

Supporting Information

Discovery of a First-in-Class Degradar for the Lipid Kinase PIKfyve

Chungen Li^{1,#}, Yuanyuan Qiao^{2,4,#}, Xia Jiang², Lianchao Liu¹, Yang Zheng², Yudi Qiu¹, Caleb Cheng², Fengtao Zhou⁸, Yang Zhou⁸, Weixue Huang¹, Xiaomei Ren¹, Yuzhuo Wang³, Zhen Wang^{1,*}, Arul M. Chinnaiyan^{2,4,5,6,*}, Ke Ding^{1,7,8,*}

¹ State Key Laboratory of Chemical Biology, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, #345 Lingling Rd., Shanghai 200032, People's Republic of China

² Michigan Center for Translational Pathology, University of Michigan, Ann Arbor, MI 48109, USA.

³ The Vancouver Prostate Centre, Vancouver General Hospital and Department of Urologic Sciences, The University of British Columbia, Vancouver, V6H 3Z6 BC, Canada.

⁴ Department of Pathology, University of Michigan, Ann Arbor, MI 48109, USA.

⁵ Howard Hughes Medical Institute, University of Michigan, Ann Arbor, MI 48109, USA.

⁶ Department of Urology, University of Michigan, Ann Arbor, MI 48109, USA.

⁷ Institute of Basic Medicine and Cancer (IBMC), Chinese Academy of Sciences, Hangzhou, Zhejiang 310022, People's Republic of China

⁸ International Cooperative Laboratory of Traditional Chinese Medicine Modernization and Innovative Drug Discovery of Chinese Ministry of Education

(MOE), Guangzhou City Key Laboratory of Precision Chemical Drug Development,
College of Pharmacy, Jinan University, 855 Xingye Avenue East, Guangzhou
511400, People's Republic of China

#C. L. and Y. Q. contributed equally to this work.

*Email: wangz@sioc.ac.cn (Z.W.);_arul@med.umich.edu (A.M.C);_dingk@sioc.ac.cn;

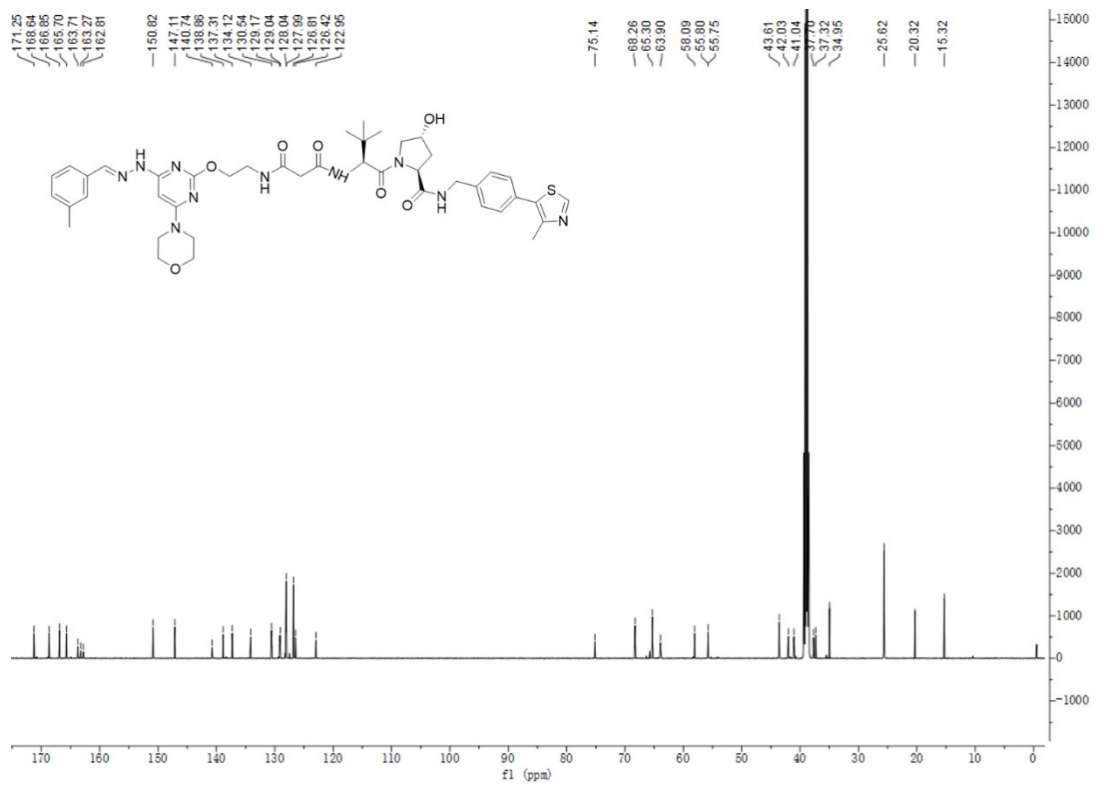
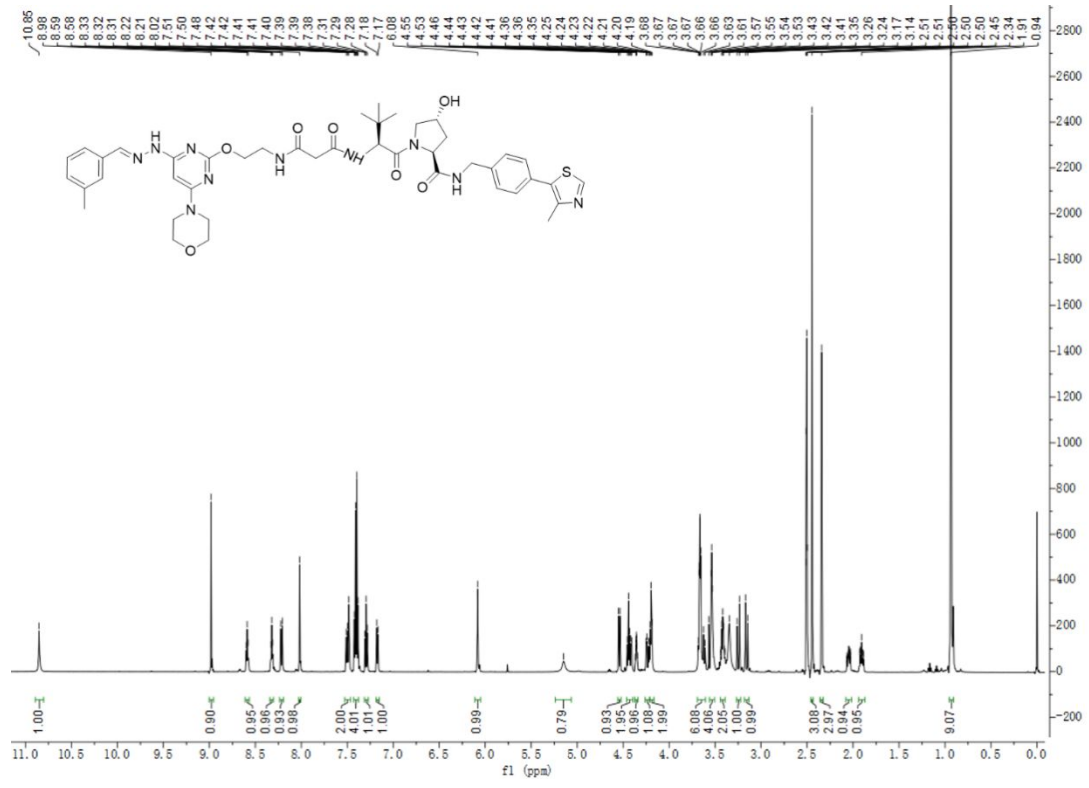
Tel: +86-21-5492 5100 (K.D.)

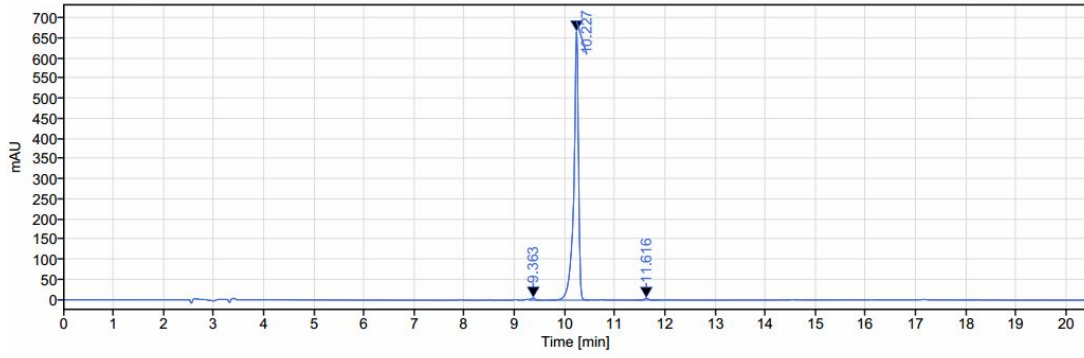
Table of Contents

1. NMR spectra and HPLC traces of final compounds.....	S3-S46
---	---------------

NMR spectra and HPLC traces of final compounds

Compound 7a

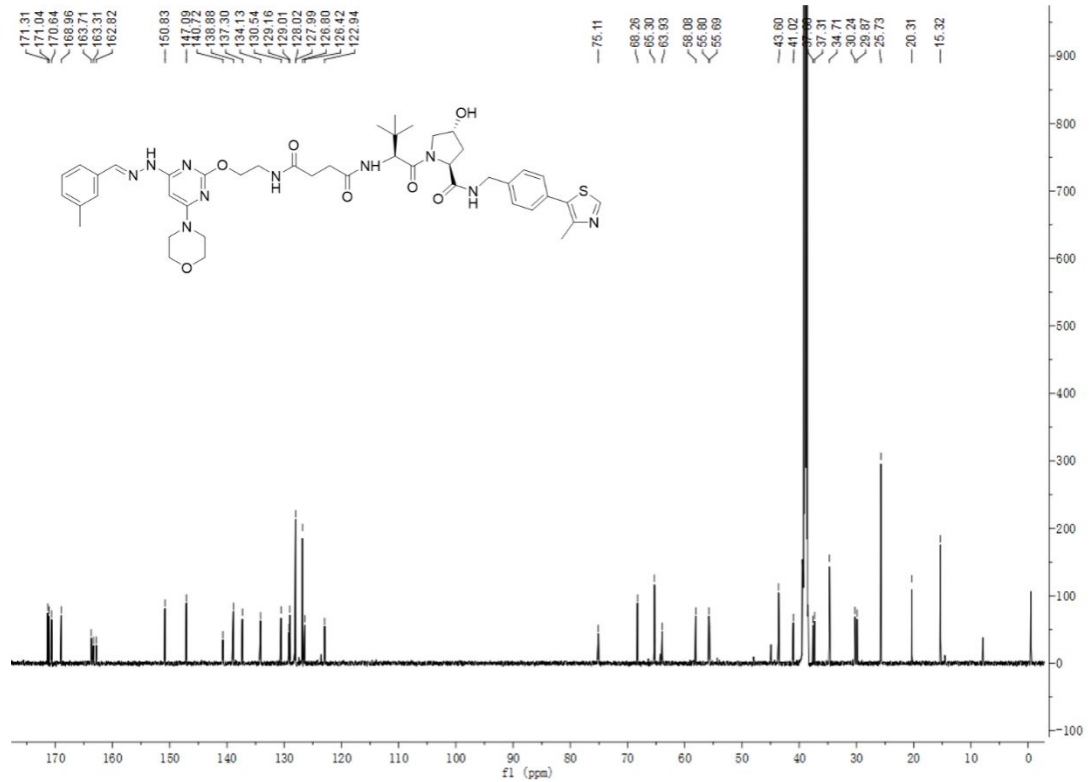
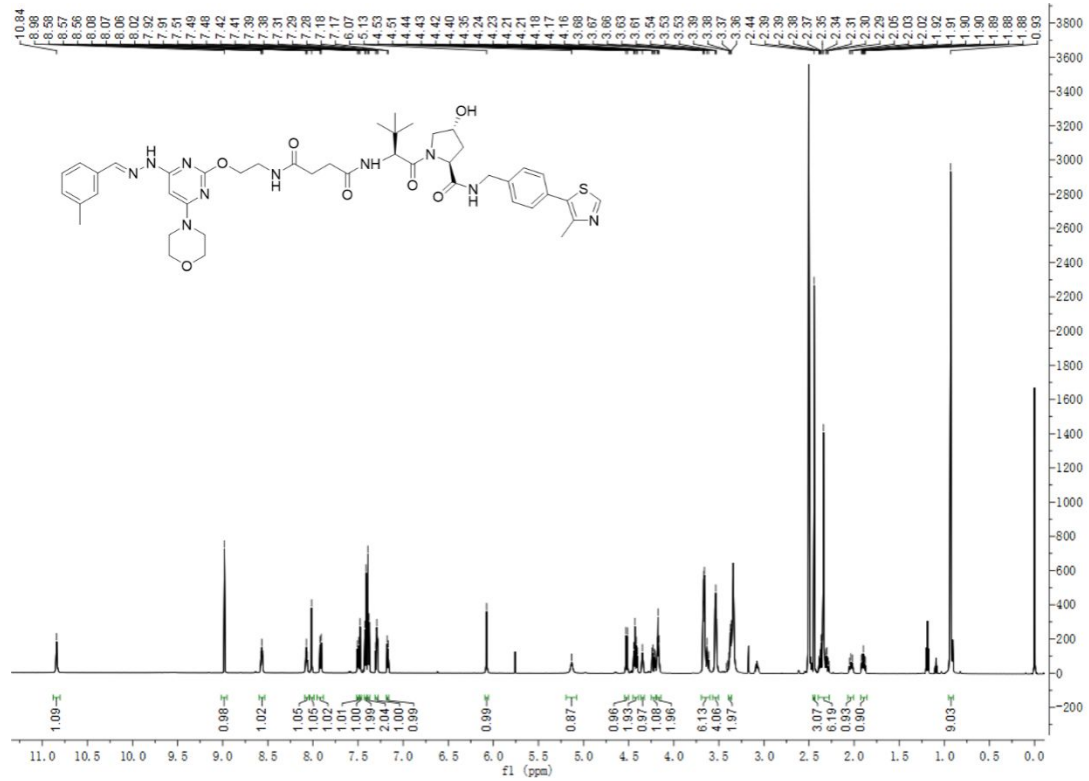


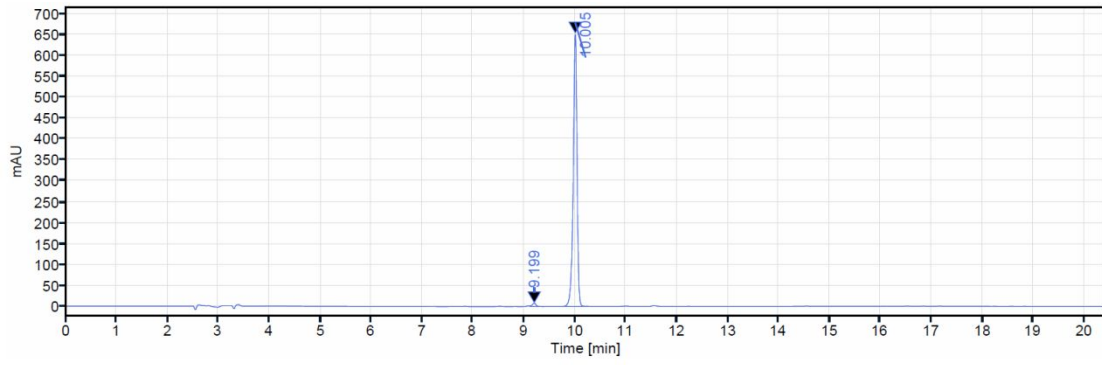


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.363	VB	0.26	31.90	5.51	0.73	
10.227	VV	0.77	4330.01	667.71	98.63	
11.616	BV	0.47	28.35	4.77	0.65	
	Sum		4390.27		100.00	

