Supporting Information for

Design, Synthesis and Anti-cervical Cancer Activity of Aroylpyrrole-Based Derivatives as Potent Histone Deacetylase 6 Inhibitors

Xingjie Wang[a], Lixuan Du[b], Yaxin Xue[c], Yitong Su[c], Xuetao Yuan[a], Shuting Yang[a], Weiyi Su[c], Wenli Gou[c, *], Xin Chen[d, *], Lu Zong[c, *]

[a]*Department of General Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, P. R. China*

[b]*Department of Urology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, P. R. China*

[c]*Department of Obstetrics & Gynecology, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, P. R. China*

[d]*Shaanxi Key Labotory of Natural Products & Chemical Biology, College of Chemistry & Pharmacy, Northwest A&F University, Yangling 712100, P. R. China*

Corresponding Author

*Wenli Gou

E-mail: 13572870556@126.com; Fax: +86-029-85323338

*Xin Chen

E-mail: chenxin1888@nwsuaf.edu.cn; Fax: +87-029-87092335

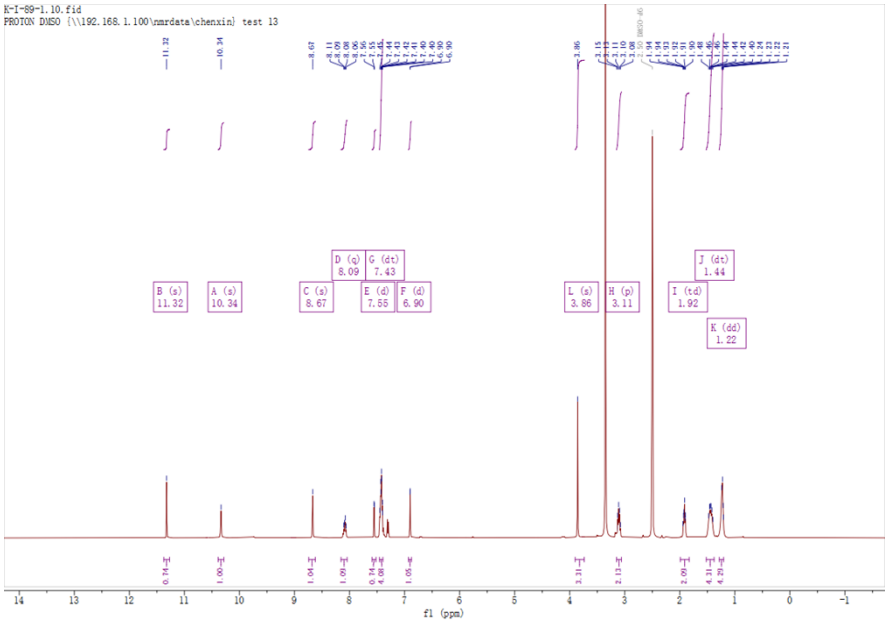
*Lu Zong

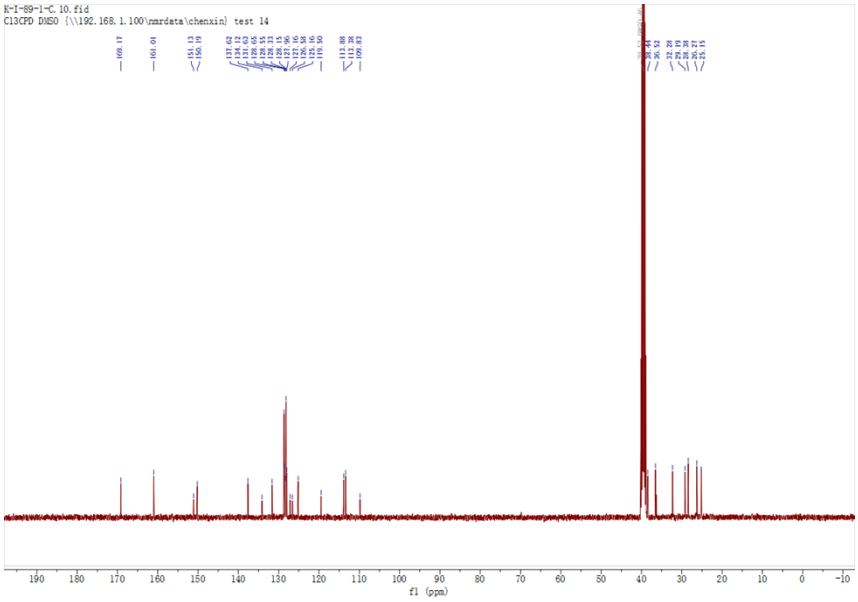
E-mail: catherazong@163.com; Fax: +86-029-85323338

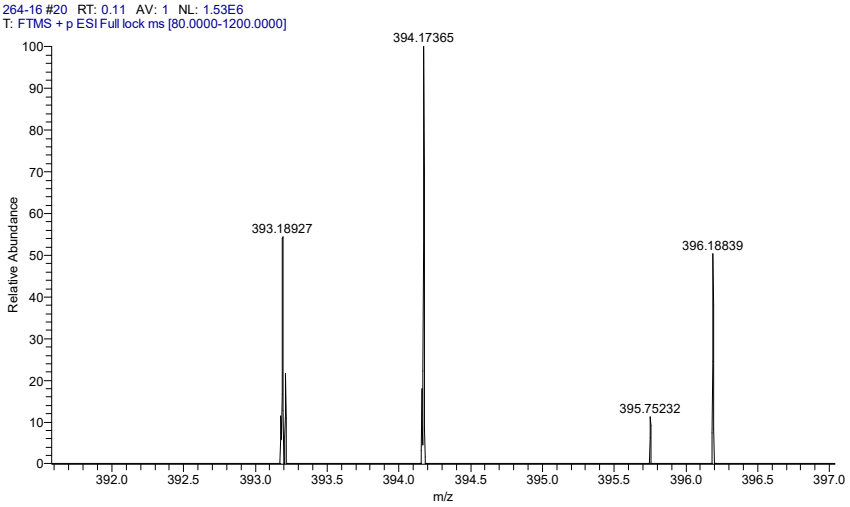
Notes

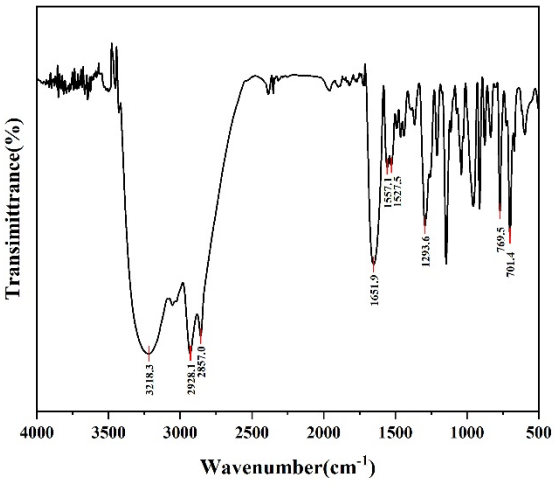
The authors declare no competing interest.

5-benzoyl-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1-methyl-1*H*-pyrrole-2-carboxamide (**10a**)

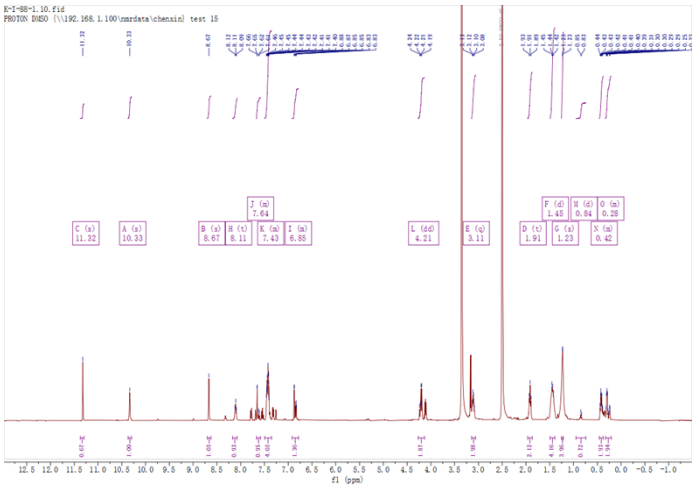


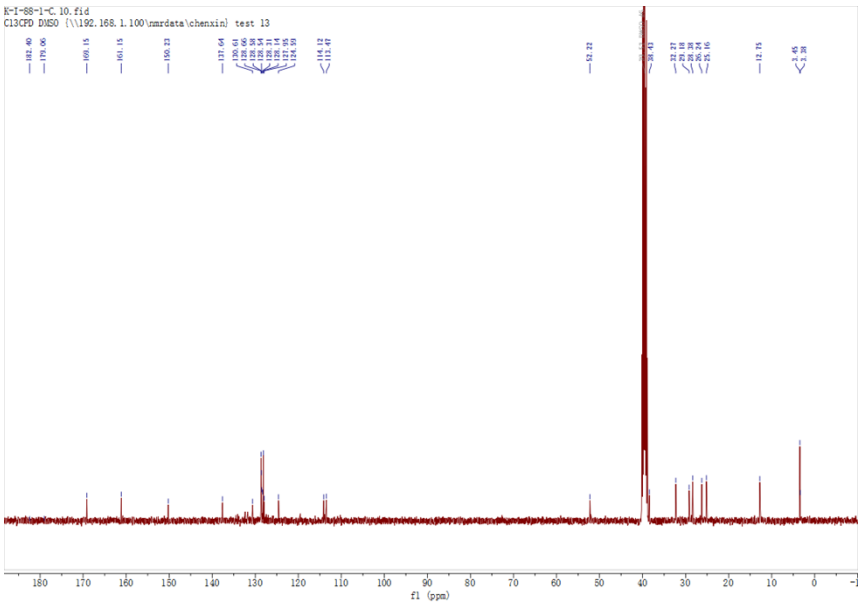


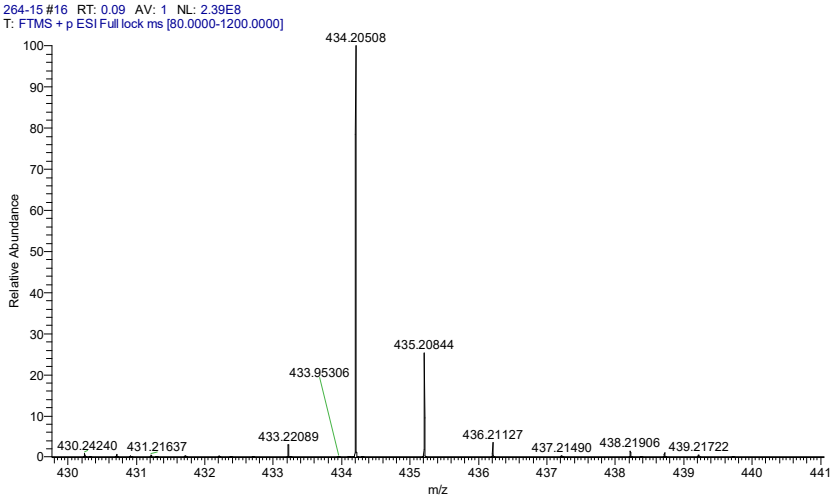


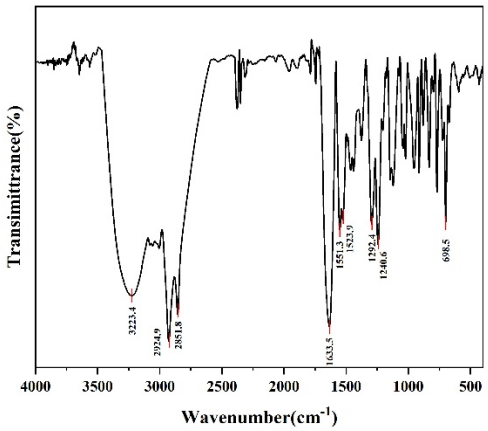


5-benzoyl-1-(cyclopropylmethyl)-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1*H*-pyrrole-2-carboxamide (**10b**)

