

Supporting Information

For

Regioselectivity of aminomethylation in 3-acetyl-7-hydroxycoumarins:

Mannich bases and Betti bases

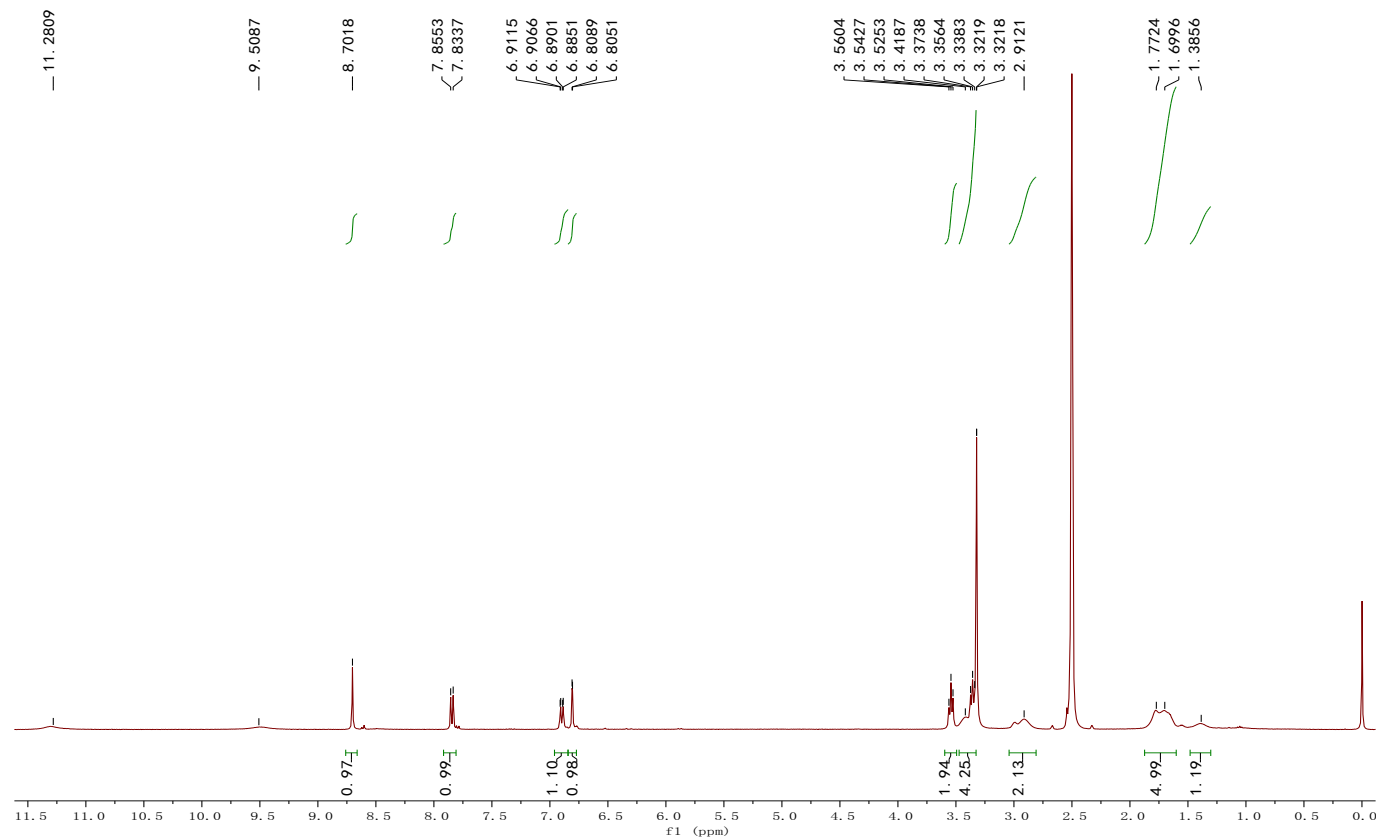
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Zhang, Li Li*

*Beijing Key Laboratory of Active Substances Discovery and Druggability Evaluation,
Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical
College, Beijing 100050, China*

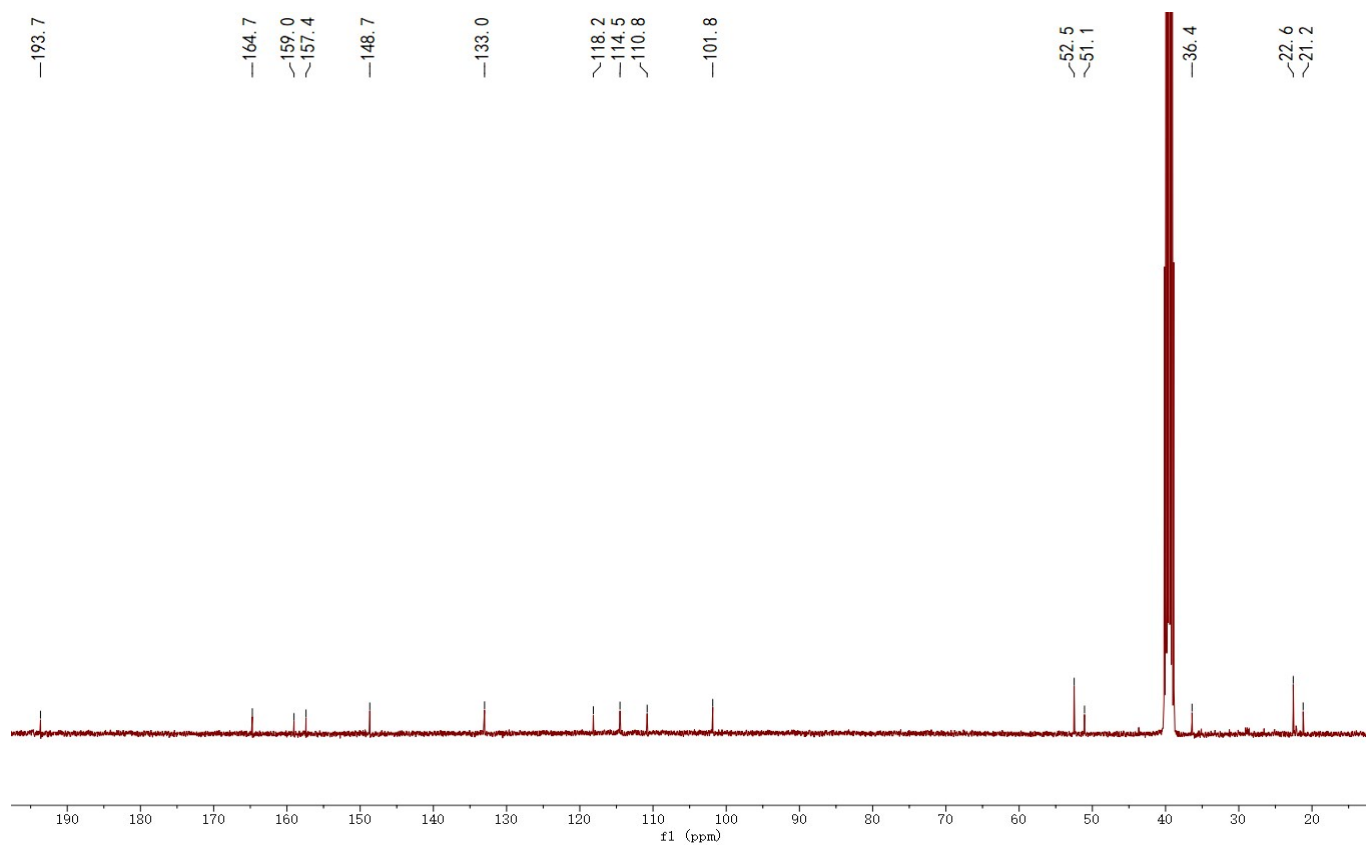
Corresponding author: annaleelin@imm.ac.cn

1 ¹H- and ¹³C-NMR spectra of compounds 8-29	S2
2 ESI-HRMS spectra of compounds 8-29	S46
3 Cartesian coordinates of compounds 6, 30-33	S68
4 Sources of the reagents used in the synthesis process	S72

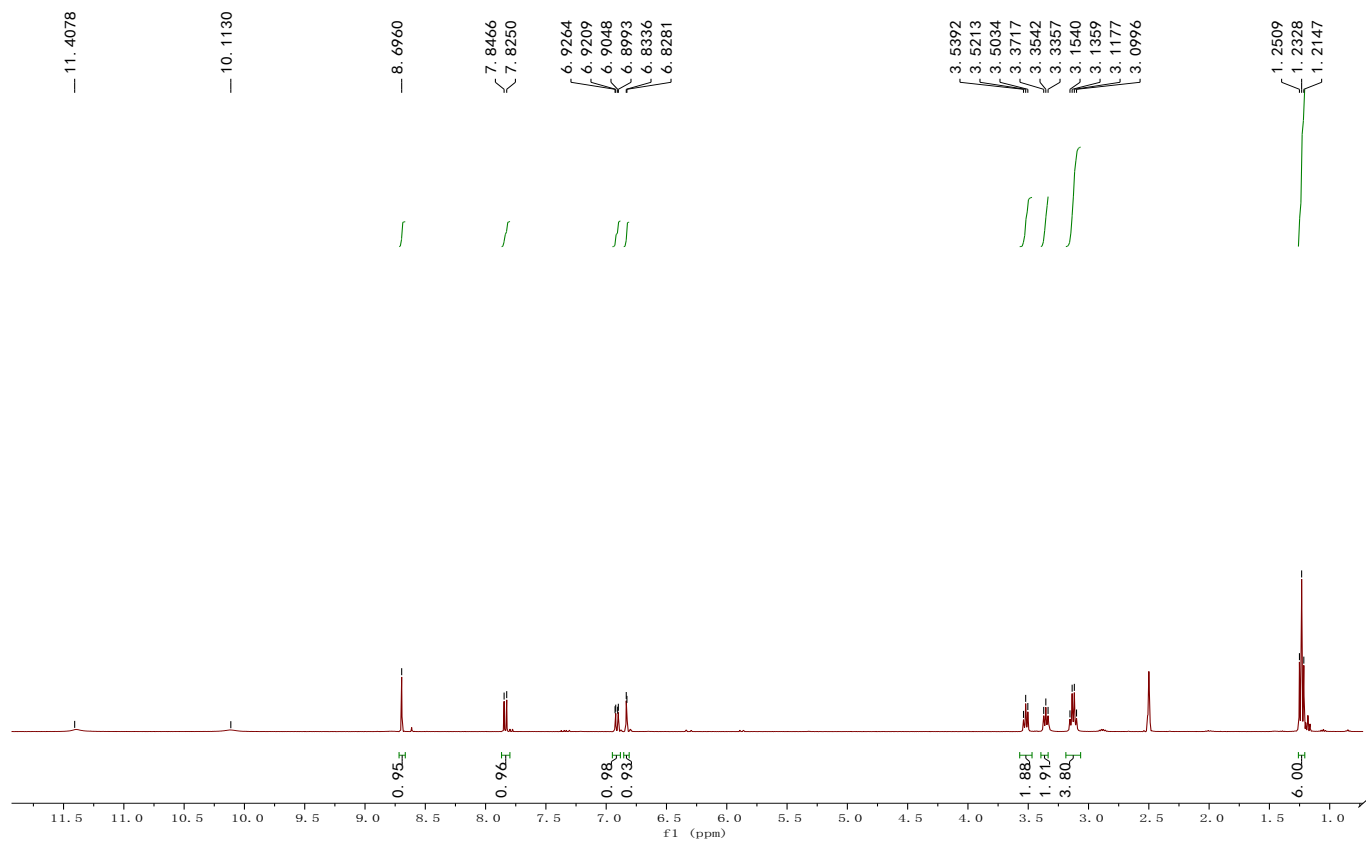
1. ^1H - and ^{13}C -NMR spectra of compounds 8-29.



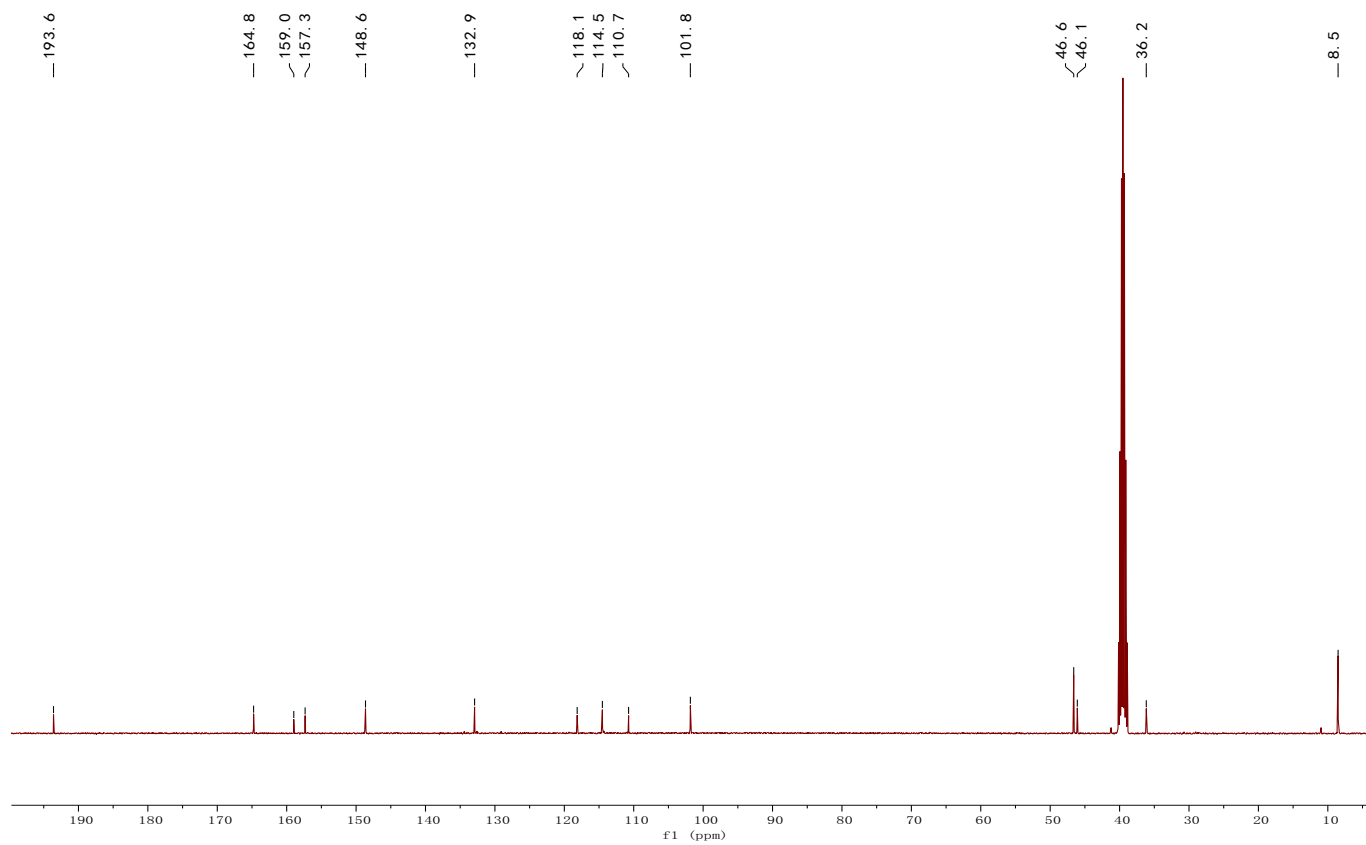
^1H -NMR (400 MHz) spectrum of compound **8** in $\text{DMSO-}d_6$



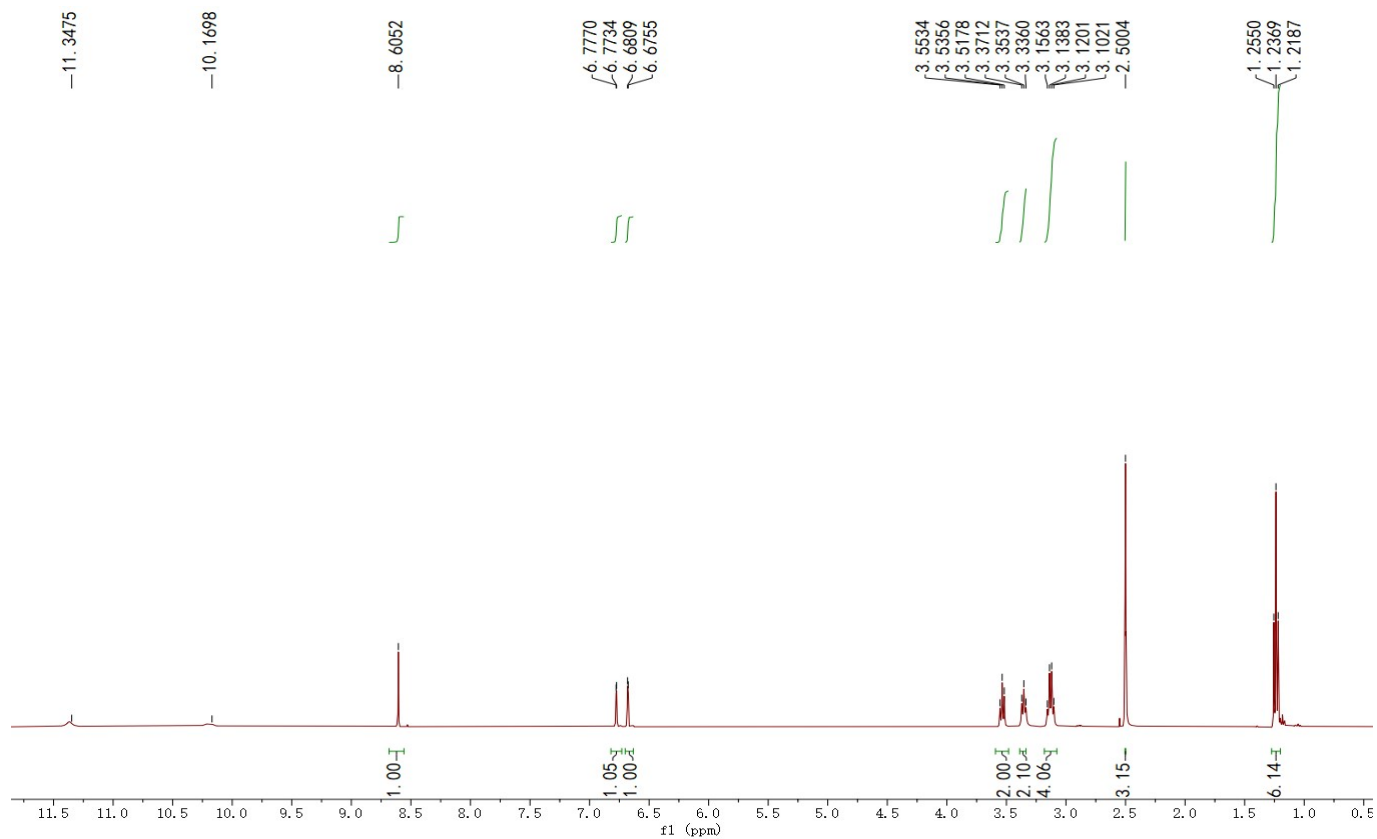
^{13}C -NMR (100 MHz) spectrum of compound **8** in $\text{DMSO-}d_6$



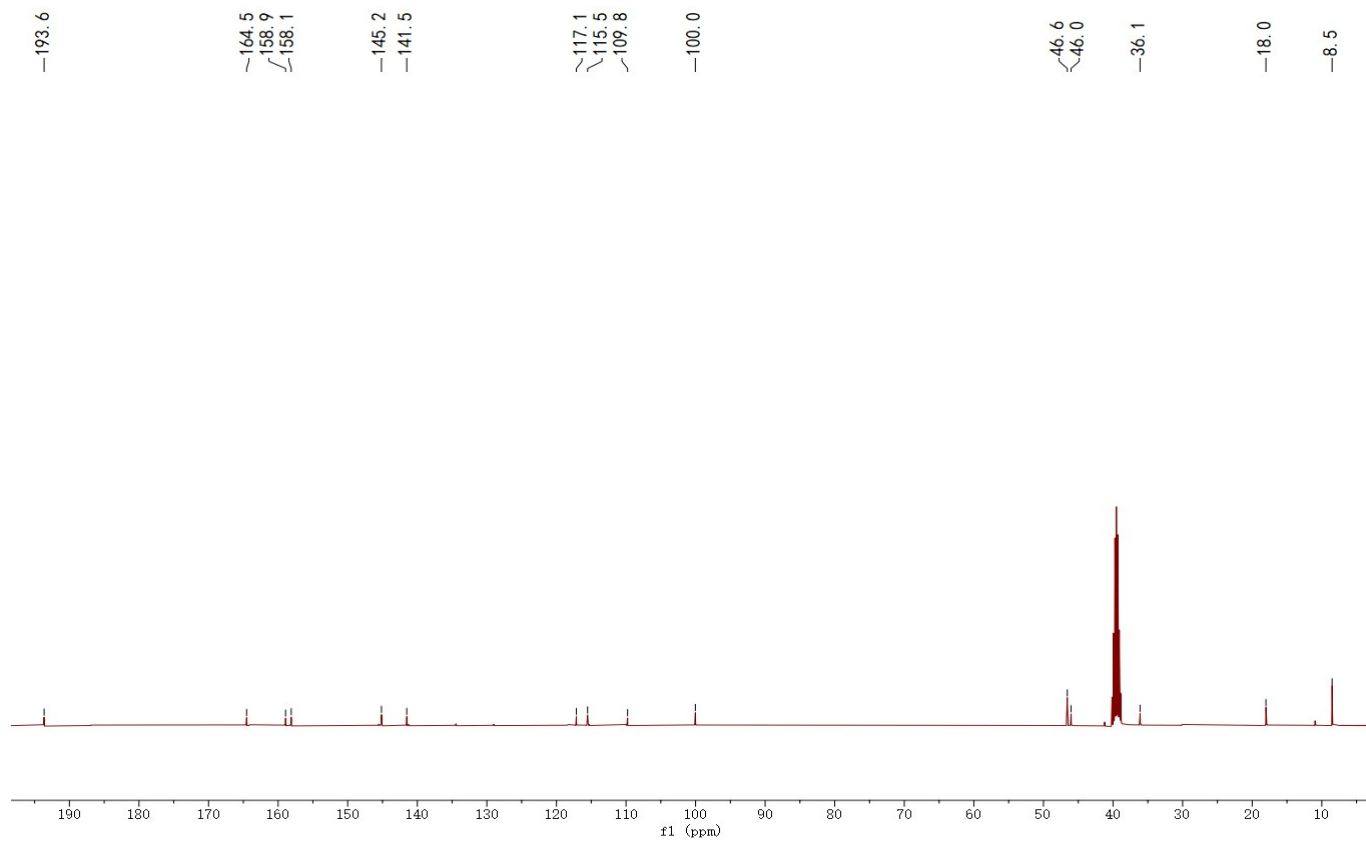
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **9** in $\text{DMSO-}d_6$



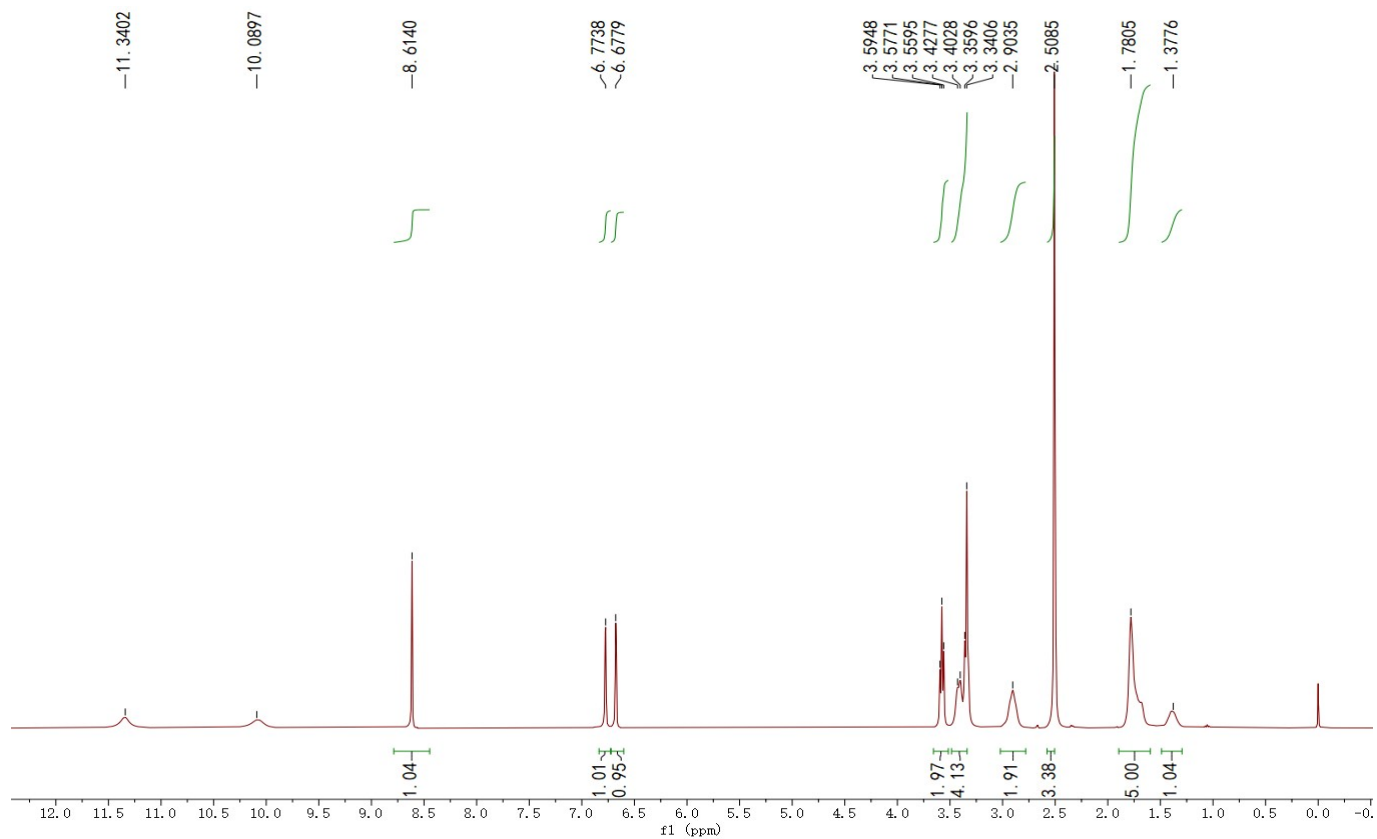
¹³C-NMR (100 MHz) spectrum of compound **9** in DMSO-*d*₆



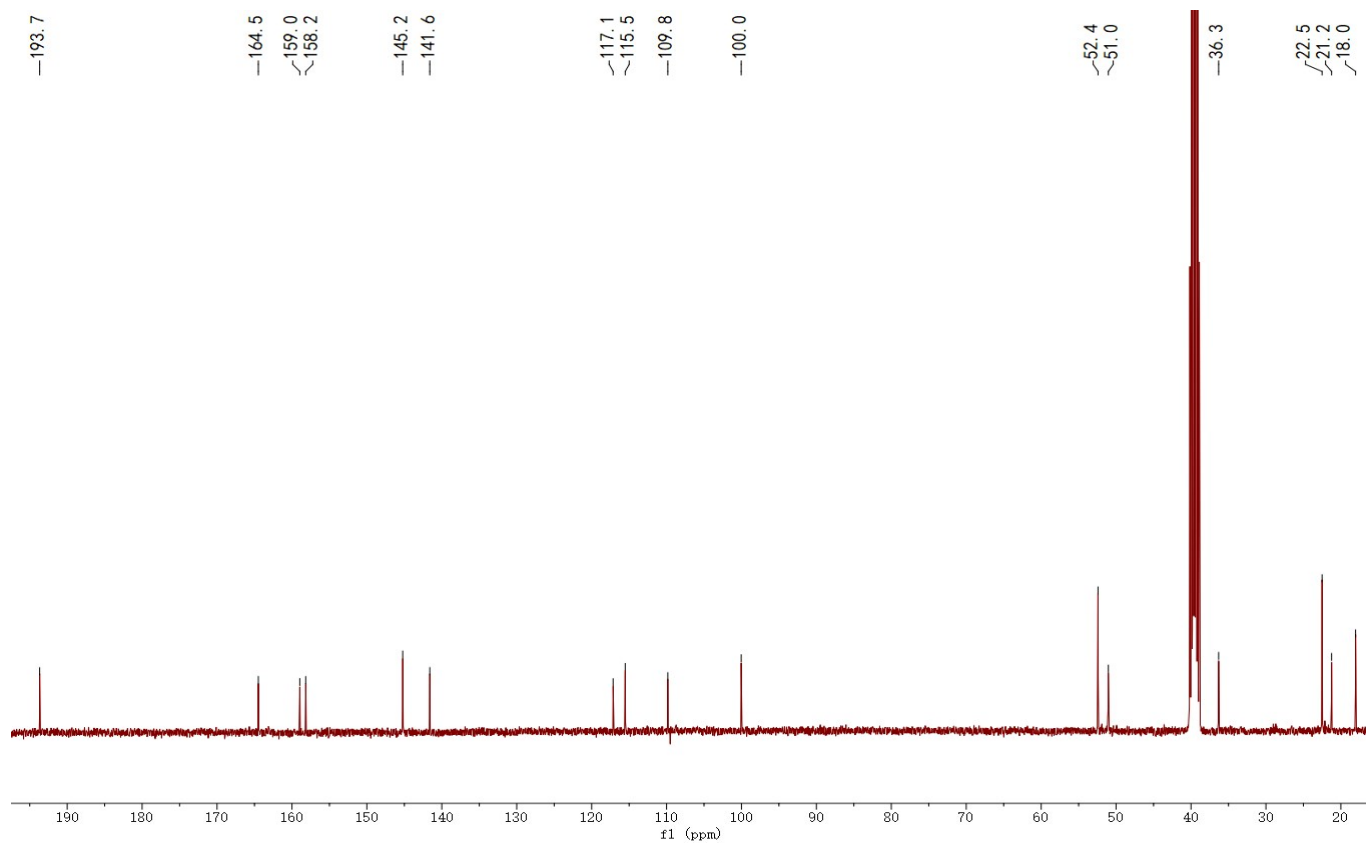
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **10** in $\text{DMSO-}d_6$



