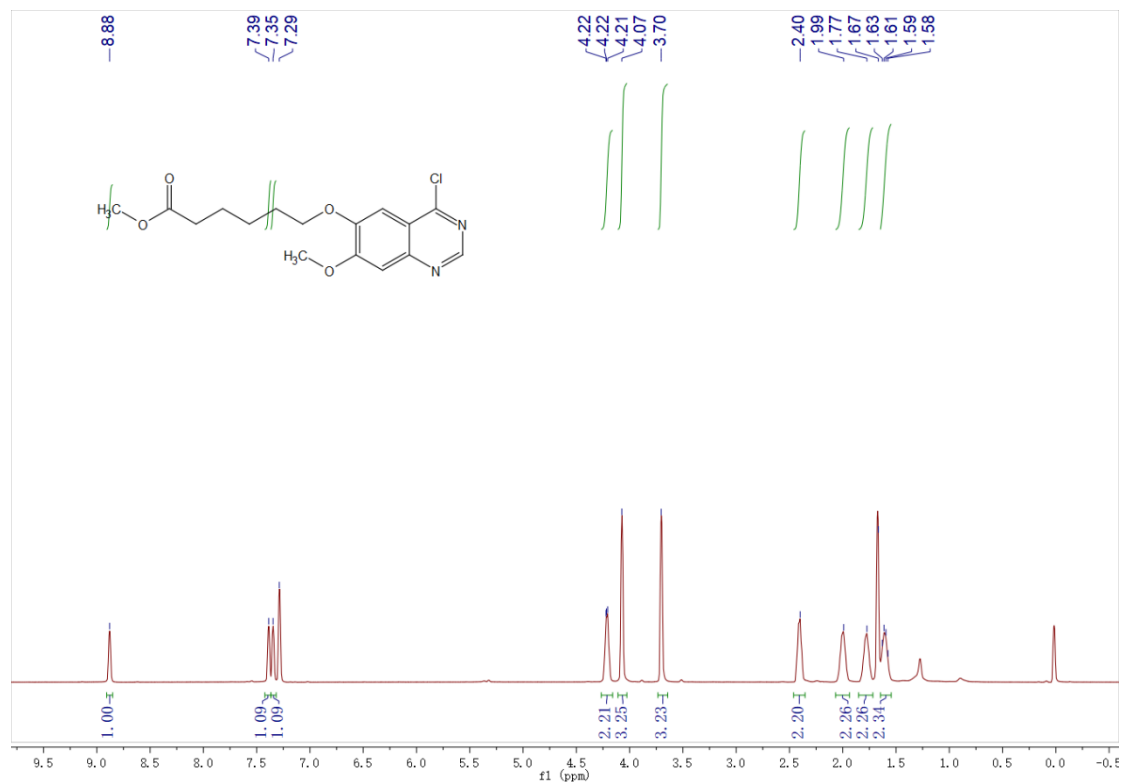
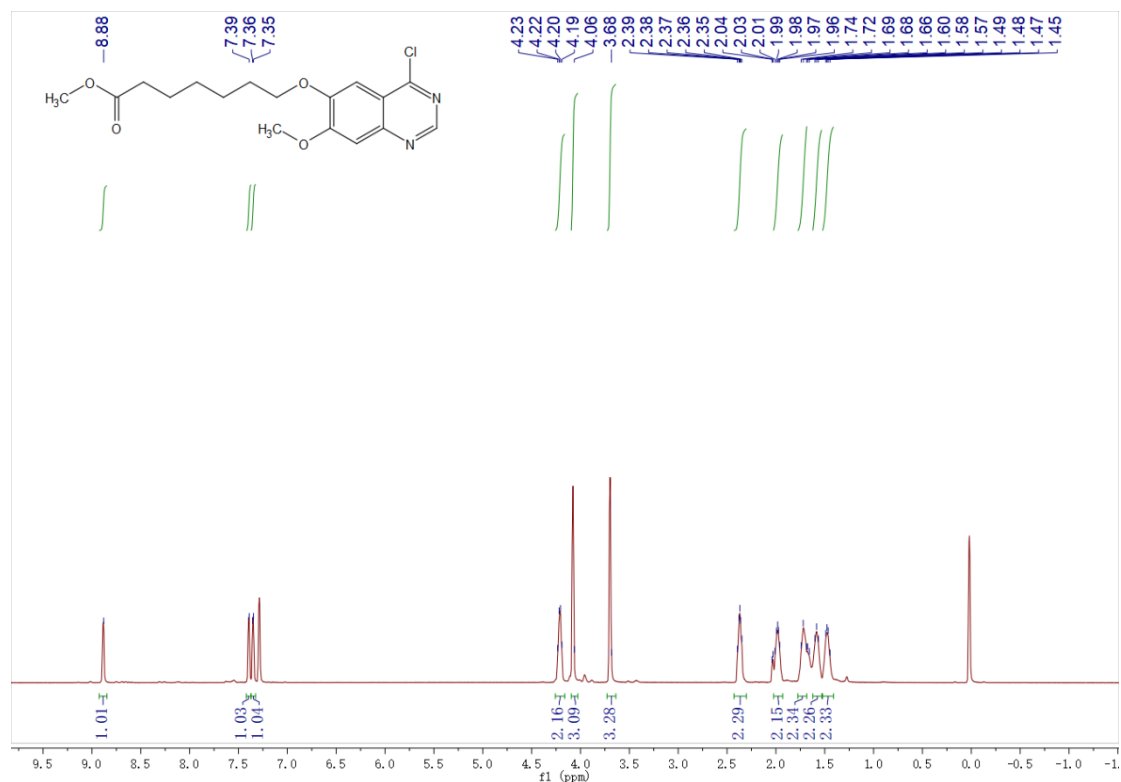


## Design, synthesis and biological evaluation of VEGFR-2/HDAC dual inhibitors as multitargeted antitumor agents based on the Fruquintinib and Vorinostat

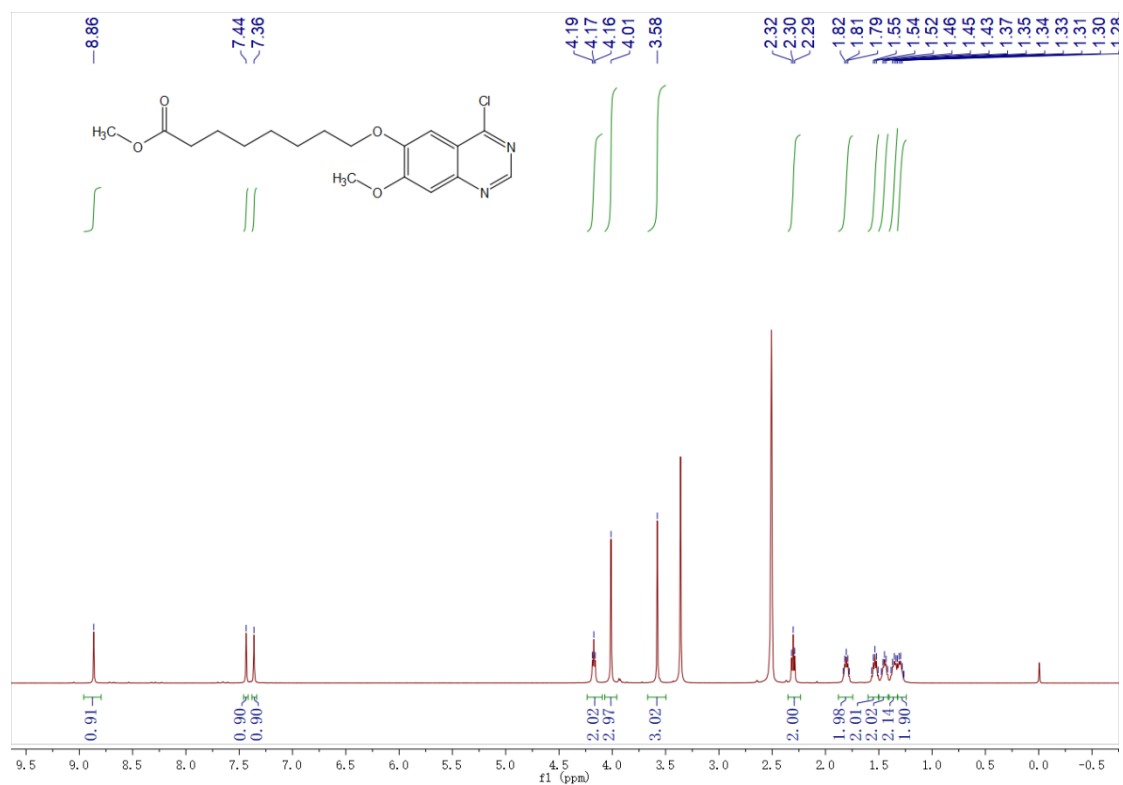
### $^1\text{H-NMR}$ of intermediate **3a**



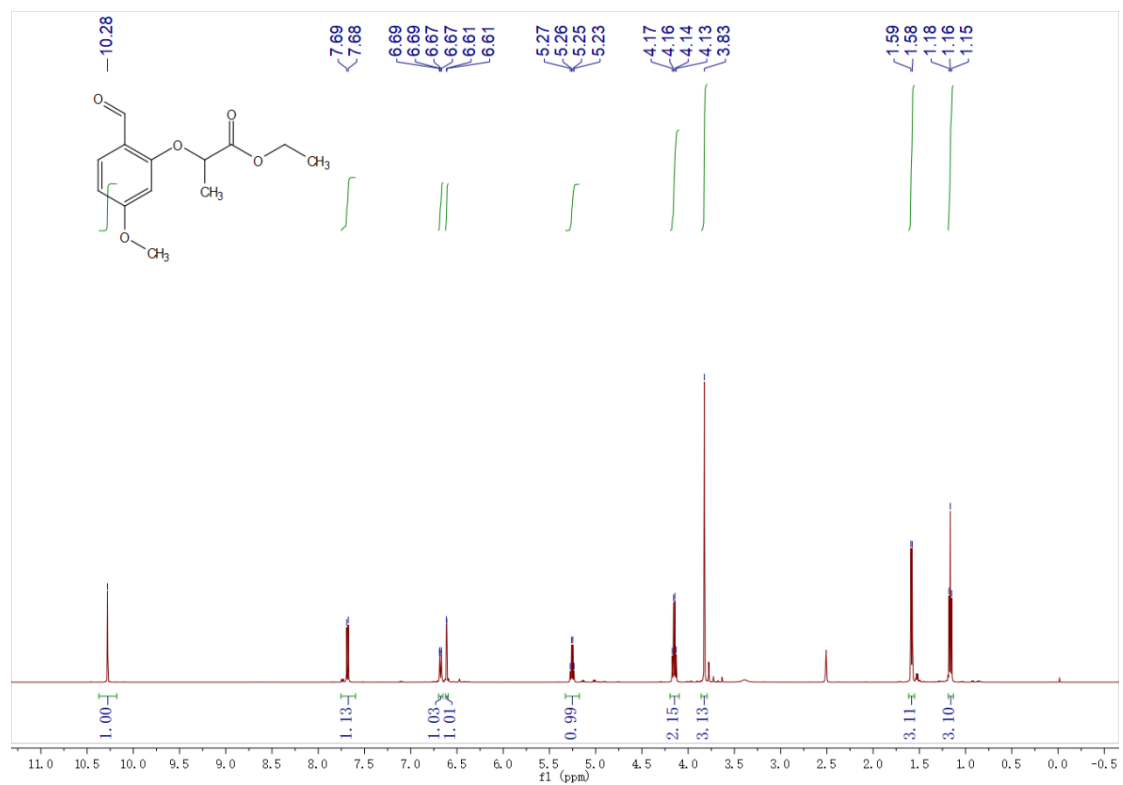
### $^1\text{H-NMR}$ of intermediate **3b**



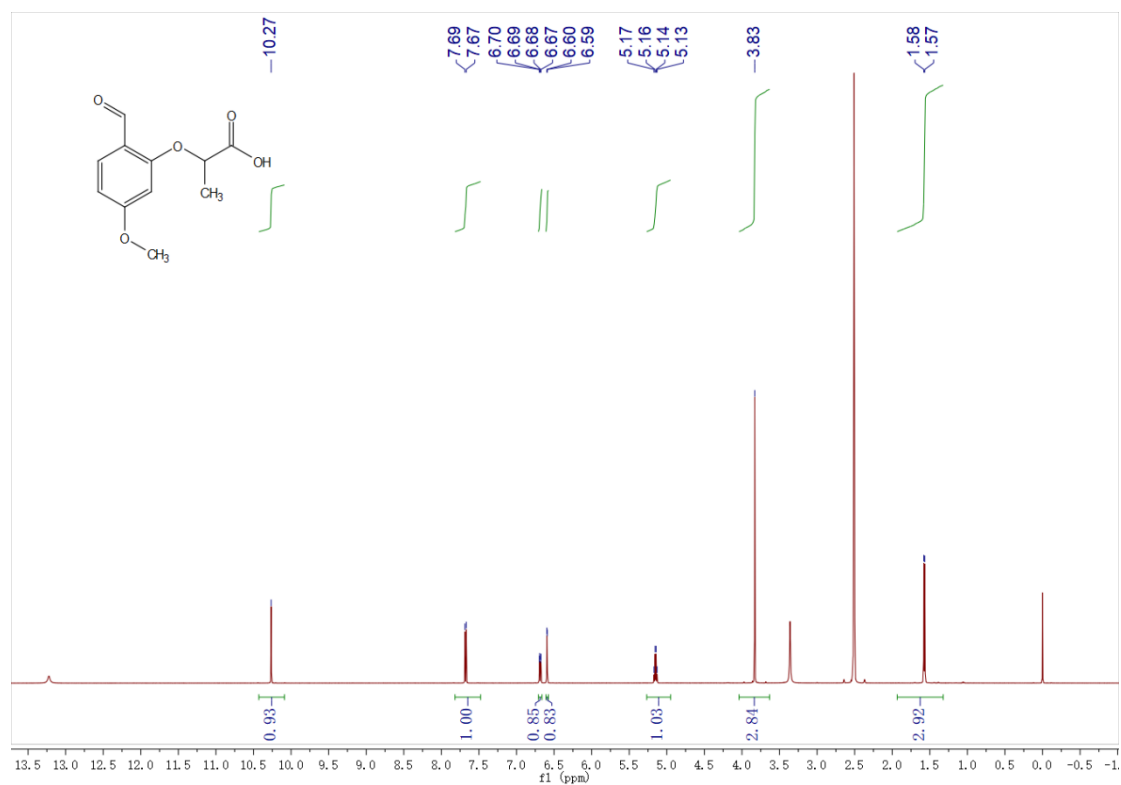
### <sup>1</sup>H-NMR of intermediate 3c



