

Solvent free synthesis and *in-silico* molecular docking study of (*E*)-3-(β -C-glycosylmethylidene)-*N*-aryl/alkyl succinimides

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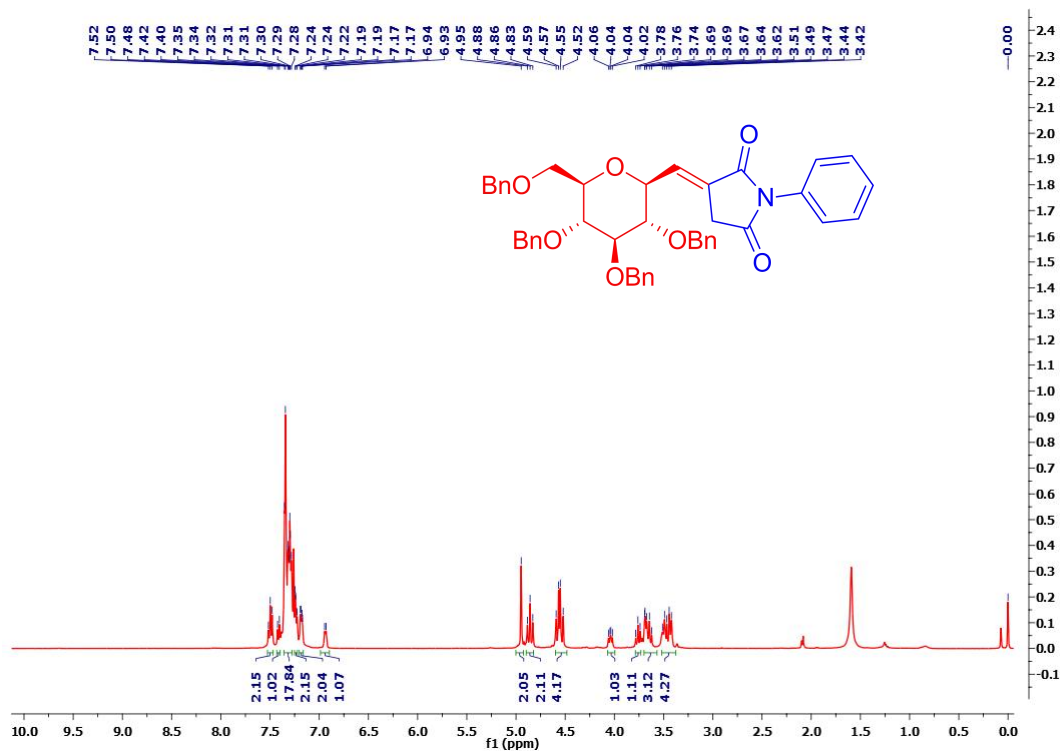


Figure S1. ^1H NMR spectrum of compound **3a** (400 MHz, CDCl_3).

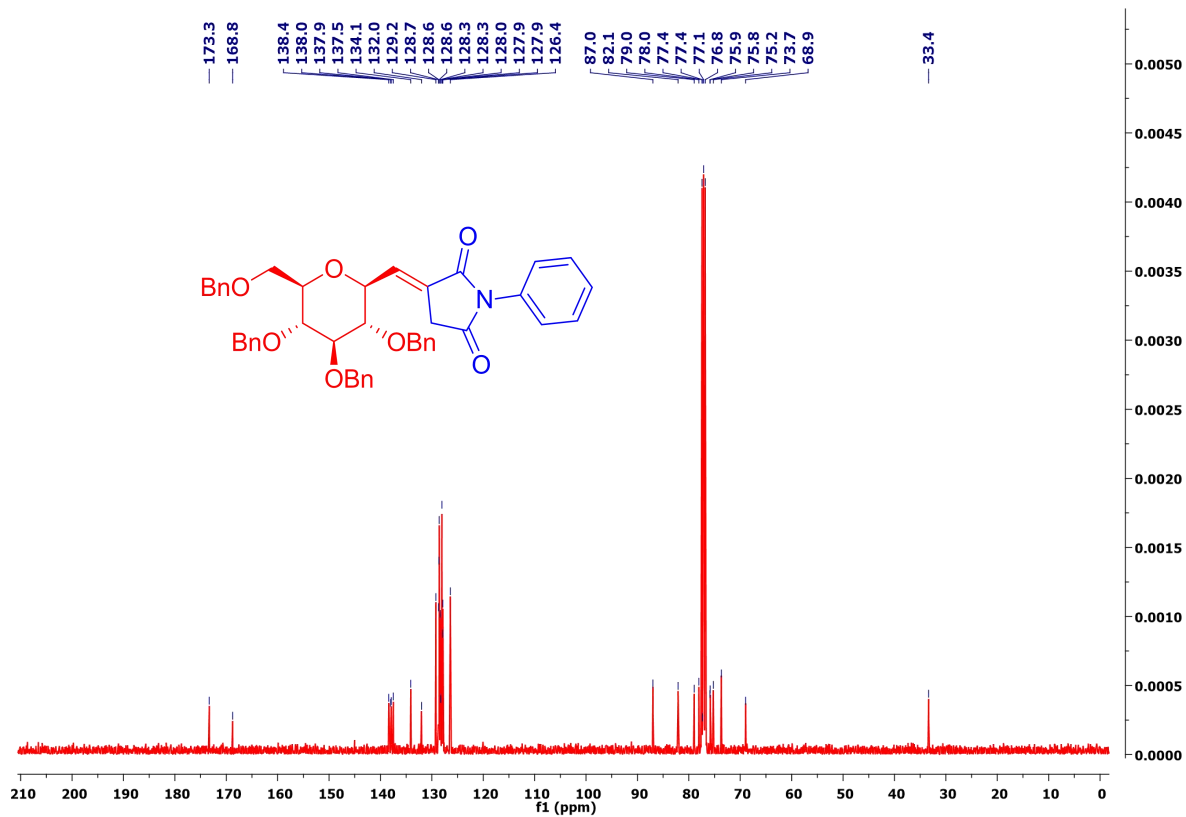


Figure S2. ^{13}C NMR spectrum of compound **3a** (100.6 MHz, CDCl_3).

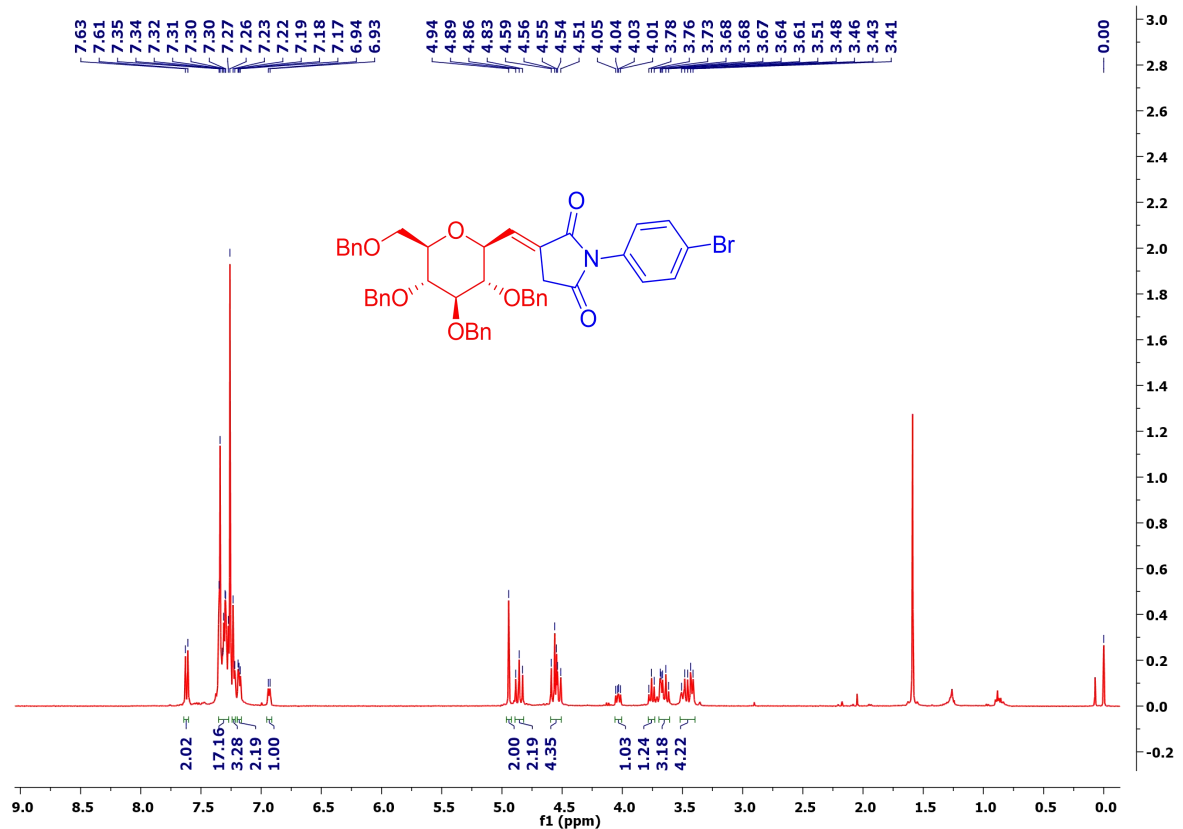


Figure S3. ¹H NMR spectrum of compound **3b** (400 MHz, CDCl₃).

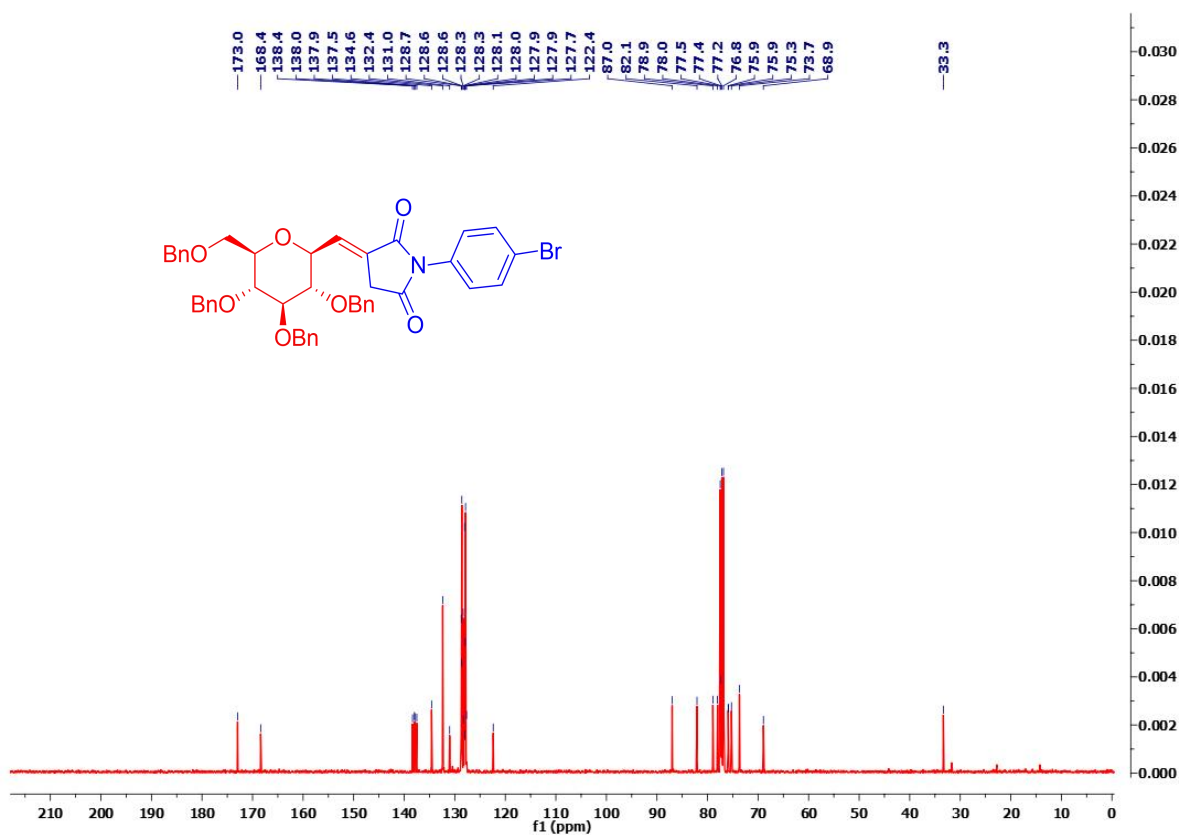


Figure S4. ¹³C NMR spectrum of compound **3b** (100.6 MHz, CDCl₃).

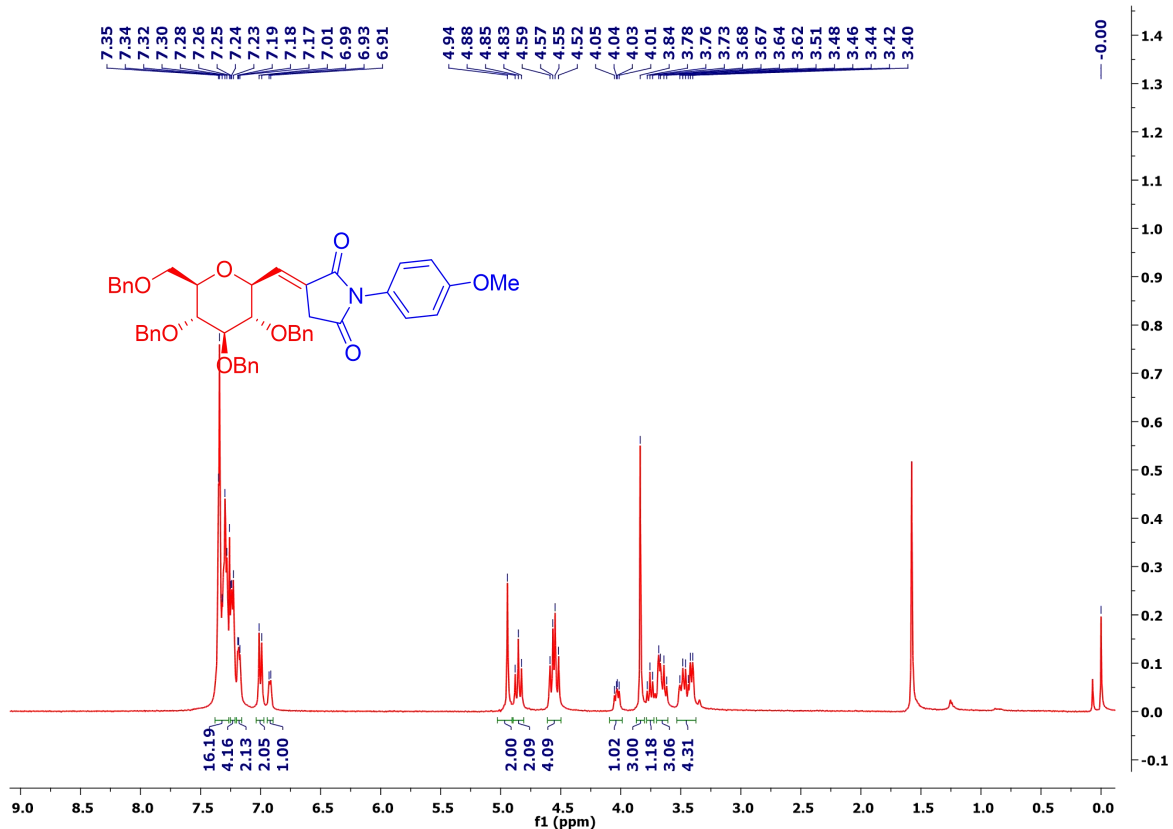


Figure S5. ^1H NMR spectrum of compound **3c** (400 MHz, CDCl_3).

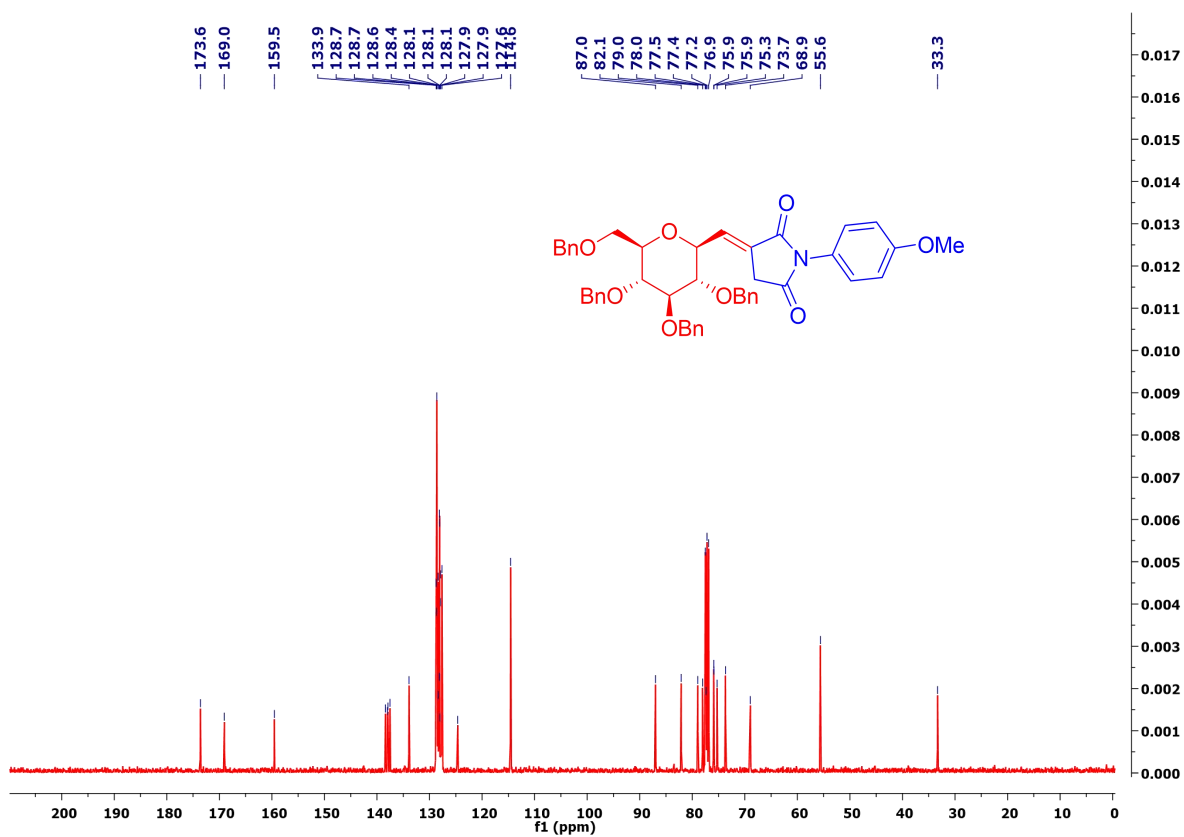
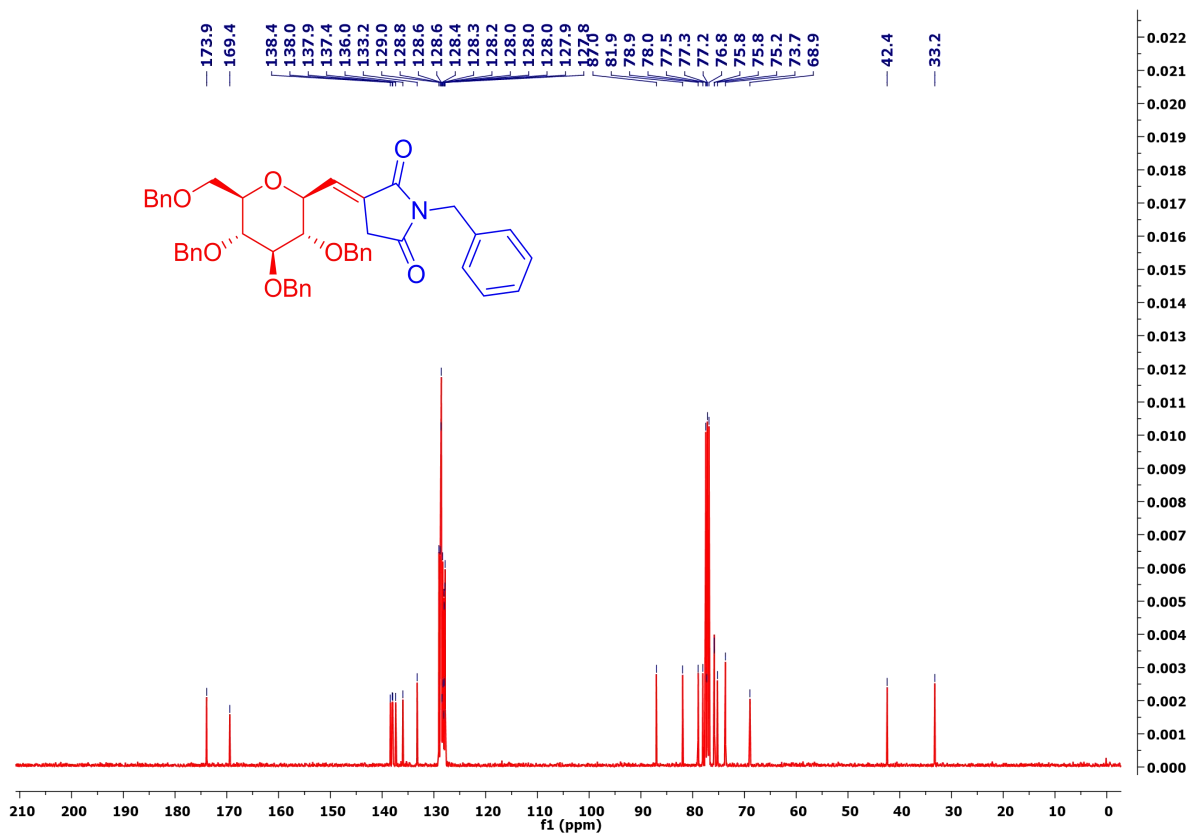
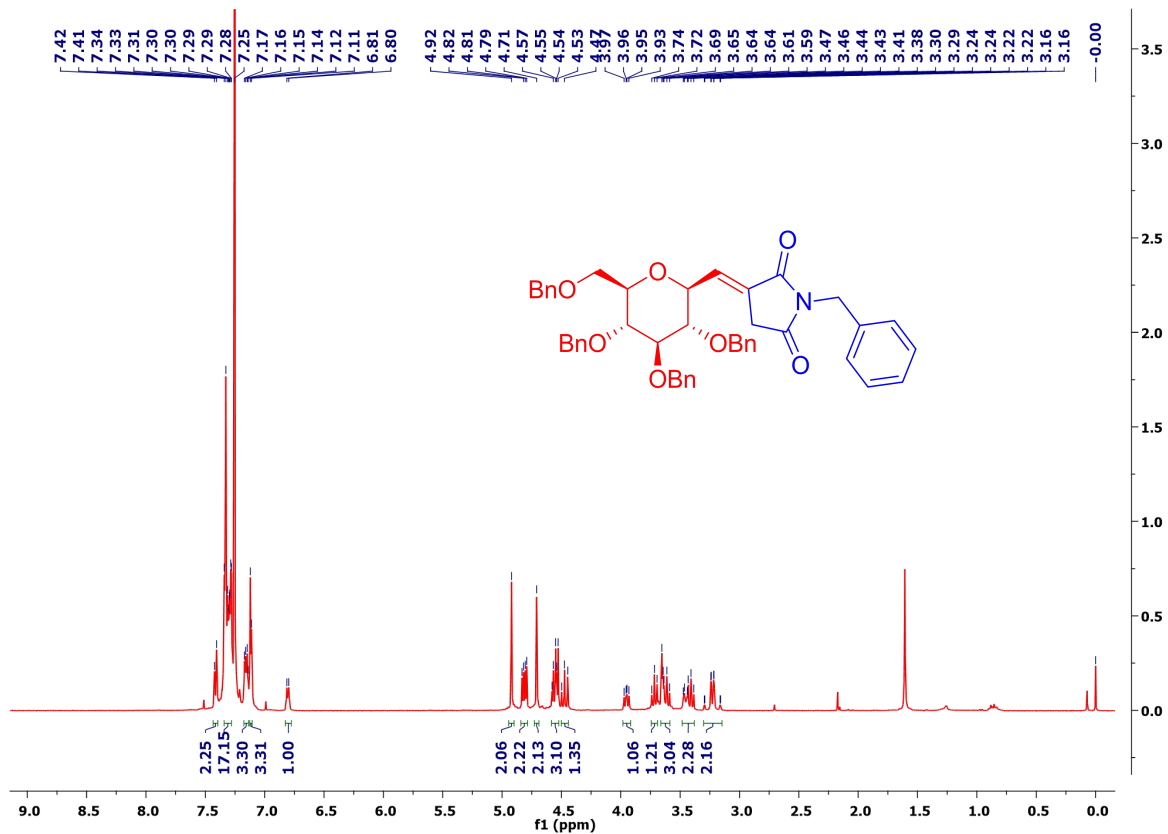


Figure S6. ^{13}C NMR spectrum of compound **3c** (100.6 MHz, CDCl_3).



