

## Supporting Information

### Discovery of Dibenzylbutane Lignan LCA Derivatives as Potent Anti-inflammatory Agents

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# 1. $^1\text{H}$ NMR and $^{13}\text{C}$ NMR spectrum of compound 2

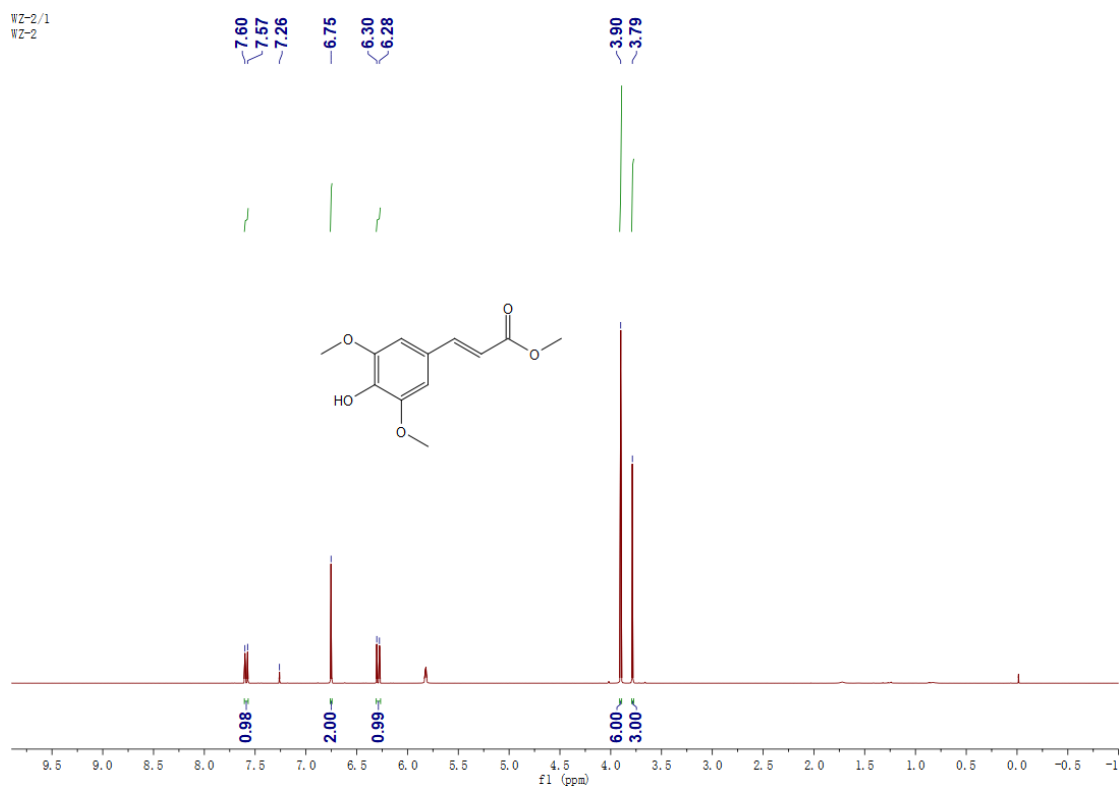


Figure S1.  $^1\text{H}$  NMR spectrum of compound 2

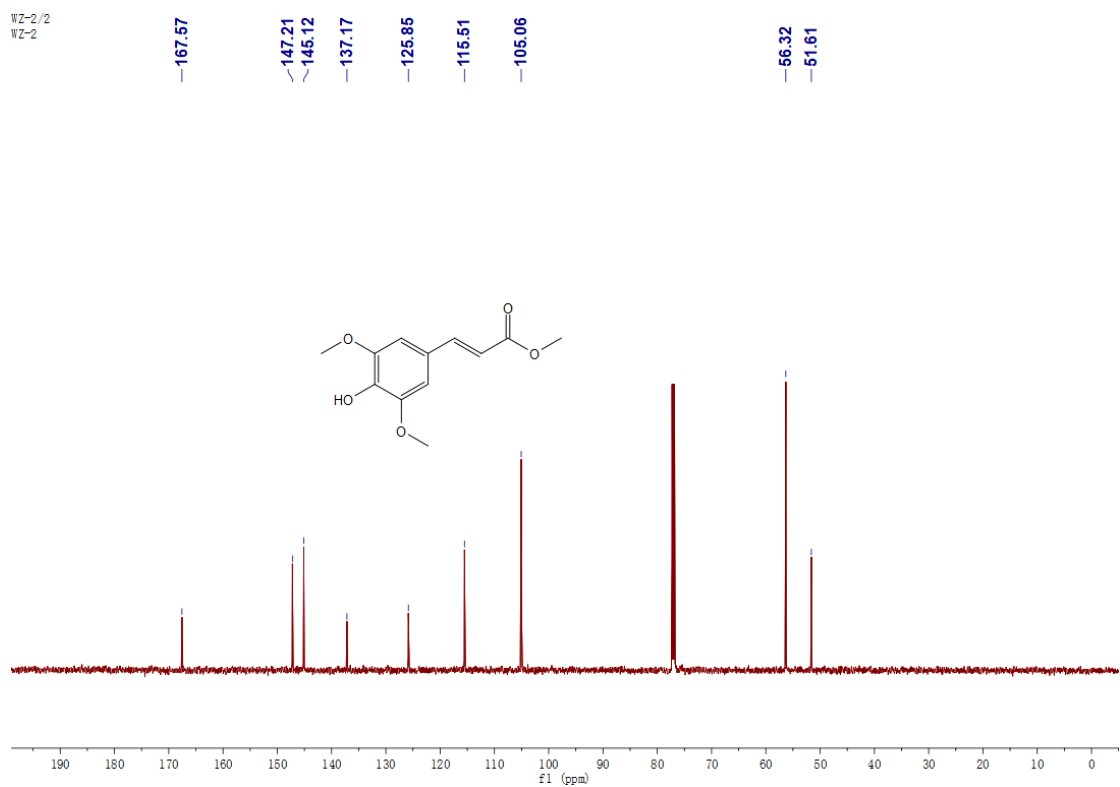


Figure S2.  $^{13}\text{C}$  NMR spectrum of compound 2

## 2. $^1\text{H}$ NMR and $^{13}\text{C}$ NMR spectrum of compound 3

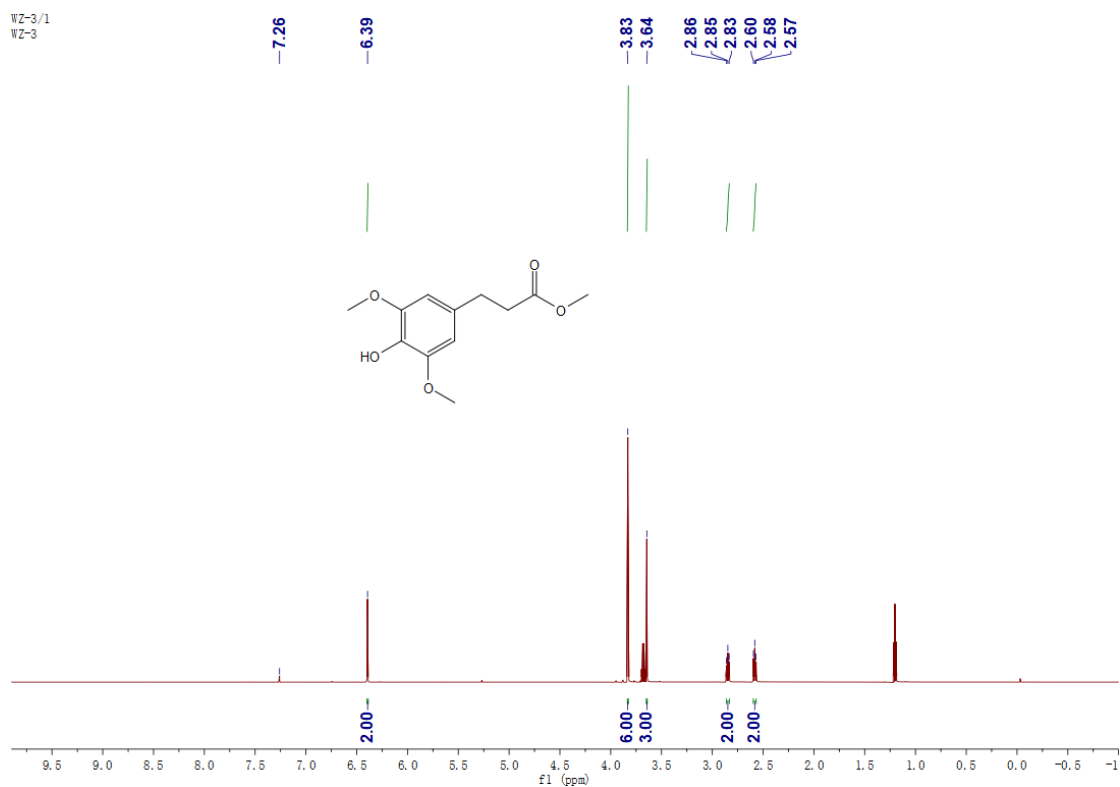


Figure S3.  $^1\text{H}$  NMR spectrum of compound 3

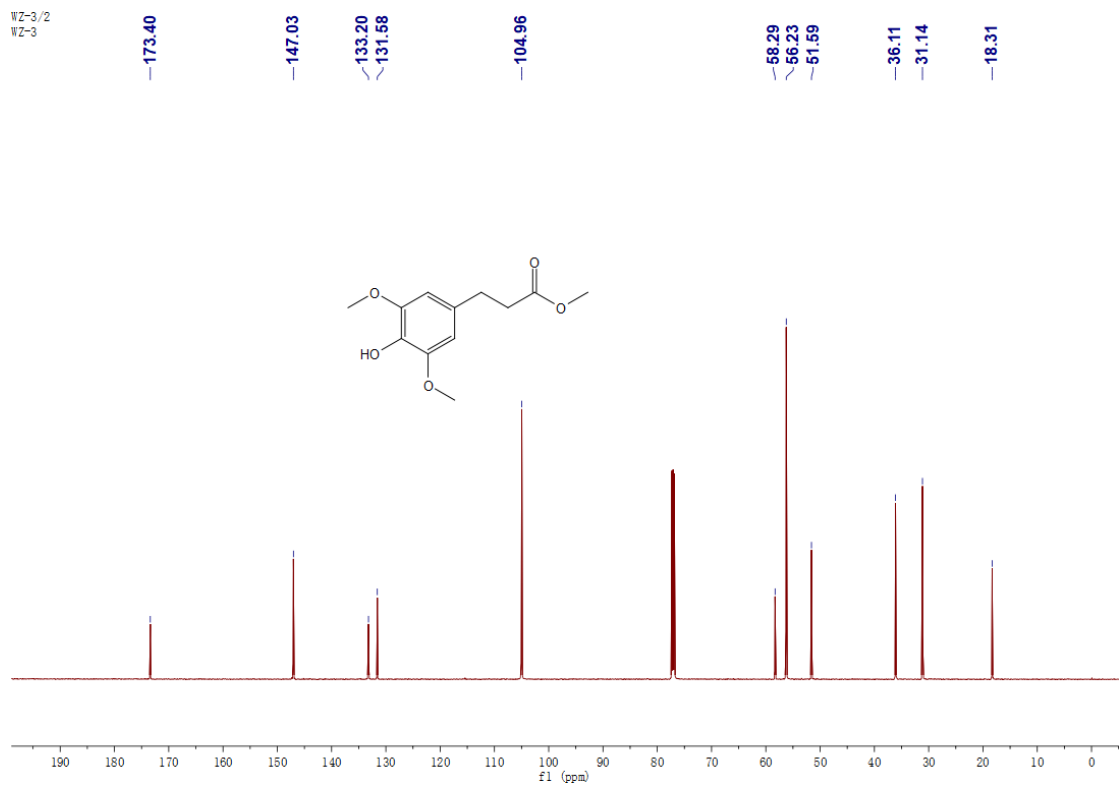


Figure S4.  $^{13}\text{C}$  NMR spectrum of compound 3

### 3. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 4



Figure S5.  $^1\text{H}$  NMR spectrum of compound 4

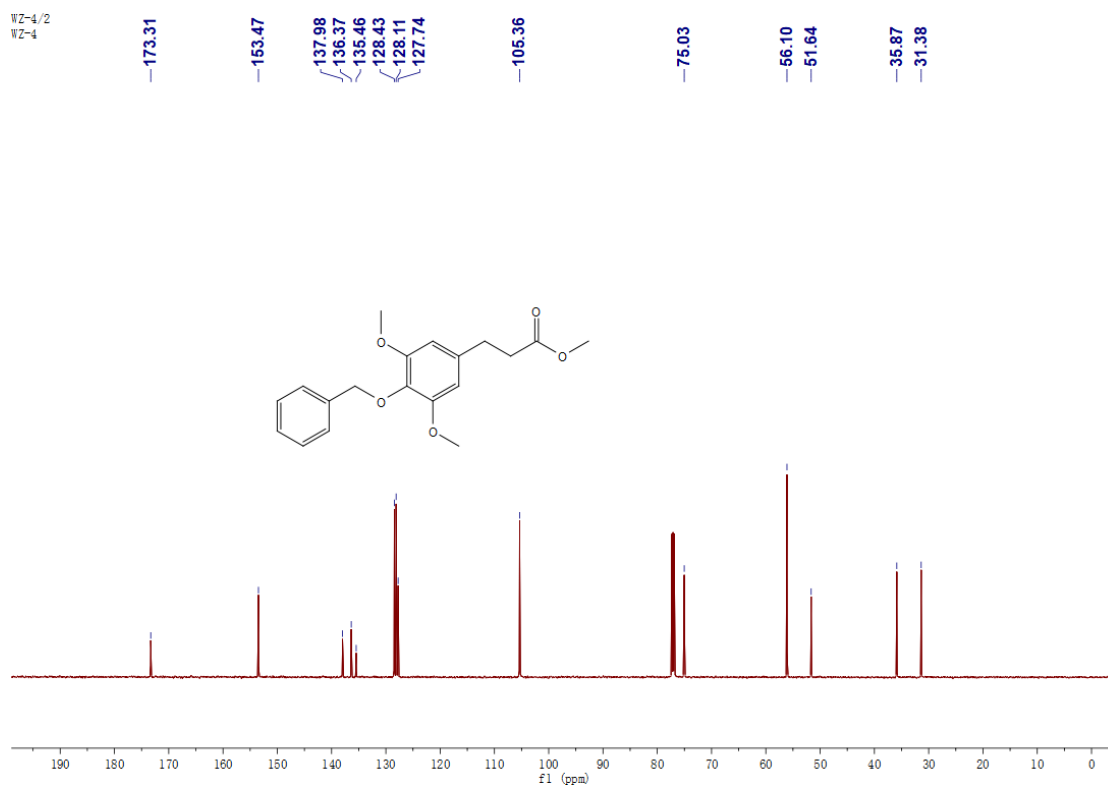


Figure S6.  $^{13}\text{C}$  NMR spectrum of compound 4

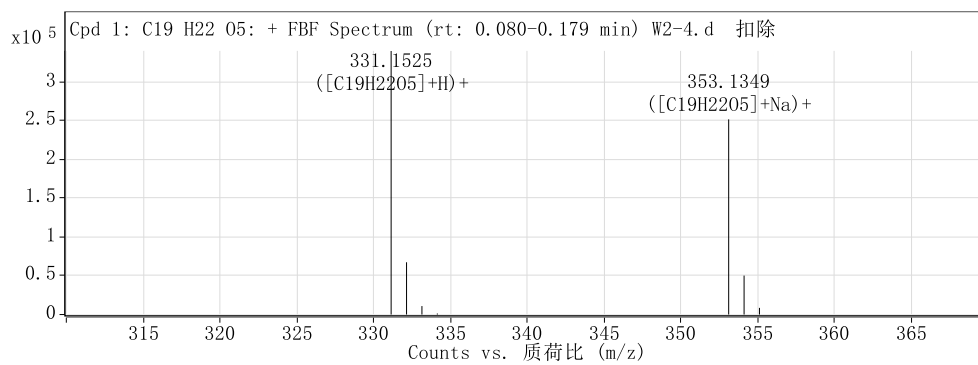


Figure S7. HRMS spectrum of compound 4

#### 4. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 5

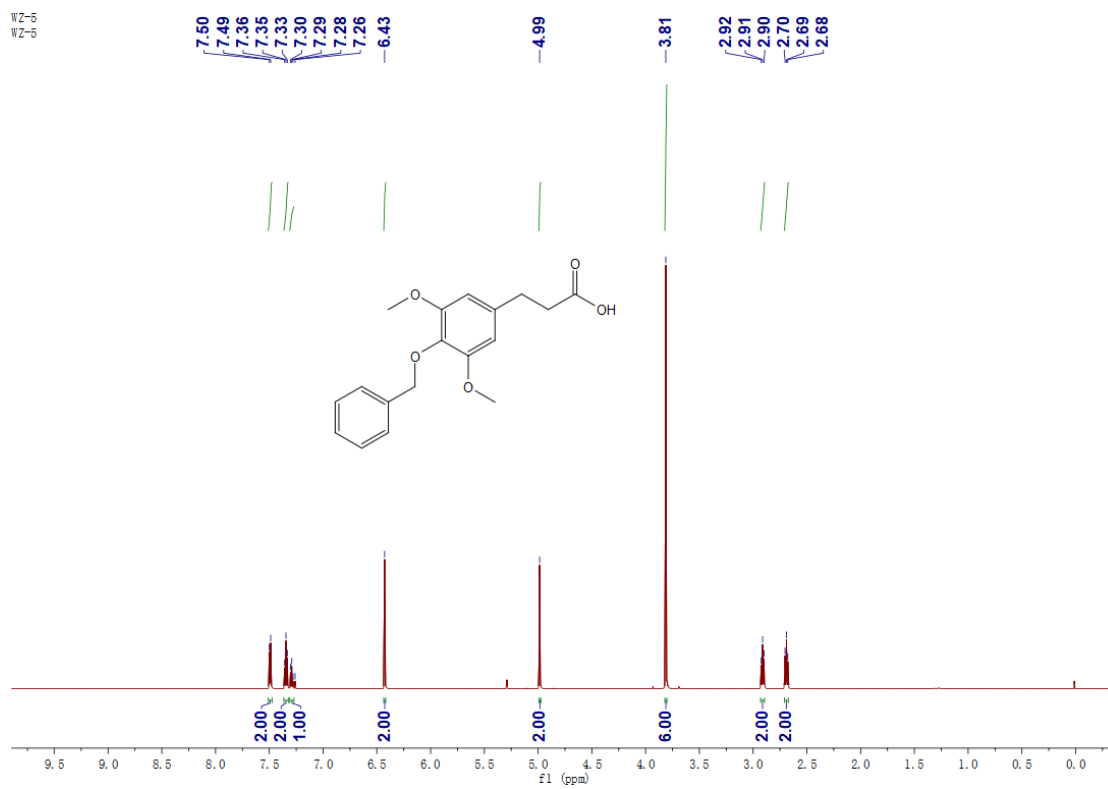


Figure S8. <sup>1</sup>H NMR spectrum of compound 5

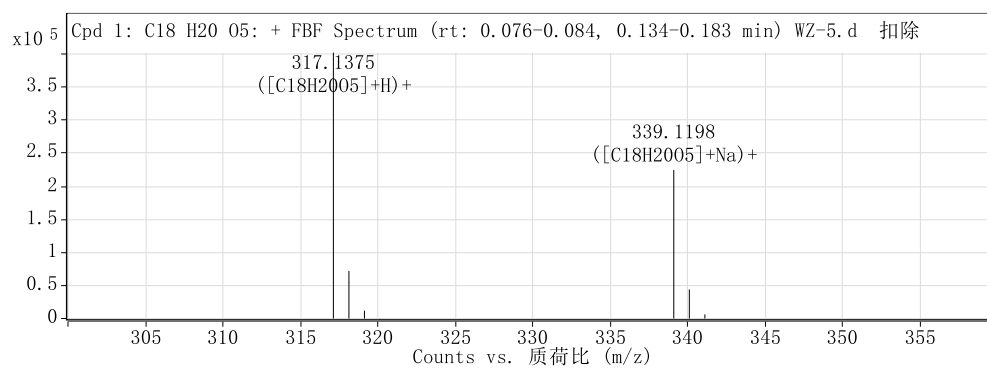
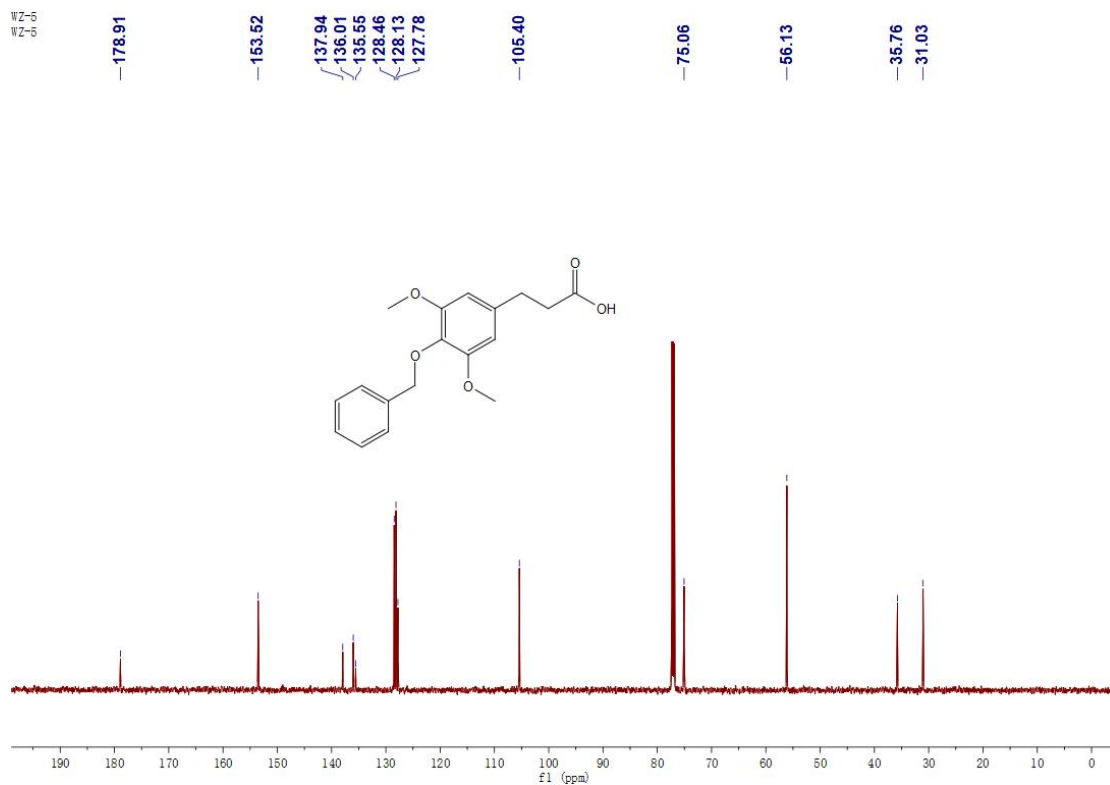


