Supporting Information for

Original article

Discovery of novel sulfonamide substituted indolylarylsulfones as potent HIV-1 inhibitors with better safety profiles

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Animal husbandry conditions

Animals are group housed during acclimation and study. The animal room environment is controlled (target conditions: temperature 20 °C to 25 °C, relative humidity 40% to 70%, 12 hours' artificial light and 12 hours' dark). In the acute toxicity experiment, subacute toxicity experiment, and PK study, All the animals will be fasted for 12 hours before dosing. The age of Sprague-Dawley rats in PK study is 6-8 weeks, and the body weights range from 180 - 220 g. The age of Kunming mice in acute/subacute toxicity study is 3-4 weeks, and the body weights are about 20 g.

***In vivo* pharmacokinetics study**

The $\mathbf{R_{10}L_4}$ (14.56 mg) was dissolved in a mixture of 0.713 mL DMSO, 1.427 mL polyethylene glycol-15 hydroxystearate (Solutol) and 12.128 mL normal saline for a 1.00 mg/mL solution. Six male Sprague-Dawley rats were randomly divided into two groups to receive intravenous (2 $mg \cdot kg^{-1}$) or oral administration (10 $mg \cdot kg^{-1}$) of a test drug. Blood samples of the intravenous group were collected from the sinus jugularis into heparinized centrifugation tubes at 5 min, 15 min, 30 min, 1 h, 2 h, 4 h, 8 h, and 24 h after dosing, and blood samples of the oral administration group were collected at 15 min, 30 min, 1 h, 2 h, 4 h, 8 h, and 24 h after dosing (250 μL of blood each time). The blood samples were centrifuged at 6000 rpm for 3 min to separate plasma, which was stored at -20 °C for next steps of analysis. Upon LC-MS analysis, plasma samples were thawed, shaken for 30 seconds, and centrifuged at 4000 rpm for 0.5 min under 4°C. The internal standard solution contains 50 μg/L tolbutamide in a 1:1 mixture of MeOH and ACN. Then 40 μL of plasma, calibration standard, quality control and dilution quality control, blank sample were added to the 96-well plate respectively. Each sample was quenched with 200 μL of internal standard respectively (blank sample was quenched with 200 μL of ACN:MeOH = 1:1), and then the mixture was vortex-mixed for 5 min and centrifuged for 5 min at 14000 rpm, 4 °C. Subsequently, 100 μL supernatant was transferred to another clean 96-well plate and diluted with 100 μL of ACN, vortex-mixed for 5 min and centrifuged for 5 min at 800 rpm, 4 °C, then injected for LC-MS/MS analysis. All samples were quantified with an LC-MS/MS-AR Triple Quad 6500+ (SCIEX, USA) and the liquid phase system was ExionLC. The mobile phase was 0.1% formic acid-water/ACN with gradient elute at a

flow rate of 0.8 mL/min (total time 2 min), and the test wavelength was 225 nm. All blood samples were centrifuged in an Eppendorf 5424R centrifuge and quantified with an LC-MS/MS-AR Triple Quad 6500+ (SCIEX, USA). Pharmacokinetic parameters were calculated by WinNolin 8.2 software.

Acute Toxicity Experiment

A group of Kunming mice (three male and three female) was supplied by the Animal Experimental Center of Shandong University. The mice were fasted for 12 h; then, a suspension of $\mathbf{R_{10}L_4}$ in 0.5% CMC-Na and 3% DMSO at the concentration of 100 mg·mL^{-1} was administered intragastrically to provide a dose of 800 mg·kg^{-1}. Experimental group is consisted of six mice (three males and three females).

Subacute Toxicity Experiment

Another batch of three male and three female Kunming mice was randomly divided into four groups (n = 3): male test group, female test group, male vehicle group, and female vehicle group. All mice were deprived of feed for 12 h and then the mice in the test groups were given 50 mg· kg^{-1} p.o. of $\mathbf{R_{10}L_4}$ once every other day for 14 days (D0, D2, D4, D6, D8, D10, and D12), while the mice in control groups received the same volume of blank solution. The mice were weighed before each dosing. All the mice were dissected after euthanasia at D14, and the heart, liver, spleen, lung, and kidney were extracted. These organs were sliced and examined by HE staining.

Molecular docking simulation

The PDB files (6C0N, 6C0L, 2OPQ) are downloaded from Protein Database Bank (rcsb.org). Protein preparation, ligand preparation and docking studies were performed by Schrödinger platform (Maestro version 13.2.128). Protein models are preprocessed, optimized, and minimized under default settings of Protein Preparation Workflow. Waters, ions and unrelated small molecules are deleted manually. Then ligand molecules in NNIBP of each model were used to locate the center of receptor grid boxes, and automatically removed in the established receptor grids. The structure of $\mathbf{R_{10}L_4}$ and **IAS-0** were prepared by LigPrep under default settings. Ligand docking

was operated by Glide XP (extra precision) module, under default settings and unadjusted van der Wall radii scaling. Upon completion, docking scores and interactions were shown in Schrödinger. 3D files are exported and visualized in Pymol (Version 2.5.2).

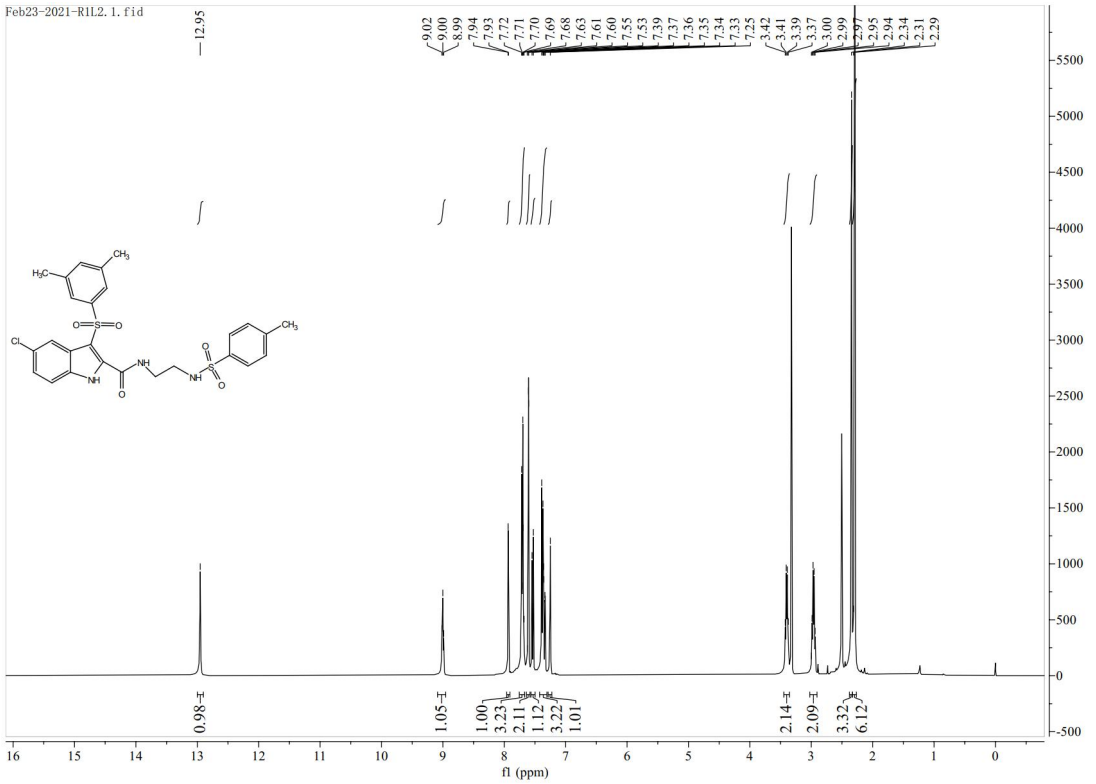
Table S1. RT inhibitory activity of target compounds.

Compound	IC_{50} ± SD (μM)[a]	Compound	IC_{50} ± SD (μM)
R_1L_2	0.075 ± 0.005	**R_1L_3**	0.160 ± 0.004
R_1L_4	0.140 ± 0.007	**R_1L_5**	0.130 ± 0.007
R_2L_2	0.094 ± 0.002	**R_2L_3**	0.130 ± 0.002
R_2L_4	0.130 ± 0.003	**R_2L_5**	0.160 ± 0.000
R_3L_2	0.100 ± 0.007	**R_3L_3**	0.120 ± 0.005
R_3L_4	0.150 ± 0.013	**R_3L_5**	0.160 ± 0.016
R_4L_2	0.066 ± 0.018	**R_4L_3**	0.100 ± 0.005
R_4L_4	0.150 ± 0.009	**R_4L_5**	0.150 ± 0.012
R_5L_2	0.110 ± 0.032	**R_5L_3**	0.100 ± 0.003
R_5L_4	0.120 ± 0.003	**R_5L_5**	0.160 ± 0.002
R_6L_2	0.120 ± 0.011	**R_6L_3**	0.160 ± 0.016
R_6L_4	0.150 ± 0.015	**R_6L_5**	0.130 ± 0.009
R_7L_2	0.055 ± 0.002	**R_7L_3**	0.078 ± 0.013
R_7L_4	0.094 ± 0.003	**R_7L_5**	0.120 ± 0.011
R_8L_2	0.140 ± 0.015	**R_8L_3**	0.190 ± 0.035
R_8L_4	0.190 ± 0.017	**R_8L_5**	0.220 ± 0.017
R_9L_2	0.055 ± 0.006	**R_9L_3**	0.084 ± 0.011
R_9L_4	0.130 ± 0.014	**R_9L_5**	0.120 ± 0.015
$R_{10}L_2$	0.060 ± 0.009	**$R_{10}L_3$**	0.041 ± 0.009
$R_{10}L_4$	0.077 ± 0.009	**$R_{10}L_5$**	0.095 ± 0.012
$R_{11}L_2$	0.083 ± 0.007	**$R_{11}L_3$**	0.076 ± 0.019
$R_{11}L_4$	0.120 ± 0.015	**$R_{12}L_2$**	0.083 ± 0.011
$R_{12}L_3$	0.130 ± 0.016	**$R_{12}L_4$**	0.150 ± 0.017
$R_{13}L_2$	0.057 ± 0.012	**$R_{14}L_2$**	0.180 ± 0.000
IAS-0	0.018 ± 0.002	**EFV[b]**	0.030 ± 0.000

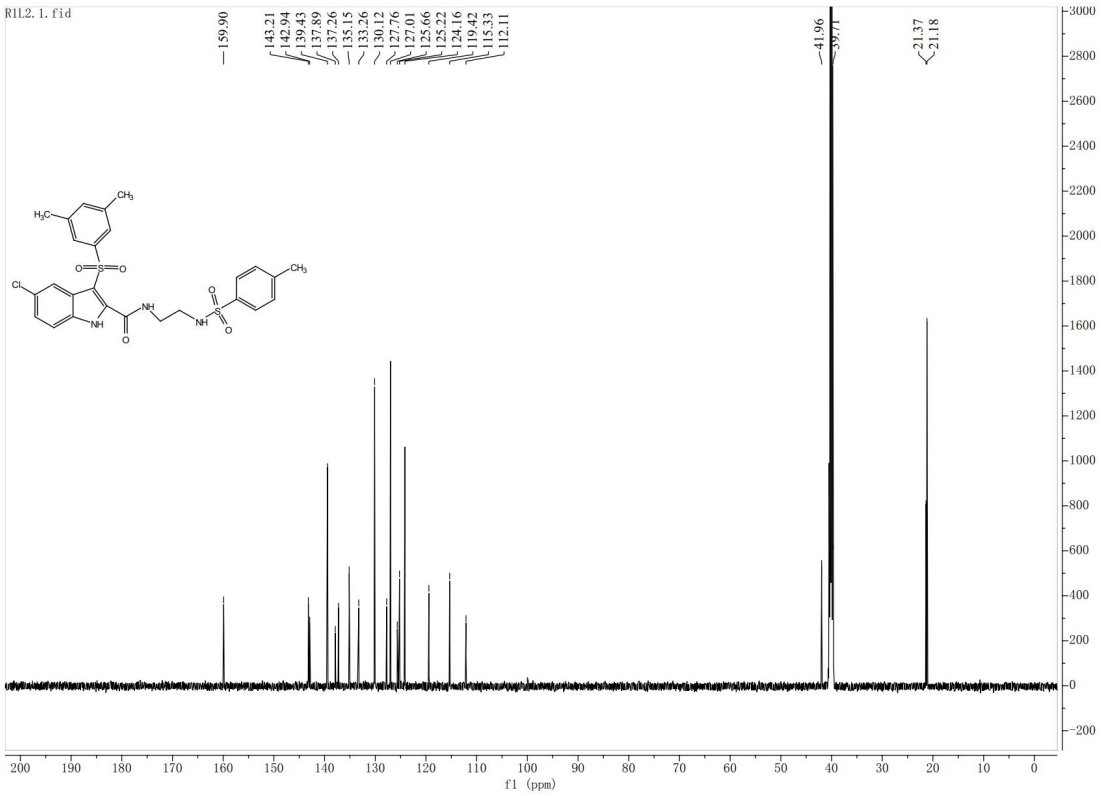
[a]IC_{50}: Compound concentration required to inhibit 50% incorporation of biotin-labeled UTP by HIV-1 (WT) RT. [b]All data were obtained from one batch with the same method.

^{1}H NMR and ^{13}C NMR spectra of final compounds

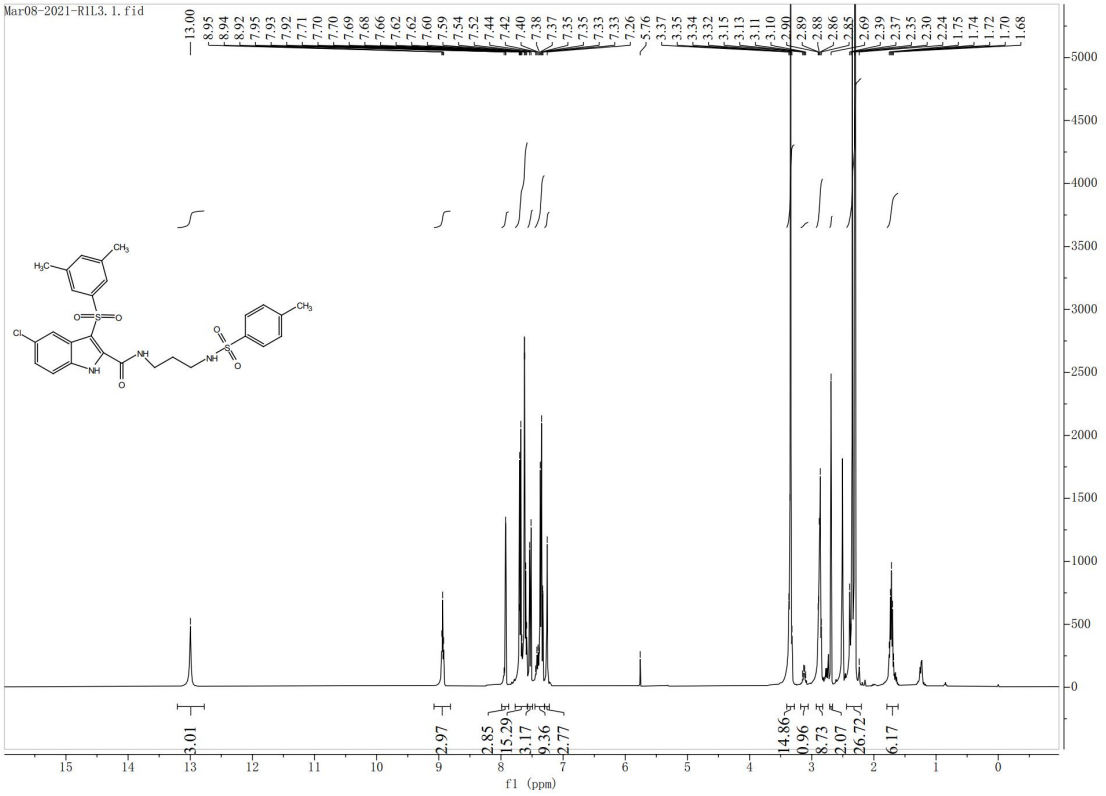
^{1}H NMR (600 MHz, DMSO-d_6) of **R_1L_2**



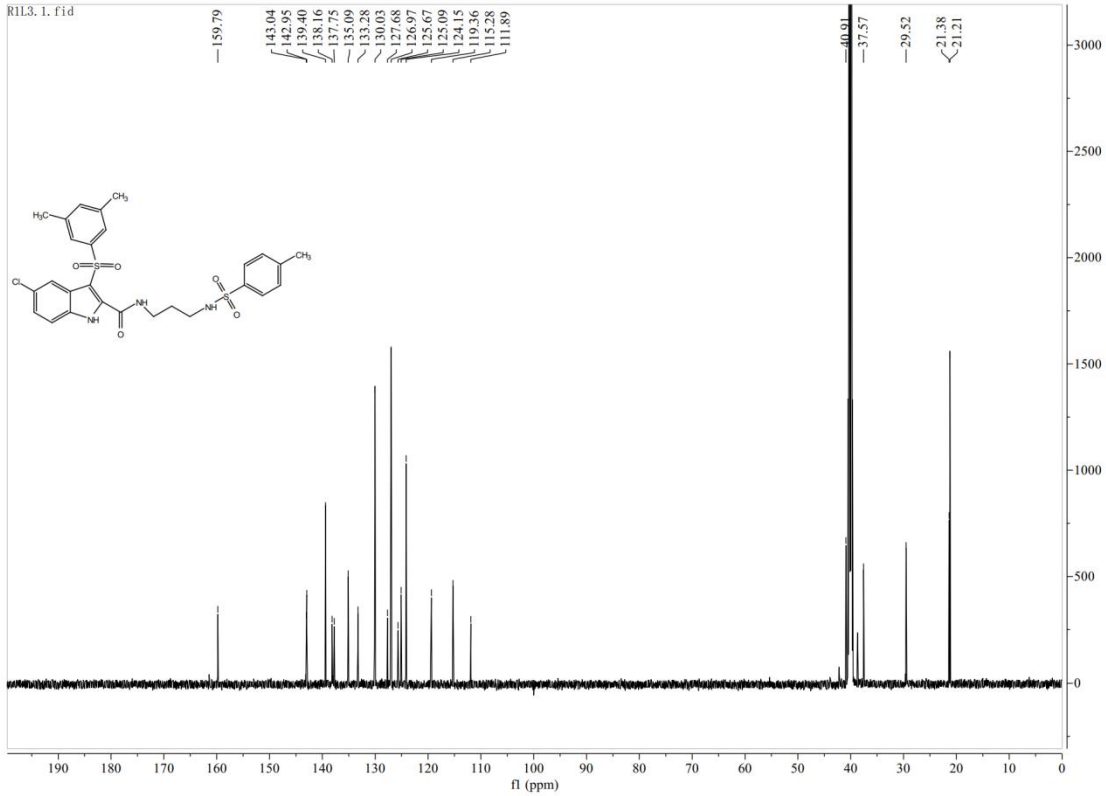
^{13}C NMR (150 MHz, DMSO-d_6) of **R_1L_2**



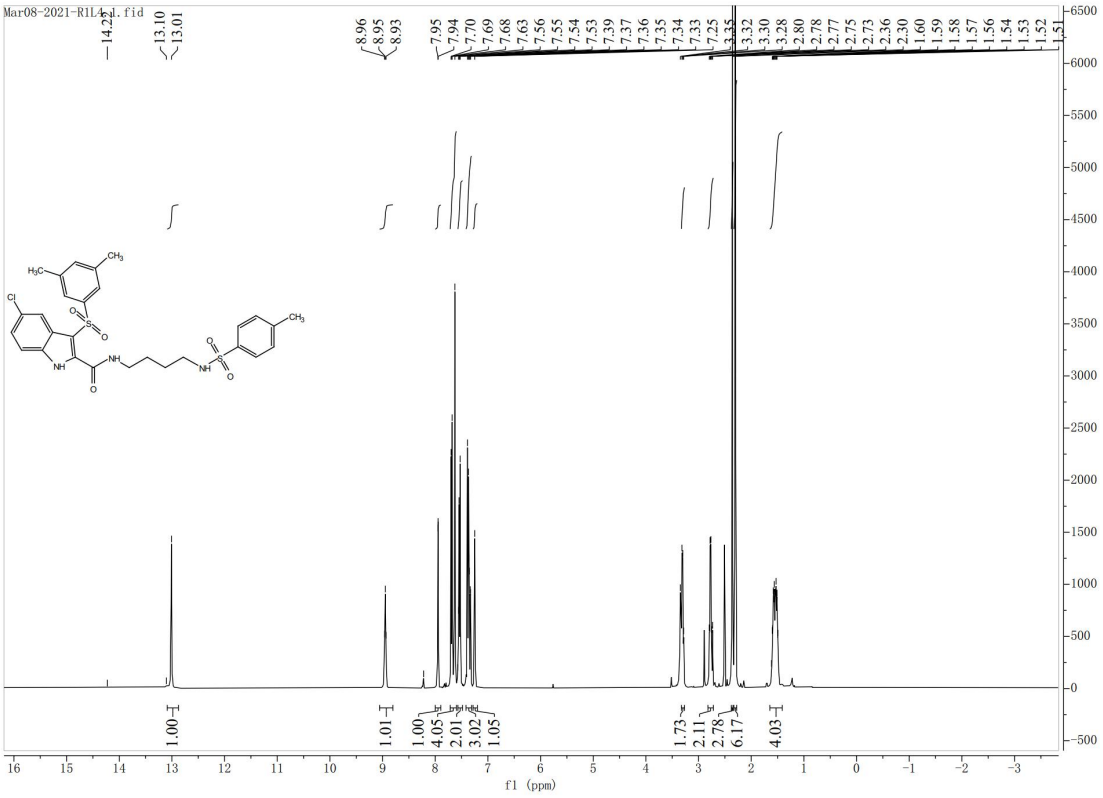
^{1}H NMR (600 MHz, DMSO-d_6) of **R_1L_3**



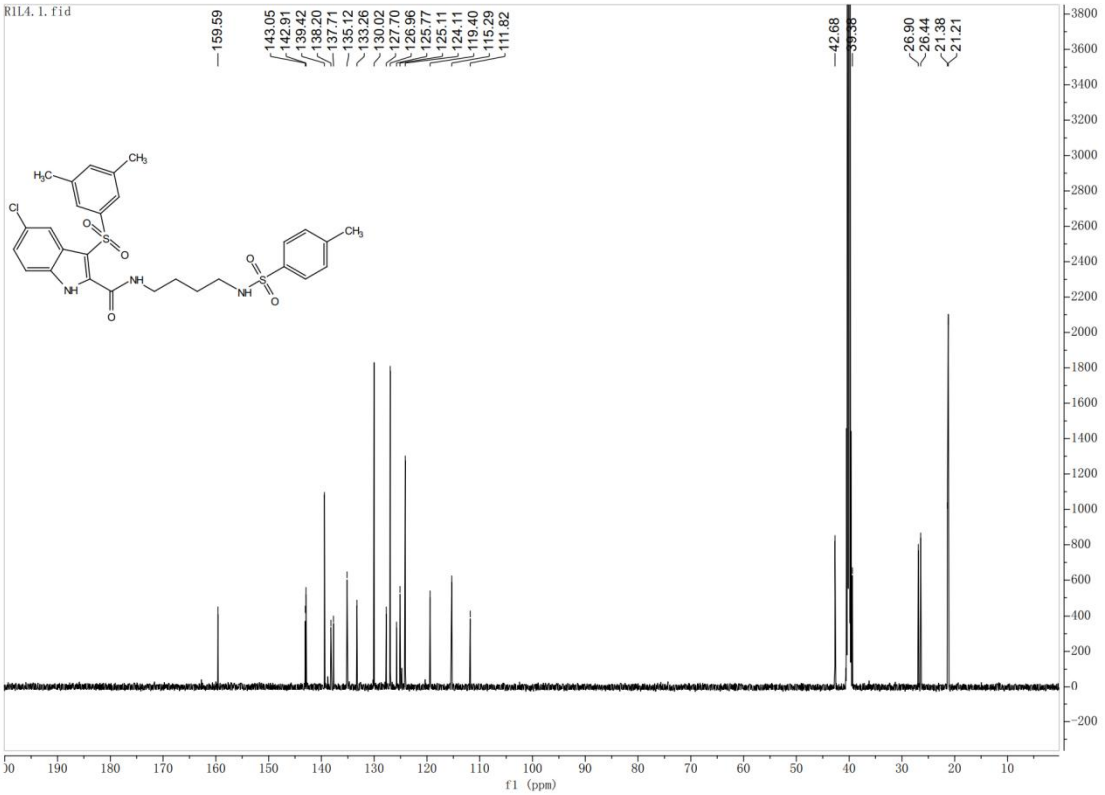
^{13}C NMR (150 MHz, DMSO-d_6) of **R_1L_3**



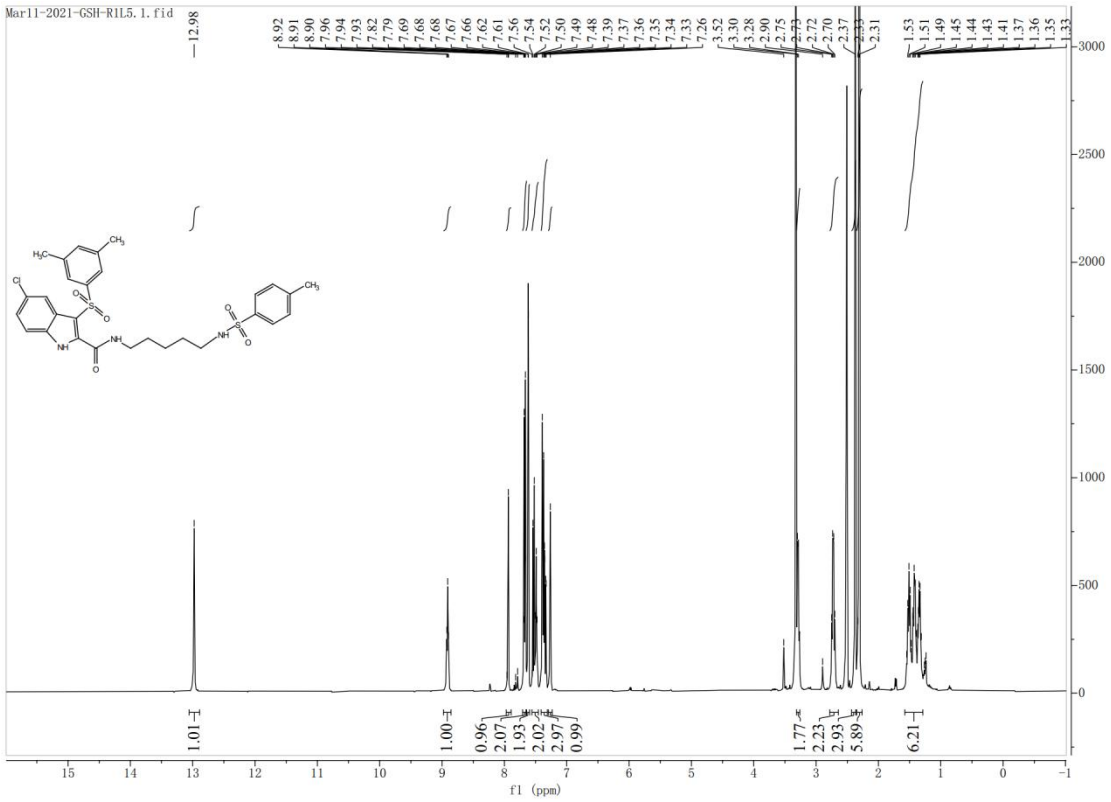
^{1}H NMR (600 MHz, DMSO-d_6) of **R_1L_4**



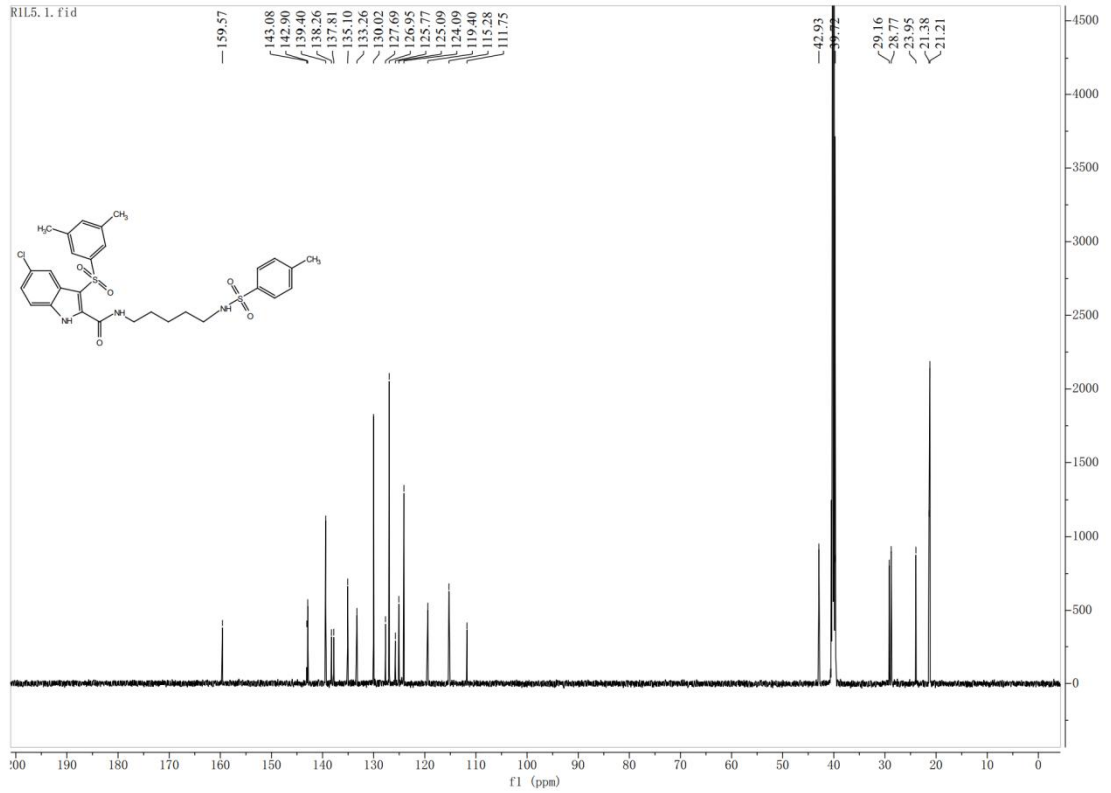
^{13}C NMR (150 MHz, DMSO-d_6) of **R_1L_4**



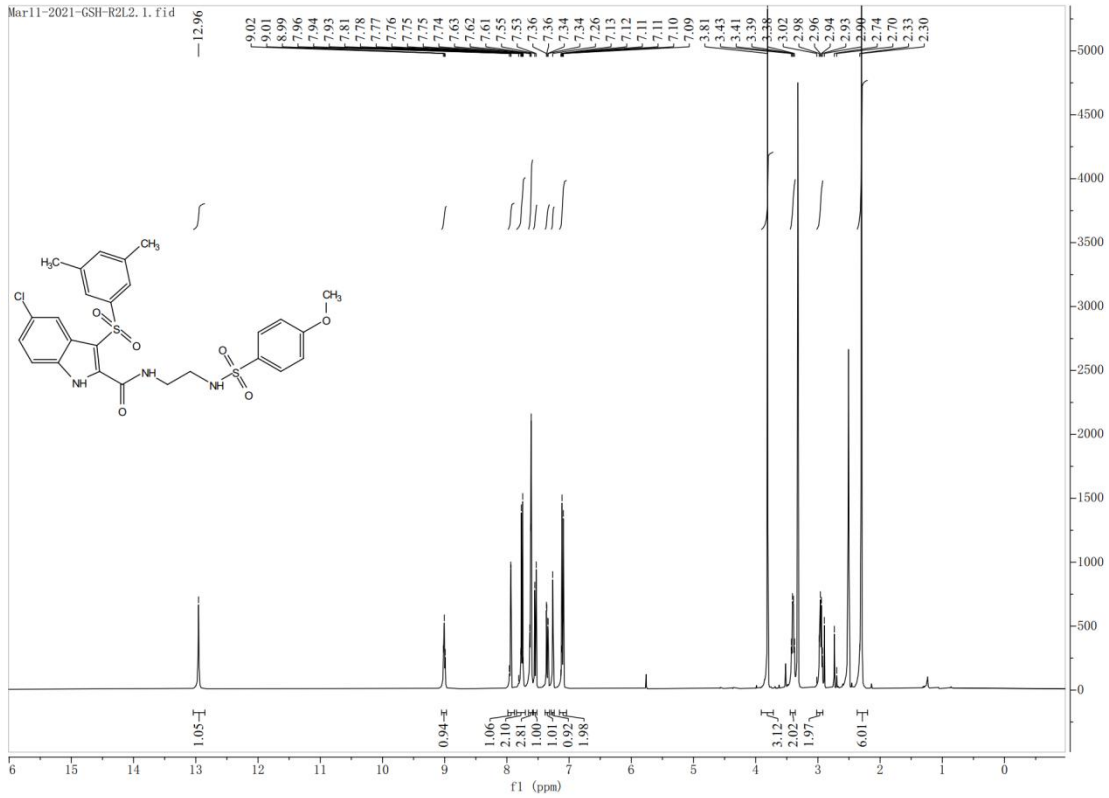
^{1}H NMR (600 MHz, DMSO-d_6) of **R_1L_5**



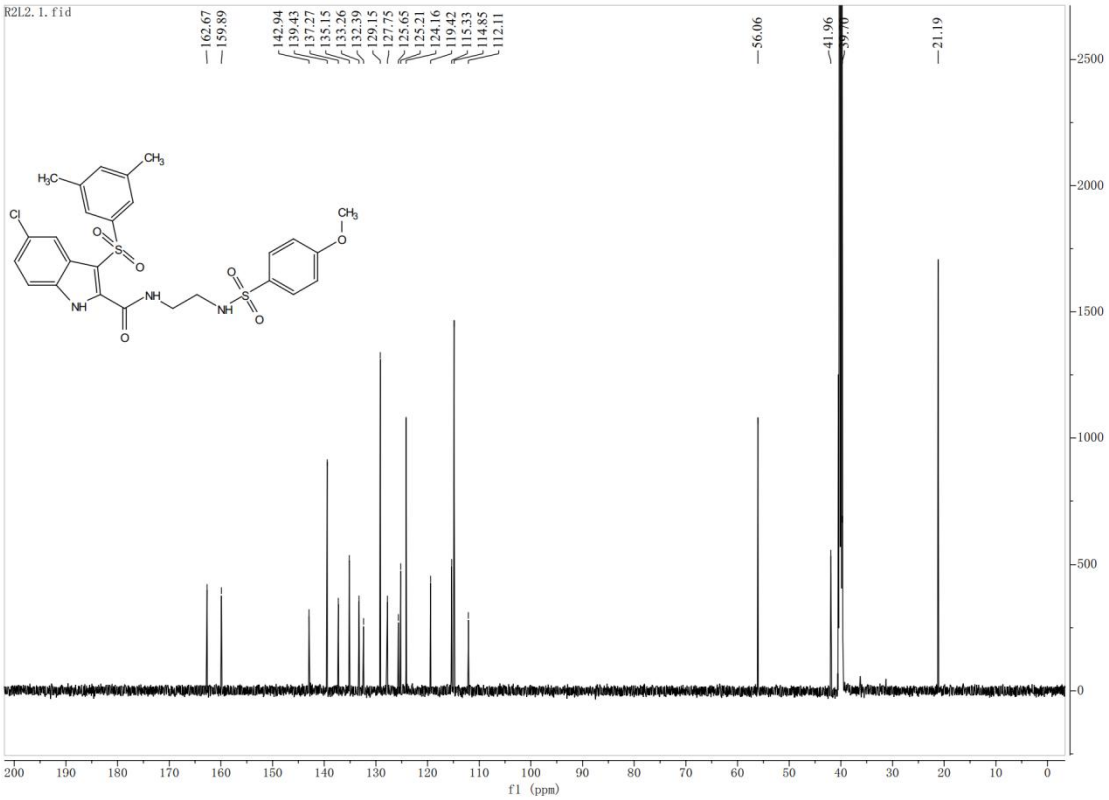
^{13}C NMR (150 MHz, DMSO-d_6) of **R_1L_5**



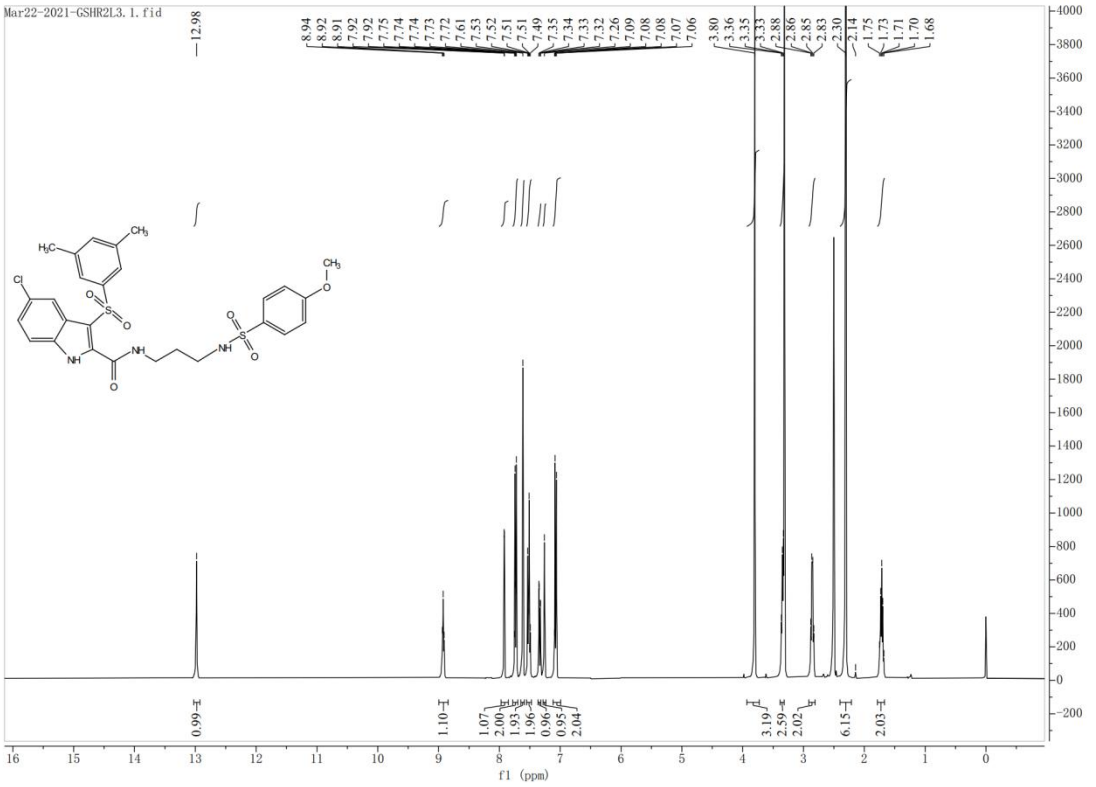
^{1}H NMR (600 MHz, DMSO-d_6) of **R_2L_2**



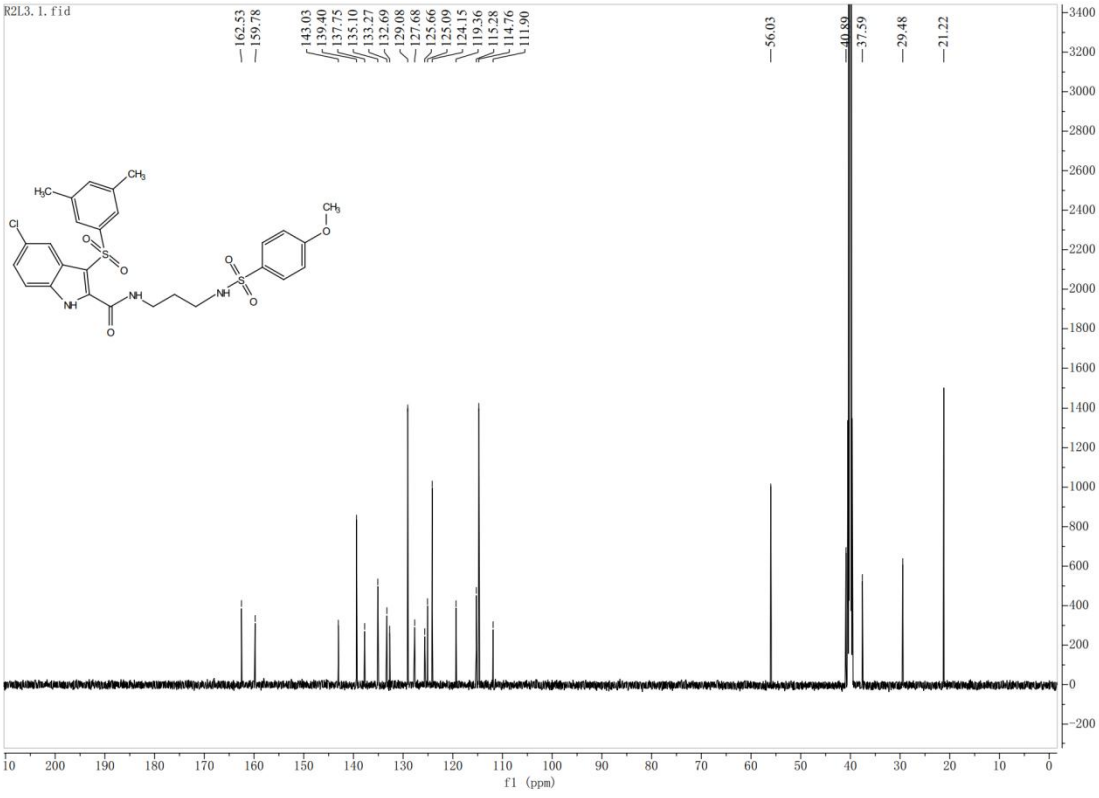
^{13}C NMR (150 MHz, DMSO-d_6) of **R_2L_2**



^{1}H NMR (600 MHz, DMSO-d_6) of **R_2L_3**



^{13}C NMR (150 MHz, DMSO-d_6) of **R_2L_3**



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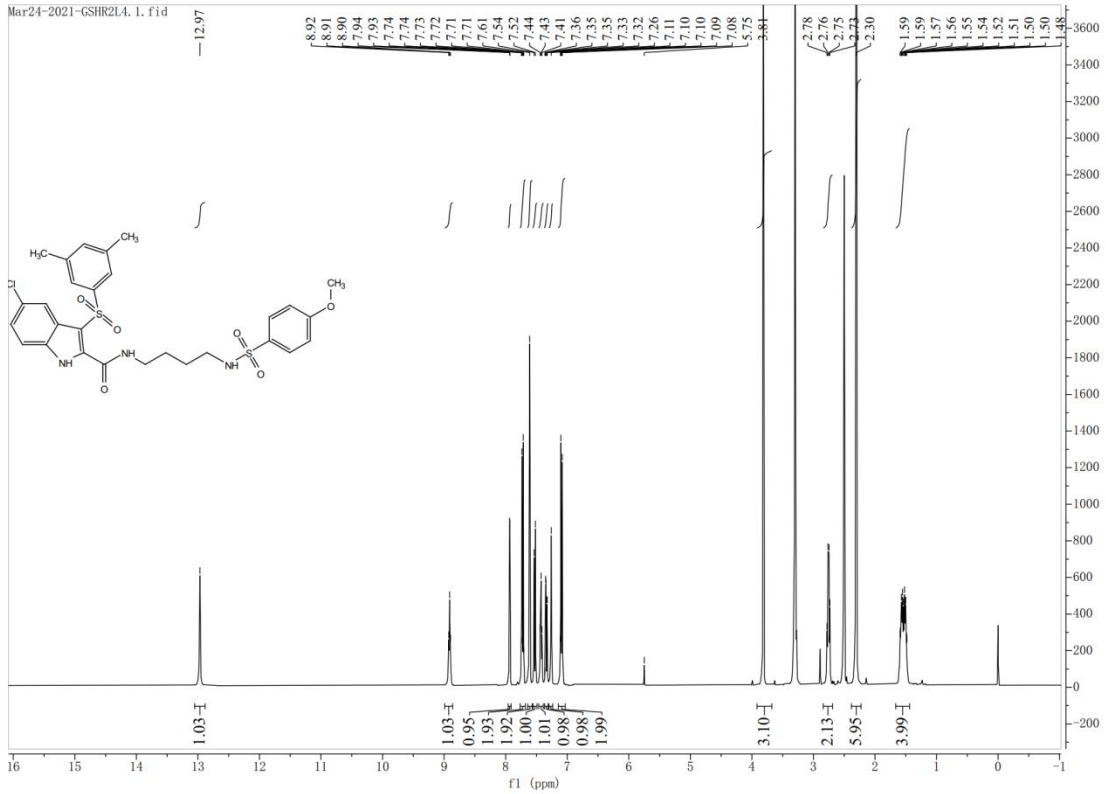

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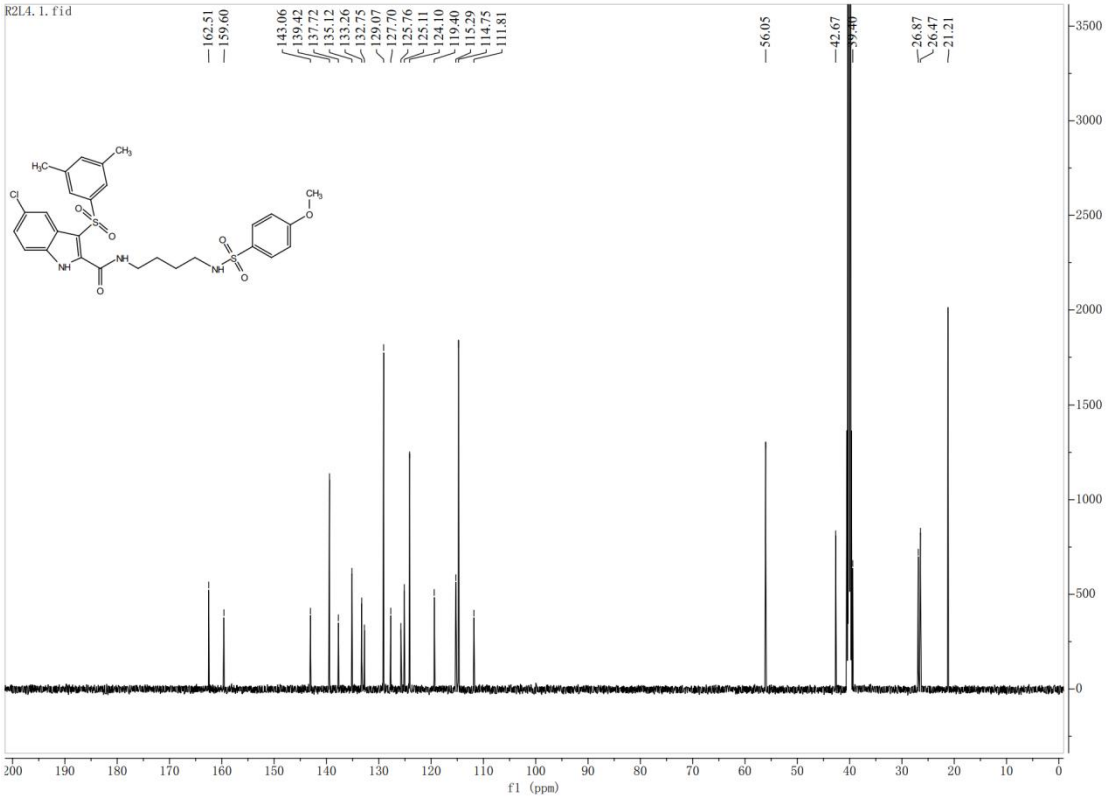
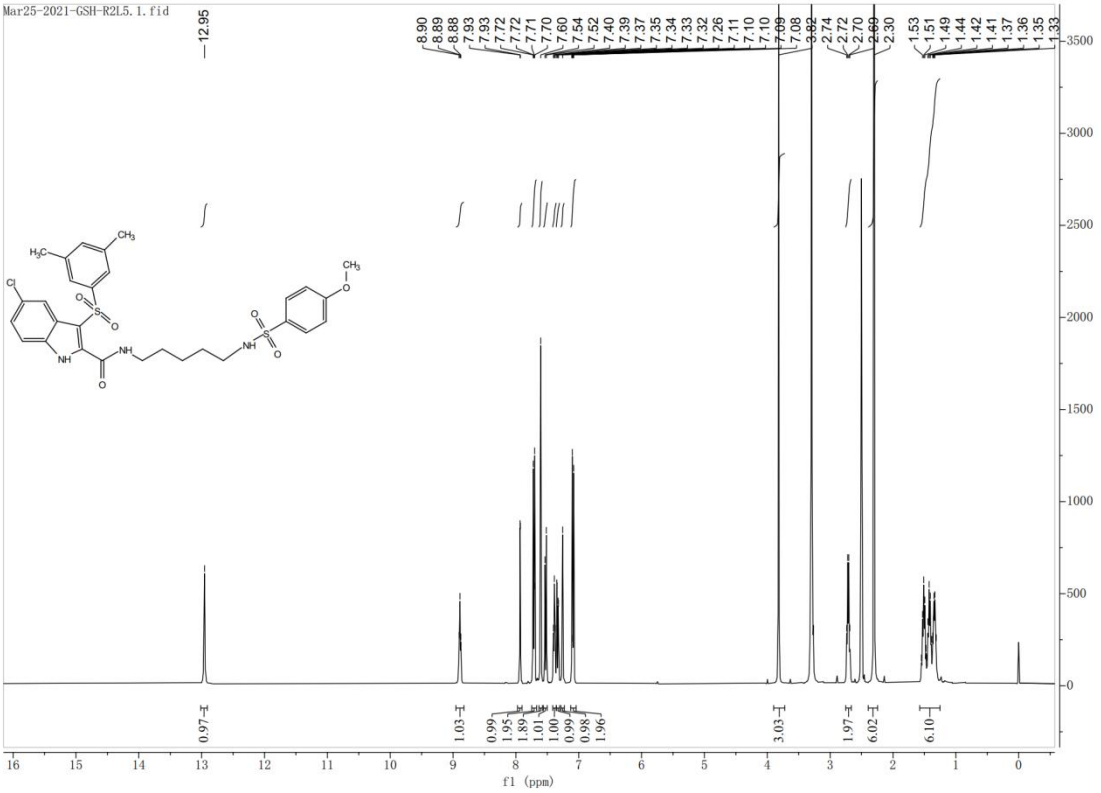
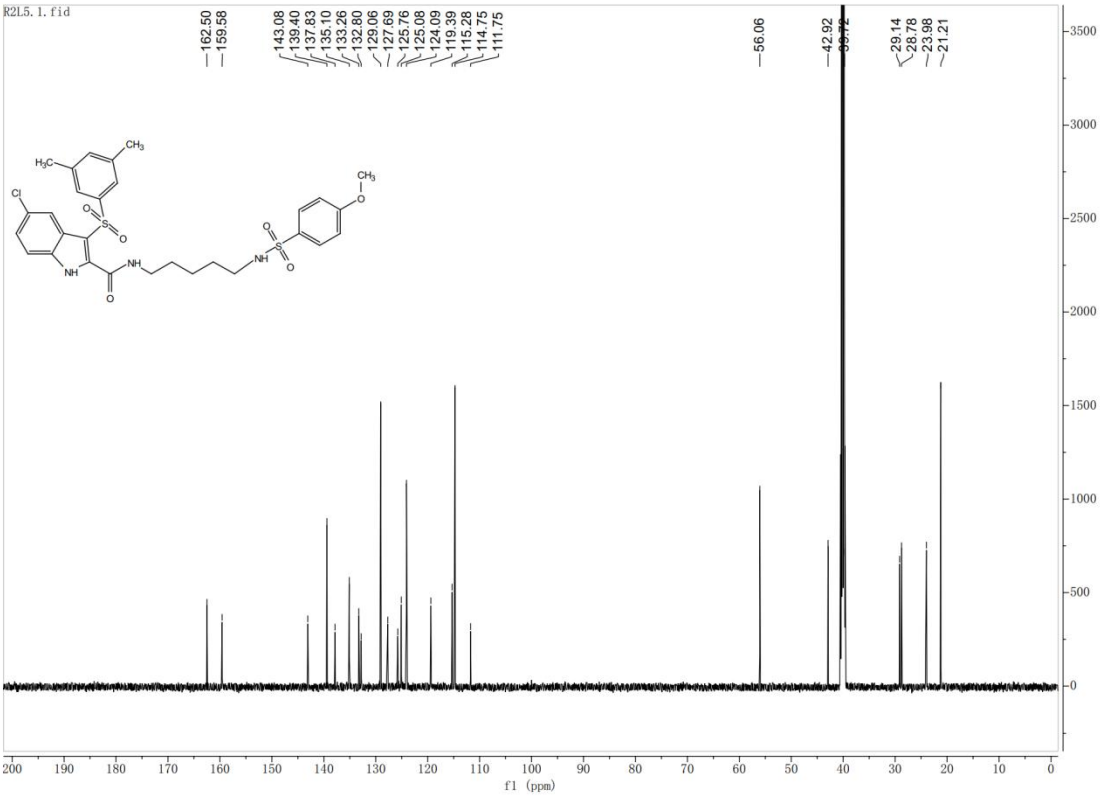