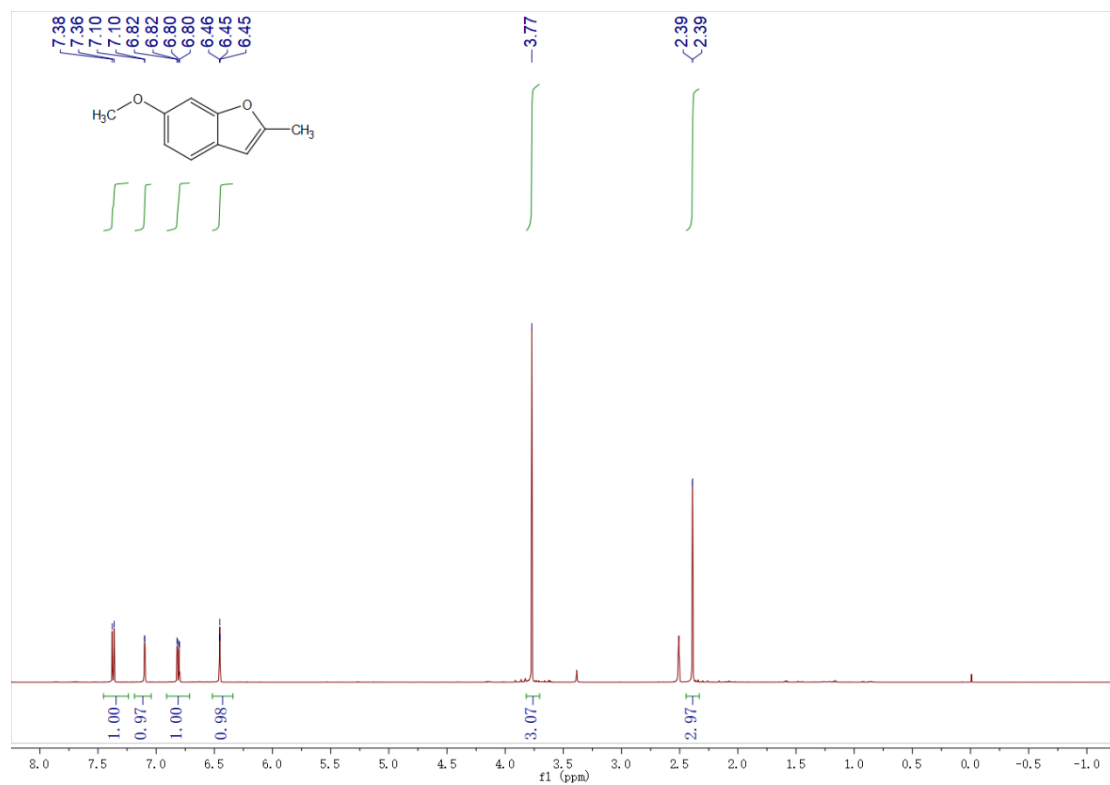
### <sup>1</sup>H-NMR of intermediate 4



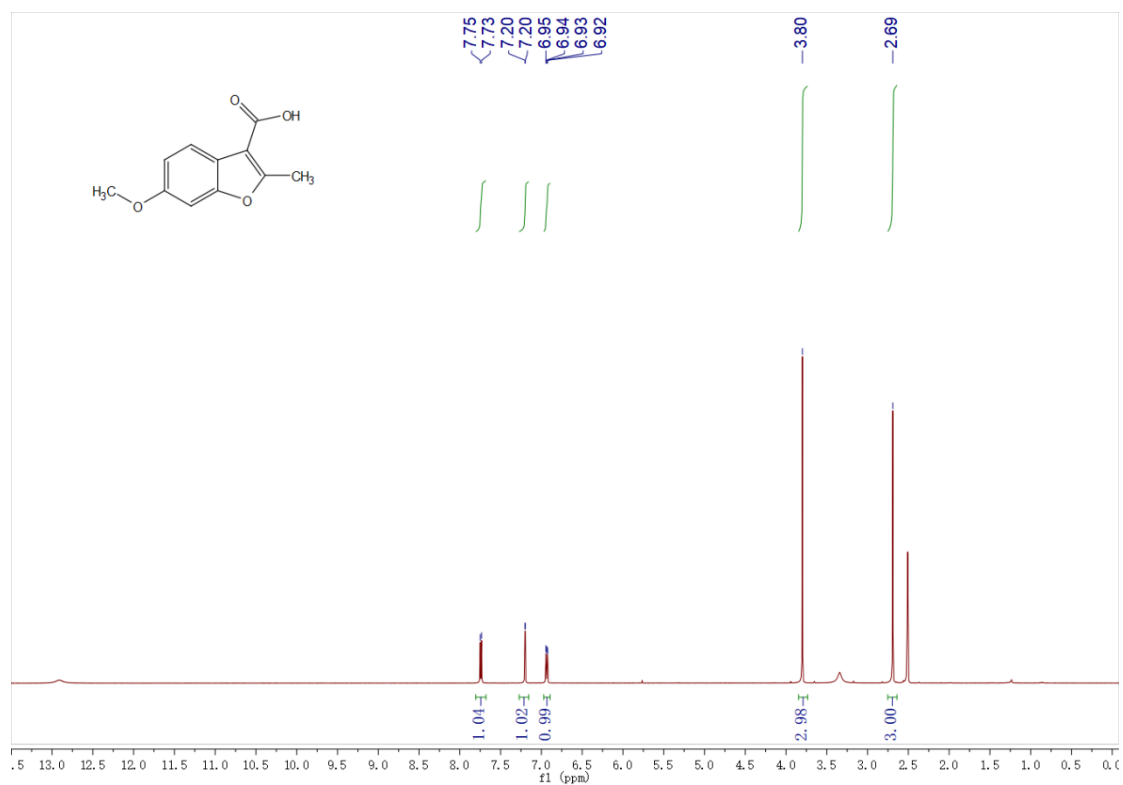
### <sup>1</sup>H-NMR of intermediate 5



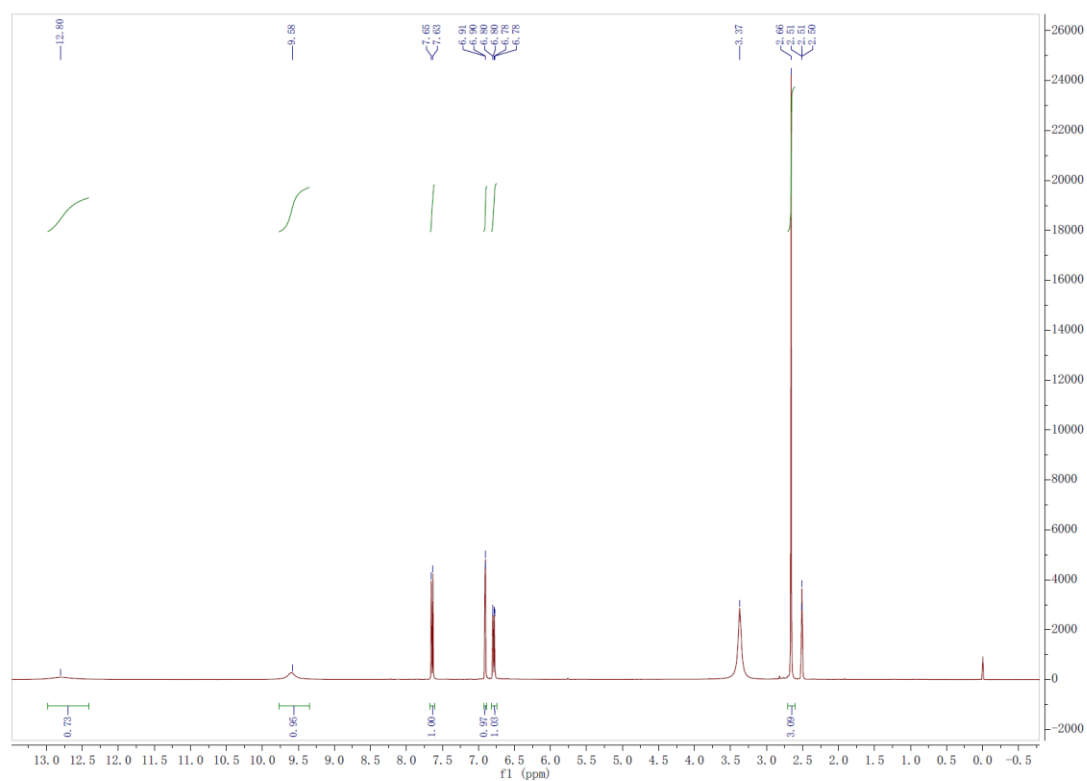
### <sup>1</sup>H-NMR of intermediate 6



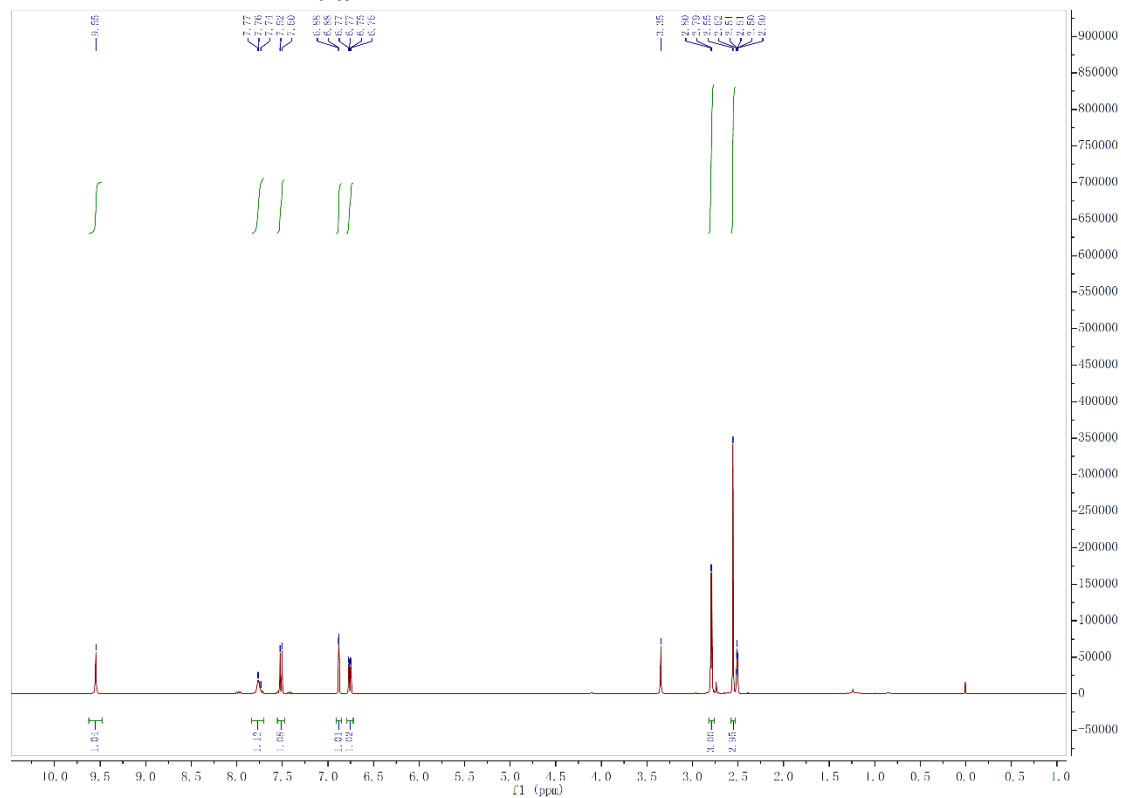
### <sup>1</sup>H-NMR of intermediate 7



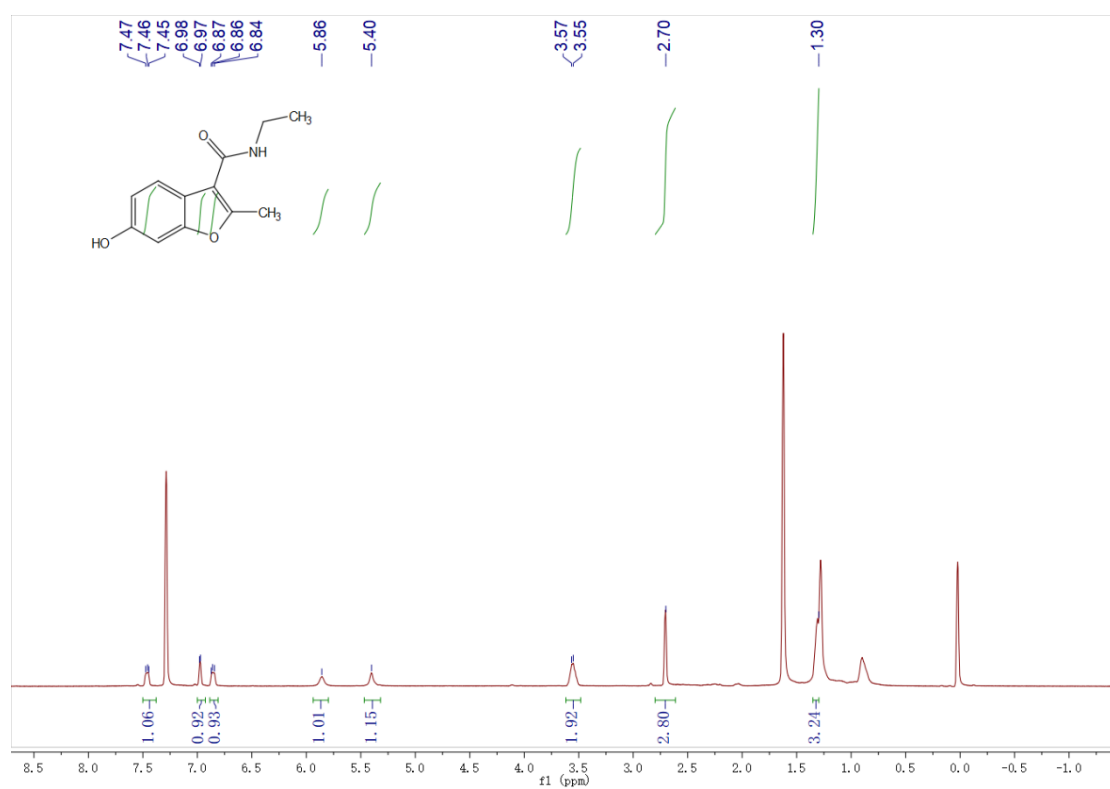
### <sup>1</sup>H-NMR of intermediate 8



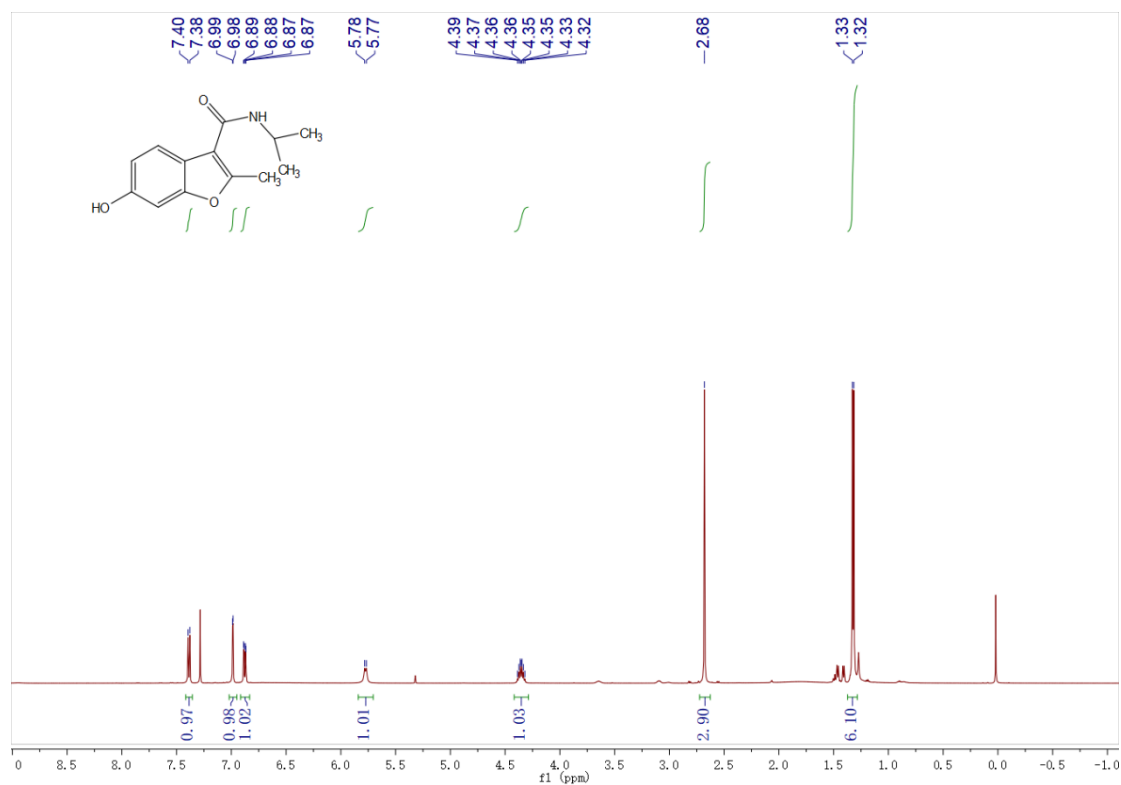
### <sup>1</sup>H-NMR of intermediate **9a**



### <sup>1</sup>H-NMR of intermediate **9b**



### <sup>1</sup>H-NMR of intermediate 9c

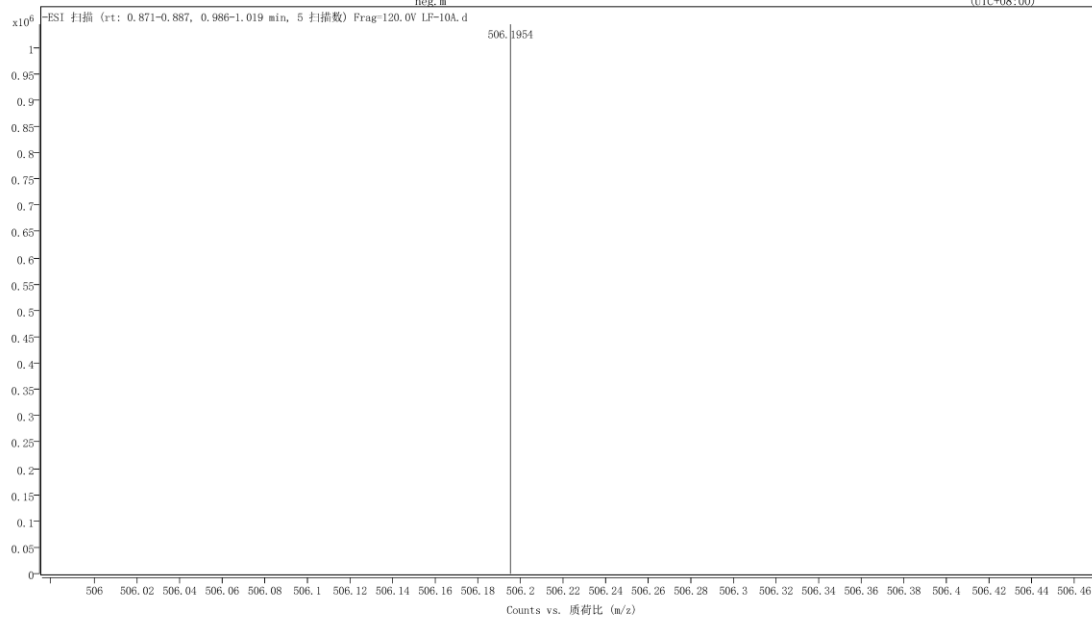


### HRMS (ESI) of intermediate 10a

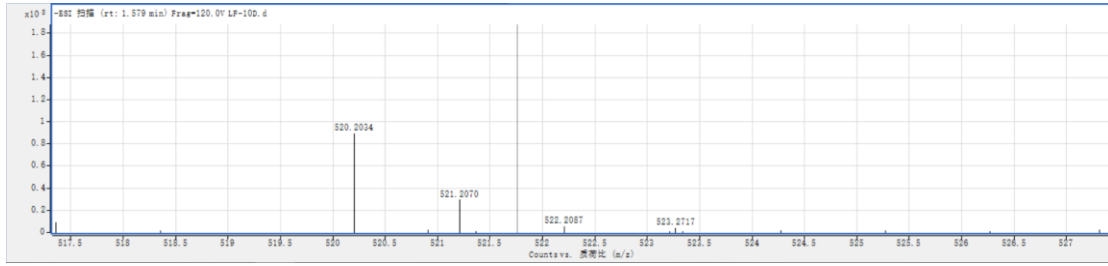
#### 谱图报告



名称	Sample29	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-10A.d	方法 (Acq)	80mech20water-10min-neg.m	采集时间 (本地)	2023/5/18 15:40:19 (UTC+08:00)



## HRMS (ESI) of intermediate 10b

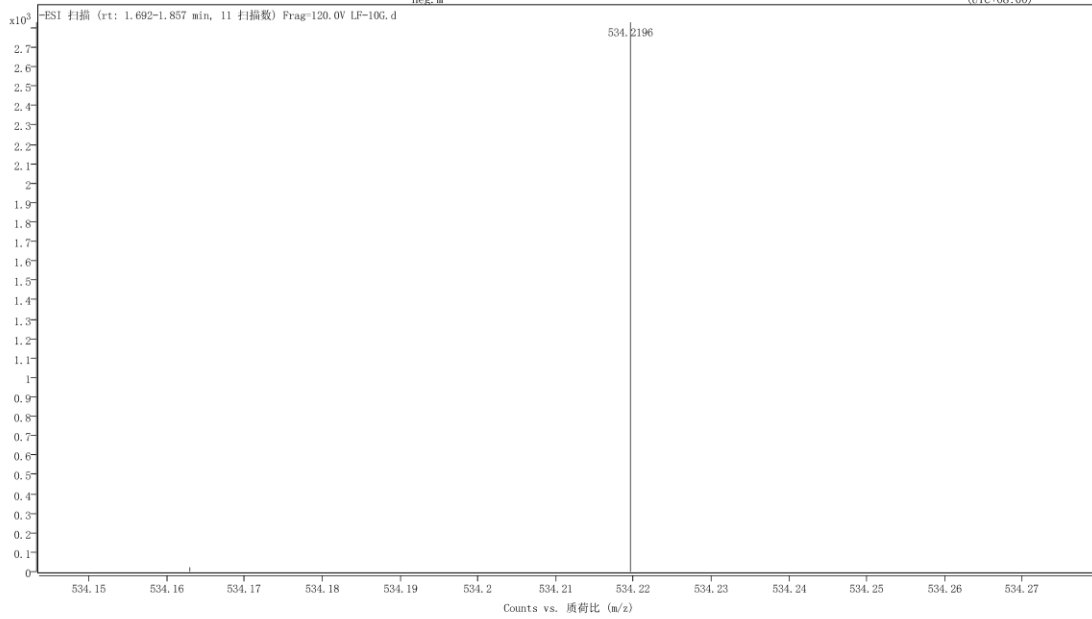


## HRMS (ESI) of intermediate 10c

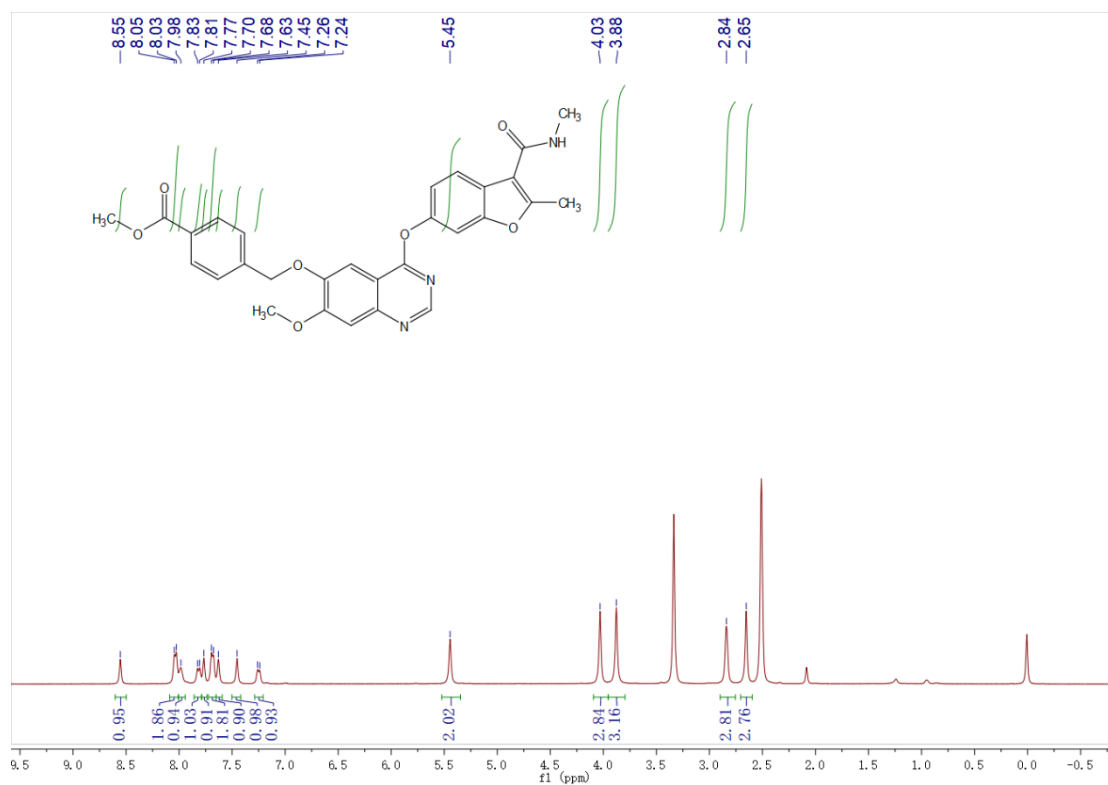
### 谱图报告



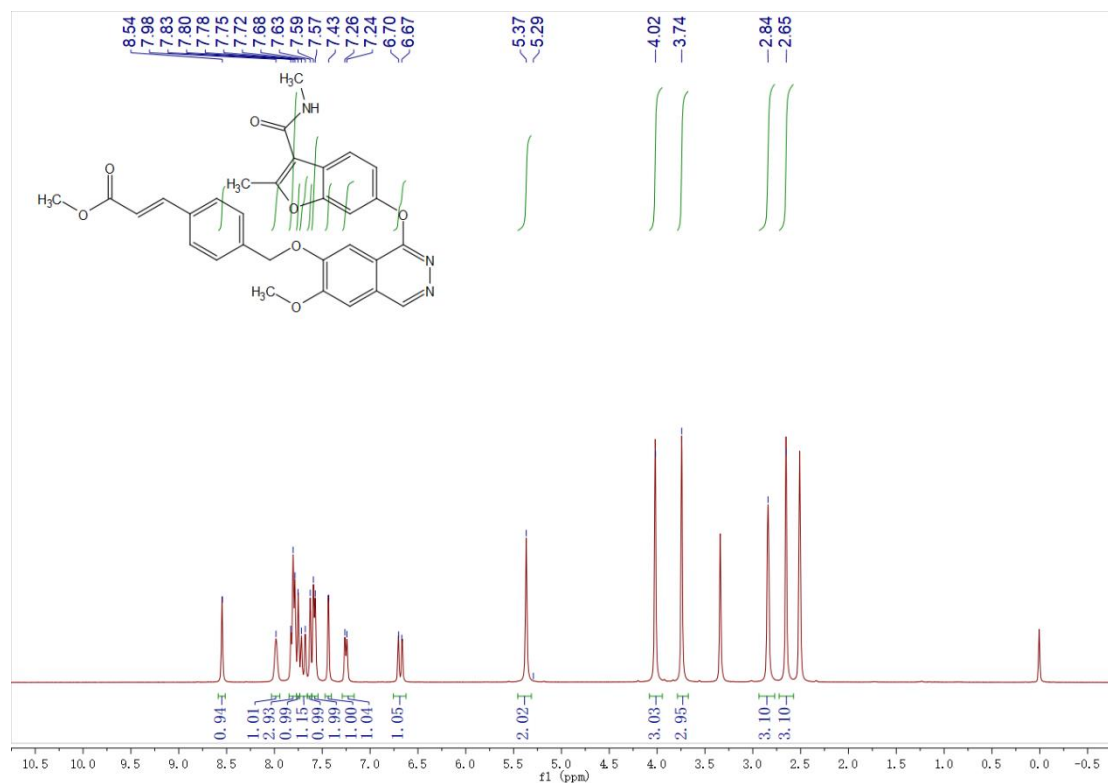
名称	Sample35	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF=10G.d	方法 (Acq)	80meoh20water=10min- neg.m	注释	采集时间 (本地) 2023/5/18 16:43:56 (UTC+08:00)



### <sup>1</sup>H-NMR of intermediate **10d**



### <sup>1</sup>H-NMR of intermediate **10e**



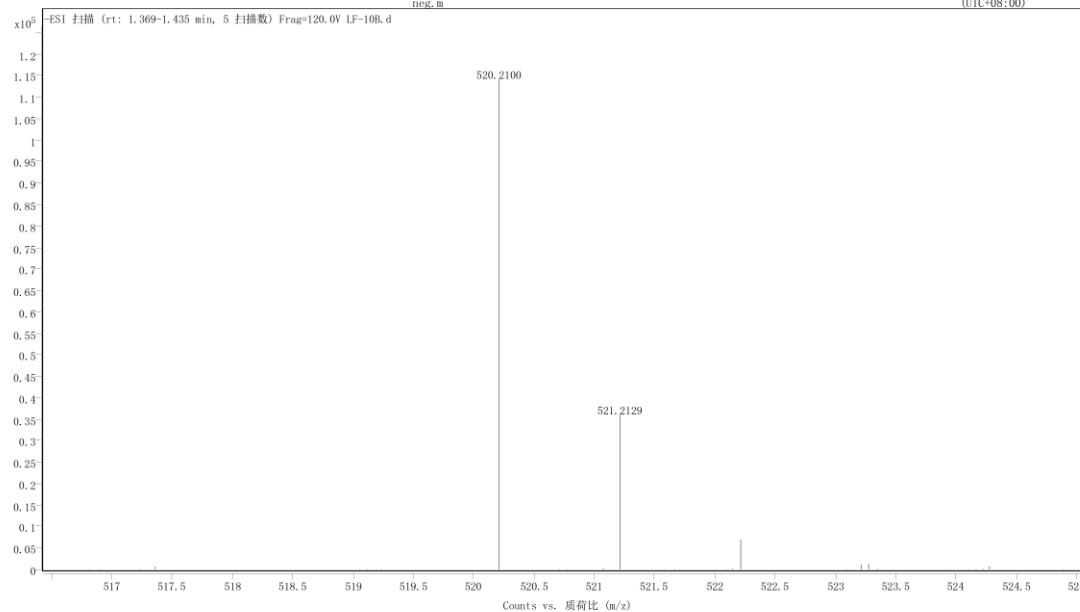


# HRMS (ESI) of intermediate 10f

## 谱图报告



名称	Sample30	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-10B.d	方法 (Acq)	80mech20water-10min- neg.m	注释	采集时间 (本地) 2023/5/18 15:50:55 (UTC+08:00)

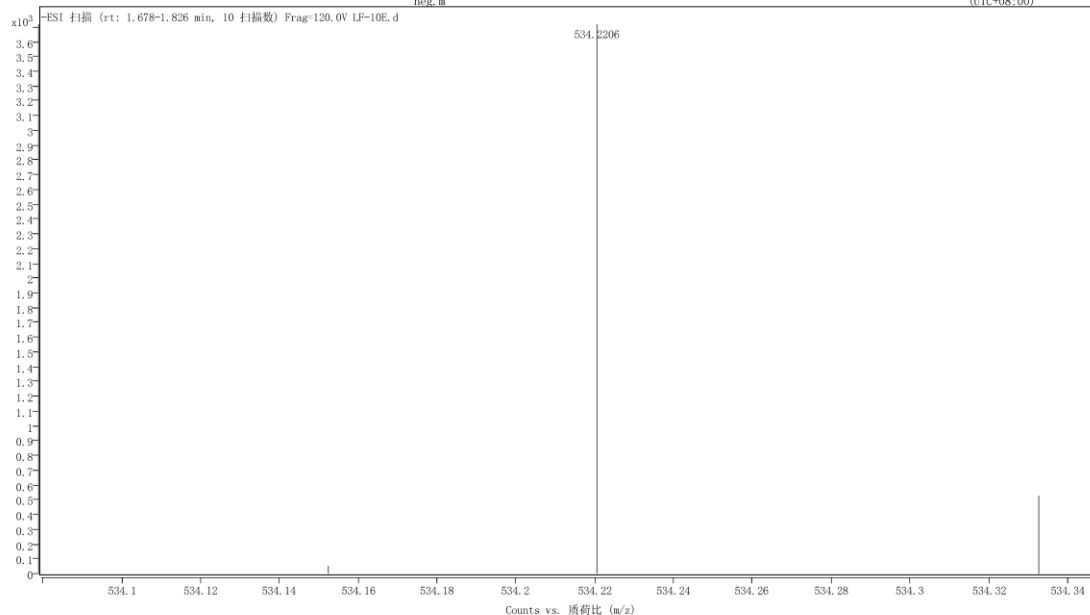


# HRMS (ESI) of intermediate 10g

## 谱图报告



名称	Sample33	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-10E.d	方法 (Acq)	80mech20water-10min- neg.m	注释	采集时间 (本地) 2023/5/18 16:22:44 (UTC+08:00)

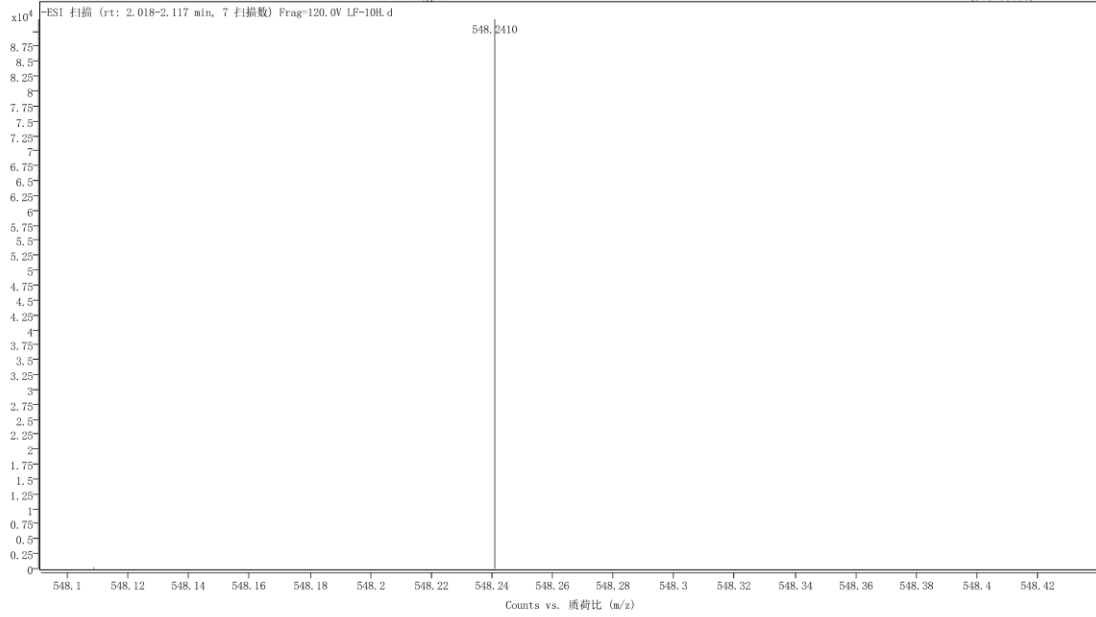


# HRMS (ESI) of intermediate 10h

## 谱图报告



名称	Sample36	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-10H.d	方法 (Acq)	80mech20water-10min- neg.m	注释	采集时间 (本地) 2023/5/18 16:54:32 (UTC+08:00)

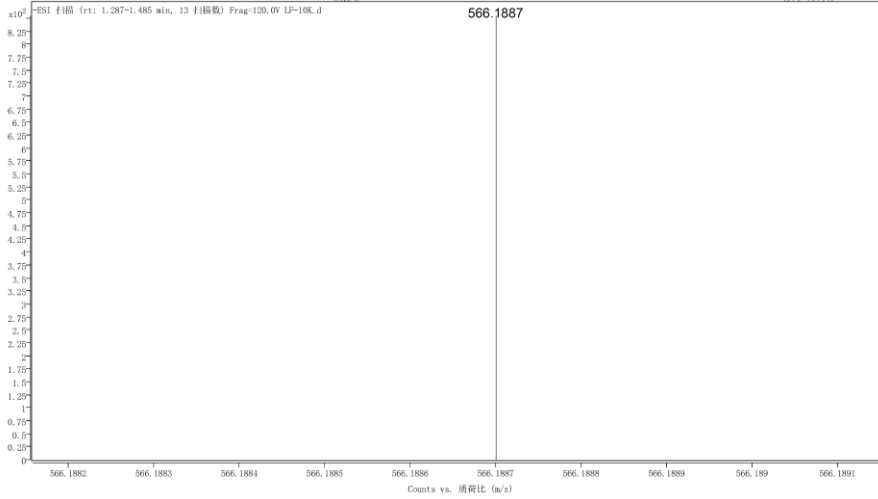


# HRMS (ESI) of intermediate 10j

## 谱图报告



名称	Sample39	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-10K.d	方法 (Acq)	80mech20water-10min- neg.m	注释	采集时间 (本地) 2023/5/18 17:26:20 (UTC+08:00)