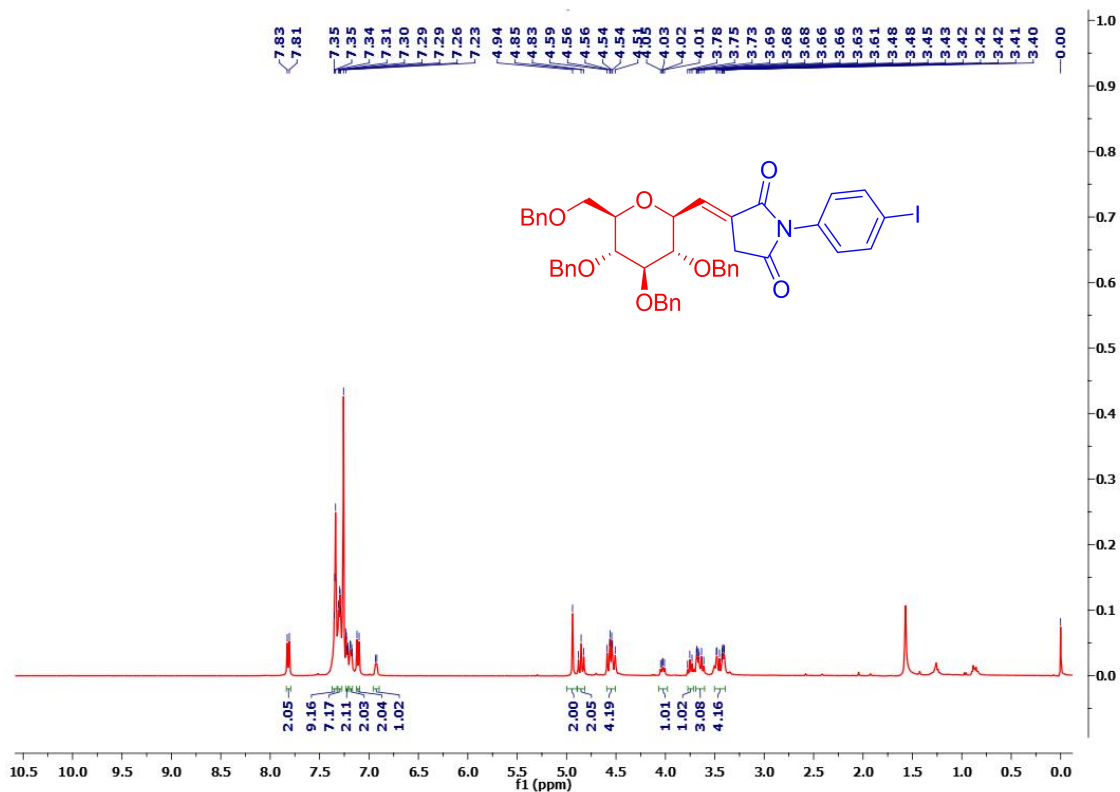


Figure S9. ^1H NMR spectrum of compound 3e (400 MHz, CDCl_3).

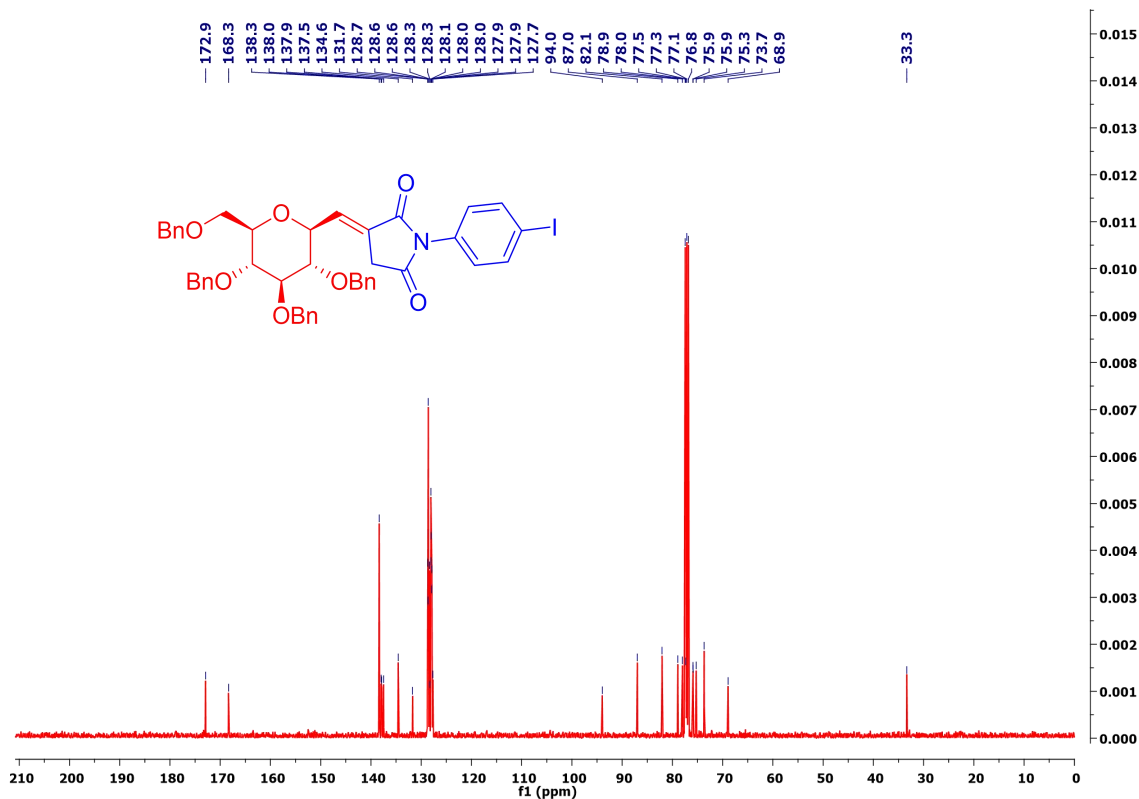


Figure S10. ^{13}C NMR spectrum of compound 3e (100.6 MHz, CDCl_3).

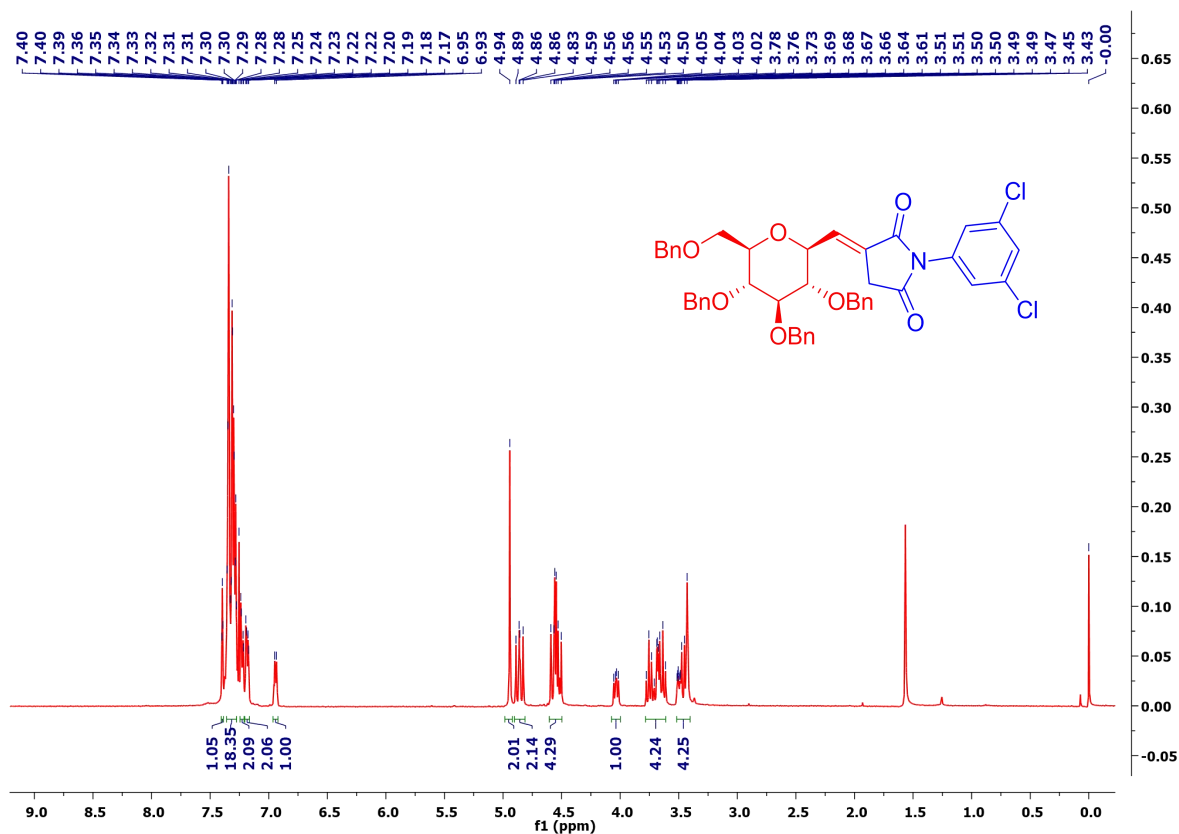


Figure S11. ^1H NMR spectrum of compound **3f** (400 MHz, CDCl_3).

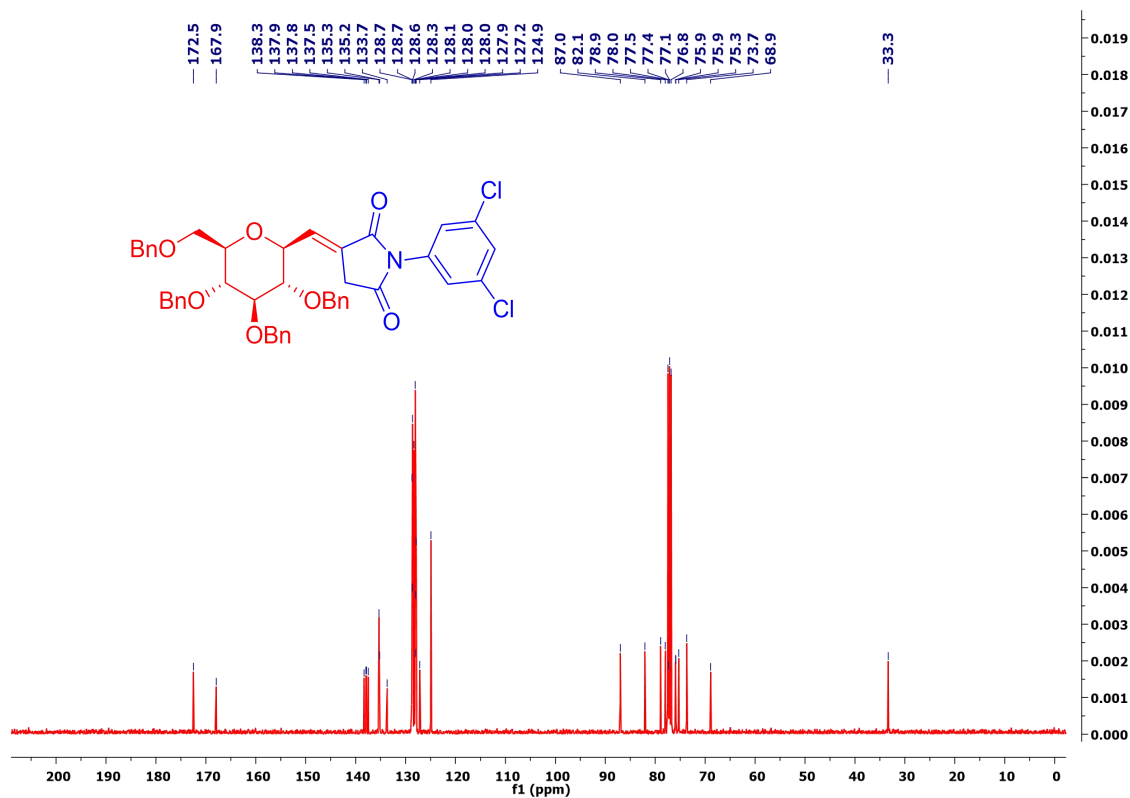
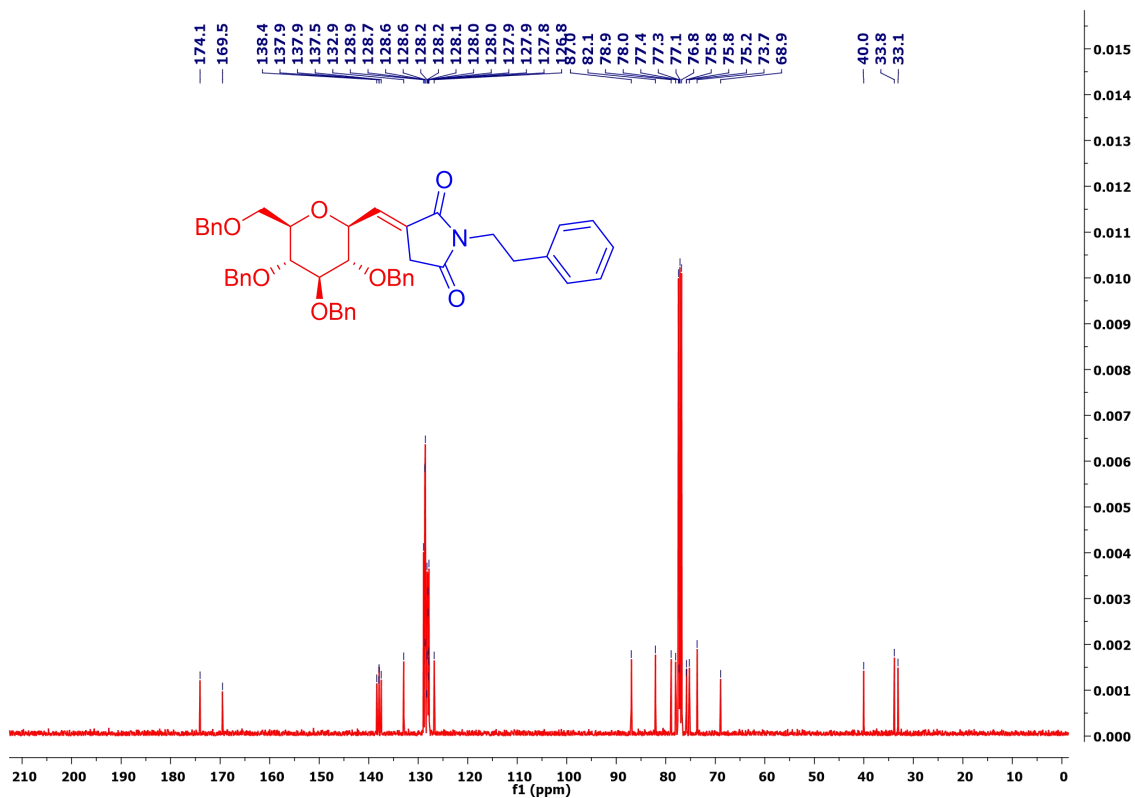
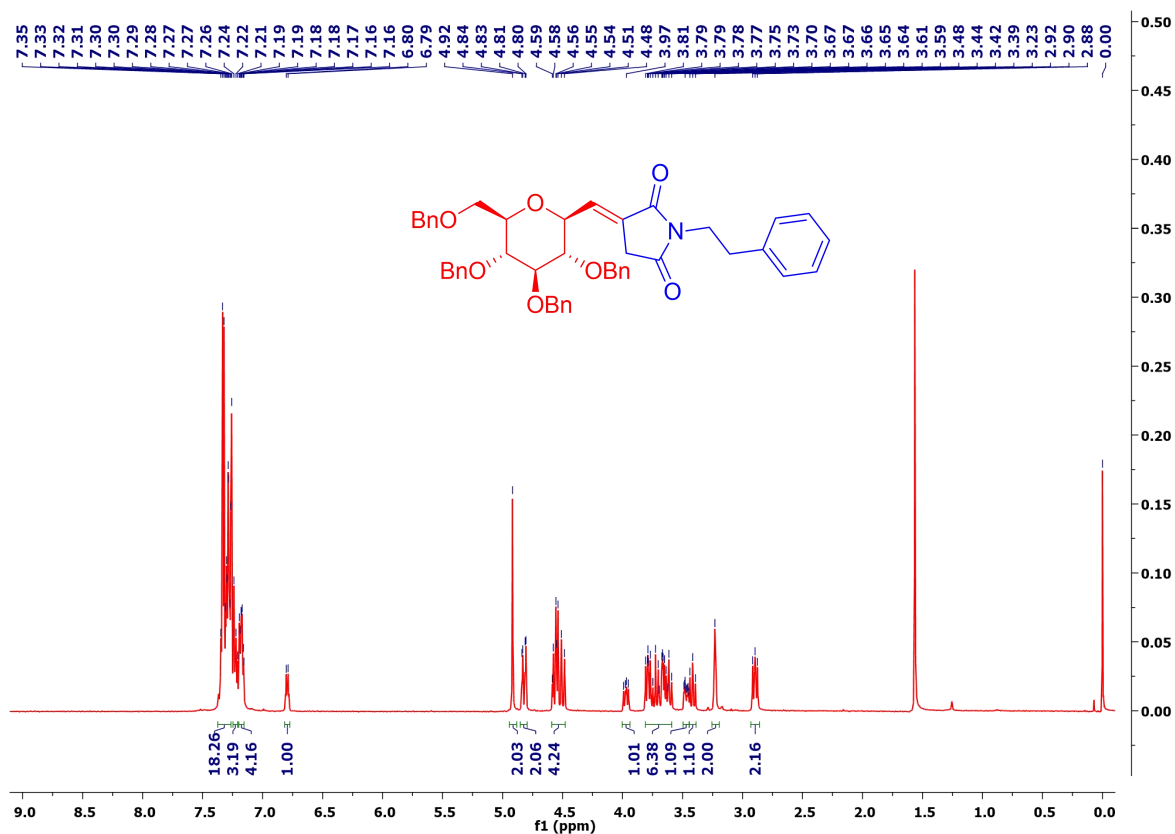


Figure S12. ^{13}C NMR spectrum of compound **3f** (100.6 MHz, CDCl_3).



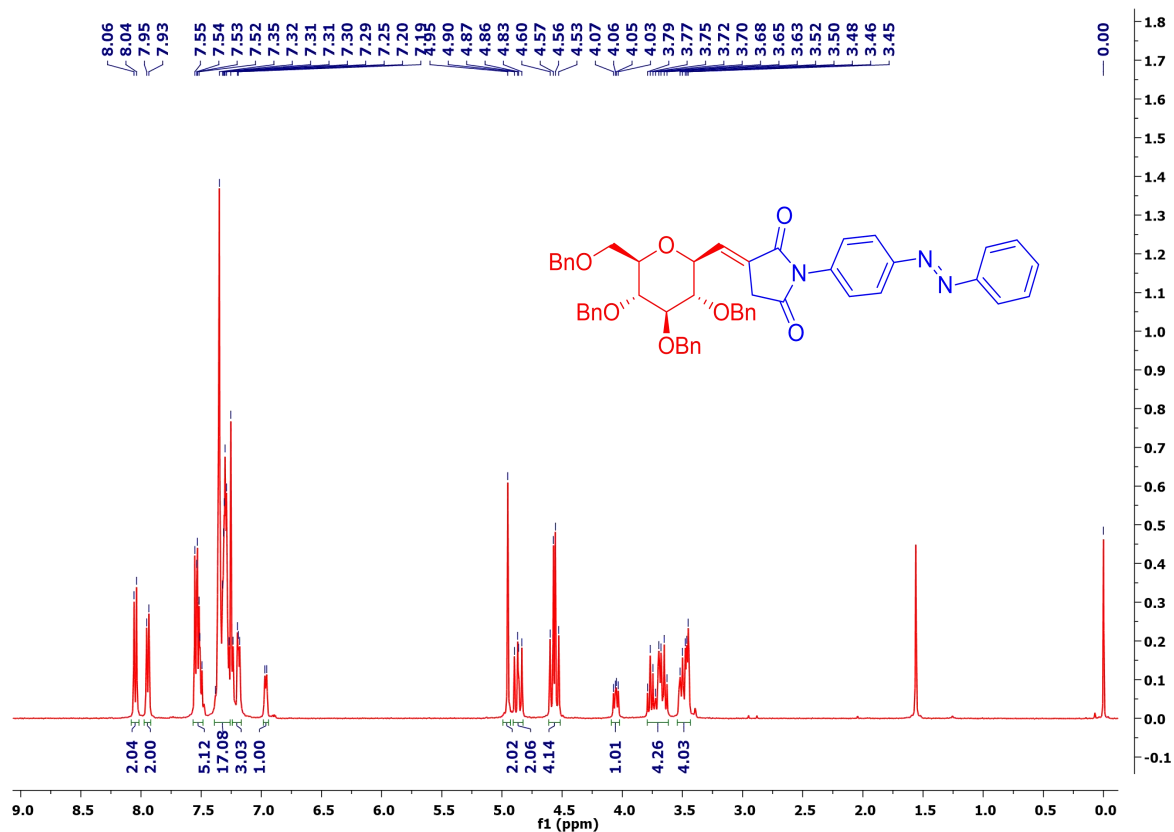


Figure S15. ^1H NMR spectrum of compound **3h** (400 MHz, CDCl_3).

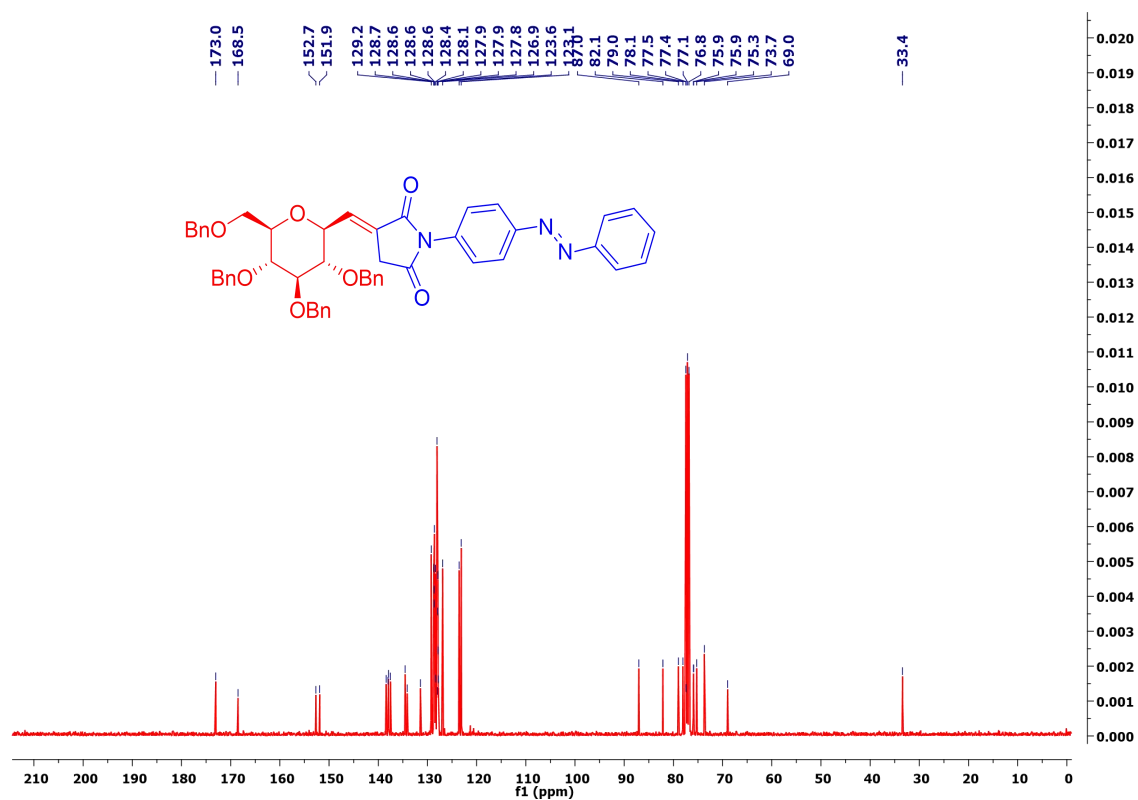


Figure S16. ^{13}C NMR spectrum of compound **3h** (100.6 MHz, CDCl_3).

