Electronic Supplementary Information

Gallium(III)-2-benzoylpyridine-thiosemicarbazone complexes promote apoptosis through Ca^{2+} signaling and ROS-mediated mitochondrial pathways

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Table S1 Crystal Data of three Ga(III)complexes.

GA(III) complexes	C1	C2	C3
Empirical formula	$C_{26}H_{24.5}GaN_9O_{4.25}S_2$	$C_{38}H_{30}GaN_9O_3S_2$	$C_{32}H_{38}GaN_9O_5S_2$
Formula weight	666.90	794.55	762.55
Temperature/K	296.15	296.15	296.15
Crystal system	monoclinic	triclinic	monoclinic
Space group	$P2_1/c$	$P\bar{1}$	$P2_1/n$
a/Å	13.263(4)	10.891(4)	18.466(3)
b/Å	11.598(4)	12.977(4)	8.9272(14)
c/Å	18.773(6)	14.074(5)	21.798(4)
α/°	90	91.872(6)	90
β/°	94.273(5)	97.259(5)	94.344(3)
γ/°	90	109.477(5)	90
Volume/Å^3	2879.8(15)	1854.4(10)	3583.0(10)
Z	4	2	4
Index ranges	$-16 \le h \le 16$, $-14 \le k \le 14$, $-23 \le l \le 23$	$-13 \le h \le 13$, $-15 \le k \le 15$, $-17 \le l \le 16$	$-23 \le h \le 22$, $-11 \le k \le 11$, $-27 \le l \le 27$
Goodness−of−fit on F^2	0.976	1.041	1.030
Final R indexes [all data]	$R_1 = 0.0424$, $wR_2 = 0.1214$	$R_1 = 0.0959$, $wR_2 = 0.2076$	$R_1 = 0.0499$, $wR_2 = 0.1362$
CCDC NO.	1488962	1488961	1488960

Table S2. Selected Bond Lengths (Å) and Angles (deg)

	C1	C2	C3
Ga1-S2	2.3536(9)	2.3595(15)	2.3660(7)
Ga1-S1	2.3728(8)	2.3390(13)	2.3666(8)
Ga1-N6	2.0822(17)	2.045(3)	2.036(2)
Ga1-N2	2.0769(17)	2.045(3)	2.051(2)
Ga1-N5	2.1292(18)	2.168(4)	2.1071(19)
Ga1-N1	2.1065(18)	2.125(3)	2.0997(19)
S2-Ga1-S1	98.30(2)	99.97(6)	99.33(3)
N6-Ga1-S2	81.88(5)	82.46(10)	82.79(6)
N6-Ga1-S1	105.19(5)	104.33(10)	102.31(6)
N6-Ga1-N5	76.91(7)	76.28(13)	77.77(8)
N6-Ga1-N1	94.67(7)	94.67(13)	97.38(8)
N2-Ga1-S2	109.16(5)	105.95(10)	100.83(6)
N2-Ga1-S1	81.83(5)	82.67(10)	82.53(5)
N2-Ga1-N6	166.24(7)	168.19(13)	173.51(7)
N2-Ga1-N5	91.51(7)	94.36(13)	98.06(8)
N2-Ga1-N1	77.33(7)	77.24(13)	77.31(7)
N5-Ga1-S2	158.65(5)	158.05(10)	159.86(6)
N5-Ga1-S1	89.63(5)	90.62(10)	89.98(6)
N1-Ga1-S2	91.14(5)	90.68(11)	90.40(6)
N1-Ga1-S1	158.98(5)	159.22(10)	158.95(6)
N1-Ga1-N5	88.22(7)	85.71(13)	86.95(7)

Table S3. Interference of ligands and Ga(III) complexes with the MTT assay in a cell-free system.

