

## Electronic Supporting Information (ESI)

# Synthesis of Cucurbitacin IIa Derivatives with Apoptosis-Inducing Capabilities in Human Cancer Cells

Kun Yu,<sup>†ab</sup> Xinmei Yang,<sup>†c</sup> Ying Li,<sup>ab</sup> Xue Cui,<sup>ab</sup> Bo Liu,<sup>\*ab</sup> and Qingqiang Yao<sup>\*ab</sup>

a. School of Medicine and Life Sciences, University of Jinan-Shandong Academy of Medical Sciences, Jinan 250200, Shandong, China

b. Institute of Materia Medica, Shandong First Medical University & Shandong Academy of Medical Sciences, Jinan 250062, Shandong, China

c. Department of Pharmacy, The First Affiliated Hospital of Shandong First Medical University, Jinan 250014, China

<sup>†</sup>These authors contributed equally to the work.

\*Corresponding authors: E-Mail: mls\_liub@ujn.edu.cn (Bo Liu), yao\_imm@163.com (Qingqiang Yao)

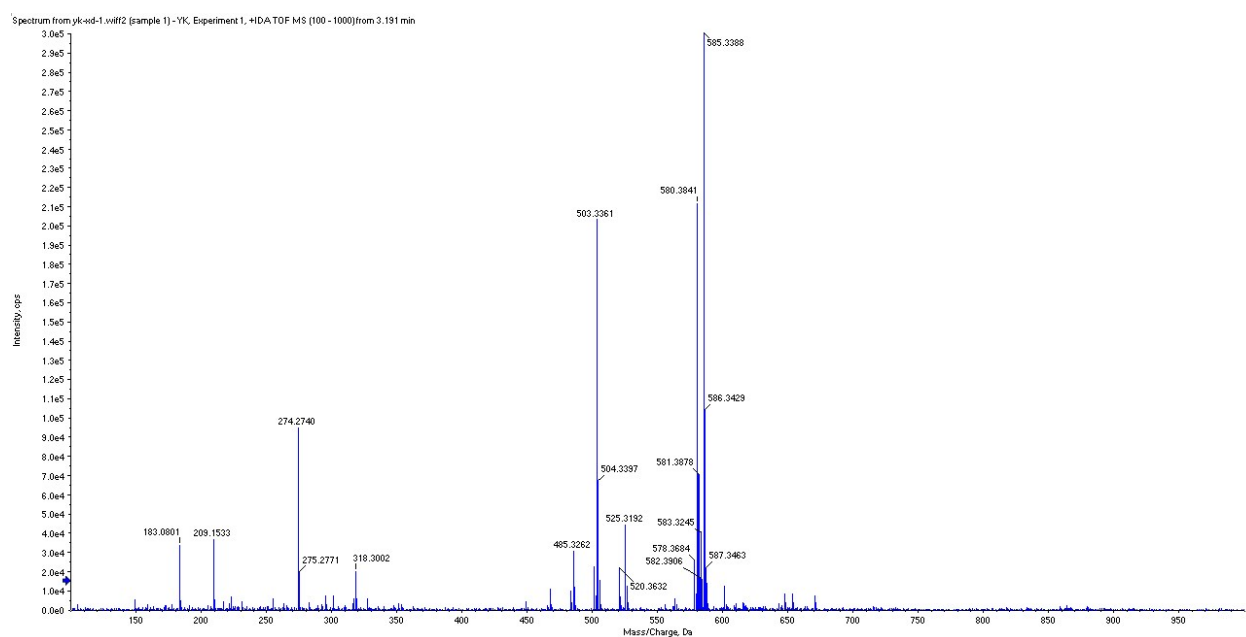


Fig. S1 HRMS spectrum of **1**

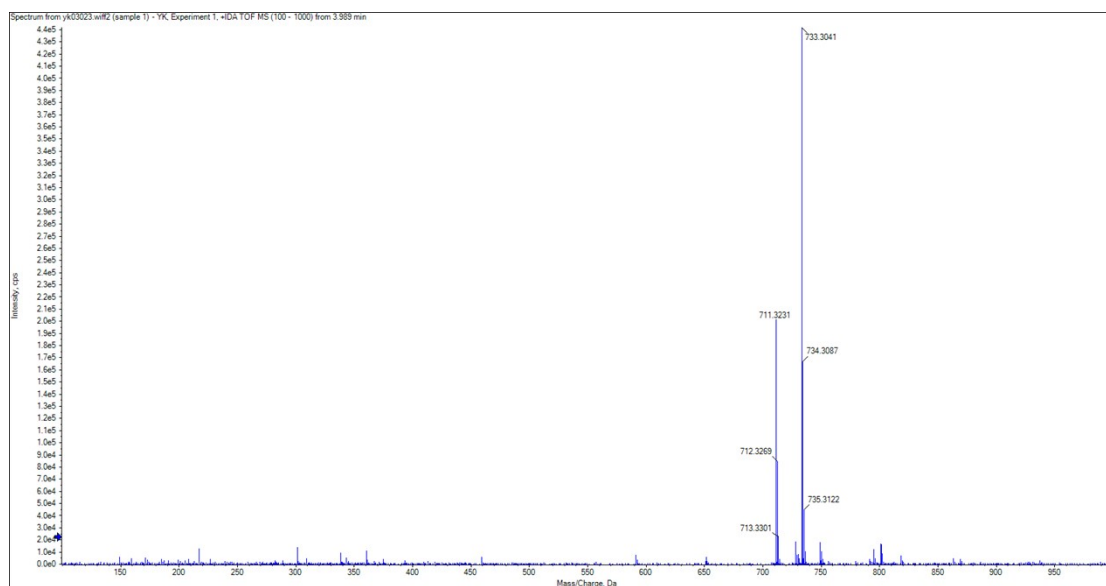


Fig. S2 HRMS spectrum of **2**

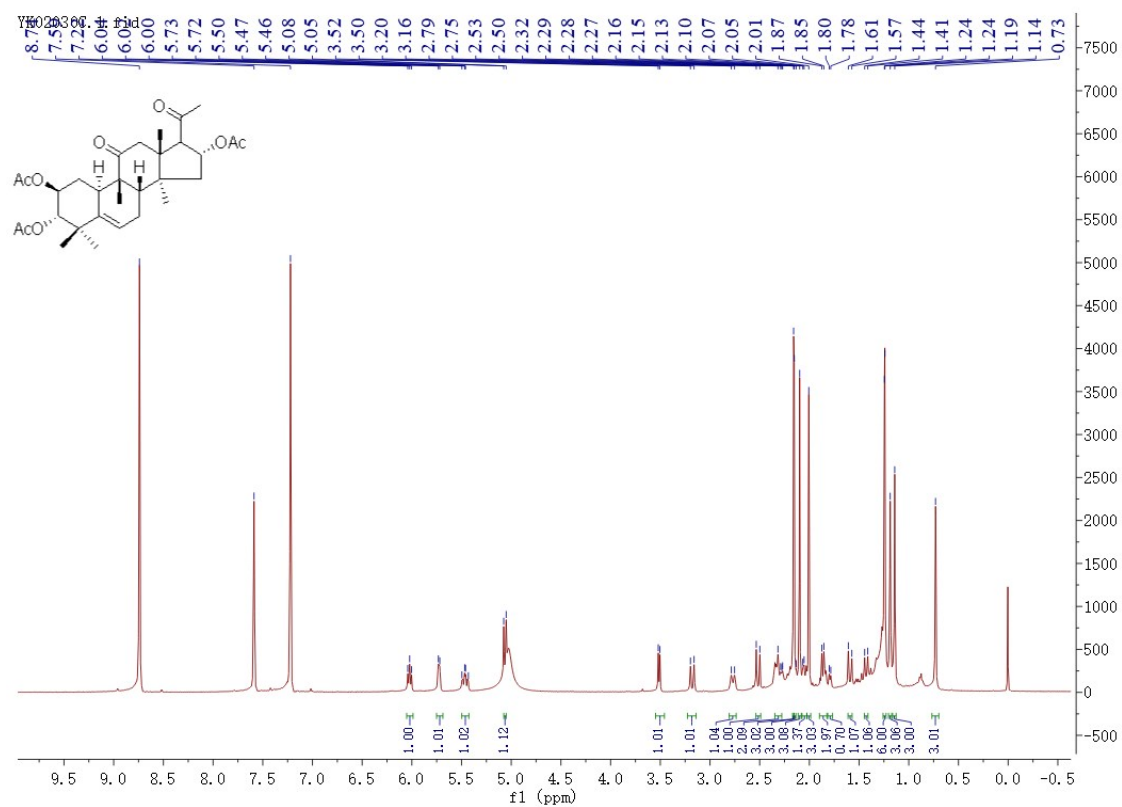


Fig. S3 <sup>1</sup>H NMR spectrum of **3**

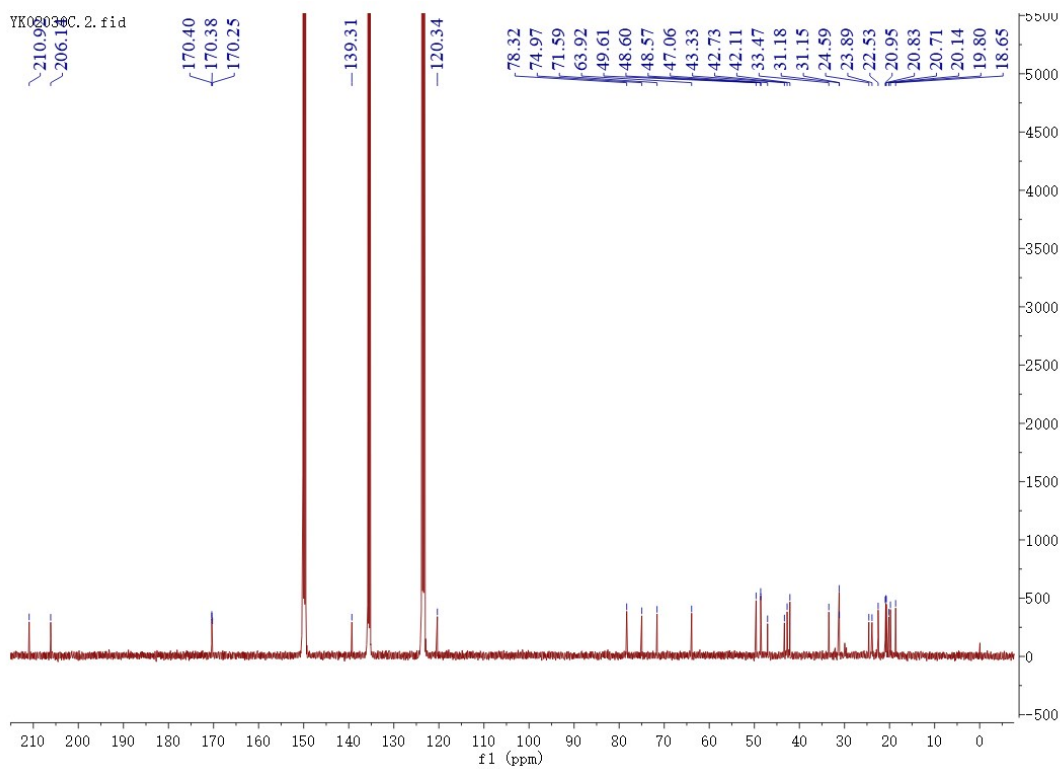


Fig. S4  $^{13}\text{C}$  NMR spectrum of **3**

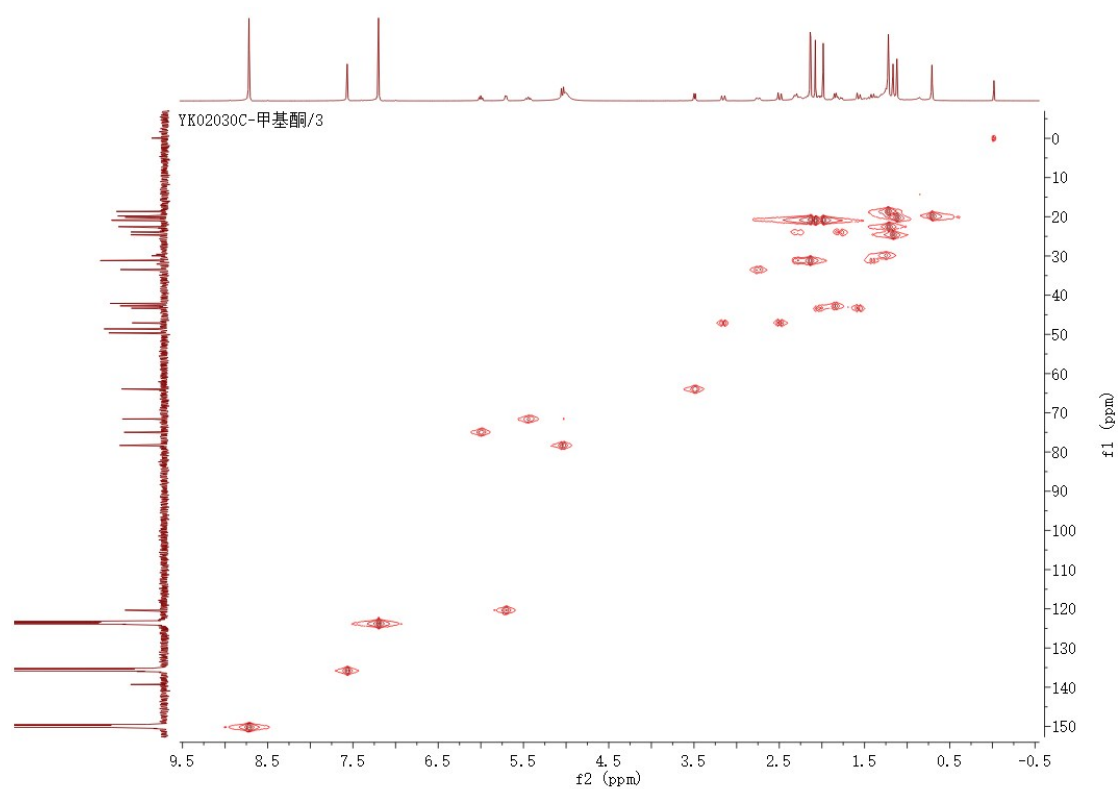


Fig. S5 HSQC spectrum of **3**

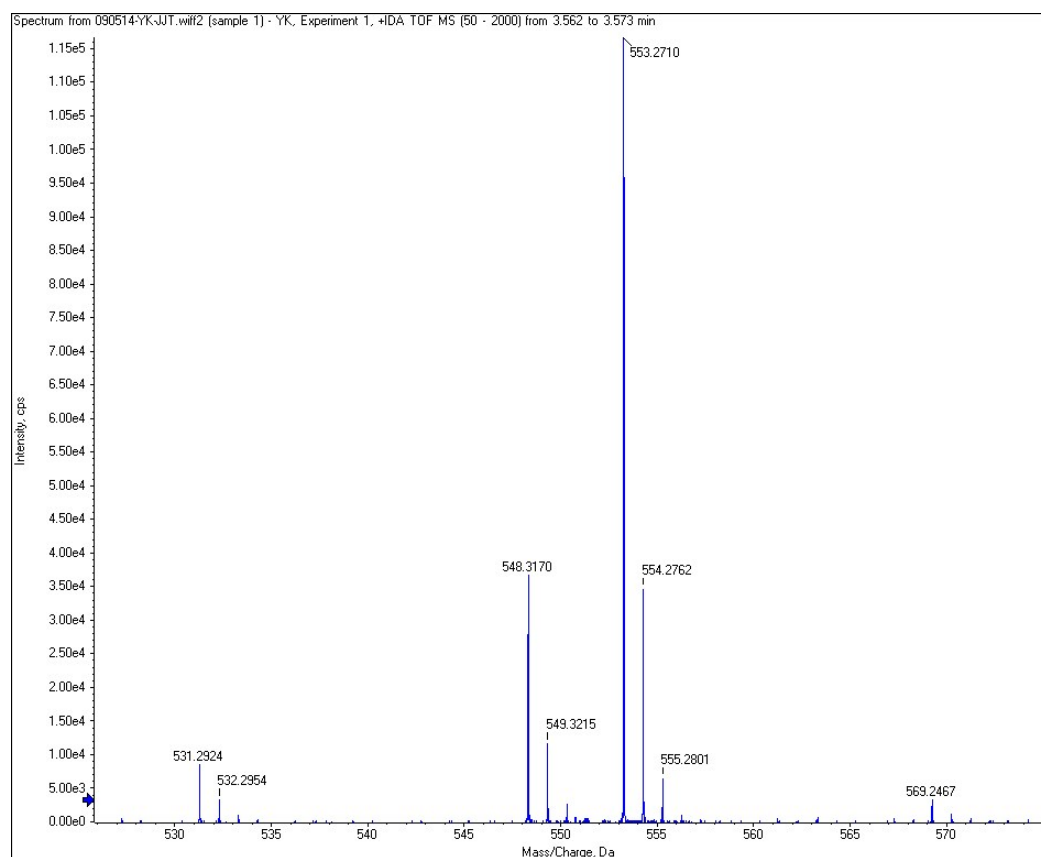


Fig. S6 HRMS spectrum of **3**

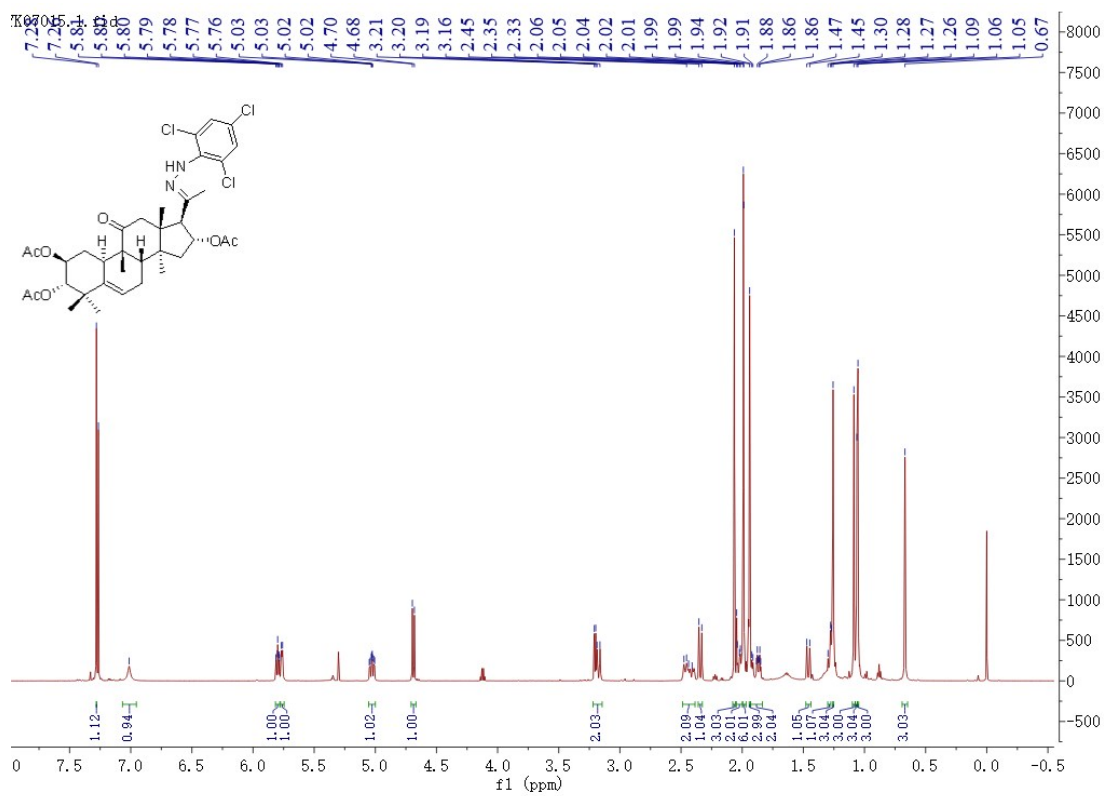


Fig. S7  $^1\text{H}$  NMR spectrum of **4a**

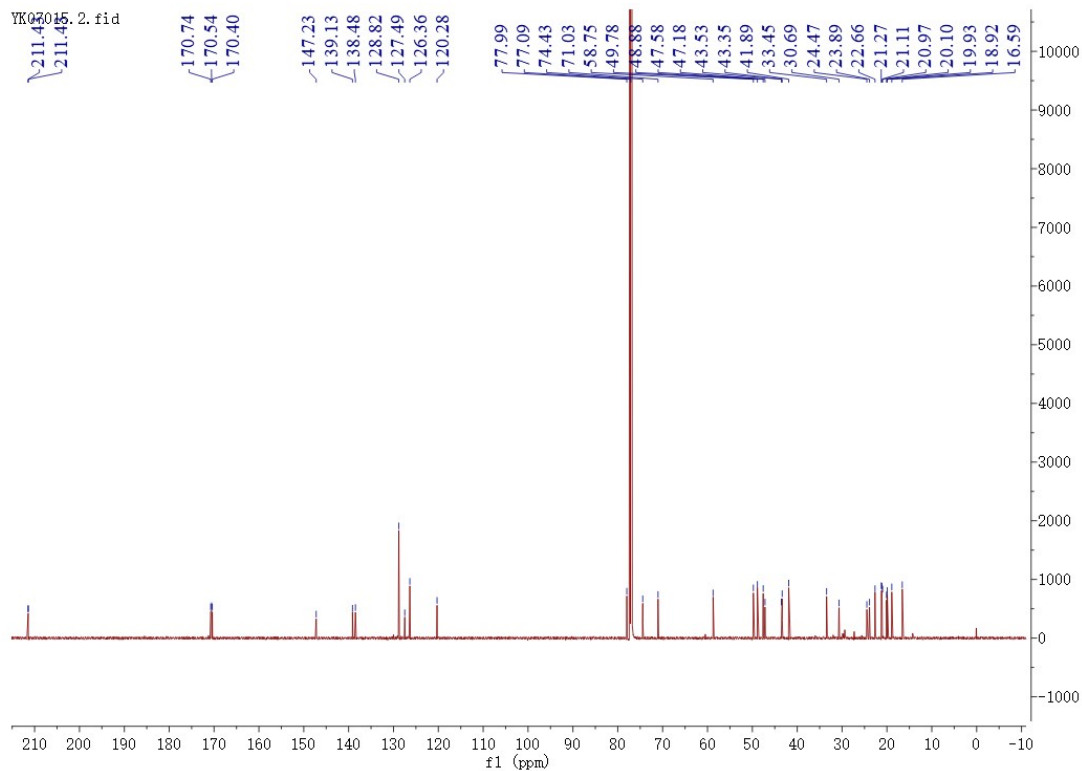


Fig. S8  $^{13}\text{C}$  NMR spectrum of **4a**

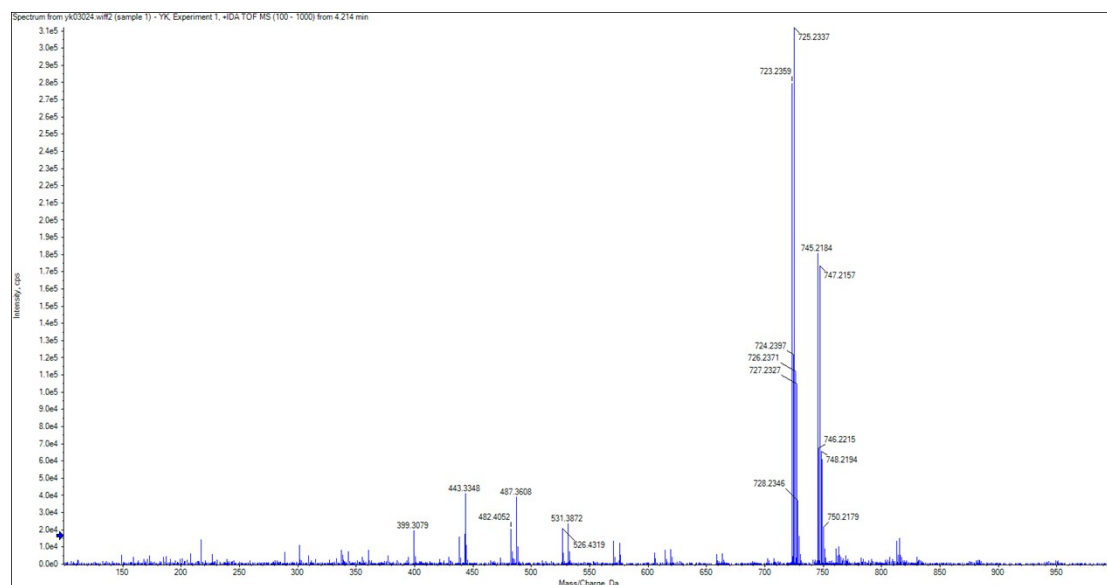


Fig. S9 HRMS spectrum of **4a**

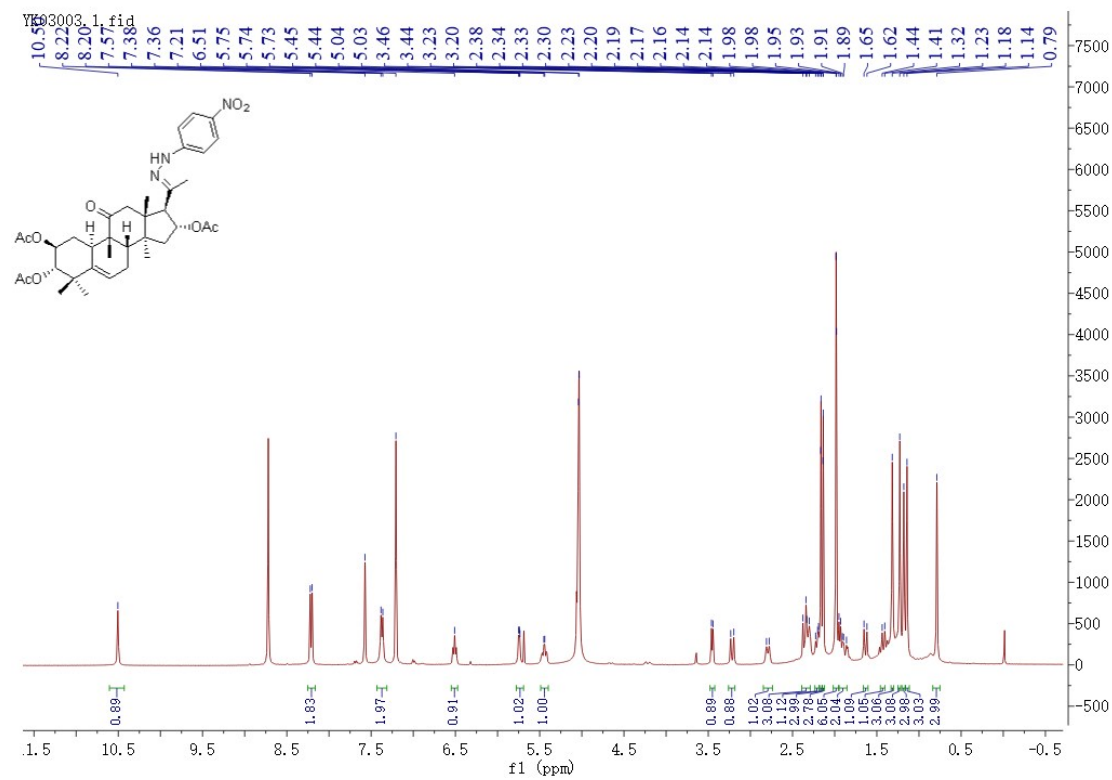


Fig. S10  $^1\text{H}$  NMR spectrum of 4b

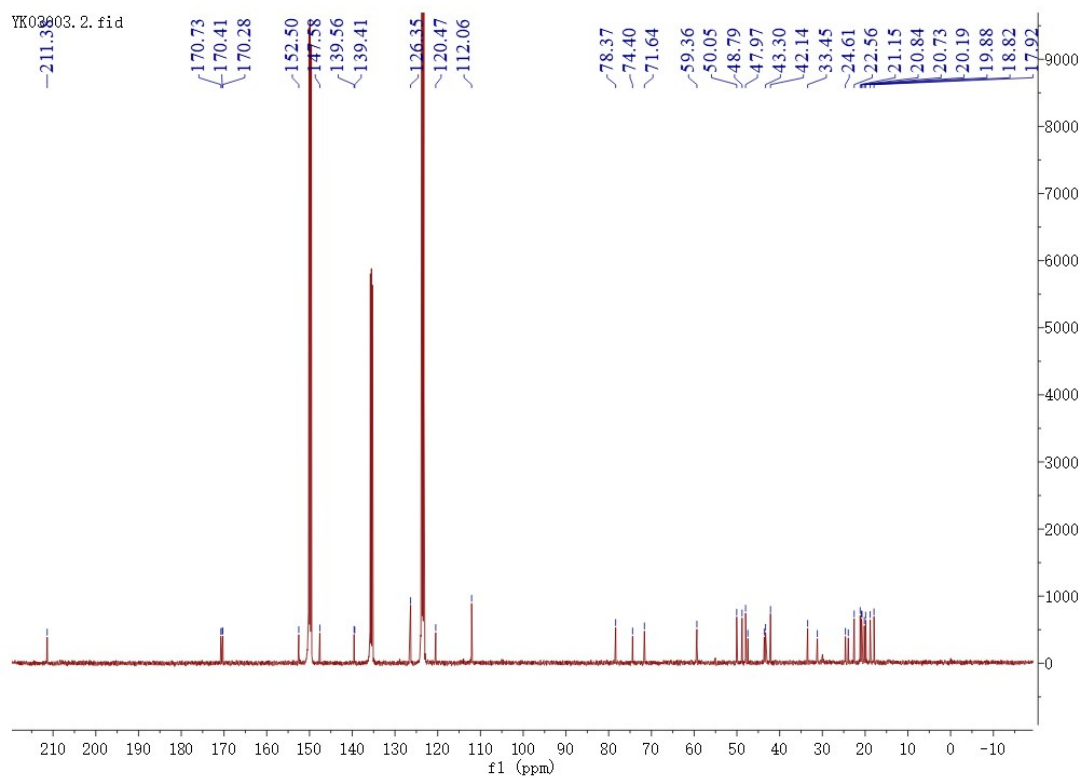


Fig. S11  $^{13}\text{C}$  NMR spectrum of 4b

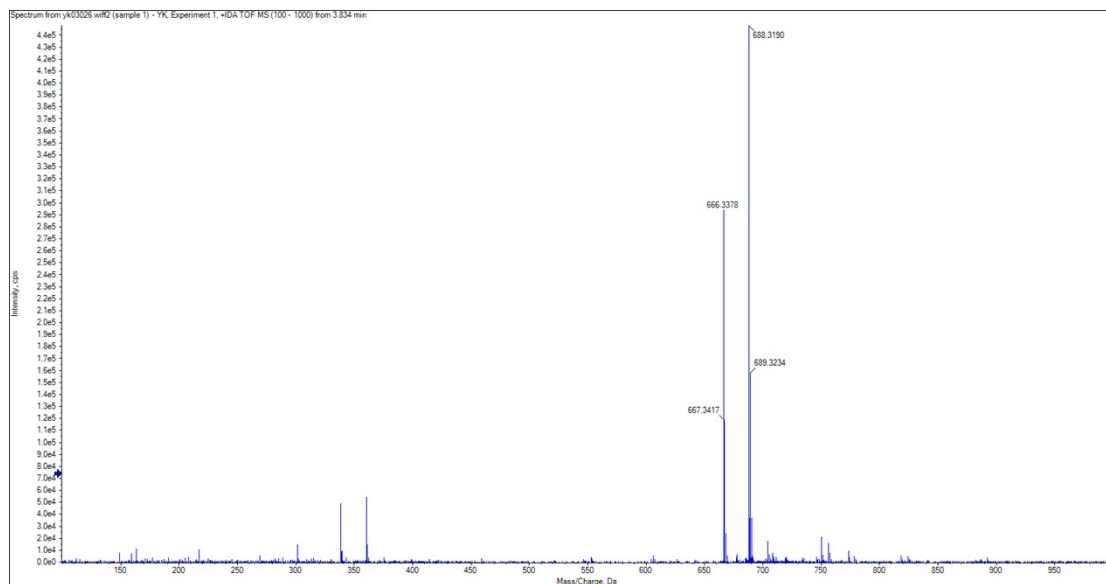


Fig. S12 HRMS spectrum of **4b**

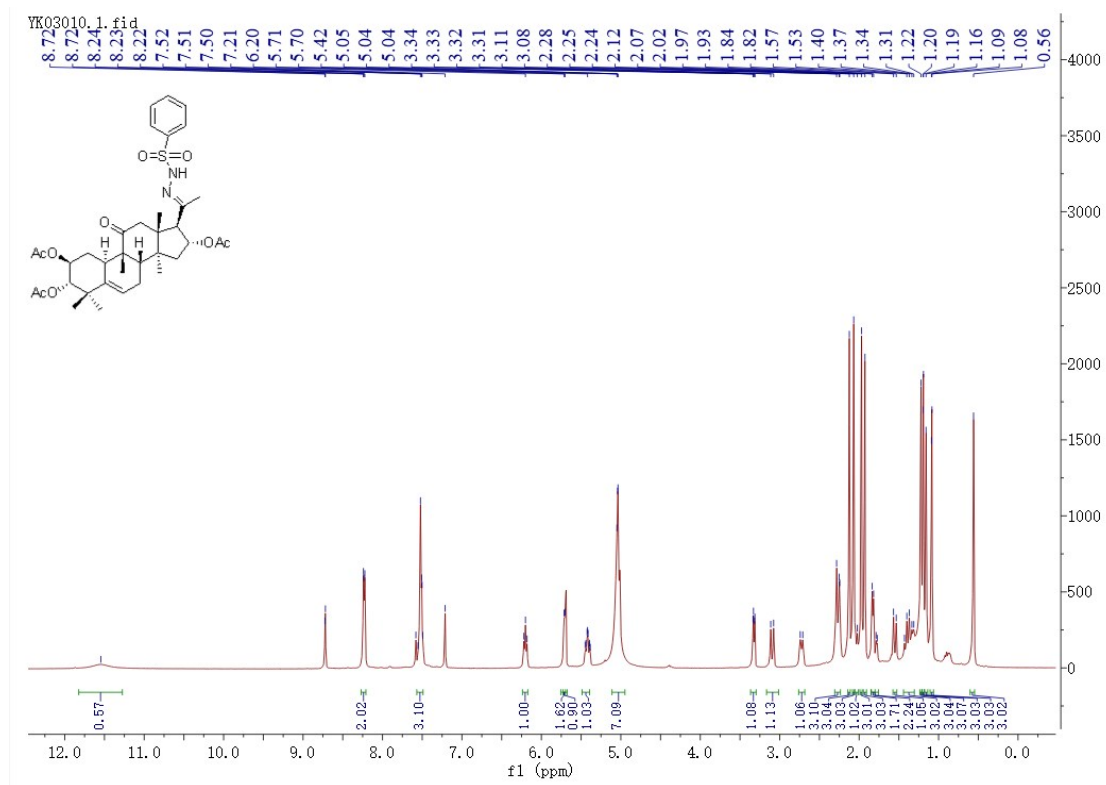


Fig. S13  $^1\text{H}$  NMR spectrum of **4c**

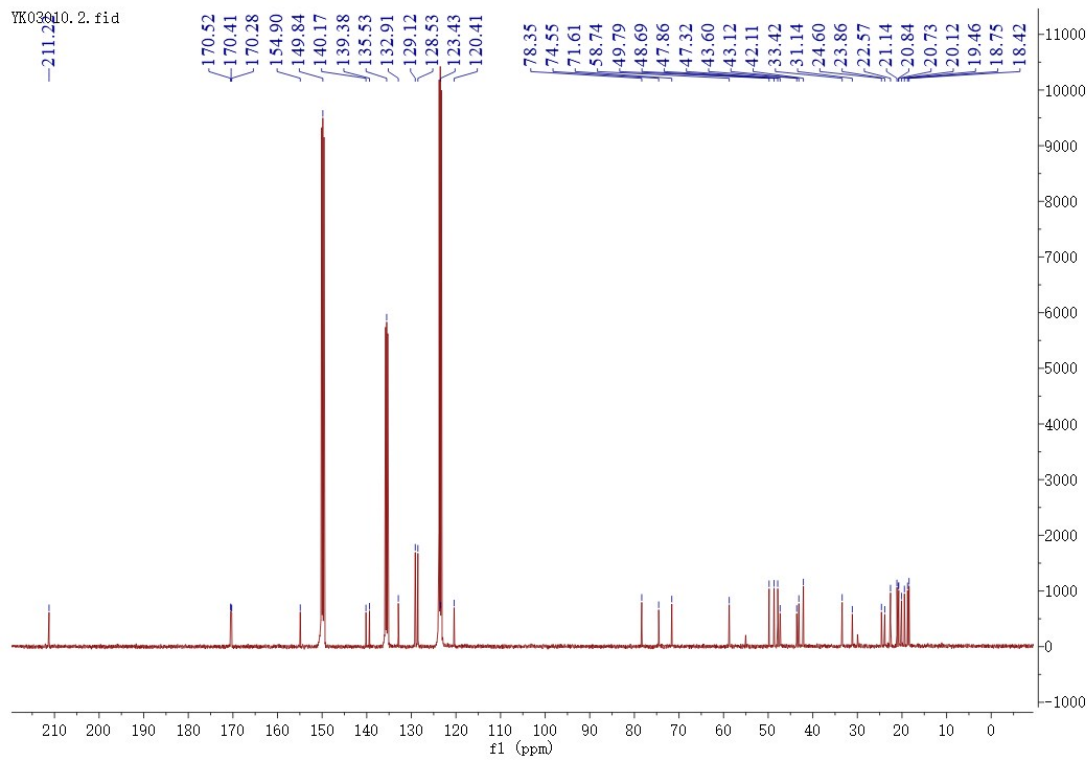