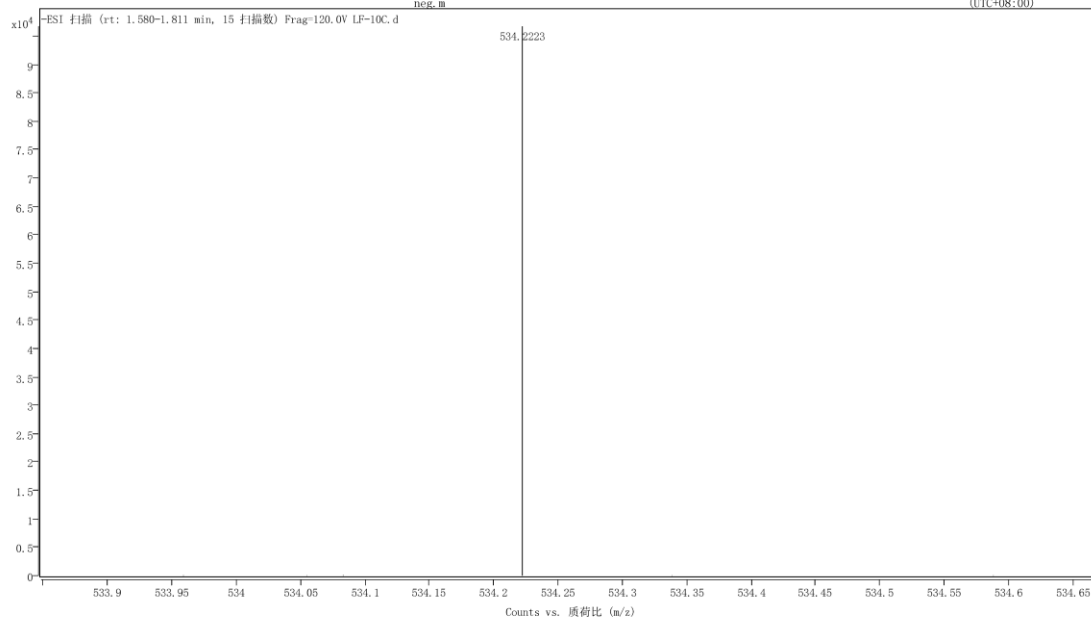


# HRMS (ESI) of intermediate 10k

## 谱图报告



名称	Sample31	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-10C.d	方法 (Acq)	80meoh20water-10min-neg.m	注释	采集时间 (本地) 2023/5/18 16:01:32 (UTC+08:00)

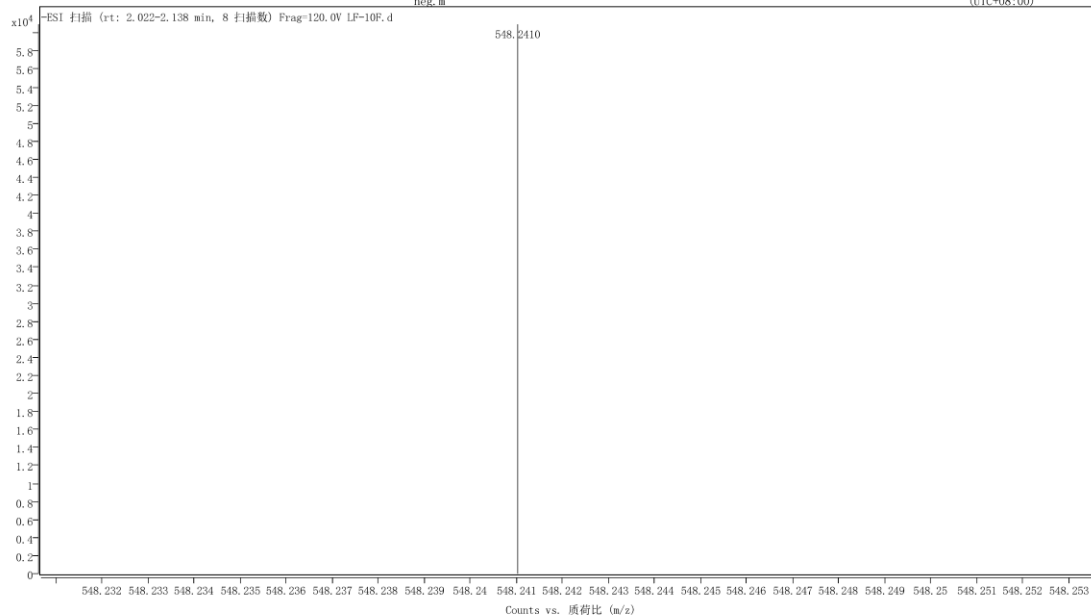


# HRMS (ESI) of intermediate 10l

## 谱图报告



名称	Sample34	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-10F.d	方法 (Acq)	80meoh20water-10min-neg.m	注释	采集时间 (本地) 2023/5/18 16:33:20 (UTC+08:00)

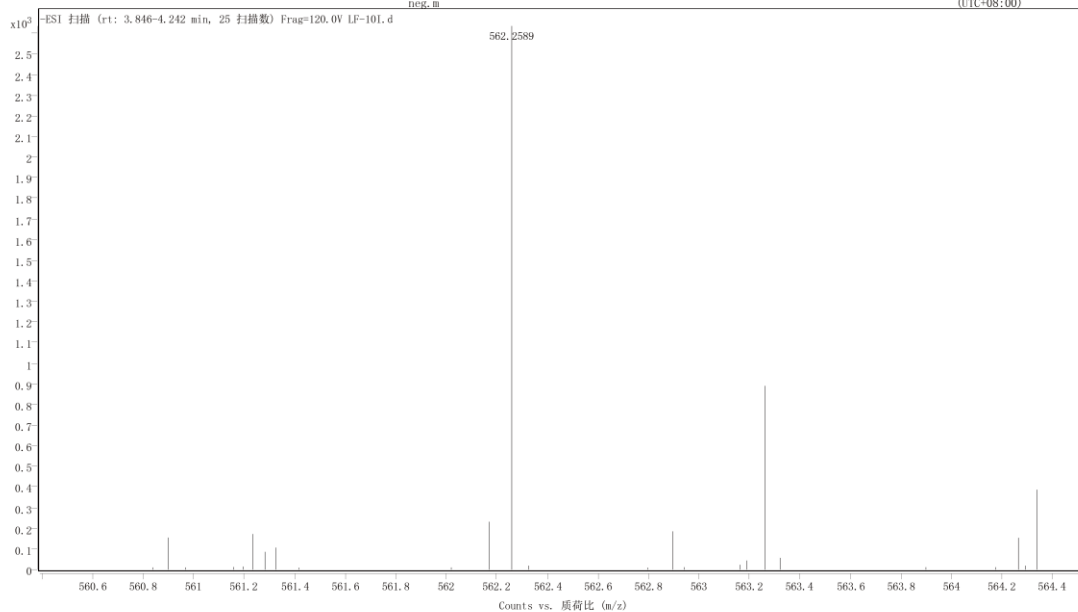


# HRMS (ESI) of intermediate 10m

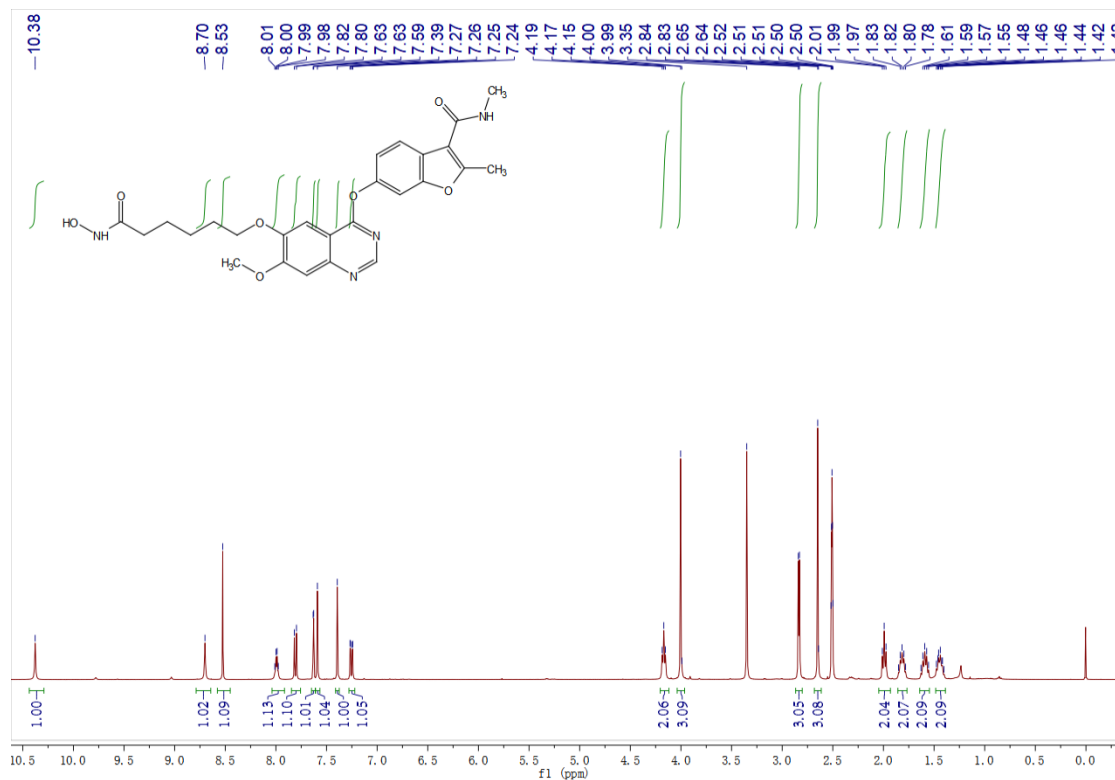
## 谱图报告



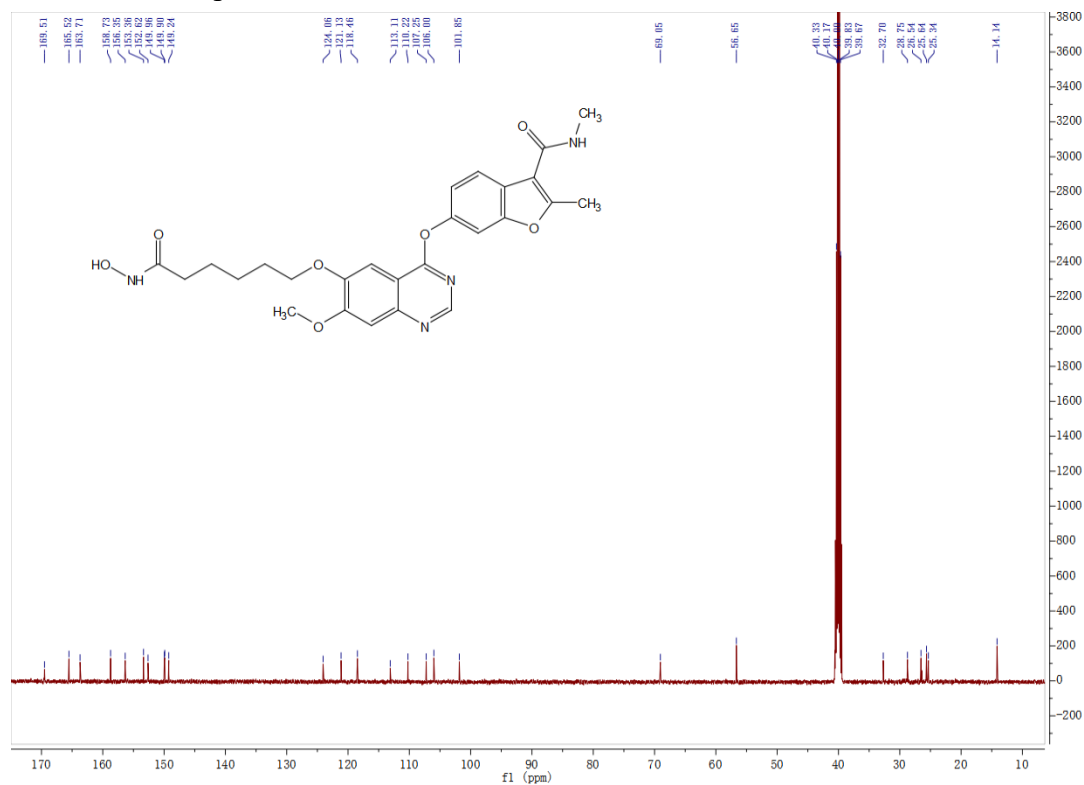
名称	Sample37	样品架位置	仪器	Instrument 1	操作者
进样体积 (ul)	5	样品盘位置	IRM 状态	所有丢失的离子	
数据文件	LF-101.d	方法 (Acq)	80vol20water-10min-neg.m	注释	采集时间 (本地) 2023/5/18 17:05:08 (UTC+08:00)



# <sup>1</sup>H-NMR of compound 12



### <sup>13</sup>C-NMR of compound 12

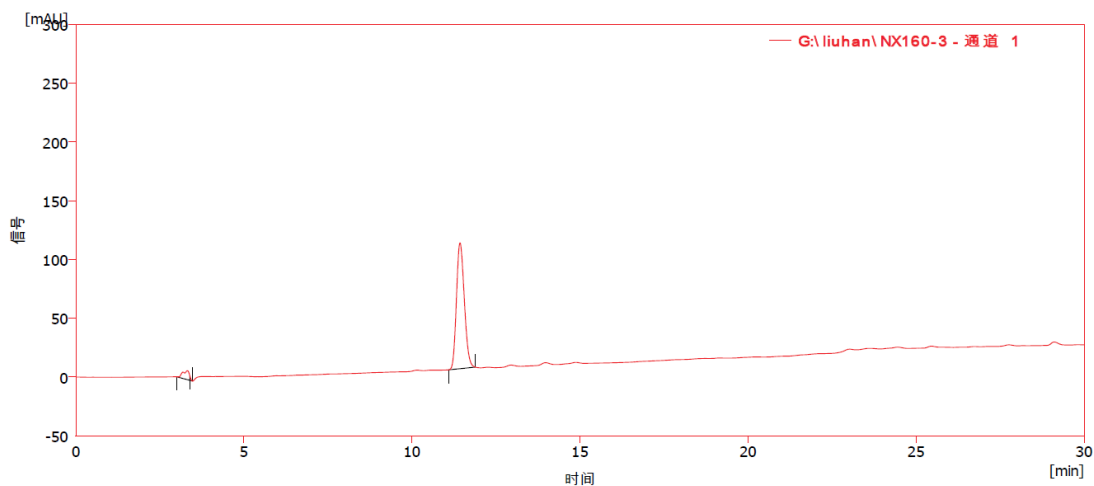


### HPLC of compound 13

2023/9/14 17:54

色谱图 G:\liuhan\NX160-3.prm

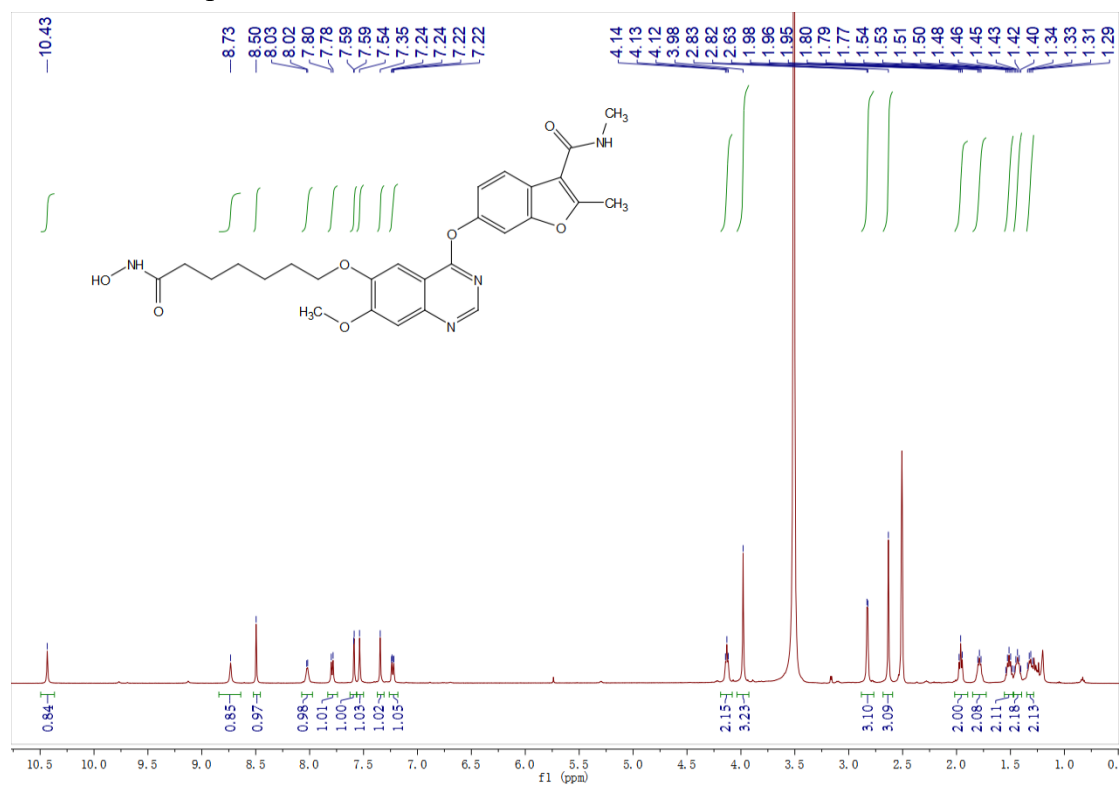
第1页/共6页



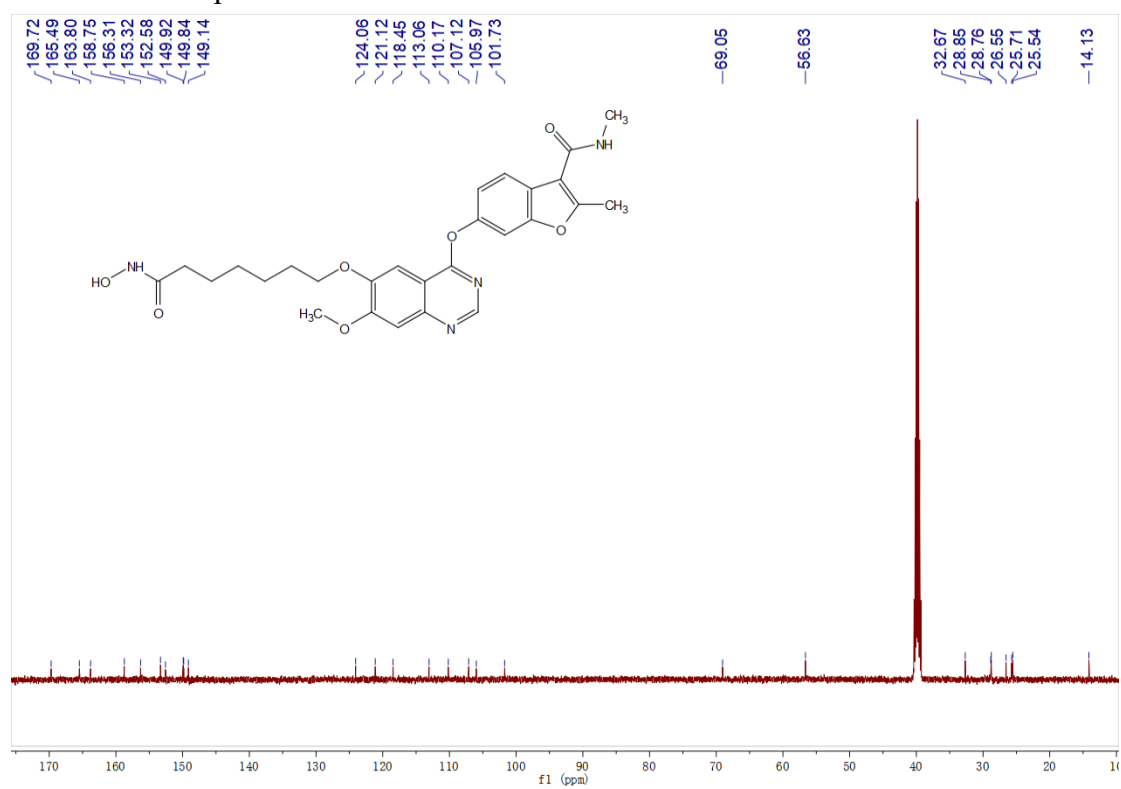
结果表(不计算 - G:\liuhan\NX160-3 - 通道 1)

	保留时间 [min]	峰面积 [mAU.s]	峰高 [mAU]	面积 [%]	峰高 [%]	W05 [min]	PDA峰纯度	化合物名称
1	3.318	97.802	7.658	5.3	6.5	0.27	838	
2	3.397	6.143	3.421	0.3	2.9	0.03	225	
3	11.430	1739.623	107.067	94.4	90.6	0.26	927	
合计		1843.569	118.145	100.0	100.0			