	Absorbance as % control						
	0μM	0.1μM	0.5μM	1μM	5μM	50μM	100μM
3−AP	100.14 ± 0.23	100.11 ± 0.24	100.00 ± 0.25	100.10 ± 0.23	99.99 ± 0.20	100.10 ± 0.21	99.89 ± 0.23
L1	100.21 ± 0.22	99.89 ± 0.25	100.10 ± 0.22	100.00 ± 0.20	100.11 ± 0.23	100.21 ± 0.23	100.00 ± 0.23
L2	100.00 ± 0.24	100.00 ± 0.21	100.19 ± 0.25	100.08 ± 0.21	99.98 ± 0.22	100.11 ± 0.20	100.21 ± 0.20
L3	100.23 ± 0.21	100.10 ± 0.22	100.11 ± 0.23	100.00 ± 0.25	100.01 ± 0.23	100.02 ± 0.23	100.23 ± 0.20
C1	99.93 ± 0.25	100.00 ± 0.24	99.82 ± 0.26	99.99 ± 0.23	100.13 ± 0.23	100.08 ± 0.20	100.09 ± 0.23
C2	100.32 ± 0.22	100.02 ± 0.20	100.00 ± 0.25	99.98 ± 0.20	100.21 ± 0.20	100.01 ± 0.23	100.02 ± 0.22
C3	100.11 ± 0.23	100.00 ± 0.22	100.05 ± 0.23	100.06 ± 0.20	100.03 ± 0.20	100.03 ± 0.21	100.00 ± 0.20
$Ga(NO_3)_3$	100.21 ± 0.21	100.00 ± 0.20	100.21 ± 0.25	99.88 ± 0.20	99.93 ± 0.21	100.00 ± 0.22	100.02 ± 0.23
Cell culture media	100.11 ± 0.12	100.11 ± 0.23	100.00 ± 0.25	99.99 ± 0.23	99.92 ± 0.23	99.93 ± 0.23	99.99 ± 0.23

Table S4. The logP predicted with Chemdraw.