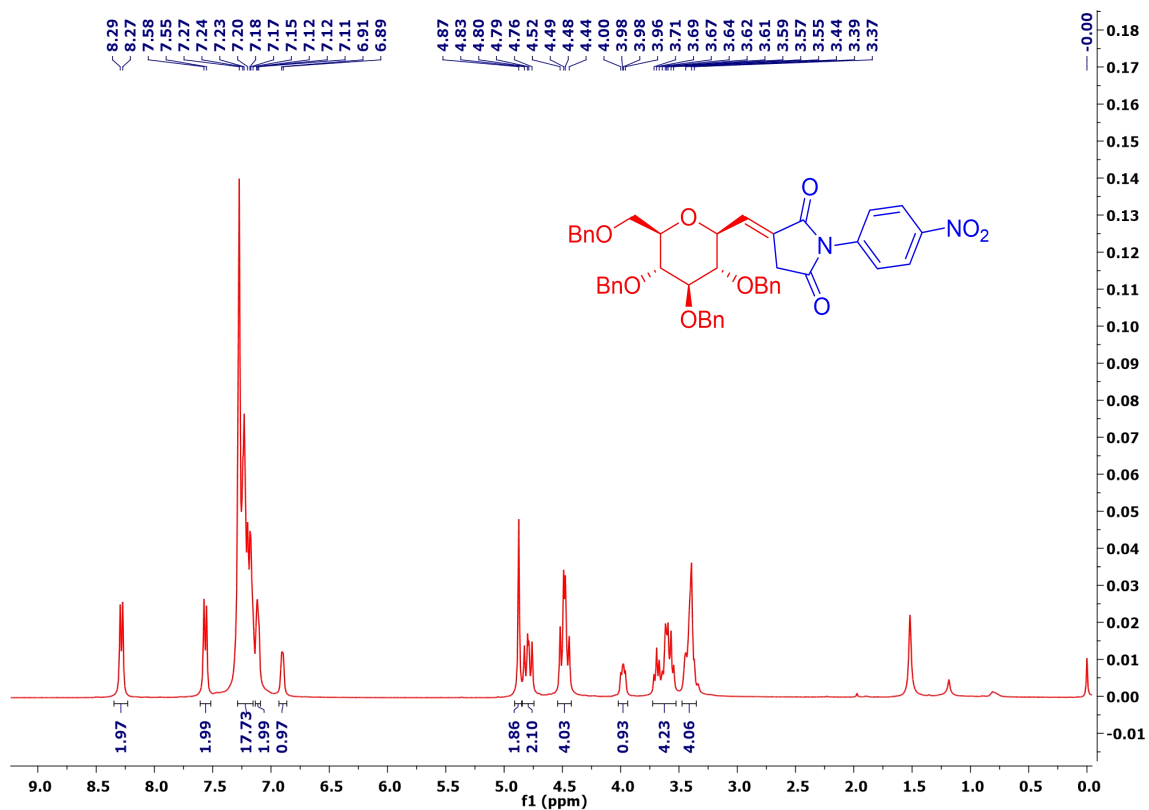


Figure S17. ^1H NMR spectrum of compound **3i** (400 MHz, CDCl_3).

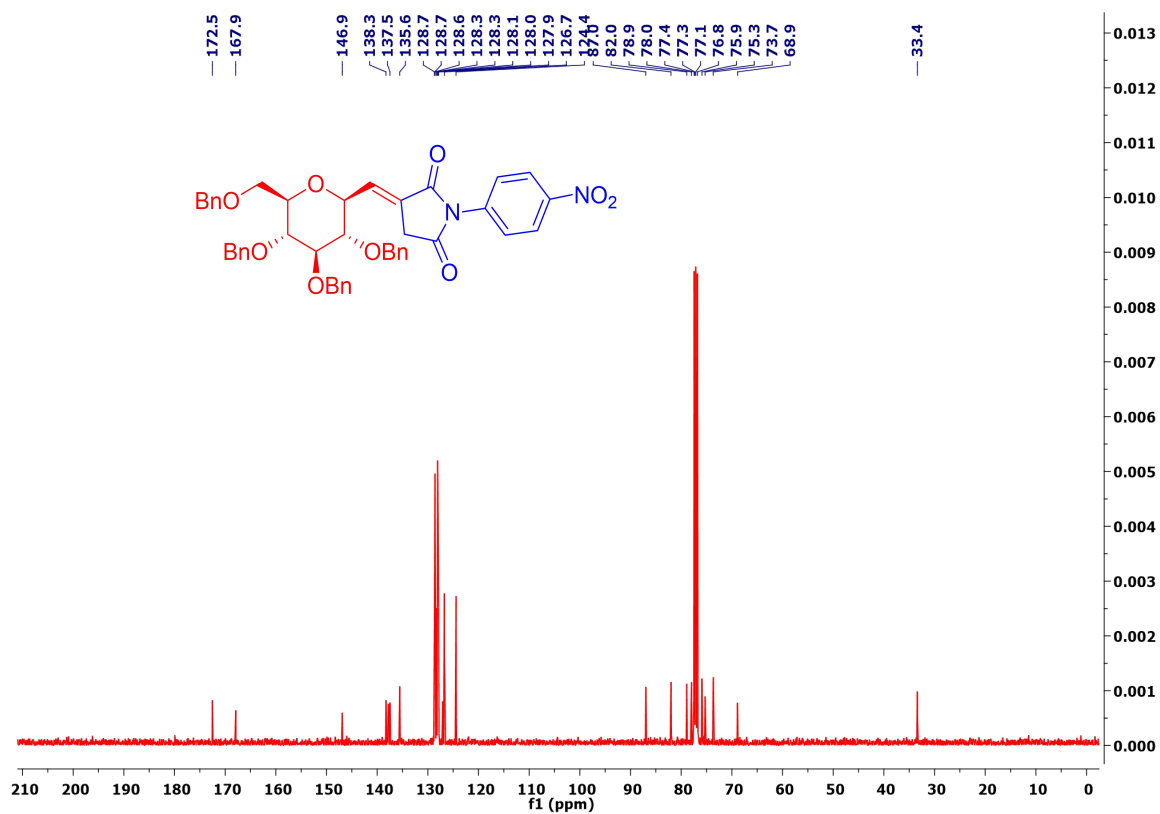
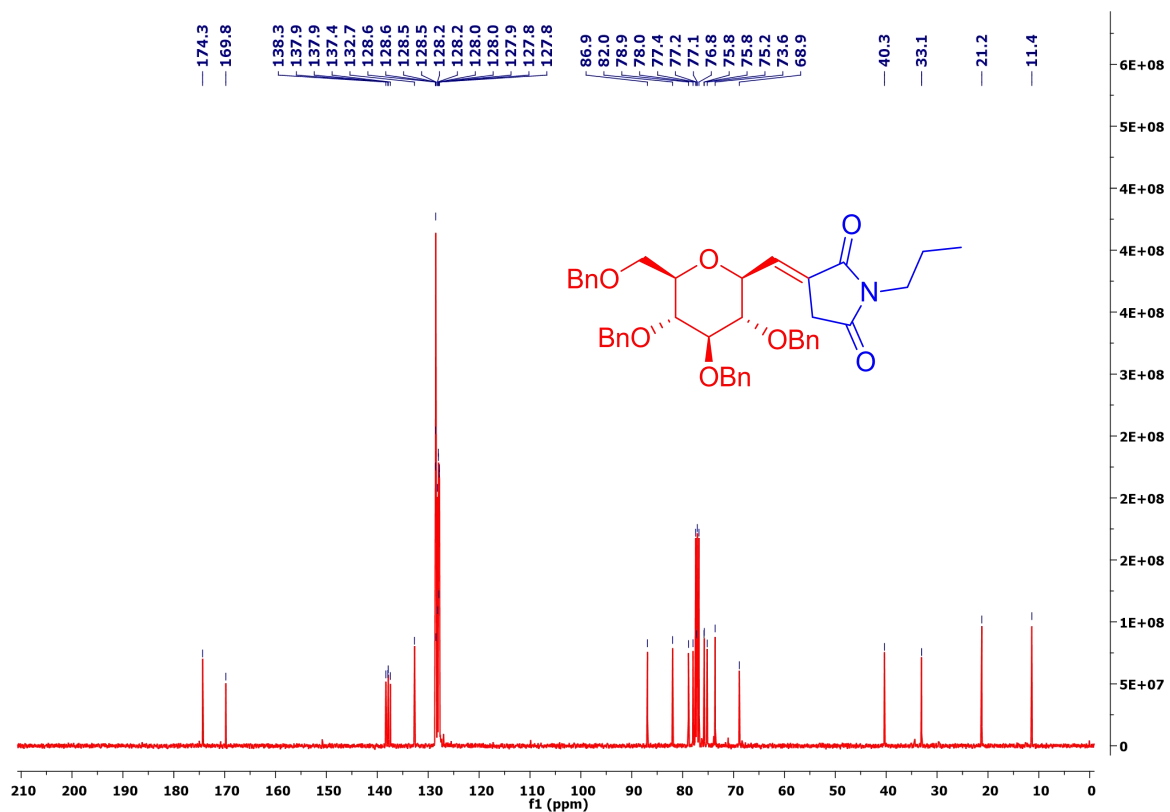
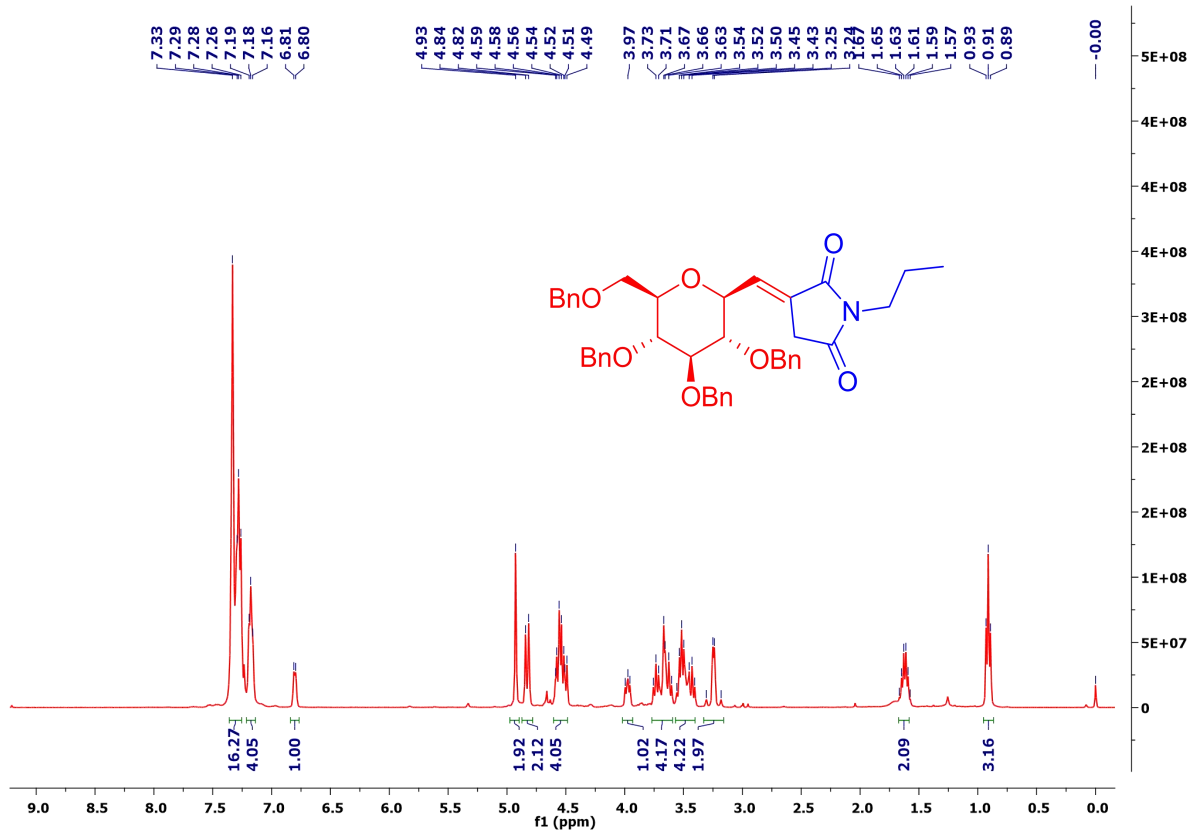


Figure S18. ^{13}C NMR spectrum of compound **3i** (100.6 MHz, CDCl_3).



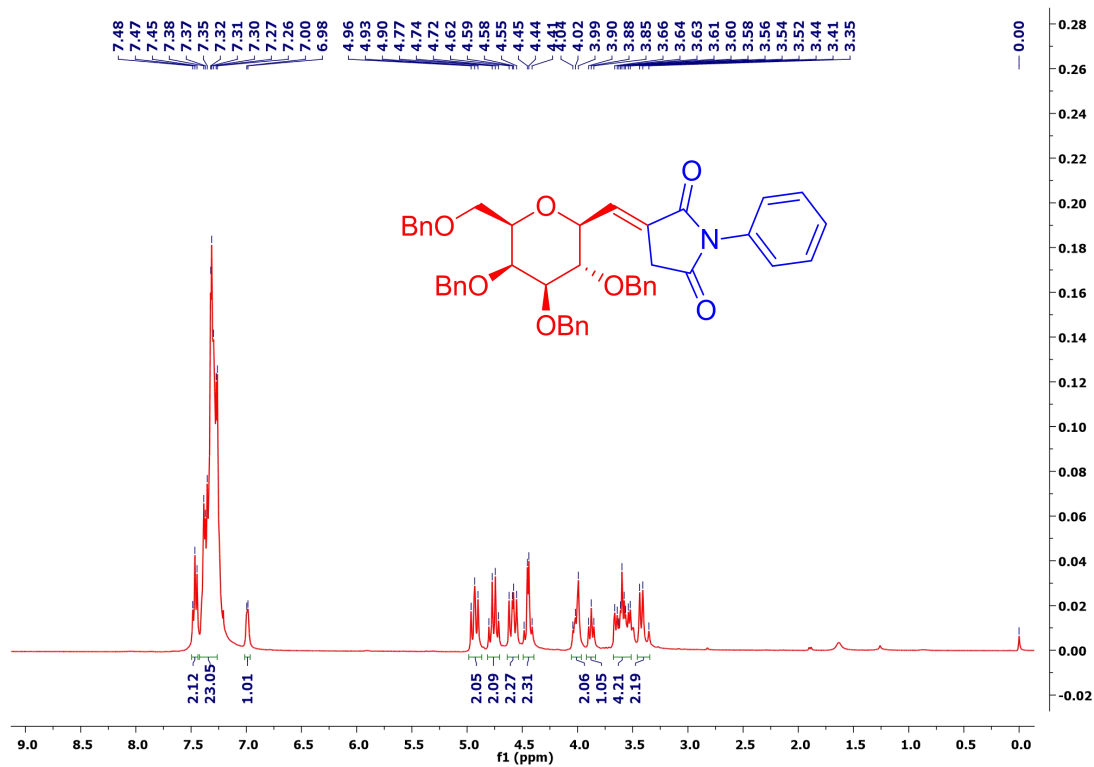


Figure S21. ^1H NMR spectrum of compound **3k** (400 MHz, CDCl_3).

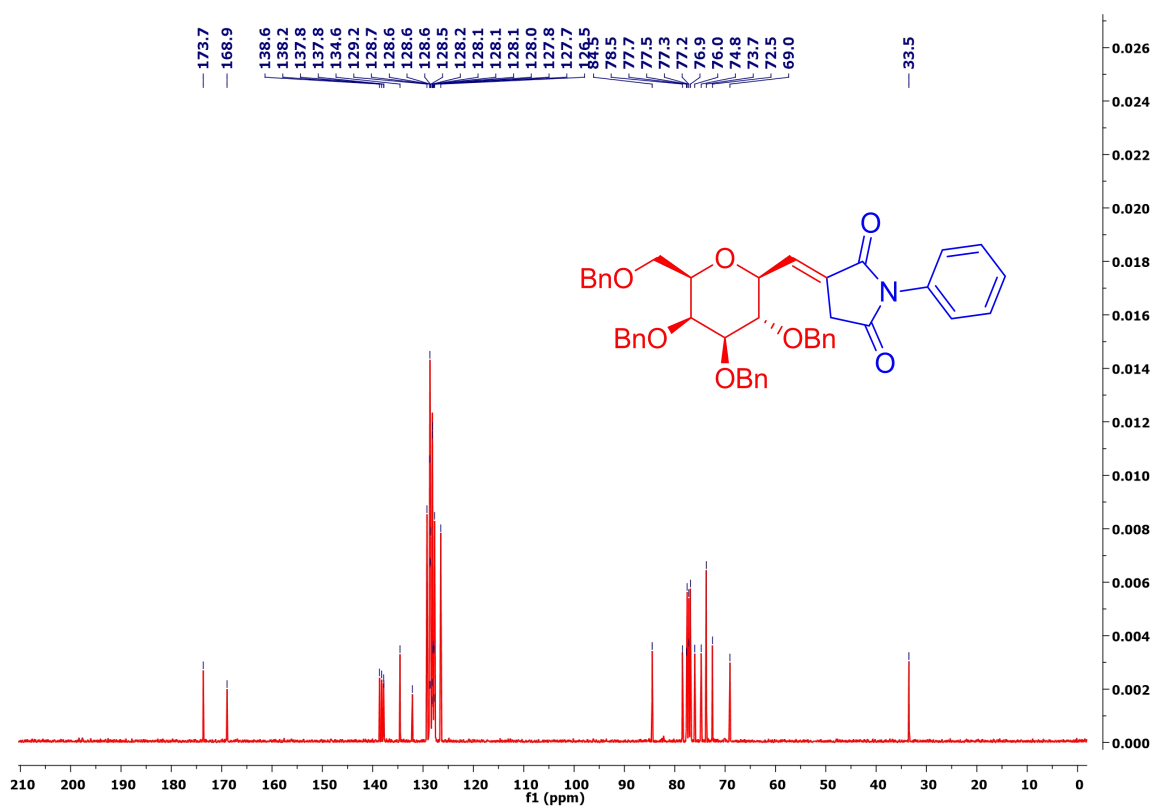
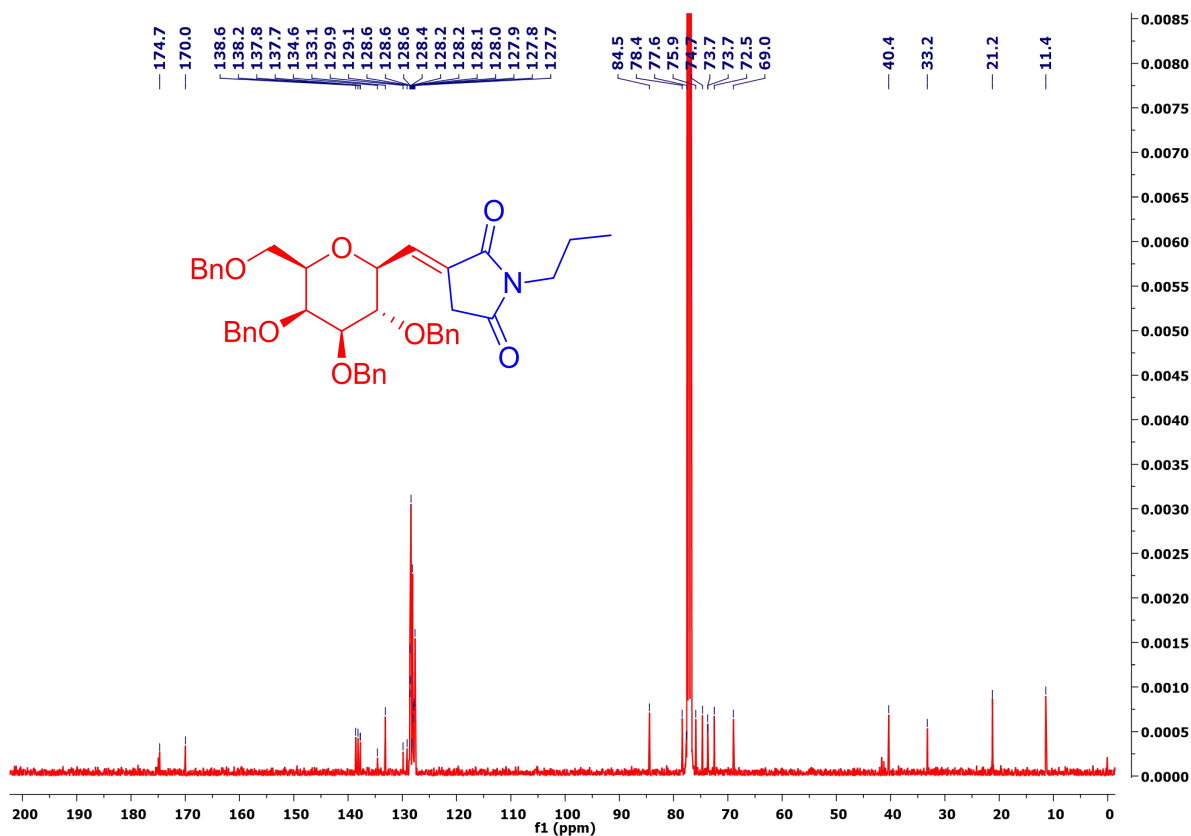
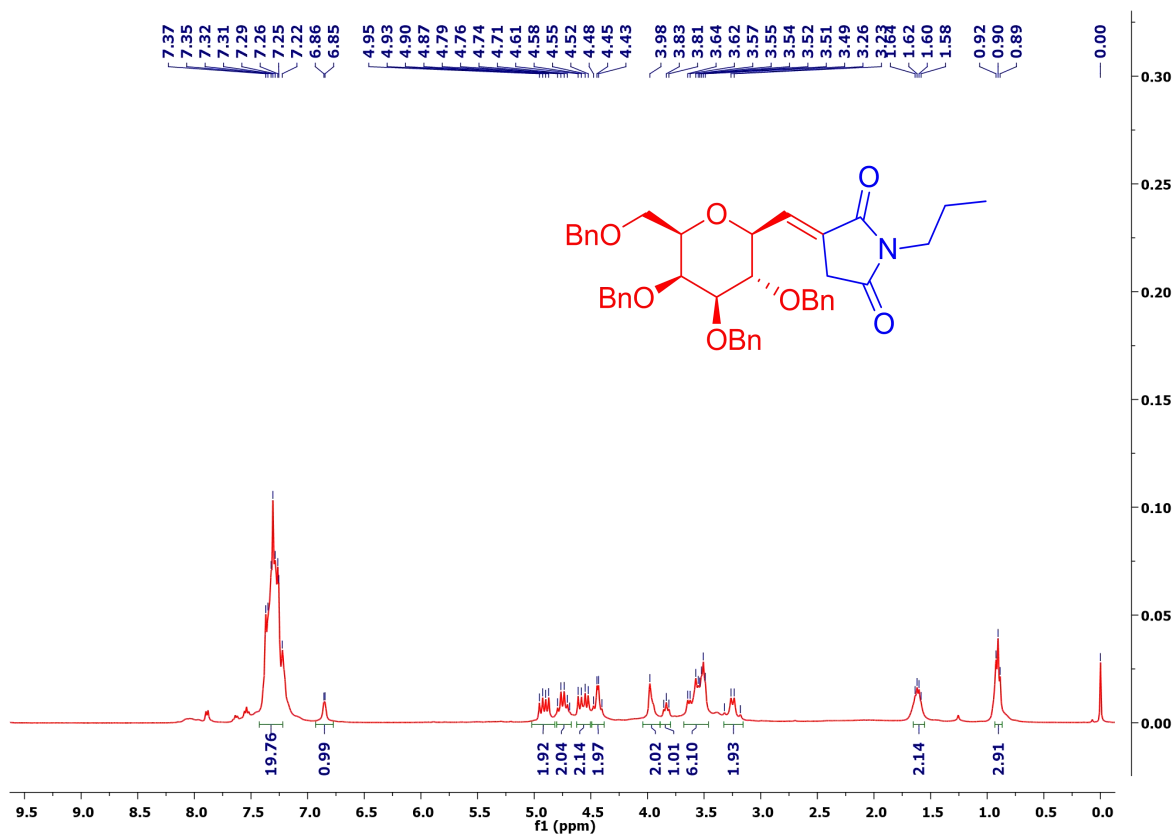


Figure S22. ^{13}C NMR spectrum of compound **3k** (100.6 MHz, CDCl_3).



