

Supplementary Materials

Synthesis and Biological Evaluation of Novel Allobetulon/Allobetulin–Nucleoside Conjugates as Antitumor Agents

Yanli Wang ^{1,2,†}, Xiaowan Huang ^{3,4,†}, Xiao Zhang ⁴, Jingchen Wang ⁴, Keyan Li ², Guotao Liu ², Kexin Lu ⁴, Xiang Zhang ³, Chengping Xie ³, Teresa Zheng ⁵, Yung-Yi Cheng ^{5,*} and Qiang Wang ^{1,2,3,4,*}

¹ School of Medicine, Huanghe Science and Technology College, Zhengzhou, China; hbyfe@163.com

² National Health Commission Key Laboratory of Birth Defect Prevention, Henan Institute of Reproductive Health Science and Technology, Zhengzhou, China; lky130277680782022@163.com (K.L.); liuguotao33@163.com (G.L.)

³ High & New Technology Research Center, Henan Academy of Science, Zhengzhou, China; 18336708203@163.com (X.H.); zxzsy0405@163.com (X.Z.); xiechp@ceprei.com (C.X.)

⁴ BGI College & Henan Institute of Medical and Pharmaceutical Science, Zhengzhou University, Zhengzhou, China; zhangxiao7011@163.com (X.Z.); chen13021083099@163.com (J.W.); kexin14590@163.com (K.L.)

⁵ Division of Pharmacoengineering and Molecular Pharmaceutics, Eshelman School of Pharmacy, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; tzheng1999@gmail.com

* Correspondence: yungyi@email.unc.edu (Y.-Y.C.); qiangwang@hhstu.edu.cn (Q.W.); Tel: +1-9843694796 (Y.-Y.C.); +86-371-65511776 (Q.W.)

† These authors contributed equally to this work.

Figure S1	¹ H NMR spectrum of compound 5.....	4
FigureS2	¹³ C NMR spectrum of compound 5.....	4
Figure S3	HRMS spectrum of compound 5.....	5
Figure S4	¹ H NMR spectrum of compound 6.....	5
Figure S5	¹³ C NMR spectrum of compound 6.....	6
Figure S6	HRMS spectrum of compound 6.....	6
Figure S7	¹ H NMR spectrum of compound 7.....	7
Figure S8	¹³ C NMR spectrum of compound 7.....	7
Figure S9	HRMS spectrum of compound 7.....	8
Figure S10	¹ H NMR spectrum of compound 8.....	8
Figure S11	Expanded NOESY spectrum (0.6-2.0 ppm) of compound 8.....	9
Figure S12	Expanded COSY spectrum (0.6-2.0 ppm) of compound 8.....	9
Figure S13	¹³ C NMR spectrum of compound 8.....	10
Figure S14	HRMS spectrum of compound 8.....	10
Figure S15	¹ H NMR spectrum of compound 9a.....	11
Figure S16	¹³ C NMR spectrum of compound 9a.....	11

Figure S17	HRMS spectrum of compound 9a.....	12
Figure S18	^1H NMR spectrum of compound 9b.....	12
Figure S19	^{13}C NMR spectrum of compound 9b.....	13
Figure S20	HRMS spectrum of compound 9b.....	13
Figure S21	^1H NMR spectrum of compound 9c.....	14
Figure S22	^{13}C NMR spectrum of compound 9c.....	14
Figure S23	HRMS spectrum of compound 9c.....	15
Figure S24	^1H NMR spectrum of compound 9d.....	15
Figure S25	^{13}C NMR spectrum of compound 9d.....	16
Figure S26	HRMS spectrum of compound 9d.....	16
Figure S27	^1H NMR spectrum of compound 9e.....	17
Figure S28	^{13}C NMR spectrum of compound 9e.....	17
Figure S29	HRMS spectrum of compound 9e.....	18
Figure S30	^1H NMR spectrum of compound 9f.....	18
Figure S31	^{13}C NMR spectrum of compound 9f.....	19
Figure S32	HRMS spectrum of compound 9f.....	19
Figure S33	^1H NMR spectrum of compound 9g.....	20
Figure S34	^{13}C NMR spectrum of compound 9g.....	20
Figure S35	HRMS spectrum of compound 9g.....	21
Figure S36	^1H NMR spectrum of compound 9h.....	21
Figure S37	^{13}C NMR spectrum of compound 9h.....	22
Figure S38	HRMS spectrum of compound 9h.....	22
Figure S39	^1H NMR spectrum of compound 9i.....	23
Figure S40	^{13}C NMR spectrum of compound 9i.....	23
Figure S41	HRMS spectrum of compound 9i.....	24
Figure S42	^1H NMR spectrum of compound 10a.....	24
Figure S43	^{13}C NMR spectrum of compound 10a.....	25
Figure S44	HRMS spectrum of compound 10a.....	25
Figure S45	^1H NMR spectrum of compound 10b.....	26
Figure S46	^{13}C NMR spectrum of compound 10b.....	26
Figure S47	HRMS spectrum of compound 10b.....	27
Figure S48	^1H NMR spectrum of compound 10c.....	27
Figure S49	^{13}C NMR spectrum of compound 10c.....	28
Figure S50	HRMS spectrum of compound 10c.....	28

Figure S51	^1H NMR spectrum of compound 10d.....	29
Figure S52	^{13}C NMR spectrum of compound 10d.....	29
Figure S53	HRMS spectrum of compound 10d.....	30
Figure S54	^1H NMR spectrum of compound 10e.....	30
Figure S55	^{13}C NMR spectrum of compound 10e.....	31
Figure S56	HRMS spectrum of compound 10e.....	31
Figure S57	^1H NMR spectrum of compound 10f.....	32
Figure S58	^{13}C NMR spectrum of compound 10f.....	32
Figure S59	HRMS spectrum of compound 10f.....	33
Figure S60	^1H NMR spectrum of compound 10g.....	33
Figure S61	^{13}C NMR spectrum of compound 10g.....	34
Figure S62	HRMS spectrum of compound 10g.....	34
Figure S63	^1H NMR spectrum of compound 10h.....	35
Figure S64	^{13}C NMR spectrum of compound 10h.....	35
Figure S65	HRMS spectrum of compound 10h.....	36
Figure S66	^1H NMR spectrum of compound 10i.....	36
Figure S67	^{13}C NMR spectrum of compound 10i.....	37
Figure S68	HRMS spectrum of compound 10i.....	37

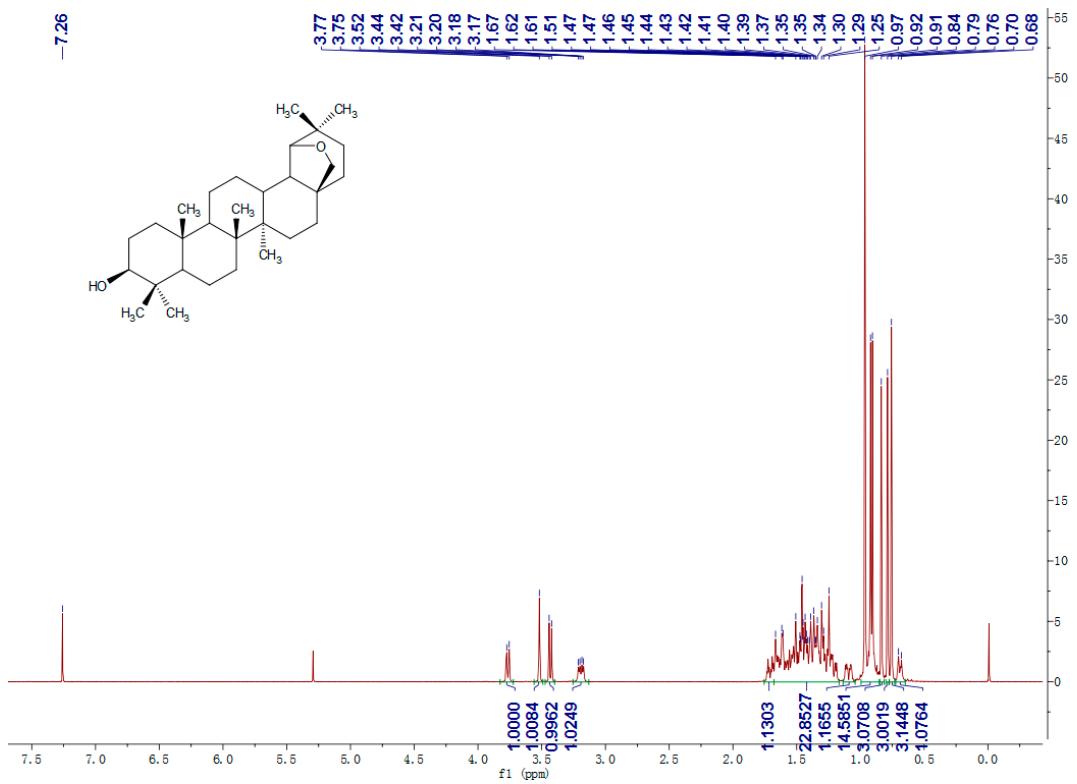


Figure S1 ^1H NMR spectrum of compound 5

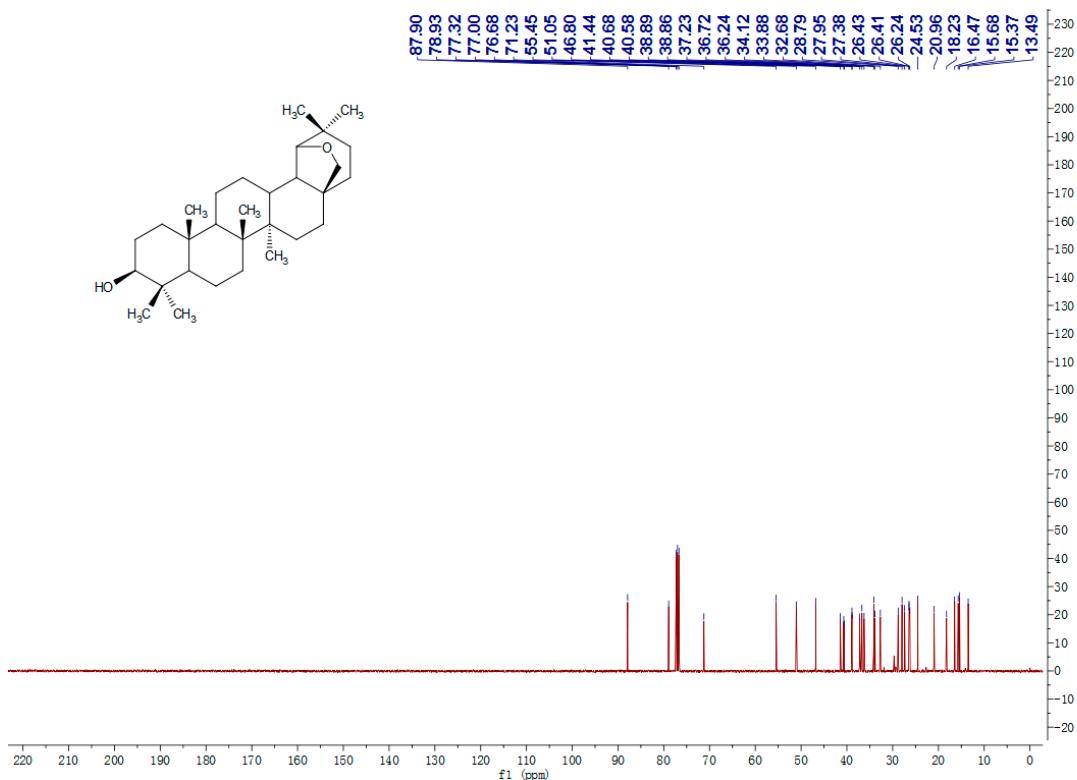


Figure S2 ^{13}C NMR spectrum of compound 5

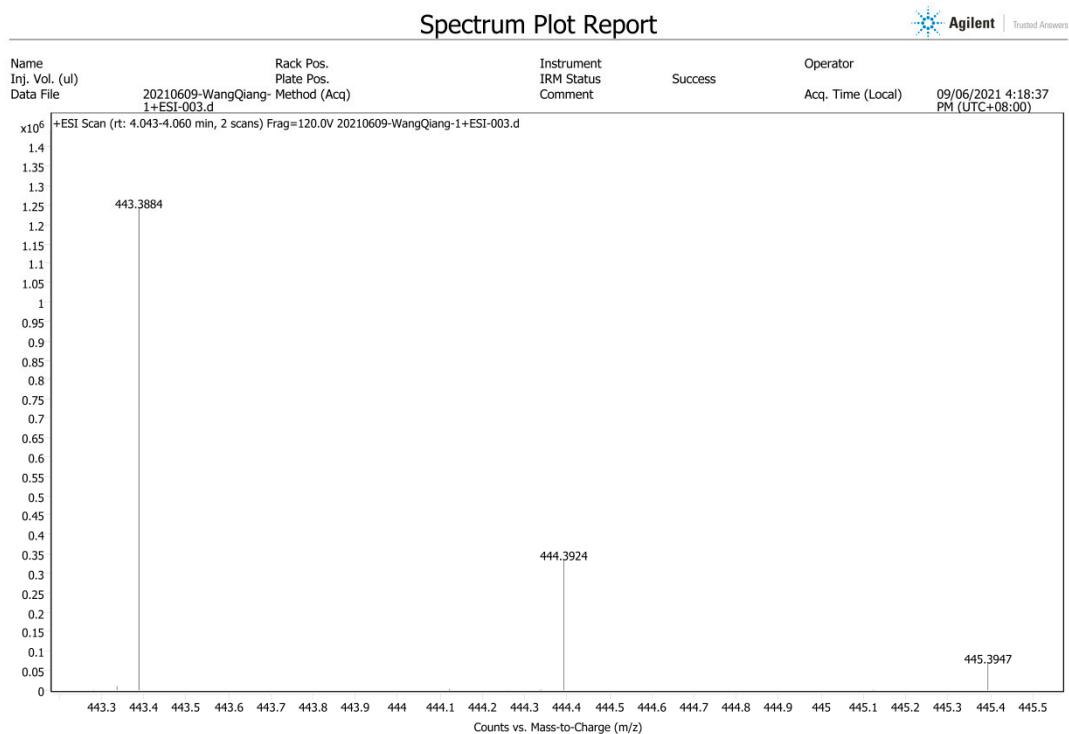


Figure S3 HRMS spectrum of compound 5

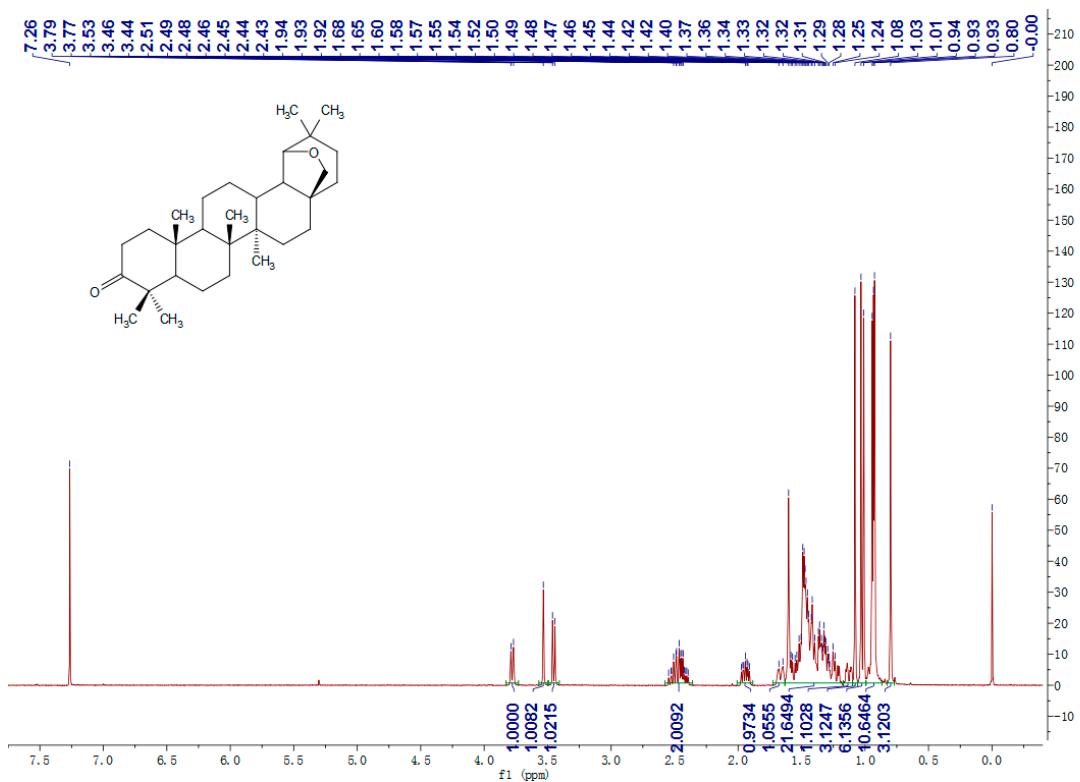


Figure S4 ^1H NMR spectrum of compound 6

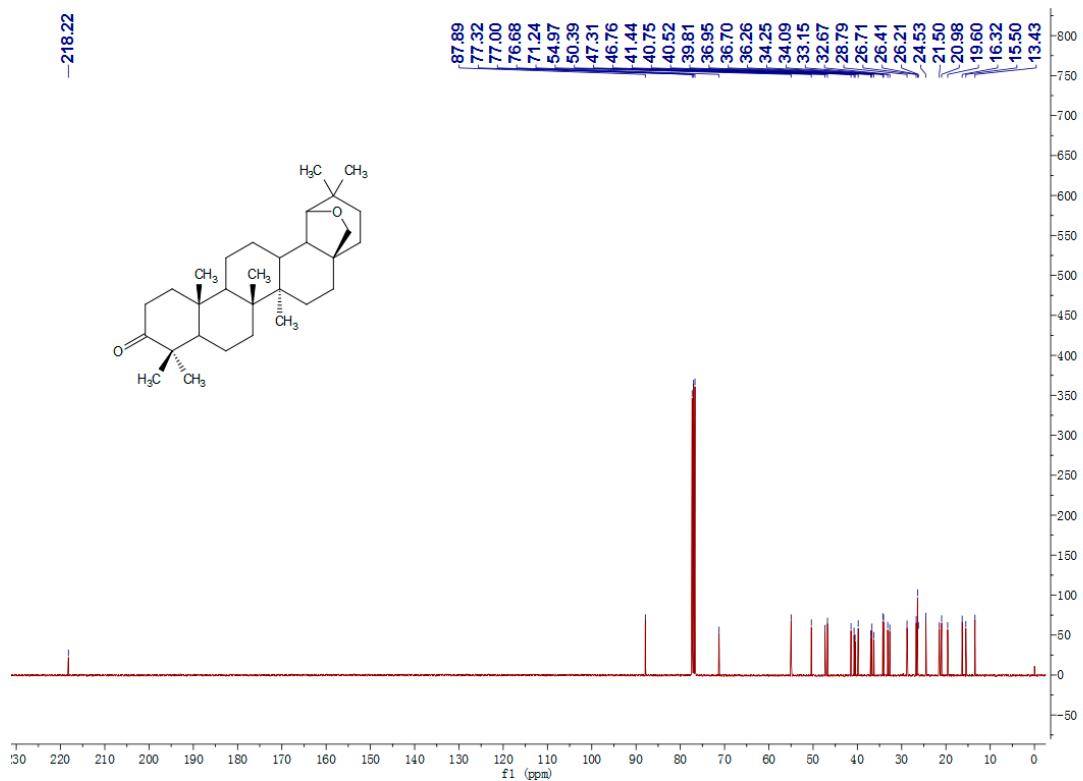
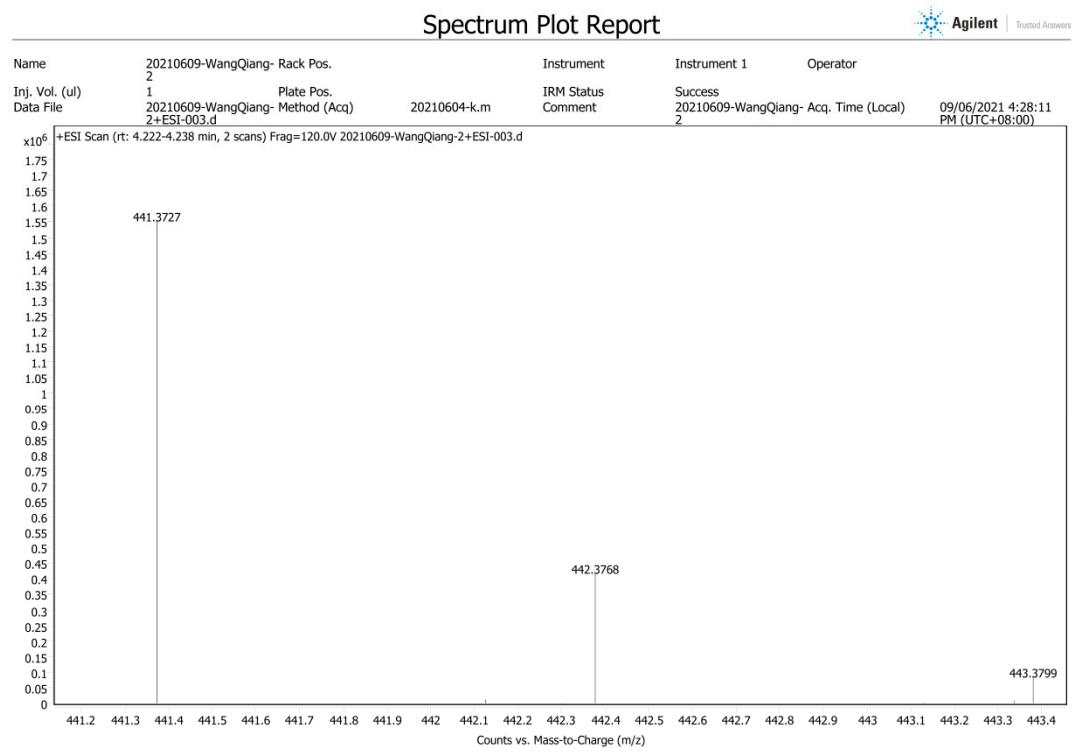