Compound 7b

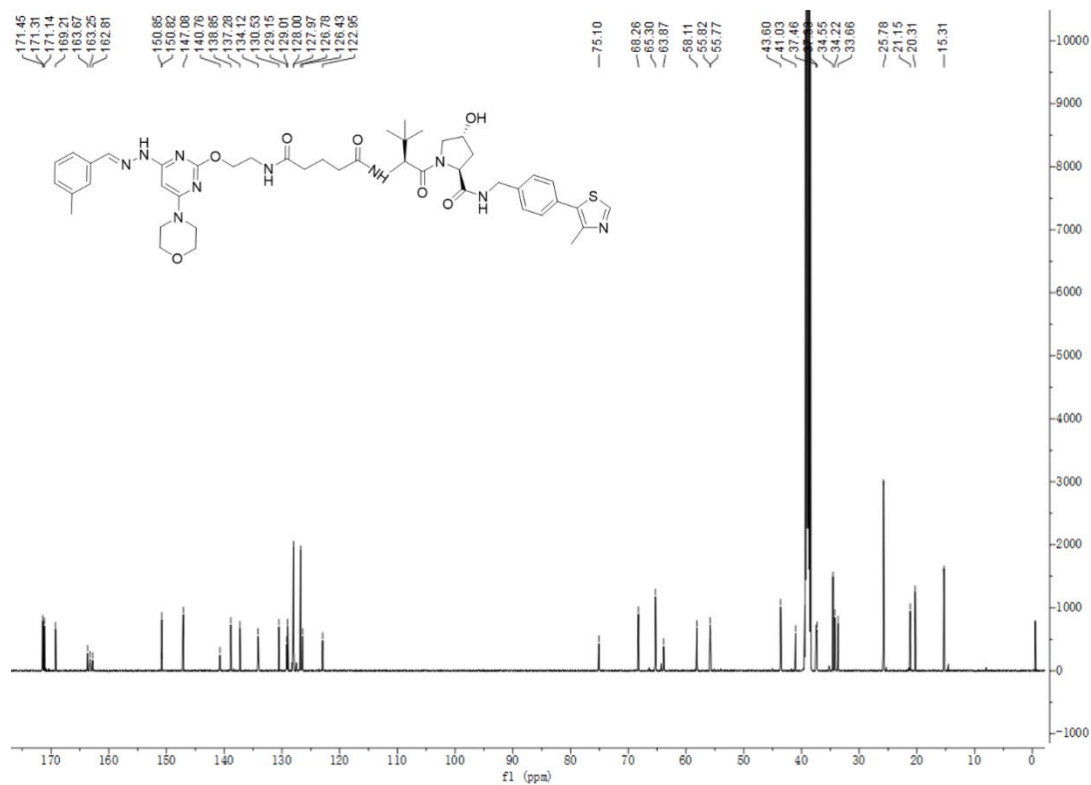
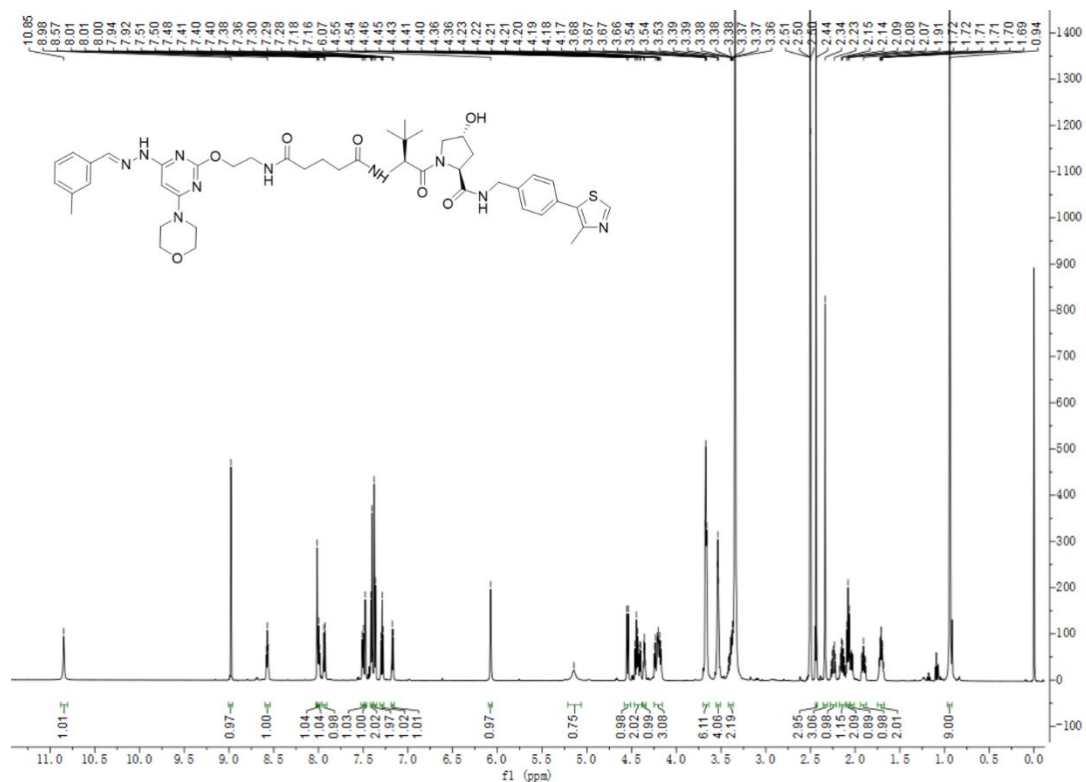


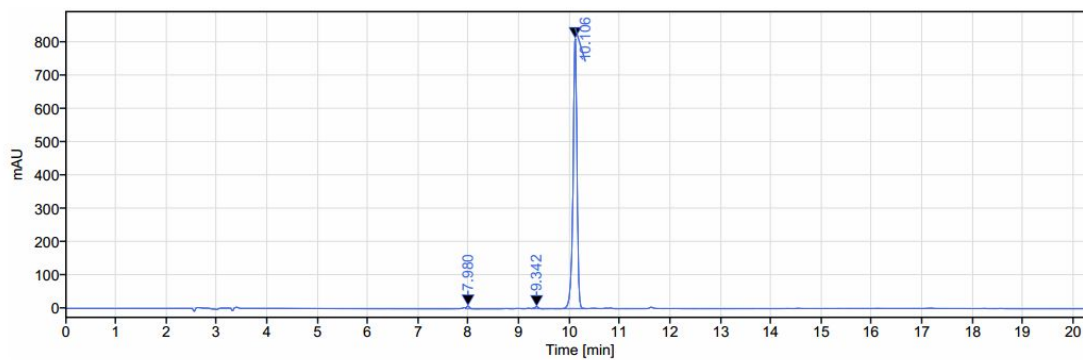


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.199	VB	0.26	43.71	8.38	1.27	
10.005	BV	0.70	3400.60	655.48	98.73	
		Sum	3444.32		100.00	

Compound 7c

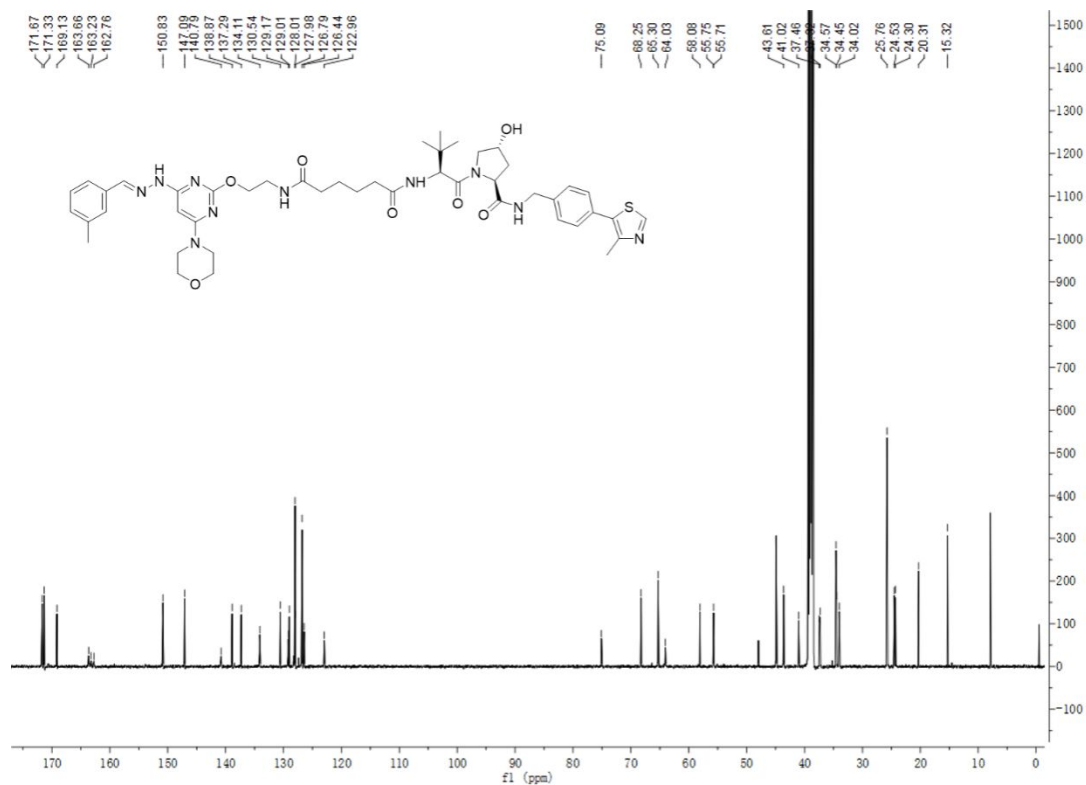
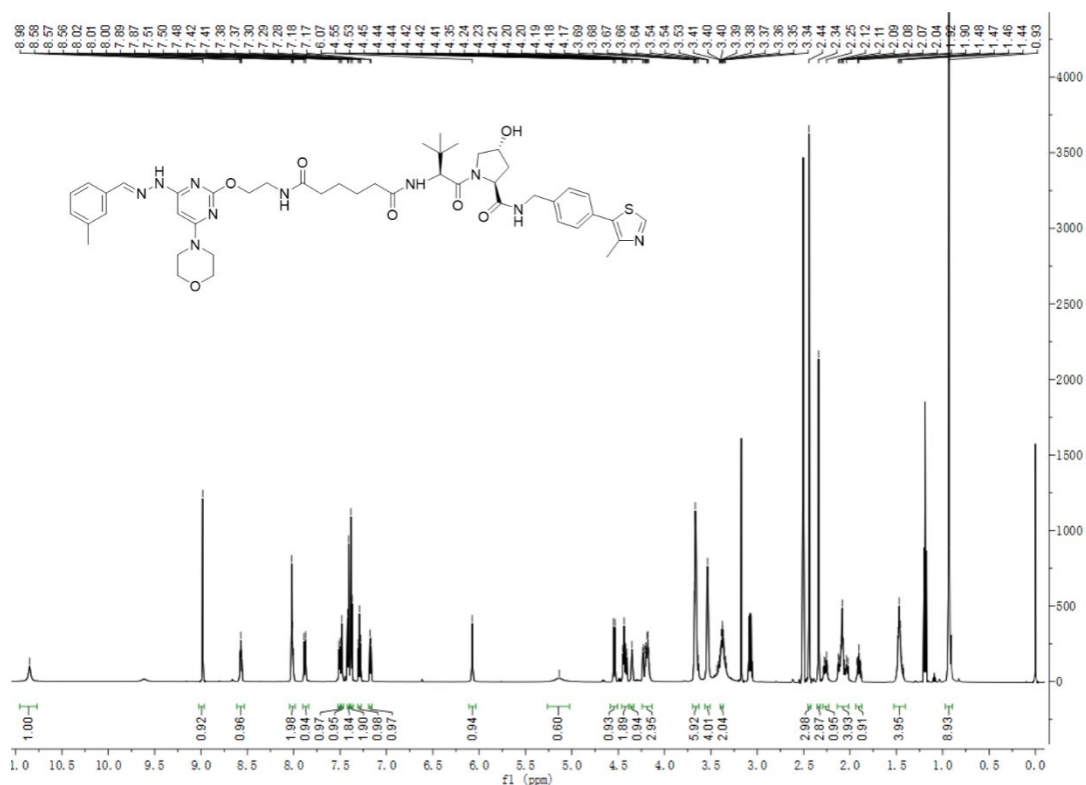


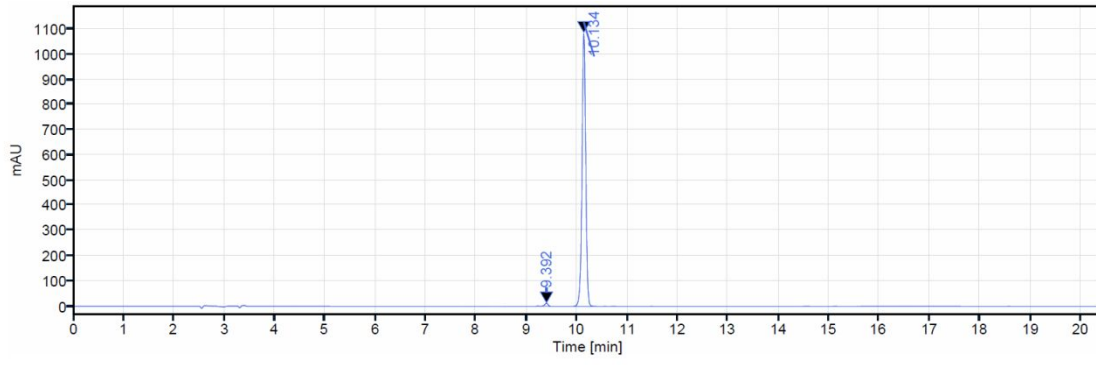


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.980	VB	0.28	35.28	8.50	0.79	
9.342	VB	0.25	35.26	6.42	0.78	
10.106	VV	0.66	4421.70	810.54	98.43	
	Sum		4492.24		100.00	

Compound 7d

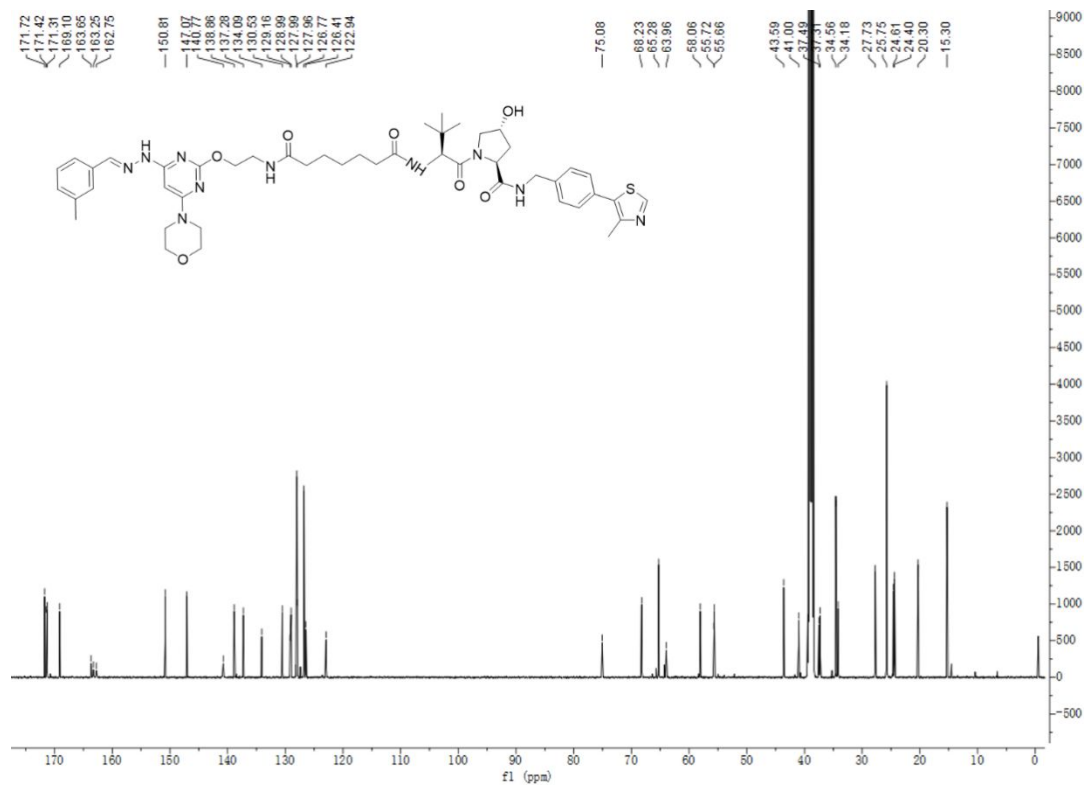
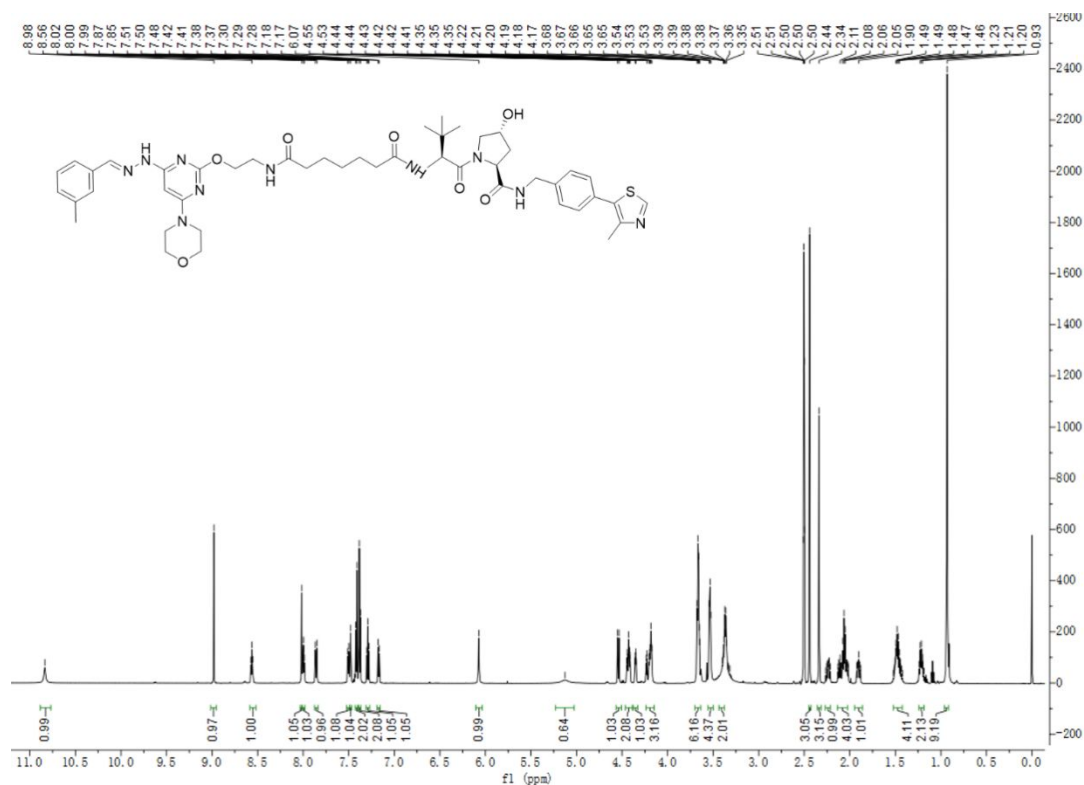


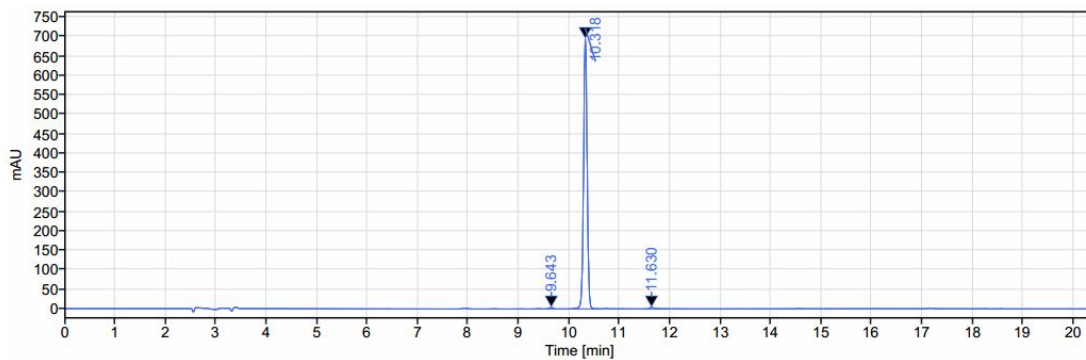


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.392	MM m	0.15	51.90	11.76	0.92	
10.134	BV	0.68	5595.25	1086.09	99.08	
		Sum	5647.15		100.00	