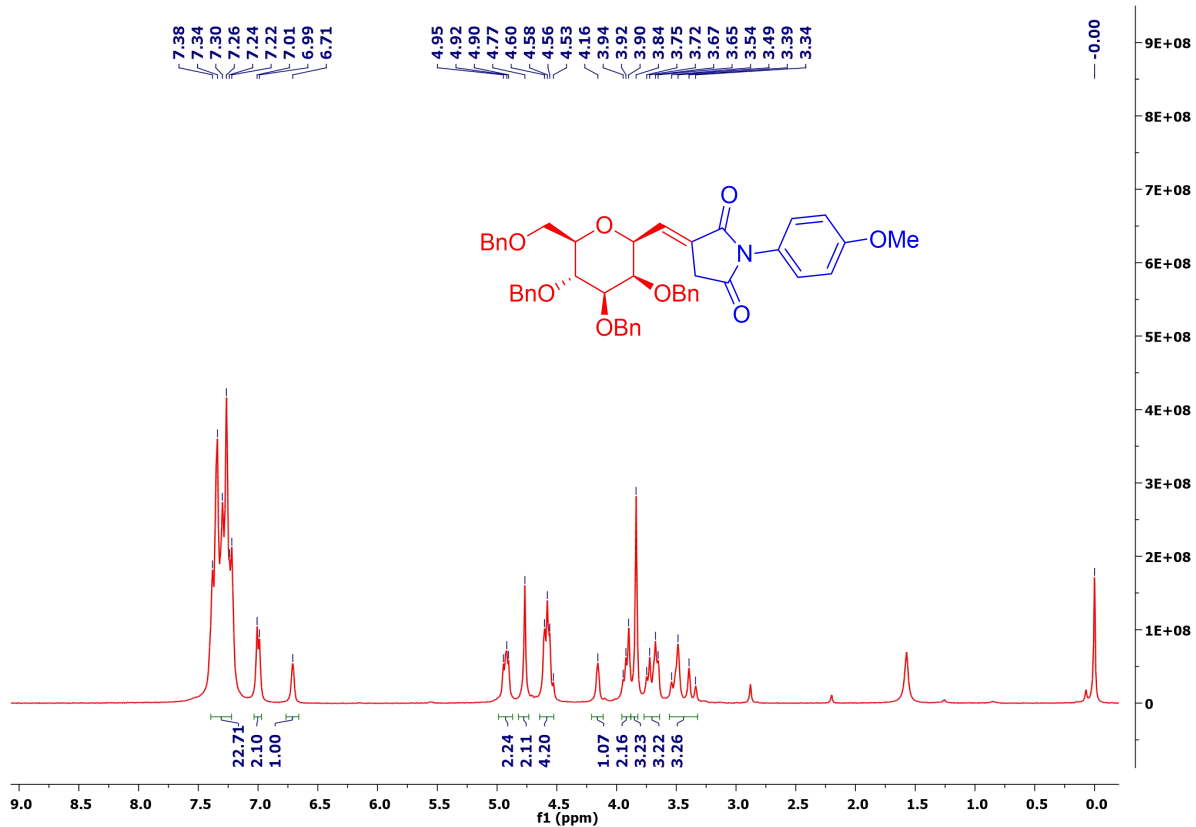


Figure S25. ¹H NMR spectrum of compound **3m** (400 MHz, CDCl₃).

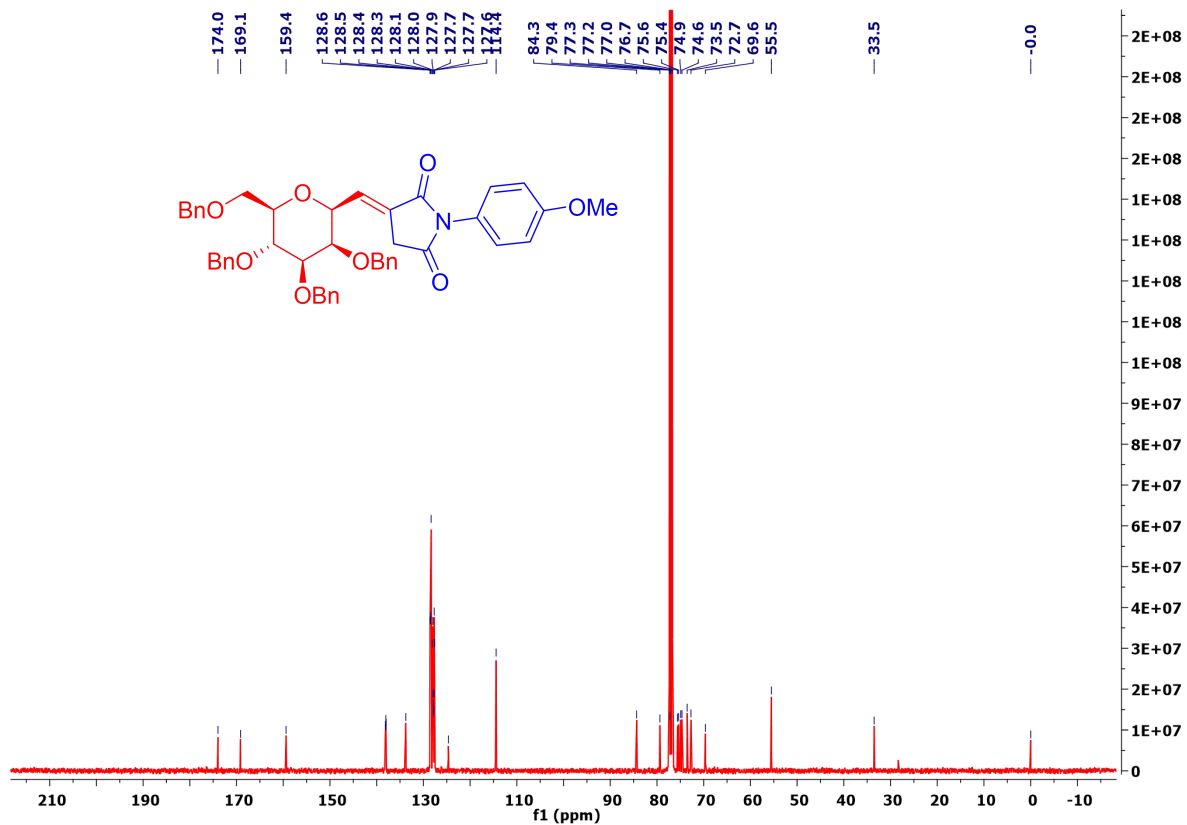


Figure S26. ¹³C NMR spectrum of compound **3m** (100.6 MHz, CDCl₃).

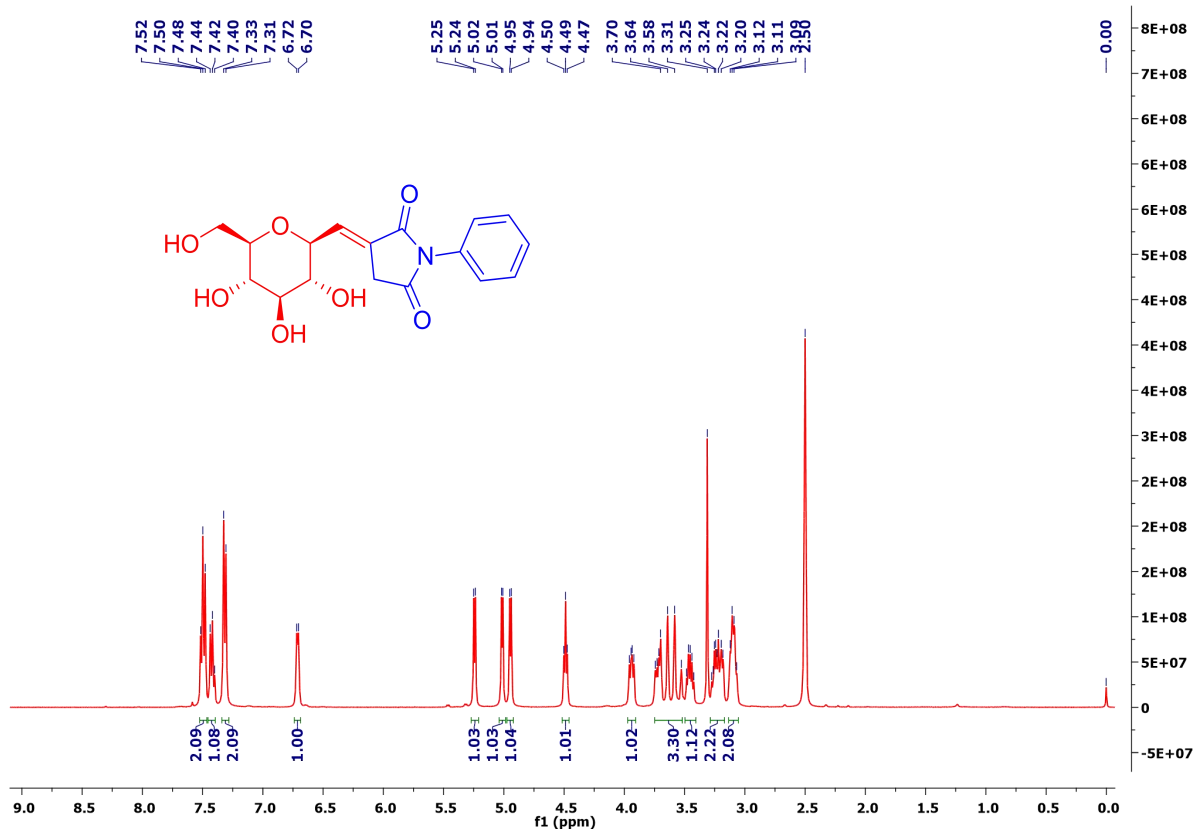


Figure S27. ^1H NMR spectrum of compound 4a (400 MHz, $\text{DMSO-}d_6$).

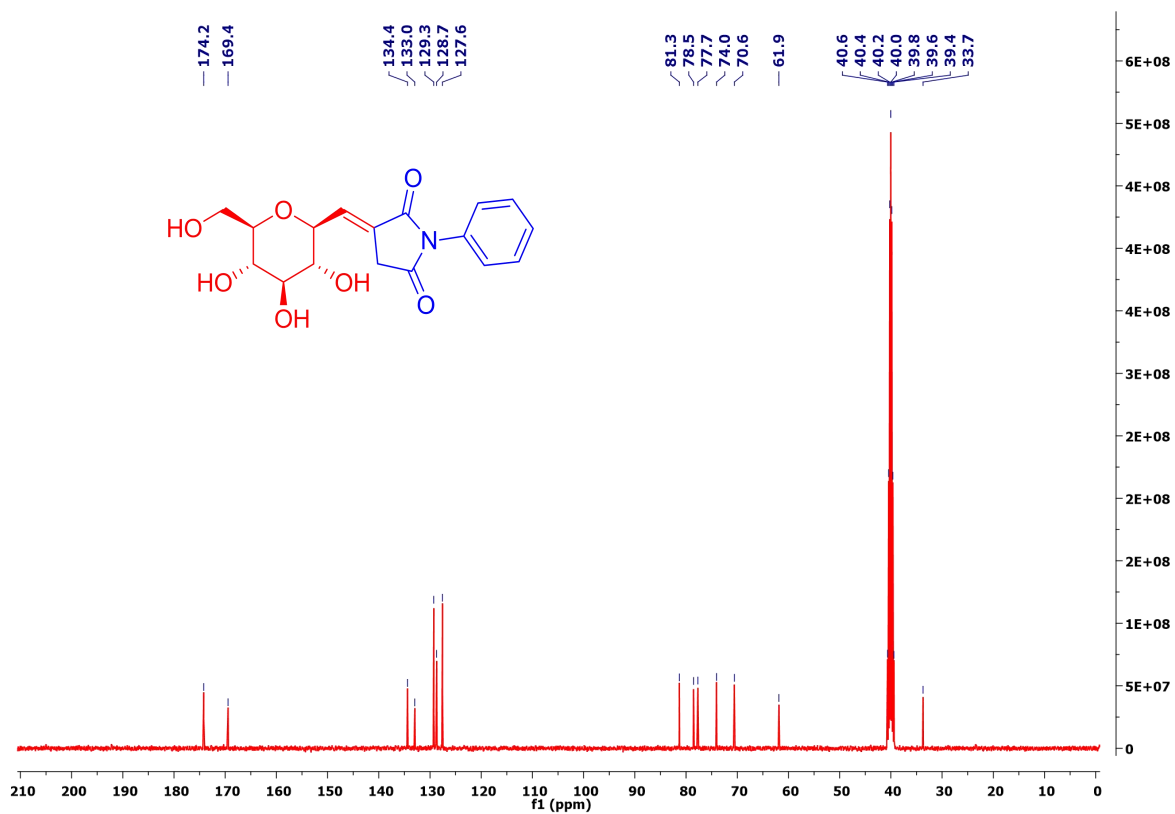


Figure S28. ^{13}C NMR spectrum of compound 4a (100.6 MHz, $\text{DMSO-}d_6$).

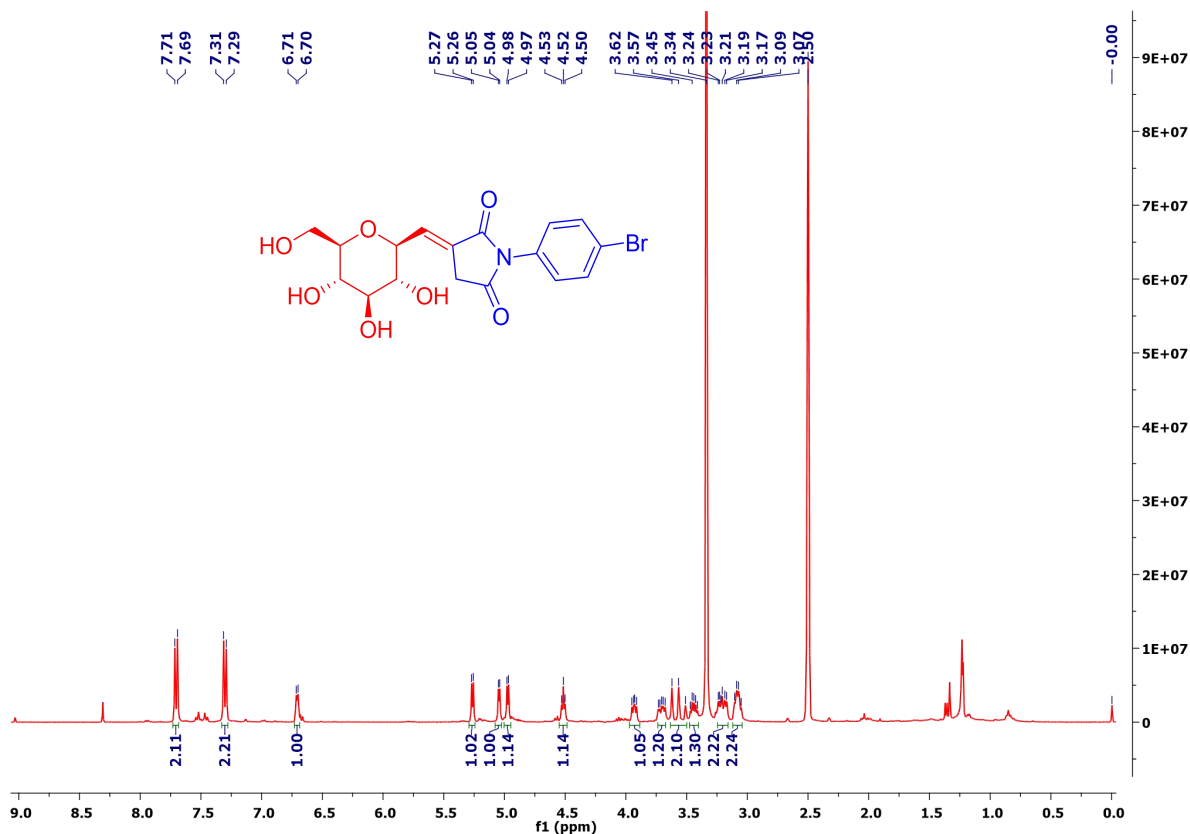


Figure S29. ¹H NMR spectrum of compound **4b** (400 MHz, DMSO-*d*₆).

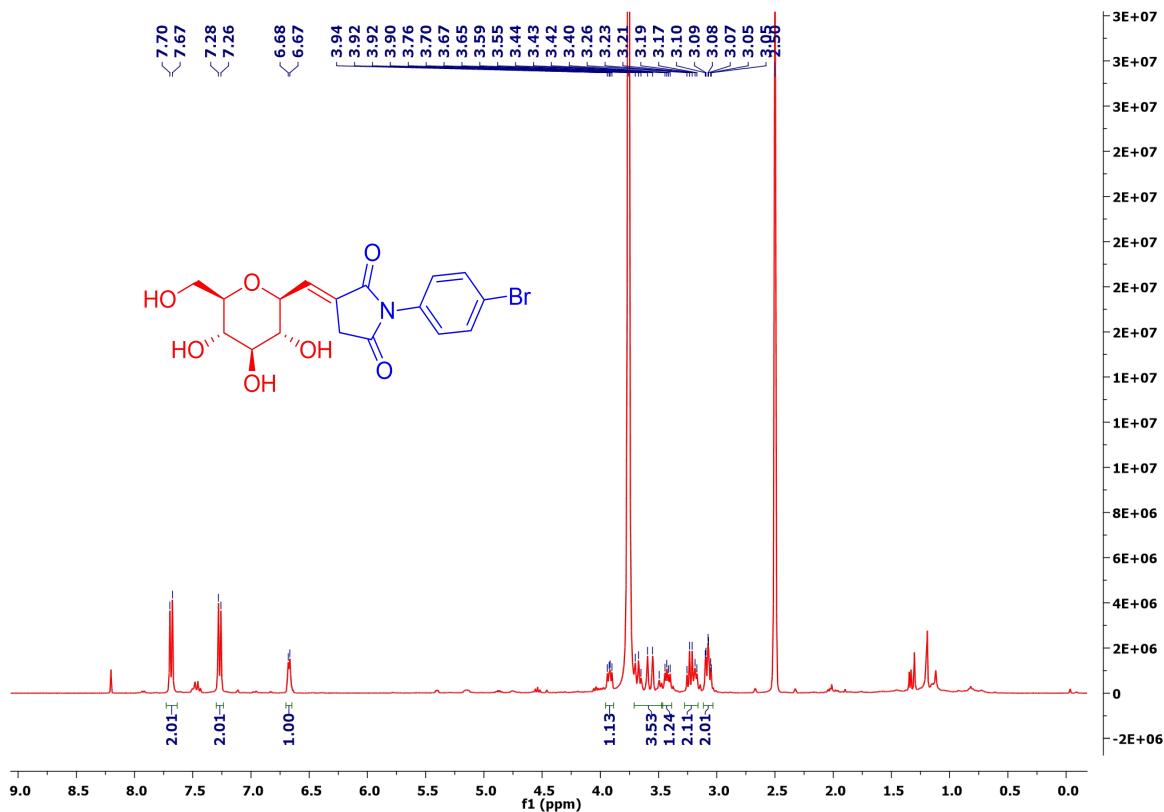


Figure S30. ¹H NMR spectrum of compound **4b** (400 MHz, D₂O-DMSO-*d*₆).

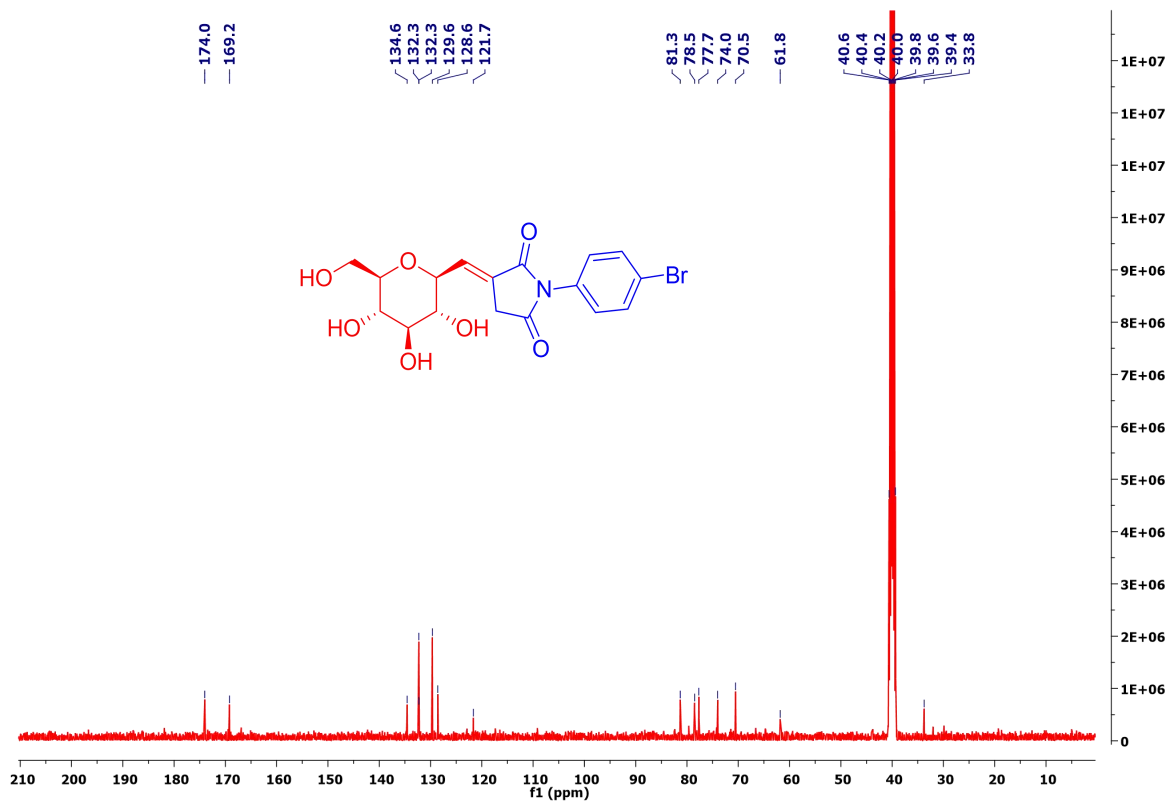


Figure S31. ^{13}C NMR spectrum of compound **4b** (100.6 MHz, $\text{DMSO-}d_6$).

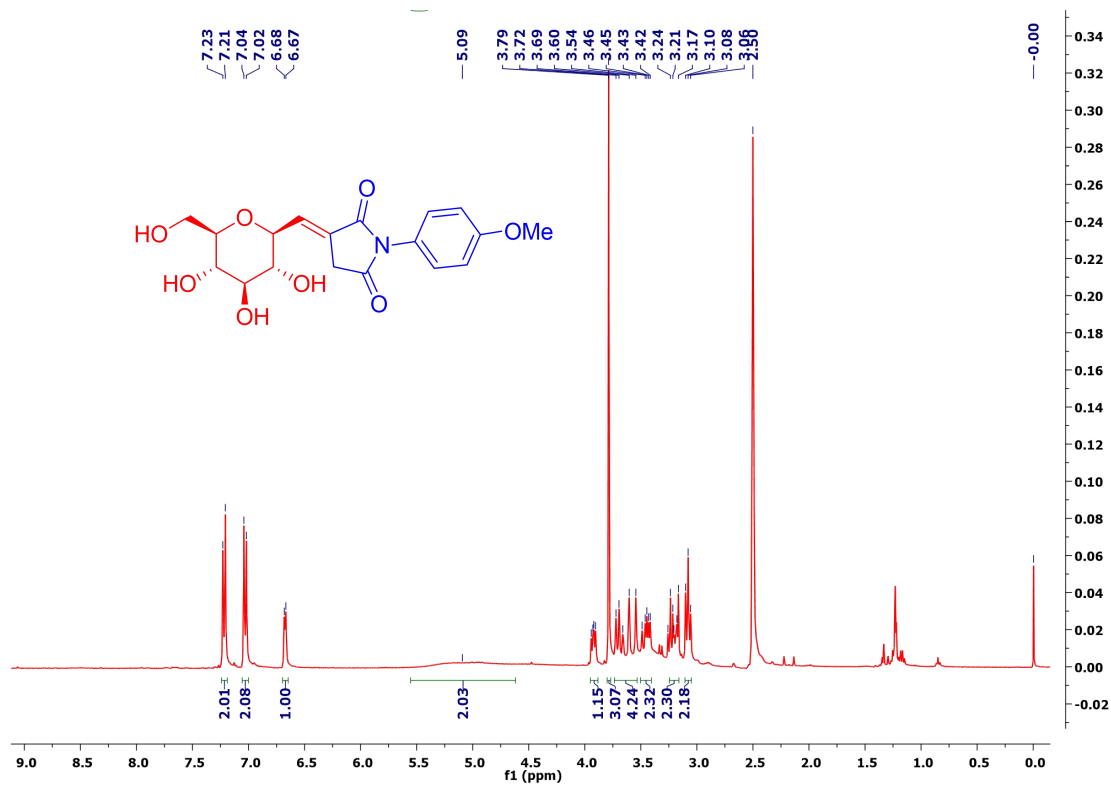


Figure S32. ^1H NMR spectrum of compound 4c (400 MHz, $\text{DMSO-}d_6$).

