

Supporting Information:

**Harnessing Hydrophobic Tag Technology to Combat Drug-Resistant
Influenza: Design, Synthesis, and Potency of Oseltamivir-Derived
HyTTDs**

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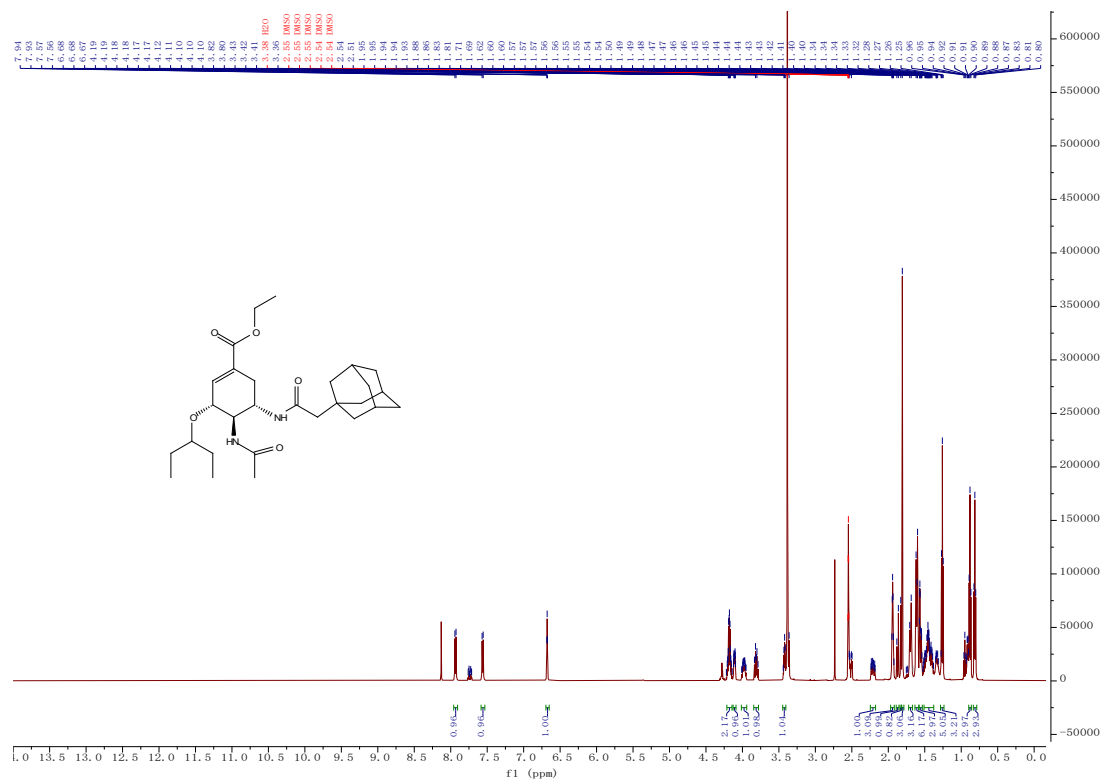
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(liusw@smu.edu.cn).

† These authors contributed equally to this work.

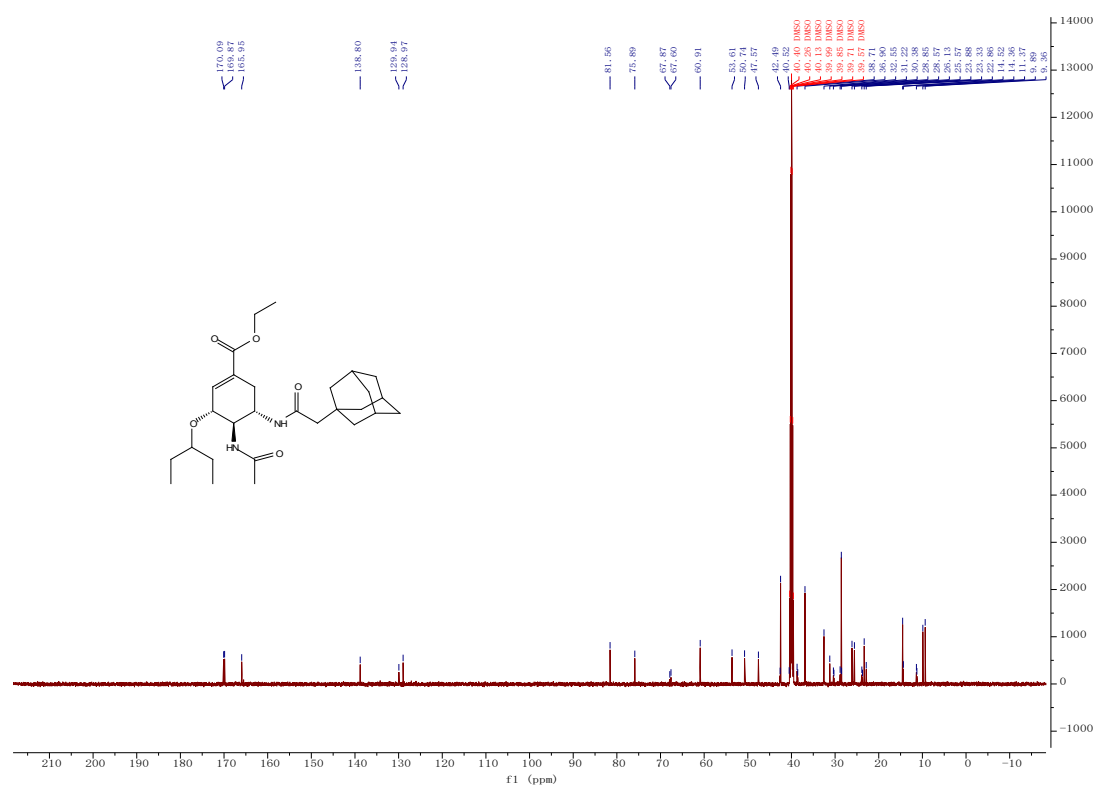
Spectrums of chemically synthesized compounds