Fig. S14  $^{13}\text{C}$  NMR spectrum of **4c**

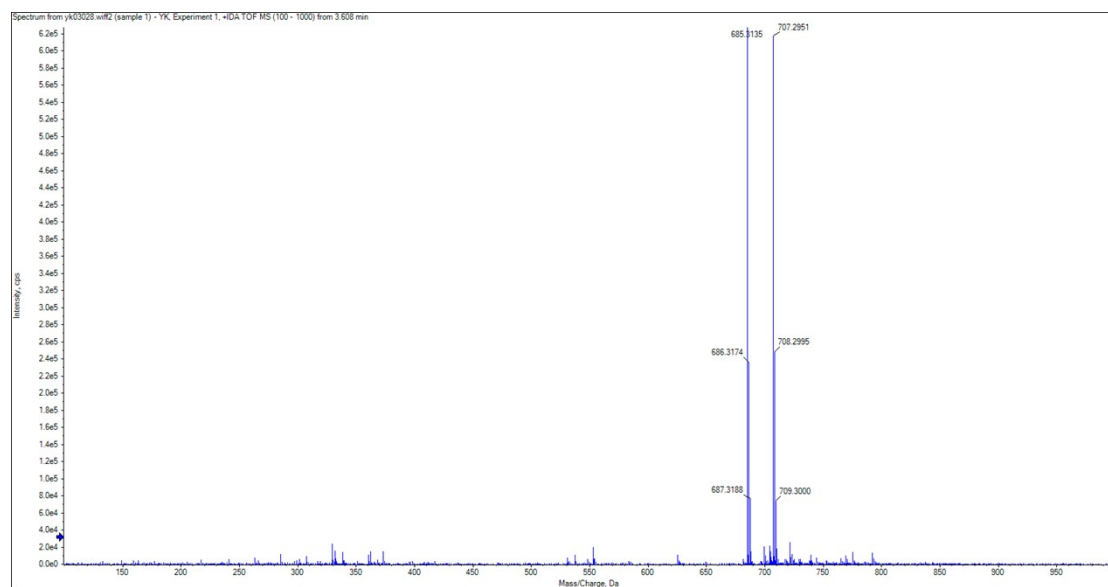


Fig. S15 HRMS spectrum of **4c**



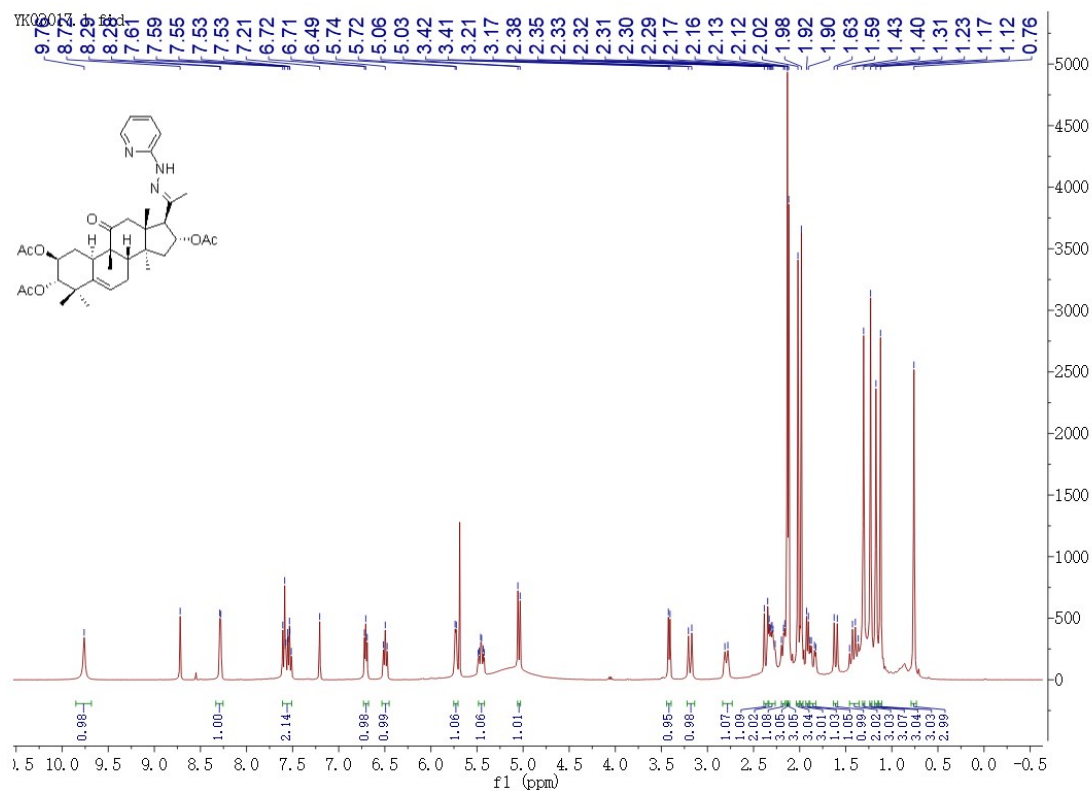


Fig. S16  $^1\text{H}$  NMR spectrum of 4d

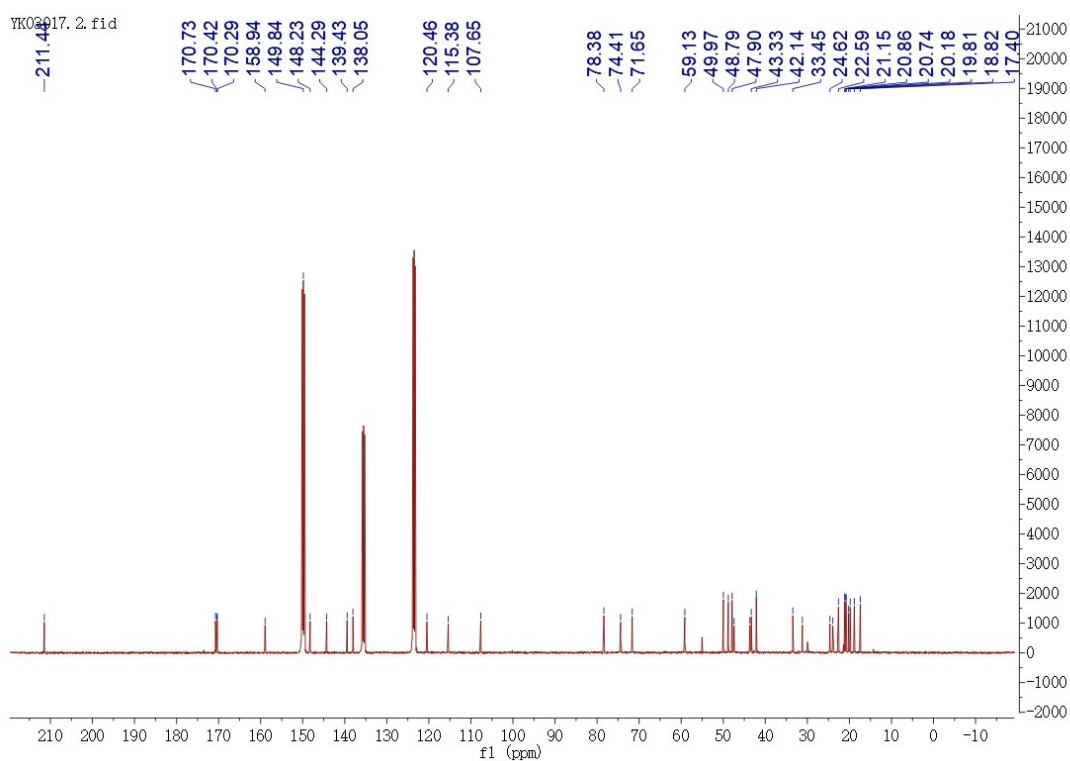


Fig. S17  $^{13}\text{C}$  NMR spectrum of 4d

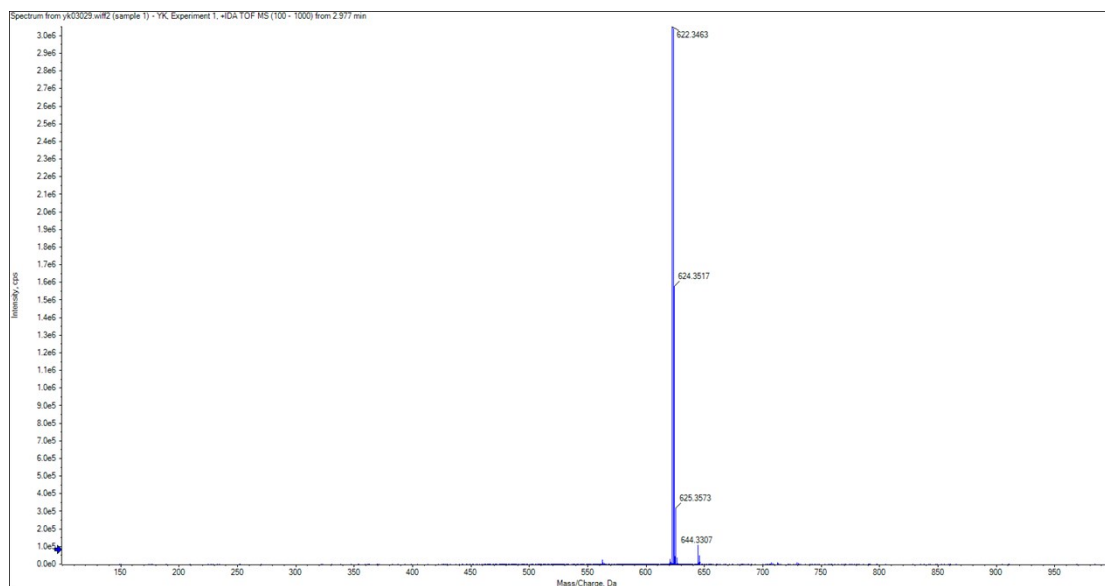


Fig. S18 HRMS spectrum of **4d**

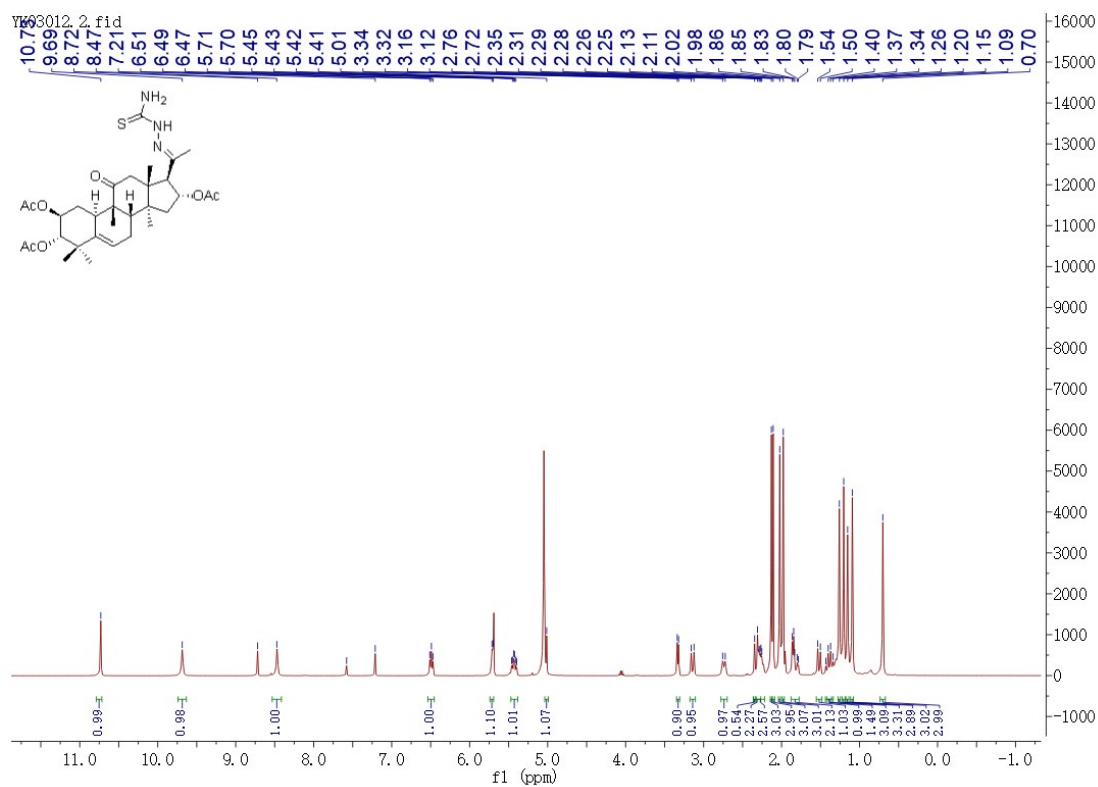


Fig. S19  $^1\text{H}$  NMR spectrum of **4e**

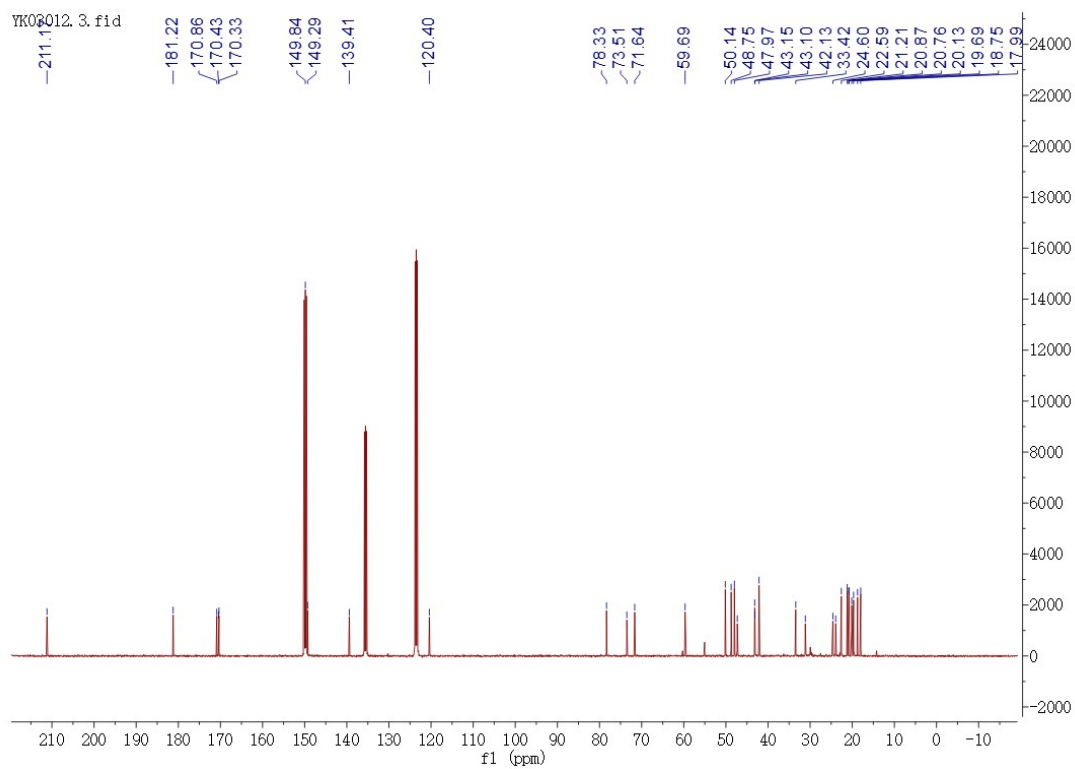


Fig. S20  $^{13}\text{C}$  NMR spectrum of **4e**

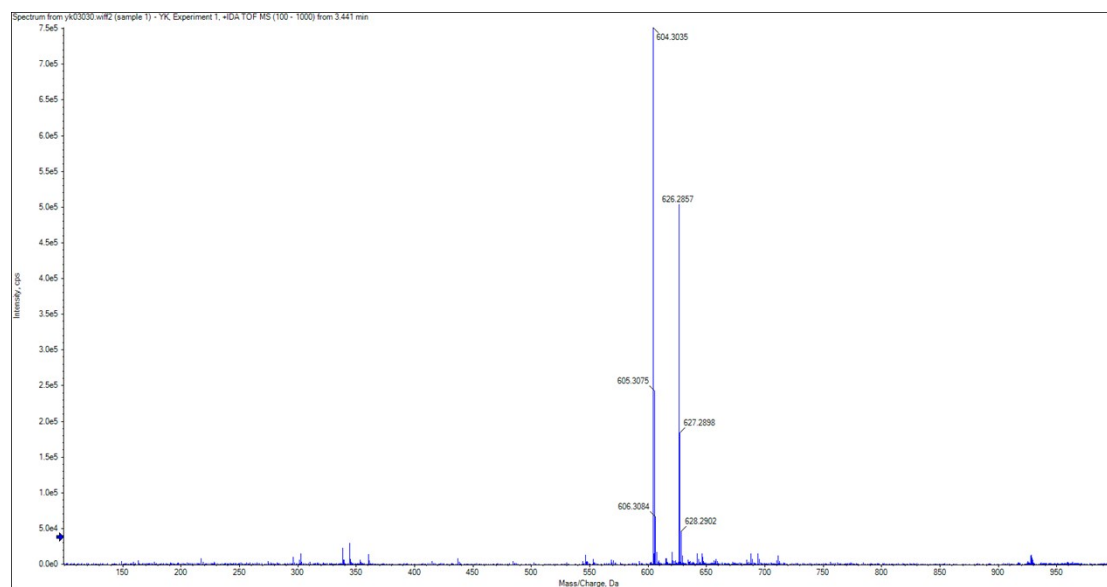


Fig. S21 HRMS spectrum of **4e**

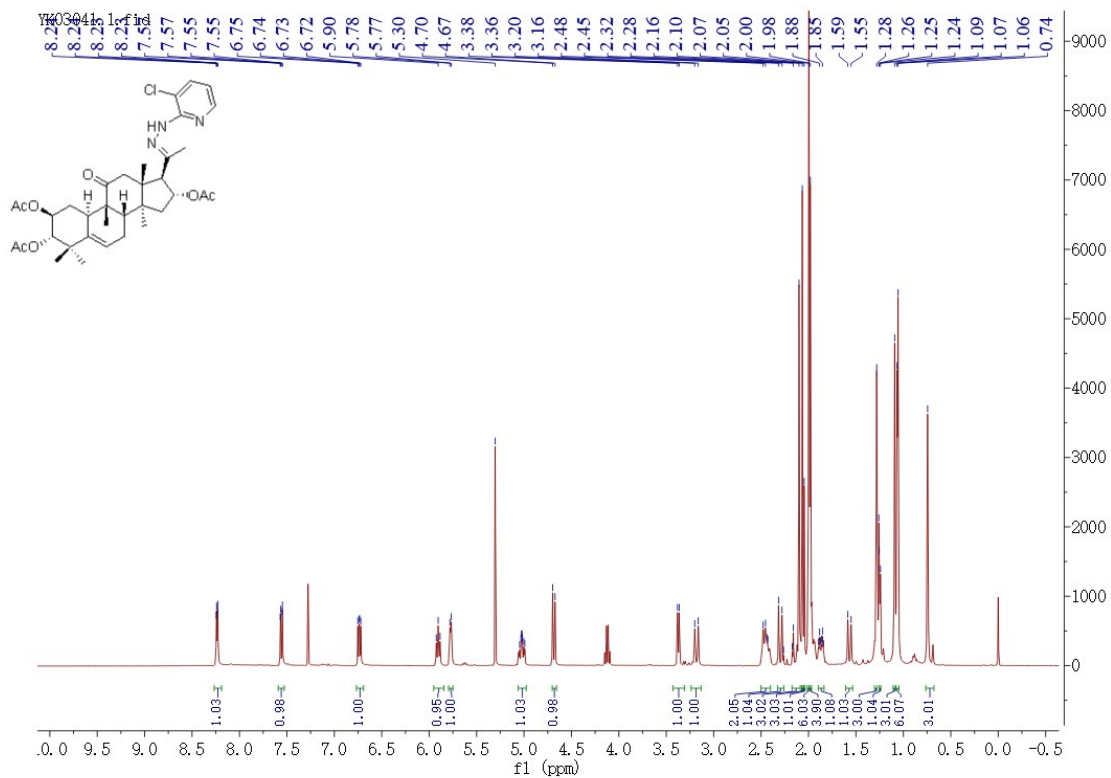


Fig. S22  $^1\text{H}$  NMR spectrum of **4f**

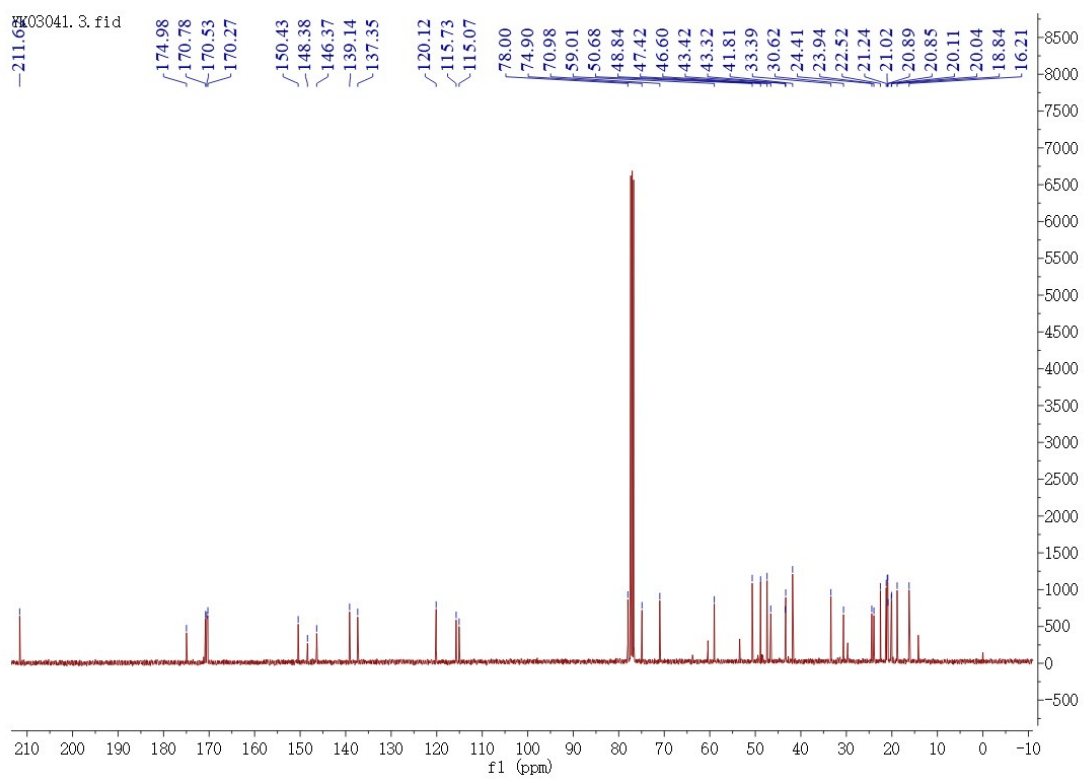


Fig. S23  $^{13}\text{C}$  NMR spectrum of **4f**

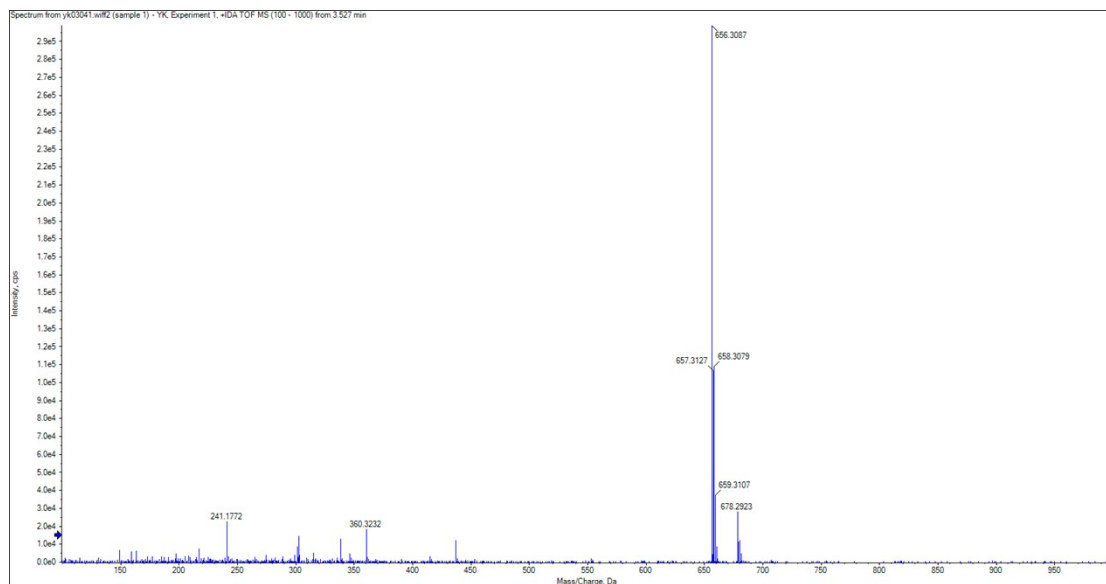


Fig. S24 HRMS spectrum of 4f

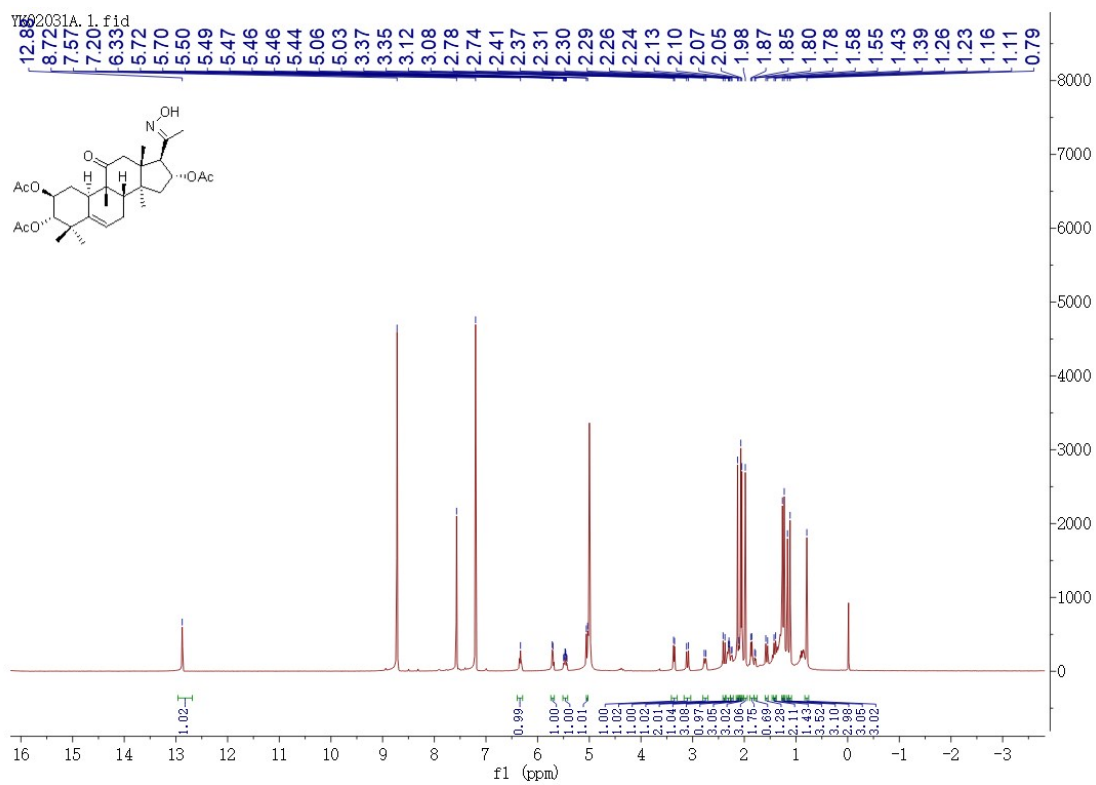


Fig. S25 <sup>1</sup>H NMR spectrum of 5a

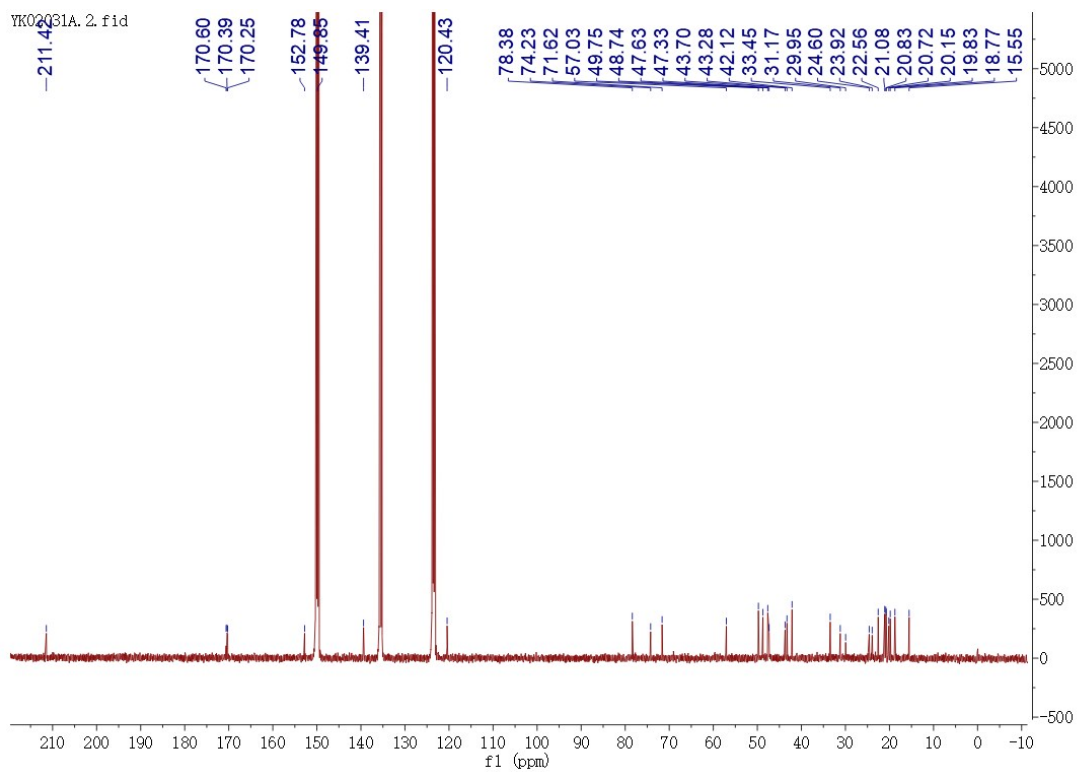


Fig. S26  $^{13}\text{C}$  NMR spectrum of **5a**

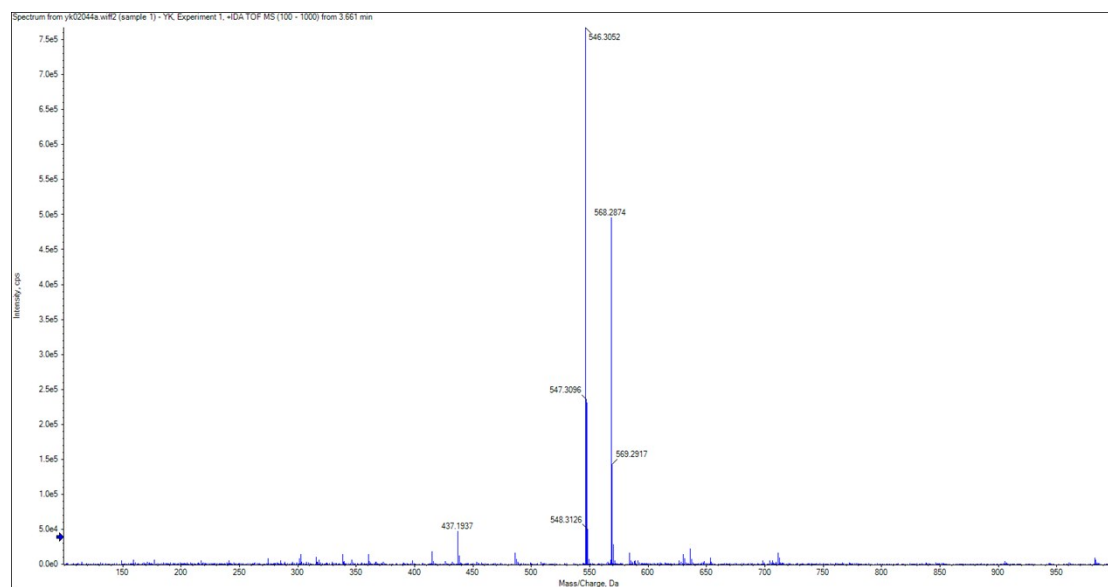


Fig. S27 HRMS spectrum of **5a**



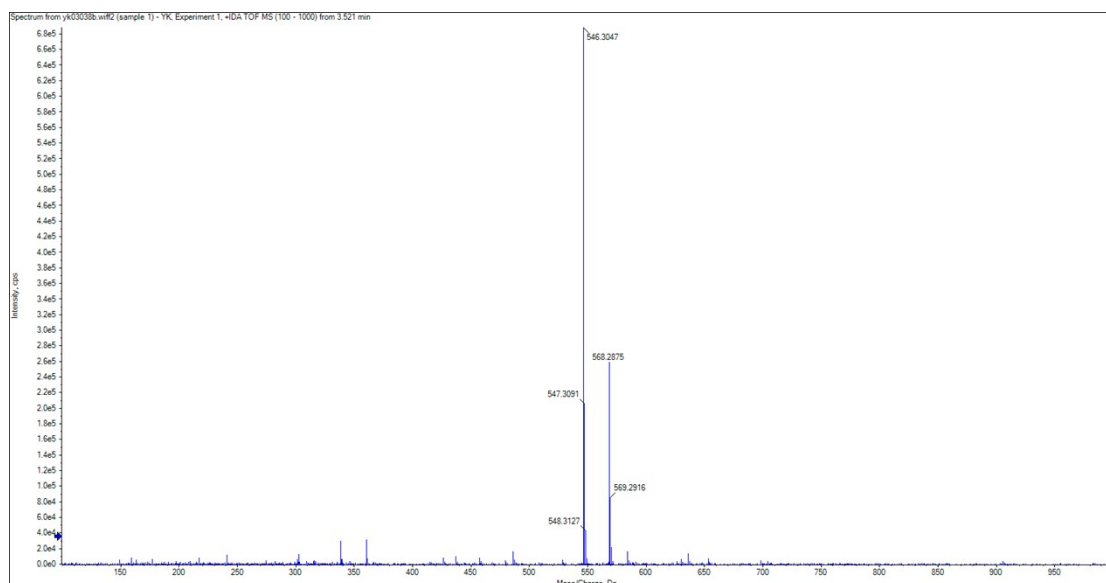


Fig. S30 HRMS spectrum of **5b**

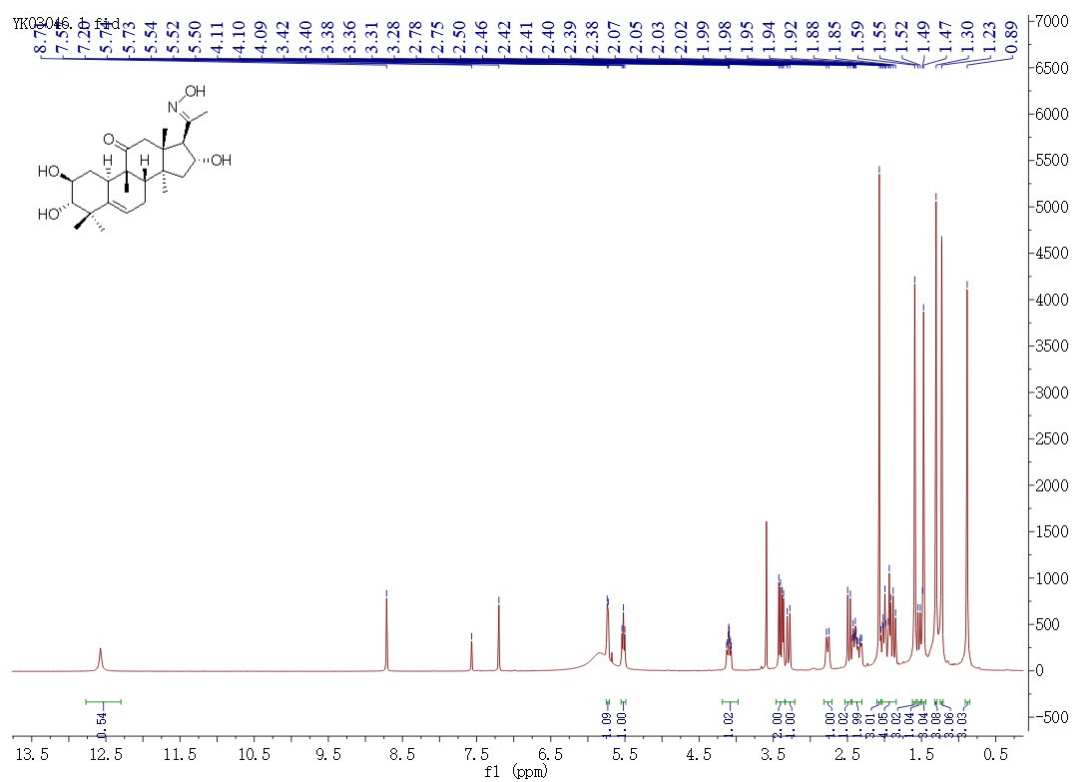


Fig. S31  $^1\text{H}$  NMR spectrum of **6a**



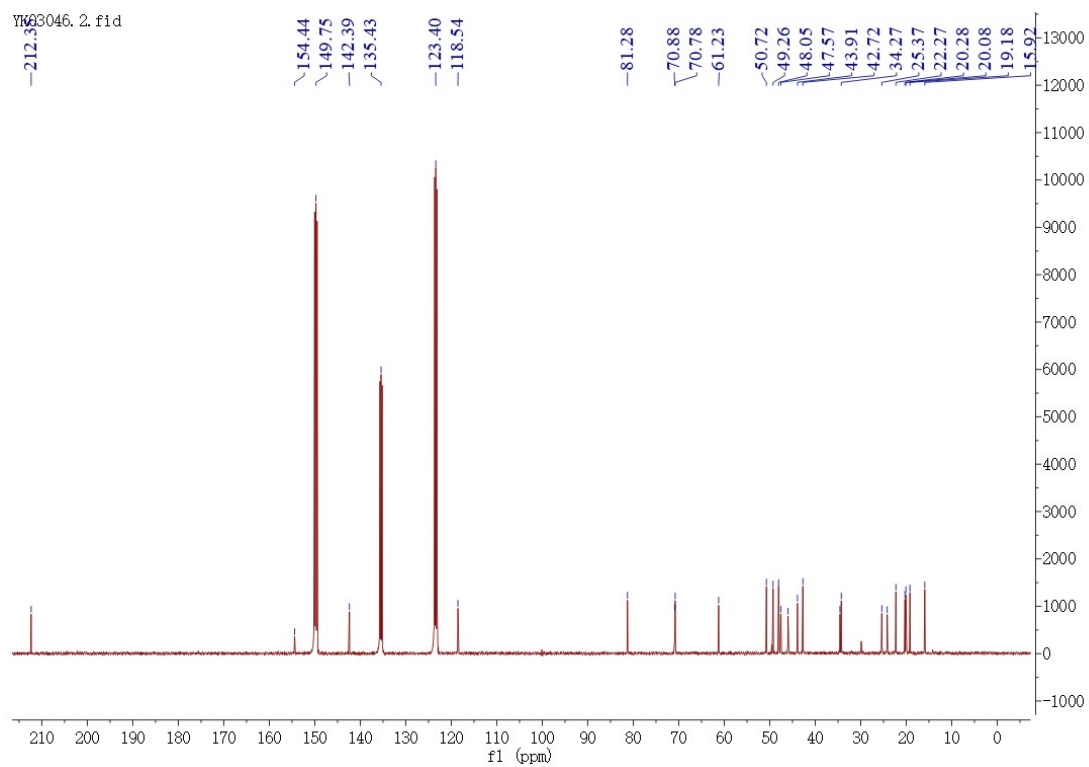


Fig. S32  $^{13}\text{C}$  NMR spectrum of **6a**

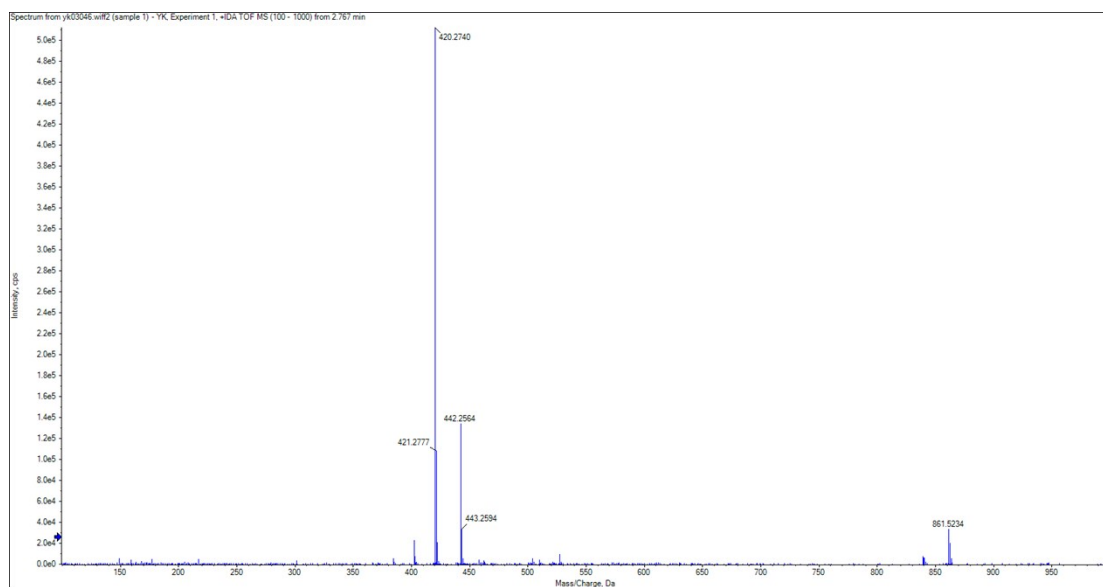


Fig. S33 HRMS spectrum of **6a**

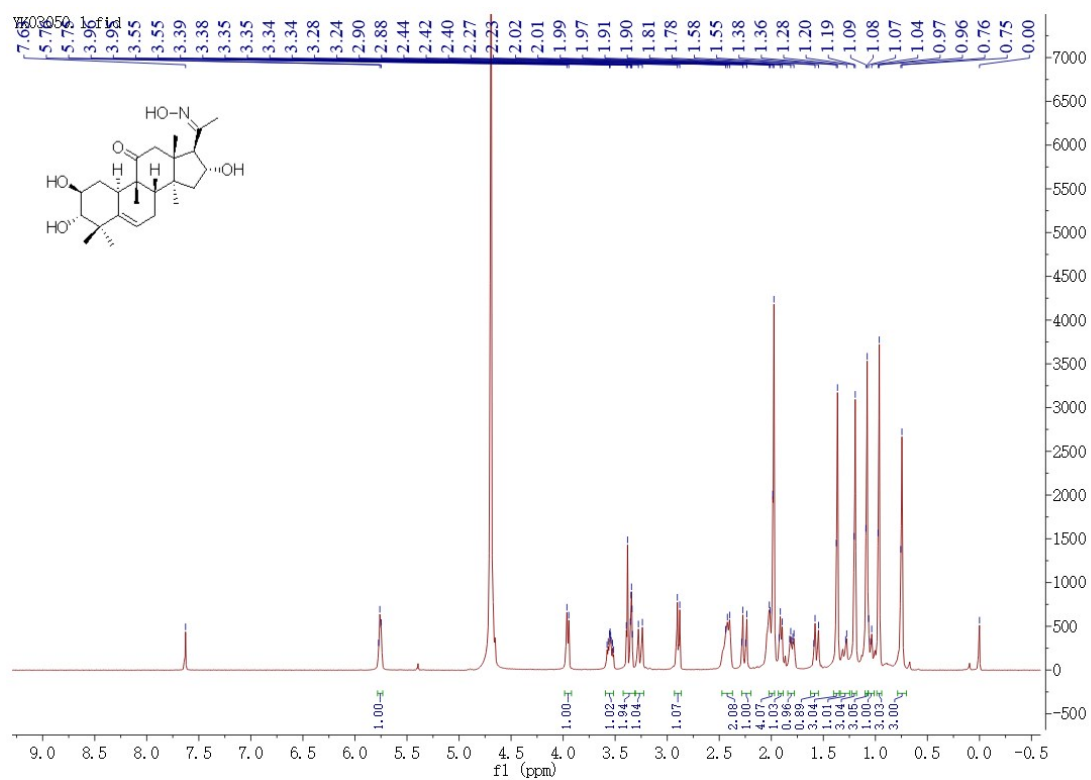


Fig. S34  $^1\text{H}$  NMR spectrum of 6b

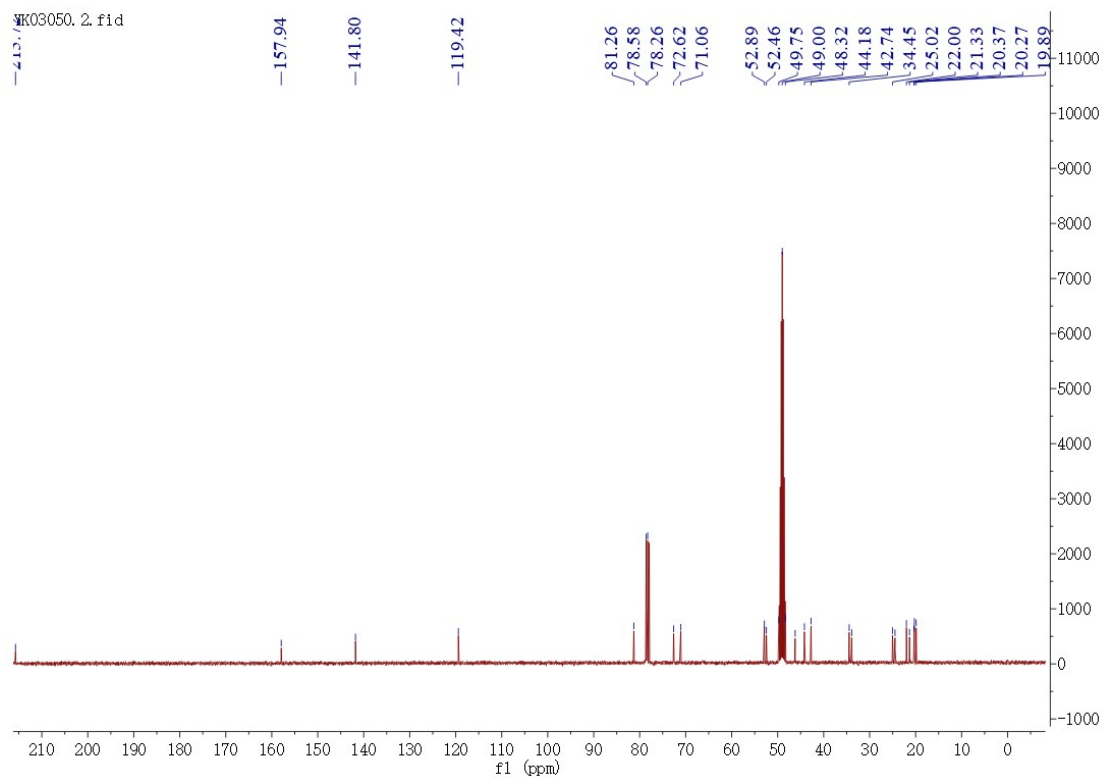


Fig. S35  $^{13}\text{C}$  NMR spectrum of 6b

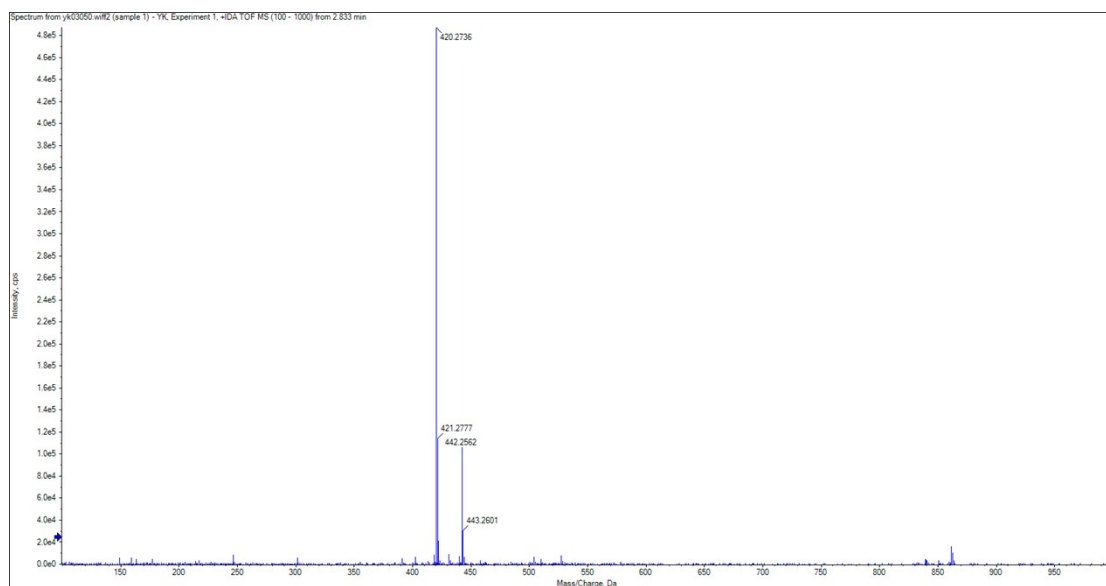


Fig. S36 HRMS spectrum of **6b**

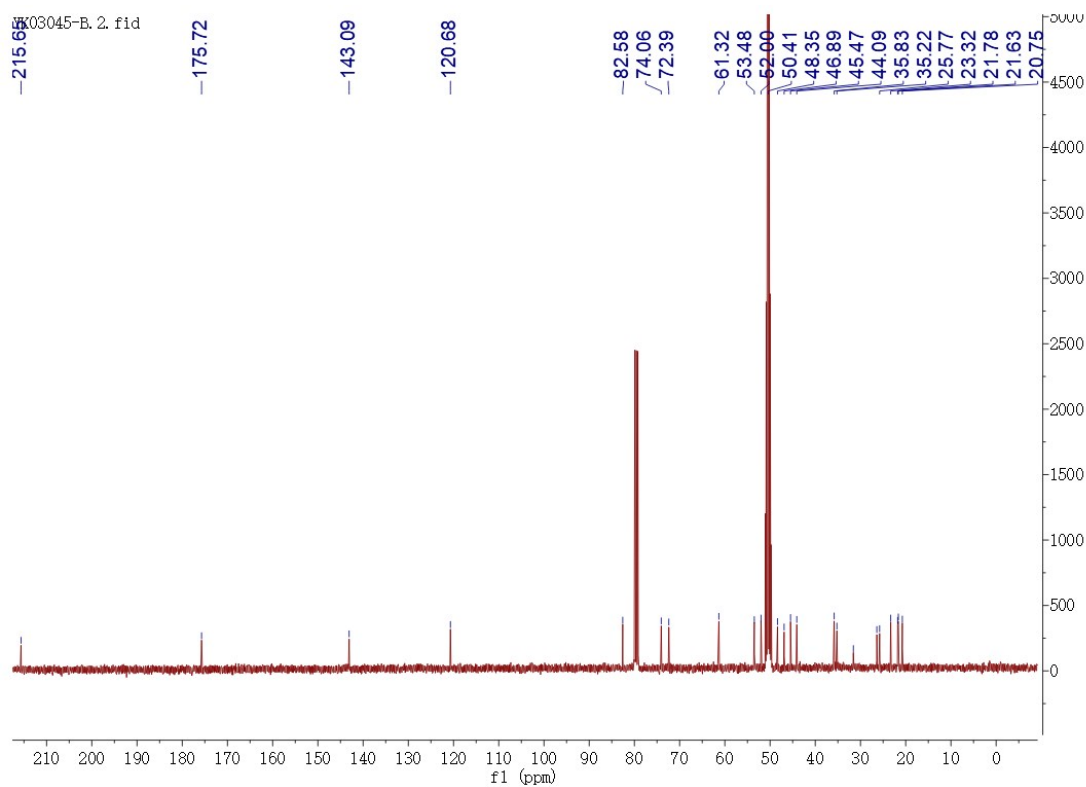


Fig. S37  $^{13}\text{C}$  NMR spectrum of **7**

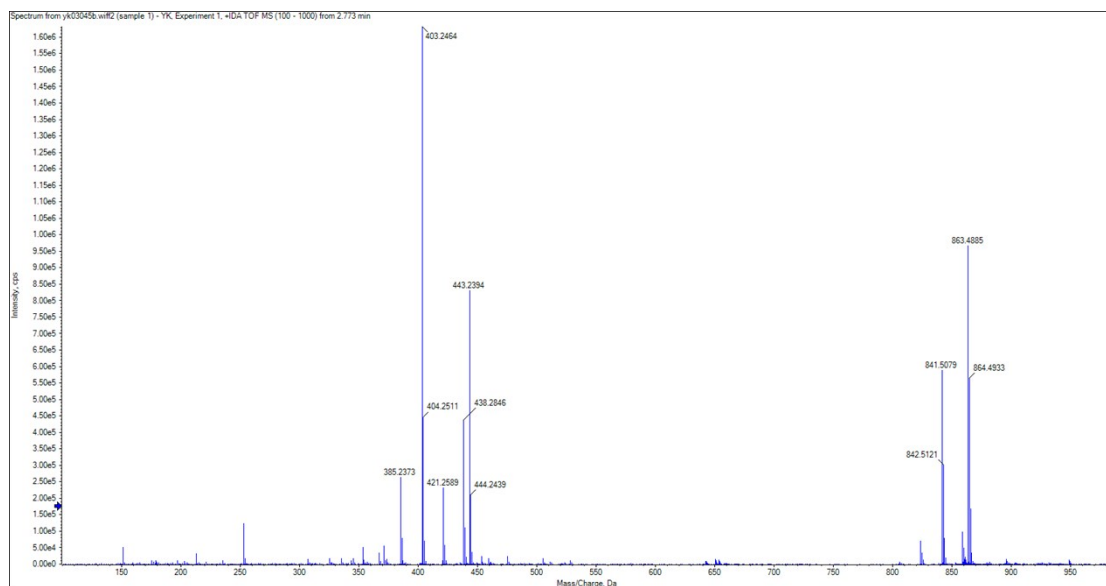


Fig. S38 HRMS spectrum of 7

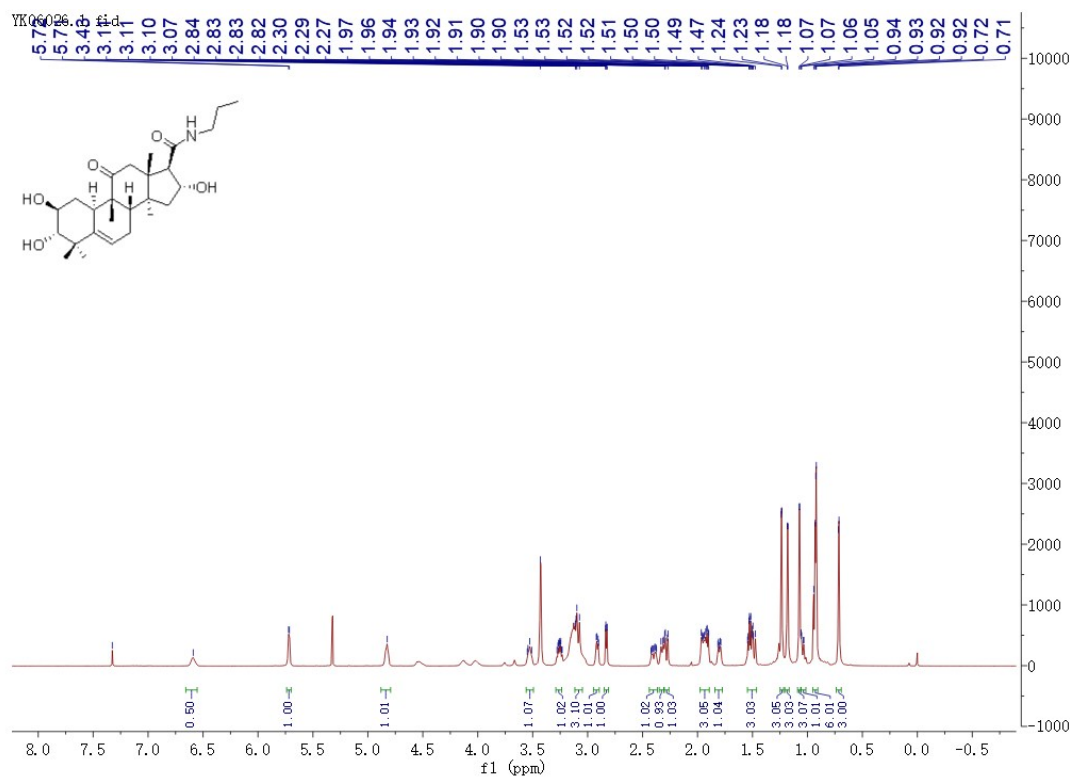


Fig. S39 <sup>1</sup>H NMR spectrum of 9a

