Supplementary Information

Development of Macrocyclic Peptides Containing Epoxyketone with Oral Availability as Proteasome Inhibitors

Daqiang Li,[†] Xiaotuan Zhang,[‡,∥] Xiaodong Ma,[⊥] Lei Xu,[‡,§,∥] Jianjun Yu,[†] Lixin Gao,[‡] Xiaobei Hu,[‡] Jiankang Zhang,[#] Xiaowu Dong,[†] Jia Li,[‡] Tao Liu,[*,†] Yubo Zhou,[*,‡] Yongzhou Hu[*,†]

[†]*ZJU-ENS Joint Laboratory of Medicinal Chemistry, Zhejiang Province Key Laboratory of Anti-Cancer Drug Research, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, 310058, People's Republic of China*

[‡]*National Center for Drug Screening, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China*

[§]*School of Life Science and Technology, ShanghaiTech University, Shanghai, 201203, China*

[∥]*University of Chinese Academy of Sciences, Graduate School, No. 19A Yuquan Road, Beijing, China*

[⊥] *Department of Medicinal Chemistry, School of Pharmacy, Anhui University of Chinese Medicine, Hefei 230031, China*

[#]*Zhejiang University City College, Hangzhou 310015, Zhejiang, China*

Supporting Information

1. HPLC analysis of final compounds……S3-S4

2. ^{13}C NMR Spectrums……S5-S19

3. HPLC Spectrums……S20-S27

HPLC analysis of final compounds

System: Agilent 1260 Series

Mobile phase: Mobile phase A: H_2O, Mobile phase B: MeCN

Detector: UV at 254 nm (220 nm for **24r**)

Column: Cosmosil 5C18-AR-II column (4.6 mm i.d. × 250 mm)

Flow rate: 0.8 mL/min

Using the listed gradients:

t/min	Mobile phase A	Mobile phase B
0	60%	40%
5	60%	40%
10	40%	60%
18	40%	60%
19	10%	90%
25	10%	90%
26	60%	40%
28	60%	40%

Purity of all final compounds

Compound	Purity / %	Retention time / min
24a	95.0	10.751
24b	95.8	17.597
24c	98.8	20.826
24d	97.3	23.682
24e	97.5	24.662
24f	96.7	25.743
24g	98.9	23.148
24h	95.8	21.528

24i	96.4	22.173
24j	98.2	20.495
24k	97.2	23.204
24l	98.7	24.259
24m	95.0	23.982
24n	99.1	15.056
24o	98.6	26.231
24p	98.7	13.224
24q	98.3	18.830
24r	97.7	15.794
24s	95.7	17.945
24t	96.3	9.847
24u	95.2	16.118
24v	95.9	9.317
24w	99.4	18.552
24x	95.5	17.052
24y	96.8	17.596
24z	95.4	18.717
24za	99.3	21.287
24zb	95.5	23.365
30a	95.7	16.689
30b	97.2	16.243

^{13}C NMR Spectrums:

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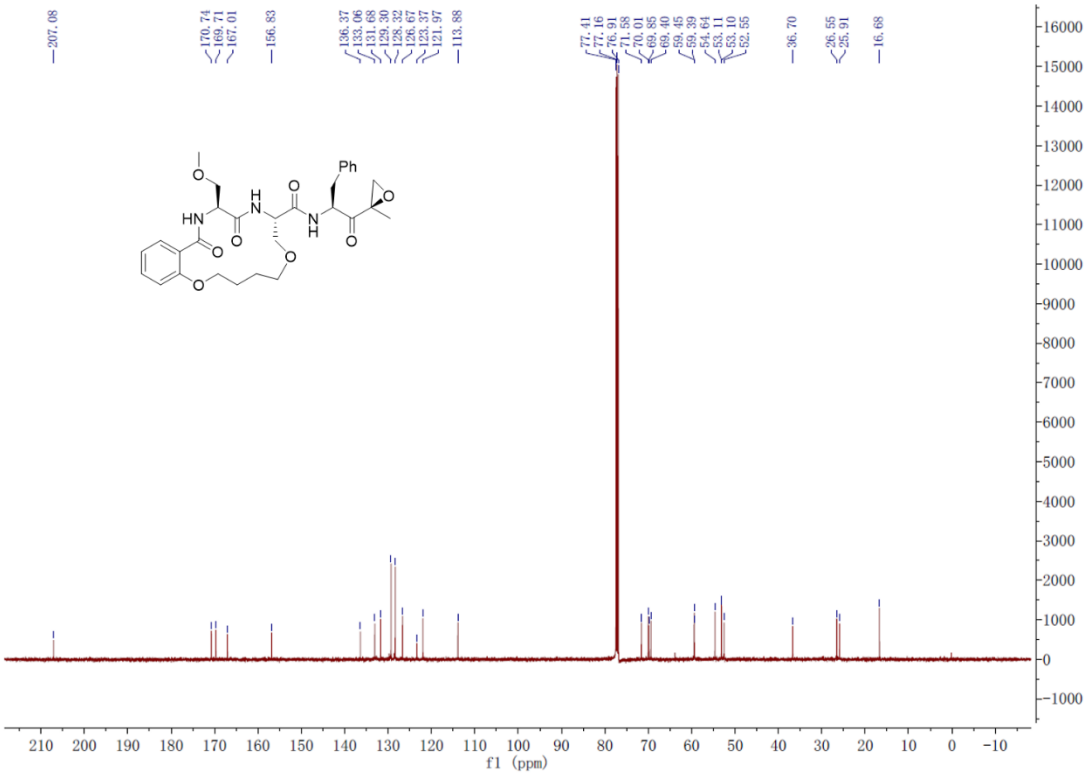

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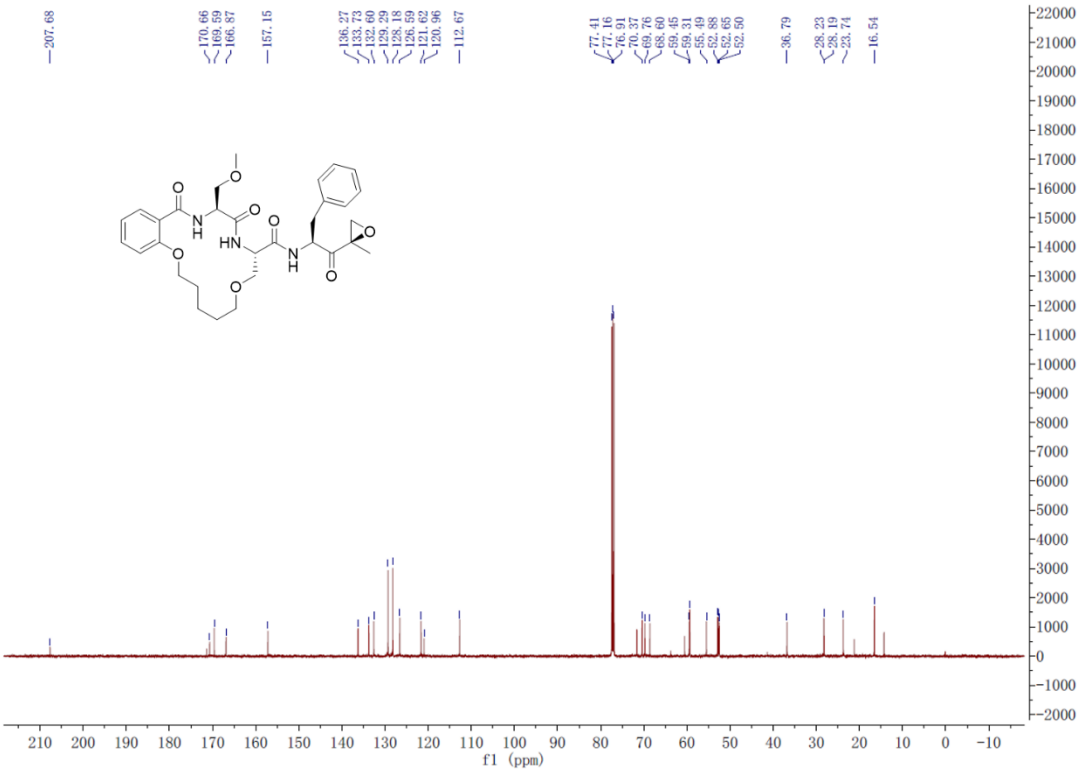

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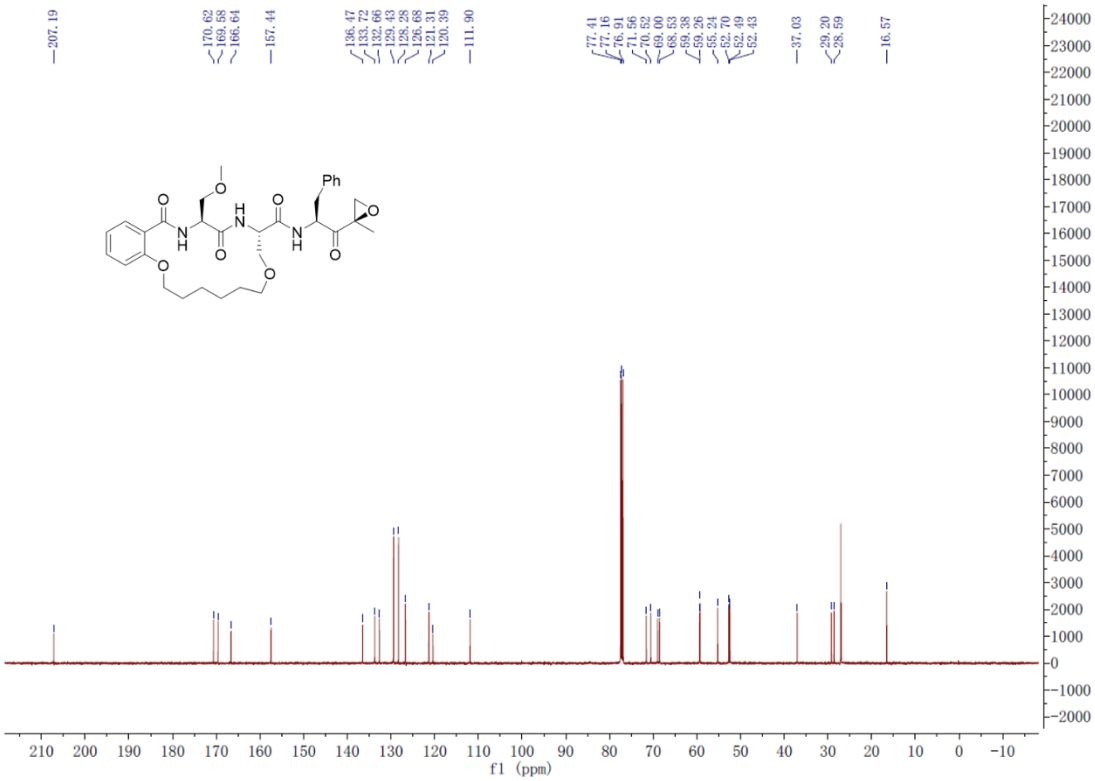
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f1 (ppm)

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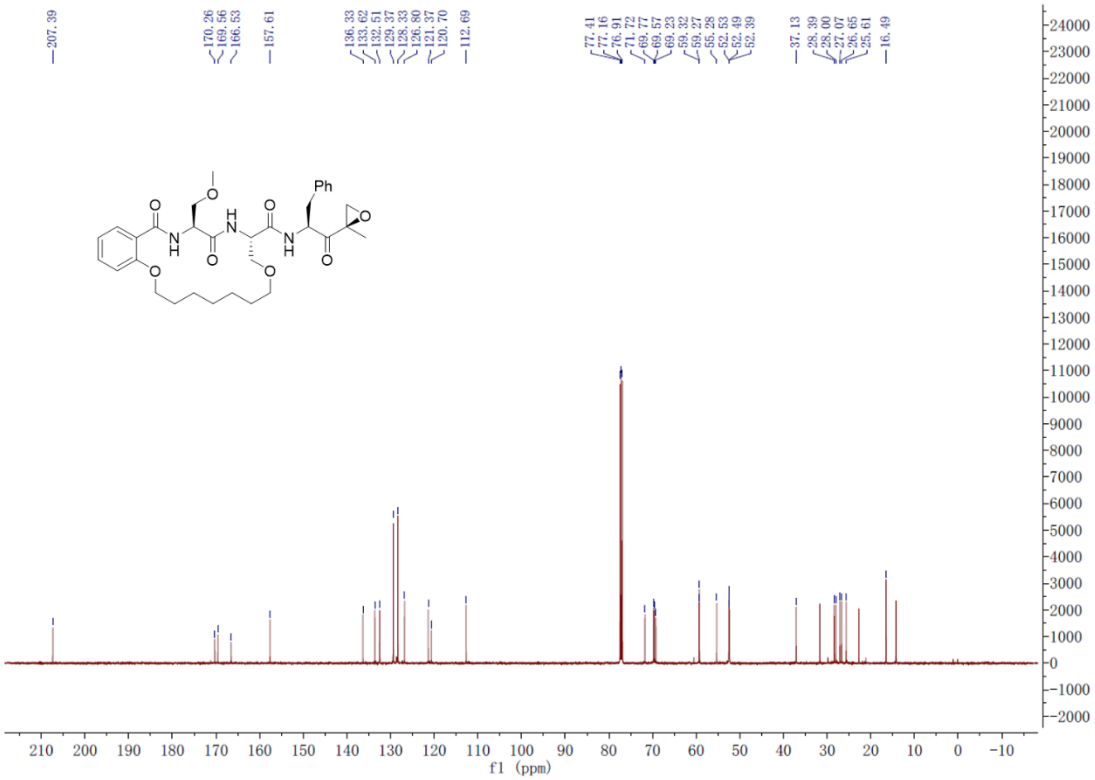
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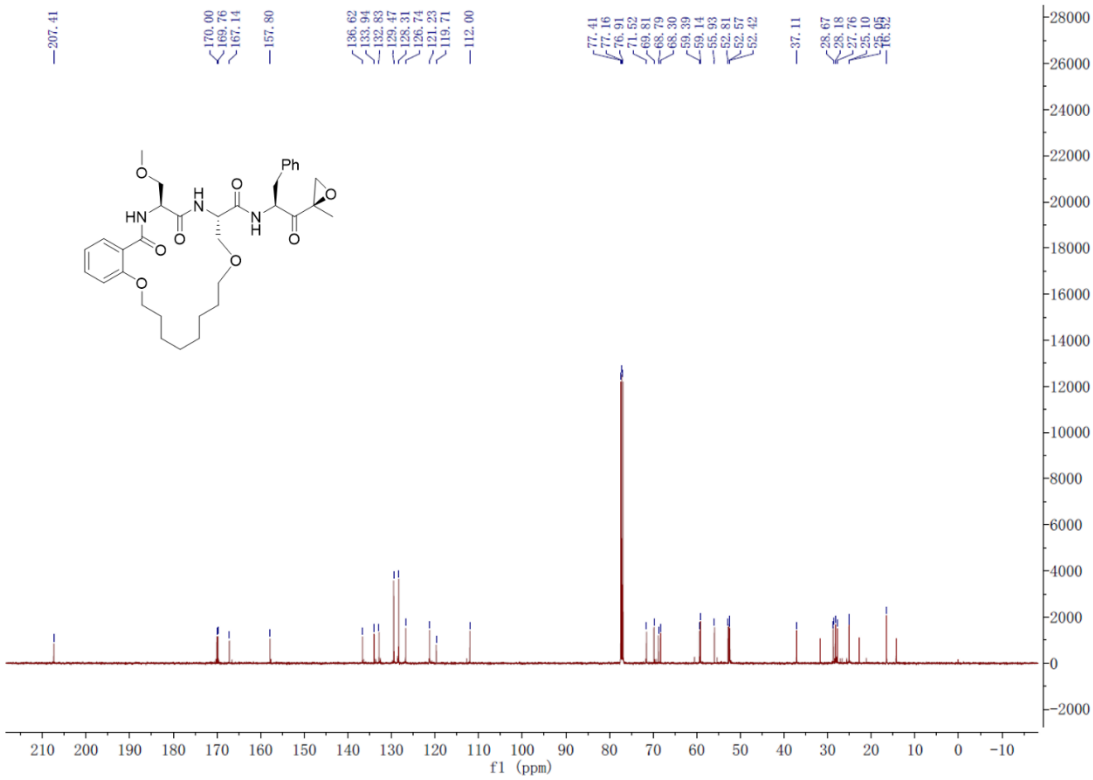
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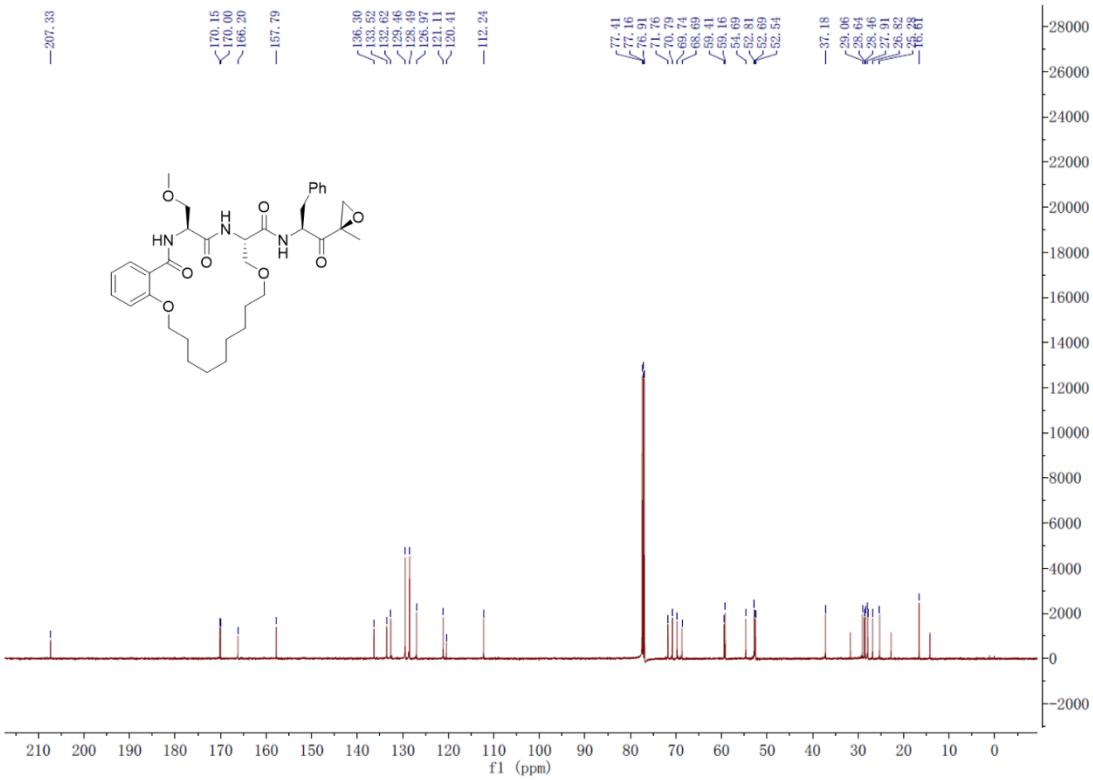
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f1 (ppm)