Spectrums of L1

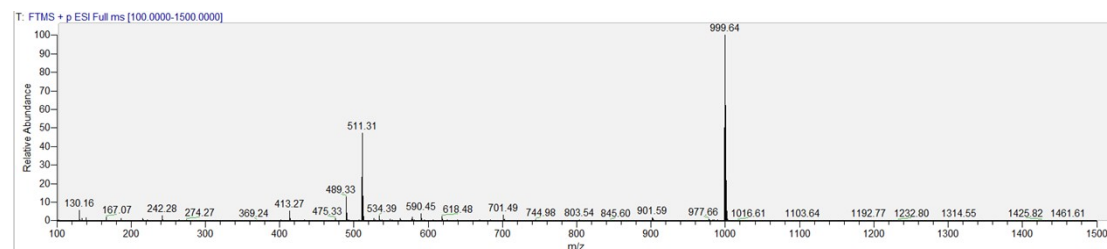
^1H NMR of L1



¹³C NMR of L1

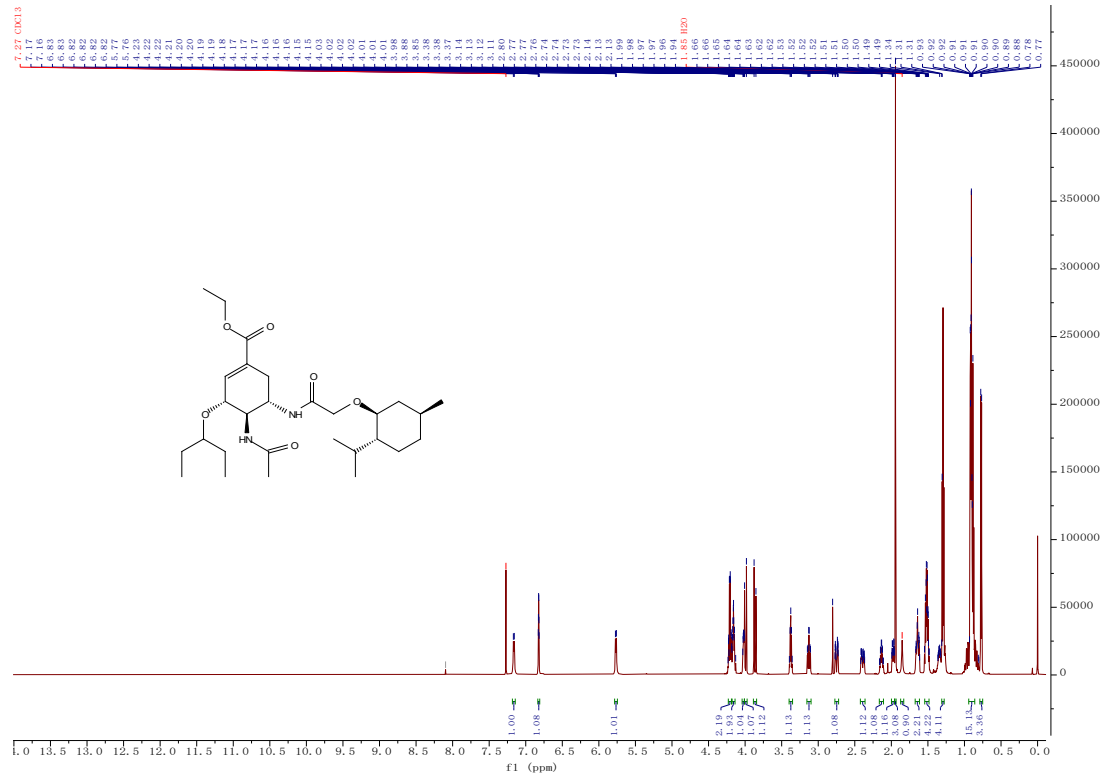


ESI-HRMS spectrum of L1

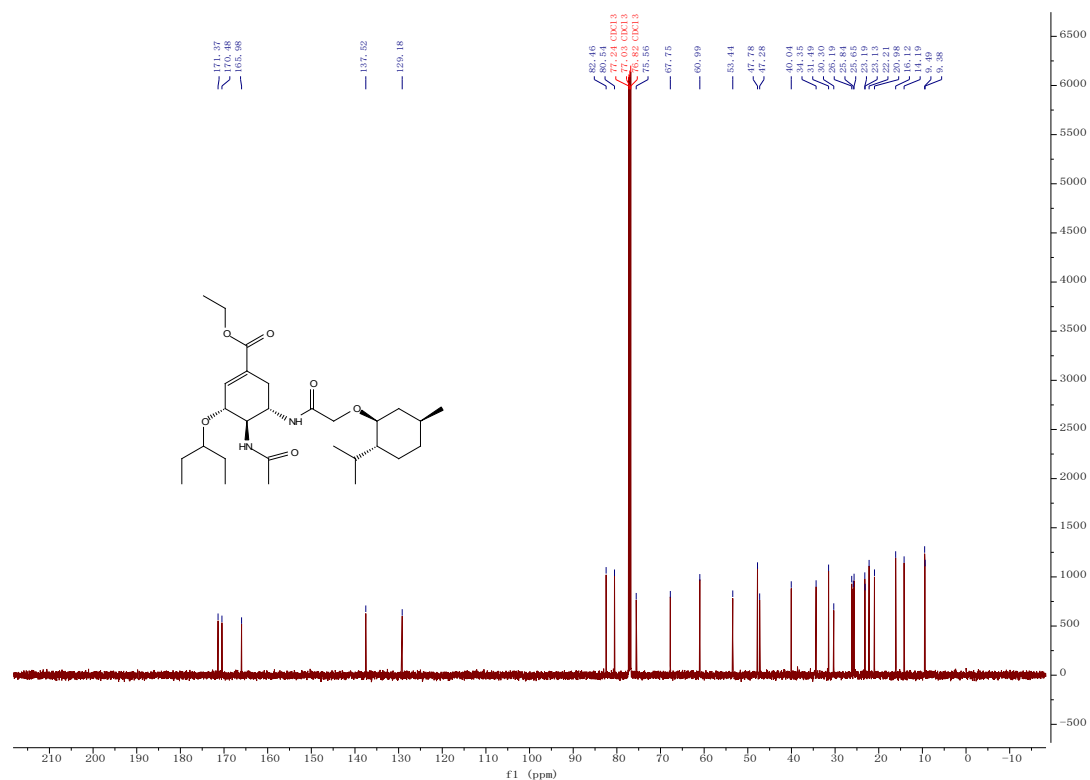


Spectrums of L2

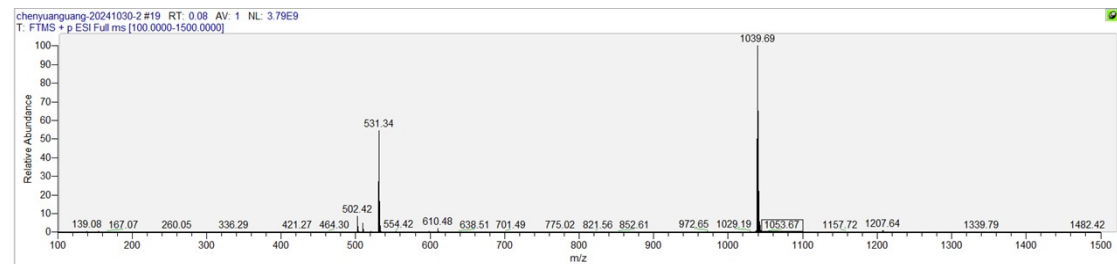
^1H NMR of L2



¹³C NMR of L2

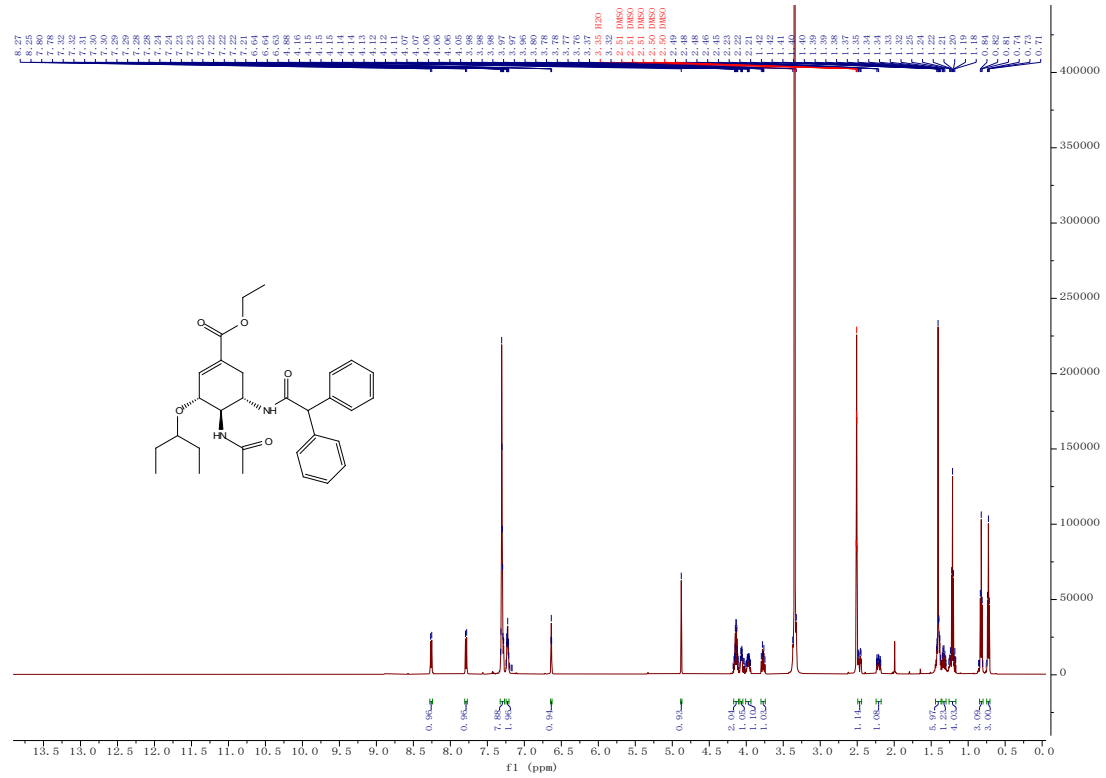


ESI-HRMS spectrum of L2

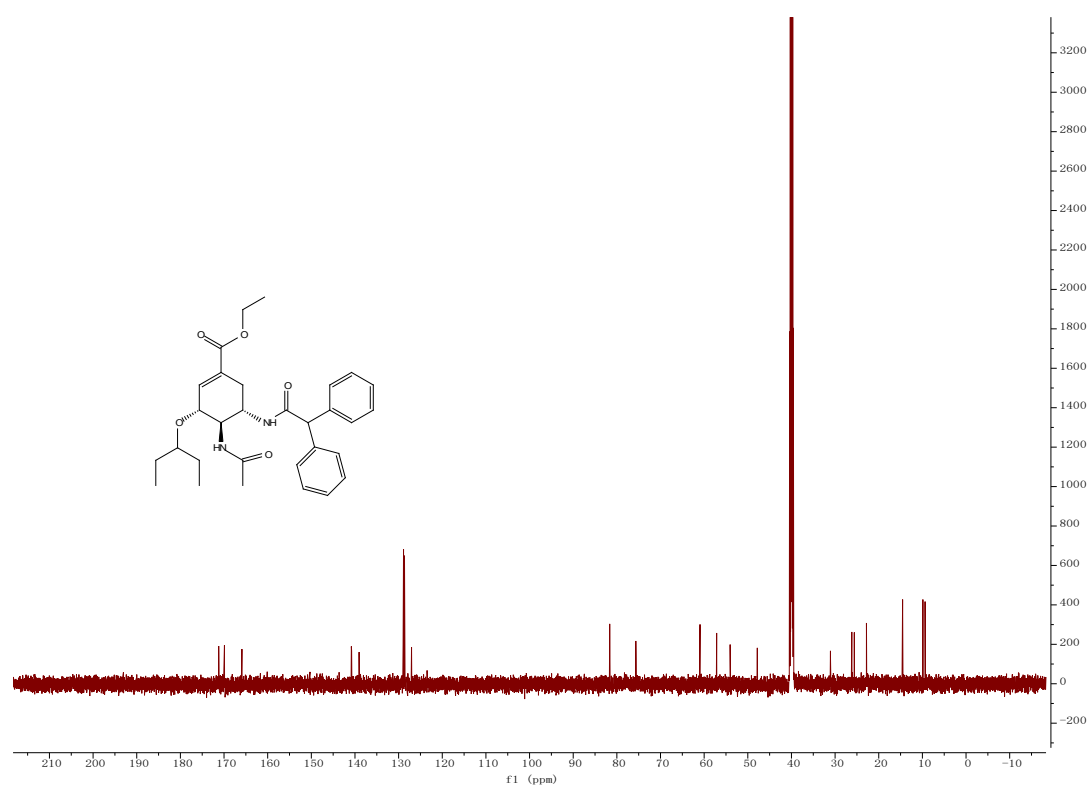


Spectrums of L3

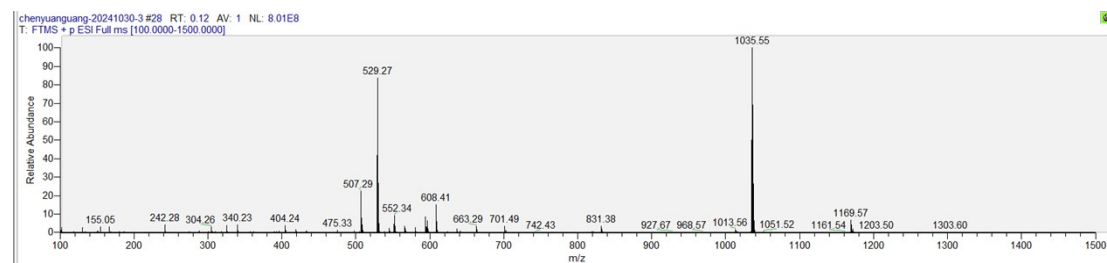
^1H NMR of L3



¹³C NMR of L3

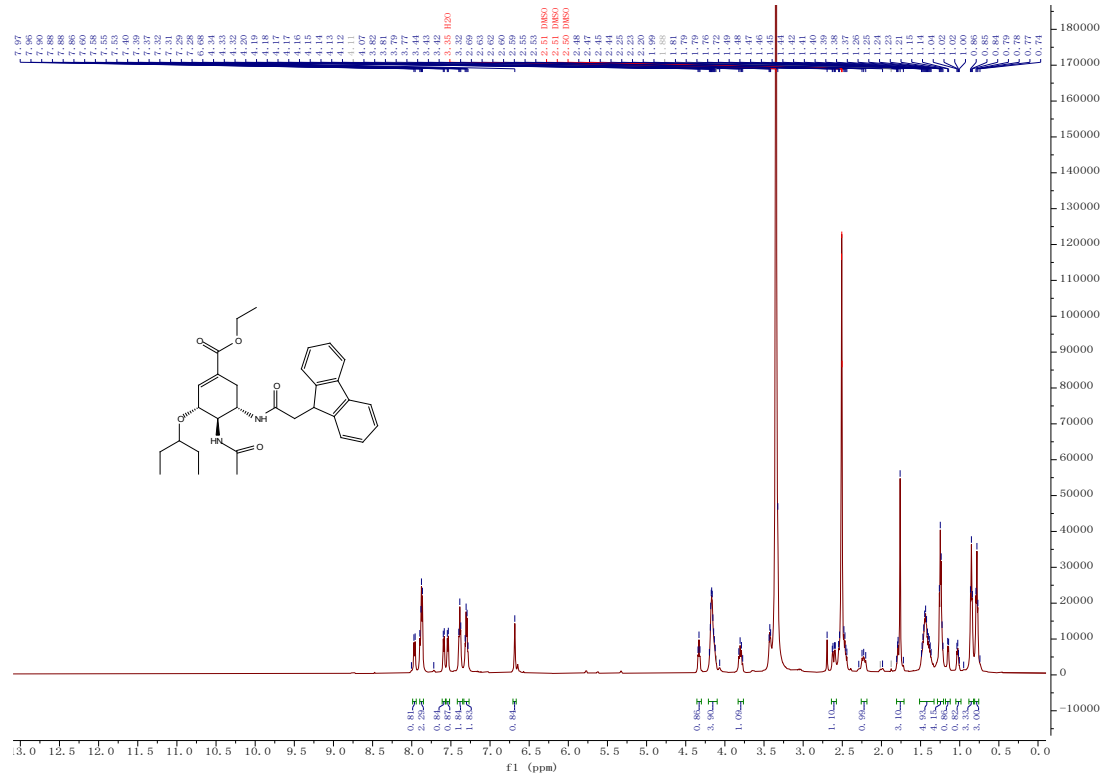


ESI-HRMS spectrum of L3

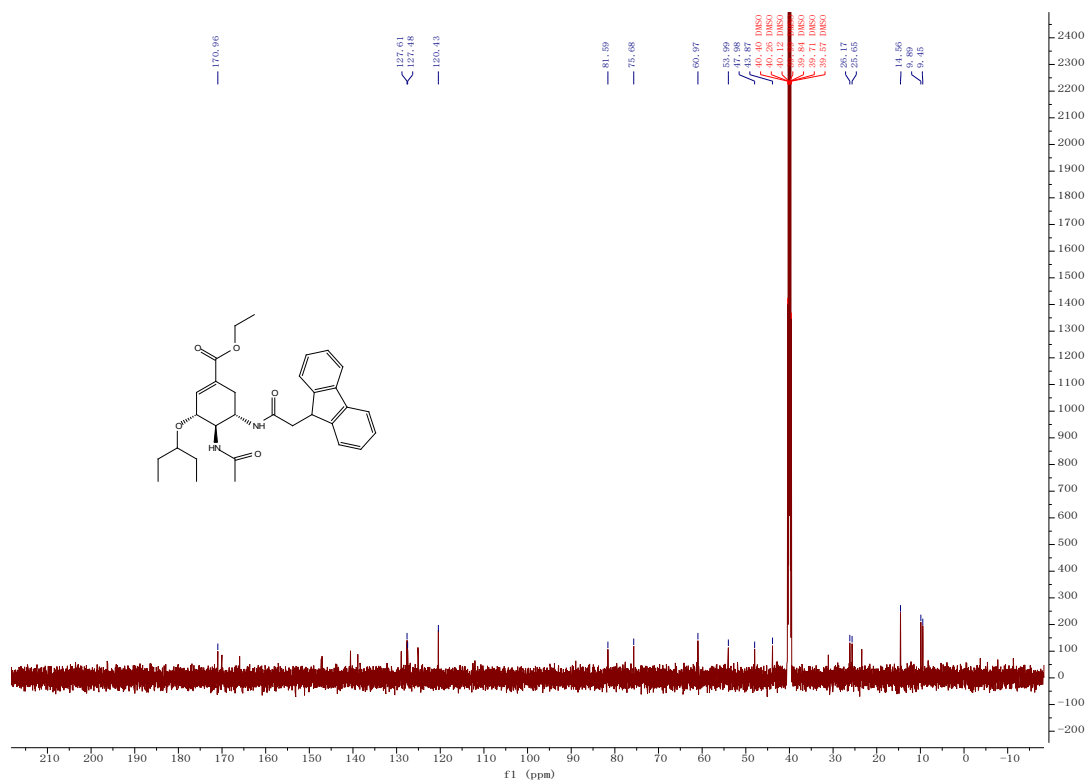


Spectrums of L4

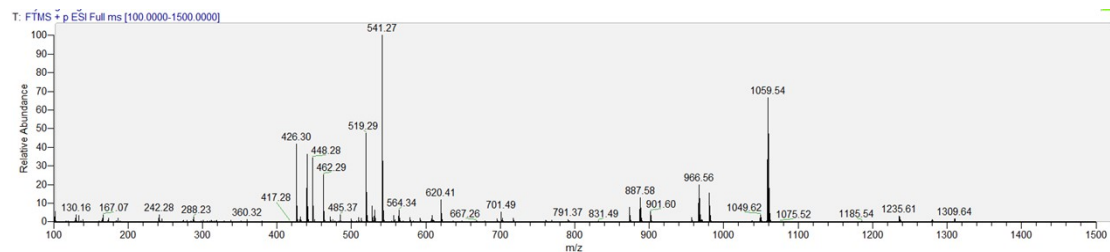
^1H NMR of L4



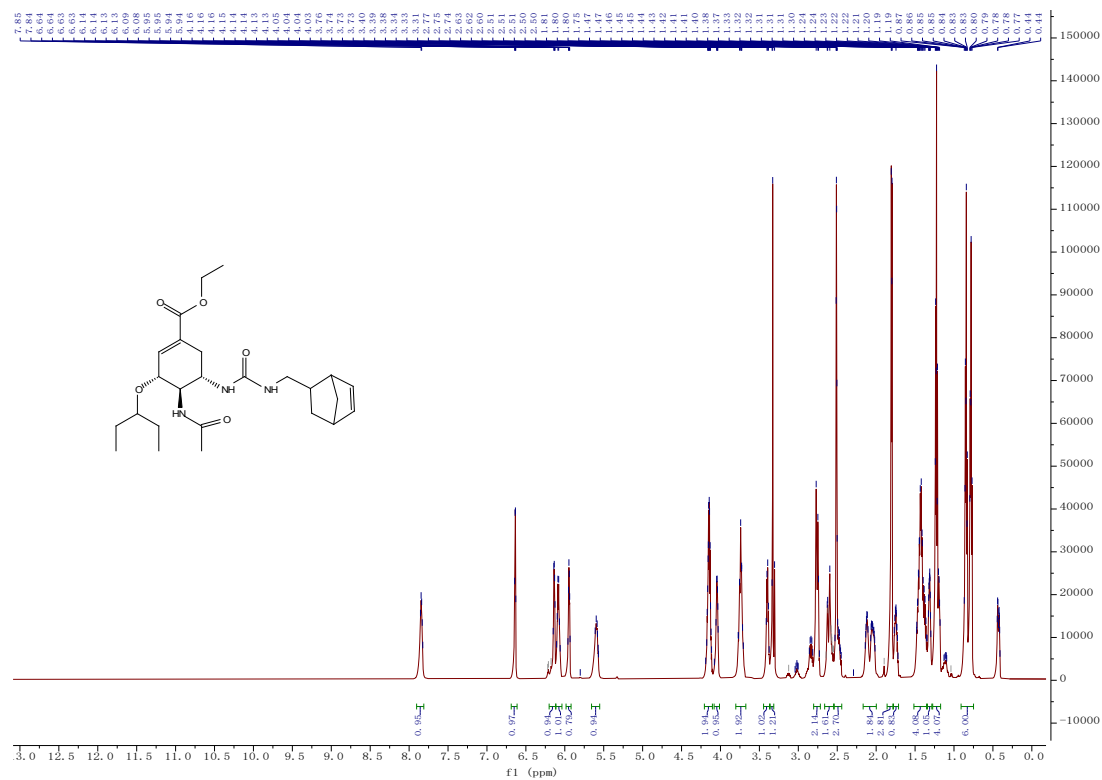