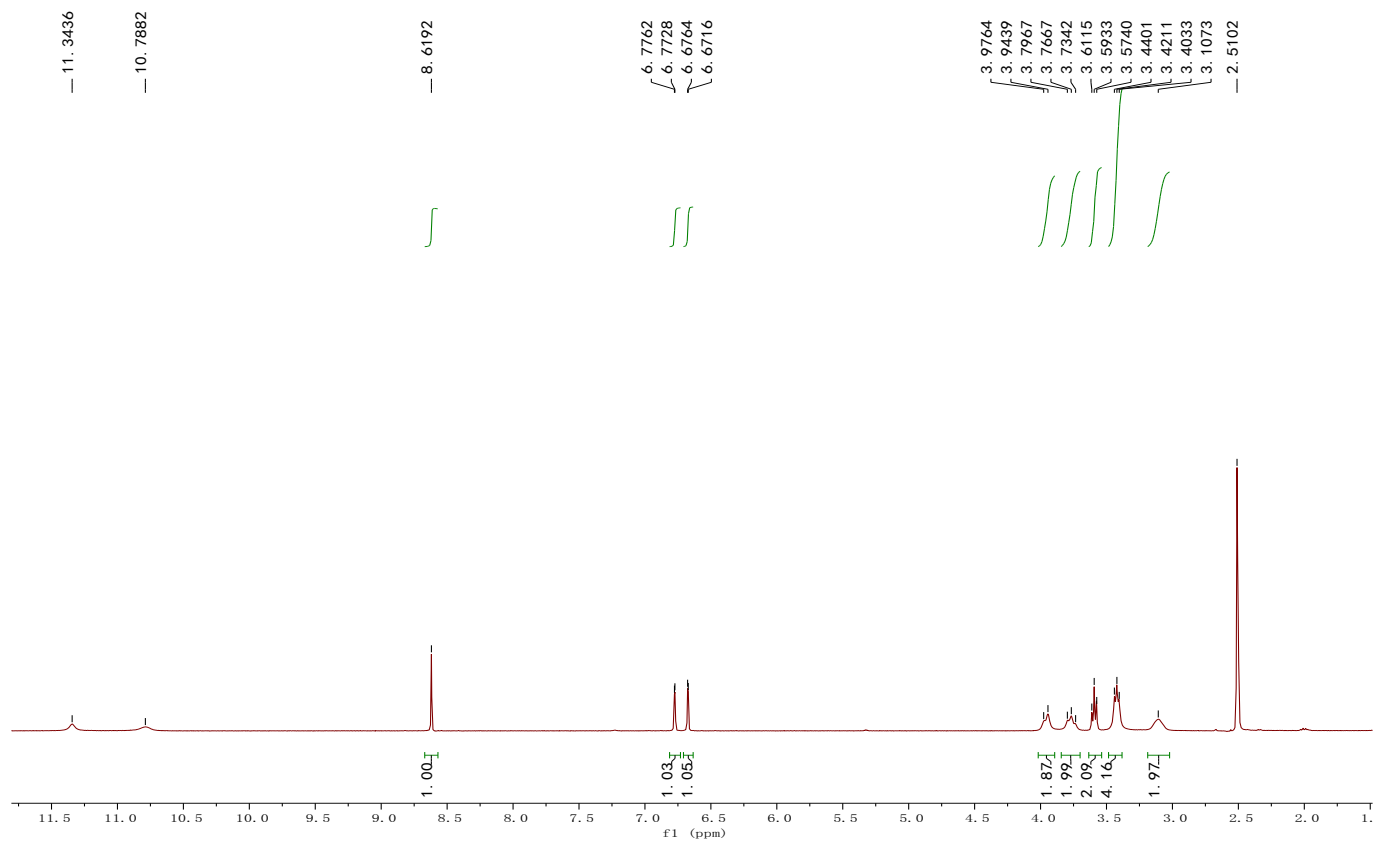
^{13}C -NMR (100 MHz) spectrum of compound **10** in $\text{DMSO-}d_6$



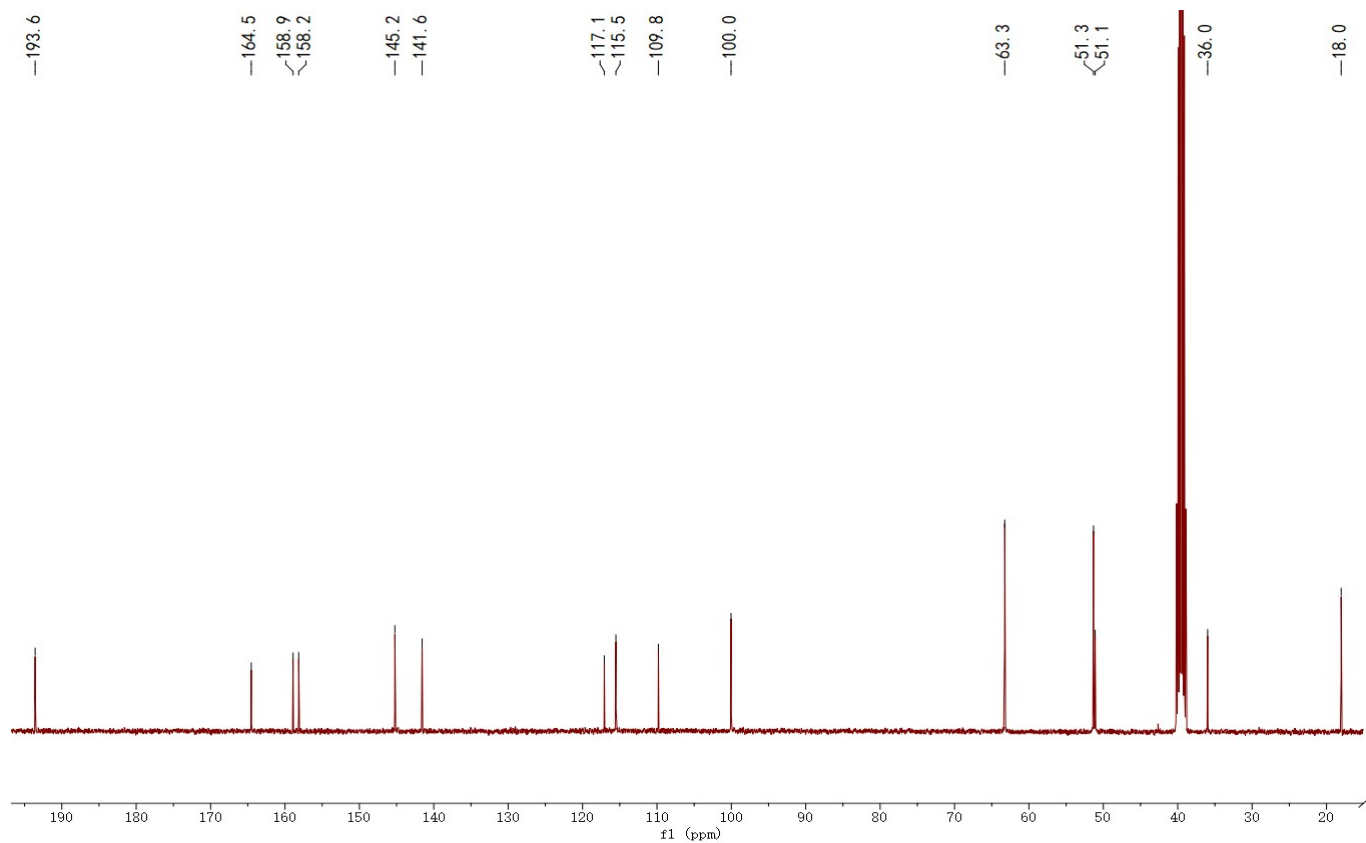
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **11** in $\text{DMSO-}d_6$



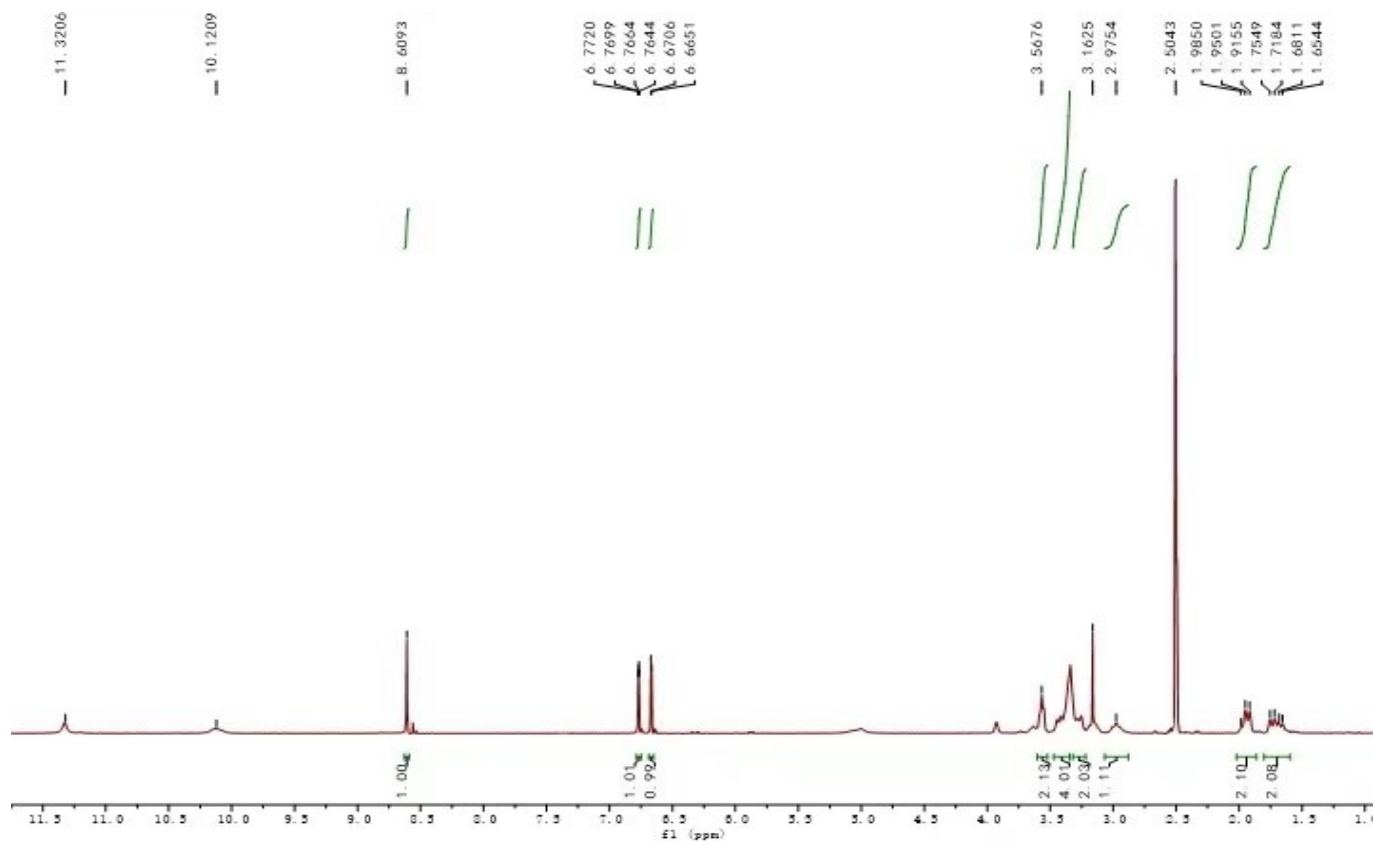
^{13}C -NMR (100 MHz) spectrum of compound **11** in $\text{DMSO-}d_6$



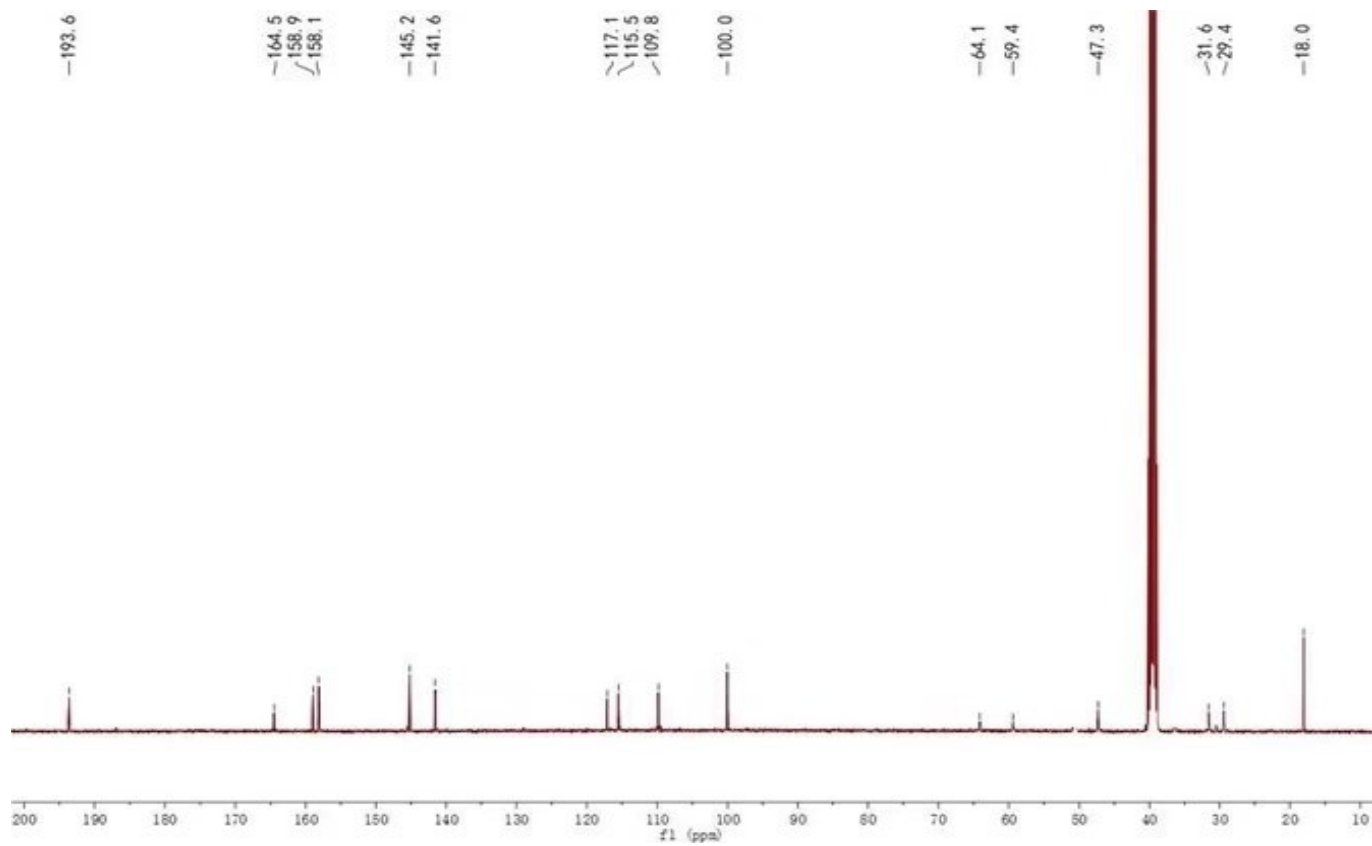
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **12** in $\text{DMSO-}d_6$



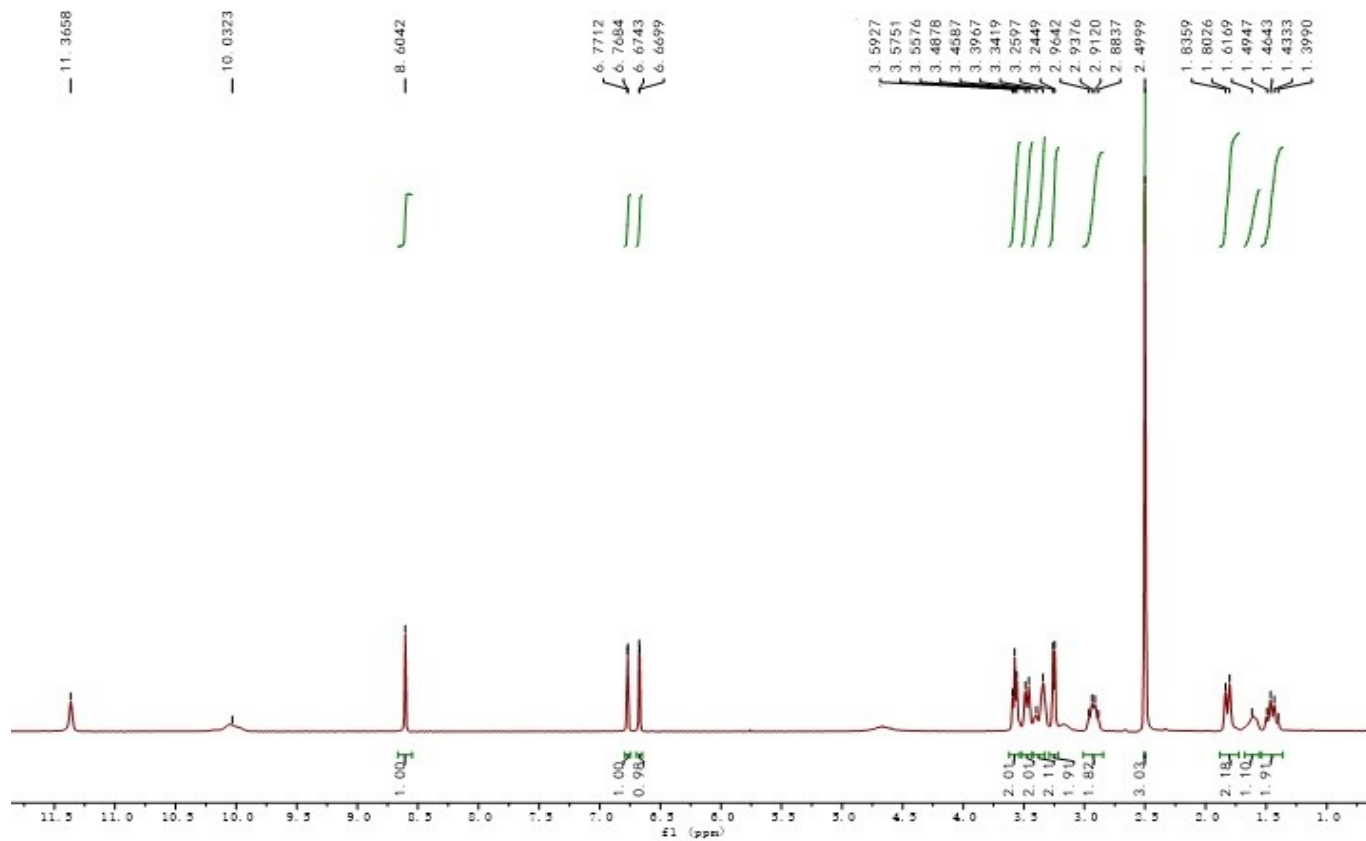
^{13}C -NMR (100 MHz) spectrum of compound **12** in $\text{DMSO-}d_6$



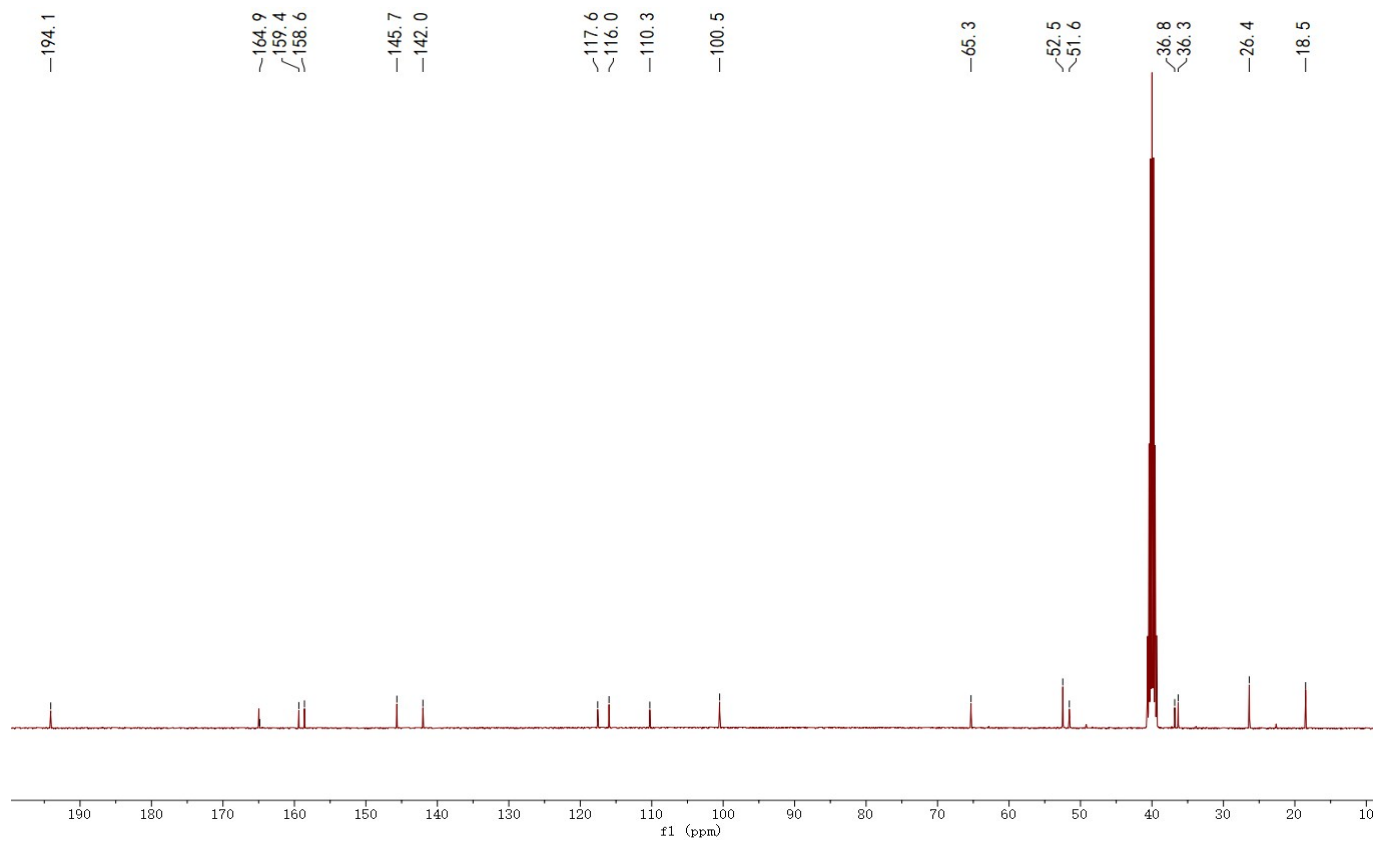
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **13** in $\text{DMSO-}d_6$



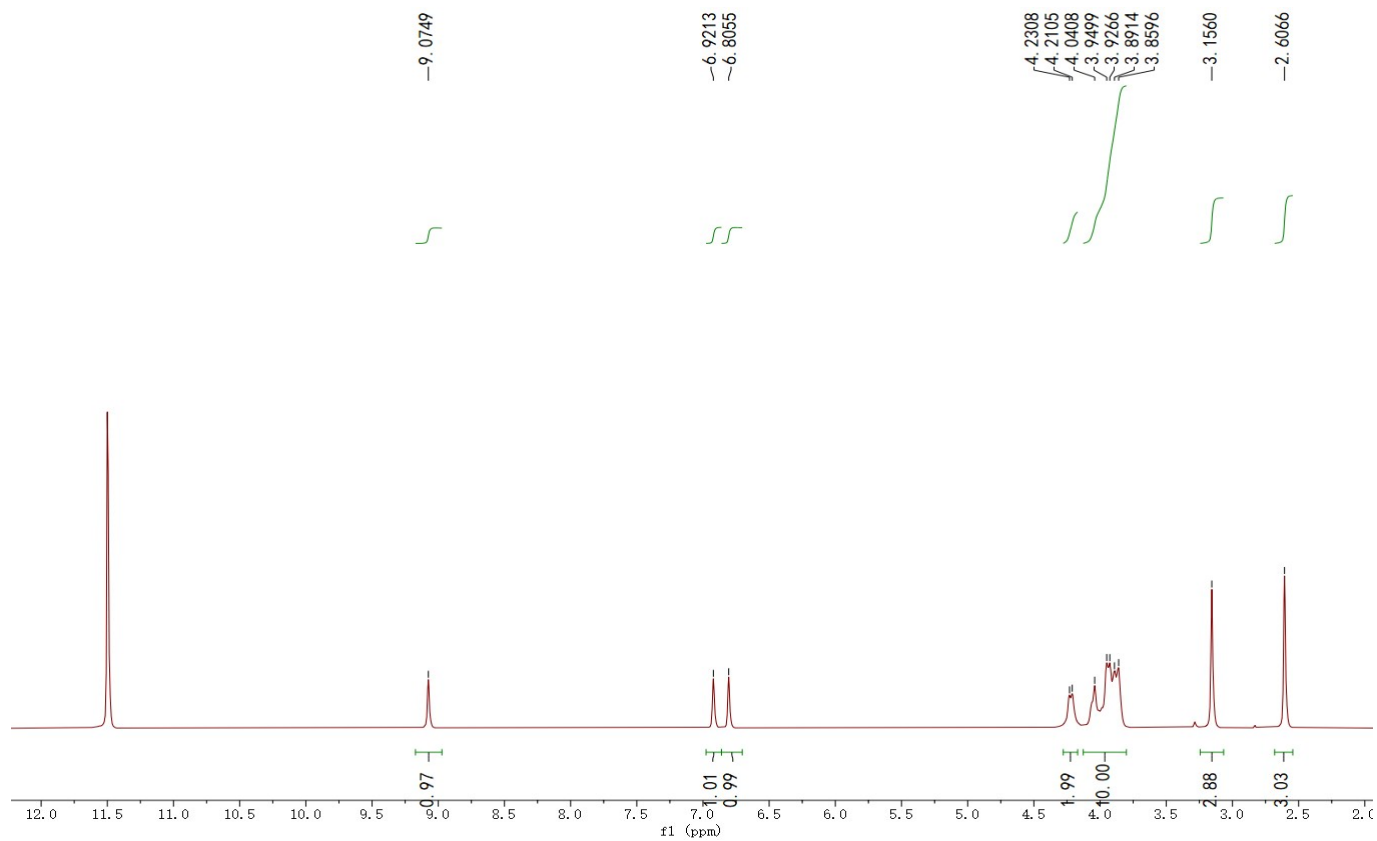
¹³C-NMR (100 MHz) spectrum of compound **13** in DMSO-*d*₆



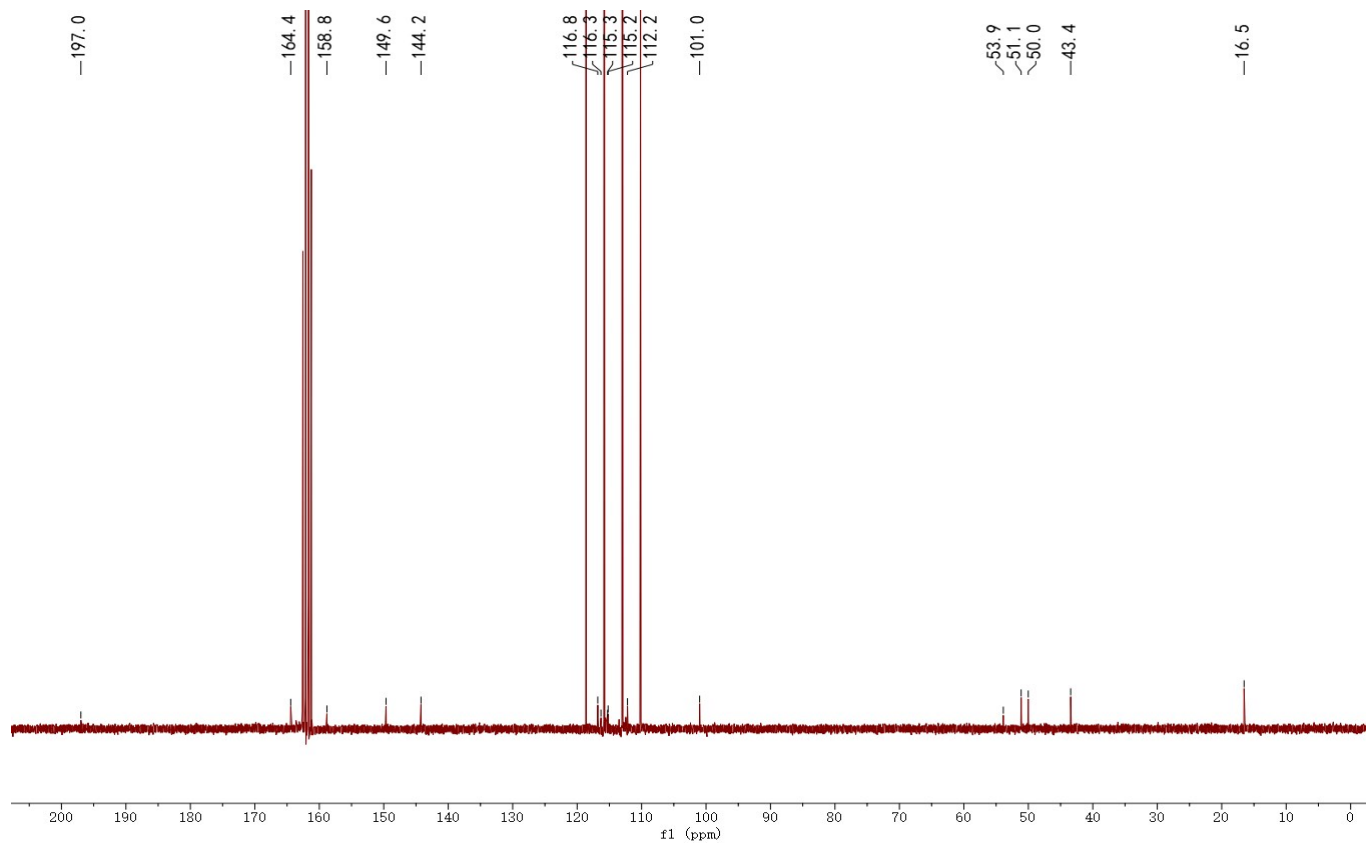
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **14** in $\text{DMSO-}d_6$



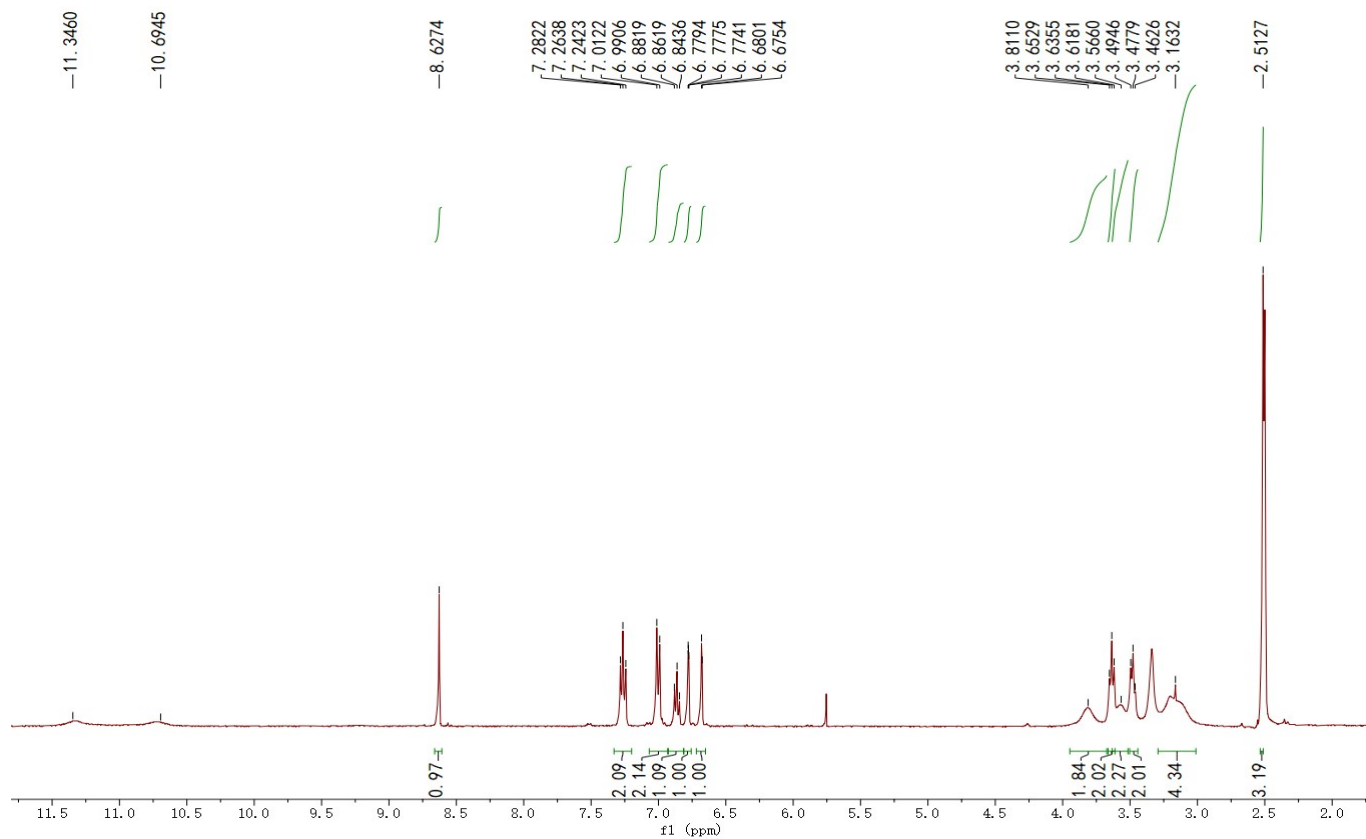
^{13}C -NMR (100 MHz) spectrum of compound **14** in $\text{DMSO-}d_6$