	logP
L1	2.25
L2	4.43
L3	3.14

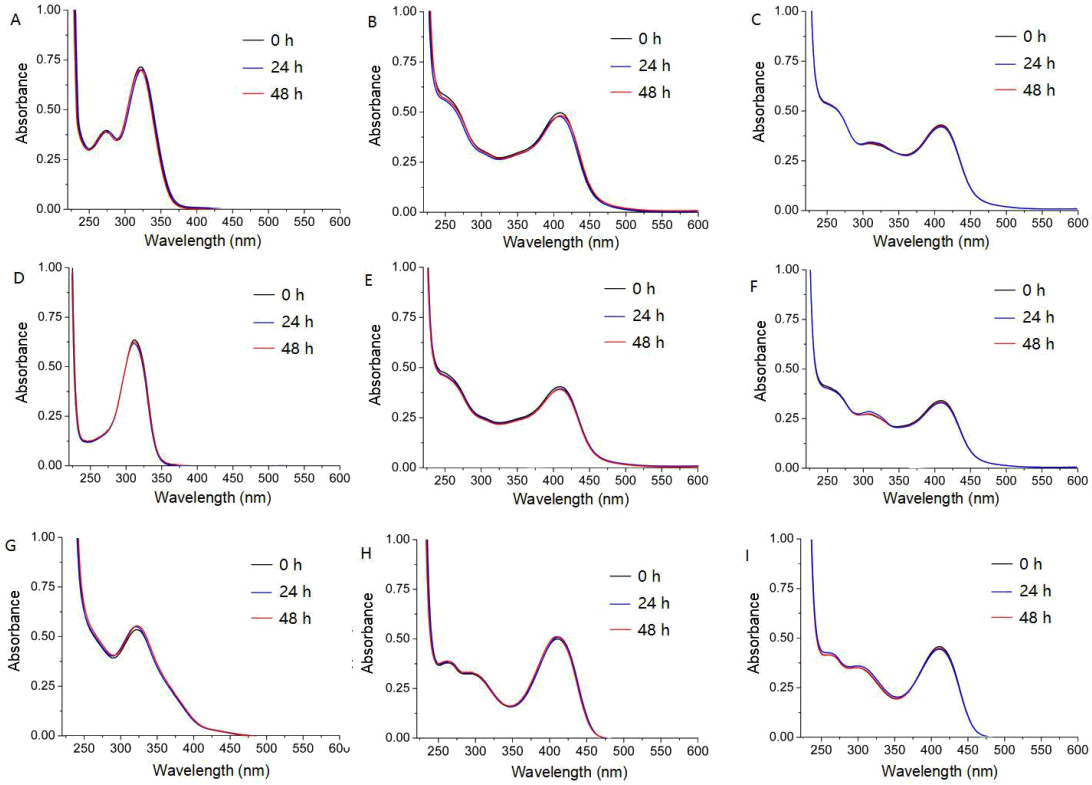
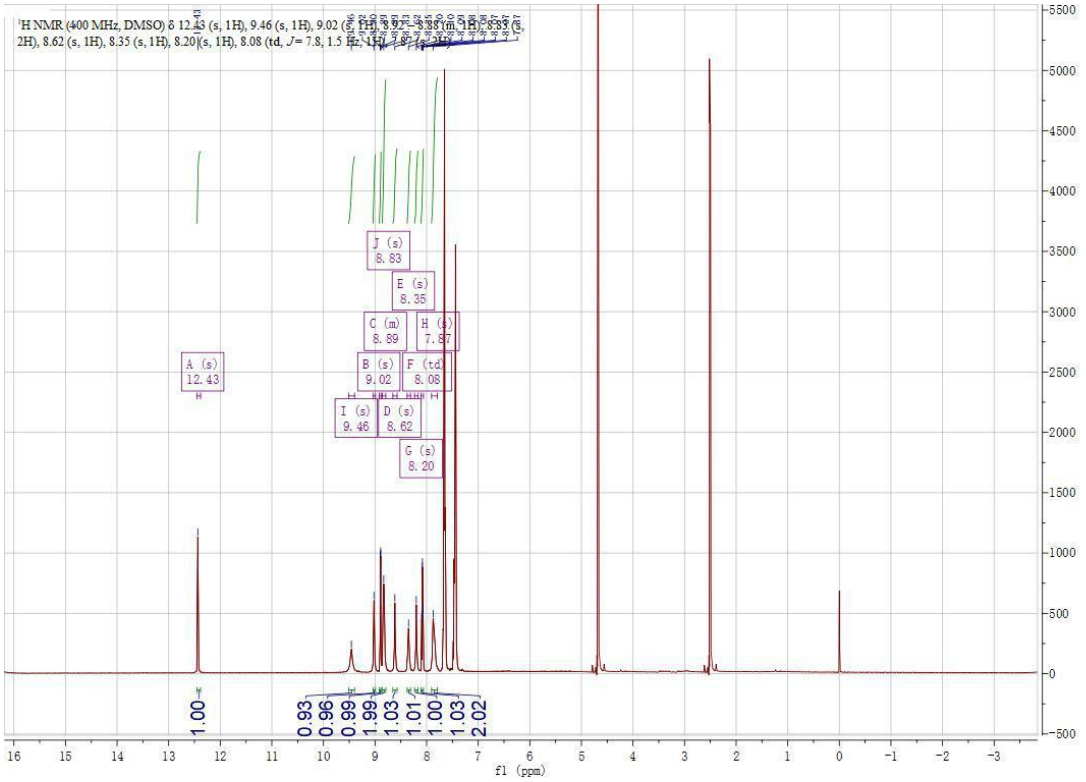
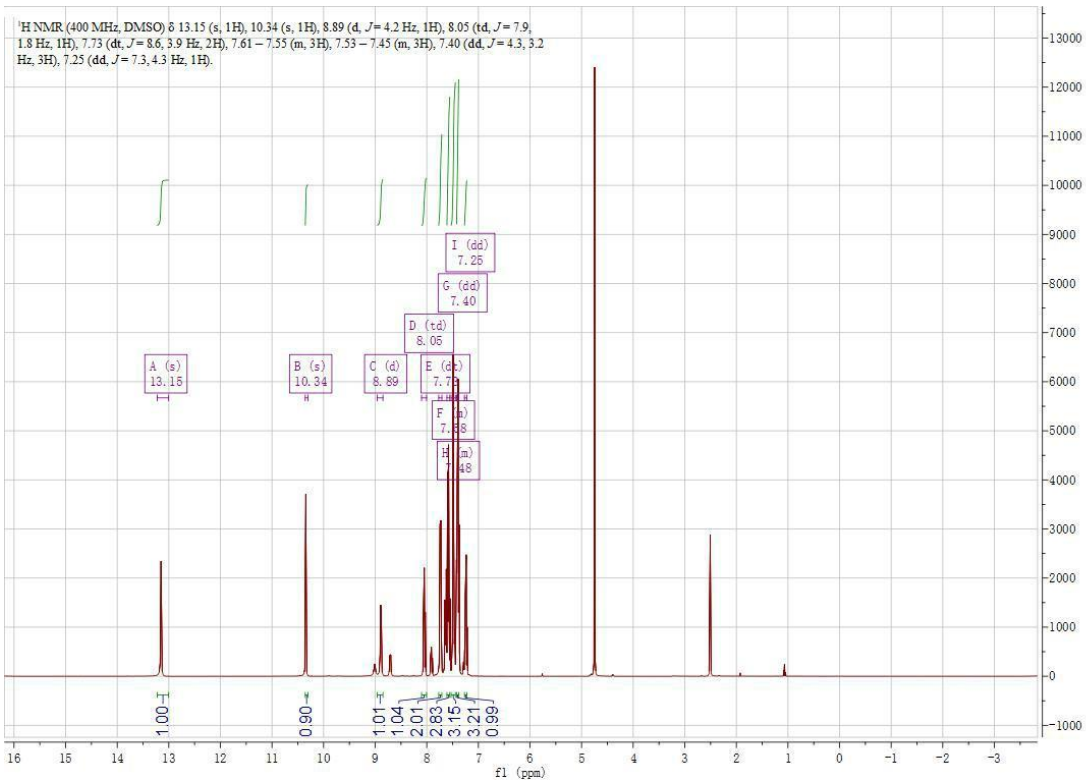