Figure S5 ^{13}C NMR spectrum of compound 6



Page 1 of 1

Generated at 4:45 PM on 09/06/2021

Figure S6 HRMS spectrum of compound 6

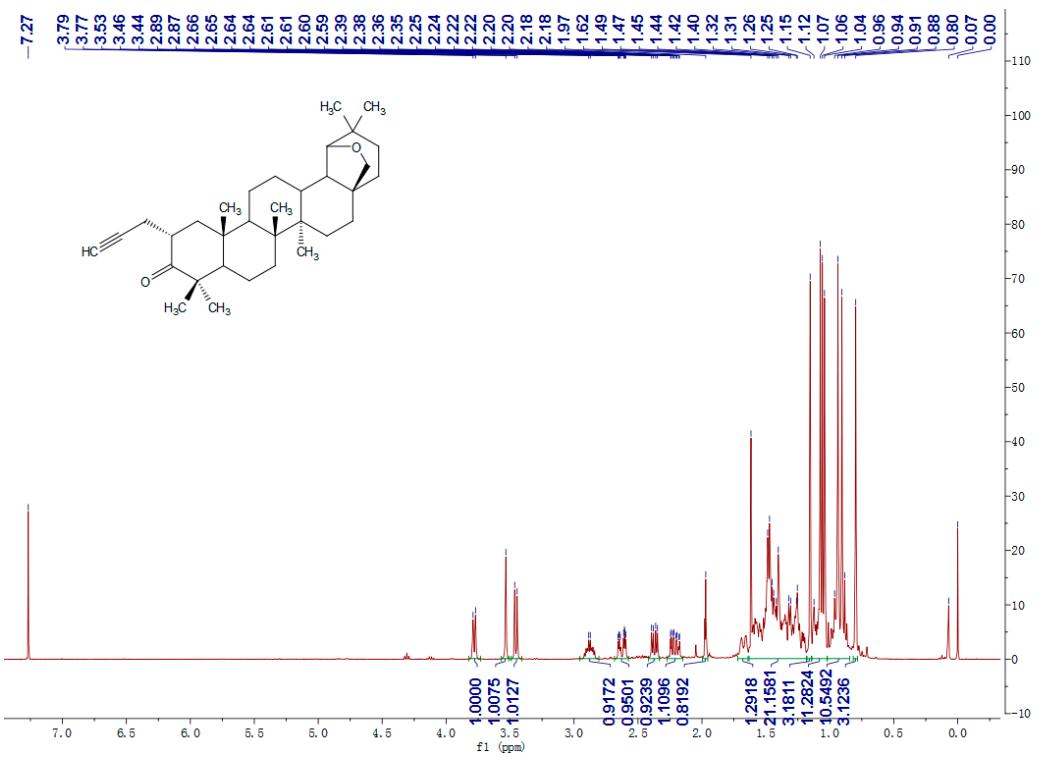


Figure S7 ¹H NMR spectrum of compound 7

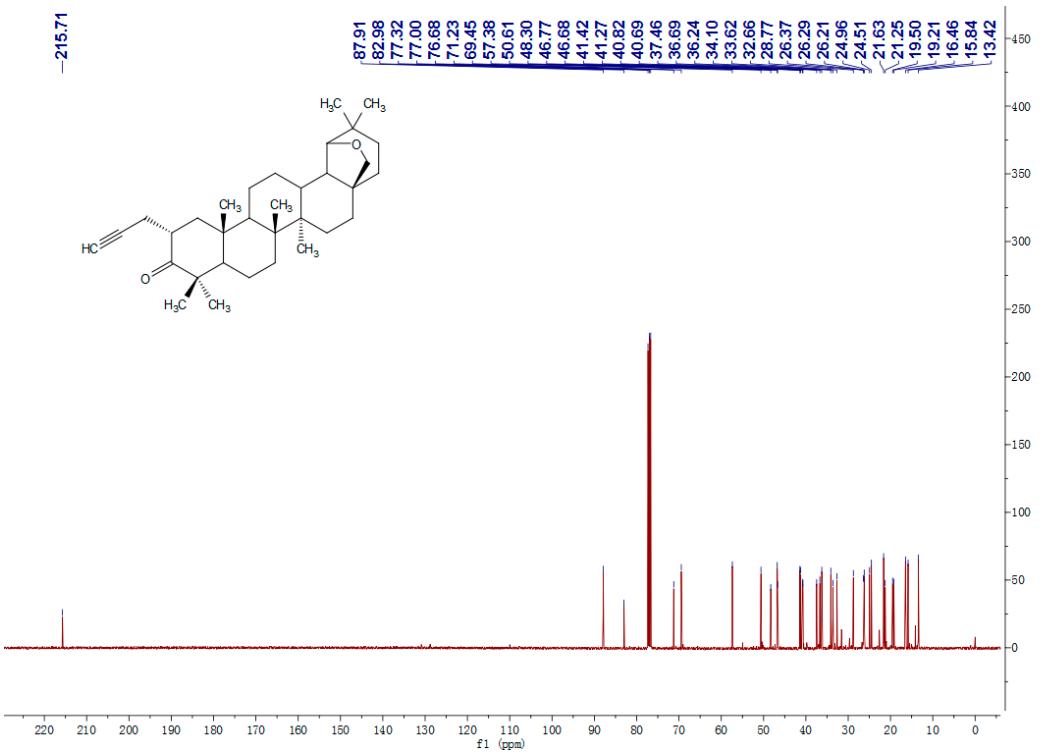


Figure S8 ¹³C NMR spectrum of compound 7

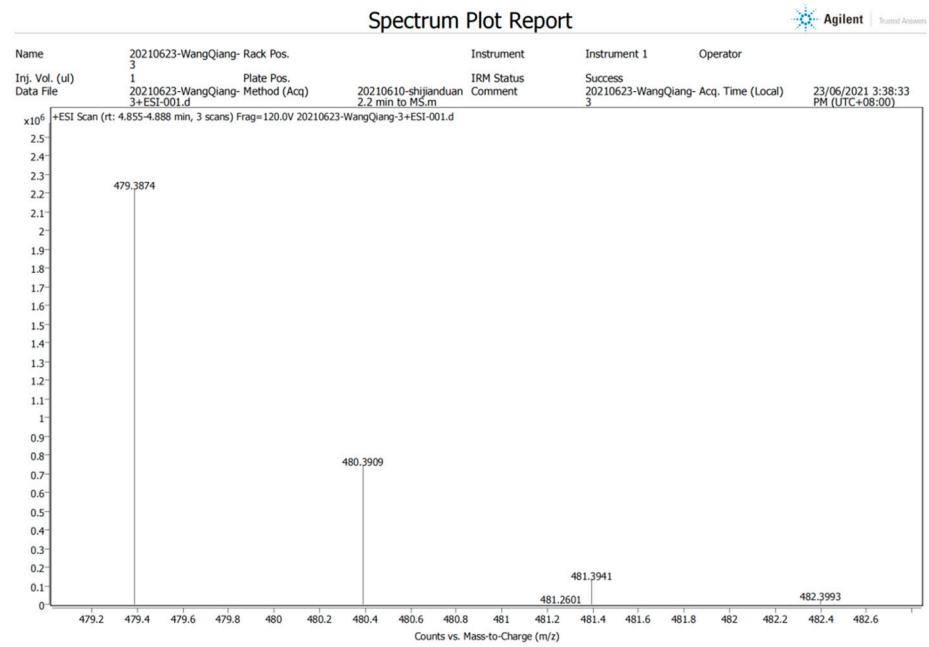


Figure S9 HRMS spectrum of compound 7

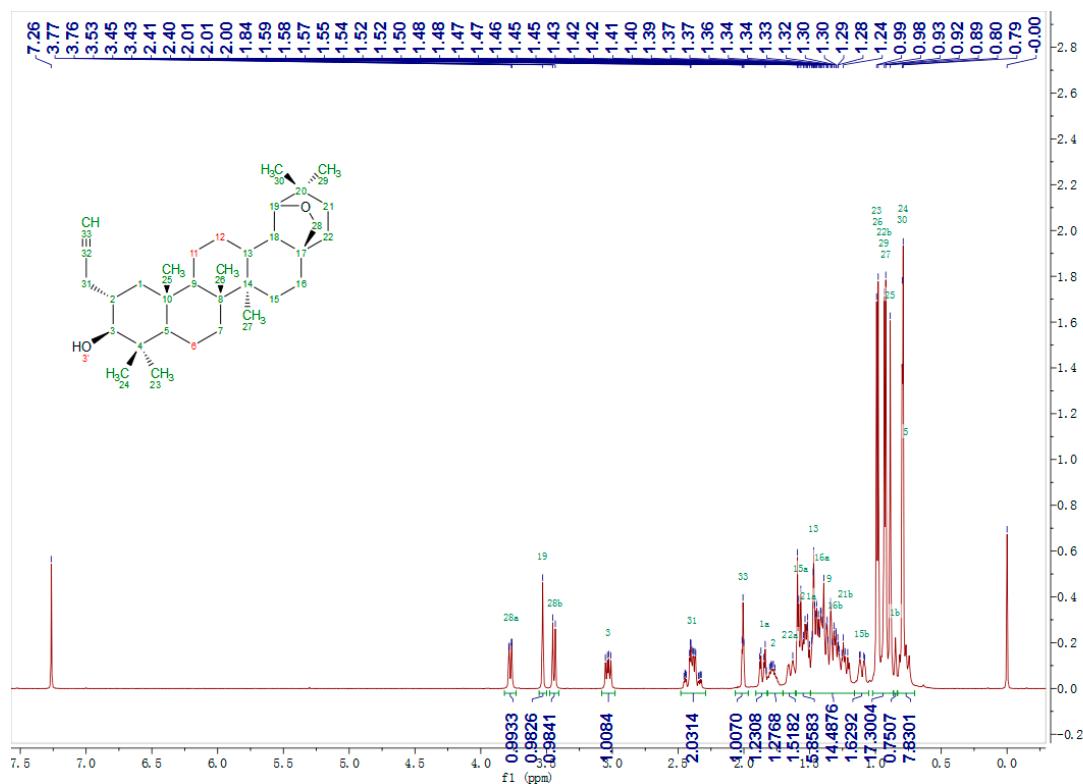


Figure S10 ^1H NMR spectrum of compound **8**

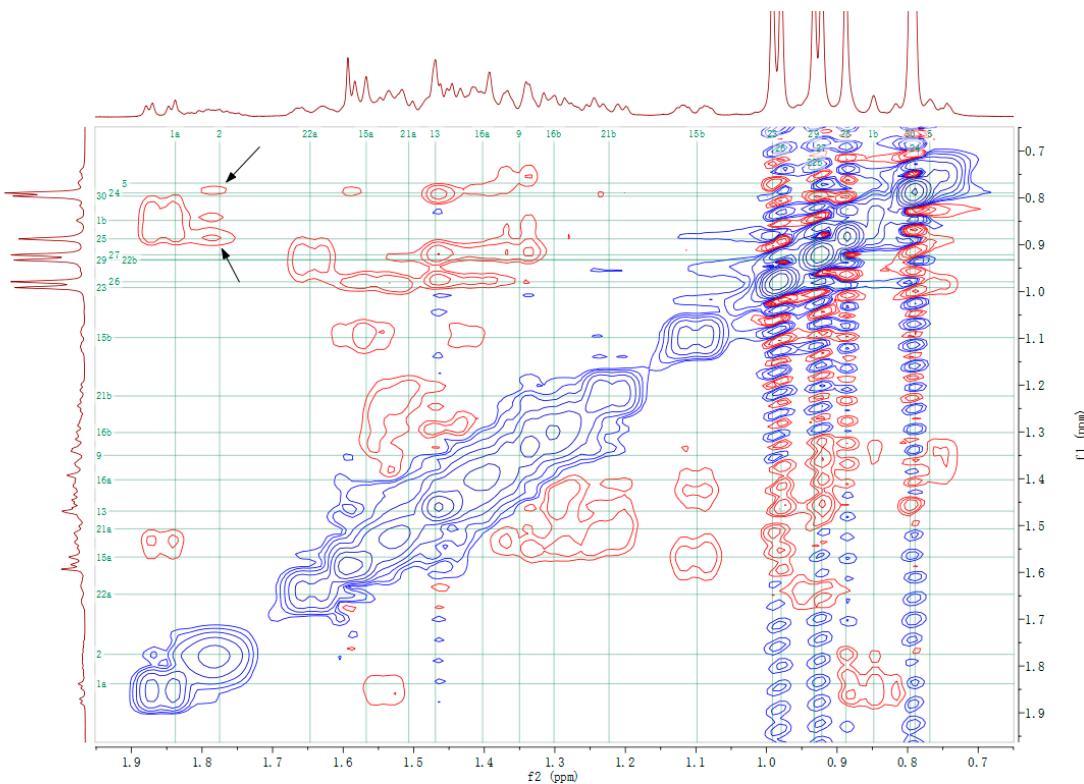


Figure S11 Expanded NOESY spectrum (0.6-2.0 ppm) of compound 8

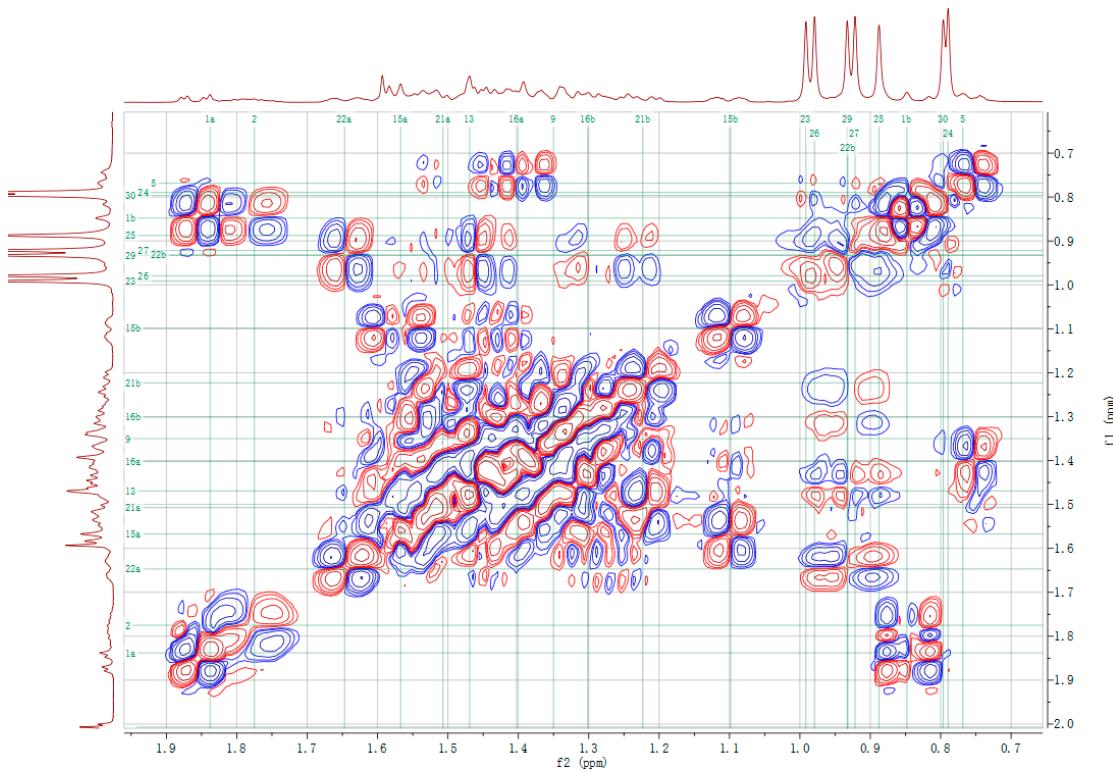


Figure S12 Expanded COSY spectrum (0.6-2.0 ppm) of compound 8

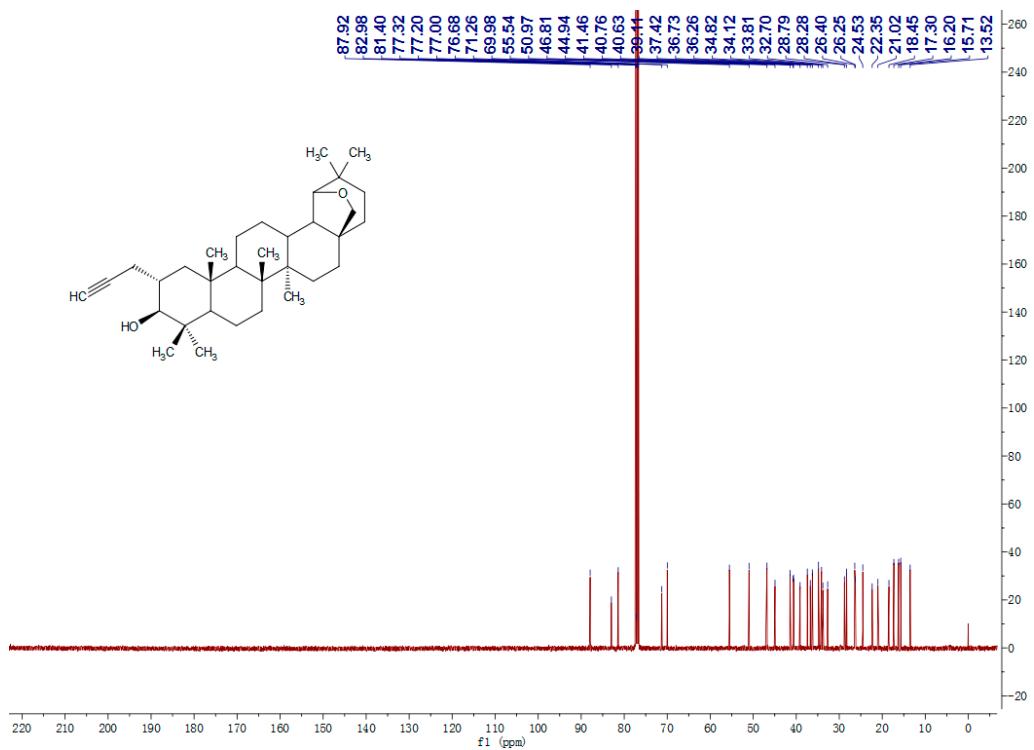


Figure S13 ^{13}C NMR spectrum of compound 8

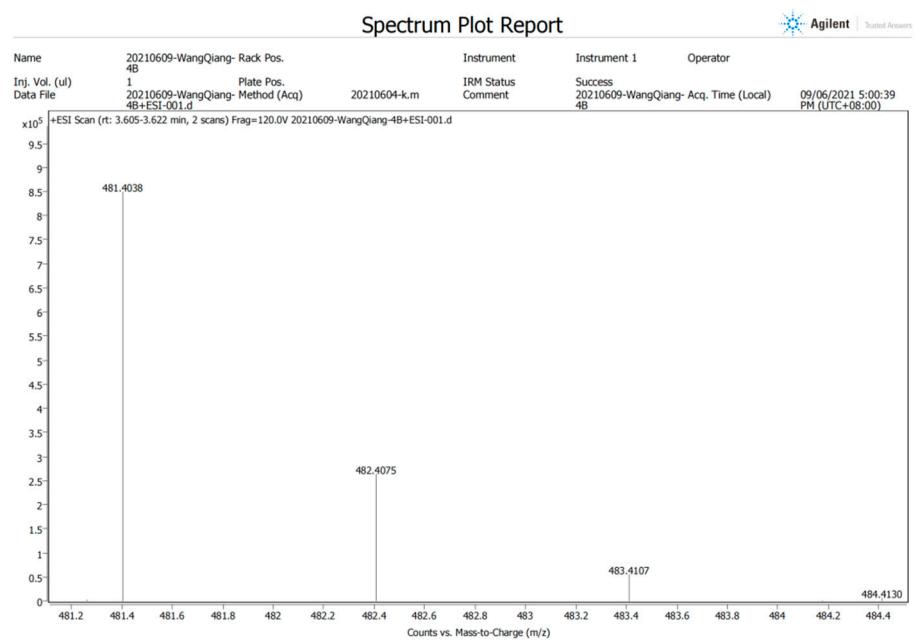