Compound 7e

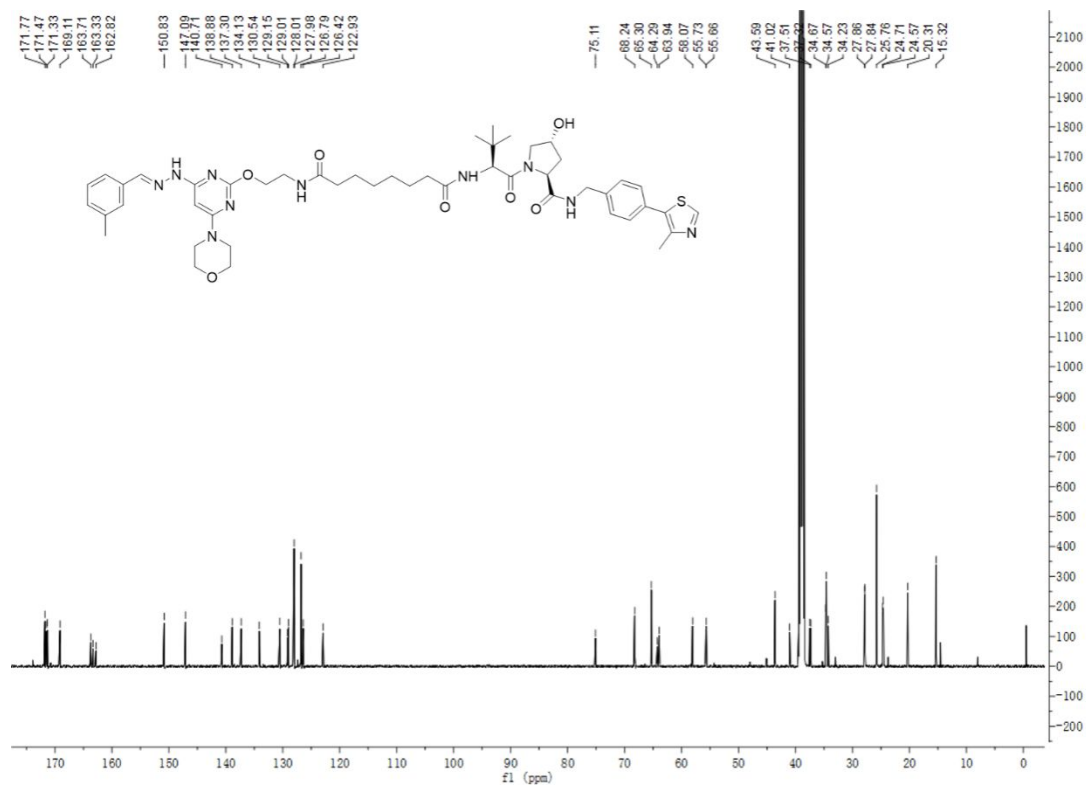
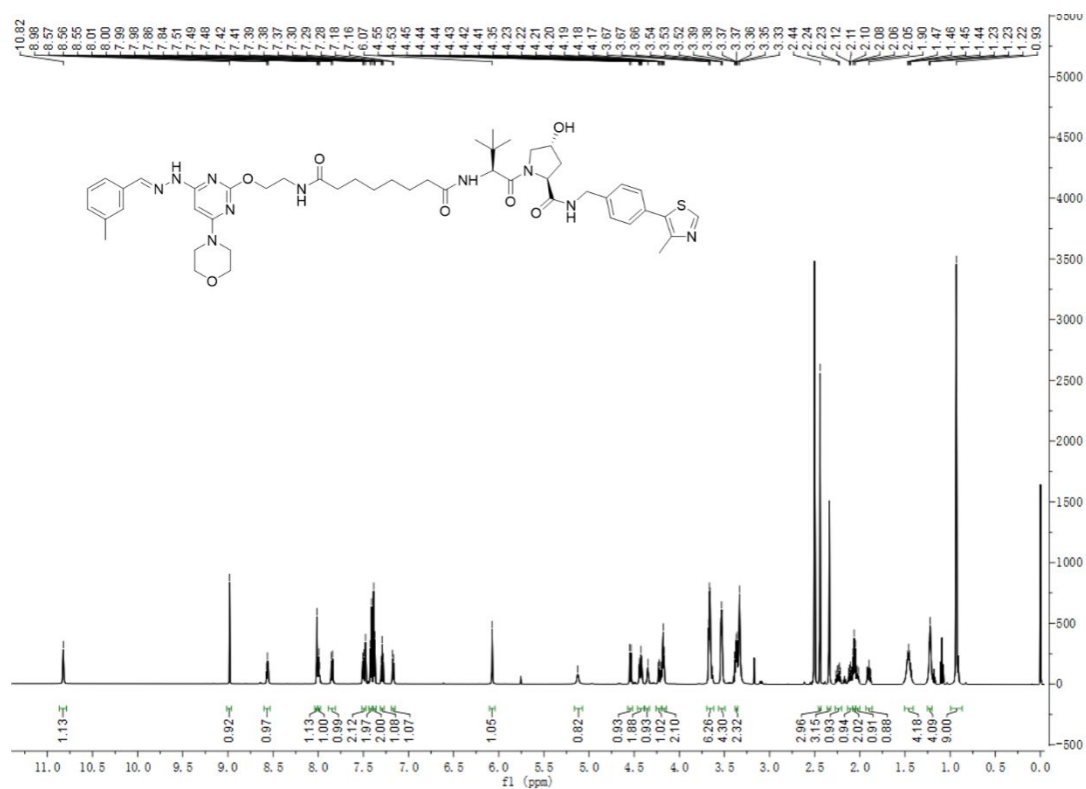


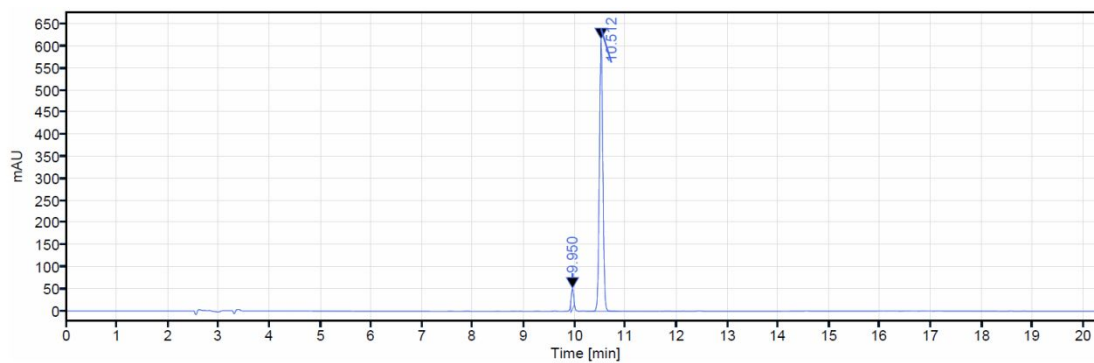


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.643	VB	0.29	24.25	4.75	0.70	
10.318	VV	0.67	3428.93	695.96	98.54	
11.630	BB	0.49	26.56	4.56	0.76	
	Sum		3479.74		100.00	

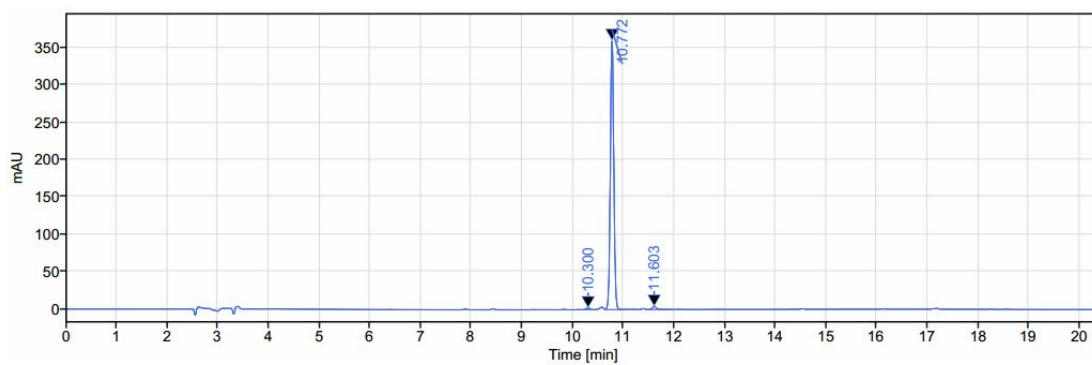
Compound 7f





Signal: DAD1A,Sig=254,4 Ref=off

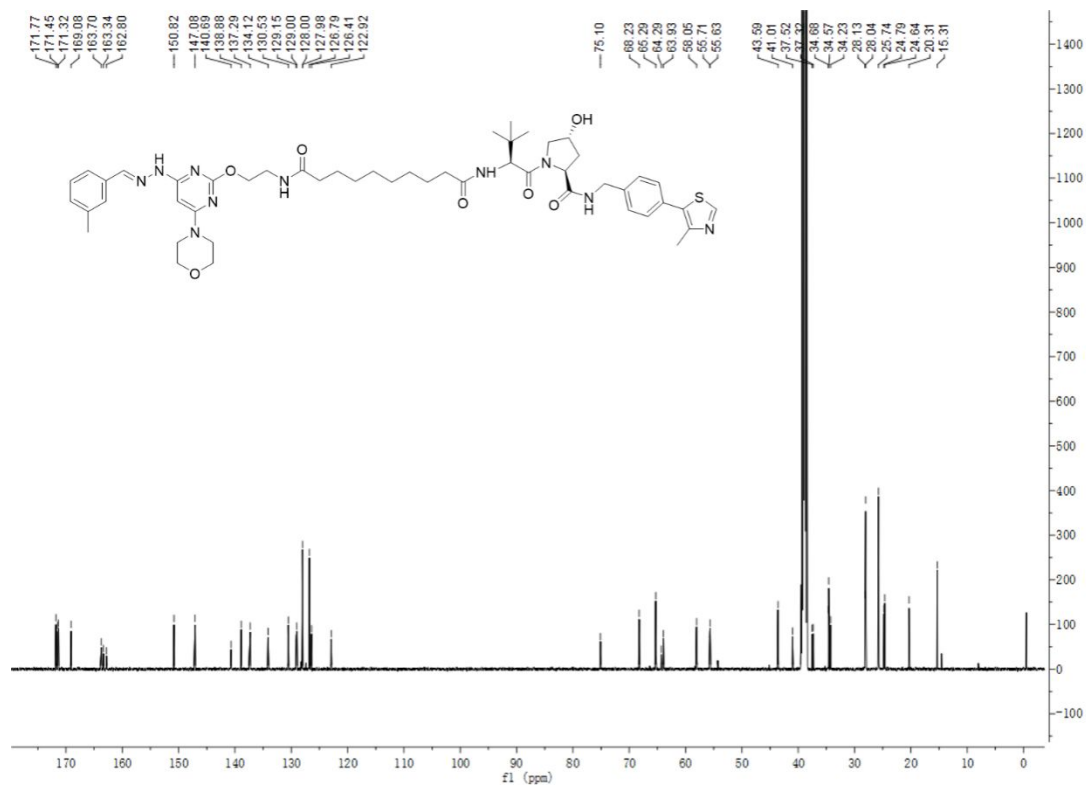
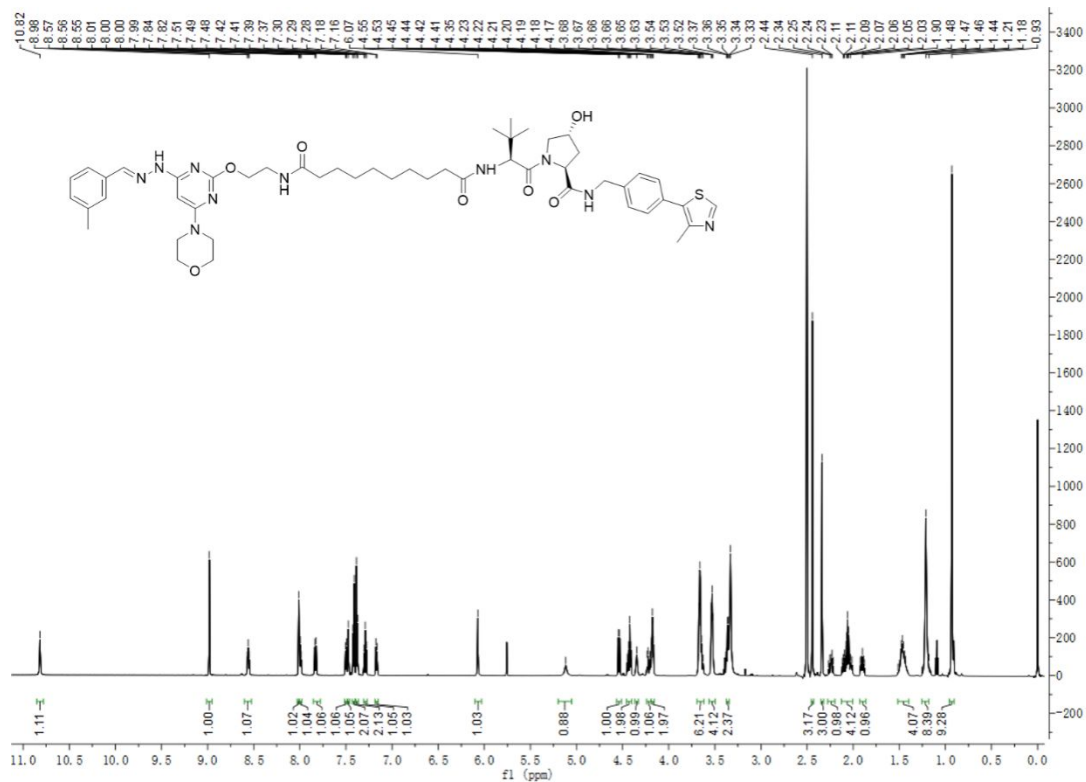
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.950	MM m	0.07	136.50	46.04	4.45	
10.512	VV	0.63	2930.35	616.79	95.55	
		Sum	3066.84		100.00	

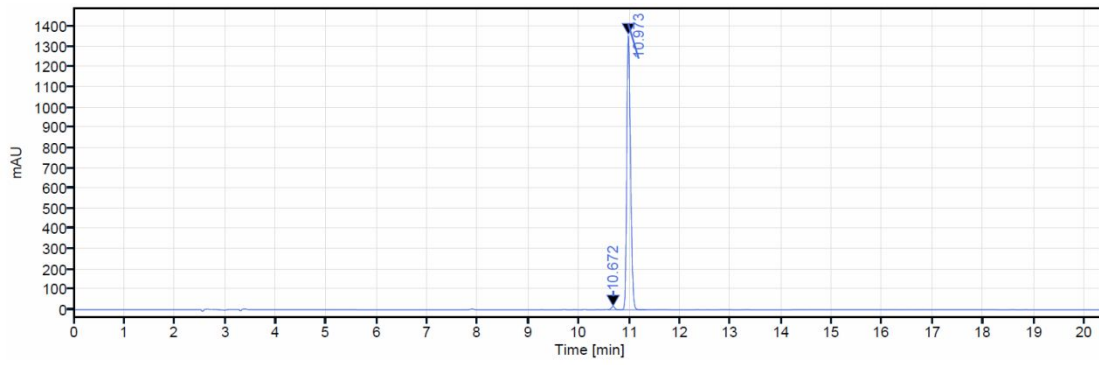


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.300	VB	0.23	12.70	2.55	0.73	
10.772	VV	0.36	1708.46	360.30	97.86	
11.603	VB	0.47	24.57	4.46	1.41	
		Sum	1745.73		100.00	

