Supplementary Materials: Synthesis and Biological Evaluation of Curcumin Derivatives with Water-Soluble Groups as Potential Antitumor Agents: An *in Vitro* Investigation Using Tumor Cell Lines

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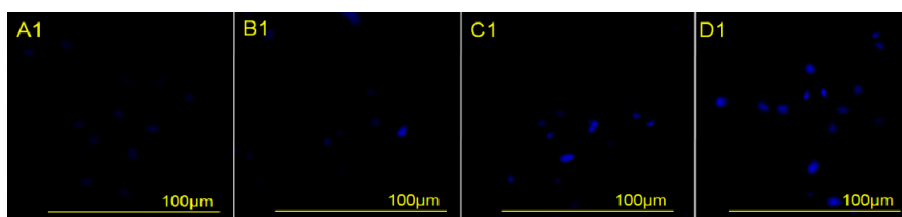## 1. Cell Apoptosis Effects of Compounds 8 and 9 on HeLa or 12 on MCF-7
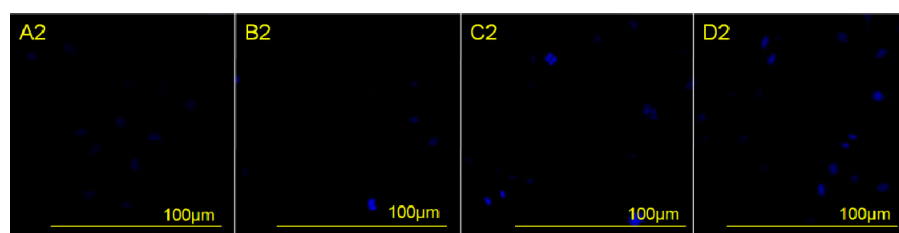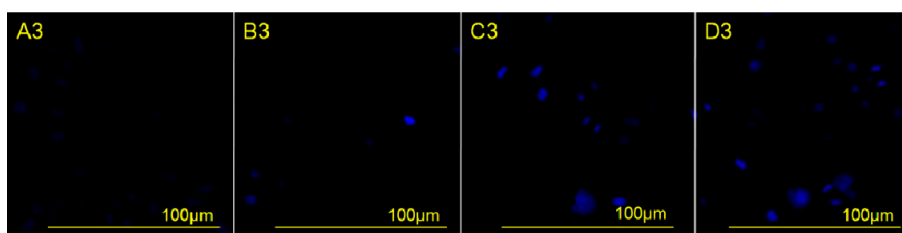

Figure S1. Effects of compound **8** on HeLa cell apoptosis was observed by DAPI staining under an inversion fluorescent microscope. HeLa cells were incubated with 0 μM (**A1**); 2.5 μM (**B1**); 5 μM (**C1**); or 10 μM (**D1**) of compound **8** for 48 h.


Figure S2. Effects of compound **9** on HeLa cell apoptosis was observed by DAPI staining under an inversion fluorescent microscope. HeLa cells were incubated with 0 μM (**A2**); 2.5 μM (**B2**); 5 μM (**C2**); or 10 μM (**D2**) of compound **9** for 48 h.

Figure S3. Effects of compound **12** on HeLa cell apoptosis was observed by DAPI staining under an inversion fluorescent microscope. HeLa cells were incubated with 0 μM (**A3**); 2.5 μM (**B3**); 5 μM (**C3**); or 10 μM (**D3**) of compound **12** for 48 h.
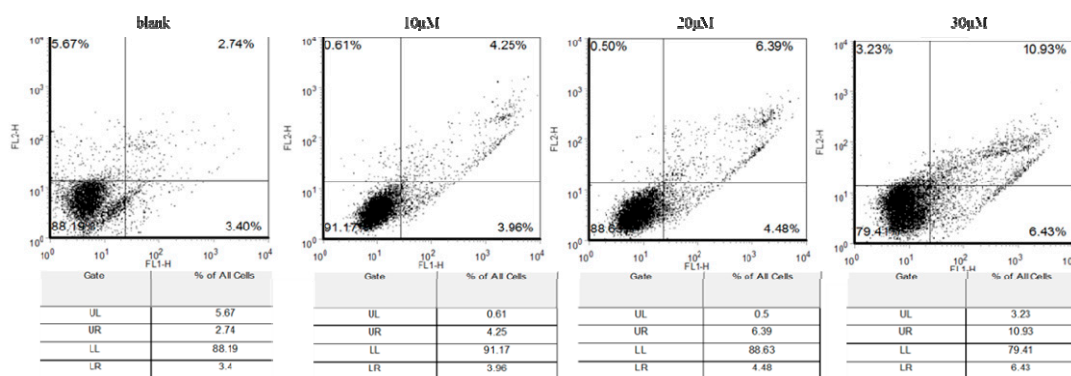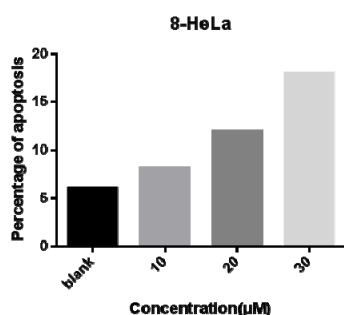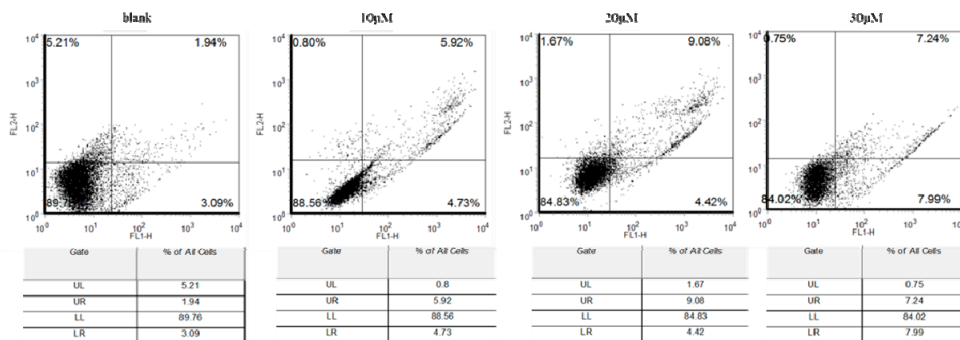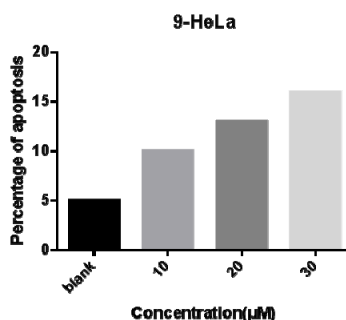
Figure S4. (A) HeLa cells were treated with compound **8** (0, 10, 20, or 30 μM) for 24 h and then analyzed by Annexin V-FITC/PI staining and flow cytometry. The apoptotic cell scatter plot is divided into four quadrants: upper left (UL), upper right (UR), lower left (LL), and lower right (LR) quadrants; **(B)** Apoptosis rate of HeLa cells treated with various concentrations of compound **8**.
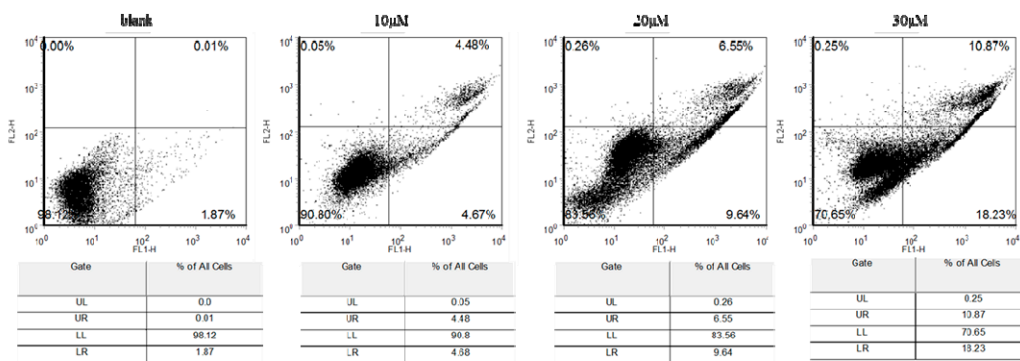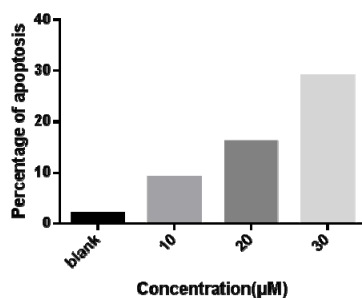

Figure S5. (A) HeLa cells were treated with compound **9** (0, 10, 20, or 30 μM) for 24 h and then analyzed by Annexin V-FITC/PI staining and flow cytometry. The apoptotic cell scatter plot is divided into four quadrants: upper left (UL), upper right (UR), lower left (LL), and lower right (LR) quadrants; **(B)** Apoptosis rate of HeLa cells treated with various concentrations of compound **9**.

A

B

Figure S6. (A) MCF-7 cells were treated with compound **12** (0, 10, 20, or 30 μM) for 24 h and then analyzed by Annexin V-FITC/PI staining and flow cytometry. The apoptotic cell scatter plot is divided into four quadrants: upper left (UL), upper right (UR), lower left (LL), and lower right (LR) quadrants. **(B)** Apoptosis rate of MCF-7 cells treated with various concentrations of compound **12**.

2. ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR, MS-ESI, and HRMS-ESI of the Synthetic Compounds
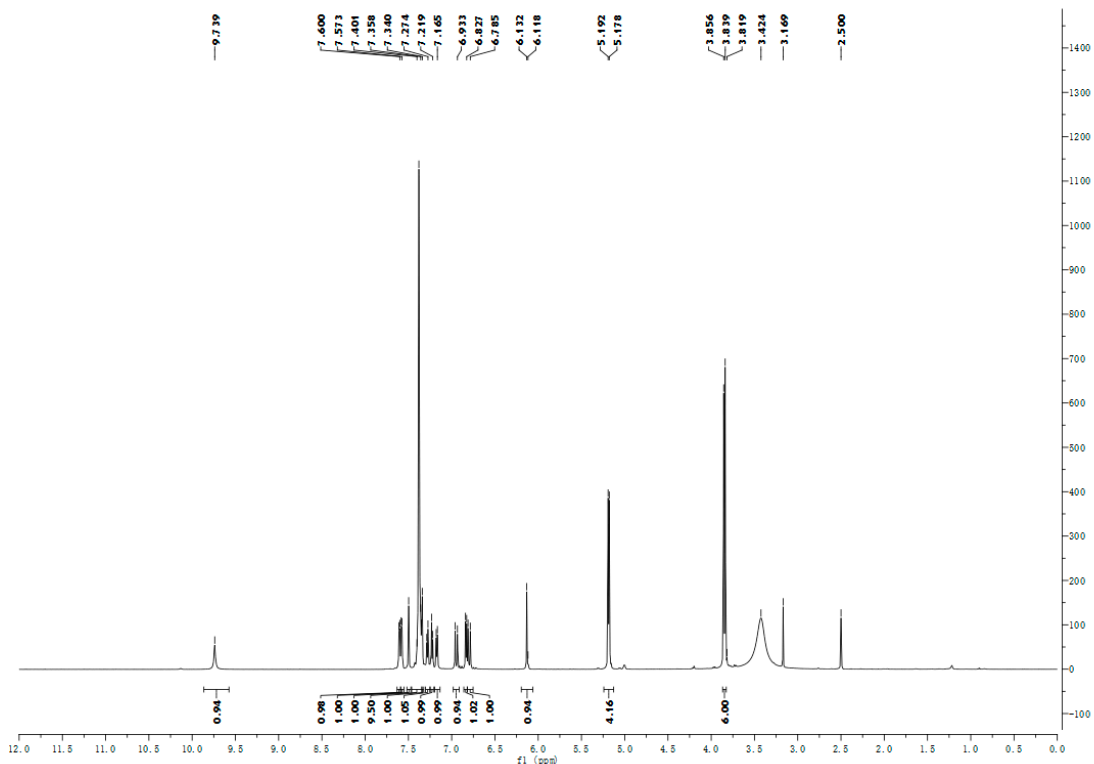
Figure S7. ^{1}H-NMR for compound **1**.

S3
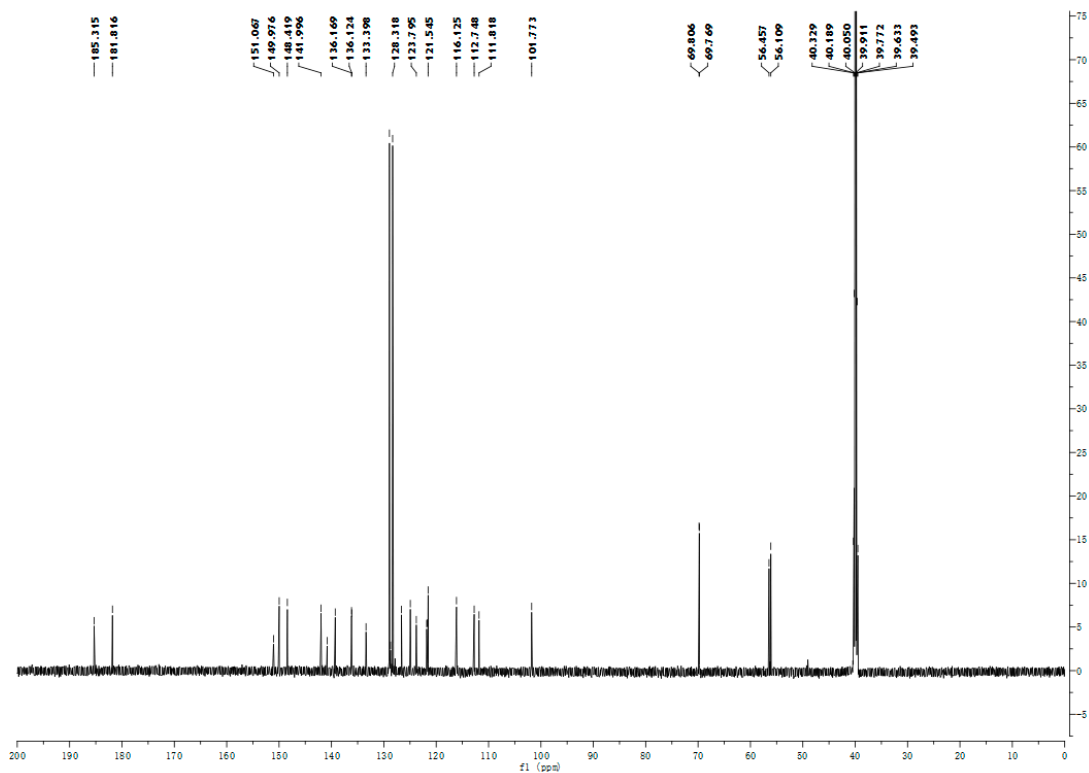
Figure S8. ^{13}C-NMR for compound **1**.

R.Time:0.983(Scan#:119)
MassPeaks:700   BasePeak:627(50711)
Spectrum Mode:Single 0.983(119)
BG Mode:Averaged 0.033-0.692(5-84) Polarity:Negative Segment 1 - Event 1
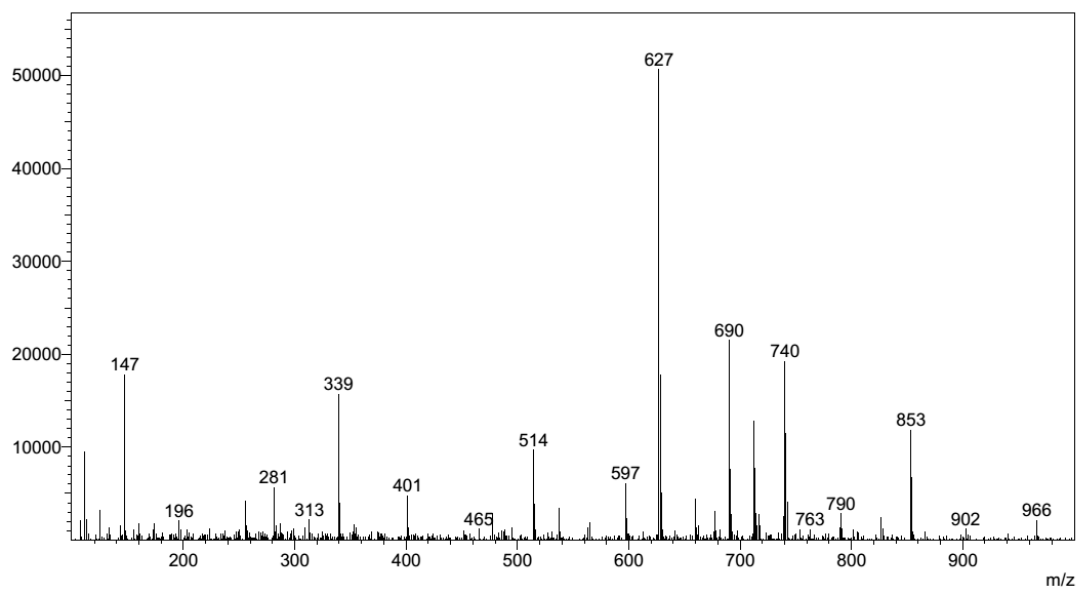
Figure S9. MS-ESI for compound **1**.
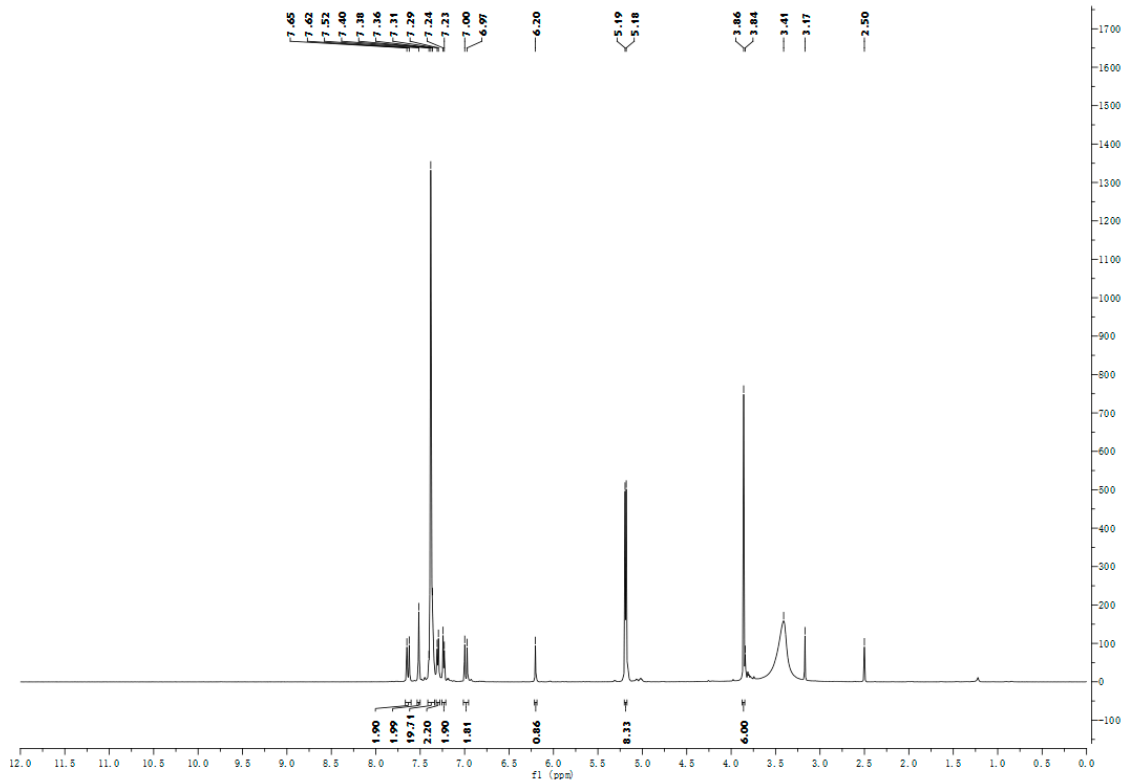
Figure S10. ^{1}H-NMR for compound **2**.
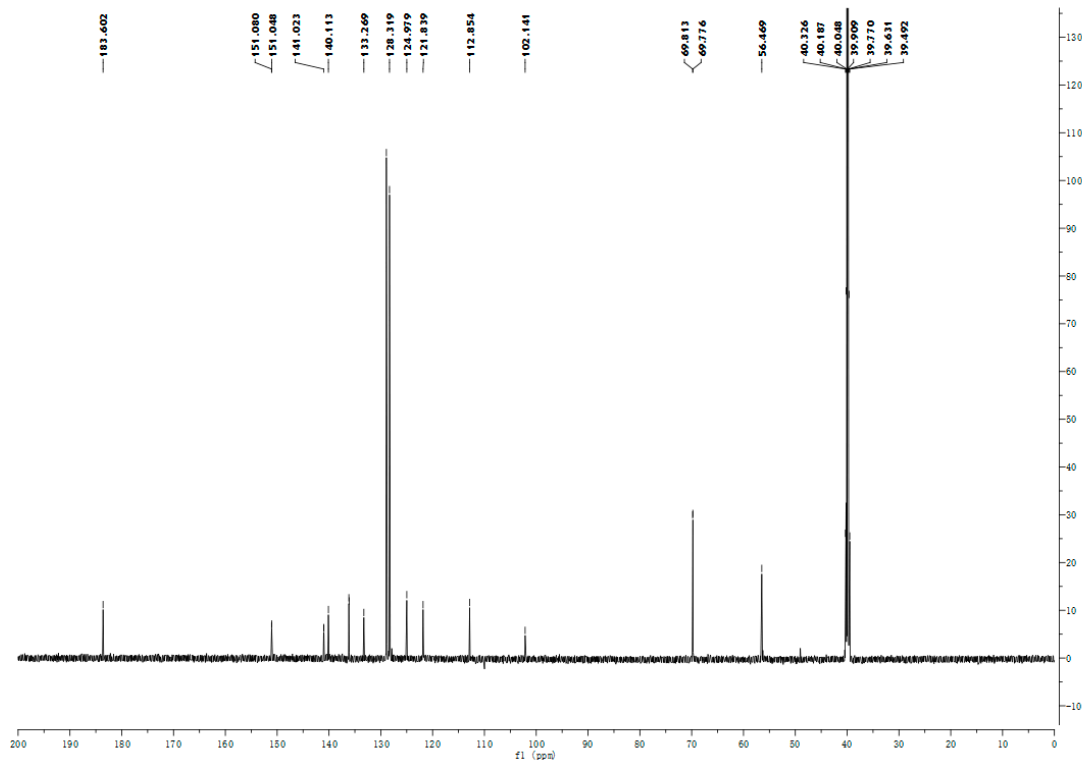
Figure S11. ^{13}C-NMR for compound **2**.
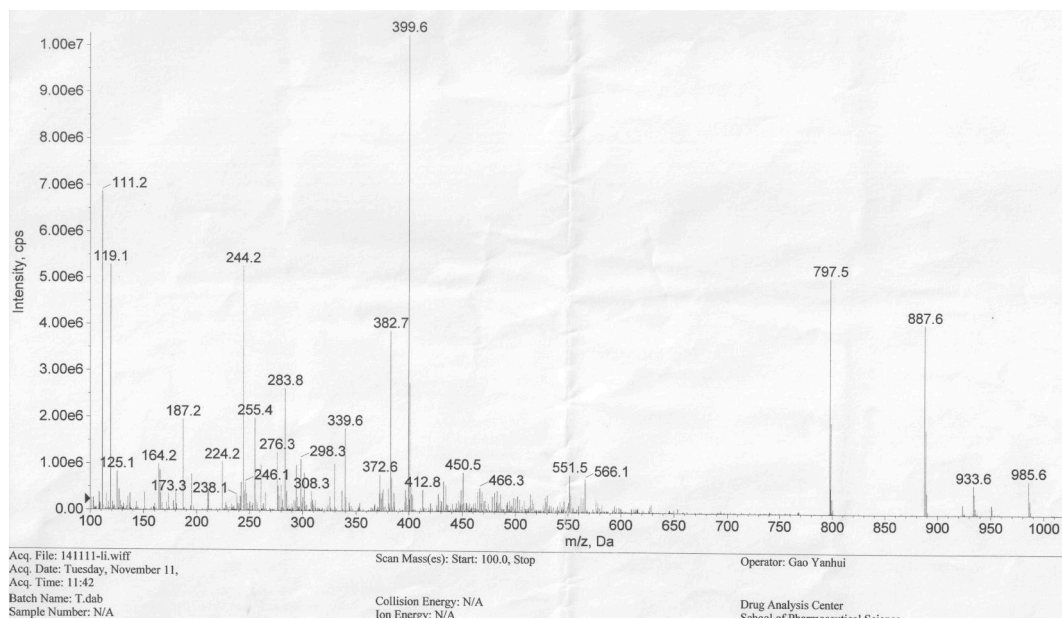
Figure S12. MS-ESI for compound **2**.
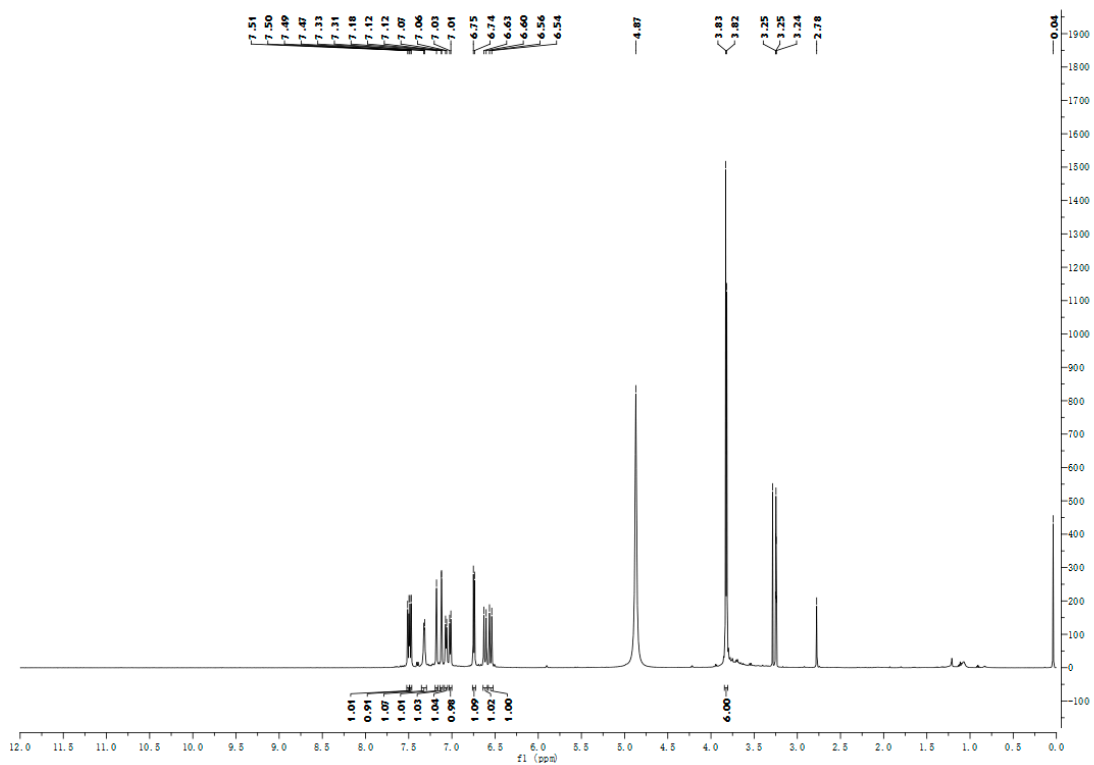
Figure S13. ^{1}H-NMR for compound **3**.
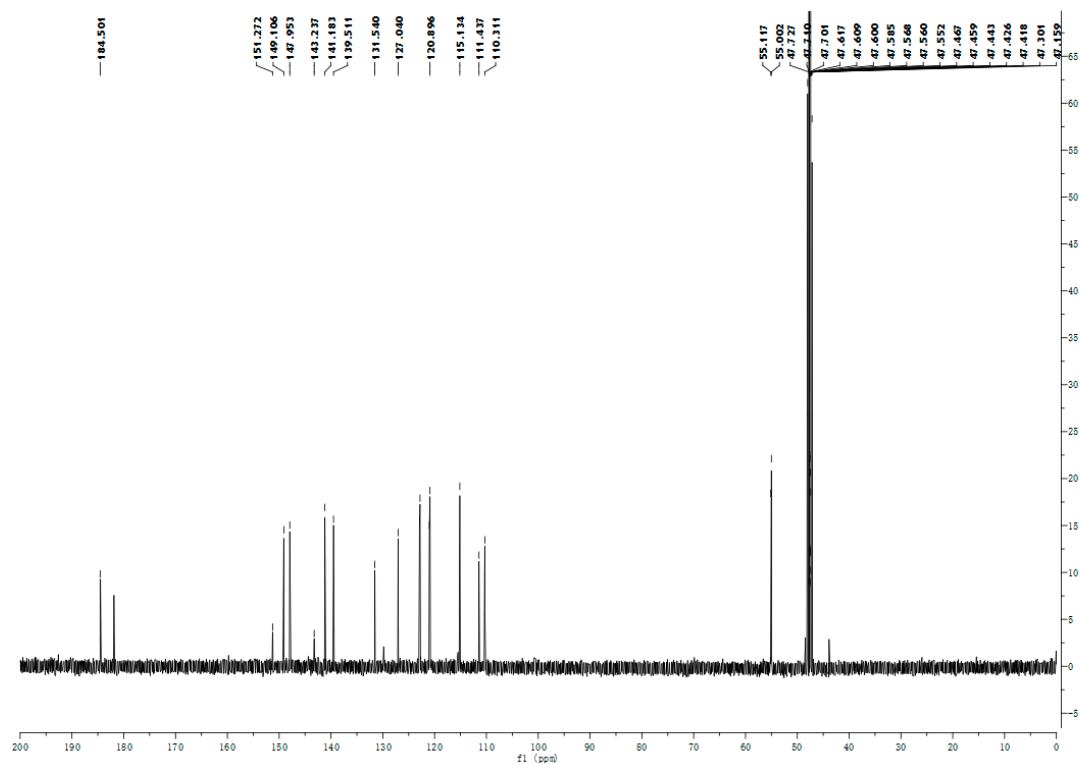
Figure S14. ^{13}C-NMR for compound **3**.
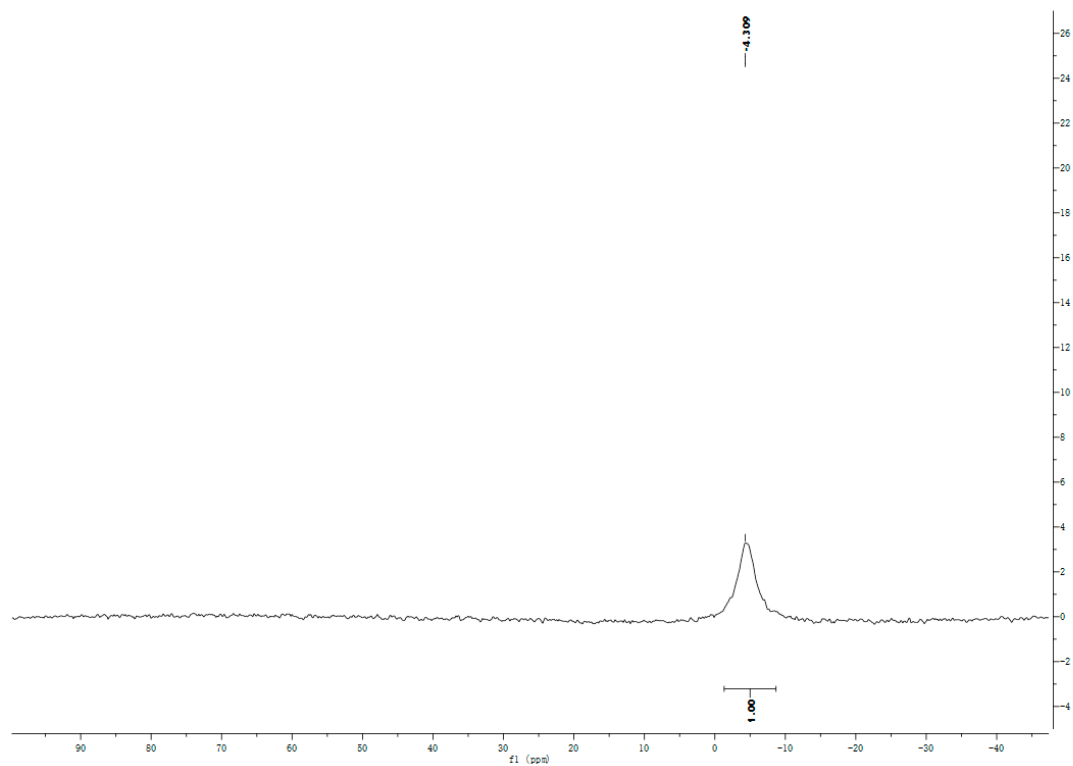
Figure S15. ^{31}P-NMR for compound **3**.

