Supporting Information

1,2,3-Triazole-ContainingFlex-Nucleoside Analogs and Sulfonamido-Ribofuranoside Conjugates: Design, Synthesis, and Antiproliferative Potential

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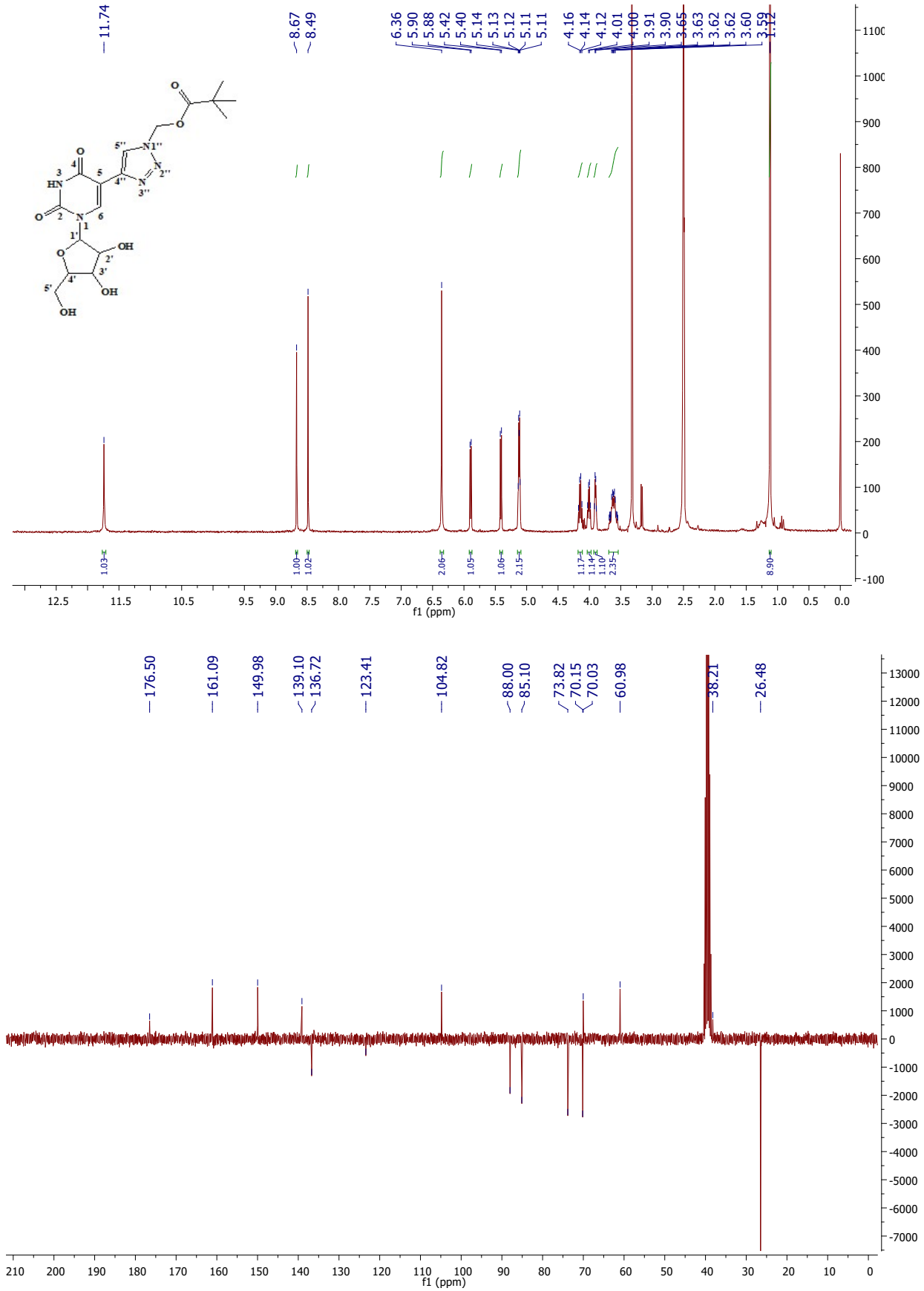


Figure S1. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **7**.

