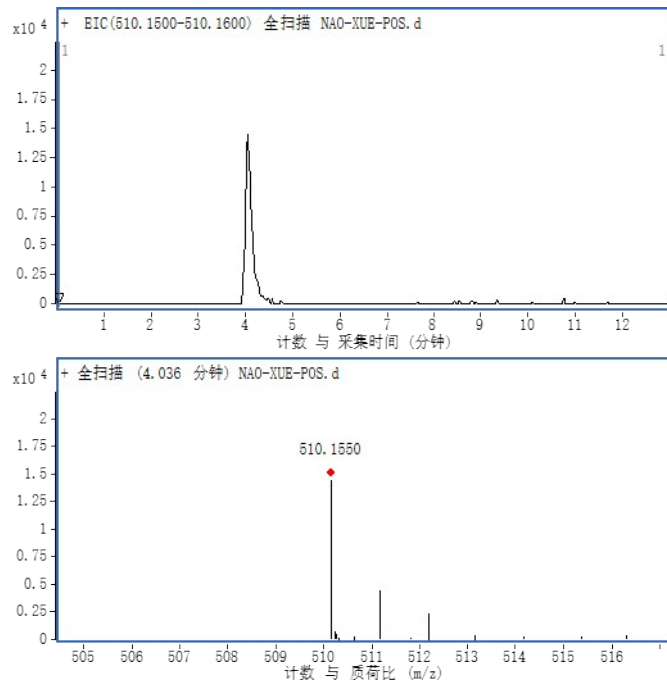


## **The synthesis and bioactivities of 1,2- dithiolan-3-yl motif based ROCK2 inhibitors**

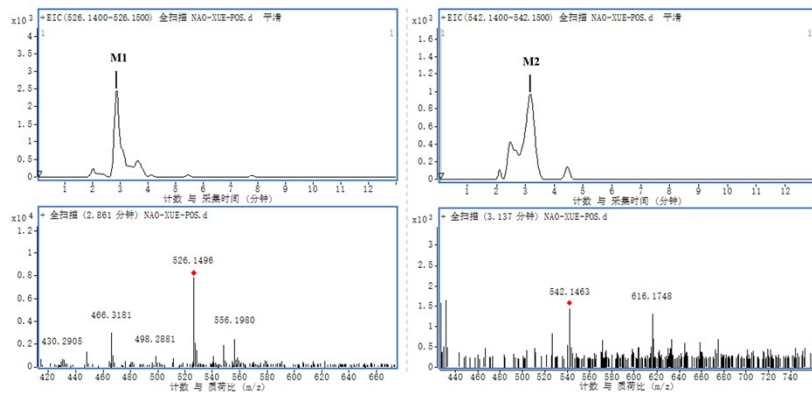
Ruolin Cao<sup>&a</sup>, Fangyu Du<sup>&a</sup>, Zhiqiang Liu<sup>a</sup>, Pengcheng Cai<sup>a</sup>, Minggang Qi<sup>a</sup>, Wei  
Xiao<sup>b\*</sup>, Xuefei Bao<sup>a\*</sup>, Guoliang Chen<sup>a\*</sup>

<sup>a</sup>Key Laboratory of Structure-Based Drug Design & Discovery of Ministry of  
Education, School of Pharmaceutical Engineering, Shenyang Pharmaceutical  
University, Shenyang 110016, PR China.

<sup>b</sup>Jiangsu Kanion Pharmaceutical Co., Ltd., Jiangning Industrial City, Economic and  
Technological Development Zone, Lianyungang, Jiangsu, 222001, China.



**Figure S1.** Extraction ion chromatography of DC01

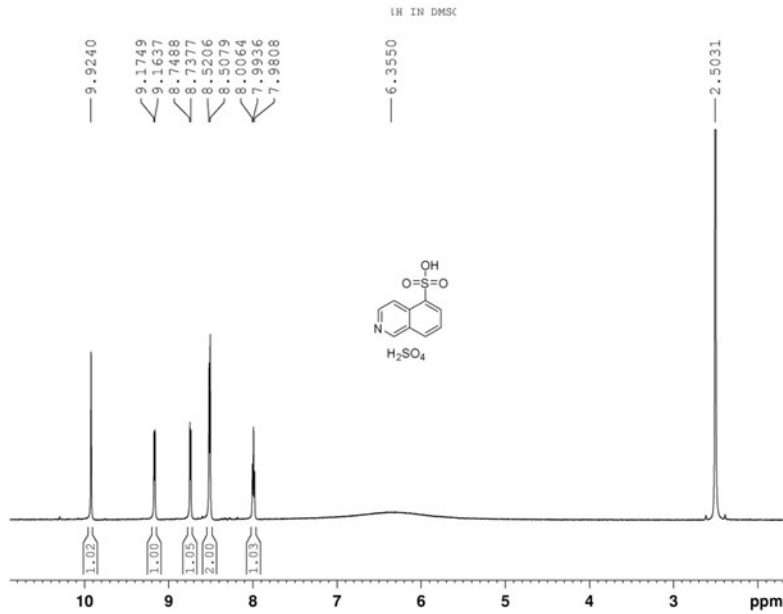


**Figure S2.** Extraction ion chromatography of metabolites M1 and M2

**General Information:**

All the starting materials, reagents and solvents are commercially available and used without further purification. Melting points were determined with a X-4 apparatus and were uncorrected. The nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Ascend 400 (Billerica, MA, USA) using tetramethylsilane as an internal standard. Electrospray ionization mass spectrometry (ESI-MS) analyses were recorded in an Agilent 1100 Series MSD Trap SL (Santa Clara, CA, USA). The reactions were monitored by thin-layer chromatography (TLC; HG/T2354-92, GF254).

# NMR Spectra:

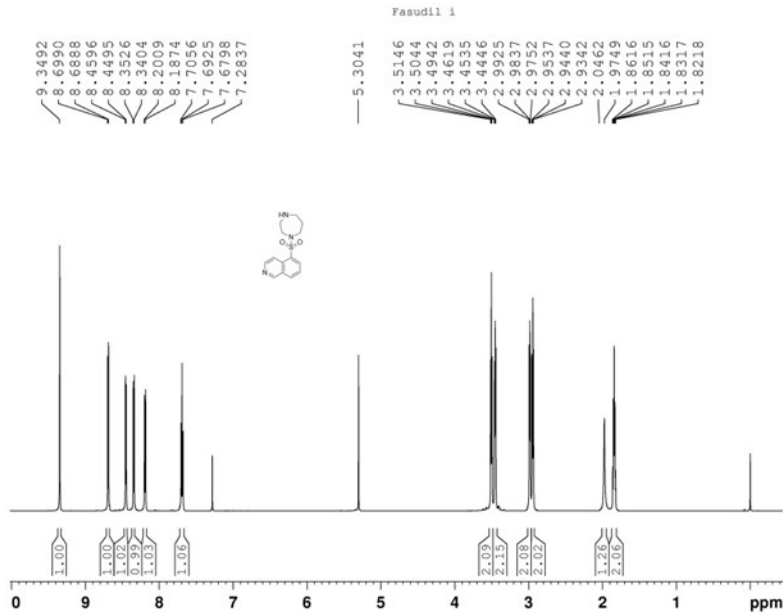


```

NAME      QISquin-5-so3H
EXPNO     1
PROCNO    1
Date_     20180904
Time      13.21
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         16
DS         2
SWH        12335.526 Hz
FIDRES     0.188223 Hz
AQ         2.6564426 sec
RG         174.88
DW         40.533 usec
DE         6.50 usec
TE         297.9 K
D1         1.00000000 sec

----- CHANNEL f1 -----
NUC1      1H
P1        12.85 usec
SI        65536
SF        600.1300053 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
    
```

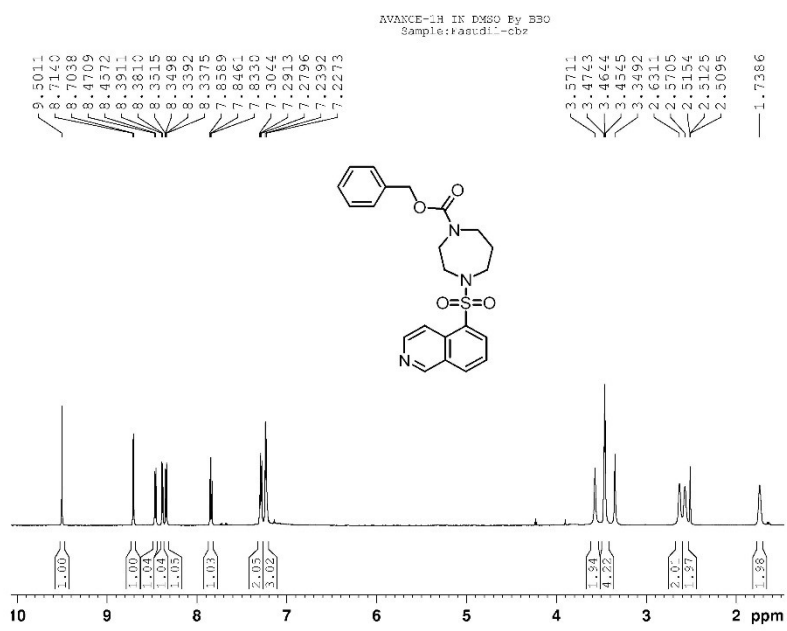
<sup>1</sup>H NMR spectrum of compound 2



```

NAME      Fasudil
EXPNO     10
PROCNO    1
Date_     20180912
Time      14.28 h
INSTRUM   spect
PROBHD    z132572_0018 (
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         8
DS         2
SWH        12019.230 Hz
FIDRES     0.183399 Hz
AQ         2.7263477 sec
RG         8.2
DW         41.600 usec
DE         10.00 usec
TE         300.1 K
D1         1.00000000 sec
TDO        1
SFO1      600.1337058 MHz
NUC1      1H
P1        12.00 usec
SI        65536
SF        600.1300004 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
    
```

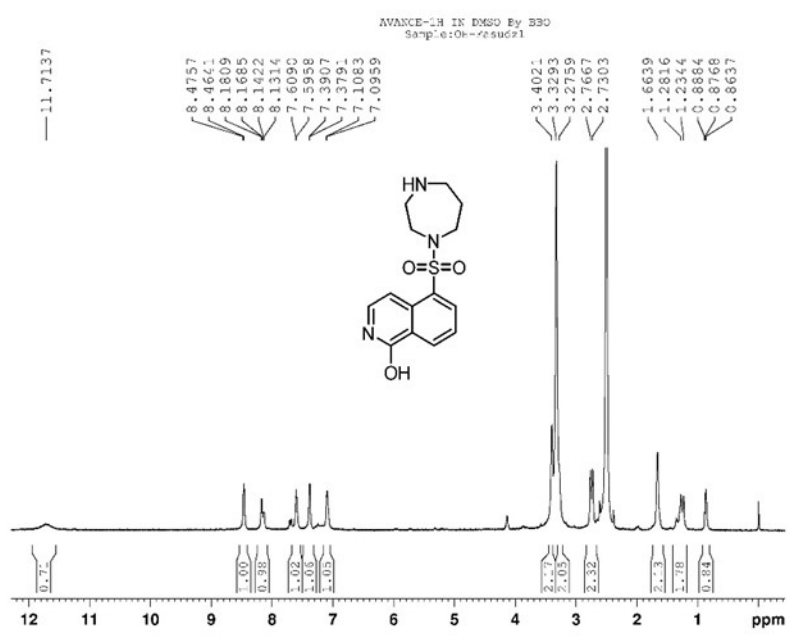
<sup>1</sup>H NMR spectrum of compound 4



```

NAME          kasudil-cbz
EXPNO         1
PROCNO        1
Date_         20181012
Time          13.12
INSTRUM       spect
PROBHD        5 mm F400 BBO
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            16
DS            2
SWH           12335.526 Hz
FIDRES        0.188225 Hz
AQ            2.6584426 s
RG            174.88
PC            1.00
SFO           600.1300051 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```

<sup>1</sup>H NMR spectrum of compound 8



```

NAME          Oh-kasudil
EXPNO         1
PROCNO        1
Date_         20181114
Time          14.50
INSTRUM       spect
PROBHD        5 mm F400 BBO
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            16
DS            2
SWH           12335.526 Hz
FIDRES        0.188225 Hz
AQ            2.6584426 s
RG            174.88
PC            1.00
SFO           600.1300051 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```

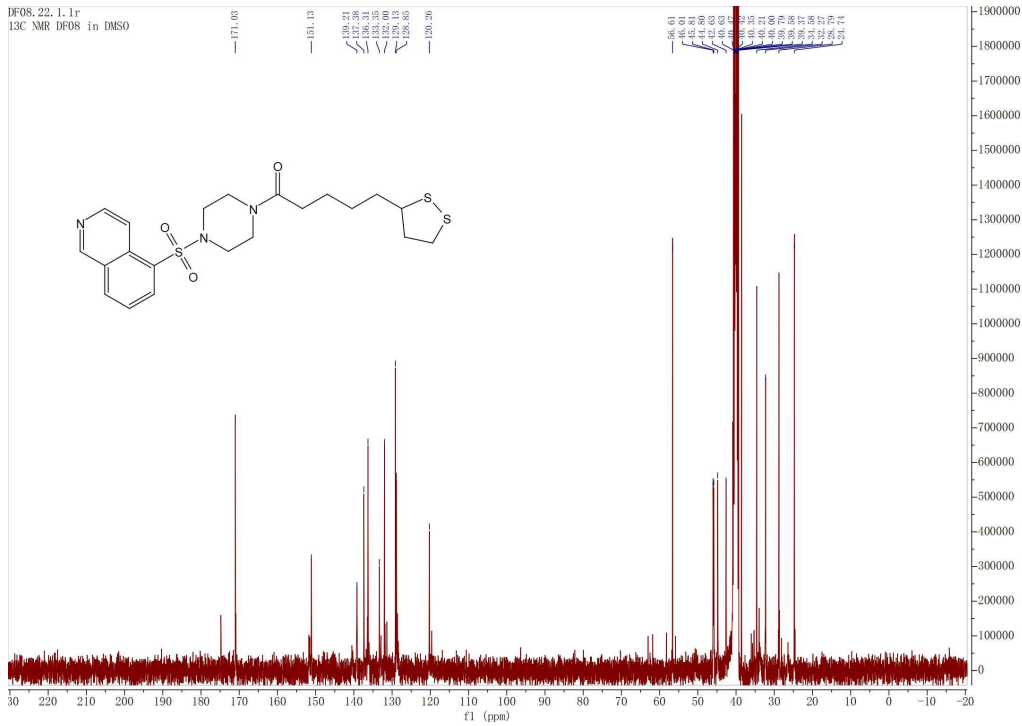
<sup>1</sup>H NMR spectrum of compound 11



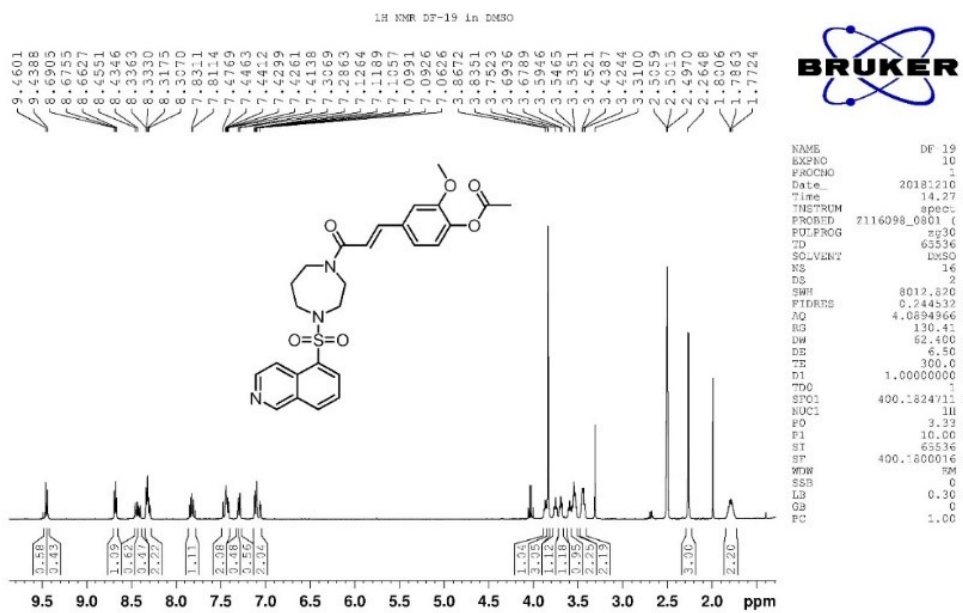




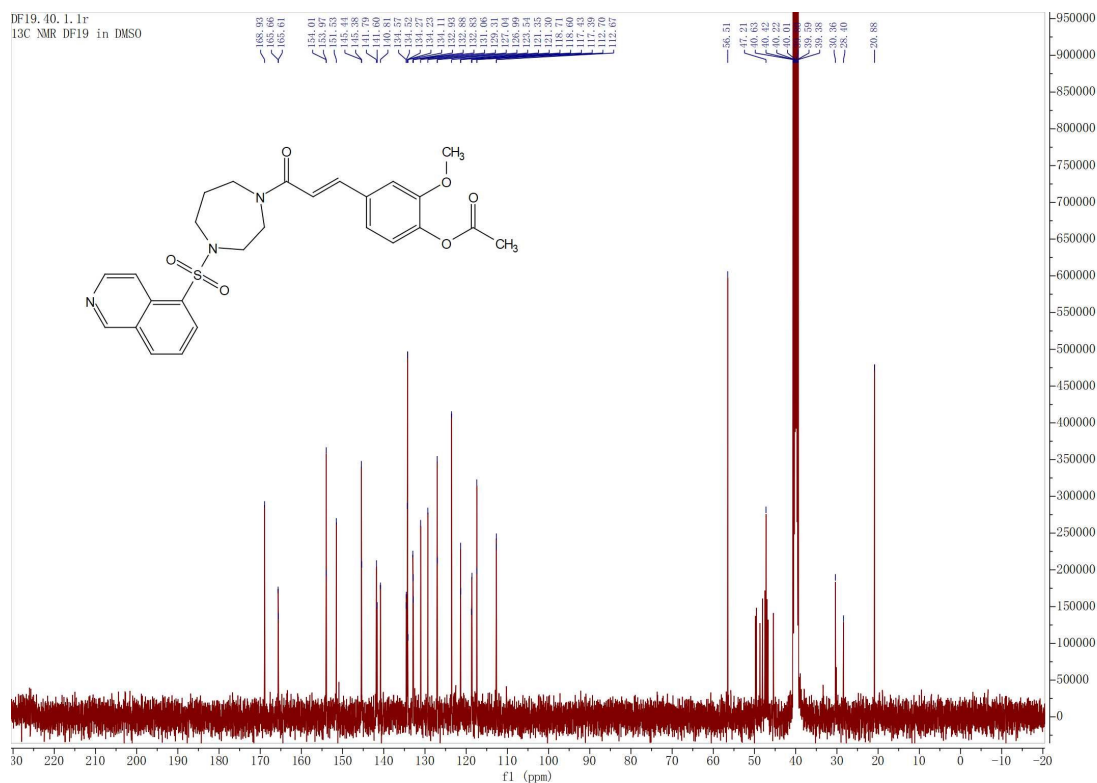




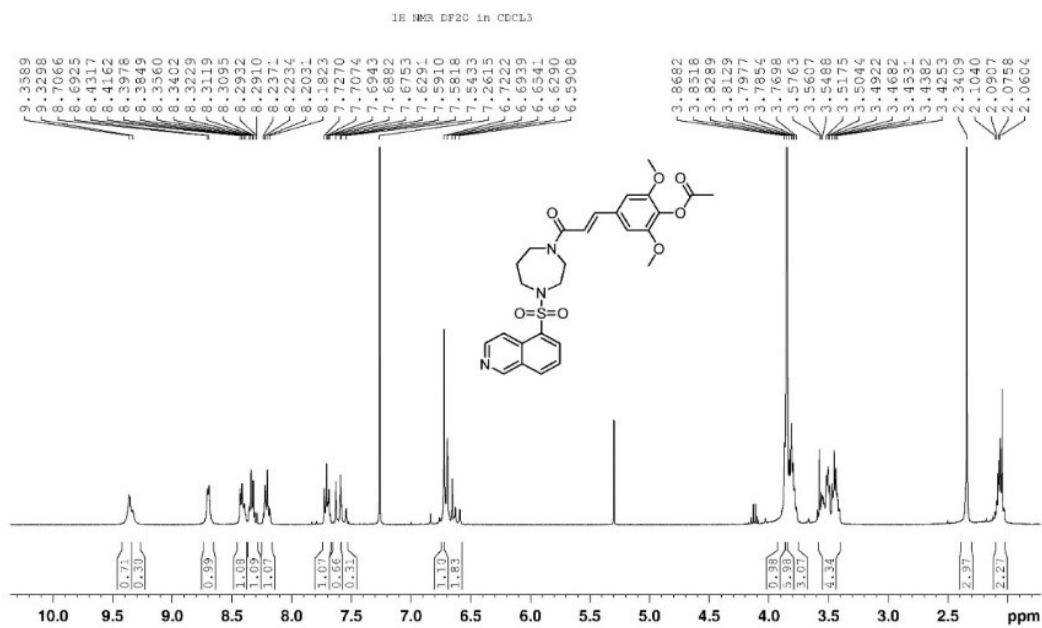
<sup>13</sup>C NMR spectrum of compound DC03