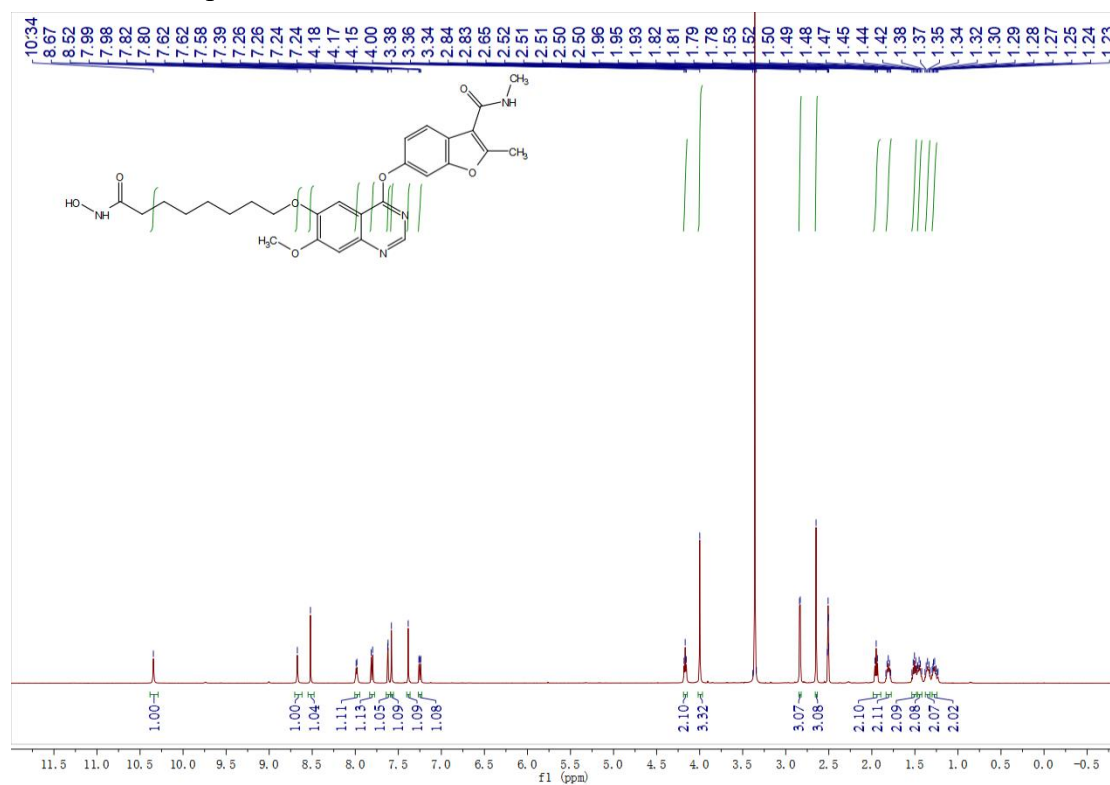
### <sup>1</sup>H-NMR of compound 13



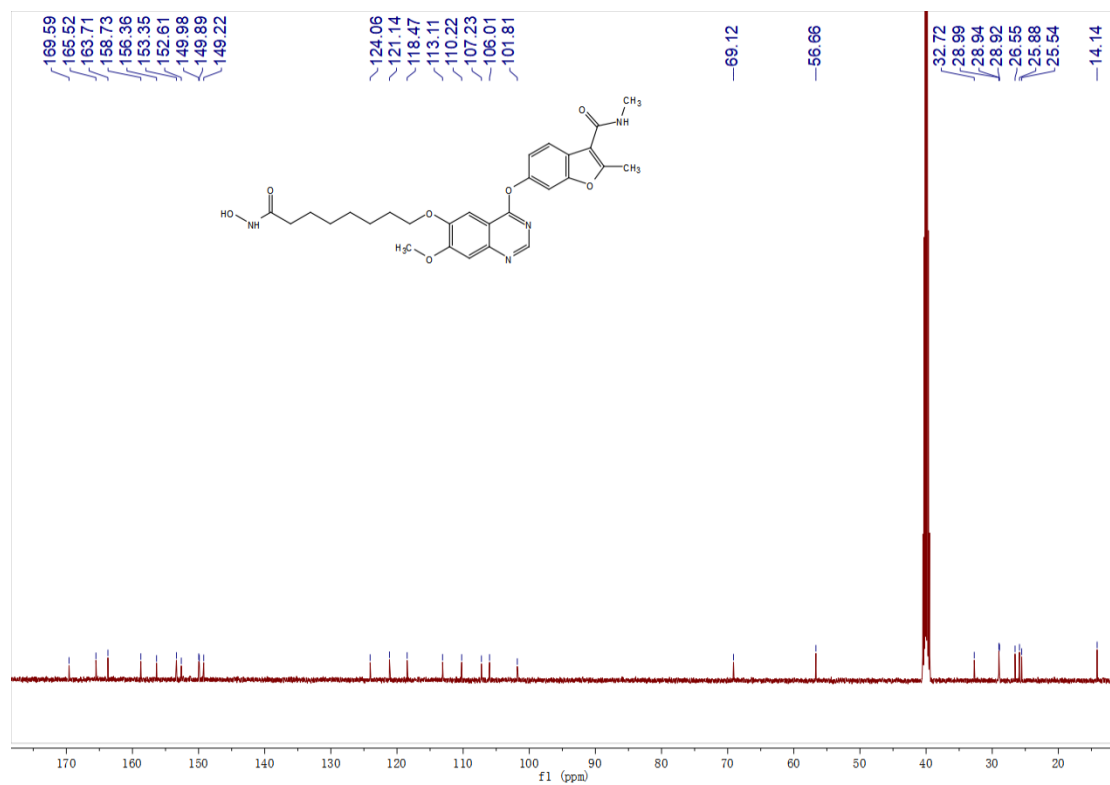
### <sup>13</sup>C-NMR of compound 13



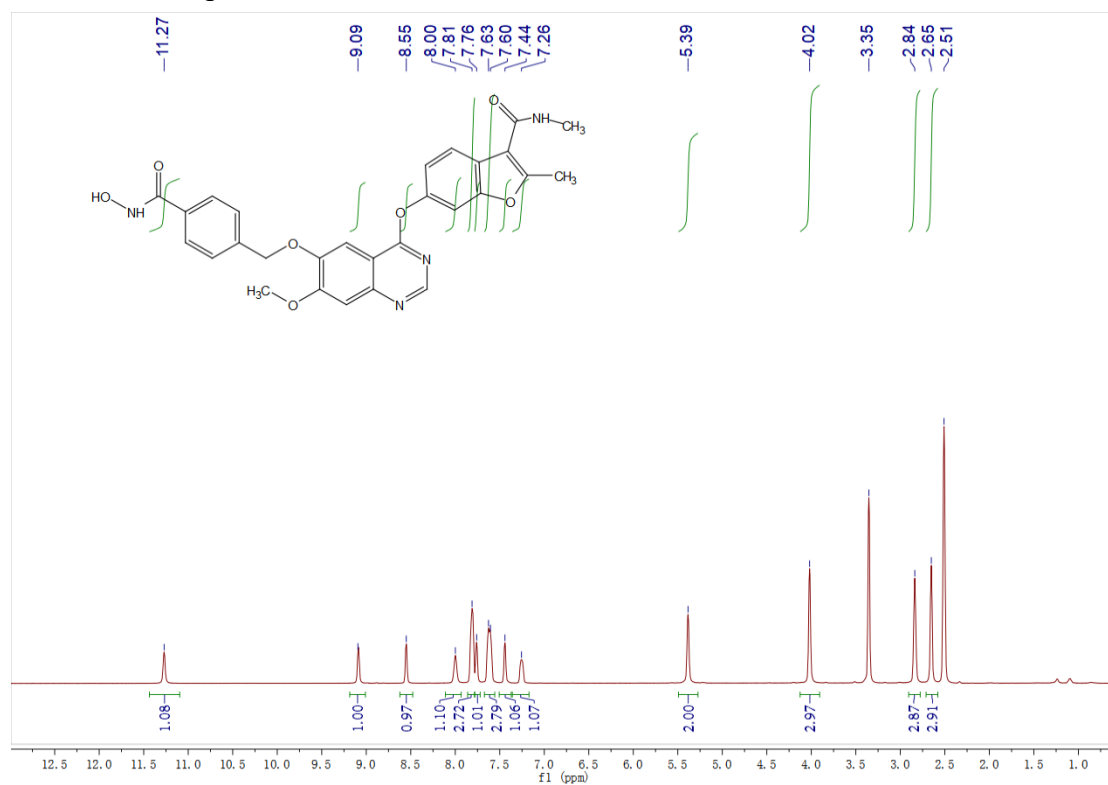
### <sup>1</sup>H-NMR of compound 14



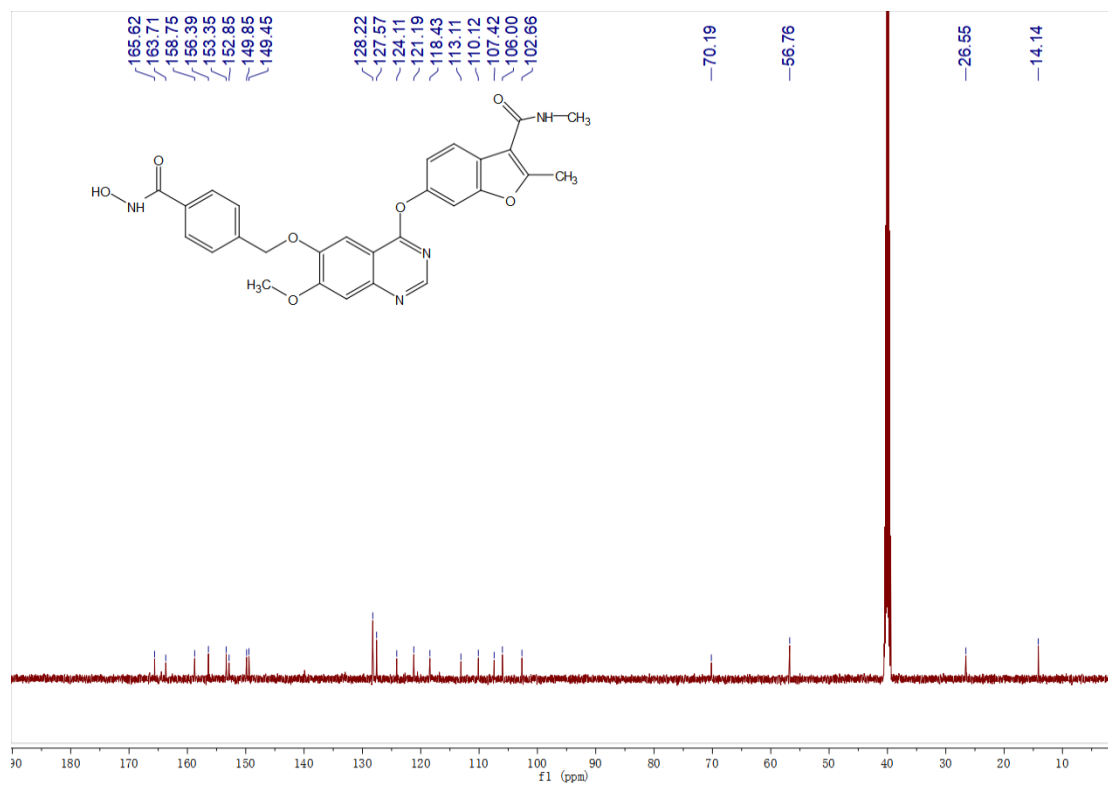
### <sup>13</sup>C-NMR of compound 14



### <sup>1</sup>H-NMR of compound 15

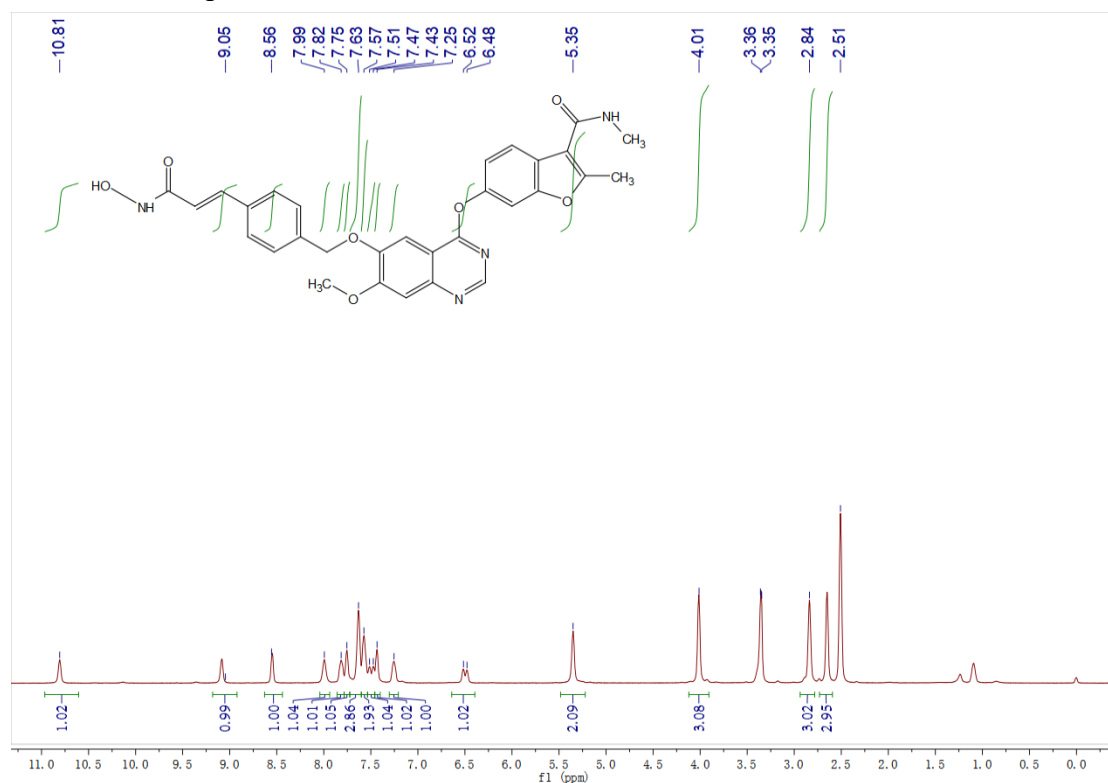


### <sup>13</sup>C-NMR of compound 15

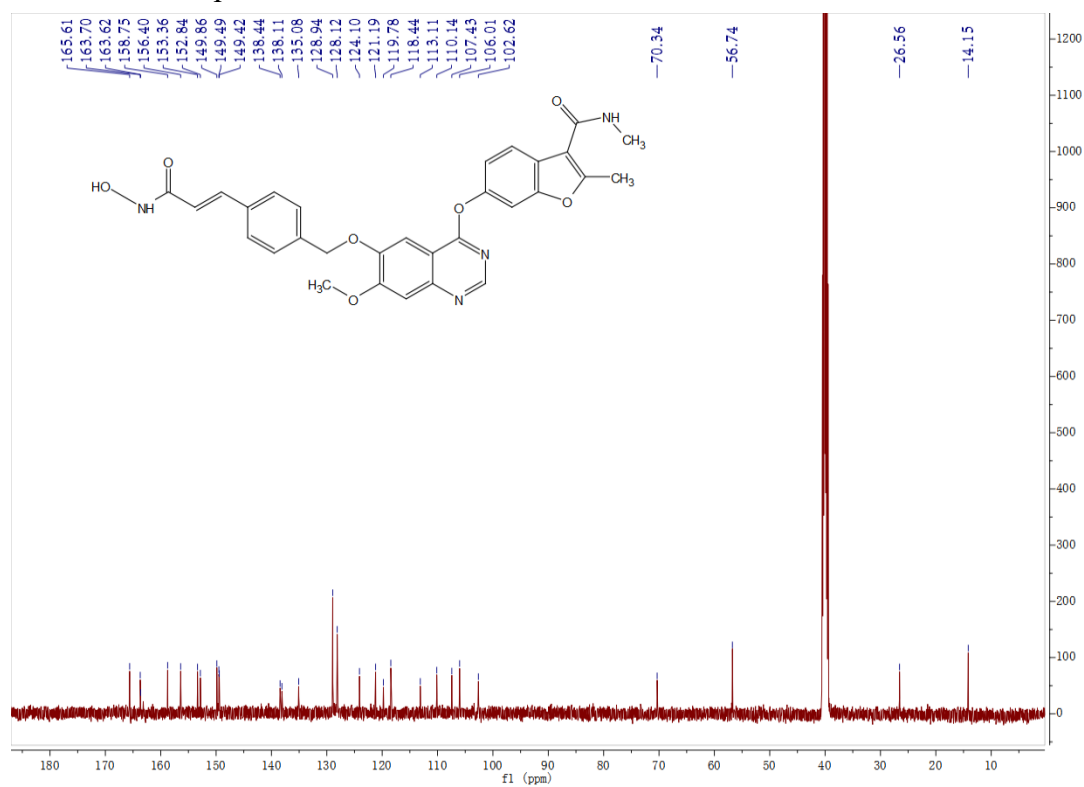




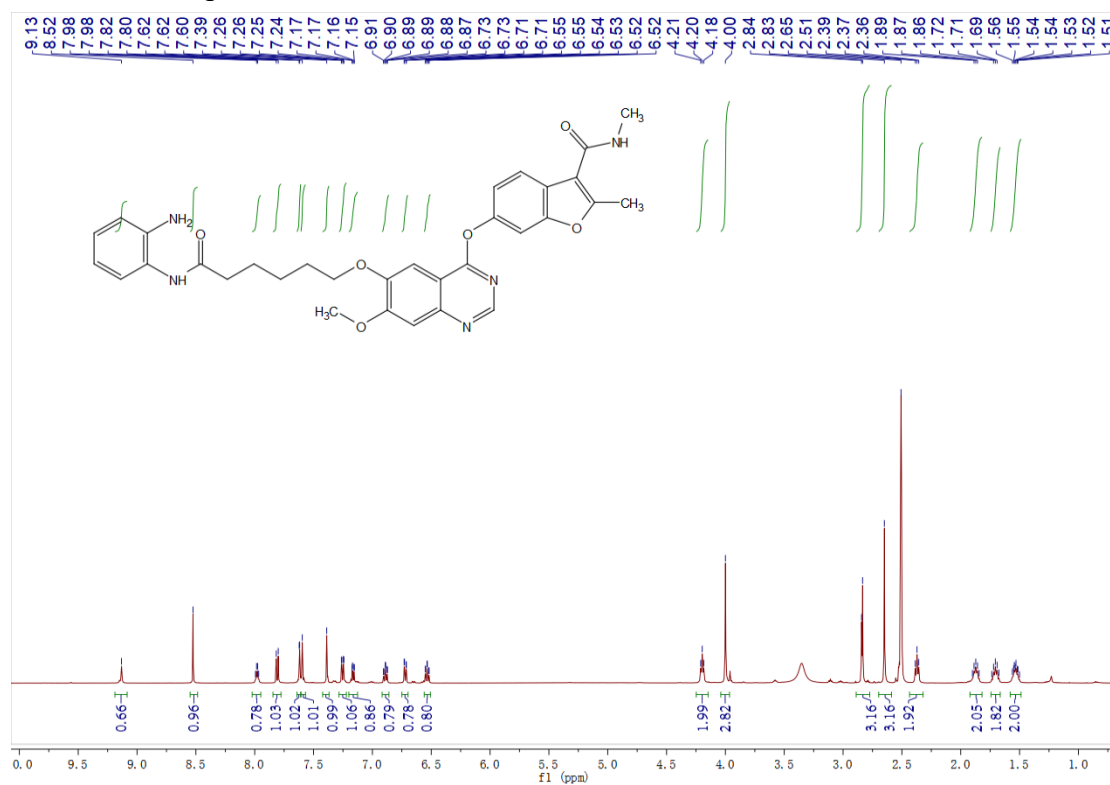
### <sup>1</sup>H-NMR of compound 16



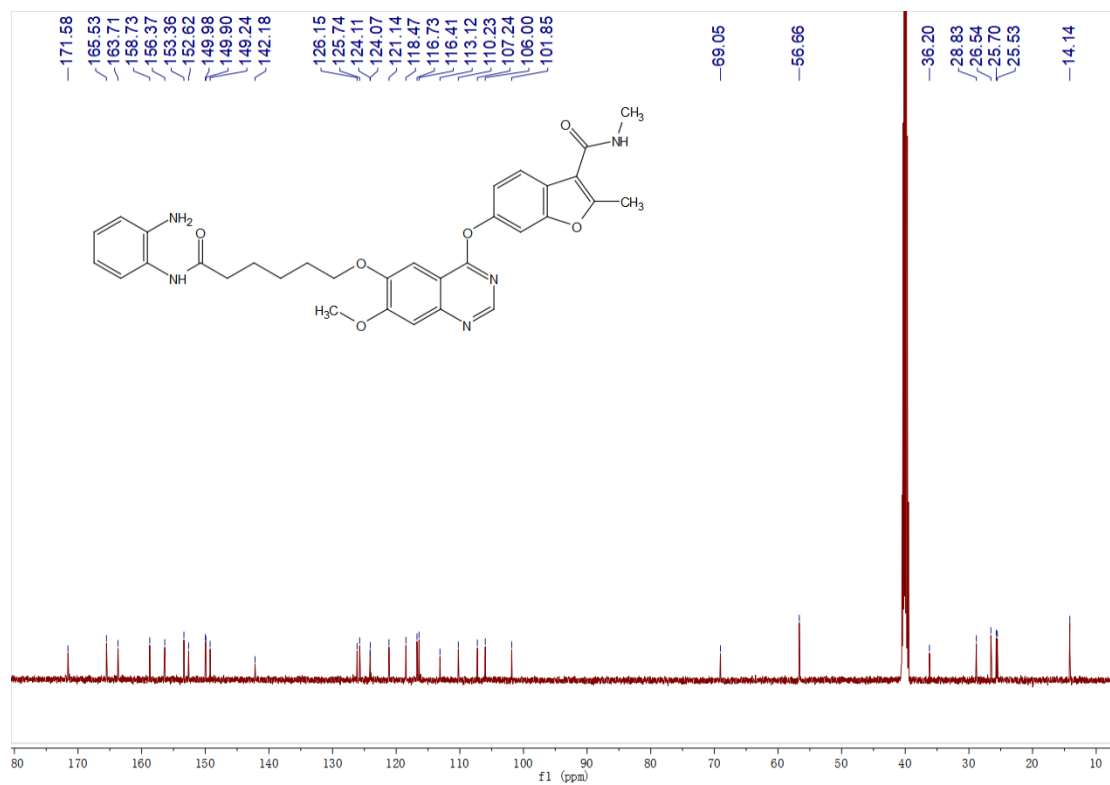
### <sup>13</sup>C-NMR of compound 16



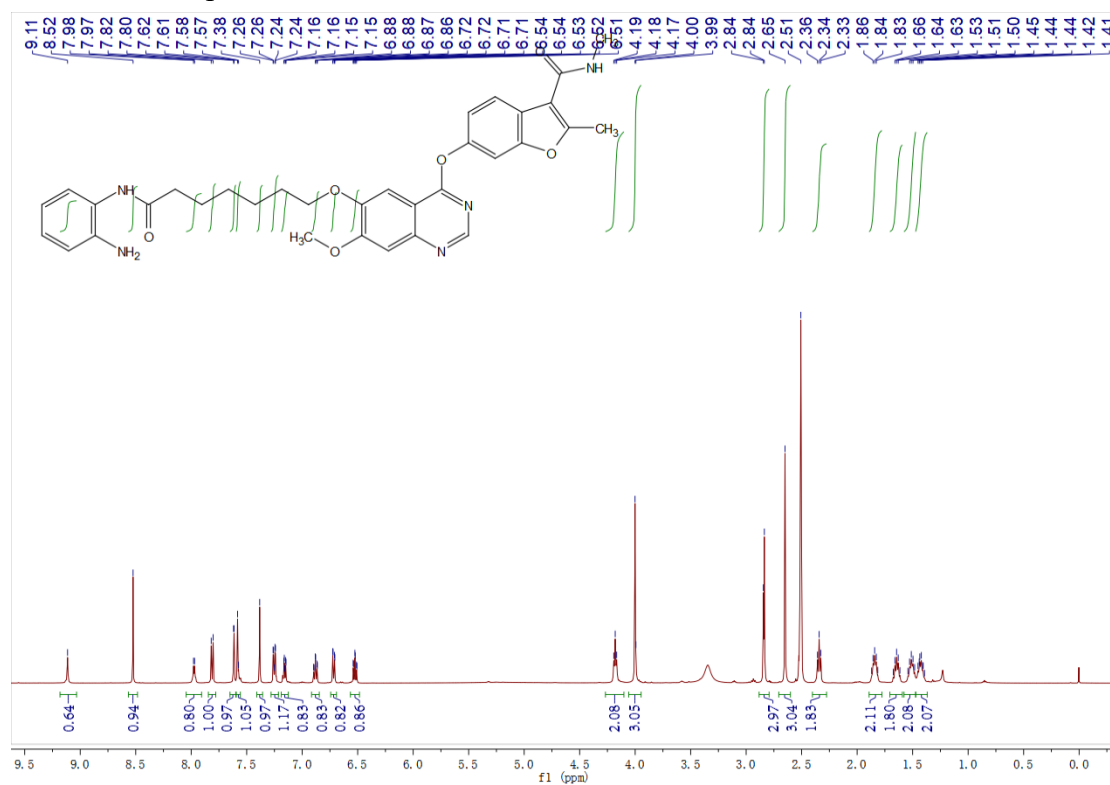
### <sup>1</sup>H-NMR of compound 17



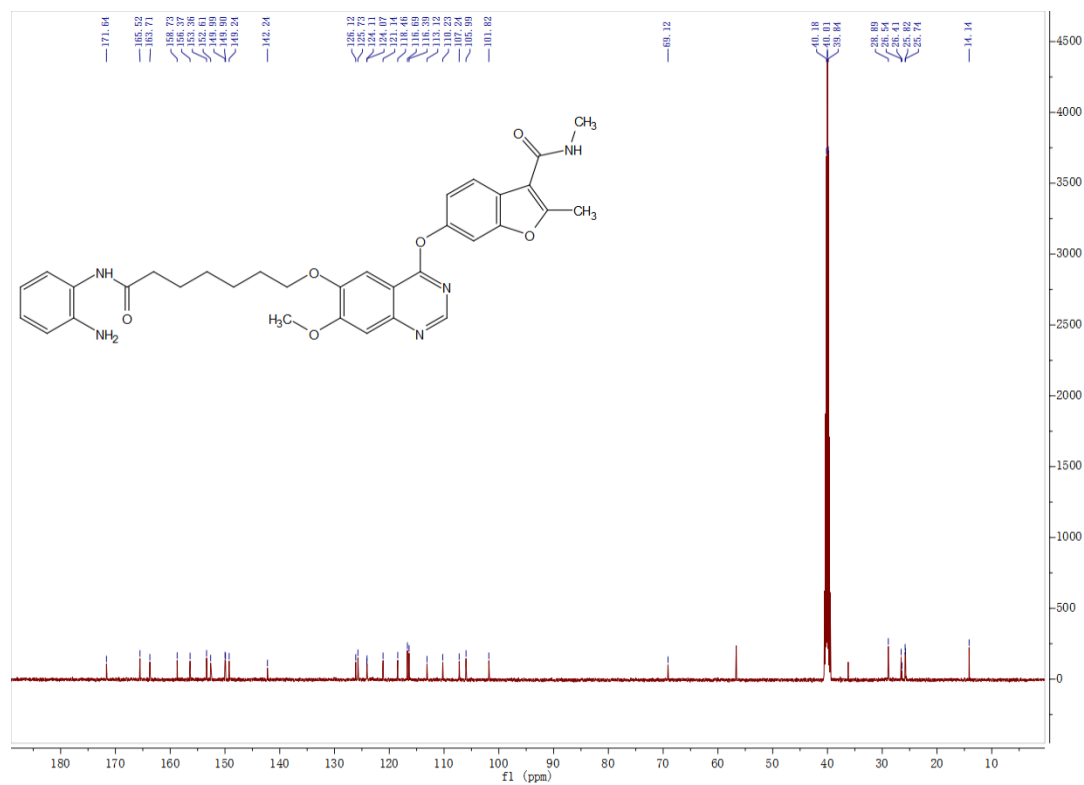
### <sup>13</sup>C-NMR of compound 17



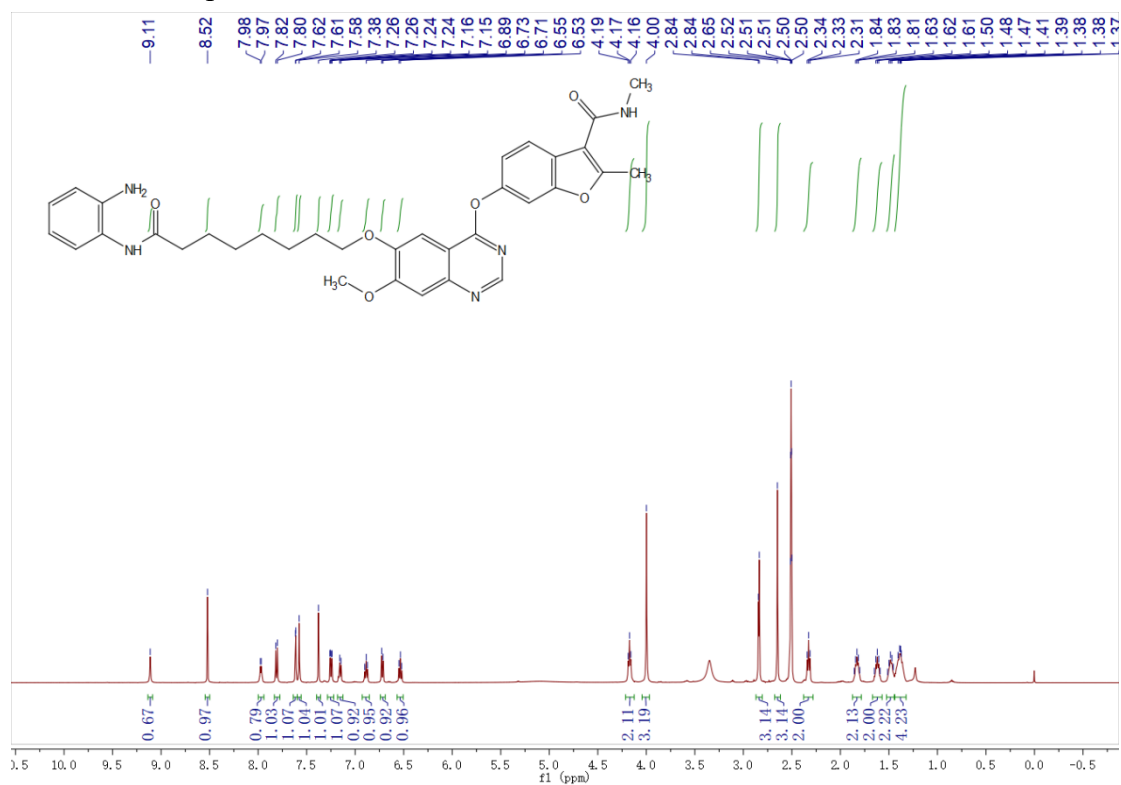
### <sup>1</sup>H-NMR of compound **18**