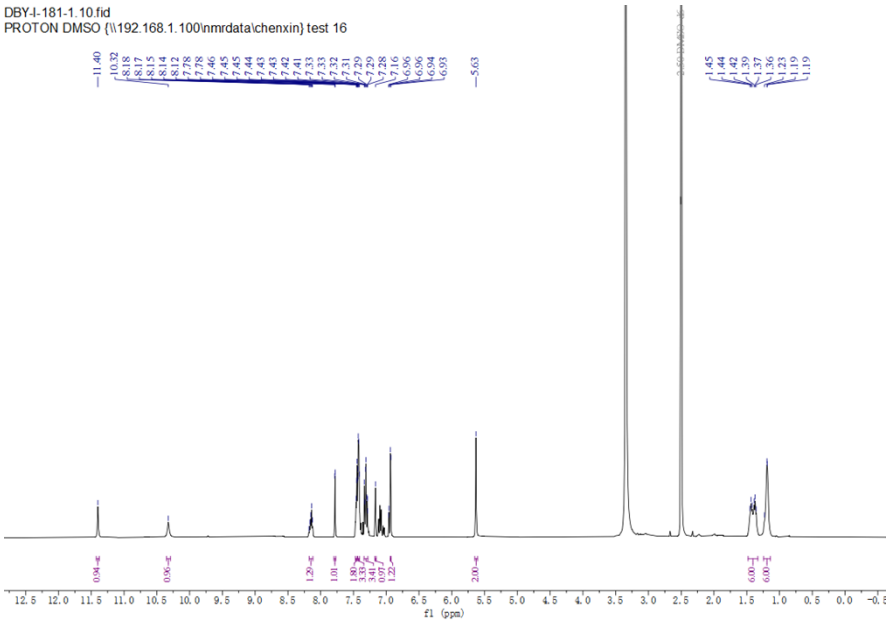


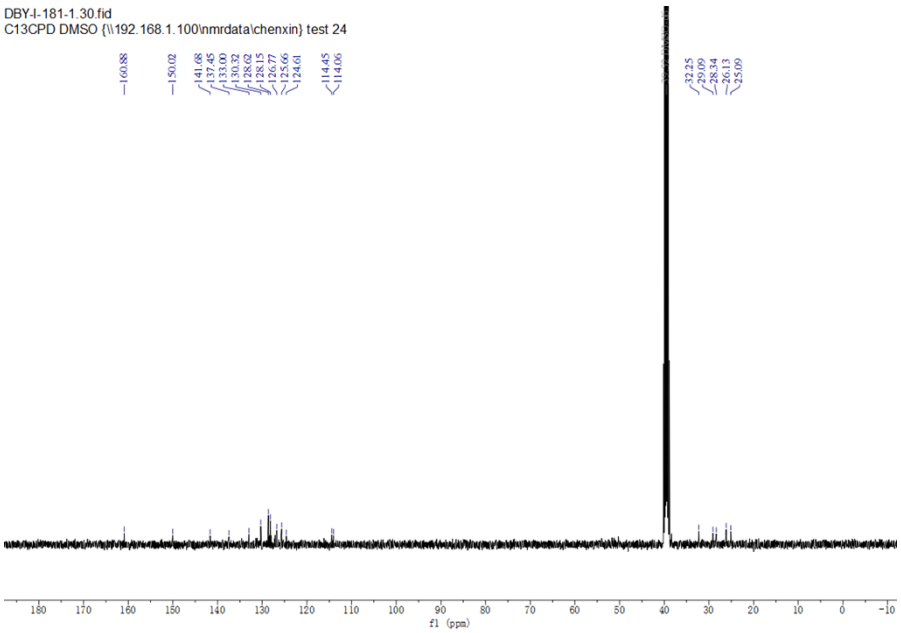


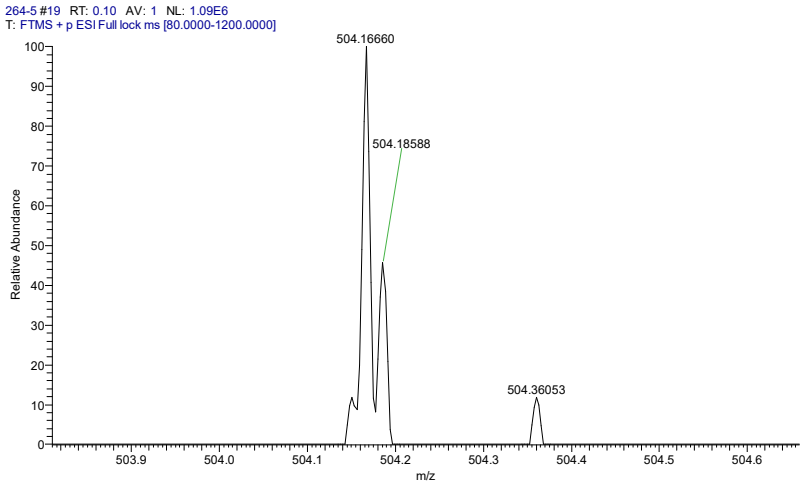


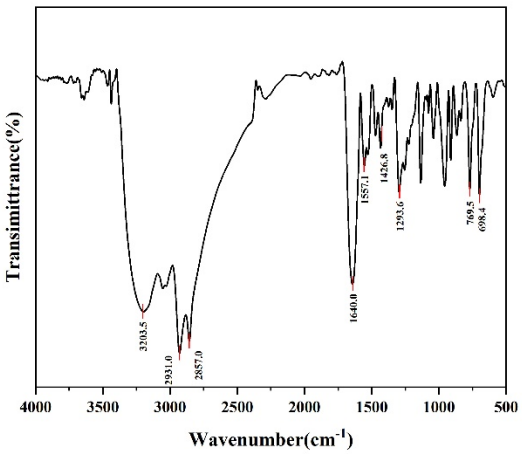


5-benzoyl-1-(3-chlorobenzyl)-*N*-(6-(hydroxyamino)-6-oxohexyl)-1*H*-pyrrole-2-carboxamide (**10c**)

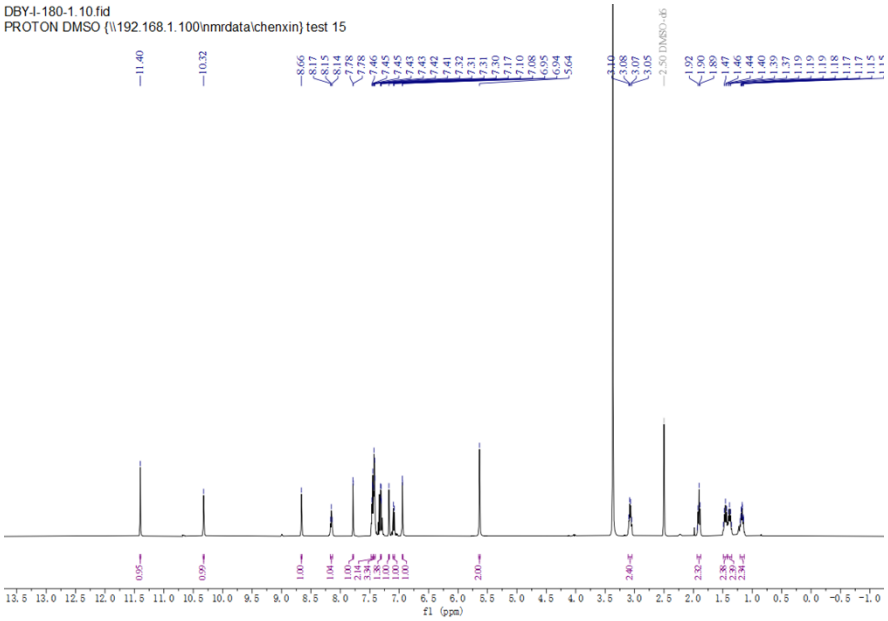


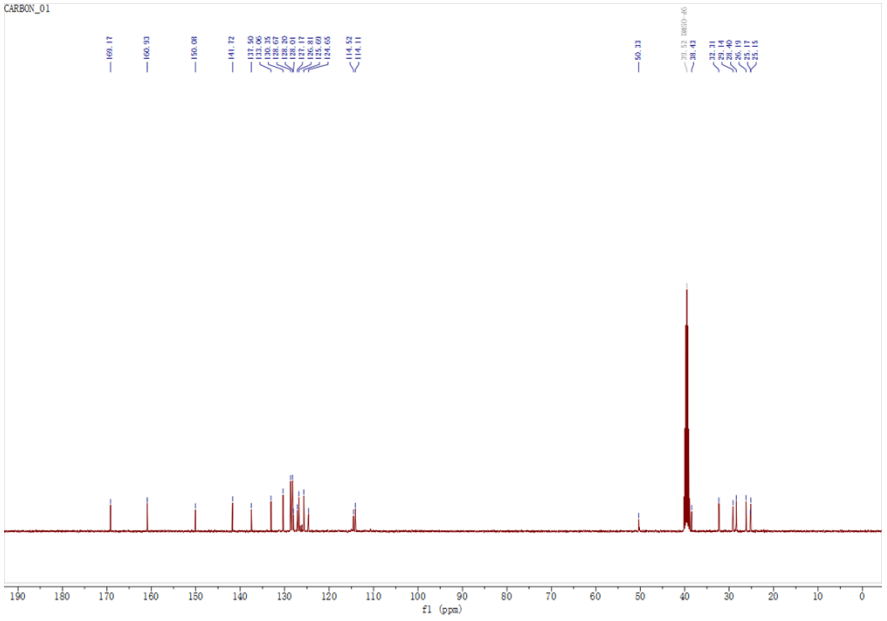


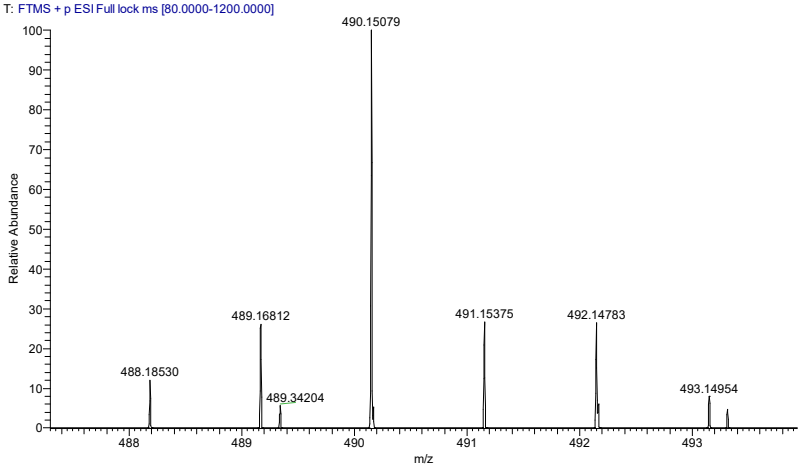


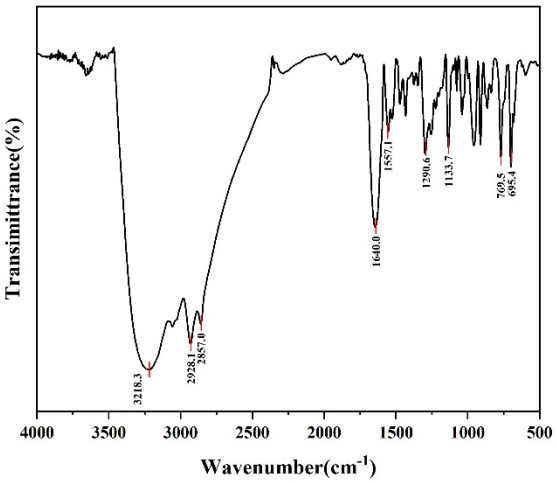


5-benzoyl-1-(3-chlorobenzyl)-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1*H*-pyrrole-2-carboxamide (**10d**)

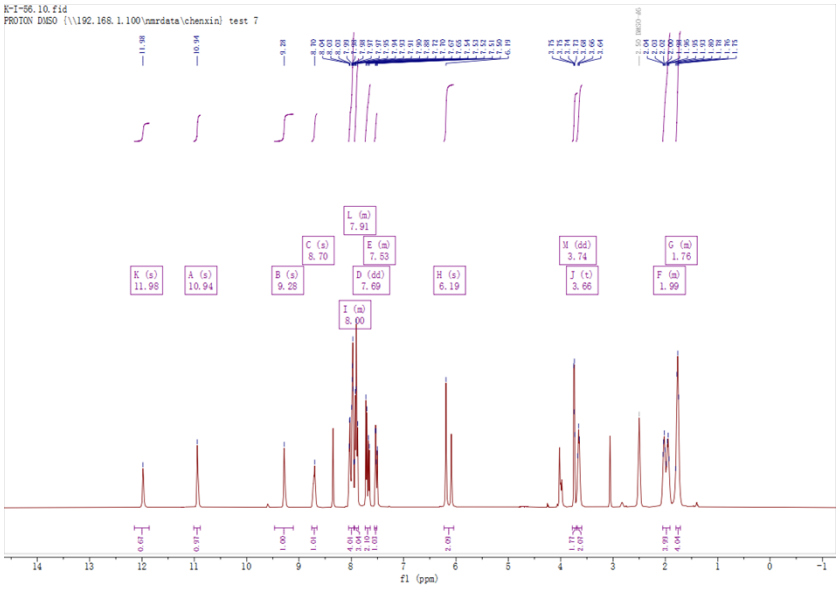

DBY-I-180-1.10.fid
PROTON DMSO {\\192.168.1.100\nmrdata\chenxin} test 15
f1 (ppm)

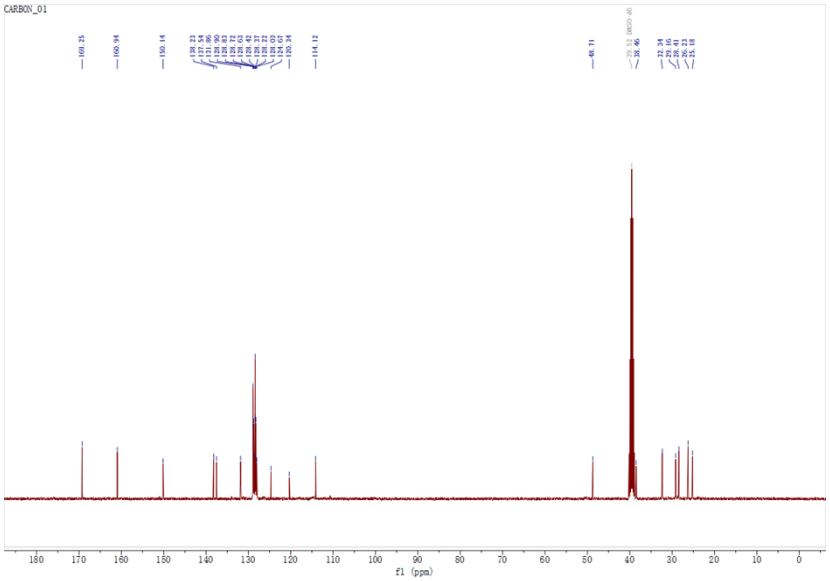

CARBON_01
f1 (ppm)