S7
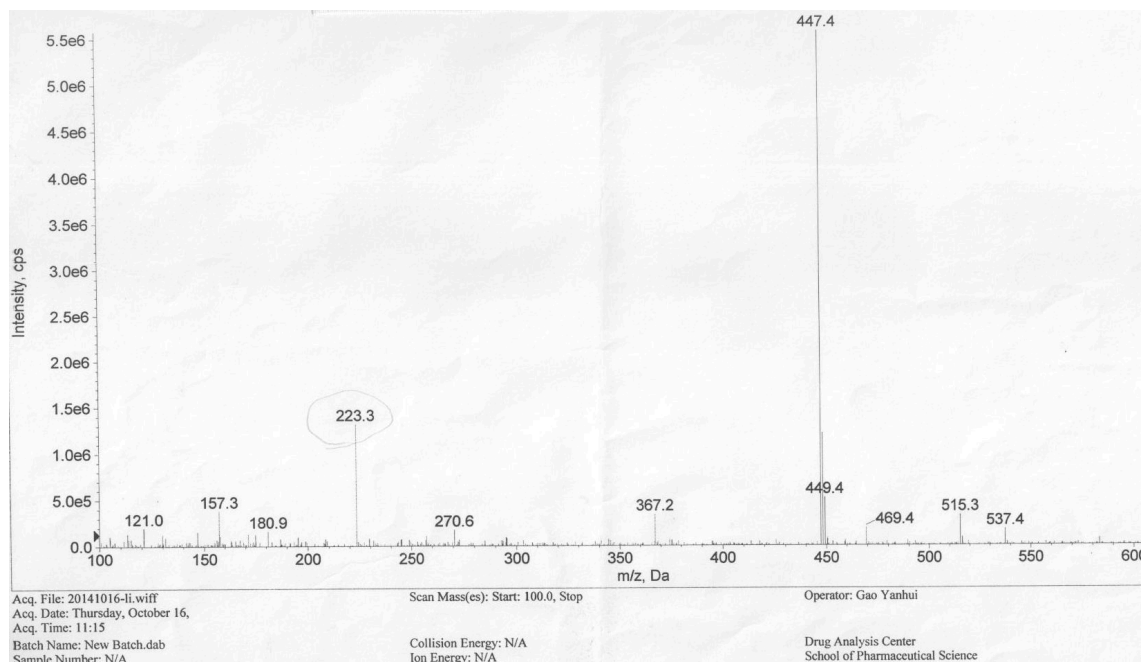
Figure S16. MS-ESI for compound **3**.
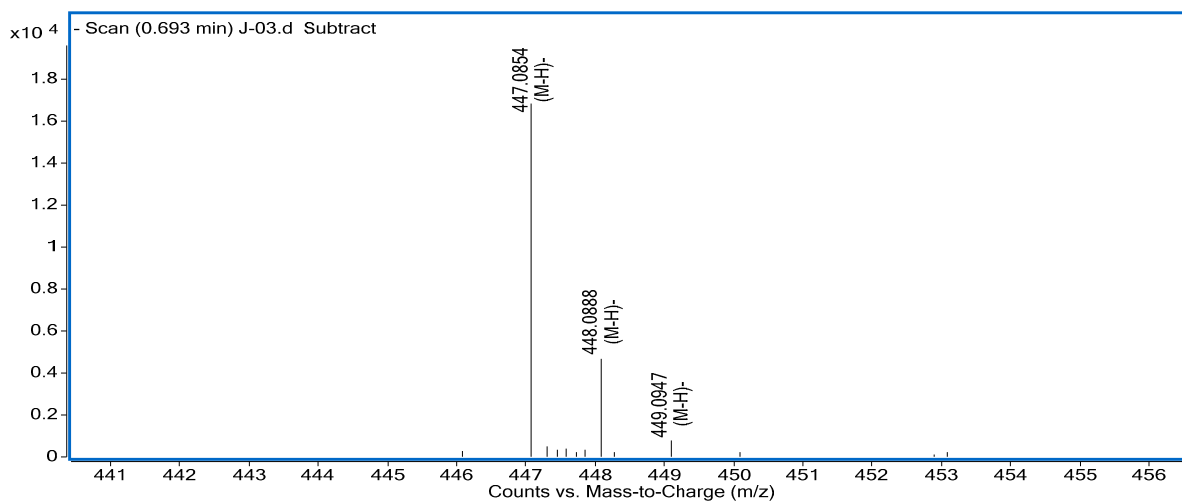
Figure S17. HRMS-ESI for compound **3**.
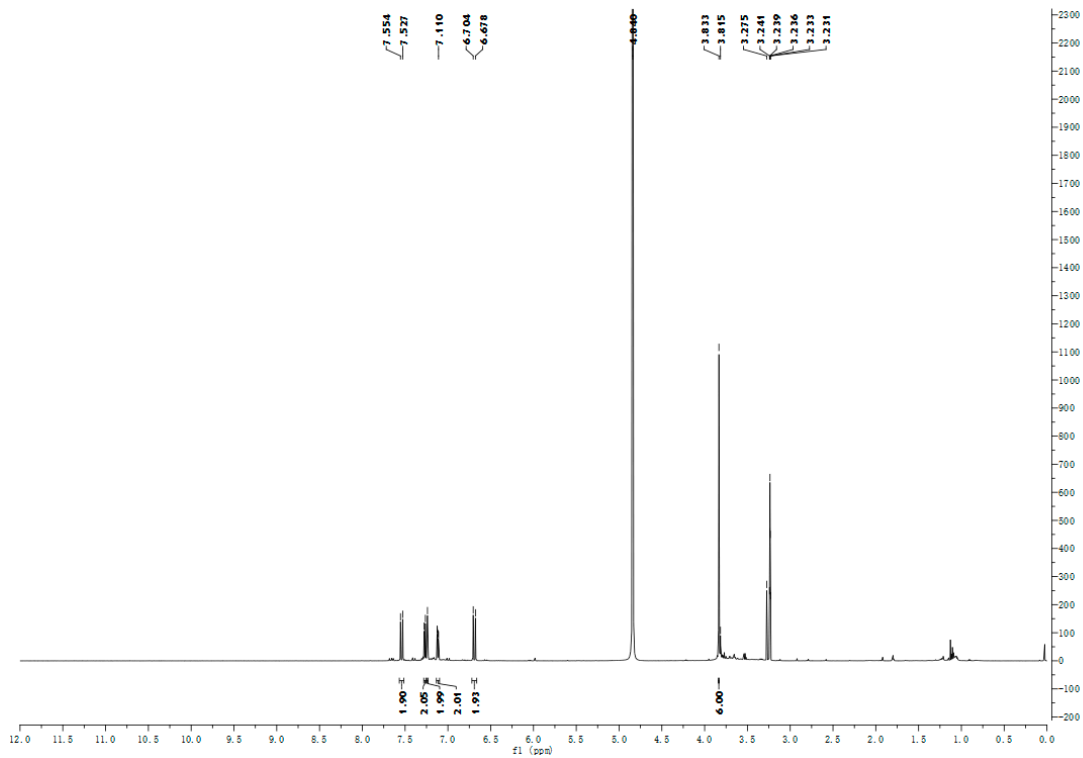
Figure S18. ^{1}H-NMR for compound **4**.
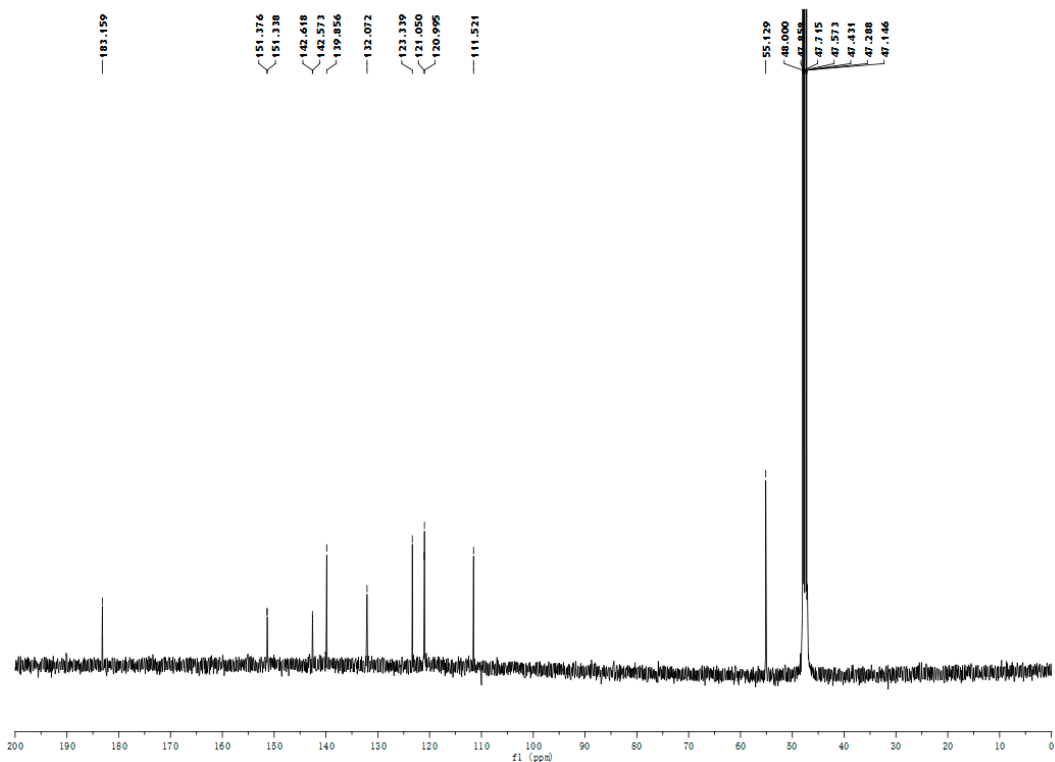
Figure S19. ^{13}C-NMR for compound **4**.
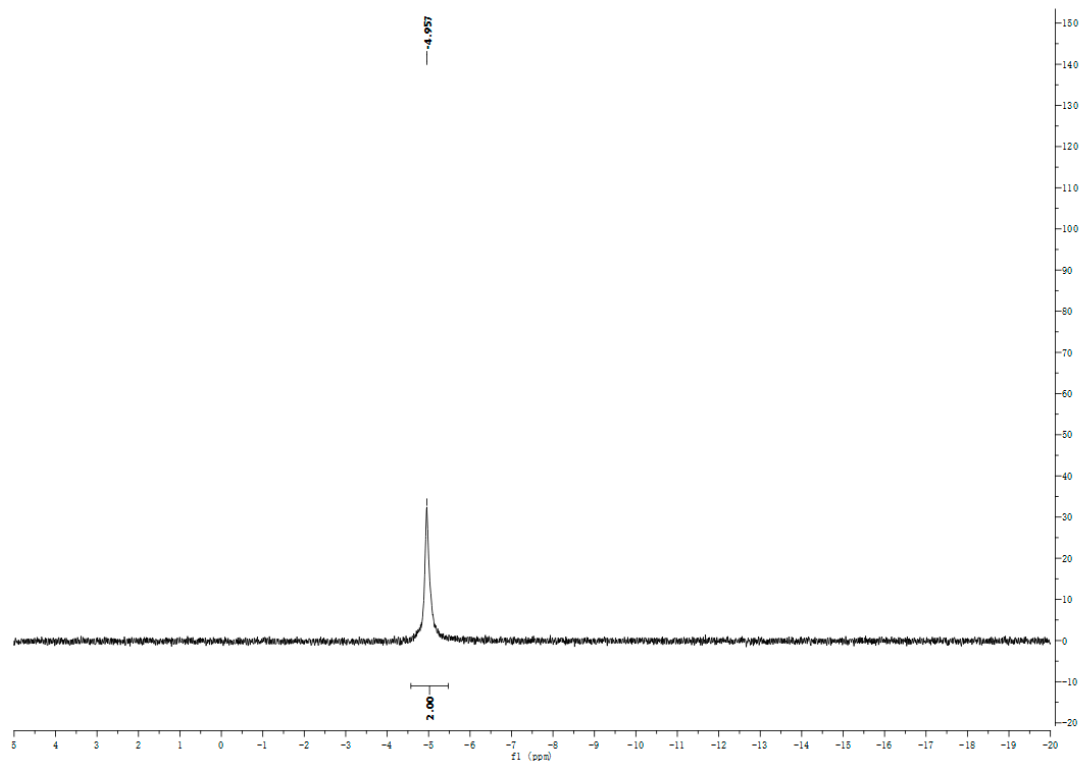
Figure S20. ^{31}P-NMR for compound **4**.