Fig. S1 The UV-Visible absorption of ligands and Ga complexes. A: L1 in 0.1% DMSO aqueous solution; B: C1 in 0.1% DMSO aqueous solution; C: C1 in Tris-HCl (0.05mol/L, pH=7.5) buffer solution; D: L2 in 0.1% DMSO aqueous solution; E: C2 in 0.1% DMSO aqueous solution; F: C2 in Tris-HCl (0.05mol/L, pH=7.5) buffer solution; G: L3 in 0.1% DMSO aqueous solution; H: C3 in 0.1% DMSO aqueous solution; I: C3 in Tris-HCl (0.05mol/L, pH=7.5) buffer solution.

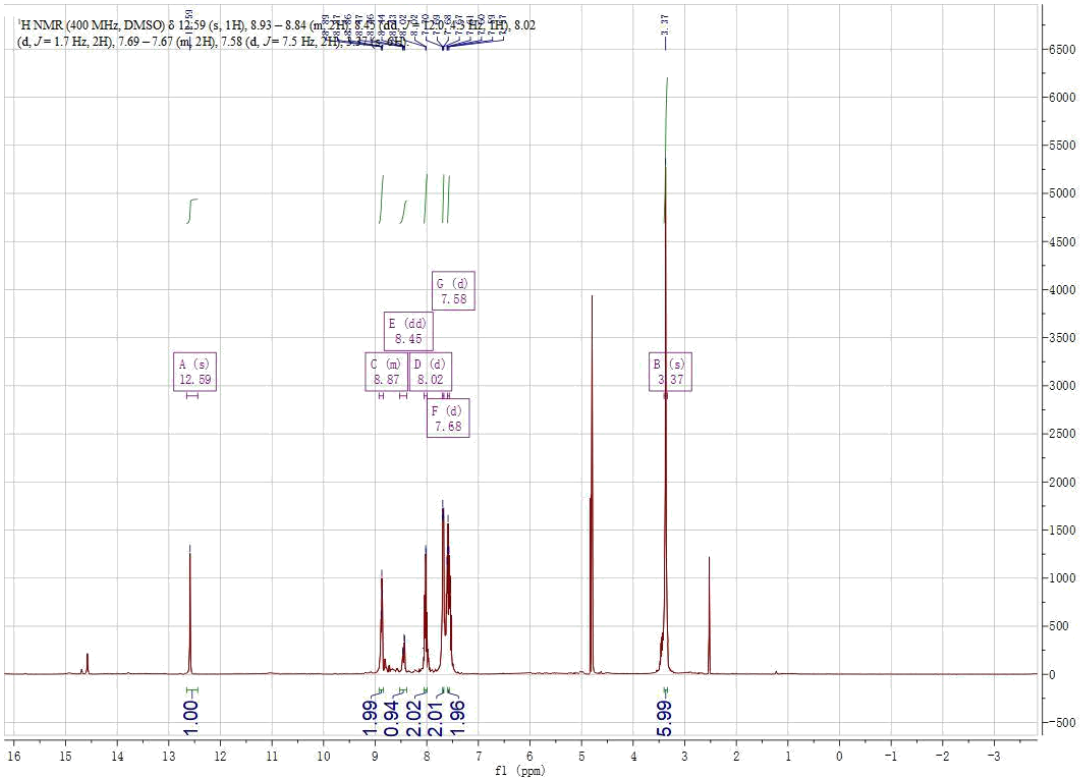
$_1$H Spectra and HRMS for target compounds in D_2O : DMSO-d_6 = 7 : 3, pH = 7.5 solution.