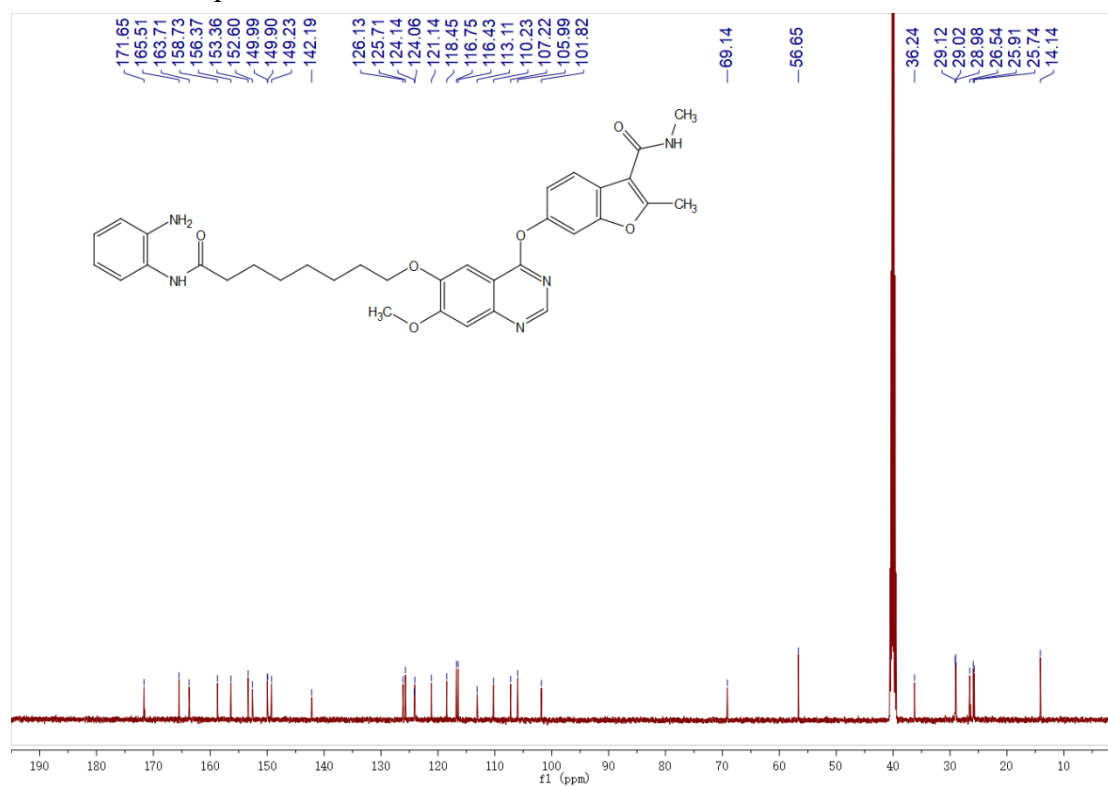
### <sup>13</sup>C-NMR of compound **18**



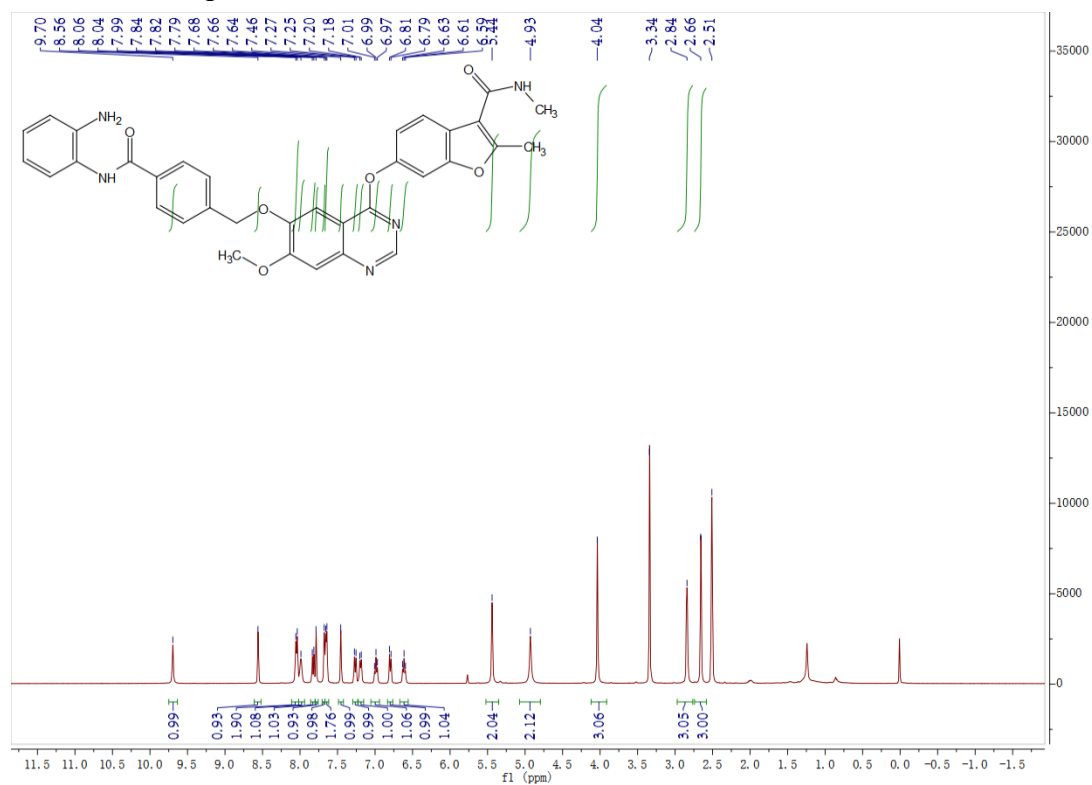
### <sup>1</sup>H-NMR of compound **19**



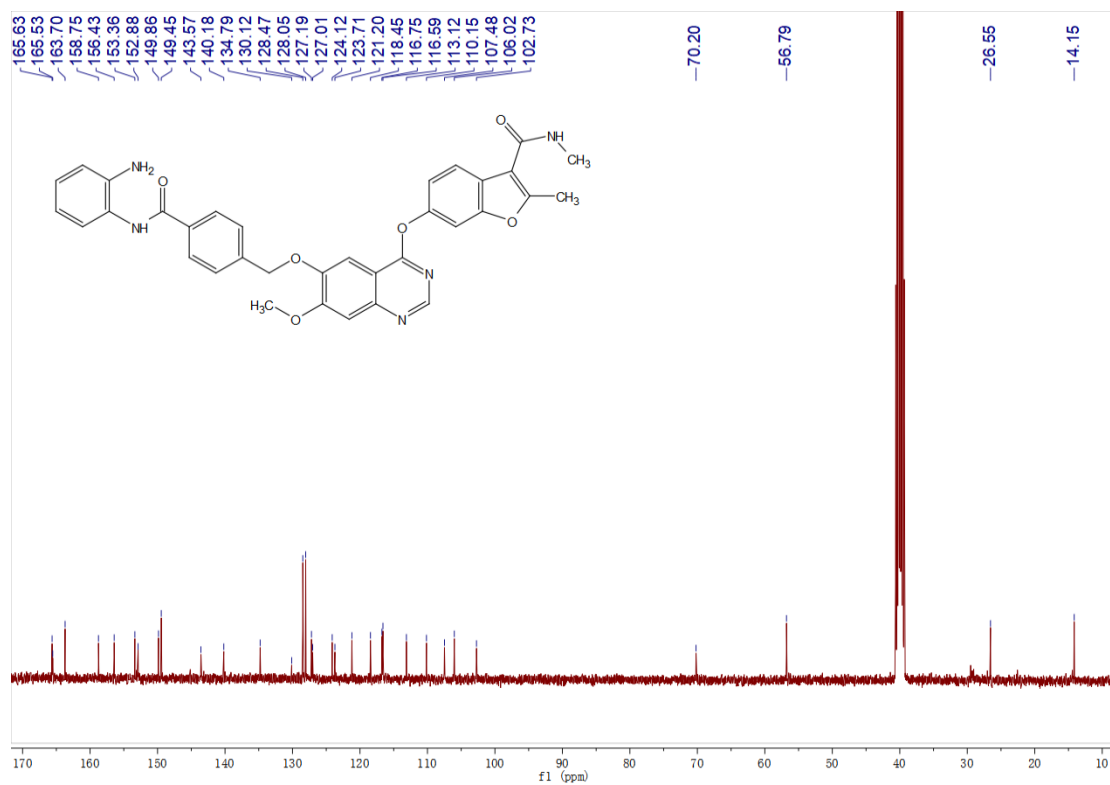
### <sup>13</sup>C-NMR of compound **19**



