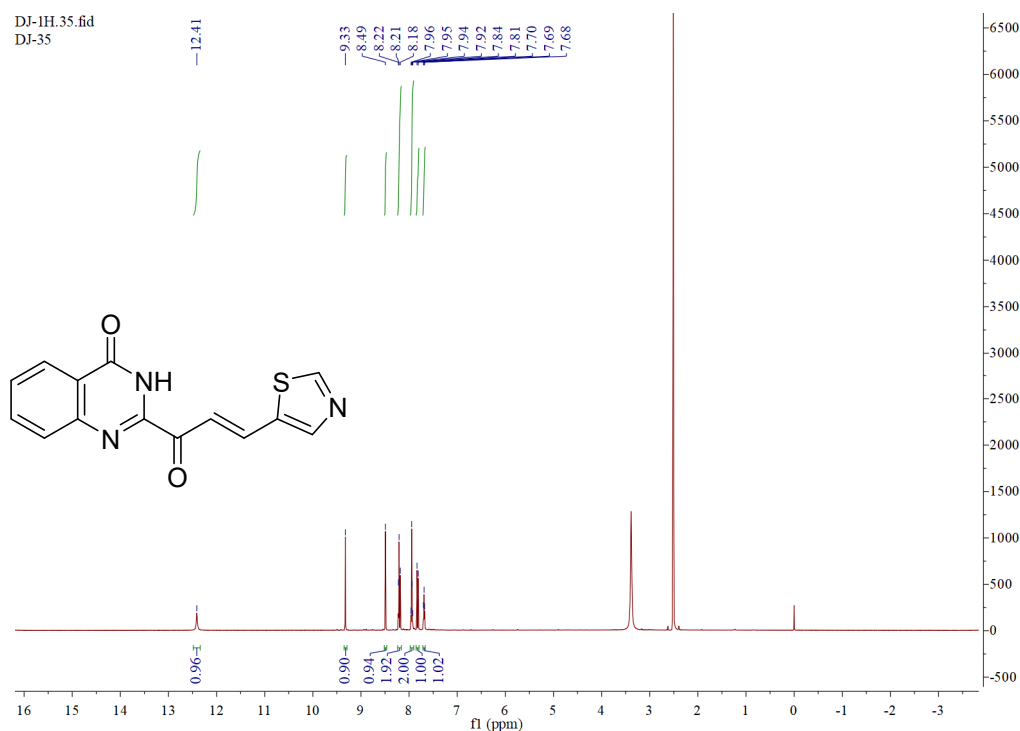


HPLC spectrum

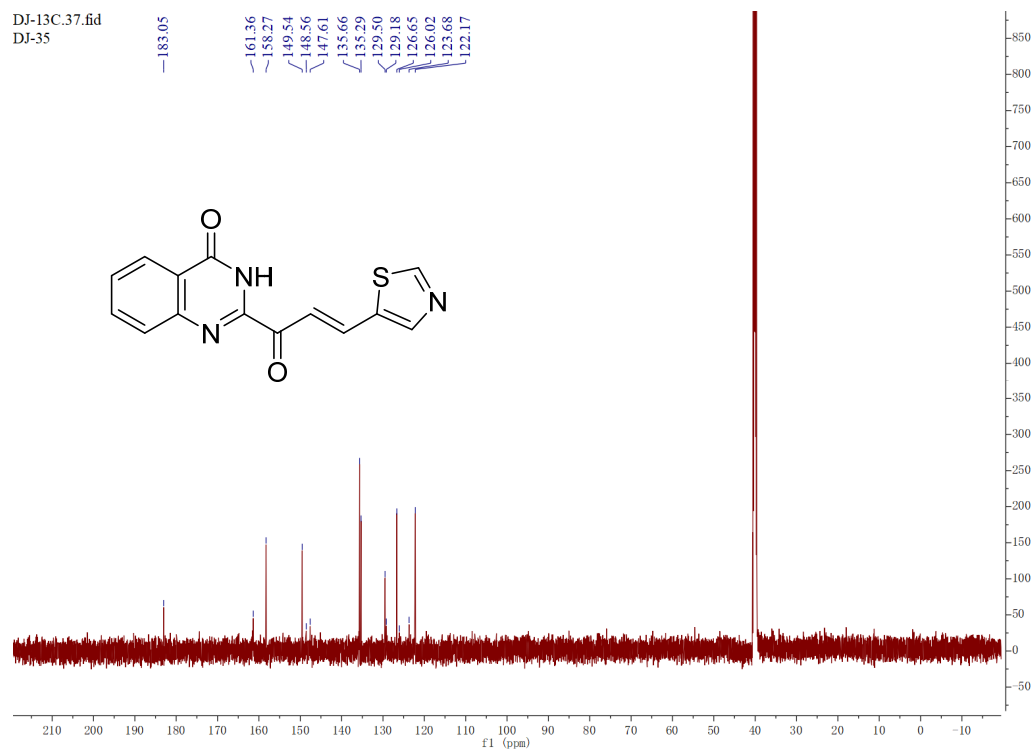


5.2 Spectra of compound **5a**

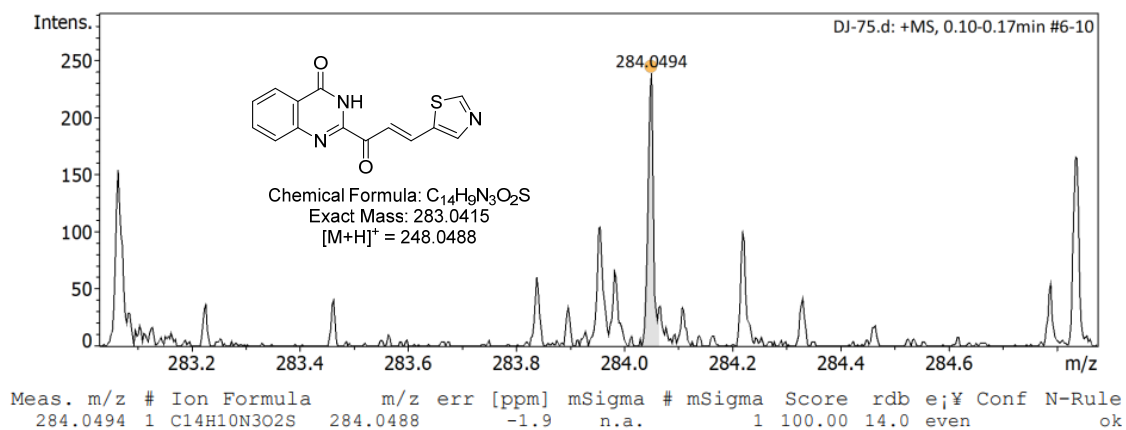
1H NMR spectrum



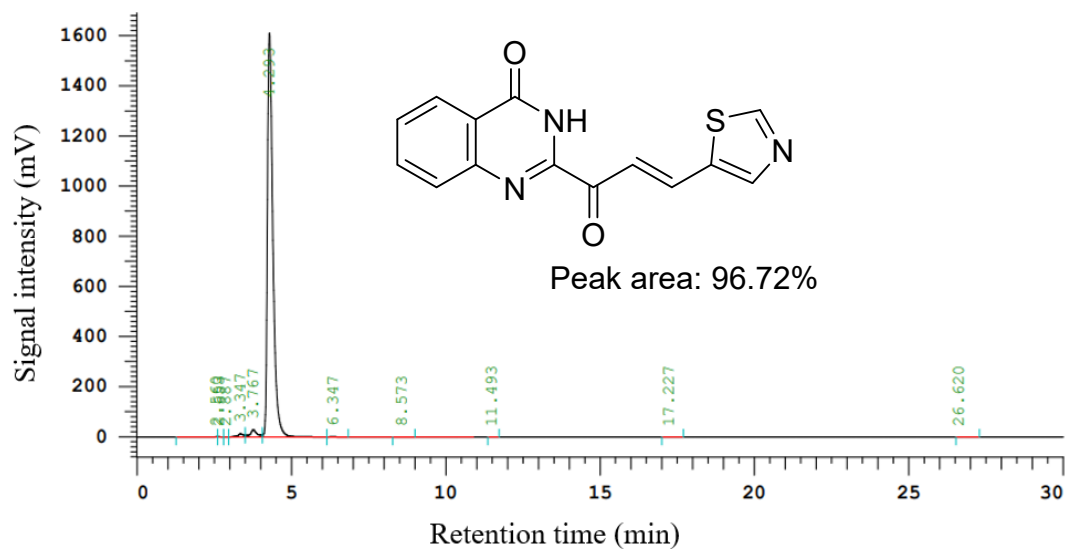
¹³C NMR spectrum



HRMS spectrum

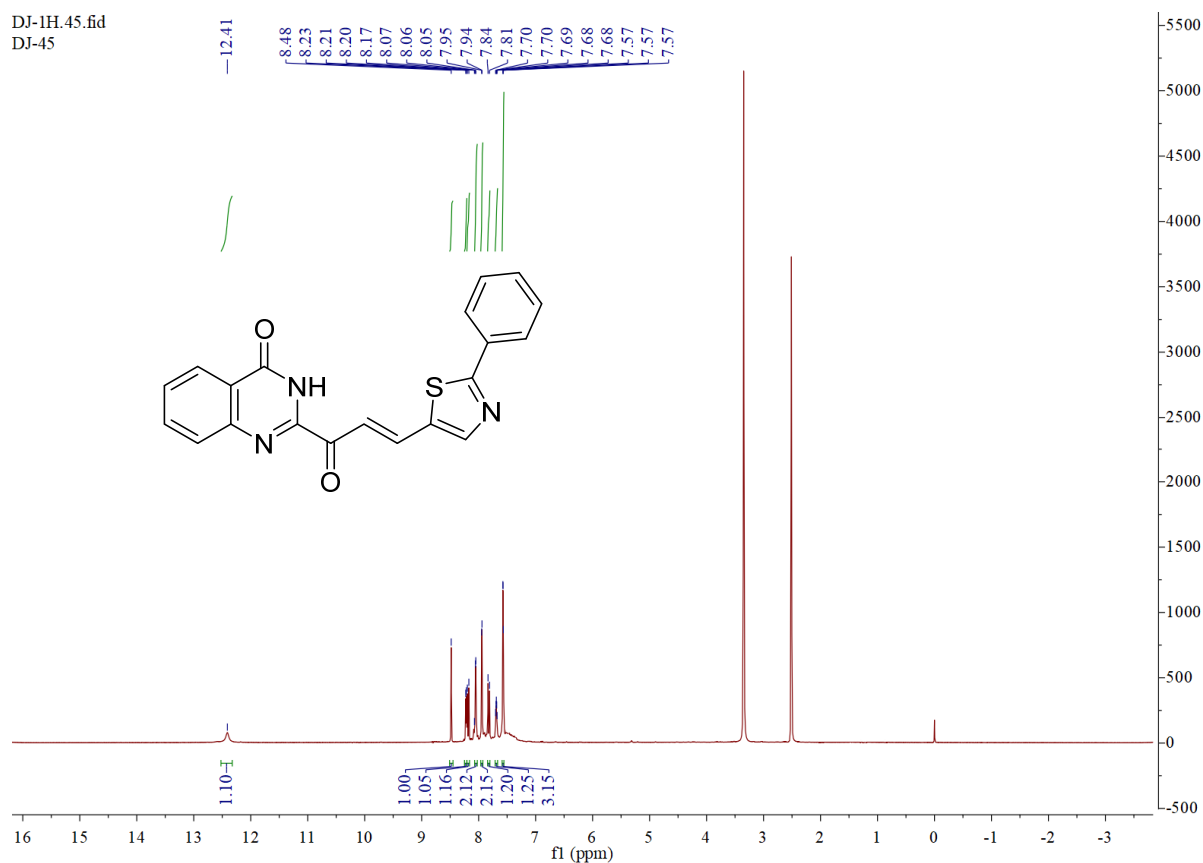


HPLC spectrum

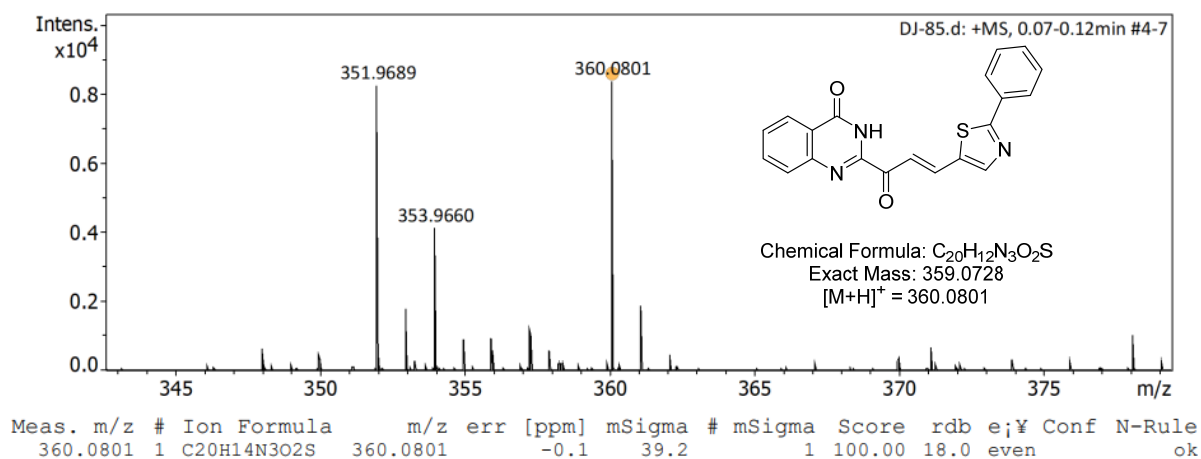


