Synthesis and Biological Evaluation of 2,2-Dimethylbenzopyran Derivatives as Potent Neuroprotection Agents

Fangyu Du [a], Qifan Zhou [a], Xiaoxiao Fu [b], Yajie Shi [a], Yuanguang Chen [a], Wuhong Fang [a], Jingyu Yang †[b], Guoliang Chen †[a]

[a] Key Laboratory of Structure-Based Drug Design & Discovery of Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, P. R. of China

[b] Department of Pharmacology, Shenyang Pharmaceutical University, Shenyang 110016, P. R. of China

†Corresponding author:

Jingyu Yang: yangjingyu2006@gmail.com; Guoliang Chen: spucgl@163.com.

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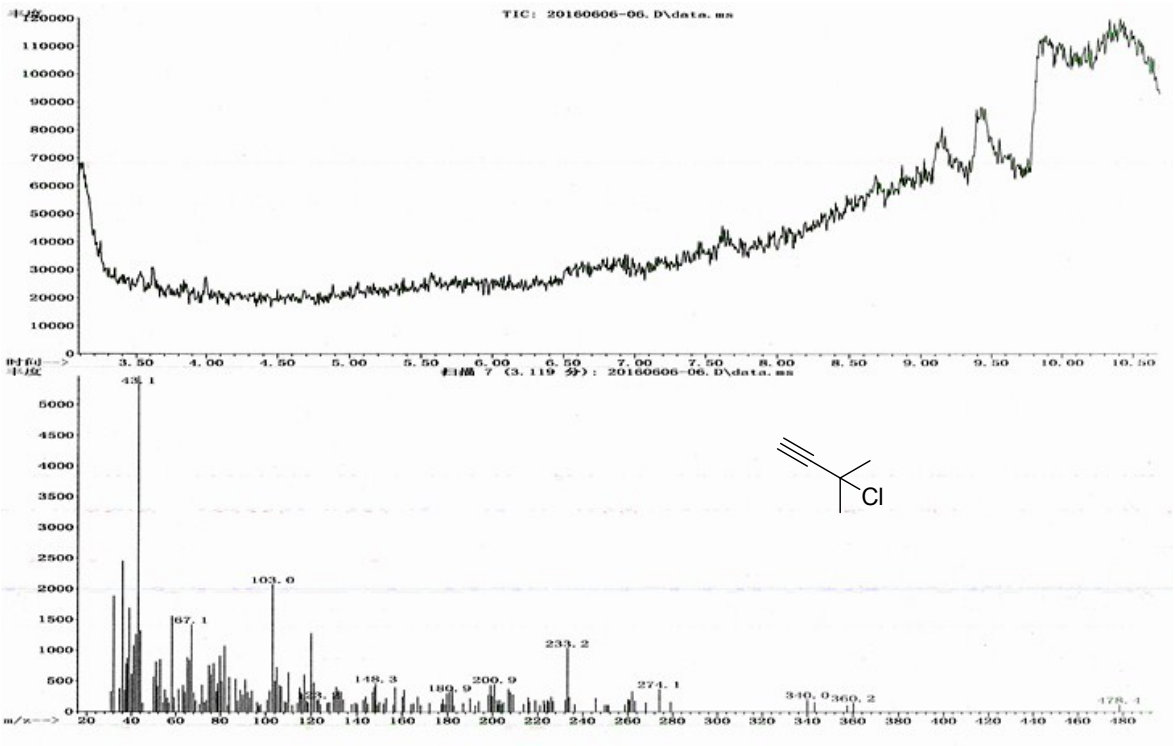
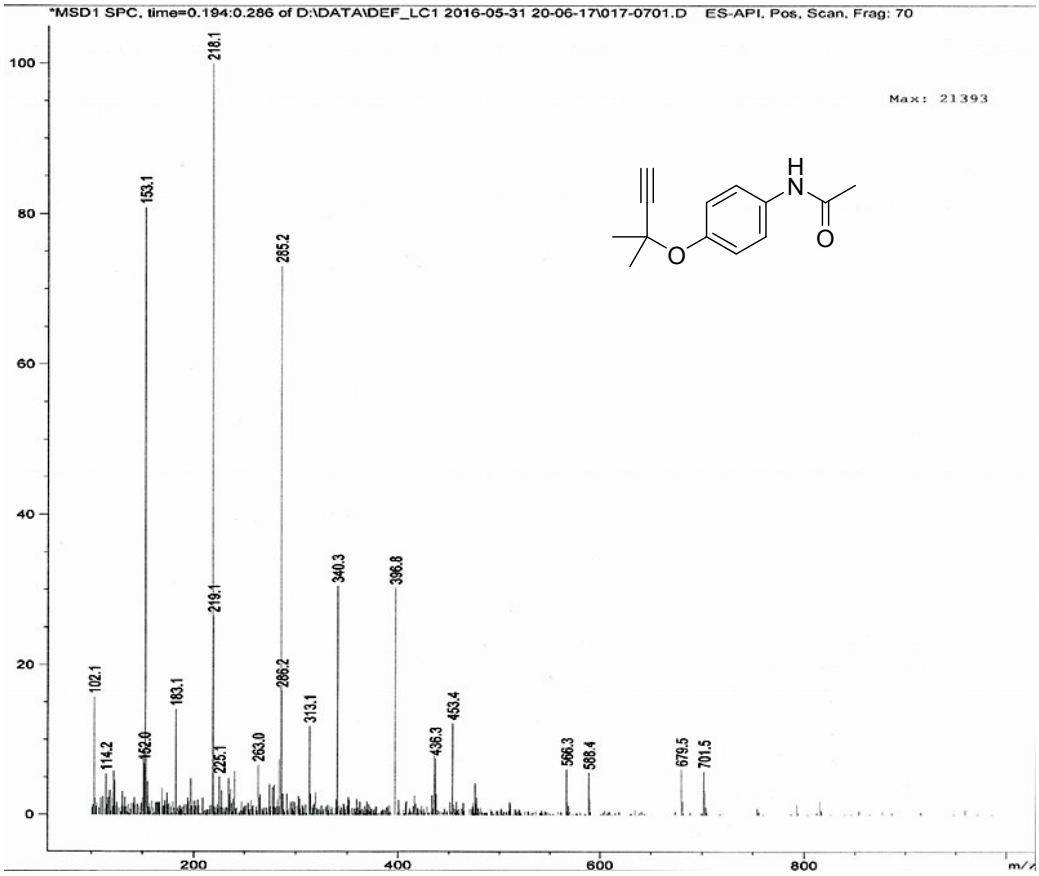
1. General procedures

All reagents used were commercially available. All the ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker 400 MHz and 600 MHz spectrometer in DMSO-d_6. Chemical shifts (δ) were expressed in parts per million using tetramethylsilane as an internal reference. ESI-MS data were obtained using an Agilent 1100 instrument. LC-MS-ESI was recorded by Agilent 1100 Series MSD Trap (SL). GC-MS-ESI was recorded by Agilent 6890-5975 GC-MS. Melting points were measured on X-4 digital melting point instrument. The purity was determined by Shimadzu LC-2010AHT high performance liquid chromatography. Reactions were monitored by thin-layer chromatography (TLC) and visualized by UV-light. Column chromatography was performed on silica gel (160-200 mesh).

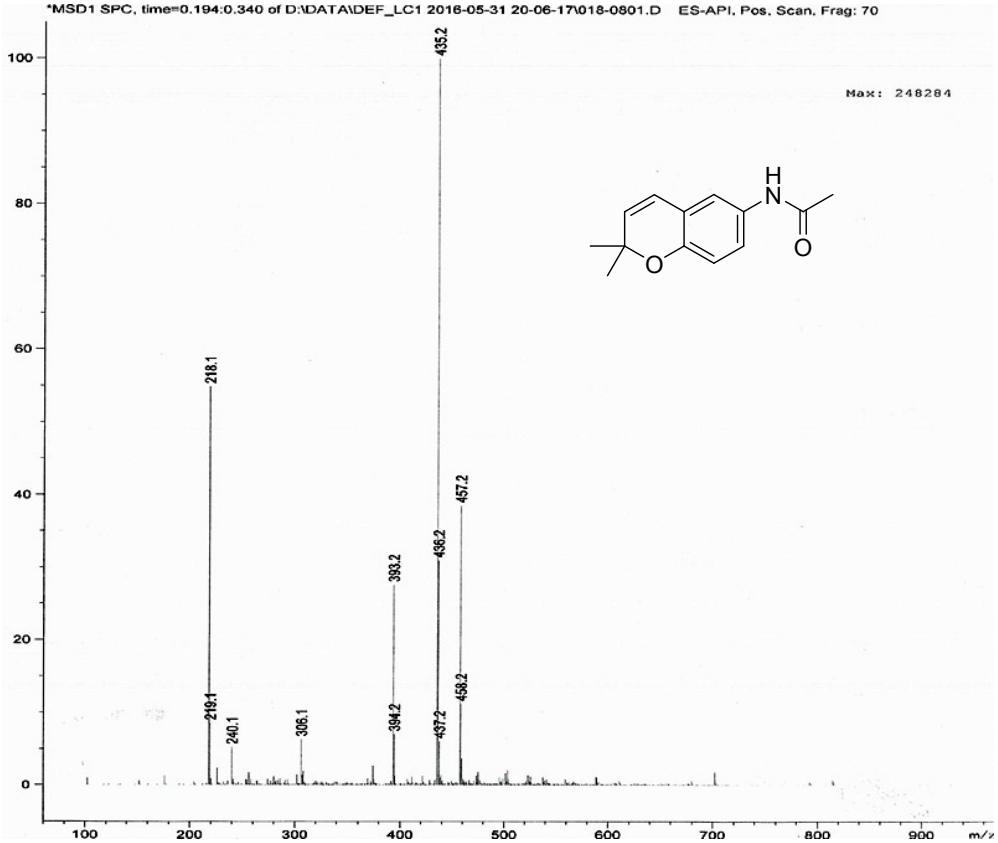
2. GC-MS spectrum of 3-Chloro-3-methylbut-1-yne (3)



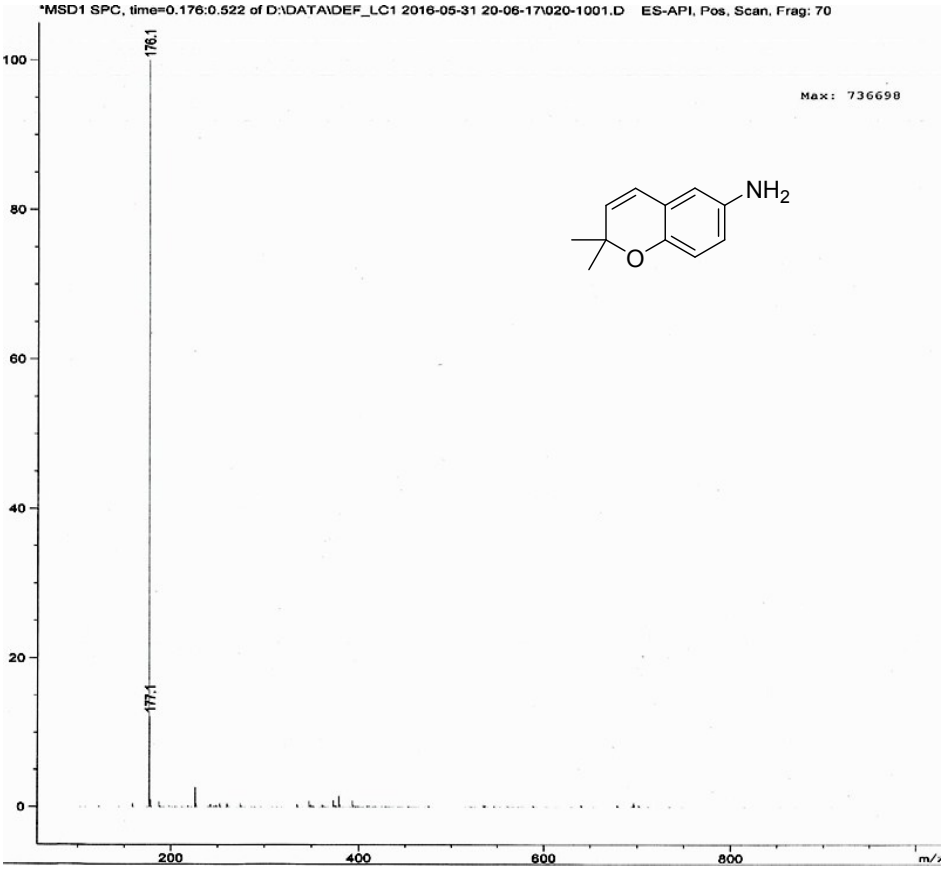
3. LC-MS spectrum of *N*-(4-((2-methylbut-3-yn-2-yl)oxy)phenyl)acetamide (7)



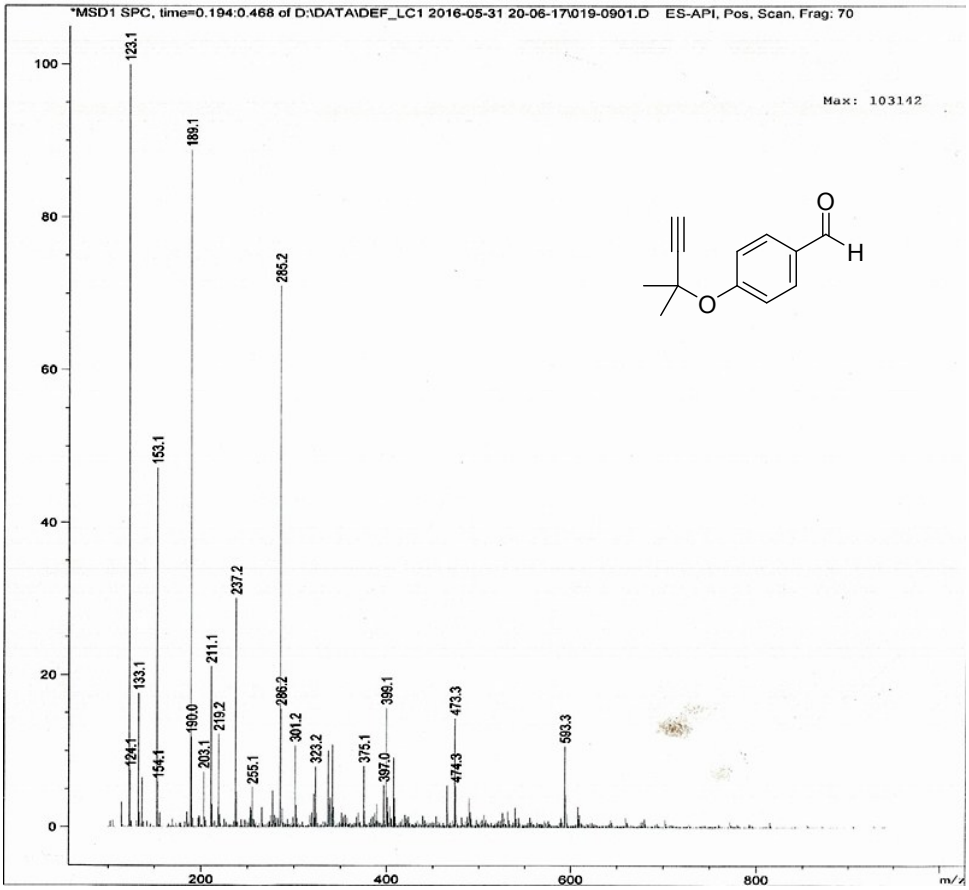
4. LC-MS spectrum of *N*-(2,2-dimethyl-2H-chromen-6-yl)acetamide (8)



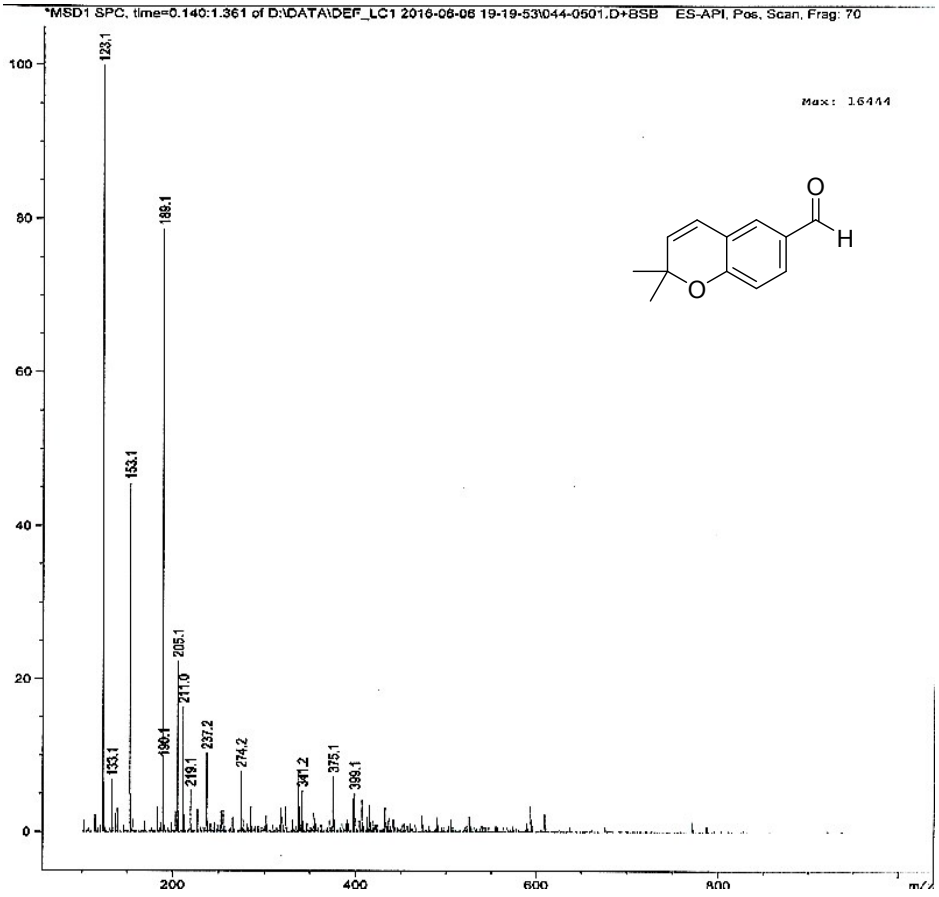
5. LC-MS spectrum of 2,2-dimethyl-2*H*-chromen-6-amine (9)



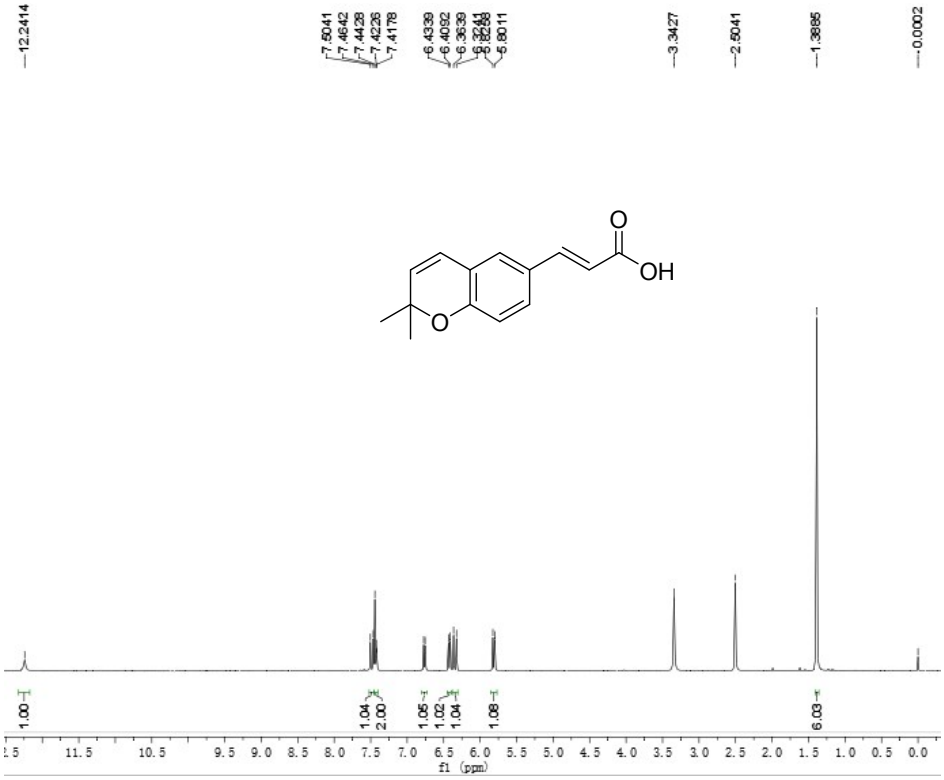
6. LC-MS spectrum of 4-((2-methylbut-3-yn-2-yl)oxy)benzaldehyde (11)



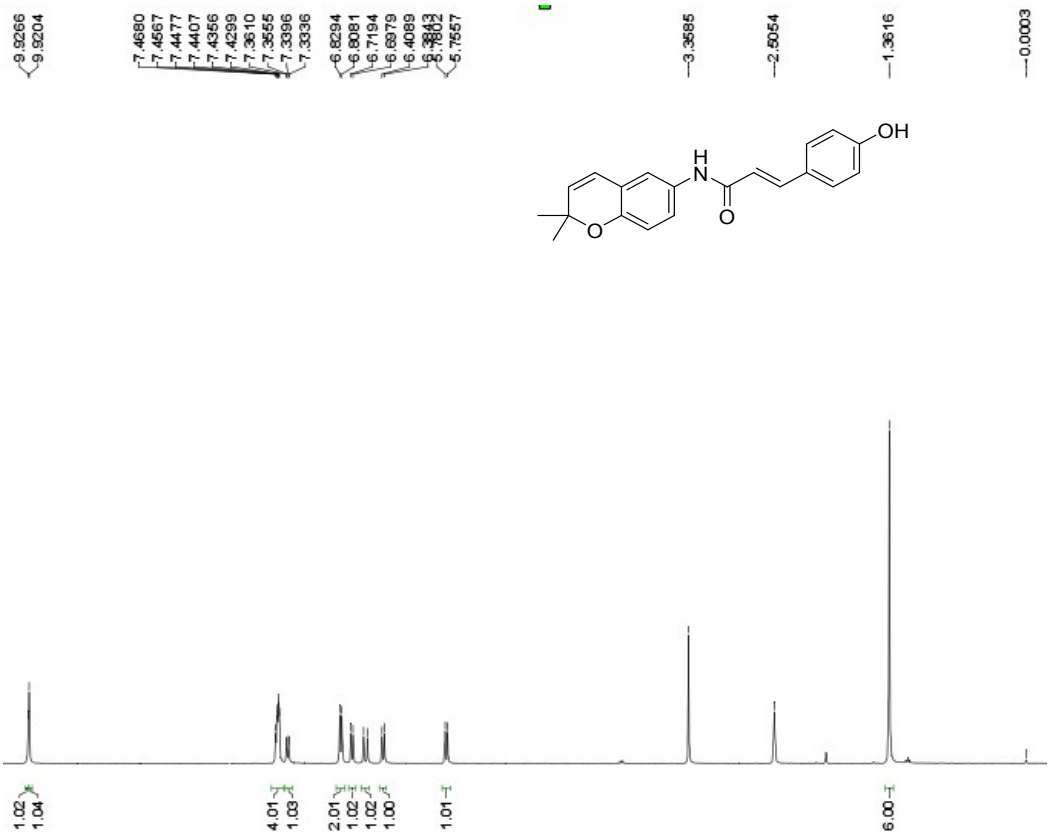
7. LC-MS spectrum 2,2-dimethyl-2*H*-chromene-6-carbaldehyde (12)



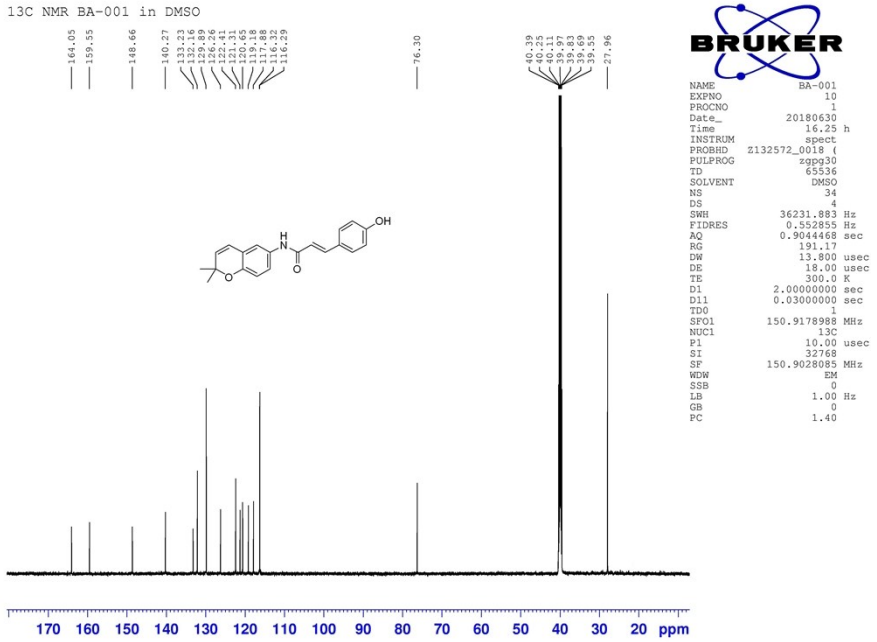
8. ^{1}H-NMR spectrum of compound 13 in $CDCl_3$