¹³C NMR of L4



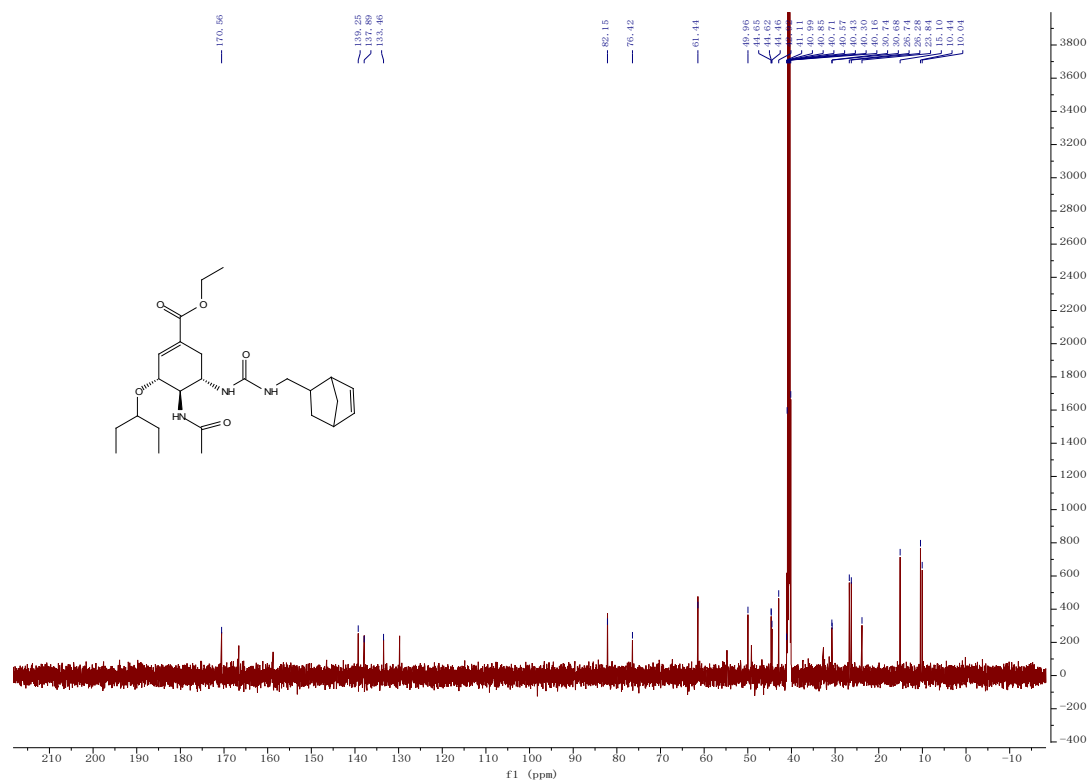
ESI-HRMS spectrum of L4



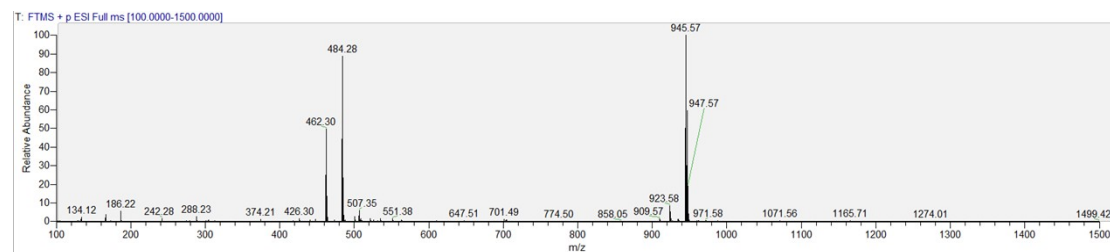
¹H NMR of L5



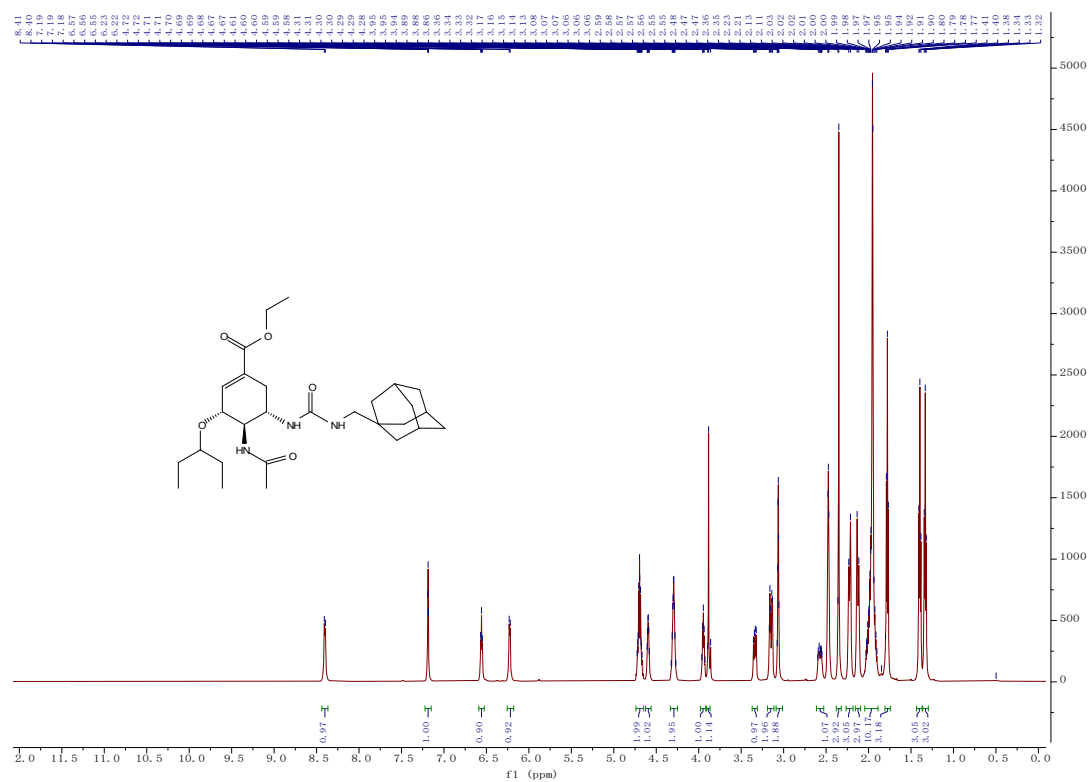
¹³C NMR of L5



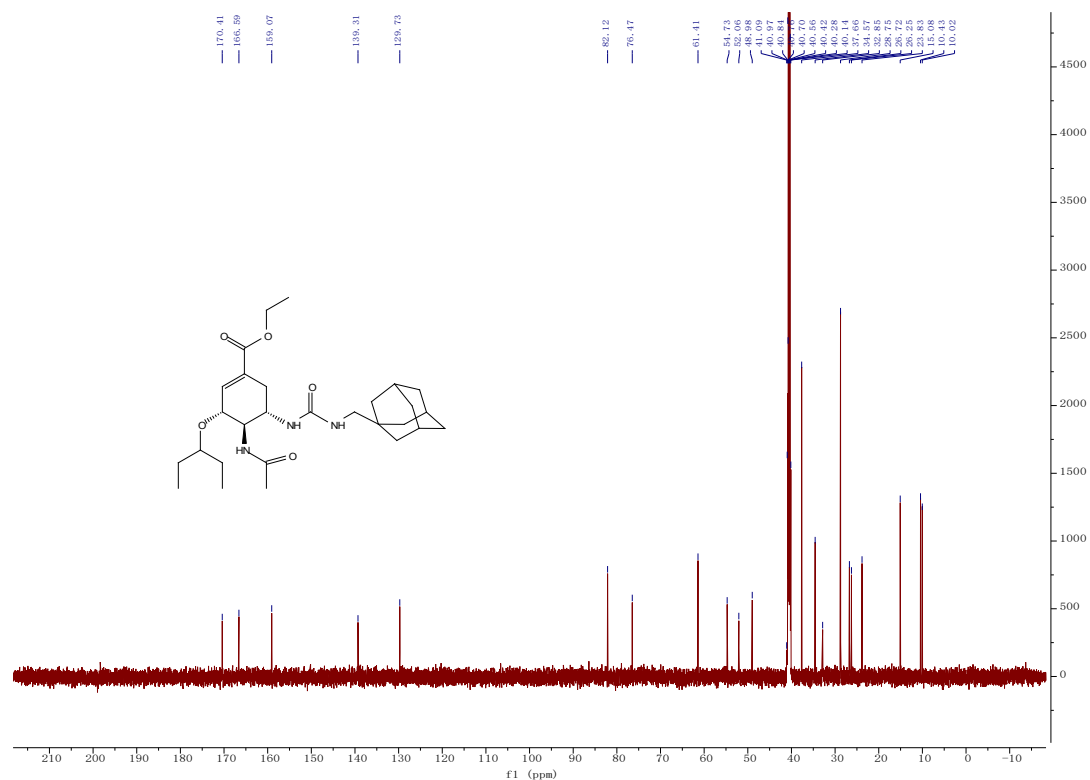
ESI-HRMS spectrum of L5



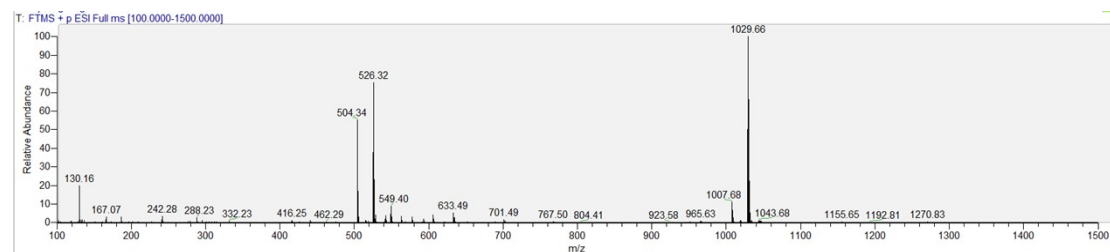
¹H NMR of L6



¹³C NMR of L6

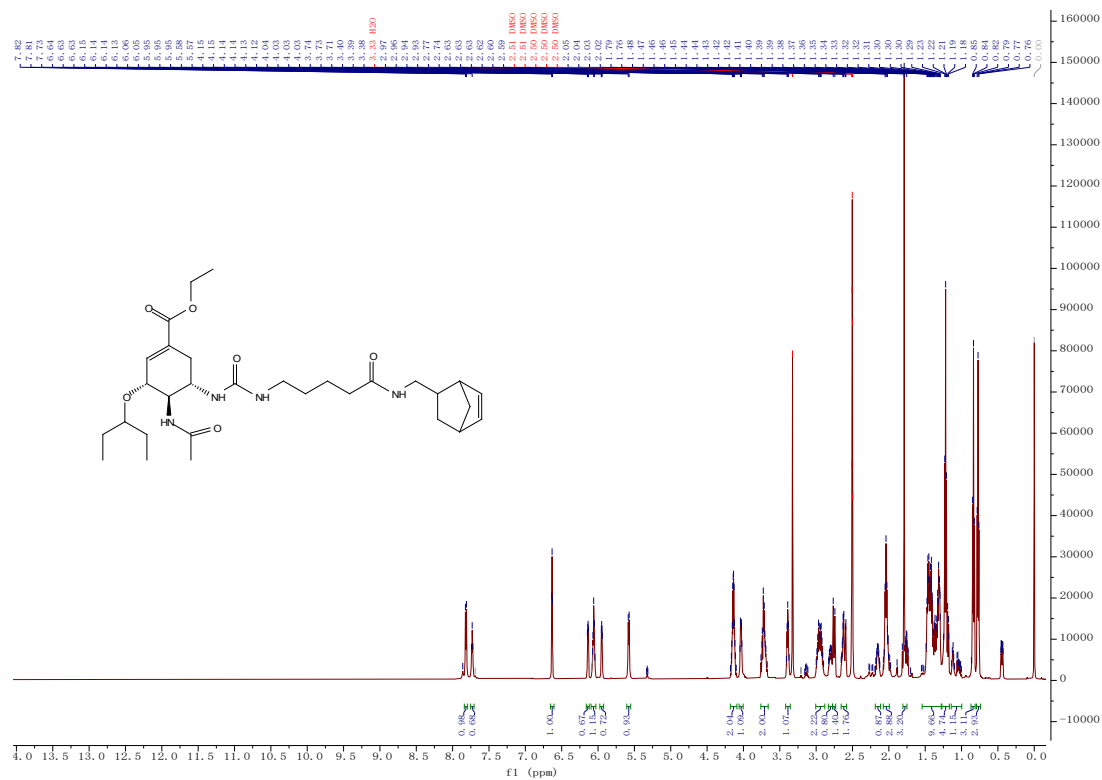


ESI-HRMS spectrum of L6

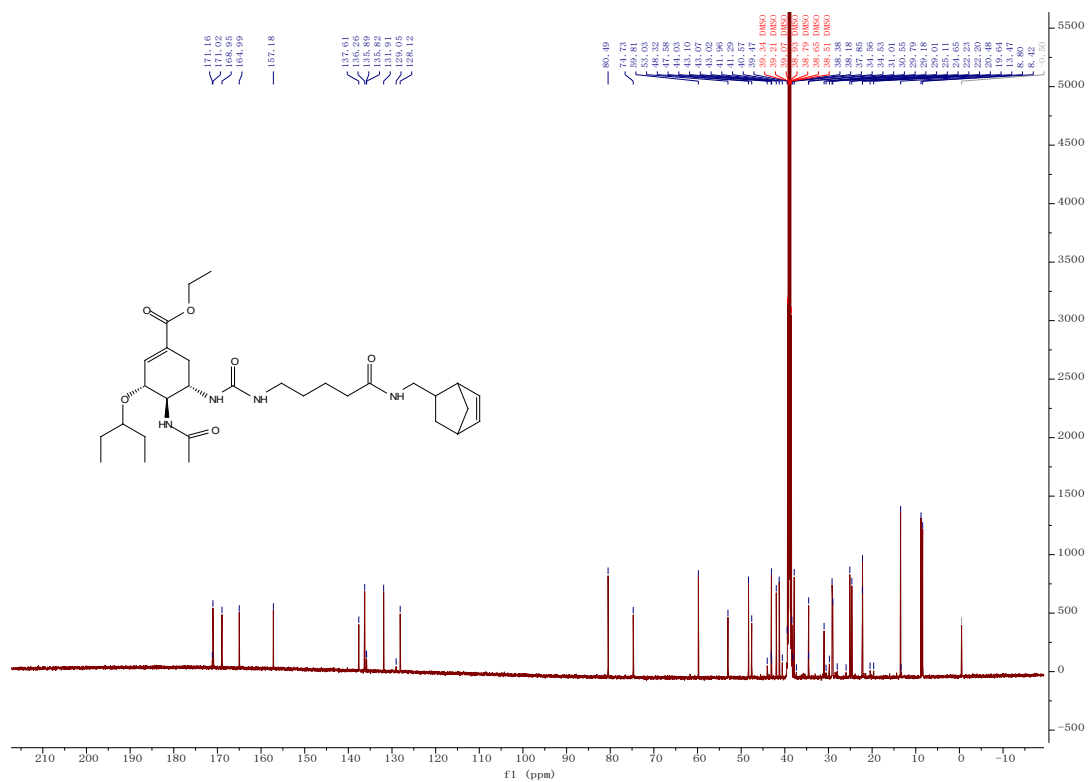


Spectrums of L7

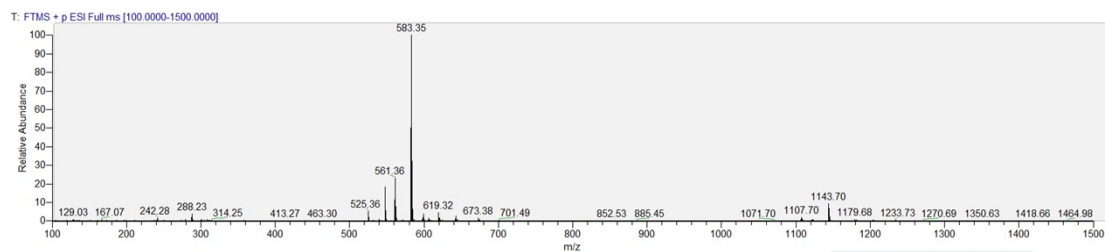
¹H NMR of L7



¹³C NMR of L7

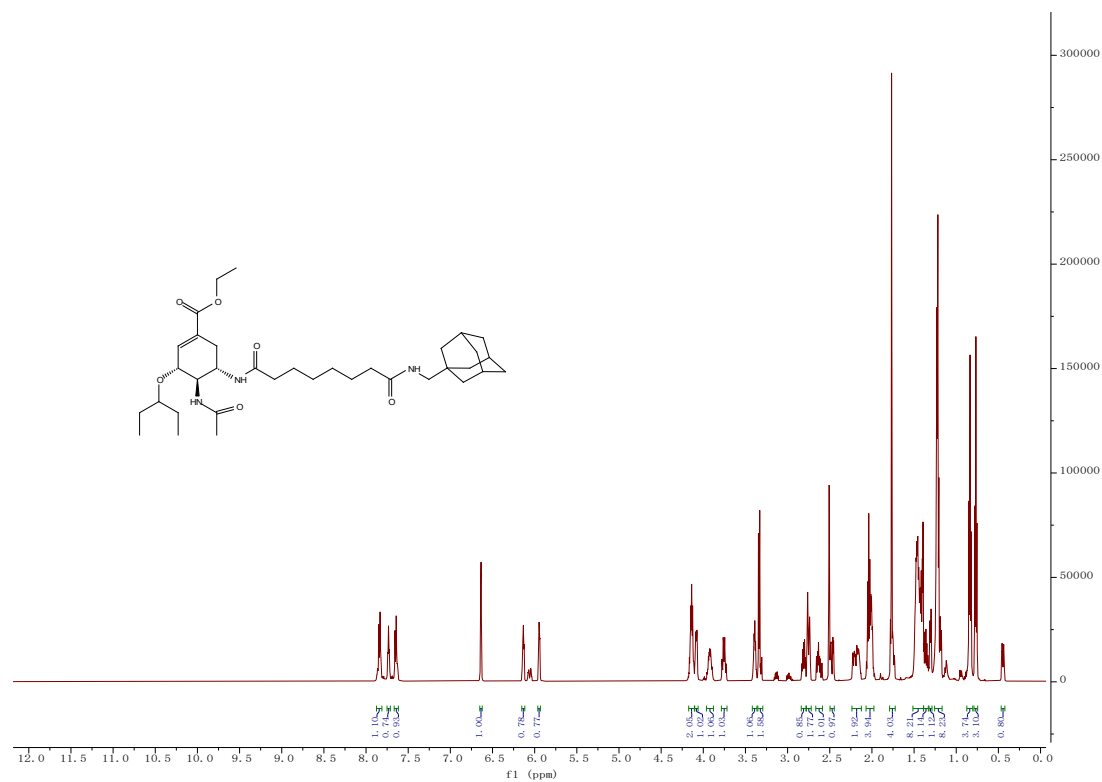


ESI-HRMS spectrum of L7

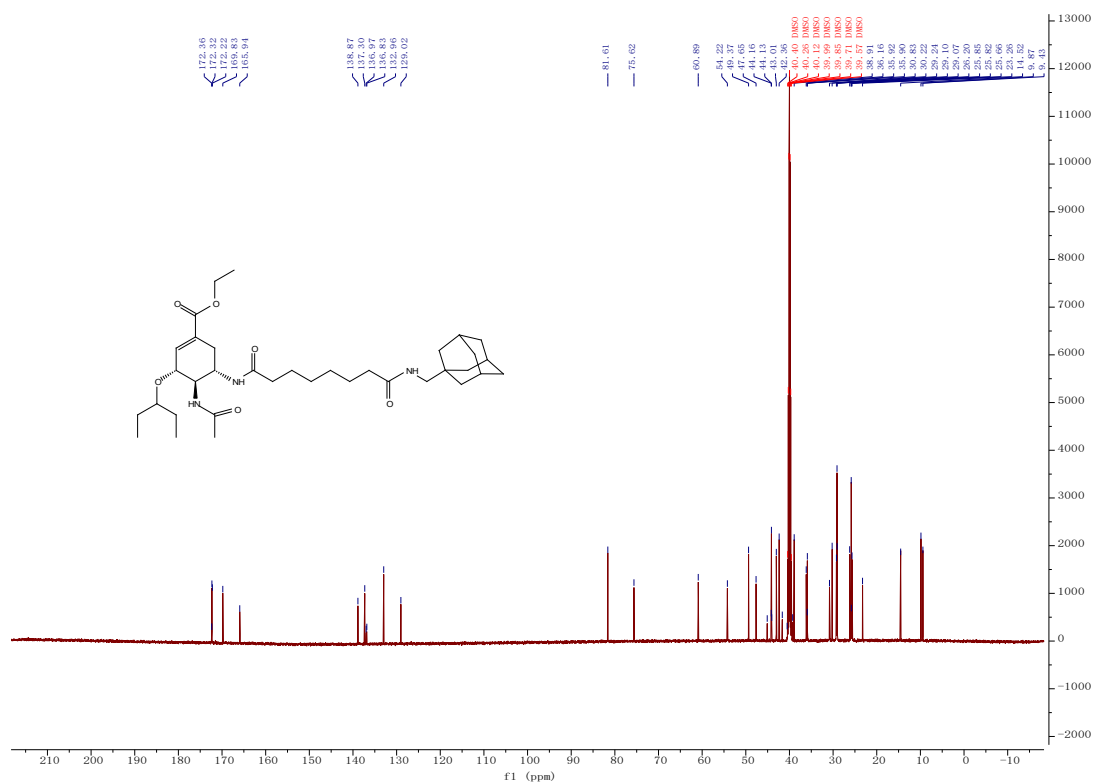


Spectrums of L8

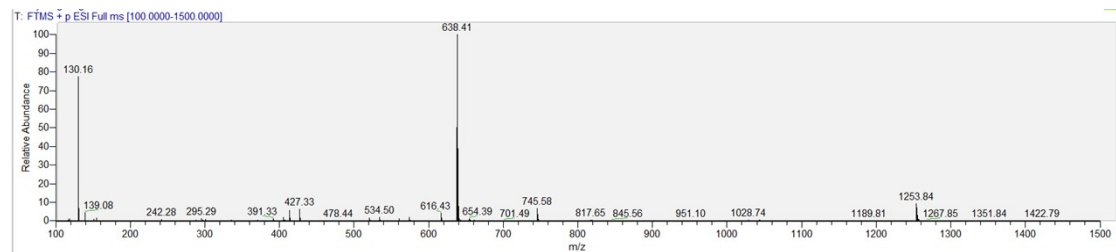
^1H NMR of L8