Figure S14 HRMS spectrum of compound 8

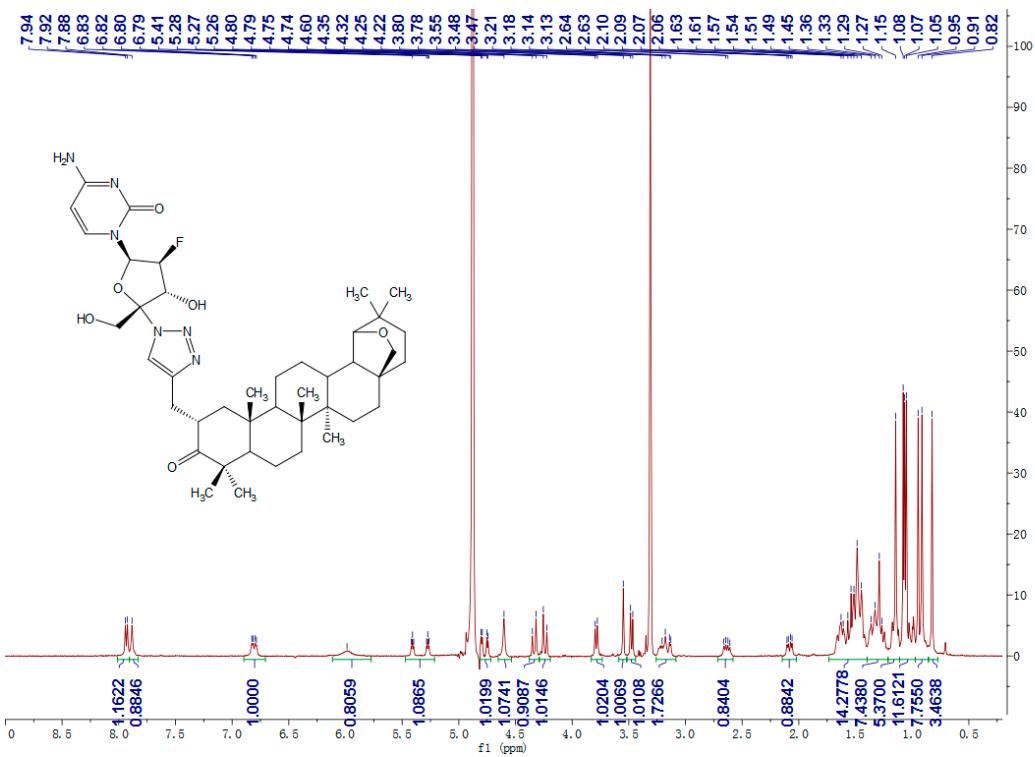


Figure S15 ¹H NMR spectrum of compound 9a

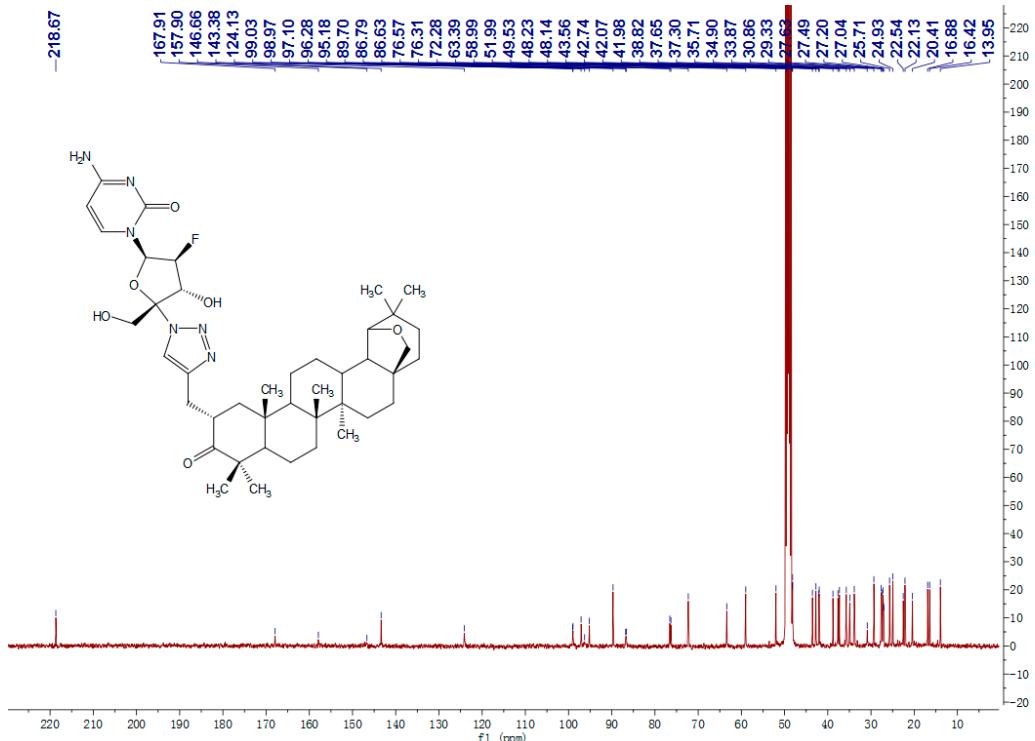
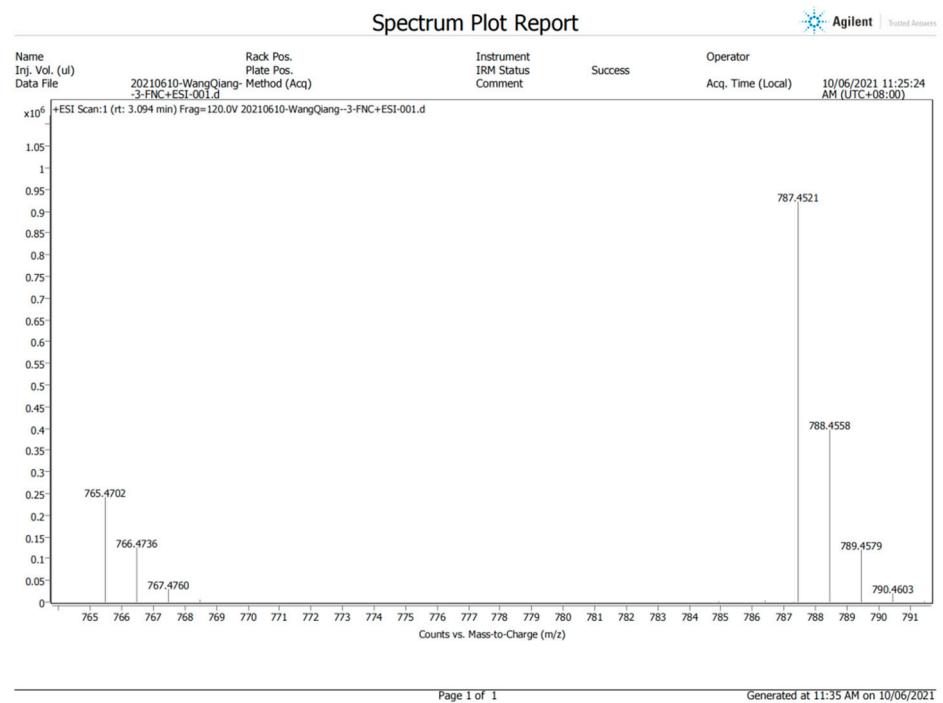


Figure S16 ¹³C NMR spectrum of compound 9a



Page 1 of 1

Generated at 11:35 AM on 10/06/2021

Figure S17 HRMS spectrum of compound **9a**

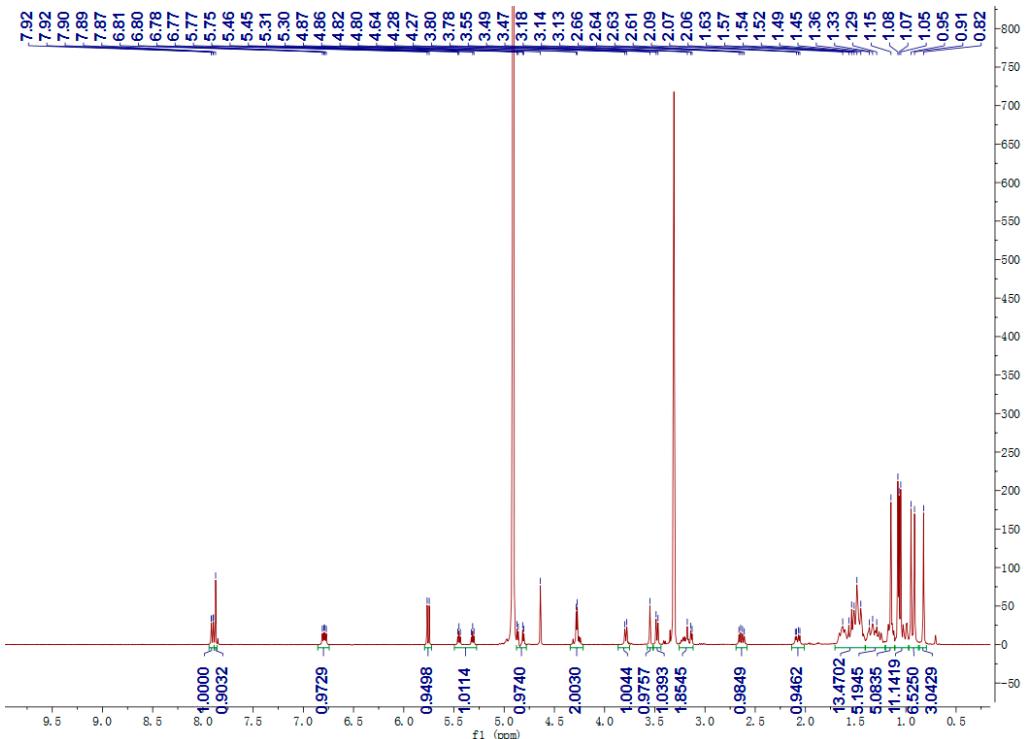


Figure S18 ^1H NMR spectrum of compound **9b**

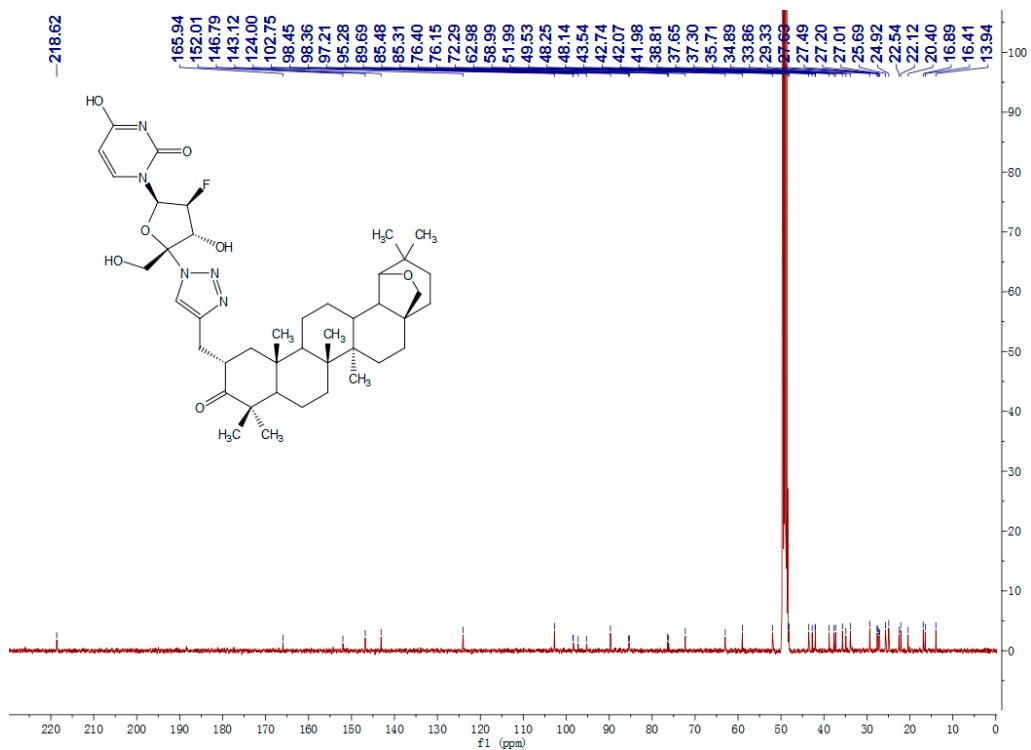


Figure S19 ^{13}C NMR spectrum of compound **9b**

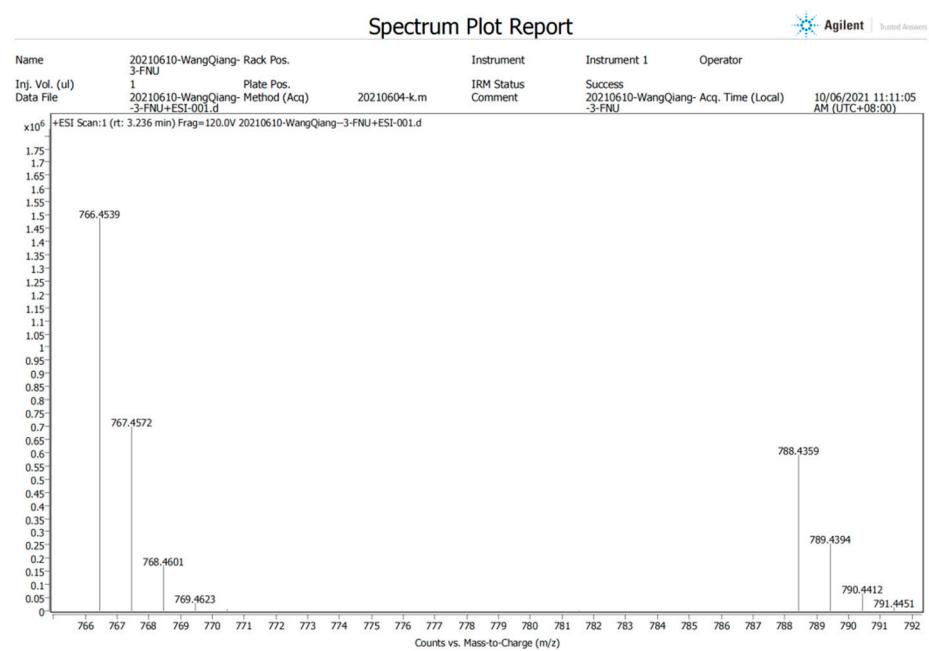


Figure S20 HRMS spectrum of compound **9b**

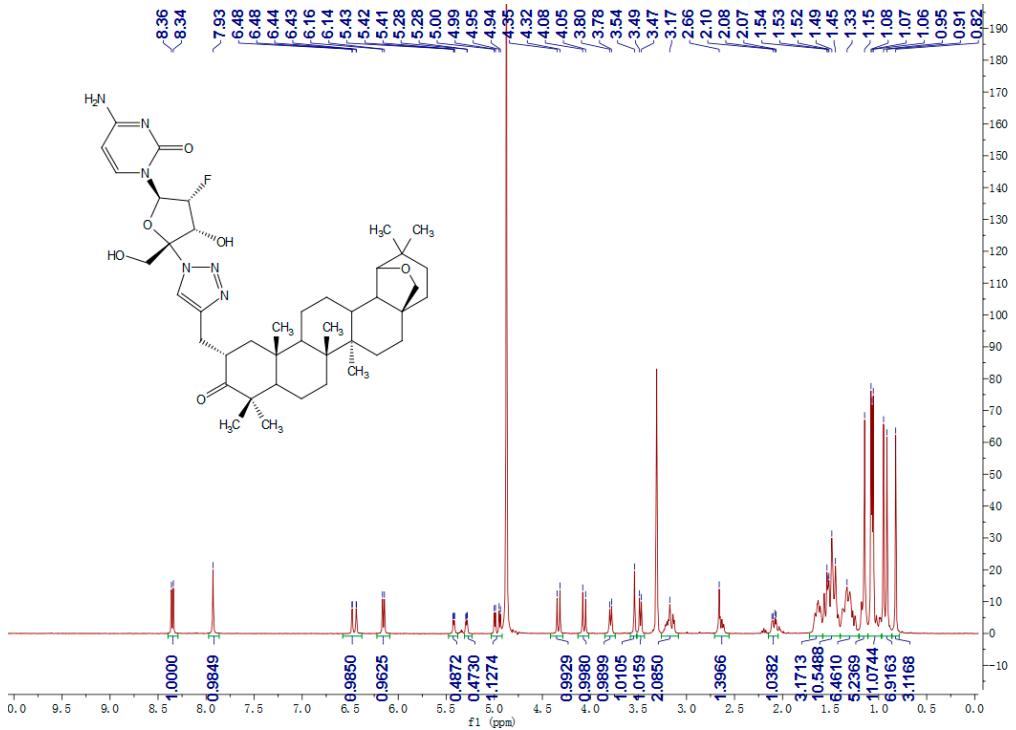


Figure S21 ¹H NMR spectrum of compound 9c

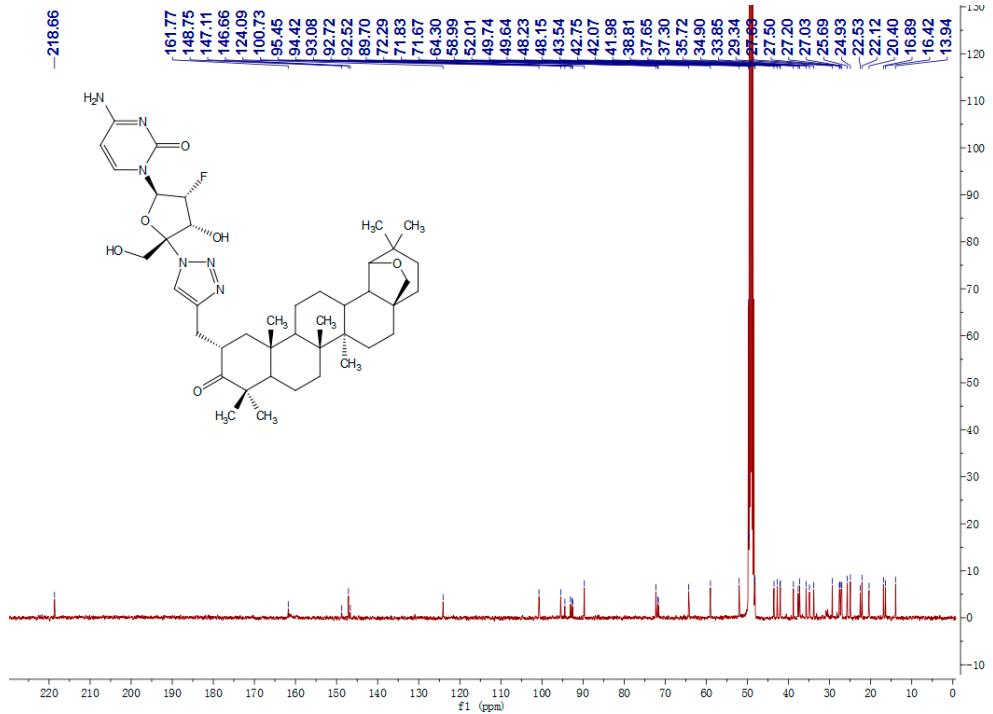
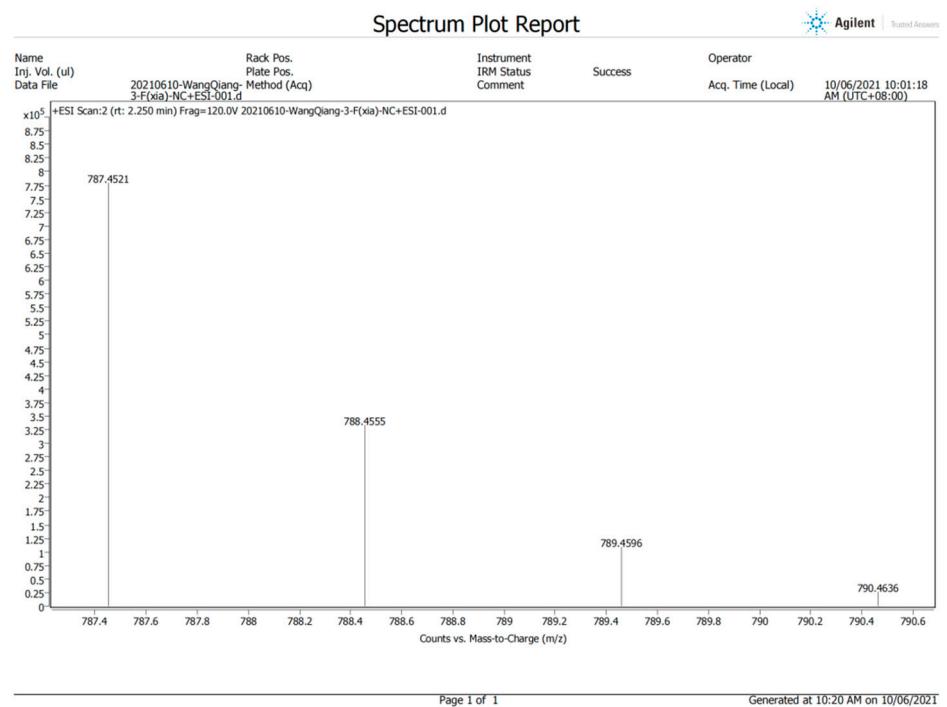