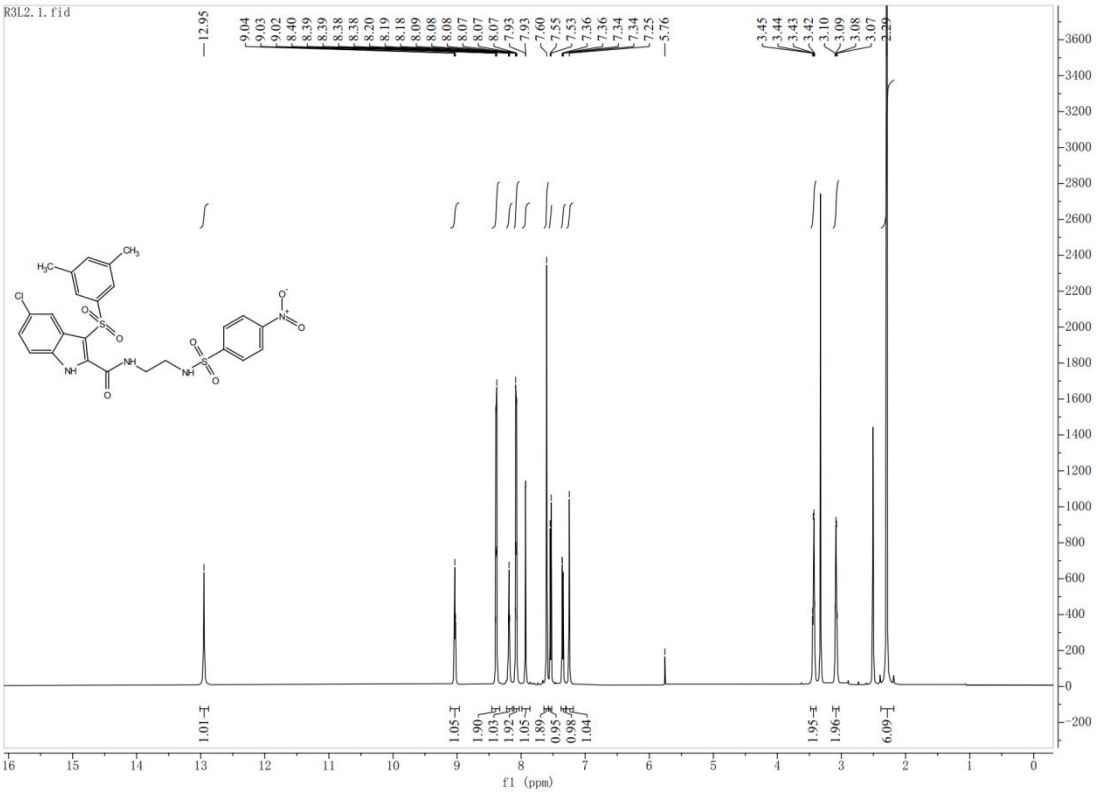
^{1}H NMR (600 MHz, DMSO-d_6) of **R_2L_5**



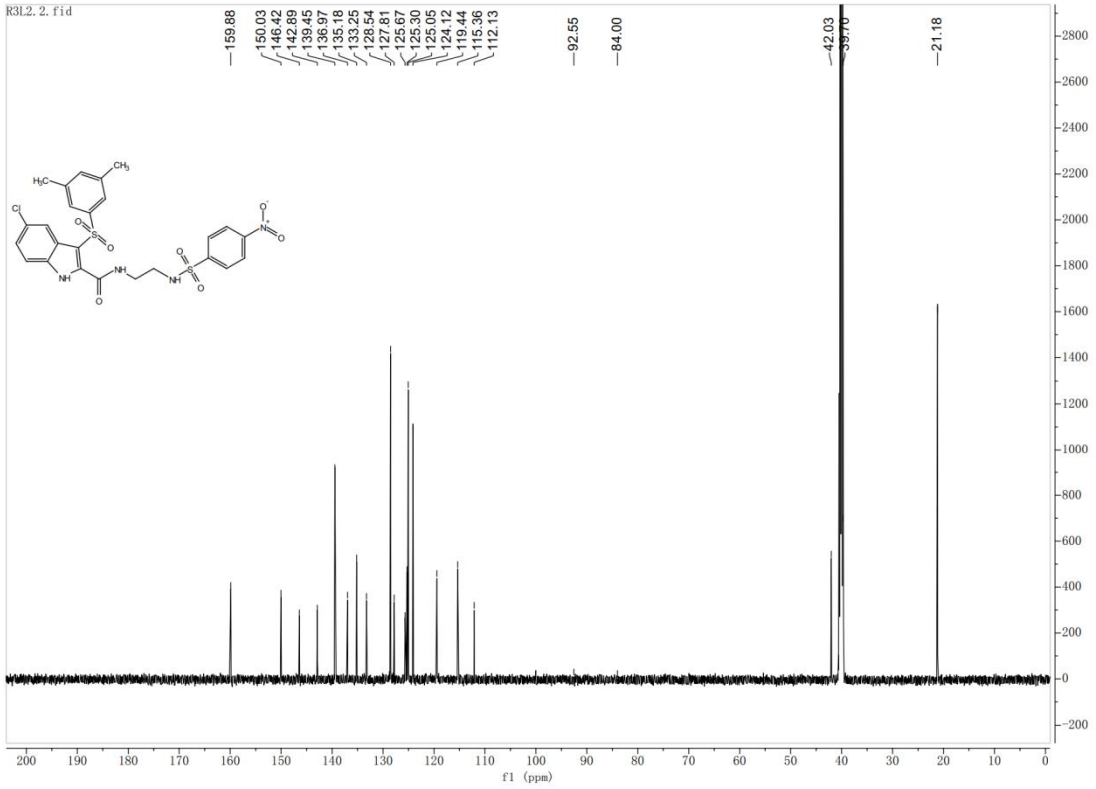
^{13}C NMR (150 MHz, DMSO-d_6) of **R_2L_5**



^{1}H NMR (600 MHz, DMSO-d_6) of **R_3L_2**



^{13}C NMR (150 MHz, DMSO-d_6) of **R_3L_2**



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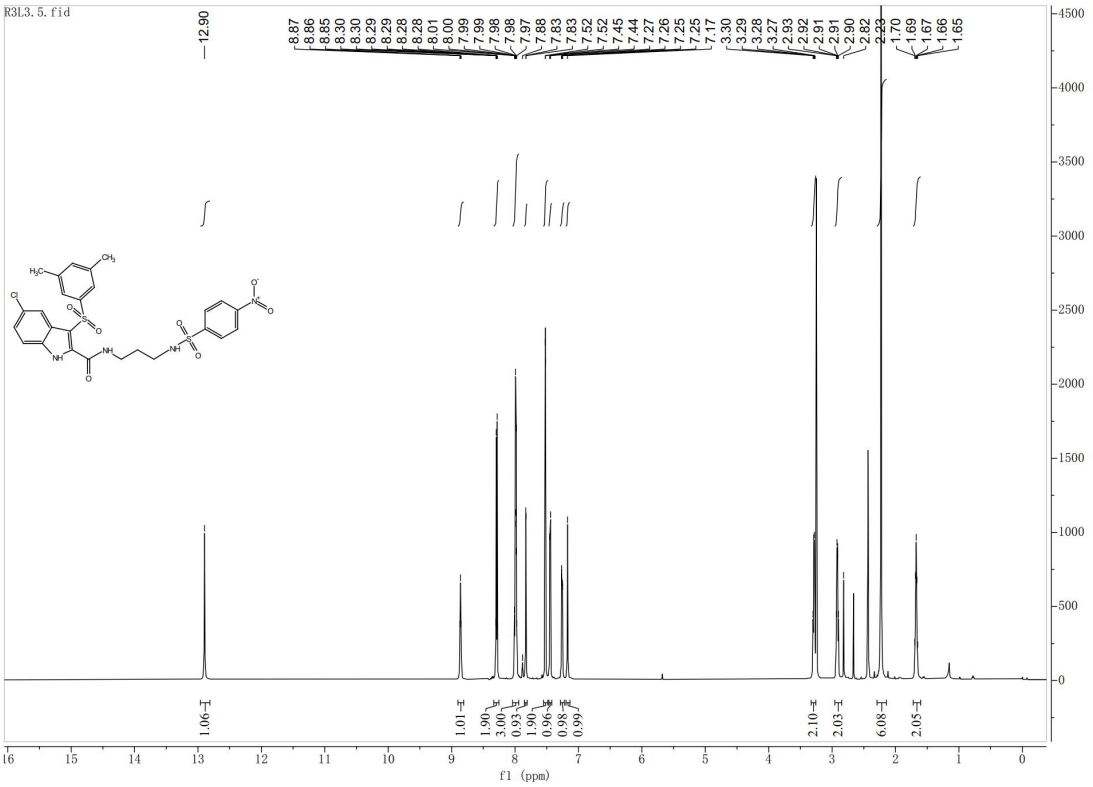

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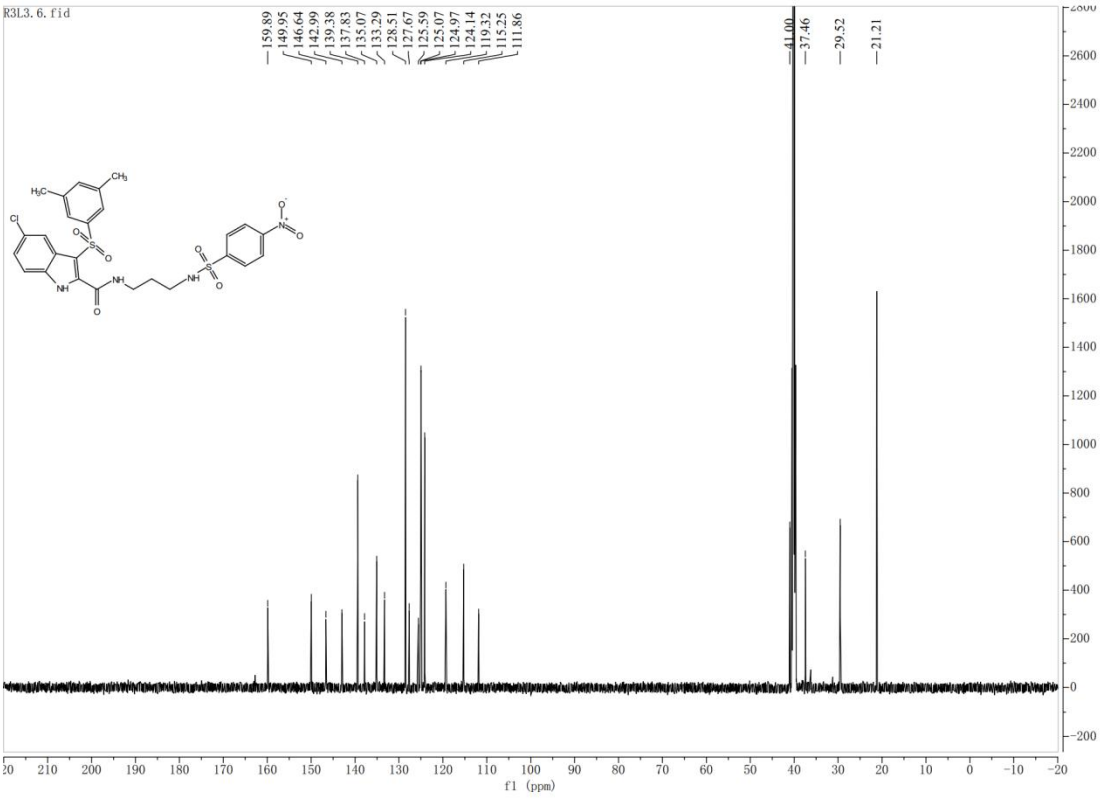

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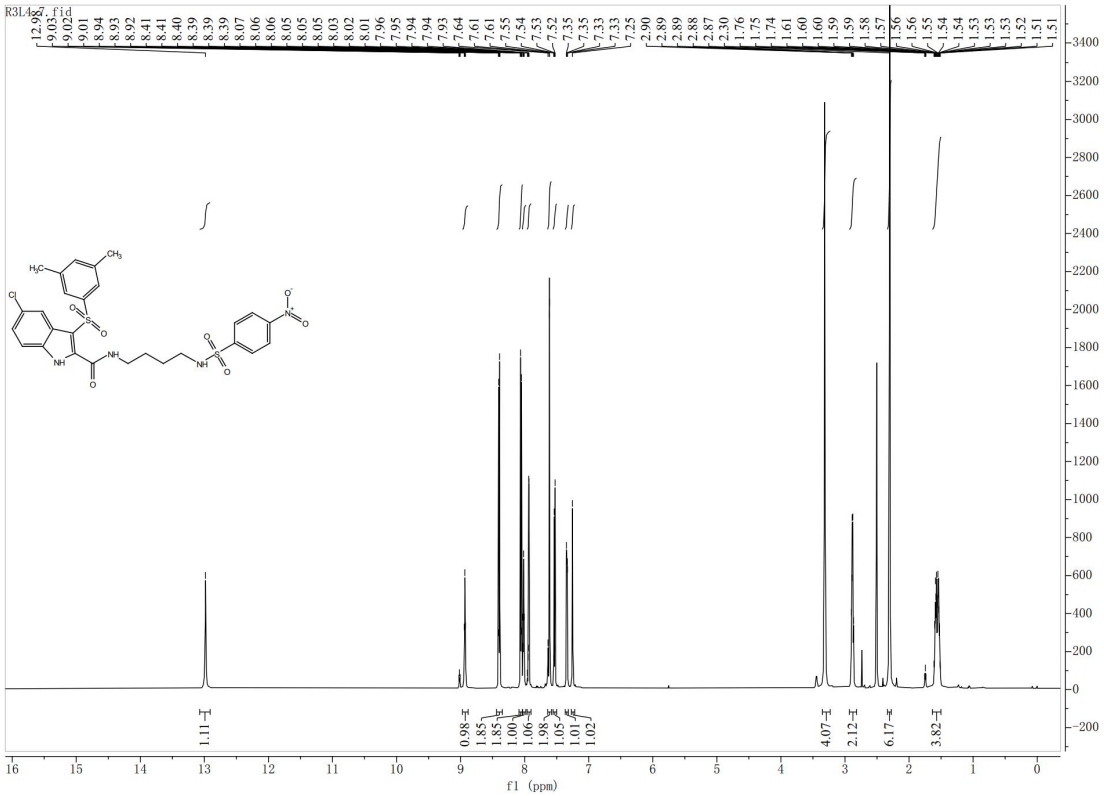

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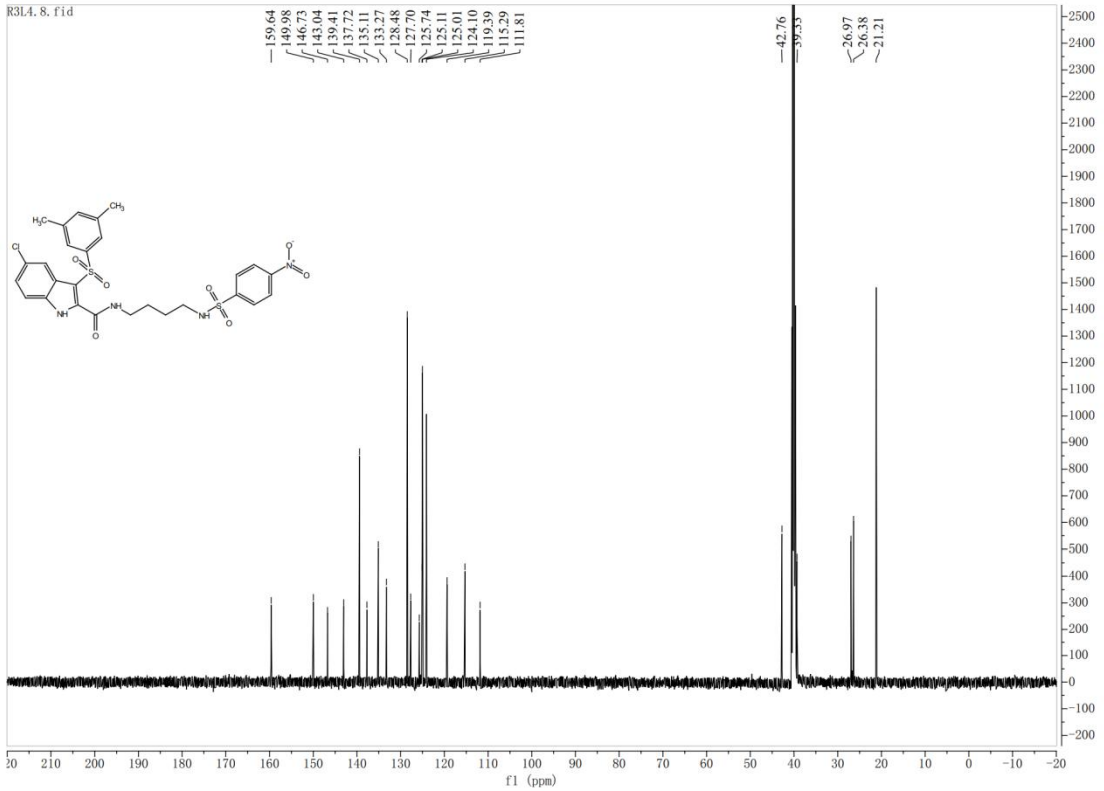
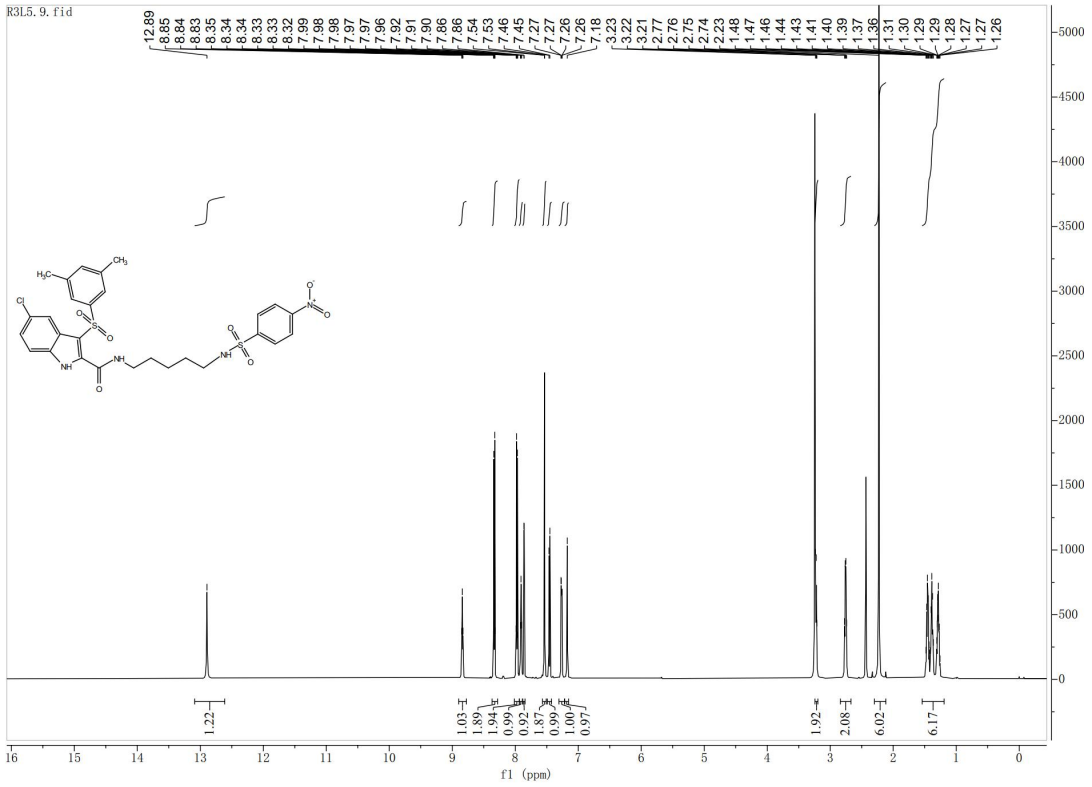


^{1}H NMR (600 MHz, DMSO-d_6) of **R_3L_5**



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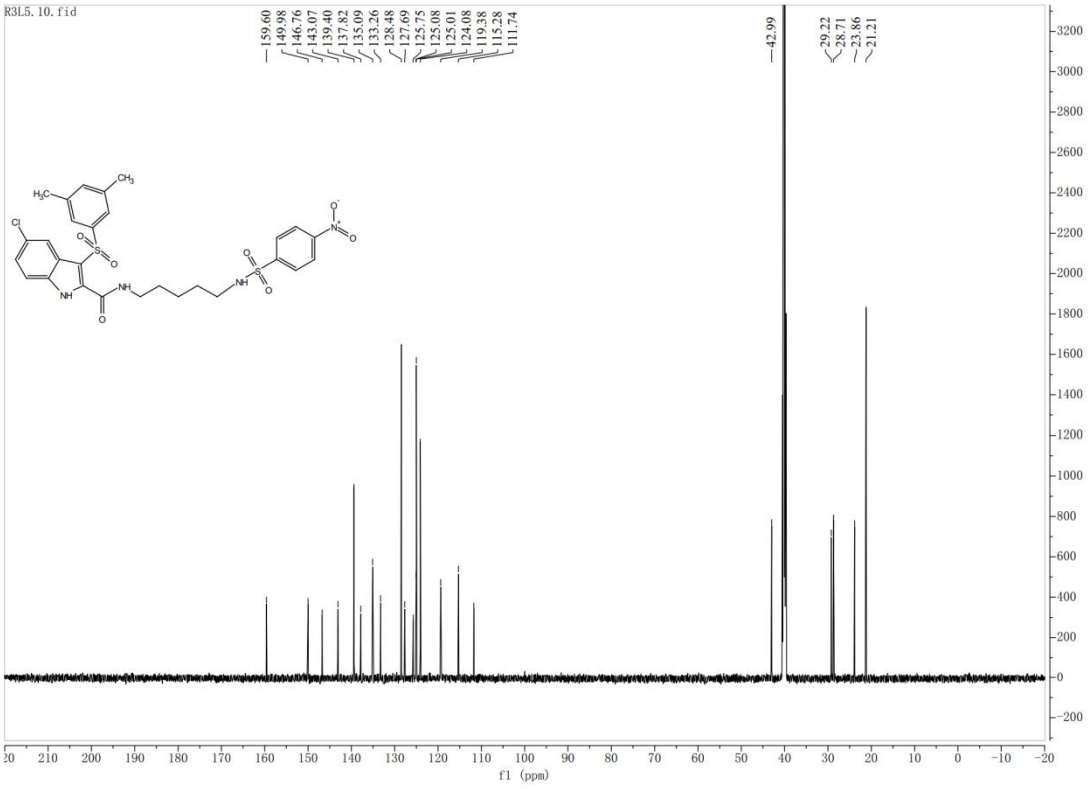

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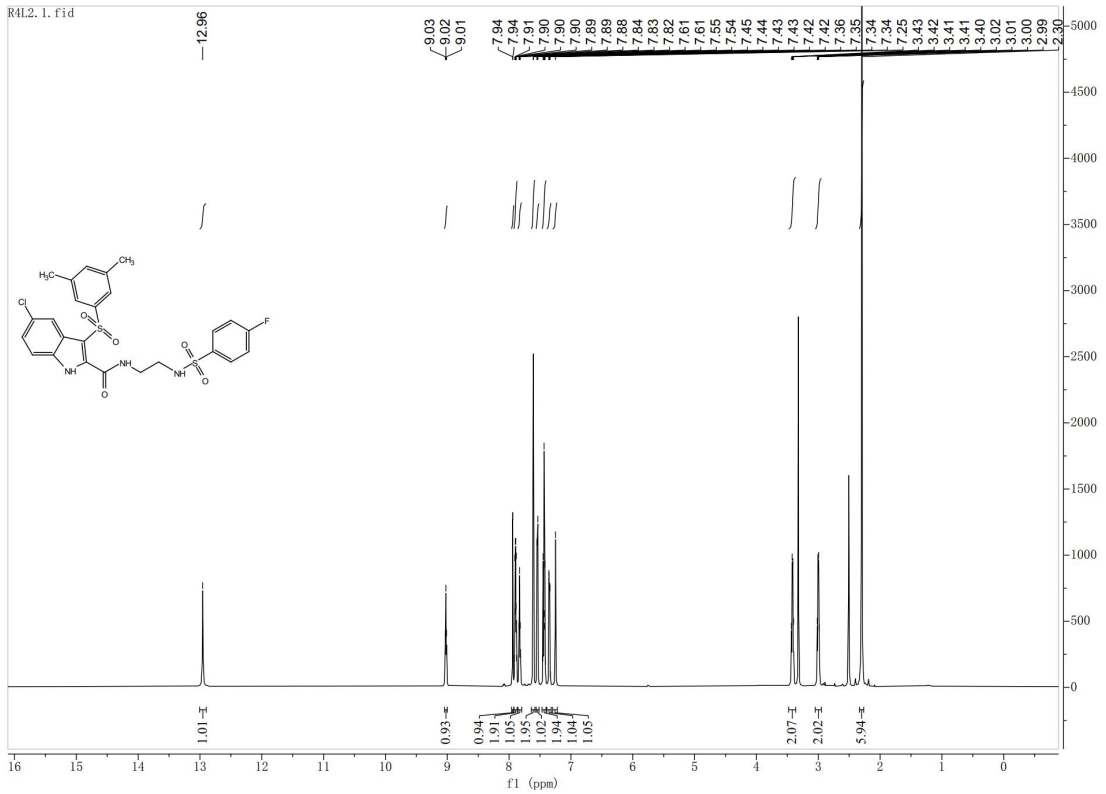
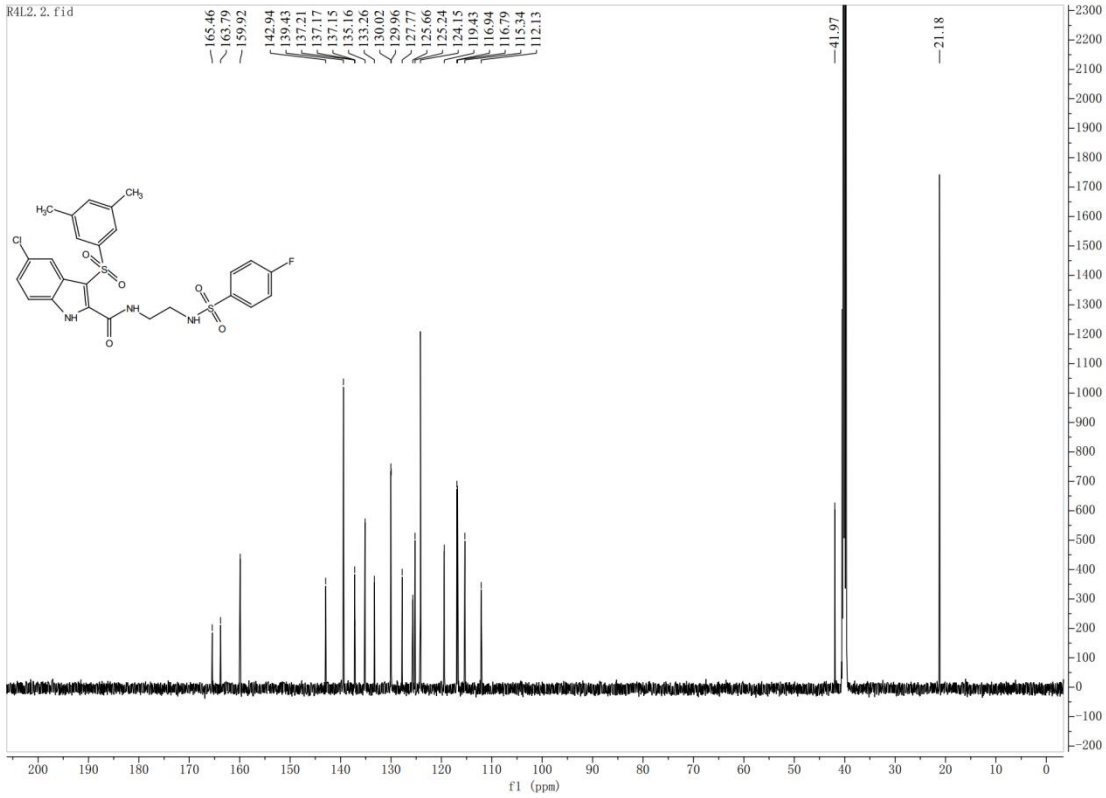


^{13}C NMR (150 MHz, DMSO-d_6) of **R_4L_2**



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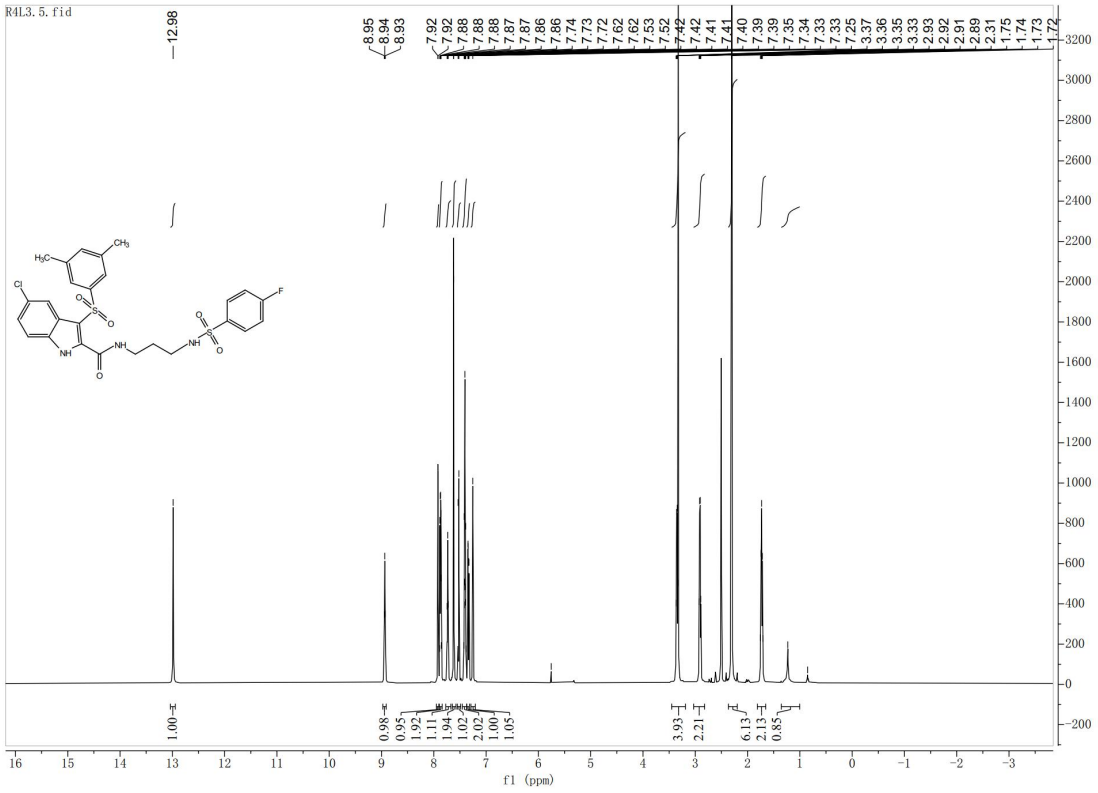

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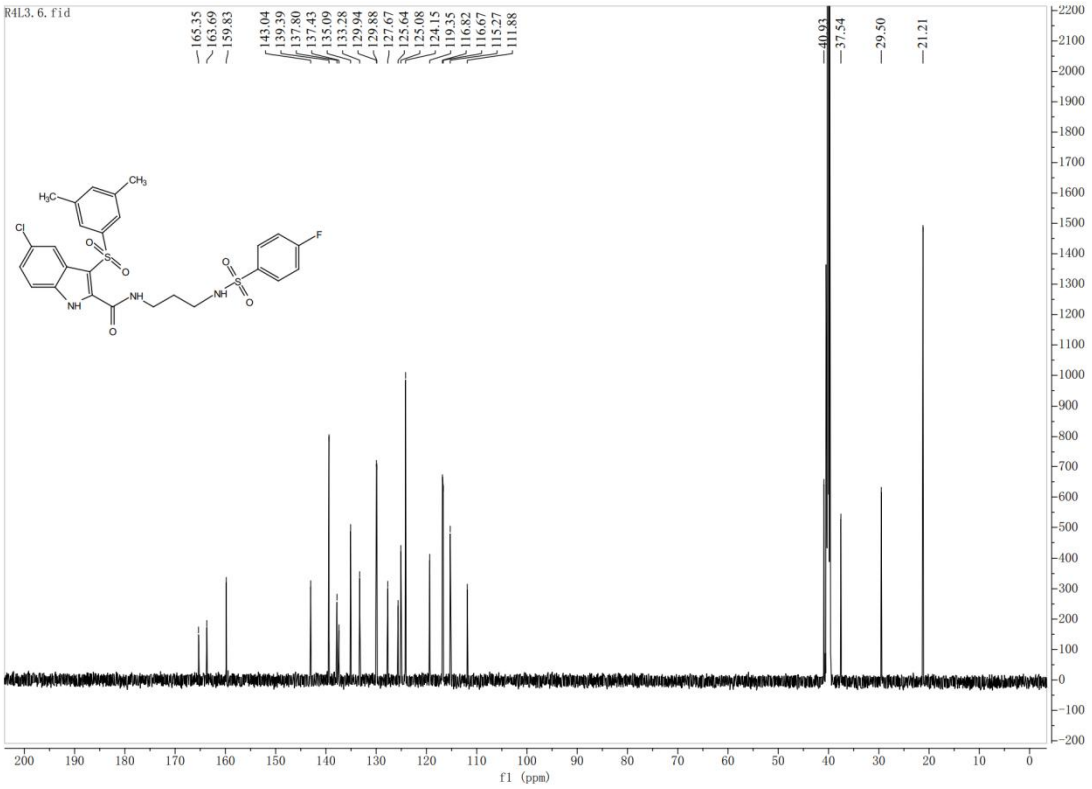

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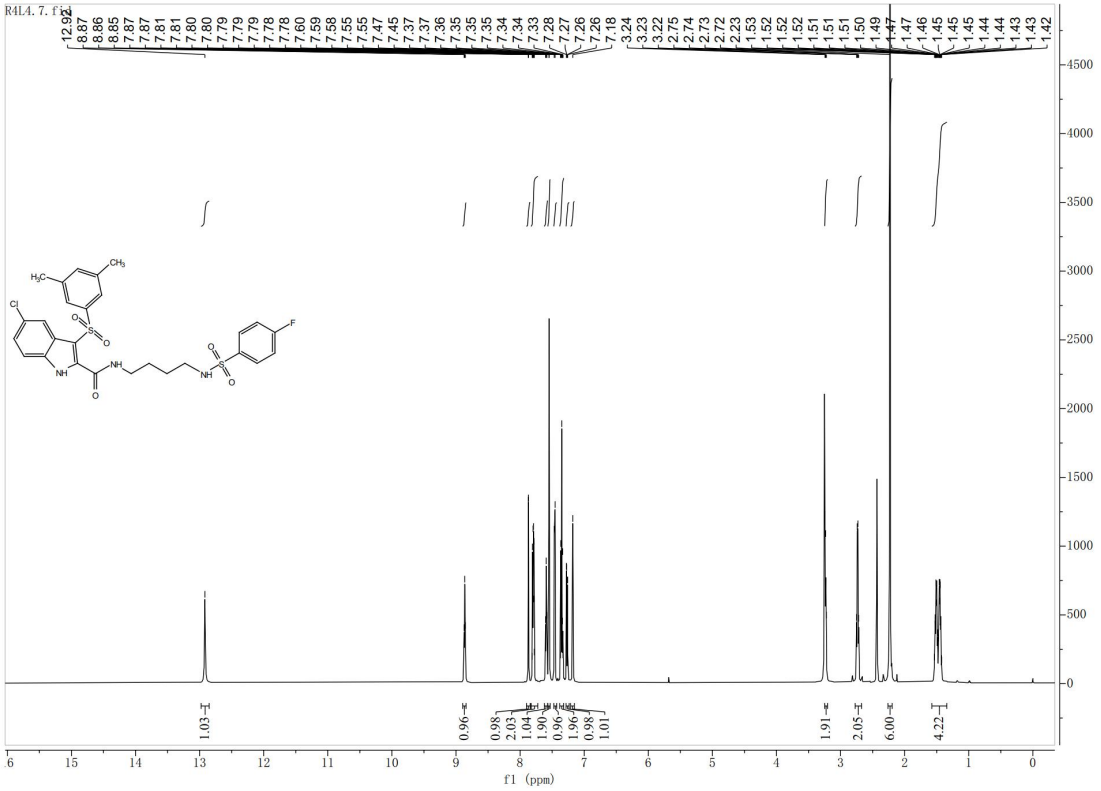
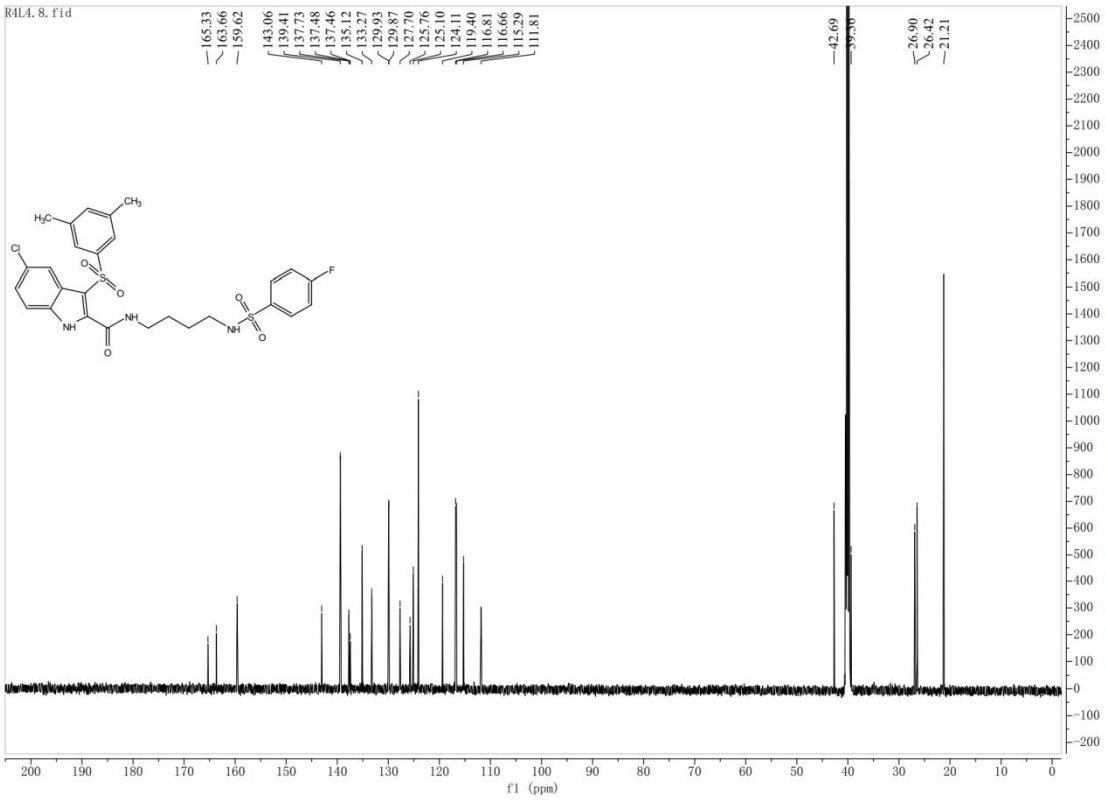
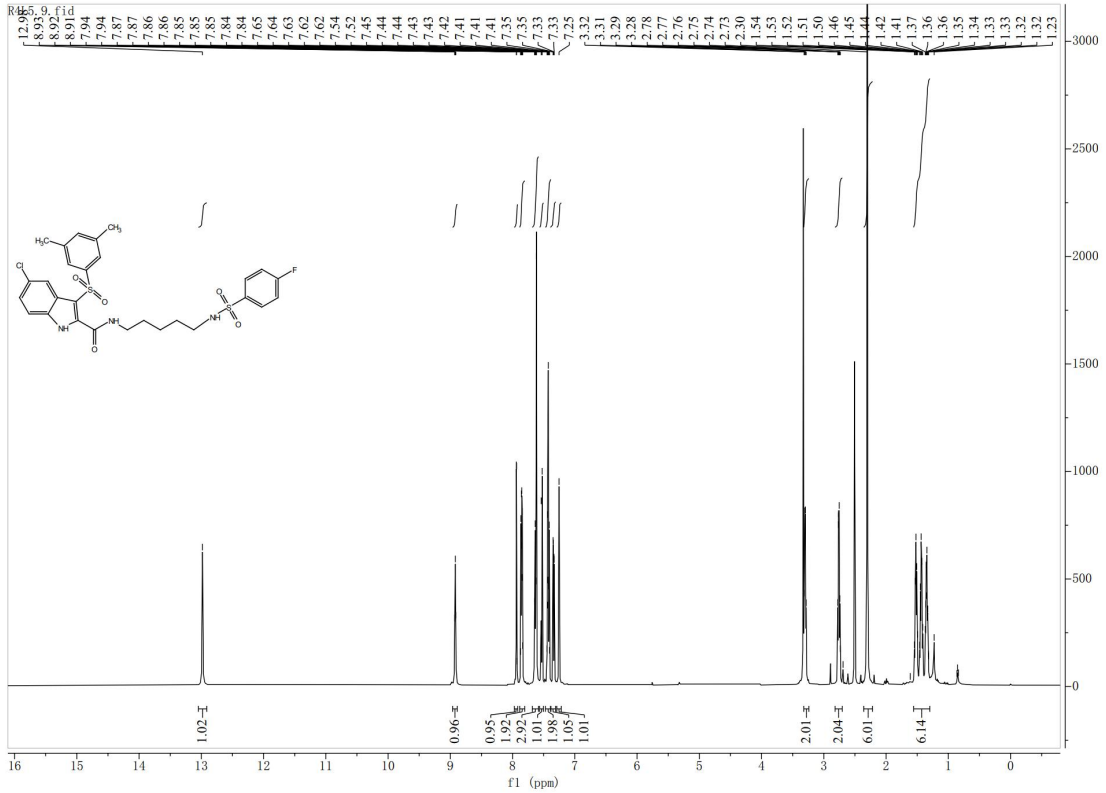


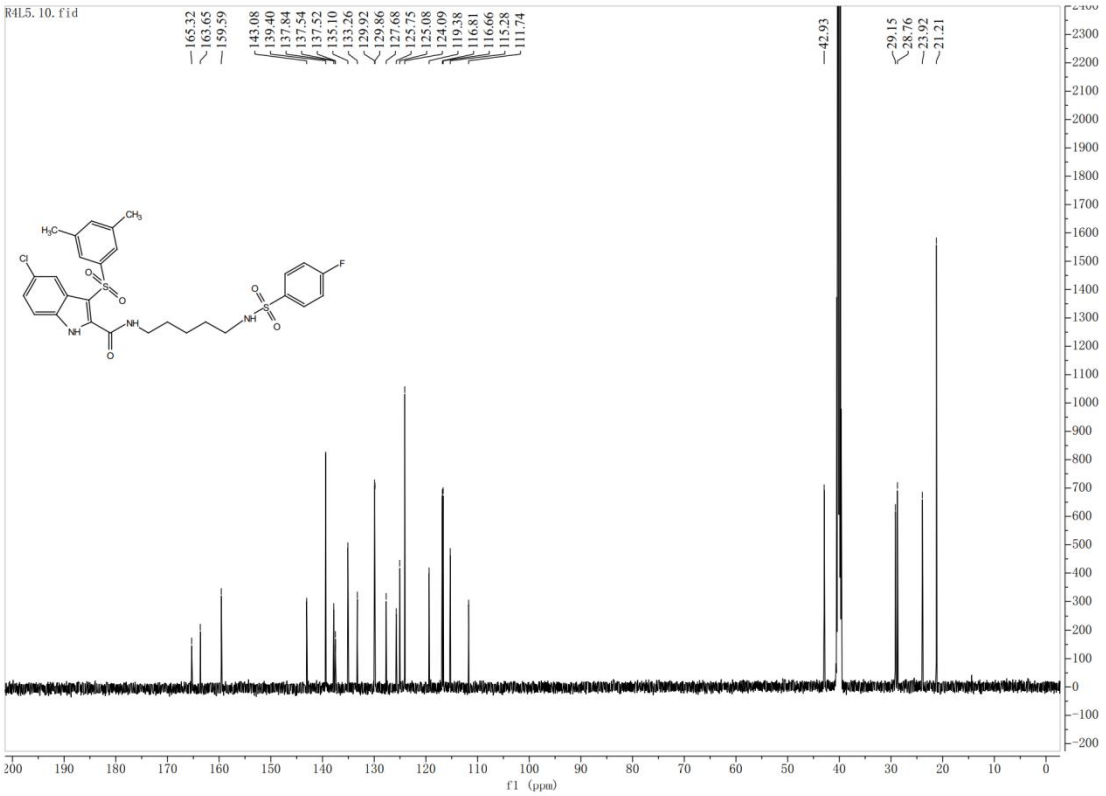
^{13}C NMR (150 MHz, DMSO-d_6) of **R_4L_4**



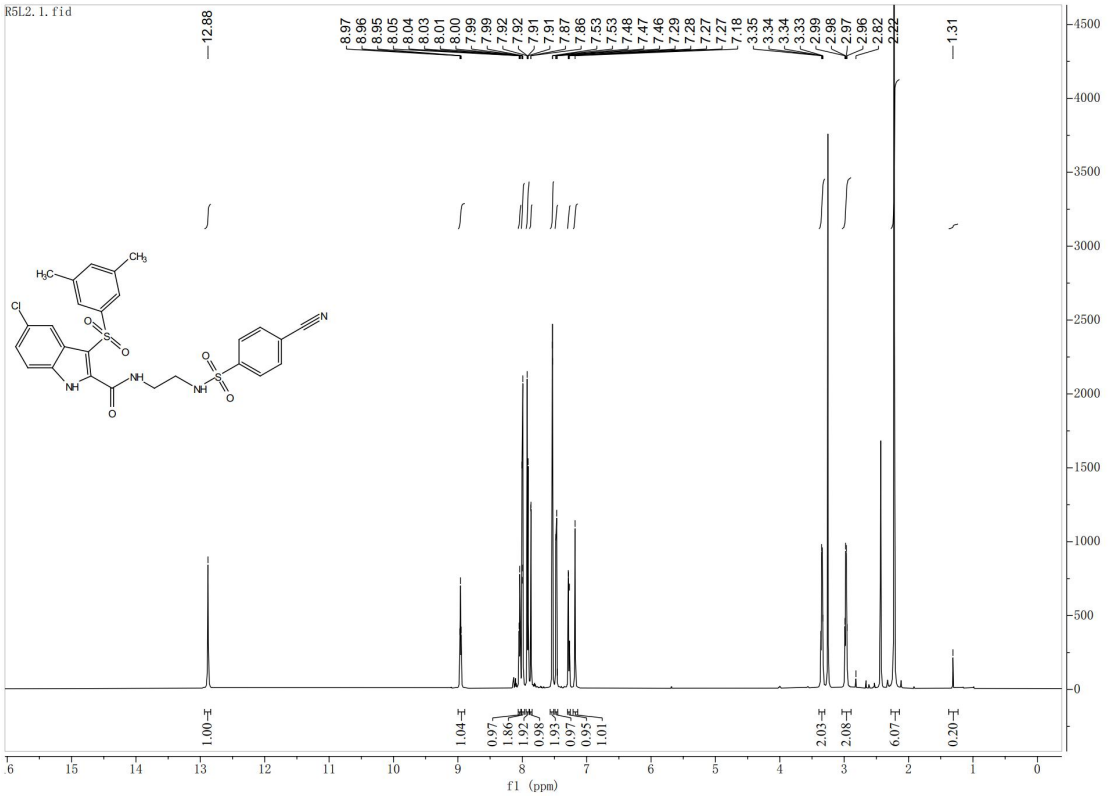
^{1}H NMR (600 MHz, DMSO-d_6) of **R_4L_5**



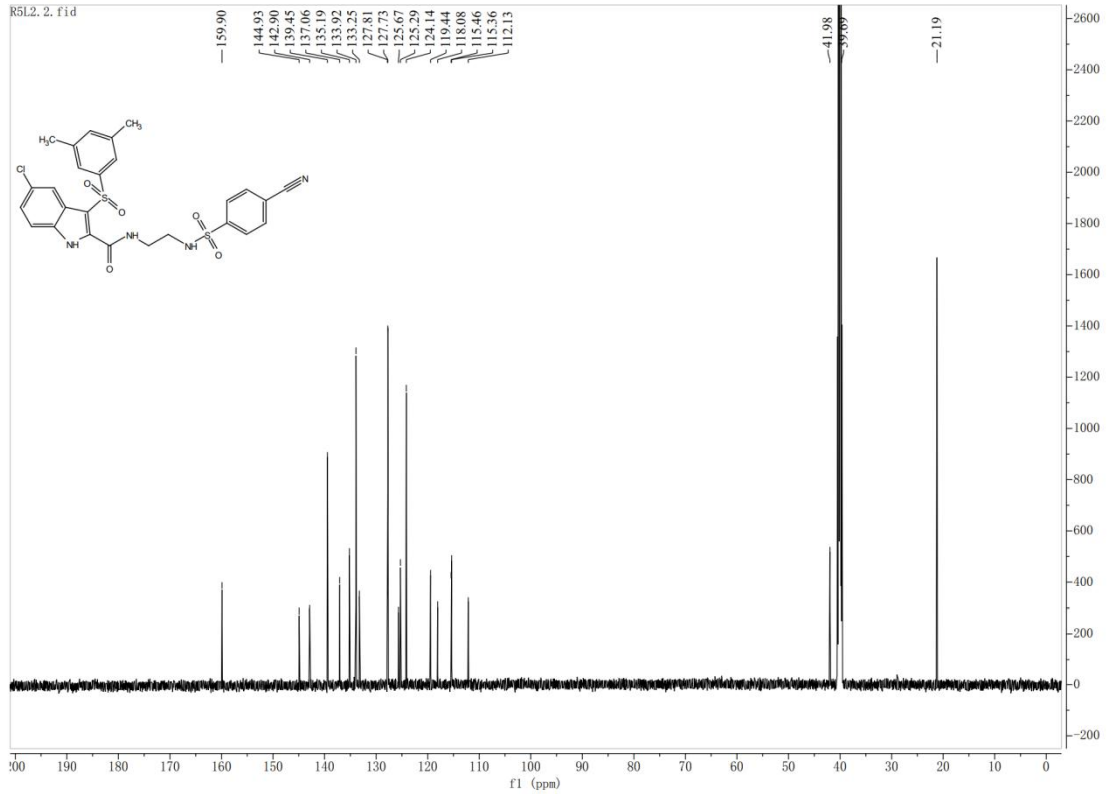
^{13}C NMR (150 MHz, DMSO-d_6) of **R_4L_5**



^{1}H NMR (600 MHz, DMSO-d_6) of **R_5L_2**



^{13}C NMR (150 MHz, DMSO-d_6) of **R_5L_2**



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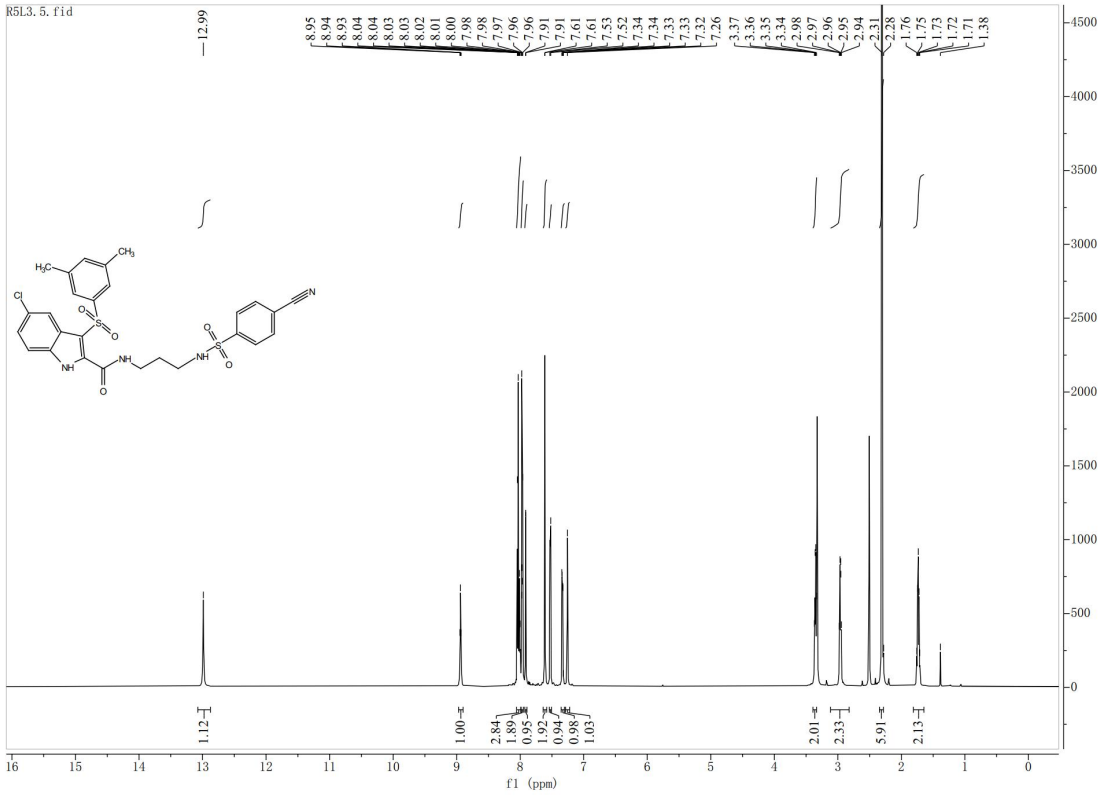
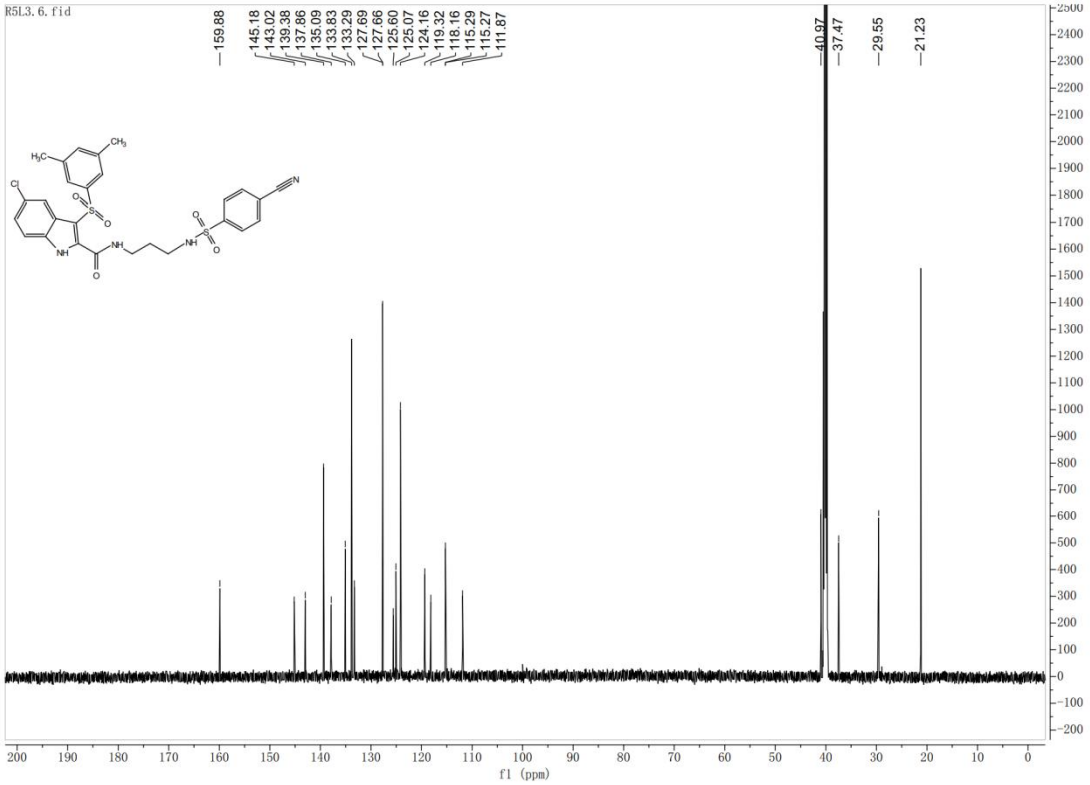
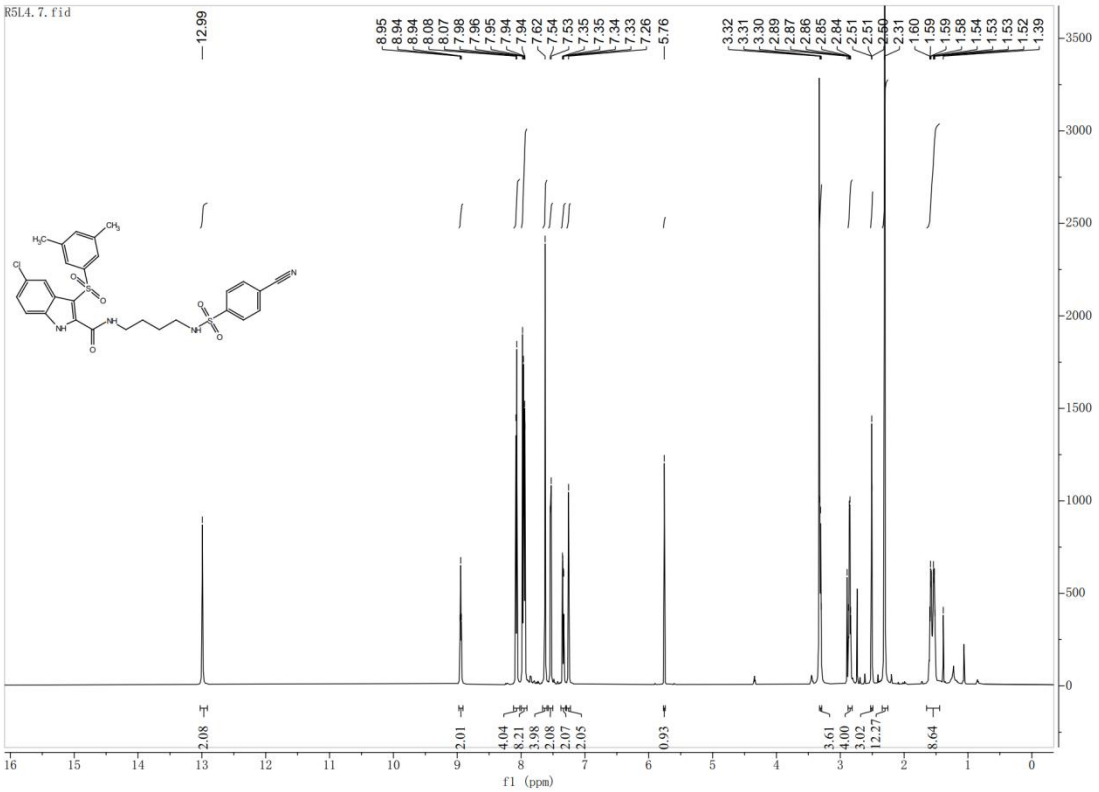


