Supporting Information

Synthesis, characterization and biological evaluation of formononetin derivatives as novel EGFR inhibitors via inhibiting growth, migration and inducing apoptosis in breast cancer cell line

Hong-Yan Lin [a,b,1], Wen-Xue Sun [a,b,1], Chao-Sai Zheng [a,b], Hong-Wei Han [a,b], Xue Wang [a,b], Ya-Han Zhang [a,b], Han-Yue Qiu [a,b], Cheng-Yi Tang [a,b], Jin-Liang Qi [a,b], Gui-Hua Lu [a,b], Rong-Wu Yang [a,b,*], Xiao-Ming Wang [a,b,*] and Yong-Hua Yang [a,b,*].

Table S1 The binding energy of the target compounds, formononetin and lapatinib

Compound	CDOCKER_INTERACTION _ENERGY (kcal/mol)	Compound	CDOCKER_INTERACTION _ENERGY (kcal/mol)
4a	-41.0285	**4m**	-49.2016
4b	-39.2586	**4n**	-48.3509
4c	-34.6878	**4o**	-41.8921
4d	-40.3325	**4p**	-54.0388
4e	-38.0547	**4q**	-45.3512
4f	-40.0058	**4r**	-44.9801
4g	-41.0508	**4s**	-51.0268
4h	-56.3879	**4t**	-52.3607
4i	-41.2687	**4u**	-48.0109
4j	-41.0207	**4v**	**-64.5264**
4k	-40.8912	Formononetin	-34.5681
4l	-42.3901	Lapatinib	-71.0407

Determination of 1-ocatanol/water partition coefficients for 4a-4v

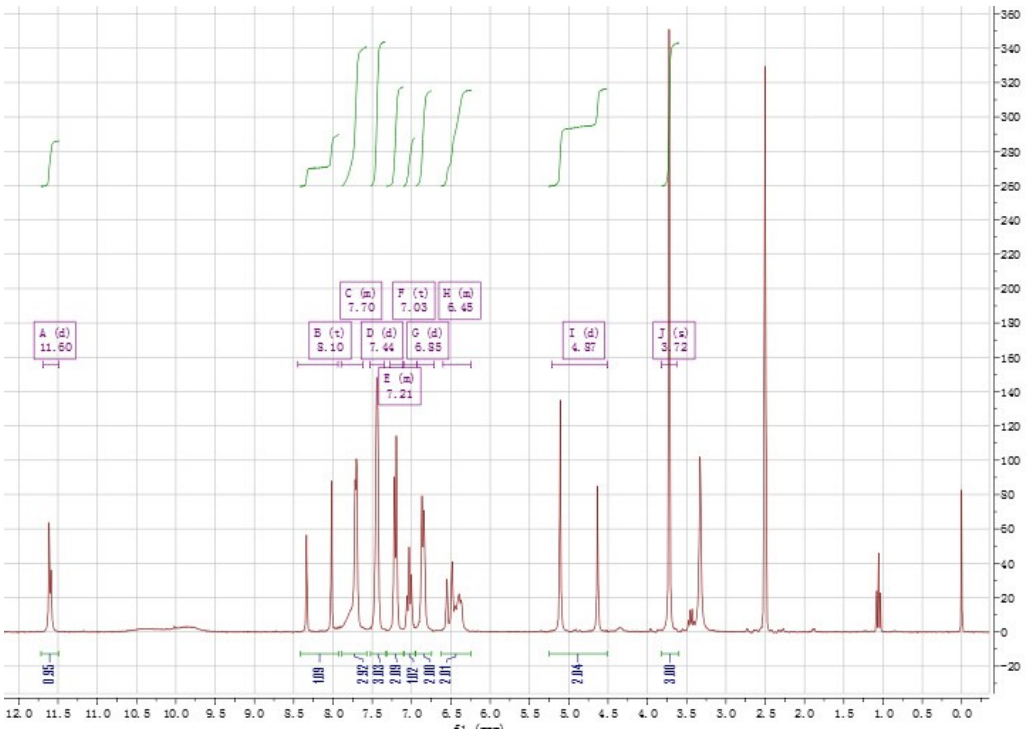
1-Ocatanol/water partition coefficients was measured by a shake-flask method [1]. Both the solvents were mutually saturated before performing the experiments. Solutions of about 300 μg/mL formononetin derivatives (**4a-4v**) were prepared in aqueous buffer solutions (pH=7.4). Then 10 mL of 1-ocatanol was added to 10 mL of the aqueous formononetin derivative solution in glass flasks. The mixtures were then stirred in a mechanical shaker for 1 hour. Samples were left in water baths and kept at 25 ℃ for at least 72 hours. After that, the aqueous phases were isolated and the concentrations were determined by measuring the UV absorbance. The partition coefficients were calculated by mass balance. All the partitioning experiments were performed in at least three times.

1-Ocatanol/water partition coefficient is defined as $P=C_0/C_w$, where C_0 is the concentration of compound in 1-ocatanol phase at equilibrium, C_w is the concentration of compound in aqueous phase at equilibrium.

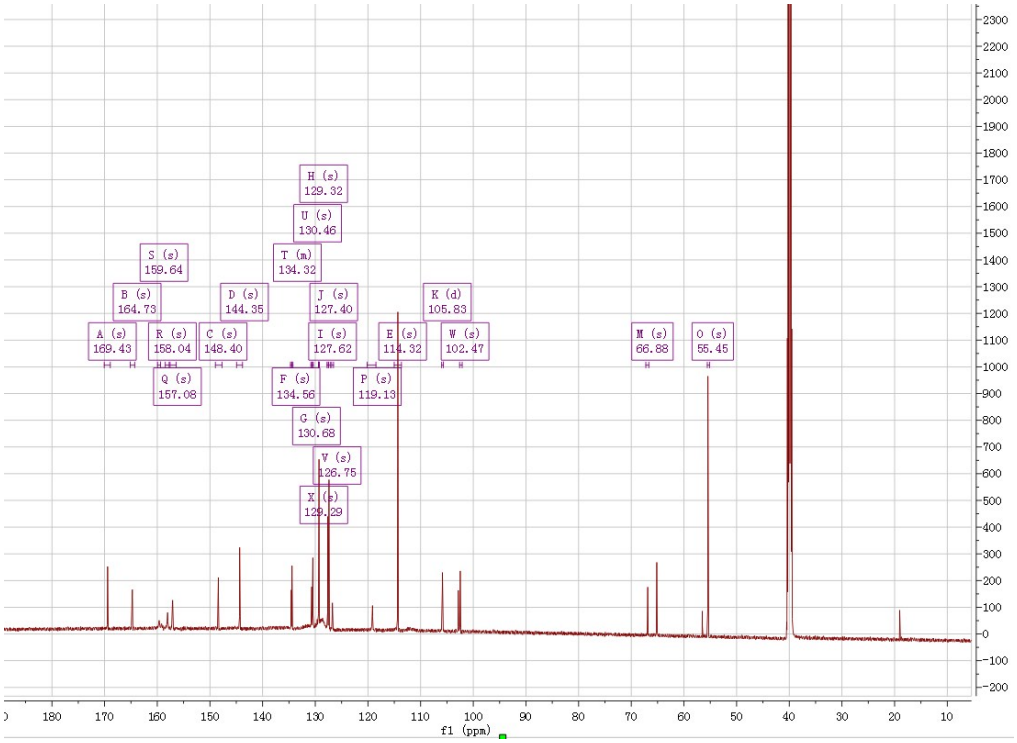
[1] Wang F. A., Molecular thermdynamics and chromatographic retention, China Meteorology Press, Beijing, 2001.

Table S2 Measurement values for 1-ocatanol/water partition coefficients (log *P*) for **4a**-**4v**.

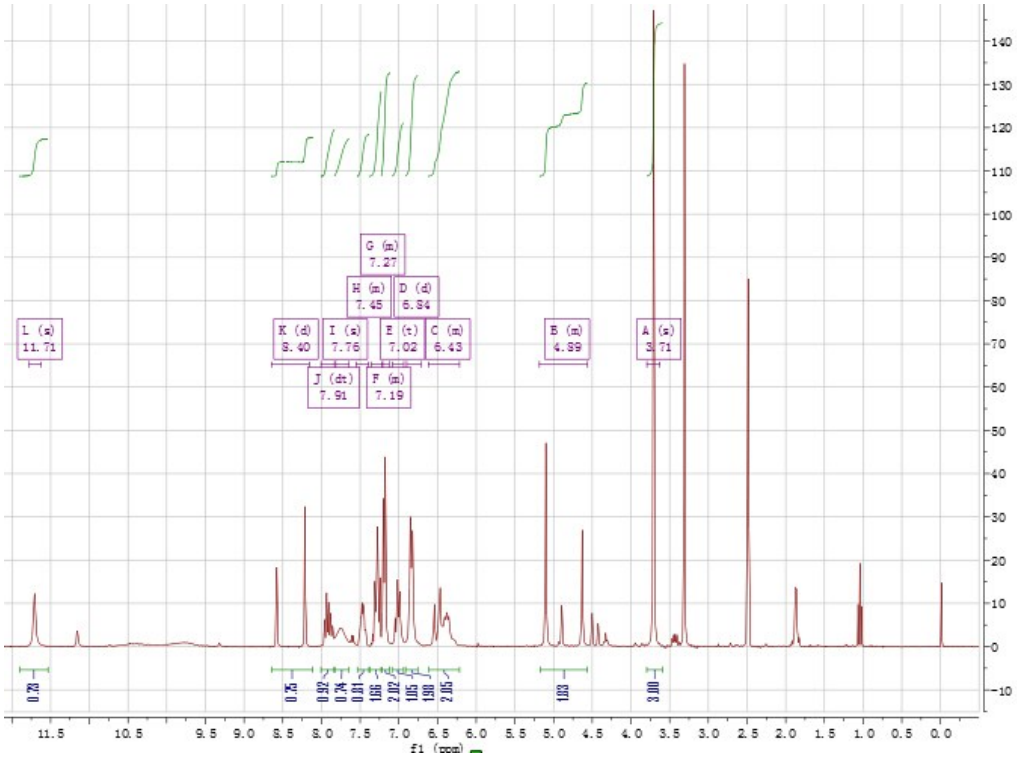
compound	log *P*	compound	log *P*	compound	log *P*
4a	2.35	**4i**	2.40	**4q**	2.42
4b	2.38	**4j**	2.48	**4r**	2.46
4c	2.39	**4k**	2.45	**4s**	2.48
4d	2.45	**4l**	2.42	**4t**	2.45
4e	2.43	**4m**	2.44	**4u**	2.49
4f	2.35	**4n**	2.39	**4v**	2.51
4g	2.38	**4o**	2.46		
4h	2.46	**4p**	2.41		