Compound 7h

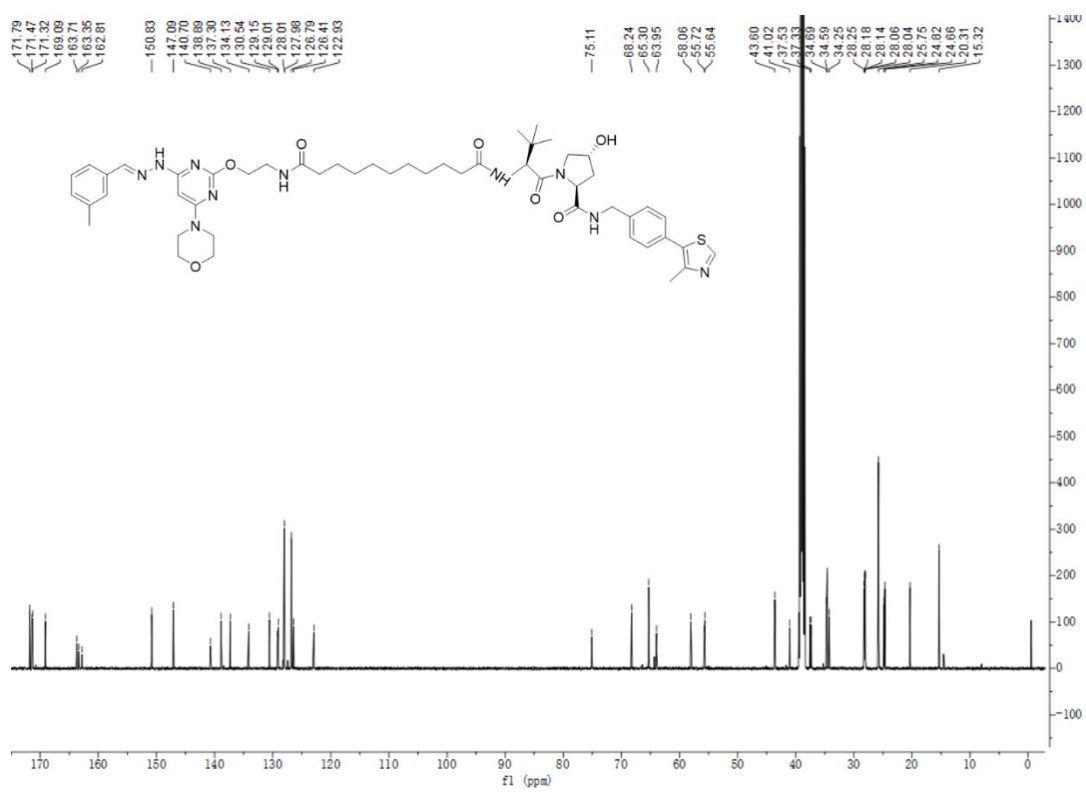
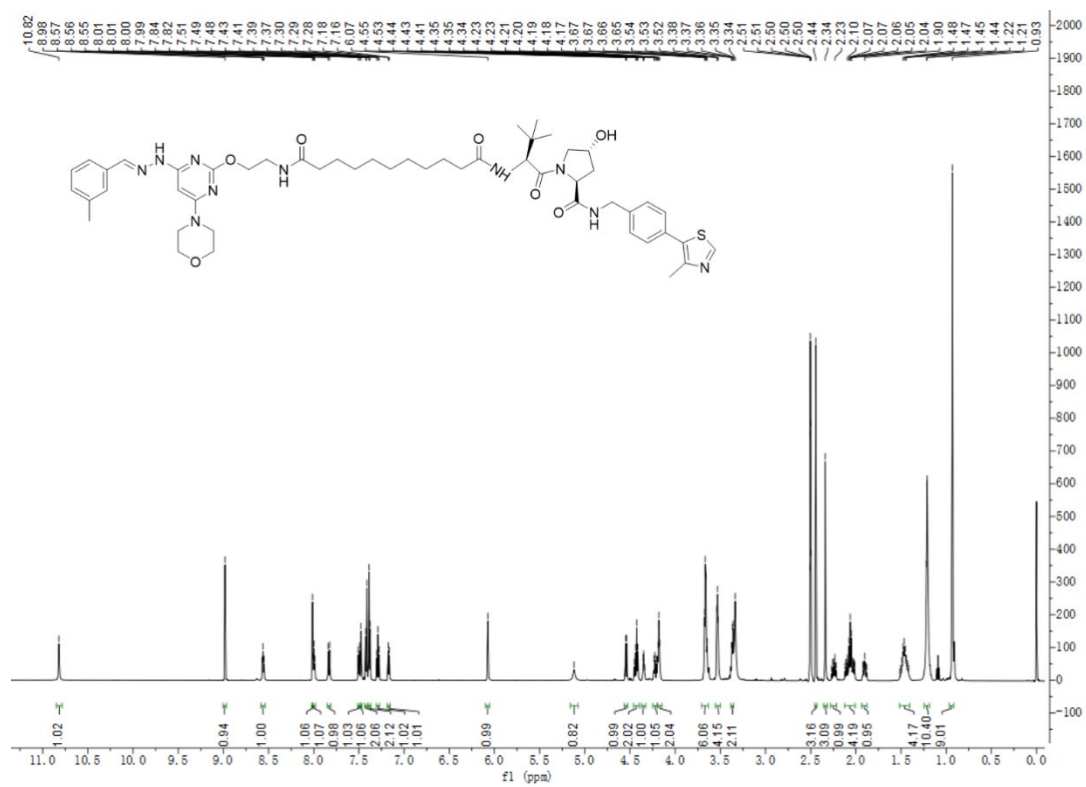


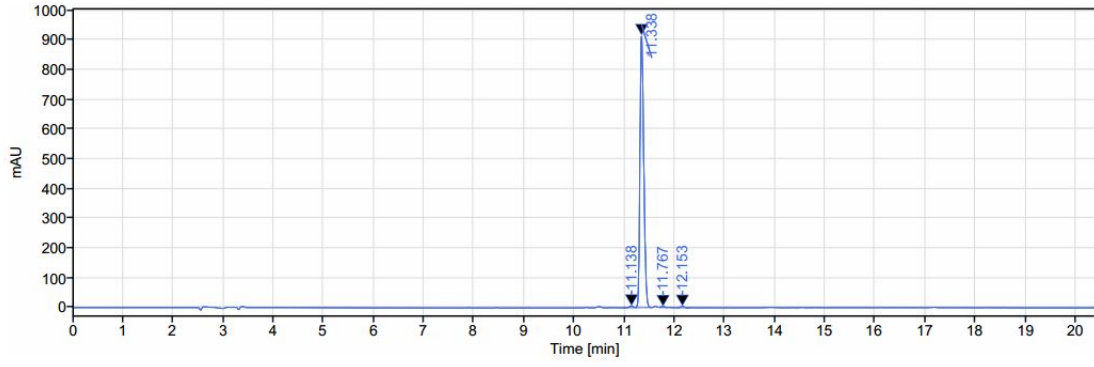


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.672	VV	0.24	85.25	16.42	1.18	
10.973	VV	0.51	7138.02	1360.86	98.82	
Sum			7223.27		100.00	

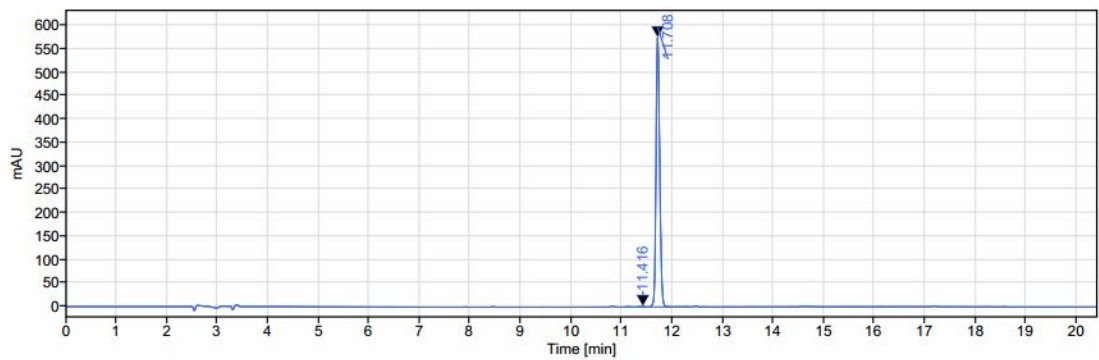
Compound **7i**





Signal: DAD1A,Sig=254,4 Ref=off

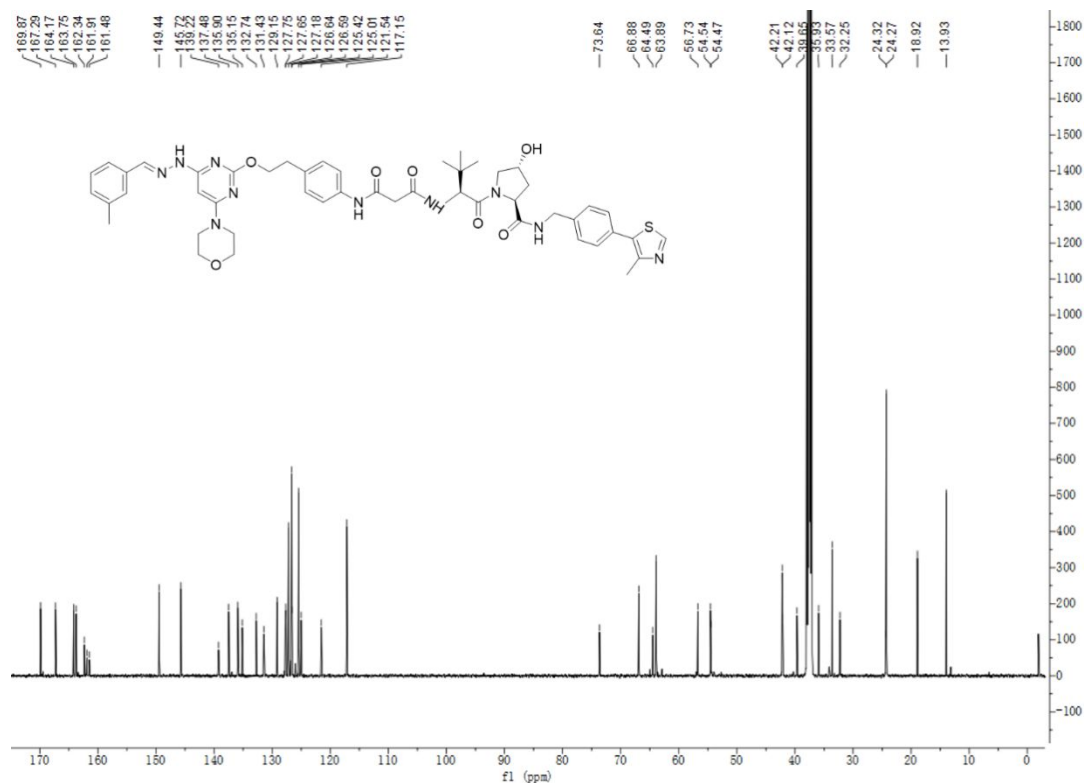
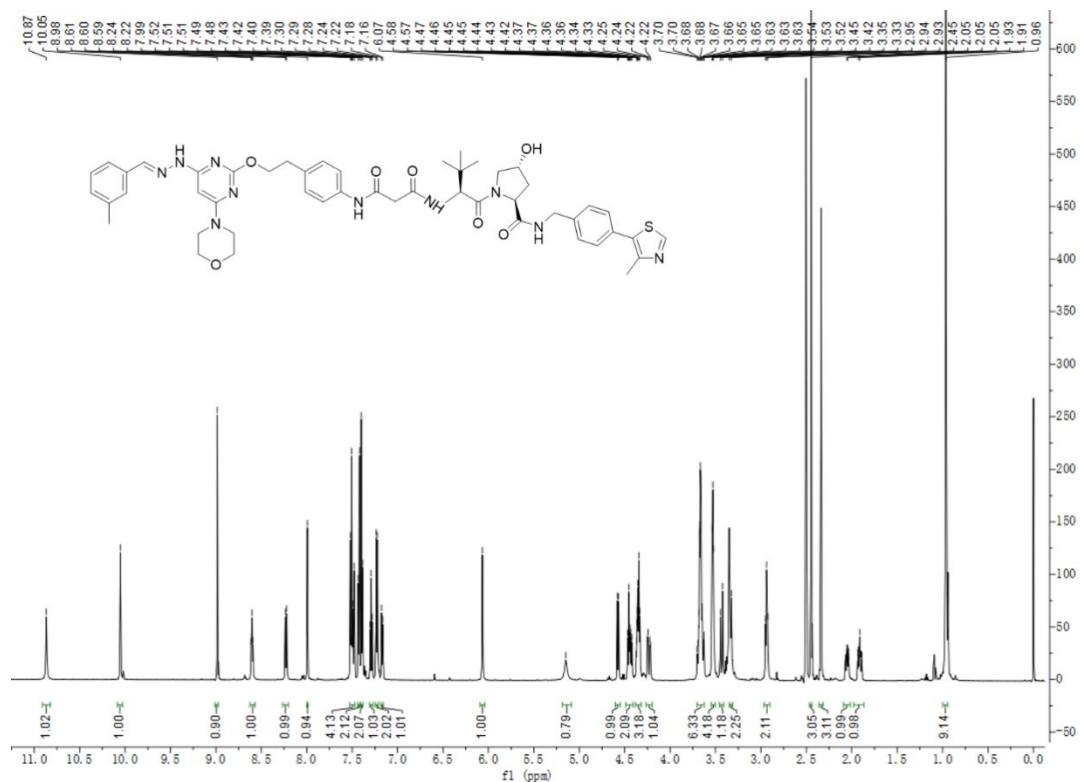
RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.138	BV	0.25	32.25	6.08	0.67	
11.338	VB	0.33	4764.93	916.26	98.36	
11.767	VV	0.17	23.28	3.86	0.48	
12.153	BB	0.25	24.11	5.15	0.50	
Sum			4844.57		100.00	

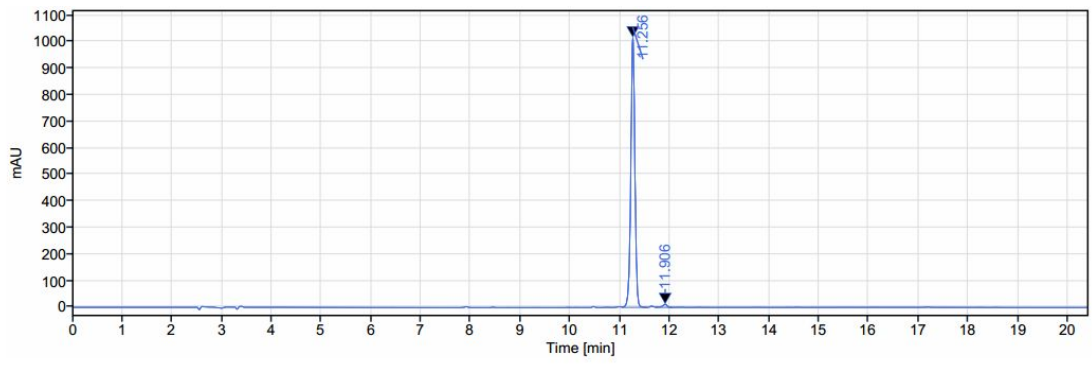


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.416	VV	0.29	10.50	1.72	0.36	
11.708	VV	0.48	2901.01	574.44	99.64	
Sum			2911.51		100.00	

Compound 12a

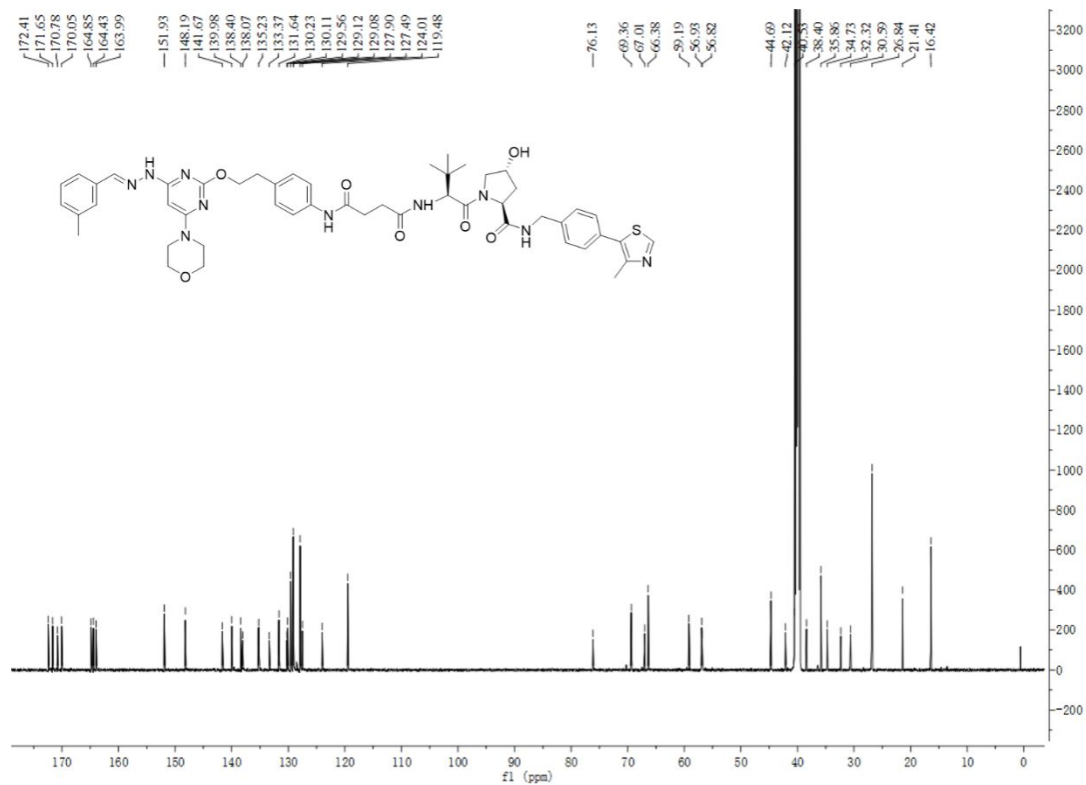
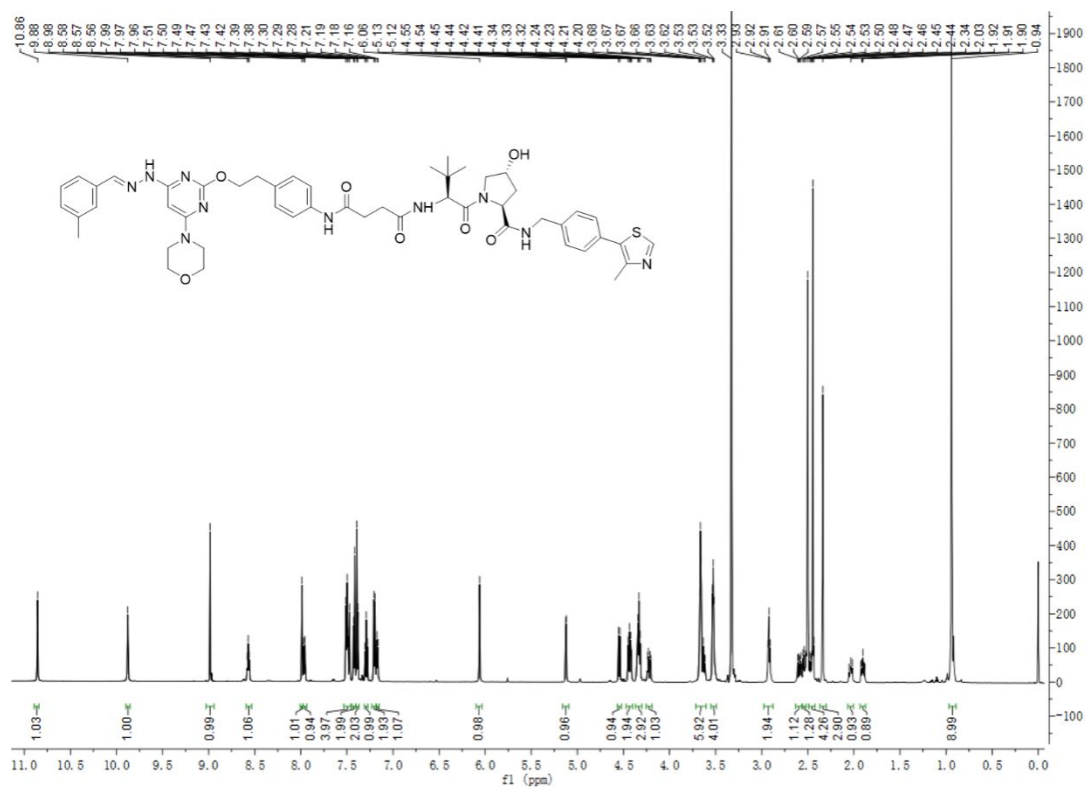