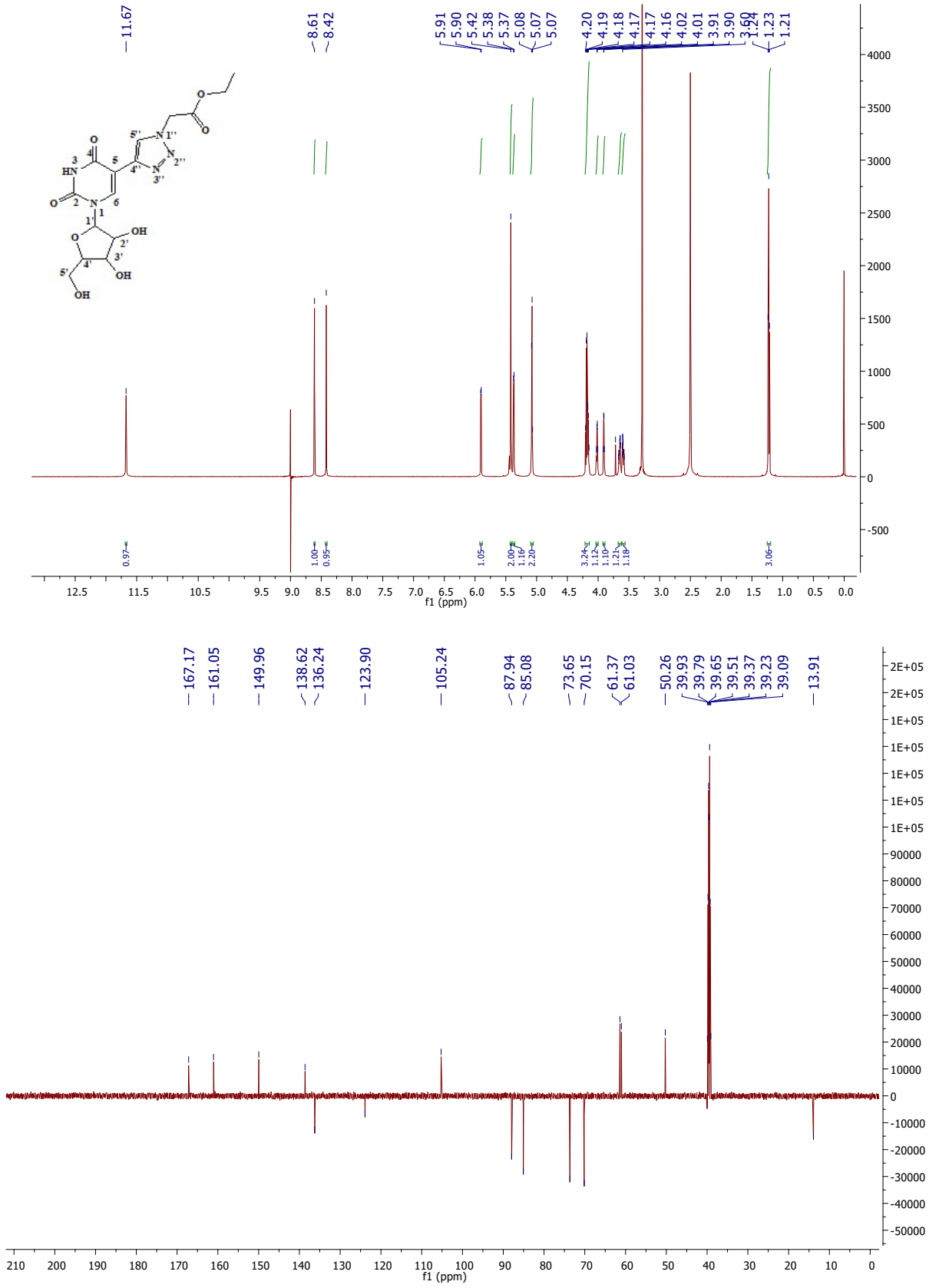


Figure S2. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **8**.