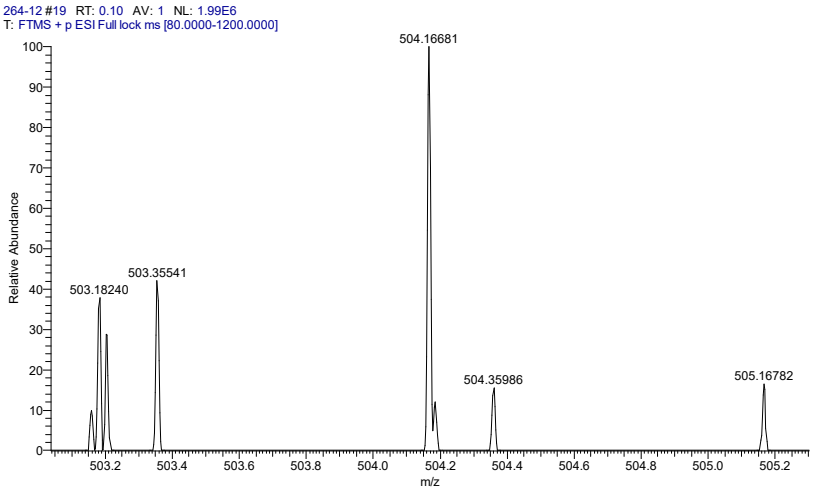

264-4 #19 RT: 0.10 AV: 1 NL: 3.79E6
T: FTMS + p ESI Full lock ms [80.0000-1200.0000]
Relative Abundance
m/z
490.15079
489.16812
491.15375
492.14783
488.18530
489.34204
493.14954

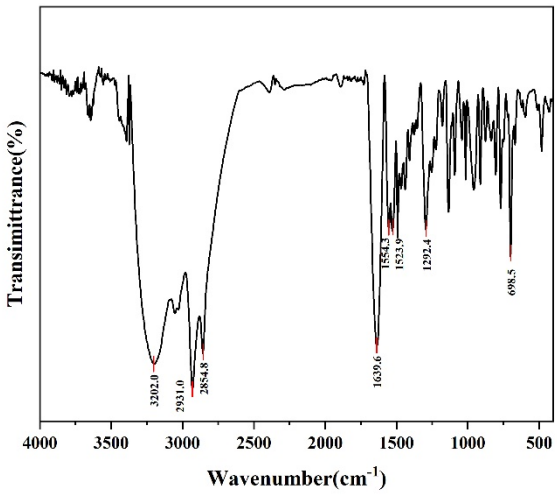


5-benzoyl-1-(4-chlorobenzyl)-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1*H*-pyrrole-2-carboxamide (**10e**)

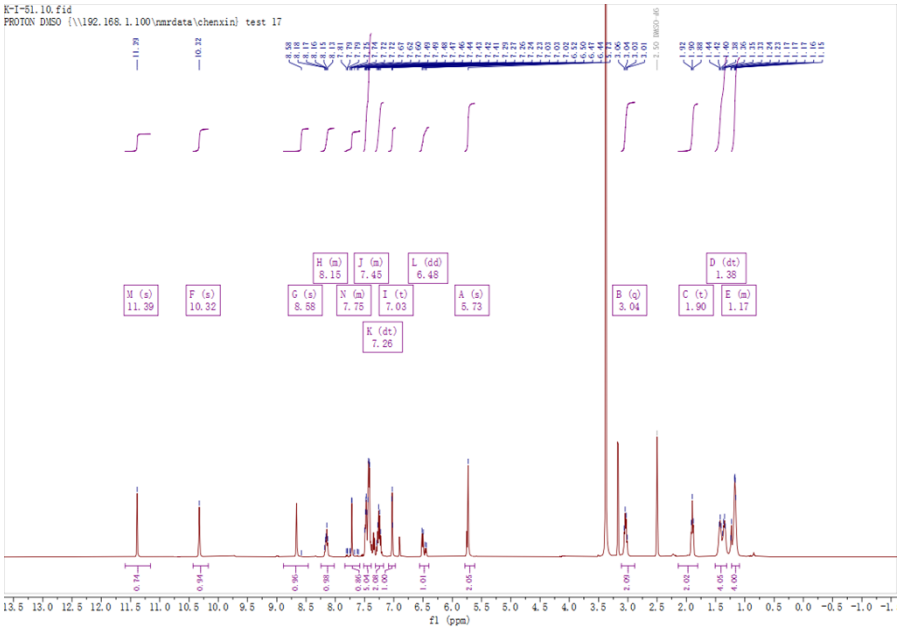


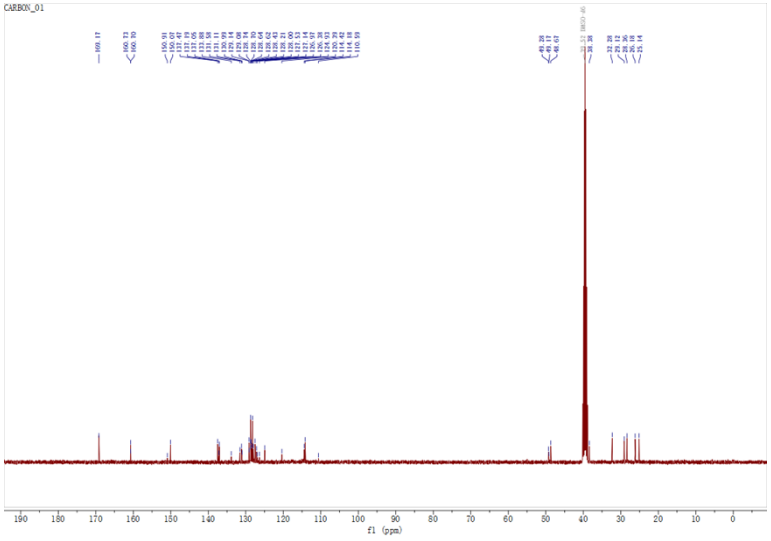


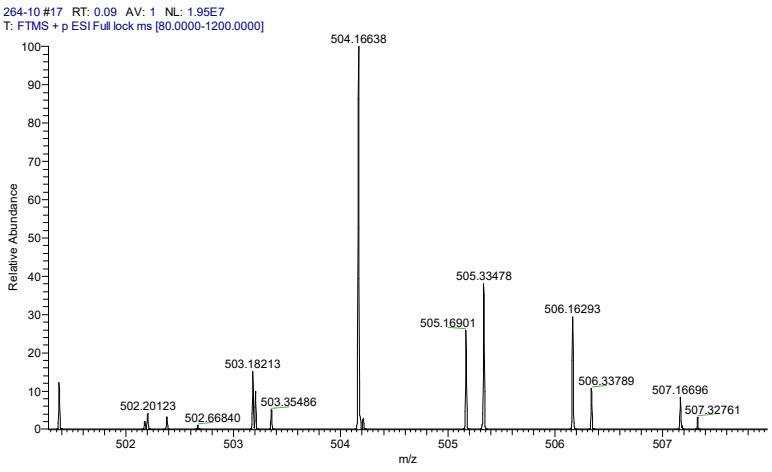


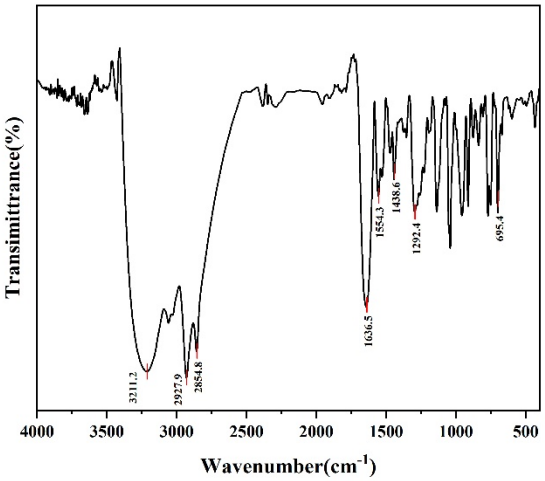


5-benzoyl-1-(2-chlorobenzyl)-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1*H*-pyrrole-2-carboxamide (**10f**)

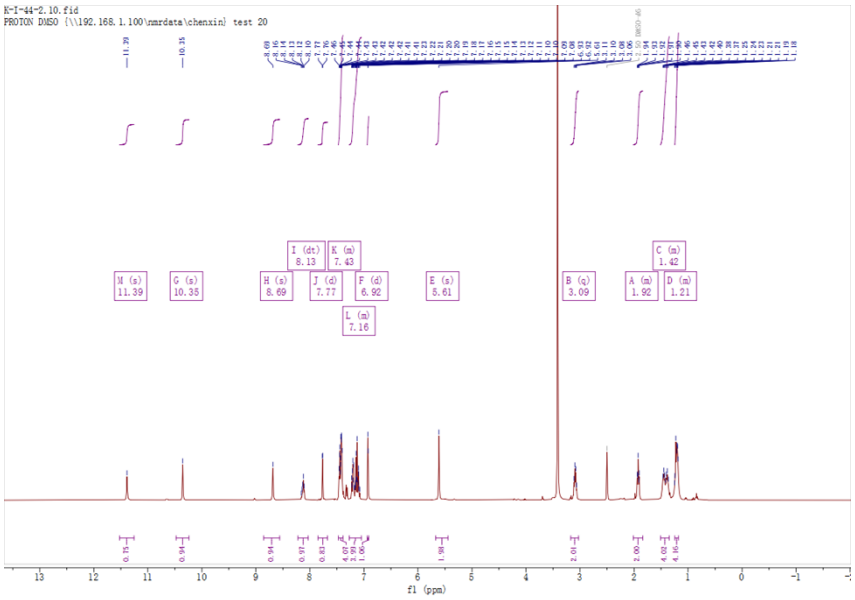


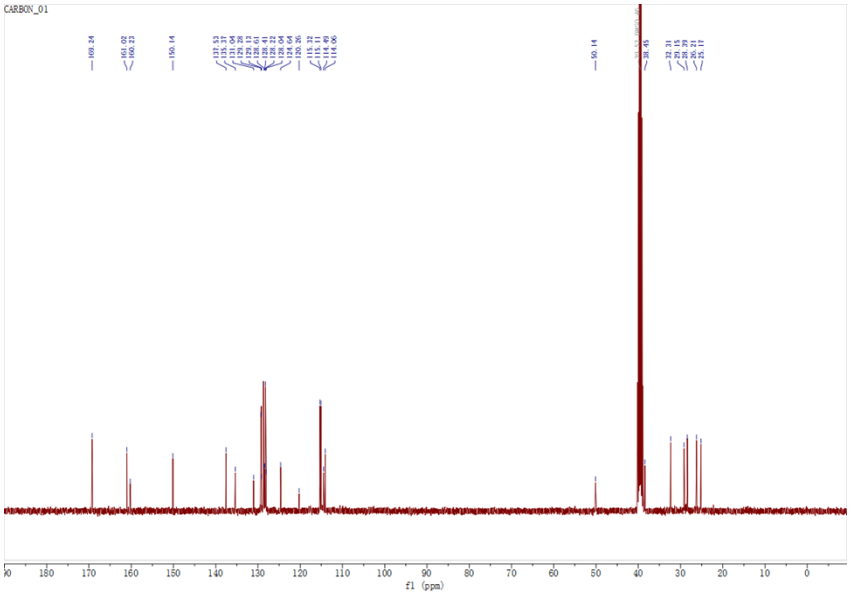


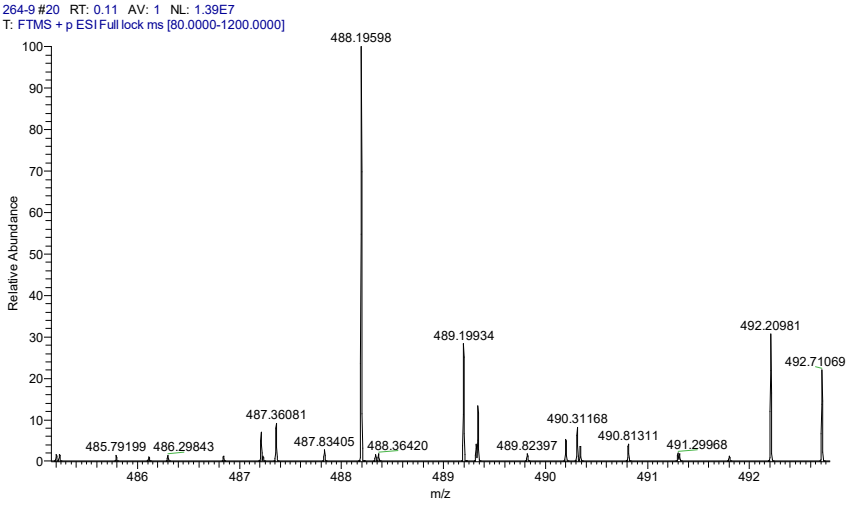


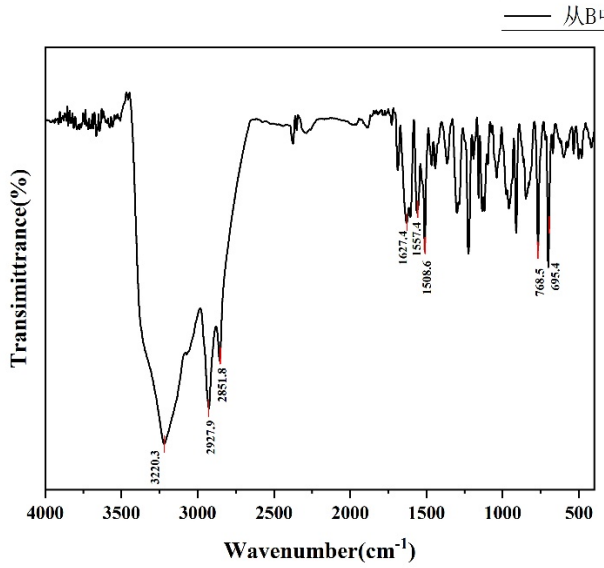


5-benzoyl-1-(4-fluorobenzyl)-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1*H*-pyrrole-2-carboxamide (**10g**)