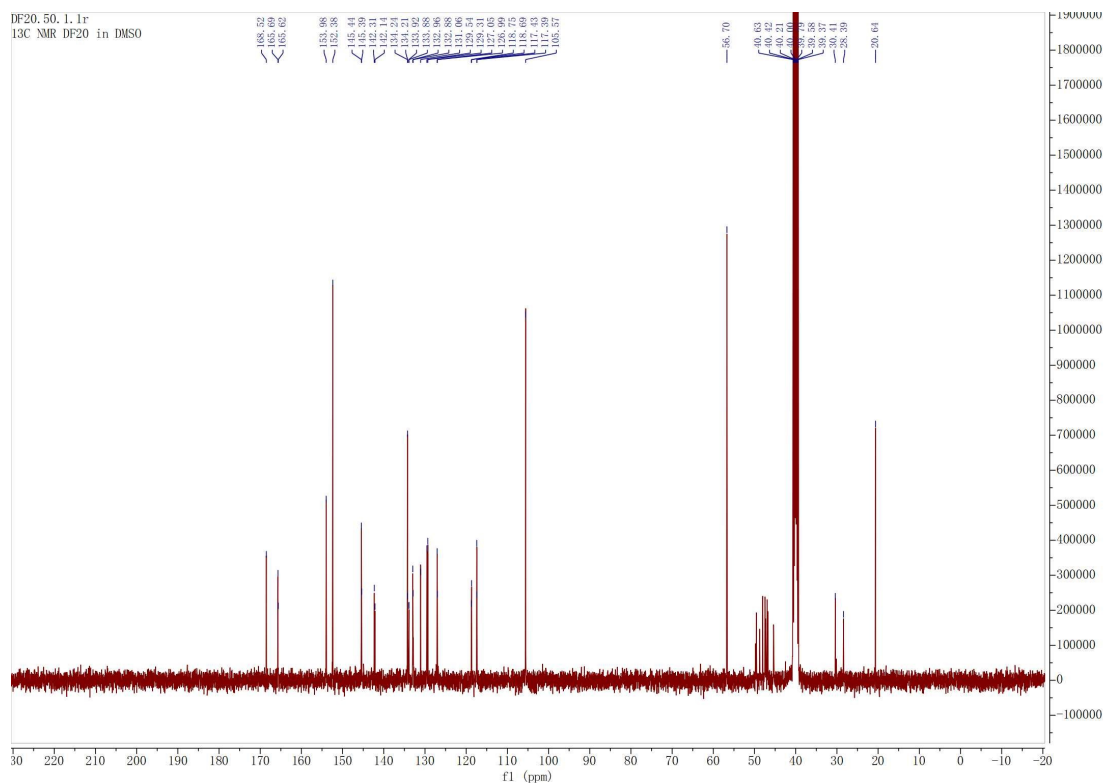
<sup>1</sup>H NMR spectrum of compound DC04



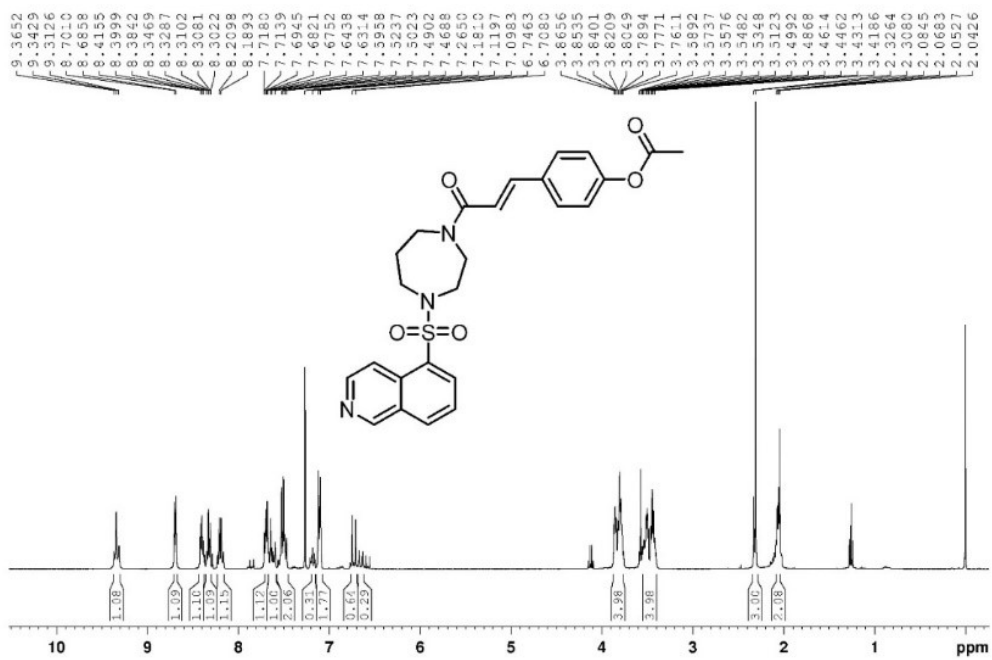
<sup>13</sup>C NMR spectrum of compound DC04



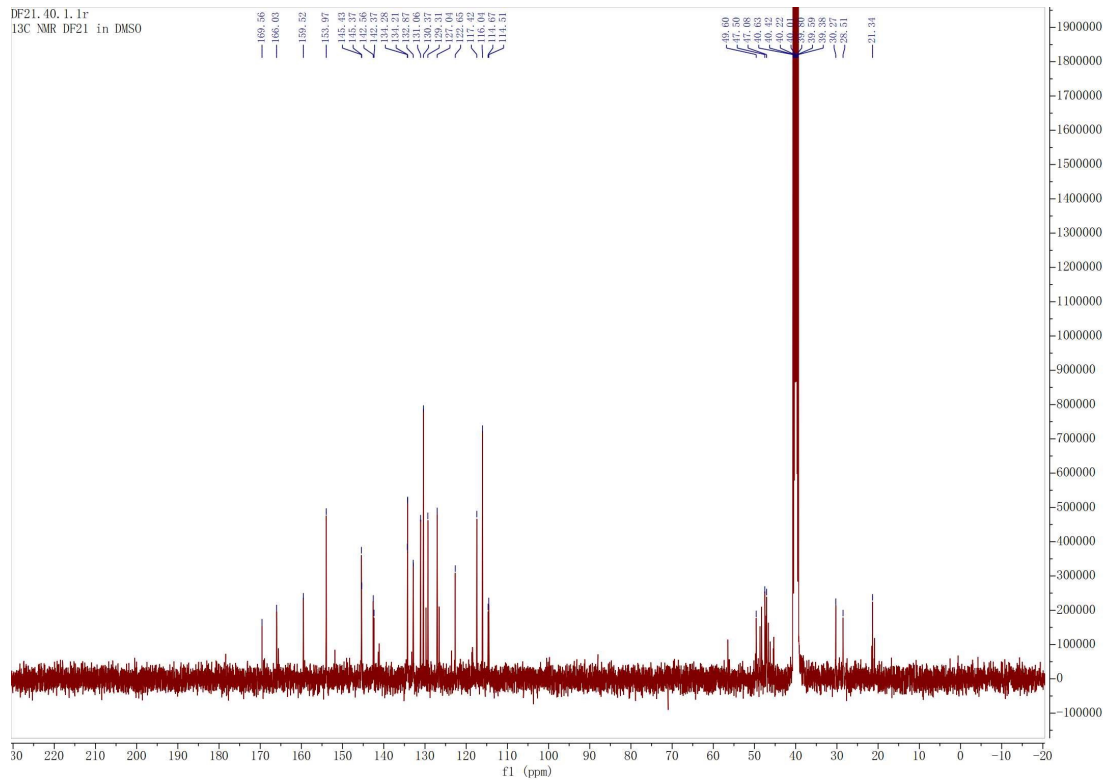
<sup>1</sup>H NMR spectrum of compound DC05



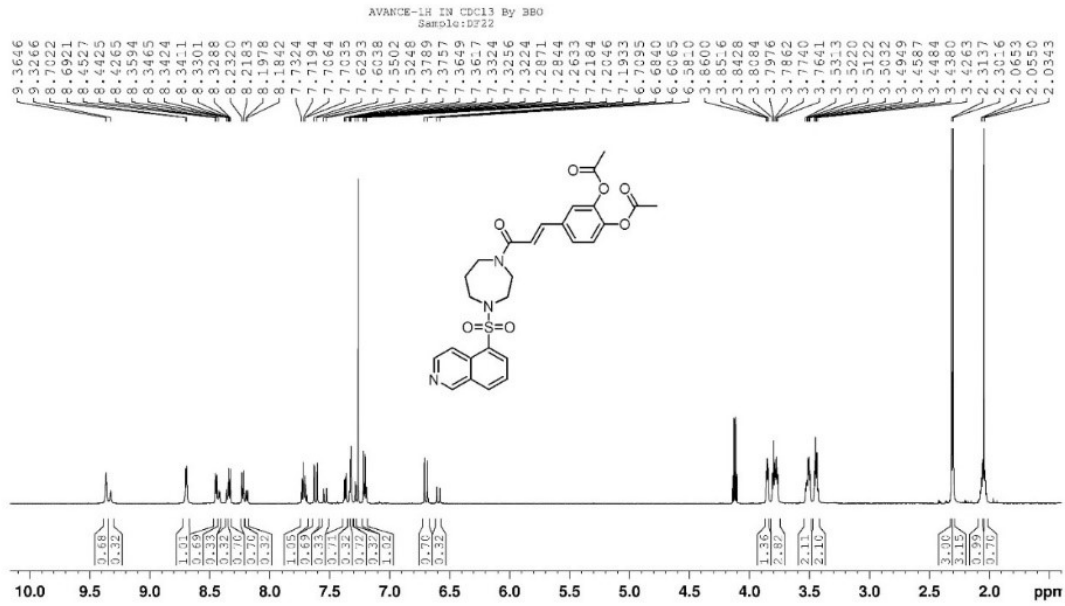
<sup>13</sup>C NMR spectrum of compound DC05



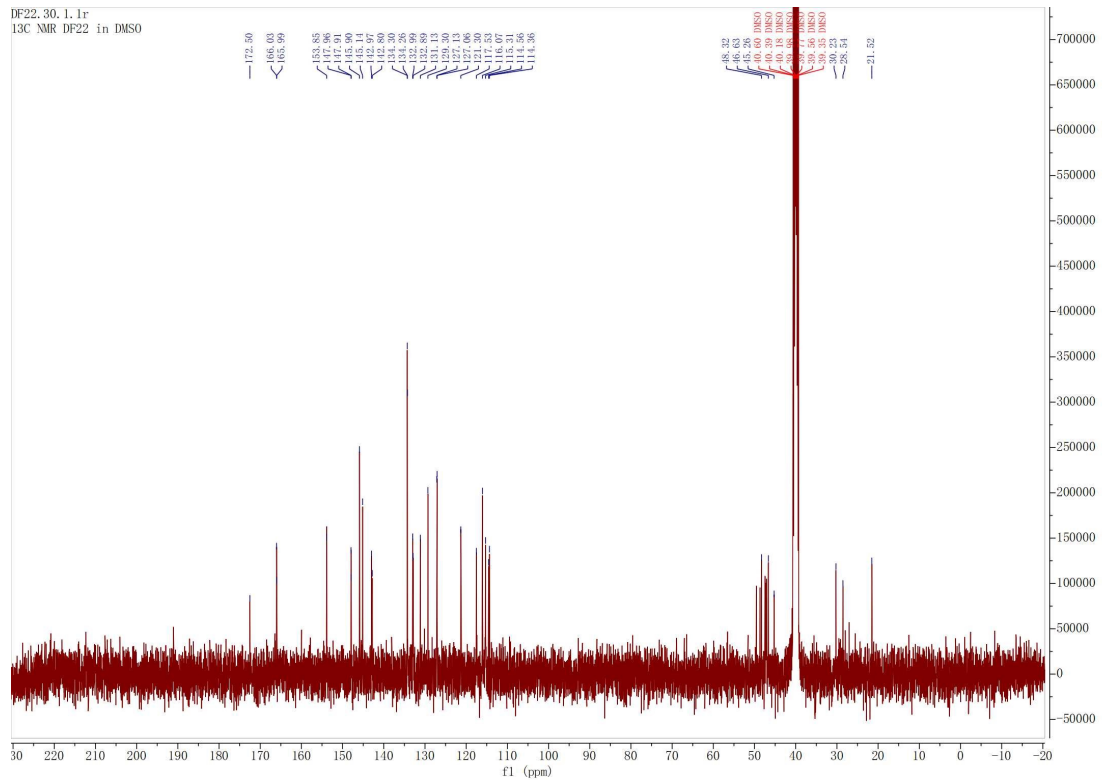
<sup>1</sup>H NMR spectrum of compound DC06



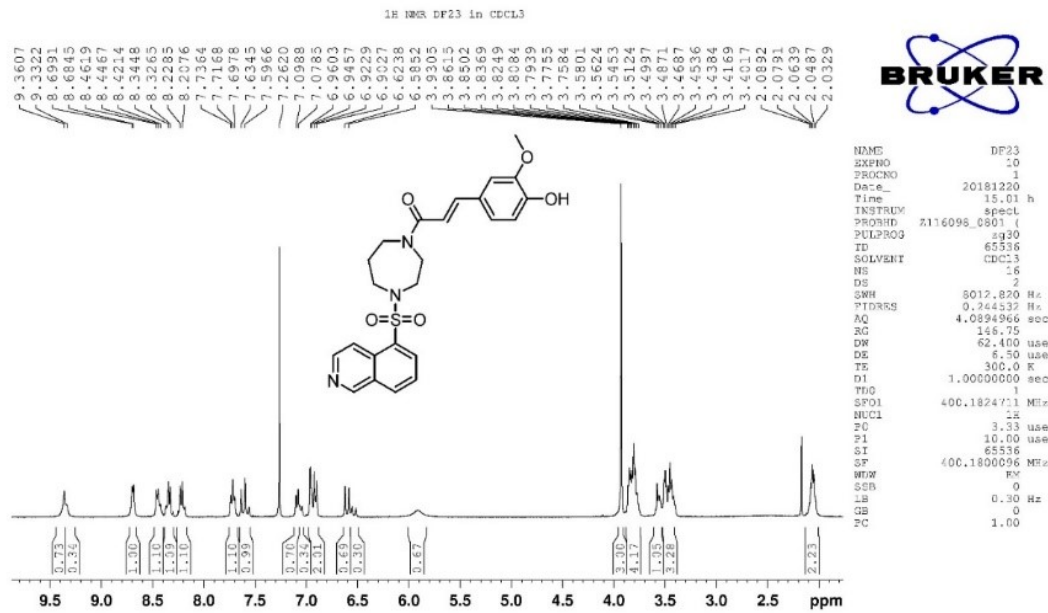
<sup>13</sup>C NMR spectrum of compound DC06



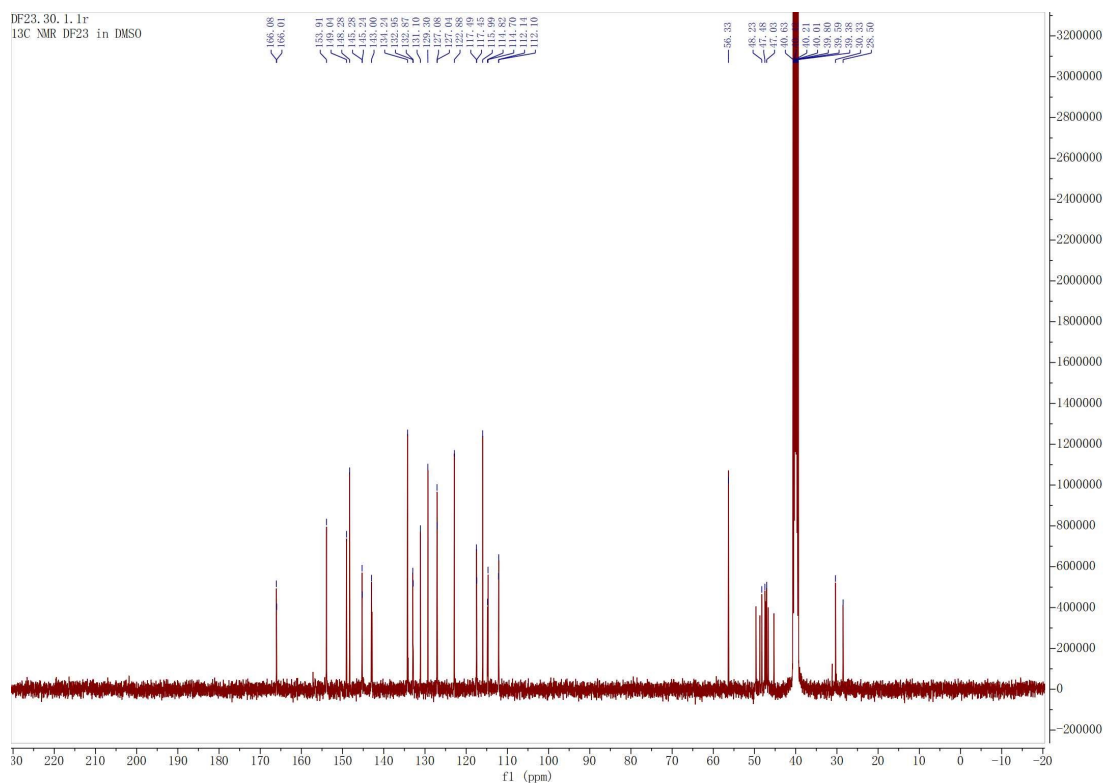
<sup>1</sup>H NMR spectrum of compound DC07



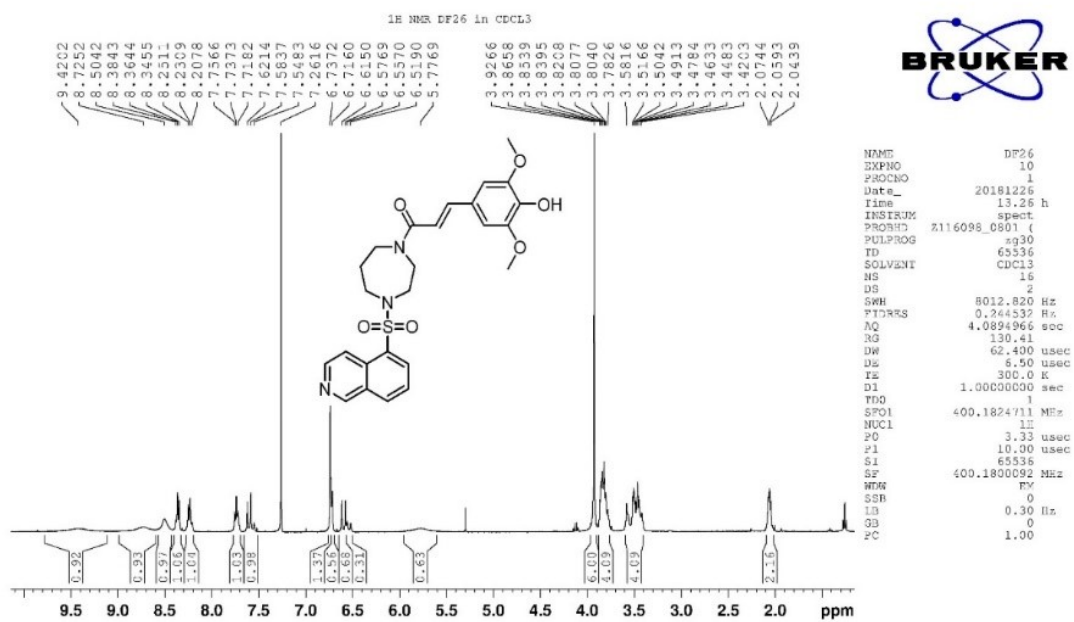
<sup>13</sup>C NMR spectrum of compound DC07



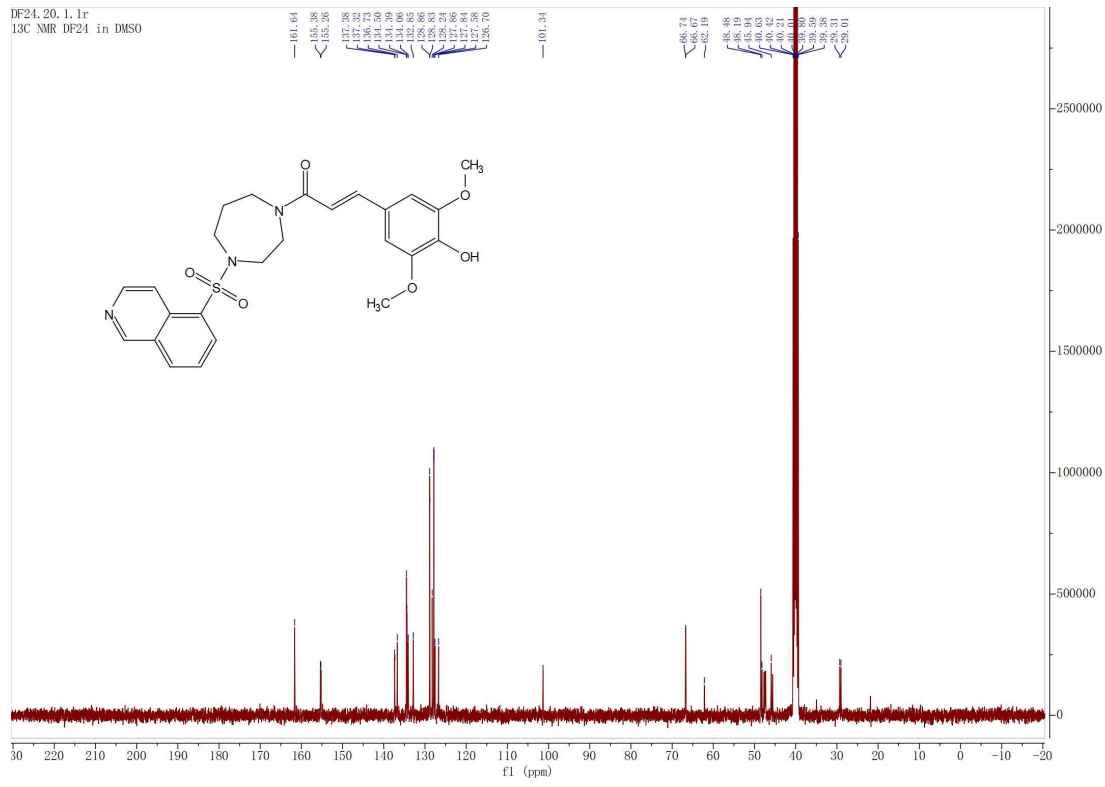
<sup>1</sup>H NMR spectrum of compound DC08