R.Time:0.183(Scan#:23)
MassPeaks:996   BasePeak:263(270259)
Spectrum Mode:Single 0.183(23)
BG Mode:None   Polarity:Negative Segment 1 - Event 1
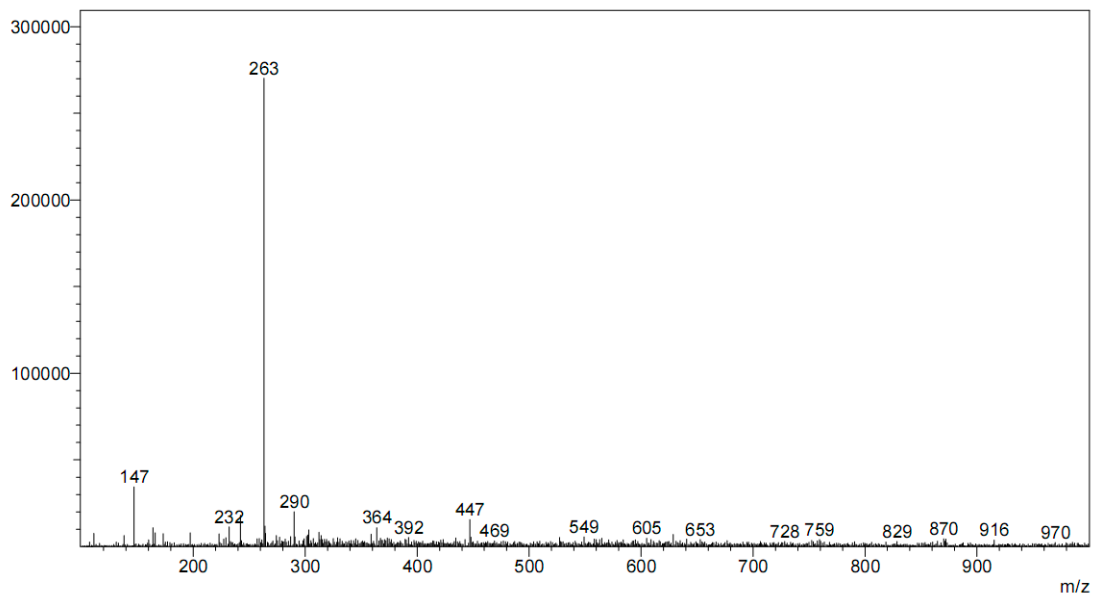
Figure S21. MS-ESI for compound **4**.
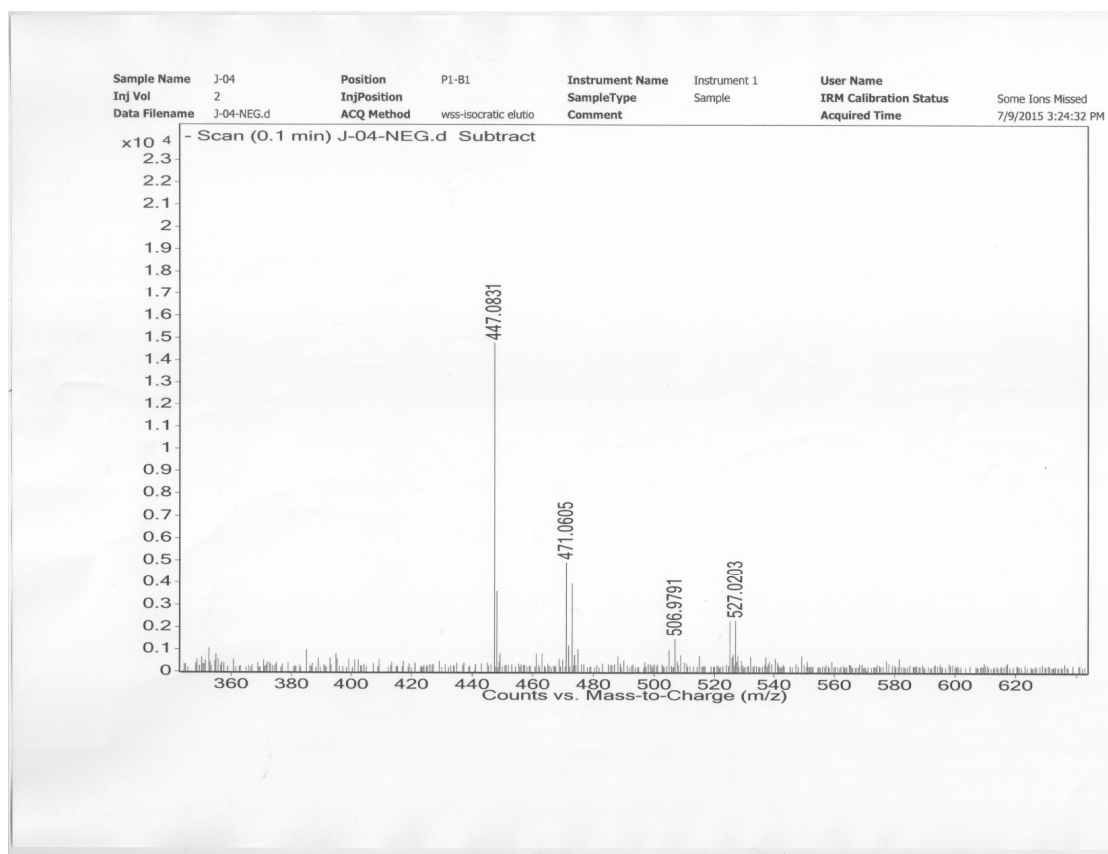
Figure S22. HRMS-ESI for compound **4**.
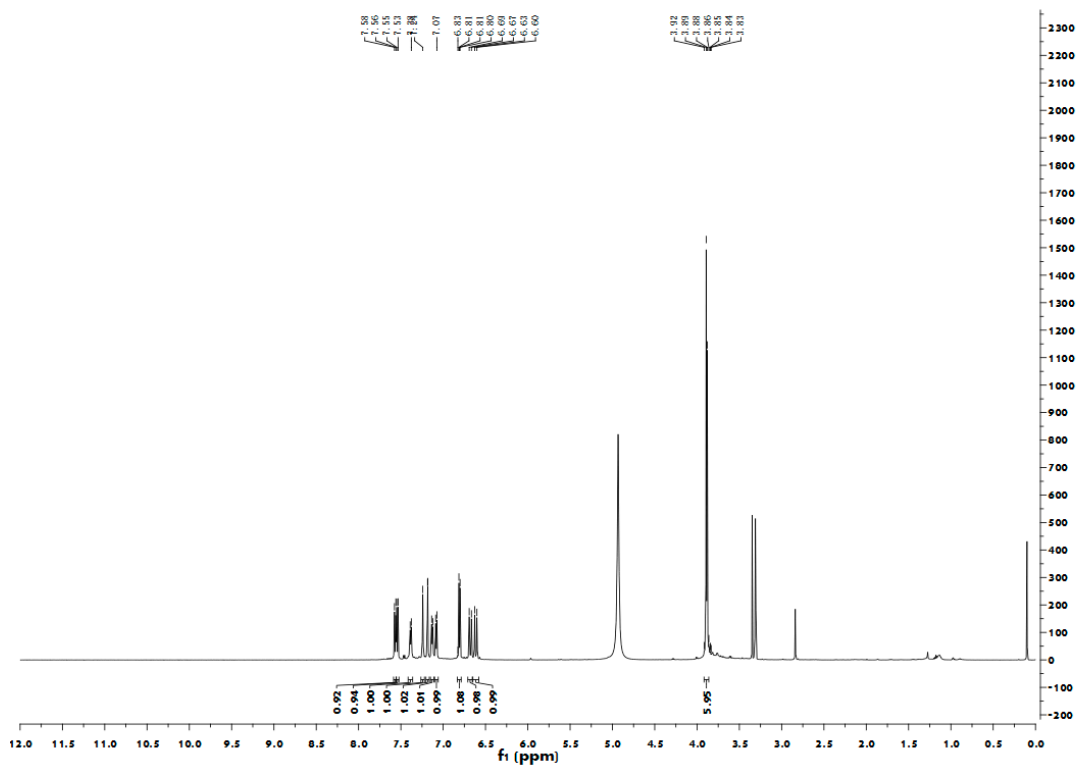
Figure S23. ^{1}H-NMR for compound **5**.
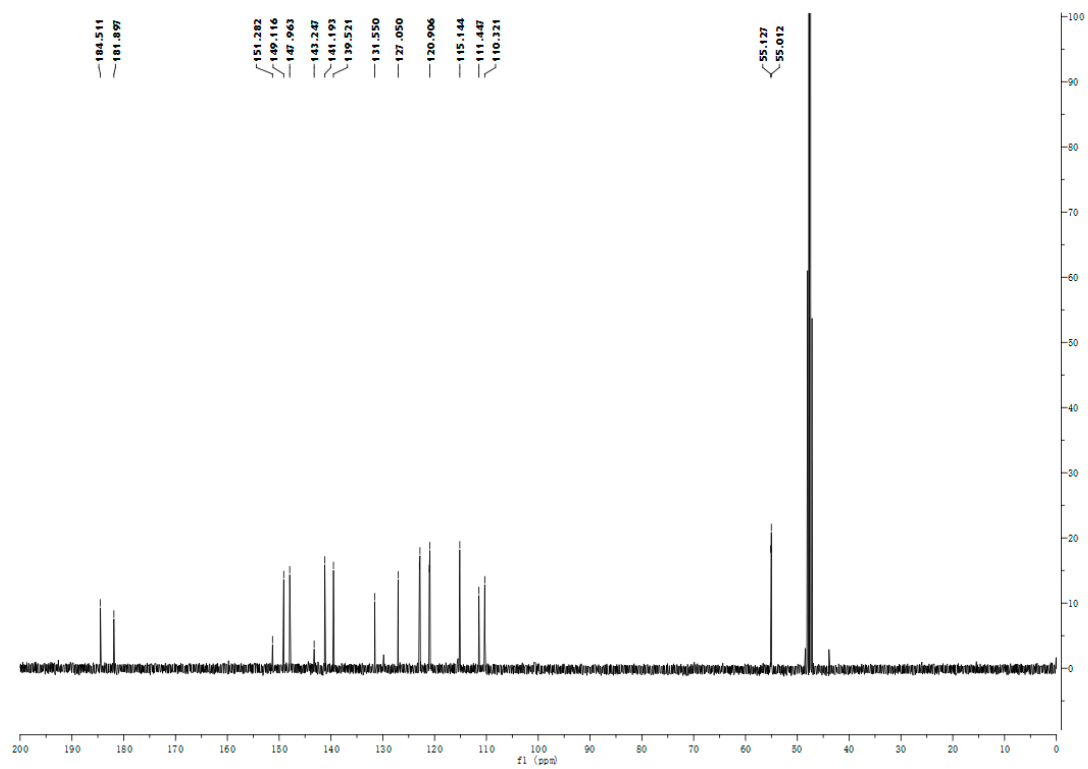
Figure S24. ^{13}C-NMR for compound **5**.
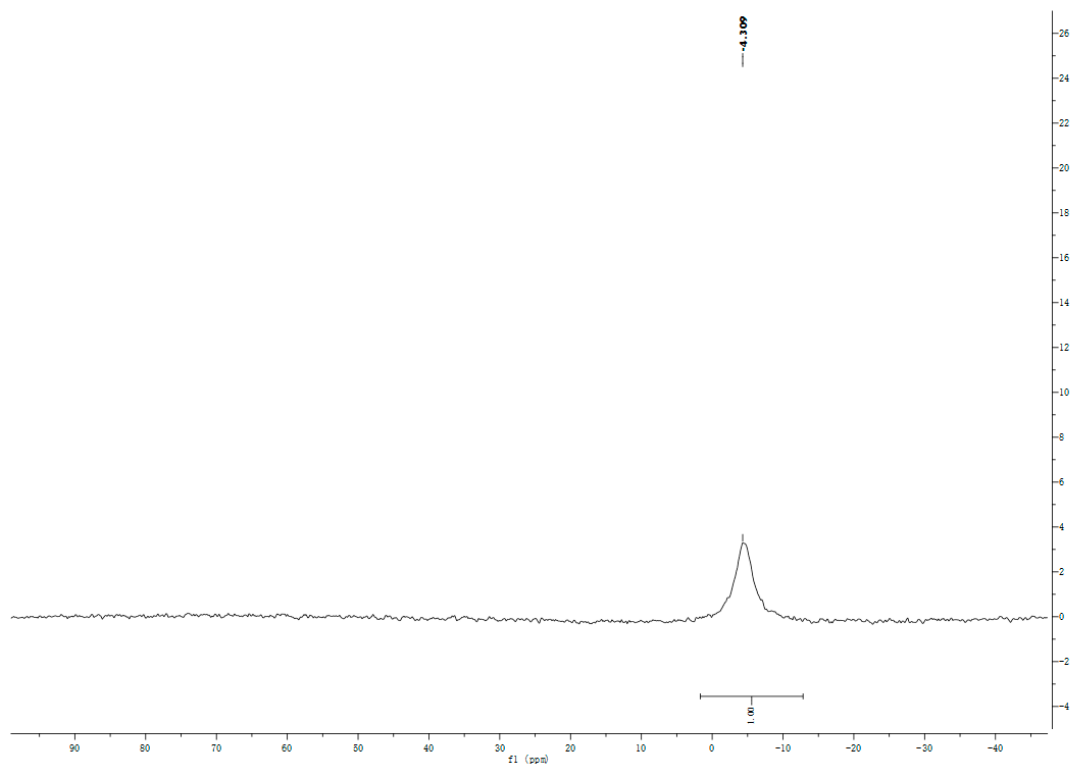
Figure S25. ^{31}P-NMR for compound **5**.
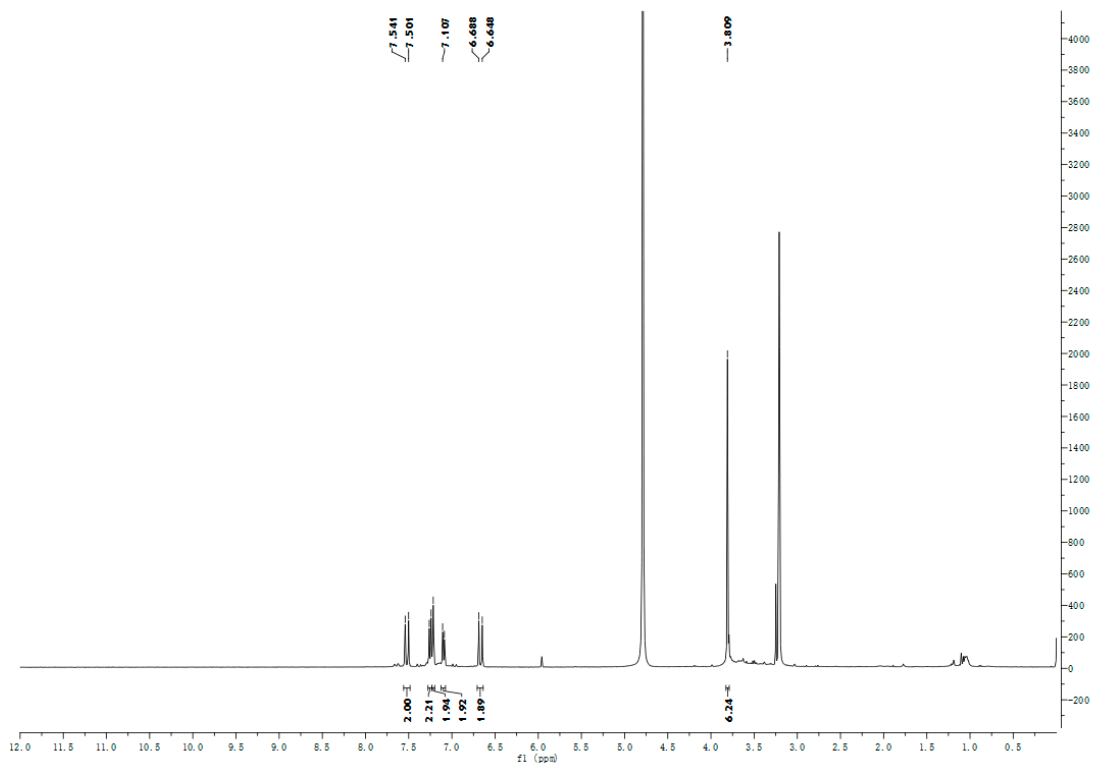
Figure S26. ^{1}H-NMR for compound **6**.
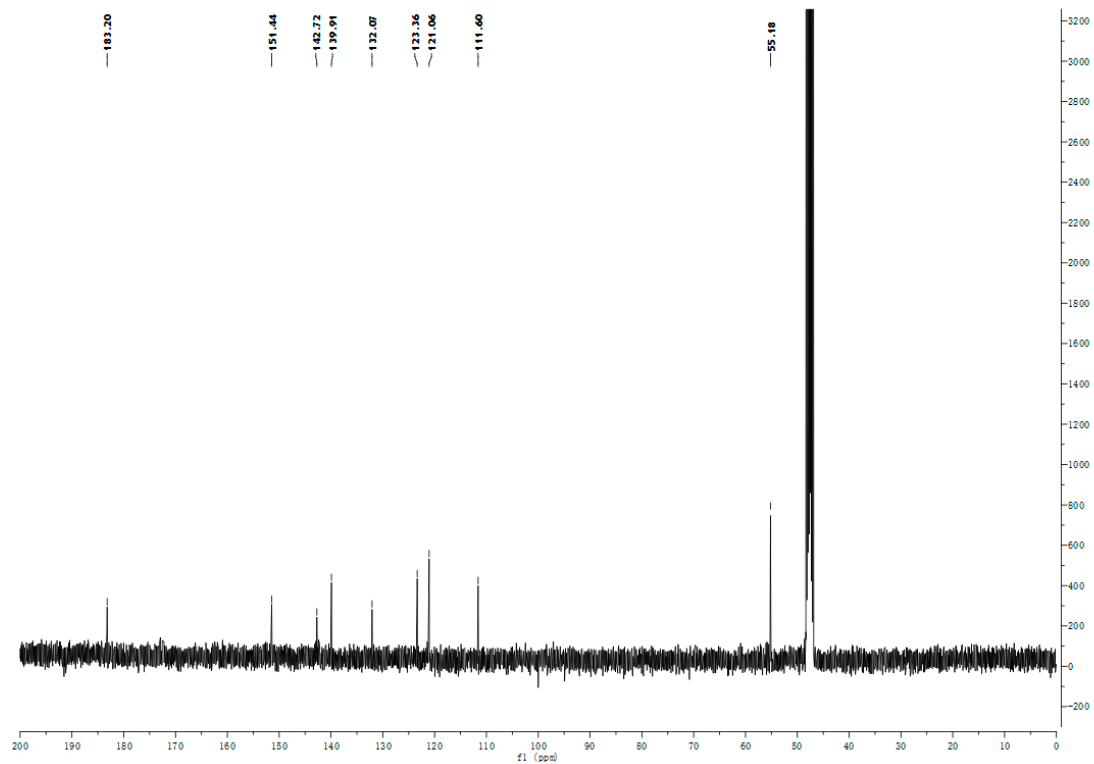
Figure S27. ^{13}C-NMR for compound **6**.
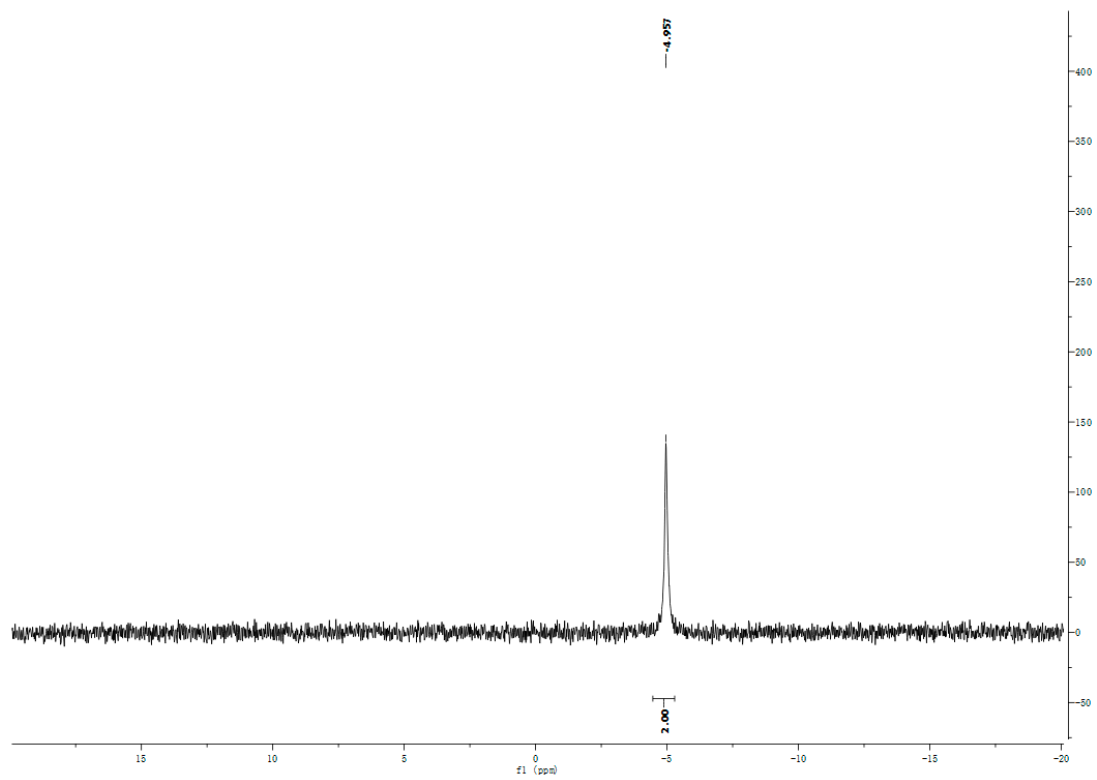
Figure S28. ^{31}P-NMR for compound **6**.
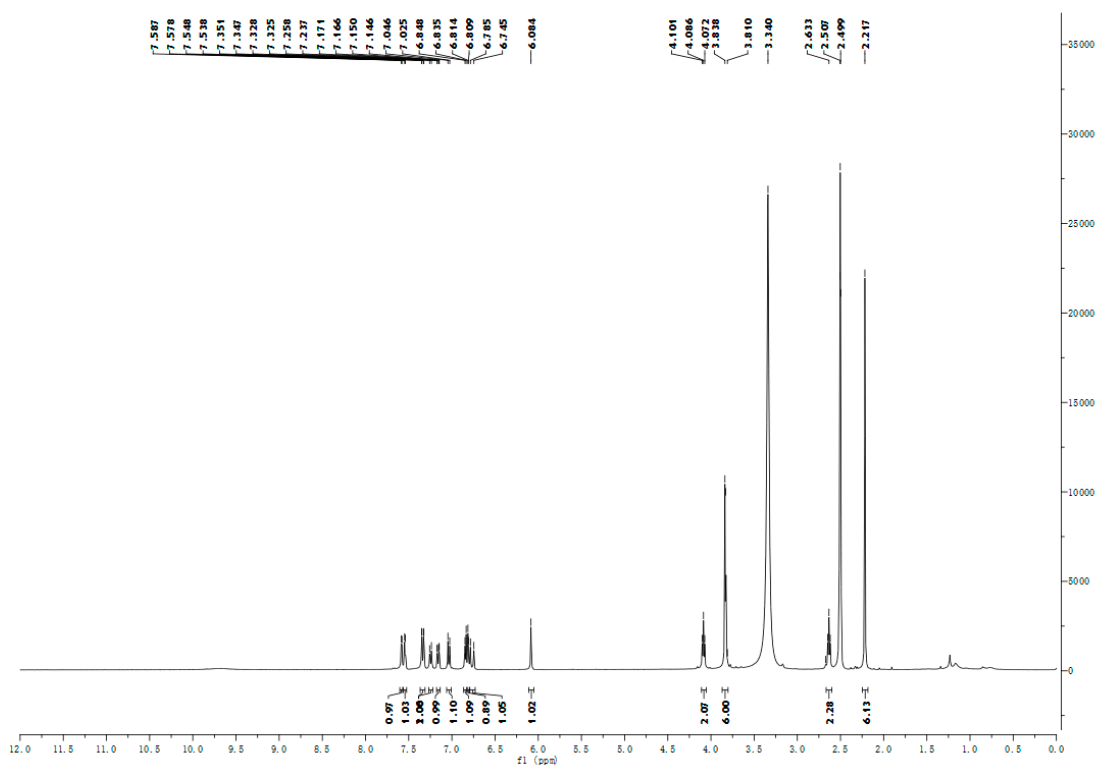
Figure S29. ^{1}H-NMR for compound **7**.
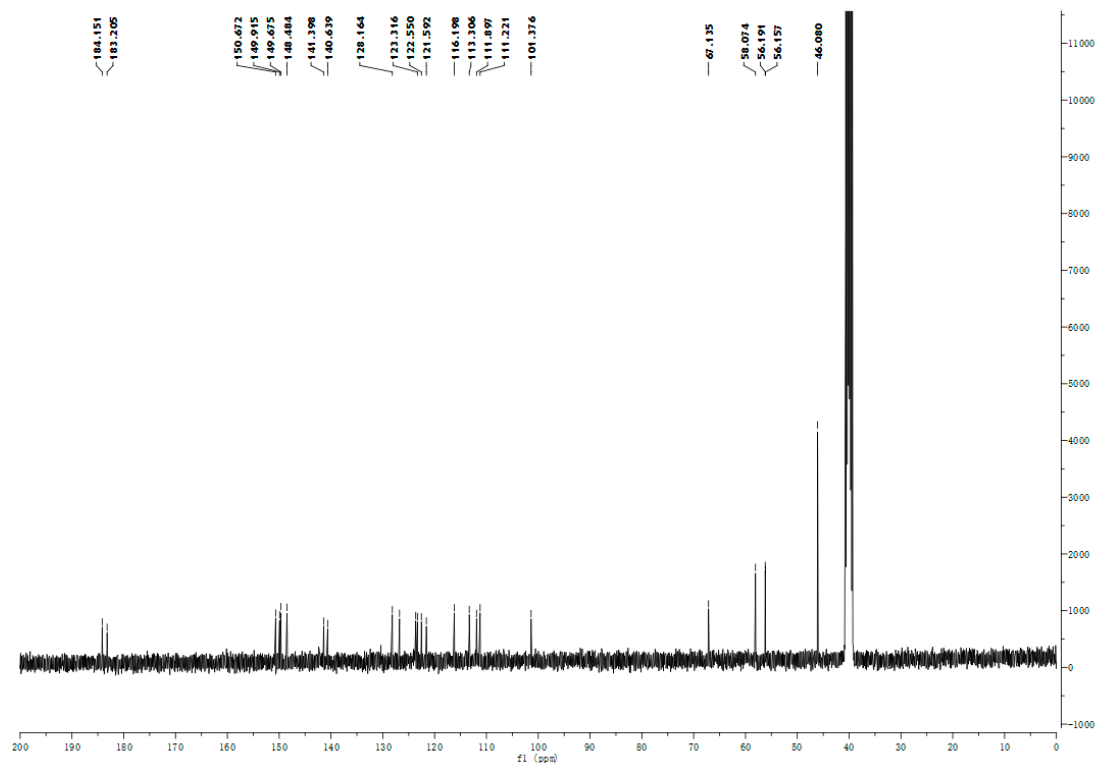
Figure S30. ^{13}C-NMR for compound **7**.

R.Time:1.292(Scan#:156)
MassPeaks:439   BasePeak:440(116788)
Spectrum Mode:Single 1.292(156)
BG Mode:Averaged 0.092-1.142(12-138) Polarity:Positive Segment 1 - Event 1
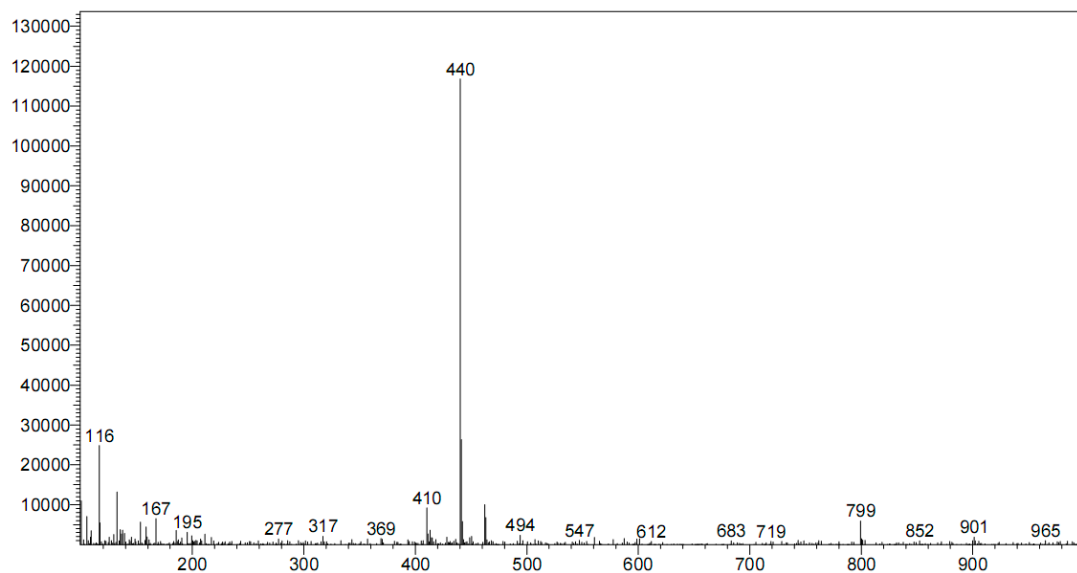
Figure S31. MS-ESI for compound **7**.
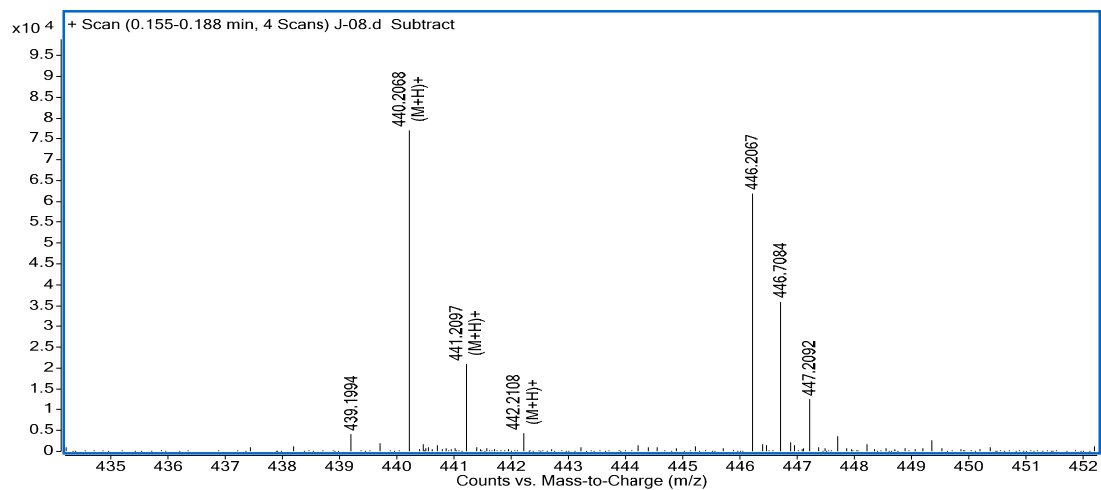
Figure S32. HRMS-ESI for compound **7**.
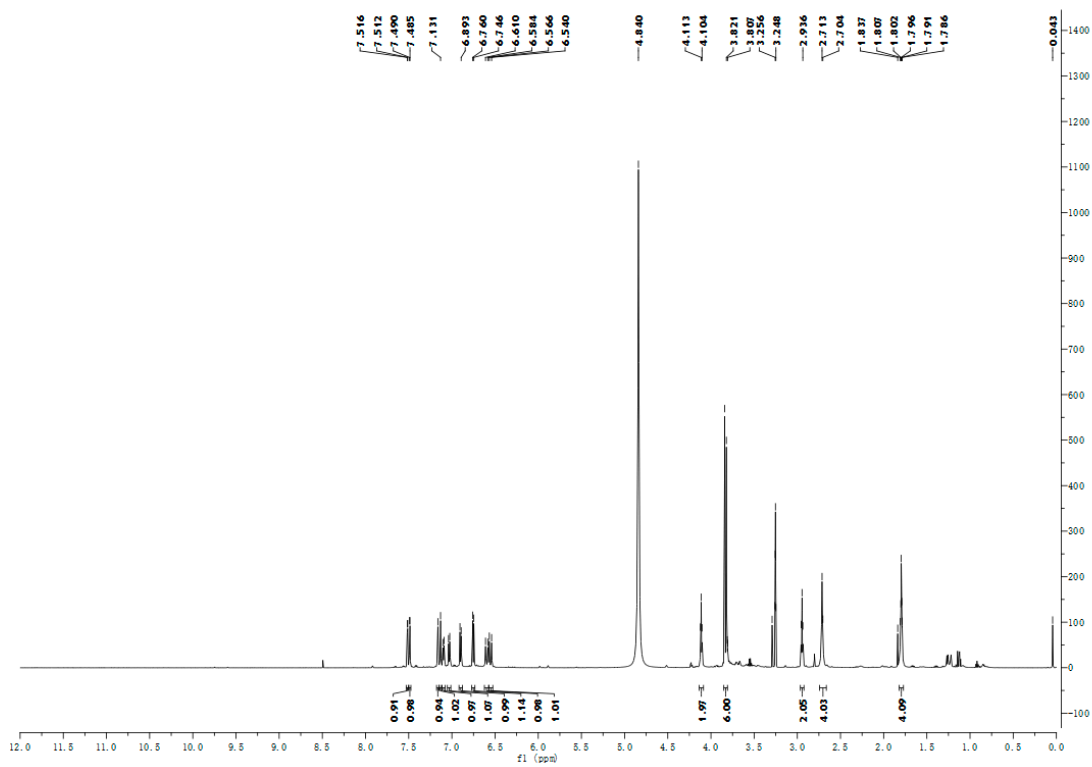
Figure S33. ^{1}H-NMR for compound **8**.
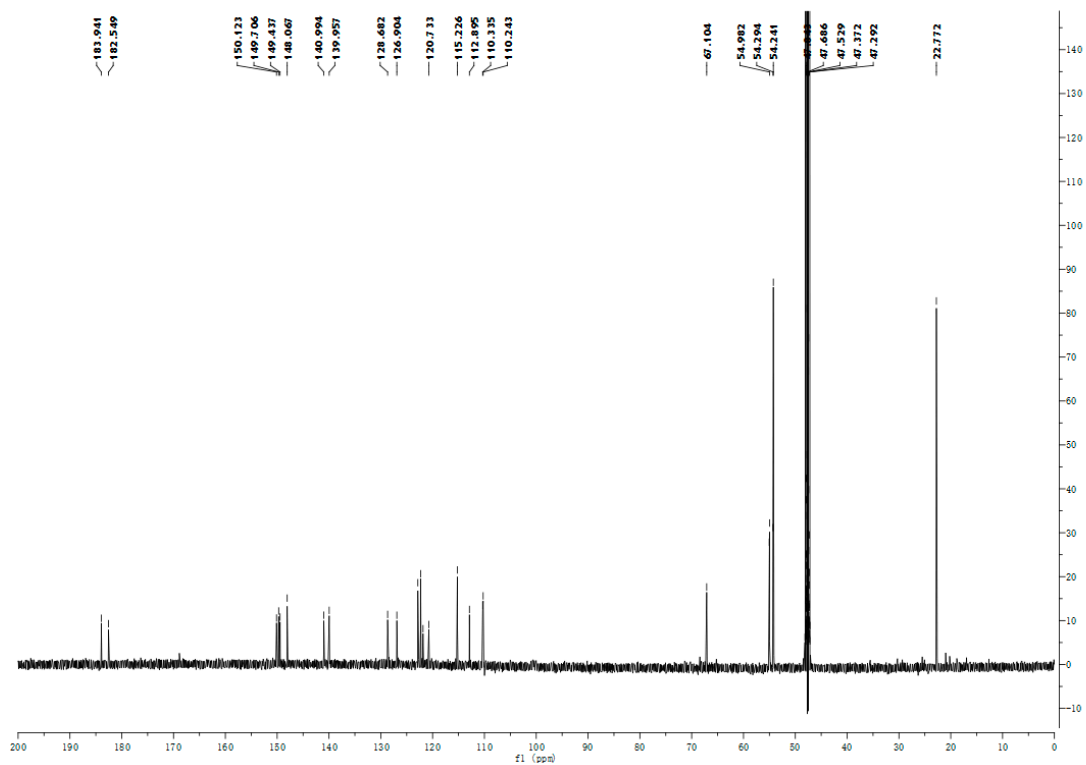
Figure S34. ^{13}C-NMR for compound **8**.

