

Supplemental Material For:

Novel Coumarin 7-Carboxamide/Sulfonamide Derivatives as Potential Fungicidal Agents: Design, Synthesis, and Biological Evaluation

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1. General Procedure for Synthesis of Starting Materials **4**

Preparation of 7-Aminocoumarins (4**).** 7-Aminocoumarins **4** were synthesized through the reported synthetic route.

Benzyl chloroformate (100.0 mmol) and *m*-aminophenol **1** (100.0 mmol) were employed as the starting materials to generate 3-hydroxyphenylurethane **2**. A solution of 3-hydroxyphenylurethane **2** (2.0 g) and un/substituted ethyl acetoacetate (1.2 eq) suspended in 20.0 mL of 70% ethanolic H₂SO₄ was stirred at room temperature for 4–6 h, and the crude products were crystallized from ethanol to obtain compounds **3** in moderate to good yields. To a 45% KOH (W/W) solution, compounds **3** were added. The mixture was heated at 100 °C for 30 min and then poured into 100 mL of ice water. Concentrated HCl was added to adjust the pH to 1–2, and then the pH was adjusted to 4–5 with ammonia. The resulting solid was dried by suction filtration and purified by flash column chromatography using petroleum ether/ethyl acetate as the eluent to yield the desired products **4**.

Please see: Zhang, S.G.; Liang, C.G.; Sun, Y.Q.; Teng, P.; Wang, J.Q.; Zhang, W.H. Design, synthesis and antifungal activities of novel pyrrole-and pyrazole-substituted coumarin derivatives. *Mol. Divers.* **2019**, *23*, 915-925; Yu, H.N.; Hou, Z.; Tian, Y.; Mou, Y.H.; Guo, C. Design, synthesis, cytotoxicity and mechanism of novel dihydroartemisinin-coumarin hybrids as potential anti-cancer agents. *Eur. J. Med. Chem.* **2018**, *151*, 434-448.

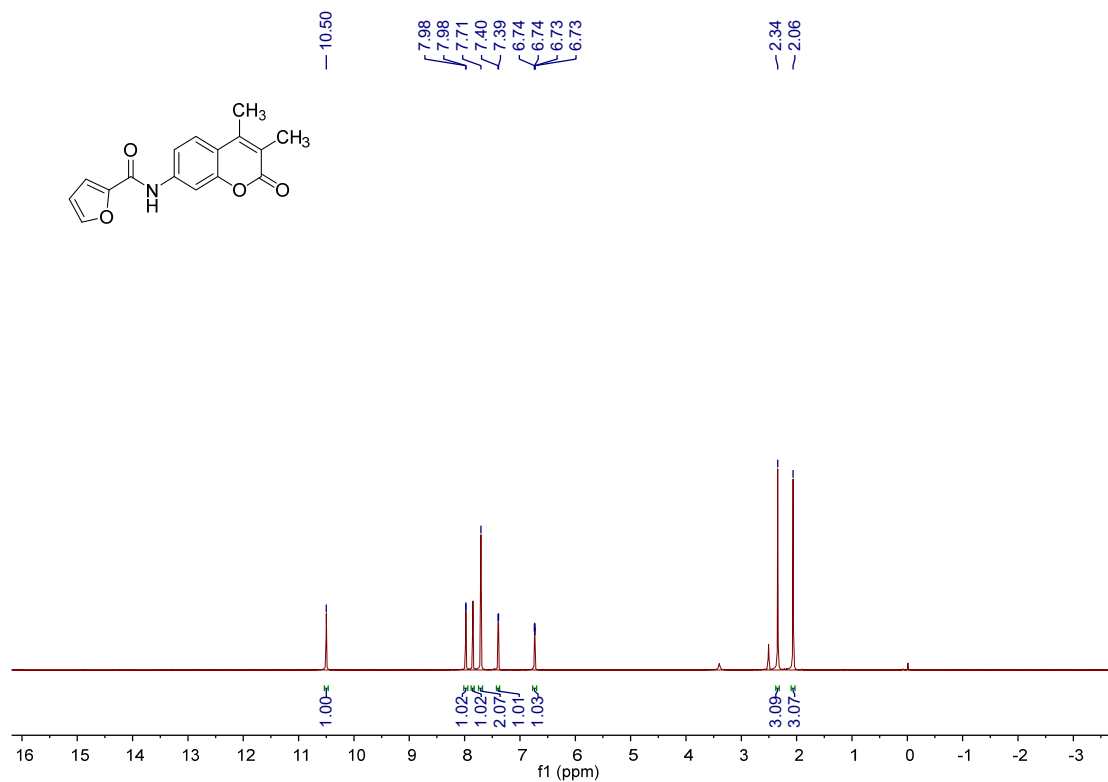
2. Biological Assays

The assay of antifungal activity toward *Botrytis cinerea*, *Alternaria solani*, *Gibberellae*, *Rhizoctoria solani*, *Cucumber anthrax*, and *Alternaria mali* was carried out on 100 mm × 15 mm Petri plates, each containing 10 mL of potato dextrose agar, under sterile conditions, on a clean bench in a sterile room. Sterile blank paper disks (0.65 cm in diameter) were placed at a distance 2.5 cm away from the rim of the mycelial

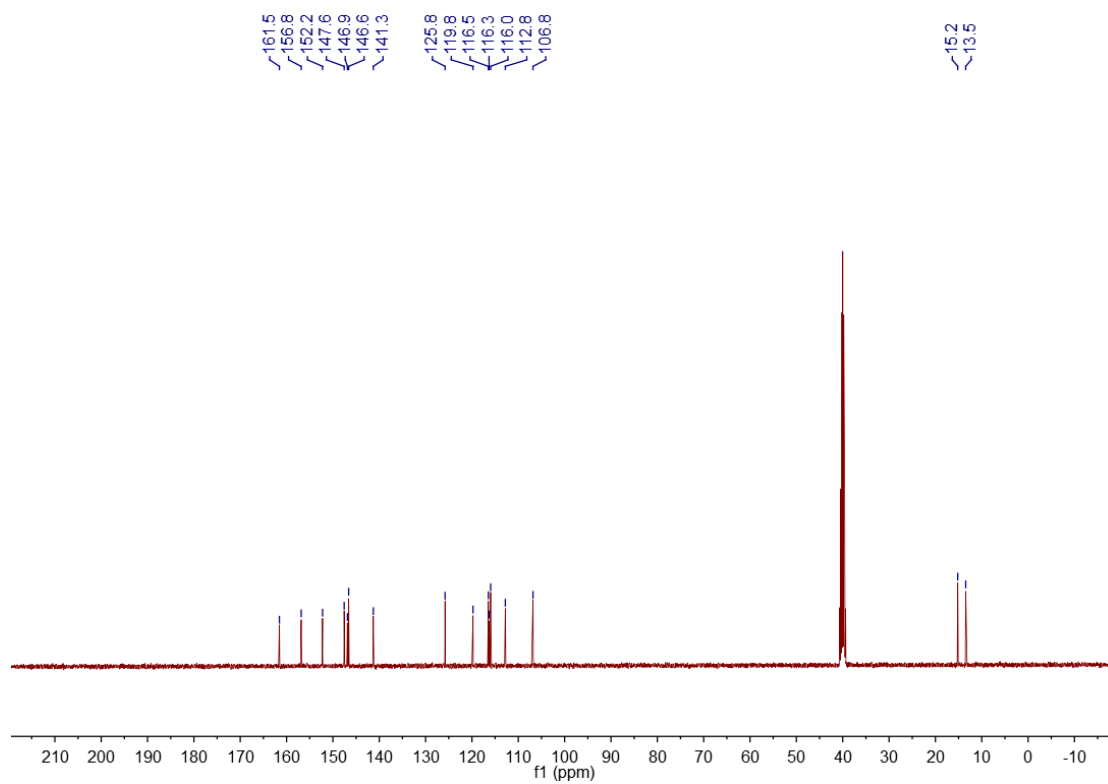
colony. The plates were sealed with parafilm and incubated at 25 °C until mycelial growth had enveloped the disks containing the control and had formed crescents of inhibition around disks containing samples with antifungal activity. When the mycelia colony of the control had grown to almost fill the plate, the area of the mycelia colony was measured, and the inhibition of fungal growth in the other plates was determined by calculating the percent reduction in the area of the mycelia colony. The resulting data were collated for each compound, and averages across replicates were used to make a judgment of the overall activity level of the compound.

4. ^1H NMR, ^{13}C NMR, and HRMS Spectra of Products

^1H NMR Spectrum of 5a (400 MHz, $\text{DMSO}-d_6$)

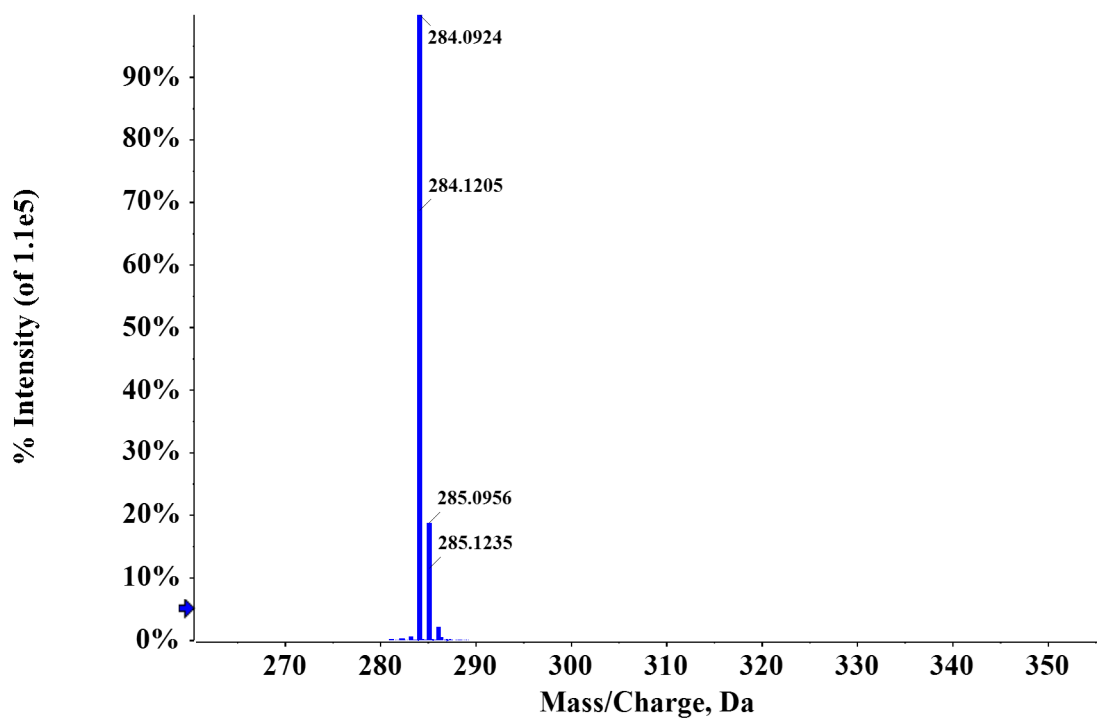


^{13}C NMR Spectrum of 5a (101 MHz, $\text{DMSO}-d_6$)

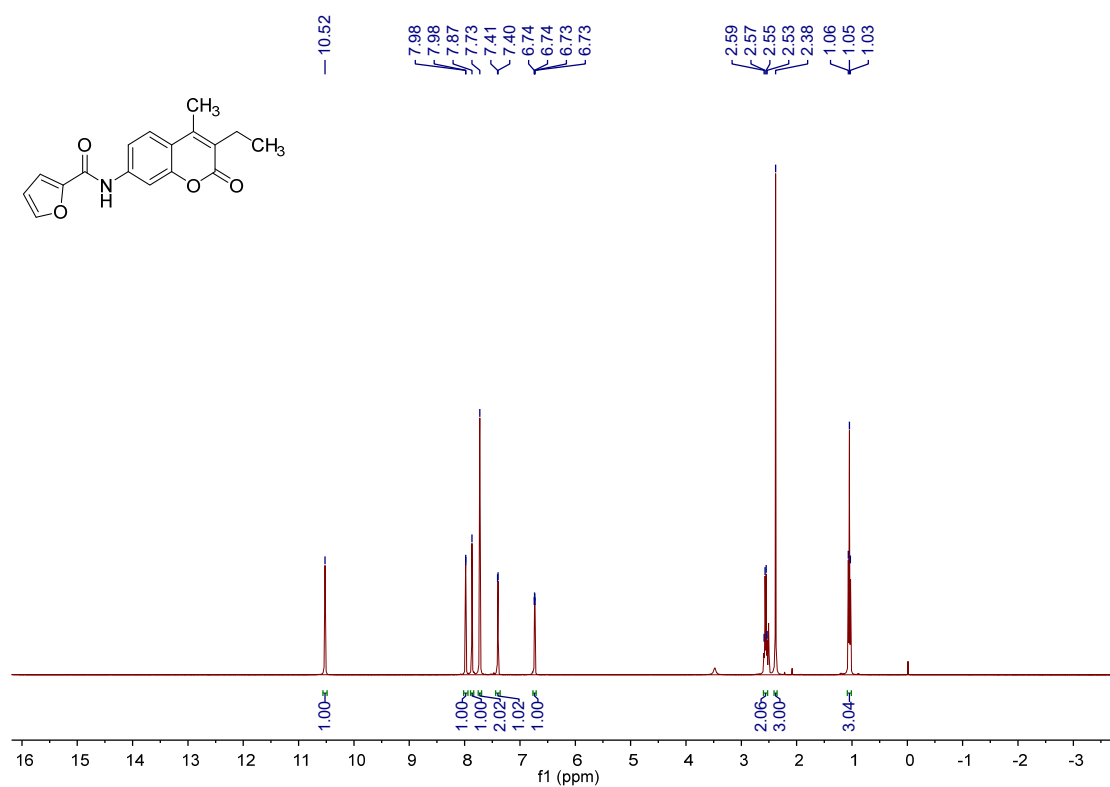


HRMS Spectrum of 5a

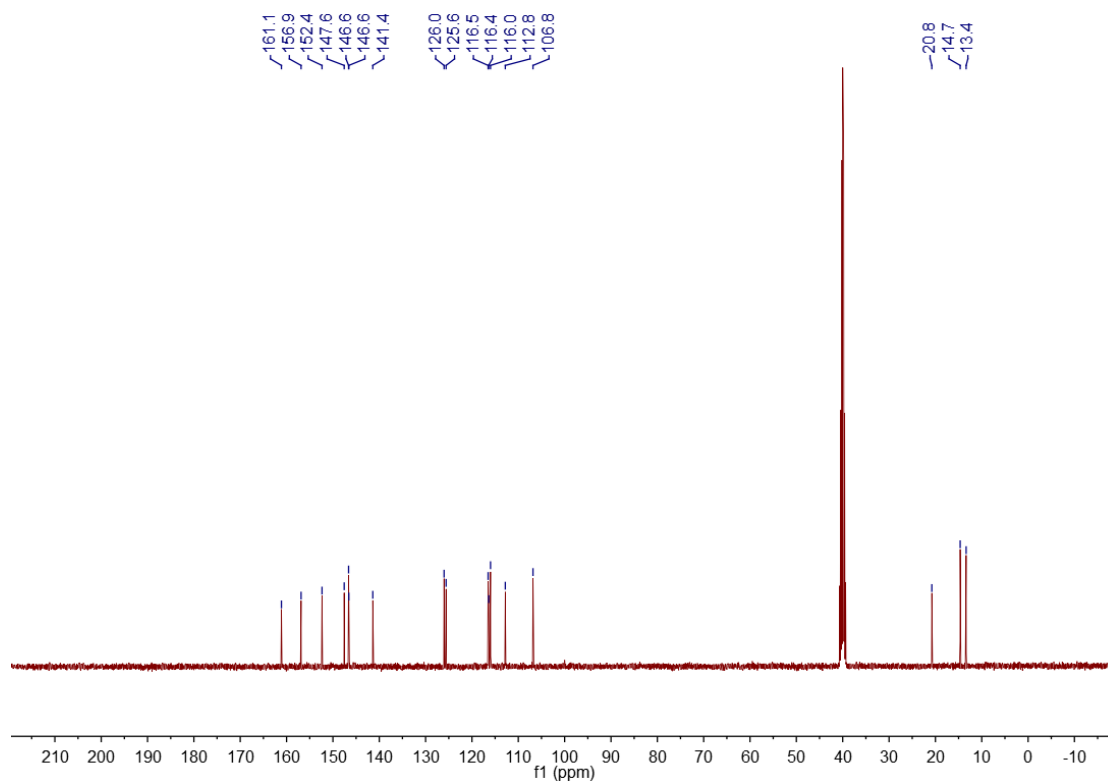
Spectrum from wenya02.wiff (sample 1) - ... MS (100 - 1000) from 0.090 to 0.107 min



¹H NMR Spectrum of 5b (400 MHz, DMSO-*d*₆)

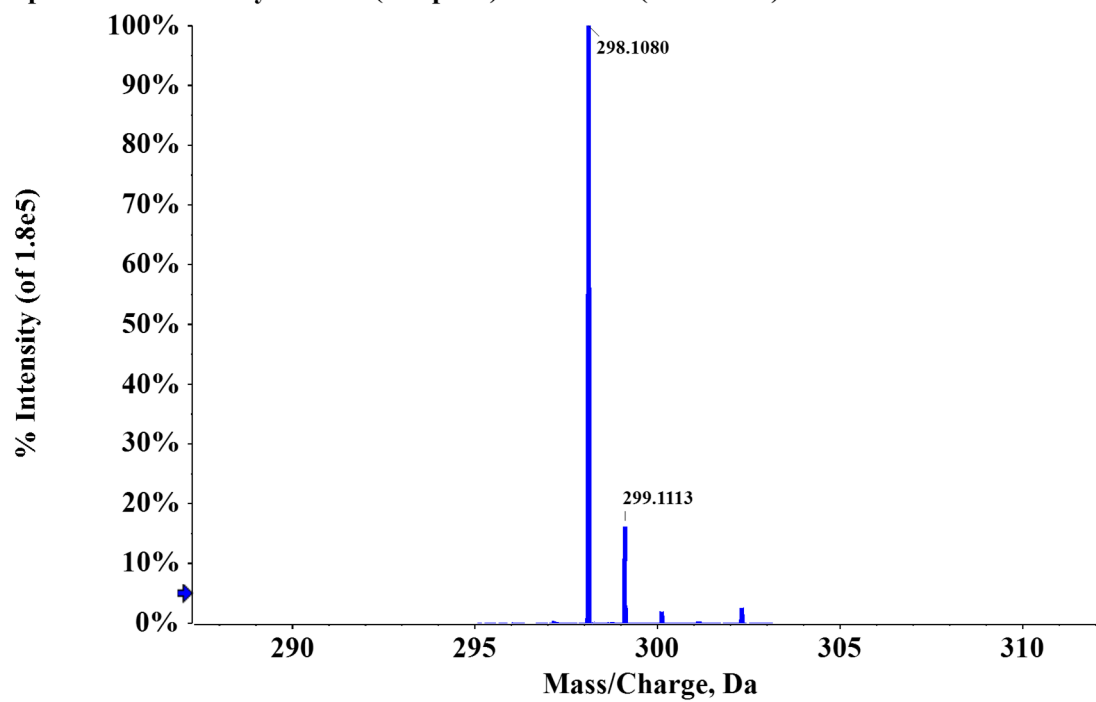


^{13}C NMR Spectrum of 5b (101 MHz, DMSO- d_6)

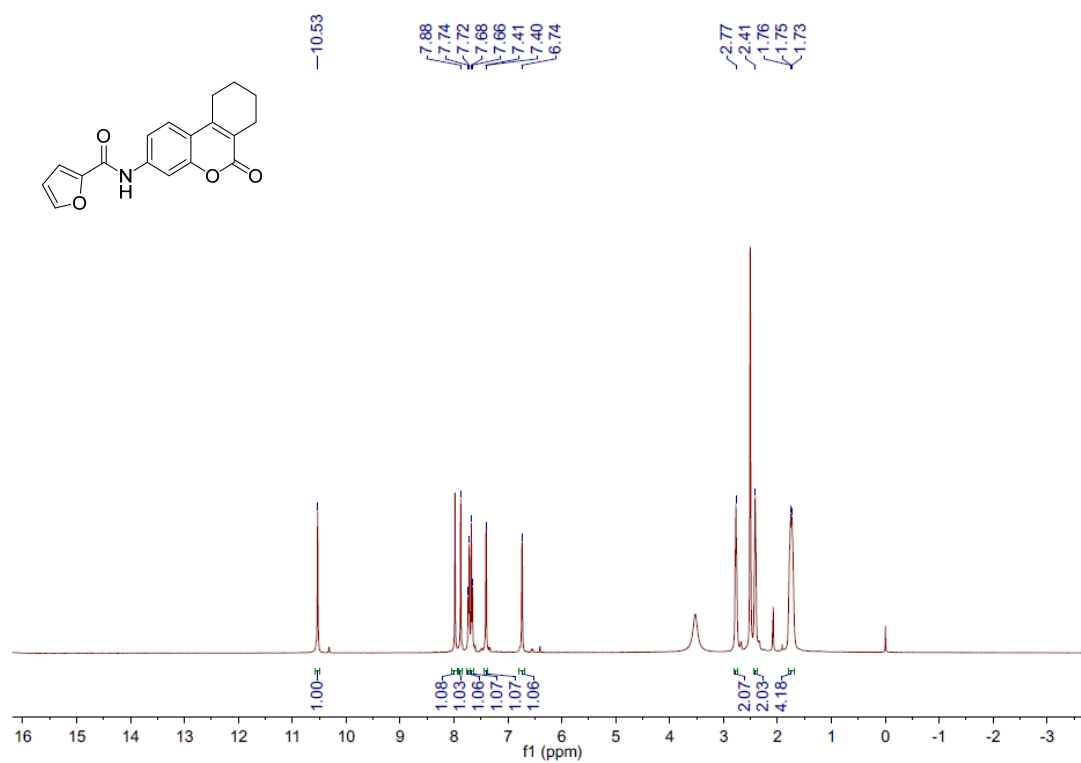


HRMS Spectrum of 5b

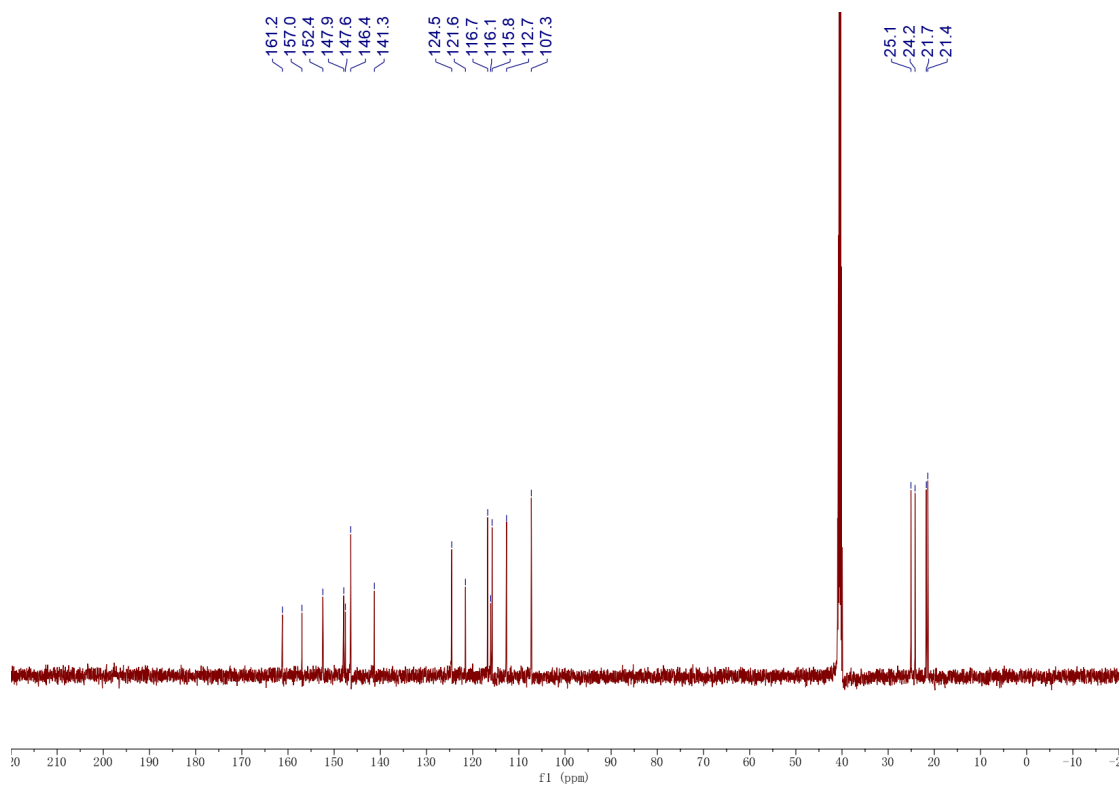
Spectrum from wenya03.wiff (sample 1) - w...F MS (100 - 1000) from 0.063 to 0.072 min



¹H NMR Spectrum of 5c (400 MHz, DMSO-*d*₆)

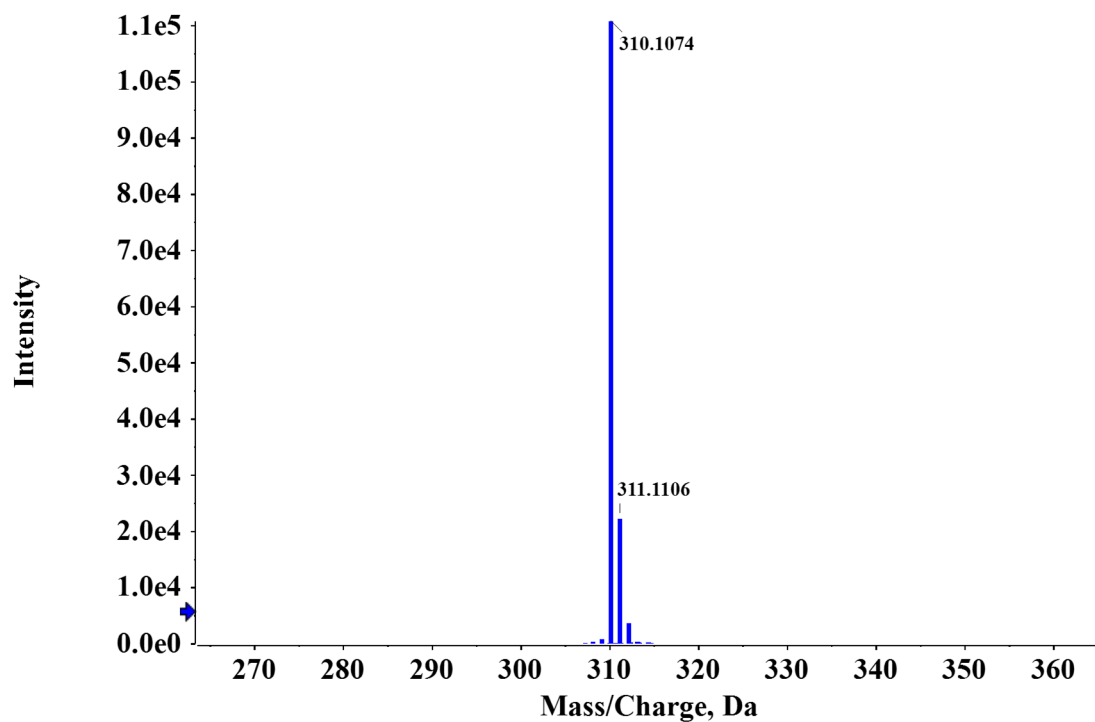


¹³C NMR Spectrum of 5c (126 MHz, DMSO-*d*₆)

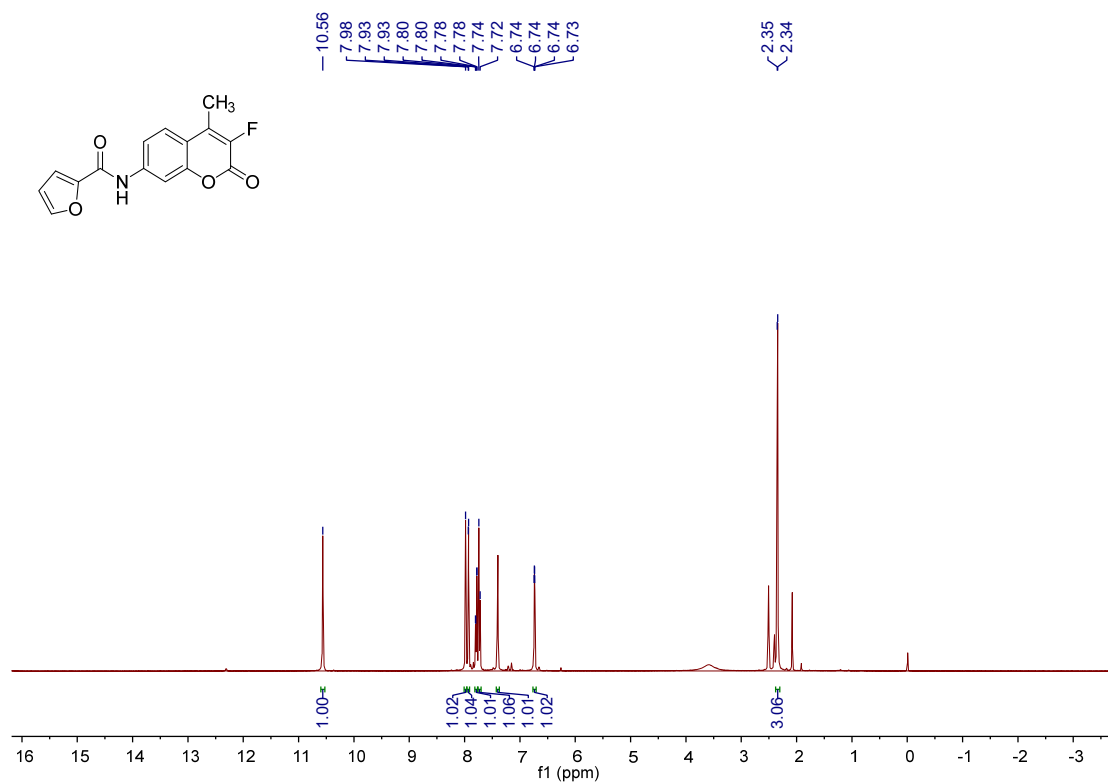


HRMS Spectrum of 5c

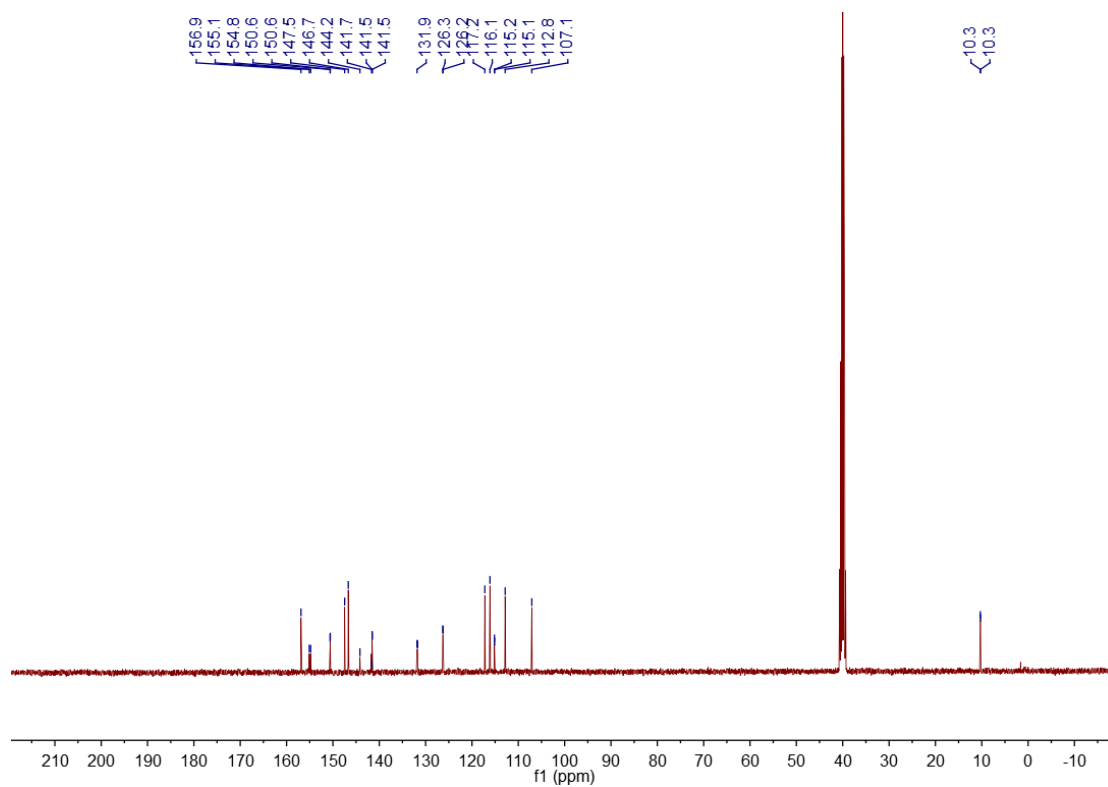
Spectrum from wenya04.wiff (sample 1) - ... MS (100 - 1000) from 0.072 to 0.081 min



¹H NMR Spectrum of 5d (400 MHz, DMSO-*d*₆)

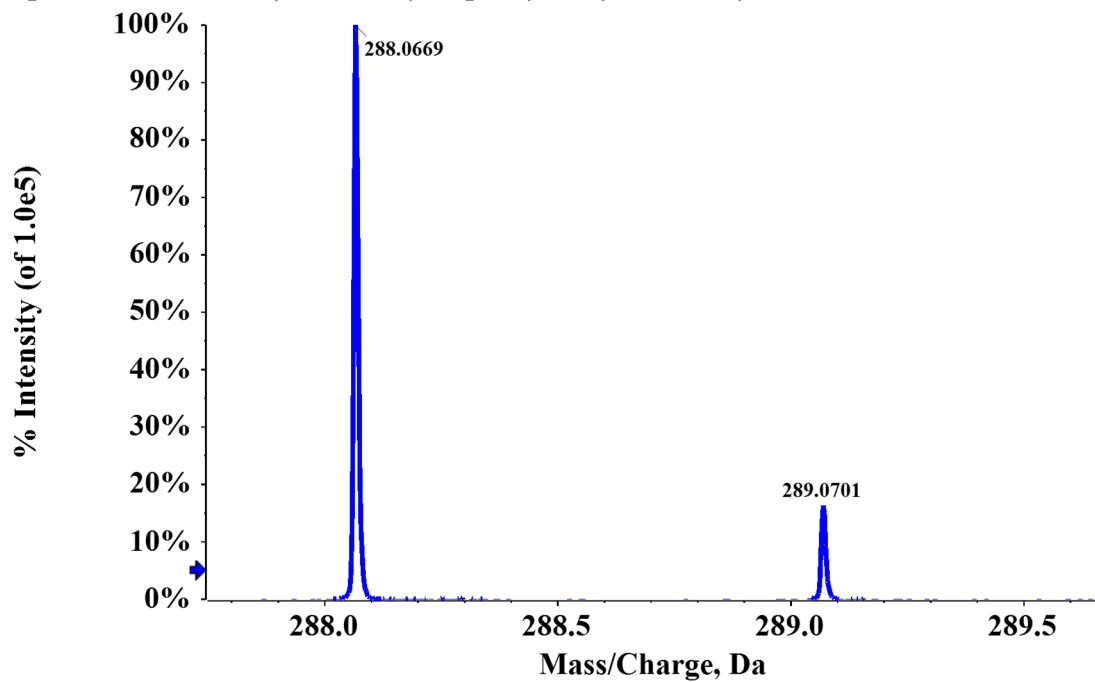


^{13}C NMR Spectrum of 5d (101 MHz, DMSO- d_6)

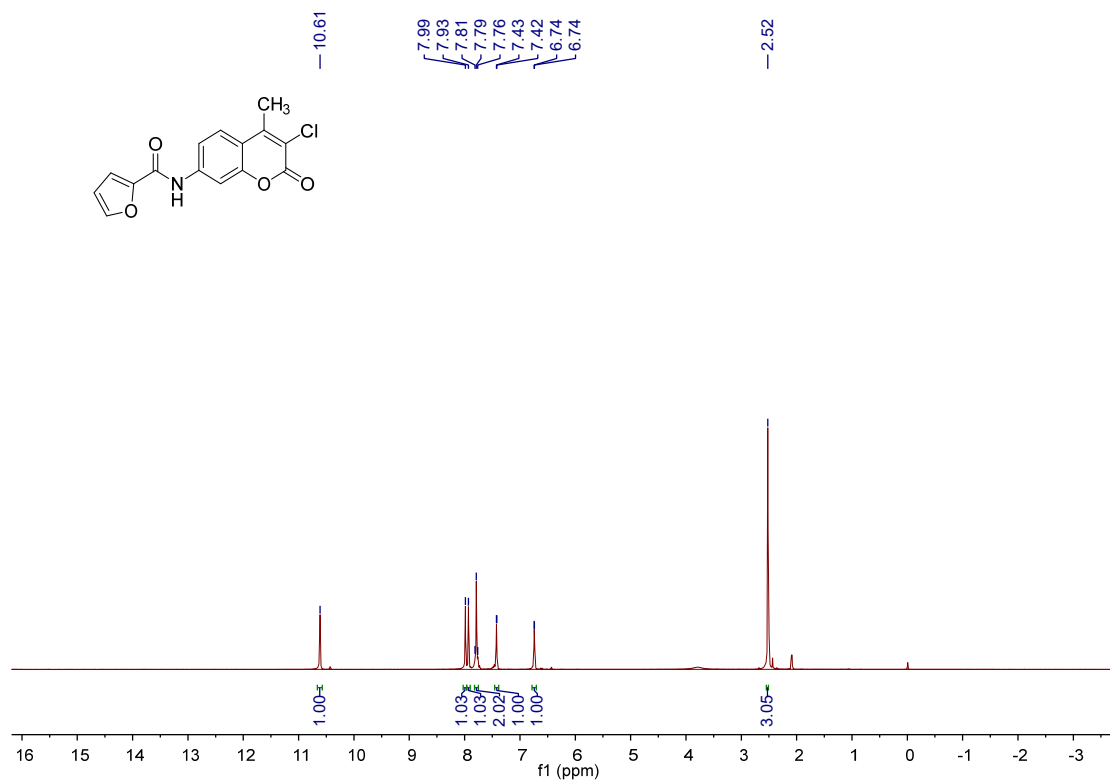


HRMS Spectrum of 5d

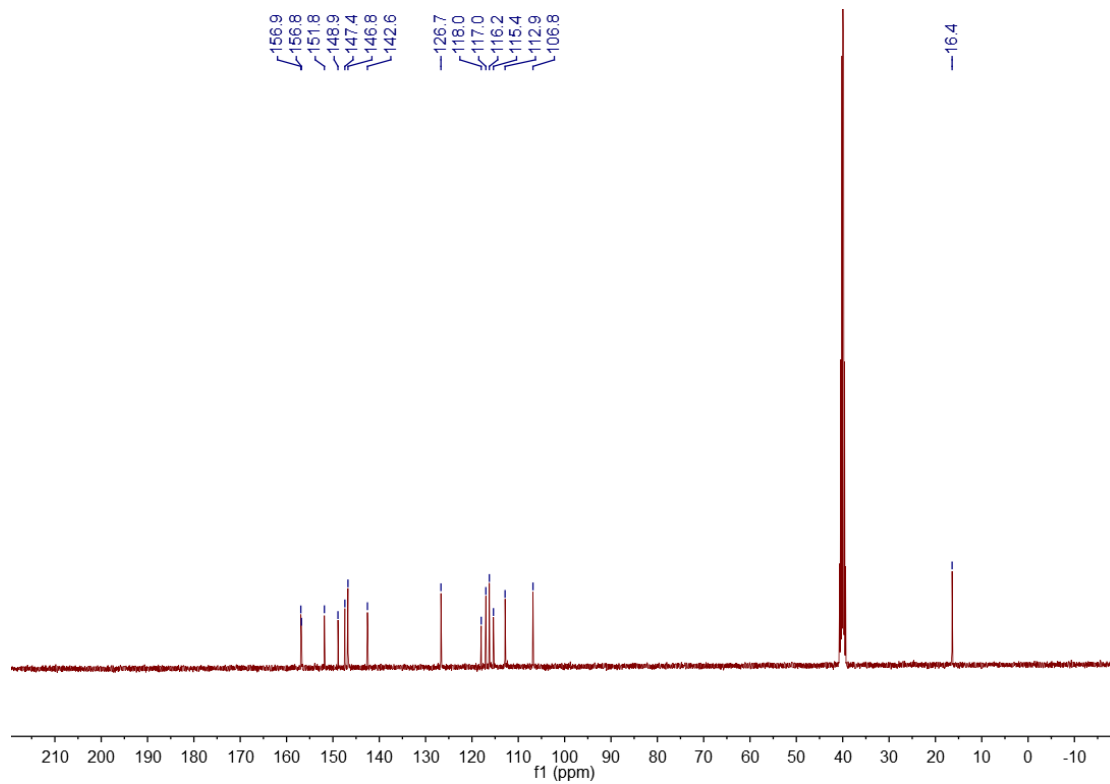
Spectrum from wenya07.wiff (sample 1) ...S (100 - 1000) from 0.067 to 0.076 min



