

Supporting Information

Design, Synthesis and Biological Evaluation of Novel Tetrahydroacridin Hybrids with Sulfur-inserted Linkers as Potential Multitarget Agents for Alzheimer's Disease

Xiuyuan Wu^{1,†}, Xiaotong Ze^{1,†}, Shuai Qin¹, Beiyu Zhang³, Xinnan Li¹, Qi Gong², Haiyan Zhang^{2,*}, Zheyang Zhu^{3,*} and Jinyi Xu^{1,*}

¹ State Key Laboratory of Natural Medicines and Department of Medicinal Chemistry, China Pharmaceutical University, 24 Tong Jia Xiang, Nanjing 210009, P. R. China.

² CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Shanghai 201203, China.

³ Therapeutics & Formulation, School of Pharmacy, The University of Nottingham, University Park Campus, Nottingham NG7 2RD, UK.

* E-mails: jinyixu@china.com; hzhang@simmm.ac.cn; Zheyang.Zhu@nottingham.ac.uk

[†] *These authors contributed equally to this work.*

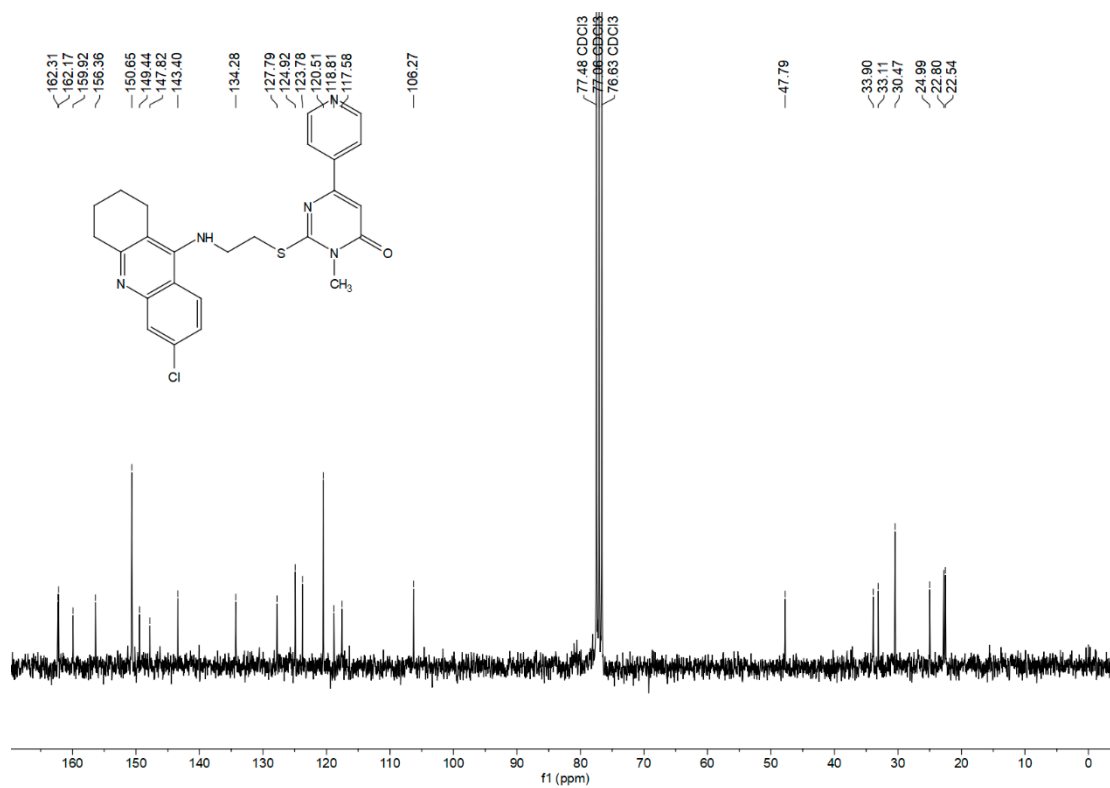
Table of contents

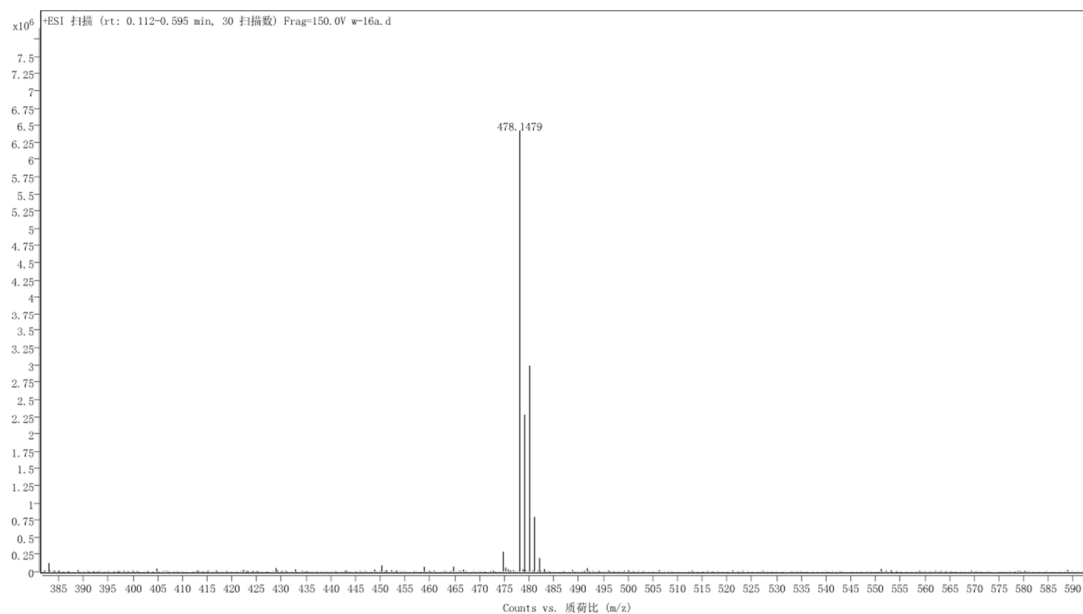
NMR and HRMS of compound 16a	S2
NMR and HRMS of compound 16b	S4
NMR and HRMS of compound 16c	S6
NMR and HRMS of compound 16d	S8
NMR and HRMS of compound 16e	S10
NMR and HRMS of compound 16f	S12
NMR and HRMS of compound 18a	S14
NMR and HRMS of compound 18b	S16
NMR and HRMS of compound 18c	S18