R.Time:0.508(Scan#:62)
MassPeaks:213   BasePeak:466(123500)
Spectrum Mode:Single 0.508(62)
BG Mode:Averaged 0.025-0.342(4-42) Polarity:Positive Segment 1 - Event 1
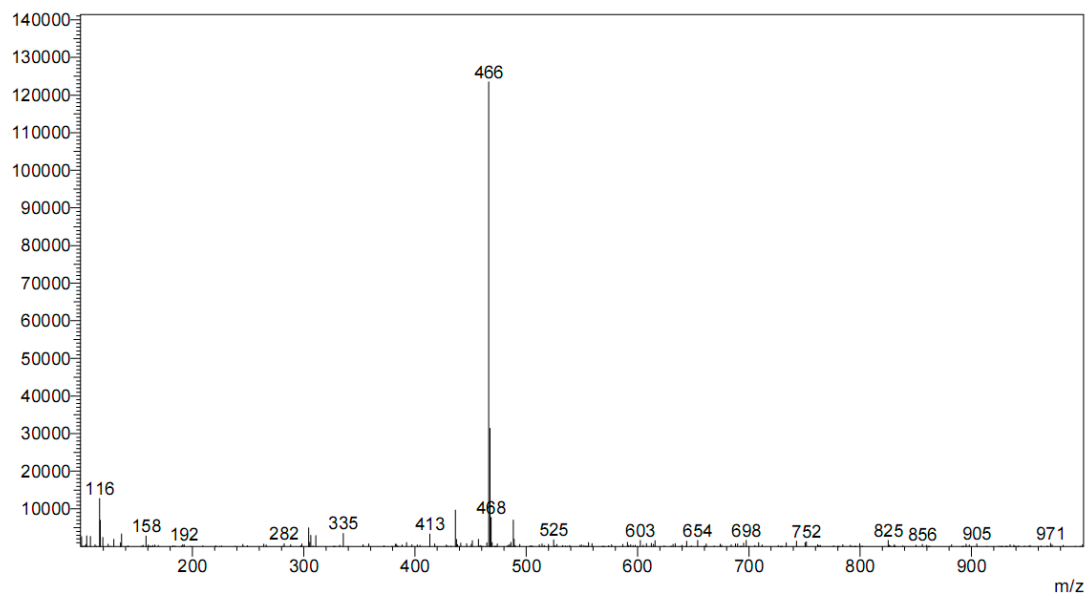
Figure S35. MS-ESI for compound **8**.
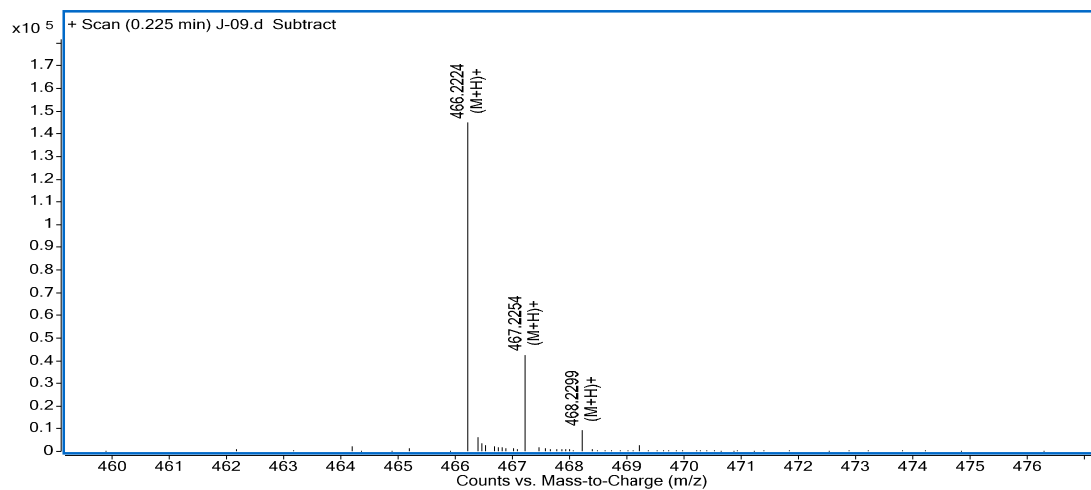
Figure S36. HRMS-ESI for compound **8**.
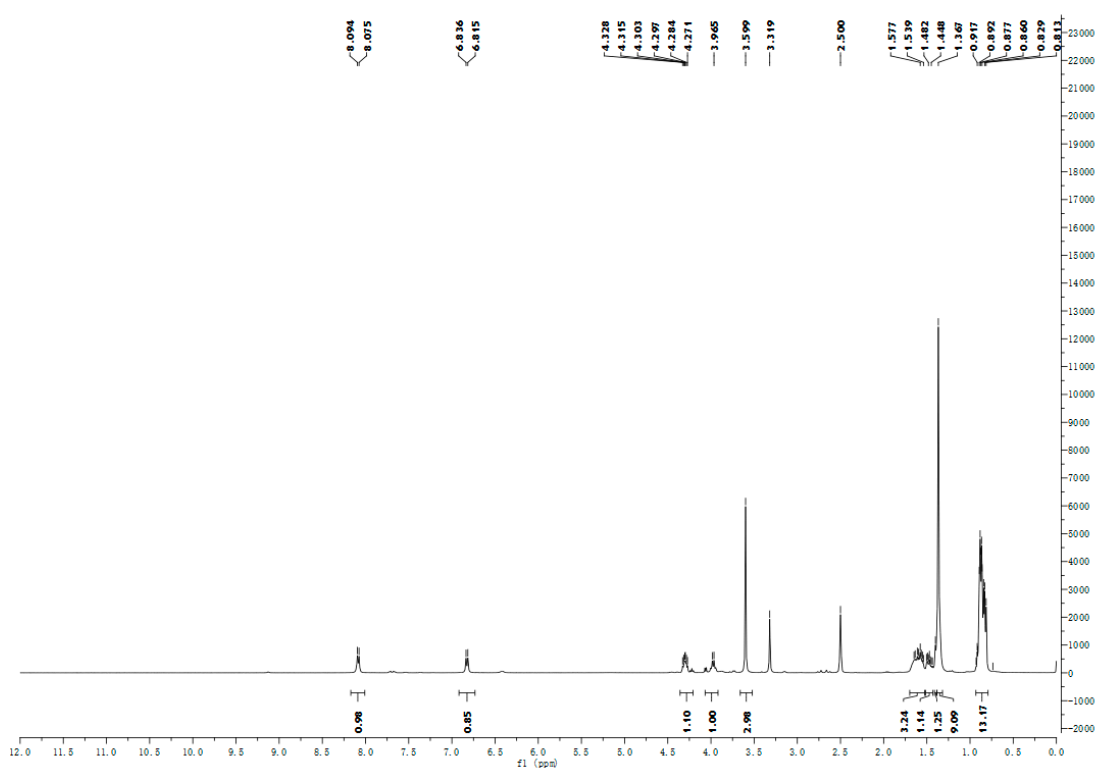
Figure S37. ^{1}H-NMR for compound **Leu-01**.
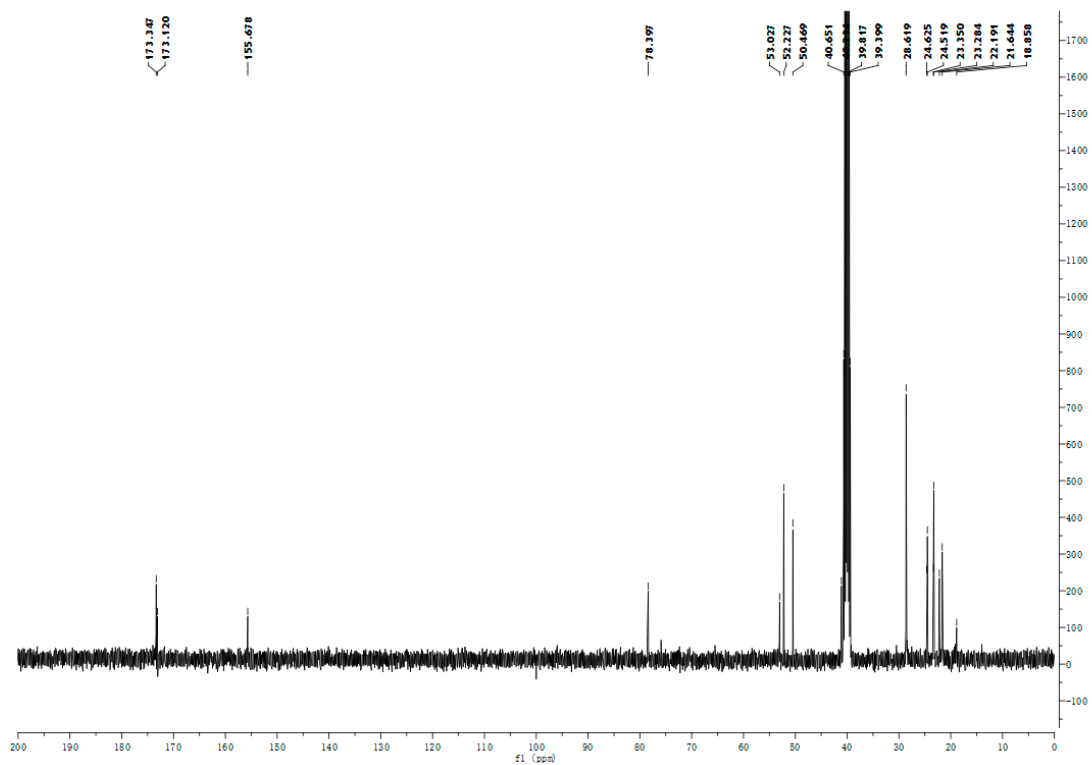
Figure S38. ^{13}C-NMR for compound **Leu-01**.

R.Time:0.783(Scan#:95)
MassPeaks:545   BasePeak:381(1481153)
Spectrum Mode:Single 0.783(95)
BG Mode:Averaged 0.042-0.458(6-56) Polarity:Positive Segment 1 - Event 1
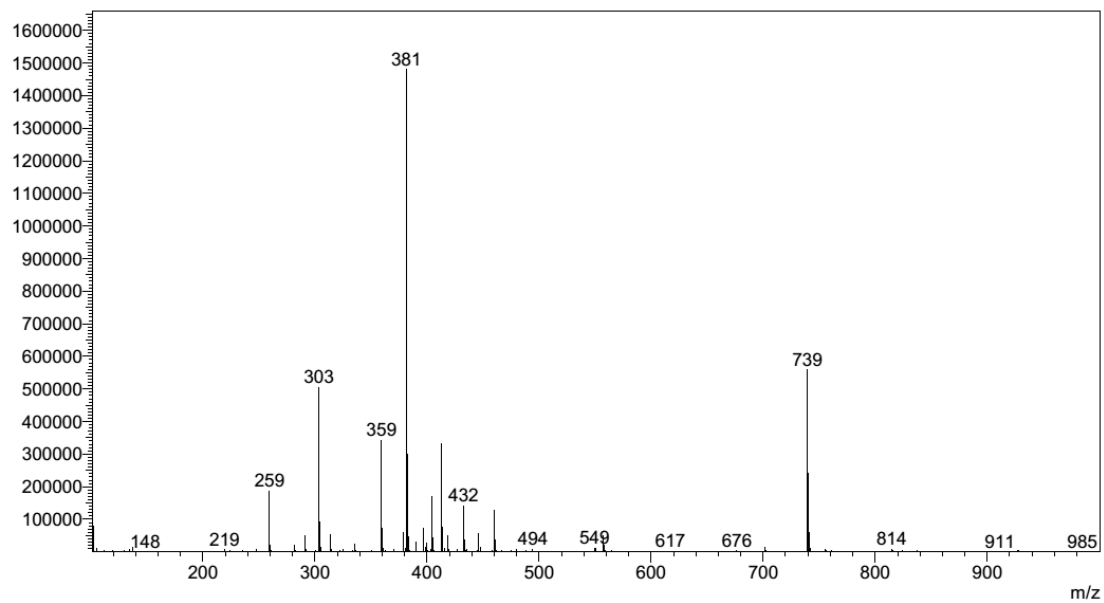
Figure S39. MS-ESI for compound **Leu-01**.
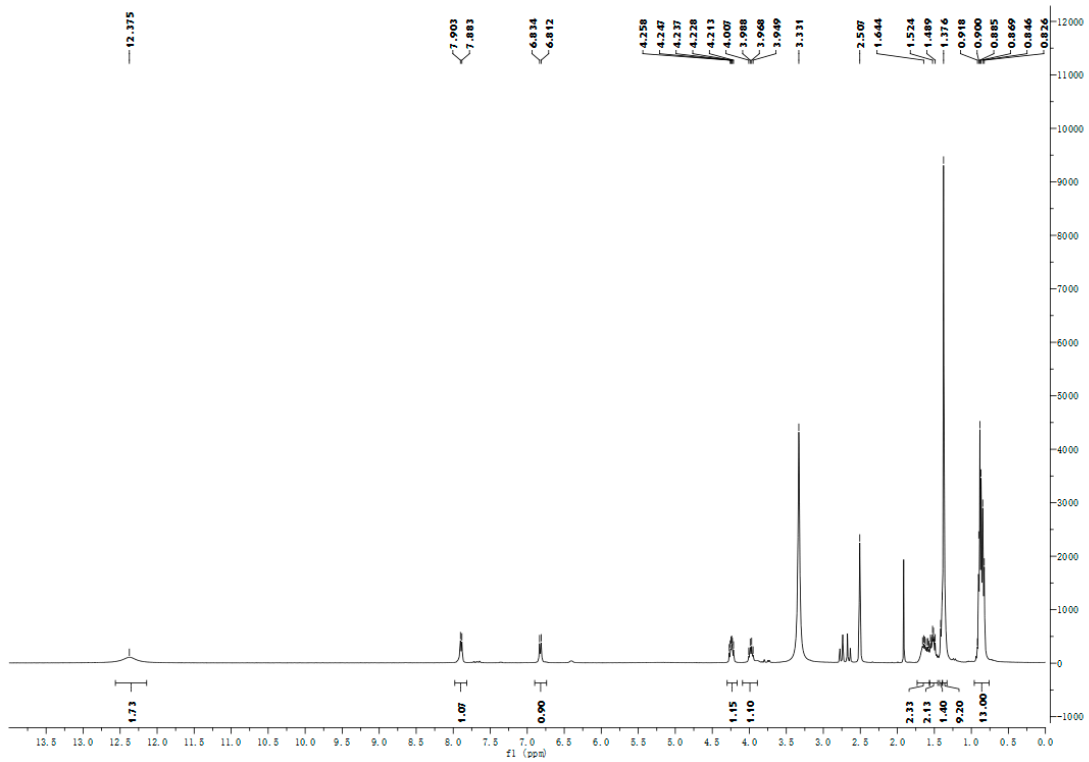
Figure S40. ¹H-NMR for compound **Leu-02**.
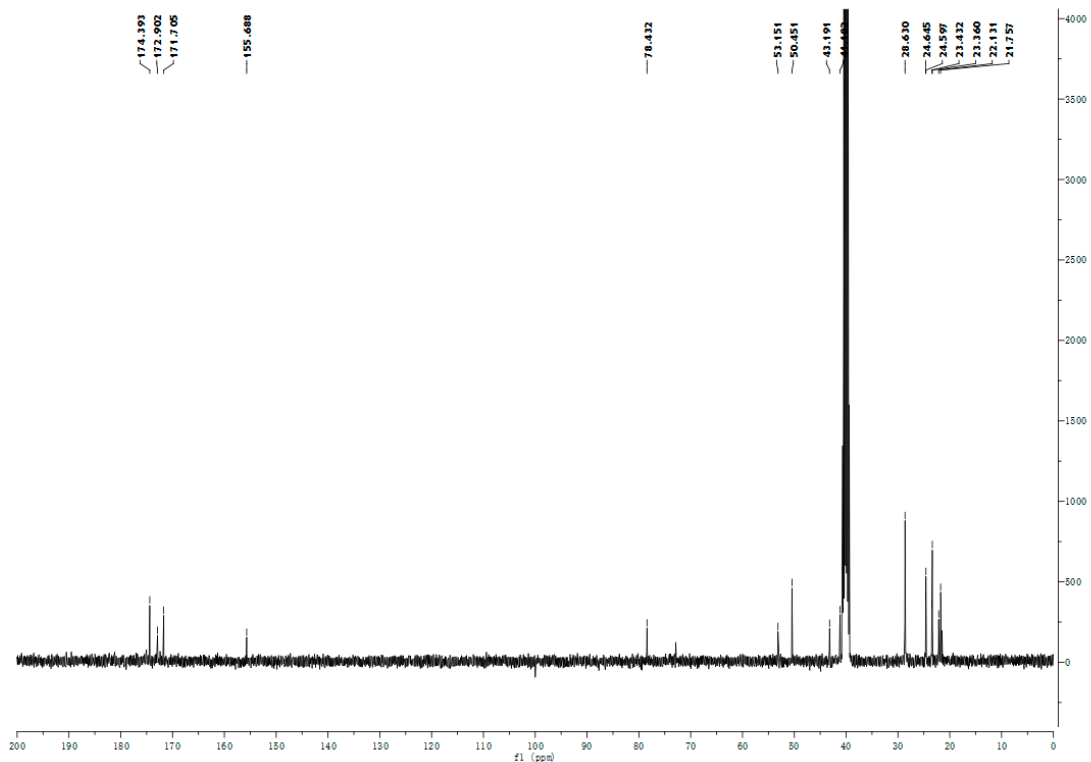
Figure S41. ¹³C-NMR for compound **Leu-02**.

Figure S42. MS-ESI for compound **Leu-02**.
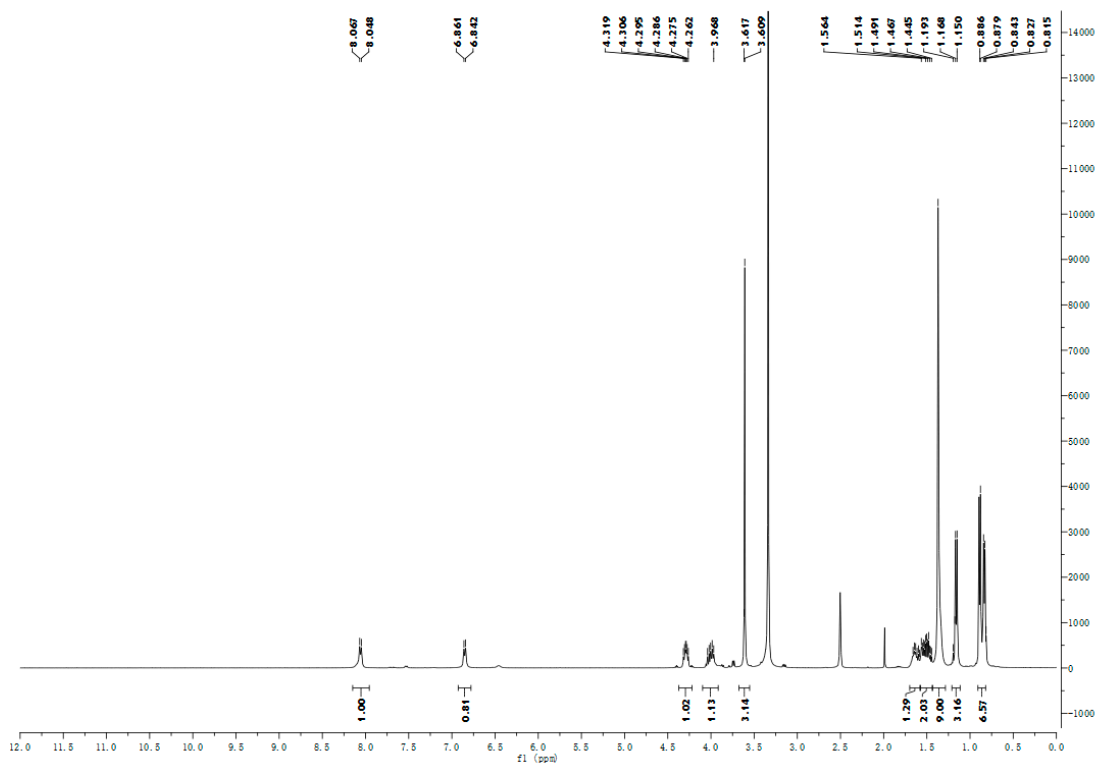
Figure S43. ¹H-NMR for compound **Leu-03**.

S21
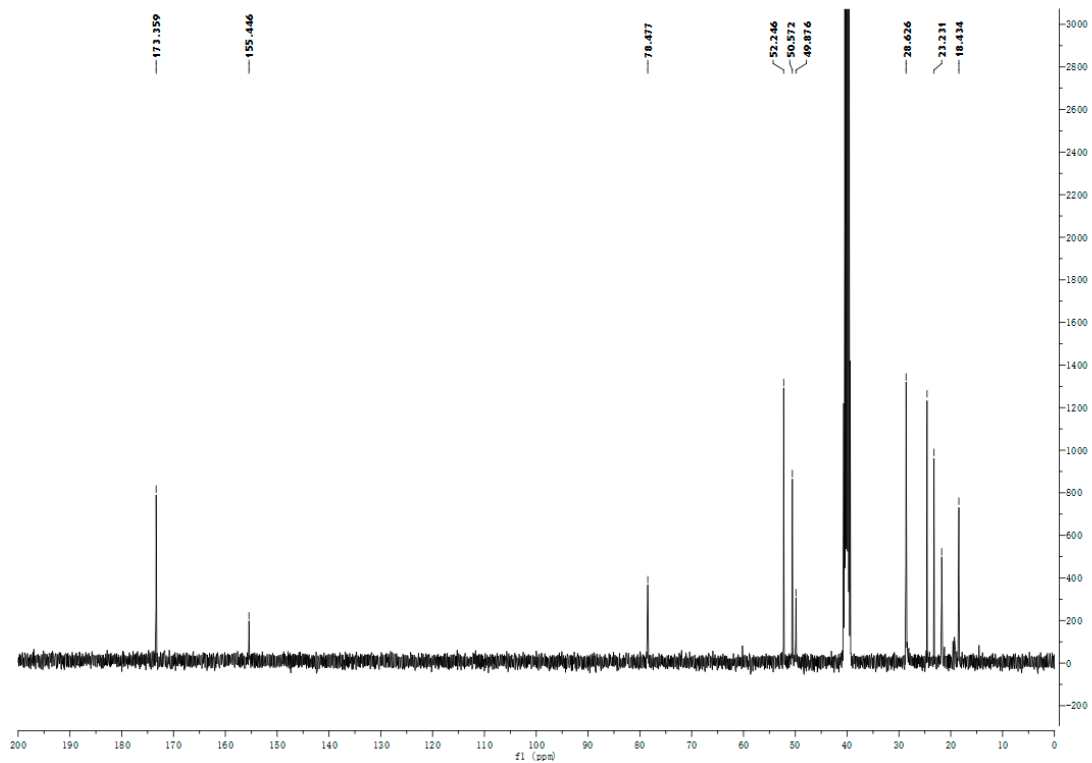
Figure S44. ^{13}C-NMR for compound **Leu-03**.

R.Time:0.208(Scan#:26)
MassPeaks:963   BasePeak:339(2375134)
Spectrum Mode:Single 0.208(26)
BG Mode:None   Polarity:Positive Segment 1 - Event 1
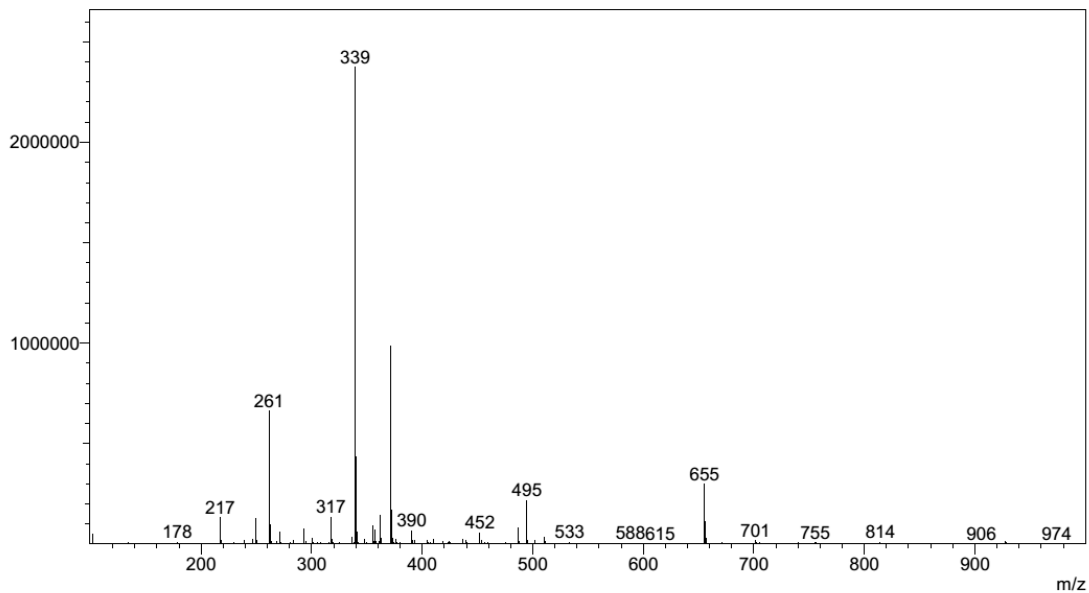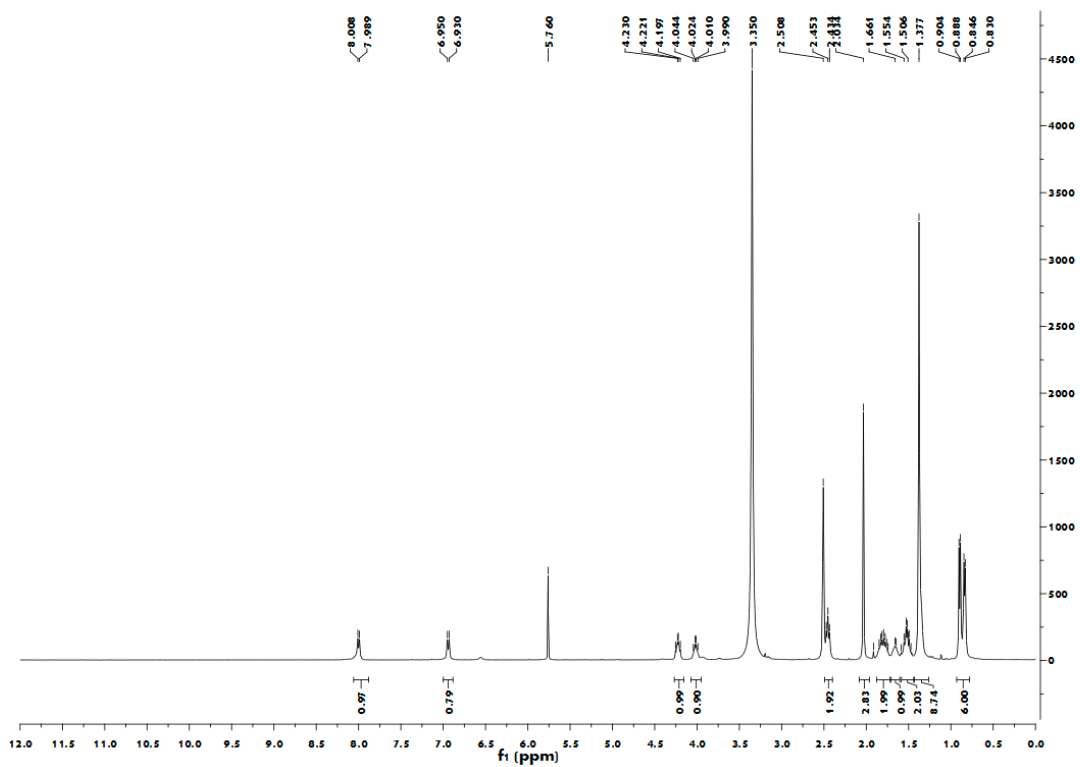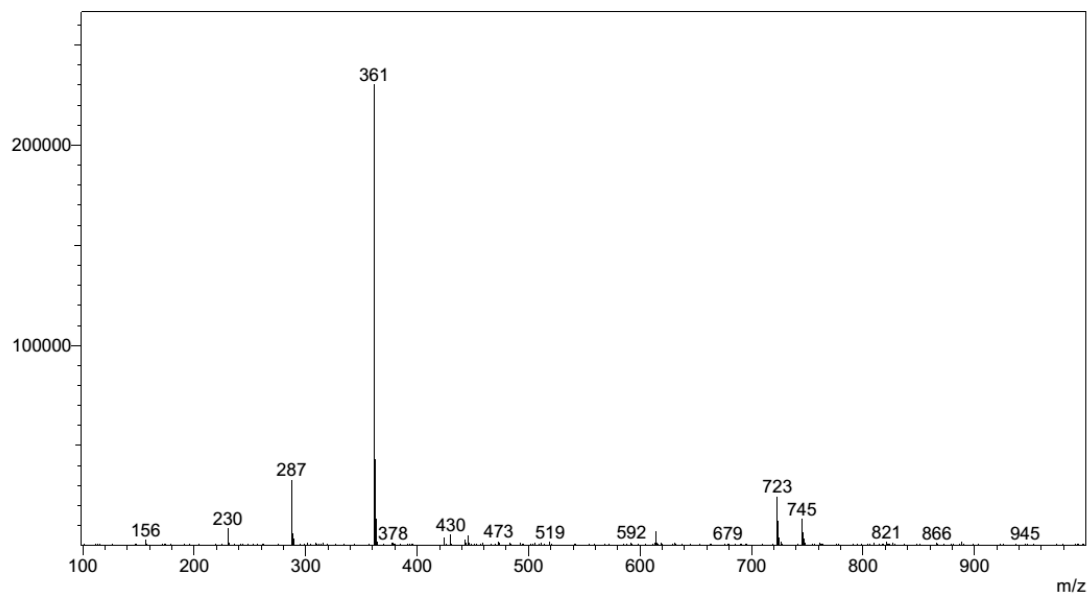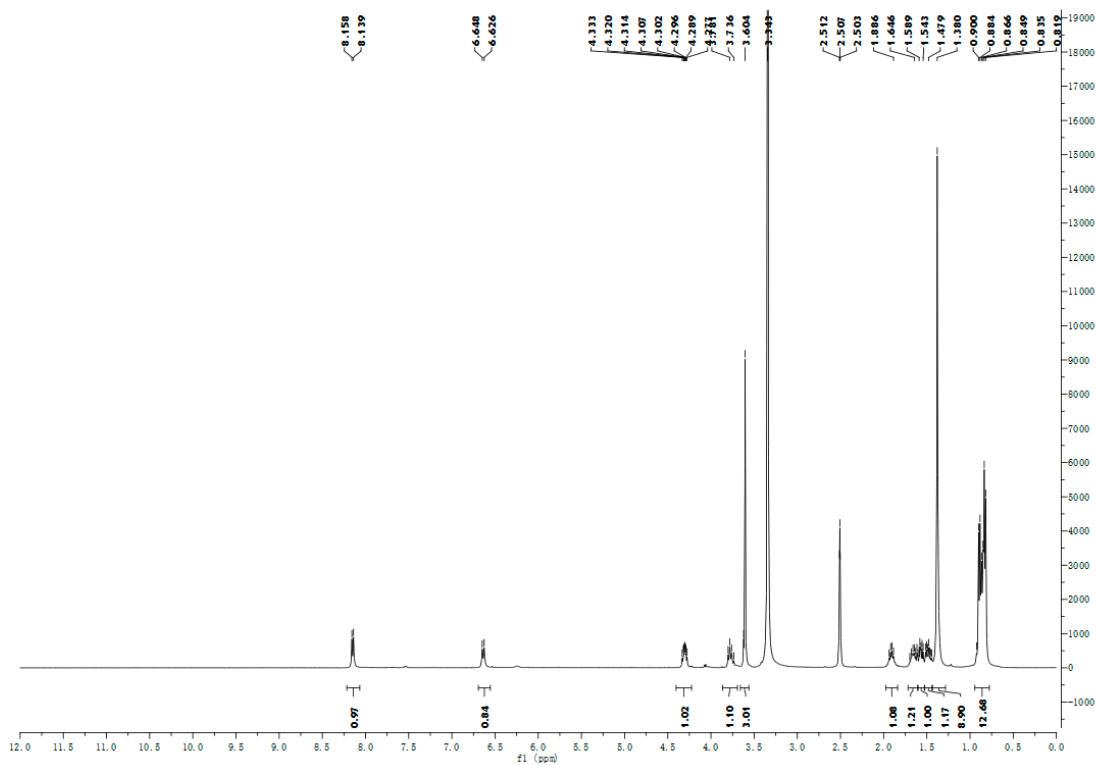

