

Supporting Information

Synthesis, Molecular Docking Analysis and Biological Evaluations of Saccharide-modified Thiadiazole Sulfonamide Derivatives

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^1H -NMR and ^{13}C -NMR Spectra

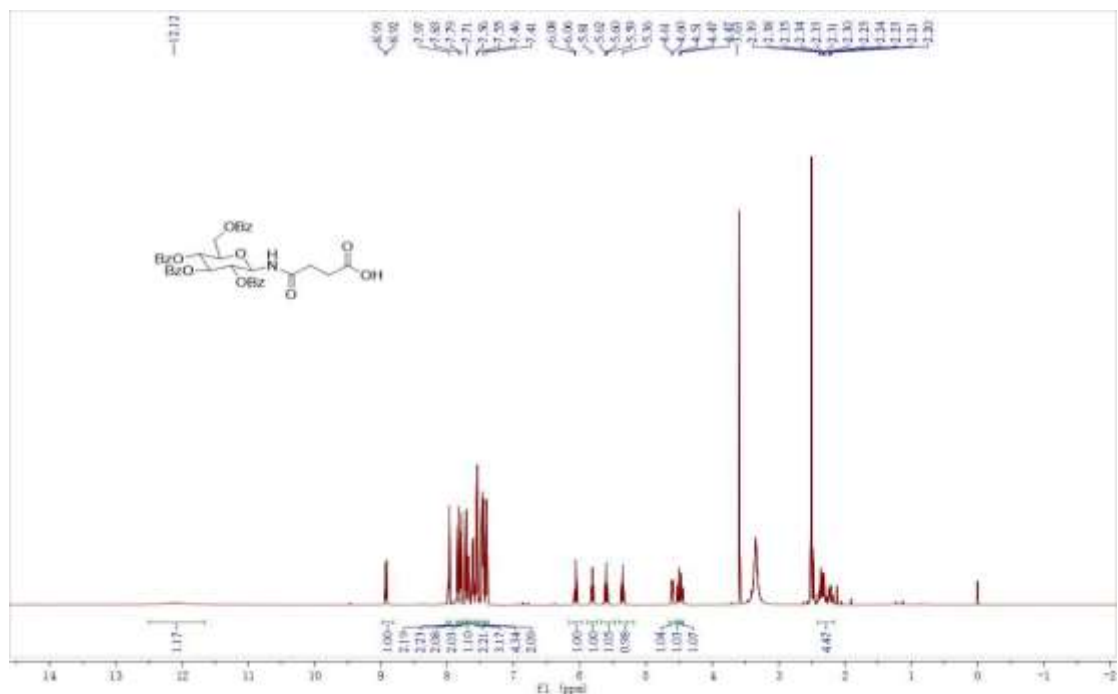


Figure S1. The ^1H -NMR of intermediate 5a.

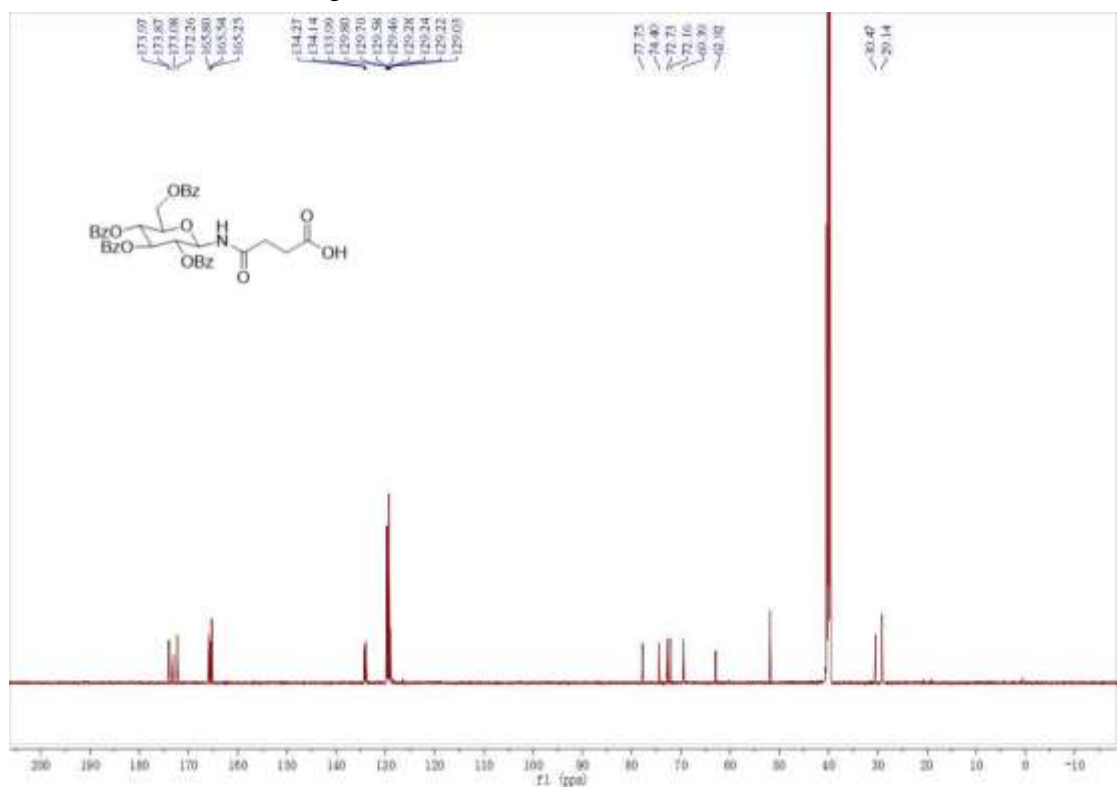


Figure S2. The ^{13}C -NMR of intermediate 5a.

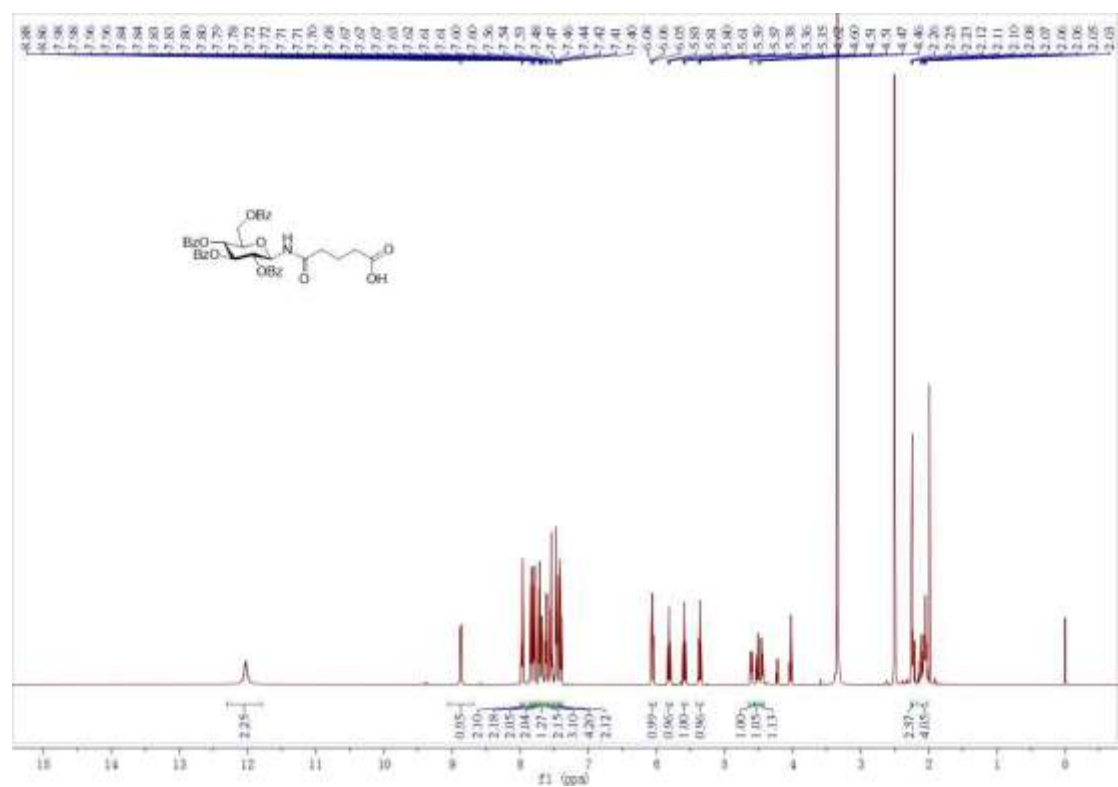


Figure S3. The ¹H-NMR of intermediate 5b.

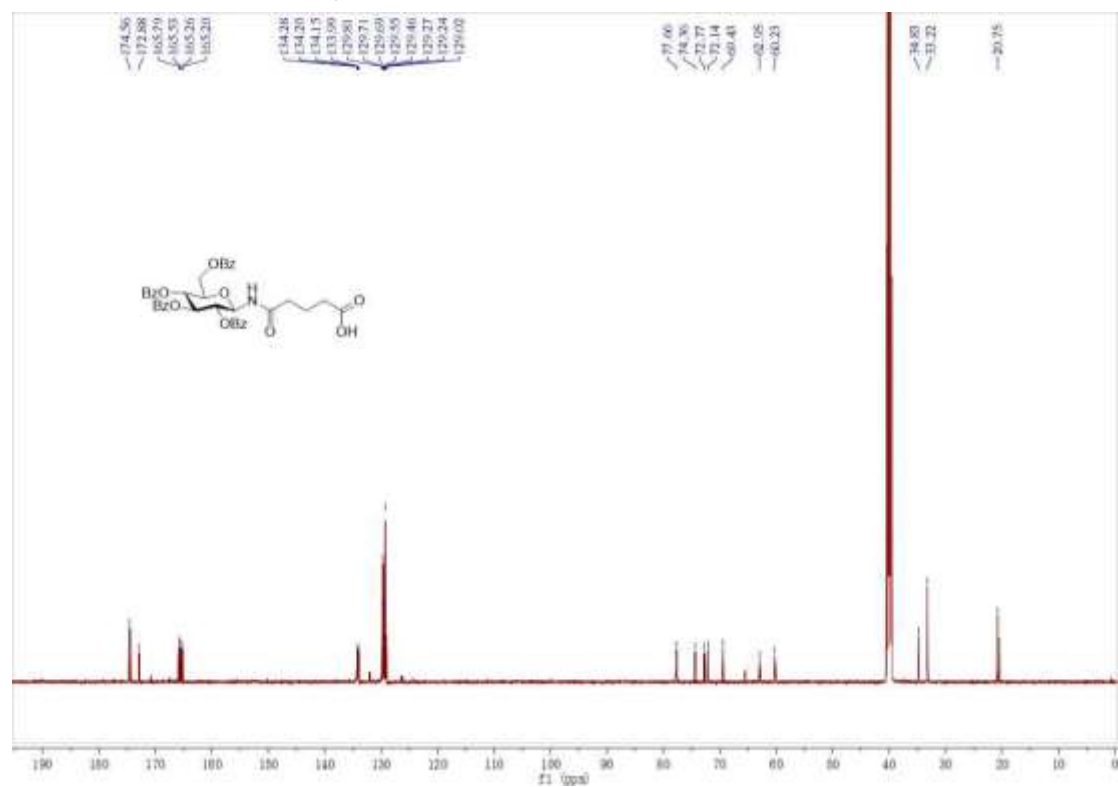


Figure 4. The ¹³C-NMR of intermediate 5b.

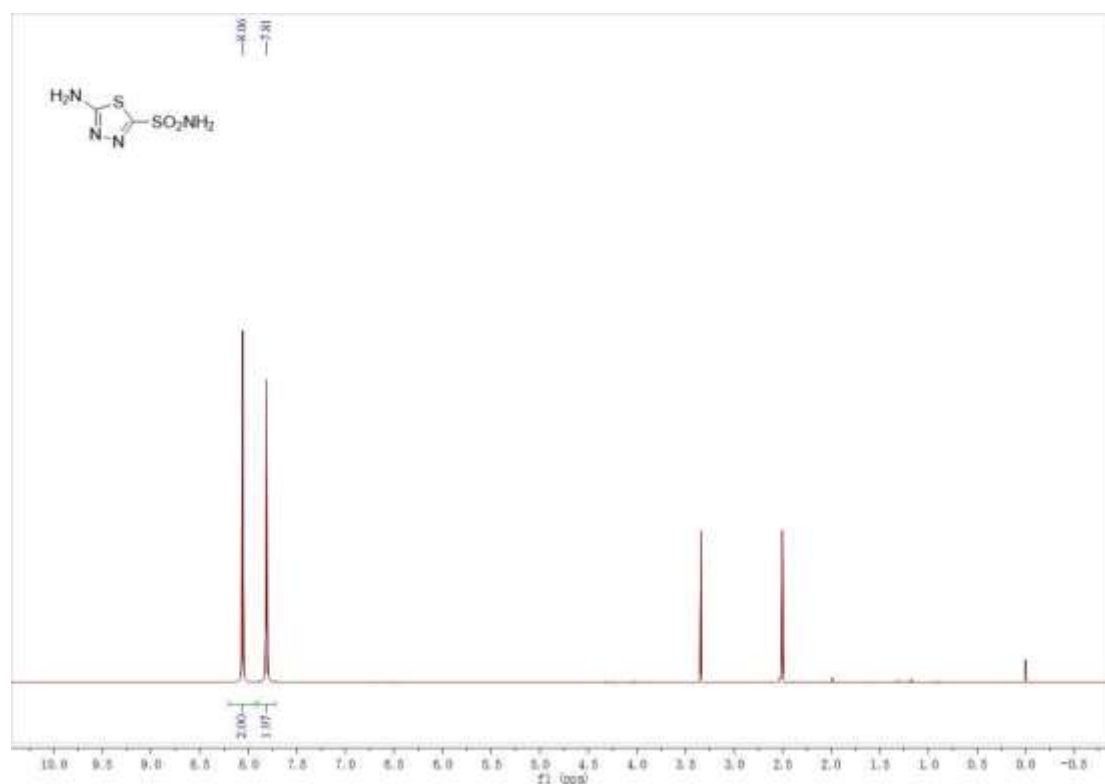


Figure S5. The ^1H -NMR of intermediate 10.

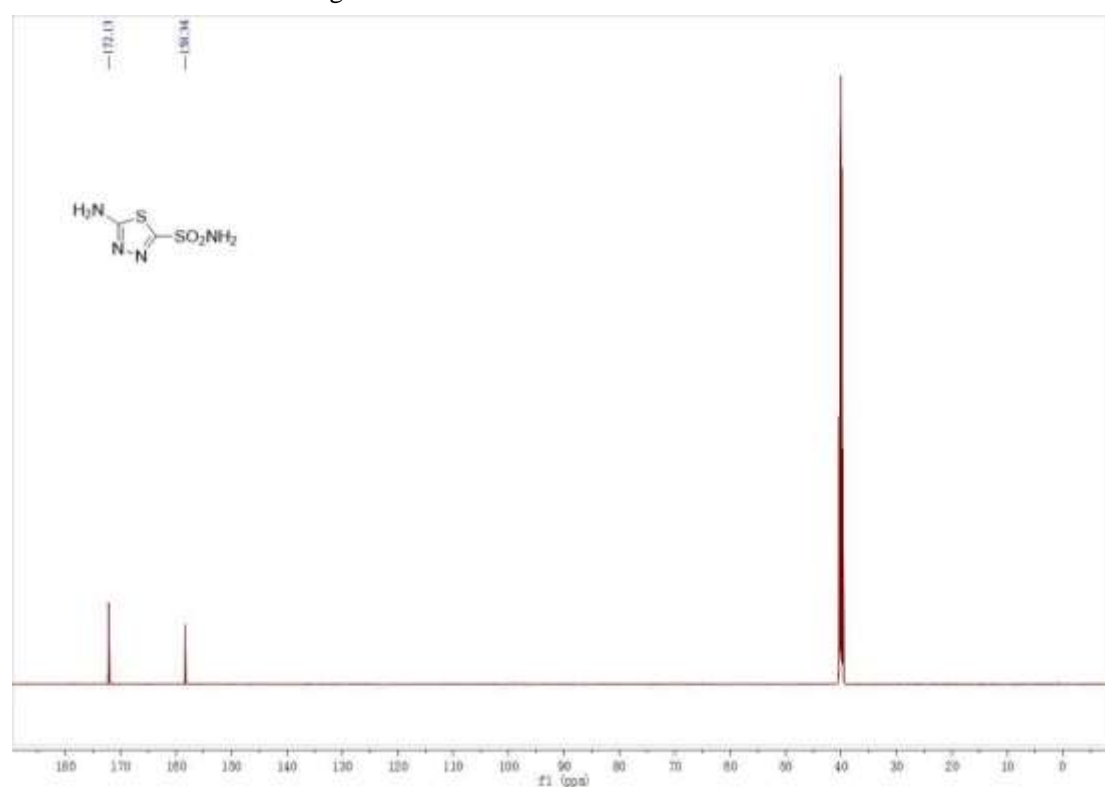


Figure S6. The ^{13}C -NMR of intermediate 10.

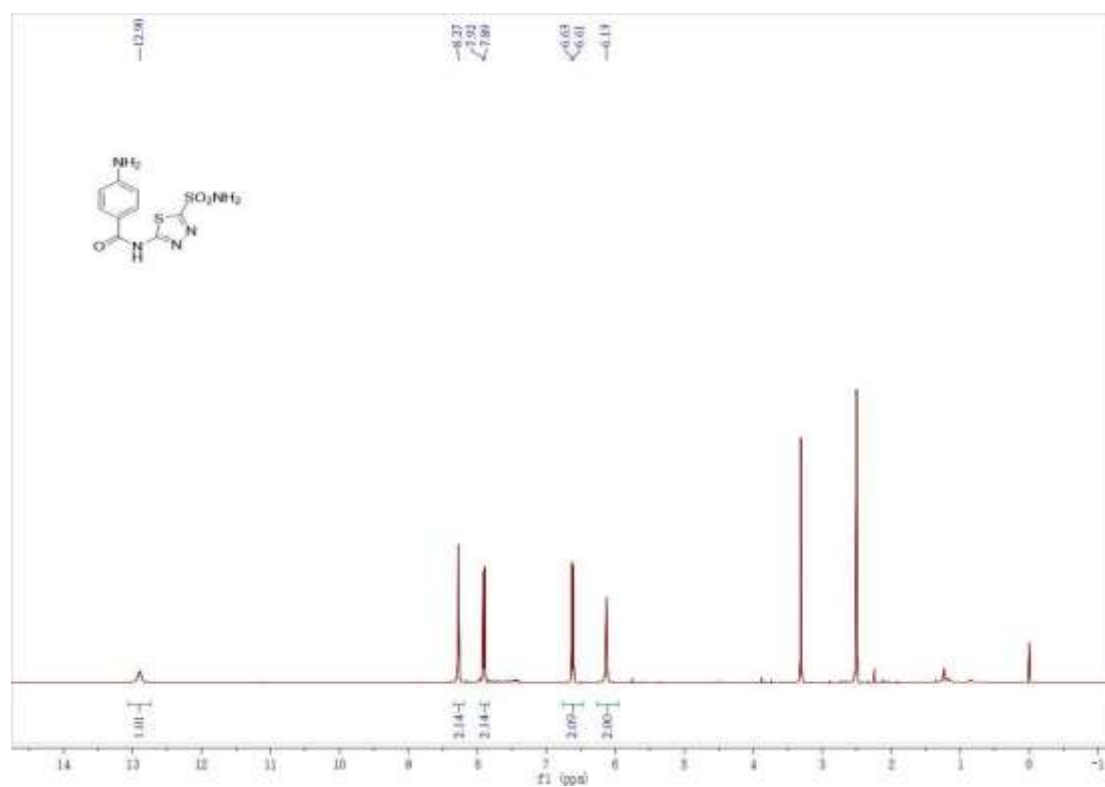


Figure S7. The ¹H-NMR of intermediate 12a.