5.3 Spectra of compound **5b**

¹H NMR spectrum

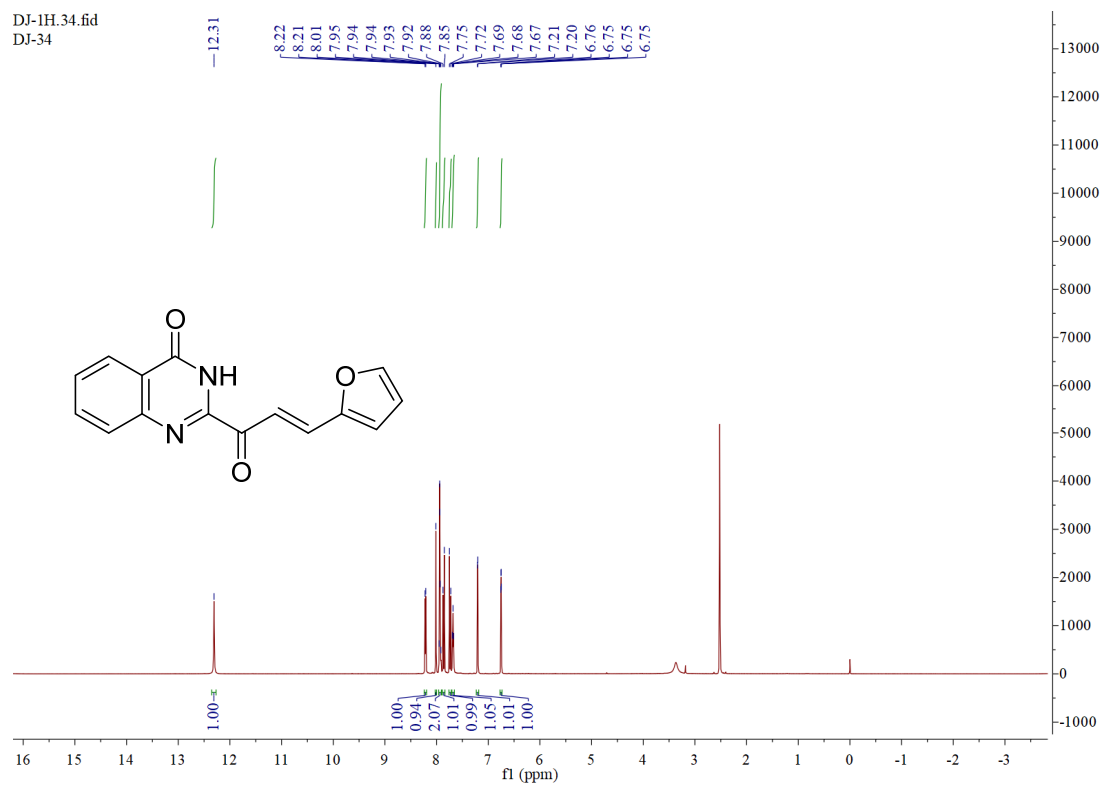


HRMS spectrum

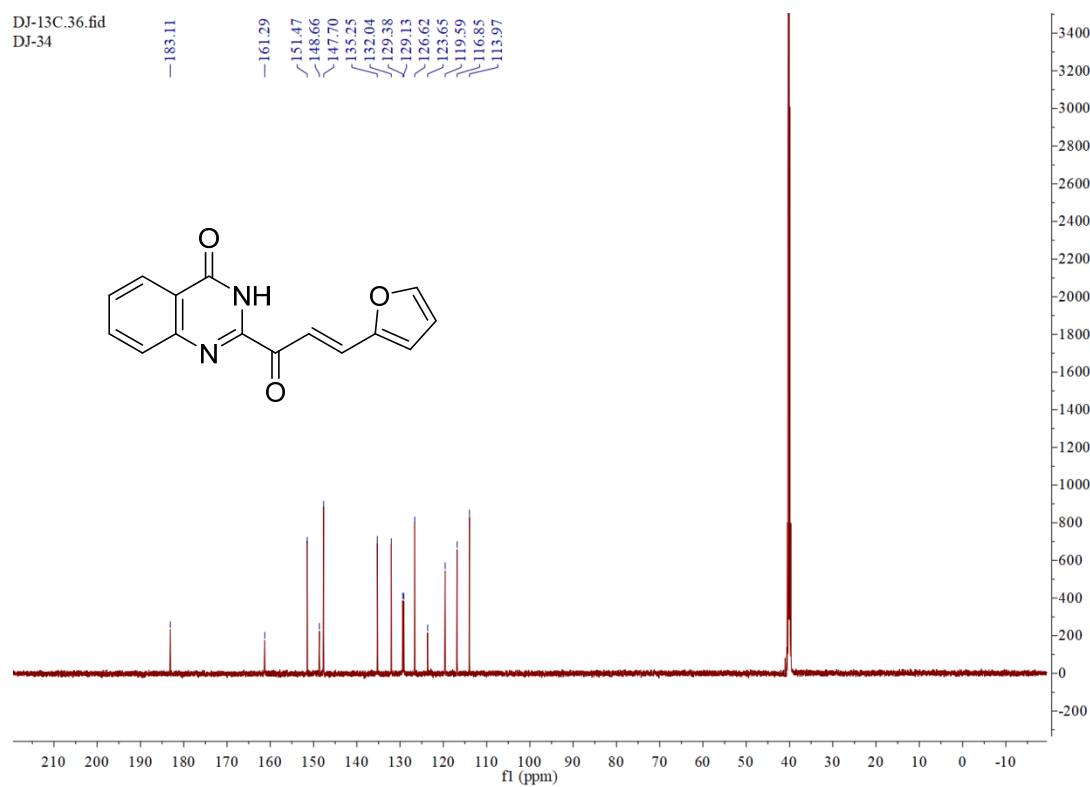


5.4 Spectra of compound **6a**

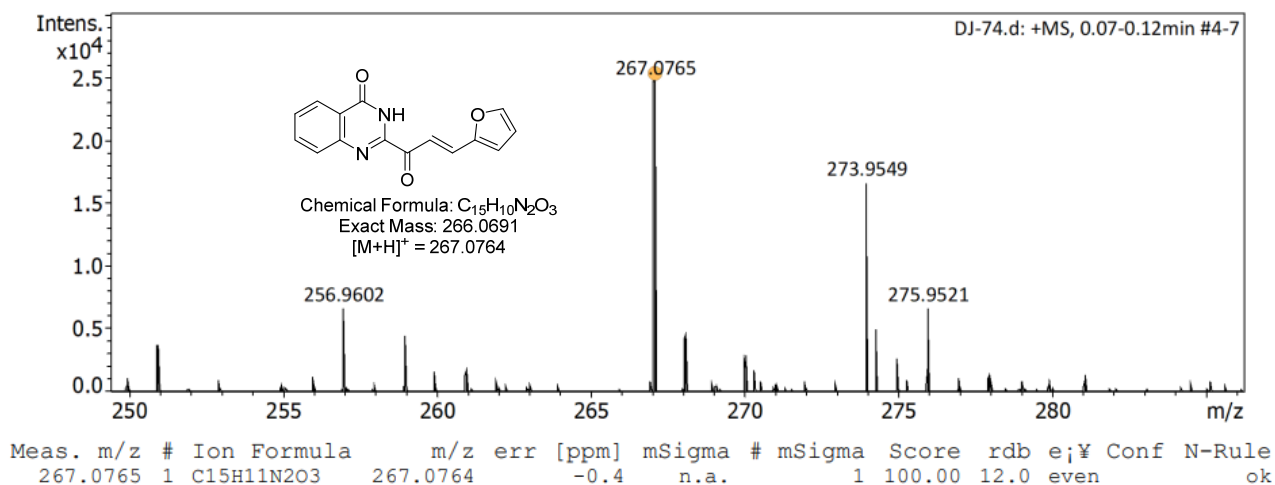
¹H NMR spectrum



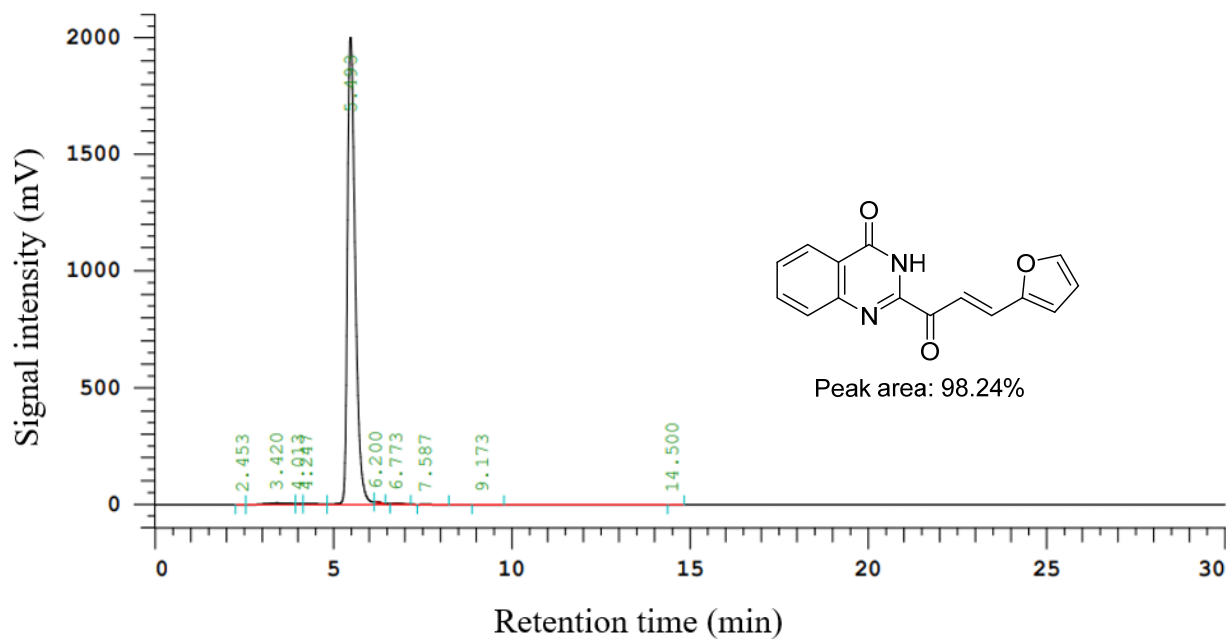
¹³C NMR spectrum



HRMS spectrum

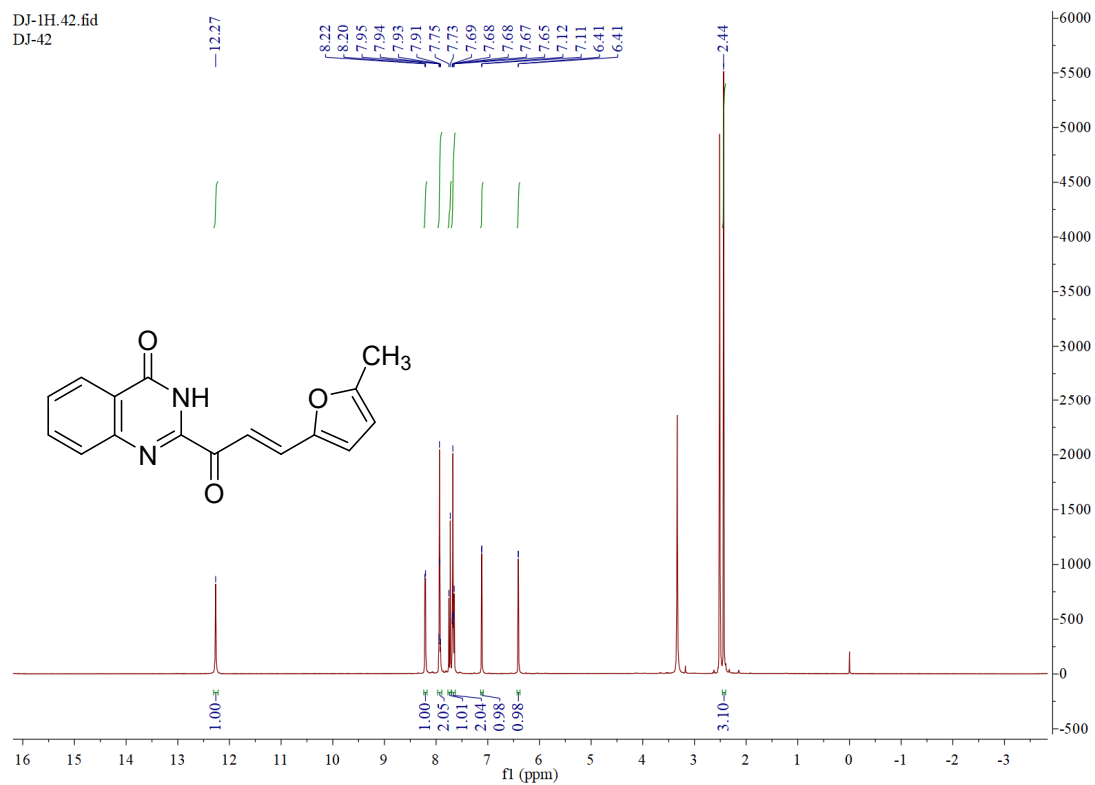


HPLC spectrum