Cc1c(C(=O)c2cc(C#N)cc2SCCNC3=C(Cl)C=CC4=C3C=CC5=C4CCCCC5)c(C#N)cc1

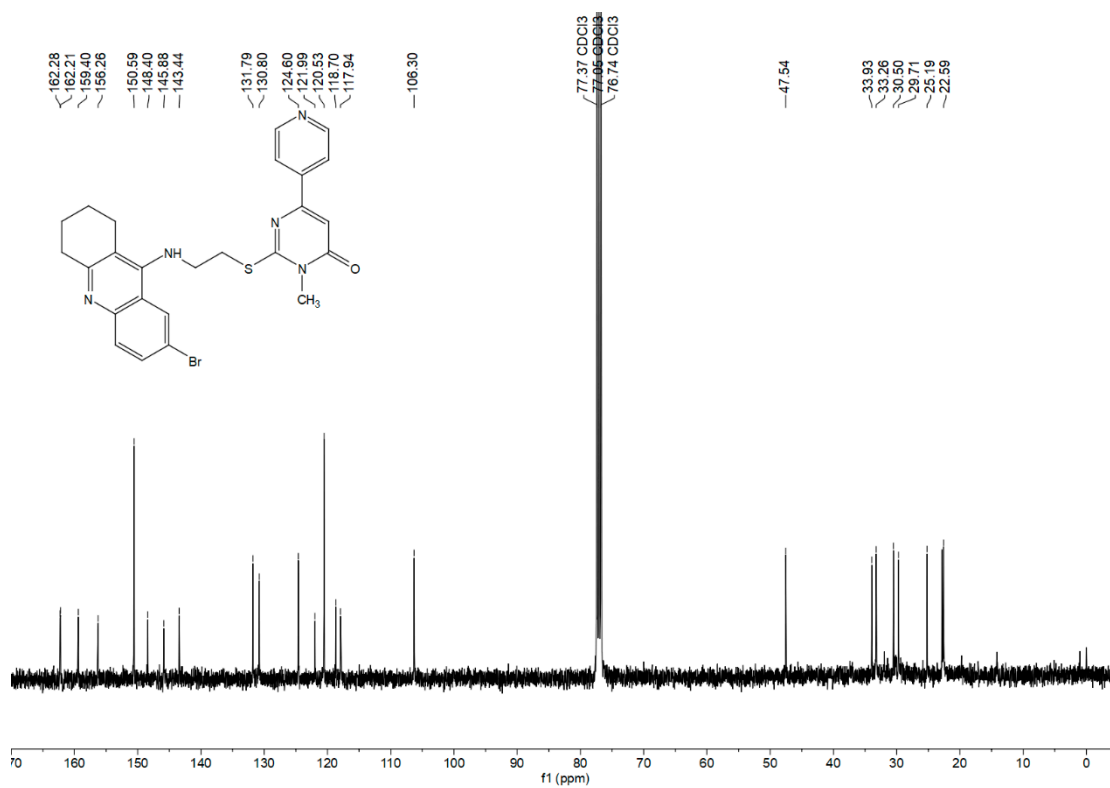
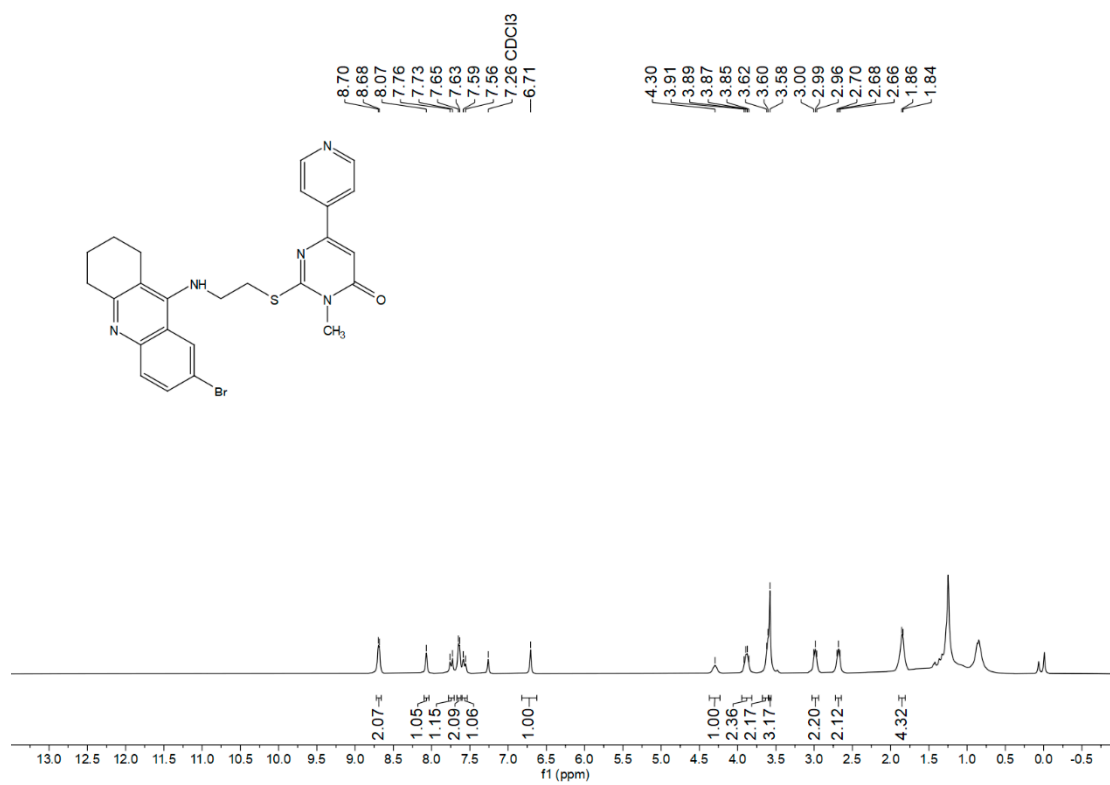
Chemical structure of compound 10 is shown above the ^1H NMR spectrum. The spectrum was recorded in CDCl_3 and shows the following chemical shifts (ppm): 8.70, 8.66, 7.86, 7.86, 7.83, 7.80, 7.65, 7.64, 7.26 (CDCl_3), 7.21, 7.20, 7.18, 7.17, 6.70, 4.36, 3.93, 3.91, 3.89, 3.87, 3.61, 3.59, 3.57, 3.55, 3.01, 2.99, 2.97, 2.65, 2.63, 2.62, 1.84, 1.82.

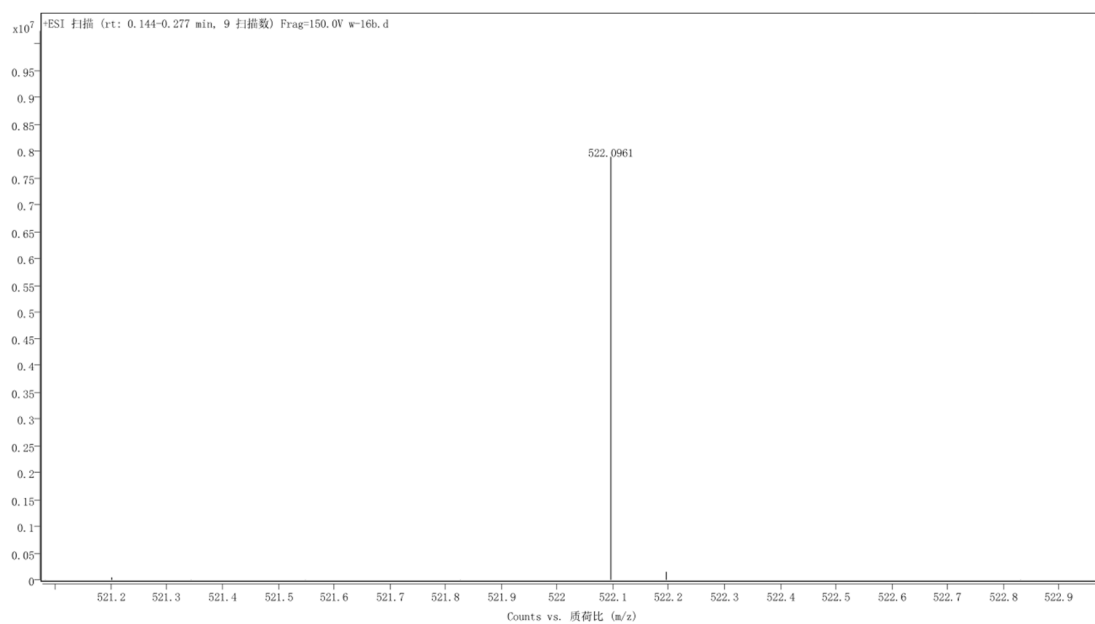
Integration values are provided below the baseline: 2.18, 2.20, 2.17, 1.01, 1.00, 0.98, 2.22, 2.14, 3.01, 2.19, 2.22, 4.18.