¹H NMR Spectrum of 5e (400 MHz, DMSO-*d*₆)

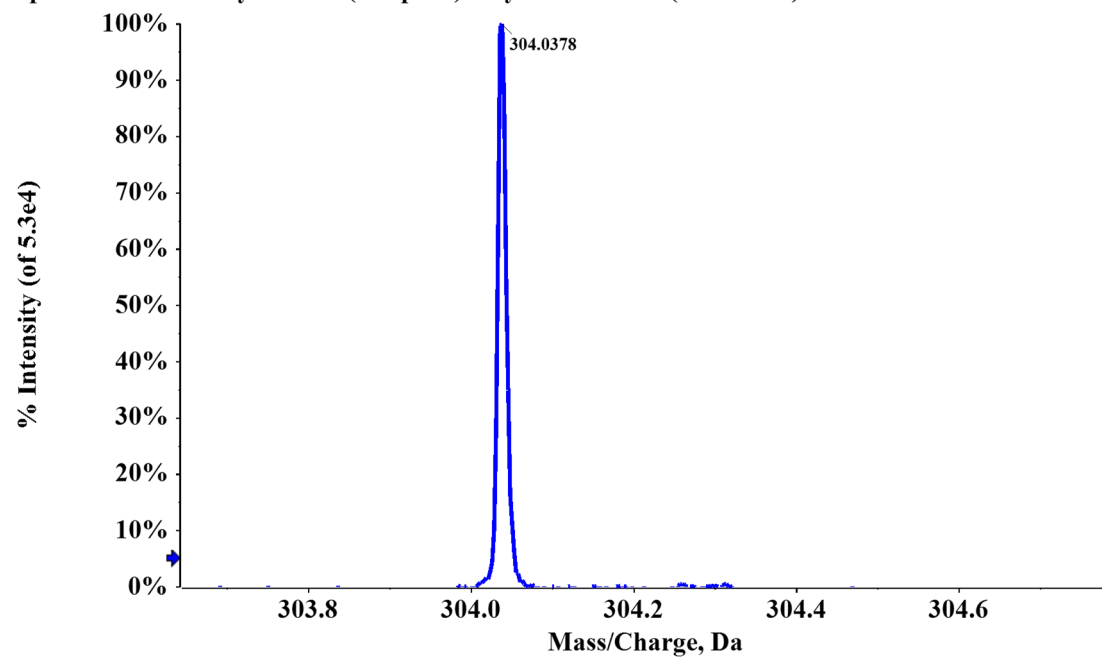


¹³C NMR Spectrum of 5e (101 MHz, DMSO-*d*₆)

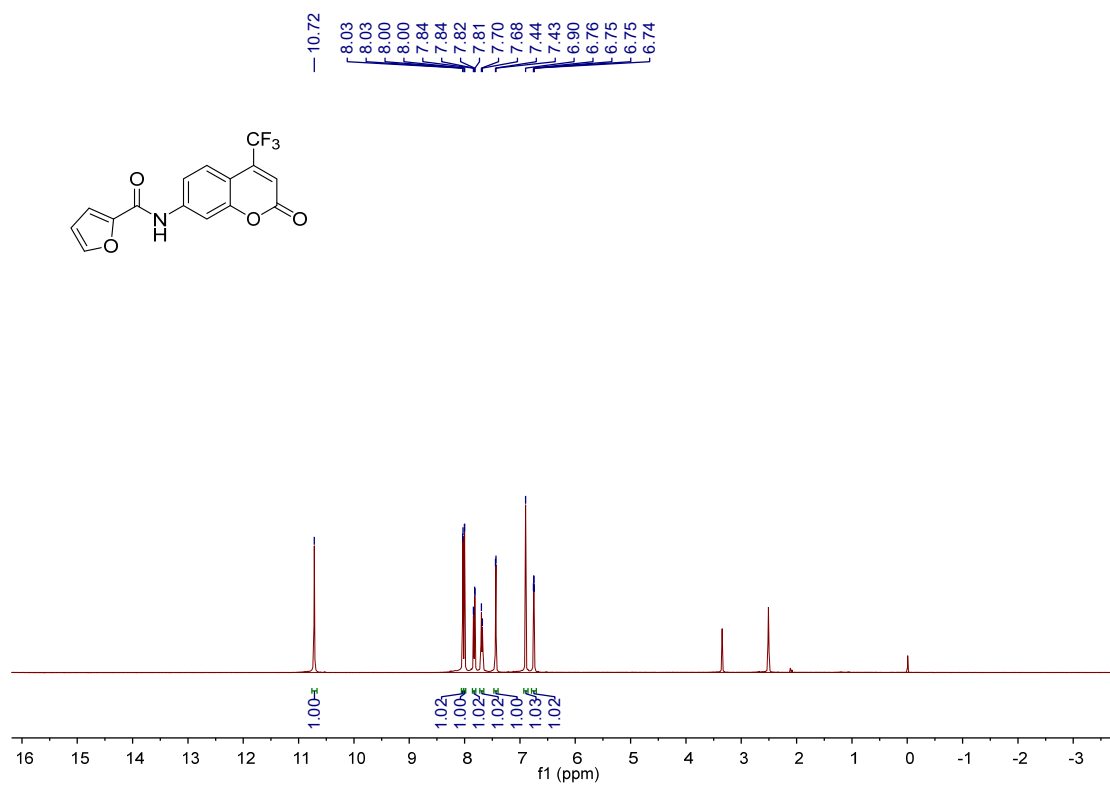


HRMS Spectrum of 5e

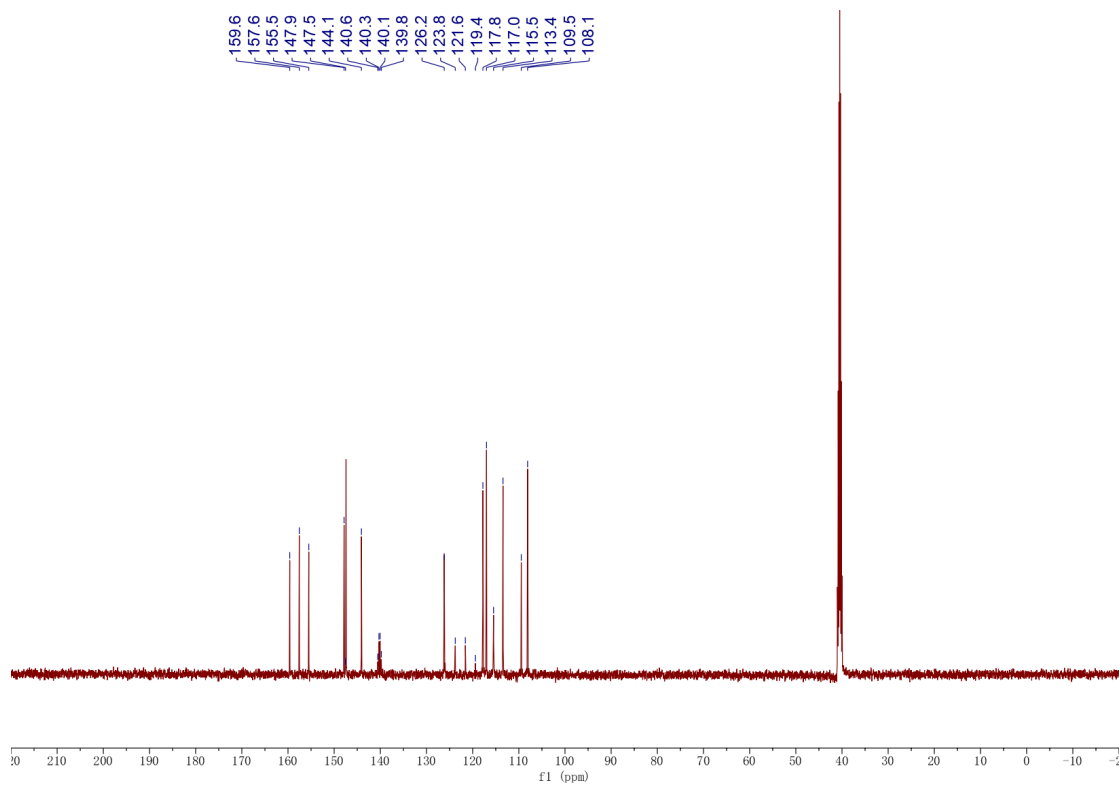
Spectrum from wenya05.wiff (sample 1) - wy05...TOF MS (100 - 1000) from 0.067 to 0.076 min



¹H NMR Spectrum of 5f (400 MHz, DMSO-*d*₆)

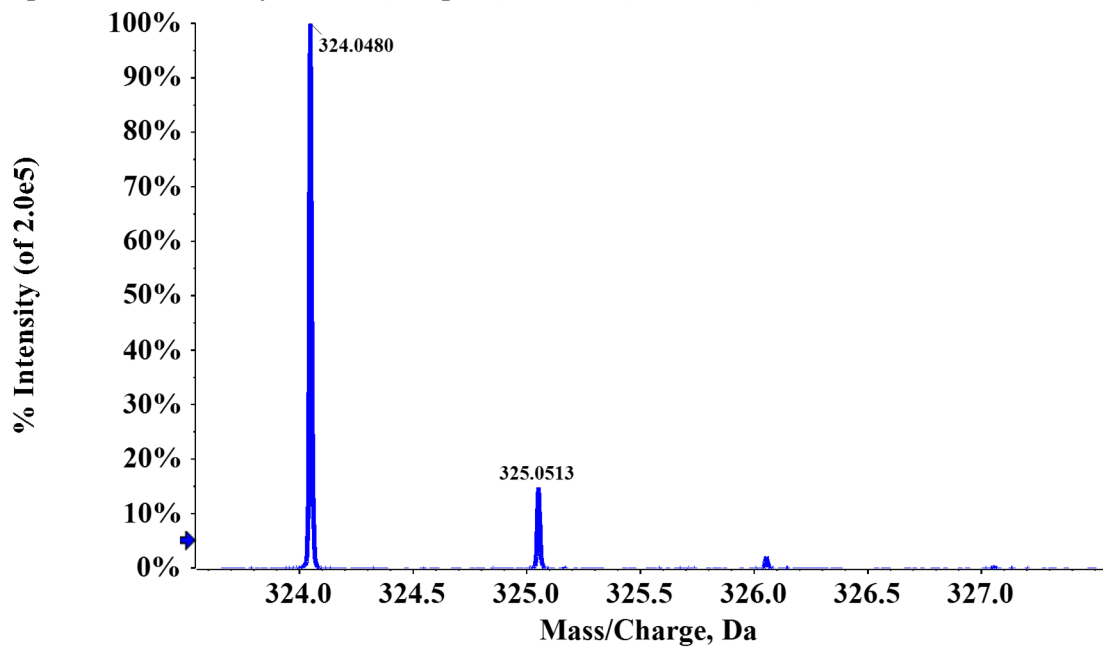


^{13}C NMR Spectrum of 5f (126 MHz, $\text{DMSO-}d_6$)

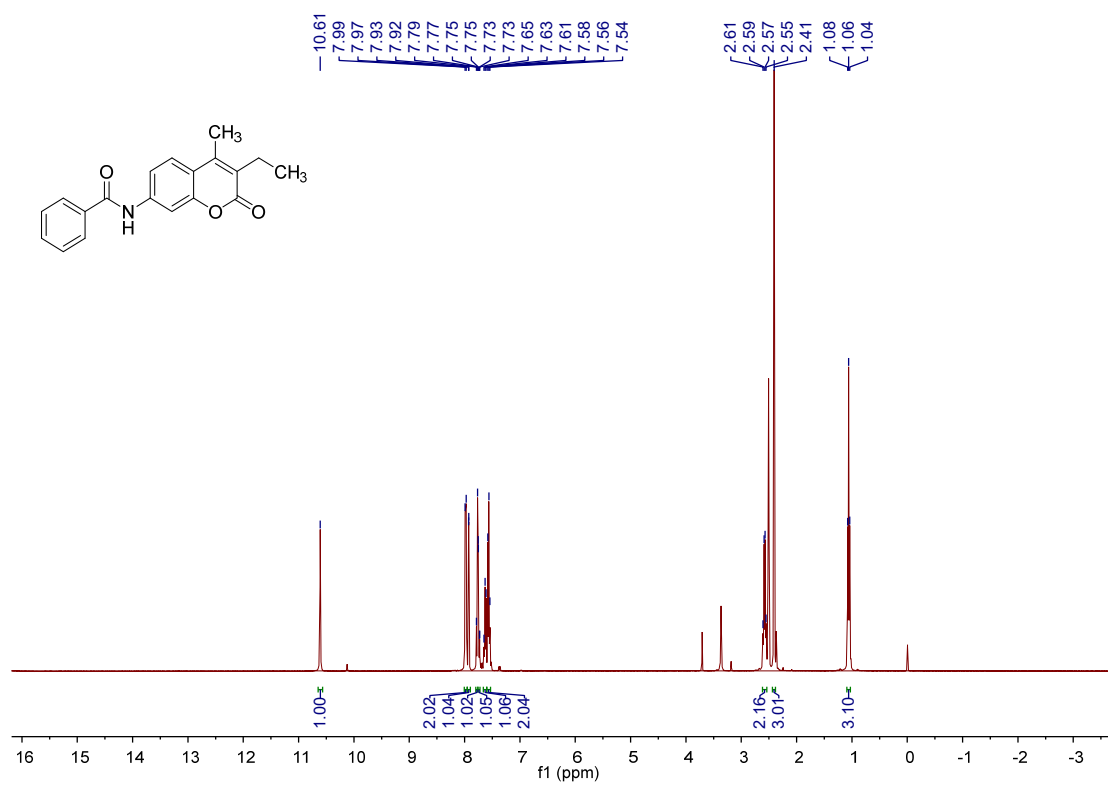


HRMS Spectrum of 5f

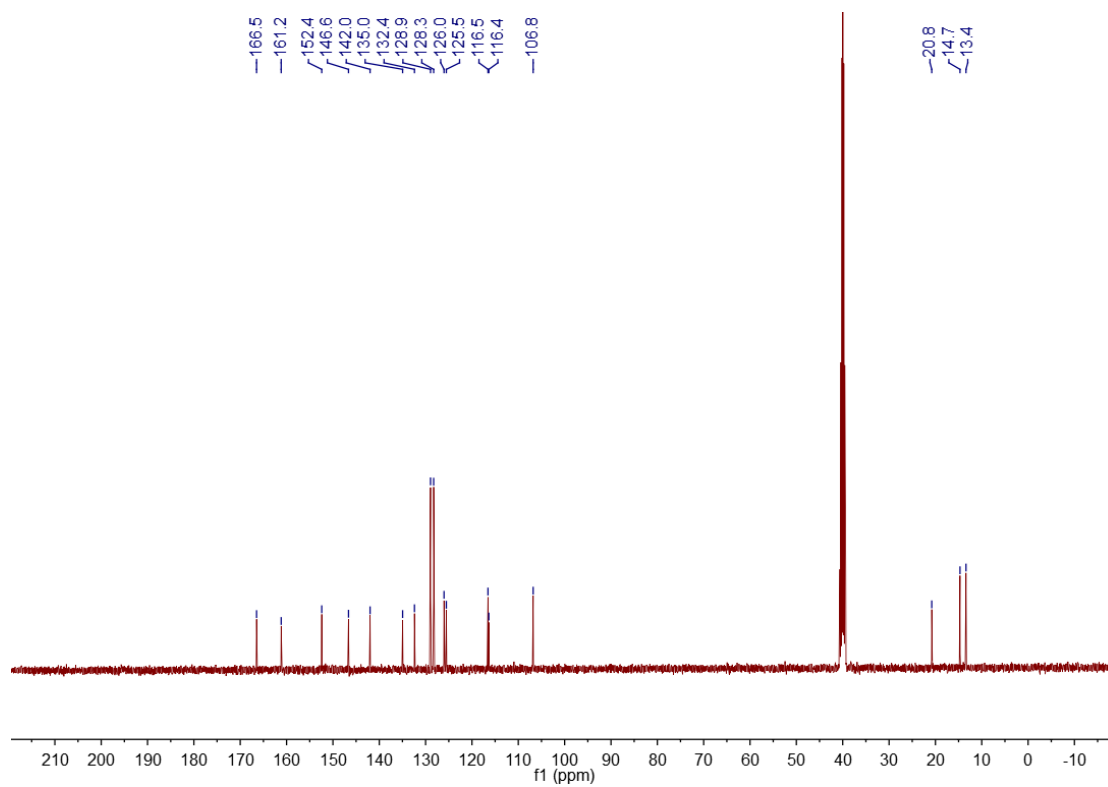
Spectrum from wenya06.wiff (sample 1) - ... MS (100 - 1000) from 0.063 to 0.072 min



¹H NMR Spectrum of 5g (400 MHz, DMSO-*d*₆)

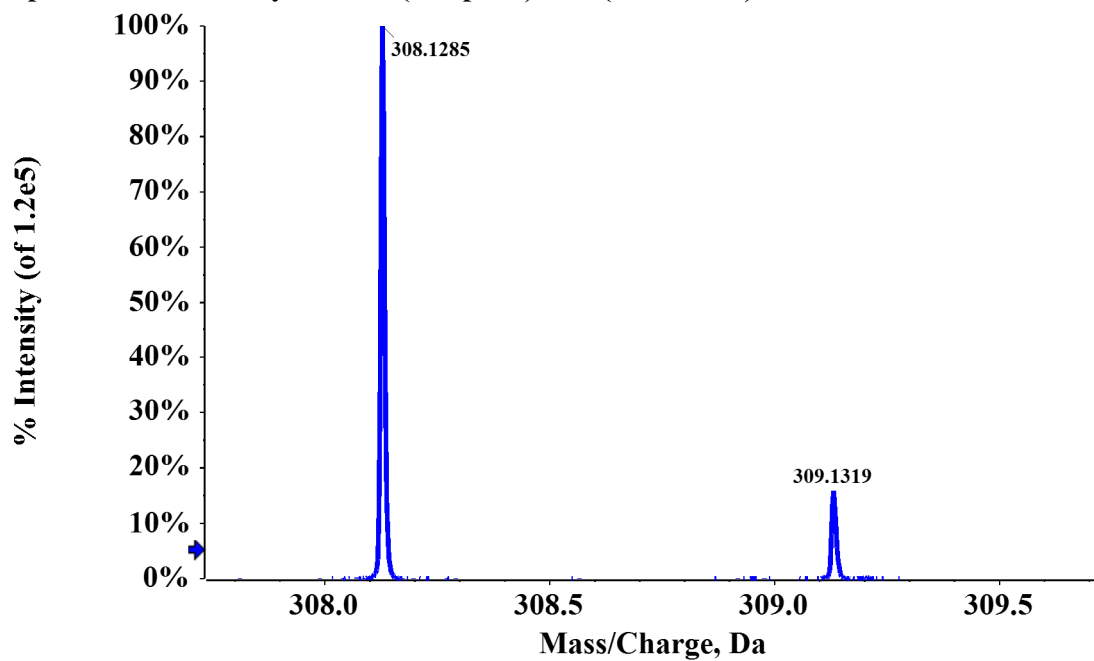


¹³C NMR Spectrum of 5g (101 MHz, DMSO-*d*₆)

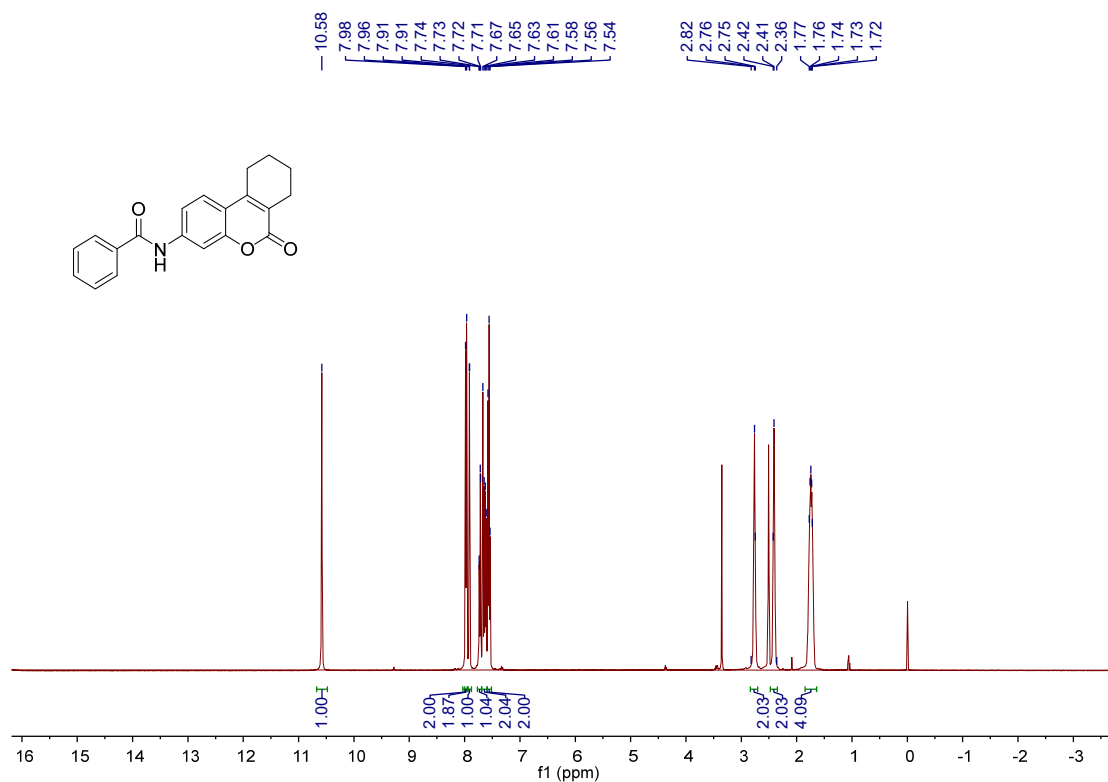


HRMS Spectrum of 5g

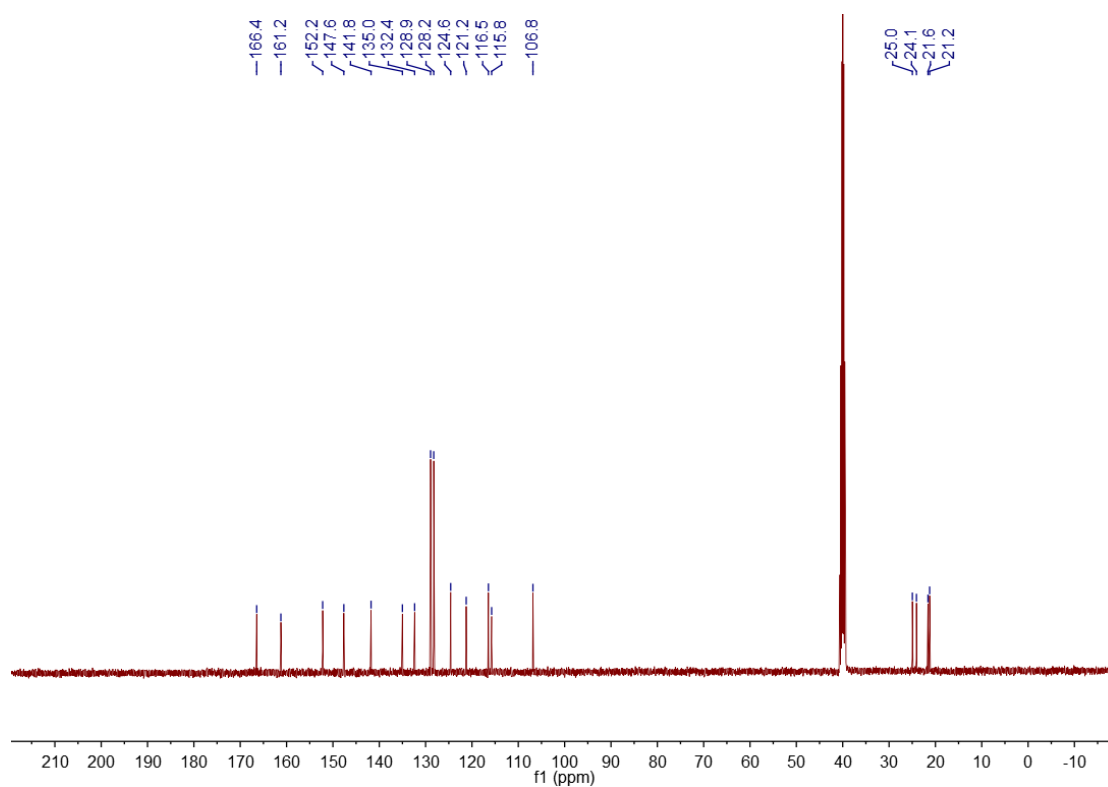
Spectrum from wenya10.wiff (sample 1) -...S (100 - 1000) from 0.053 to 0.062 min



^1H NMR Spectrum of 5h (400 MHz, $\text{DMSO}-d_6$)

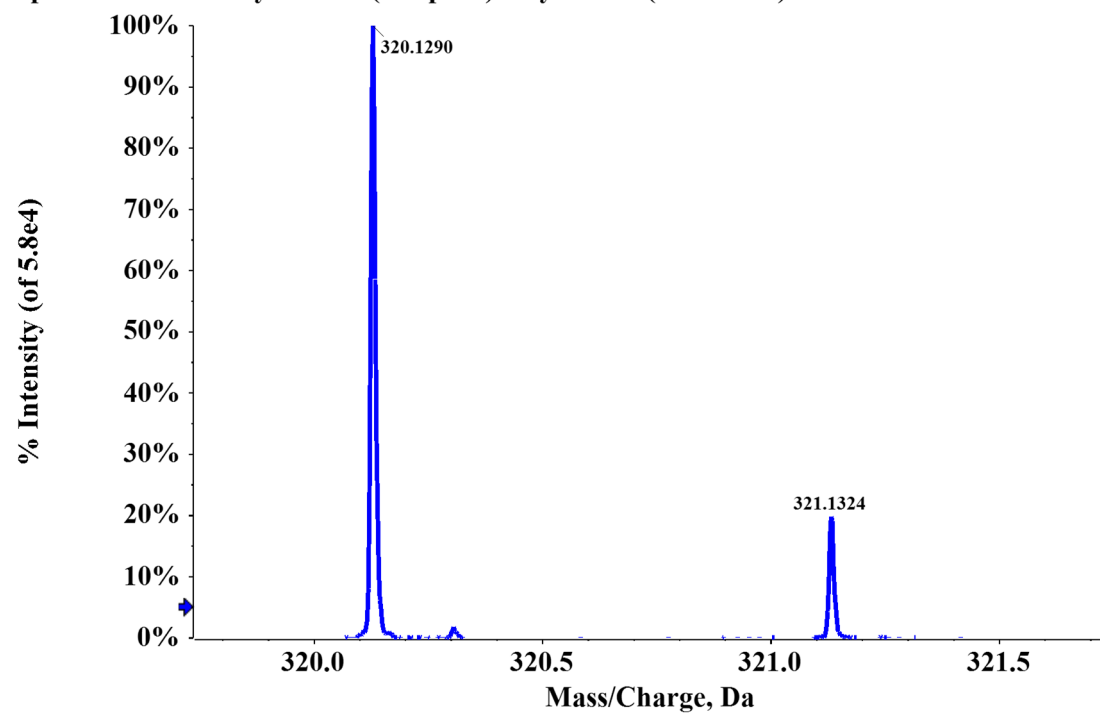


^{13}C NMR Spectrum of 5h (101 MHz, $\text{DMSO}-d_6$)

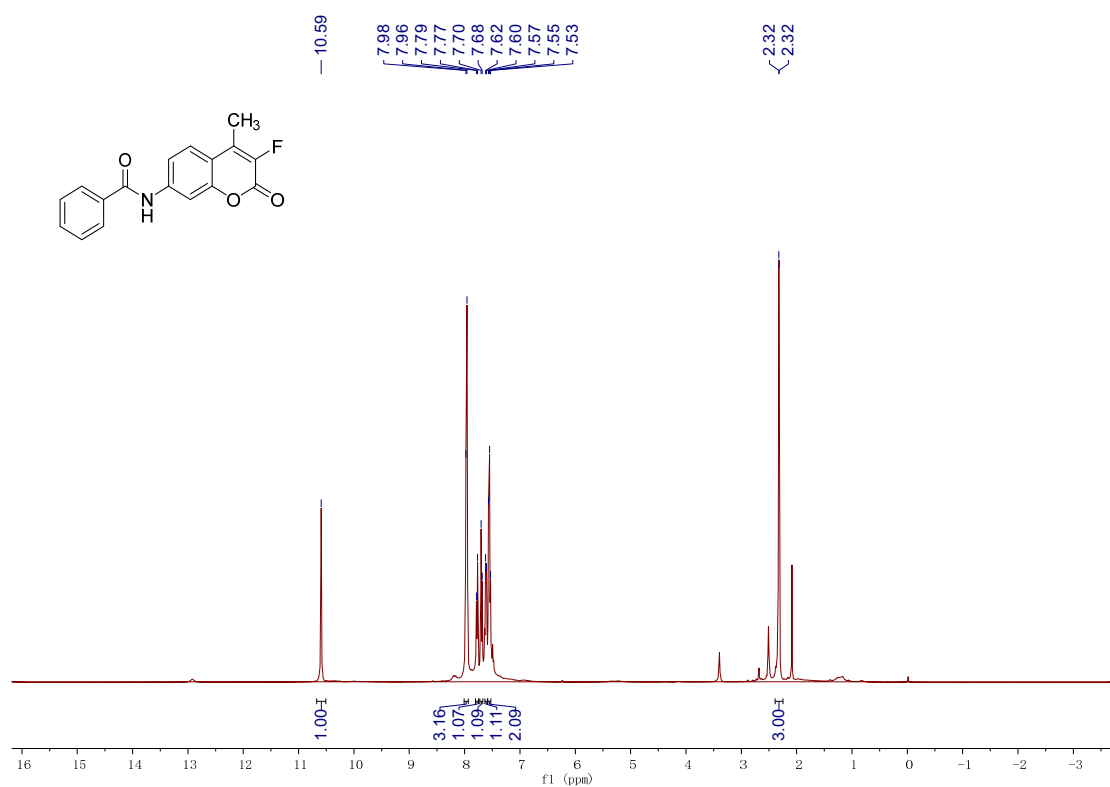


HRMS Spectrum of 5h

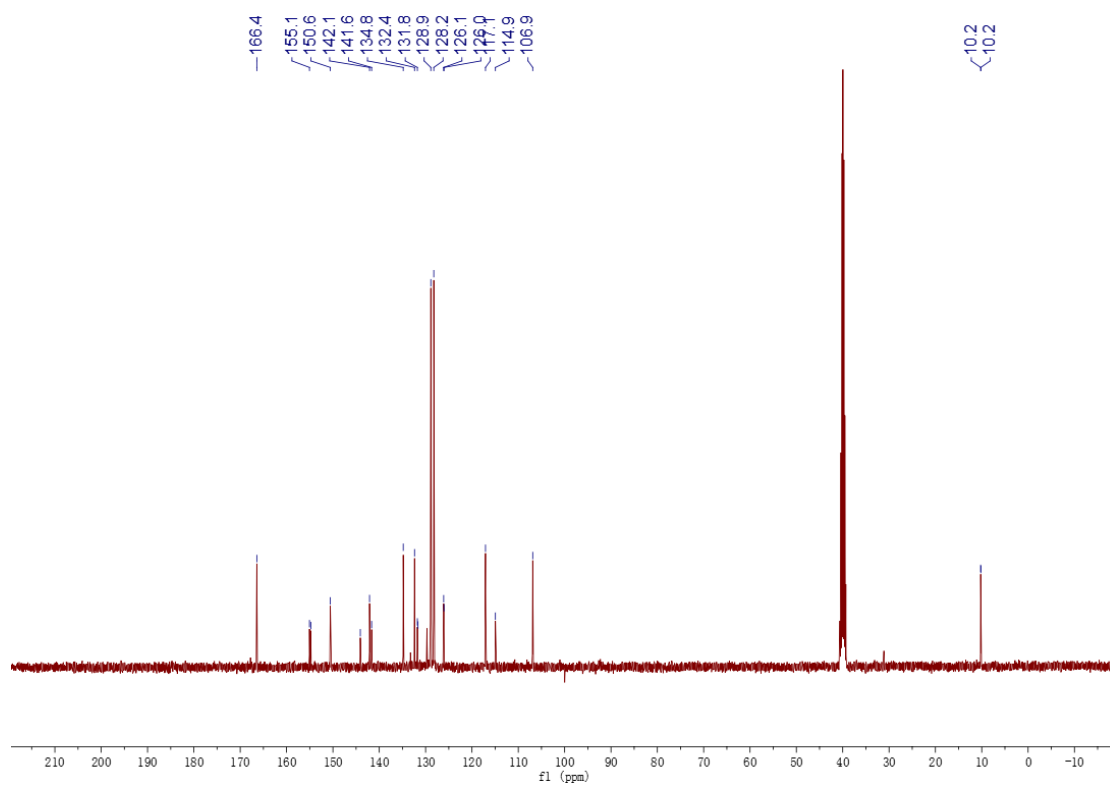
Spectrum from wenya11.wiff (sample 1) - wy...F MS (100 - 1000) from 0.085 to 0.094 min



¹H NMR Spectrum of 5i (400 MHz, DMSO-*d*₆)

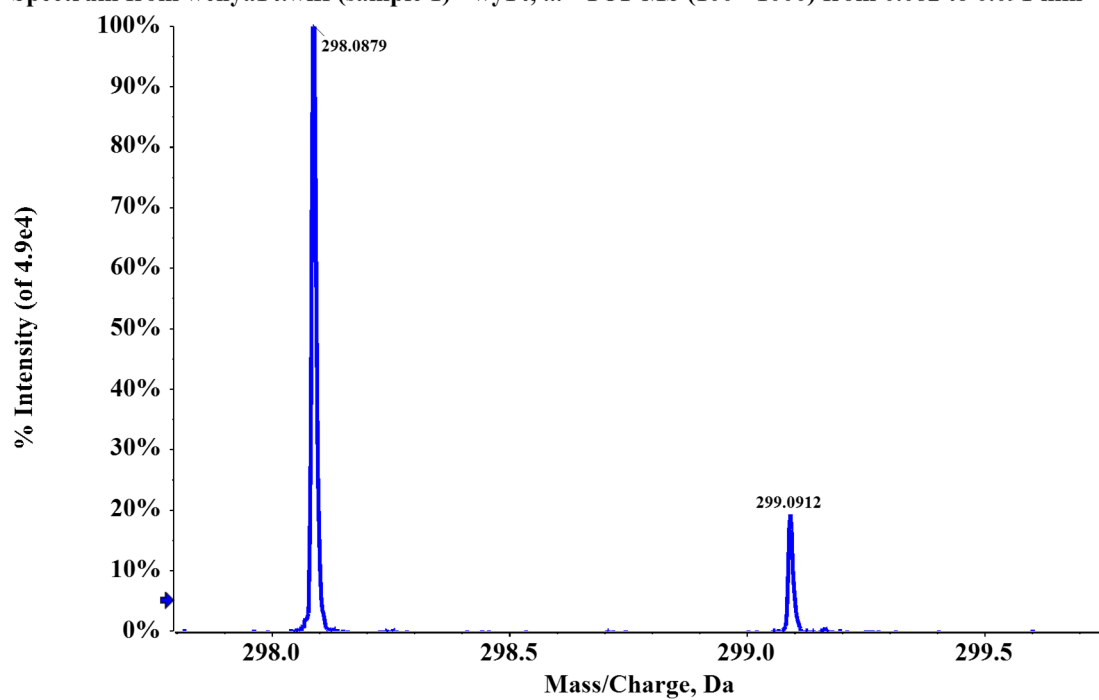


¹³C NMR Spectrum of 5i (101 MHz, DMSO-*d*₆)