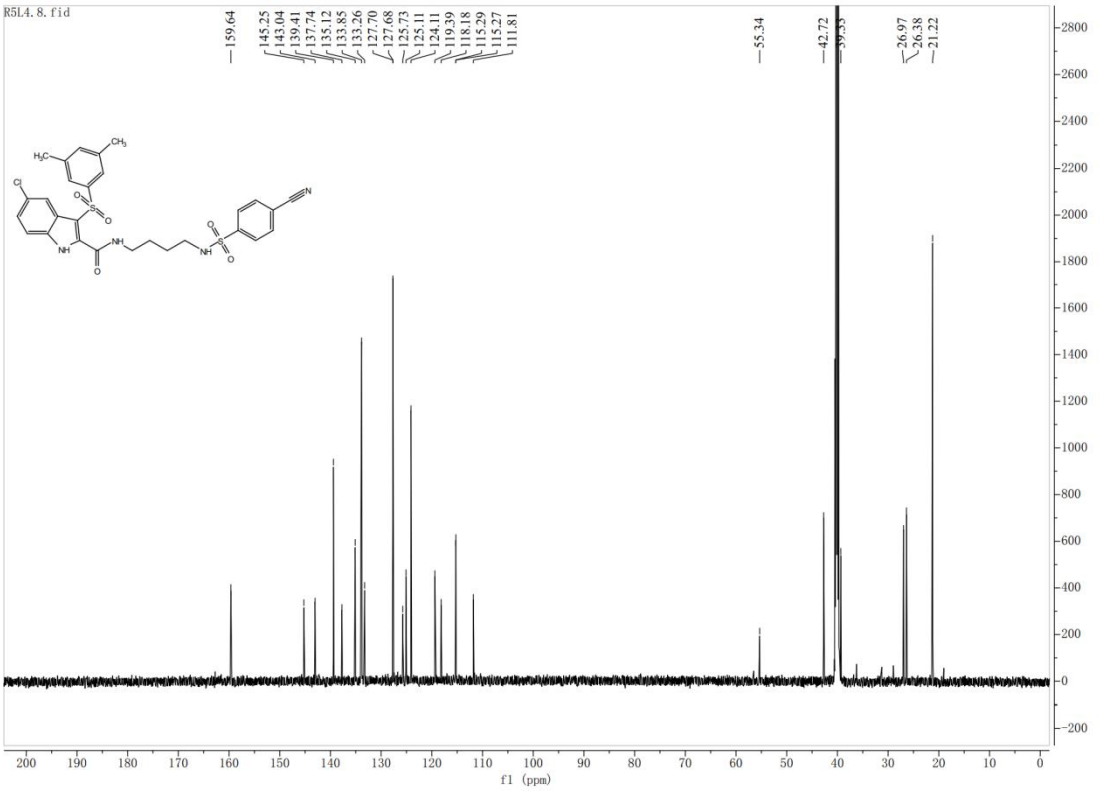
^{13}C NMR (150 MHz, DMSO-d_6) of **R_5L_3**



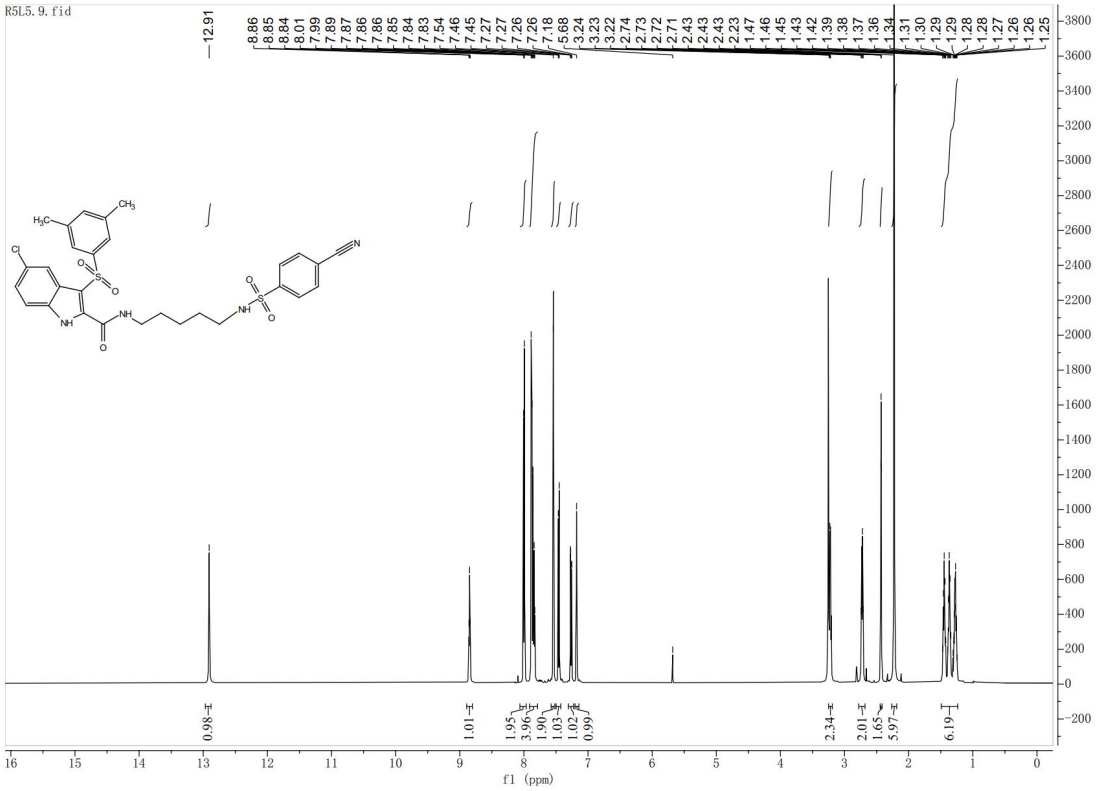
^{1}H NMR (600 MHz, DMSO-d_6) of **R_5L_4**



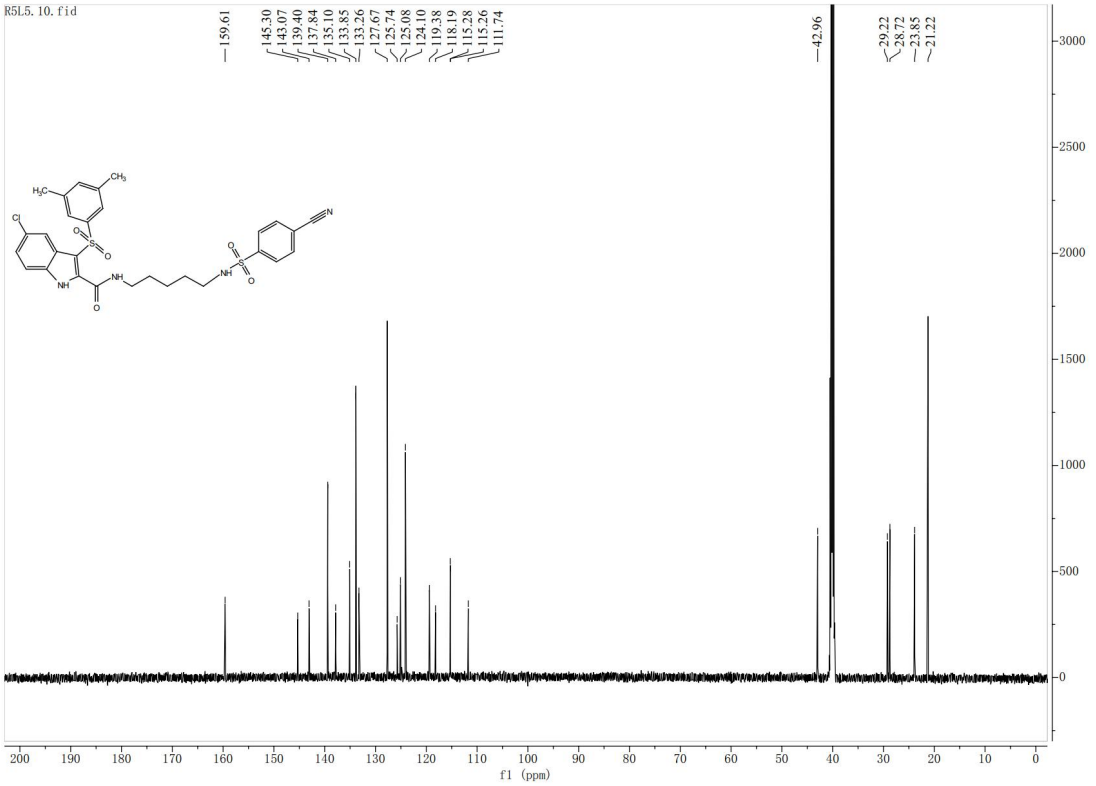
^{13}C NMR (150 MHz, DMSO-d_6) of **R_5L_4**



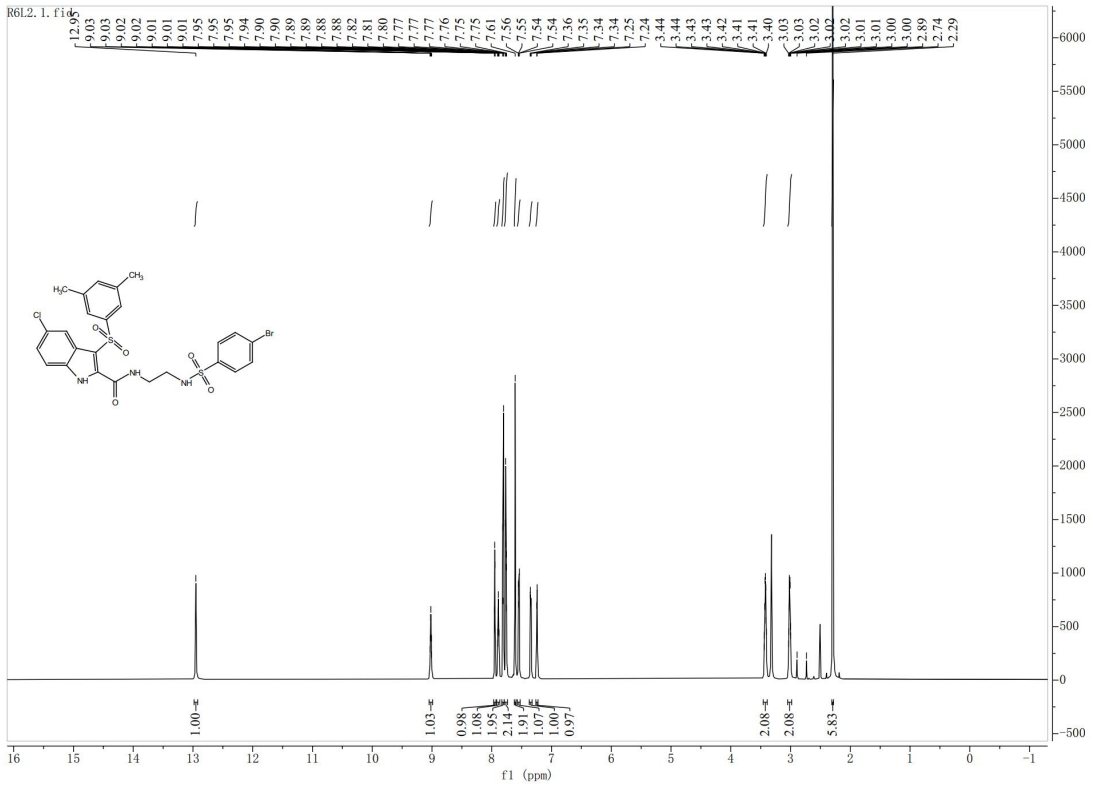
^{1}H NMR (600 MHz, DMSO-d_6) of **R_5L_5**



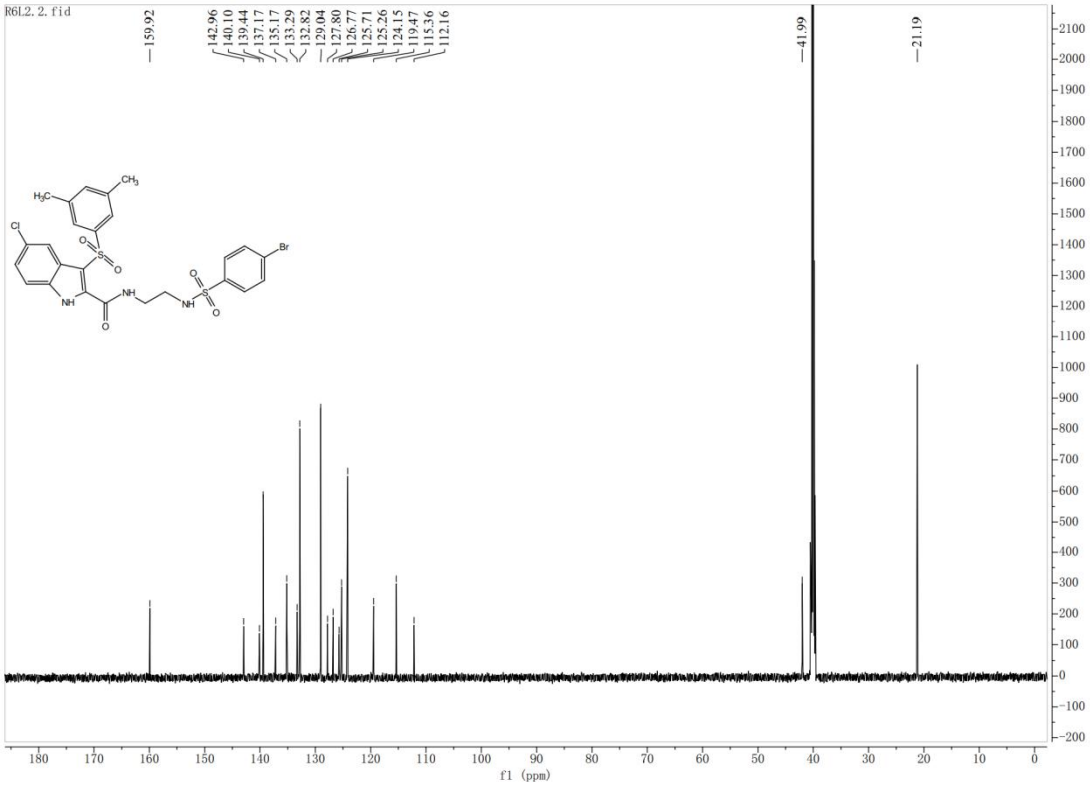
^{13}C NMR (150 MHz, DMSO-d_6) of **R_5L_5**



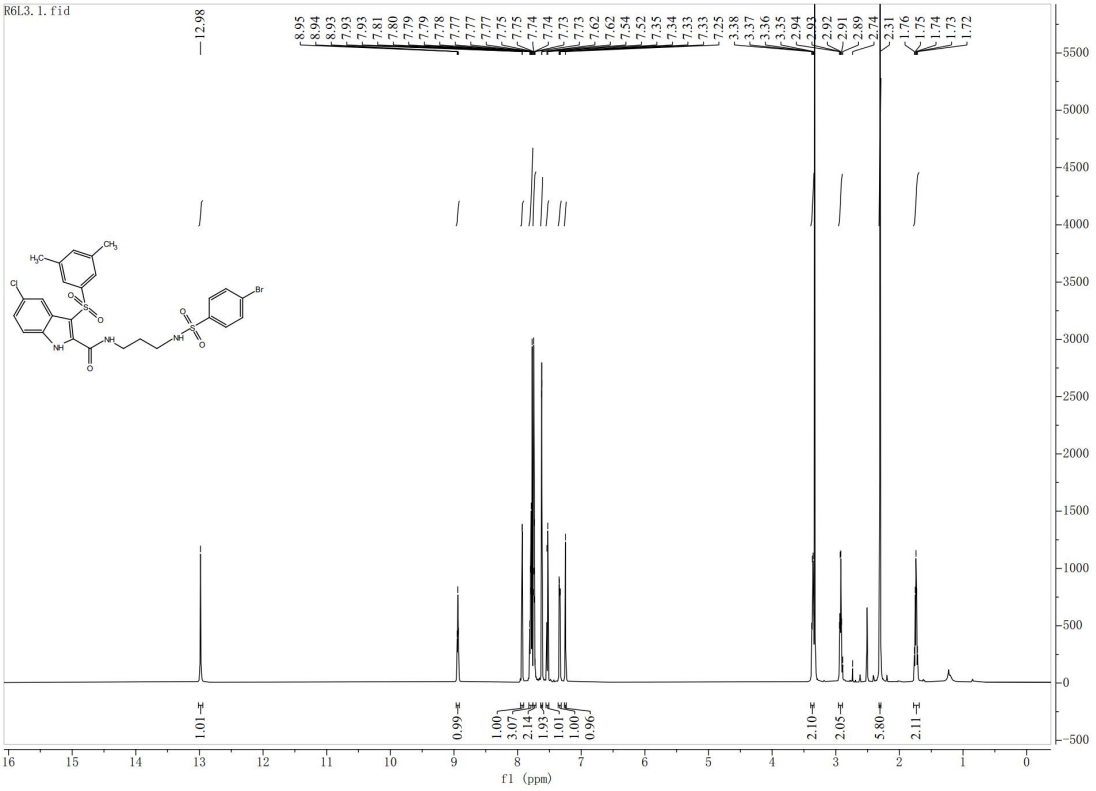
^{1}H NMR (600 MHz, DMSO-d_6) of **R_6L_2**



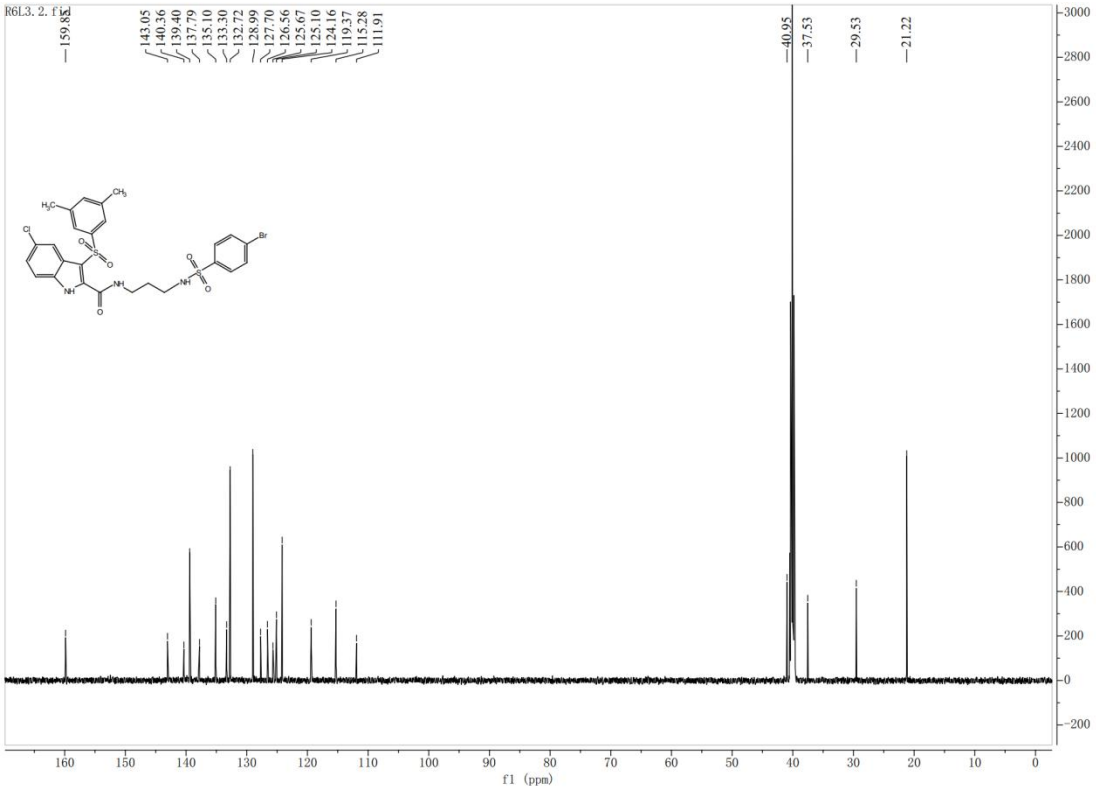
^{13}C NMR (150 MHz, DMSO-d_6) of **R_6L_2**



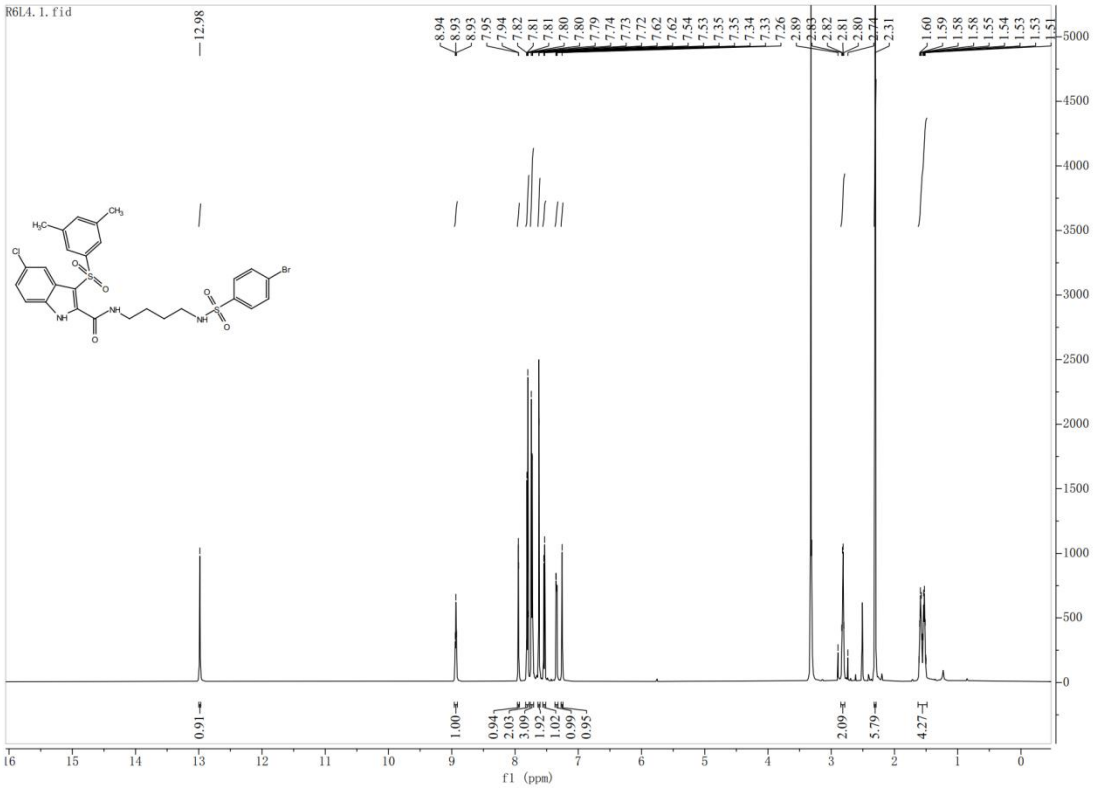
^{1}H NMR (600 MHz, DMSO-d_6) of **R_6L_3**



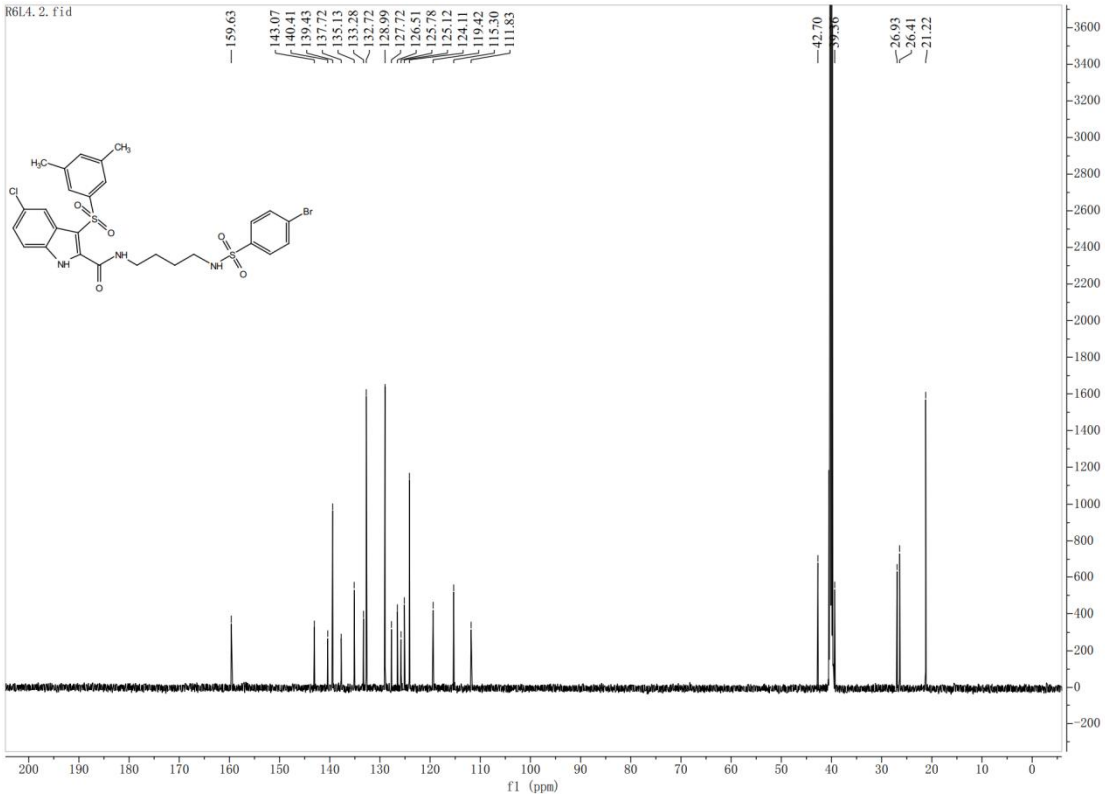
^{13}C NMR (150 MHz, DMSO-d_6) of **R_6L_3**



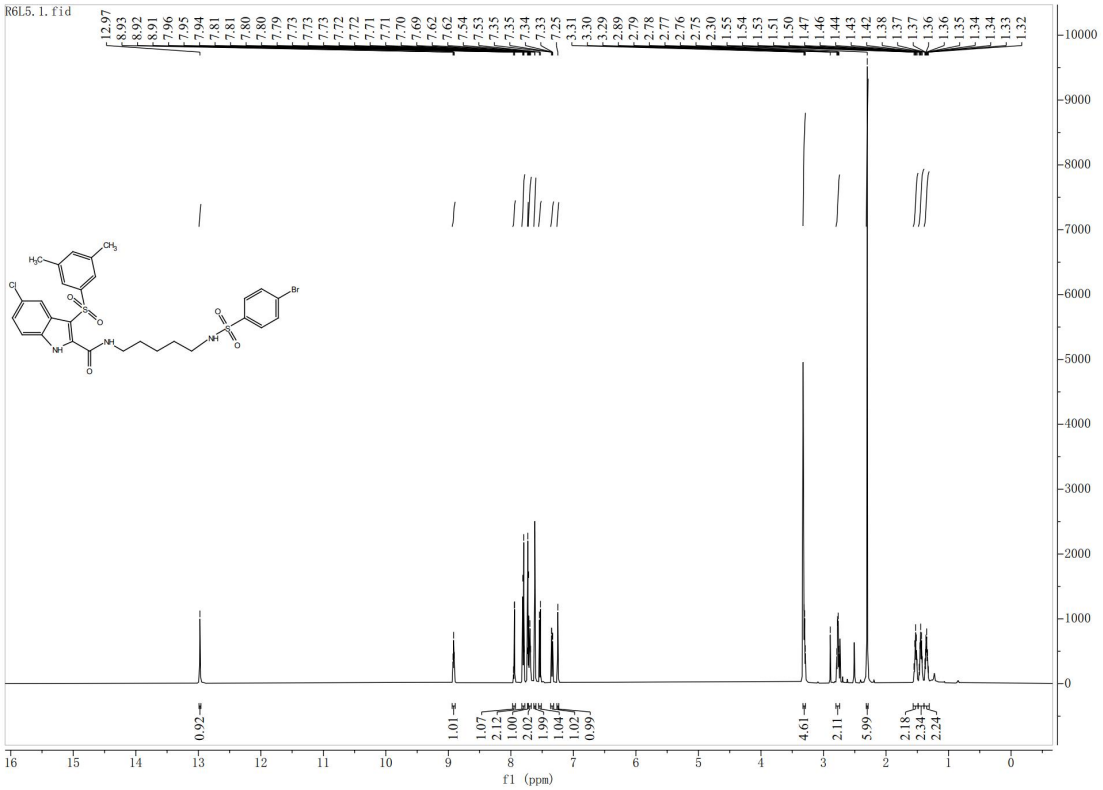
^{1}H NMR (600 MHz, DMSO-d_6) of **R_6L_4**



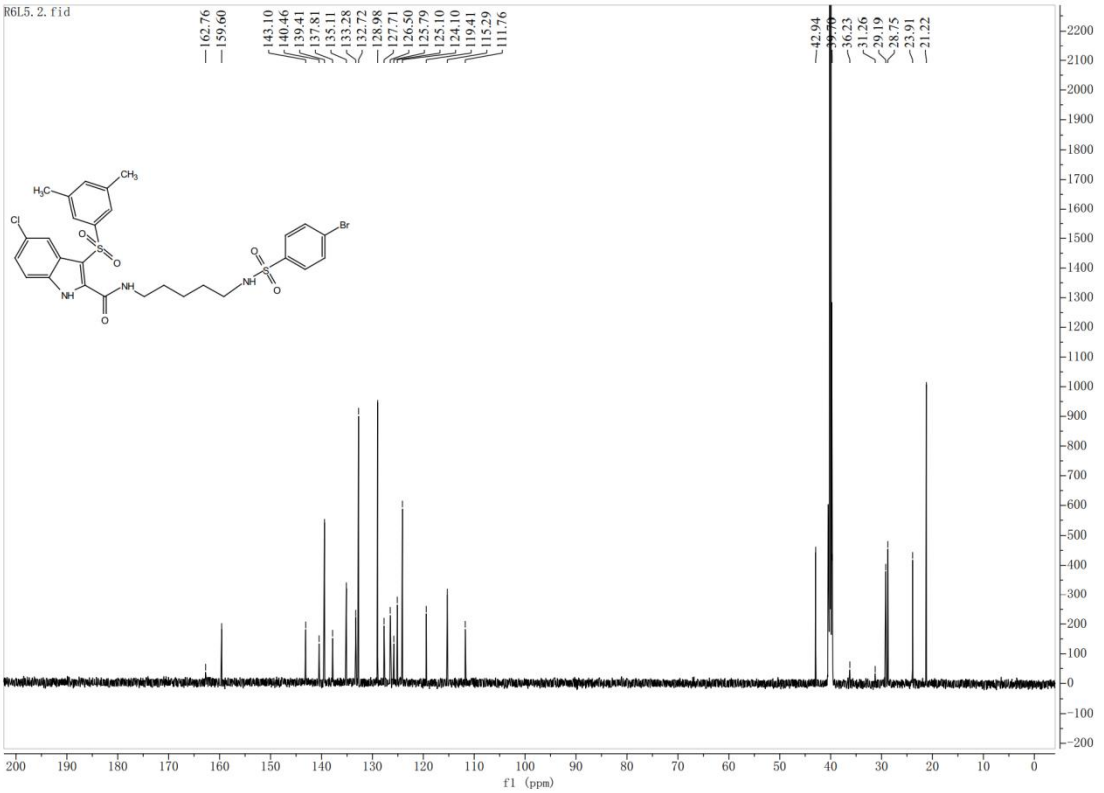
^{13}C NMR (150 MHz, DMSO-d_6) of **R_6L_4**



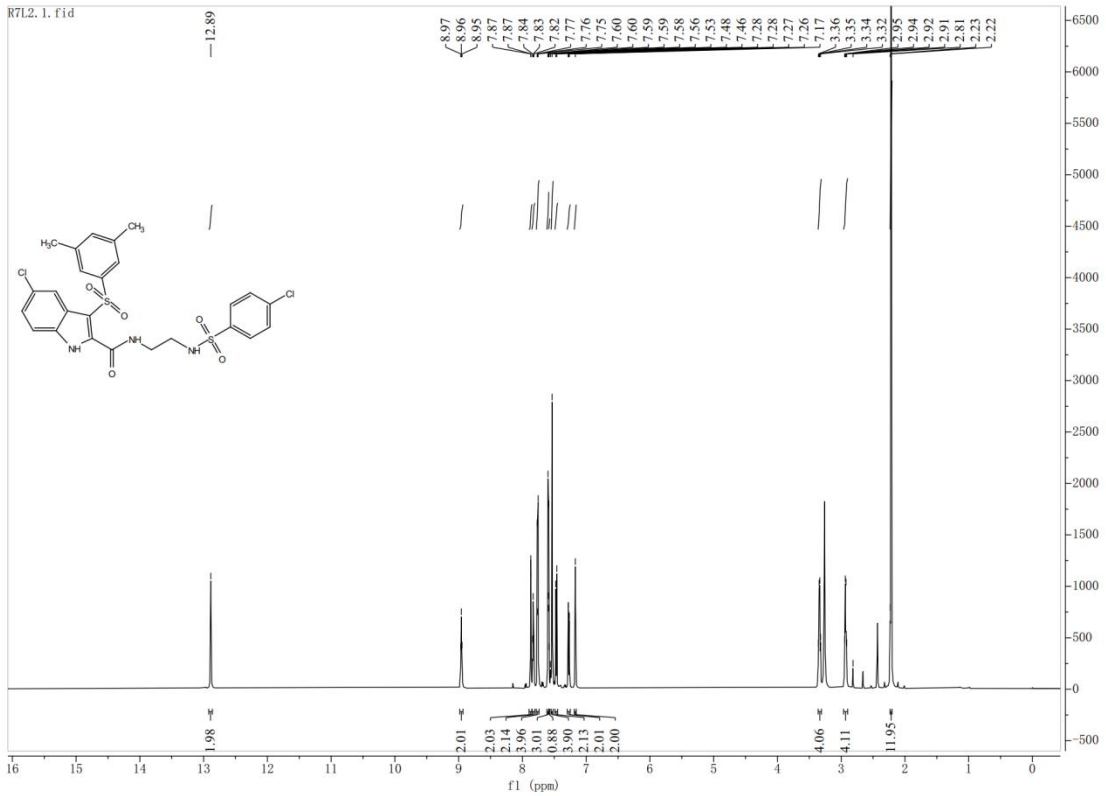
^{1}H NMR (600 MHz, DMSO-d_6) of **R_6L_5**



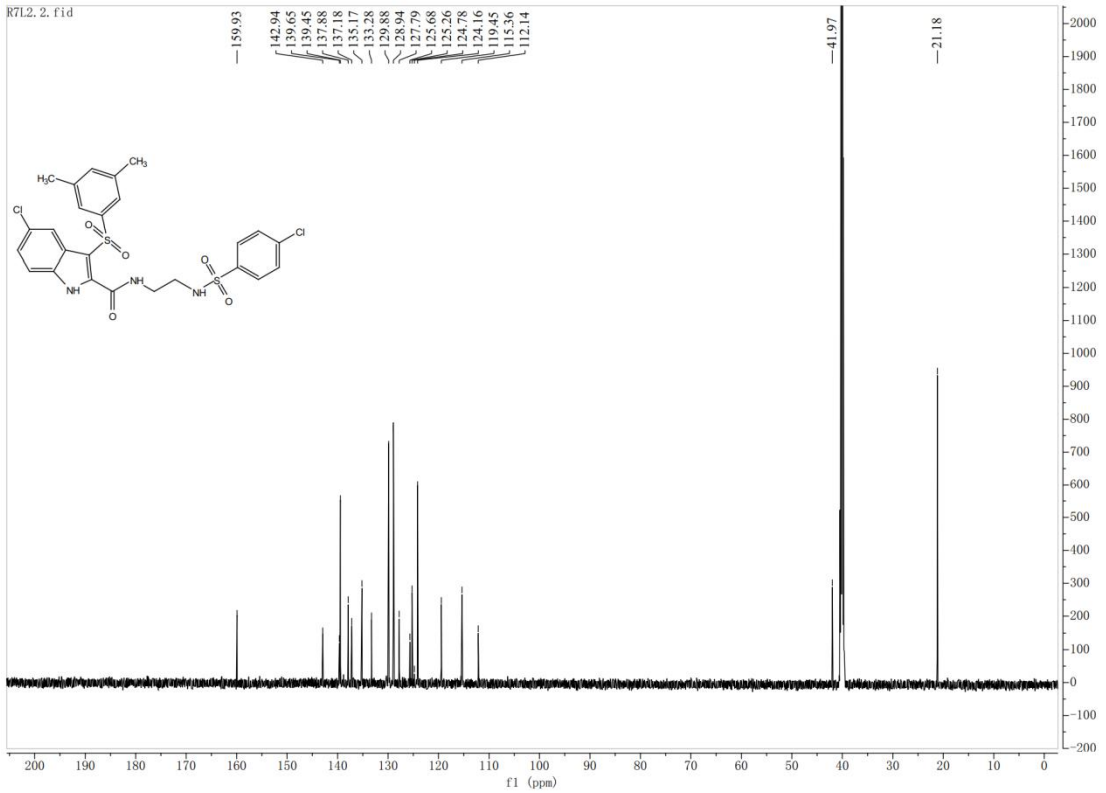
^{13}C NMR (150 MHz, DMSO-d_6) of **R_6L_5**



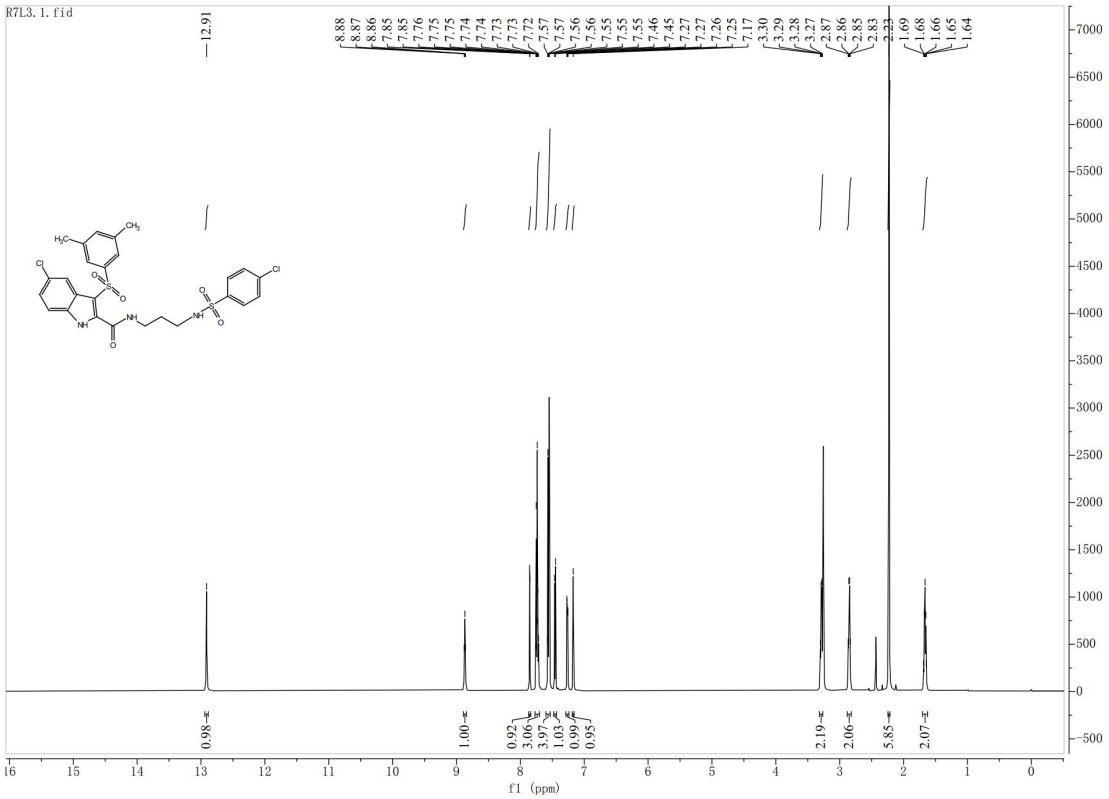
^{1}H NMR (600 MHz, DMSO-d_6) of $\mathbf{R_7L_2}$



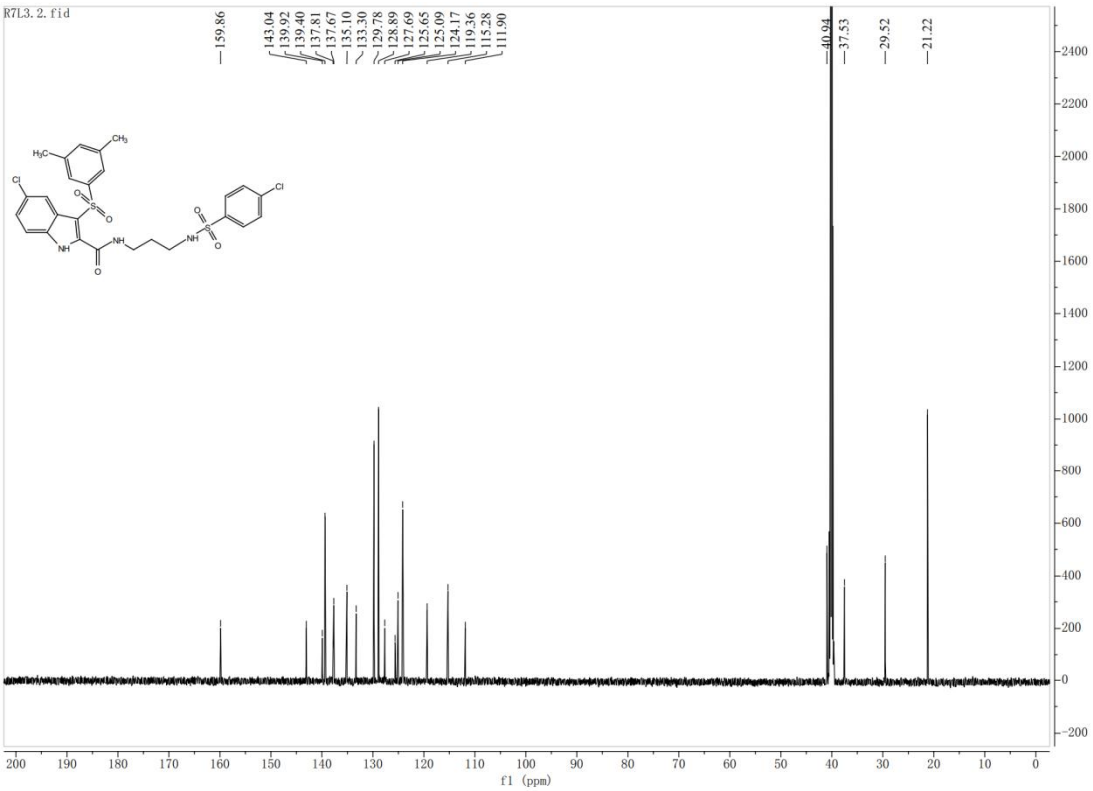
^{13}C NMR (150 MHz, DMSO-d_6) of $\mathbf{R_7L_2}$



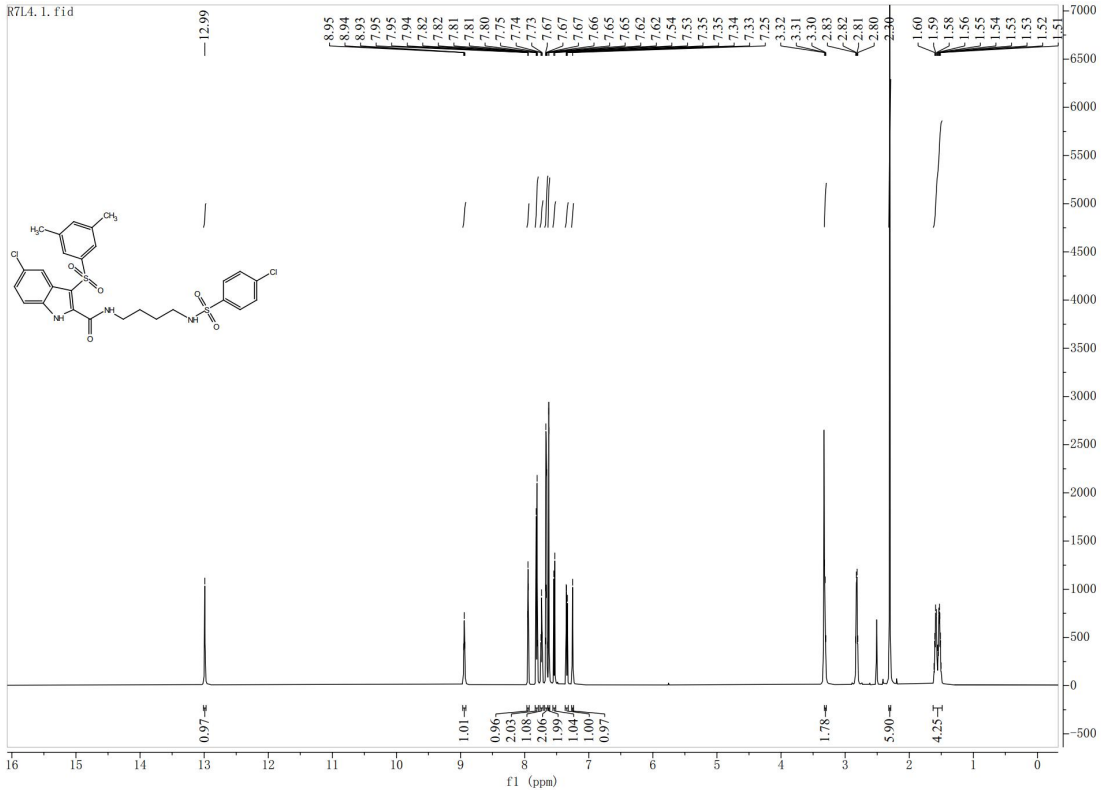
^{1}H NMR (600 MHz, DMSO-d_6) of **R_7L_3**



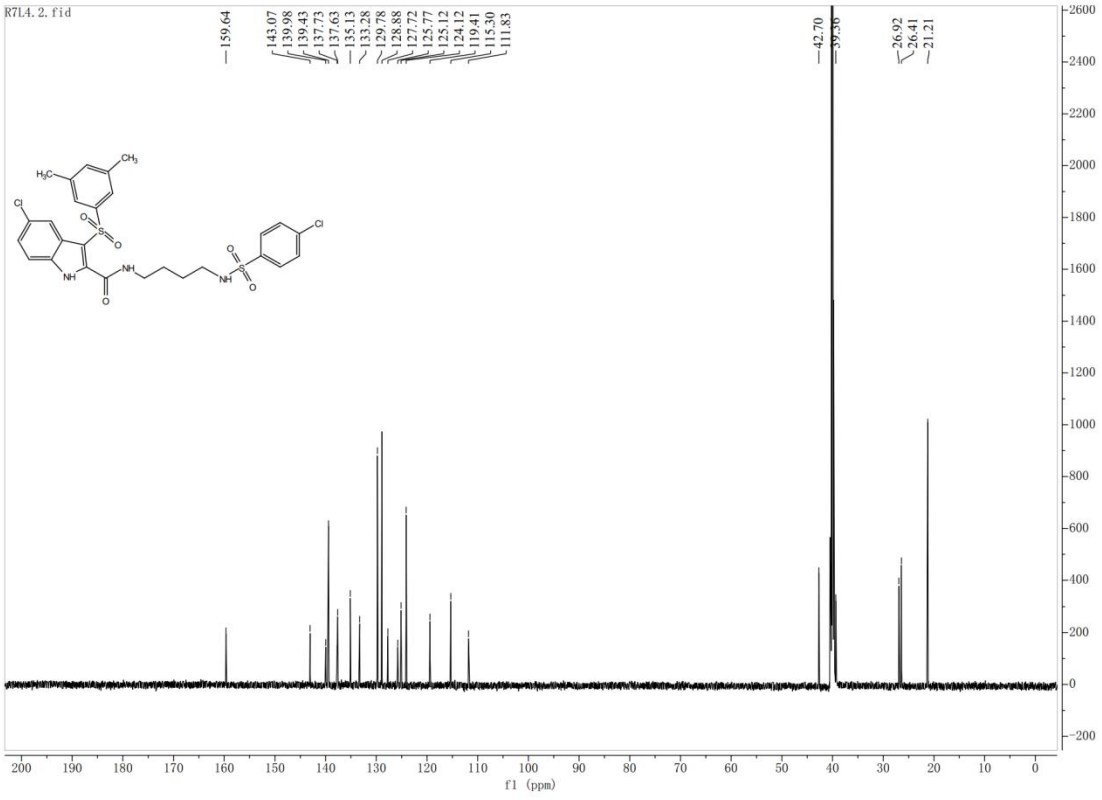
^{13}C NMR (150 MHz, DMSO-d_6) of **R_7L_3**



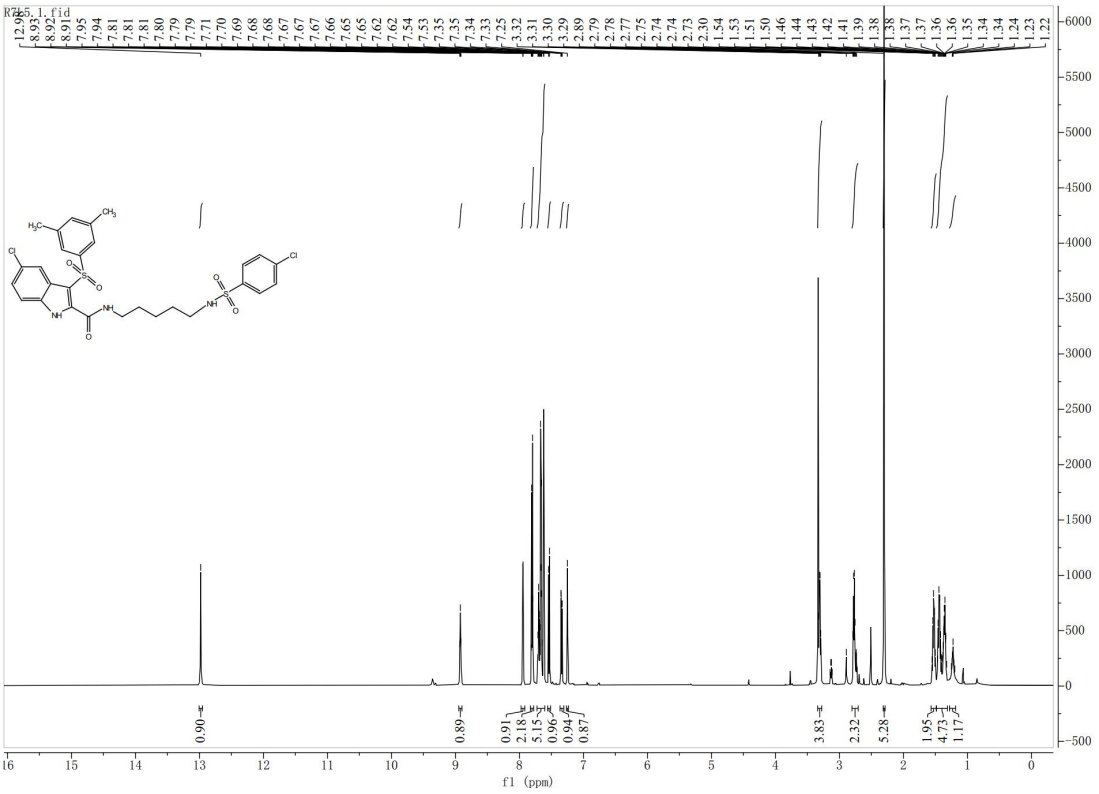
^{1}H NMR (600 MHz, DMSO-d_6) of **R_7L_4**