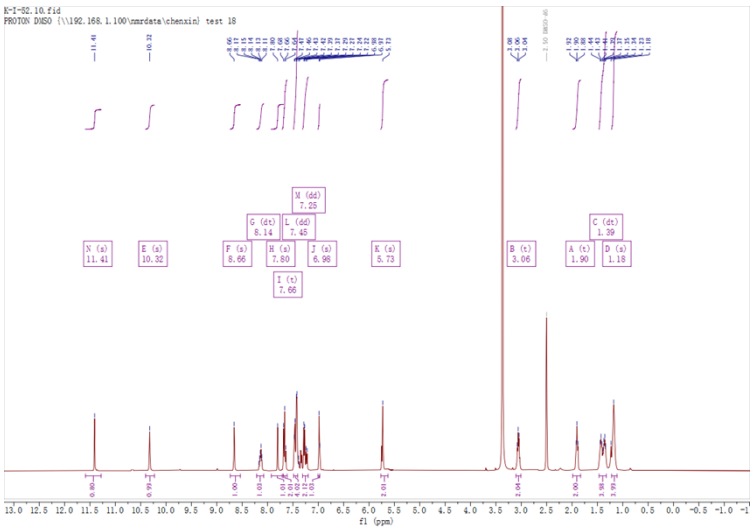

K-I-44-2.10.fid
PROTON DMSO {\\192.168.1.100\nmrdata\chenxin} test 20
I (dt) 8.13
K (m) 7.43
C (m) 1.42
M (s) 11.39
G (s) 10.35
H (s) 8.69
J (d) 7.77
F (d) 6.92
E (s) 5.61
B (q) 3.09
A (m) 1.92
D (m) 1.21
L (m) 7.16
f1 (ppm)

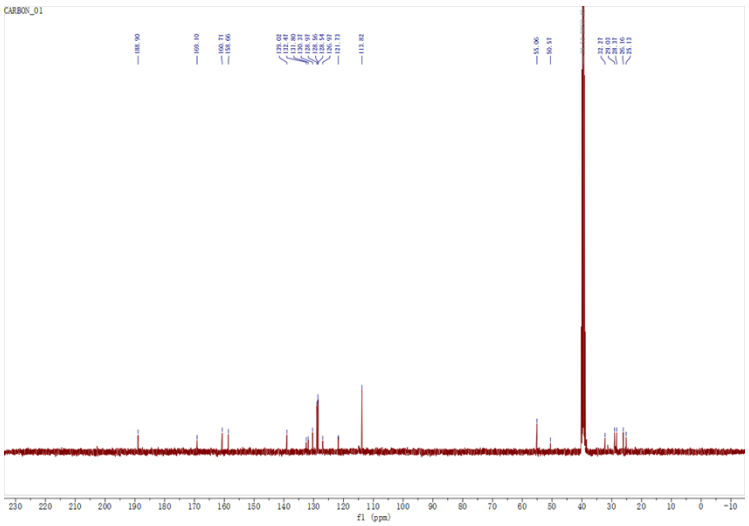

CARBON_01
f1 (ppm)

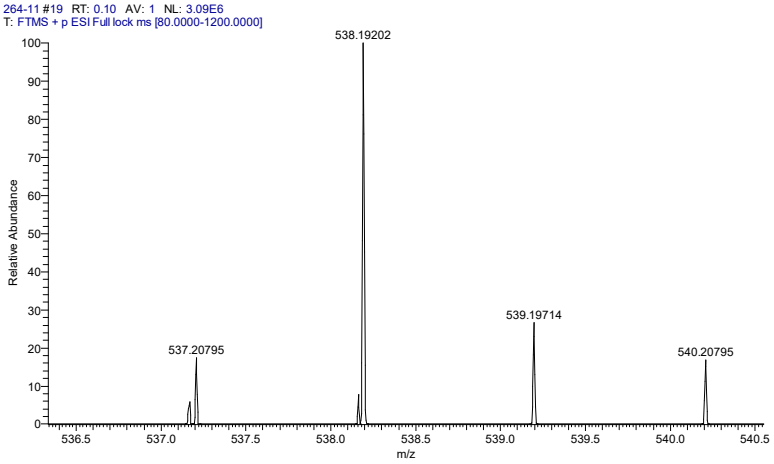

264-9 #20 RT: 0.11 AV: 1 NL: 1.39E7
T: FTMS + p ESI Full lock ms [80.0000-1200.0000]
Relative Abundance
m/z
488.19598
489.19934
492.20981
492.71069
487.36081
487.83405
488.36420
485.79199
486.29843
489.82397
490.31168
490.81311
491.29968

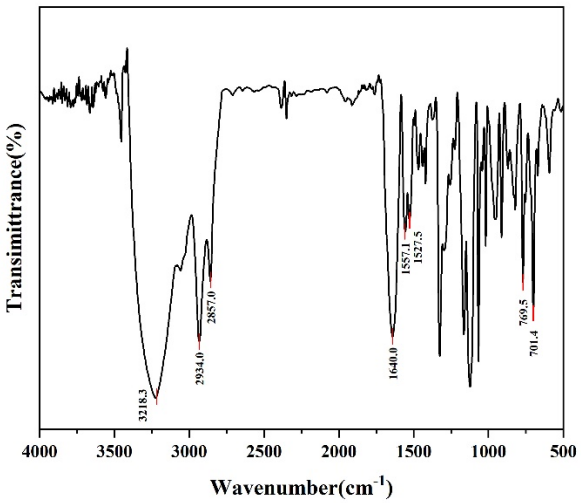


5-benzoyl-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1-(4-(trifluoromethyl)benzyl)-1*H*-pyrrole-2-carboxamide **(10h)**

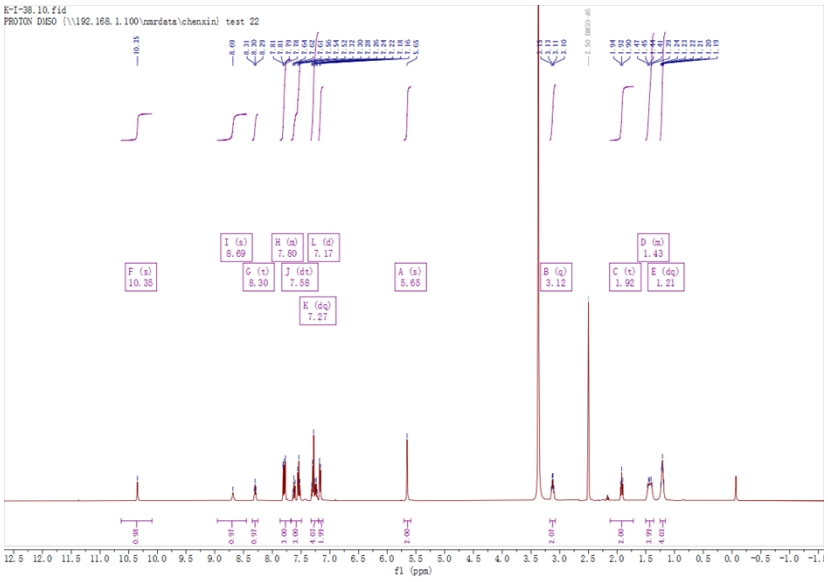


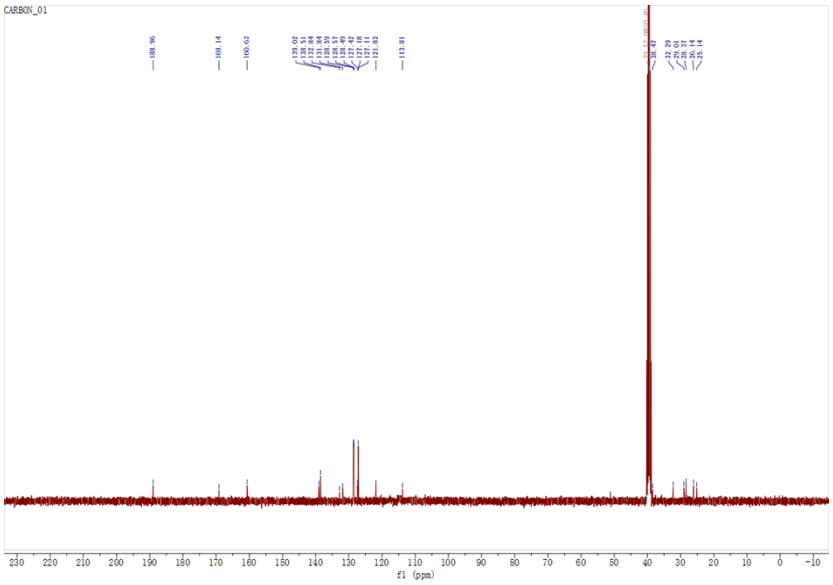


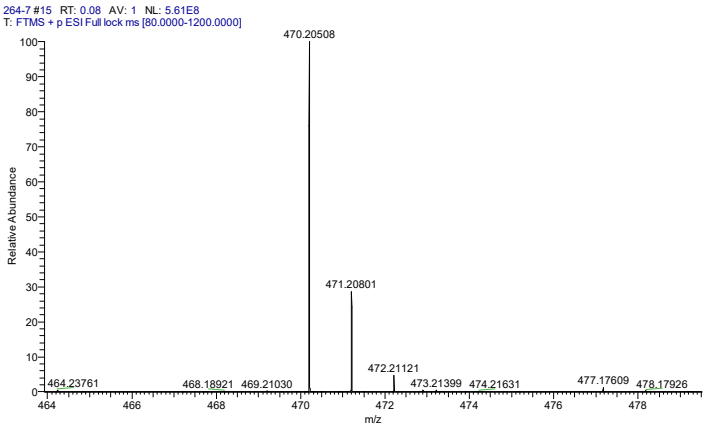


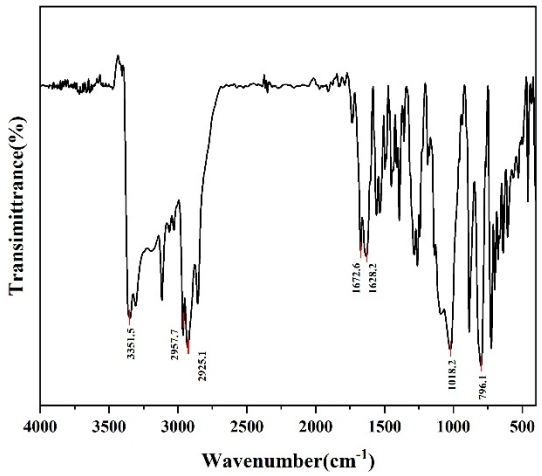


5-benzoyl-1-benzyl-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1*H*-pyrrole-2-carboxamide (**10i**)