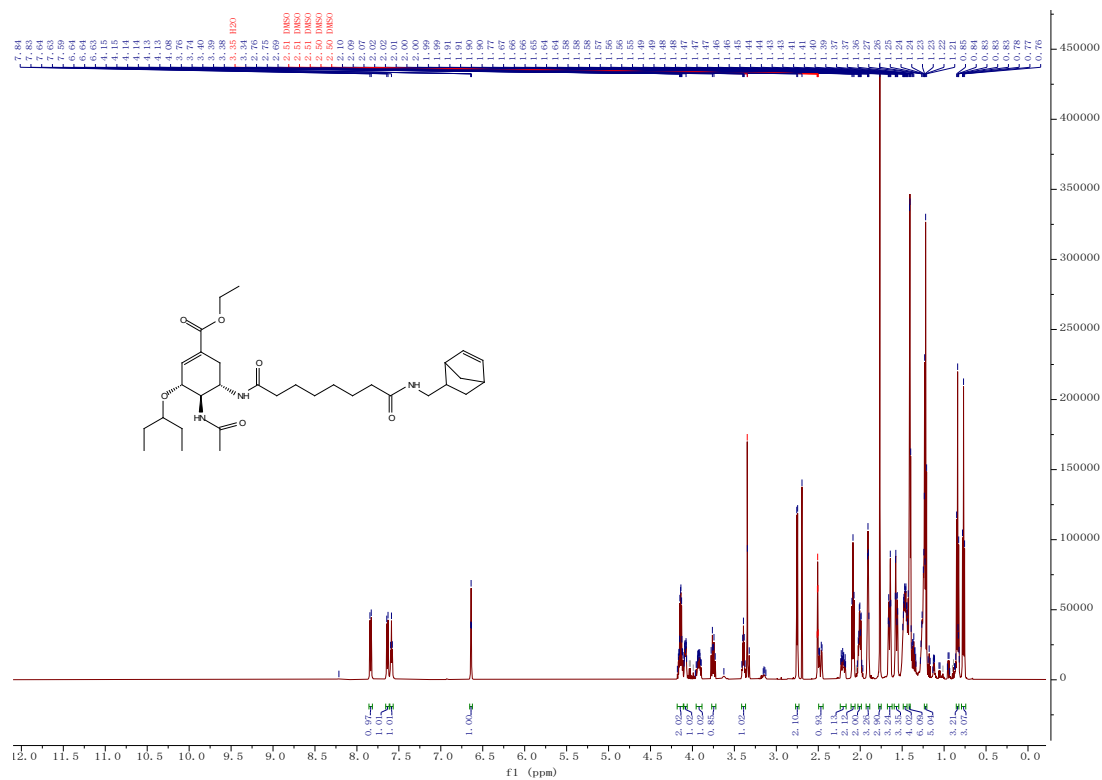
¹³C NMR of L8



ESI-HRMS spectrum of L8



¹H NMR of L9



Chemical structure of compound 10 is shown above the spectra.

¹H NMR spectrum (top) shows peaks (ppm): 8.1, 8.02, 7.6, 6.02, 5.8, 5.6, 5.4, 5.2, 5.0, 4.8, 4.6, 4.4, 4.2, 4.0, 3.8, 3.6, 3.4, 3.2, 3.0, 2.8, 2.6, 2.4, 2.2, 2.0, 1.8, 1.6, 1.4, 1.2, 1.0, 0.8.

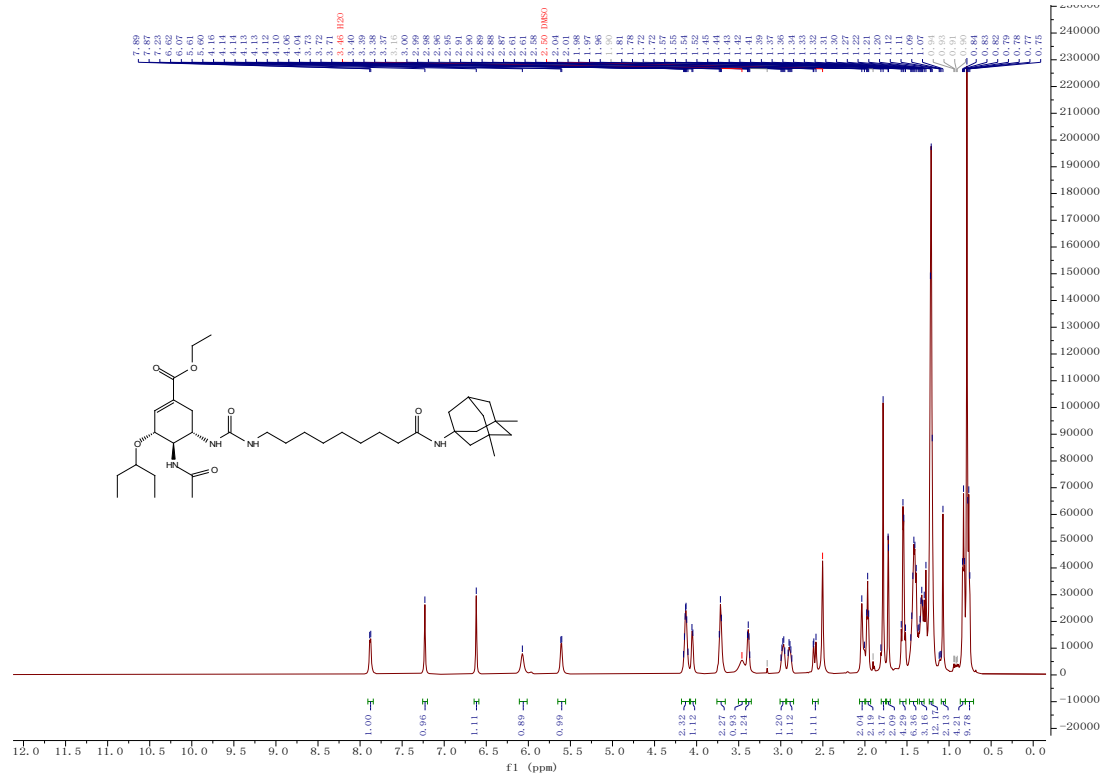
¹³C NMR spectrum (bottom) shows peaks (ppm): 172.70, 172.30, 168.84, 165.93, 138.87, 129.02, 81.02, 76.02, 74.02, 60.88, 60.20, 58.02, 54.07, 50.46, 48.02, 44.93, 40.51, 38.09, 36.17, 35.89, 34.07, 32.02, 30.64, 28.99, 28.63, 26.82, 25.21, 25.07, 23.23, 21.19, 21.00, 20.68, 18.52, 17.17, 14.40, 13.99, 12.00.