Figure S10. HRMS spectrum of compound 5



## 5. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 6

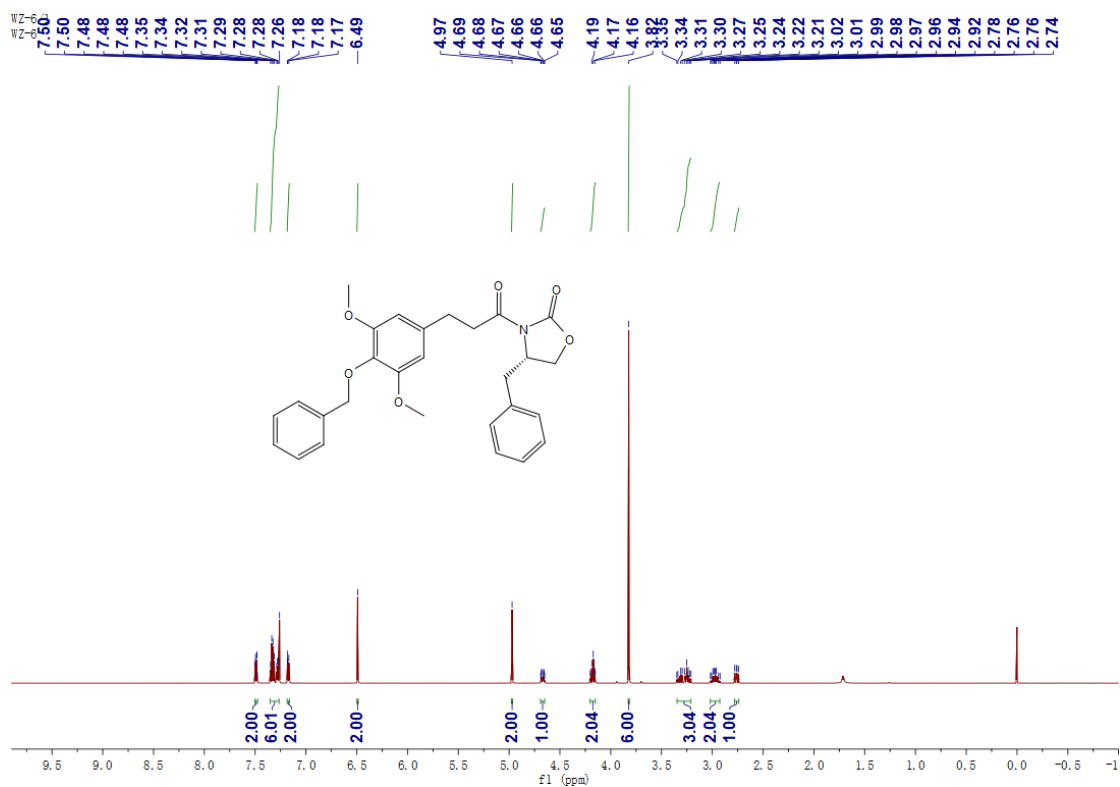


Figure S11.  $^1\text{H}$  NMR spectrum of compound 6

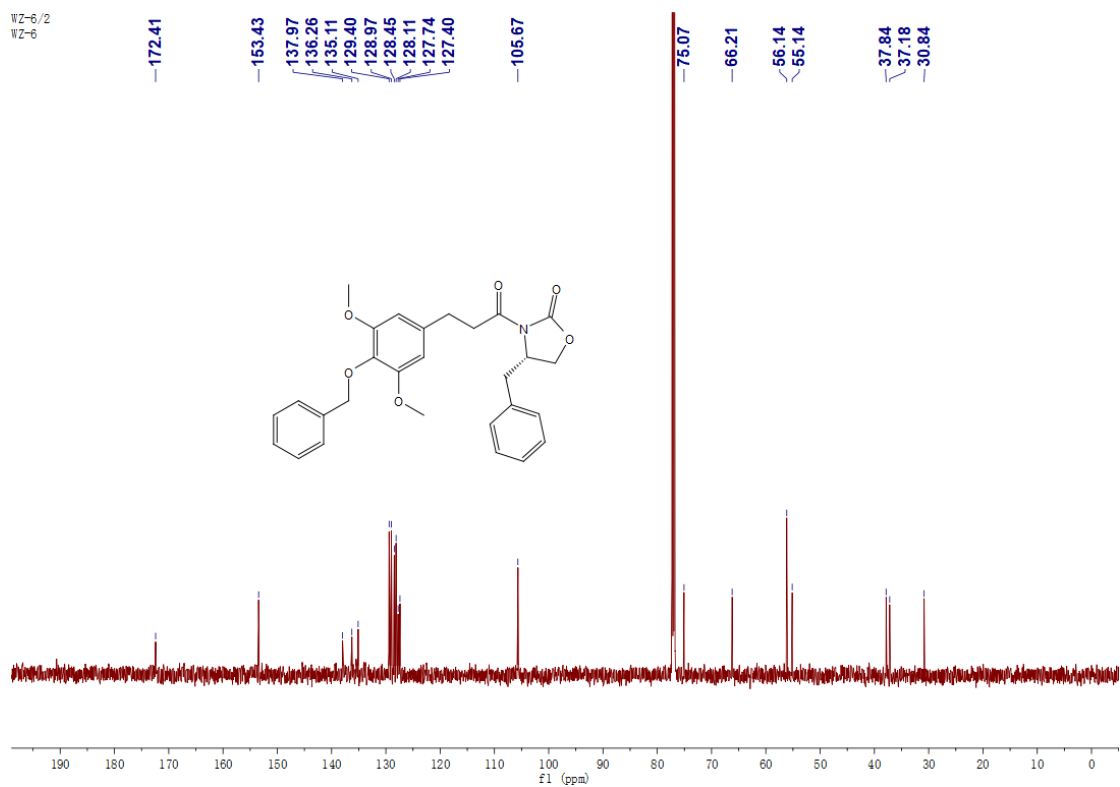


Figure S12.  $^{13}\text{C}$  NMR spectrum of compound 6

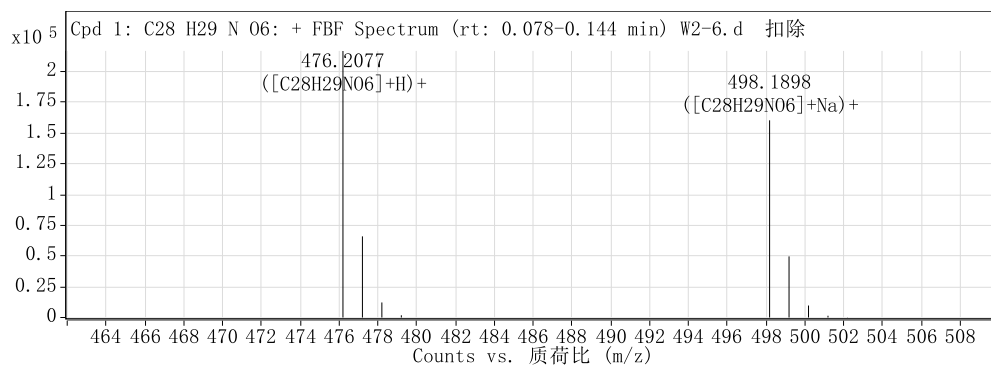


Figure S13. HRMS spectrum of compound 6

## 6. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectrum of compound 7

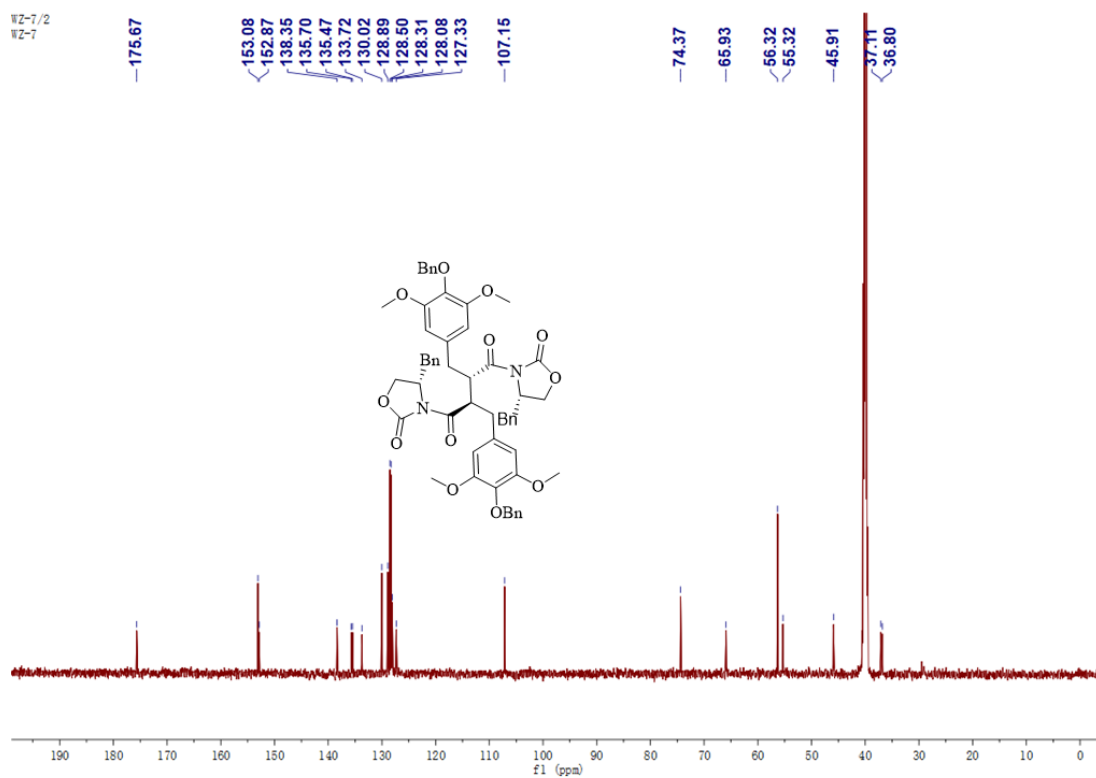


Figure S14. <sup>13</sup>C NMR spectrum of compound 7

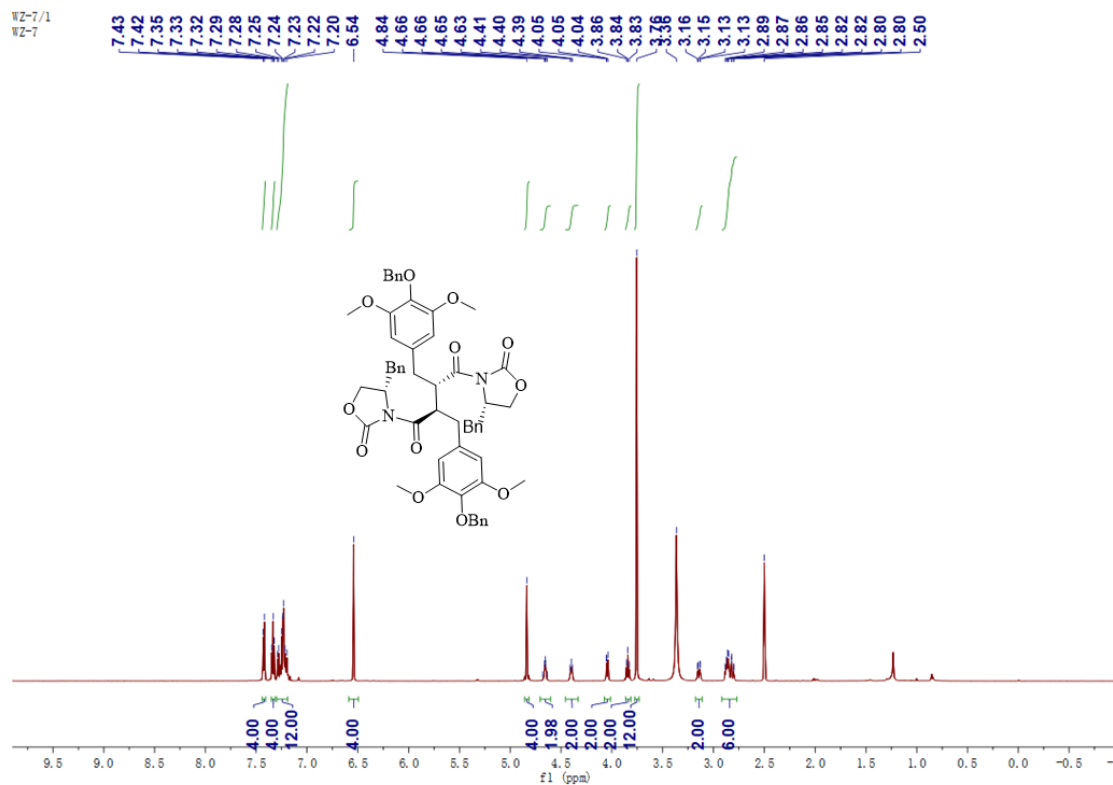


Figure S15.  $^{13}\text{C}$  NMR spectrum of compound 7

### 7. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 8

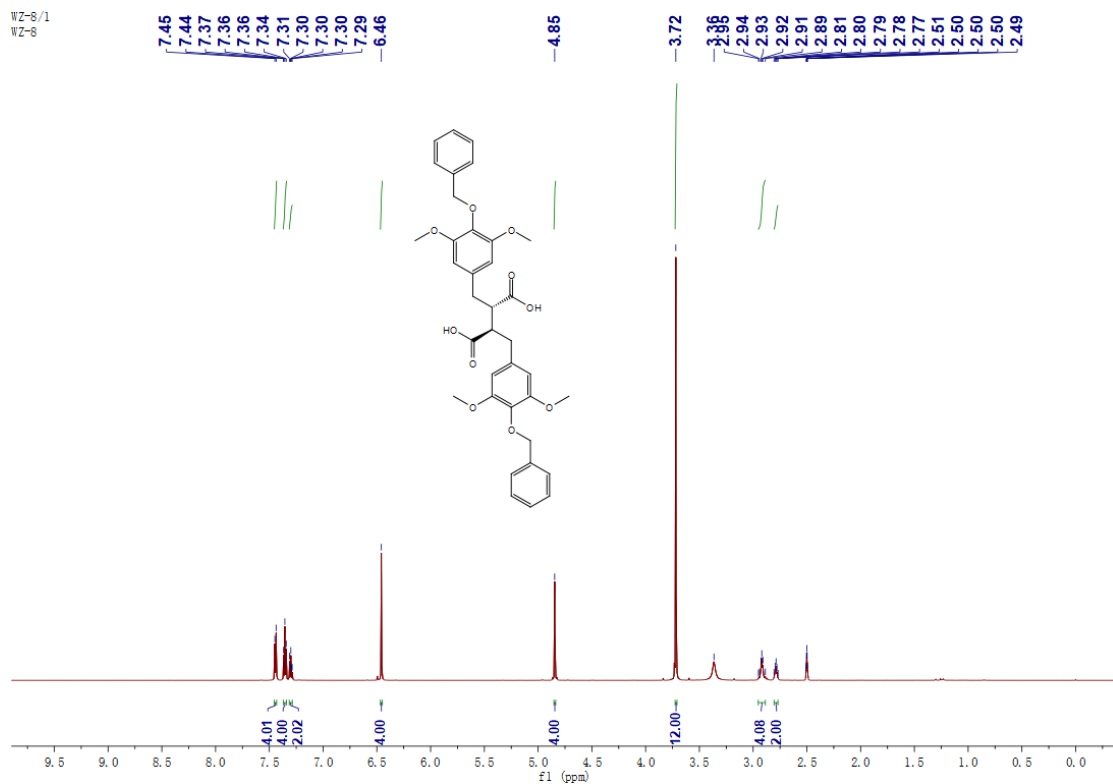
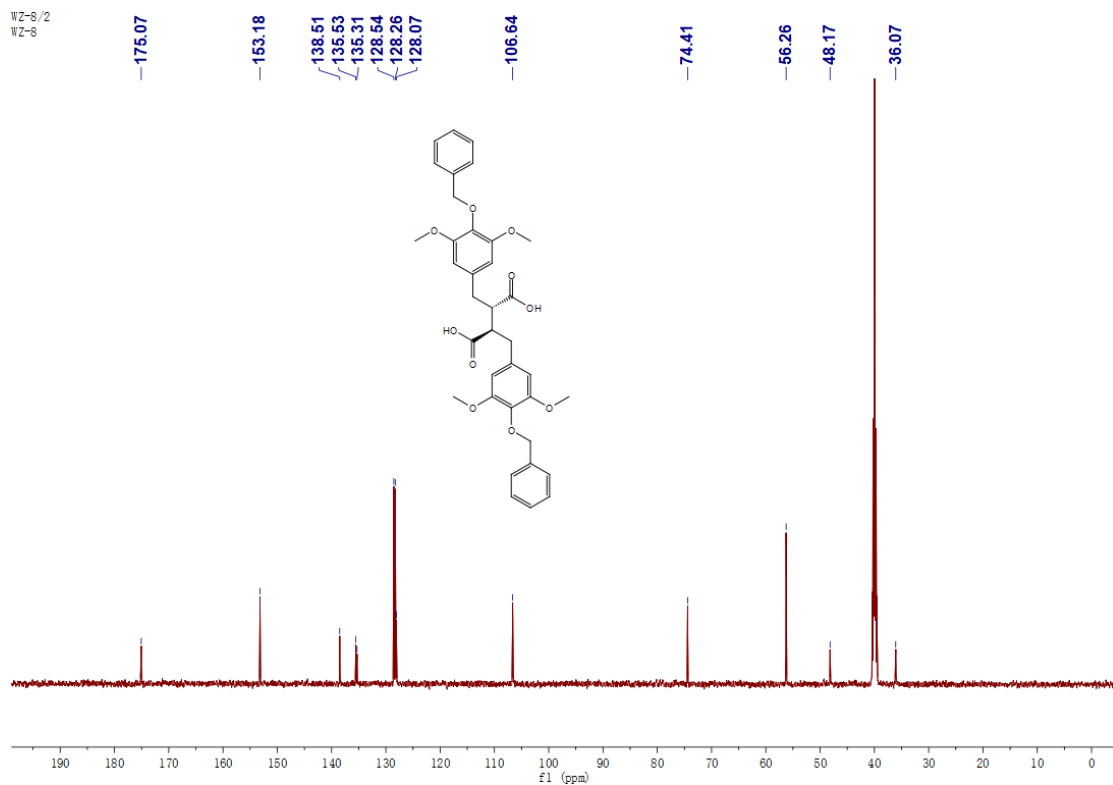
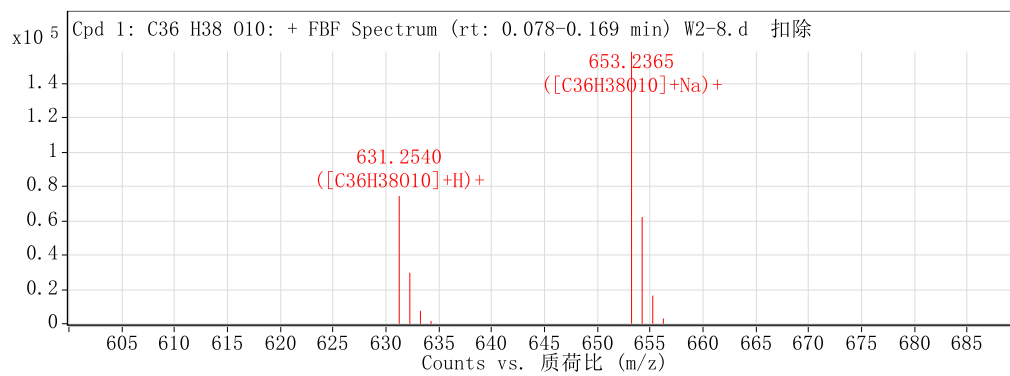