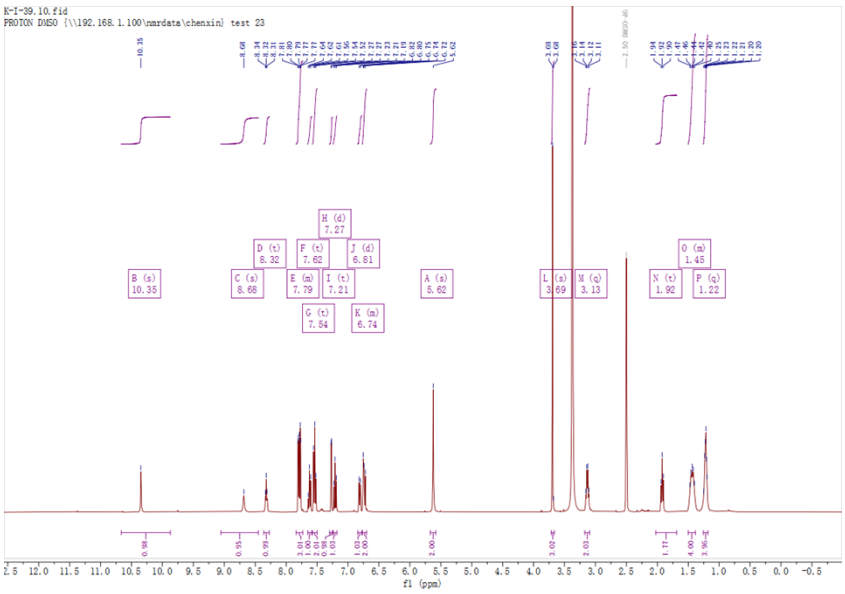


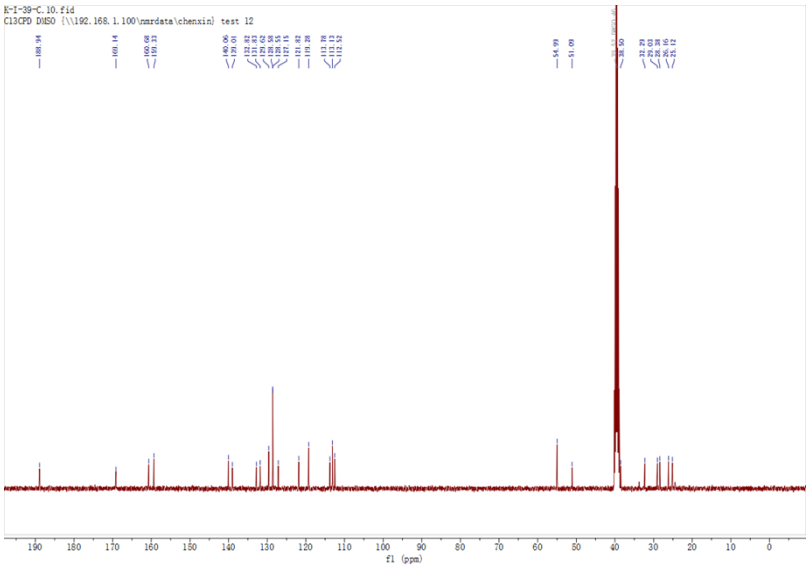


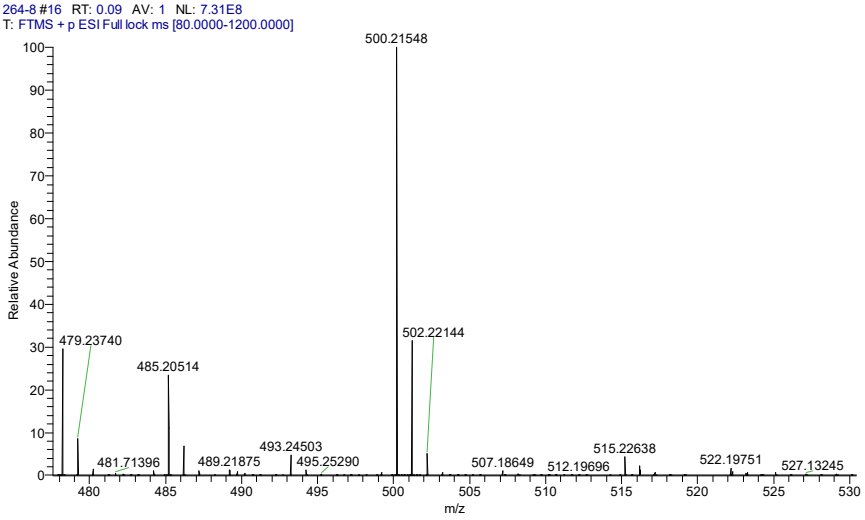


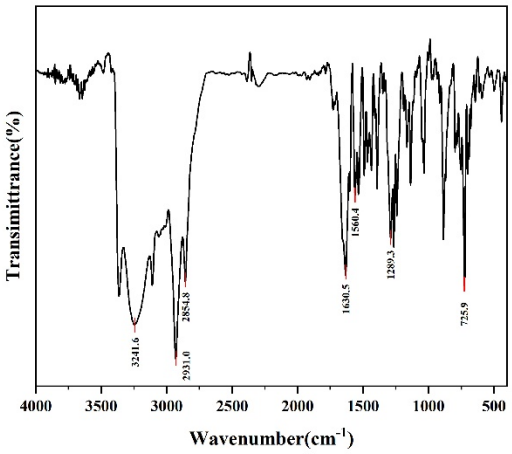


5-benzoyl-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1-(3-methoxybenzyl)-1*H*-pyrrole-2-carboxamide (**10j**)

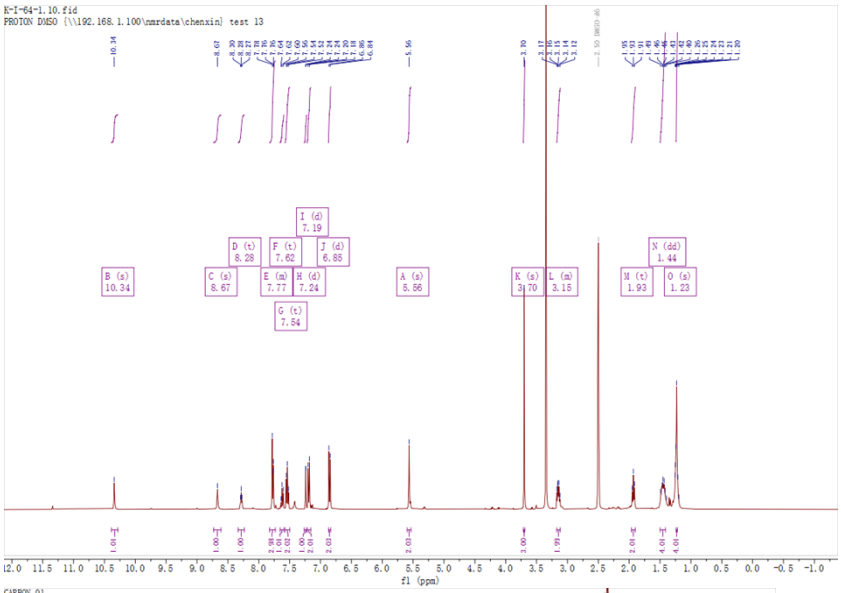

K-I-39.10.fid
PROTON DMSO {\\192.168.1.100\nmrdata\chenxin} test 23
H (d) 7.27
D (t) 8.32
F (t) 7.62
J (d) 6.81
O (m) 1.45
B (s) 10.35
C (s) 8.68
E (m) 7.79
I (t) 7.21
A (s) 5.62
L (s) 3.69
M (q) 3.13
N (t) 1.92
P (q) 1.22
G (t) 7.54
K (m) 6.74
f1 (ppm)

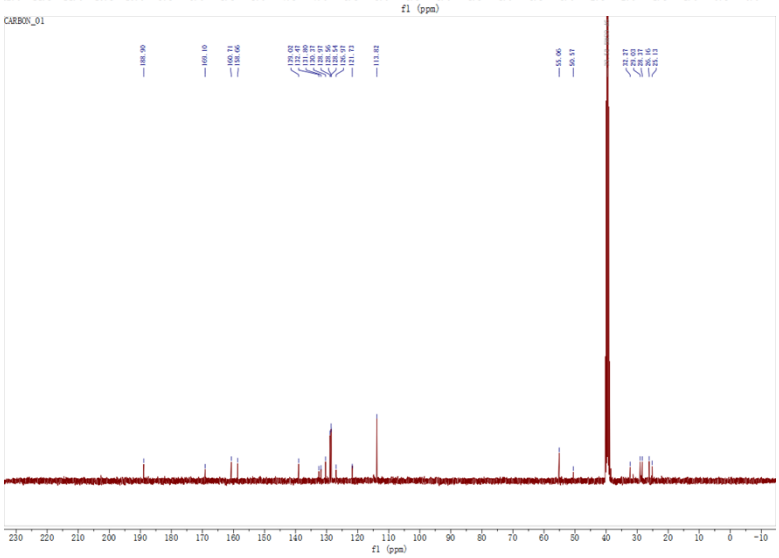

K-I-39-C.10.fid
C13CPD DMSO {\\192.168.1.100\nmrdata\chenxin} test 12
f1 (ppm)

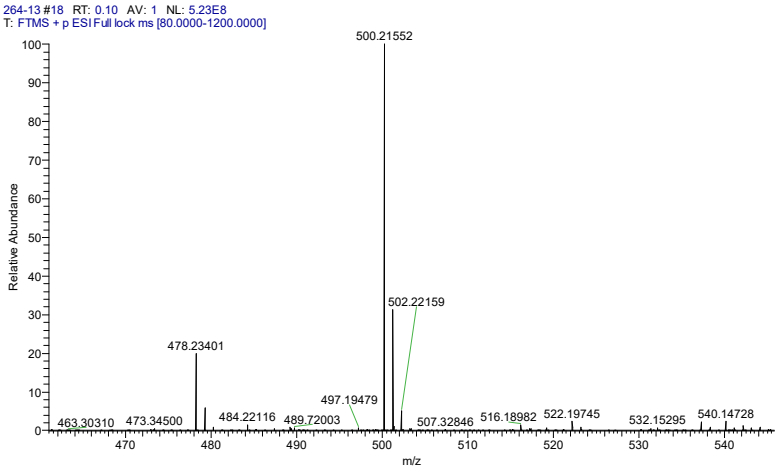

264-8 #16 RT: 0.09 AV: 1 NL: 7.31E8
T: FTMS + p ESI Full lock ms [80.0000-1200.0000]
Relative Abundance
m/z
500.21548
502.22144
479.23740
485.20514
493.24503
481.71396
489.21875
495.25290
507.18649
512.19696
515.22638
522.19751
527.13245

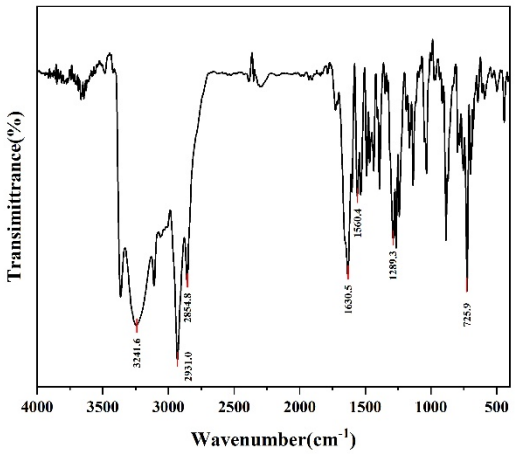


5-benzoyl-*N*-(7-(hydroxyamino)-7-oxoheptyl)-1-(4-methoxybenzyl)-1*H*-pyrrole-2-carboxamide (**10k**)

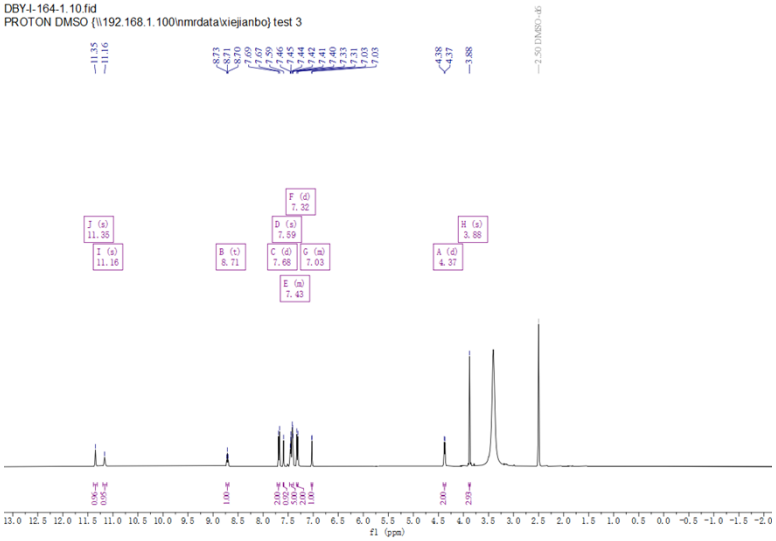


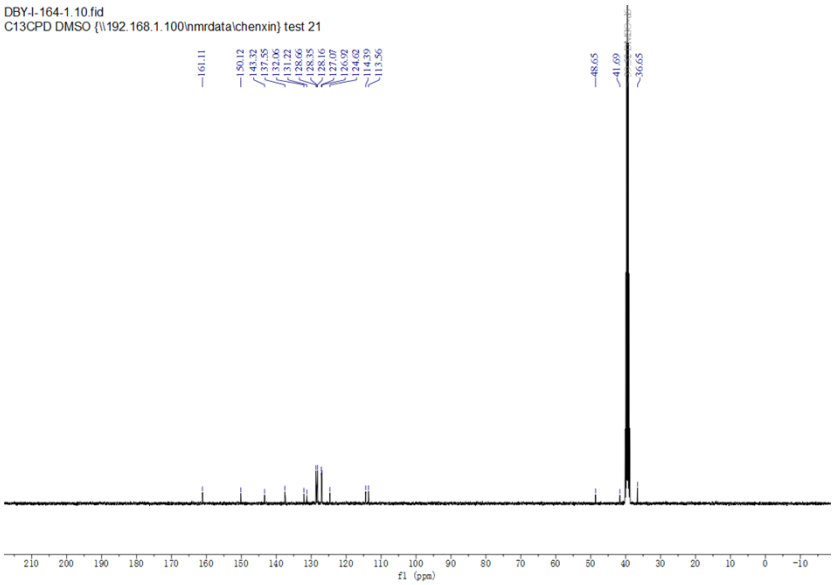


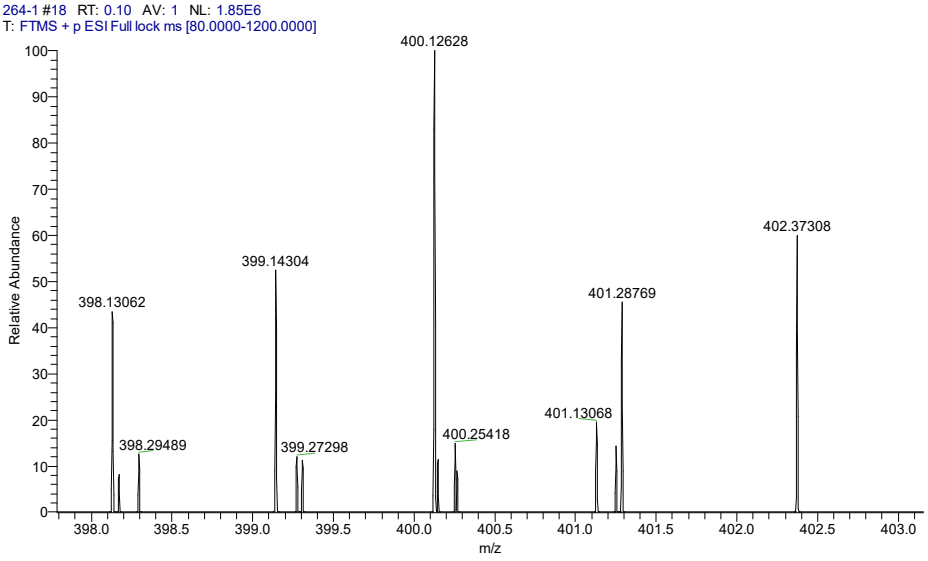


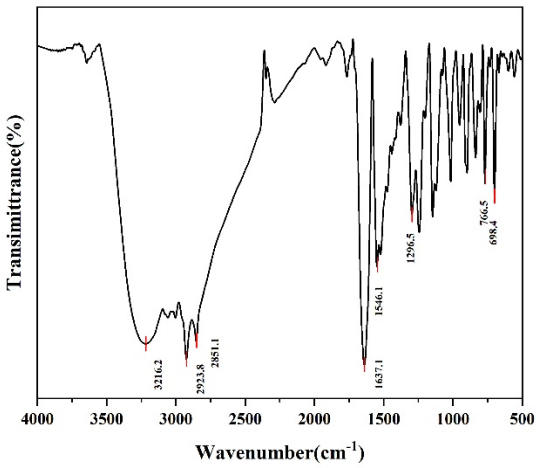


5-benzoyl-*N*-(4-(hydroxycarbamoyl)benzyl)-1-methyl-1*H*-pyrrole-2-carboxamide (**11a**)