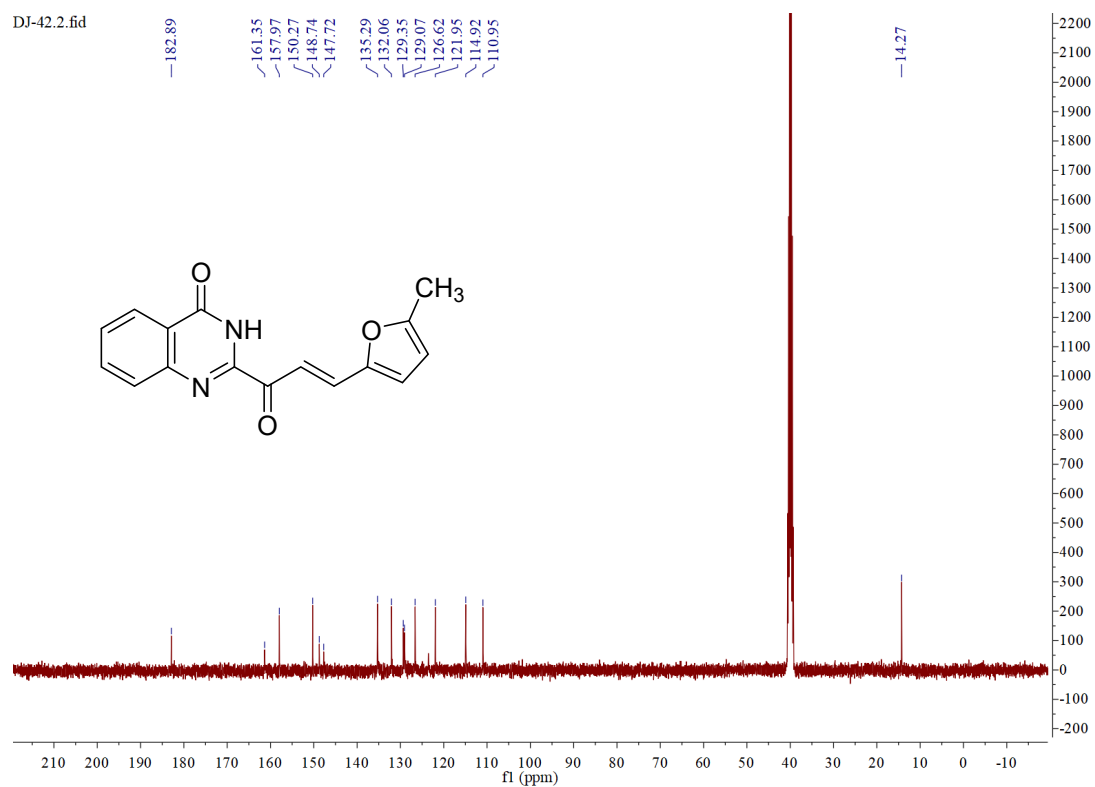


5.5 Spectra of compound **6b**

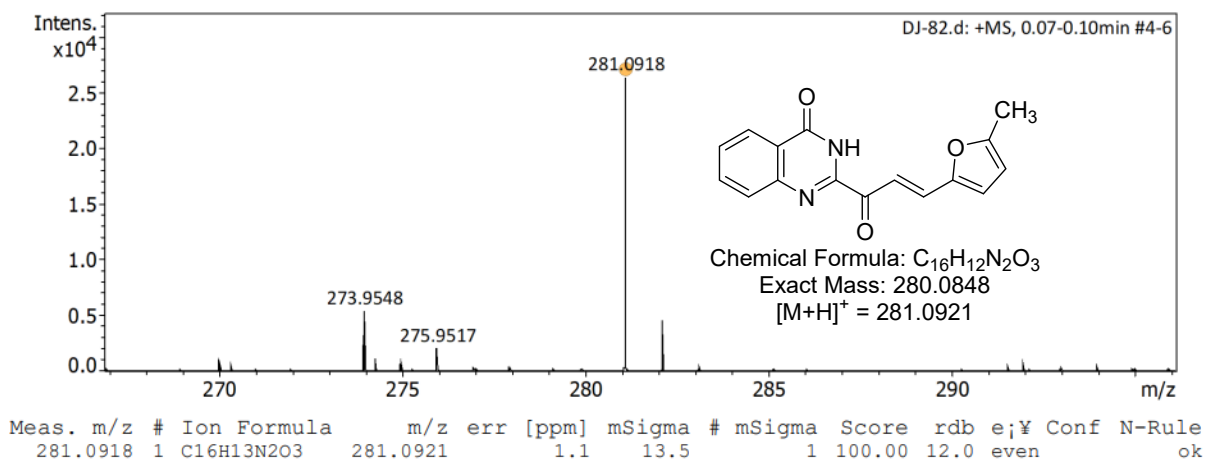
1H NMR spectrum



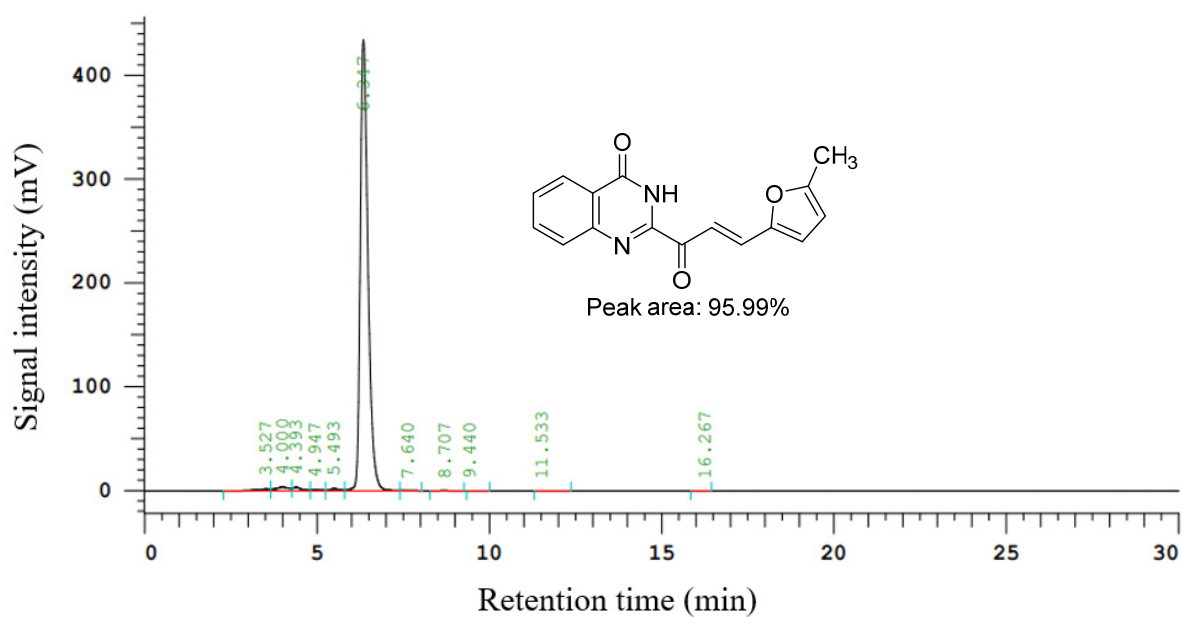
¹³C NMR spectrum



HRMS spectrum

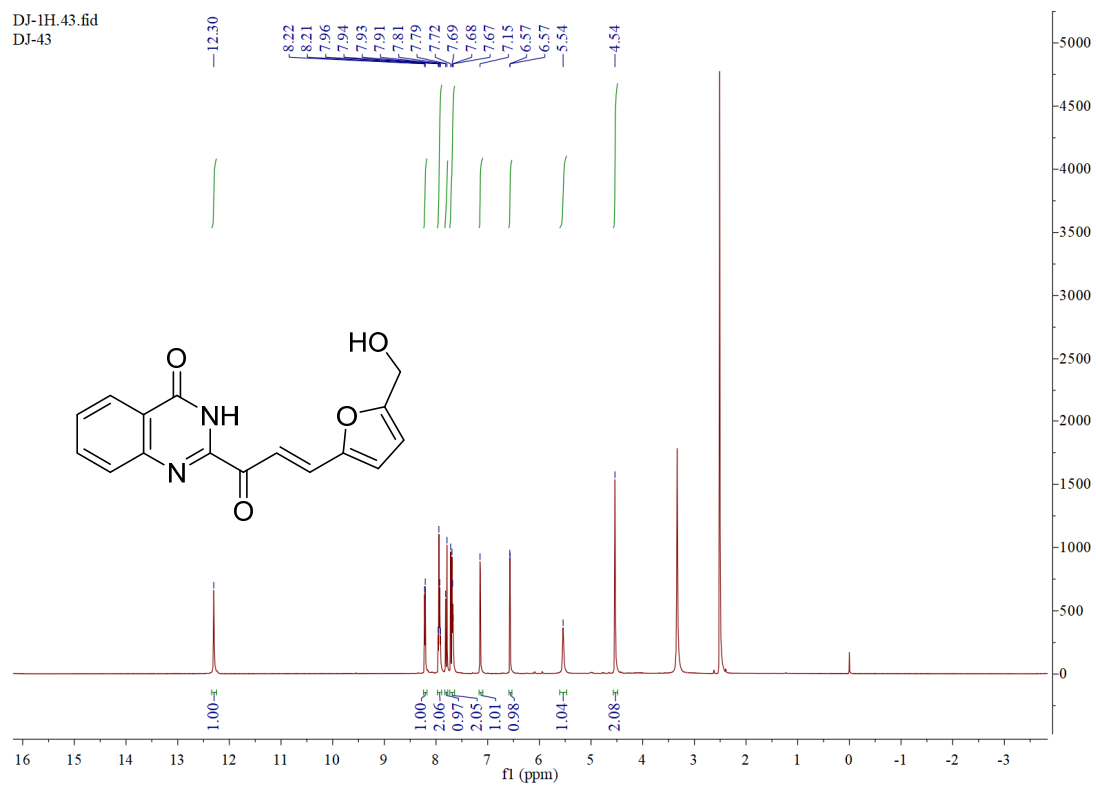


HPLC spectrum

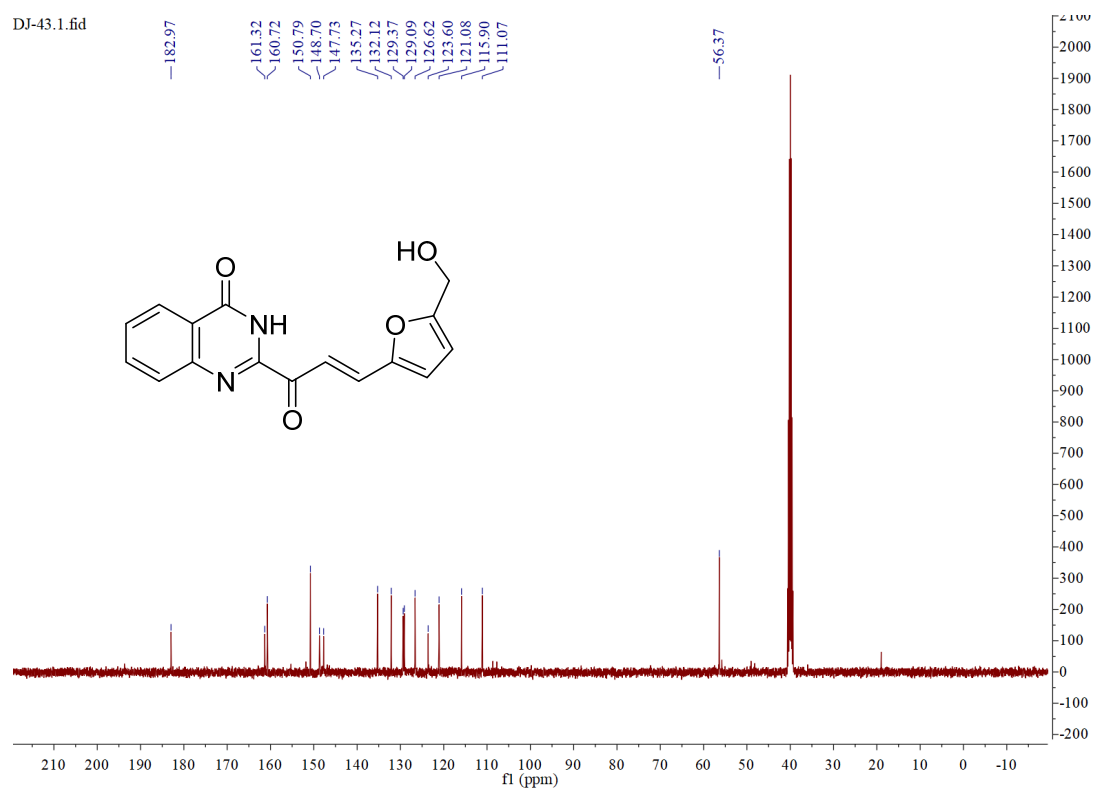


5.6 Spectra of compound 6c

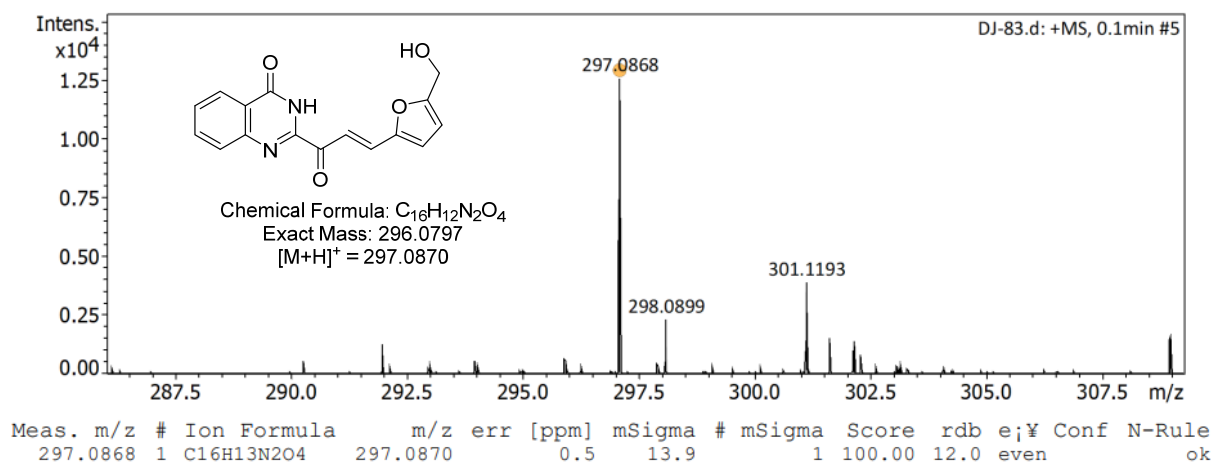