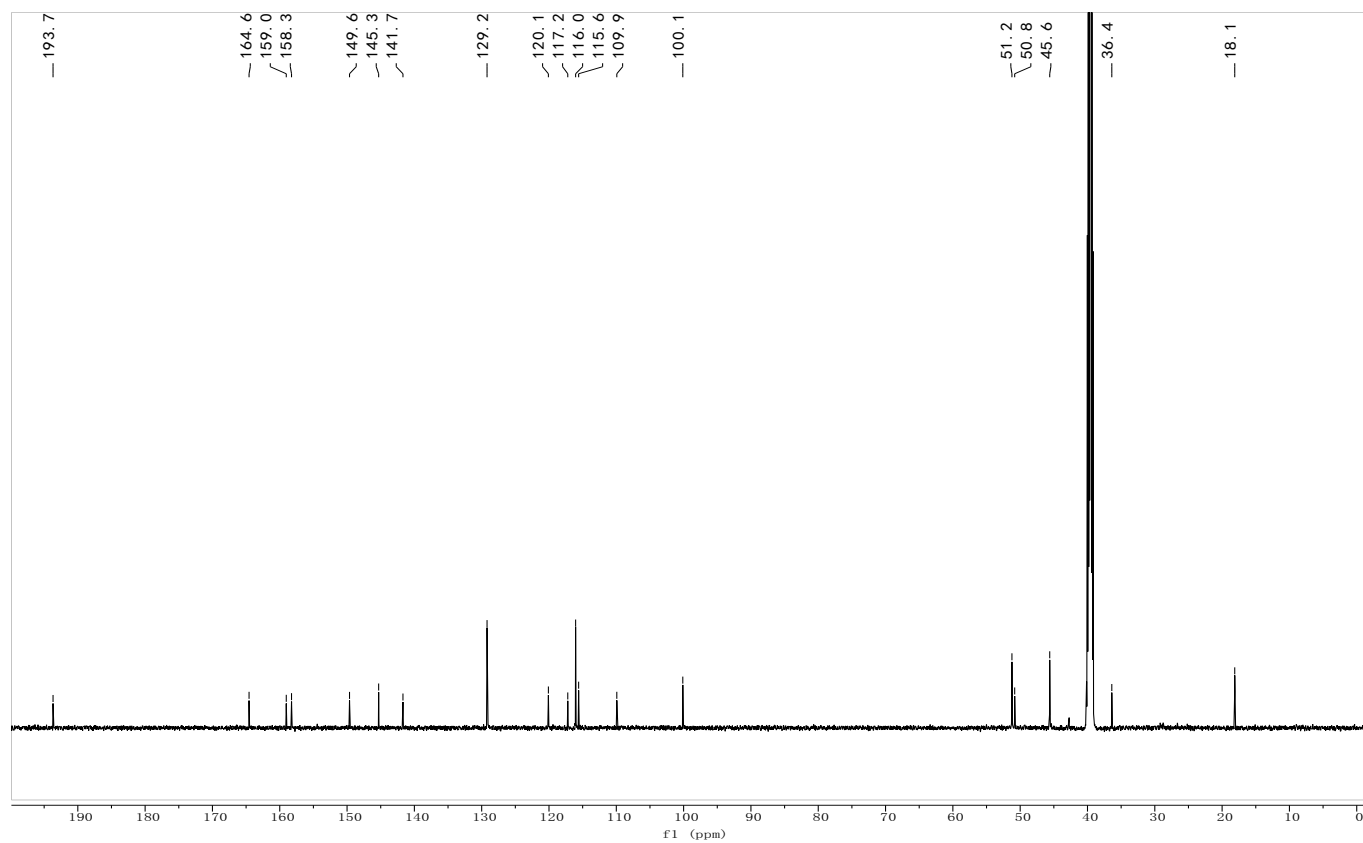
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **15** in trifluoroacetic acid-*d*



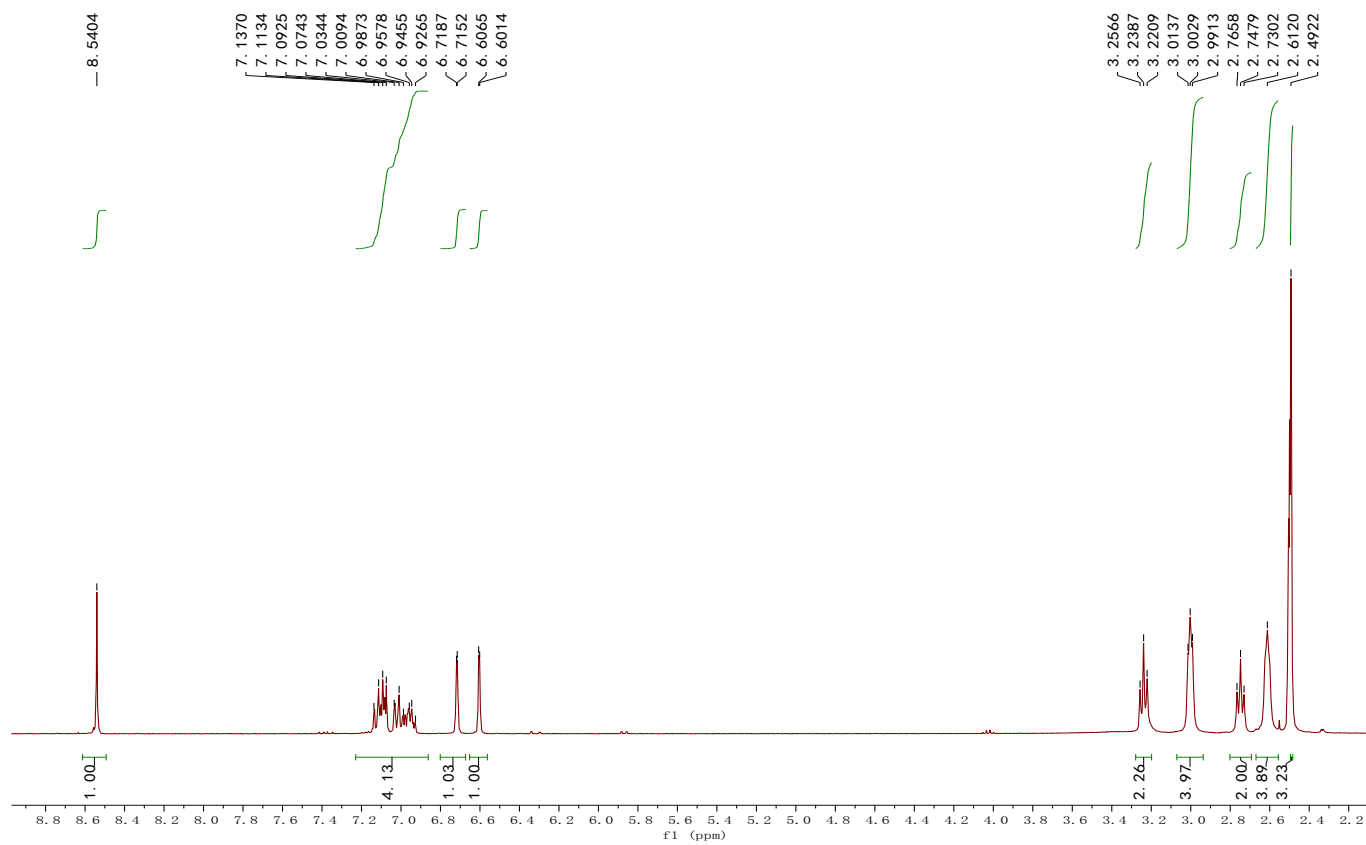
^{13}C -NMR (100 MHz) spectrum of compound **15** in trifluoroacetic acid-*d*



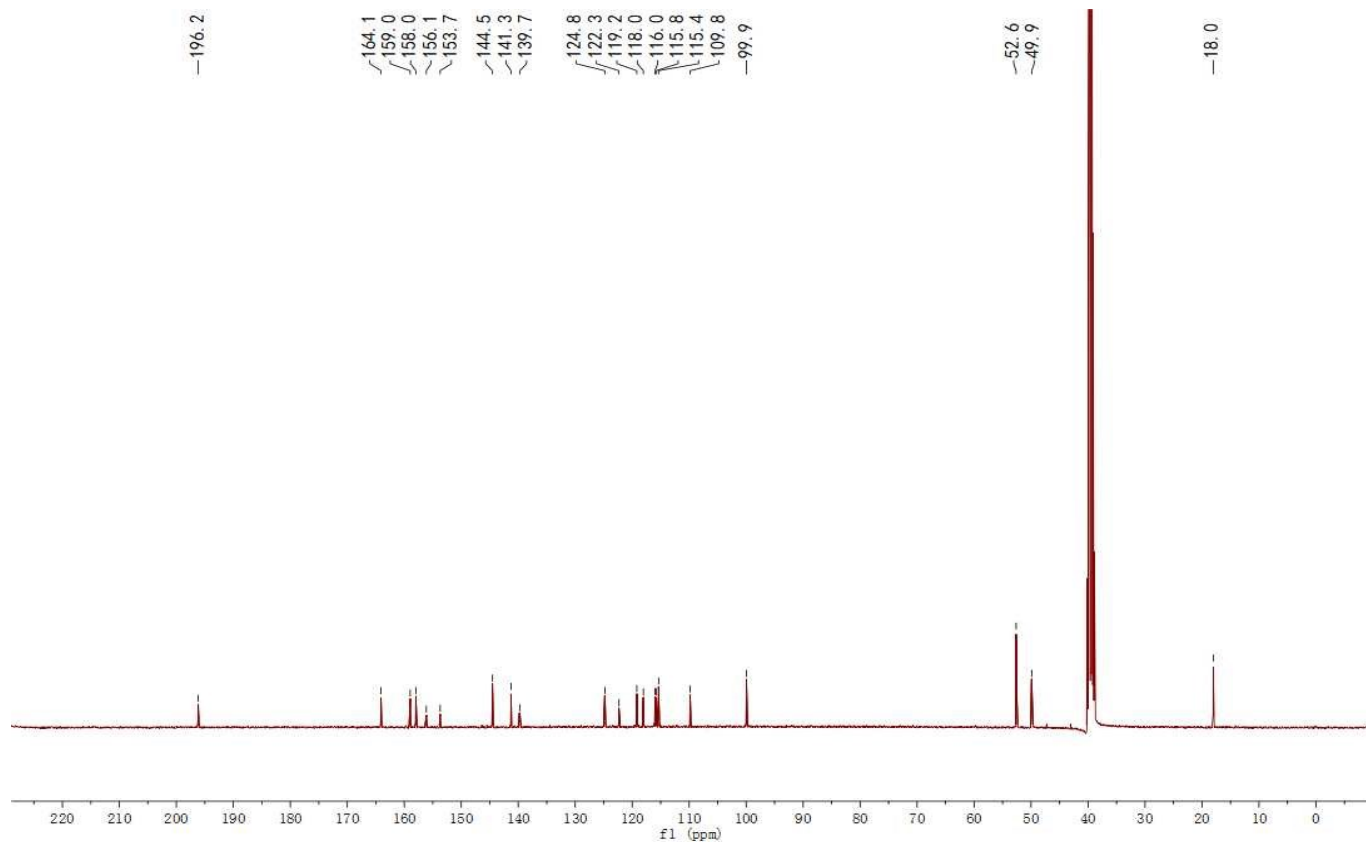
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **16** in $\text{DMSO-}d_6$



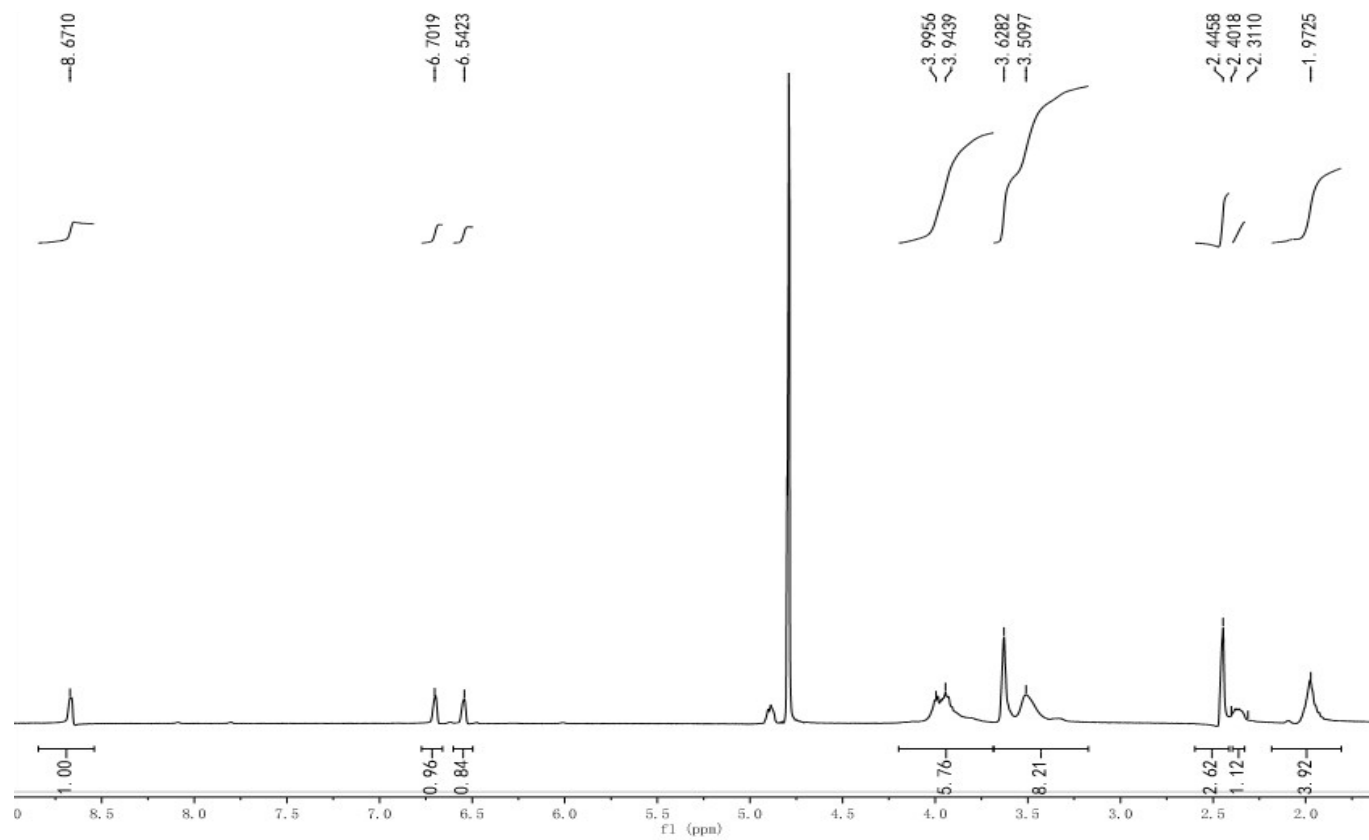
¹³C-NMR (150 MHz) spectrum of compound **16** in DMSO-*d*₆



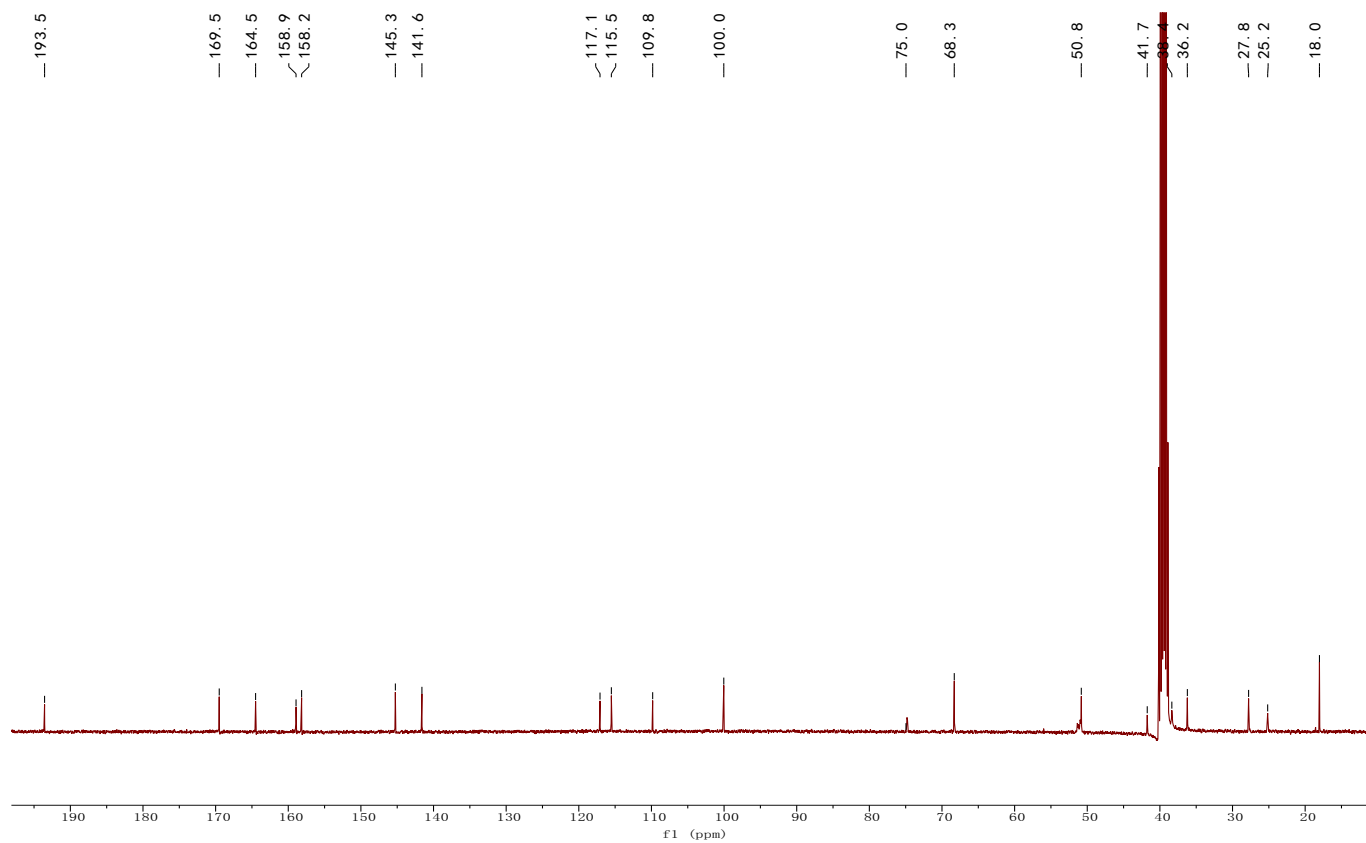
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **17** in $\text{DMSO-}d_6$



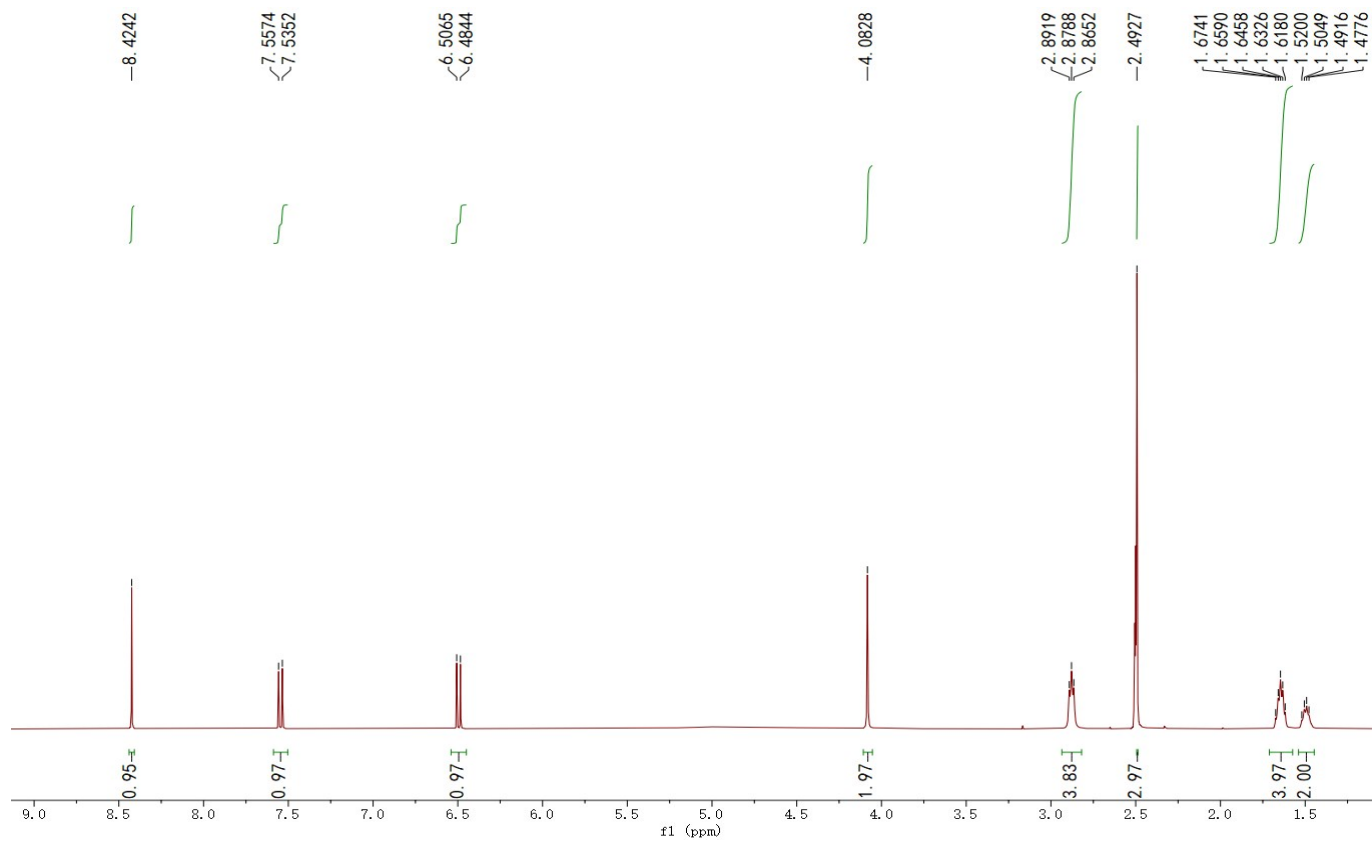
¹³C-NMR (100 MHz) spectrum of compound **17** in DMSO-*d*₆



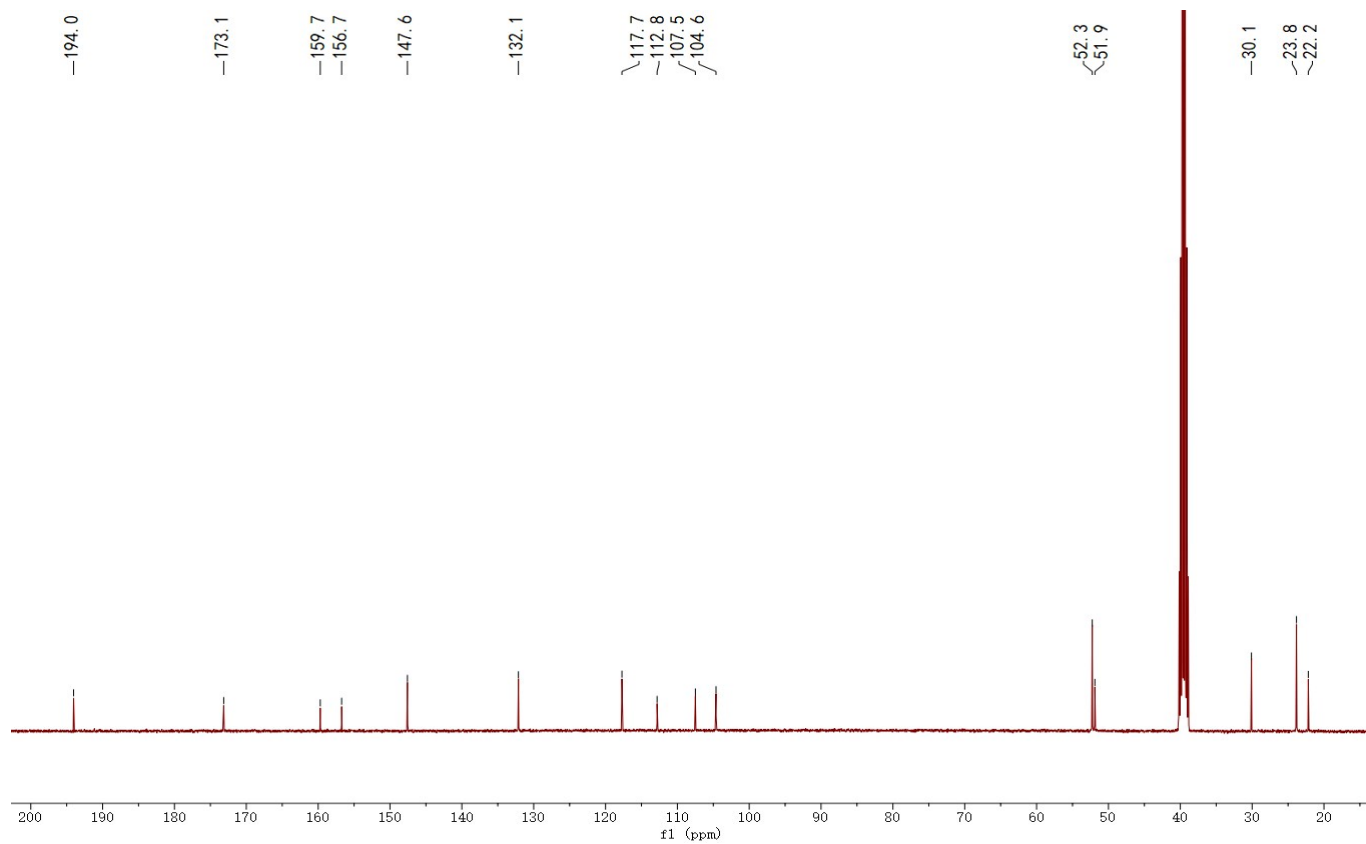
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **18** in D_2O



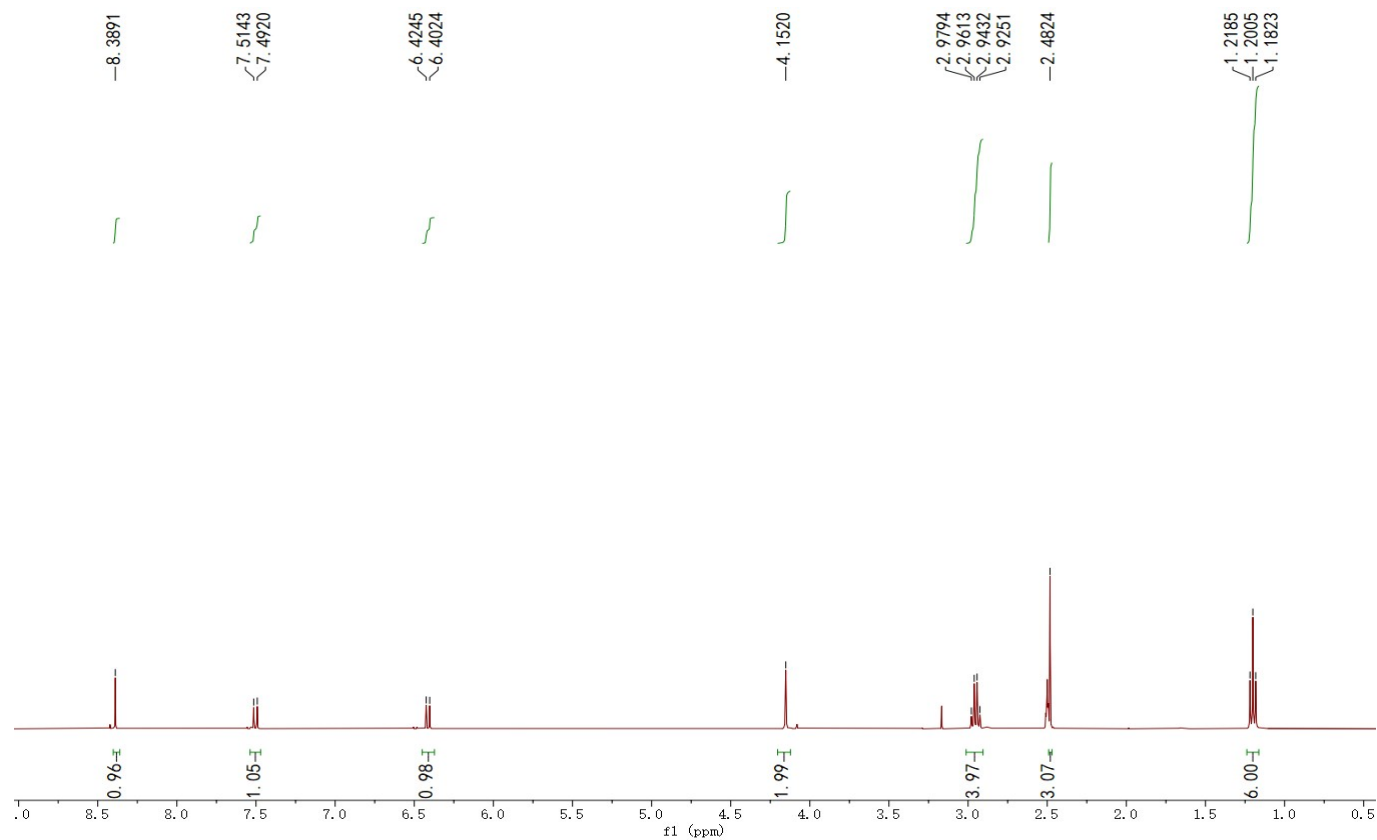
¹³C-NMR (100 MHz) spectrum of compound **18** in DMSO-*d*₆



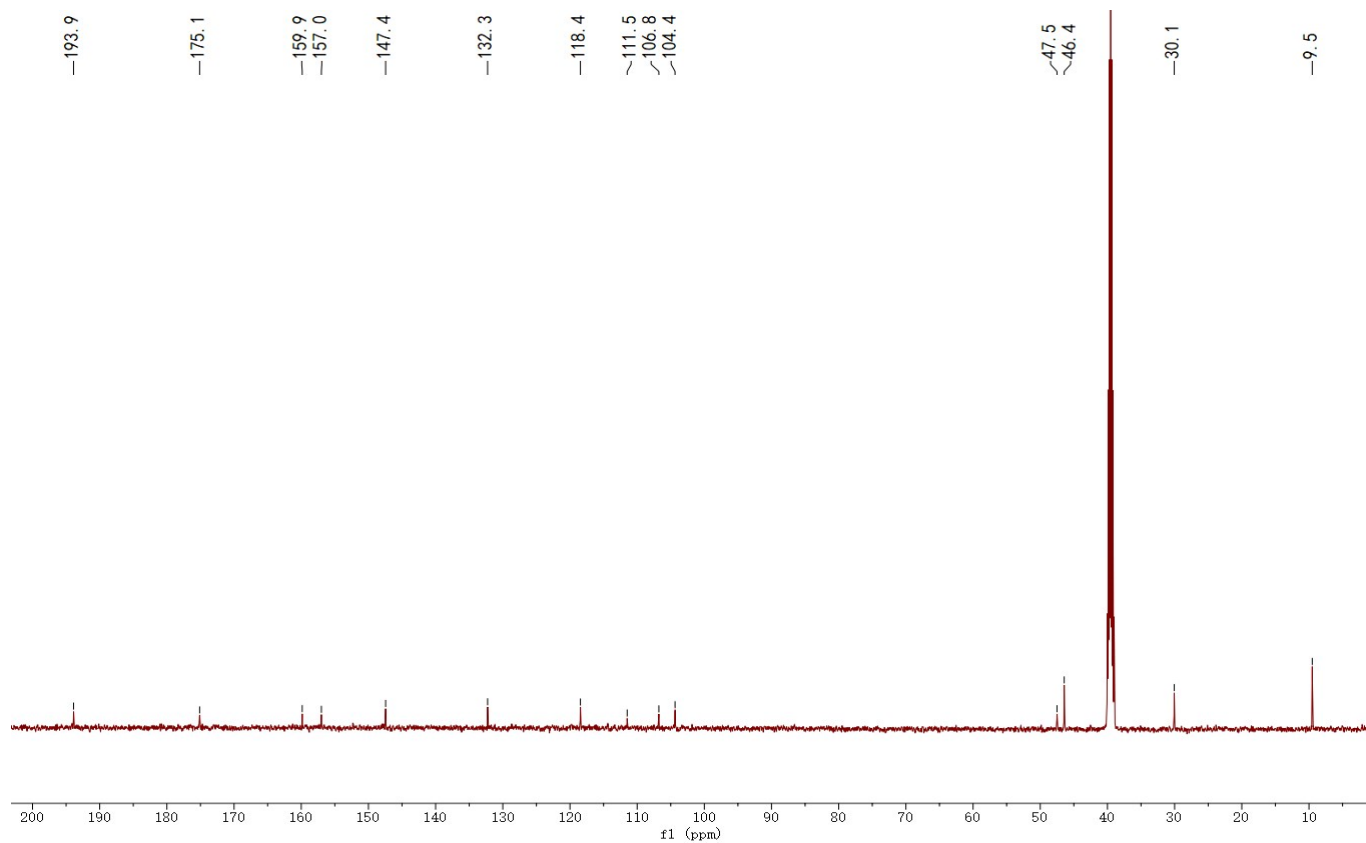
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **19** in $\text{DMSO-}d_6$