Figure S16.  $^1\text{H}$  NMR spectrum of compound 8



**Figure S17.**  $^{13}\text{C}$  NMR spectrum of compound **8**



**Figure S18.** HRMS spectrum of compound **8**

## 8. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 10a

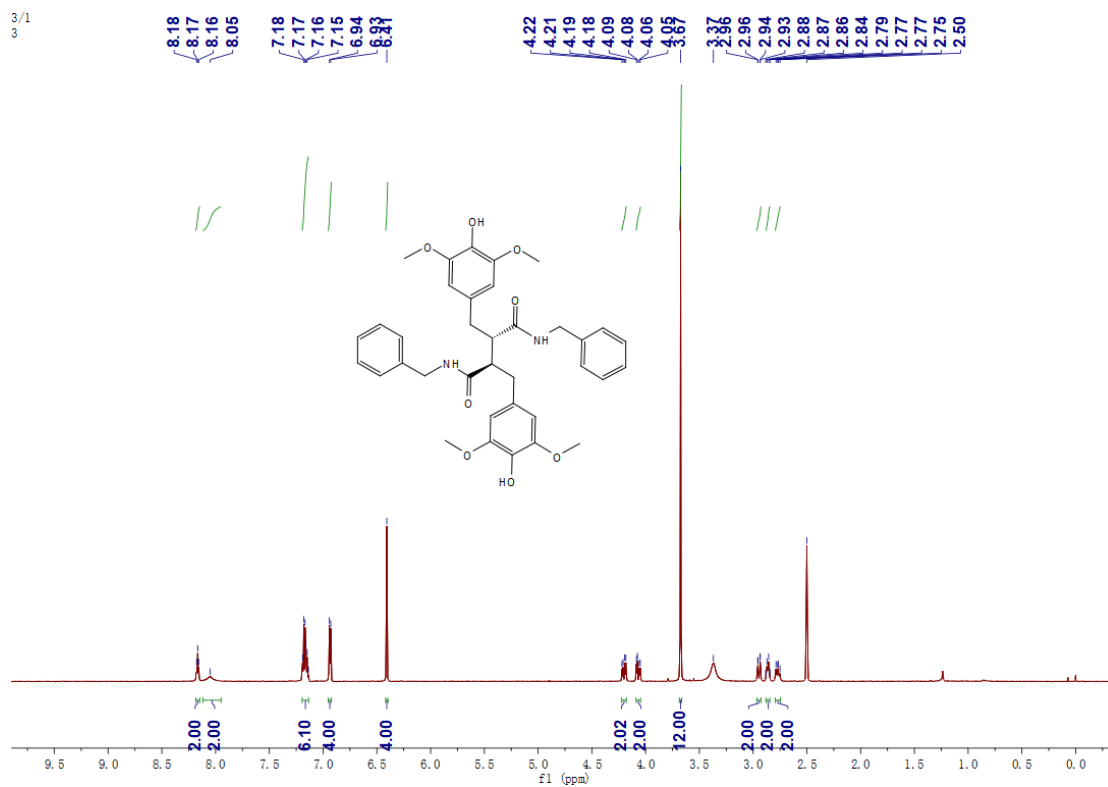


Figure S19.  $^1\text{H}$  NMR spectrum of compound 10a

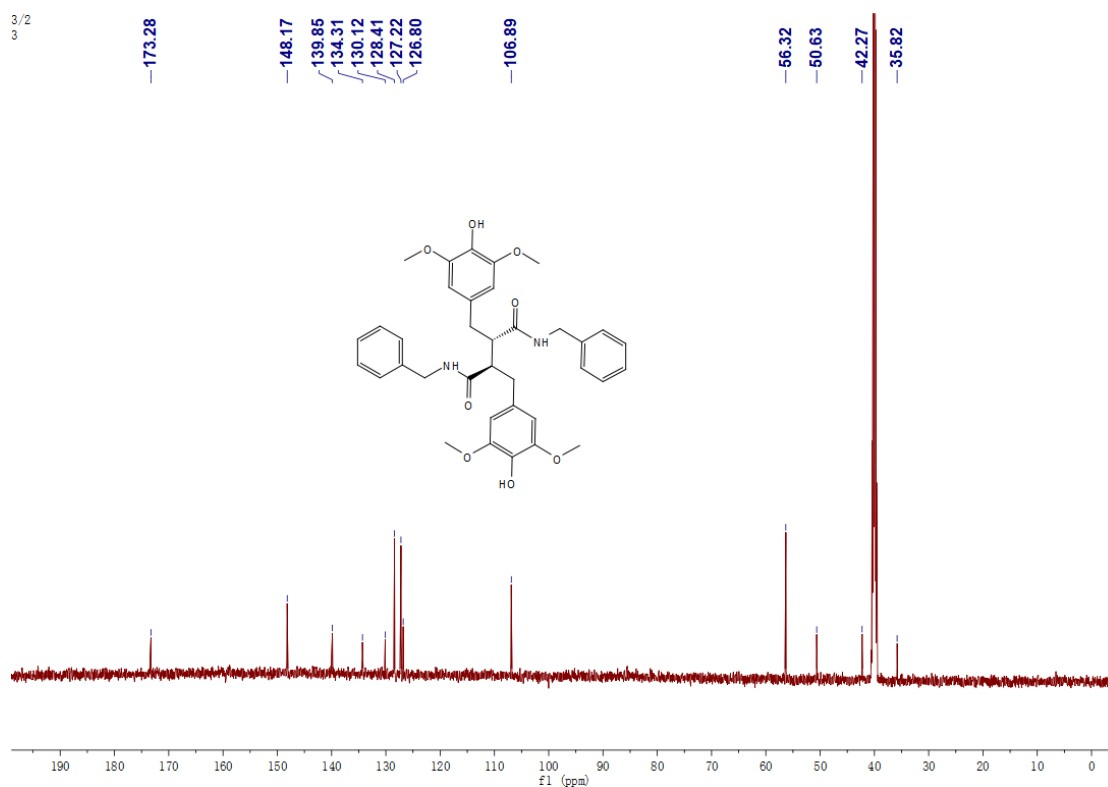


Figure S20.  $^{13}\text{C}$  NMR spectrum of compound 10a

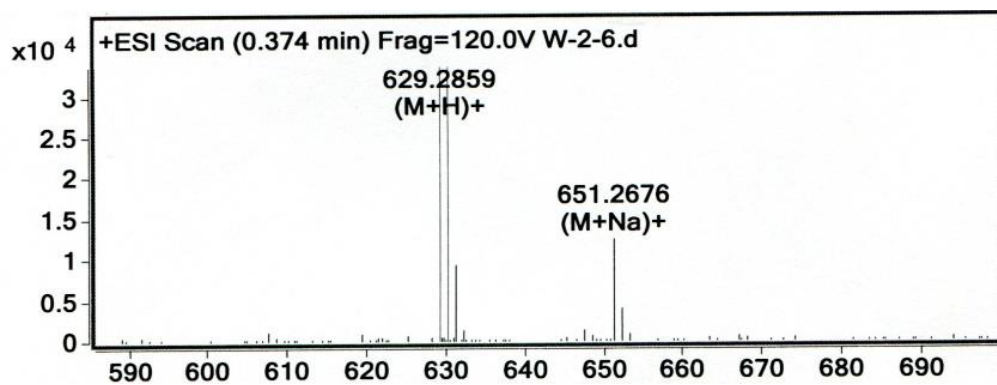


Figure S21. HRMS spectrum of compound 10a

9. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10b

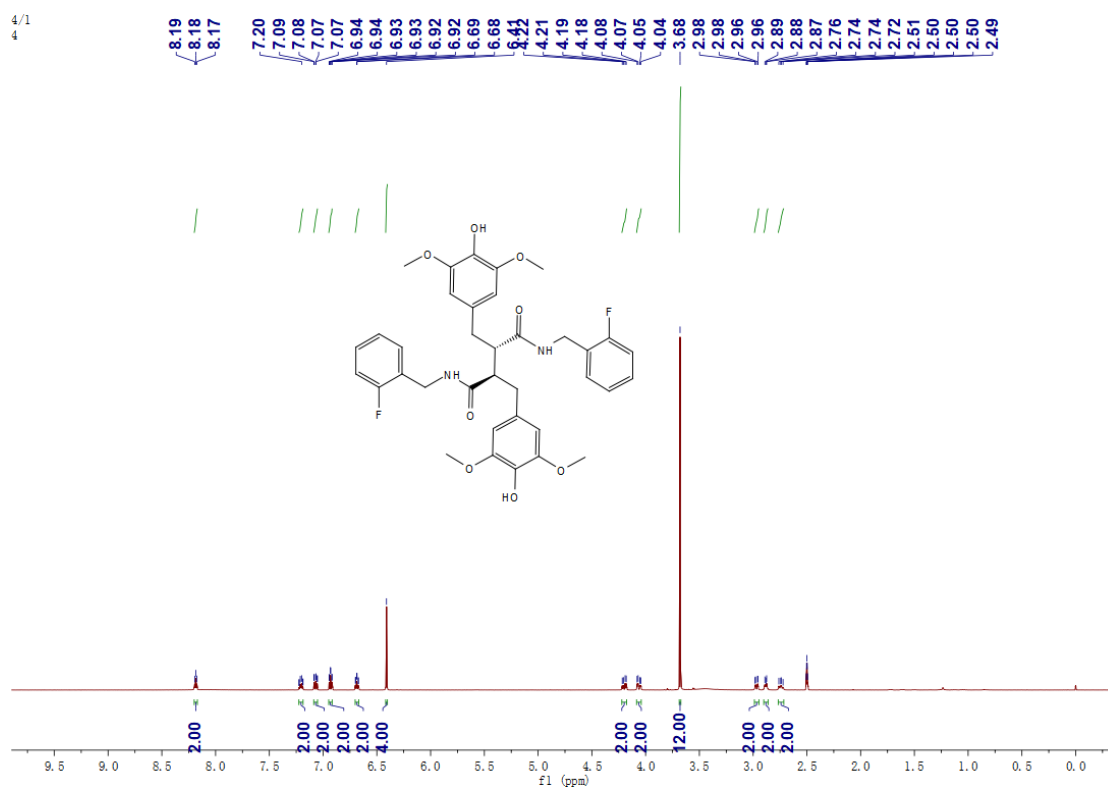


Figure S22. <sup>1</sup>H NMR spectrum of compound 10b

4/2  
4

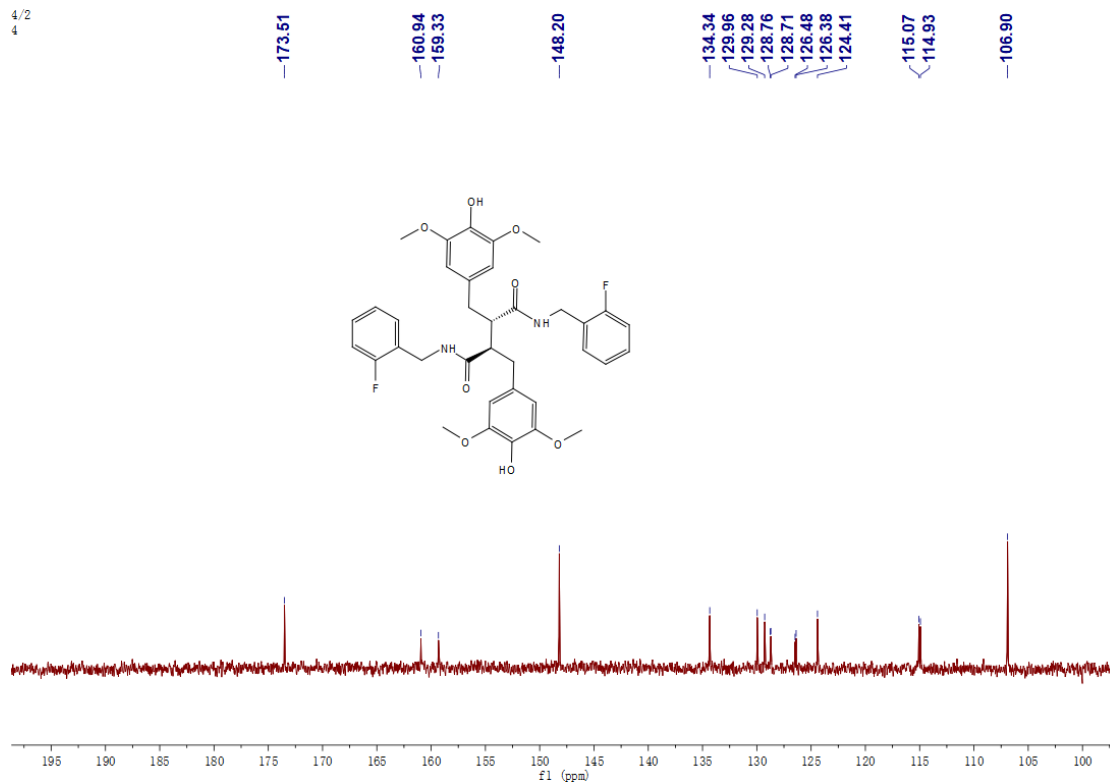


Figure S23. <sup>13</sup>C NMR spectrum of compound 10b

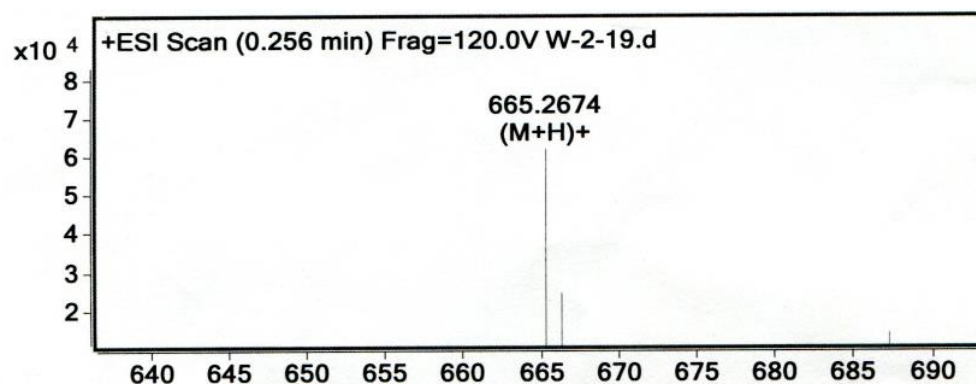
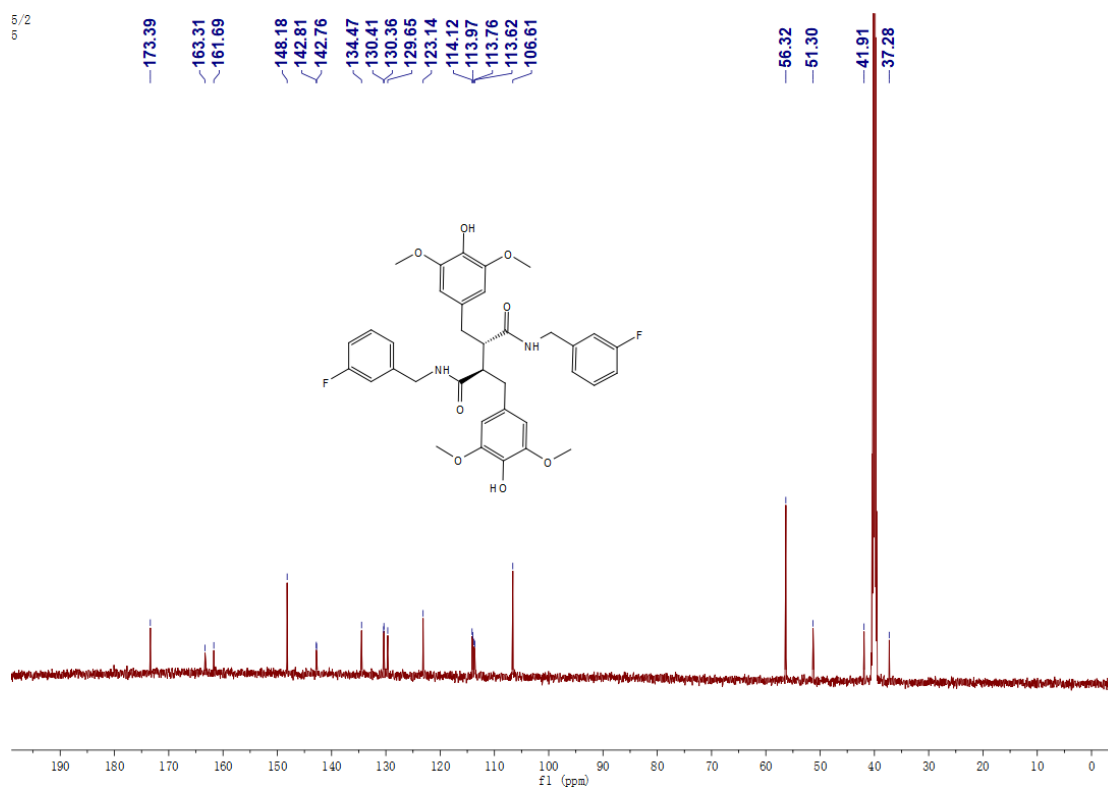
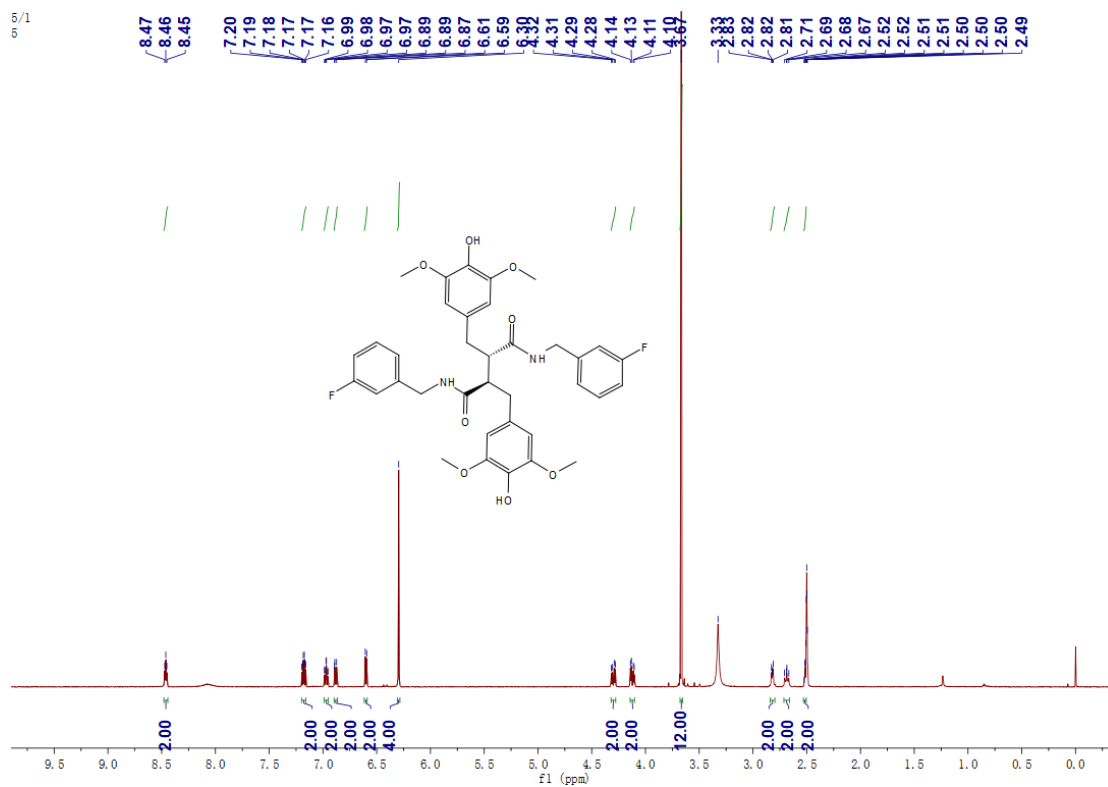


Figure S24. HRMS spectrum of compound 10b

## 10. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10c





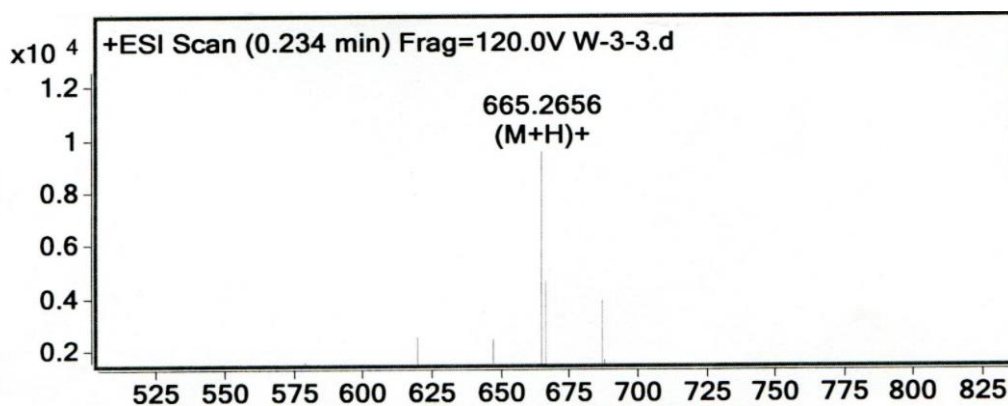


Figure S27. HRMS spectrum of compound 10c

11. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10d

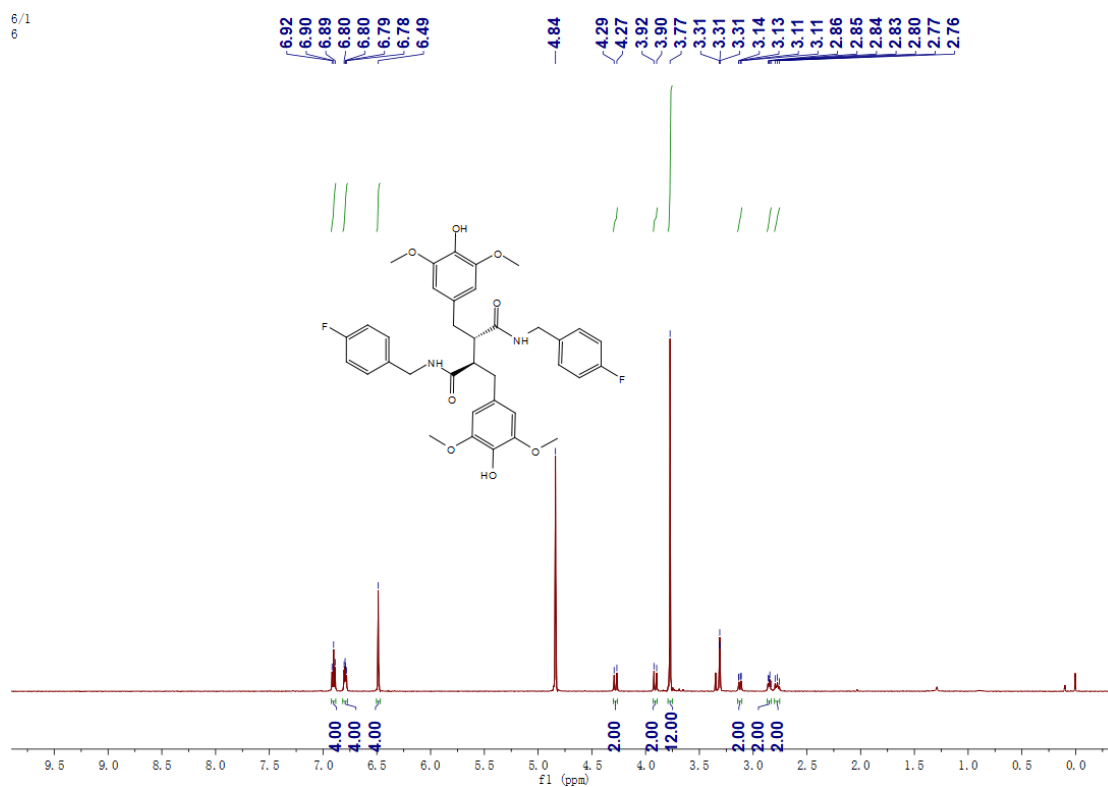
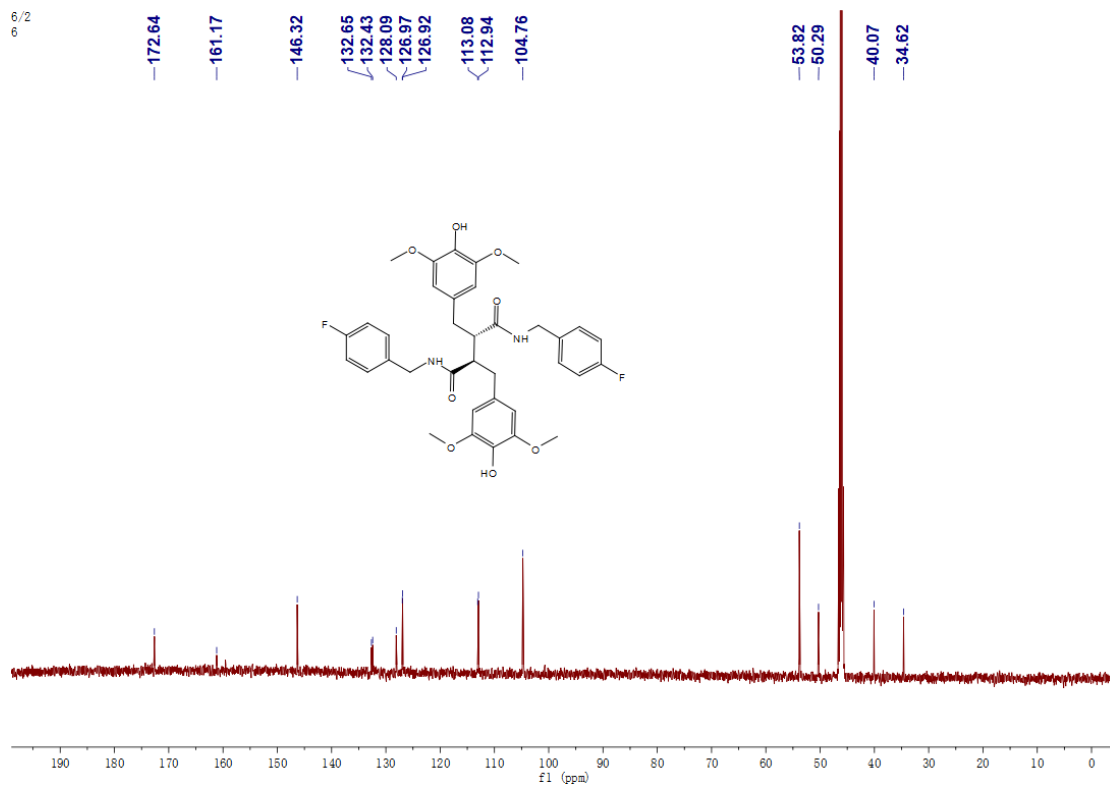
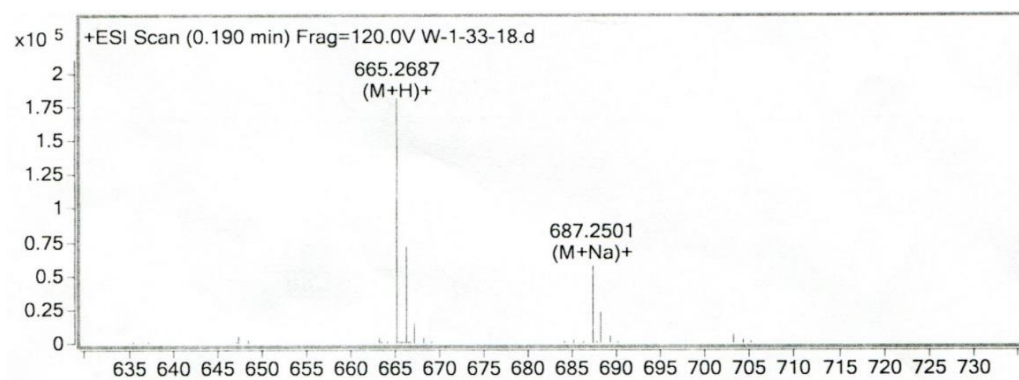