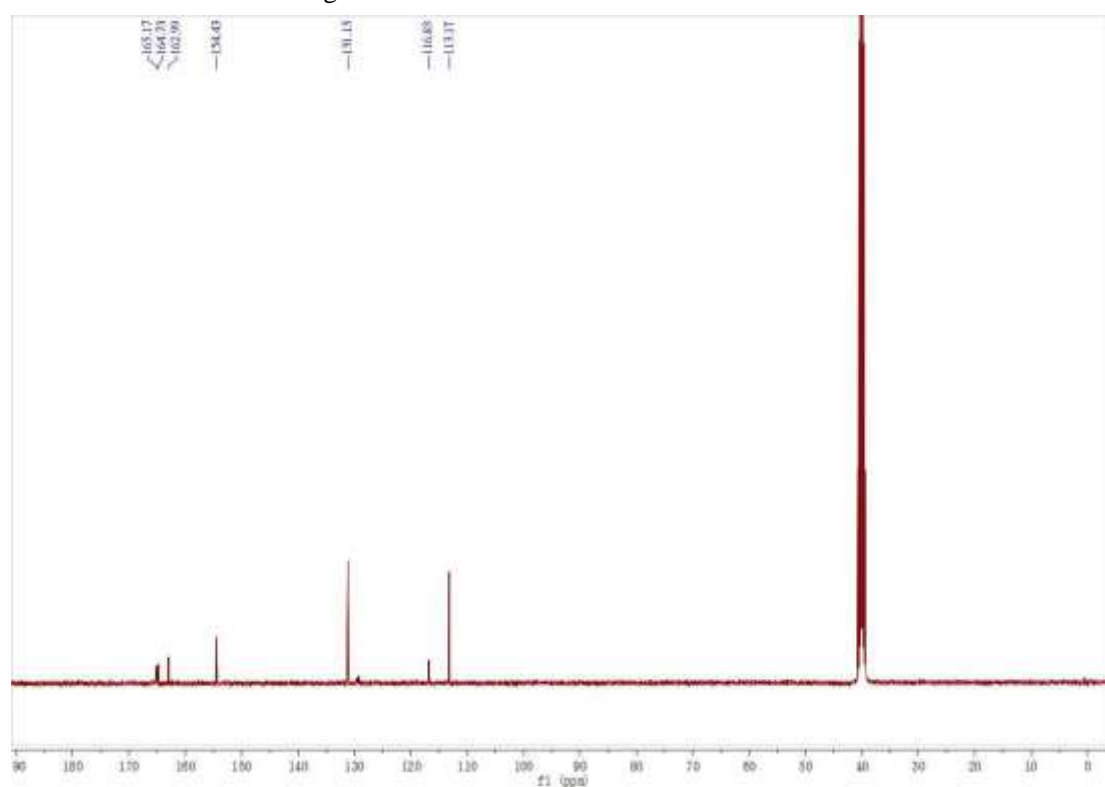
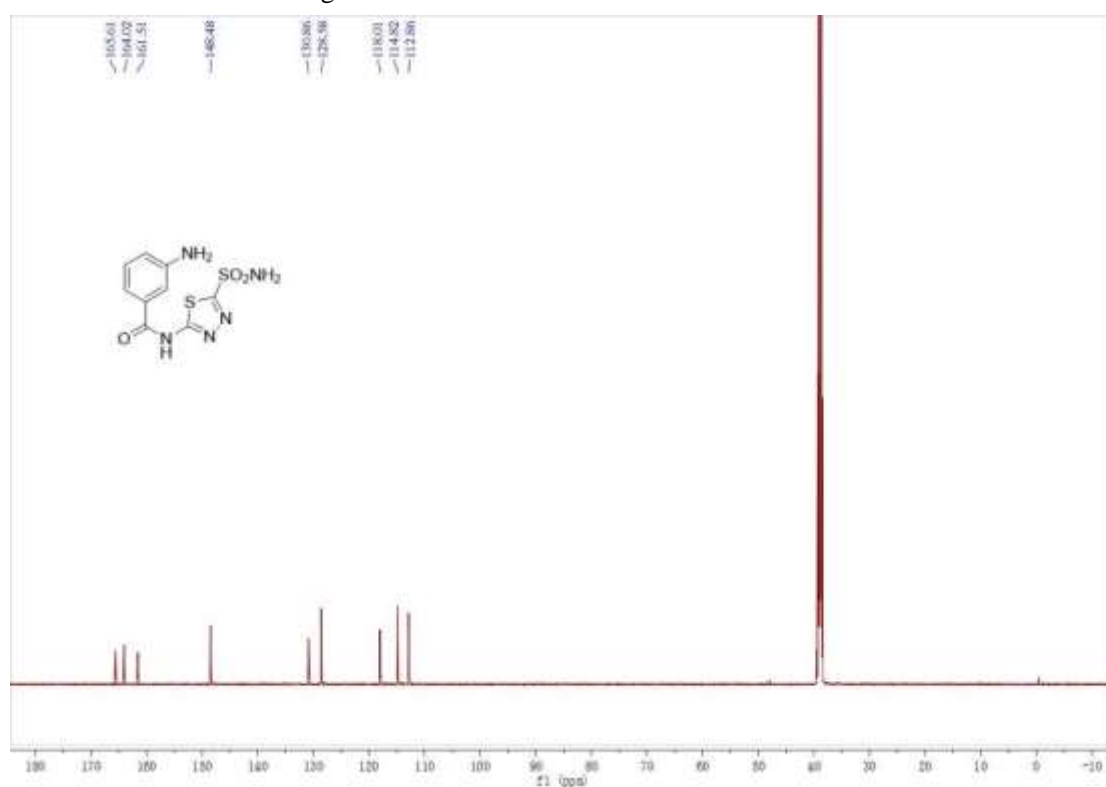
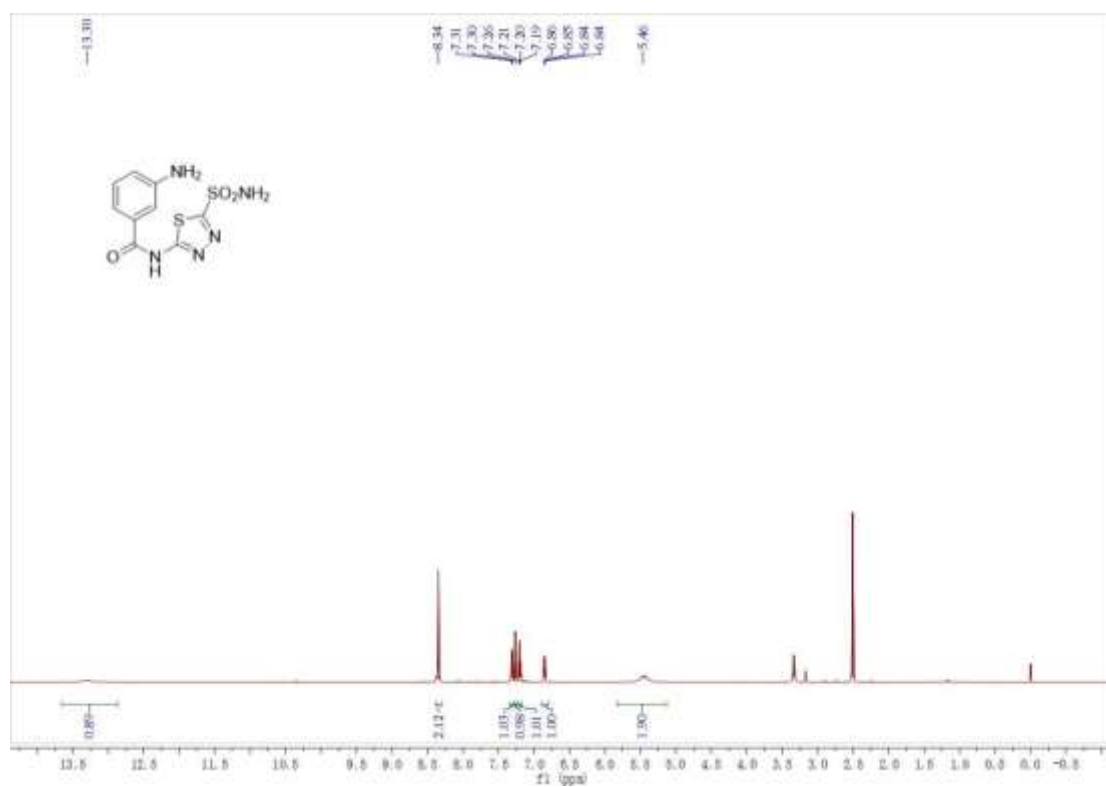
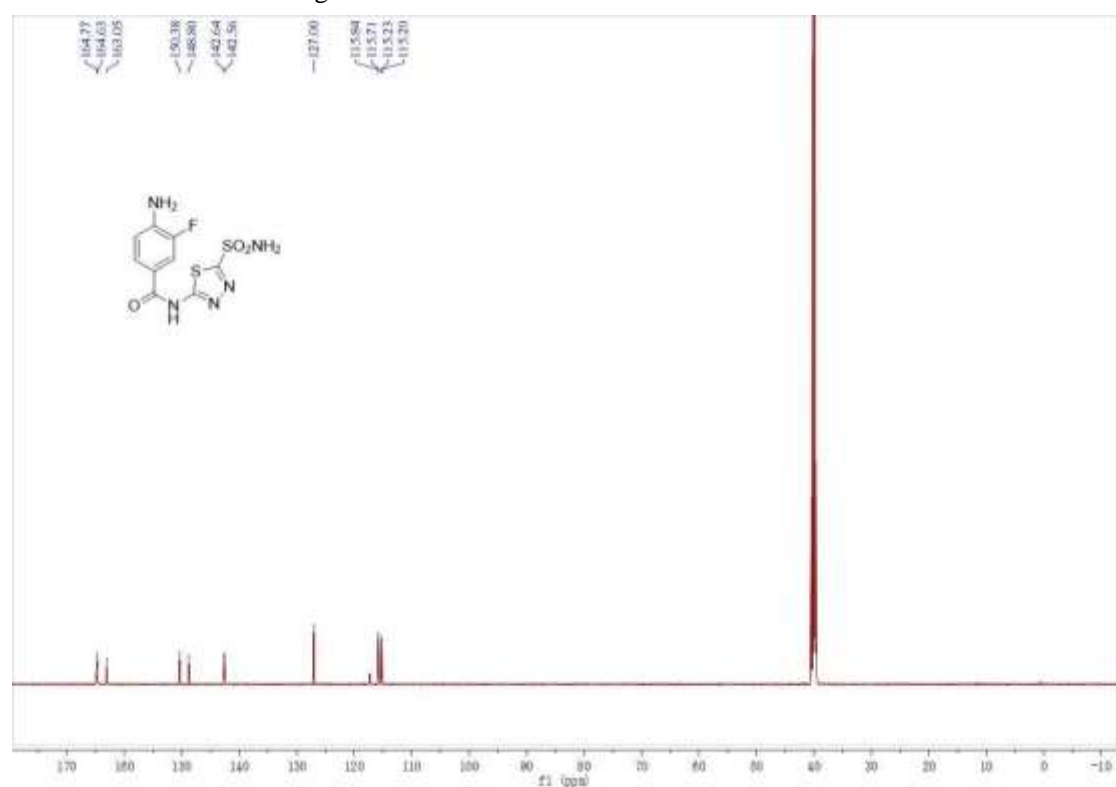
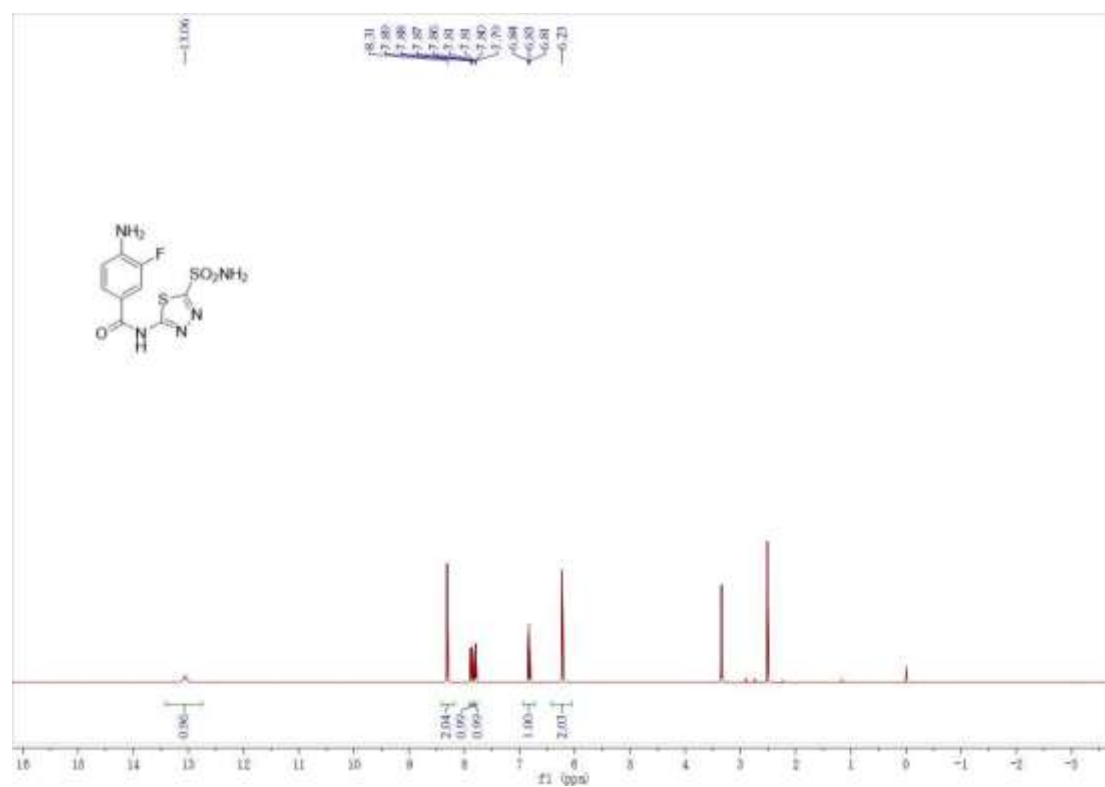


Figure S8. The ¹³C-NMR of intermediate 12a.





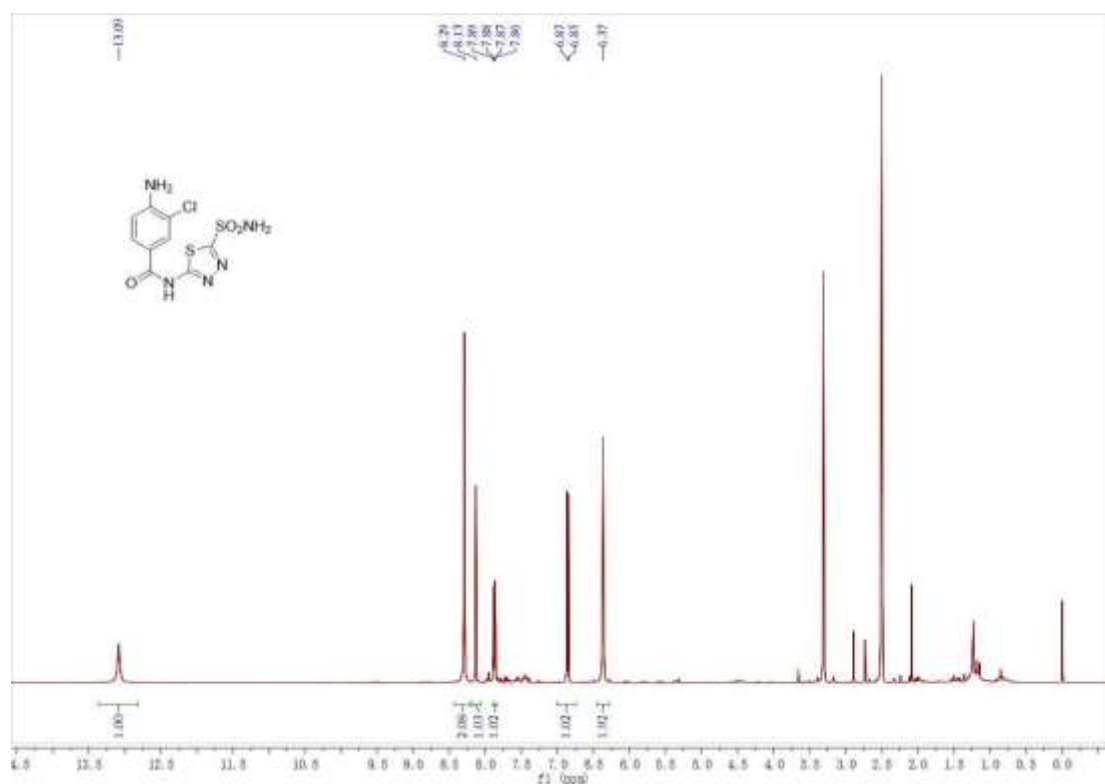


Figure S13. The ¹H-NMR of intermediate 12d.

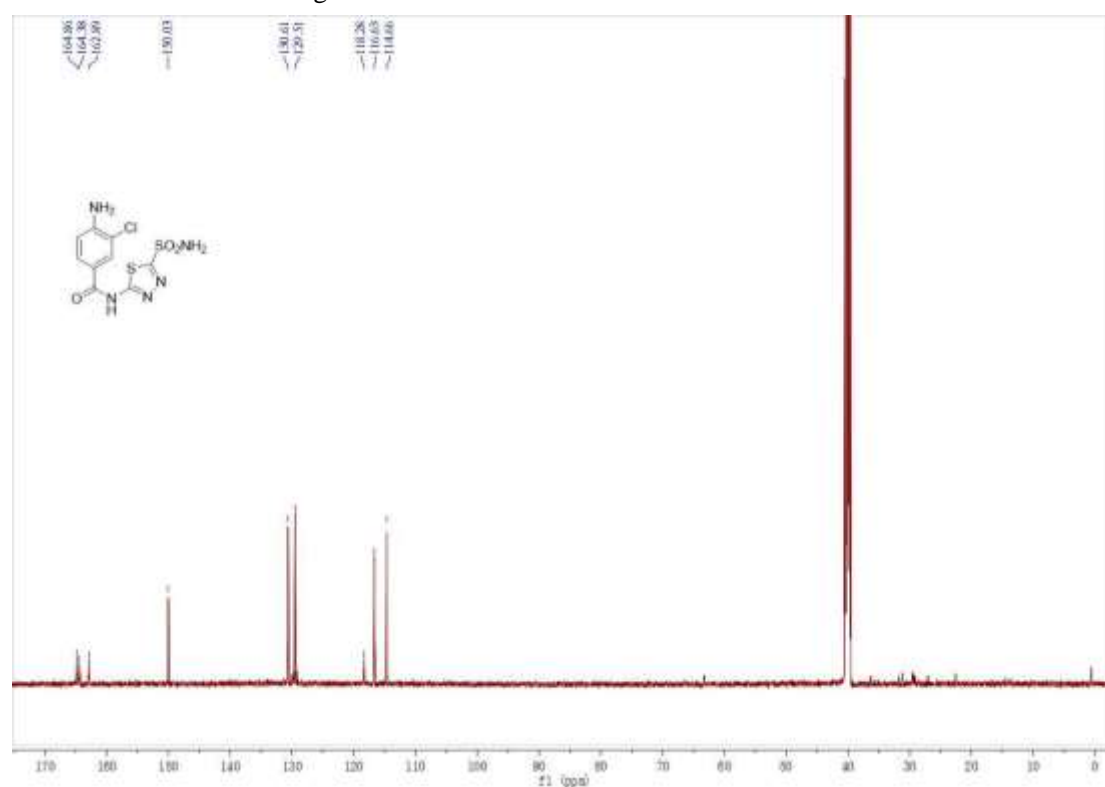


Figure S14. The ¹³C-NMR of intermediate 12d.

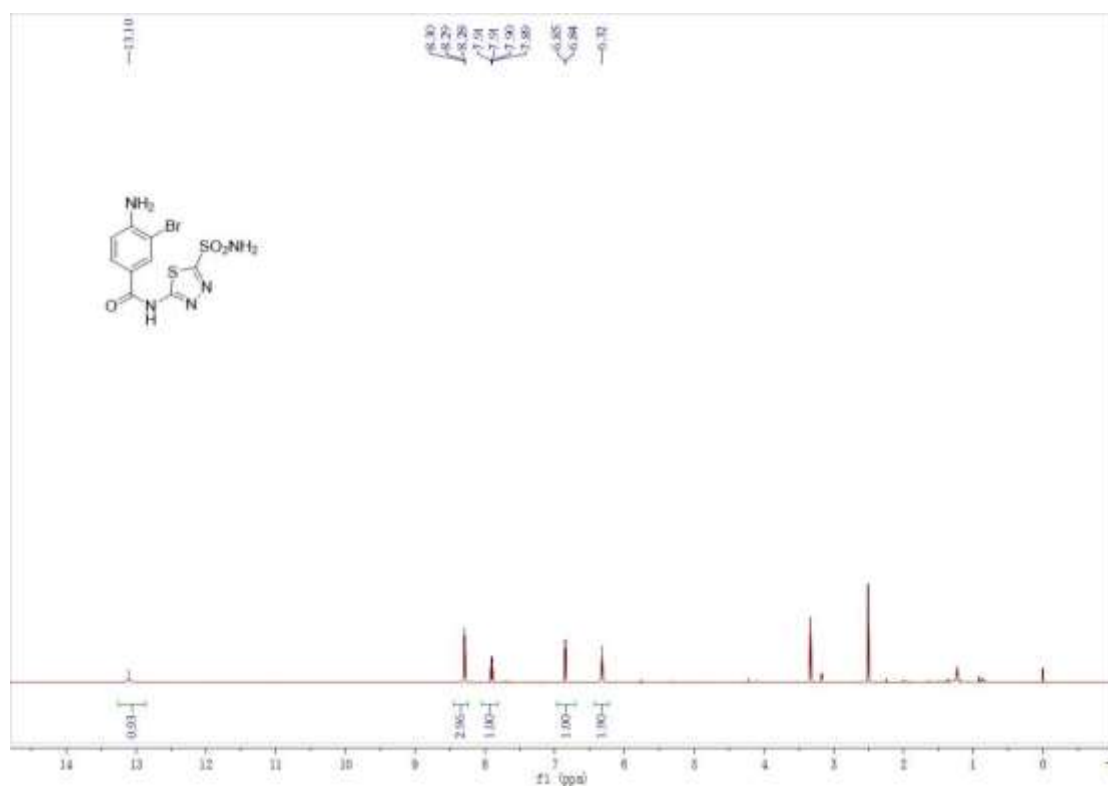


Figure S15. The ¹H-NMR of intermediate 12e.