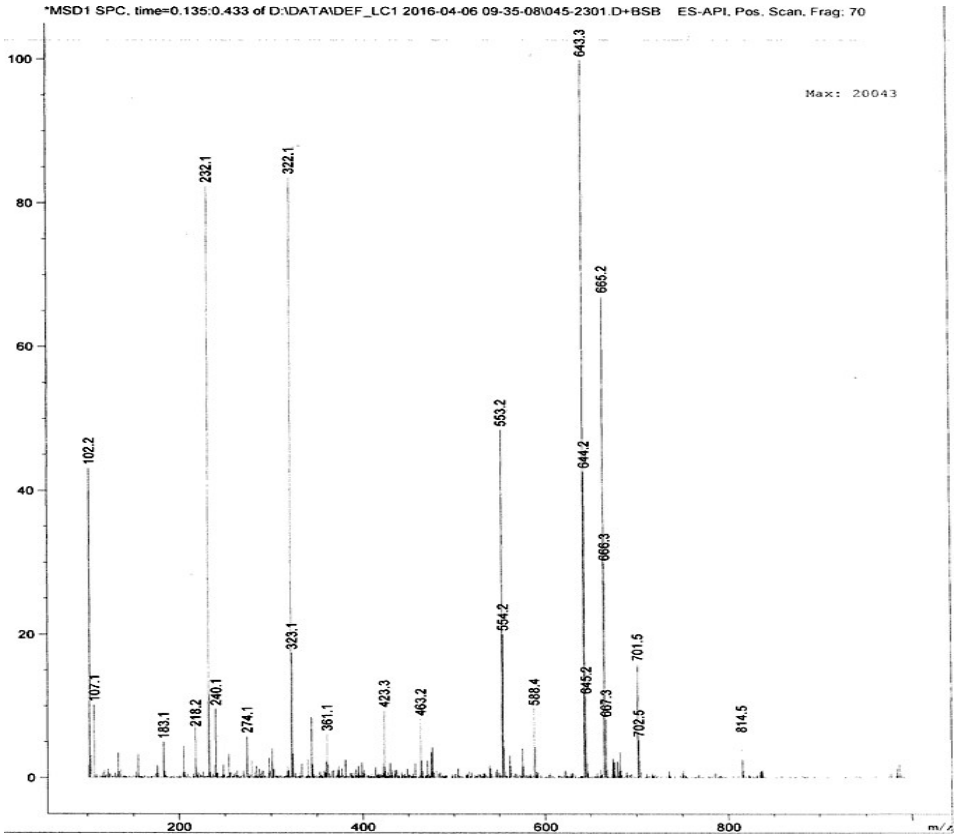
9. ^{1}H, ^{13}C NMR spectra and MS spectra of BA-01~BA-11



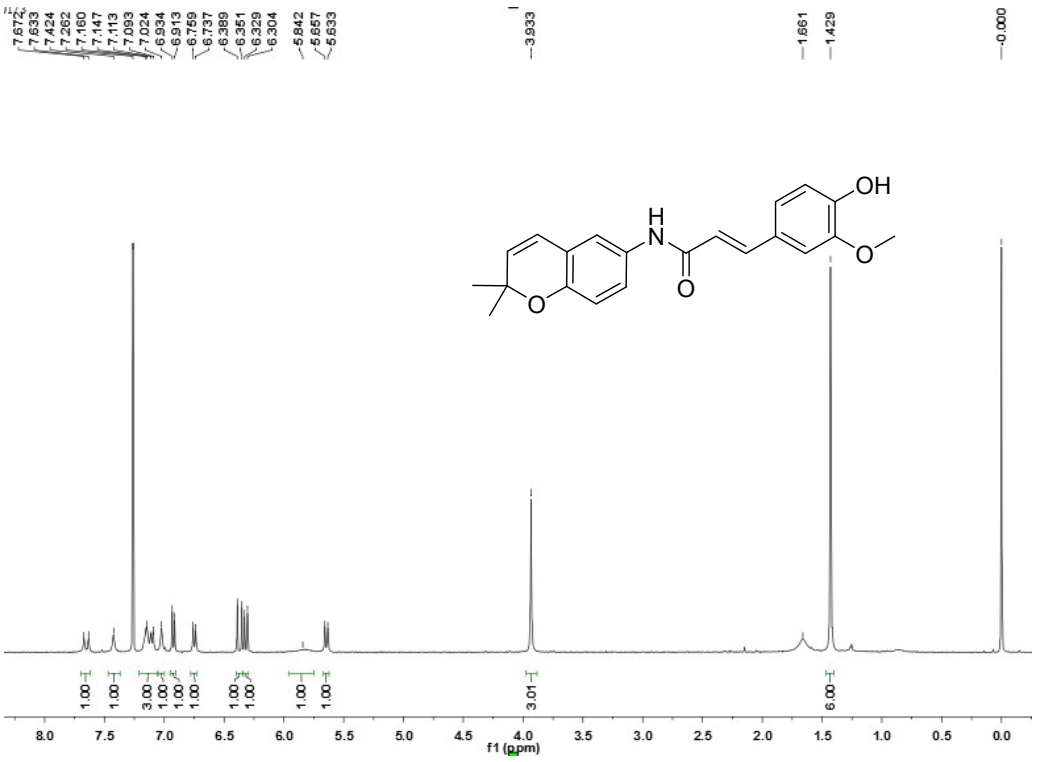
^{1}H-NMR spectrum of compound **BA-01** in DMSO-d_6



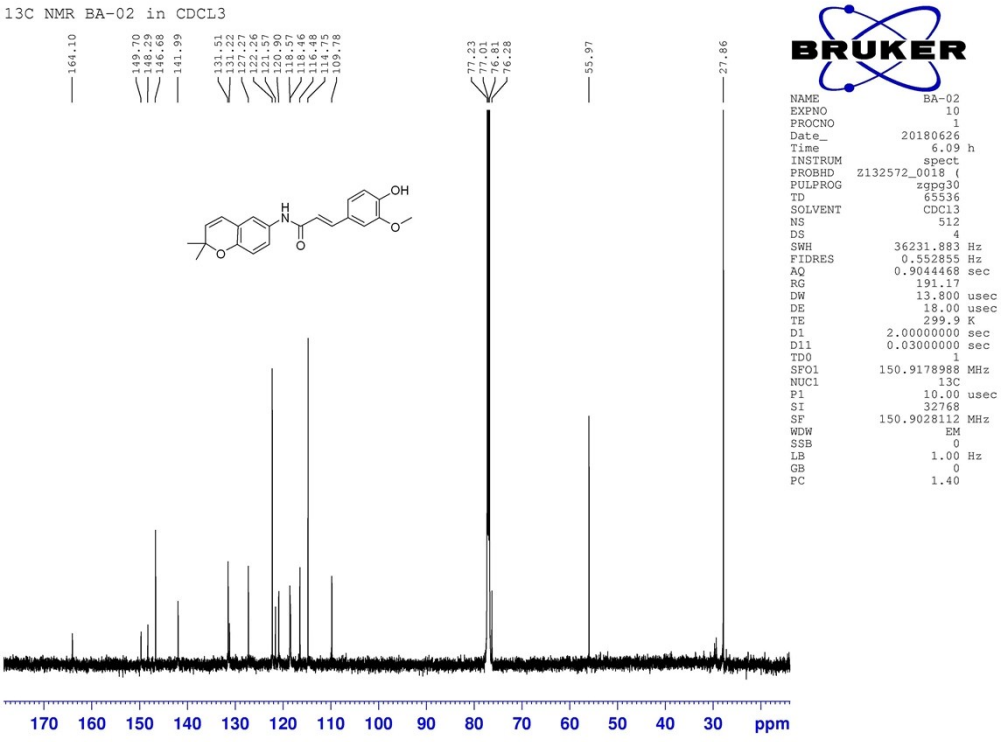
^{13}C-NMR spectrum of compound **BA-01** in DMSO-d_6



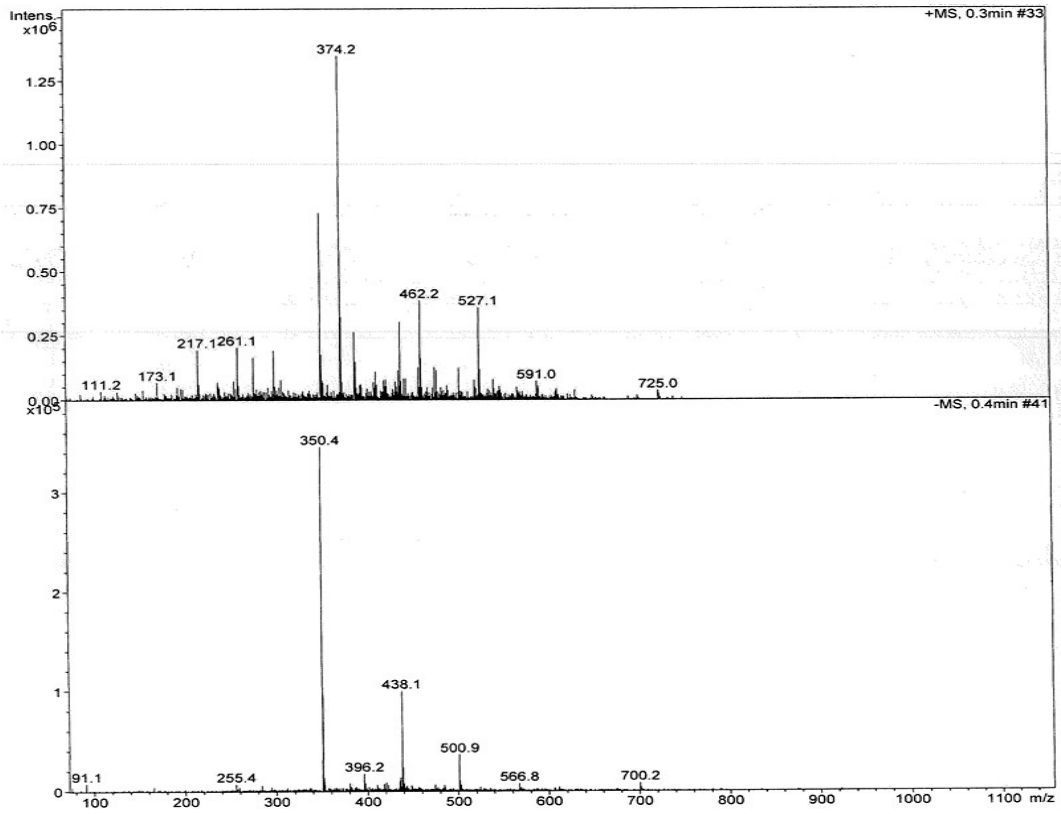
LC-MS spectrum of compound **BA-01**



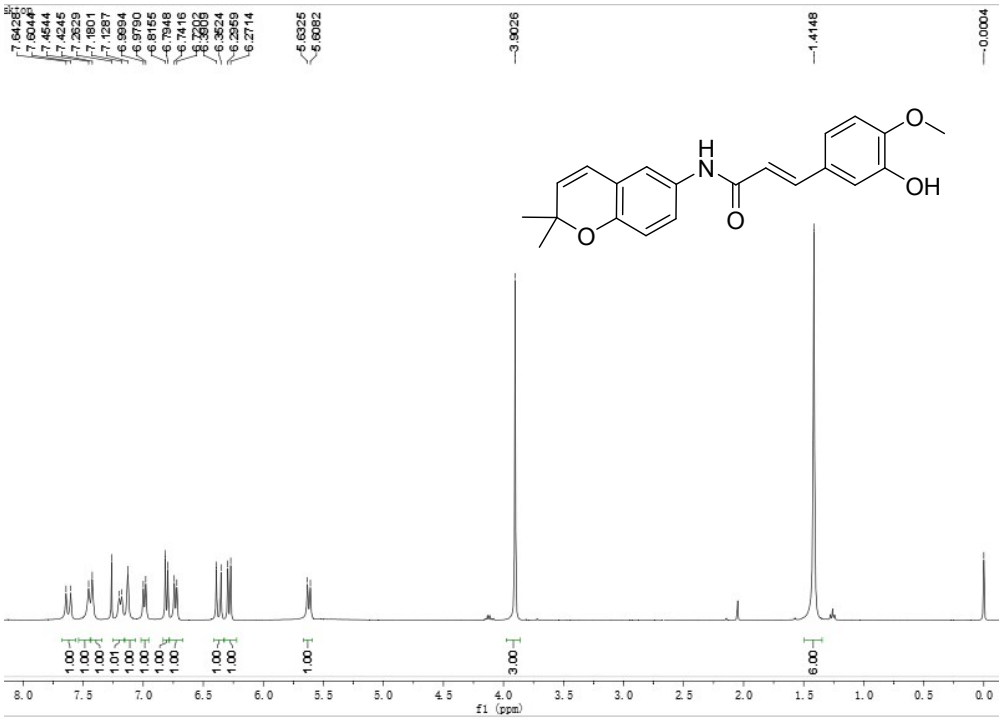
^{1}H-NMR spectrum of compound **BA-02** in $CDCl_3$



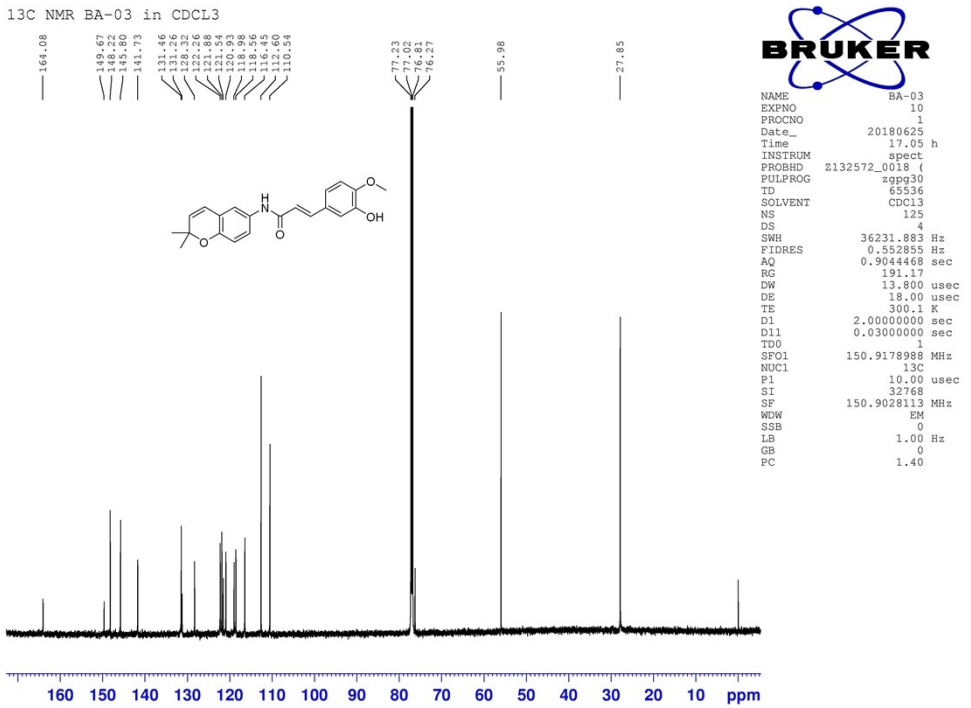
^{13}C-NMR spectrum of compound **BA-02** in $CDCl_3$



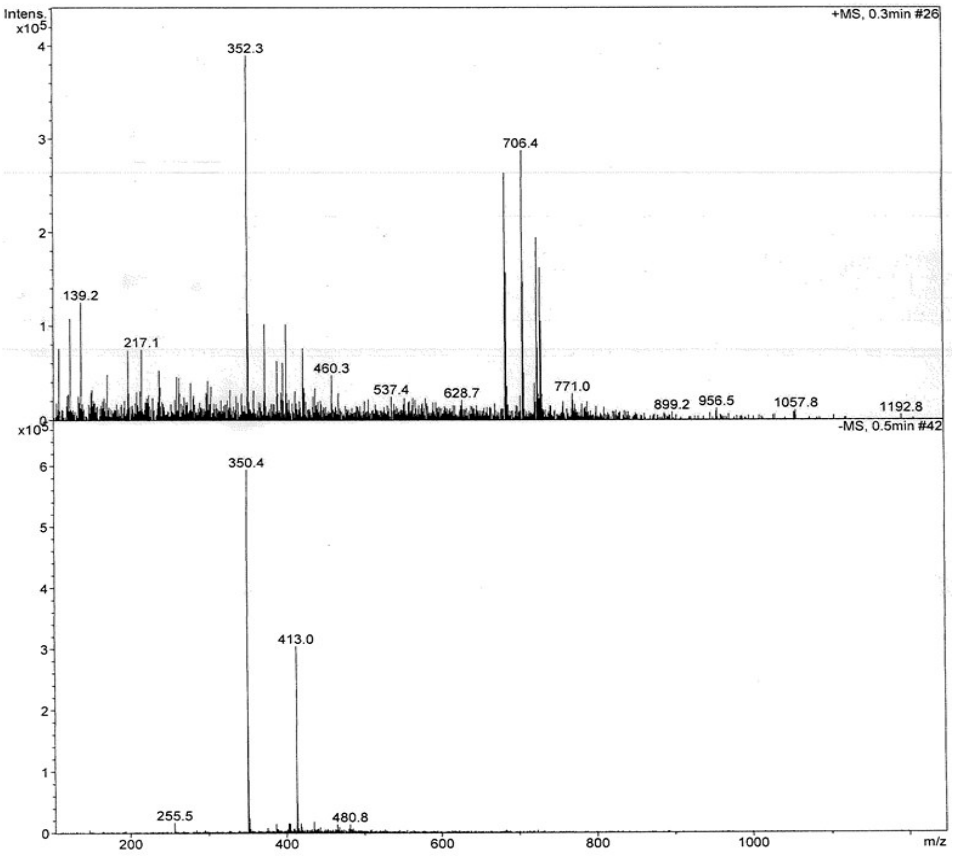
LC-MS spectrum of compound **BA-02**



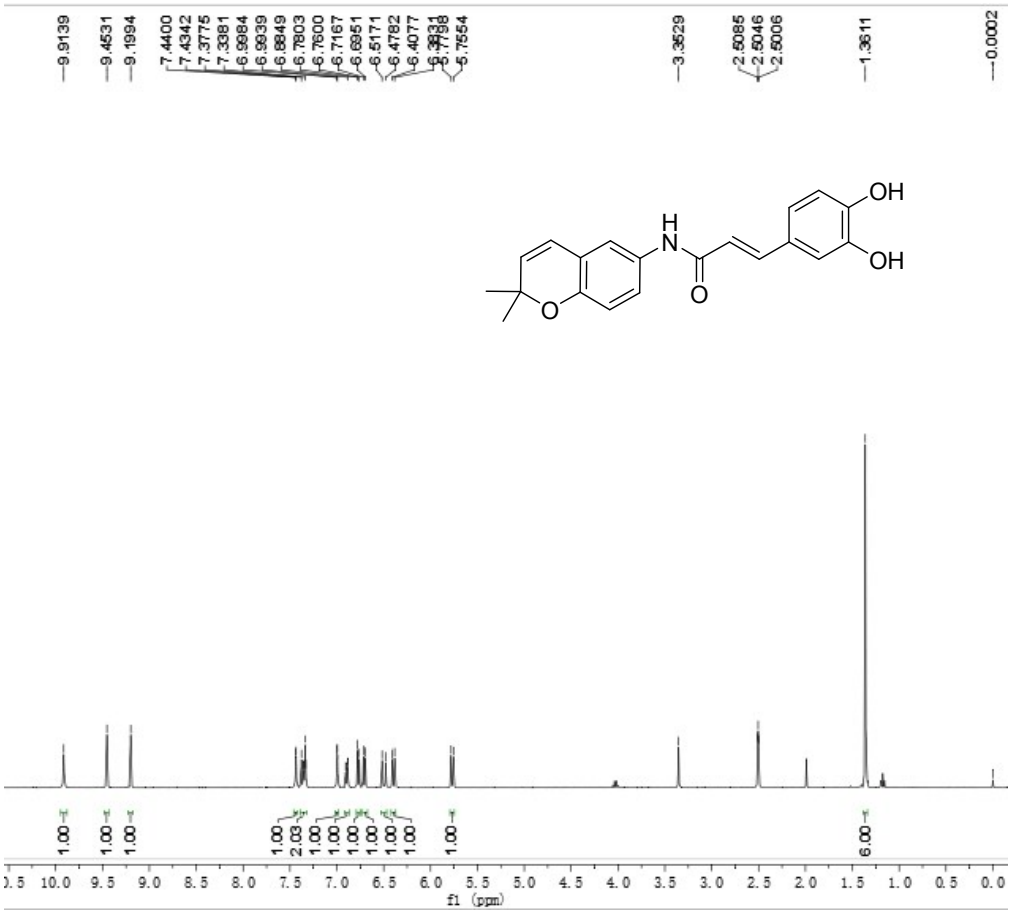
^{1}H-NMR spectrum of compound **BA-03** in $CDCl_3$



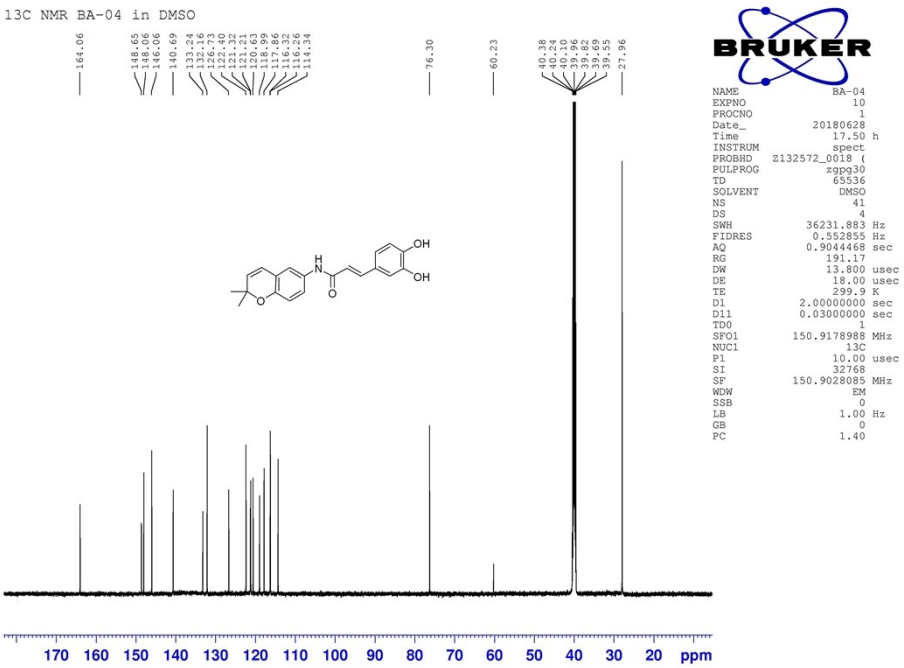
^{13}C-NMR spectrum of compound **BA-03** in $CDCl_3$