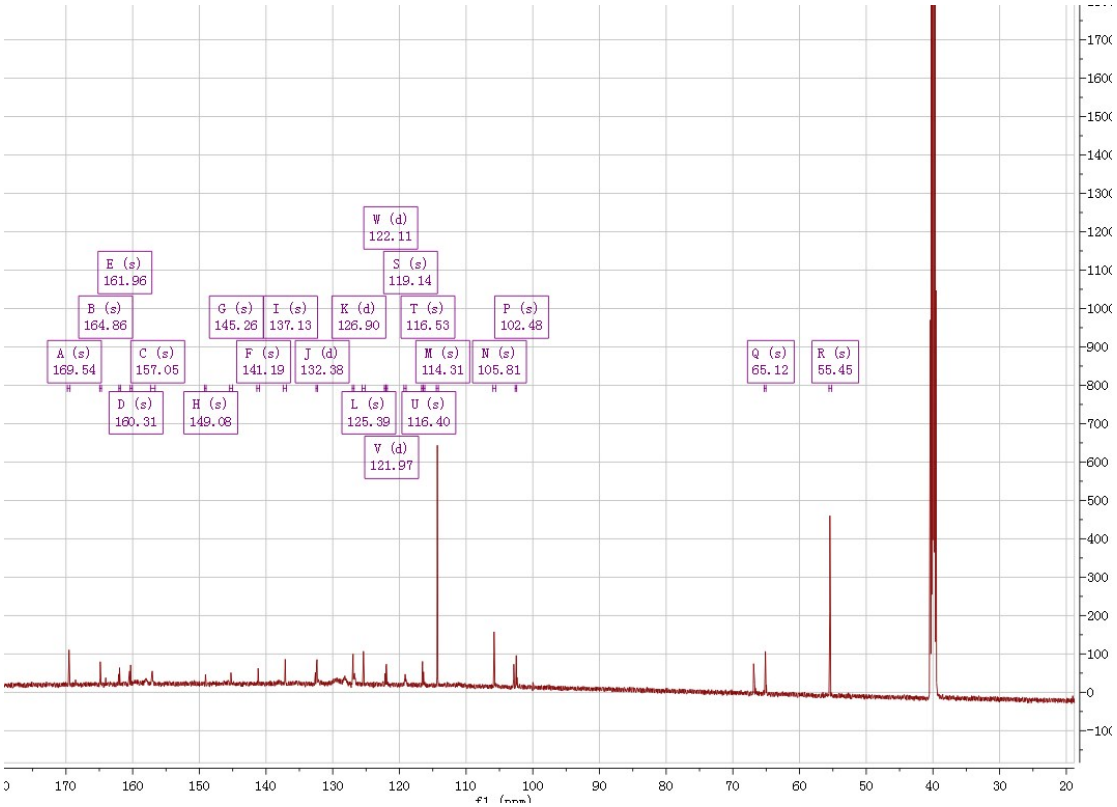
^{1}H NMR spectrum of **4a**



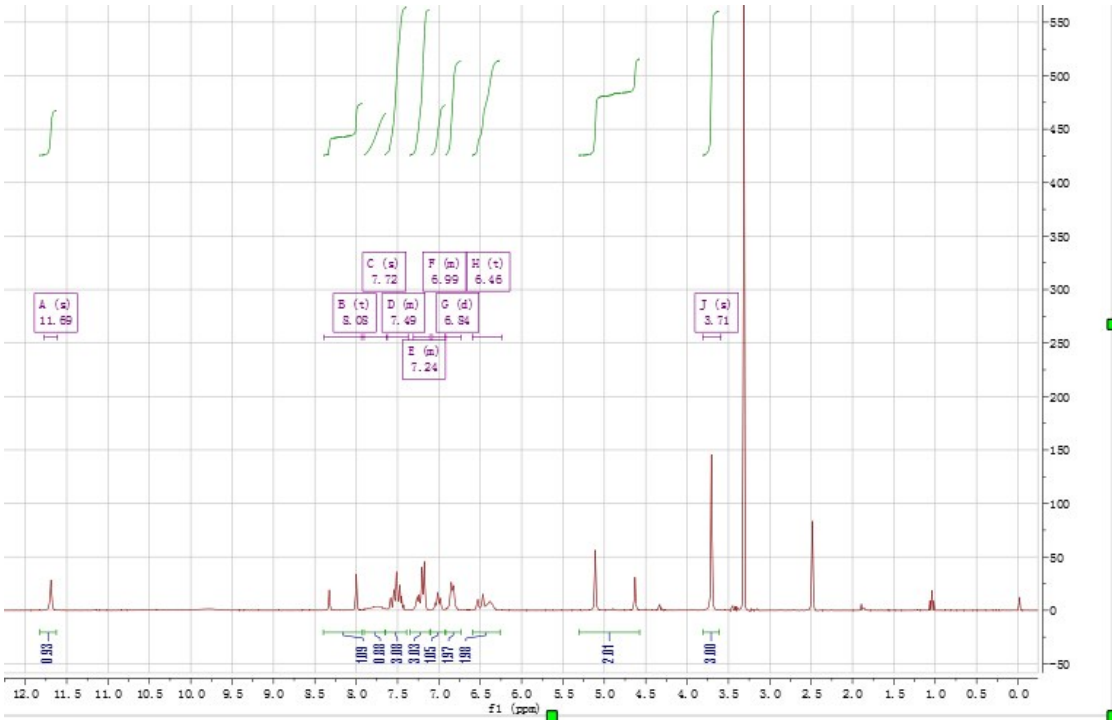
^{13}C NMR spectrum of **4a**



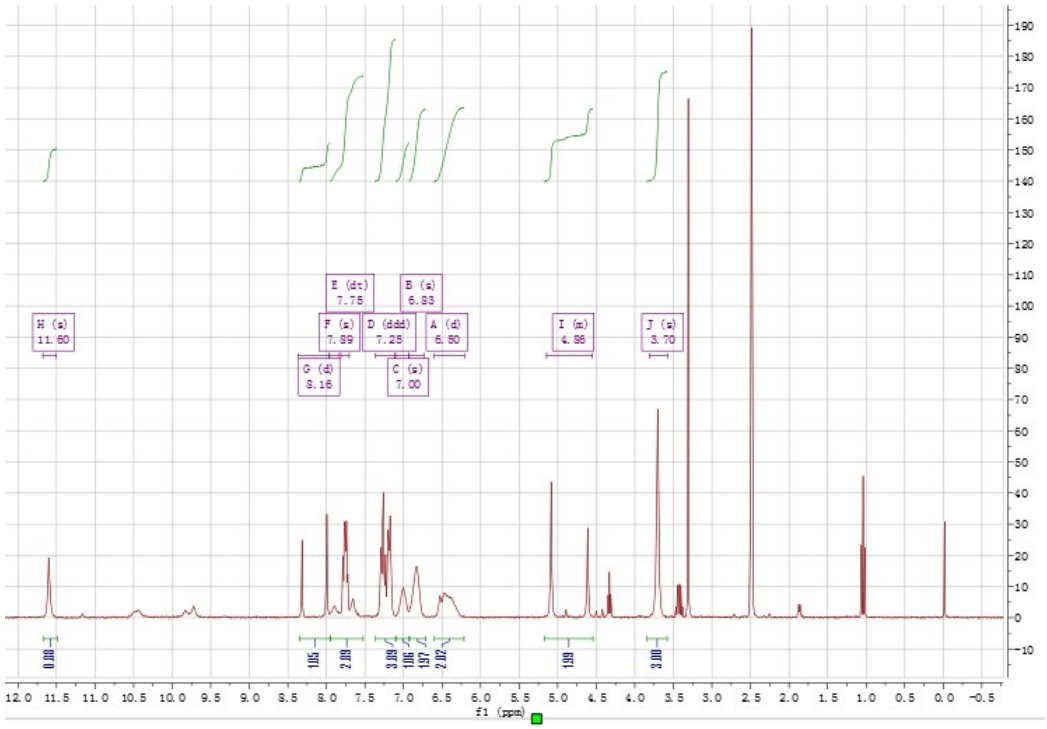
^{1}H NMR spectrum of **4b**



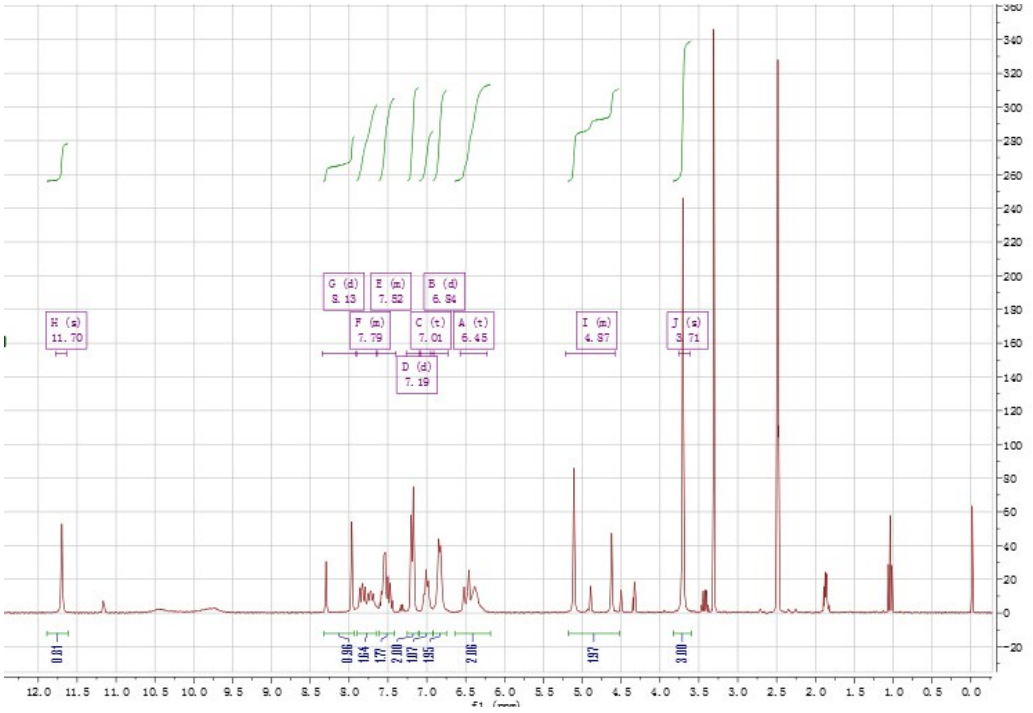
^{13}C NMR spectrum of **4b**