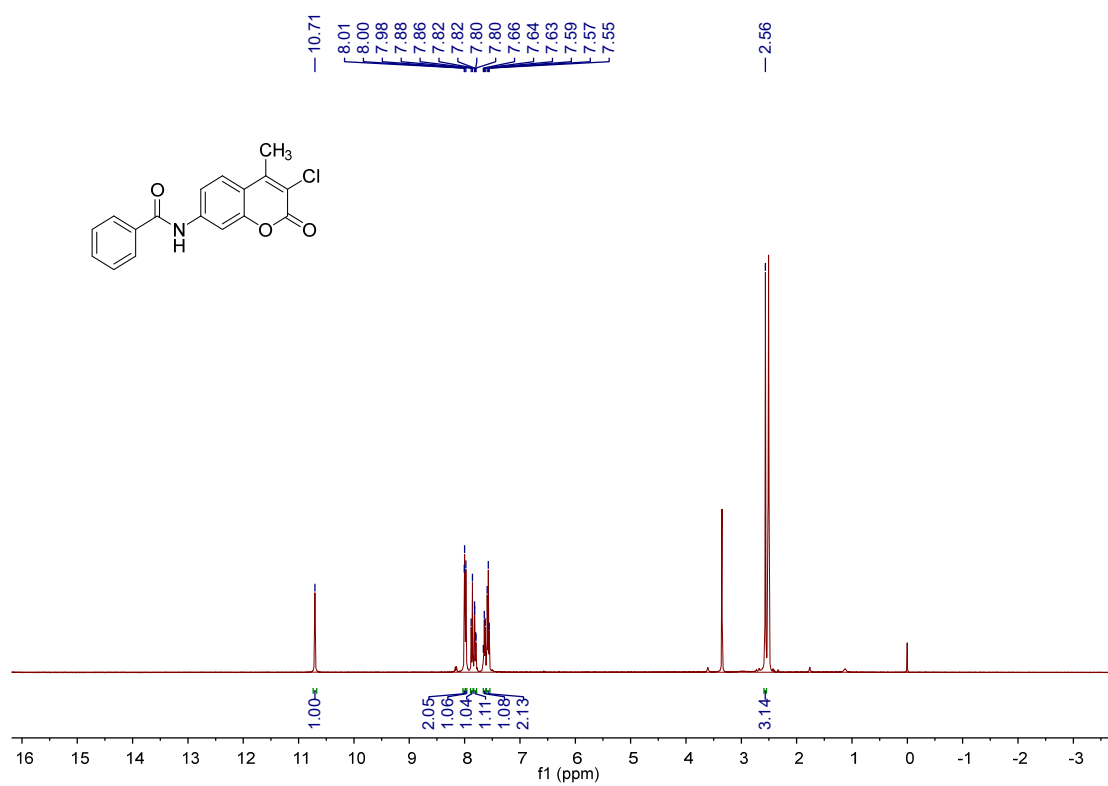


HRMS Spectrum of 5i

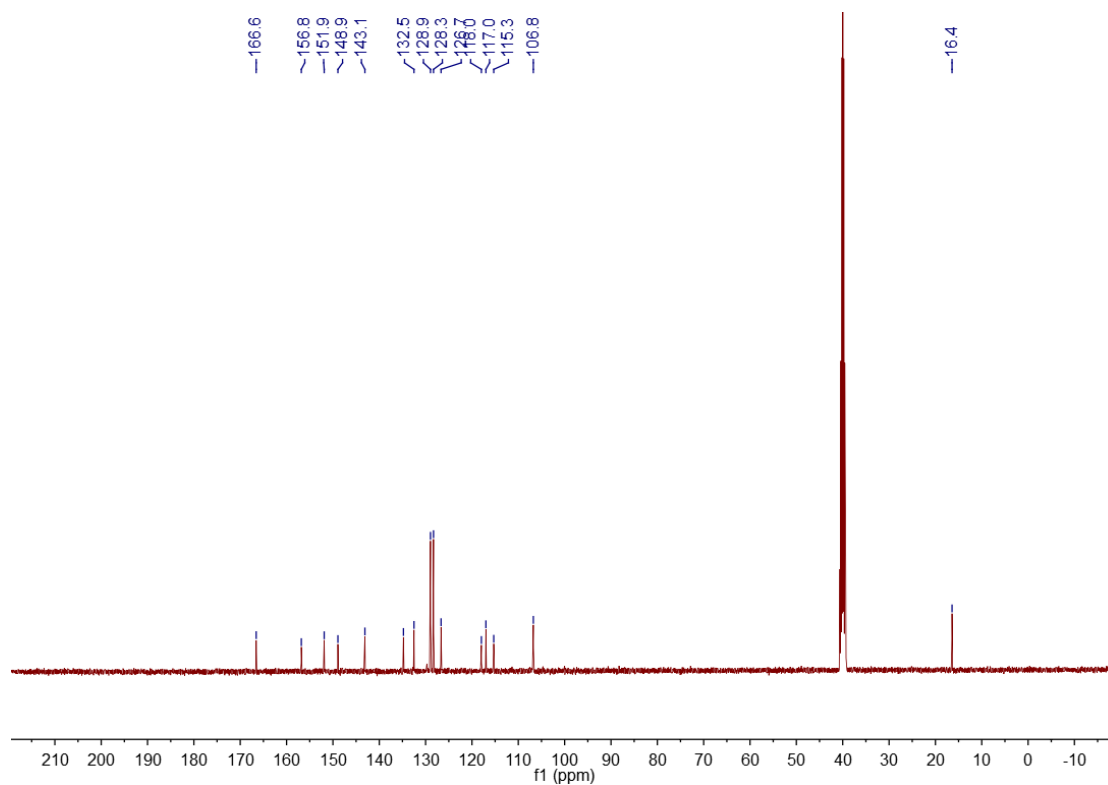
Spectrum from wenya14.wiff (sample 1) - wy14, ... +TOF MS (100 - 1000) from 0.082 to 0.091 min



^1H NMR Spectrum of 5j (400 MHz, $\text{DMSO-}d_6$)

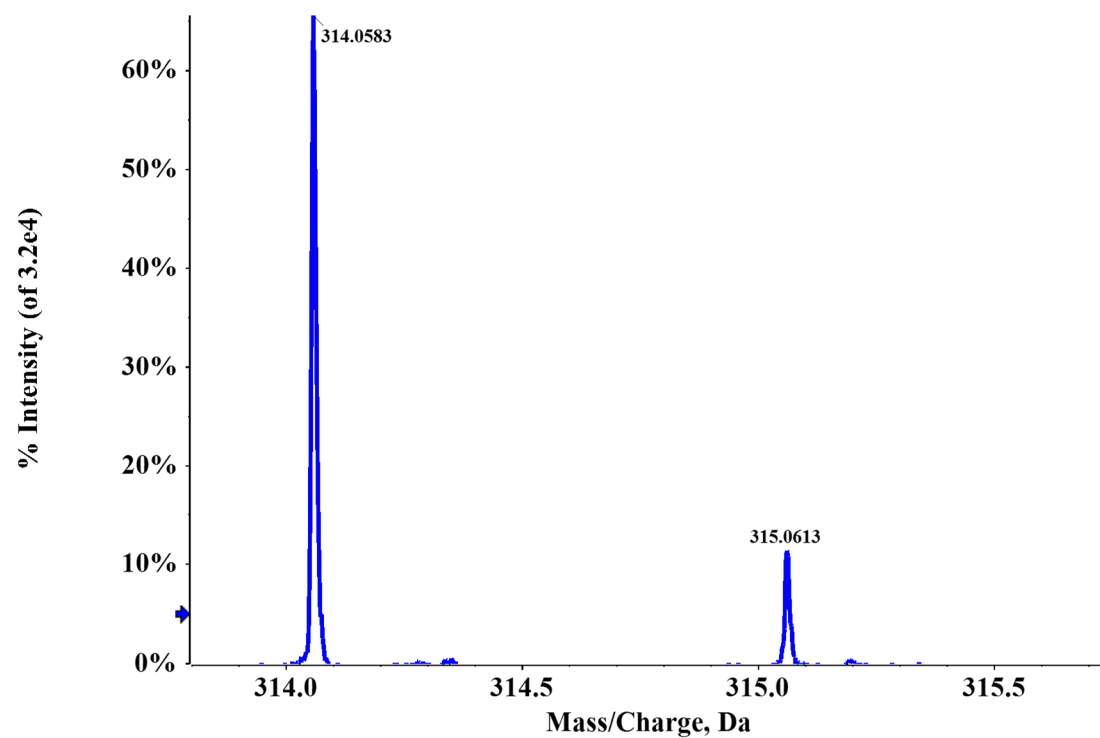


^{13}C NMR Spectrum of 5j (101 MHz, $\text{DMSO-}d_6$)

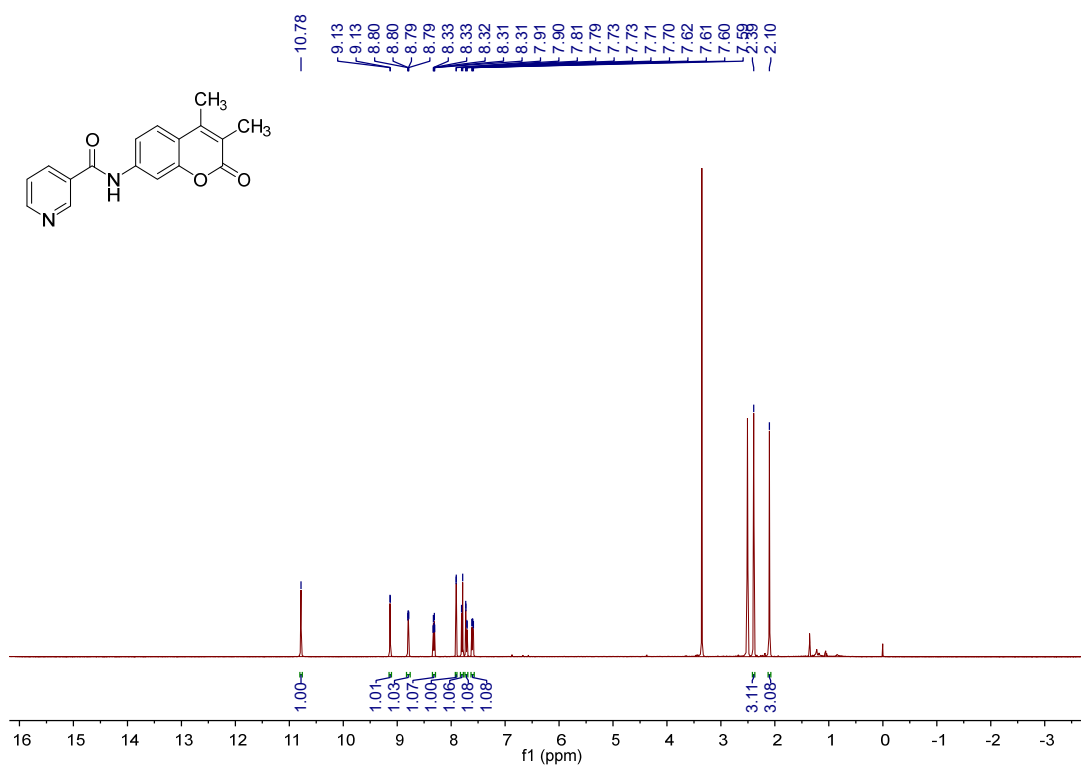


HRMS Spectrum of 5j

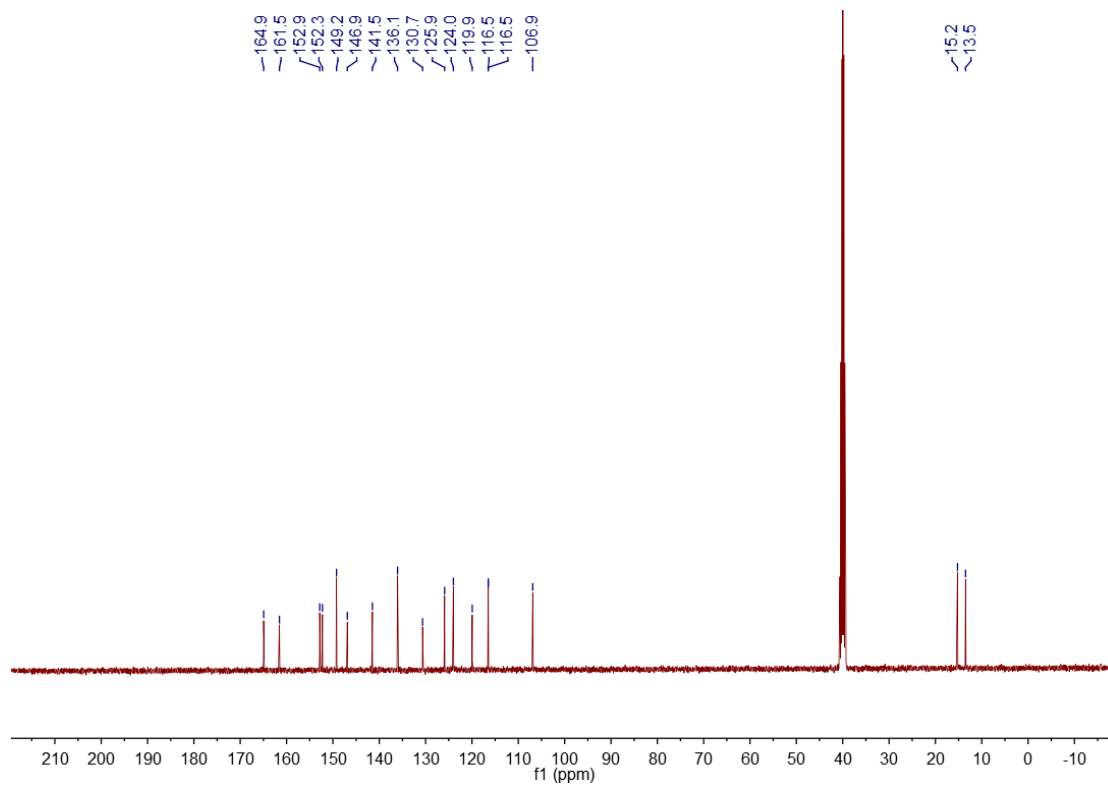
Spectrum from wenya12.wiff (sample 1) - wy...F MS (100 - 1000) from 0.072 to 0.082 min



^1H NMR Spectrum of 5k (400 MHz, $\text{DMSO}-d_6$)

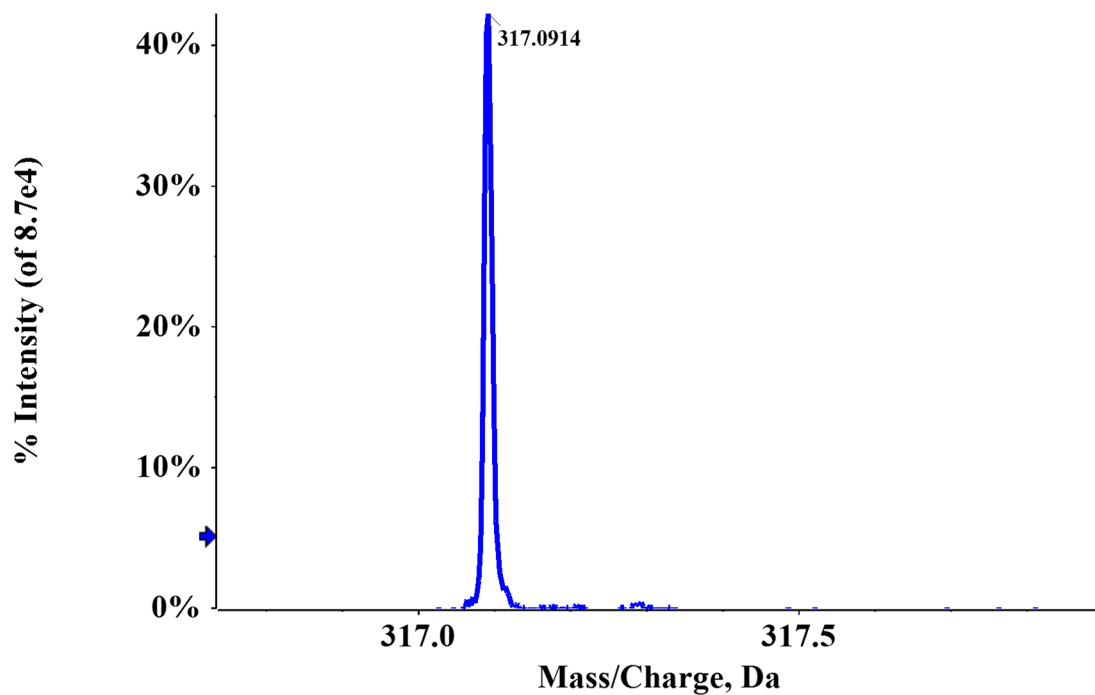


¹³C NMR Spectrum of 5k (101 MHz, DMSO-*d*₆)

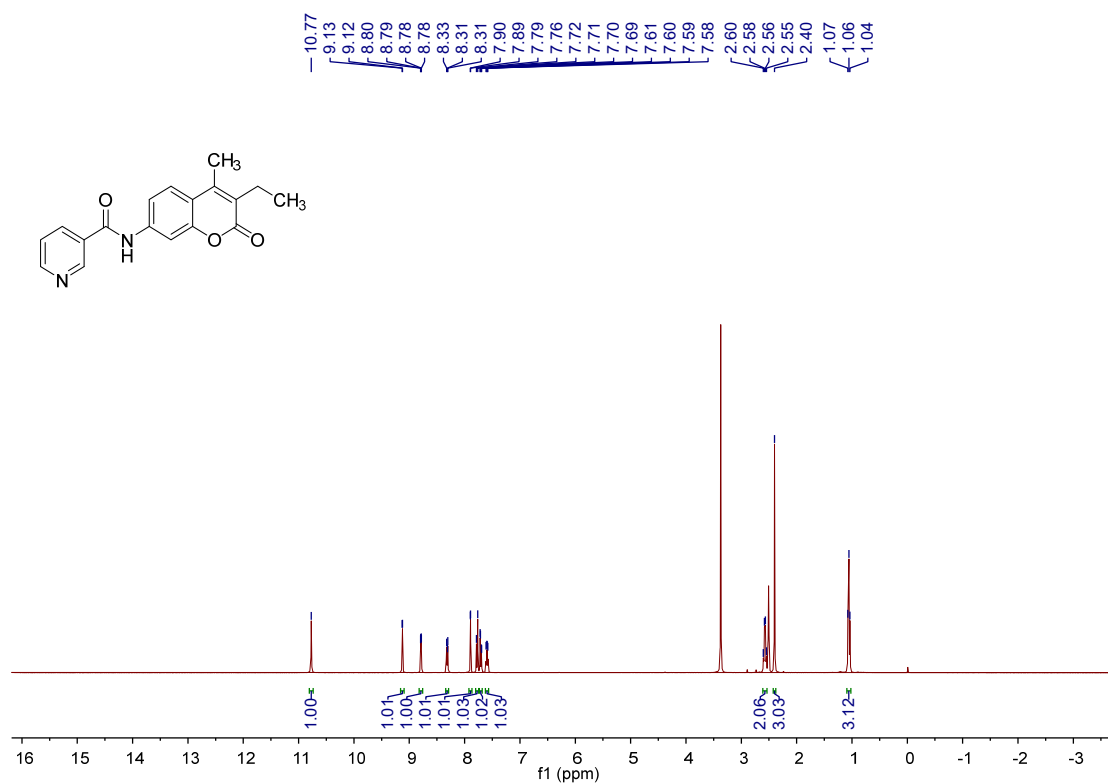


HRMS Spectrum of 5k

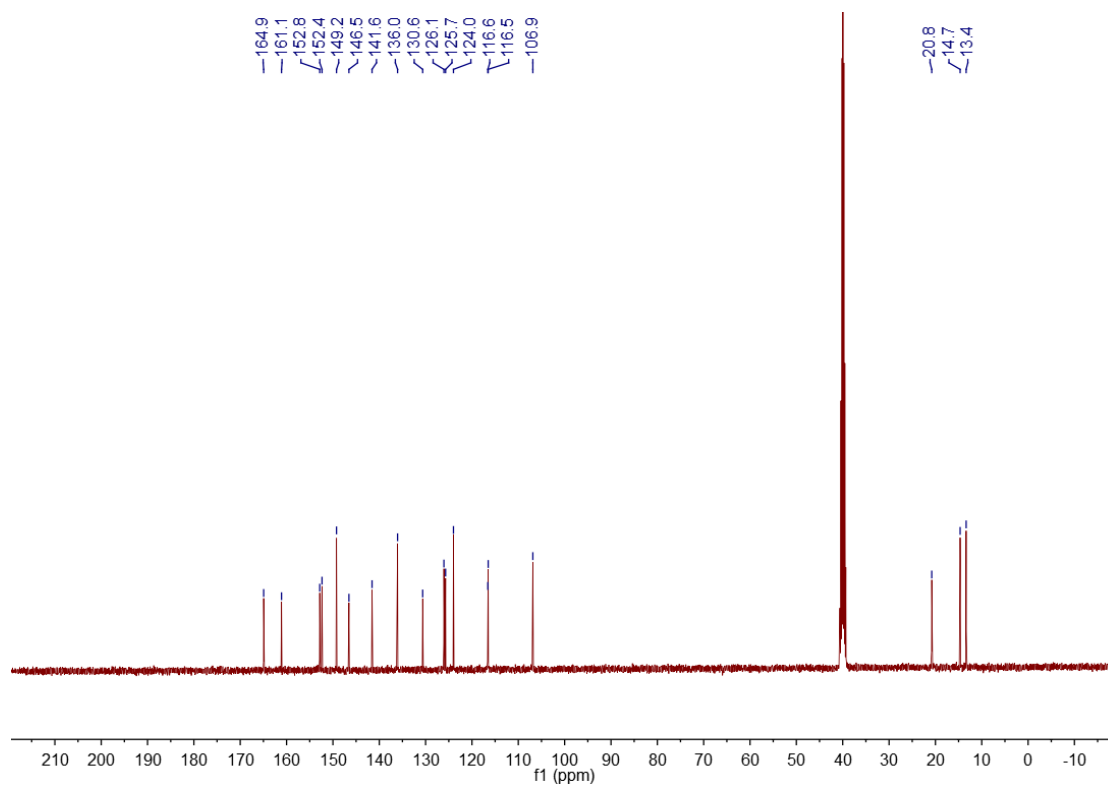
Spectrum from wenya29.wiff (sample 1...100 - 1000) from 0.081 to 0.090 min



¹H NMR Spectrum of 5l (400 MHz, DMSO-*d*₆)

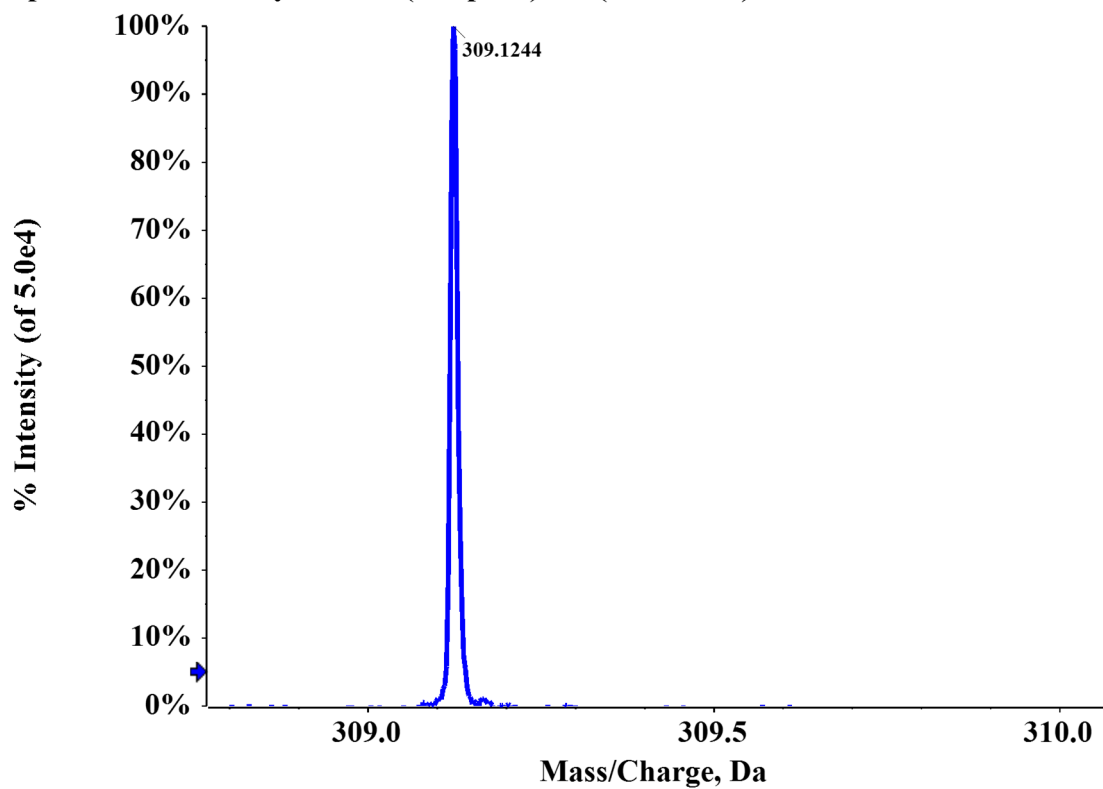


¹³C NMR Spectrum of 5l (101 MHz, DMSO-*d*₆)

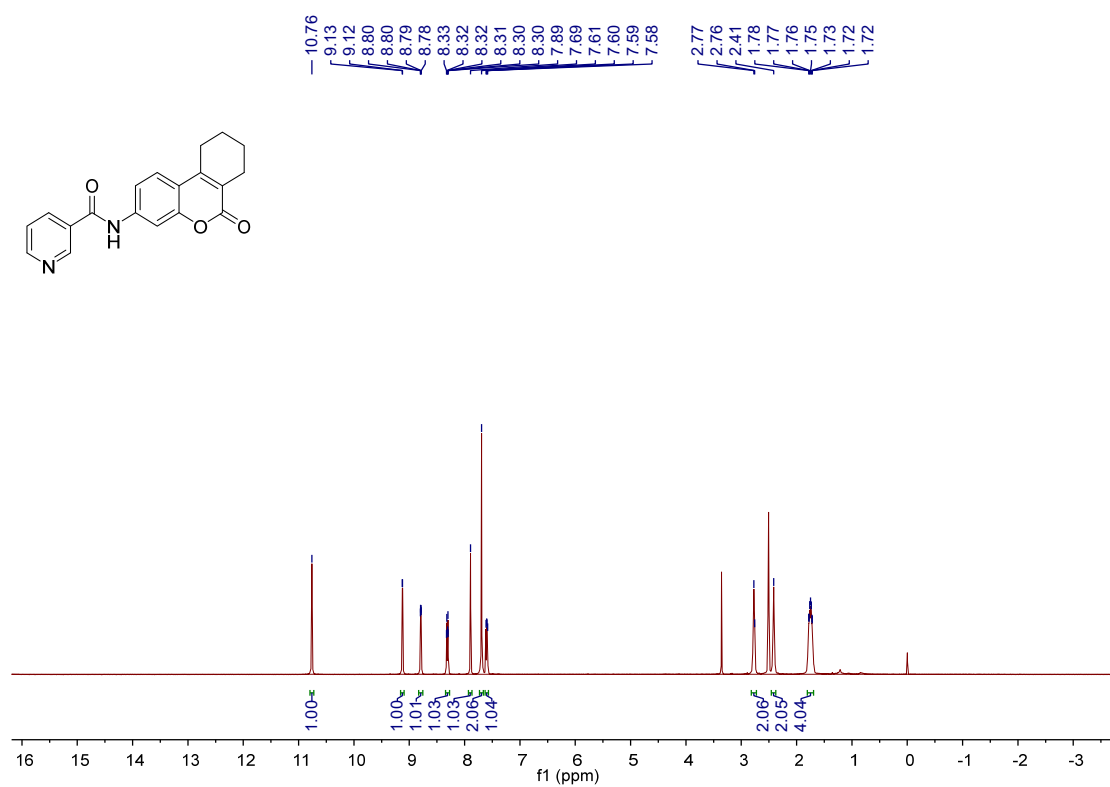


HRMS Spectrum of 5I

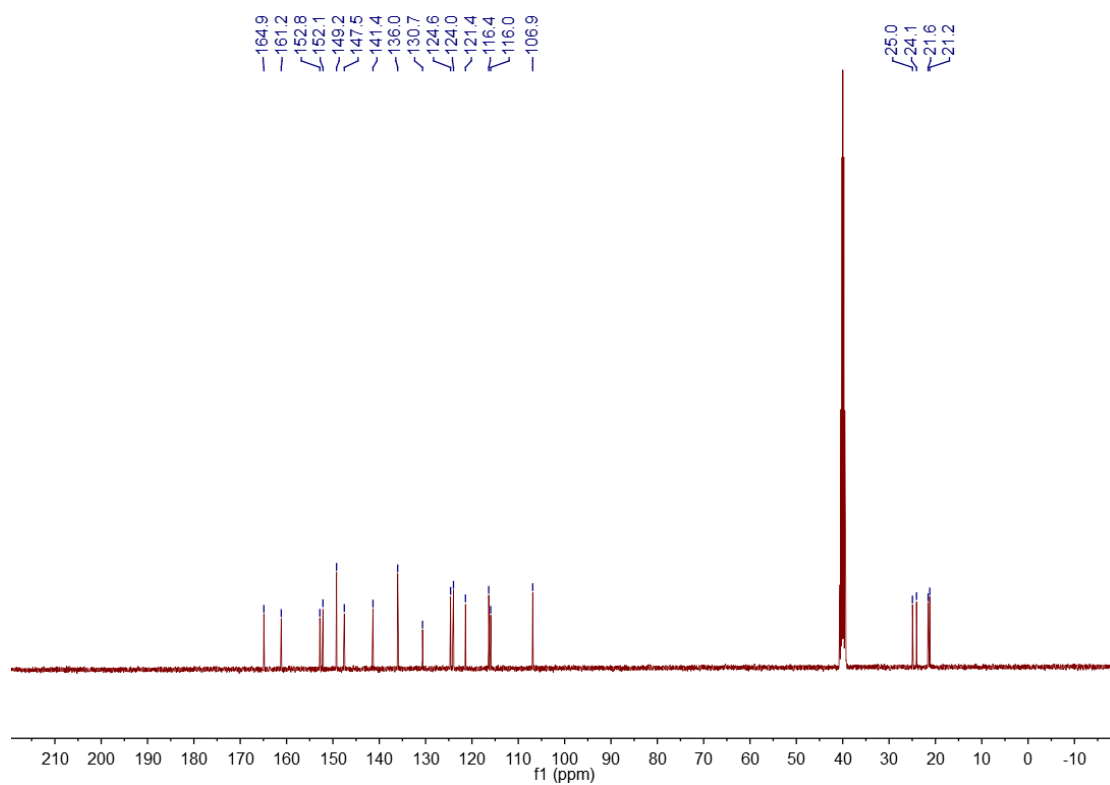
Spectrum from wenya30.wiff (sample 1) ...S (100 - 1000) from 0.072 to 0.081 min



^1H NMR Spectrum of 5m (400 MHz, $\text{DMSO}-d_6$)

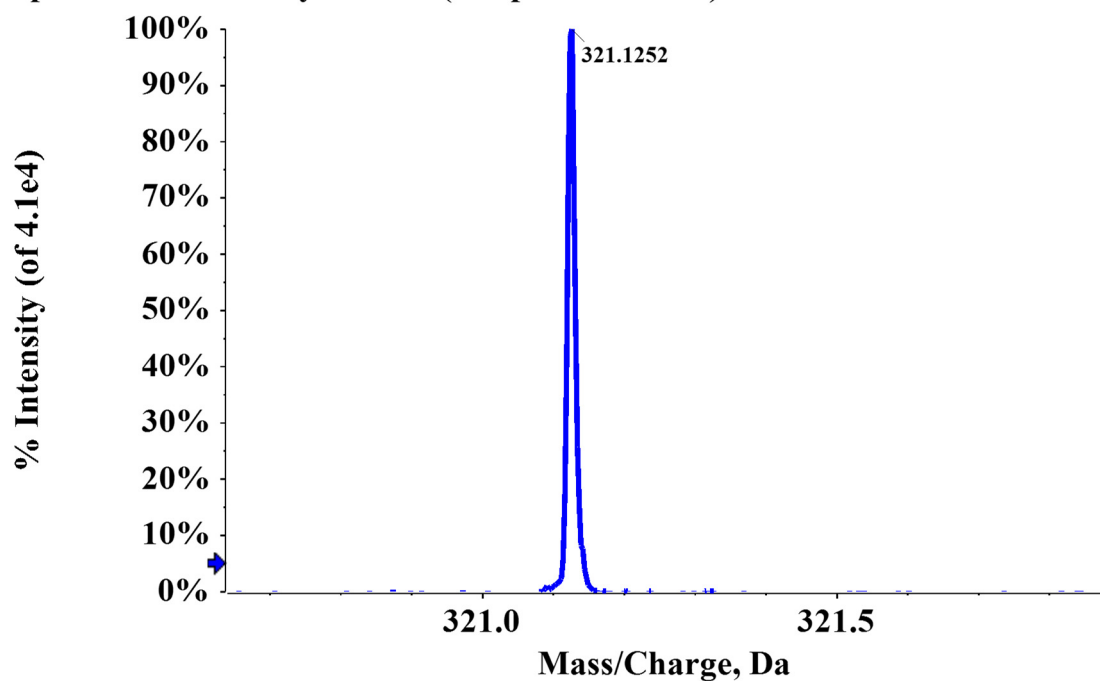


¹³C NMR Spectrum of 5m (101 MHz, DMSO-*d*₆)

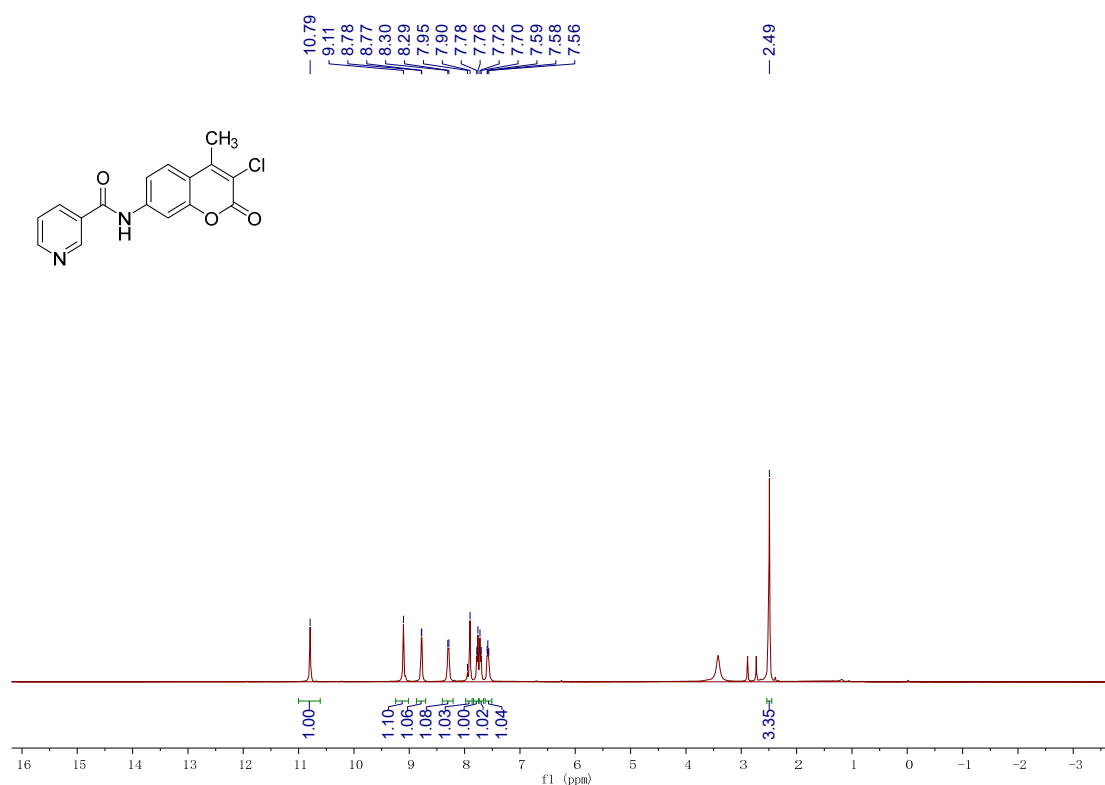


HRMS Spectrum of 5m

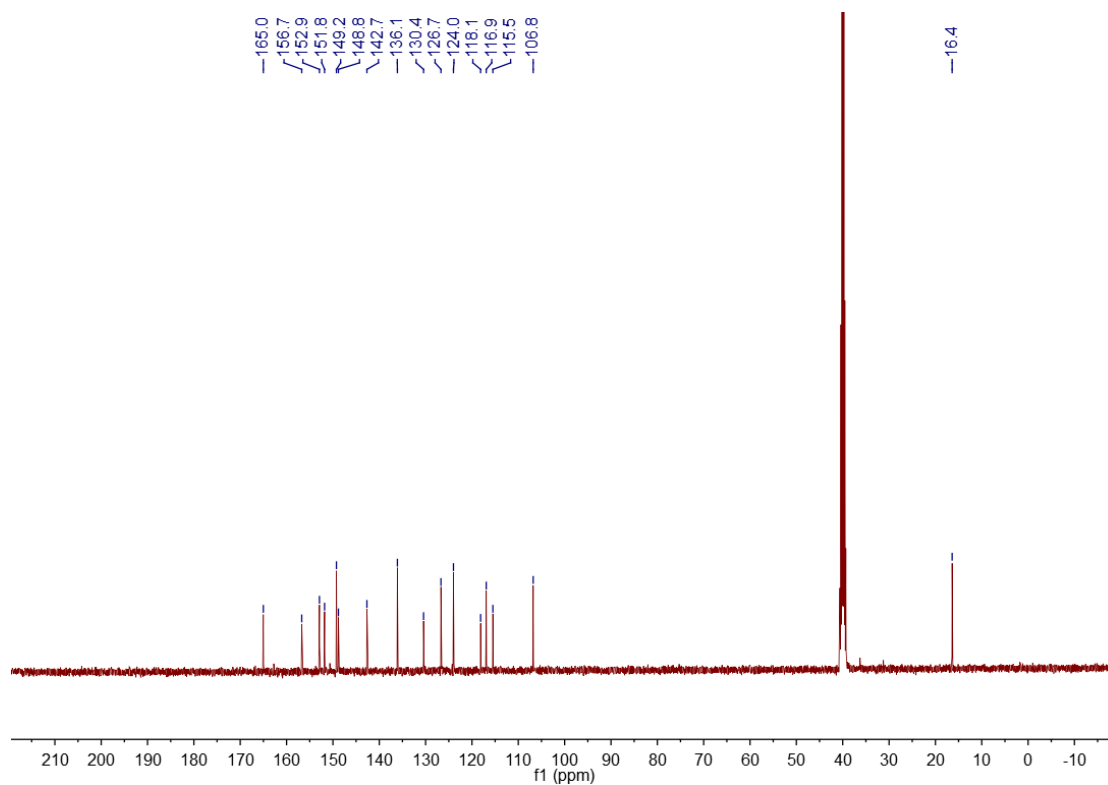
Spectrum from wenya31.wiff (sample...00 - 1000) from 0.067 to 0.076 min



^1H NMR Spectrum of 5n (400 MHz, $\text{DMSO-}d_6$)

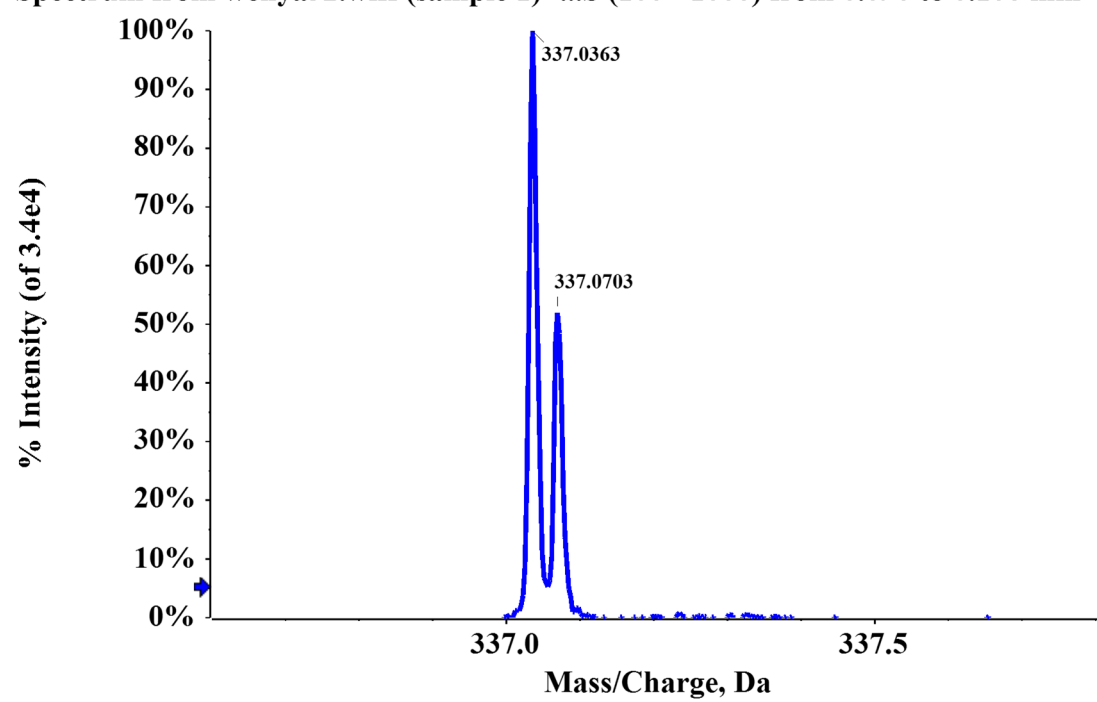


^{13}C NMR Spectrum of 5n (101 MHz, $\text{DMSO-}d_6$)