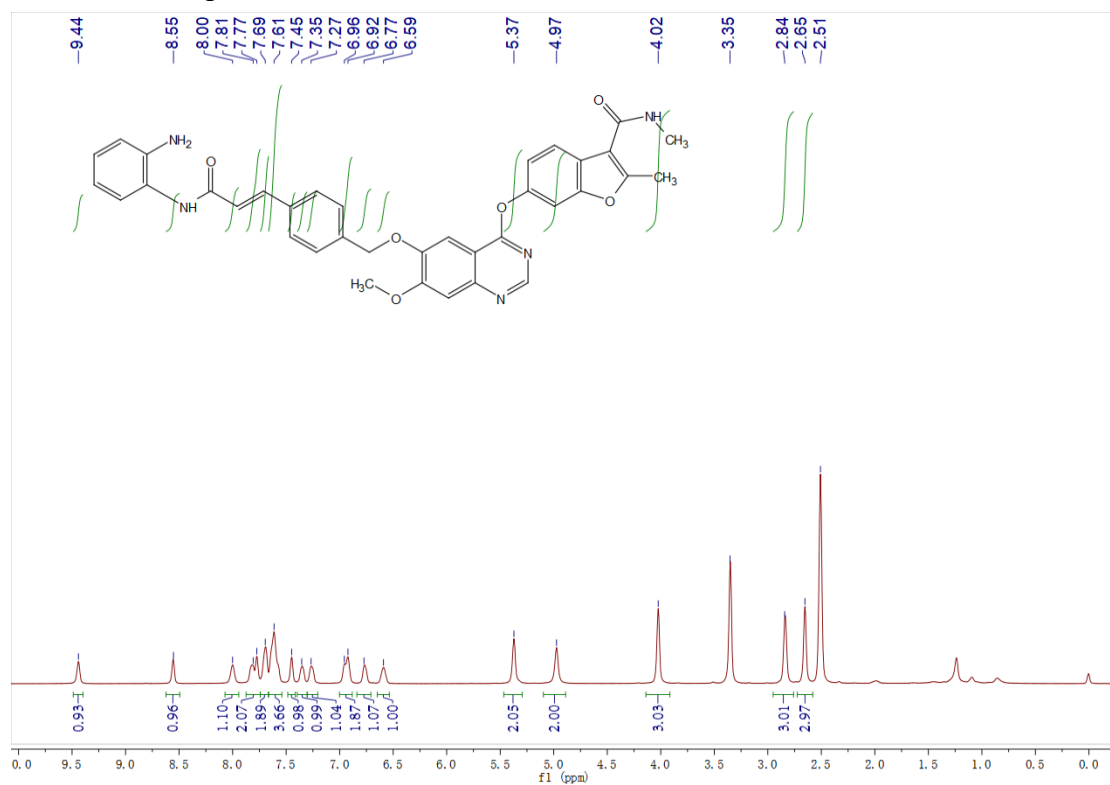
### <sup>1</sup>H-NMR of compound 20



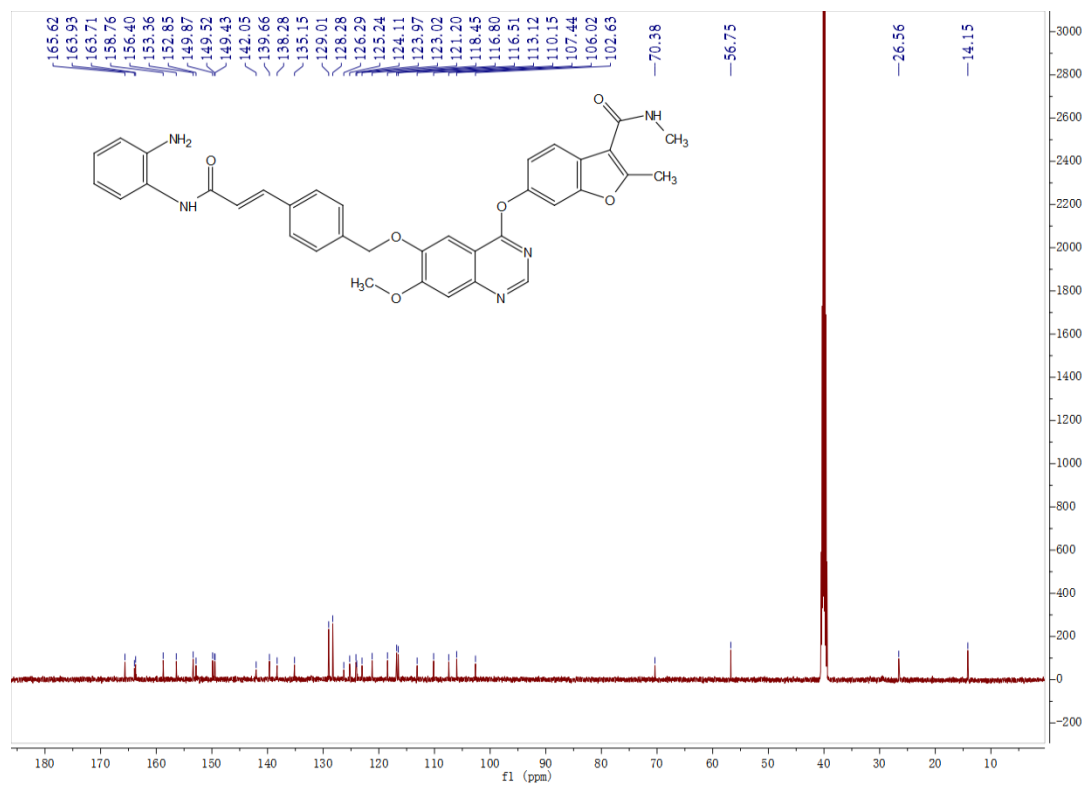
### <sup>13</sup>C-NMR of compound 20



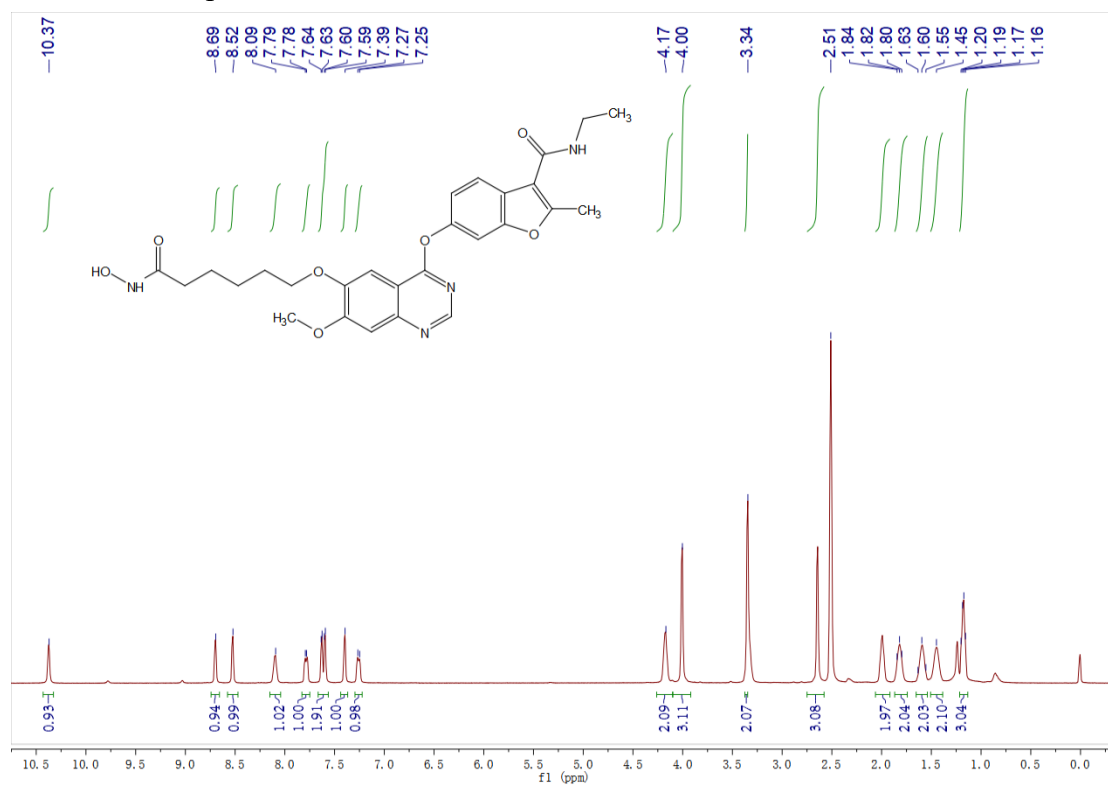
### <sup>1</sup>H-NMR of compound 21



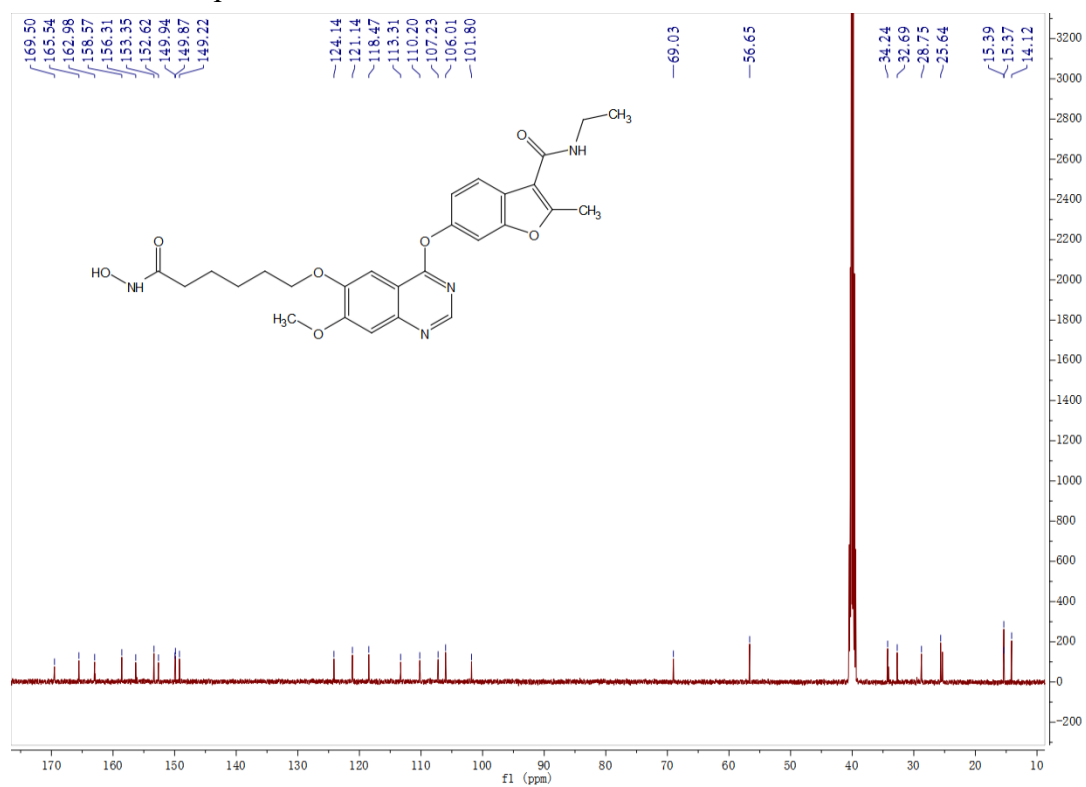
### <sup>13</sup>C-NMR of compound 21



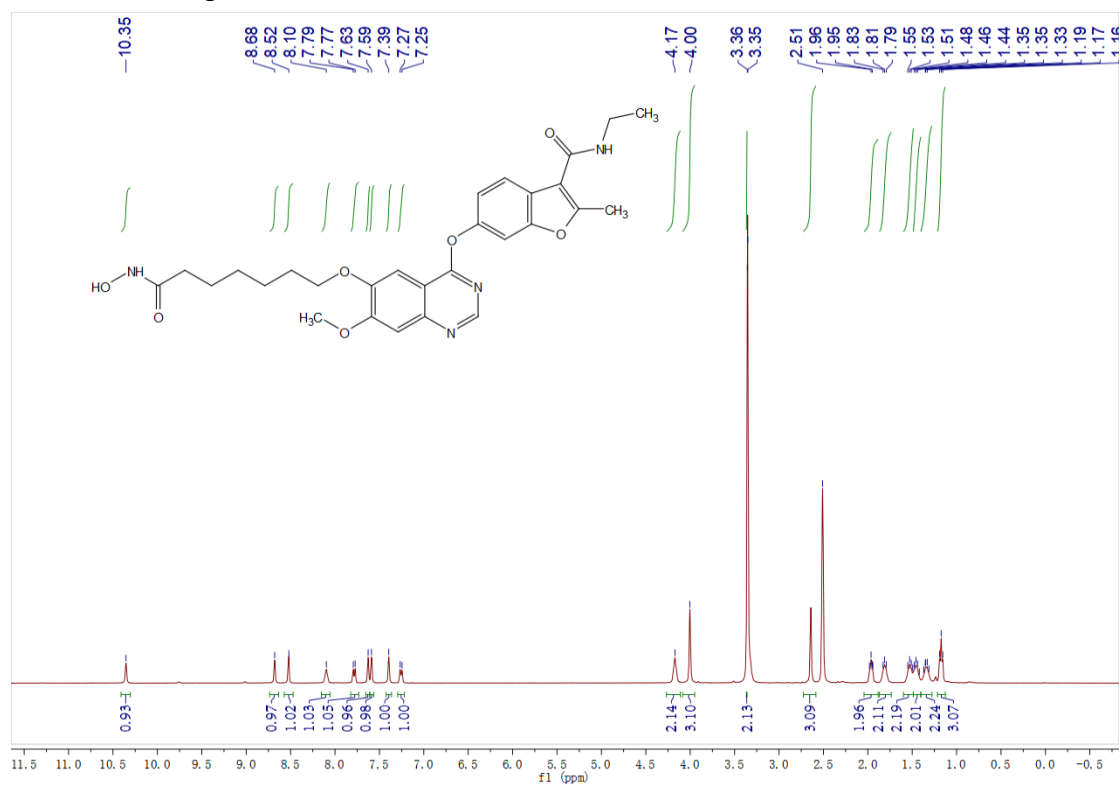
### <sup>1</sup>H-NMR of compound 22



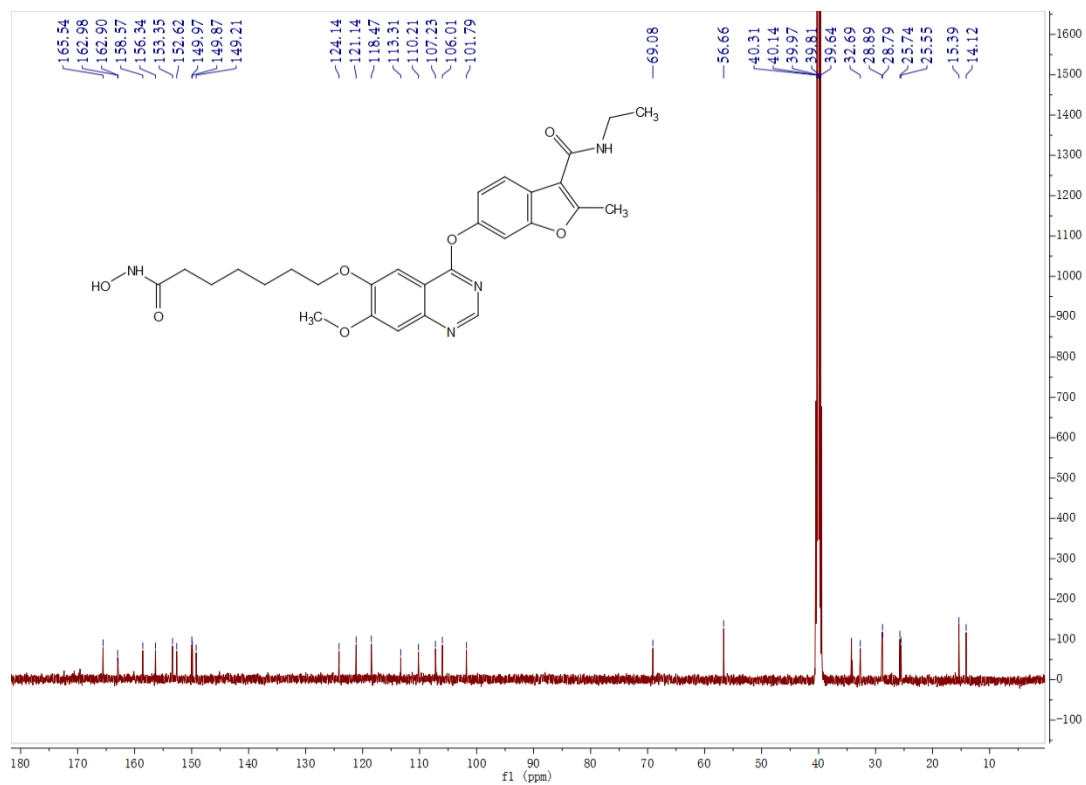
### <sup>13</sup>C-NMR of compound 22



### <sup>1</sup>H-NMR of compound 23

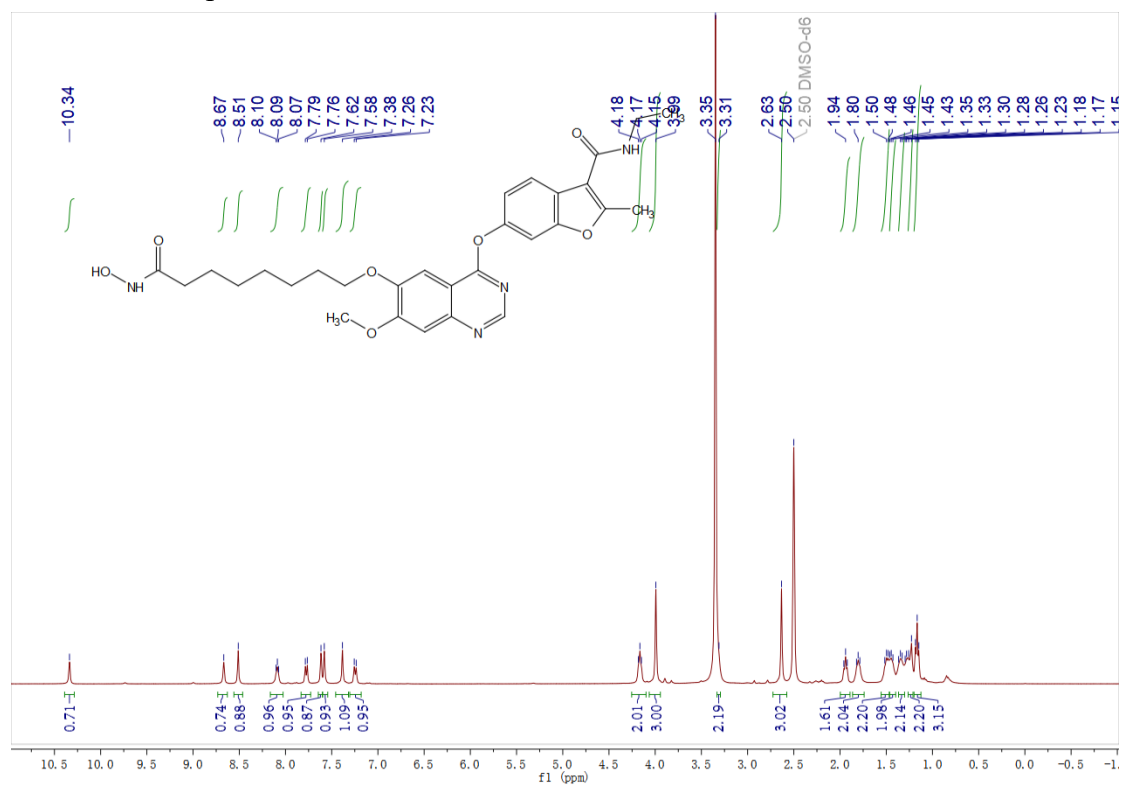


### <sup>13</sup>C-NMR of compound 23

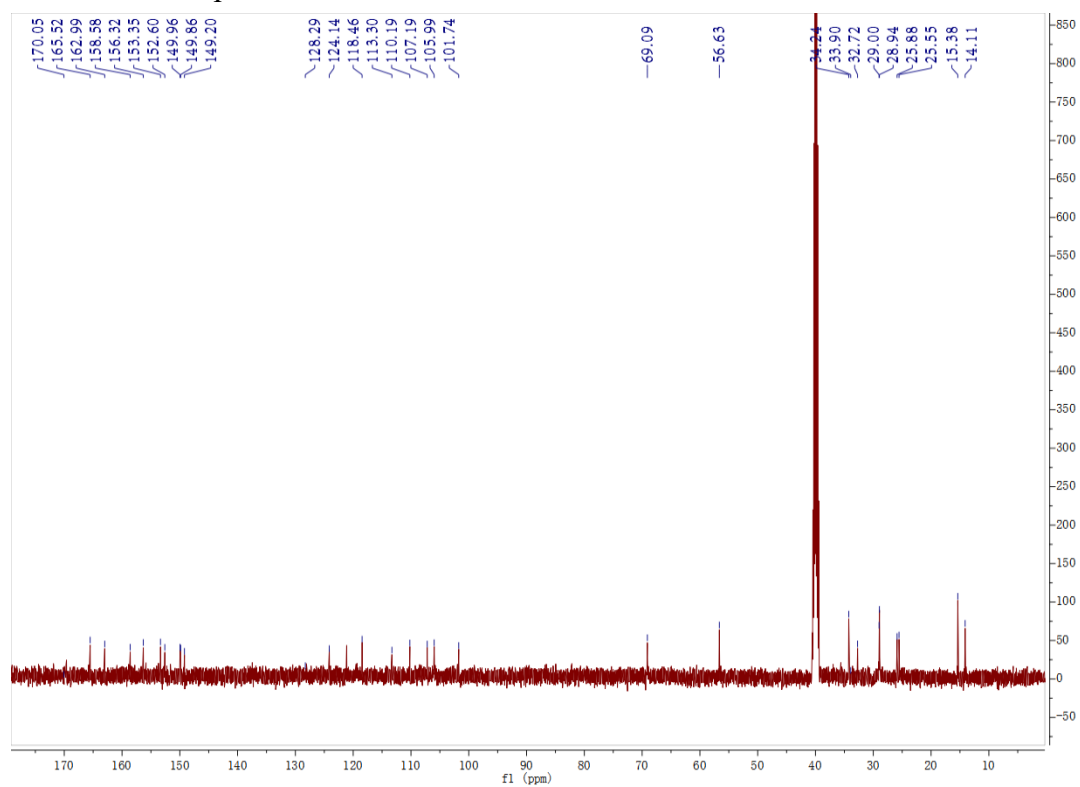




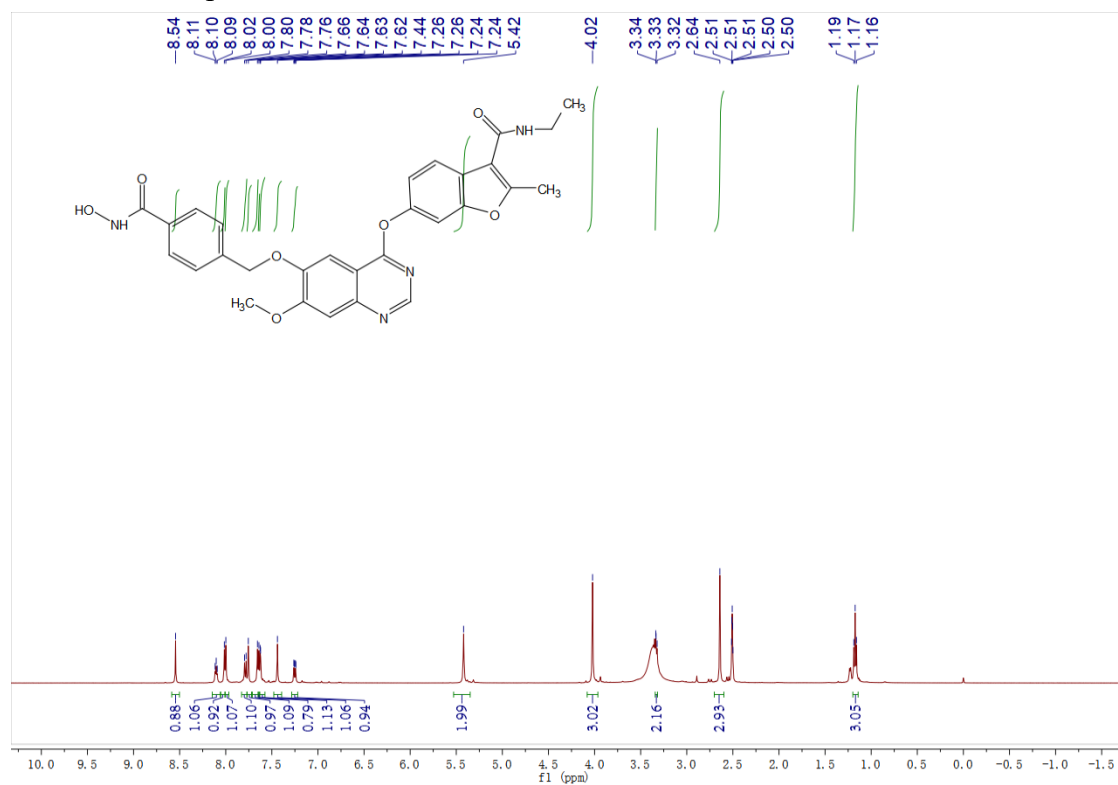
### <sup>1</sup>H-NMR of compound 24



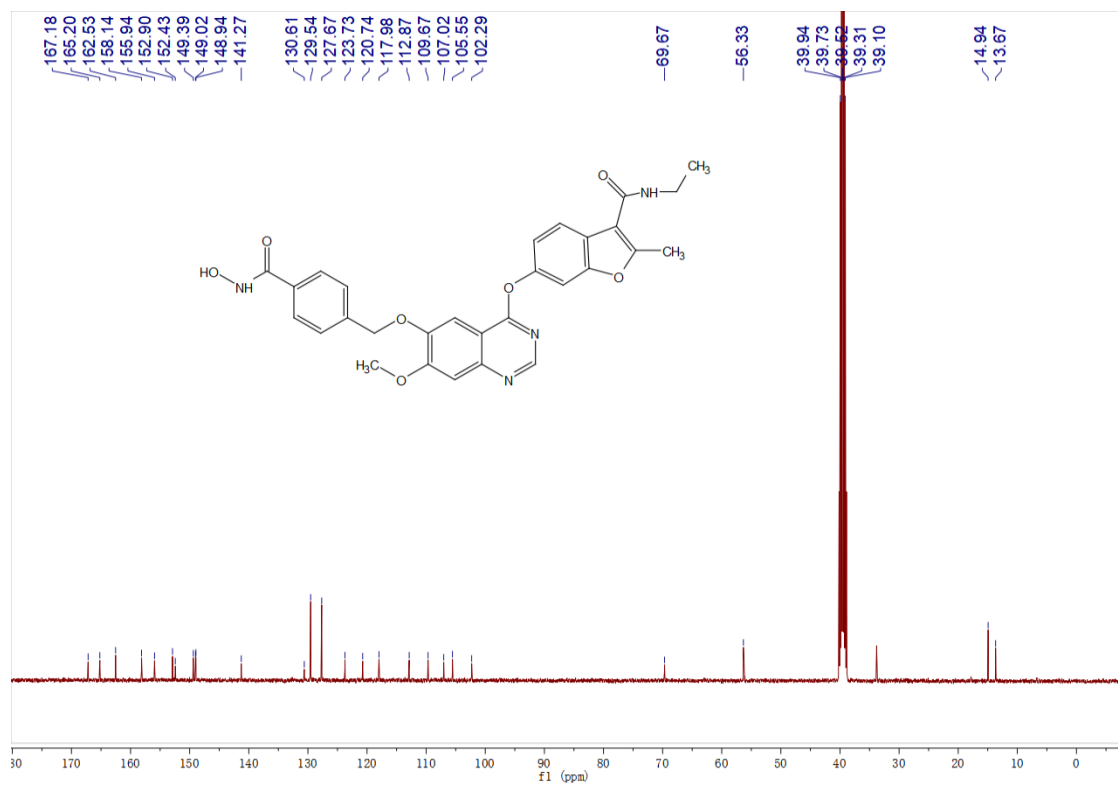
### <sup>13</sup>C-NMR of compound 24



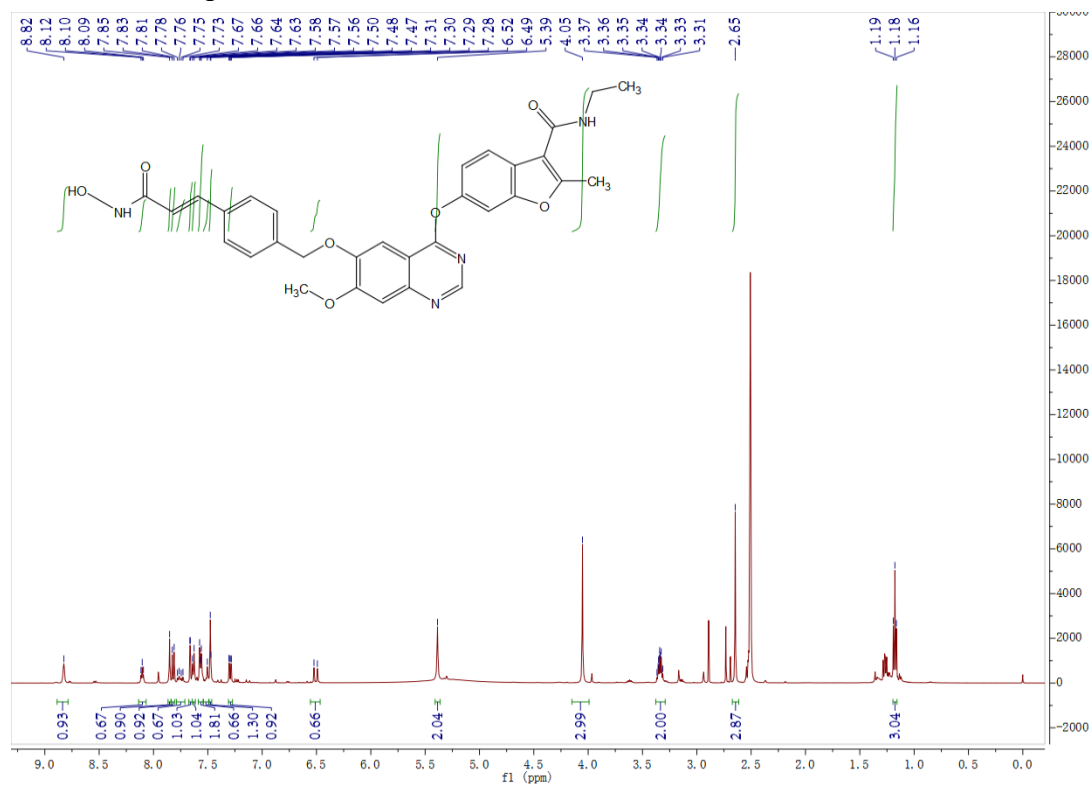
### <sup>1</sup>H-NMR of compound 25



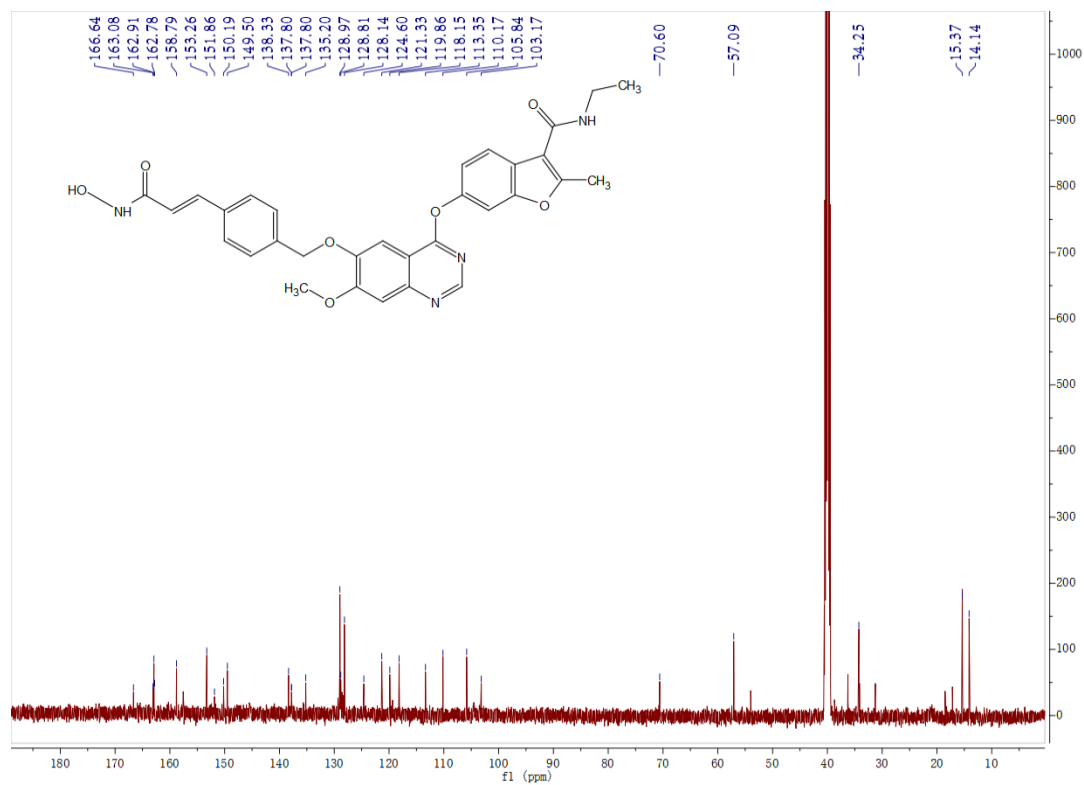
### <sup>13</sup>C-NMR of compound 25



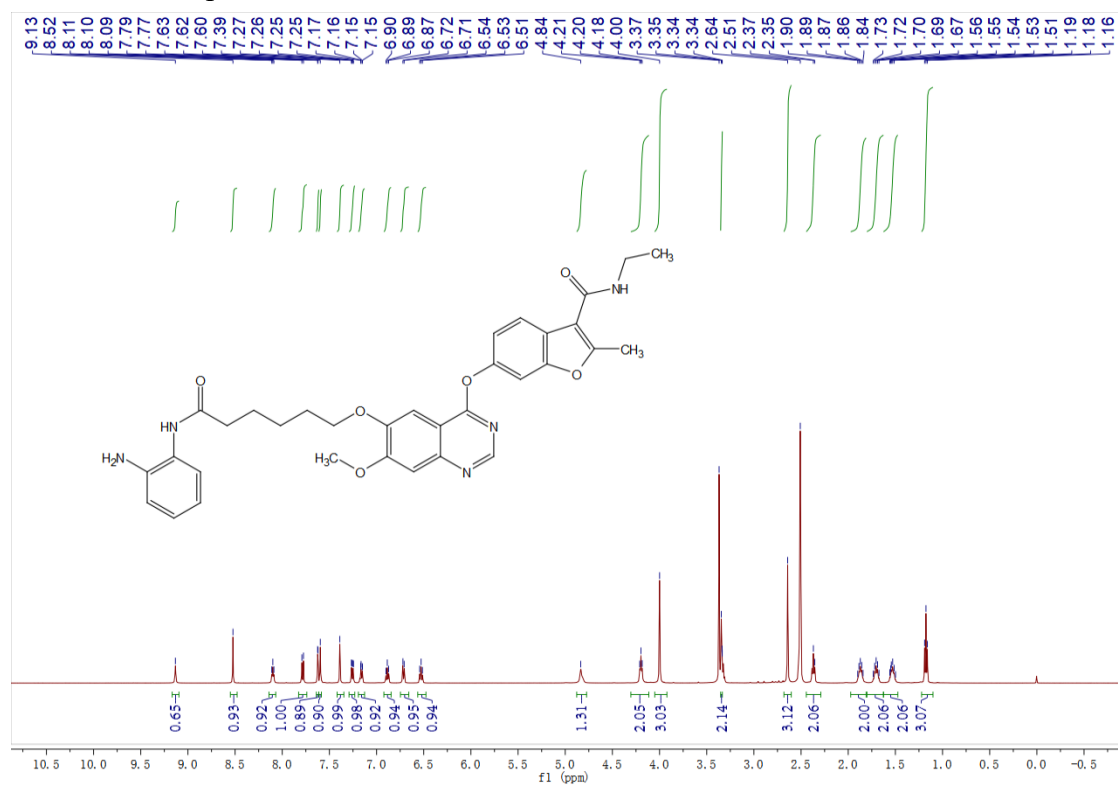