Figure S28. <sup>1</sup>H NMR spectrum of compound 10d

6/2  
6



**Figure S29.** <sup>13</sup>C NMR spectrum of compound **10d**



**Figure S30.** HRMS spectrum of compound **10d**

## 12. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10e

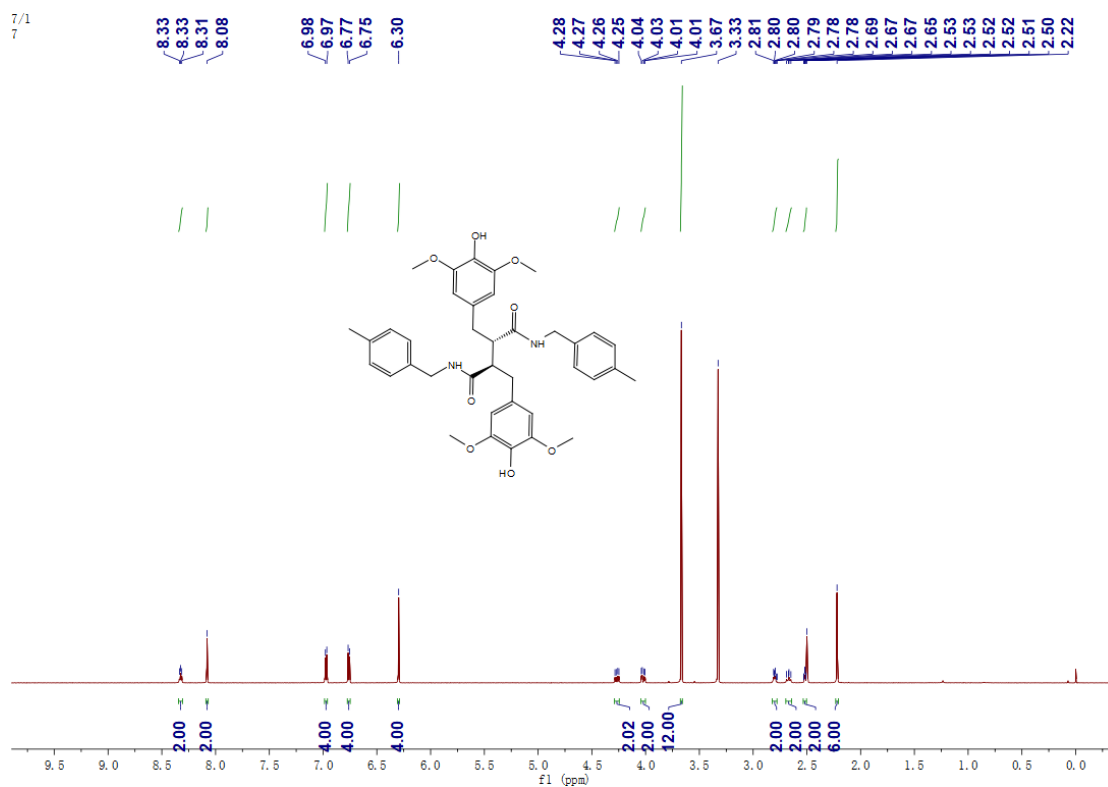


Figure S31. <sup>1</sup>H NMR spectrum of compound 10e

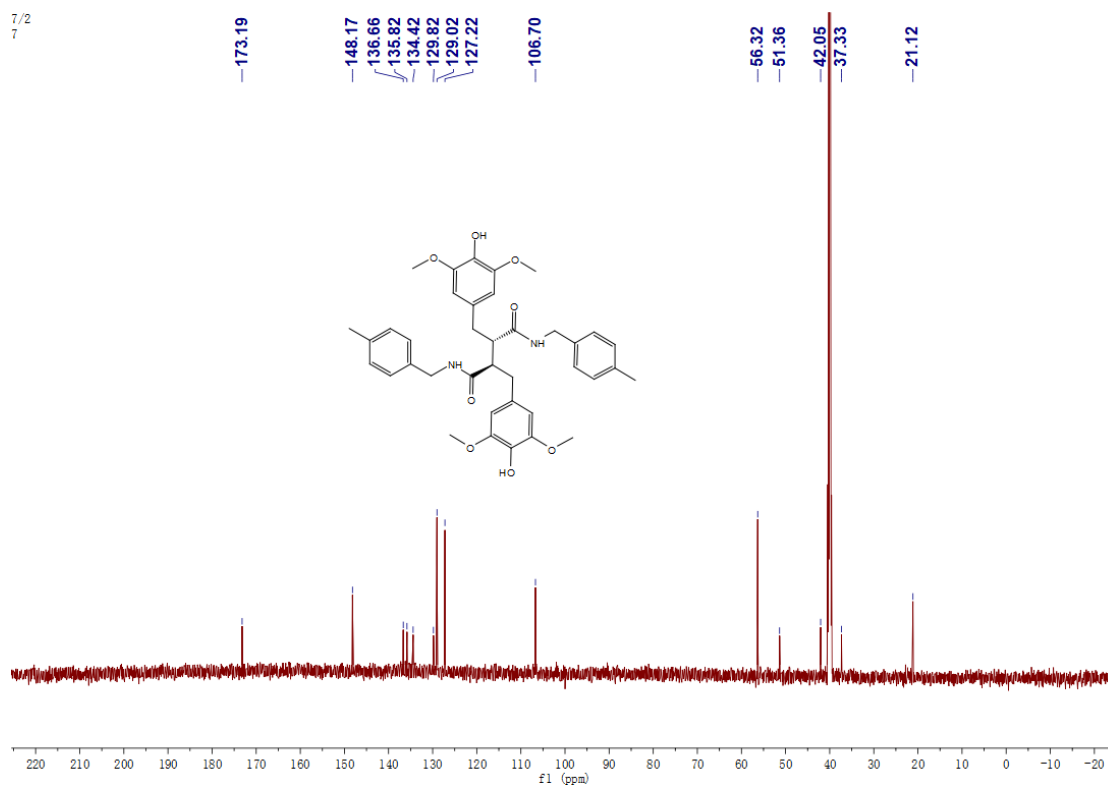


Figure S32. <sup>13</sup>C NMR spectrum of compound 10e

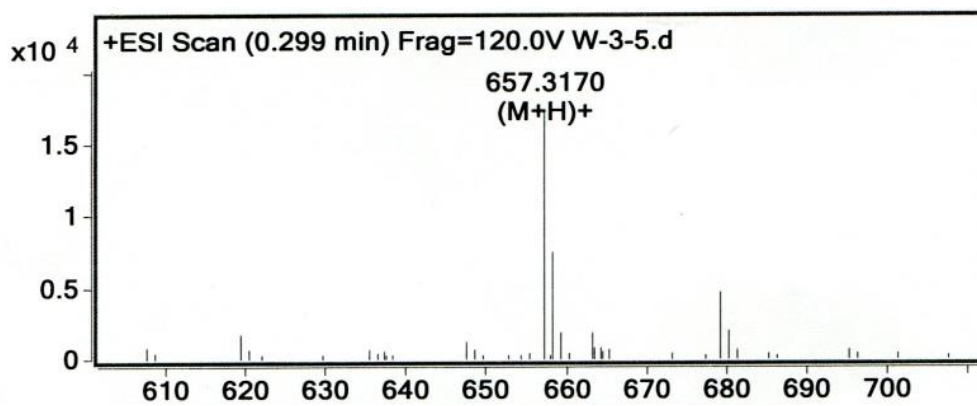


Figure S33. HRMS spectrum of compound 10e

13. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10f

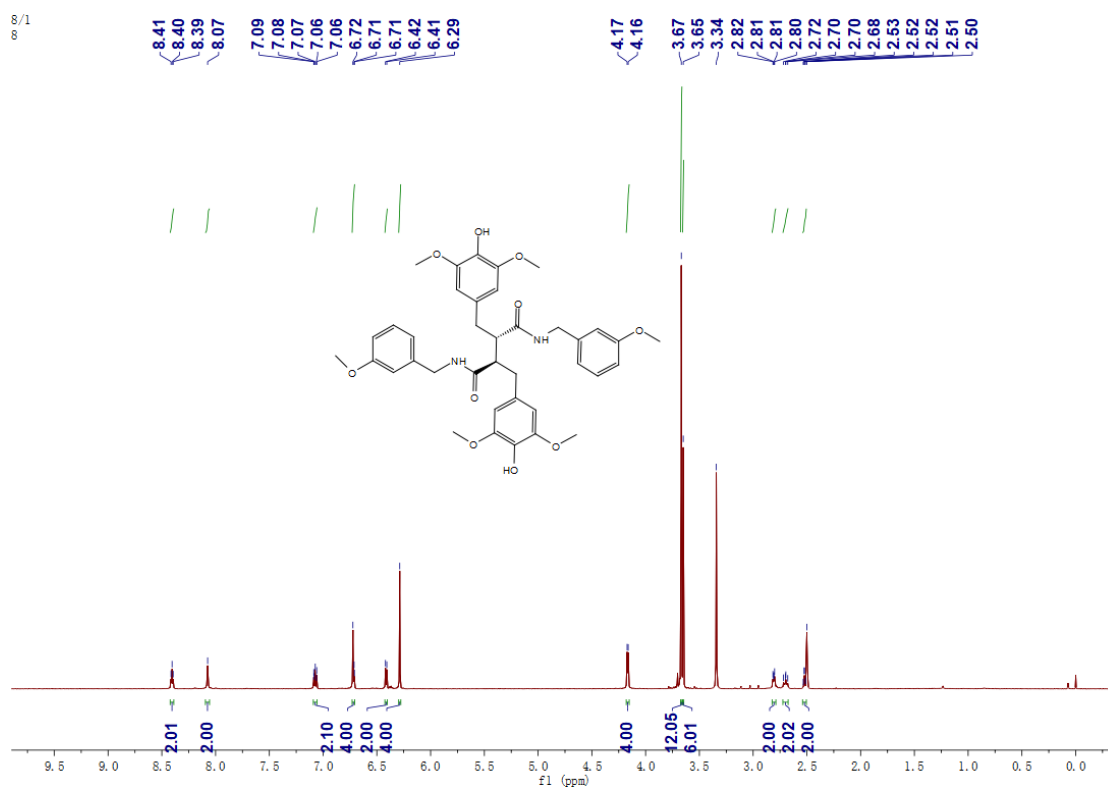


Figure S34. <sup>1</sup>H NMR spectrum of compound 10f

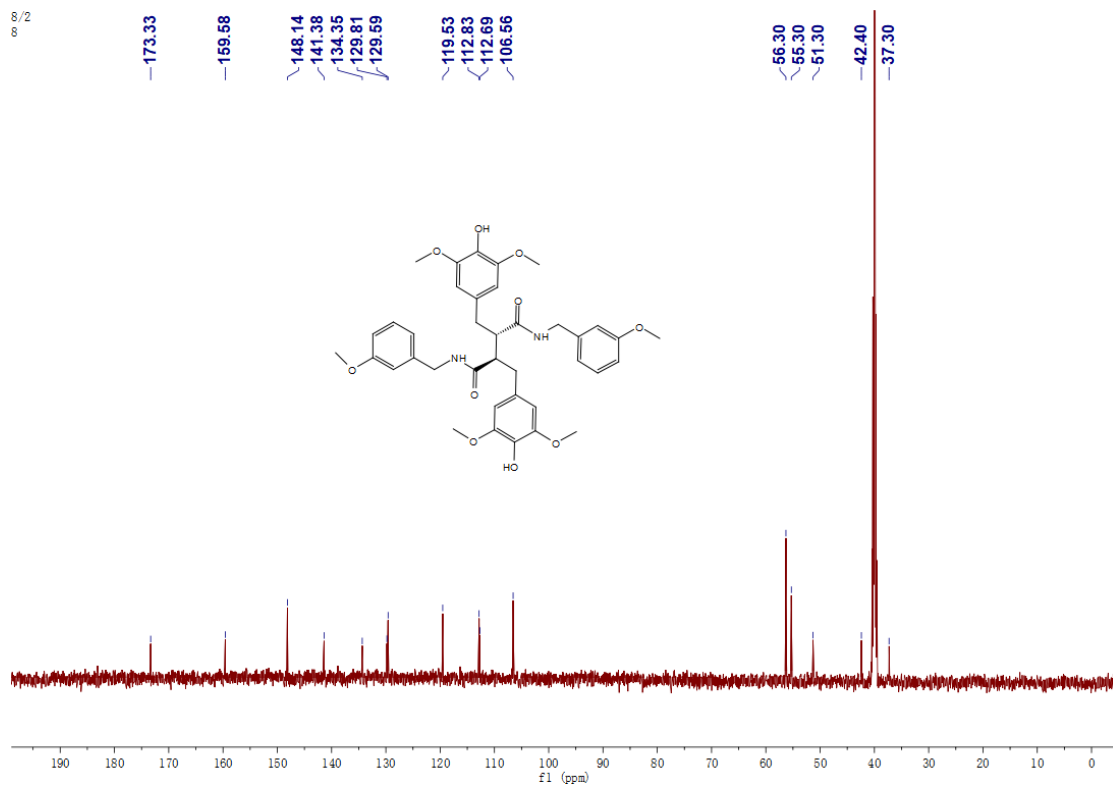


Figure S35 <sup>13</sup>C NMR spectrum of compound 10f

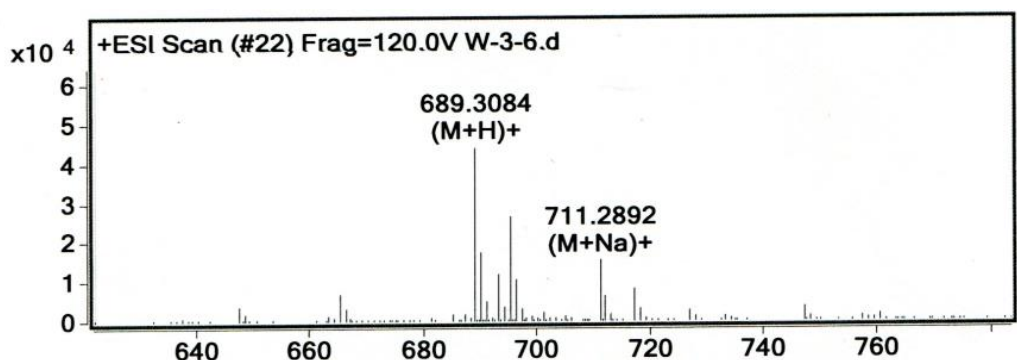


Figure S36 HRMS spectrum of compound 10f

# 14. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10g

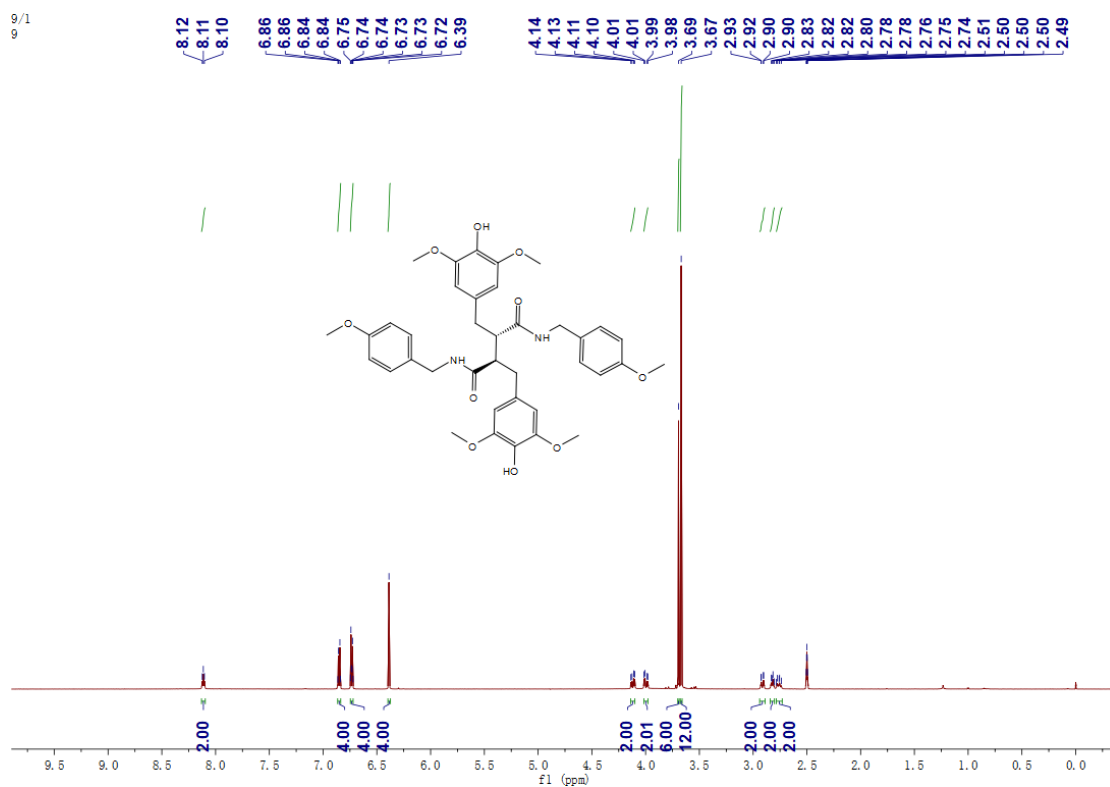


Figure S37 <sup>1</sup>H NMR spectrum of compound 10g

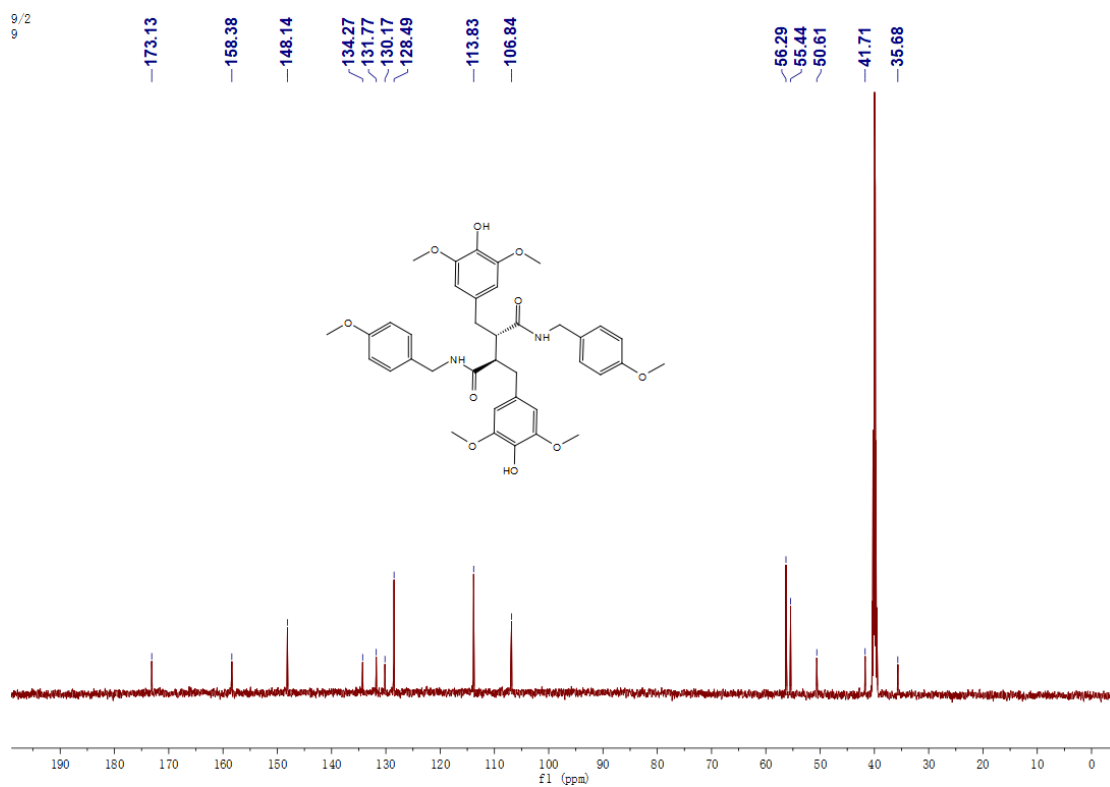


Figure S38 <sup>13</sup>C NMR spectrum of compound 10g

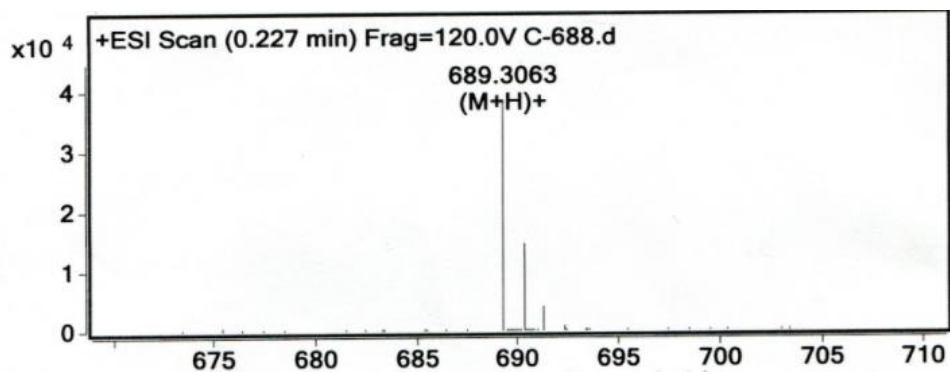


Figure S39 HRMS spectrum of compound 10g

15. <sup>1</sup>H NMR, <sup>13</sup>C NMR, <sup>19</sup>F NMR and HRMS spectrum of compound 10h