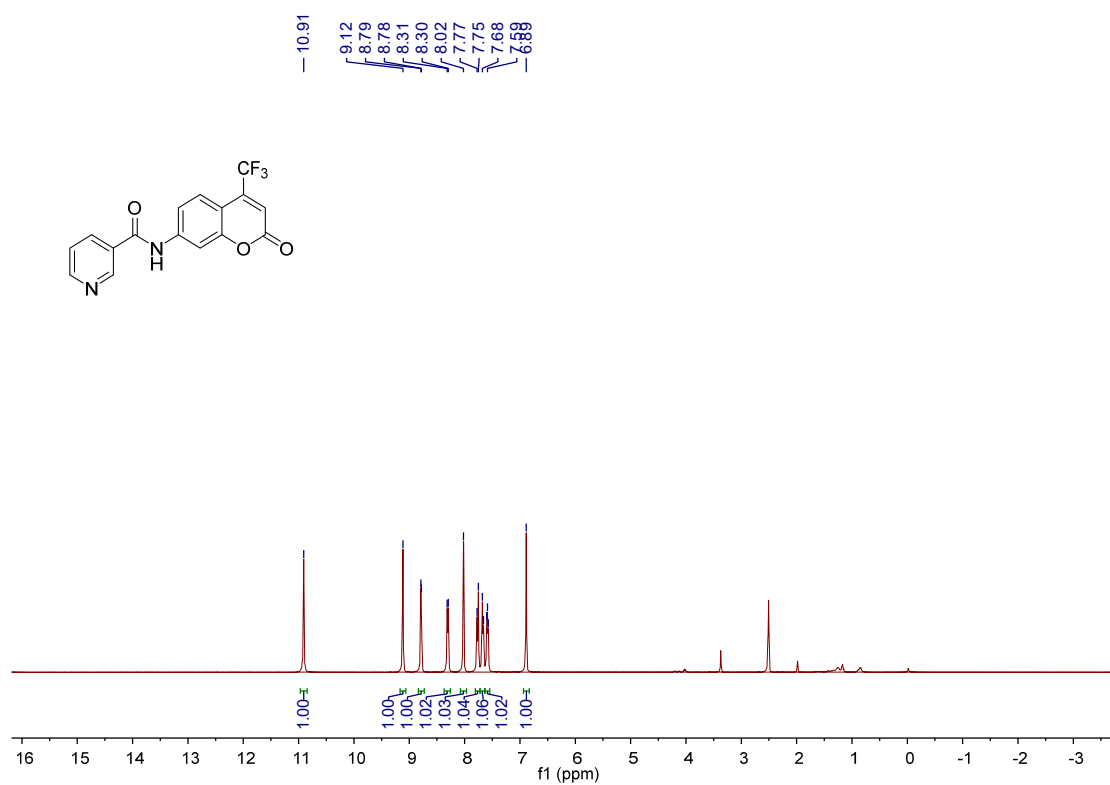


HRMS Spectrum of 5n

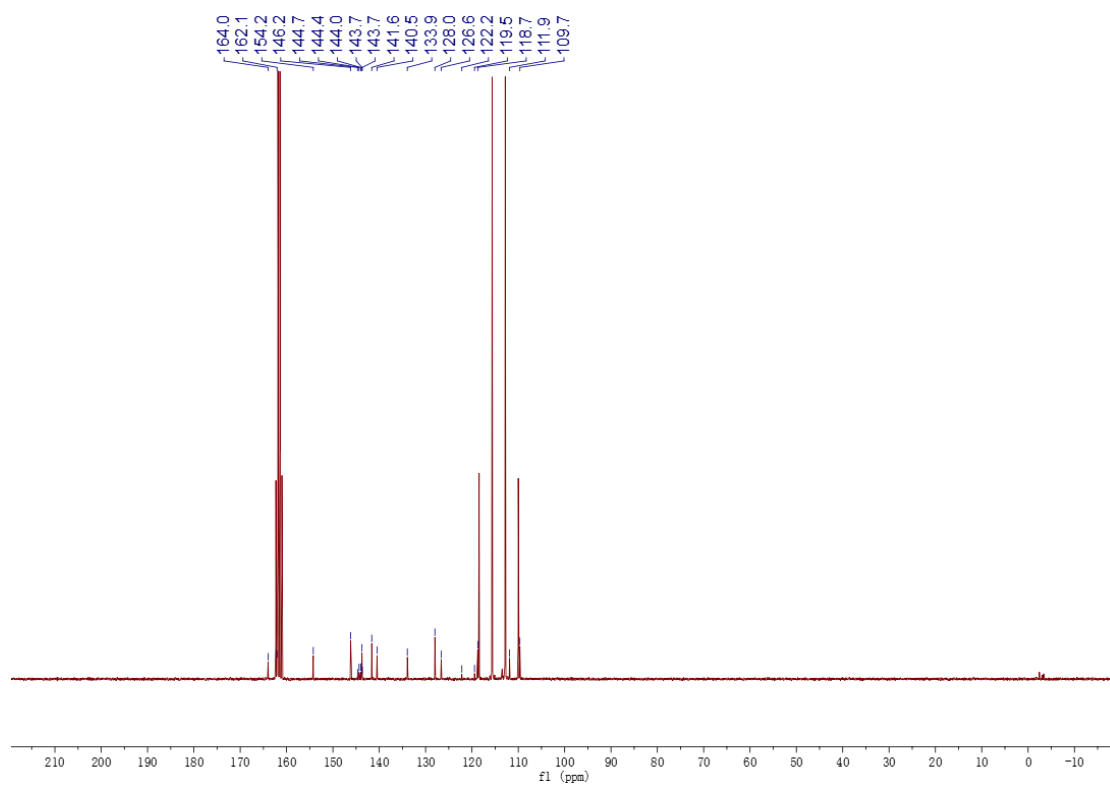
Spectrum from wenya32.wiff (sample 1) -...S (100 - 1000) from 0.090 to 0.106 min



^1H NMR Spectrum of 5o (400 MHz, $\text{DMSO}-d_6$)

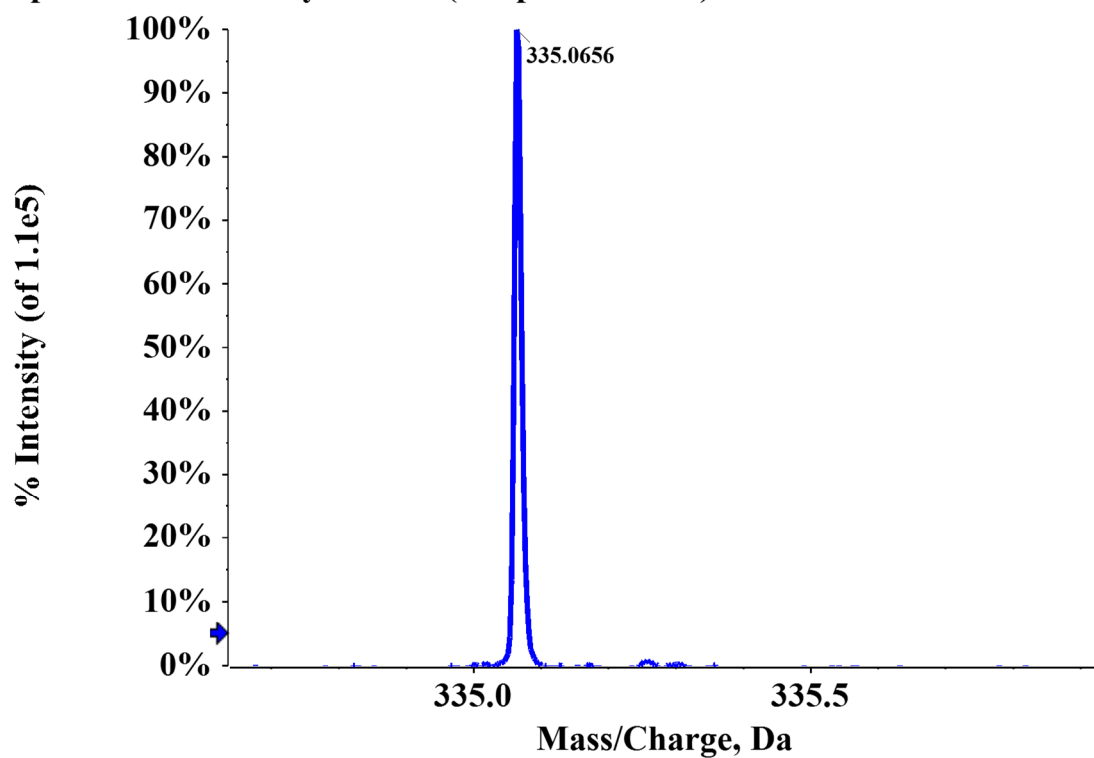


¹³C NMR Spectrum of 5o (101 MHz, CF₃COOD)

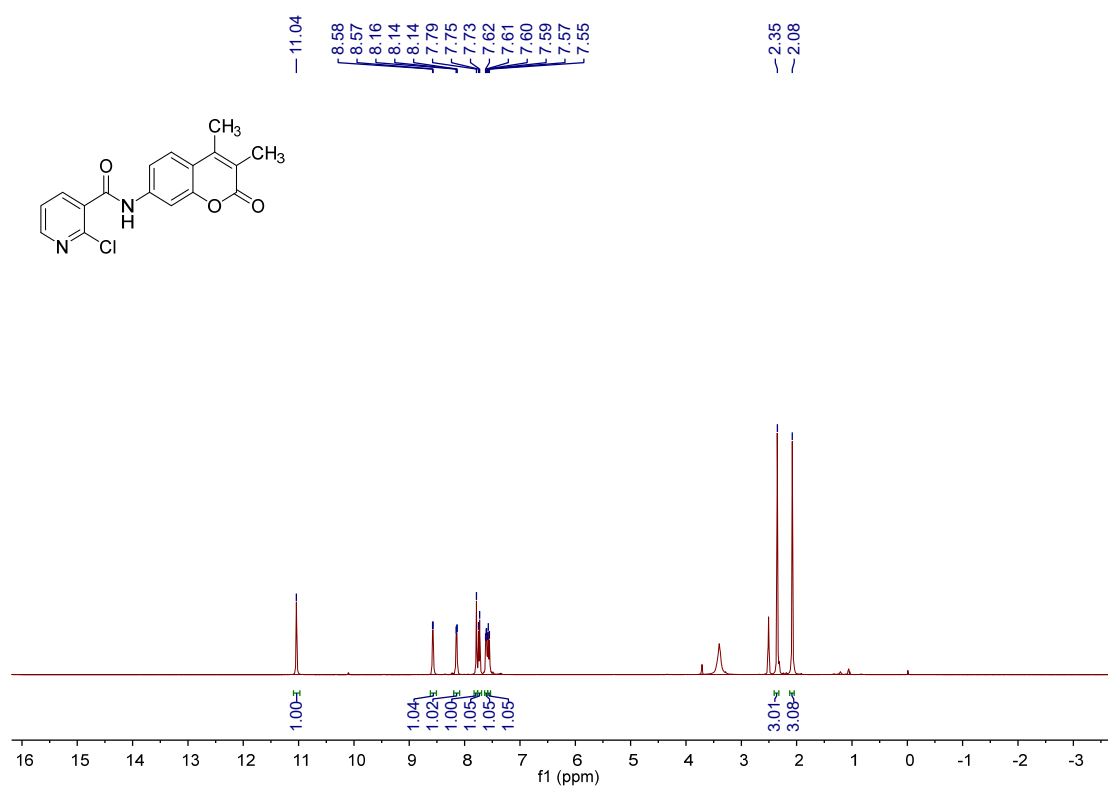


HRMS Spectrum of 5o

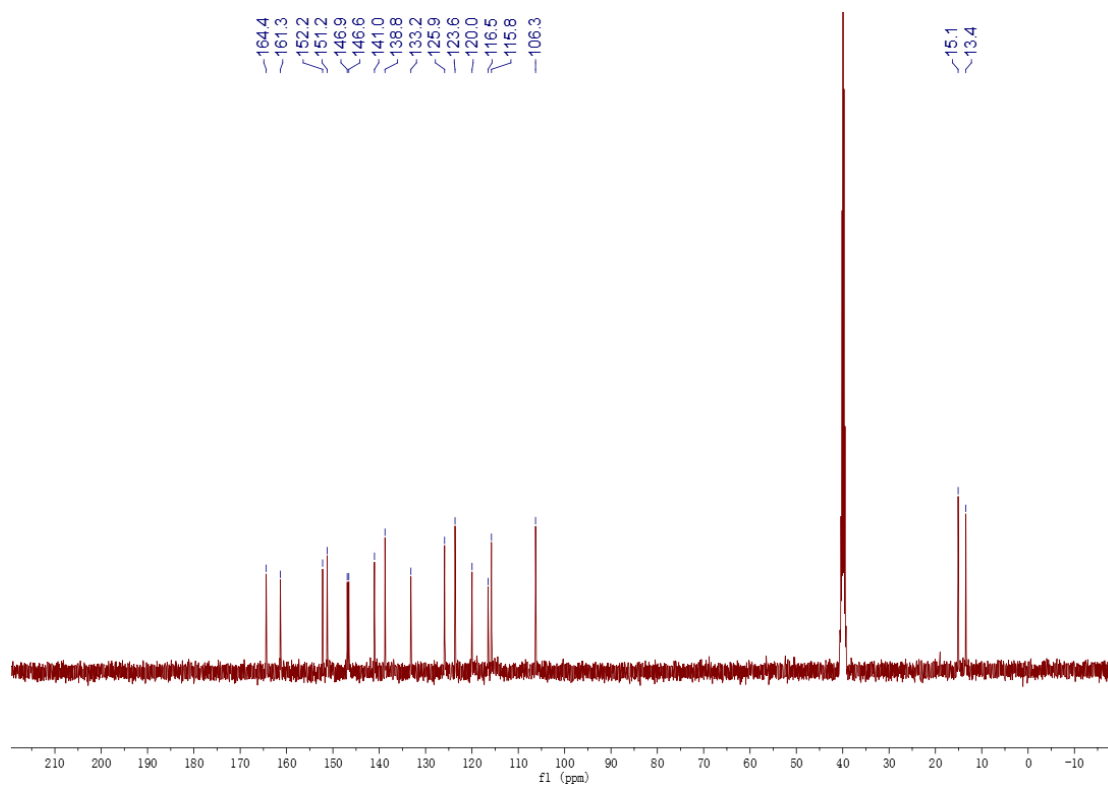
Spectrum from wenya33.wiff (sample...0 - 1000) from 0.067 to 0.076 min



^1H NMR Spectrum of 5p (400 MHz, $\text{DMSO-}d_6$)

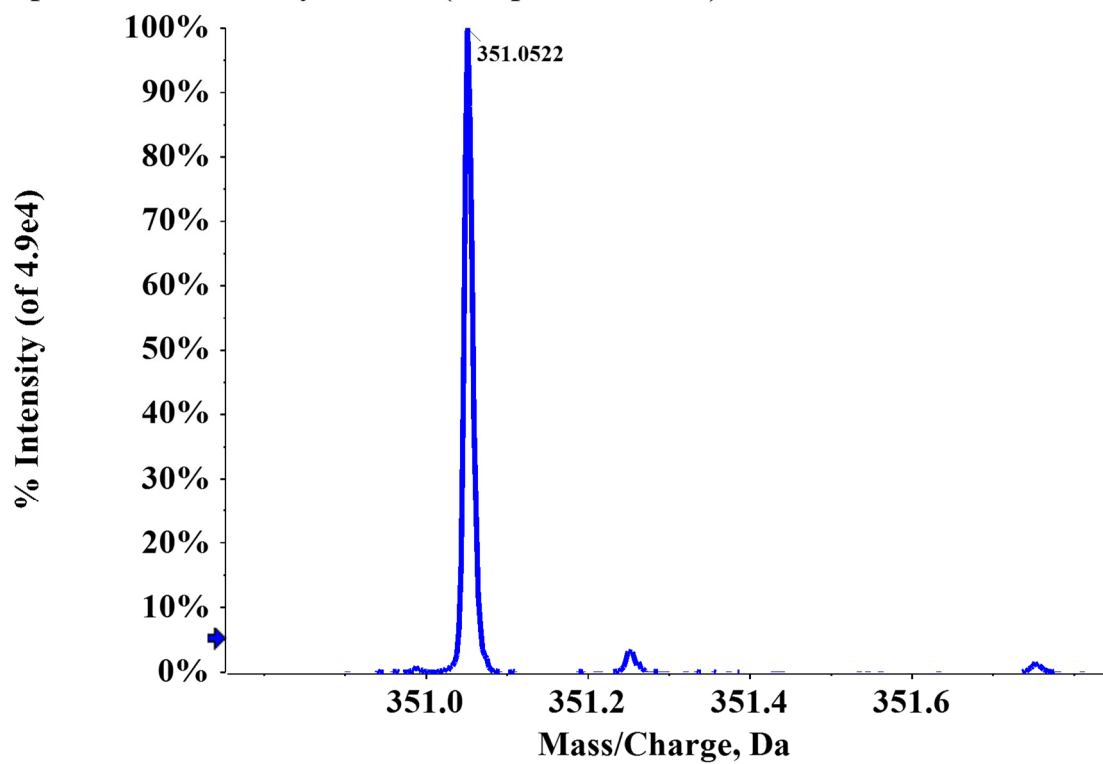


^{13}C NMR Spectrum of 5p (101 MHz, $\text{DMSO-}d_6$)

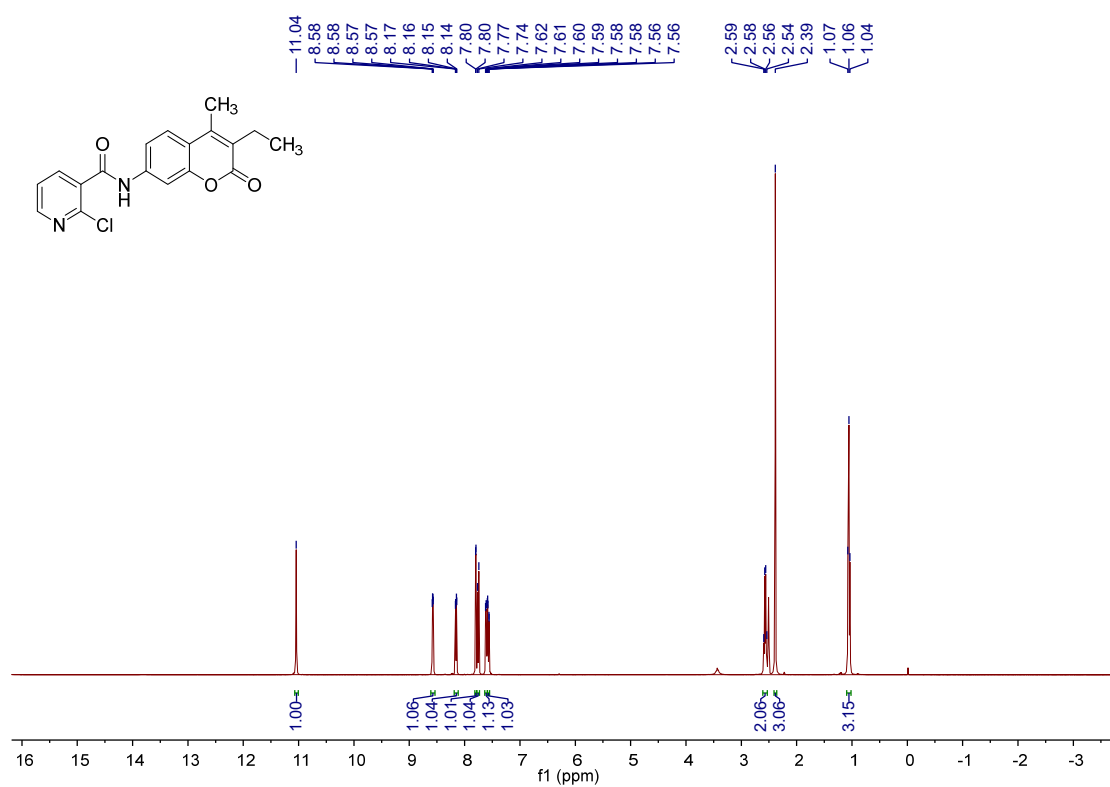


HRMS Spectrum of 5p

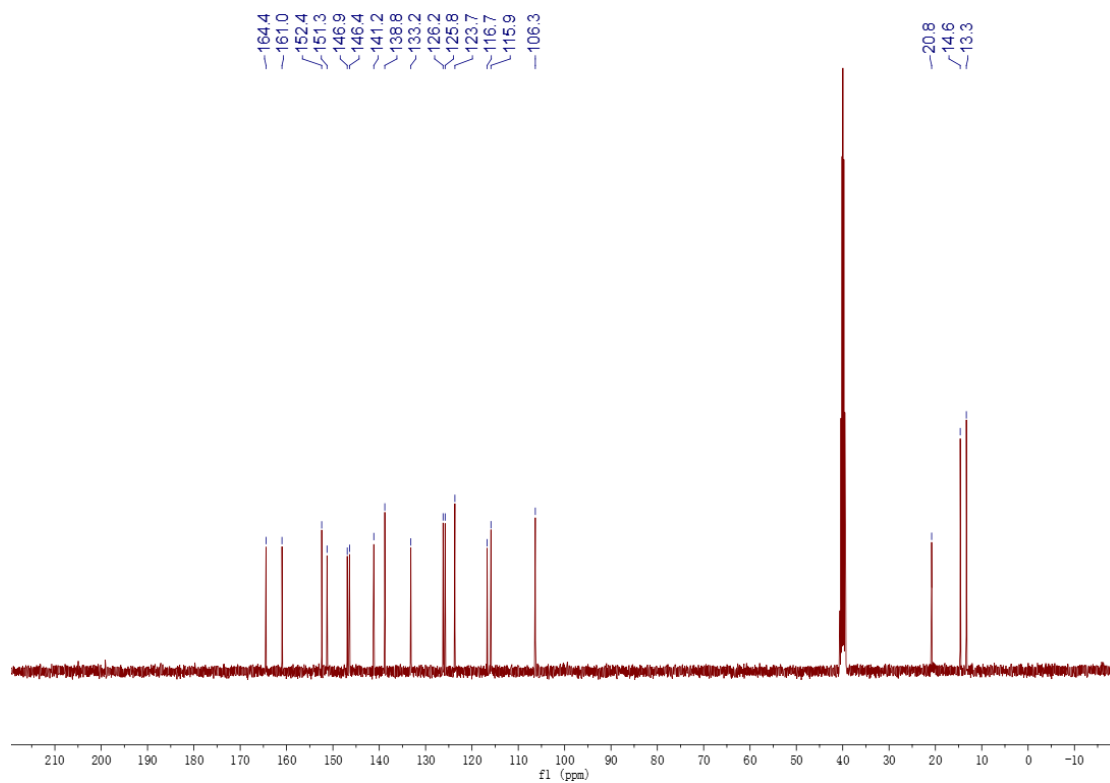
Spectrum from wenya35.wiff (sample...00 - 1000) from 0.058 to 0.067 min



¹H NMR Spectrum of 5q (400 MHz, DMSO-*d*₆)

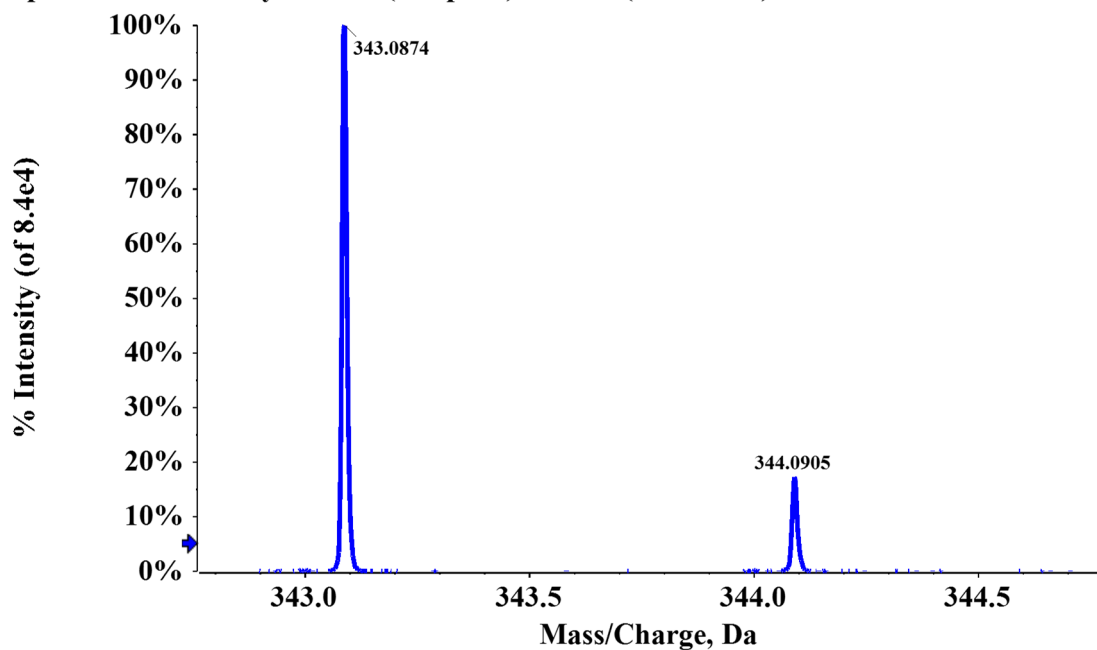


¹³C NMR Spectrum of 5q (101 MHz, DMSO-*d*₆)

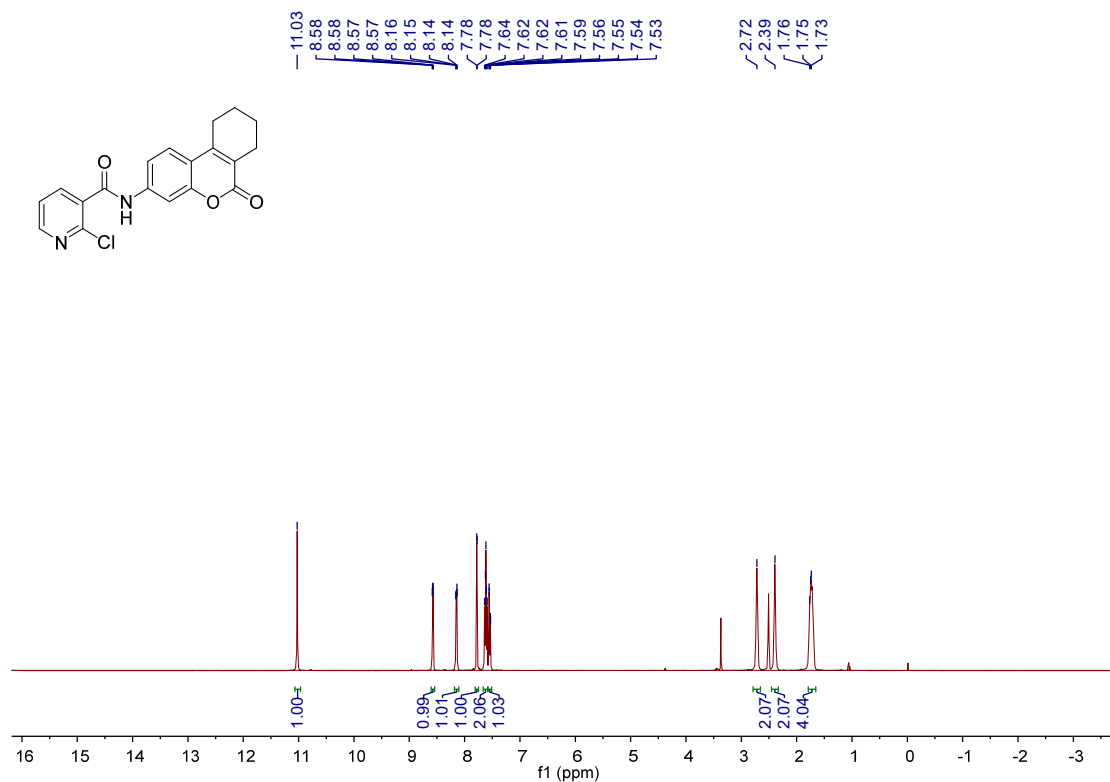


HRMS Spectrum of 5q

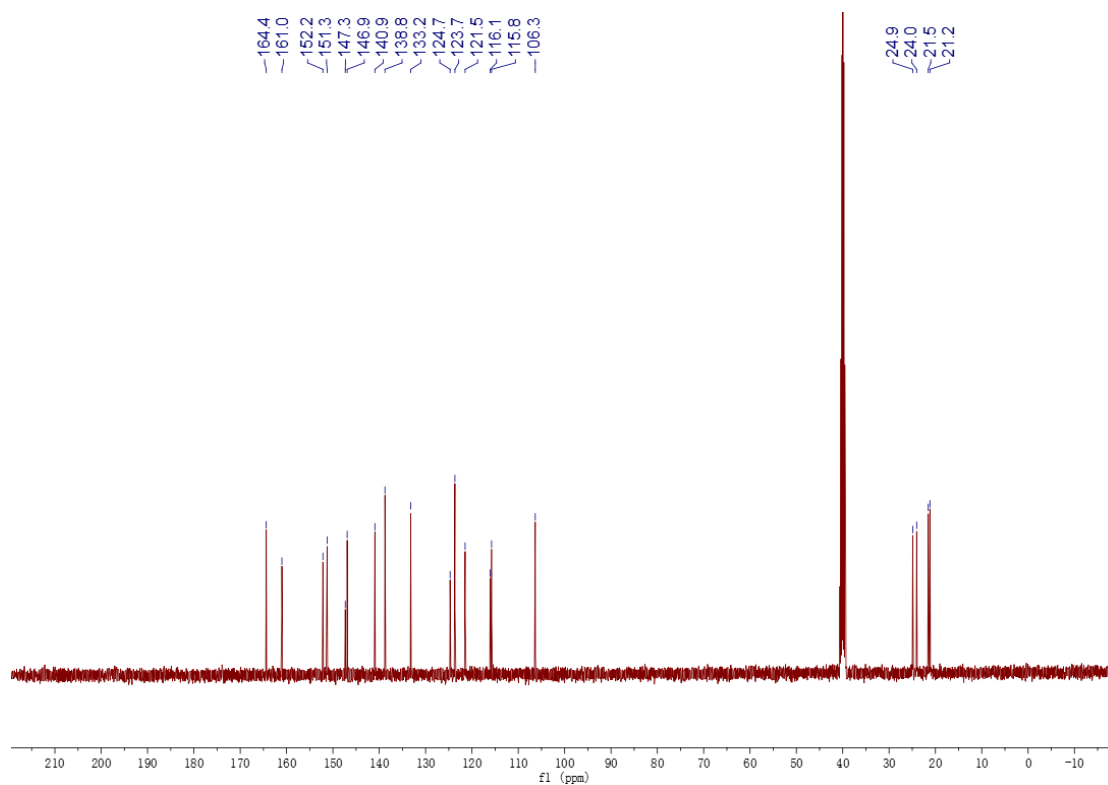
Spectrum from wenya36.wiff (sample 1) - ... MS (100 - 1000) from 0.058 to 0.067 min



^1H NMR Spectrum of 5r (400 MHz, DMSO- d_6)

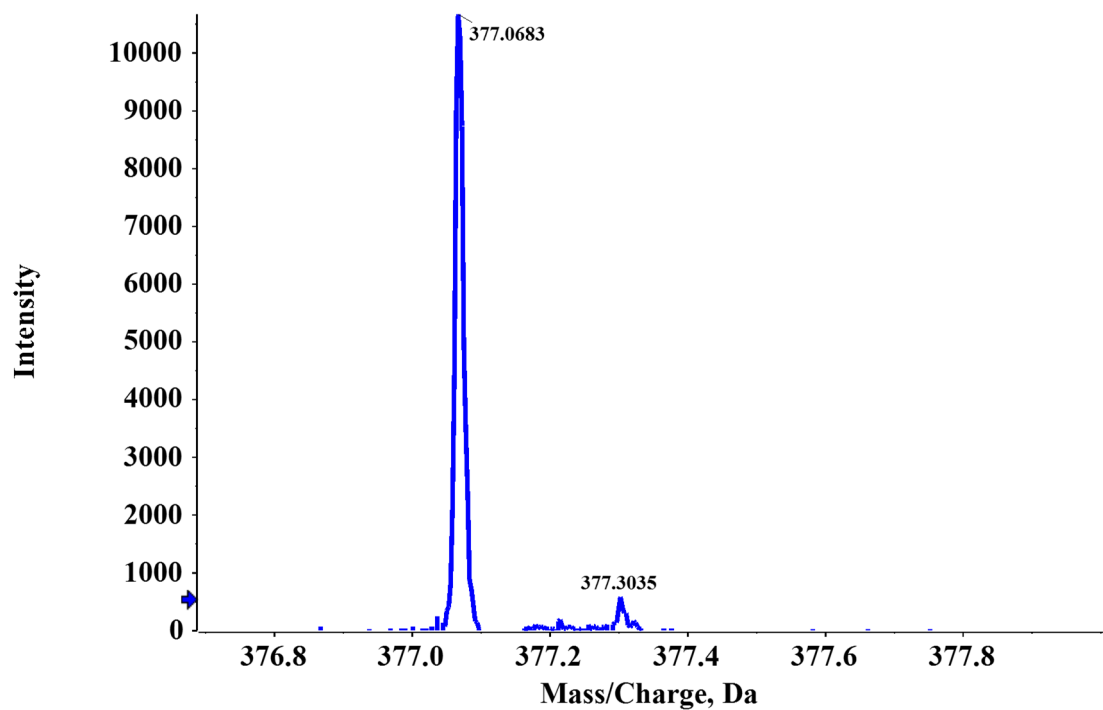


^{13}C NMR Spectrum of 5r (101 MHz, DMSO- d_6)

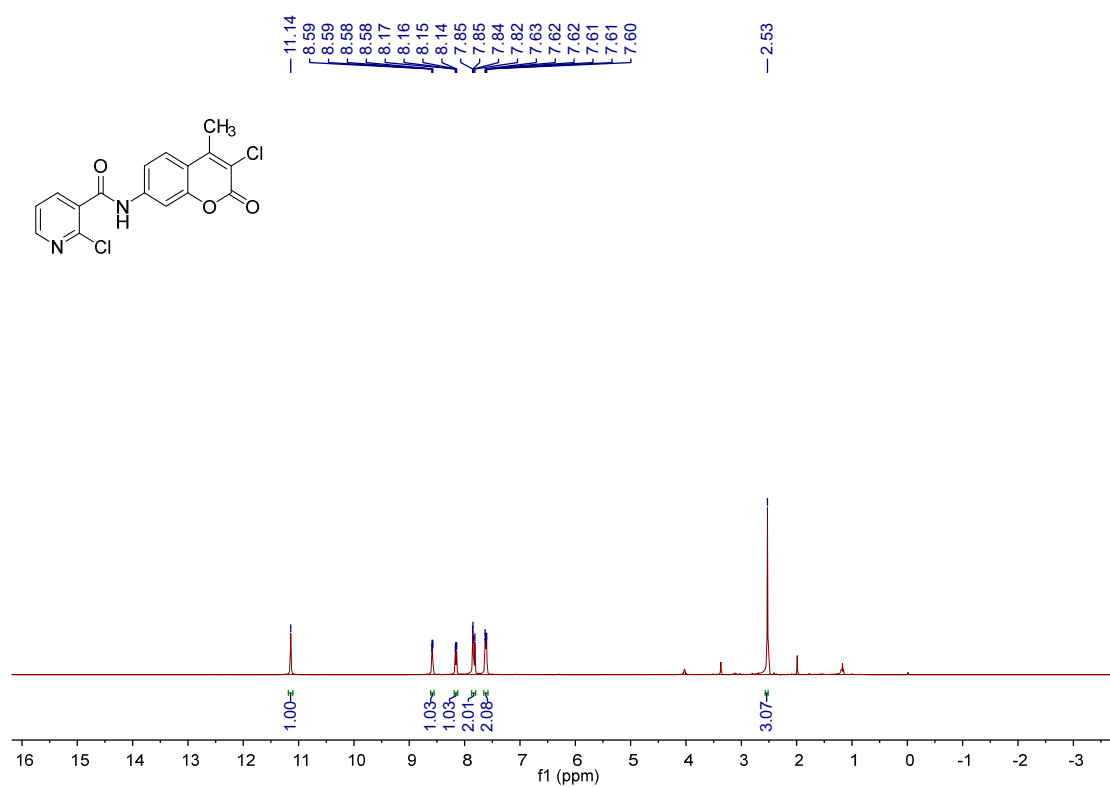


HRMS Spectrum of 5r

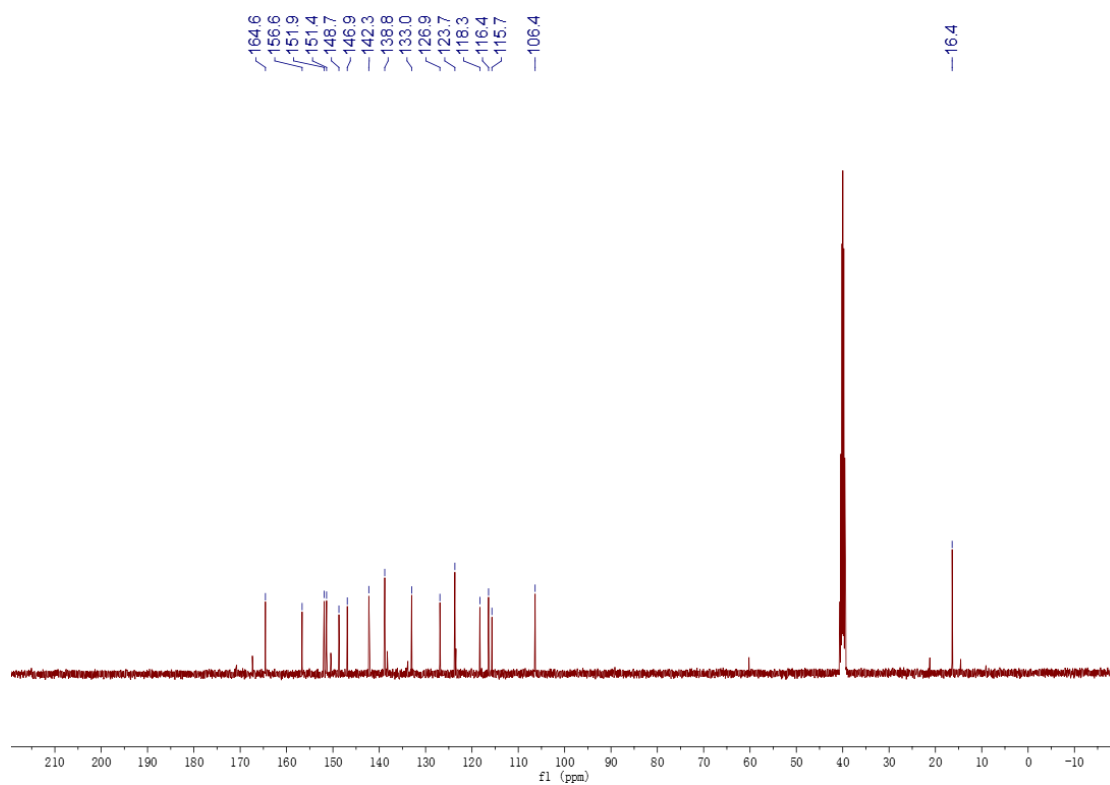
Spectrum from wenya37.wiff (sample 1) - ... MS (100 - 1000) from 0.082 to 0.091 min