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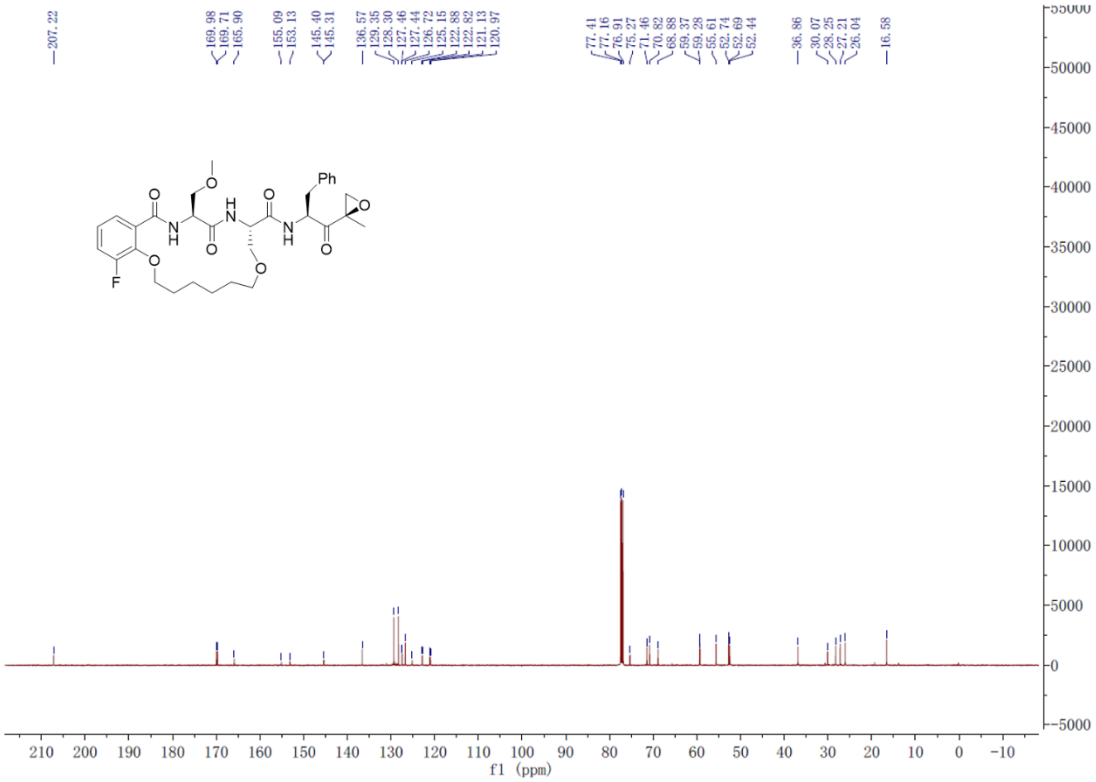
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Ph
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f1 (ppm)

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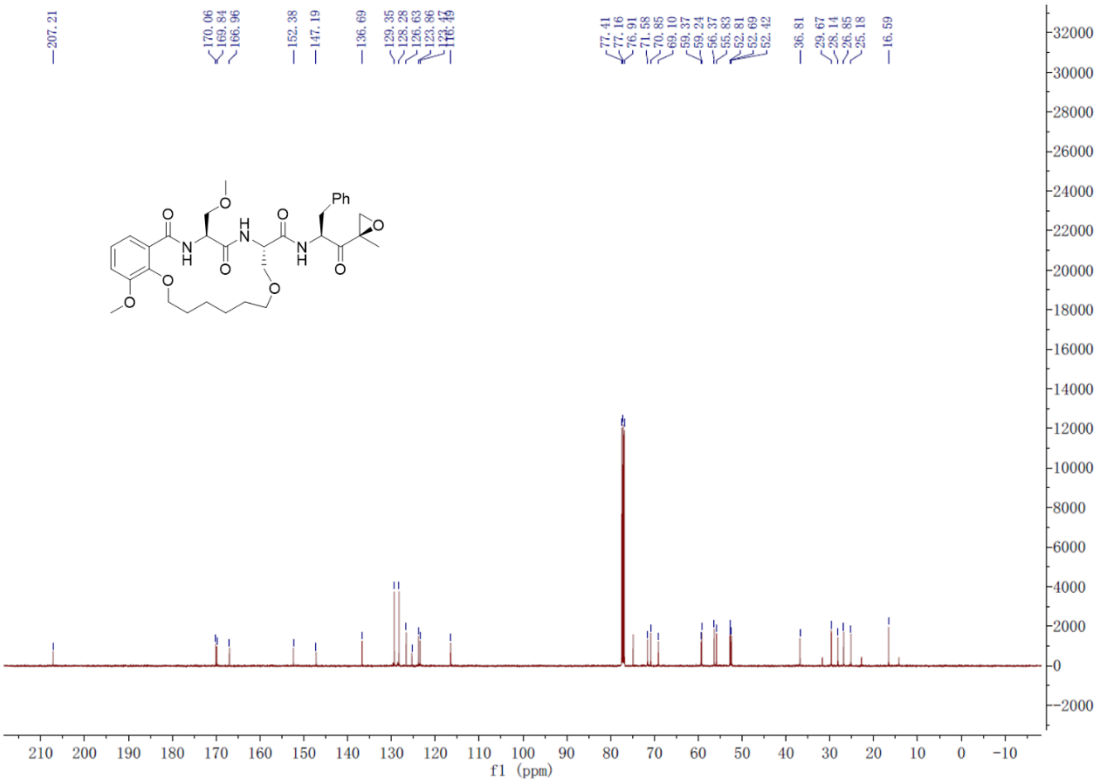
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Ph
f1 (ppm)

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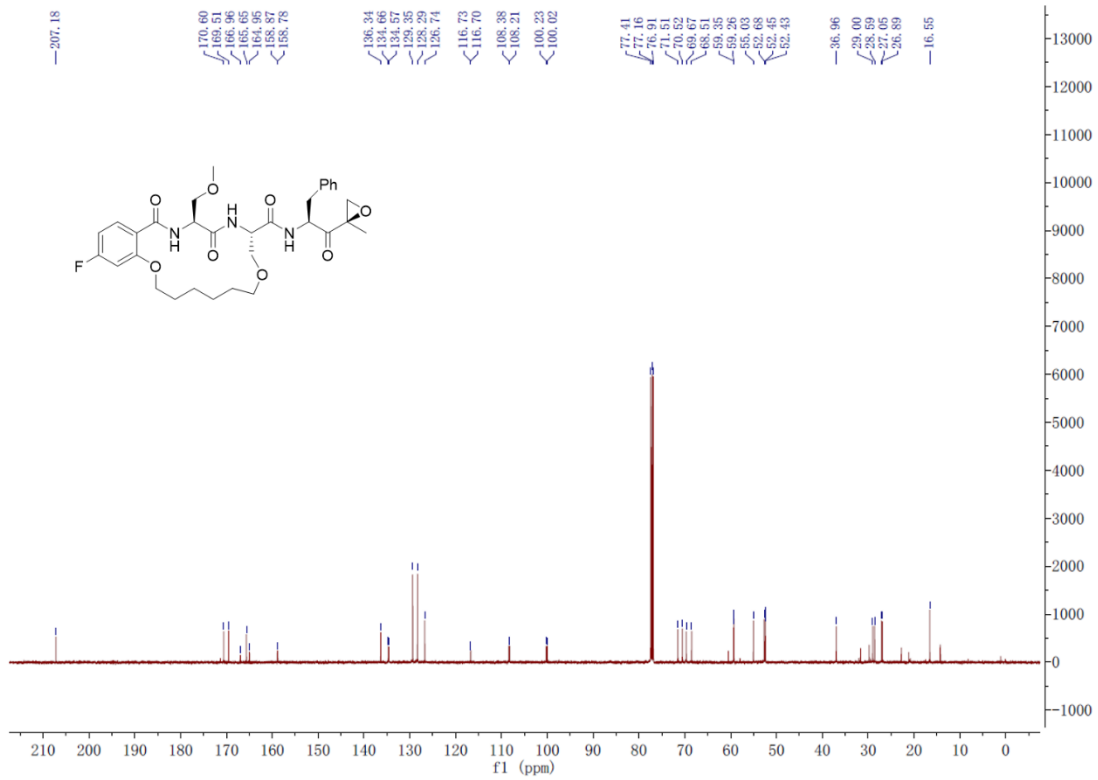
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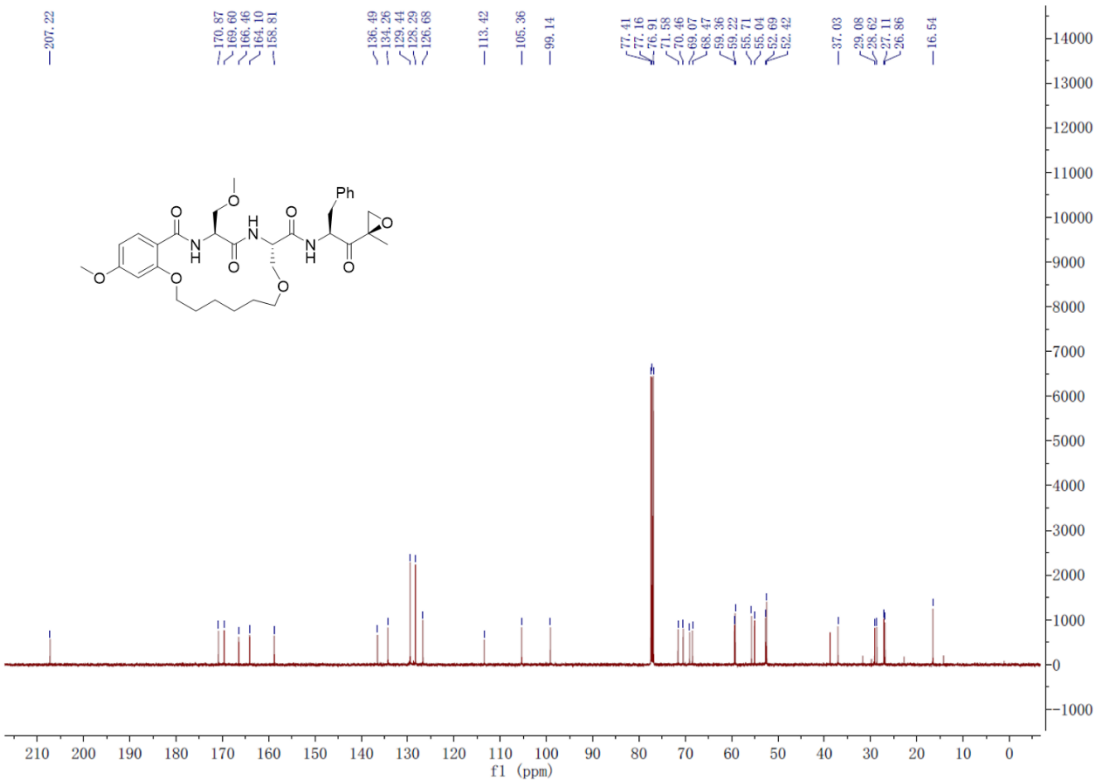
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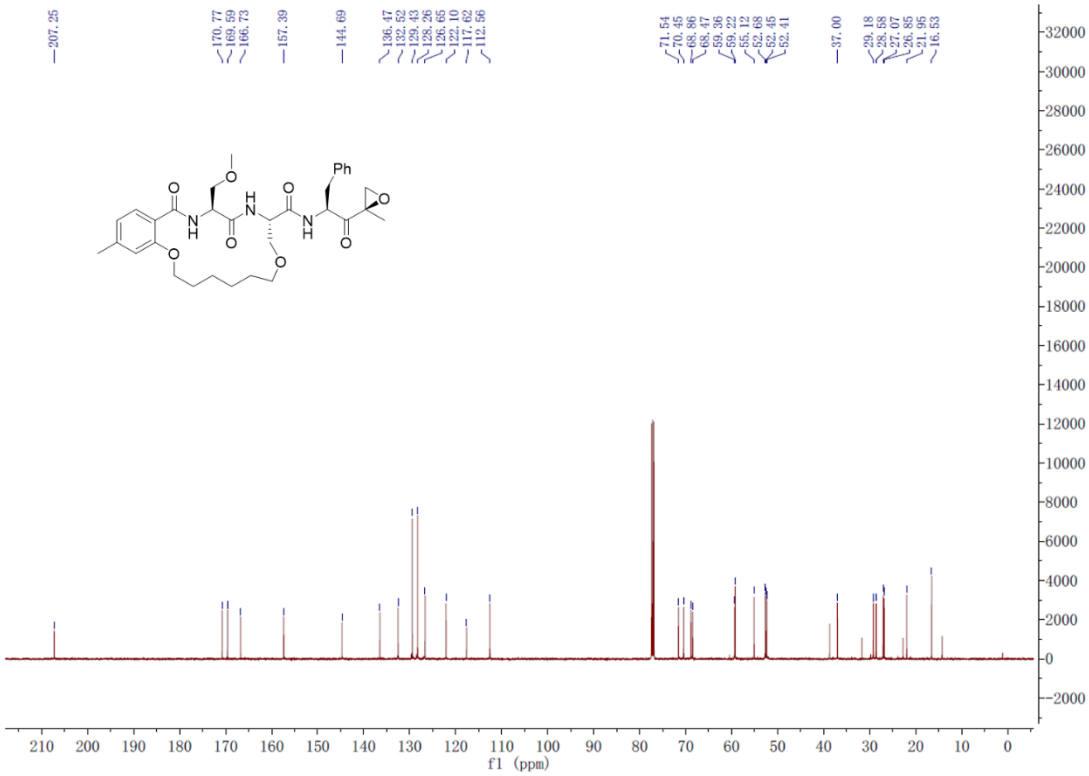
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Ph
f1 (ppm)