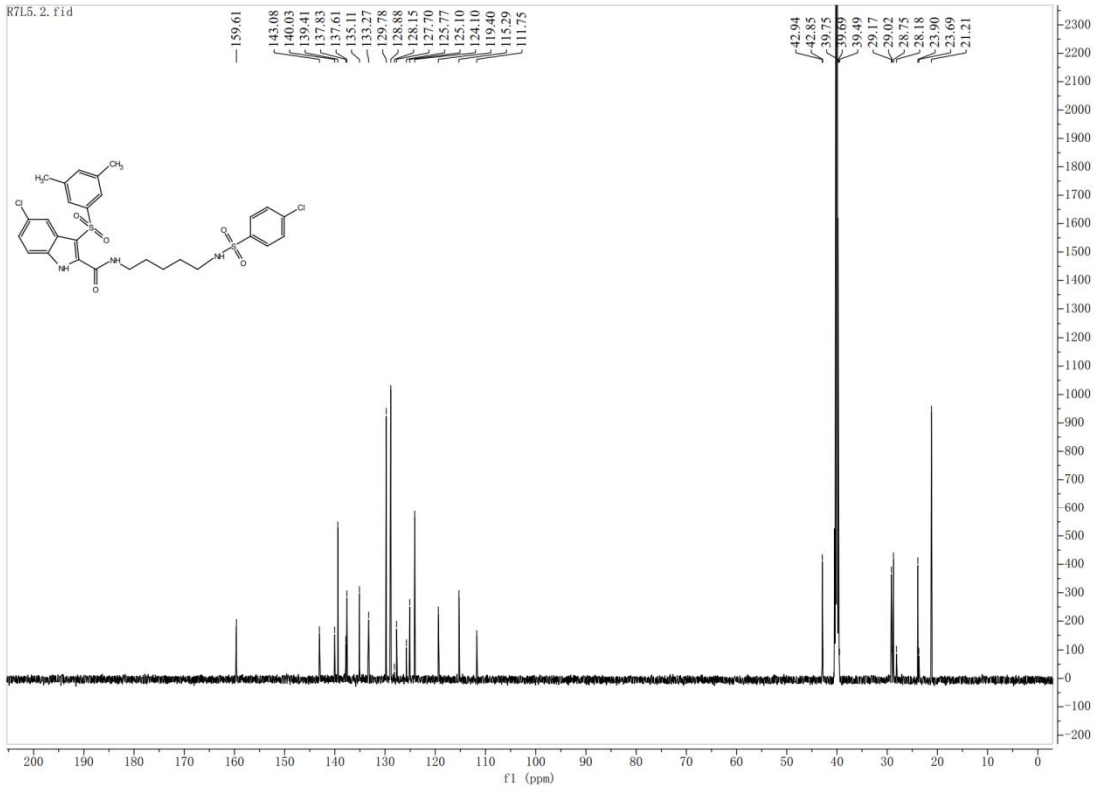
^{13}C NMR (150 MHz, DMSO-d_6) of **R_7L_4**



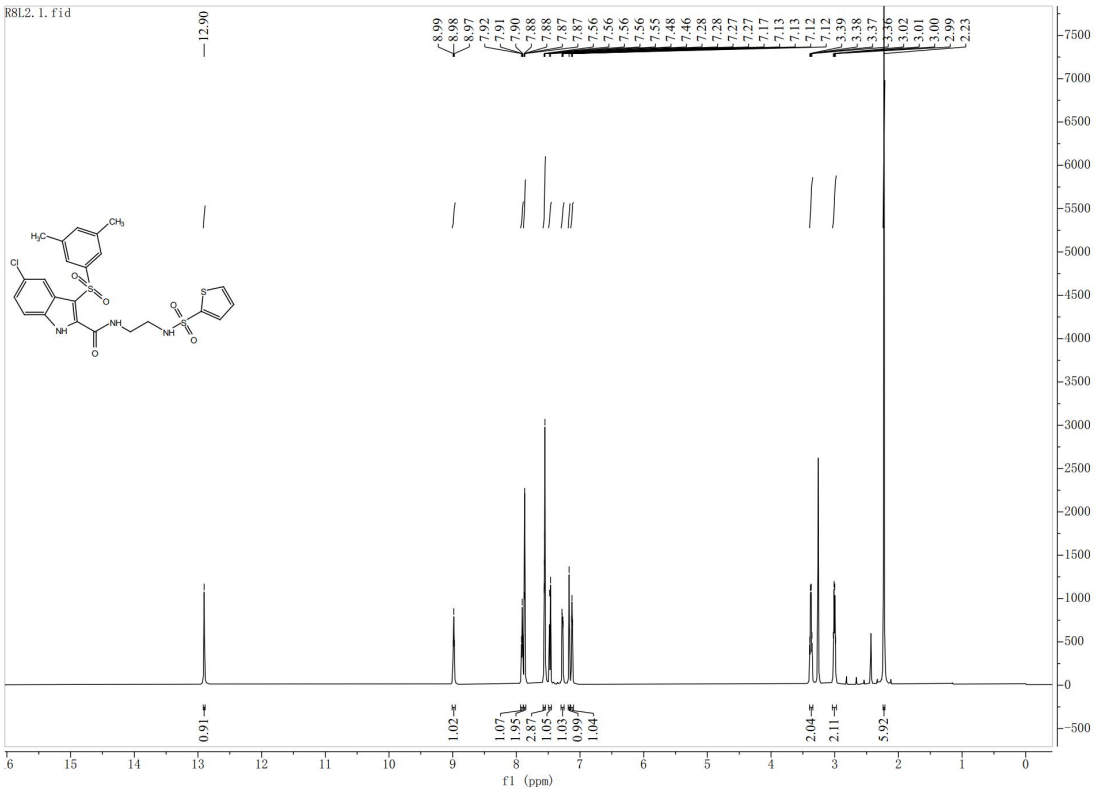
^{1}H NMR (600 MHz, DMSO-d_6) of **R_7L_5**



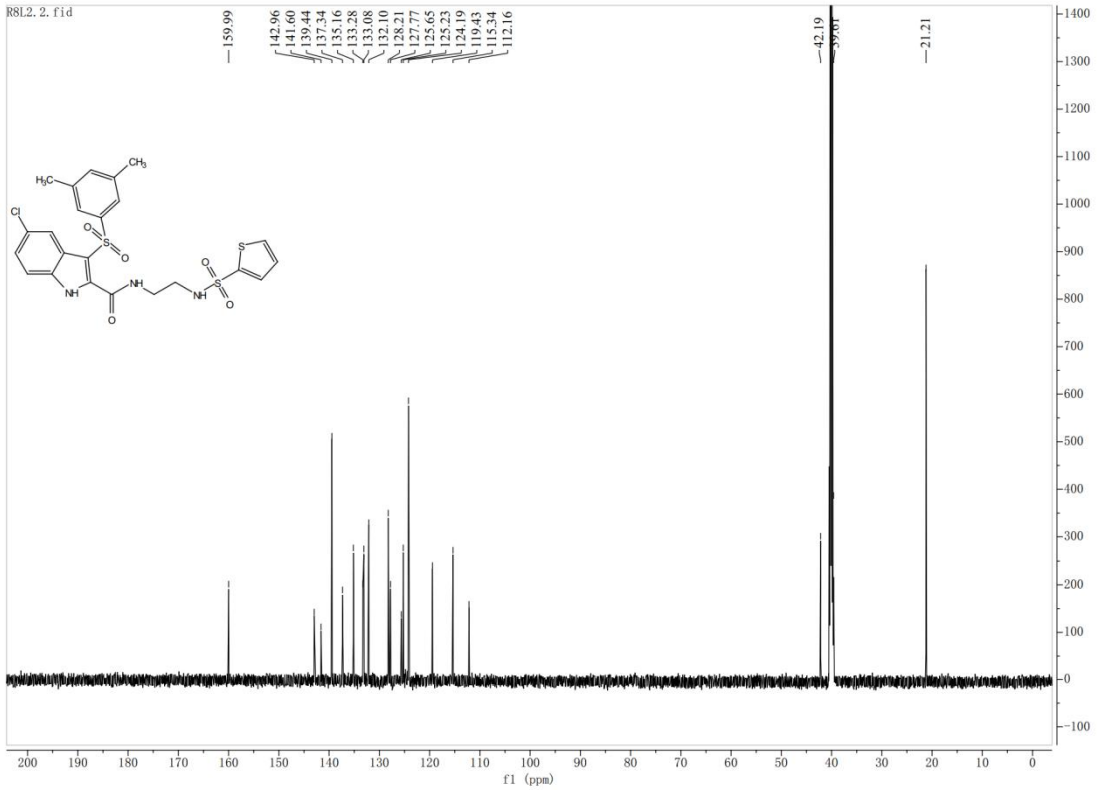
^{13}C NMR (150 MHz, DMSO-d_6) of **R_7L_5**



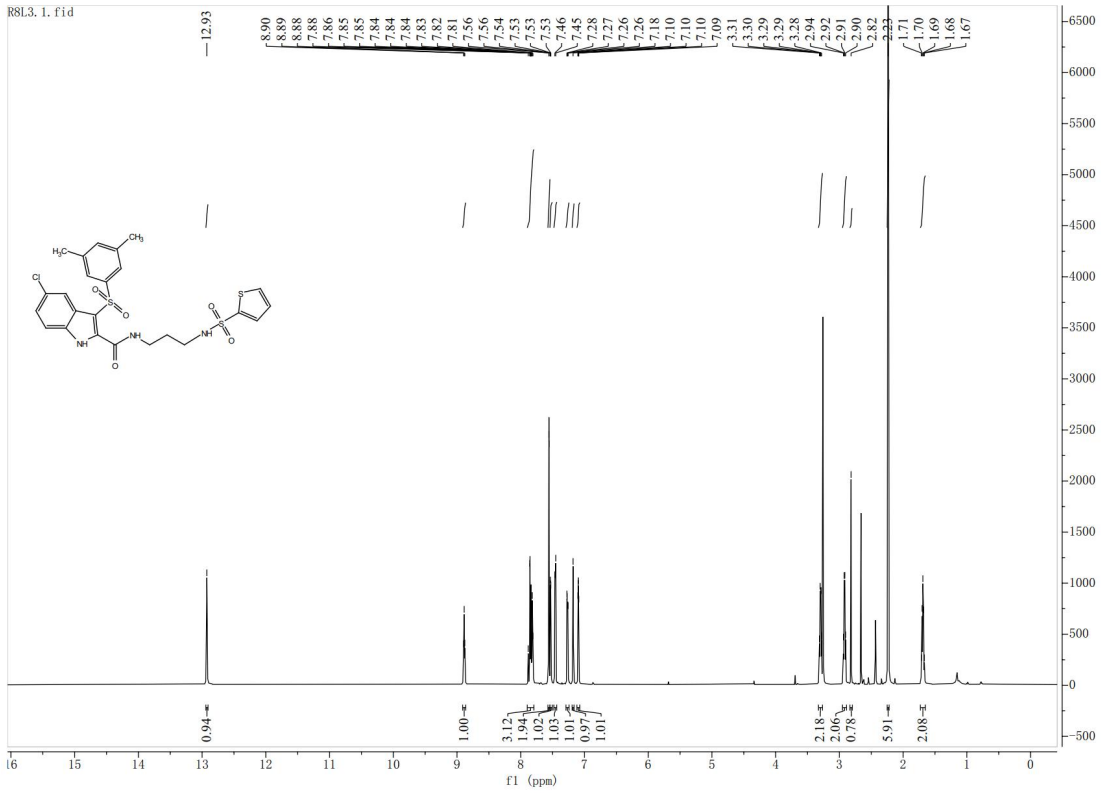
^{1}H NMR (600 MHz, DMSO-d_6) of **R_8L_2**



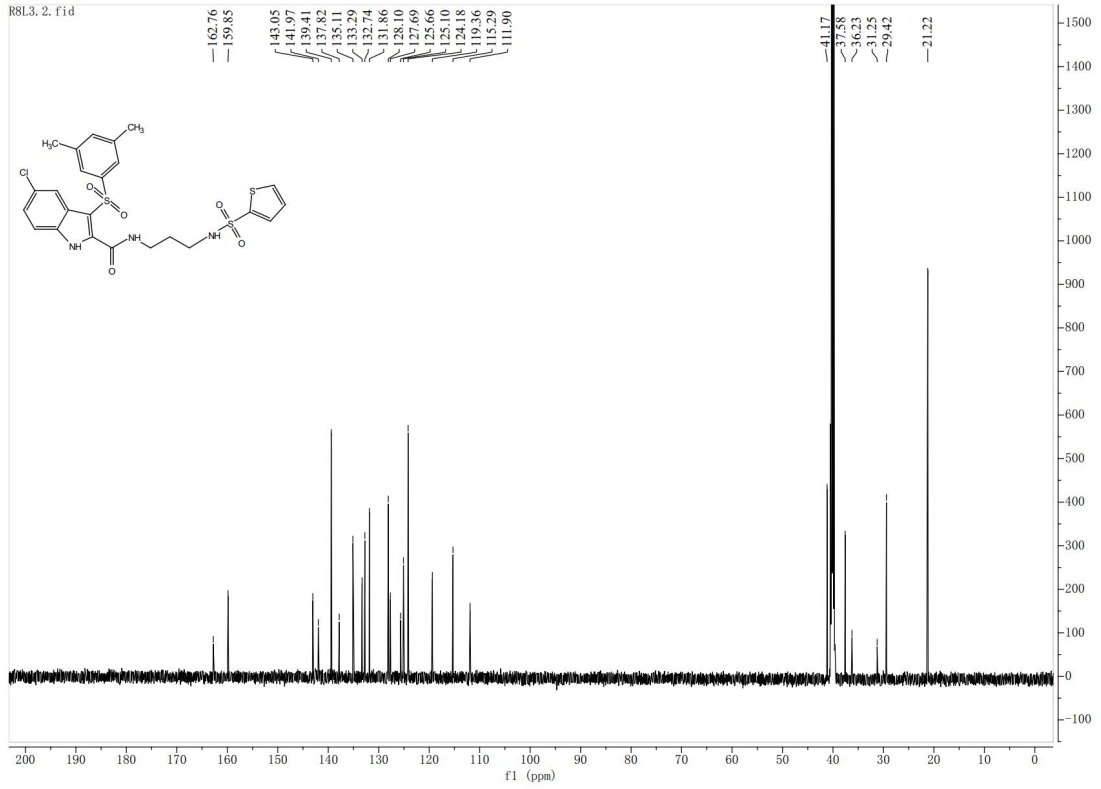
^{13}C NMR (150 MHz, DMSO-d_6) of **R_8L_2**



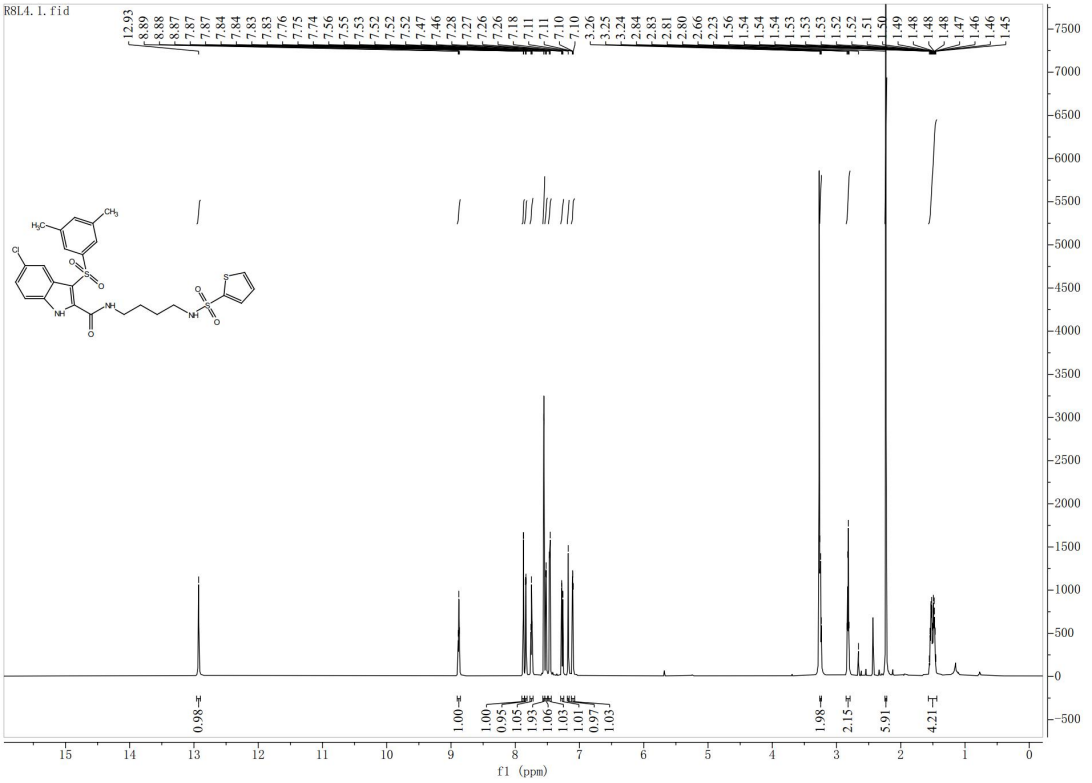
^{1}H NMR (600 MHz, DMSO-d_6) of **R_8L_3**



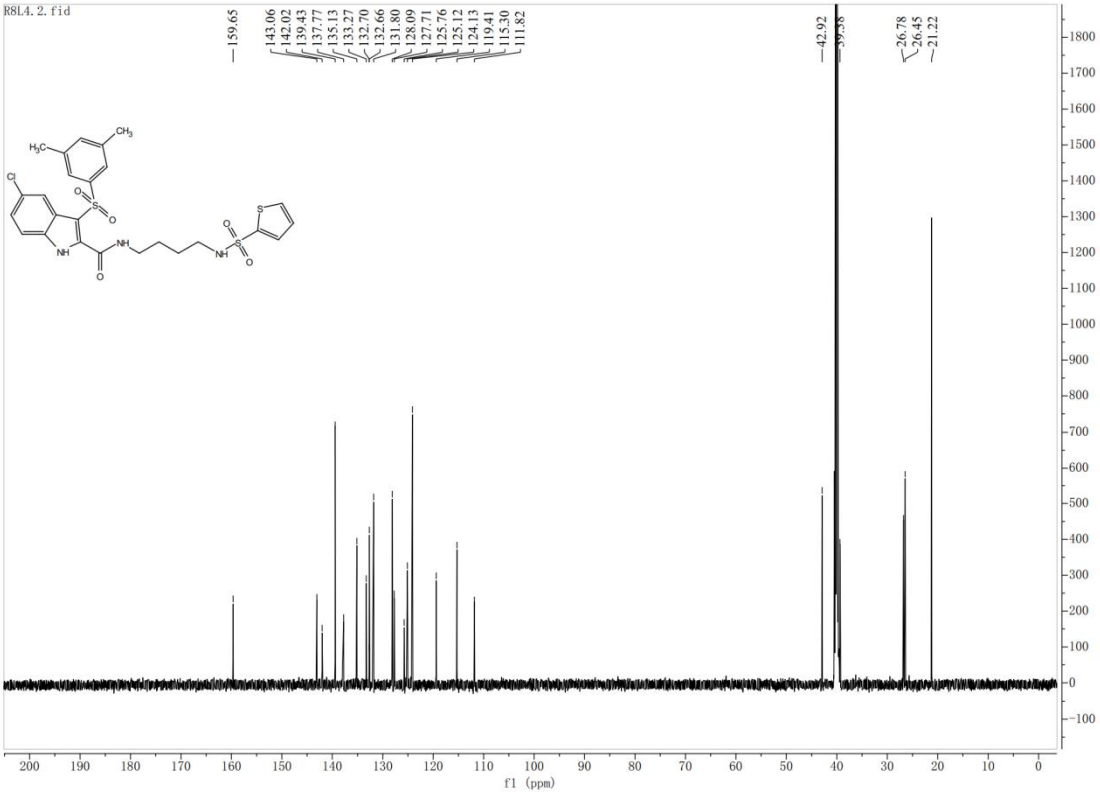
^{13}C NMR (150 MHz, DMSO-d_6) of **R_8L_3**



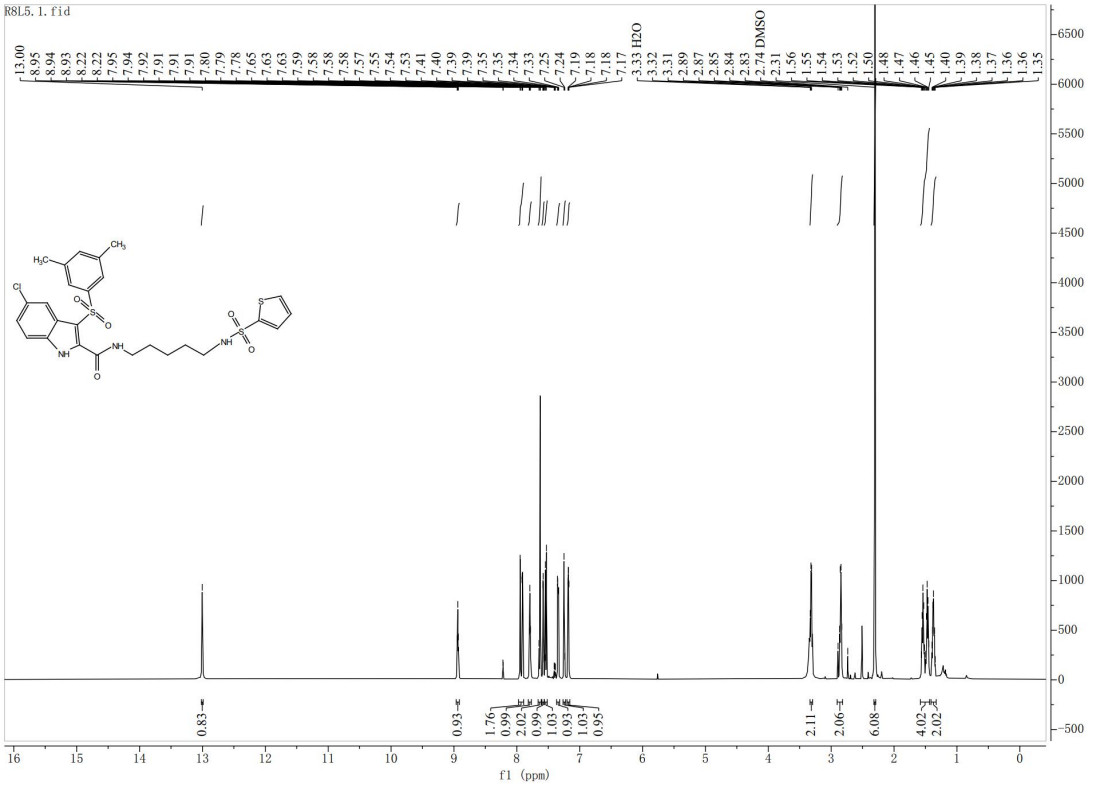
^{1}H NMR (600 MHz, DMSO-d_6) of **R_8L_4**



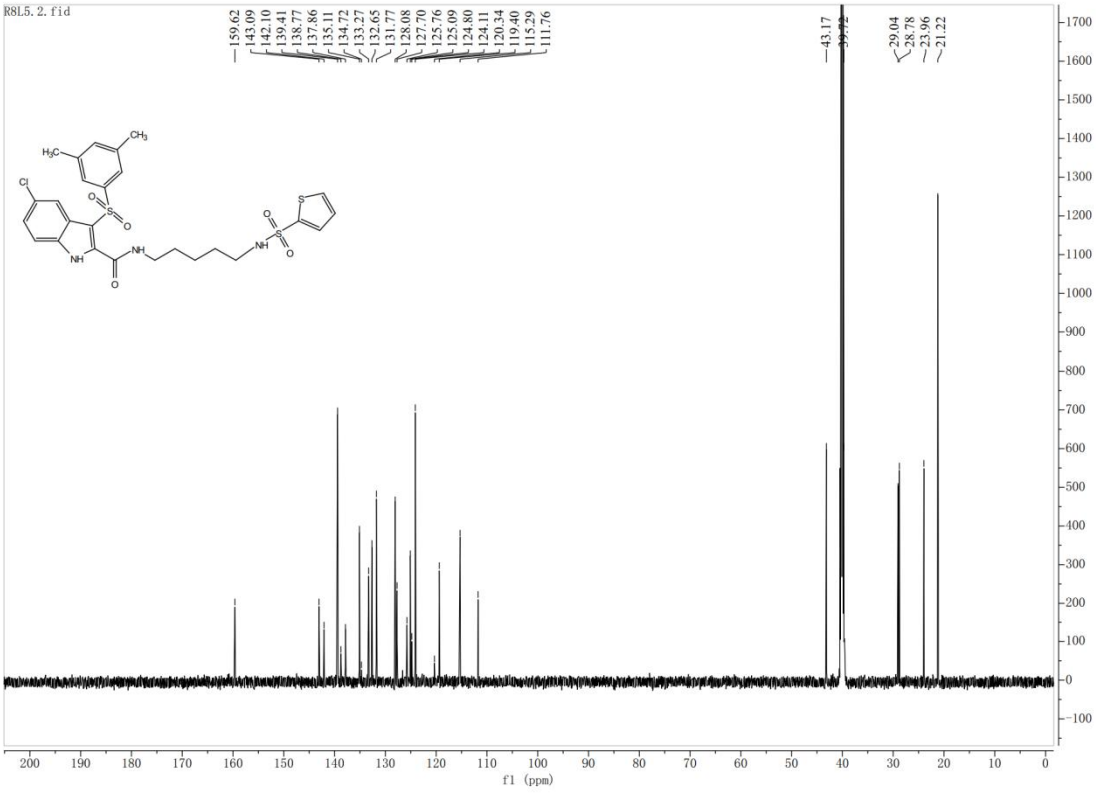
^{13}C NMR (150 MHz, DMSO-d_6) of **R_8L_4**



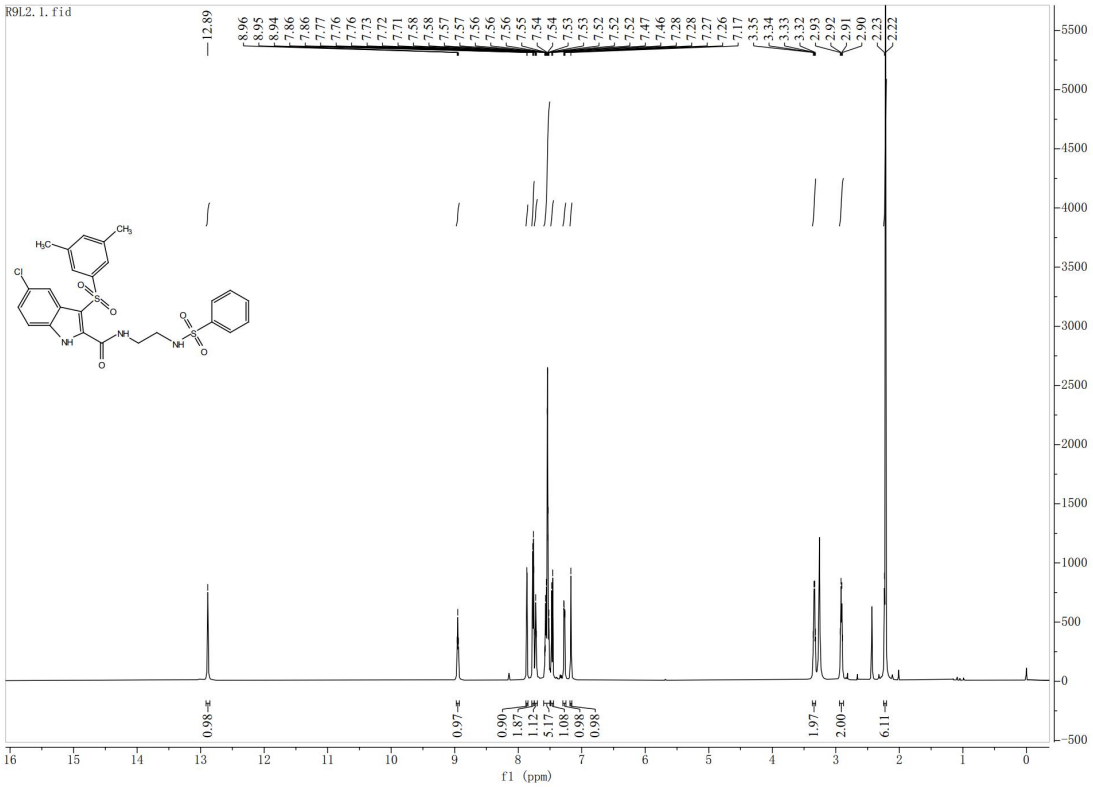
^{1}H NMR (600 MHz, DMSO-d_6) of **R_8L_5**



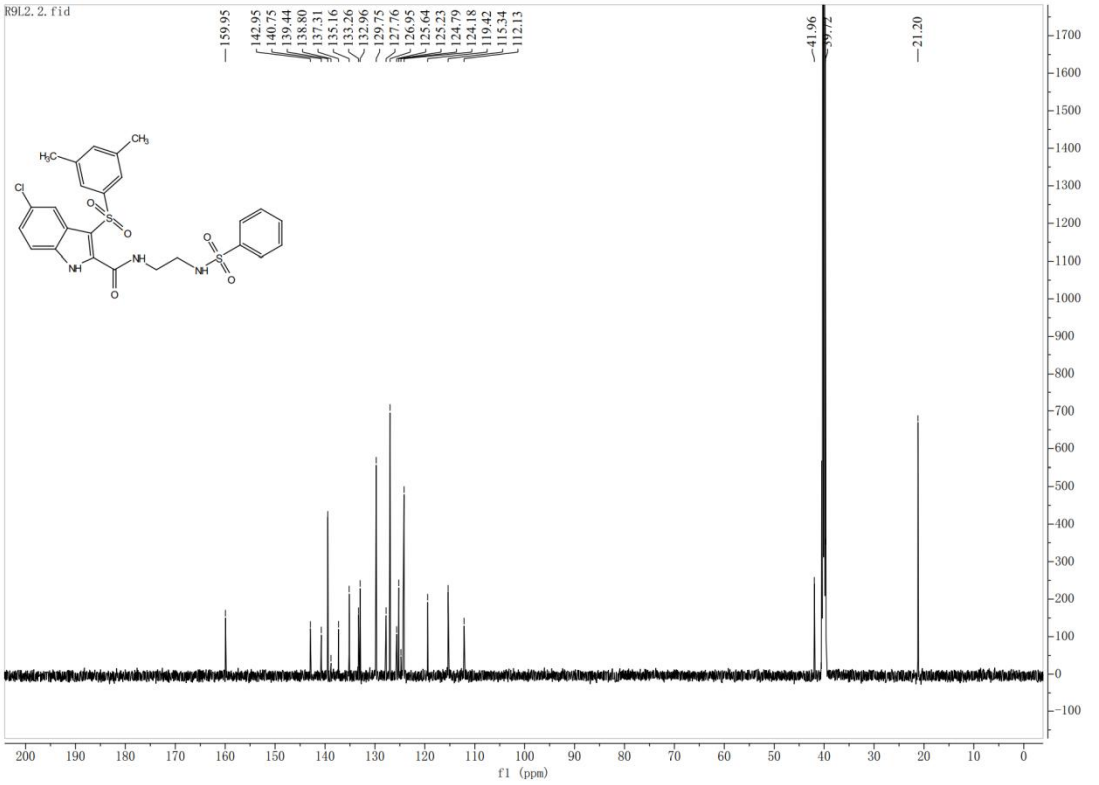
^{13}C NMR (150 MHz, DMSO-d_6) of **R_8L_5**



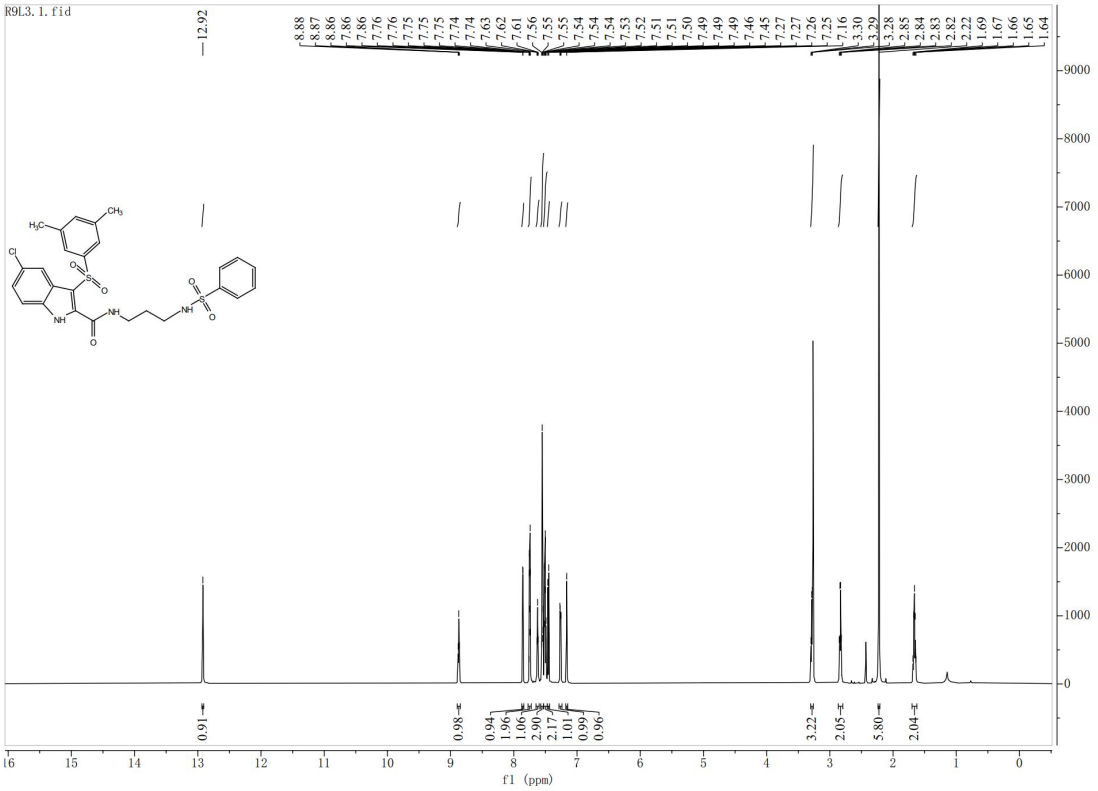
^{1}H NMR (600 MHz, DMSO-d_6) of **R_9L_2**



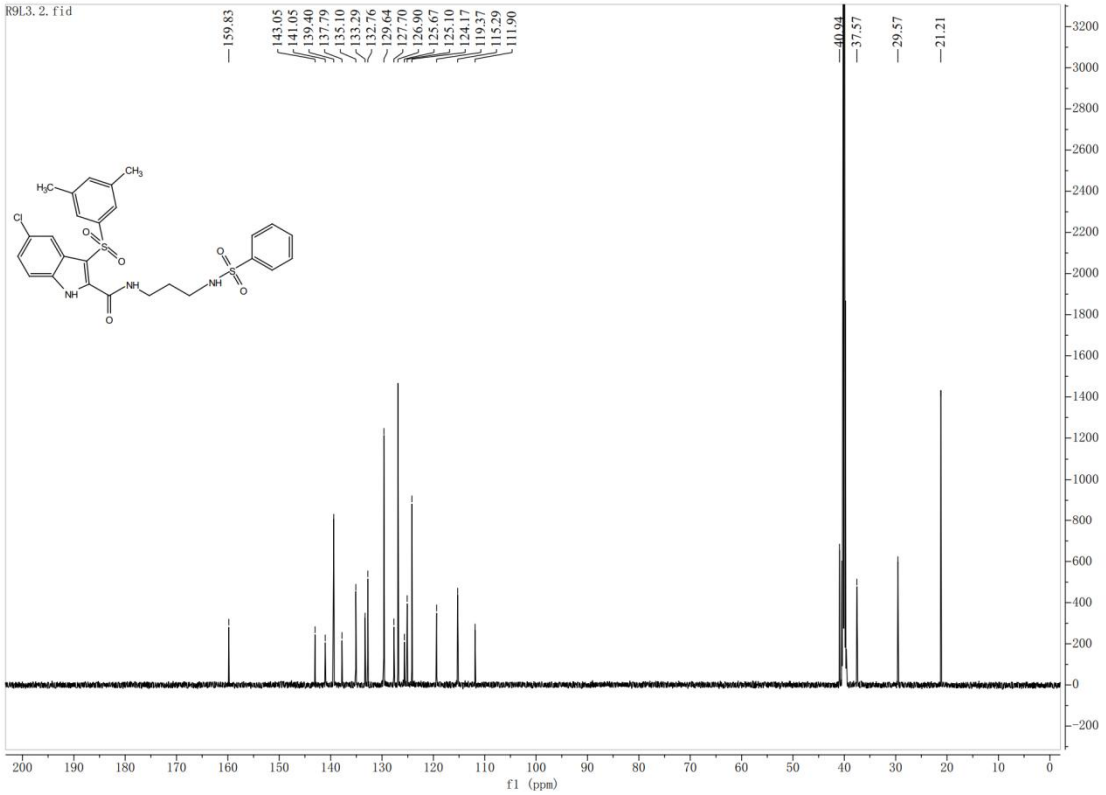
^{13}C NMR (150 MHz, DMSO-d_6) of **R_9L_2**



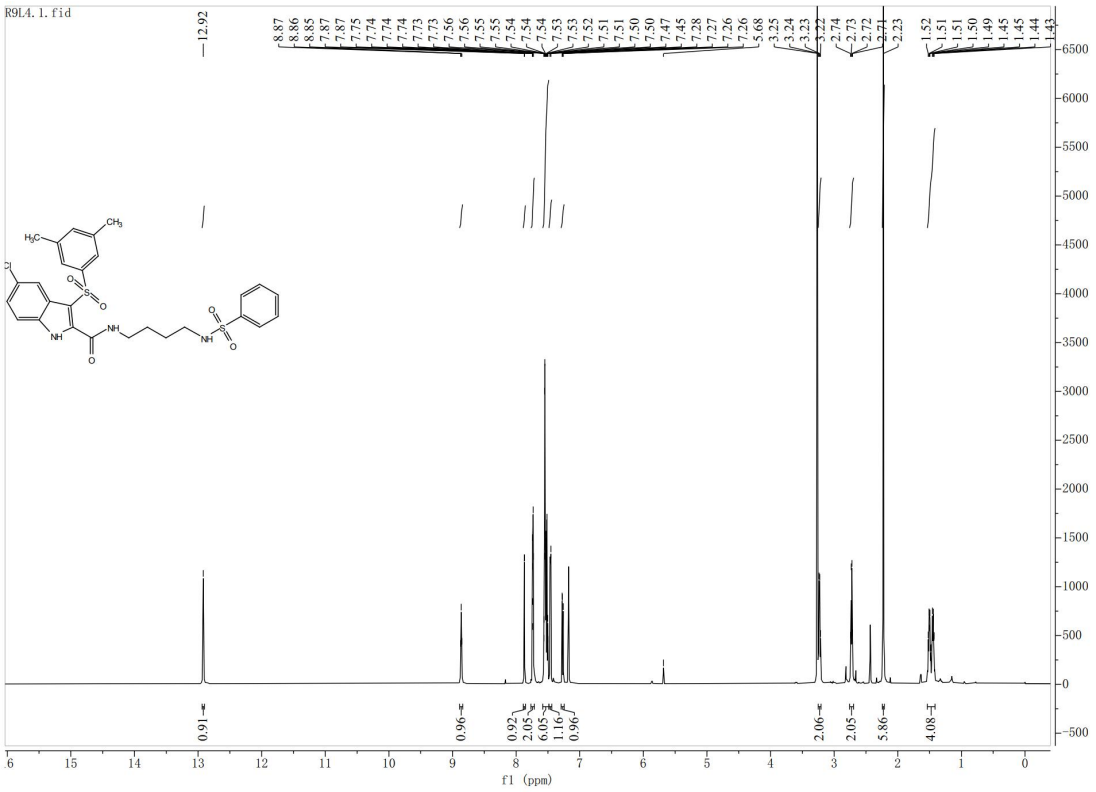
^{1}H NMR (600 MHz, DMSO-d_6) of **R_9L_3**



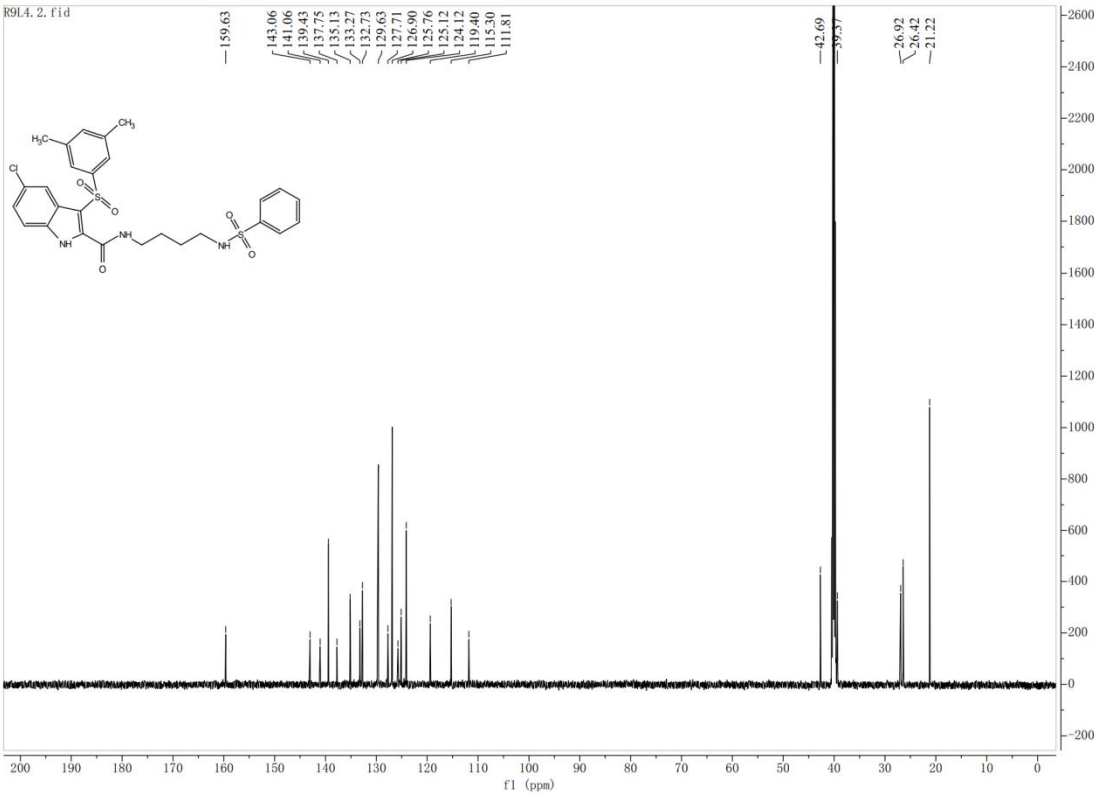
^{13}C NMR (150 MHz, DMSO-d_6) of **R_9L_3**



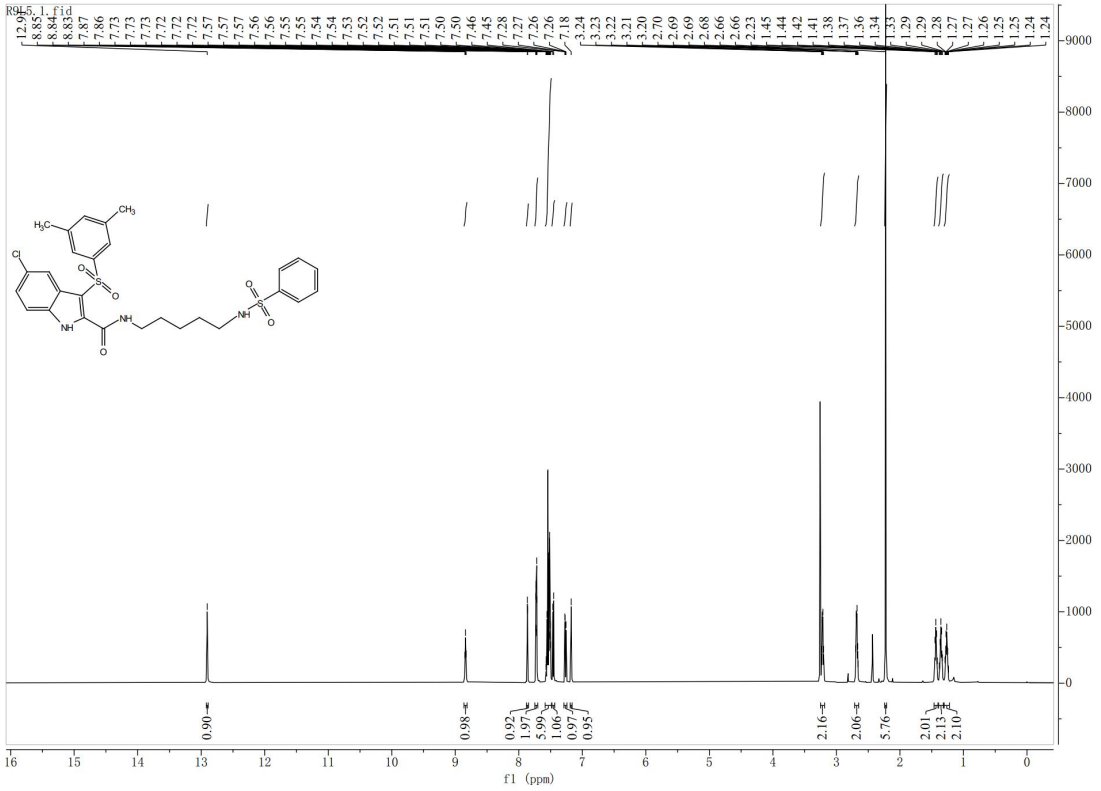
^{1}H NMR (600 MHz, DMSO-d_6) of **R_9L_4**



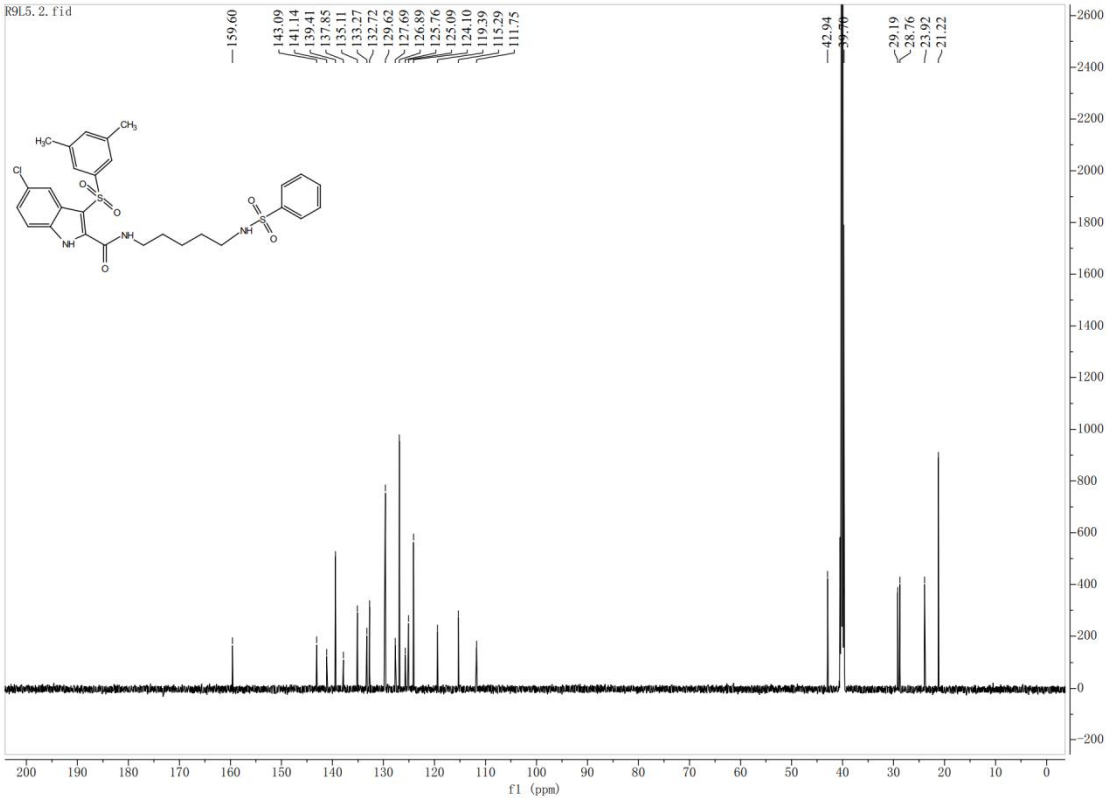
^{13}C NMR (150 MHz, DMSO-d_6) of **R_9L_4**



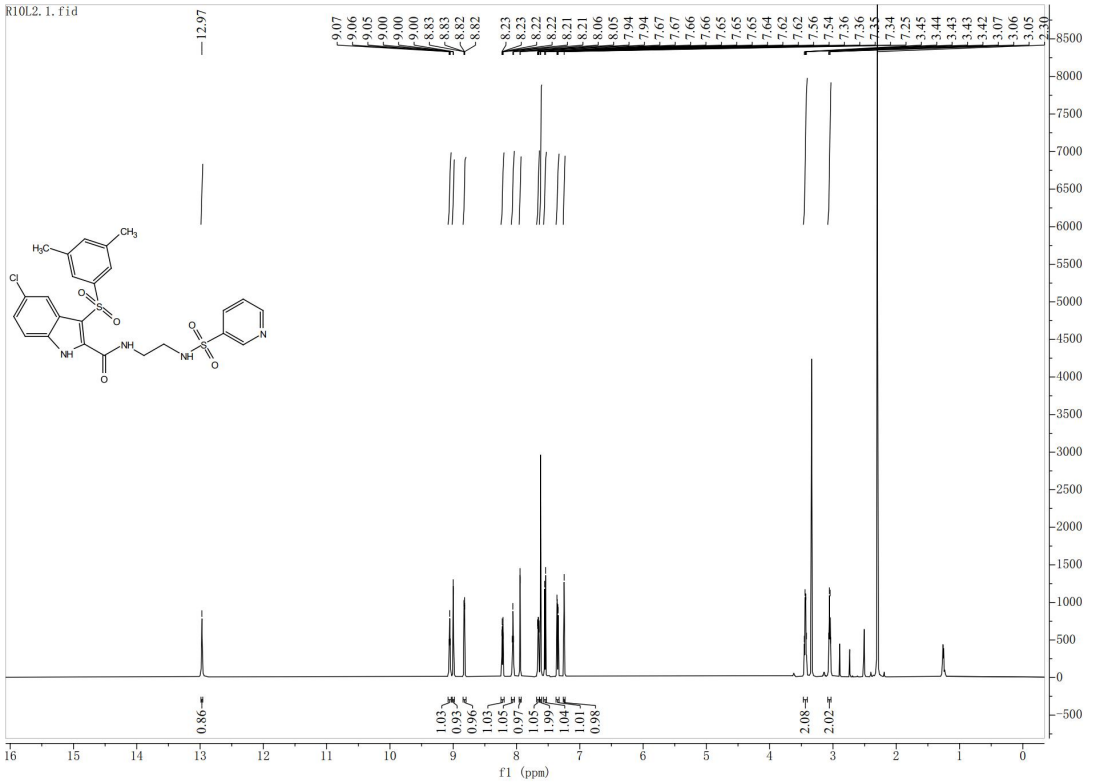
^{1}H NMR (600 MHz, DMSO-d_6) of **R_9L_5**



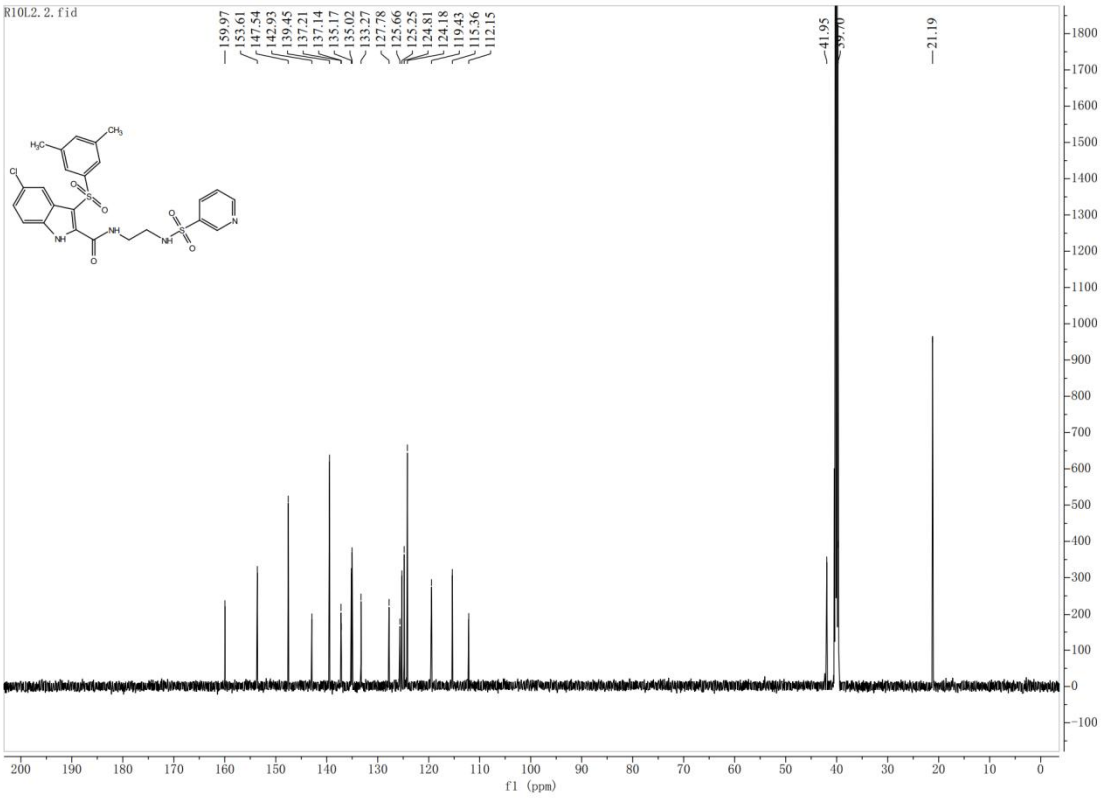
^{13}C NMR (150 MHz, DMSO-d_6) of **R_9L_5**