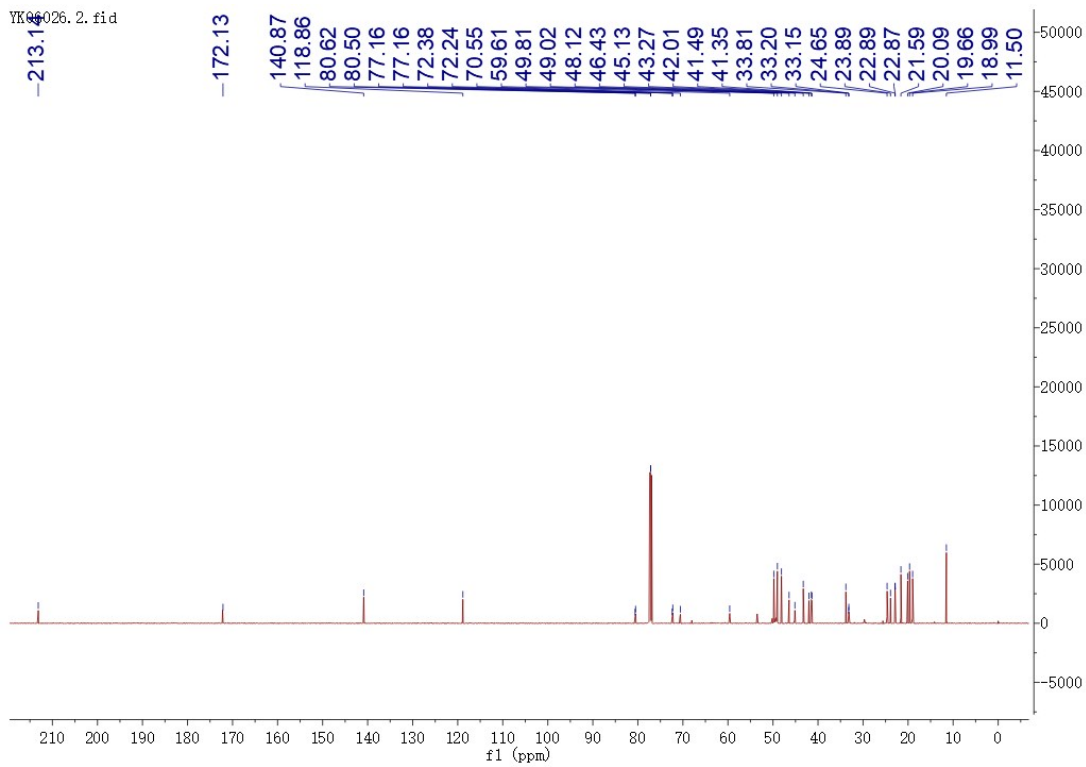


Fig. S40  $^{13}\text{C}$  NMR spectrum of **9a**

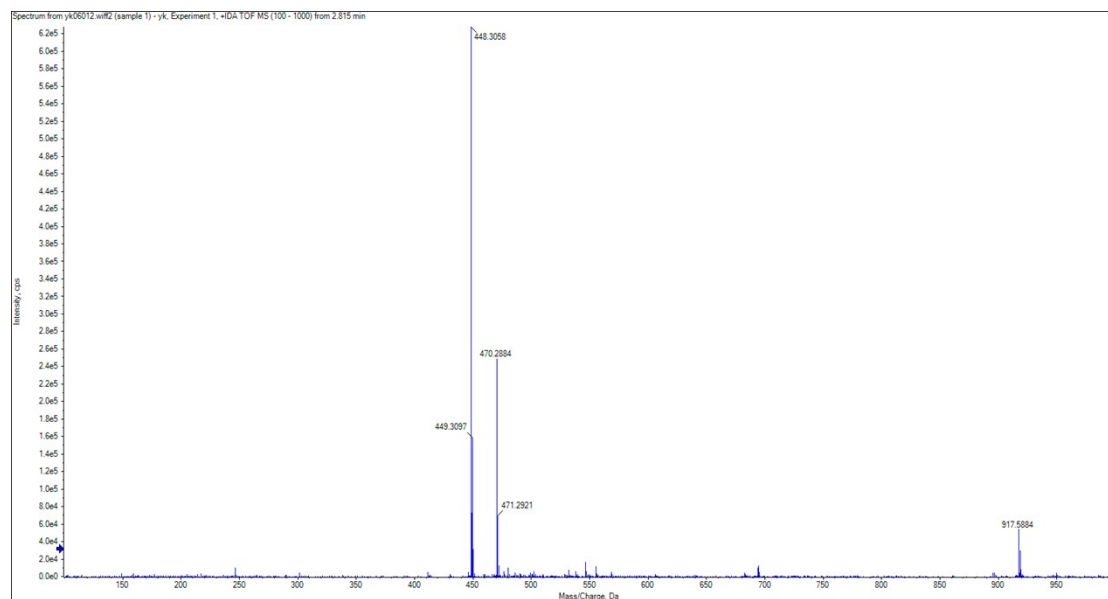


Fig. S41 HRMS spectrum of **9a**

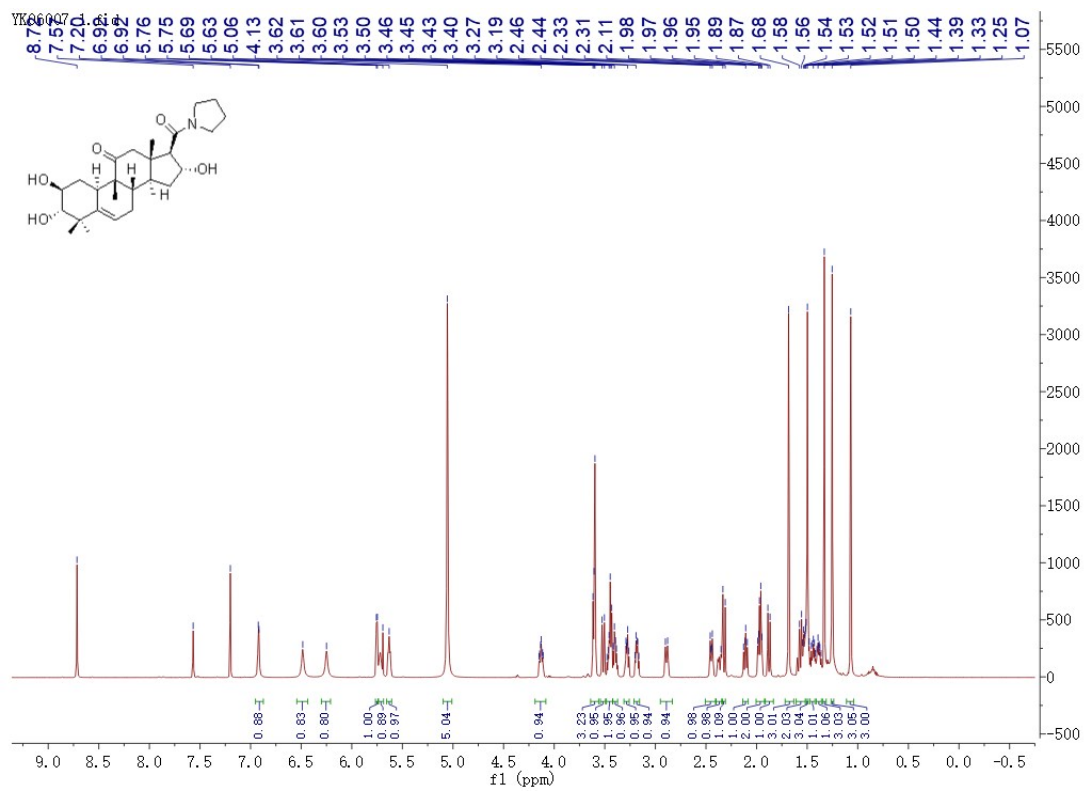


Fig. S42  $^1\text{H}$  NMR spectrum of 9b

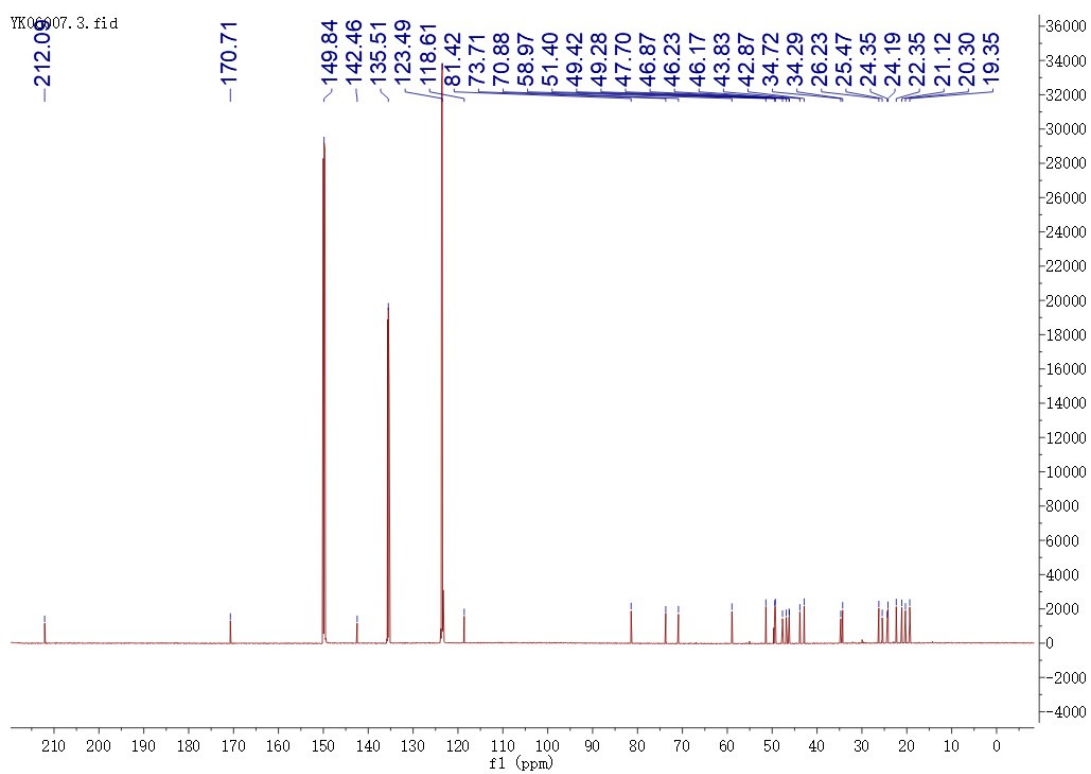


Fig. S43  $^{13}\text{C}$  NMR spectrum of 9b

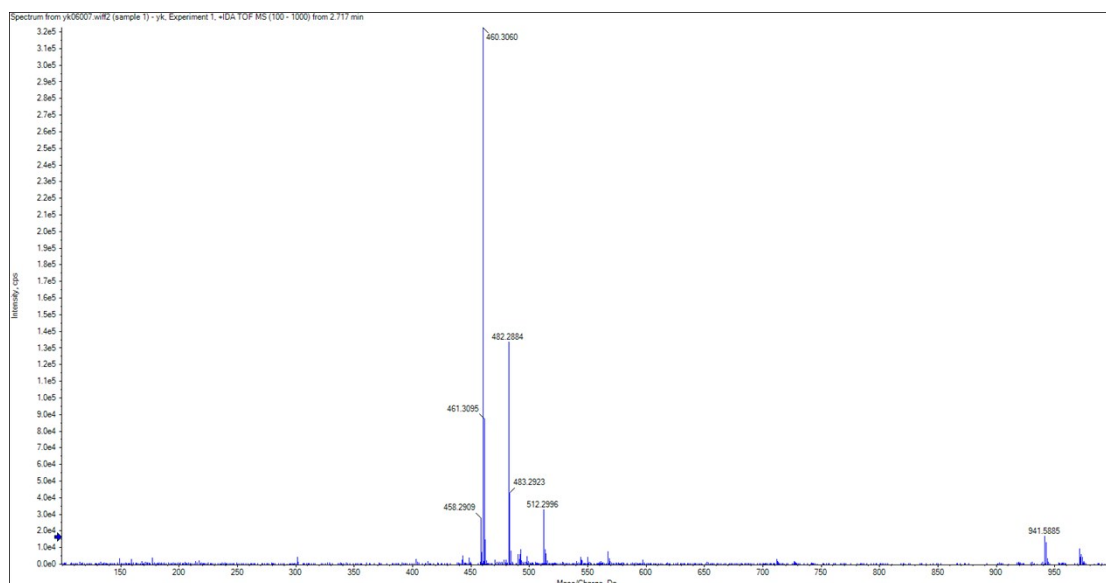


Fig. S44 HRMS spectrum of 9b

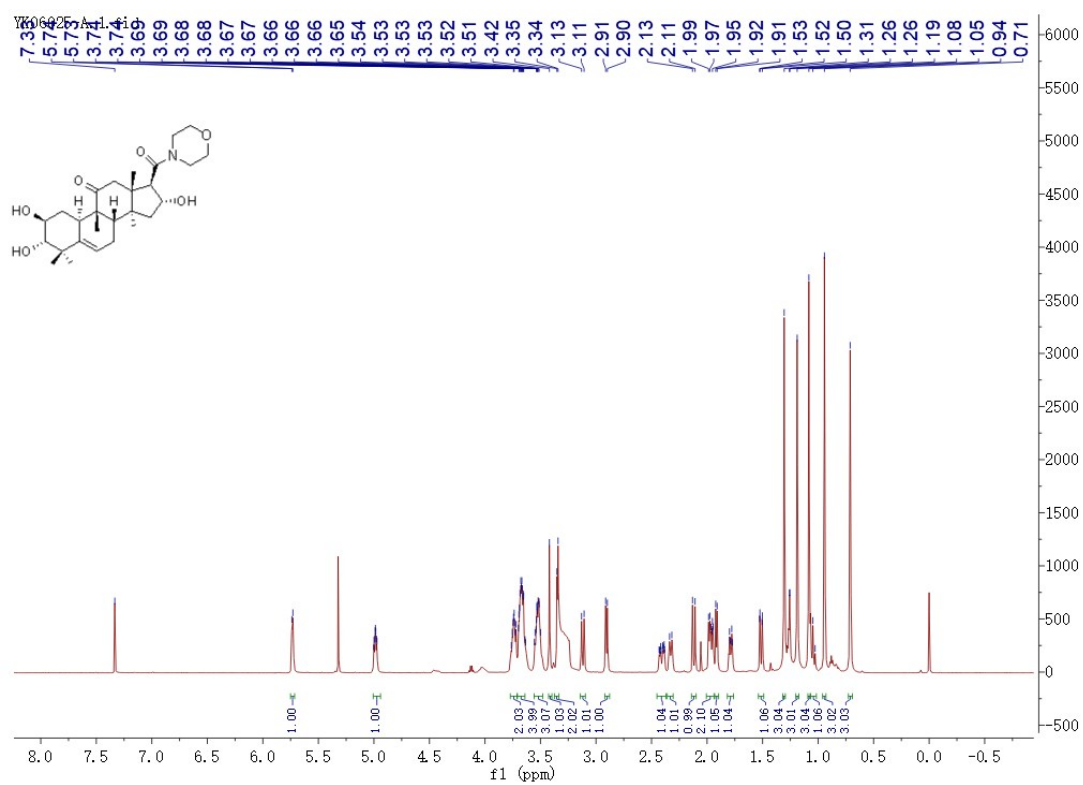


Fig. S45 <sup>1</sup>H NMR spectrum of 9c

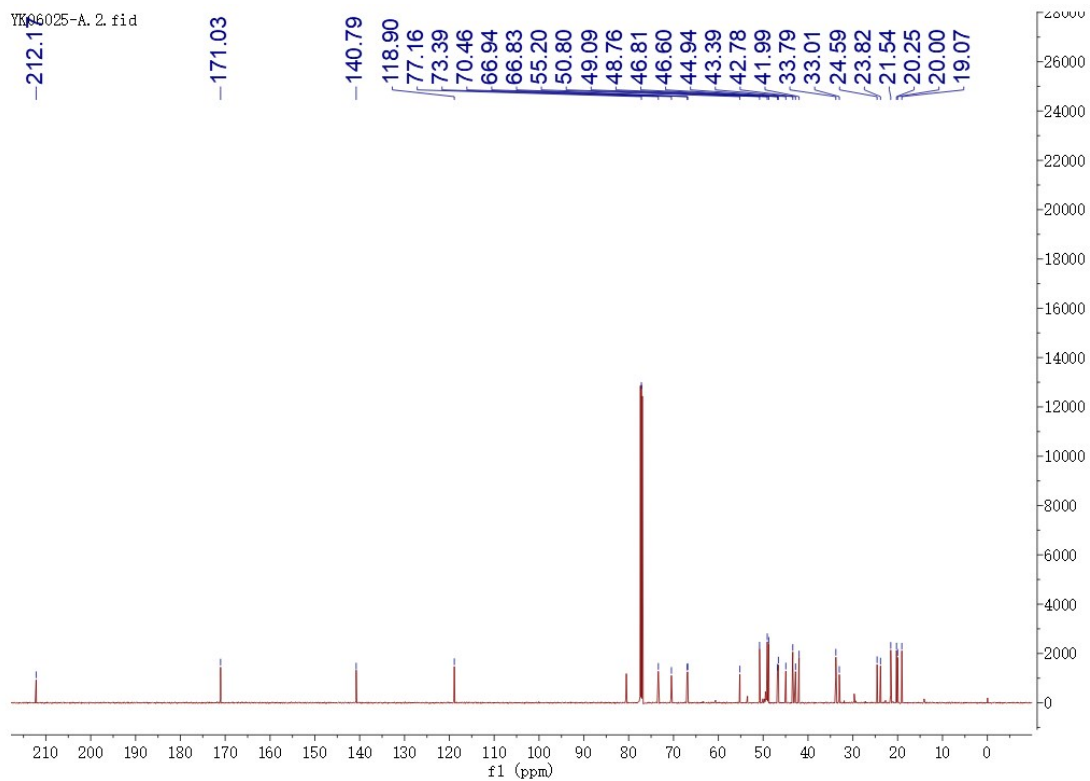


Fig. S46  $^{13}\text{C}$  NMR spectrum of **9c**

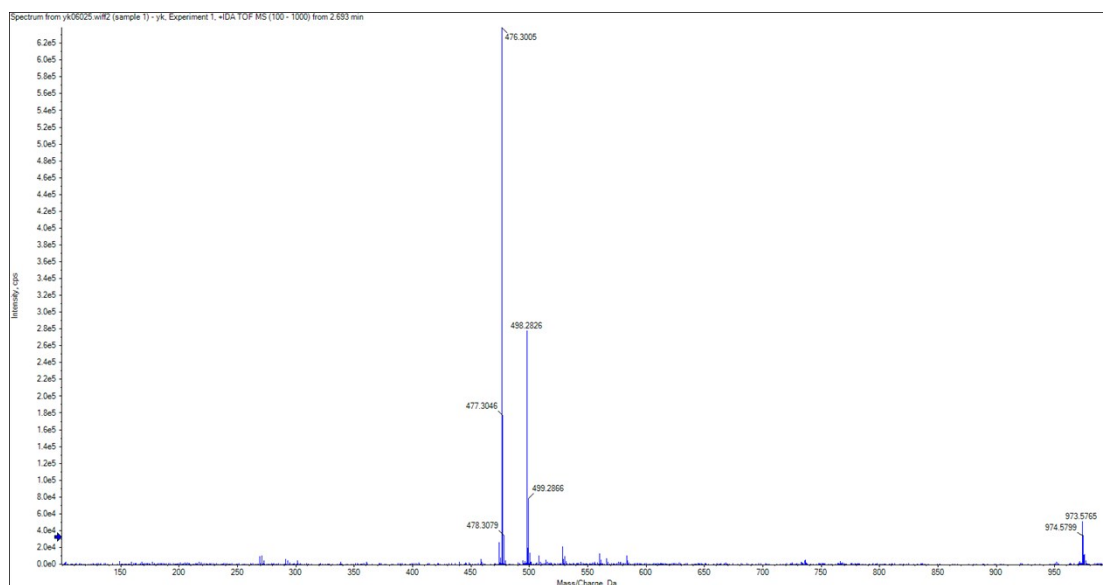


Fig. S47 HRMS spectrum of **9c**



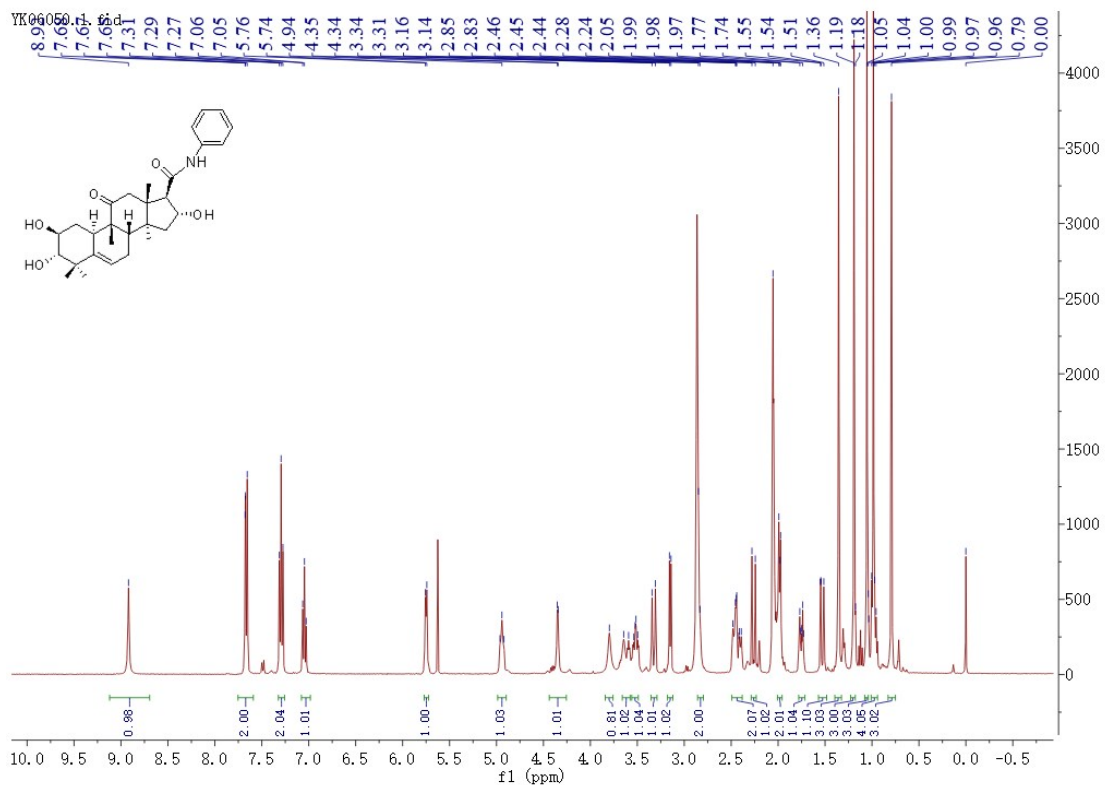


Fig. S48 <sup>1</sup>H NMR spectrum of 9d

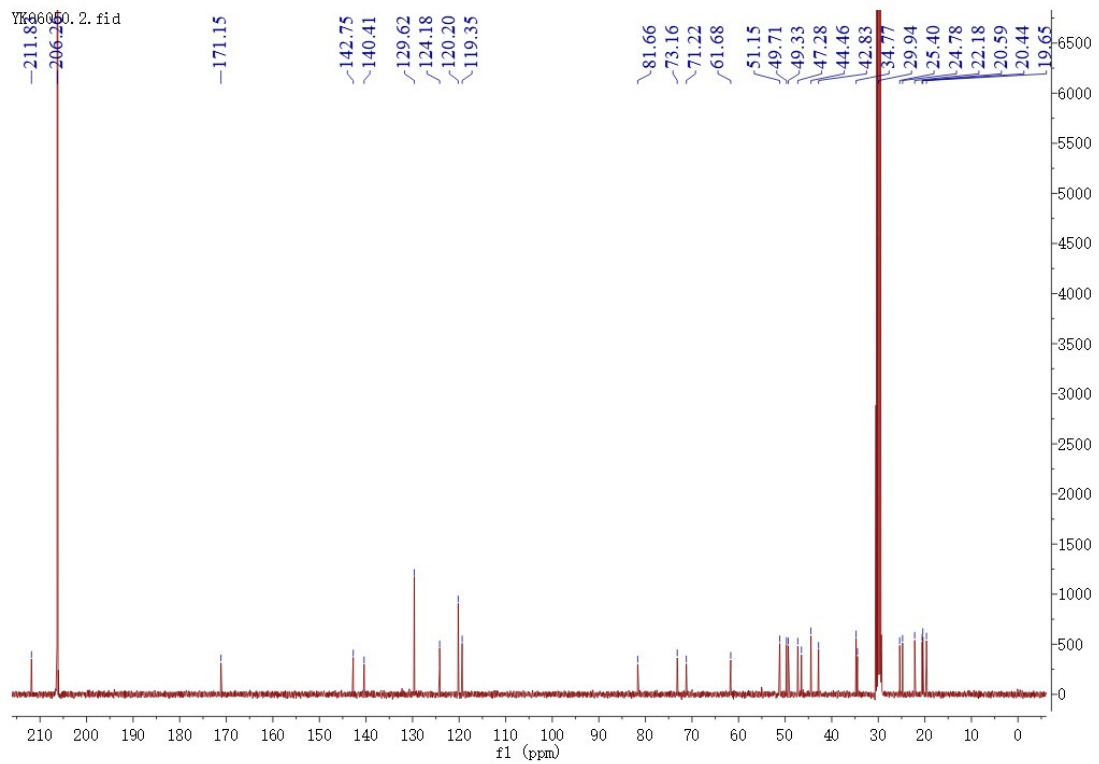


Fig. S49 <sup>13</sup>C NMR spectrum of 9d

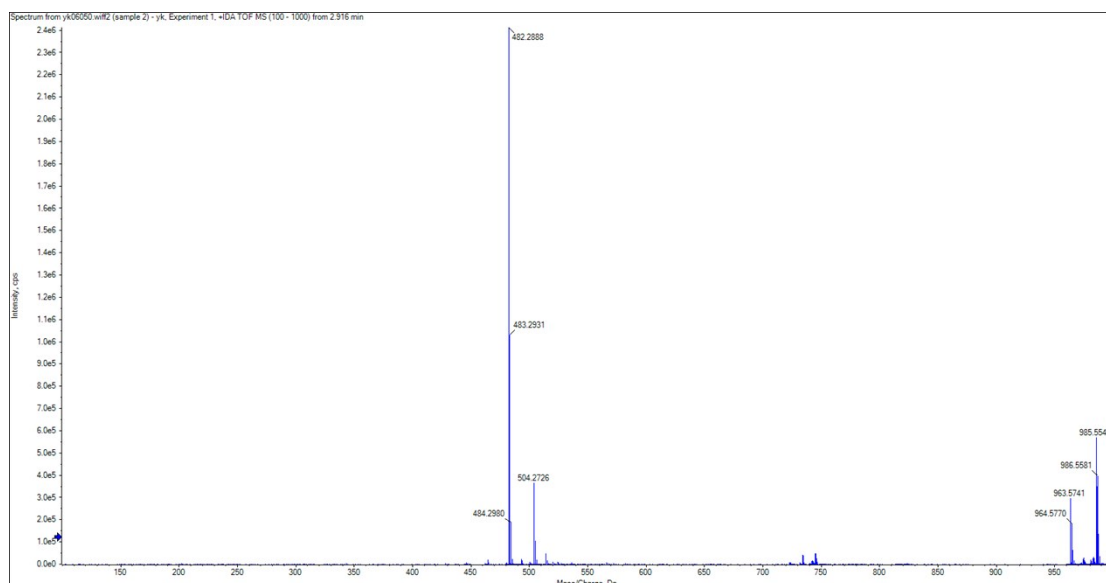


Fig. S50 HRMS spectrum of 9d

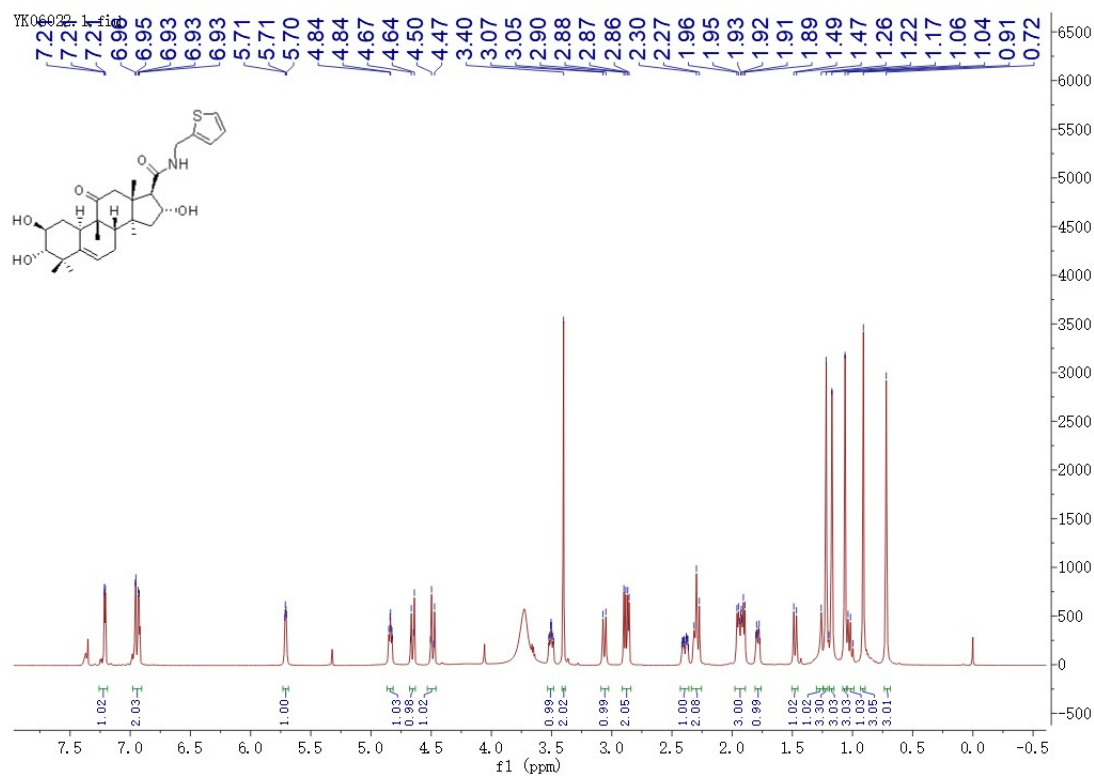


Fig. S51 <sup>1</sup>H NMR spectrum of 9e

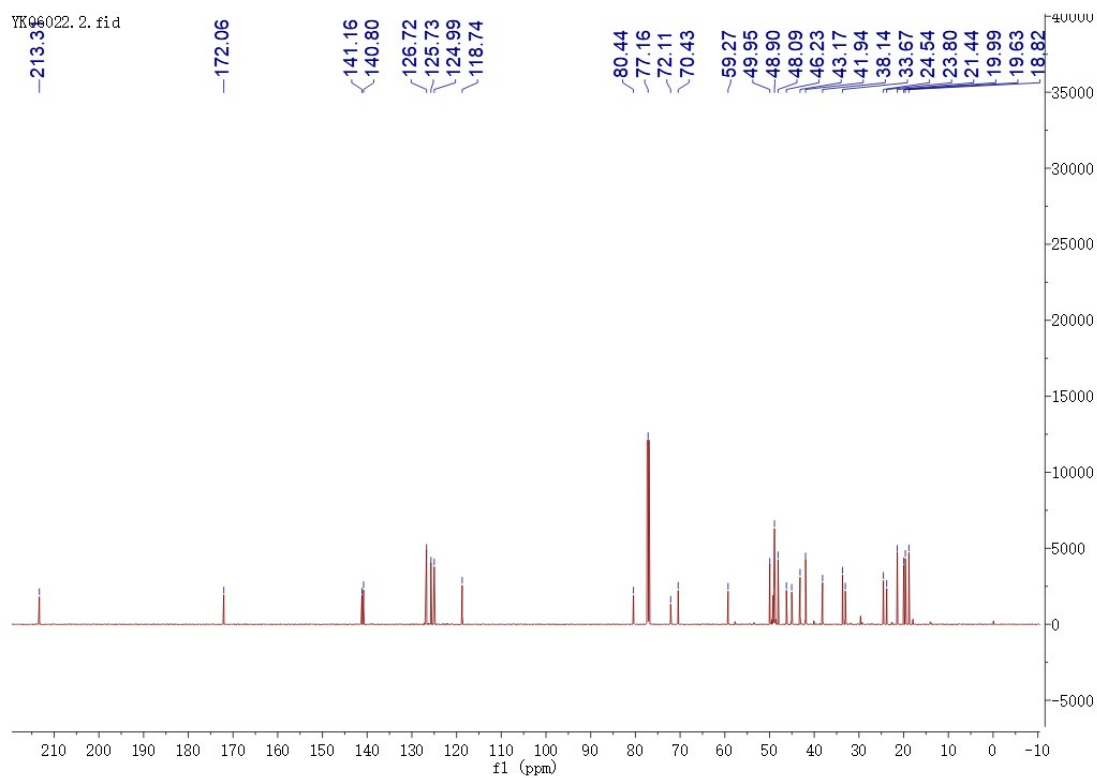


Fig. S52 <sup>13</sup>C NMR spectrum of 9e

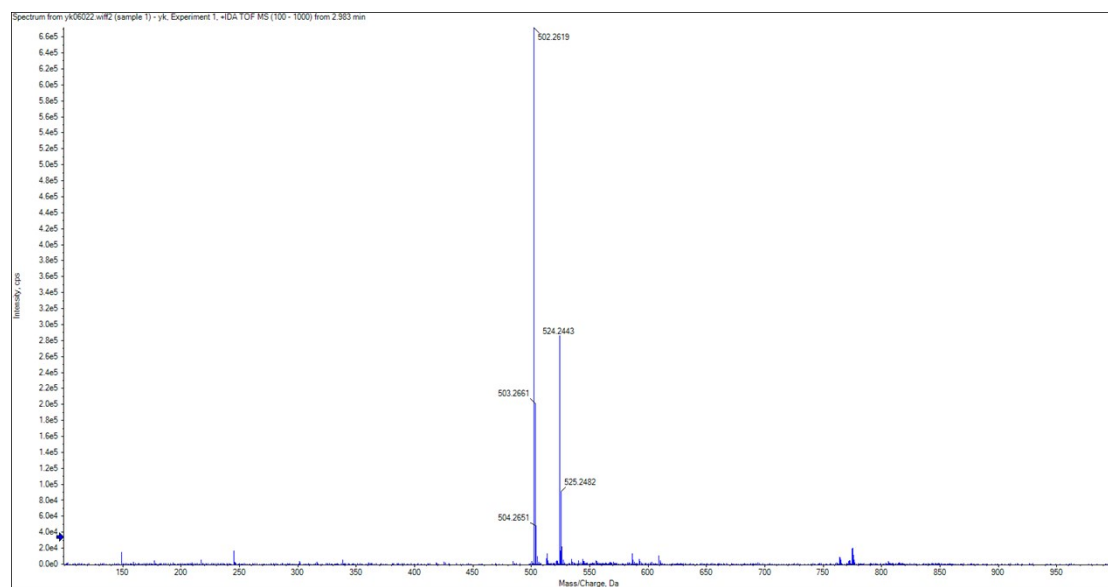


Fig. S53 HRMS spectrum of 9e

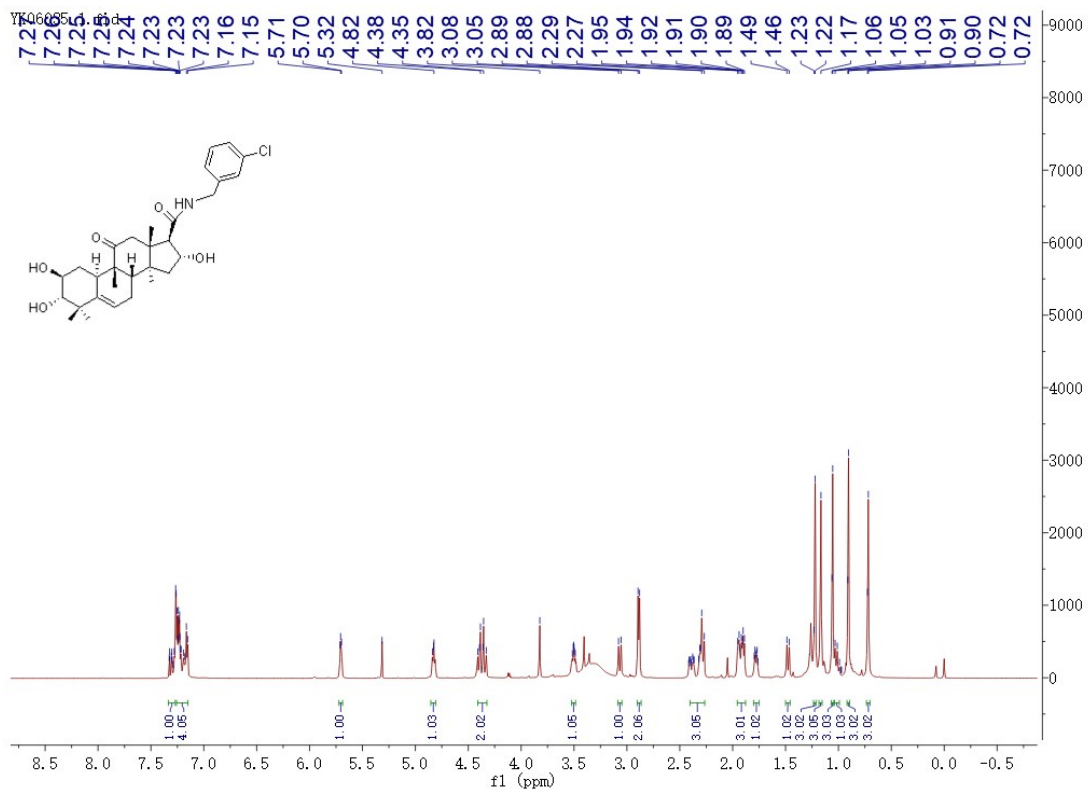


Fig. S54  $^1\text{H}$  NMR spectrum of 9f

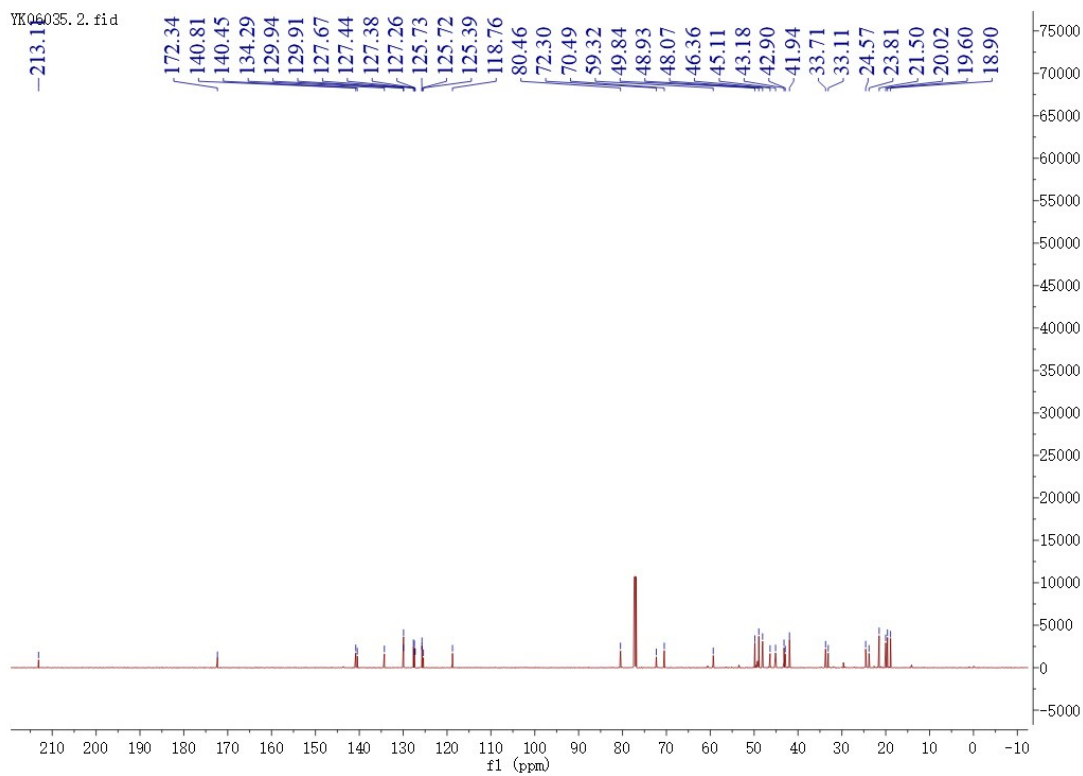


Fig. S55  $^{13}\text{C}$  NMR spectrum of 9f

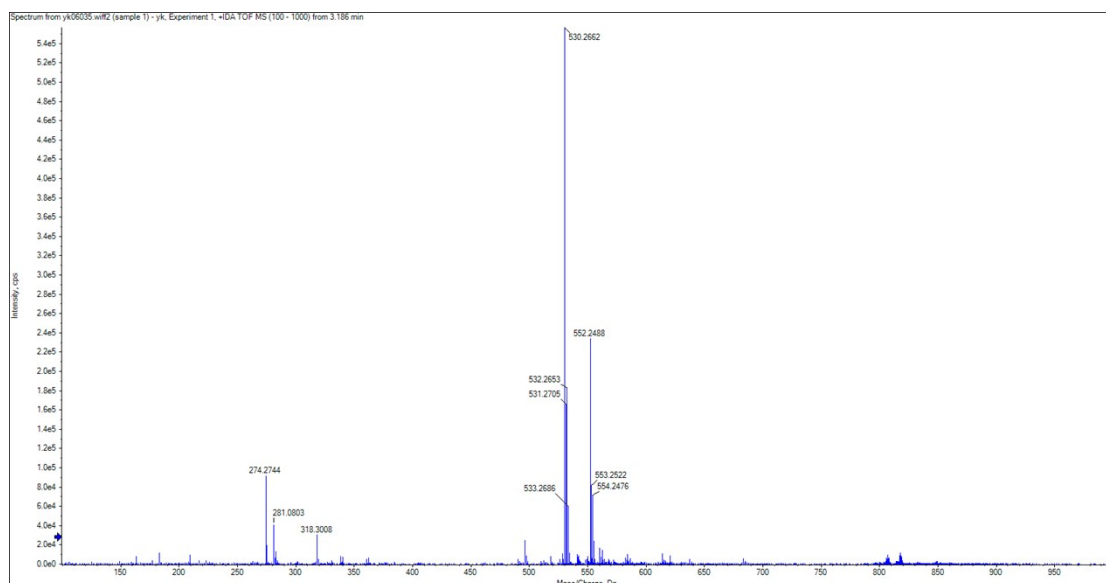


Fig. S56 HRMS spectrum of **9f**

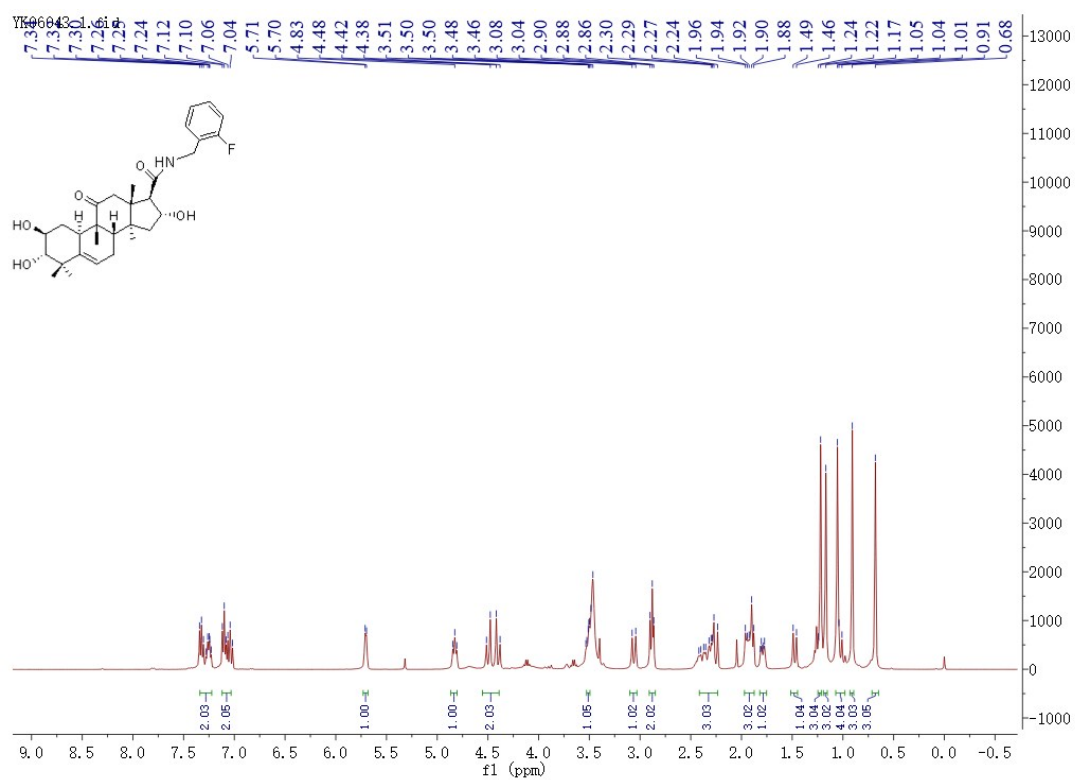


Fig. S57 <sup>1</sup>H NMR spectrum of **9g**

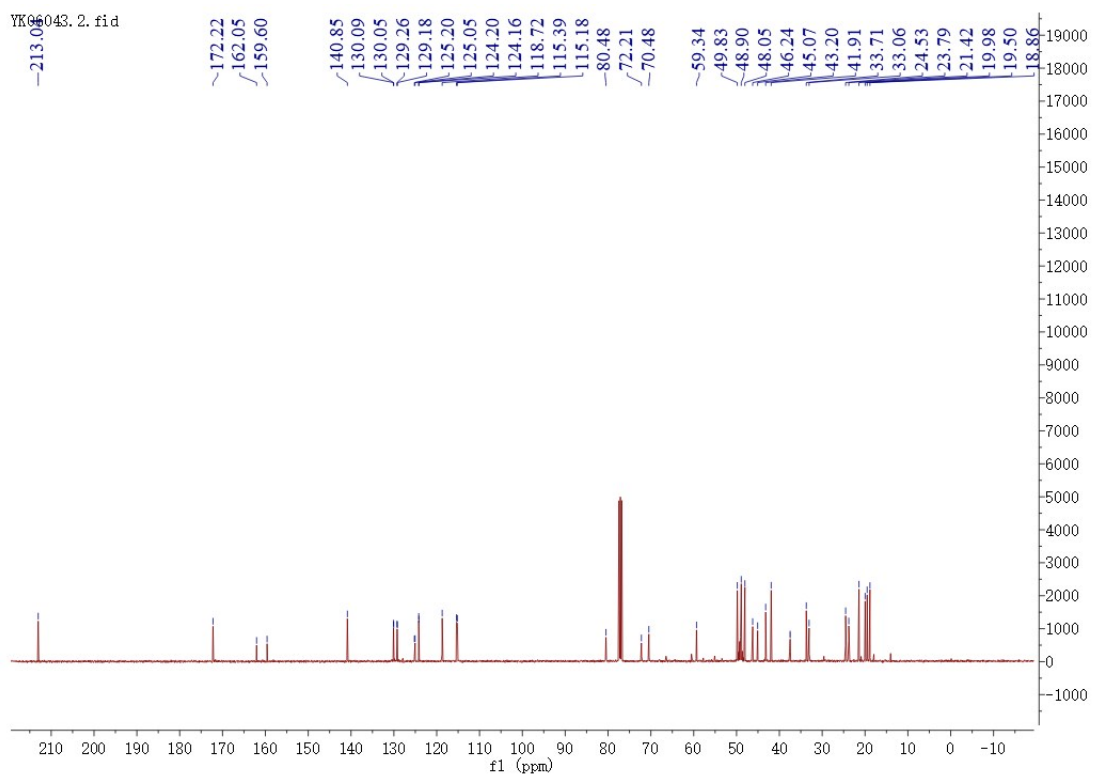


Fig. S58  $^{13}\text{C}$  NMR spectrum of **9g**

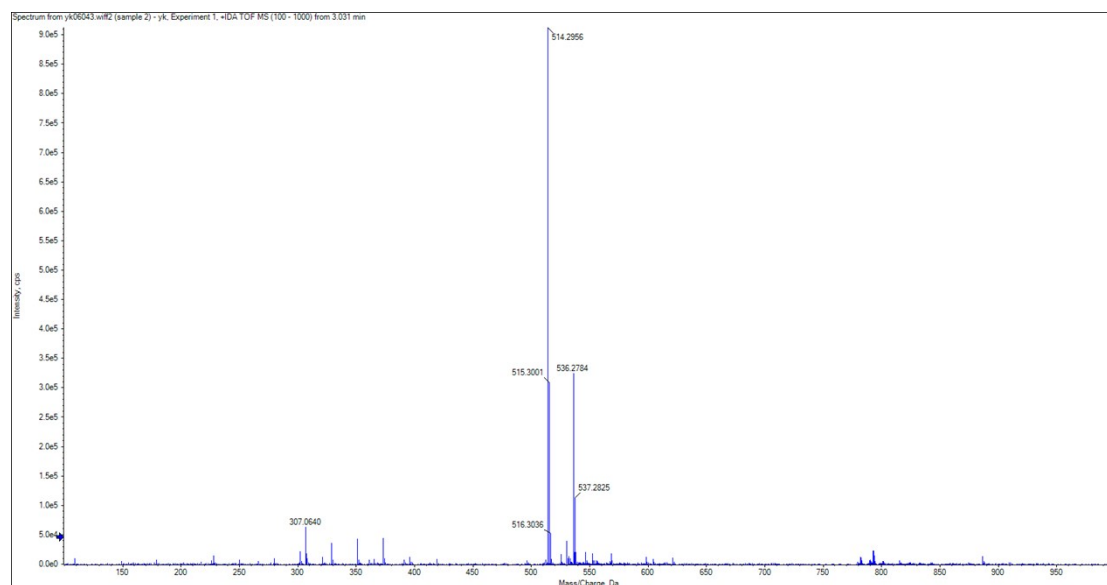


Fig. S59 HRMS spectrum of **9g**

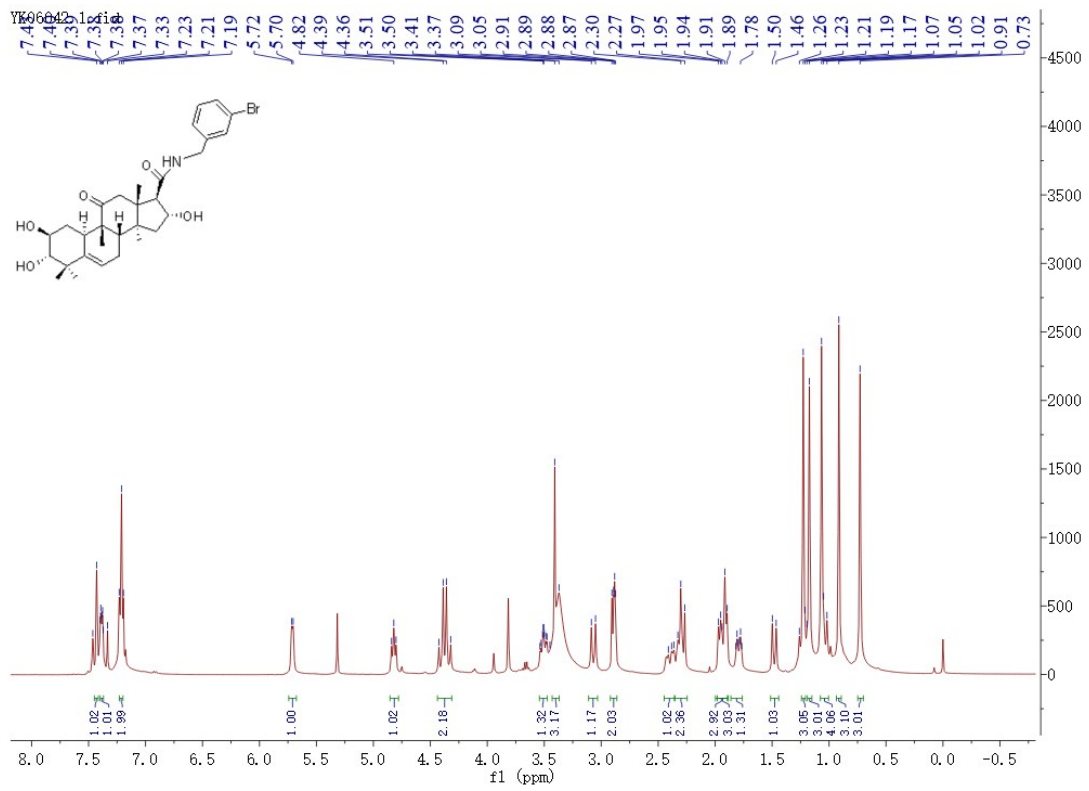


Fig. S60  $^1\text{H}$  NMR spectrum of 9h

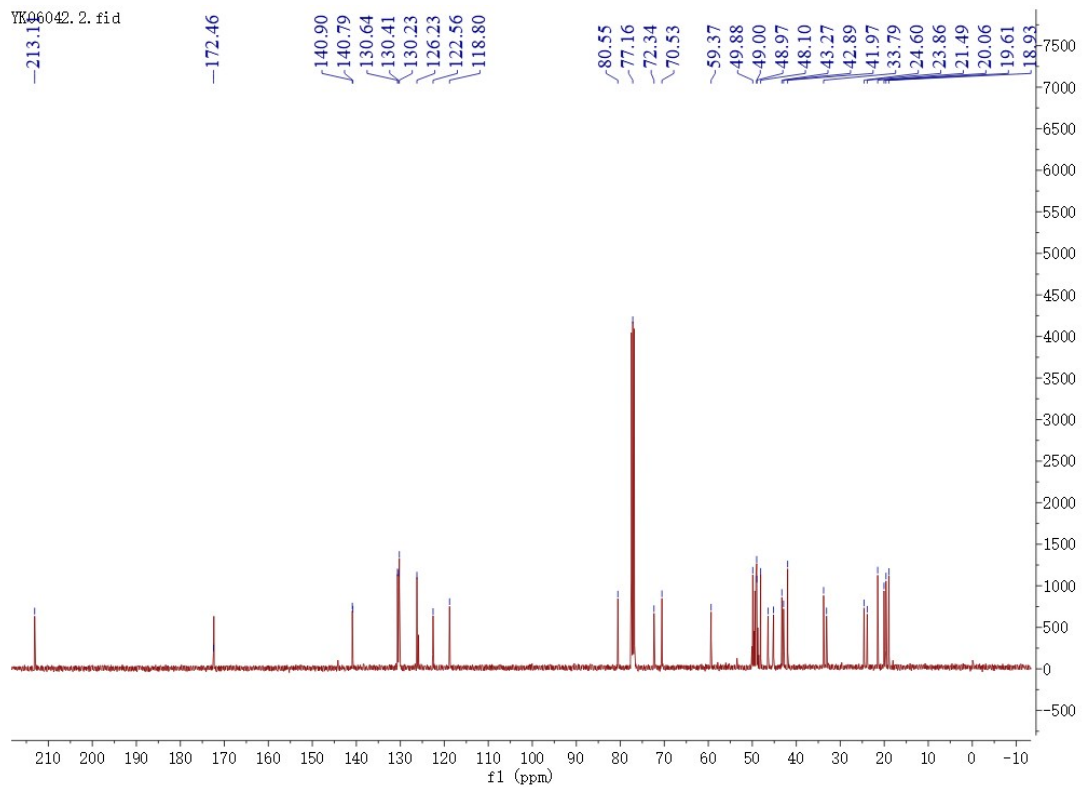
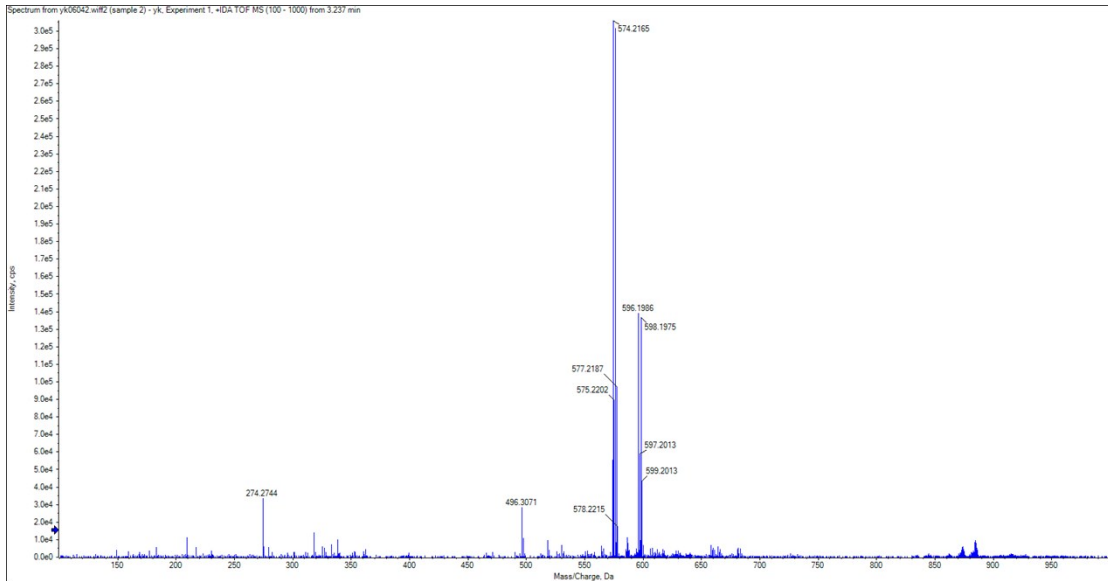
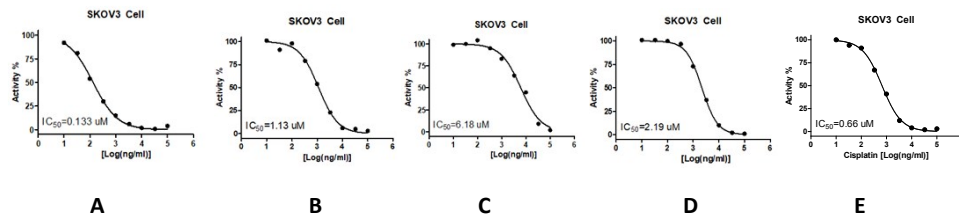


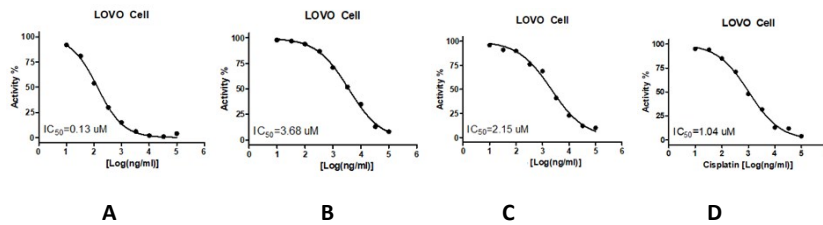
Fig. S61  $^{13}\text{C}$  NMR spectrum of 9h