T: FTMS + p ESI Full ms [100.0000-1500.0000]

Mass spectrum plot showing relative abundance versus m/z. The x-axis ranges from 100 to 1500 m/z, and the y-axis ranges from 0 to 100 relative abundance. The base peak is at m/z 596.37. Other significant peaks are labeled at m/z 130.16, 186.22, 242.28, 288.23, 377.20, 414.30, 486.30, 560.37, 574.38, 619.44, 703.54, 731.42, 872.56, 946.07, 1007.23, 1103.70, 1147.76, 1169.74, 1227.70, 1295.73, and 1461.14.

Spectrums of L10

¹H NMR of L10



Chemical structure of compound 10 is shown in the top left corner of the spectrum.

¹H NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift in ppm (f1), ranging from 210 to -10. The y-axis represents the intensity, ranging from 0 to 3200. The spectrum shows several peaks, with the following chemical shifts (ppm) labeled above the peaks:

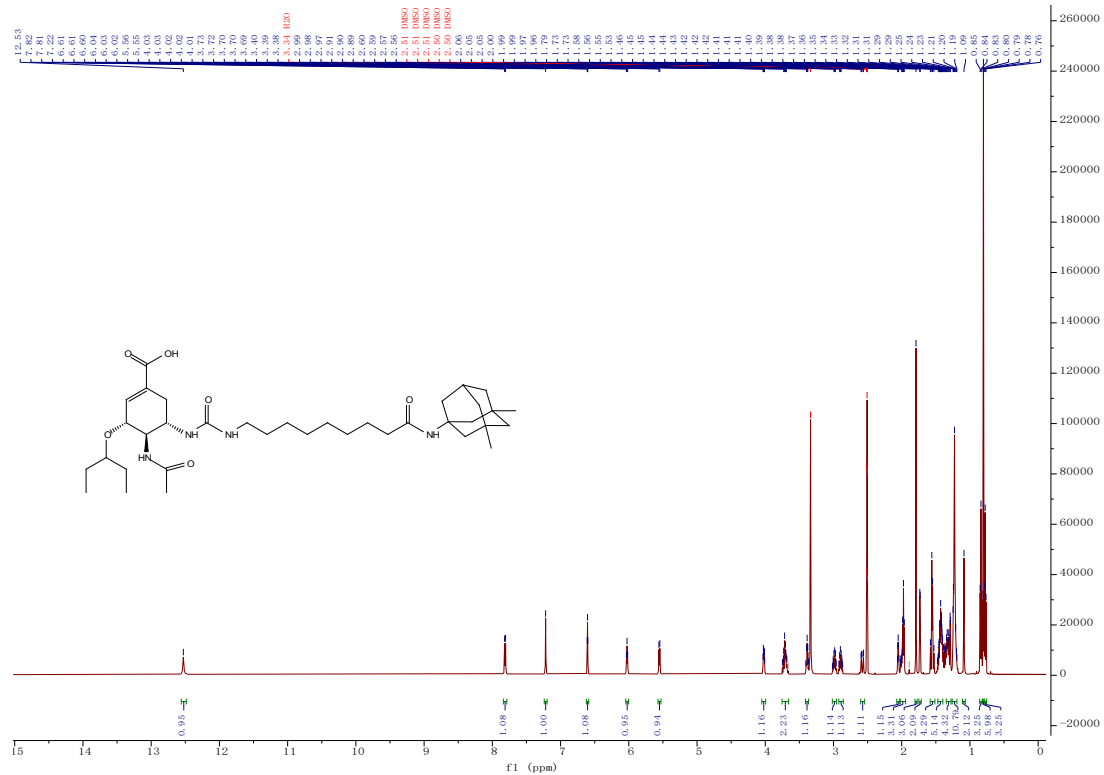
- 172.08
- 165.05
- 158.23
- 138.69
- 129.19
- 81.57
- 75.80
- 60.87
- 58.12
- 52.31
- 50.78
- 48.65
- 46.56
- 42.83
- 40.53
- 37.24
- 36.50
- 36.40
- 30.40
- 29.17
- 29.05
- 26.79
- 26.68
- 25.71
- 23.27
- 23.27
- 19.88
- 0.59

T: FTMS • p ESI Full ms [100 0000-1500 0000]

Mass spectrum plot showing relative abundance versus m/z. The x-axis ranges from 100 to 1500 m/z, and the y-axis ranges from 0 to 100 relative abundance. The base peak is at m/z 673.49. Other significant peaks are labeled at m/z 150.10, 186.22, 288.23, 348.23, 356.22, 415.27, 475.32, 530.23, 585.40, 652.53, 695.47, 711.44, 718.55, 774.61, 802.64, 854.65, 1007.79, 1029.20, 1036.69, 1092.19, 1190.67, 1357.96, 1367.95, 1383.93, and 1493.83.

Spectrums of L11

^1H NMR of L11



Chemical structure of compound 10 is shown in the top left. The ^1H NMR spectrum (CDCl₃) is displayed below, with peaks labeled by their chemical shifts (ppm):

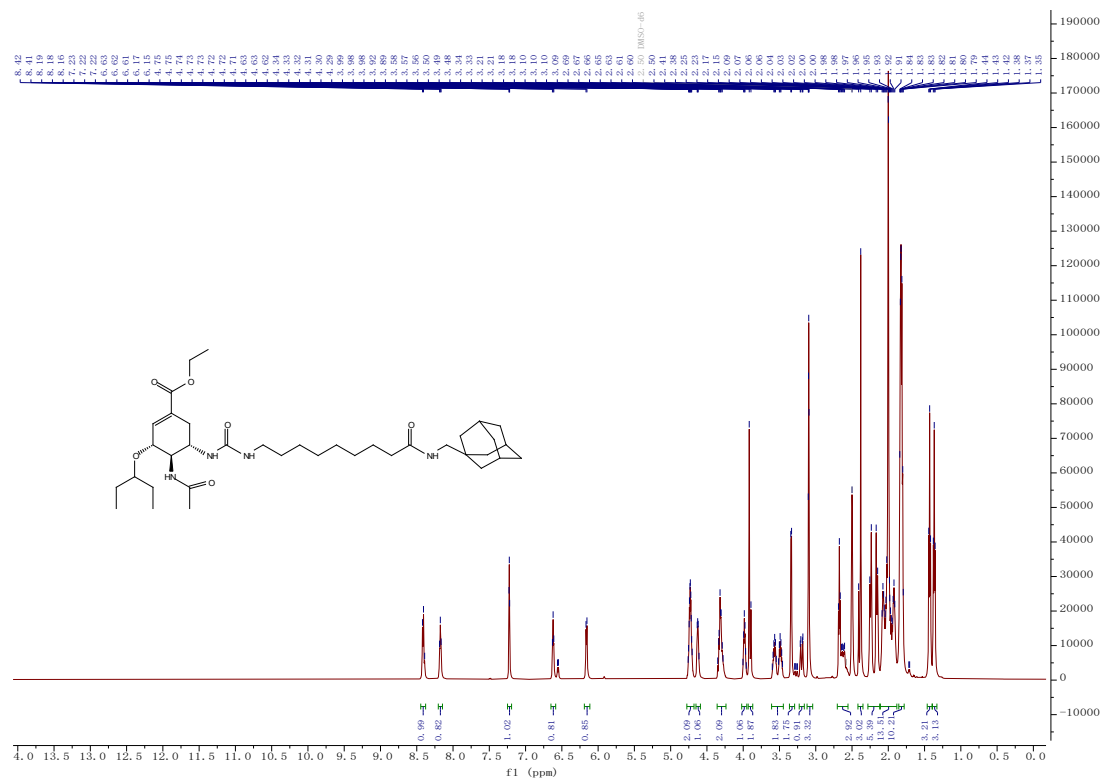
- 172.10, 169.97, 167.75, 168.27, 138.18, 129.81
- 81.53, 75.93
- 54.27, 52.51, 52.40, 52.35, 48.72, 47.96, 47.85, 42.83, 40.53, 40.13, 40.27, 39.89, 39.71, 39.65, 39.62, 32.27, 32.14, 30.99, 30.41, 29.57, 29.26, 29.25, 29.18, 28.67, 28.61, 26.79, 26.19, 25.70, 23.27, 23.18, 18.98, 18.18

T: FTMS + p ESI Full ms [100.0000-1500.0000]

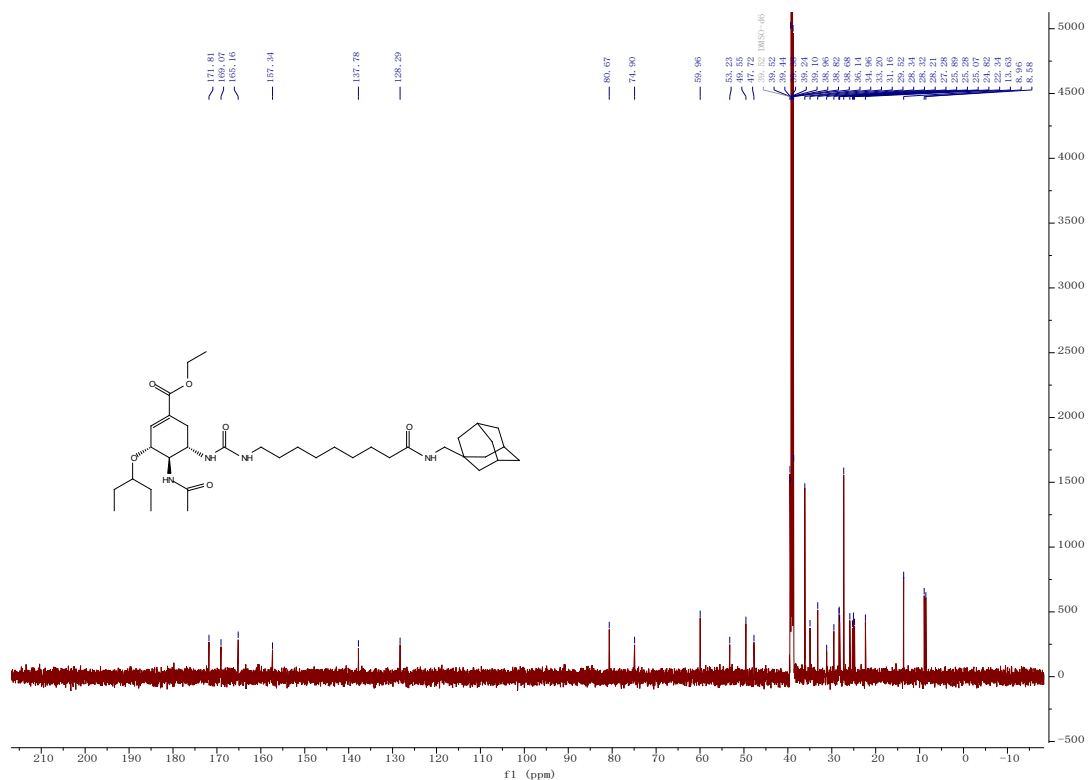
Mass spectrum plot showing relative abundance versus m/z. The x-axis ranges from 100 to 1500 m/z, and the y-axis ranges from 0 to 100 relative abundance. The base peak is at m/z 667.44. Other significant peaks are labeled with their m/z values.

m/z	Relative Abundance (approx)
130.16	1
167.07	1
242.28	1
288.23	1
350.23	1
437.19	1
475.32	1
529.27	1
596.37	1
645.46	35
667.44	100
695.47	10
701.49	5
774.61	1
816.42	1
927.66	1
986.66	1
1035.54	1
1174.72	1
1311.89	10
1368.96	1
1450.79	1

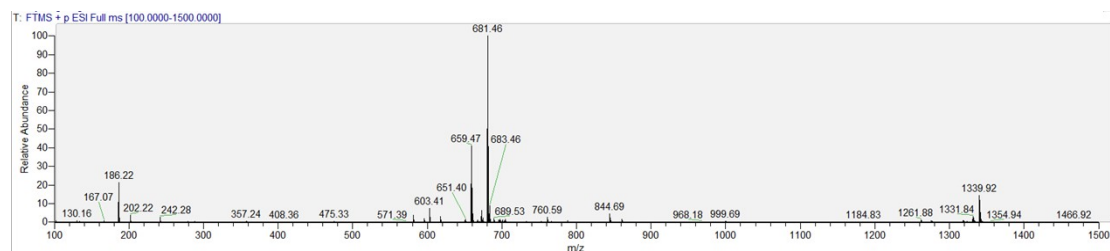
¹H NMR of L12



¹³C NMR of L12

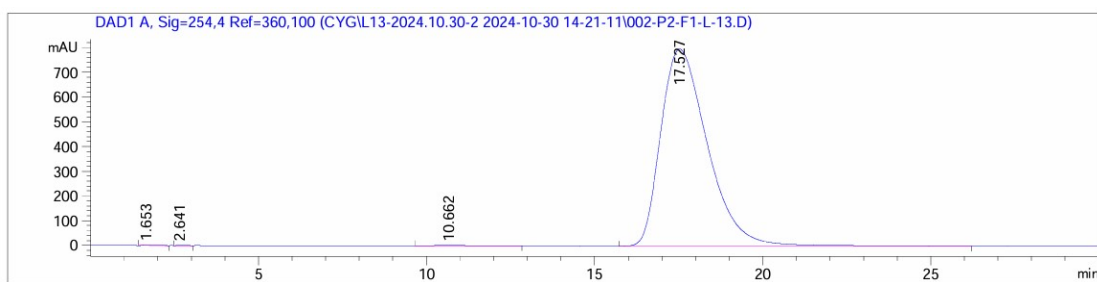


ESI-HRMS spectrum of L12



HPLC spectrum of L12

The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AS-3 column (0.01×25 cm), Hexane/*i*PrOH = 80:20, flow rate = 0.4 mL/min, λ = 254 nm, $t_{1/2}$: 17.527 min.