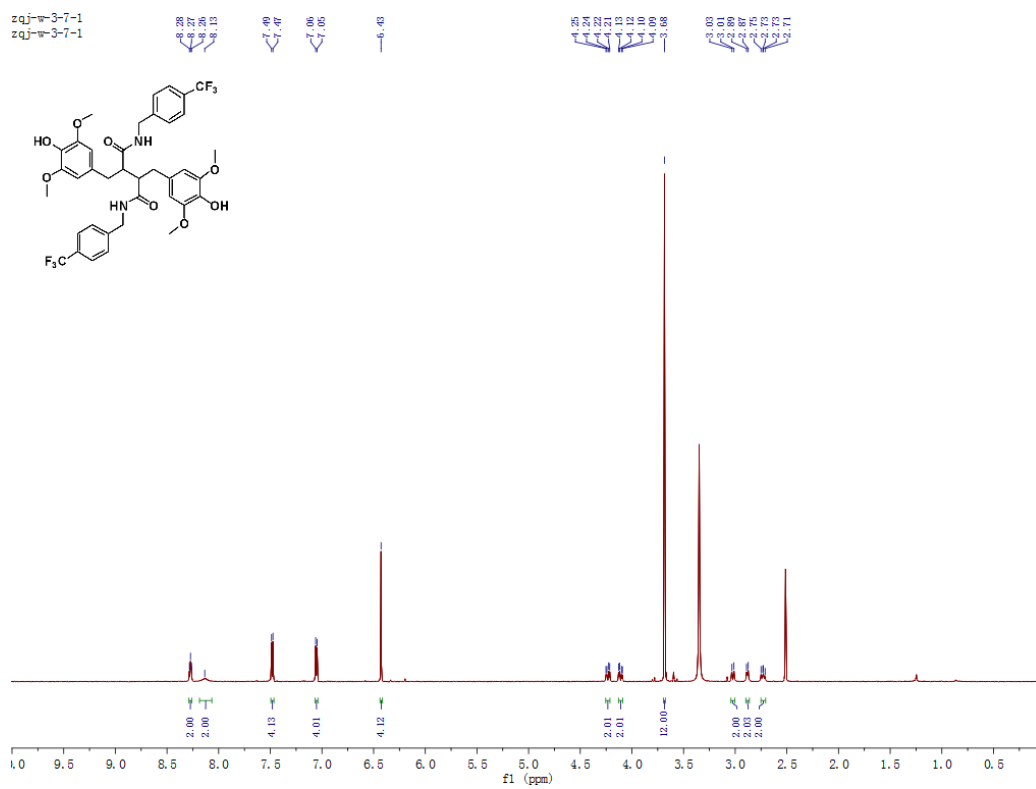


Figure S40 <sup>1</sup>H NMR spectrum of compound 10h

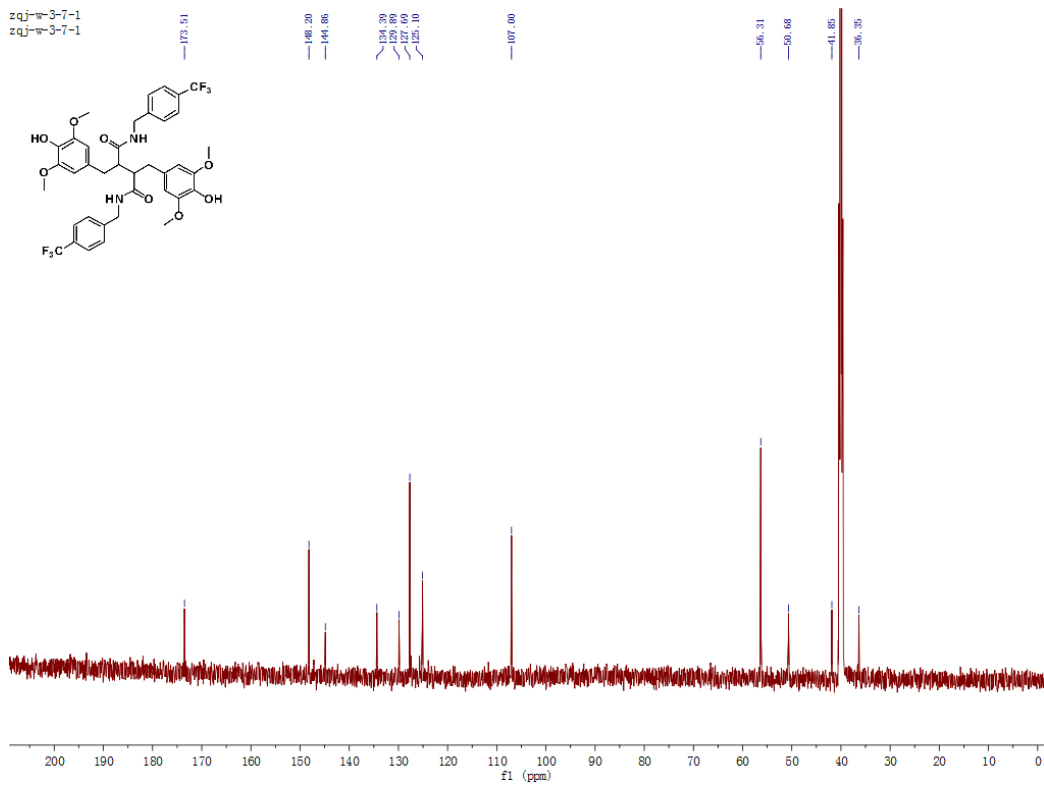


Figure S41  $^{13}\text{C}$  NMR spectrum of compound **10h**

S217-3

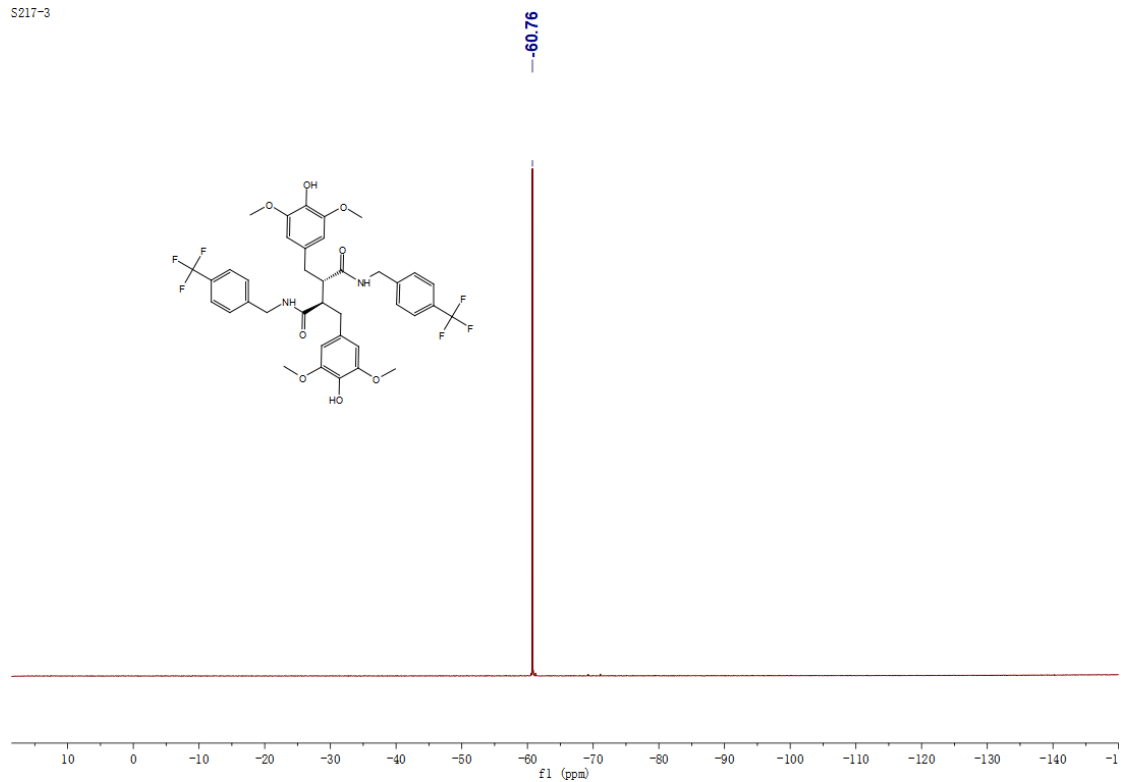


Figure S42  $^{19}\text{F}$  NMR spectrum of compound **10h**



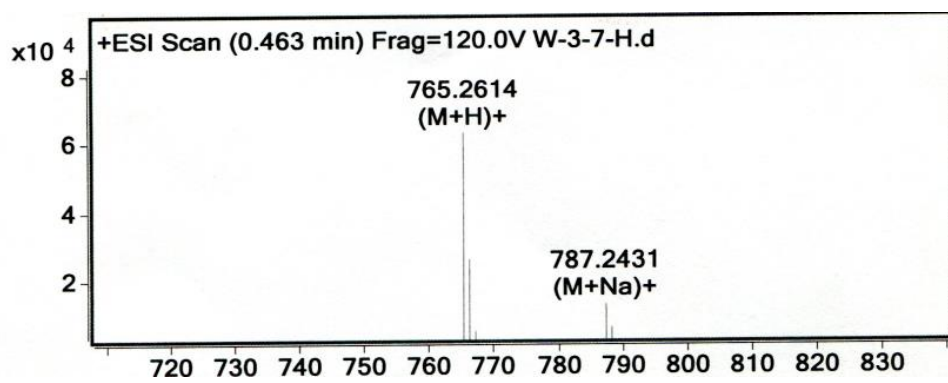


Figure S43 HRMS spectrum of compound 10h

16. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10i

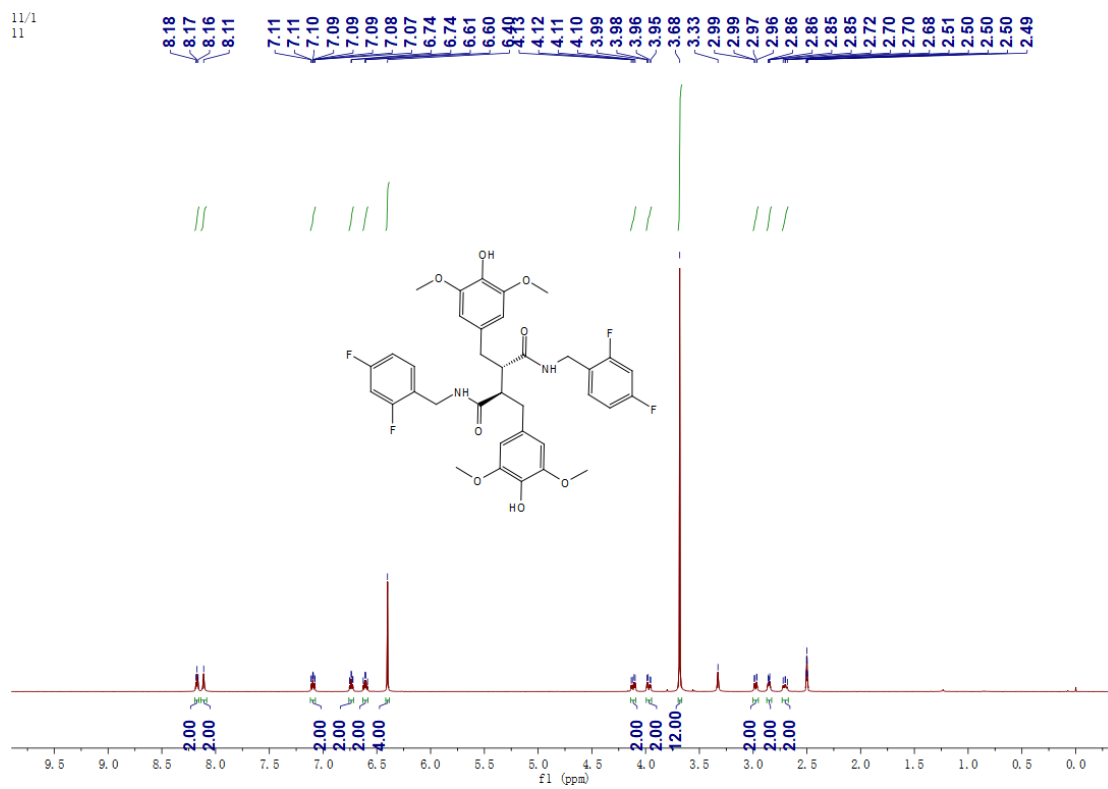


Figure S44 <sup>1</sup>H NMR spectrum of compound 10i

11/2  
11

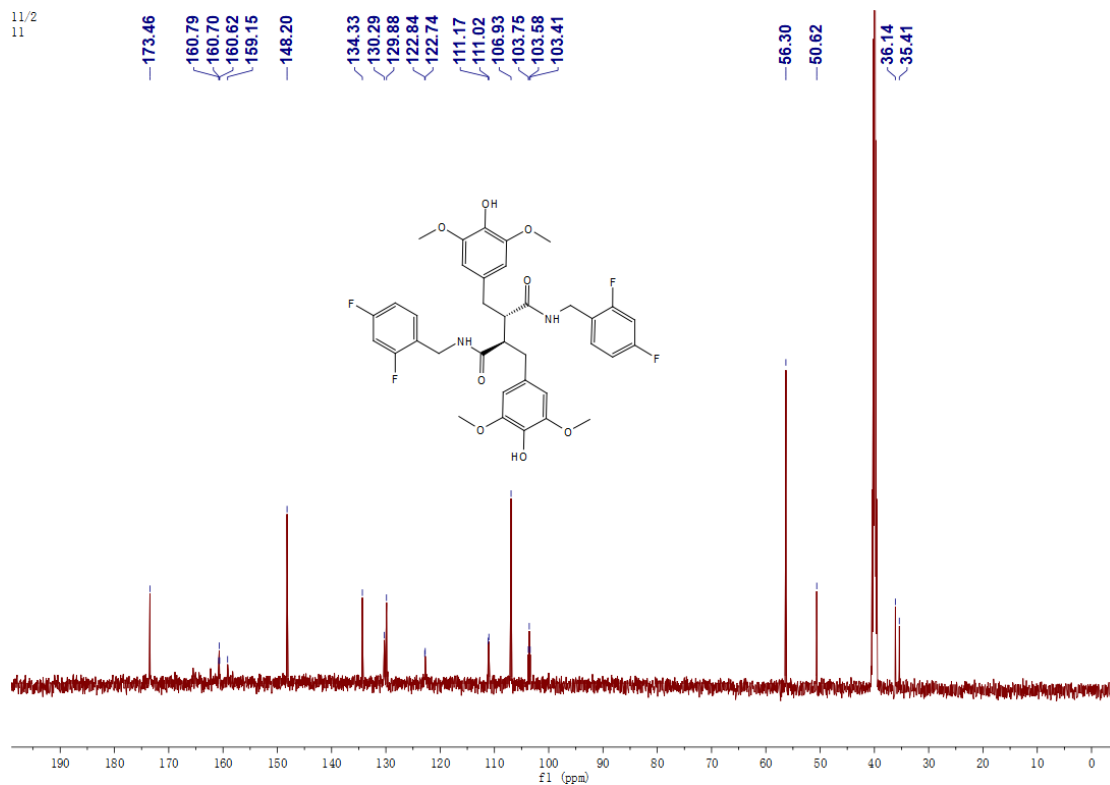


Figure S45 <sup>13</sup>C NMR spectrum of compound 10i

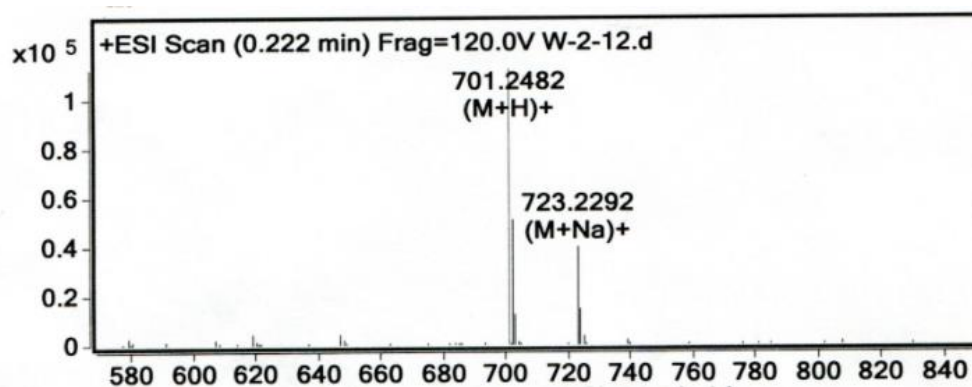


Figure S46 HRMS spectrum of compound 10i

## 17. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10j

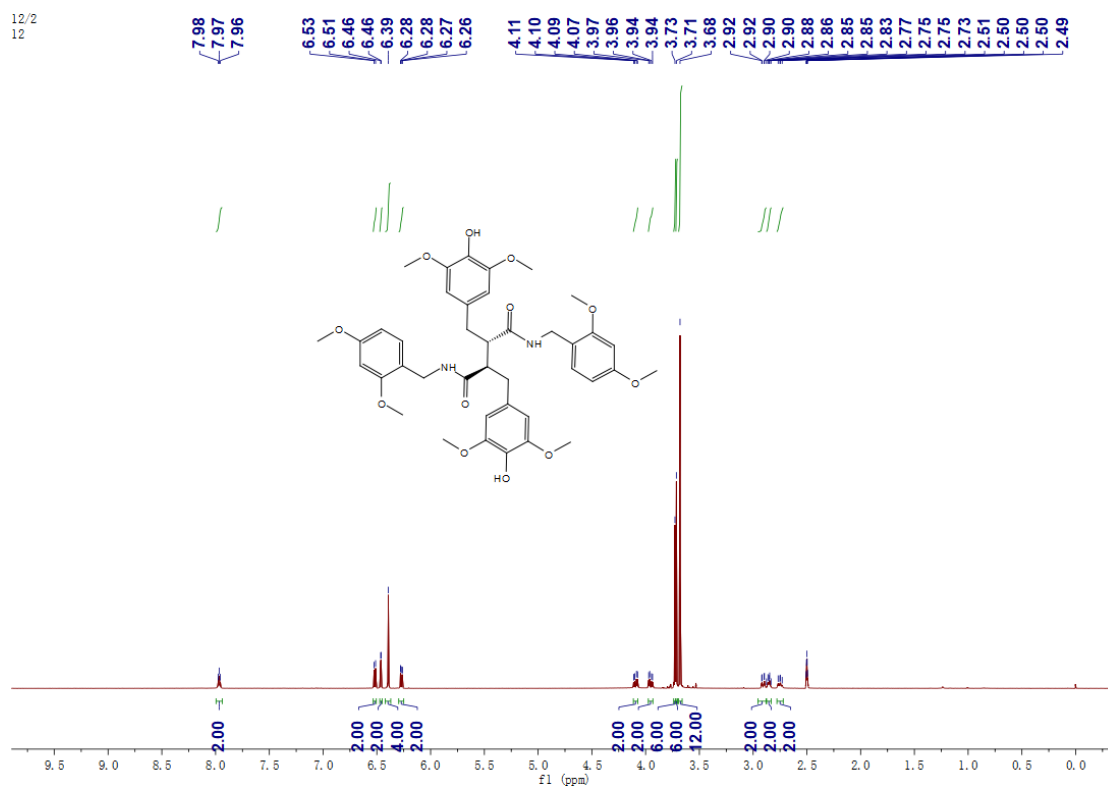


Figure S47 <sup>1</sup>H NMR spectrum of compound 10j

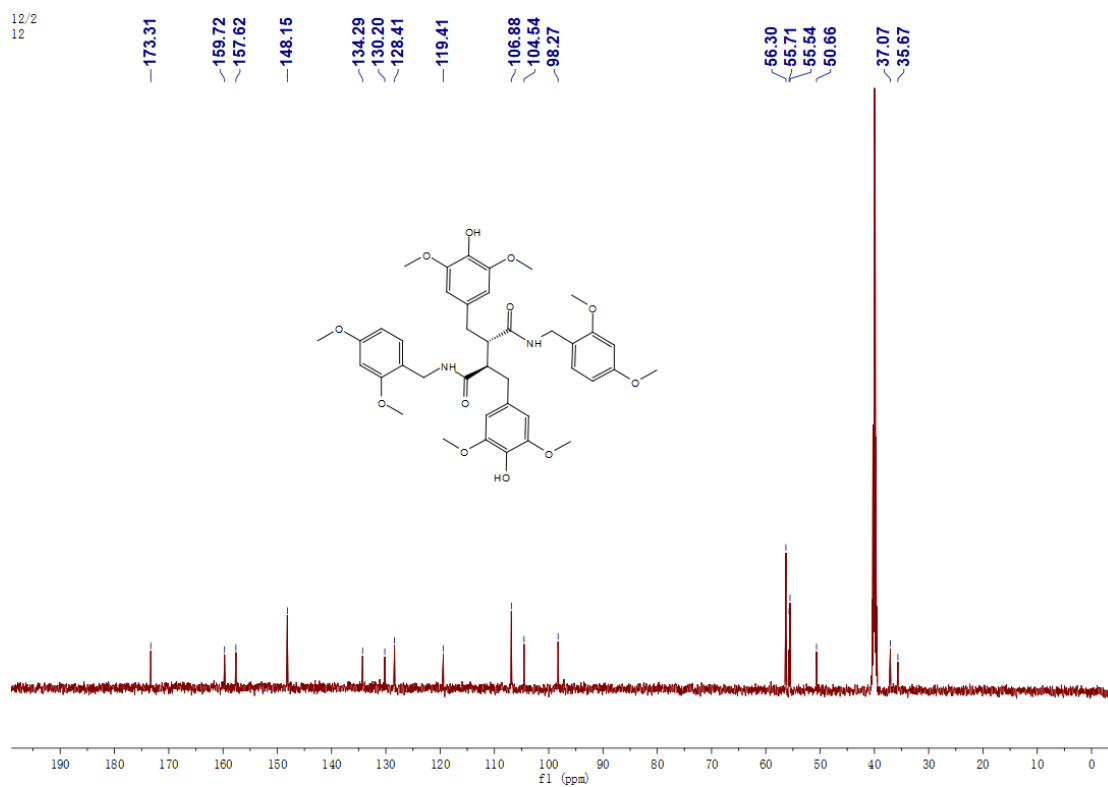


Figure S48 <sup>13</sup>C NMR spectrum of compound 10j

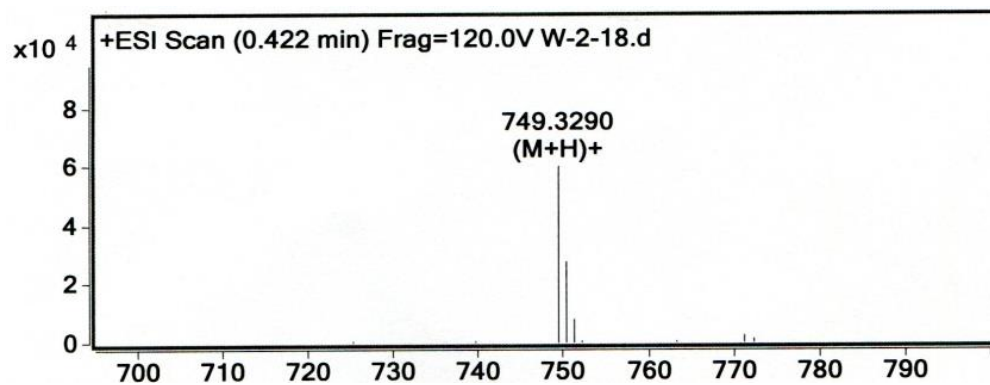


Figure S49 HRMS spectrum of compound 10j

18. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10k

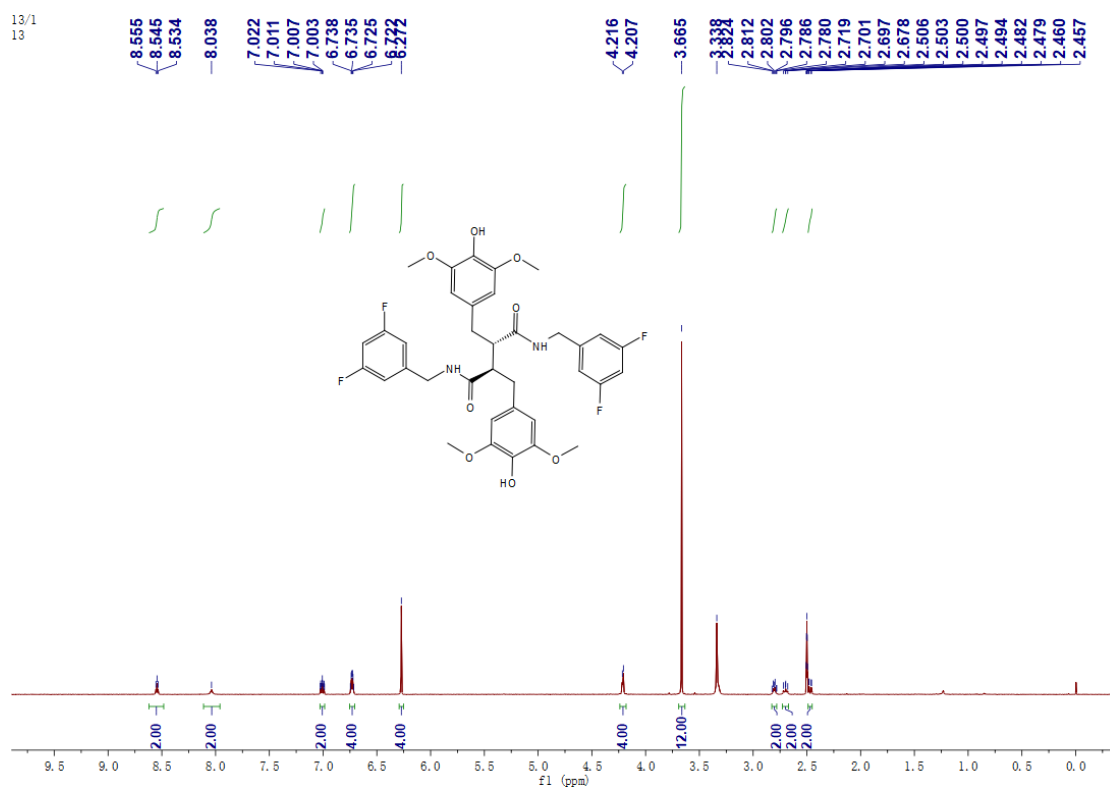


Figure S50 <sup>1</sup>H NMR spectrum of compound 10k

13/2  
13

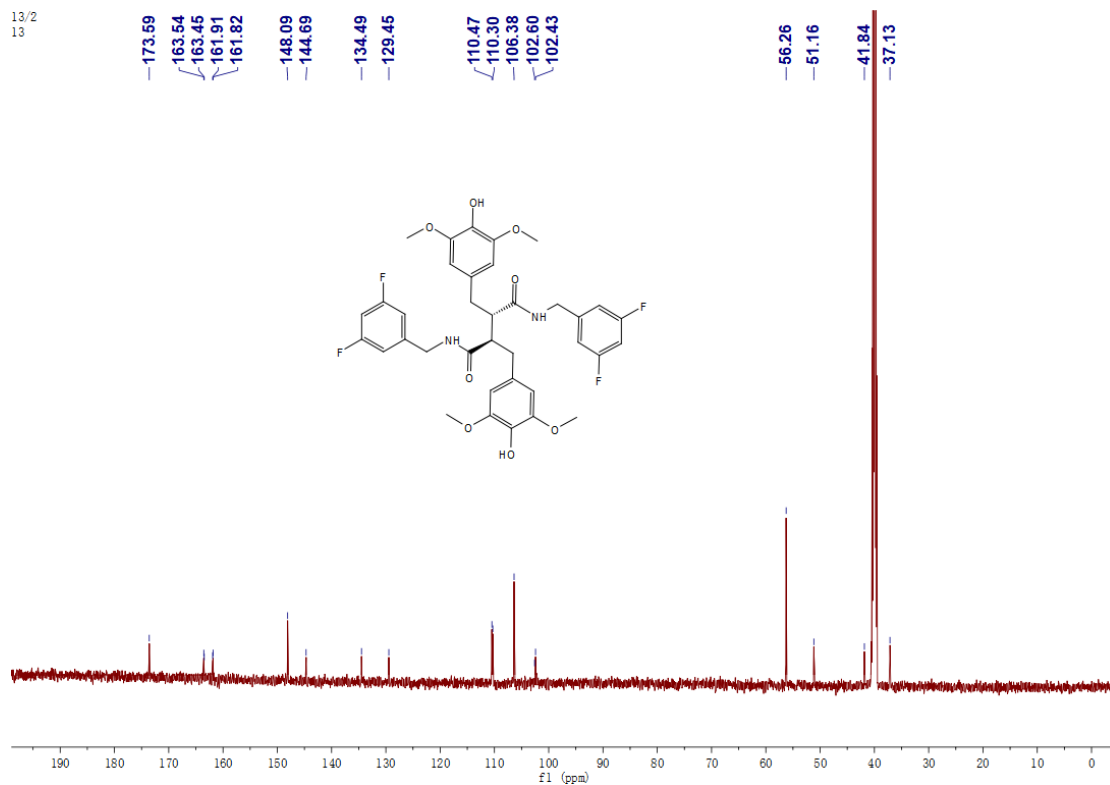


Figure S51 <sup>13</sup>C NMR spectrum of compound 10k