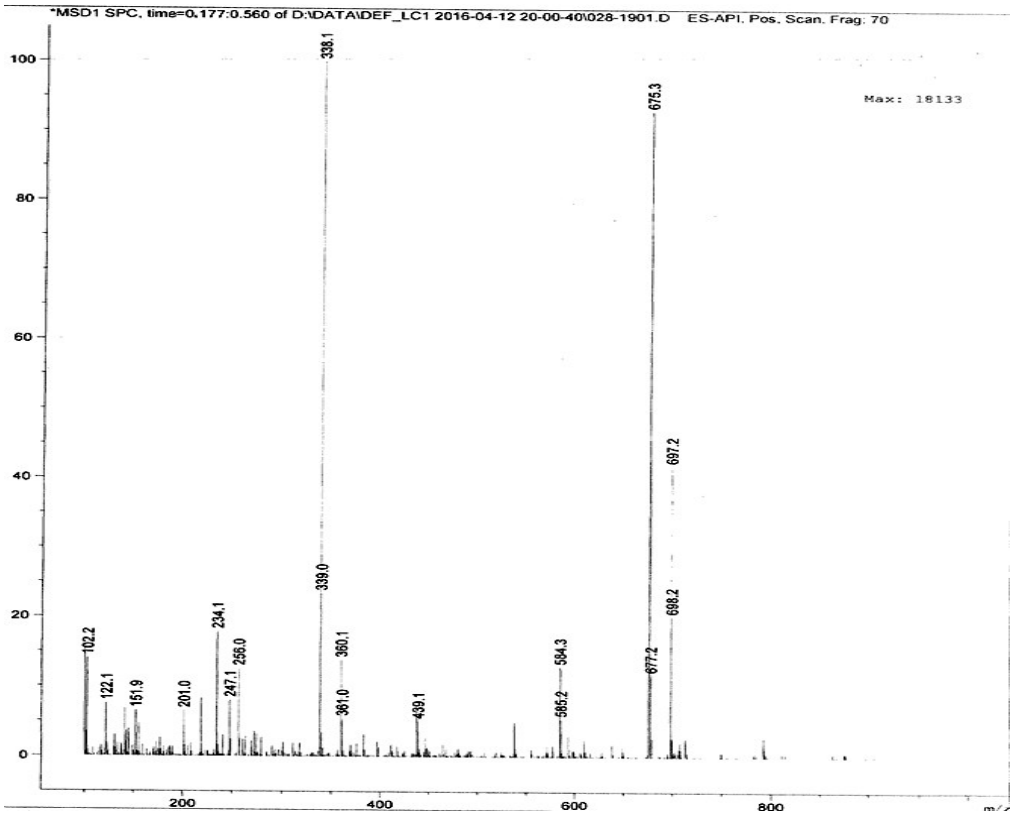
LC-MS spectrum of compound **BA-03**



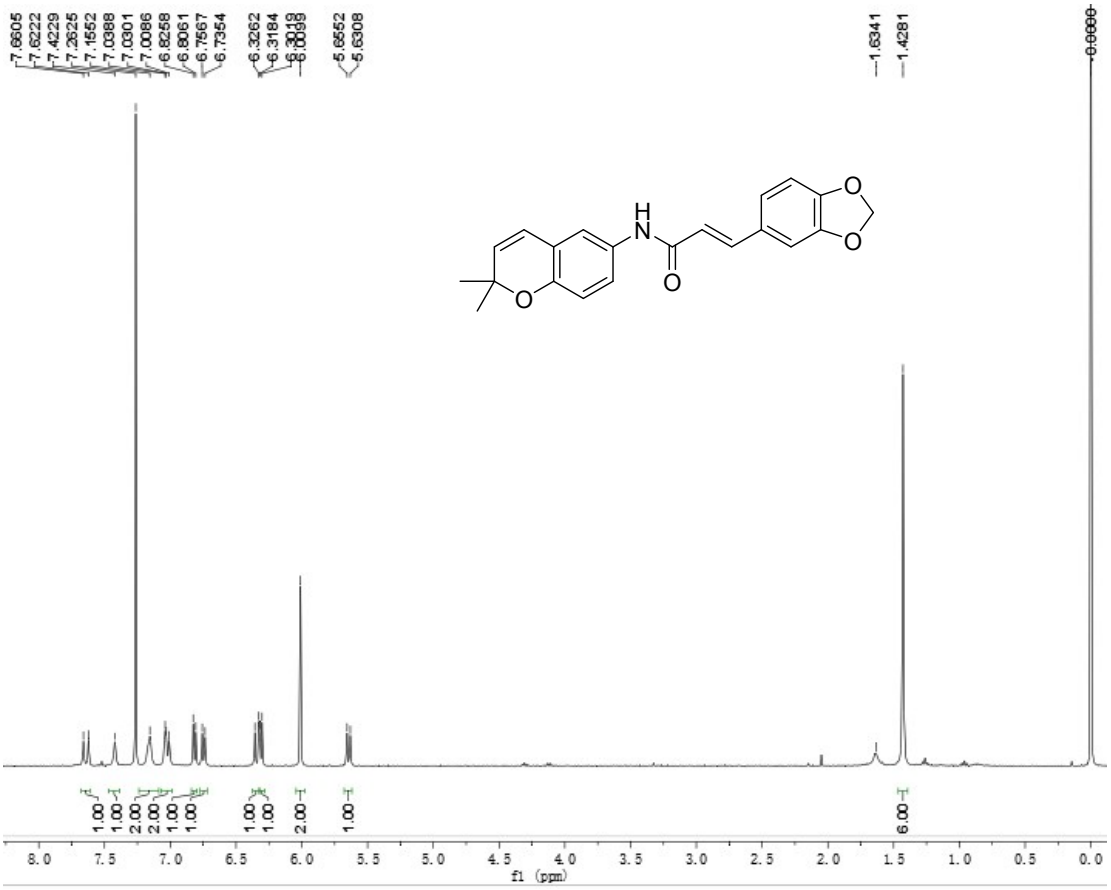
^{1}H-NMR spectrum of compound **BA-04** in DMSO-d_6



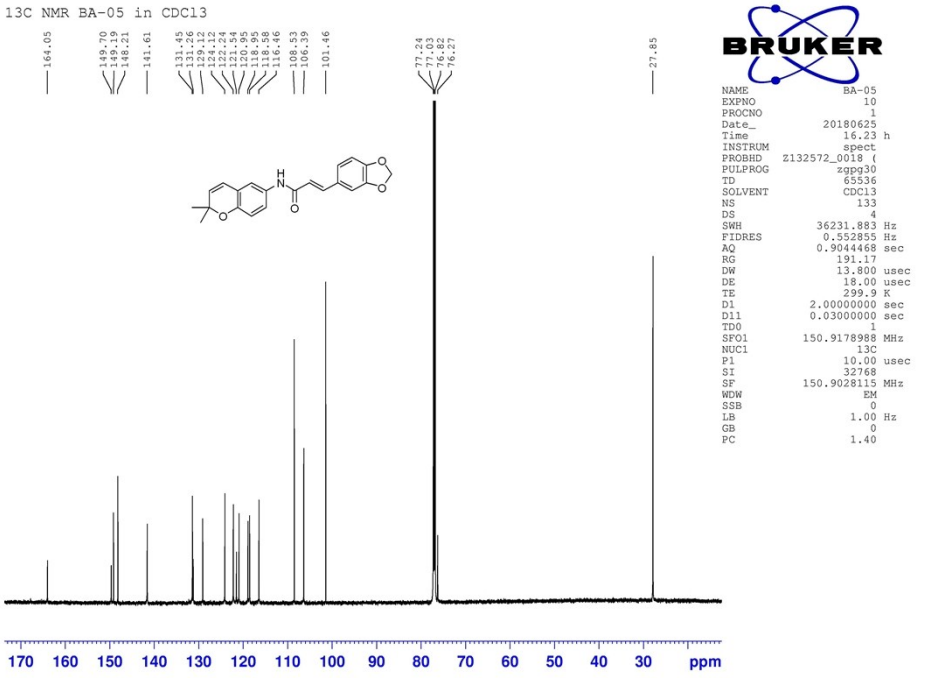
^{13}C-NMR spectrum of compound **BA-04** in DMSO-d_6



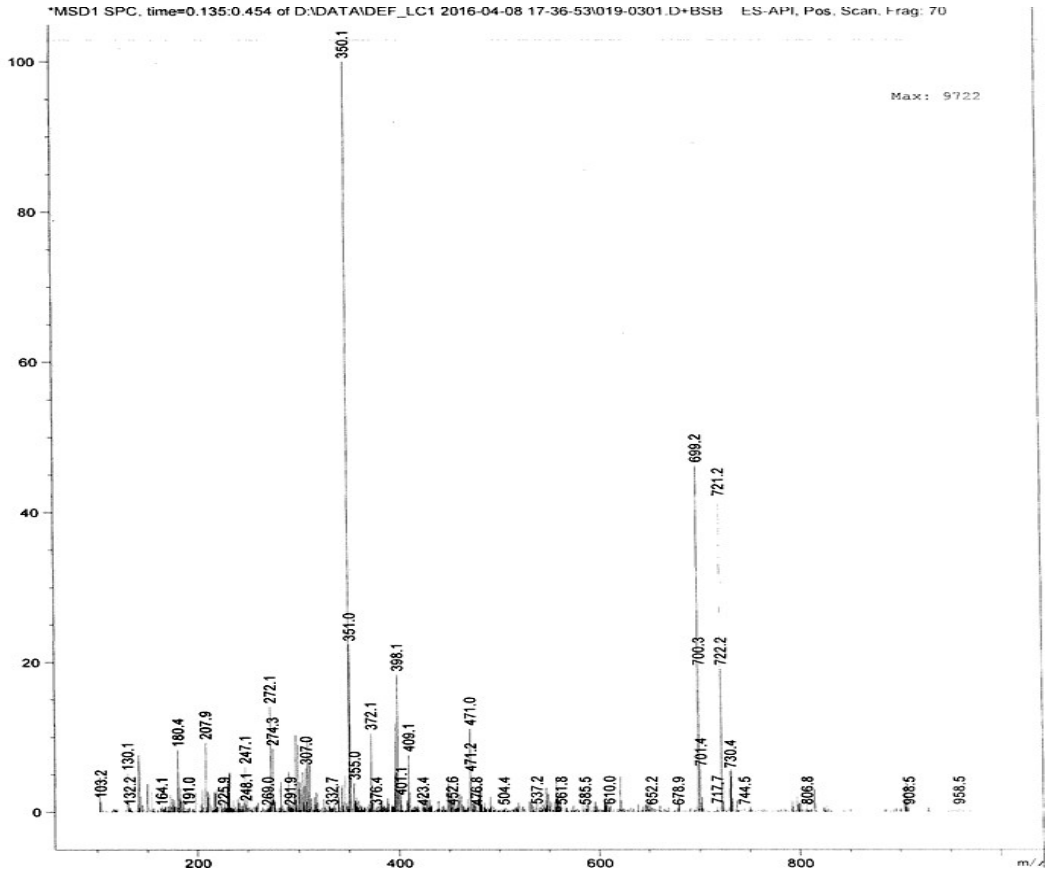
LC-MS spectrum of compound **BA-04**



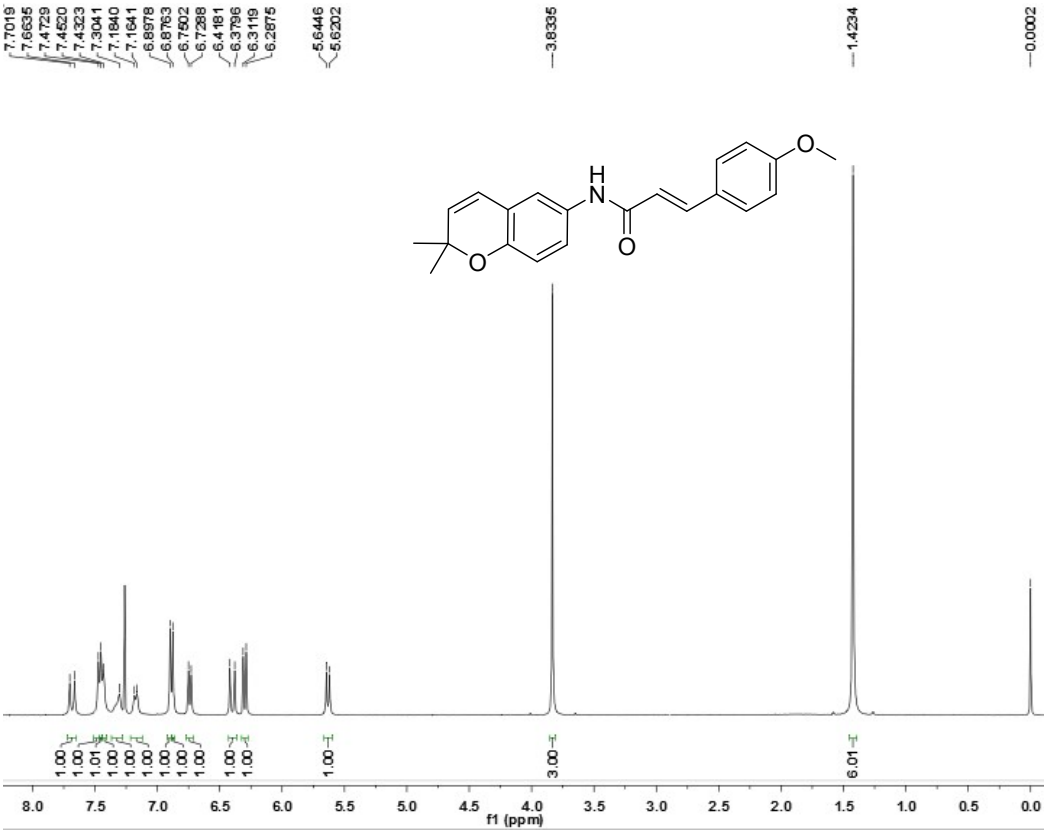
^{1}H-NMR spectrum of compound **BA-05** in $CDCl_3$



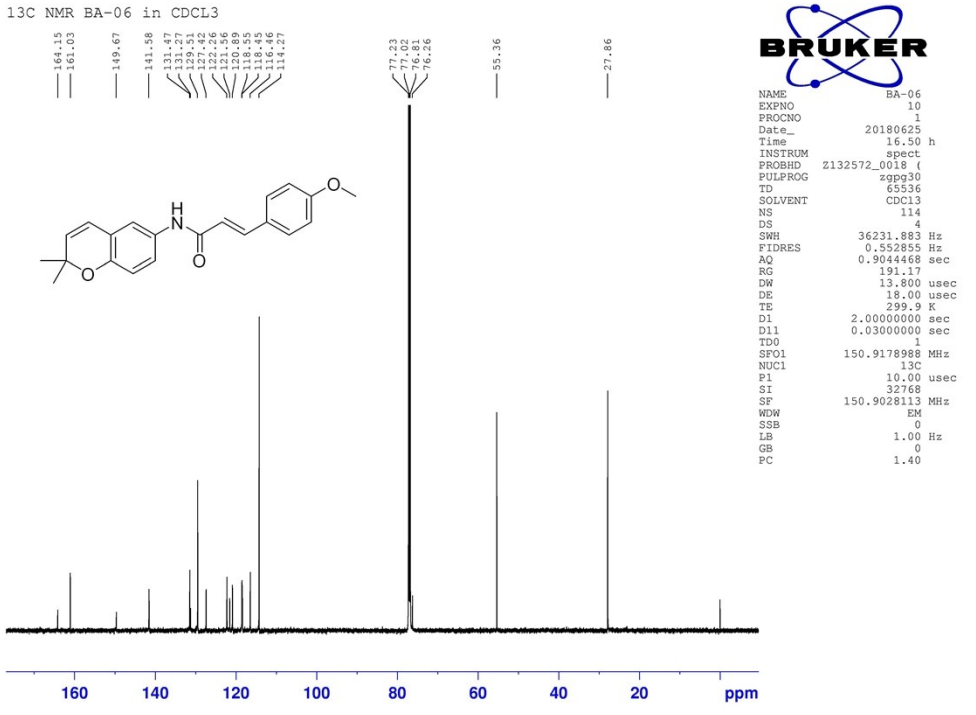
^{13}C-NMR spectrum of compound **BA-05** in $CDCl_3$



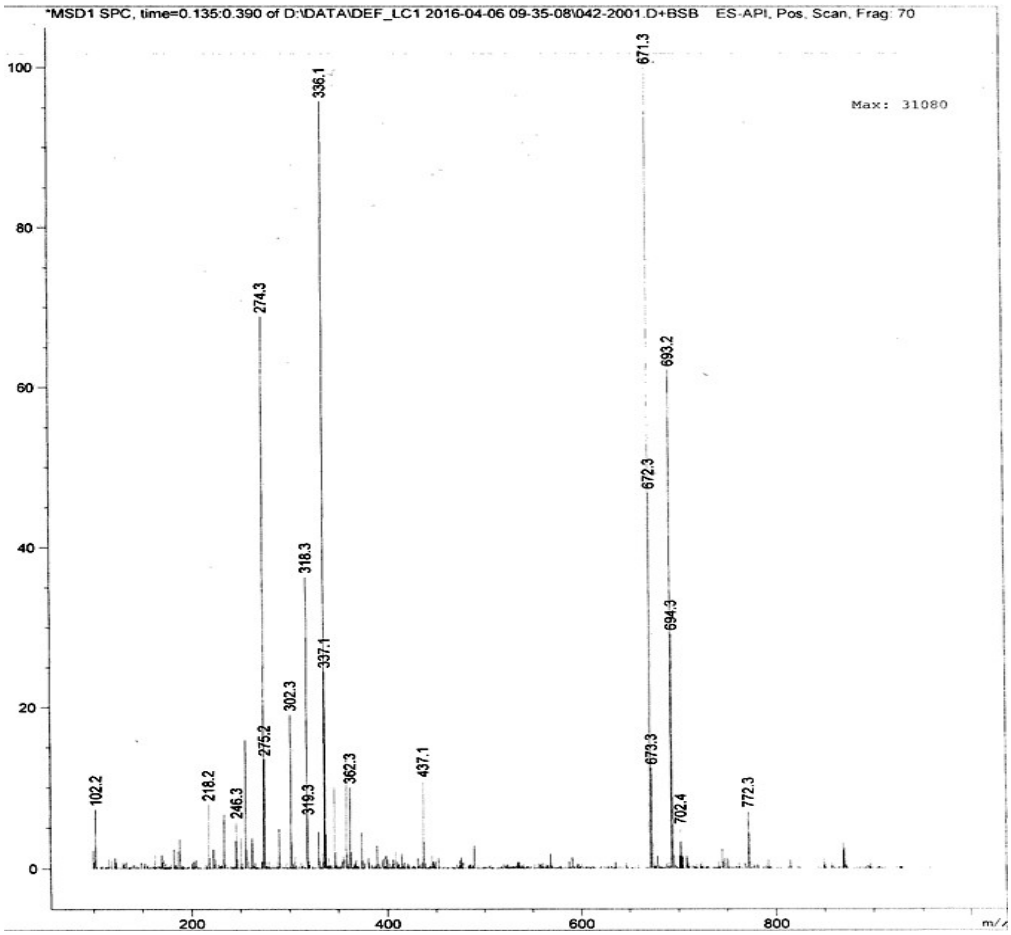
LC-MS spectrum of compound **BA-05**



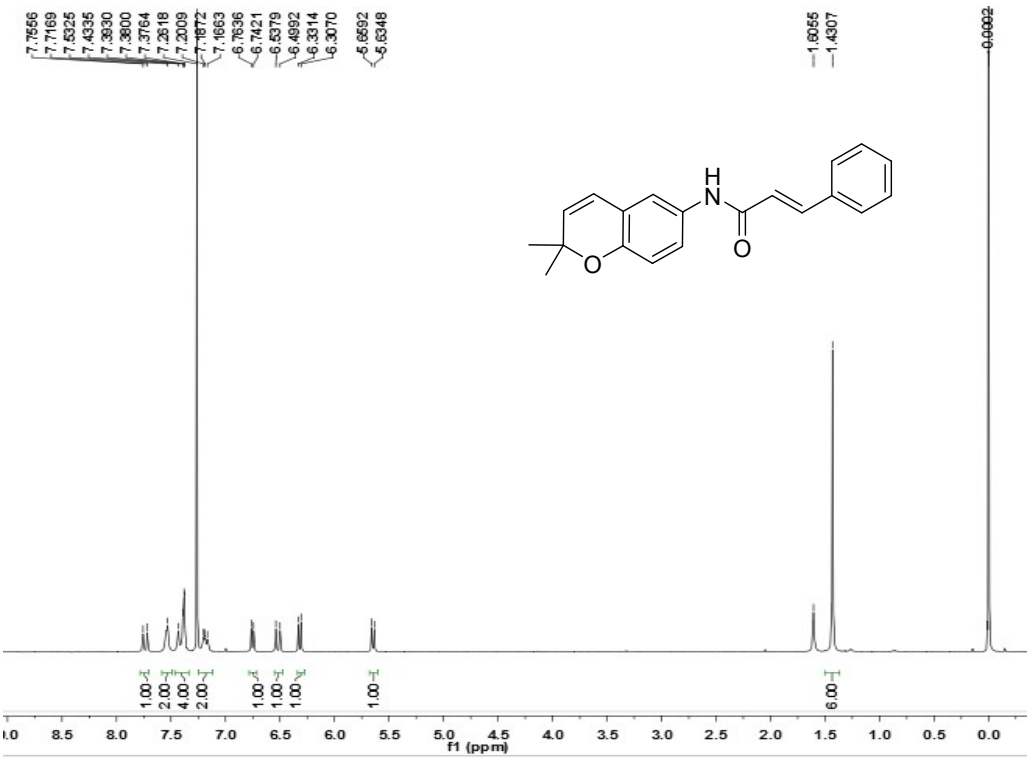
^{1}H-NMR spectrum of compound **BA-06** in $CDCl_3$



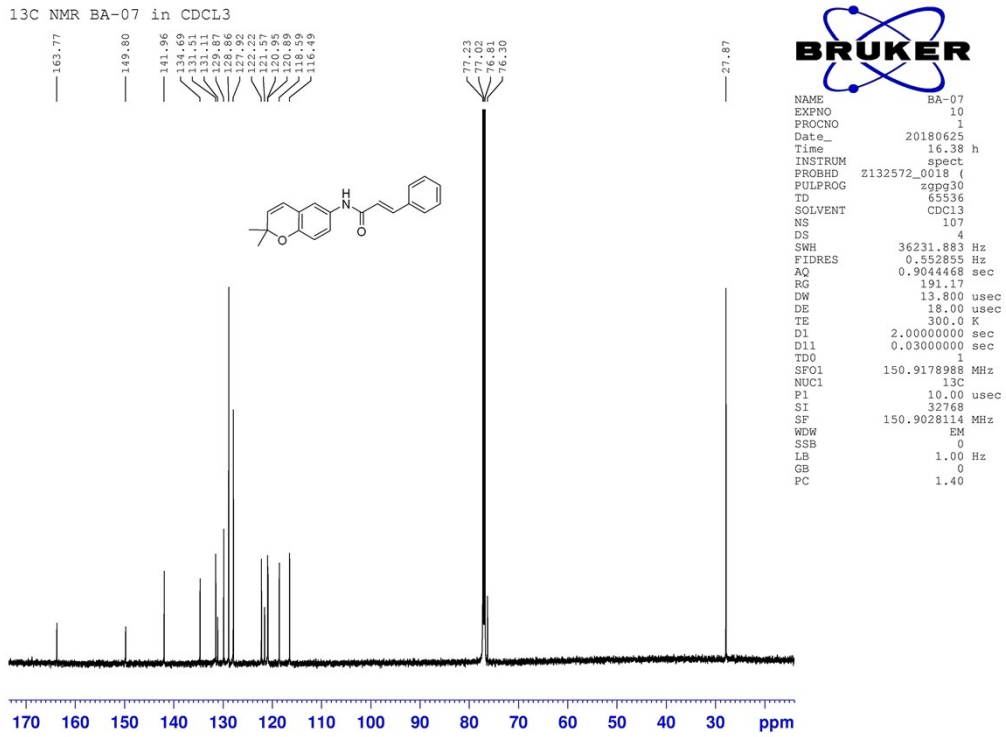
^{13}C-NMR spectrum of compound **BA-06** in $CDCl_3$