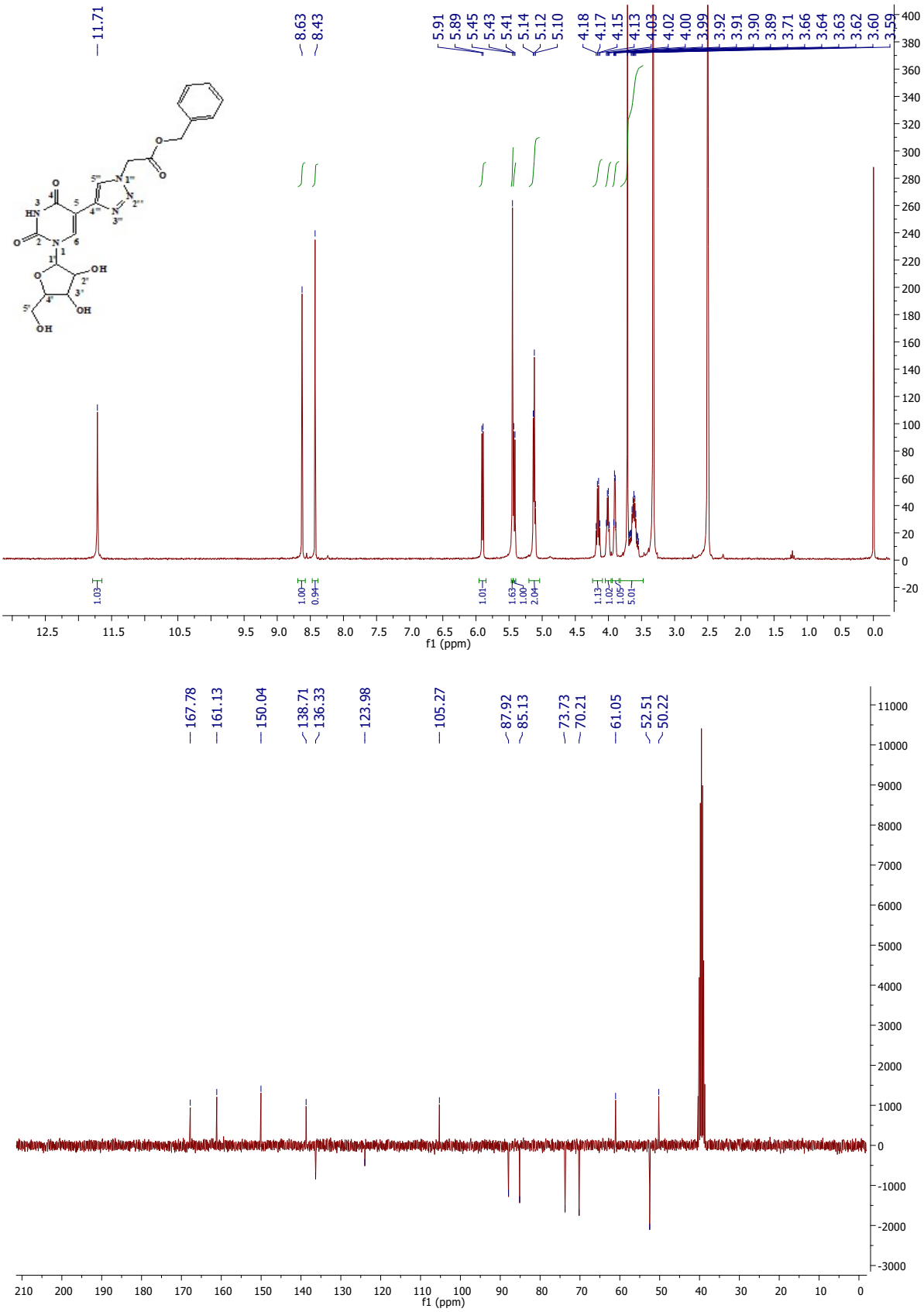


Figure S3. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **9**.