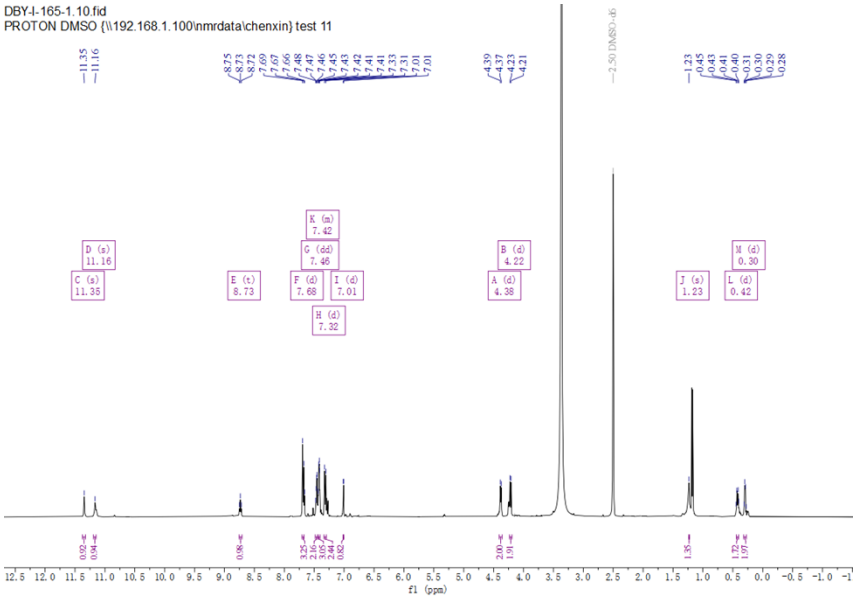


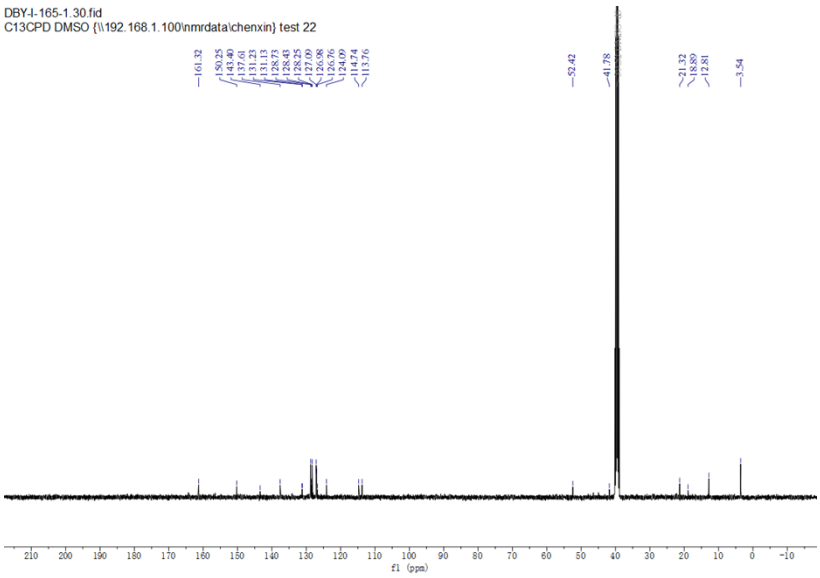


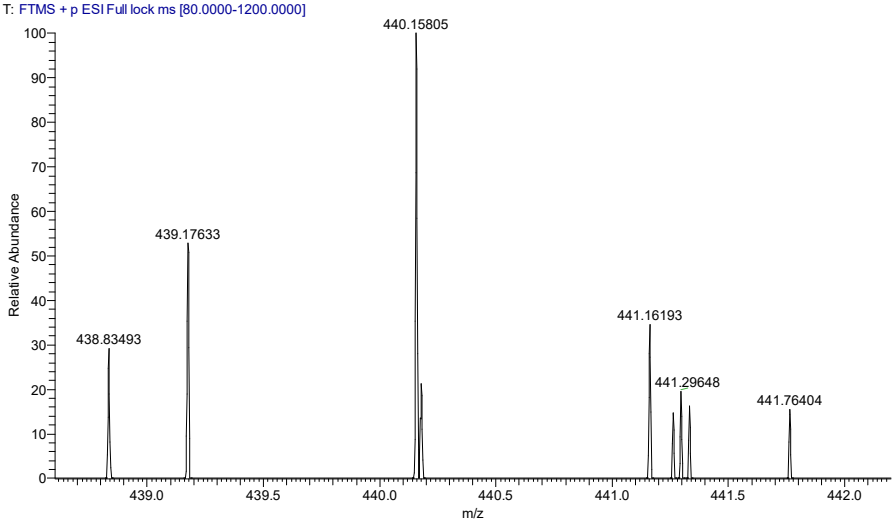


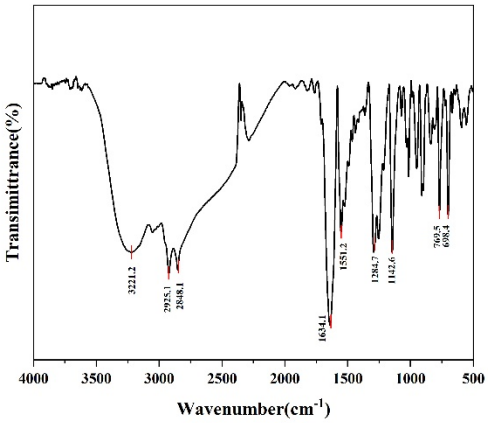


5-benzoyl-1-(cyclopropylmethyl)-*N*-(4-(hydroxycarbamoyl)benzyl)-1*H*-pyrrole-2-carboxamide (**11b**)

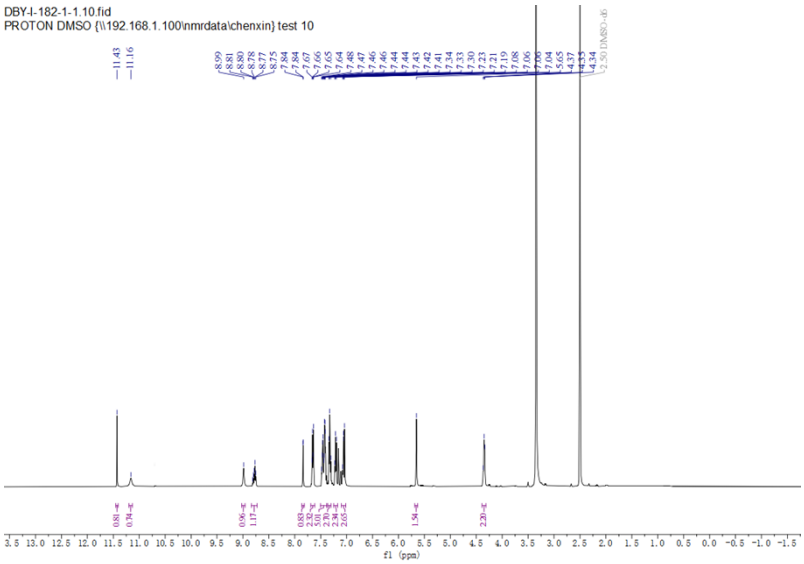

DBY-I-165-1.10.fid
PROTON DMSO {\\192.168.1.100\nmrdata\chenxin} test 11
D (s) 11.16
C (s) 11.35
E (t) 8.73
K (m) 7.42
G (dd) 7.46
F (d) 7.68
I (d) 7.01
H (d) 7.32
B (d) 4.22
A (d) 4.38
J (s) 1.23
M (d) 0.30
L (d) 0.42
f1 (ppm)

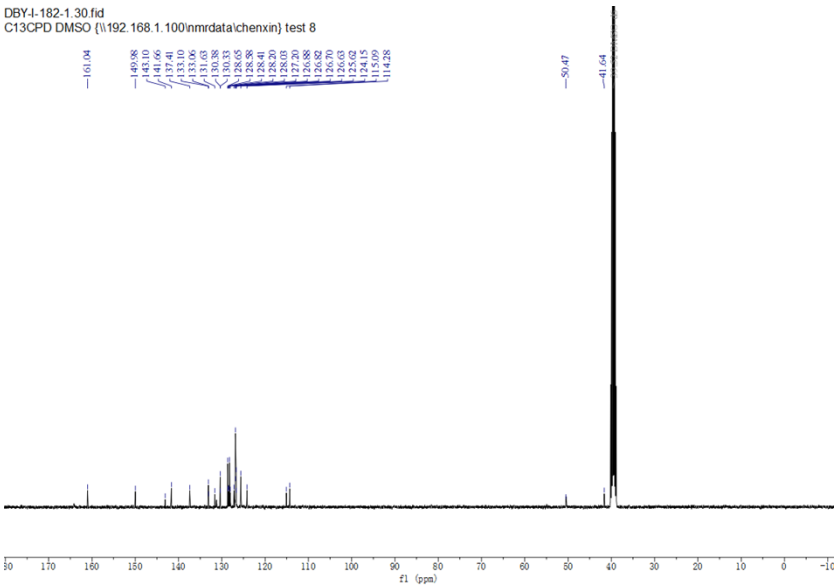

DBY-I-165-1.30.fid
C13CPD DMSO {\\192.168.1.100\nmrdata\chenxin} test 22
f1 (ppm)

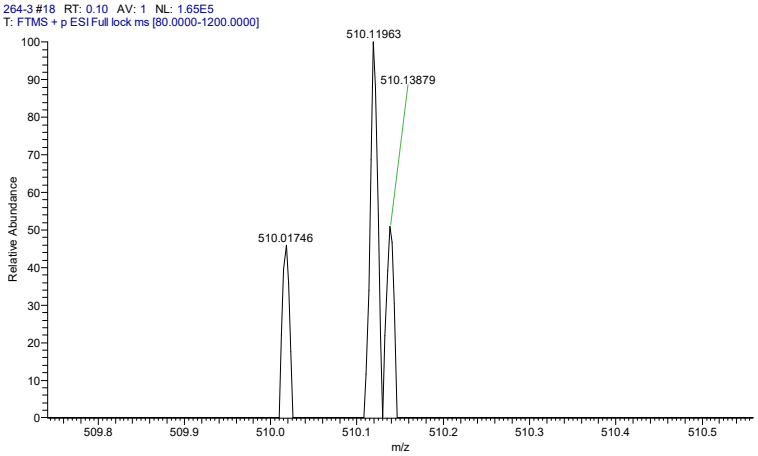

264-2 #16 RT: 0.09 AV: 1 NL: 6.39E5
T: FTMS + p ESI Full lock ms [80.0000-1200.0000]
440.15805
439.17633
438.83493
441.16193
441.29648
441.76404
Relative Abundance
m/z

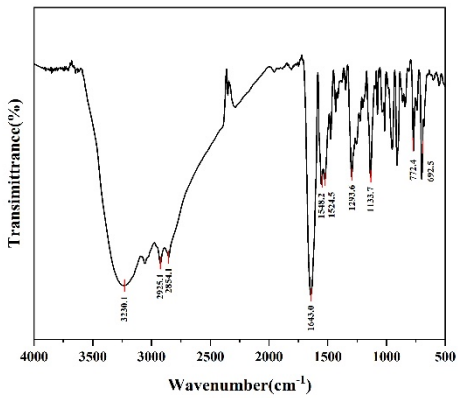


5-benzoyl-1-(3-chlorobenzyl)-*N*-(4-(hydroxycarbamoyl)benzyl)-1*H*-pyrrole-2-carboxamide (**11c**)