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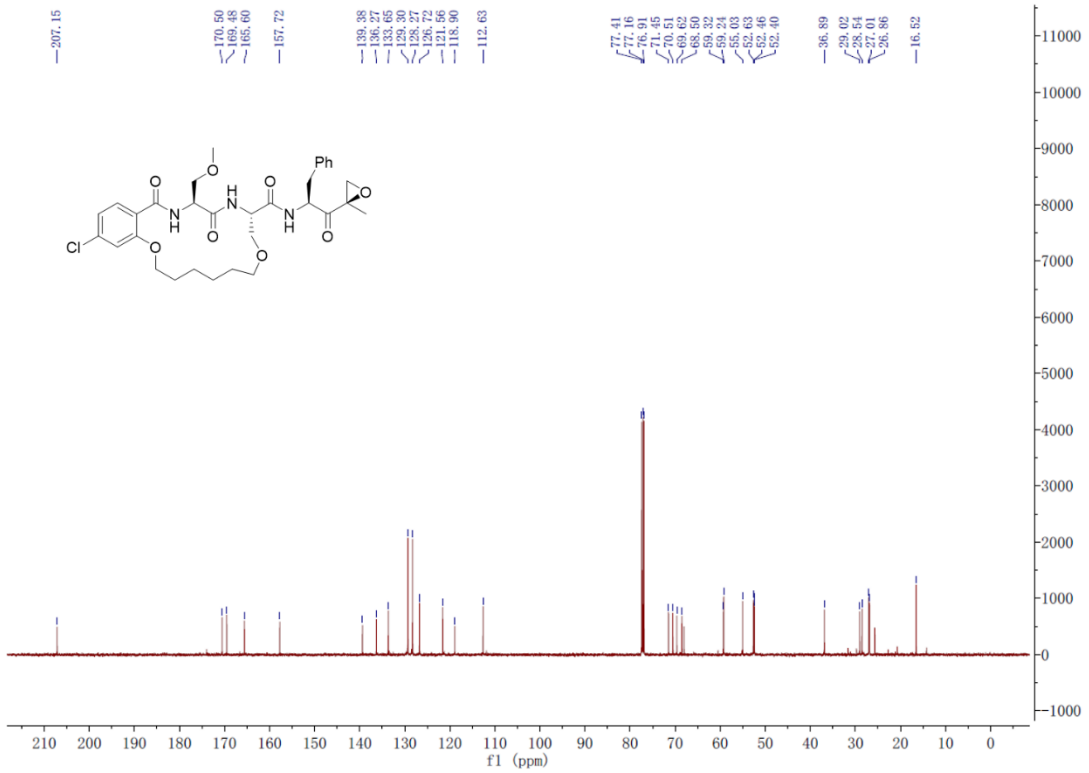
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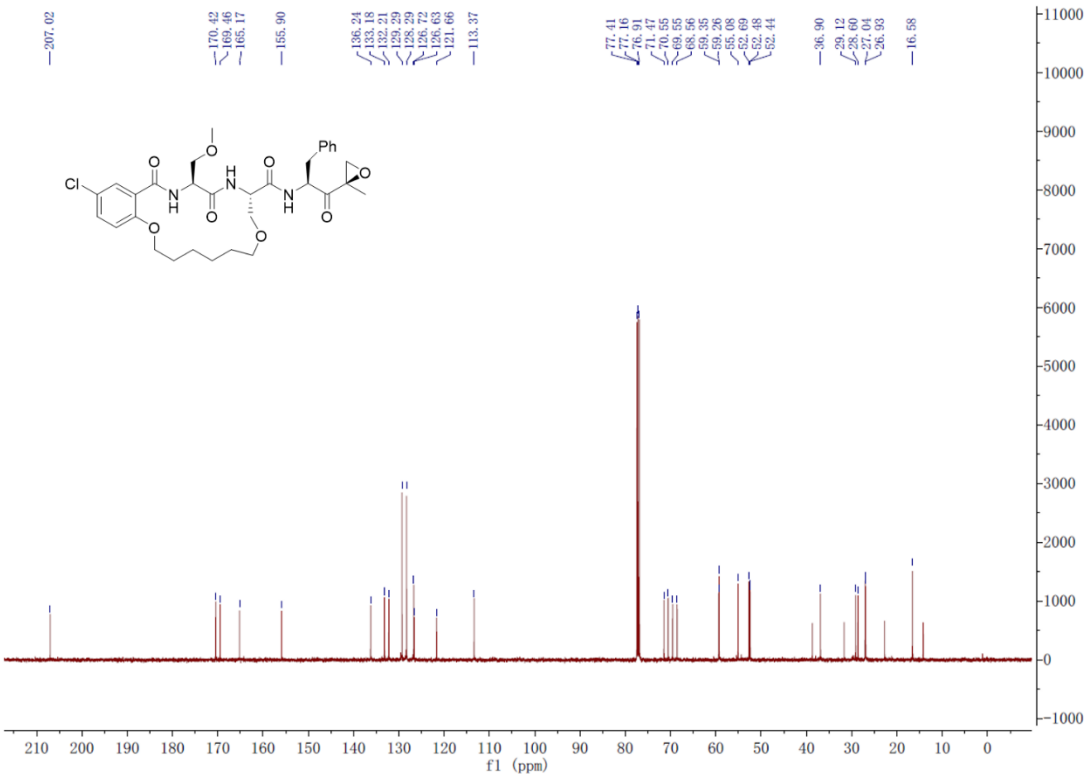
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Ph
f1 (ppm)