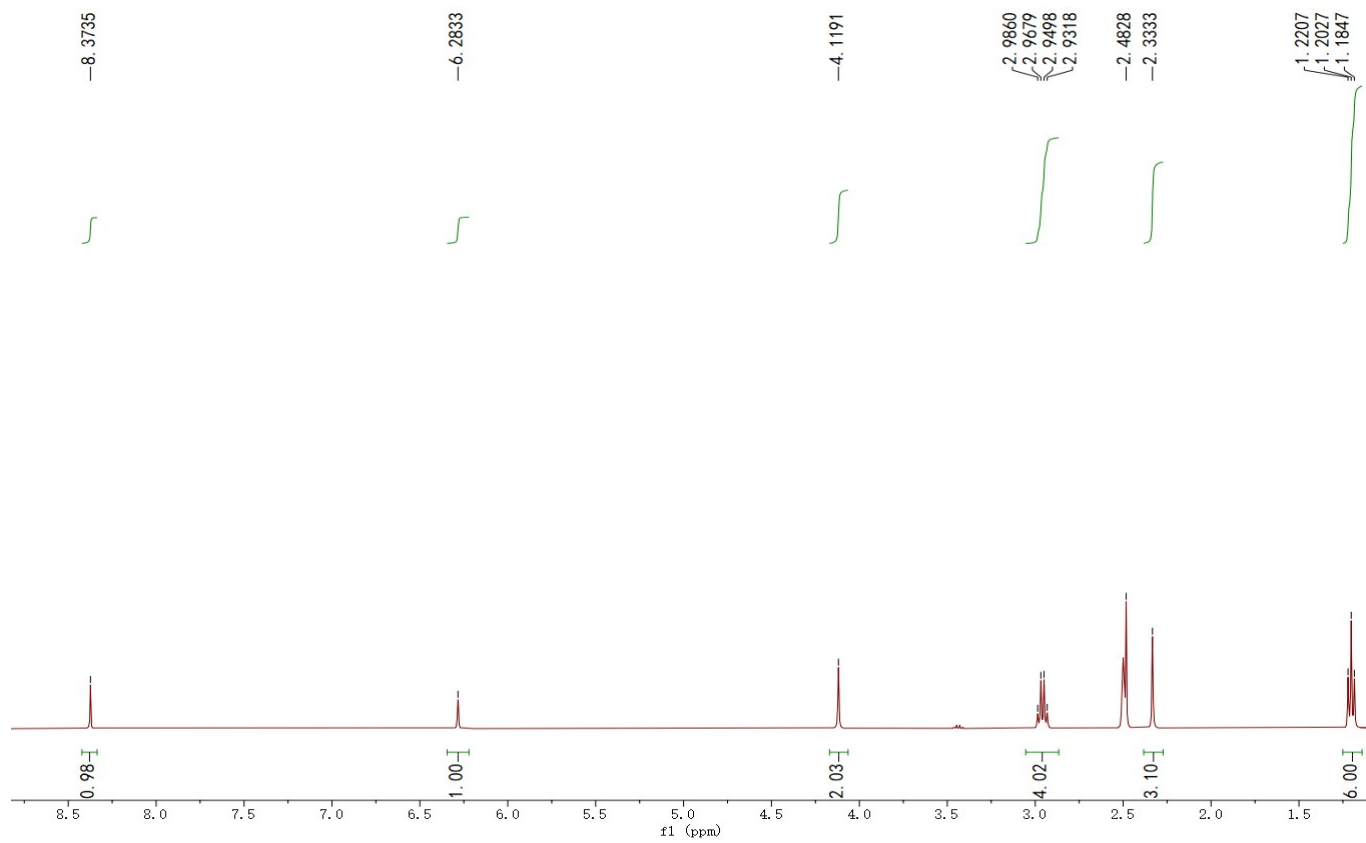
¹³C-NMR (125 MHz) spectrum of compound **19** in DMSO-*d*₆



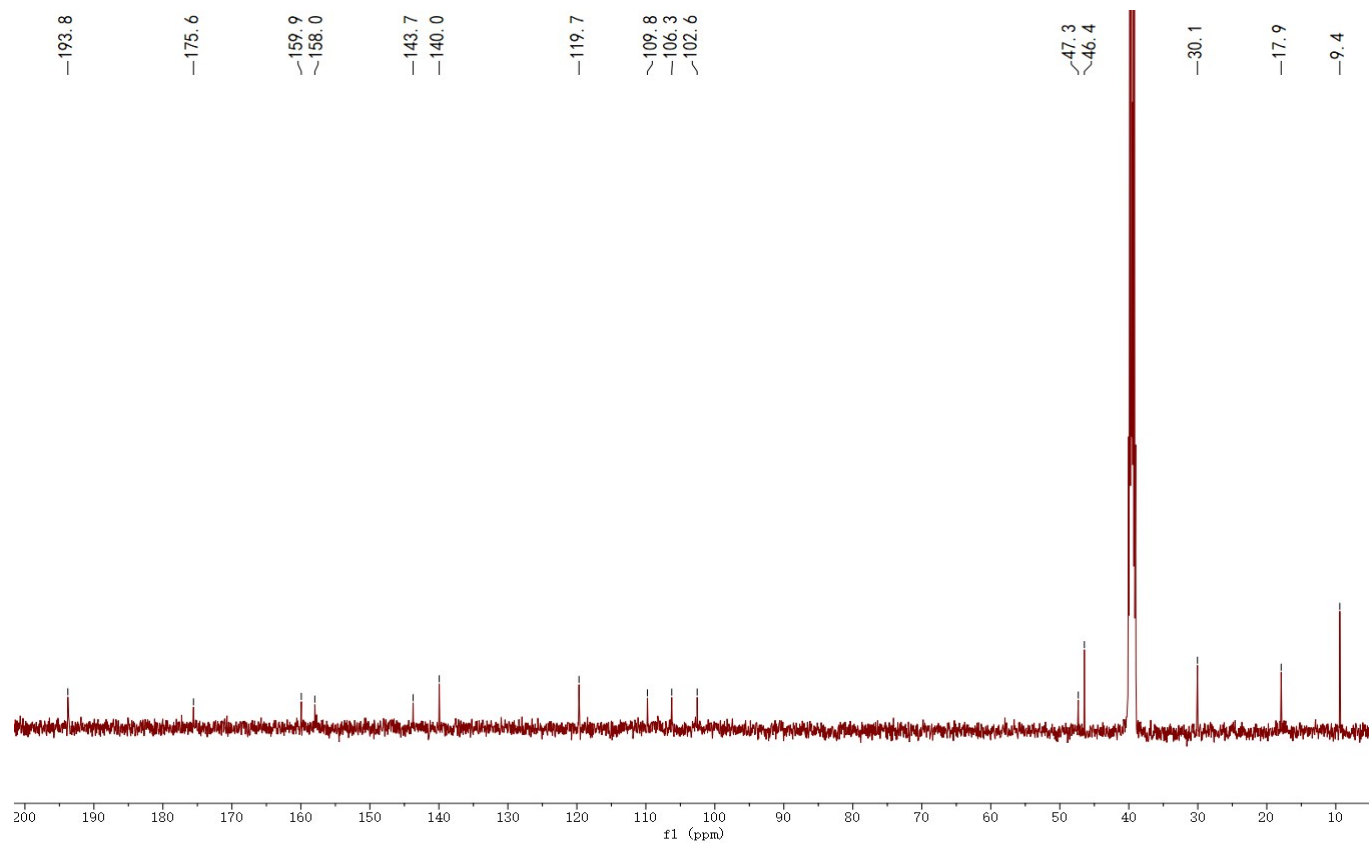
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **20** in $\text{DMSO-}d_6$



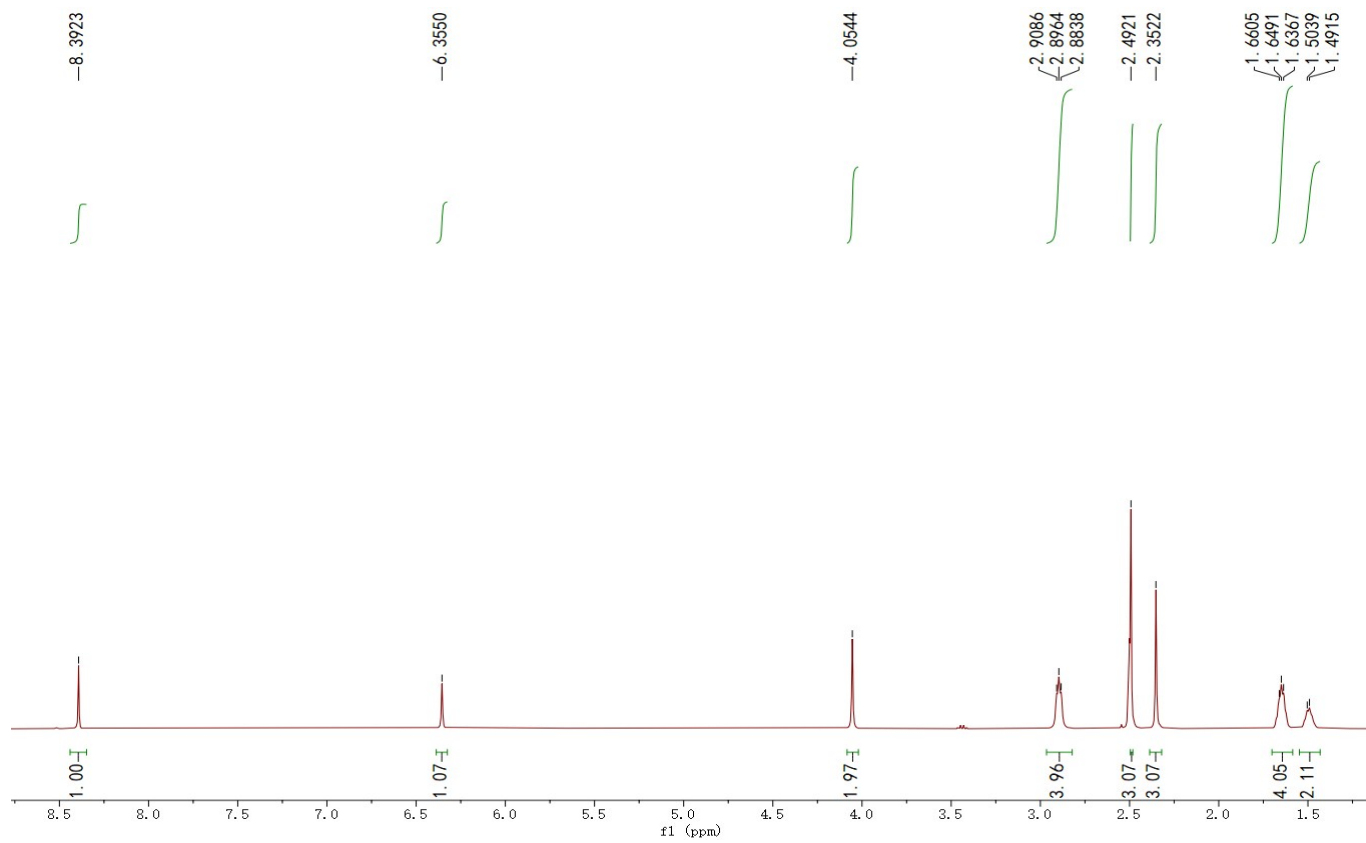
¹³C-NMR (100 MHz) spectrum of compound **20** in DMSO-*d*₆



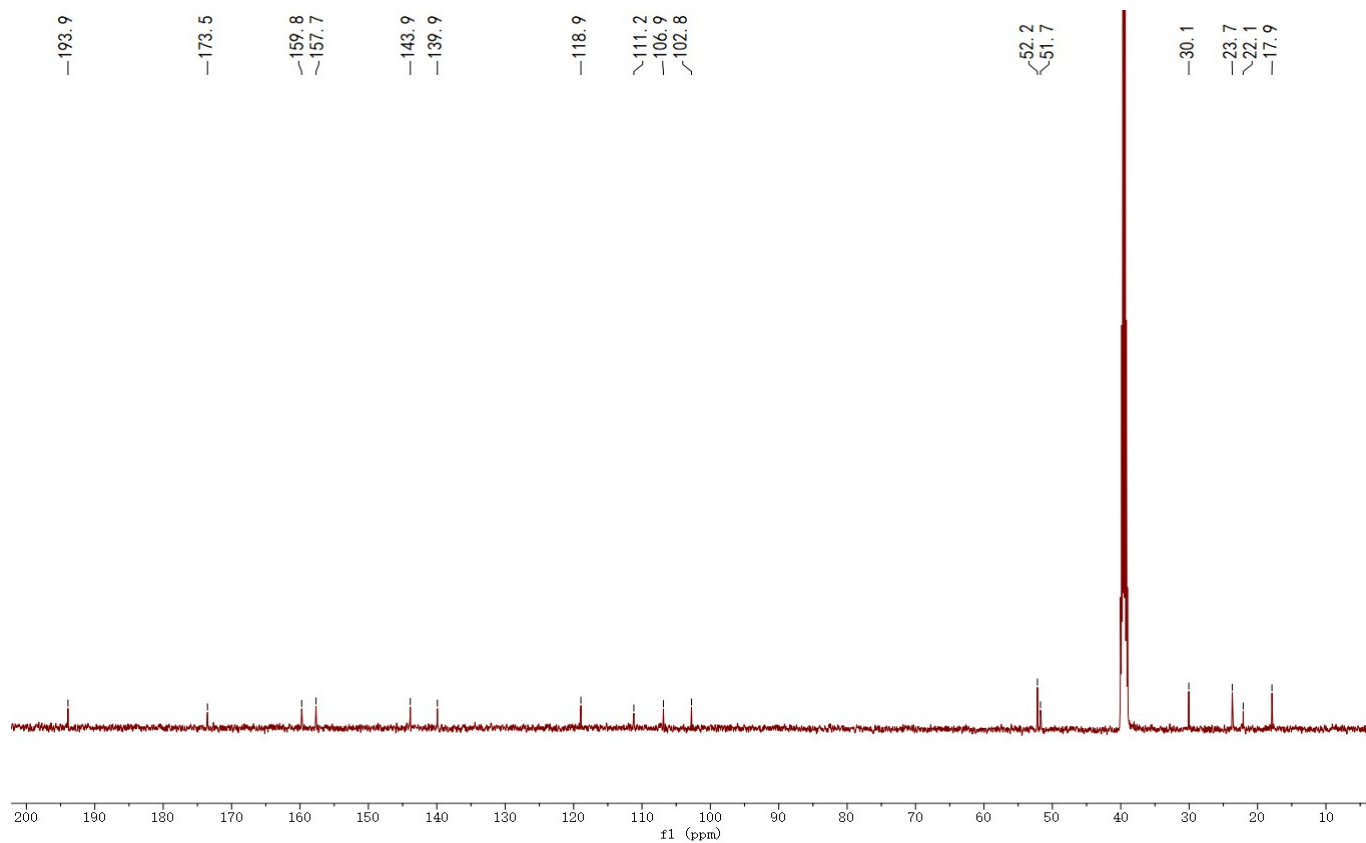
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **21** in $\text{DMSO-}d_6$



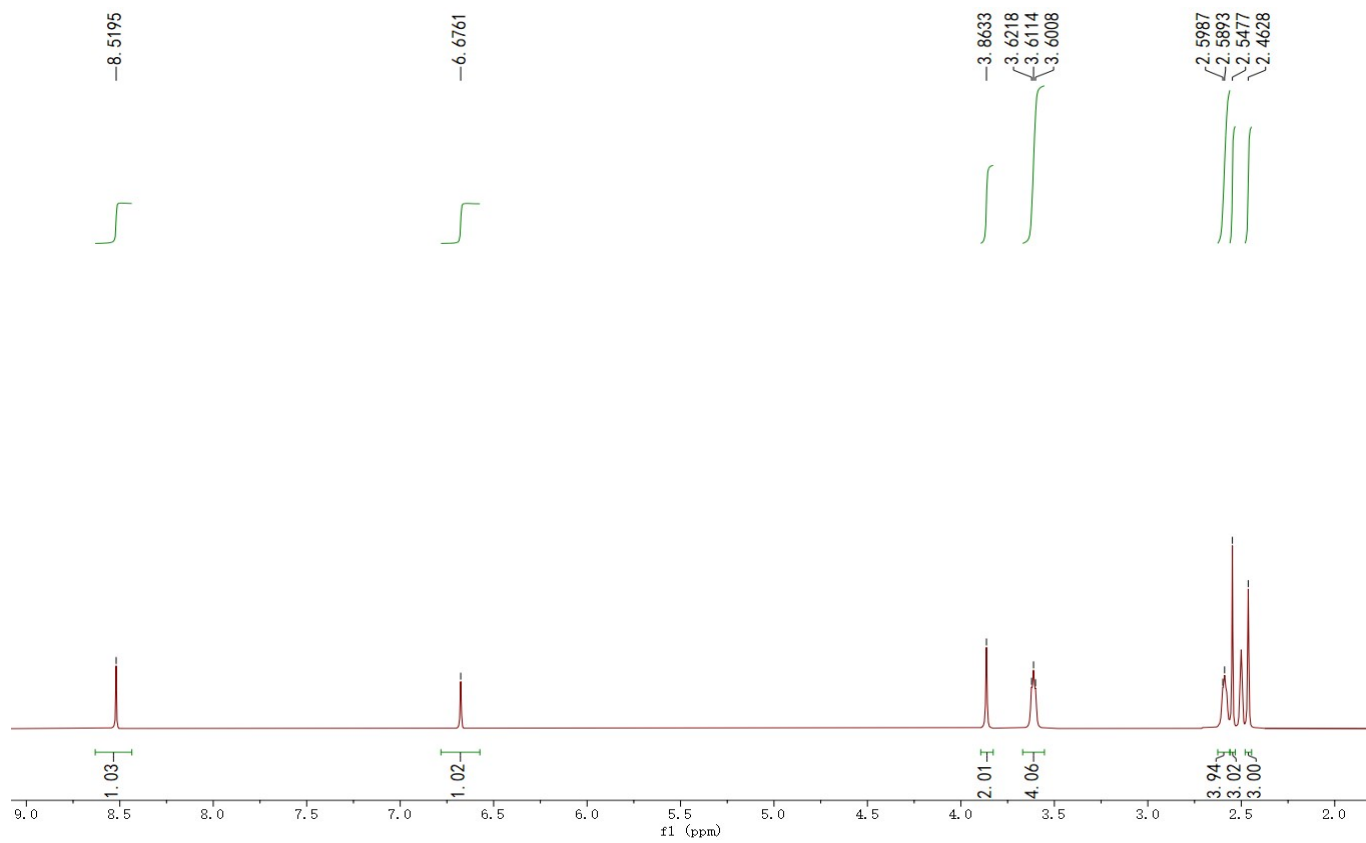
¹³C-NMR (125 MHz) spectrum of compound **21** in DMSO-*d*₆



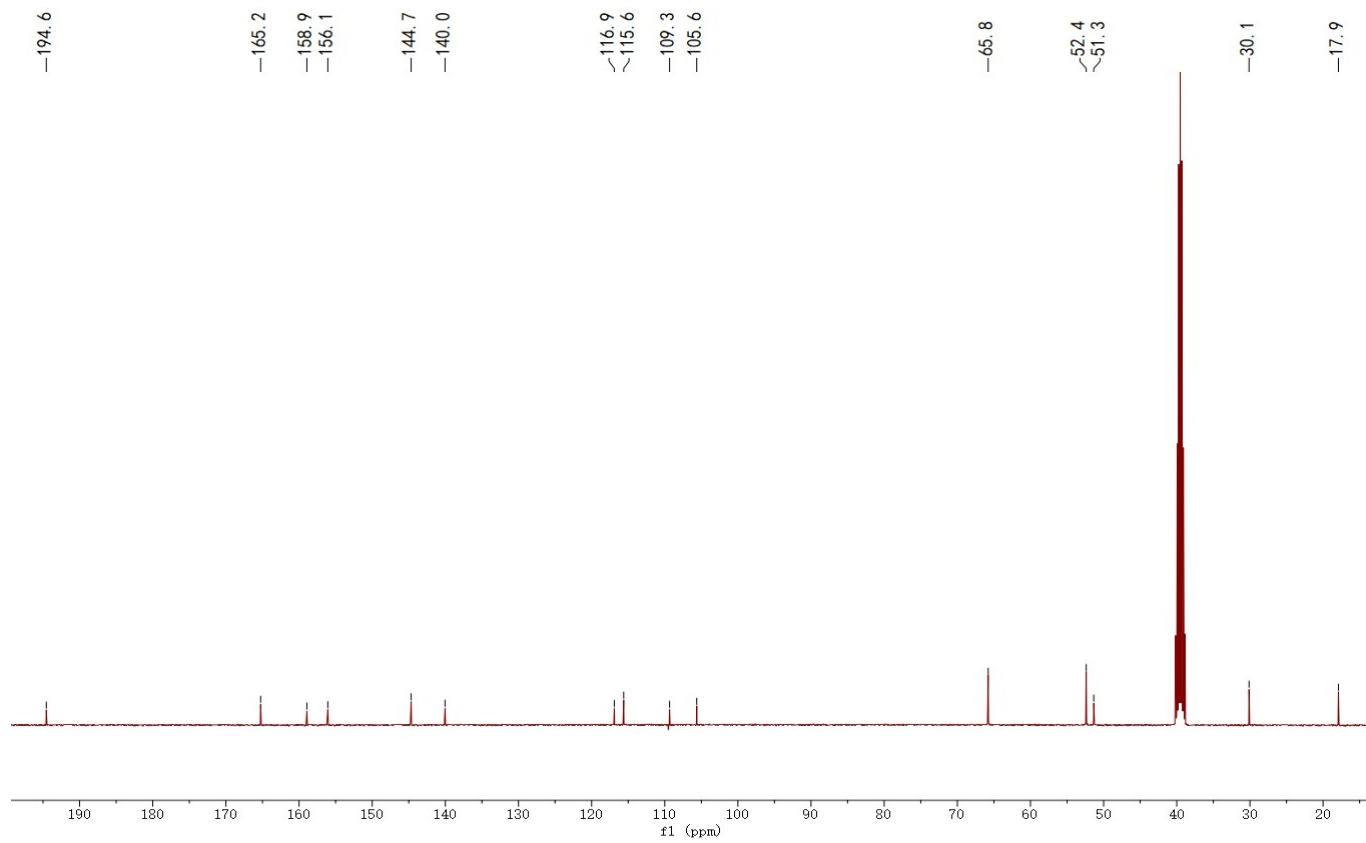
¹H-NMR (400 MHz) spectrum of compound **22** in DMSO-*d*₆



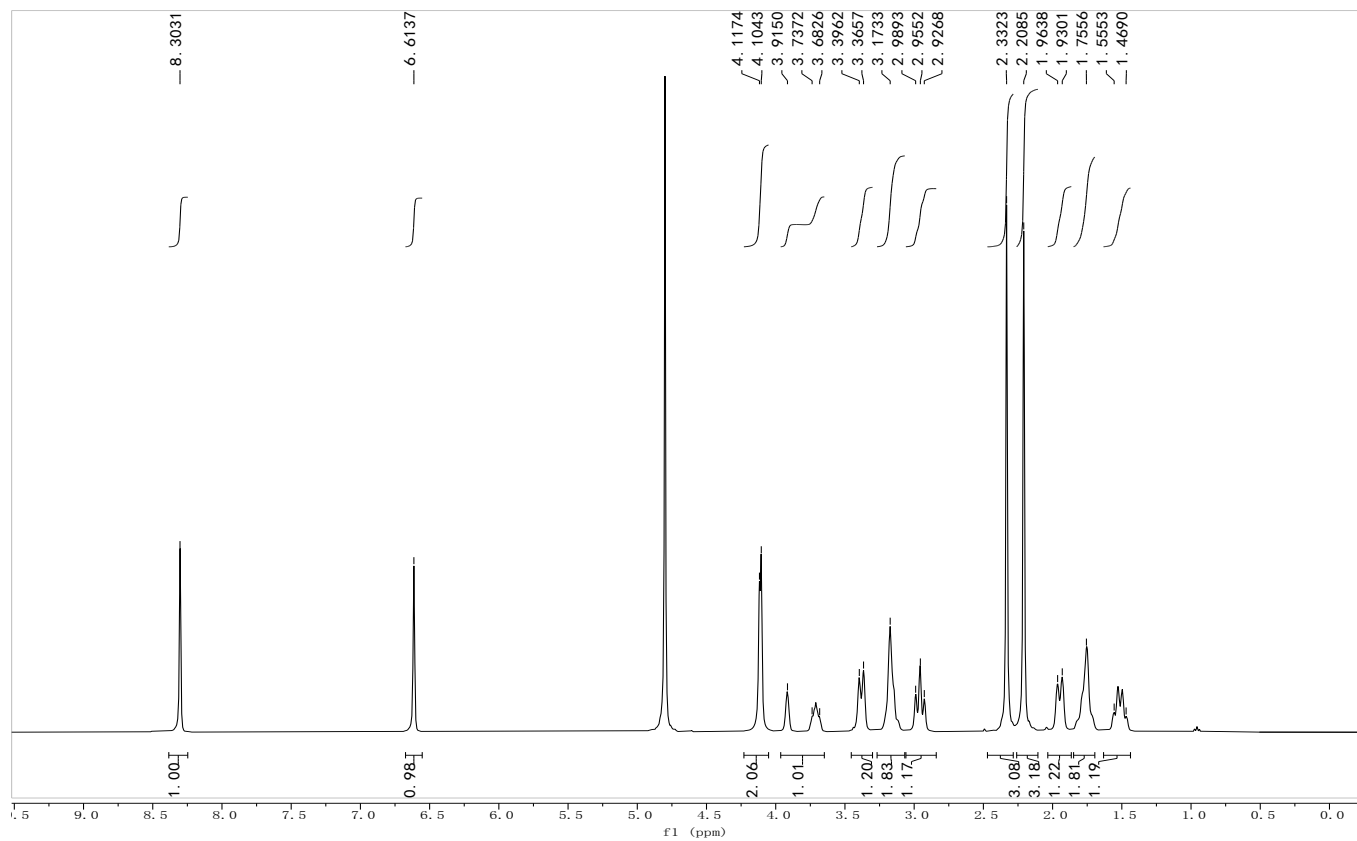
^{13}C -NMR (125 MHz) spectrum of compound **22** in $\text{DMSO-}d_6$



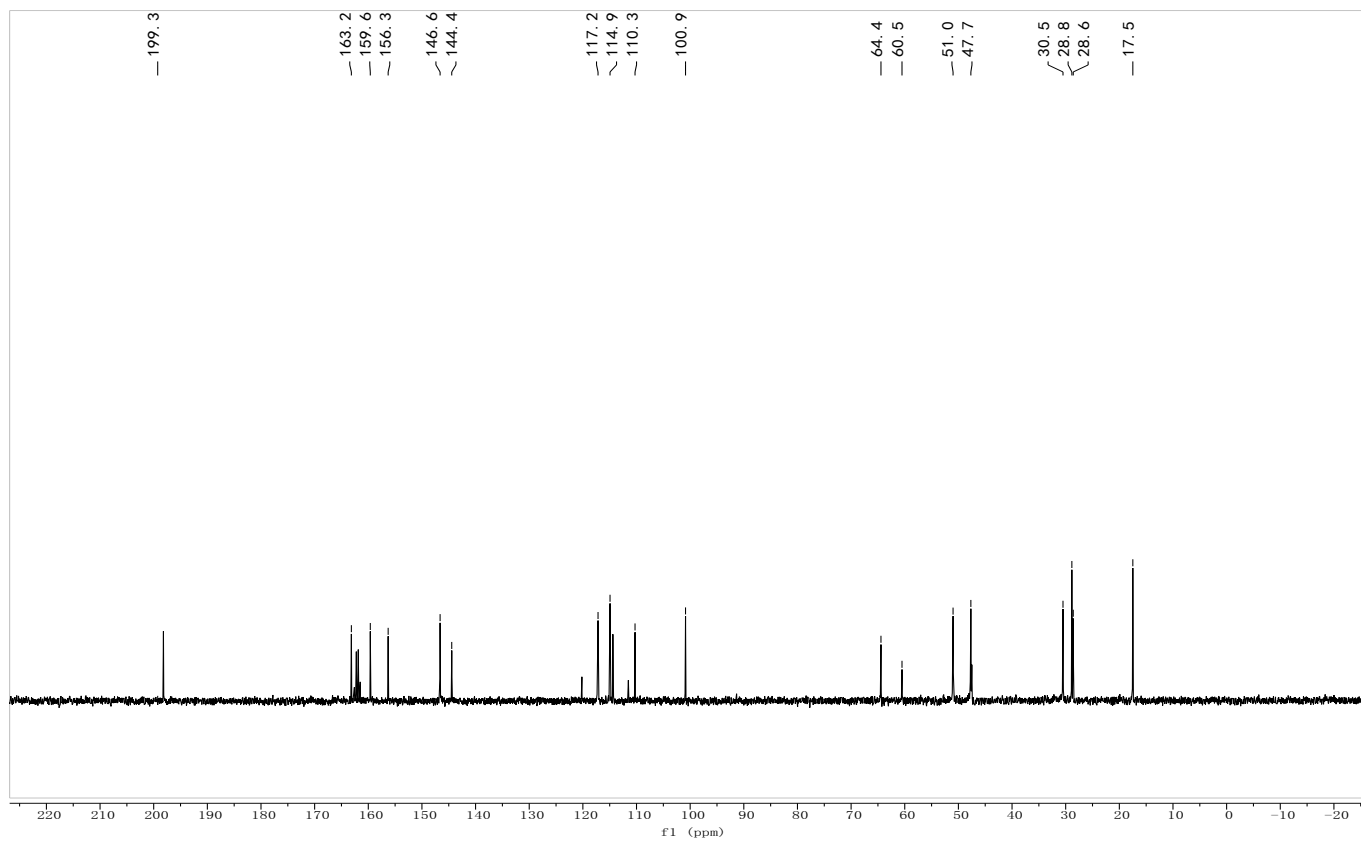
¹H-NMR (400 MHz) spectrum of compound **23** in DMSO-*d*₆