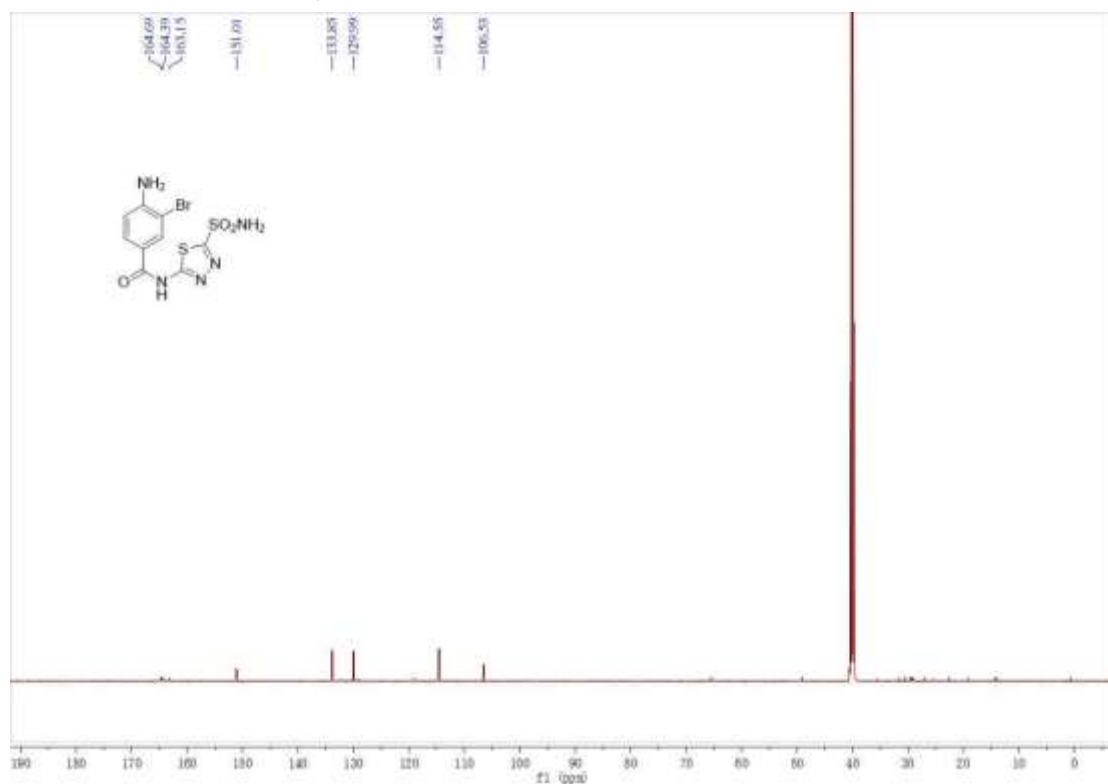


Figure S16. The ¹³C-NMR of intermediate 12e.

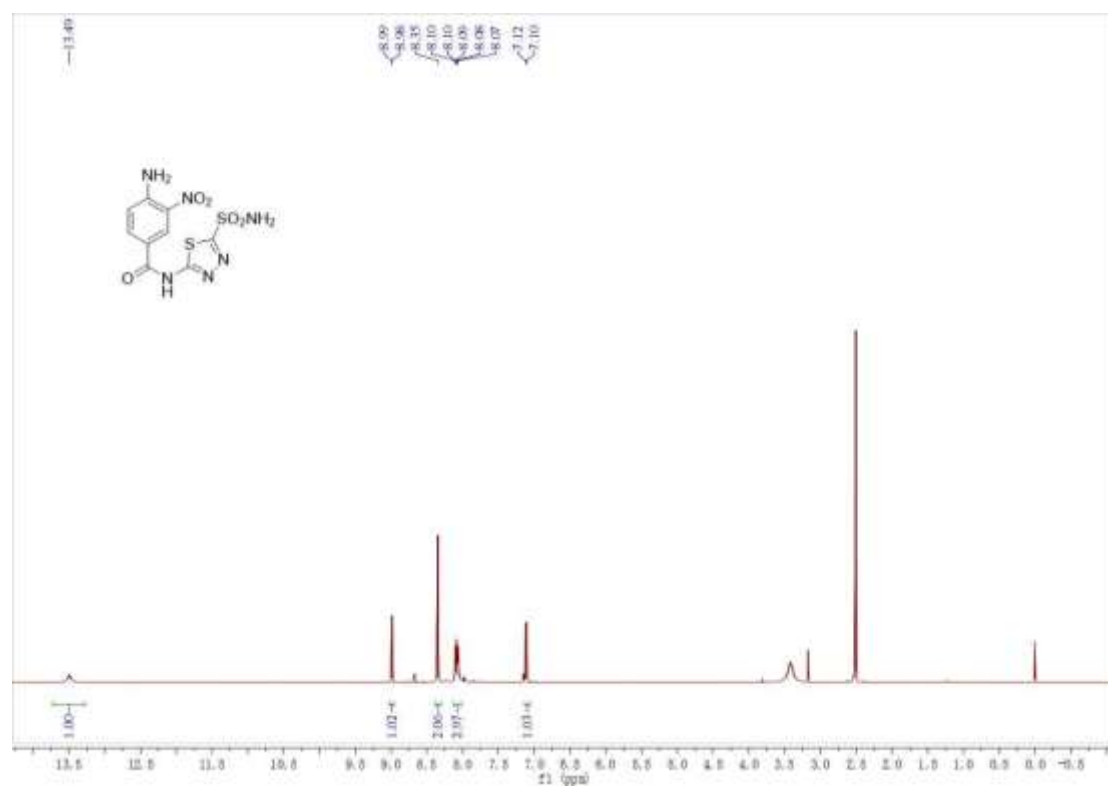


Figure S17. The ¹H-NMR of intermediate 12f.

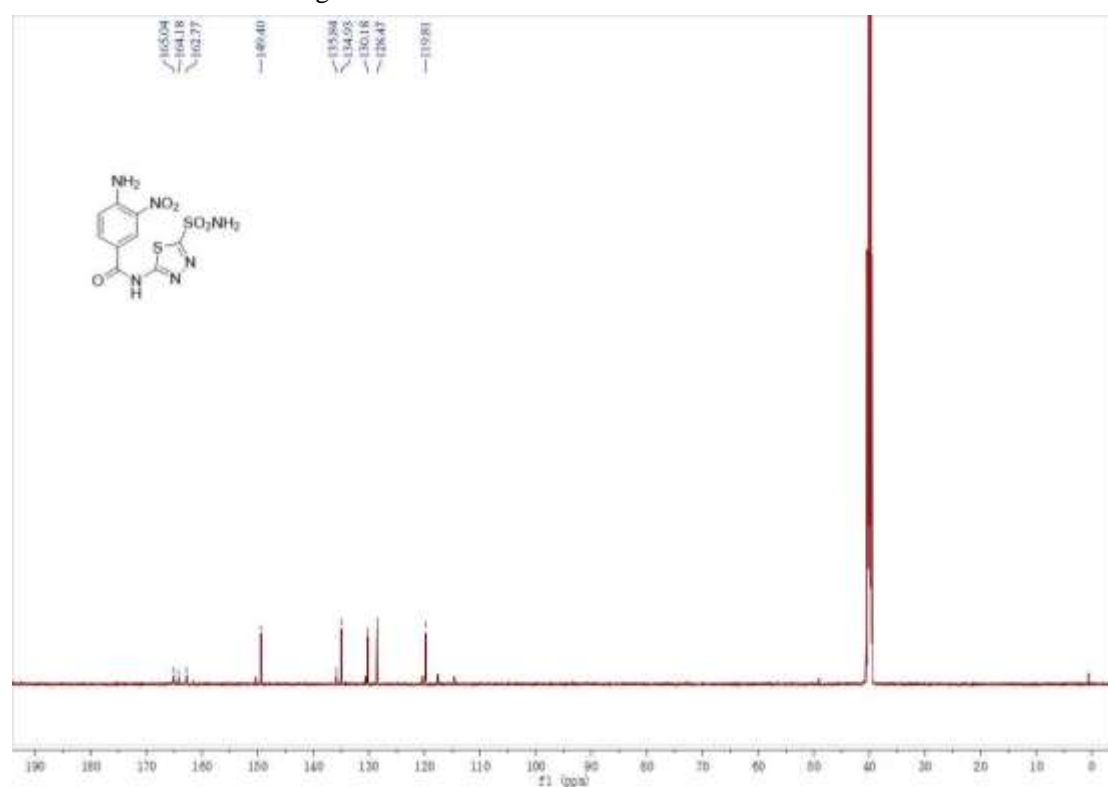
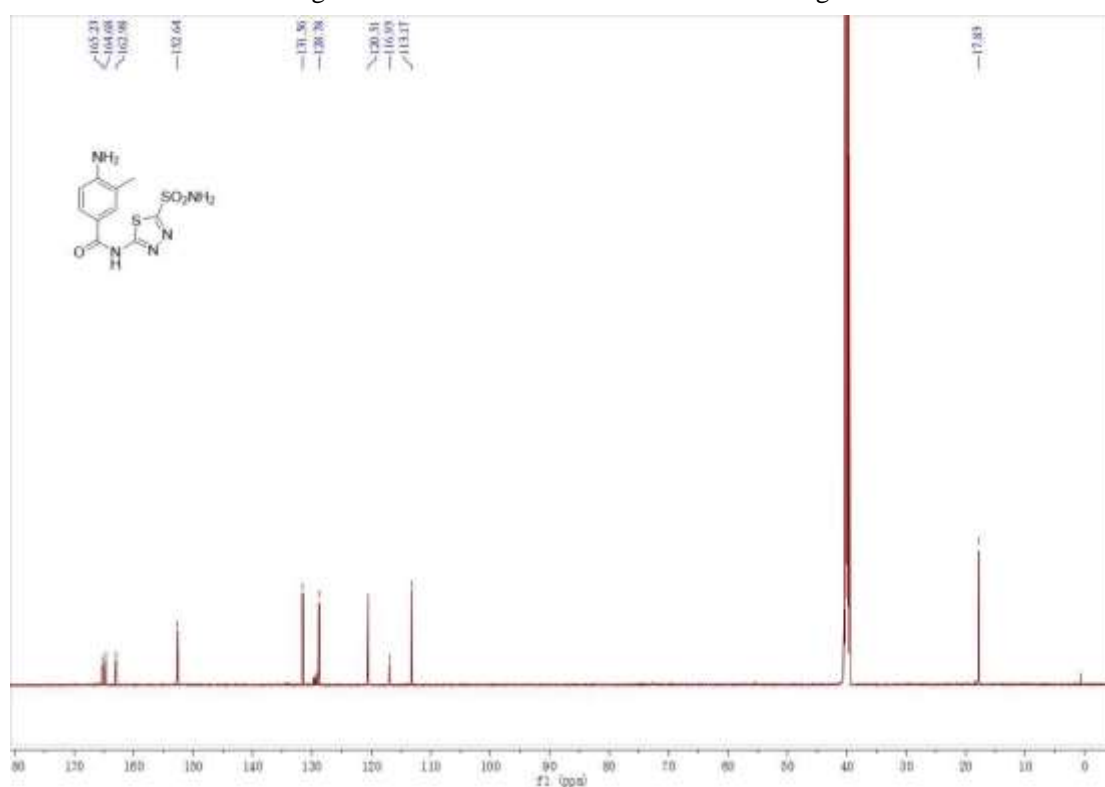
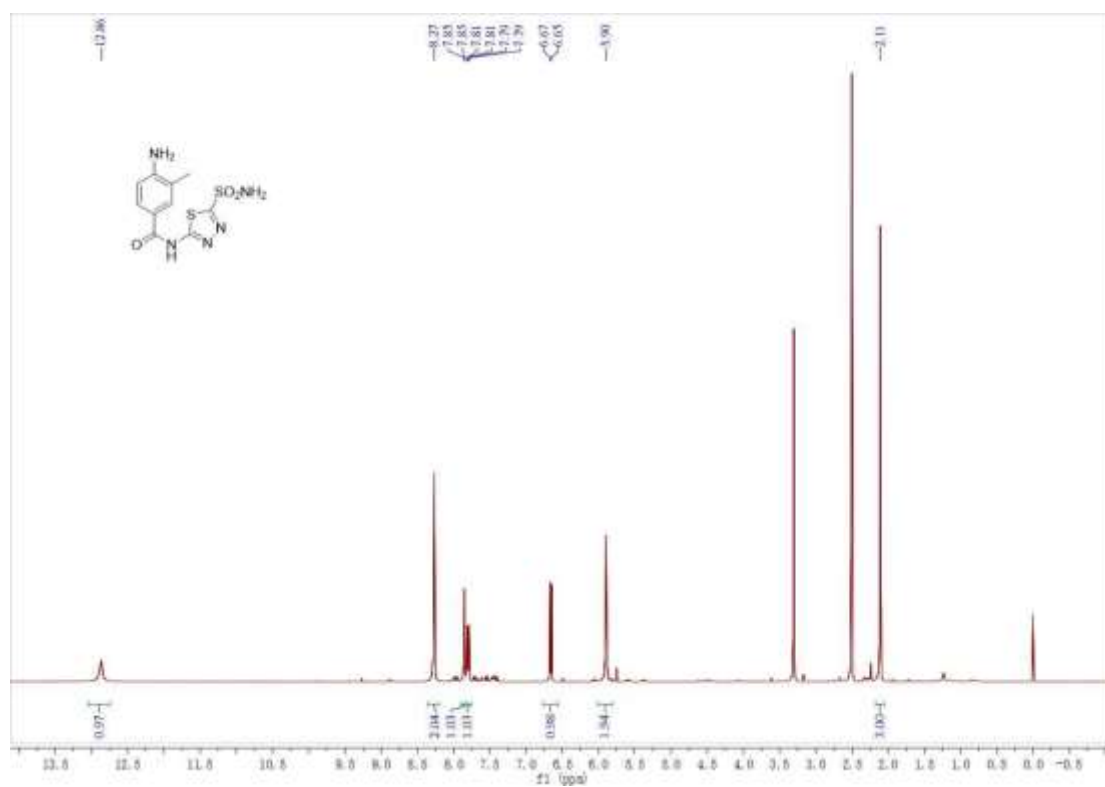


Figure S18. The ¹³C-NMR of intermediate 12f.



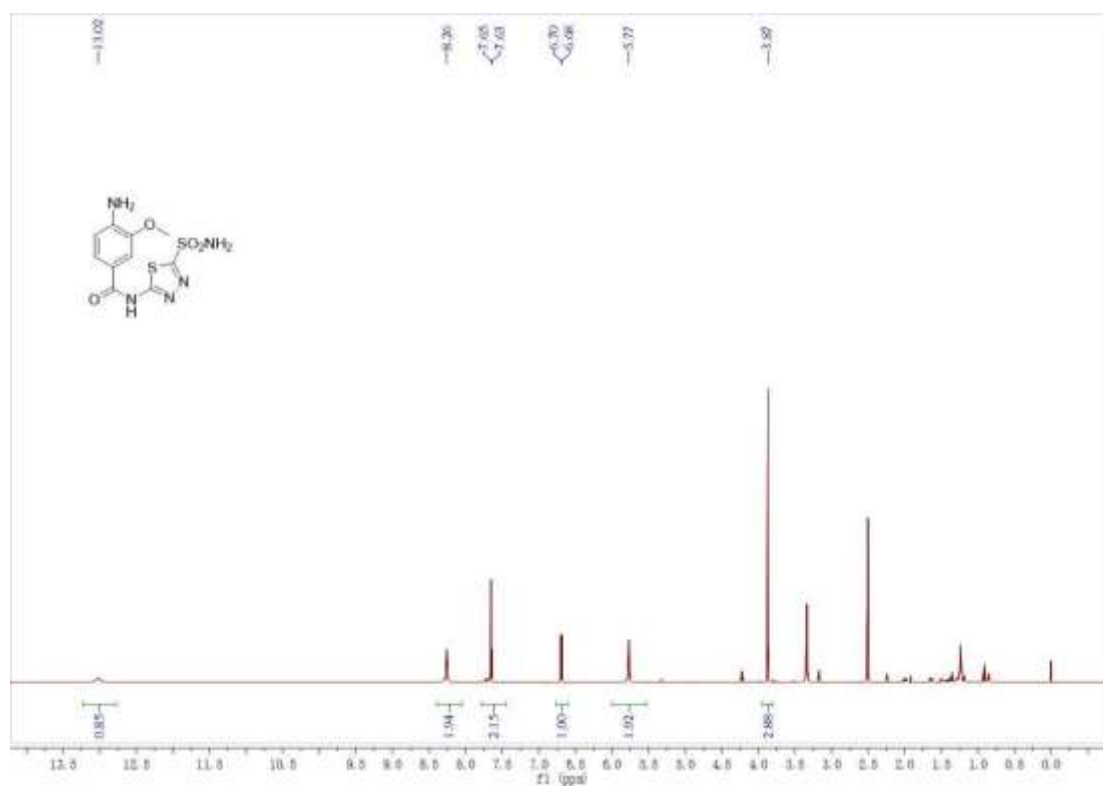


Figure S21. The ¹H-NMR of intermediate 12h.

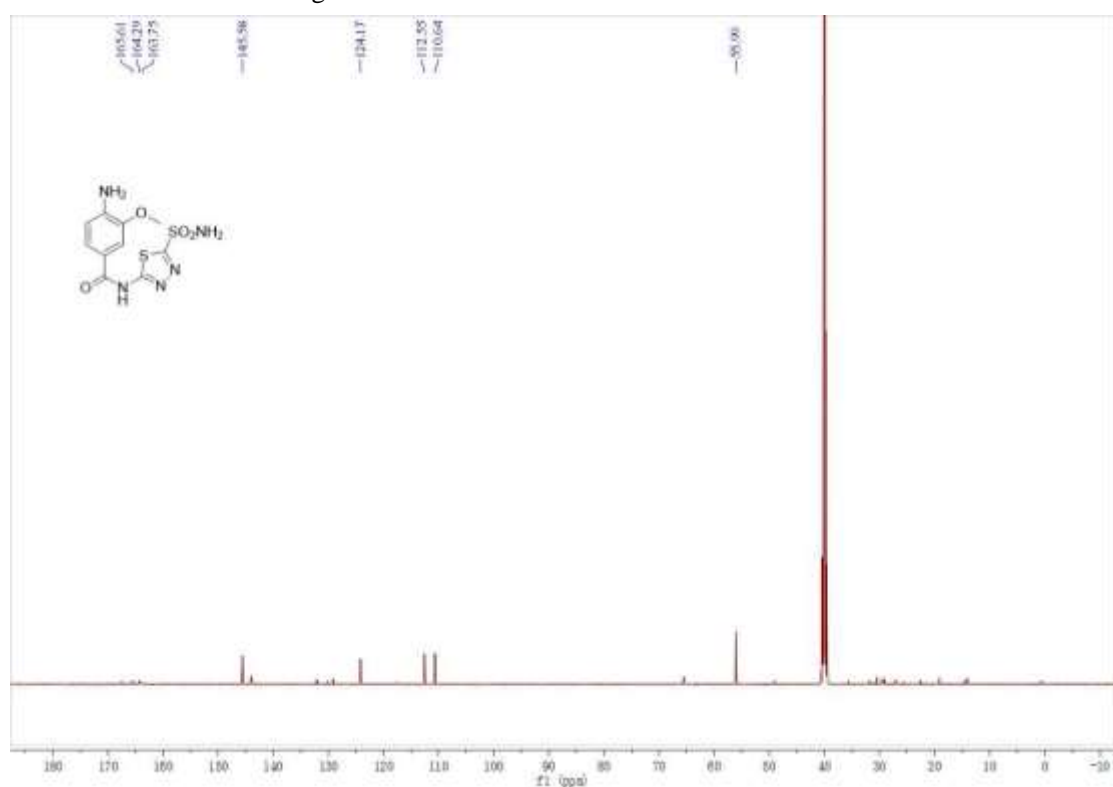


Figure S22. The ¹³C-NMR of intermediate 12h.

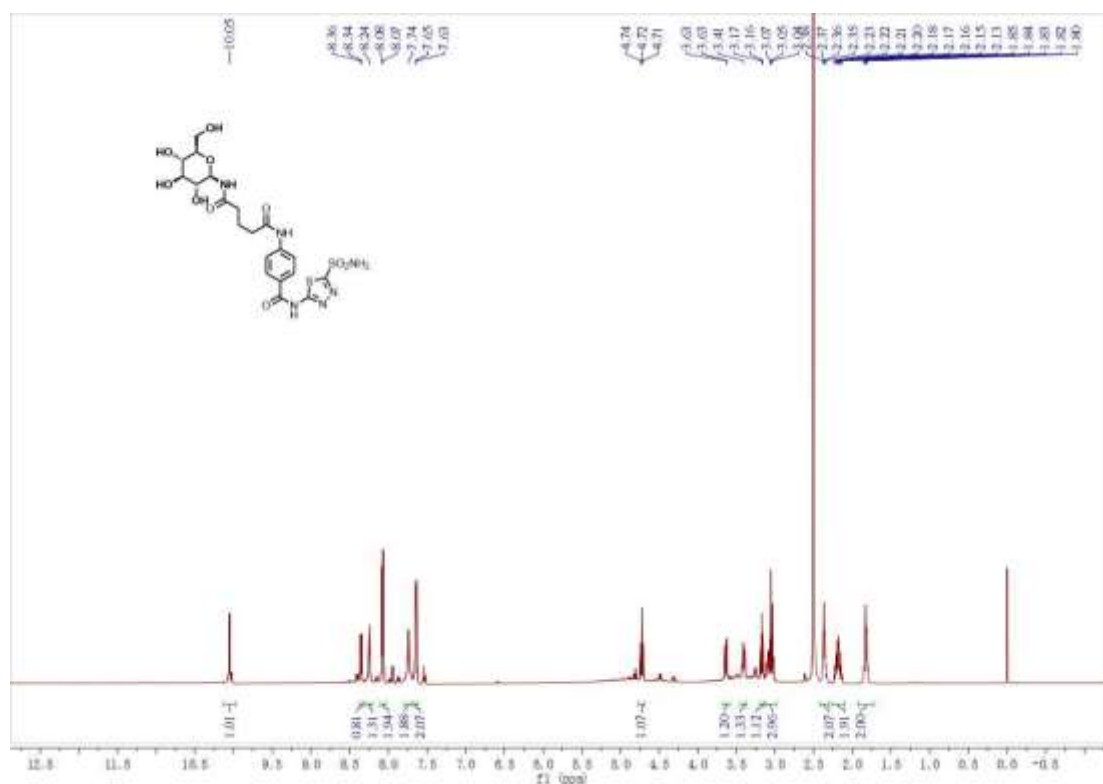


Figure S23. The ^1H -NMR of compound 14a.