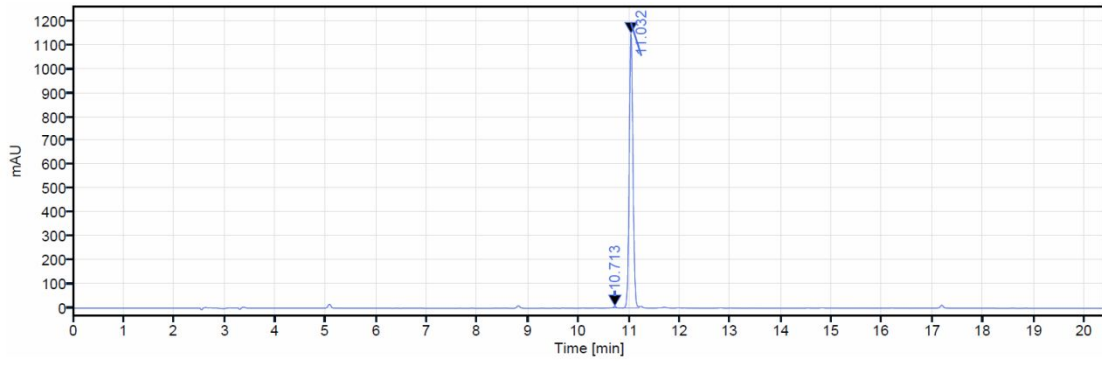


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.256	VB	0.49	5800.71	1016.46	98.68	
11.906	VB	0.34	77.57	11.73	1.32	
Sum			5878.28		100.00	

Compound 12b

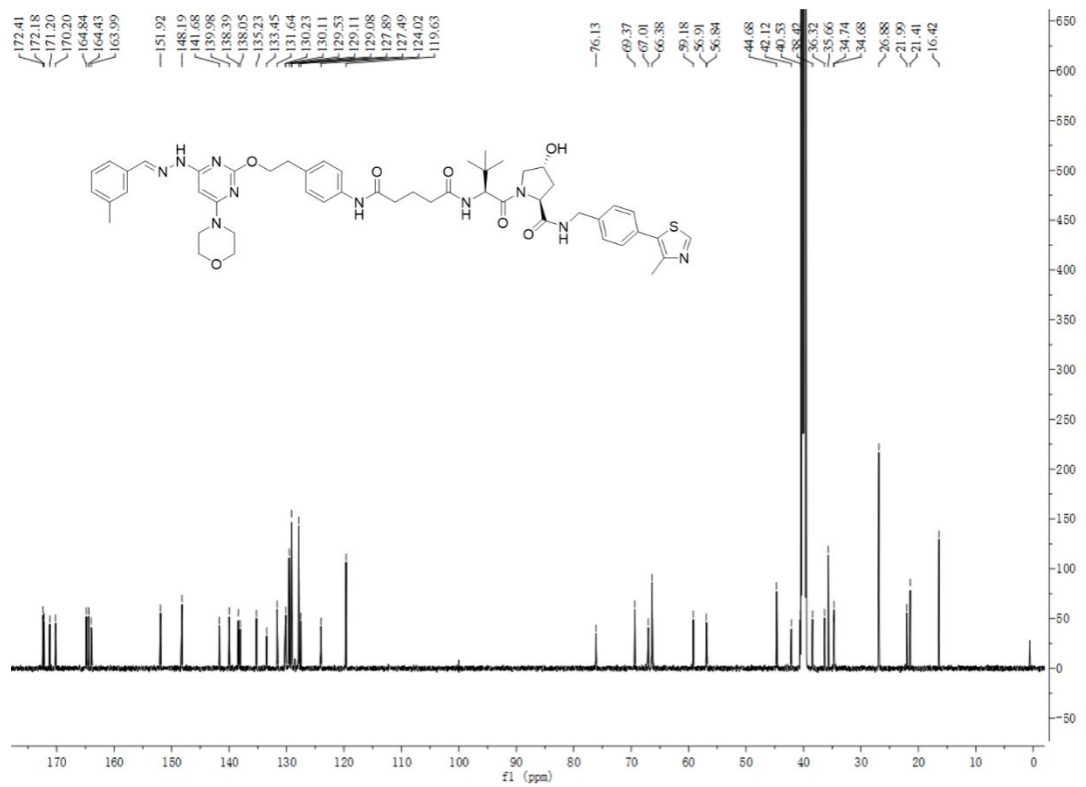
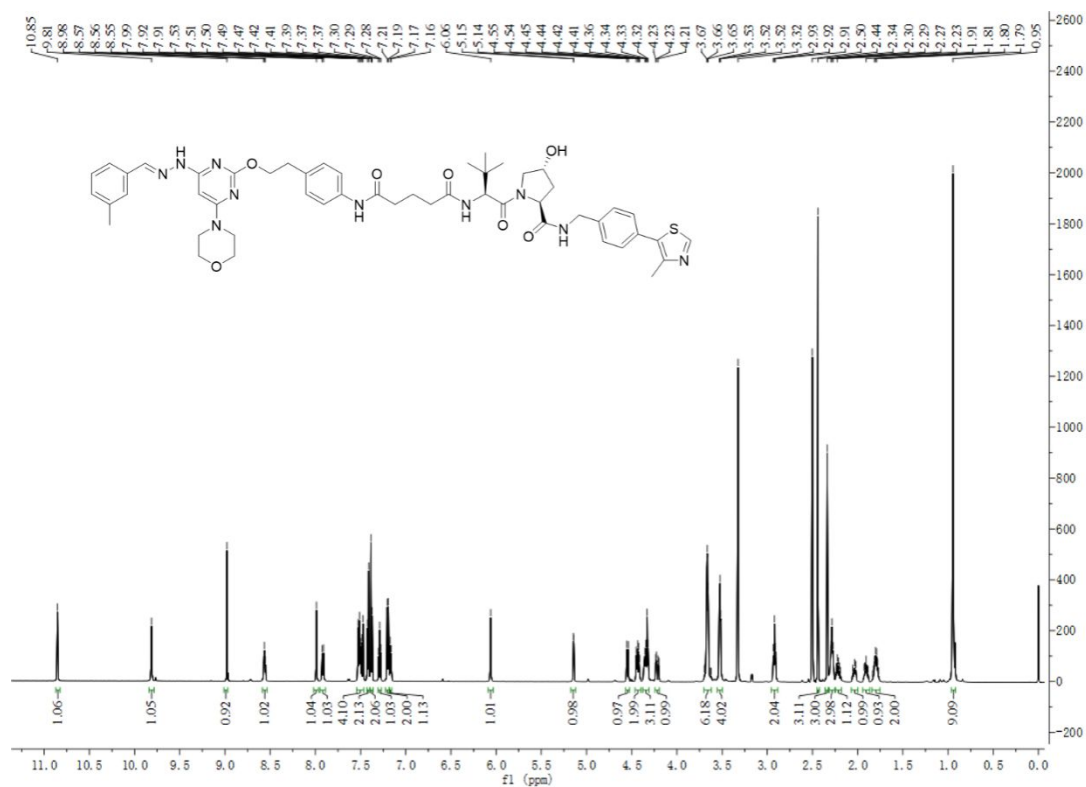


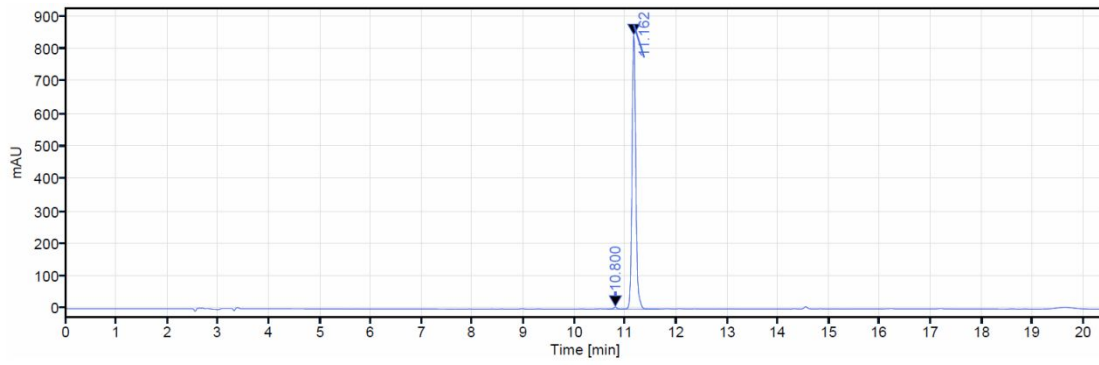


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.713	MM m	0.11	19.40	5.93	0.33	
11.032	BV	0.32	5896.41	1147.04	99.67	
		Sum	5915.81		100.00	

Compound 12c

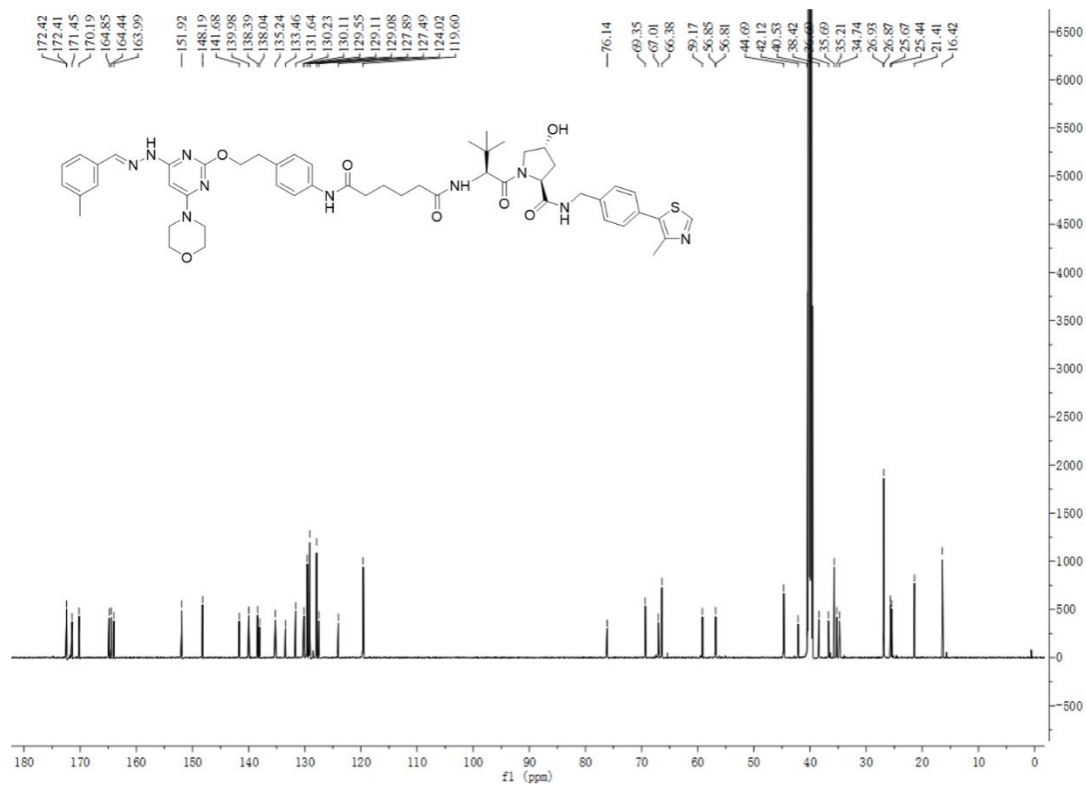
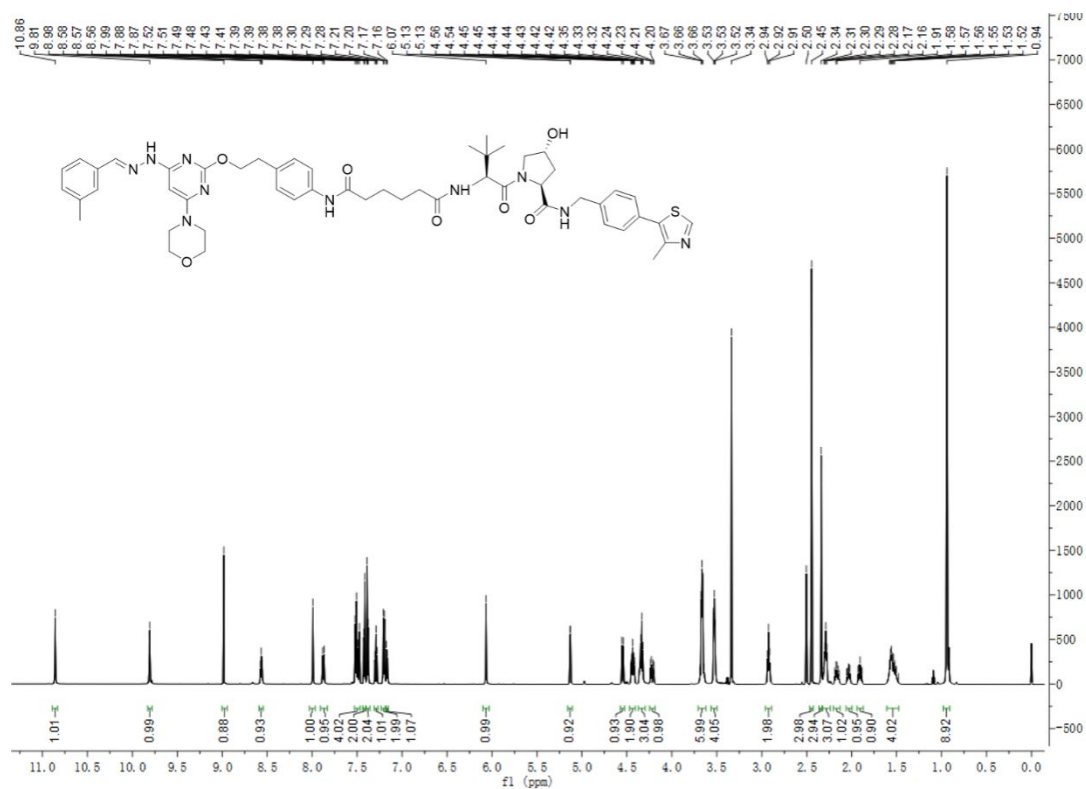


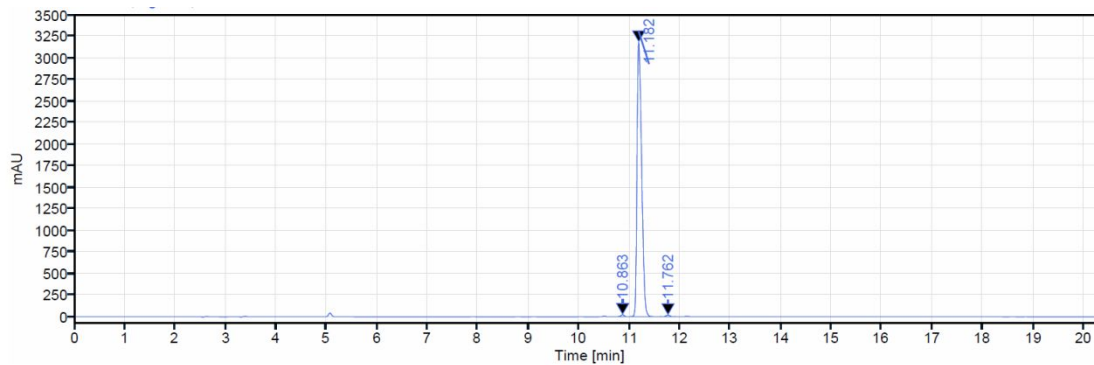


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.800	VV	0.30	31.43	6.64	0.72	
11.162	VV	0.73	4311.28	842.84	99.28	
		Sum	4342.71		100.00	