Figure S45. MS-ESI for compound **Leu-03**.
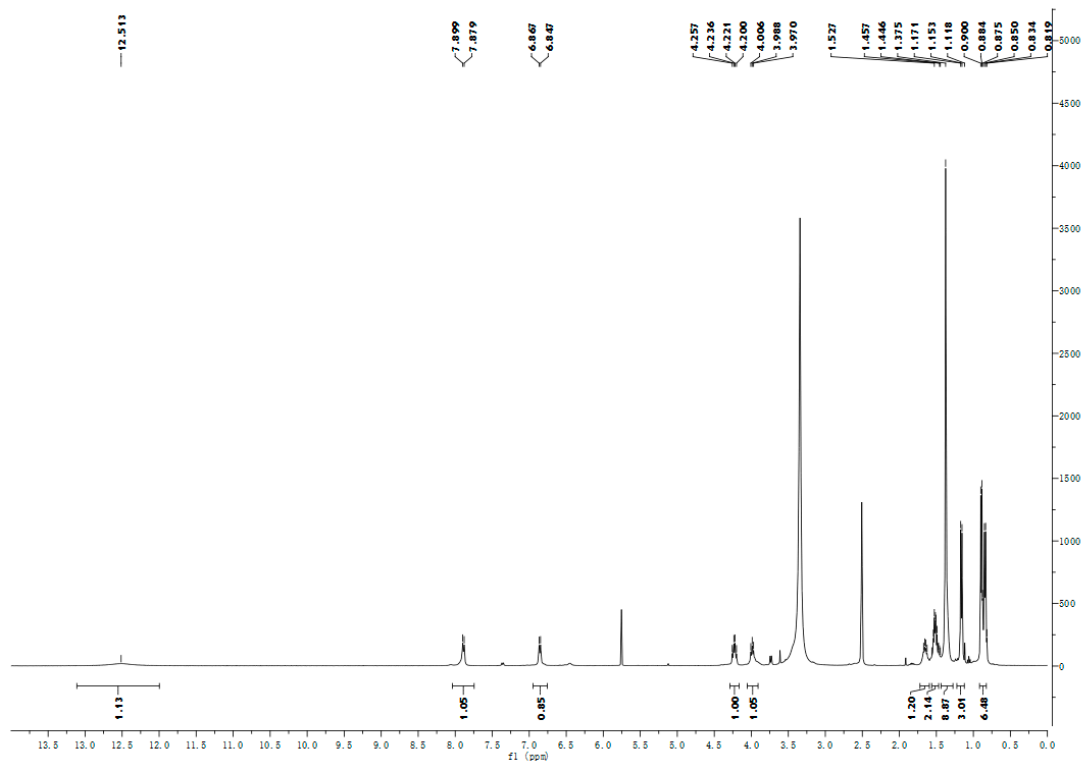
Figure S46. ¹H-NMR for compound **Leu-04**.
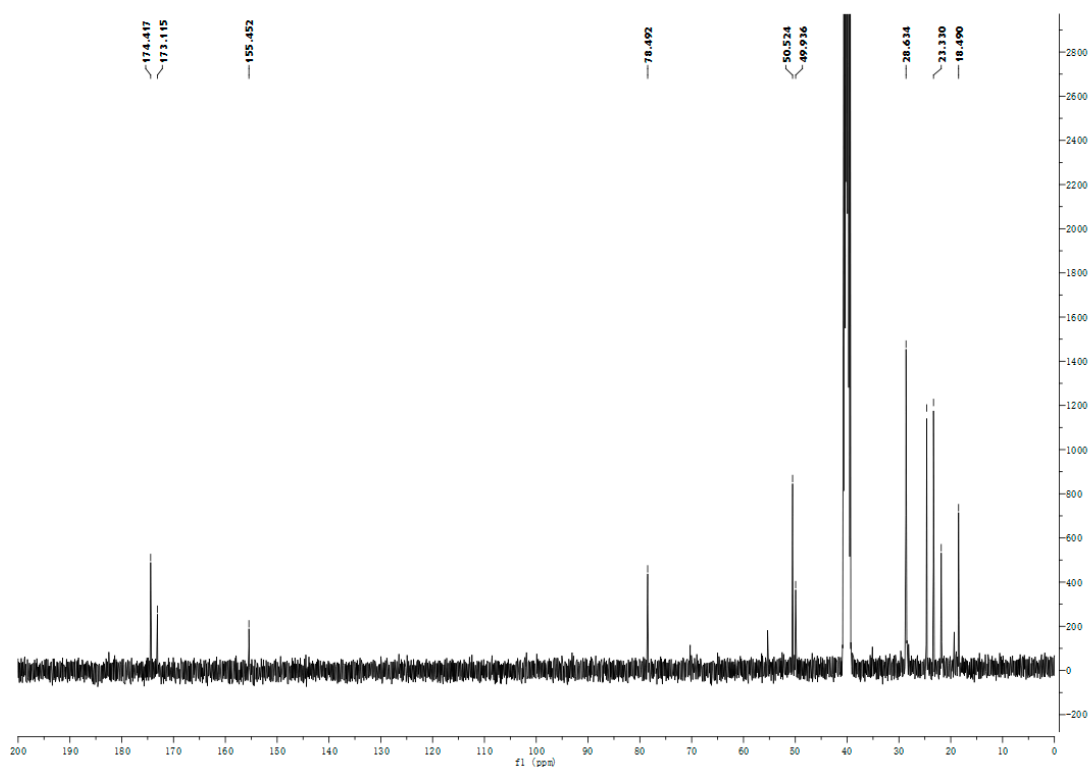
Figure S47. ¹³C-NMR for compound **Leu-04**.

Figure S48. MS-ESI for compound **Leu-04**.
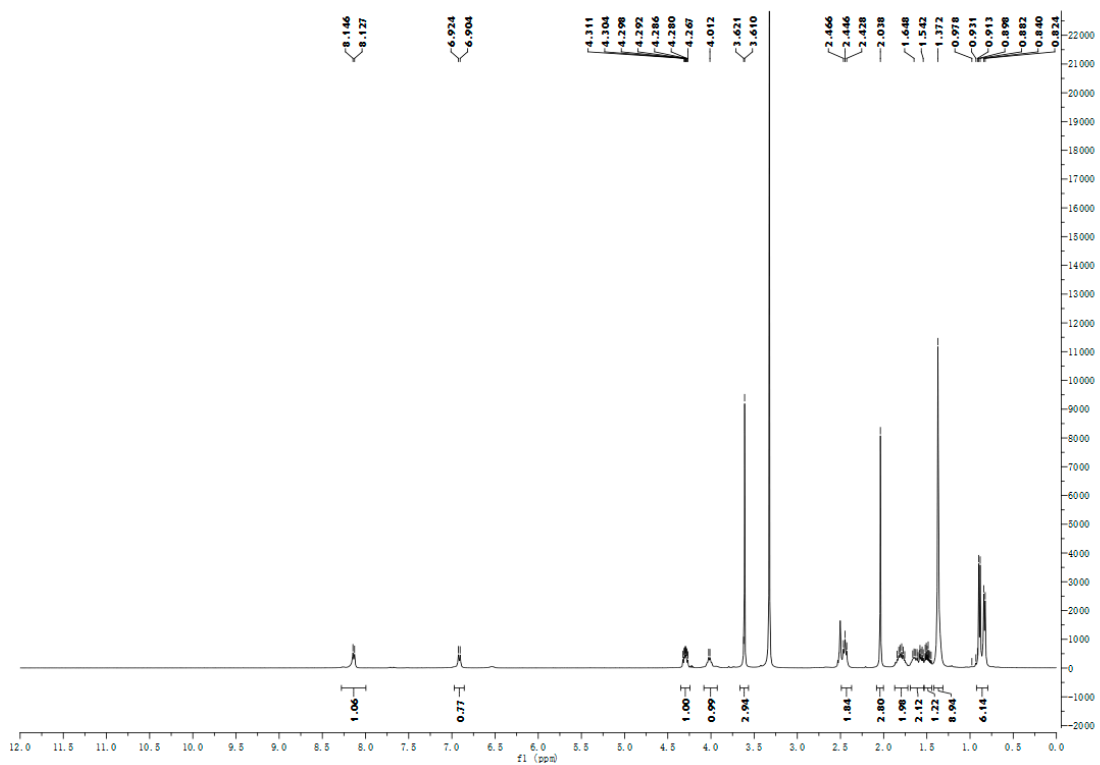
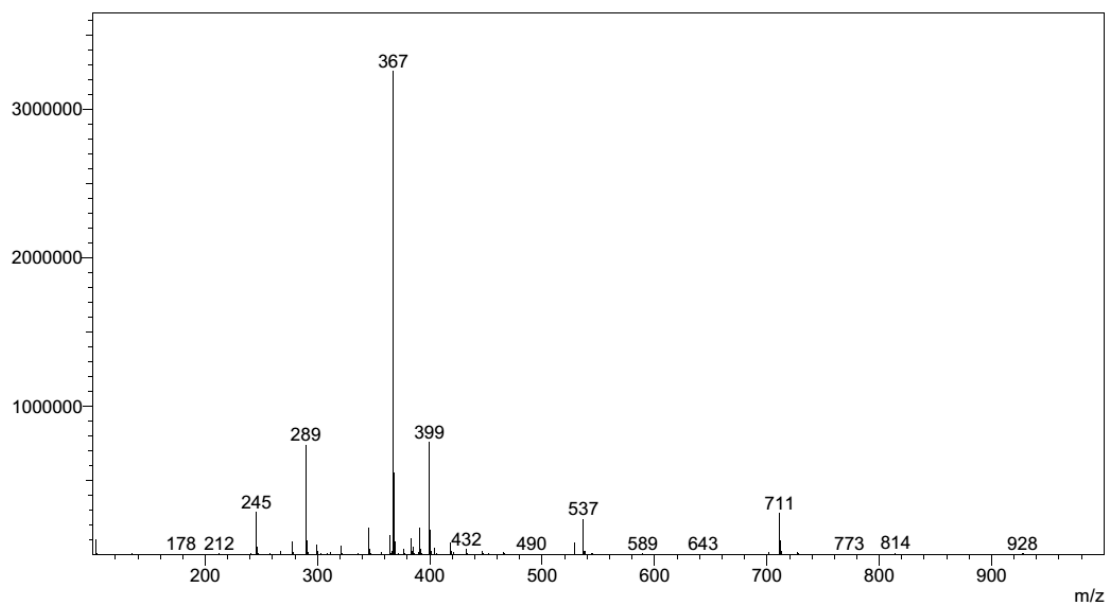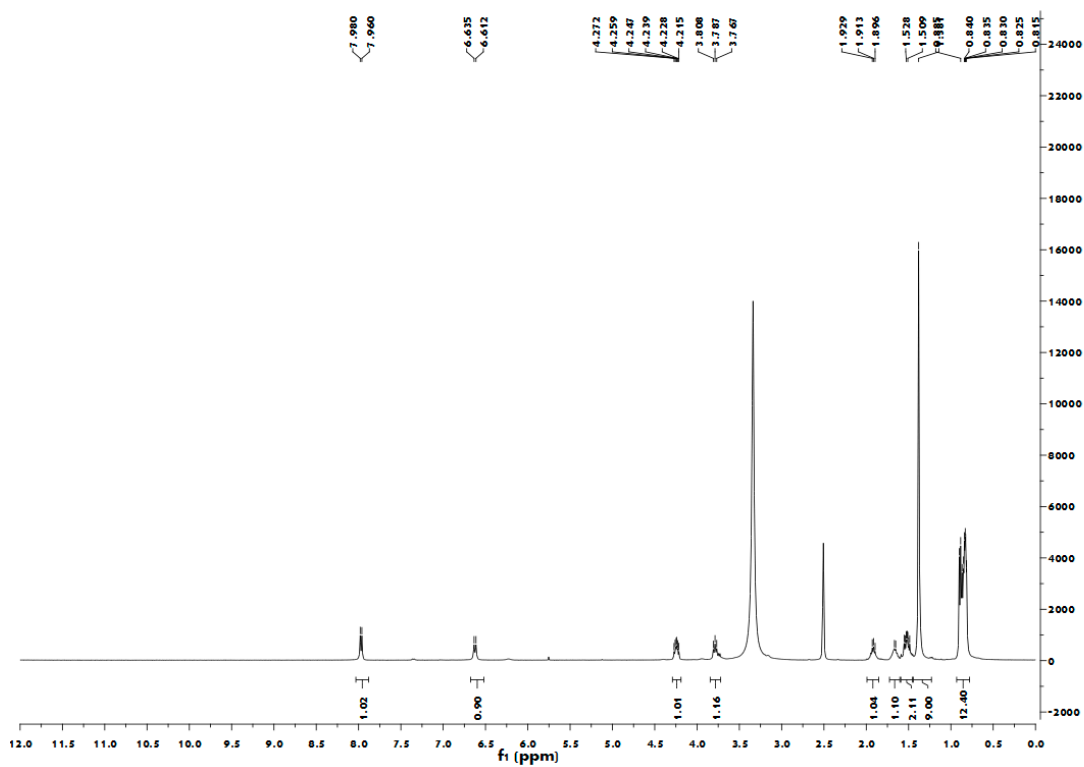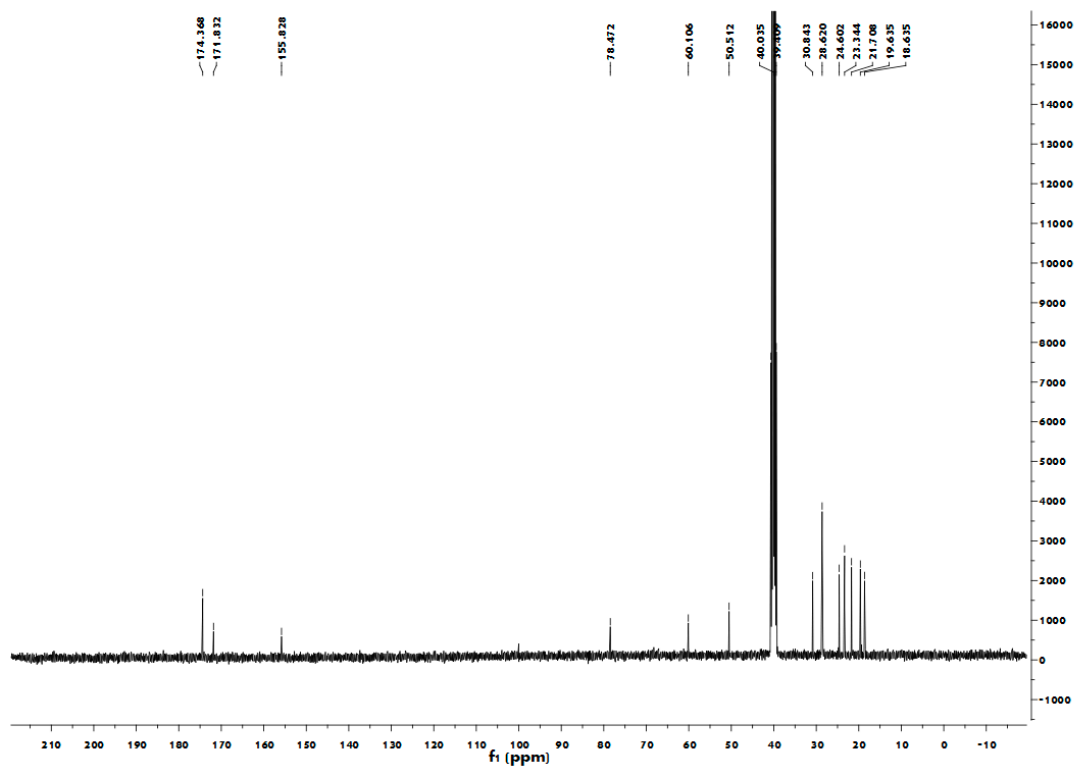**Figure S49.** ¹H-NMR for compound **Leu-05**.
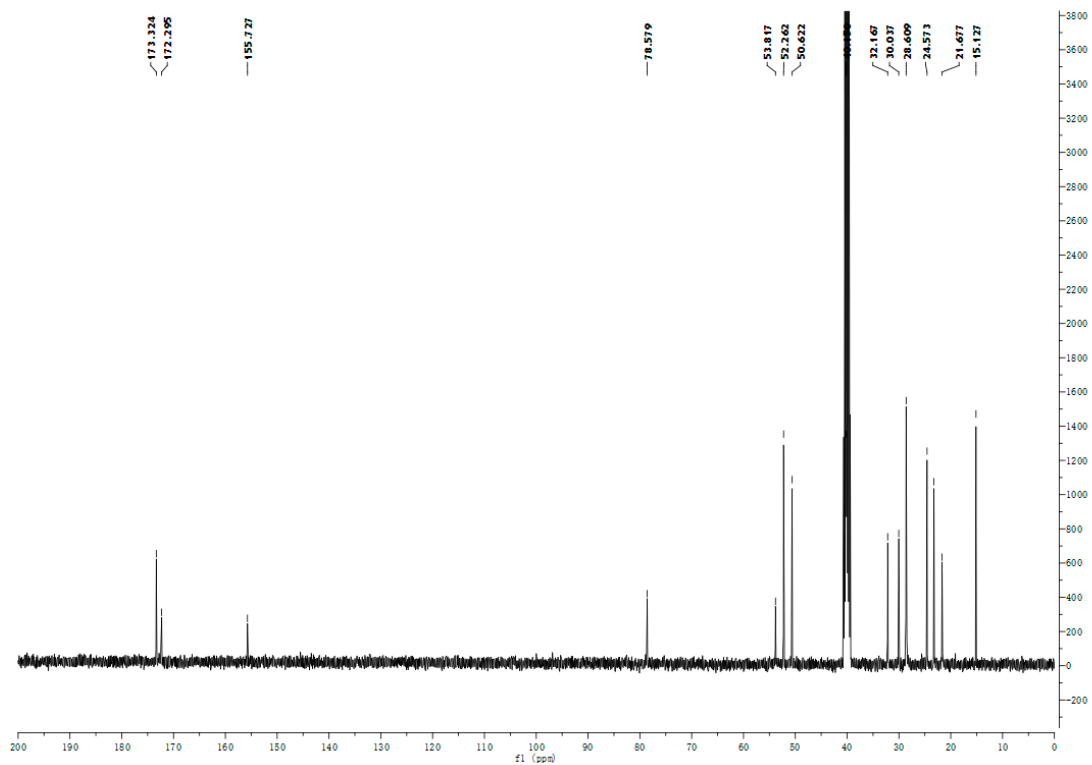
Figure S50. ^{13}C-NMR for compound **Leu-05**.

R.Time:0.242(Scan#:30)
MassPeaks:552   BasePeak:399(2512602)
Spectrum Mode:Single 0.242(30)
BG Mode:Averaged 0.008-0.142(2-18) Polarity:Positive Segment 1 - Event 1
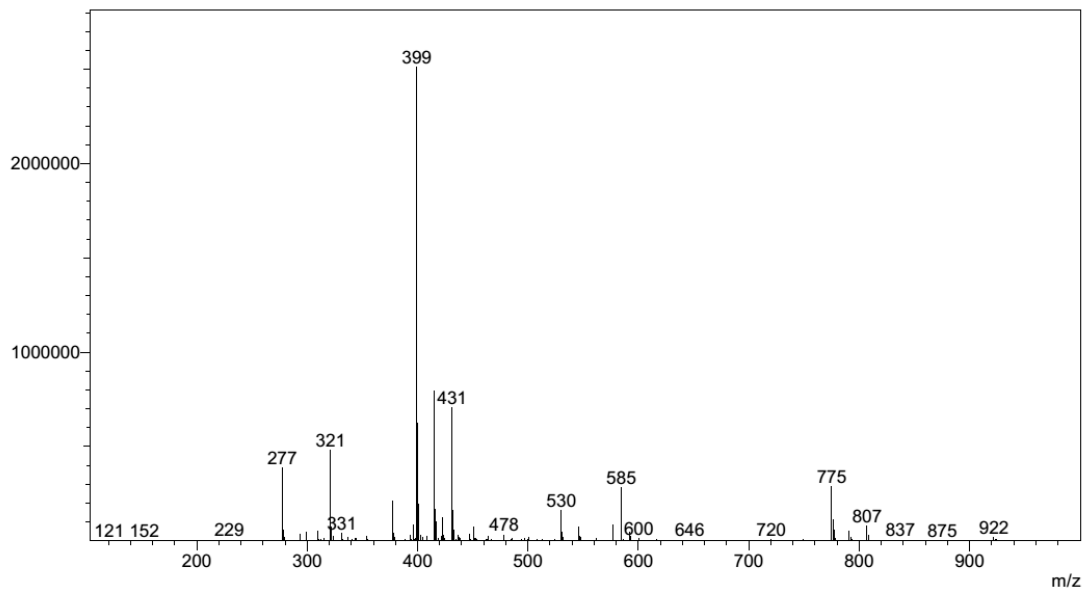
Figure S51. MS-ESI for compound **Leu-05**.

Figure S52. ^{1}H-NMR for compound **Leu-06**.
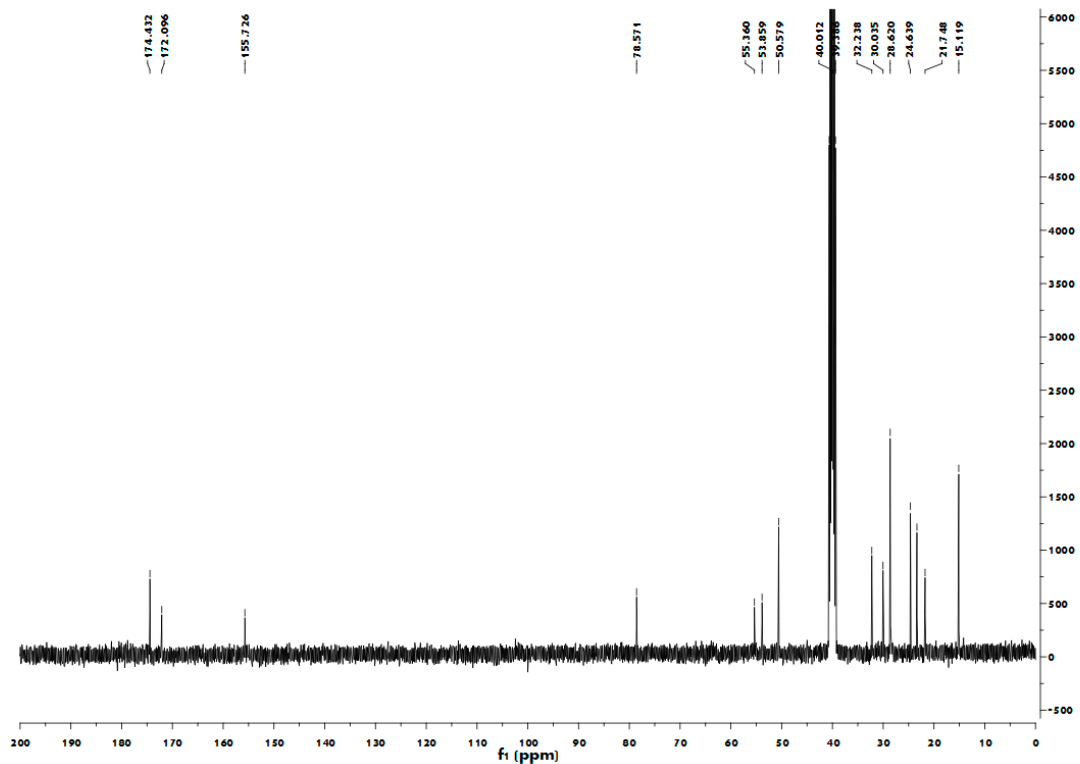
Figure S53. ^{13}C-NMR for compound **Leu-06**.

Figure S54. MS-ESI for compound **Leu-06**.

Figure S55. ¹H-NMR for compound **Leu-07**.

S27
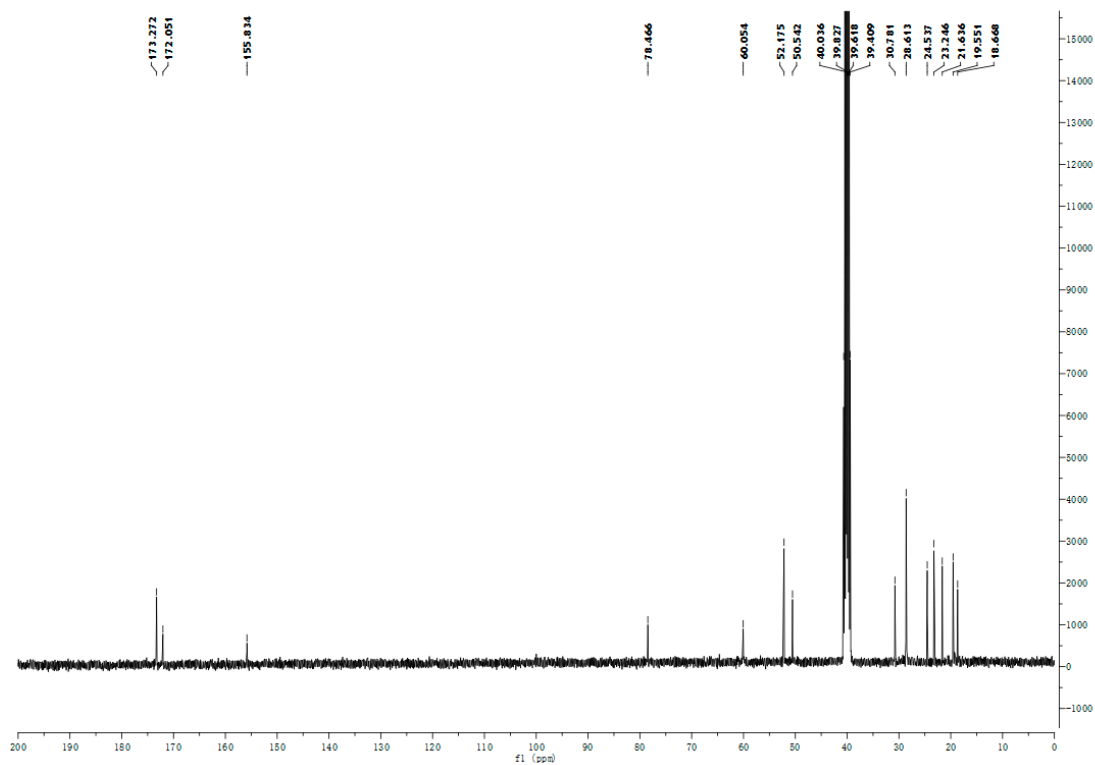
Figure S56. ^{13}C-NMR for compound **Leu-07**.

R.Time:0.225(Scan#:28)
MassPeaks:944   BasePeak:367(3256550)
Spectrum Mode:Single 0.225(28)
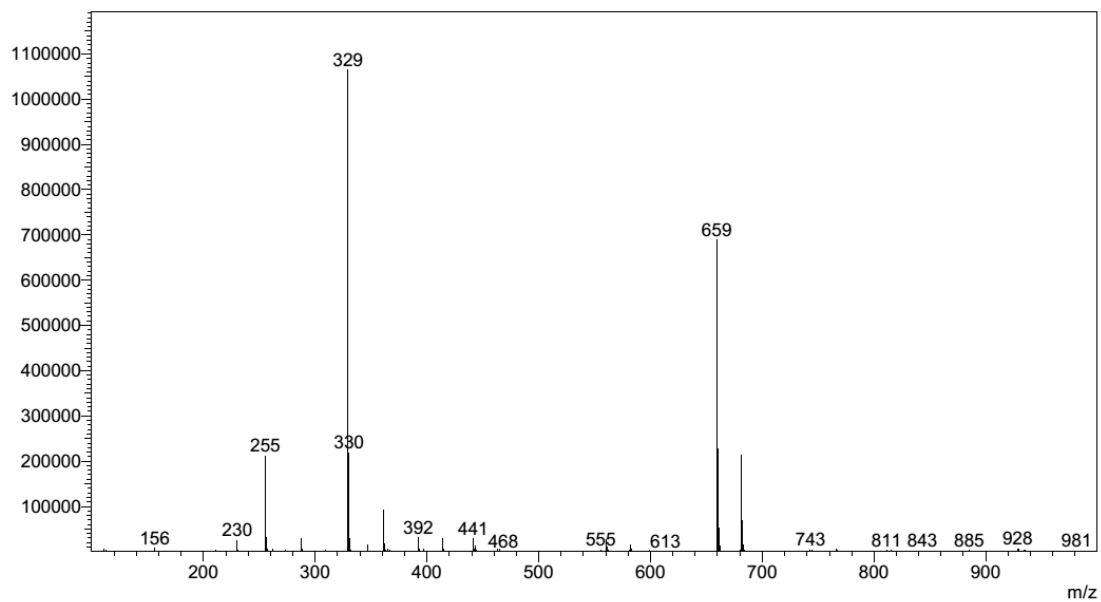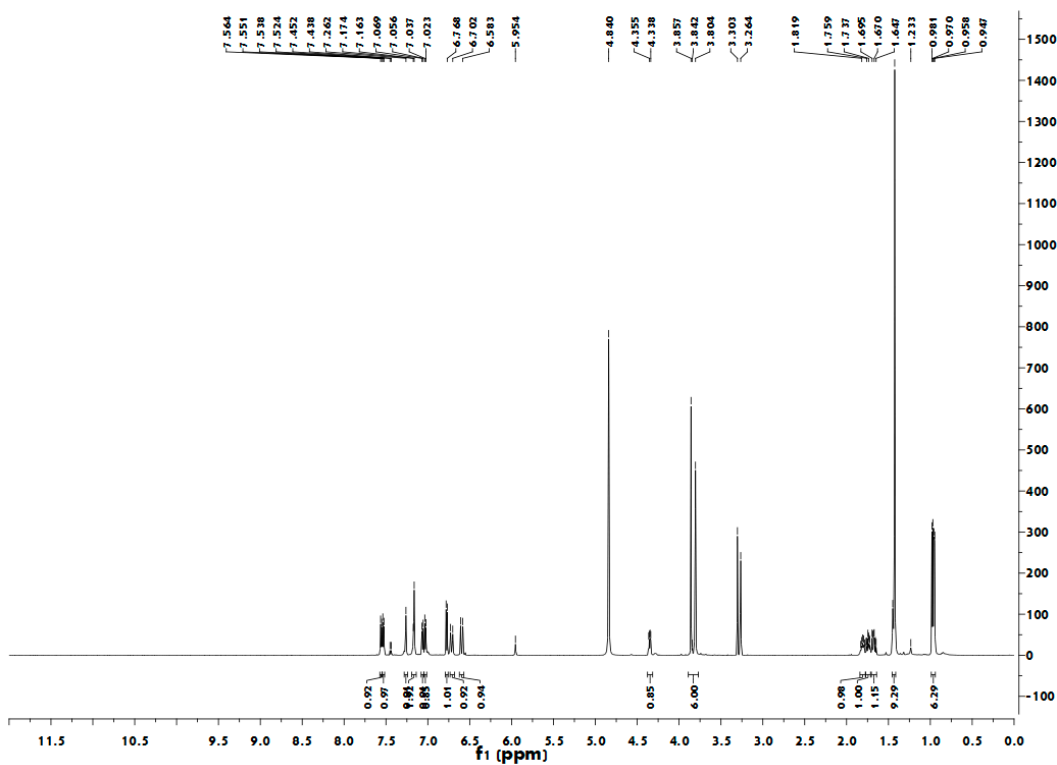BG Mode:None   Polarity:Positive Segment 1 - Event 1

Figure S57. MS-ESI for compound **Leu-07**.