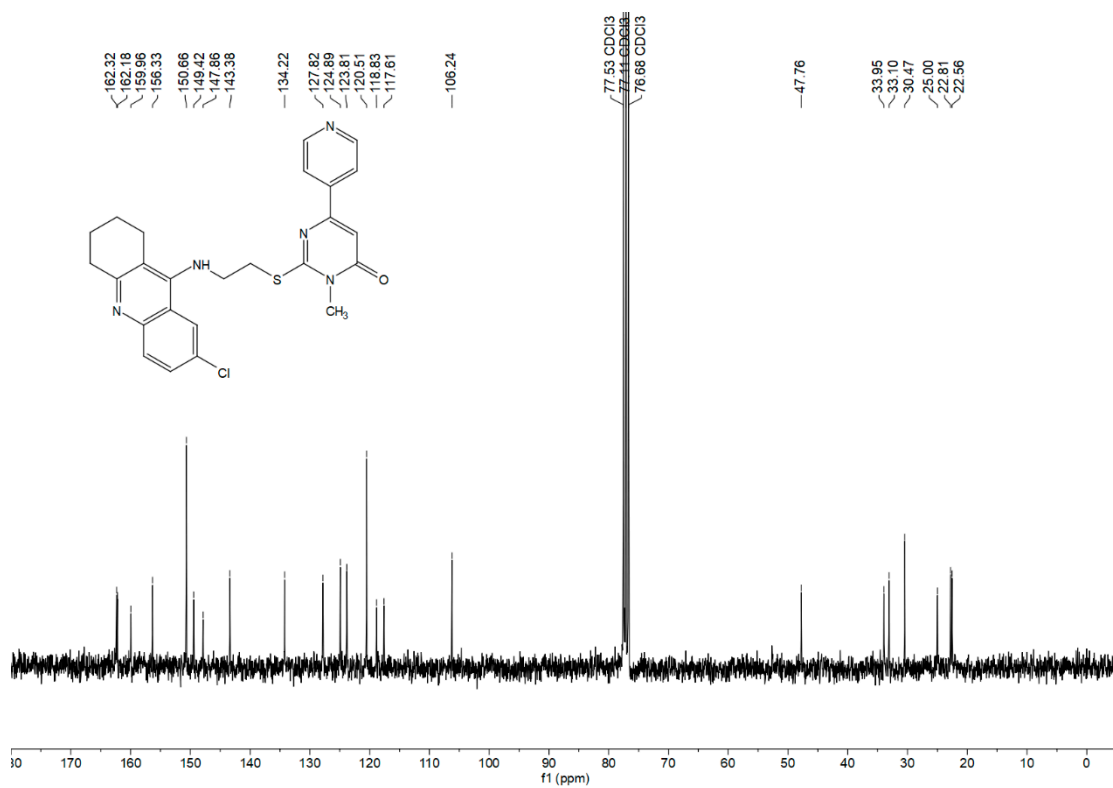
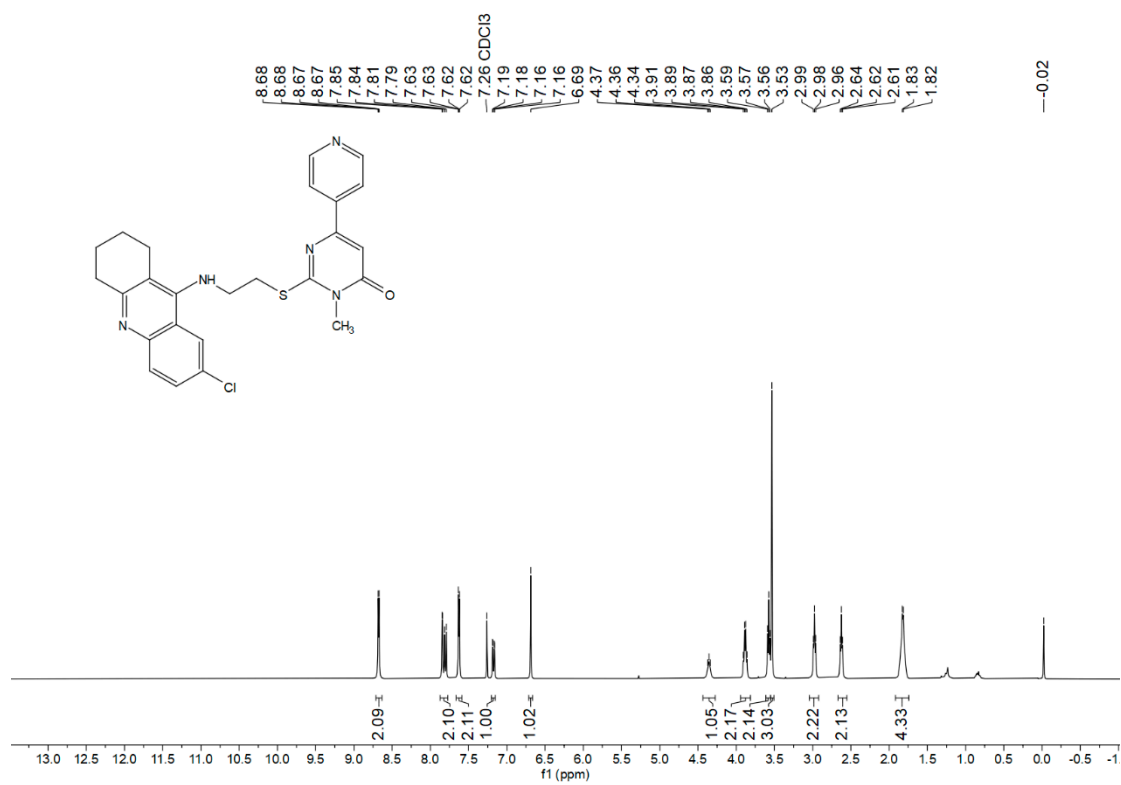