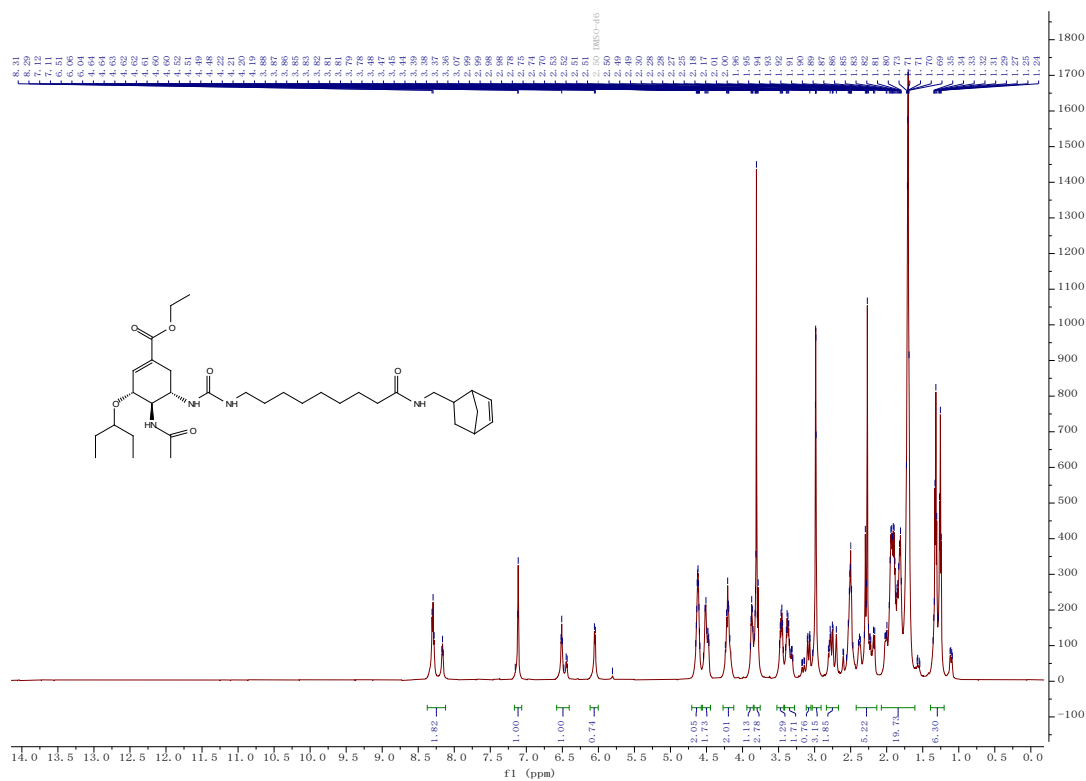
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.653	BB	0.1782	46.82692	3.41114	0.0609
2	2.641	BV	0.1682	18.22373	1.45404	0.0237
3	10.662	BB	0.7094	195.31413	3.26759	0.2539
4	17.527	BB	1.4794	7.66740e4	796.26025	99.6616

Totals : 7.69344e4 804.39303

Spectrums of L13

¹H NMR of L13



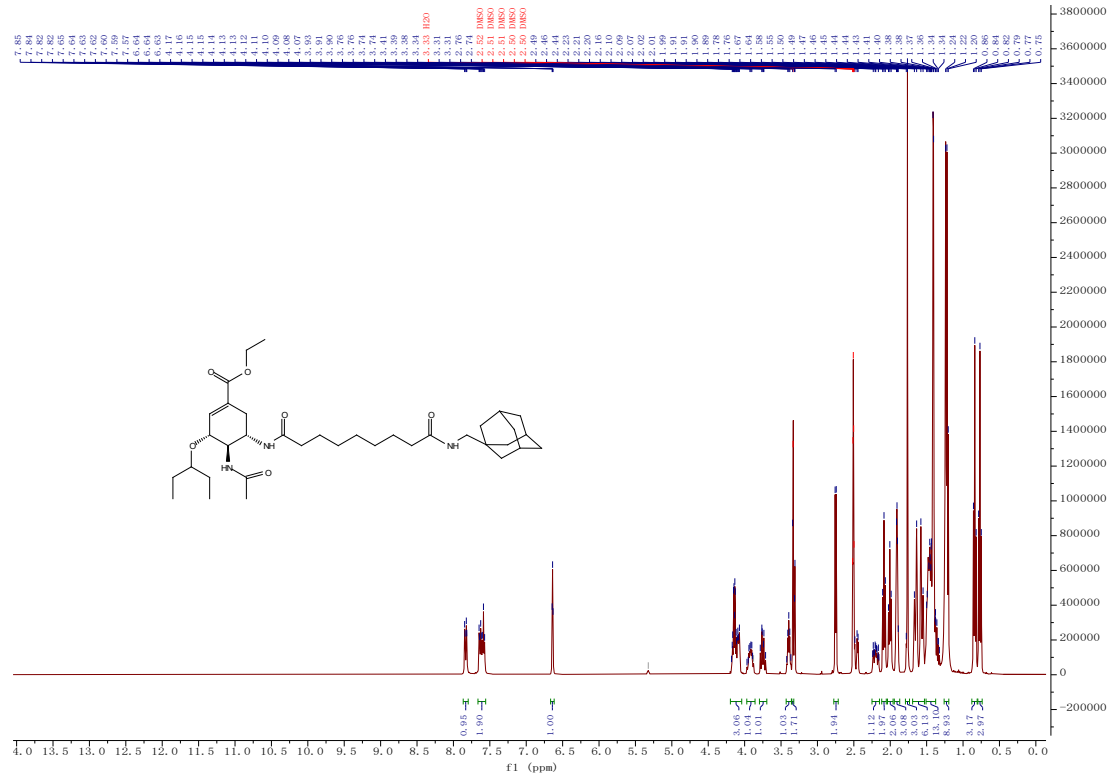
[illegible]

T: FIMS pESI Full ms [100 0000-1500 0000]

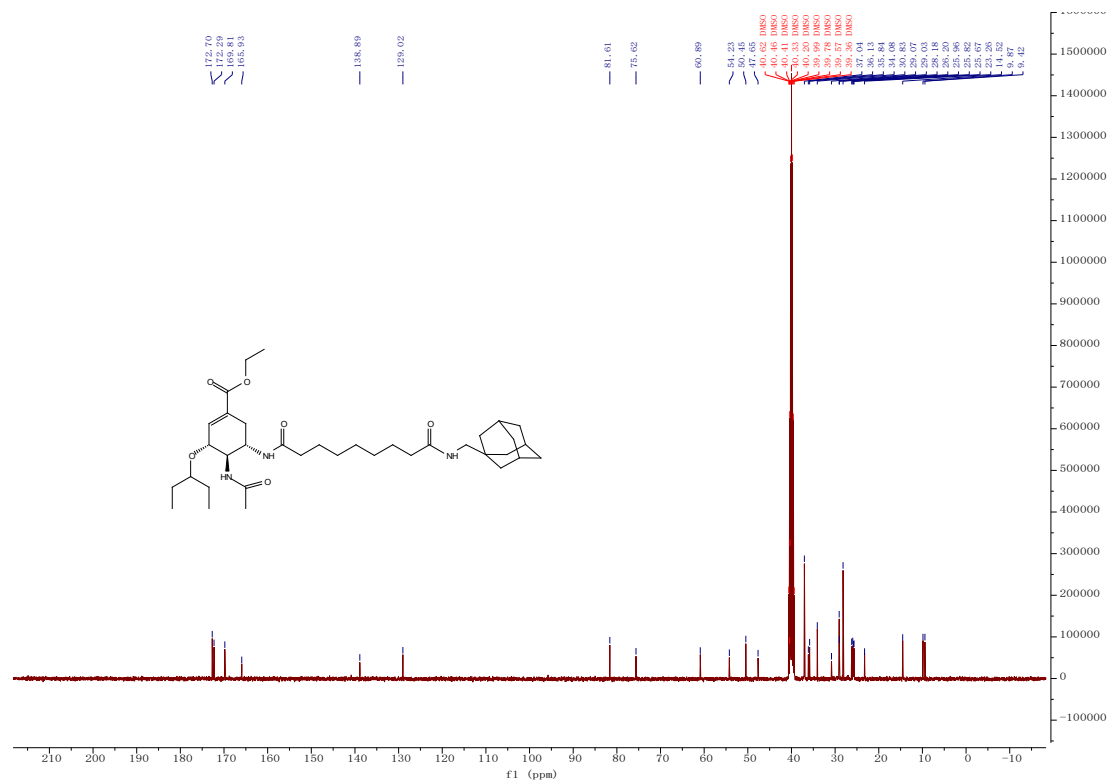
Mass spectrum showing Relative Abundance (Y-axis, 0 to 100) versus m/z (X-axis, 100 to 1500). The base peak is at m/z 675.38. Other labeled peaks include: 129.03, 186.22, 242.28, 289.23, 373.26, 463.30, 507.33, 573.36, 581.43, 603.41, 639.41, 653.40, 678.39, 681.45, 766.64, 838.62, 991.08, 1090.52, 1184.83, 1255.80, 1327.78, and 1369.77. A bracket labeled 'x2' indicates a 2-fold increase in relative abundance for the peak at m/z 675.38.