Figure S58. ^{1}H-NMR for compound **Leu-08**.

Figure S59. ^{13}C-NMR for compound **Leu-08**.

Figure S60. MS-ESI for compound **Leu-08**.

Figure S61. ^{1}H-NMR for compound **9**.
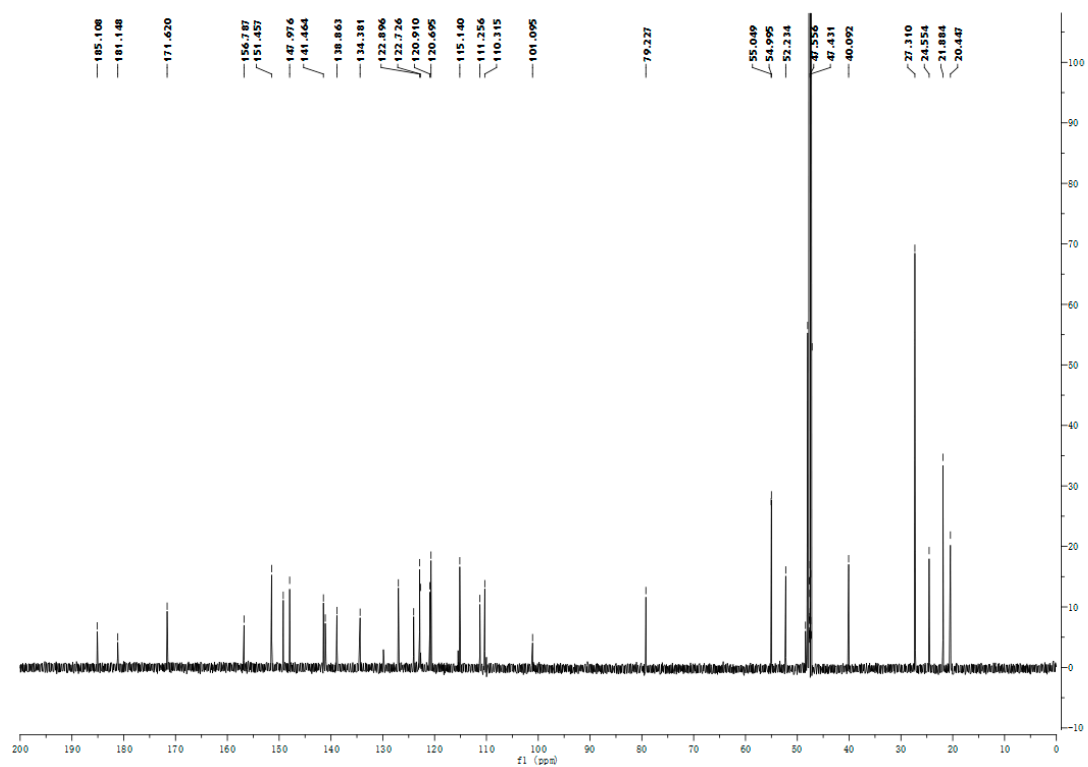
Figure S62. ^{13}C-NMR for compound **9**.

R.Time:0.375(Scan#:46)
MassPeaks:502   BasePeak:580(48435)
Spectrum Mode:Single 0.375(46)
BG Mode:Averaged 0.033-0.283(5-35) Polarity:Negative Segment 1 - Event 1
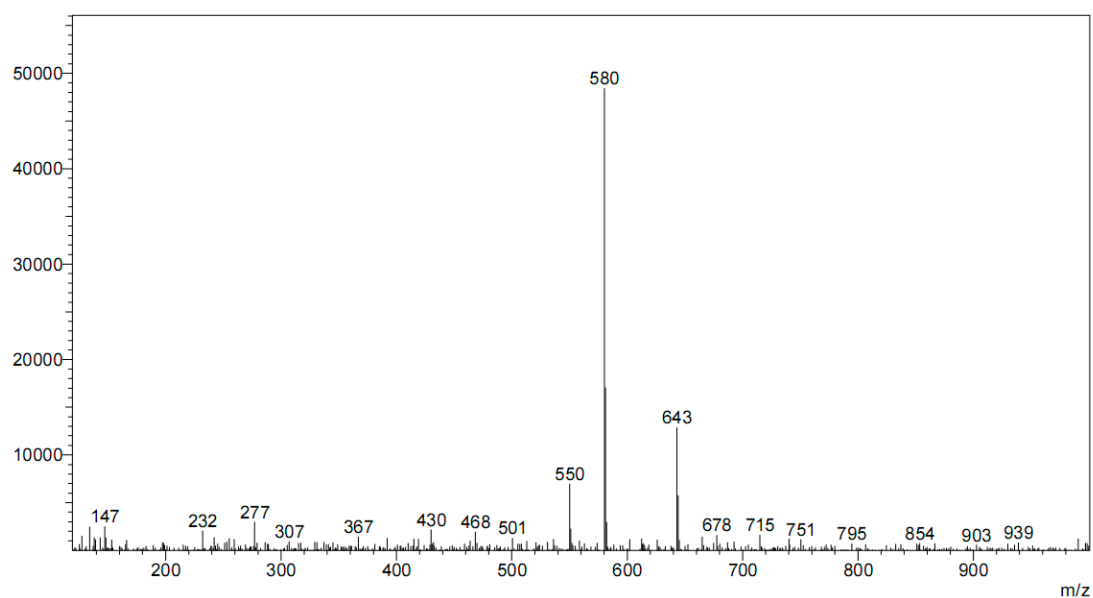
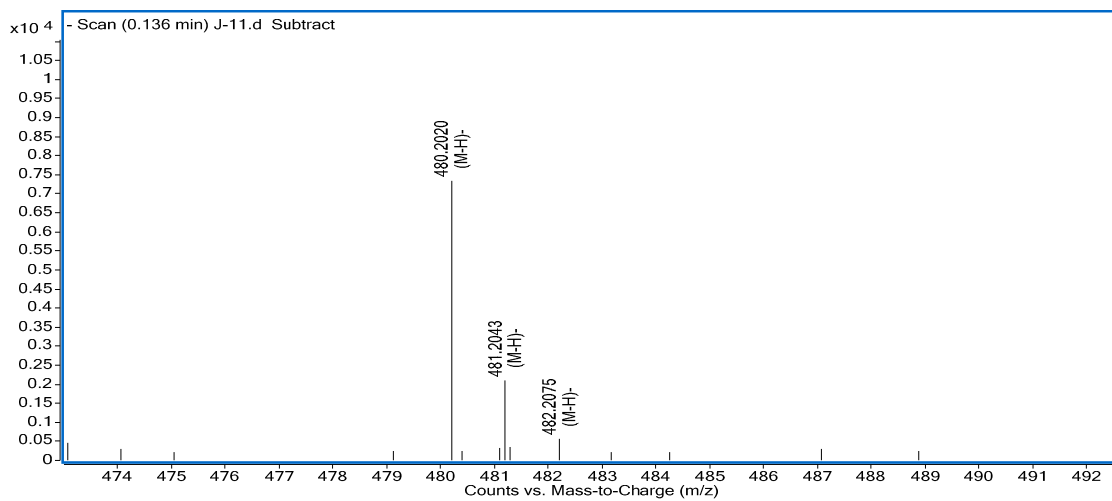

Figure S63. MS-ESI for compound **9**.
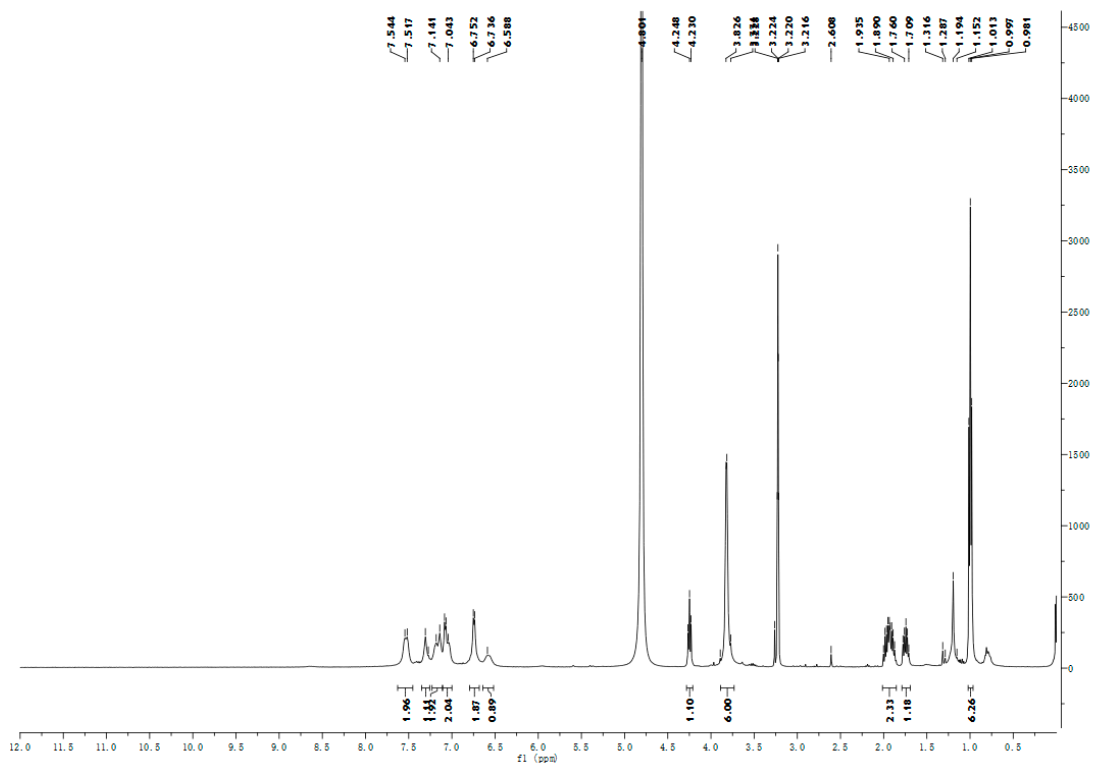
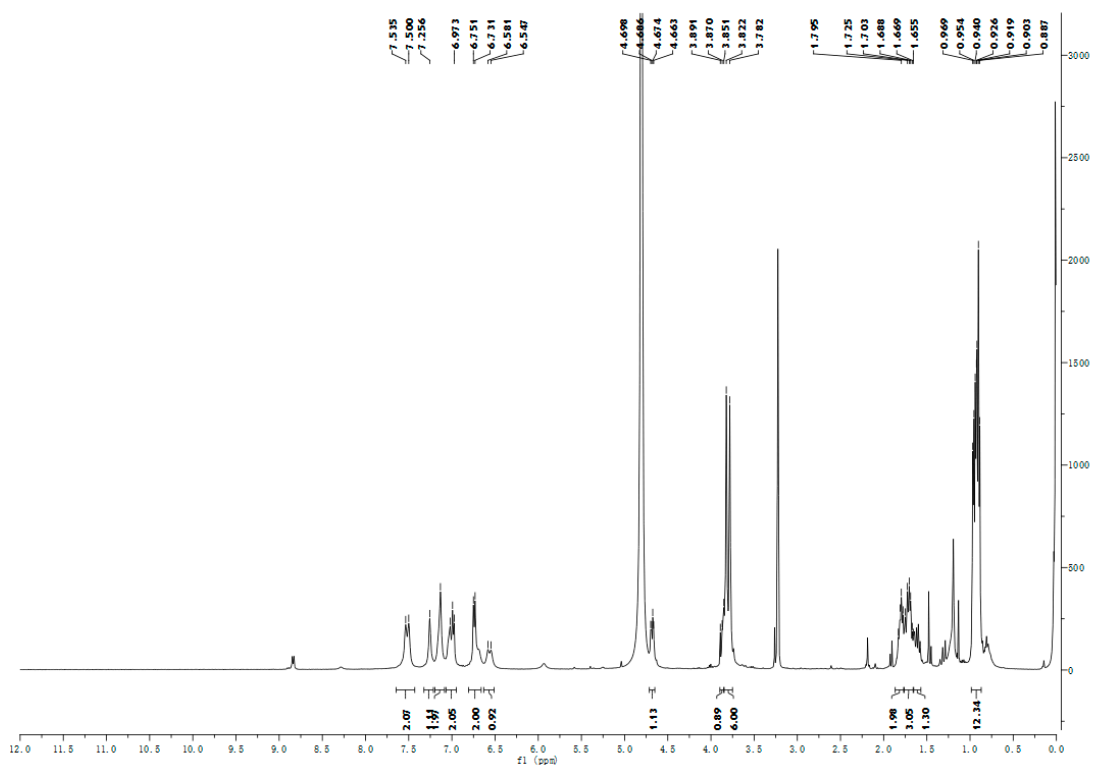**Figure S64.** ^{1}H-NMR for compound **10**.
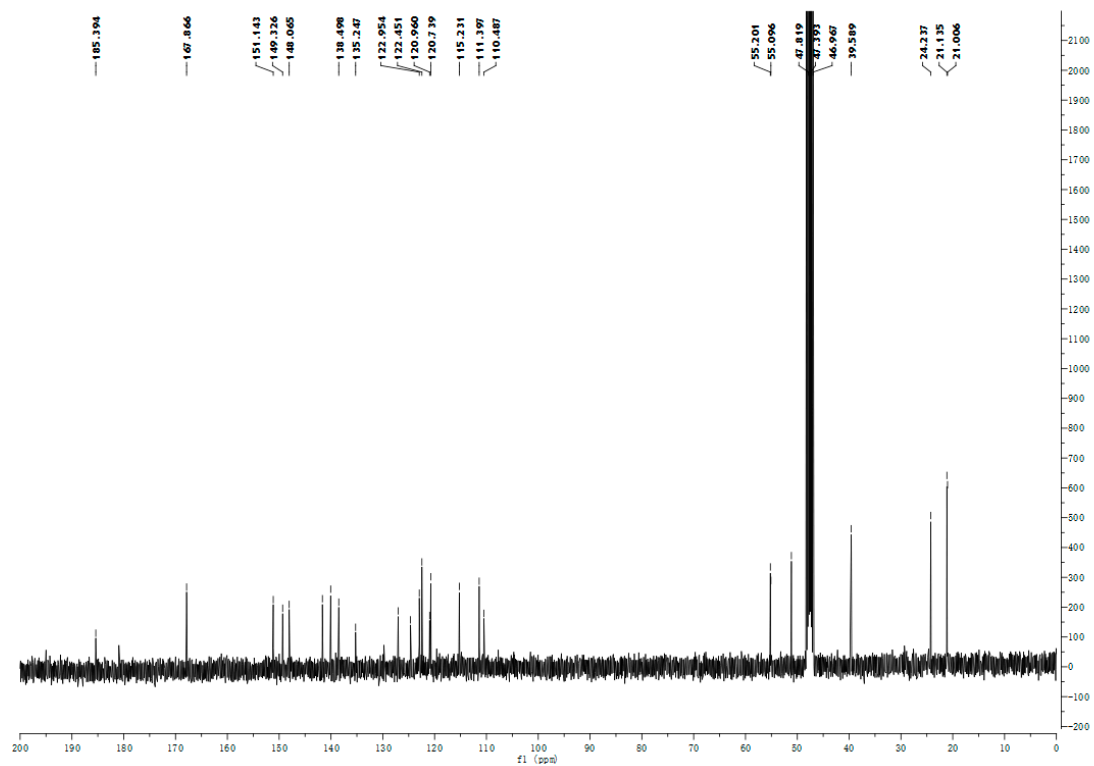
Figure S65. ^{13}C-NMR for compound **10**.
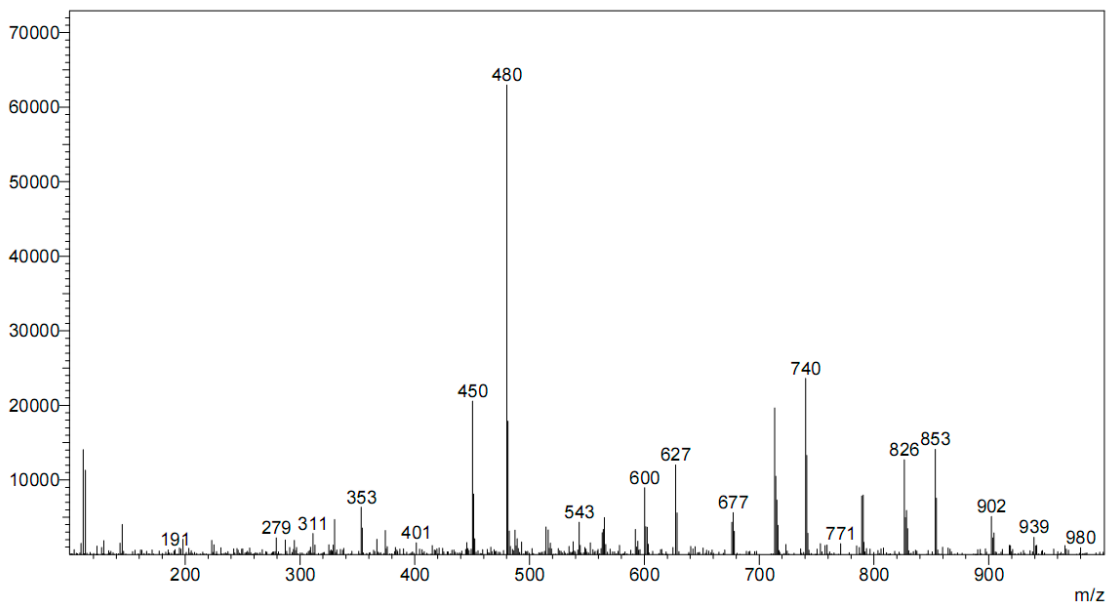
Figure S66. MS-ESI for compound **10**.

Figure S67. HRMS-ESI for compound **10**.
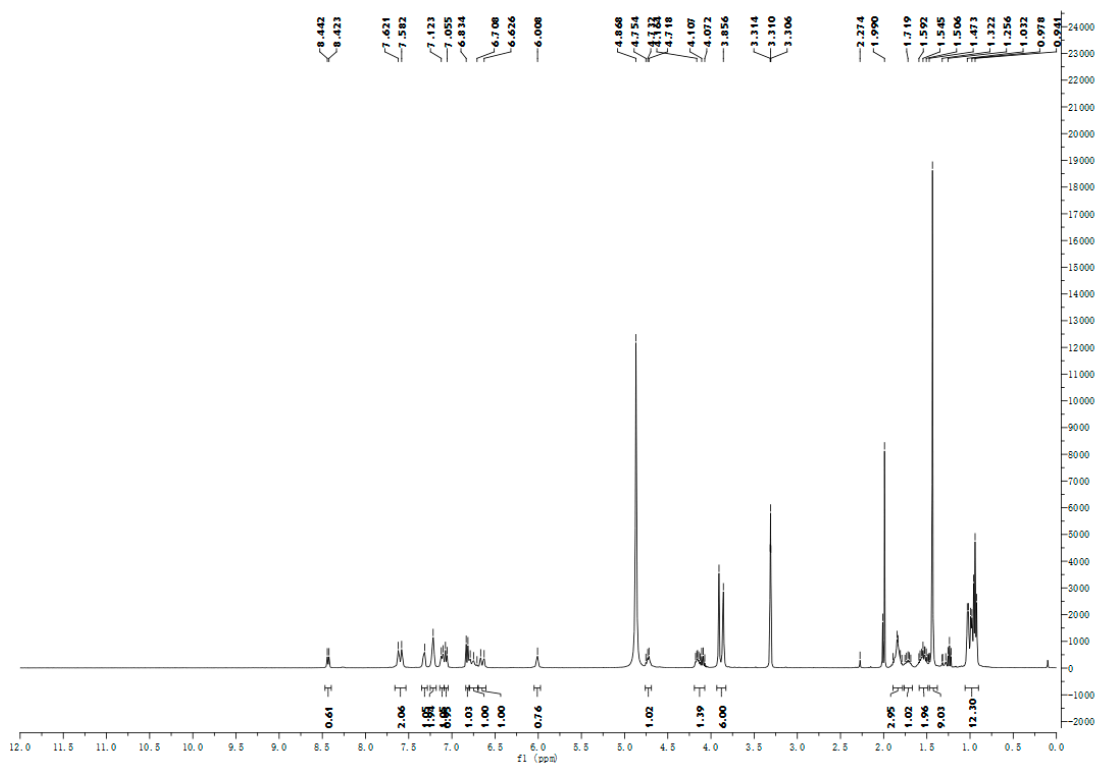
Figure S68. ^{1}H-NMR for compound **11**.
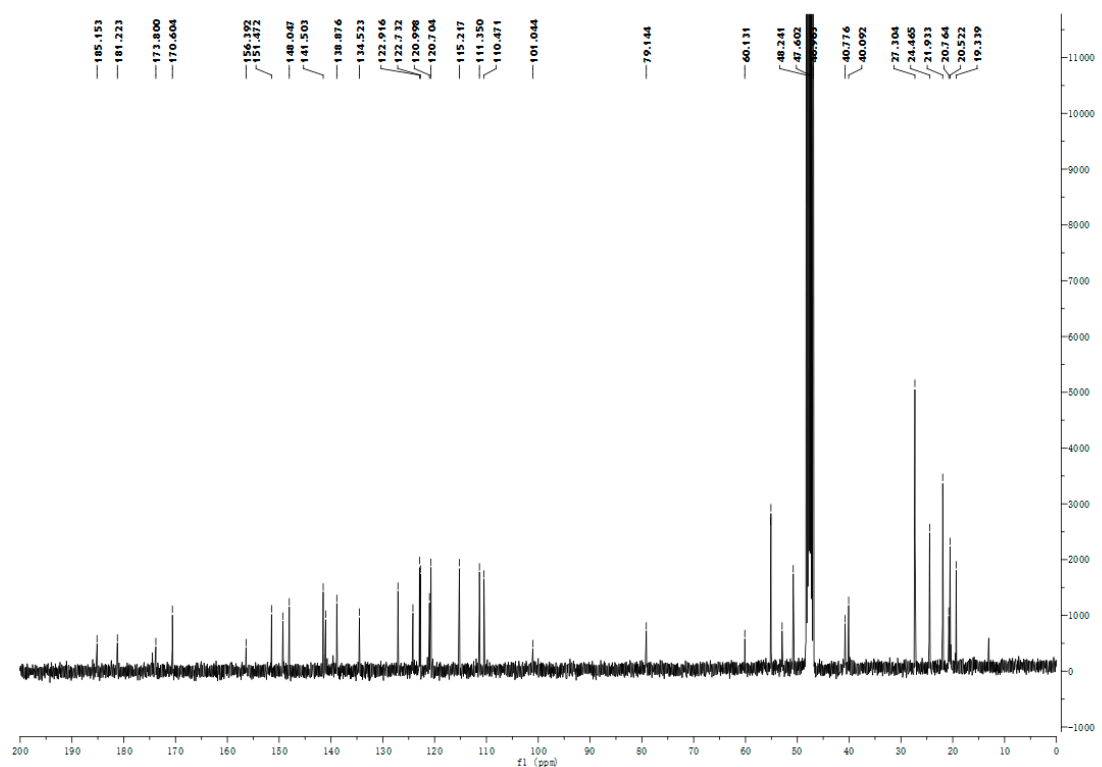
Figure S69. ^{13}C-NMR for compound **11**.
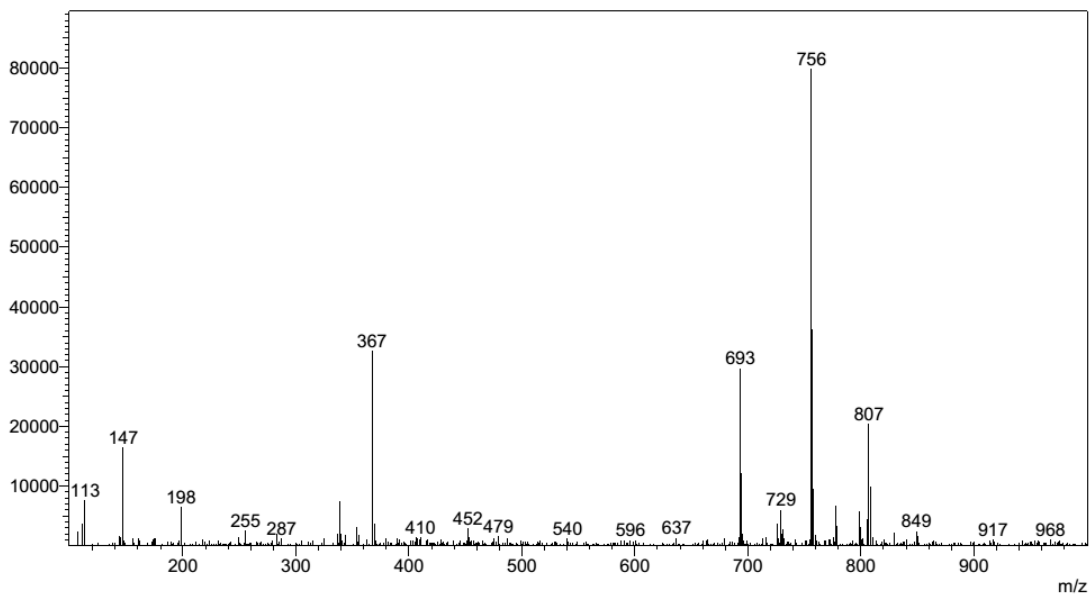
Figure S70. MS-ESI for compound **11**.

Figure S71. ¹H-NMR for compound **12**.
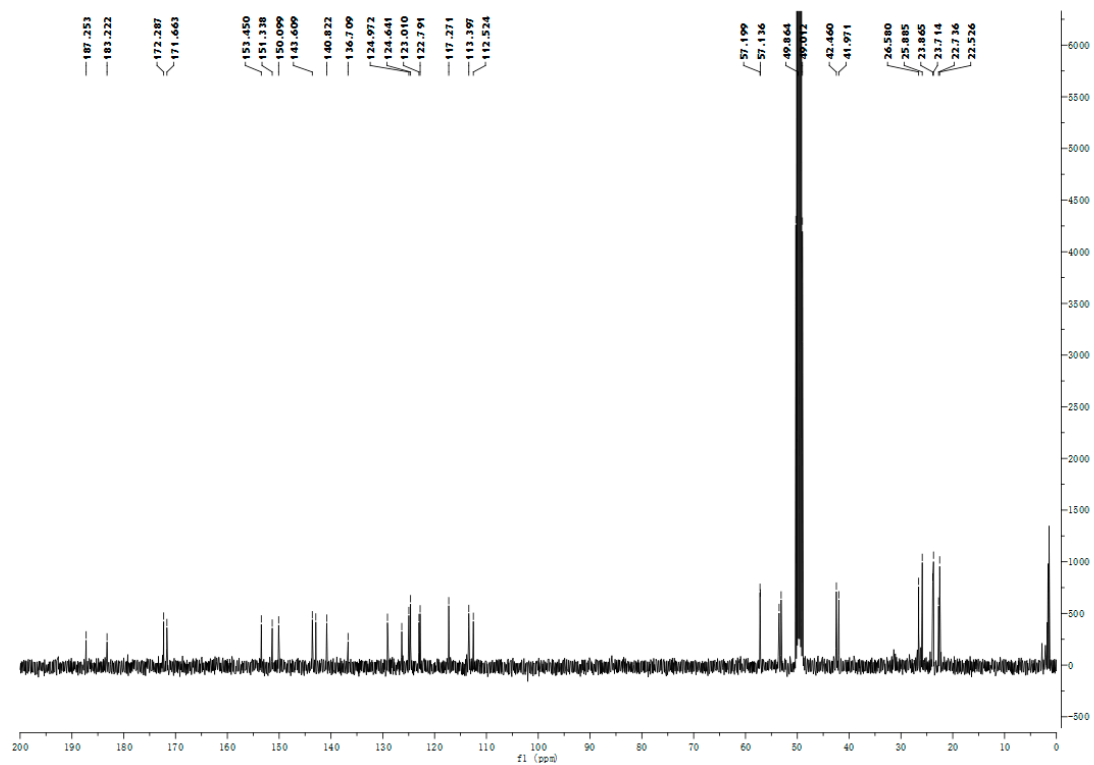
Figure S72. ^{13}C-NMR for compound **12**.