¹H NMR spectrum



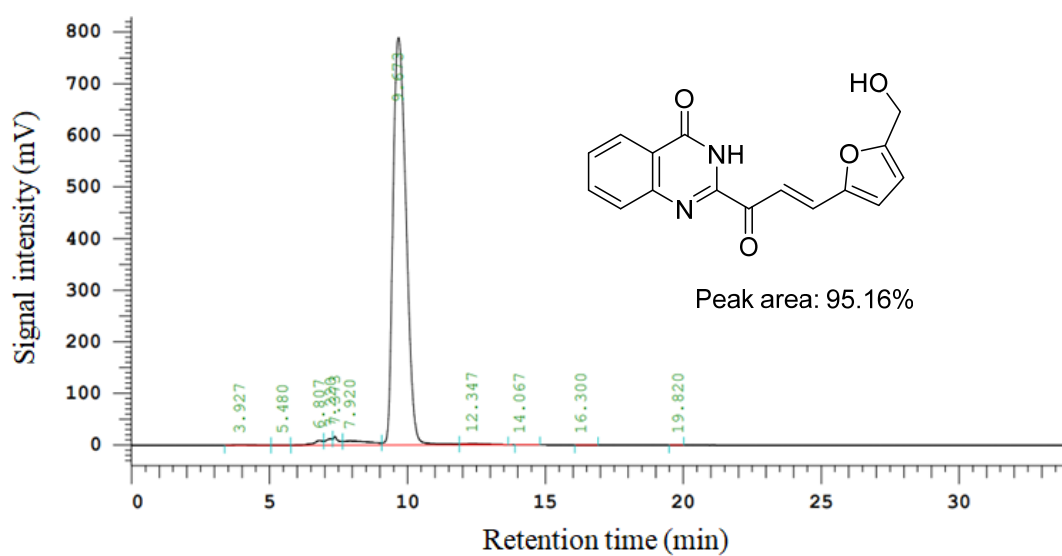
¹³C NMR spectrum



HRMS spectrum

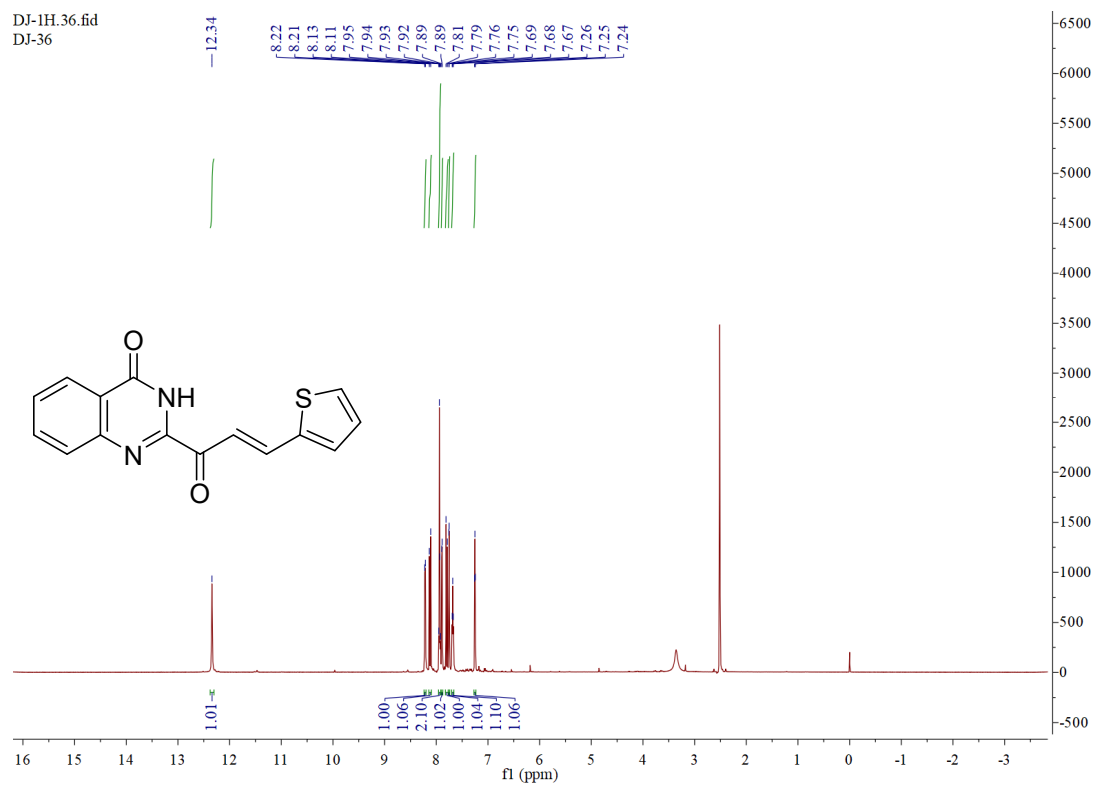


HPLC spectrum

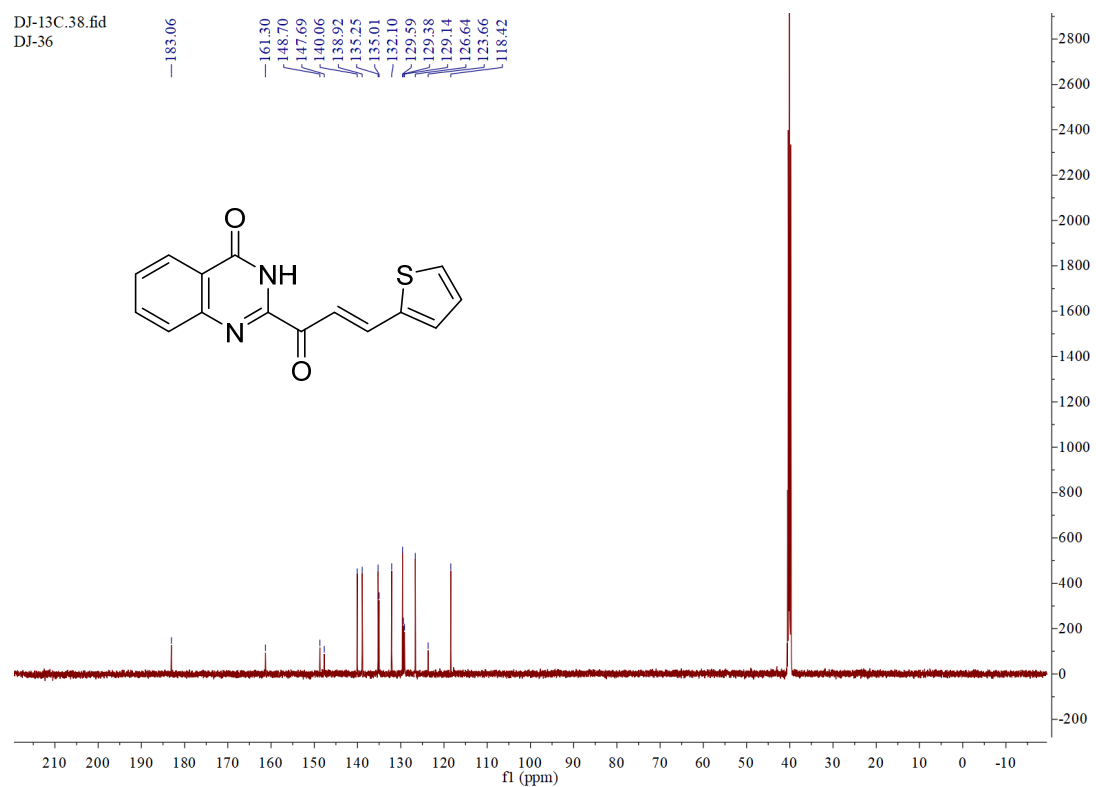


5.7 Spectra of compound **7a**

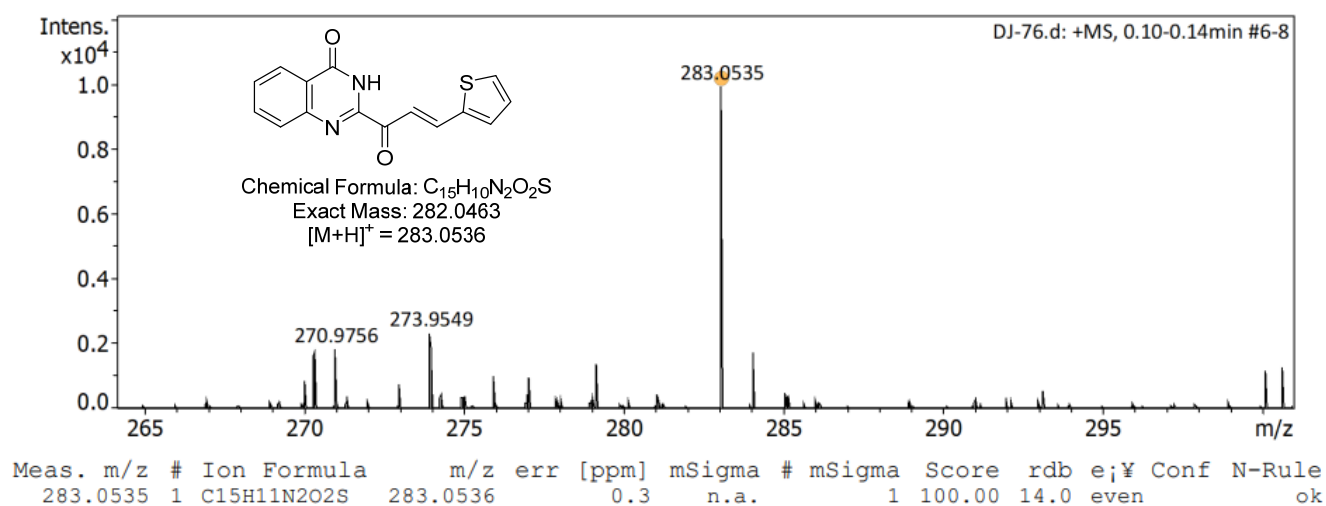
1H NMR spectrum



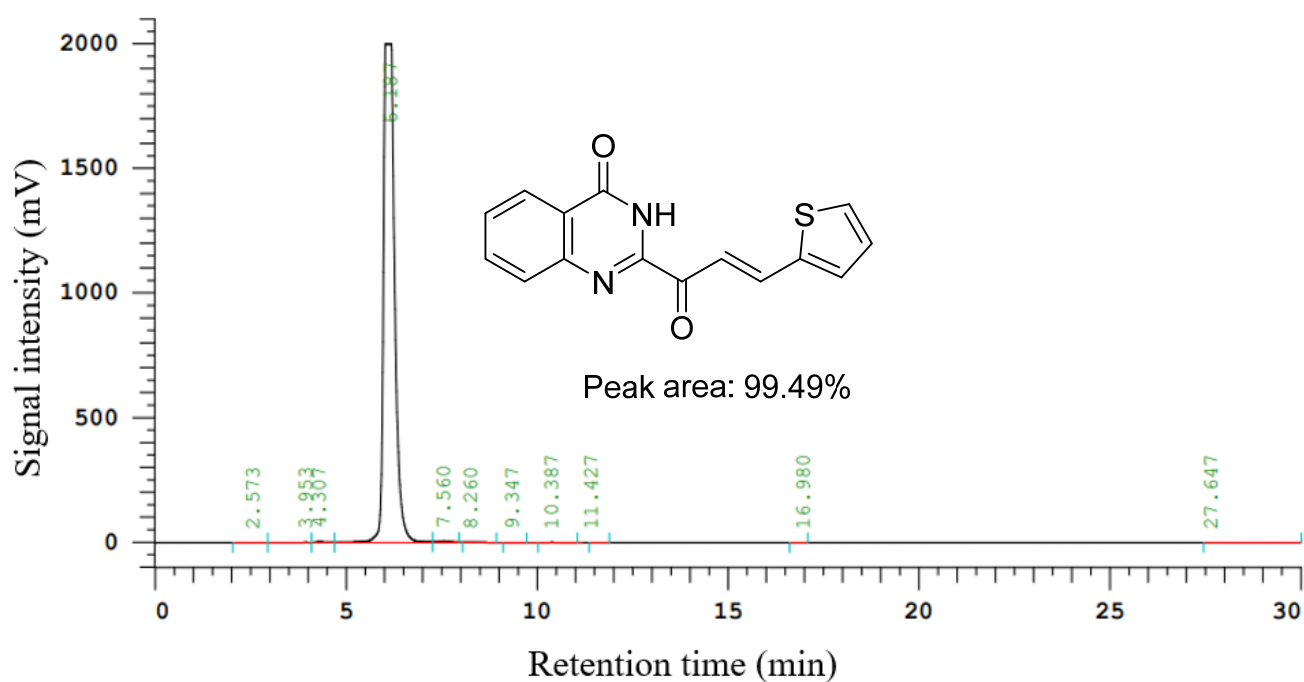
¹³C NMR spectrum



HRMS spectrum