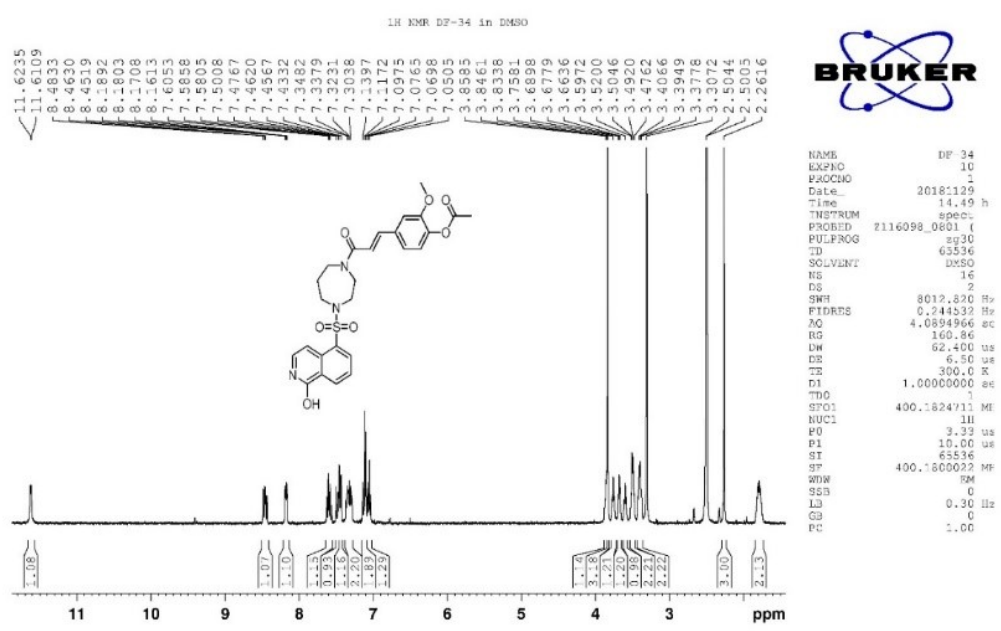
<sup>13</sup>C NMR spectrum of compound DC08



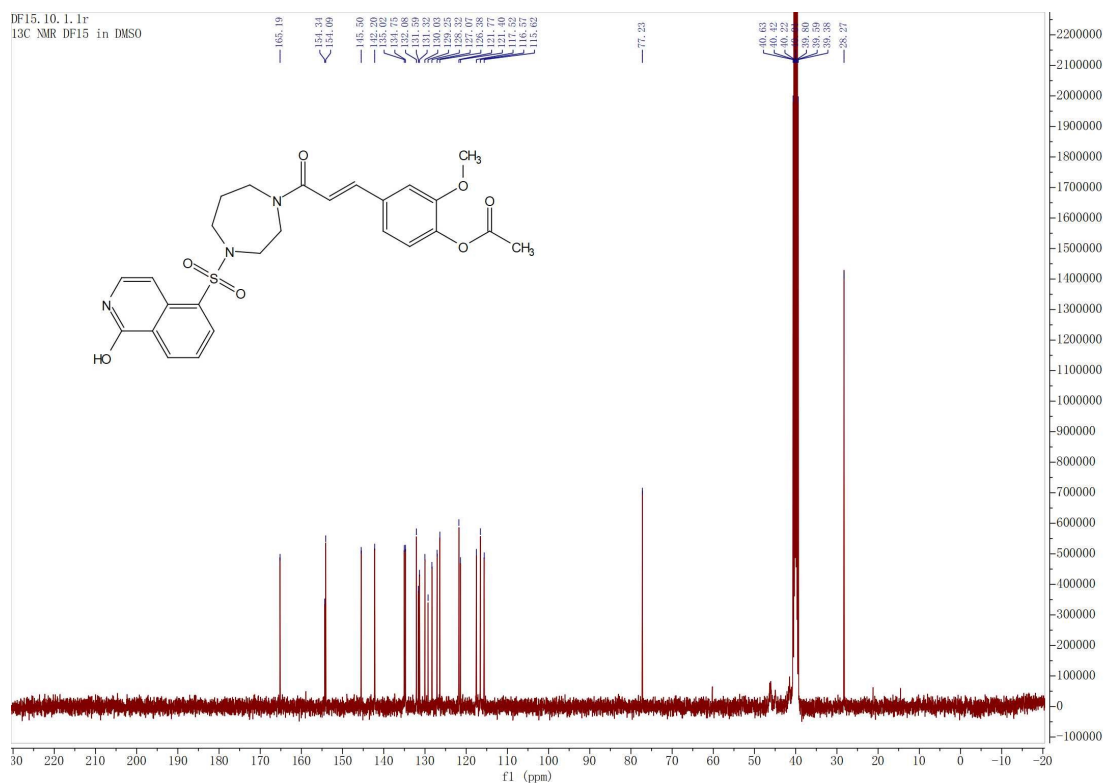
<sup>1</sup>H NMR spectrum of compound DC09



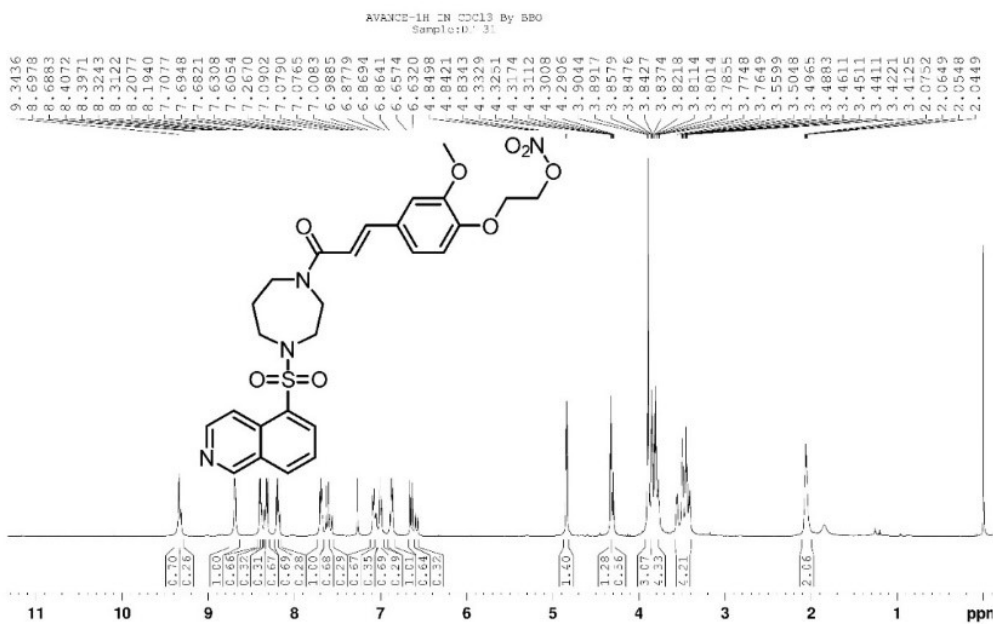
<sup>13</sup>C NMR spectrum of compound DC09



<sup>1</sup>H NMR spectrum of compound DC10

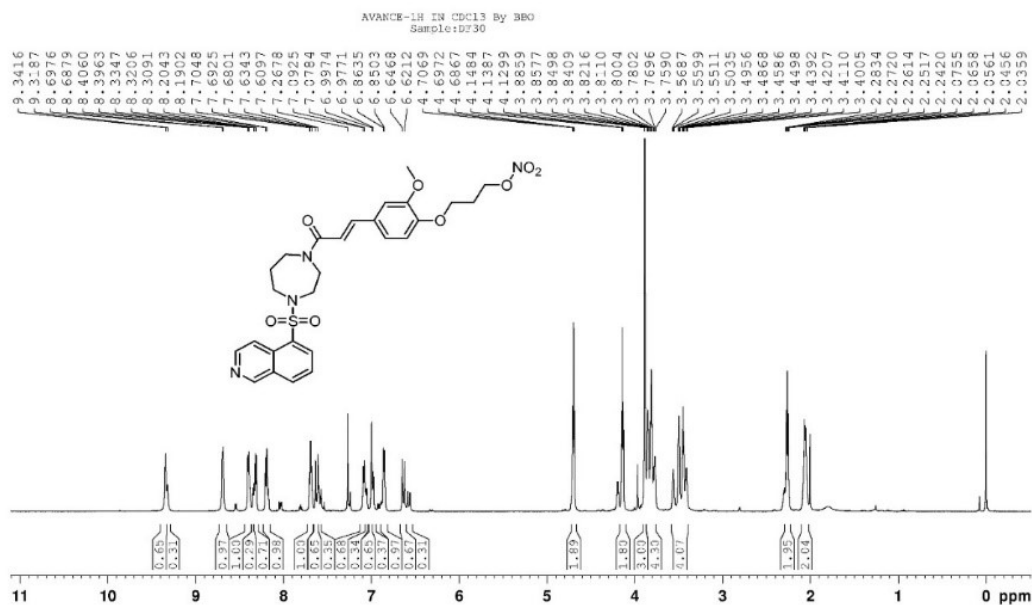


<sup>13</sup>C NMR spectrum of compound DC10

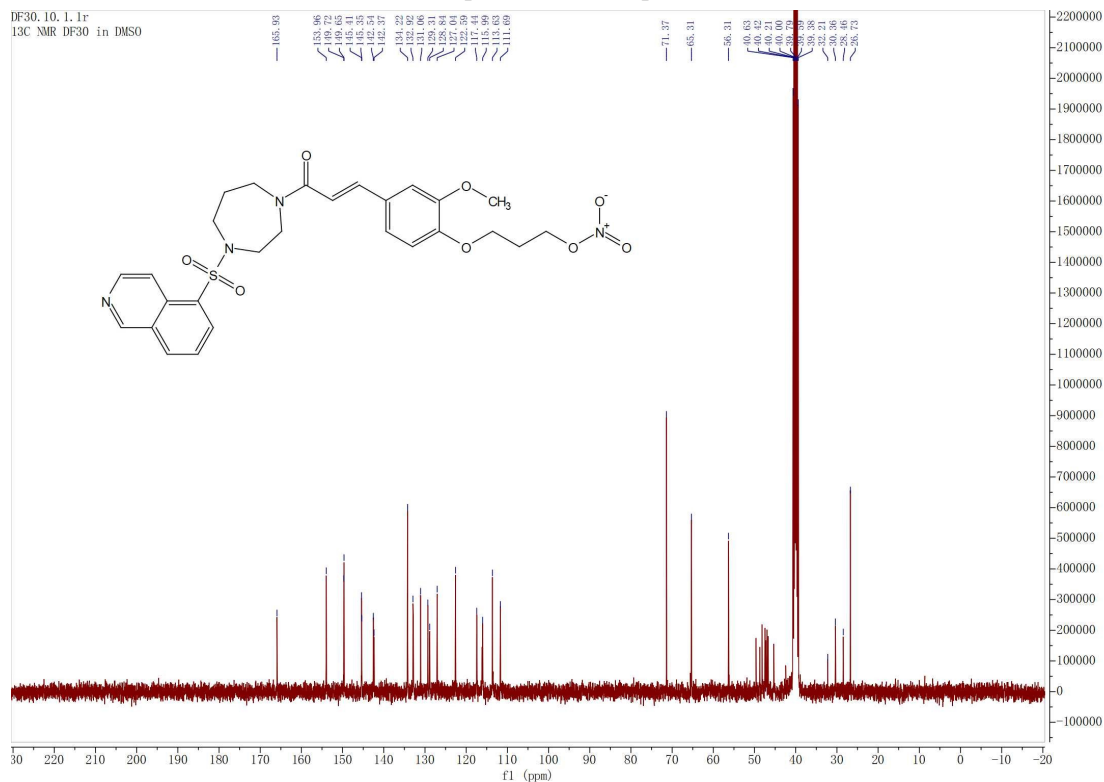


<sup>1</sup>H NMR spectrum of compound DC11

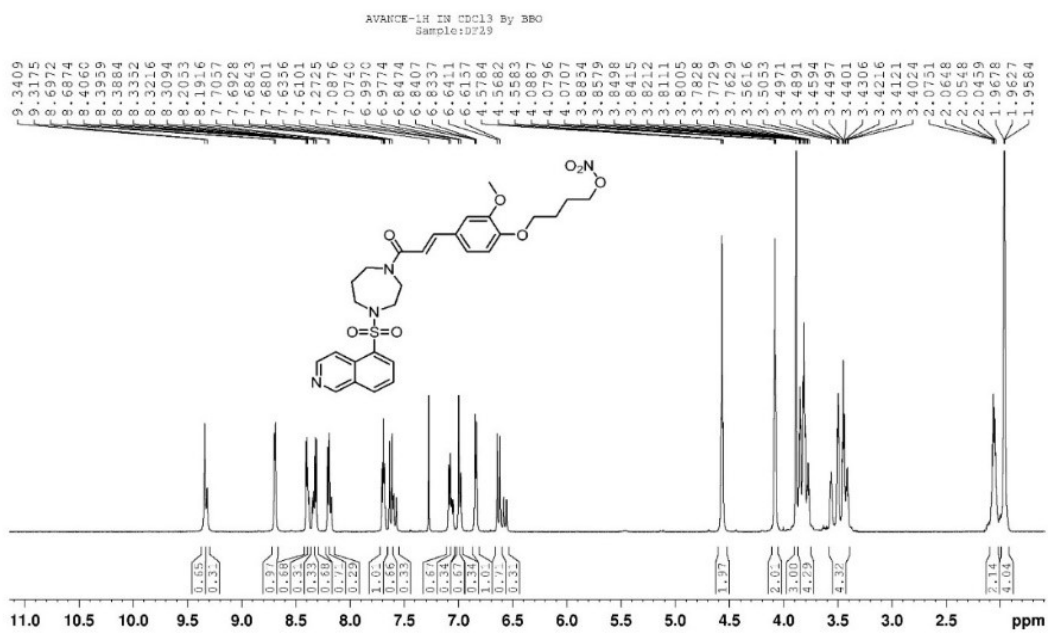




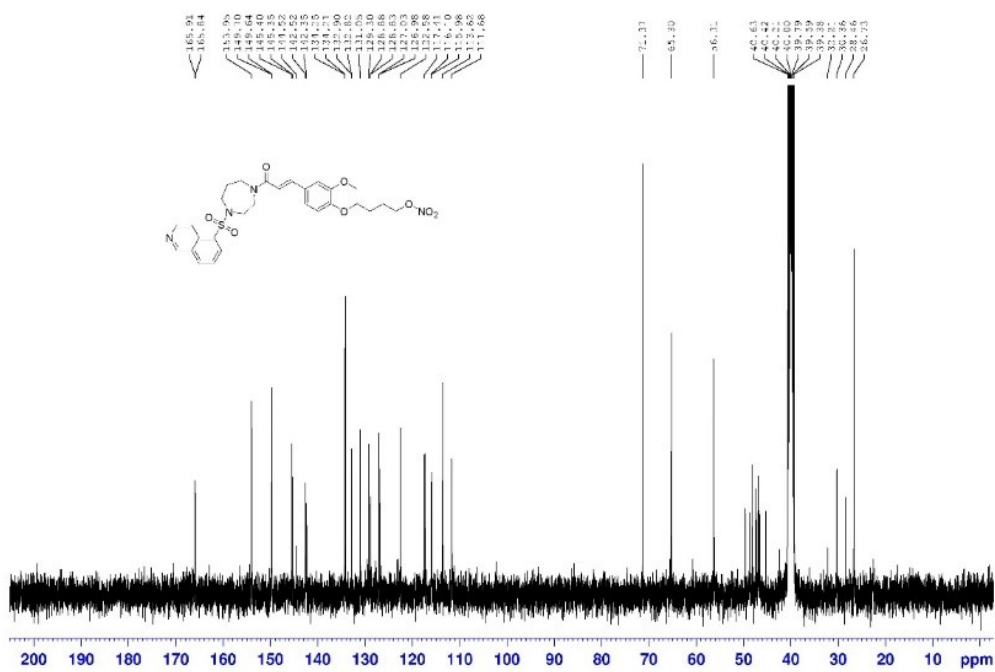
<sup>1</sup>H NMR spectrum of compound DC12



<sup>13</sup>C NMR spectrum of compound DC12

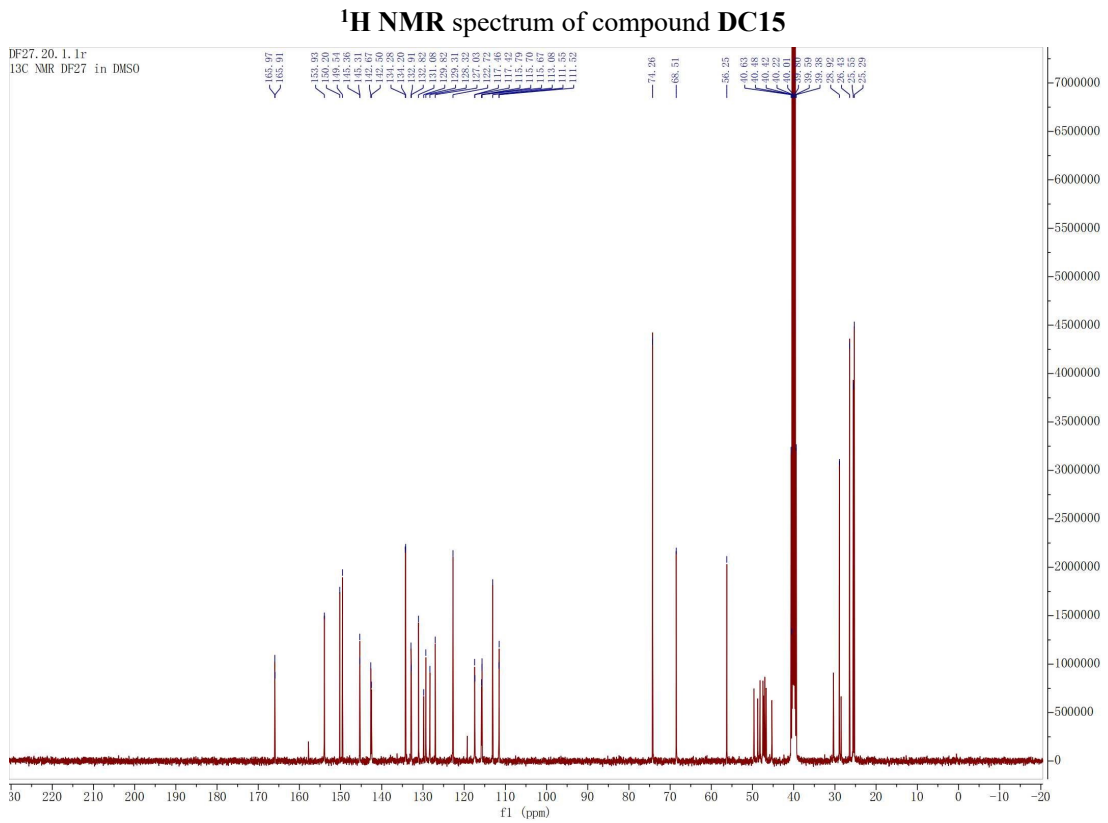
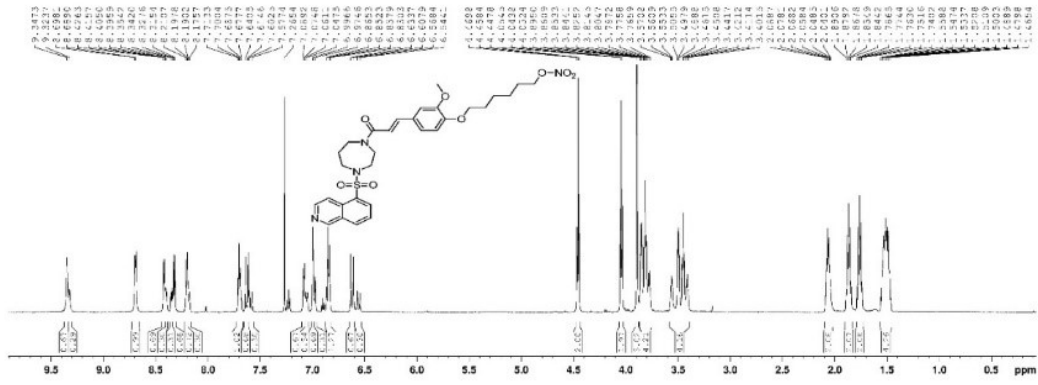


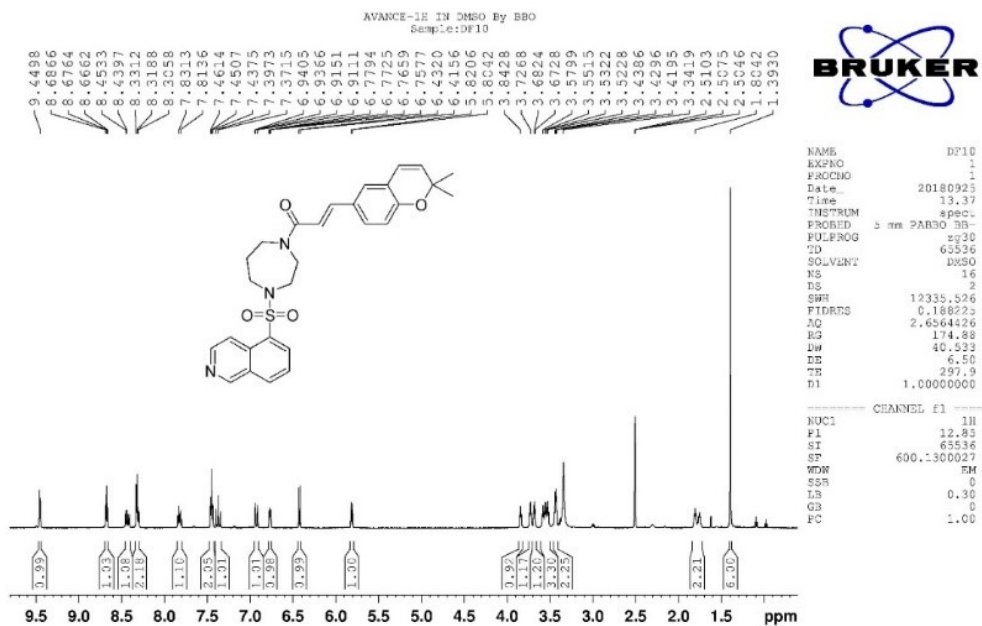
<sup>1</sup>H NMR spectrum of compound DC13