### <sup>1</sup>H-NMR of compound 26



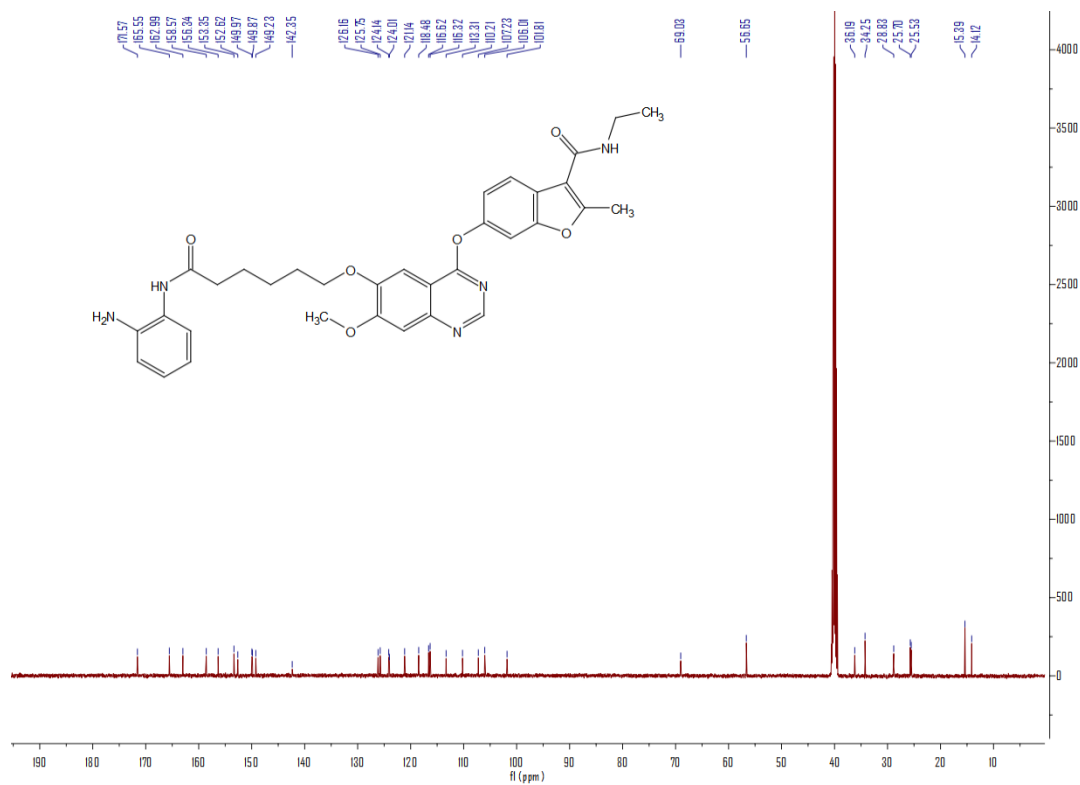
### <sup>13</sup>C-NMR of compound 26



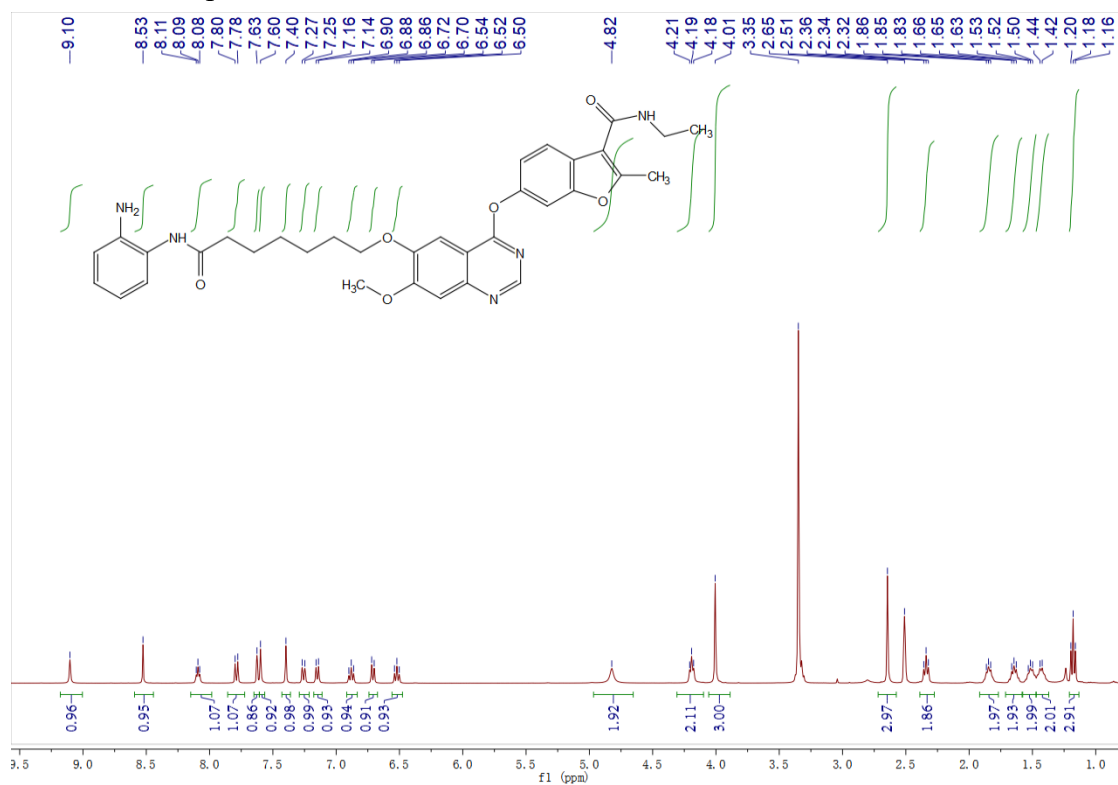
### <sup>1</sup>H-NMR of compound 27



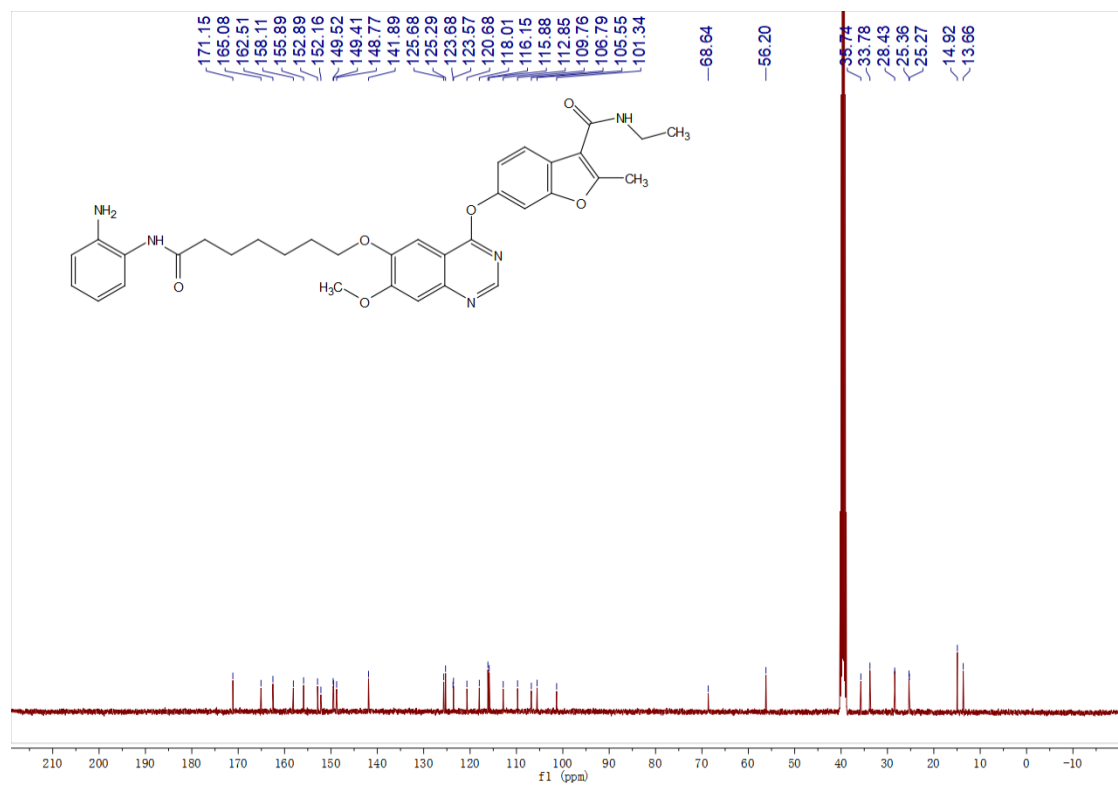
### <sup>13</sup>C-NMR of compound 27



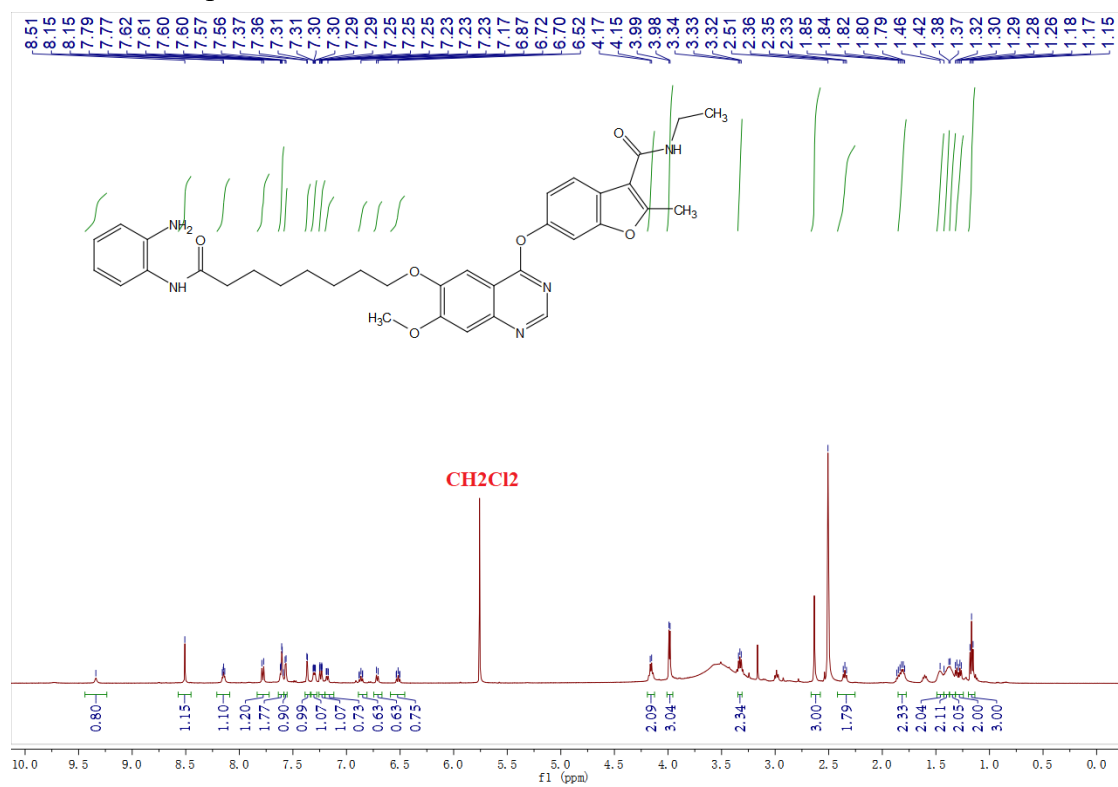
### <sup>1</sup>H-NMR of compound 28



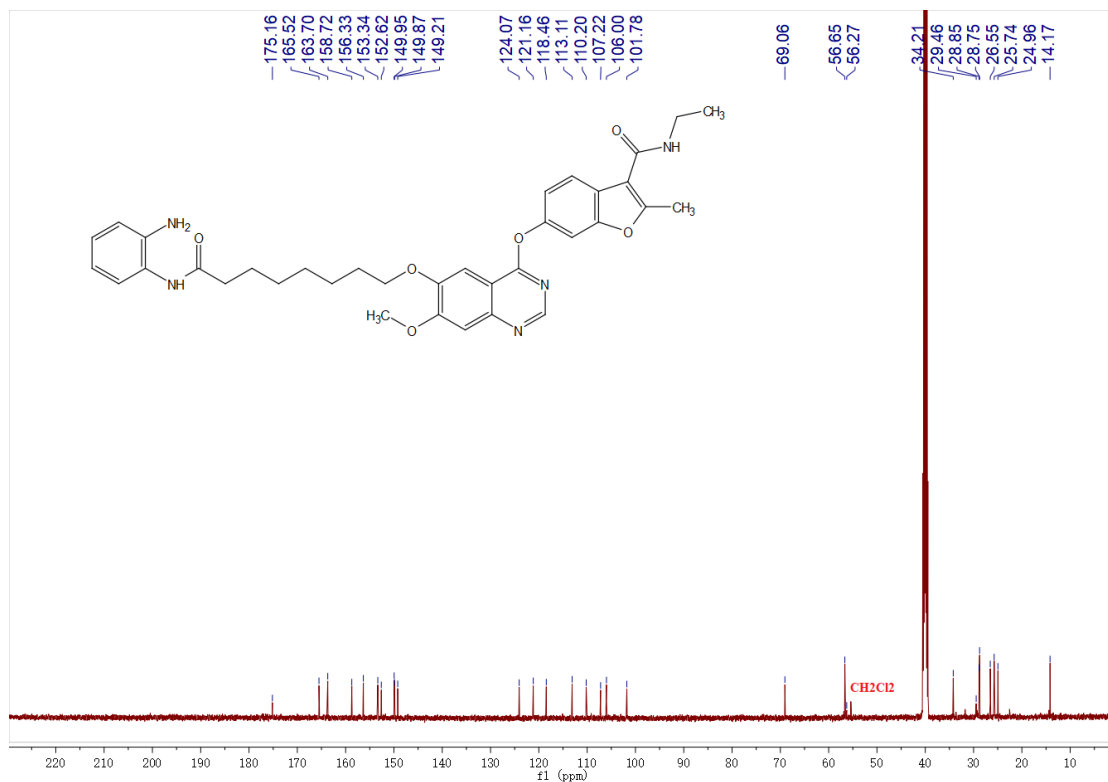
### <sup>13</sup>C-NMR of compound 28



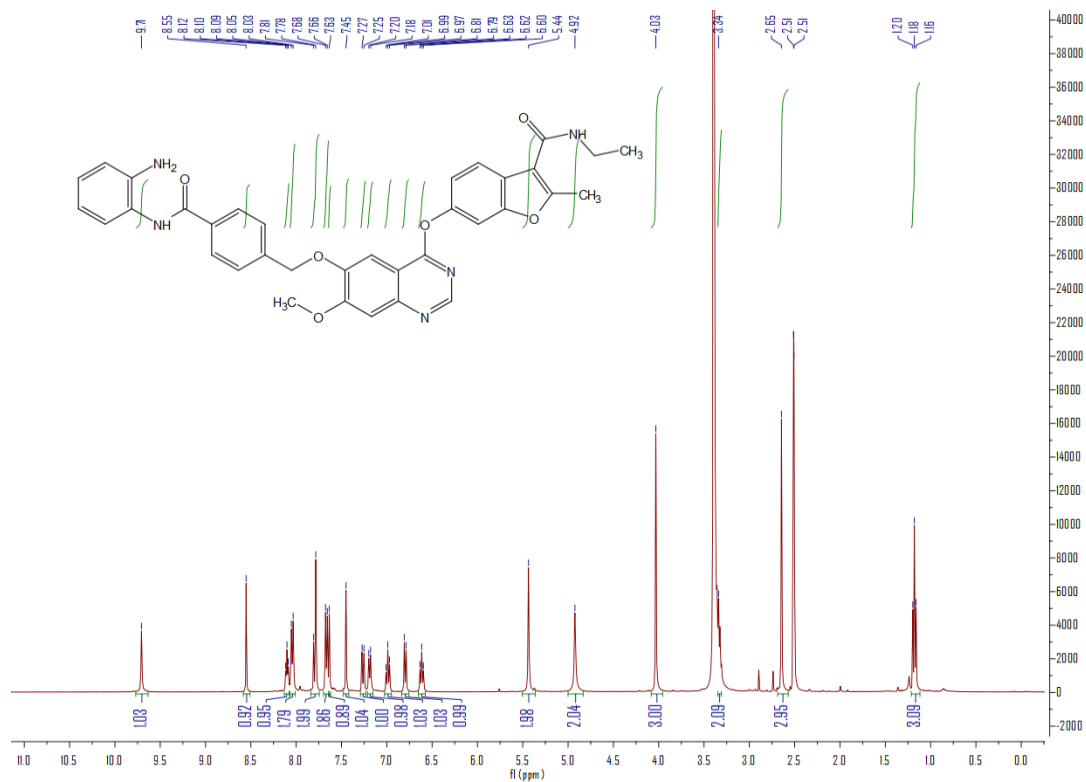
### <sup>1</sup>H-NMR of compound 29



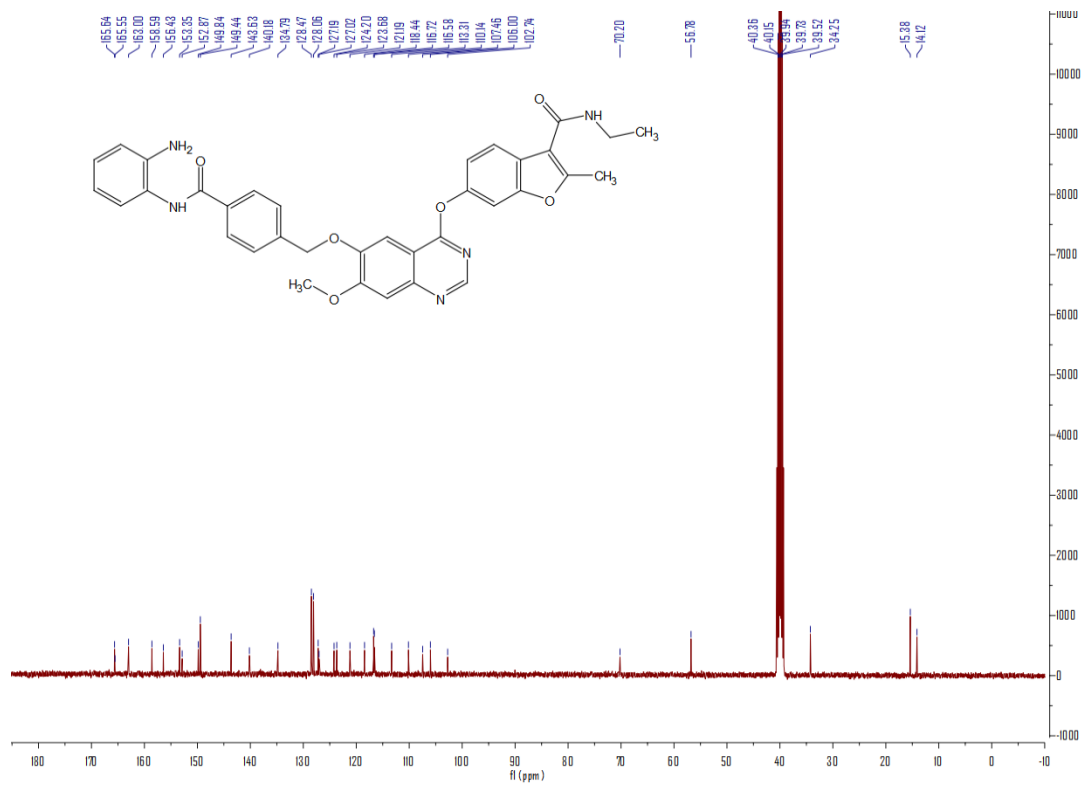
### <sup>13</sup>C-NMR of compound 29



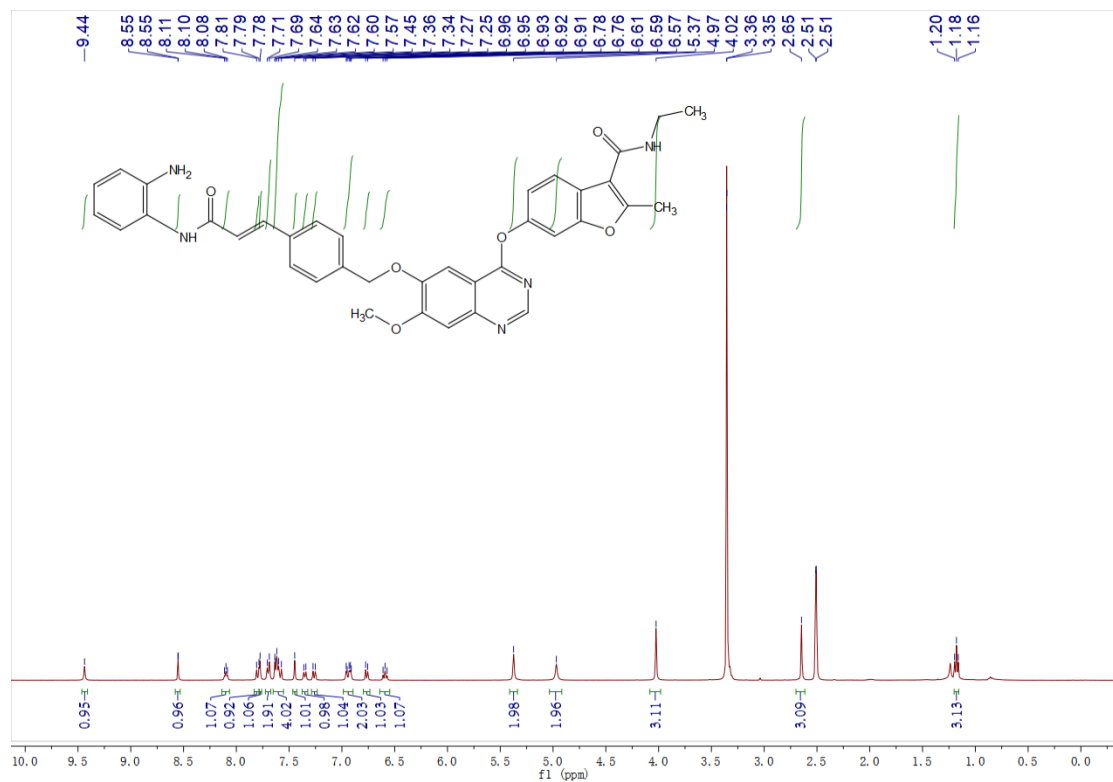
**<sup>1</sup>H-NMR of compound 30**



**<sup>13</sup>C-NMR of compound 30**

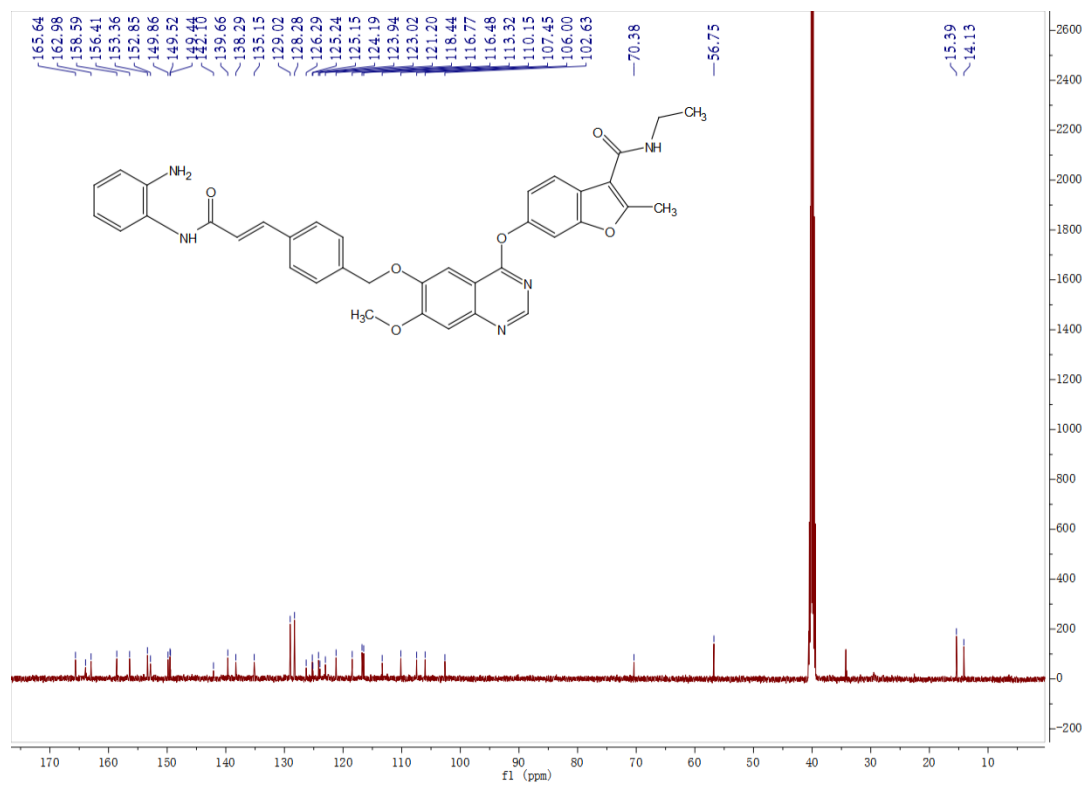


**<sup>1</sup>H-NMR of compound 31**

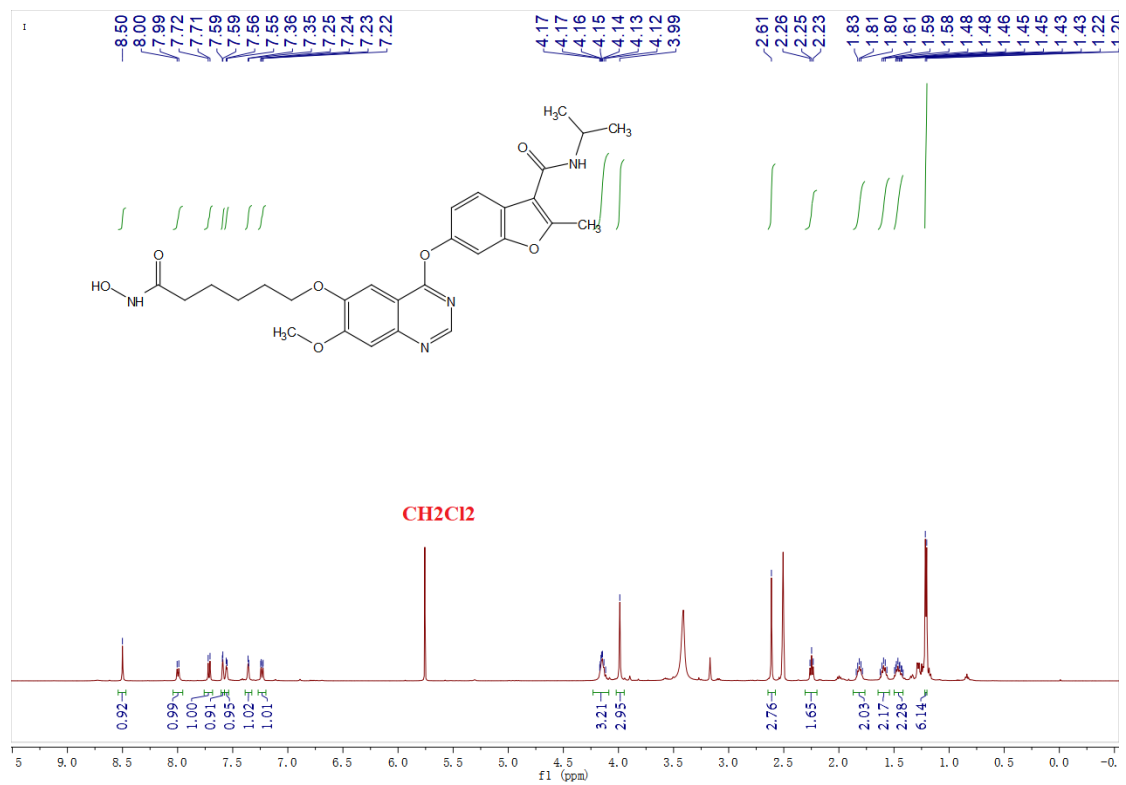


**<sup>13</sup>C-NMR of compound 31**

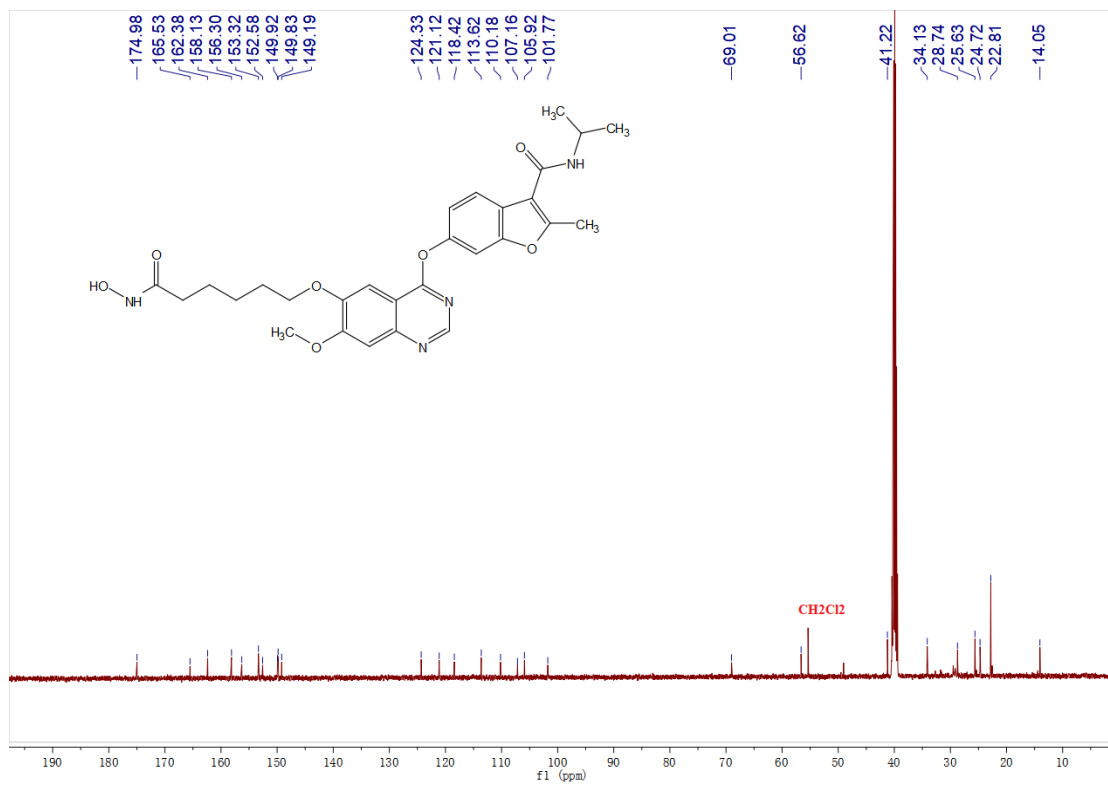