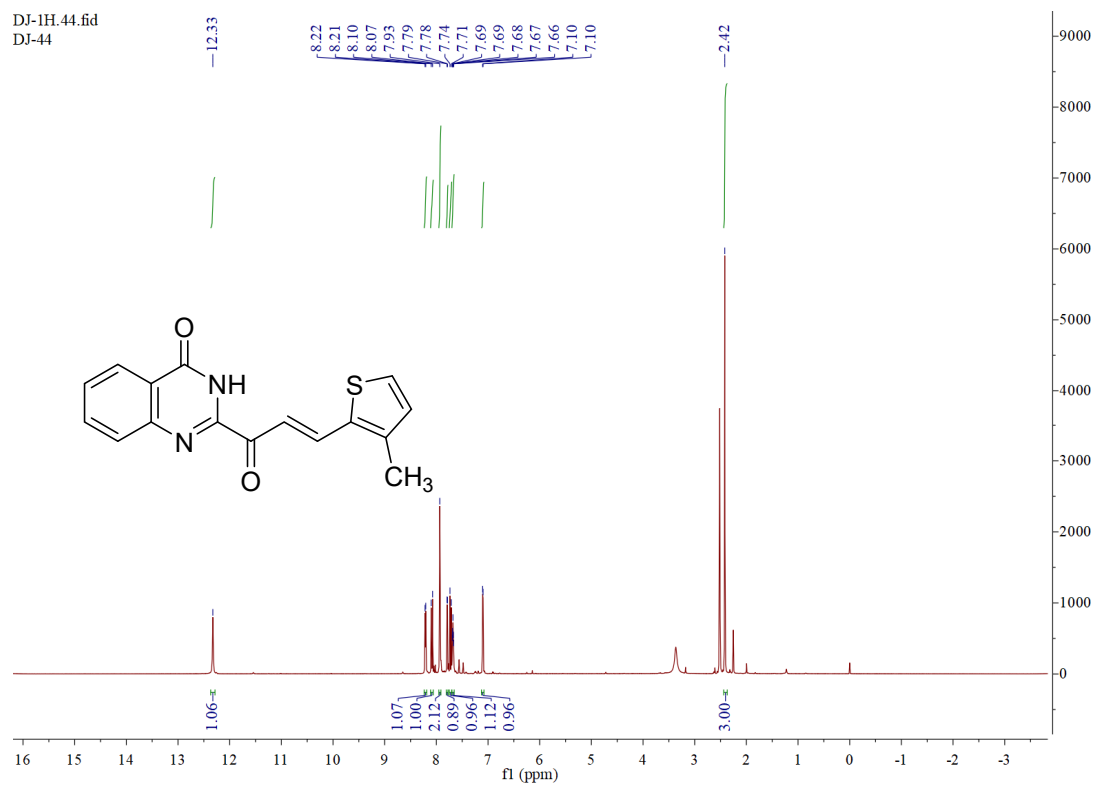


HPLC spectrum

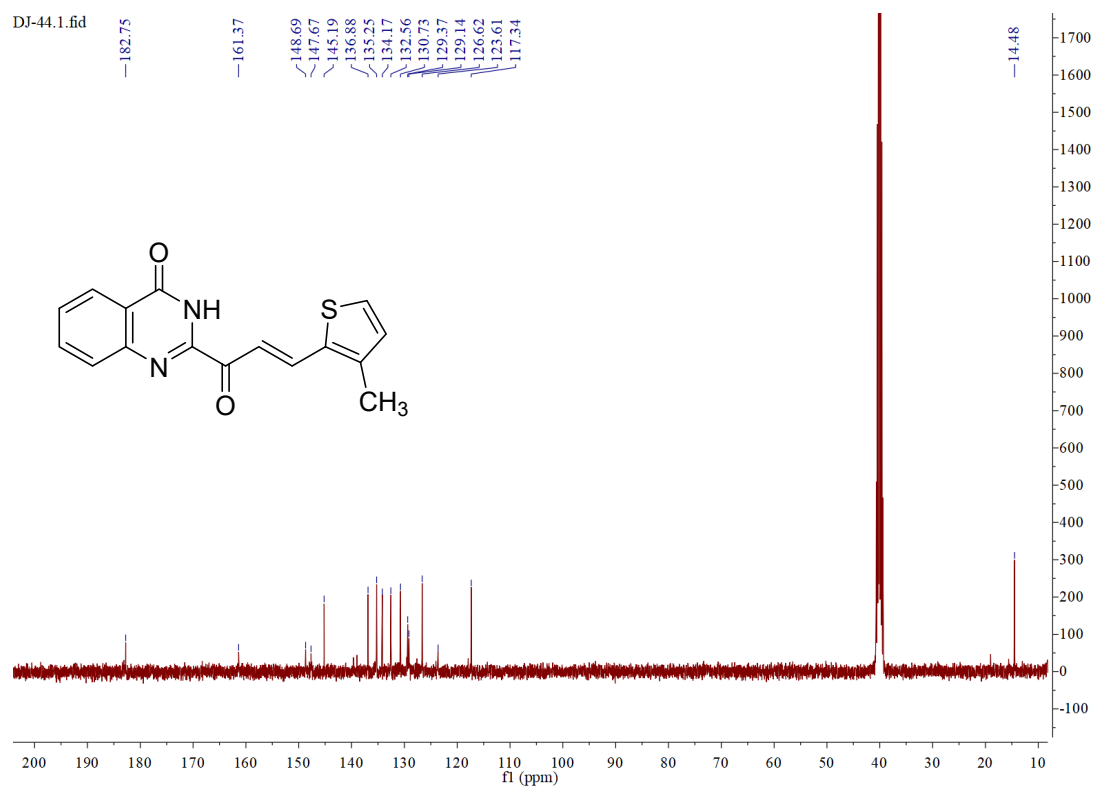


5.8 Spectra of compound 7b

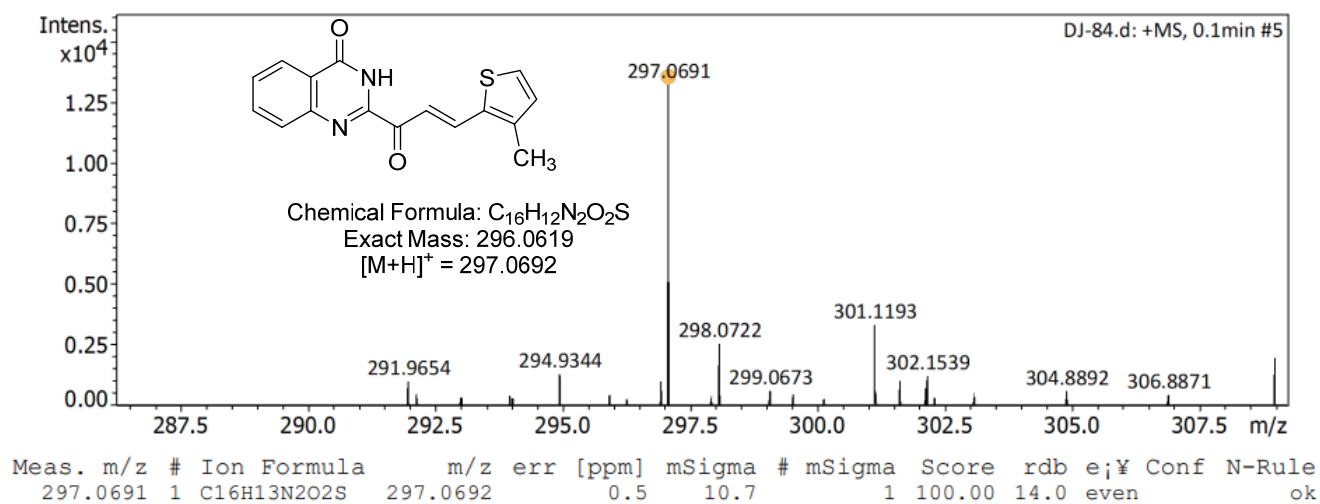
¹H NMR spectrum



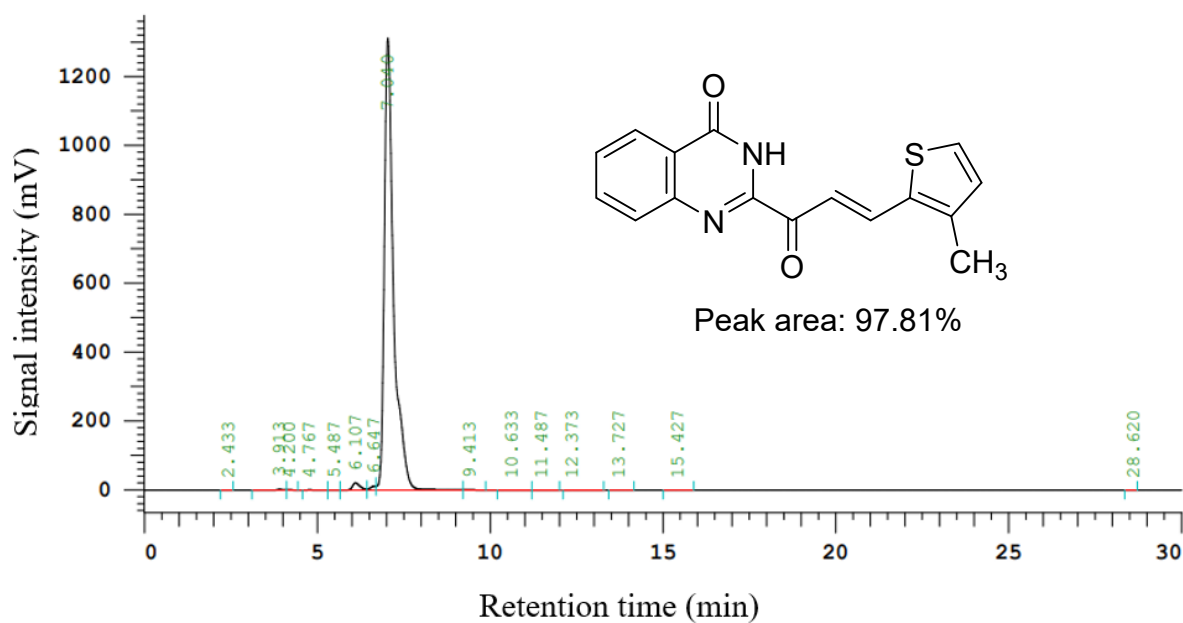
¹³C NMR spectrum



HRMS spectrum

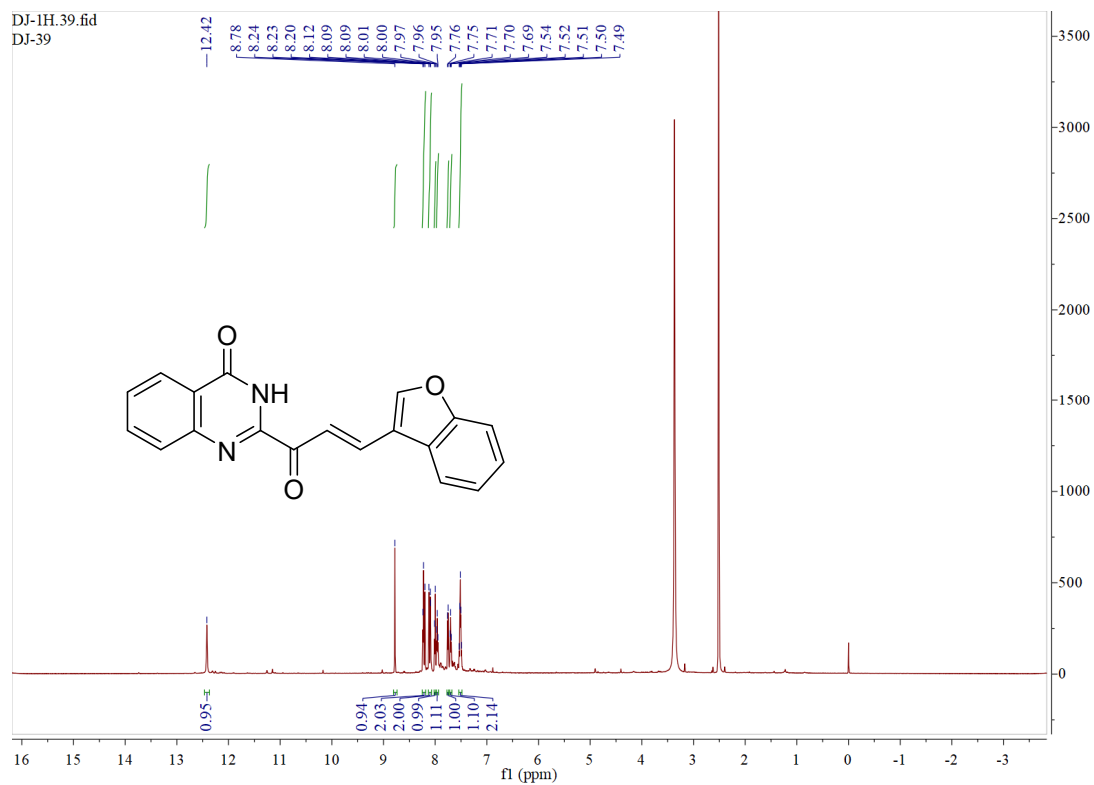


HPLC spectrum

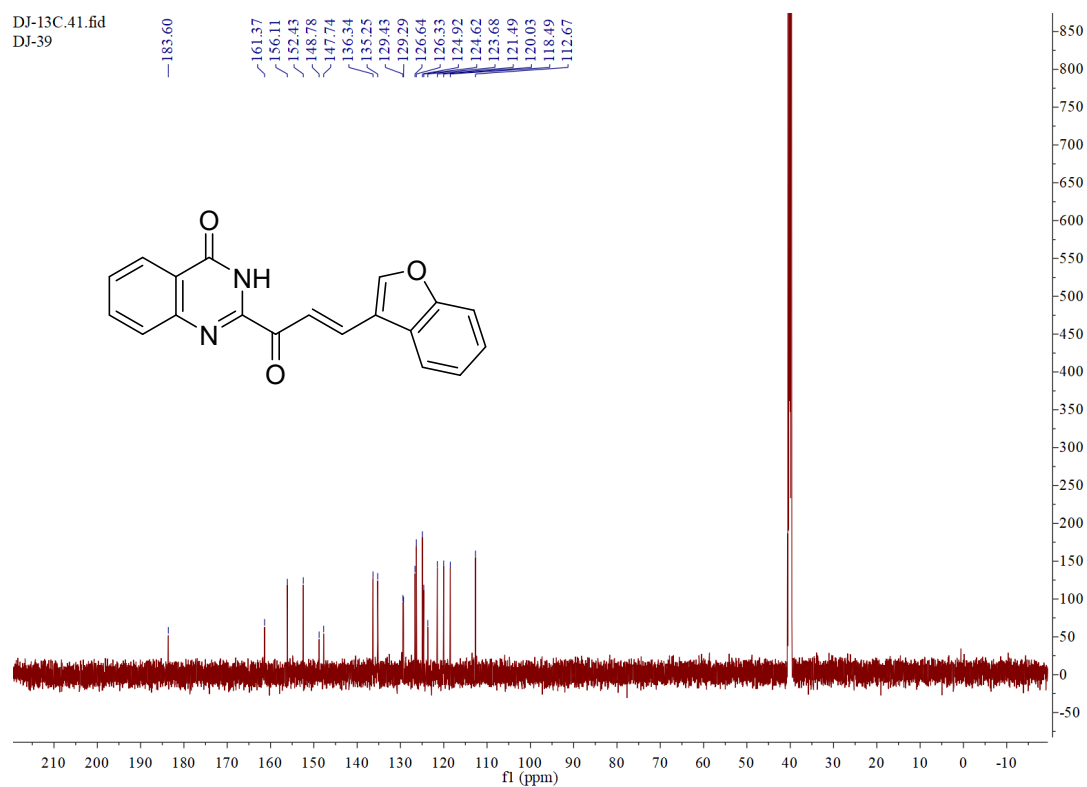


5.9 Spectra of compound **8a**