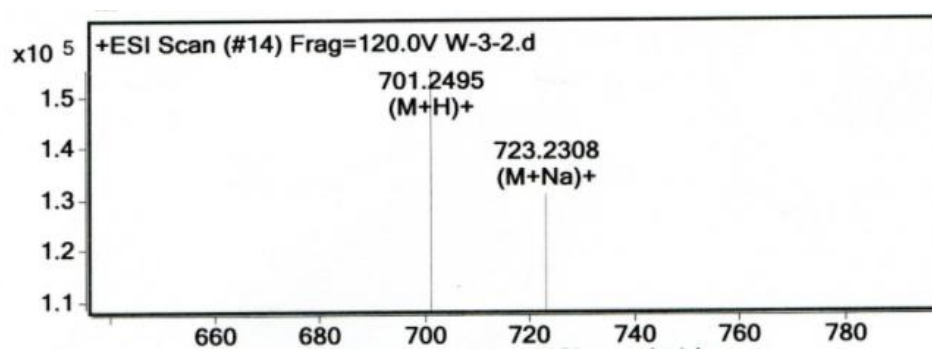


Figure S52 HRMS spectrum of compound 10k

## 19. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 101

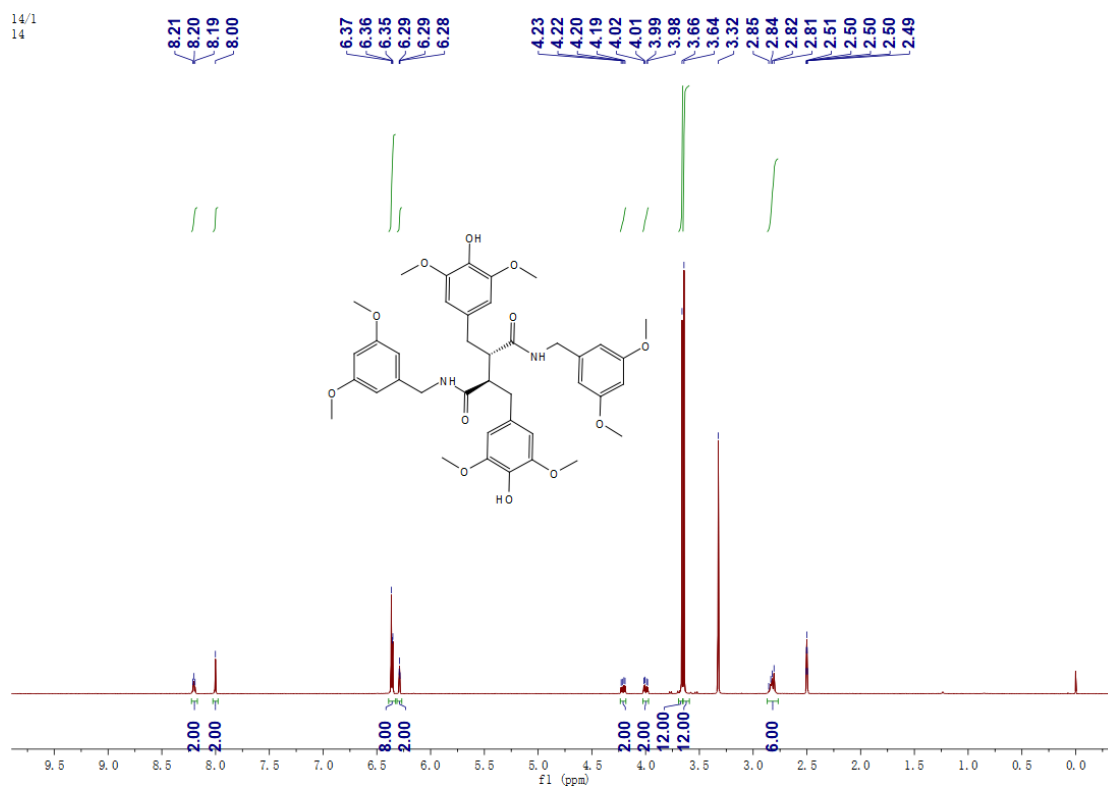


Figure S53  $^1\text{H}$  NMR spectrum of compound 101

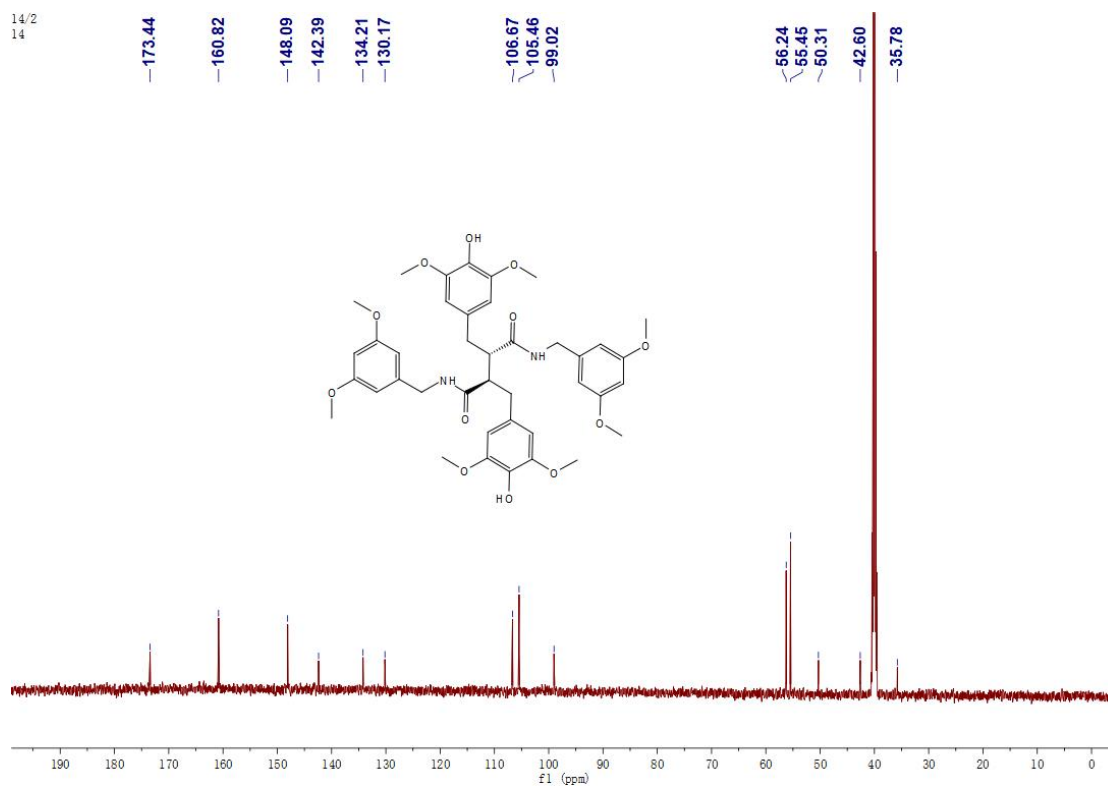


Figure S54  $^{13}\text{C}$  NMR spectrum of compound 101

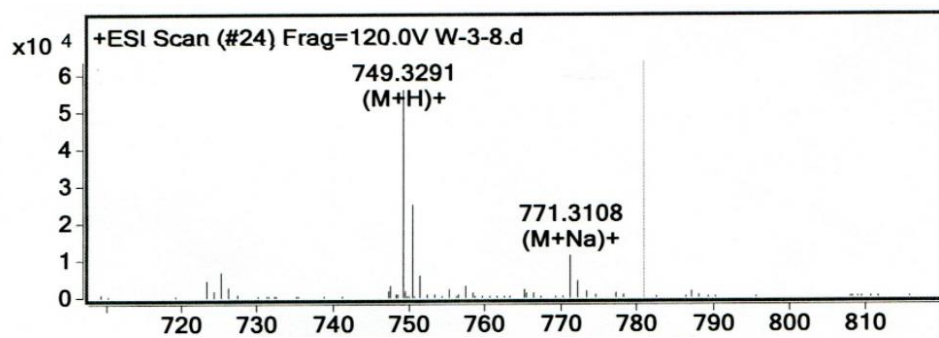


Figure S55 HRMS spectrum of compound 10l

20. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 10m

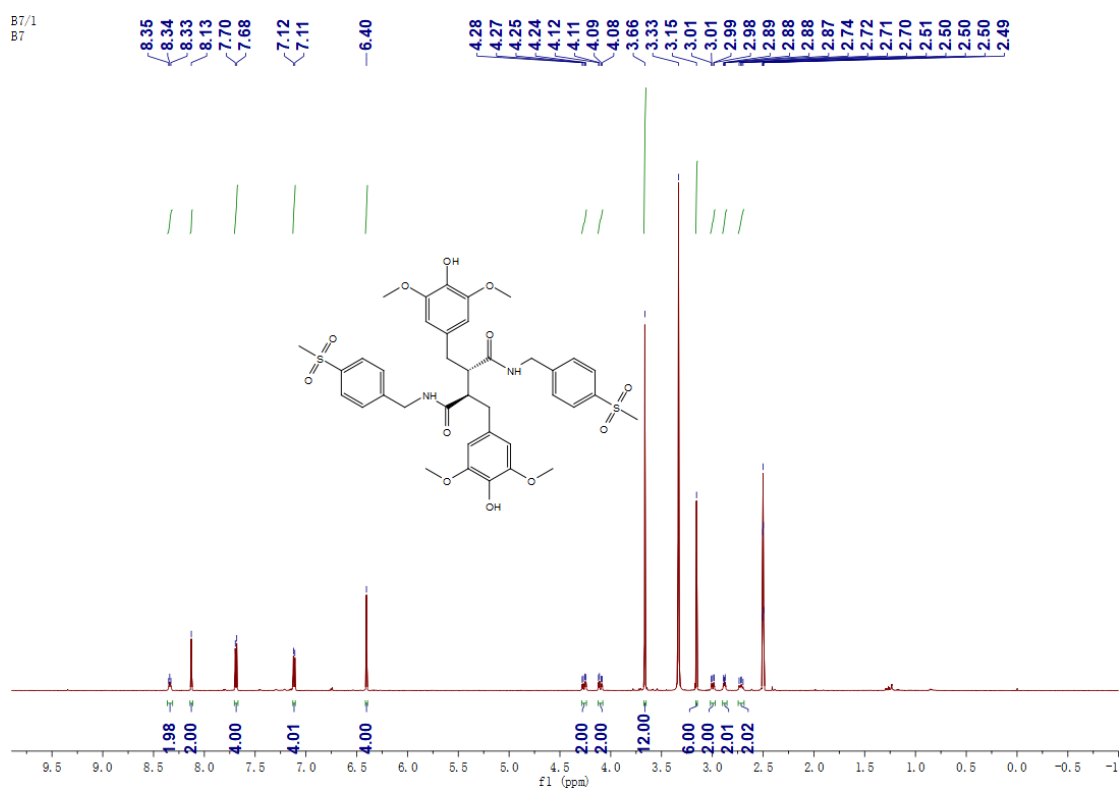
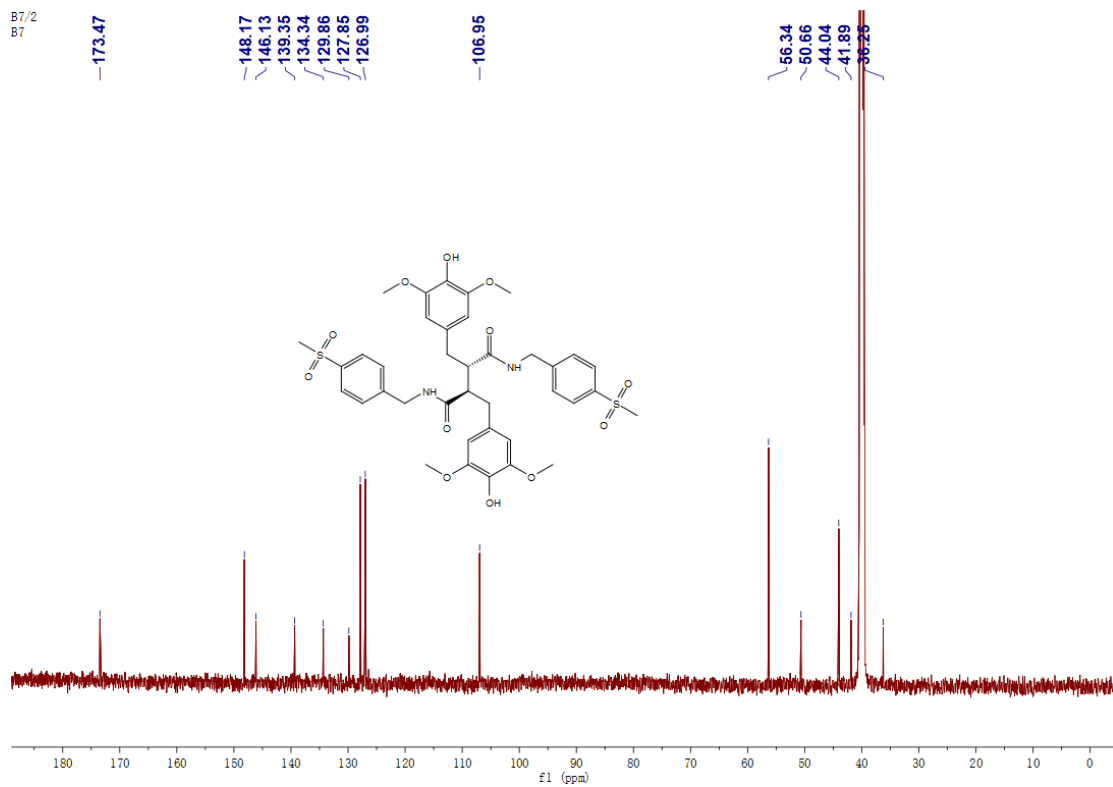
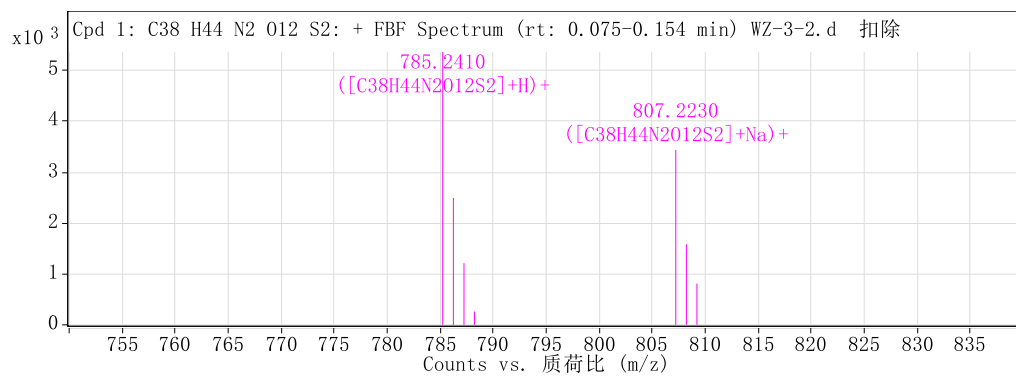


Figure S56 <sup>1</sup>H NMR spectrum of compound 10m



**Figure S57**  $^{13}\text{C}$  NMR spectrum of compound **10m**



**Figure S58** HRMS spectrum of compound **10m**



## 21. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 10n

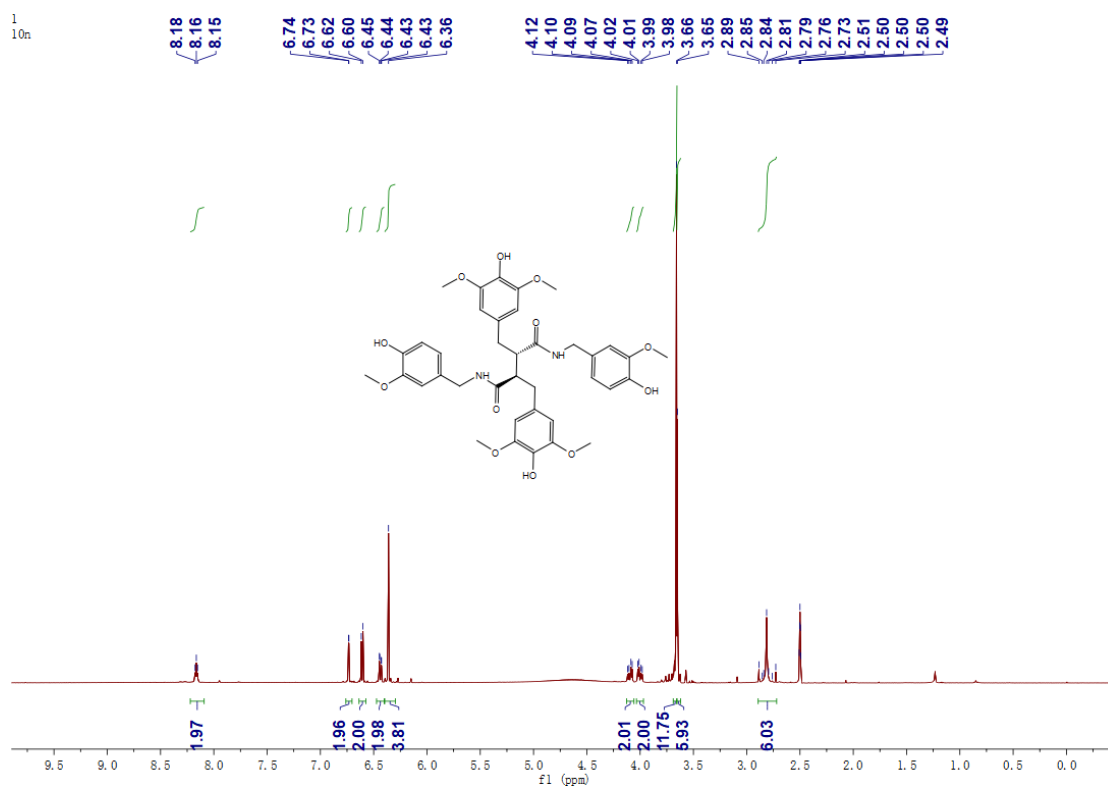


Figure S59  $^1\text{H}$  NMR spectrum of compound 10n

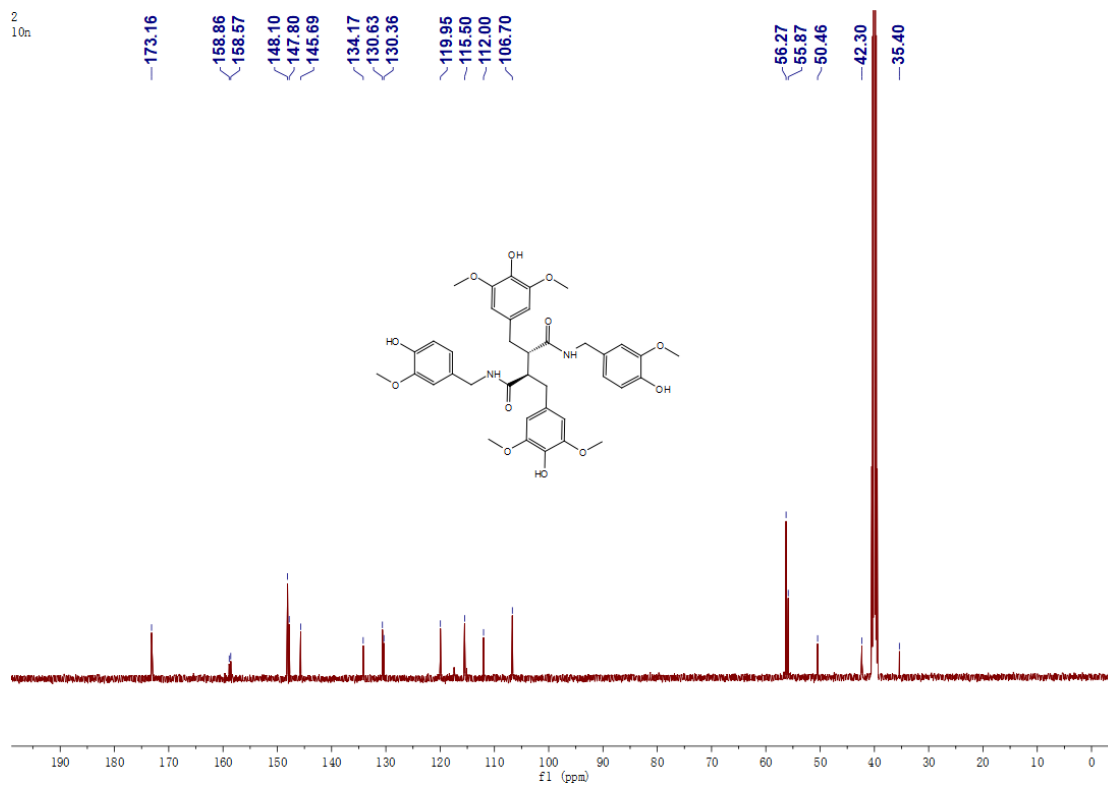


Figure S60  $^{13}\text{C}$  NMR spectrum of compound 10n

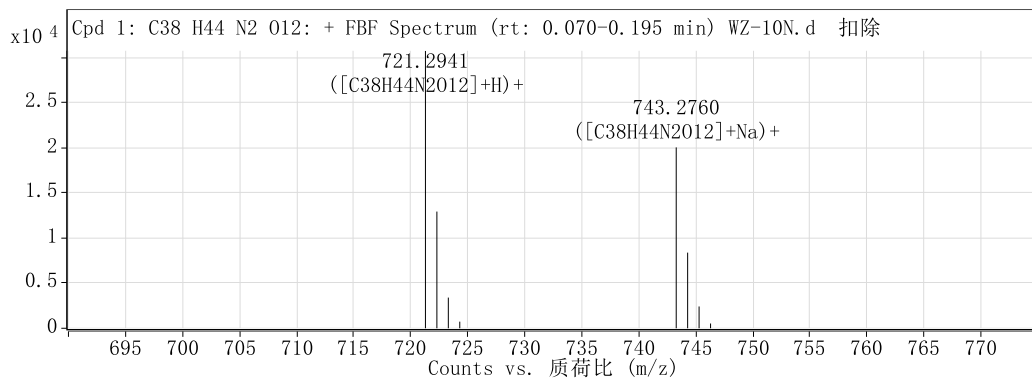


Figure S61 HRMS spectrum of compound 10n

22. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 12a

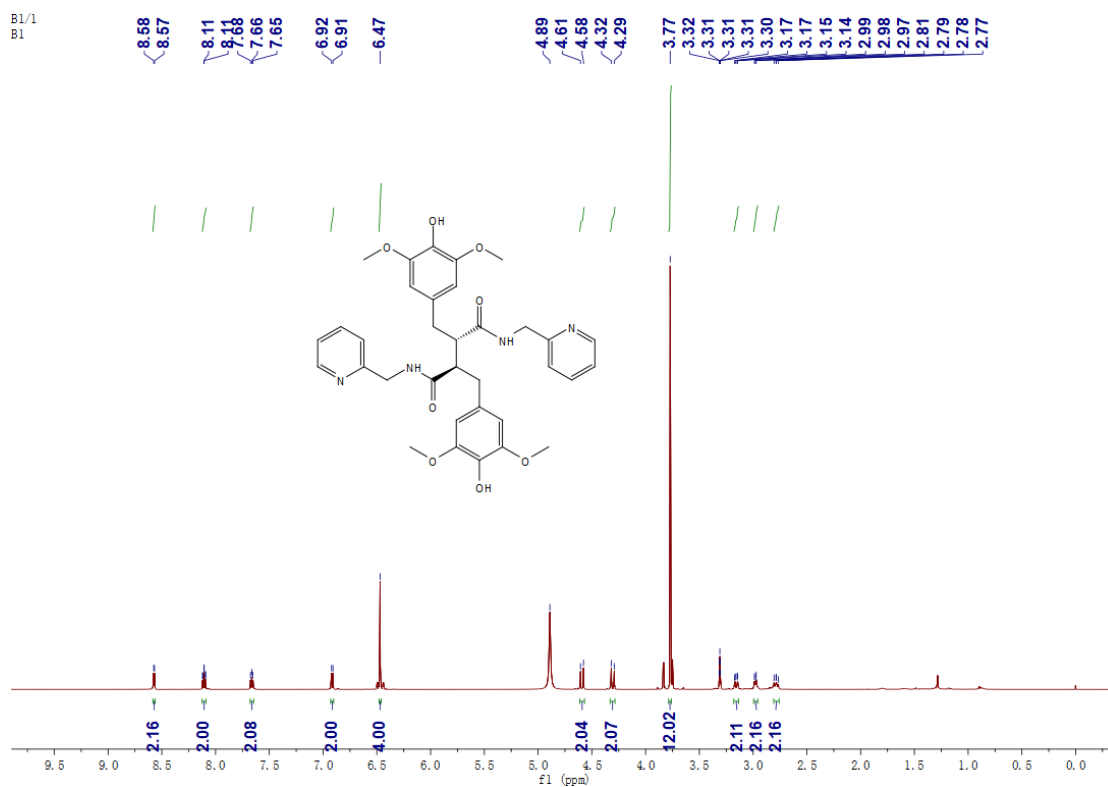
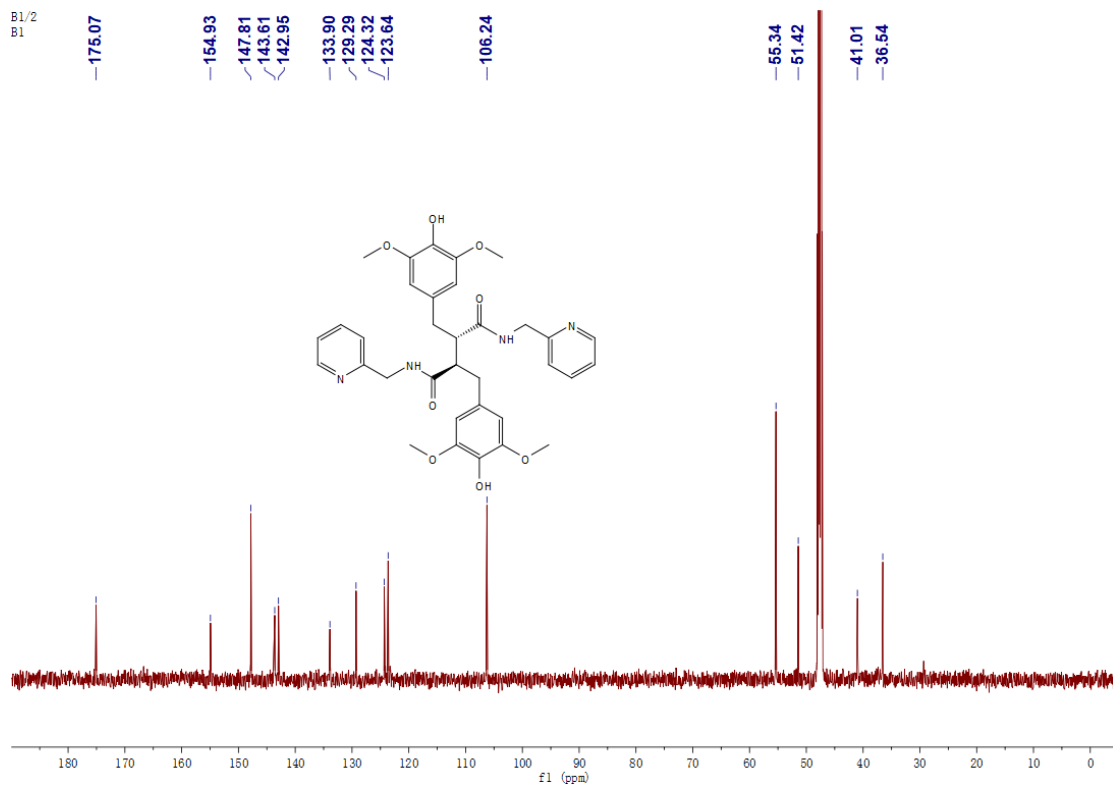
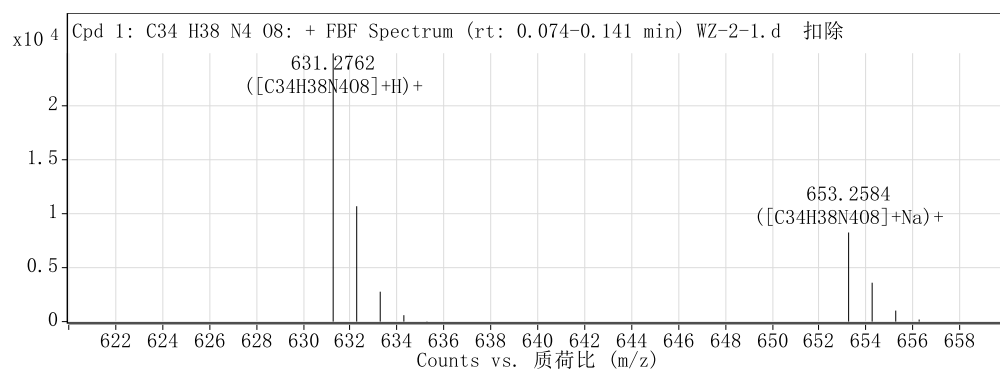