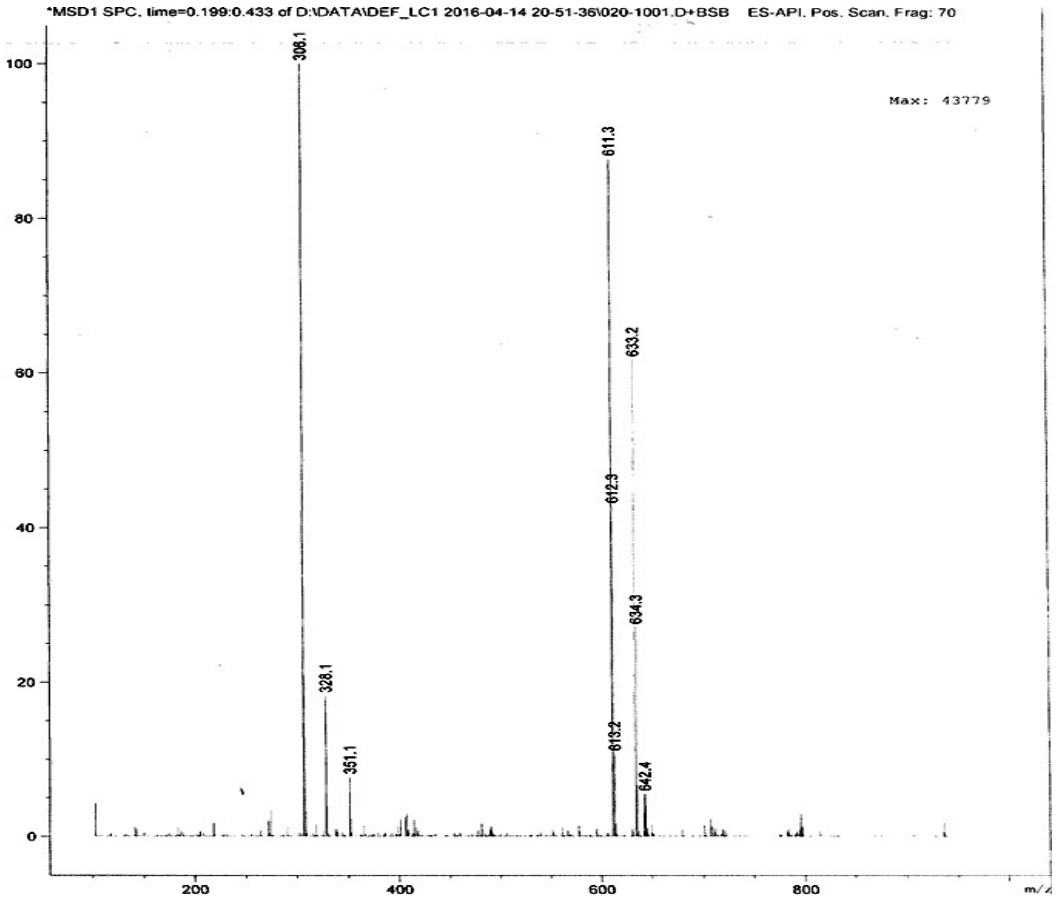
LC-MS spectrum of compound **BA-06**



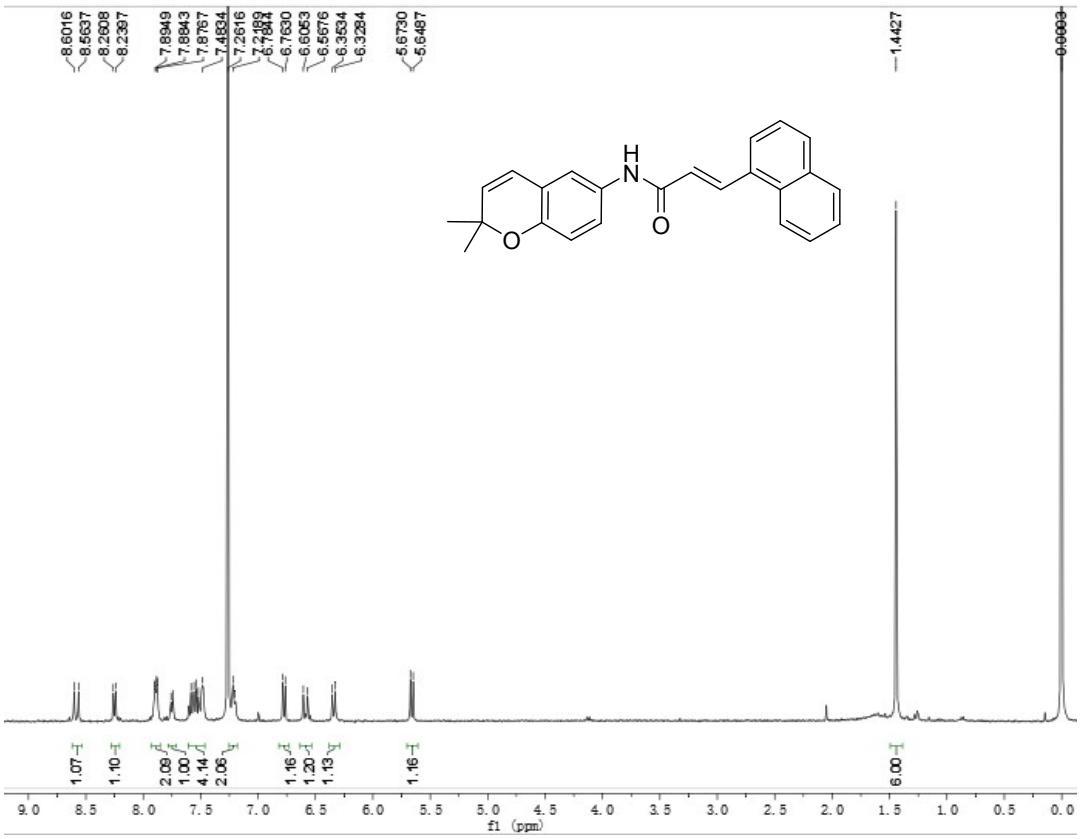
^{1}H-NMR spectrum of compound **BA-07** in $CDCl_3$



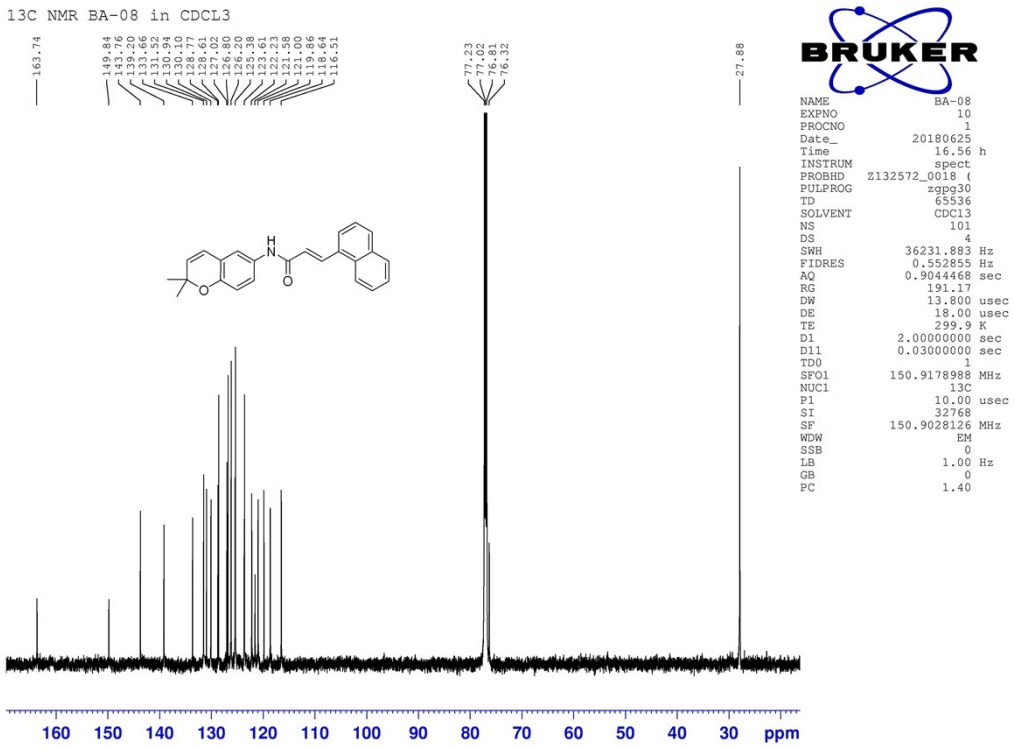
^{13}C-NMR spectrum of compound **BA-07** in $CDCl_3$



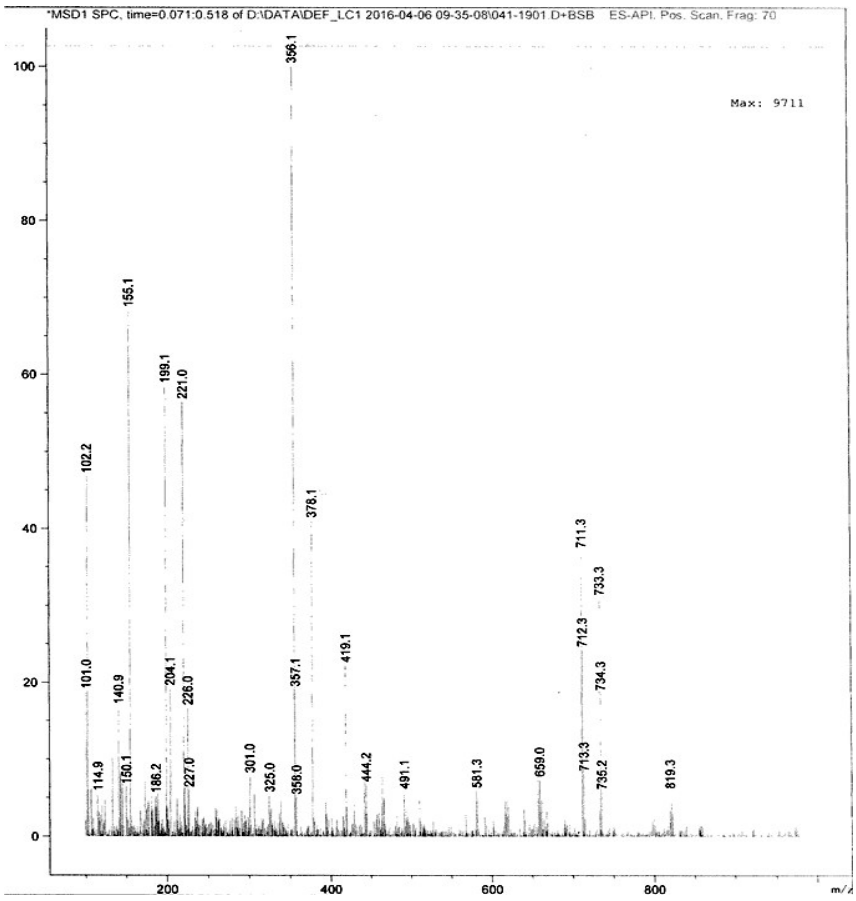
LC-MS spectrum of compound **BA-07**



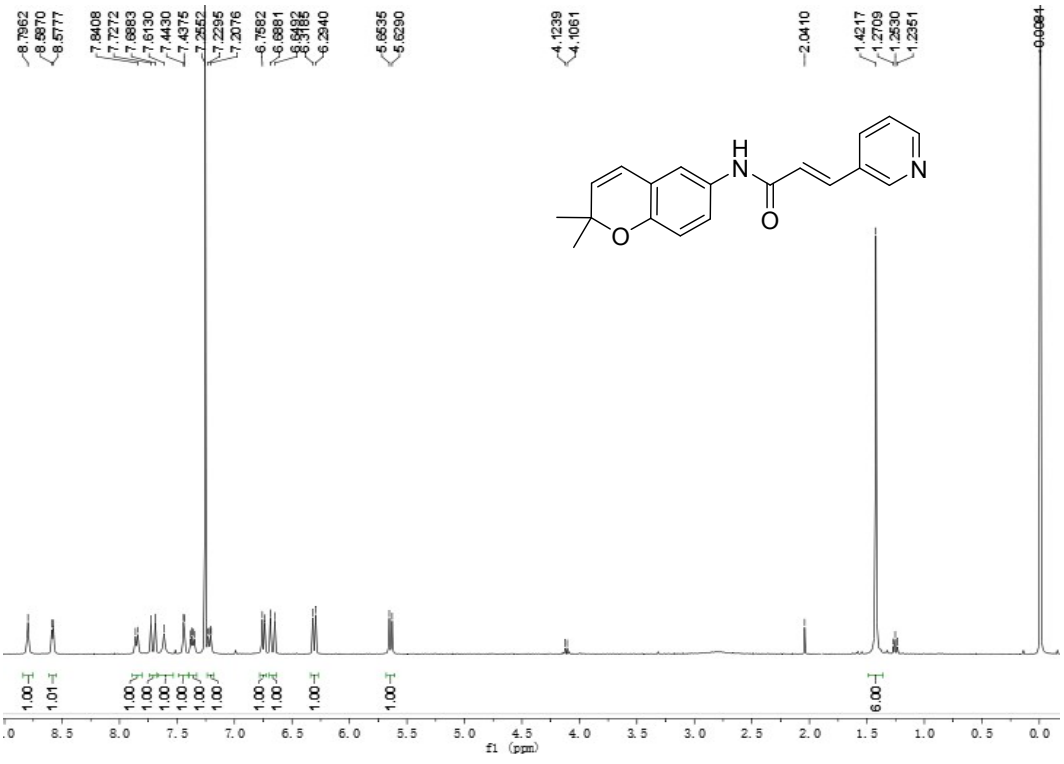
^{1}H-NMR spectrum of compound **BA-08** in $CDCl_3$



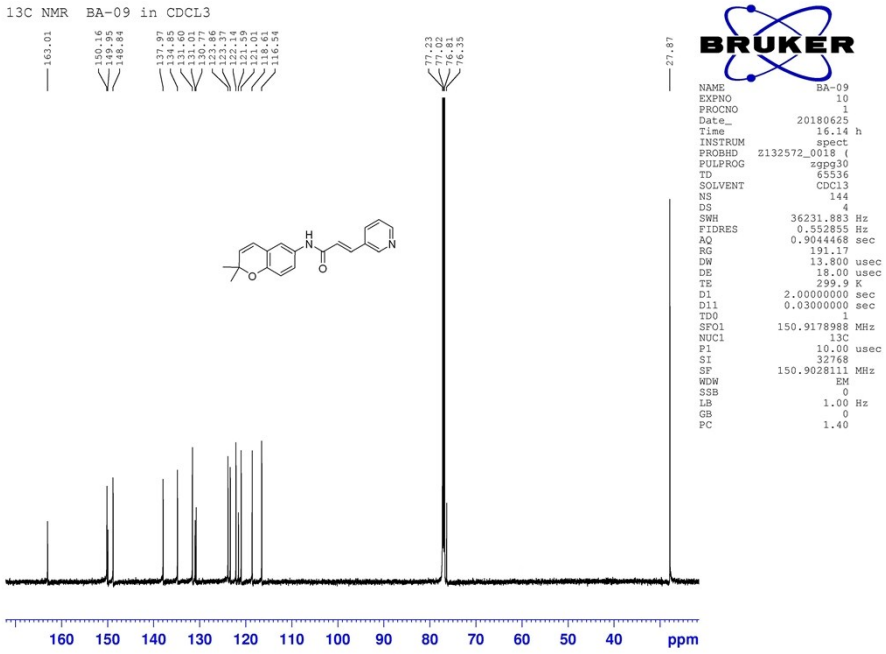
^{13}C-NMR spectrum of compound **BA-08** in $CDCl_3$



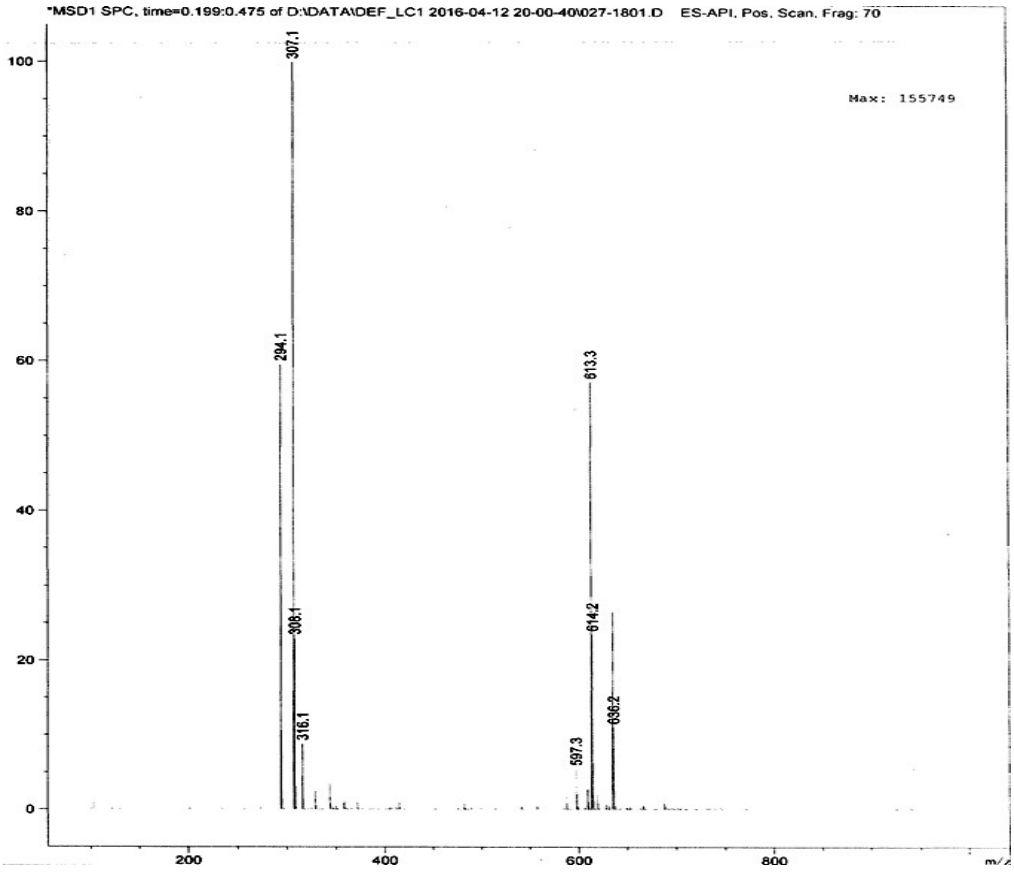
LC-MS spectrum of compound **BA-08**



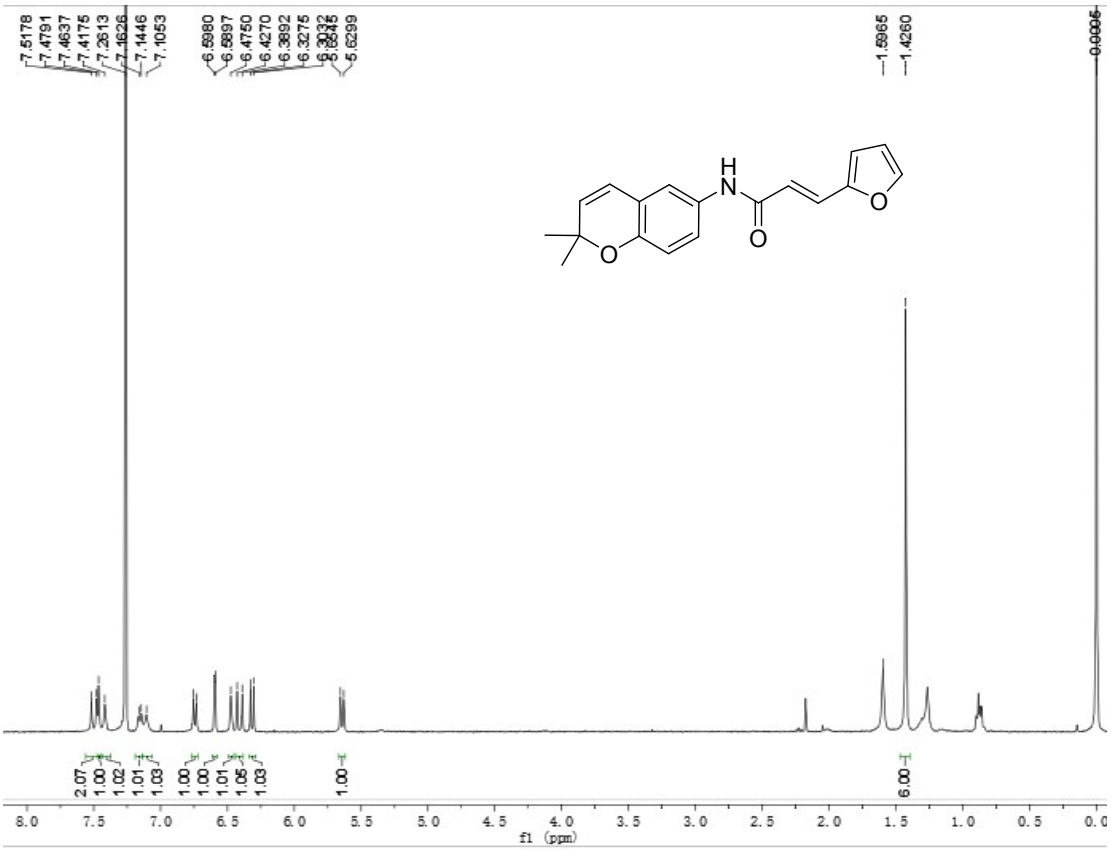
^{1}H-NMR spectrum of compound **BA-09** in $CDCl_3$



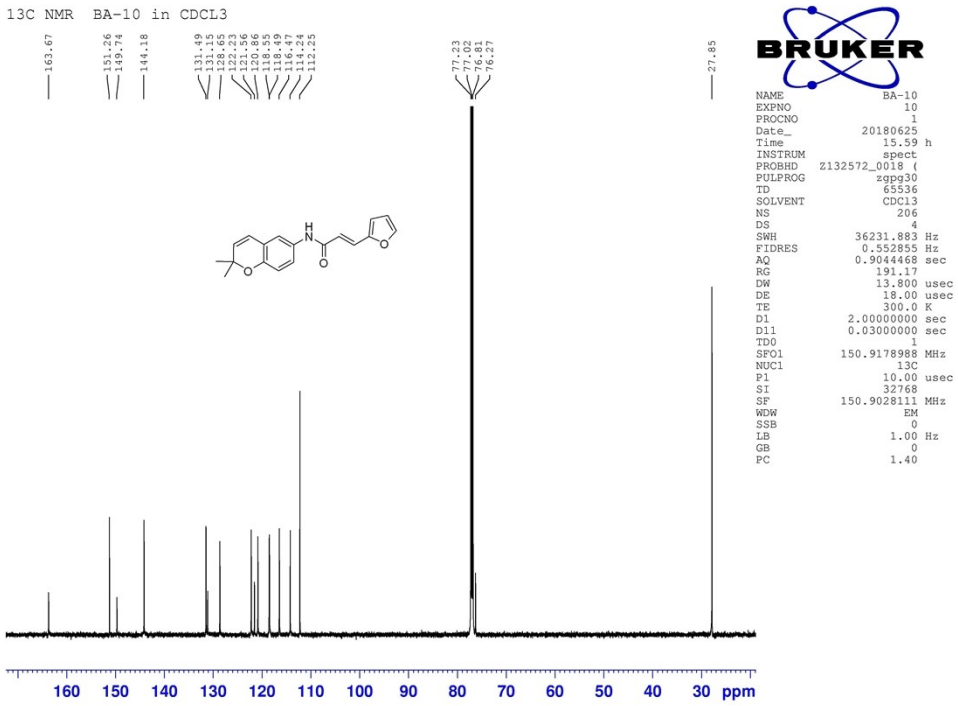
^{13}C-NMR spectrum of compound **BA-09** in $CDCl_3$