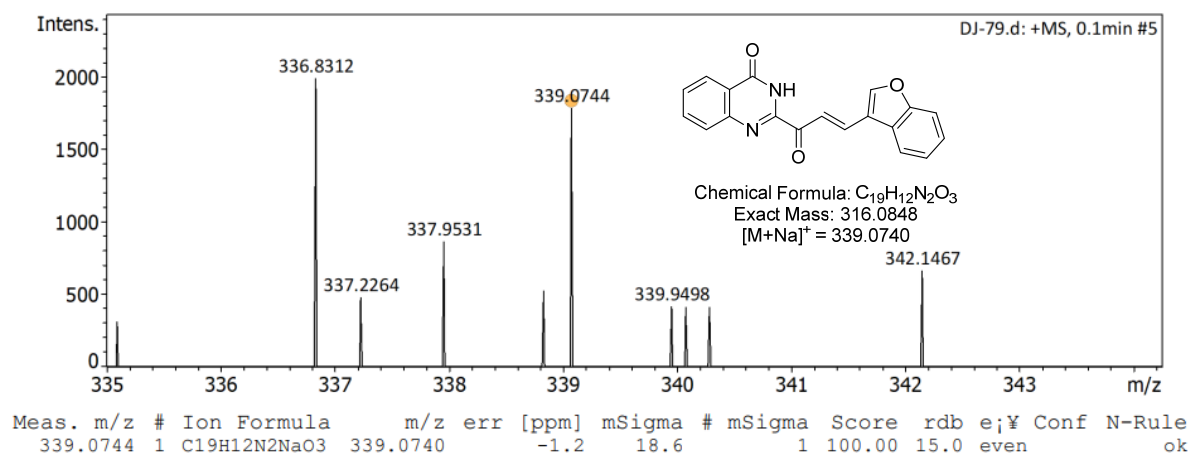
¹H NMR spectrum



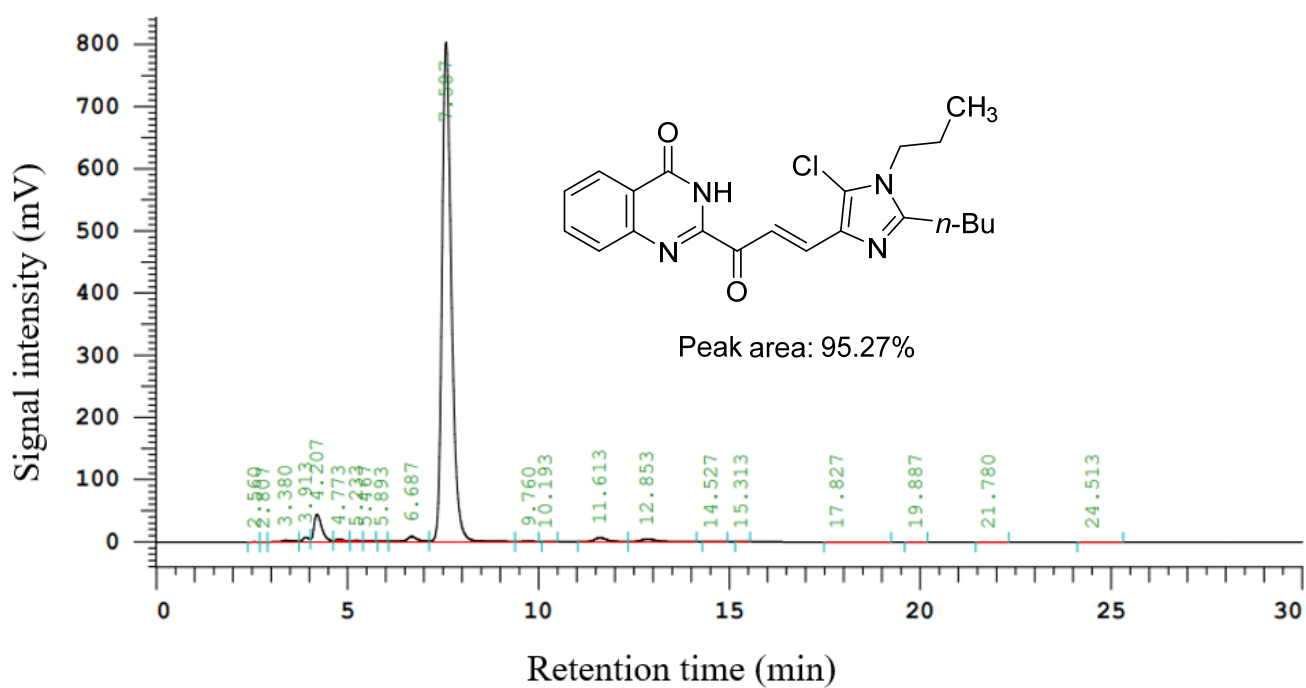
¹³C NMR spectrum



HRMS spectrum

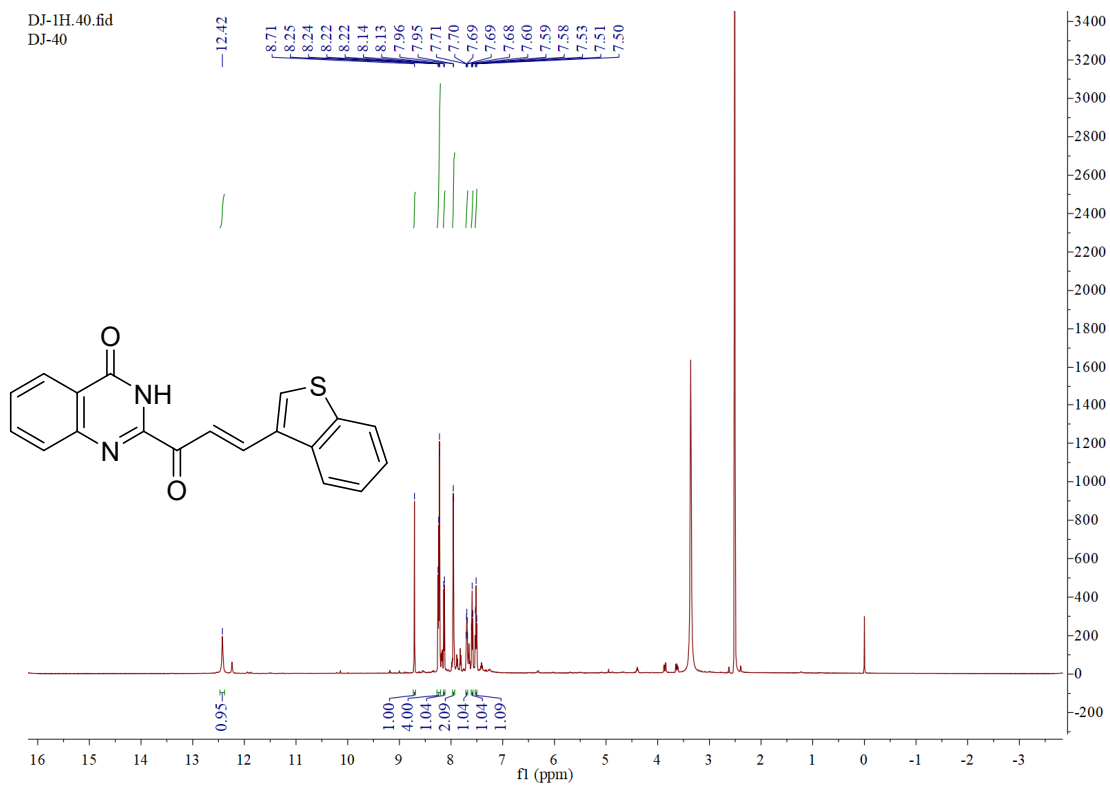


HPLC spectrum

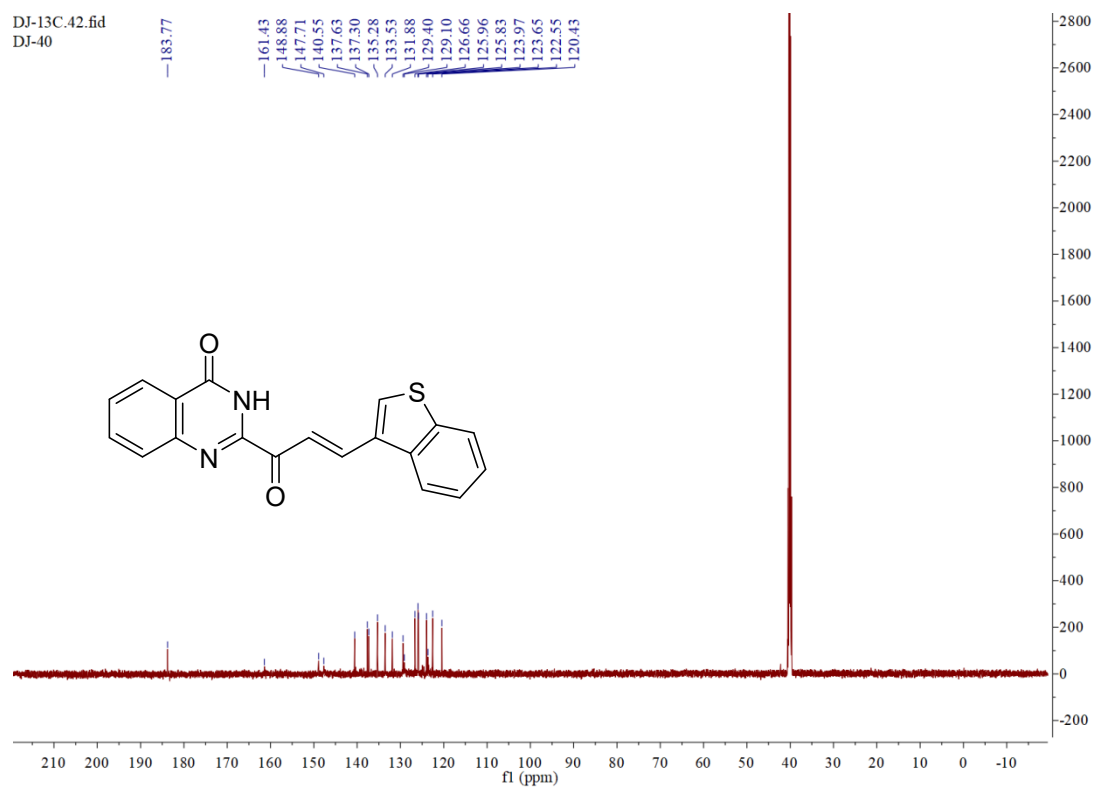


5.10 Spectra of compound **8b**

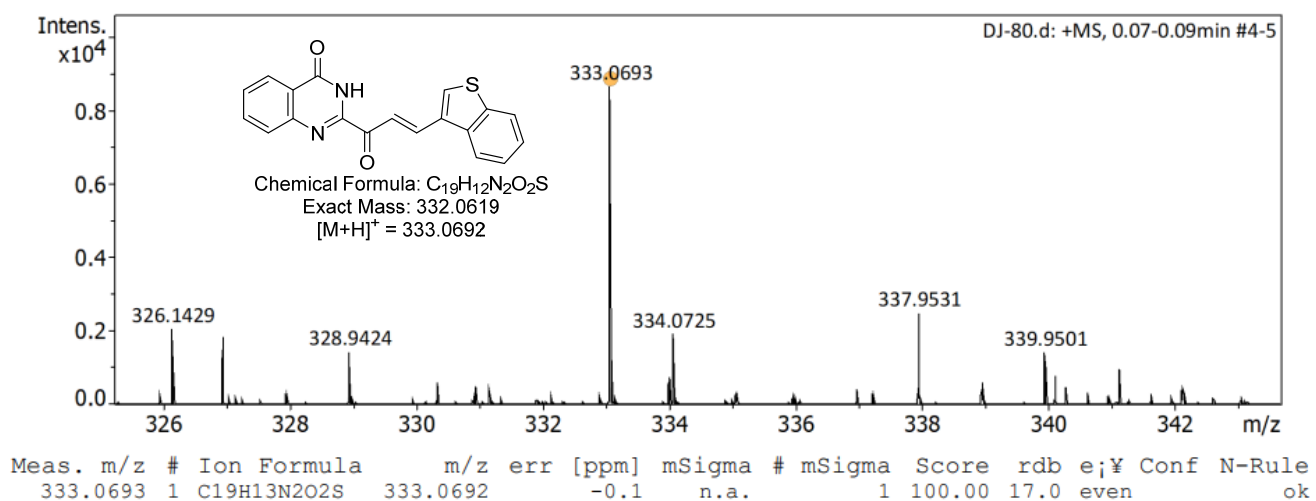
1H NMR spectrum



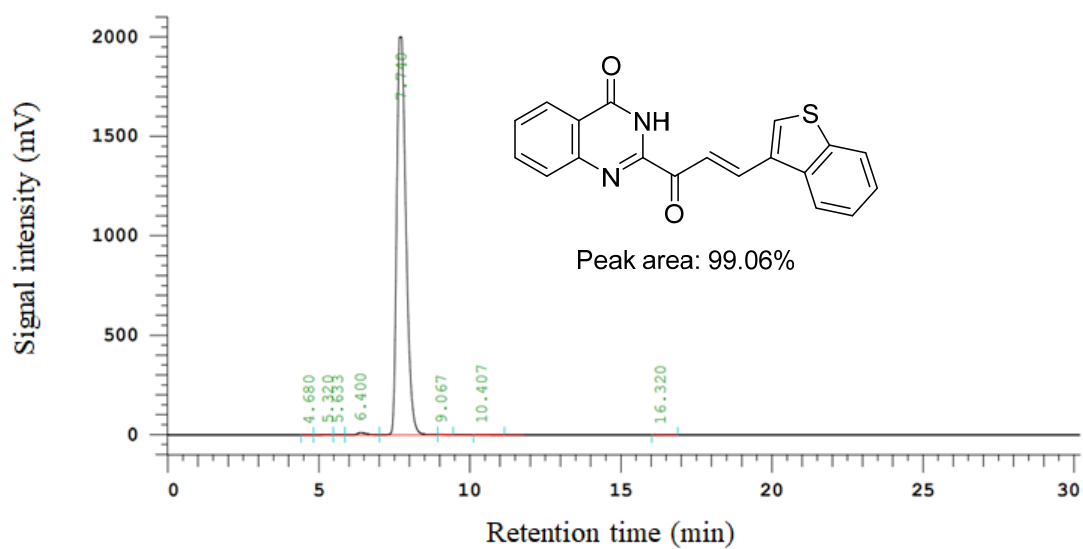