Spectrums of L14

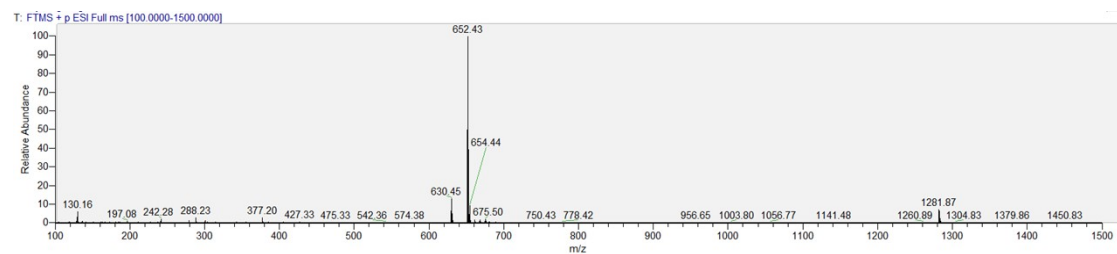
¹H NMR of L14



¹³C NMR of L14

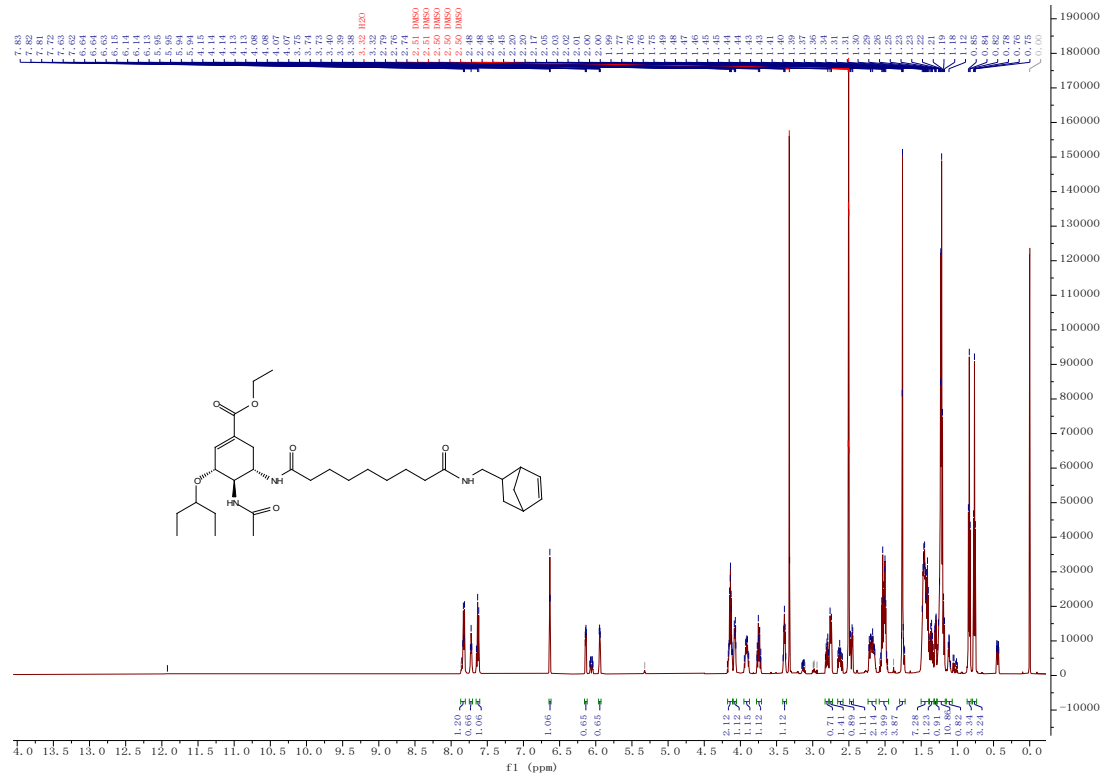


ESI-HRMS spectrum of L14

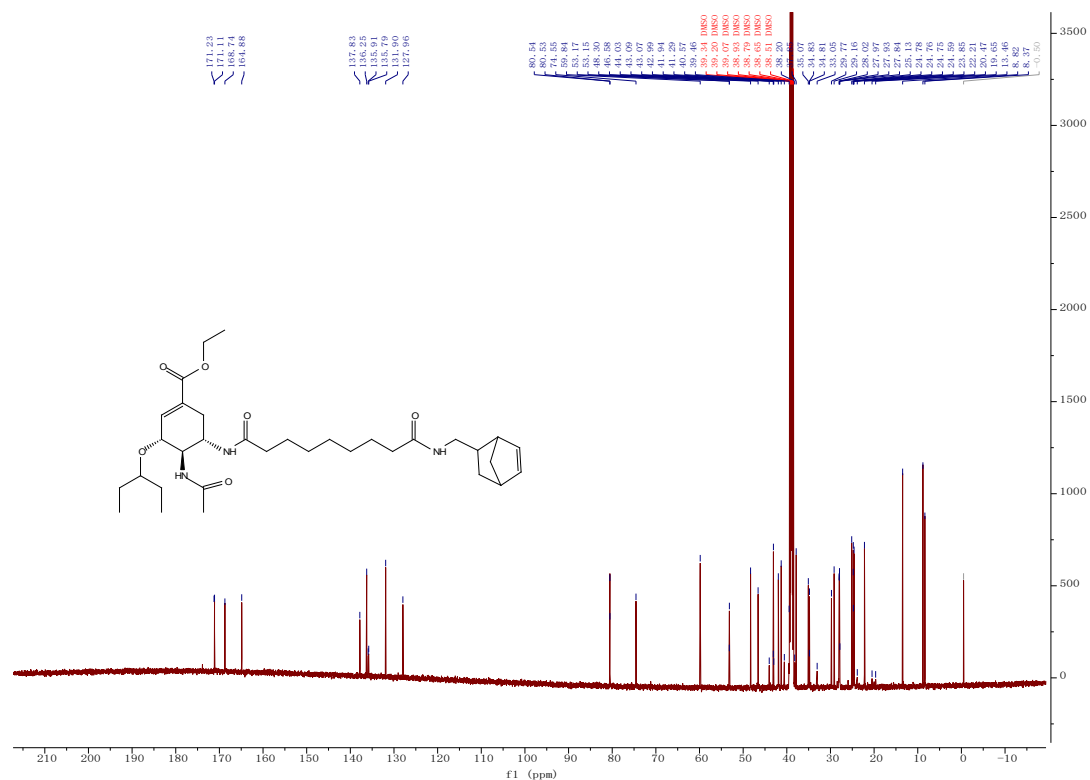


Spectrums of L15

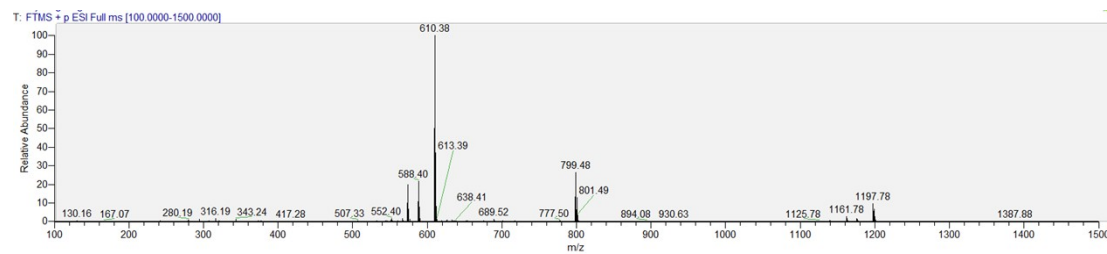
¹H NMR of L15



¹³C NMR of L15

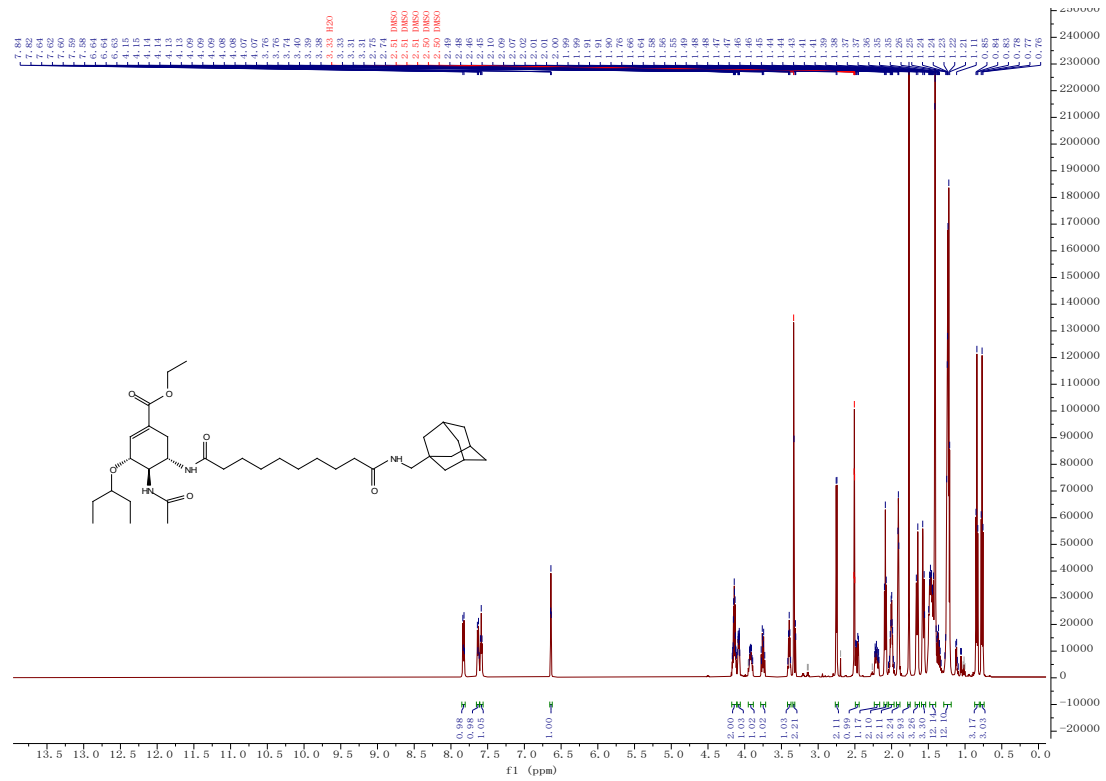


ESI-HRMS spectrum of L15

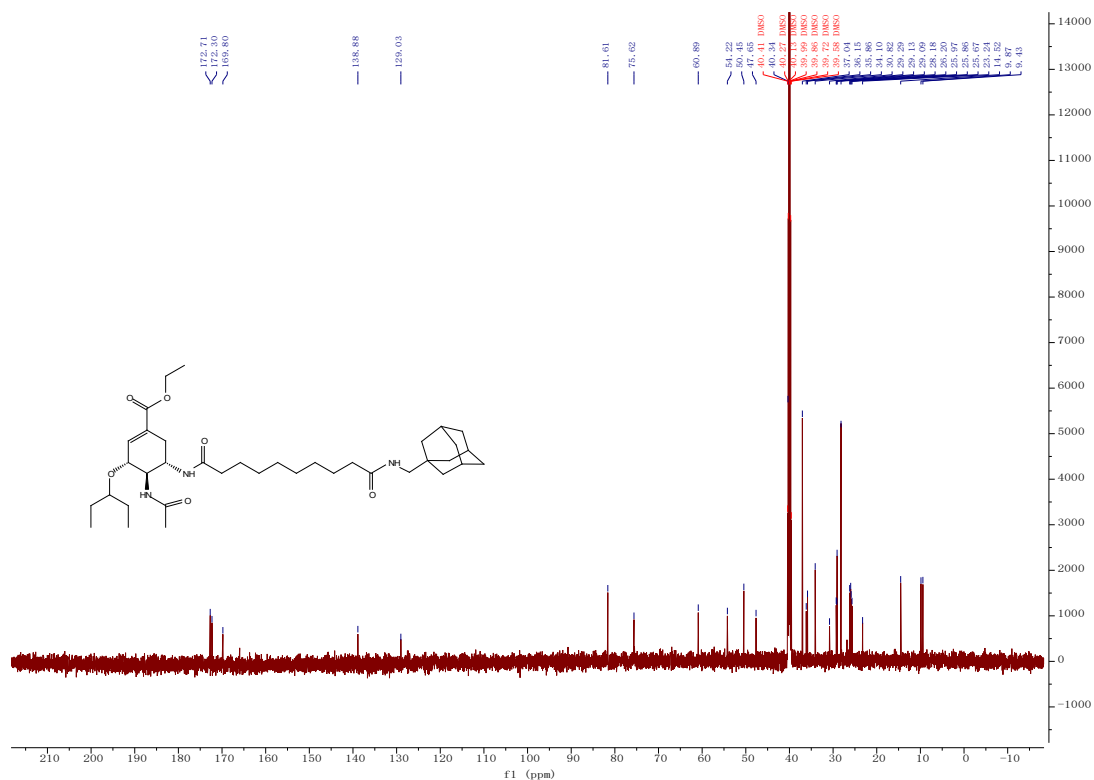


Spectrums of L16

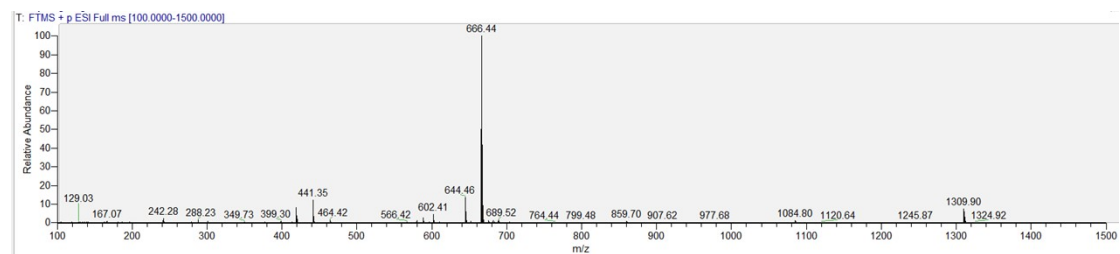
¹H NMR of L16



¹³C NMR of L16

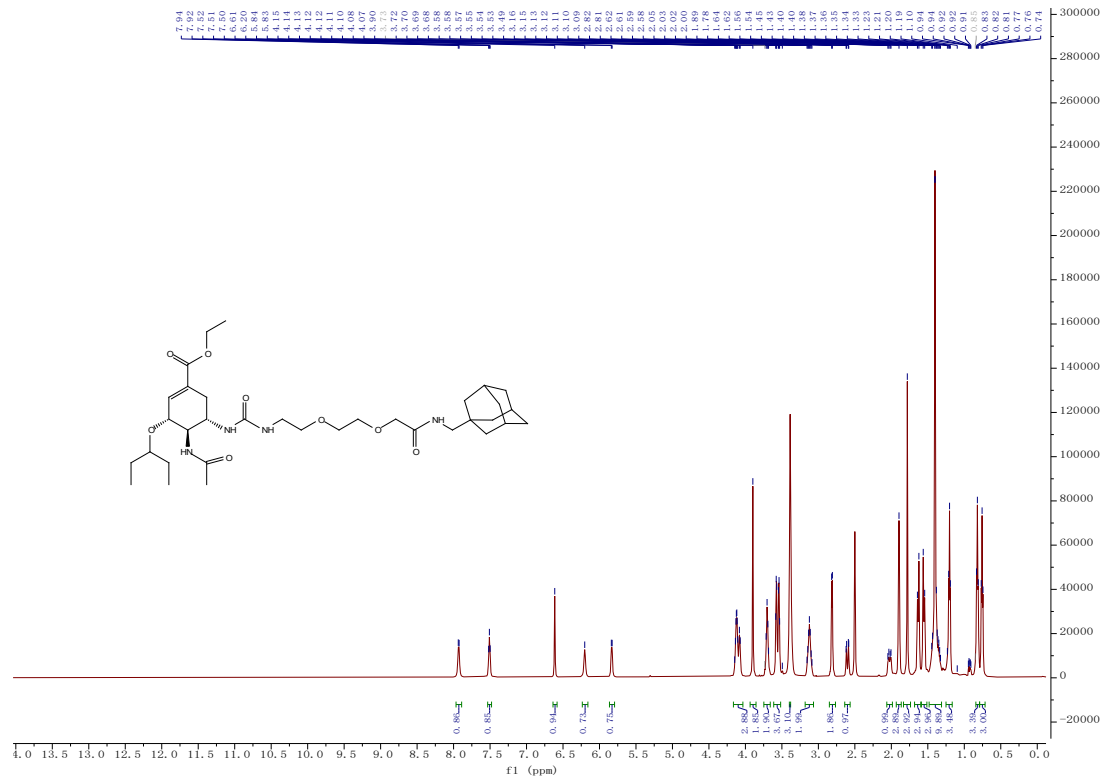