Figure S22 ¹³C NMR spectrum of compound 9c



Page 1 of 1

Generated at 10:20 AM on 10/06/2021

Figure S23 HRMS spectrum of compound **9c**

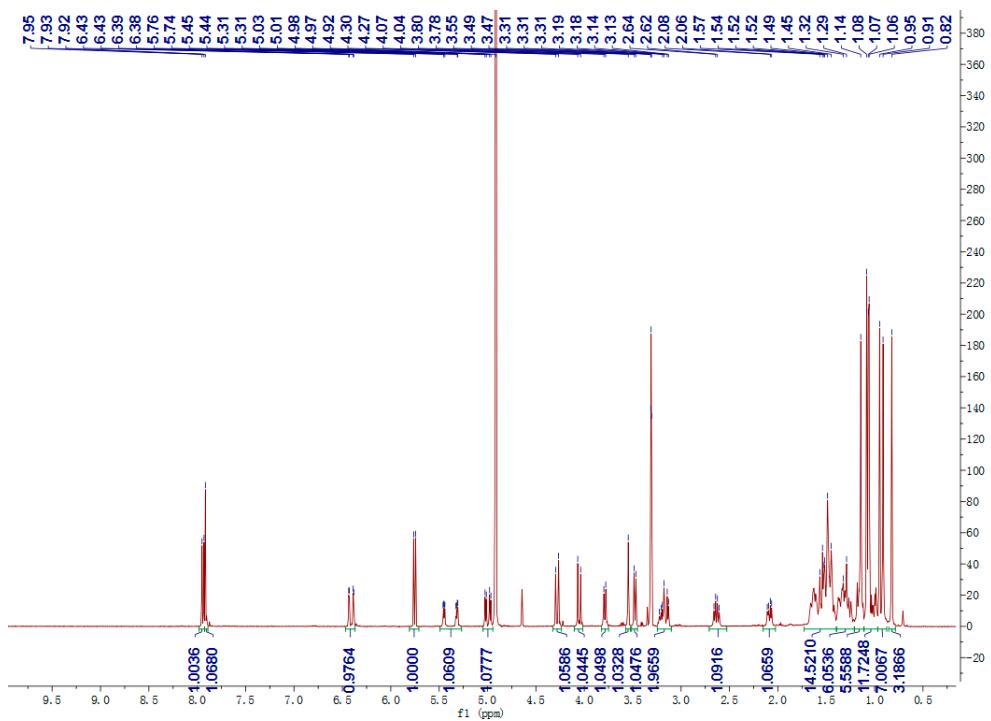


Figure S24 ^1H NMR spectrum of compound **9d**

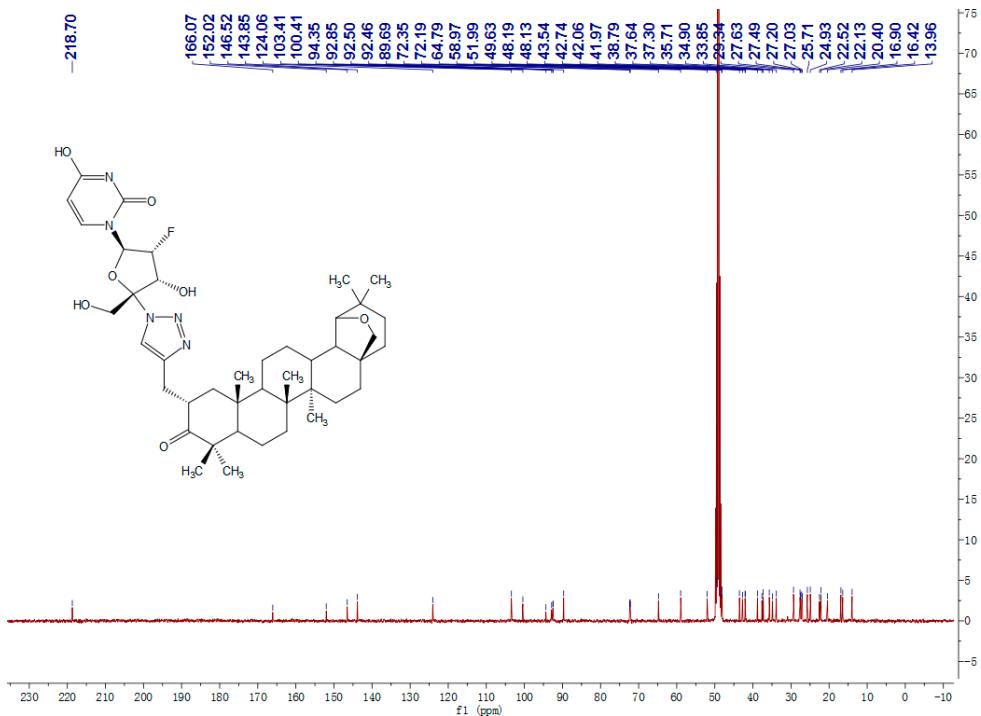


Figure S25 ¹³C NMR spectrum of compound 9d

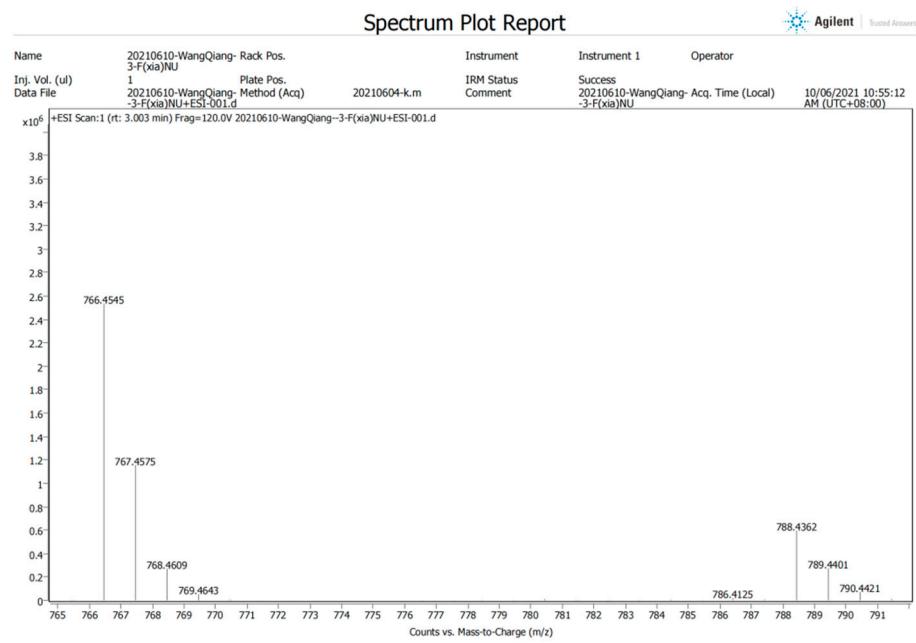


Figure S26 HRMS spectrum of compound 9d

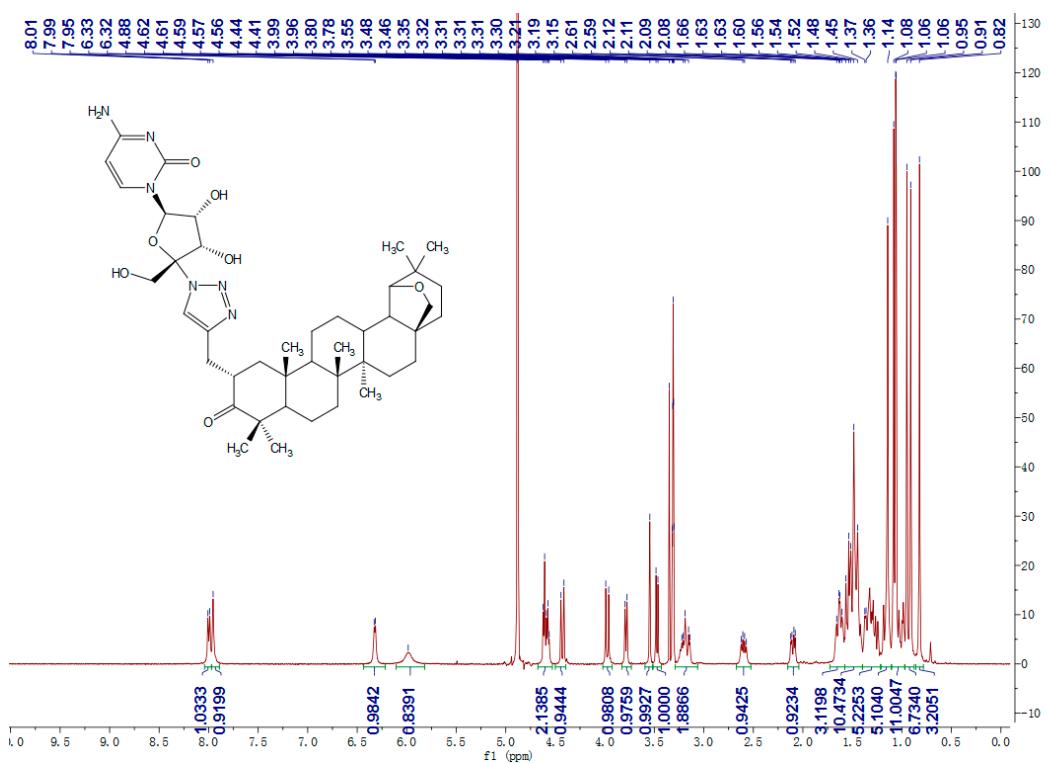


Figure S27 ¹H NMR spectrum of compound 9e

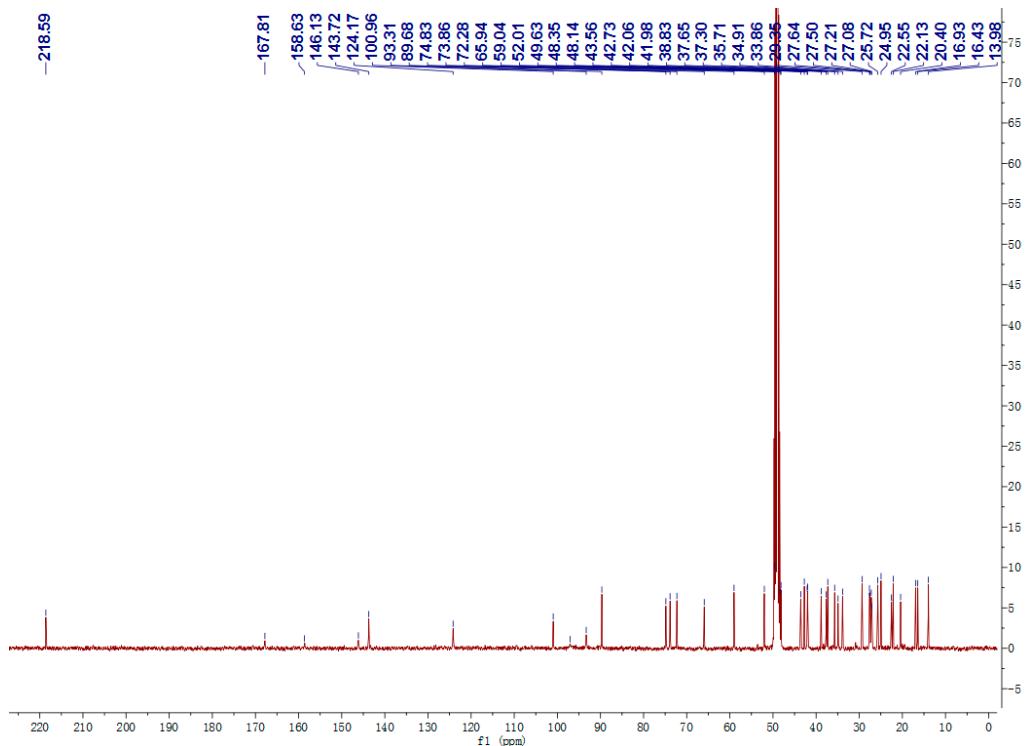
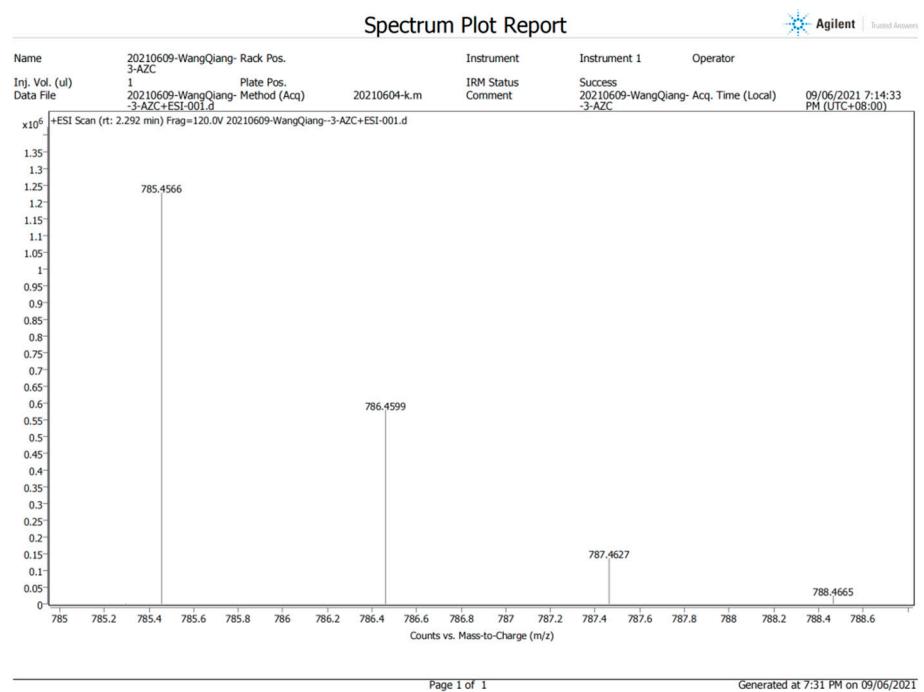