R.Time:0.900(Scan#:109)
MassPeaks:635   BasePeak:595(359918)
Spectrum Mode:Single 0.900(109)
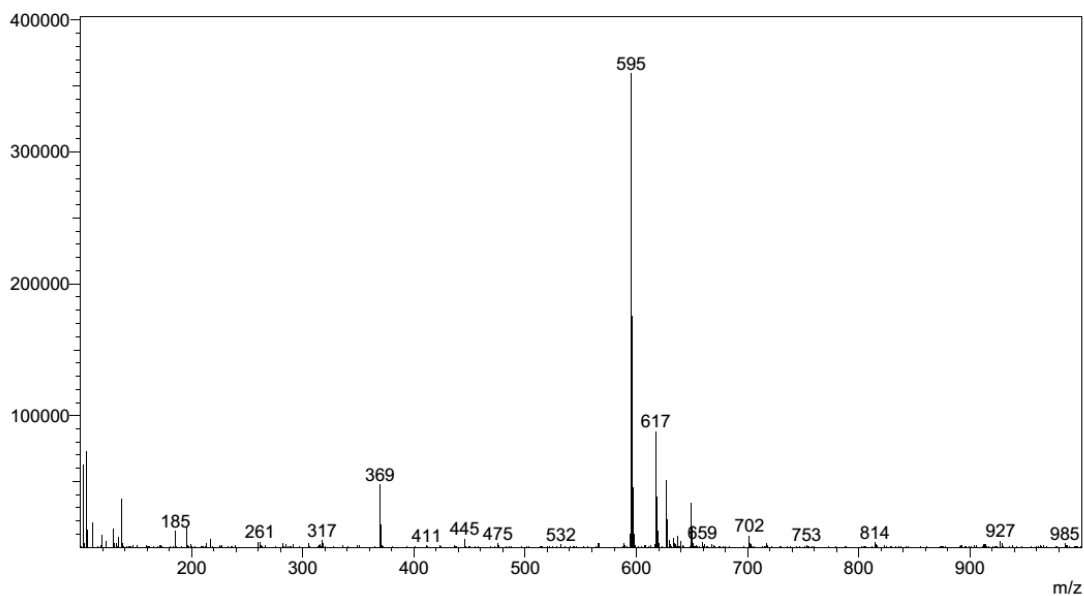BG Mode:Averaged 0.025-0.700(4-85) Polarity:Positive Segment 1 - Event 1
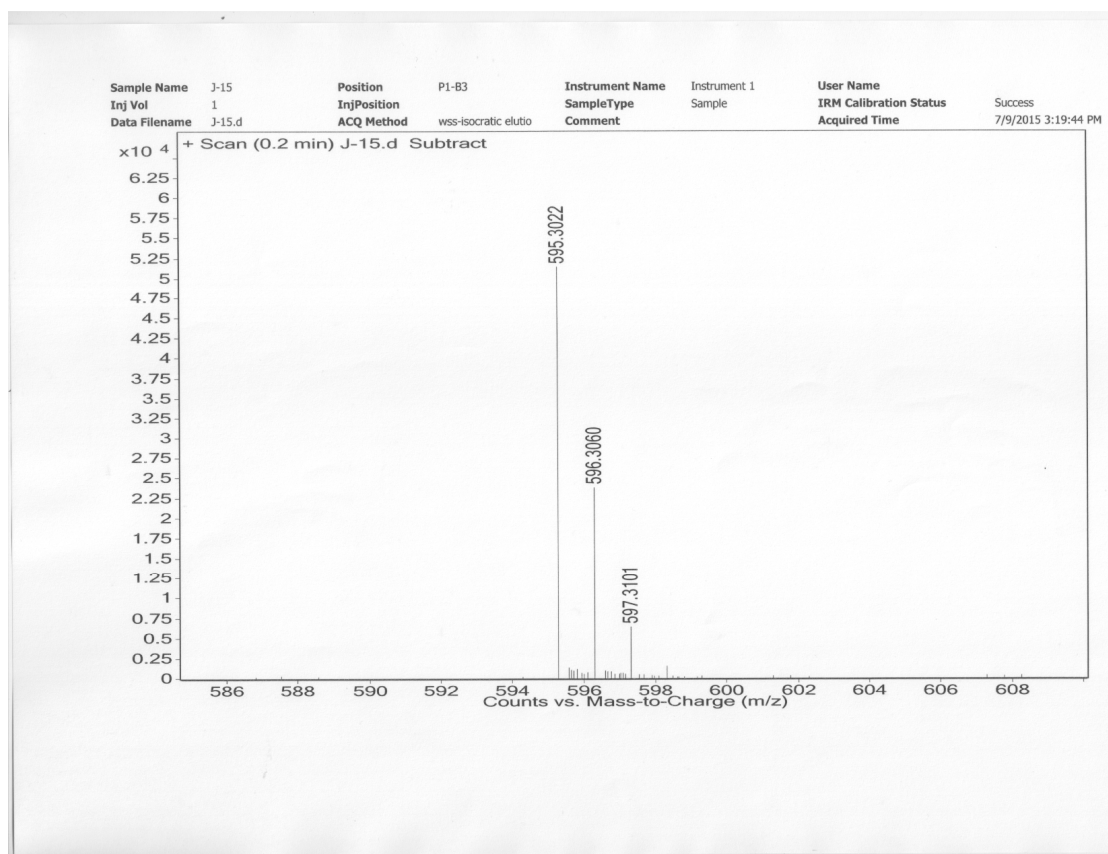

Figure S73. MS-ESI for compound **12**.
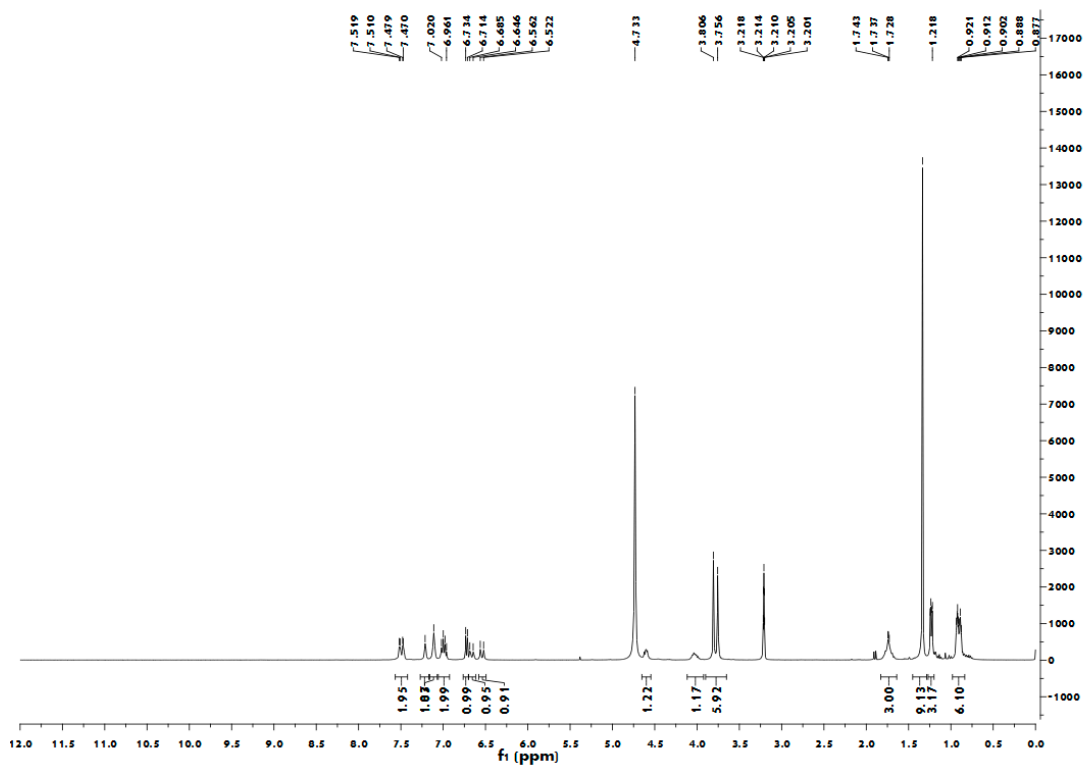
Figure S74. HRMS-ESI for compound **12**.

Figure S75. ^{1}H-NMR for compound **13**.
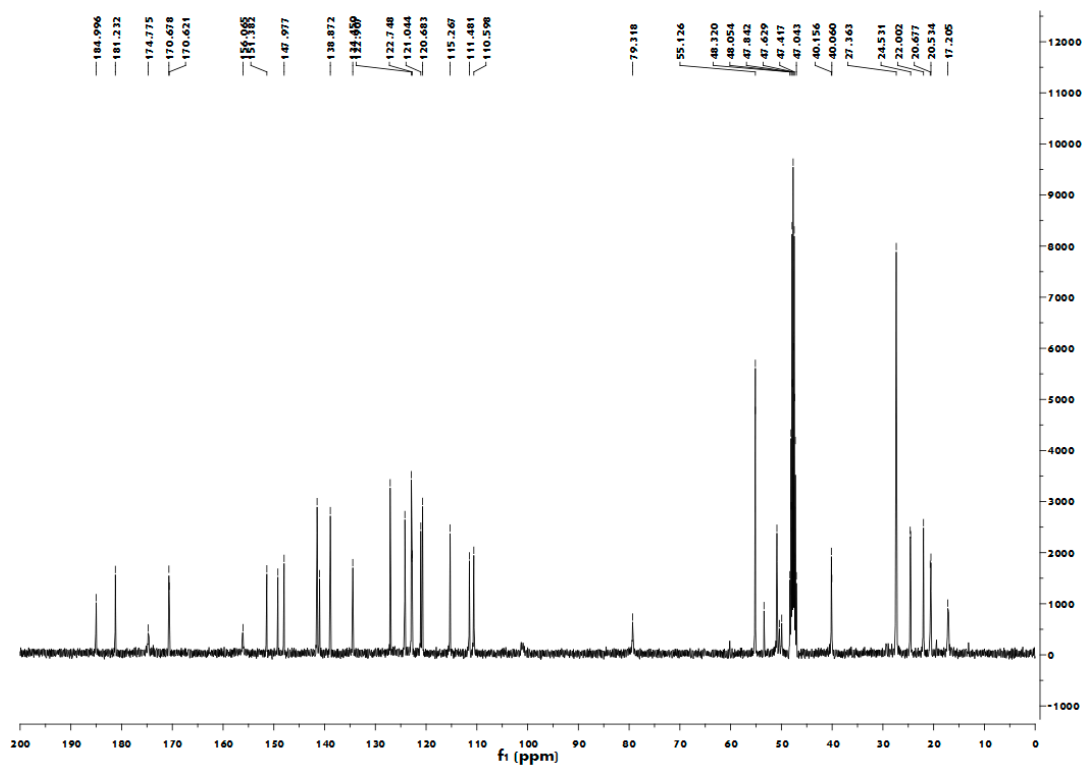
Figure S76. ^{13}C-NMR for compound **13**.

R.Time:0.292(Scan#:36)
MassPeaks:467   BasePeak:367(31008)
Spectrum Mode:Single 0.292(36)
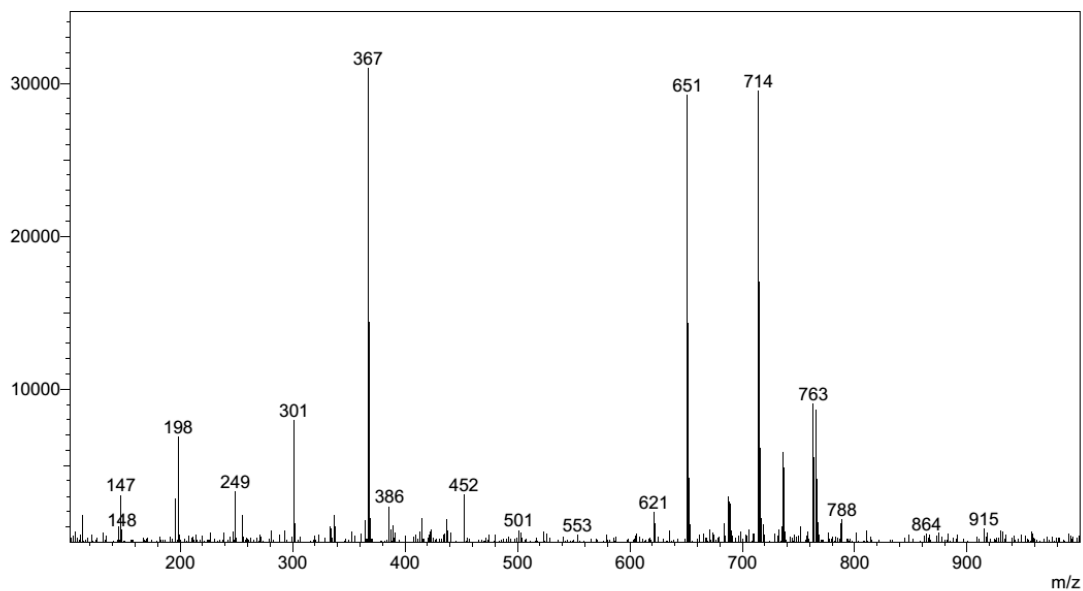BG Mode:Averaged 0.008-0.150(2-19) Polarity:Negative Segment 1 - Event 1
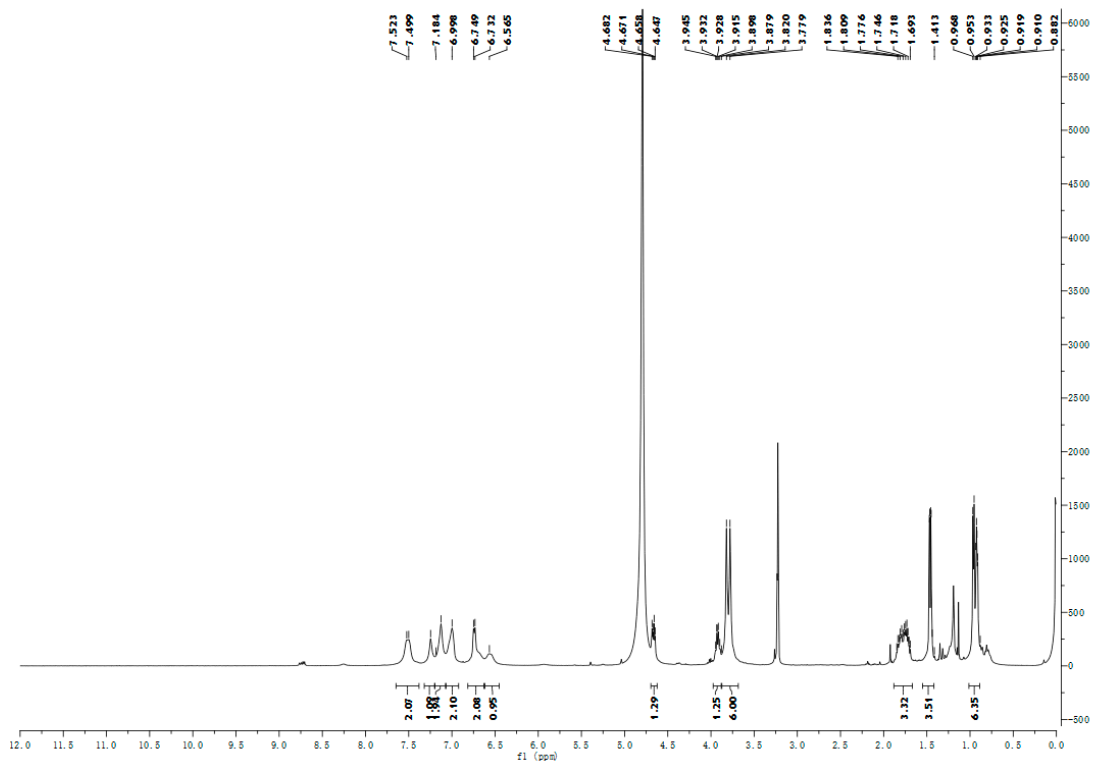

Figure S77. MS-ESI for compound **13**.
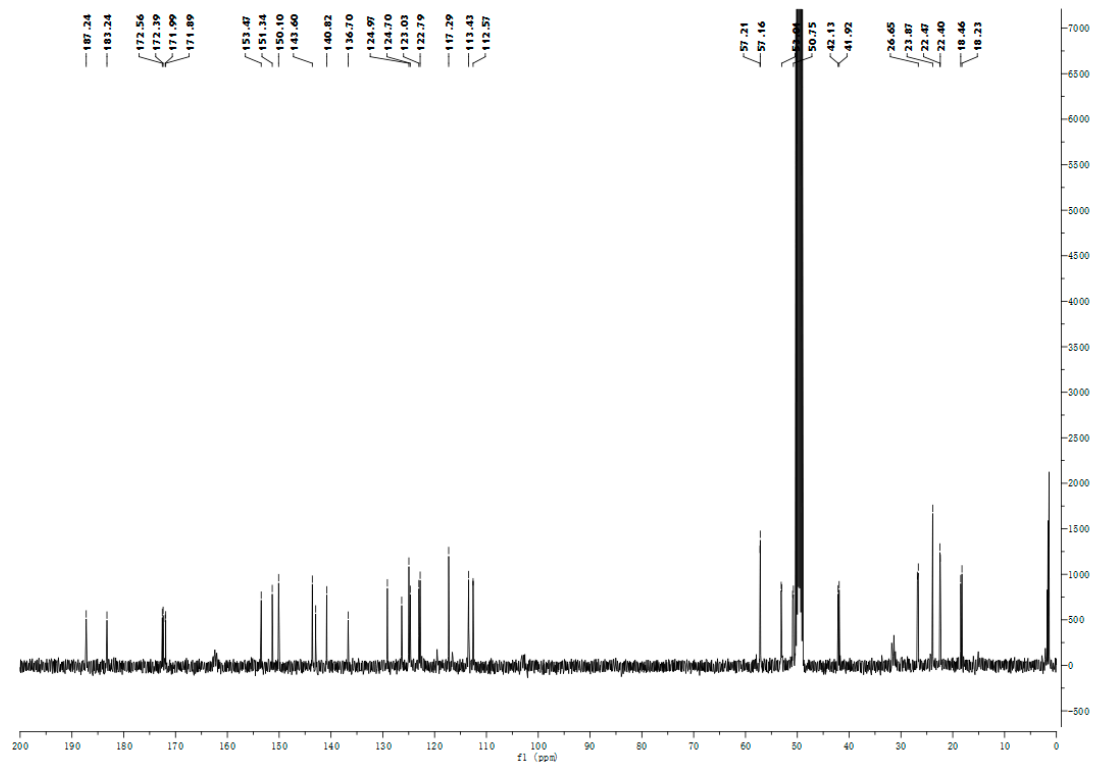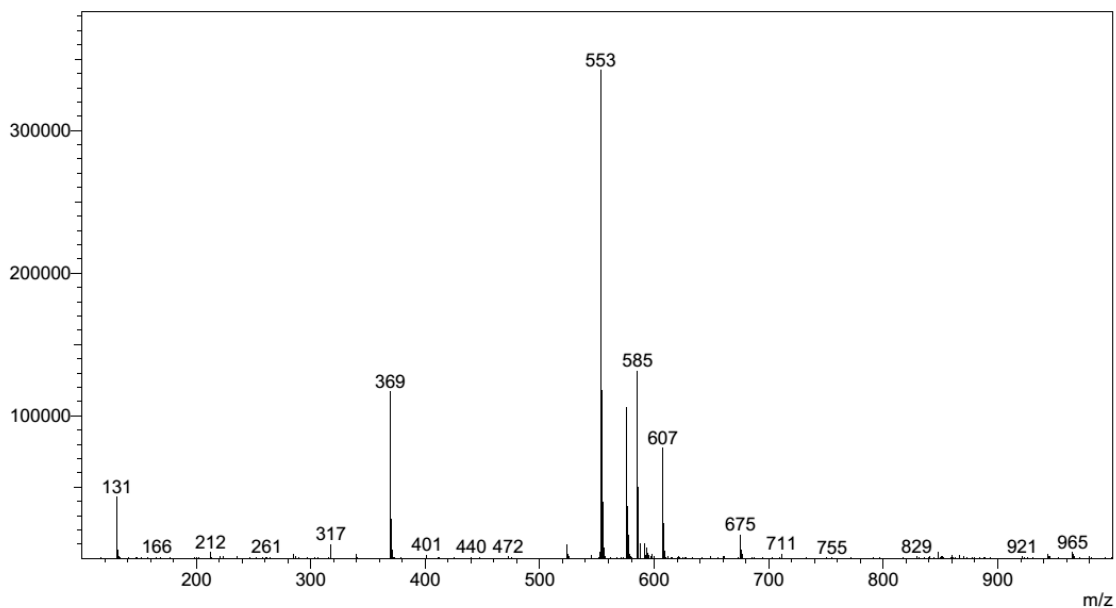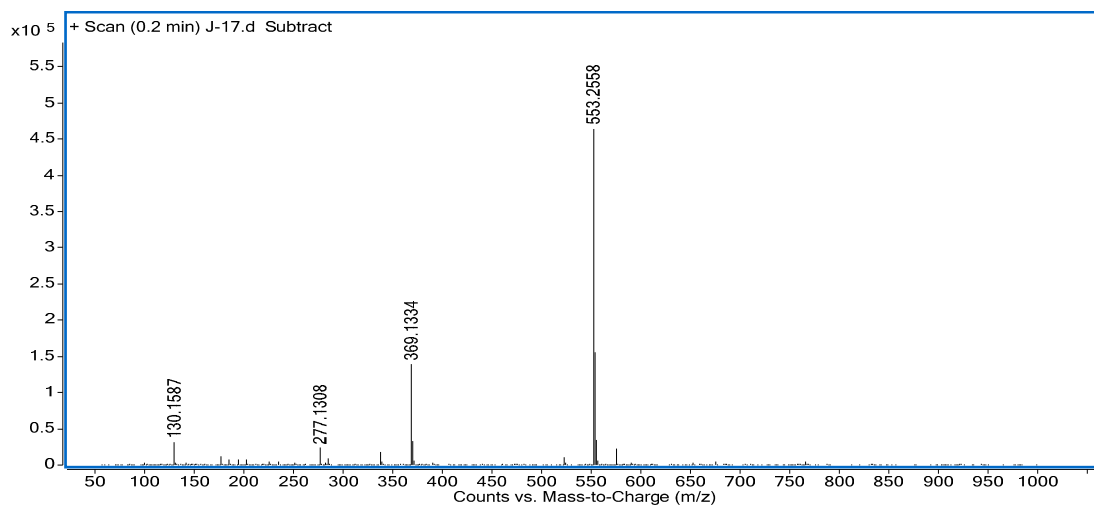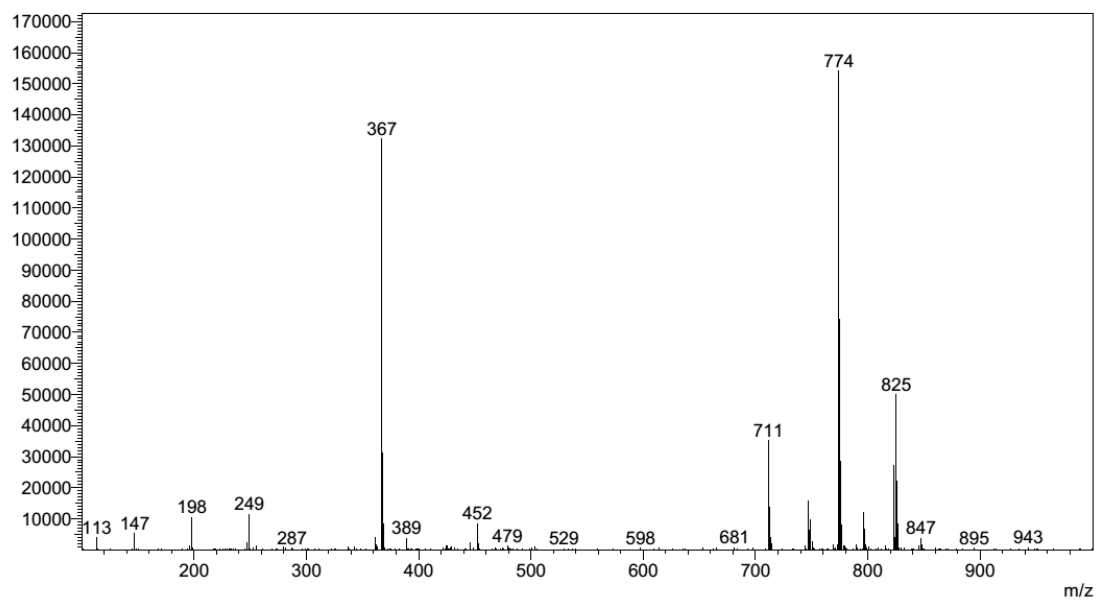
Figure S78. ^{1}H-NMR for compound **14**.

Figure S79. ^{13}C-NMR for compound **14**.

Figure S80. MS-ESI for compound **14**.

Figure S81. HRMS-ESI for compound **14**.
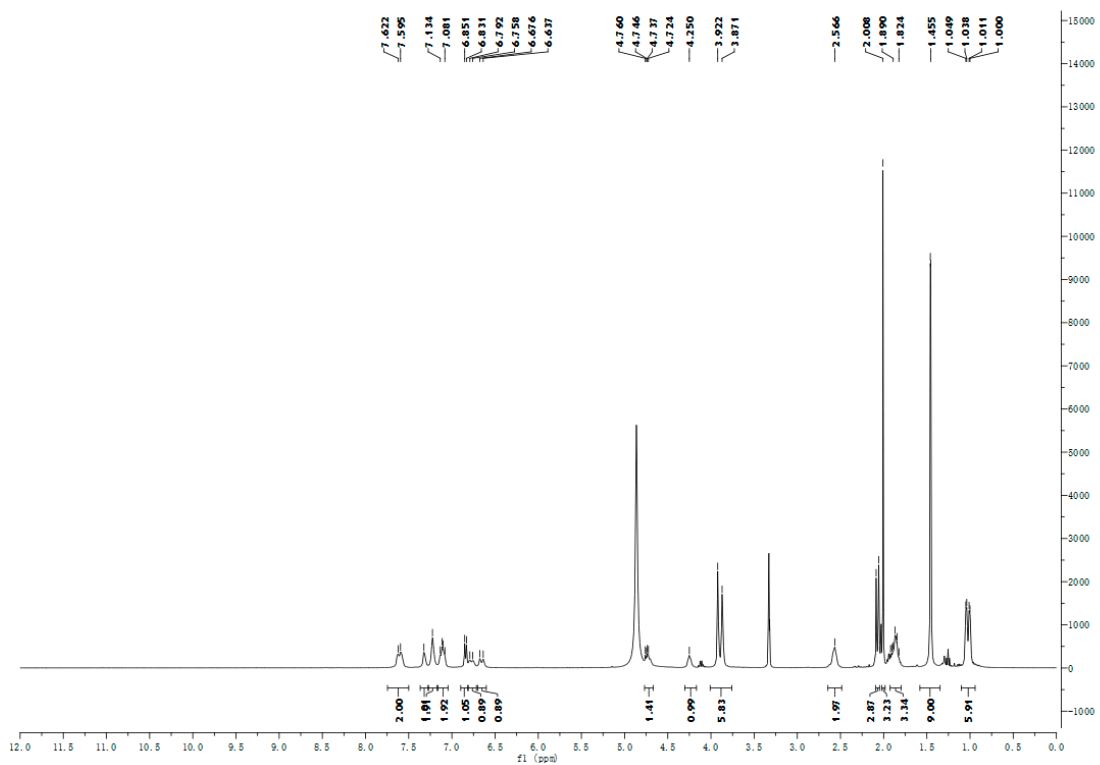
Figure S82. ^{1}H-NMR for compound **15**.
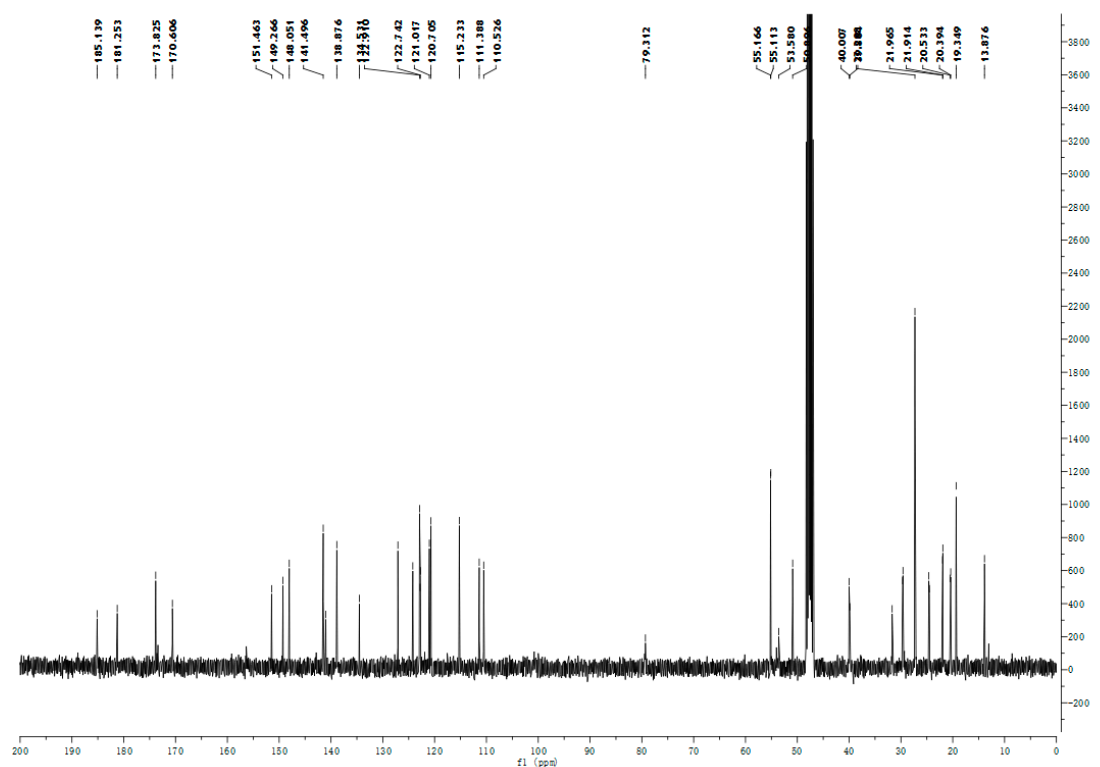
Figure S83. ^{13}C-NMR for compound **15**.