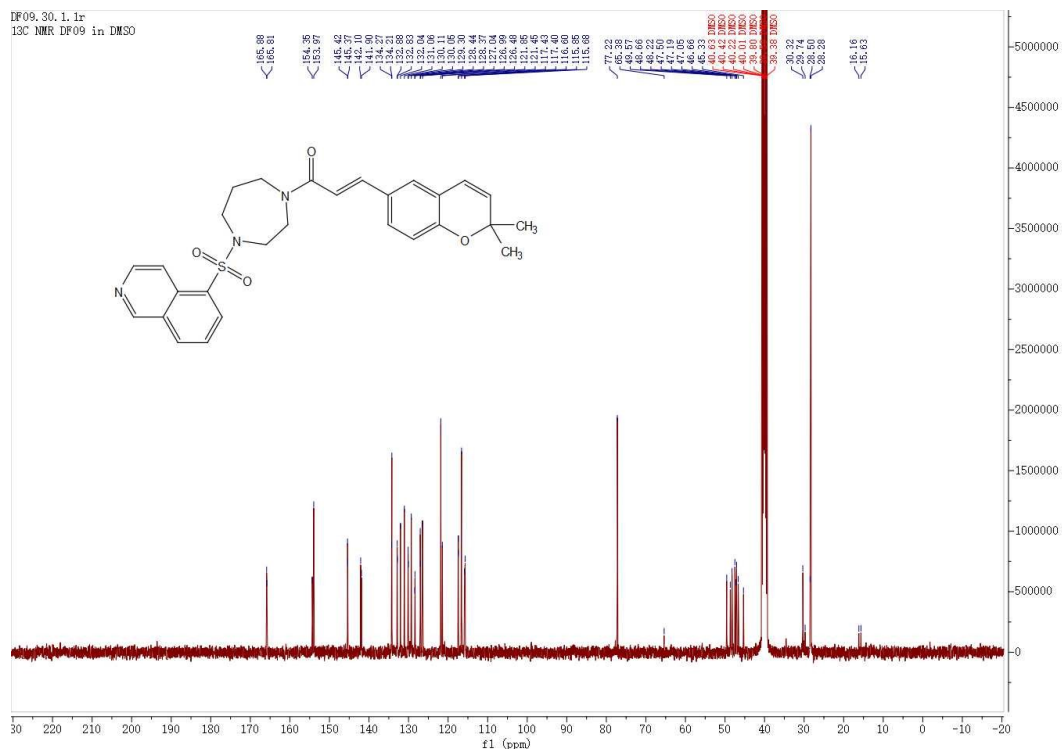
<sup>13</sup>C NMR spectrum of compound DC13



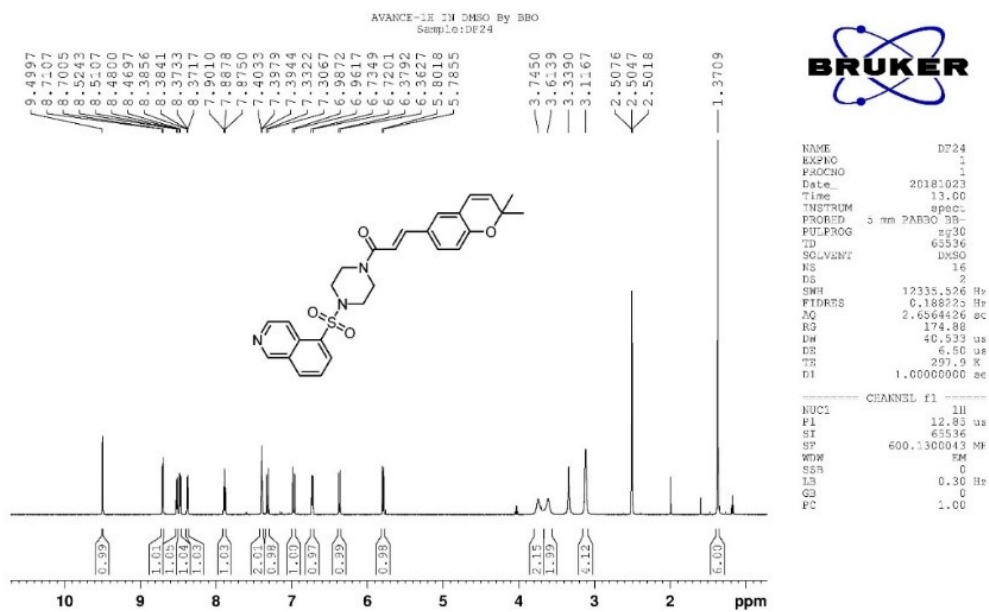




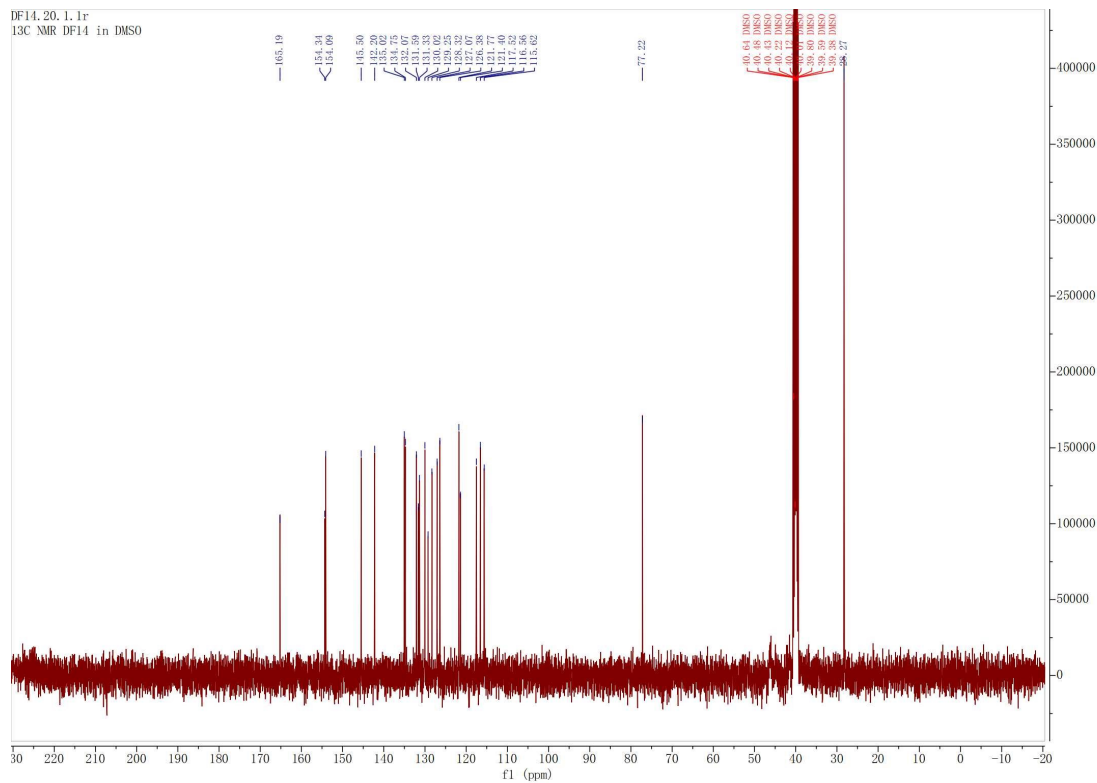
**<sup>1</sup>H NMR spectrum of compound DC16**



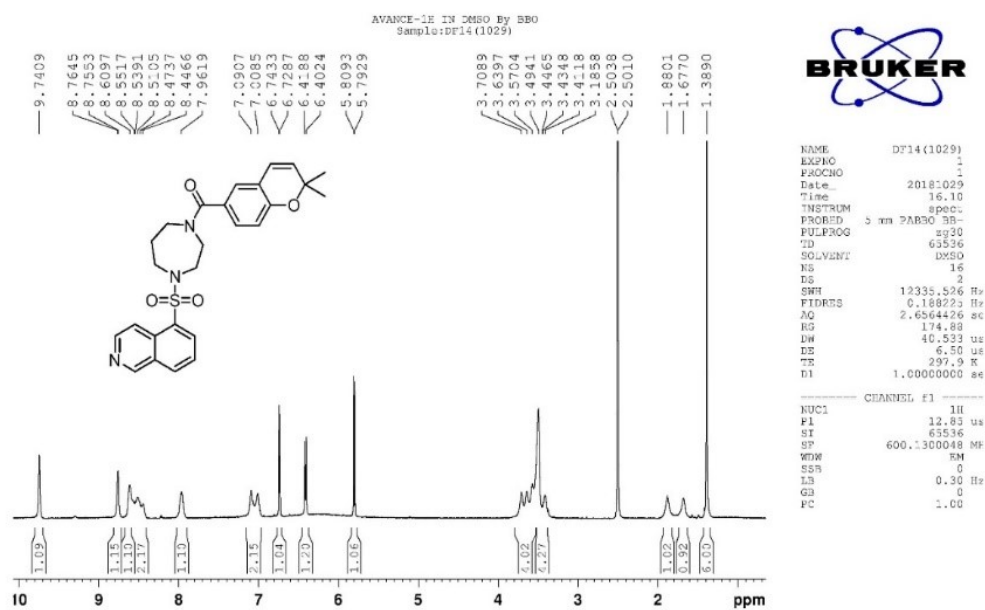
**<sup>13</sup>C NMR spectrum of compound DC16**



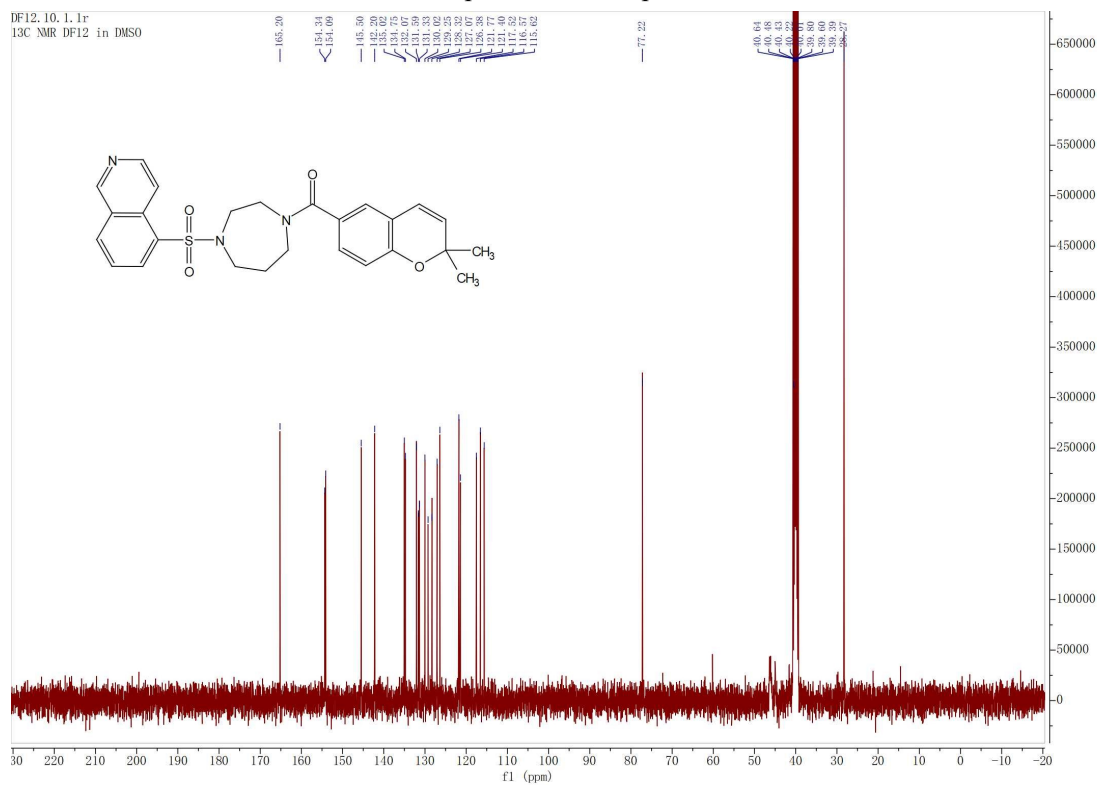
<sup>1</sup>H NMR spectrum of compound DC17



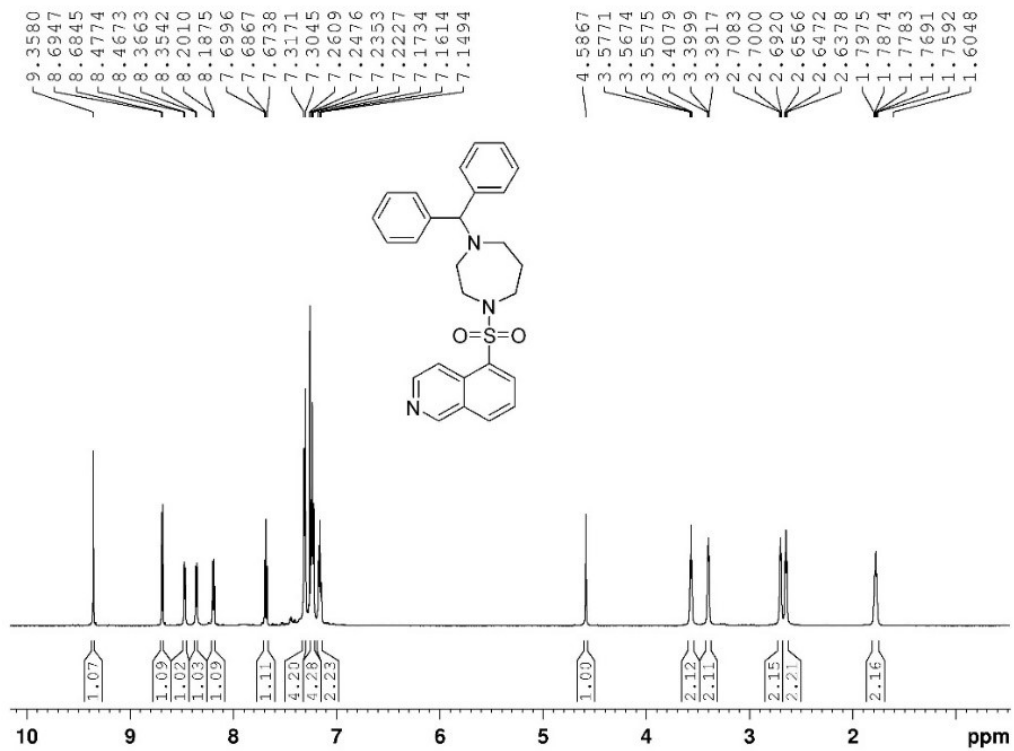
<sup>13</sup>C NMR spectrum of compound DC17



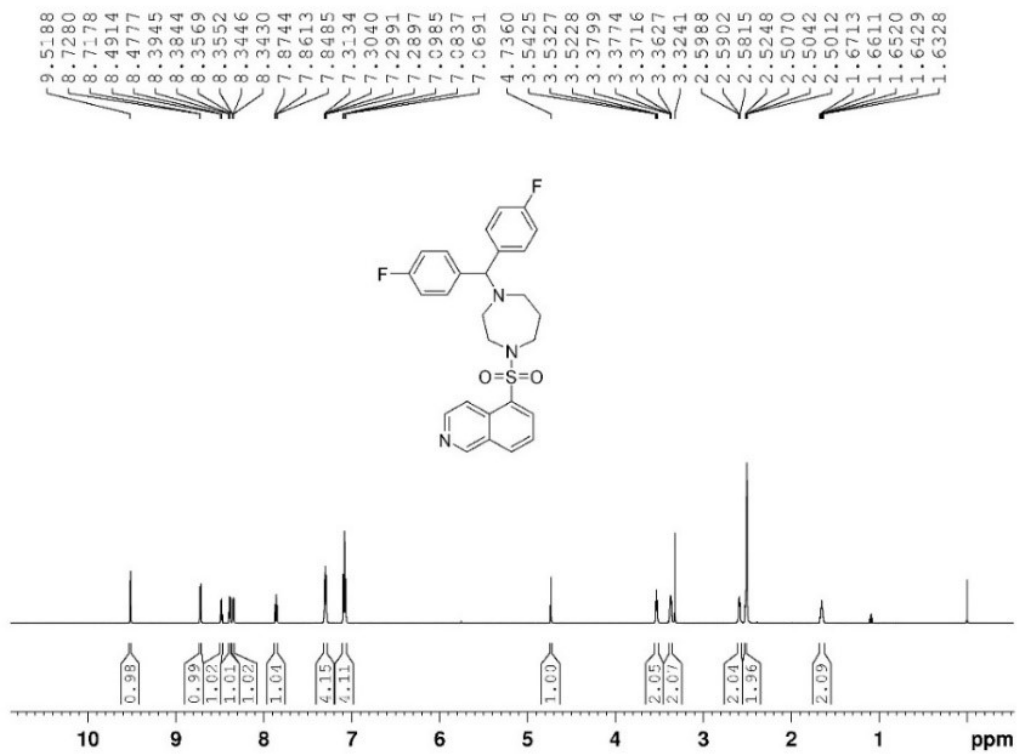
<sup>1</sup>H NMR spectrum of compound DC18