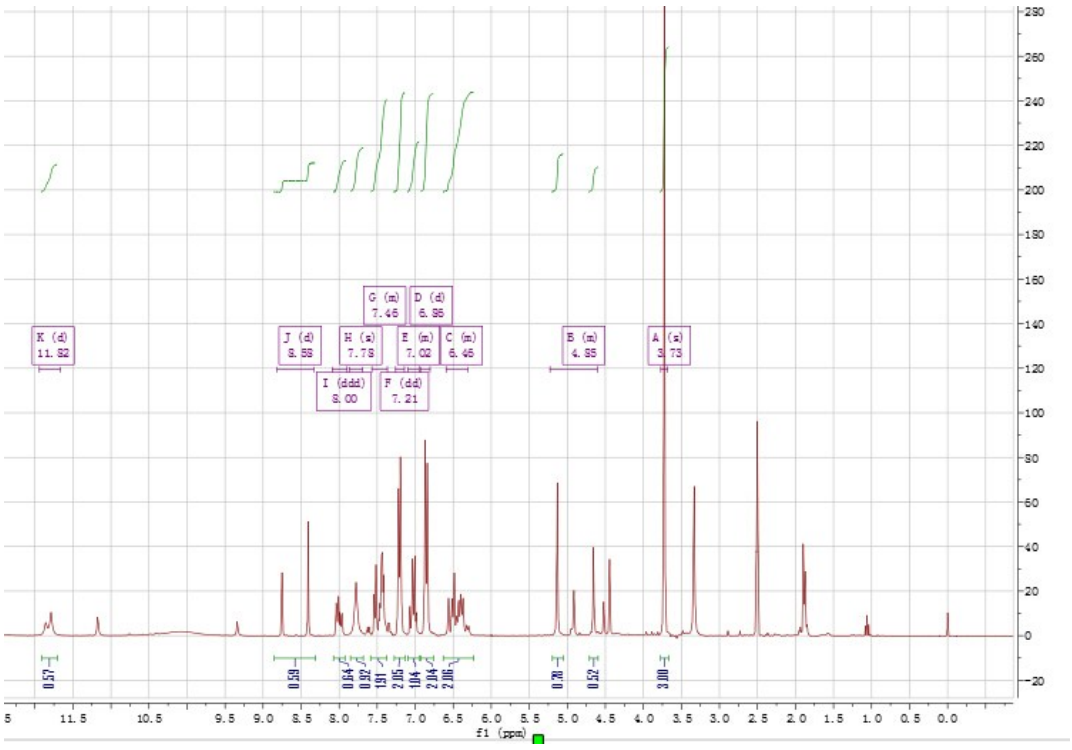
^{1}H NMR spectrum of **4c**



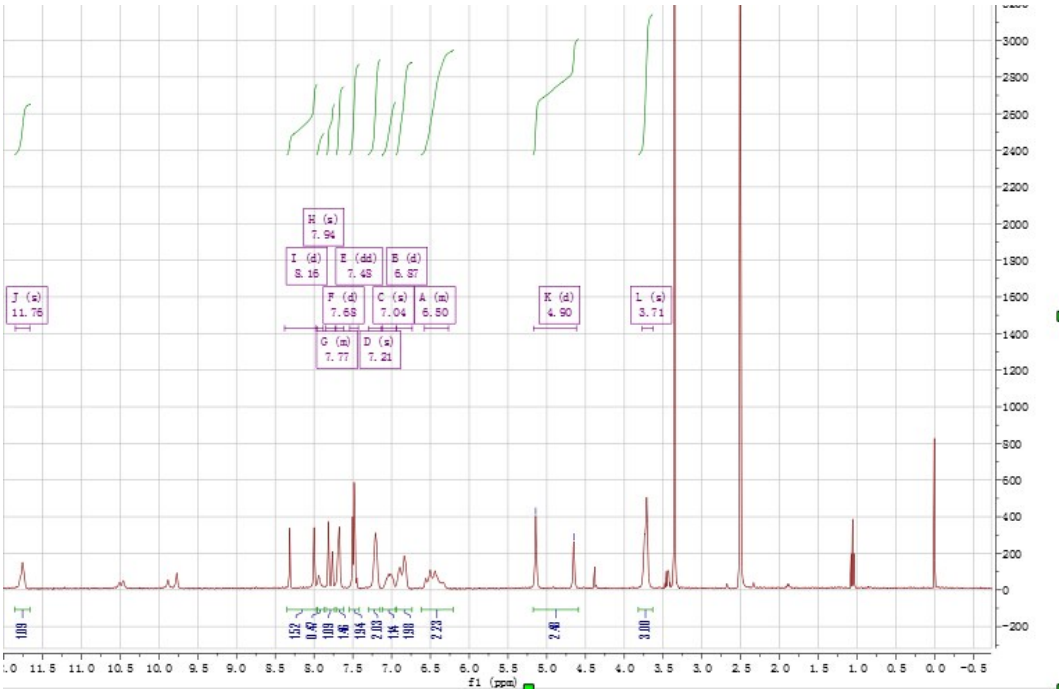
^{1}H NMR spectrum of **4d**



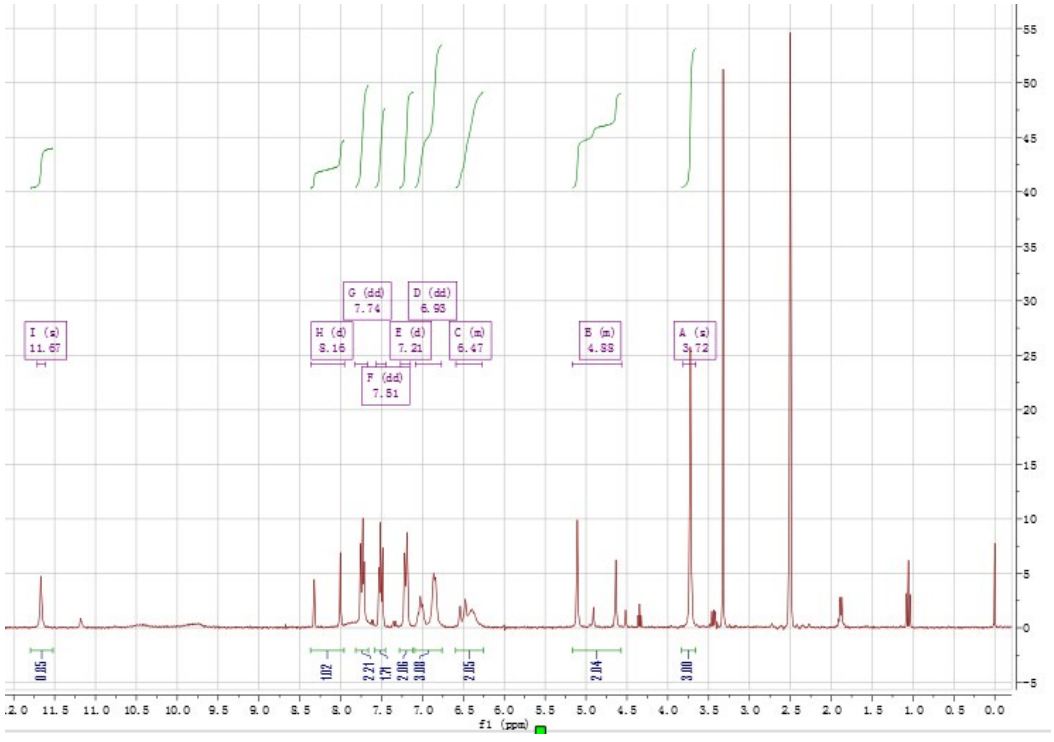
^{1}H NMR spectrum of **4e**



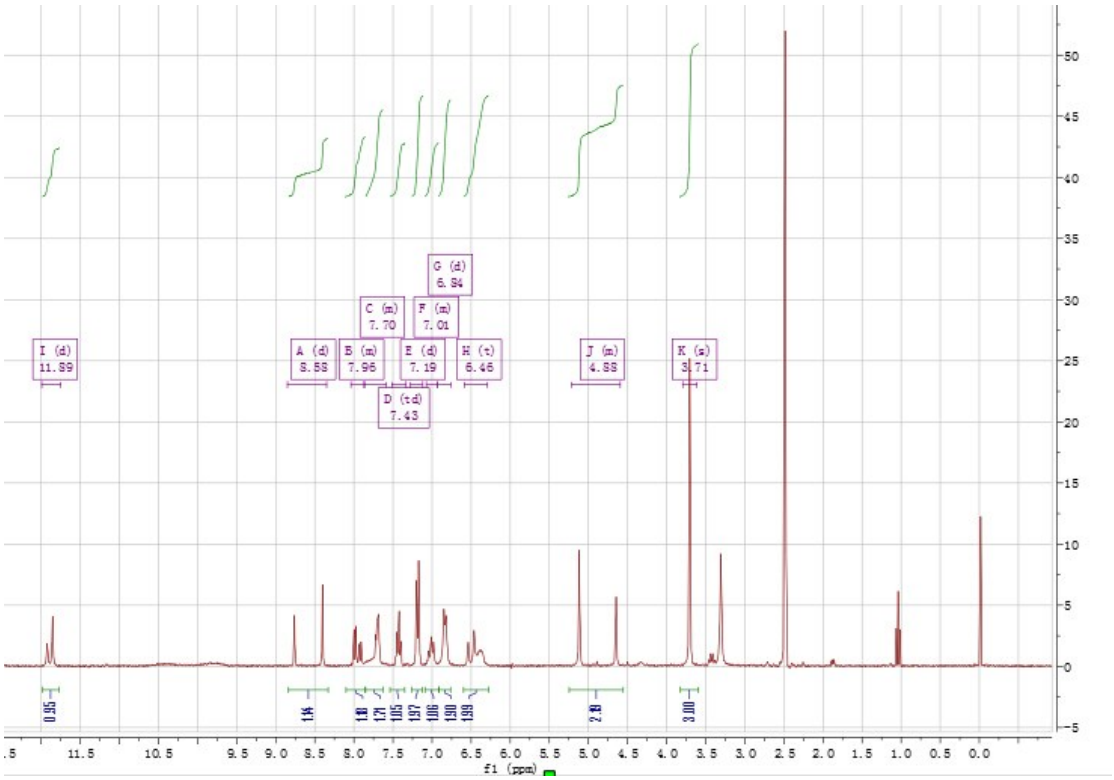
^{1}H NMR spectrum of **4f**