Figure S28 ¹³C NMR spectrum of compound 9e



Page 1 of 1

Generated at 7:31 PM on 09/06/2021

Figure S29 HRMS spectrum of compound **9e**

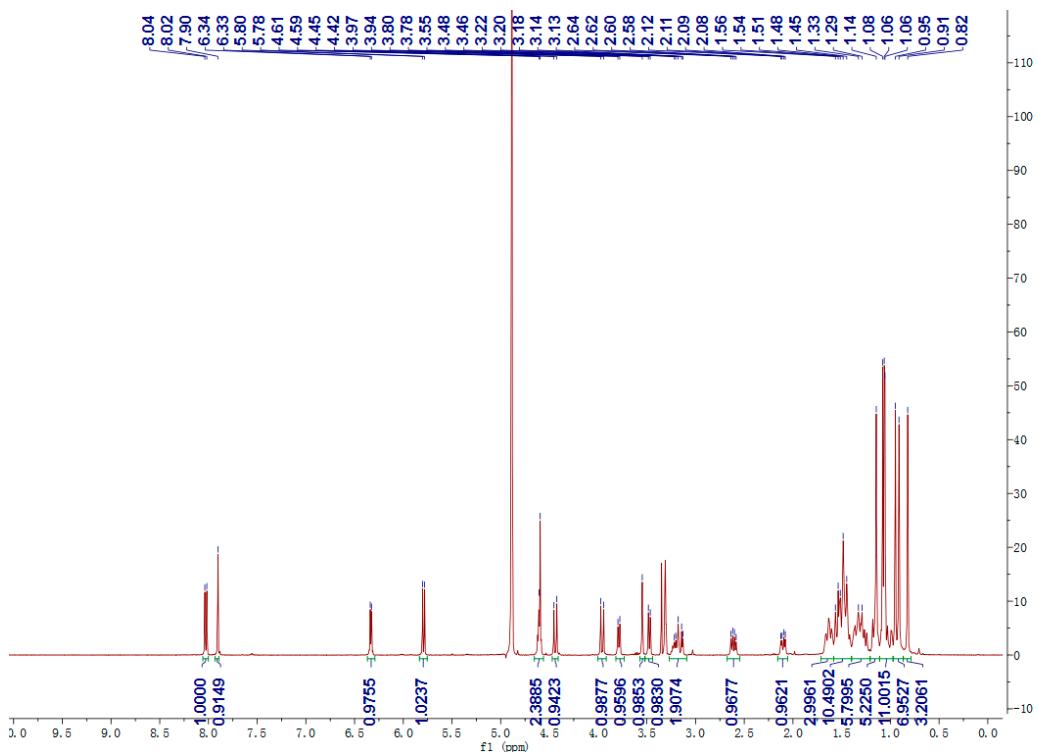


Figure S30 ^1H NMR spectrum of compound **9f**

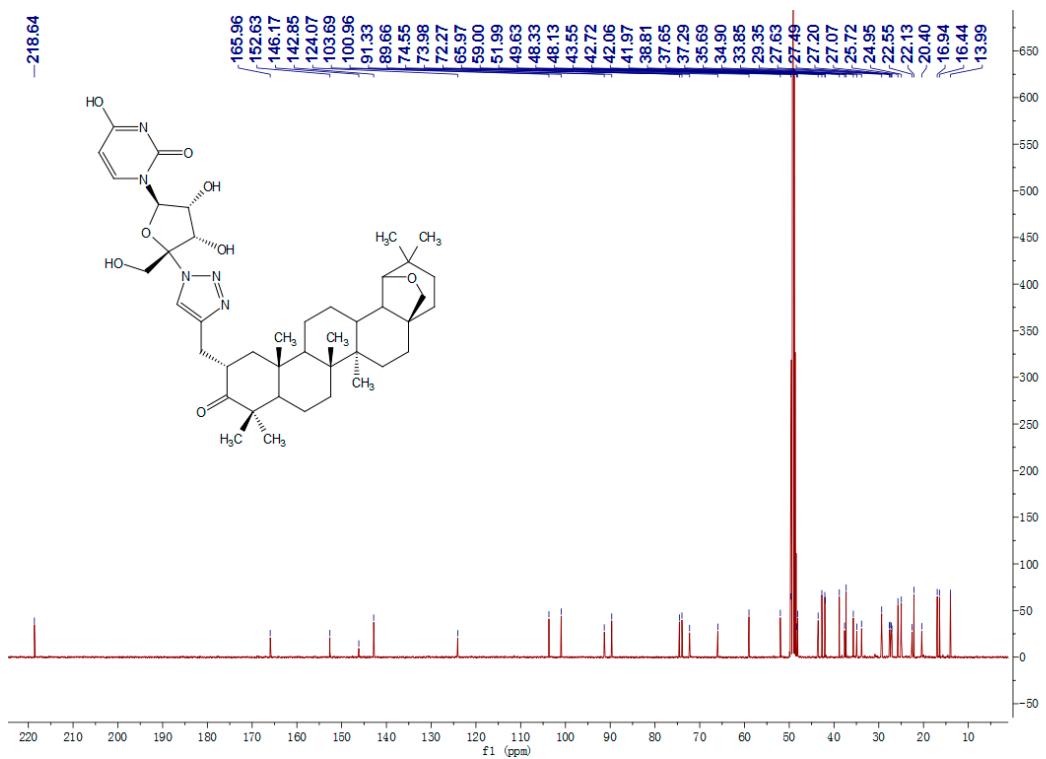


Figure S31 ¹³C NMR spectrum of compound 9f

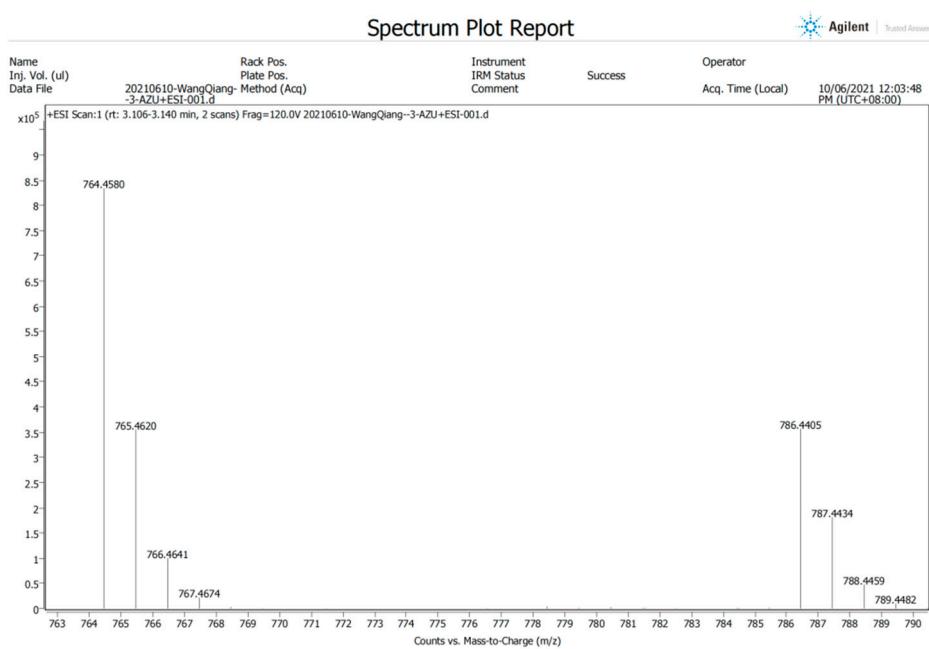


Figure S32 HRMS spectrum of compound 9f

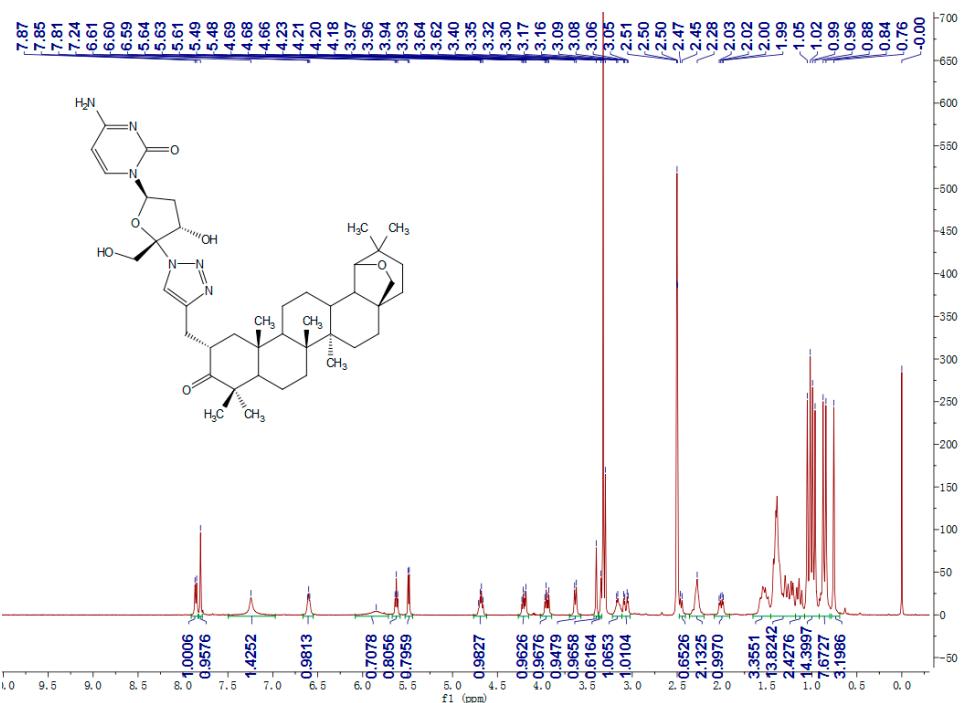


Figure S33 ¹H NMR spectrum of compound 9g

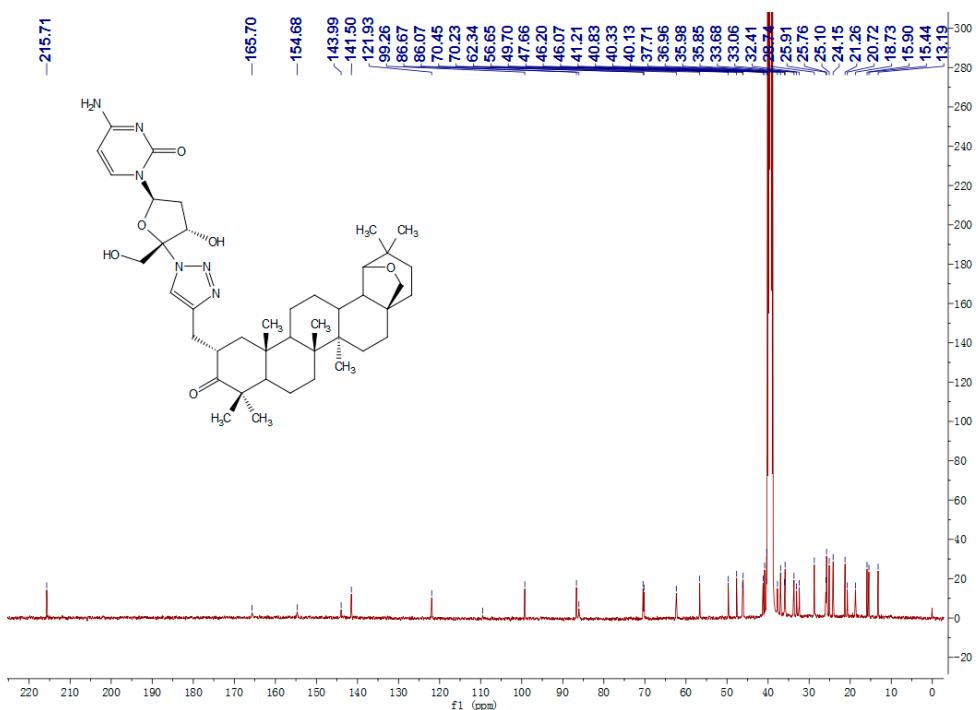
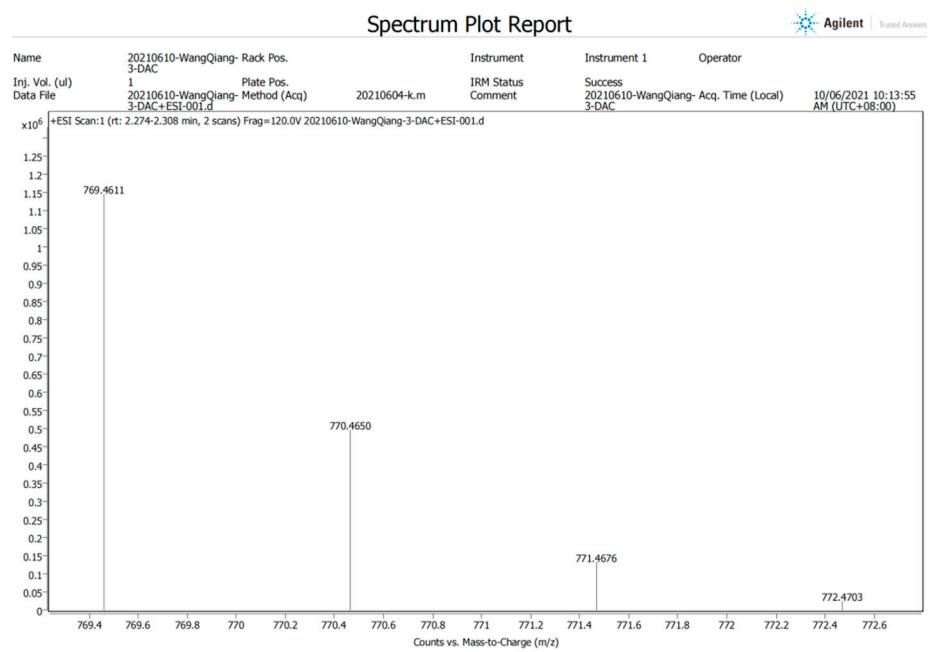


Figure S34 ¹³C NMR spectrum of compound 9g



Page 1 of 2

Generated at 10:26 AM on 10/06/2021

Figure S35 HRMS spectrum of compound **9g**

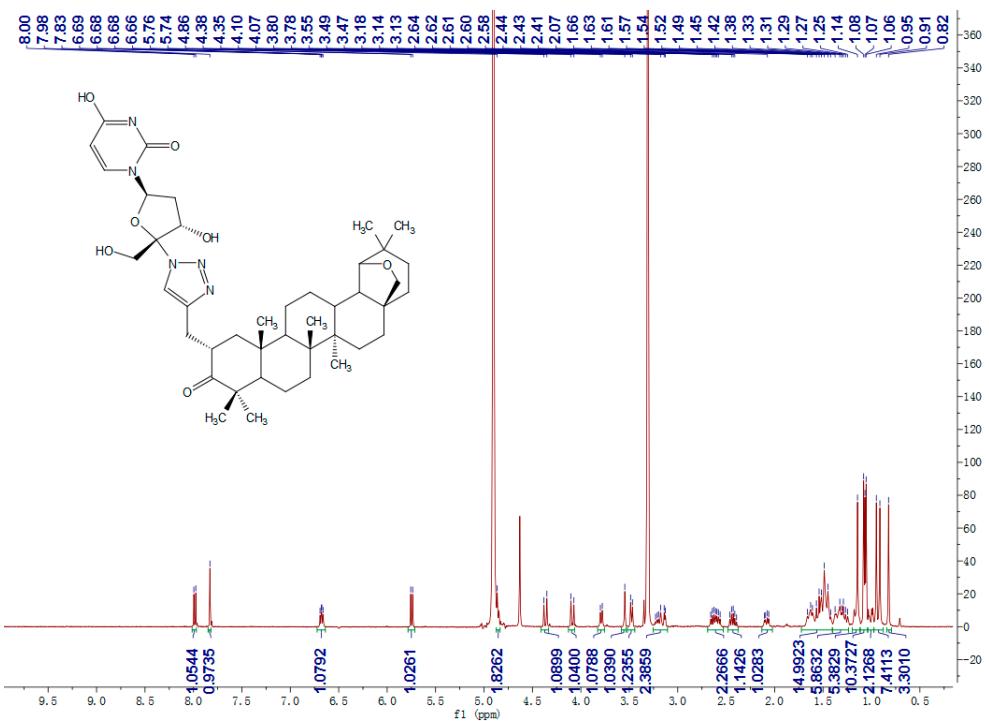


Figure S36 ^1H NMR spectrum of compound **9h**

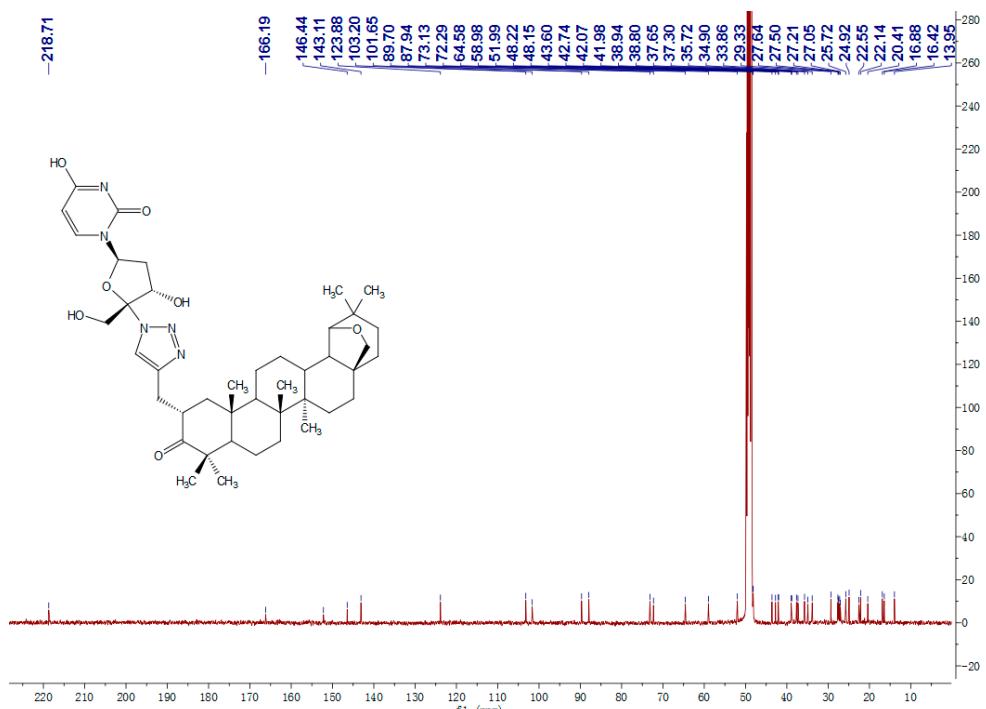


Figure S37 ^{13}C NMR spectrum of compound **9h**

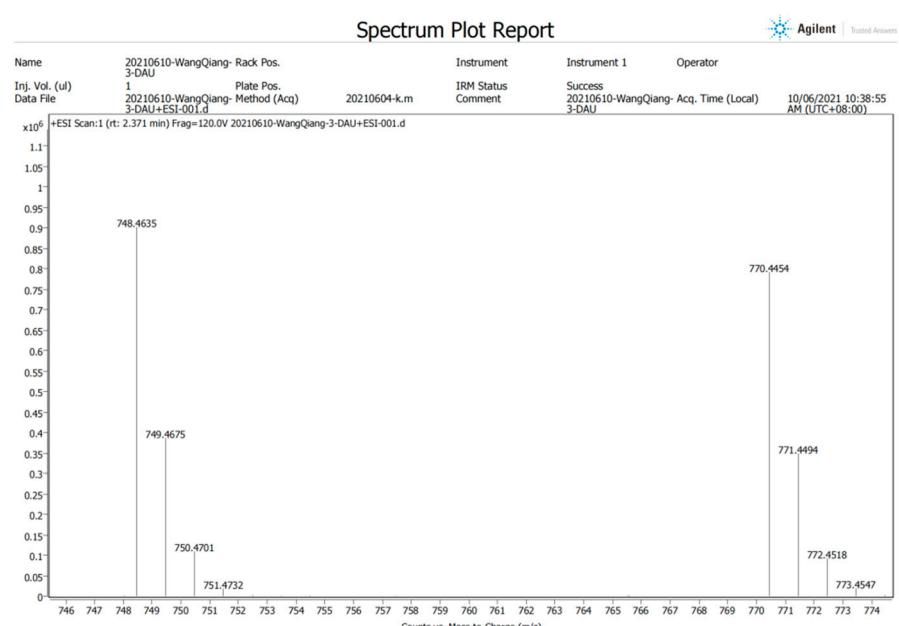


Figure S38 HRMS spectrum of compound **9h**

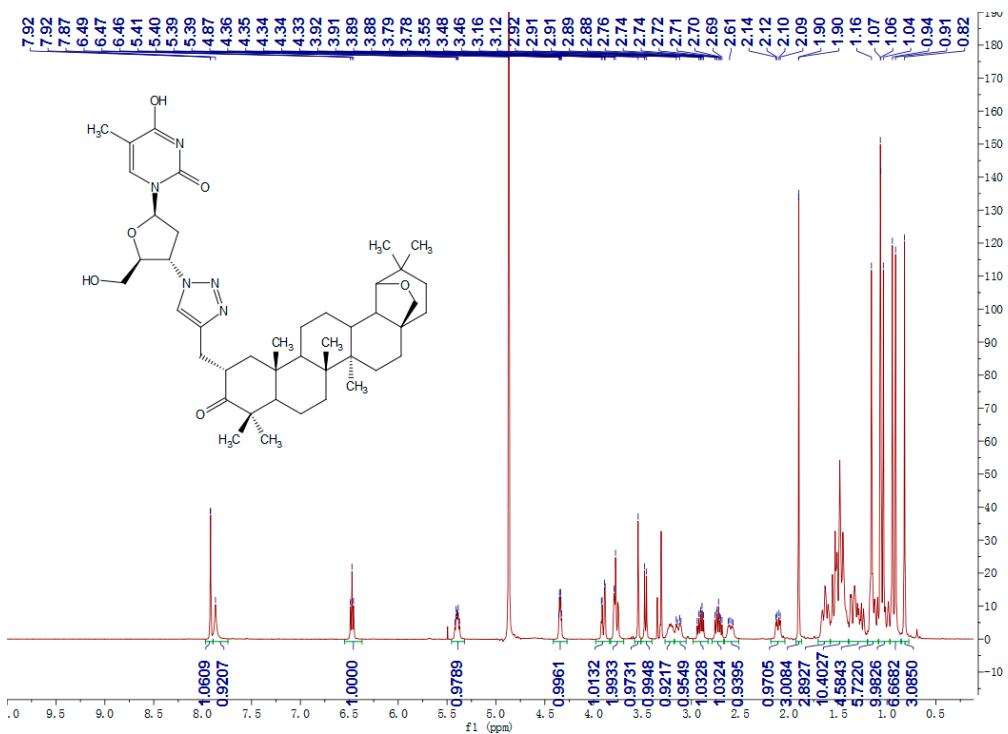


Figure S39 ^1H NMR spectrum of compound **9i**

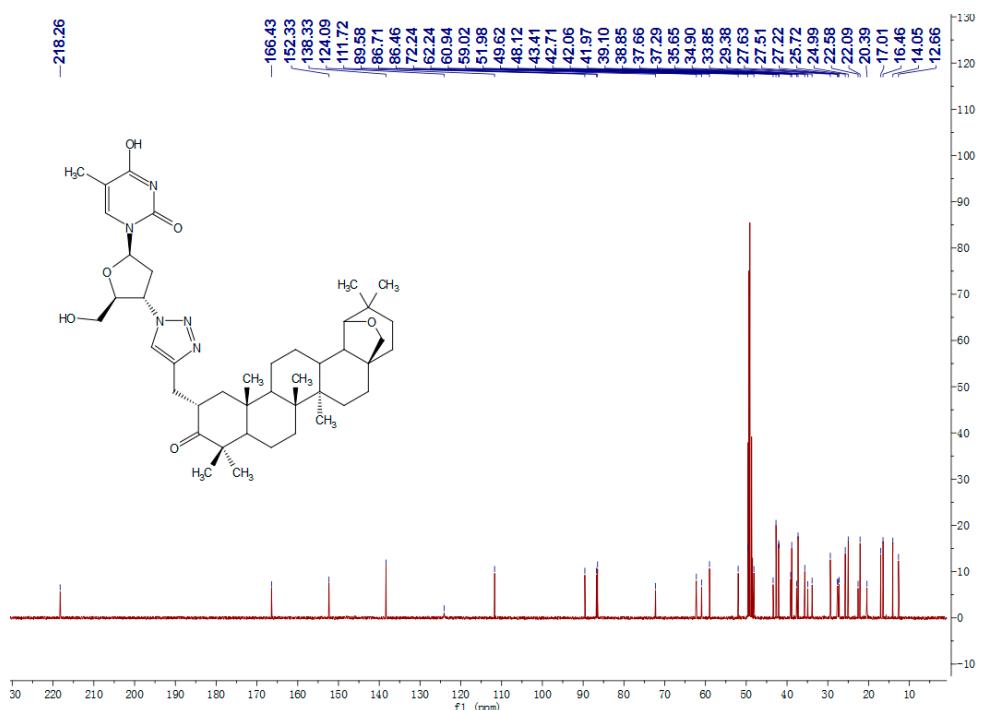
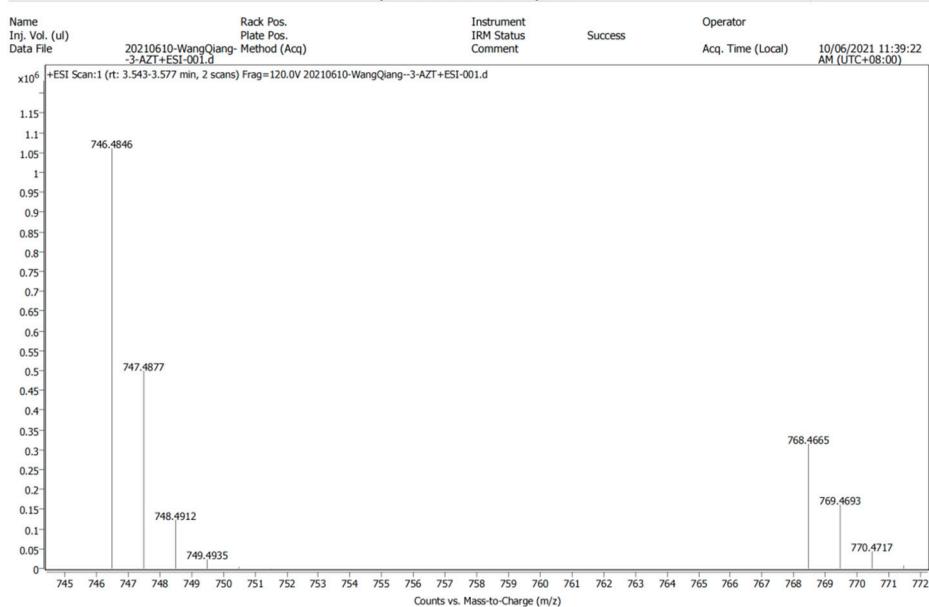