Figure S62 <sup>1</sup>H NMR spectrum of compound 12a



**Figure S63**  $^{13}\text{C}$  NMR spectrum of compound **12a**



**Figure S64** HRMS spectrum of compound **12a**

### 23. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 12b

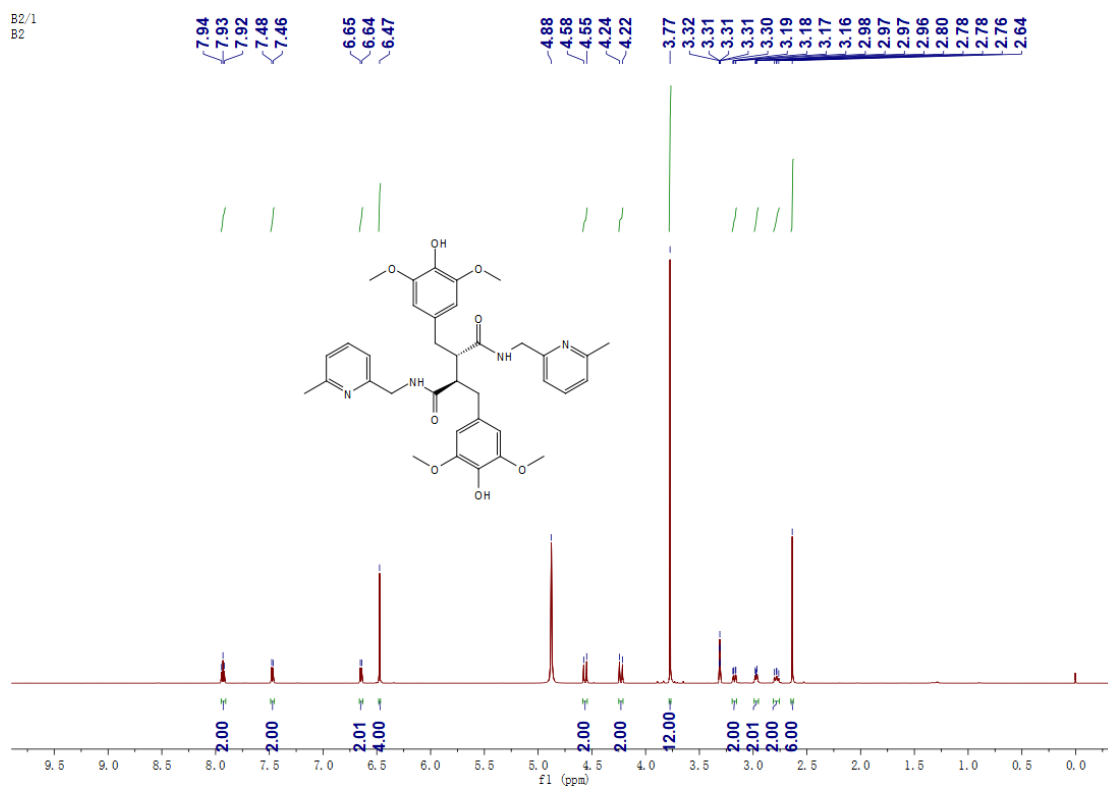


Figure S65  $^1\text{H}$  NMR spectrum of compound 12b

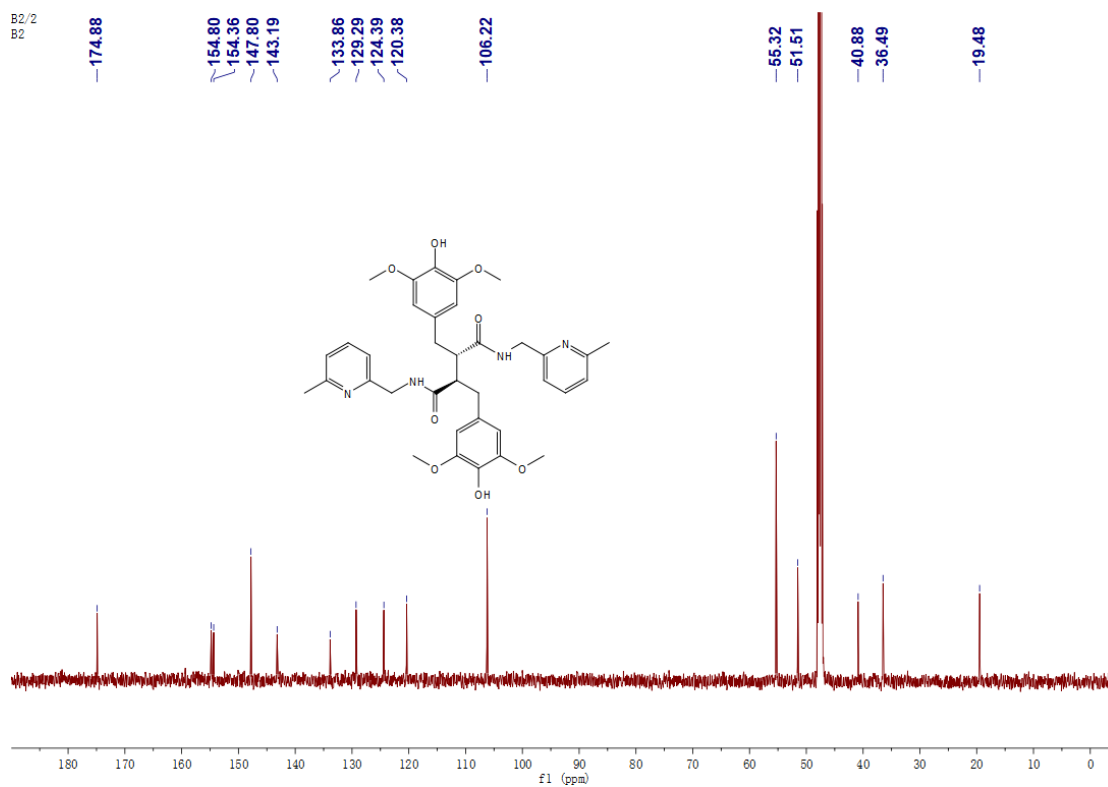


Figure S66  $^{13}\text{C}$  NMR spectrum of compound 12b

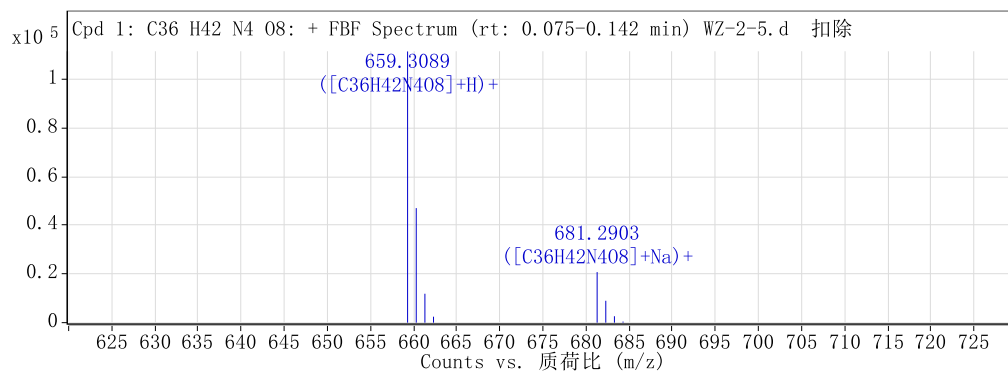


Figure S67 HRMS spectrum of compound 12b

24. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 12c

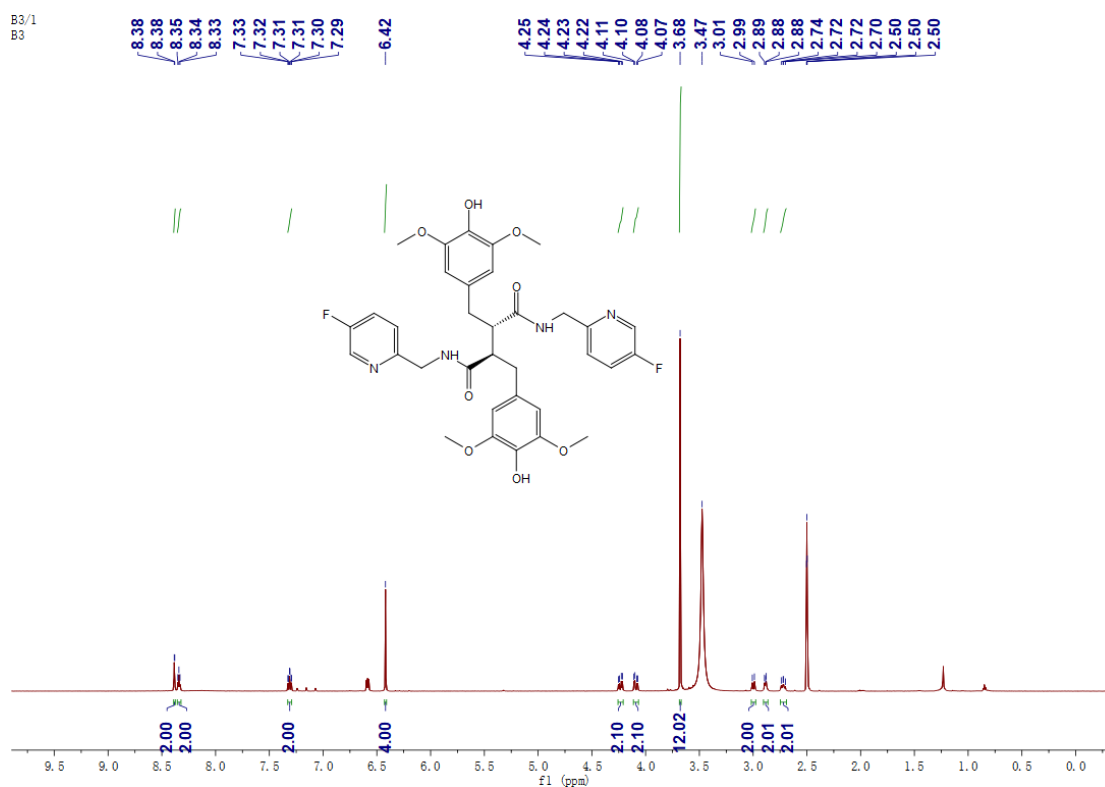


Figure S68 <sup>1</sup>H NMR spectrum of compound 12c

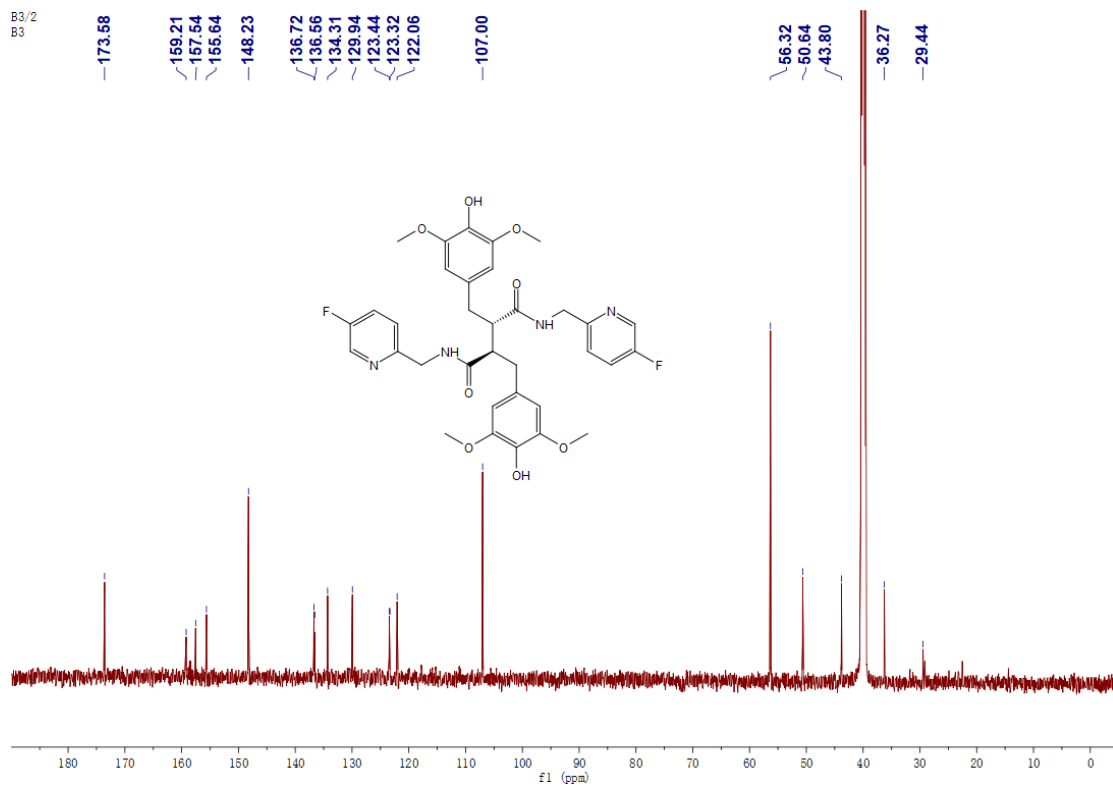


Figure S69  $^{13}\text{C}$  NMR spectrum of compound 12c

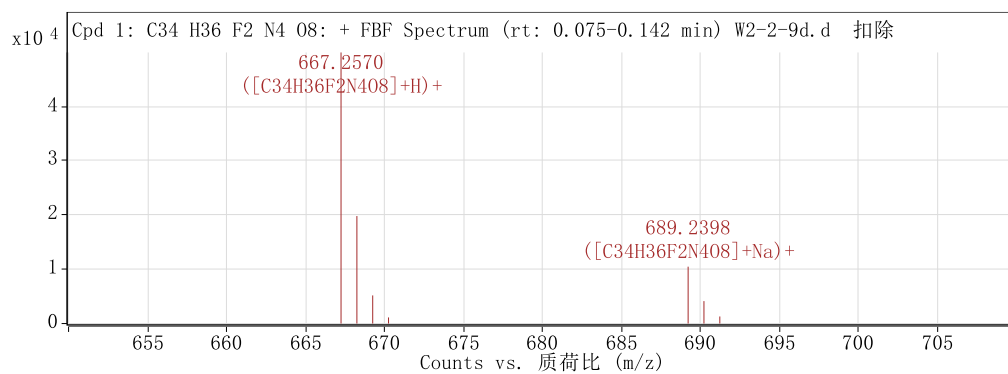


Figure S70 HRMS spectrum of compound 12c

## 25. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 12d

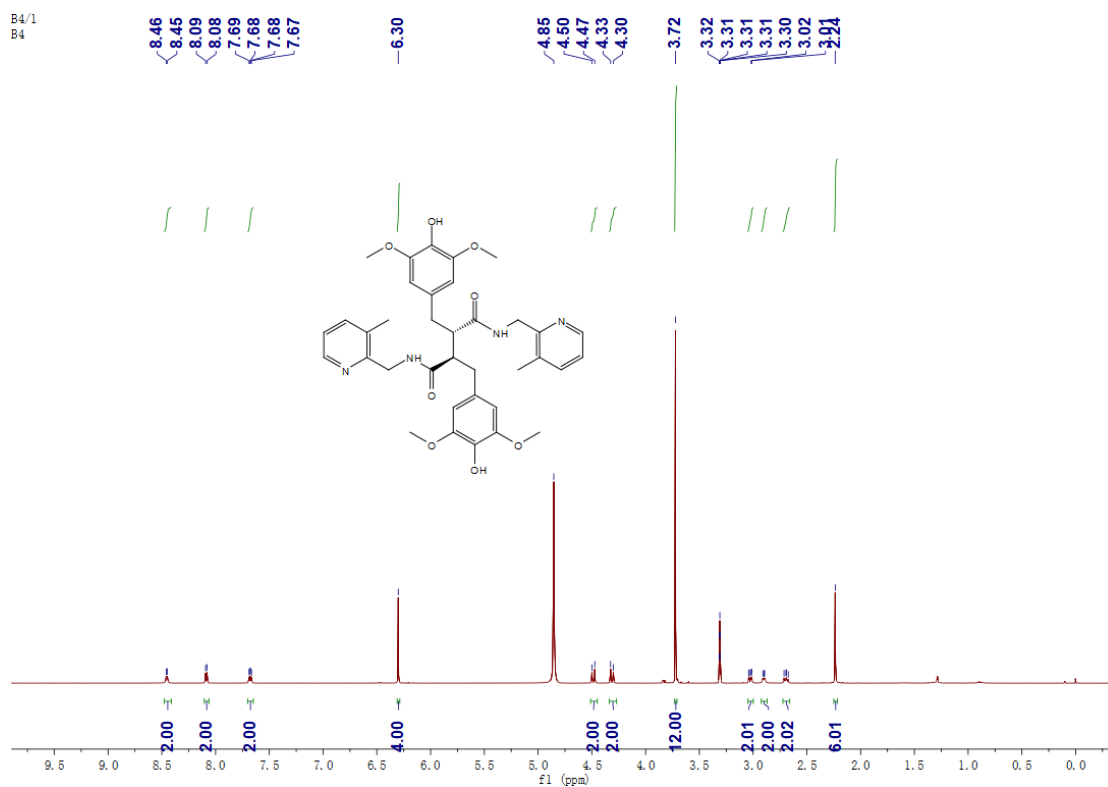


Figure S71  $^1\text{H}$  NMR spectrum of compound 12d

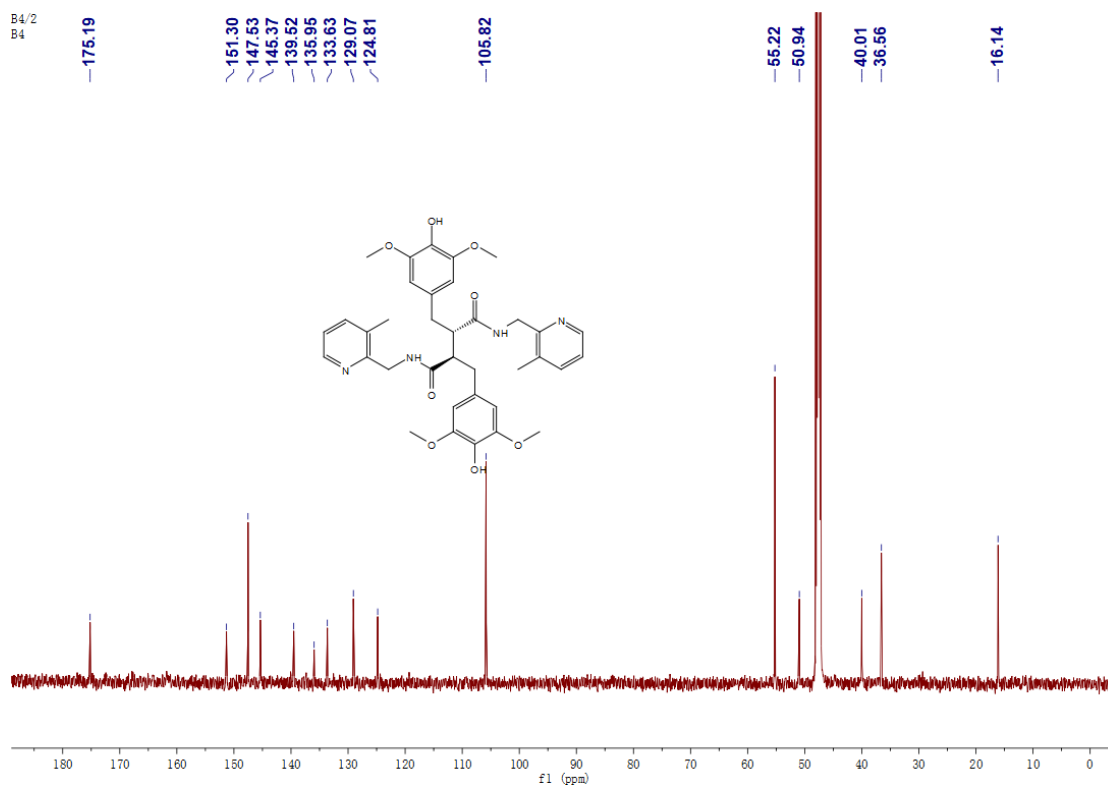


Figure S72  $^{13}\text{C}$  NMR spectrum of compound 12d

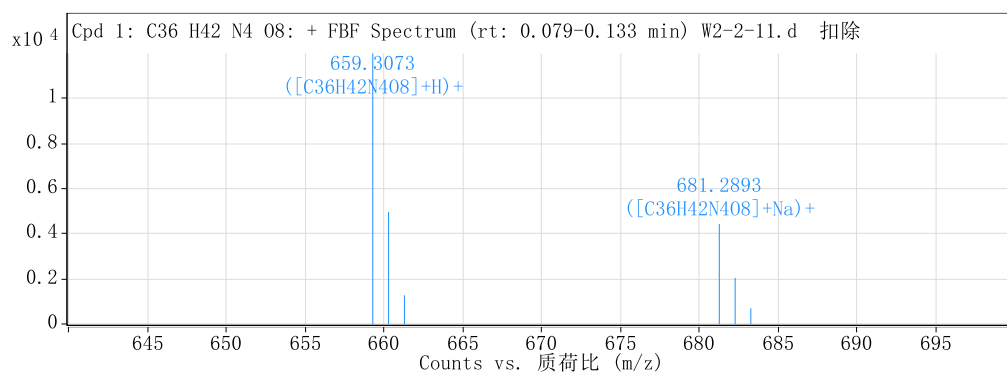


Figure S73 HRMS spectrum of compound 12d

26. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 12e

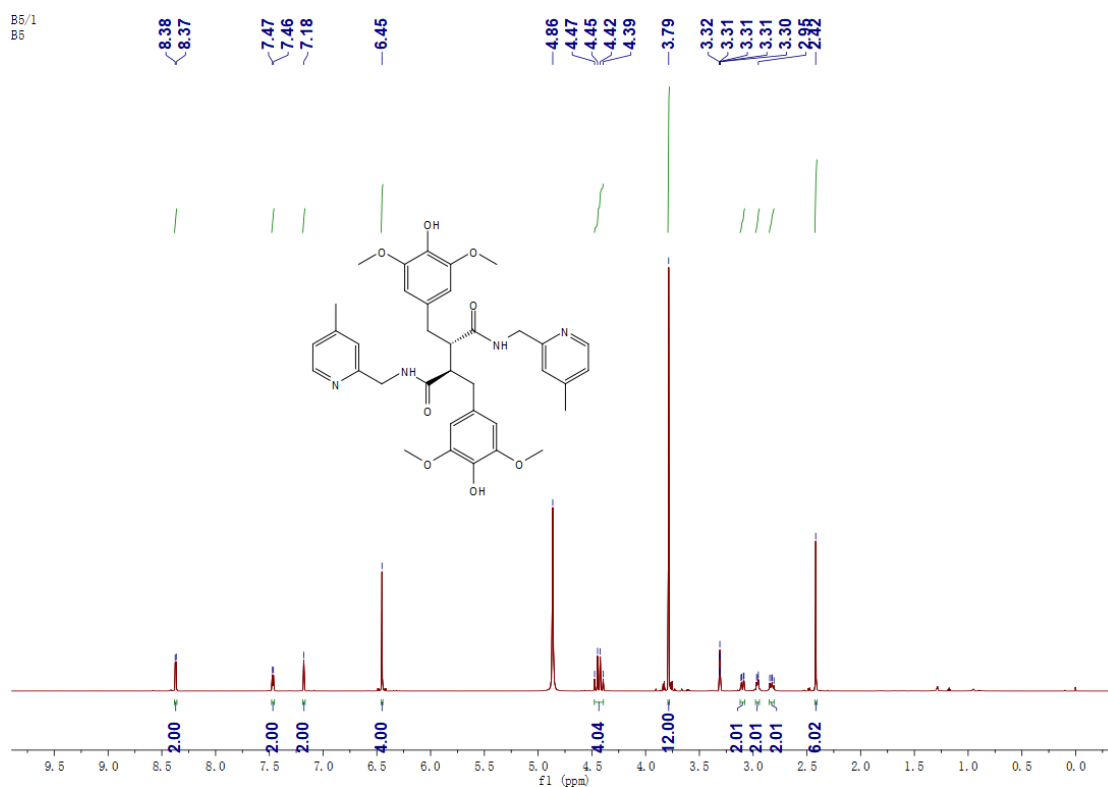


Figure S74 <sup>1</sup>H NMR spectrum of compound 12e



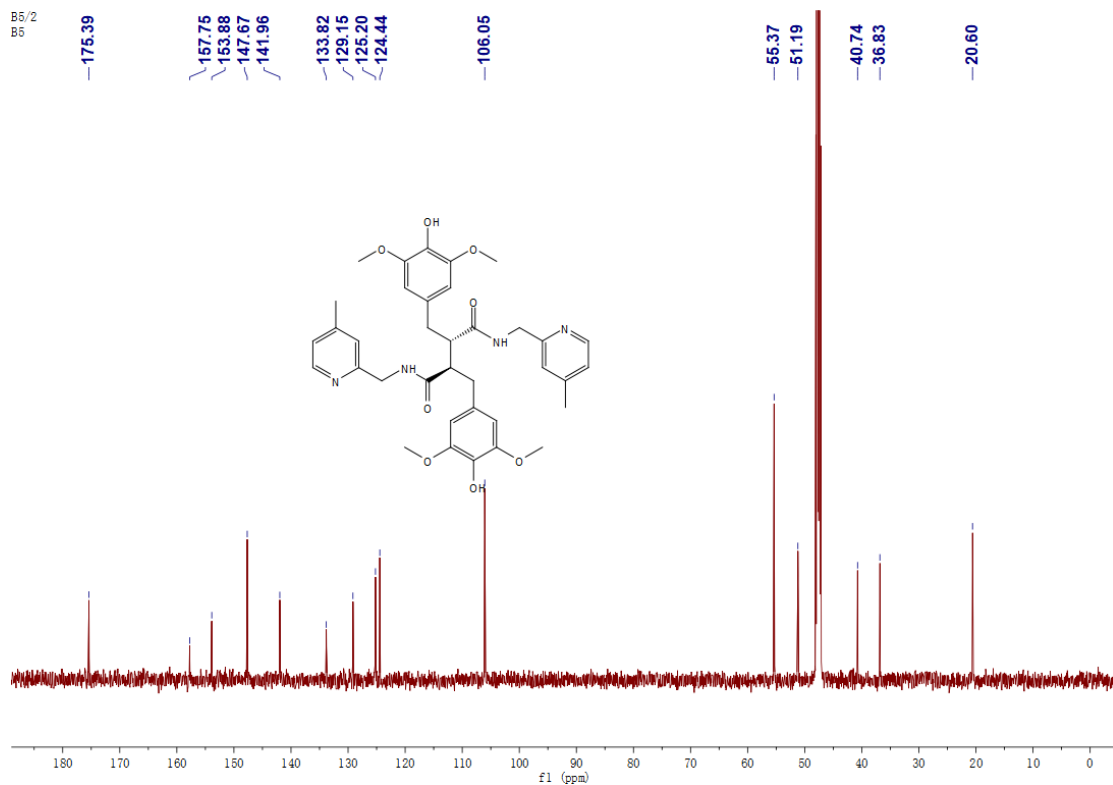


Figure S75  $^{13}\text{C}$  NMR spectrum of compound 12e

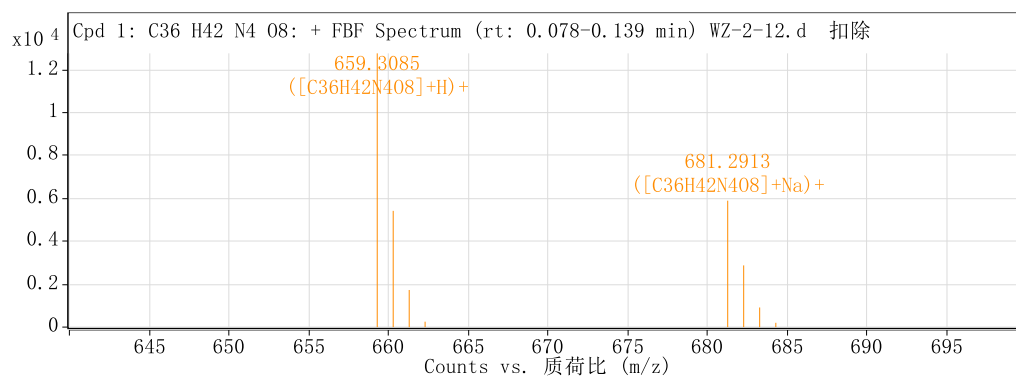


Figure S76 HRMS spectrum of compound 12e

## 27. <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectrum of compound 12f

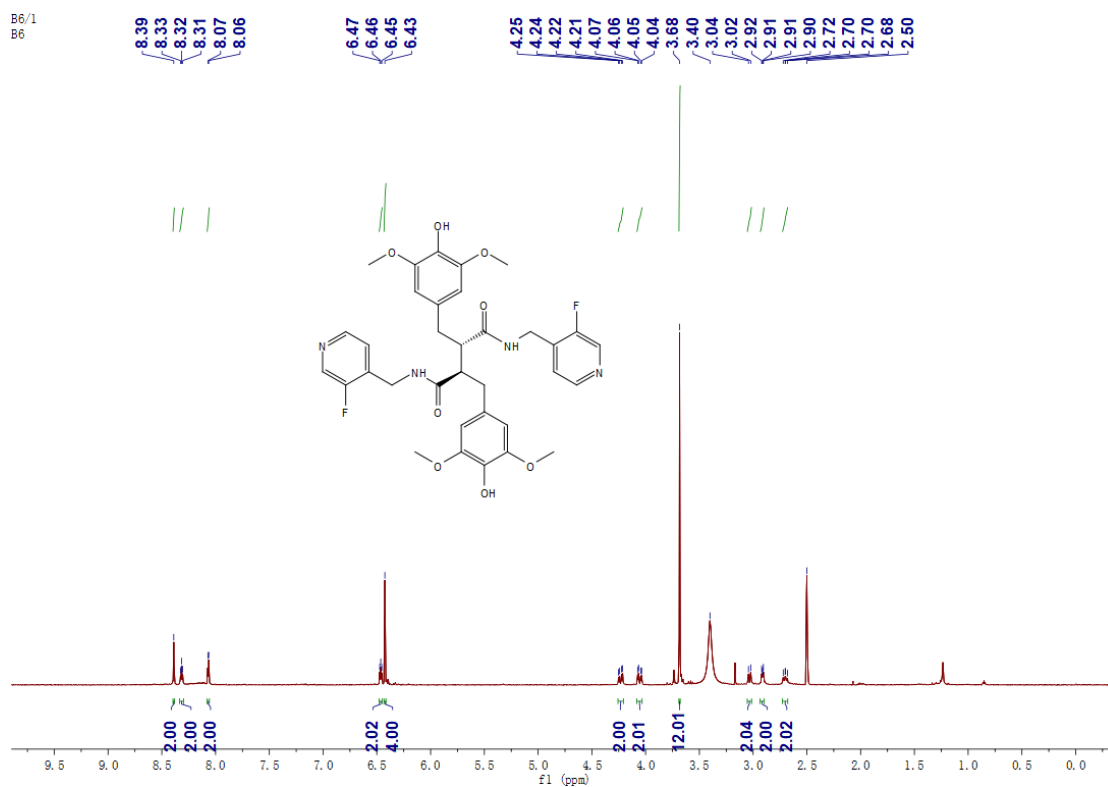


Figure S77 <sup>1</sup>H NMR spectrum of compound 12f

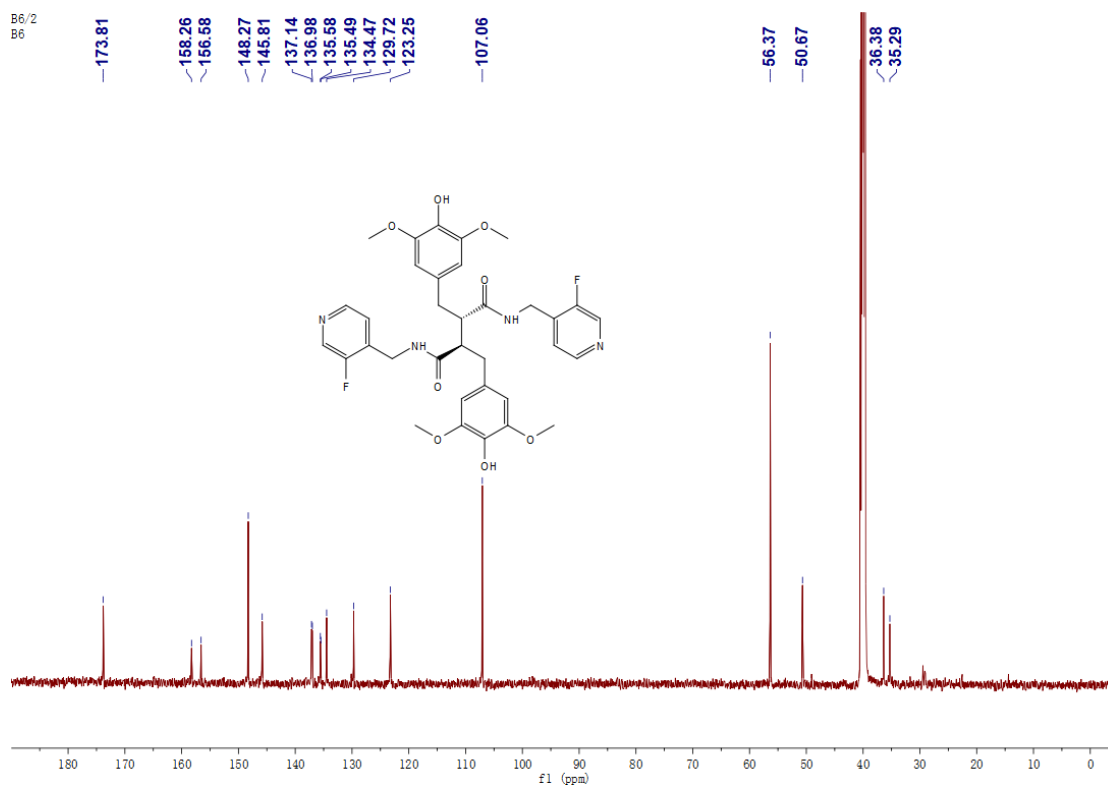


Figure S78 <sup>13</sup>C NMR spectrum of compound 12f

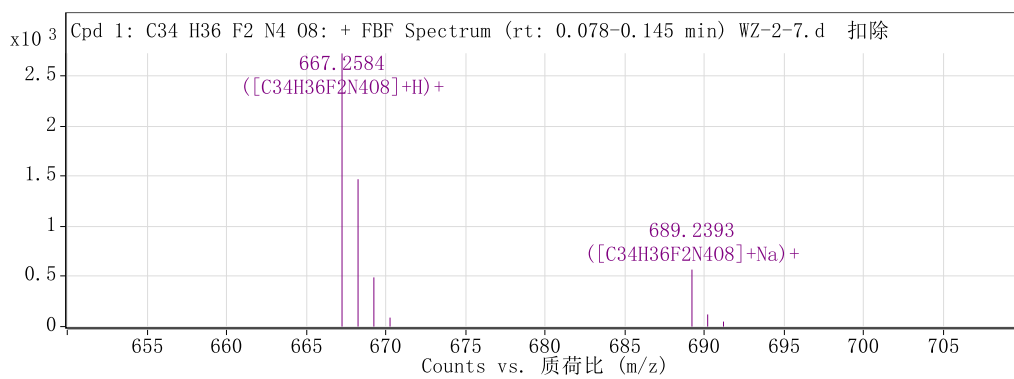


Figure S79 HRMS spectrum of compound 12f

28.  $^1H$  NMR,  $^{13}C$  NMR and HRMS spectrum of compound 12g

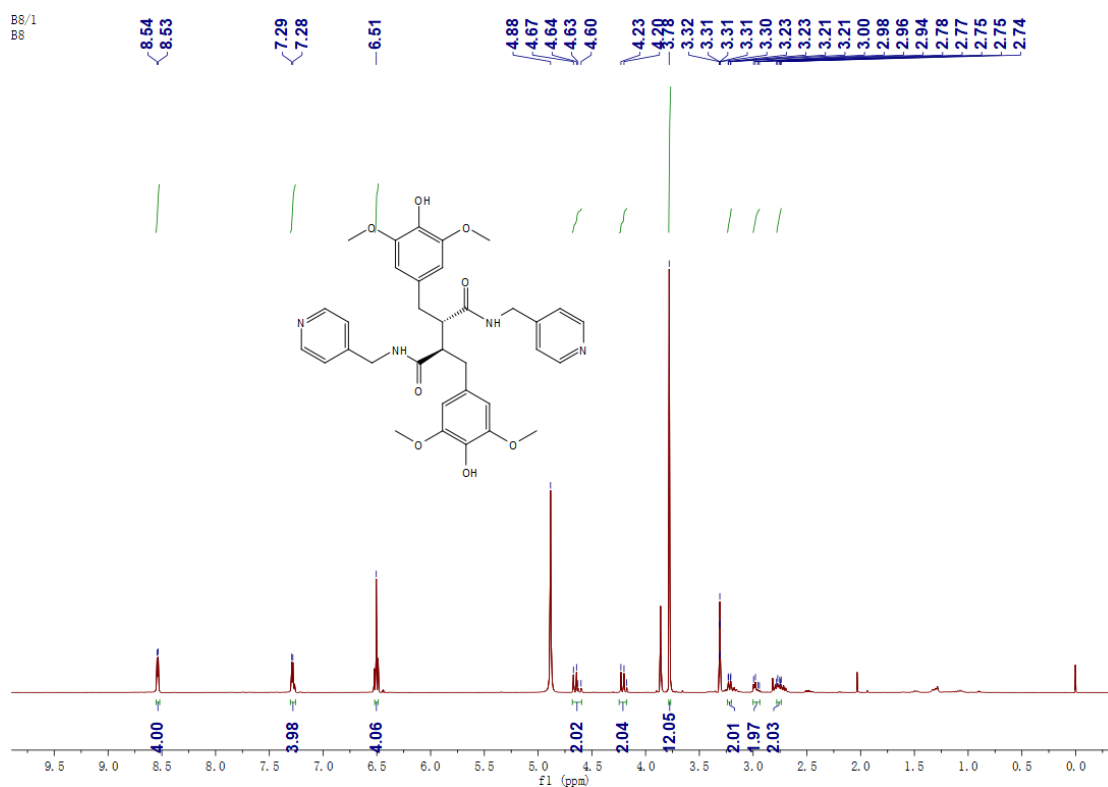
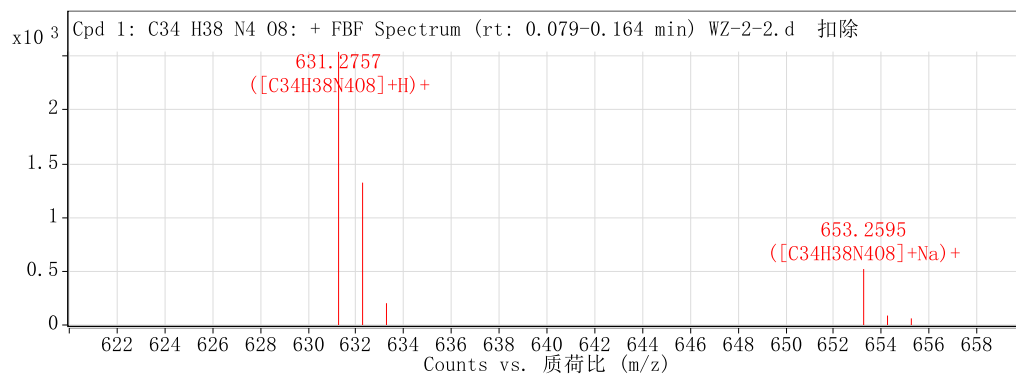
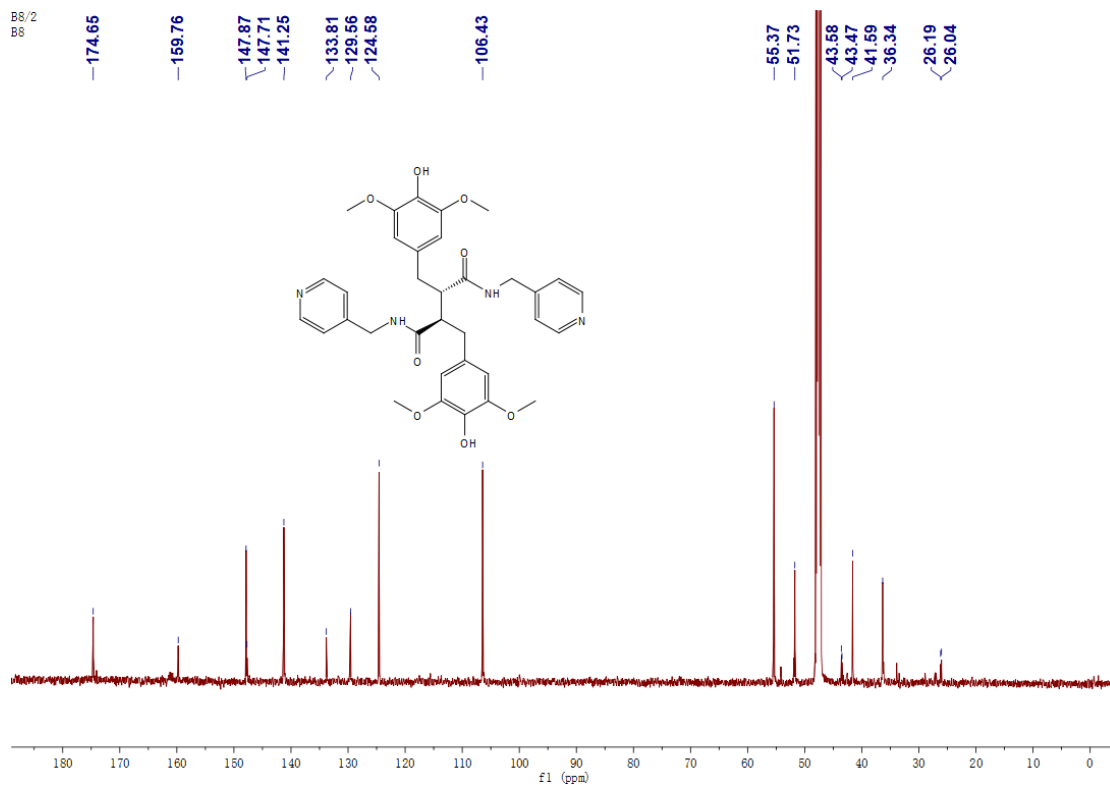


Figure S80  $^1H$  NMR spectrum of compound 12g