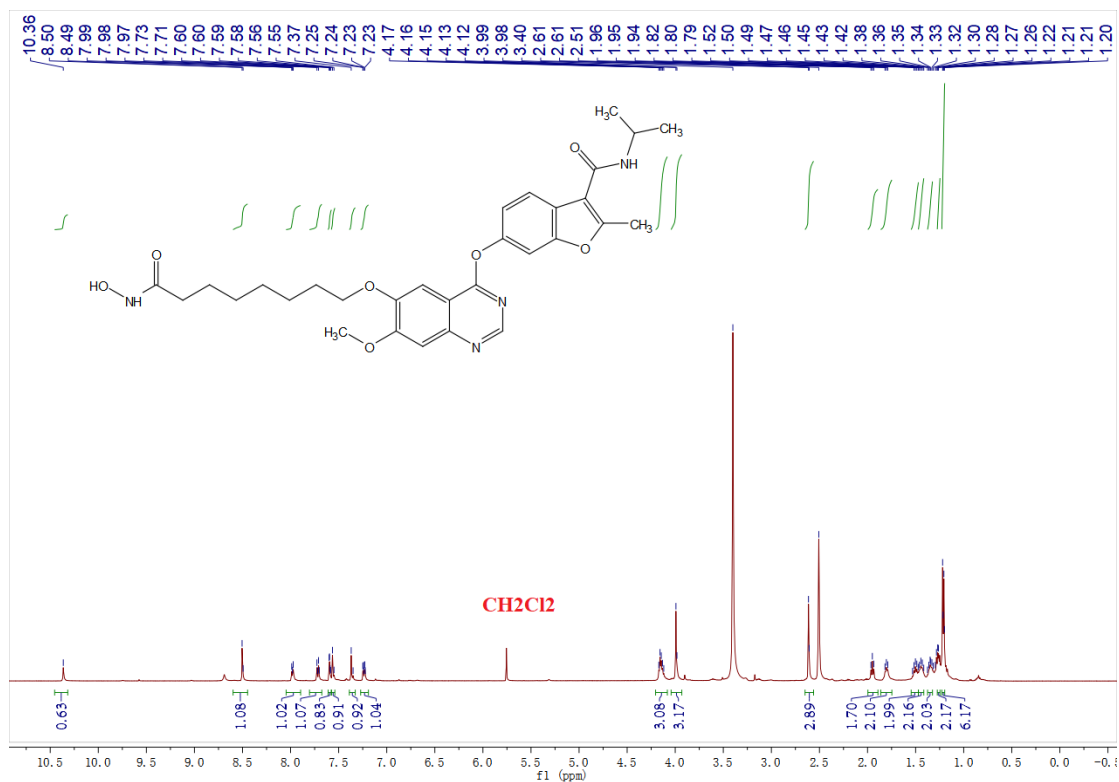
**<sup>1</sup>H-NMR of compound 32**



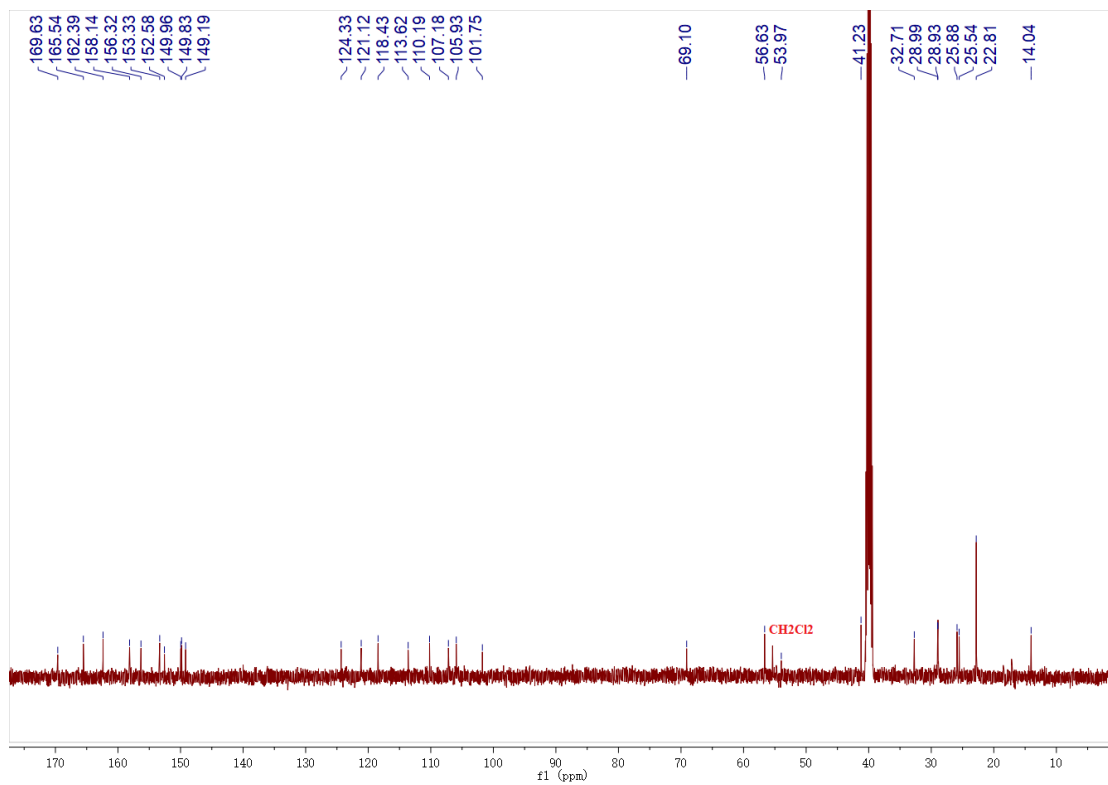
**<sup>13</sup>C-NMR of compound 32**



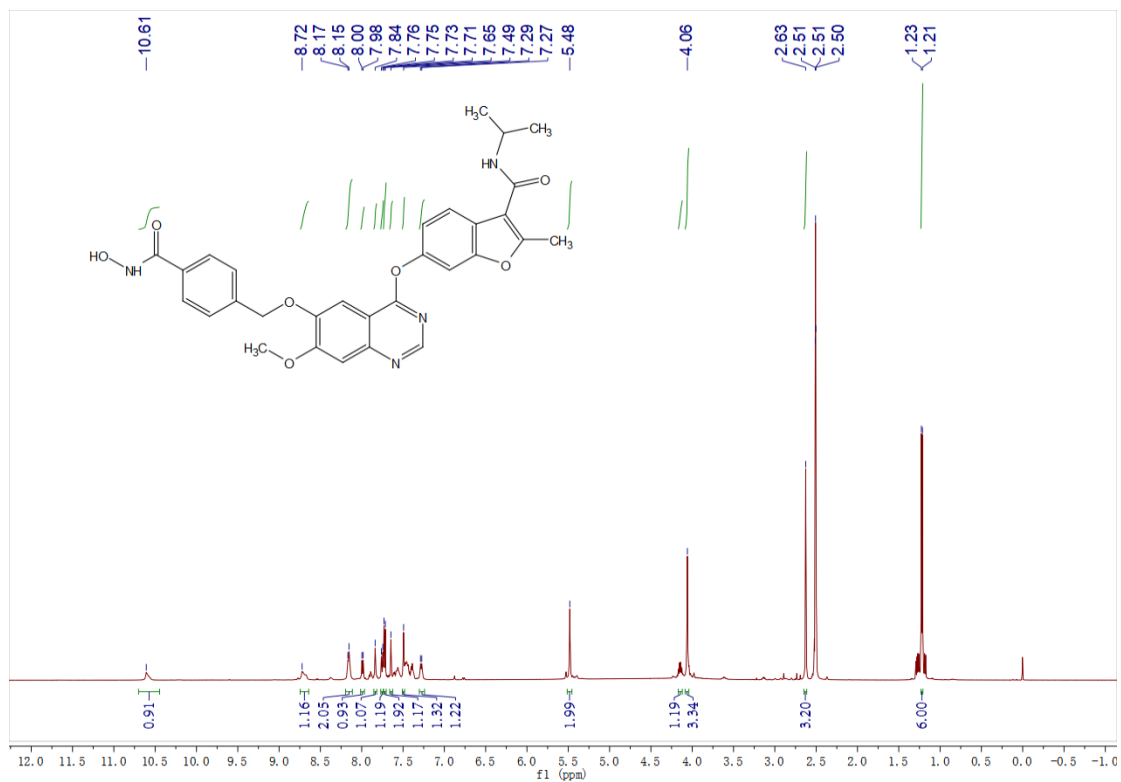
**<sup>1</sup>H-NMR of compound 33**



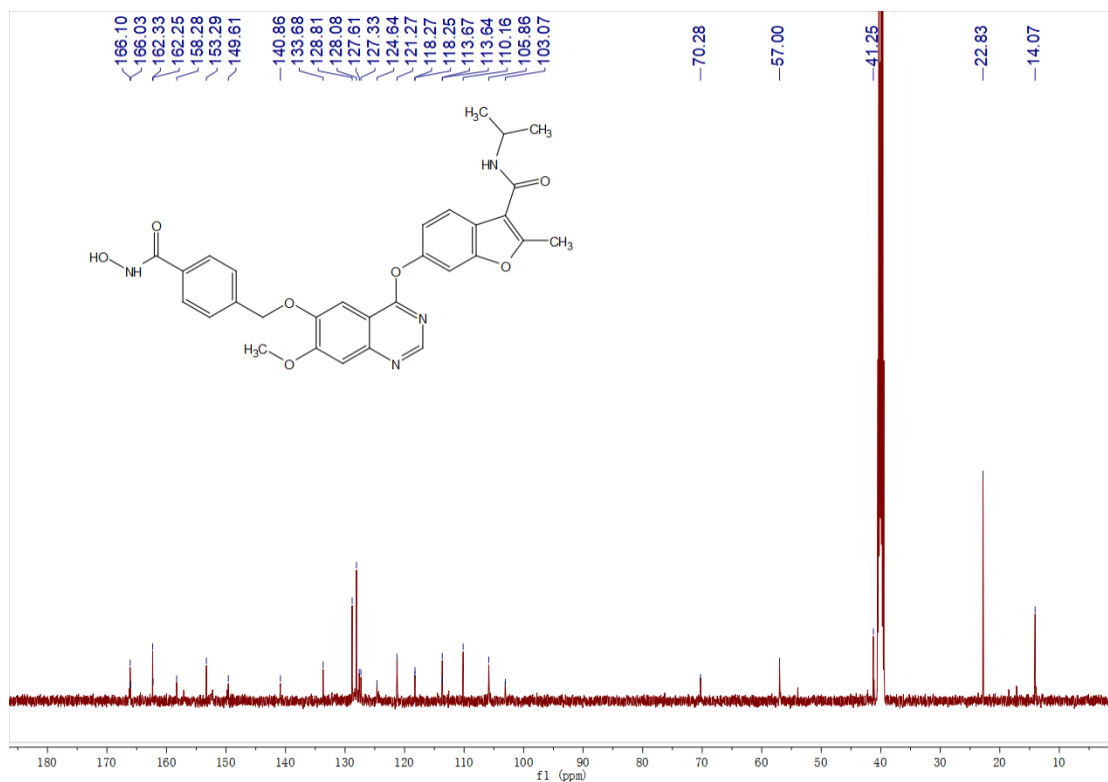
**<sup>13</sup>C-NMR of compound 33**



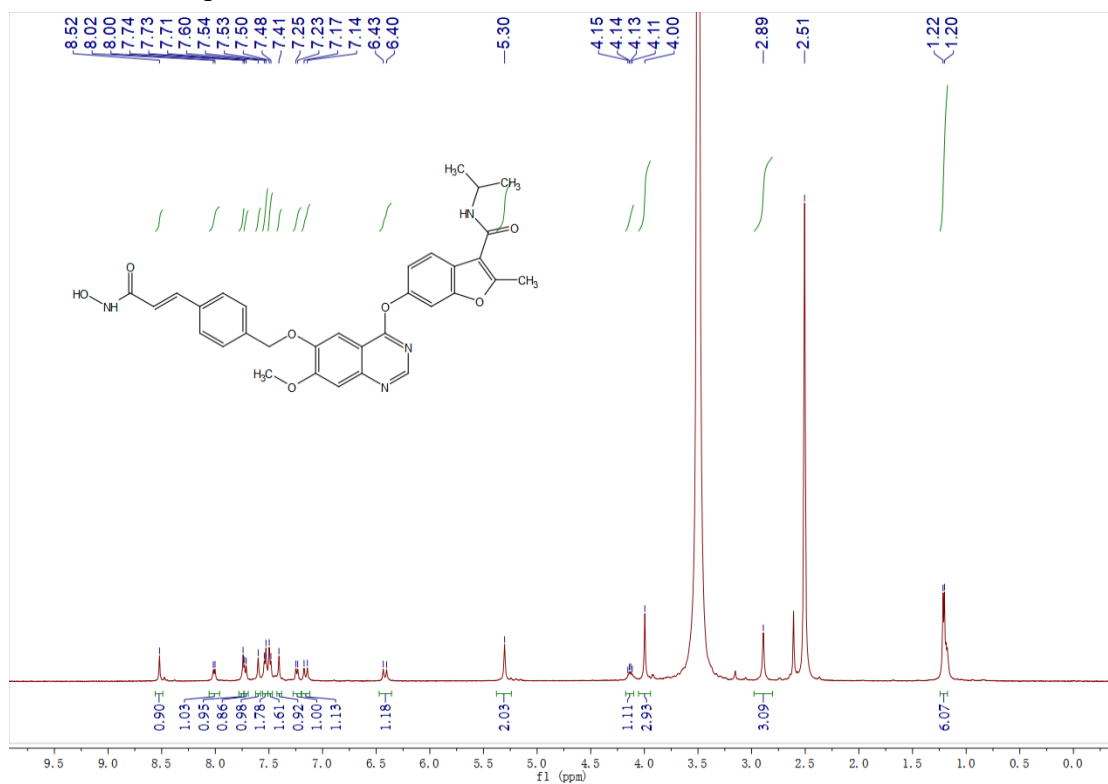
**<sup>1</sup>H-NMR of compound 34**



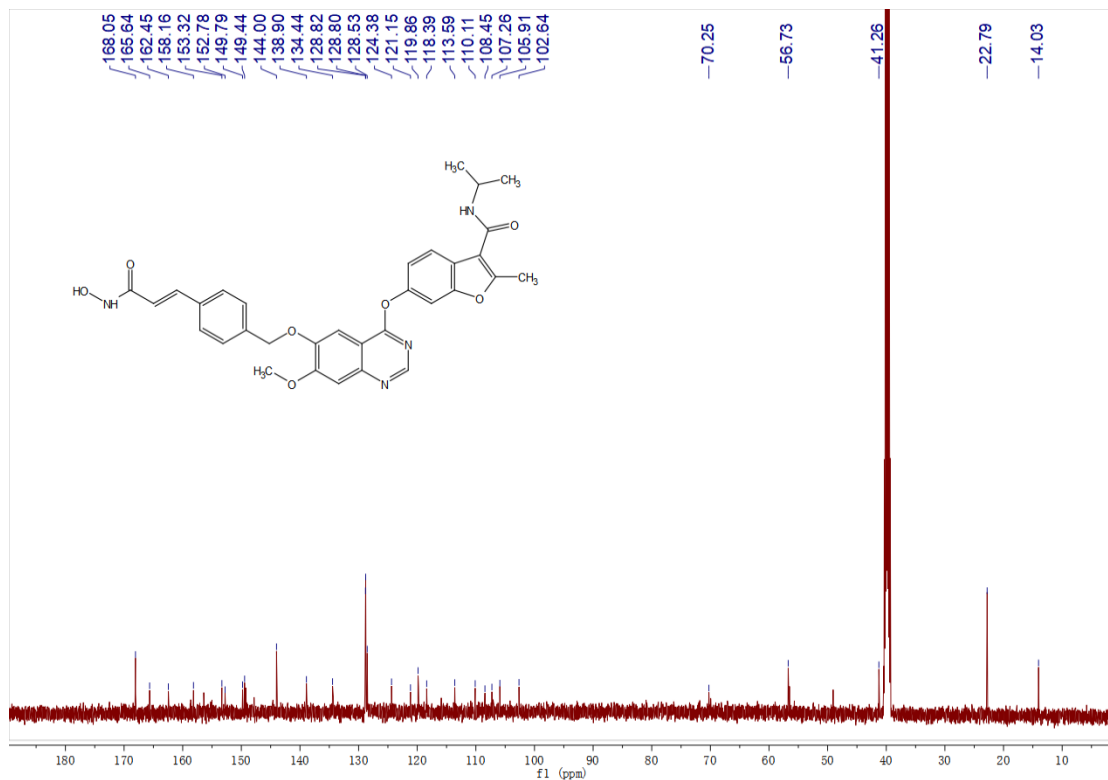
**<sup>13</sup>C-NMR of compound 34**



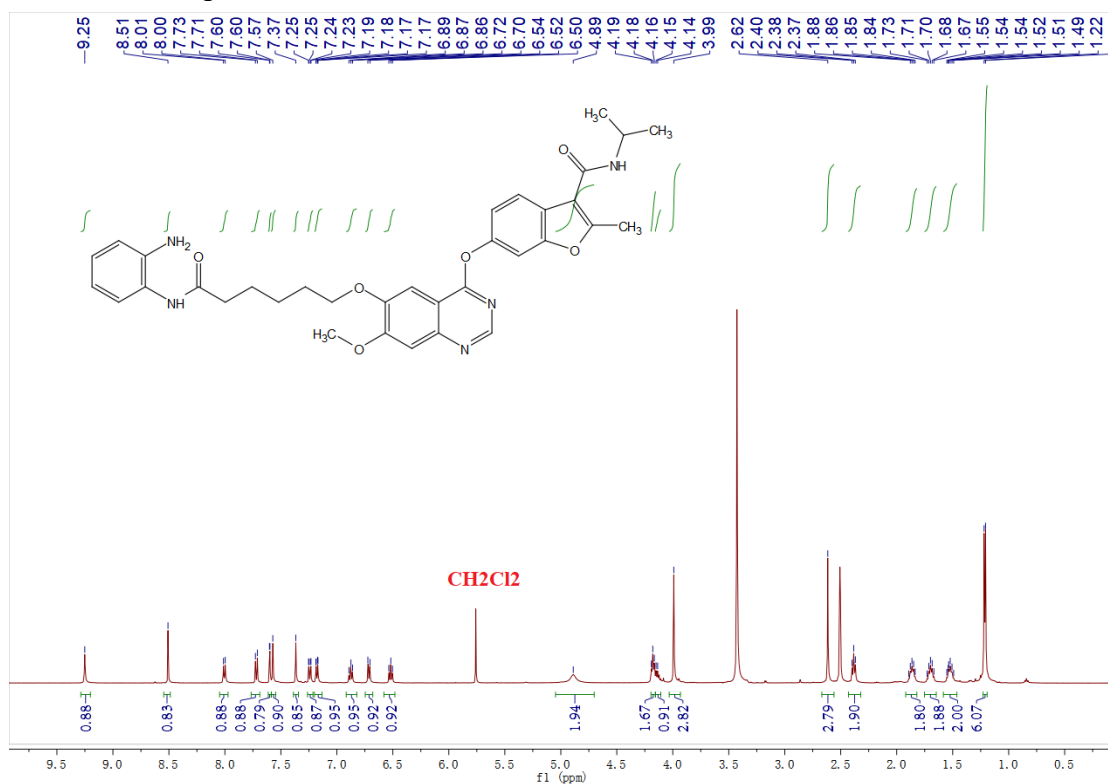
**<sup>1</sup>H-NMR of compound 35**



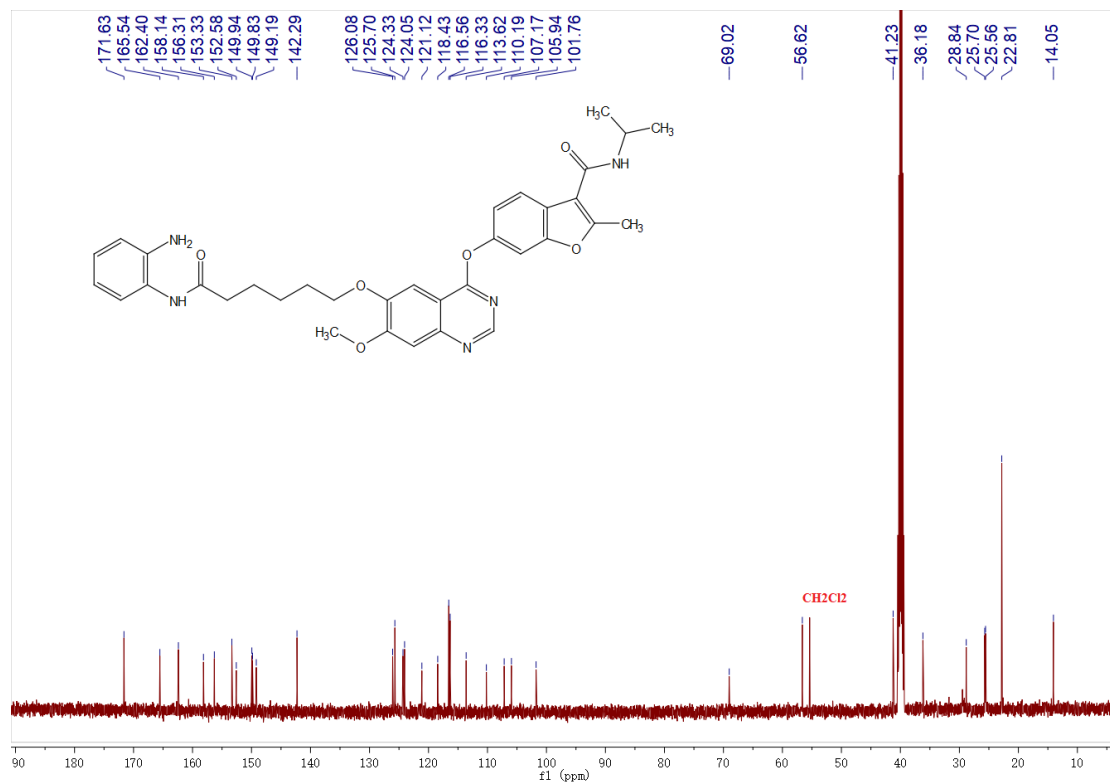
**<sup>13</sup>C-NMR of compound 35**



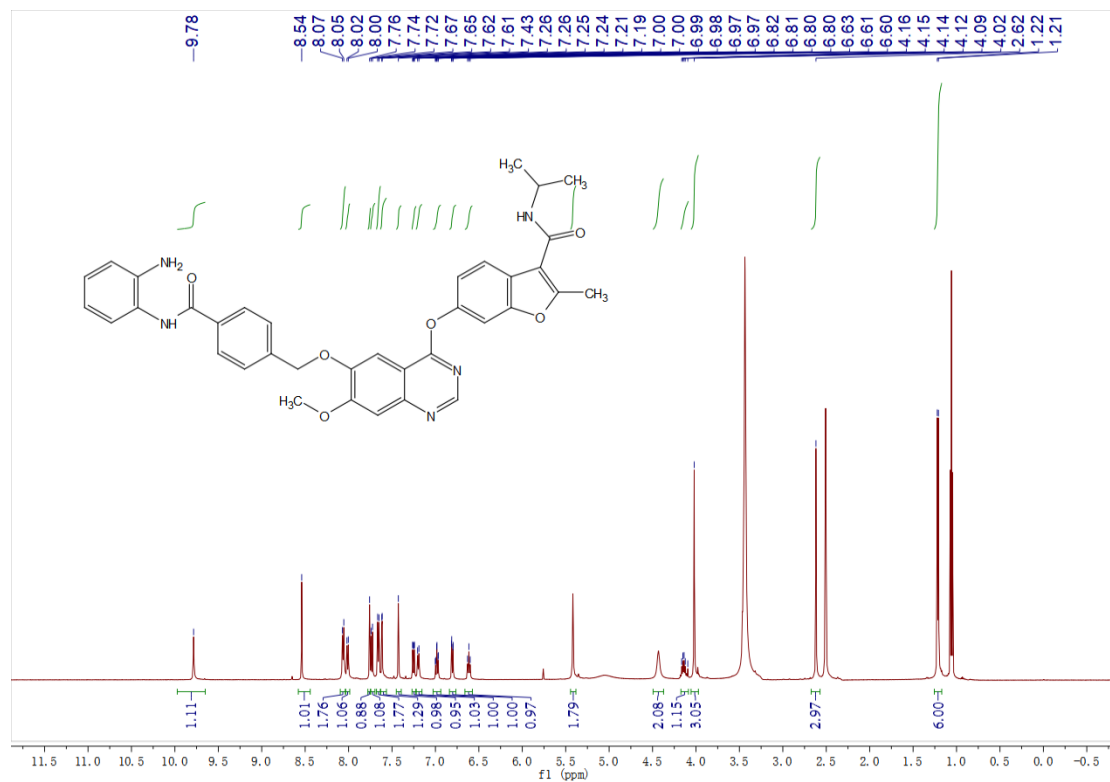
**<sup>1</sup>H-NMR of compound 36**



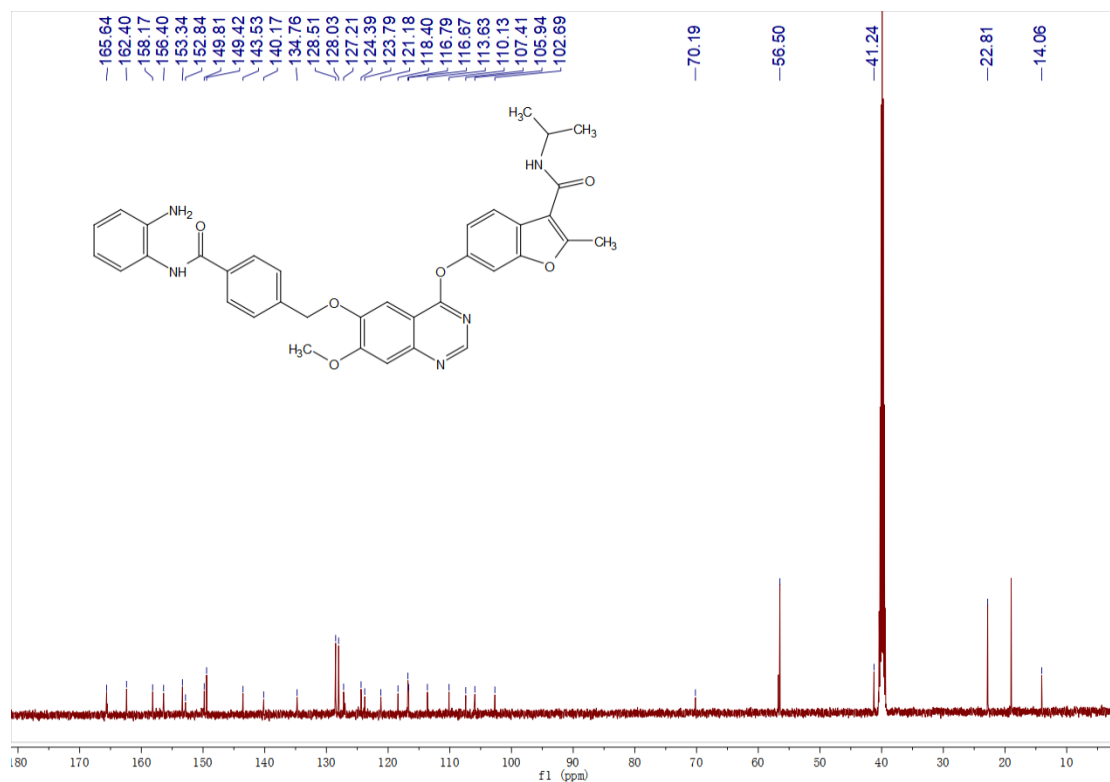
**<sup>13</sup>C-NMR of compound 36**



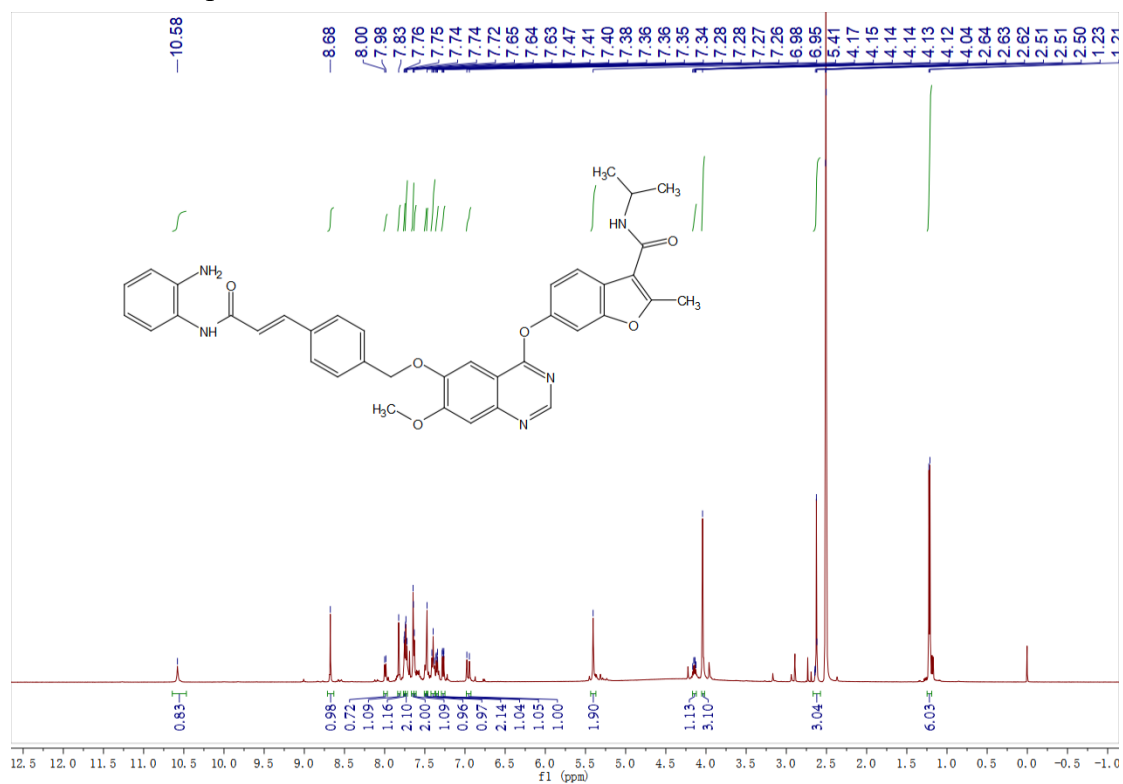
<sup>1</sup>H-NMR of compound 37



<sup>13</sup>C-NMR of compound 37



<sup>1</sup>H-NMR of compound 38



<sup>13</sup>C-NMR of compound 38