^1H NMR Spectrum of 5s (400 MHz, $\text{DMSO}-d_6$)

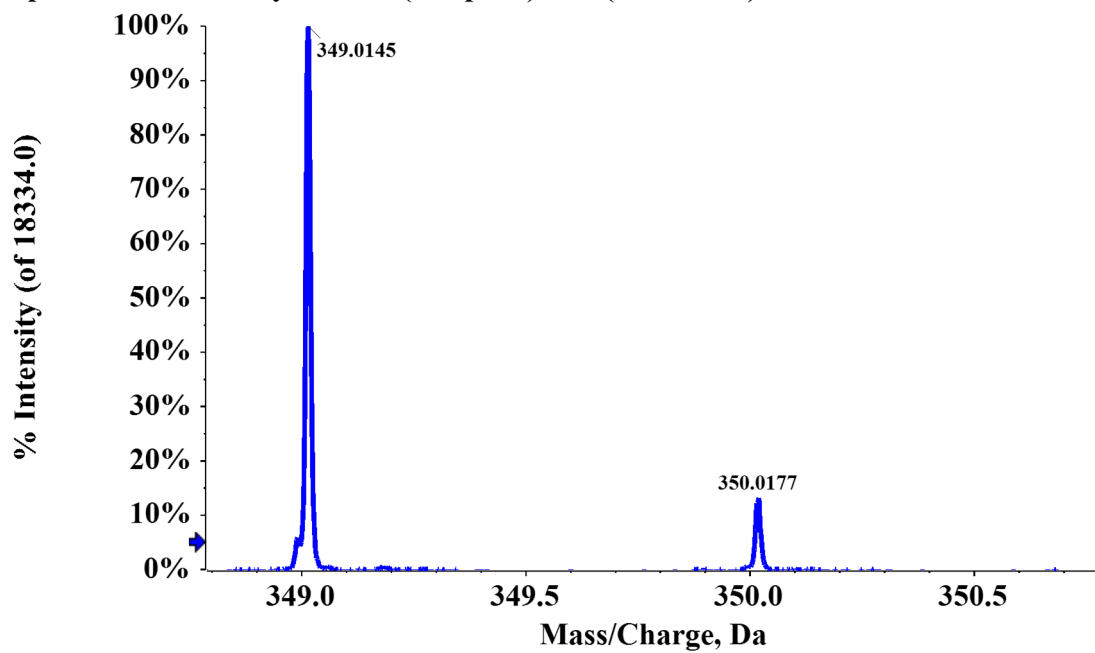


¹³C NMR Spectrum of 5s (101 MHz, DMSO-*d*₆)

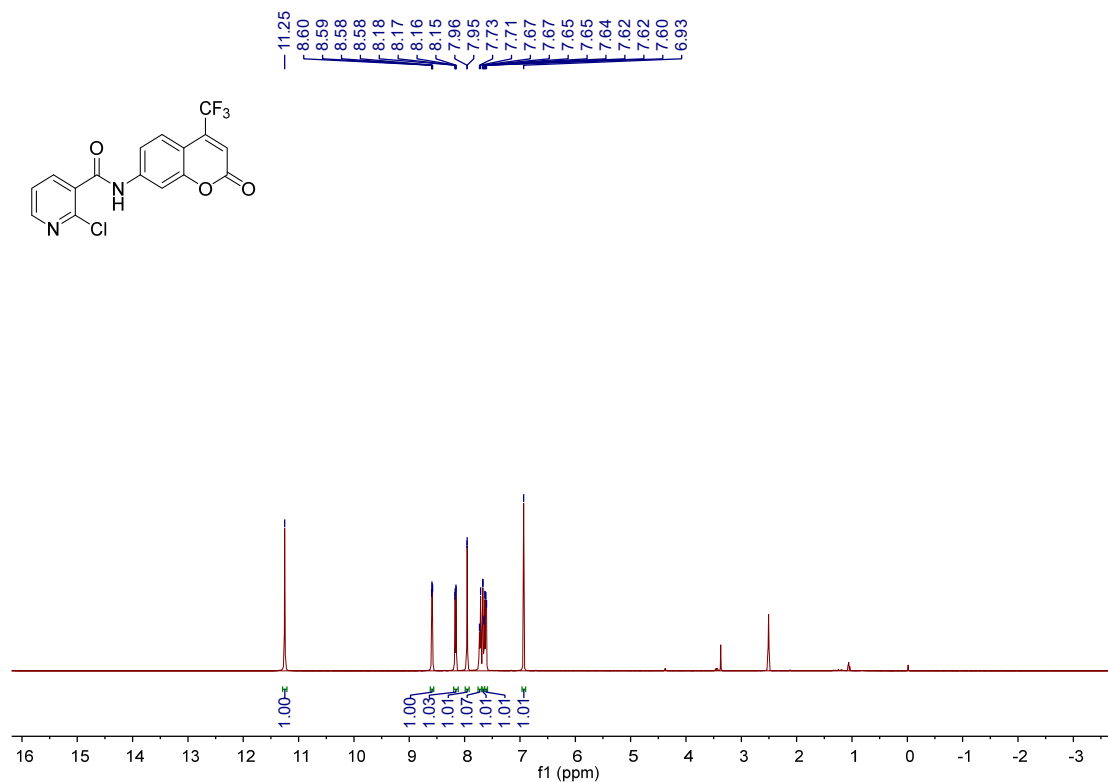


HRMS Spectrum of 5s

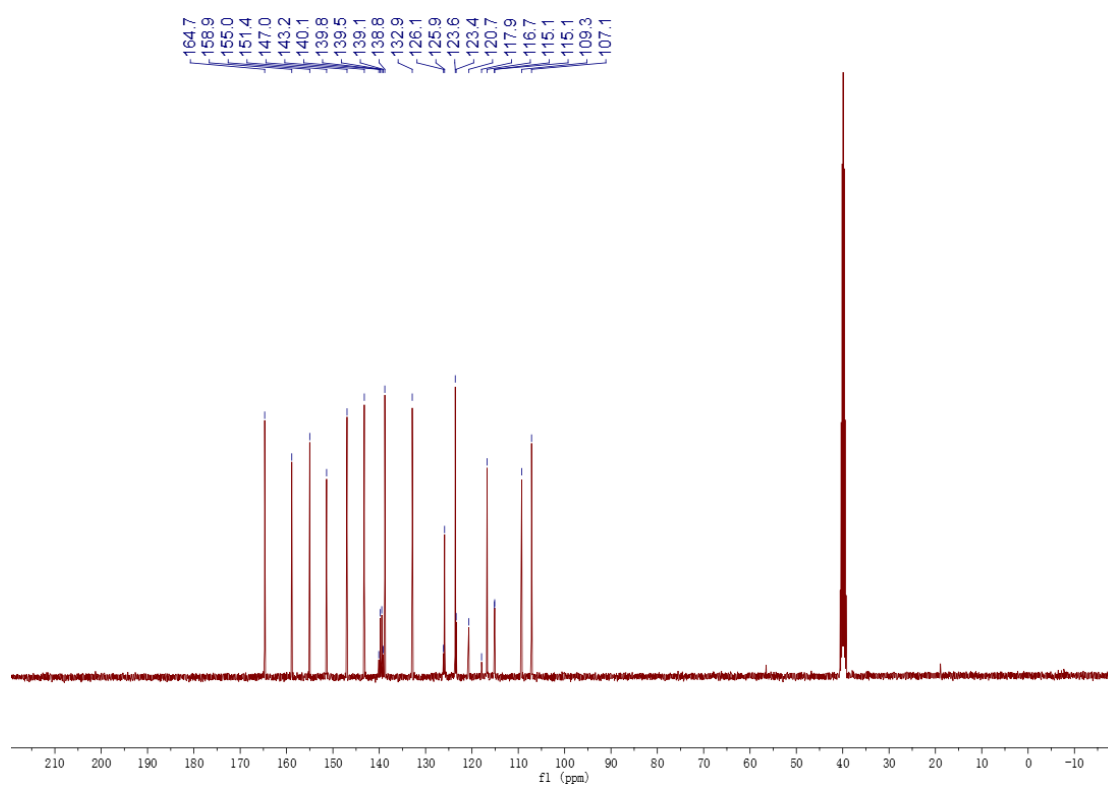
Spectrum from wenya38.wiff (sample 1) -...S (100 - 1000) from 0.053 to 0.063 min



^1H NMR Spectrum of 5t (400 MHz, DMSO- d_6)

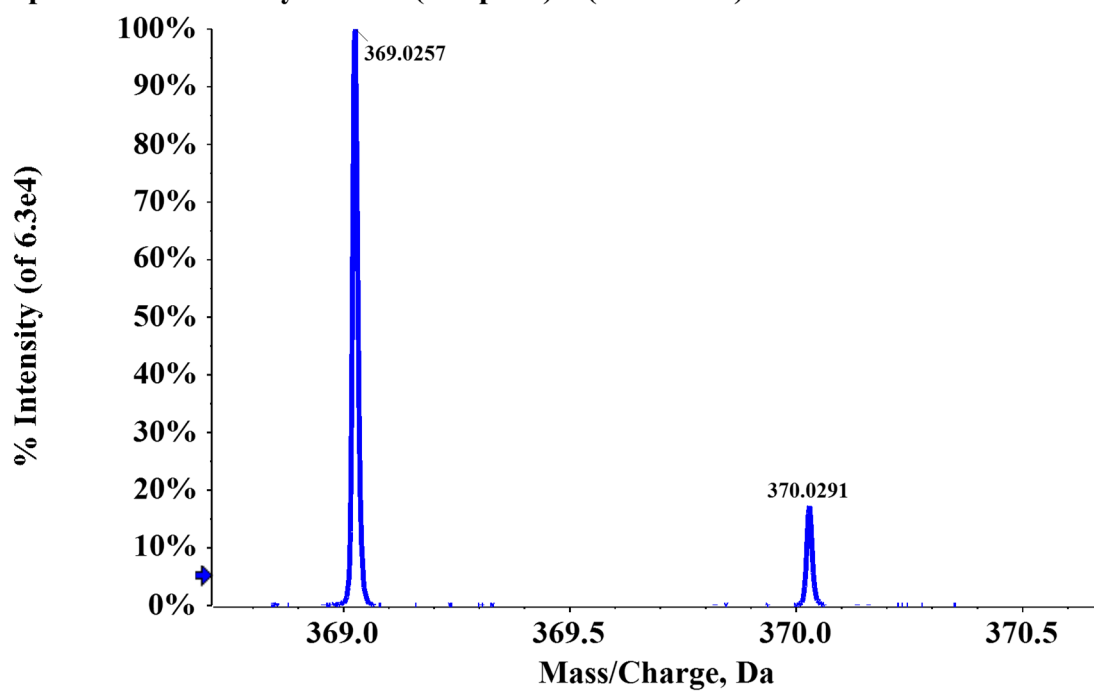


^{13}C NMR Spectrum of 5t (101 MHz, DMSO- d_6)

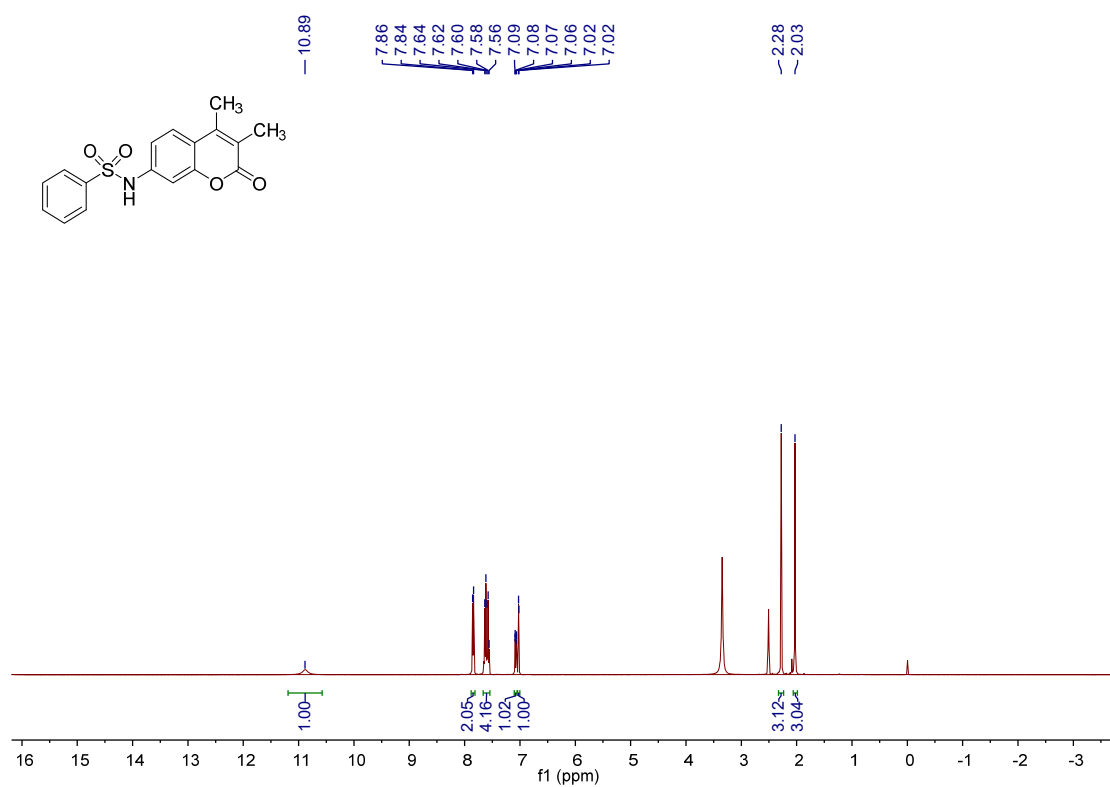


HRMS Spectrum of 5t

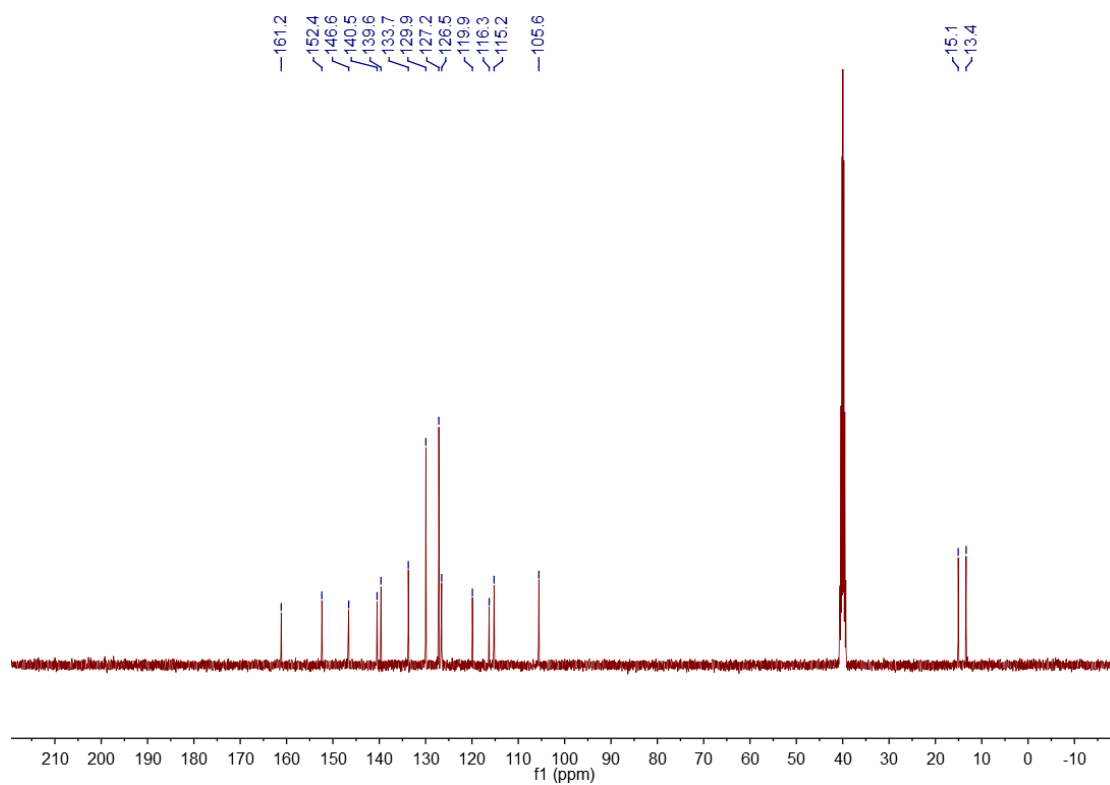
Spectrum from wenya39.wiff (sample 1)... (100 - 1000) from 0.067 to 0.076 min



^1H NMR Spectrum of 6a (400 MHz, $\text{DMSO}-d_6$)

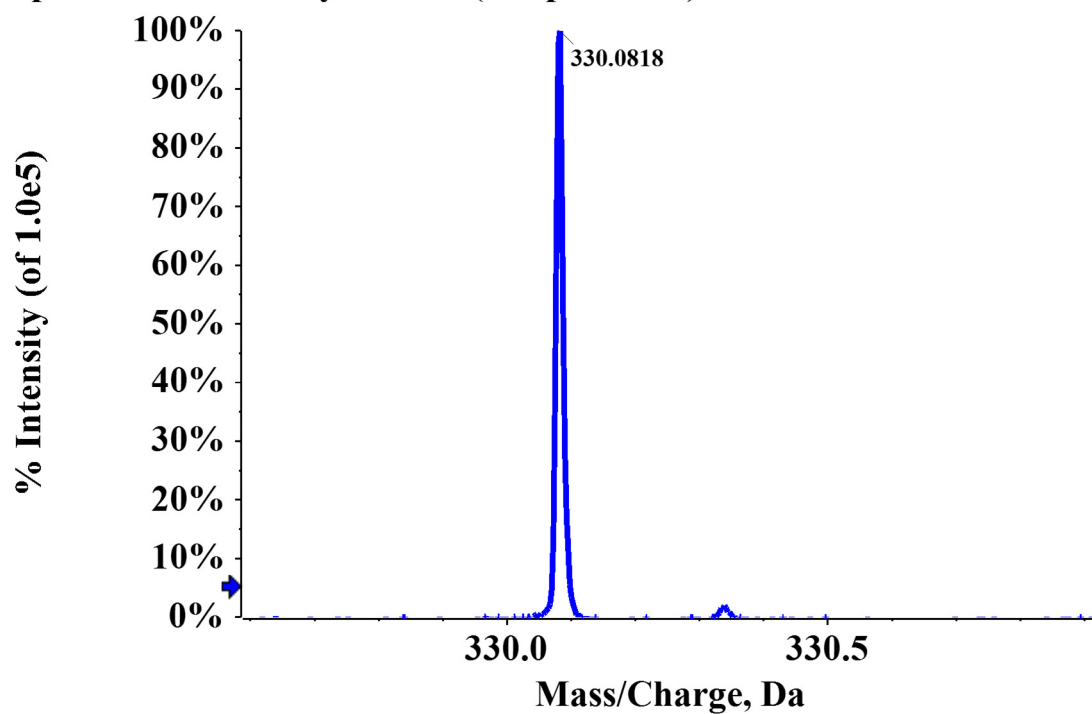


¹³C NMR Spectrum of 6a (101 MHz, DMSO-*d*₆)

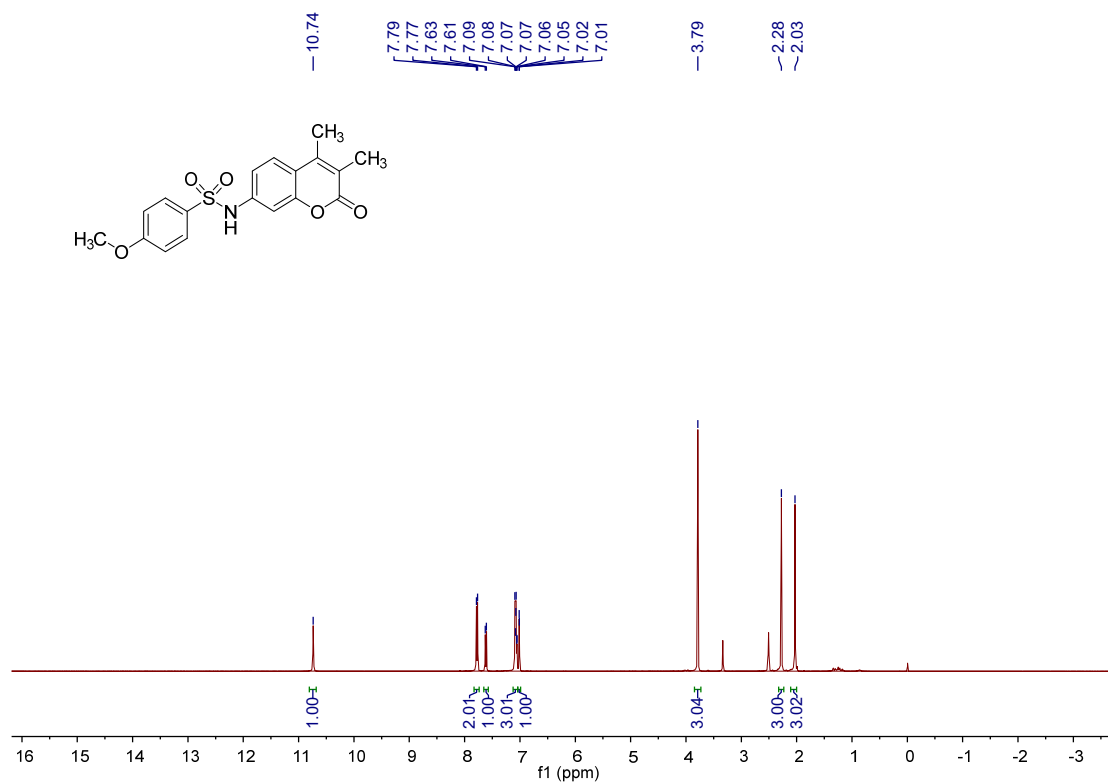


HRMS Spectrum of 6a

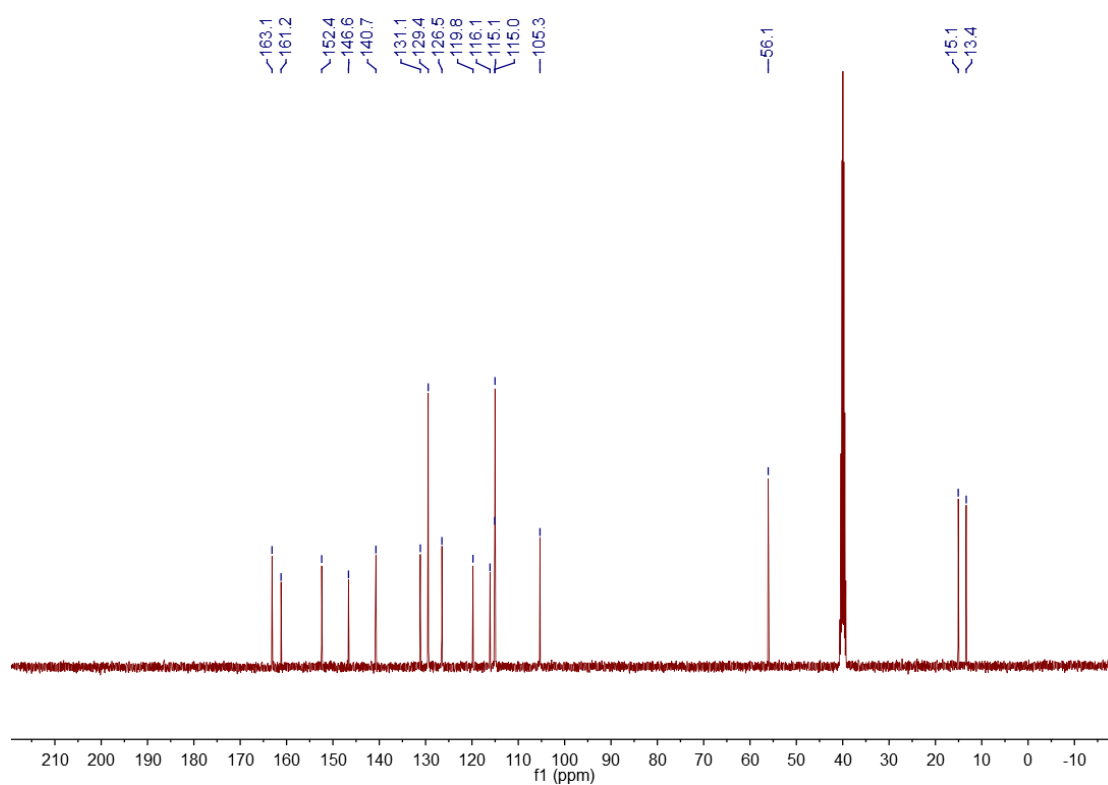
Spectrum from wenya45.wiff (samp...- 1000) from 0.072 to 0.081 min



^1H NMR Spectrum of 6b (400 MHz, $\text{DMSO}-d_6$)

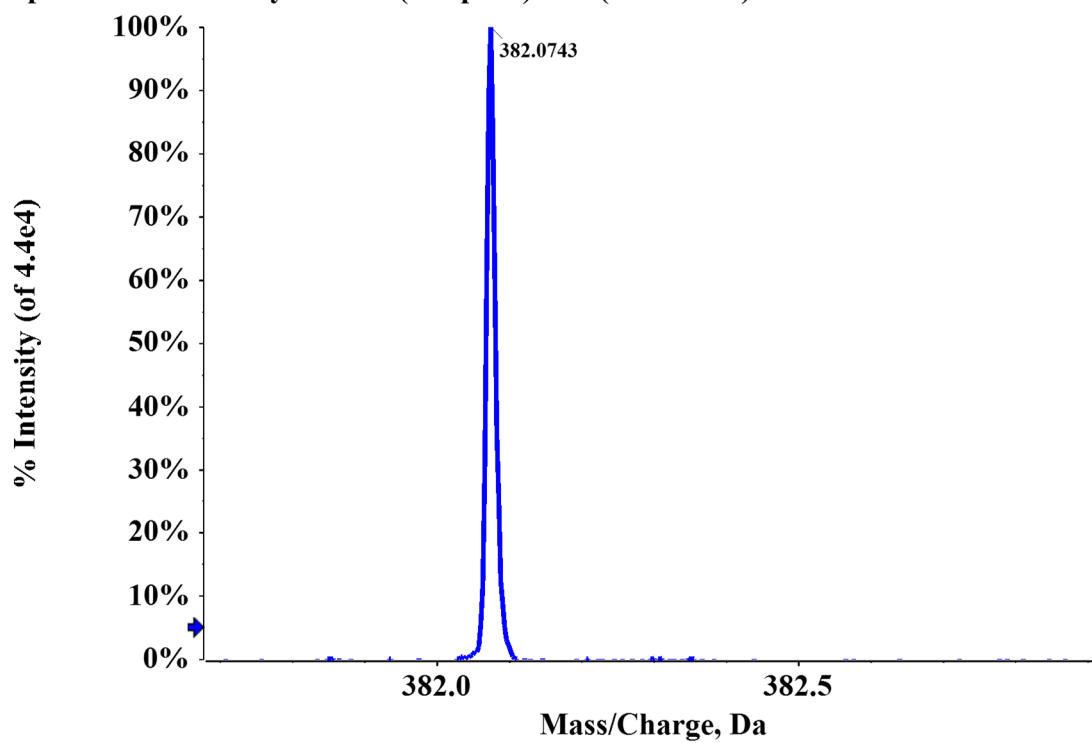


^{13}C NMR Spectrum of 6b (101 MHz, $\text{DMSO}-d_6$)

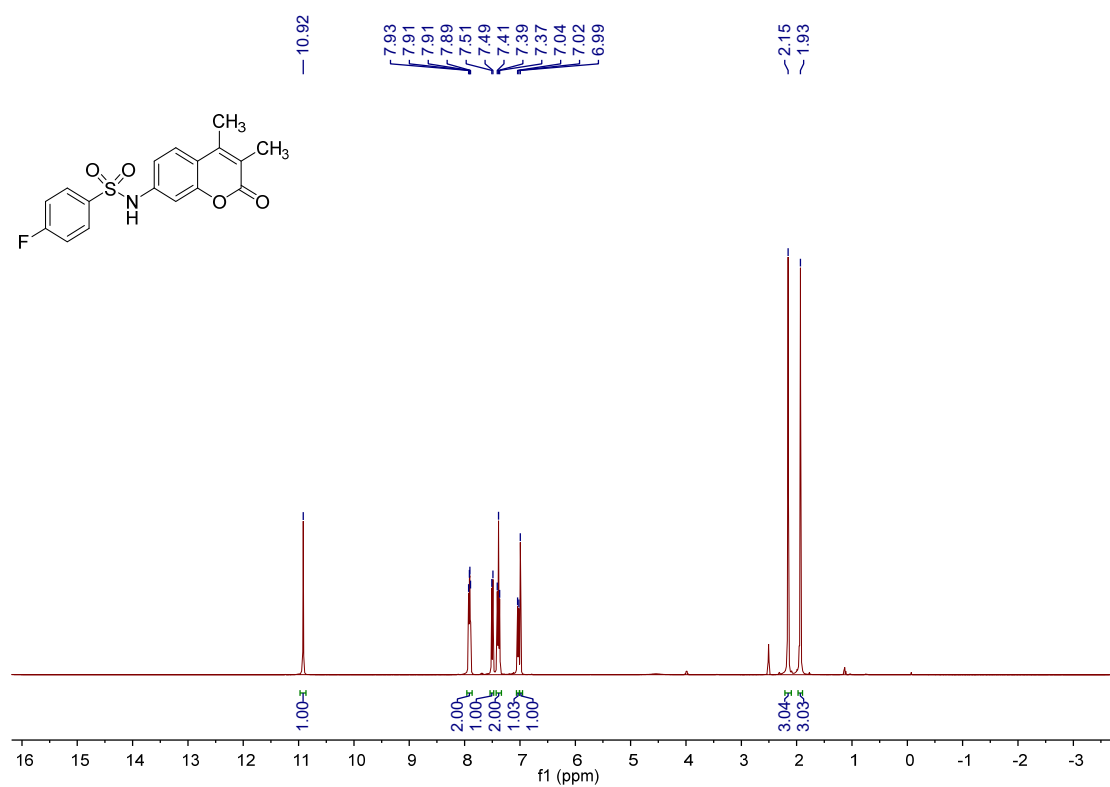


HRMS Spectrum of 6b

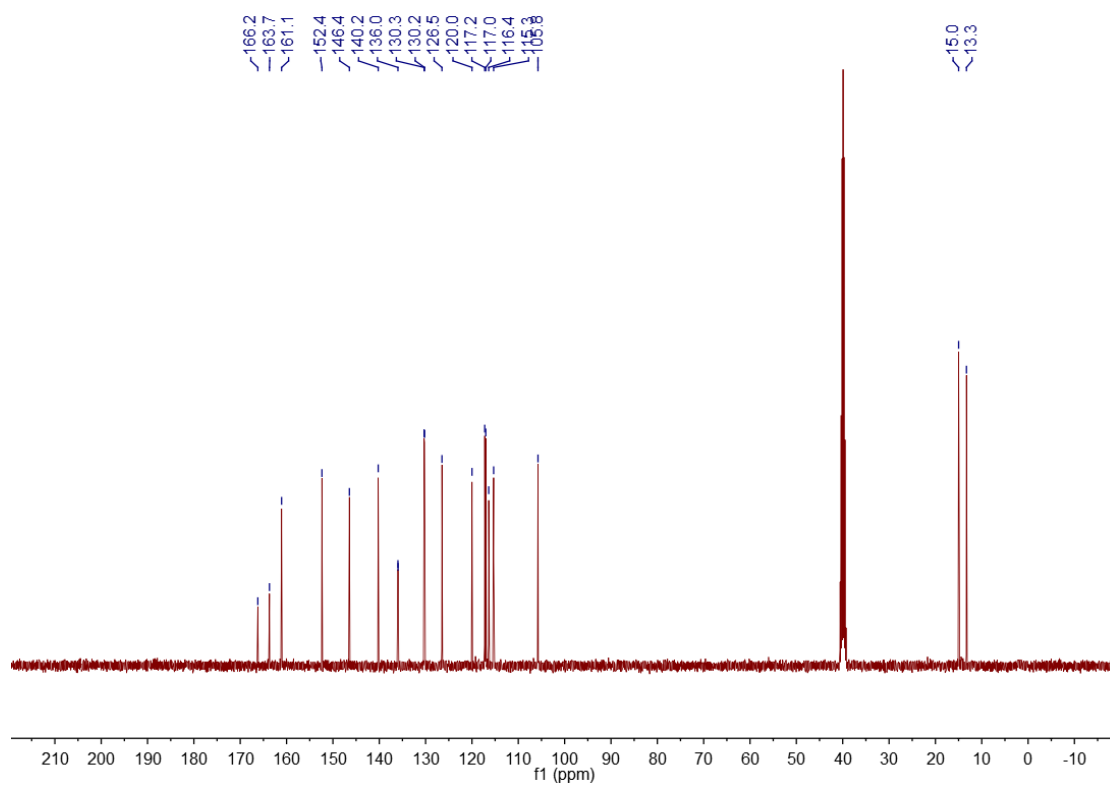
Spectrum from wenya46.wiff (sample 1) -...S (100 - 1000) from 0.080 to 0.089 min



¹H NMR Spectrum of 6c (400 MHz, DMSO-*d*₆)

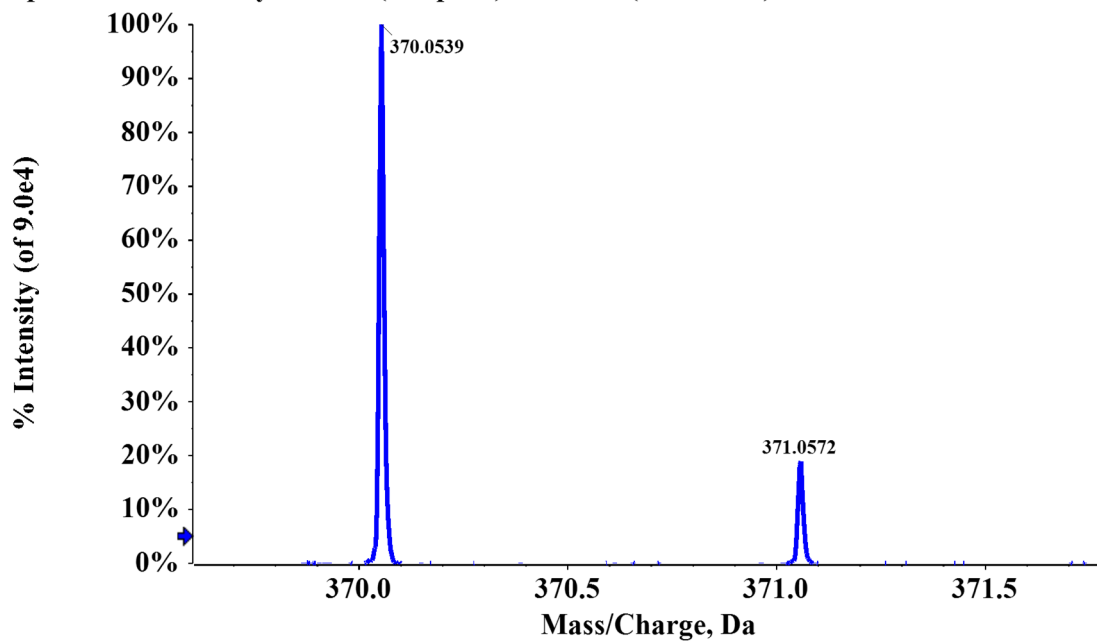


¹³C NMR Spectrum of 6c (101 MHz, DMSO-*d*₆)

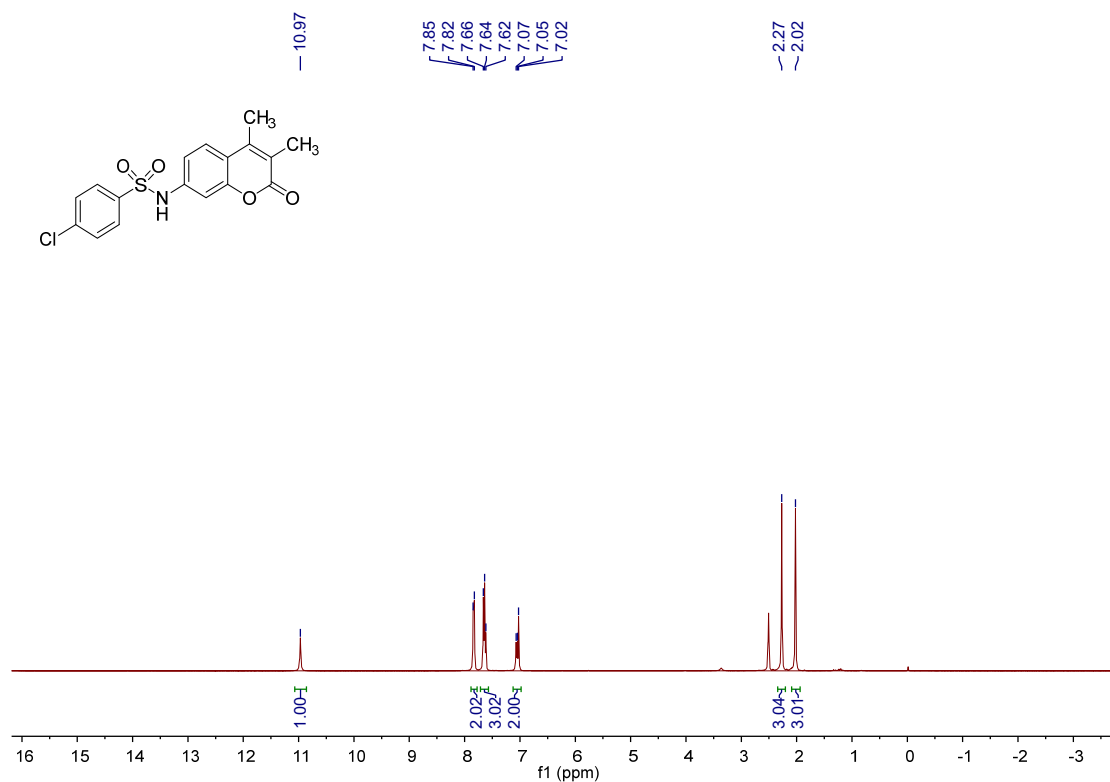


HRMS Spectrum of 6c

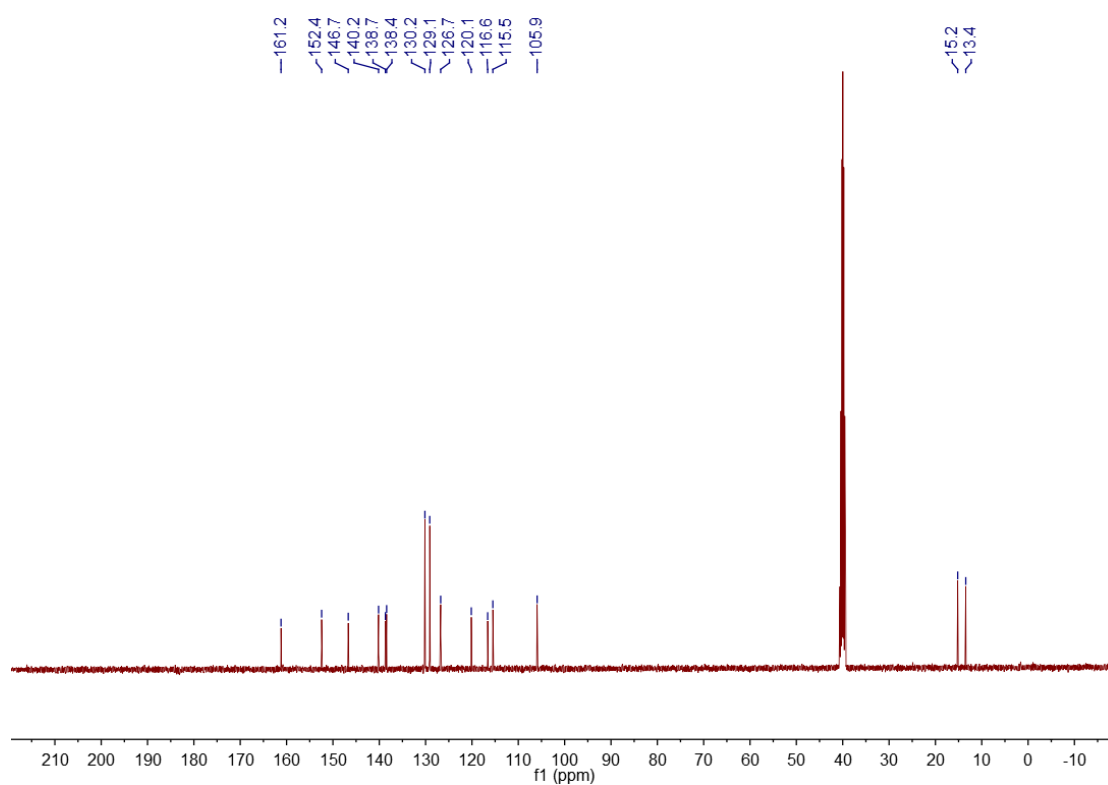
Spectrum from wenya47.wiff (sample 1) - w... MS (100 - 1000) from 0.084 to 0.093 min