Figure S40 ^{13}C NMR spectrum of compound **9i**

Spectrum Plot Report

Agilent | Trained Analysts



Page 1 of 2

Generated at 11:48 AM on 10/06/2021

Figure S41 HRMS spectrum of compound **9i**

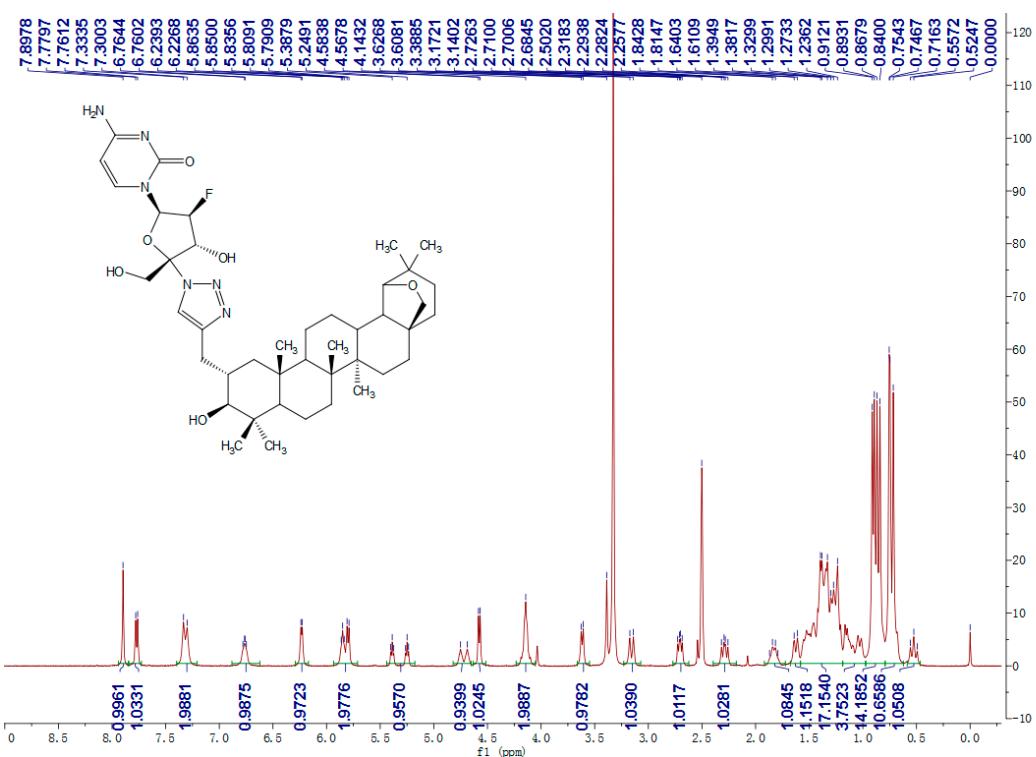


Figure S42 ¹H NMR spectrum of compound **10a**

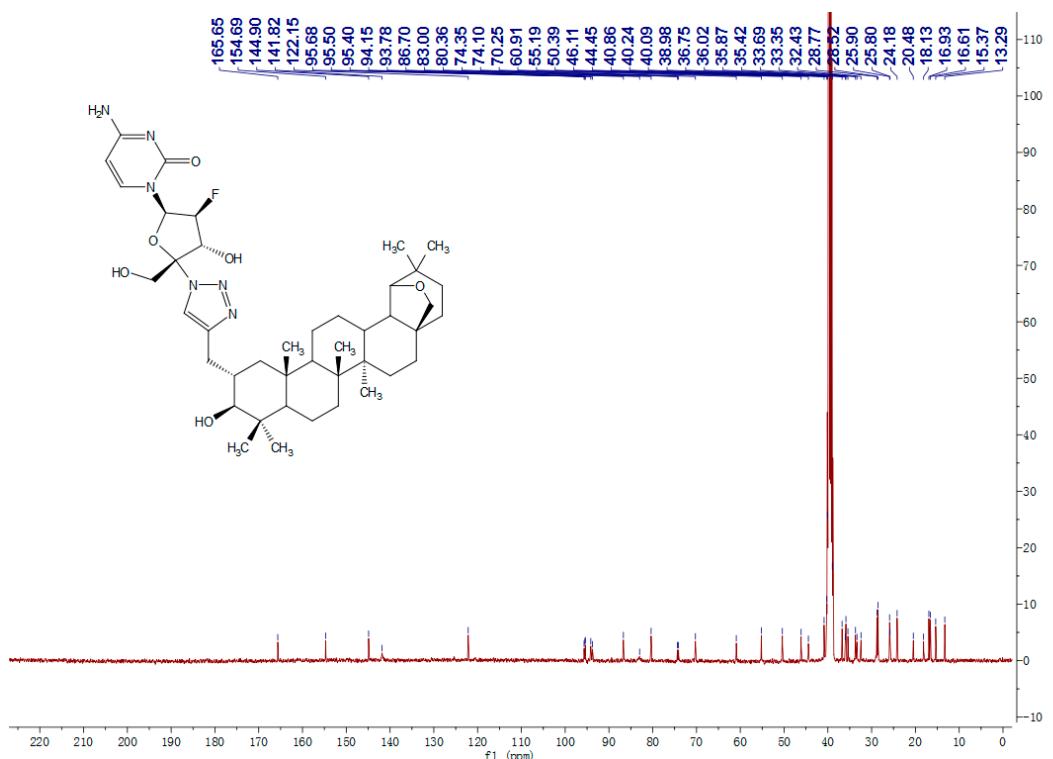


Figure S43 ^{13}C NMR spectrum of compound **10a**

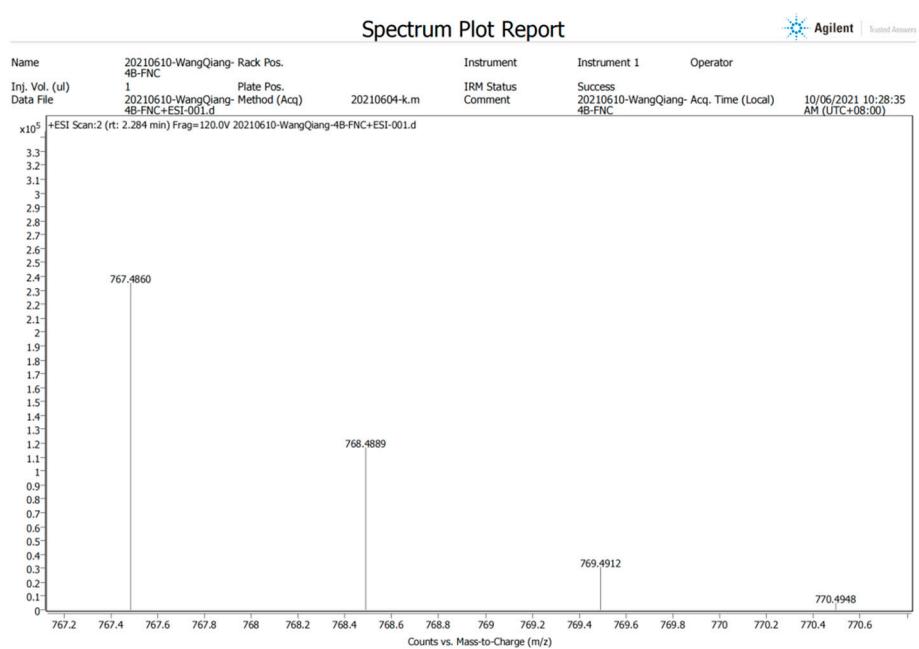


Figure S44 HRMS spectrum of compound **10a**

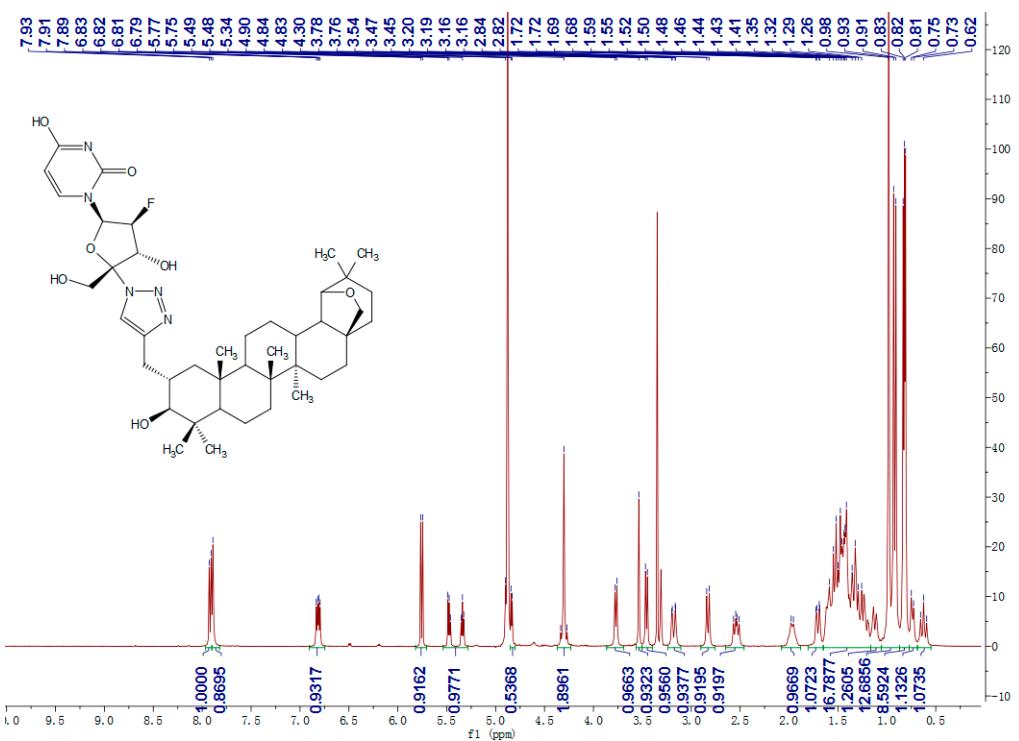


Figure S45 ¹H NMR spectrum of compound **10b**

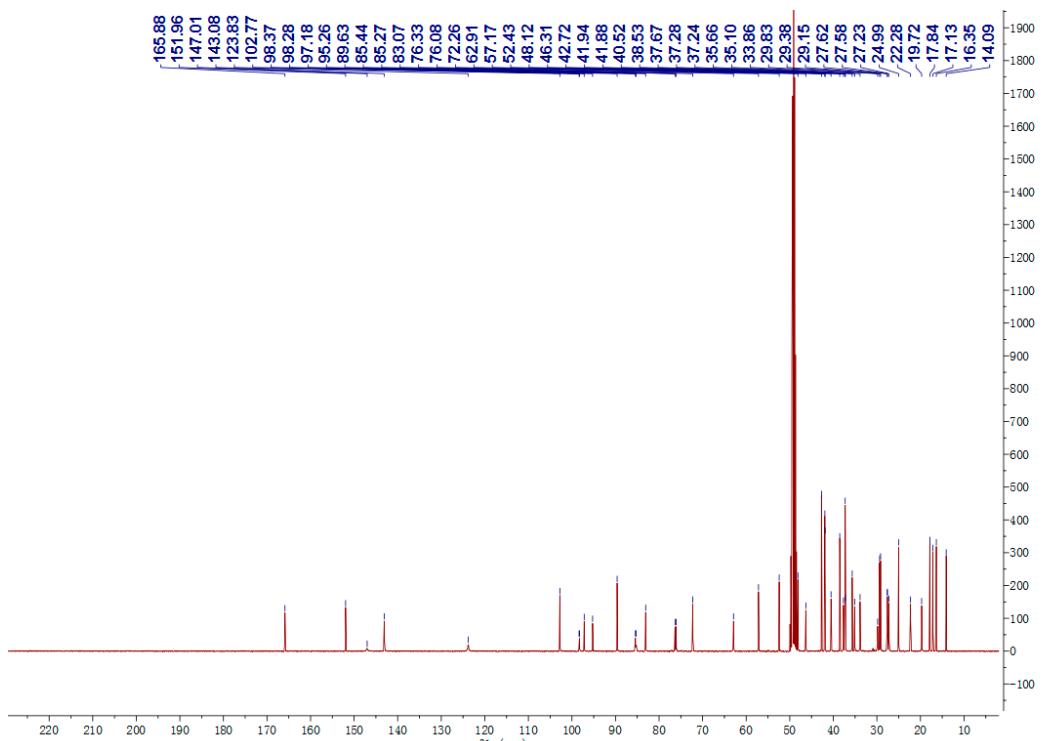
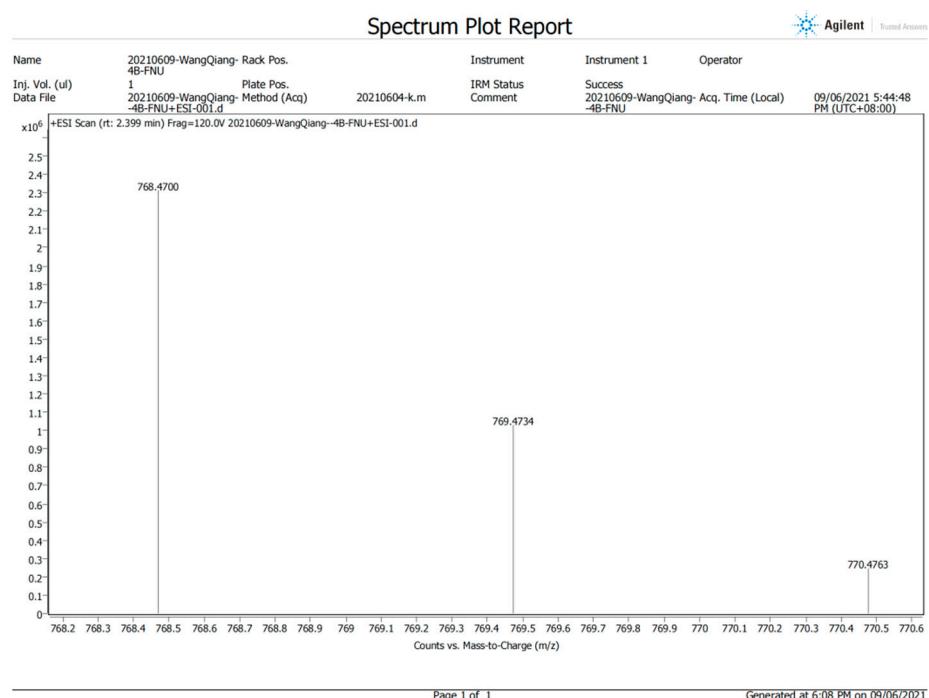