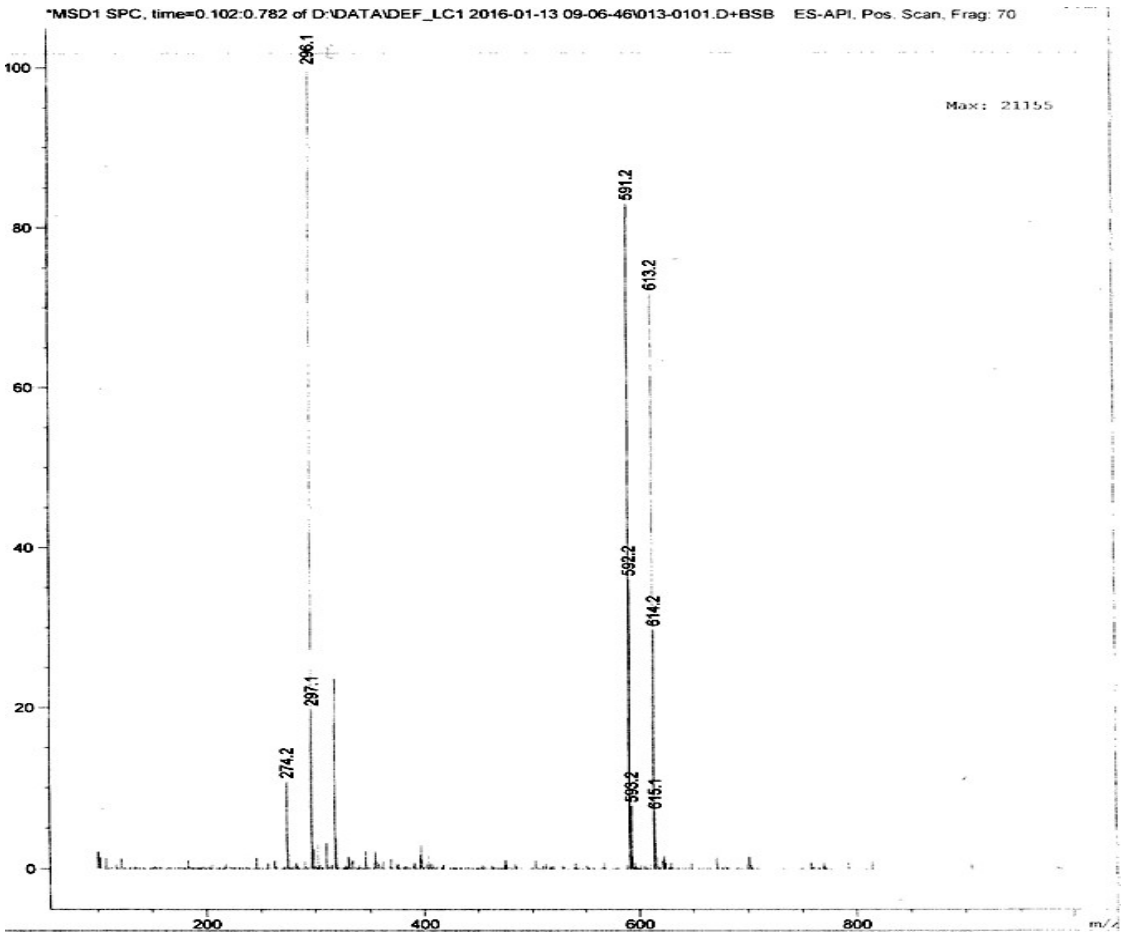
LC-MS spectrum of compound **BA-09**



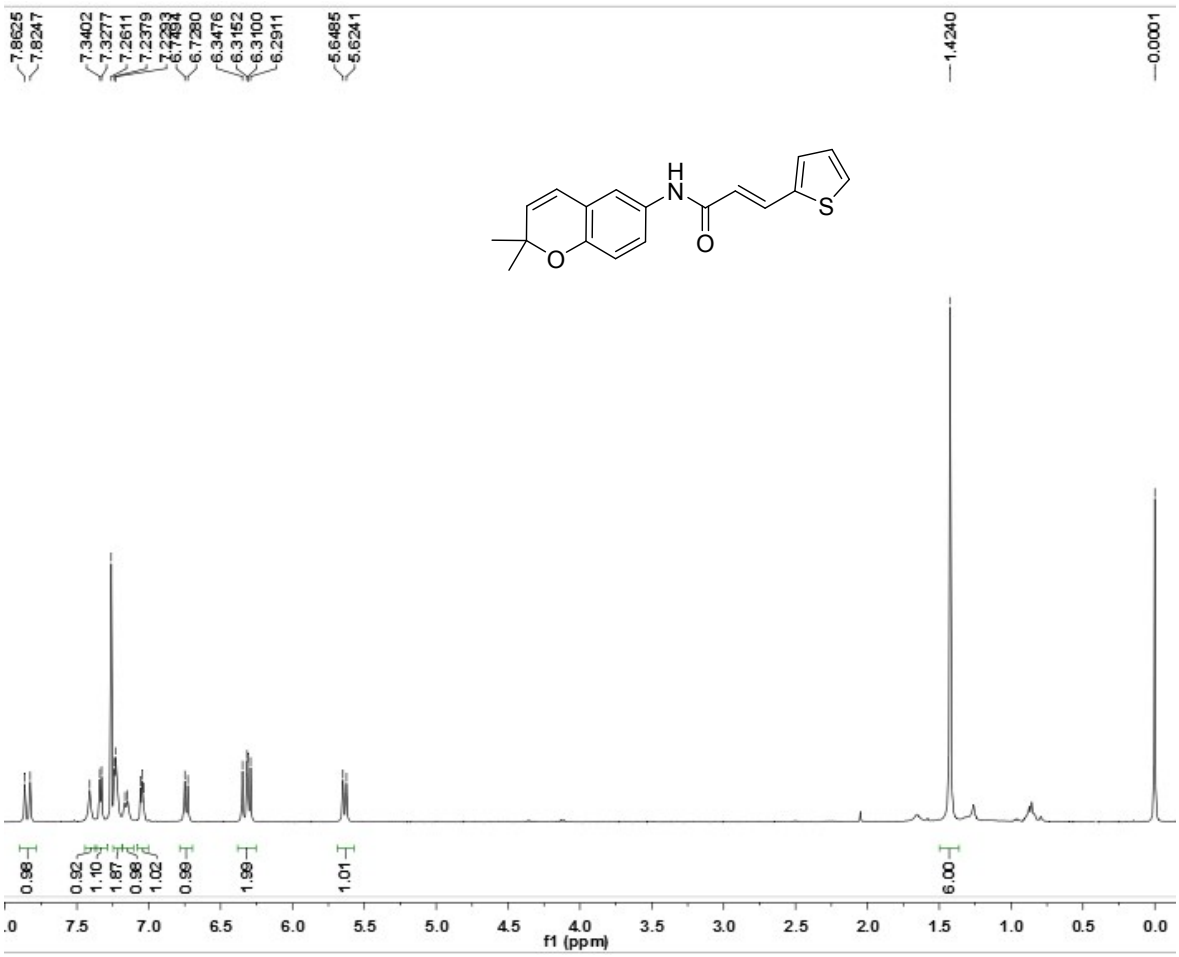
^{1}H-NMR spectrum of compound **BA-10** in $CDCl_3$



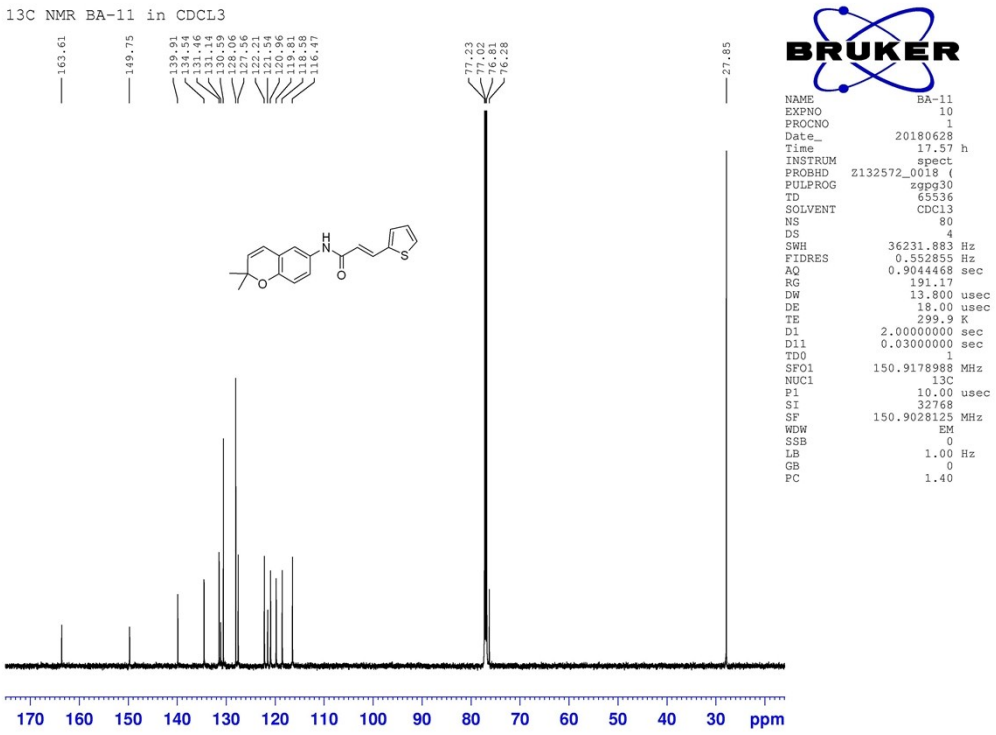
^{13}C-NMR spectrum of compound **BA-10** in $CDCl_3$



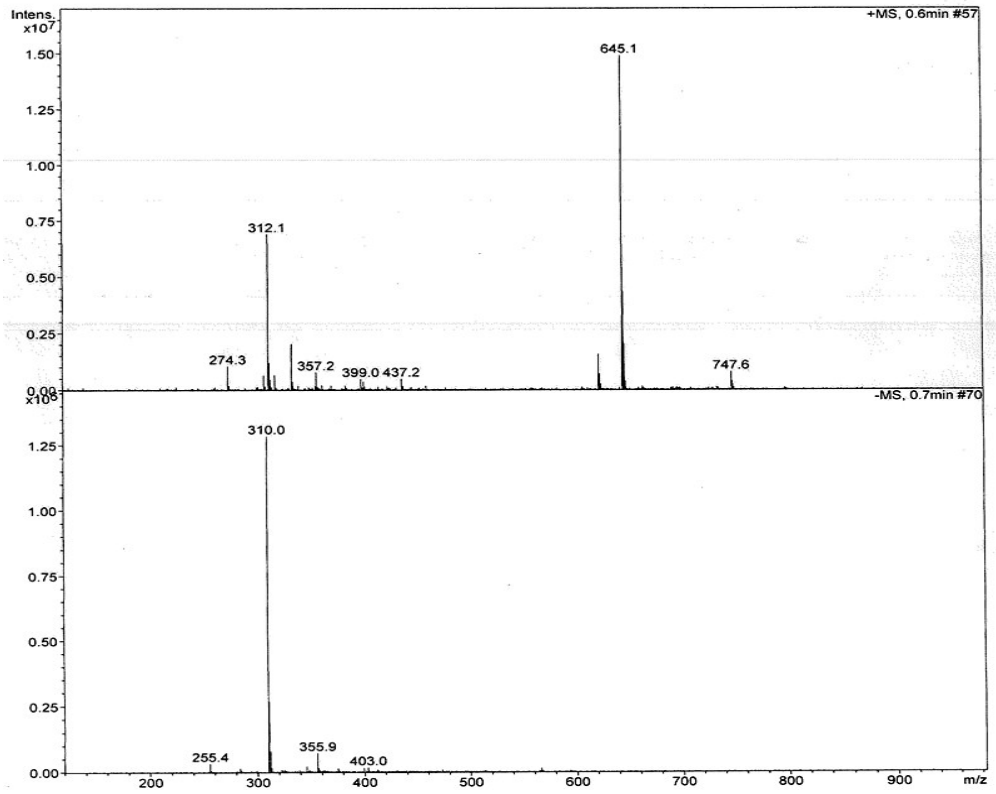
LC-MS spectrum of compound **BA-10**



^{1}H-NMR spectrum of compound **BA-11** in $CDCl_3$

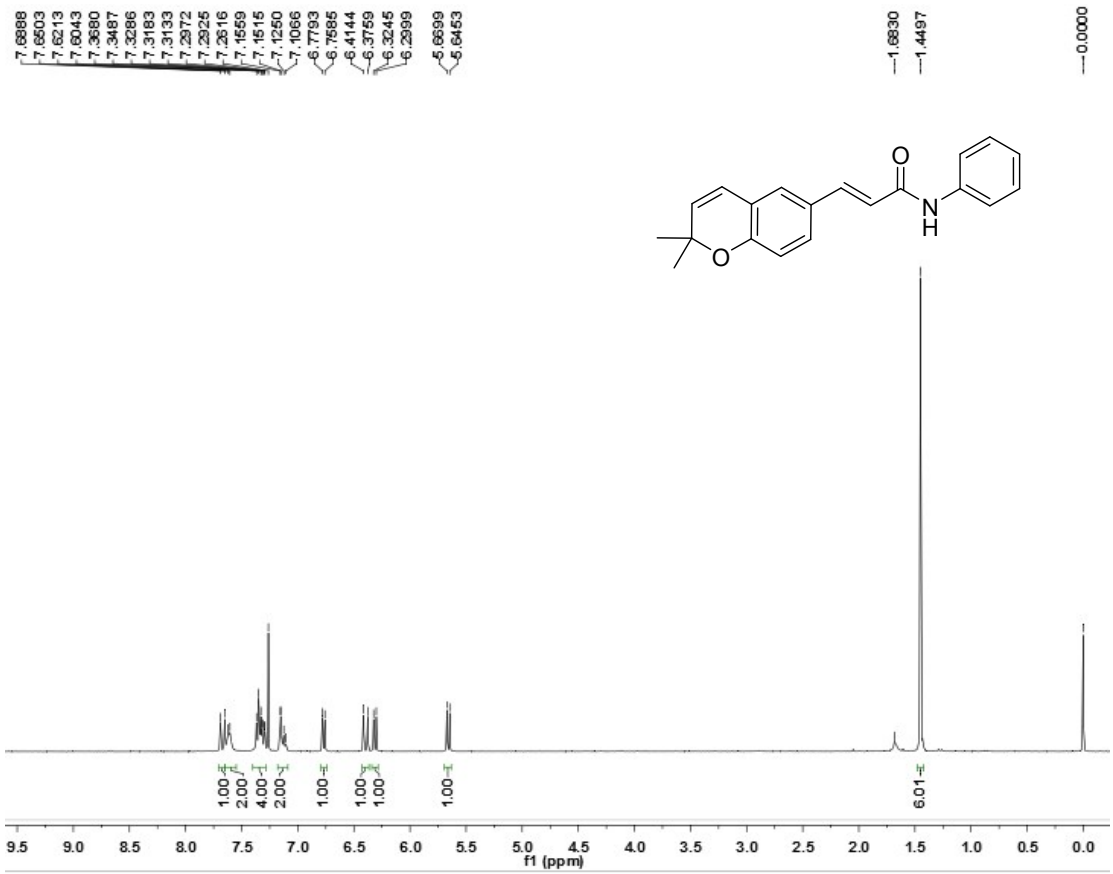


^{13}C-NMR spectrum of compound **BA-11** in $CDCl_3$

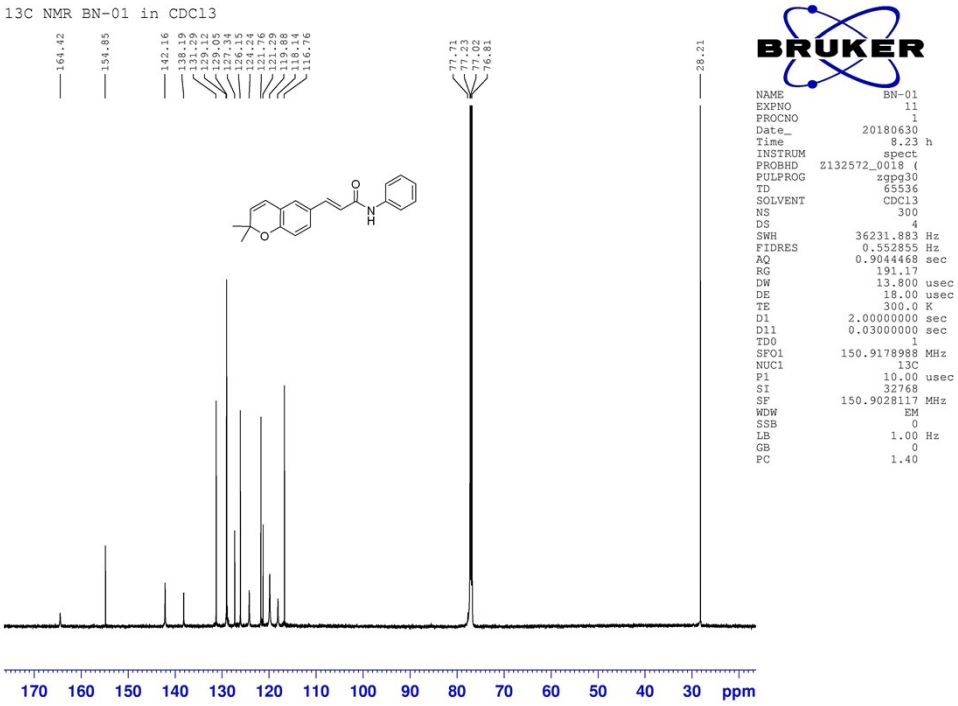


LC-MS spectrum of compound **BA-11**

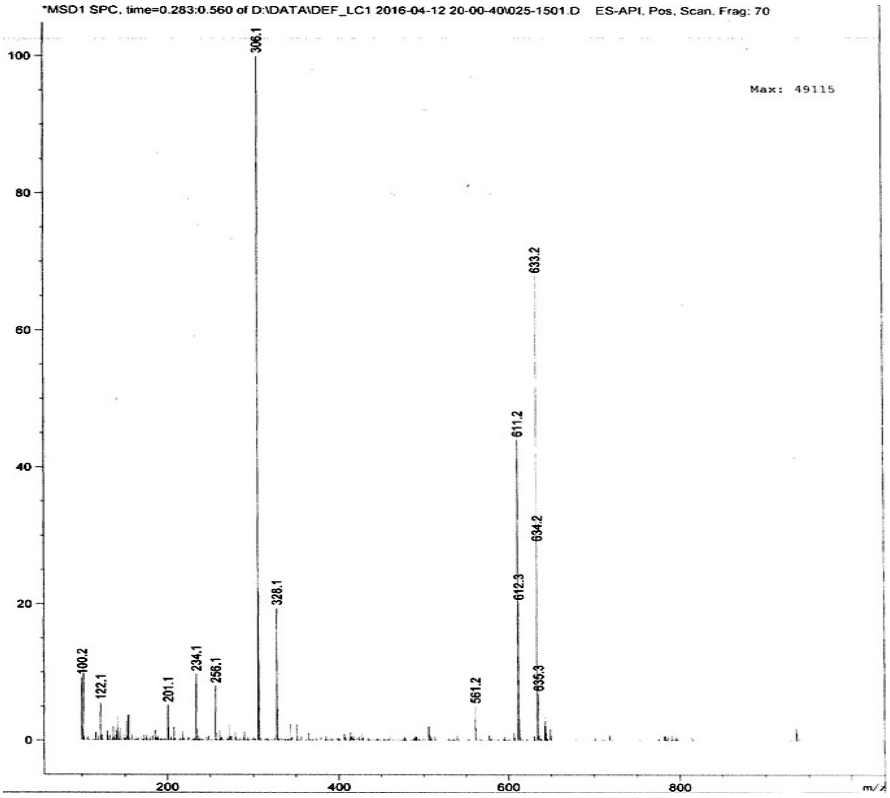
10. ^{1}H, ^{13}C NMR spectra and MS spectra of BA-01~BN-10



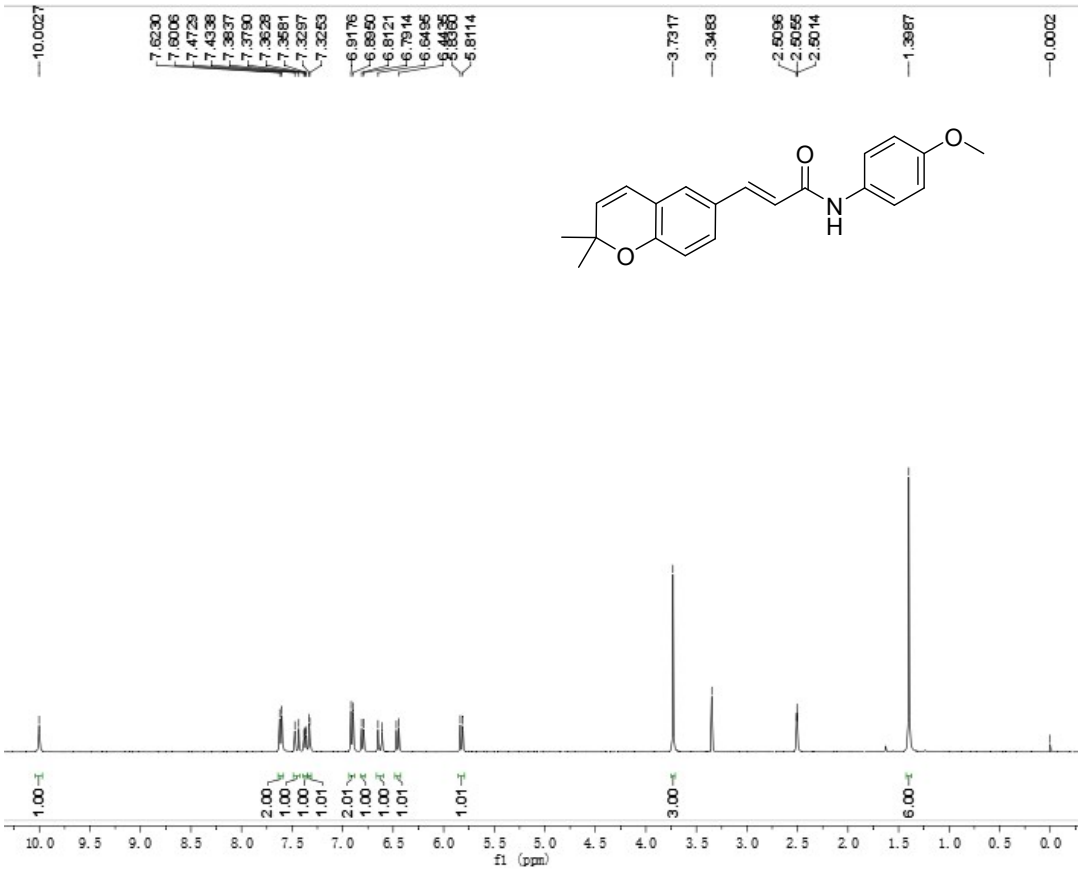
^{1}H-NMR spectrum of compound **BN-01** in $CDCl_3$



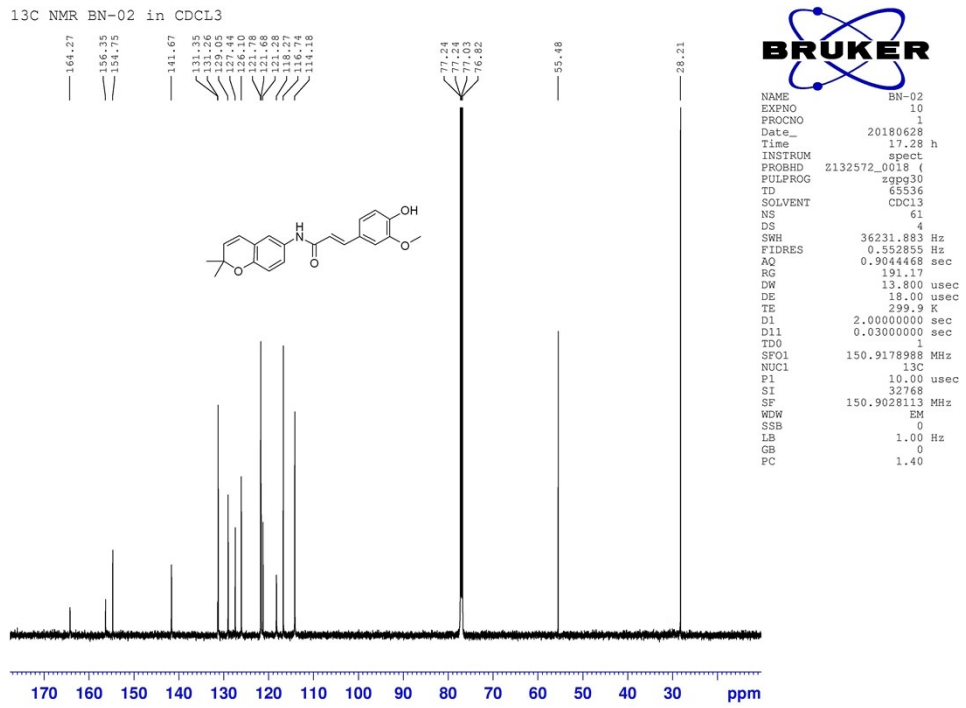
^{13}C-NMR spectrum of compound **BN-01** in $CDCl_3$