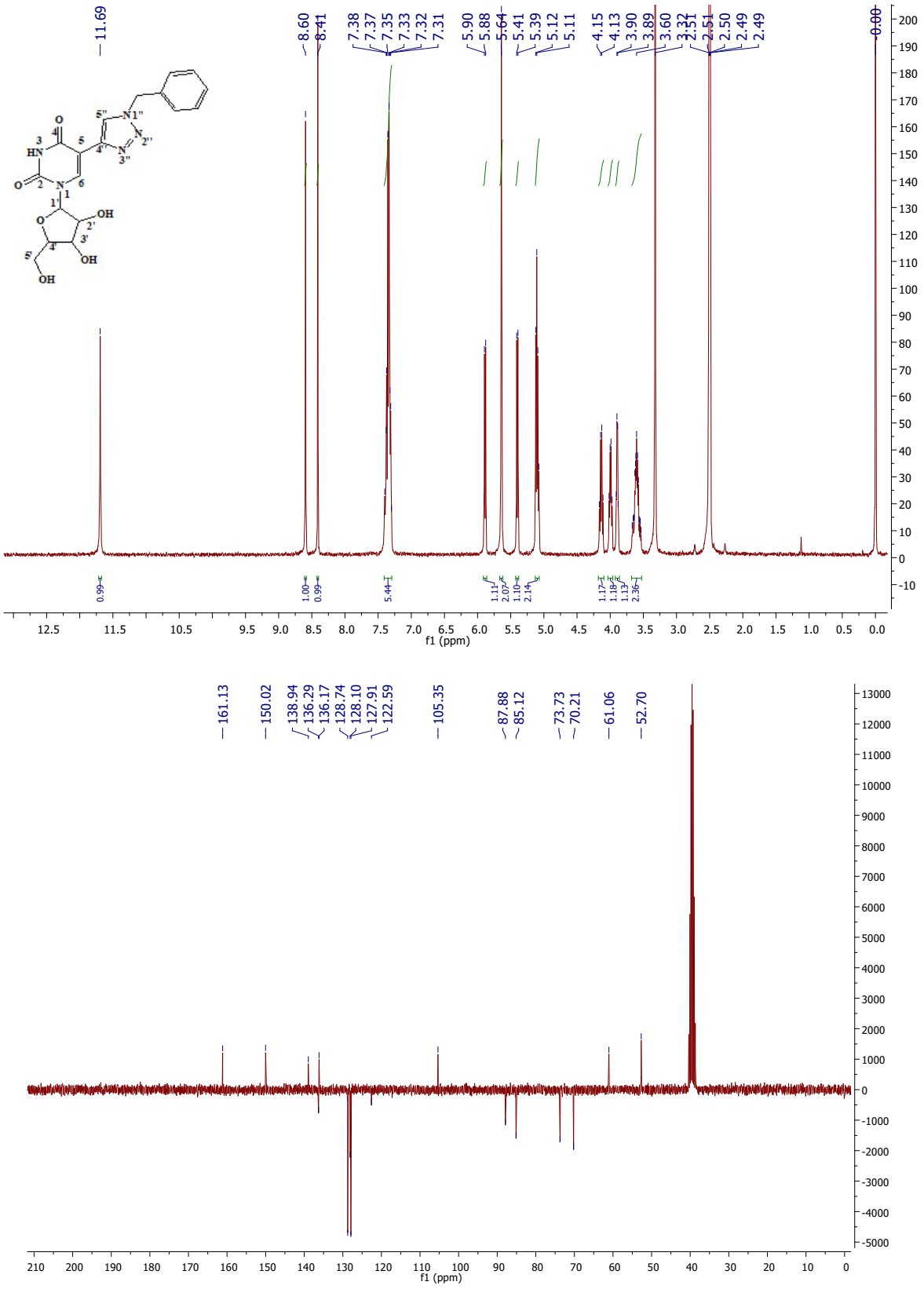


Figure S4. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **10**.