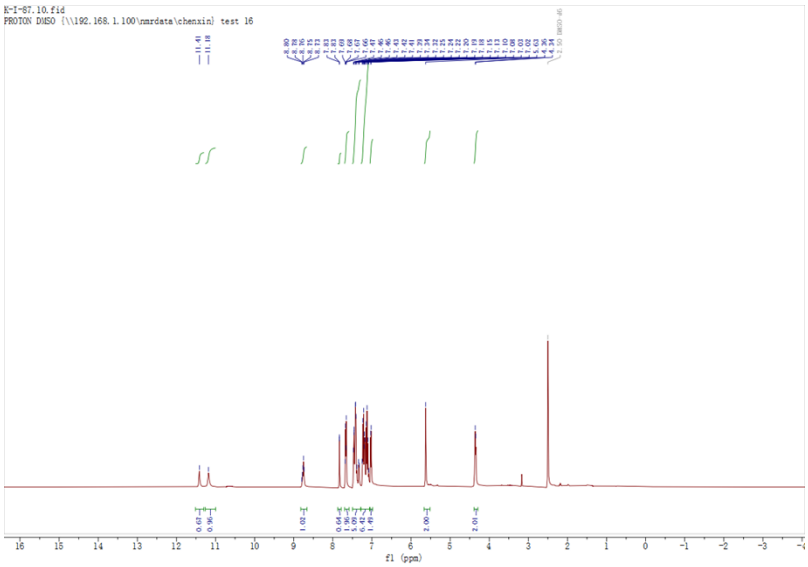


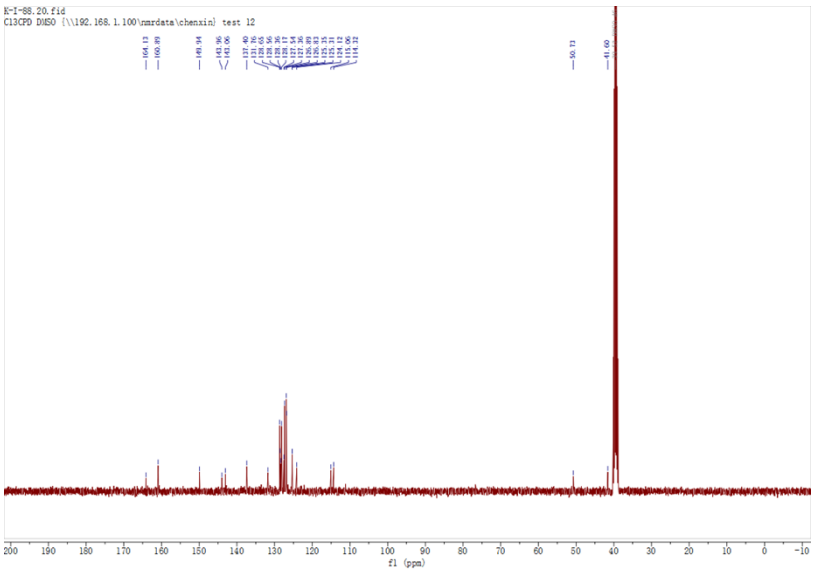


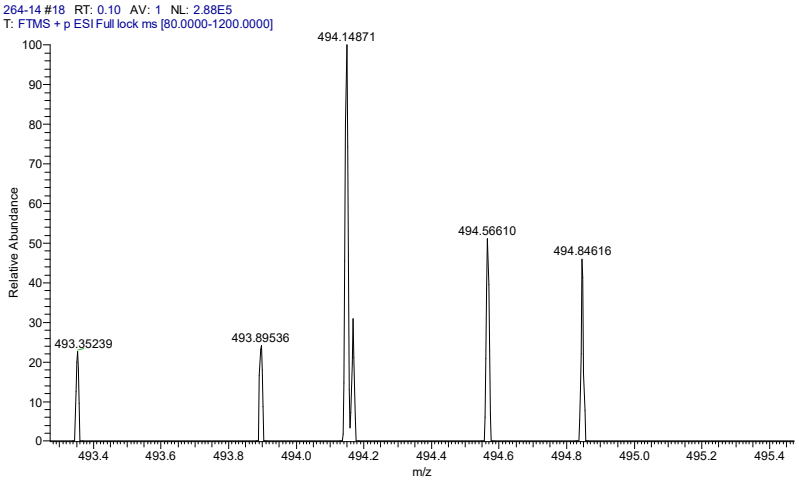


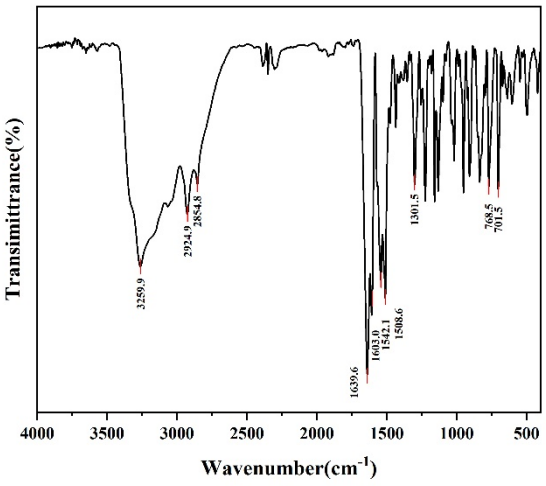


5-benzoyl-1-(4-fluorobenzyl)-*N*-(4-(hydroxycarbamoyl)benzyl)-1*H*-pyrrole-2-carboxamide (**11d**)

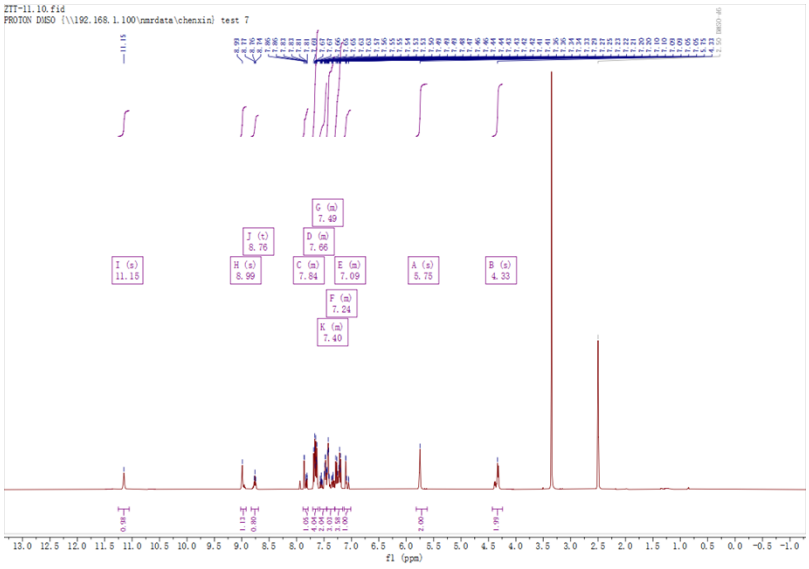


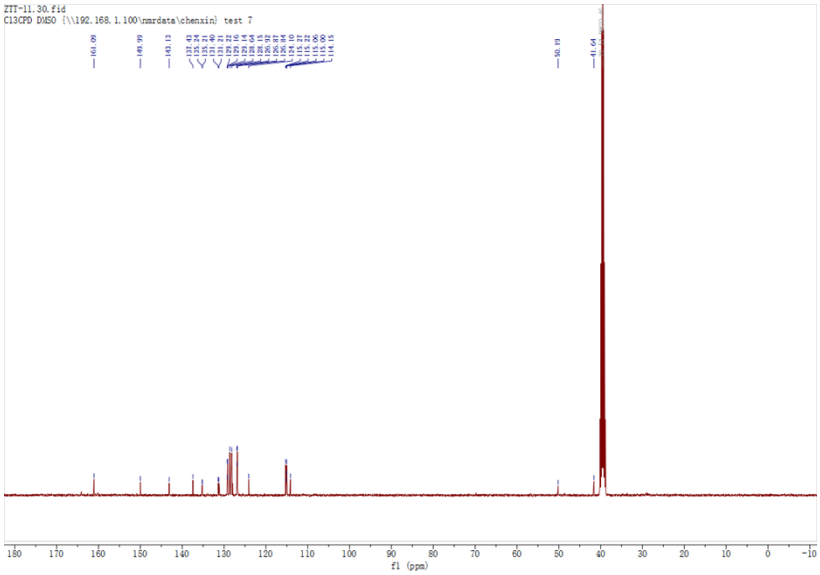




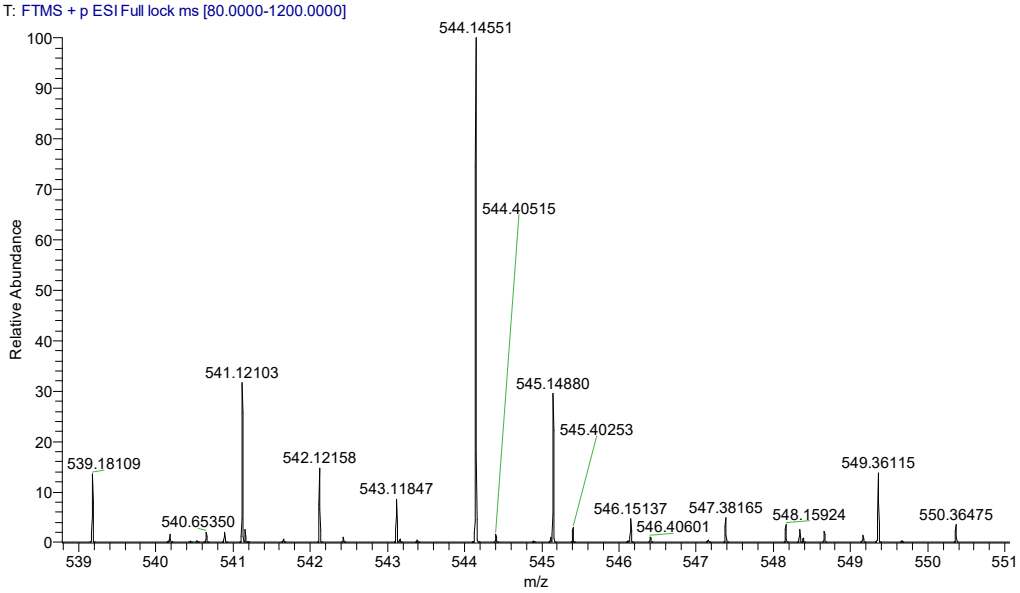


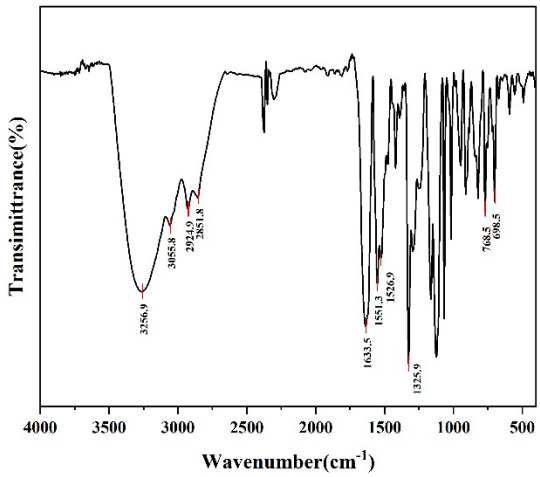
5-benzoyl-*N*-(4-(hydroxycarbamoyl)benzyl)-1-(4-(trifluoromethyl)benzyl)-1*H*-pyrrole-2-carboxamide (**11e**)



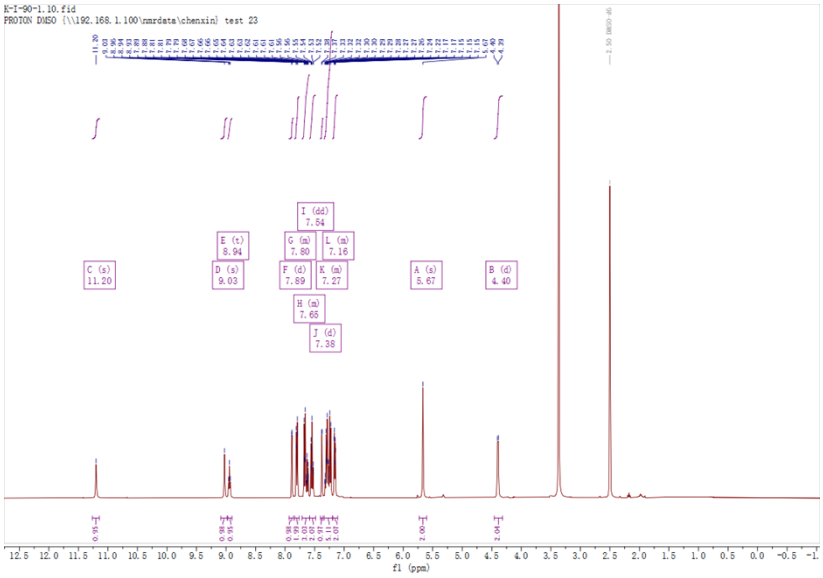


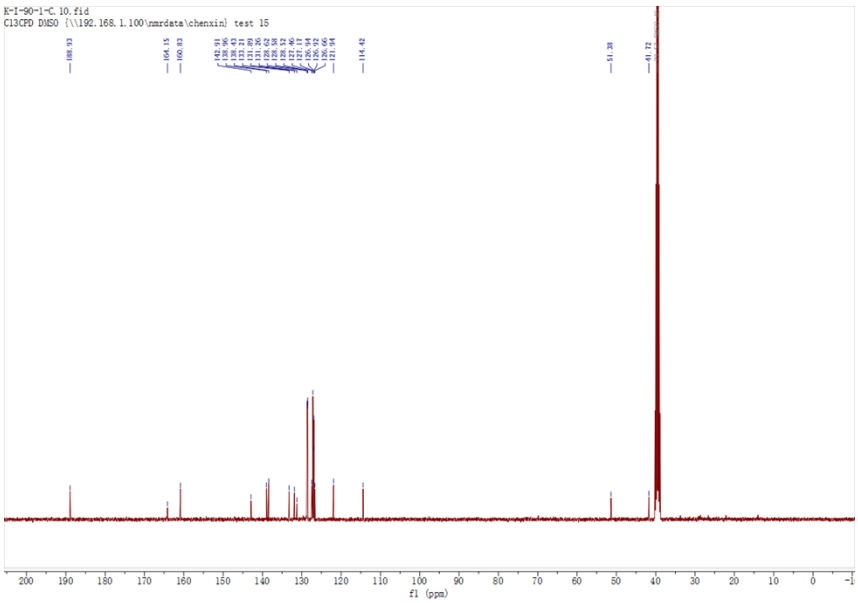
264-19 #19 RT: 0.10 AV: 1 NL: 2.76E7
T: FTMS + p ESI Full lock ms [80.0000-1200.0000]