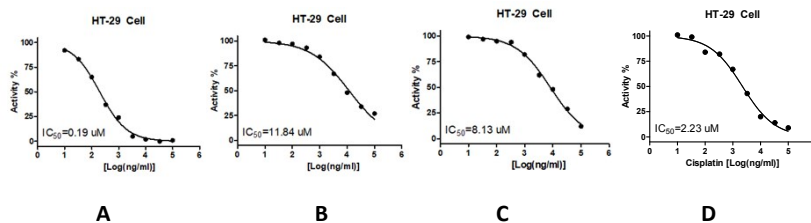
**Fig. S62** HRMS spectrum of **9h**



**Fig. S63** Cell viability assay after 72 hours treatment of compounds in SKOV3 cell line. A: compound **1**, B: compound **2**, C: compound **4a**, D: compound **4d**, E: compound **Cisplatin**.

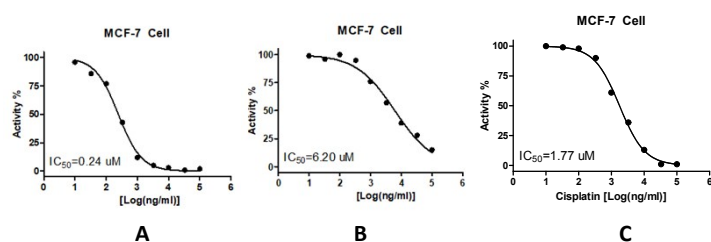


**Fig. S64** Cell viability assay after 72 hours treatment of compounds in LOVO cell line. A: compound **1**, B: compound **4a**, C: compound **4d**, D: compound **Cisplatin**.

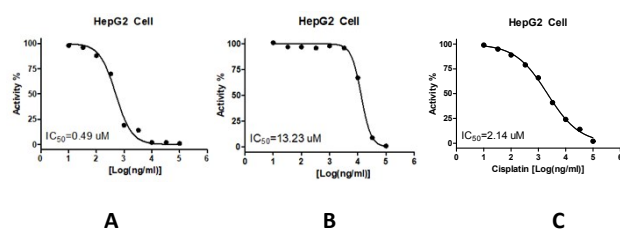


**Fig. S65** Cell viability assay after 72 hours treatment of compounds in HT-29 cell line. A: compound **1**, B: compound **4a**, C: compound **4d**, D: compound **Cisplatin**.

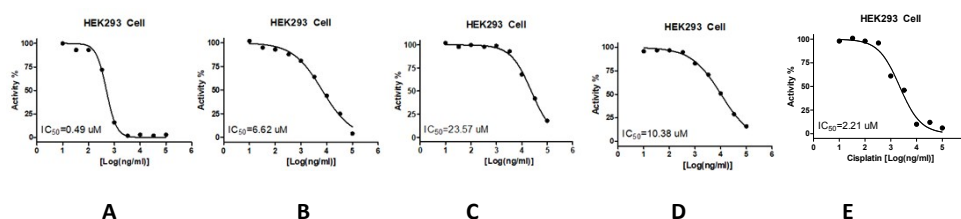




**Fig. S66** Cell viability assay after 72 hours treatment of compounds in MCF-7 cell line. A: compound **1**, B: compound **4a**, C: compound **Cisplatin**.



**Fig. S67** Cell viability assay after 72 hours treatment of compounds in HepG2 cell line. A: compound **1**, B: compound **4a**, C: compound **Cisplatin**.



**Fig. S68** Cell viability assay after 72 hours treatment of compounds in HEK 293 cell line. A: compound **1**, B: compound **2**, C: compound **4a**, D: compound **4d**, E: compound **Cisplatin**.

**Tab. S1** Crystal data and structure refinement for **4b**

Identification code	cu_20181106zinz_0m_a	
Empirical formula	C36 H47 N3 O9	
Formula weight	665.76	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	
Unit cell dimensions	a = 10.8304(3) Å	α = 90°.
	b = 15.9589(4) Å	β = 90°.
	c = 21.2922(5) Å	γ = 90°.
Volume	3680.17(16) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.202 Mg/m <sup>3</sup>	

Absorption coefficient	0.709 mm <sup>-1</sup>
F(000)	1424
Crystal size	? x ? x ? mm <sup>3</sup>
Theta range for data collection	3.461 to 58.926°.
Index ranges	-11<=h<=11, -16<=k<=17, -18<=l<=23
Reflections collected	10488
Independent reflections	4789 [R(int) = 0.0360]