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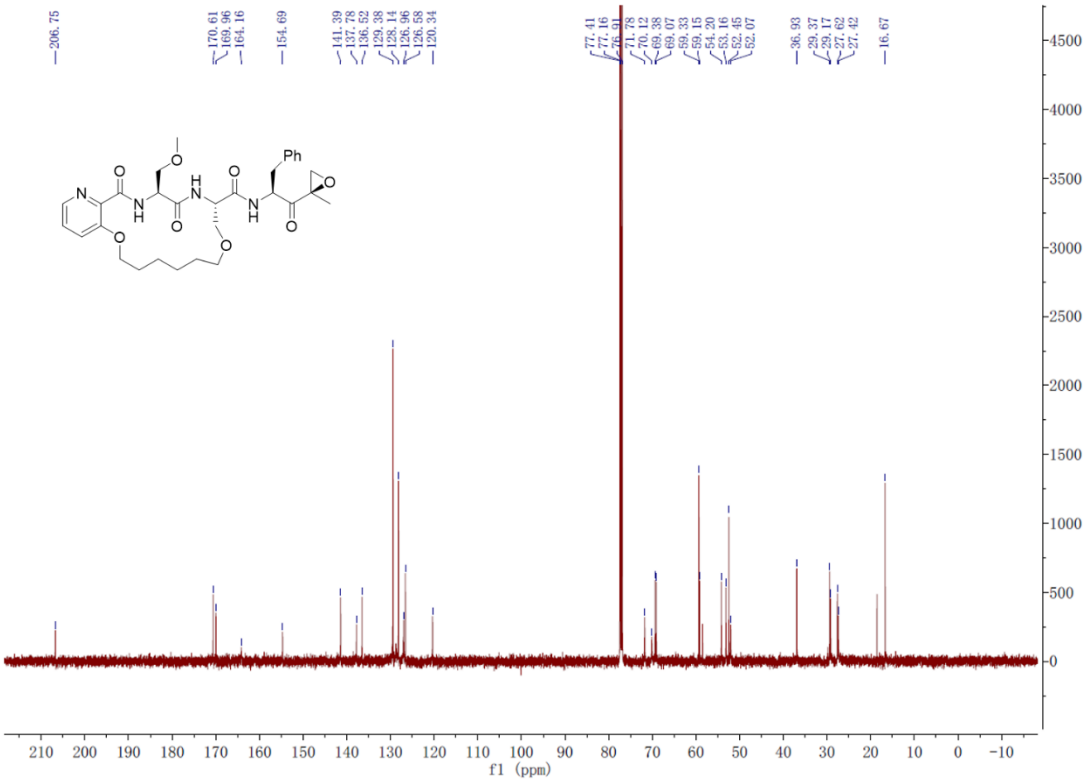
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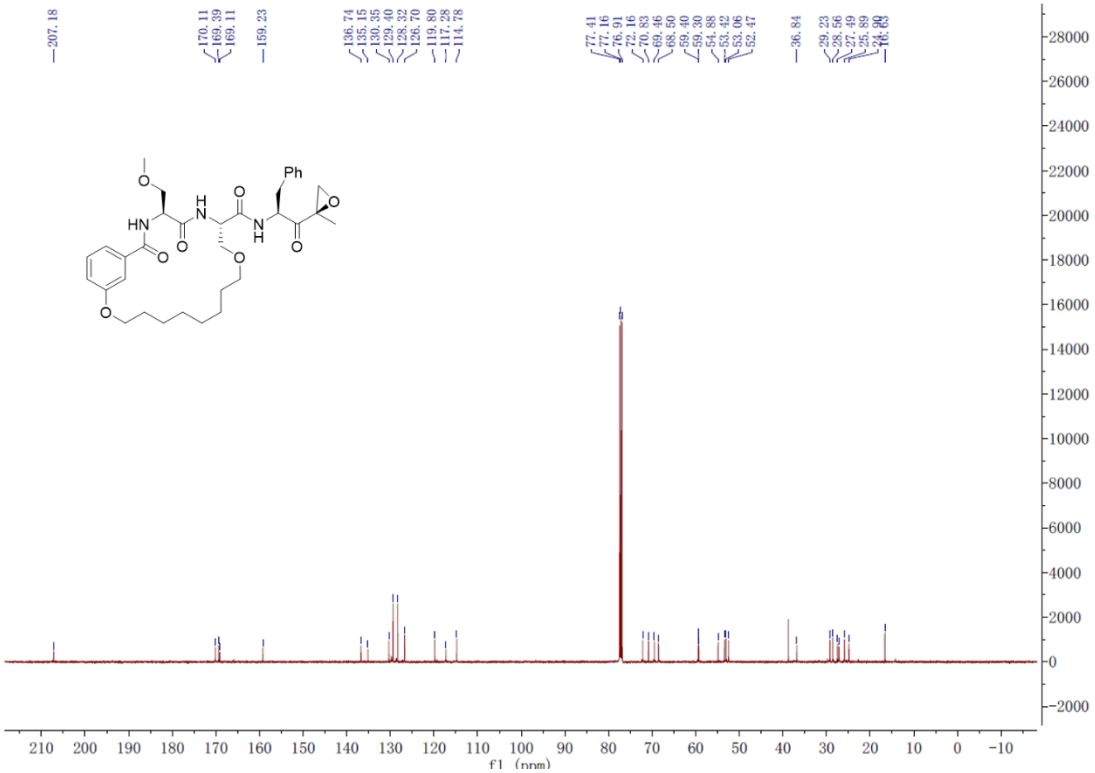
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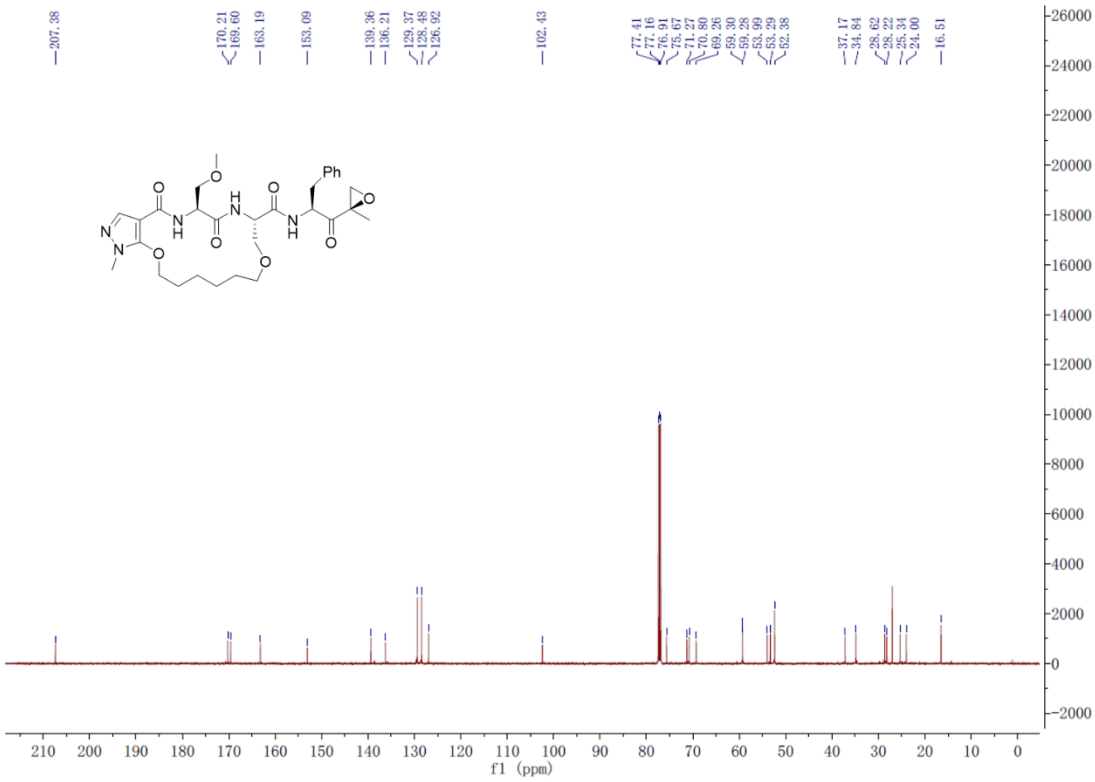
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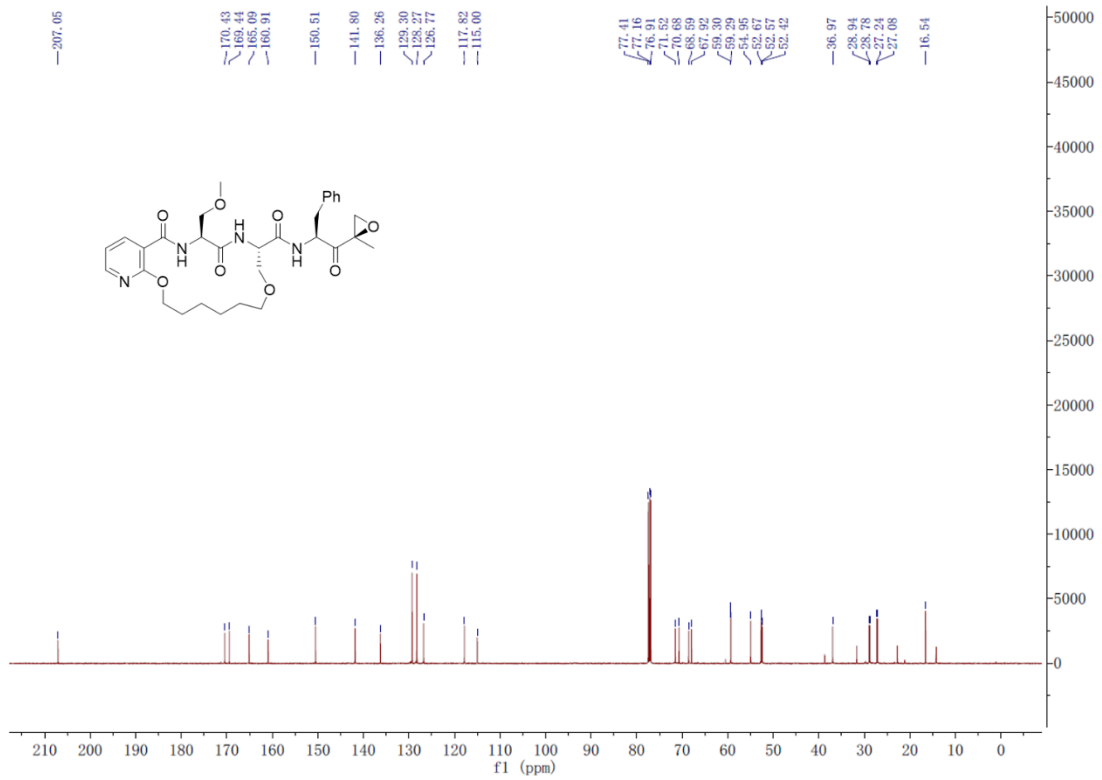
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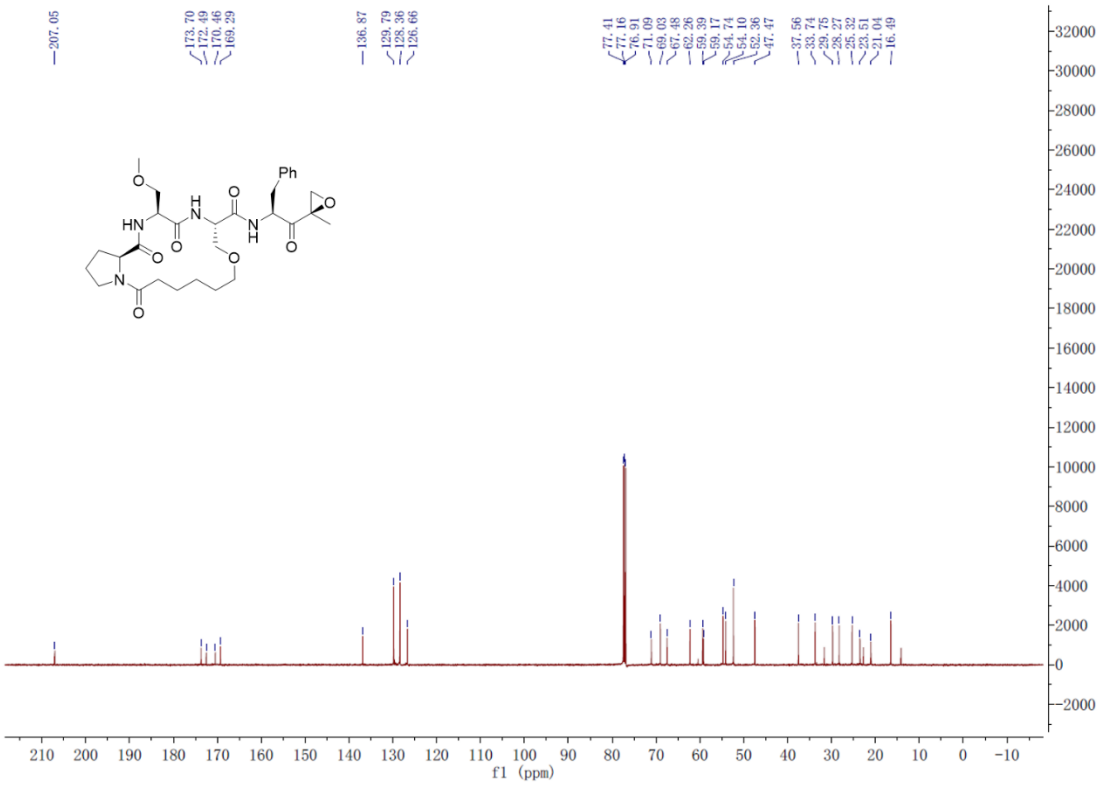
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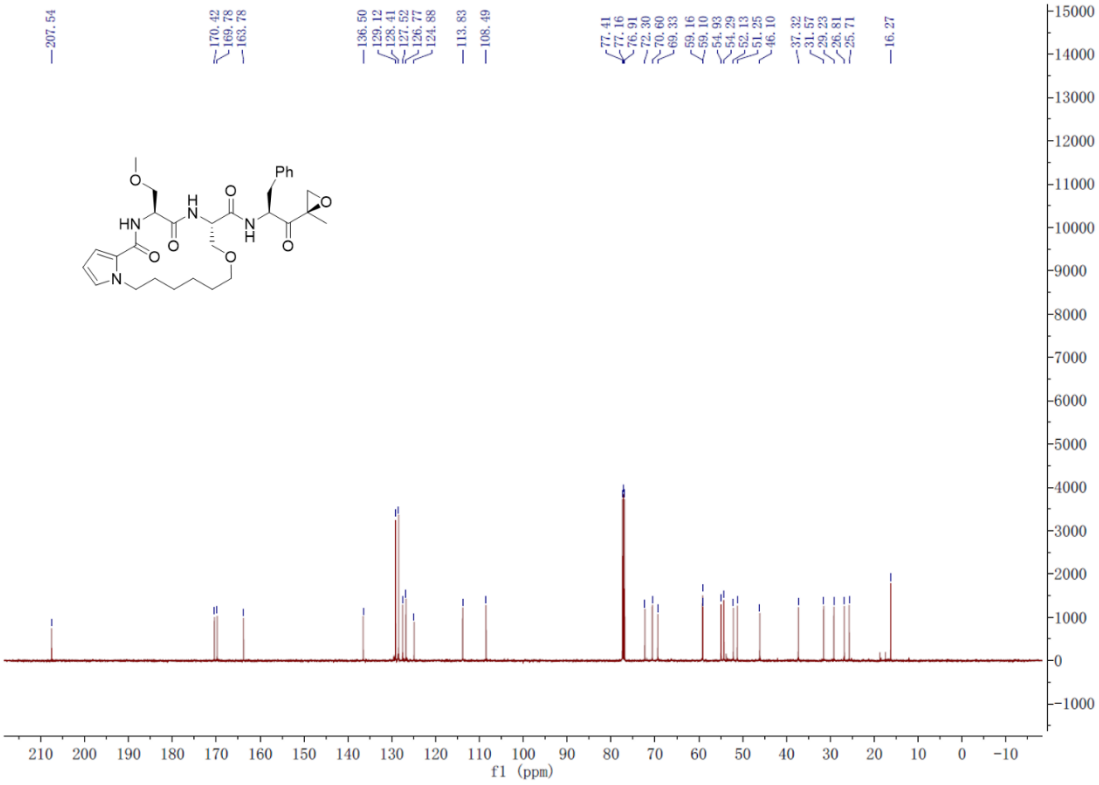
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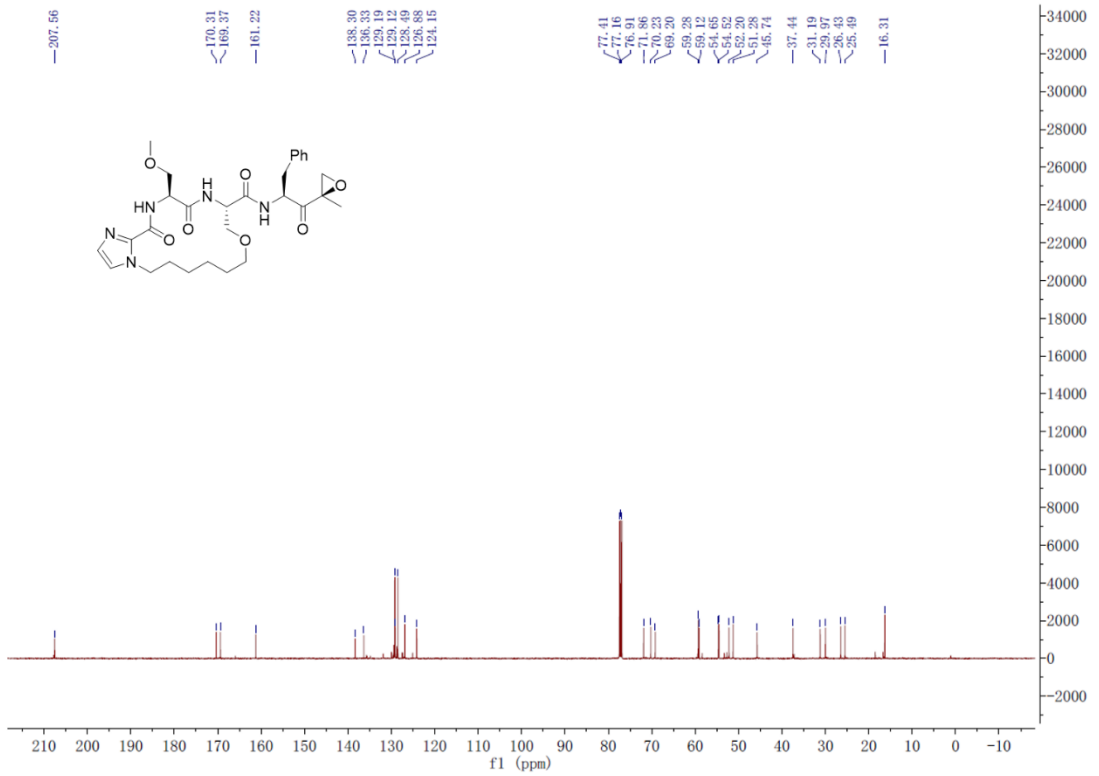
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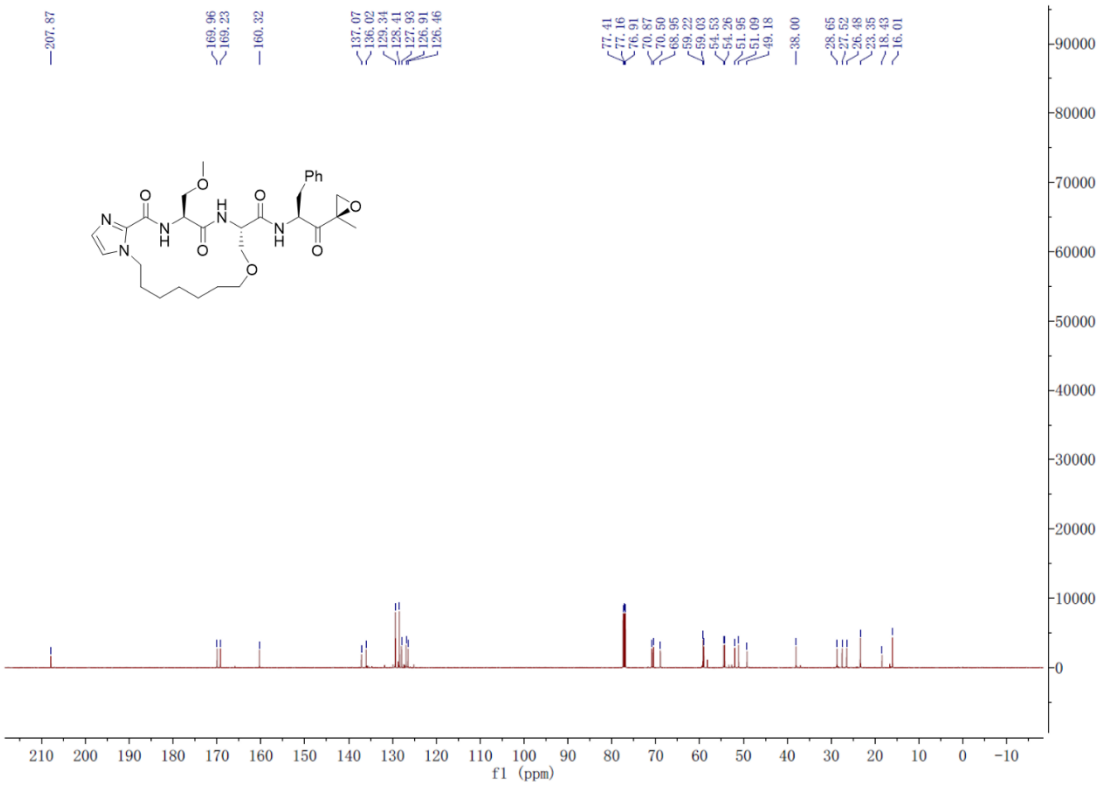
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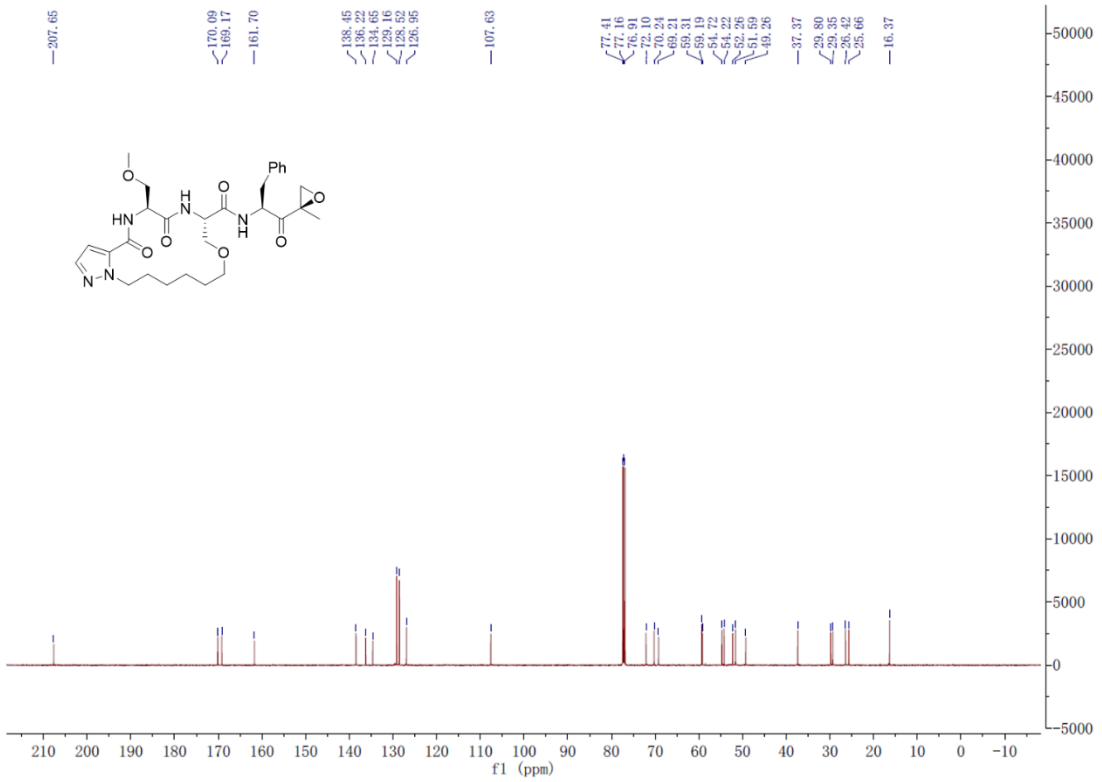
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f1 (ppm)