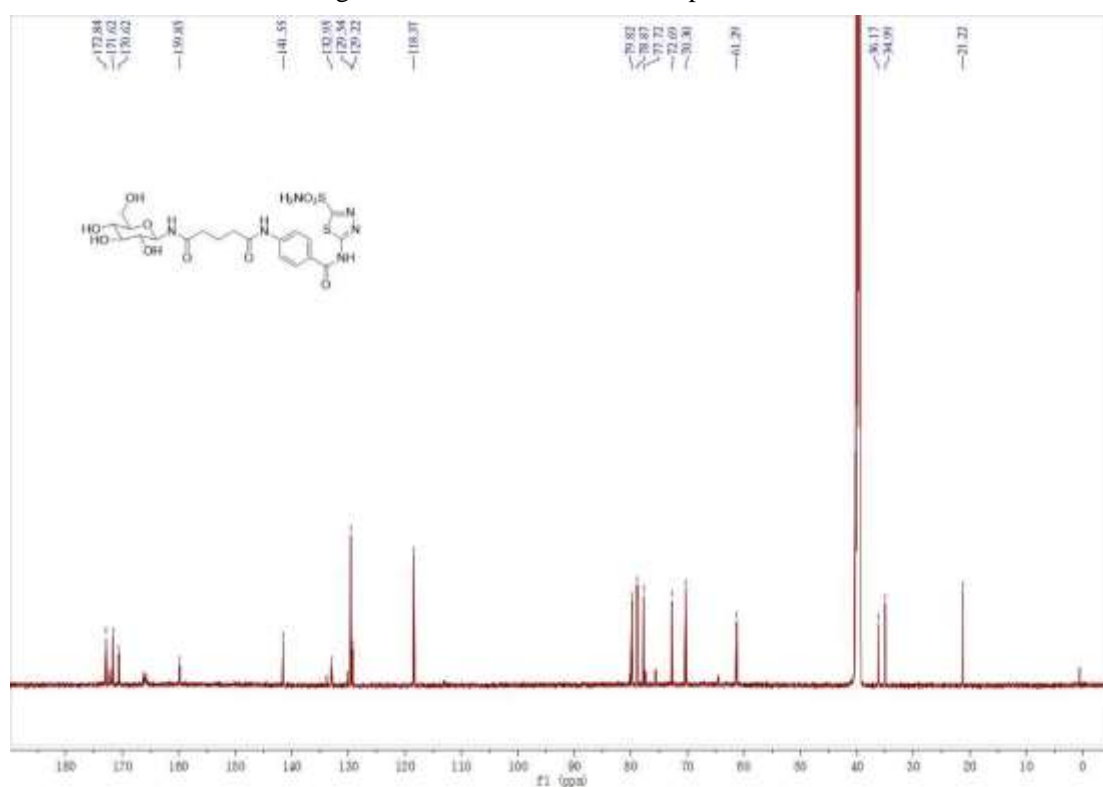


Figure S24. The ^{13}C -NMR of compound 14a.

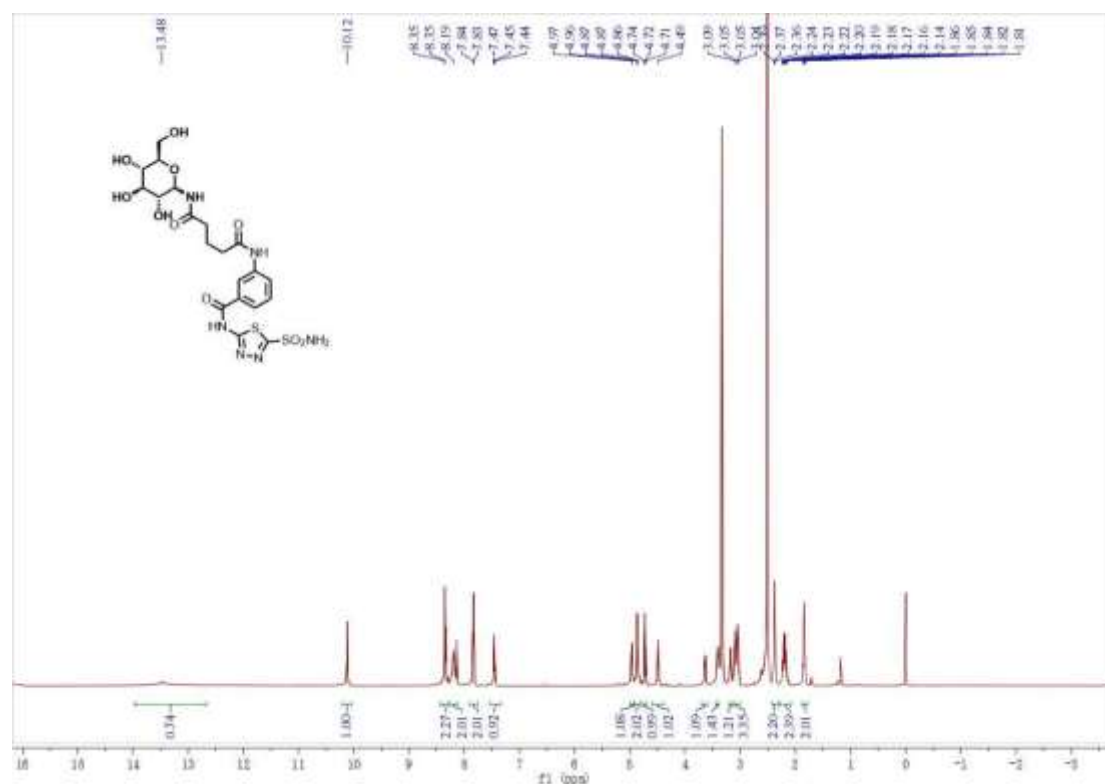


Figure S25. The ^1H -NMR of compound 14b.

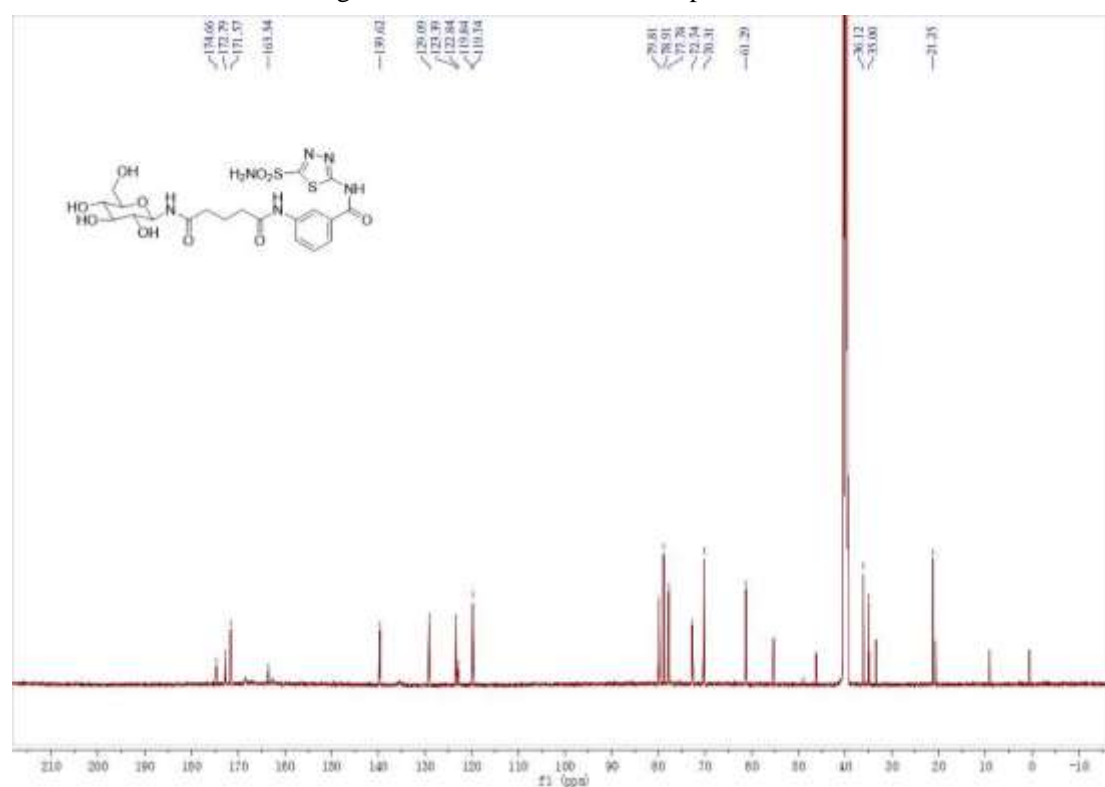


Figure S26. The ^{13}C -NMR of compound 14b.

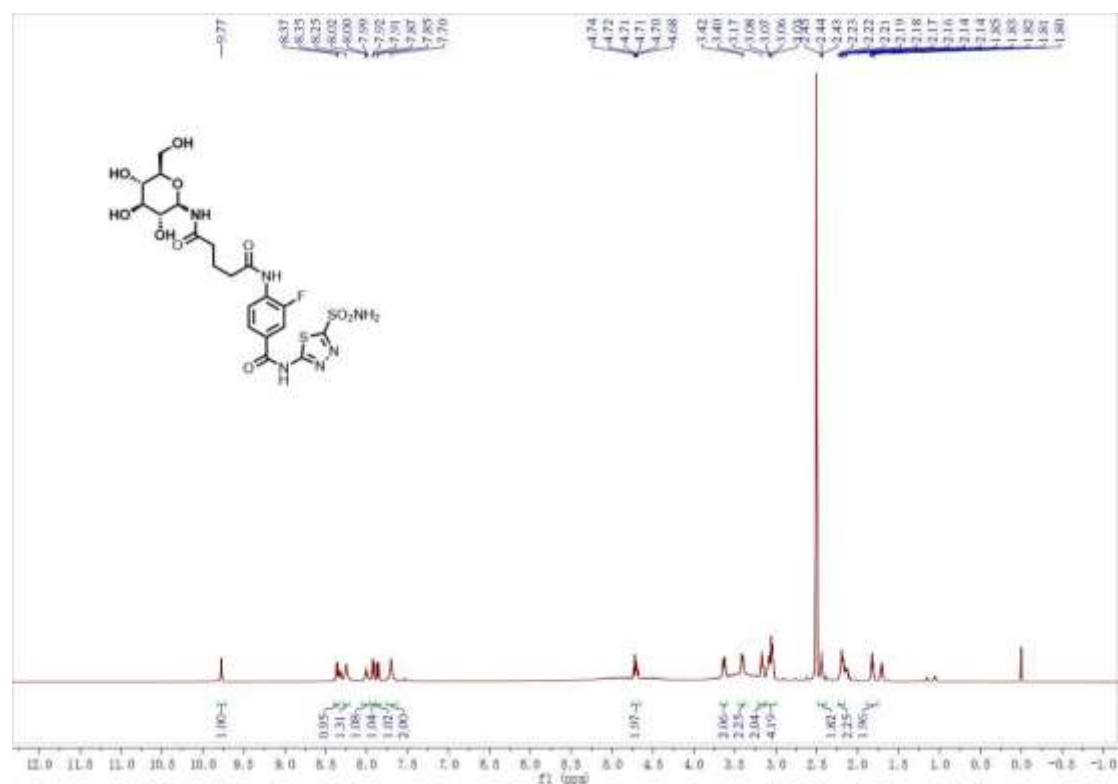


Figure S27. The ^1H -NMR of compound 14c.

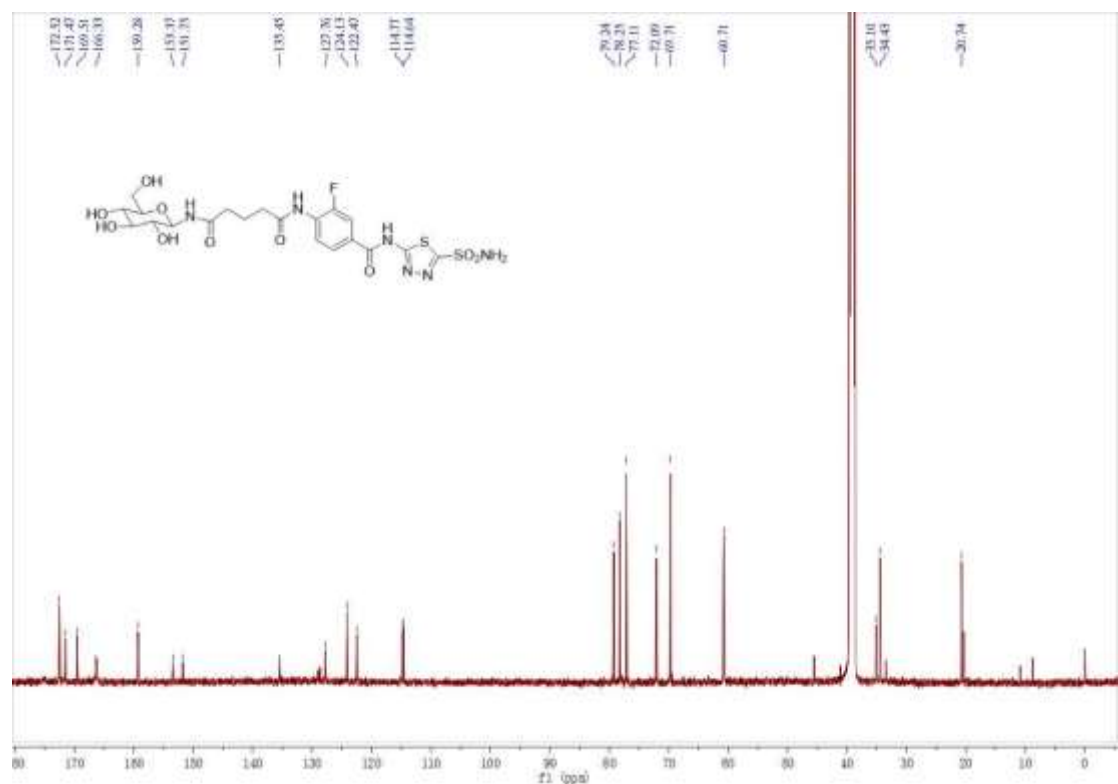
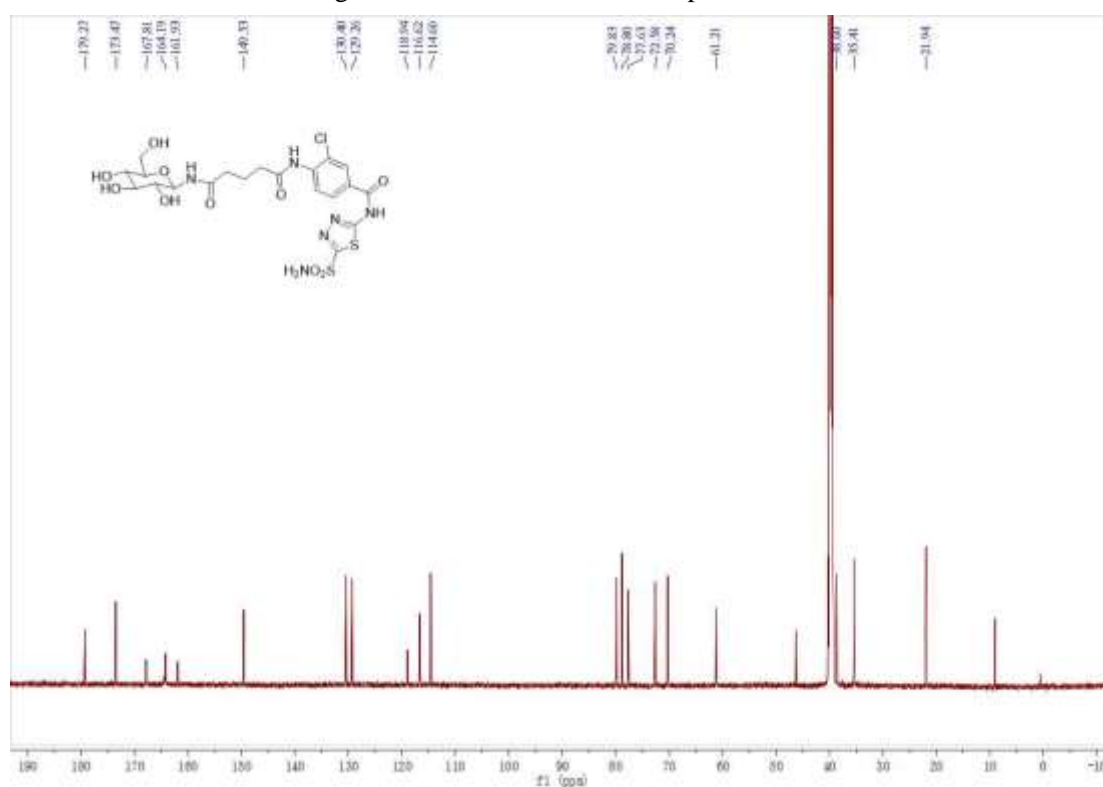
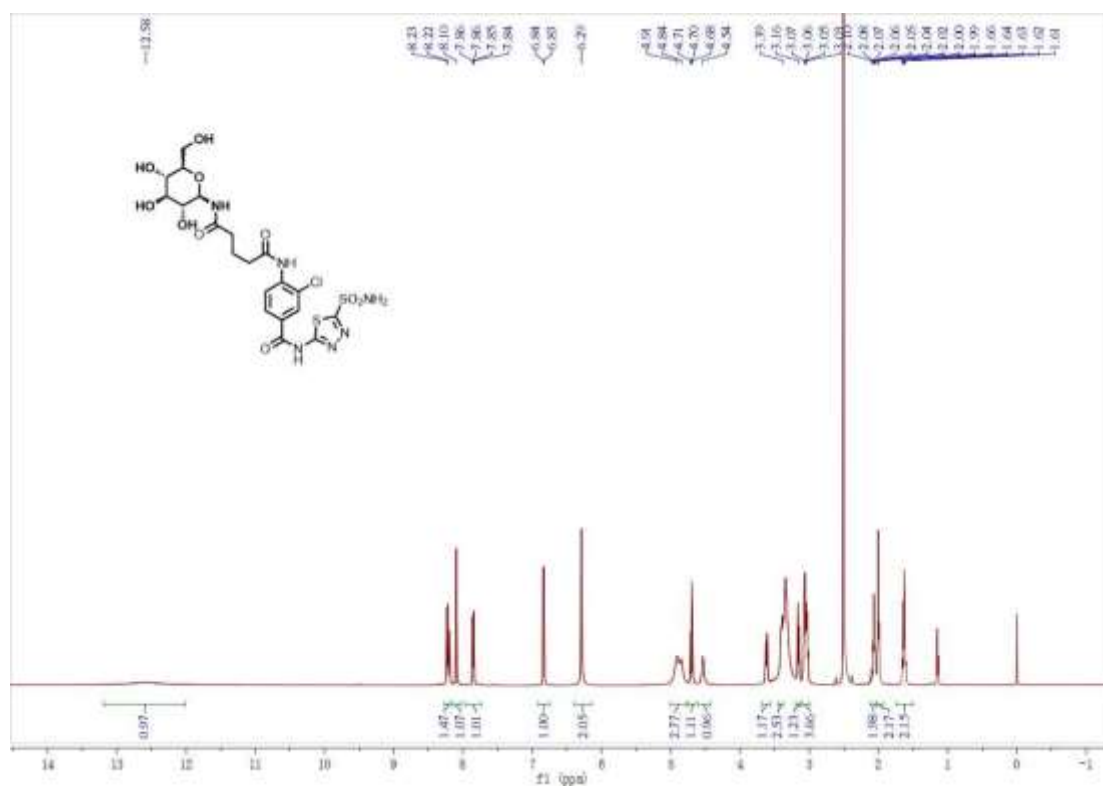


Figure S28. The ^{13}C -NMR of compound 14c.



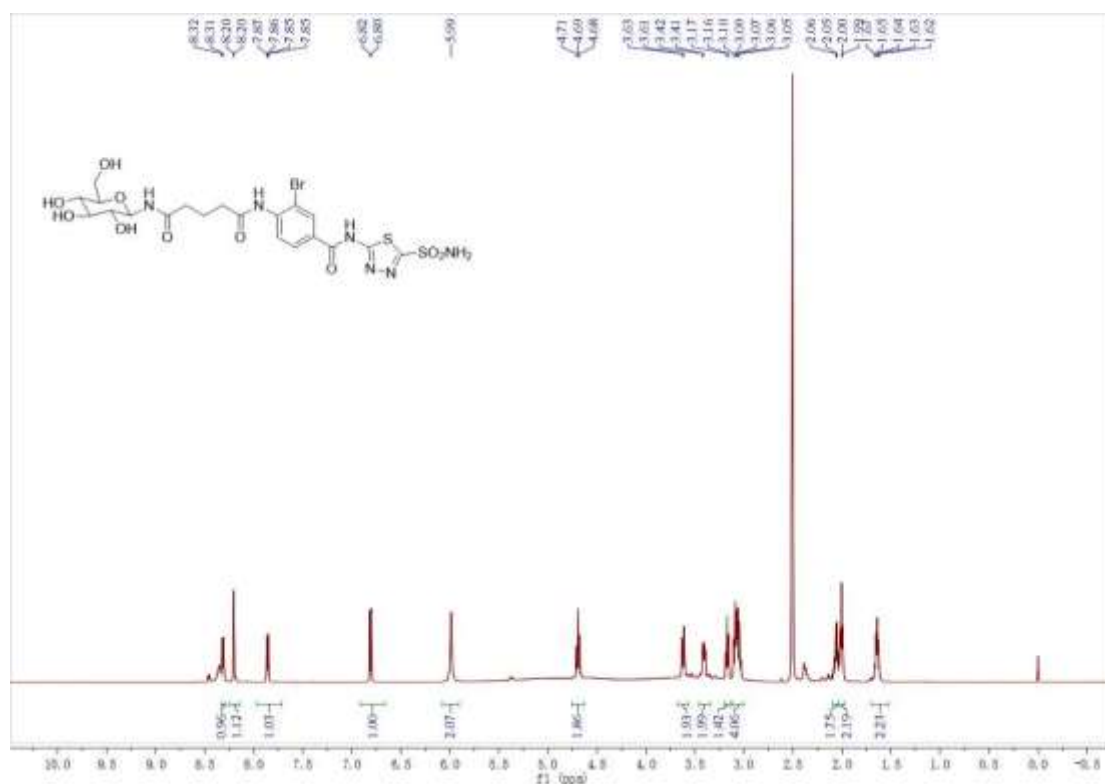


Figure S31. The ¹H-NMR of compound 14e.