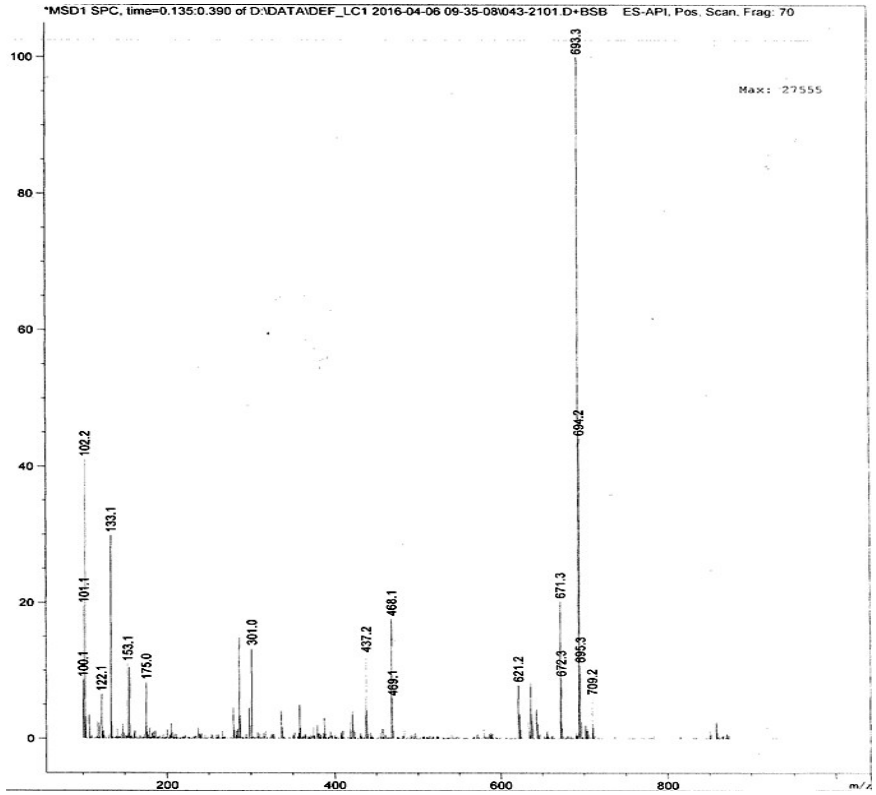
LC-MS spectrum of compound **BN-01**



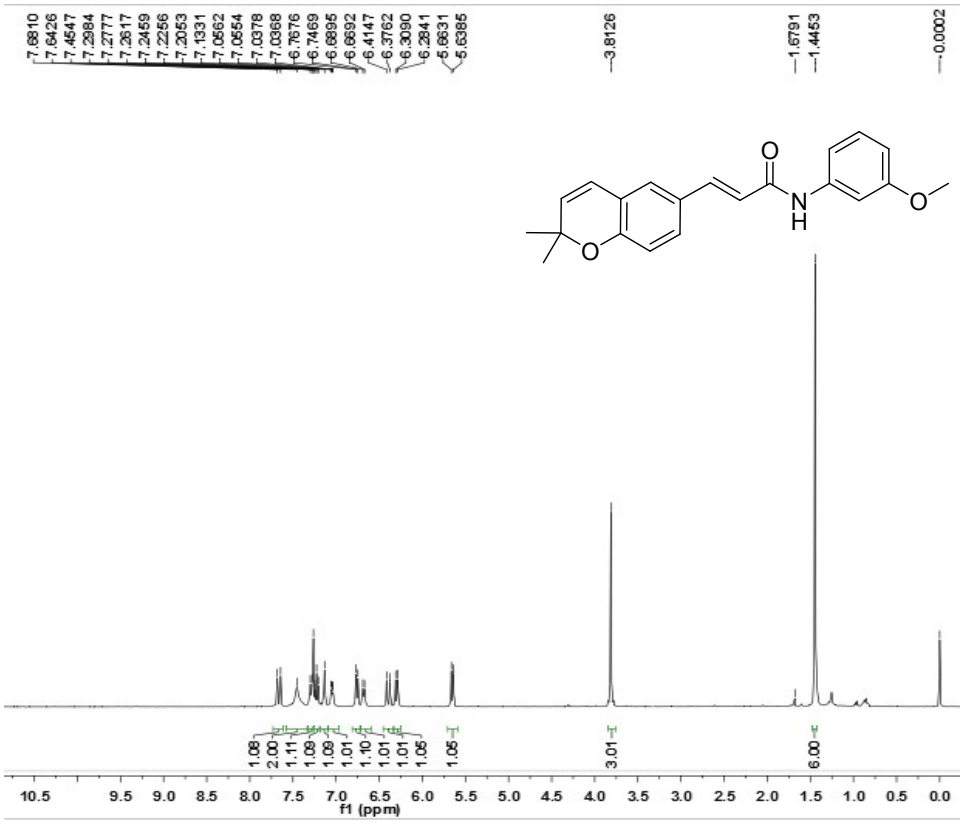
^{1}H-NMR spectrum of compound **BN-02** in DMSO-d_6



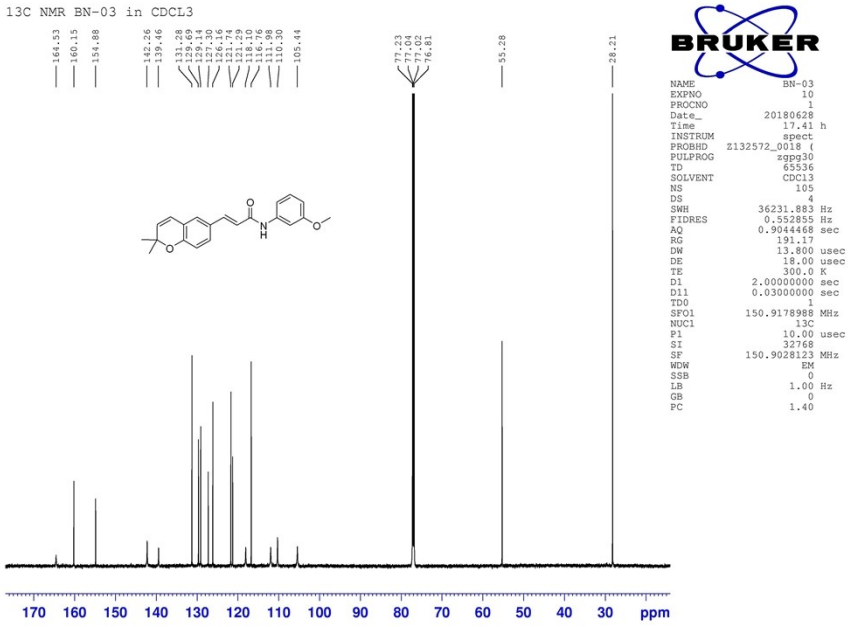
^{13}C-NMR spectrum of compound **BN-02** in $CDCl_3$



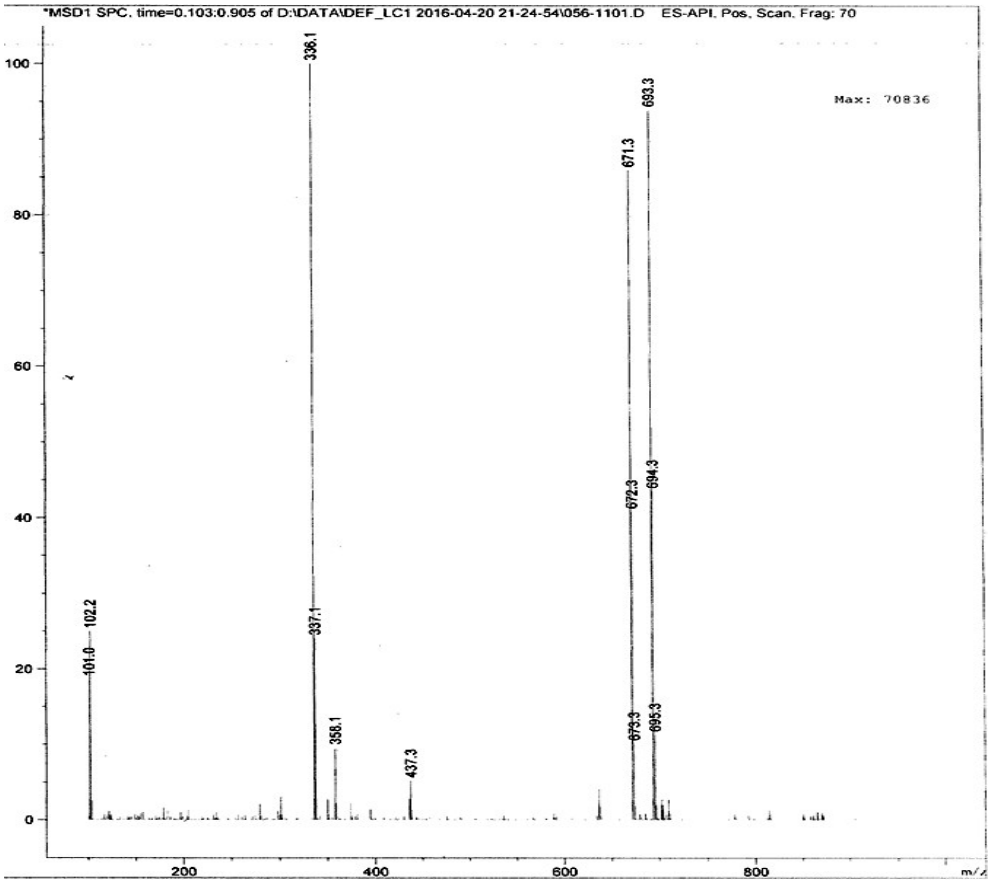
LC-MS spectrum of compound **BN-02**



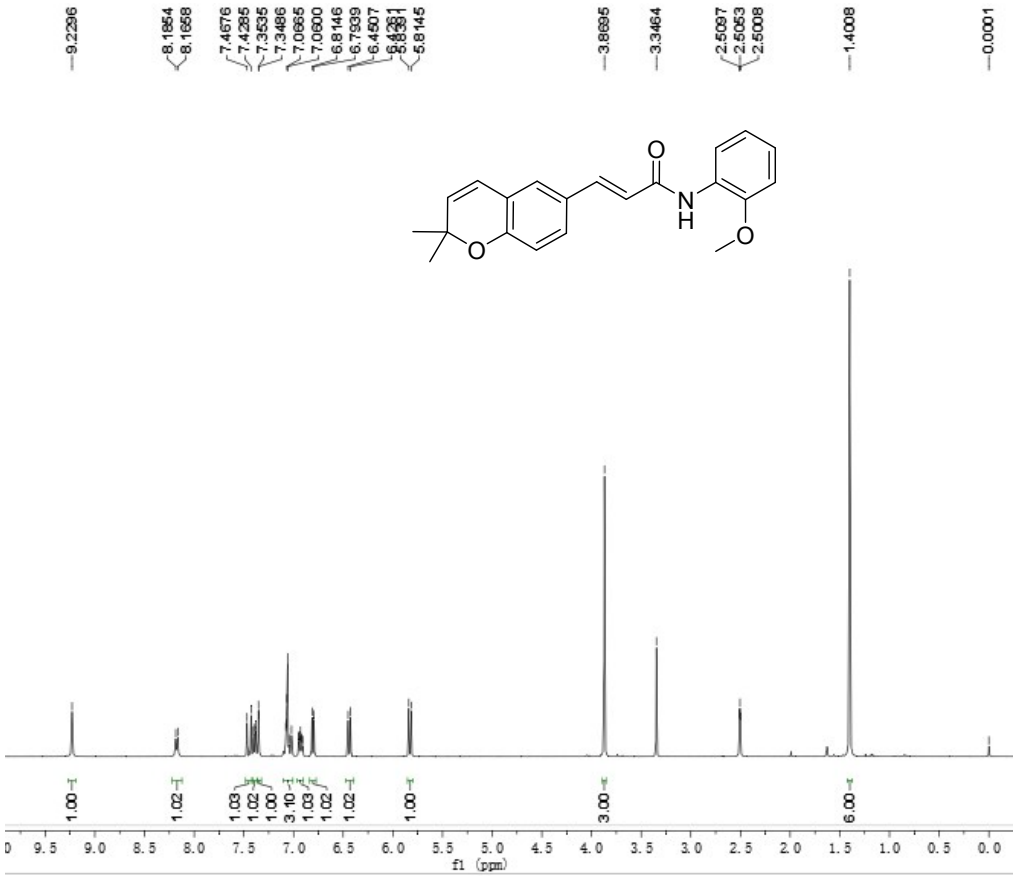
^{1}H-NMR spectrum of compound **BN-03** in $CDCl_3$



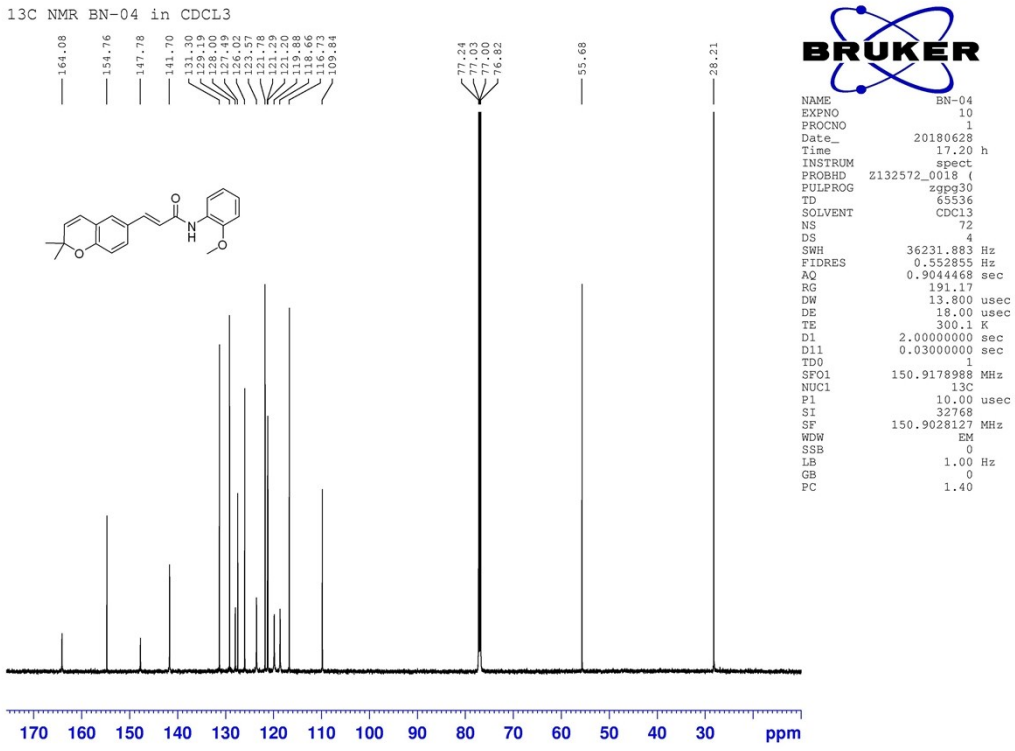
^{13}C-NMR spectrum of compound **BN-03** in $CDCl_3$



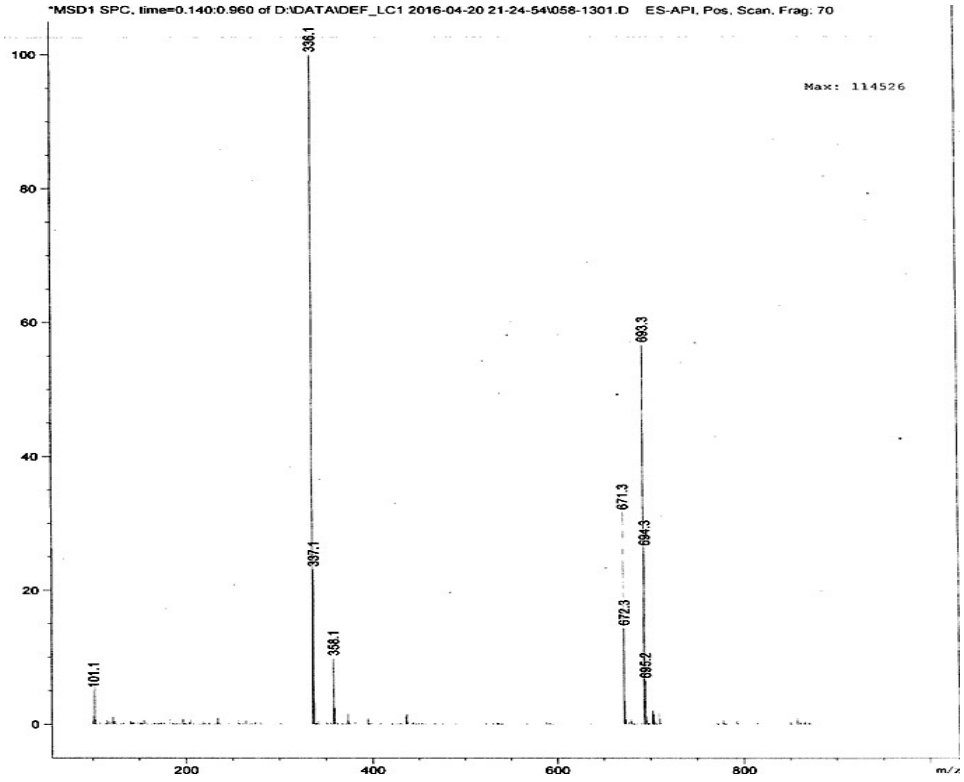
LC-MS spectrum of compound **BN-03**



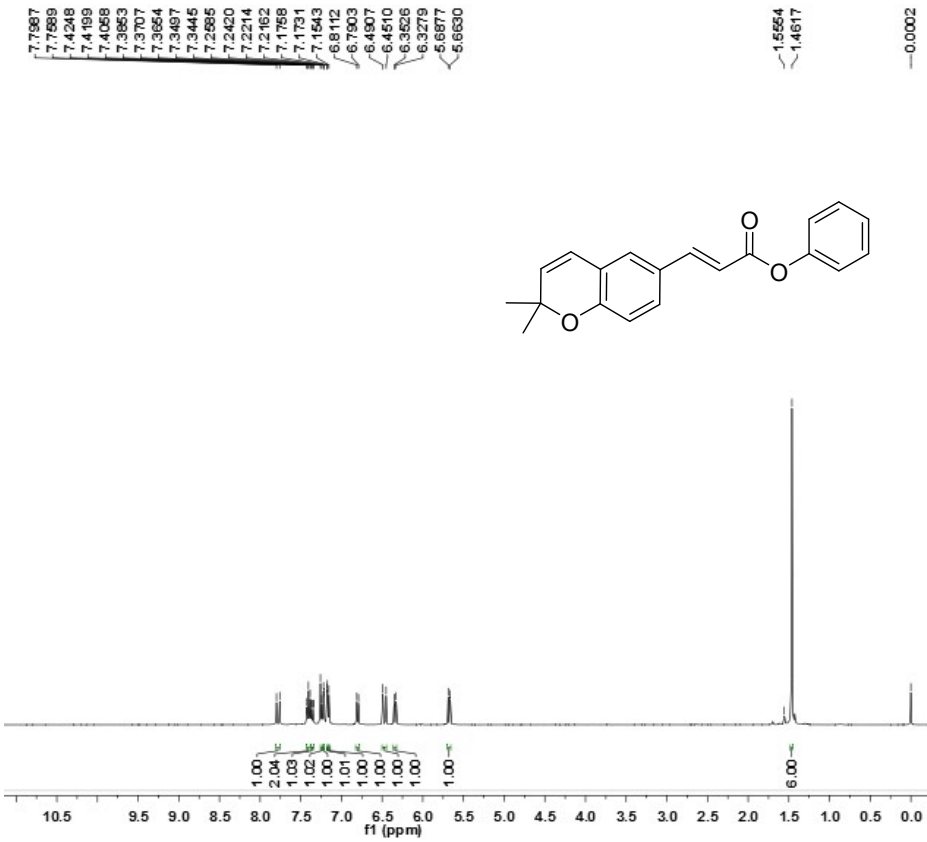
^{1}H-NMR spectrum of compound **BN-04** in DMSO-d_6



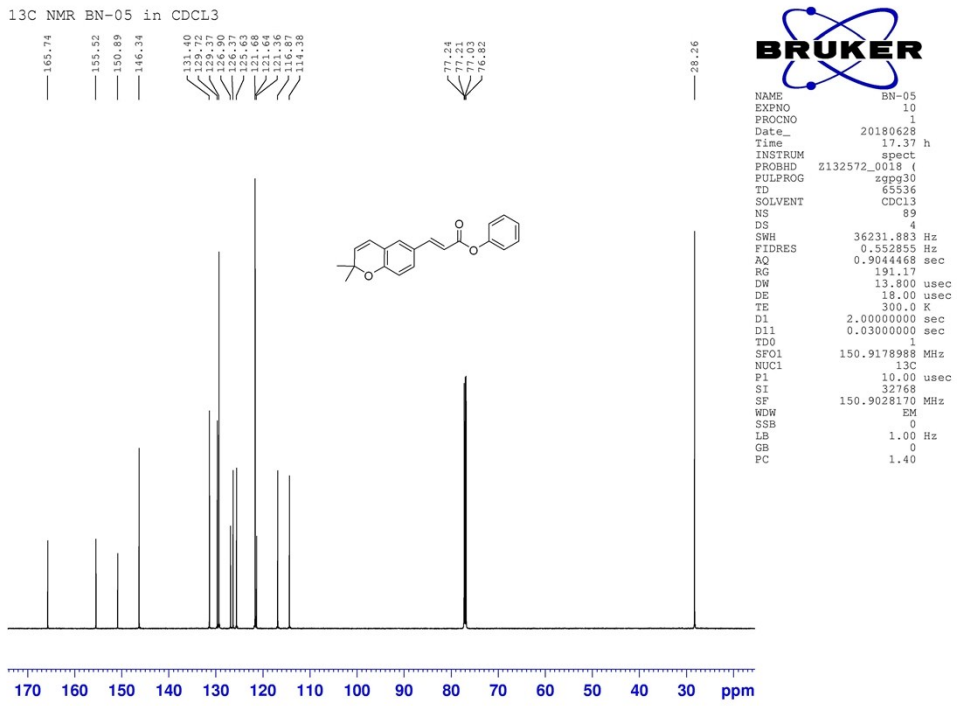
^{13}C-NMR spectrum of compound **BN-04** in $CDCl_3$



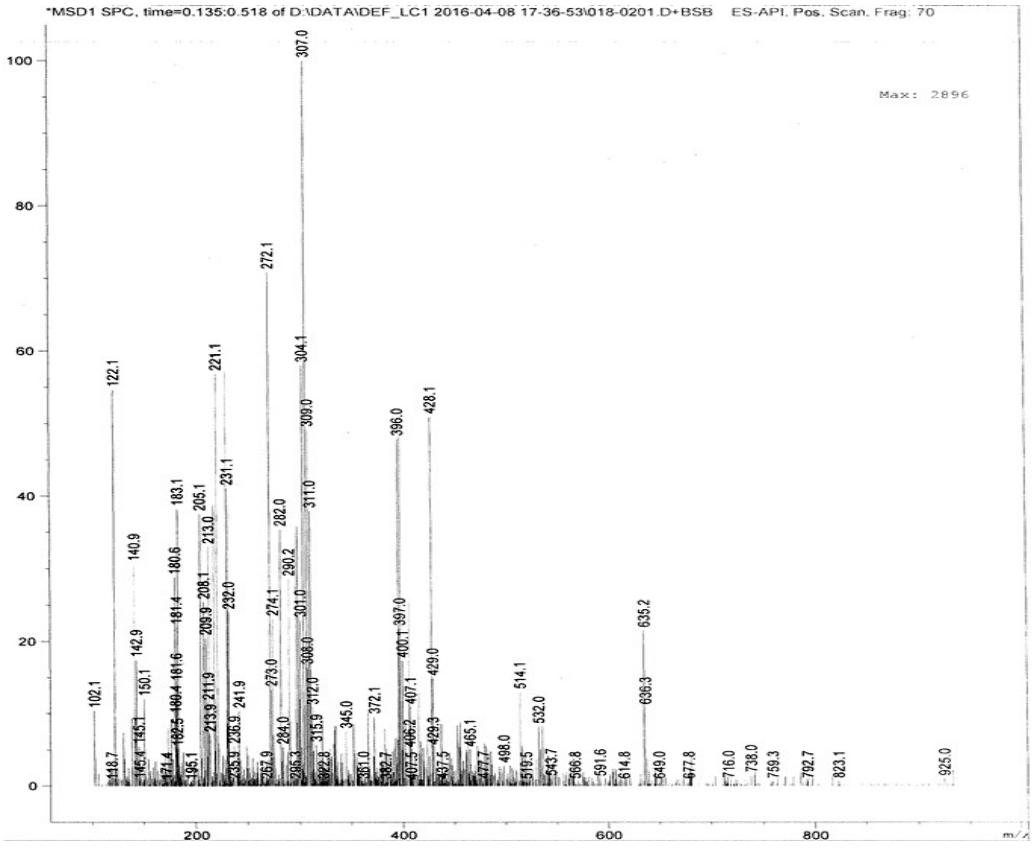
LC-MS spectrum of compound **BN-04**



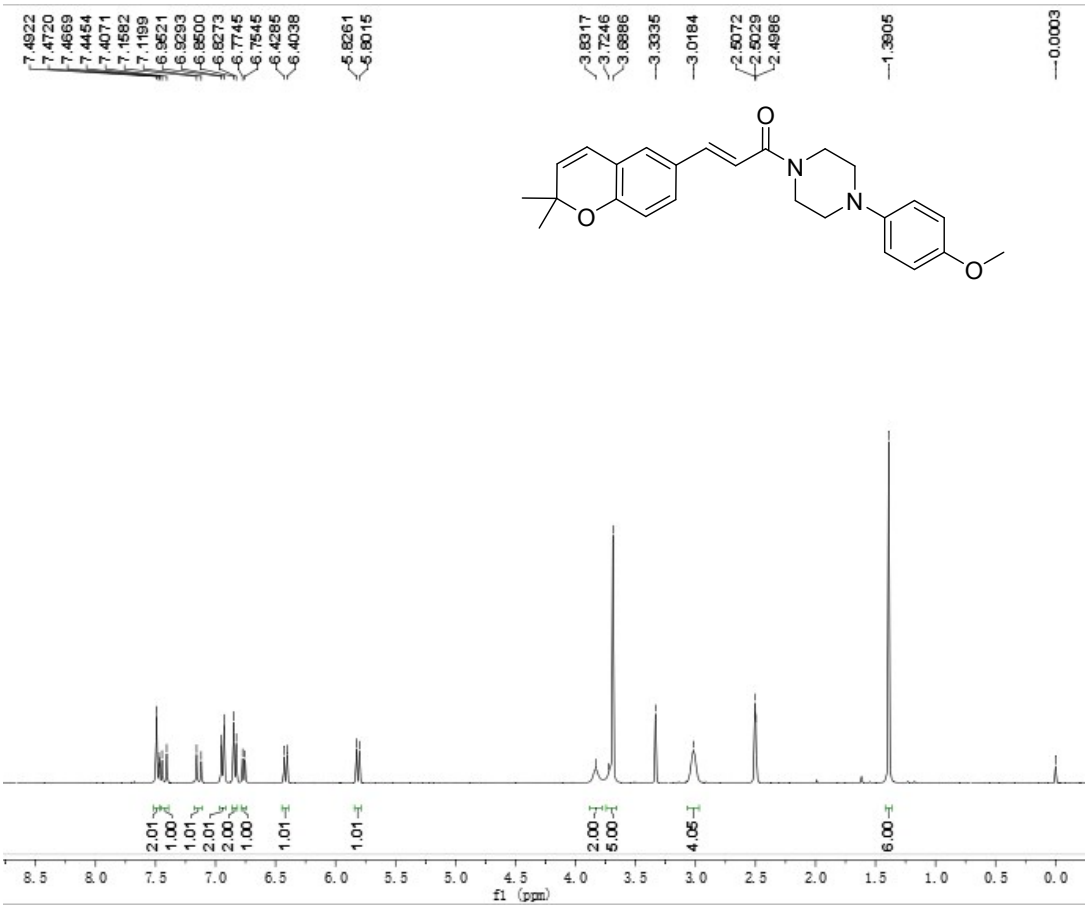
^{1}H-NMR spectrum of compound **BN-05** in $CDCl_3$