¹³C NMR spectrum



HRMS spectrum

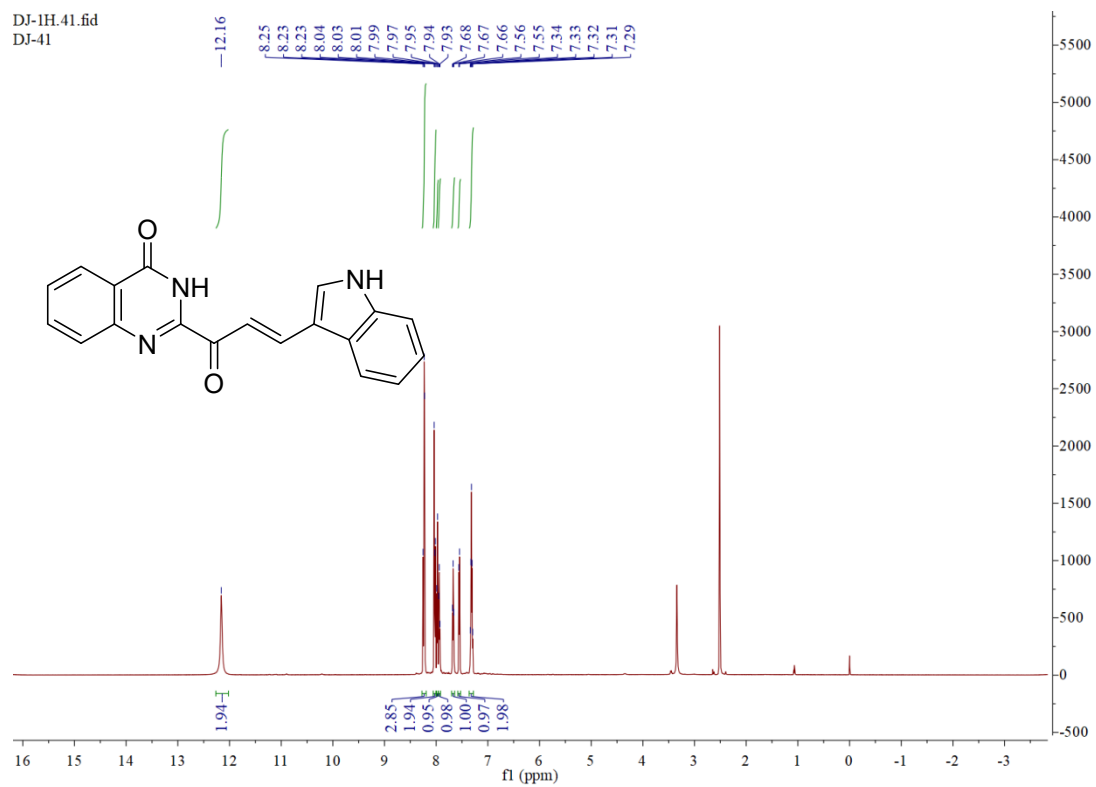


HPLC spectrum

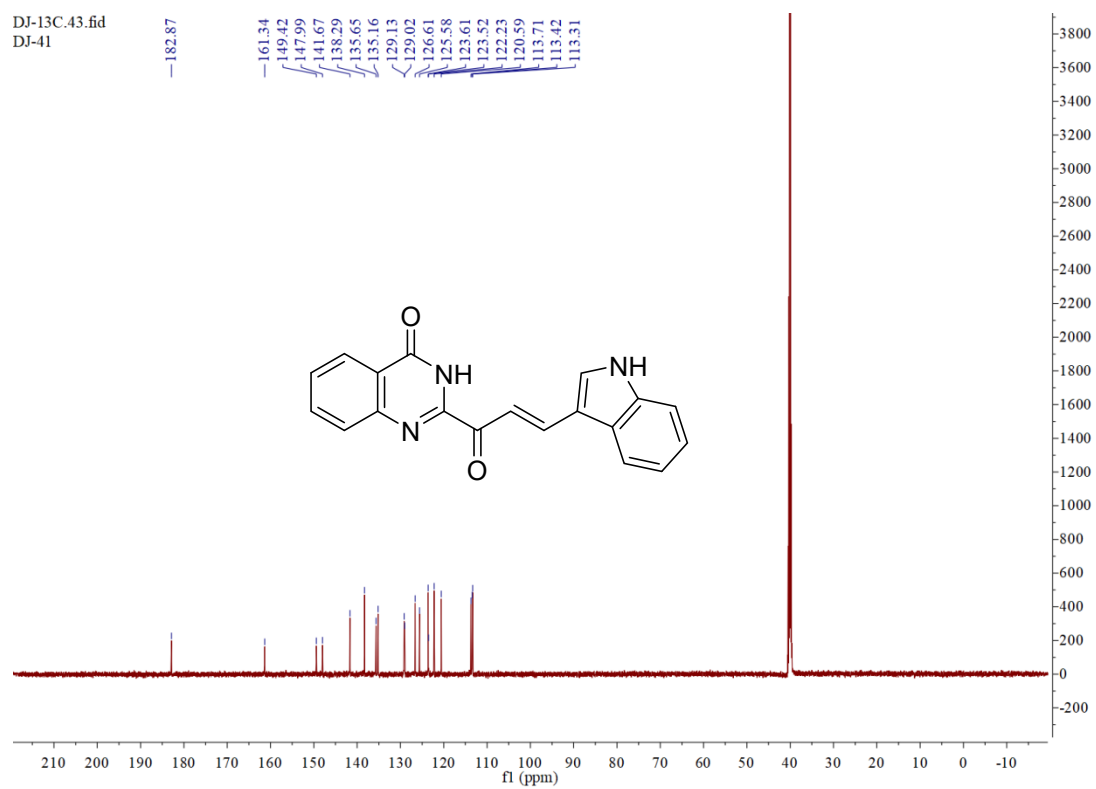


5.11 Spectra of compound **8c**

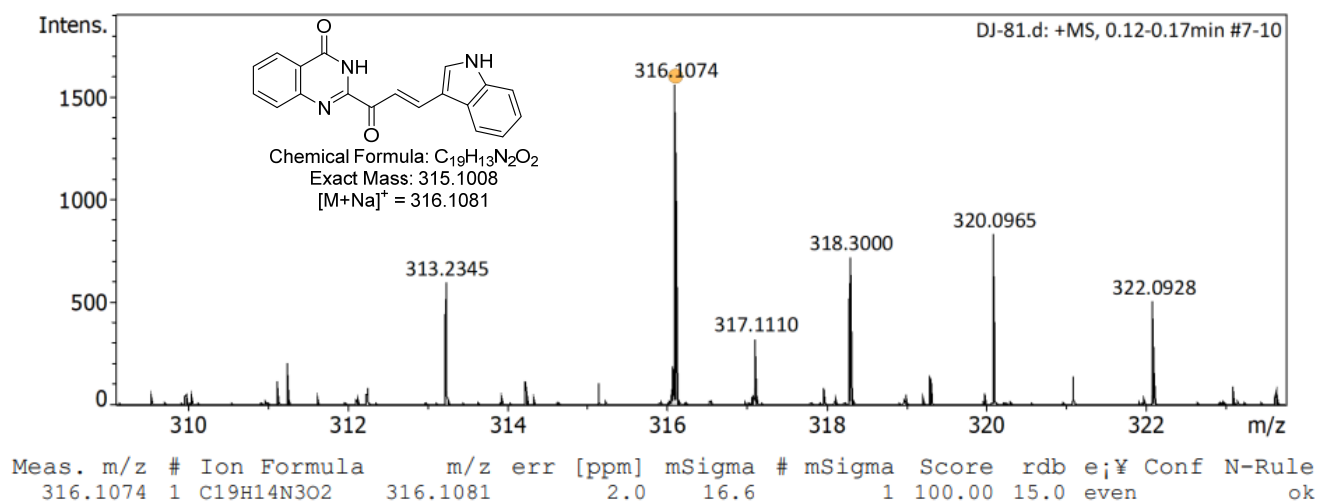
1H NMR spectrum



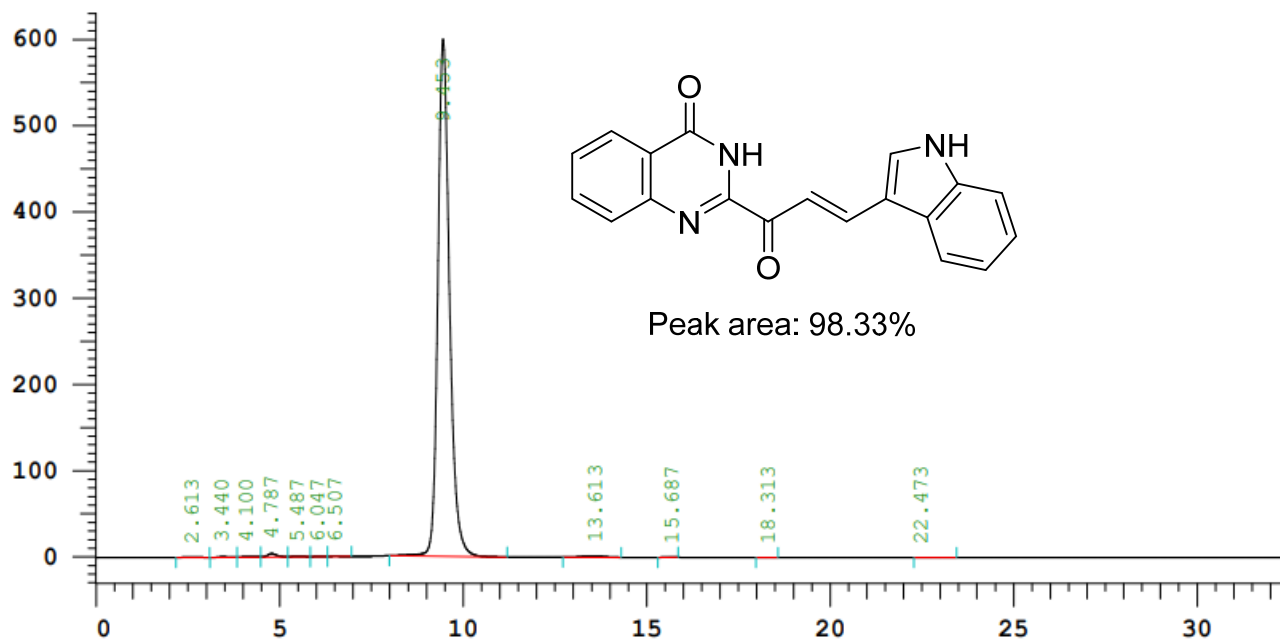
¹³C NMR spectrum



HRMS spectrum

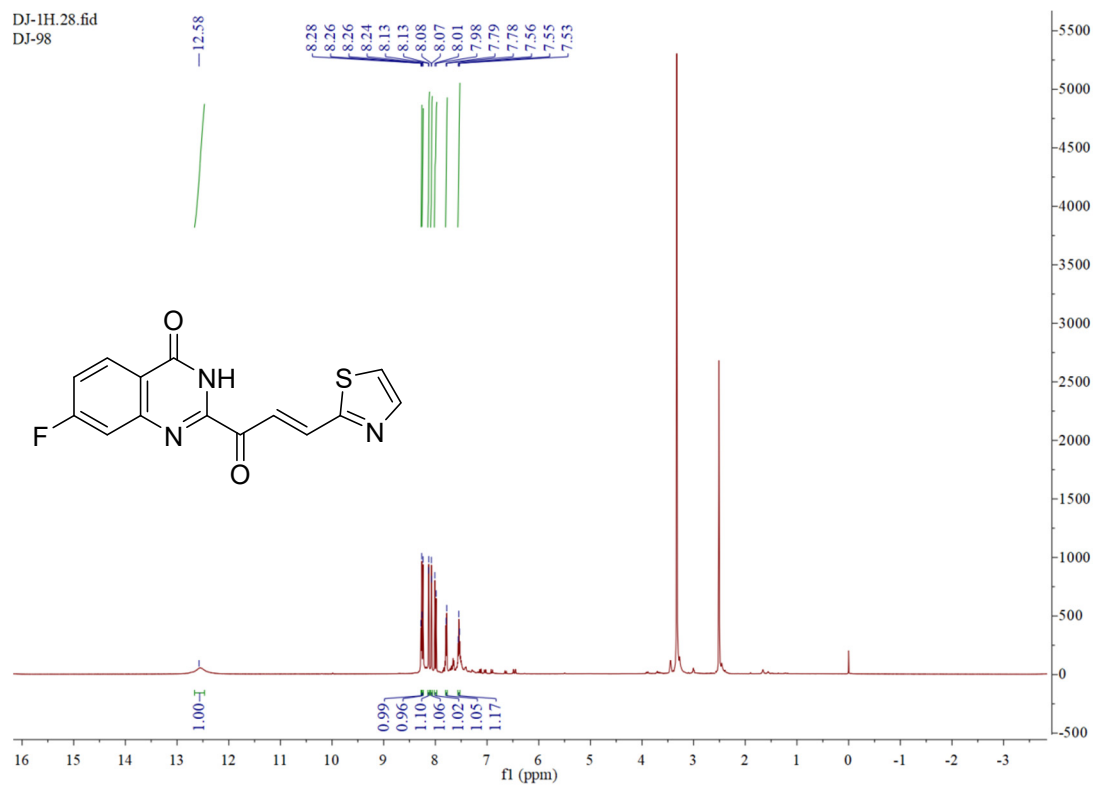


HPLC spectrum