Completeness to theta = 58.926°	94.2 %
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	4789 / 132 / 442
Goodness-of-fit on F <sup>2</sup>	1.062
Final R indices [I>2sigma(I)]	R1 = 0.0434, wR2 = 0.1158
R indices (all data)	R1 = 0.0441, wR2 = 0.1166
Absolute structure parameter	0.00(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.274 and -0.464 e.Å <sup>-3</sup>

**Tab. S2** Bond lengths [Å] and angles [°] for **4a**

C(1)-C(6)	4a
C(1)-C(2)	1.381(6)
C(1)-N(1)	1.452(5)
C(2)-C(3)	1.368(5)
C(2)-H(2)	0.9500
C(3)-C(4)	1.386(5)
C(3)-H(3)	0.9500
C(4)-N(2)	1.379(5)
C(4)-C(5)	1.393(5)
C(5)-C(6)	1.381(6)
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(7)-N(3)	1.287(4)
C(7)-C(8)	1.488(5)
C(7)-C(9)	1.509(4)
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(9)-C(10)	1.535(5)
C(9)-C(13)	1.563(4)

C(9)-H(9)	1.0000
C(10)-O(5)	1.443(5)
C(10)-C(11)	1.527(5)
C(10)-H(10)	1.0000
C(11)-C(12)	1.544(5)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-C(15)	1.535(5)
C(12)-C(19)	1.543(5)
C(12)-C(13)	1.565(4)
C(13)-C(16)	1.525(4)
C(13)-C(14)	1.535(5)
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(17)	1.519(5)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(17)-O(3)	1.210(4)
C(17)-C(18)	1.537(5)
C(18)-C(20)	1.546(5)
C(18)-C(19)	1.571(5)
C(18)-C(21)	1.583(4)
C(19)-C(24)	1.530(5)
C(19)-H(19)	1.0000
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-C(22)	1.523(4)
C(21)-C(25)	1.538(4)
C(21)-H(21)	1.0000
C(22)-C(23)	1.327(5)
C(22)-C(28)	1.531(5)
C(23)-C(24)	1.484(6)
C(23)-H(23)	0.9500

C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-C(26)	1.508(5)
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900
C(26)-O(6)	1.443(4)
C(26)-C(27)	1.513(4)
C(26)-H(26)	1.0000
C(27)-O(8)	1.456(4)
C(27)-C(28)	1.539(5)
C(27)-H(27)	1.0000
C(28)-C(29)	1.536(4)
C(28)-C(30)	1.548(4)
C(29)-H(29A)	0.9800
C(29)-H(29B)	0.9800
C(29)-H(29C)	0.9800
C(30)-H(30A)	0.9800
C(30)-H(30B)	0.9800
C(30)-H(30C)	0.9800
C(31)-O(9)	1.186(4)
C(31)-O(8)	1.348(4)
C(31)-C(32)	1.493(5)
C(32)-H(32A)	0.9800