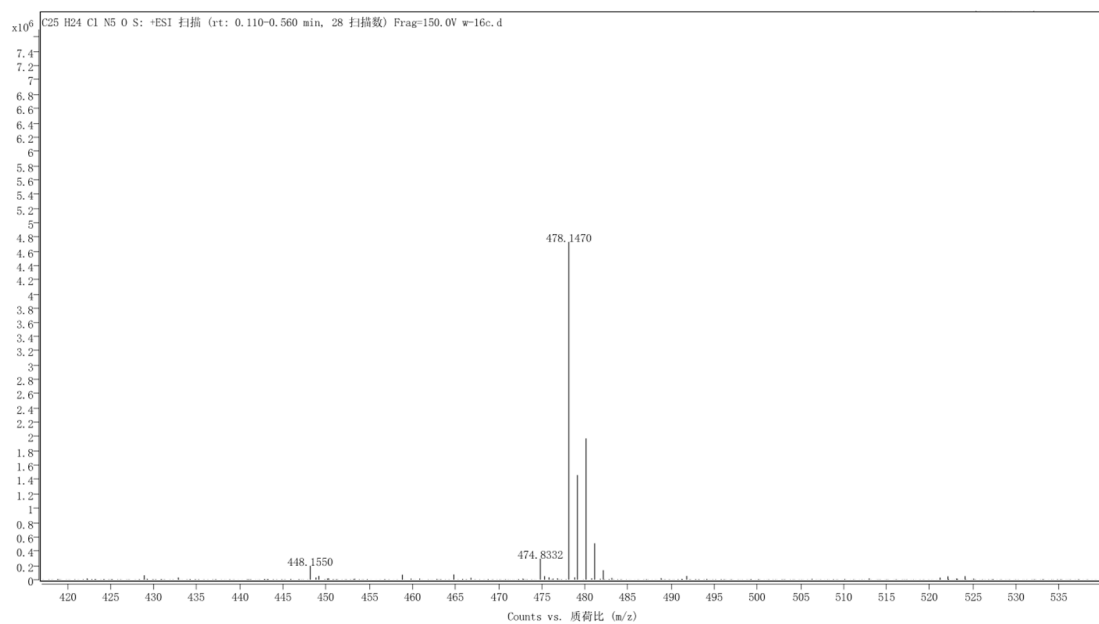
NMR and HRMS of compound **16b**



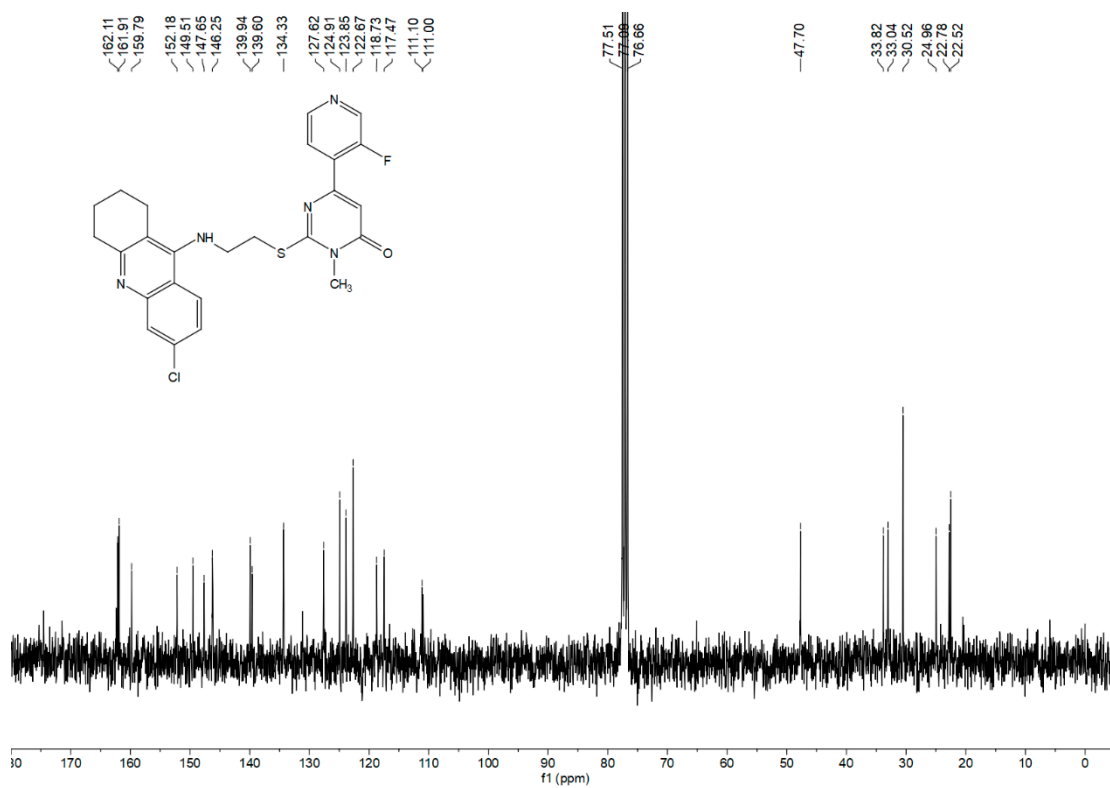
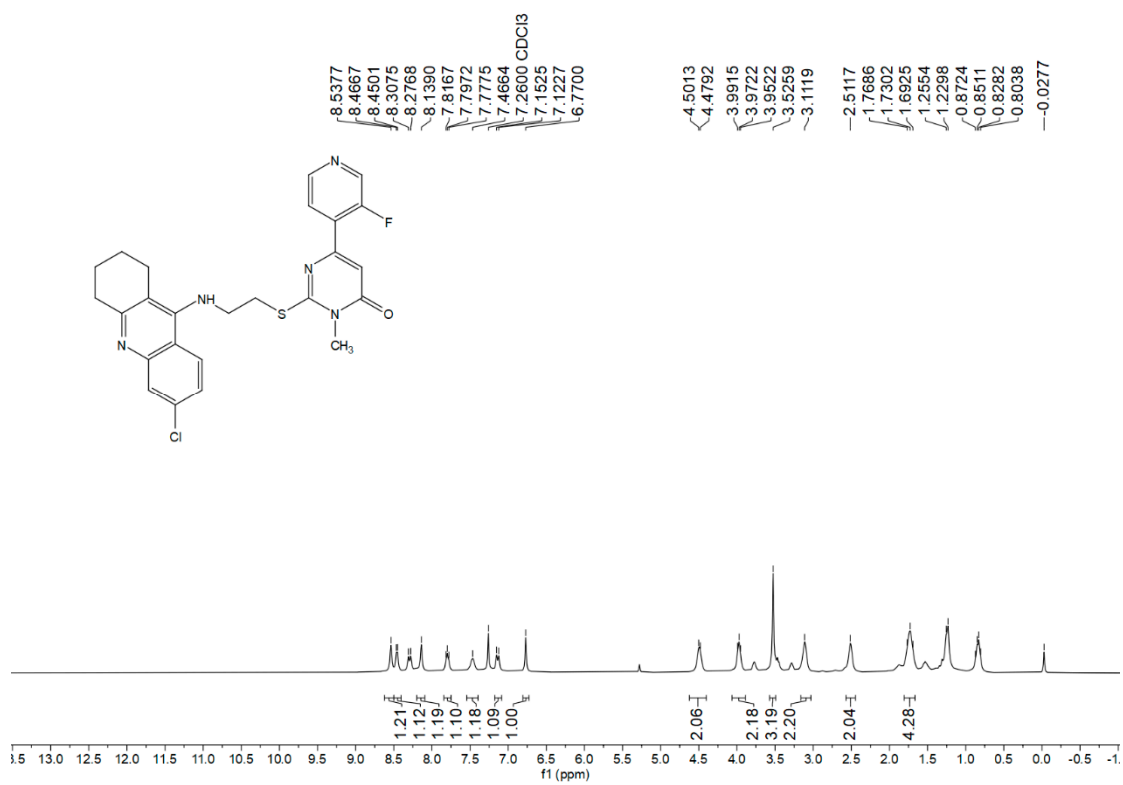