^1H NMR Spectrum of 6d (400 MHz, $\text{DMSO}-d_6$)

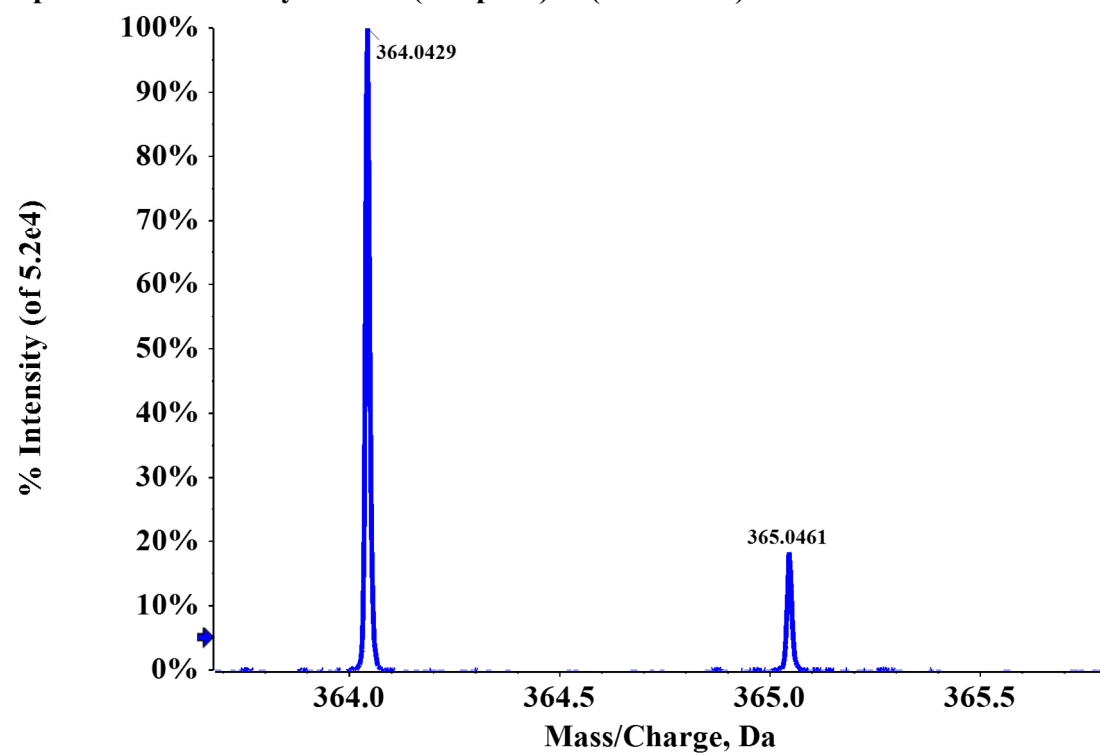


^{13}C NMR Spectrum of 6d (101 MHz, $\text{DMSO}-d_6$)

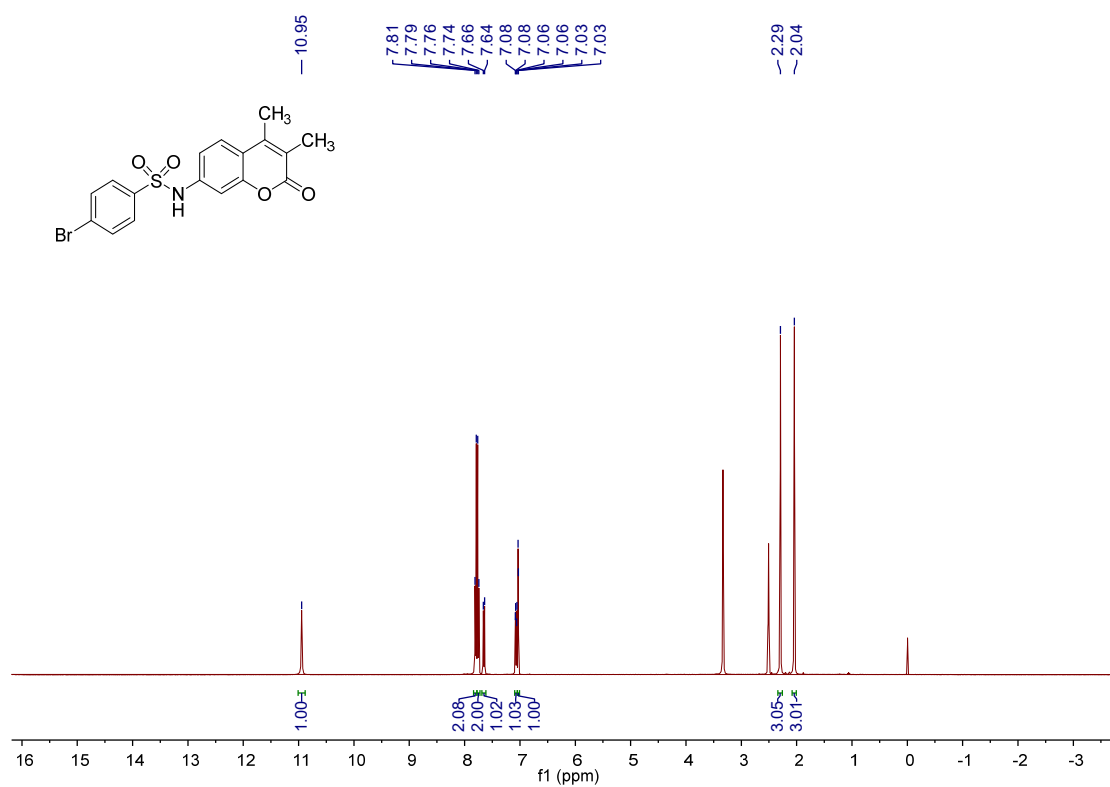


HRMS Spectrum of 6d

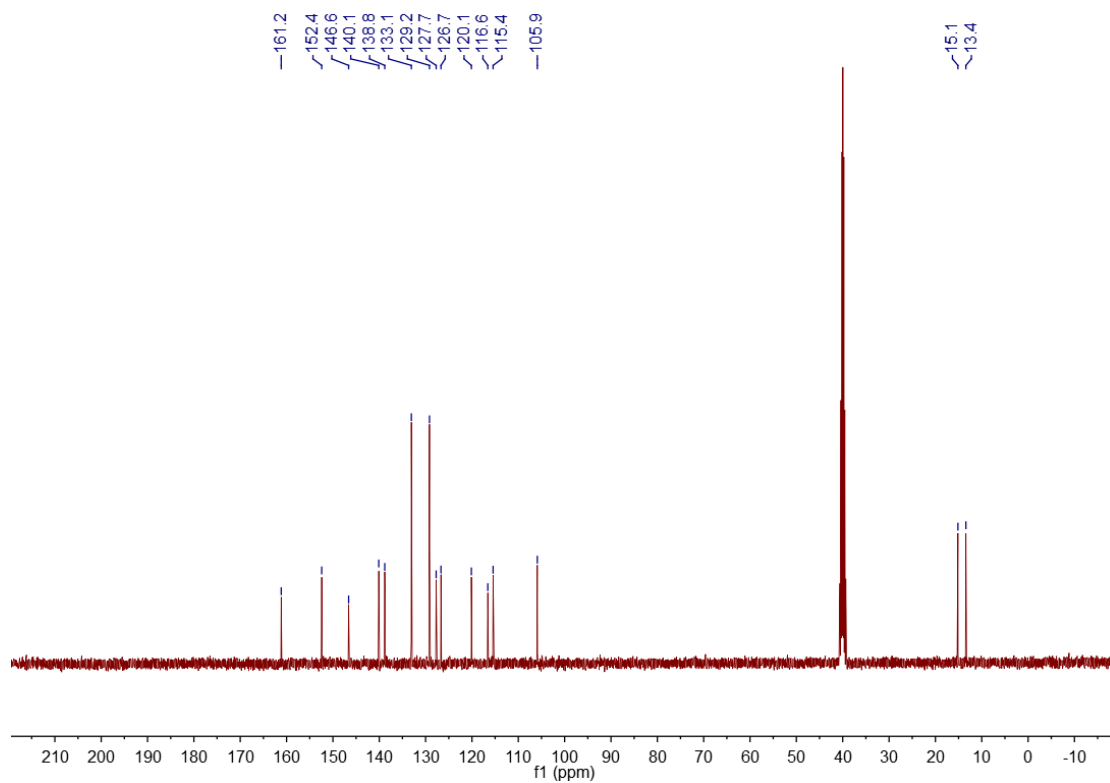
Spectrum from wenya48.wiff (sample 1) ... (100 - 1000) from 0.053 to 0.063 min



¹H NMR Spectrum of 6e (400 MHz, DMSO-*d*₆)

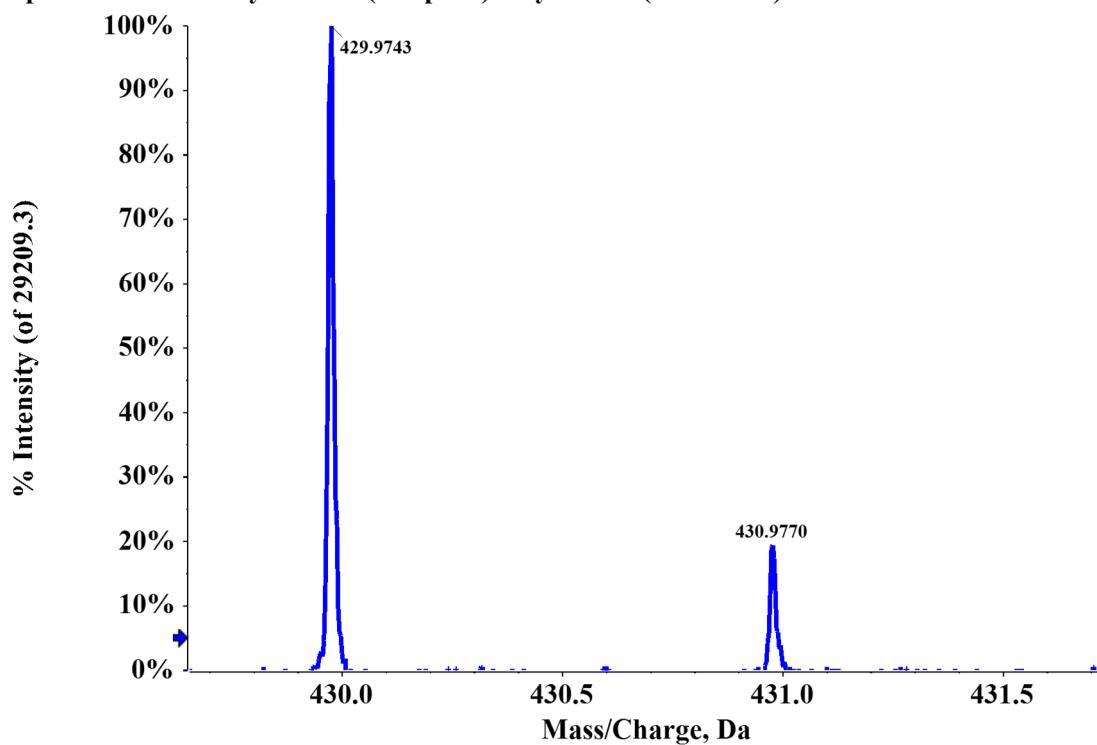


^{13}C NMR Spectrum of 6e (101 MHz, $\text{DMSO}-d_6$)

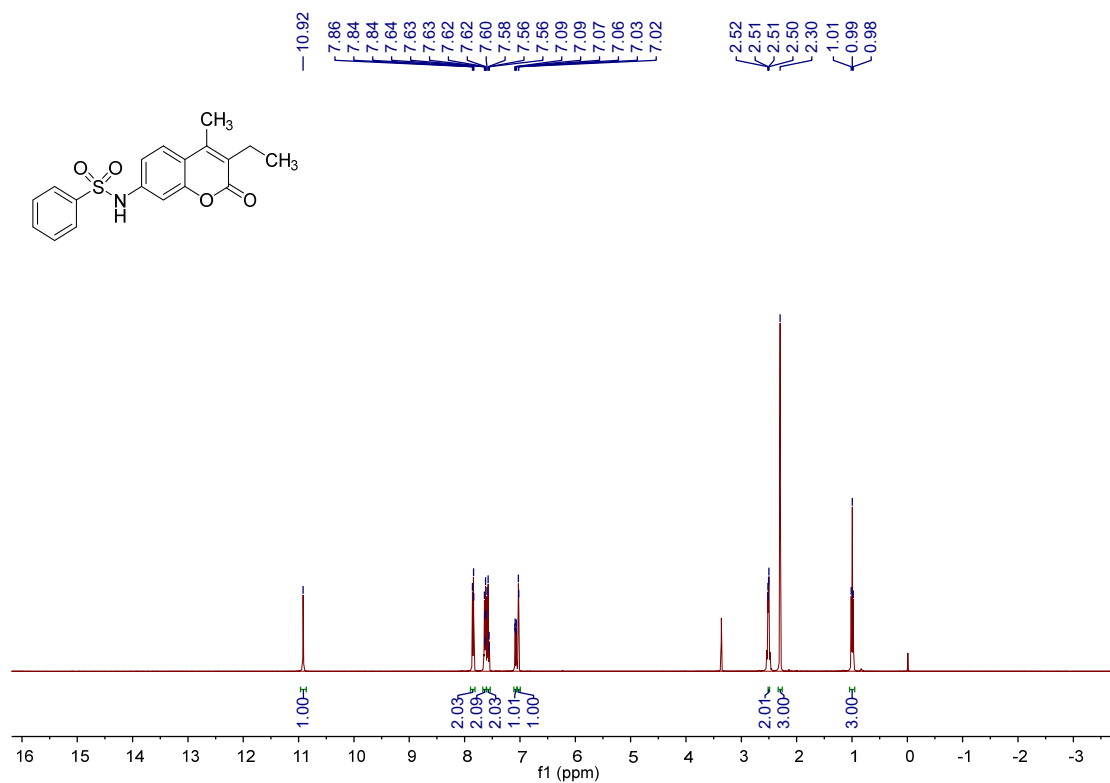


HRMS Spectrum of 6e

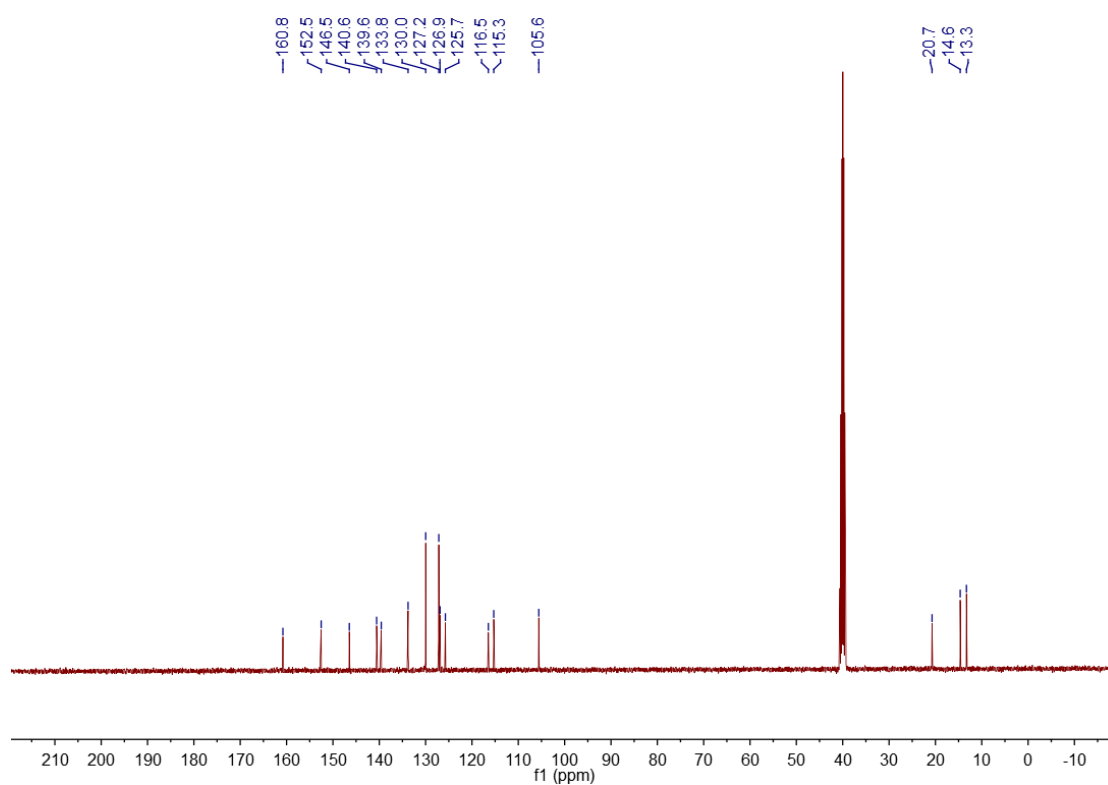
Spectrum from wenya49.wiff (sample 1) - wy...F MS (100 - 1000) from 0.081 to 0.090 min



^1H NMR Spectrum of 6f (400 MHz, $\text{DMSO}-d_6$)

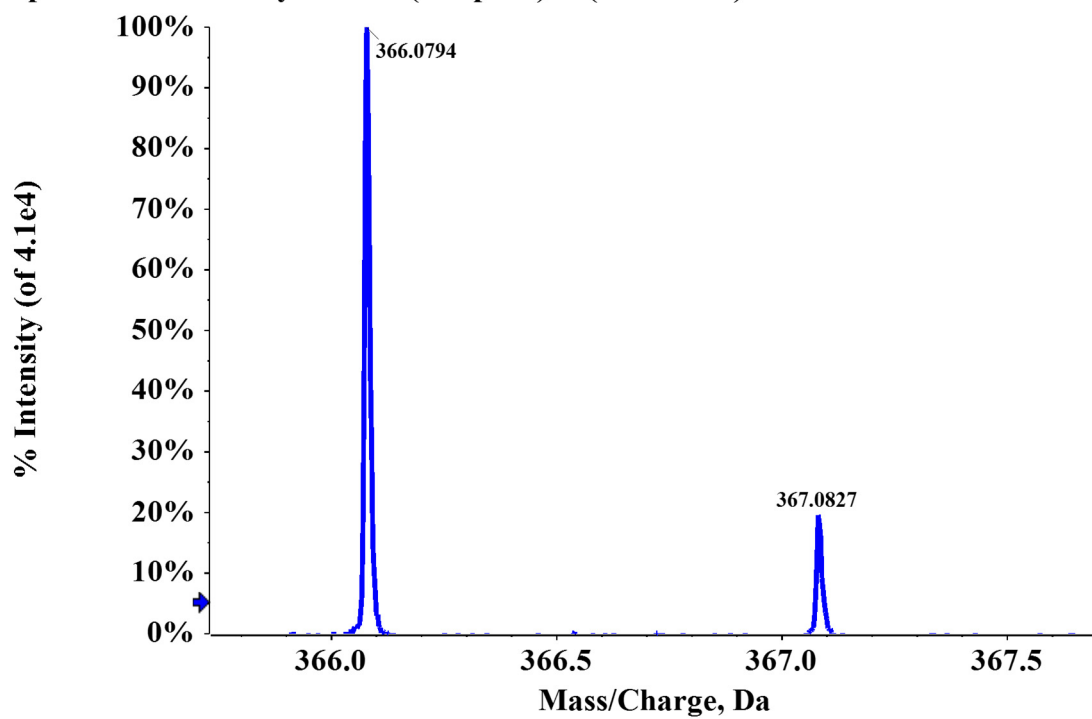


^{13}C NMR Spectrum of 6f (101 MHz, $\text{DMSO}-d_6$)

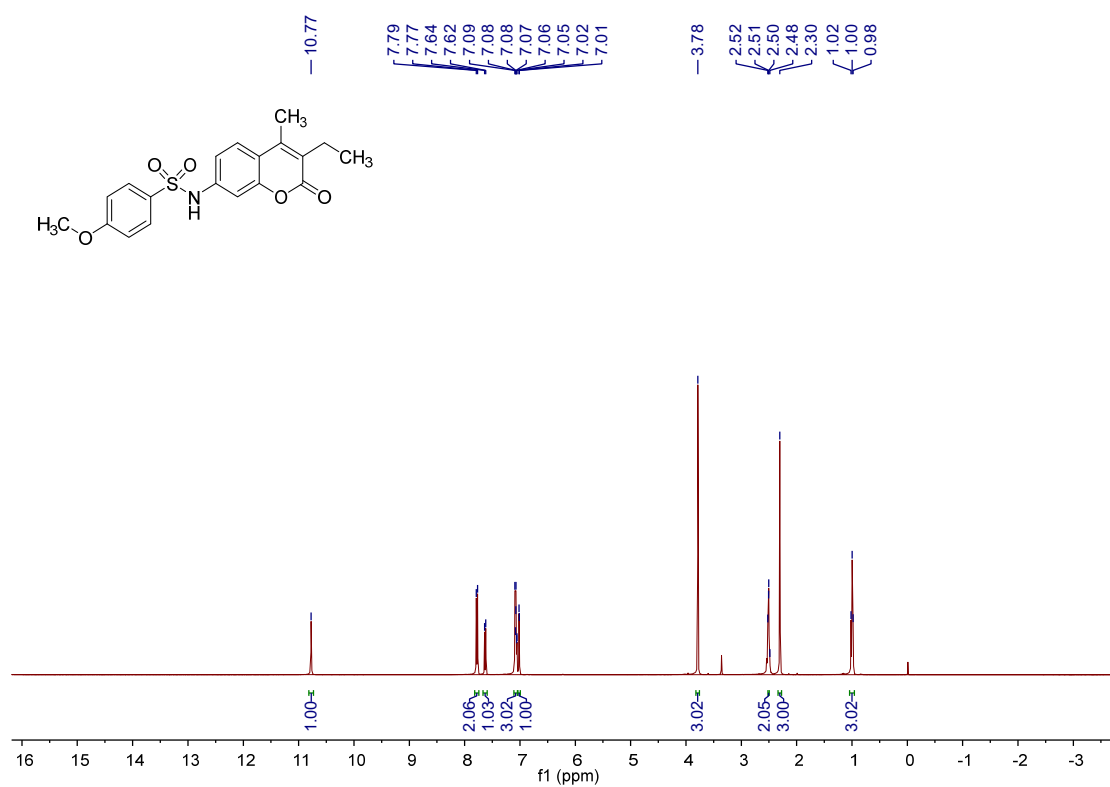


HRMS Spectrum of 6f

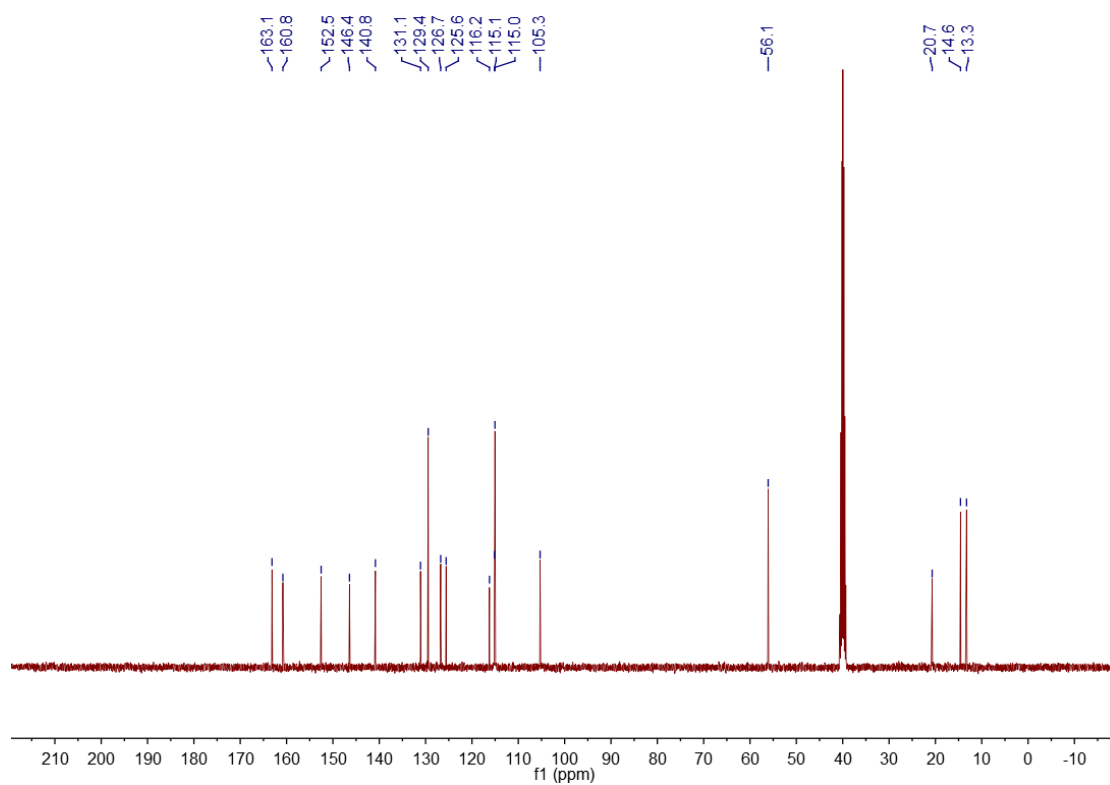
Spectrum from wenya50.wiff (sample 1) ... (100 - 1000) from 0.072 to 0.080 min



^1H NMR Spectrum of 6g (400 MHz, $\text{DMSO}-d_6$)

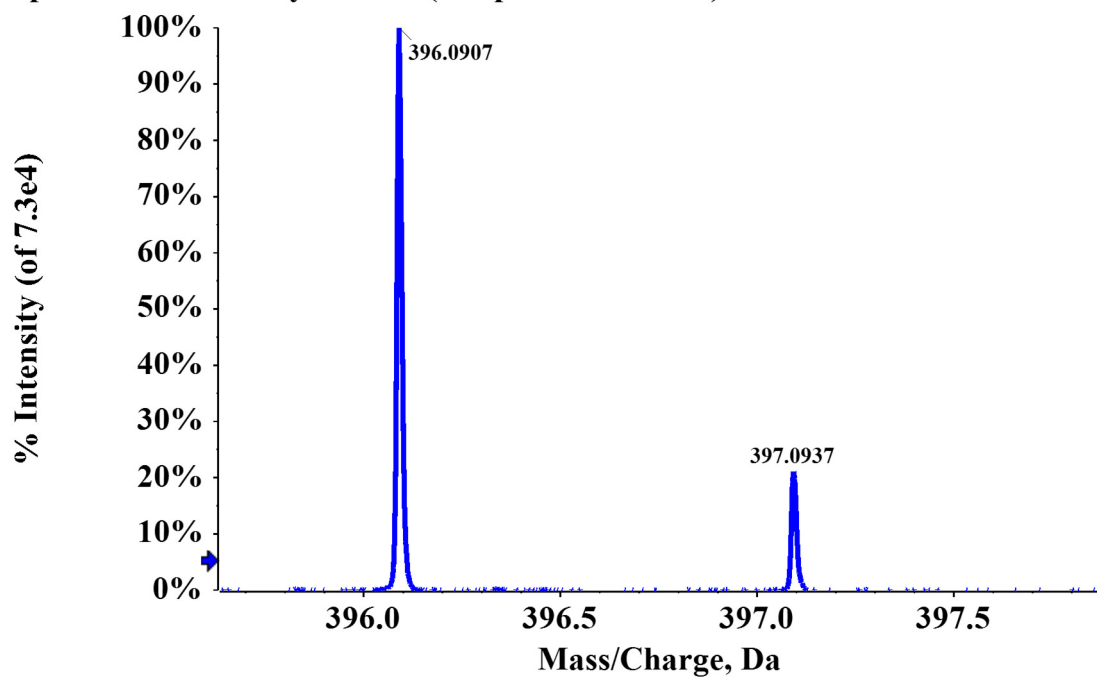


¹³C NMR Spectrum of 6g (101 MHz, DMSO-*d*₆)

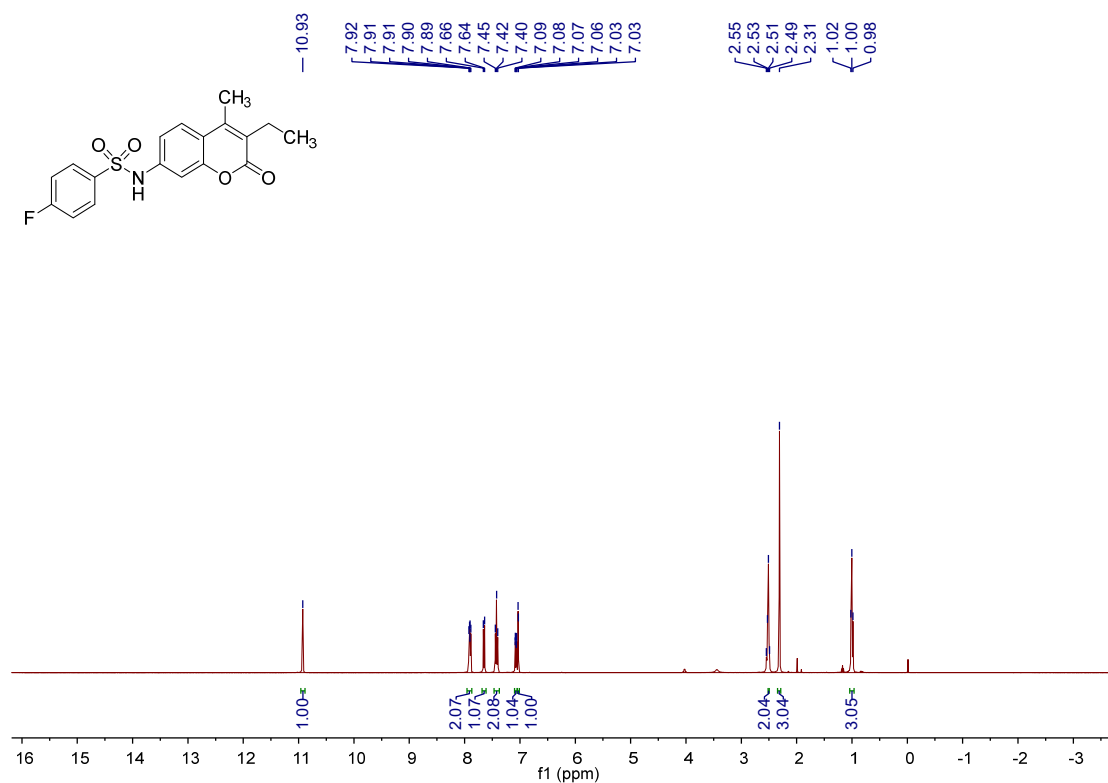


HRMS Spectrum of 6g

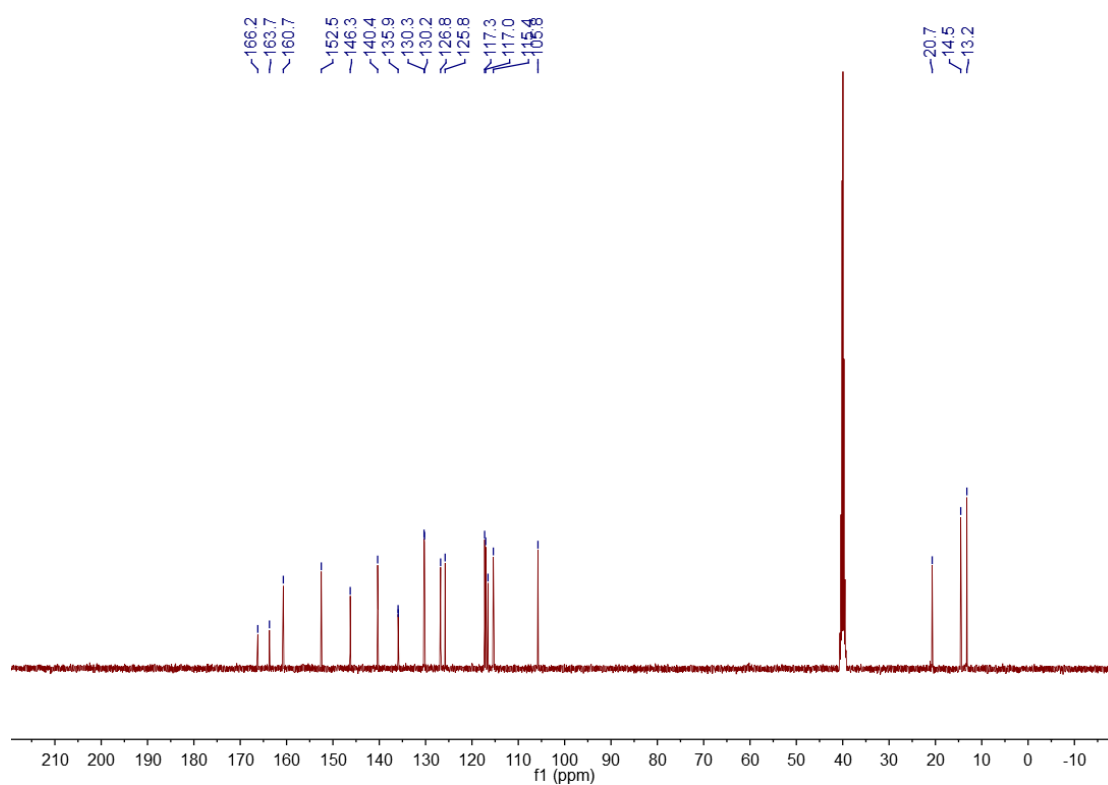
Spectrum from wenya51.wiff (sample ...100 - 1000) from 0.405 to 0.431 min



^1H NMR Spectrum of 6h (400 MHz, $\text{DMSO}-d_6$)

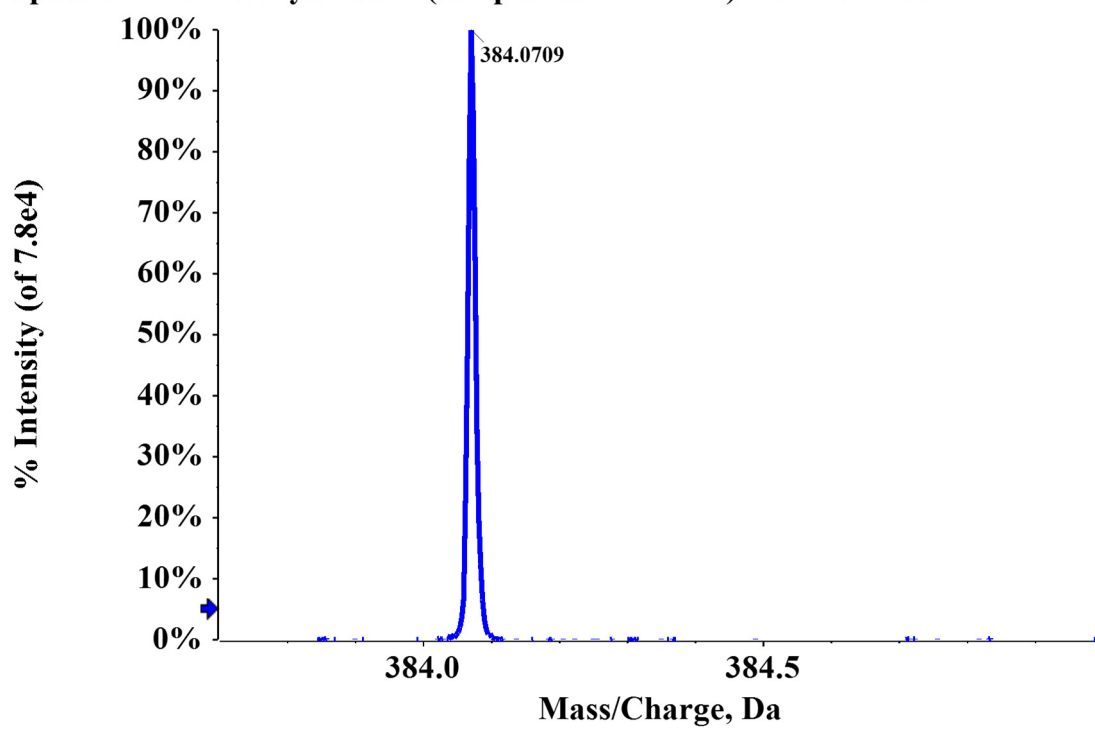


^{13}C NMR Spectrum of 6h (101 MHz, $\text{DMSO}-d_6$)