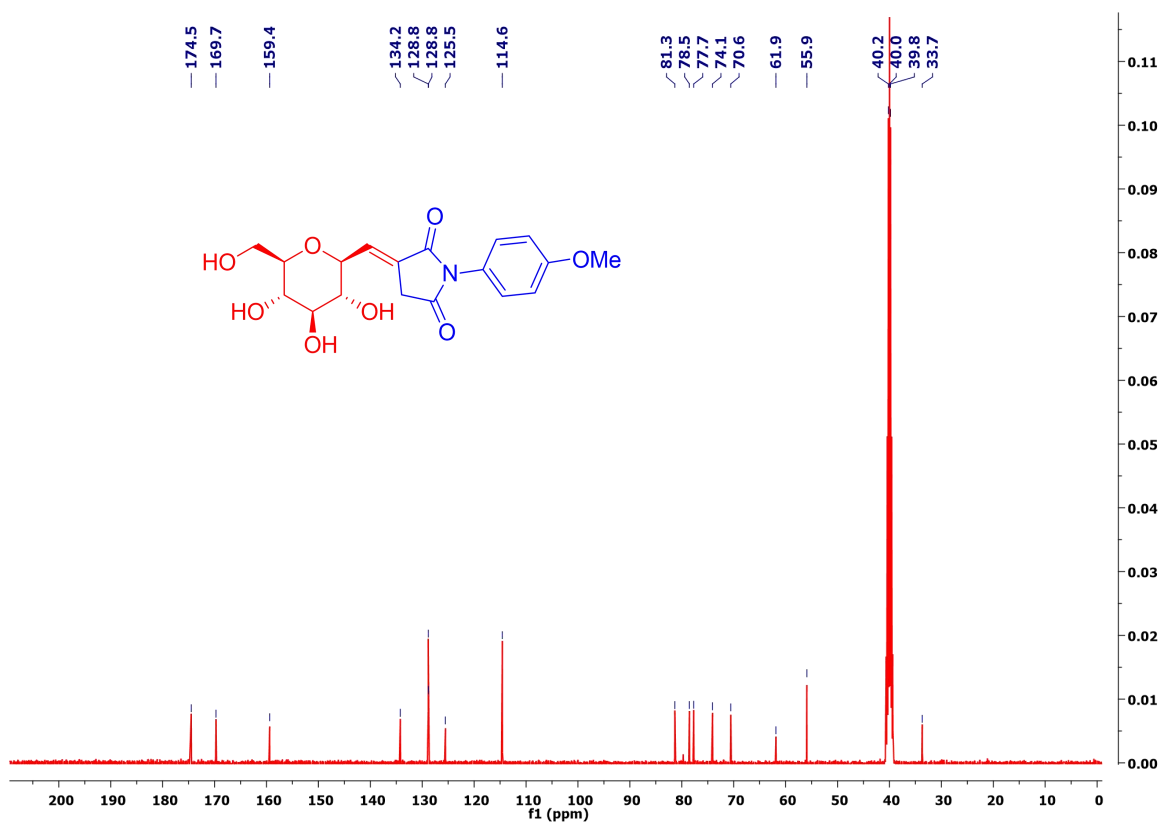


Figure S33. ^{13}C NMR spectrum of compound 4c (100.6 MHz, $\text{DMSO-}d_6$).

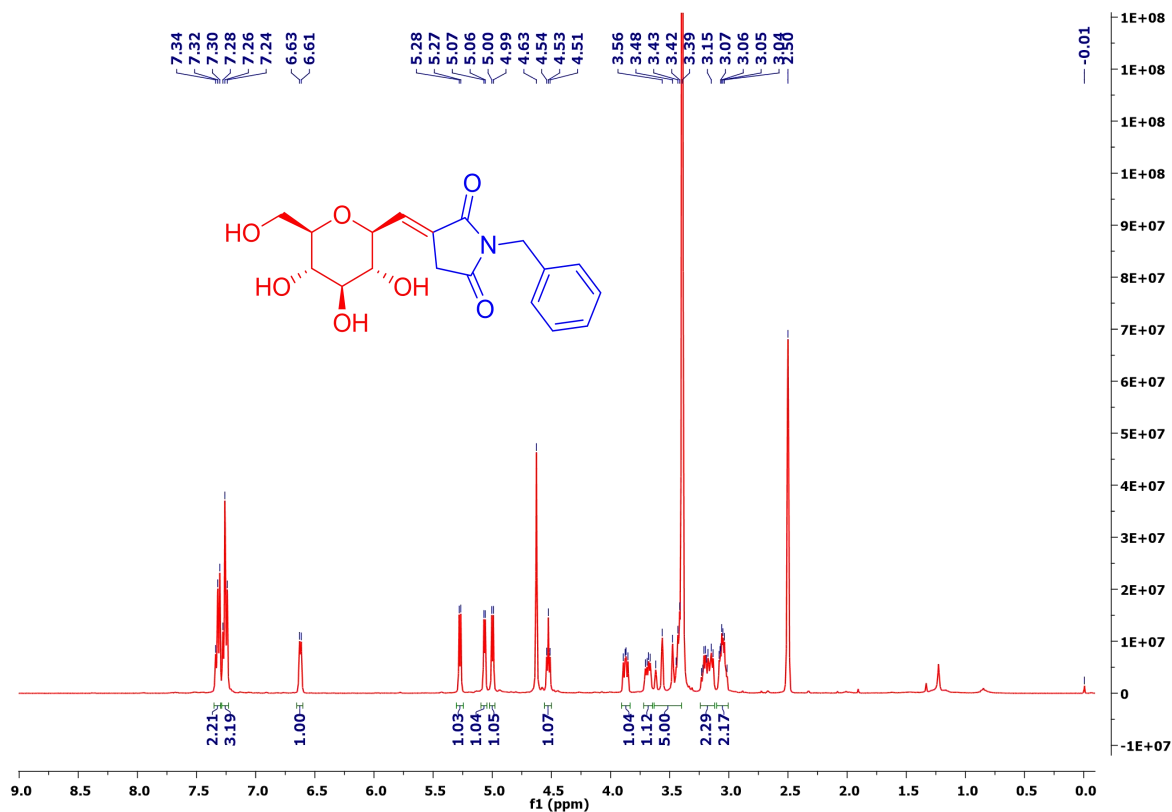


Figure S34. ¹H NMR spectrum of compound 4d (400 MHz, DMSO-*d*₆).

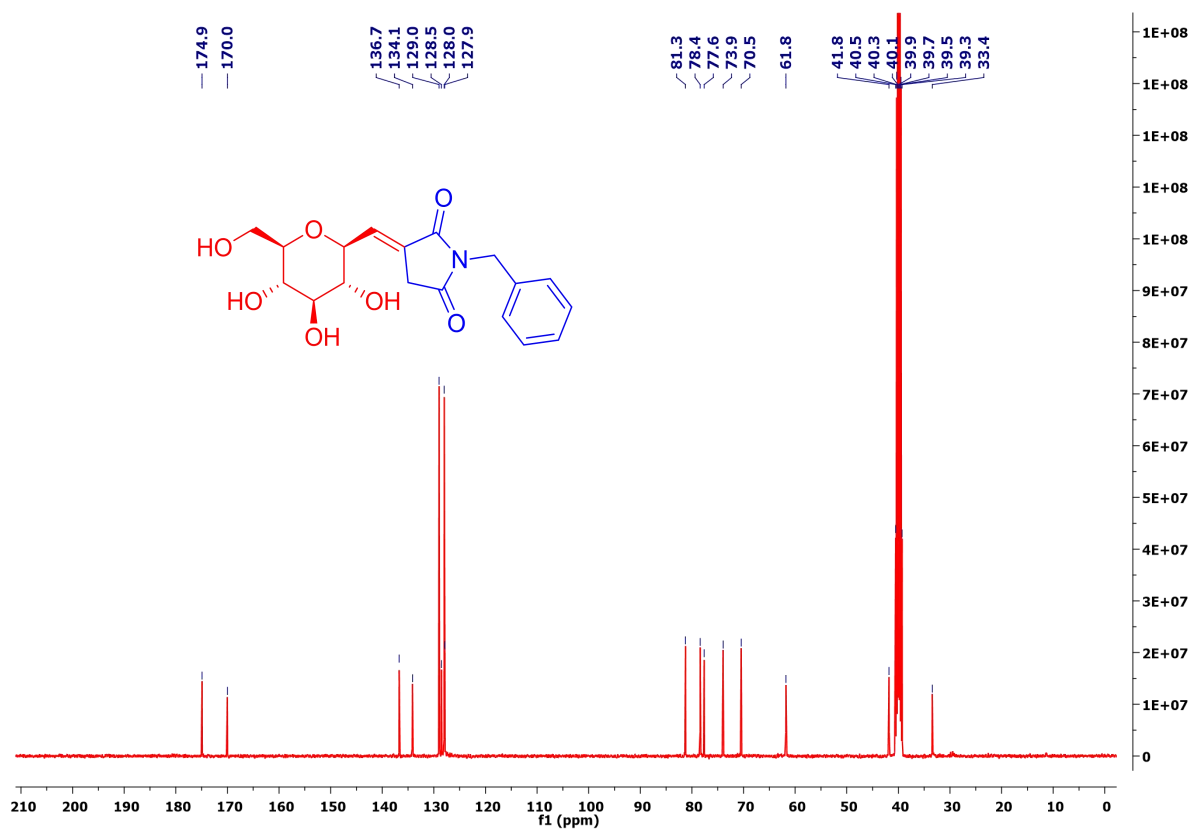


Figure S35. ¹³C NMR spectrum of compound 4d (100.6 MHz, DMSO-*d*₆).

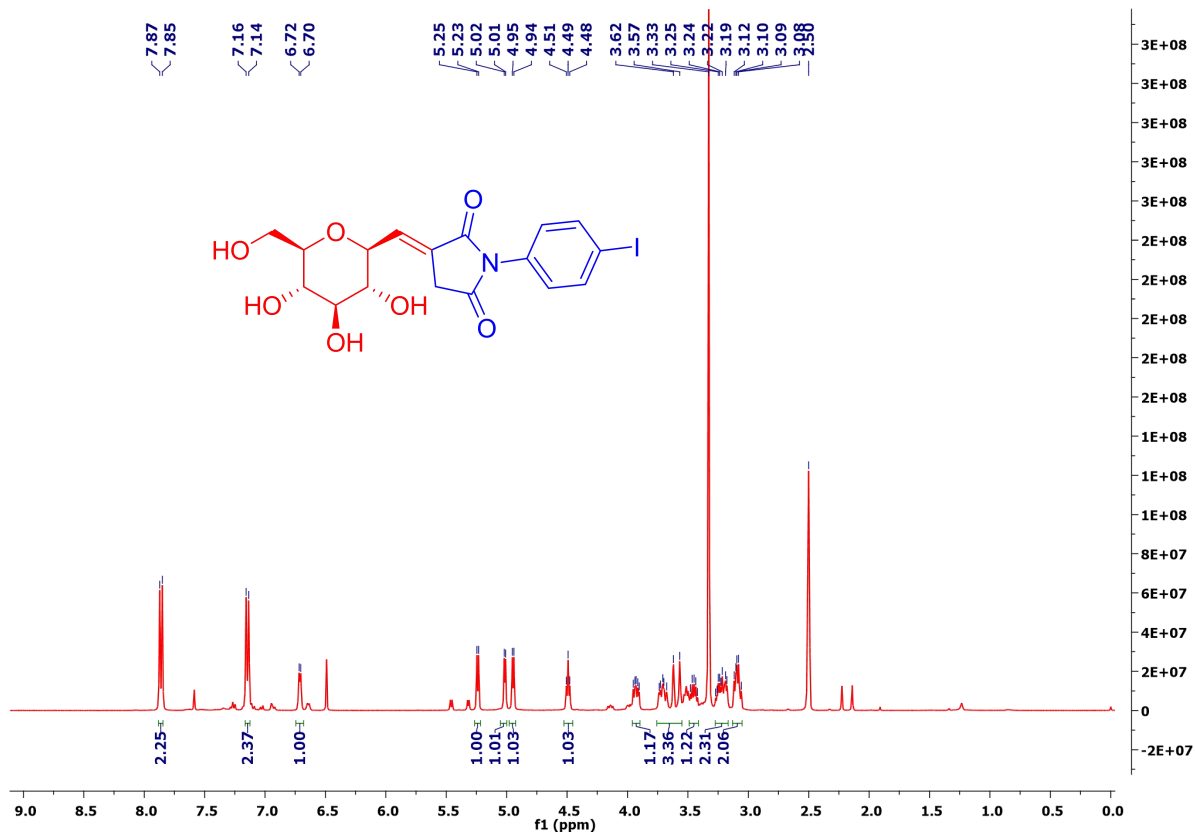


Figure S36. ^1H NMR spectrum of compound **4e** (400 MHz, $\text{DMSO-}d_6$).

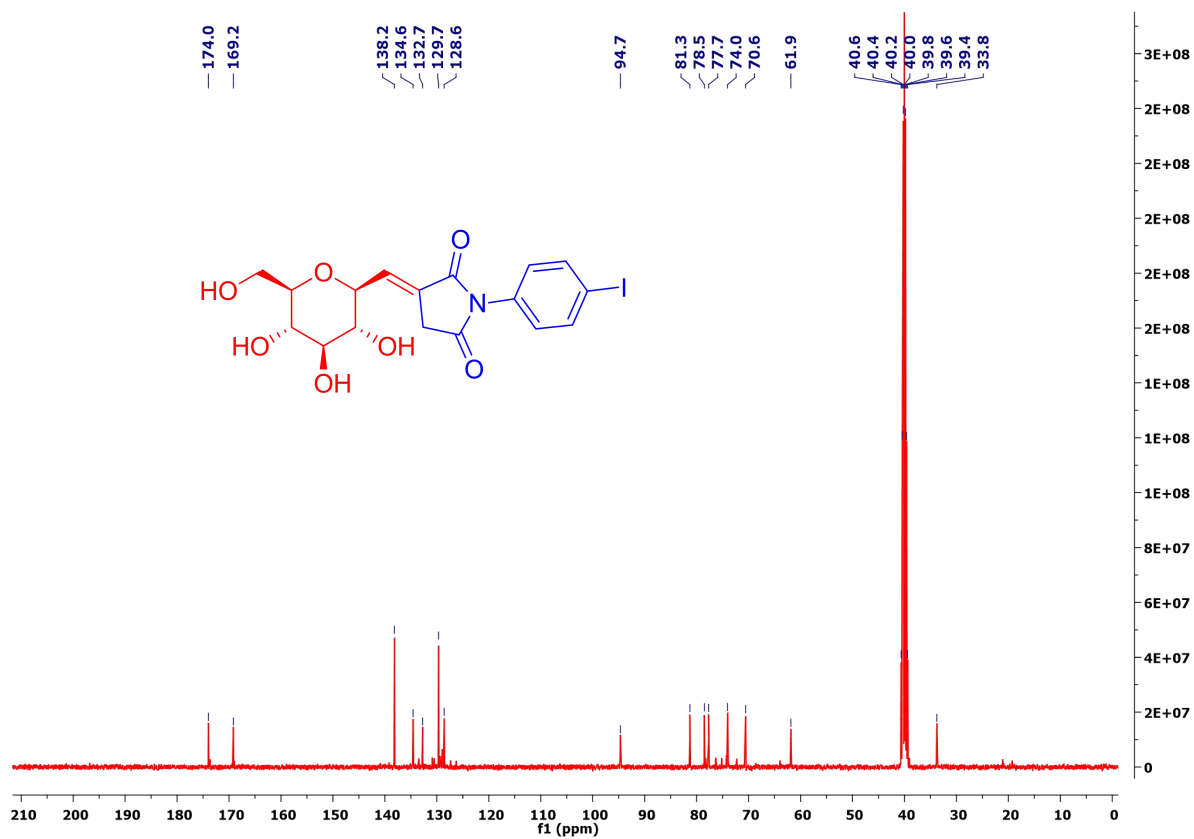


Figure S37. ^{13}C NMR spectrum of compound **4e** (100.6 MHz, $\text{DMSO-}d_6$).

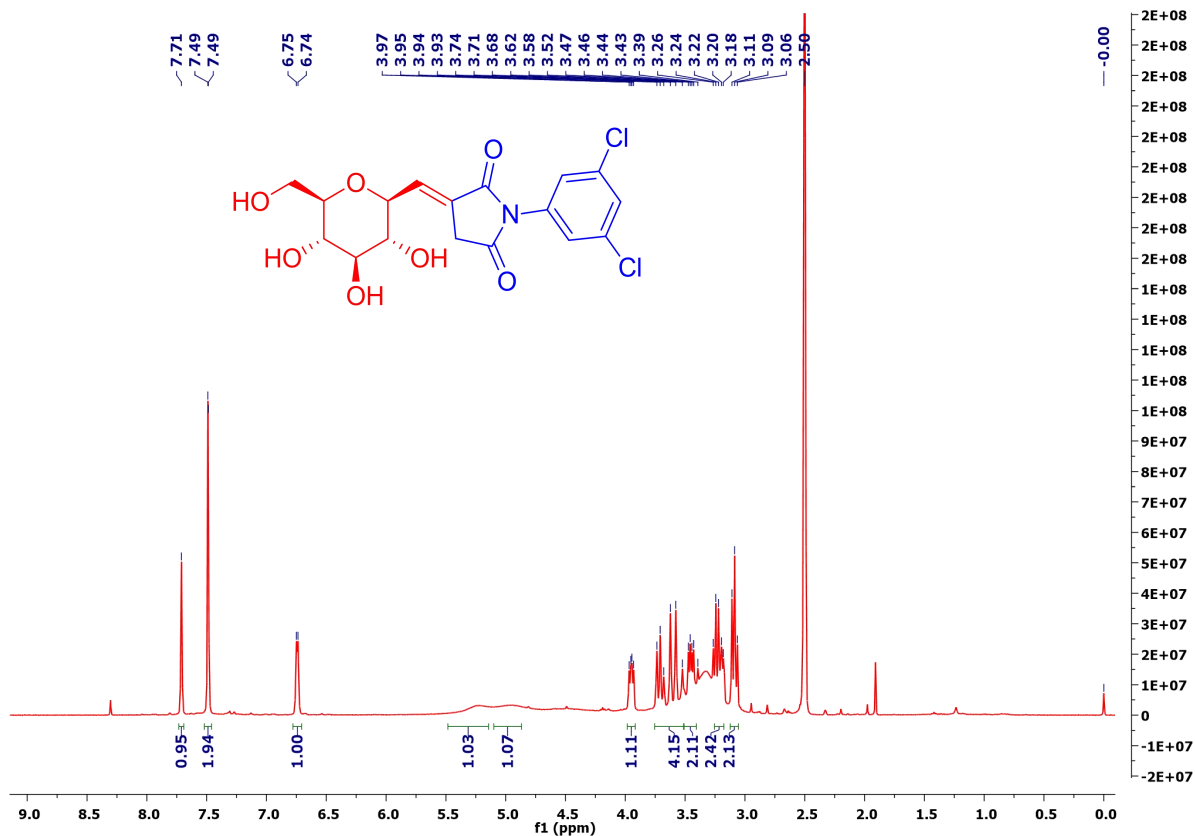


Figure S38. ¹H NMR spectrum of compound 4f (400 MHz, DMSO-*d*₆).

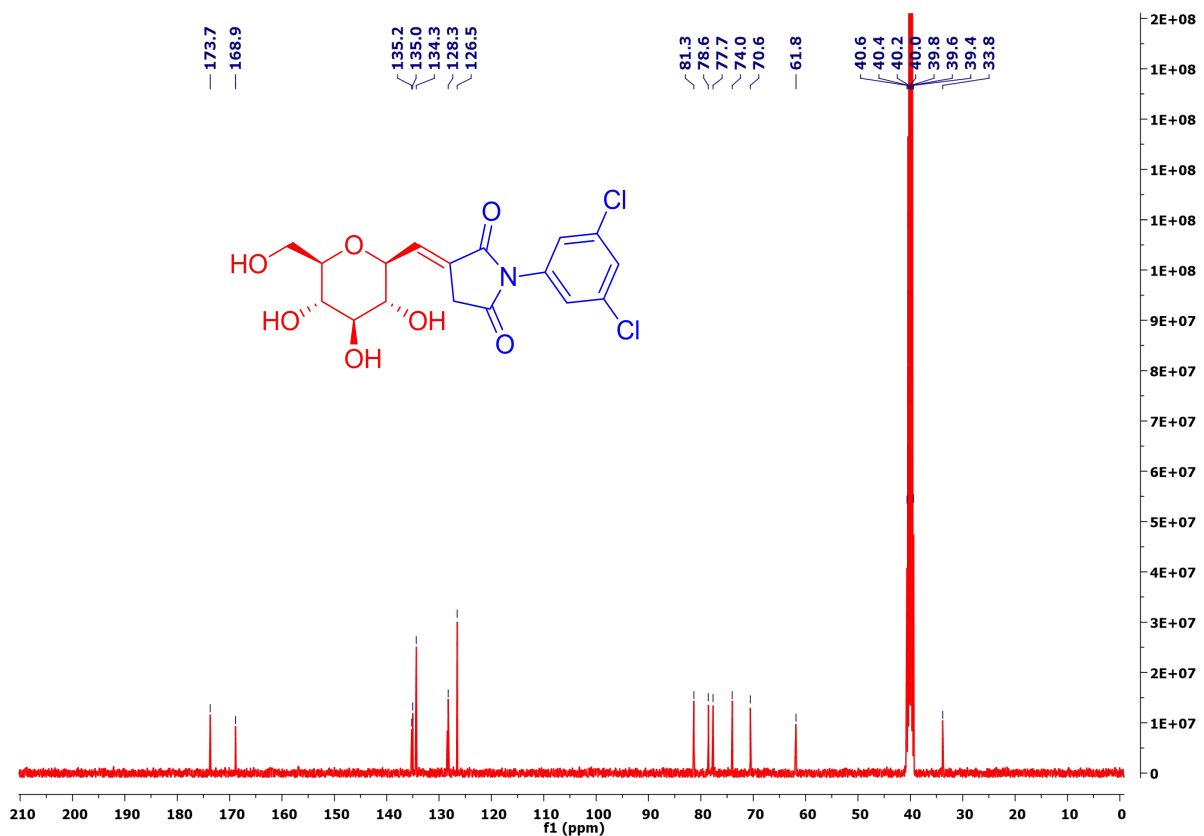


Figure S39. ¹³C NMR spectrum of compound 4f (100.6 MHz, DMSO-*d*₆).