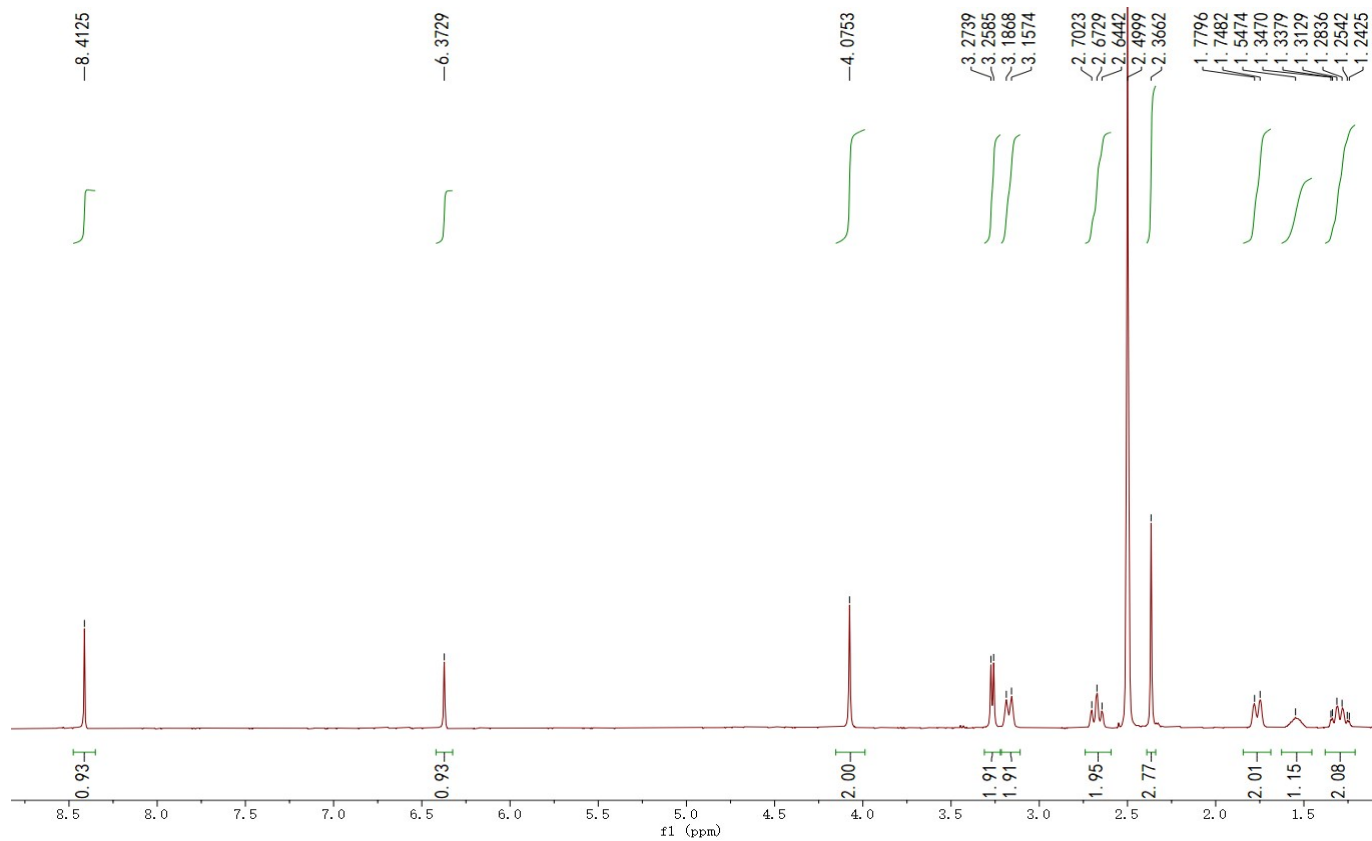
¹³C-NMR (100 MHz) spectrum of compound **23** in DMSO-*d*₆



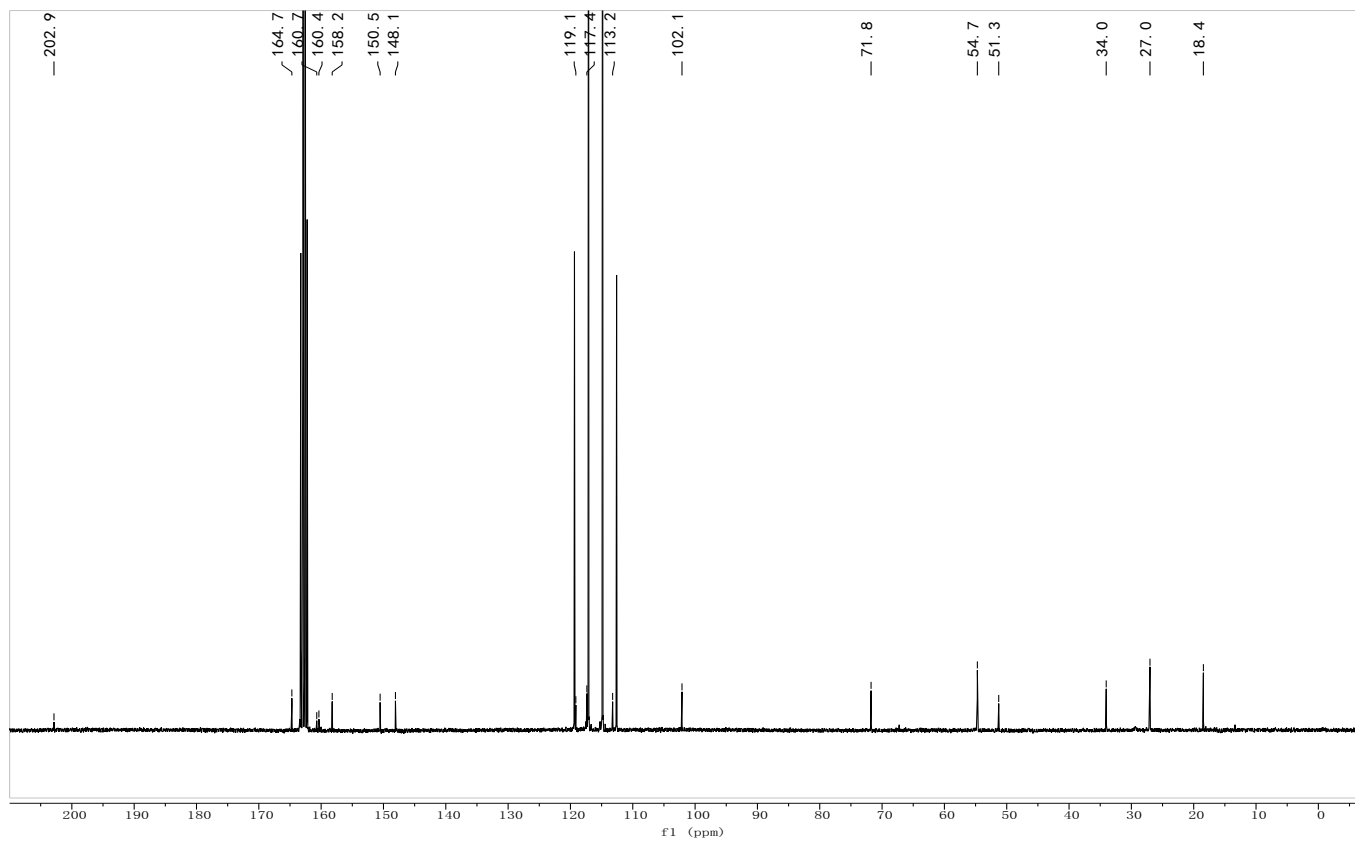
$^1\text{H-NMR}$ (500 MHz) spectrum of compound **24** in D_2O and CF_3COOD



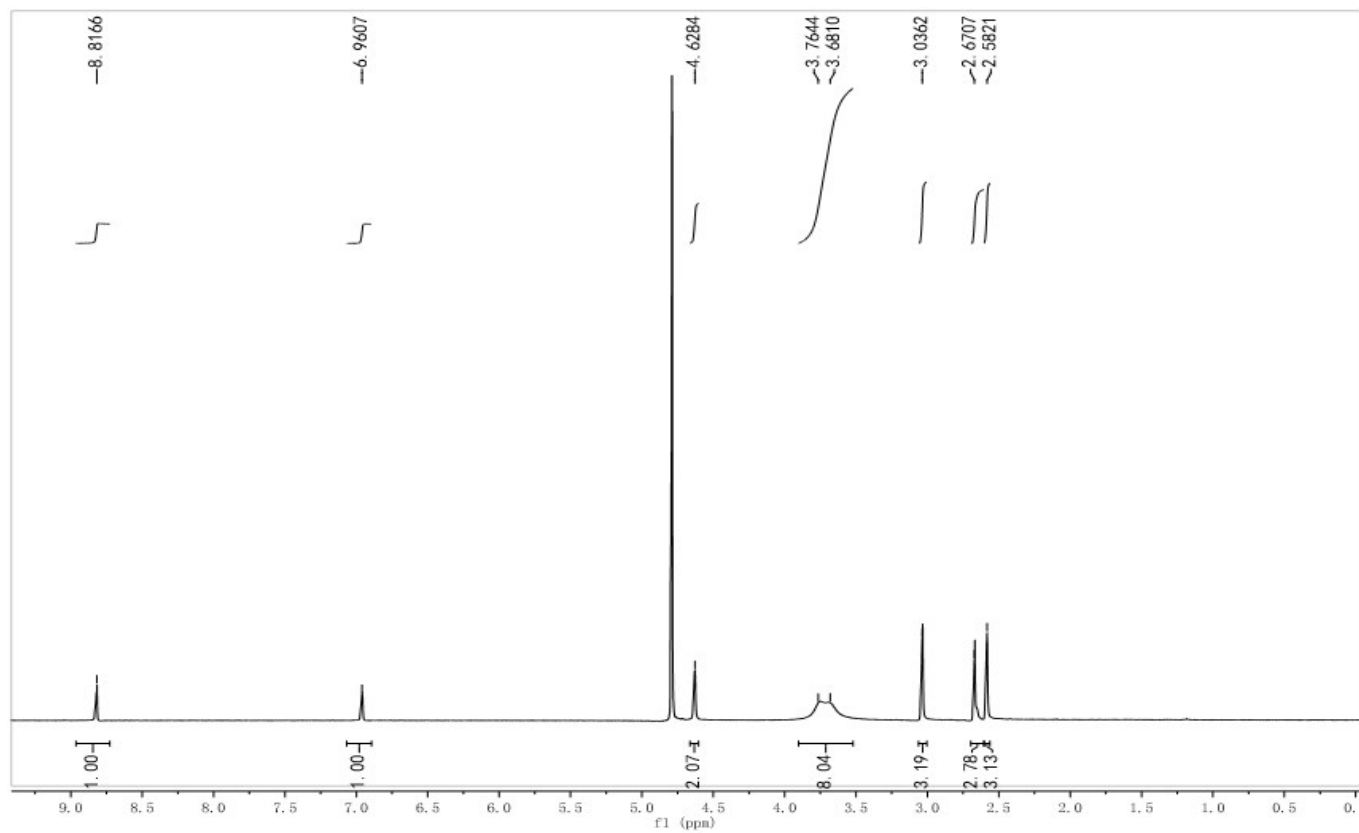
^{13}C -NMR (125 MHz) spectrum of compound **24** in D_2O and CF_3COOD



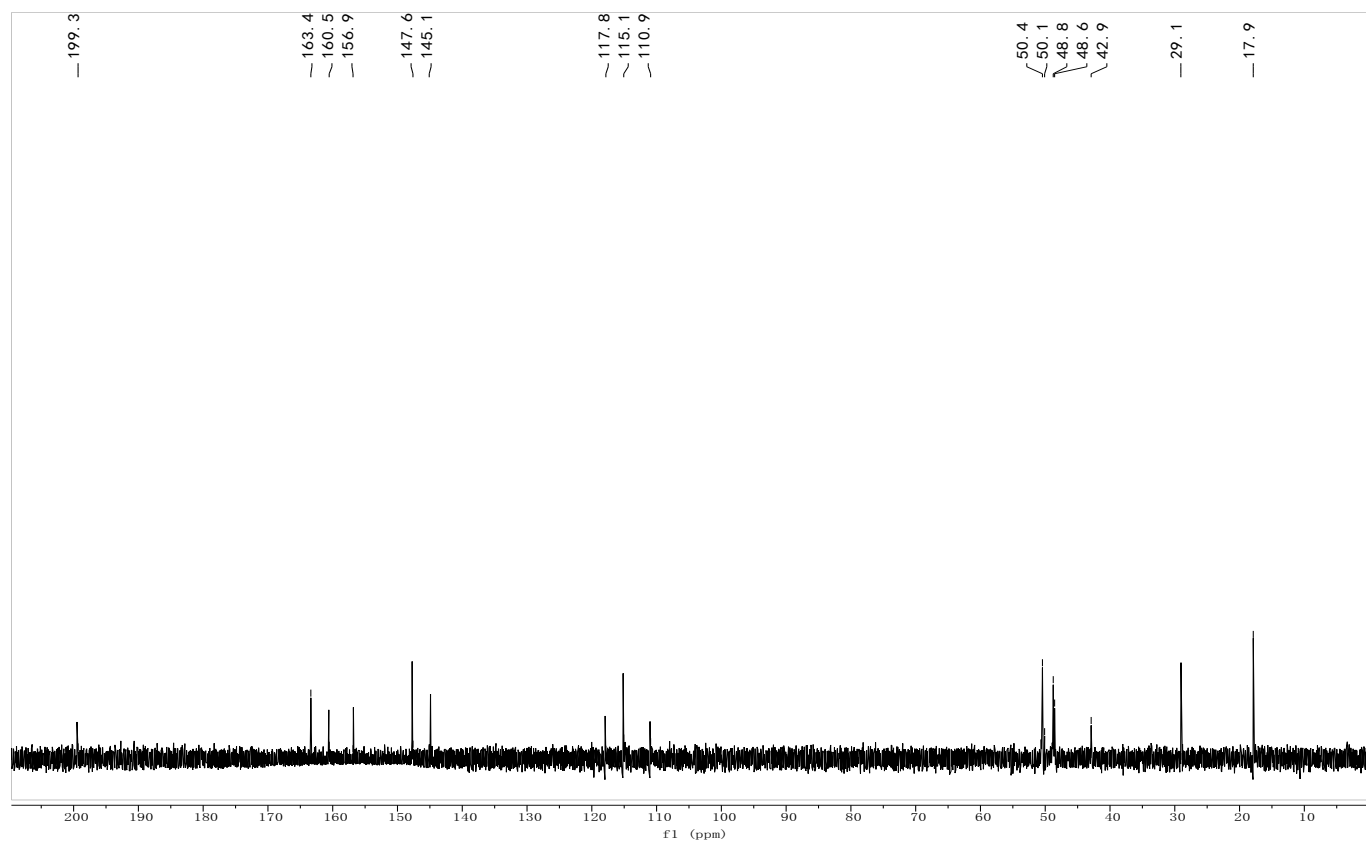
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **25** in $\text{DMSO-}d_6$



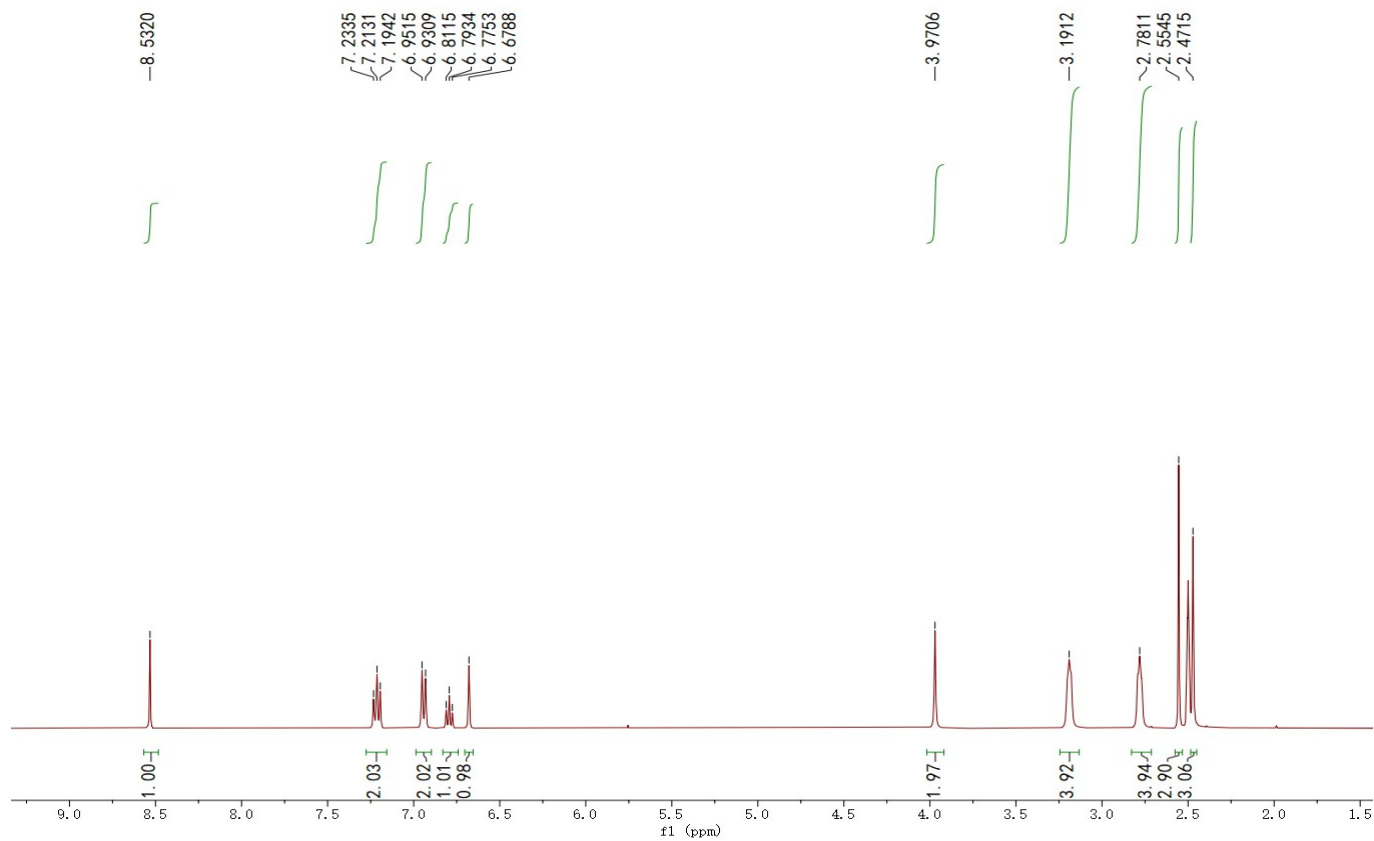
^{13}C -NMR (125 MHz) spectrum of compound **25** in D_2O and CF_3COOD



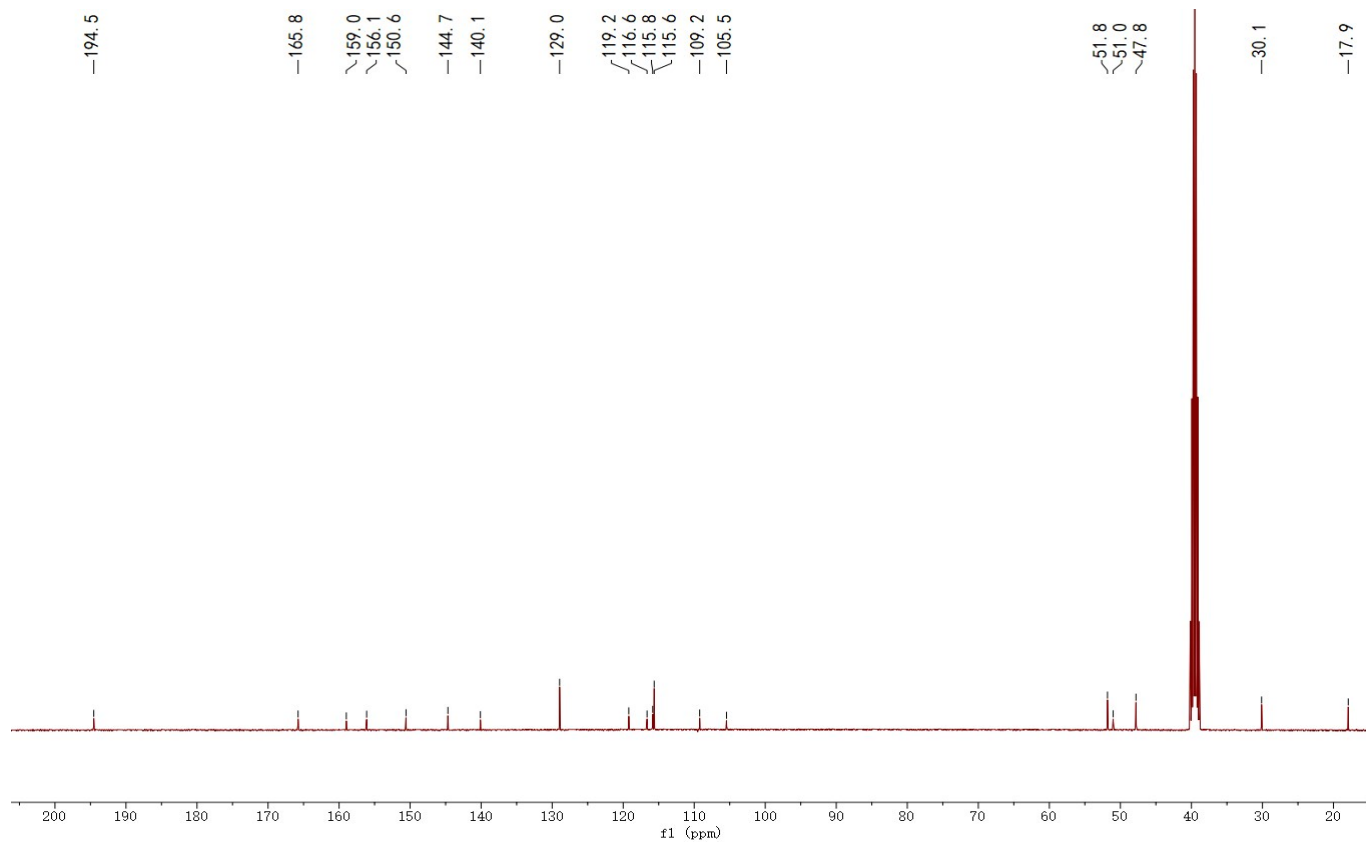
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **26** in D_2O



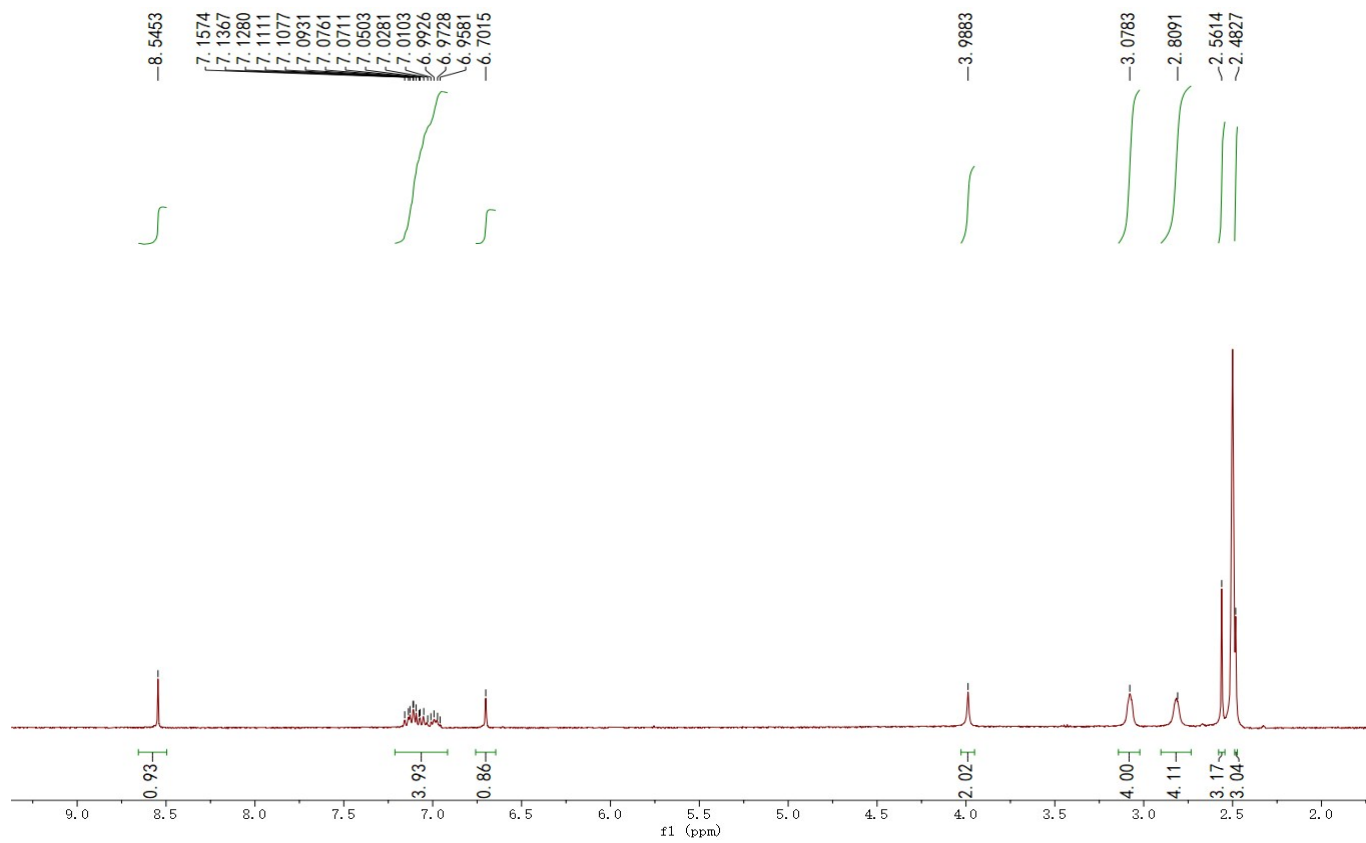
^{13}C -NMR (125 MHz) spectrum of compound **26** in D_2O



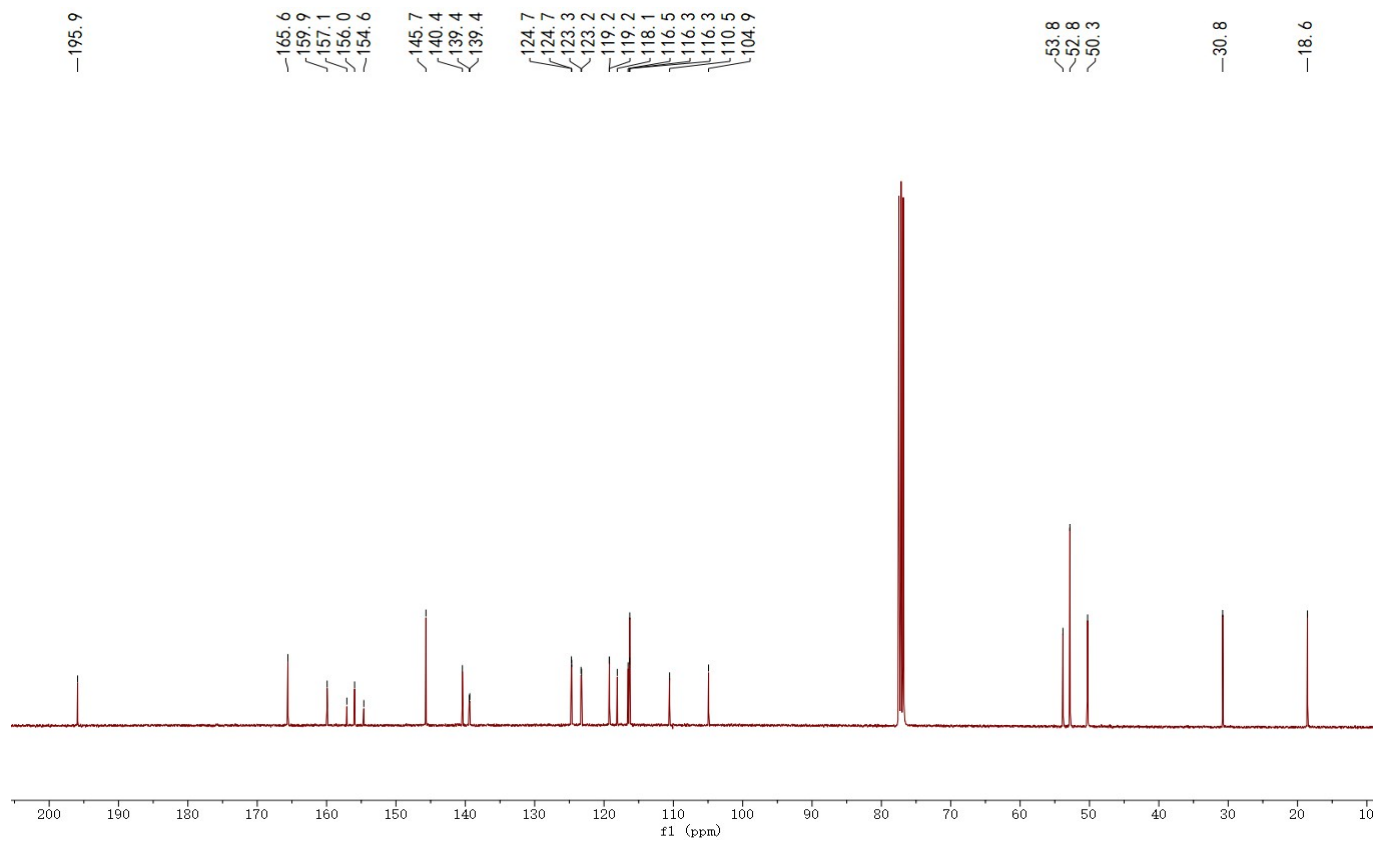
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **27** in $\text{DMSO-}d_6$



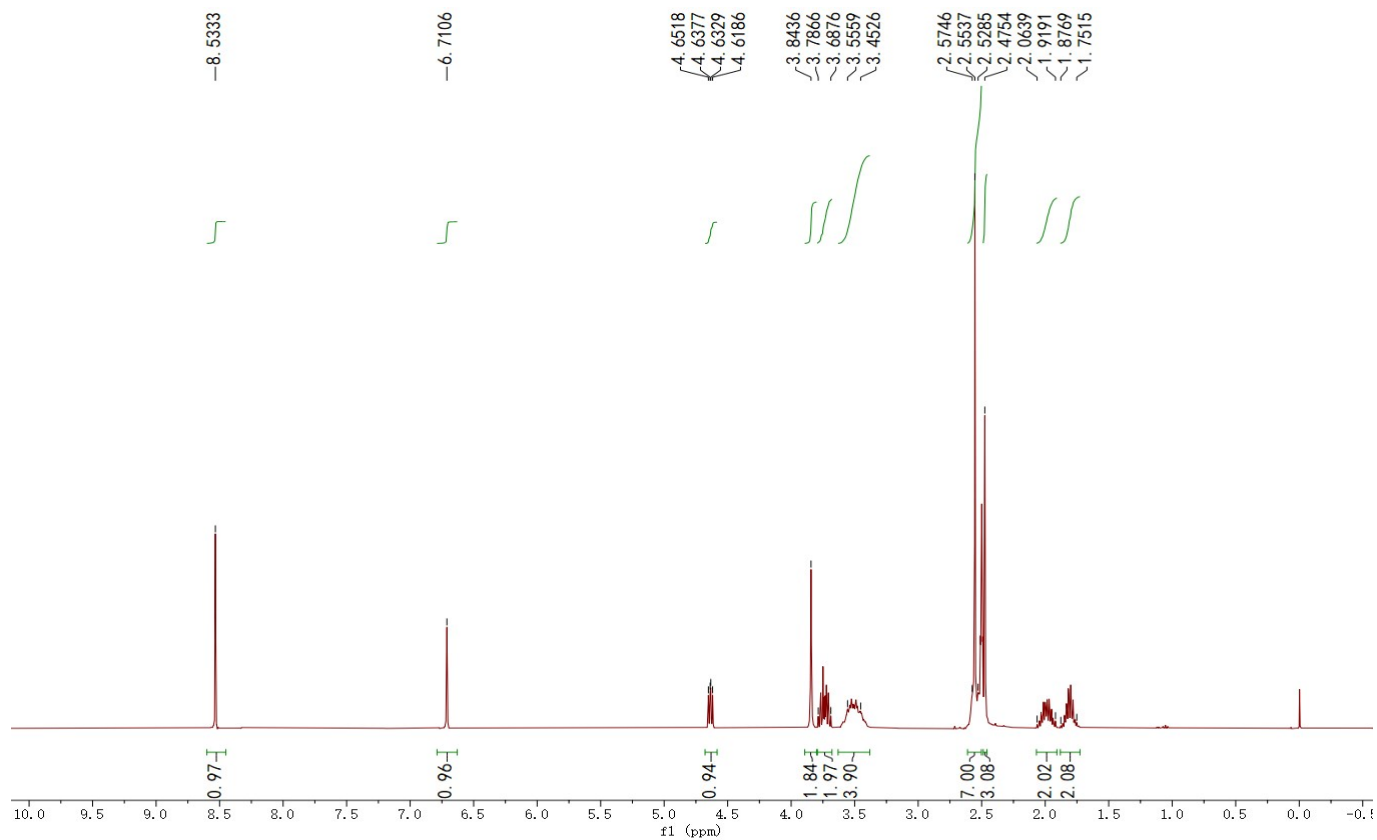
¹³C-NMR (100 MHz) spectrum of compound **27** in DMSO-*d*₆