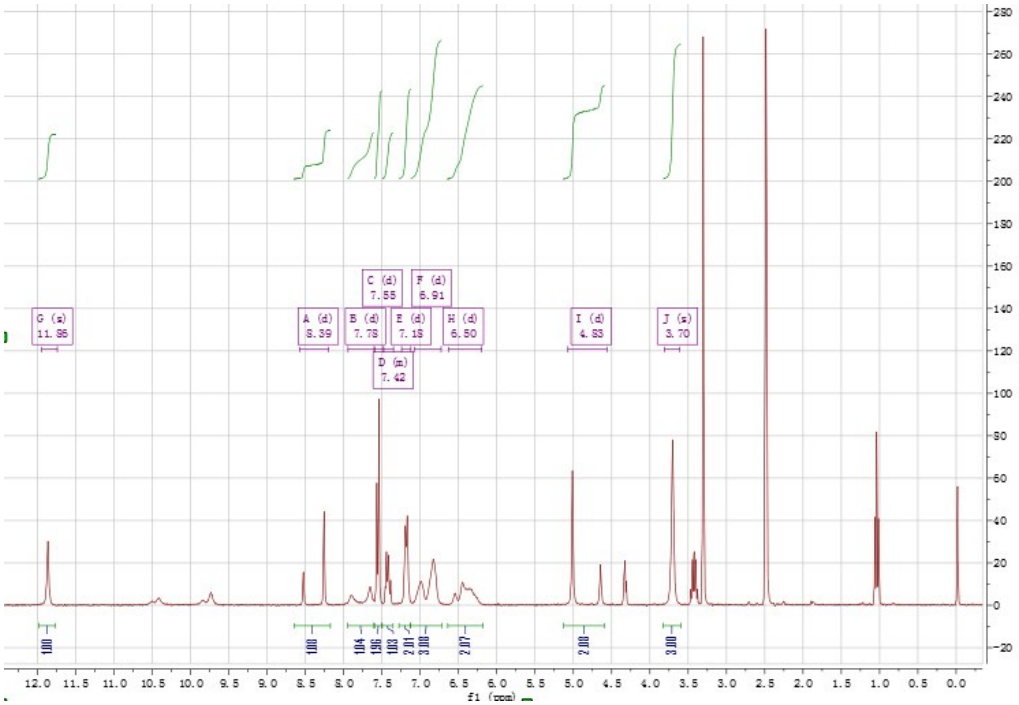
^{1}H NMR spectrum of **4g**



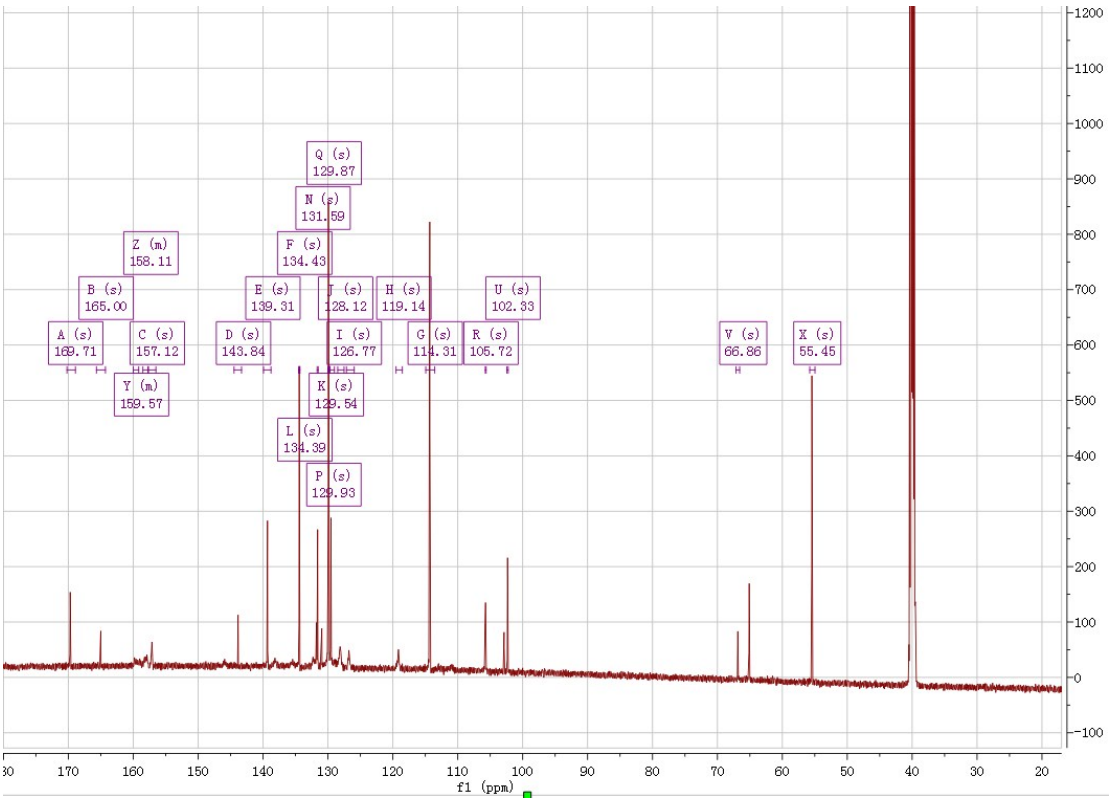
^{1}H NMR spectrum of **4h**



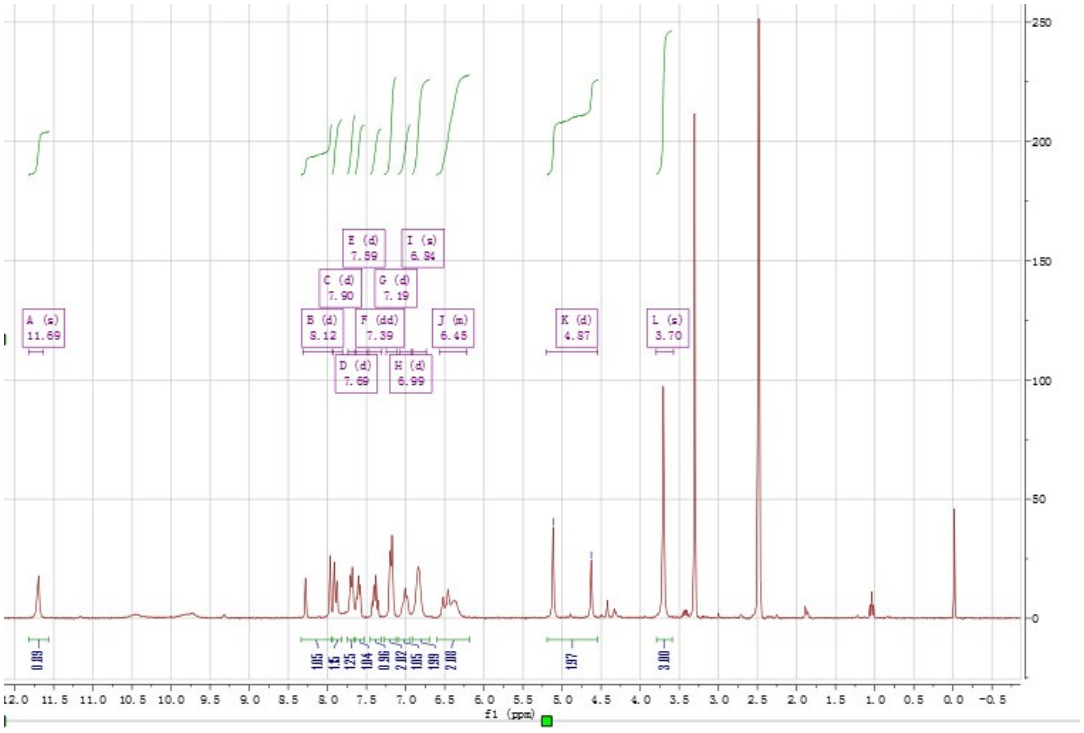
^{1}H NMR spectrum of **4i**



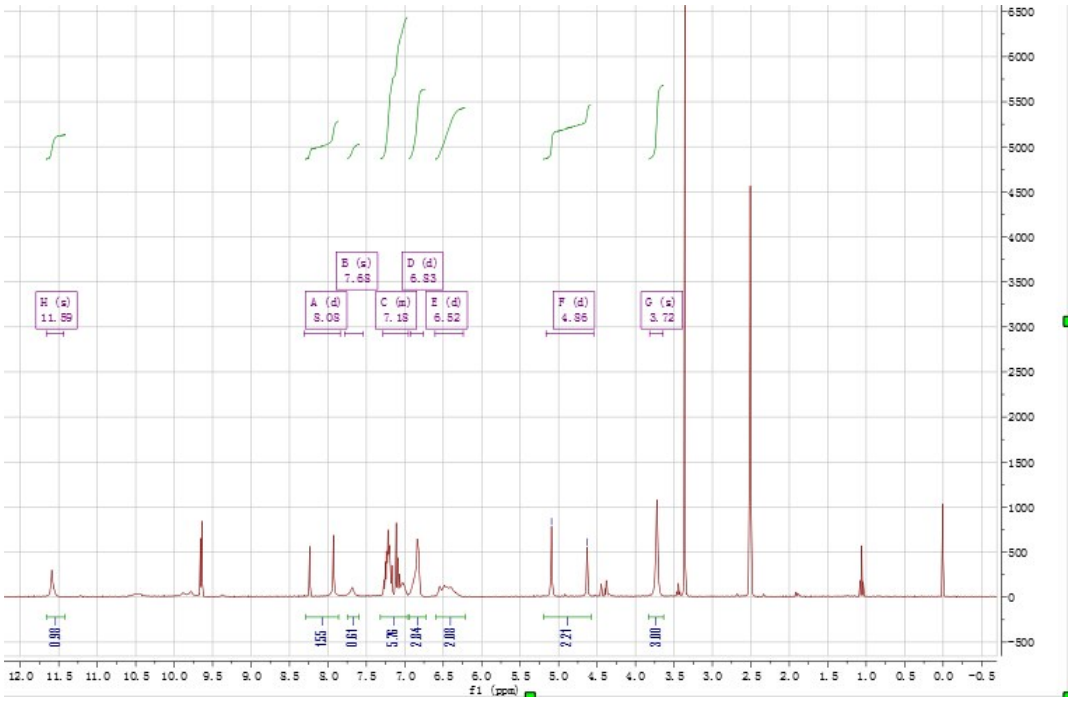
^{1}H NMR spectrum of **4j**