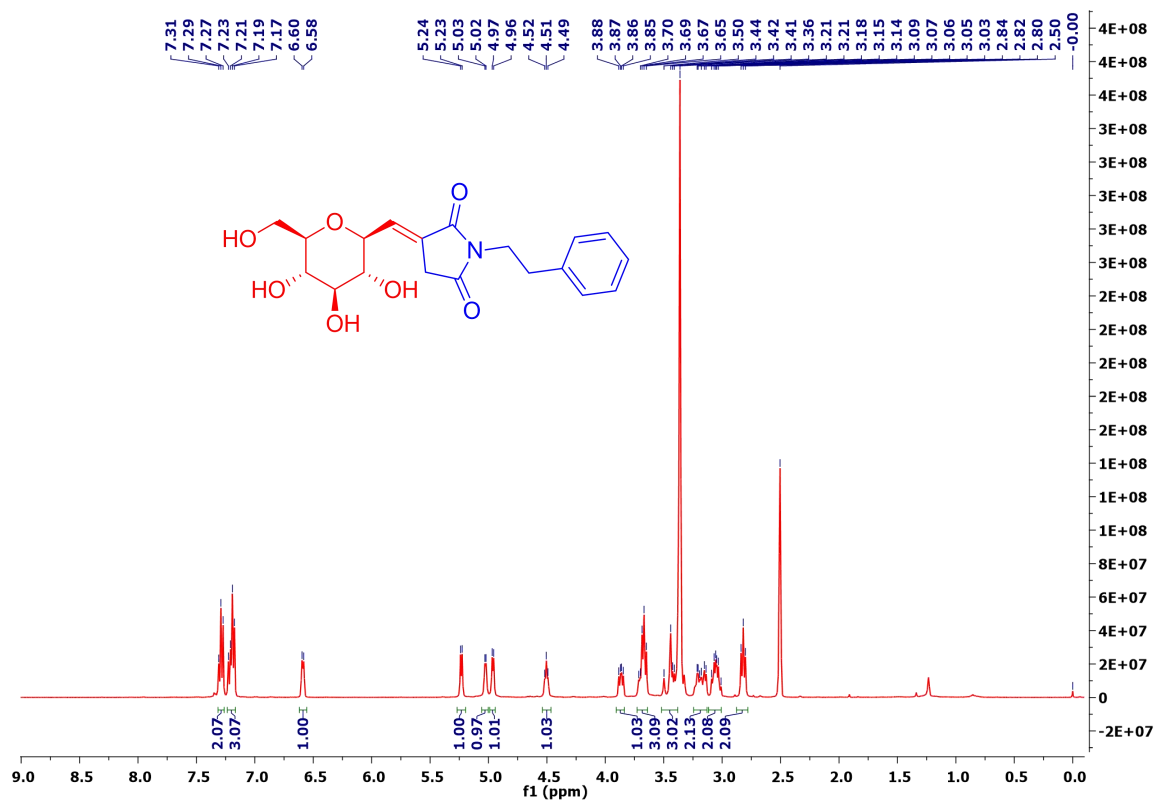


Figure S40. ^1H NMR spectrum of compound **4g** (400 MHz, $\text{DMSO-}d_6$).

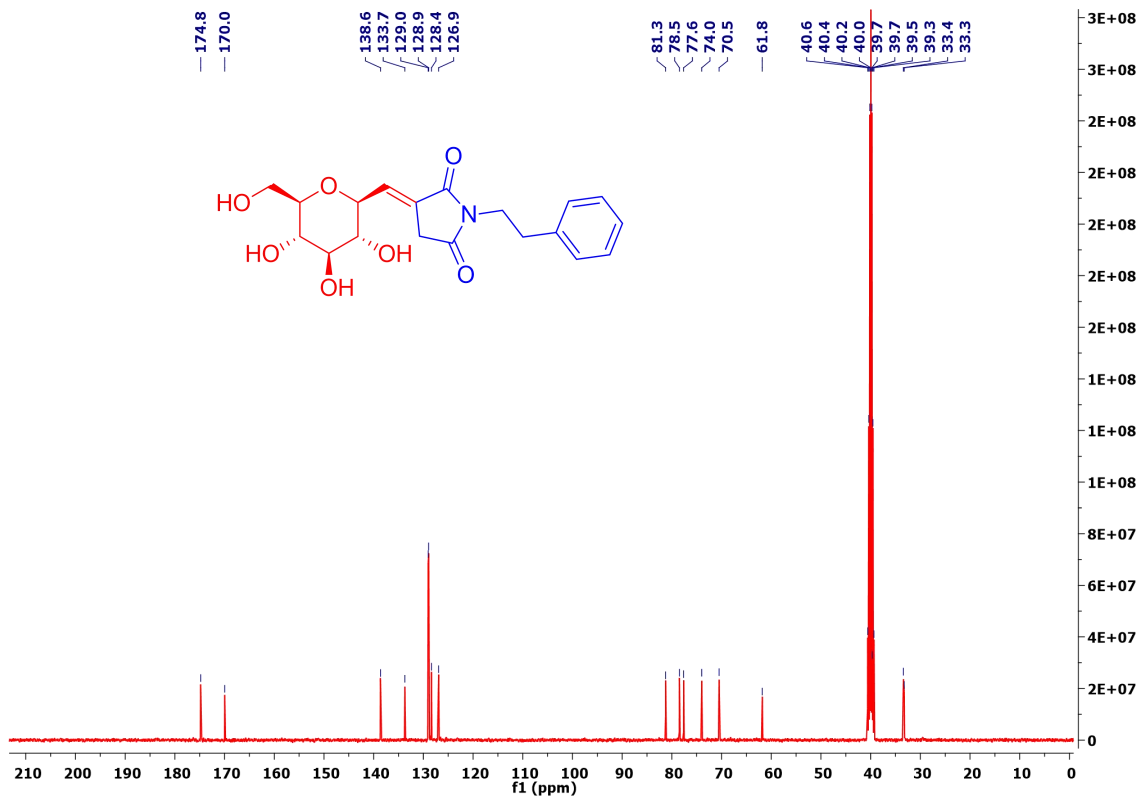


Figure S41. ^{13}C NMR spectrum of compound **4g** (100.6 MHz, $\text{DMSO-}d_6$).

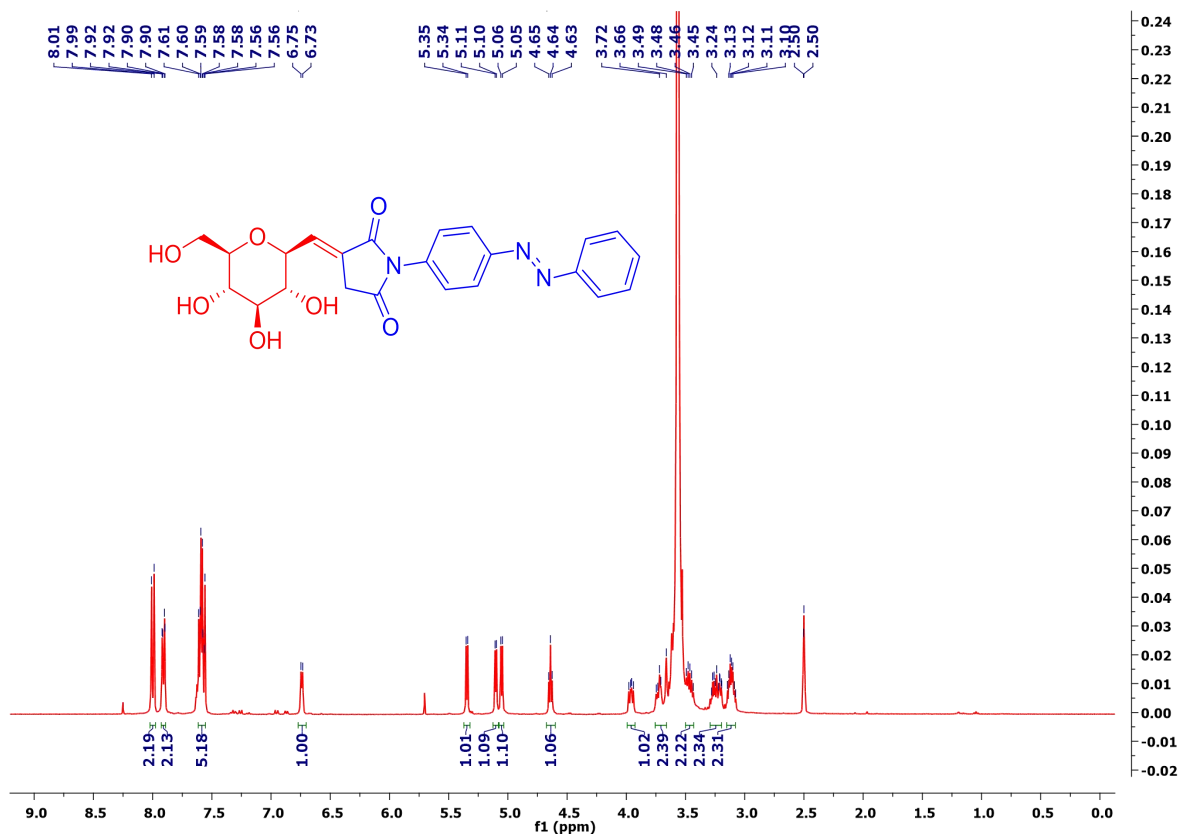


Figure S42. ^1H NMR spectrum of compound 4h (400 MHz, $\text{DMSO}-d_6$).

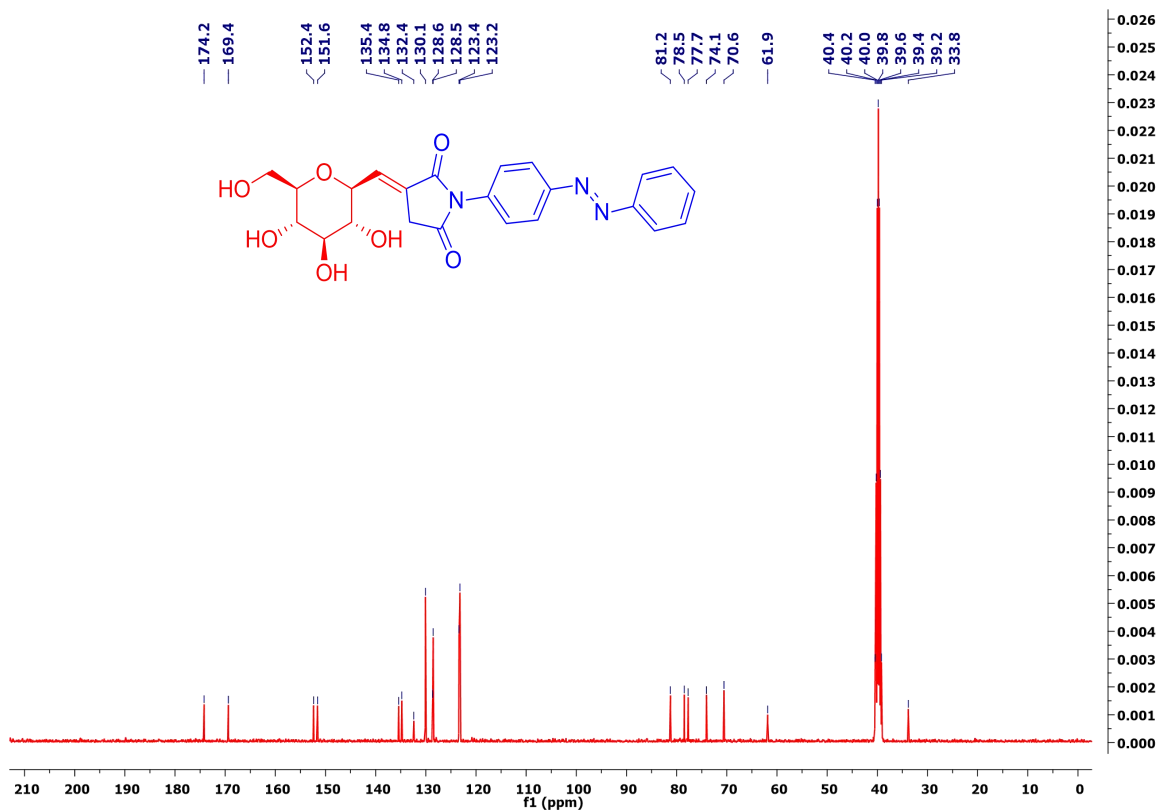


Figure S43. ^{13}C NMR spectrum of compound 4h (100.6 MHz, $\text{DMSO}-d_6$).

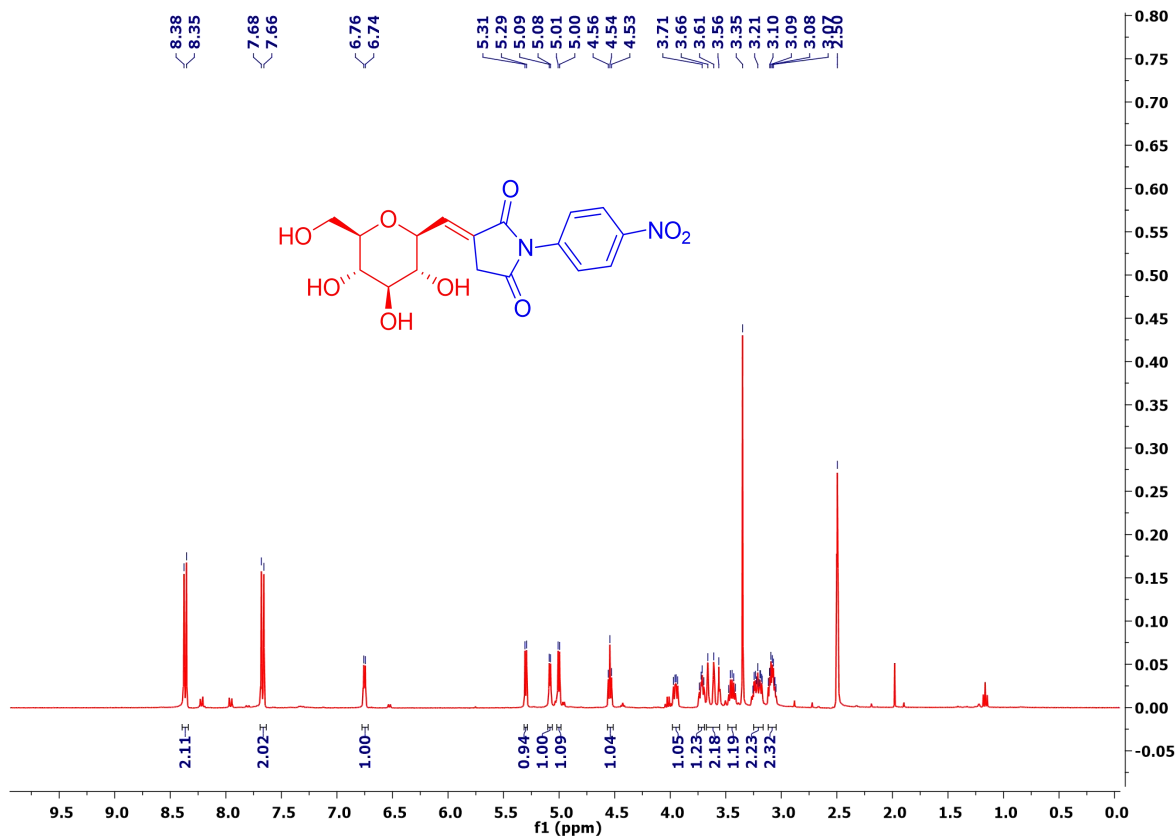


Figure S44. ^1H NMR spectrum of compound **4i** (400 MHz, $\text{DMSO-}d_6$).

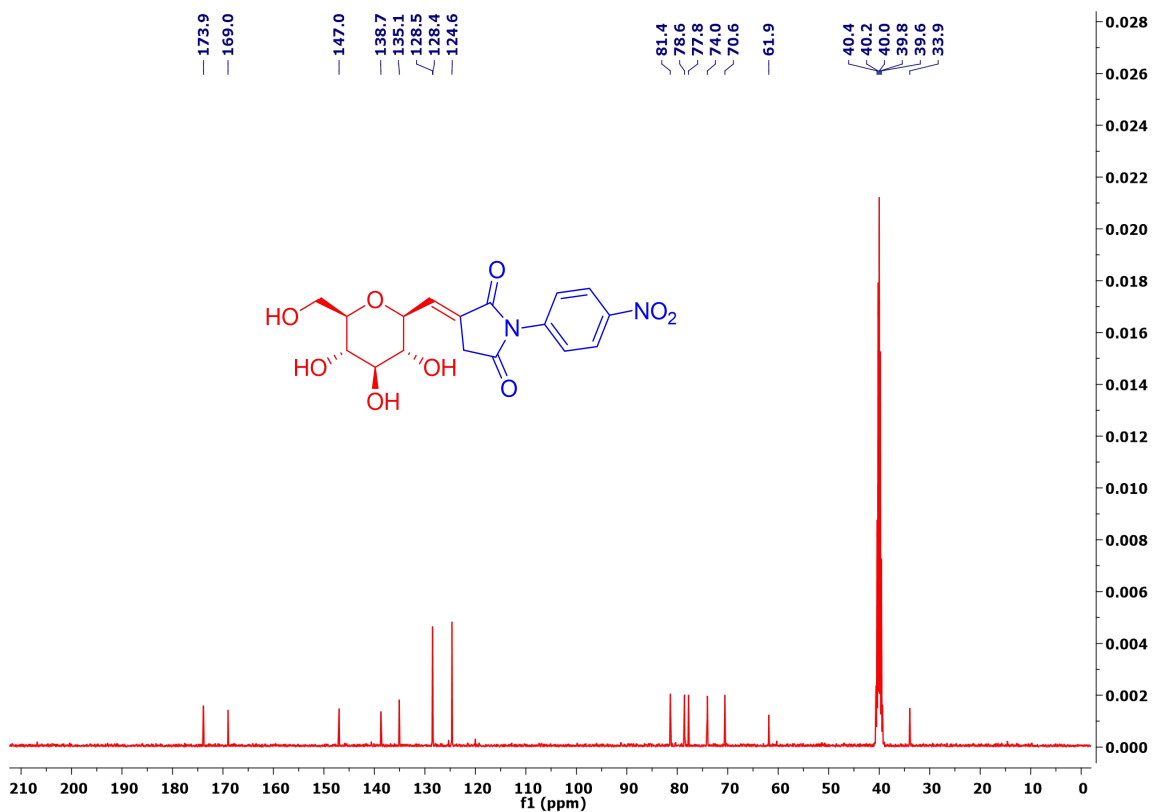


Figure S45. ^{13}C NMR spectrum of compound **4i** (100.6 MHz, $\text{DMSO-}d_6$).

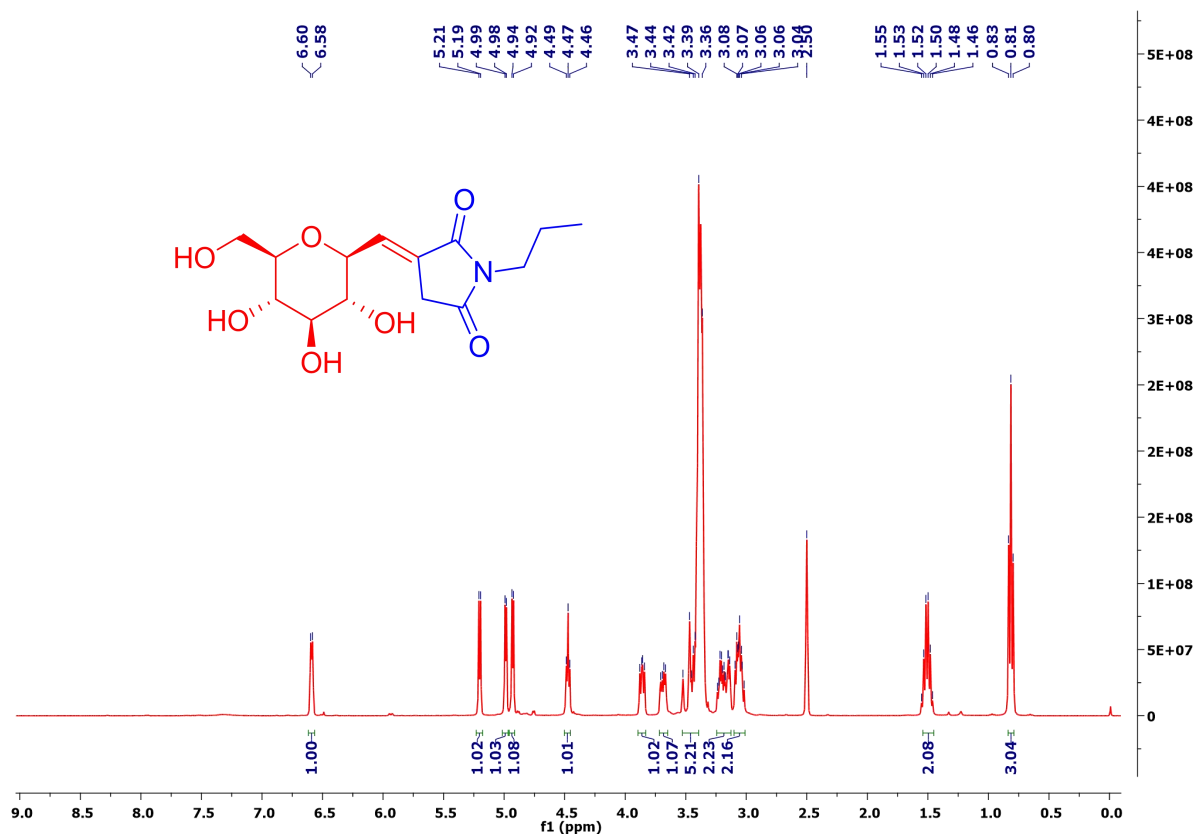


Figure S46. ^1H NMR spectrum of compound 4j (400 MHz, $\text{DMSO-}d_6$).

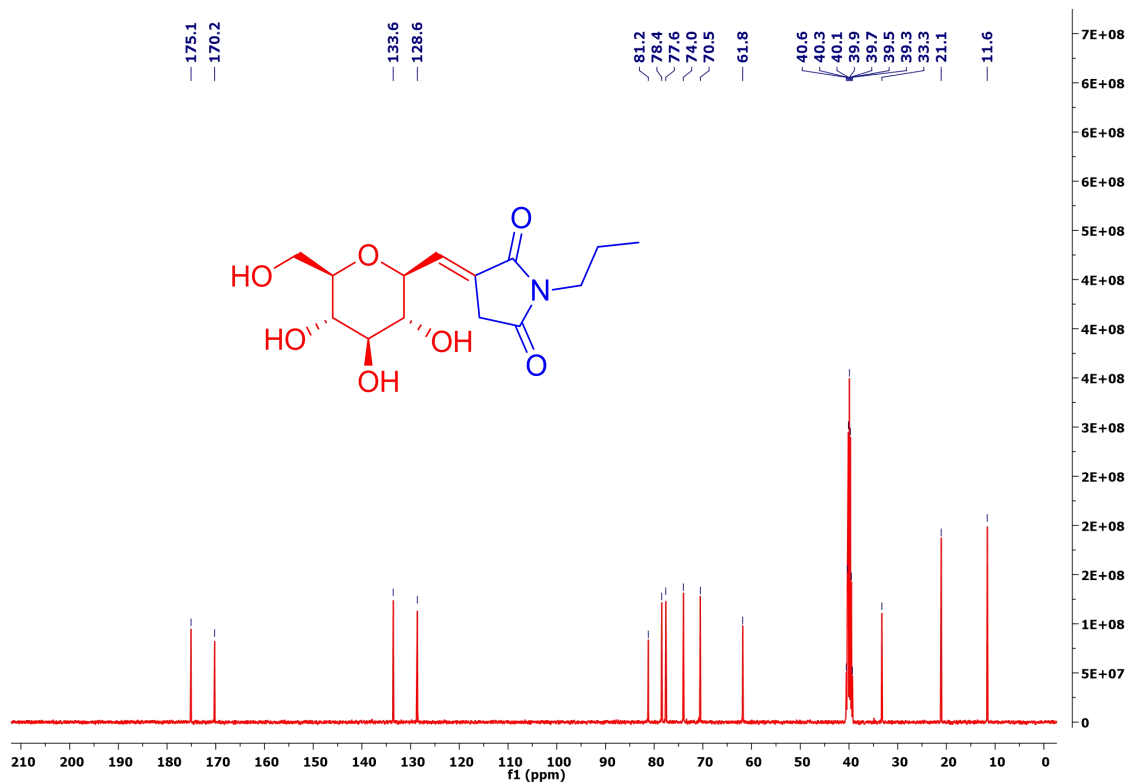


Figure S47. ^{13}C NMR spectrum of compound 4j (100.6 MHz, $\text{DMSO-}d_6$).