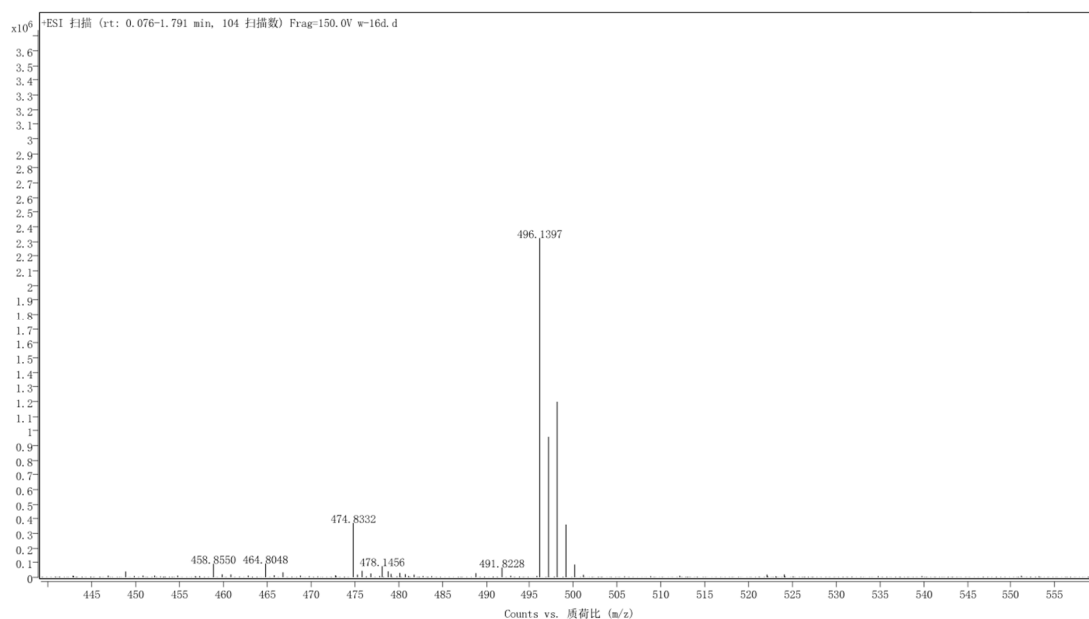
NMR and HRMS of compound **16c**



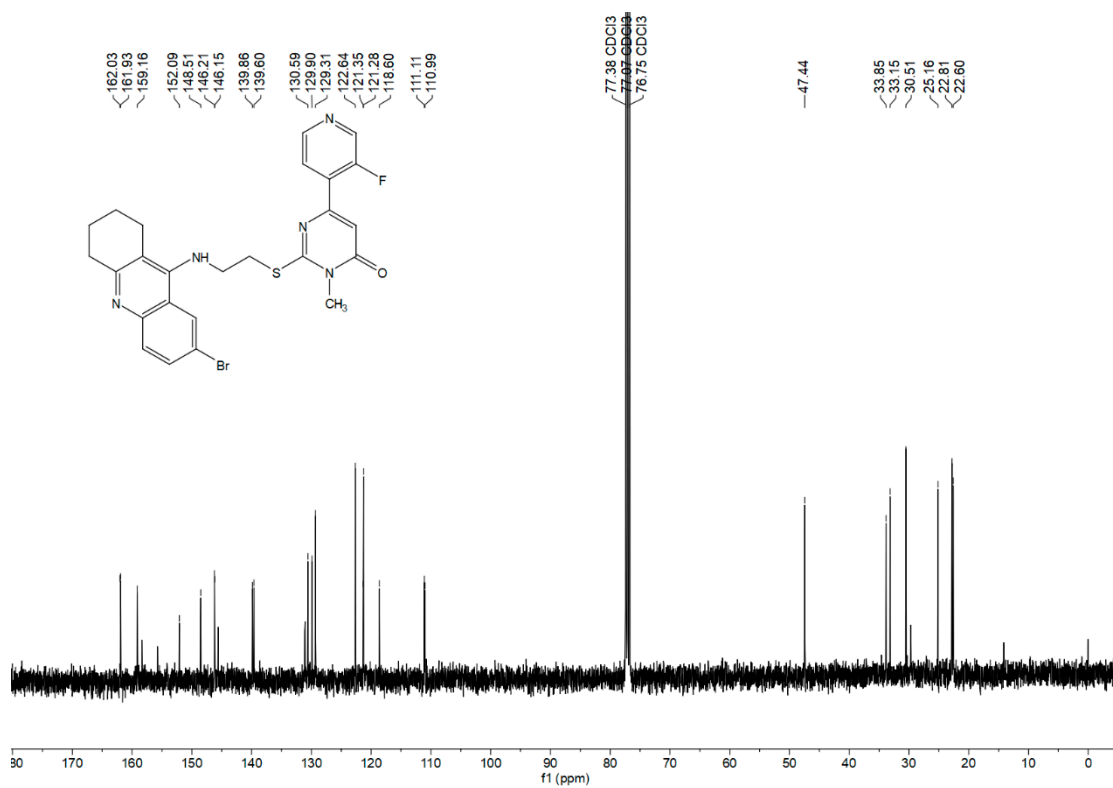
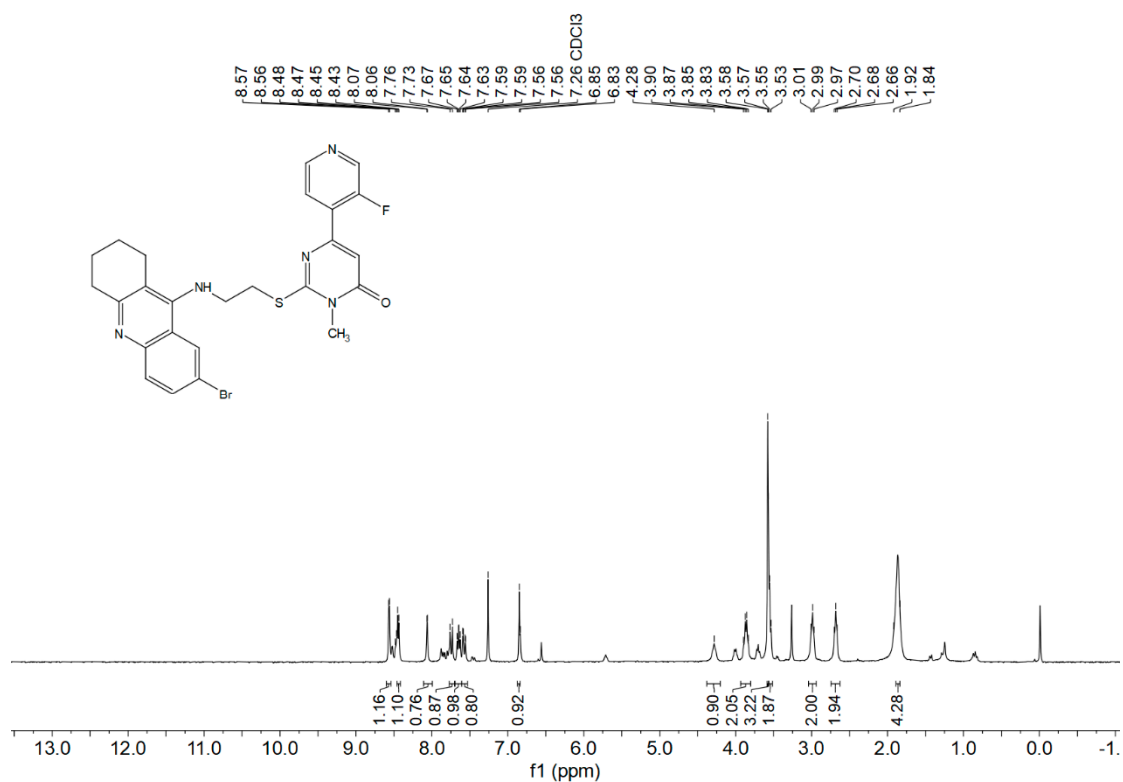