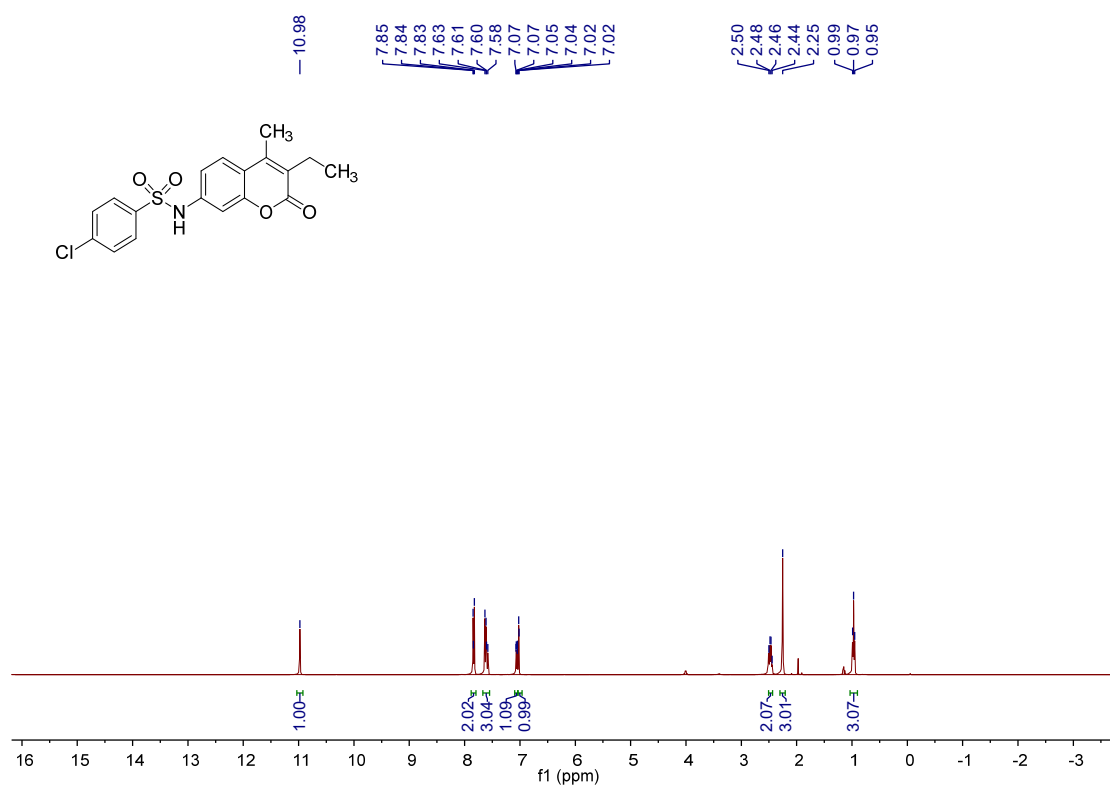


HRMS Spectrum of 6h

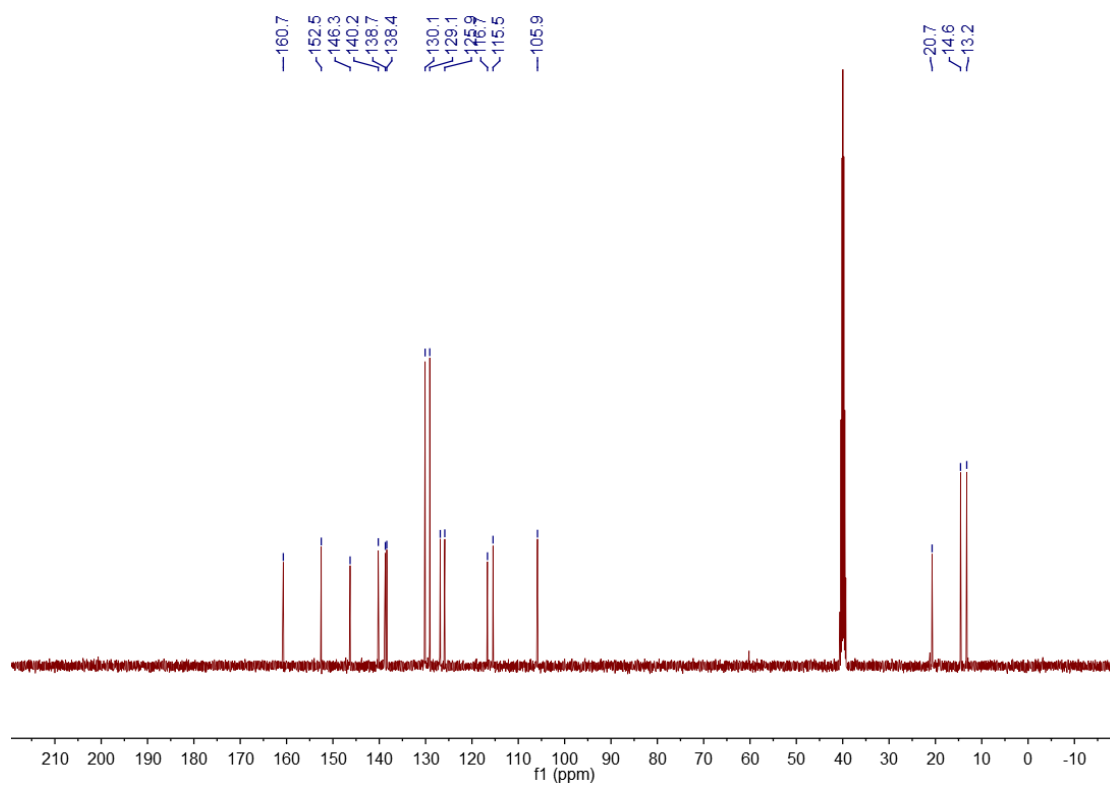
Spectrum from wenya52.wiff (sample 1...100 - 1000) from 0.058 to 0.066 min



¹H NMR Spectrum of 6i (400 MHz, DMSO-*d*₆)

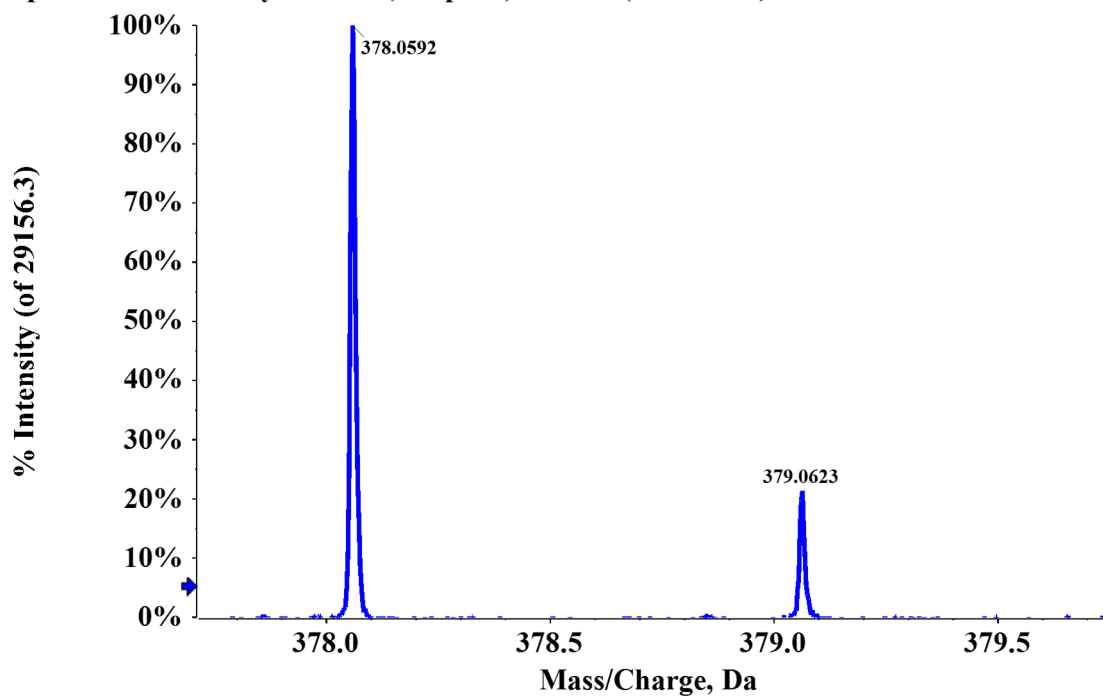


¹³C NMR Spectrum of **6i (101 MHz, DMSO-*d*₆)**

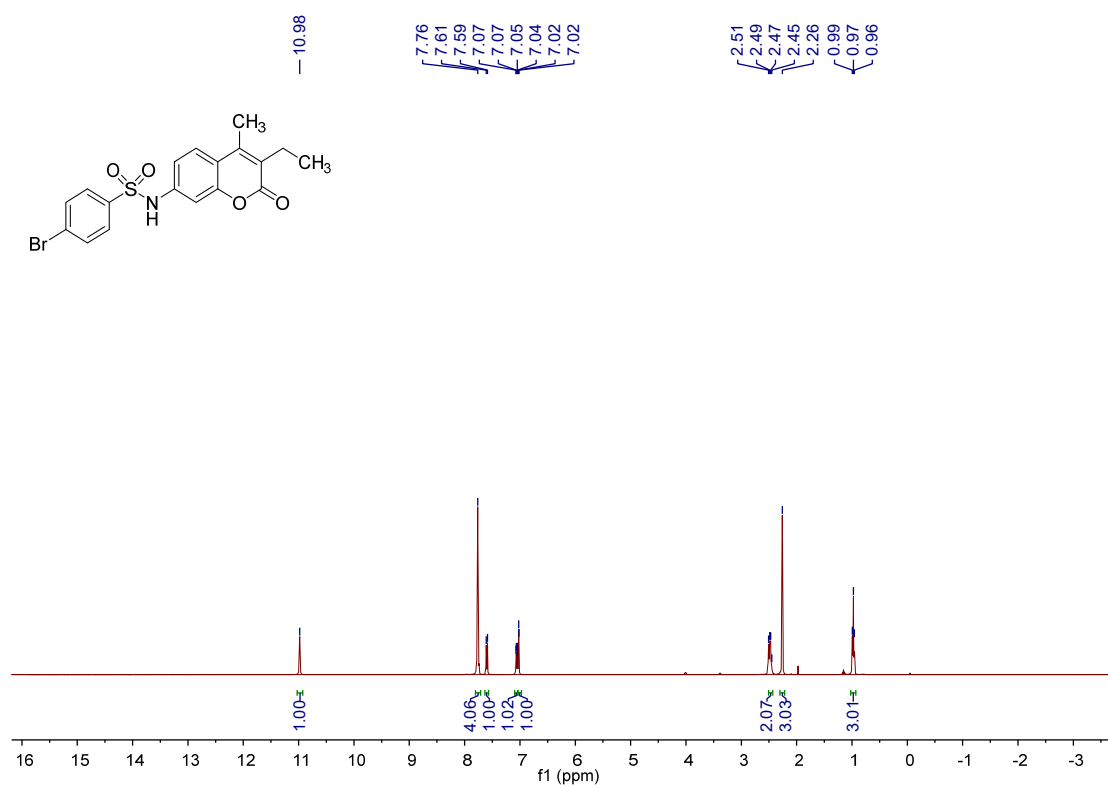


HRMS Spectrum of **6i**

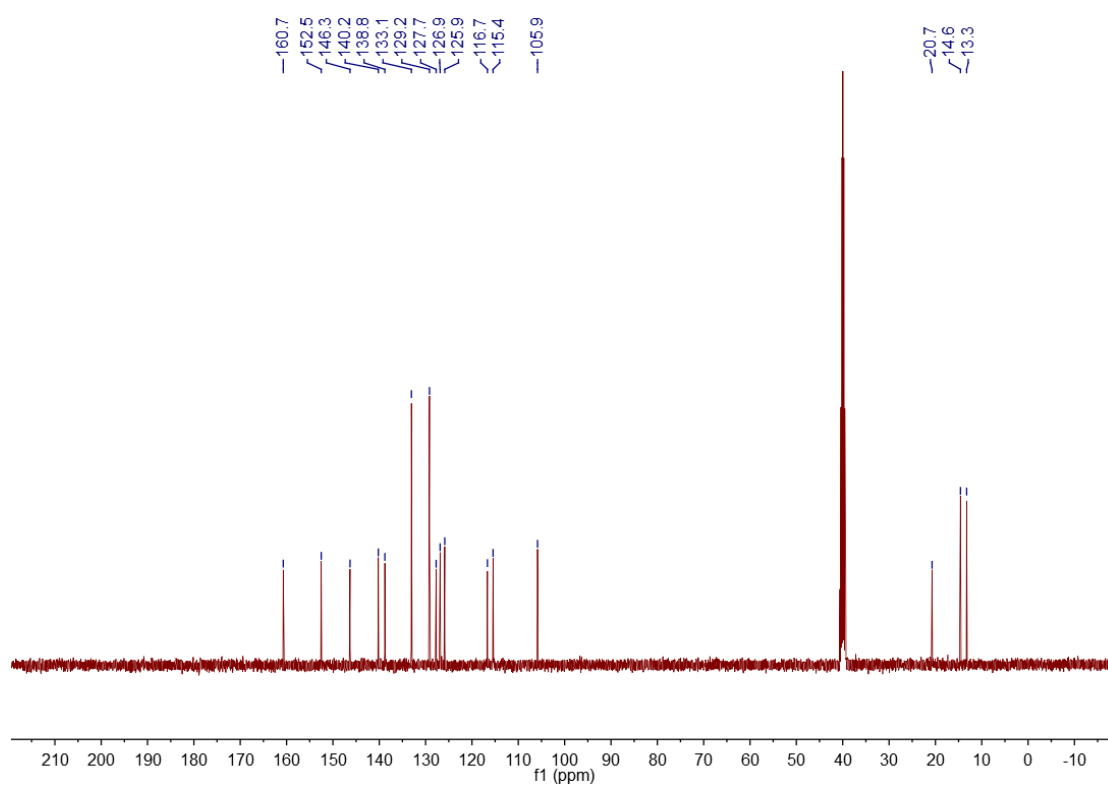
Spectrum from wenya53.wiff (sample 1) - ... MS (100 - 1000) from 0.076 to 0.085 min



^1H NMR Spectrum of 6j (400 MHz, DMSO- d_6)

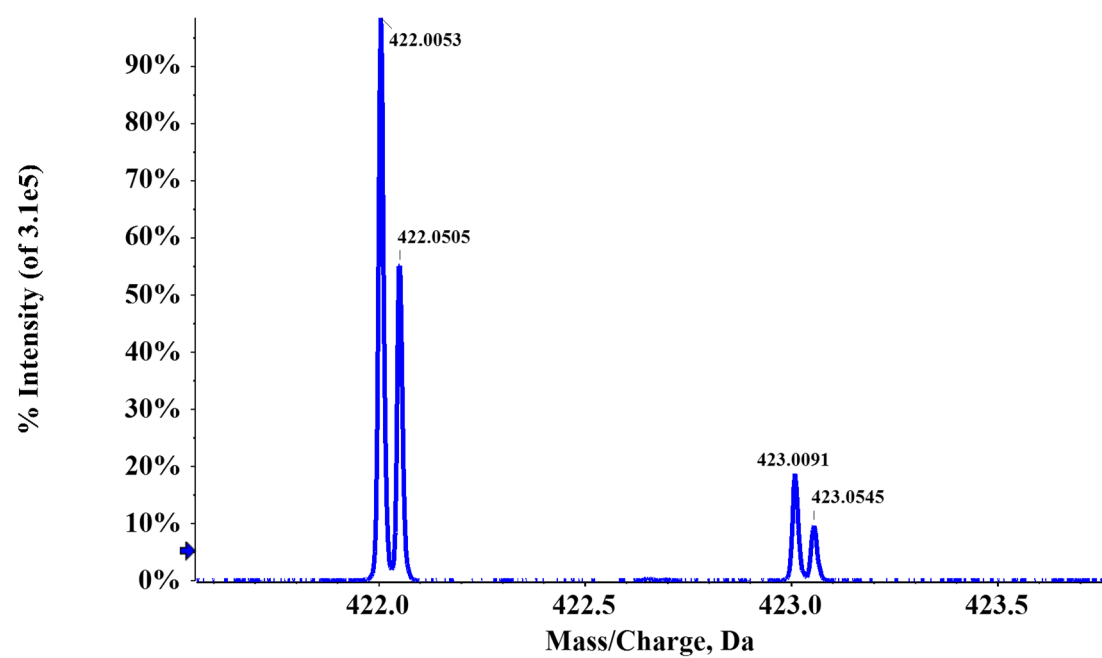


^{13}C NMR Spectrum of 6j (101 MHz, DMSO- d_6)

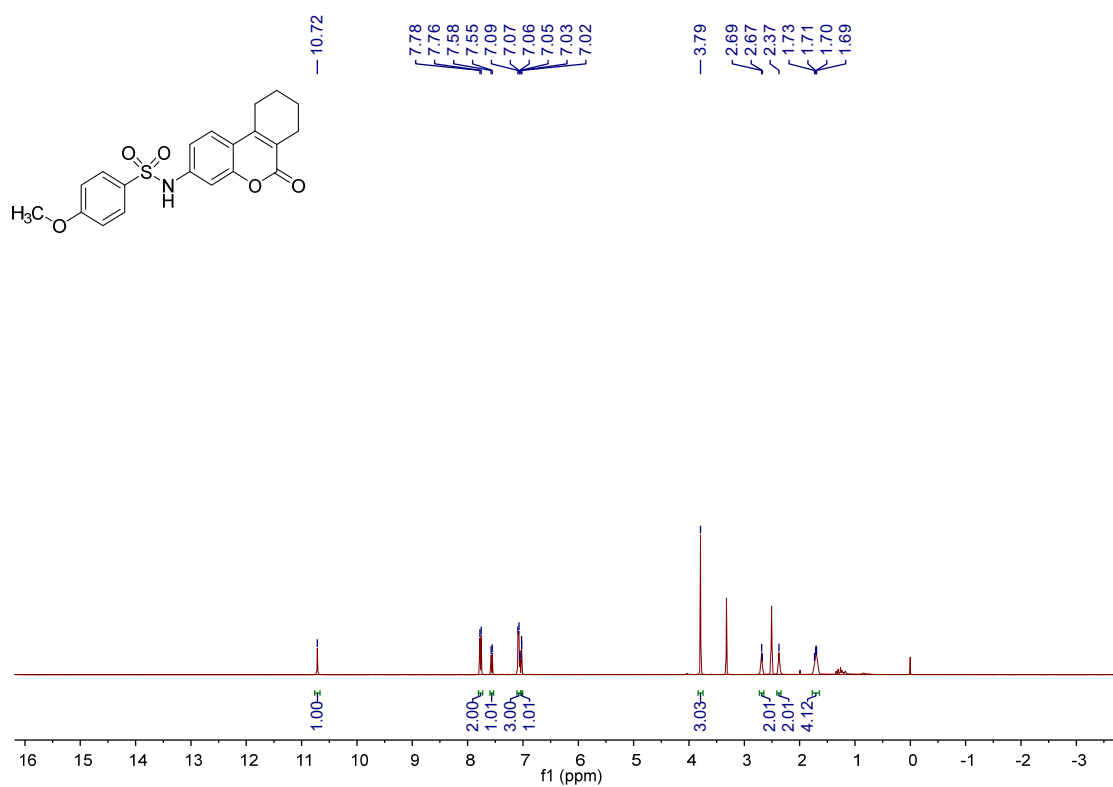


HRMS Spectrum of 6j

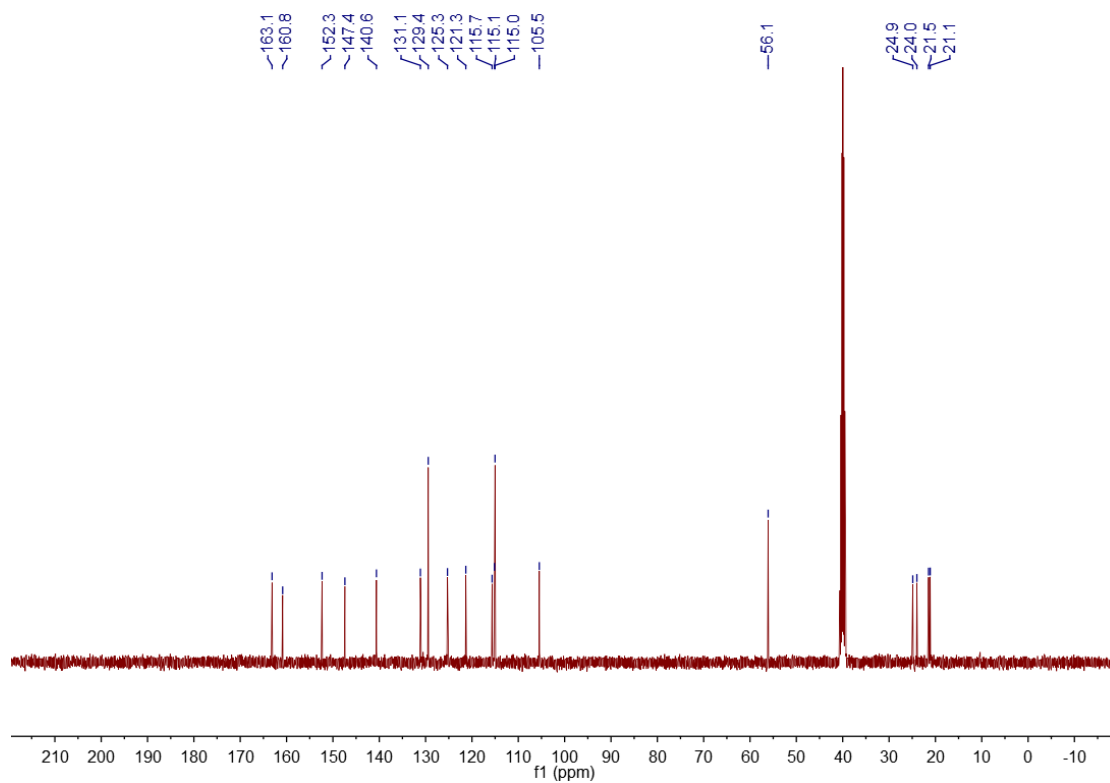
Spectrum from wy54.wiff (sample 1) - wy54...F MS (100 - 1000) from 0.409 to 0.435 min



^1H NMR Spectrum of 6k (400 MHz, $\text{DMSO}-d_6$)

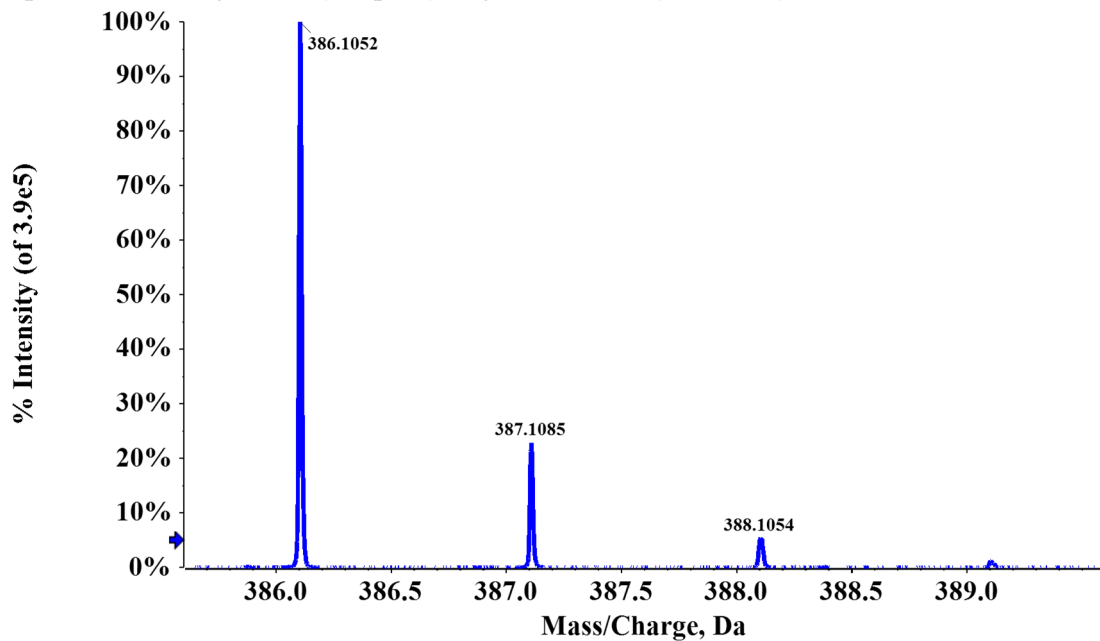


¹³C NMR Spectrum of 6k (101 MHz, DMSO-*d*₆)

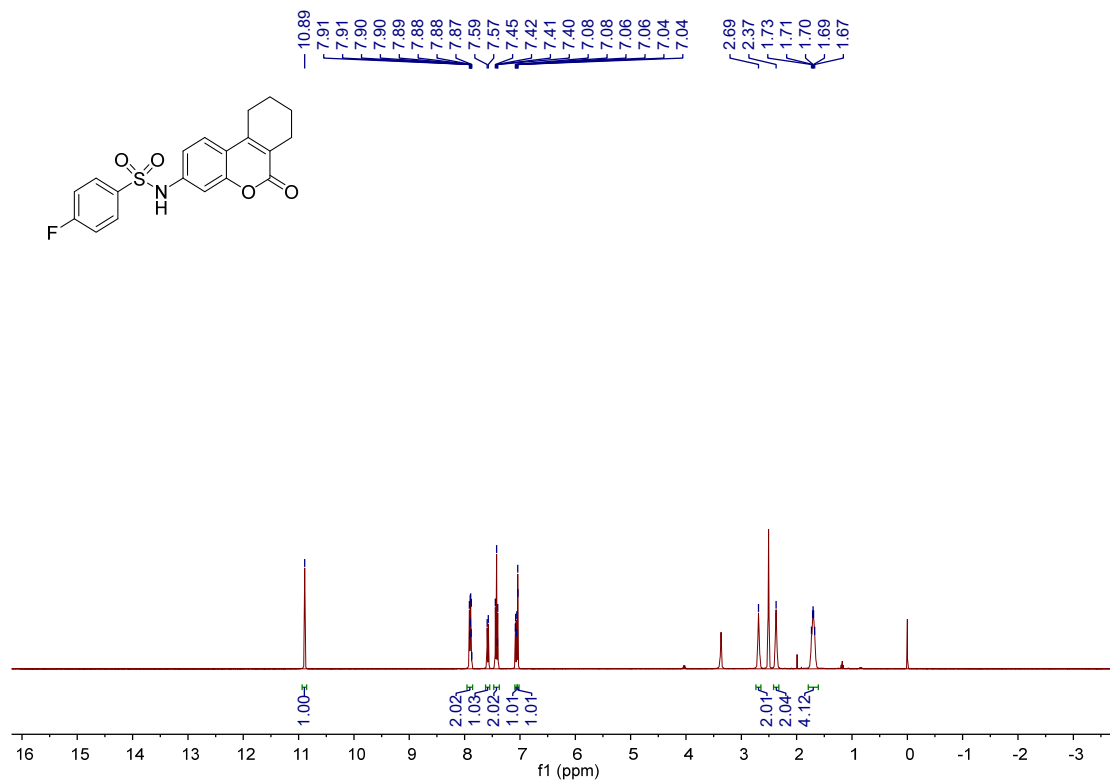


HRMS Spectrum of 6k

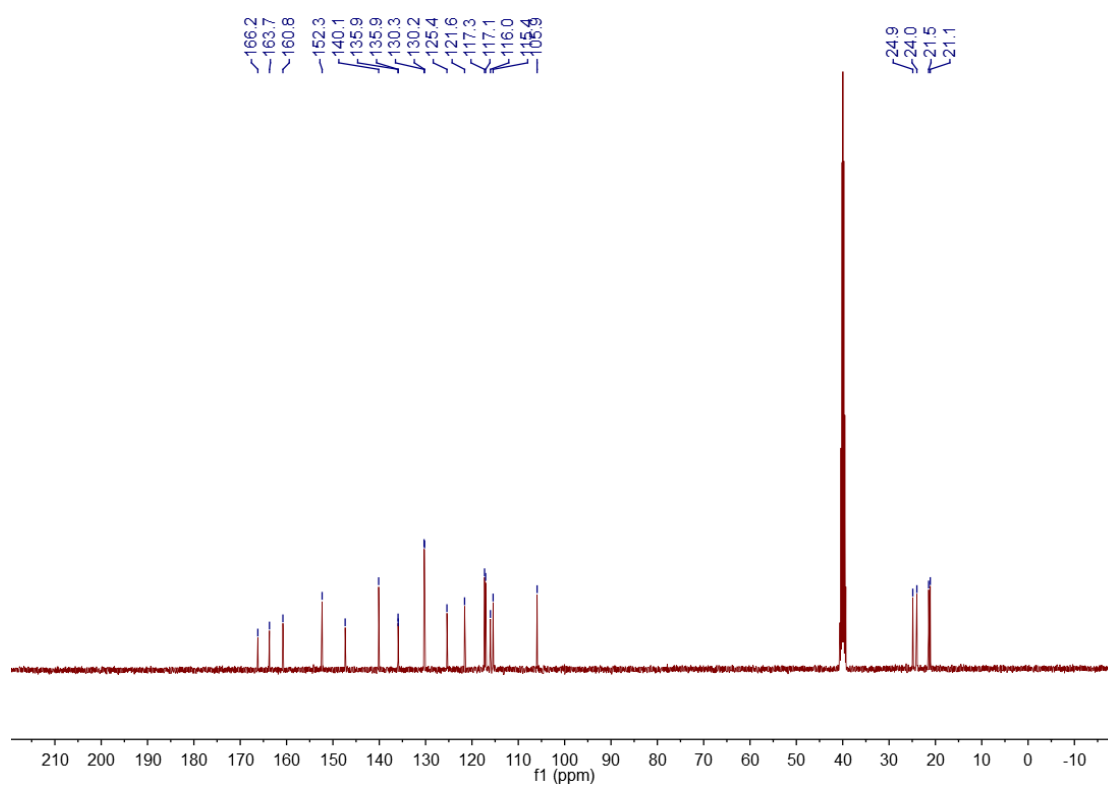
Spectrum from wy56.wiff (sample 1) - wy56, ...OF MS (100 - 1000) from 0.839 to 0.863 min



^1H NMR Spectrum of 6l (400 MHz, $\text{DMSO}-d_6$)

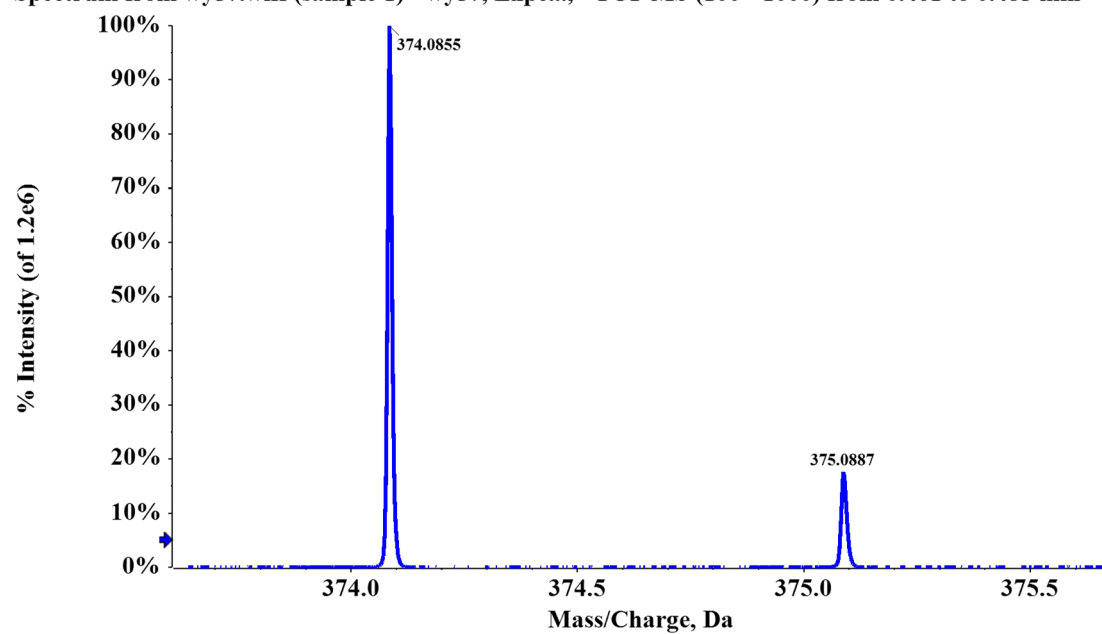


^{13}C NMR Spectrum of 6l (101 MHz, $\text{DMSO}-d_6$)

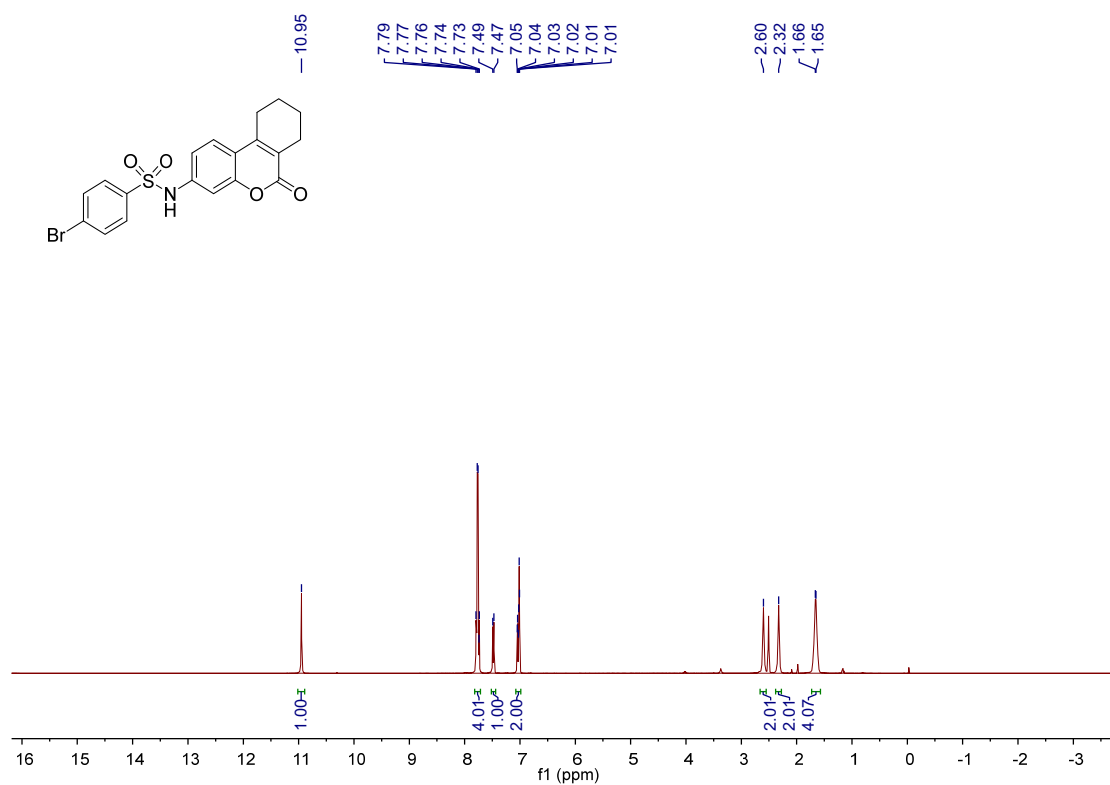


HRMS Spectrum of 6l

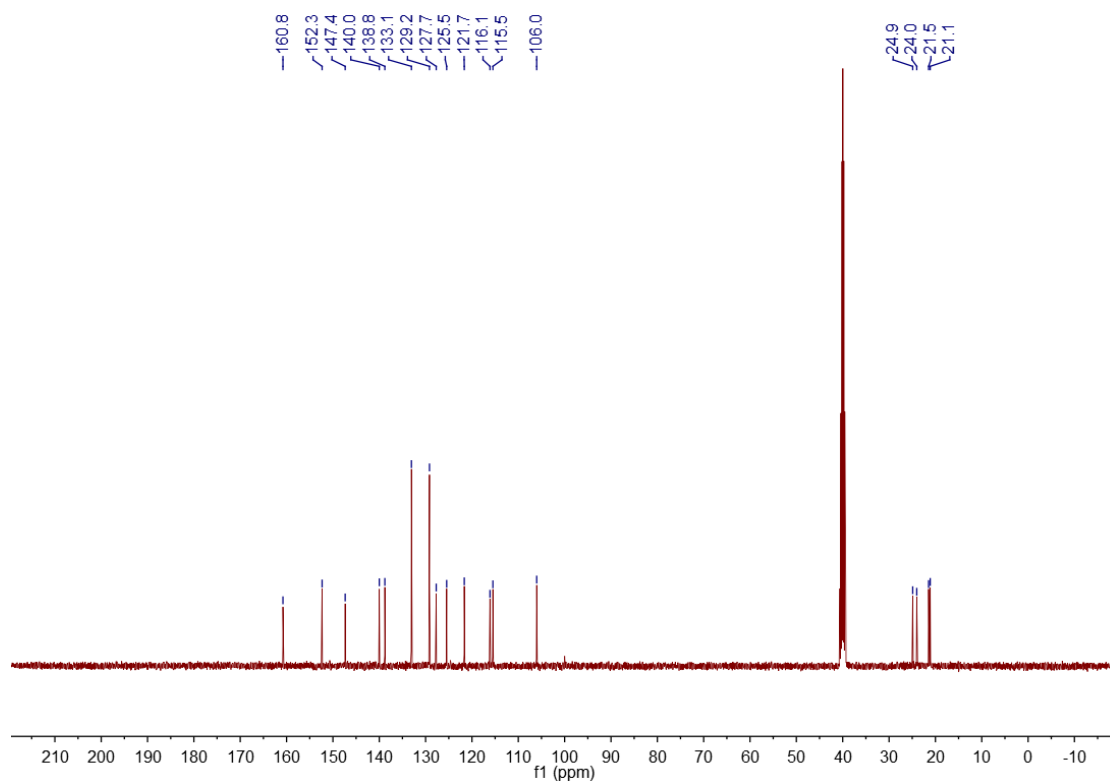
Spectrum from wy57.wiff (sample 1) - wy57, Expe..., +TOF MS (100 - 1000) from 0.461 to 0.485 min



^1H NMR Spectrum of 6m (400 MHz, $\text{DMSO}-d_6$)

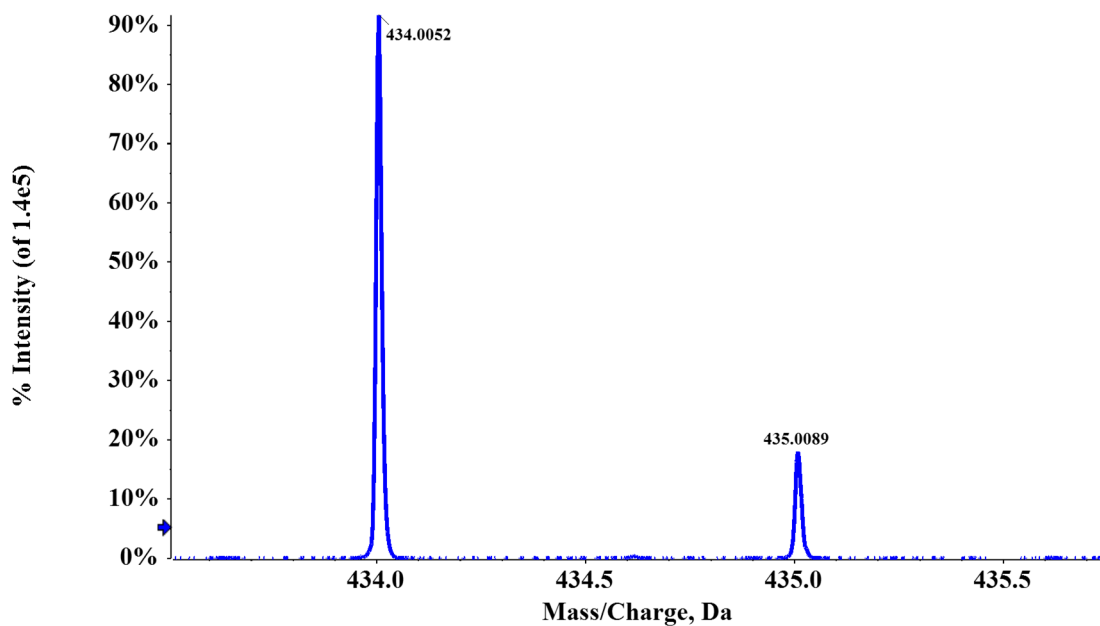


^{13}C NMR Spectrum of 6m (101 MHz, $\text{DMSO}-d_6$)