<sup>13</sup>C NMR spectrum of compound DC18

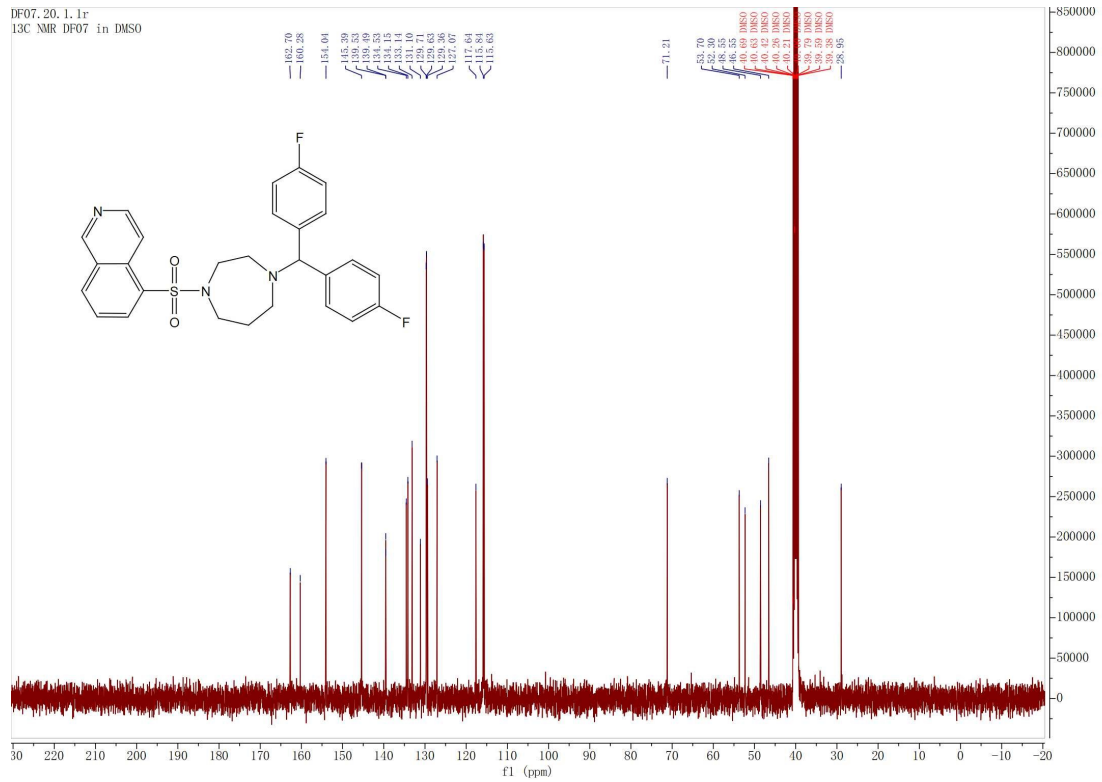


**<sup>1</sup>H NMR spectrum of compound DC19**

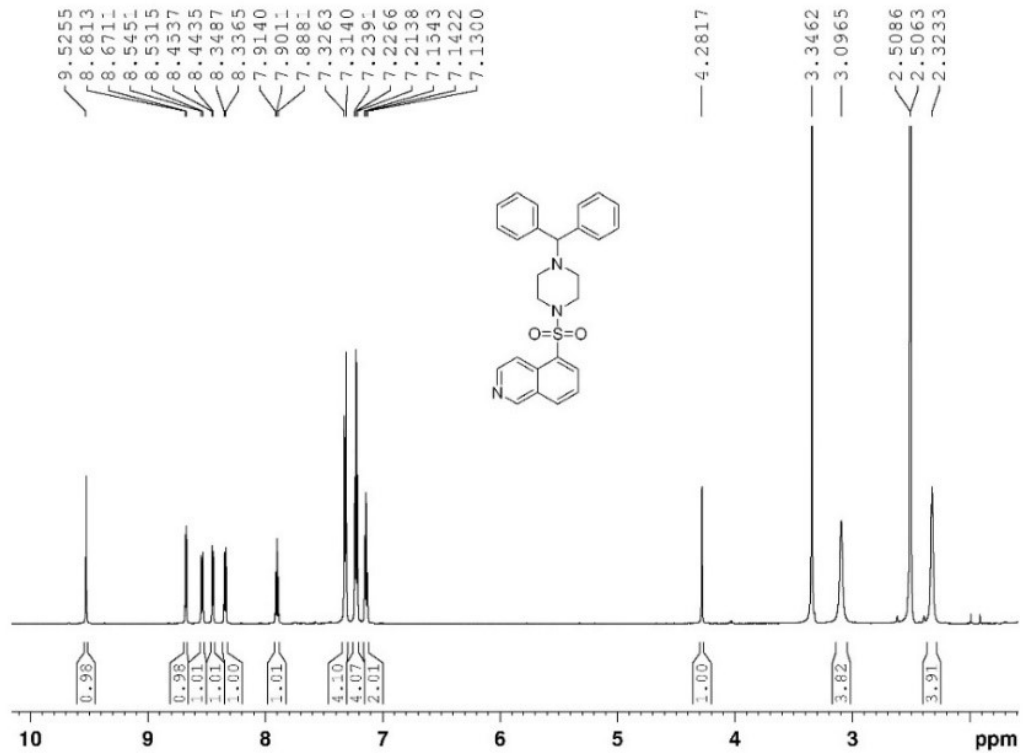


**<sup>1</sup>H NMR spectrum of compound DC20**

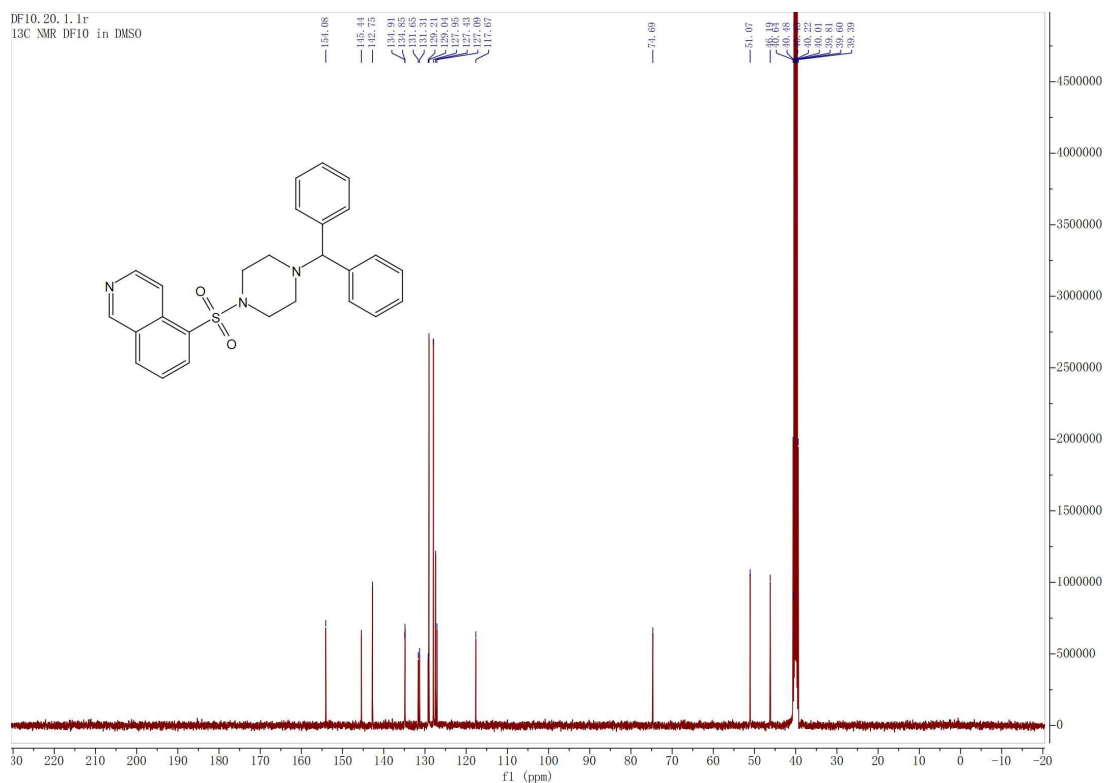


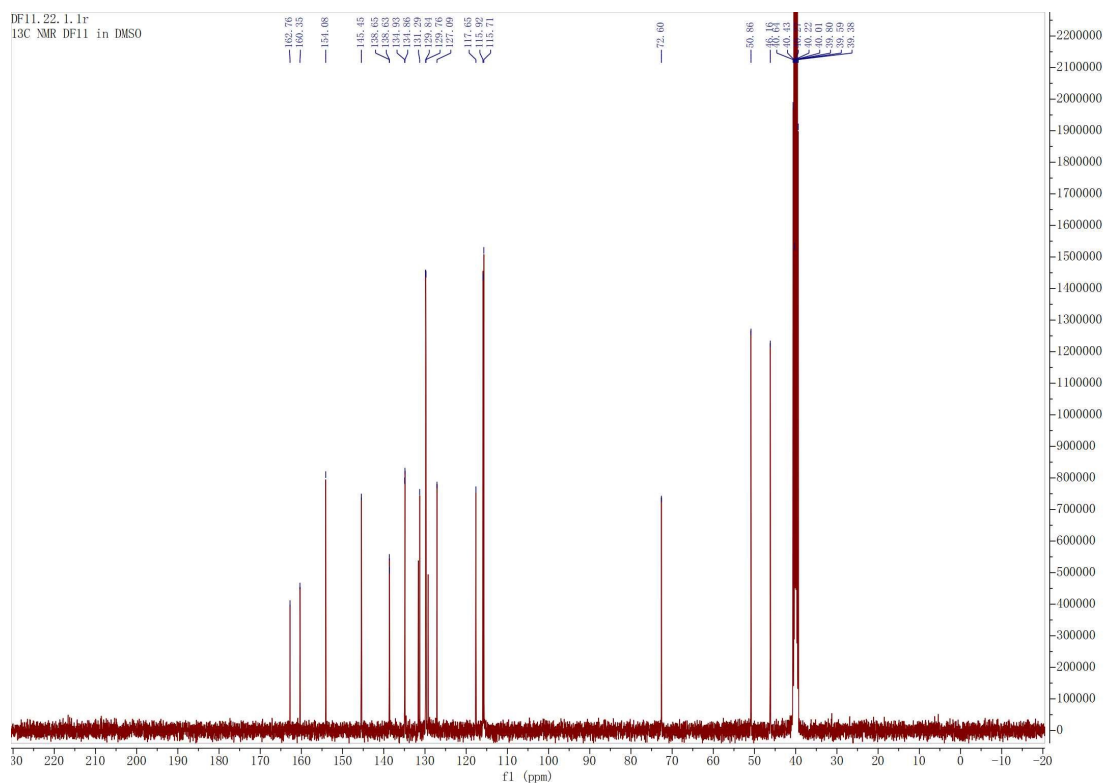


<sup>13</sup>C NMR spectrum of compound DC20

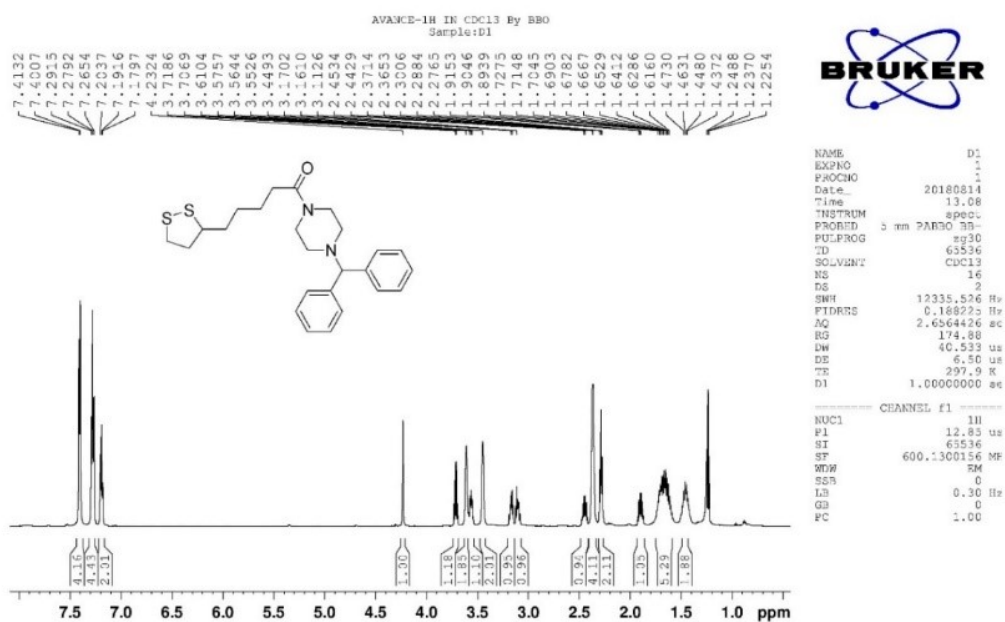


<sup>1</sup>H NMR spectrum of compound DC21

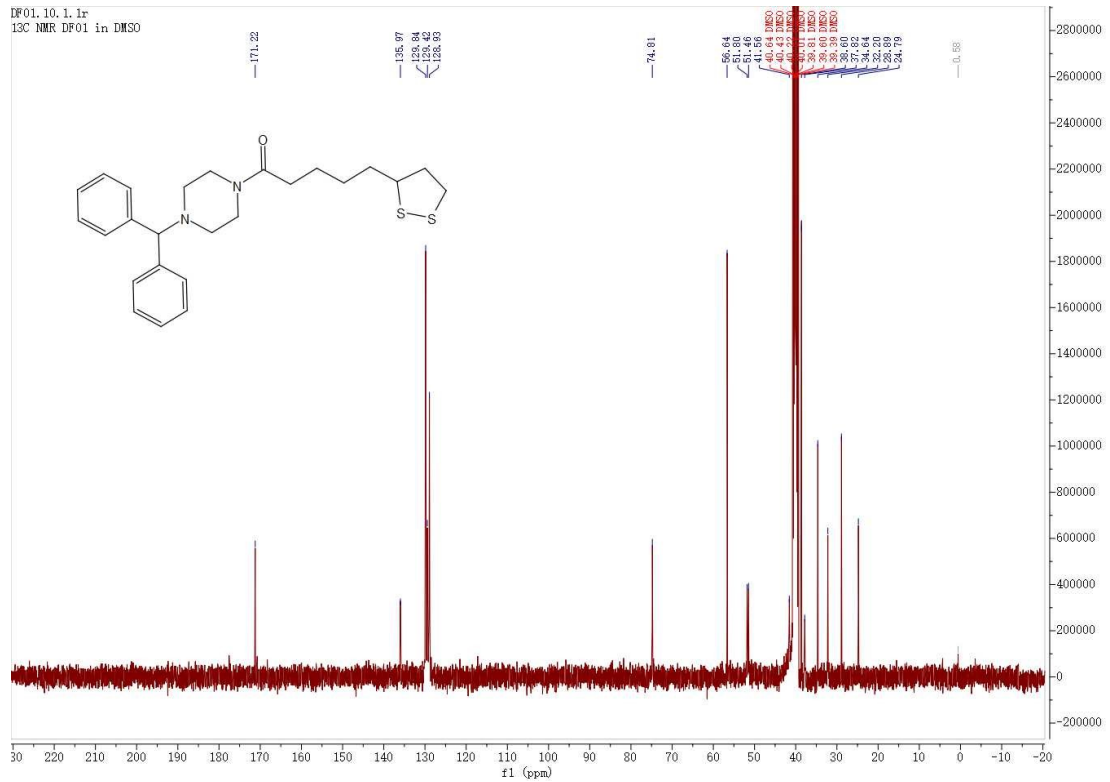




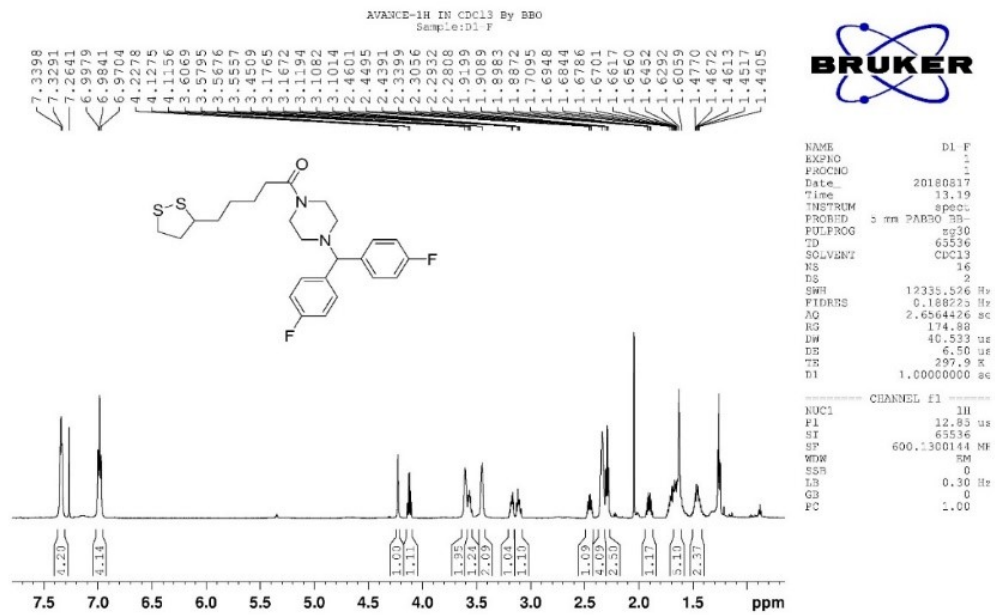
<sup>13</sup>C NMR spectrum of compound DC22



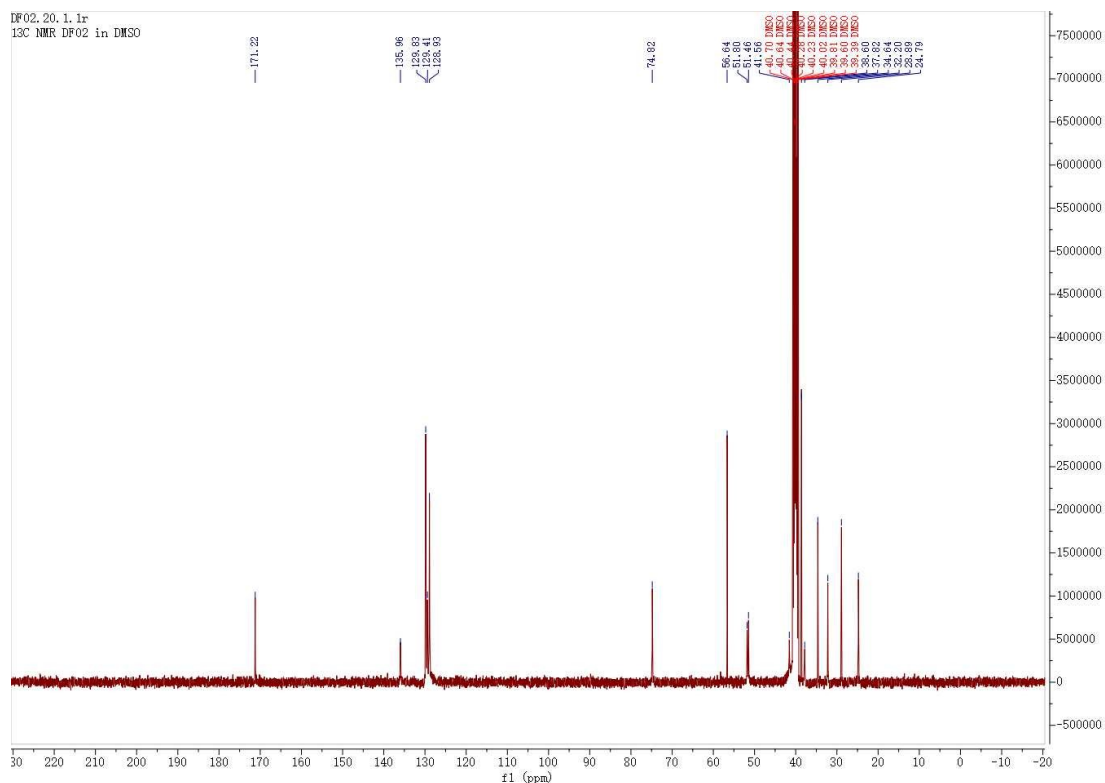
<sup>1</sup>H NMR spectrum of compound DC23



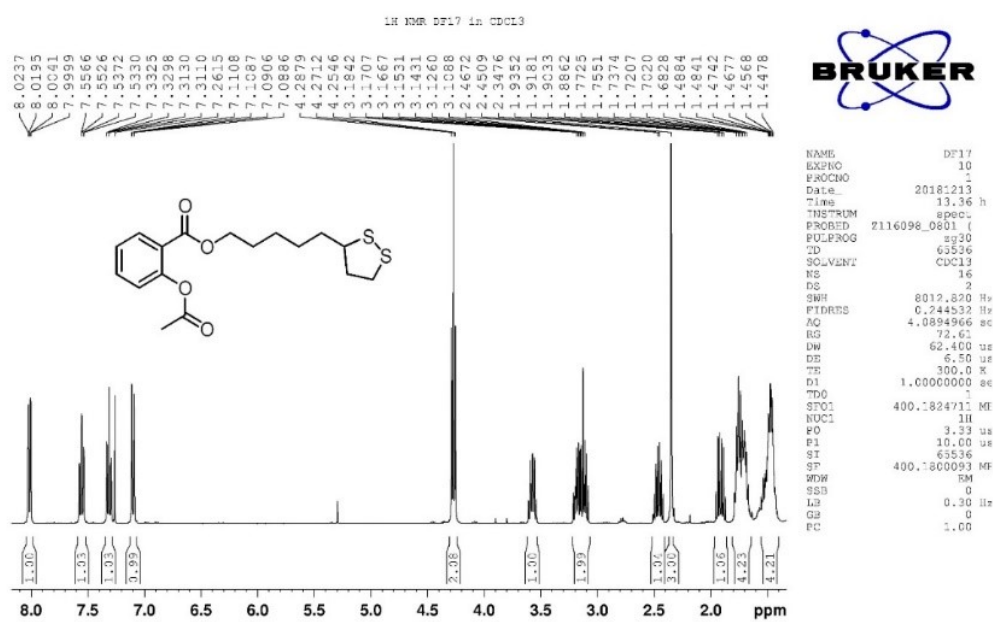
<sup>13</sup>C NMR spectrum of compound DC23



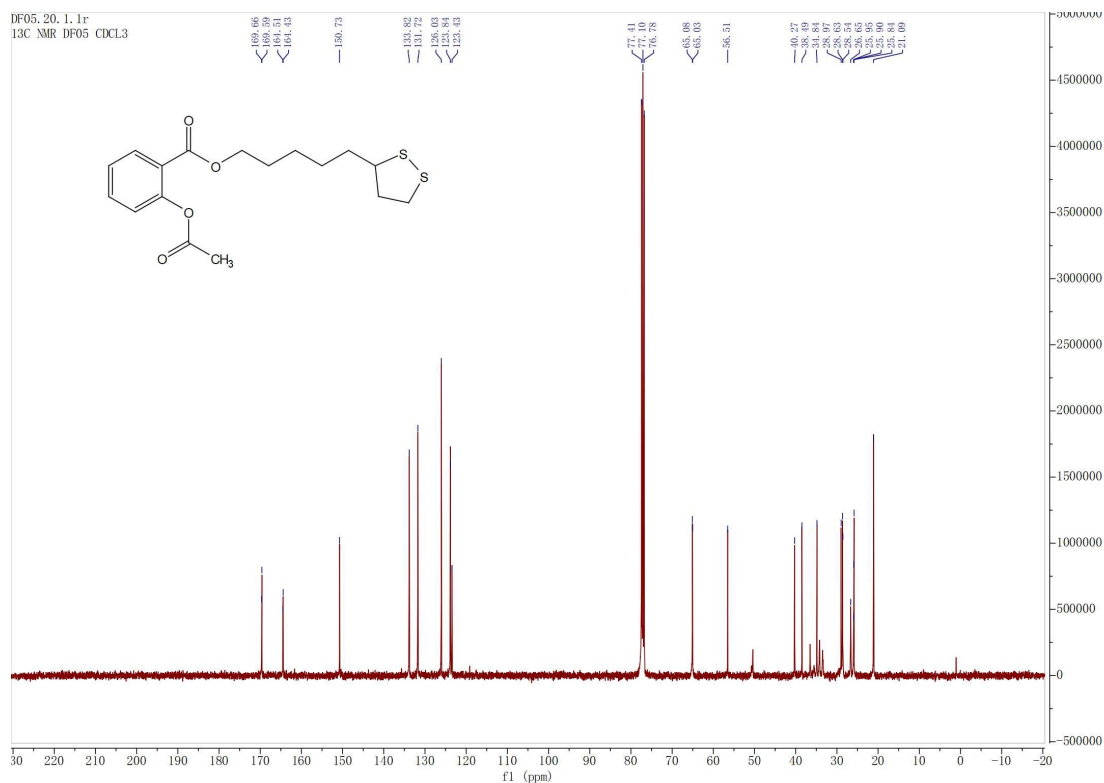
<sup>1</sup>H NMR spectrum of compound DC24



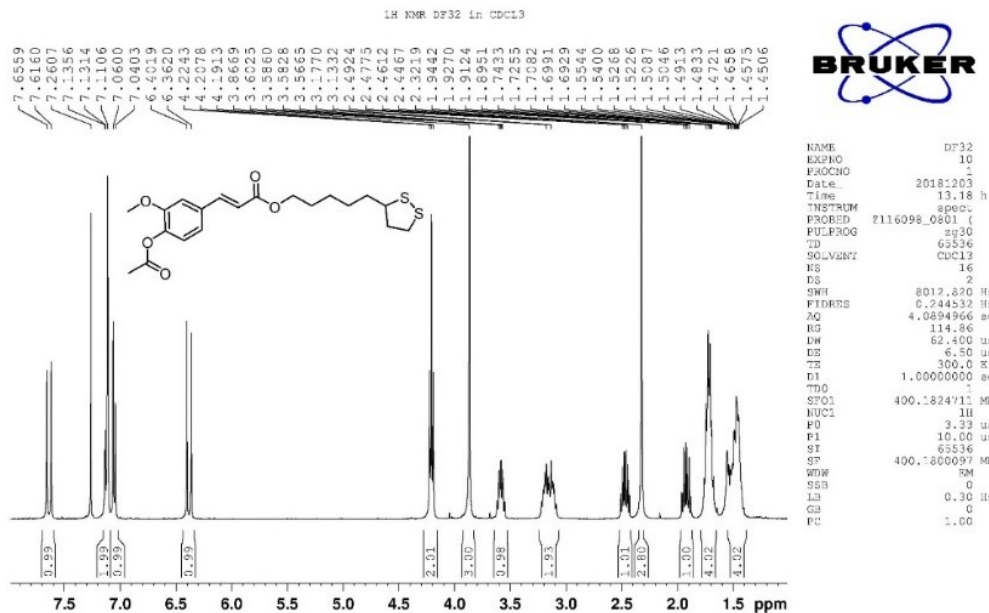
<sup>13</sup>C NMR spectrum of compound DC24



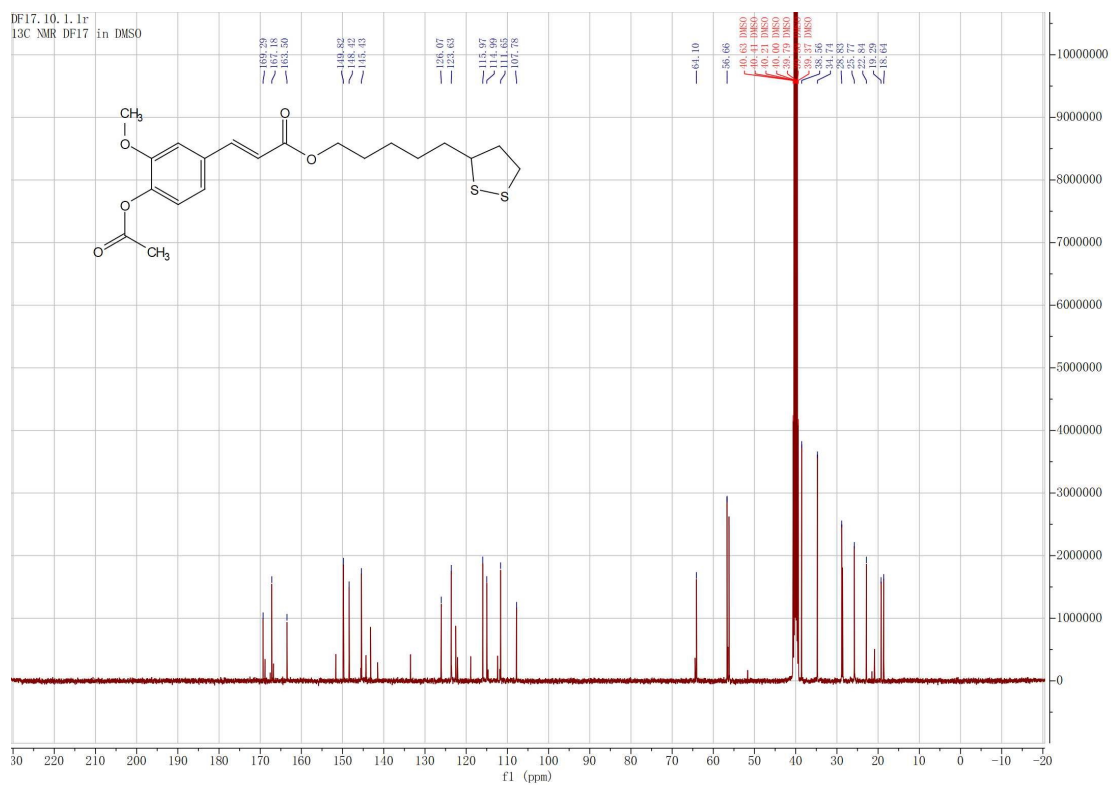
<sup>1</sup>H NMR spectrum of compound DC25