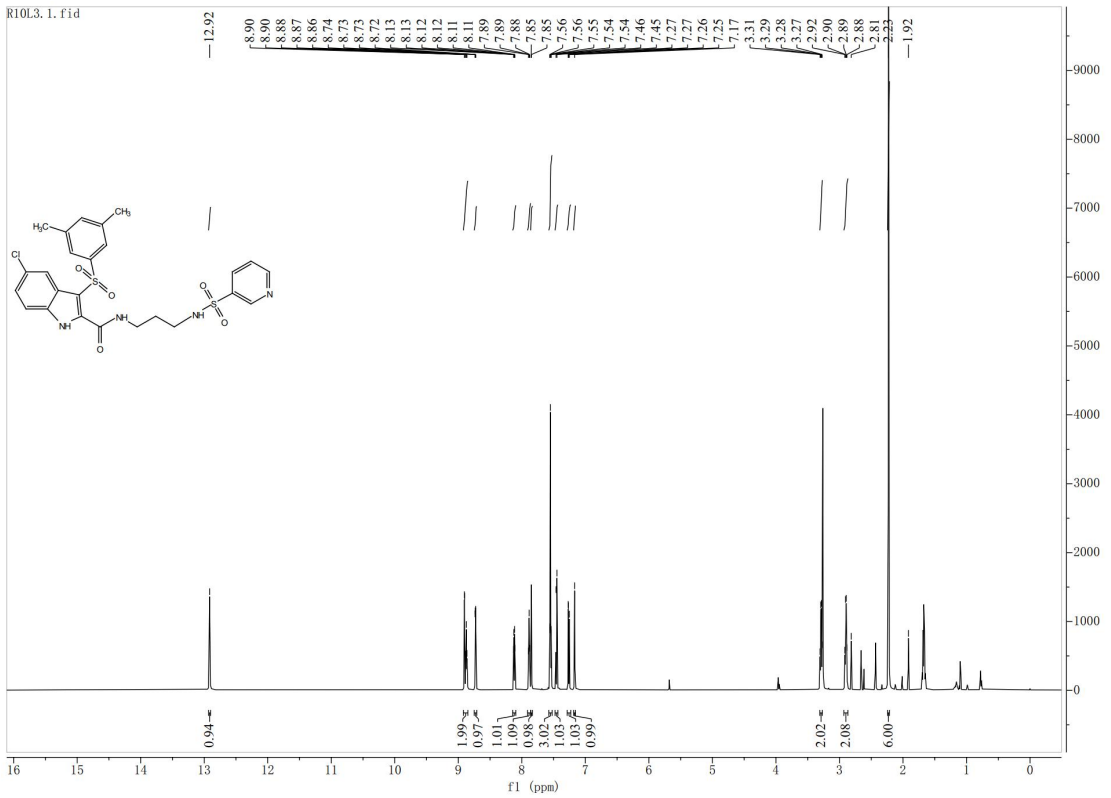
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{10}L_2$**



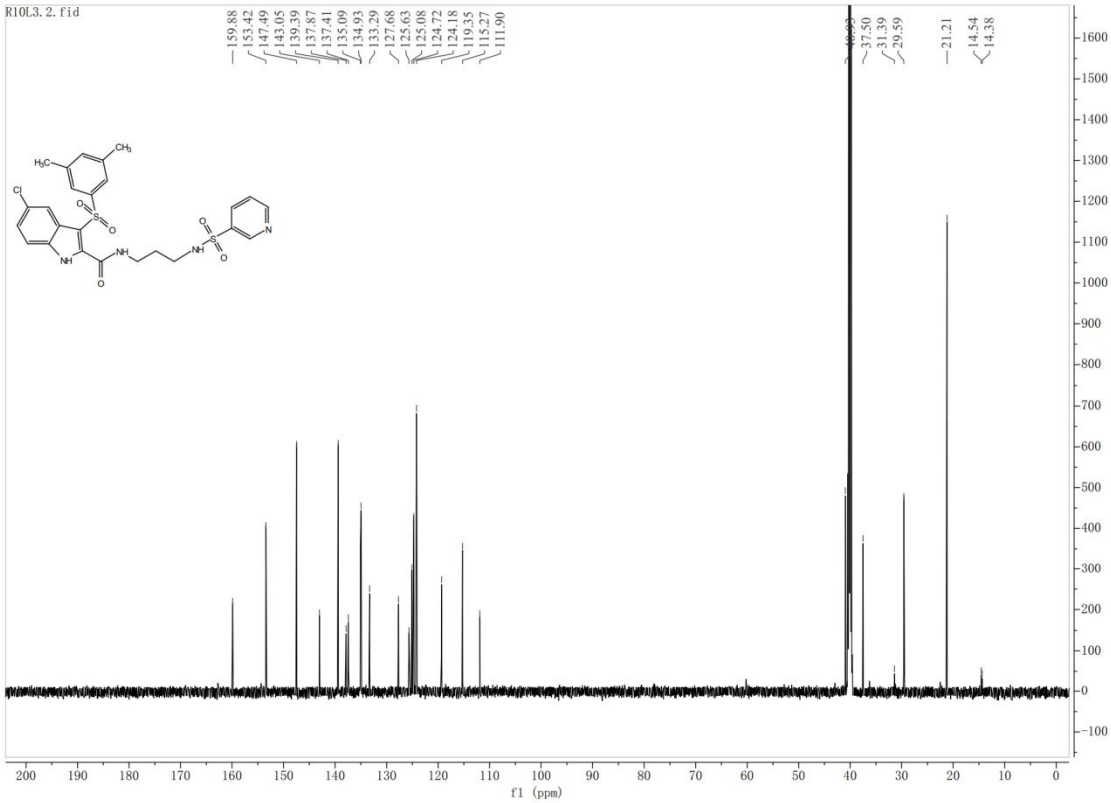
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{10}L_2$**



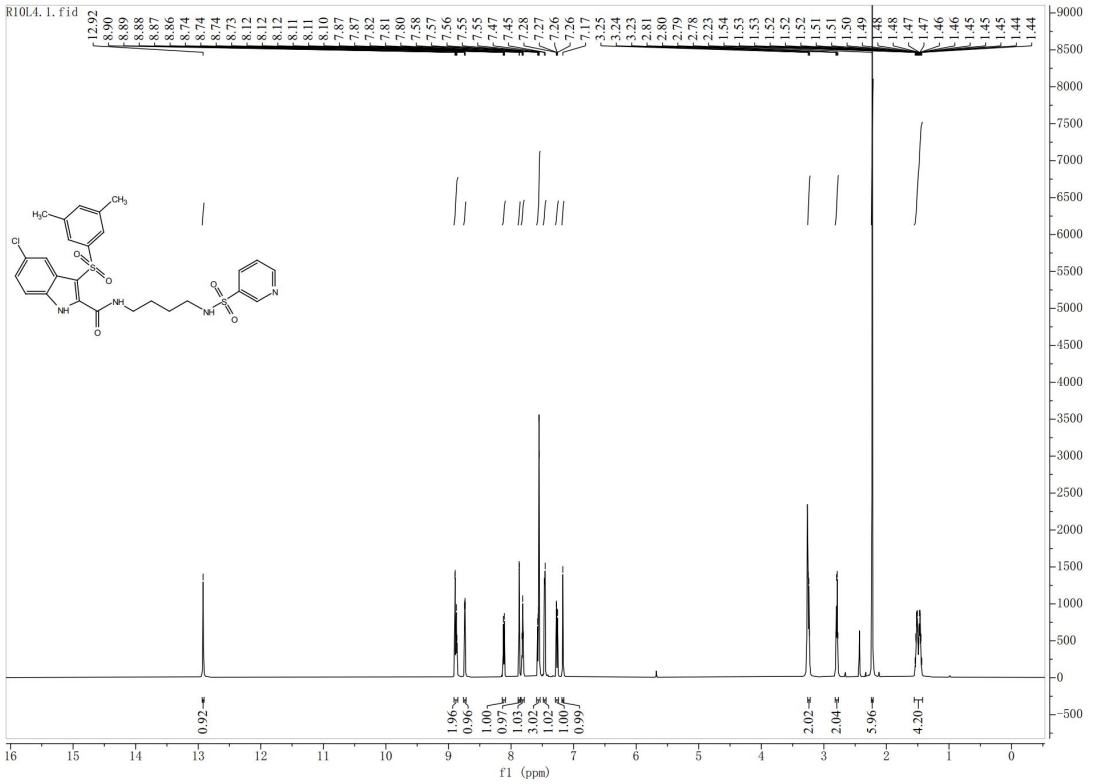
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{10}L_3$**



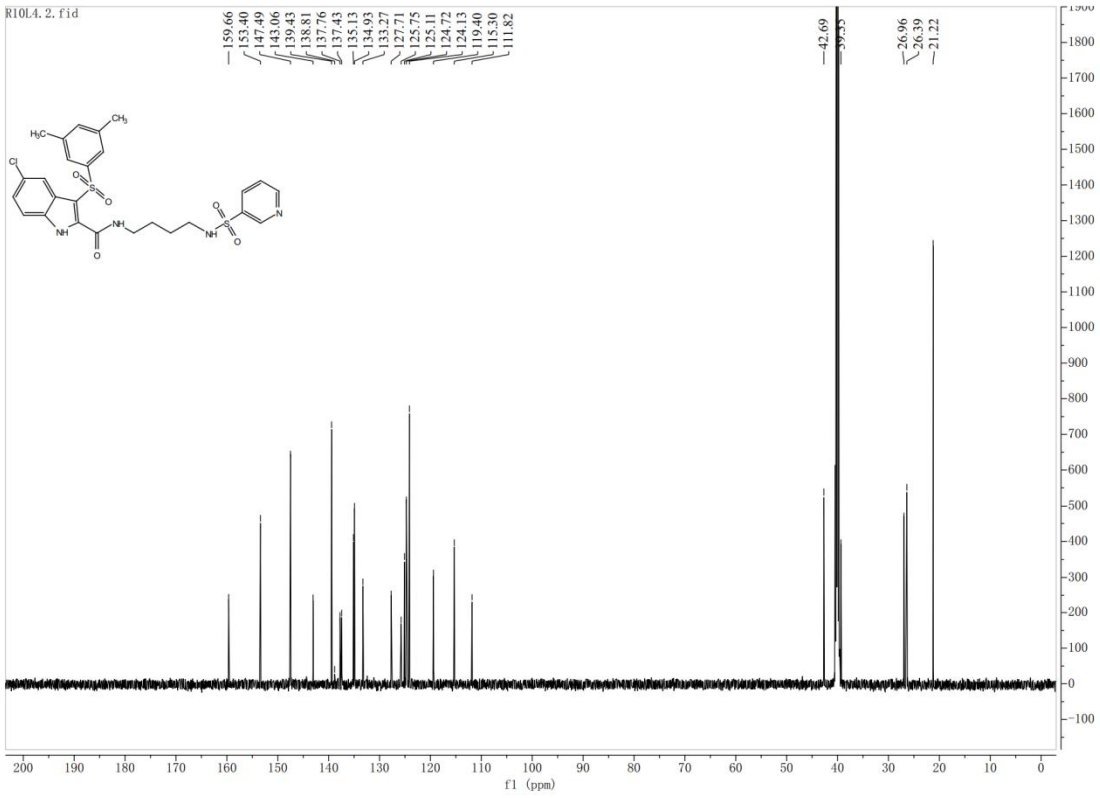
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{10}L_3$**



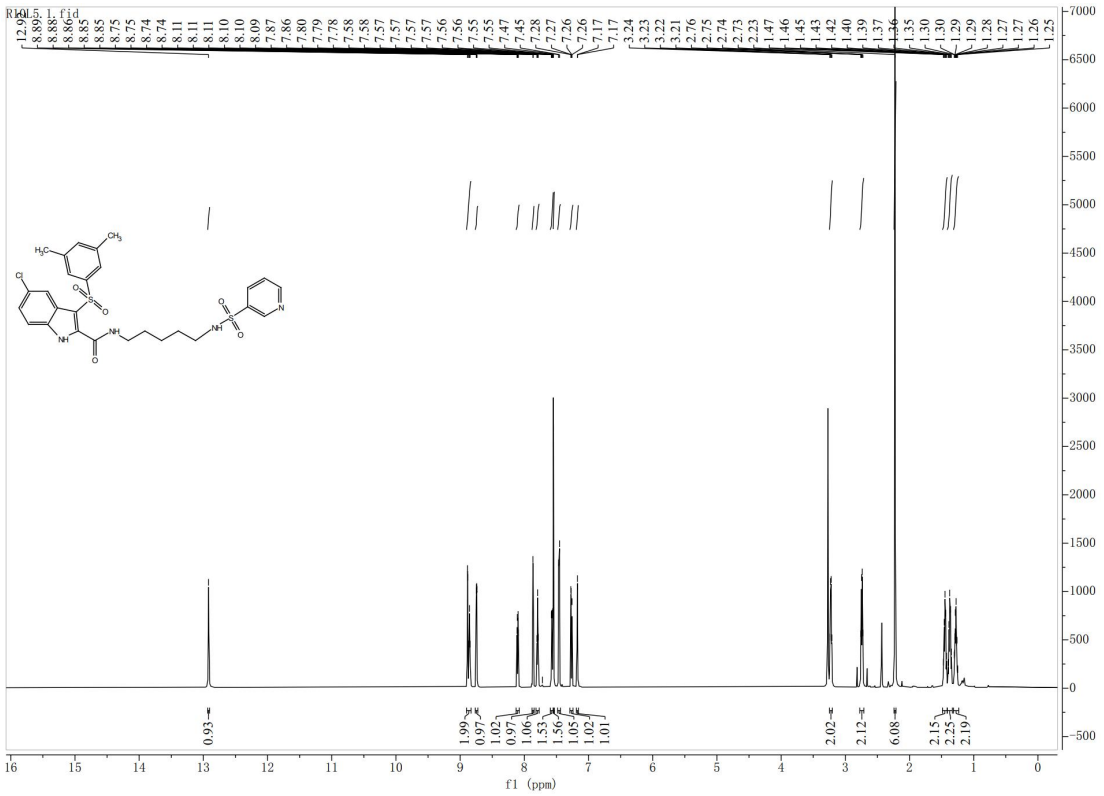
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{10}L_4$**



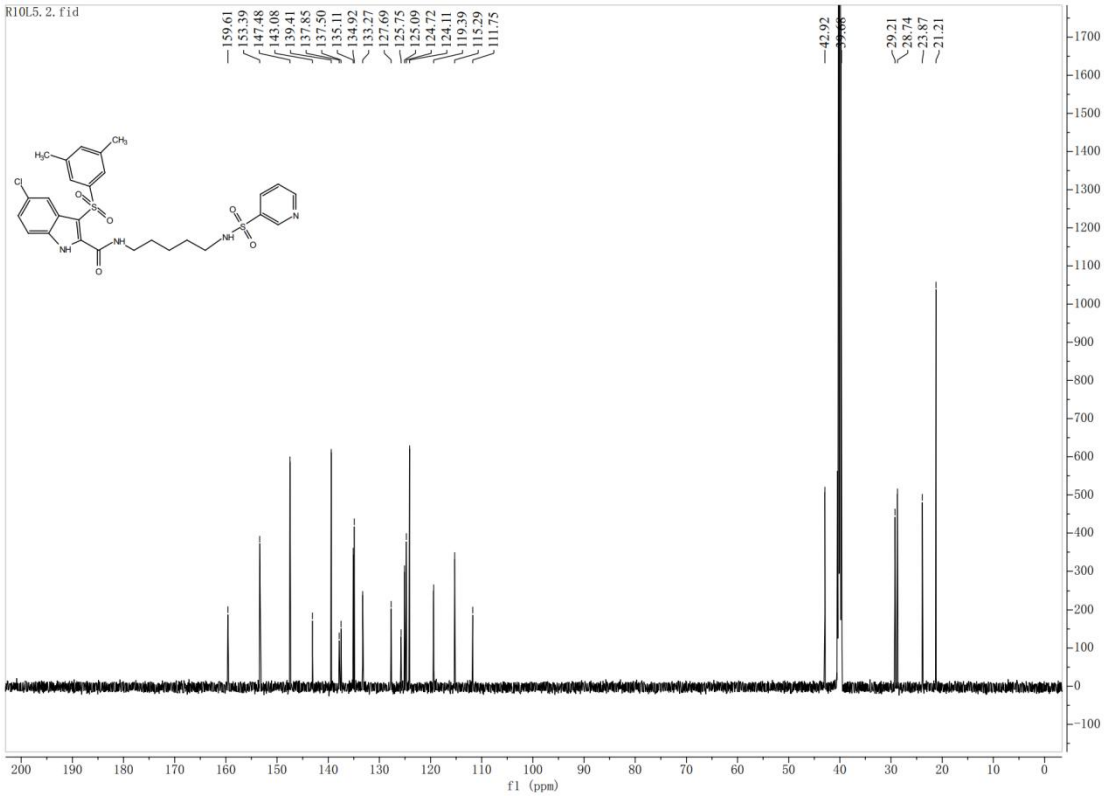
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{10}L_4$**



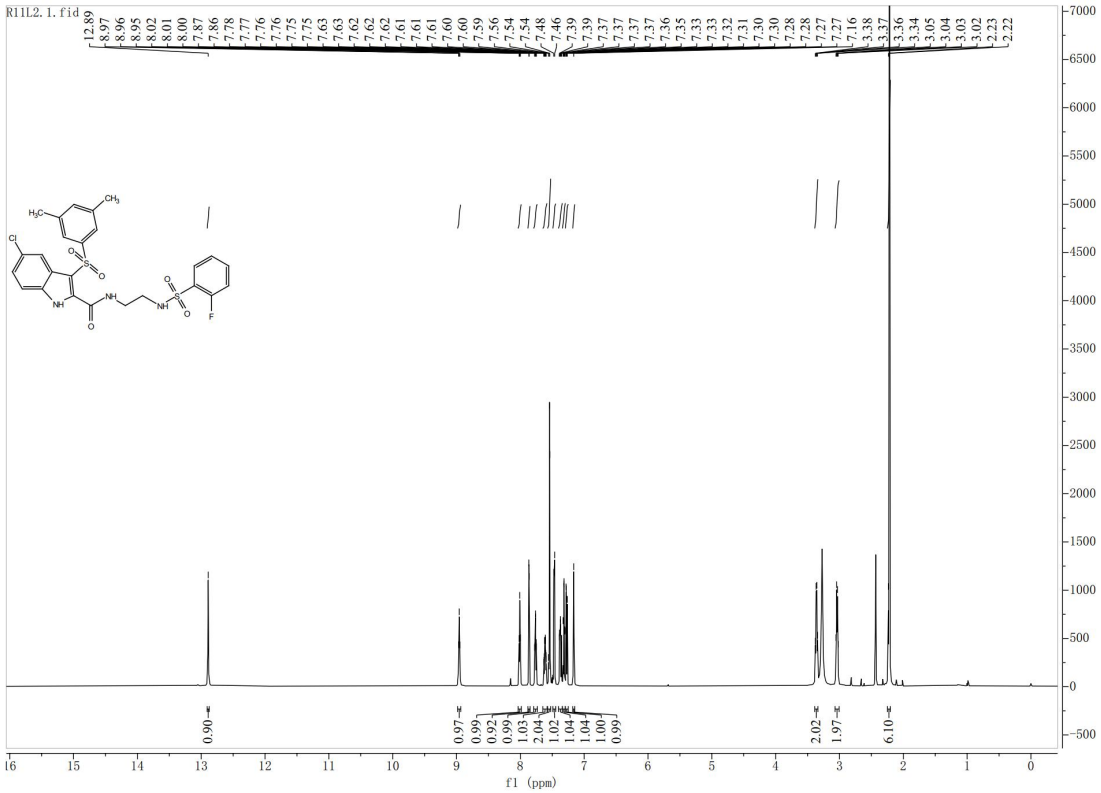
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{10}L_5$**



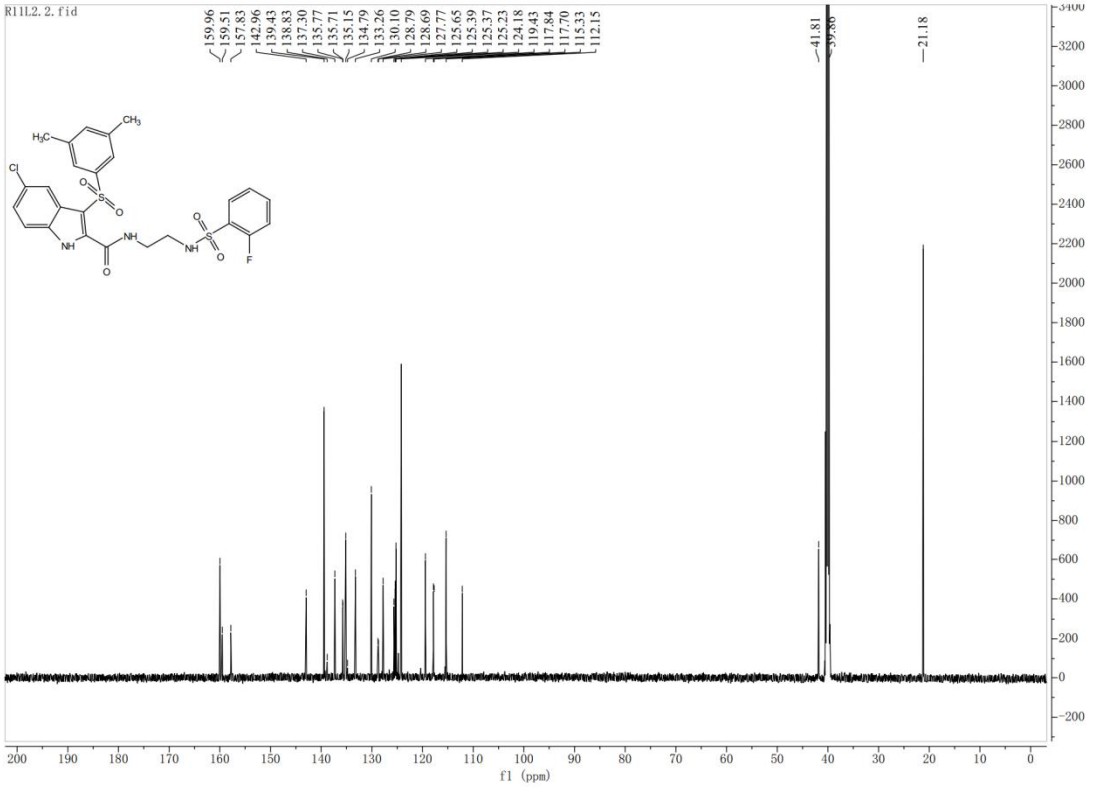
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{10}L_5$**



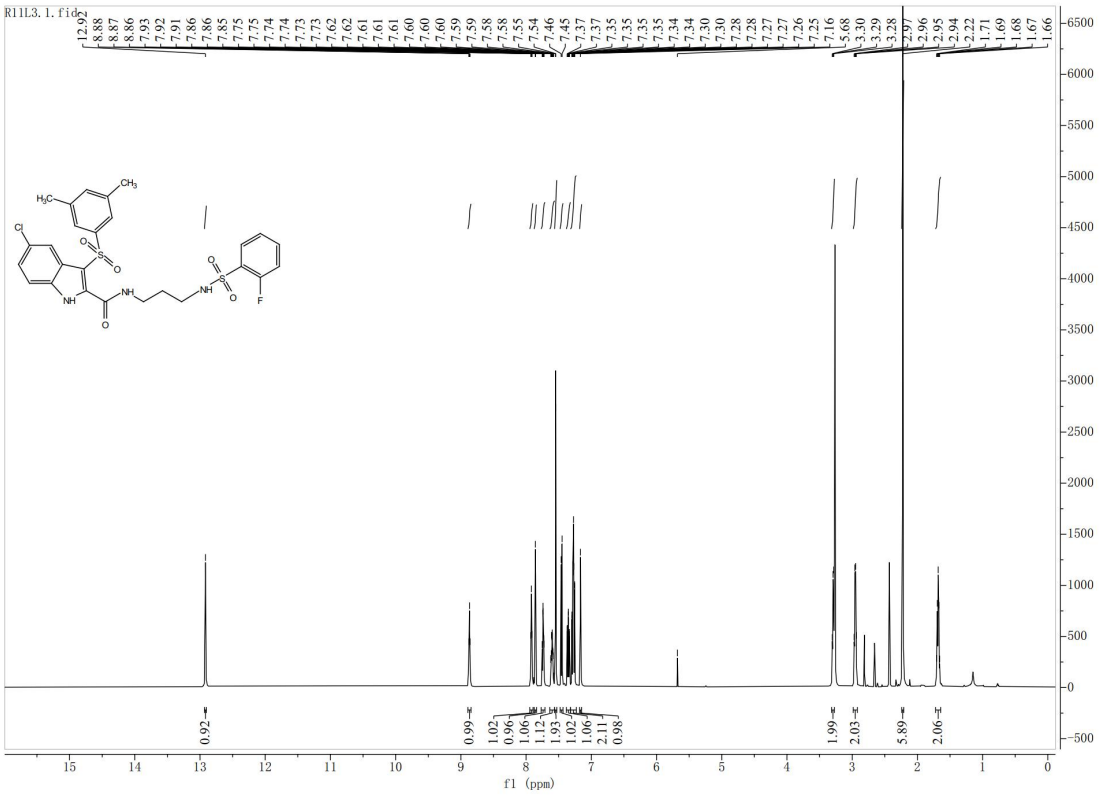
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{11}L_2$**



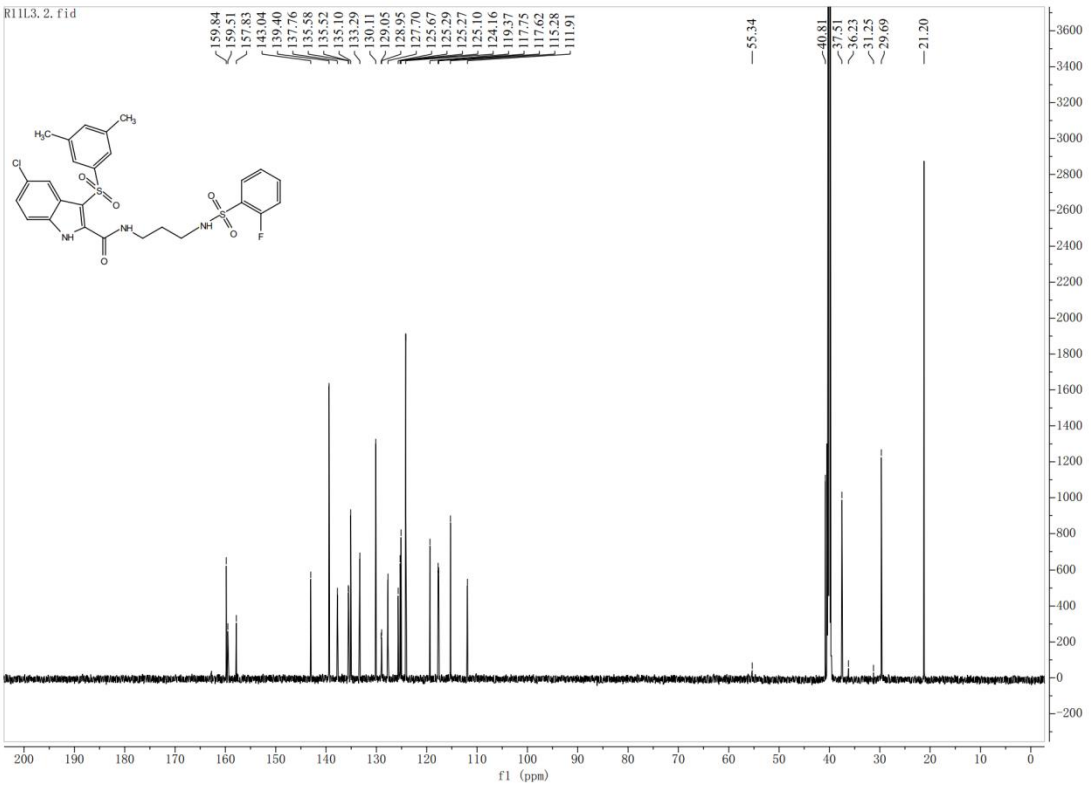
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{11}L_2$**



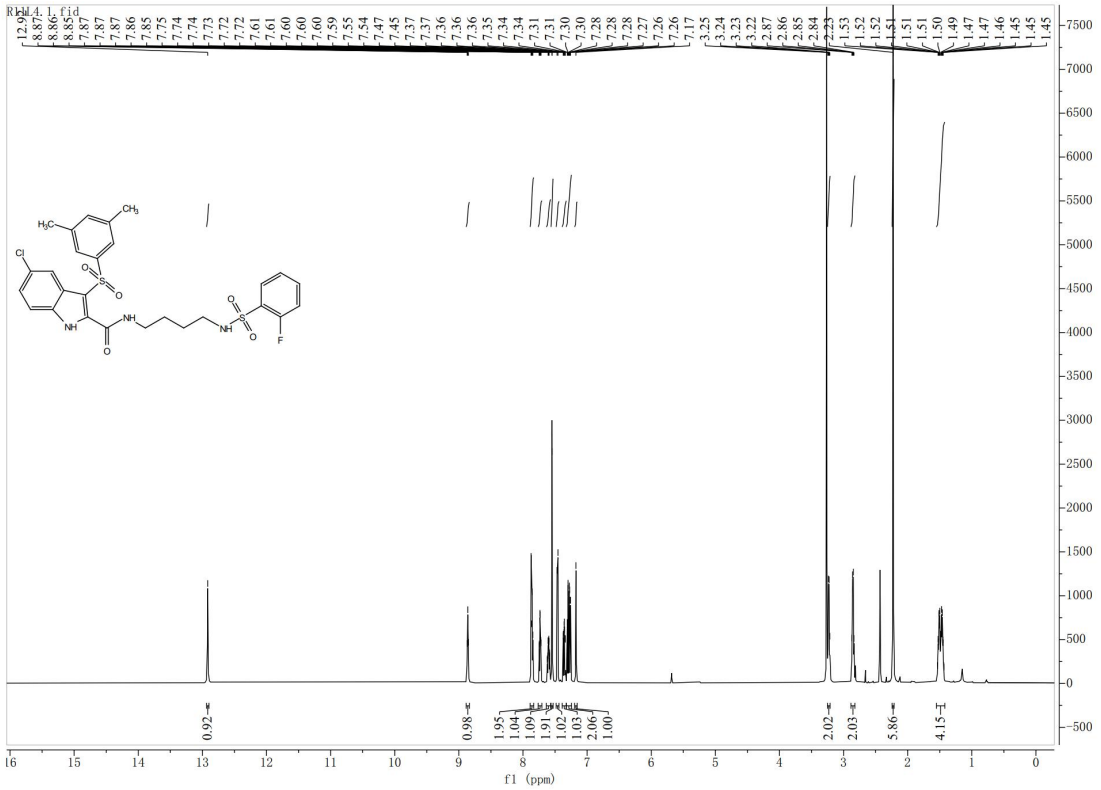
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{11}L_3$**



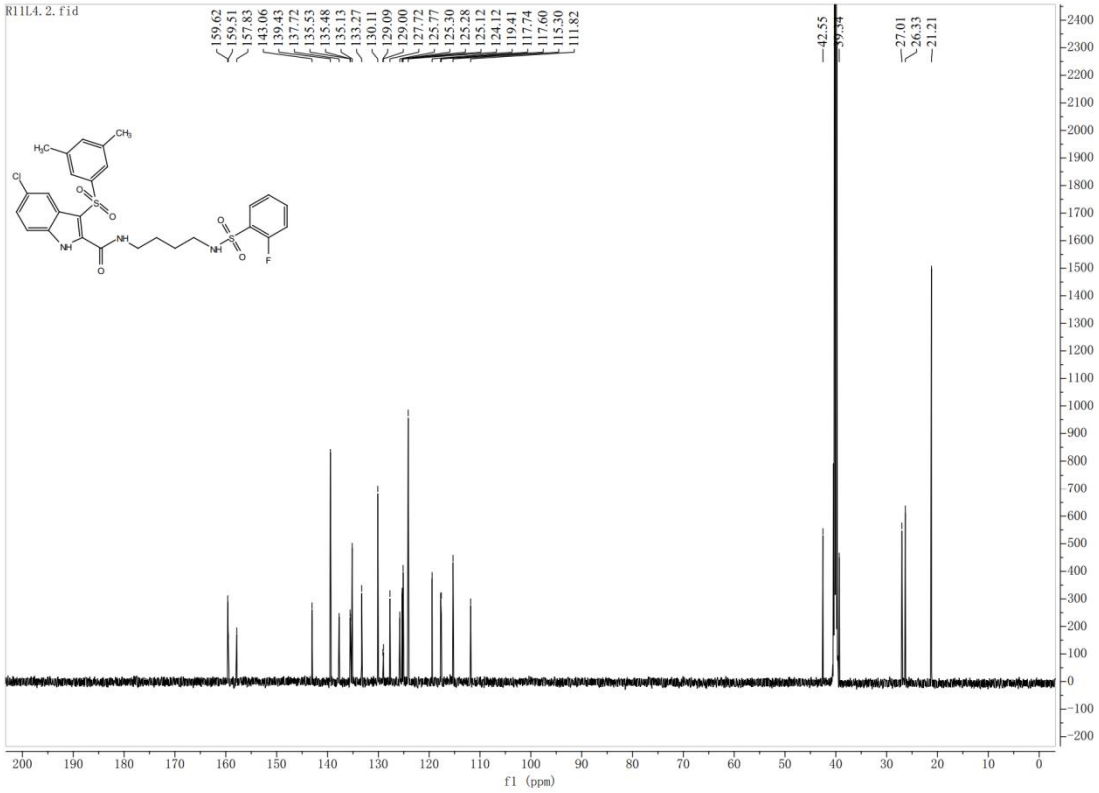
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{11}L_3$**



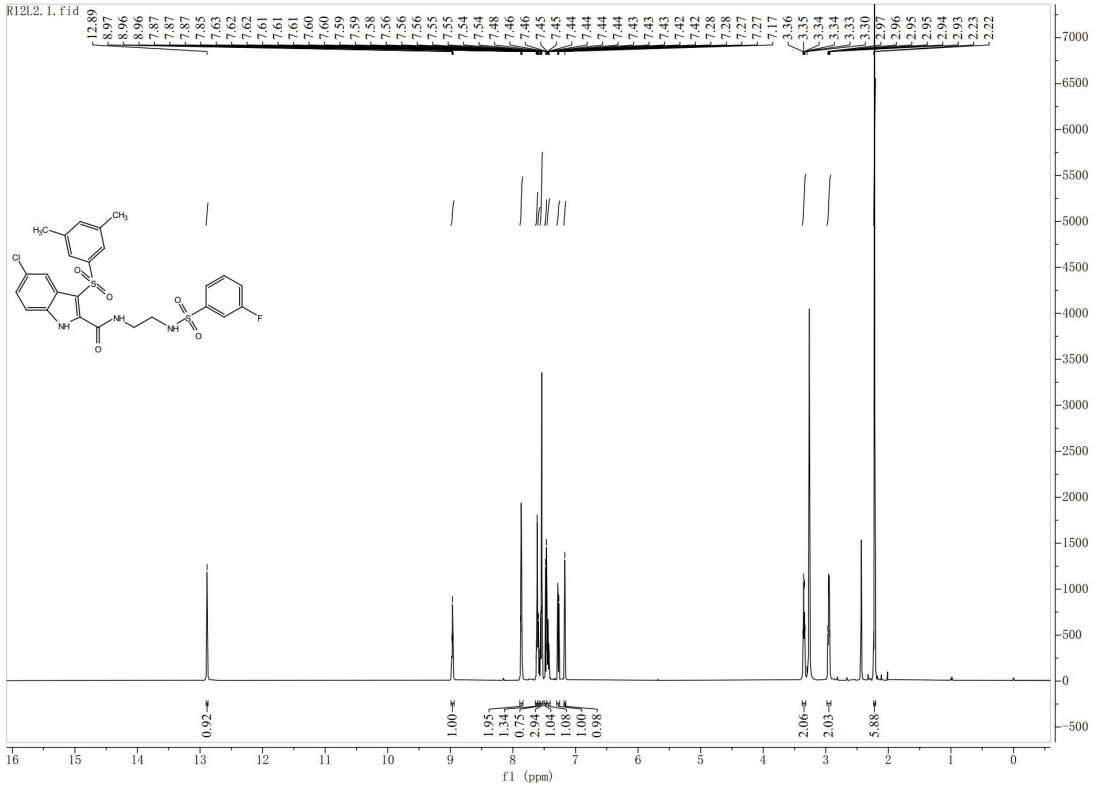
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{11}L_3$**



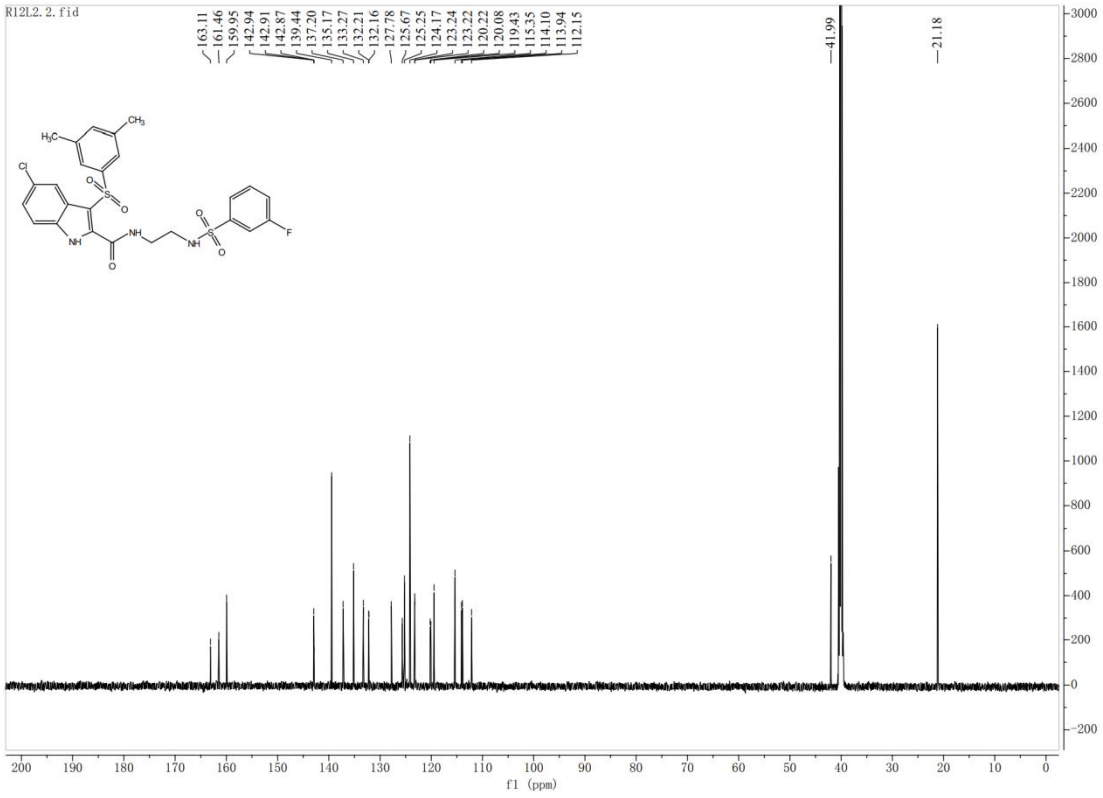
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{11}L_3$**



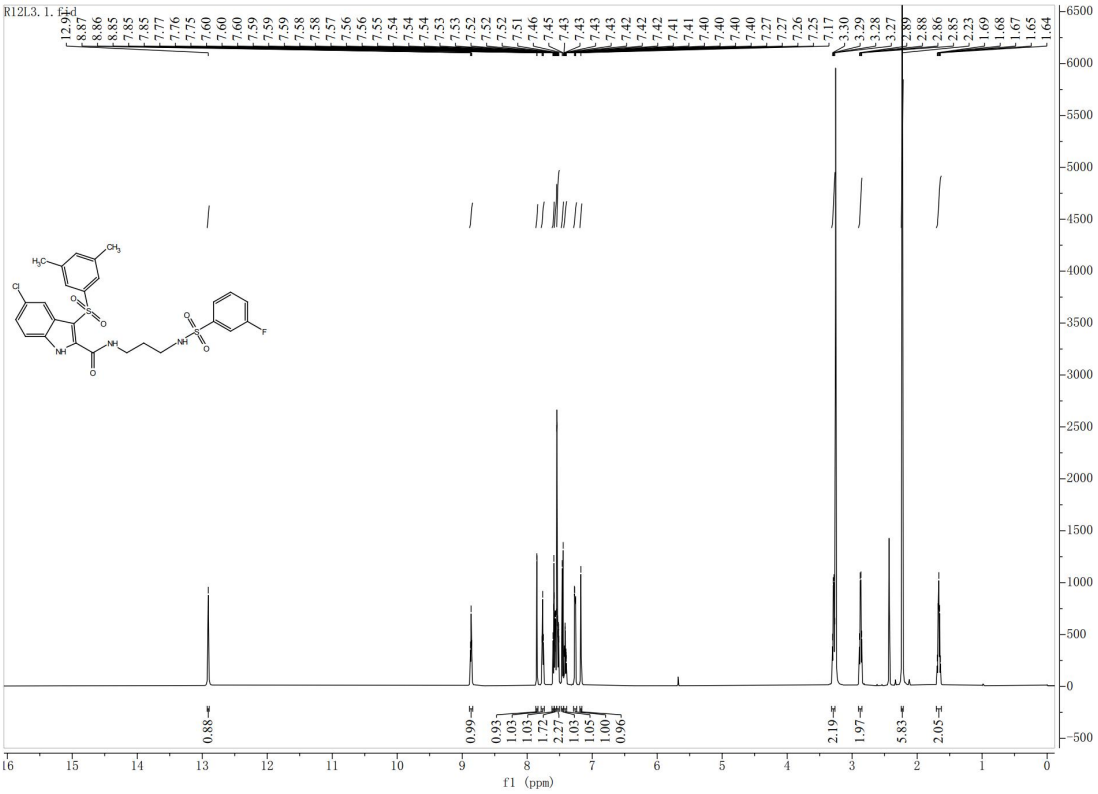
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{12}L_2$**



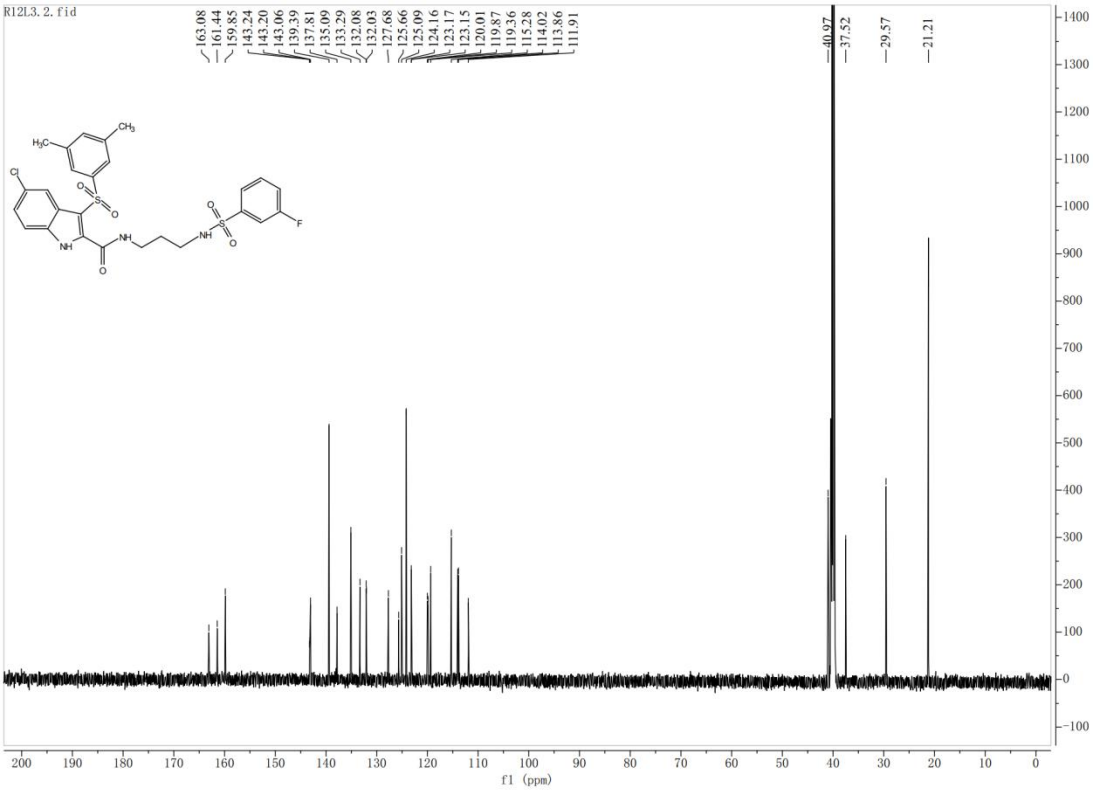
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{12}L_2$**



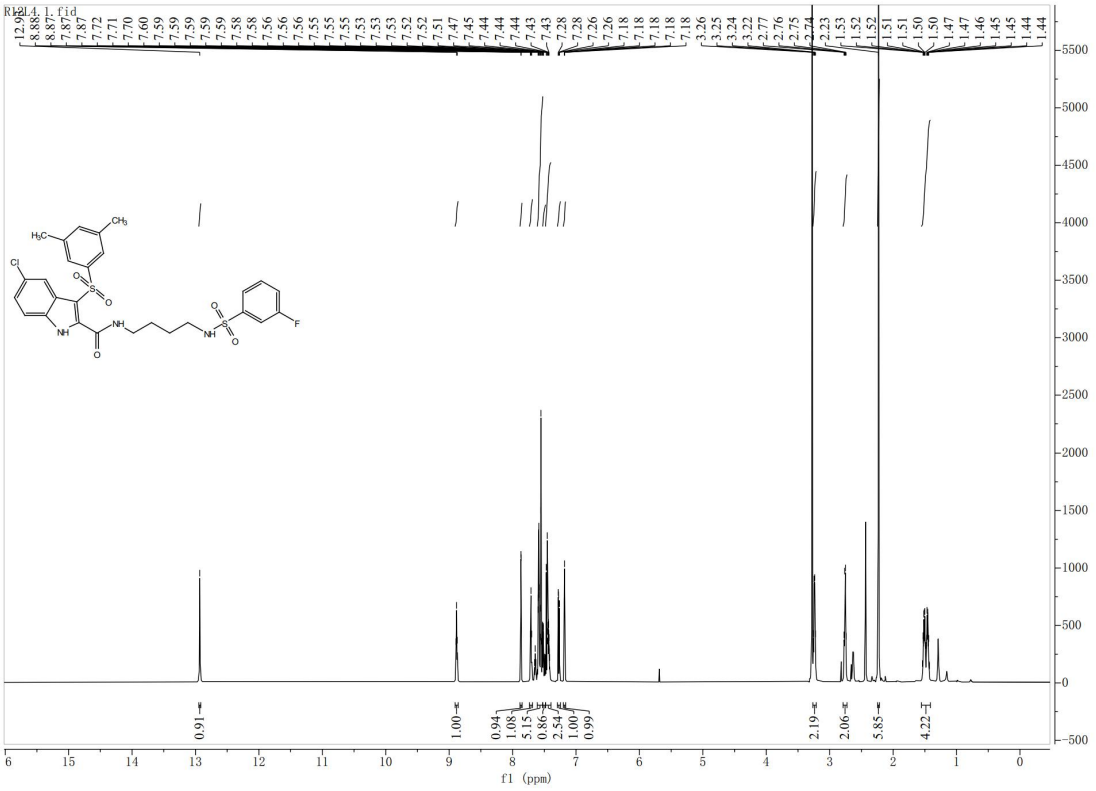
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{12}L_3$**



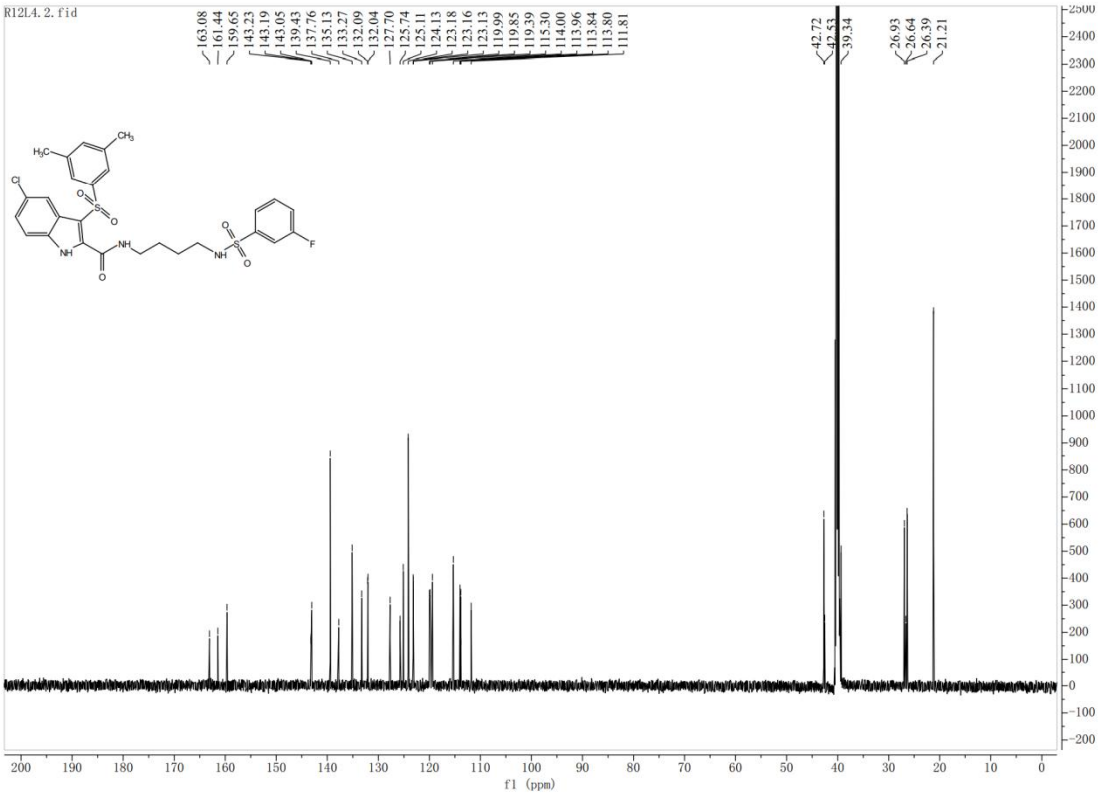
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{12}L_3$**



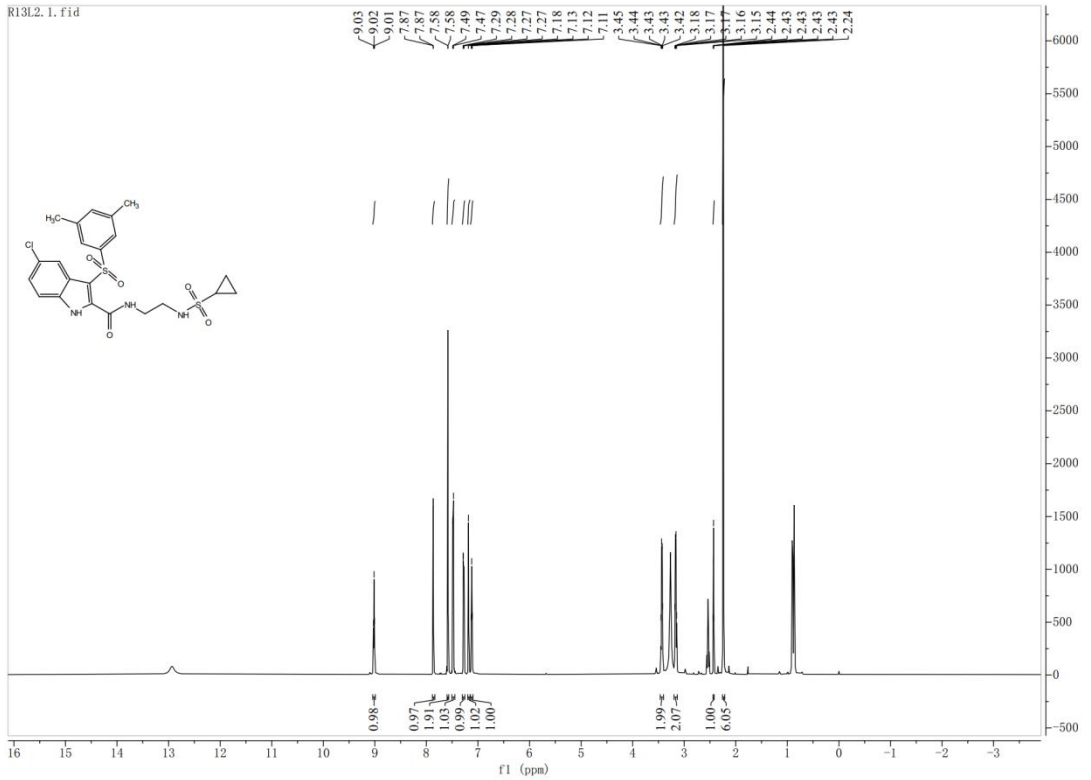
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{12}L_4$**