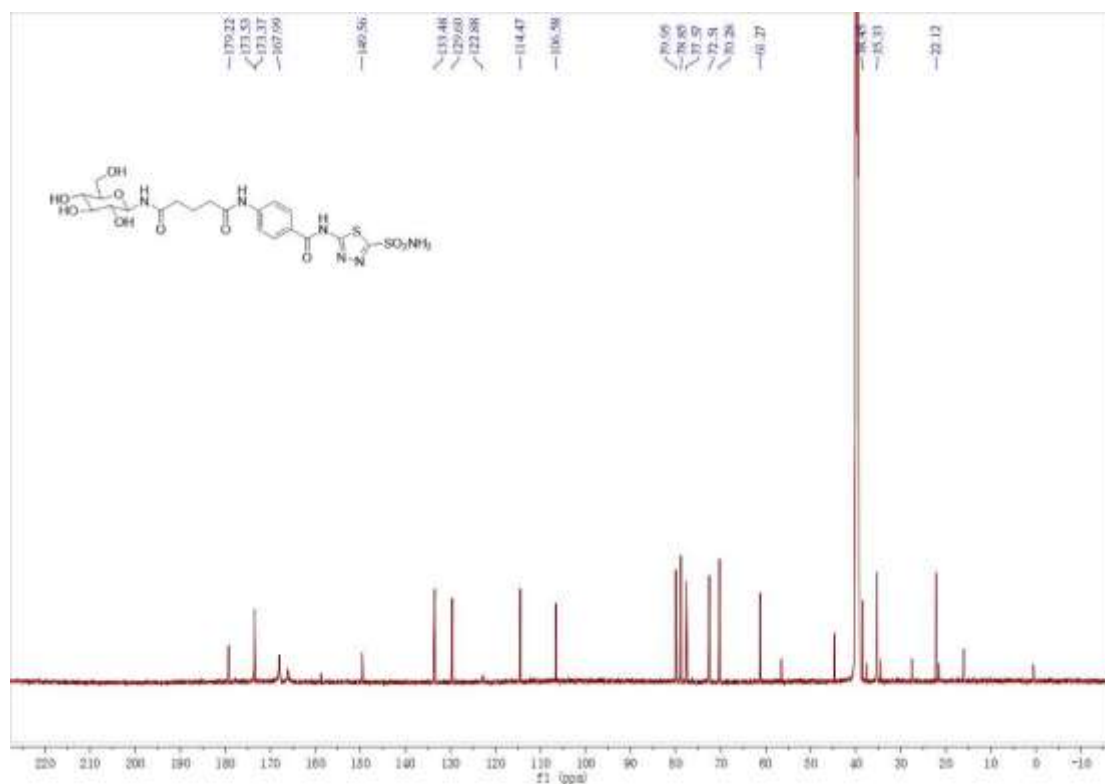


Figure S32. The ¹³C-NMR of compound 14e.

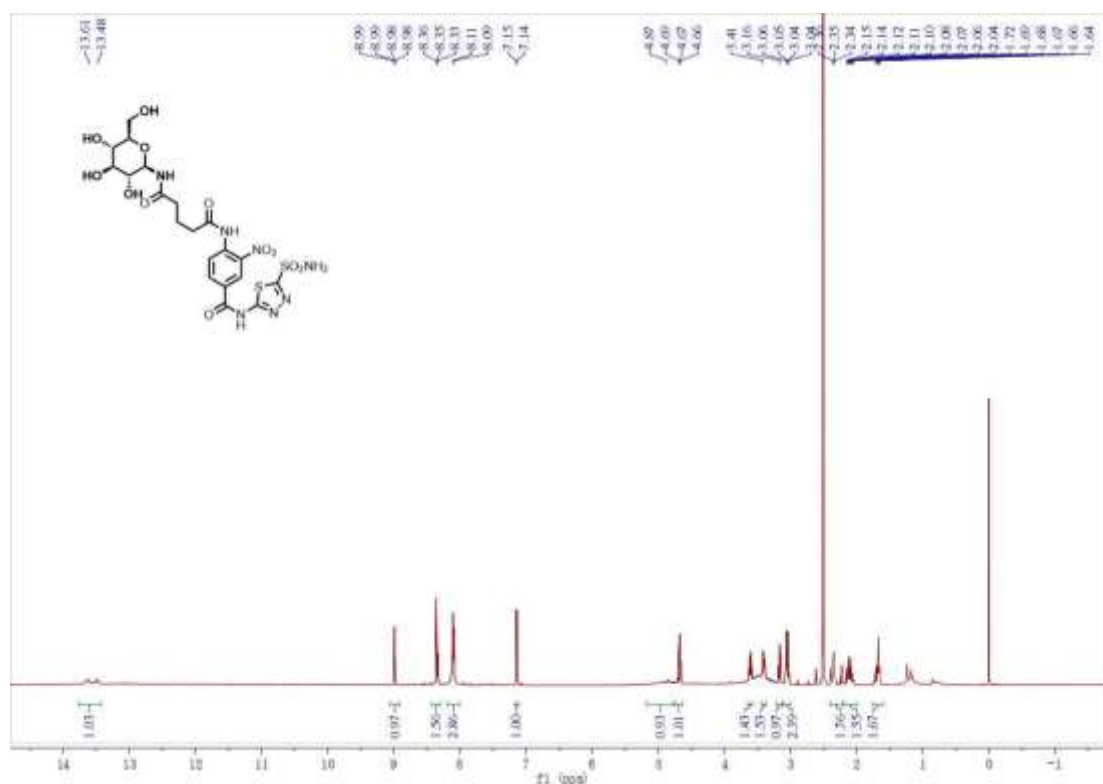


Figure S33. The ^1H -NMR of compound 14f.

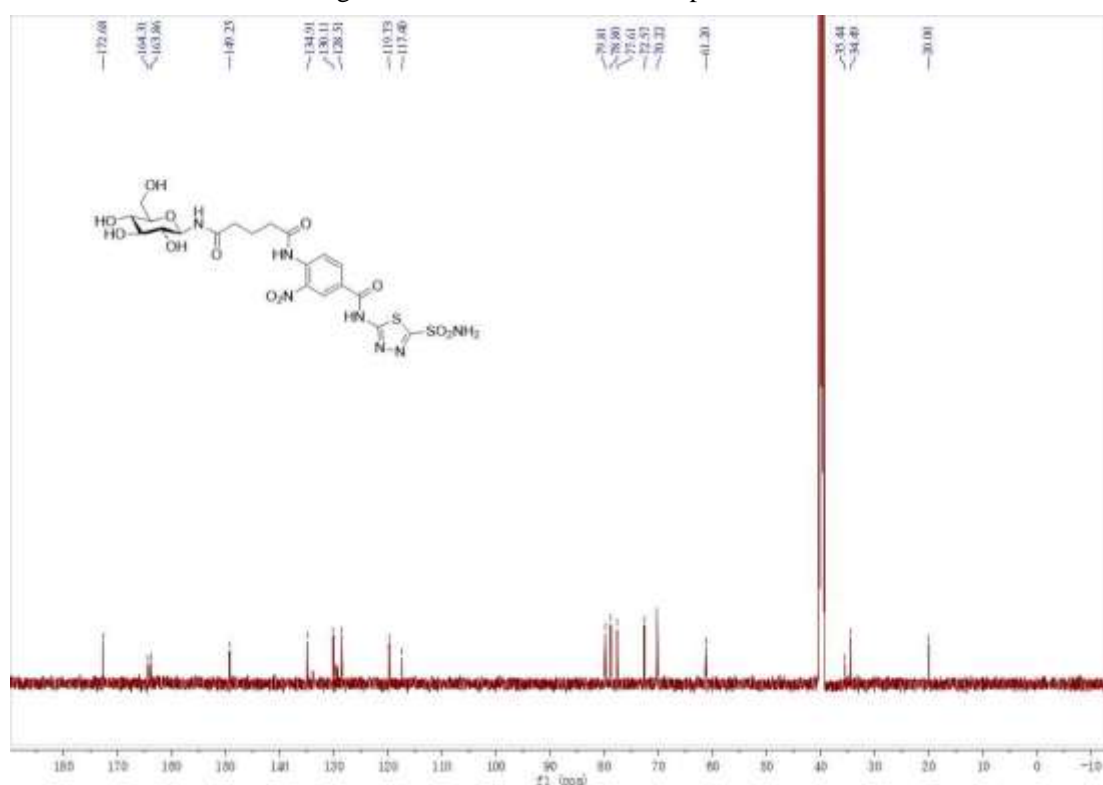


Figure S34. The ^{13}C -NMR of compound 14f.

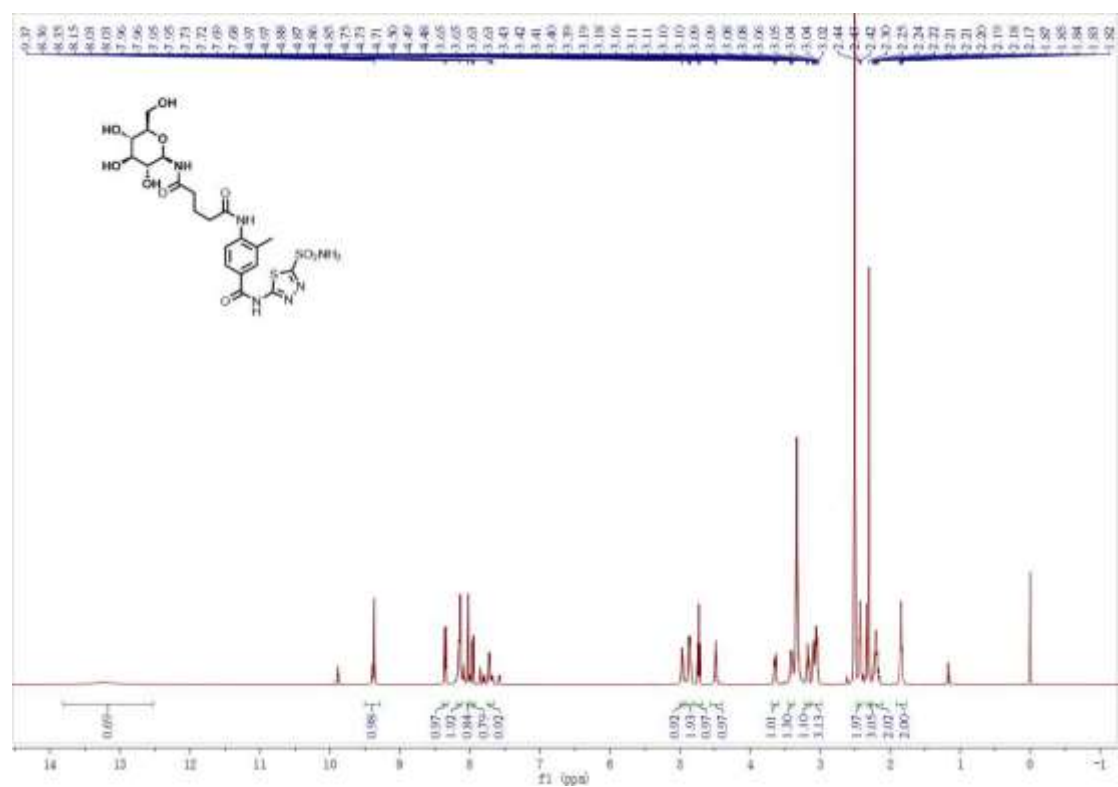


Figure S35. The ^1H -NMR of compound 14g.

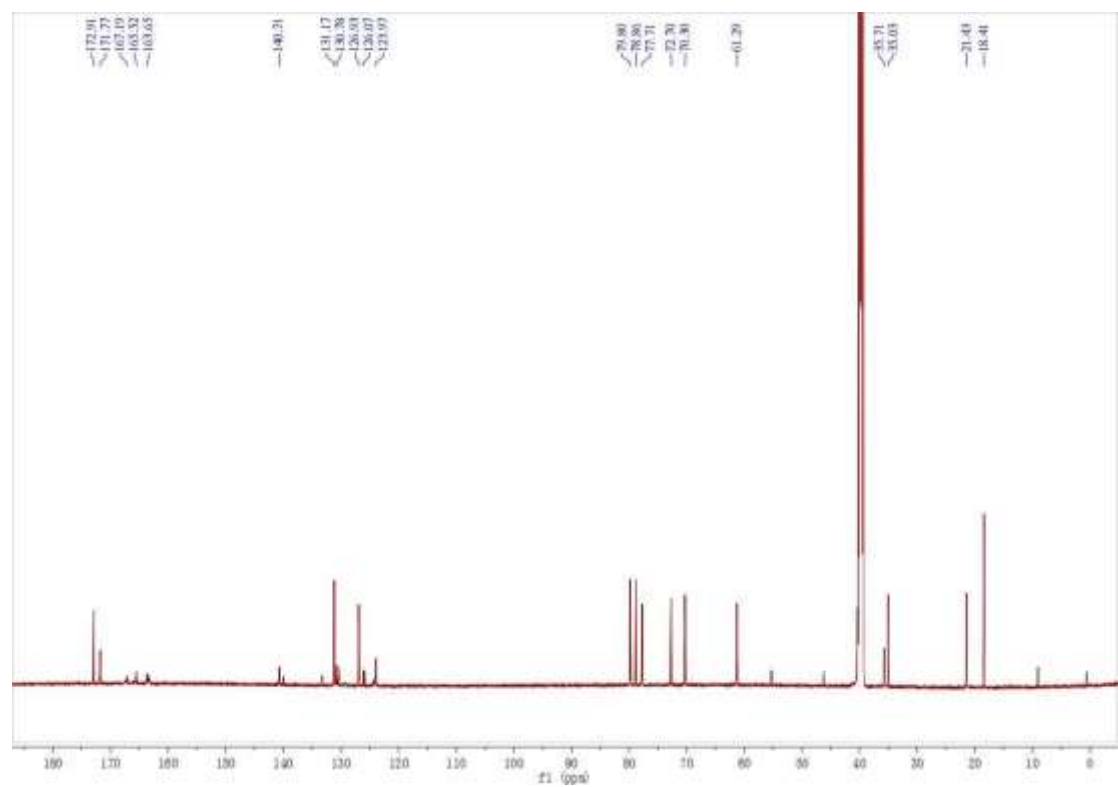
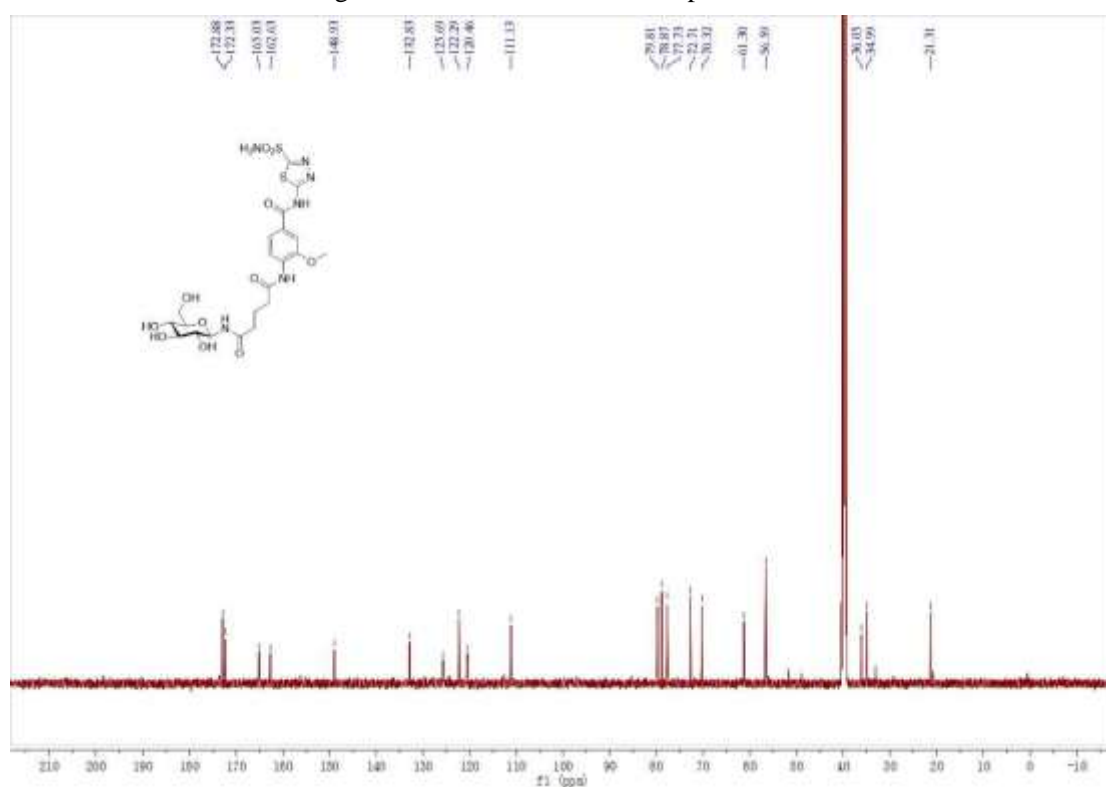
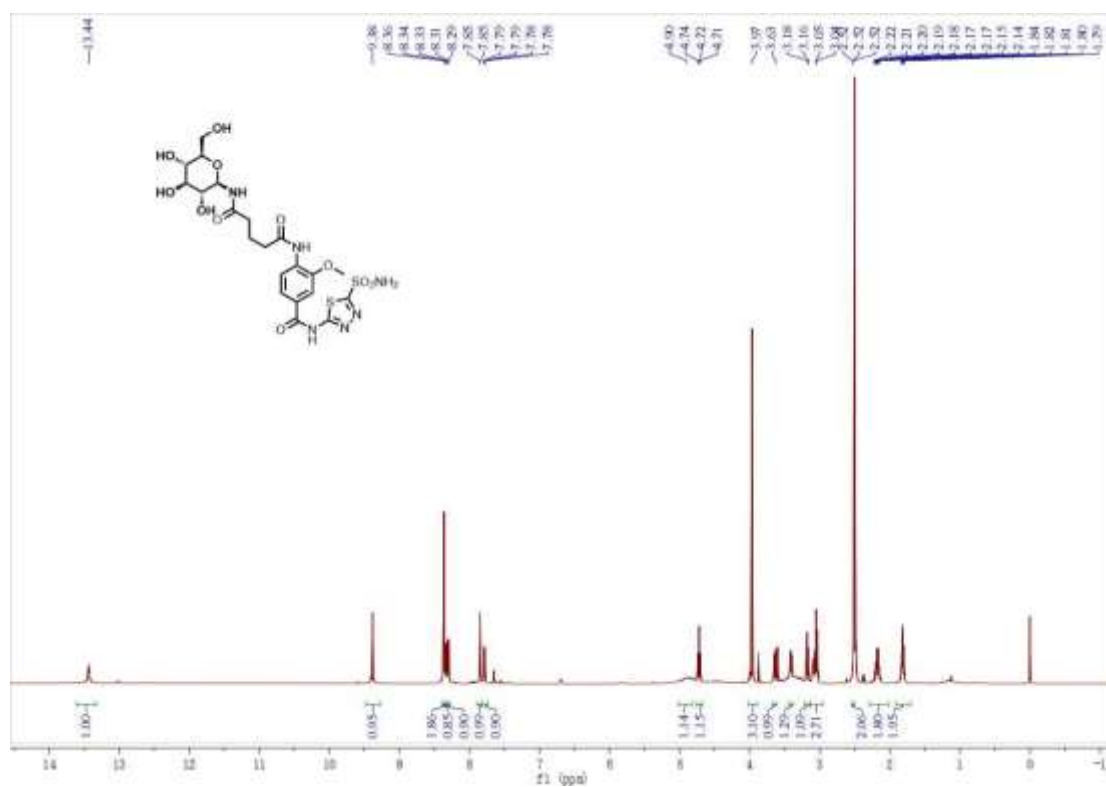


Figure S36. The ^{13}C -NMR of compound 14g.



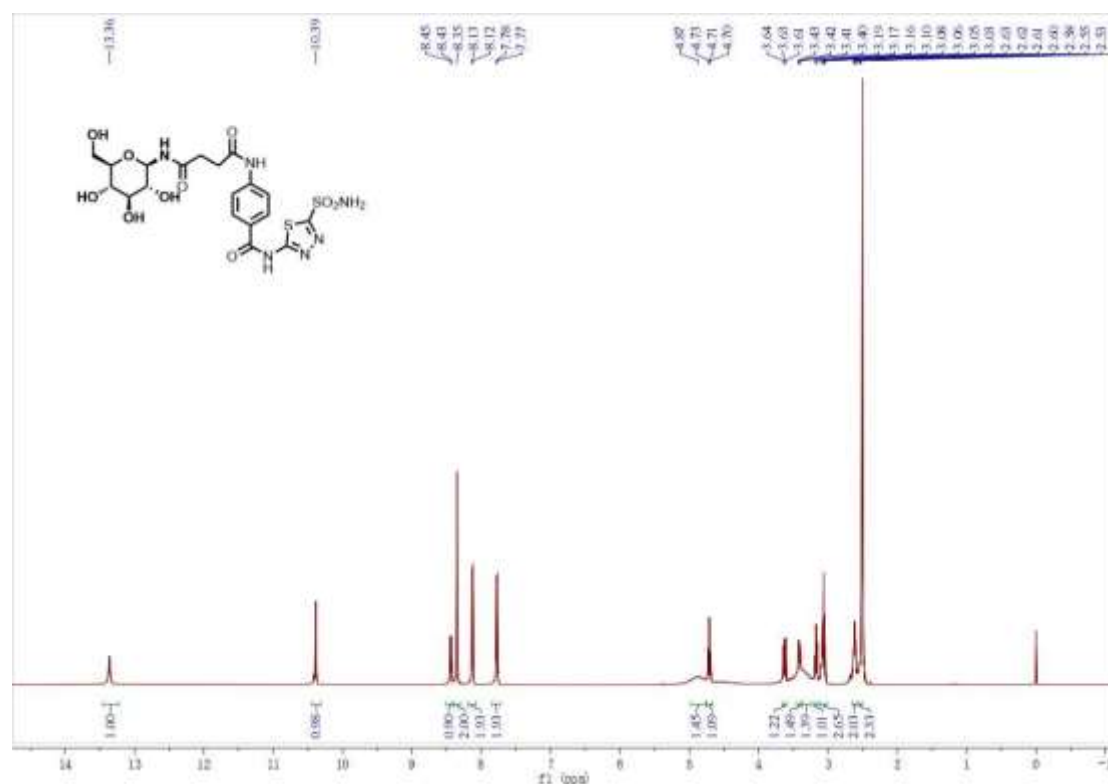


Figure S39. The ¹H-NMR of compound 14i.