<sup>13</sup>C NMR spectrum of compound DC25

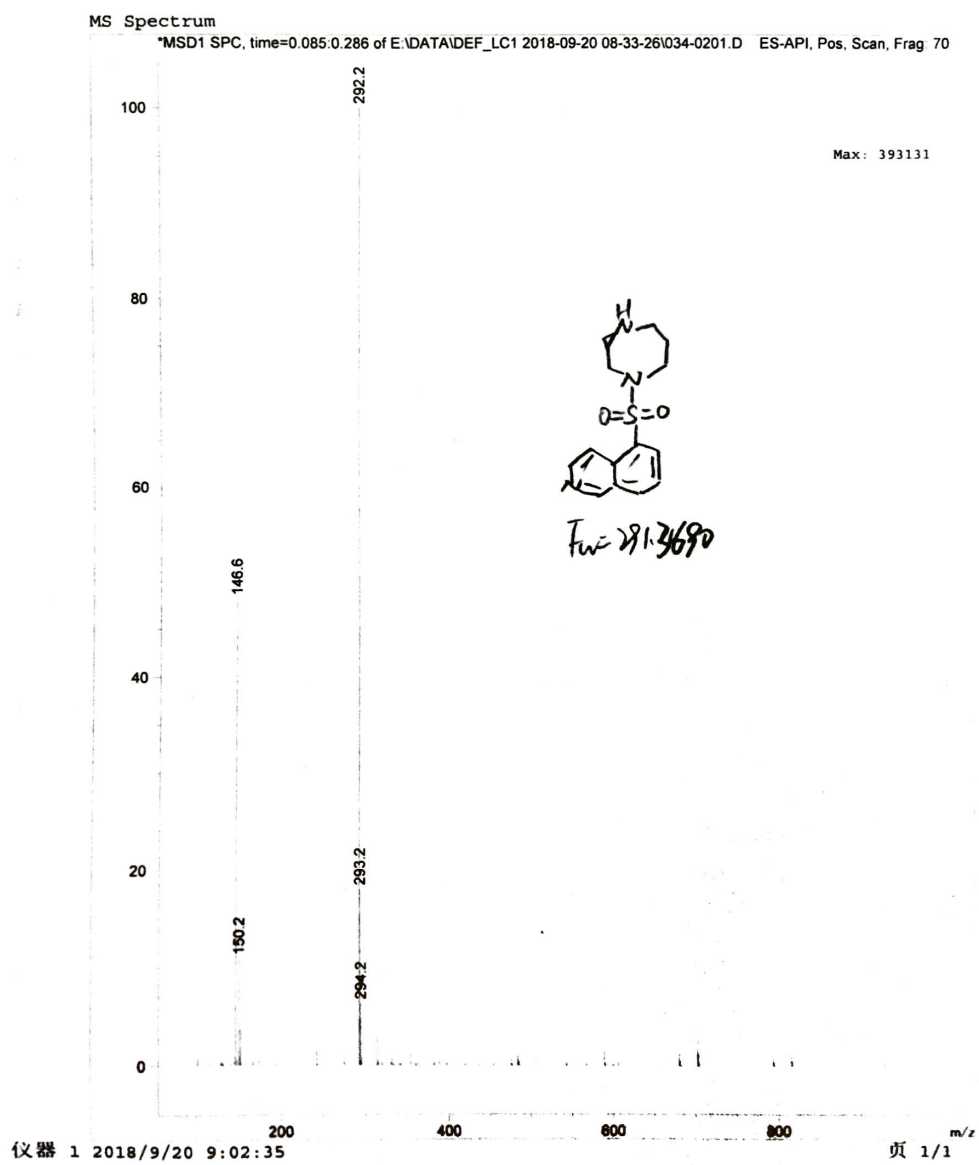


<sup>1</sup>H NMR spectrum of compound DC26



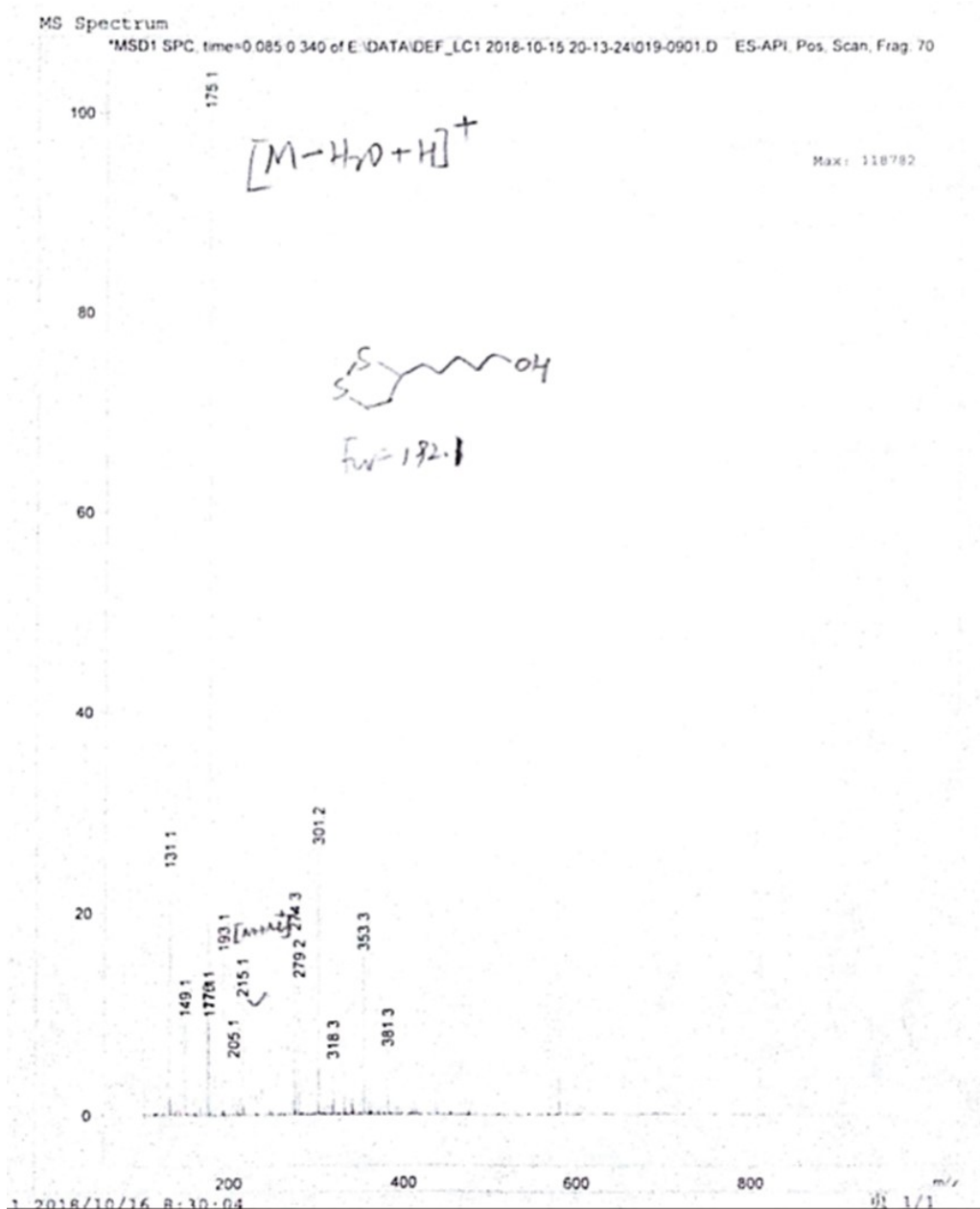
<sup>13</sup>C NMR spectrum of compound DC26

# MS Spectra:



MS spectrum of compound 4

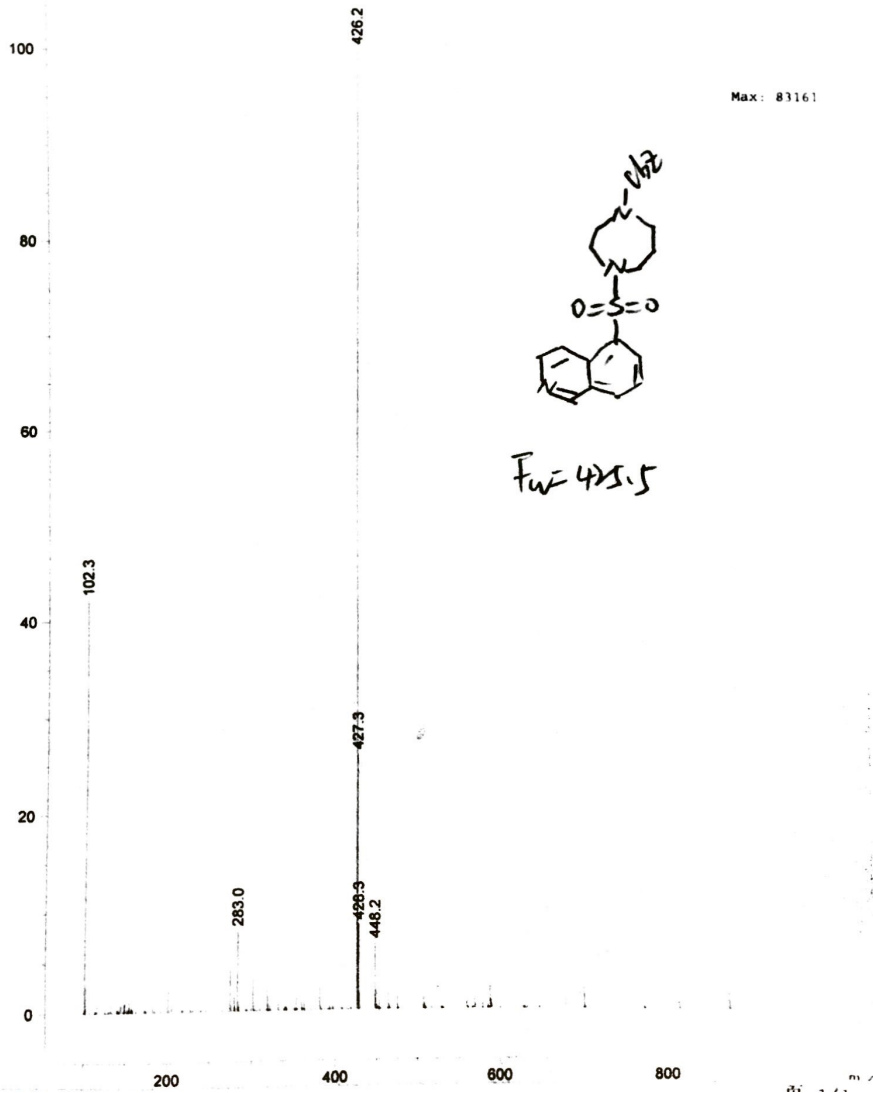




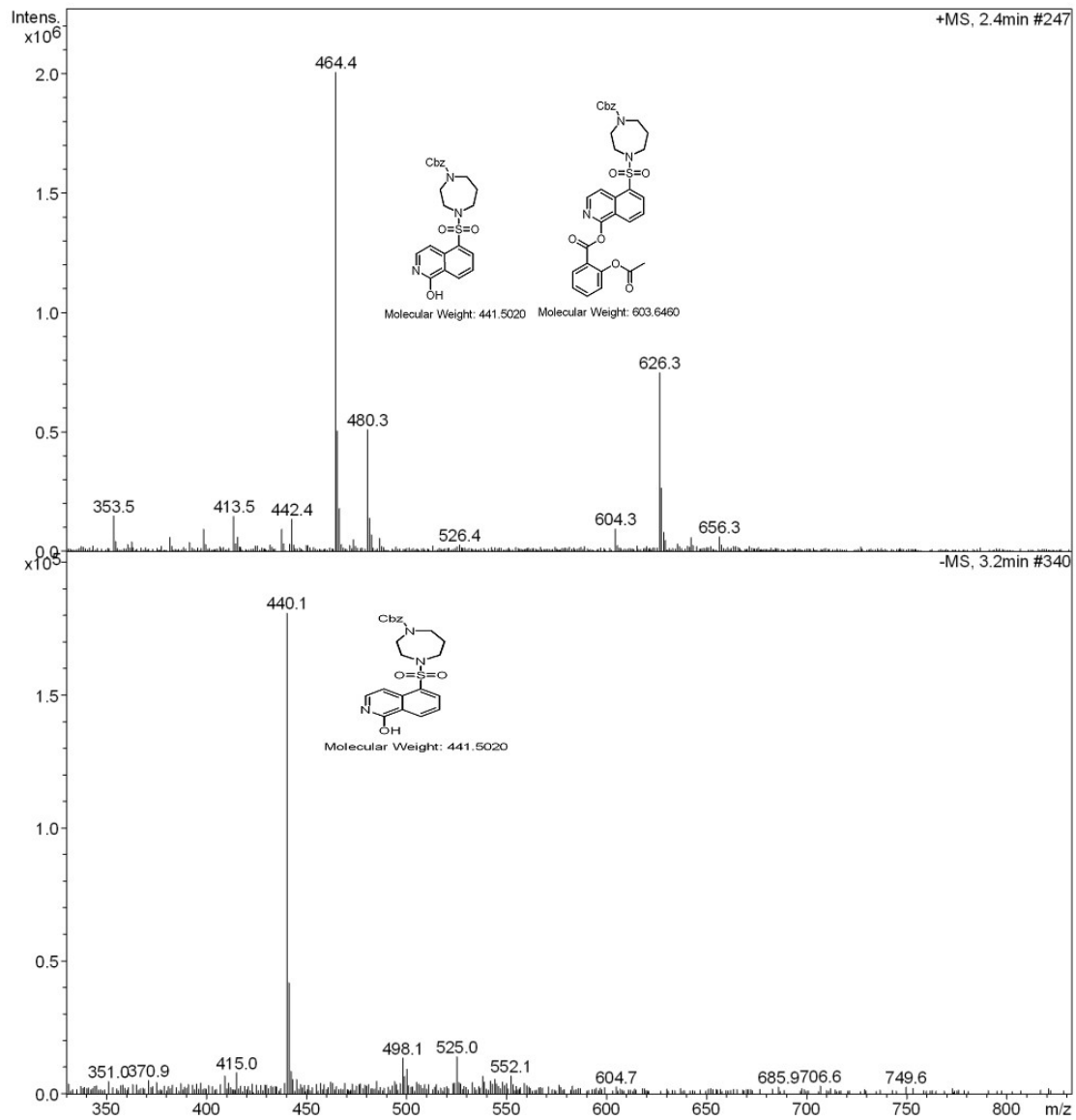
MS spectrum of compound 6

MS Spectrum

\*MSD1 SPC, time=0.016: 1.273 of E:\DATA\DEF\_LC1 2018-11-04 13-04-19\071-0101.D ES-API, Pos. Scan, Frag 70



MS spectrum of compound 8



MS spectrum of compound 10

打印窗口 80: MS Spectrum

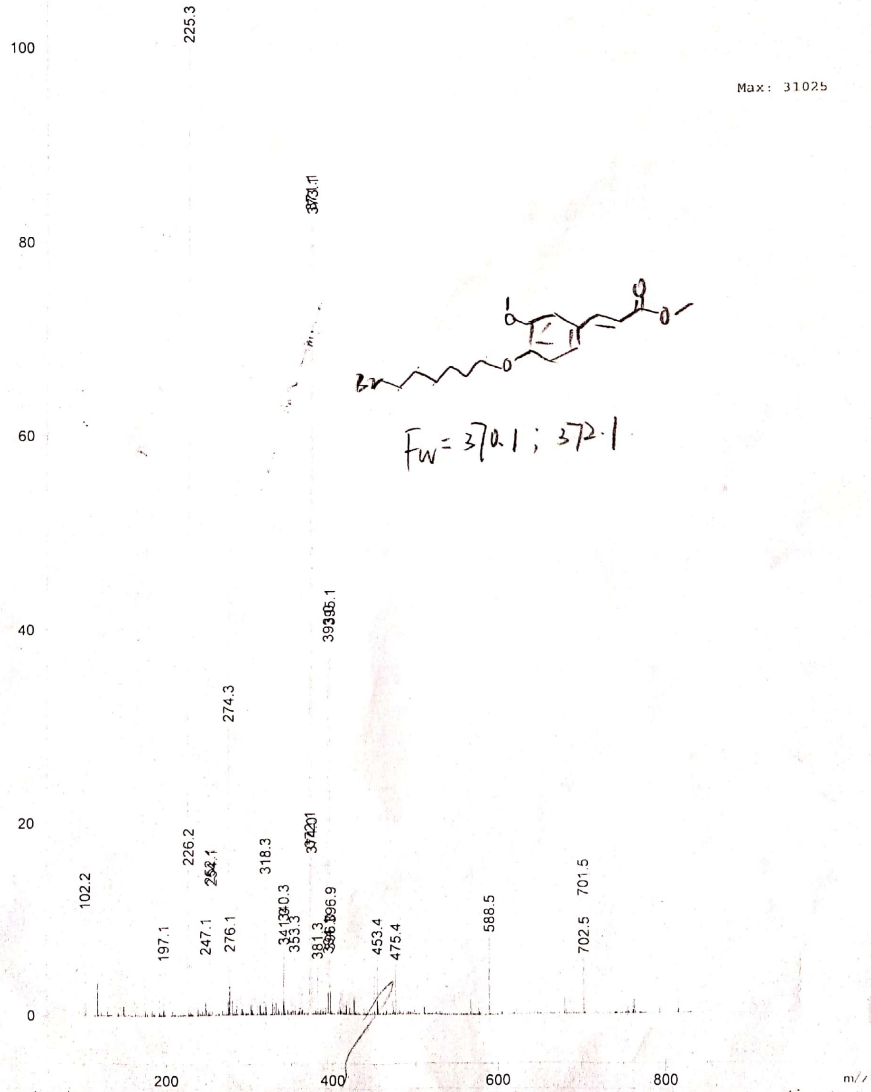
数据文件: : E:\DATA\DEF\_LC1 2018-12-10 20-38-36\035-2601.D

样品名称 : BR-J

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操作者 : 序列行 : 26  
仪器 : 仪器 1 位置 : 样品瓶 35  
进样日期 : 2018/12/10 23:21:53 进样次数 : 1  
进样量 : 5.000 µl  
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最后修改 : 2018/9/25 19:47:22  
分析方法 : C:\CHEM32\1\METHODS\100TO1000P\_AND\_N.M  
最后修改 : 2018/12/11 8:23:23  
(调用后修改)  
方法信息 : 2080F

MS Spectrum

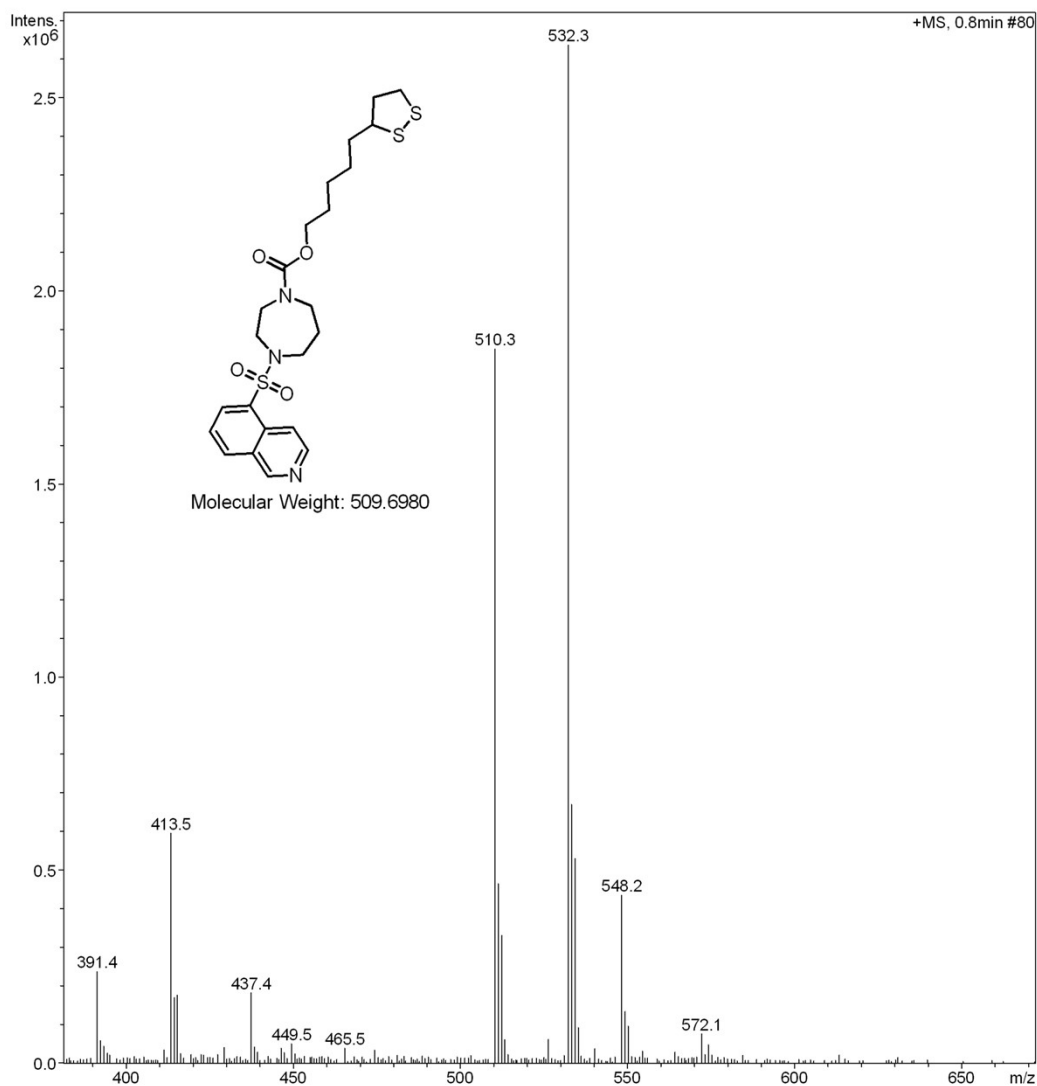
\*MSD1 SPC, time=0.072:1.222 of E:\DATA\DEF\_LC1 2018-12-10 20-38-36\035-2601.D ES-API, Pos. Scan, Frag: 70