## 29. $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and HRMS spectrum of compound 12h

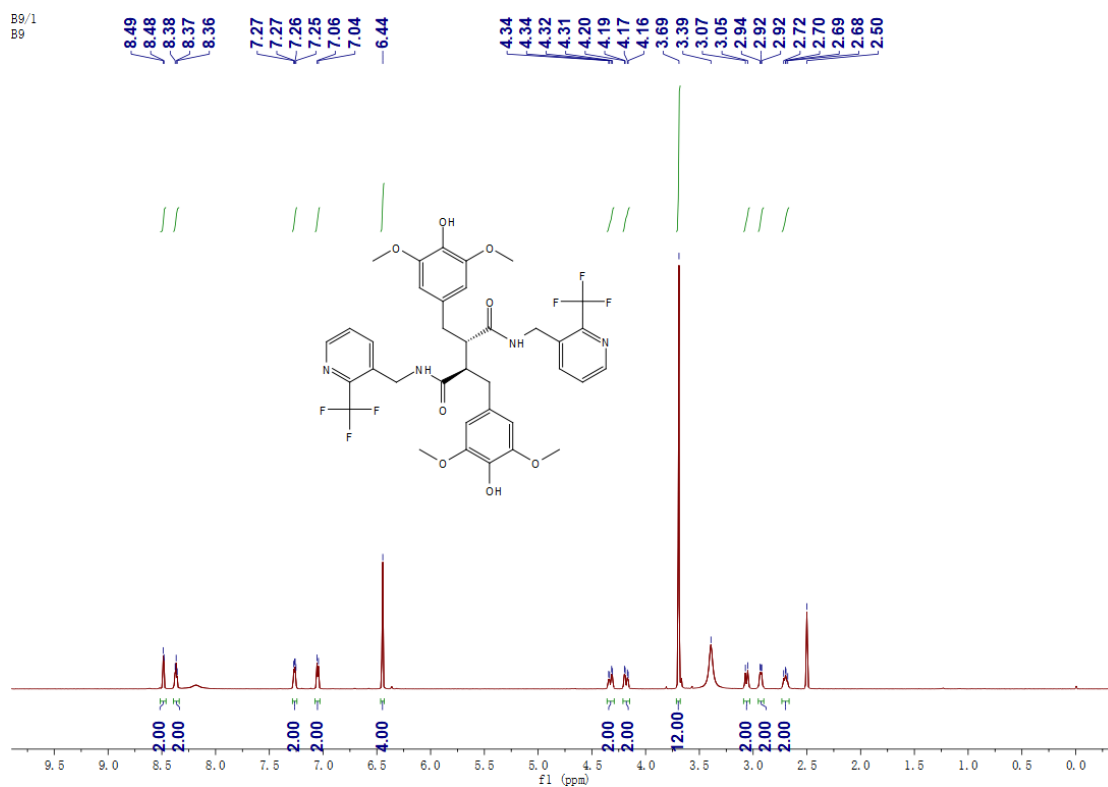


Figure S83  $^1\text{H}$  NMR spectrum of compound 12h

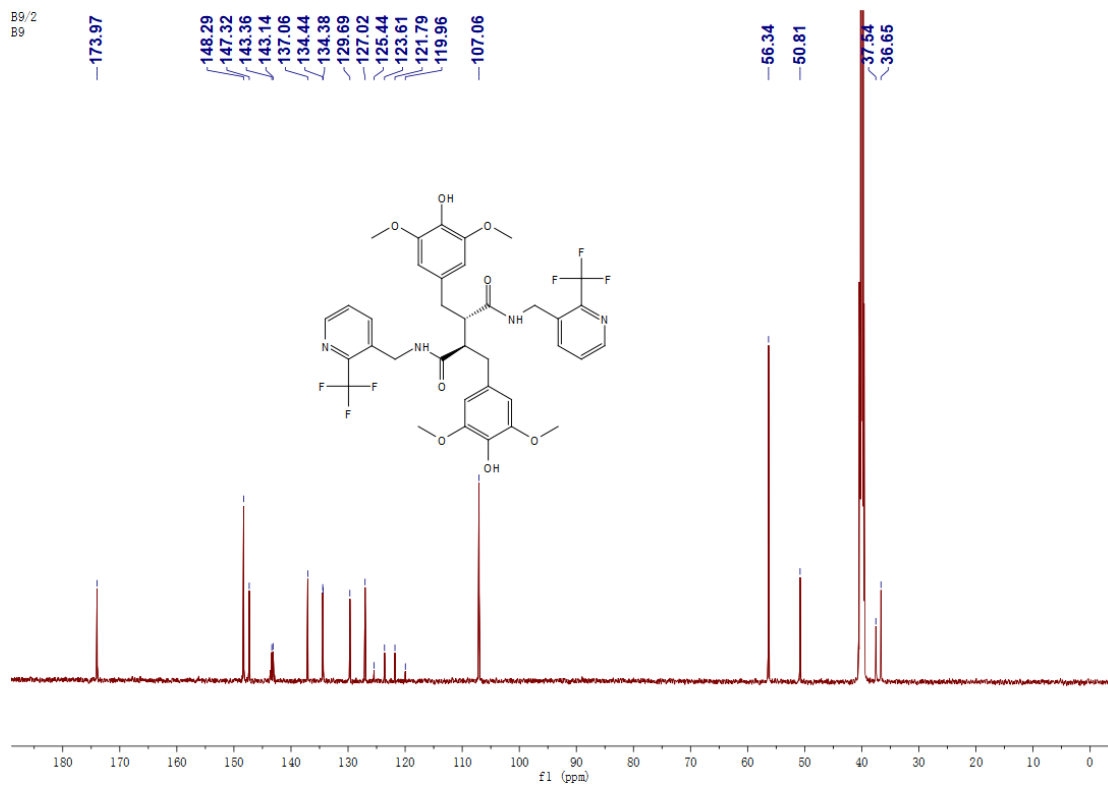


Figure S84  $^{13}\text{C}$  NMR spectrum of compound 12h

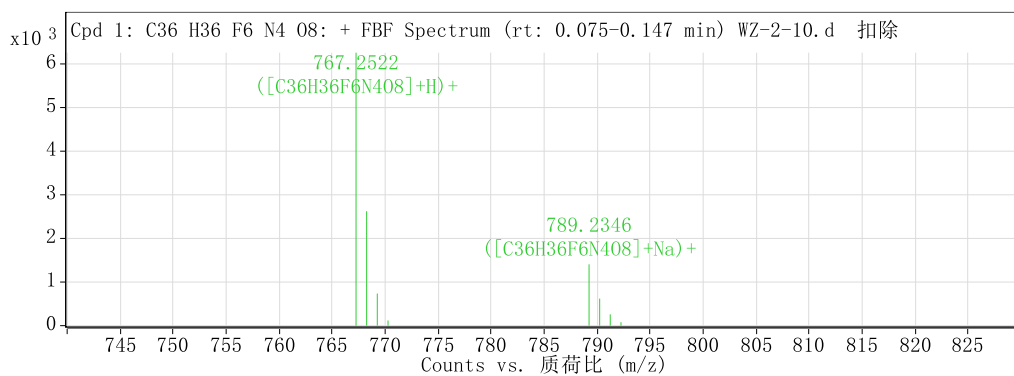


Figure S85 HRMS spectrum of compound 12h

30.  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and HRMS spectrum of compound 12i

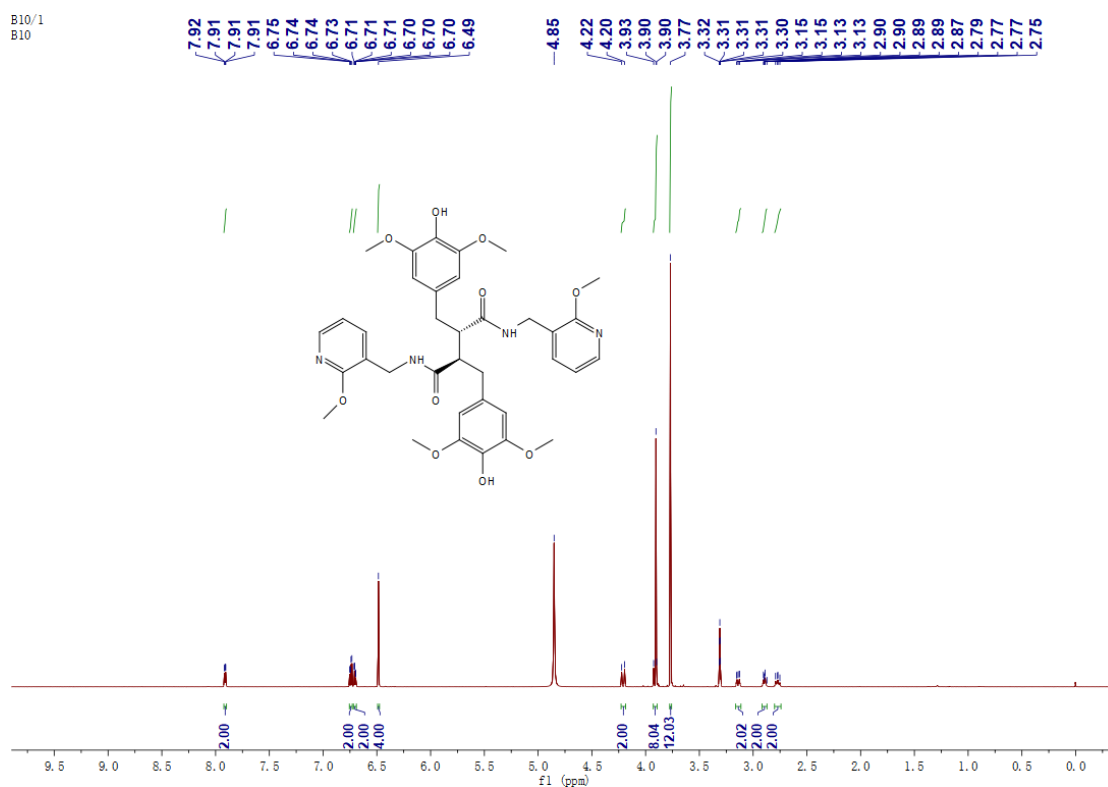


Figure S86  $^1\text{H}$  NMR spectrum of compound 12i

B10/2  
B10

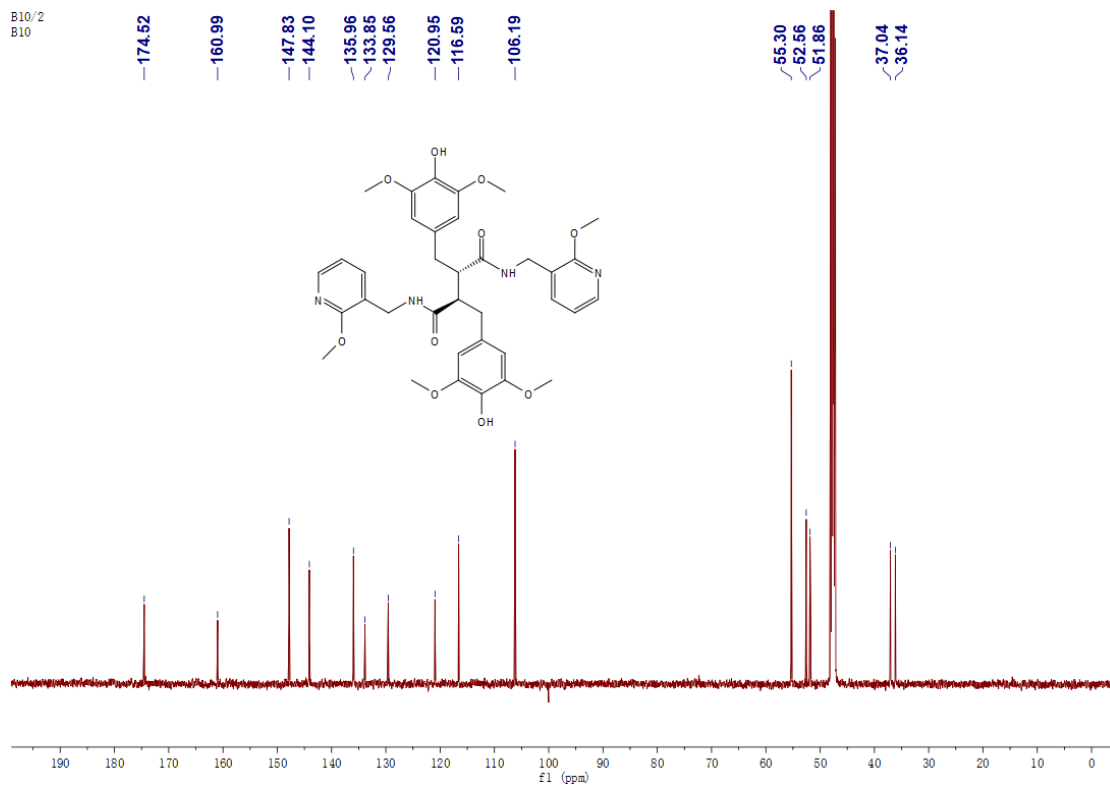


Figure S87  $^{13}\text{C}$  NMR spectrum of compound 12i

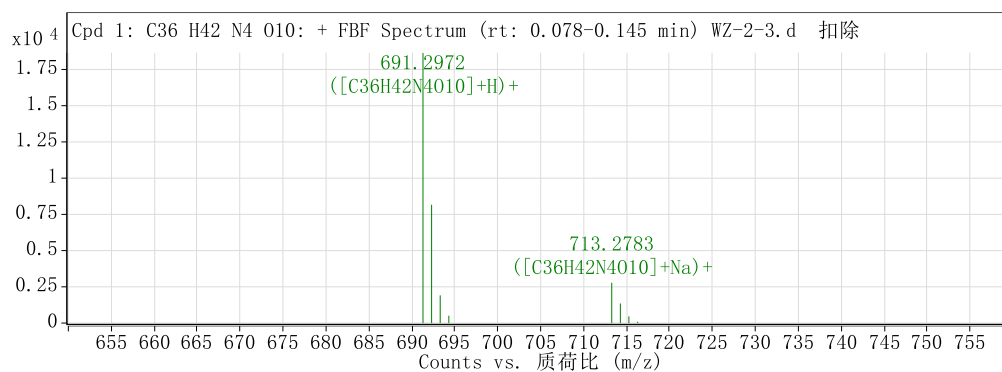


Figure S88 HRMS spectrum of compound 12i

### 31. Paw swelling thickness of mice in the *in vivo* anti-inflammatory experiments

Time (min)	CON					
0	2.557	2.463	2.477	2.435	2.603	2.617
15	2.4	2.291	2.528	2.477	2.679	2.682
30	2.507	2.532	2.699	2.23	2.373	2.56
60	2.403	2.52	2.603	2.496	2.425	2.389
120	2.442	2.415	2.385	2.439	2.665	2.631
240	2.37	2.233	2.634	2.625	2.764	2.427
	Carr.					
0	2.535	2.491	2.618	2.577	2.872	2.761
15	4.014	3.976	4.047	3.781	4.241	4.017
30	3.921	3.964	3.782	3.929	3.871	3.776
60	3.822	3.661	3.953	3.816	3.761	3.712
120	3.887	3.827	4.271	3.353	3.761	3.799
240	3.926	3.866	4.074	3.479	3.703	3.724
	Carr.+20 mg/kg LCA					
0	2.678	2.642	2.644	2.584	2.612	2.584
15	3.466	3.474	3.329	3.421	3.596	3.510
30	3.305	3.199	3.205	3.287	3.315	3.225
60	3.122	3.180	2.943	2.985	3.251	2.913
120	3.016	3.016	2.959	3.135	3.063	2.914
240	3.159	3.158	2.931	2.976	2.936	2.776
	Carr.+5 mg/kg 10h					
0	2.648	2.557	2.633	2.708	2.621	2.600
15	3.881	3.812	3.659	4.052	3.821	3.669
30	3.685	3.496	3.603	3.647	3.725	3.552
60	3.619	3.953	3.180	2.946	3.457	3.647
120	3.643	3.550	3.332	3.495	3.193	3.643
240	3.855	3.741	2.982	3.474	3.279	3.739
	Carr.+20 mg/kg 10h					
0	2.839	2.430	2.706	2.590	2.643	2.228
15	3.510	3.451	3.833	3.404	3.401	2.959
30	3.318	3.243	3.475	3.252	3.390	3.222
60	3.268	3.109	3.411	3.063	3.138	2.728
120	2.945	3.072	3.106	3.199	3.097	3.011
240	3.203	2.986	3.164	2.904	2.953	3.118