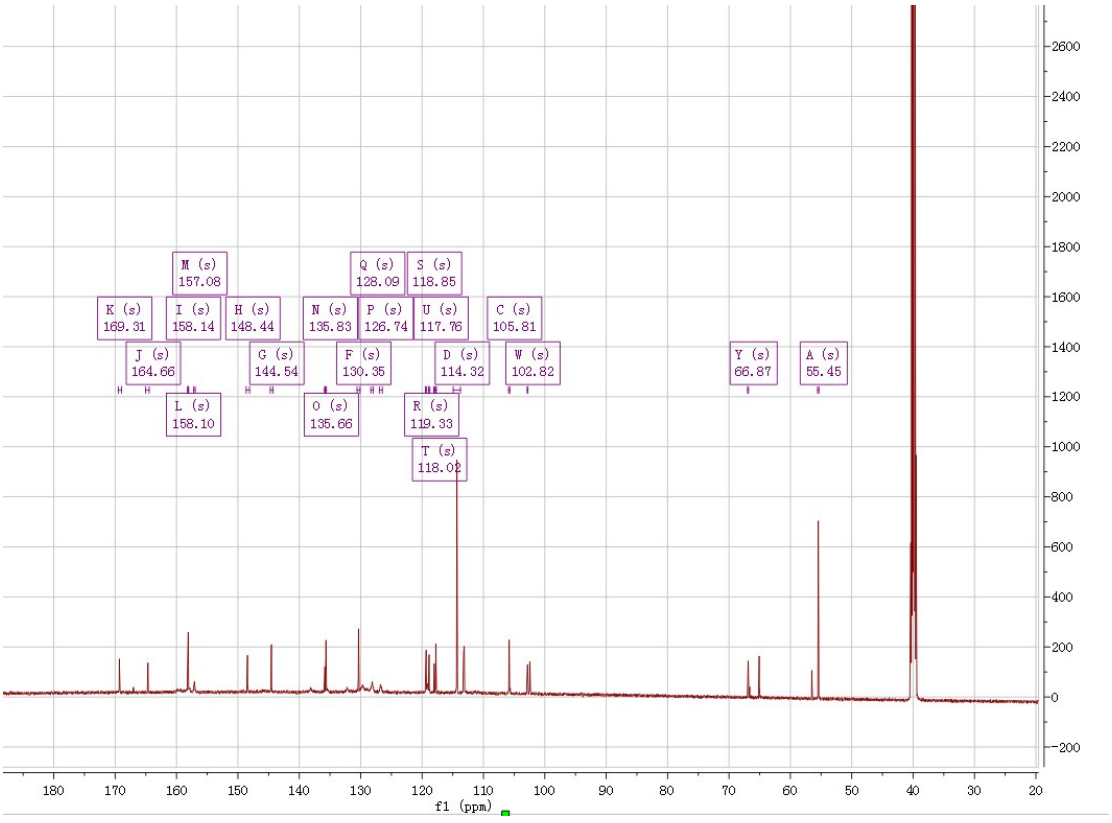
^{13}C NMR spectrum of **4j**



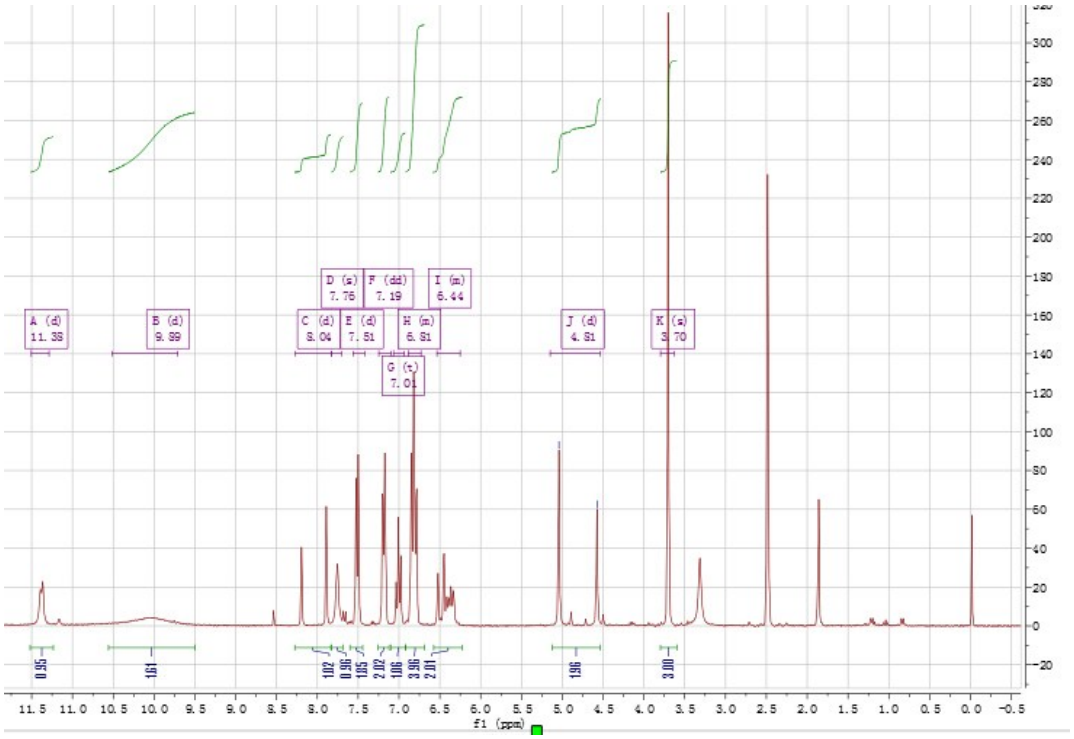
^{1}H NMR spectrum of **4k**



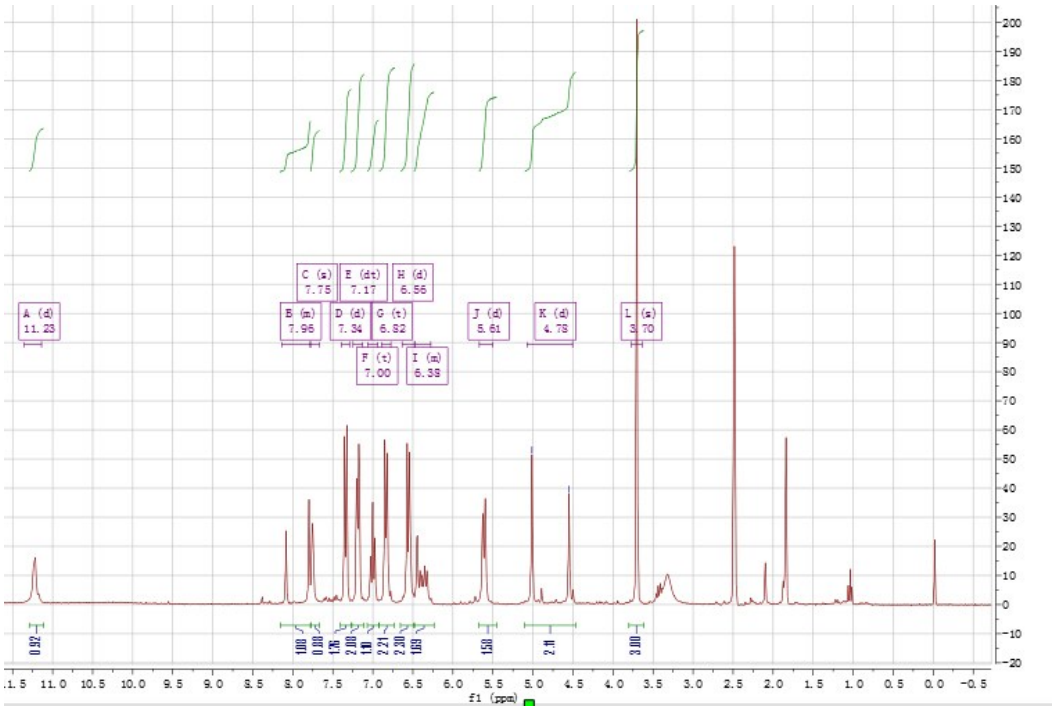
^{1}H NMR spectrum of **4l**



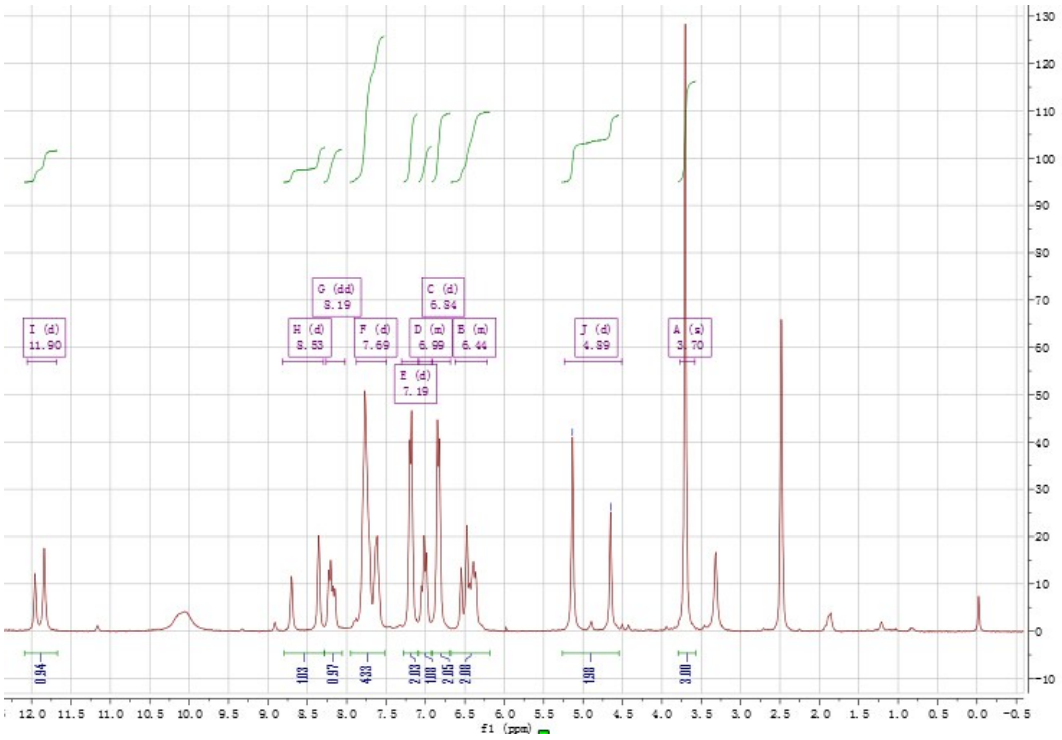
^{13}C NMR spectrum of **4l**