Compound 12d

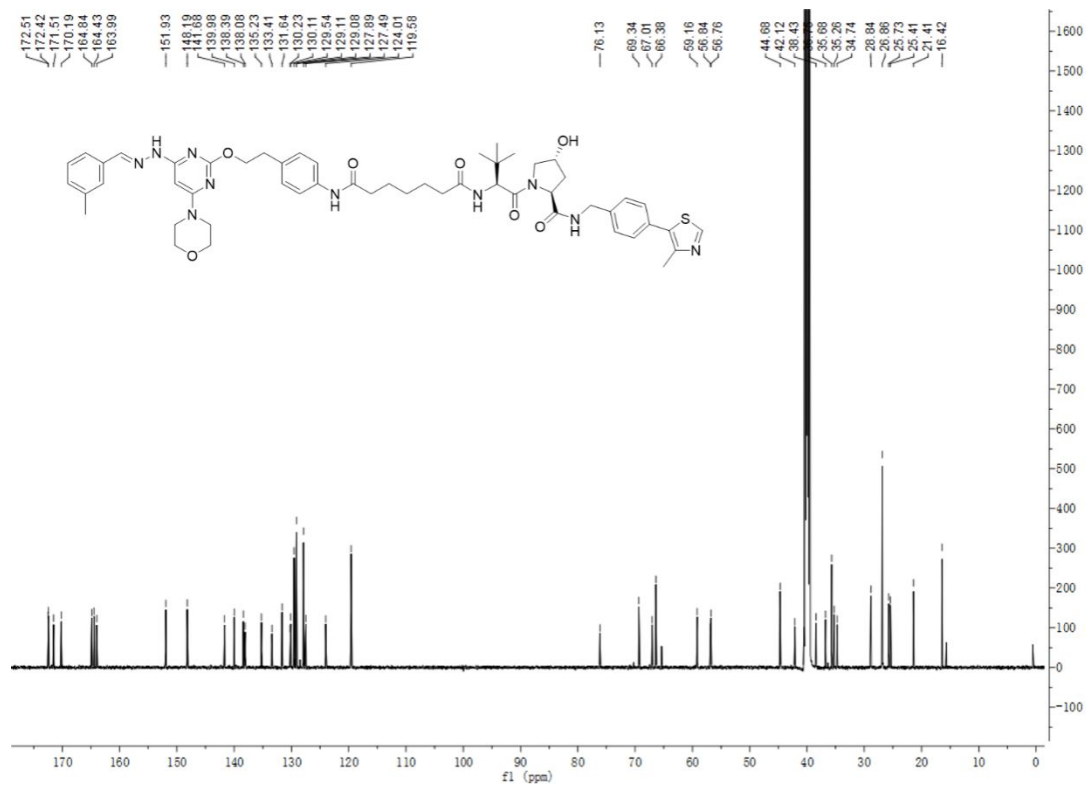
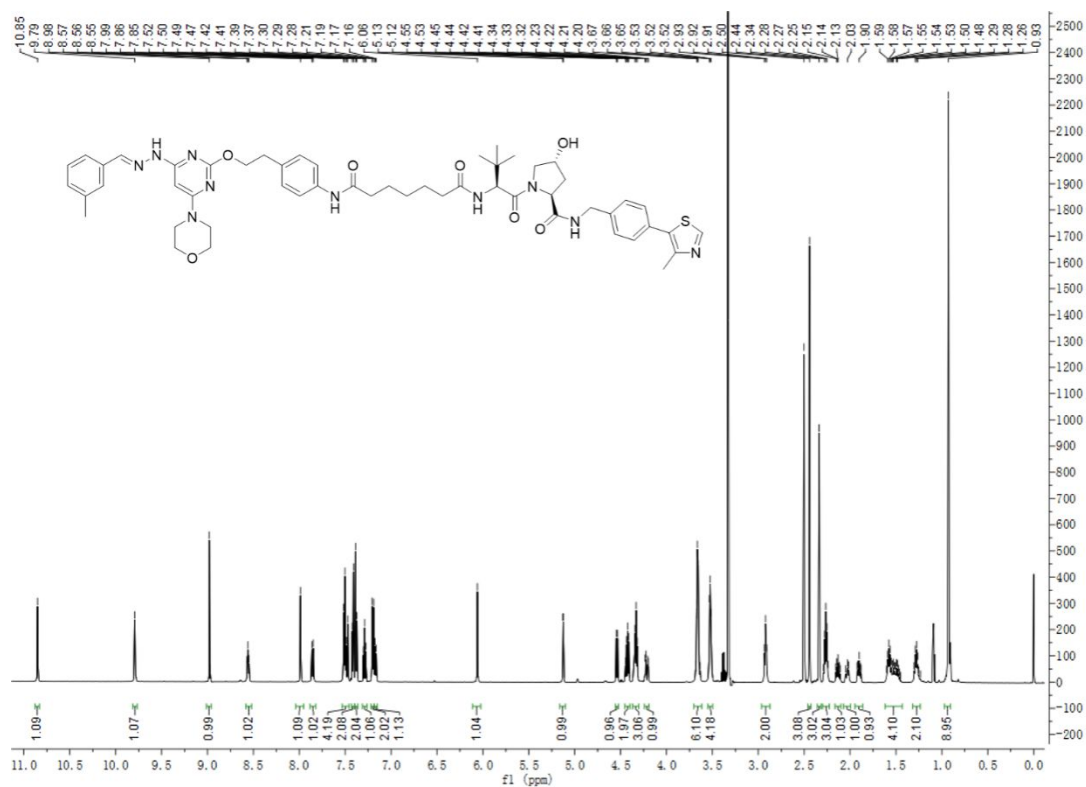


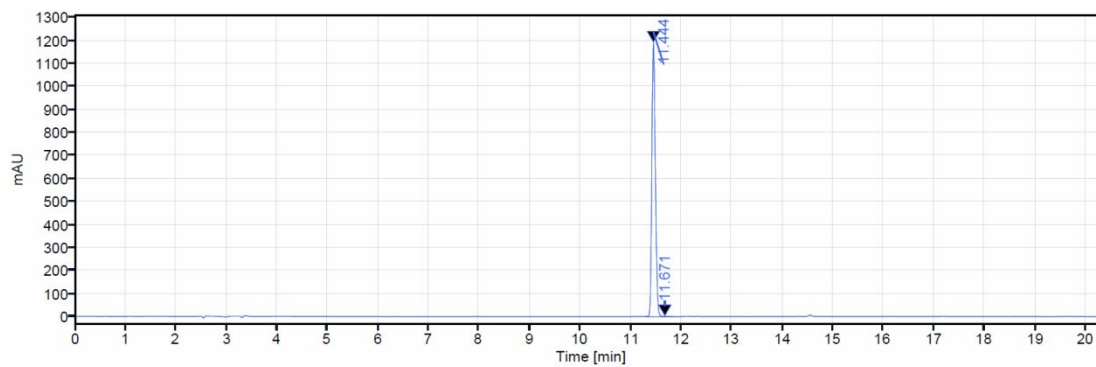


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.863	VB	0.22	106.41	22.51	0.52	
11.182	BB	0.59	20180.56	3185.79	99.00	
11.762	VV	0.20	98.33	19.57	0.48	
Sum			20385.29		100.00	

Compound 12e

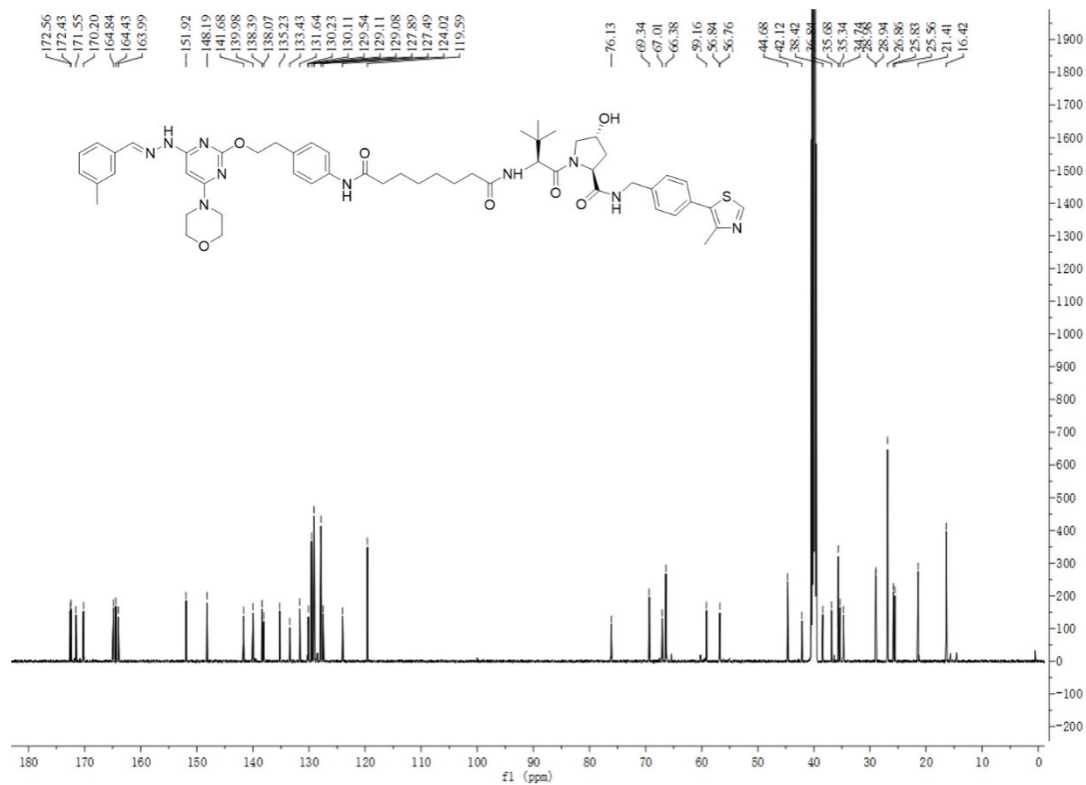
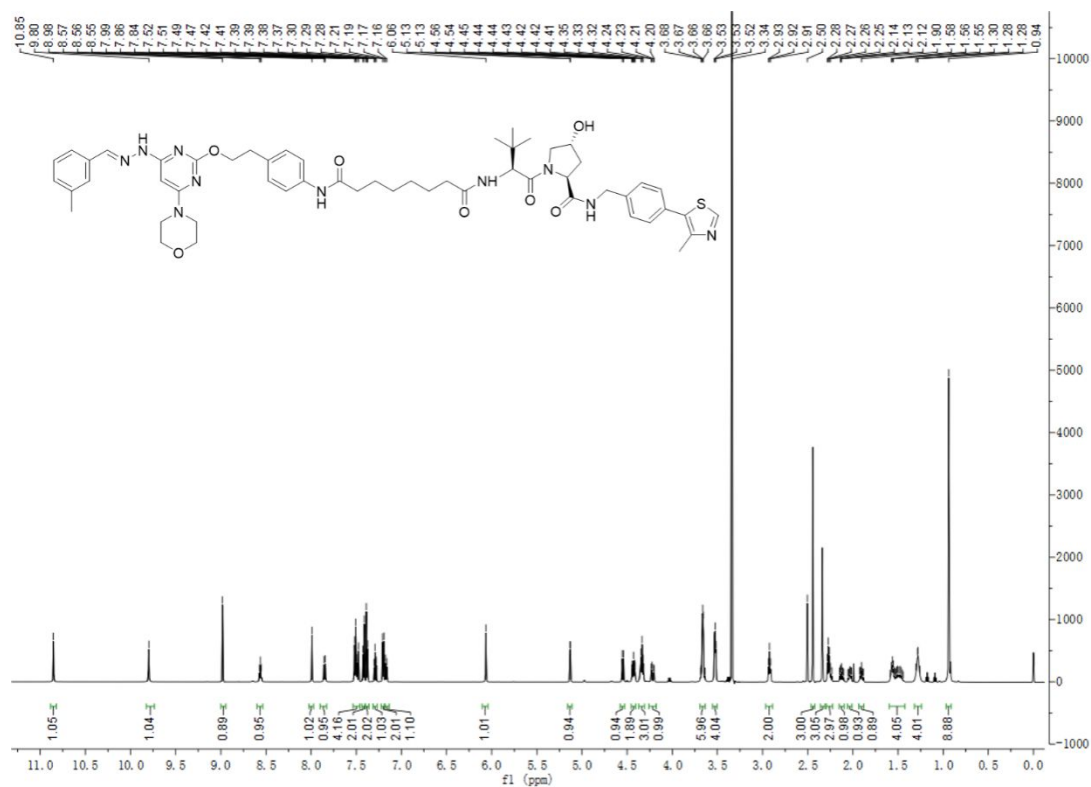


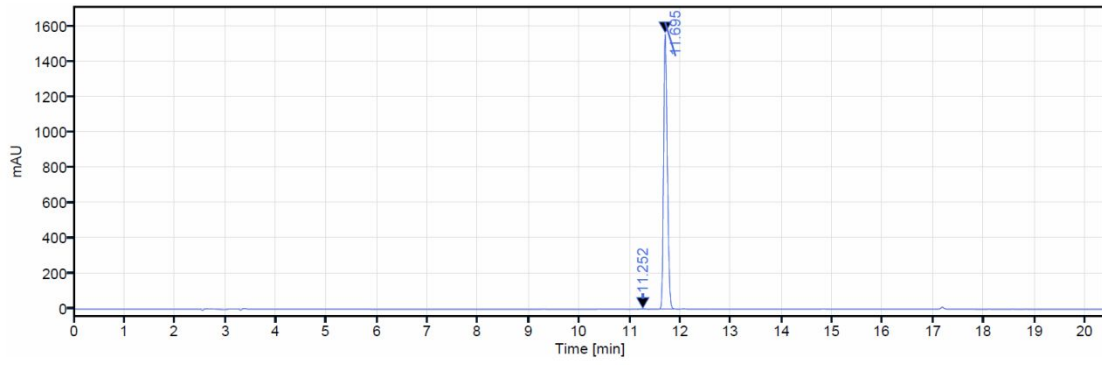


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.444	VV	0.35	5748.64	1192.91	99.85	
11.671	VB	0.24	8.86	1.85	0.15	
Sum			5757.50		100.00	

Compound 12f

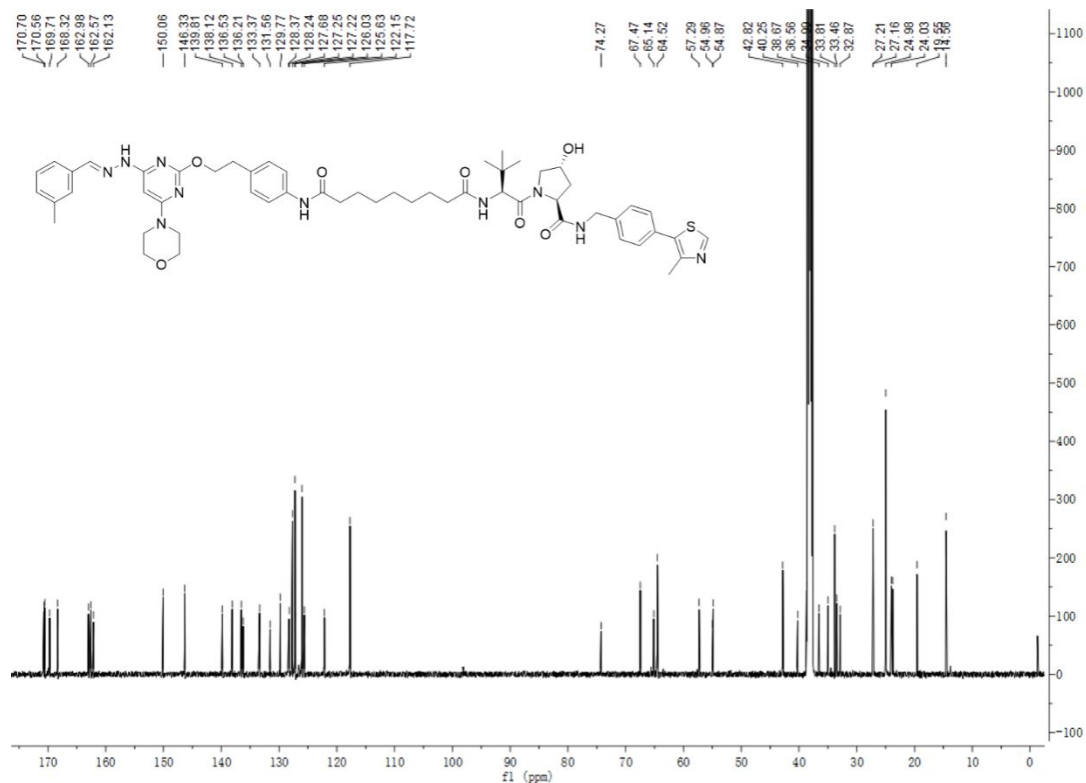
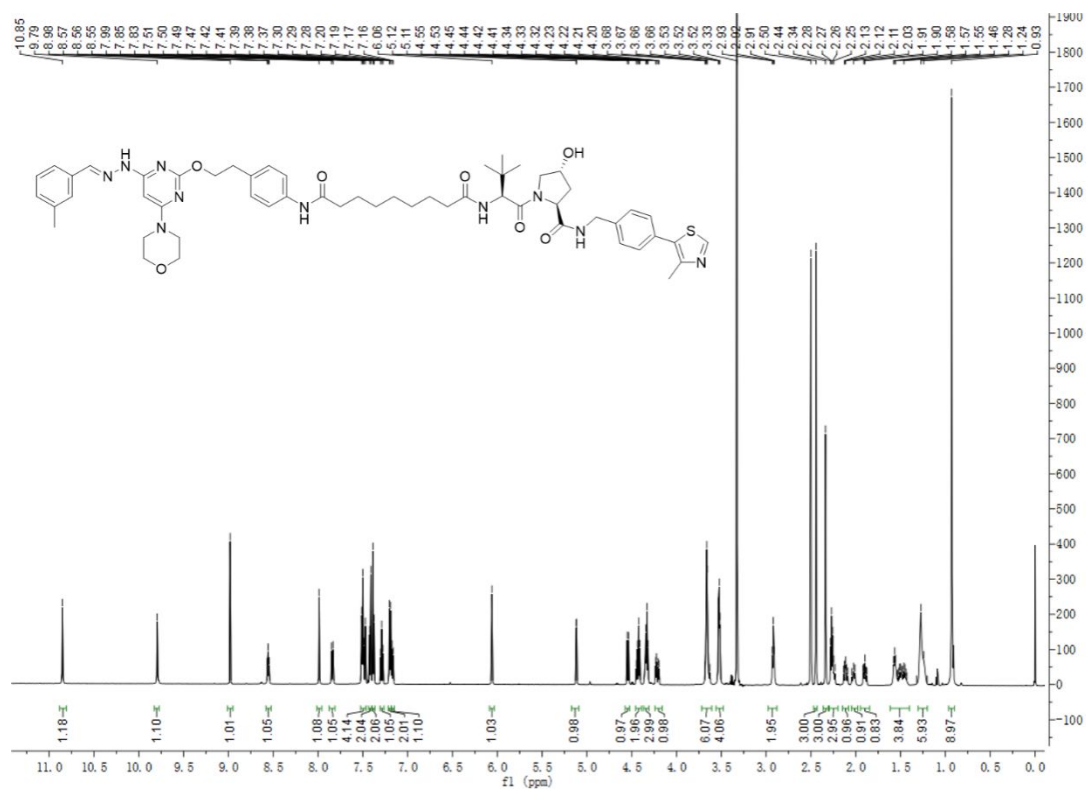