C(32)-H(32B)	0.9800
C(32)-H(32C)	0.9800
C(33)-O(7)	1.199(4)
C(33)-O(6)	1.334(4)
C(33)-C(34)	1.495(5)
C(34)-H(34A)	0.9800
C(34)-H(34B)	0.9800
C(34)-H(34C)	0.9800
C(35)-C(36)	1.471(10)
C(35)-H(35A)	0.9800
C(35)-H(35B)	0.9800
C(35)-H(35C)	0.9800
C(36)-O(4)	1.226(9)
C(36)-O(5)	1.292(7)
N(1)-O(1)	1.221(5)

N(1)-O(2)	1.226(6)
N(2)-N(3)	1.368(4)
N(2)-H(2A)	0.8800
C(6)-C(1)-C(2)	121.6(4)
C(6)-C(1)-N(1)	118.8(4)
C(2)-C(1)-N(1)	119.6(4)
C(3)-C(2)-C(1)	119.3(3)
C(3)-C(2)-H(2)	120.4
C(1)-C(2)-H(2)	120.4
C(2)-C(3)-C(4)	120.2(3)
C(2)-C(3)-H(3)	119.9
C(4)-C(3)-H(3)	119.9
N(2)-C(4)-C(3)	119.0(3)
N(2)-C(4)-C(5)	121.0(3)
C(3)-C(4)-C(5)	120.0(3)
C(6)-C(5)-C(4)	119.7(4)
C(6)-C(5)-H(5)	120.2
C(4)-C(5)-H(5)	120.2
C(1)-C(6)-C(5)	119.2(4)
C(1)-C(6)-H(6)	120.4
C(5)-C(6)-H(6)	120.4
N(3)-C(7)-C(8)	124.5(3)
N(3)-C(7)-C(9)	116.1(3)
C(8)-C(7)-C(9)	119.4(3)
C(7)-C(8)-H(8A)	109.5
C(7)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(7)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
C(7)-C(9)-C(10)	114.6(3)
C(7)-C(9)-C(13)	117.0(3)
C(10)-C(9)-C(13)	101.5(3)
C(7)-C(9)-H(9)	107.8
C(10)-C(9)-H(9)	107.8
C(13)-C(9)-H(9)	107.8
O(5)-C(10)-C(11)	113.2(3)
O(5)-C(10)-C(9)	106.6(3)

C(11)-C(10)-C(9)	107.9(3)
O(5)-C(10)-H(10)	109.7
C(11)-C(10)-H(10)	109.7
C(9)-C(10)-H(10)	109.7
C(10)-C(11)-C(12)	105.2(3)
C(10)-C(11)-H(11A)	110.7
C(12)-C(11)-H(11A)	110.7
C(10)-C(11)-H(11B)	110.7
C(12)-C(11)-H(11B)	110.7
H(11A)-C(11)-H(11B)	108.8
C(15)-C(12)-C(19)	112.7(3)
C(15)-C(12)-C(11)	106.8(3)
C(19)-C(12)-C(11)	114.4(3)
C(15)-C(12)-C(13)	113.4(3)
C(19)-C(12)-C(13)	107.7(3)
C(11)-C(12)-C(13)	101.3(2)
C(16)-C(13)-C(14)	106.8(3)
C(16)-C(13)-C(9)	118.0(3)
C(14)-C(13)-C(9)	108.4(3)
C(16)-C(13)-C(12)	109.1(2)
C(14)-C(13)-C(12)	114.1(3)
C(9)-C(13)-C(12)	100.6(2)
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(12)-C(15)-H(15A)	109.5
C(12)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(12)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(17)-C(16)-C(13)	109.3(3)
C(17)-C(16)-H(16A)	109.8