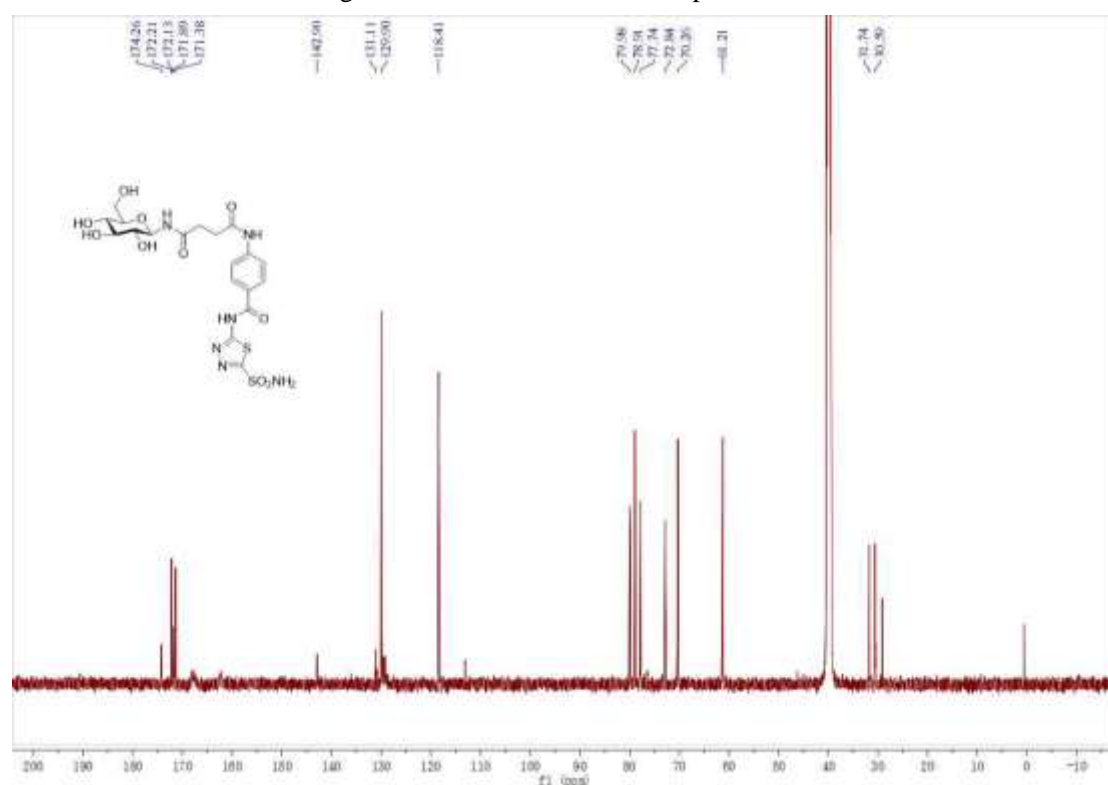


Figure S40. The ¹³C-NMR of compound 14i.

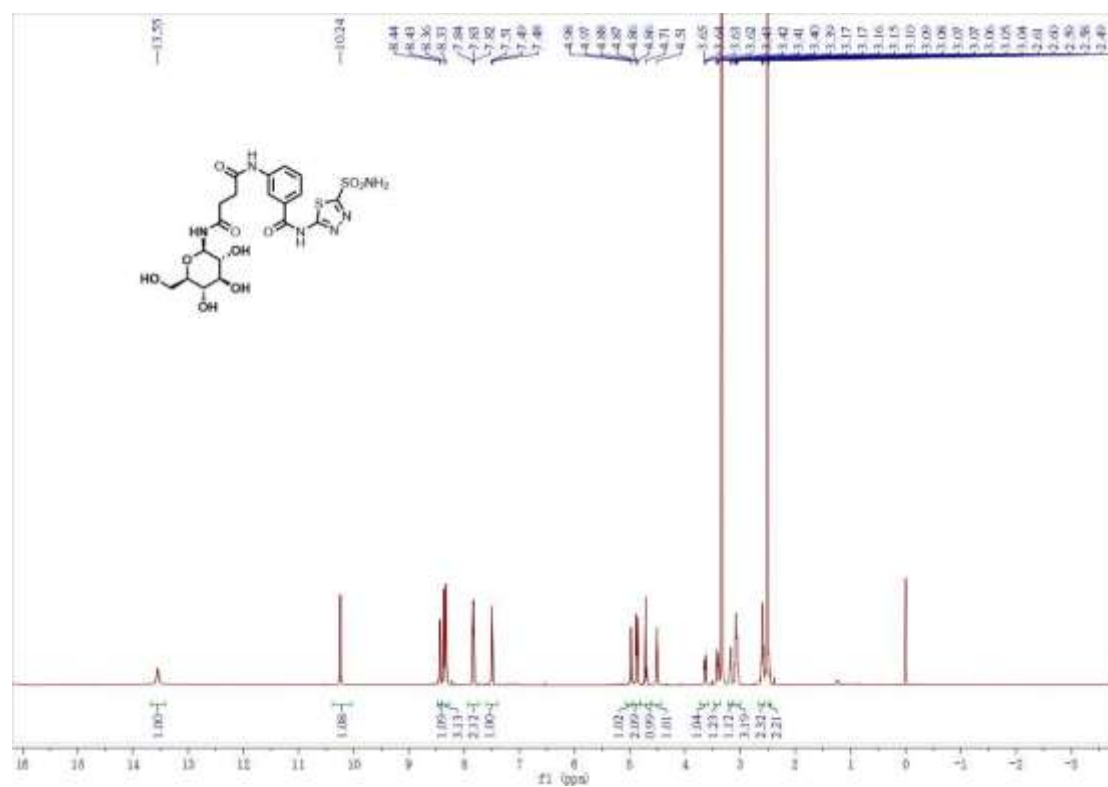


Figure S41. The ¹H-NMR of compound 14j.

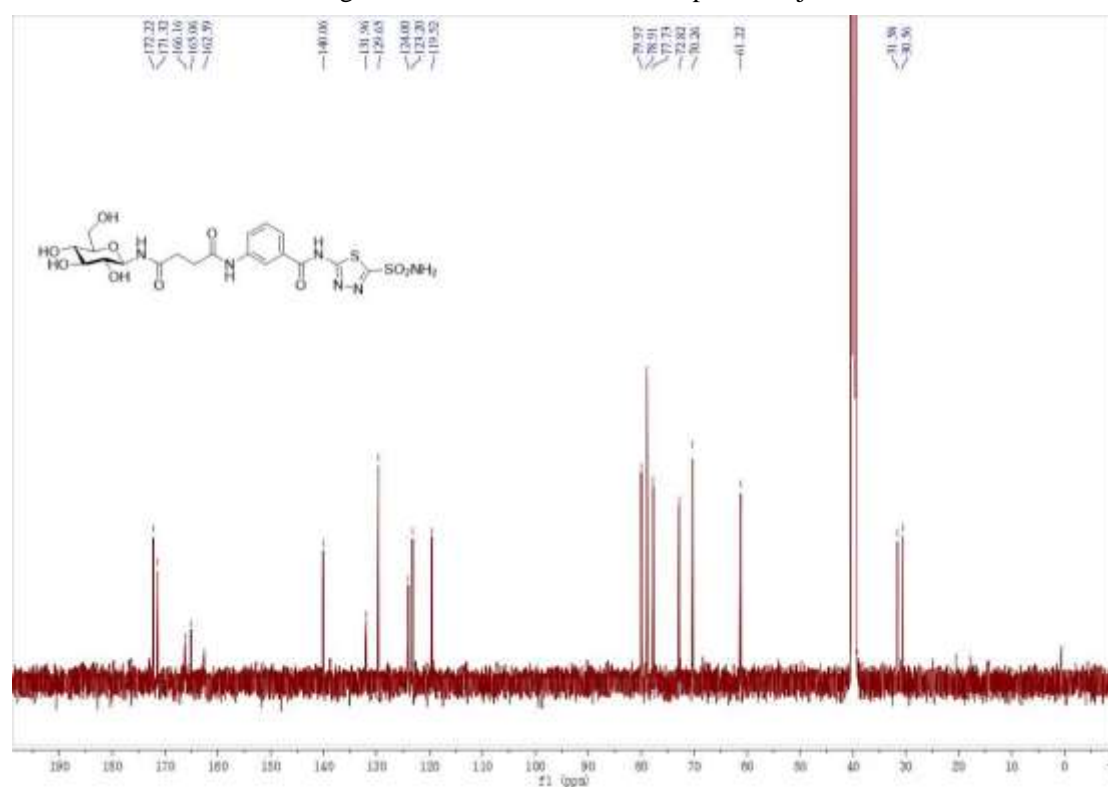


Figure S42. The ¹³C-NMR of compound 14j.

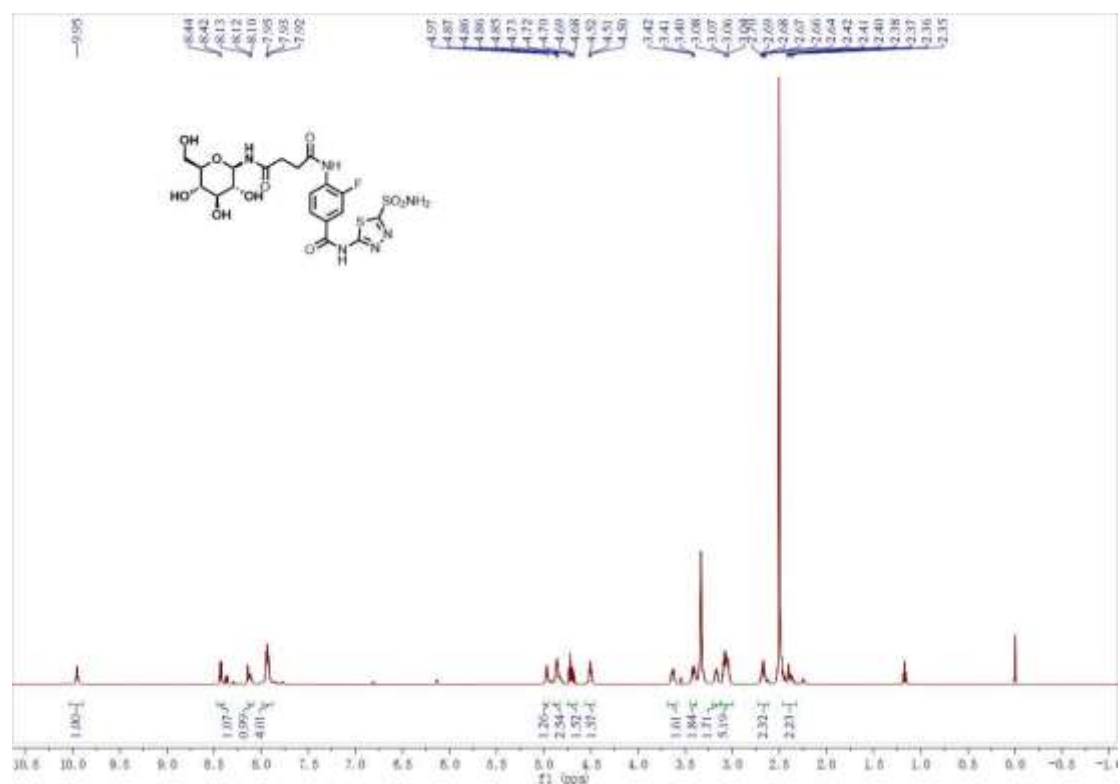


Figure S43. The ^1H -NMR of compound 14k.

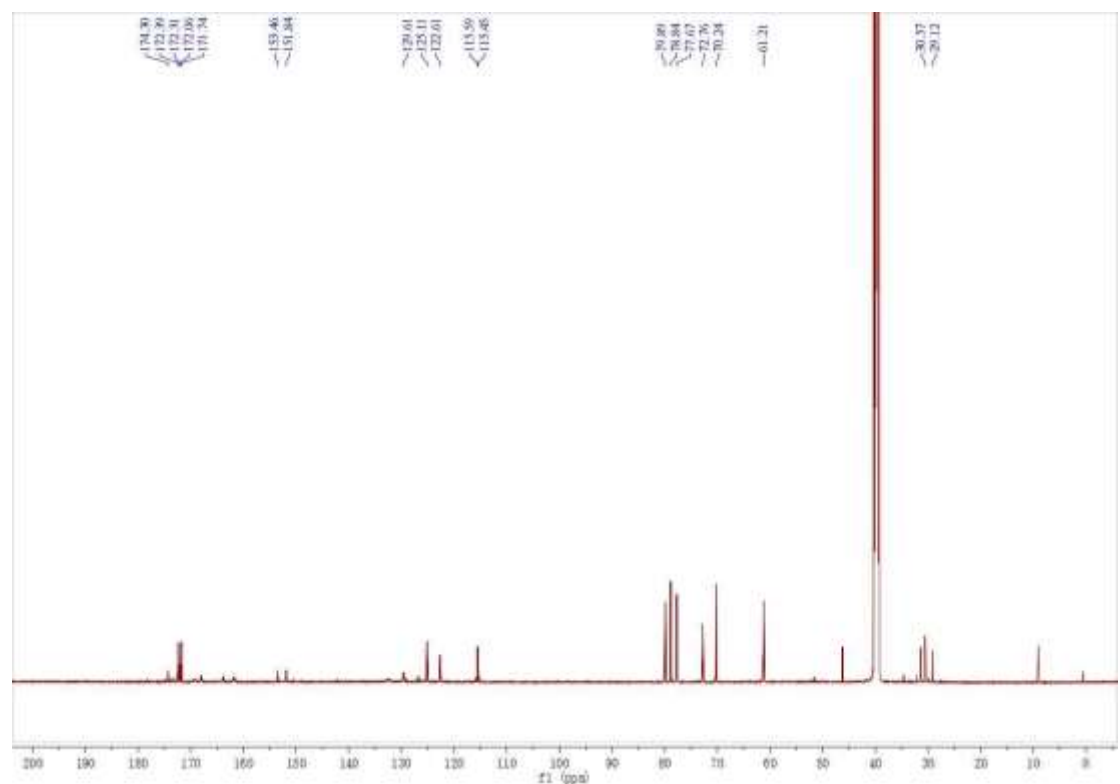
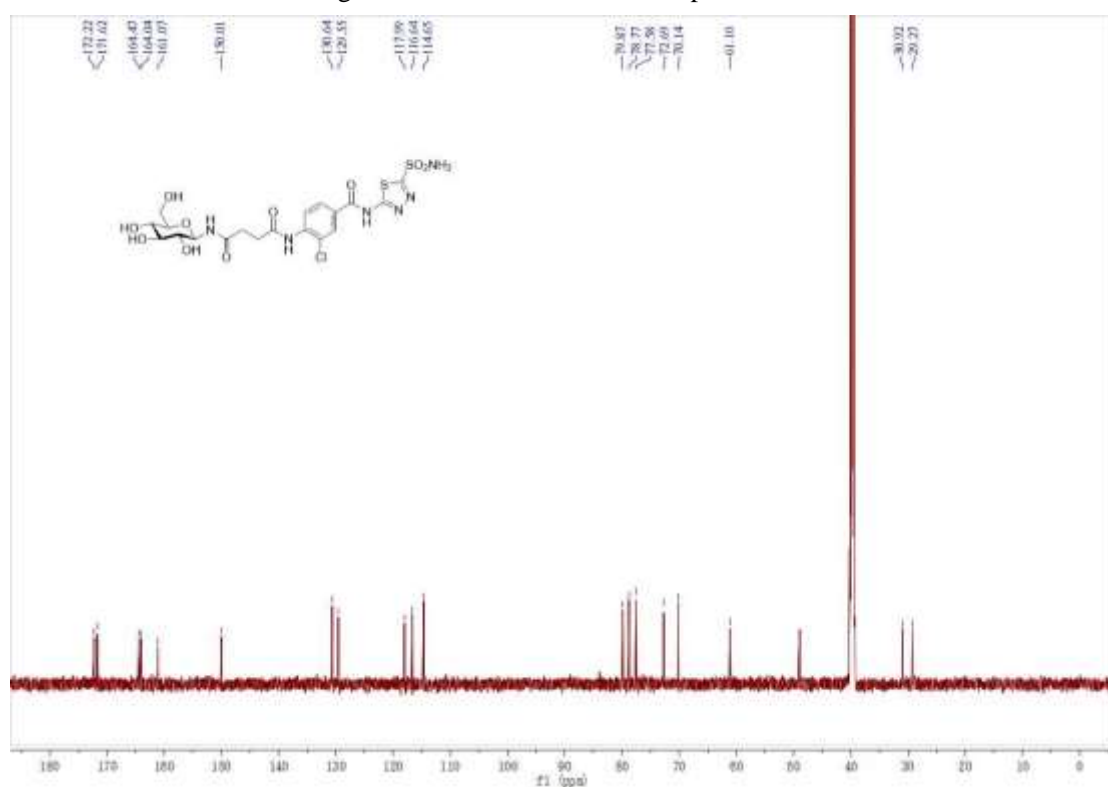
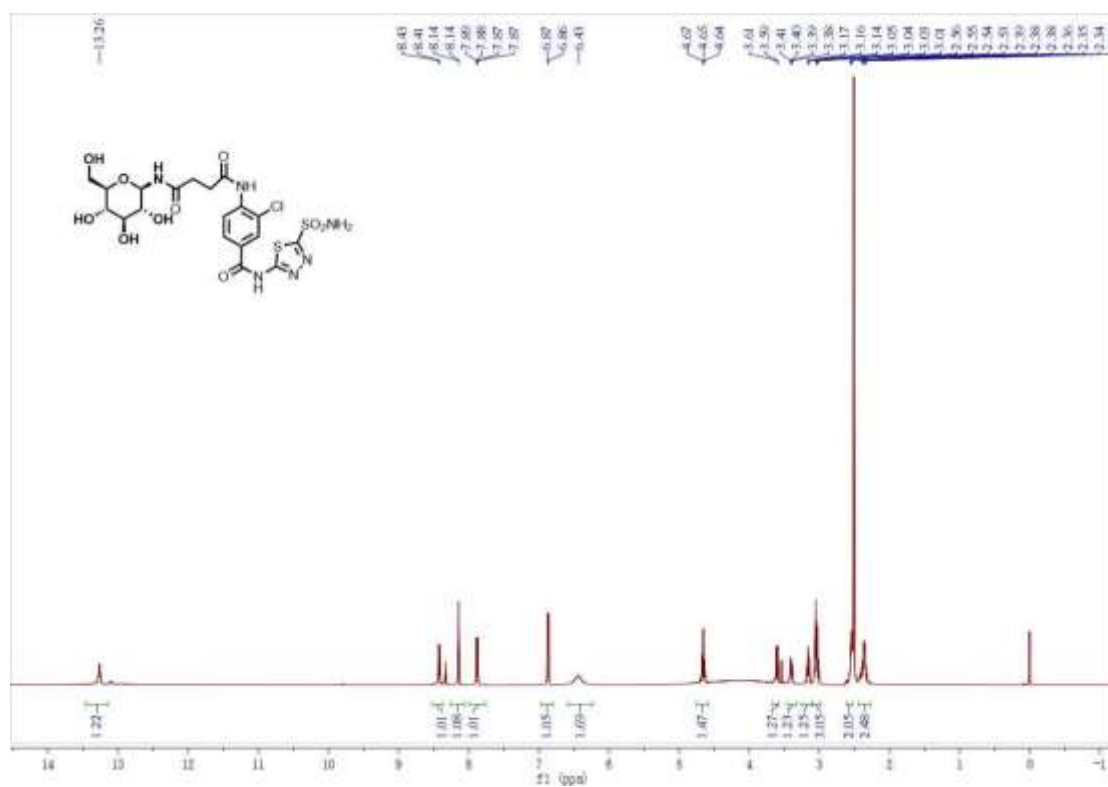


Figure S44. The ^{13}C -NMR of compound 14k.