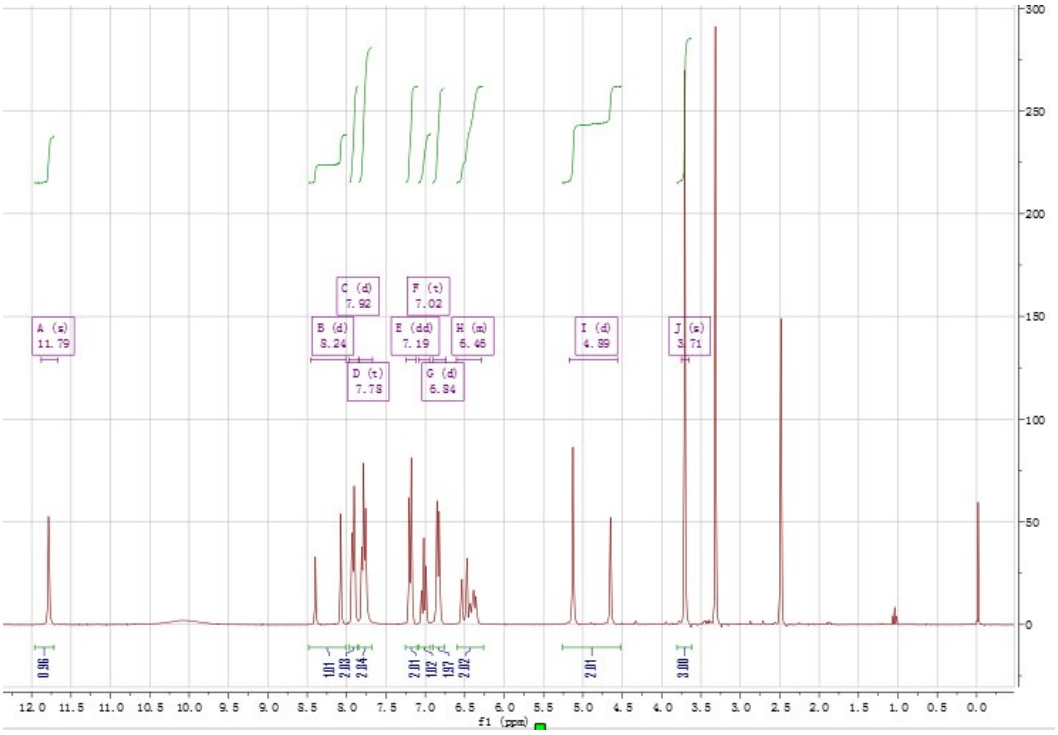
^{1}H NMR spectrum of **4m**



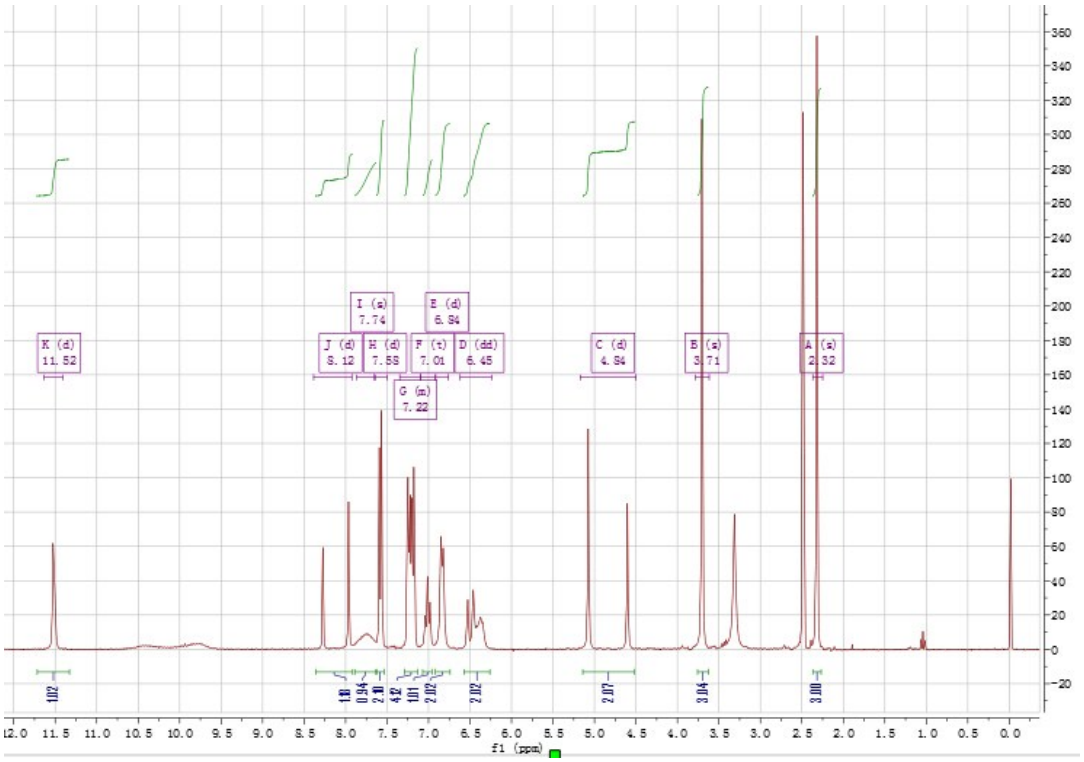
^{1}H NMR spectrum of **4n**



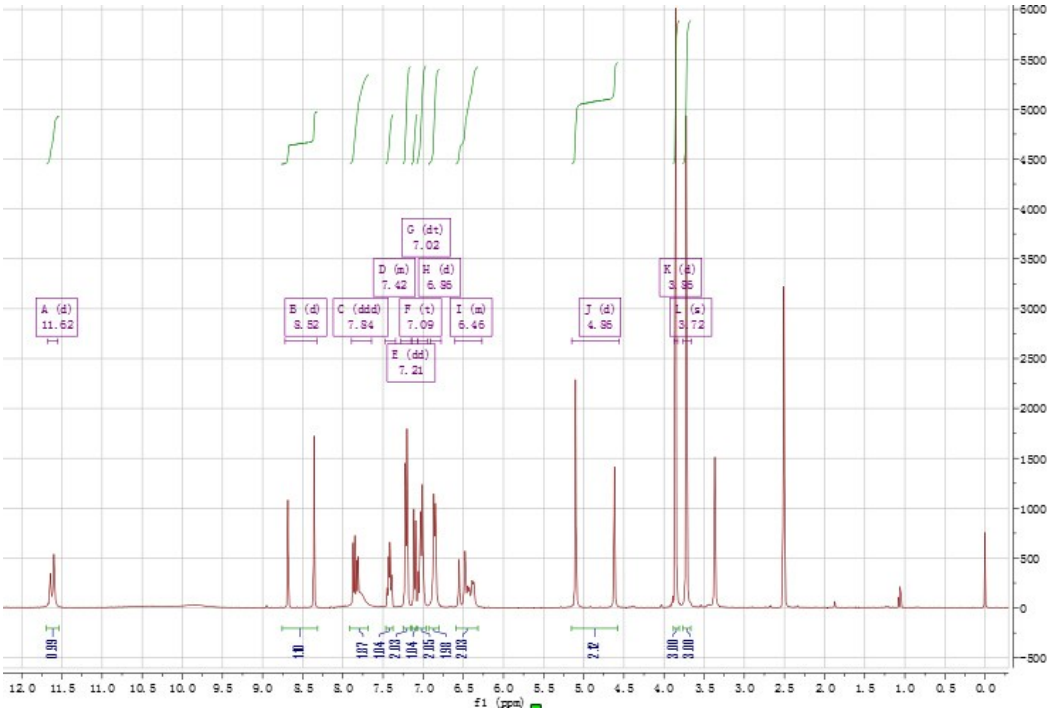
^{1}H NMR spectrum of **4o**



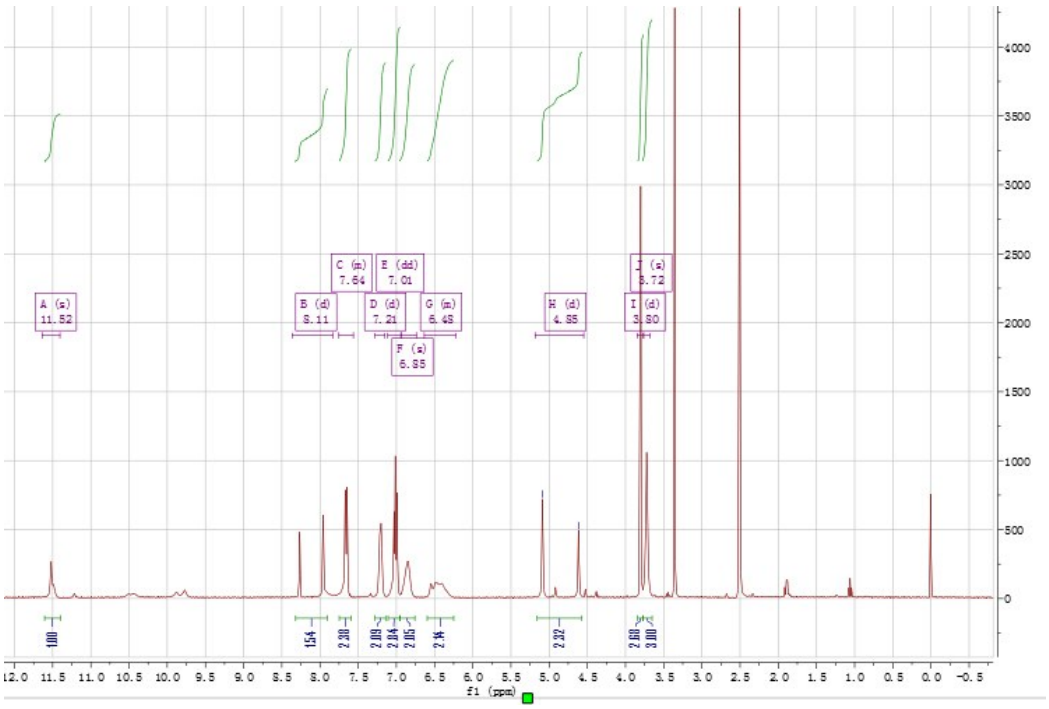
^{1}H NMR spectrum of **4p**