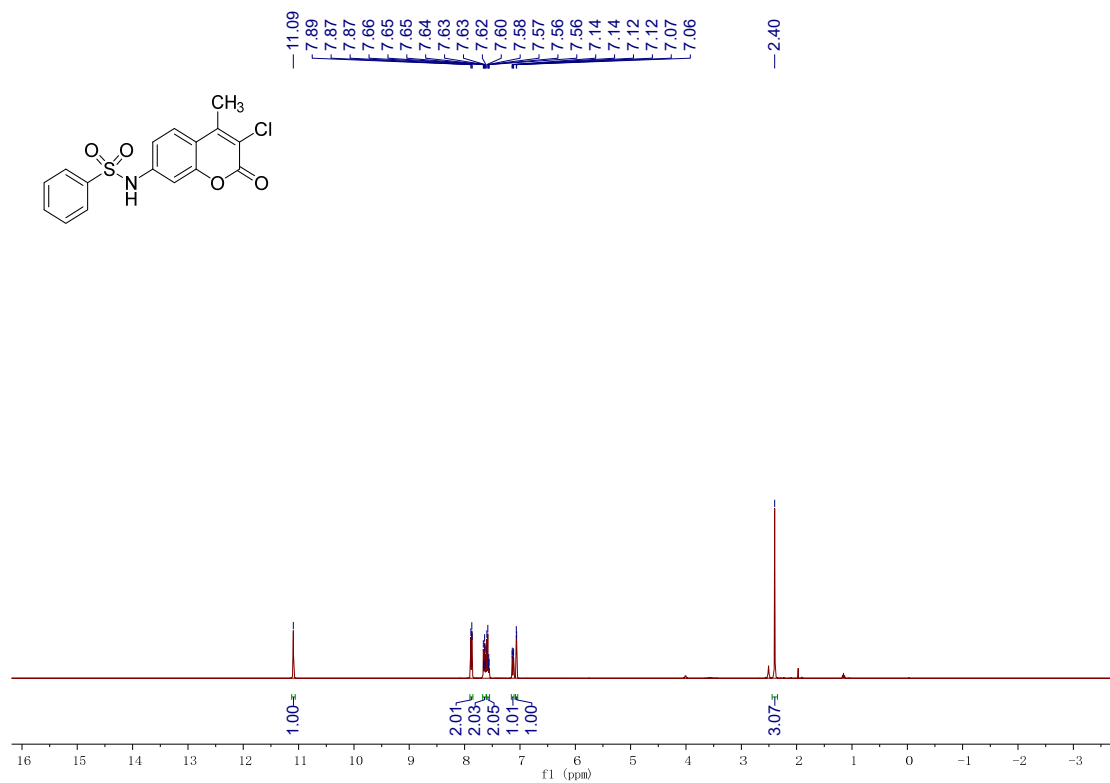


HRMS Spectrum of 6m

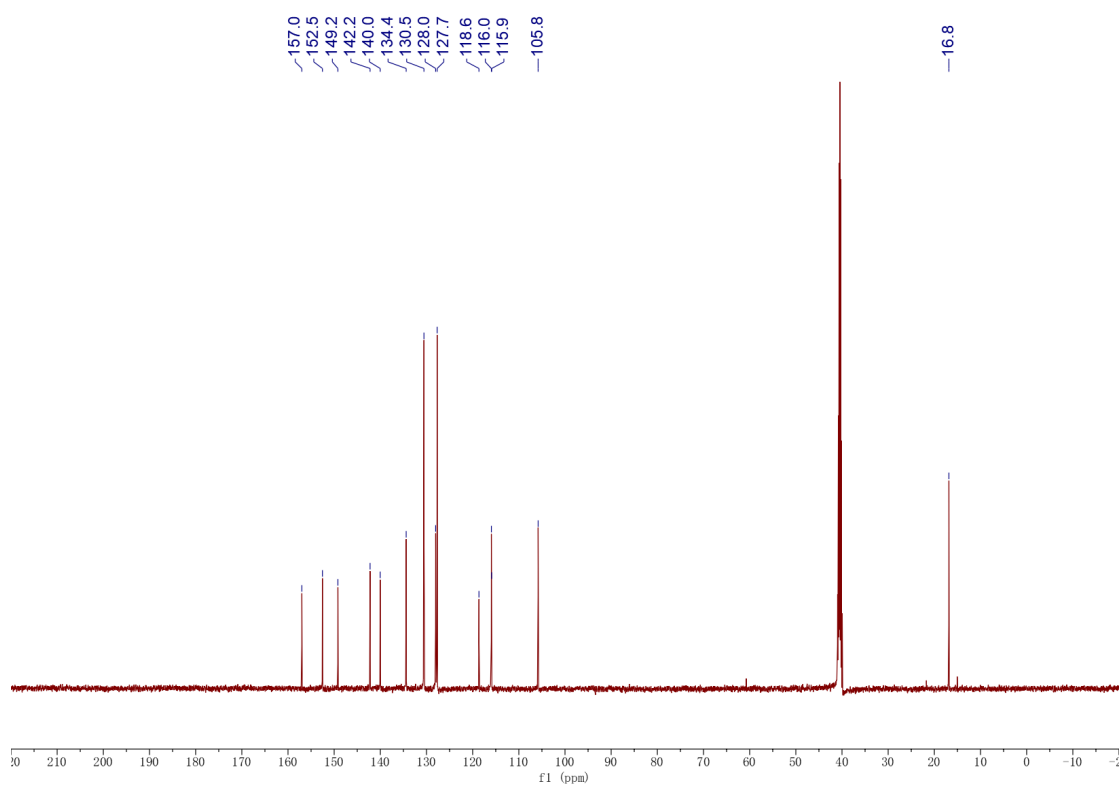
Spectrum from wy59.wiff (sample 1) - wy59, Ex... +TOF MS (100 - 1000) from 0.754 to 0.779 min



^1H NMR Spectrum of 6n (400 MHz, $\text{DMSO}-d_6$)

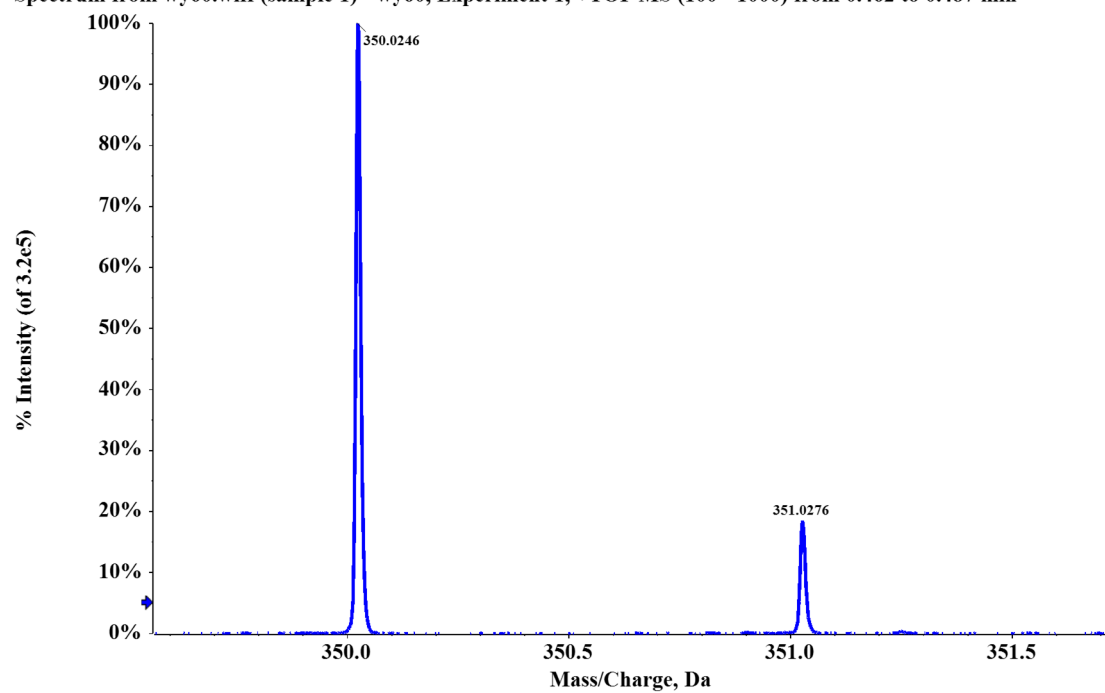


^{13}C NMR Spectrum of 6n (126 MHz, $\text{DMSO}-d_6$)

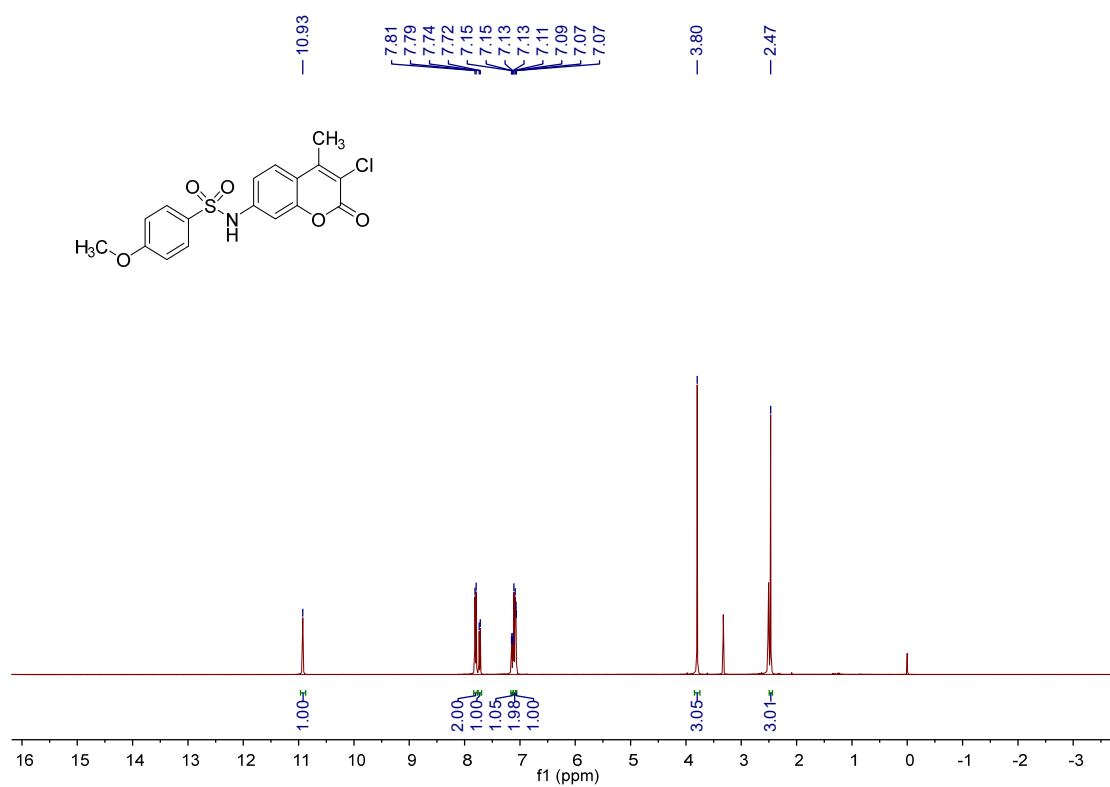


HRMS Spectrum of 6n

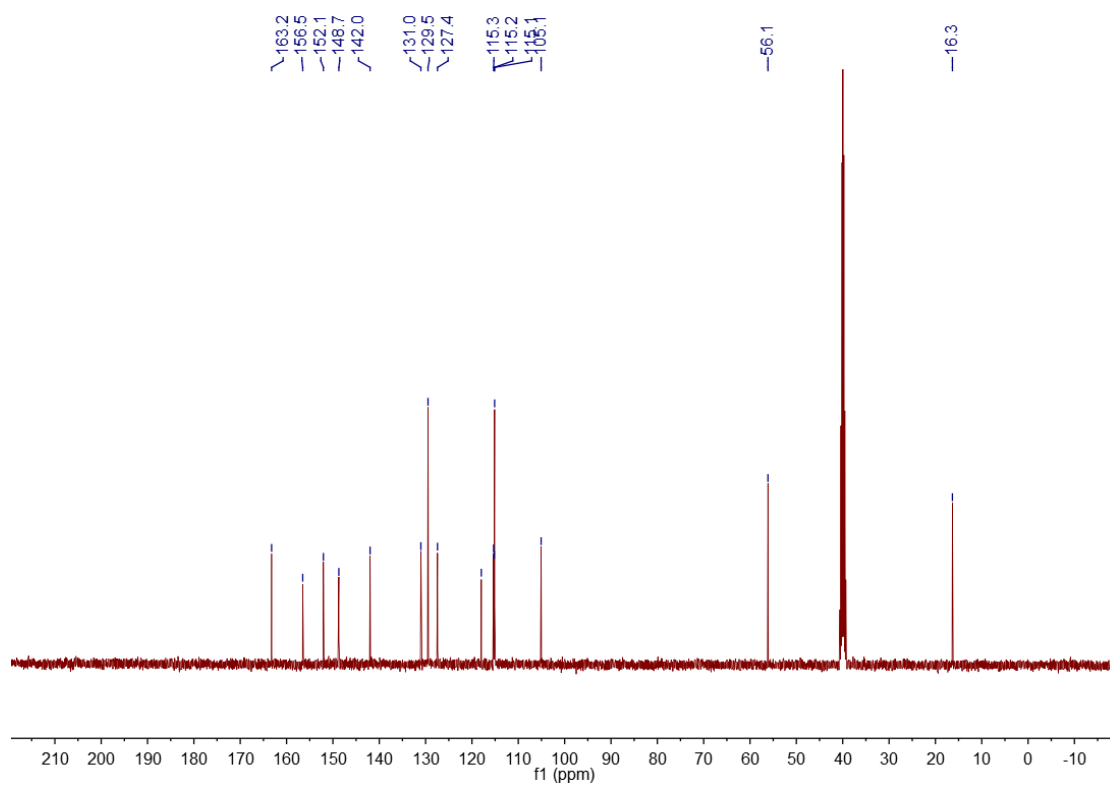
Spectrum from wy60.wiff (sample 1) - wy60, Experiment 1, +TOF MS (100 - 1000) from 0.462 to 0.487 min



¹H NMR Spectrum of 6o (400 MHz, DMSO-*d*₆)

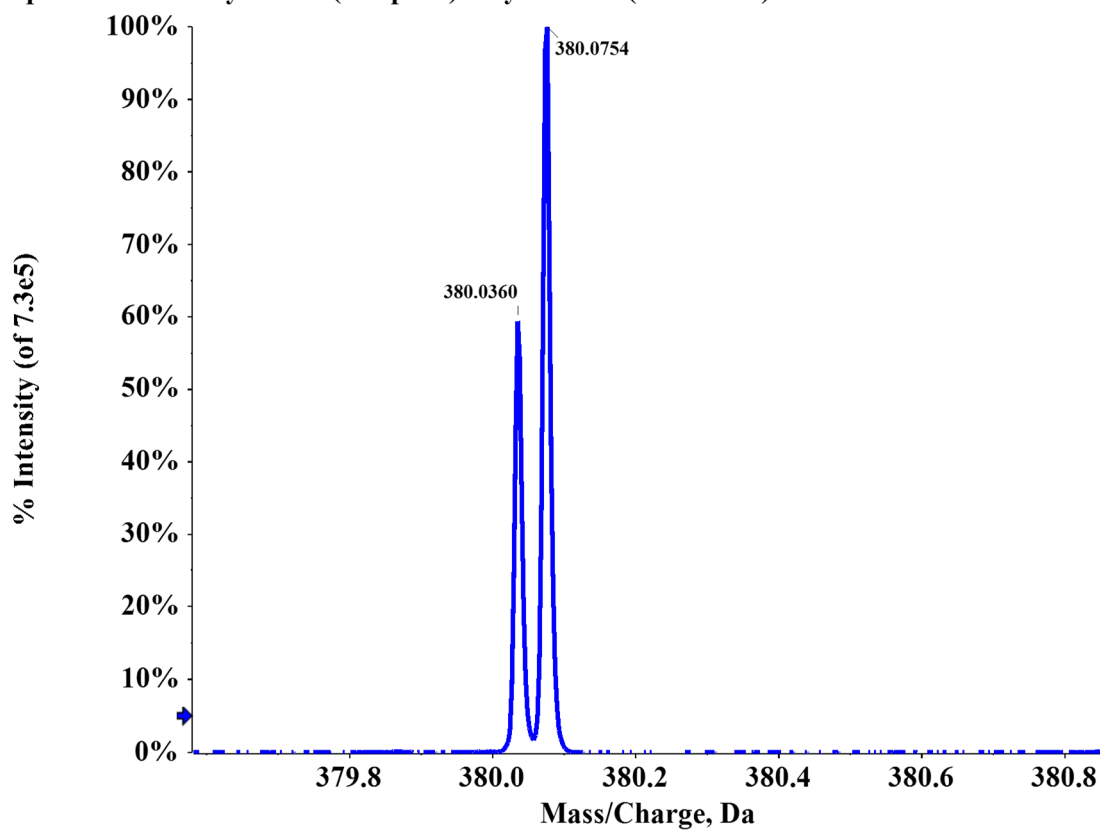


^{13}C NMR Spectrum of 60 (101 MHz, $\text{DMSO}-d_6$)

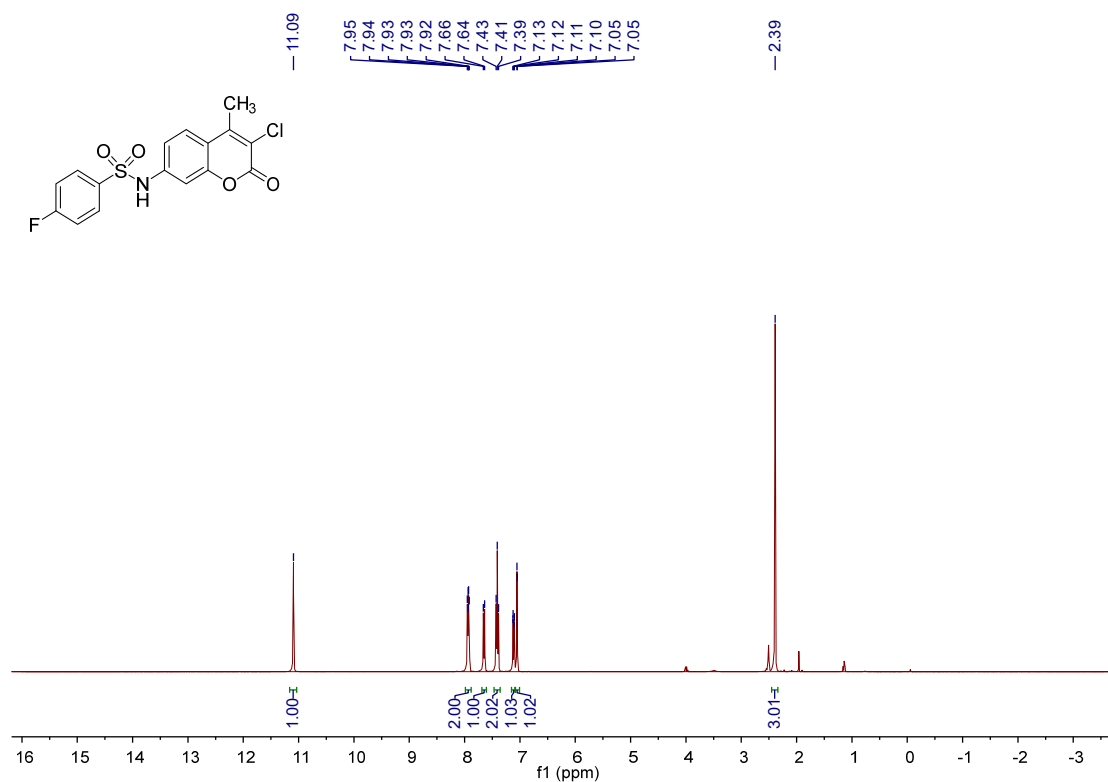


HRMS Spectrum of 60

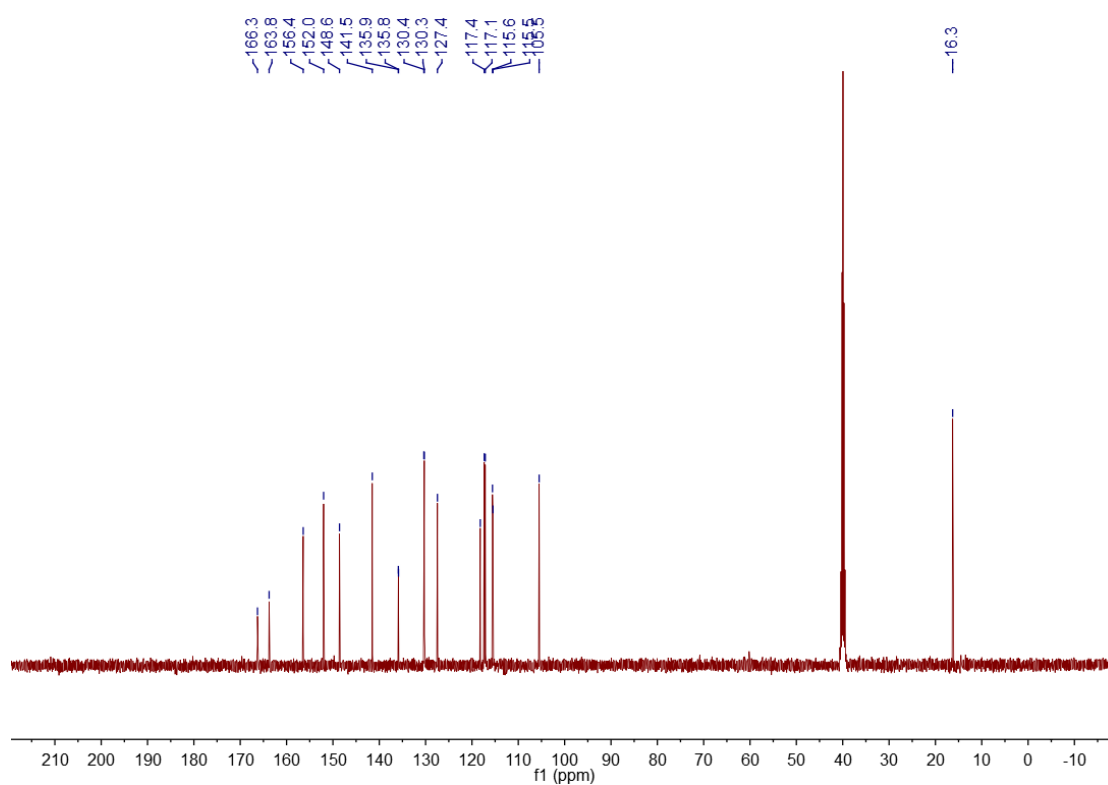
Spectrum from wy61.wiff (sample 1) - wy61... MS (100 - 1000) from 0.338 to 0.363 min



^1H NMR Spectrum of 6p (400 MHz, DMSO- d_6)

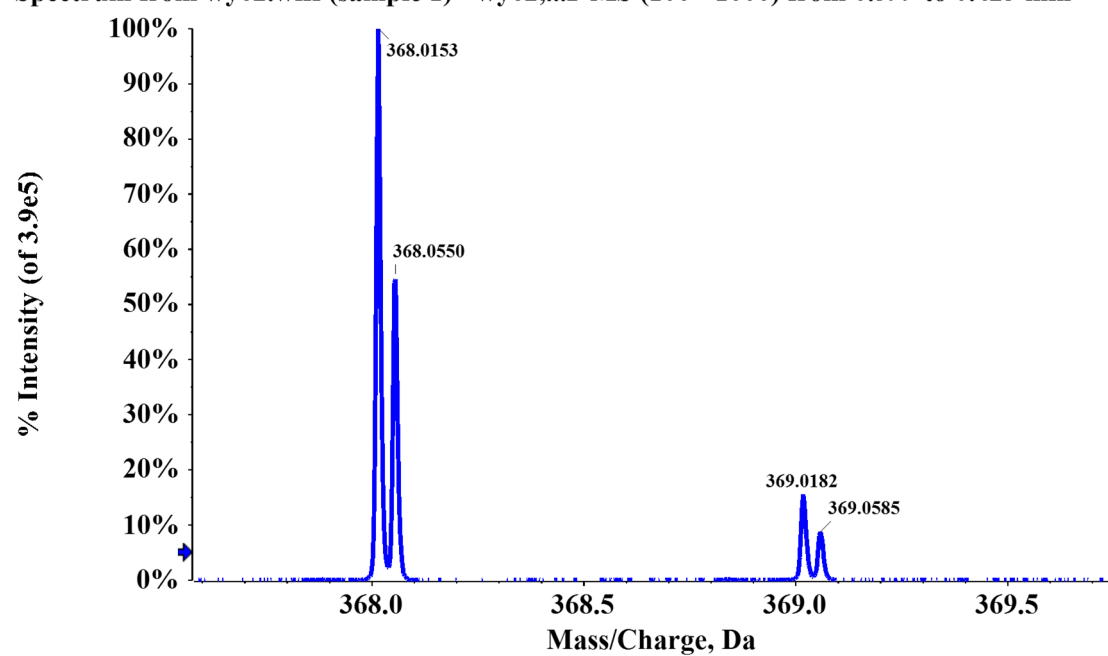


^{13}C NMR Spectrum of 6p (101 MHz, DMSO- d_6)

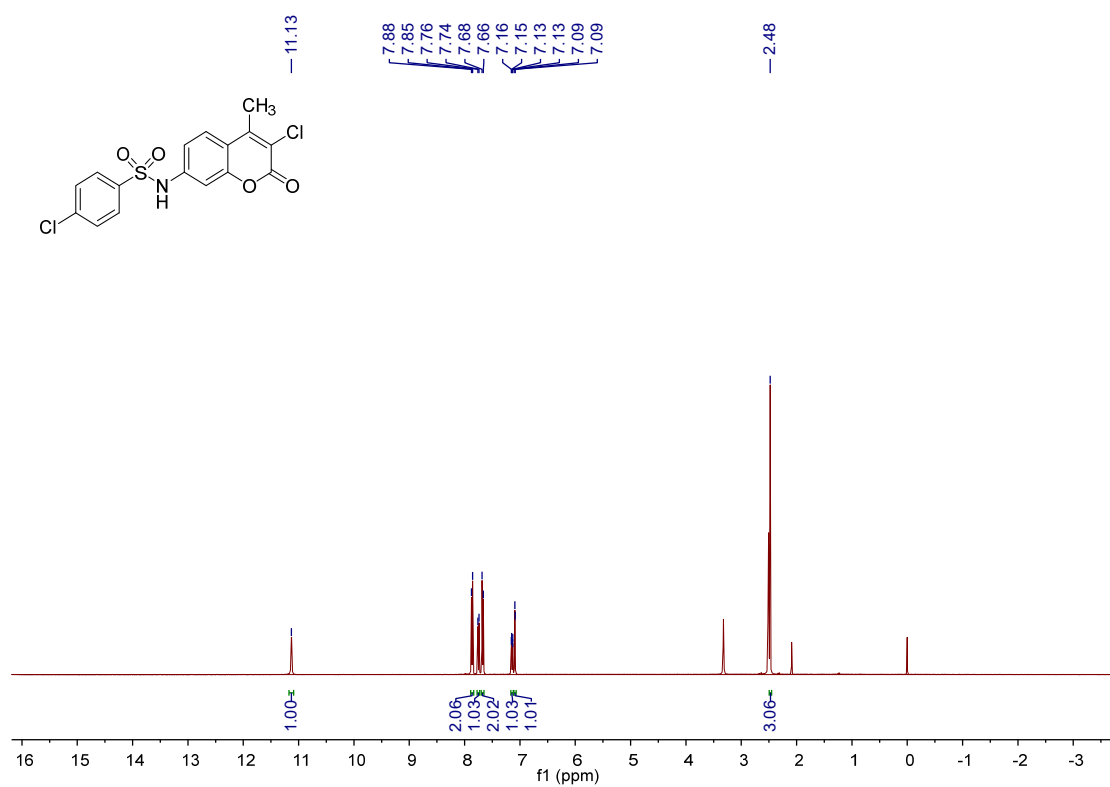


HRMS Spectrum of 6p

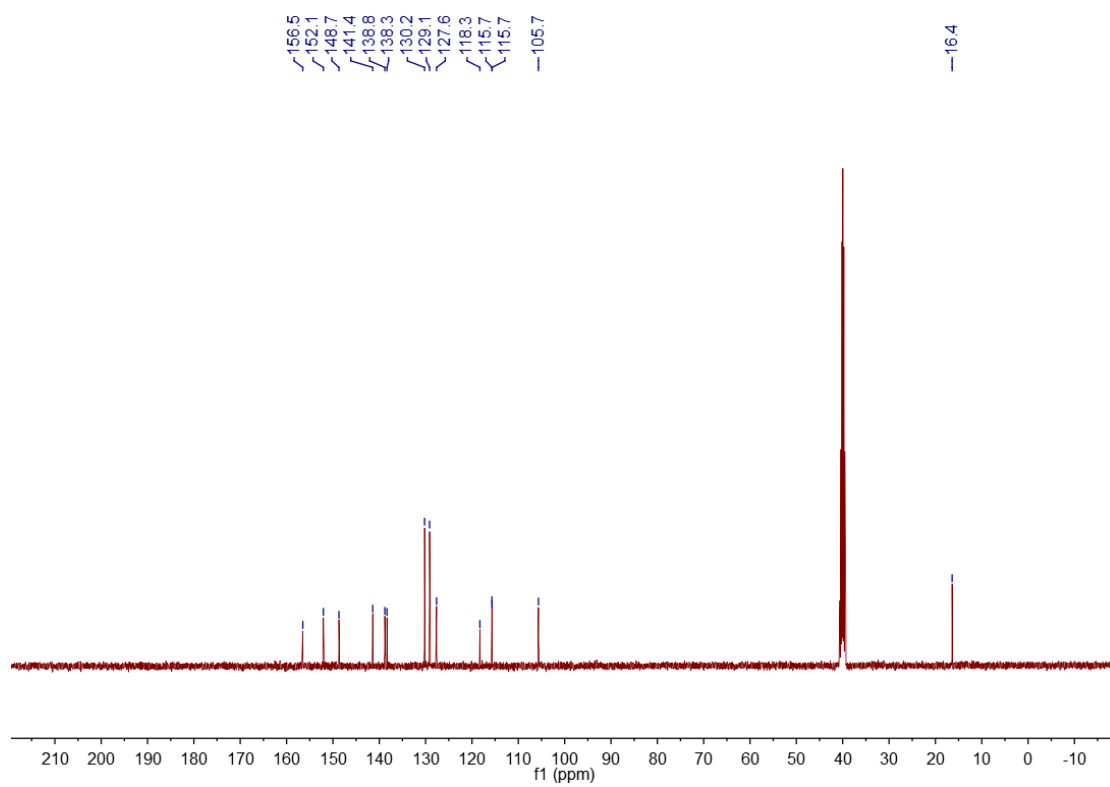
Spectrum from wy62.wiff (sample 1) - wy62,...F MS (100 - 1000) from 0.399 to 0.423 min



¹H NMR Spectrum of 6q (400 MHz, DMSO-*d*₆)

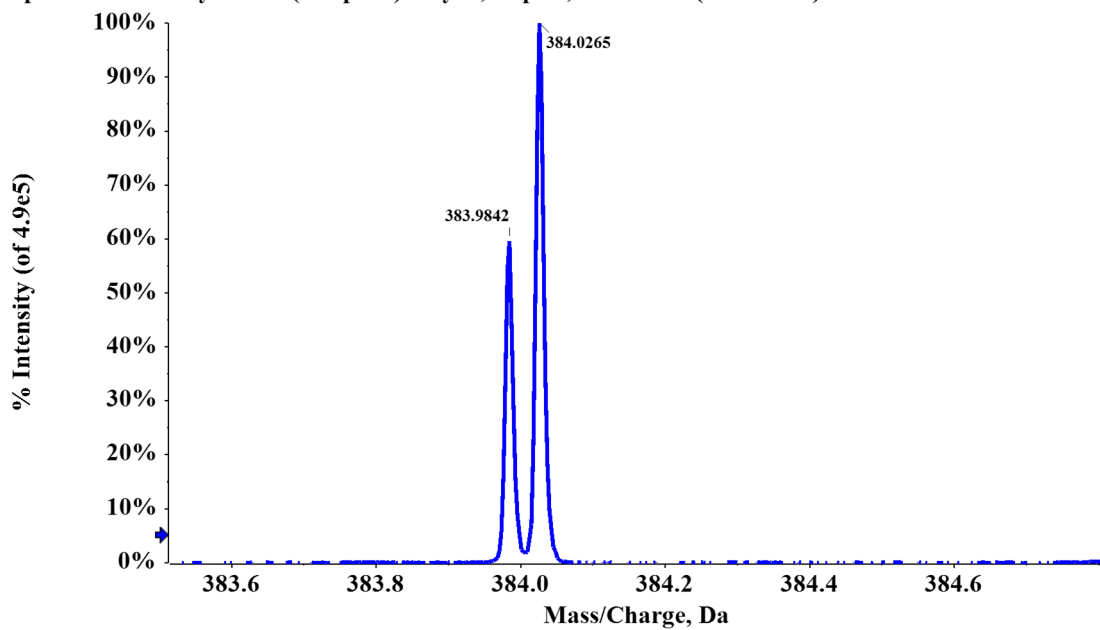


^{13}C NMR Spectrum of 6q (101 MHz, DMSO- d_6)

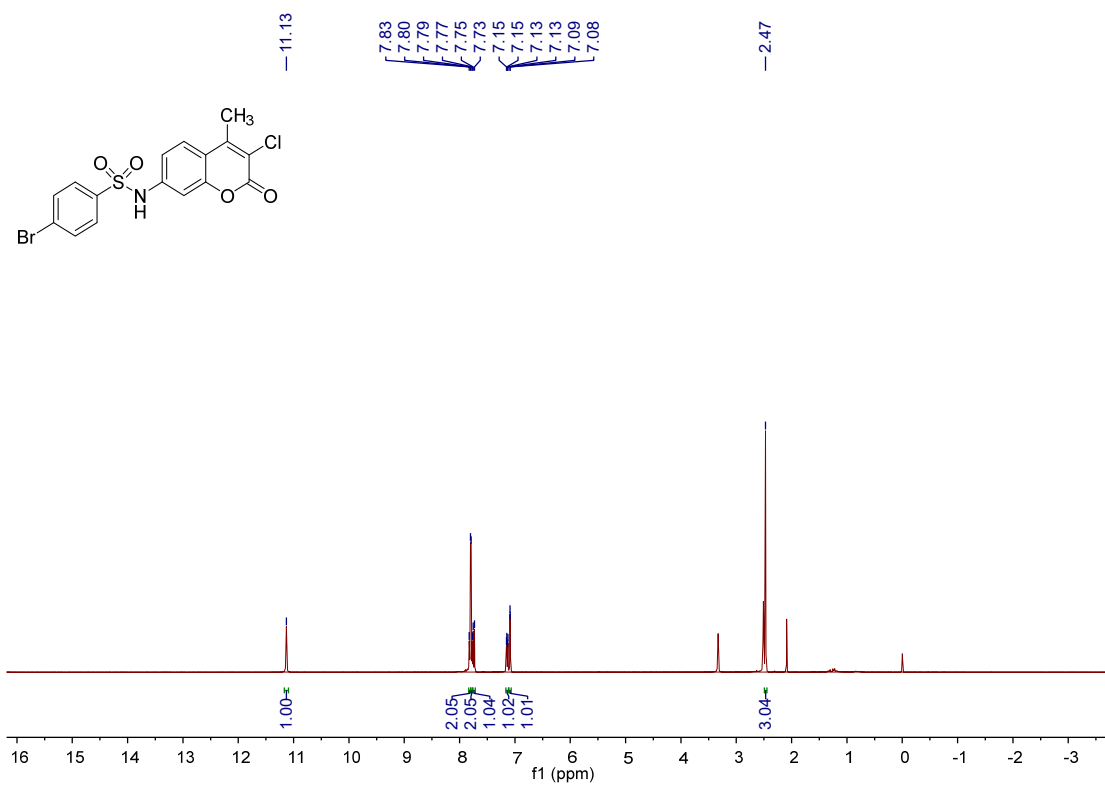


HRMS Spectrum of 6q

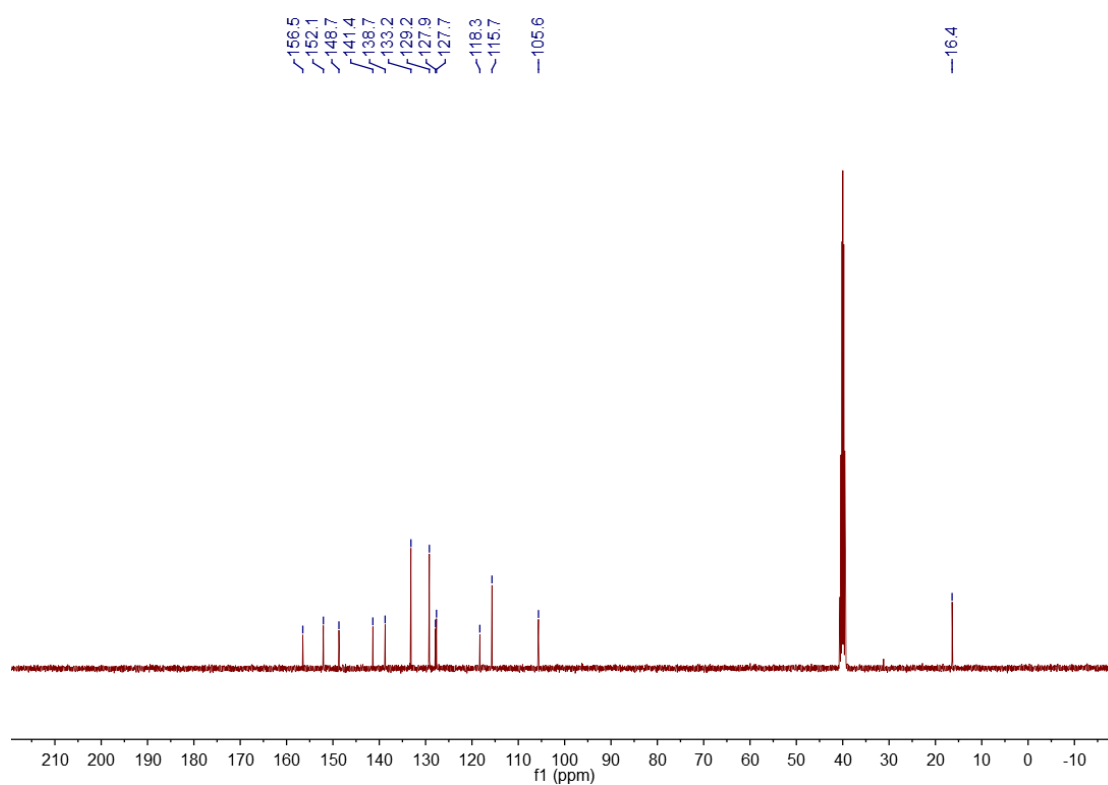
Spectrum from wy63.wiff (sample 1) - wy63, Expe..., +TOF MS (100 - 1000) from 0.316 to 0.340 min



¹H NMR Spectrum of 6r (400 MHz, DMSO-*d*₆)



¹³C NMR Spectrum of 6r (101 MHz, DMSO-*d*₆)



HRMS Spectrum of 6r

Spectrum from wy64.wiff (sample 1) - wy64, Expe...1, +TOF MS (100 - 1000) from 0.697 to 0.722 min