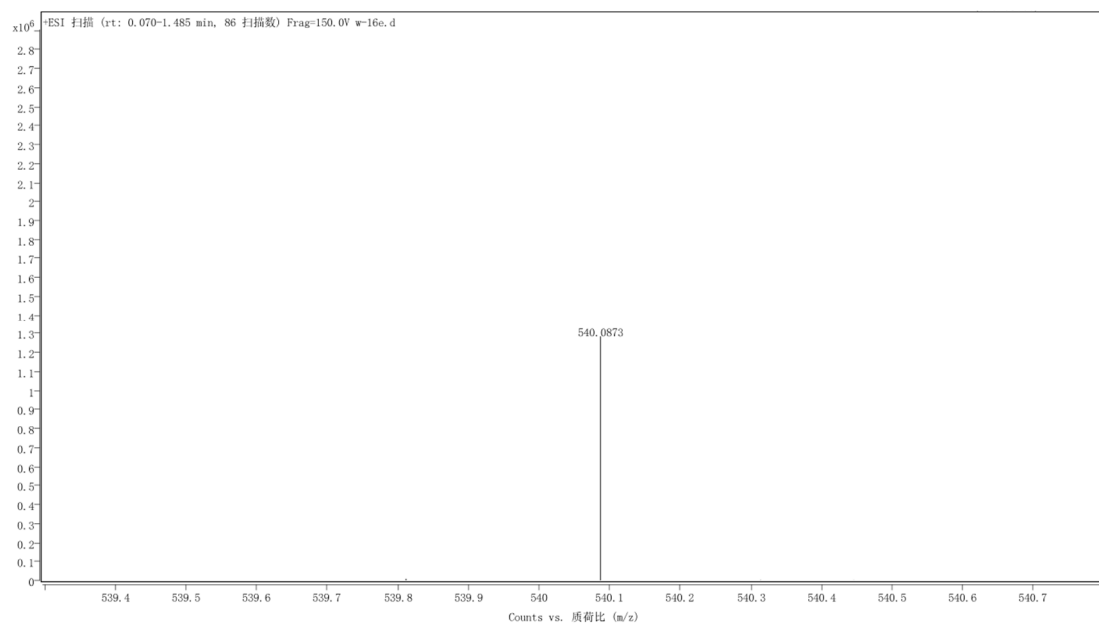
NMR and HRMS of compound **16d**



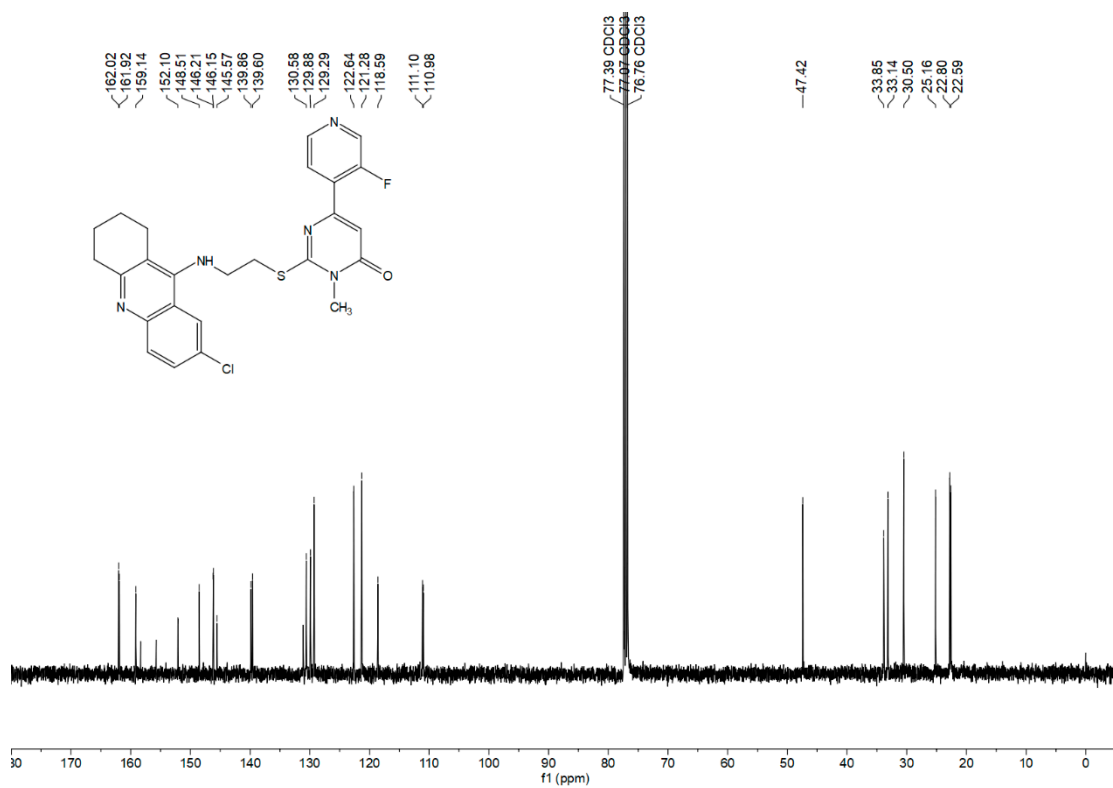
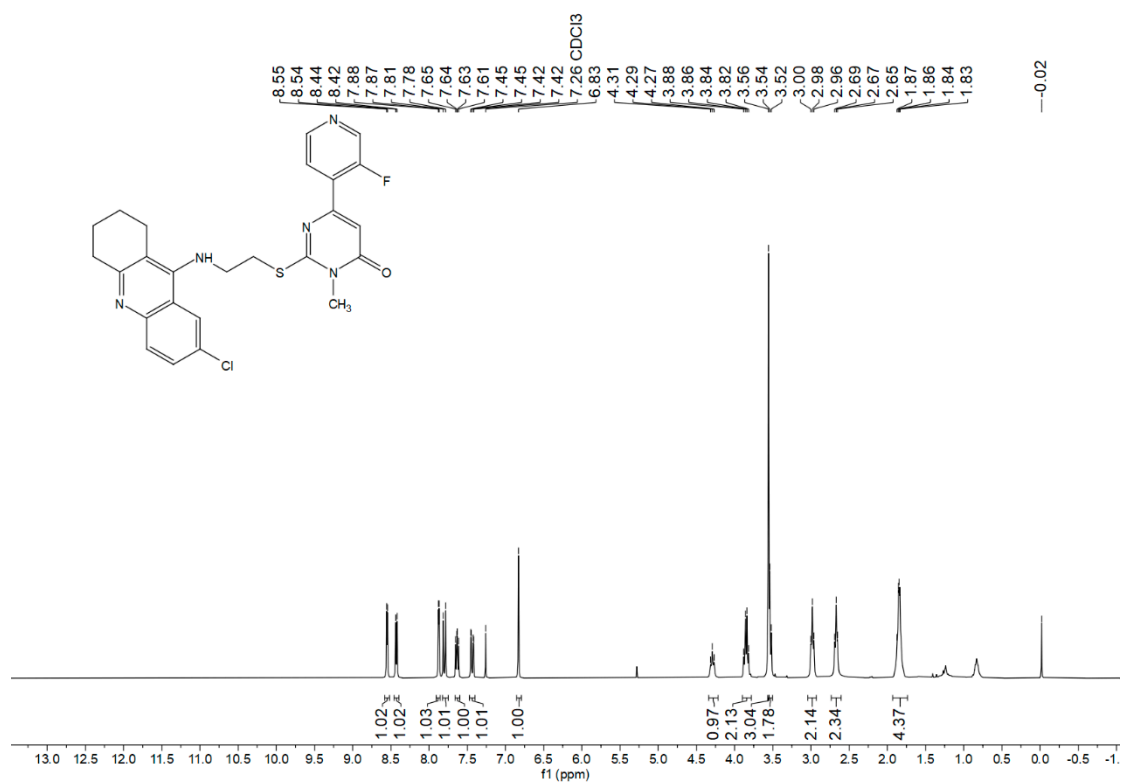