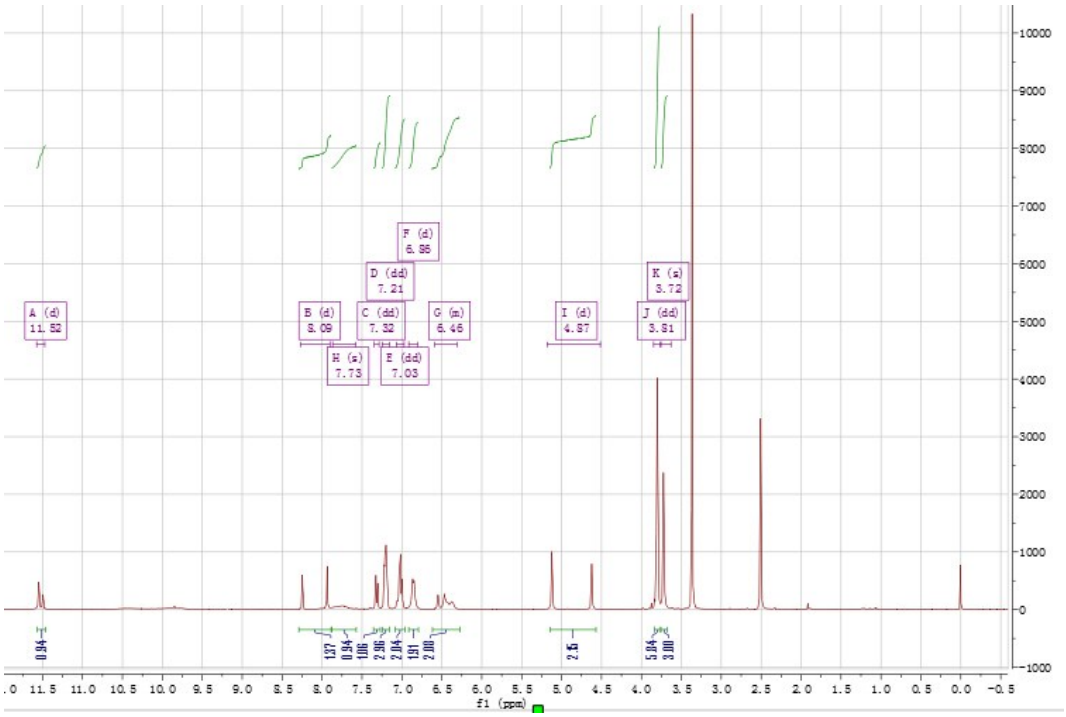
^{1}H NMR spectrum of **4q**



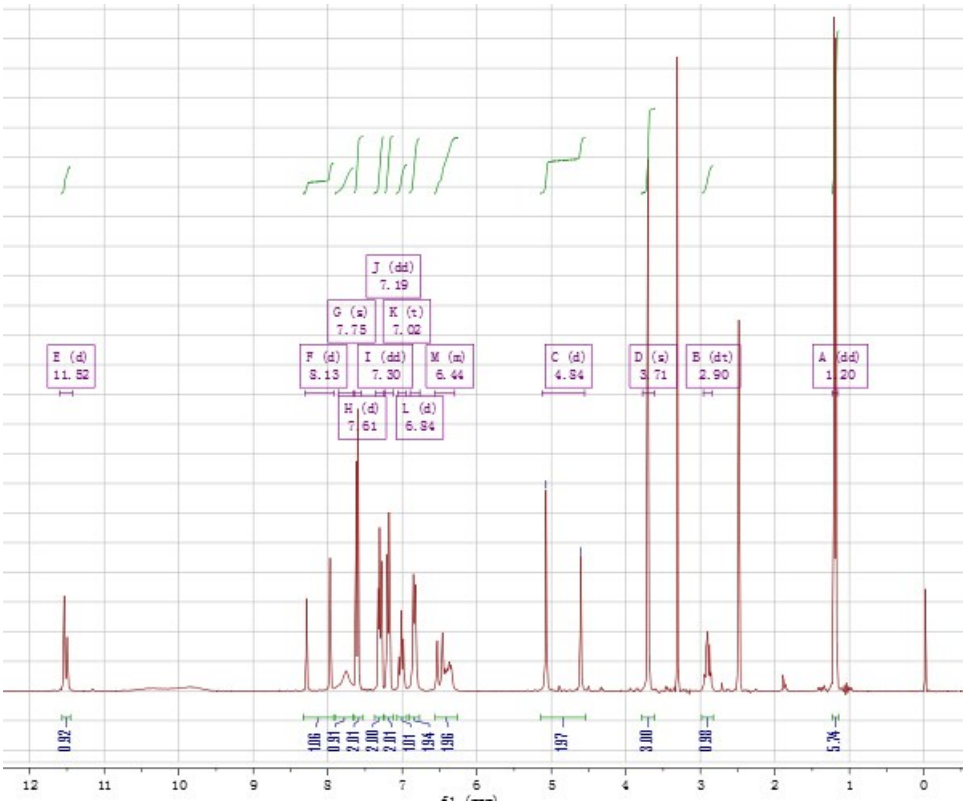
^{1}H NMR spectrum of **4r**



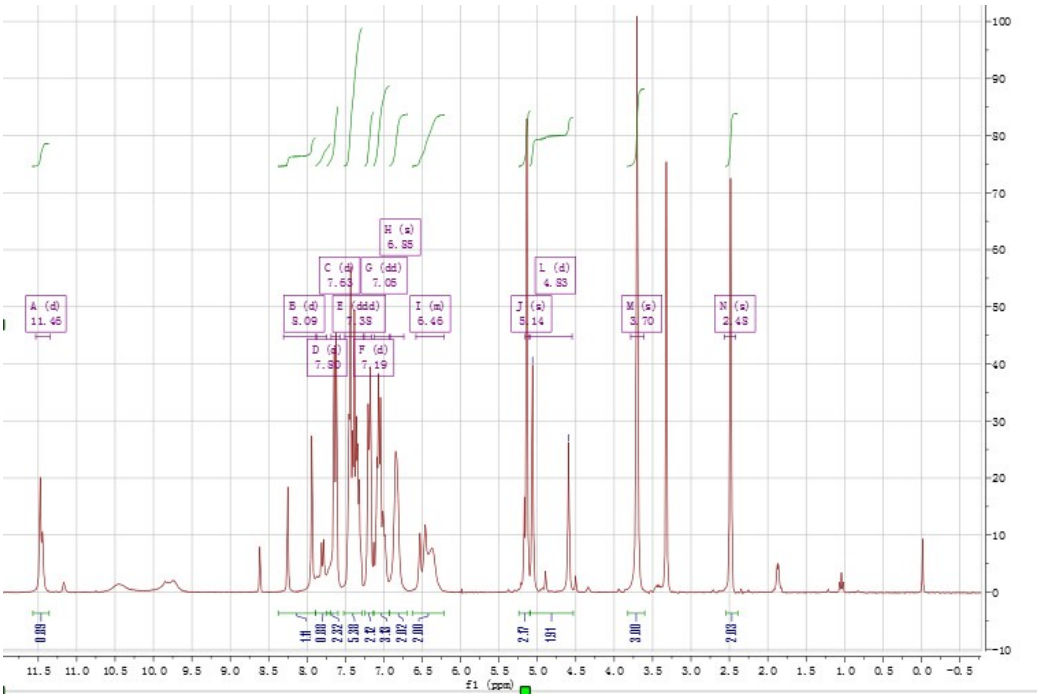
^{1}H NMR spectrum of **4s**



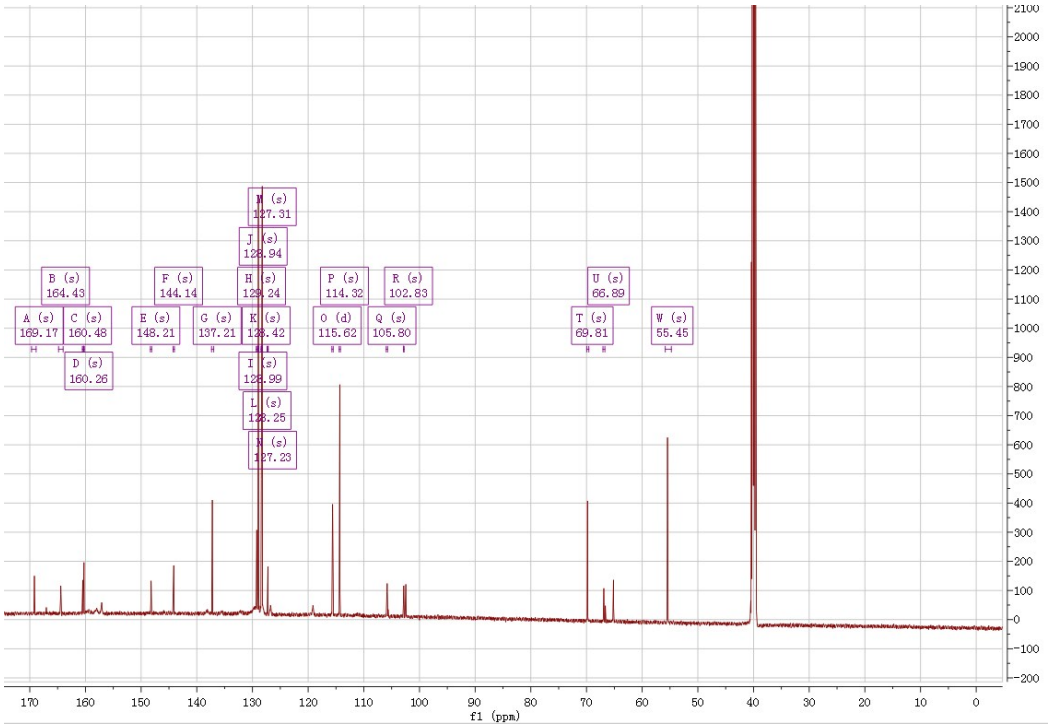
^{1}H NMR spectrum of **4t**