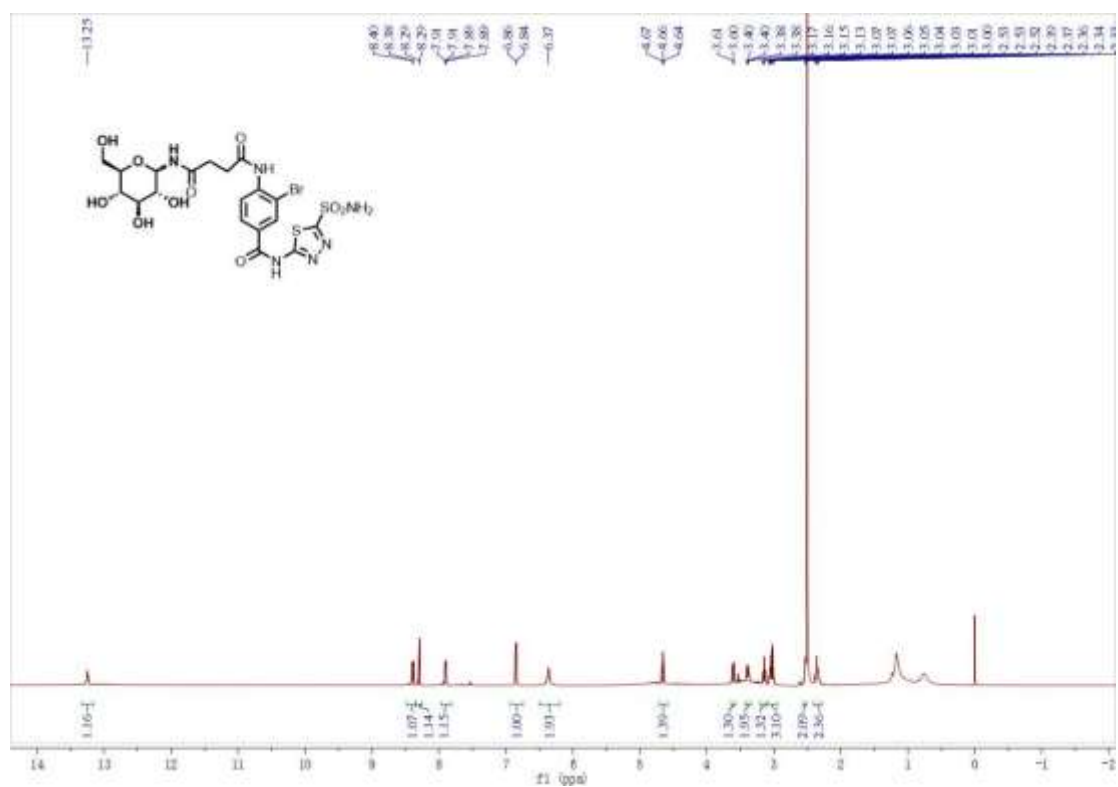


Figure S47. The ^1H -NMR of compound 14m.

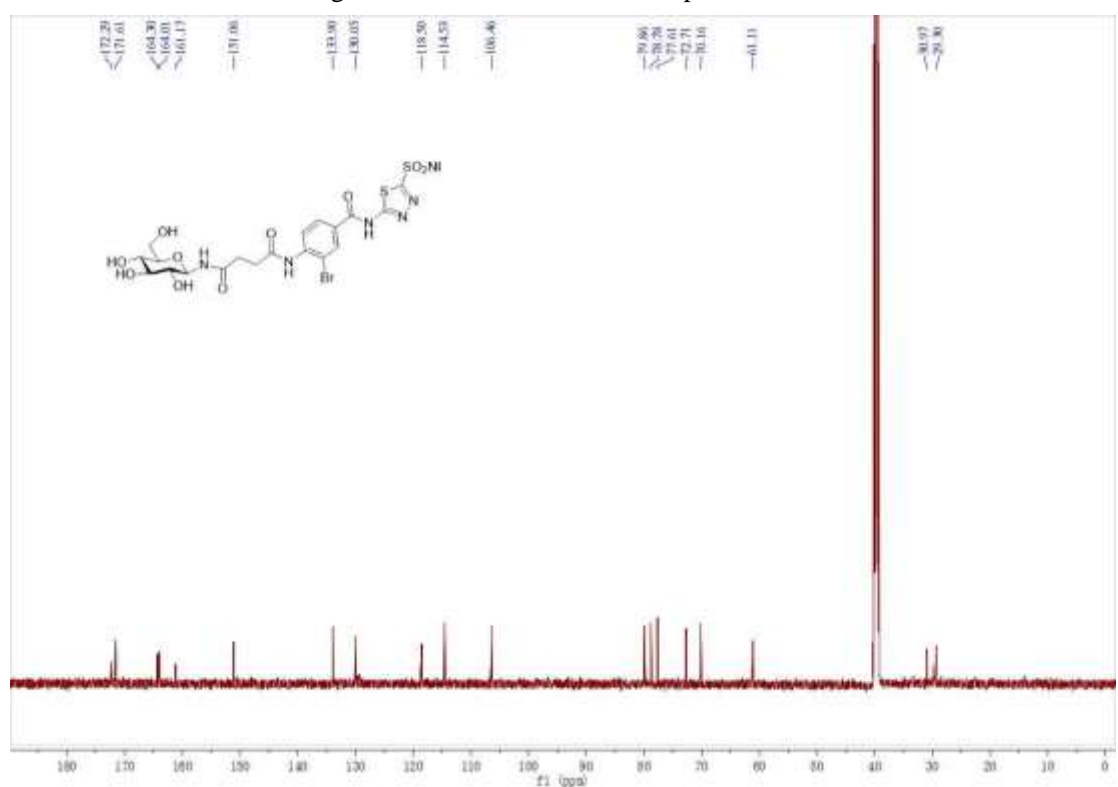
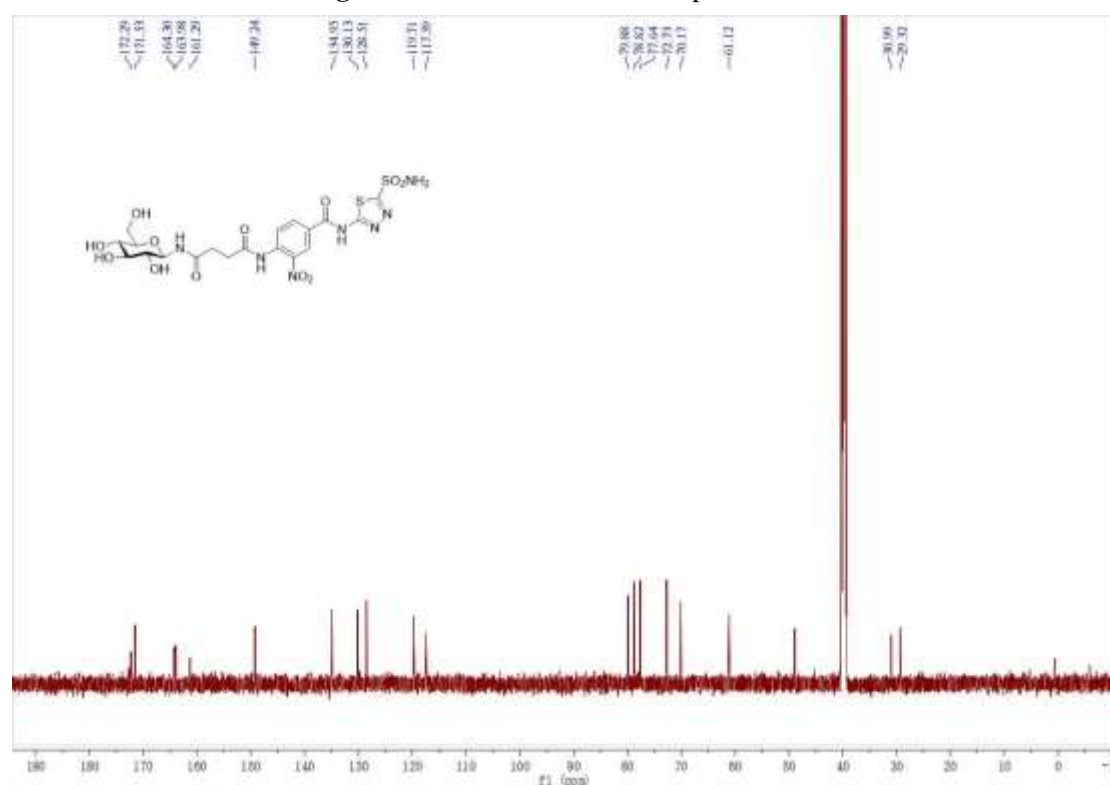
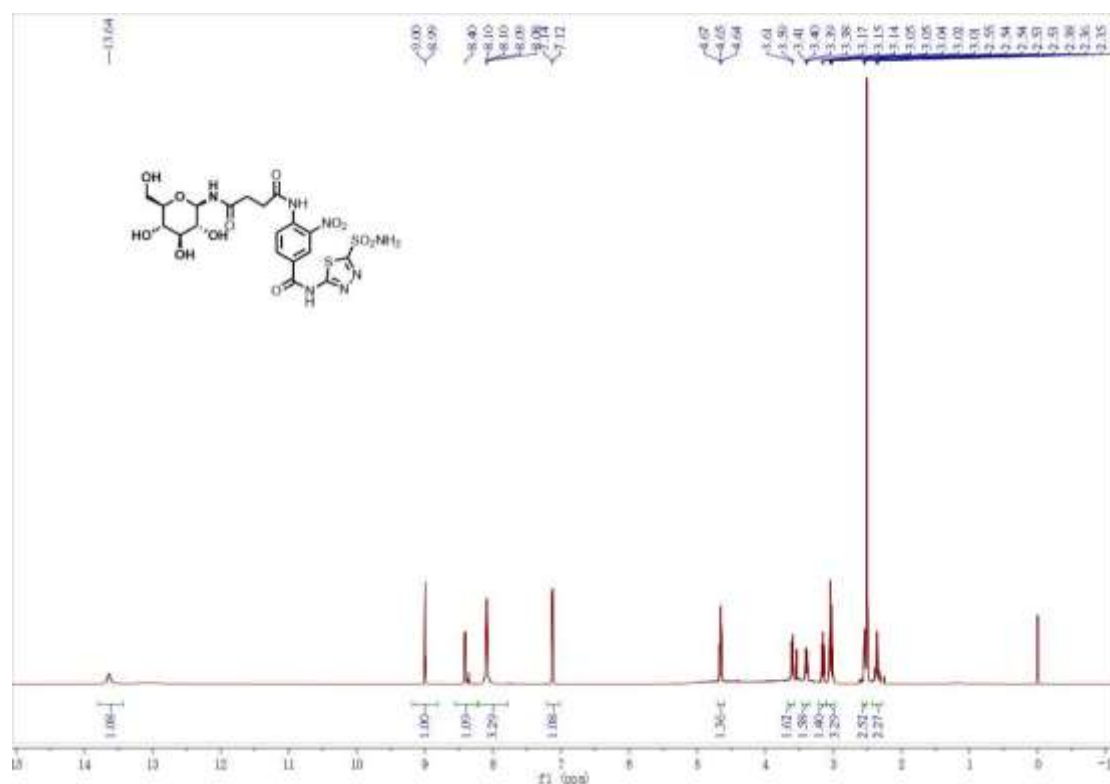


Figure S48. The ^{13}C -NMR of compound 14m.



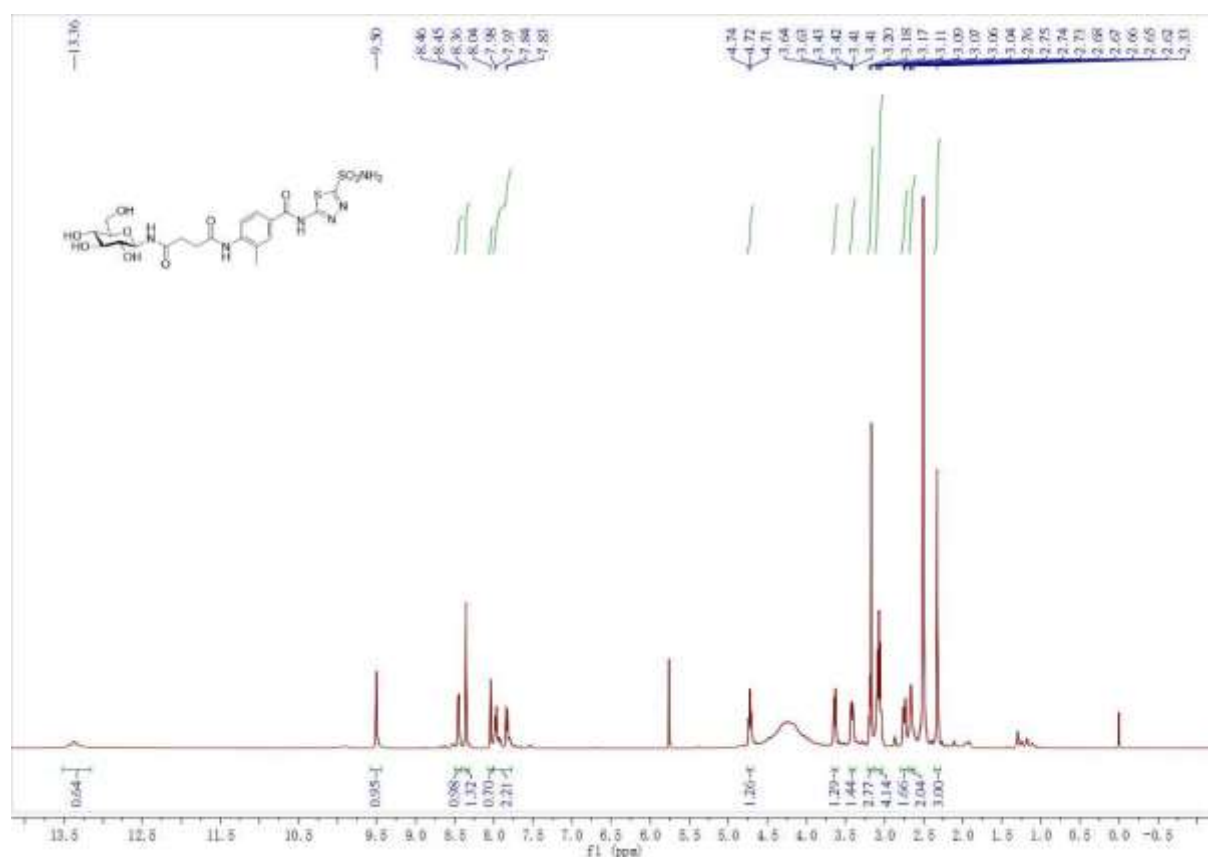


Figure S51. The ^1H -NMR of compound 14o.

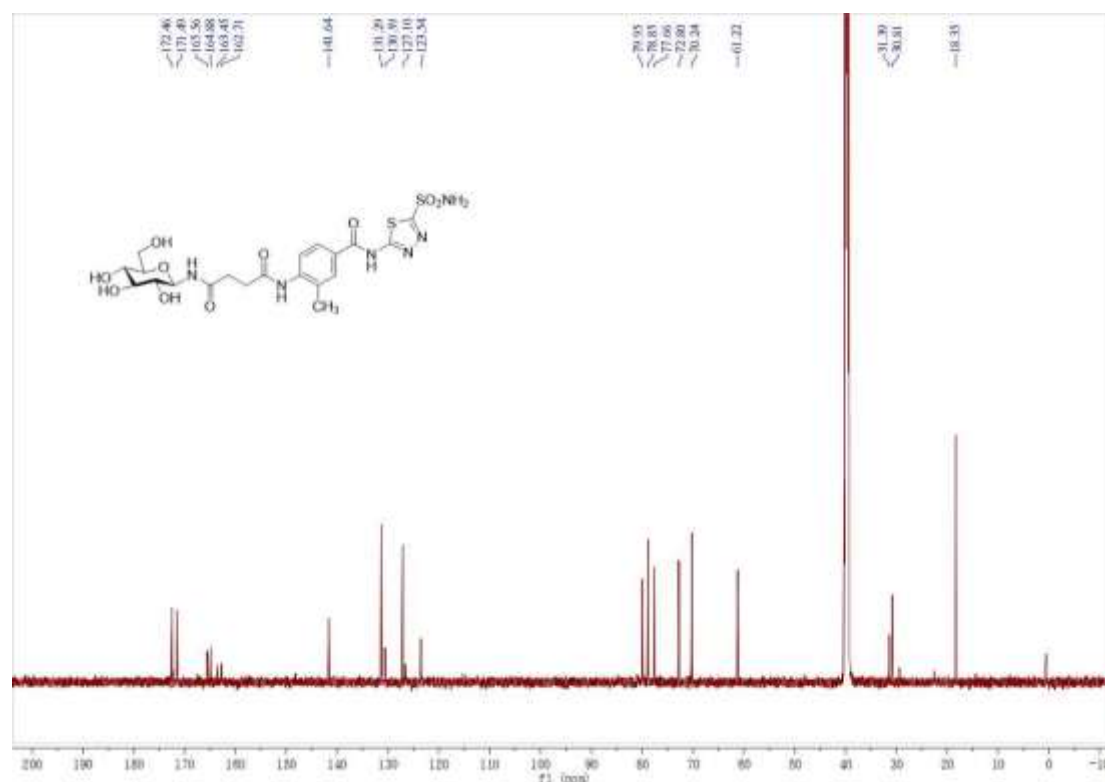


Figure S52. The ^{13}C -NMR of compound 14o.

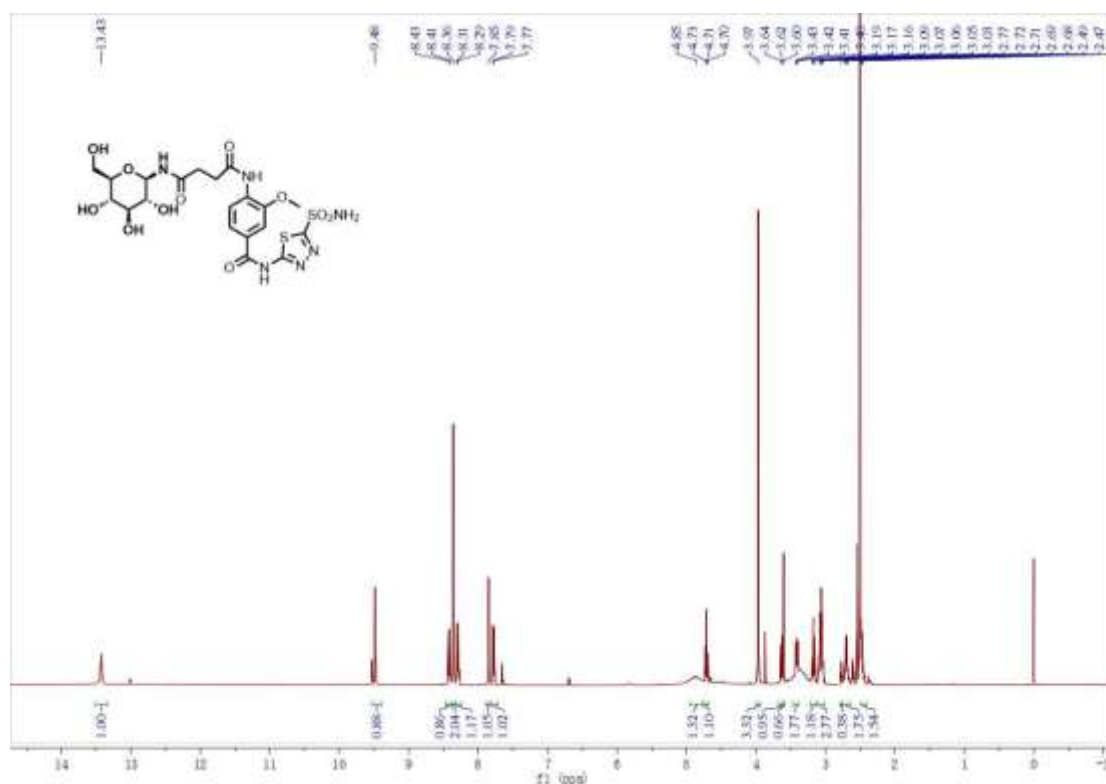


Figure S53. The ^1H -NMR of compound 14p.

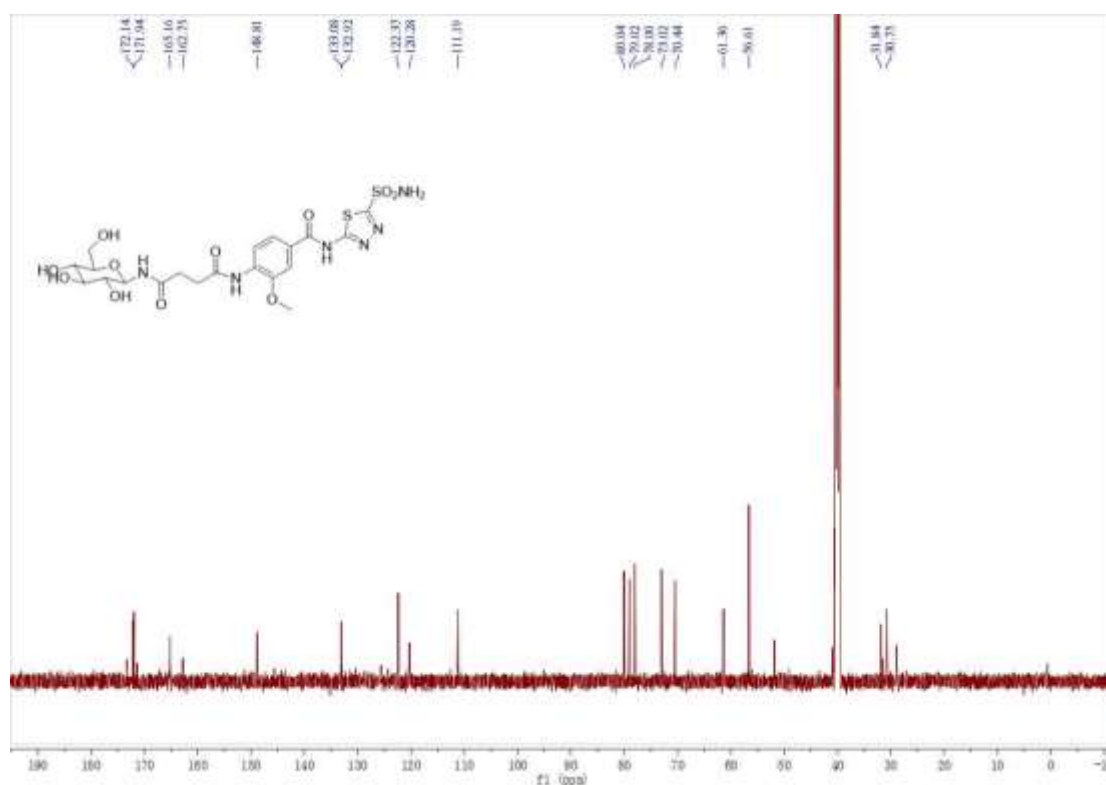


Figure S54. The ^{13}C -NMR of compound 14p.