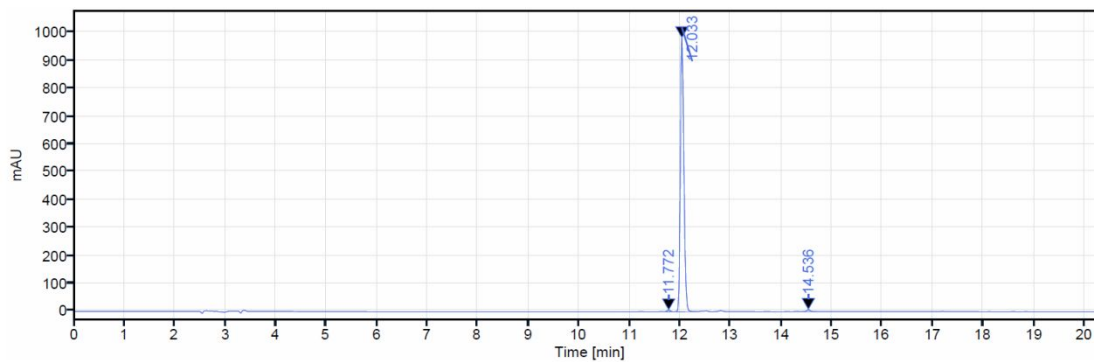


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.252	VB	0.26	21.25	2.48	0.26	
11.695	BV	0.56	8063.57	1564.25	99.74	
		Sum	8084.82		100.00	

Compound 12g

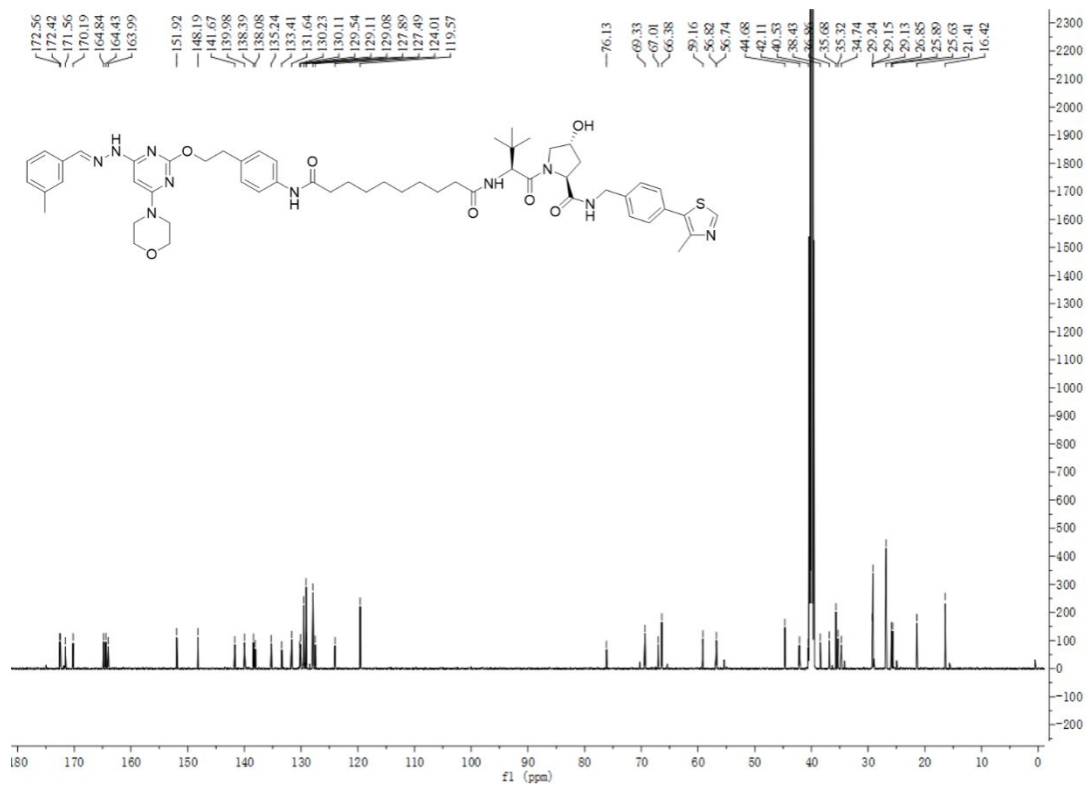
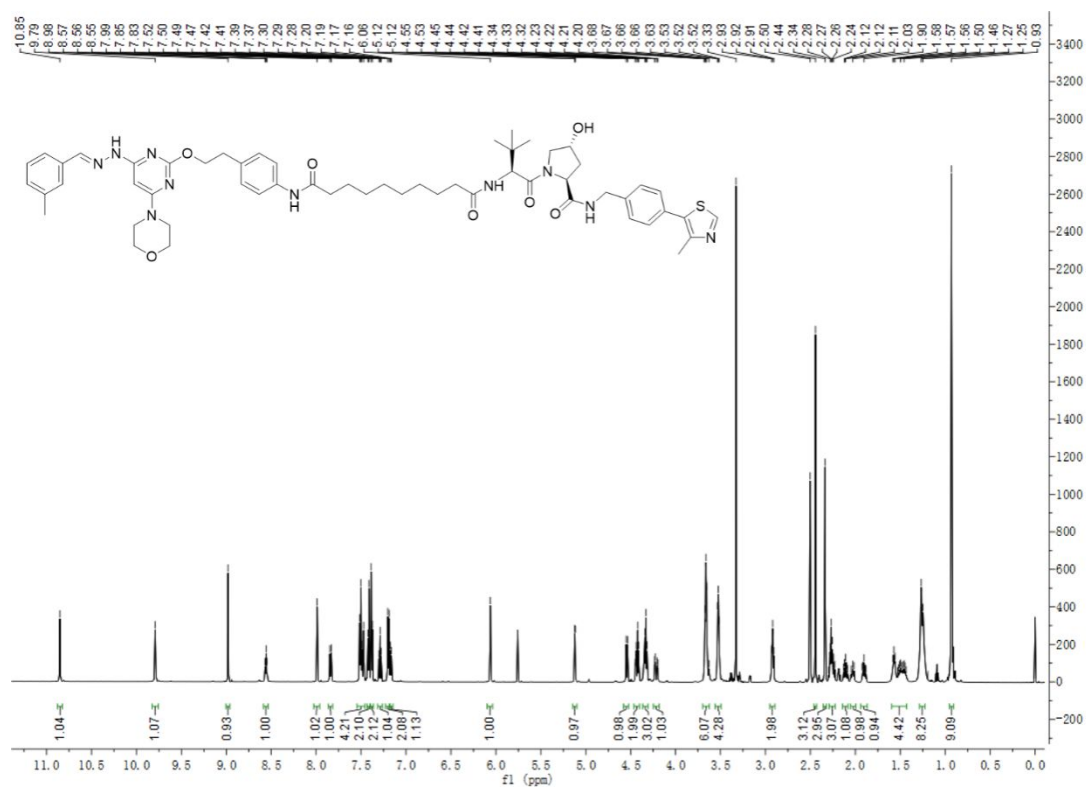


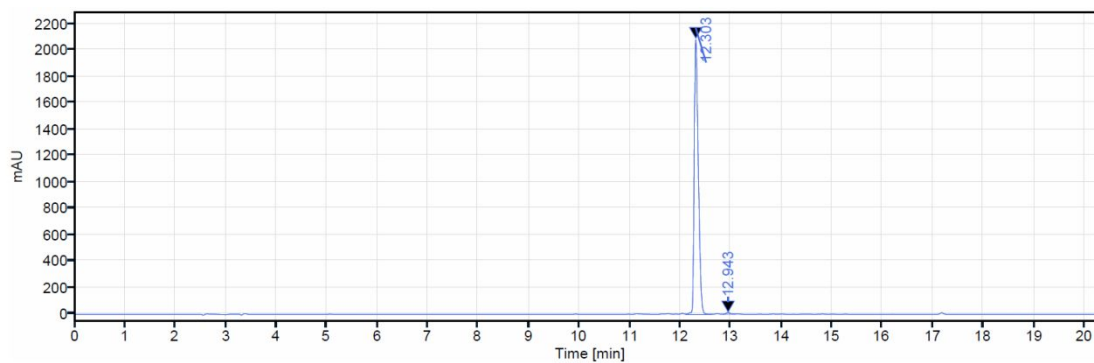


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.772	VB	0.19	23.32	5.25	0.48	
12.033	BB	0.46	4783.57	982.78	98.87	
14.536	VB	0.27	31.17	6.84	0.64	
Sum			4838.07		100.00	

Compound 12h

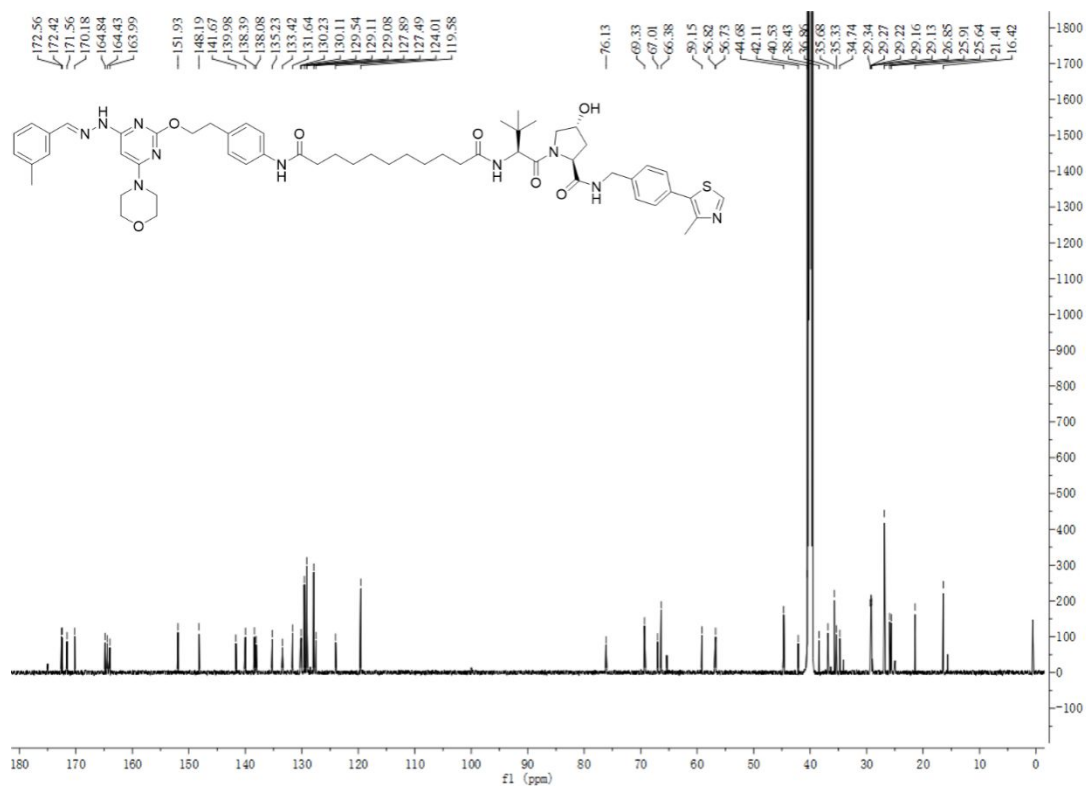
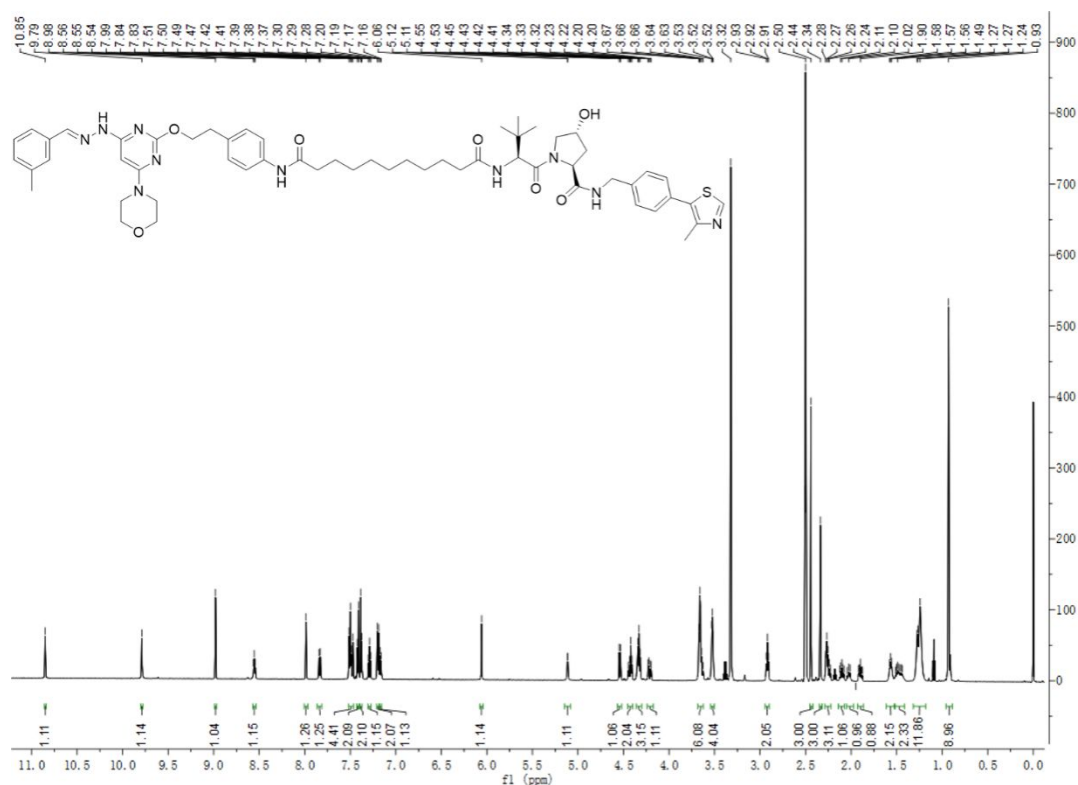


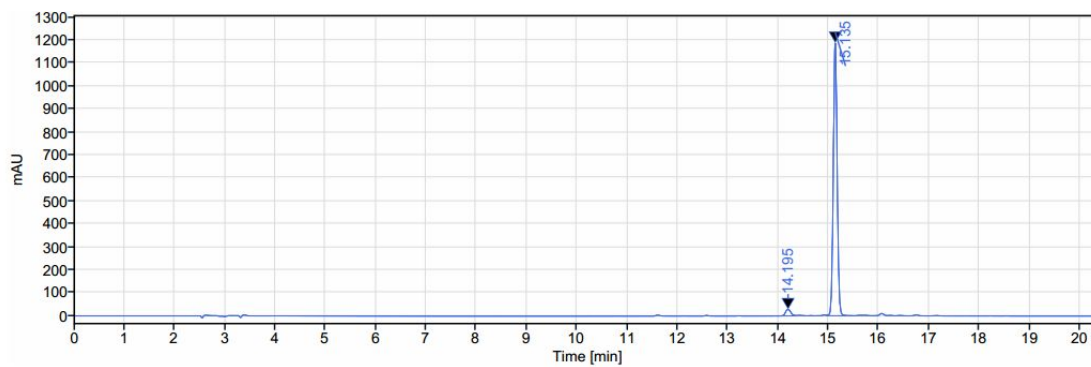


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.303	VB	0.51	11762.95	2084.50	99.35	
12.943	BV	0.24	77.33	14.17	0.65	
Sum			11840.29		100.00	

Compound 12i

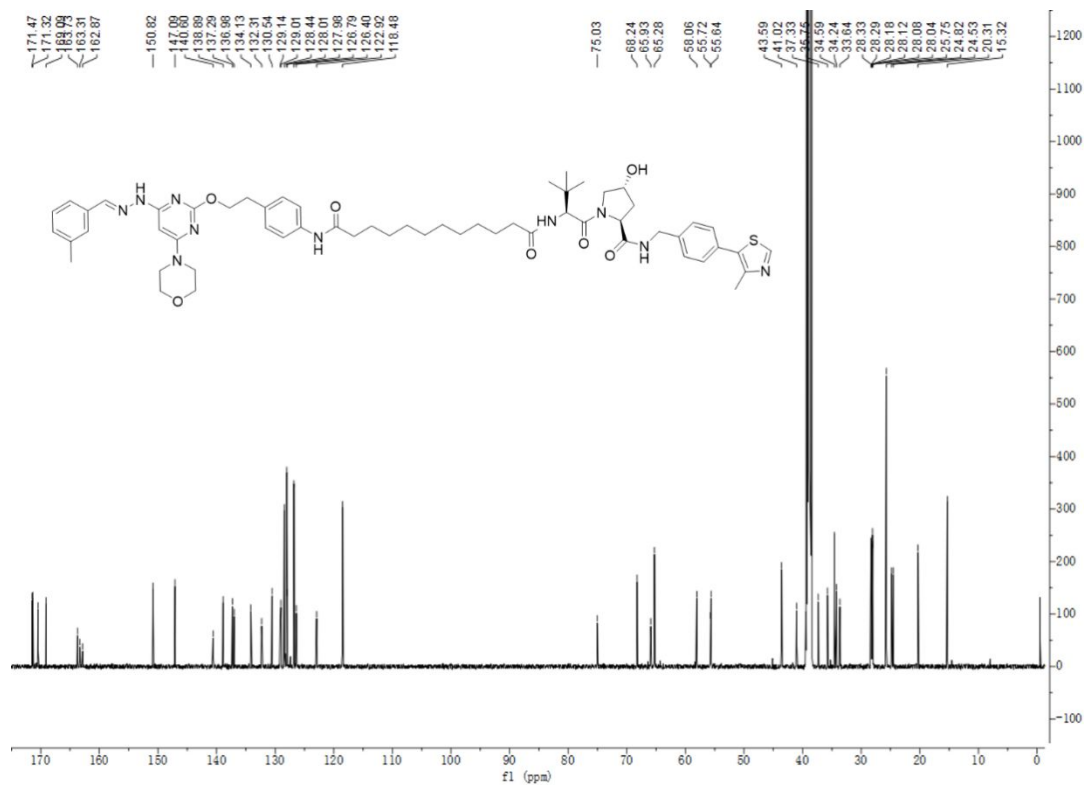
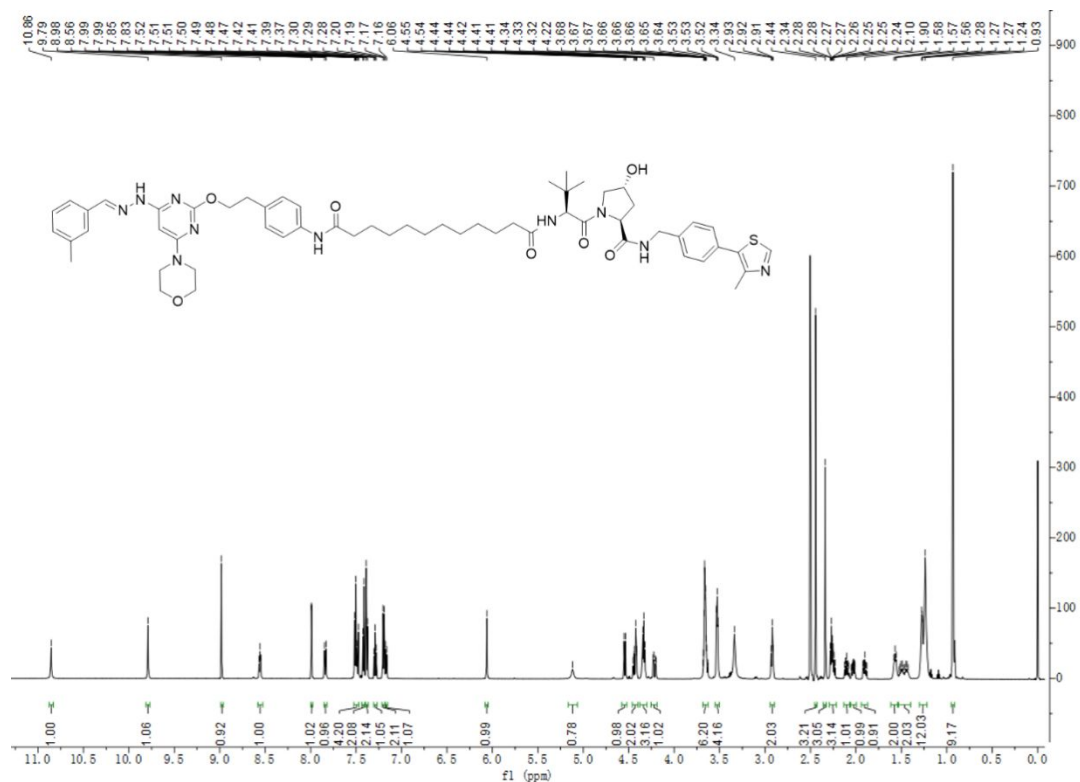