Figure S46 ¹³C NMR spectrum of compound **10b**



Page 1 of 1

Generated at 6:08 PM on 09/06/2021

Figure S47 HRMS spectrum of compound 10b

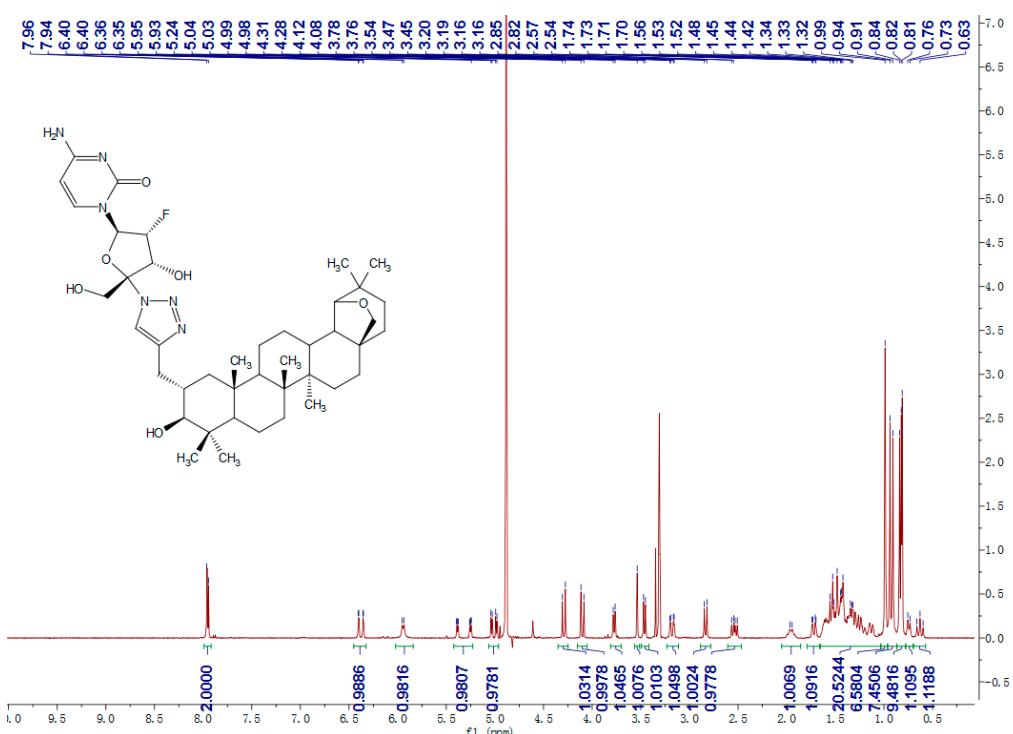


Figure S48 ^1H NMR spectrum of compound 10c

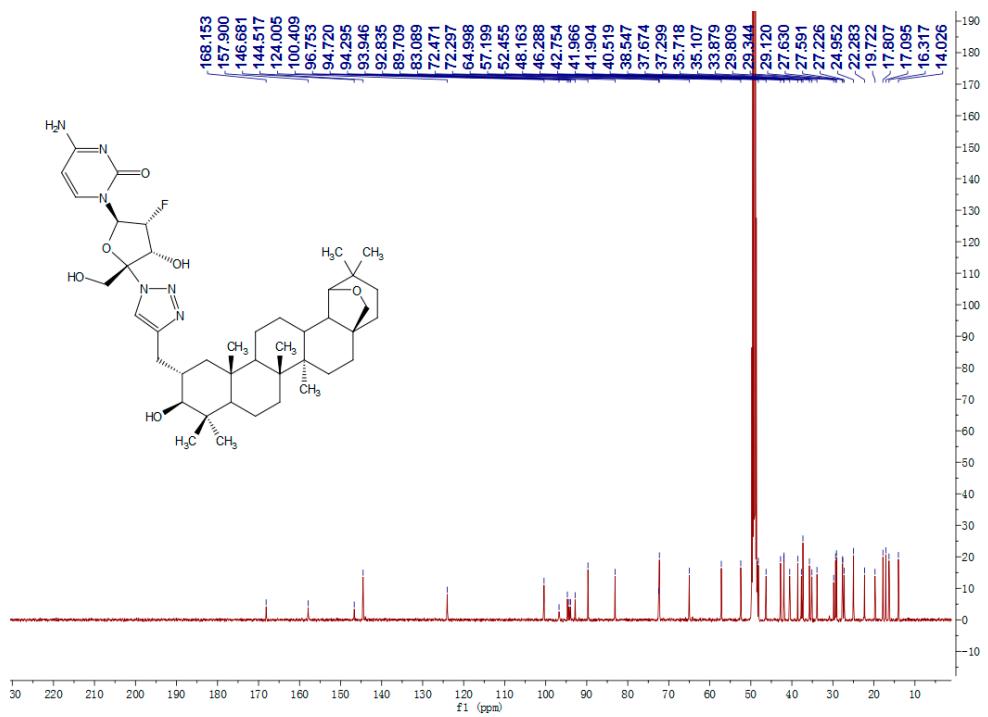


Figure S49 ^{13}C NMR spectrum of compound **10c**

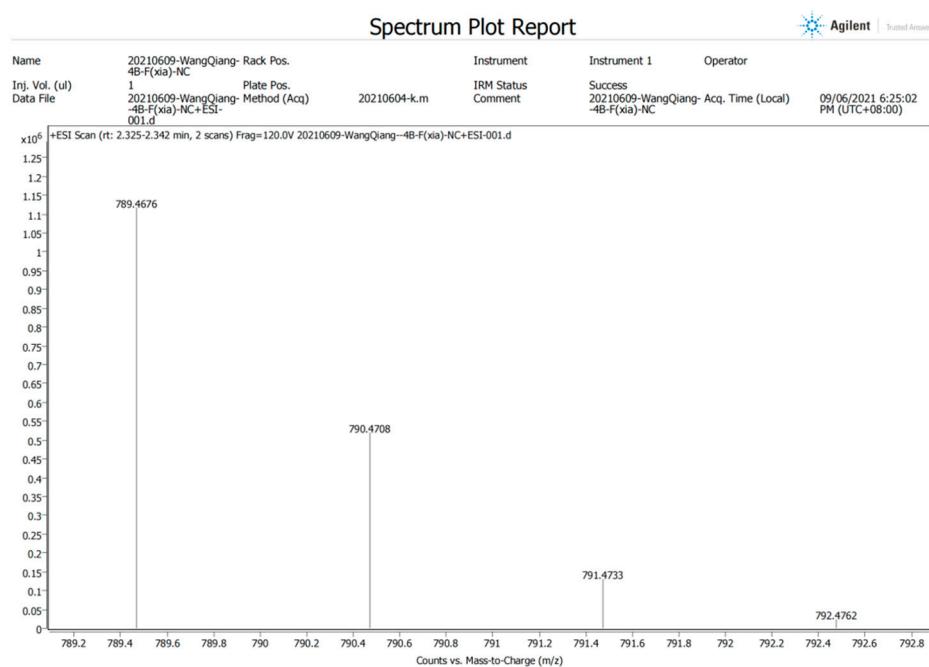


Figure S50 HRMS spectrum of compound **10c**

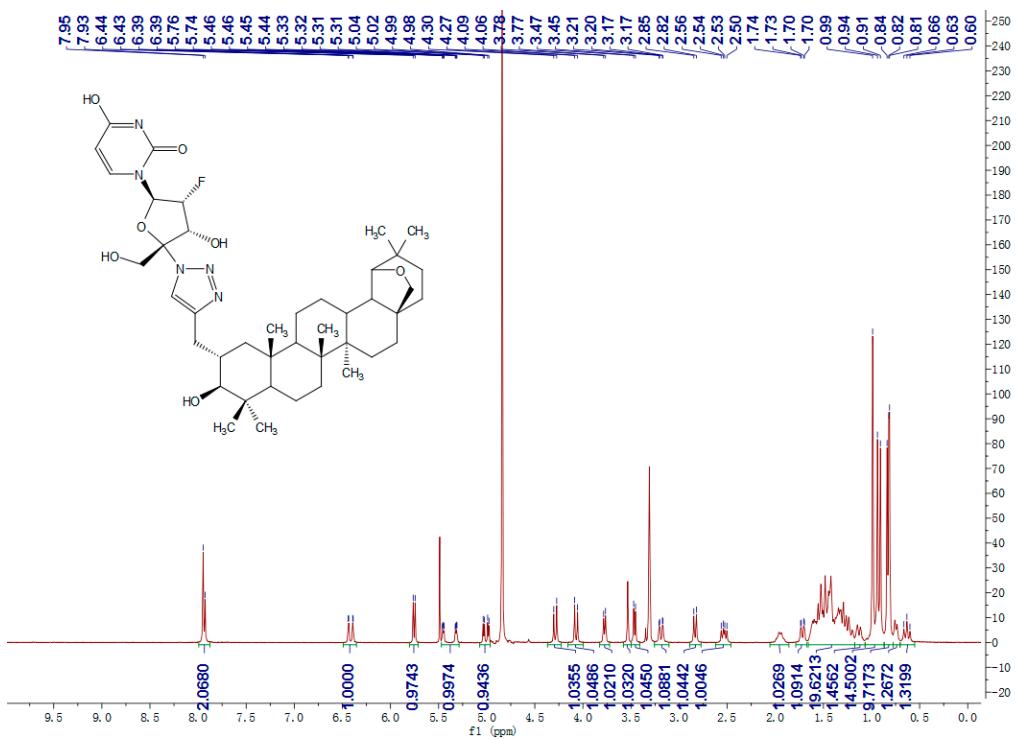


Figure S51 ¹H NMR spectrum of compound 10d

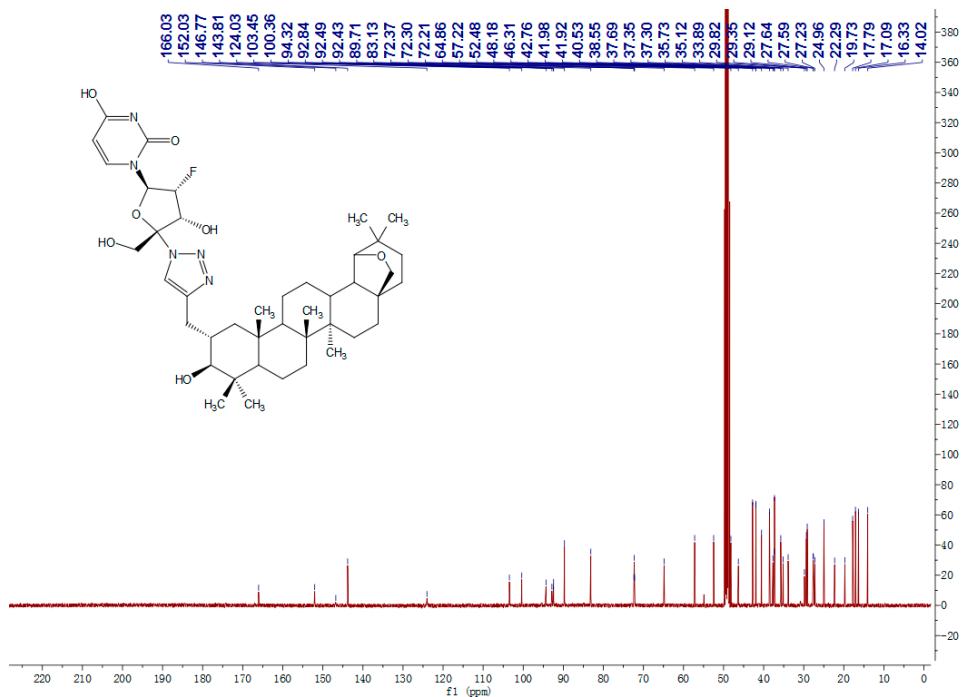


Figure S52 ¹³C NMR spectrum of compound 10d

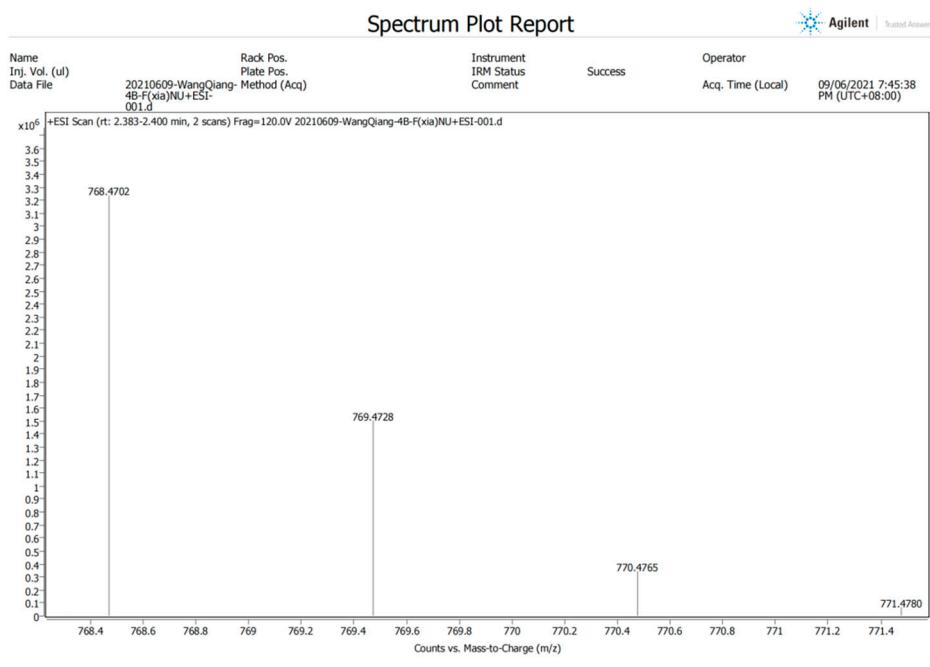


Figure S53 HRMS spectrum of compound **10d**

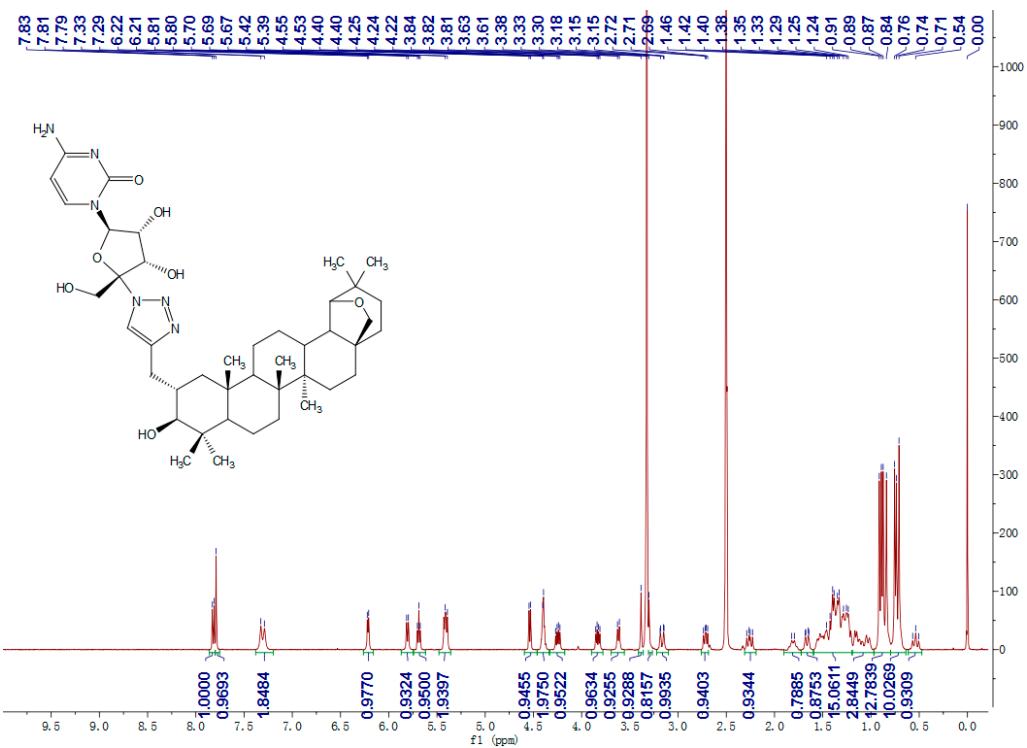


Figure S54 ^1H NMR spectrum of compound **10e**

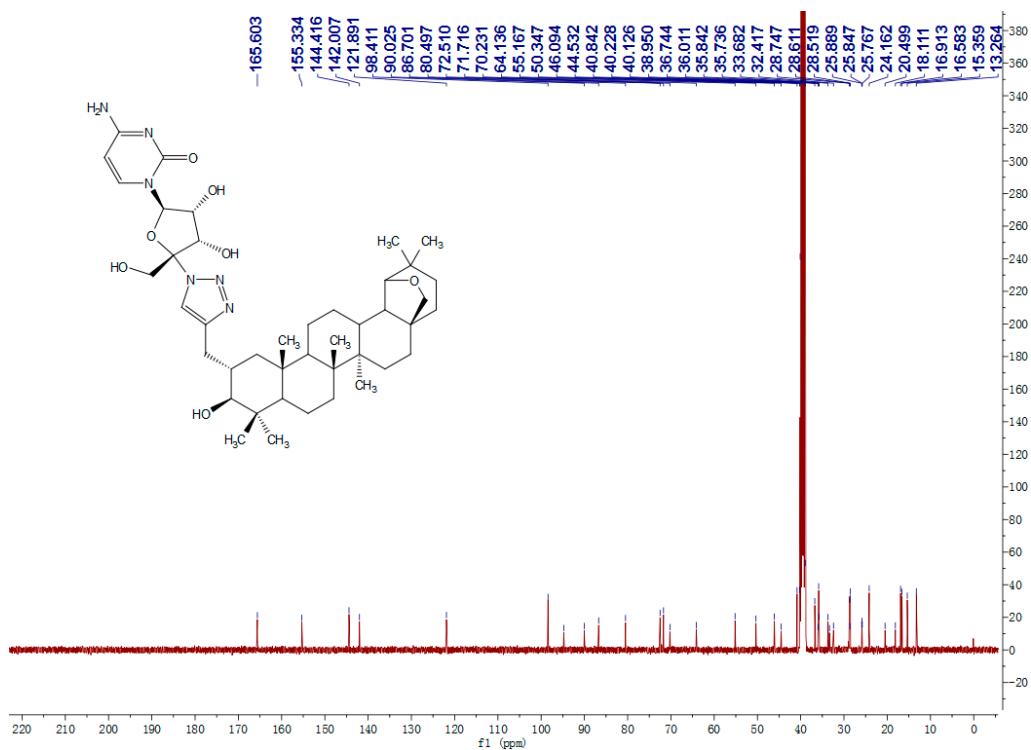


Figure S55 ^{13}C NMR spectrum of compound **10e**

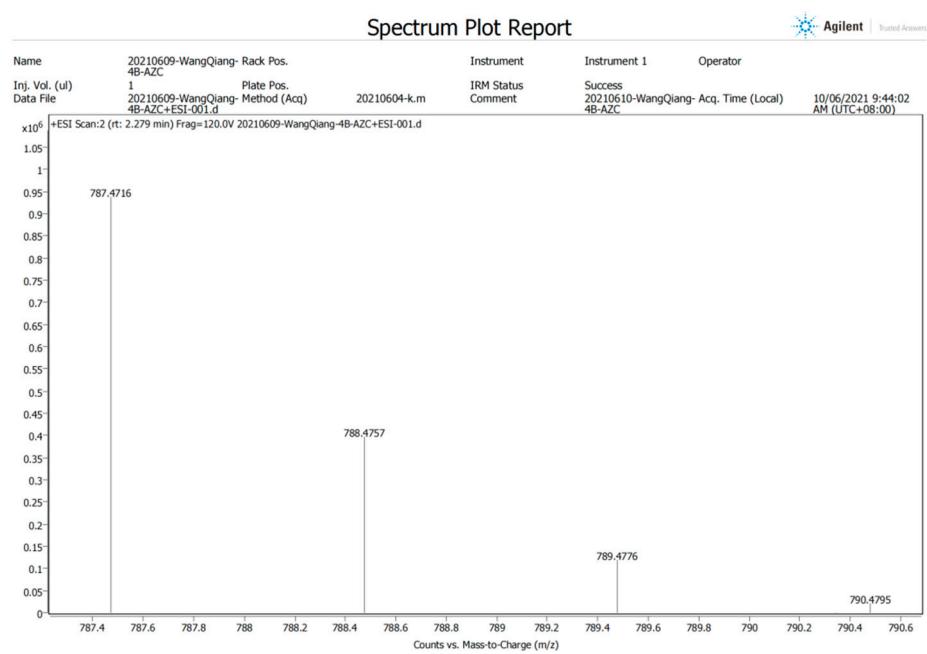


Figure S56 HRMS spectrum of compound **10e**

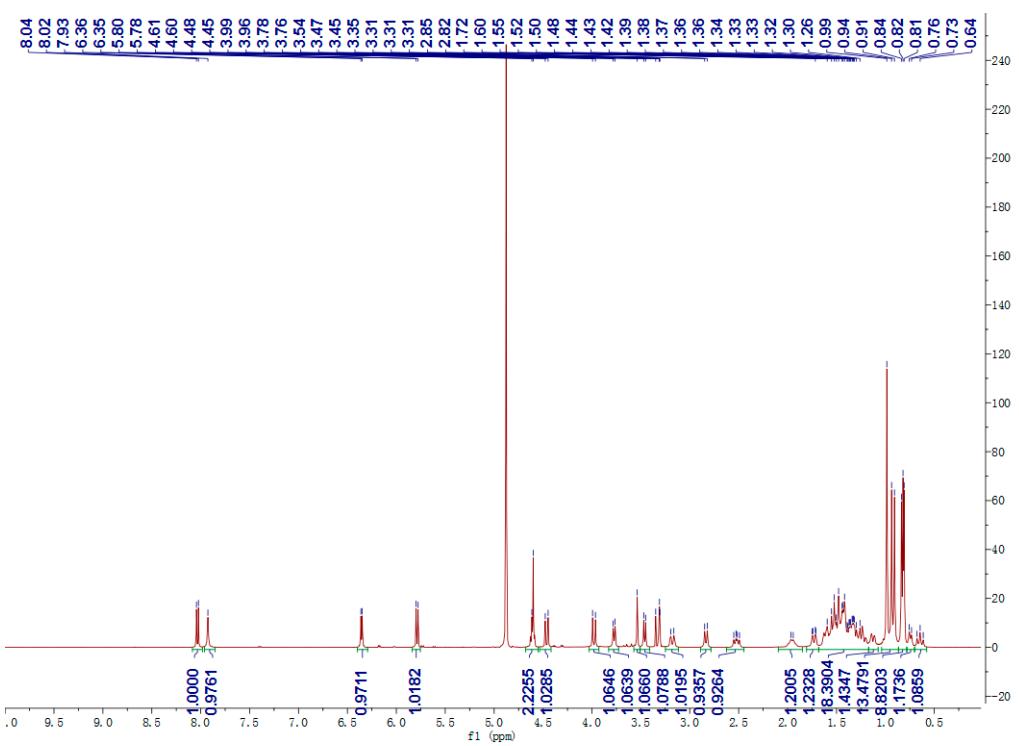


Figure S57 ¹H NMR spectrum of compound 10f

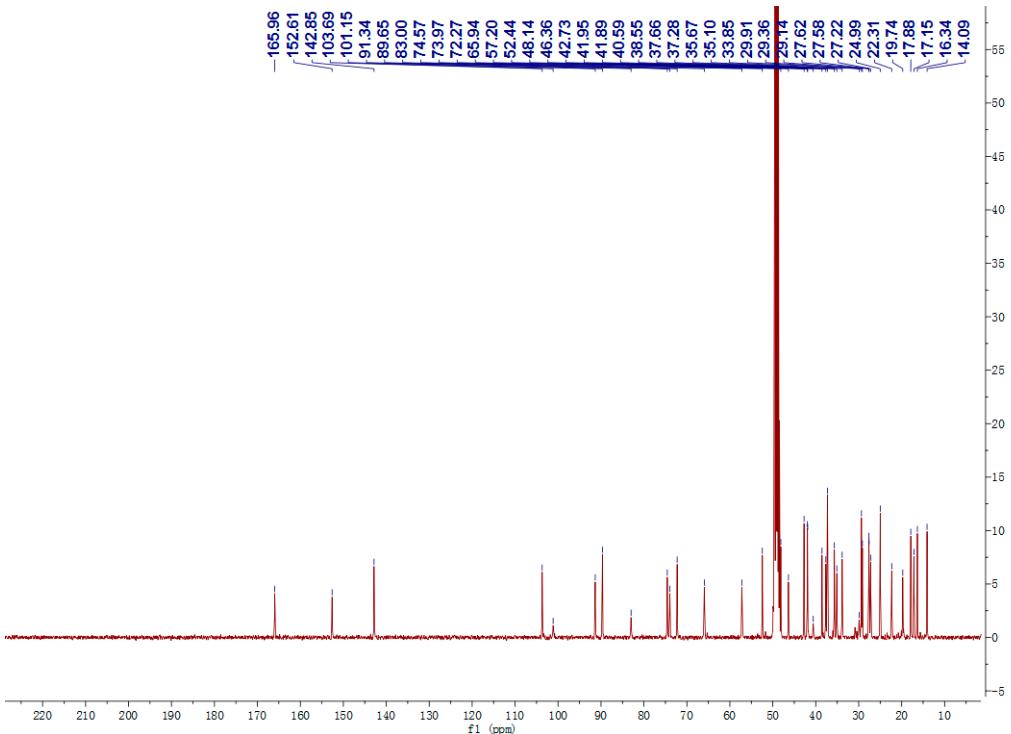
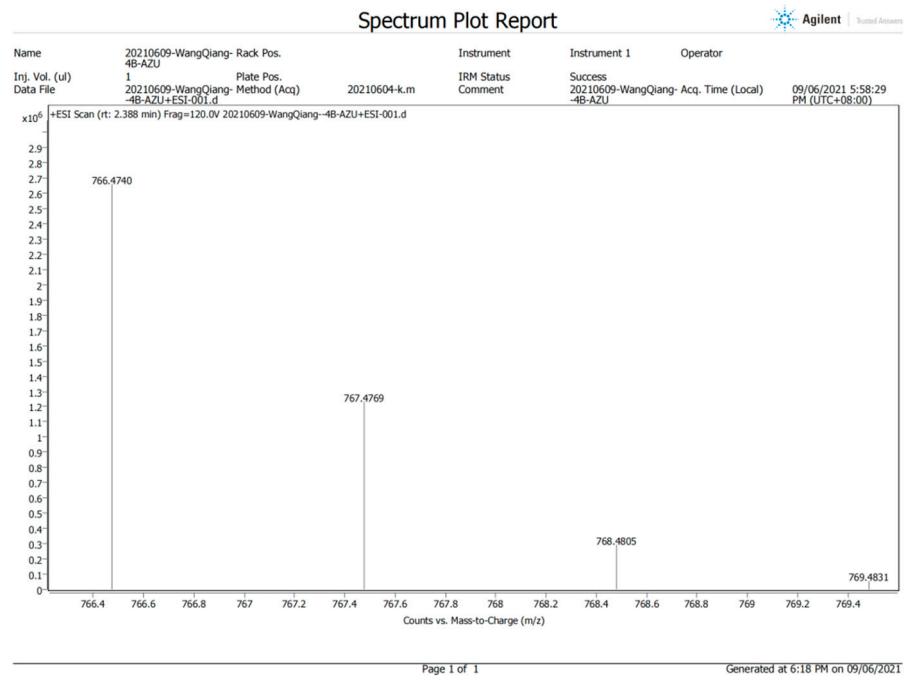