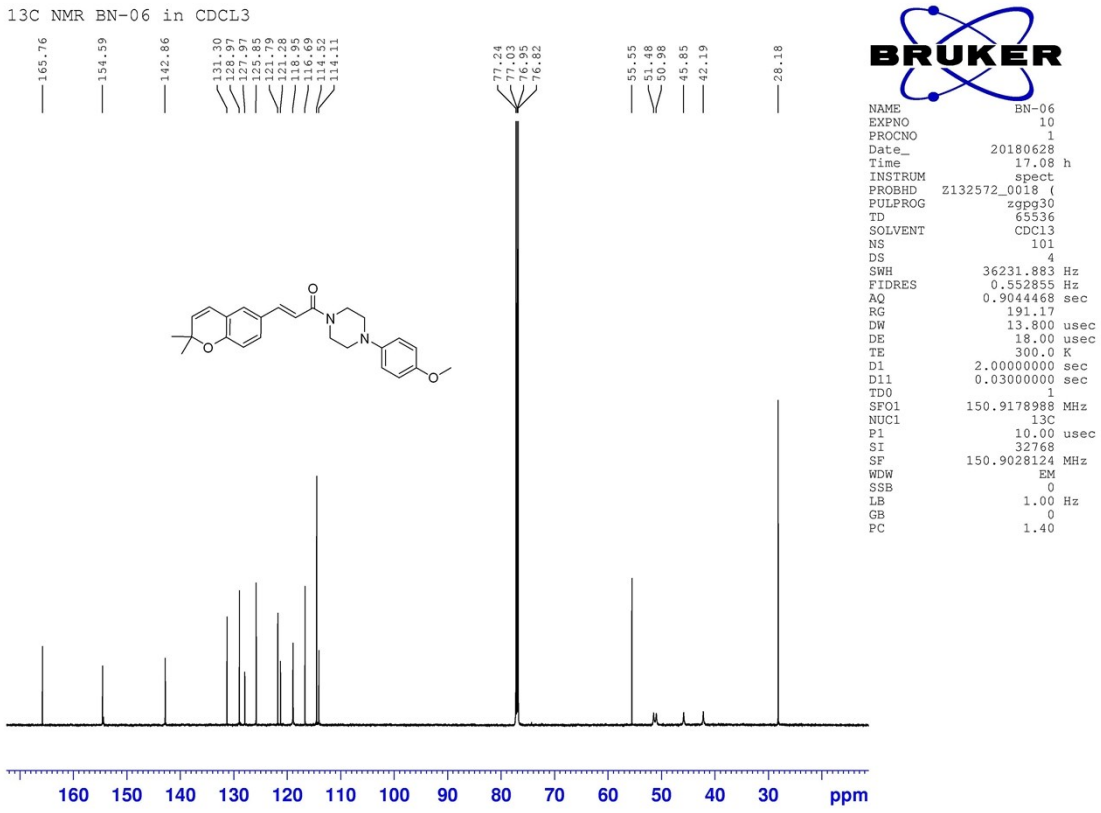
^{13}C-NMR spectrum of compound **BN-05** in $CDCl_3$



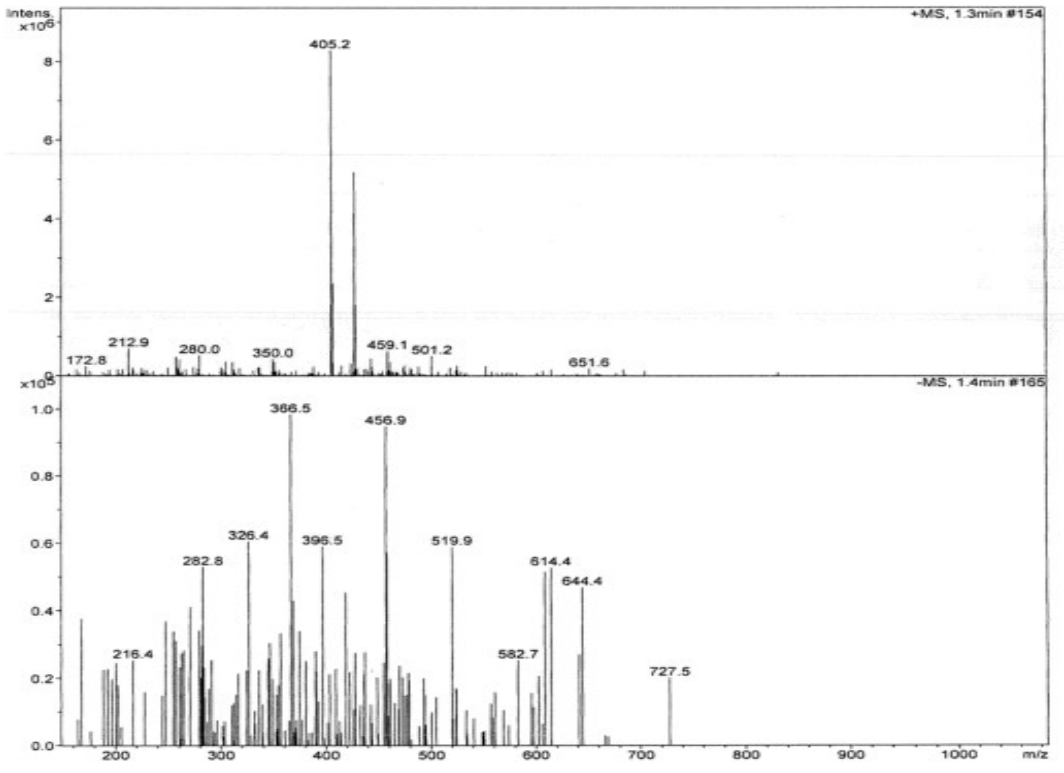
LC-MS spectrum of compound **BN-05**



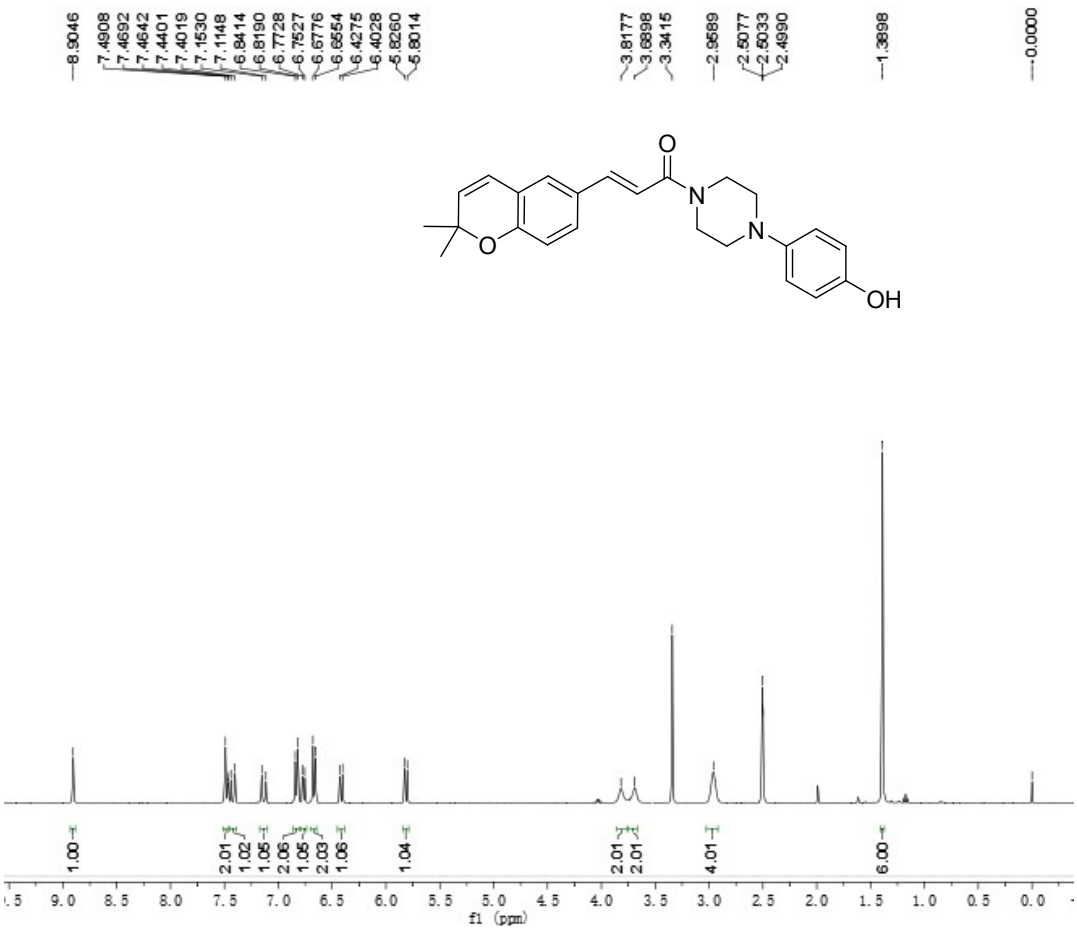
^{1}H-NMR spectrum of compound **BN-06** in DMSO-d_6



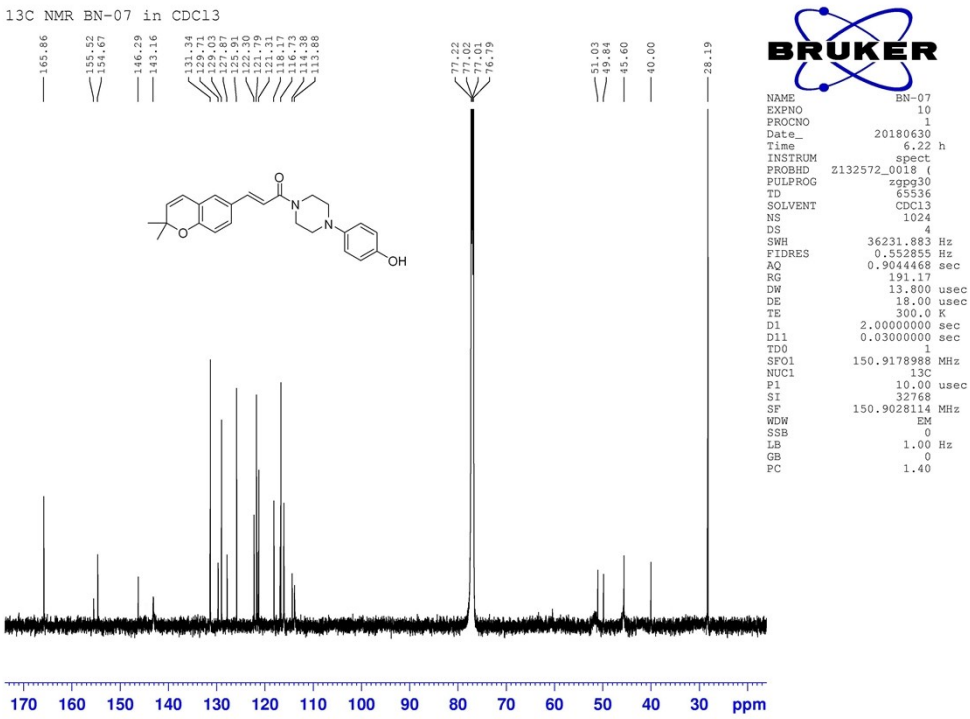
^{13}C-NMR spectrum of compound **BN-06** in $CDCl_3$



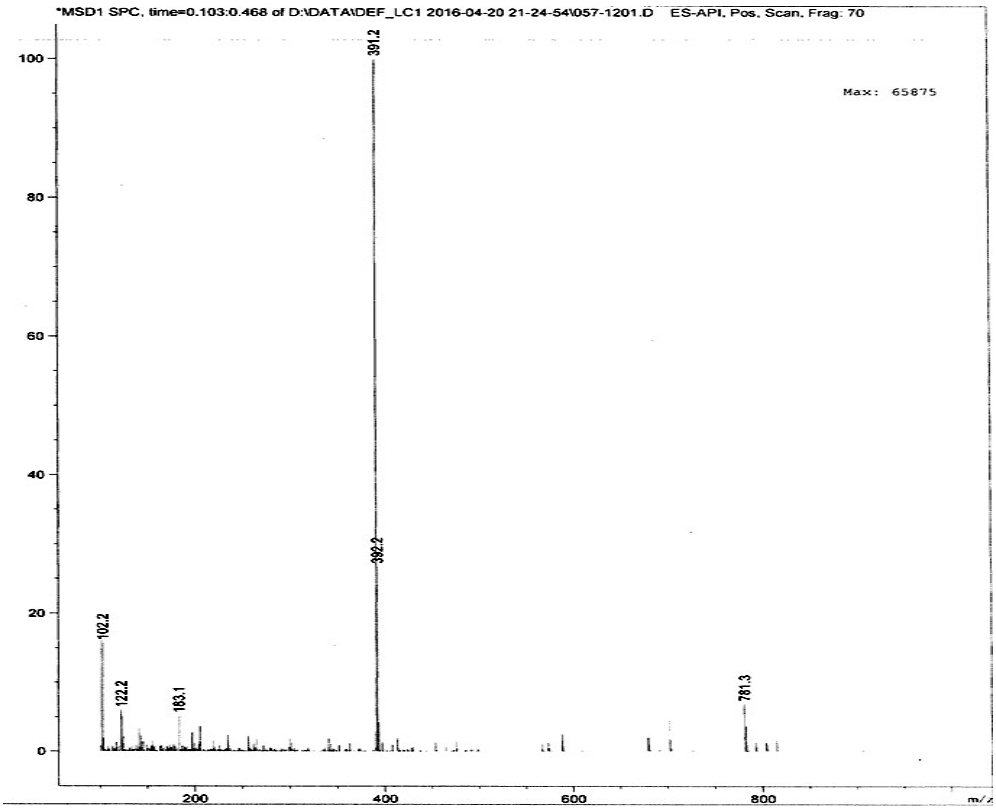
LC-MS spectrum of compound **BN-06**



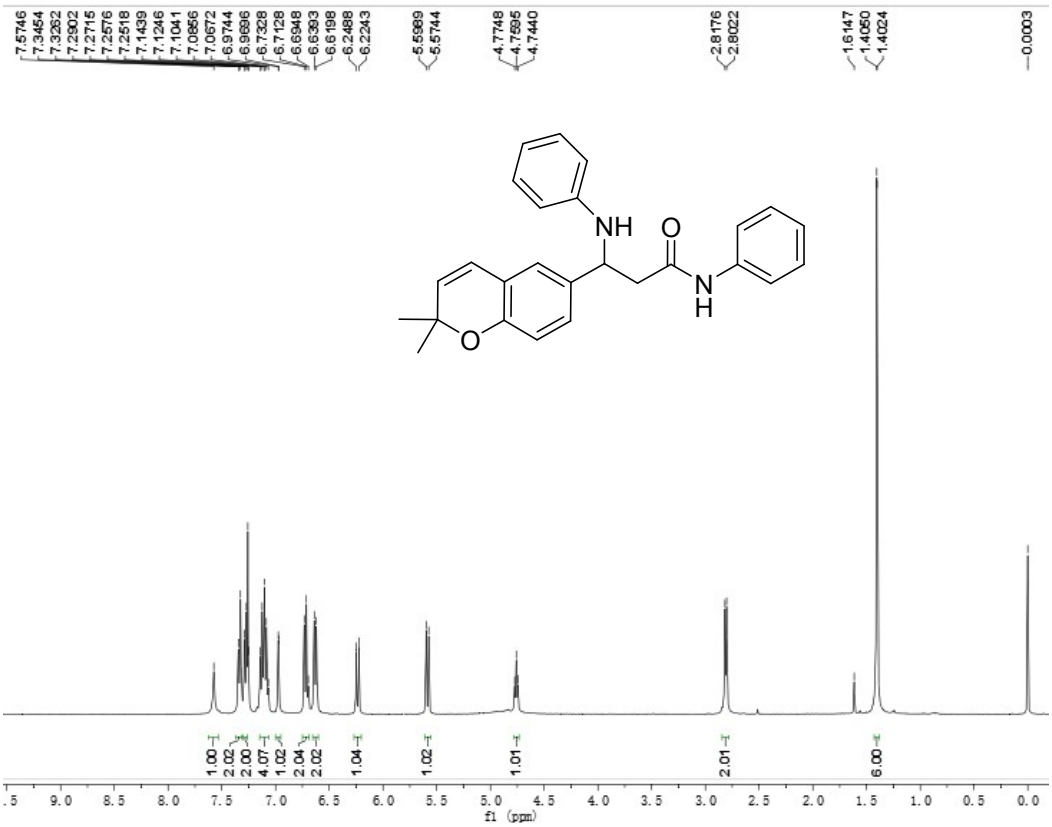
^{1}H-NMR spectrum of compound **BN-07** in DMSO-d_6



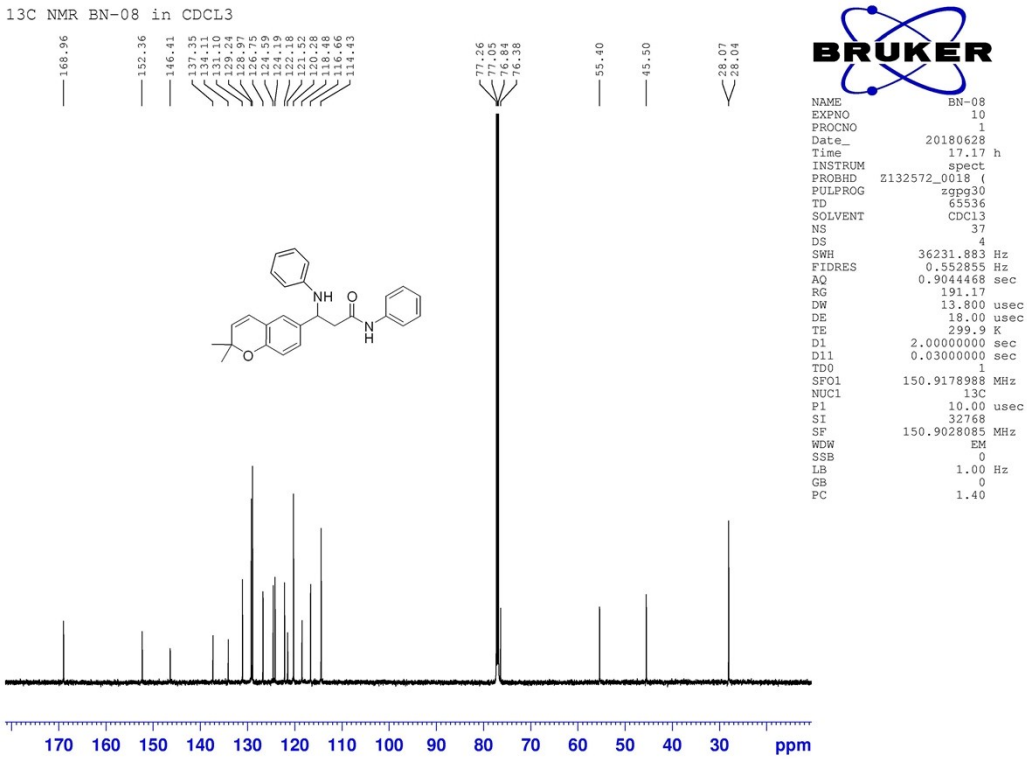
^{13}C-NMR spectrum of compound **BN-07** in $CDCl_3$



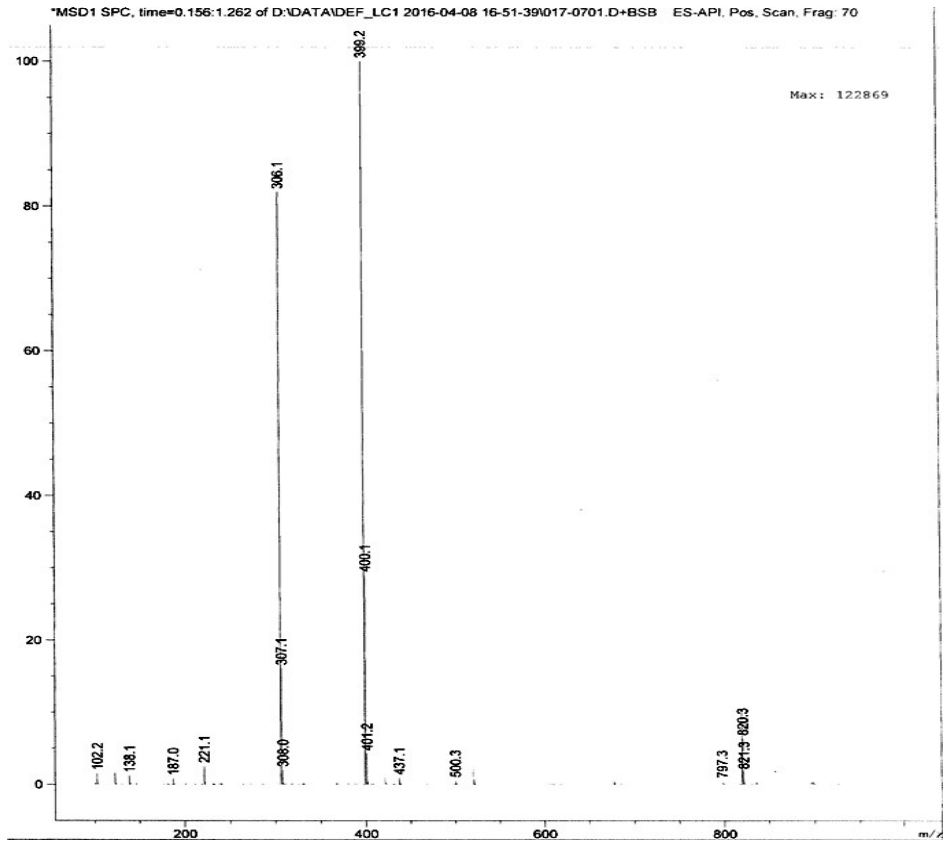
LC-MS spectrum of compound **BN-07**



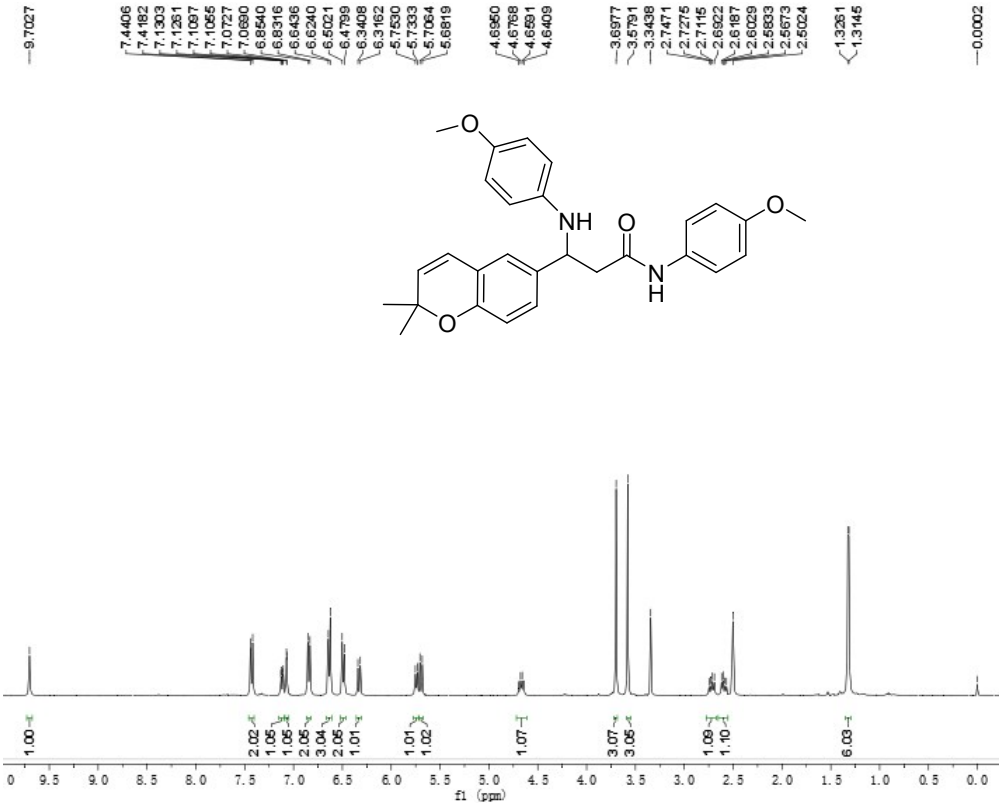
^{1}H-NMR spectrum of compound **BN-08** in $CDCl_3$