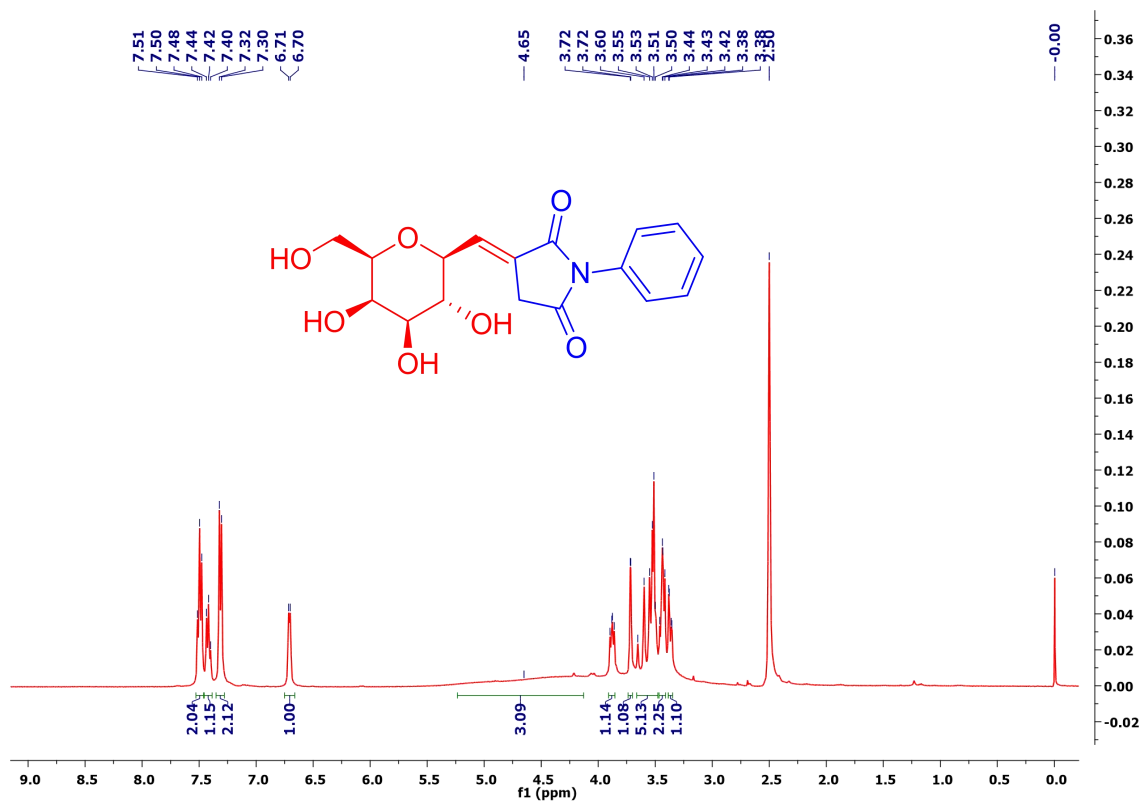


Figure S48. ^1H NMR spectrum of compound **4k** (400 MHz, $\text{DMSO-}d_6$).

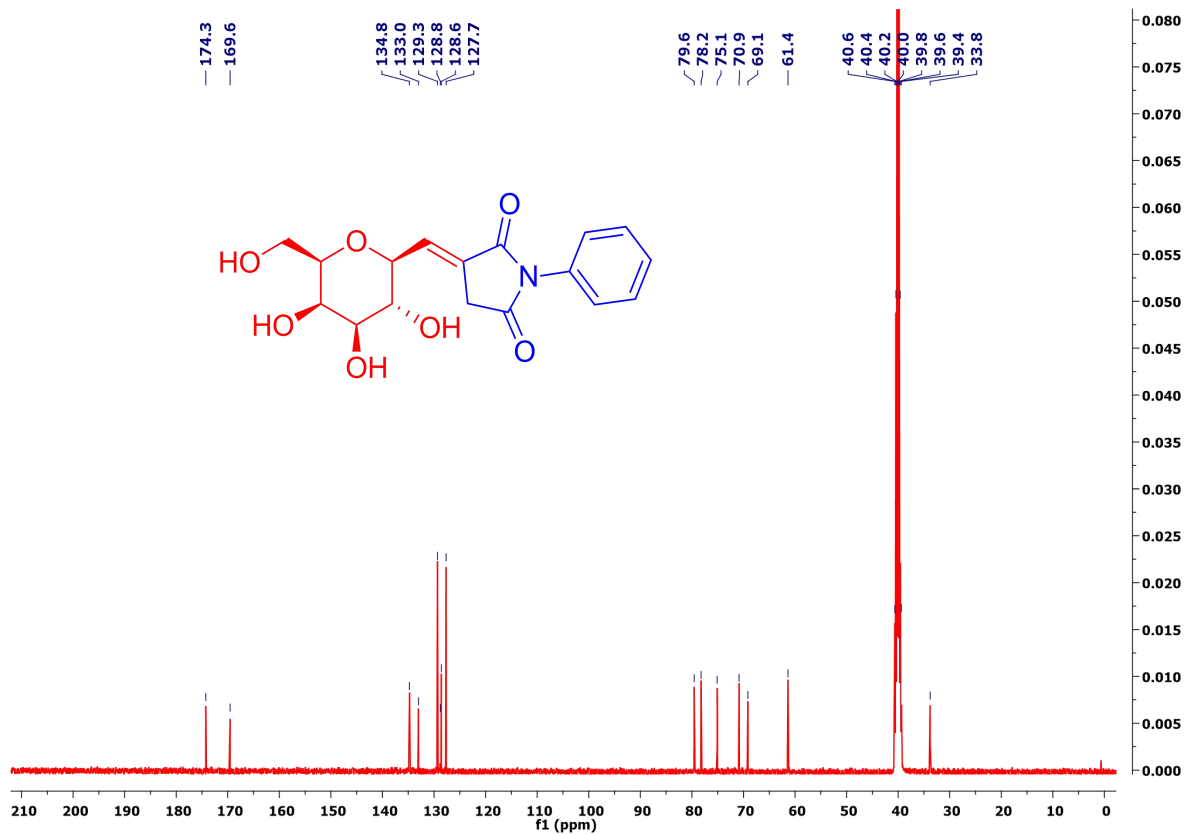


Figure S49. ^{13}C NMR spectrum of compound **4k** (100.6 MHz, $\text{DMSO-}d_6$).

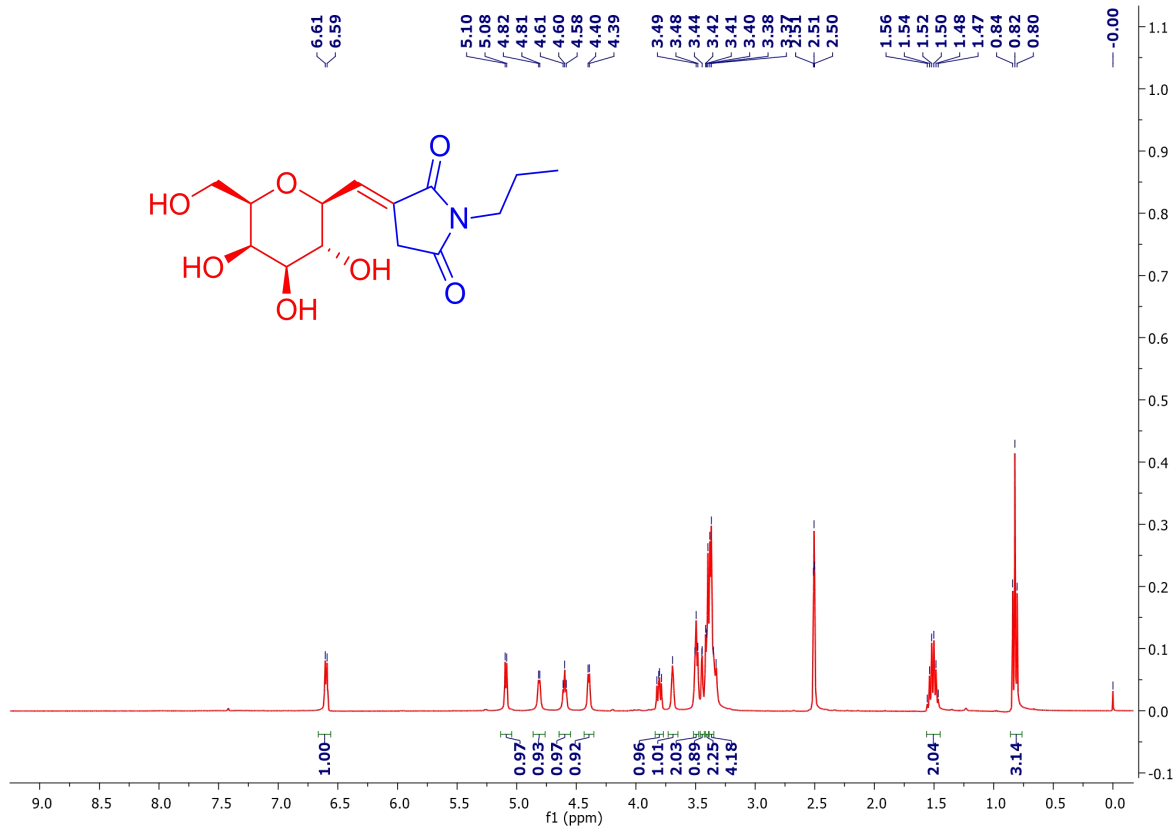


Figure S50. ^1H NMR spectrum of compound 4l (400 MHz, $\text{DMSO-}d_6$).

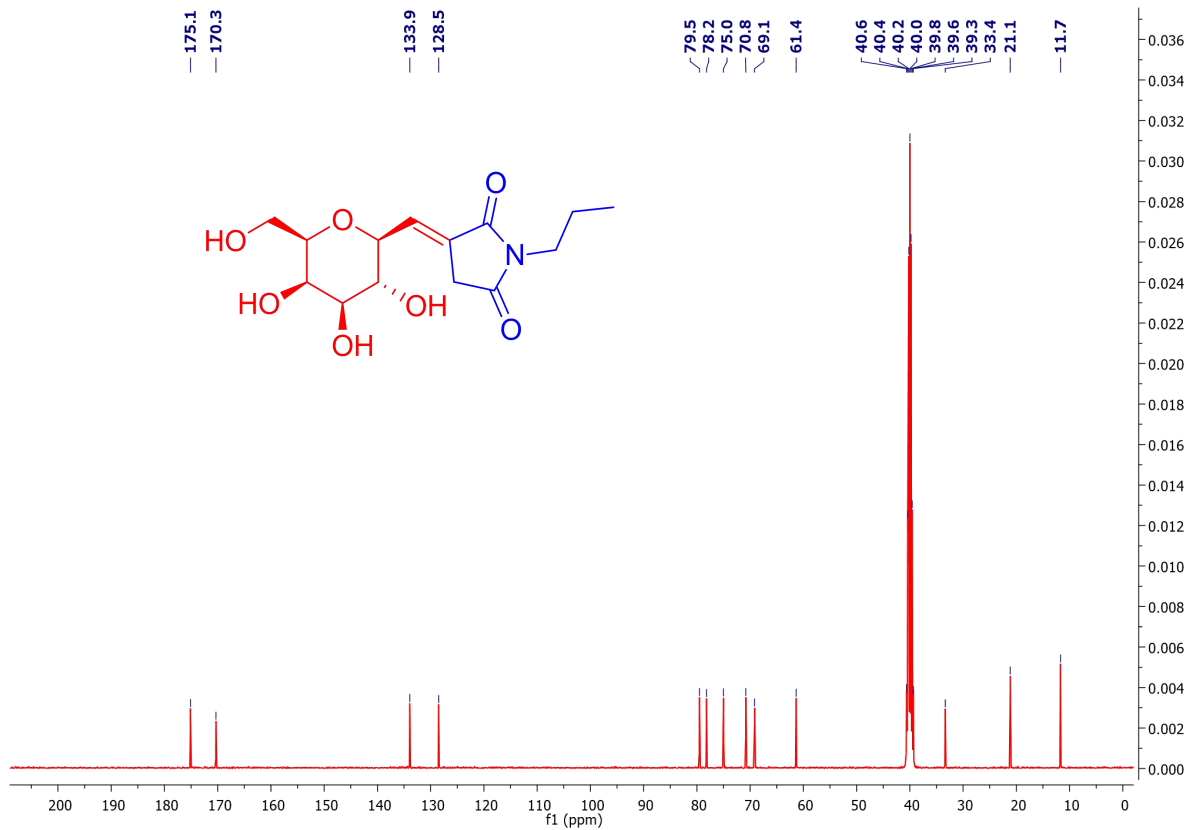


Figure S51. ^{13}C NMR spectrum of compound 4l (100.6 MHz, $\text{DMSO-}d_6$).

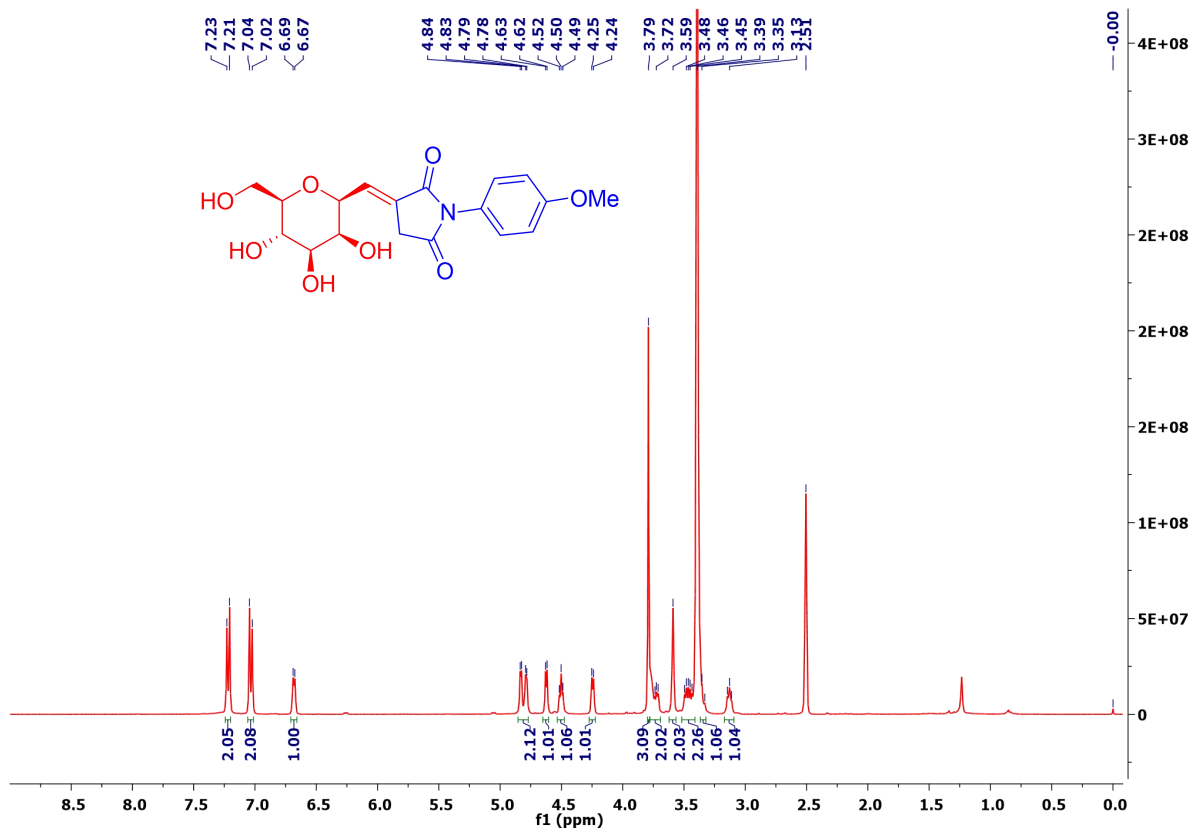


Figure S52. ^1H NMR spectrum of compound 4m (400 MHz, $\text{DMSO-}d_6$).

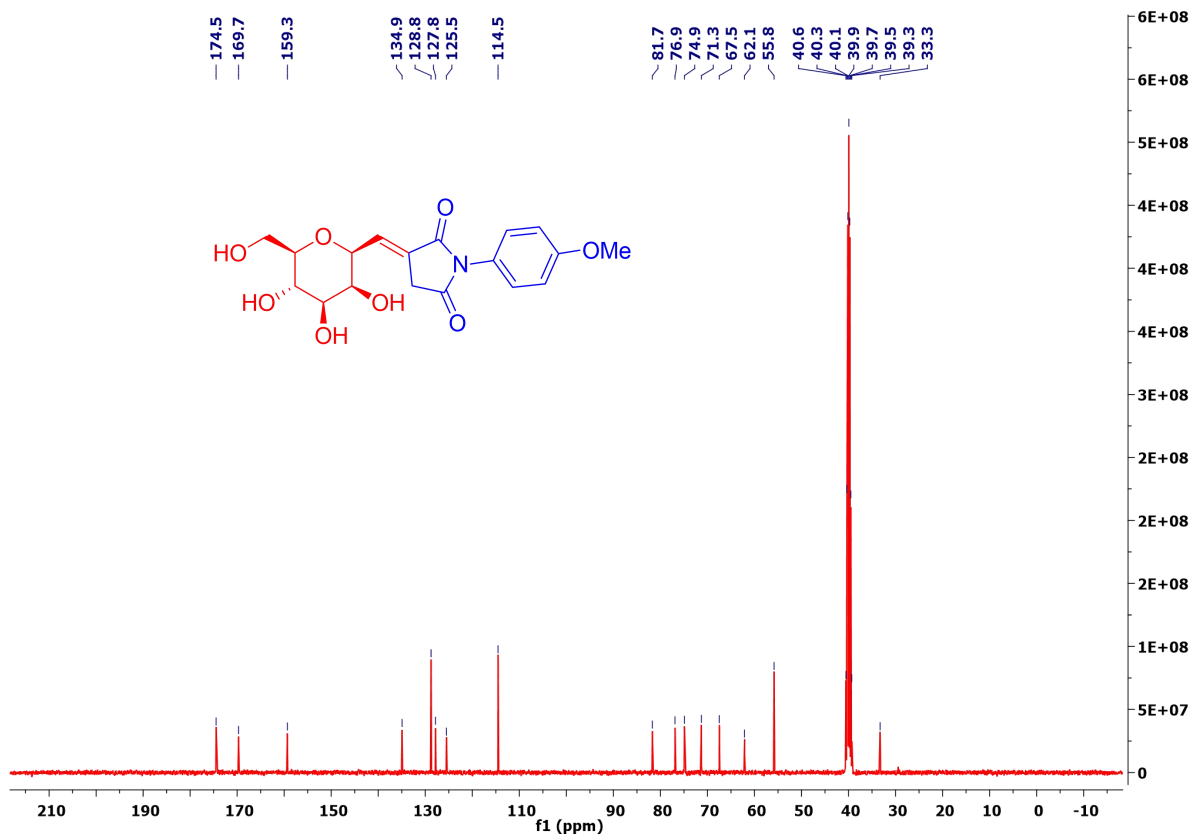


Figure S53. ^{13}C NMR spectrum of compound 4m (100.6 MHz, $\text{DMSO-}d_6$).

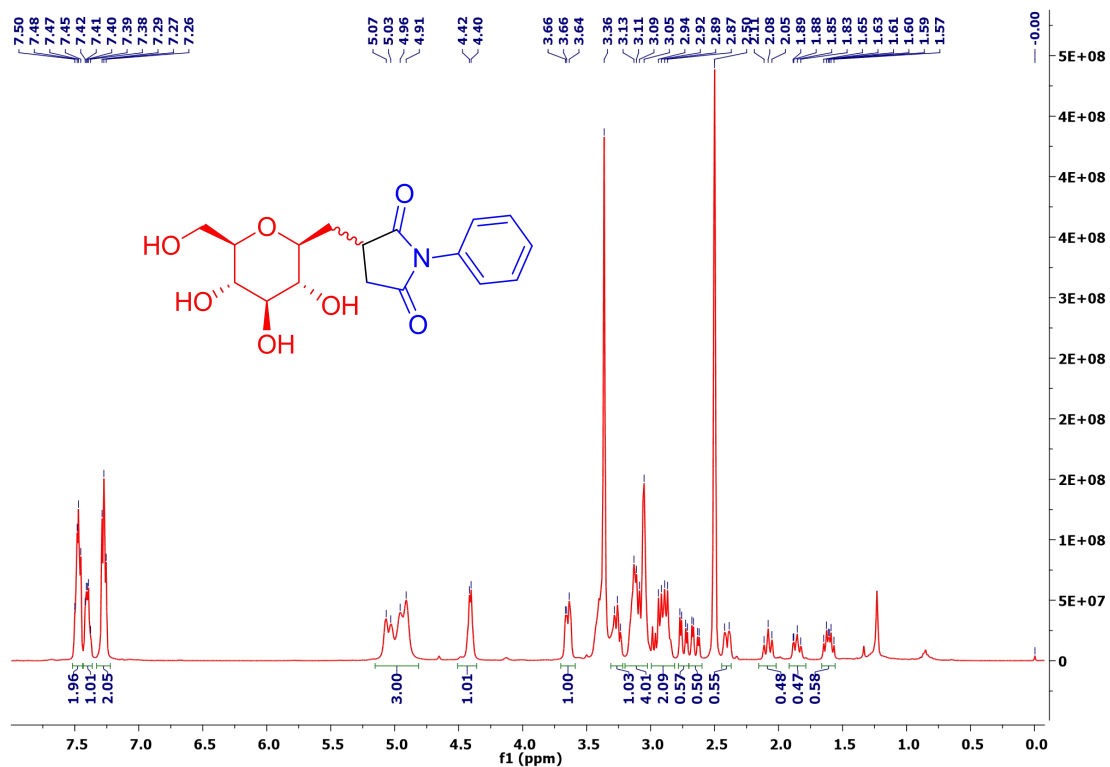


Figure S54. ^1H NMR spectrum of compound **5a** (400 MHz, $\text{DMSO-}d_6$).