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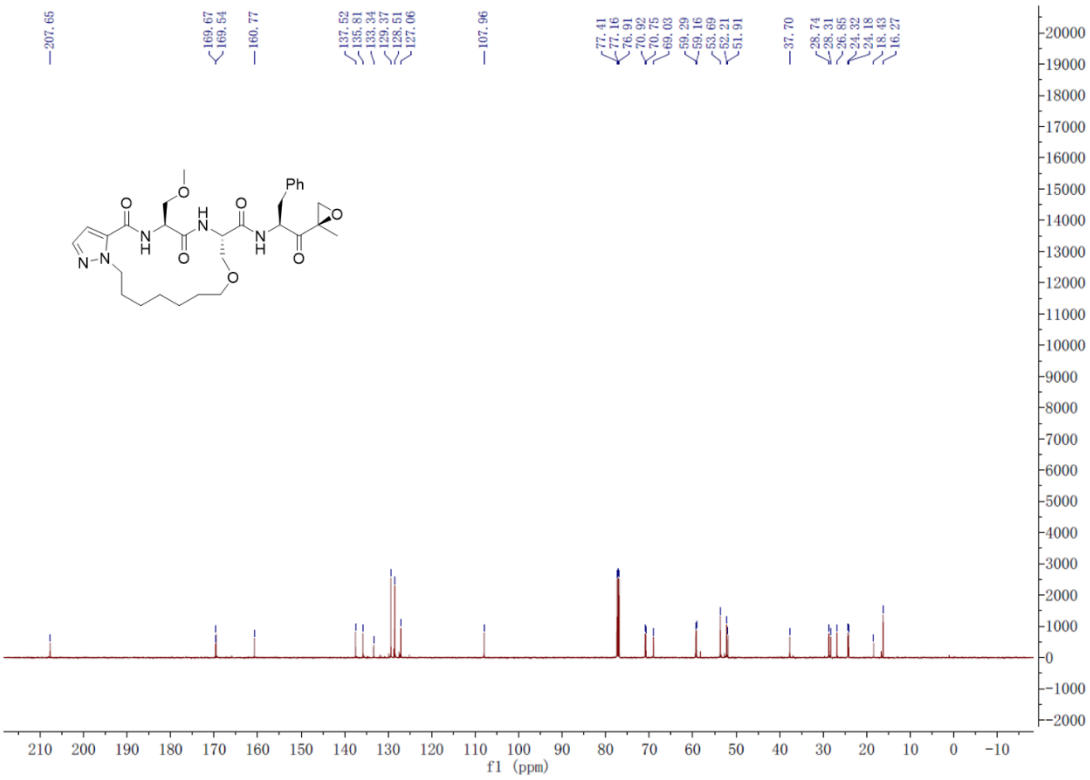
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Ph
f1 (ppm)

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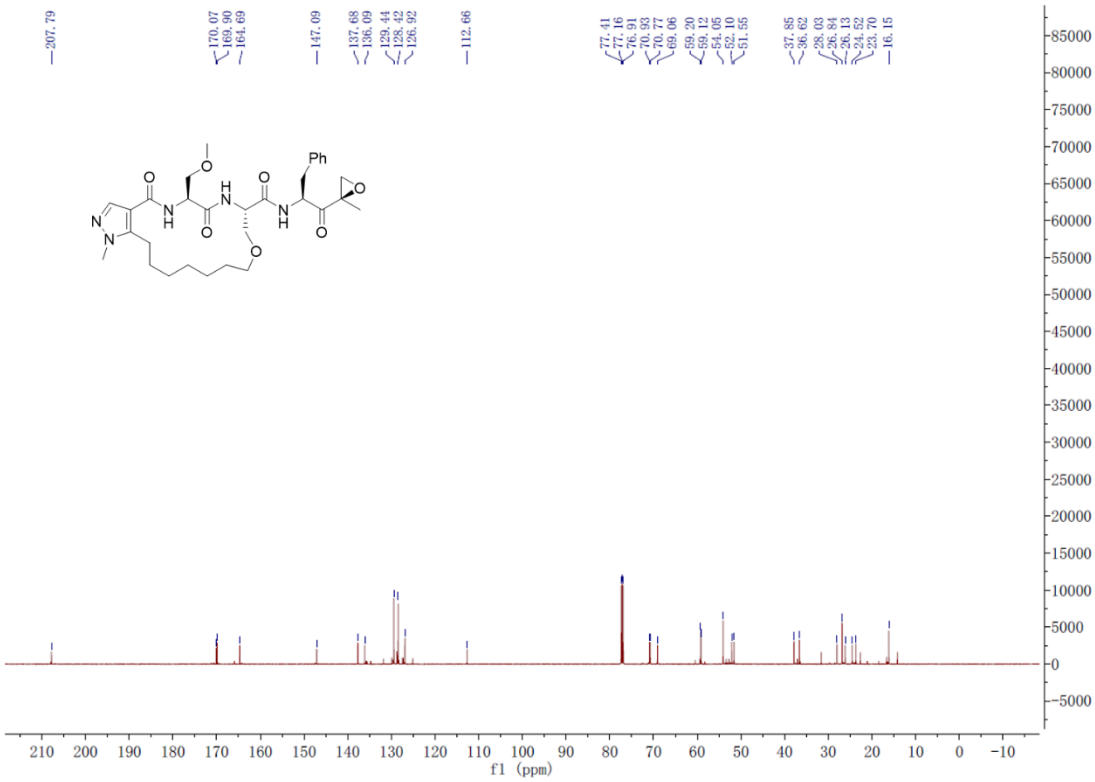
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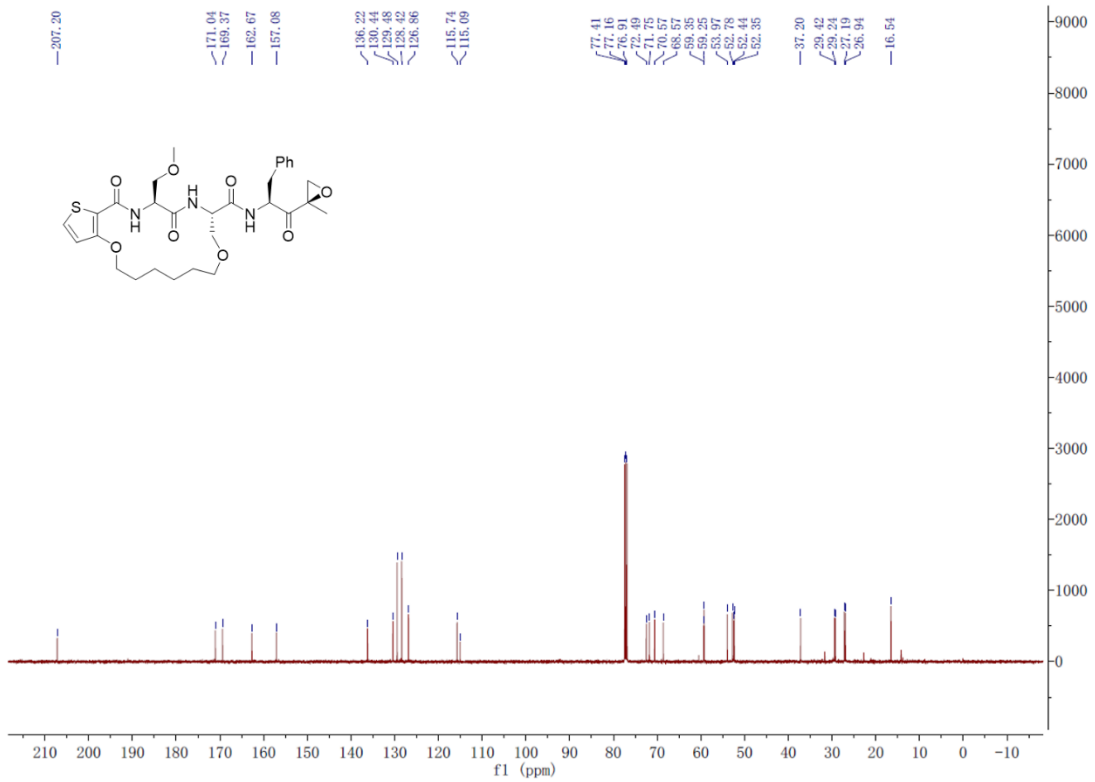
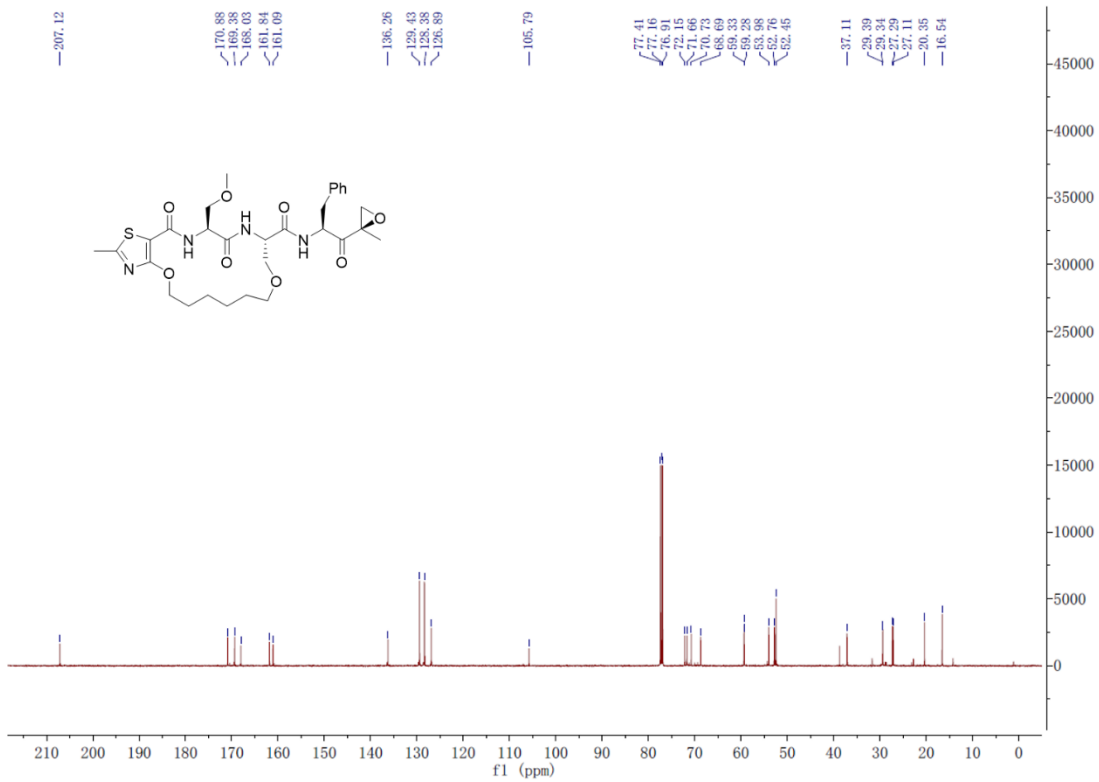
70.77
69.06
59.20
59.12
54.05
52.10
51.55
37.85
36.62
28.03
26.84
26.13
24.52
23.70
16.15
Ph
f1 (ppm)

24y:


207.20
171.04
169.37
162.67
157.08
136.22
130.44
129.48
128.42
126.86
115.74
115.09
77.41
77.16
76.91
72.49
71.75
70.57
68.57
59.35
59.25
53.97
52.78
52.44
52.35
37.20
29.42
29.24
27.19
26.94
16.54
f1 (ppm)

24z: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161.84
161.09
136.26
129.43
128.38
126.89
105.79
77.41
77.16
76.91
72.15
71.66
70.73
68.69
59.33
59.28
53.98
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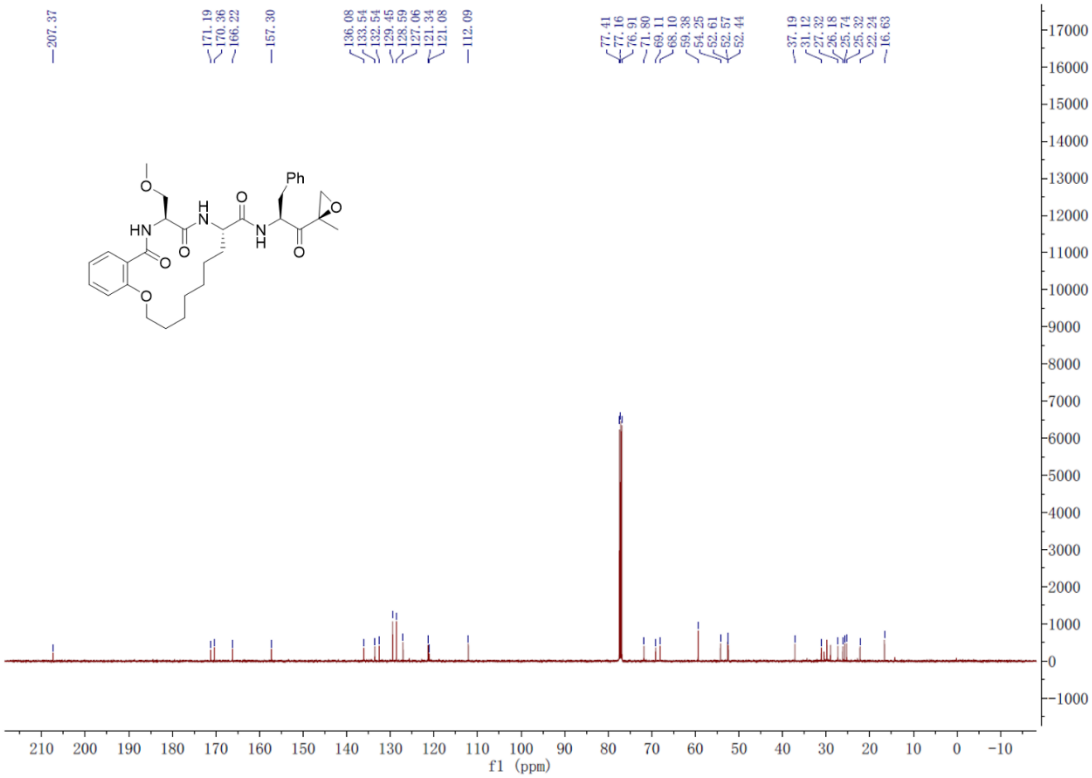
52.45
37.11
29.39
29.34
27.29
27.11
20.35
16.54
f1 (ppm)