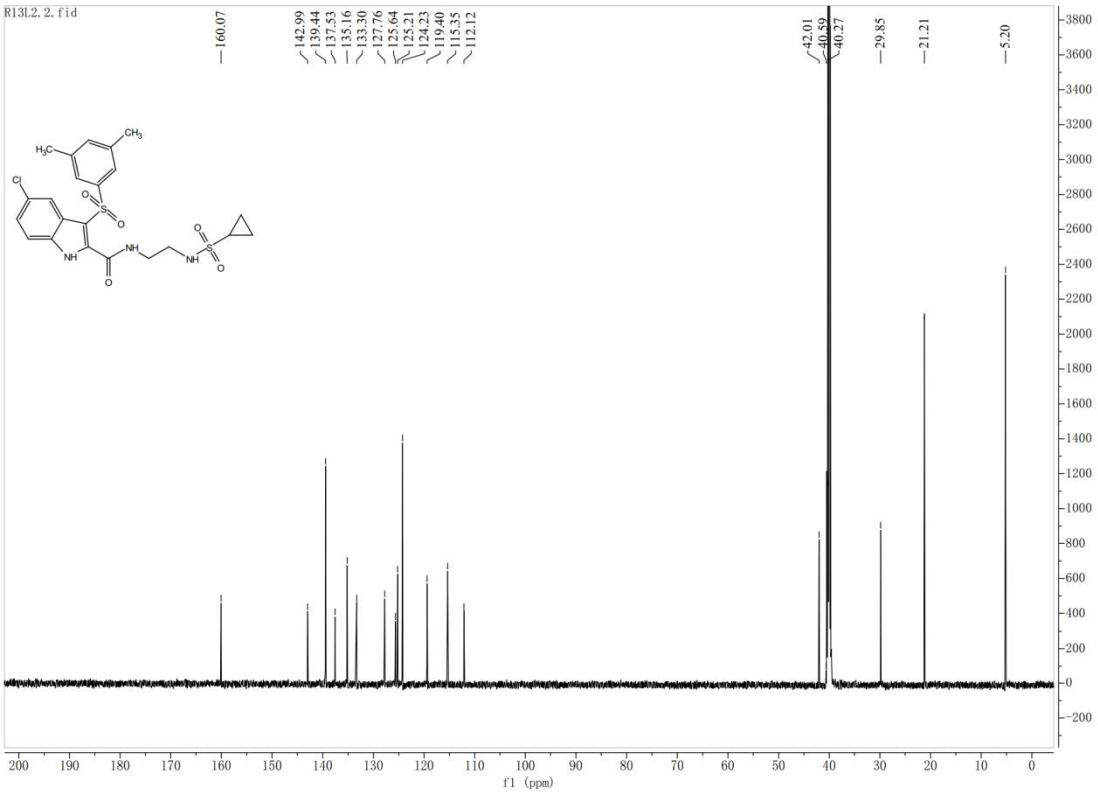
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{12}L_4$**



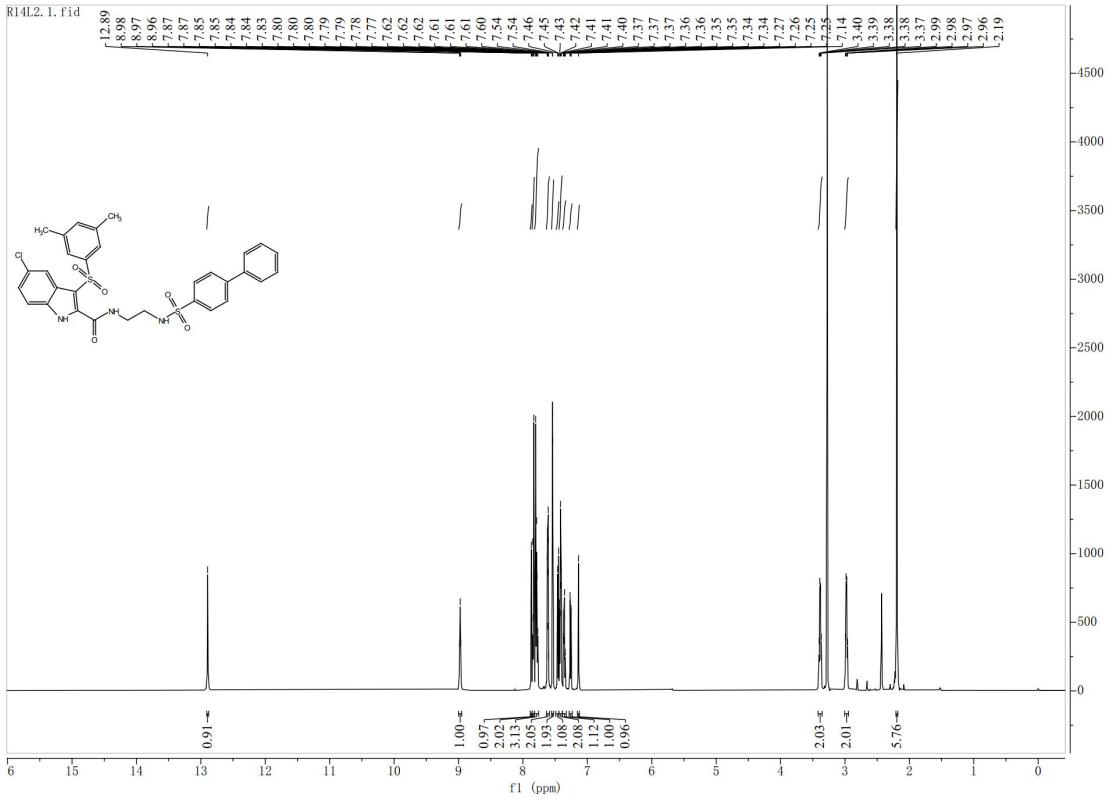
^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{13}L_2$**



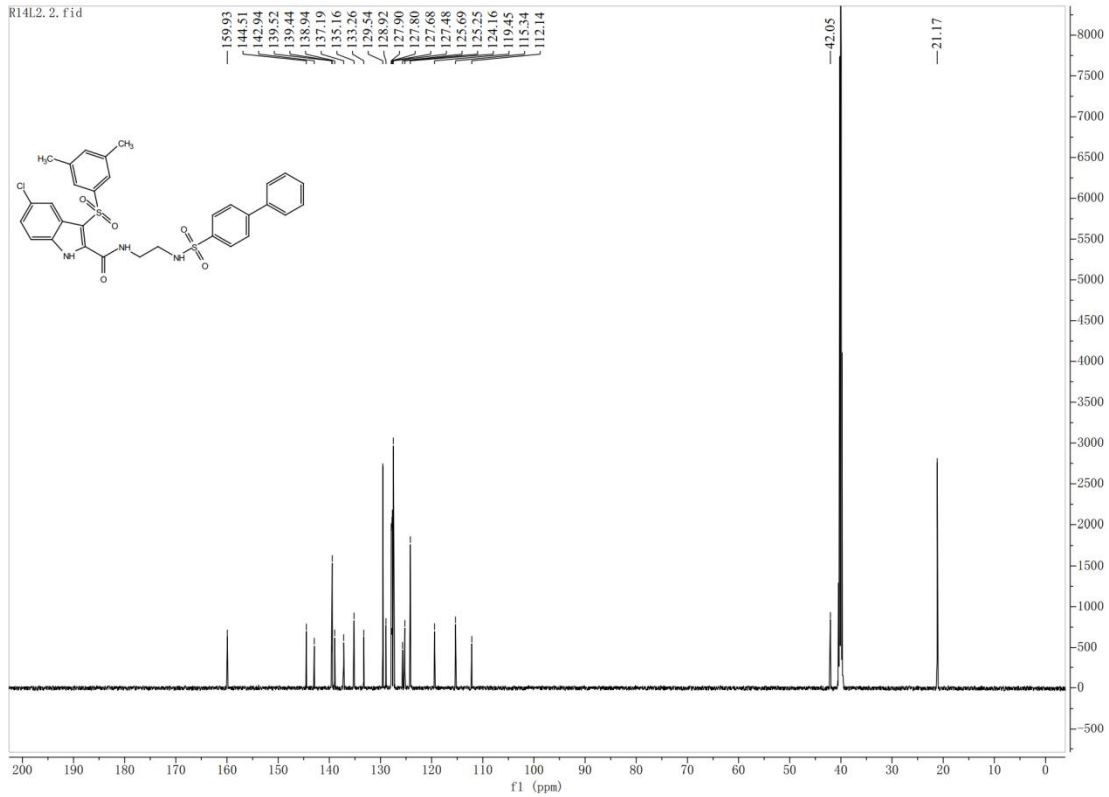
^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{13}L_2$**