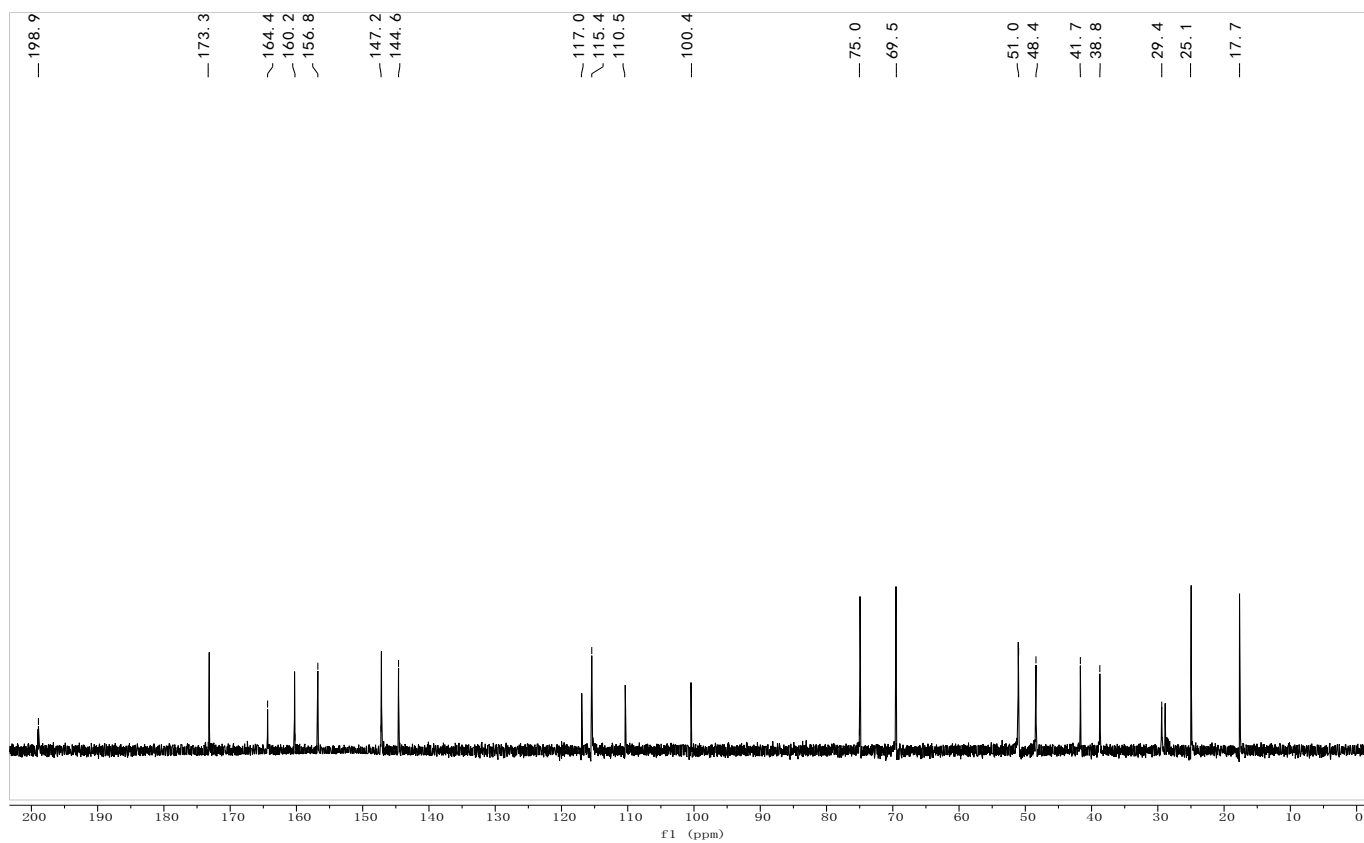
¹H-NMR (400 MHz) spectrum of compound **28** in DMSO-*d*₆



^{13}C -NMR (100 MHz) spectrum of compound **28** in chloroform-*d*



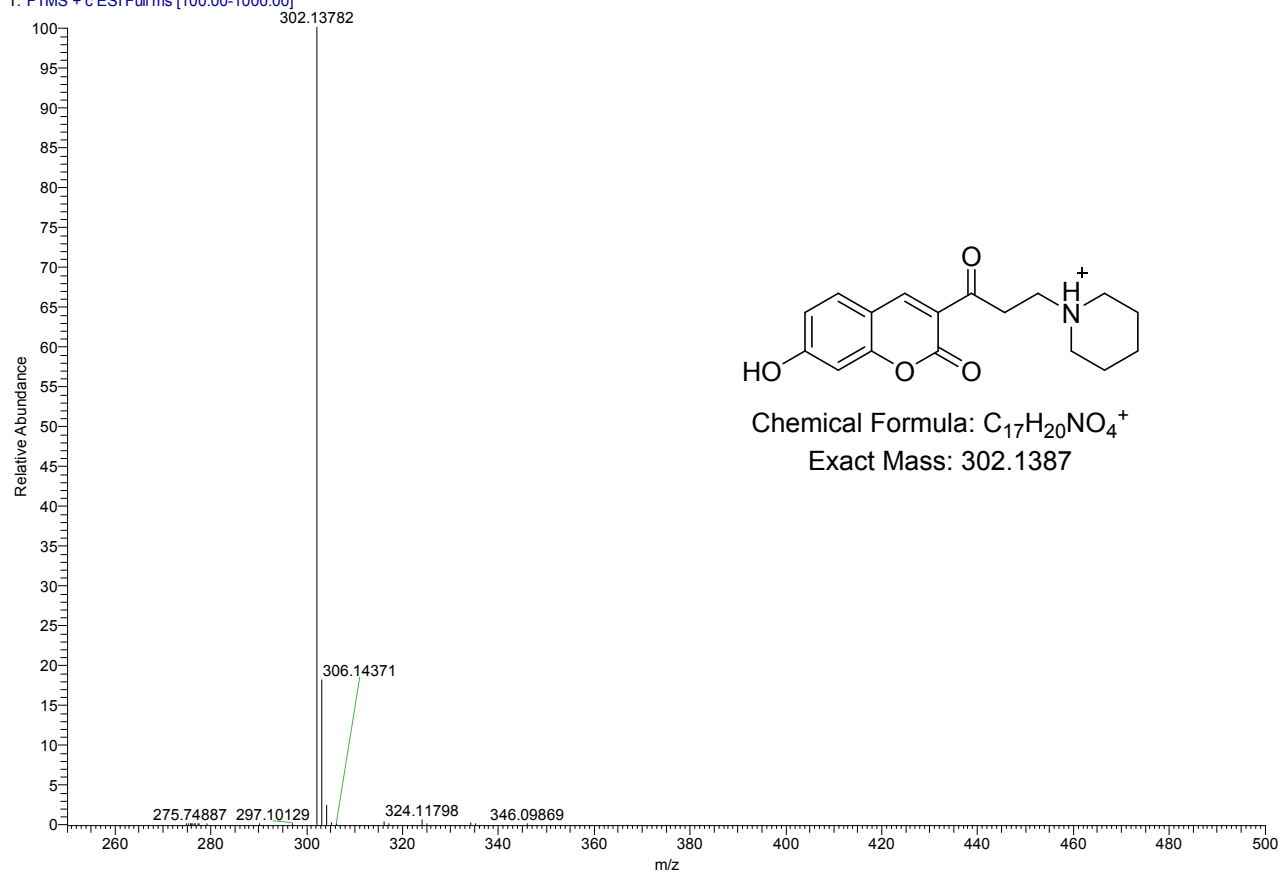
$^1\text{H-NMR}$ (400 MHz) spectrum of compound **29** in $\text{DMSO-}d_6$



^{13}C -NMR (125 MHz) spectrum of compound **29** in D_2O

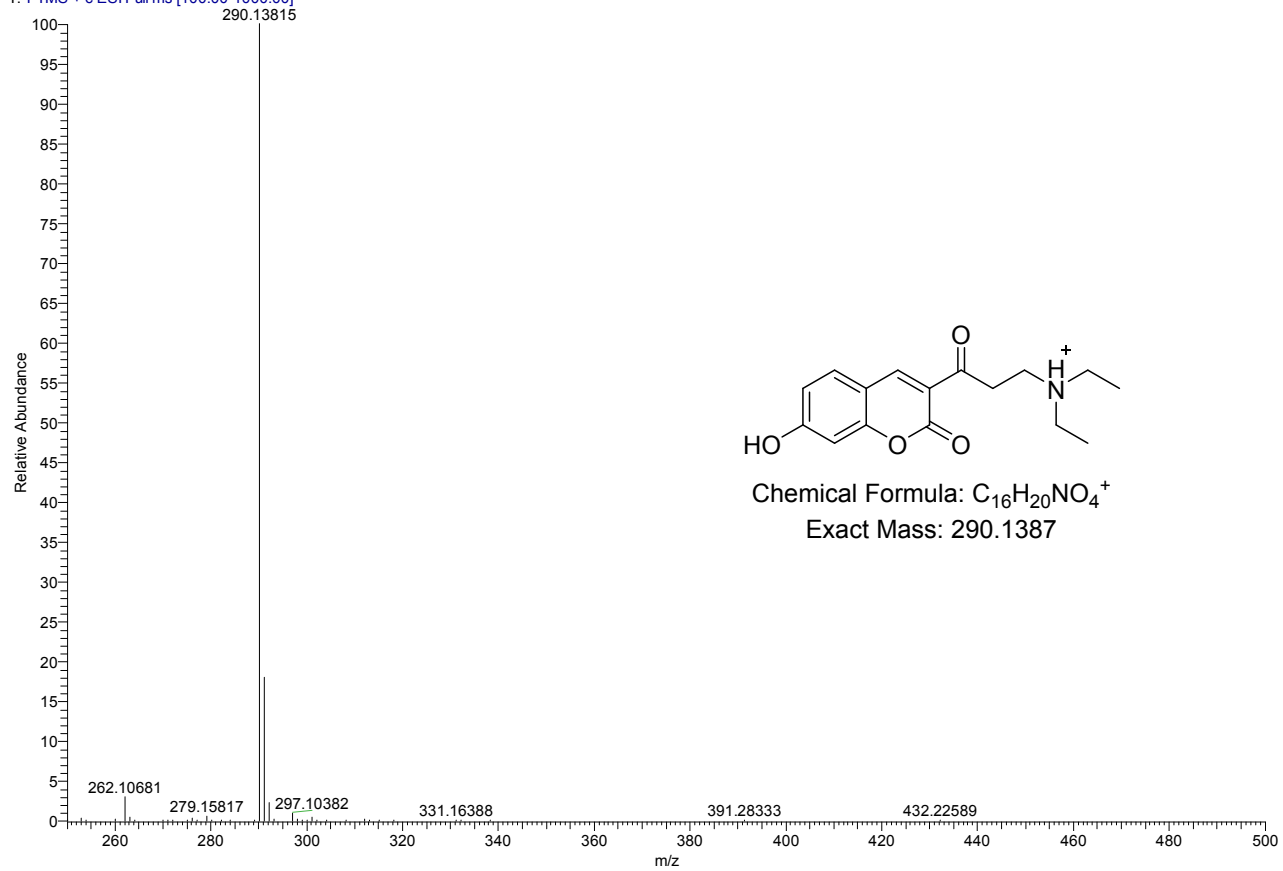
2. ESI-HRMS spectra of compounds 8-29.

8 #691 RT: 2.54 AV: 1 NL: 1.65E8
T: FTMS + c ESI Full ms [100.00-1000.00]



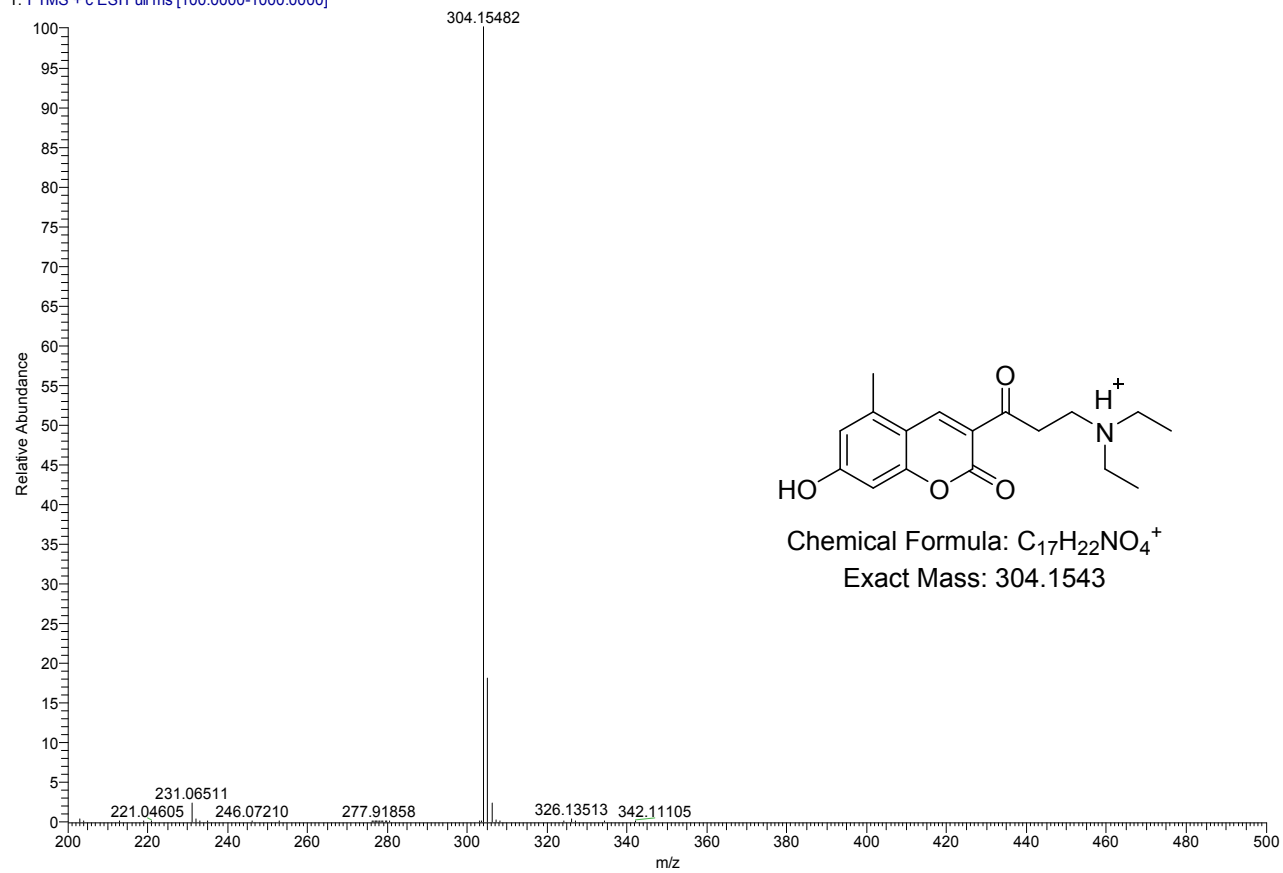
ESI-HRMS spectrum of compound **8**

6 #647 RT: 2.40 AV: 1 NL: 1.36E7
T: FTMS + c ESI Full ms [100.00-1000.00]



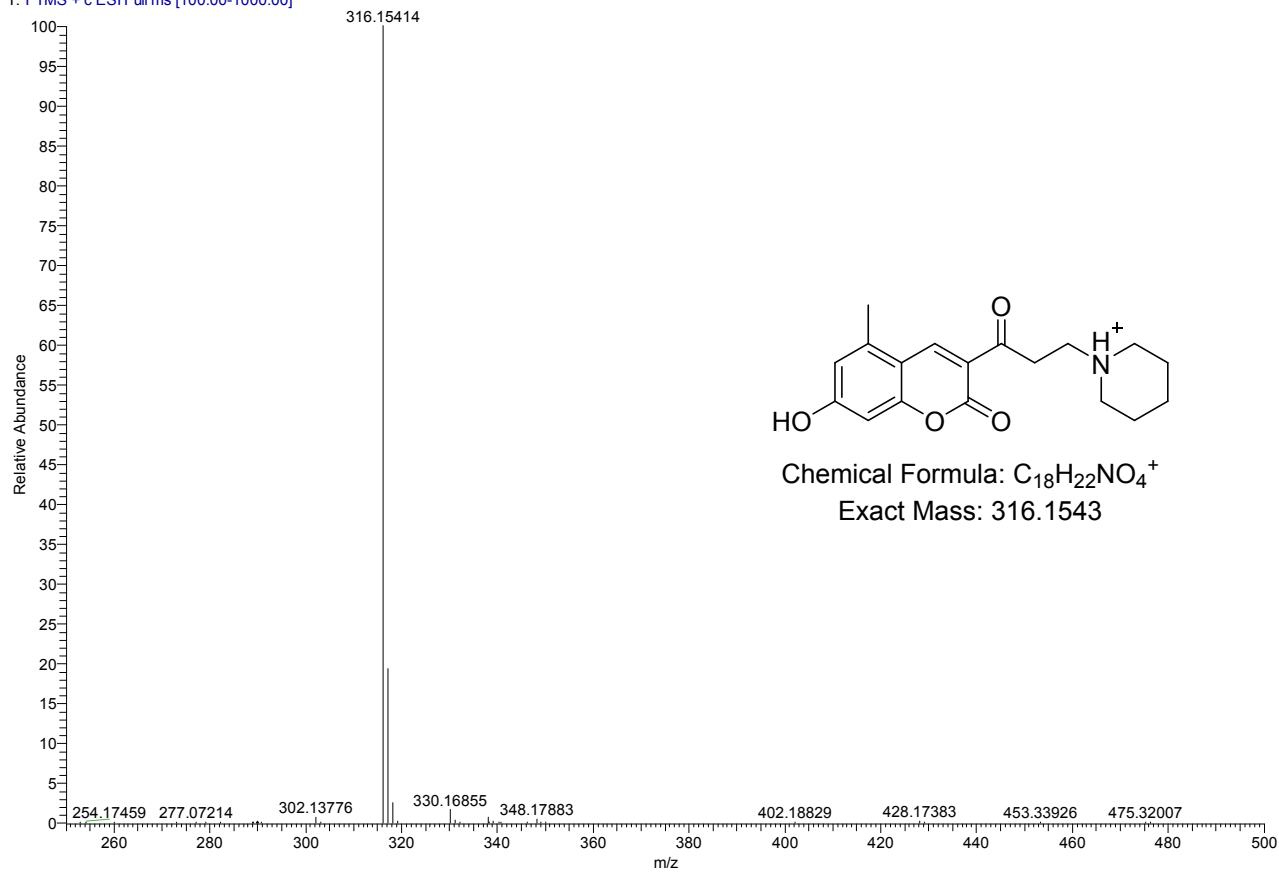
ESI-HRMS spectrum of compound **9**

CMB-A3 #842 RT: 2.59 AV: 1 NL: 2.69E9
T: FTMS + c ESI Full ms [100.0000-1000.0000]



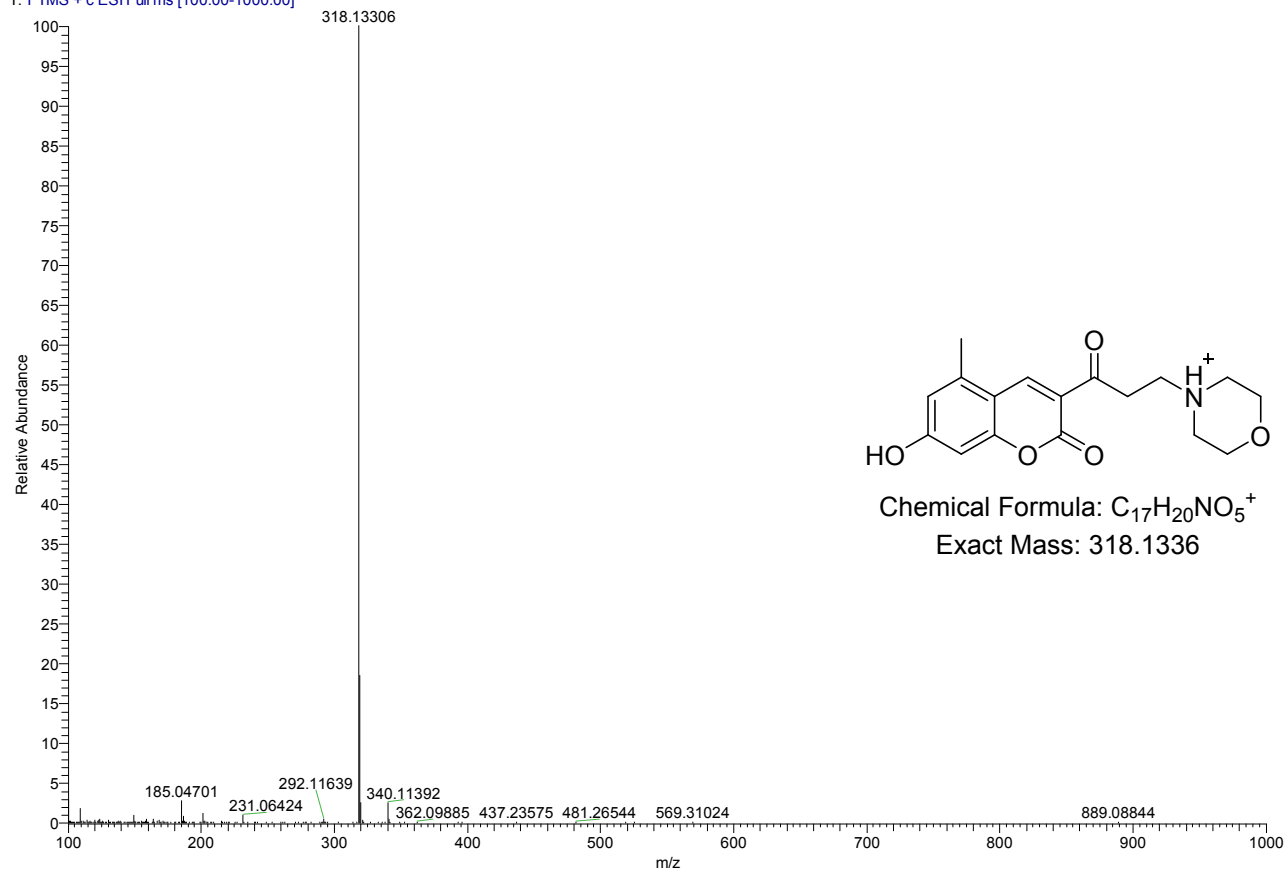
ESI-HRMS spectrum of compound **10**

20 #738 RT: 2.74 AV: 1 NL: 5.57E7
T: FTMS + c ESI Full ms [100.00-1000.00]



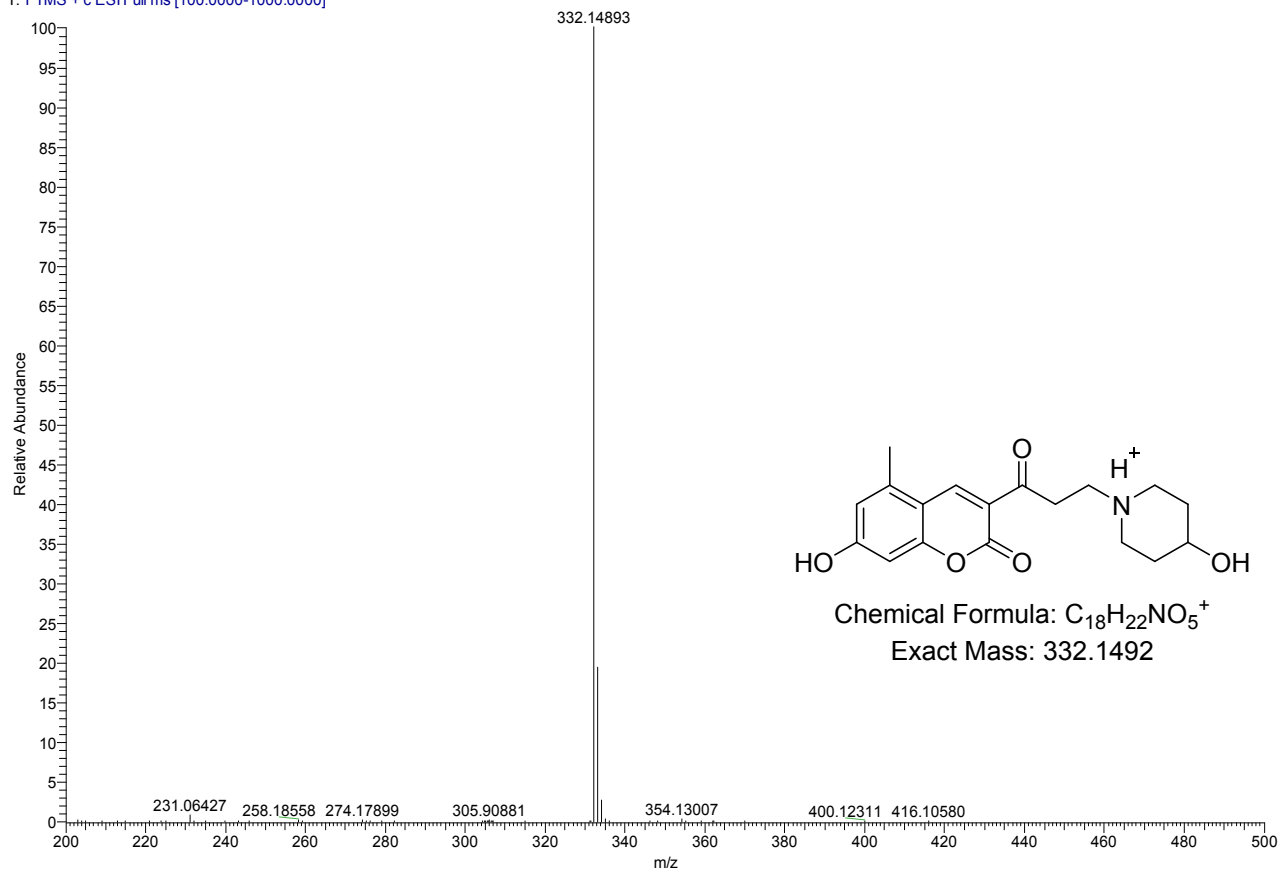
ESI-HRMS spectrum of compound **11**

19 #667 RT: 2.47 AV: 1 NL: 8.67E7
T: FTMS + c ESI Full ms [100.00-1000.00]



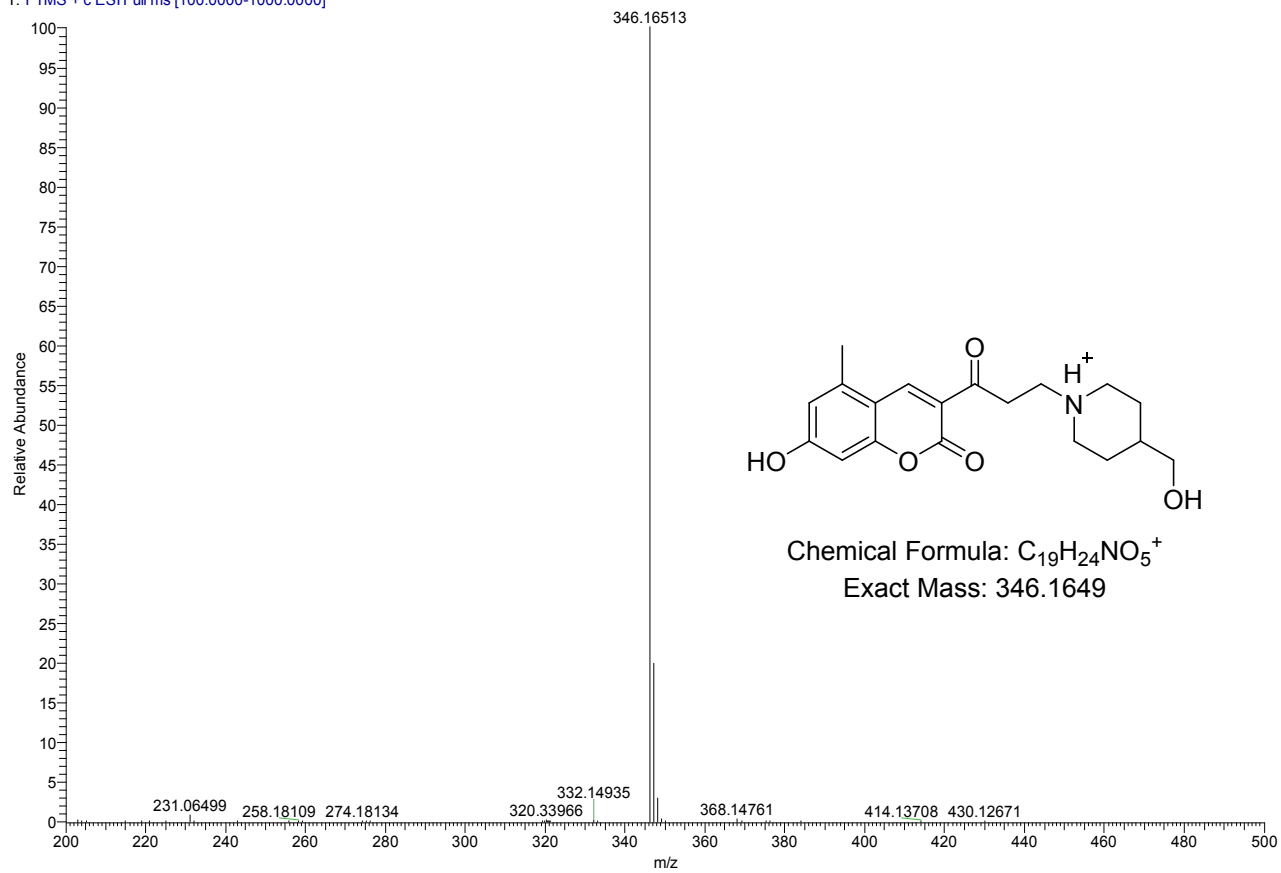
ESI-HRMS spectrum of compound 12

CMB-A20 #791 RT: 2.45 AV: 1 NL: 1.17E9
T: FTMS + c ESIFull ms [100.0000-1000.0000]