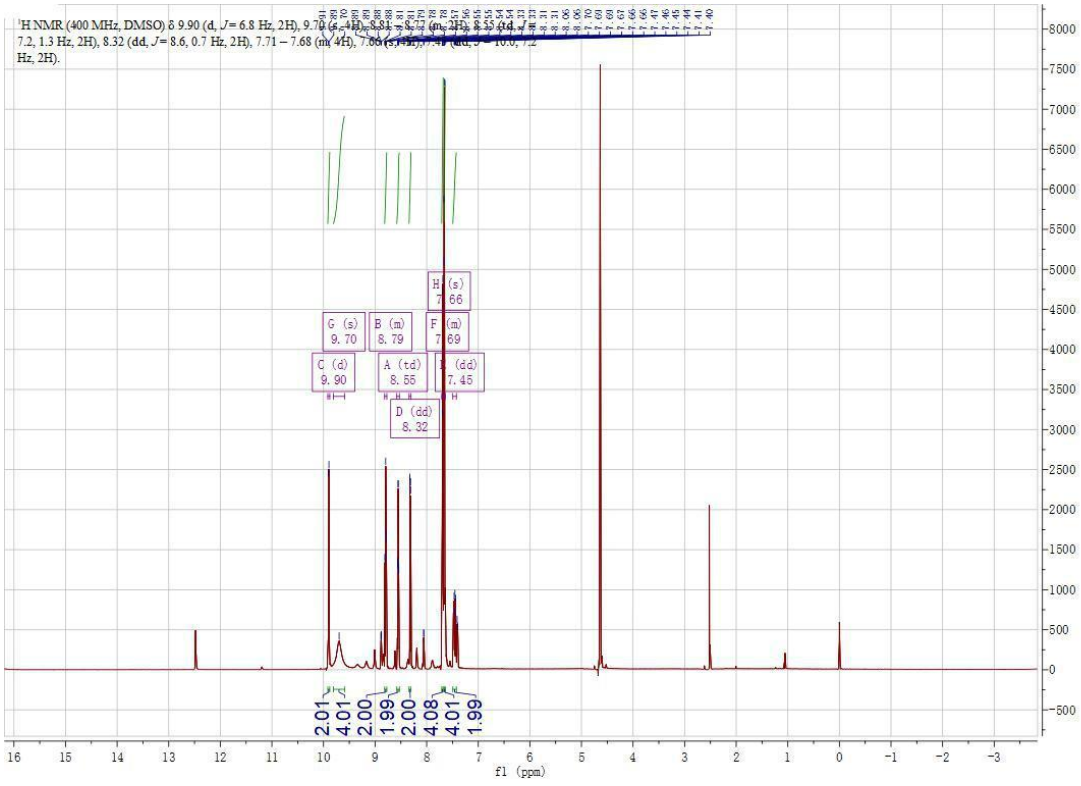
^{1}H NMR Spectra for L1



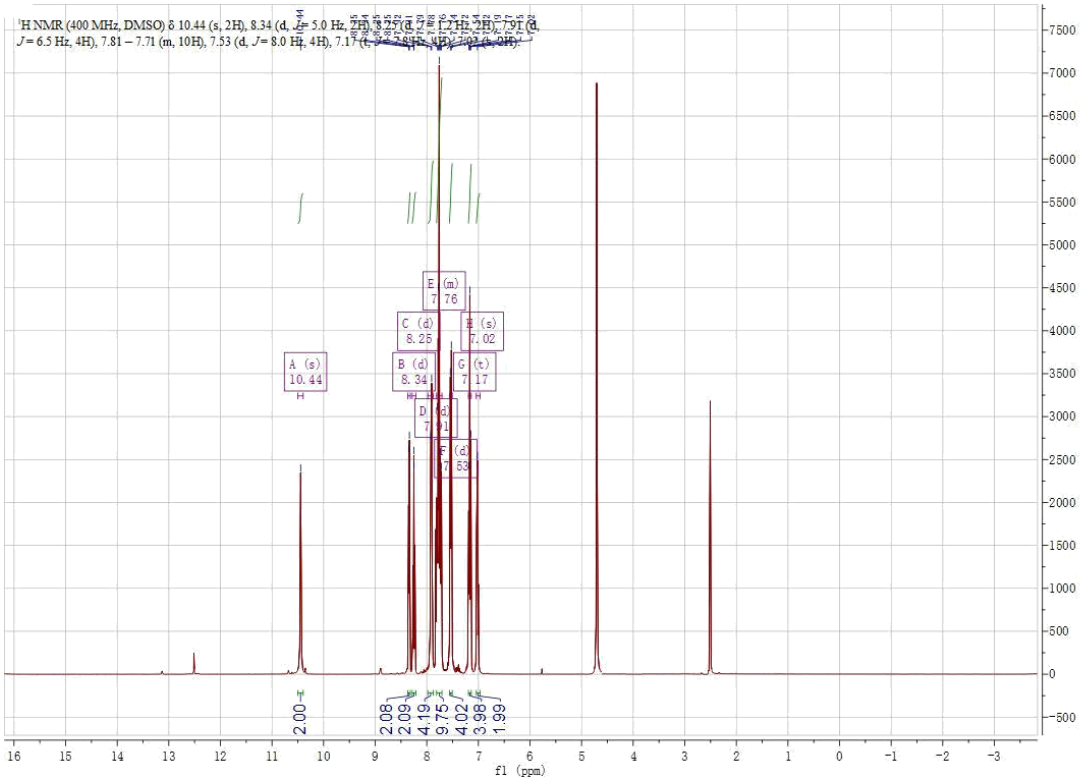
^{1}H NMR Spectra for L2