Figure S58 ¹³C NMR spectrum of compound 10f



Page 1 of 1

Generated at 6:18 PM on 09/06/2021

Figure S59 HRMS spectrum of compound **10f**

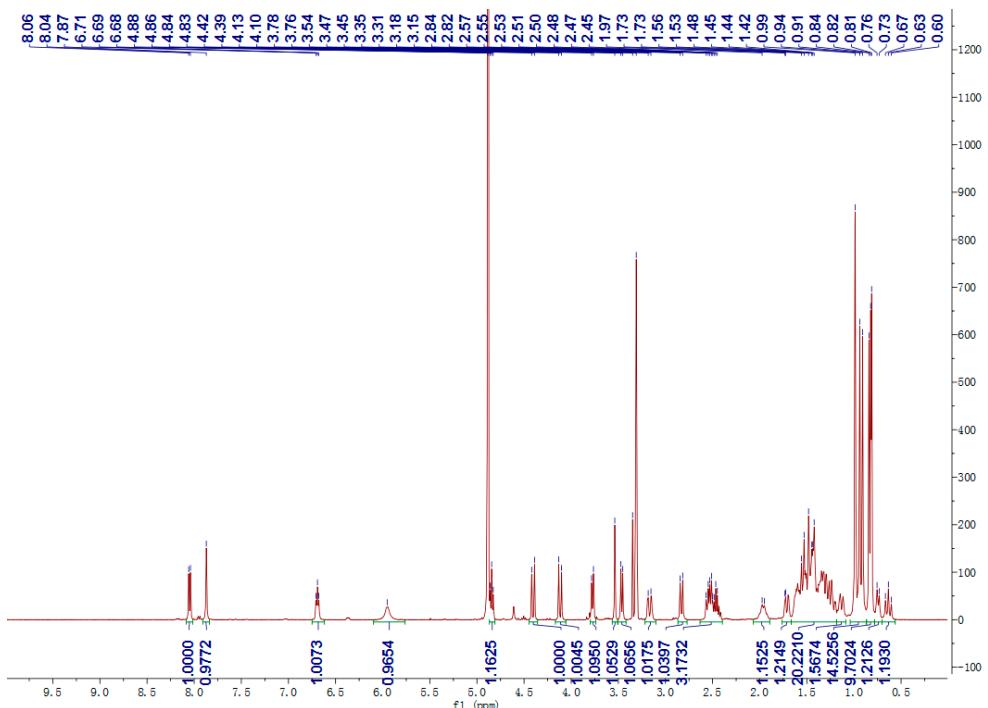


Figure S60 ^1H NMR spectrum of compound **10g**

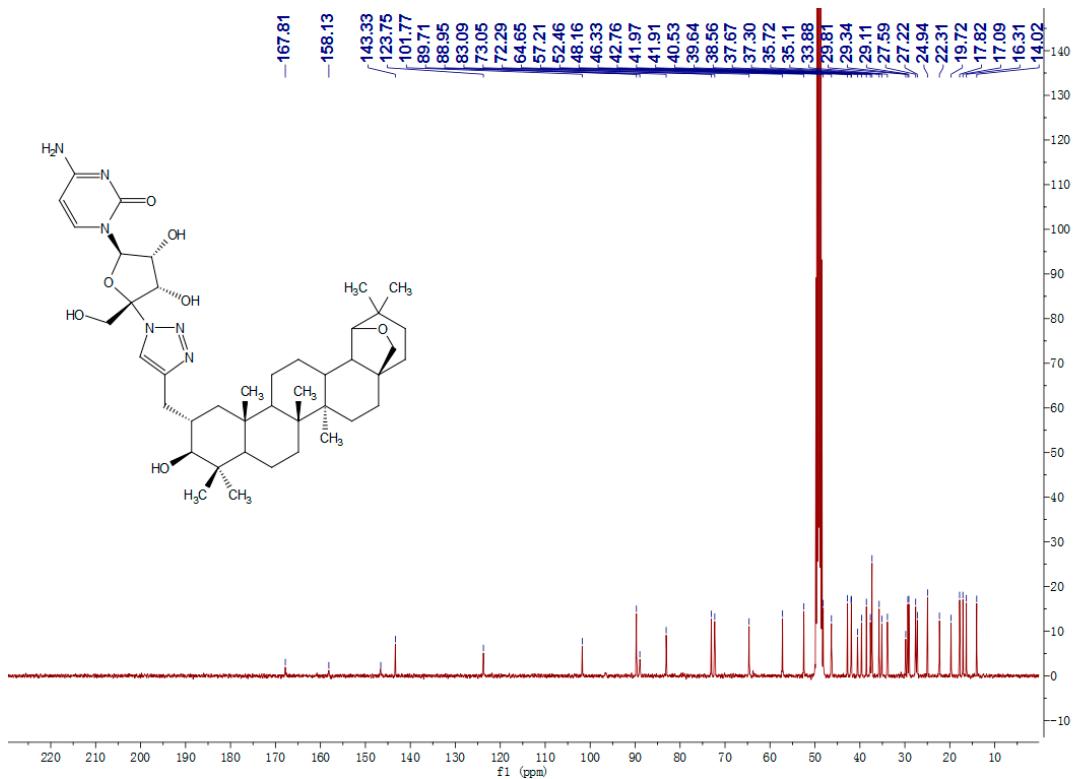


Figure S61 ^{13}C NMR spectrum of compound **10g**

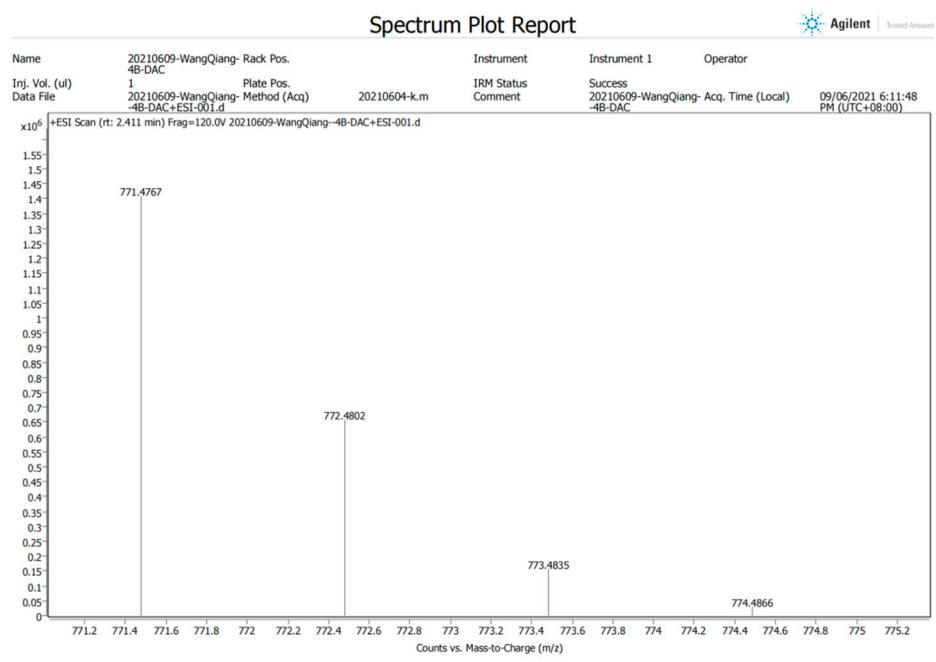


Figure S62 HRMS spectrum of compound **10g**

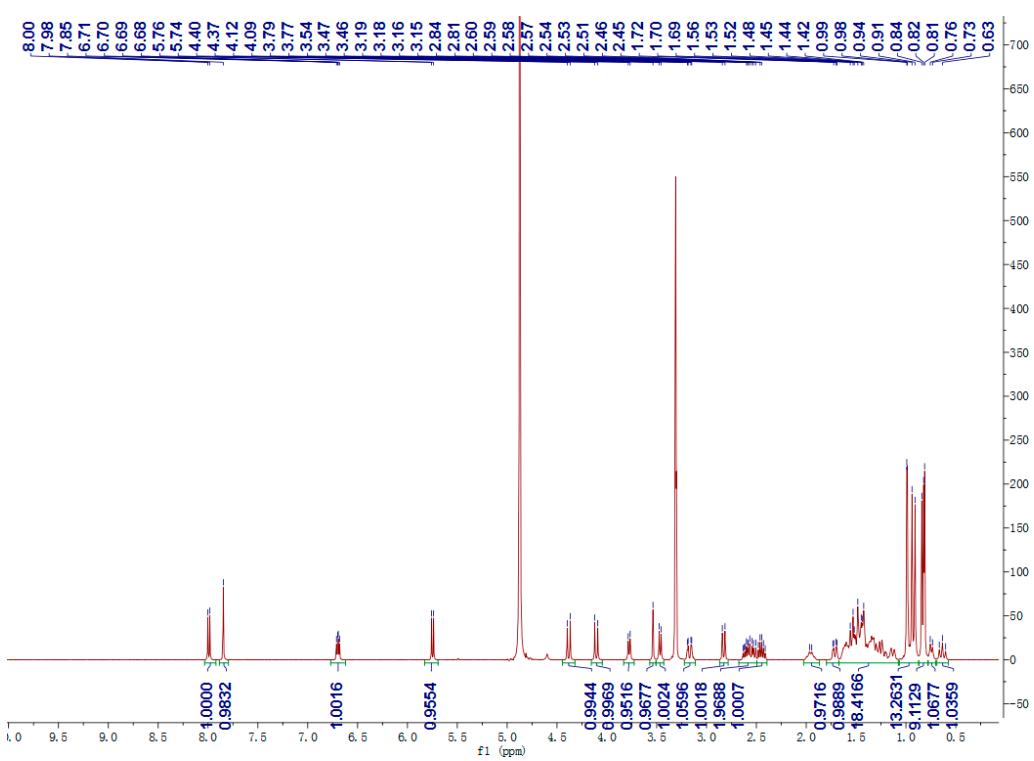


Figure S63 ¹H NMR spectrum of compound **10h**

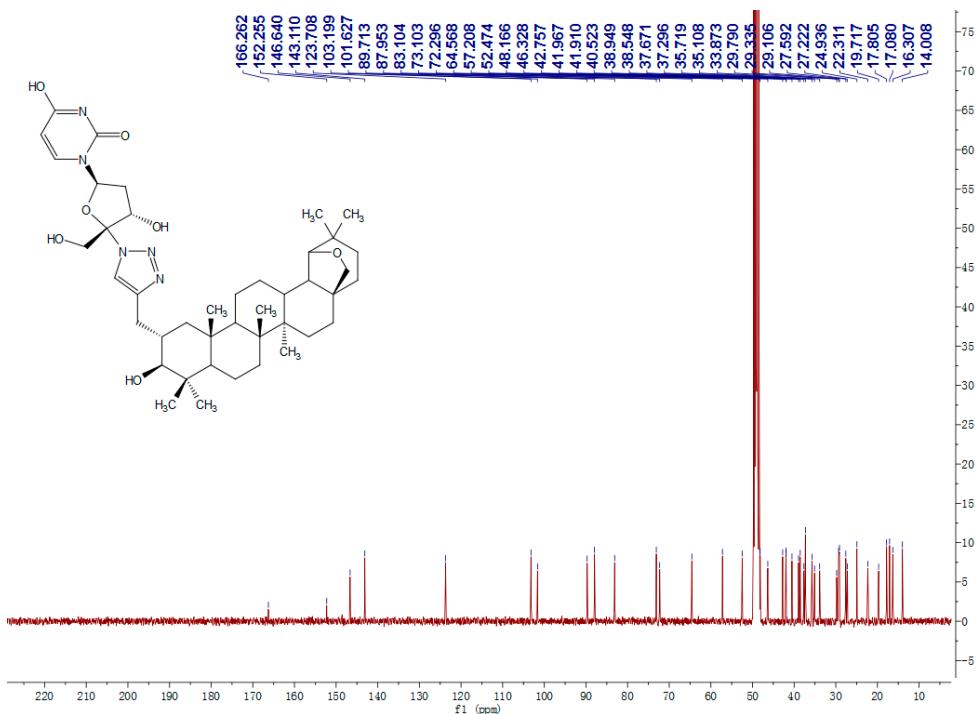
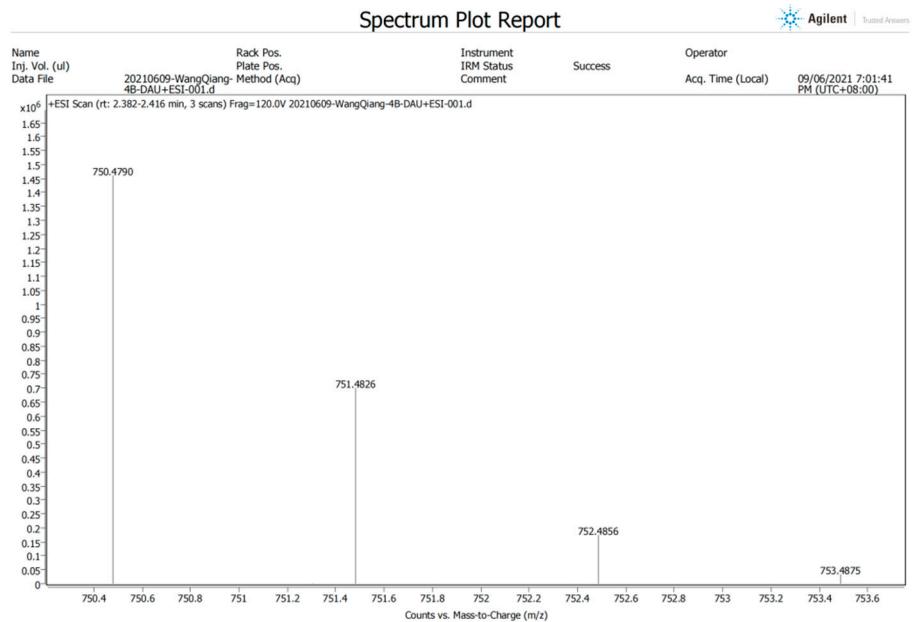


Figure S64 ¹³C NMR spectrum of compound **10h**



Page 1 of 1

Generated at 7:08 PM on 09/06/2021

Figure S65 HRMS spectrum of compound **10h**

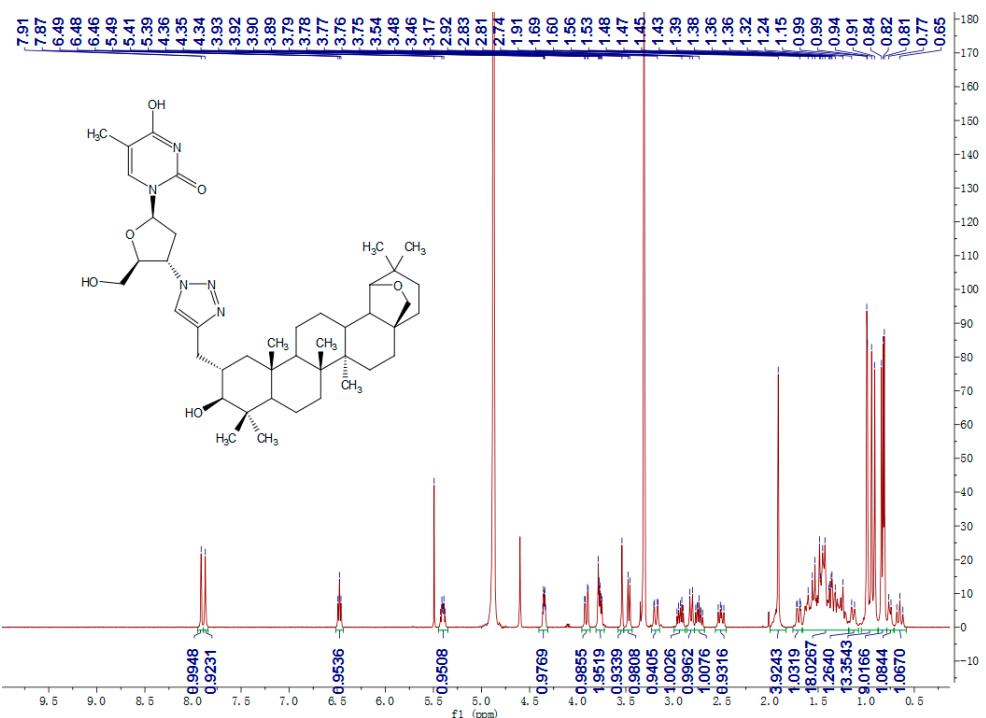


Figure S66 ^1H NMR spectrum of compound **10i**

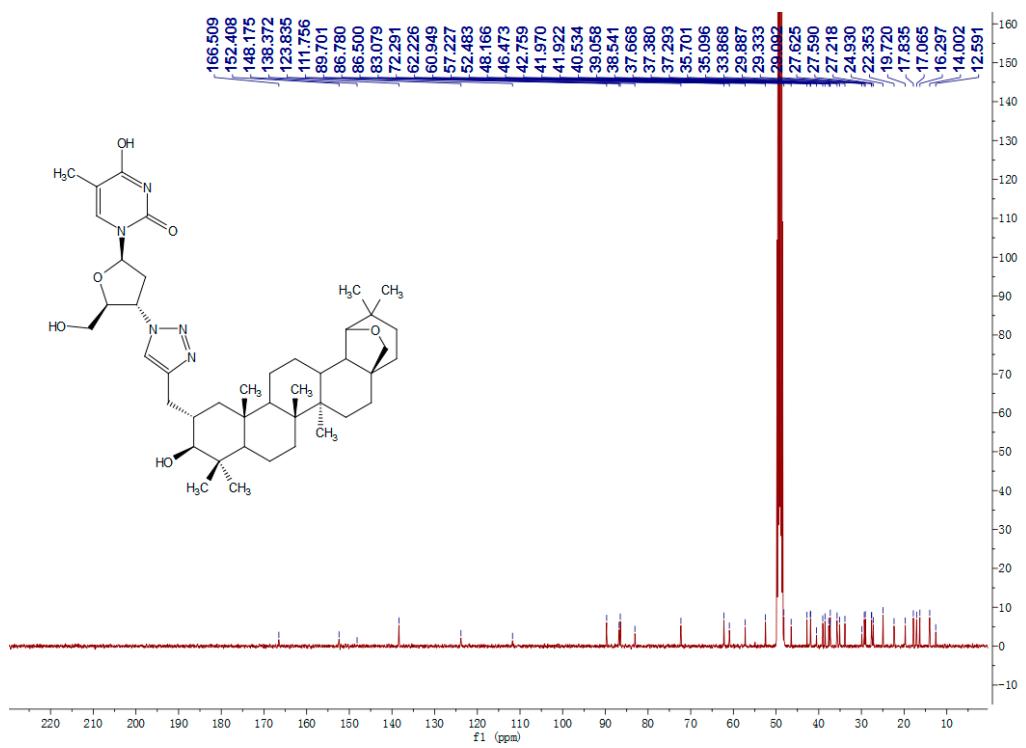


Figure S67 ^{13}C NMR spectrum of compound **10i**

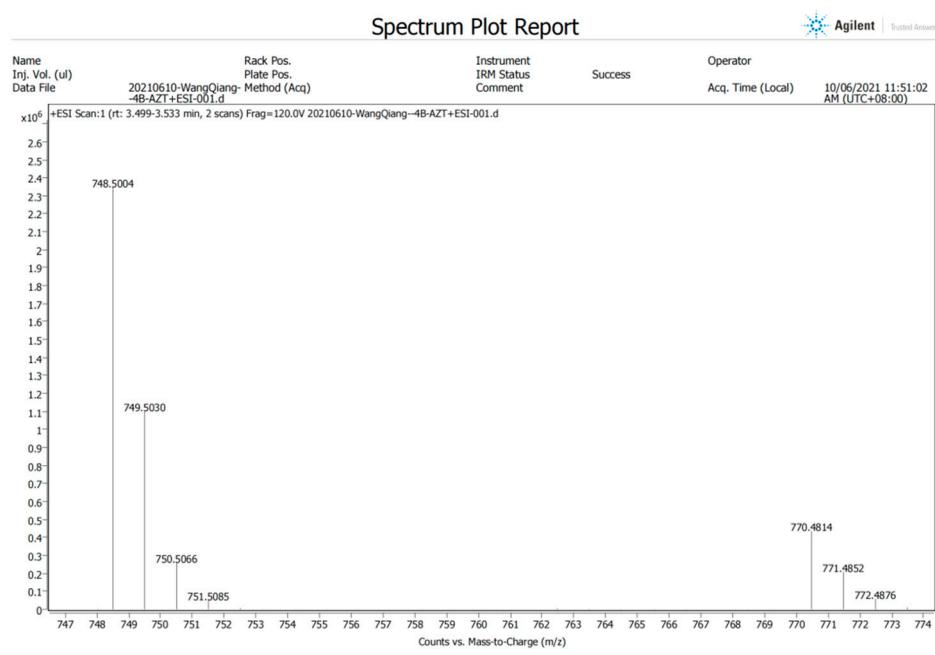


Figure S68 HRMS spectrum of compound **10i**