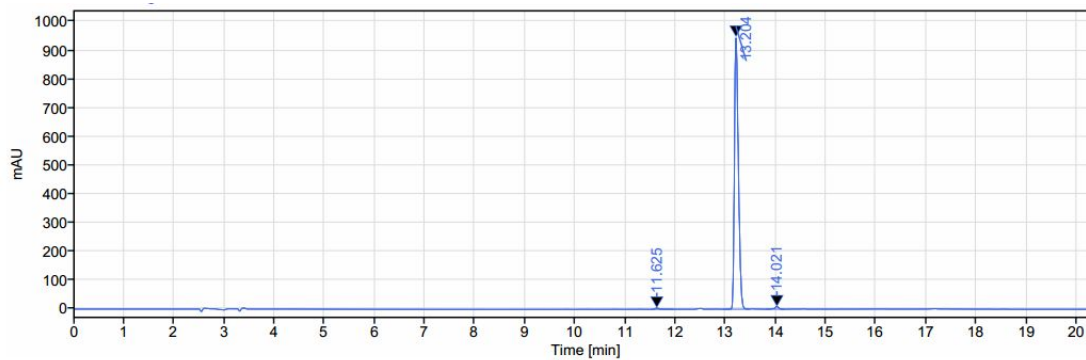


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
14.195	BV	0.37	209.99	27.74	3.19	
15.135	VB	0.55	6364.19	1187.27	96.81	
		Sum	6574.18		100.00	

Compound 12j

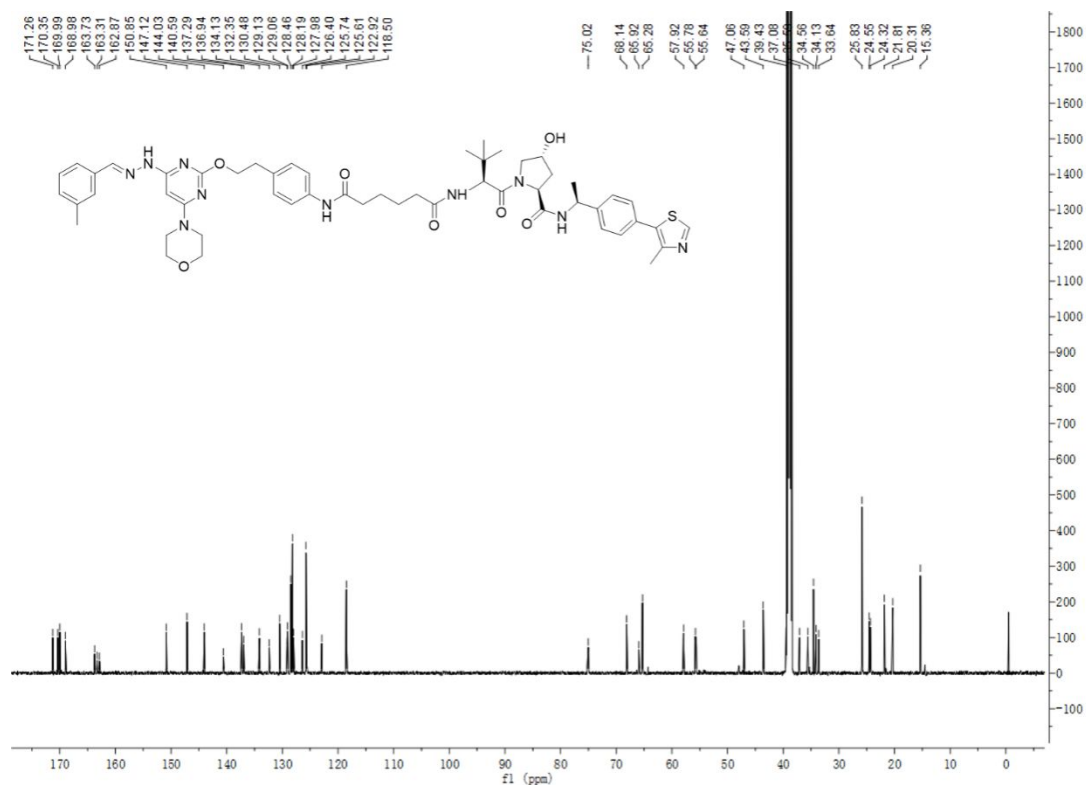
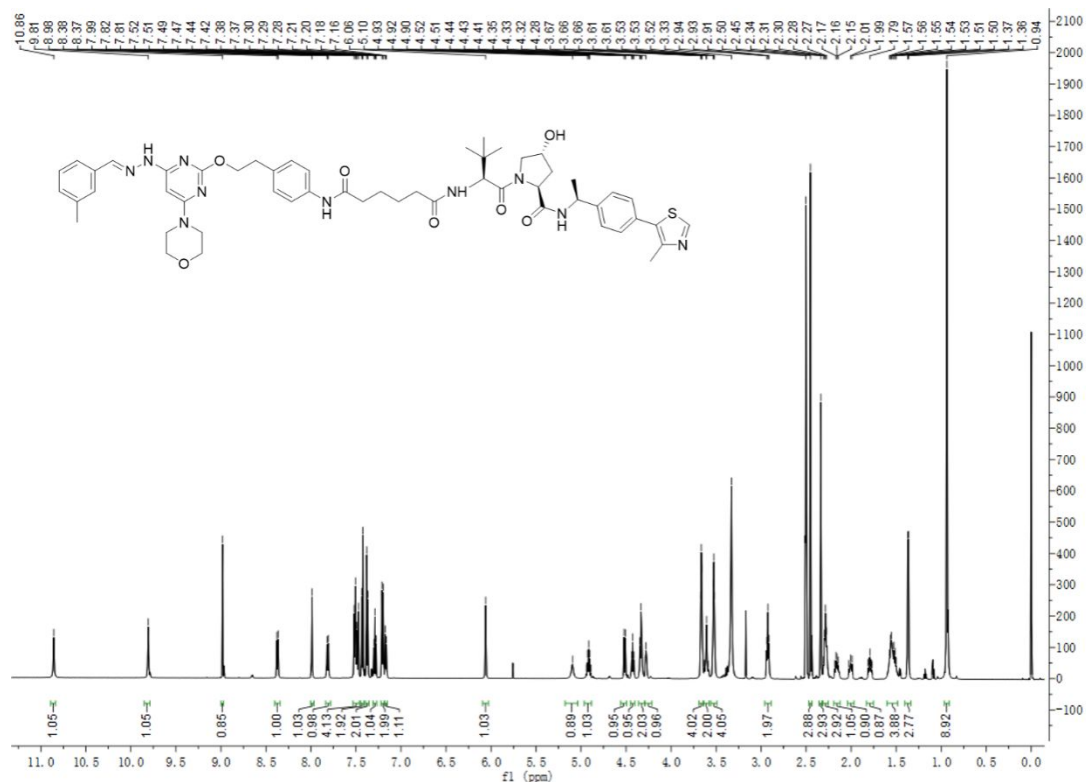


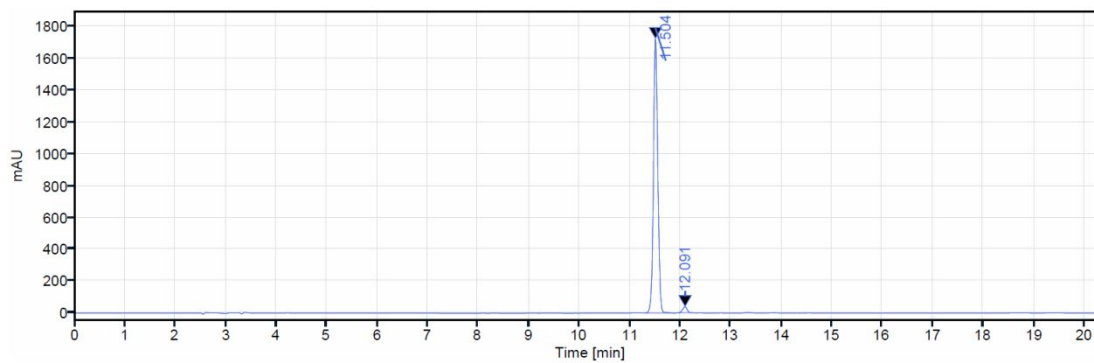


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.625	BB	0.46	26.19	4.53	0.50	
13.204	BV	0.53	5207.71	947.49	98.53	
14.021	BB	0.37	51.76	9.03	0.98	
Sum			5285.66		100.00	

Compound 13a

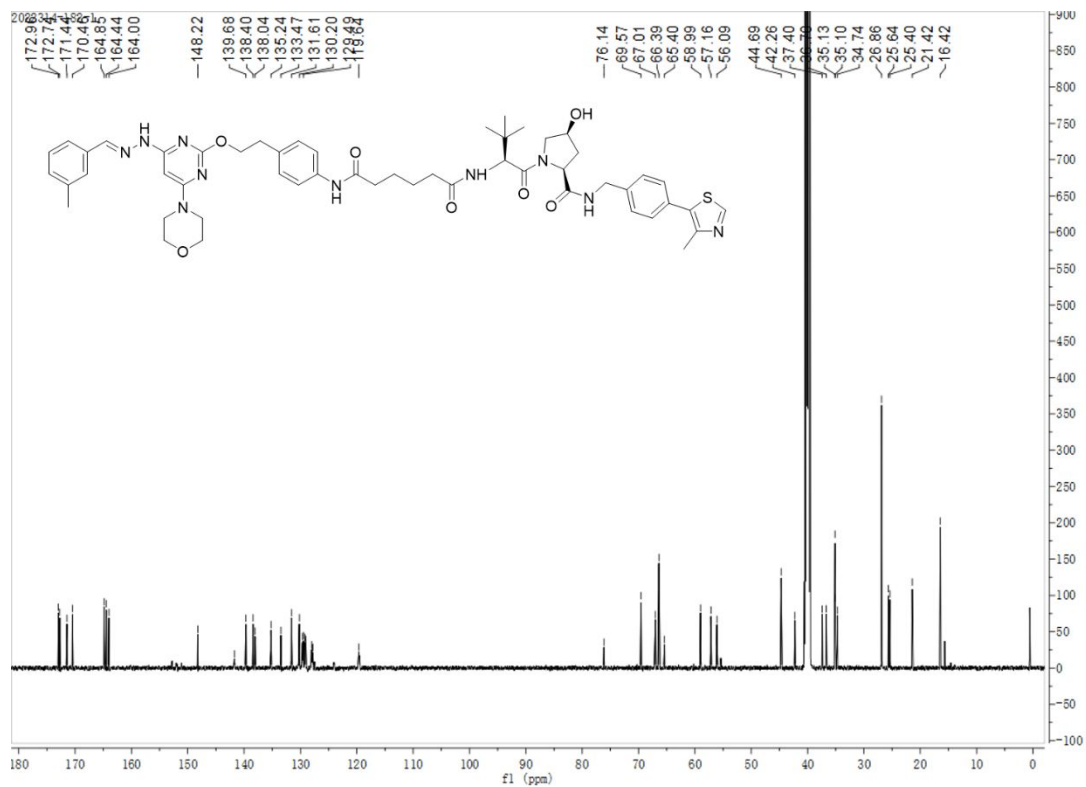
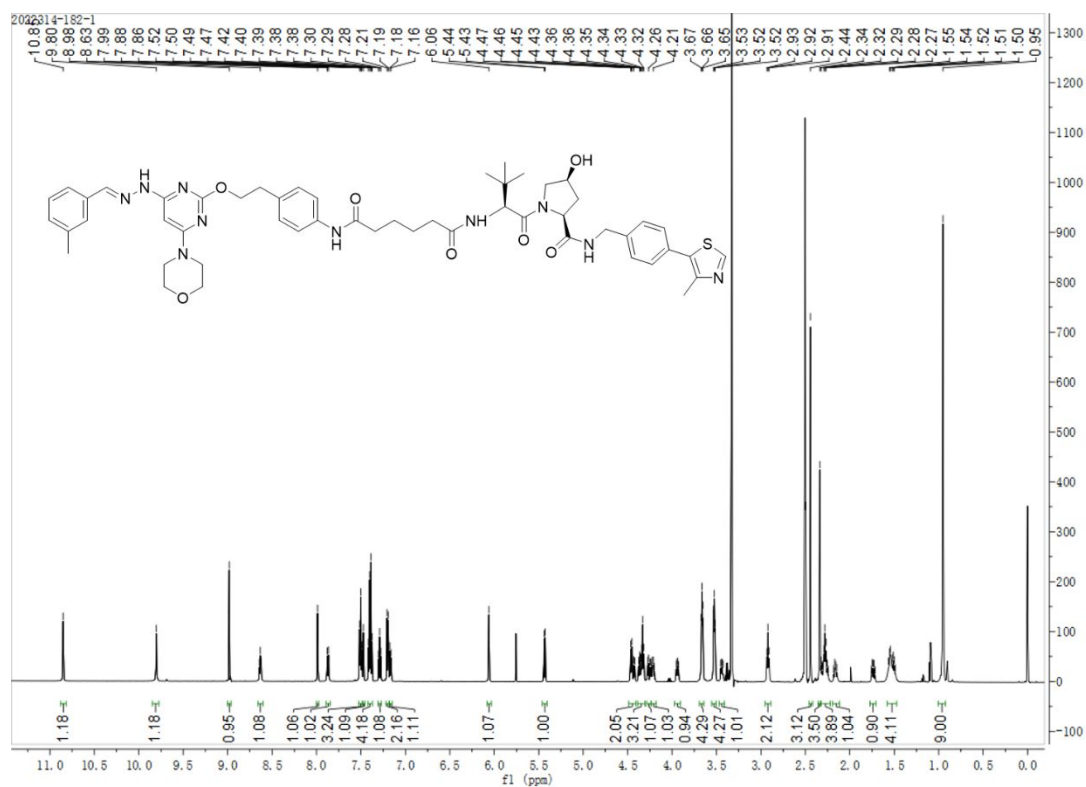


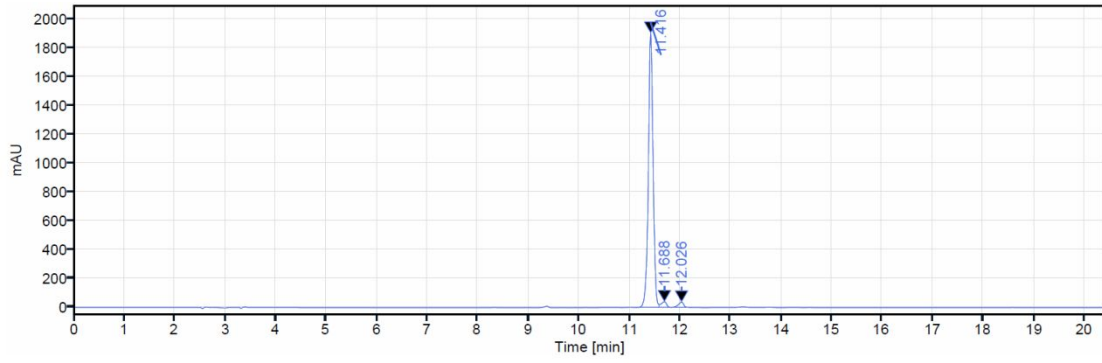


Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.504	VM m	0.59	10338.98	1726.43	97.91	
12.091	MM m	0.32	220.46	37.12	2.09	
Sum			10559.44		100.00	

Compound 12dN





Signal: DAD1A,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.416	MV m	0.45	12348.51	1898.63	95.44	
11.688	VV	0.23	304.65	40.06	2.35	
12.026	VB	0.42	285.92	37.39	2.21	
Sum			12939.08		100.00	