^{1}H NMR (600 MHz, DMSO-d_6) of **$R_{14}L_2$**

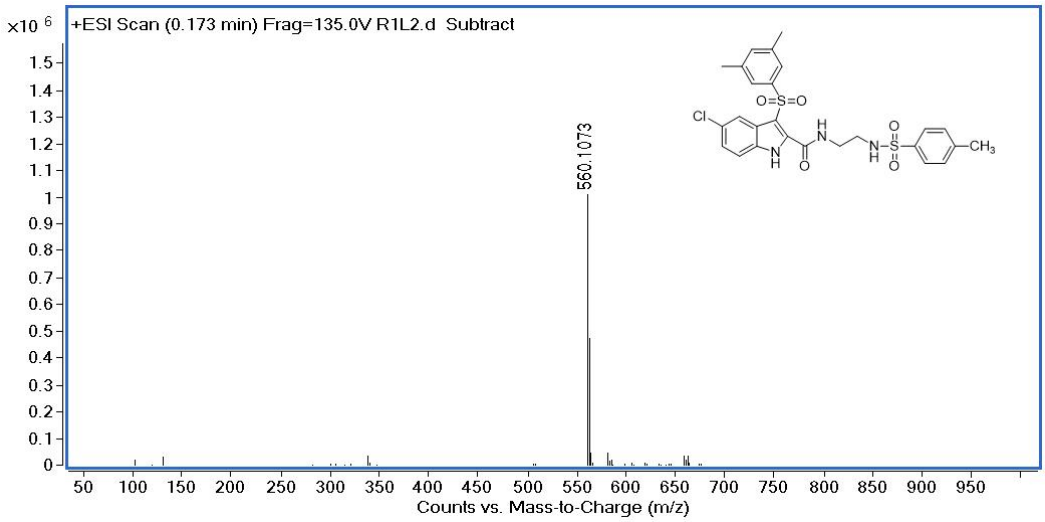


^{13}C NMR (150 MHz, DMSO-d_6) of **$R_{14}L_2$**

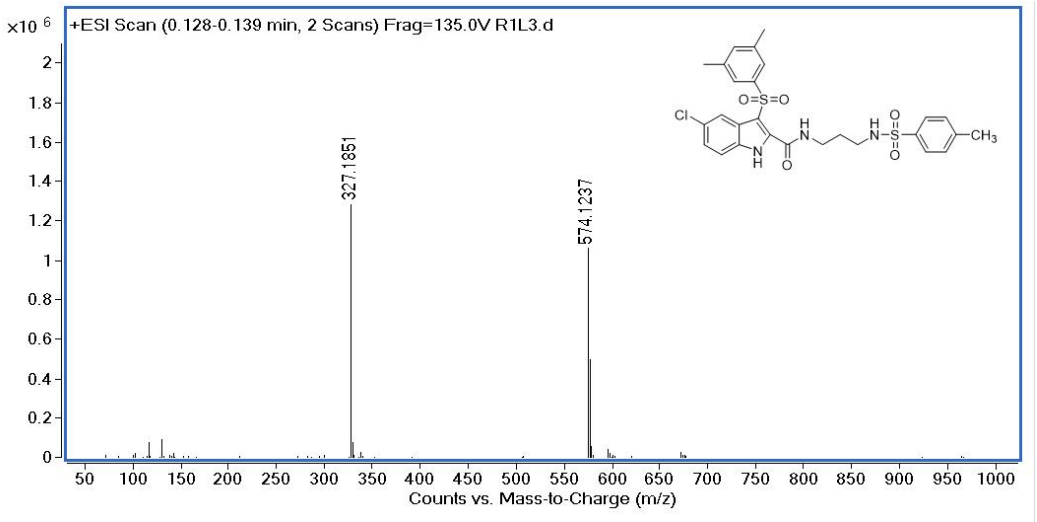


HRMS spectra of representative final compounds

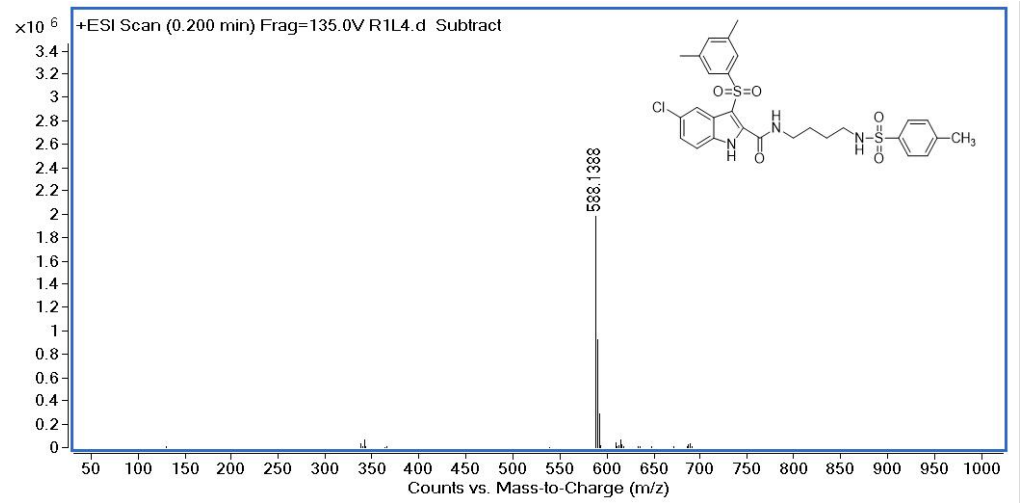
HRMS spectrum of R_1L_2



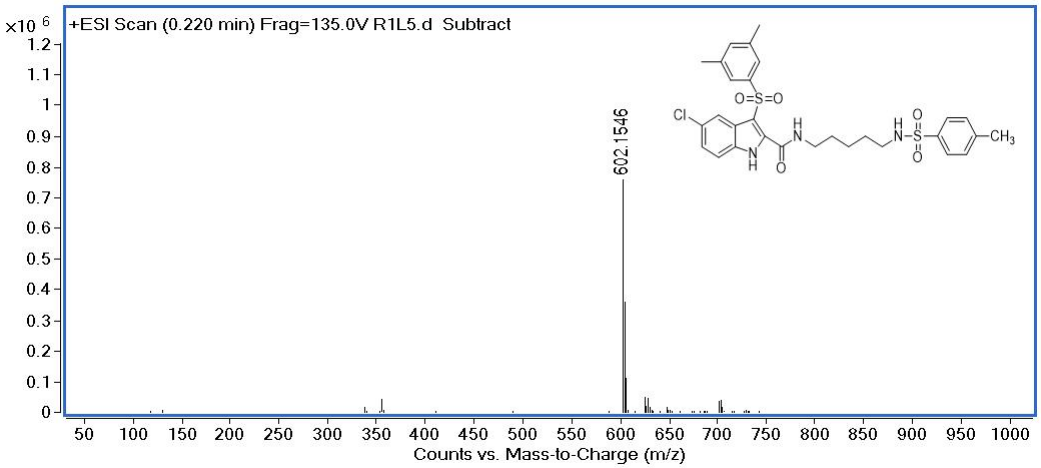
HRMS spectrum of R_1L_3



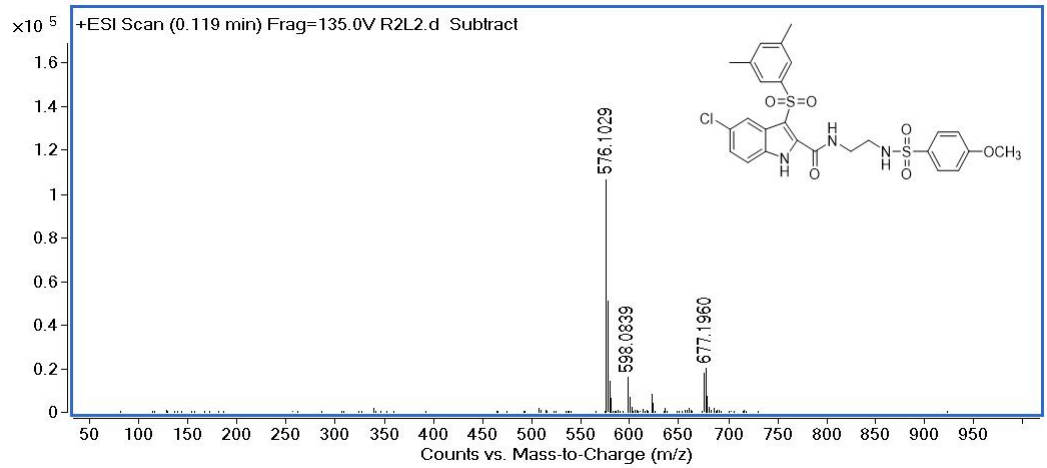
HRMS spectrum of R_1L_4



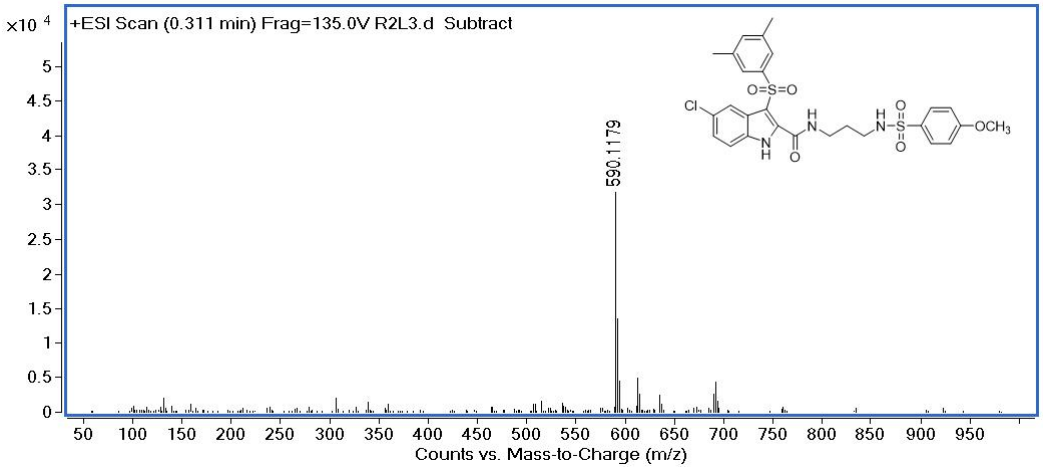
HRMS spectrum of R_1L_5



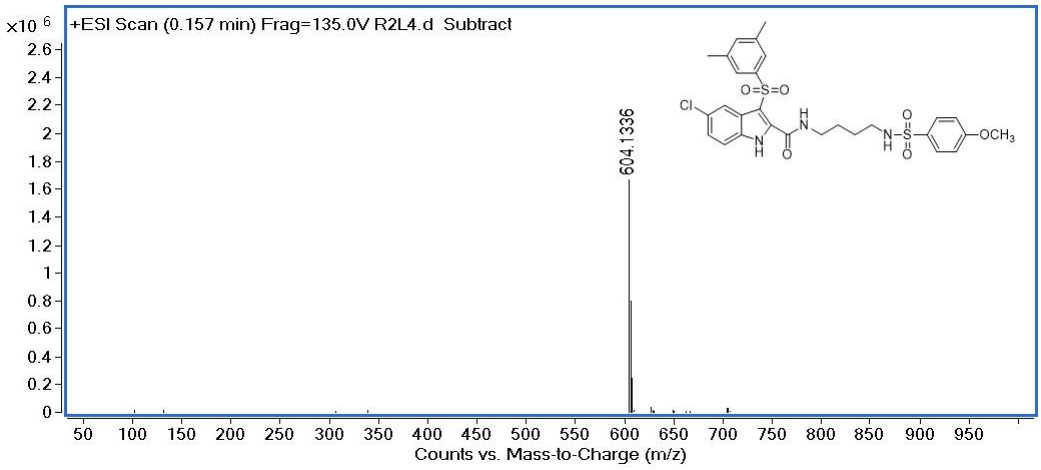
HRMS spectrum of R_2L_2



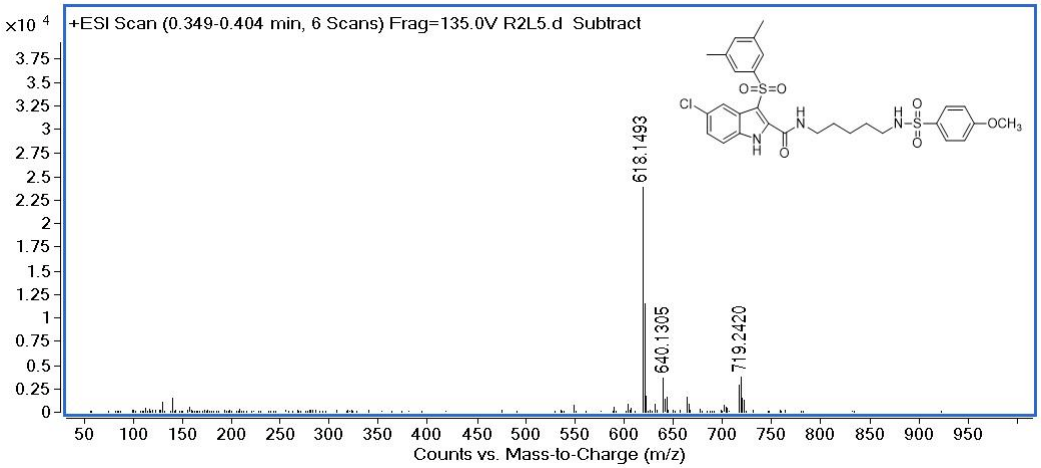
HRMS spectrum of R_2L_3



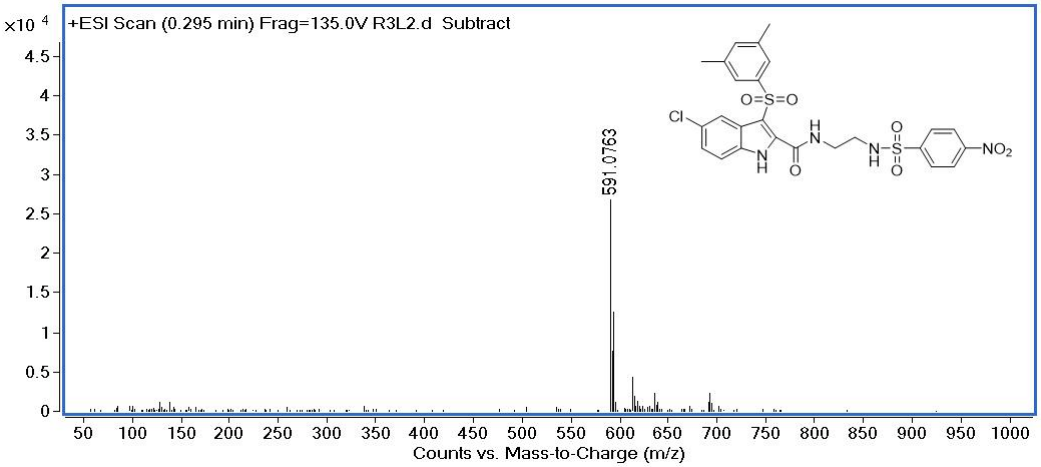
HRMS spectrum of R_2L_4



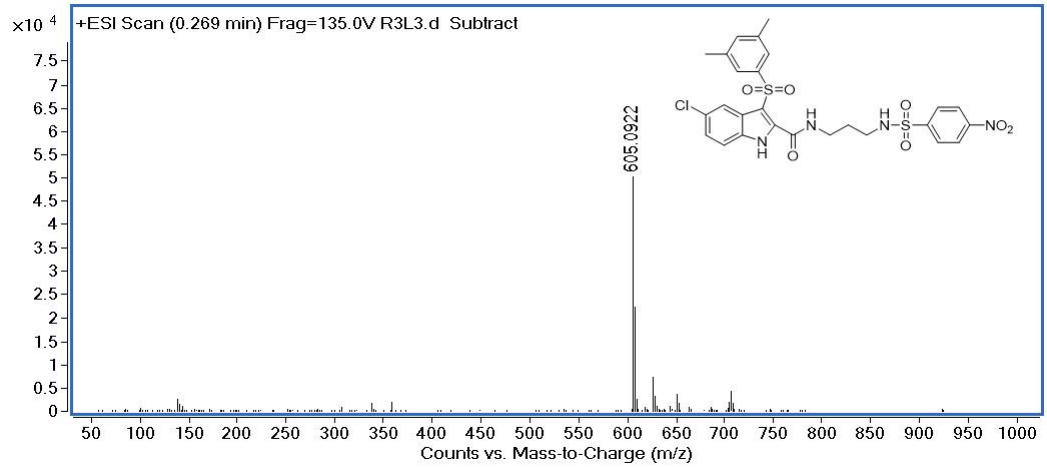
HRMS spectrum of R_2L_5



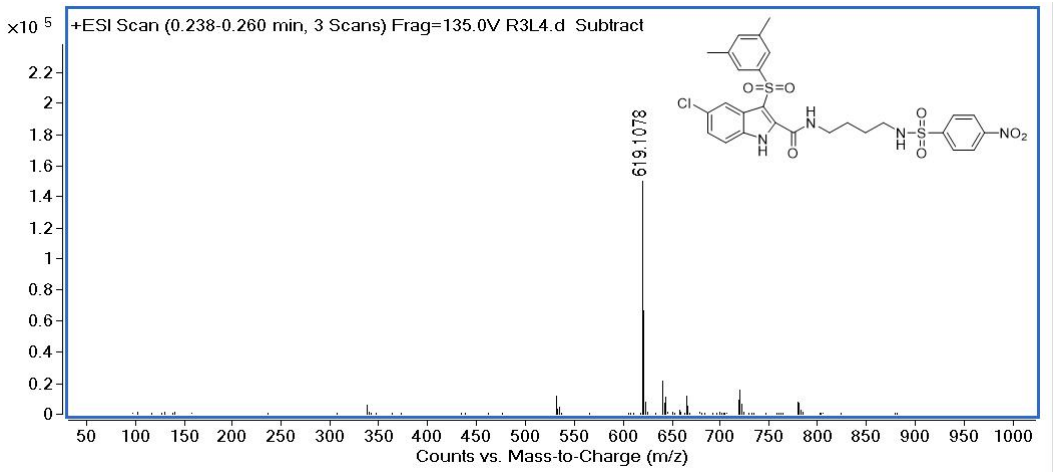
HRMS spectrum of R_3L_2



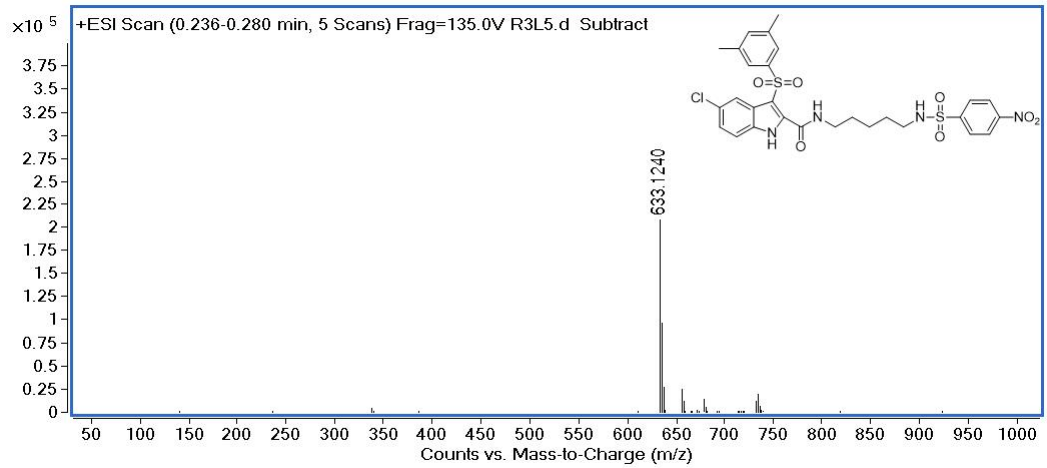
HRMS spectrum of R_3L_3



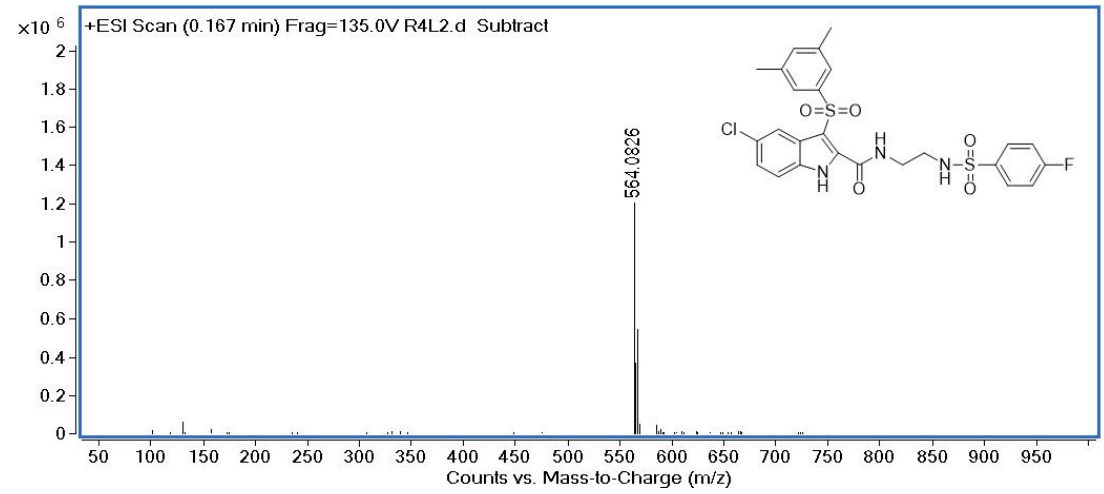
HRMS spectrum of R_3L_4



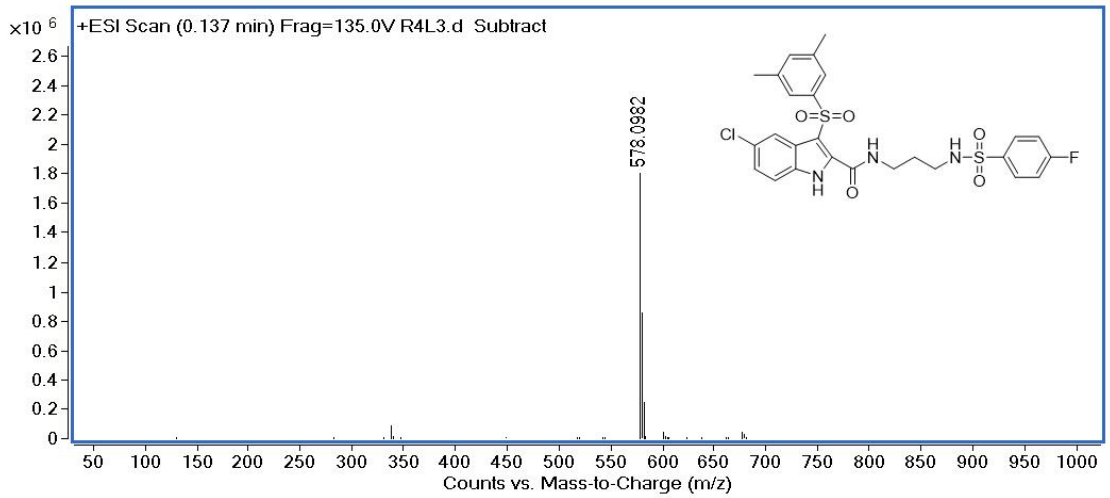
HRMS spectrum of R_3L_5



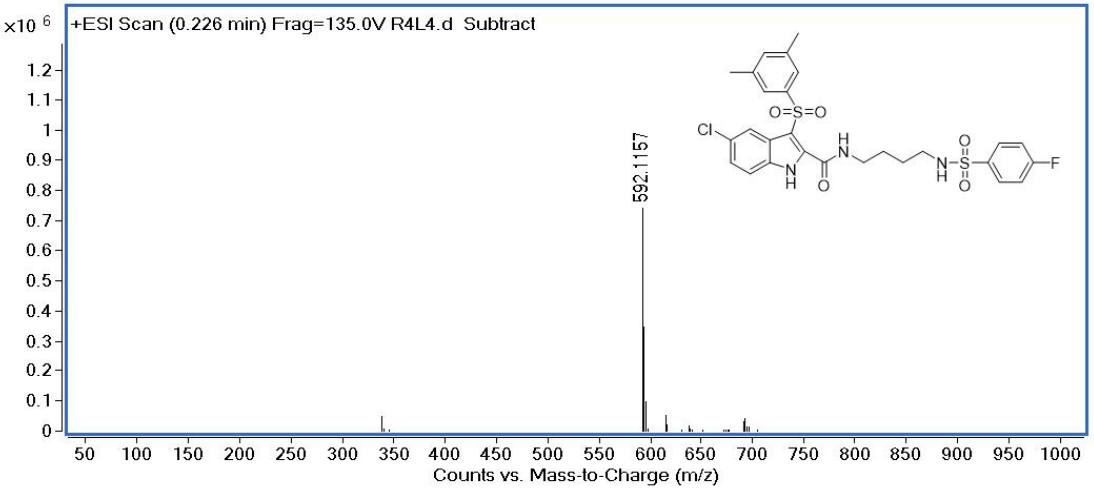
HRMS spectrum of R_4L_2



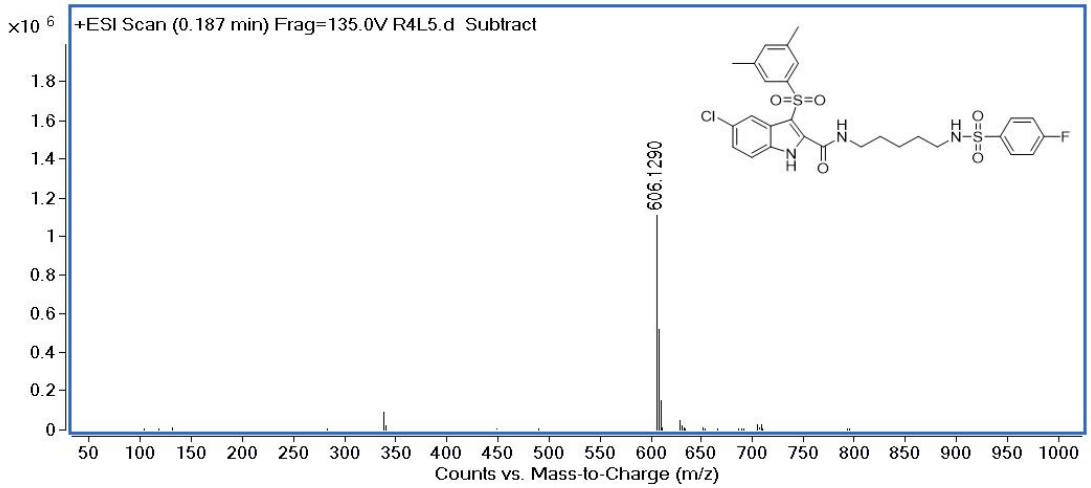
HRMS spectrum of R_4L_3



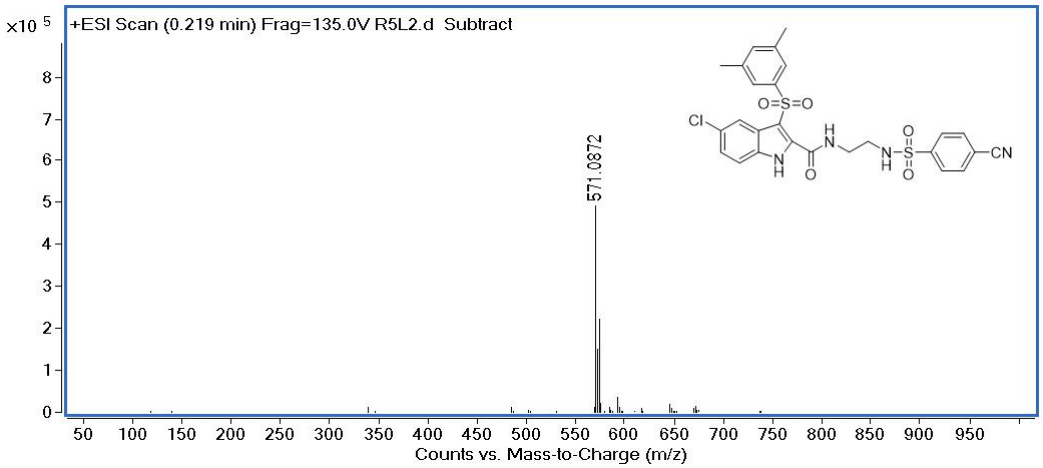
HRMS spectrum of R_4L_4



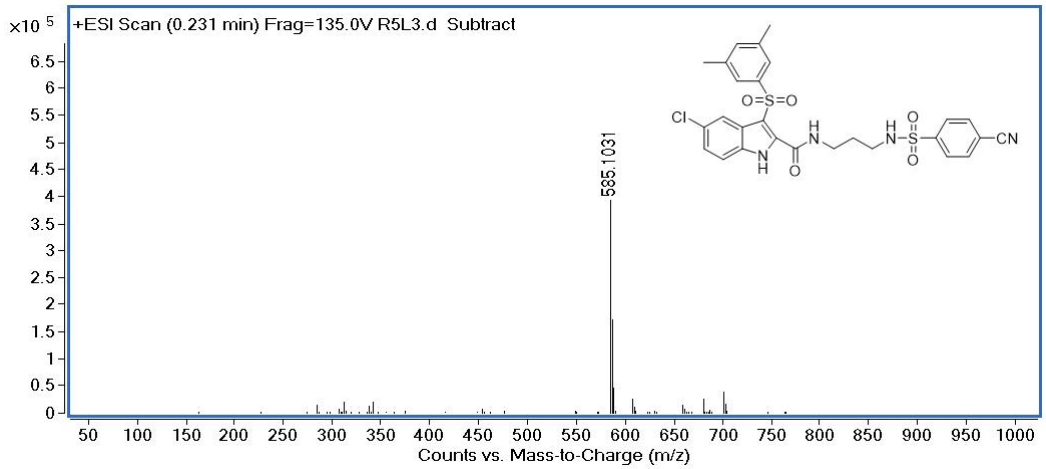
HRMS spectrum of R_4L_5



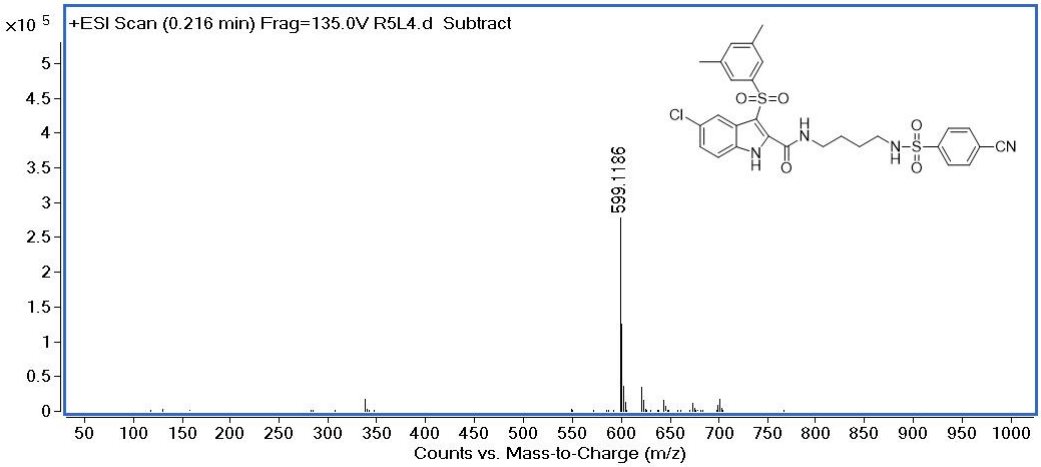
HRMS spectrum of R_5L_2



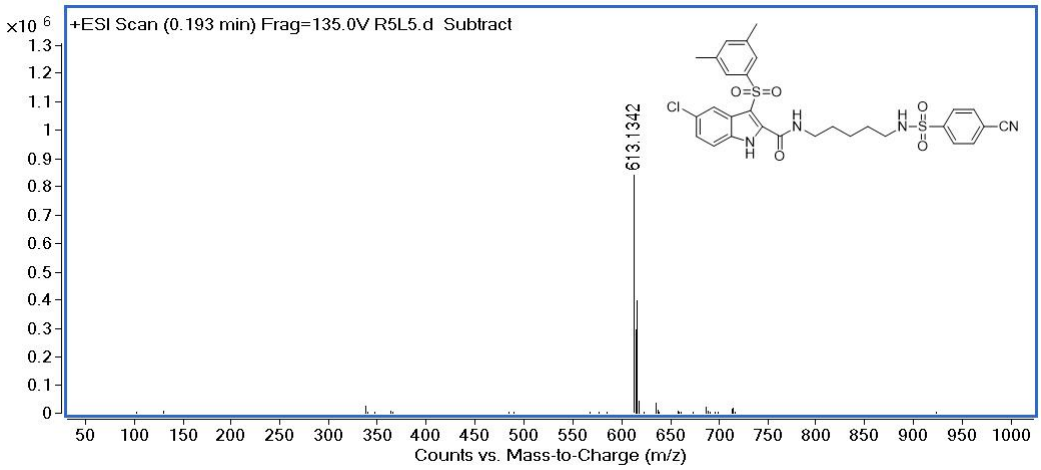
HRMS spectrum of R_5L_3



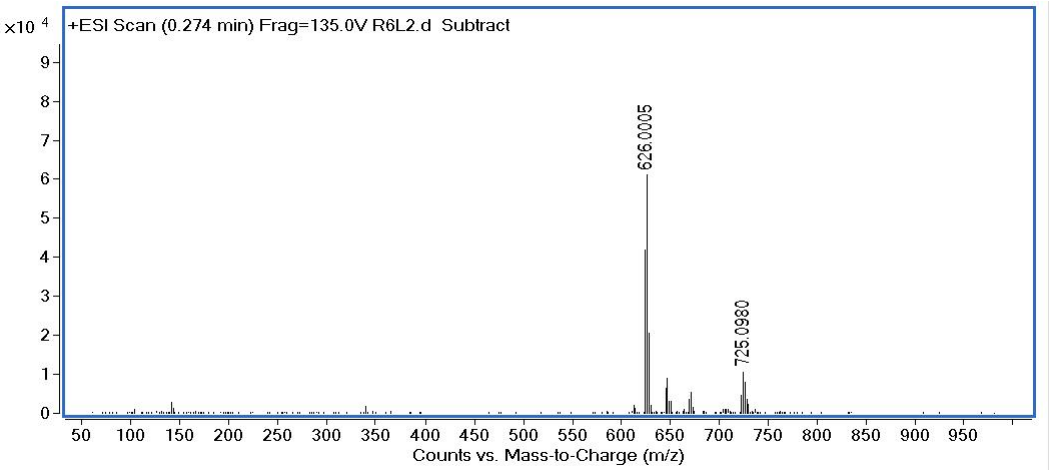
HRMS spectrum of R_5L_4

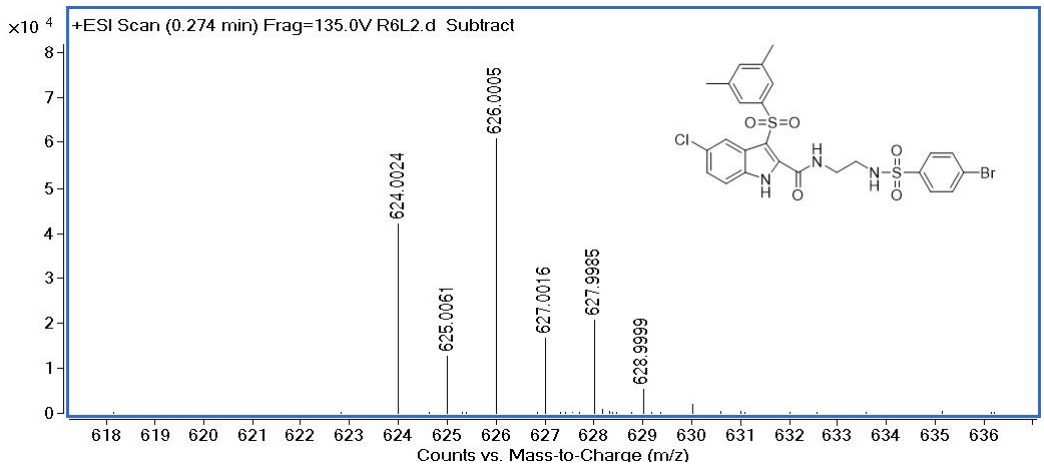


HRMS spectrum of R_5L_5

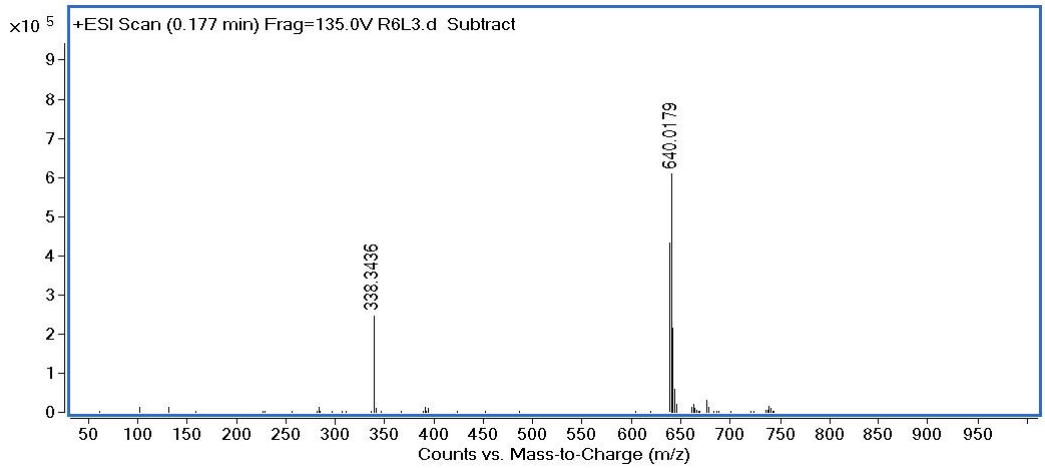


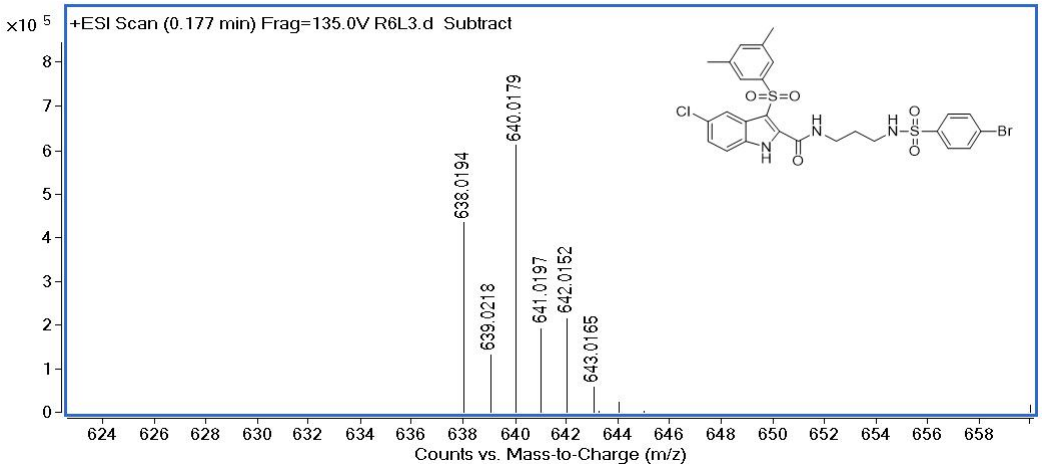
HRMS spectra of R_6L_2



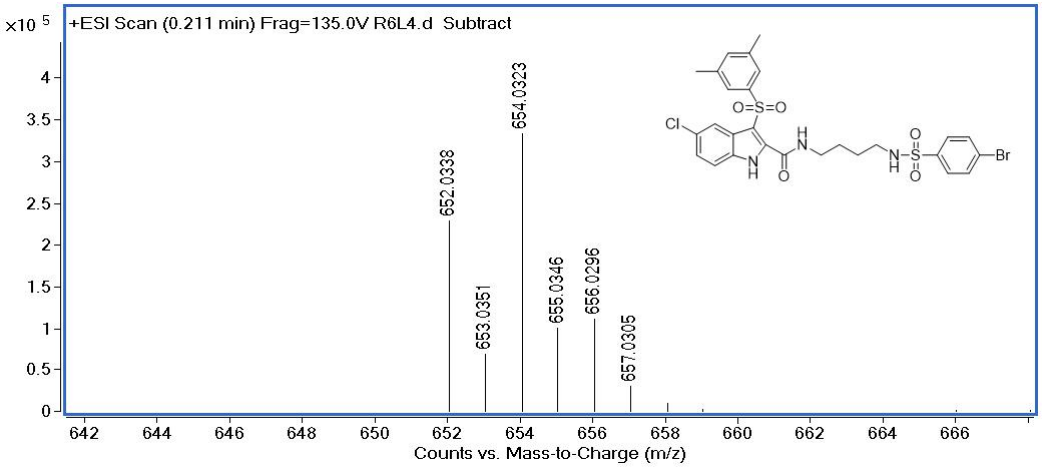


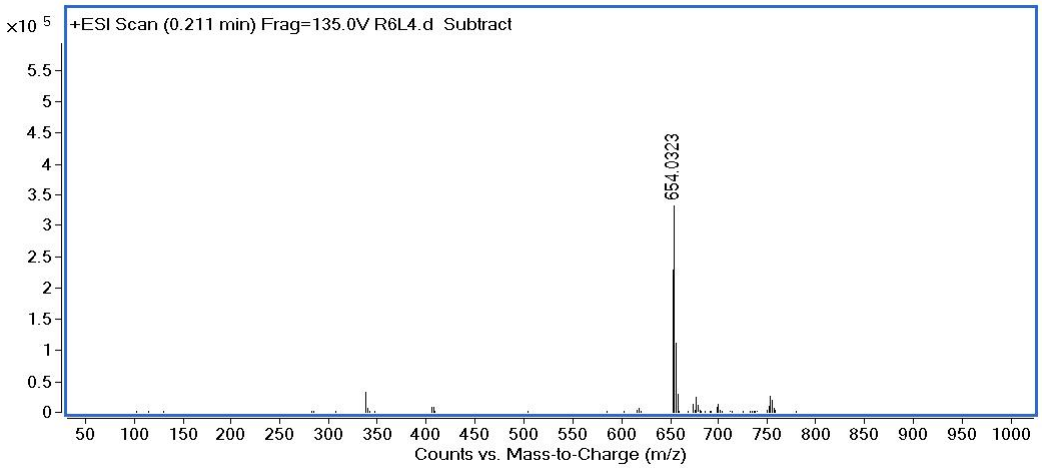
HRMS spectra of R_6L_3



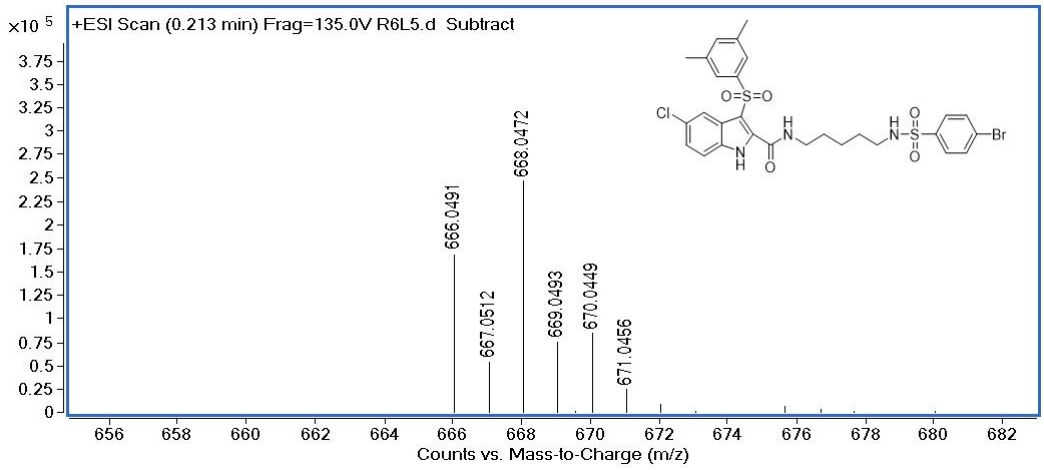


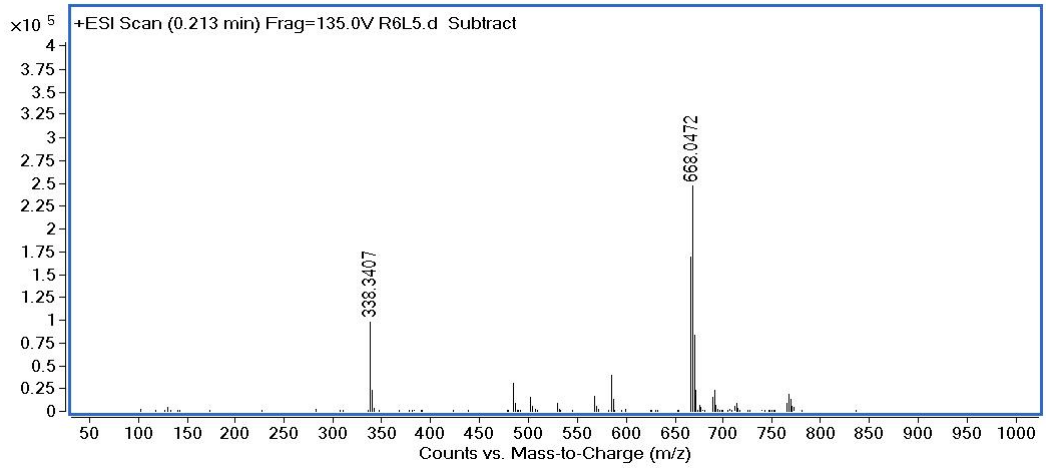
HRMS spectra of R_6L_4



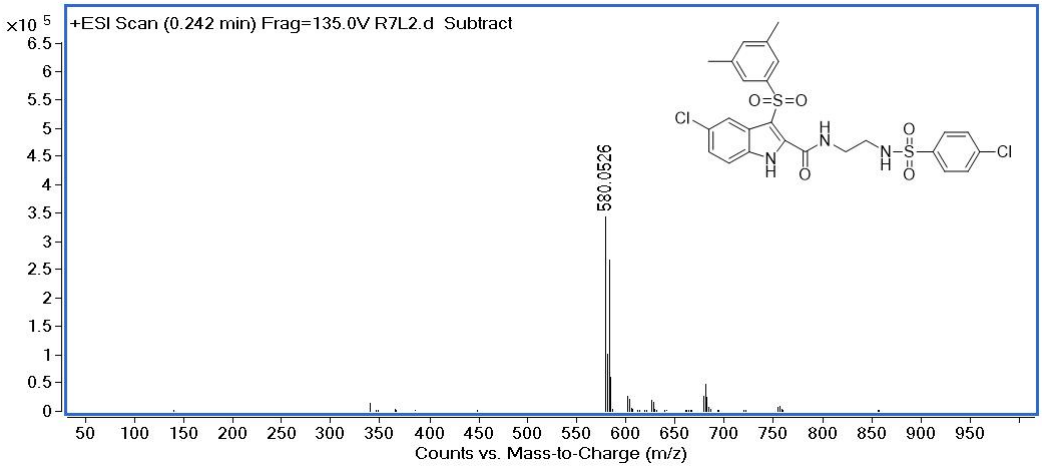


HRMS spectra of R_6L_5

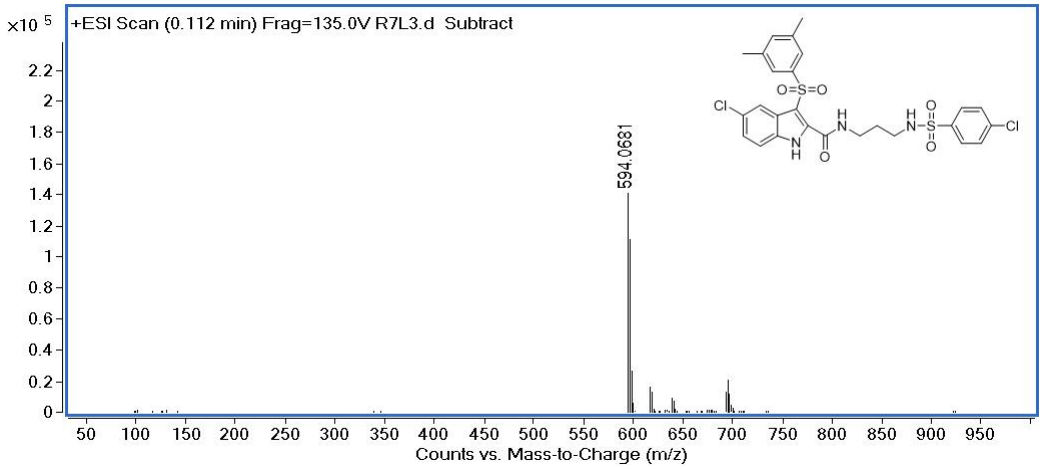




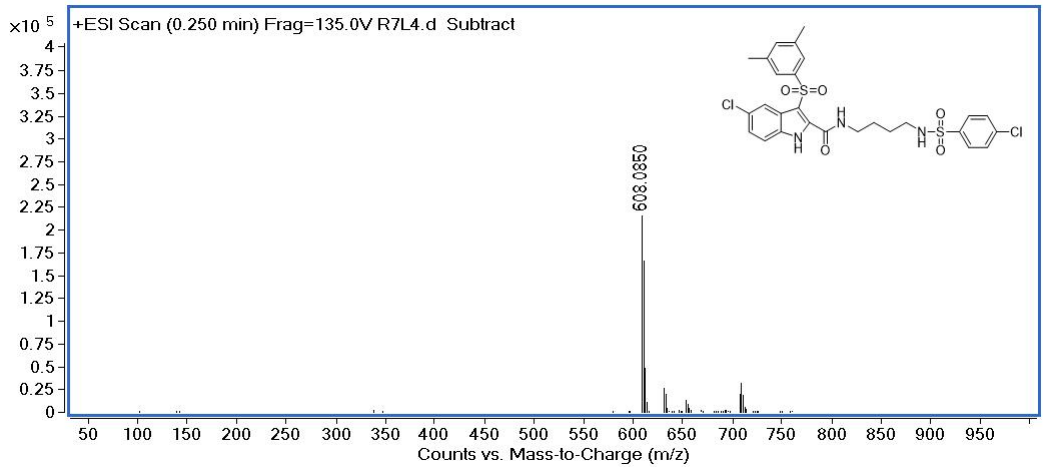
HRMS spectrum of R_7L_2



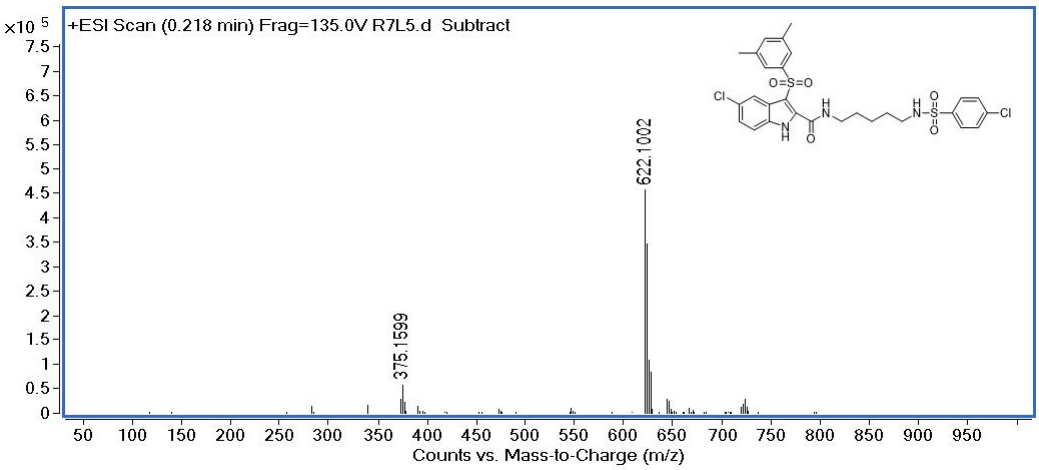
HRMS spectrum of R_7L_3



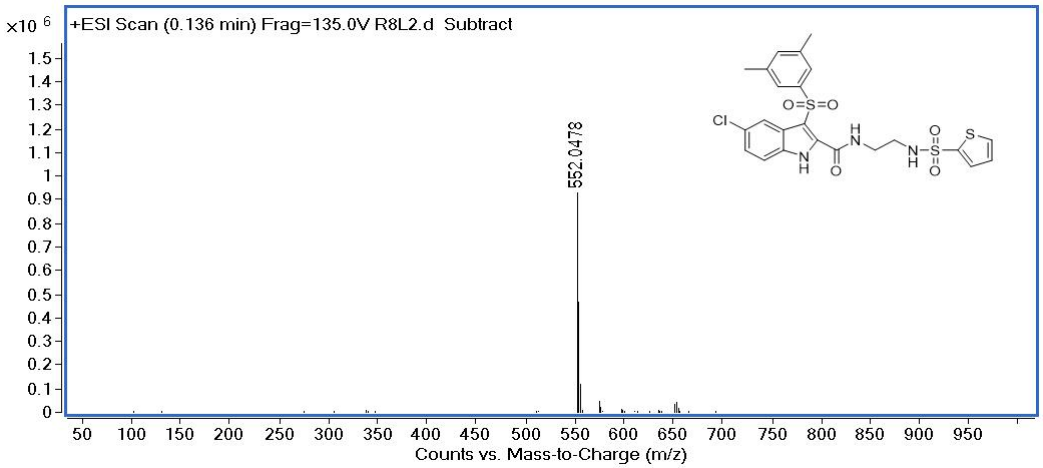
HRMS spectrum of R_7L_4



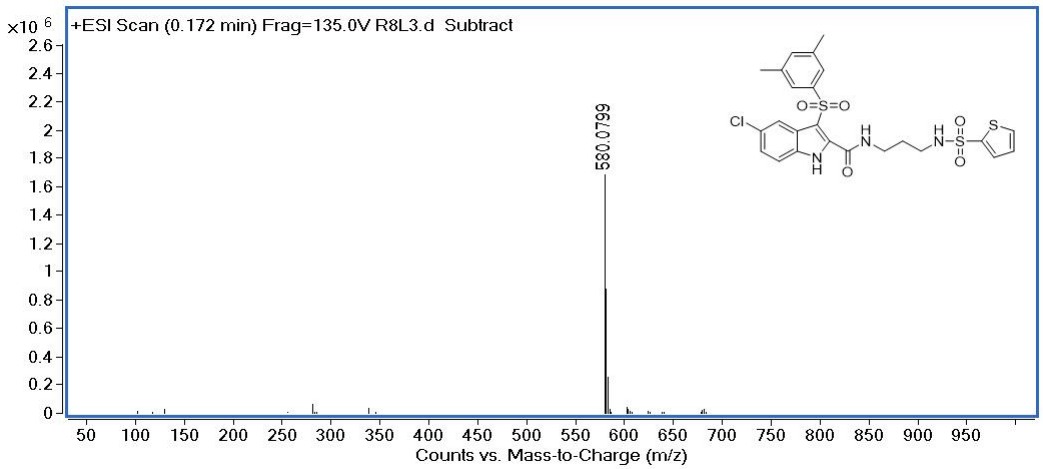
HRMS spectrum of R_7L_5



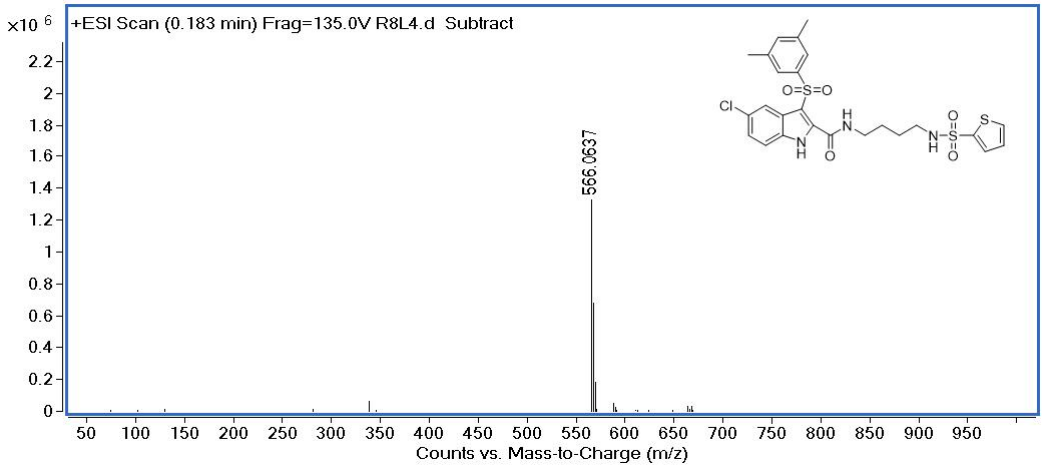
HRMS spectrum of R_8L_2



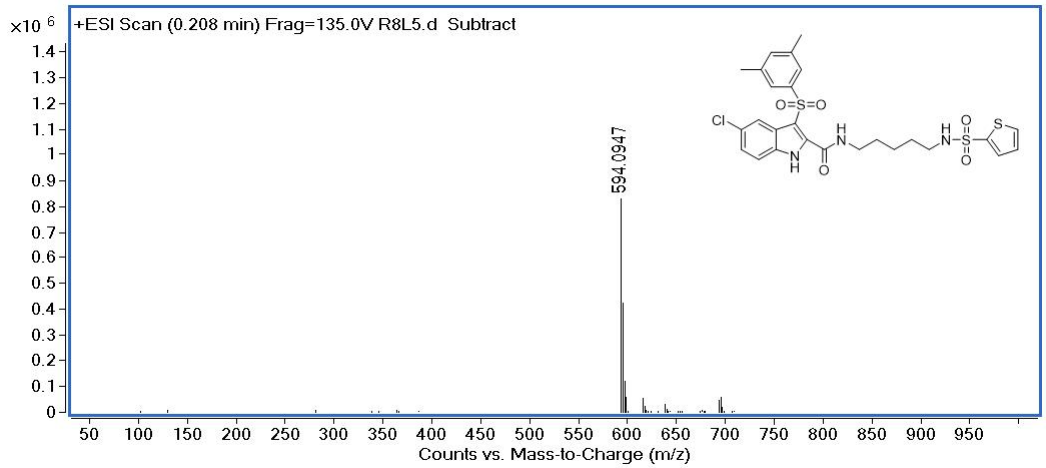
HRMS spectrum of R_8L_3



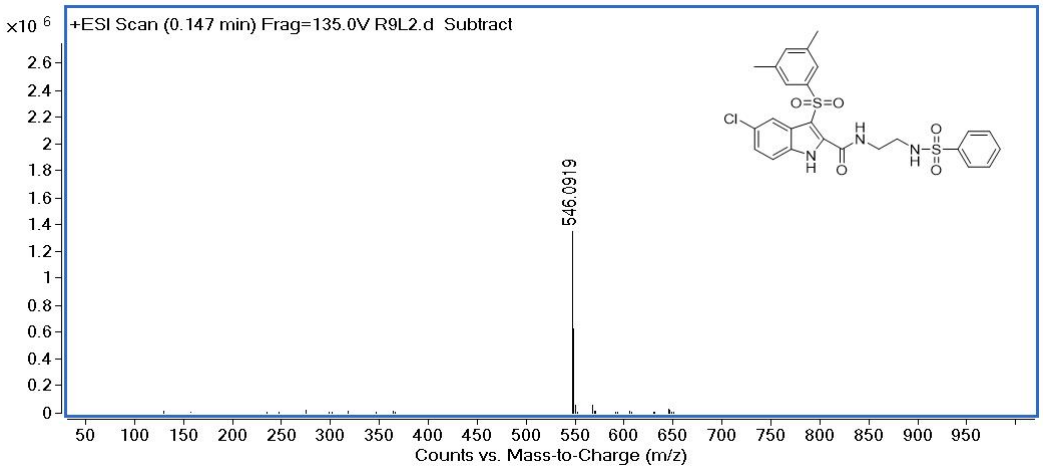
HRMS spectrum of R_8L_4



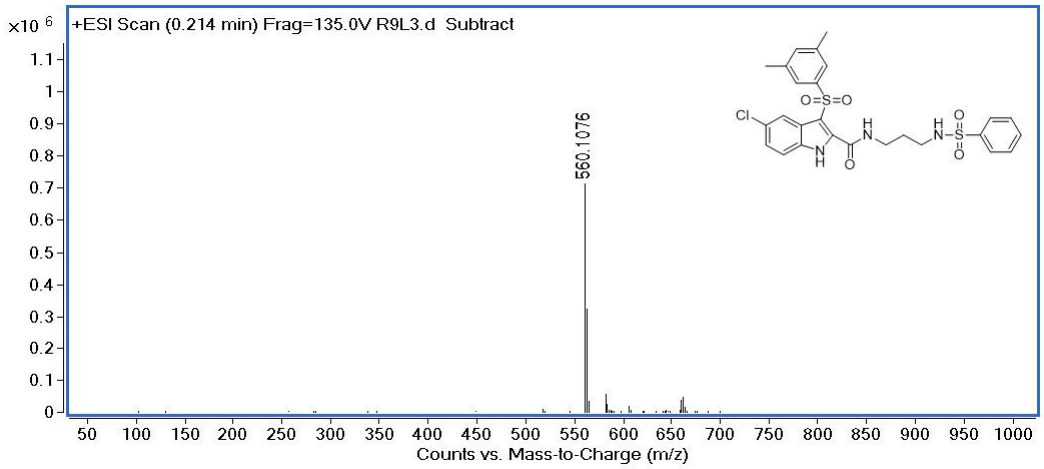
HRMS spectrum of R_8L_5



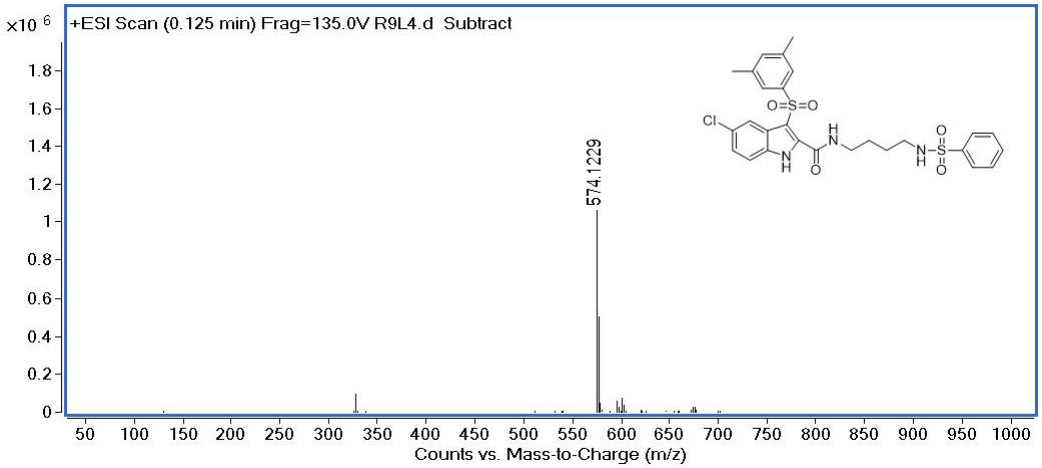
HRMS spectrum of R_9L_2



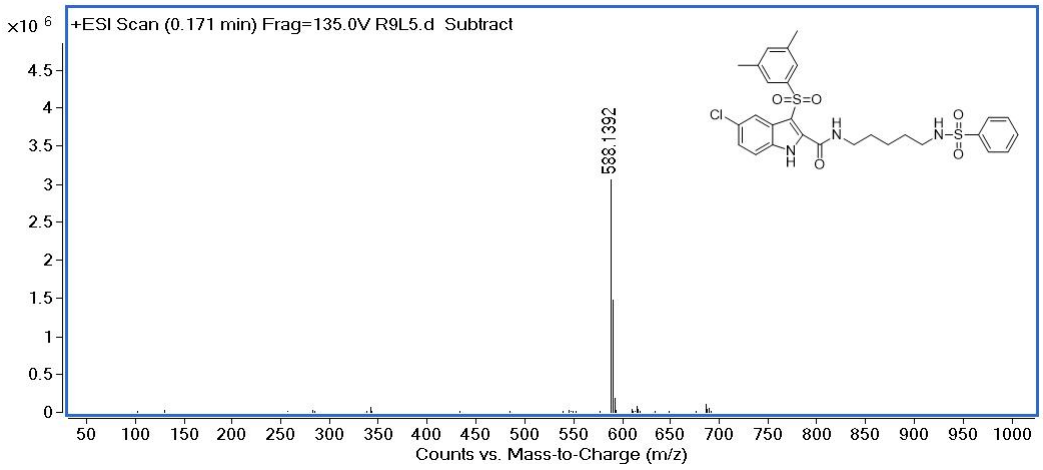
HRMS spectrum of R_9L_3



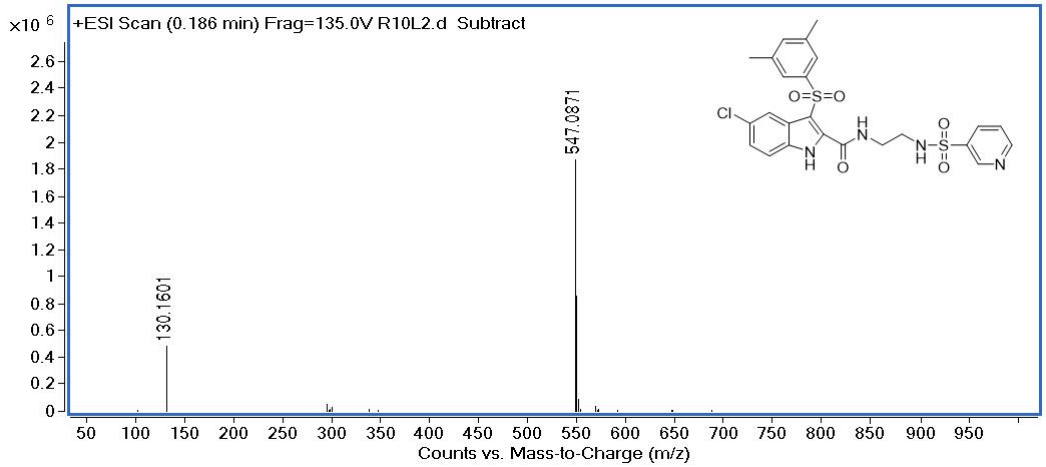
HRMS spectrum of R_9L_4



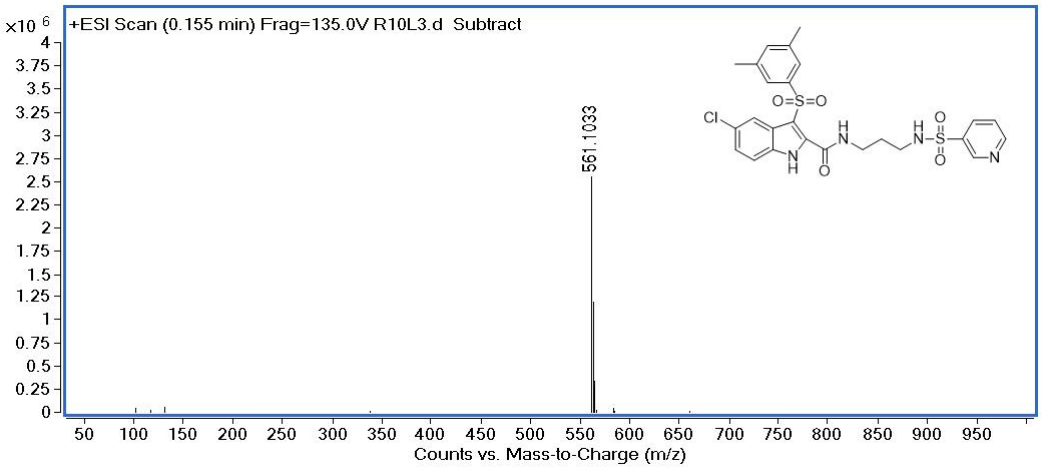
HRMS spectrum of R_9L_5



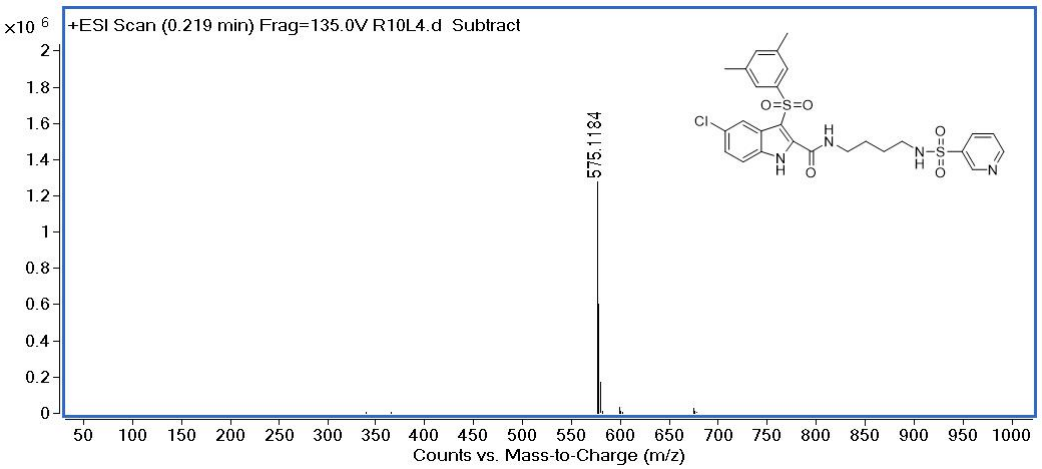
HRMS spectrum of $R_{10}L_2$



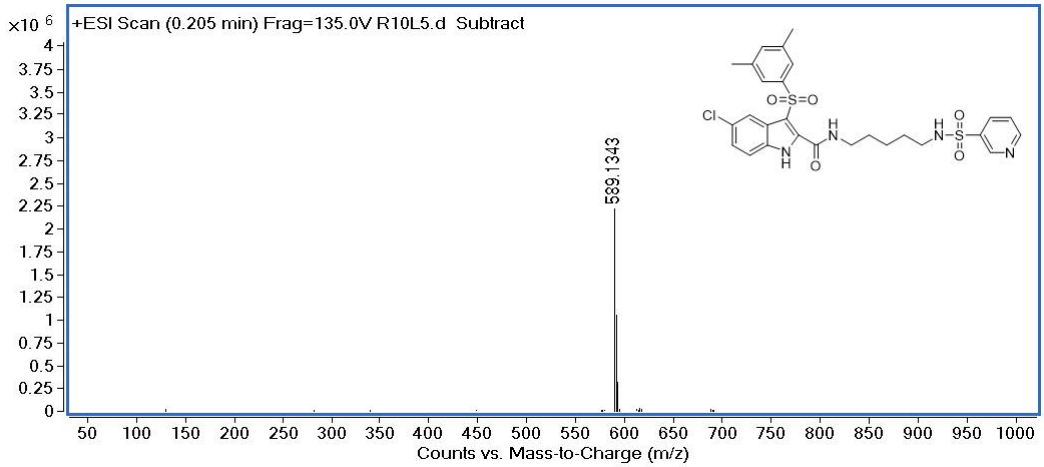
HRMS spectrum of $R_{10}L_3$



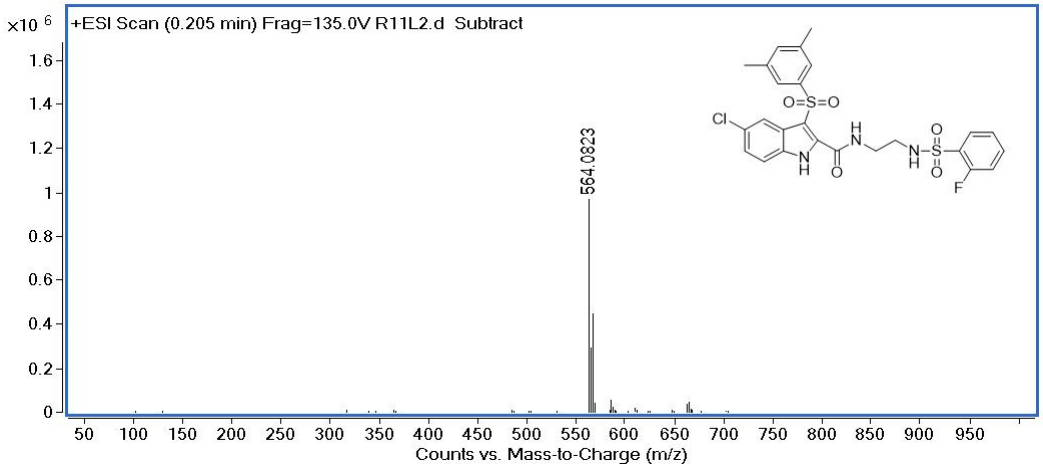
HRMS spectrum of $R_{10}L_4$



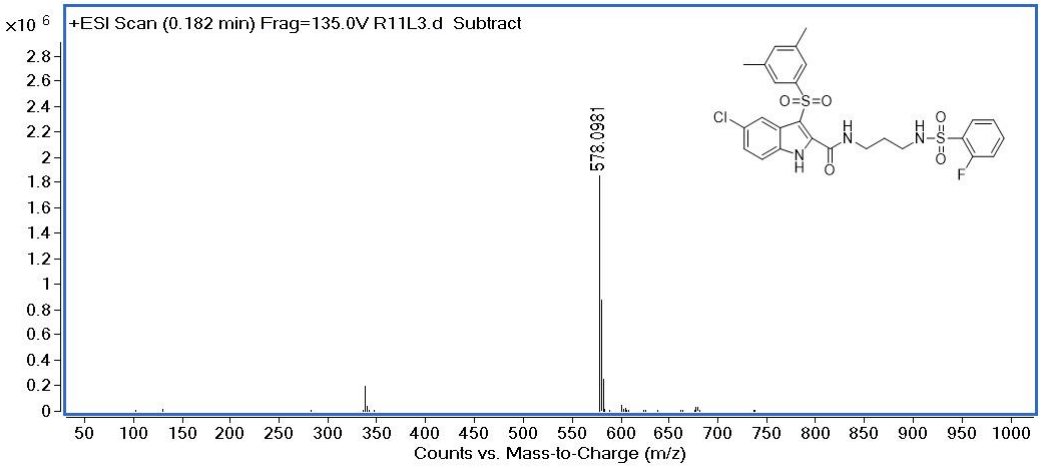
HRMS spectrum of $R_{10}L_5$



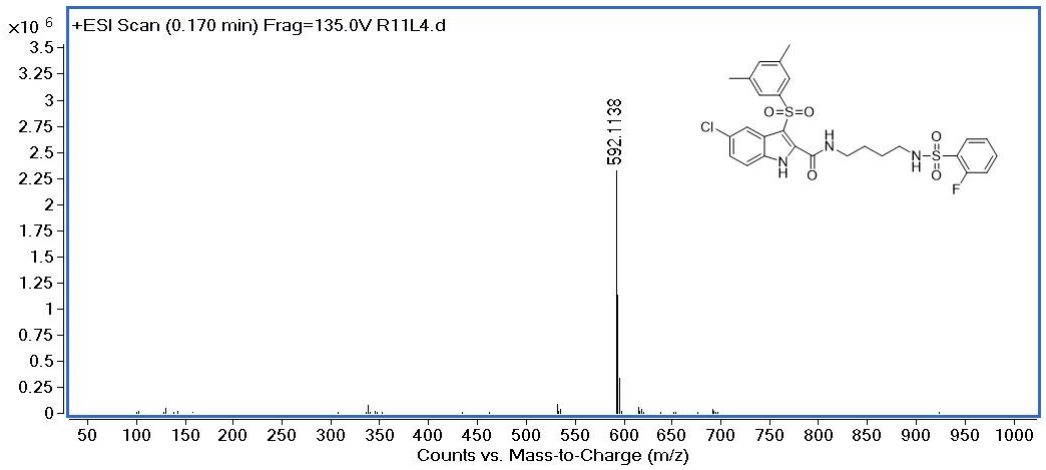
HRMS spectrum of $R_{11}L_2$



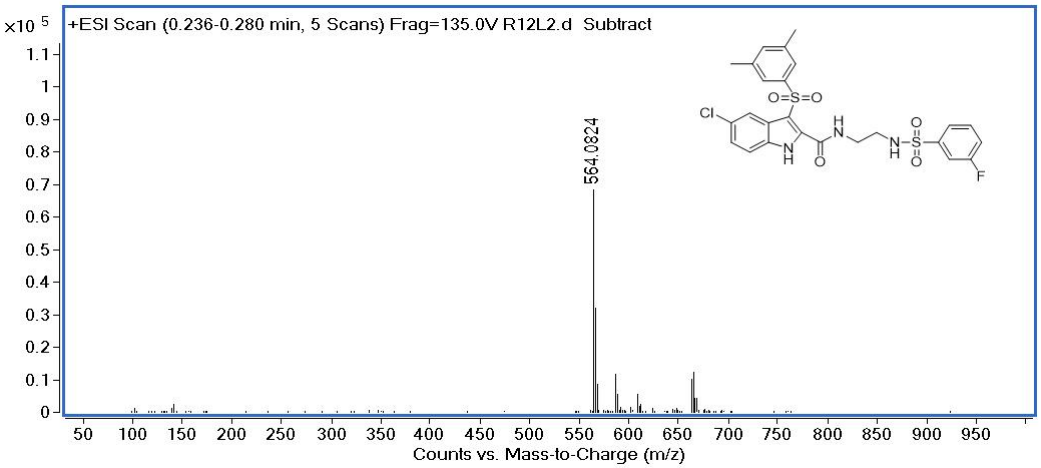
HRMS spectrum of $R_{11}L_3$



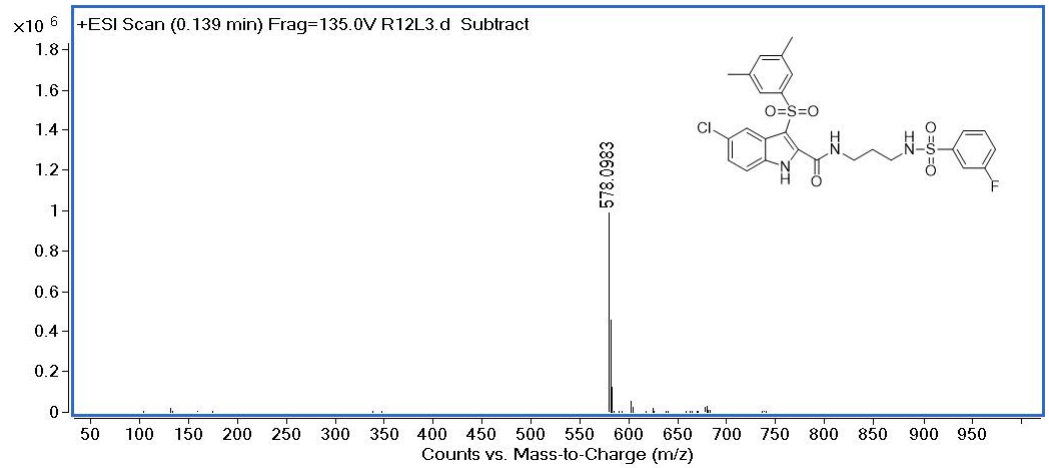
HRMS spectrum of $R_{11}L_4$



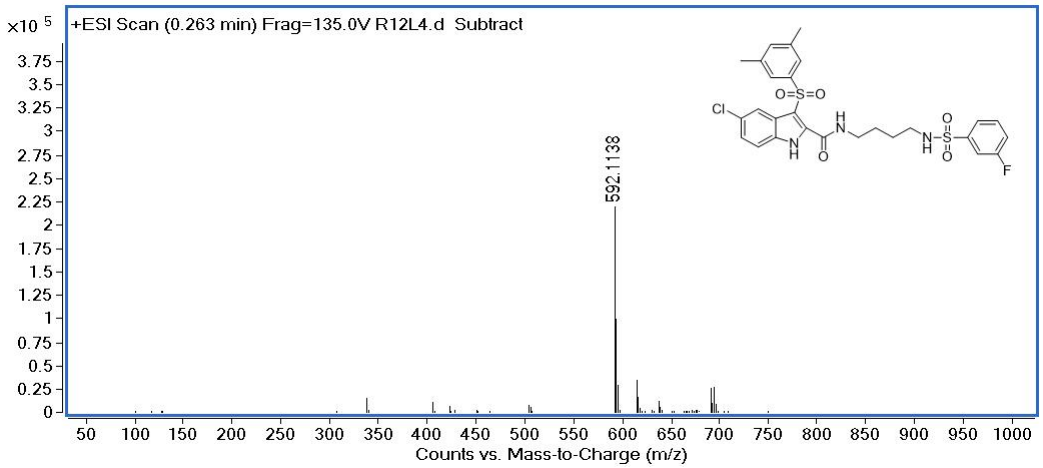
HRMS spectrum of $R_{12}L_2$



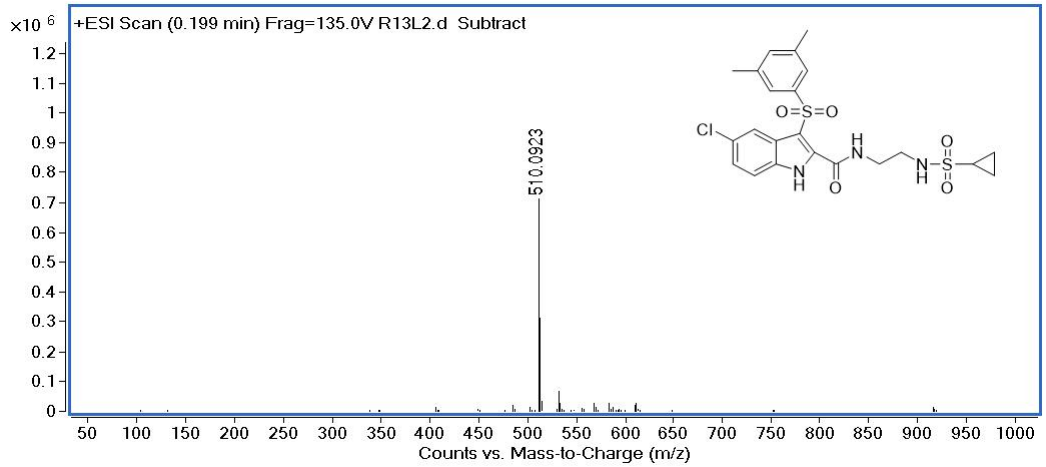
HRMS spectrum of $R_{12}L_3$



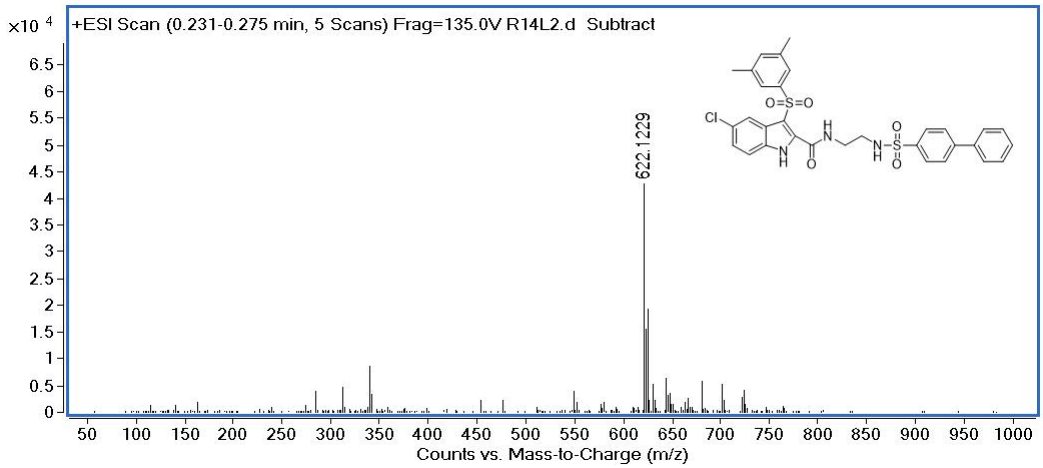
HRMS spectrum of $R_{12}L_4$



HRMS spectrum of $R_{13}L_2$

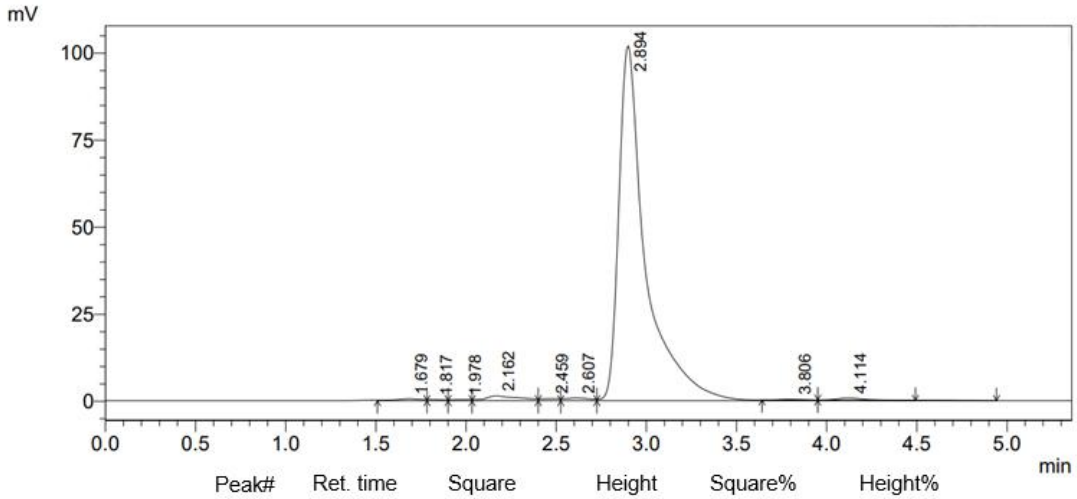


HRMS spectrum of $R_{14}L_2$



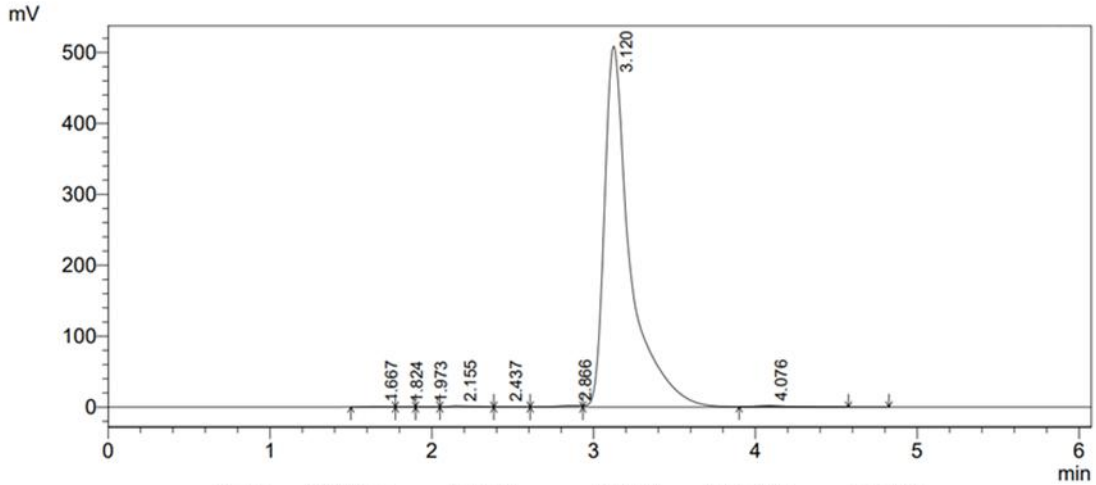
HPLC trace of representative final compounds

HPLC trace of **R_2L_2**



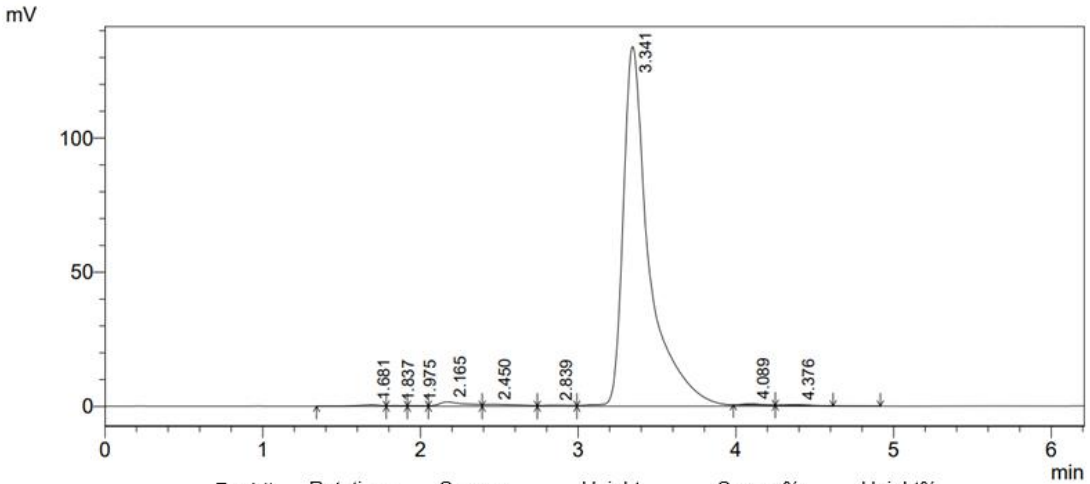
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.679	5174	552	0.470	0.518
2	1.817	1886	297	0.171	0.278
3	1.978	2299	316	0.209	0.296
4	2.162	17597	1354	1.598	1.269
5	2.459	3974	570	0.361	0.534
6	2.607	7179	776	0.652	0.727
7	2.894	1053968	101952	95.685	95.561
8	3.806	1957	217	0.178	0.203
9	4.114	7463	655	0.678	0.614
Total		1101496	106688	100.000	100.000

HPLC trace of **R_2L_4**



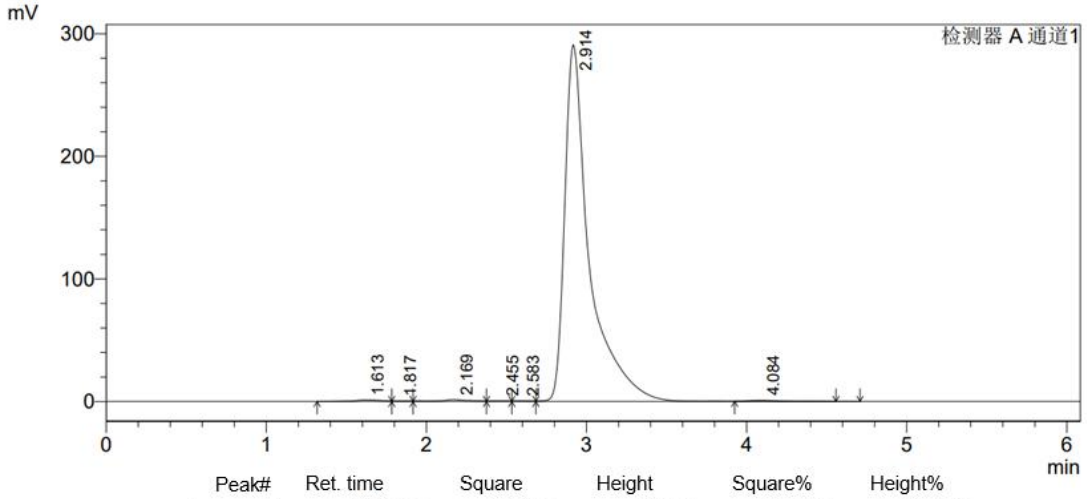
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.667	7337	714	0.128	0.138
2	1.824	2685	385	0.047	0.075
3	1.973	3264	386	0.057	0.075
4	2.155	18321	1589	0.319	0.308
5	2.437	7758	669	0.135	0.130
6	2.866	24123	2208	0.420	0.427
7	3.120	5661679	509073	98.556	98.528
8	4.076	19478	1655	0.339	0.320
Total		5744645	516680	100.000	100.000

HPLC trace of $\mathbf{R_2L_5}$



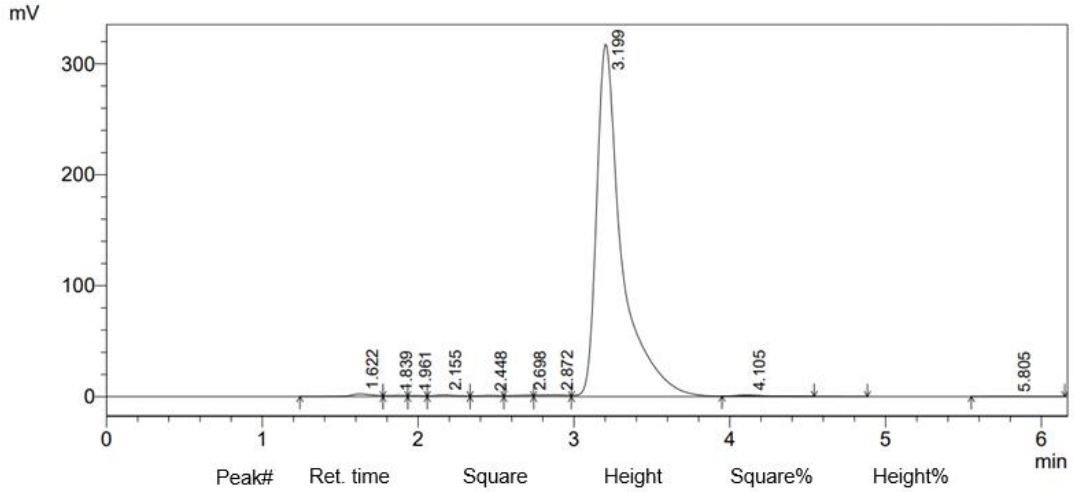
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.681	5170	523	0.326	0.378
2	1.837	1755	243	0.111	0.176
3	1.975	1765	228	0.111	0.165
4	2.165	18766	1590	1.182	1.149
5	2.450	10549	723	0.665	0.522
6	2.839	4802	366	0.303	0.265
7	3.341	1537998	133925	96.894	96.793
8	4.089	3564	470	0.225	0.339
9	4.376	2927	295	0.184	0.213
Total		1587296	138362	100.000	100.000

HPLC trace of $\mathbf{R_3L_2}$



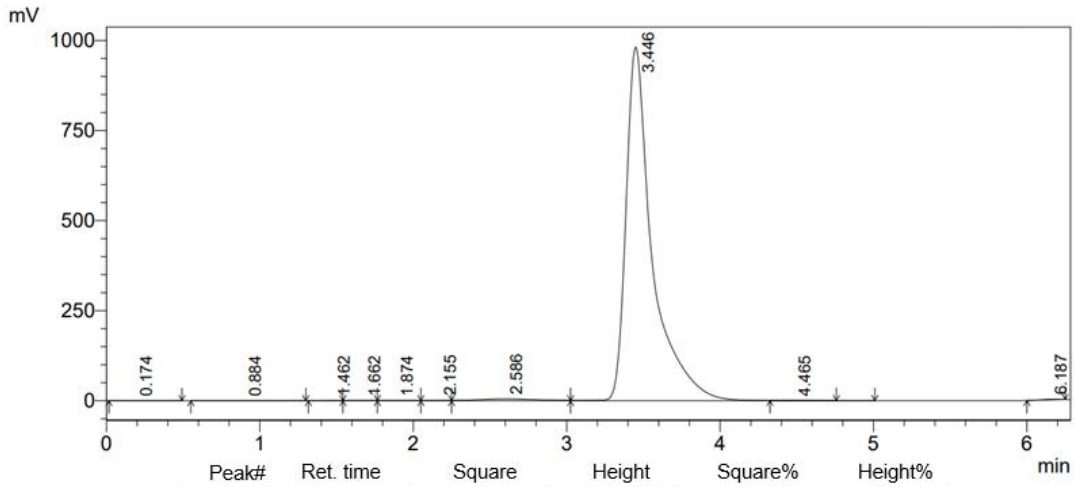
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.613	15125	1228	0.476	0.414
2	1.817	3700	514	0.116	0.173
3	2.169	19344	1420	0.609	0.479
4	2.455	5356	621	0.169	0.210
5	2.583	4908	584	0.155	0.197
6	2.914	3117601	291090	98.153	98.225
7	4.084	10242	894	0.322	0.302
Total		3176275	296351	100.000	100.000

HPLC trace of **R_3L_4**



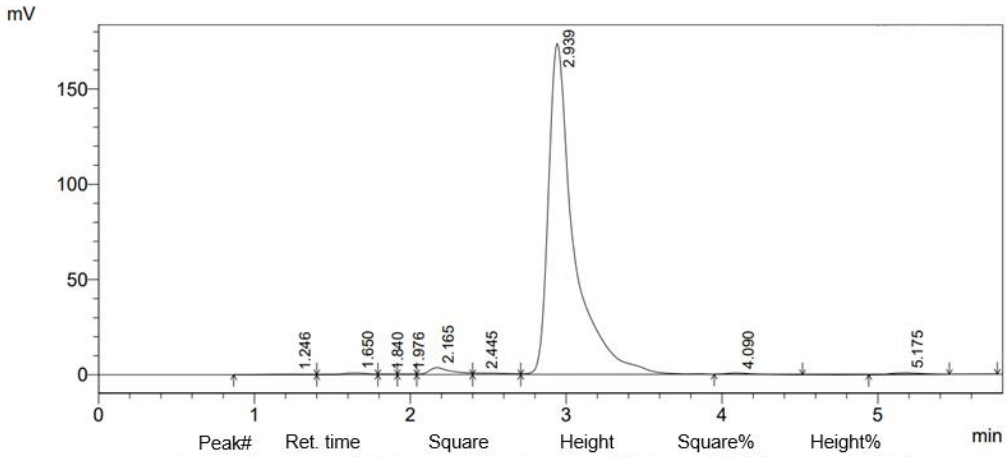
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.622	23953	2414	0.651	0.737
2	1.839	8209	941	0.223	0.287
3	1.961	5512	820	0.150	0.250
4	2.155	15214	1412	0.414	0.431
5	2.448	10307	951	0.280	0.290
6	2.698	11169	1130	0.304	0.345
7	2.872	17553	1336	0.477	0.408
8	3.199	3573088	317545	97.121	96.902
9	4.105	12880	1091	0.350	0.333
10	5.805	1118	56	0.030	0.017
Total		3679001	327696	100.000	100.000

HPLC trace of **R_3L_5**



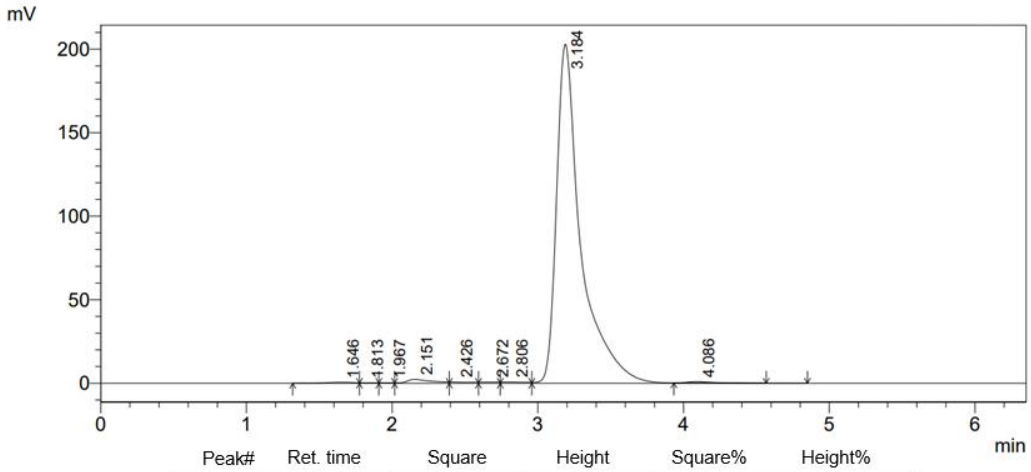
Peak#	Ret. time	Square	Height	Square%	Height%
1	0.174	1677	114	0.014	0.012
2	0.884	2074	95	0.018	0.010
3	1.462	2965	420	0.025	0.042
4	1.662	7375	749	0.062	0.075
5	1.874	8284	643	0.070	0.065
6	2.155	10767	1251	0.091	0.126
7	2.586	136540	5199	1.155	0.524
8	3.446	11638276	982291	98.428	98.977
9	4.465	3860	352	0.033	0.036
10	6.187	12336	1325	0.104	0.134
Total		11824154	992438	100.000	100.000