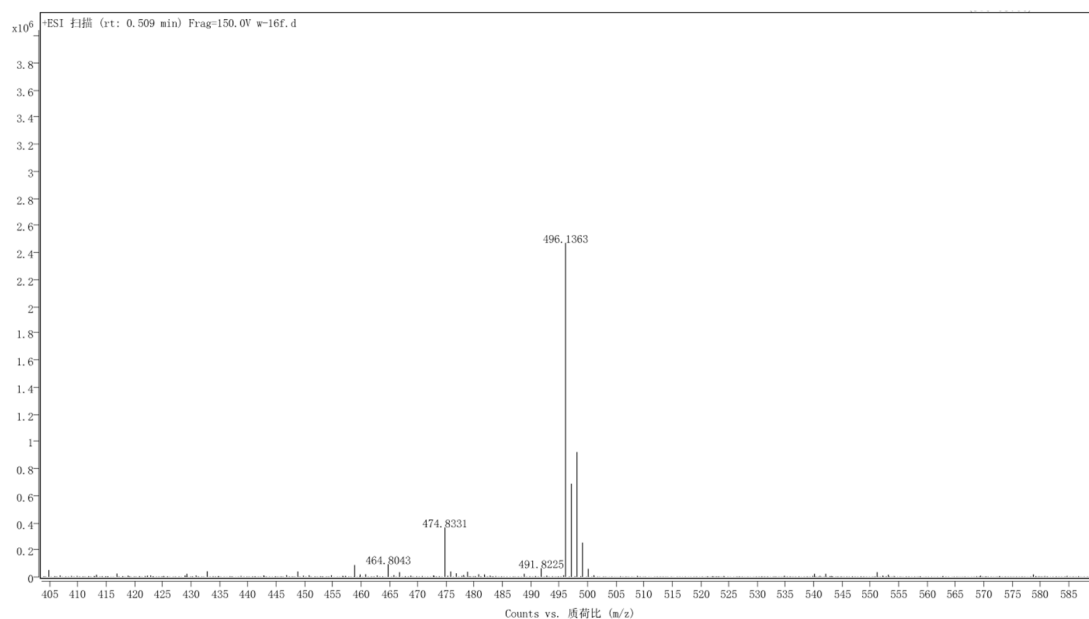
NMR and HRMS of compound **16e**



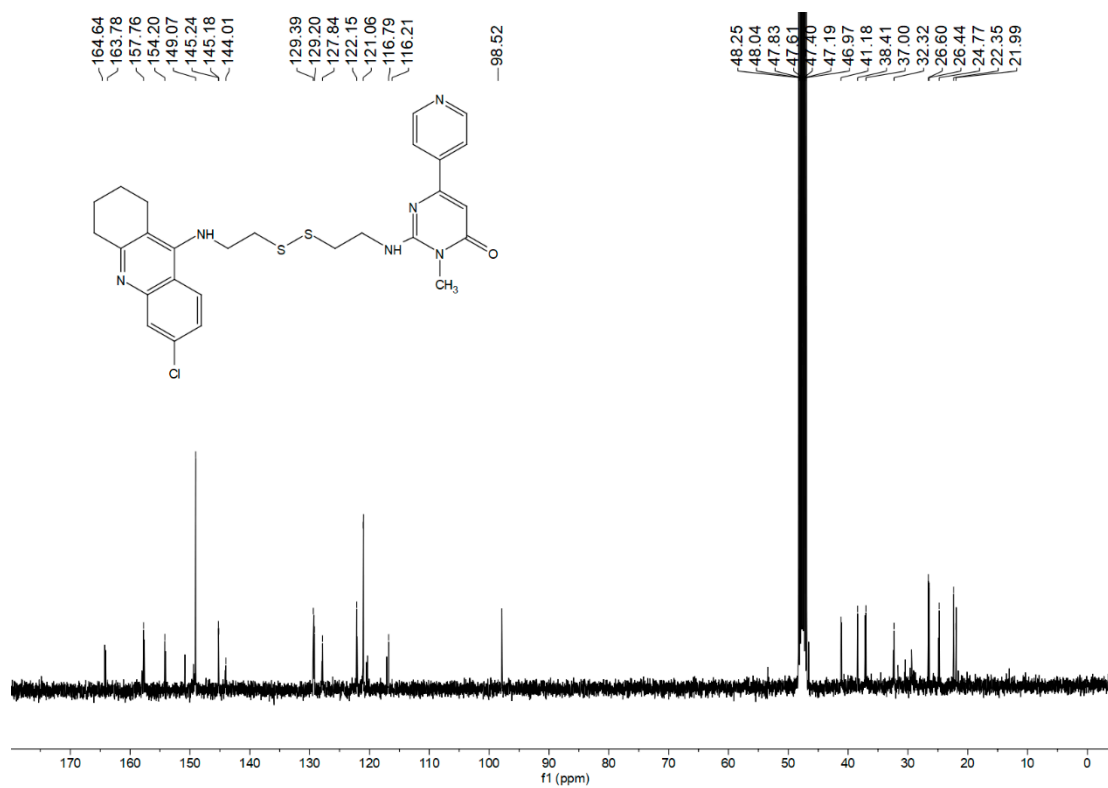
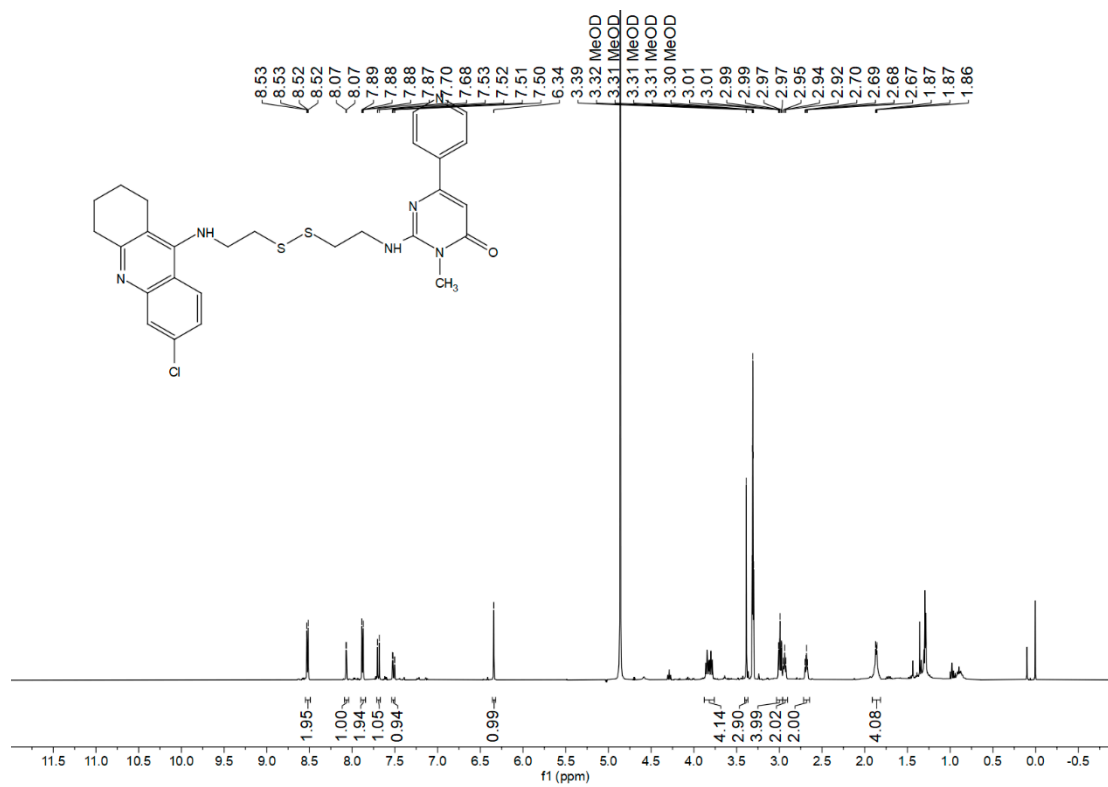