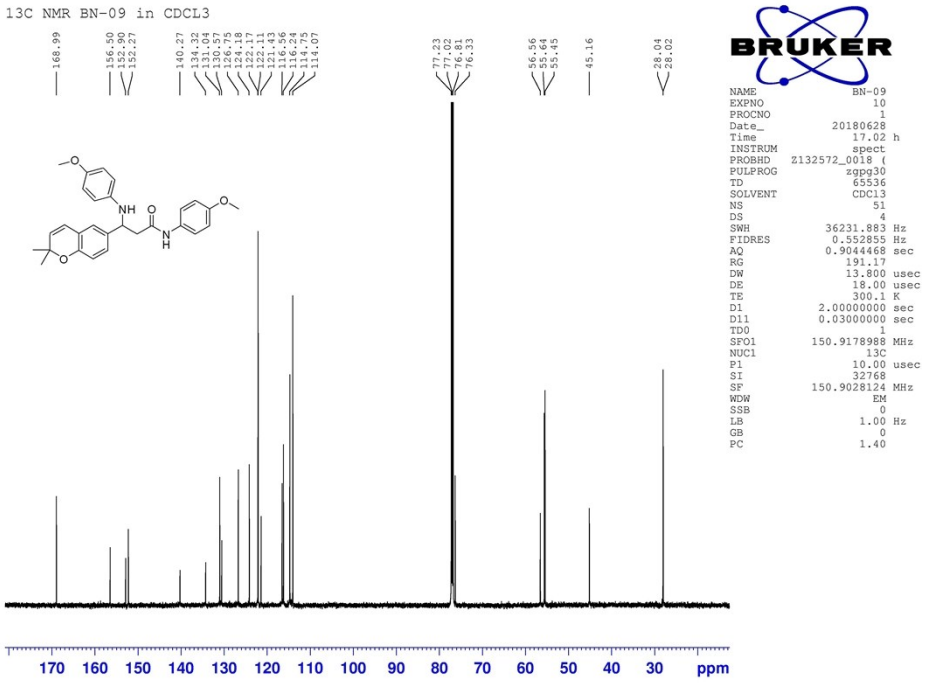
^{13}C-NMR spectrum of compound **BN-08** in $CDCl_3$



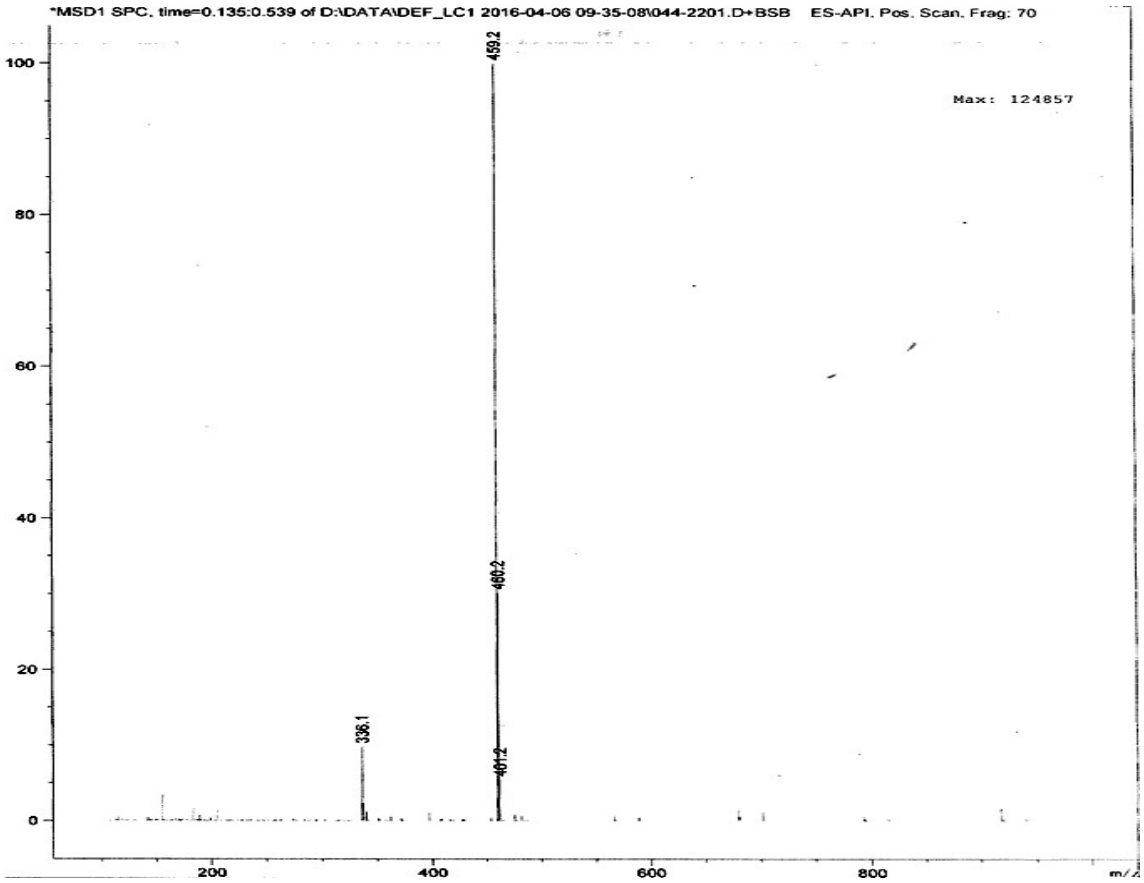
LC-MS spectrum of compound **BN-08**



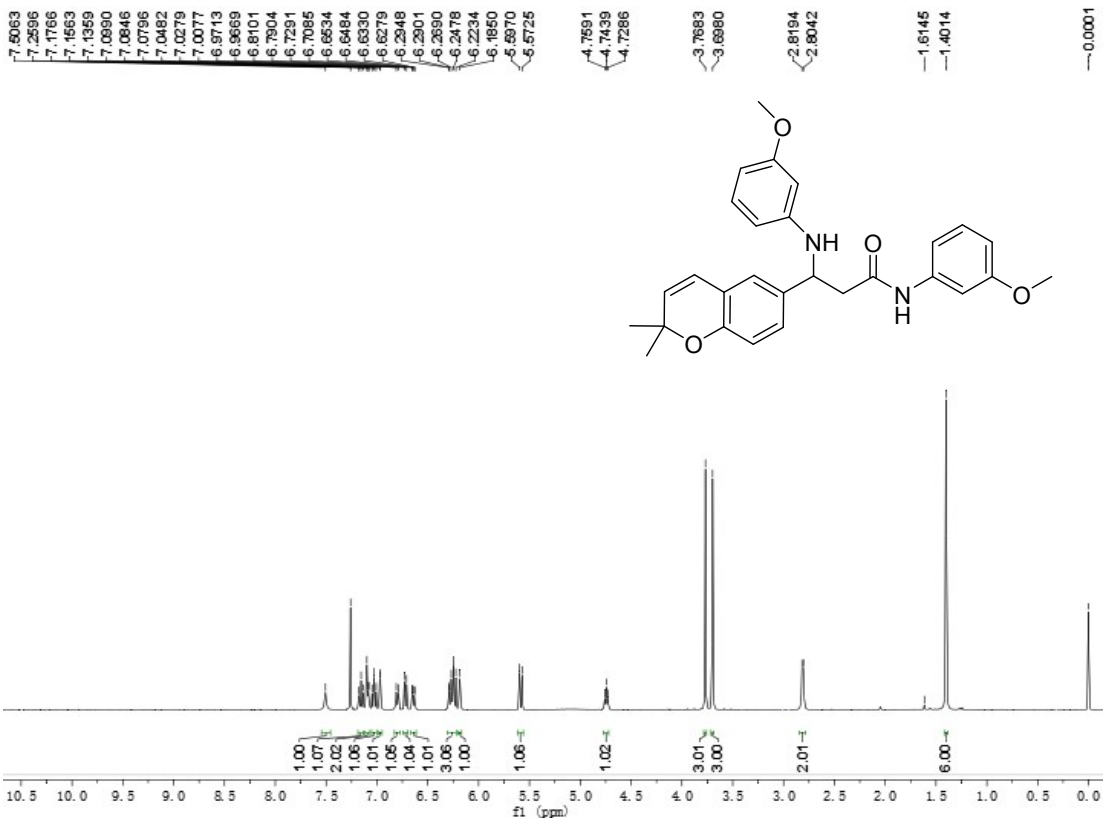
^{1}H-NMR spectrum of compound **BN-09** in DMSO-d_6



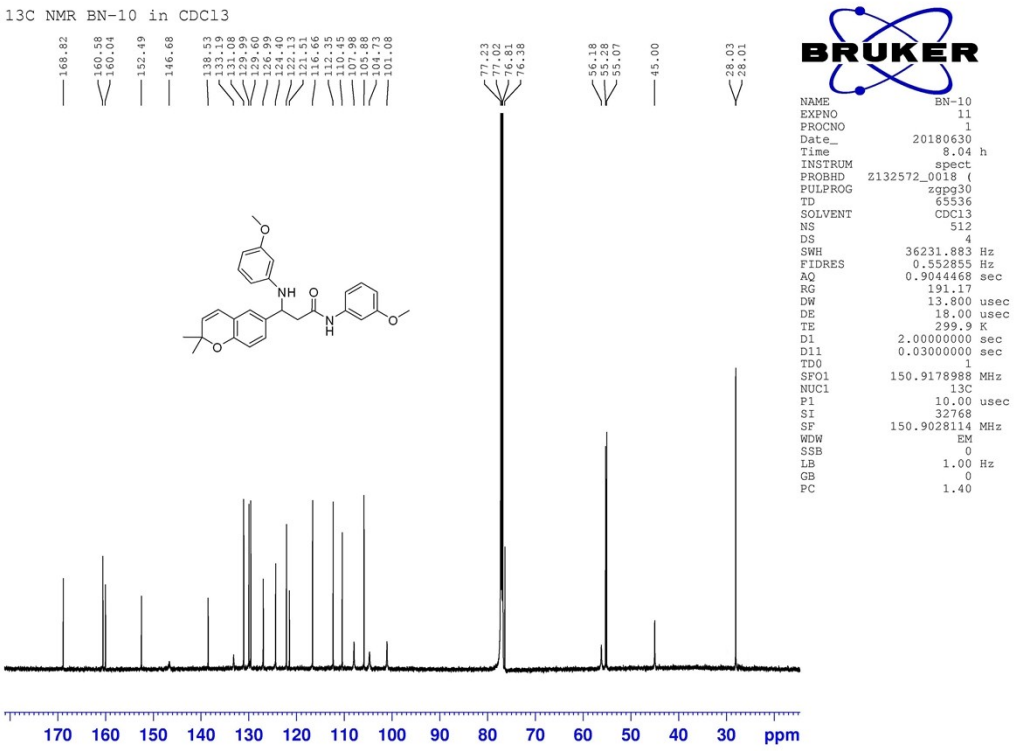
^{13}C-NMR spectrum of compound **BN-09** in $CDCl_3$



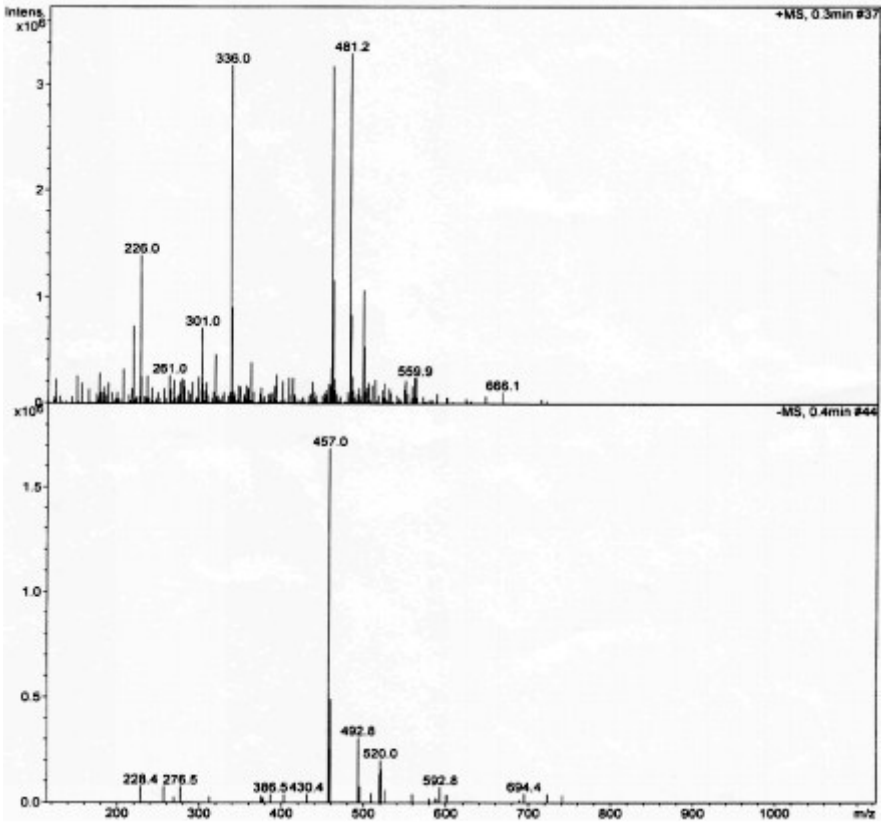
LC-MS spectrum of compound **BN-09**



The ^{1}H-NMR spectrum of compound **BN-10** in $CDCl_3$



^{13}C-NMR spectrum of compound **BN-10** in $CDCl_3$



The LC-MS spectrum of compound **BN-10**

11. Morphology of primary cortical neurons of the rats

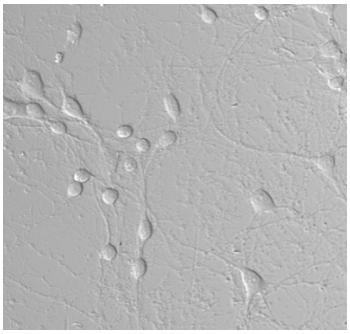


Fig. S1. Primary cortical neurons

12. Cell survival rate of primary neurons after administration in BA compounds (%)

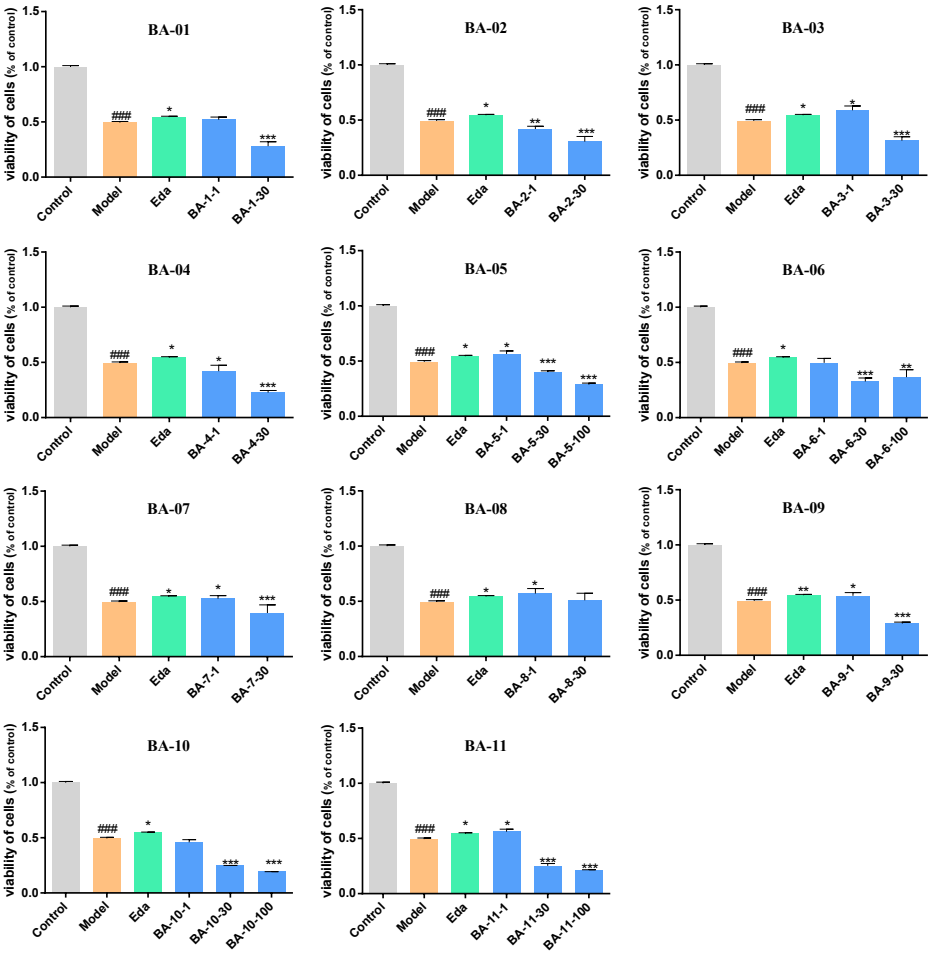


Fig. S2. Cell survival rate of primary neurons after administration in BA compounds (%)

13. Cell survival rate of primary neurons after administration in BN compounds (%)

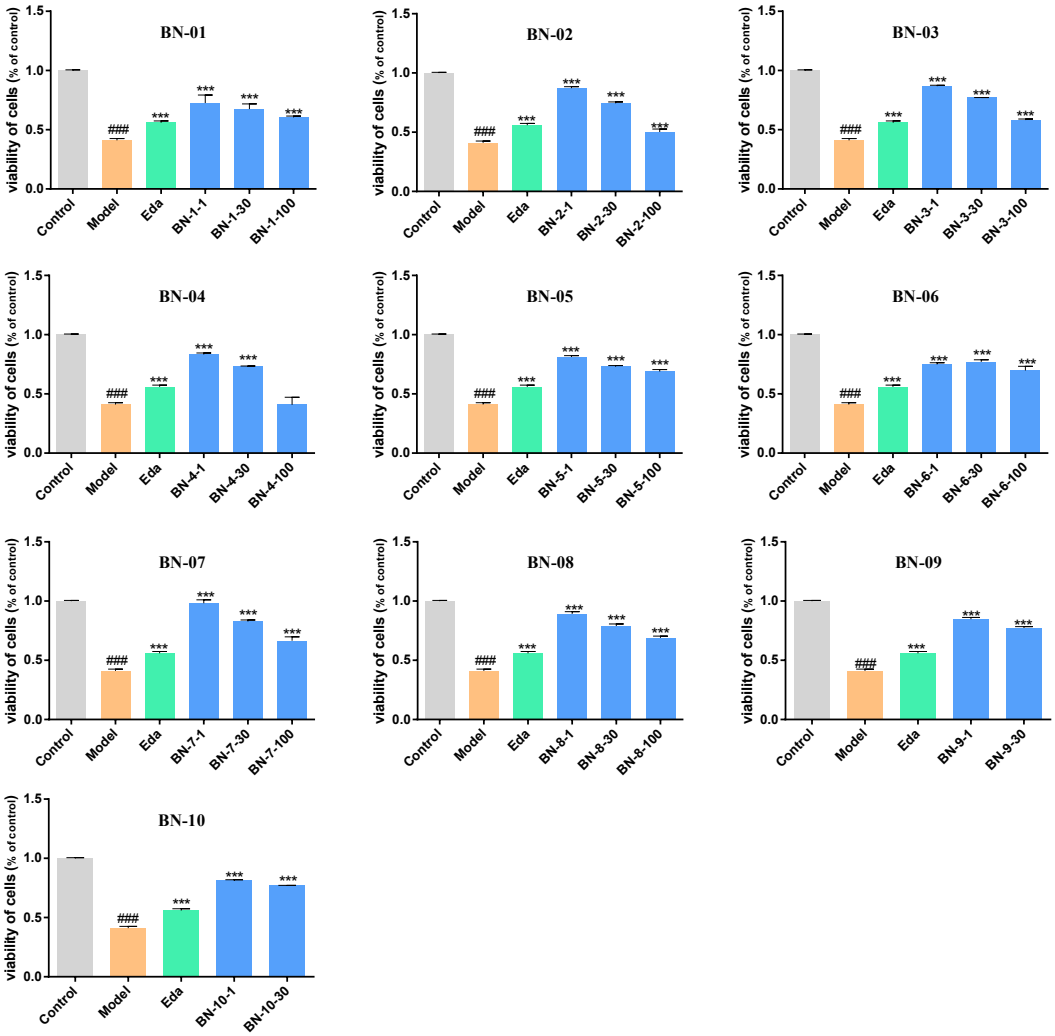


Fig. S3. Cell survival rate of primary neurons after administration in BN compounds (%)

14. The morphological changes of neurons after administration in BN compounds

Fig. S4. The morphological changes of neurons after administration in BN compounds

15. ADMET plot

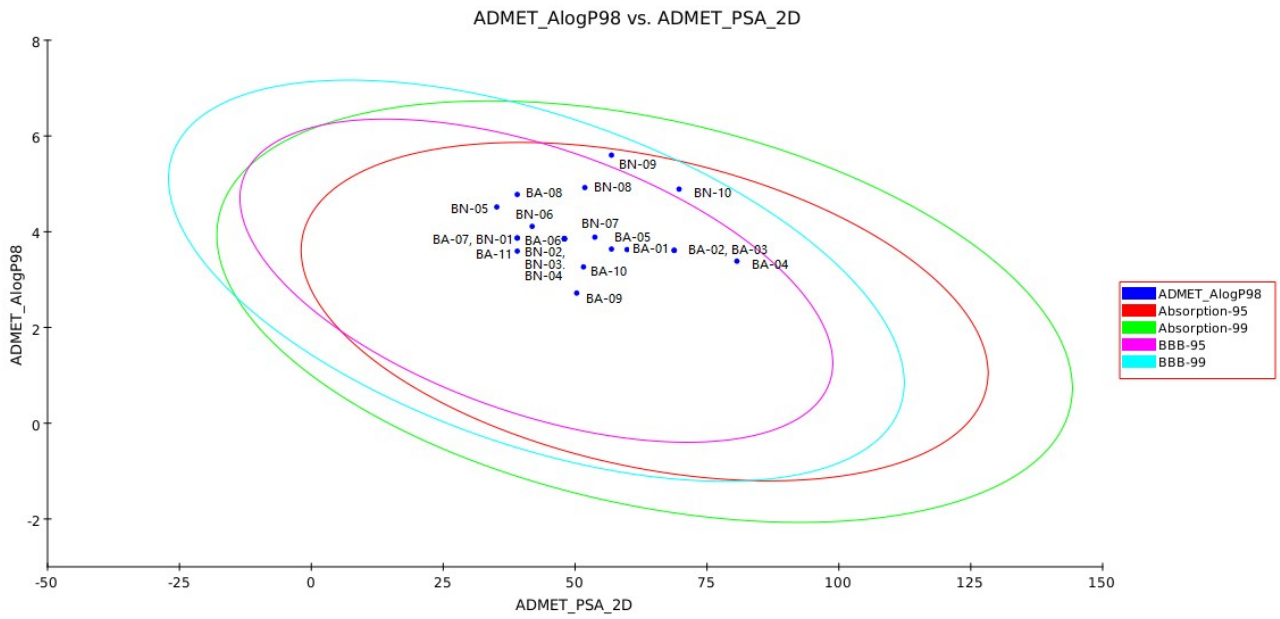


Fig. S5. ADMET plot