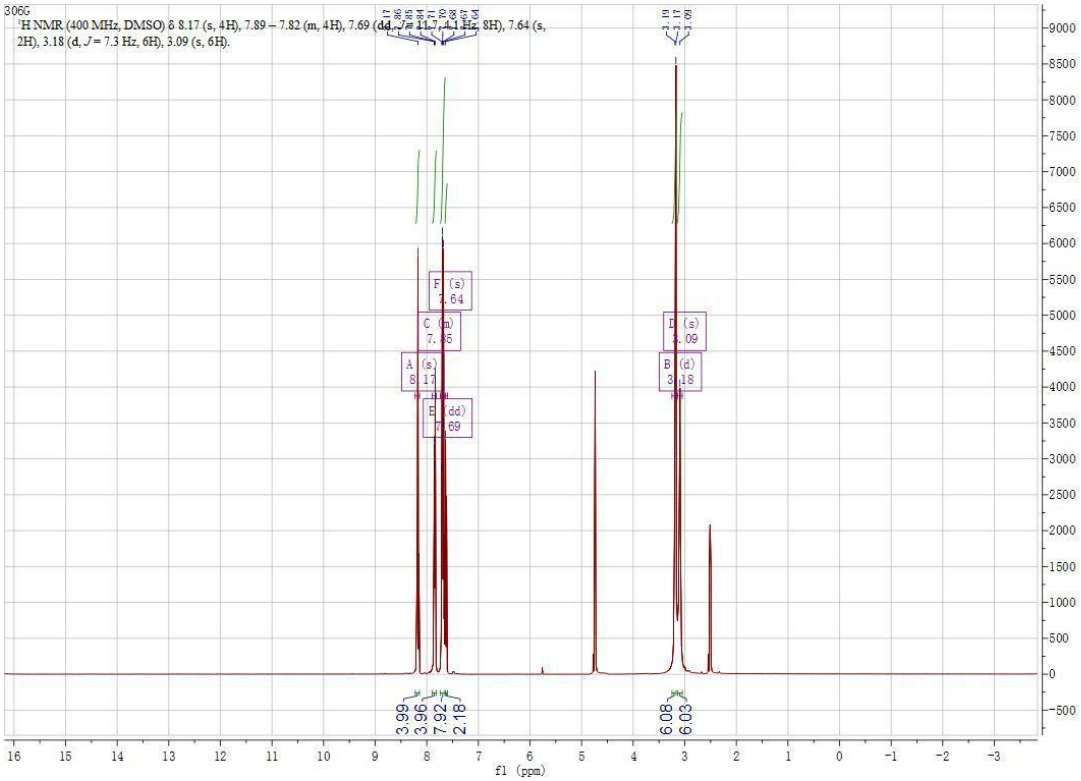
^{1}H NMR Spectra for L3



^{1}H NMR Spectra for C1



^{1}H NMR Spectra for C2



^{1}H NMR Spectra for C3