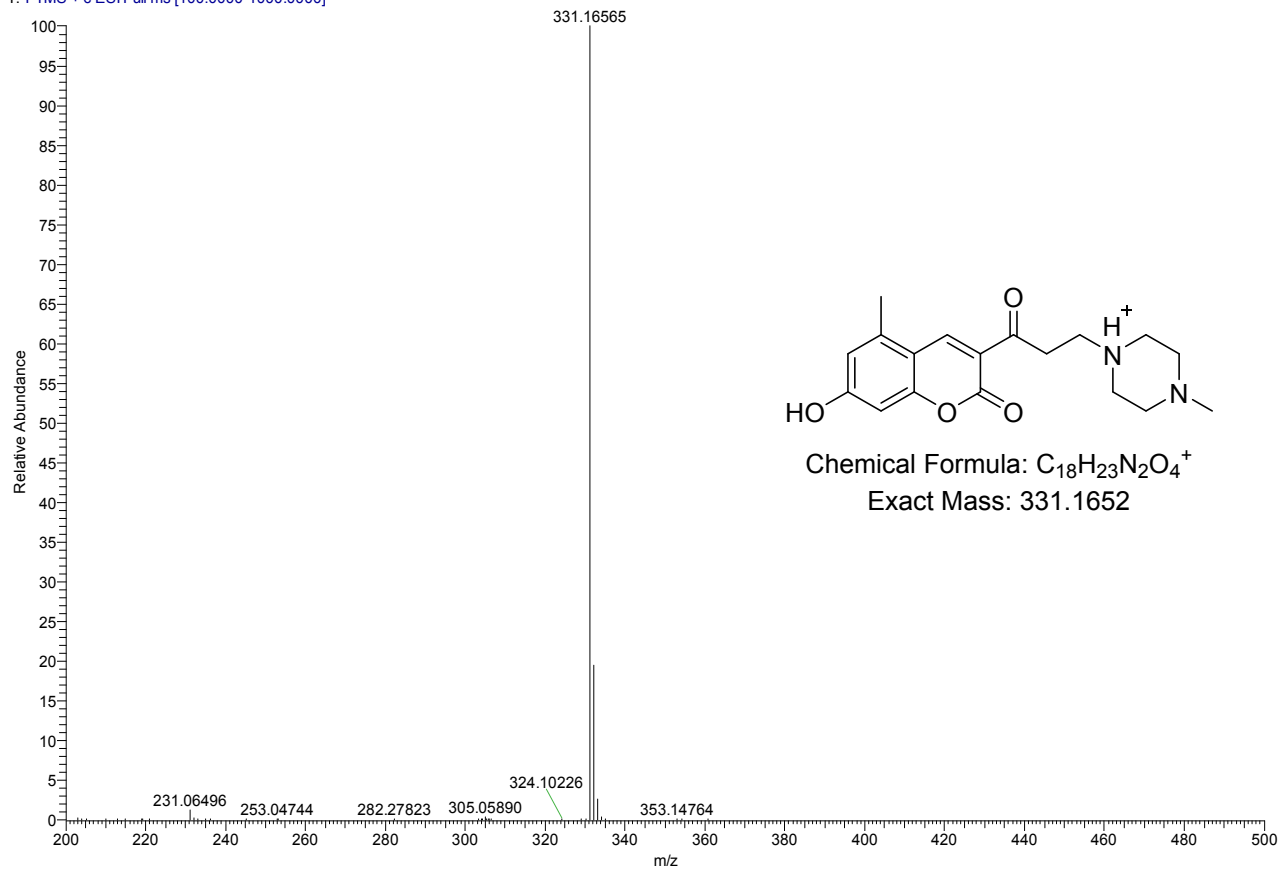
ESI-HRMS spectrum of compound **13**

CMB-A21 #842 RT: 2.53 AV: 1 NL: 1.50E9
T: FTMS + c ESI Full ms [100.0000-1000.0000]



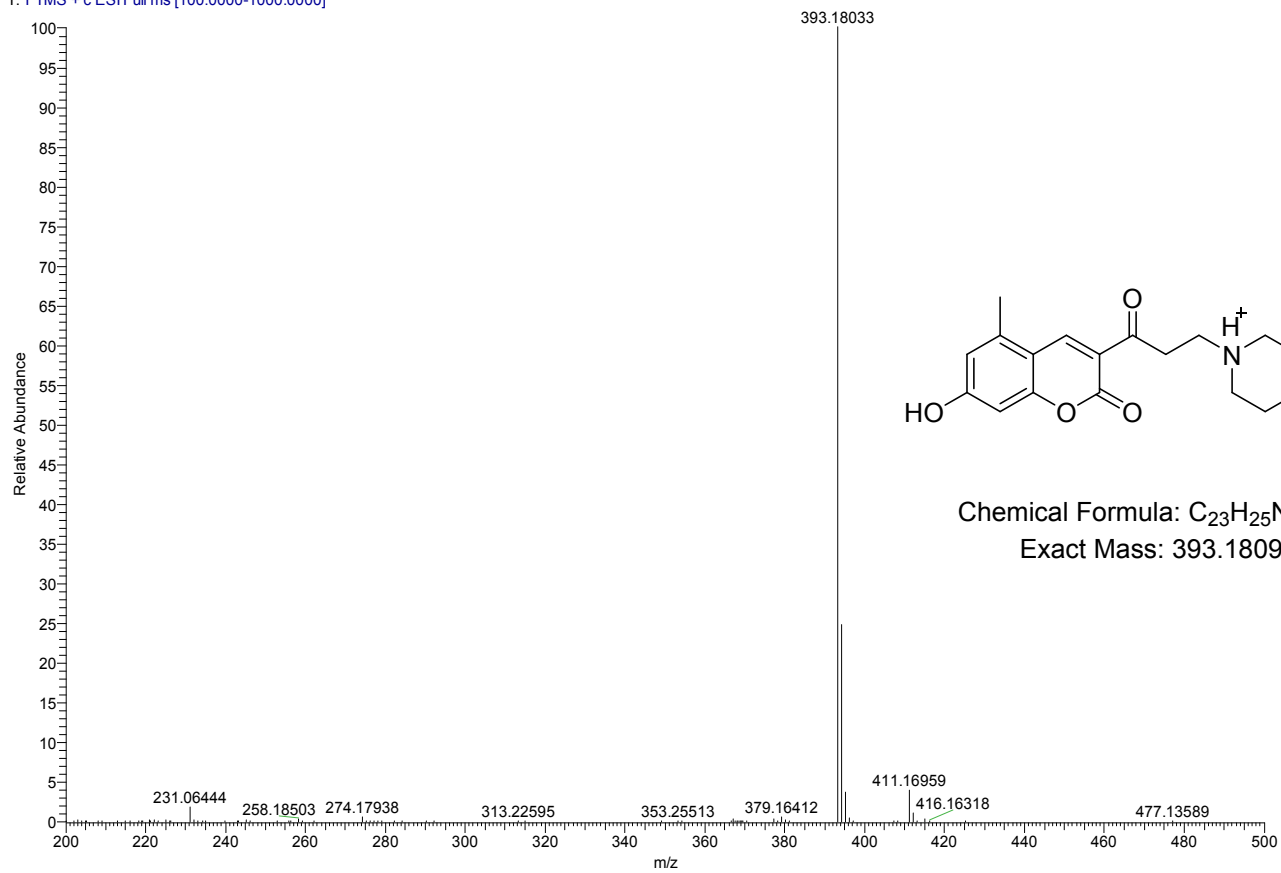
ESI-HRMS spectrum of compound **14**

CMB-A6 #787 RT: 2.34 AV: 1 NL: 1.51E9
T: FTMS + c ESIFull ms [100.0000-1000.0000]



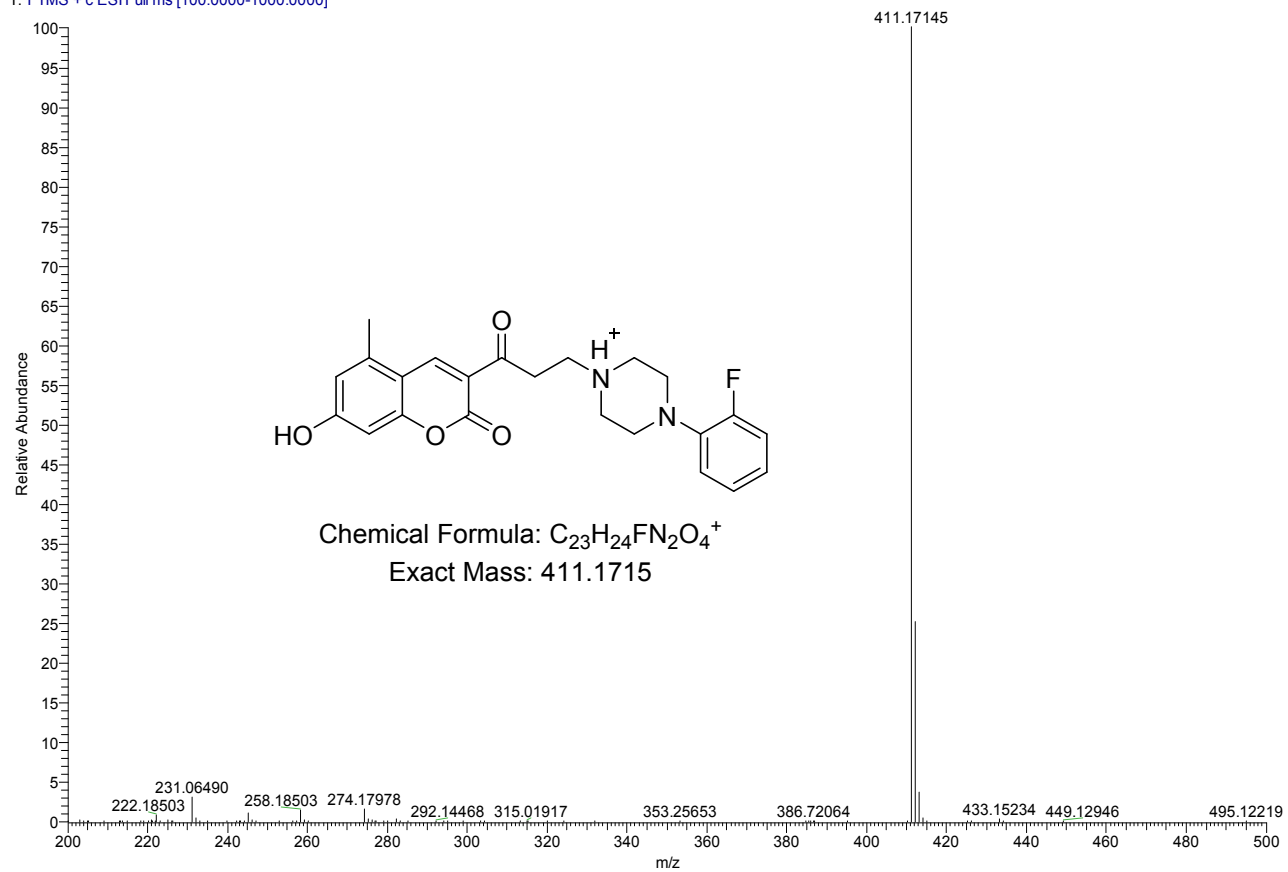
ESI-HRMS spectrum of compound **15**

CMB-A15 #1098 RT: 3.20 AV: 1 NL: 6.83E8
T: FTMS + c ESI Full ms [100.0000-1000.0000]



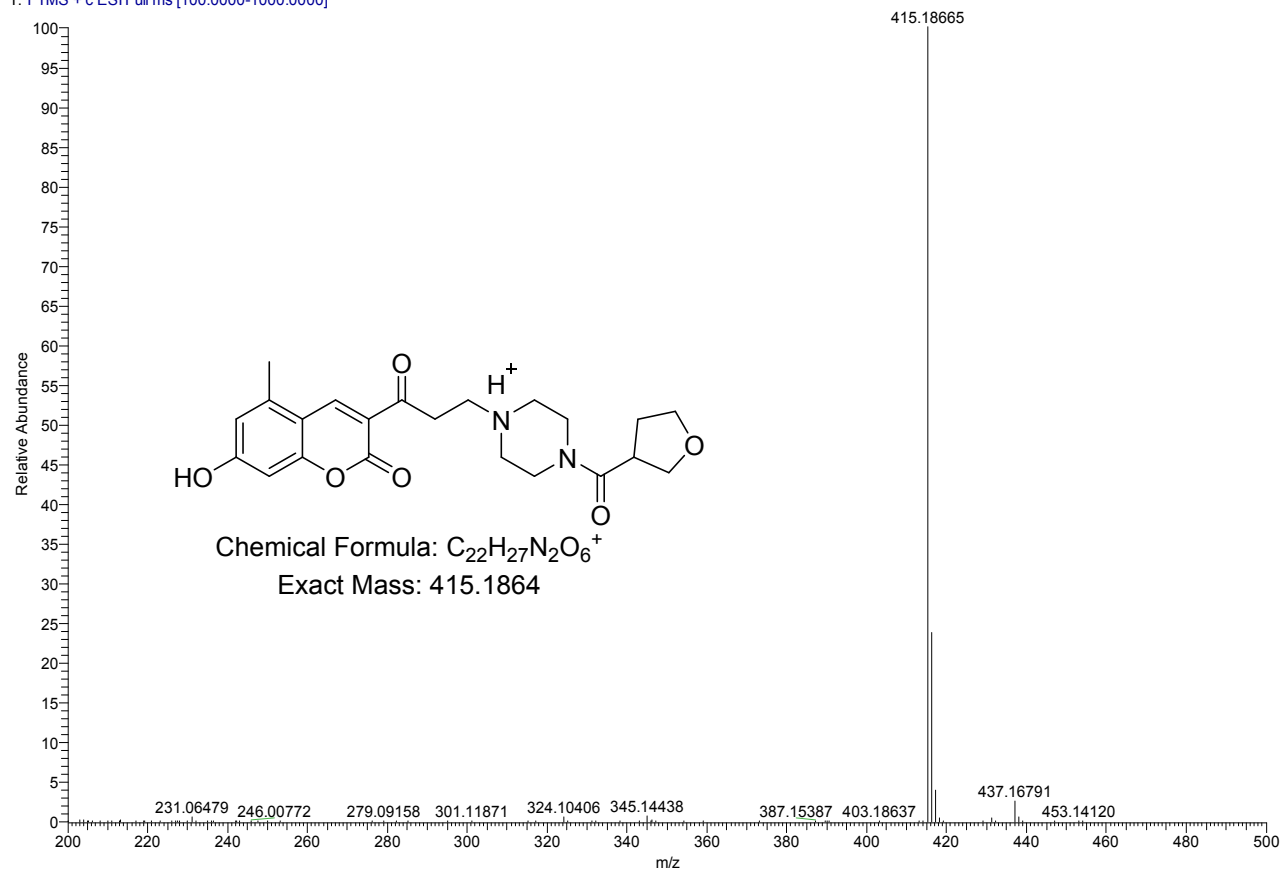
ESI-HRMS spectrum of compound **16**

CMB-A10-2 #1224 RT: 3.27 AV: 1 NL: 6.76E8
T: FTMS + c ESI Full ms [100.0000-1000.0000]



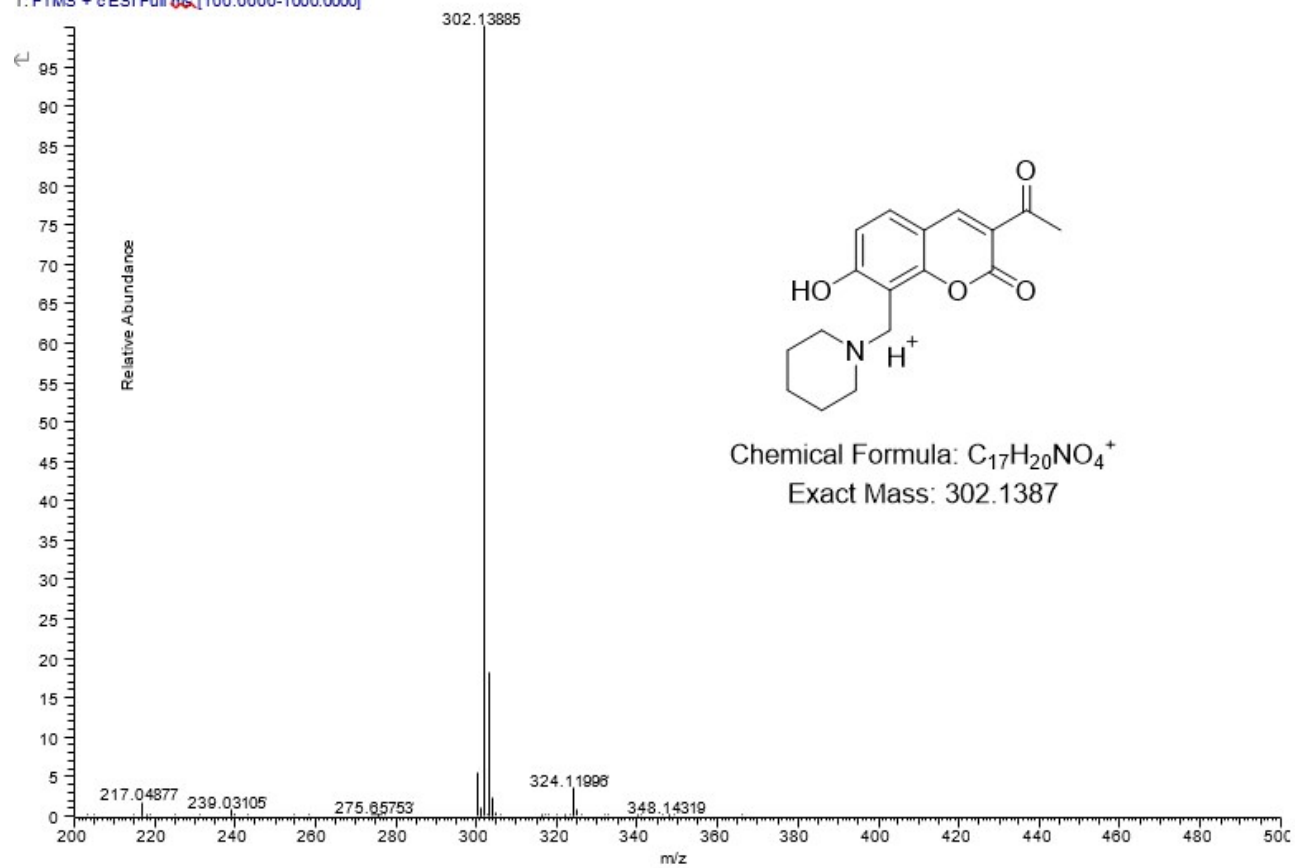
ESI-HRMS spectrum of compound **17**

CMB-A13_190328211107 #843 RT: 2.44 AV: 1 NL: 5.13E8
T: FTMS + c ESI Full ms [100.0000-1000.0000]



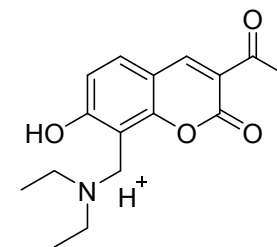
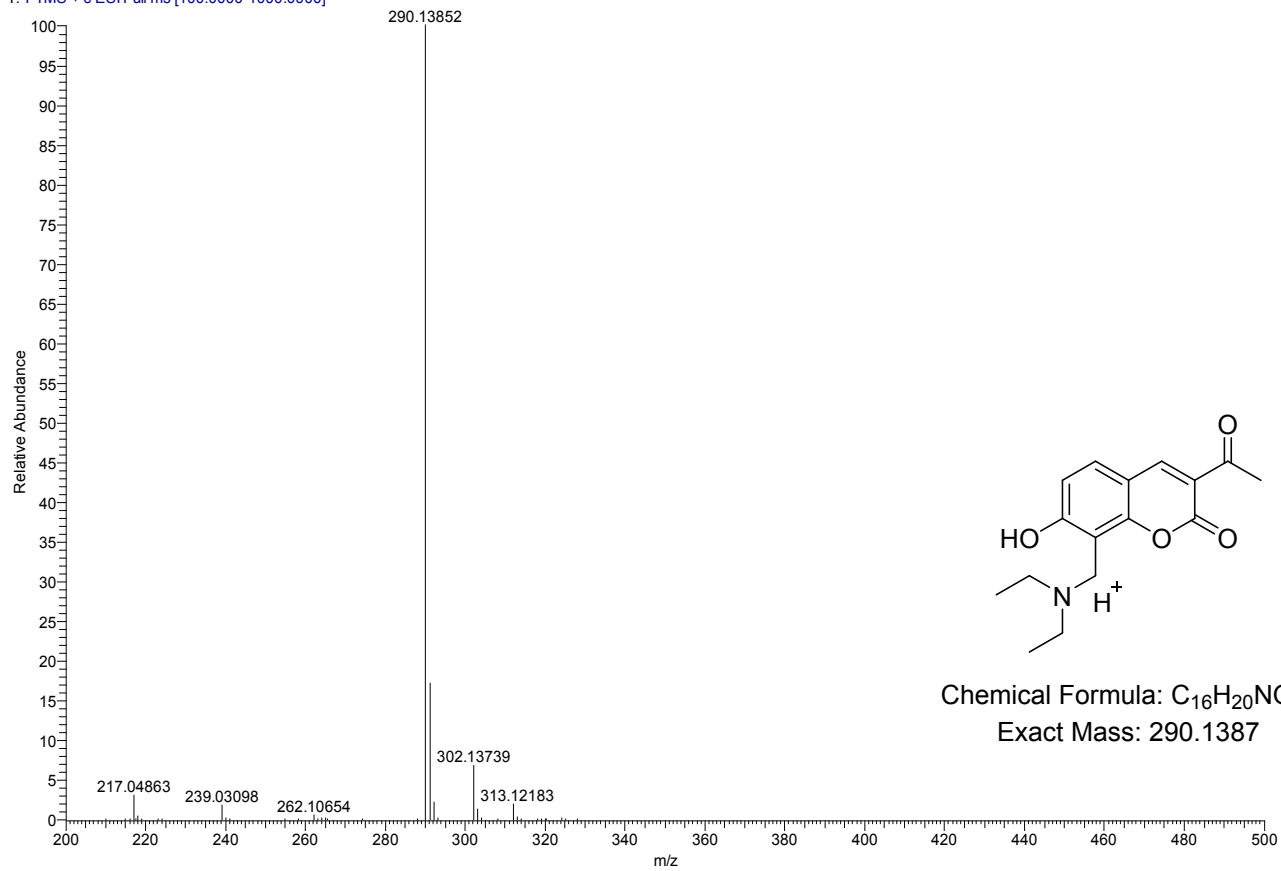
ESI-HRMS spectrum of compound **18**

QMB-C8-15_19032917401#834 RT: 2.56 AV: 1 NL: 1.86E9
T: FTMS + cESI Full ps.[100.0000-1000.0000]



ESI-HRMS spectrum of compound **19**

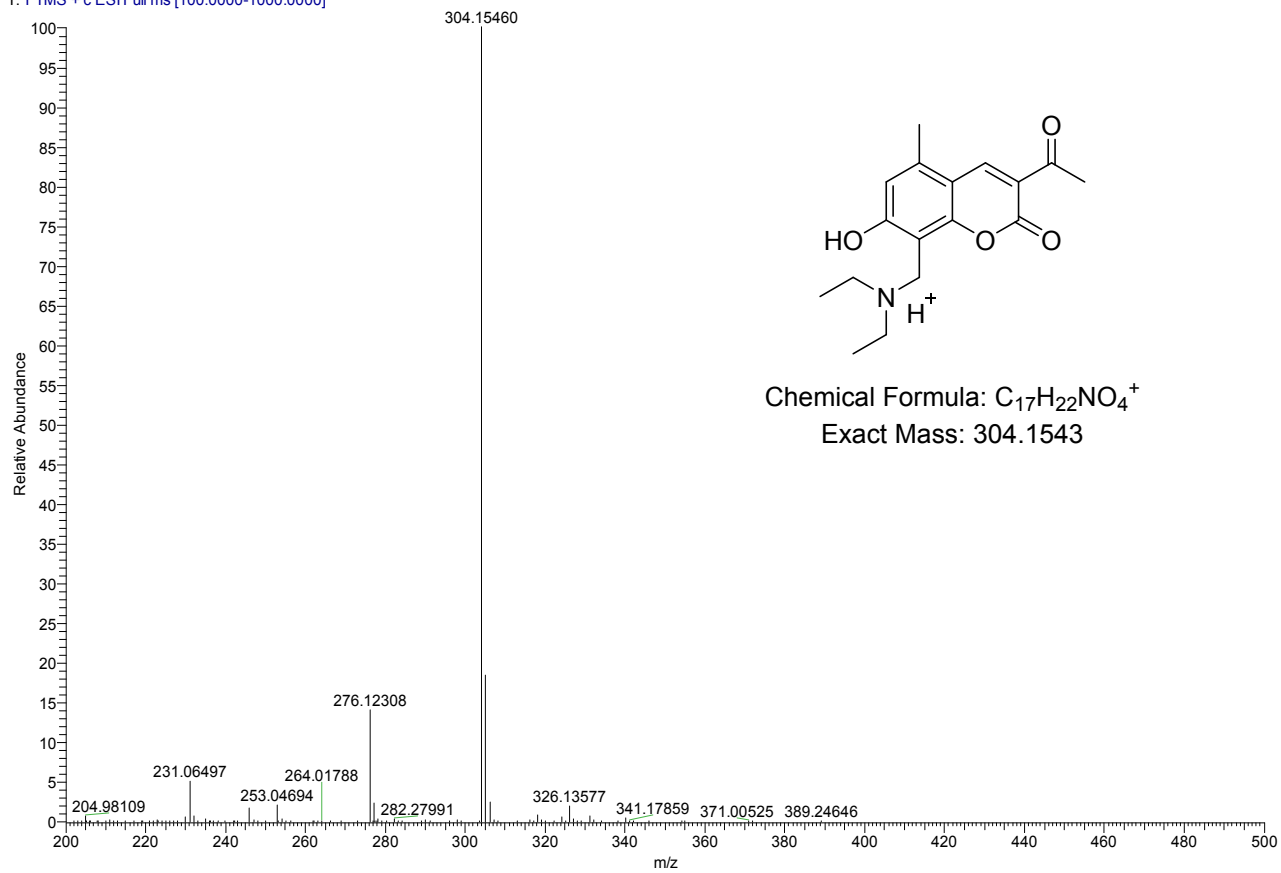
CMB-C8-16_190329174847 #765 RT: 2.41 AV: 1 NL: 2.39E9
T: FTMS + c ESI Full ms [100.0000-1000.0000]



Chemical Formula: $C_{16}H_{20}NO_4^+$
Exact Mass: 290.1387

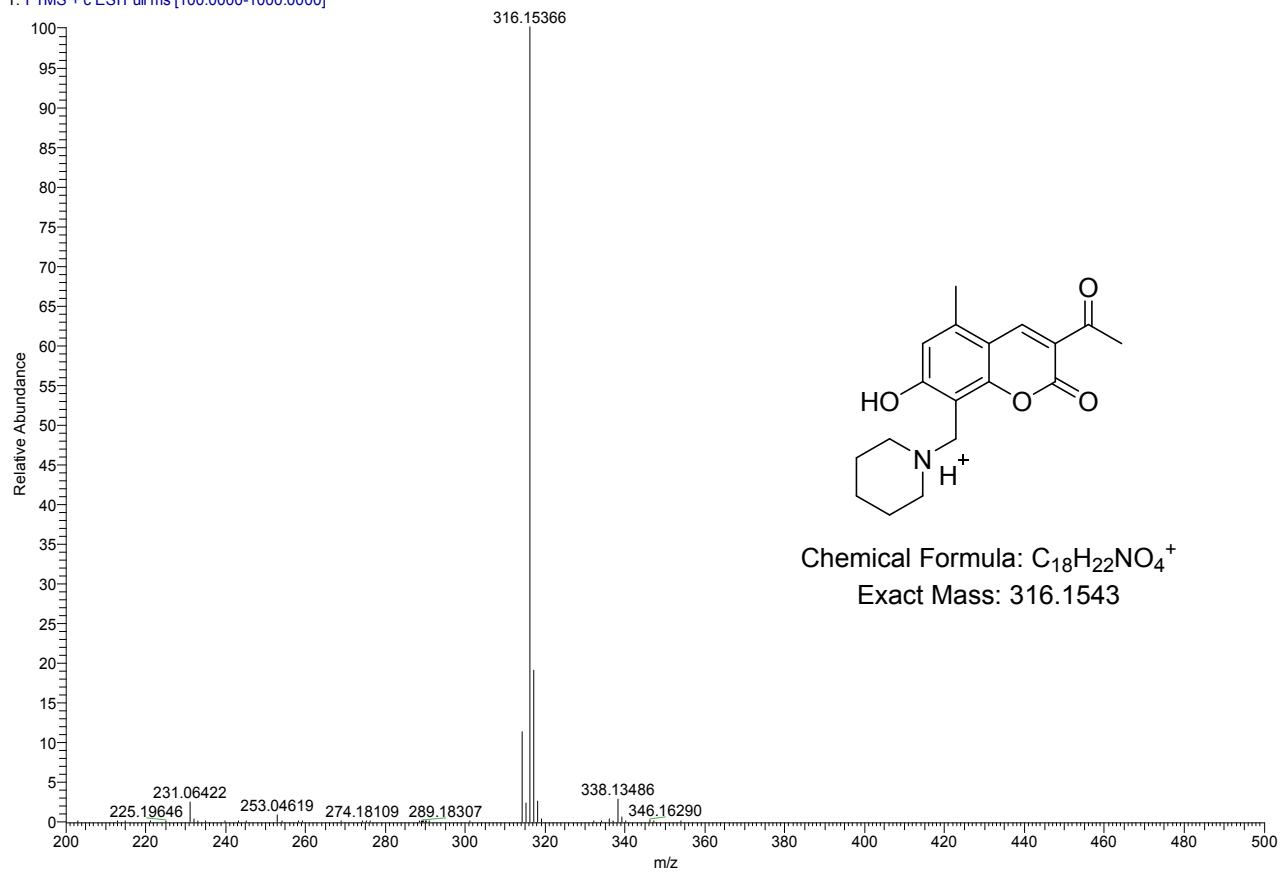
ESI-HRMS spectrum of compound 20

CMB-C8-9_190328213646 #804 RT: 2.45 AV: 1 NL: 3.94E8
T: FTMS + c ESI Full ms [100.0000-1000.0000]



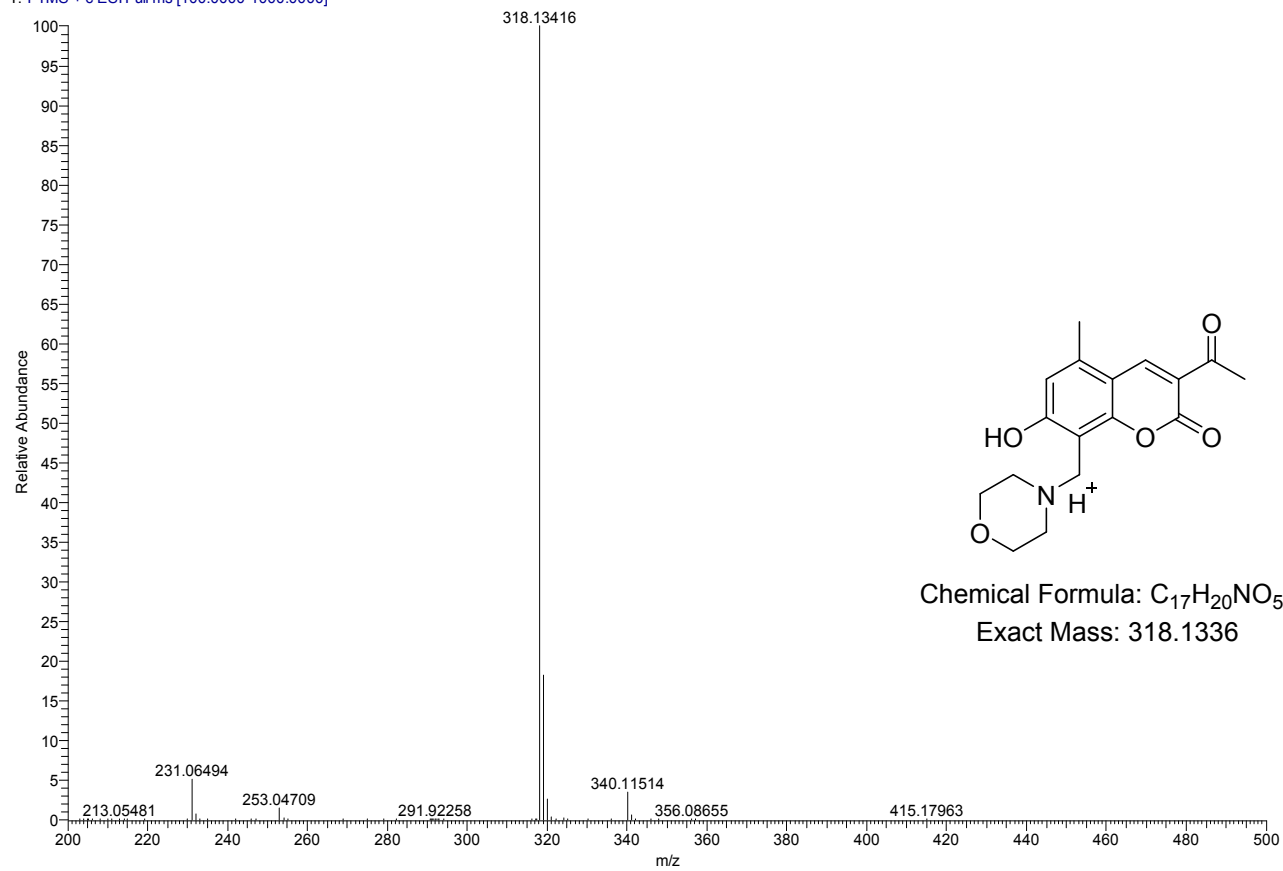
ESI-HRMS spectrum of compound **21**

CMB-C8-2_190329173142 #863 RT: 2.65 AV: 1 NL: 1.27E9
T: FTMS + c ESI Full ms [100.0000-1000.0000]