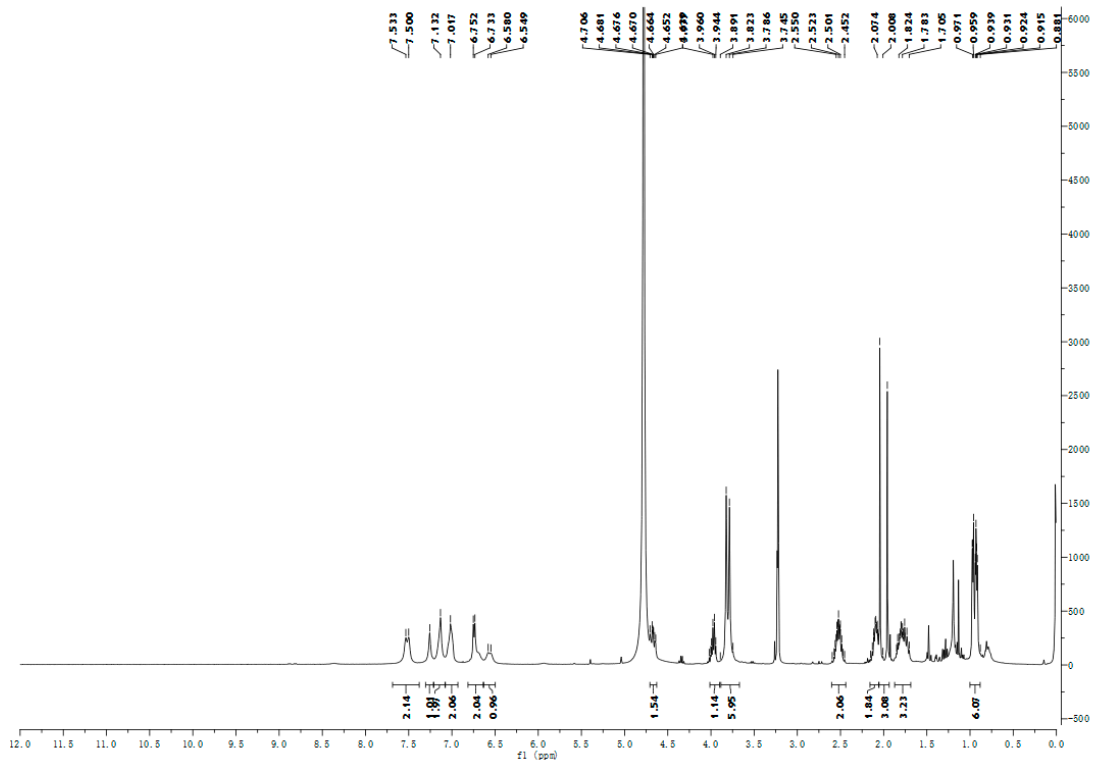**Figure S84.** MS-ESI for compound **15**.

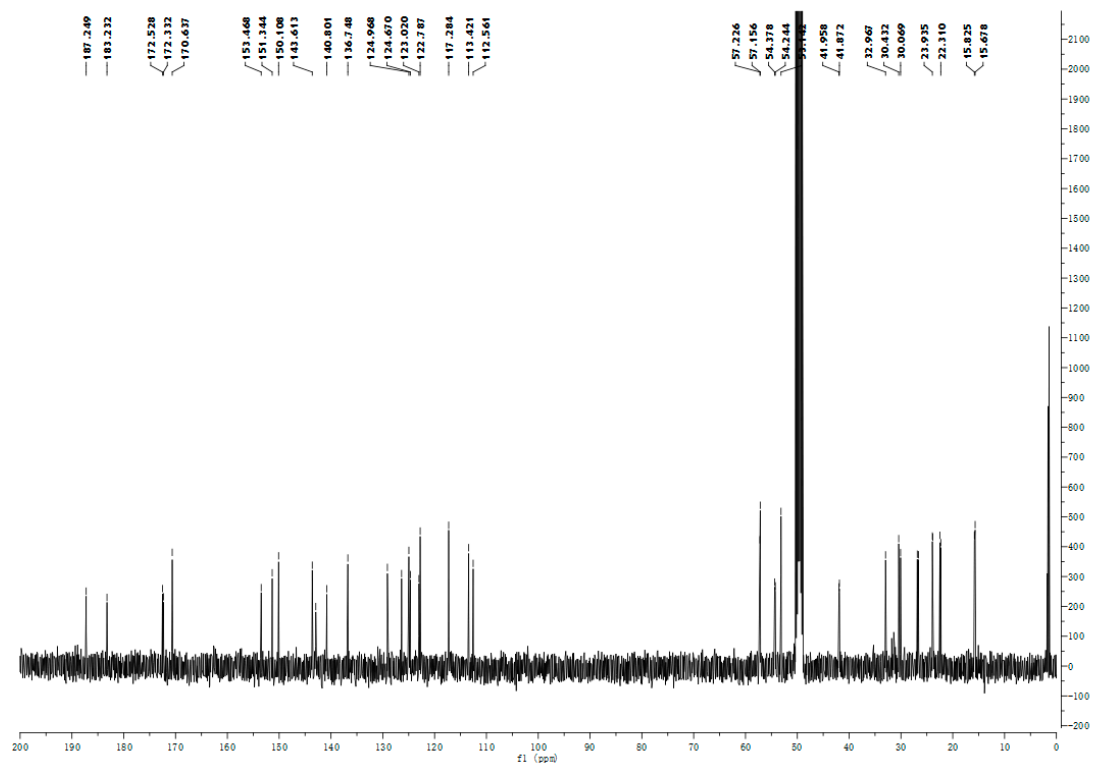**Figure S85.** ¹H-NMR for compound **16**.

Figure S86. ¹³C-NMR for compound **16**.

R.Time:0.292(Scan#:36)
MassPeaks:341   BasePeak:613(459275)
Spectrum Mode:Single 0.292(36)
BG Mode:Averaged 0.008-0.083(2-11) Polarity:Positive Segment 1 - Event 1
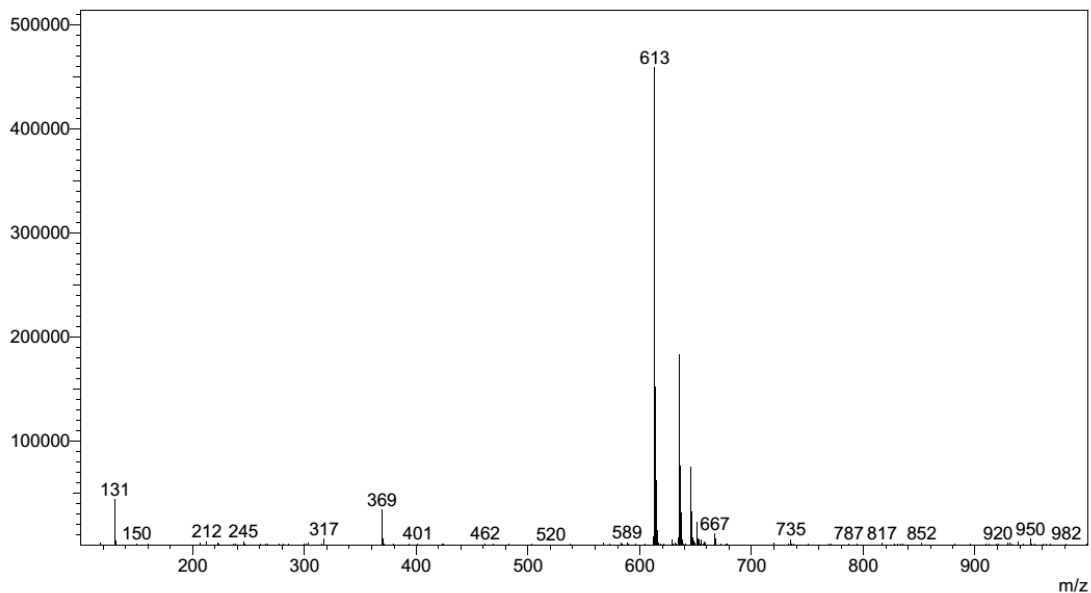

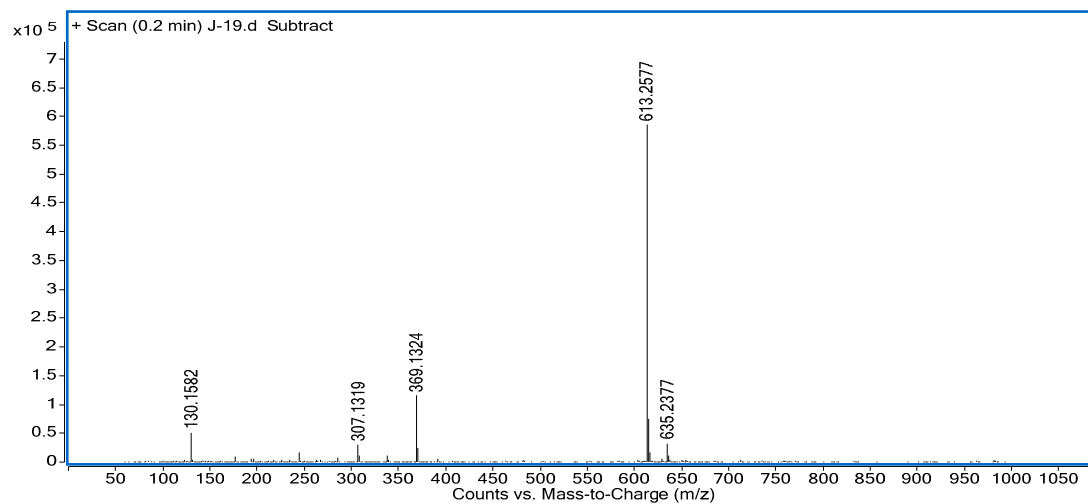**Figure S87.** MS-ESI for compound **16**.
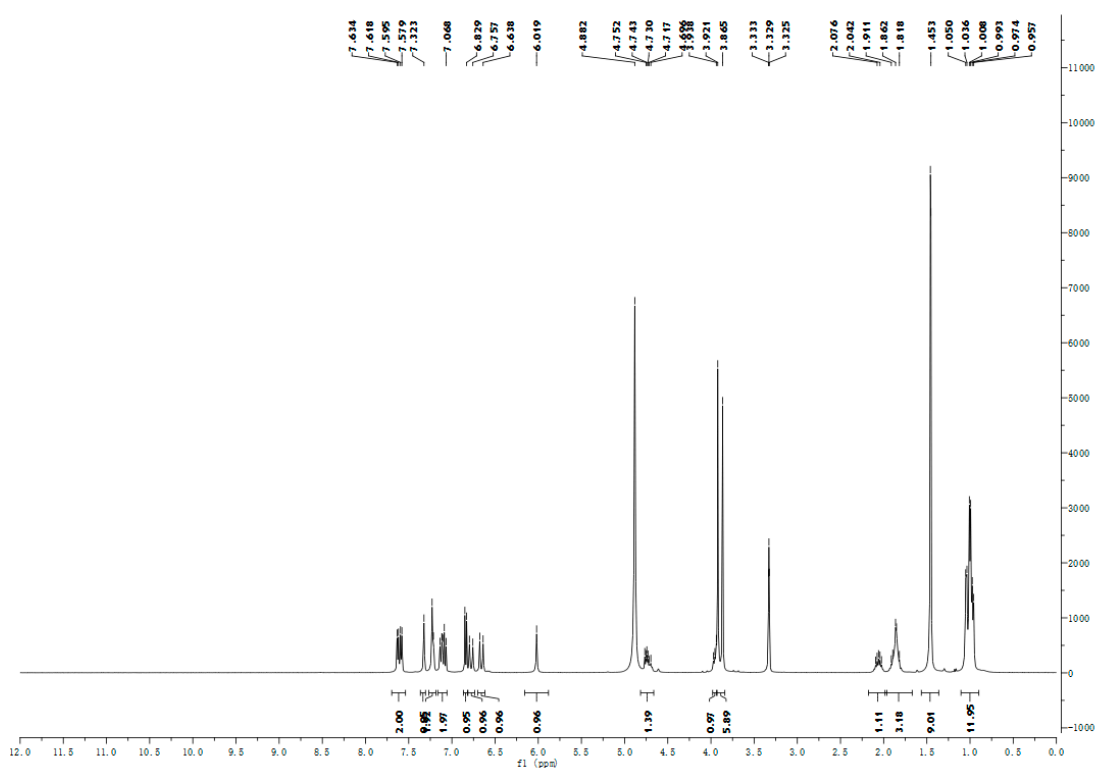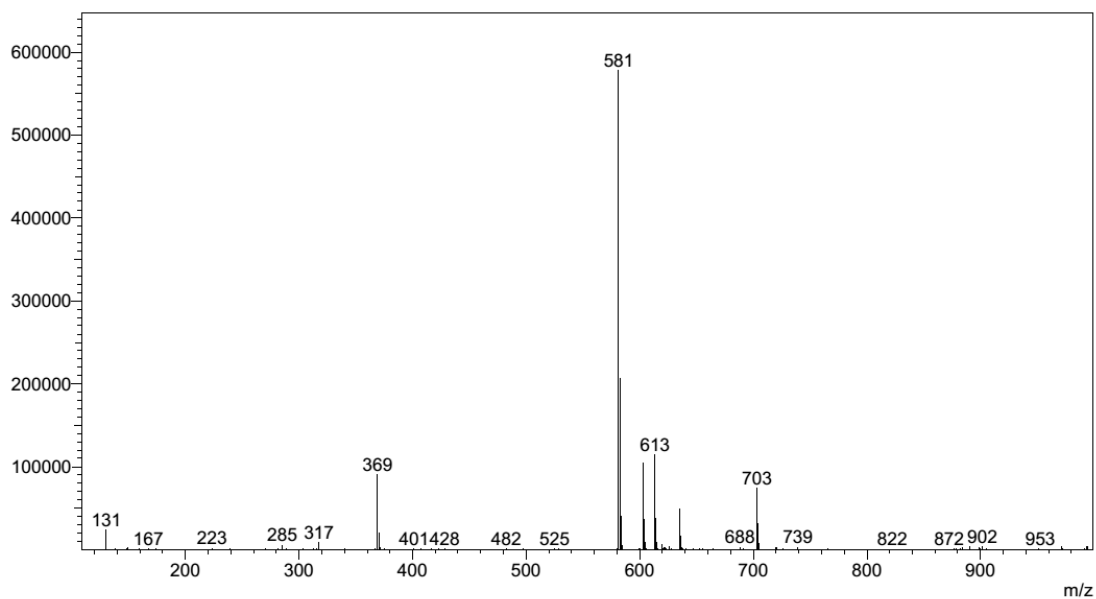
Figure S88. HRMS-ESI for compound **16**.

Figure S89. ^{1}H-NMR for compound **17**.
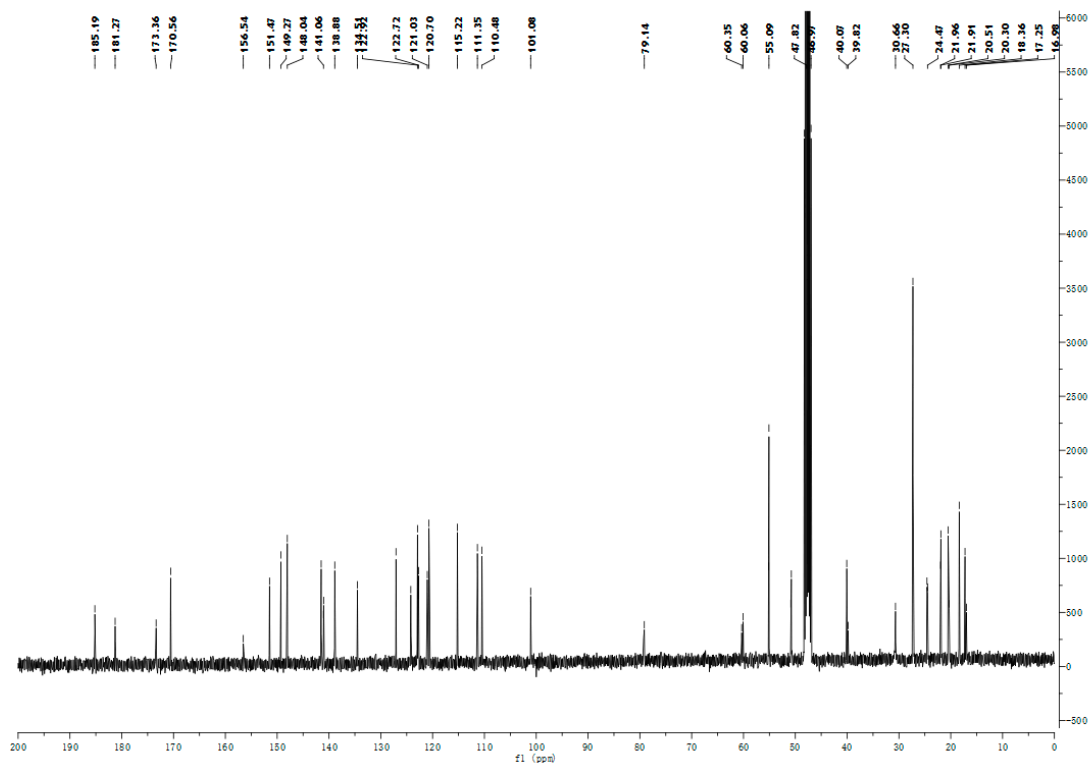
Figure S90. ^{13}C-NMR for compound **17**.
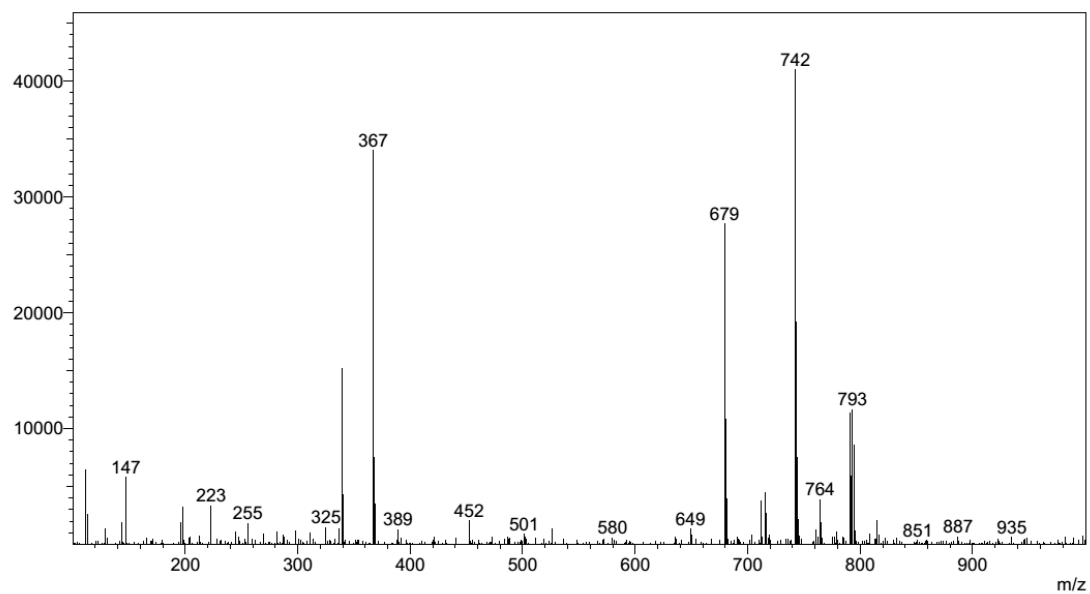
Figure S91. MS-ESI for compound **17**.
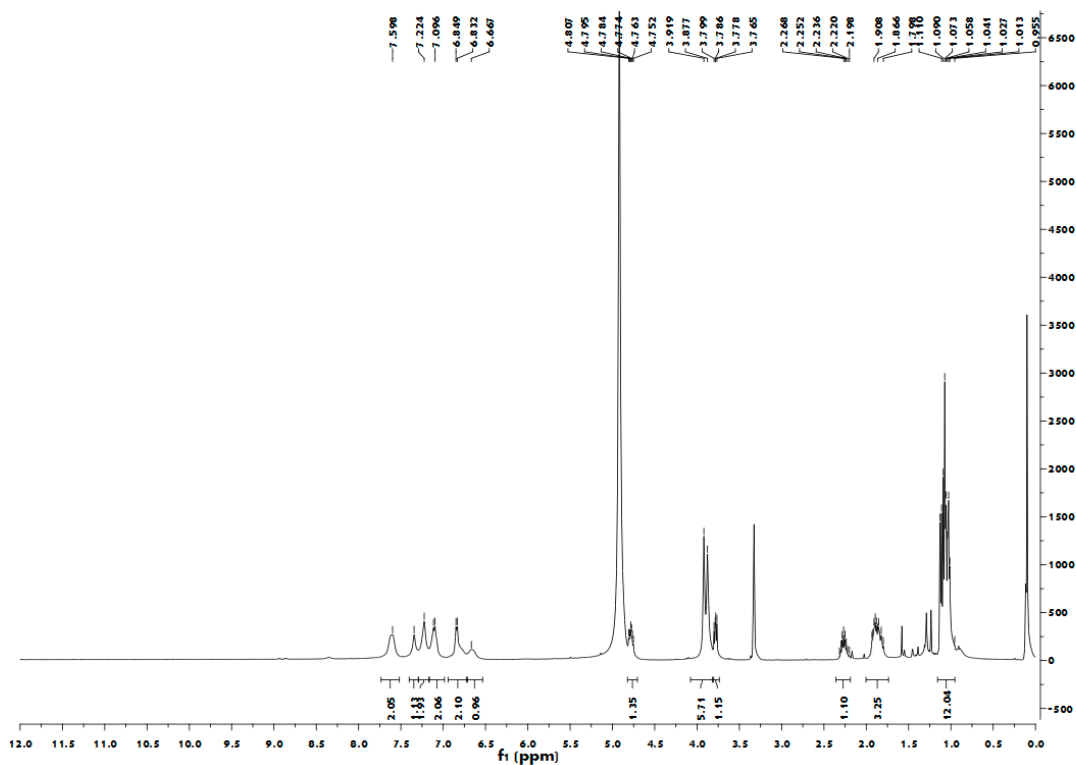
Figure S92. ^{1}H-NMR for compound **18**.
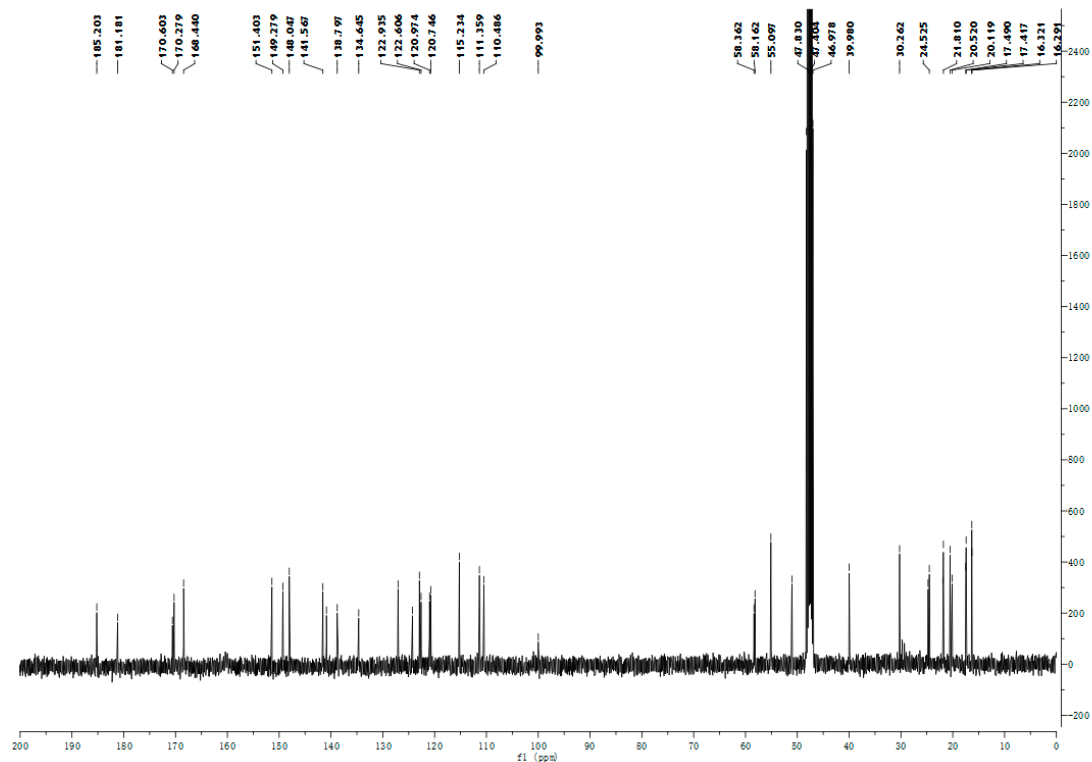
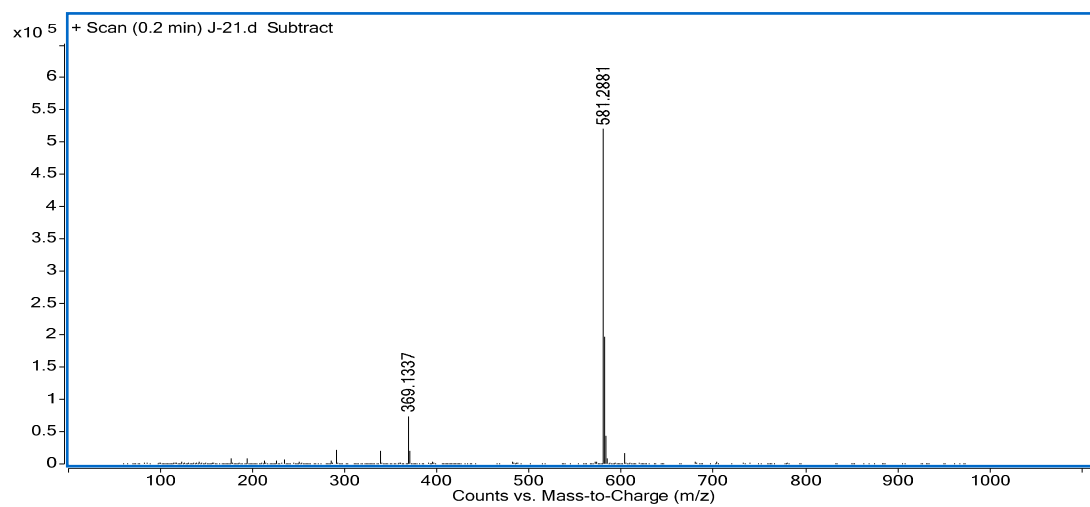**Figure S93.** ^{13}C-NMR for compound **18**.

Figure S94. MS-ESI for compound **18**.

Figure S95. HRMS-ESI for compound **18**.