C(13)-C(16)-H(16A)	109.8
C(17)-C(16)-H(16B)	109.8

C(13)-C(16)-H(16B)	109.8
H(16A)-C(16)-H(16B)	108.3
O(3)-C(17)-C(16)	119.2(3)
O(3)-C(17)-C(18)	121.1(3)
C(16)-C(17)-C(18)	119.7(3)
C(17)-C(18)-C(20)	108.6(3)
C(17)-C(18)-C(19)	113.5(3)
C(20)-C(18)-C(19)	107.2(3)
C(17)-C(18)-C(21)	103.9(2)
C(20)-C(18)-C(21)	110.8(3)
C(19)-C(18)-C(21)	112.9(3)
C(24)-C(19)-C(12)	114.9(3)
C(24)-C(19)-C(18)	111.1(3)
C(12)-C(19)-C(18)	114.6(2)
C(24)-C(19)-H(19)	105.0
C(12)-C(19)-H(19)	105.0
C(18)-C(19)-H(19)	105.0
C(18)-C(20)-H(20A)	109.5
C(18)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(18)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(22)-C(21)-C(25)	109.2(2)
C(22)-C(21)-C(18)	114.8(3)
C(25)-C(21)-C(18)	111.6(3)
C(22)-C(21)-H(21)	107.0
C(25)-C(21)-H(21)	107.0
C(18)-C(21)-H(21)	107.0
C(23)-C(22)-C(21)	121.9(3)
C(23)-C(22)-C(28)	122.5(3)
C(21)-C(22)-C(28)	115.5(3)
C(22)-C(23)-C(24)	125.3(3)
C(22)-C(23)-H(23)	117.3
C(24)-C(23)-H(23)	117.3
C(23)-C(24)-C(19)	115.3(3)
C(23)-C(24)-H(24A)	108.5
C(19)-C(24)-H(24A)	108.5

C(23)-C(24)-H(24B)	108.5
C(19)-C(24)-H(24B)	108.5
H(24A)-C(24)-H(24B)	107.5
C(26)-C(25)-C(21)	112.2(3)
C(26)-C(25)-H(25A)	109.2
C(21)-C(25)-H(25A)	109.2
C(26)-C(25)-H(25B)	109.2
C(21)-C(25)-H(25B)	109.2
H(25A)-C(25)-H(25B)	107.9
O(6)-C(26)-C(25)	109.4(3)
O(6)-C(26)-C(27)	104.7(2)
C(25)-C(26)-C(27)	110.1(3)
O(6)-C(26)-H(26)	110.8
C(25)-C(26)-H(26)	110.8
C(27)-C(26)-H(26)	110.8
O(8)-C(27)-C(26)	106.2(3)
O(8)-C(27)-C(28)	109.8(3)
C(26)-C(27)-C(28)	114.0(2)
O(8)-C(27)-H(27)	108.9
C(26)-C(27)-H(27)	108.9
C(28)-C(27)-H(27)	108.9
C(22)-C(28)-C(29)	113.0(3)
C(22)-C(28)-C(27)	108.4(3)
C(29)-C(28)-C(27)	107.8(3)
C(22)-C(28)-C(30)	109.0(3)
C(29)-C(28)-C(30)	107.9(3)
C(27)-C(28)-C(30)	110.6(3)
C(28)-C(29)-H(29A)	109.5
C(28)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29B)	109.5
C(28)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5
C(28)-C(30)-H(30A)	109.5
C(28)-C(30)-H(30B)	109.5
H(30A)-C(30)-H(30B)	109.5
C(28)-C(30)-H(30C)	109.5
H(30A)-C(30)-H(30C)	109.5