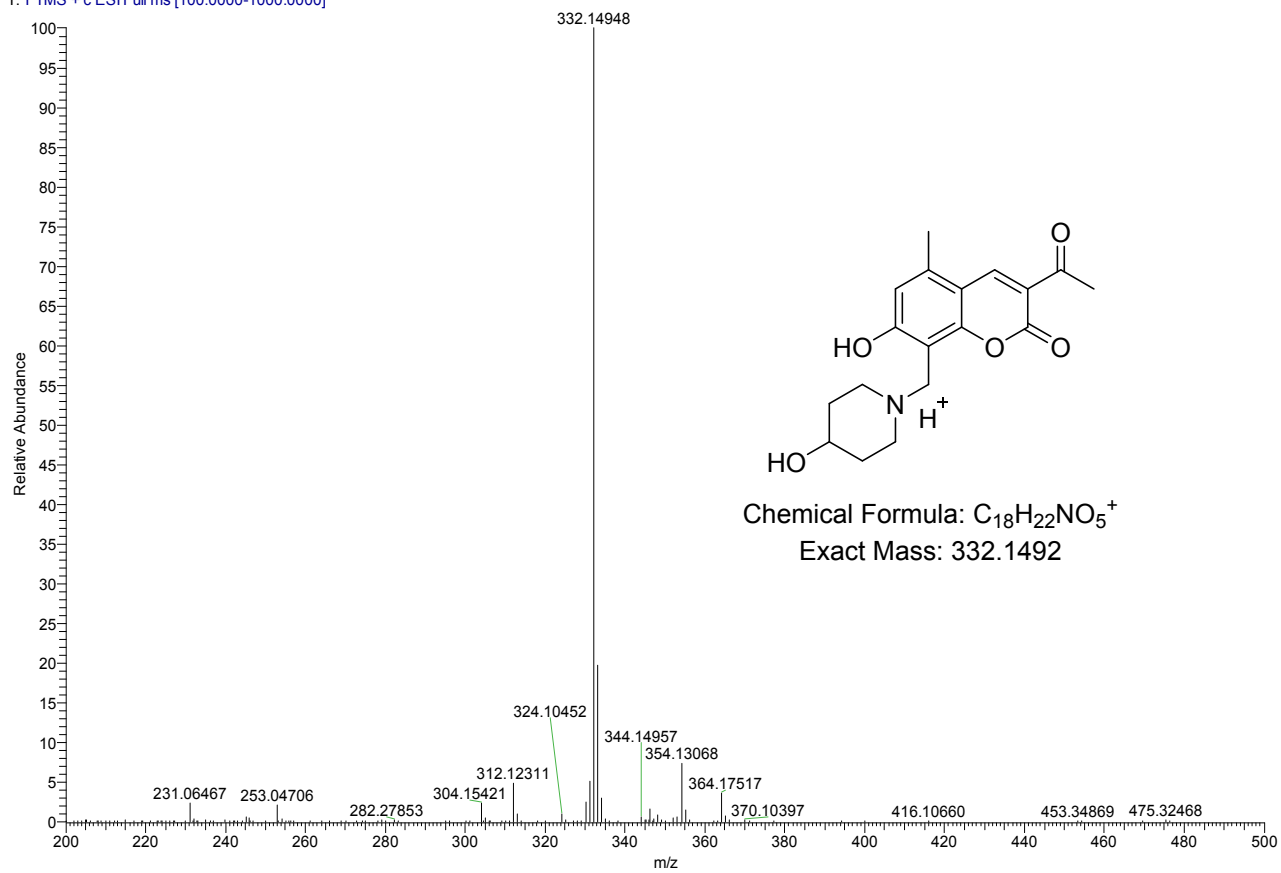
ESI-HRMS spectrum of compound **22**

CMB-C8-1_190328211942 #861 RT: 2.50 AV: 1 NL: 1.74E9
T: FTMS + c ESI Full ms [100.0000-1000.0000]



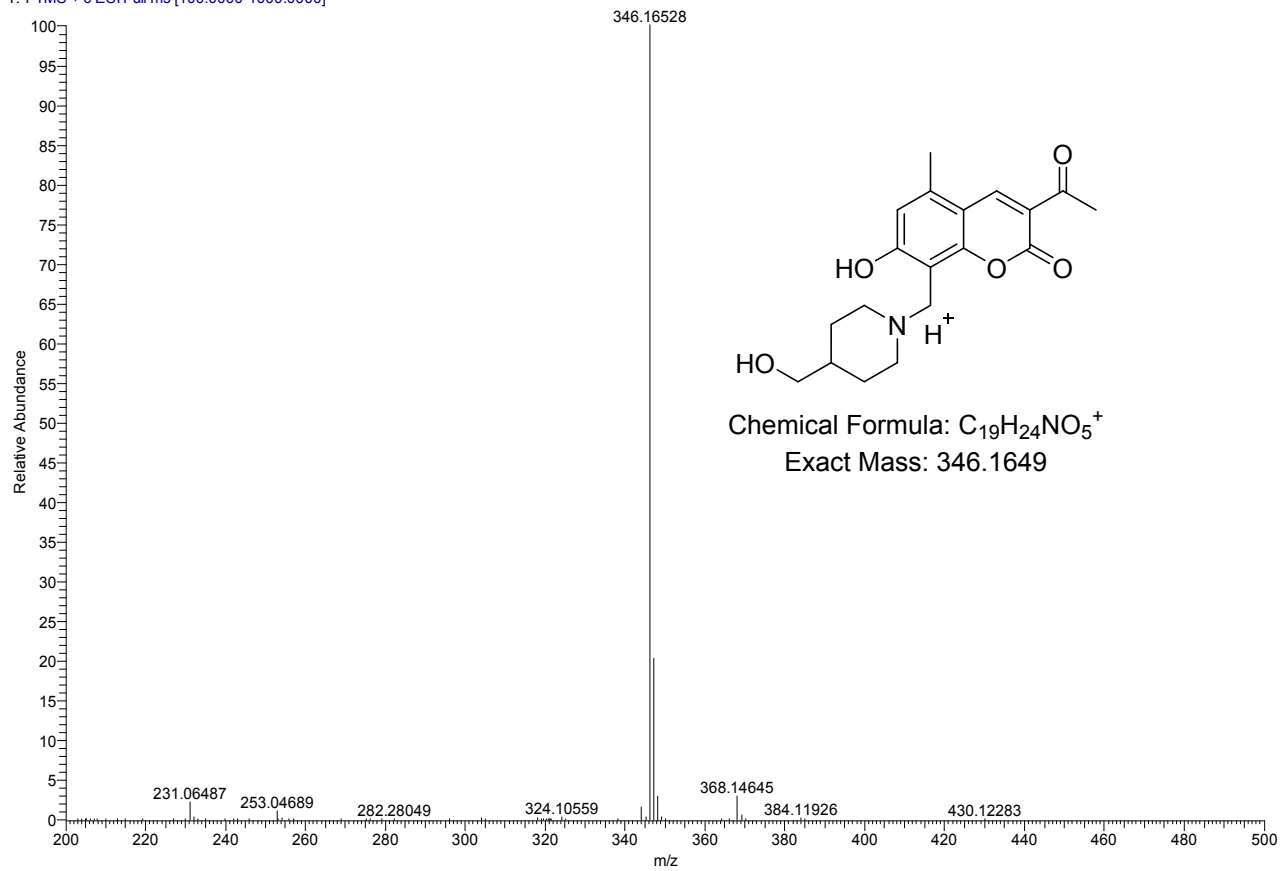
ESI-HRMS spectrum of compound **23**

CMB-C8-6_190328222805 #845 RT: 2.57 AV: 1 NL: 2.11E8
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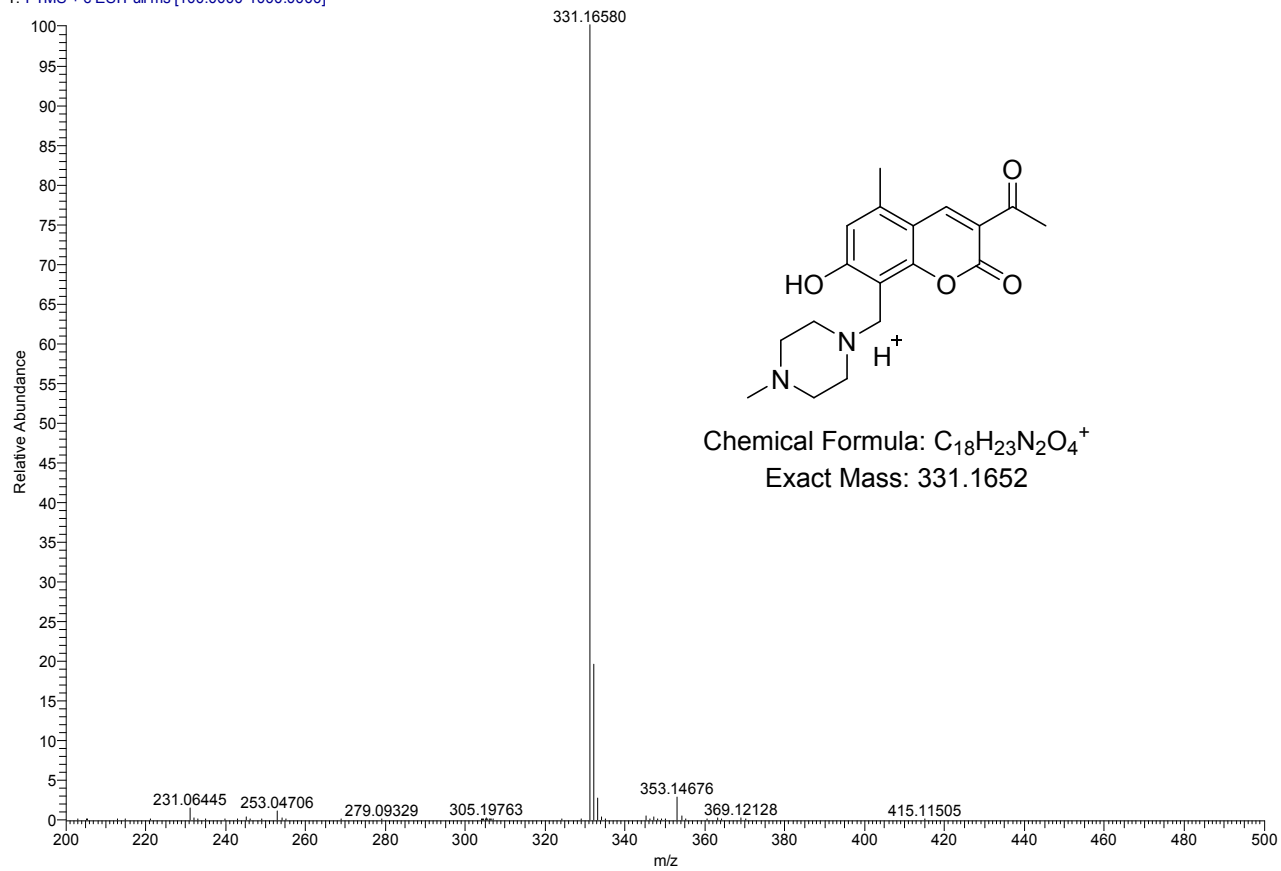
ESI-HRMS spectrum of compound 24

CMB-C8-4_190328214519 #804 RT: 2.46 AV: 1 NL: 8.37E8
T: FTMS + c ESI Full ms [100.0000-1000.0000]



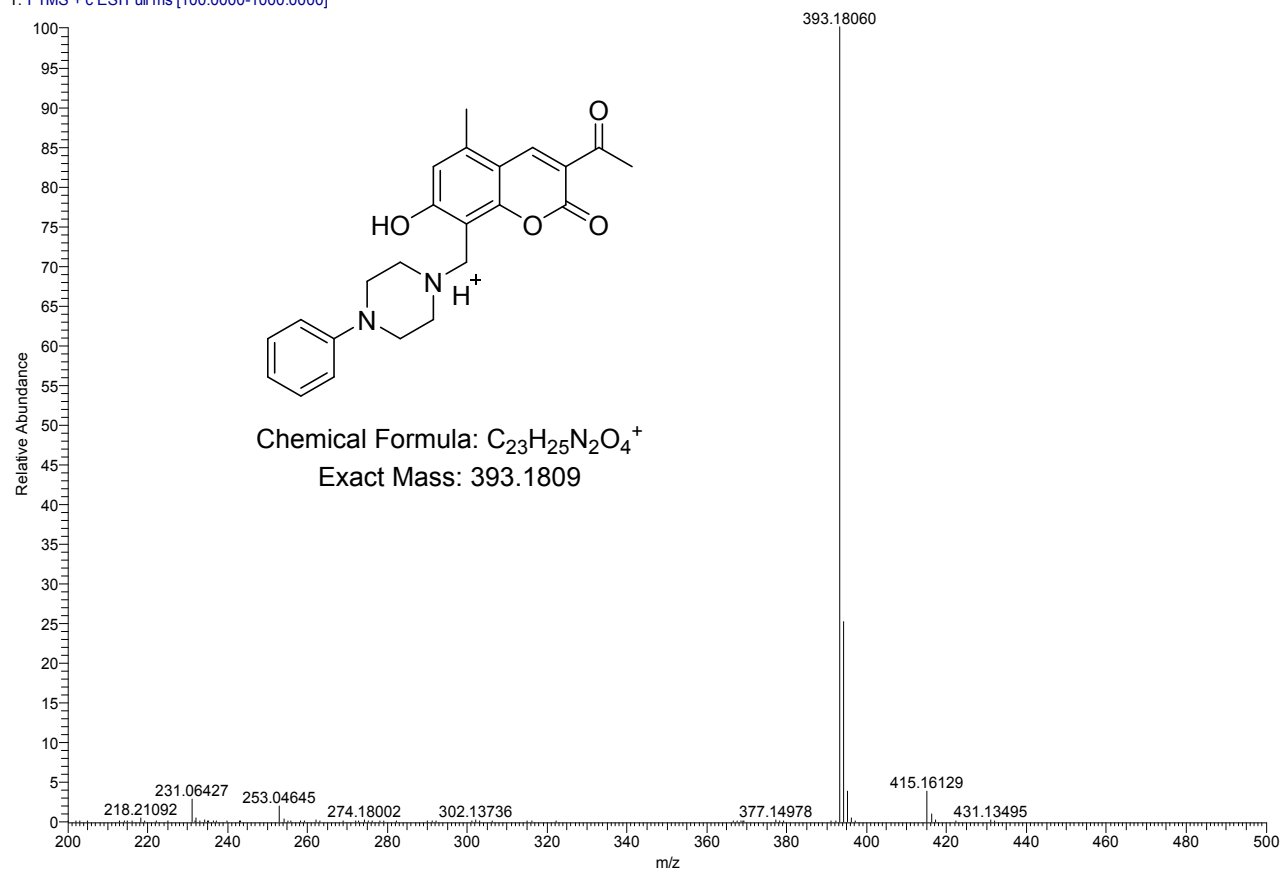
ESI-HRMS spectrum of compound **25**

CMB-C8-17_190328221931 #779 RT: 2.39 AV: 1 NL: 1.59E9
T: FTMS + c_ESIFull ms [100.0000-1000.0000]



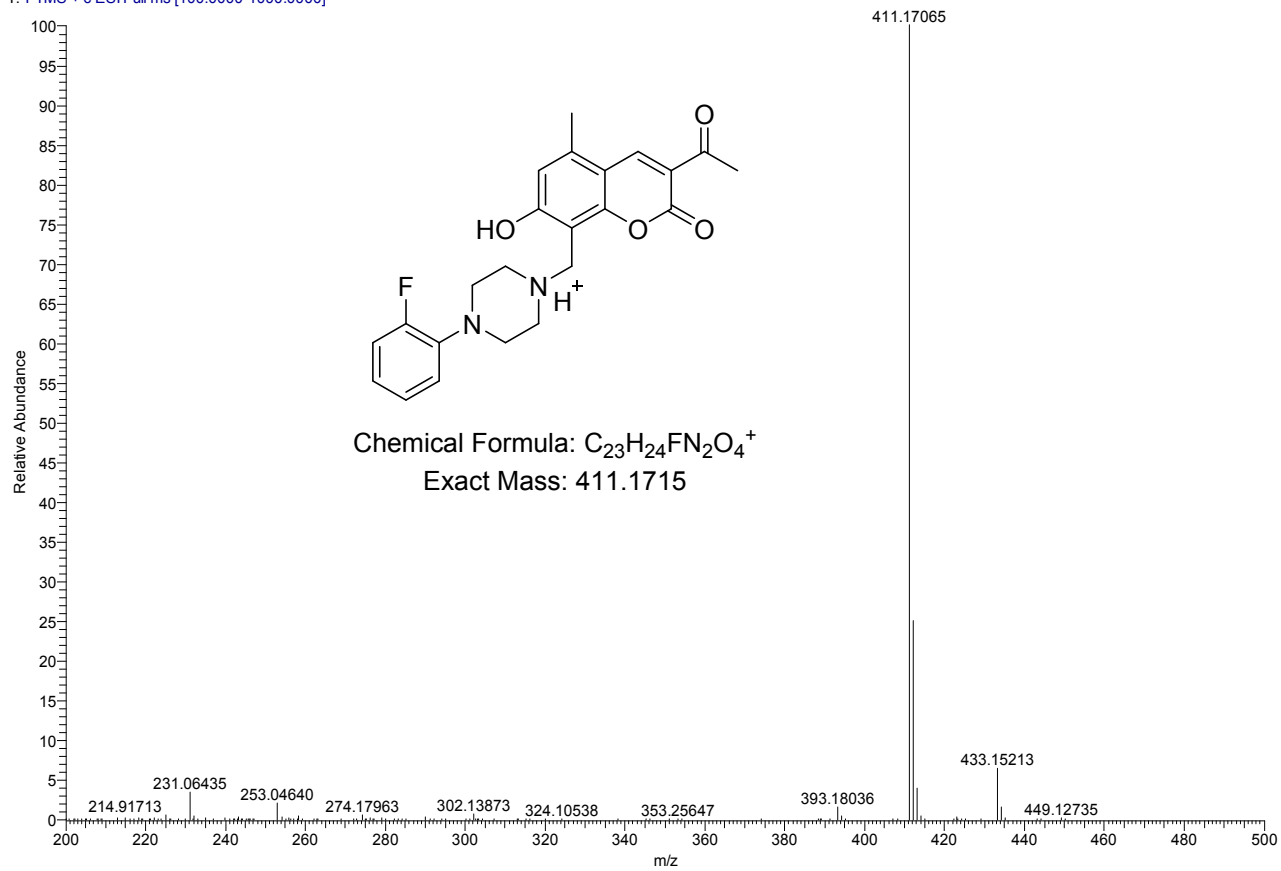
ESI-HRMS spectrum of compound **26**

CMB-C8-18_190329180553 #960 RT: 3.12 AV: 1 NL: 5.76E8
T: FTMS + c_ESIFull ms [100.0000-1000.0000]



ESI-HRMS spectrum of compound **27**

CMB-C8-10_190329181426 #1008 RT: 3.27 AV: 1 NL: 1.58E8
T: FTMS + c_ESIFull ms [100.0000-1000.0000]



ESI-HRMS spectrum of compound **28**

CMB-C8-8_190329175720 #758 RT: 2.46 AV: 1 NL: 6.19E8
T: FTMS + c ESI Full ms [100.0000-1000.0000]

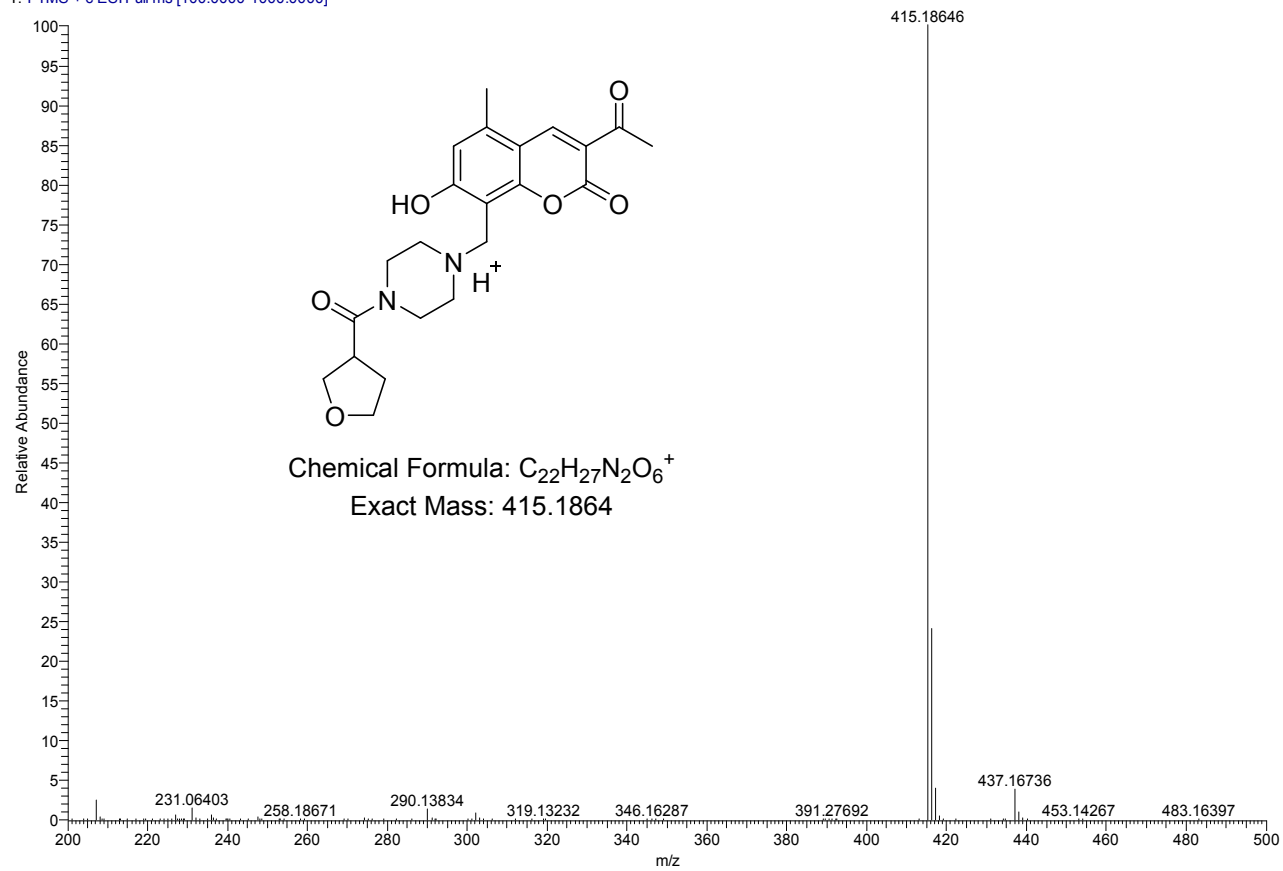


Figure S76. ESI-HRMS spectrum of compound 29

3. Cartesian coordinates of compounds 6, 30-33.

1) Compound 6 under neutral conditions

C	2.99045523	1.36371915	-0.00530994
C	3.34159626	-0.00273095	-0.00444494
C	2.35909420	-0.99348503	-0.00028794
C	1.02748010	-0.60737501	0.00310806
C	0.64548606	0.74836609	0.00171106
C	1.66157913	1.72662616	-0.00247494
O	0.08370803	-1.58381509	0.00850206
C	-1.30251407	-1.34227807	0.01217506
C	-1.70834110	0.06830102	0.00184106
C	-0.74348504	1.04039910	0.00143306
O	-1.99419011	-2.32506015	0.02682906
O	4.62785935	-0.41385197	-0.00738694
C	-3.16008621	0.42152804	-0.01264094
C	-3.53314925	1.89560614	0.03198906
O	-4.03500927	-0.42428403	-0.06087295
H	3.76850728	2.11815420	-0.00846494
H	2.63117222	-2.04041510	0.00065606
H	1.38504710	2.77444524	-0.00367394
H	-1.03231807	2.08417417	-0.00267794
H	5.22316139	0.34639108	-0.00979294
H	-4.61933033	1.96599215	0.03895306
H	-3.13609922	2.38402218	0.92555512
H	-3.14777622	2.43126618	-0.83971601

2) Compound 6 under acidic conditions

C	-3.05553722	1.31779510	-0.09458001
C	-3.35357524	-0.05582900	0.01599400
C	-2.33052617	-1.00166007	0.07820001
C	-1.01694507	-0.55593104	0.03115700
C	-0.68447805	0.80427006	-0.07260901
C	-1.74405913	1.73500013	-0.13889801
O	-0.03053800	-1.49980711	0.07844101
C	1.30740409	-1.19196209	0.03989900
C	1.68658912	0.21503202	-0.00985500
C	0.69554705	1.15226408	-0.09909401
O	2.07524015	-2.14273516	0.04091300
O	-4.66266534	-0.39254803	0.05506500
C	3.13323622	0.56825304	0.02254200
C	3.59022026	1.78323213	0.36101203
H	2.92857321	2.58293519	0.65720505
H	4.65438234	1.97940014	0.34444802
O	4.02144429	-0.40549703	-0.32981202

H	3.55553226	-1.26435809	-0.29666102
H	-3.87400028	2.02452414	-0.14176601
H	-2.53655018	-2.06211315	0.15801901
H	-1.51260411	2.79038520	-0.22101202
H	0.95397507	2.20034616	-0.19516401
H	-4.76441734	-1.34918810	0.13547801

3) Compound **30**

C	-2.35700000	0.66900000	0.04300000
H	-3.31000000	1.19500000	0.05400000
C	-2.30300000	-0.72500000	0.05000000
C	-1.08300000	-1.39100000	0.03700000
H	-1.04200000	-2.47700000	0.04200000
C	0.08800000	-0.63800000	0.01700000
C	0.06300000	0.75600000	0.01000000
C	-1.17000000	1.41000000	0.02400000
H	-1.22300000	2.49800000	0.01900000
O	1.30900000	-1.34000000	0.00500000
C	2.52600000	-0.66700000	-0.01500000
C	2.47500000	0.80500000	-0.02200000
H	3.43000000	1.31800000	-0.03800000
C	1.32200000	1.48200000	-0.01000000
H	1.30900000	2.56700000	-0.01600000
O	-3.44200000	-1.47900000	0.06900000
H	-4.22200000	-0.88000000	0.07700000
O	3.59800000	-1.27100000	-0.02600000

4) Compound **31**

C	3.25200000	-6.03500000	-1.11200000
H	2.41700000	-5.62100000	-1.67300000
C	3.29400000	-7.38600000	-0.77500000
C	4.36400000	-7.90500000	-0.05900000
H	4.39700000	-8.95900000	0.20400000
C	5.39800000	-7.04900000	0.31900000
C	5.39000000	-5.69100000	-0.00100000
C	4.30000000	-5.19100000	-0.72500000
H	4.24500000	-4.13800000	-0.99900000
O	6.45900000	-7.62300000	1.04300000
C	7.53200000	-6.85400000	1.46200000
C	7.51100000	-5.42500000	1.11800000
H	8.37200000	-4.86300000	1.46700000
C	6.51400000	-4.84600000	0.42900000

O	8.46700000	-7.34500000	2.09700000
O	2.29100000	-8.23900000	-1.13600000
H	1.60700000	-7.73800000	-1.63400000
C	6.65500000	-3.40000000	0.17100000
C	6.15000000	-2.46700000	1.08600000
H	5.64700000	-2.79900000	1.99300000
C	6.28400000	-1.09900000	0.84000000
H	5.88900000	-0.37800000	1.55300000
C	6.92400000	-0.65700000	-0.31700000
H	7.02900000	0.41000000	-0.50700000
C	7.43100000	-1.58100000	-1.23200000
H	7.93000000	-1.23400000	-2.13500000
C	7.29800000	-2.94900000	-0.99000000
H	7.69600000	-3.66000000	-1.71200000

5) Compound **32**

C	4.78300000	-5.38200000	-0.11000000
C	4.80800000	-6.77400000	-0.14800000
H	3.89100000	-7.35500000	-0.21500000
C	6.03400000	-7.43200000	-0.09900000
H	6.07200000	-8.51900000	-0.12800000
C	7.21000000	-6.68400000	-0.01300000
C	7.20400000	-5.28800000	0.02600000
C	5.96300000	-4.64000000	-0.02400000
H	5.89400000	-3.55500000	0.00300000
O	8.41200000	-7.41600000	0.03200000
C	9.63700000	-6.77500000	0.11800000
C	9.61700000	-5.30400000	0.15900000
H	10.59300000	-4.83500000	0.22600000
C	8.48800000	-4.58000000	0.11700000
O	10.69500000	-7.40300000	0.15900000
O	3.60300000	-4.69500000	-0.15500000
H	2.86000000	-5.33700000	-0.21400000
C	8.52200000	-3.07900000	0.16100000
H	9.54600000	-2.69600000	0.22800000
H	7.97800000	-2.70400000	1.03500000
H	8.07600000	-2.65400000	-0.74400000

6) Compound **33**

C	4.75200000	-5.29600000	-0.24700000
H	3.81000000	-4.76800000	-0.39700000
C	4.73000000	-6.68200000	-0.06100000
C	5.93900000	-7.35400000	0.10500000

H	5.95800000	-8.43500000	0.23300000
C	7.13900000	-6.63600000	0.10700000
C	7.19600000	-5.24600000	-0.06100000
C	5.96600000	-4.59000000	-0.24200000
O	8.30100000	-7.41400000	0.29100000
C	9.55700000	-6.83800000	0.31600000
C	9.61400000	-5.38100000	0.14300000
H	10.61400000	-4.96100000	0.16900000
C	8.53000000	-4.60900000	-0.03500000
O	10.57700000	-7.50800000	0.47500000
C	8.69300000	-3.12500000	-0.20300000
H	8.17300000	-2.58200000	0.59300000
H	9.74500000	-2.82200000	-0.15300000
H	8.31900000	-2.79800000	-1.17800000
O	5.91900000	-3.23100000	-0.42300000
H	4.98600000	-2.94200000	-0.53200000
C	3.43400000	-7.43800000	-0.10100000
H	2.61500000	-6.82900000	0.29700000
H	3.49000000	-8.34400000	0.51000000
H	3.19700000	-7.72000000	-1.13200000

4. Sources of the reagents used in the synthesis process

Reagent	Brand	Catalogue number
Piperidine hydrochloride	Aladdin	P194173-10g
Diethylamine hydrochloride	Alfa	A13637
Morpholine hydrochloride	ARK	AK116221
4-Hydroxypiperidine	Alfa	B22723
4-Piperidinemethanol	Innochem	A37590
1-Methylpiperazine	Innochem	A59775
1-Phenylpiperazine	Innochem	A61669
1-(2-Fluorophenyl)piperazine	Aladdin	F156585-5g
1-(2-Tetrahydrofuroyl)piperazine	TCI	T2617