HPLC trace of **R_4L_2**



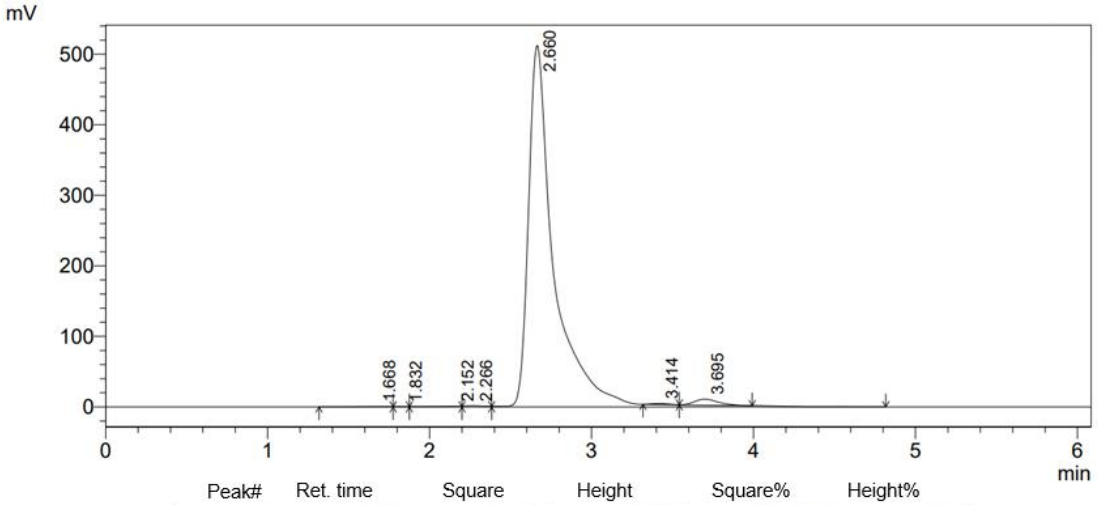
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.246	4551	260	0.222	0.143
2	1.650	11033	830	0.539	0.457
3	1.840	2455	346	0.120	0.191
4	1.976	2367	331	0.116	0.182
5	2.165	37152	3627	1.815	1.996
6	2.445	12074	868	0.590	0.478
7	2.939	1957549	173785	95.635	95.634
8	4.090	7121	695	0.348	0.382
9	5.175	12599	977	0.616	0.537
Total		2046901	181720	100.000	100.000

HPLC trace of **R_4L_4**



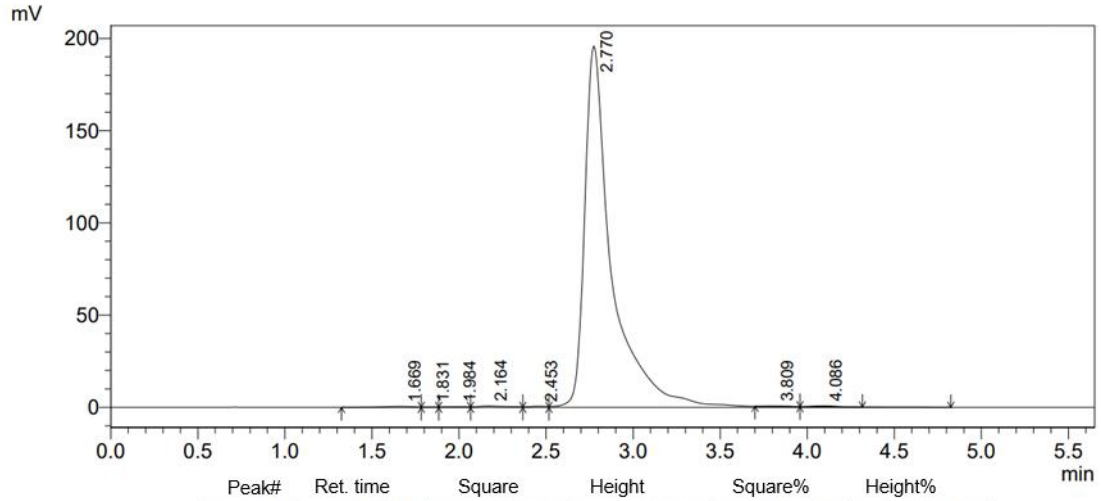
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.646	7280	614	0.300	0.293
2	1.813	1884	258	0.078	0.123
3	1.967	1364	215	0.056	0.103
4	2.151	27011	2288	1.113	1.093
5	2.426	7342	704	0.302	0.337
6	2.672	5646	696	0.233	0.333
7	2.806	8086	704	0.333	0.336
8	3.184	2358954	202961	97.172	96.987
9	4.086	10034	826	0.413	0.395
Total		2427600	209265	100.000	100.000

HPLC trace of **R_5L_2**



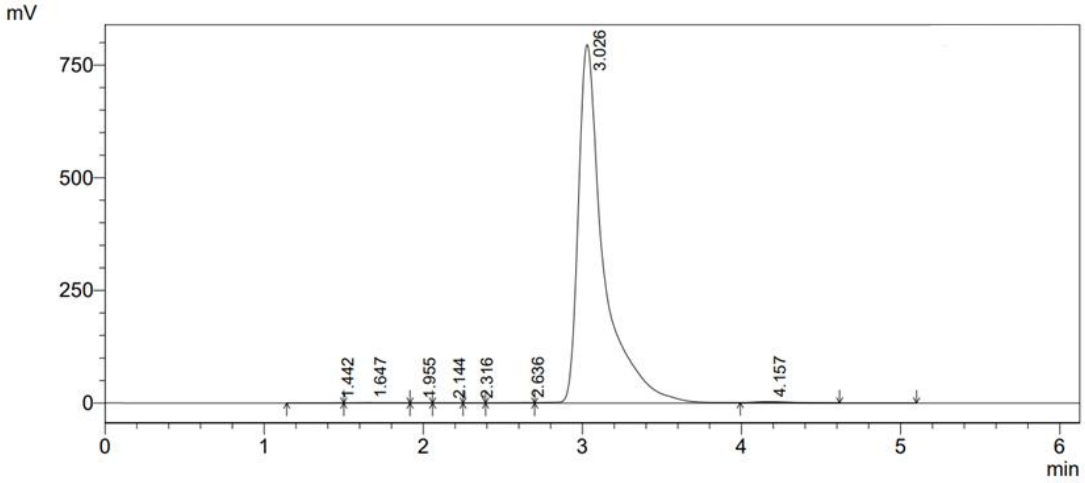
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.668	7176	588	0.124	0.112
2	1.832	1851	320	0.032	0.061
3	2.152	12928	1219	0.223	0.232
4	2.266	12874	1511	0.222	0.287
5	2.660	5659898	512600	97.687	97.390
6	3.414	11594	1596	0.200	0.303
7	3.695	87595	8505	1.512	1.616
Total		5793917	526339	100.000	100.000

HPLC trace of **R_5L_3**



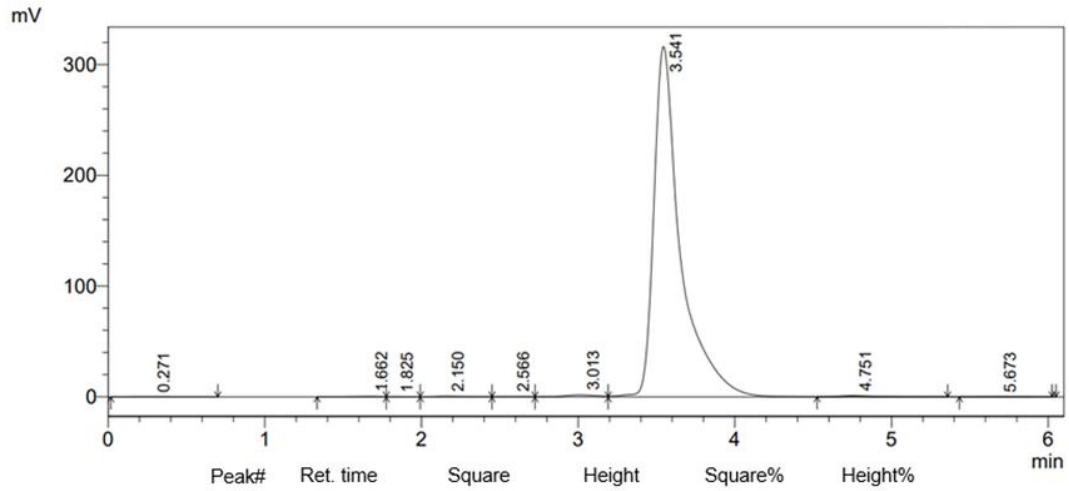
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.669	6521	528	0.302	0.265
2	1.831	1476	256	0.068	0.128
3	1.984	3564	395	0.165	0.198
4	2.164	8872	739	0.410	0.371
5	2.453	4417	598	0.204	0.300
6	2.770	2131049	195982	98.558	98.371
7	3.809	1731	208	0.080	0.104
8	4.086	4597	523	0.213	0.263
Total		2162227	199228	100.000	100.000

HPLC trace of **R_5L_5**



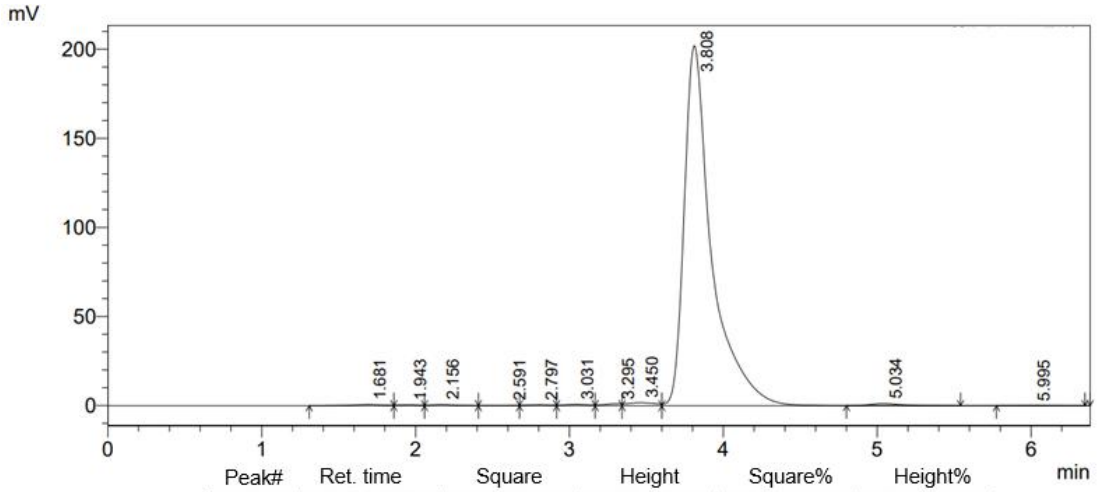
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.442	1855	193	0.021	0.024
2	1.647	14058	844	0.158	0.105
3	1.955	3089	414	0.035	0.052
4	2.144	5075	573	0.057	0.072
5	2.316	3322	431	0.037	0.054
6	2.636	12766	1176	0.143	0.147
7	3.026	8837219	795004	99.161	99.220
8	4.157	34572	2616	0.388	0.326
Total		8911955	801252	100.000	100.000

HPLC trace of **R_6L_2**



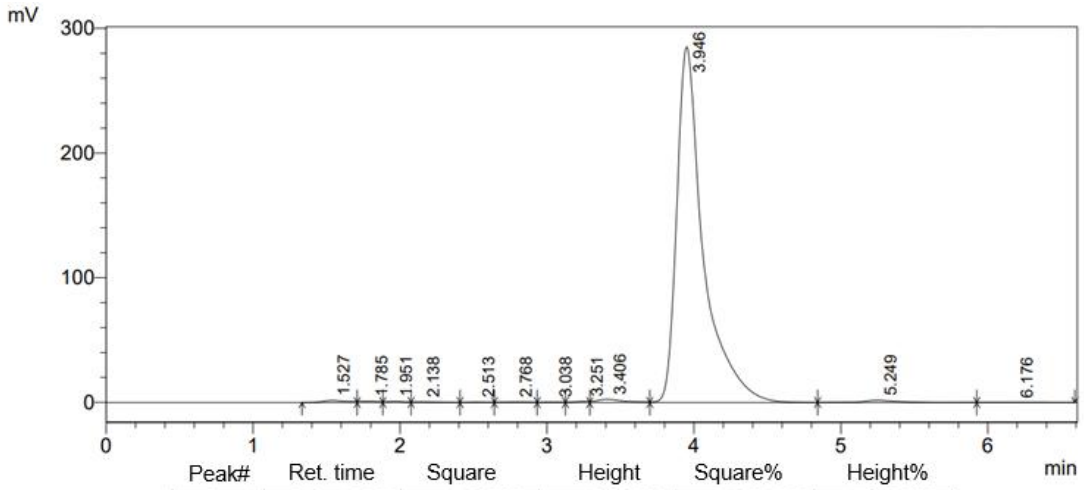
Peak#	Ret. time	Square	Height	Square%	Height%
1	0.271	1972	100	0.052	0.031
2	1.662	4085	421	0.107	0.131
3	1.825	1040	105	0.027	0.033
4	2.150	7837	675	0.205	0.210
5	2.566	4086	367	0.107	0.114
6	3.013	25929	1850	0.680	0.576
7	3.541	3751390	316291	98.335	98.498
8	4.751	15444	1076	0.405	0.335
9	5.673	3114	230	0.082	0.072
Total		3814897	321115	100.000	100.000

HPLC trace of **R_6L_3**



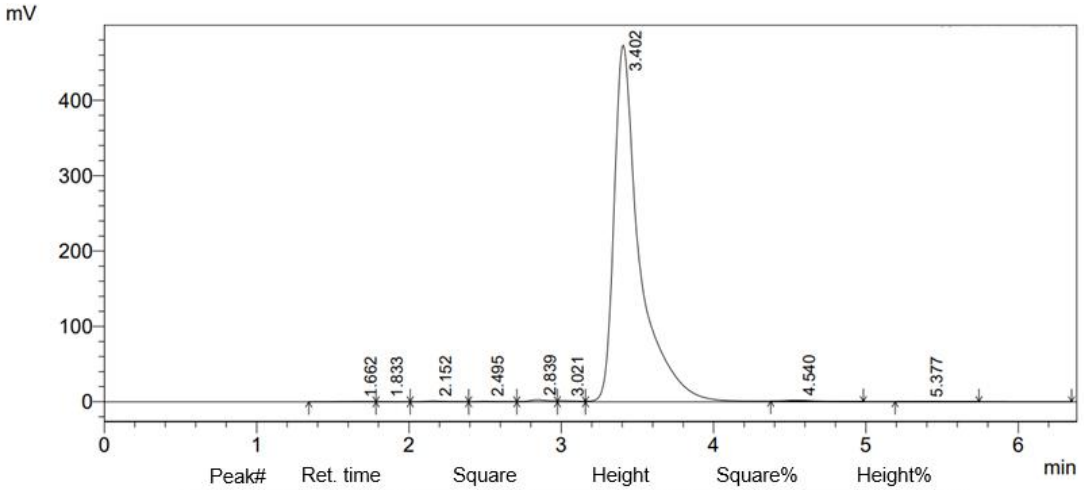
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.681	10367	680	0.399	0.324
2	1.943	5490	657	0.212	0.313
3	2.156	7801	718	0.301	0.342
4	2.591	3256	247	0.125	0.118
5	2.797	5923	545	0.228	0.260
6	3.031	8568	772	0.330	0.368
7	3.295	8741	1098	0.337	0.523
8	3.450	21346	1700	0.823	0.810
9	3.808	2504592	202094	96.511	96.311
10	5.034	16830	1160	0.649	0.553
11	5.995	2231	164	0.086	0.078
Total		2595147	209835	100.000	100.000

HPLC trace of **R_6L_4**



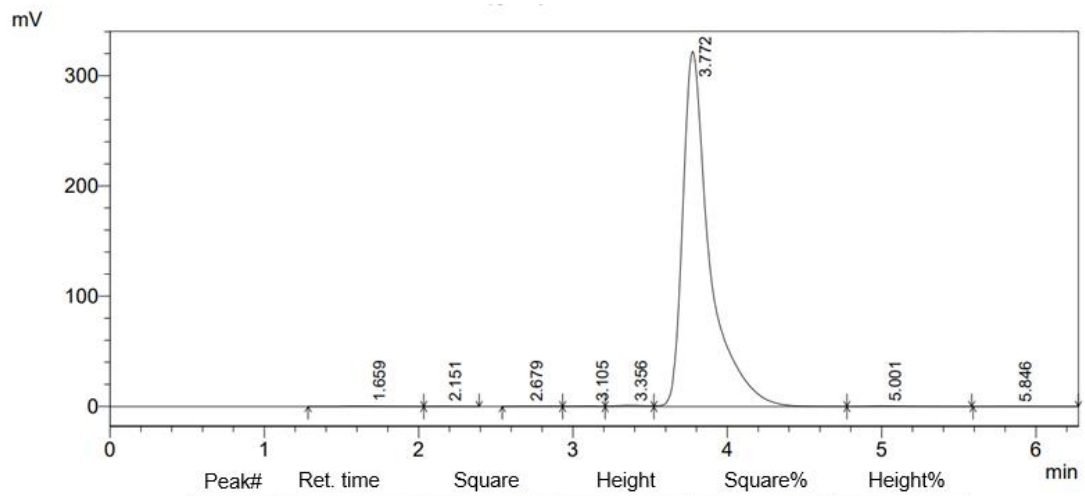
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.527	19808	1793	0.533	0.603
2	1.785	10156	1166	0.273	0.392
3	1.951	8968	1110	0.241	0.373
4	2.138	6915	620	0.186	0.209
5	2.513	3624	390	0.097	0.131
6	2.768	6768	609	0.182	0.205
7	3.038	4045	420	0.109	0.141
8	3.251	7387	1018	0.199	0.342
9	3.406	33925	2646	0.913	0.890
10	3.946	3579740	285388	96.292	96.010
11	5.249	32087	1827	0.863	0.615
12	6.176	4146	263	0.112	0.088
Total		3717571	297250	100.000	100.000

HPLC trace of **R_7L_2**



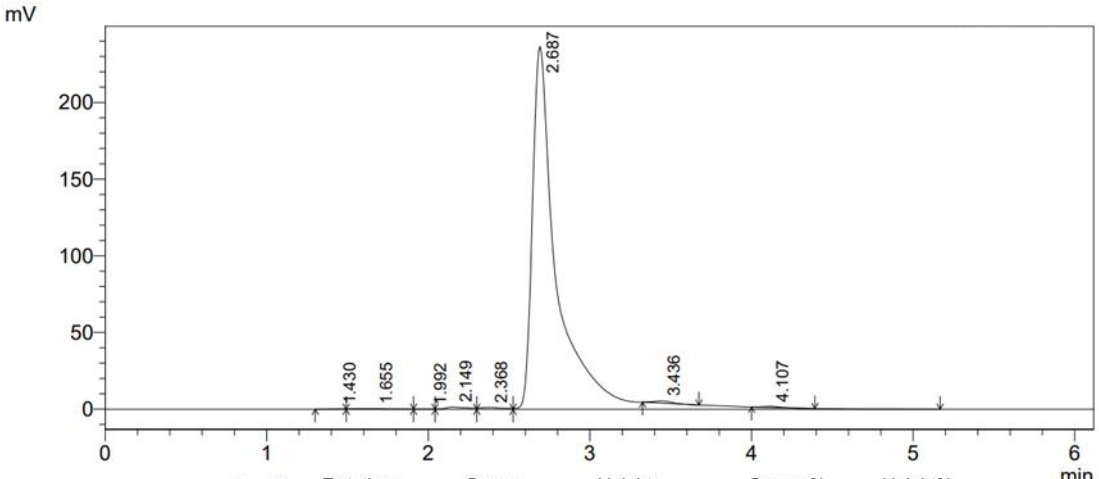
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.662	5250	452	0.093	0.094
2	1.833	1476	141	0.026	0.029
3	2.152	10283	1025	0.183	0.213
4	2.495	8284	691	0.147	0.144
5	2.839	23649	2658	0.420	0.552
6	3.021	11103	1179	0.197	0.245
7	3.402	5552687	473405	98.598	98.391
8	4.540	15544	1323	0.276	0.275
9	5.377	3353	271	0.060	0.056
Total		5631629	481145	100.000	100.000

HPLC trace of **R_7L_4**



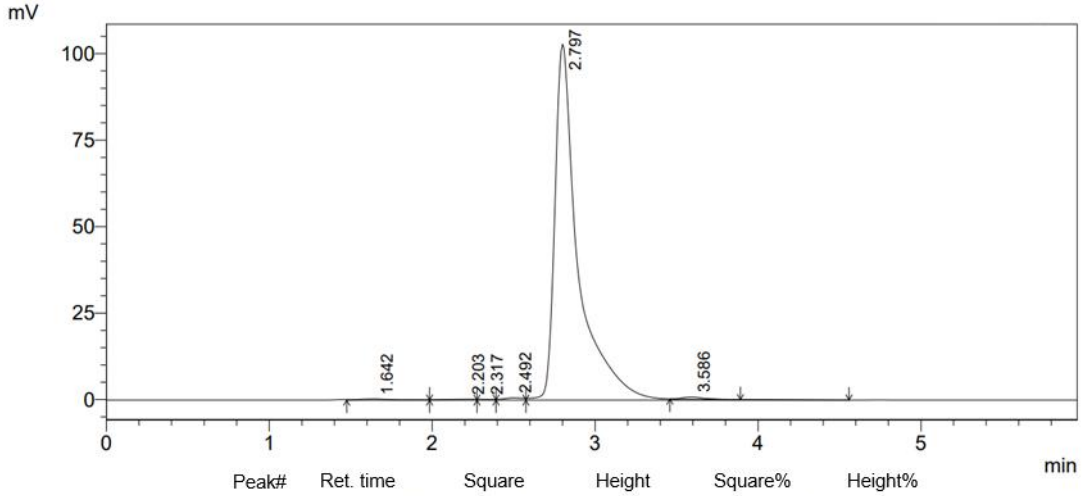
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.659	6823	516	0.172	0.159
2	2.151	2430	311	0.061	0.095
3	2.679	3636	312	0.092	0.096
4	3.105	4858	421	0.123	0.129
5	3.356	12810	896	0.324	0.275
6	3.772	3914044	322368	98.951	99.026
7	5.001	8910	579	0.225	0.178
8	5.846	2029	136	0.051	0.042
Total		3955540	325539	100.000	100.000

HPLC trace of **R_8L_2**



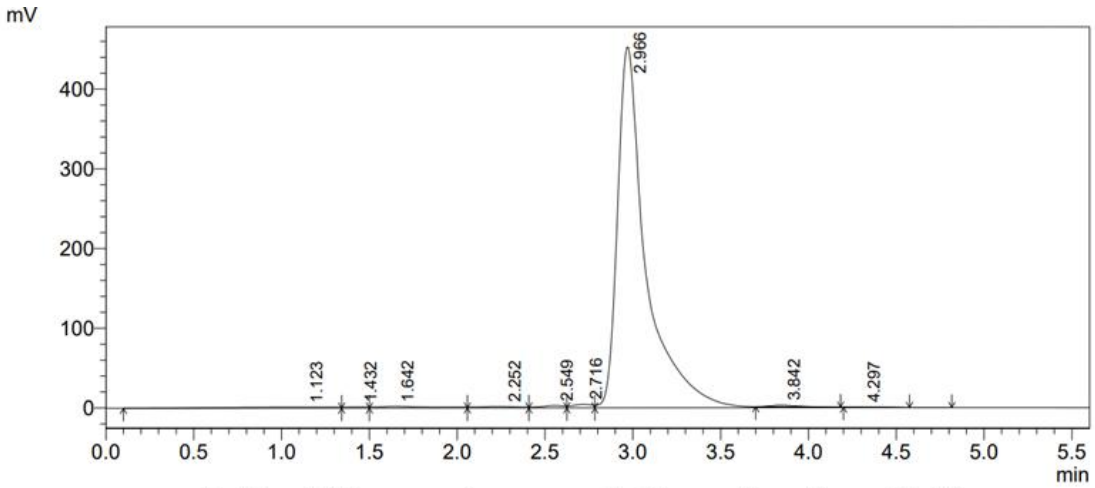
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.430	1504	245	0.057	0.101
2	1.655	6951	448	0.264	0.185
3	1.992	1019	131	0.039	0.054
4	2.149	13725	1429	0.522	0.590
5	2.368	11935	1260	0.454	0.520
6	2.687	2579395	236665	98.022	97.667
7	3.436	10469	1333	0.398	0.550
8	4.107	6438	806	0.245	0.333
Total		2631434	242317	100.000	100.000

HPLC trace of **R_8L_3**



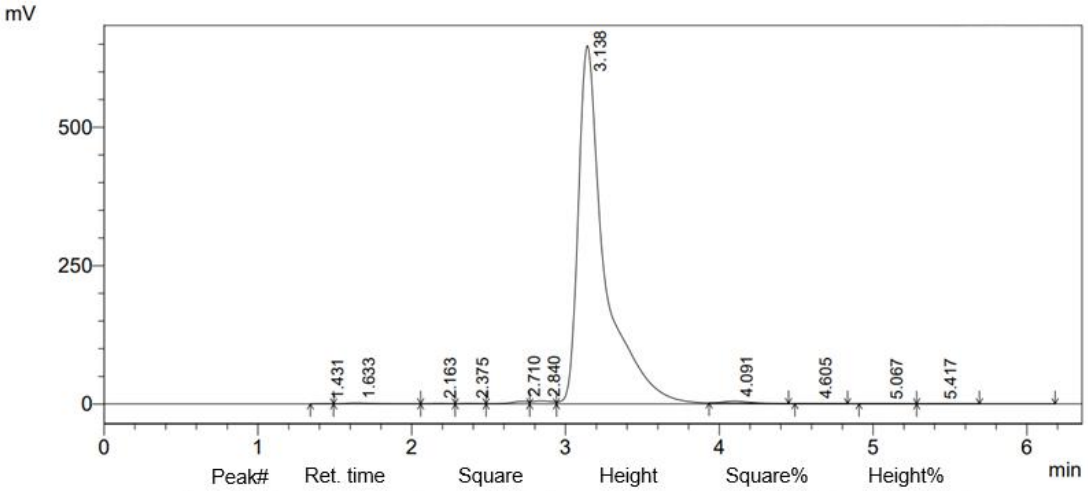
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.642	4951	305	0.473	0.291
2	2.203	3246	280	0.310	0.266
3	2.317	1489	233	0.142	0.222
4	2.492	5460	655	0.522	0.624
5	2.797	1025846	102905	97.995	97.990
6	3.586	5841	638	0.558	0.608
Total		1046834	105016	100.000	100.000

HPLC trace of **R_8L_4**



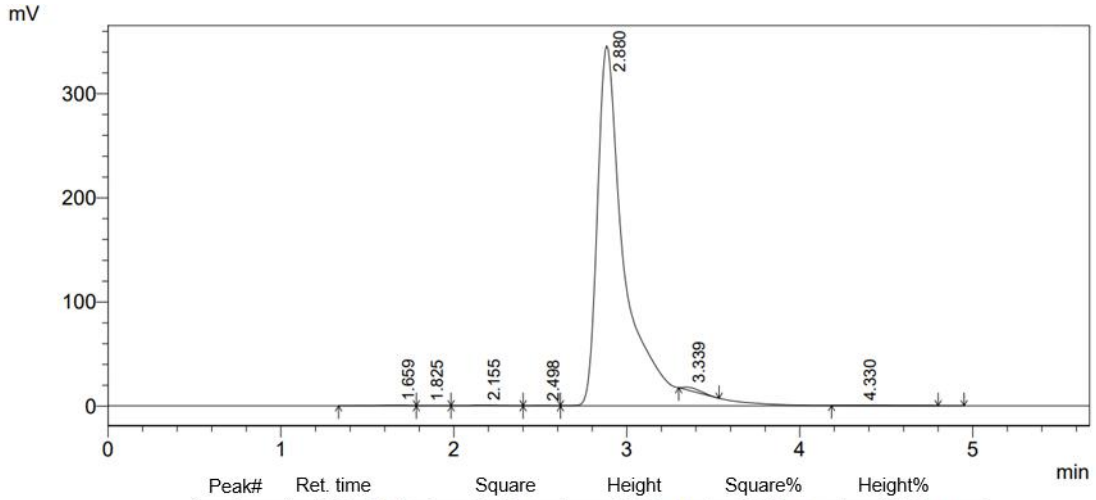
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.123	58048	1236	1.086	0.263
2	1.432	12364	1387	0.231	0.296
3	1.642	46213	2052	0.865	0.437
4	2.252	29076	1758	0.544	0.375
5	2.549	28317	3074	0.530	0.656
6	2.716	34732	4400	0.650	0.938
7	2.966	5108807	452638	95.612	96.513
8	3.842	23002	2171	0.430	0.463
9	4.297	2704	274	0.051	0.058
Total		5343263	468990	100.000	100.000

HPLC trace of **R_8L_5**



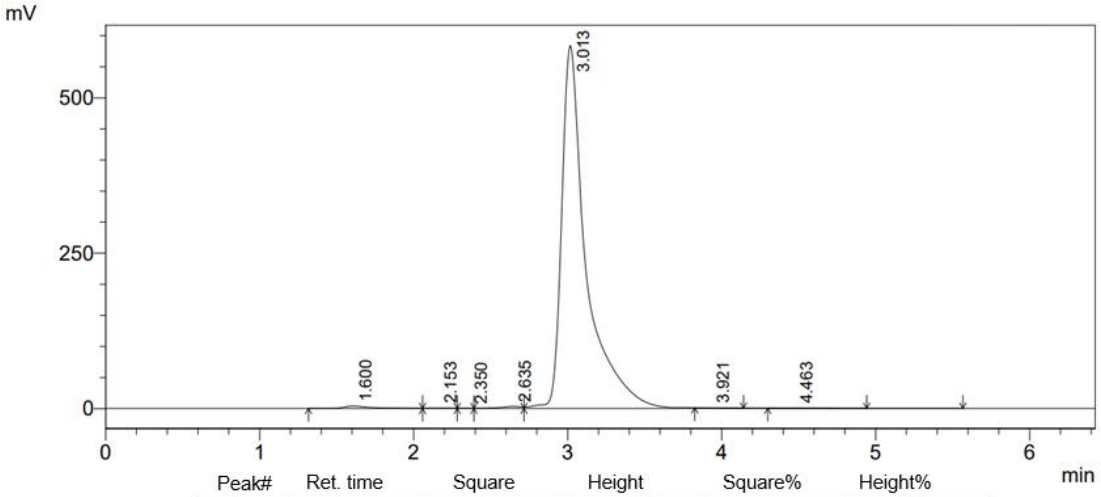
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.431	2271	381	0.029	0.057
2	1.633	23404	1627	0.294	0.245
3	2.163	6964	750	0.087	0.113
4	2.375	9053	994	0.114	0.149
5	2.710	38322	4512	0.481	0.678
6	2.840	48300	5333	0.606	0.802
7	3.138	7795194	647362	97.811	97.319
8	4.091	39965	3668	0.501	0.551
9	4.605	3607	384	0.045	0.058
10	5.067	1400	109	0.018	0.016
11	5.417	1156	76	0.015	0.011
Total		7969637	665195	100.000	100.000

HPLC trace of **R_9L_2**



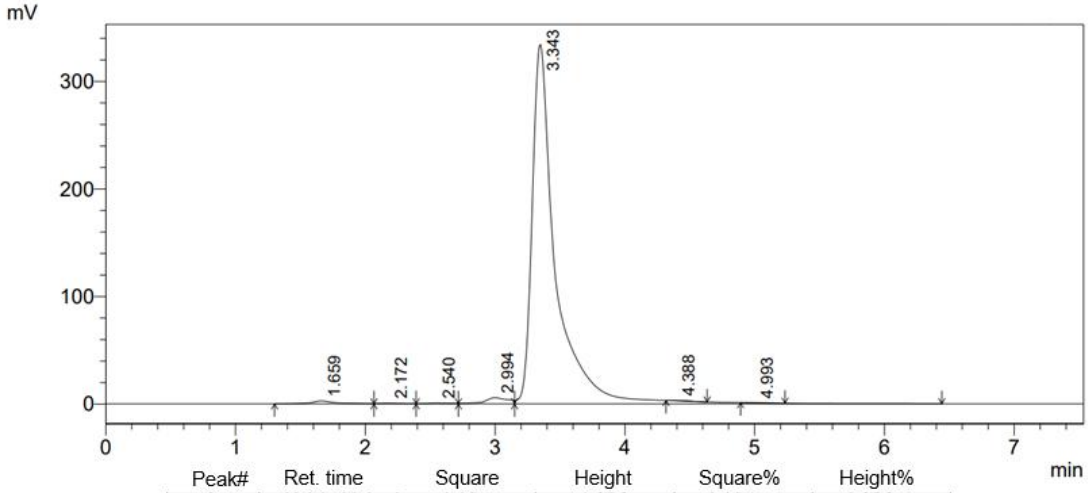
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.659	5485	493	0.137	0.141
2	1.825	1228	132	0.031	0.038
3	2.155	7257	684	0.182	0.196
4	2.498	2363	254	0.059	0.073
5	2.880	3954709	345791	99.028	98.863
6	3.339	18736	2111	0.469	0.604
7	4.330	3736	303	0.094	0.087
Total		3993515	349769	100.000	100.000

HPLC trace of **R_9L_3**



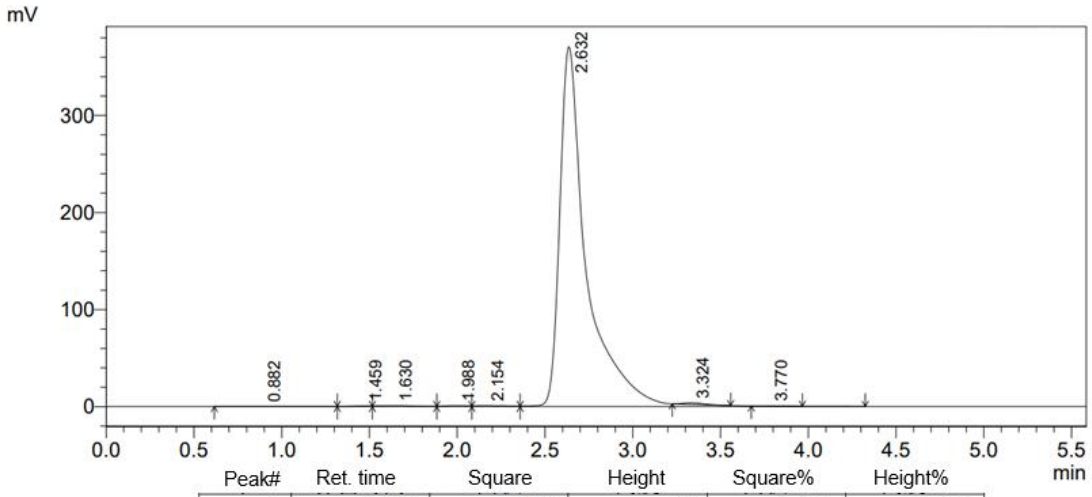
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.600	47945	3759	0.731	0.634
2	2.153	6042	613	0.092	0.103
3	2.350	2096	335	0.032	0.057
4	2.635	32103	3277	0.490	0.553
5	3.013	6457905	583877	98.488	98.468
6	3.921	3841	476	0.059	0.080
7	4.463	7141	621	0.109	0.105
Total		6557073	592959	100.000	100.000

HPLC trace of **R_9L_5**



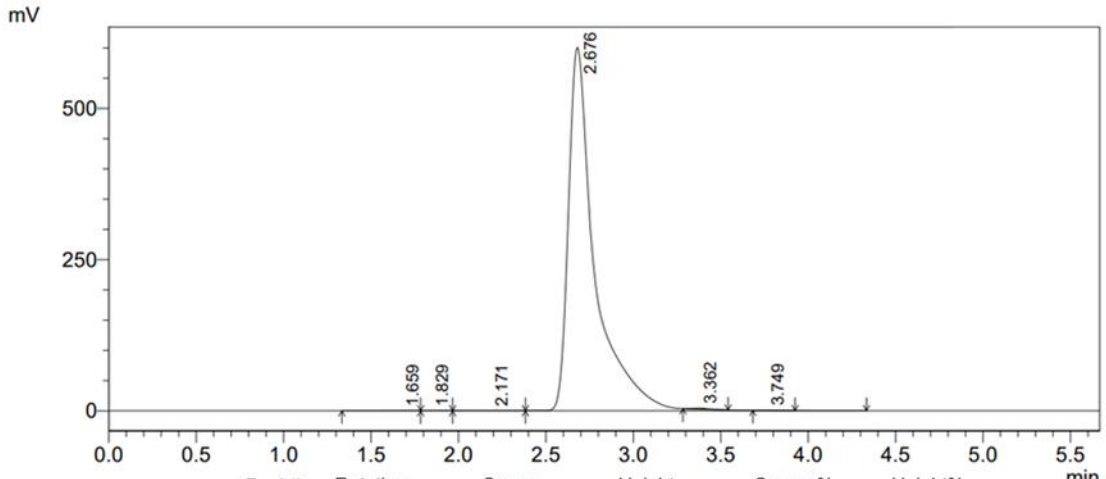
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.659	34807	2689	0.800	0.781
2	2.172	6368	573	0.146	0.167
3	2.540	9069	734	0.208	0.213
4	2.994	71724	5626	1.649	1.634
5	3.343	4221216	334035	97.041	97.011
6	4.388	4353	431	0.100	0.125
7	4.993	2410	238	0.055	0.069
Total		4349946	344327	100.000	100.000

HPLC trace of **$R_{10}L_2$**



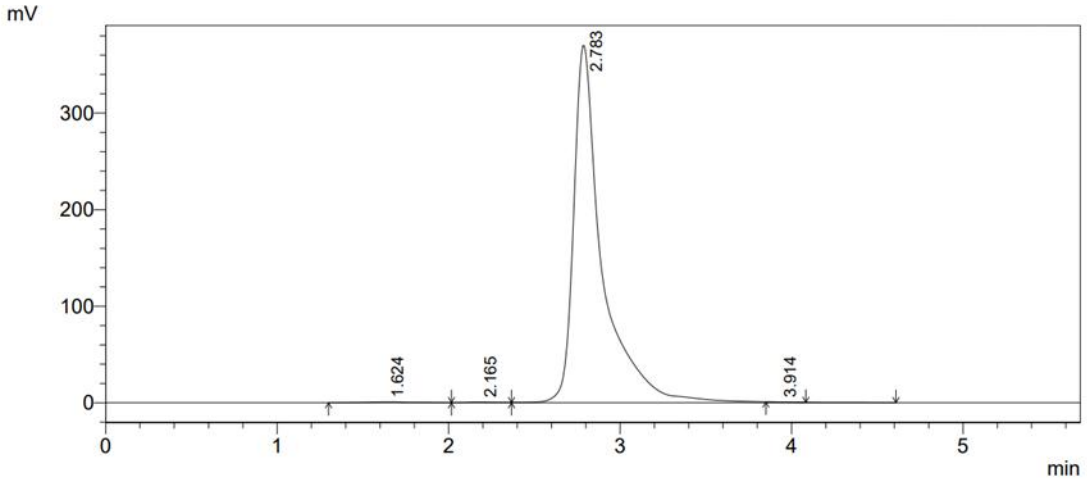
Peak#	Ret. time	Square	Height	Square%	Height%
1	0.882	1233	60	0.031	0.016
2	1.459	4400	629	0.110	0.167
3	1.630	13558	972	0.340	0.258
4	1.988	8261	901	0.207	0.239
5	2.154	10498	864	0.264	0.230
6	2.632	3929199	370705	98.637	98.576
7	3.324	14049	1629	0.353	0.433
8	3.770	2311	302	0.058	0.080
Total		3983508	376061	100.000	100.000

HPLC trace of **$R_{10}L_3$**



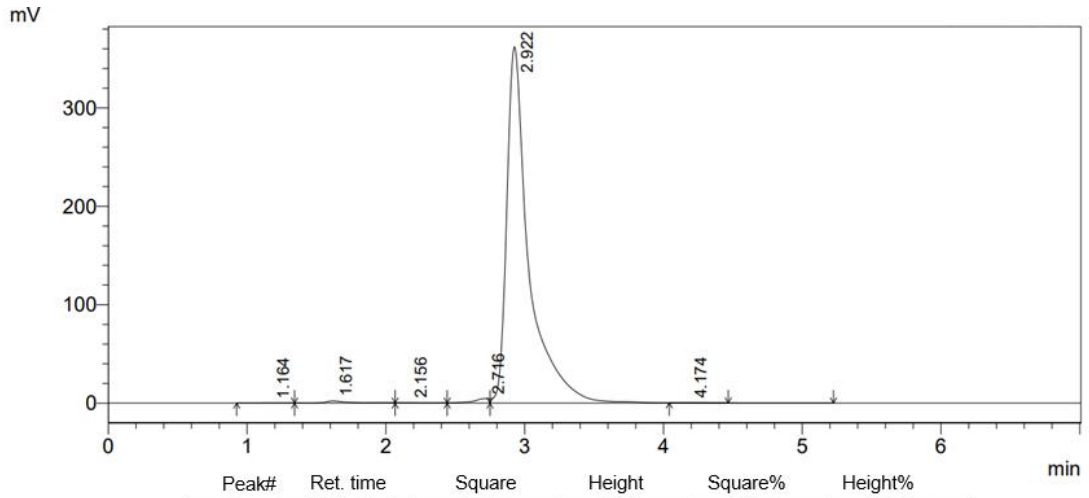
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.659	6883	559	0.108	0.093
2	1.829	2011	214	0.032	0.035
3	2.171	7716	503	0.122	0.083
4	2.676	6314067	600779	99.513	99.454
5	3.362	12851	1833	0.203	0.303
6	3.749	1429	187	0.023	0.031
Total		6344957	604075	100.000	100.000

HPLC trace of **$R_{10}L_4$**



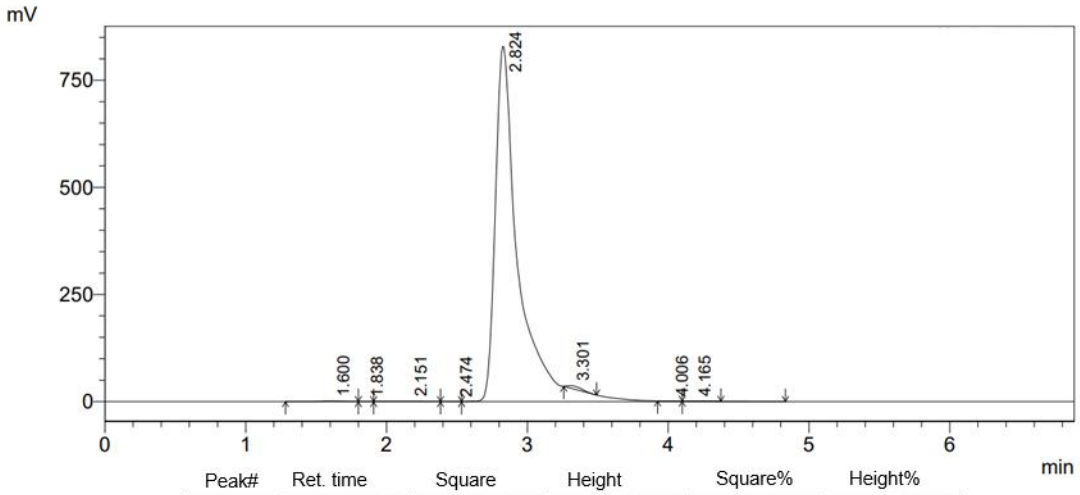
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.624	15189	902	0.351	0.243
2	2.165	8092	684	0.187	0.184
3	2.783	4299117	369902	99.431	99.527
4	3.914	1320	173	0.031	0.046
Total		4323718	371661	100.000	100.000

HPLC trace of **$R_{10}L_5$**



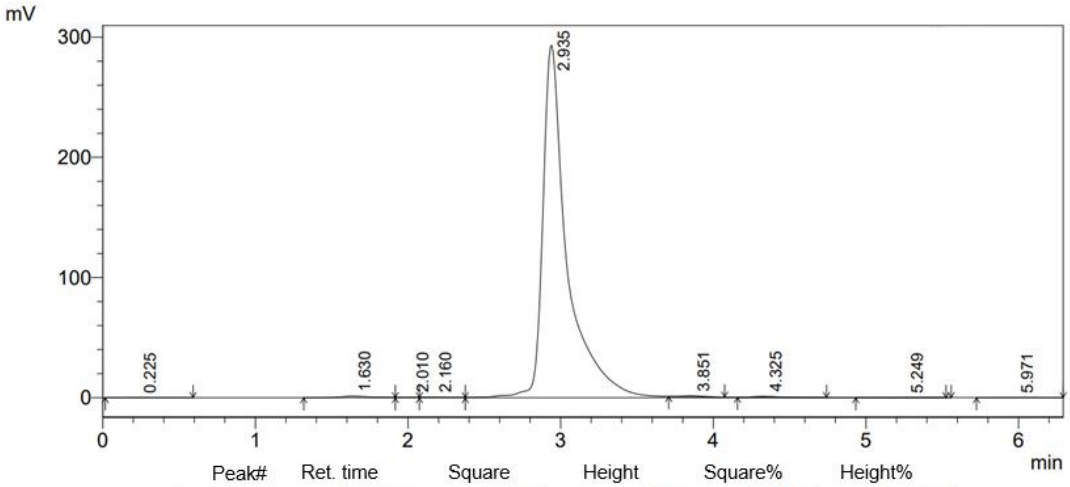
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.164	1160	75	0.028	0.020
2	1.617	26281	2072	0.643	0.561
3	2.156	6941	428	0.170	0.116
4	2.716	36602	4516	0.896	1.222
5	2.922	4010723	362186	98.189	97.996
6	4.174	2988	318	0.073	0.086
Total		4084695	369595	100.000	100.000

HPLC trace of **$R_{11}L_2$**



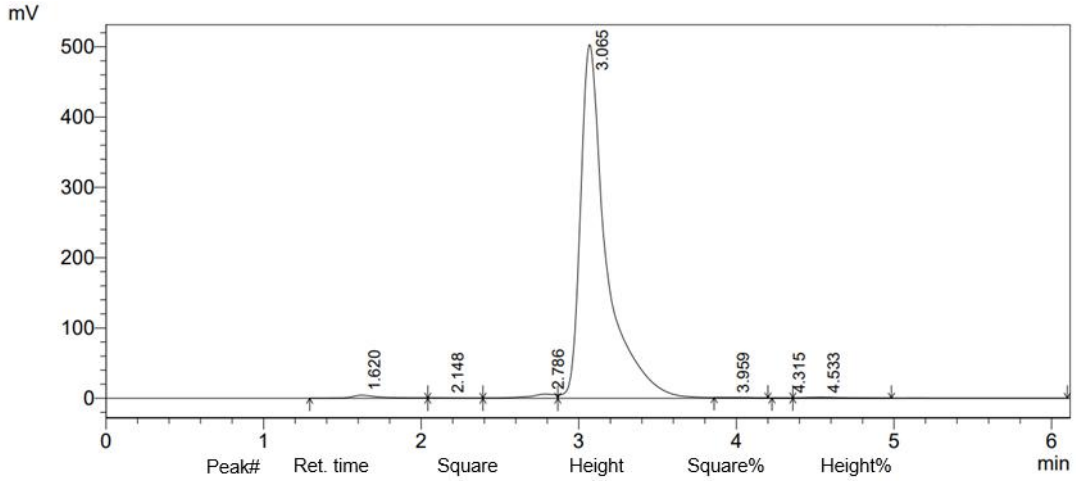
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.600	18878	1592	0.196	0.190
2	1.838	2908	479	0.030	0.057
3	2.151	15689	931	0.163	0.111
4	2.474	3630	474	0.038	0.056
5	2.824	9547890	829578	99.037	98.831
6	3.301	43442	5403	0.451	0.644
7	4.006	2725	336	0.028	0.040
8	4.165	5580	597	0.058	0.071
Total		9640741	839391	100.000	100.000

HPLC trace of **$R_{11}L_3$**



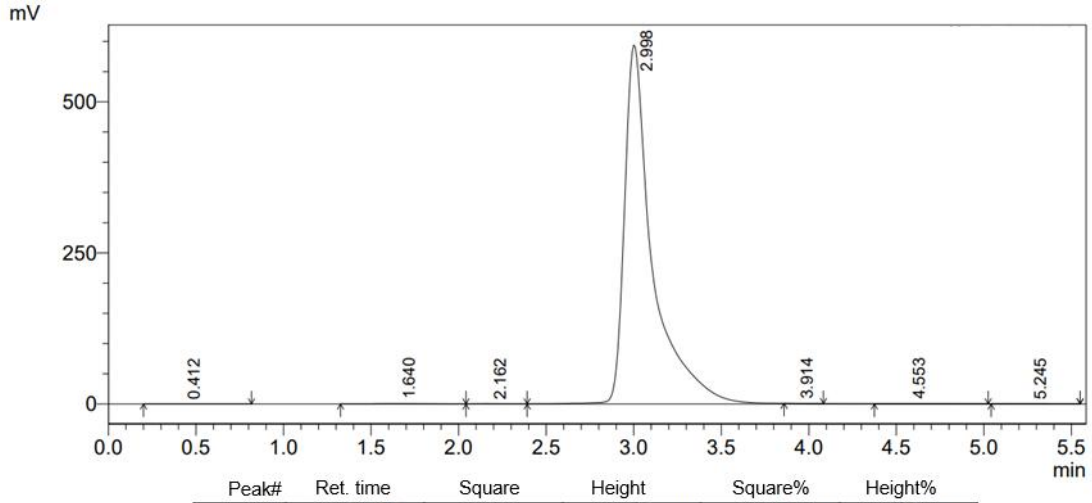
Peak#	Ret. time	Square	Height	Square%	Height%
1	0.225	1184	73	0.036	0.025
2	1.630	18232	1283	0.549	0.431
3	2.010	3838	444	0.116	0.149
4	2.160	8123	605	0.244	0.203
5	2.935	3270726	293295	98.444	98.570
6	3.851	7767	813	0.234	0.273
7	4.325	9680	845	0.291	0.284
8	5.249	1200	74	0.036	0.025
9	5.971	1663	118	0.050	0.040
Total		3322412	297550	100.000	100.000

HPLC trace of **$R_{11}L_4$**



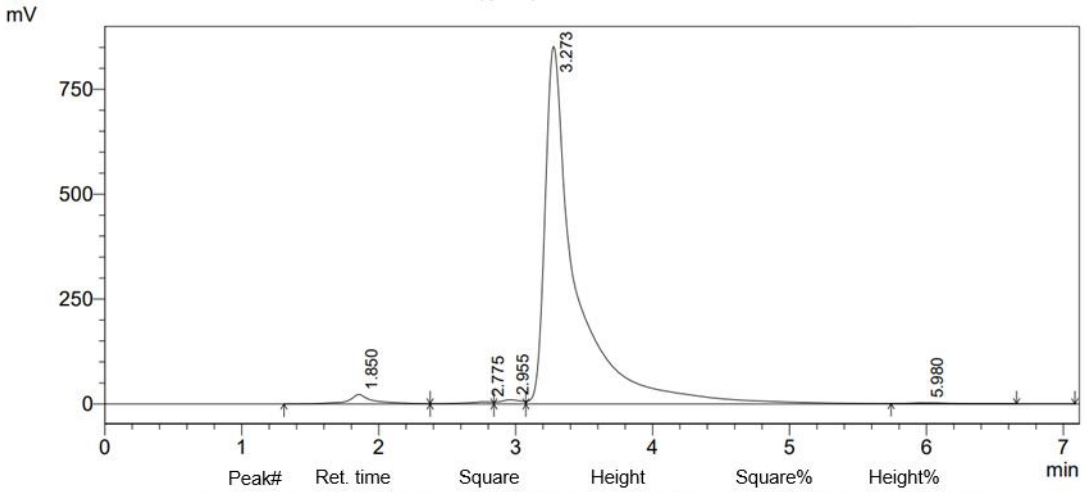
Peak#	Ret. time	Square	Height	Square%	Height%
1	1.620	56956	4293	0.960	0.832
2	2.148	10470	697	0.177	0.135
3	2.786	72398	5996	1.221	1.162
4	3.065	5767821	503228	97.242	97.492
5	3.959	4726	446	0.080	0.086
6	4.315	1449	262	0.024	0.051
7	4.533	17615	1250	0.297	0.242
Total		5931435	516171	100.000	100.000

HPLC trace of $\mathbf{R_{12}L_2}$



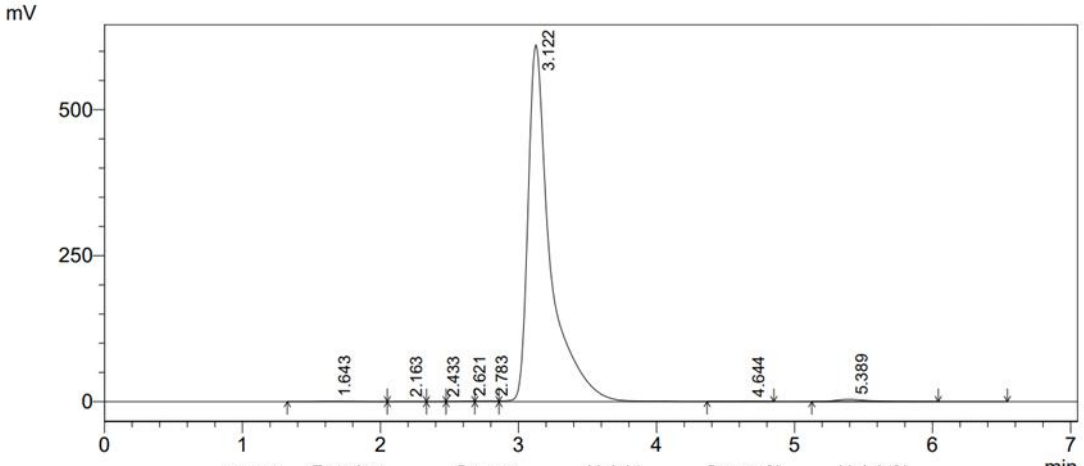
Peak#	Ret. time	Square	Height	Square%	Height%
1	0.412	1425	82	0.021	0.014
2	1.640	9749	632	0.146	0.106
3	2.162	4771	424	0.072	0.071
4	2.998	6630484	594058	99.578	99.632
5	3.914	1703	213	0.026	0.036
6	4.553	7307	592	0.110	0.099
7	5.245	3152	251	0.047	0.042
Total		6658591	596253	100.000	100.000

HPLC trace of $\mathbf{R_{12}L_4}$



Peak#	Ret. time	Square	Height	Square%	Height%
1	1.850	285447	22662	2.058	2.540
2	2.775	70997	5165	0.512	0.579
3	2.955	104285	9875	0.752	1.107
4	3.273	13373237	852241	96.408	95.519
5	5.980	37604	2282	0.271	0.256
Total		13871570	892225	100.000	100.000

HPLC trace of $\mathbf{R_{13}L_2}$



Peak#	Ret. time	Square	Height	Square%	Height%
1	1.643	10817	684	0.155	0.111
2	2.163	3441	346	0.049	0.056
3	2.433	1320	180	0.019	0.029
4	2.621	8013	995	0.115	0.161
5	2.783	11079	1152	0.159	0.186
6	3.122	6891356	611216	98.601	98.779
7	4.644	4071	353	0.058	0.057
8	5.389	59040	3848	0.845	0.622
Total		6989138	618774	100.000	100.000