H(30B)-C(30)-H(30C)	109.5
O(9)-C(31)-O(8)	124.9(3)
O(9)-C(31)-C(32)	124.6(3)
O(8)-C(31)-C(32)	110.5(3)
C(31)-C(32)-H(32A)	109.5
C(31)-C(32)-H(32B)	109.5
H(32A)-C(32)-H(32B)	109.5
C(31)-C(32)-H(32C)	109.5
H(32A)-C(32)-H(32C)	109.5
H(32B)-C(32)-H(32C)	109.5
O(7)-C(33)-O(6)	123.8(3)
O(7)-C(33)-C(34)	125.0(3)
O(6)-C(33)-C(34)	111.2(3)
C(33)-C(34)-H(34A)	109.5
C(33)-C(34)-H(34B)	109.5
H(34A)-C(34)-H(34B)	109.5
C(33)-C(34)-H(34C)	109.5
H(34A)-C(34)-H(34C)	109.5
H(34B)-C(34)-H(34C)	109.5
C(36)-C(35)-H(35A)	109.5
C(36)-C(35)-H(35B)	109.5
H(35A)-C(35)-H(35B)	109.5
C(36)-C(35)-H(35C)	109.5
H(35A)-C(35)-H(35C)	109.5
H(35B)-C(35)-H(35C)	109.5
O(4)-C(36)-O(5)	121.4(7)
O(4)-C(36)-C(35)	124.9(6)
O(5)-C(36)-C(35)	113.6(7)
O(1)-N(1)-O(2)	123.1(4)
O(1)-N(1)-C(1)	118.2(4)
O(2)-N(1)-C(1)	118.7(4)
N(3)-N(2)-C(4)	116.7(3)
N(3)-N(2)-H(2A)	121.6
C(4)-N(2)-H(2A)	121.6
C(7)-N(3)-N(2)	119.1(3)
C(36)-O(5)-C(10)	118.3(5)
C(33)-O(6)-C(26)	119.3(2)
C(31)-O(8)-C(27)	118.8(2)

---

**Tab. S3** Crystal data and structure refinement for **5a**

---

Identification code	5a	
Empirical formula	C30 H43 N O8	
Formula weight	545.65	
Temperature	173(2) K	
Wavelength	1.34139 Å	
Crystal system	Monoclinic	
Space group	P2 <sub>1</sub>	
Unit cell dimensions	a = 8.5713(6) Å	α = 90°.
	b = 31.375(2) Å	β = 105.525(2)°.
	c = 11.2567(8) Å	γ = 90°.
Volume	2916.8(4) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.243 Mg/m <sup>3</sup>	
Absorption coefficient	0.466 mm <sup>-1</sup>	
F(000)	1176	
Crystal size	0.220 x 0.180 x 0.160 mm <sup>3</sup>	
Theta range for data collection	2.450 to 52.999°.	
Index ranges	-9 ≤ h ≤ 10, -37 ≤ k ≤ 37, -13 ≤ l ≤ 13	
Reflections collected	58880	
Independent reflections	10226 [R(int) = 0.0733]	
Completeness to theta = 52.999°	99.5 %	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	10226 / 109 / 723	
Goodness-of-fit on F <sup>2</sup>	1.013	
Final R indices [I > 2σ(I)]	R1 = 0.0354, wR2 = 0.0909	
R indices (all data)	R1 = 0.0379, wR2 = 0.0931	
Absolute structure parameter	0.18(7)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.250 and -0.180 e.Å <sup>-3</sup>	

---

**Tab. S4** Bond lengths [Å] and angles [°] for **4a**

---

C(1)-C(2)	1.493(4)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(1)-H(1C)	0.9800
C(2)-O(1)	1.192(4)
C(2)-O(2)	1.343(4)
C(3)-C(4)	1.496(4)
C(3)-H(3A)	0.9800
C(3)-H(3B)	0.9800
C(3)-H(3C)	0.9800
C(4)-O(3)	1.197(3)
C(4)-O(4)	1.336(3)
C(5)-O(4)	1.458(3)
C(5)-C(6)	1.508(3)
C(5)-C(10)	1.515(3)
C(5)-H(5)	1.0000
C(6)-O(2)	1.454(3)
C(6)-C(7)	1.542(4)
C(6)-H(6)	1.0000
C(7)-C(12)	1.526(4)
C(7)-C(8)	1.543(4)
C(7)-C(11)	1.543(4)
C(8)-C(17)	1.326(4)
C(8)-C(9)	1.513(3)
C(9)-C(10)	1.534(3)
C(9)-C(13)	1.569(3)
C(9)-H(9)	1.0000
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-C(14)	1.540(4)
C(13)-C(23)	1.538(4)

C(13)-C(15)	1.562(3)
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-C(19)	1.539(4)
C(15)-C(16)	1.536(4)
C(15)-H(15)	1.0000
C(16)-C(17)	1.495(4)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(17)-H(17)	0.9500
C(18)-C(19)	1.543(4)
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-C(24)	1.544(4)
C(19)-C(20)	1.561(3)
C(20)-C(22)	1.531(3)
C(20)-C(21)	1.541(4)
C(20)-C(26)	1.548(4)
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-C(23)	1.515(4)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-O(5)	1.215(3)
C(24)-C(25)	1.542(4)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-O(6)	1.466(4)
C(25)-C(26)	1.535(4)
C(25)-H(25)	1.0000
C(26)-C(27)	1.514(4)
C(26)-H(26)	1.0000
C(27)-N(1)	1.275(4)
C(27)-C(28)	1.480(4)
C(28)-H(28A)	0.9800

C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-O(7)	1.233(7)
C(29)-O(6)	1.333(5)
C(29)-C(30)	1.510(8)
C(30)-H(30A)	0.9800
C(30)-H(30B)	0.9800
C(30)-H(30C)	0.9800
C(31)-C(32)	1.499(4)
C(31)-H(31A)	0.9800
C(31)-H(31B)	0.9800
C(31)-H(31C)	0.9800
C(32)-O(9)	1.200(3)
C(32)-O(10)	1.354(3)
C(33)-C(34)	1.489(4)
C(33)-H(33A)	0.9800
C(33)-H(33B)	0.9800
C(33)-H(33C)	0.9800
C(34)-O(11)	1.208(3)
C(34)-O(12)	1.337(3)
C(35)-O(10)	1.451(3)
C(35)-C(40)	1.507(3)
C(35)-C(36)	1.516(3)
C(35)-H(35)	1.0000
C(36)-O(12)	1.458(3)
C(36)-C(37)	1.544(3)
C(36)-H(36)	1.0000
C(37)-C(42)	1.529(3)
C(37)-C(38)	1.538(3)
C(37)-C(41)	1.544(3)
C(38)-C(46)	1.326(4)
C(38)-C(39)	1.525(3)
C(39)-C(40)	1.538(3)
C(39)-C(43)	1.574(3)
C(39)-H(39)	1.0000
C(40)-H(40A)	0.9900
C(40)-H(40B)	0.9900
C(41)-H(41A)	0.9800

C(41)-H(41B)	0.9800
C(41)-H(41C)	0.9800
C(42)-H(42A)	0.9800
C(42)-H(42B)	0.9800
C(42)-H(42C)	0.9800
C(43)-C(47)	1.530(4)
C(43)-C(53)	1.548(4)
C(43)-C(44)	1.559(3)
C(44)-C(45)	1.537(3)
C(44)-C(48)	1.540(3)
C(44)-H(44)	1.0000
C(45)-C(46)	1.494(3)
C(45)-H(45A)	0.9900
C(45)-H(45B)	0.9900
C(46)-H(46)	0.9500
C(47)-H(47A)	0.9800
C(47)-H(47B)	0.9800
C(47)-H(47C)	0.9800
C(48)-C(49)	1.543(4)
C(48)-C(54)	1.544(3)
C(48)-C(50)	1.567(3)
C(49)-H(49A)	0.9800
C(49)-H(49B)	0.9800
C(49)-H(49C)	0.9800
C(50)-C(52)	1.533(3)
C(50)-C(51)	1.550(3)
C(50)-C(56)	1.552(3)
C(51)-H(51A)	0.9800
C(51)-H(51B)	0.9800
C(51)-H(51C)	0.9800
C(52)-C(53)	1.518(4)
C(52)-H(52A)	0.9900
C(52)-H(52B)	0.9900
C(53)-O(13)	1.211(3)
C(54)-C(55)	1.545(4)
C(54)-H(54A)	0.9900
C(54)-H(54B)	0.9900
C(55)-O(16)	1.455(3)

C(55)-C(56)	1.538(3)
C(55)-H(55)	1.0000
C(56)-C(59)	1.512(3)
C(56)-H(56)	1.0000
C(57)-C(58)	1.491(5)
C(57)-H(57A)	0.9800
C(57)-H(57B)	0.9800
C(57)-H(57C)	0.9800
C(58)-O(15)	1.198(4)
C(58)-O(16)	1.348(4)
C(59)-N(2)	1.273(3)
C(59)-C(60)	1.494(4)
C(60)-H(60A)	0.9800
C(60)-H(60B)	0.9800
C(60)-H(60C)	0.9800
N(1)-O(8)	1.412(3)
N(2)-O(14)	1.417(3)
O(8)-H(8)	0.8400
O(14)-H(14)	0.8400

C(2)-C(1)-H(1A)	109.5
C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
C(2)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
O(1)-C(2)-O(2)	124.2(3)
O(1)-C(2)-C(1)	124.8(3)
O(2)-C(2)-C(1)	111.1(3)
C(4)-C(3)-H(3A)	109.5
C(4)-C(3)-H(3B)	109.5
H(3A)-C(3)-H(3B)	109.5
C(4)-C(3)-H(3C)	109.5
H(3A)-C(3)-H(3C)	109.5
H(3B)-C(3)-H(3C)	109.5
O(3)-C(4)-O(4)	124.2(2)
O(3)-C(4)-C(3)	124.9(3)
O(4)-C(4)-C(3)	110.9(2)

O(4)-C(5)-C(6)	108.13(19)
O(4)-C(5)-C(10)	106.19(19)
C(6)-C(5)-C(10)	110.2(2)
O(4)-C(5)-H(5)	110.7
C(6)-C(5)-H(5)	110.7
C(10)-C(5)-H(5)	110.7
O(2)-C(6)-C(5)	106.8(2)
O(2)-C(6)-C(7)	109.2(2)
C(5)-C(6)-C(7)	113.1(2)
O(2)-C(6)-H(6)	109.2
C(5)-C(6)-H(6)	109.2
C(7)-C(6)-H(6)	109.2
C(12)-C(7)-C(6)	108.2(2)
C(12)-C(7)-C(8)	112.4(2)
C(6)-C(7)-C(8)	109.79(19)
C(12)-C(7)-C(11)	108.6(2)
C(6)-C(7)-C(11)	110.5(2)
C(8)-C(7)-C(11)	107.4(2)
C(17)-C(8)-C(9)	122.1(2)
C(17)-C(8)-C(7)	122.0(2)
C(9)-C(8)-C(7)	115.6(2)
C(8)-C(9)-C(10)	110.1(2)
C(8)-C(9)-C(13)	113.8(2)
C(10)-C(9)-C(13)	111.62(19)
C(8)-C(9)-H(9)	107.0
C(10)-C(9)-H(9)	107.0
C(13)-C(9)-H(9)	107.0
C(5)-C(10)-C(9)	110.1(2)
C(5)-C(10)-H(10A)	109.6
C(9)-C(10)-H(10A)	109.6
C(5)-C(10)-H(10B)	109.6
C(9)-C(10)-H(10B)	109.6
H(10A)-C(10)-H(10B)	108.2
C(7)-C(11)-H(11A)	109.5
C(7)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(7)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5



H(11B)-C(11)-H(11C)	109.5
C(7)-C(12)-H(12A)	109.5
C(7)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(7)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(14)-C(13)-C(23)	109.1(2)
C(14)-C(13)-C(15)	107.4(2)
C(23)-C(13)-C(15)	112.3(2)
C(14)-C(13)-C(9)	110.6(2)
C(23)-C(13)-C(9)	104.5(2)
C(15)-C(13)-C(9)	112.9(2)
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(19)-C(15)-C(16)	115.2(2)
C(19)-C(15)-C(13)	114.5(2)
C(16)-C(15)-C(13)	110.2(2)
C(19)-C(15)-H(15)	105.3
C(16)-C(15)-H(15)	105.3
C(13)-C(15)-H(15)	105.3
C(17)-C(16)-C(15)	114.8(2)
C(17)-C(16)-H(16A)	108.6
C(15)-C(16)-H(16A)	108.6
C(17)-C(16)-H(16B)	108.6
C(15)-C(16)-H(16B)	108.6
H(16A)-C(16)-H(16B)	107.5
C(8)-C(17)-C(16)	125.2(3)
C(8)-C(17)-H(17)	117.4
C(16)-C(17)-H(17)	117.4
C(19)-C(18)-H(18A)	109.5
C(19)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(19)-C(18)-H(18C)	109.5

H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(15)-C(19)-C(24)	114.7(2)
C(15)-C(19)-C(18)	112.8(2)
C(24)-C(19)-C(18)	105.7(2)
C(15)-C(19)-C(20)	108.8(2)
C(24)-C(19)-C(20)	101.3(2)
C(18)-C(19)-C(20)	113.1(2)
C(22)-C(20)-C(21)	106.7(2)
C(22)-C(20)-C(26)	118.5(2)
C(21)-C(20)-C(26)	108.1(2)
C(22)-C(20)-C(19)	109.4(2)
C(21)-C(20)-C(19)	113.8(2)
C(26)-C(20)-C(19)	100.6(2)
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(23)-C(22)-C(20)	109.2(2)
C(23)-C(22)-H(22A)	109.8
C(20)-C(22)-H(22A)	109.8
C(23)-C(22)-H(22B)	109.8
C(20)-C(22)-H(22B)	109.8
H(22A)-C(22)-H(22B)	108.3
O(5)-C(23)-C(22)	120.0(3)
O(5)-C(23)-C(13)	120.9(3)
C(22)-C(23)-C(13)	119.1(2)
C(25)-C(24)-C(19)	104.2(2)
C(25)-C(24)-H(24A)	110.9
C(19)-C(24)-H(24A)	110.9
C(25)-C(24)-H(24B)	110.9
C(19)-C(24)-H(24B)	110.9
H(24A)-C(24)-H(24B)	108.9
O(6)-C(25)-C(26)	106.6(2)
O(6)-C(25)-C(24)	112.4(2)
C(26)-C(25)-C(24)	107.6(2)

O(6)-C(25)-H(25)	110.1
C(26)-C(25)-H(25)	110.1
C(24)-C(25)-H(25)	110.1
C(27)-C(26)-C(25)	114.1(2)
C(27)-C(26)-C(20)	117.4(2)
C(25)-C(26)-C(20)	102.0(2)
C(27)-C(26)-H(26)	107.6
C(25)-C(26)-H(26)	107.6
C(20)-C(26)-H(26)	107.6
N(1)-C(27)-C(28)	124.8(3)
N(1)-C(27)-C(26)	116.1(2)
C(28)-C(27)-C(26)	119.0(2)
C(27)-C(28)-H(28A)	109.5
C(27)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
C(27)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
O(7)-C(29)-O(6)	123.0(4)
O(7)-C(29)-C(30)	126.3(4)
O(6)-C(29)-C(30)	110.7(5)
C(29)-C(30)-H(30A)	109.5
C(29)-C(30)-H(30B)	109.5
H(30A)-C(30)-H(30B)	109.5
C(29)-C(30)-H(30C)	109.5
H(30A)-C(30)-H(30C)	109.5
H(30B)-C(30)-H(30C)	109.5
C(32)-C(31)-H(31A)	109.5
C(32)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31B)	109.5
C(32)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
O(9)-C(32)-O(10)	124.4(2)
O(9)-C(32)-C(31)	125.1(2)
O(10)-C(32)-C(31)	110.4(2)
C(34)-C(33)-H(33A)	109.5
C(34)-C(33)-H(33B)	109.5

H(33A)-C(33)-H(33B)	109.5
C(34)-C(33)-H(33C)	109.5
H(33A)-C(33)-H(33C)	109.5
H(33B)-C(33)-H(33C)	109.5
O(11)-C(34)-O(12)	123.3(2)
O(11)-C(34)-C(33)	125.0(2)
O(12)-C(34)-C(33)	111.7(2)
O(10)-C(35)-C(40)	106.61(19)
O(10)-C(35)-C(36)	108.62(18)
C(40)-C(35)-C(36)	109.19(19)
O(10)-C(35)-H(35)	110.8
C(40)-C(35)-H(35)	110.8
C(36)-C(35)-H(35)	110.8
O(12)-C(36)-C(35)	105.69(18)
O(12)-C(36)-C(37)	110.94(18)
C(35)-C(36)-C(37)	112.39(19)
O(12)-C(36)-H(36)	109.2
C(35)-C(36)-H(36)	109.2
C(37)-C(36)-H(36)	109.2
C(42)-C(37)-C(38)	112.4(2)
C(42)-C(37)-C(36)	108.35(19)
C(38)-C(37)-C(36)	108.94(19)
C(42)-C(37)-C(41)	107.8(2)
C(38)-C(37)-C(41)	108.9(2)
C(36)-C(37)-C(41)	110.4(2)
C(46)-C(38)-C(39)	121.5(2)
C(46)-C(38)-C(37)	121.5(2)
C(39)-C(38)-C(37)	116.66(19)
C(38)-C(39)-C(40)	111.05(19)
C(38)-C(39)-C(43)	113.1(2)
C(40)-C(39)-C(43)	111.06(19)
C(38)-C(39)-H(39)	107.1
C(40)-C(39)-H(39)	107.1
C(43)-C(39)-H(39)	107.1
C(35)-C(40)-C(39)	110.6(2)
C(35)-C(40)-H(40A)	109.5
C(39)-C(40)-H(40A)	109.5
C(35)-C(40)-H(40B)	109.5

C(39)-C(40)-H(40B)	109.5
H(40A)-C(40)-H(40B)	108.1
C(37)-C(41)-H(41A)	109.5
C(37)-C(41)-H(41B)	109.5
H(41A)-C(41)-H(41B)	109.5
C(37)-C(41)-H(41C)	109.5
H(41A)-C(41)-H(41C)	109.5
H(41B)-C(41)-H(41C)	109.5
C(37)-C(42)-H(42A)	109.5
C(37)-C(42)-H(42B)	109.5
H(42A)-C(42)-H(42B)	109.5
C(37)-C(42)-H(42C)	109.5
H(42A)-C(42)-H(42C)	109.5
H(42B)-C(42)-H(42C)	109.5
C(47)-C(43)-C(53)	109.8(2)
C(47)-C(43)-C(44)	107.7(2)
C(53)-C(43)-C(44)	111.32(19)
C(47)-C(43)-C(39)	110.8(2)
C(53)-C(43)-C(39)	105.1(2)
C(44)-C(43)-C(39)	112.22(19)
C(45)-C(44)-C(48)	114.5(2)
C(45)-C(44)-C(43)	110.5(2)
C(48)-C(44)-C(43)	114.7(2)
C(45)-C(44)-H(44)	105.4
C(48)-C(44)-H(44)	105.4
C(43)-C(44)-H(44)	105.4
C(46)-C(45)-C(44)	115.0(2)
C(46)-C(45)-H(45A)	108.5
C(44)-C(45)-H(45A)	108.5
C(46)-C(45)-H(45B)	108.5
C(44)-C(45)-H(45B)	108.5
H(45A)-C(45)-H(45B)	107.5
C(38)-C(46)-C(45)	125.7(2)
C(38)-C(46)-H(46)	117.1
C(45)-C(46)-H(46)	117.1
C(43)-C(47)-H(47A)	109.5
C(43)-C(47)-H(47B)	109.5
H(47A)-C(47)-H(47B)	109.5

C(43)-C(47)-H(47C)	109.5
H(47A)-C(47)-H(47C)	109.5
H(47B)-C(47)-H(47C)	109.5
C(44)-C(48)-C(49)	113.2(2)
C(44)-C(48)-C(54)	113.9(2)
C(49)-C(48)-C(54)	106.5(2)
C(44)-C(48)-C(50)	109.2(2)
C(49)-C(48)-C(50)	112.2(2)
C(54)-C(48)-C(50)	101.16(19)
C(48)-C(49)-H(49A)	109.5
C(48)-C(49)-H(49B)	109.5
H(49A)-C(49)-H(49B)	109.5
C(48)-C(49)-H(49C)	109.5
H(49A)-C(49)-H(49C)	109.5
H(49B)-C(49)-H(49C)	109.5
C(52)-C(50)-C(51)	106.4(2)
C(52)-C(50)-C(56)	119.6(2)
C(51)-C(50)-C(56)	108.3(2)
C(52)-C(50)-C(48)	109.24(19)
C(51)-C(50)-C(48)	113.4(2)
C(56)-C(50)-C(48)	100.10(19)
C(50)-C(51)-H(51A)	109.5
C(50)-C(51)-H(51B)	109.5
H(51A)-C(51)-H(51B)	109.5
C(50)-C(51)-H(51C)	109.5
H(51A)-C(51)-H(51C)	109.5
H(51B)-C(51)-H(51C)	109.5
C(53)-C(52)-C(50)	108.8(2)
C(53)-C(52)-H(52A)	109.9
C(50)-C(52)-H(52A)	109.9
C(53)-C(52)-H(52B)	109.9
C(50)-C(52)-H(52B)	109.9
H(52A)-C(52)-H(52B)	108.3
O(13)-C(53)-C(52)	119.9(2)
O(13)-C(53)-C(43)	120.9(2)
C(52)-C(53)-C(43)	119.2(2)
C(48)-C(54)-C(55)	104.6(2)
C(48)-C(54)-H(54A)	110.8

C(55)-C(54)-H(54A)	110.8
C(48)-C(54)-H(54B)	110.8
C(55)-C(54)-H(54B)	110.8
H(54A)-C(54)-H(54B)	108.9
O(16)-C(55)-C(56)	109.4(2)
O(16)-C(55)-C(54)	112.3(2)
C(56)-C(55)-C(54)	107.24(19)
O(16)-C(55)-H(55)	109.3
C(56)-C(55)-H(55)	109.3
C(54)-C(55)-H(55)	109.3
C(59)-C(56)-C(55)	114.4(2)
C(59)-C(56)-C(50)	118.9(2)
C(55)-C(56)-C(50)	100.5(2)
C(59)-C(56)-H(56)	107.4
C(55)-C(56)-H(56)	107.4
C(50)-C(56)-H(56)	107.4
C(58)-C(57)-H(57A)	109.5
C(58)-C(57)-H(57B)	109.5
H(57A)-C(57)-H(57B)	109.5
C(58)-C(57)-H(57C)	109.5
H(57A)-C(57)-H(57C)	109.5
H(57B)-C(57)-H(57C)	109.5
O(15)-C(58)-O(16)	124.1(3)
O(15)-C(58)-C(57)	124.2(3)
O(16)-C(58)-C(57)	111.7(3)
N(2)-C(59)-C(60)	125.7(2)
N(2)-C(59)-C(56)	115.8(2)
C(60)-C(59)-C(56)	118.2(2)
C(59)-C(60)-H(60A)	109.5
C(59)-C(60)-H(60B)	109.5
H(60A)-C(60)-H(60B)	109.5
C(59)-C(60)-H(60C)	109.5
H(60A)-C(60)-H(60C)	109.5
H(60B)-C(60)-H(60C)	109.5
C(27)-N(1)-O(8)	112.4(2)
C(59)-N(2)-O(14)	112.5(2)
C(2)-O(2)-C(6)	118.8(2)
C(4)-O(4)-C(5)	118.90(19)

C(29)-O(6)-C(25)	117.0(4)
N(1)-O(8)-H(8)	109.5
C(32)-O(10)-C(35)	117.36(19)
C(34)-O(12)-C(36)	118.43(19)
N(2)-O(14)-H(14)	109.5
C(58)-O(16)-C(55)	115.6(2)

---