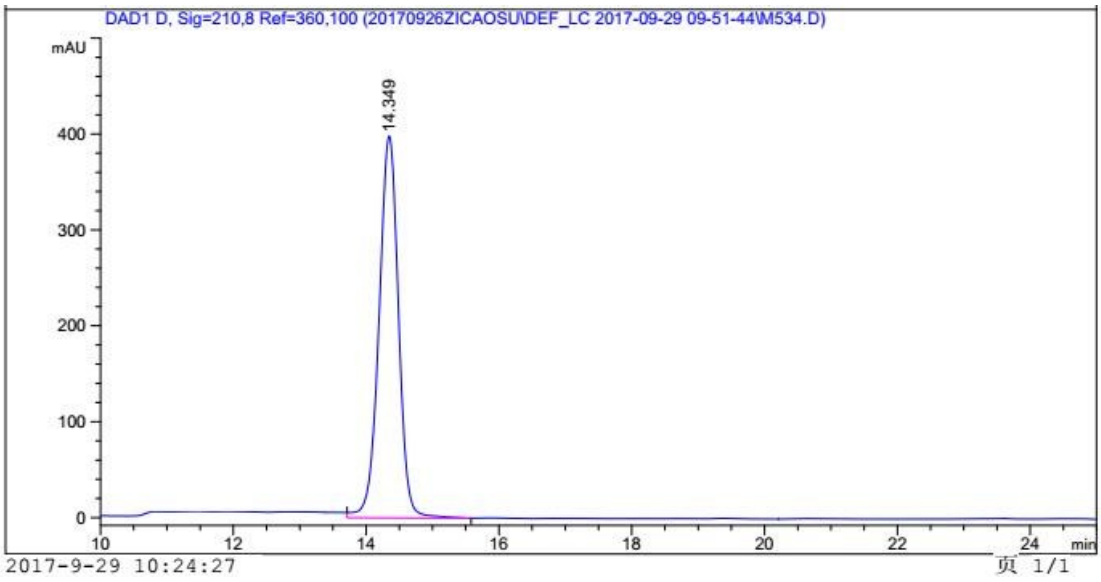
^{1}H NMR spectrum of **4u**



^{1}H NMR spectrum of **4v**



^{13}C NMR spectrum of **4v**



HPLC spectrum of **4v**

Flow rate: 1mL/min, Mobile phase: 50% ACN and 50% 0.1%TFA, Rt=14.349min, Column temperature: 30°C, Column model: Thermo Hypersil Gold 250mm × 4.6mm × 5μm