24za: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171.19
170.36
166.22
157.30
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133.54
132.54
129.45
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127.06
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121.08
112.09
77.41
77.16
76.91
71.80
69.11
68.10
59.38
54.25
52.61
52.57
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27.32
26.18
25.74
25.32
22.24
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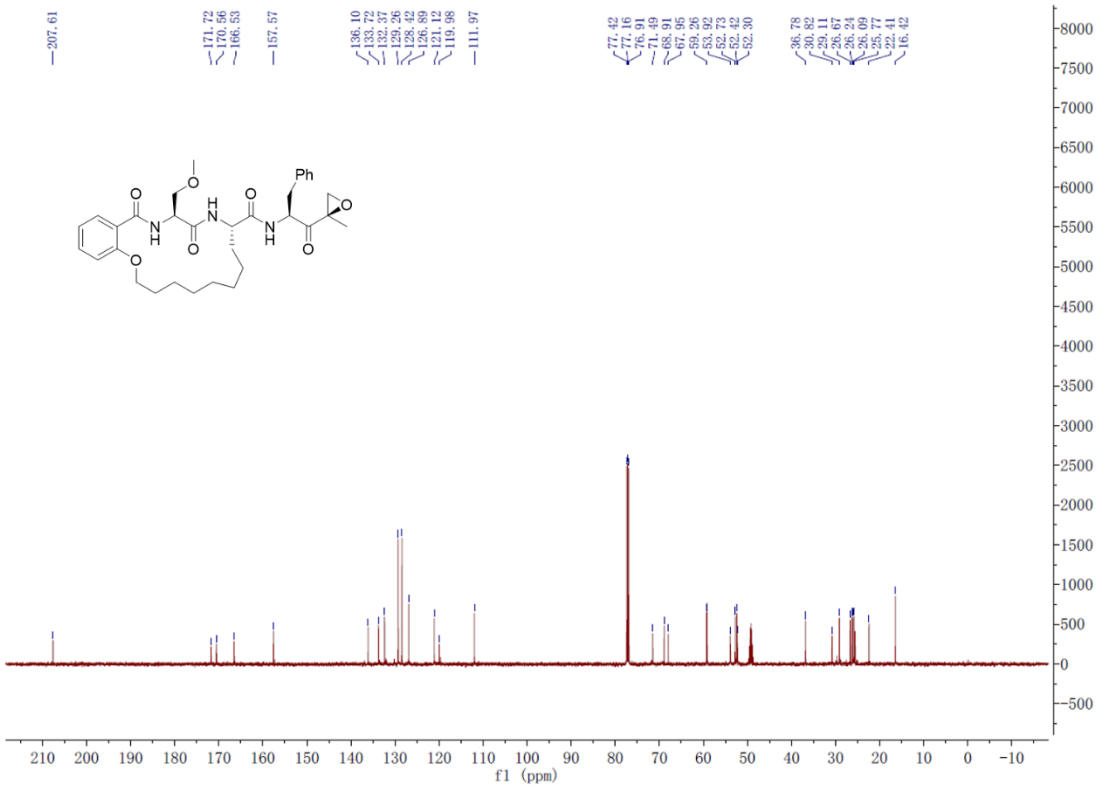
f1 (ppm)

24zb: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136.10
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121.12
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111.97
77.42
77.16
76.91
71.49
68.91
67.95
59.26
53.92
52.73
52.42
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29.11
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26.24
26.09
25.77
22.41
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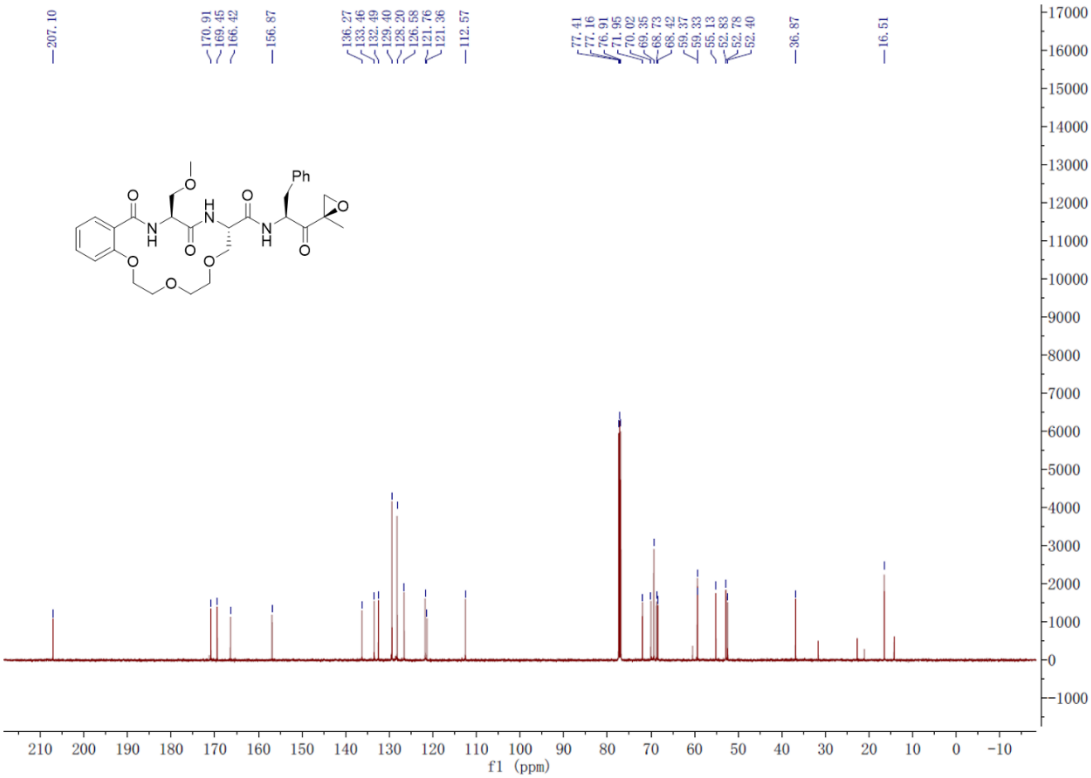
f1 (ppm)

30a: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132.49
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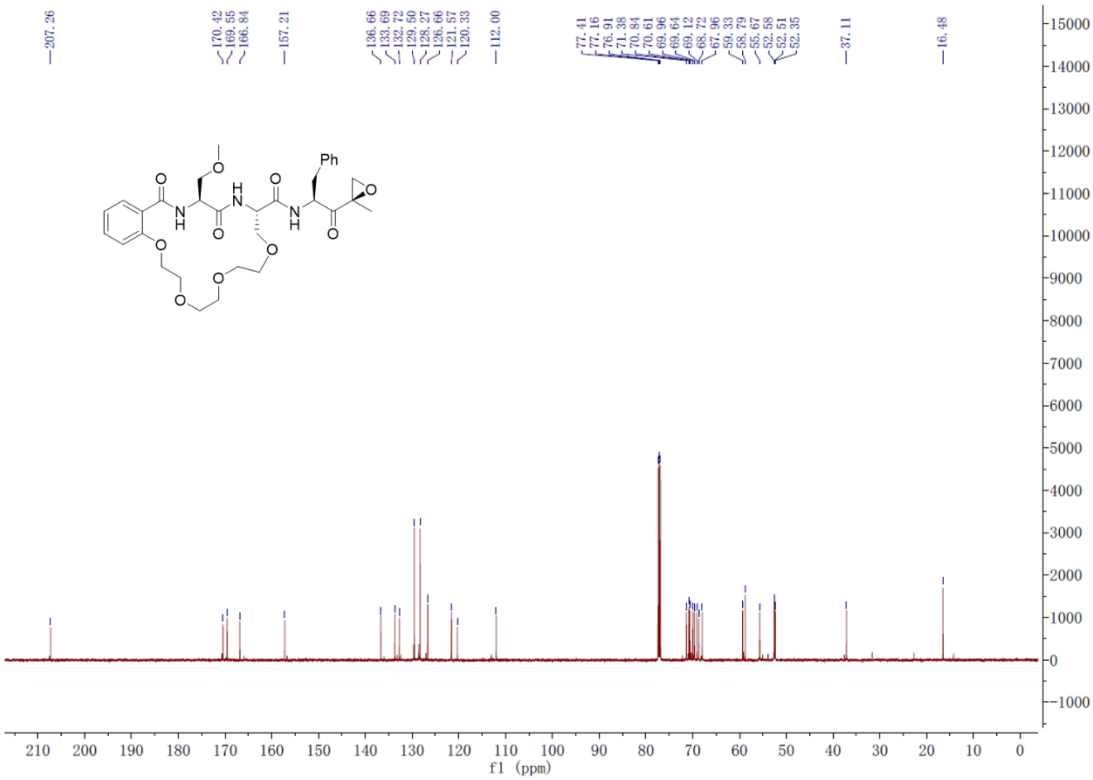
126.58
121.76
121.36
112.57
77.41
77.16
76.91
71.95
70.02
69.35
68.73
68.42
59.37
59.33
55.13
52.83
52.78
52.40
36.87
16.51
f1 (ppm)

30b: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166.84
157.21
136.66
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132.72
129.50
128.27
126.66
121.57
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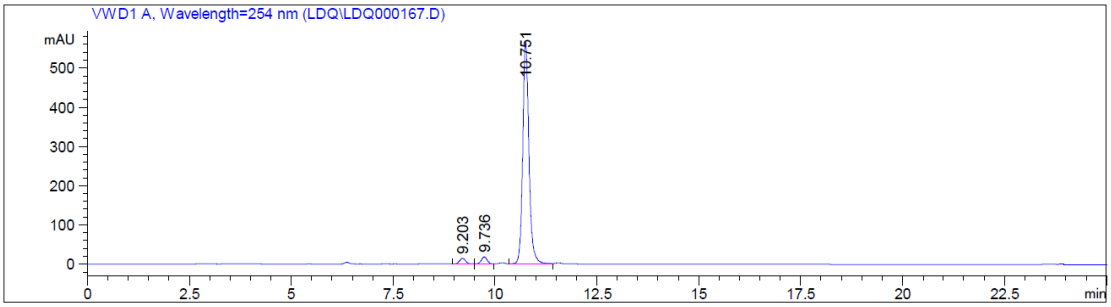
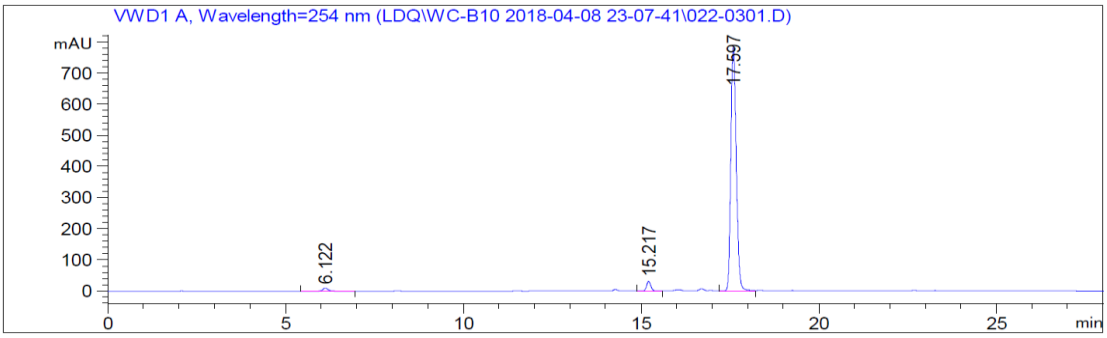
112.00
77.41
77.16
76.91
71.38
70.84
70.61
69.96
69.64
69.12
68.72
67.96
59.33
58.79
55.67
52.58
52.51
52.35
37.11
16.48
f1 (ppm)

HPLC Spectrum

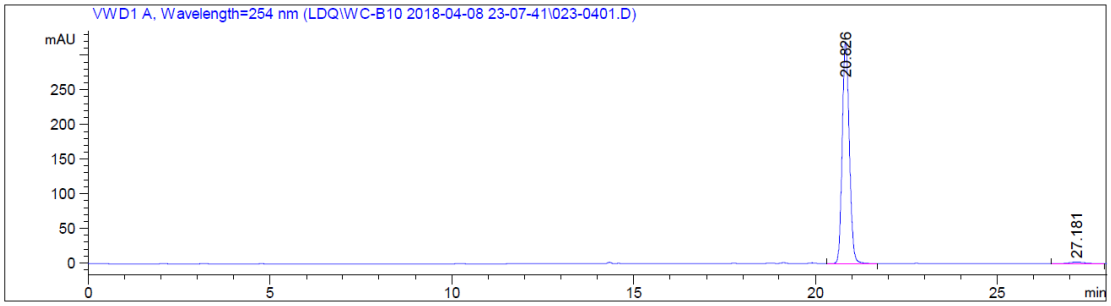
24a:



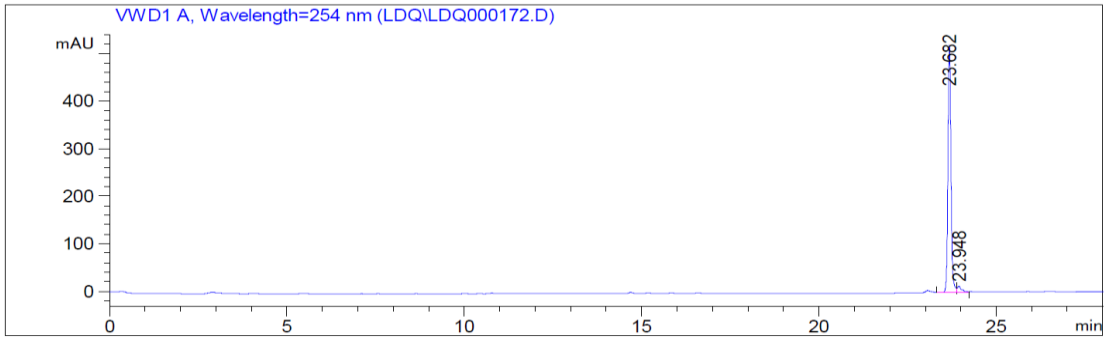
24b:



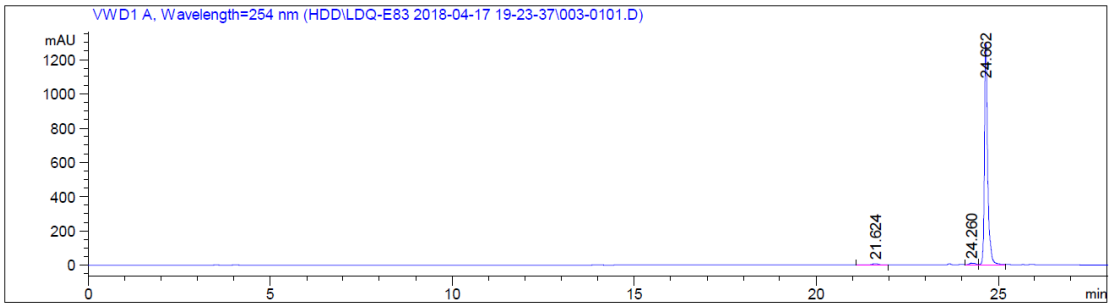
24c:



24d:



24e:



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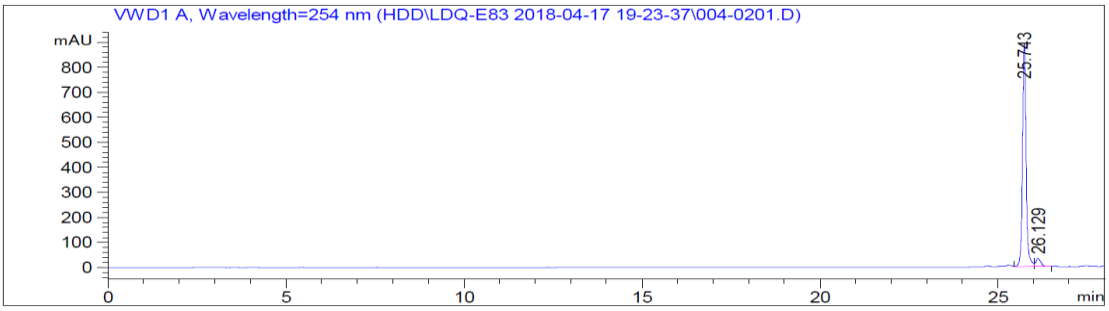
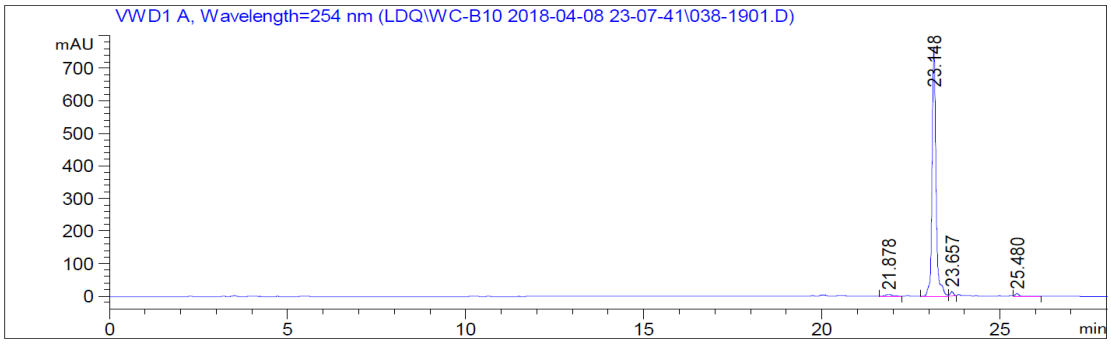
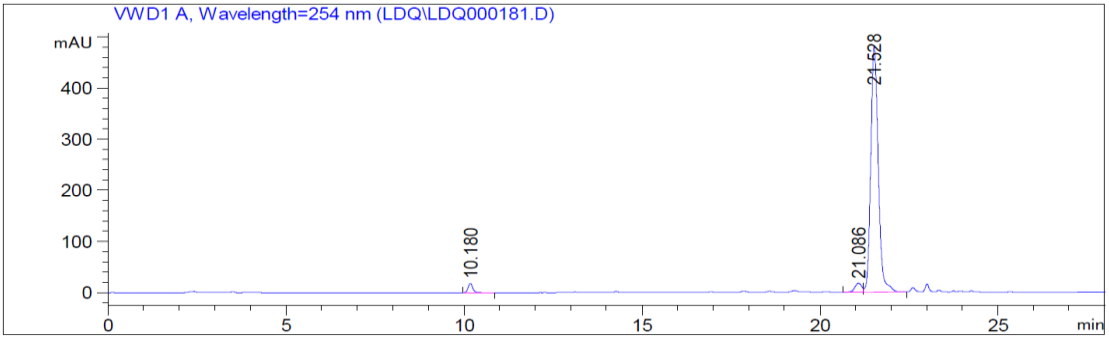


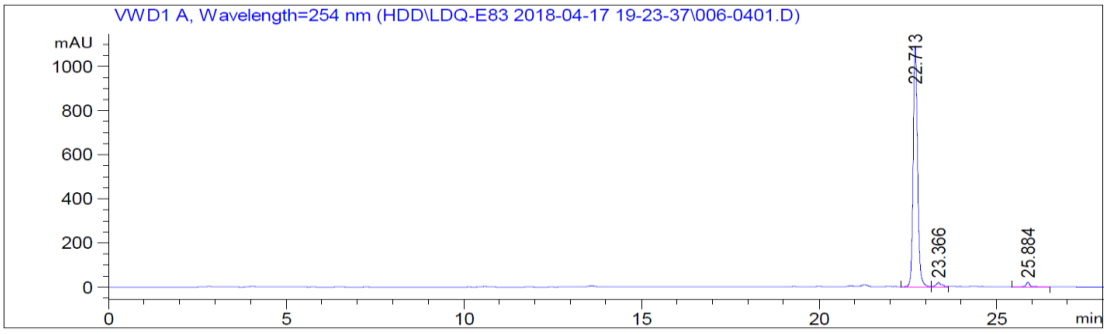
24g:



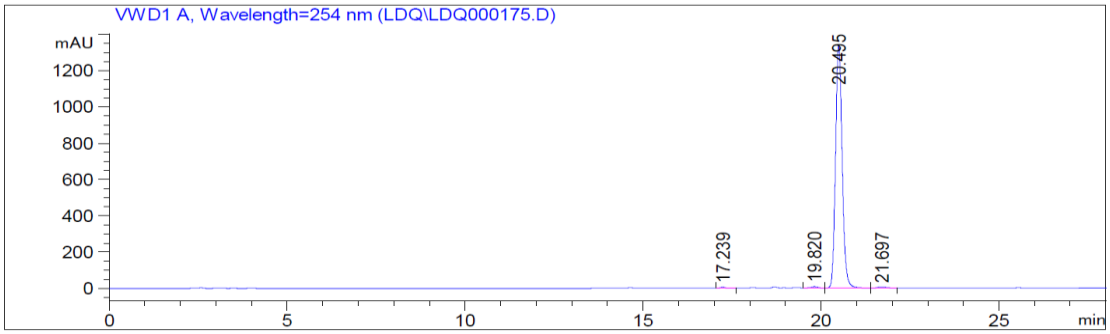
24h:



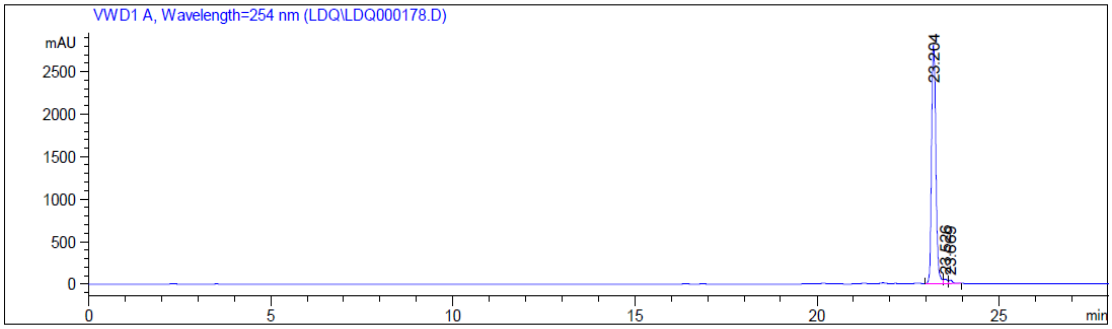
24i:



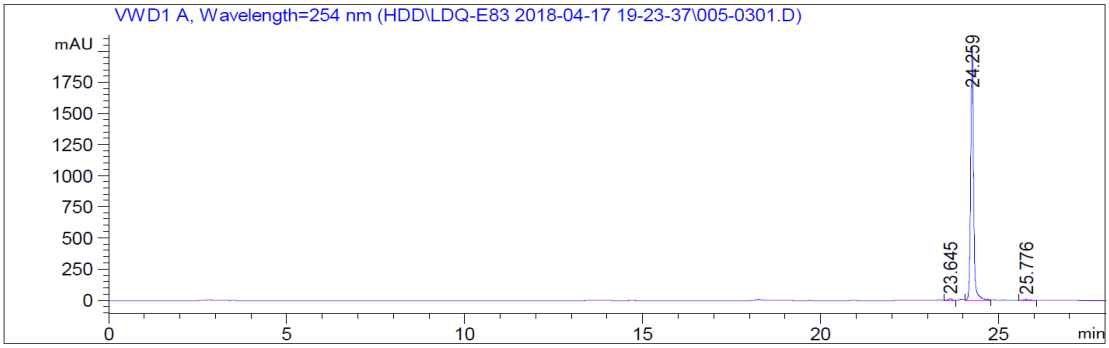
24j:



24k:



24l:



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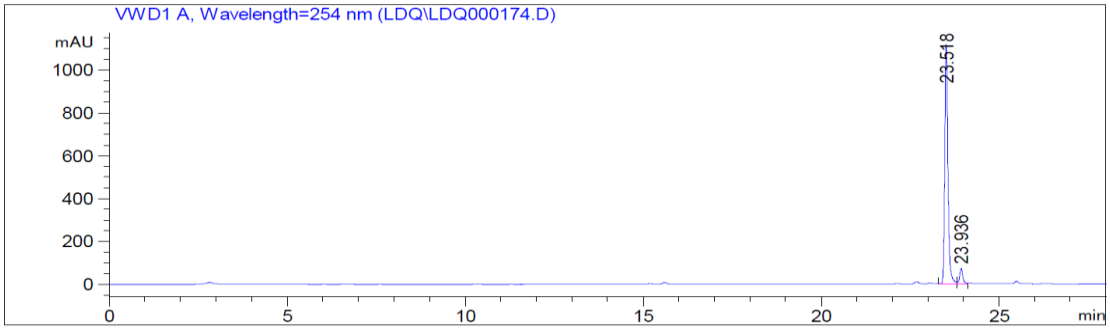
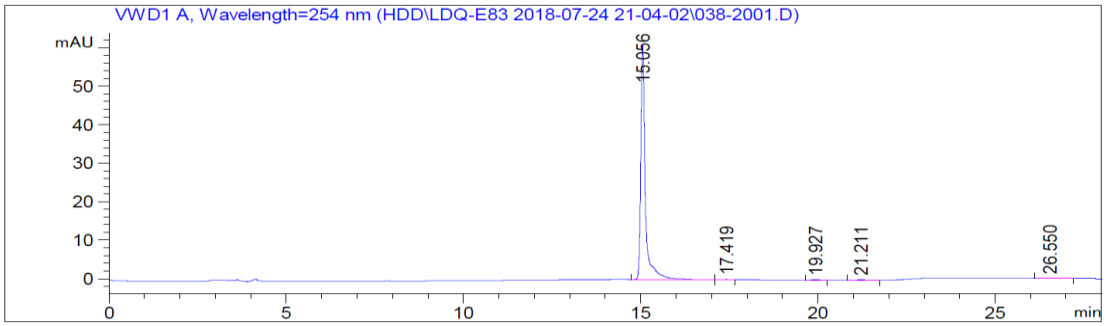
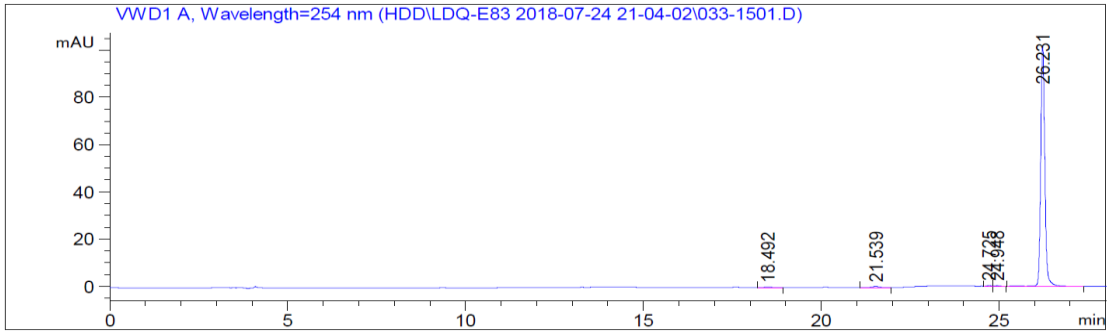


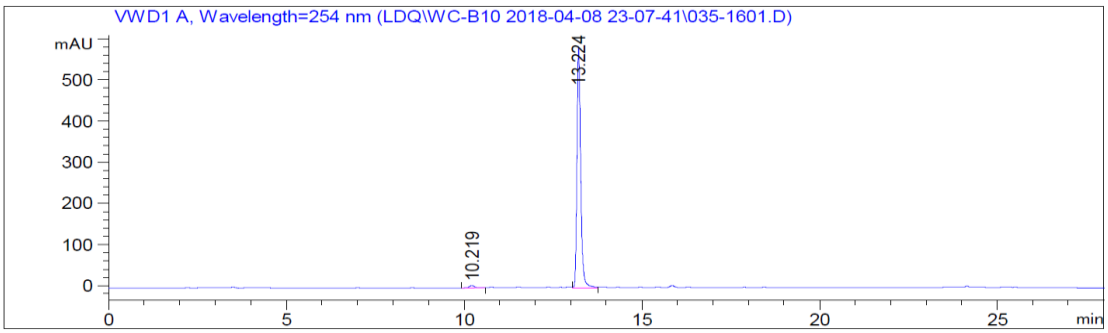
24n:



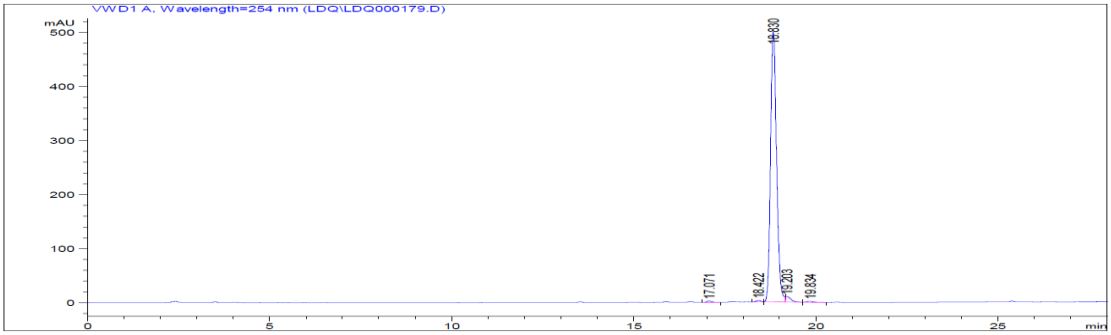
24o:



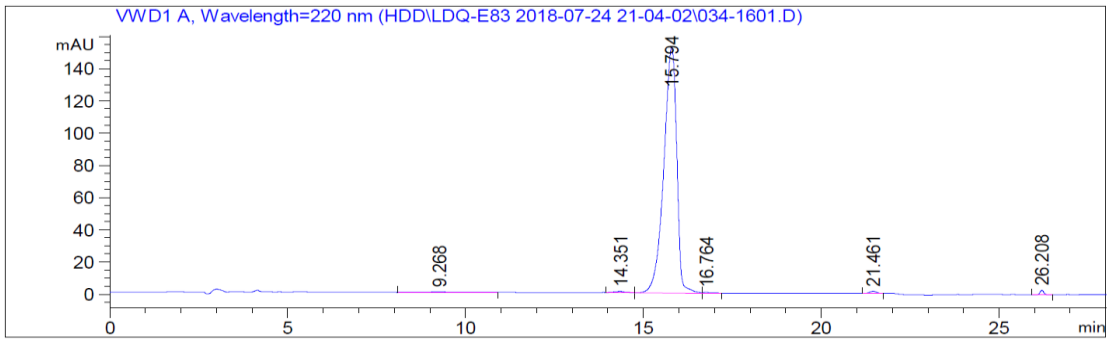
24p:



24q:



24r:



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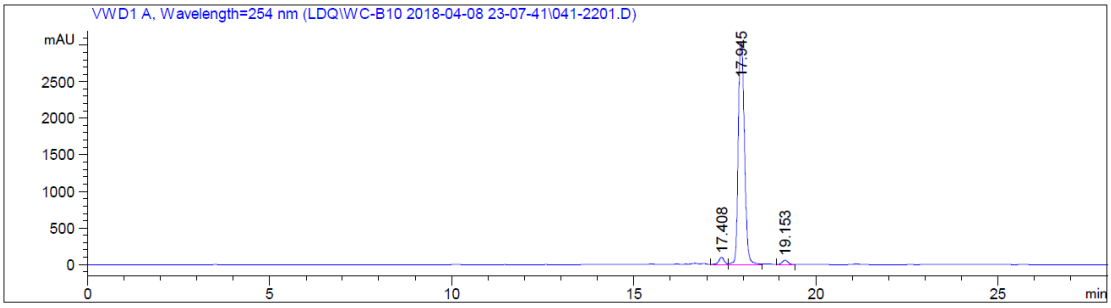
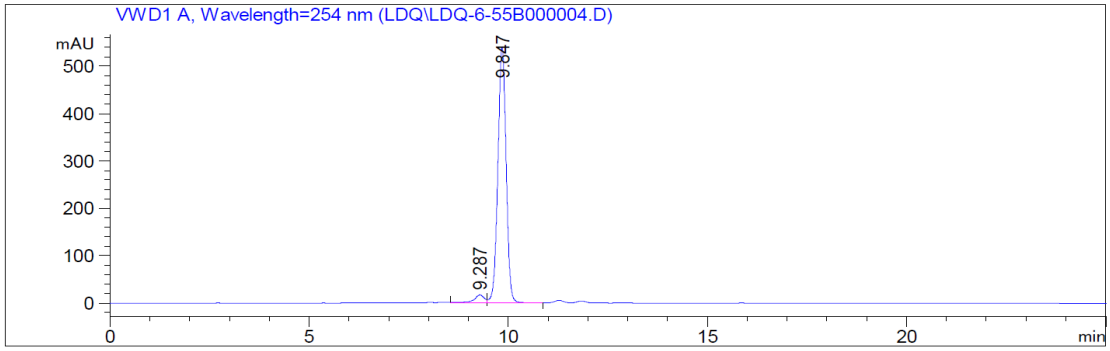
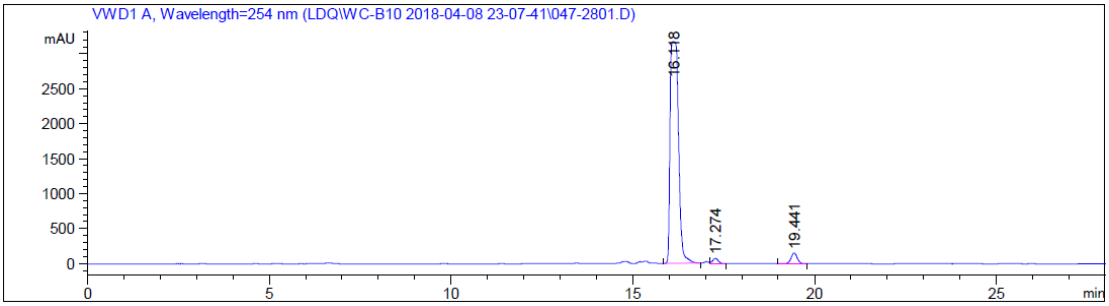


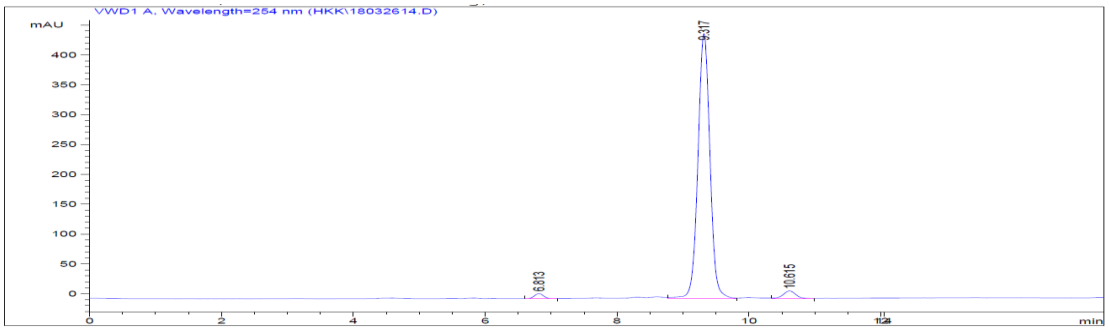
24t:



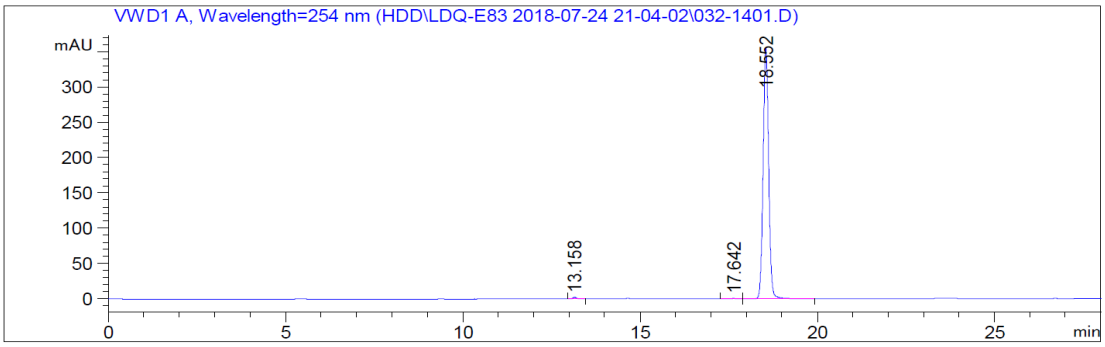
24u:



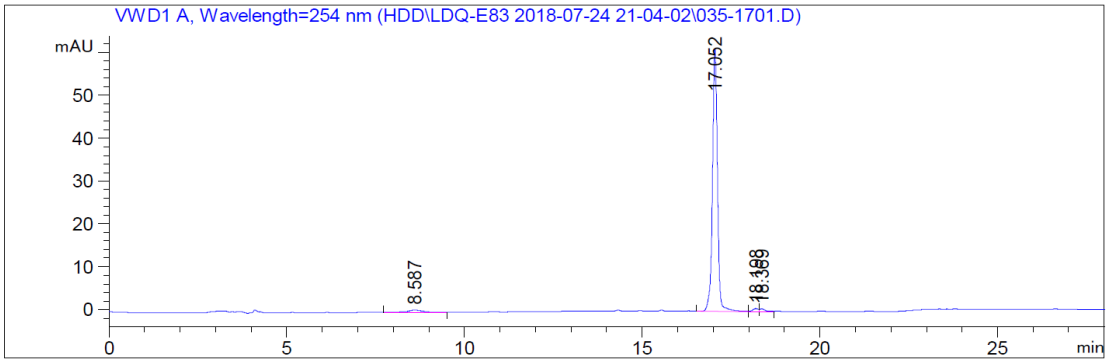
24v:



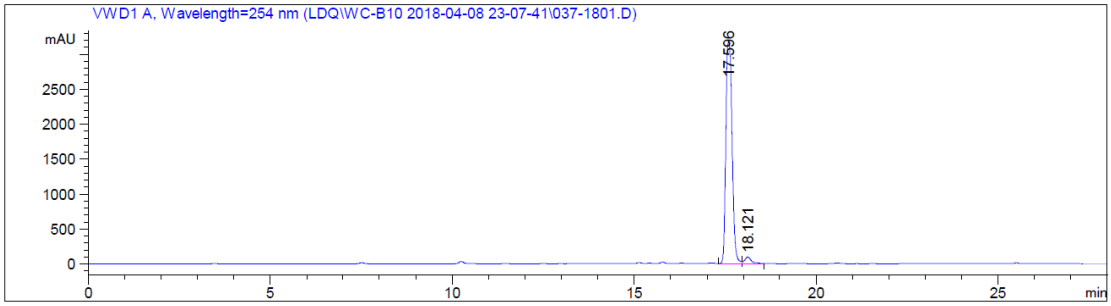
24w:



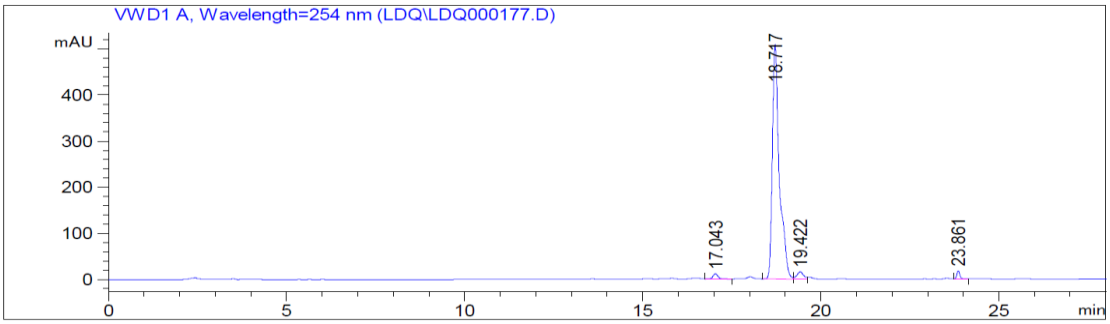
24x:



24y:



24z:



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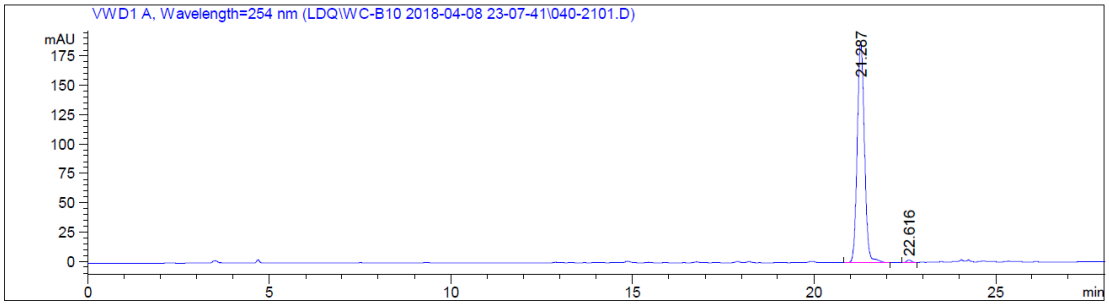
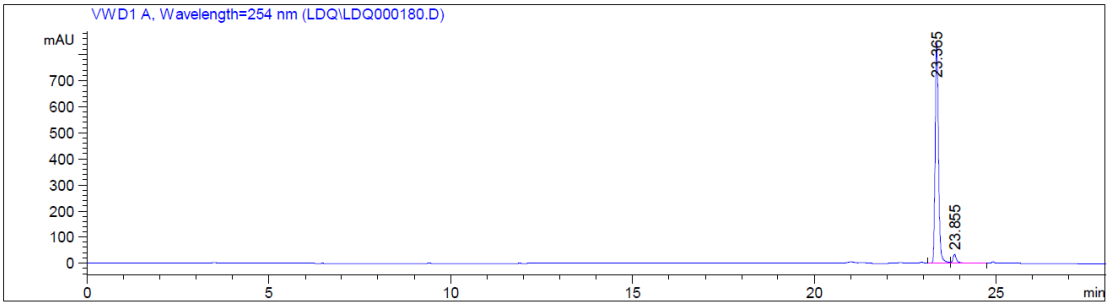


24za:



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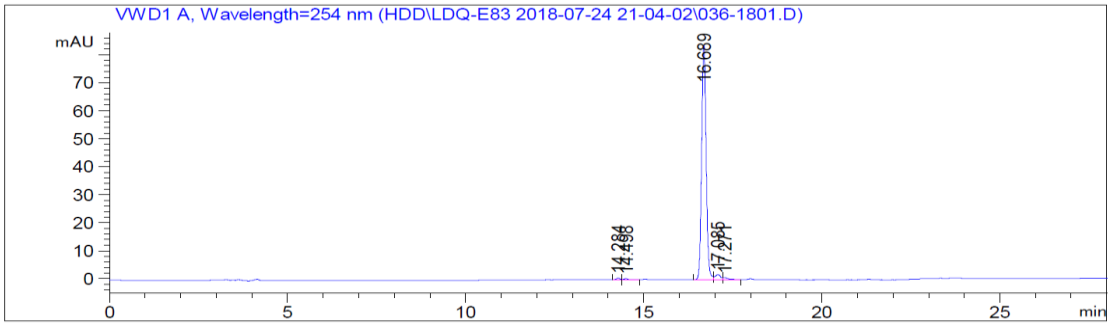
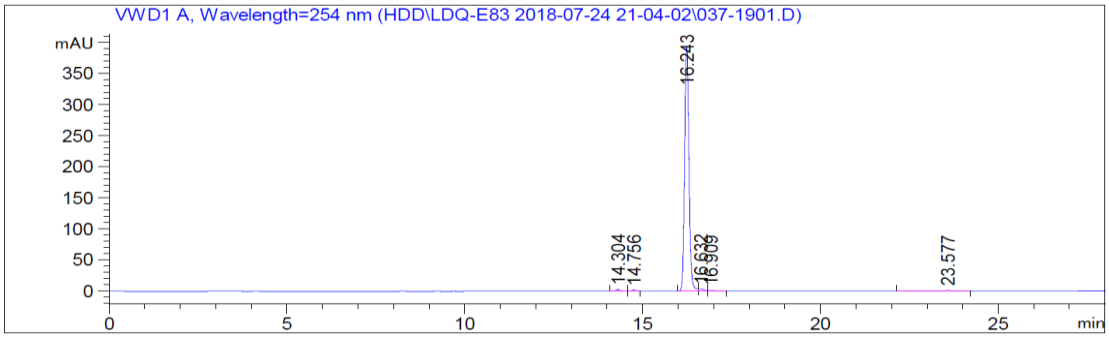

VWD1 A, Wavelength=254 nm (HDD\LDQ-E83 2018-07-24 21-04-02\036-1801.D)
mAU
70
60
50
40
30
20
10
0
16.669
0
5
10
15
20
25
min

30b:


VWD1 A, Wavelength=254 nm (HDD\LDQ-E83 2018-07-24 21-04-02\037-1901.D)
mAU
350
300
250
200
150
100
50
0
16.243
14.304
14.756
23.577
0
5
10
15
20
25
min