ESI-HRMS spectrum of L16

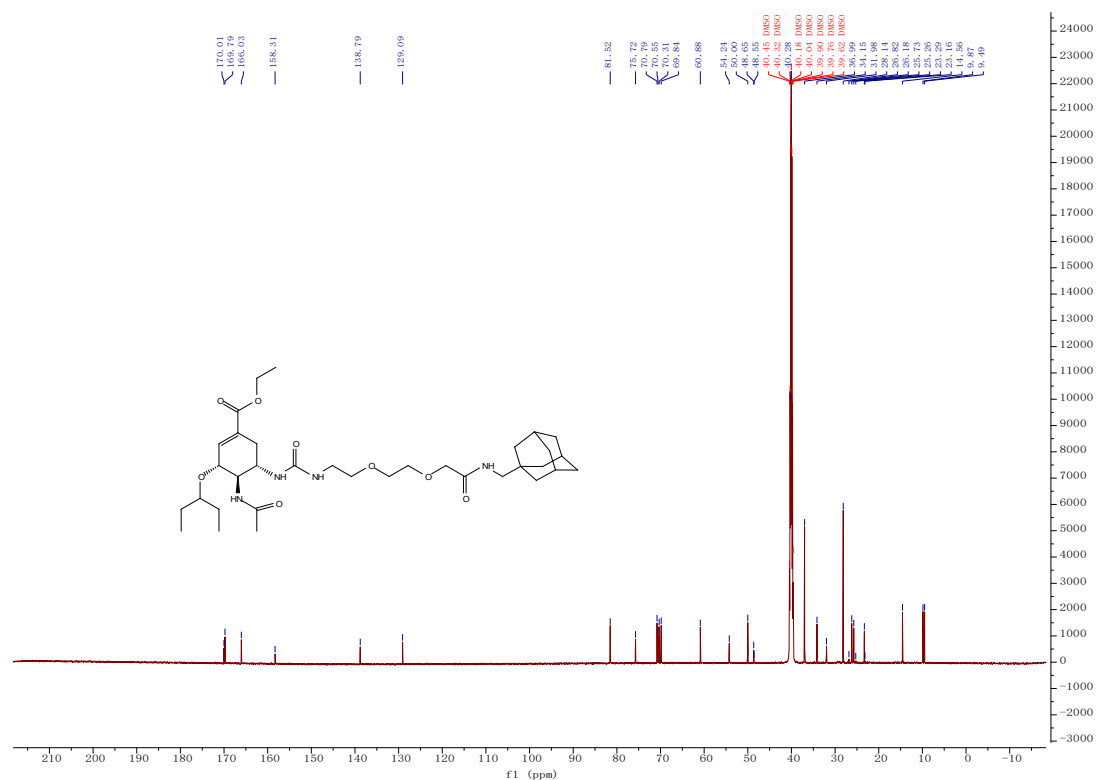


Spectrums of L17

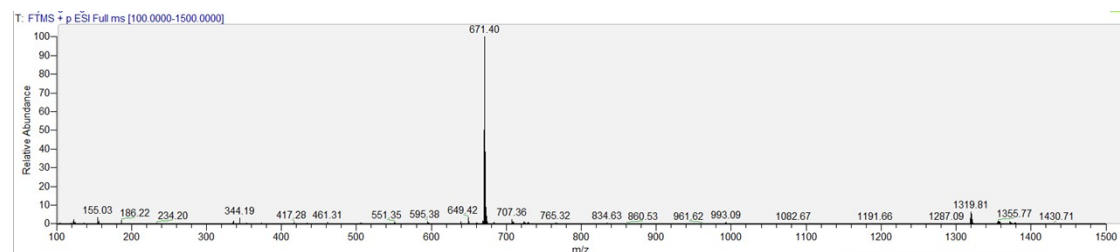
^1H NMR of L17



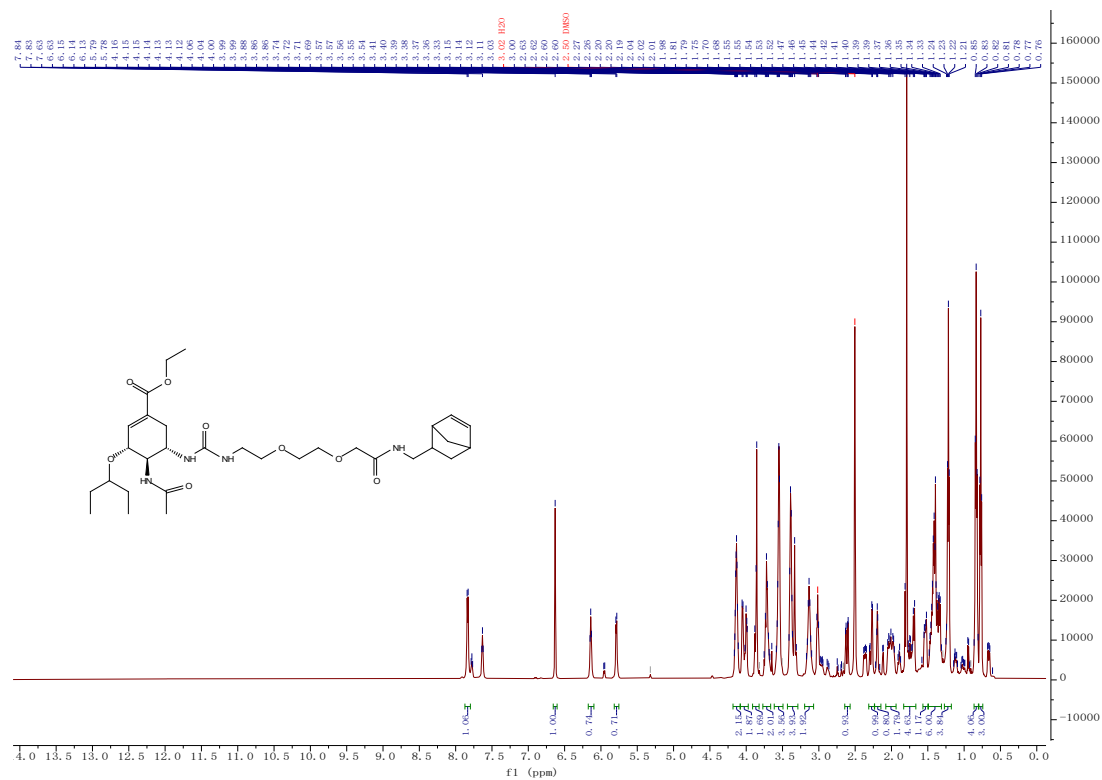
¹³C NMR of L17



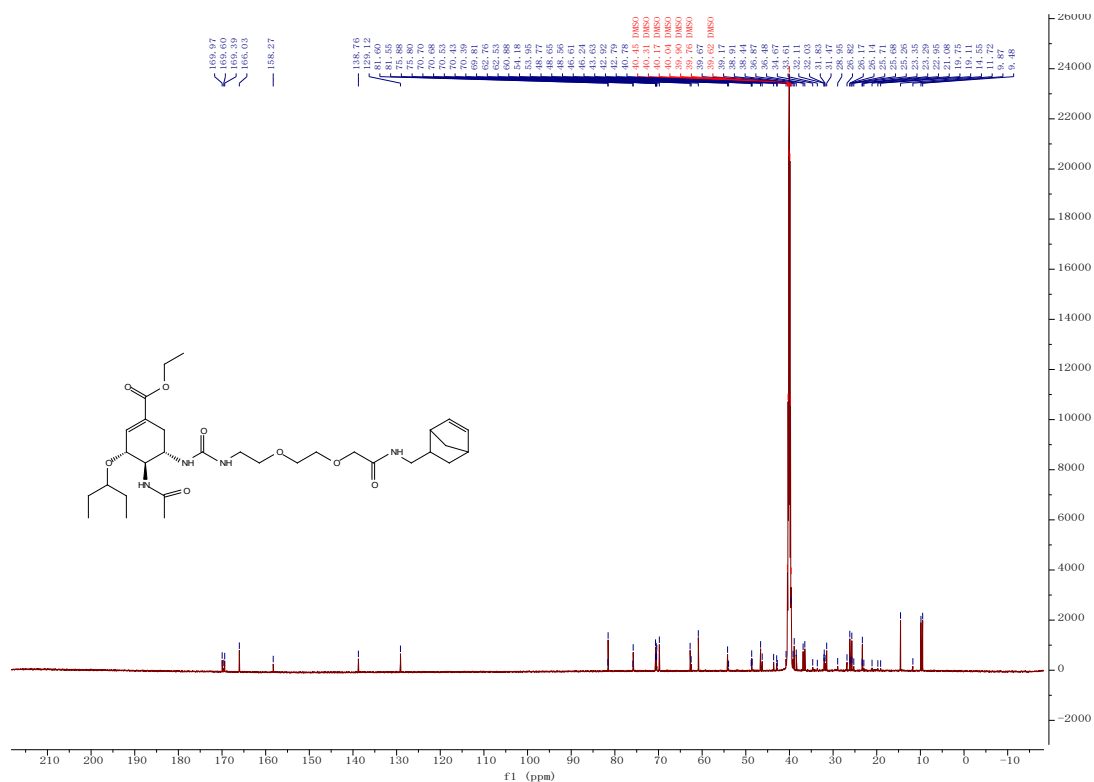
ESI-HRMS spectrum of L17



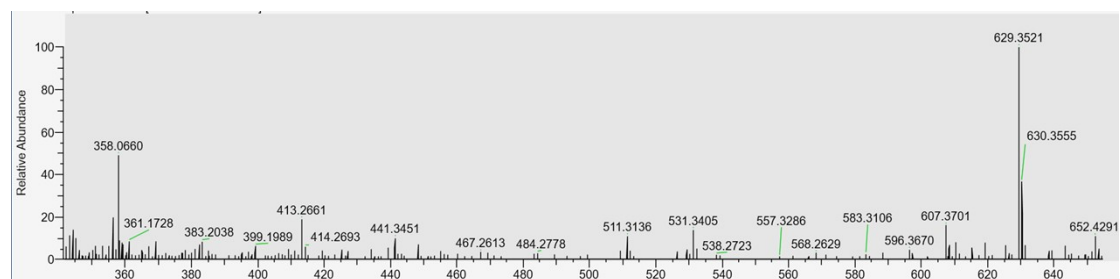
¹H NMR of L18



¹³C NMR of L18

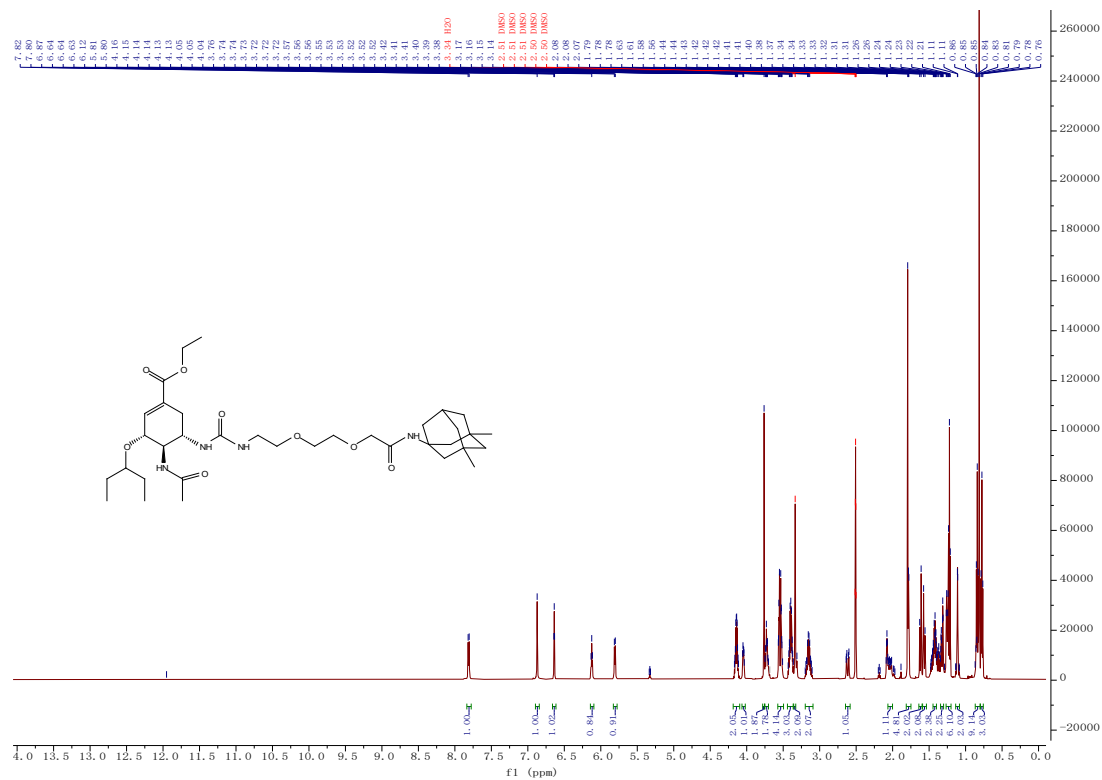


ESI-HRMS spectrum of L18

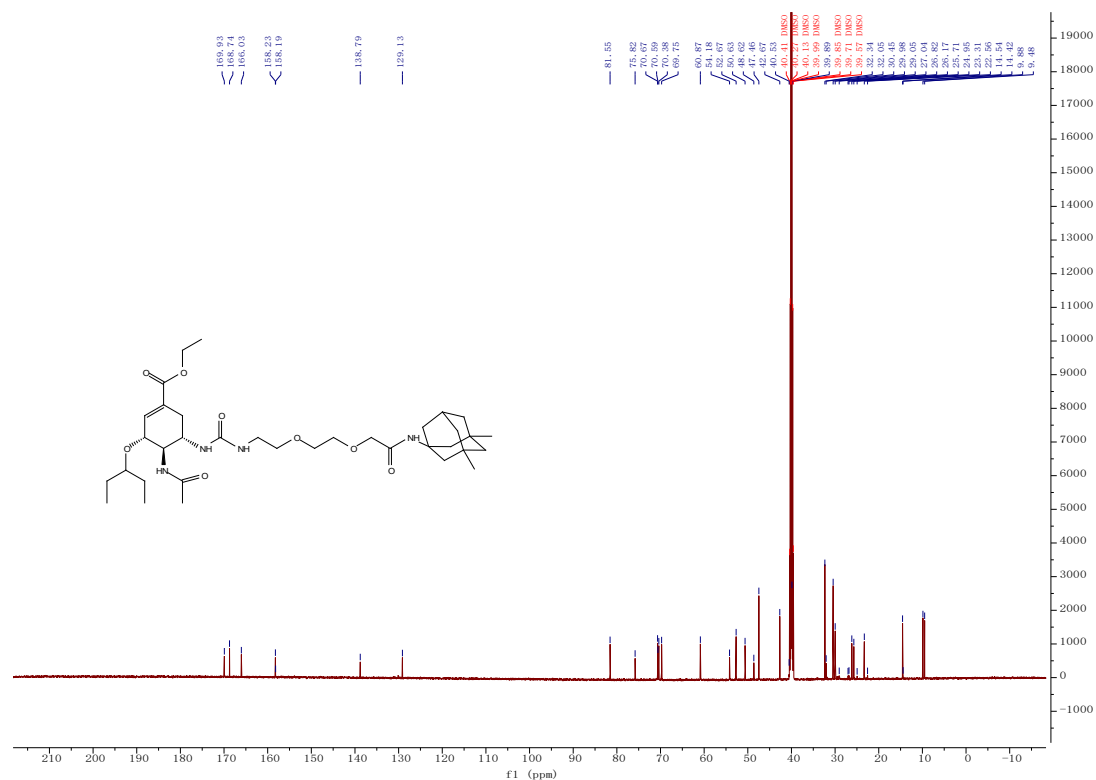


Spectrums of L19

¹H NMR of L19



^{13}C NMR of L19



ESI-HRMS spectrum of L19