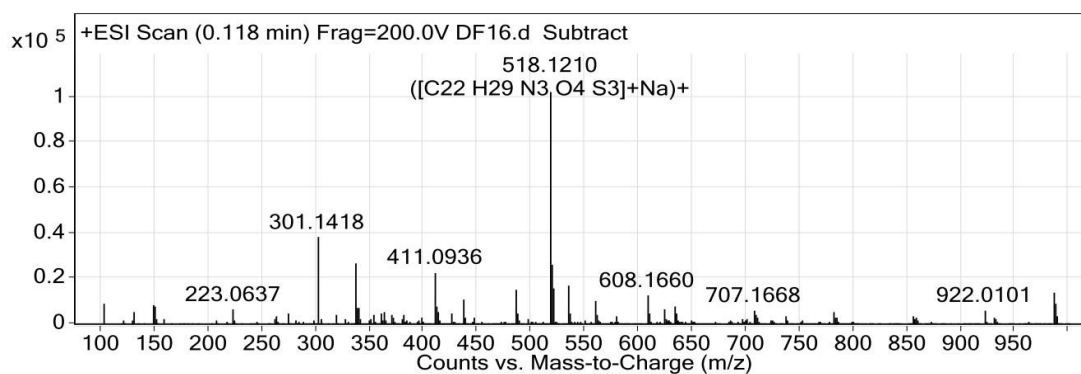
仪器 1 2018/12/11 8:34:30

页 1/1

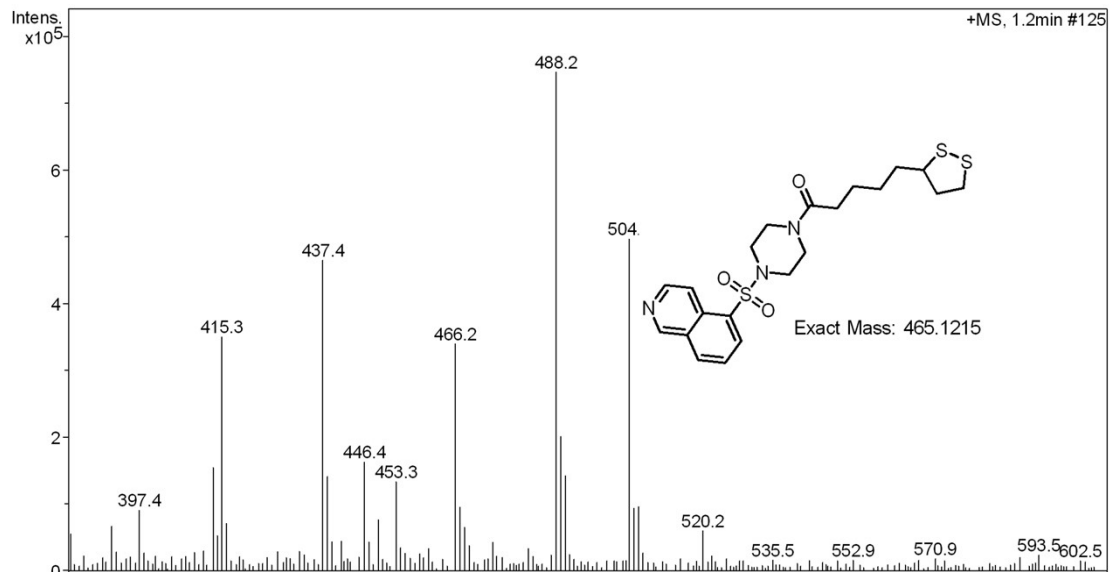
MS spectrum of compound 16



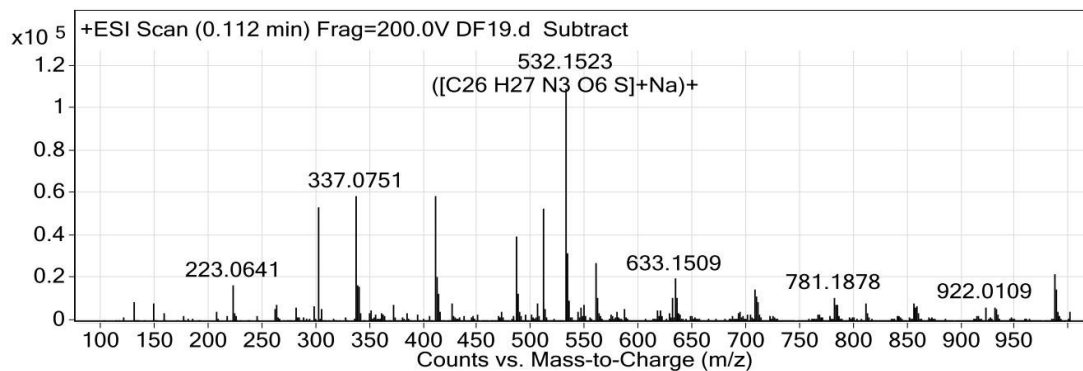
MS spectrum of compound DC01



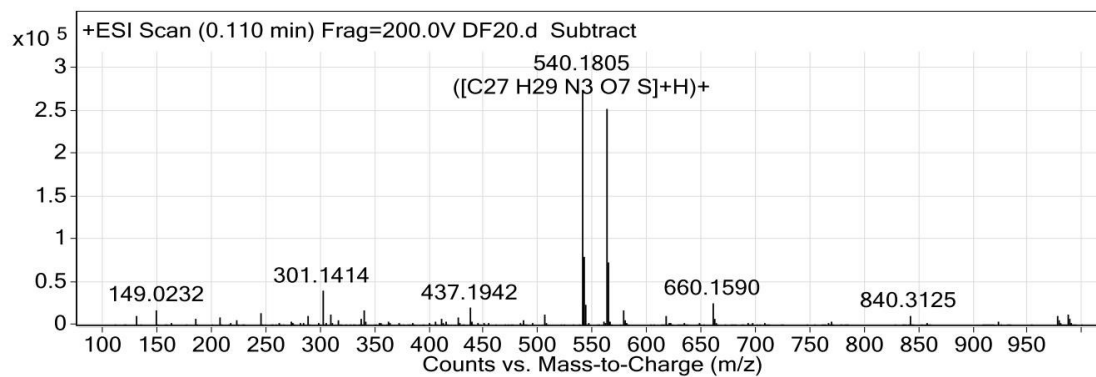
MS spectrum of compound DC02



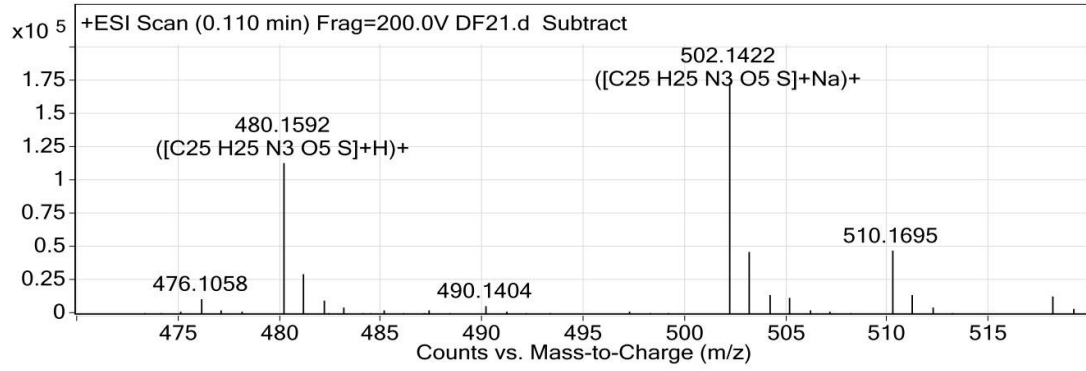
MS spectrum of compound DC03



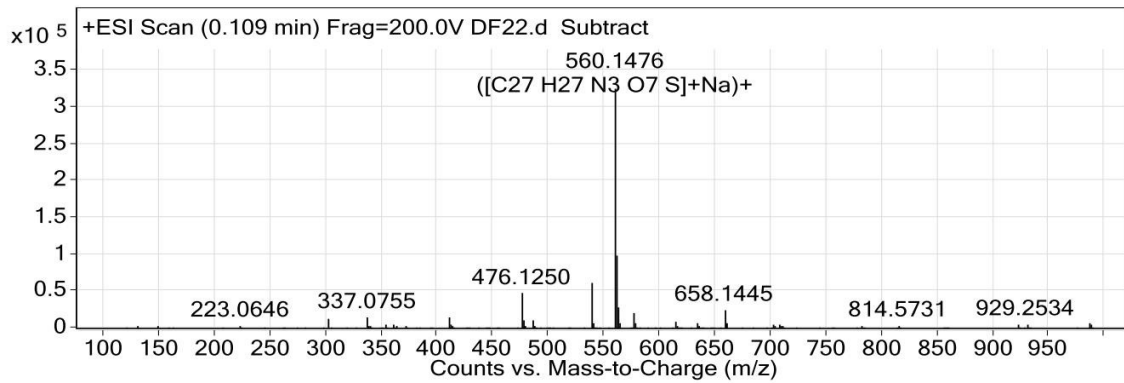
MS spectrum of compound DC04



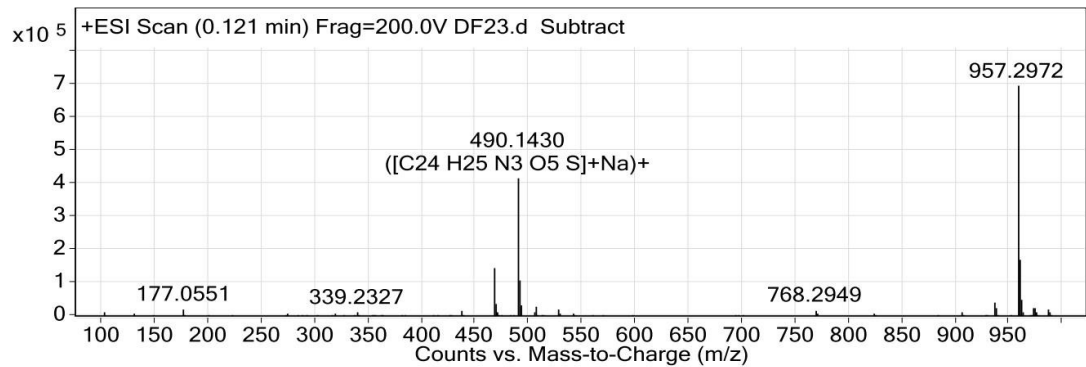
MS spectrum of compound DC05



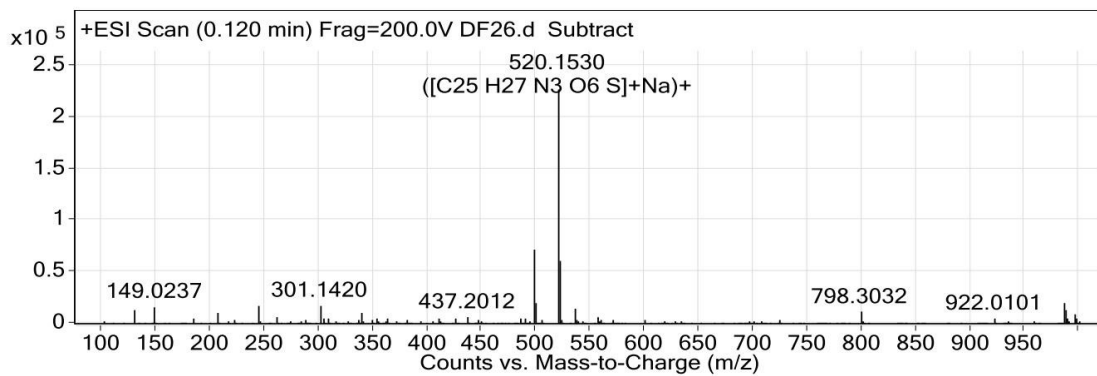
MS spectrum of compound **DC06**



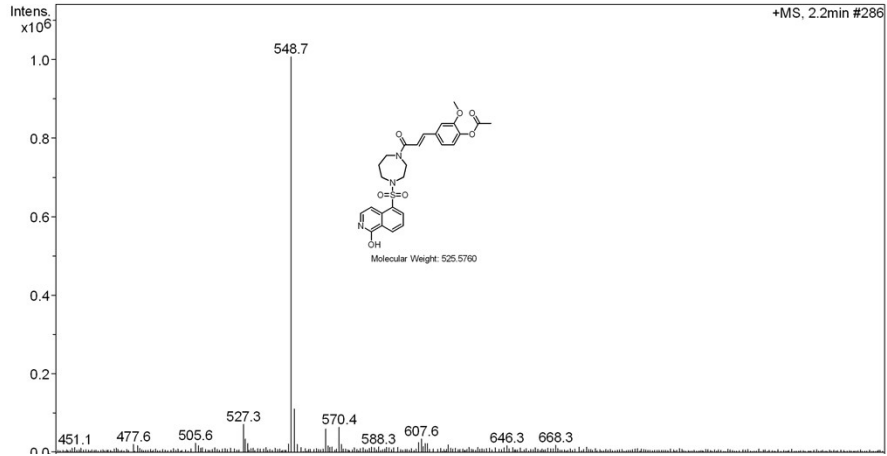
MS spectrum of compound **DC07**



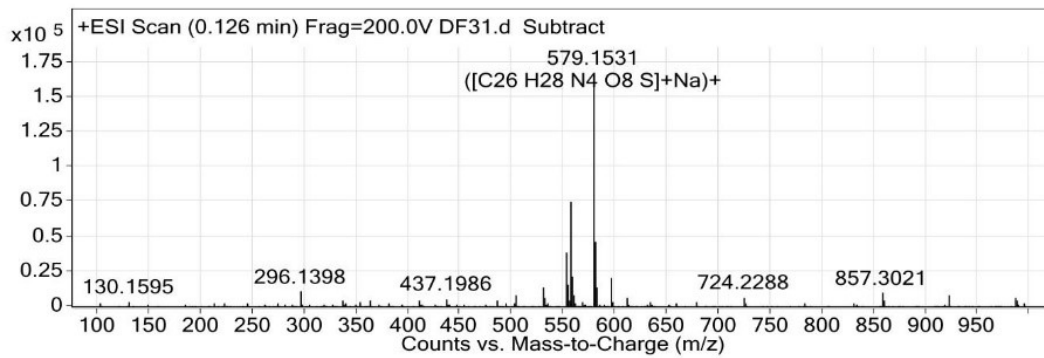
MS spectrum of compound **DC08**



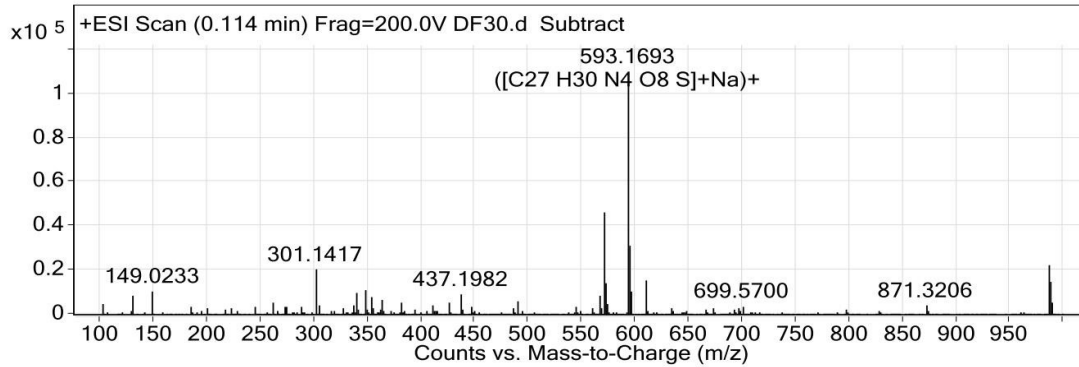
MS spectrum of compound **DC09**



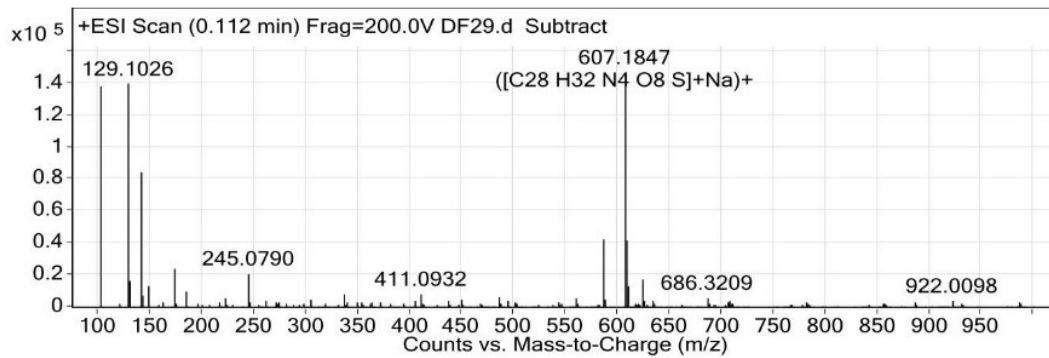
MS spectrum of compound DC10



MS spectrum of compound DC11

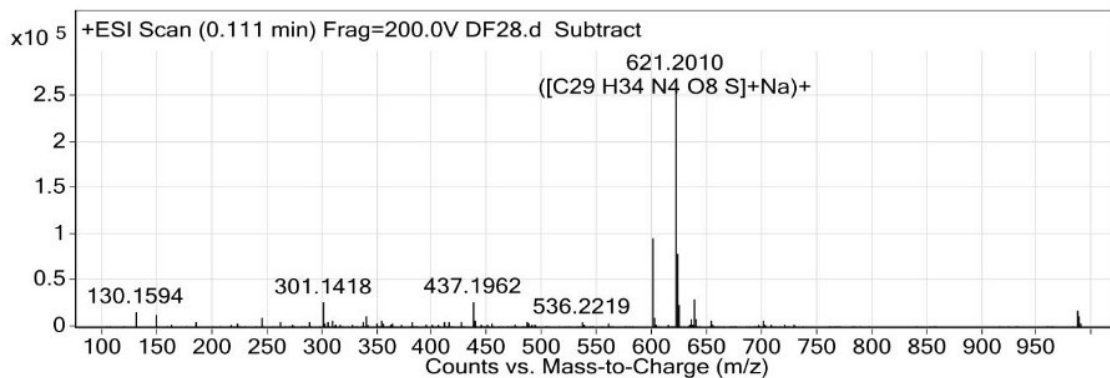


MS spectrum of compound DC12

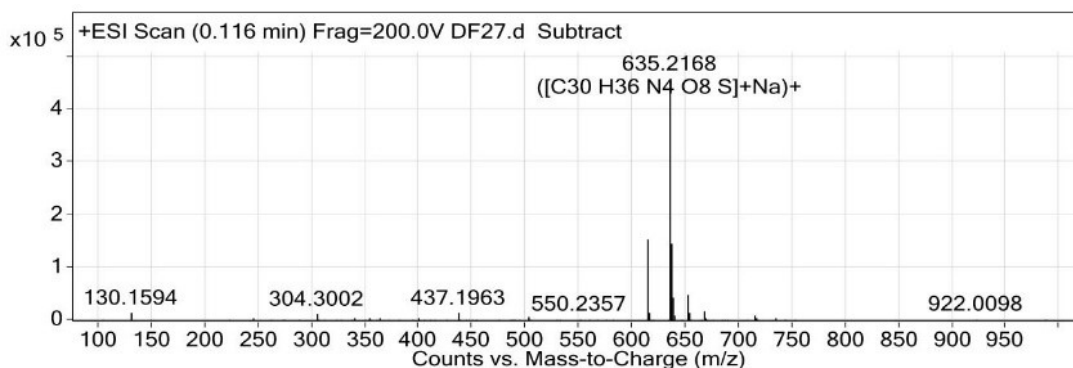


MS spectrum of compound DC13