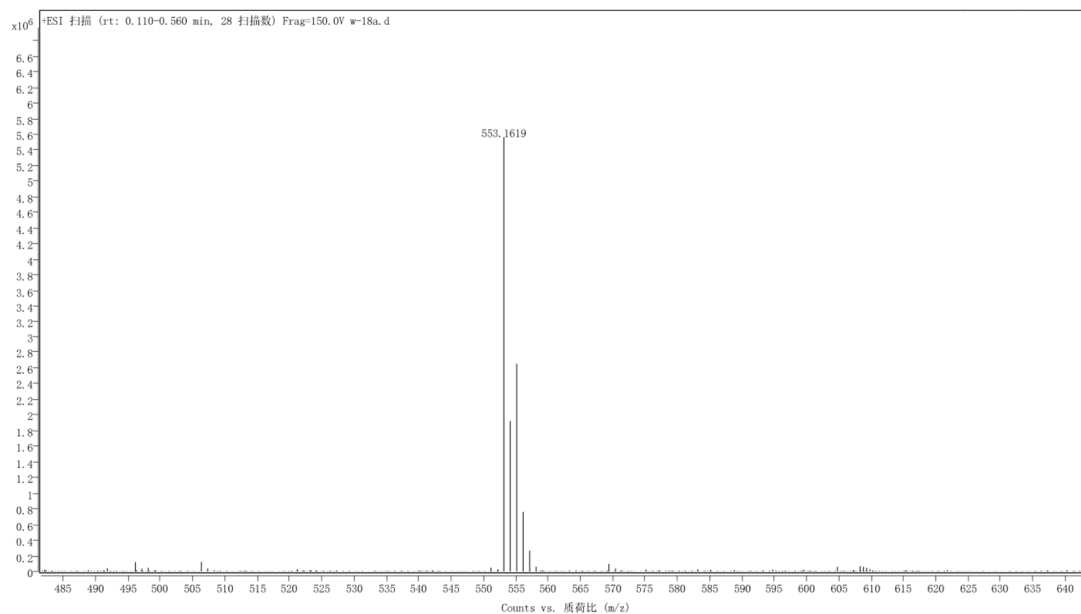
NMR and HRMS of compound **16f**



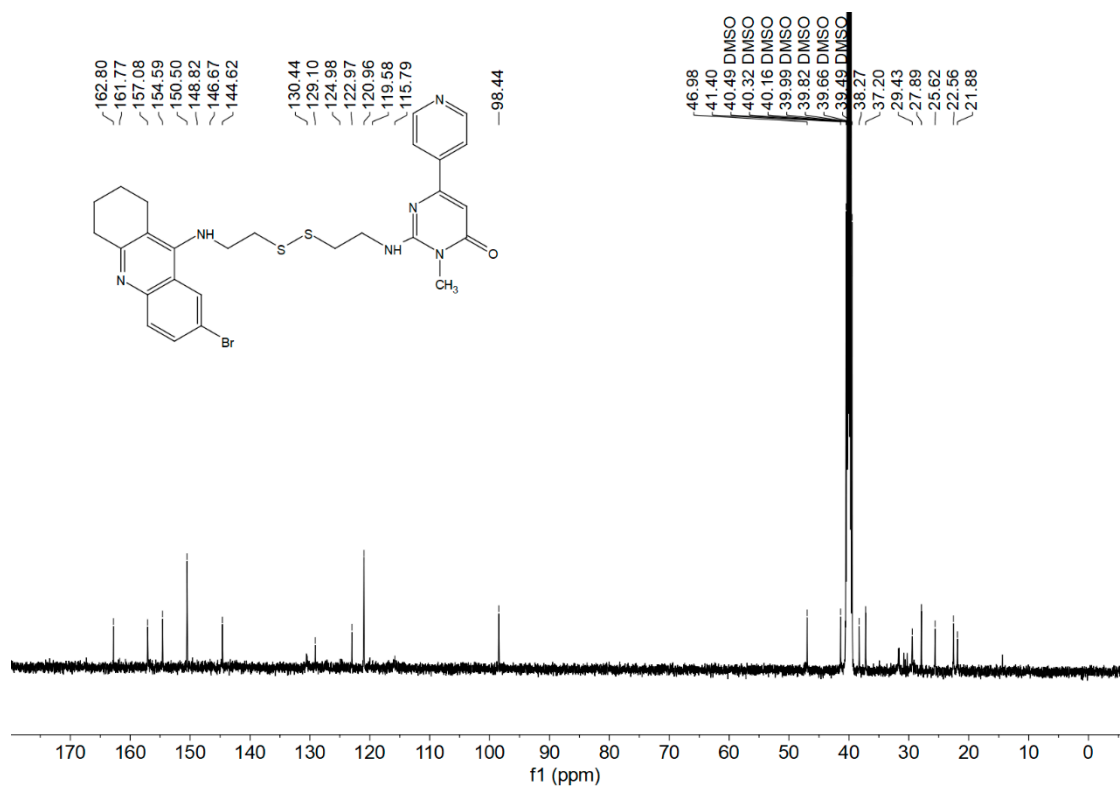
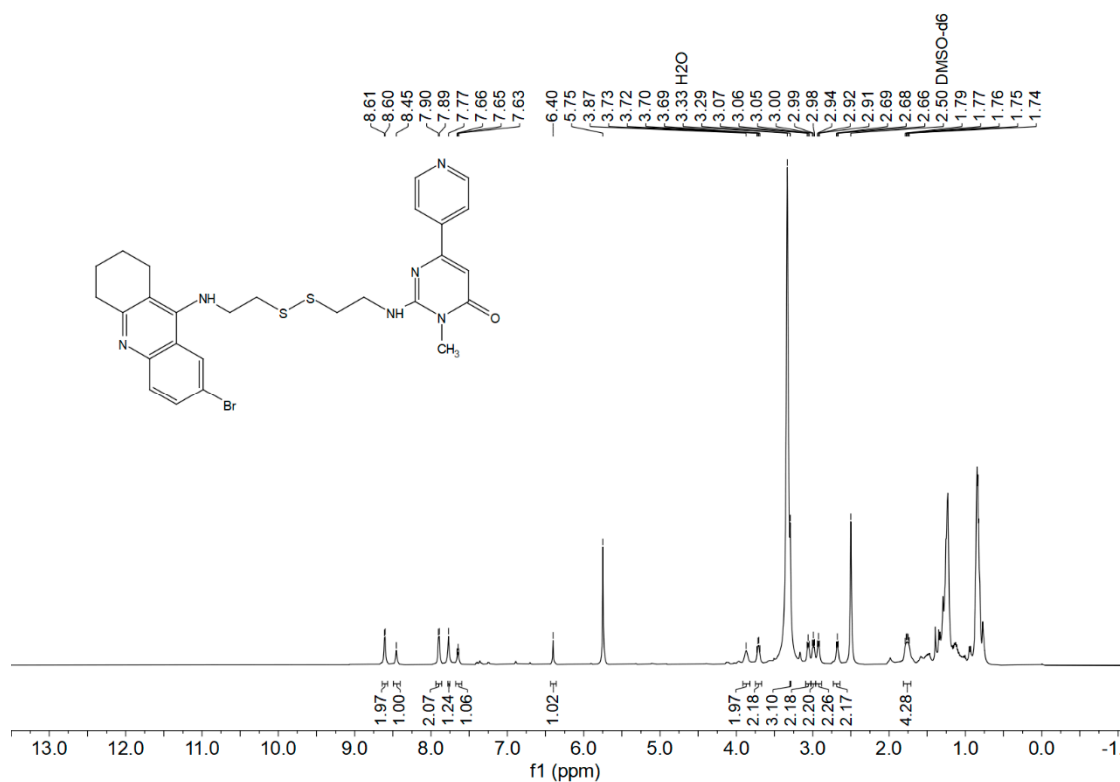


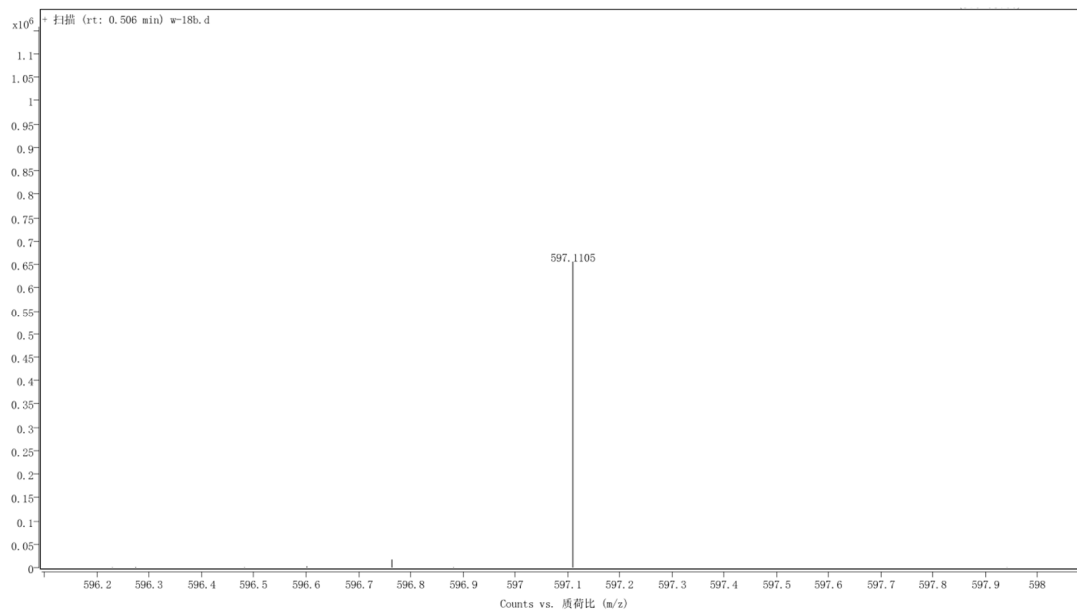
NMR and HRMS of compound **18a**





NMR and HRMS of compound **18b**





NMR and HRMS of compound **18c**