2D-NMR Spectra

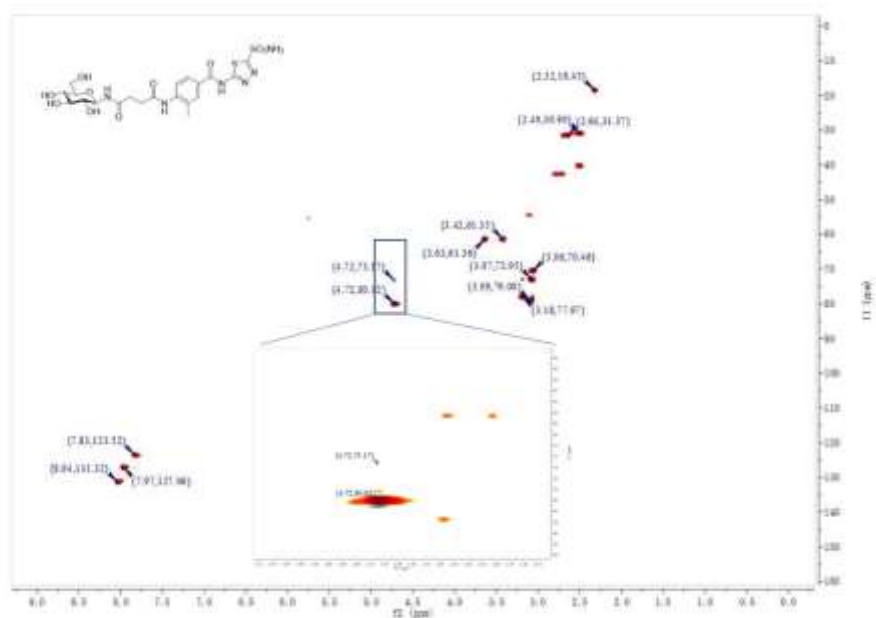


Figure S55. The HSQC spectra of compound 14o.

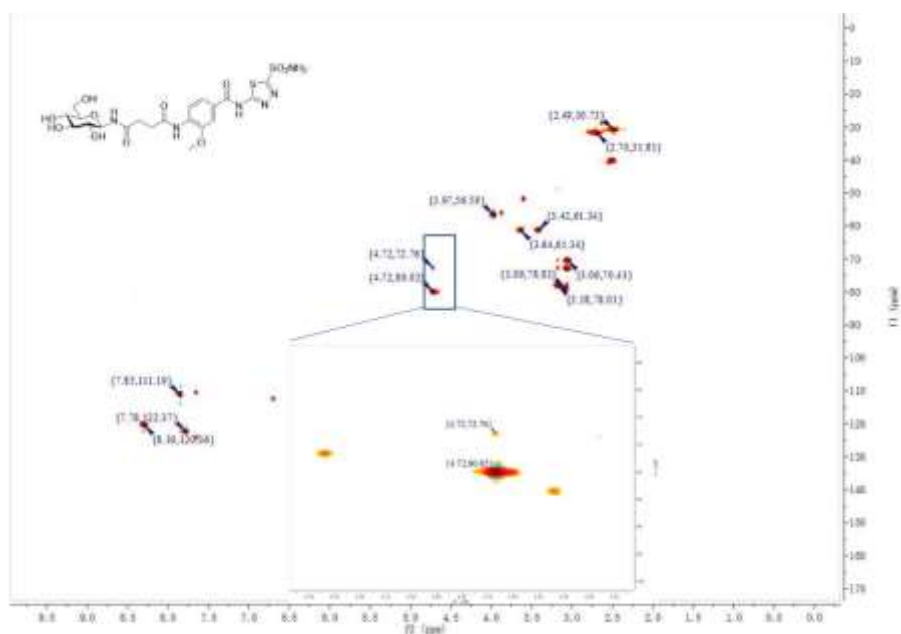


Figure S56. The HSQC spectra of compound 14p.

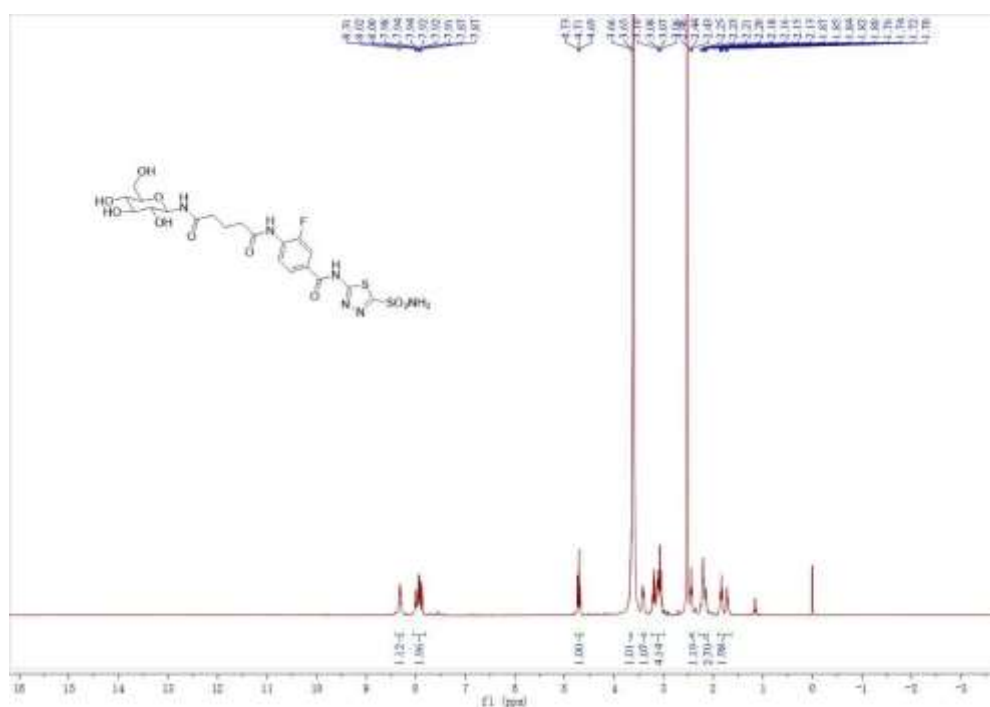


Figure S57. The ^1H -NMR of compound 14c with D_2O -exchange.

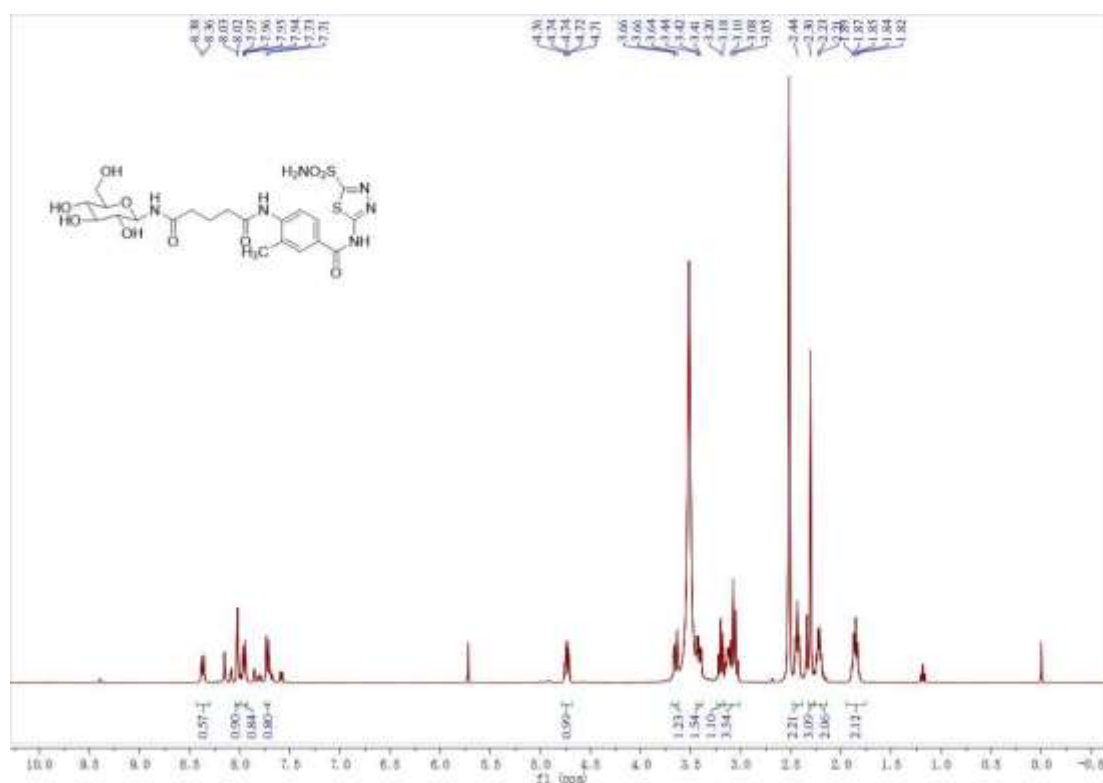


Figure S58. The ^1H -NMR of compound 14g with D_2O -exchange.

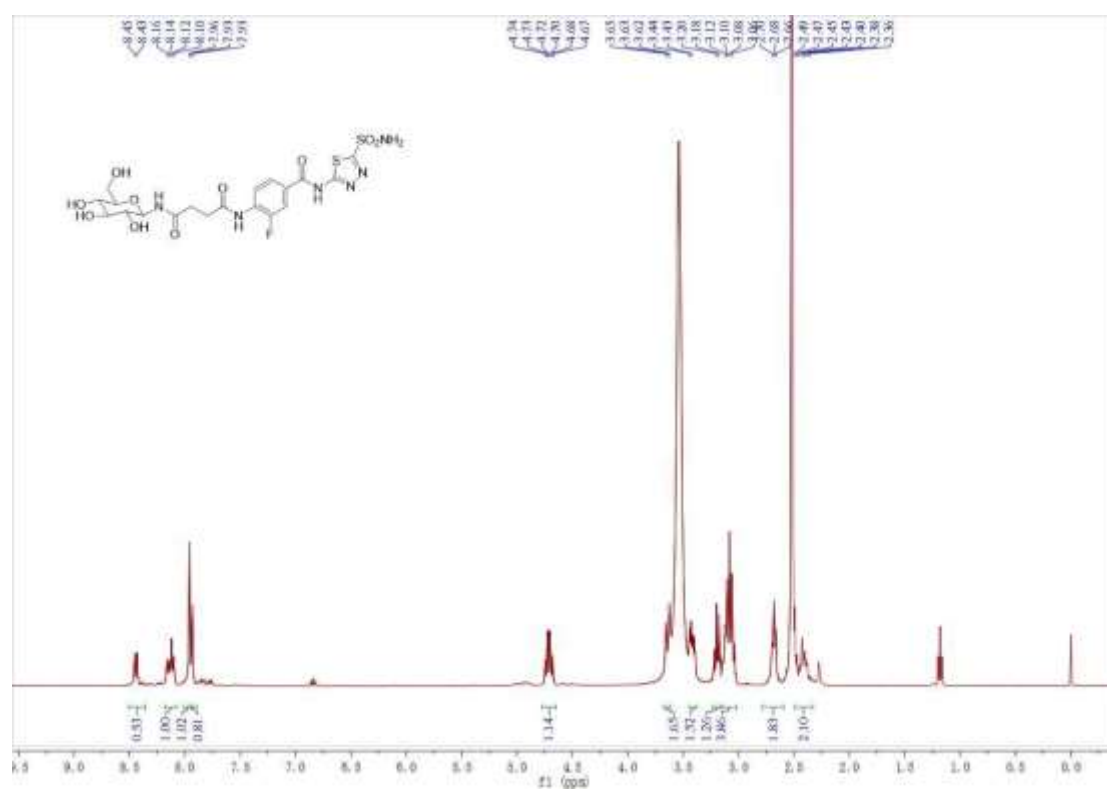


Figure S59. The ¹H-NMR of compound 14k with D₂O-exchange.

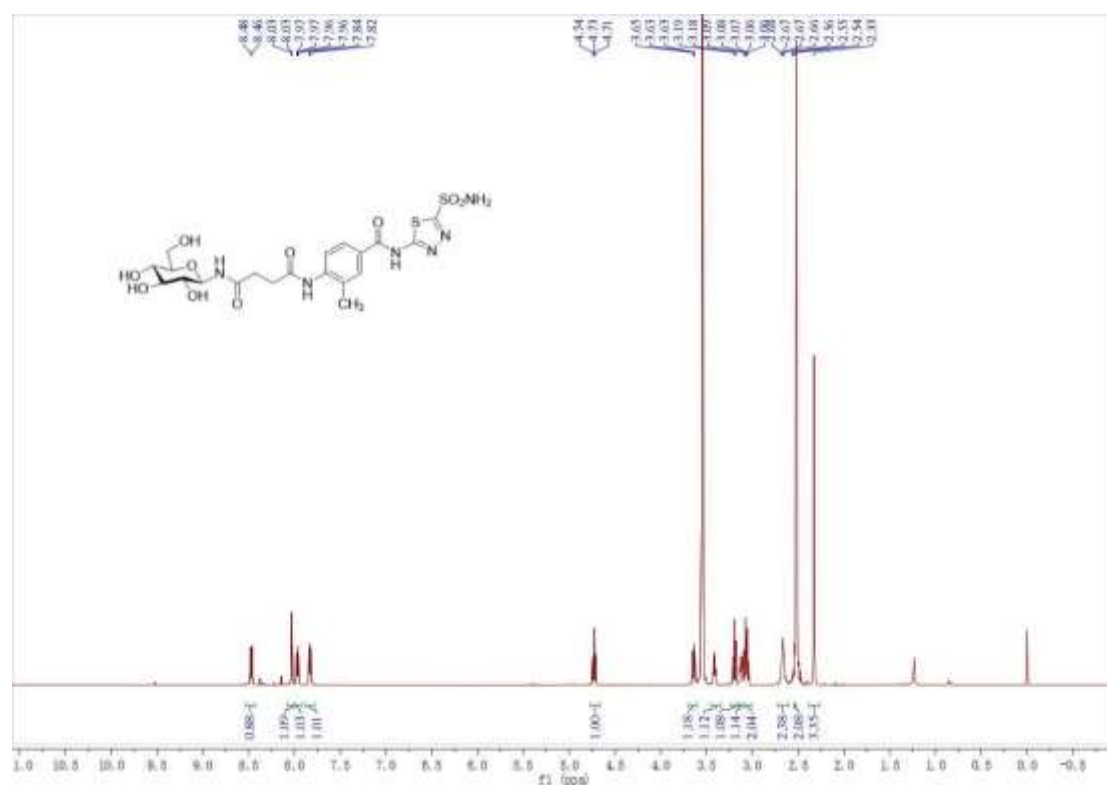


Figure S60. The ¹H-NMR of compound 14o with D₂O-exchange.

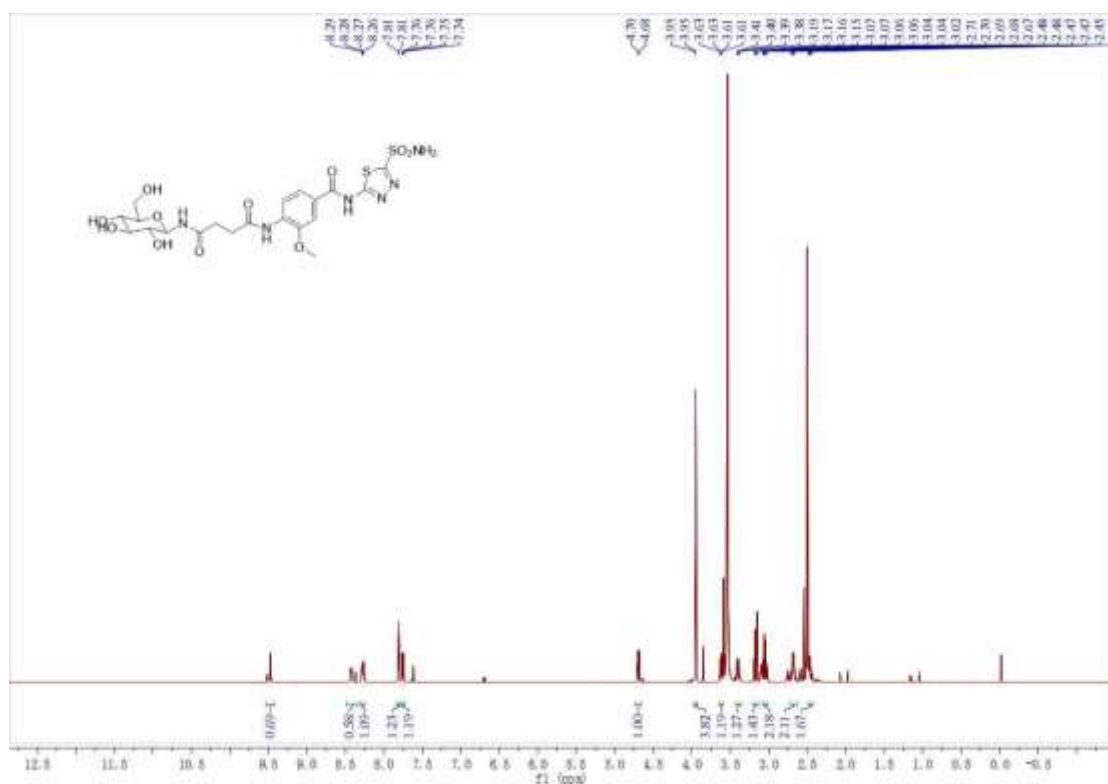


Figure S61. The ^1H -NMR of compound 14p with D_2O -exchange.

Modes of binding figures

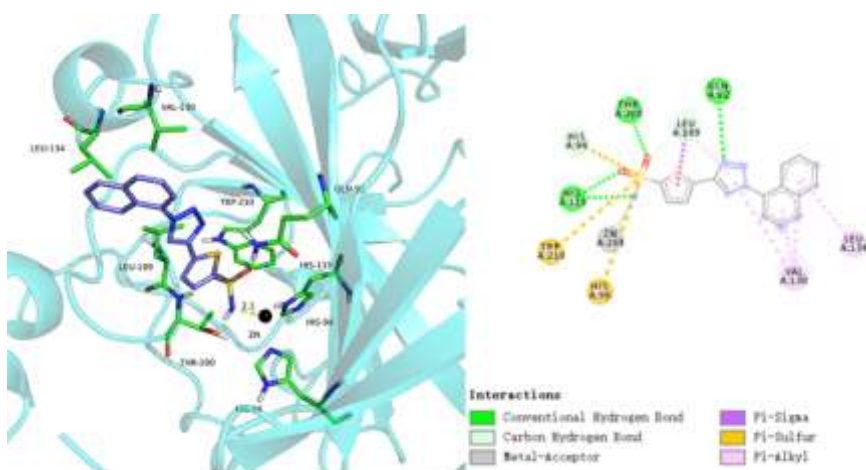


Figure S62. The modes of binding for co-crystal structure 5FL4 in CA IX.

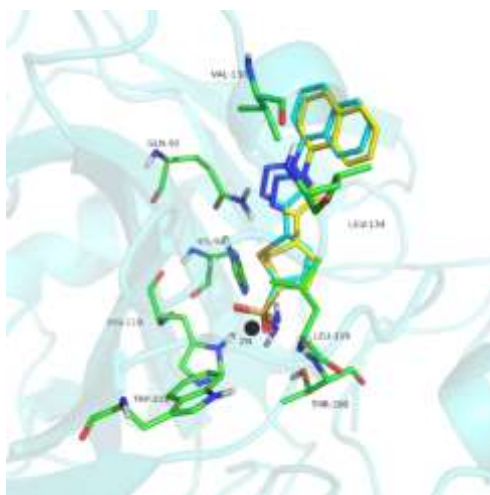


Figure S63. Co-crystallized pose (yellow) and the re-docked pose (blue) of 5FL4.

Supplementary data

Table S1. Binding energy, hydrogen bonding interacting residues, H-binding distance, hydrophobic interacting residues of 14a, 14e and 14i.

Compound	binding energy	hydrogen bonding interacting residues	H-binding distance (Å)	hydrophobic interacting residues
14a	-4.543	Gln71	2.28856	His68 His94 His96 Leu199
		Gln92	3.08217	
		His119	2.75462	
		His119	2.55636	
		Thr200	1.78295	
14e	-3.130	Gln71	1.80873	His94 His94 Leu199
		His119	2.67012	
		Thr200	1.82586	
		Thr201	2.74211	
		Thr201	3.02351	
14i	-4.508	Gln71	1.8855	His94 His96 Val121 Leu199
		Gln92	2.25552	
		Gln92	2.62697	
		Thr200	1.8108	
		Thr201	2.76773	
		Asp131	2.03706	
		Asp131	2.04039	

Table S2. The IC₅₀ of Taxol

Compound	HT-29	MDA-MB-231
Taxol	111 ng/mL	99 ng/mL

Table S3. The calculated ADMET information of some compounds

Compounds	ADMET Solubility	ADMET Solubility Level	ADMET BBB Level	ADMET Absorption Level	ADMET clogP
14a	-4.668	2	4	3	-2.069
14b	-4.784	2	4	3	-2.069
14c	-5.6	2	4	3	-1.864
14g	-5.079	2	4	3	-1.583
14i	-5.23	2	4	3	-2.086
14j	-4.565	2	4	3	-2.526
14h	-4.675	2	4	3	-2.526
14p	-5.146	2	4	3	-2.542