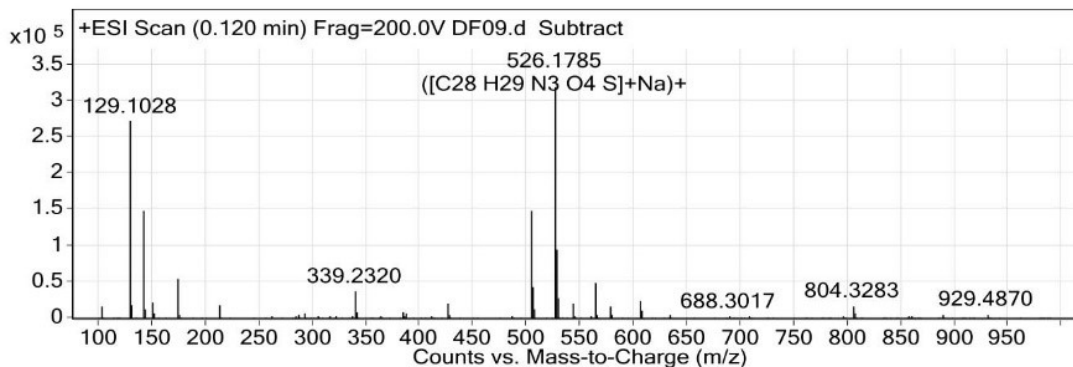




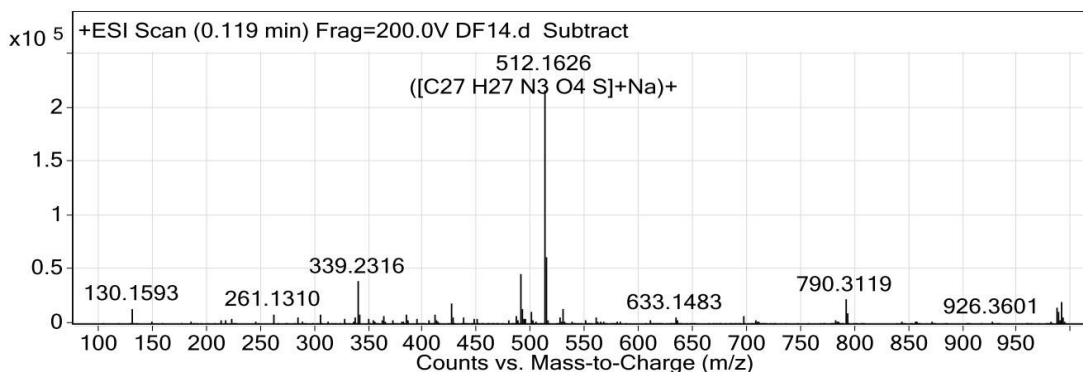
MS spectrum of compound DC14



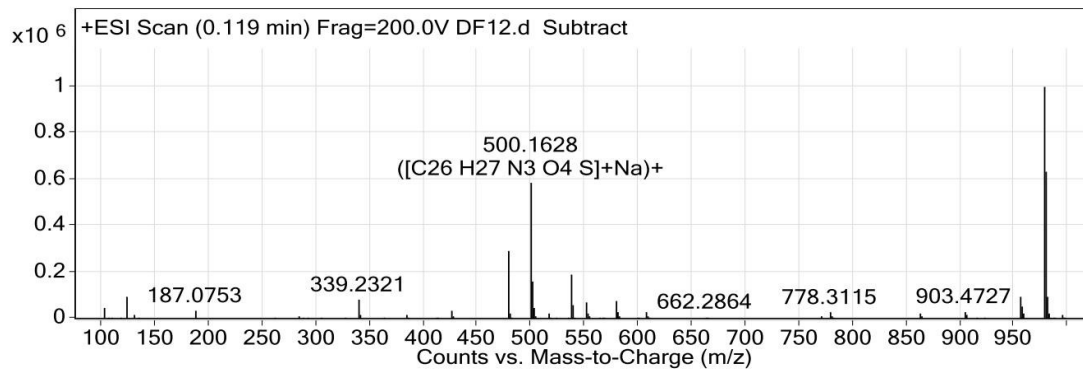
MS spectrum of compound DC15



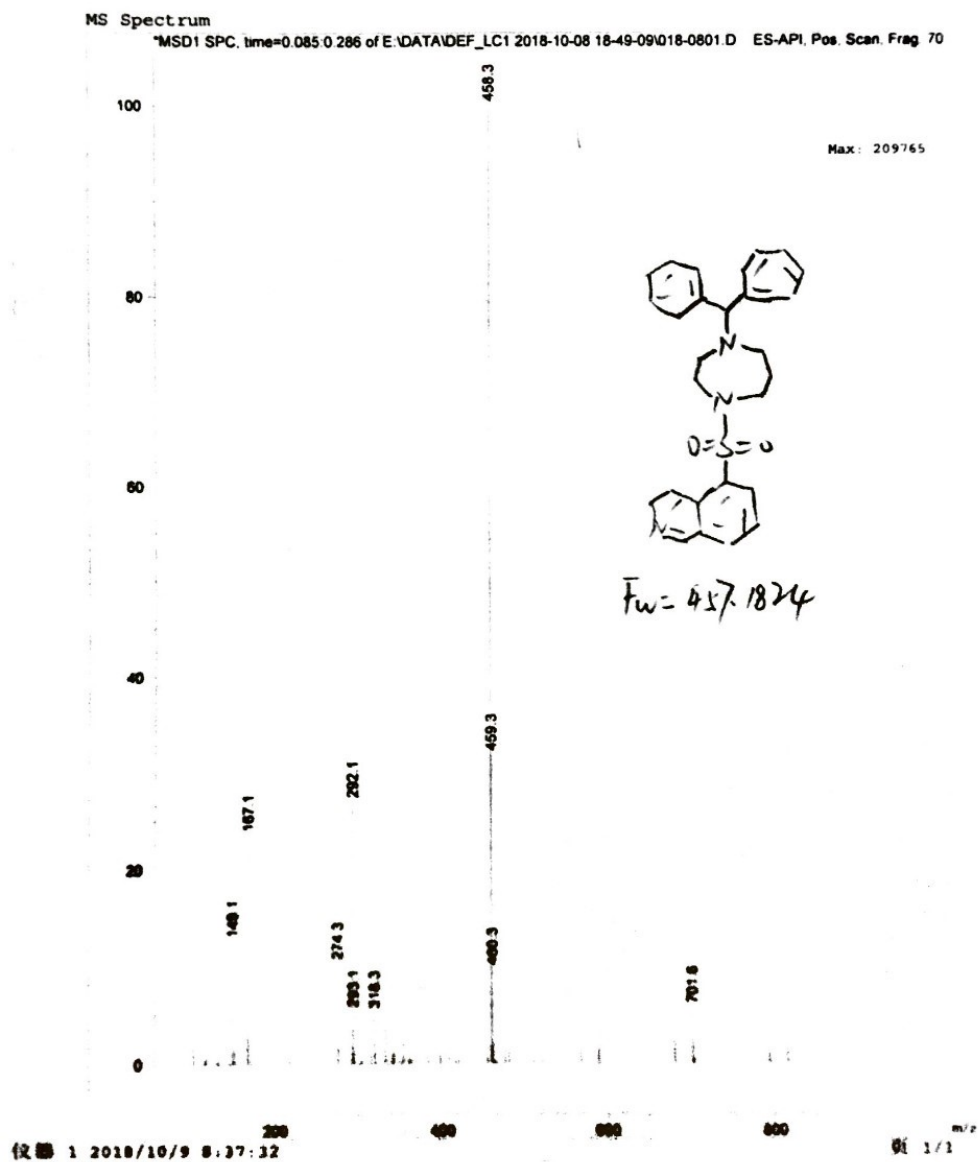
MS spectrum of compound DC16



MS spectrum of compound DC17



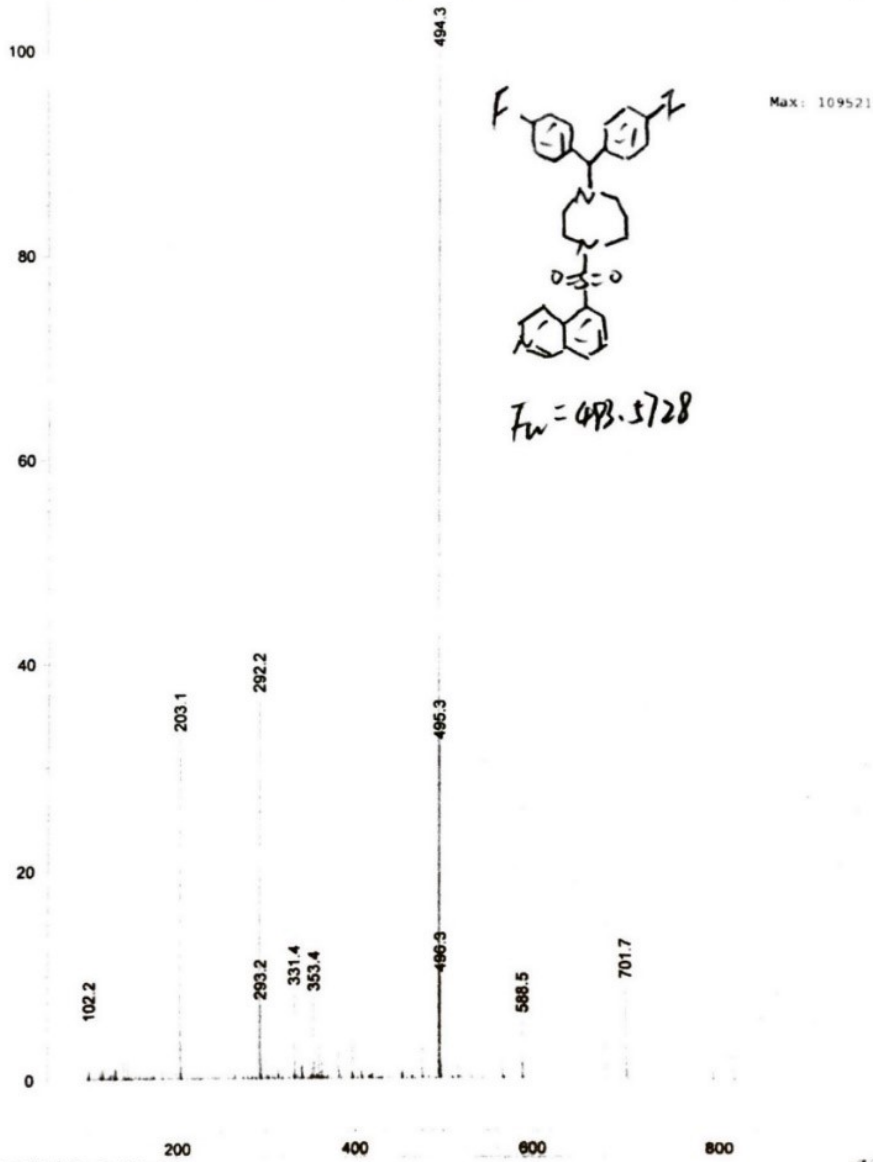
MS spectrum of compound DC18



MS spectrum of compound DC19

MS Spectrum

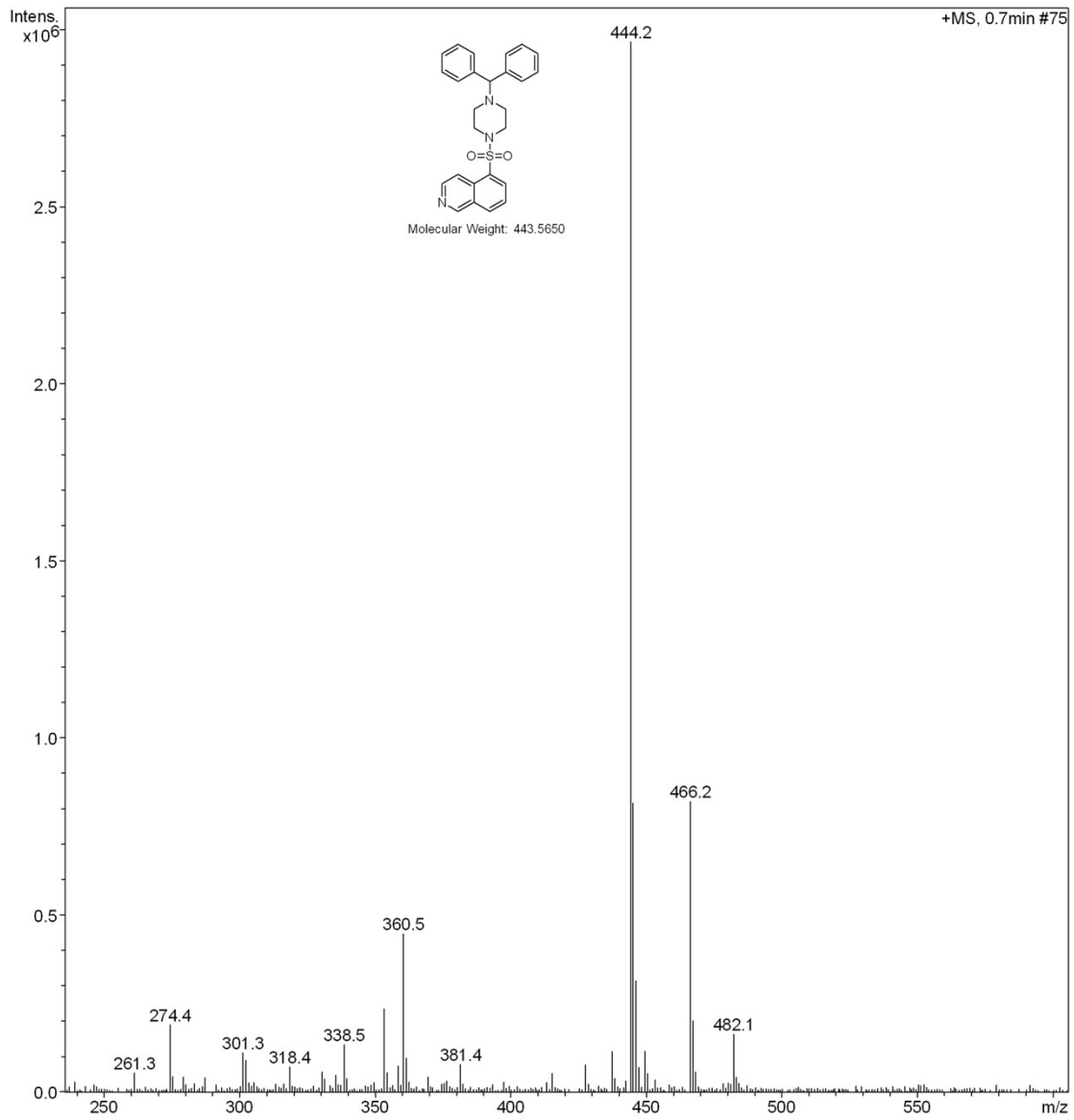
\*MSD1 SPC. time=0.0850.267 of E:\DATA\DEF\_LC1 2018-09-20 08-33-26\036-0401.D ES-API. Pos. Scan. Frag. 70



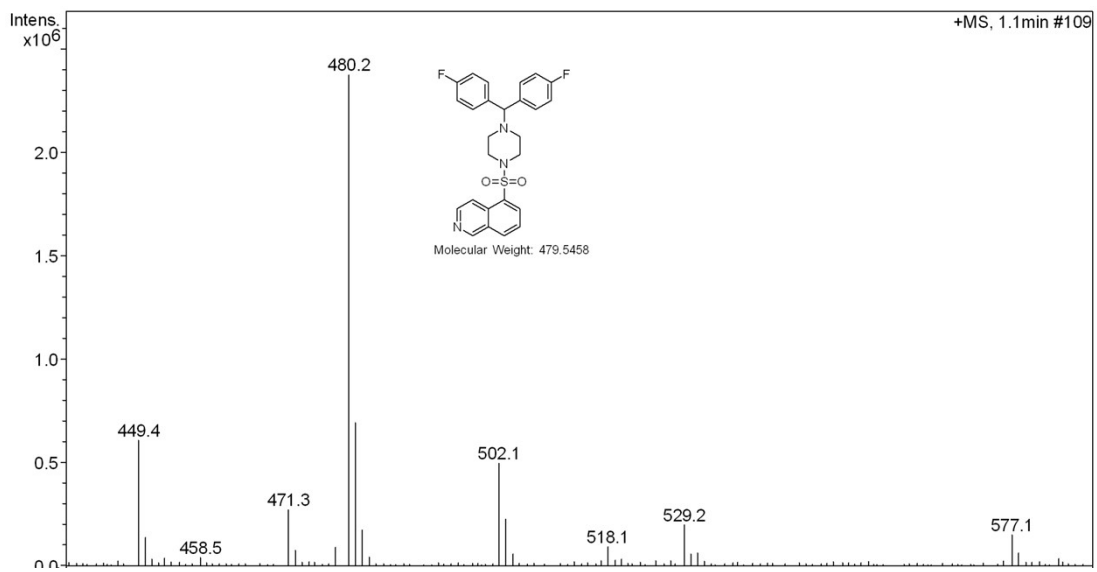
仪器 1 2018/9/20 9:03:19

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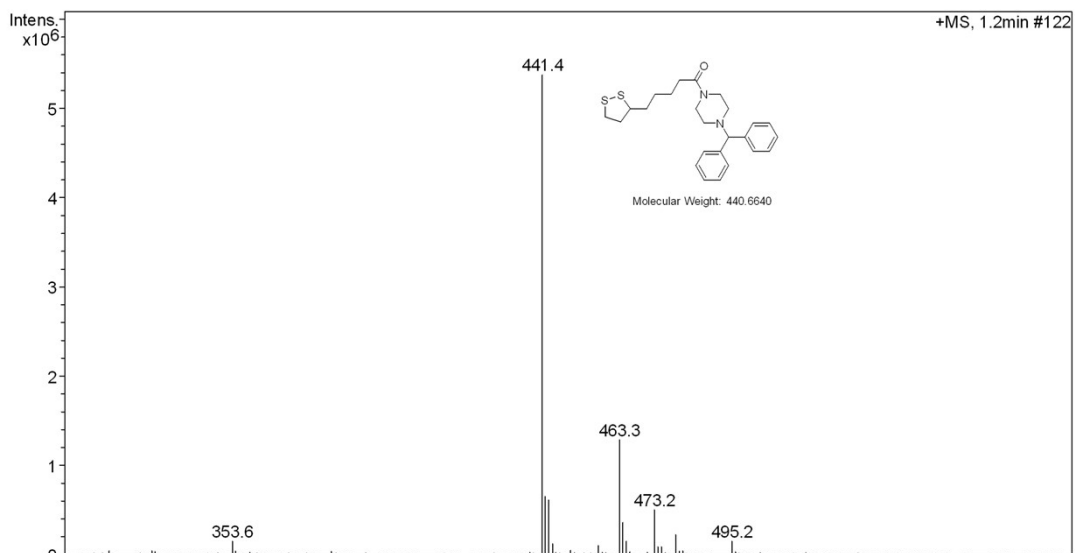
MS spectrum of compound DC20



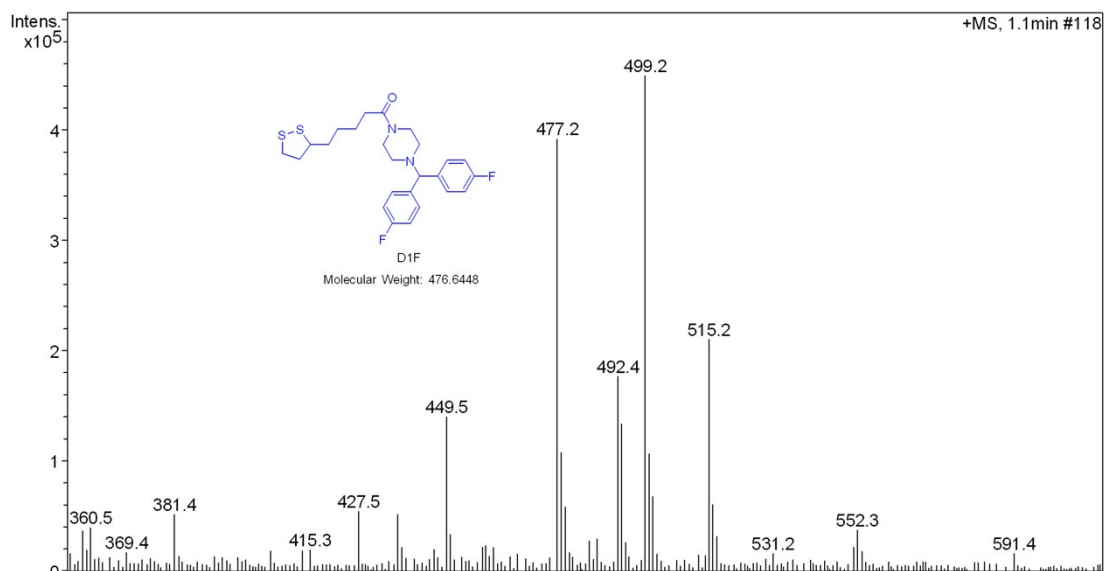
MS spectrum of compound DC21



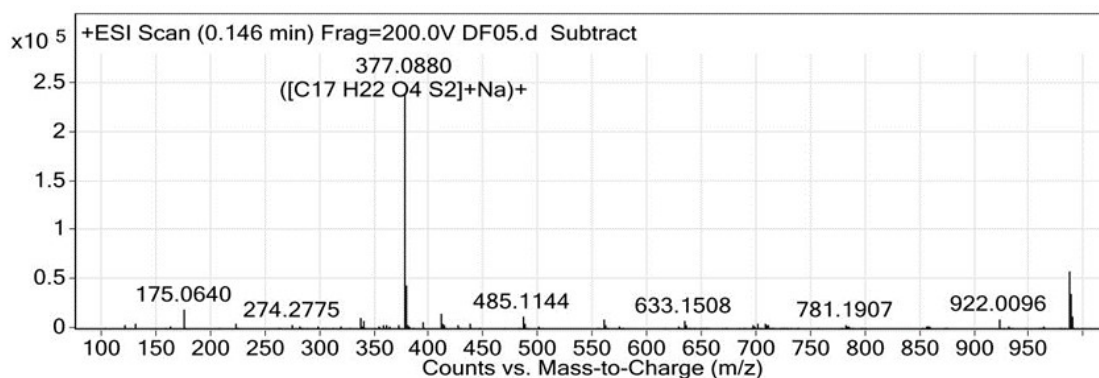
MS spectrum of compound DC22



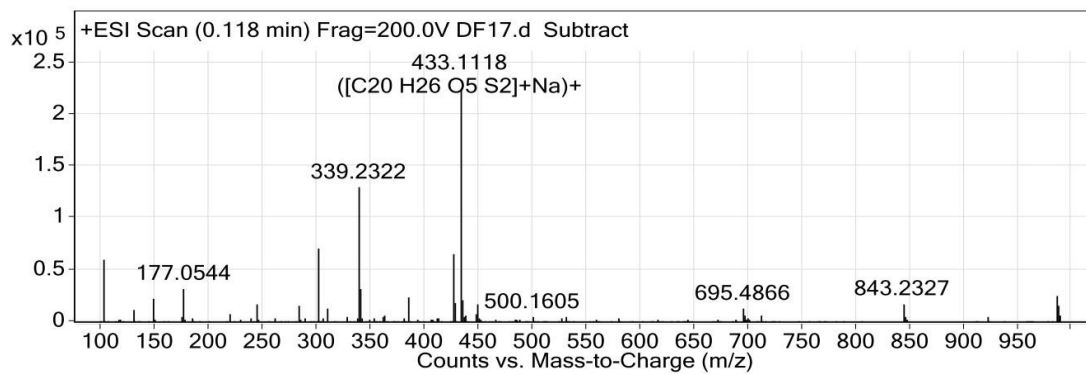
MS spectrum of compound DC23



MS spectrum of compound DC24



MS spectrum of compound DC25



MS spectrum of compound DC26