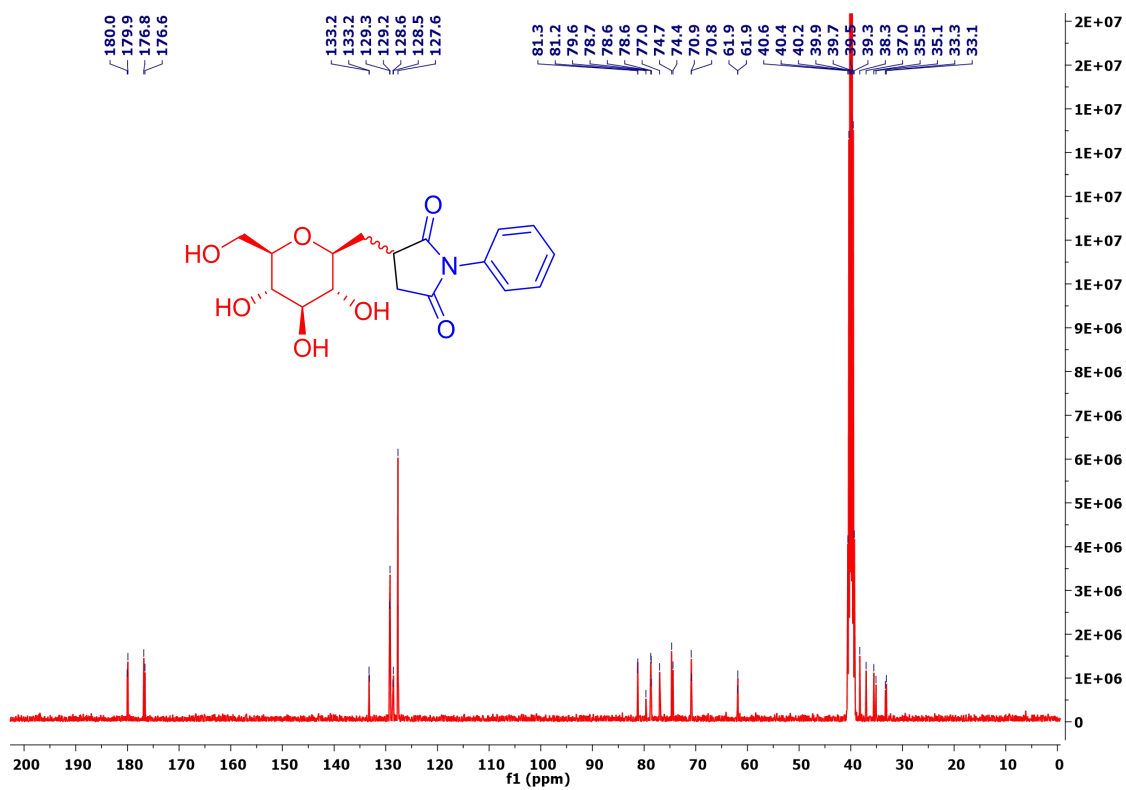
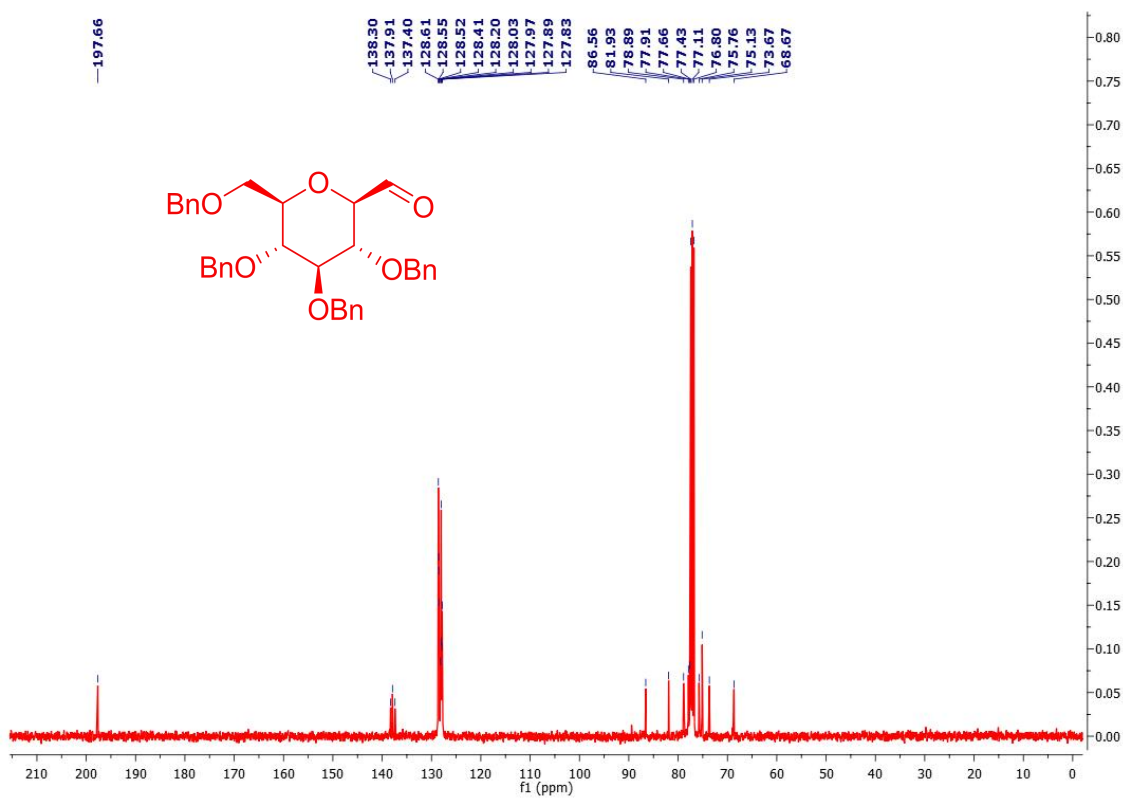
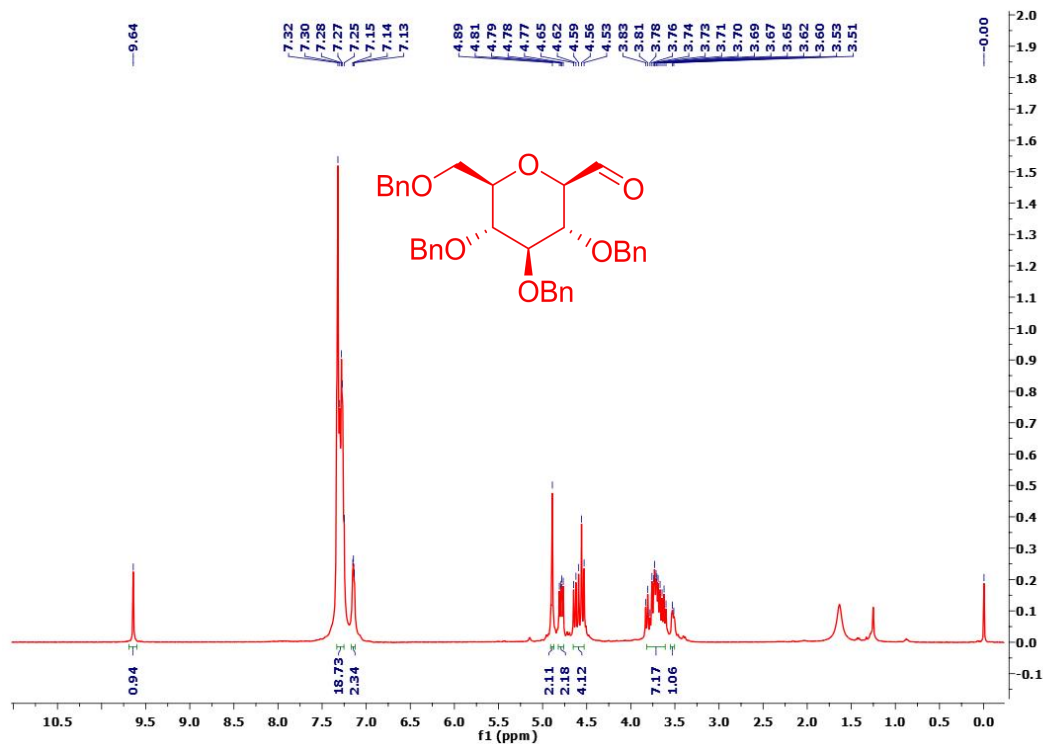


Figure S55. ^{13}C NMR spectrum of compound **5a** (100.6 MHz, $\text{DMSO-}d_6$).



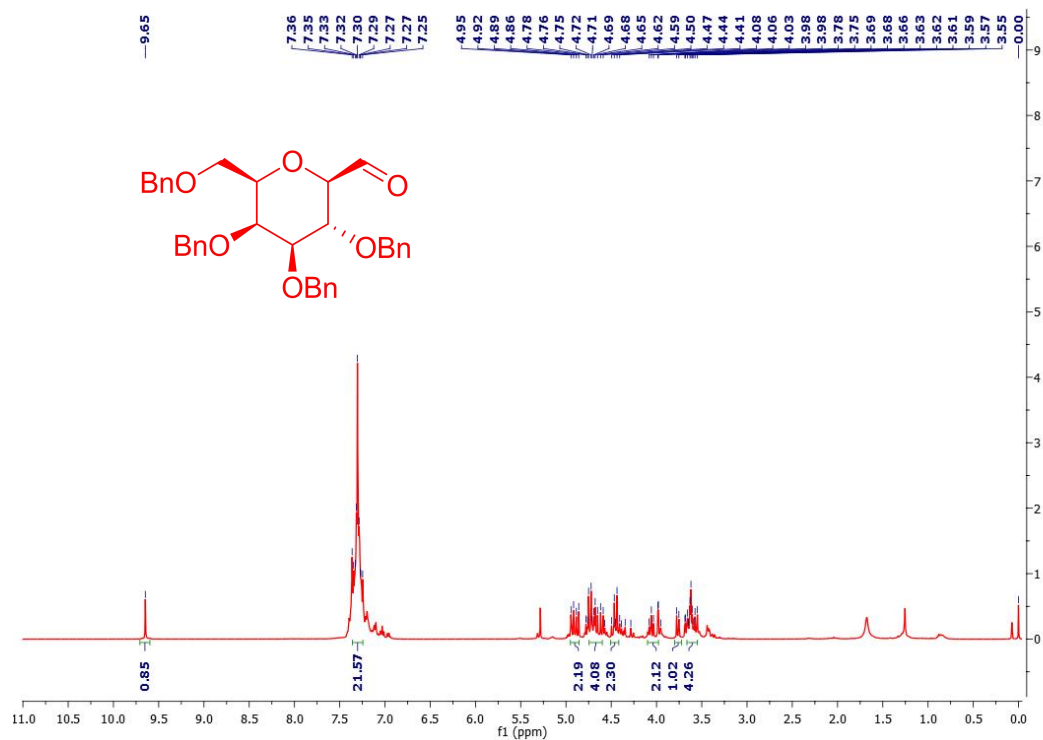


Figure S58. ^1H NMR spectrum of compound **1b** (400 MHz, CDCl_3).

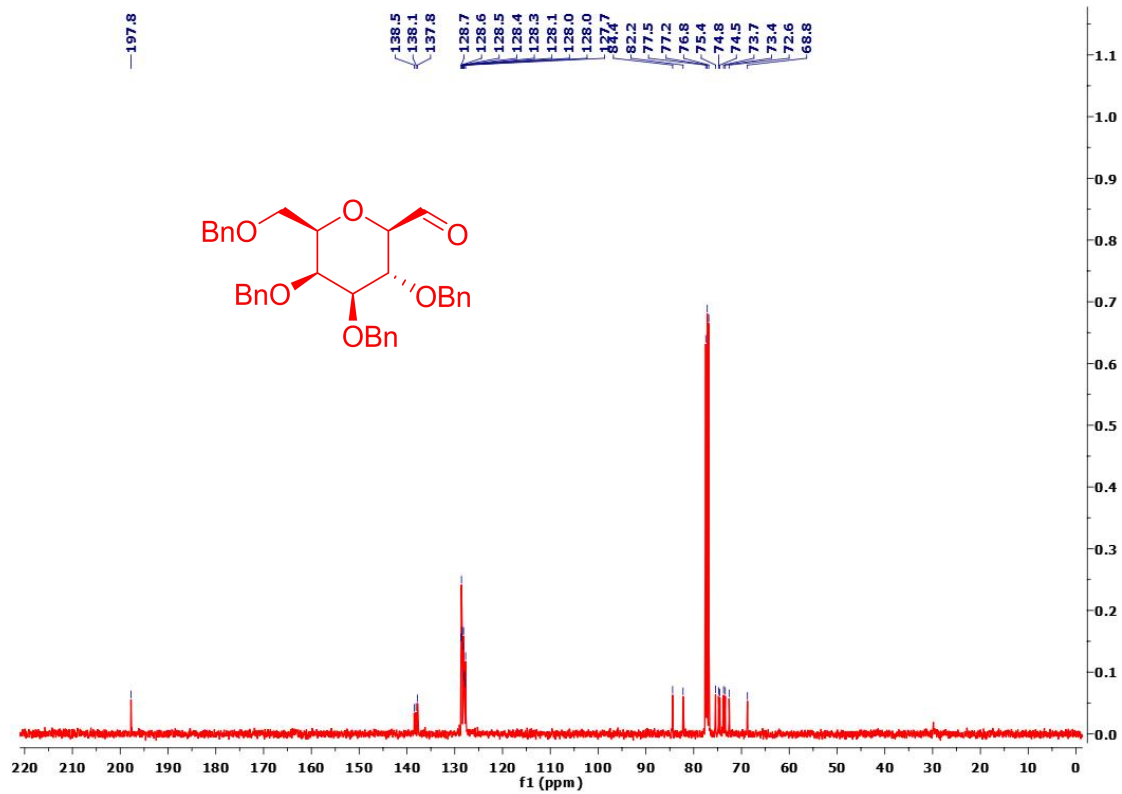


Figure S59. ^{13}C NMR spectrum of compound **1b** (100.6 MHz, CDCl_3).

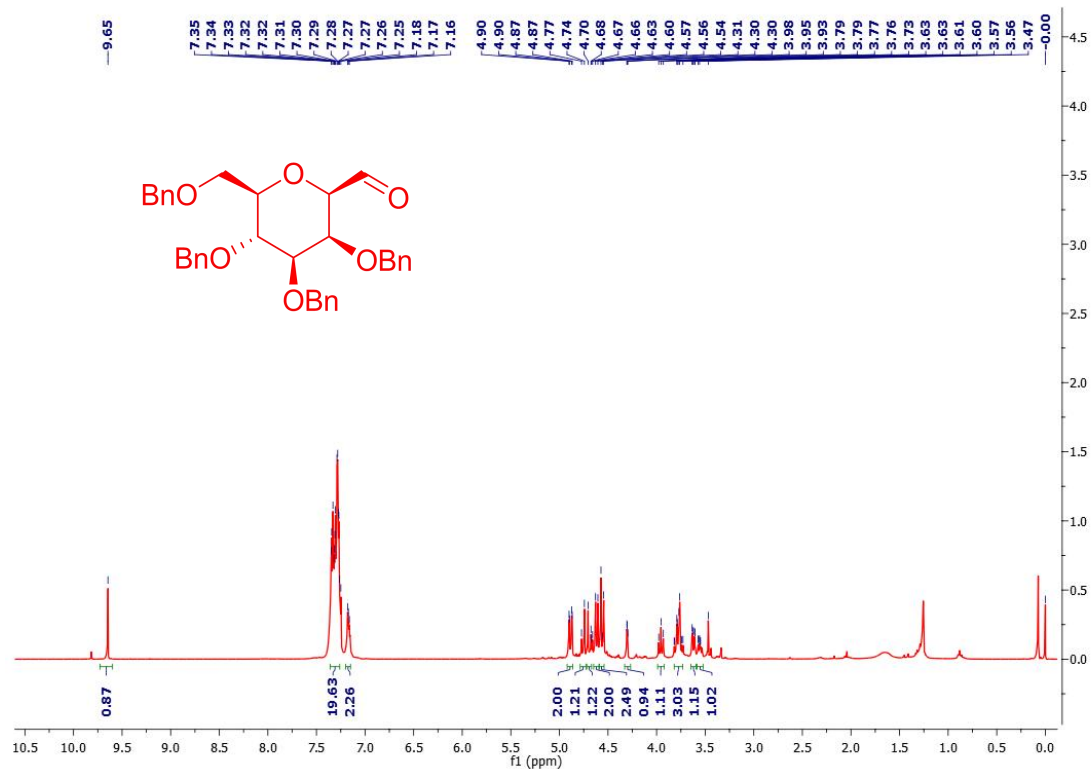


Figure S60. ¹H NMR spectrum of compound 1c (400 MHz, CDCl₃).

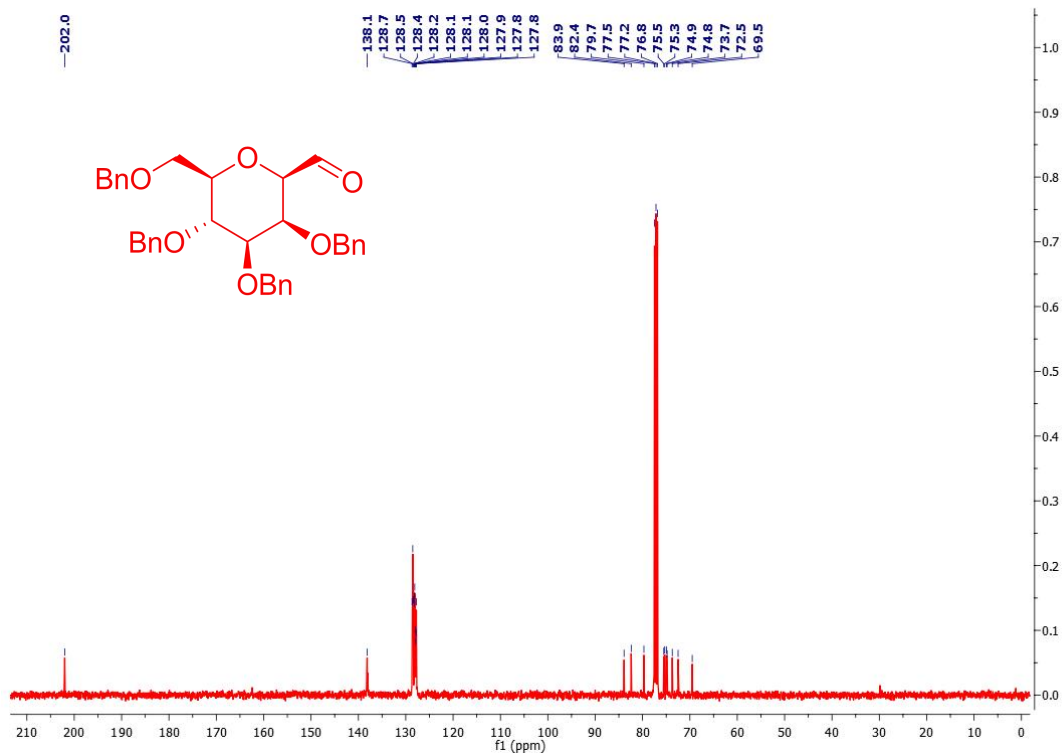


Figure S61. ¹³C NMR spectrum of compound 1c (100.6 MHz, CDCl₃).

Single crystal X-ray diffraction analysis of (*E*)-3-(*C*-Galactosylmethylidene)-*N*-phenyl succinimide (4k)

Compound **4k** was dissolved in a mixture of ethyl alcohol and water (1:1) to grow single crystals appropriate for X-ray diffraction studies by allowing slow evaporation of the solvent at room temperature. The X-ray diffraction data was collected on X'calibur CCD diffractometer with graphite monochromatized Mo/K α radiation ($\lambda = 0.71073 \text{ \AA}$) at temperature 273 K. The structure was solved and all necessary calculations were carried out using the OLEX2 package of the crystallographic programs.¹ For drawing the molecular graphics, the program Mercury² was used. The selected bond lengths, bond angles, *etc.* are given in Table S1.

Table S1. Crystal data and structure refinement for compound 4k.

Identification code	4k
Empirical formula	C ₃₄ H ₃₈ N ₂ O ₁₄ .H ₂ O
Formula weight	732.68
Temperature/K	273
Crystal system	monoclinic
Space group	C 2
a/ \AA	46.814 (6)
b/ \AA	5.8604 (8)
c/ \AA	12.4797 (16)
α / $^\circ$	90
β / $^\circ$	105.085 (7)
γ / $^\circ$	90
Volume/ \AA^3	3305.8 (8)
Z	4
$\rho_{\text{calc}}/\text{g/cm}^3$	1.472
μ/mm^{-1}	0.118
F(000)	1544.0
Radiation	Mo/K α ($\lambda = 0.71073$)
2 Θ range for data collection/ $^\circ$	3.330 to 29.389
Index ranges	$-10 \leq h \leq 10$, $-10 \leq k \leq 10$, $-20 \leq l \leq 20$
Reflections collected	6262
Independent reflections	9342 [$R_{\text{int}} = 0.0200$, $R_{\text{sigma}} = 0.0391$]
Goodness-of-fit on F ²	1.057

Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0407,$
Final R indexes [all data]	$wR_2 = 0.0990$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.358/-0.285
Flack parameter	0.1(1)
CCDC No.	2109526

***In-silico* Molecular Docking Study:**

Table S2: Binding energy of interactions of different ligands with amino acid residues of HPV16 E6 protein

S.No.	Ligand	No. of conformations		Conformations										AA-interaction	H-BOND
				1	2	3	4	5	6	7	8	9	10		
1	3a	6	B.E.	-3.6	-3.3	-3.1	-2.9	-2	-0.7					R17, K18, F20, Q21, D56, D105, L107,	
			I.C.	2.2	3.8	4.6	6.5	21	270						
2	3b	10	B.E.	-5.4	-3.4	-2.7	-2.1	-2	-1.3	-1.1	0	0	5.6	R17, K18, V38, Y39, F52, D56, V60, R62, A68, V69, L74, S81, L107, R109, R138	
			I.C.	108	3.2	10.1	25.2	45	99.9	142	933	##	2.2		
3	3c	2	B.E.	-757	-3.5									F20, A53, L107, F116,	
			I.C.	0	2.7										
4	3d	4	B.E.	-3.4	-2.3	-1.2	-1.1							R15, R17, C58, V60, S81, Q114, I135, R138	
			I.C.	3.1	20.1	122	149								
5	3e	10	B.E.	-5.49	-4.8	-4.4	-4.3	-4	-4.2	-3.9	-4	-4	-3	Y39, F52, L57, C58, V60, V69, S81, Q114, I135, R138	R17,138
			I.C.	94.2	322	577	707	826	861	1.46	1.6	3	3.6		
6	3f	1	B.E.	-3.11										F54, D56, D105, L106, L107, P119,	NA
			I.C.	5.28											
7	3g	8	B.E.	-4.27	-2.7	-760	4.4	###	0.94	-788	2.1			R15, R17, K18, V38, F52, D56, C58, V60, Y61, R62, D63, V69, L107, R138	R62
			I.C.	741	10.4	0	0	0	0	0	0				
8	3h	4	B.E.	-4.5	-2.7	-1.2	-0.3							R15, K18, C58, V60, L107, R109, Q114, R138	
			I.C.	475	9.9	124	516								
9	3i	1	B.E.	-81	-114									Y88, Q98, Y99, N134, G137, R138, W139,	Y99, T140
			I.C.	0	0										
10	3j	3	B.E.	-2.96	-1.3	0								F54, K115, P116, L117, K122,	K115
			I.C.	6.82	112	868									
11	3k	1	B.E.	-1.37										R17, K18, D56, L57, C58, L107, R138	
			I.C.	99.3											
12	4a	10	B.E.	-5	-4.6	-4.4	-4.2	-4	-4	-4	-3	-4	-4	Y39, L57, V69, Y77, I80, H85	

			I.C.	212	415	583	824	1	1.1	1.13	1.9	2	2.3		
13	4b	10	B.E.	-107	-106	-5	-4.2	-4	-3.8	-3.5	-3	-3	-3	P76, Y77, S78, K79, I80, S81, E82, Y83, Y86, I111, Q114, I135	S81
			I.C.	1	0	201	769	945	1.52	2.6	2.9	-3	3.6		
14	4c	10	B.E.	-4	-3.9	-3.9	-3.8	-4	-3.5	-3.3	-3	-3	-3	C58, V60, L74, Y77, I80, S81,	C58
			I.C.	1	1.2	1.37	1.4	1.8	2.6	3.6	3.7	4	6.4		
15	4d	10	B.E.	-4.8	-3.9	-3.8	-3.8	-4	-3.6	-3.5	-3	-3	-3	P54, C104, K115, P116, P119, K122	
			I.C.	304	1.24	1.5	1.5	2.1	2.1	2.6	2.8	3	5		
16	4e	10	B.E.	-4.11										P20, A53, F54, K115, C118	K115
			I.C.	972											
17	4f	10	B.E.	-4.6	-4.1	-3.6								Y39, C58, L74, Y77, S81	C58
			I.C.	425	987	2.13									
18	4g	10	B.E.	-2.76	-3.2	-3.4	-4.4	-4	-4	-2.5	-4	-3	-3	L107, R138, W139,	R138,W139
			I.C.	9.48	4.27	3.39	601	2.6	1.11	14.8	999	12	3.1		
19	4h	10	B.E.	-859	-839	-823	-816	-5	-4.3	-4.1	-4	-4	-3	I30, A53, F54, L106, P116, L117, K112	
			I.C.	0	0	0	0	348	644	918	985	2	4.8		
20	4i	10	B.E.	-6.02	-6	-5.9	5.7	-5	-5	-4.8	-5	-5	-5	P20, D56, L107, I108, P116, K122	I108,K122
			I.C.	38.9	40	49	66.5	104	202	312	322	##	446		
21	4j	2	B.E.	-3.19	-2.8									D56, R115, P116, L117	
			I.C.	4.59	8.79										
22	4k	10	B.E.	-4.8	-4.5	-4.5	-4.1	-4	-3.9	-3.9	-4	-4	-3	Y39, L57, L74, Y77, S78, I80, S81, Q114	
			I.C.	287	433	471	862	1	1.1	1.3	1.5	2	6.6		
23	4l	10	B.E.	-4.1	-4.1	-3.9	-3.8	-4	-3.5	-3.1	-3	-3	-3	A53, F54, D56, K115, C118	K115
			I.C.	911	920	1.2	1.4	1.6	2.4	5.1	5.4	7	11		
24	4m	10	B.E.	-5.3	-4.8	-4.7	-4.4	-4	-4.3	-4.2	-4	-4	-4	F54, C104, L106, L107, I108, F116, L117, K112,	I108
			I.C.	130	300	325	574	643	679	765	881	1	1.6		
25	5-FU	10	B.E.	-3.89	-3.9	-3.9	-3.9	-4	-3.3	-3.3	-3	-3	-3	L106, L107, G137, R138	L107, L139
	(Positive Control)		I.C.	1.42	1.41	1.44	1.51	1.9	3.54	3.7	3.7	4	3.8		

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