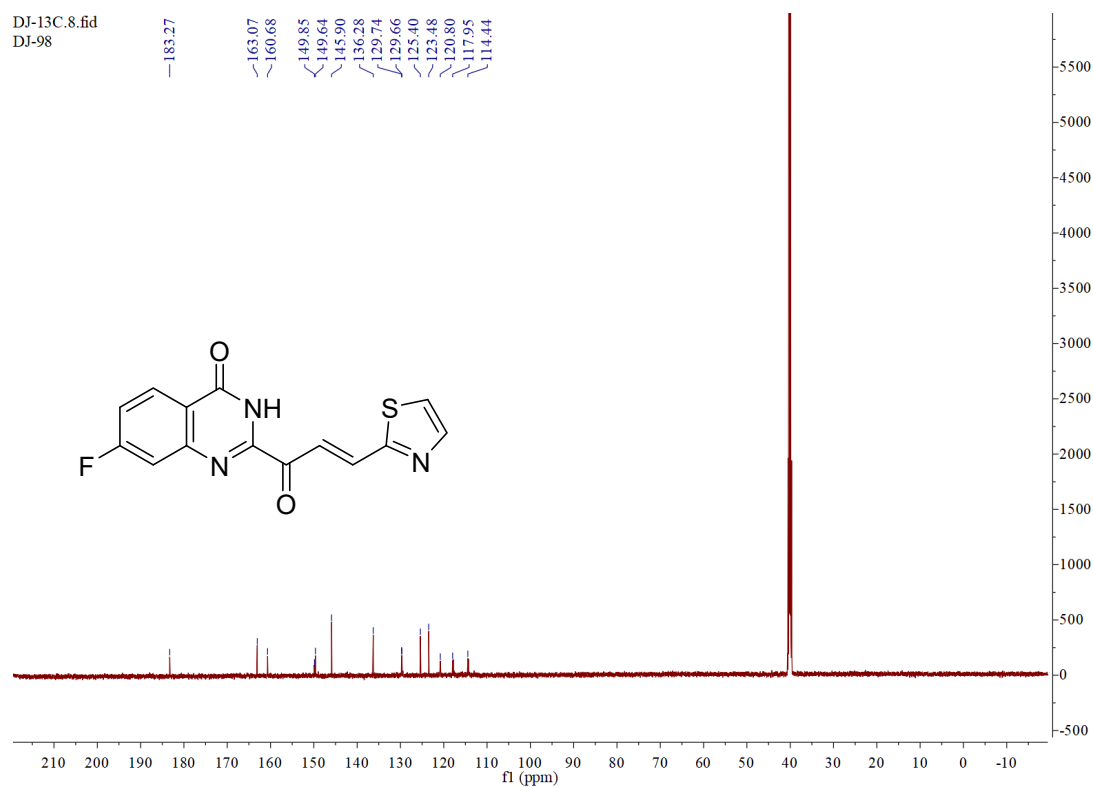


5.12 Spectra of compound **17a**

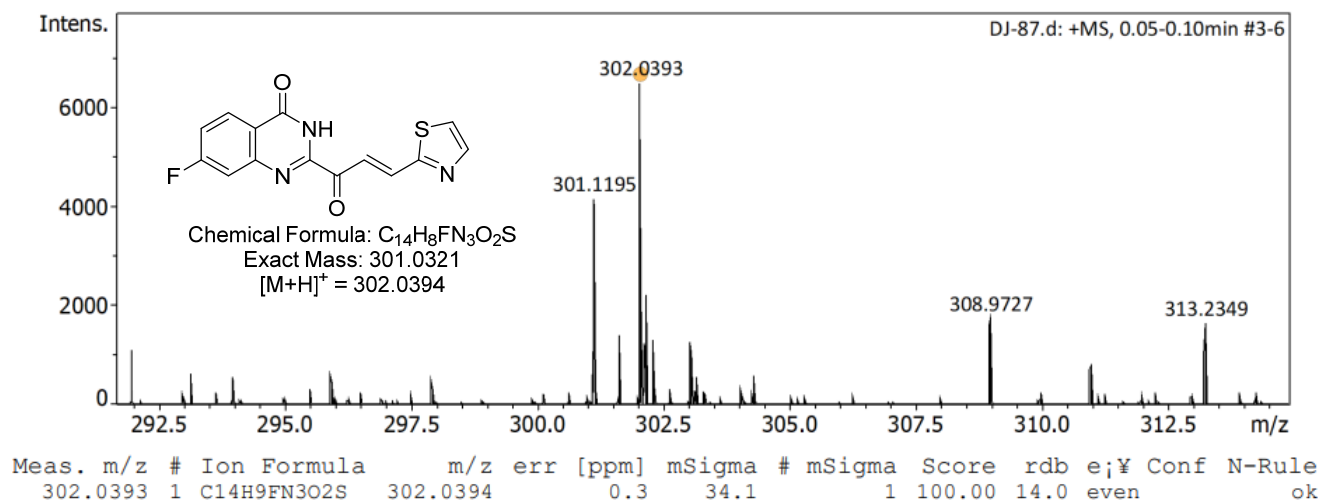
1H NMR spectrum



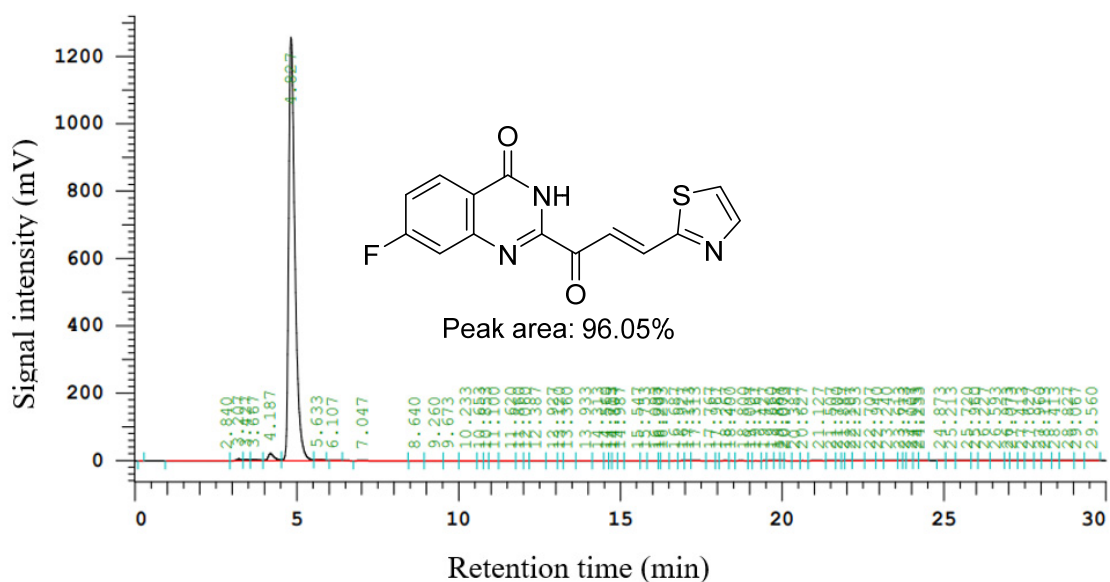
¹³C NMR spectrum



HRMS spectrum

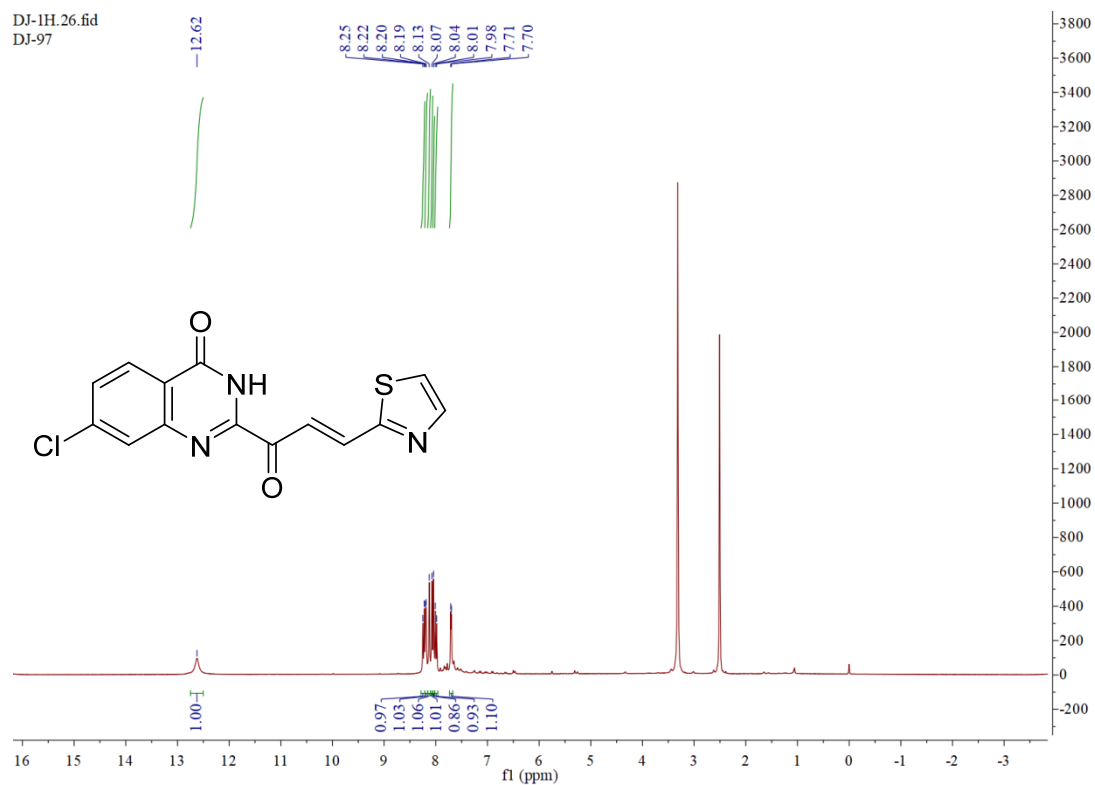


HPLC spectrum

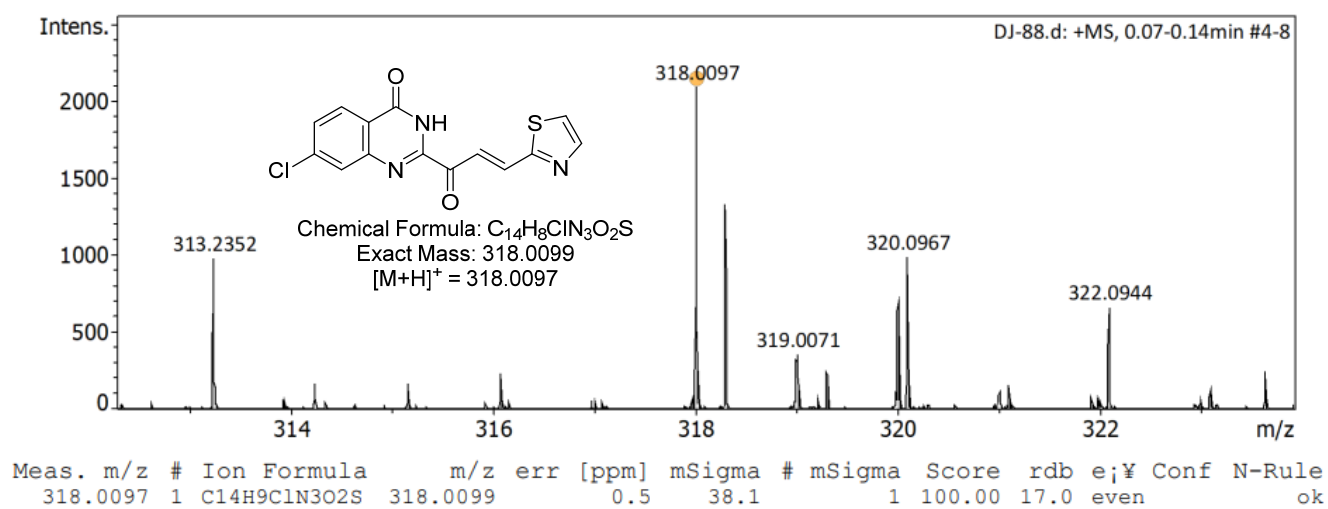


5.13 Spectra of compound **17b**

1H NMR spectrum



HRMS spectrum



HPLC spectrum