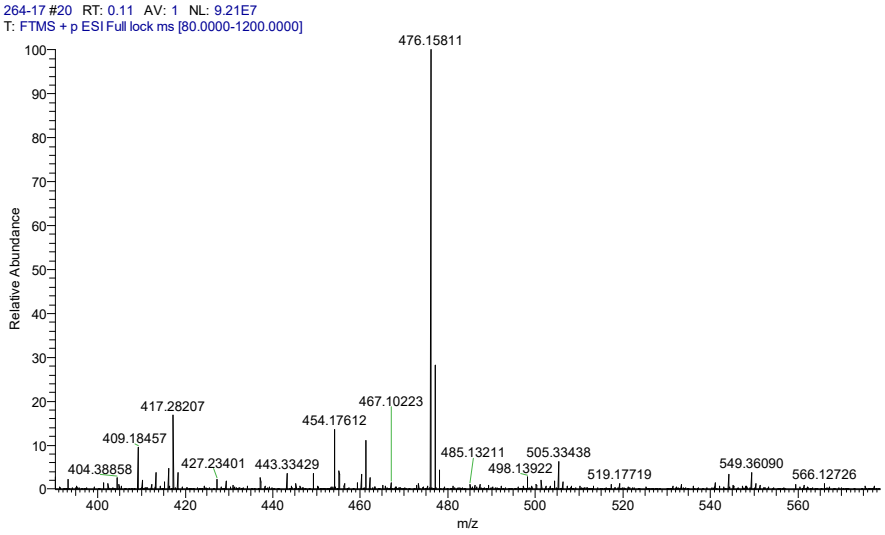


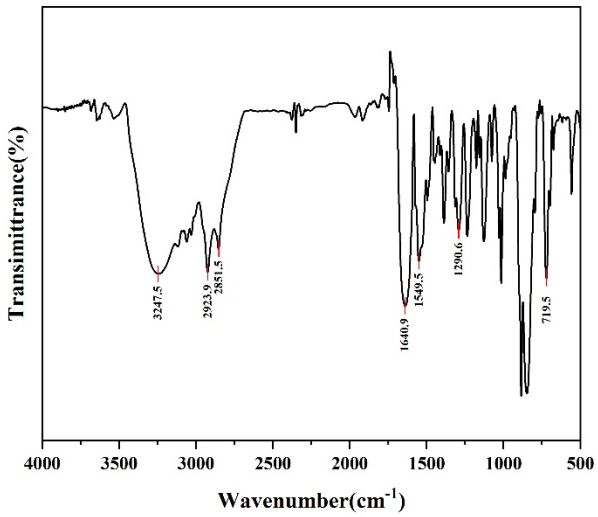


5-benzoyl-1-benzyl-*N*-(4-(hydroxycarbamoyl)benzyl)-1*H*-pyrrole-2-carboxamide (**11f**)

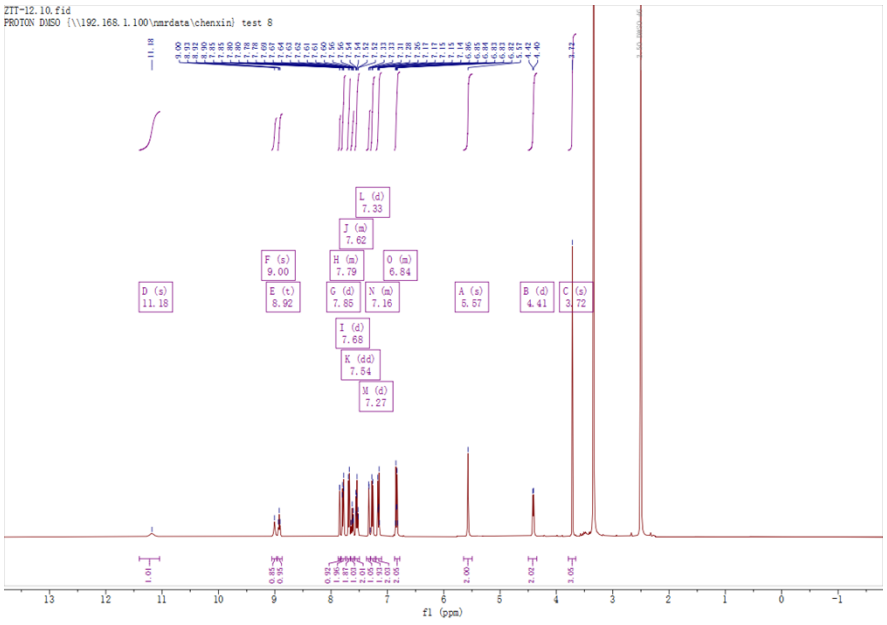


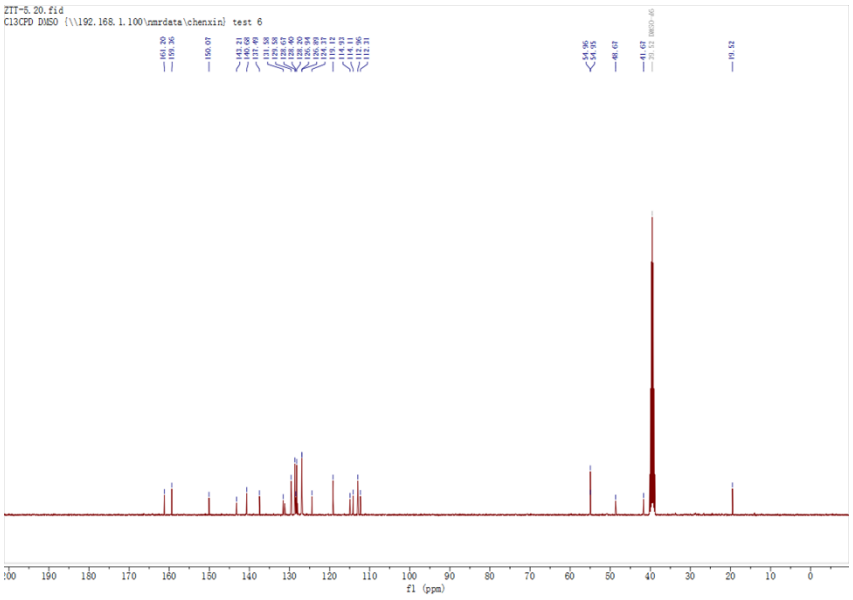


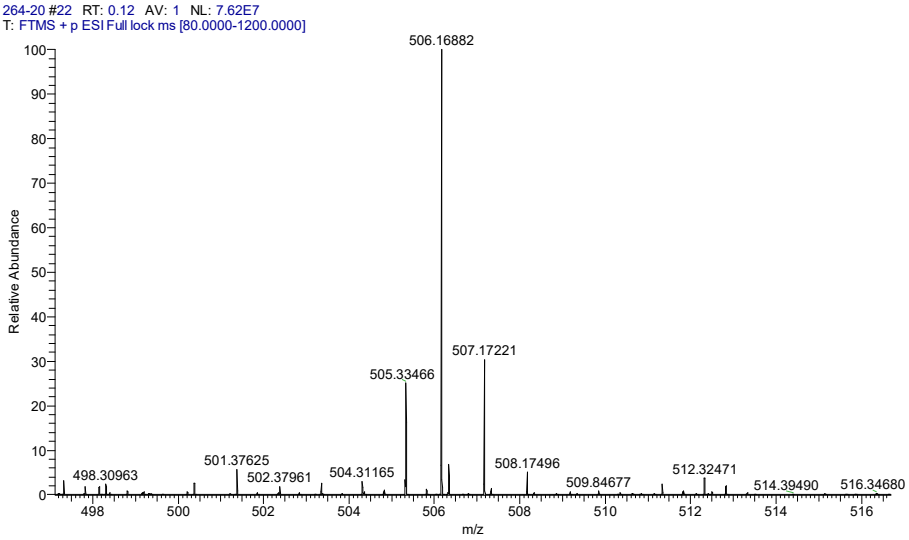


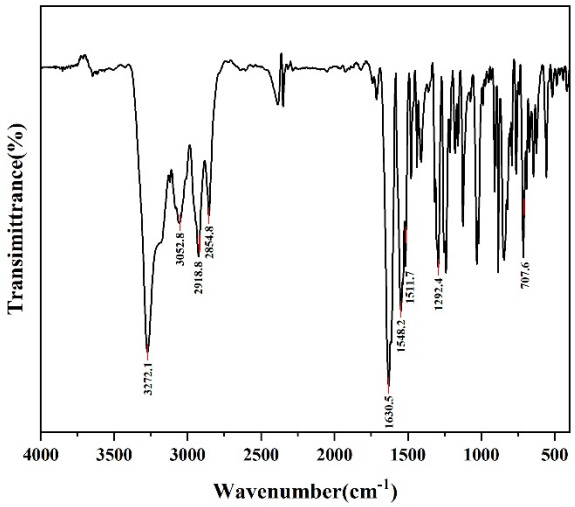


5-benzoyl-*N*-(4-(hydroxycarbamoyl)benzyl)-1-(4-methoxybenzyl)-1*H*-pyrrole-2-carboxamide (**11g**)

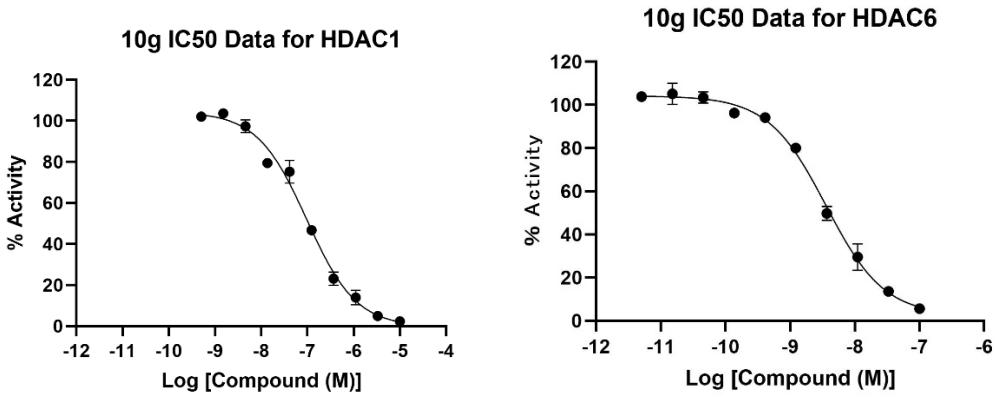



ZTT-6.20.fid
C13CPD DMSO {\\192.168.1.100\nmrdata\chenxin} test 6
f1 (ppm)

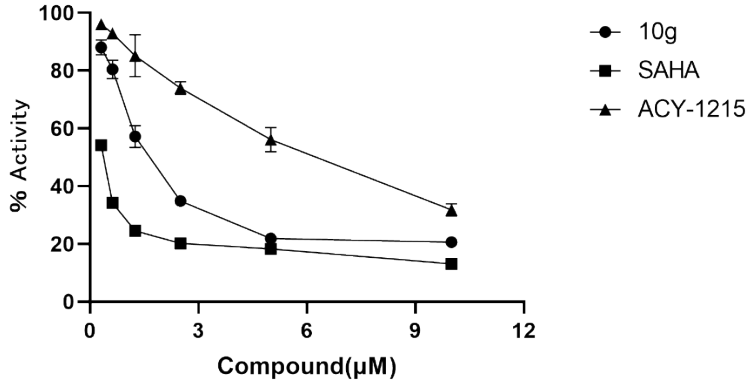

264-20 #22 RT: 0.12 AV: 1 NL: 7.62E7
T: FTMS + p ESI Full lock ms [80.0000-1200.0000]
Relative Abundance
m/z
506.16882
507.17221
505.33466
501.37625
502.37961
504.31165
498.30963
508.17496
509.84677
512.32471
514.39490
516.34680


Transimittrance(%)
Wavenumber(cm-1)
3272.1
3052.8
2918.8
2854.8
1630.5
1548.2
1511.7
1292.4
707.6

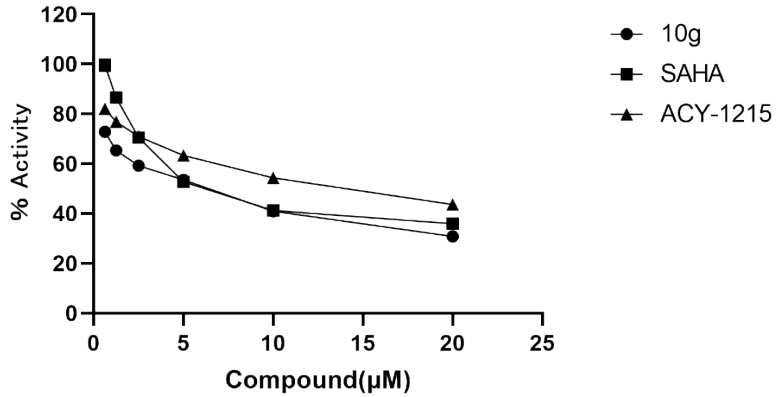
Representative graphs of enzyme activity for **10g** (RBC Company).



Antiproliferative activity graph of representative compound 10g.



Hela cell



SiHa cell