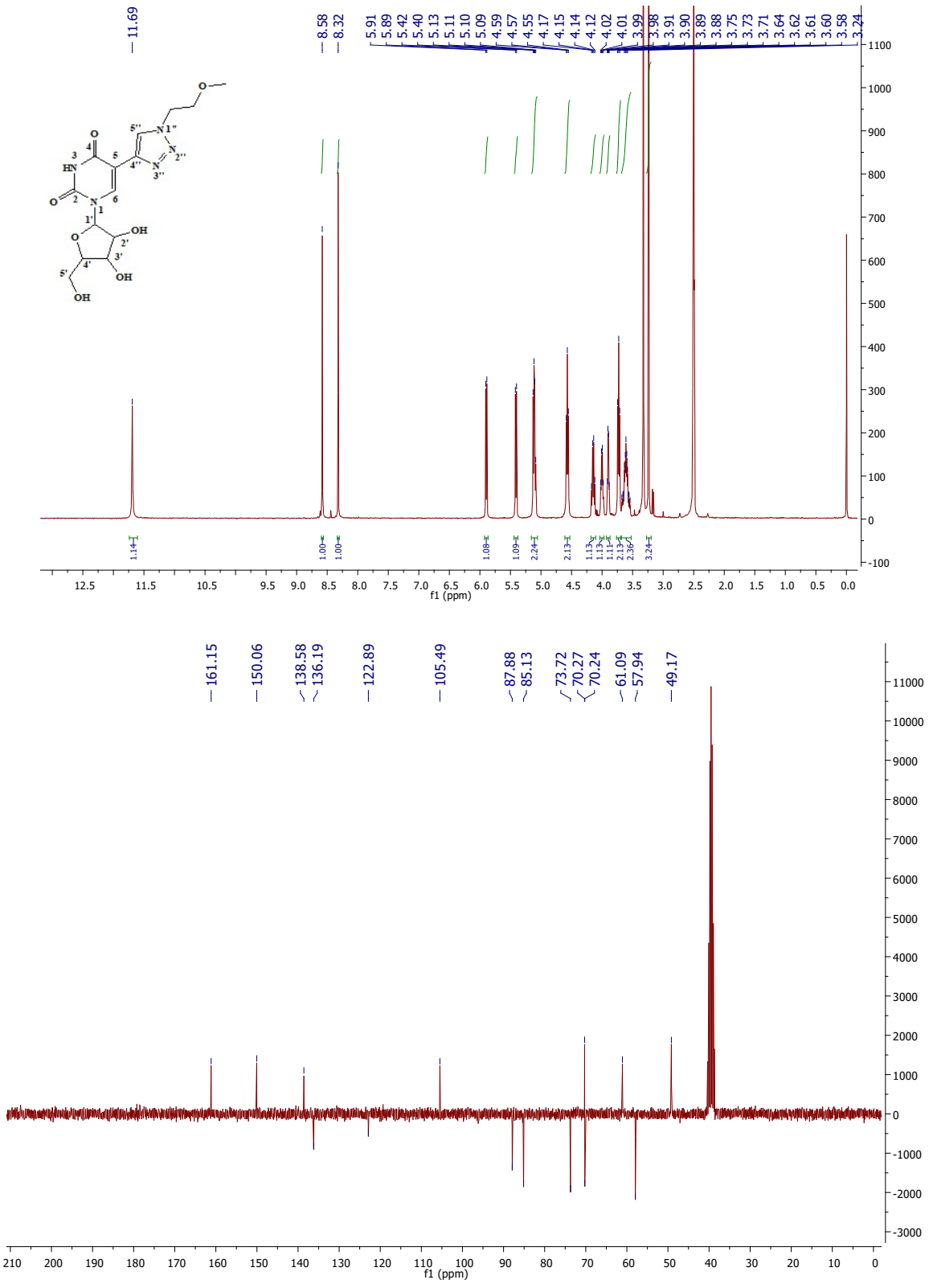


Figure S5. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **11**.

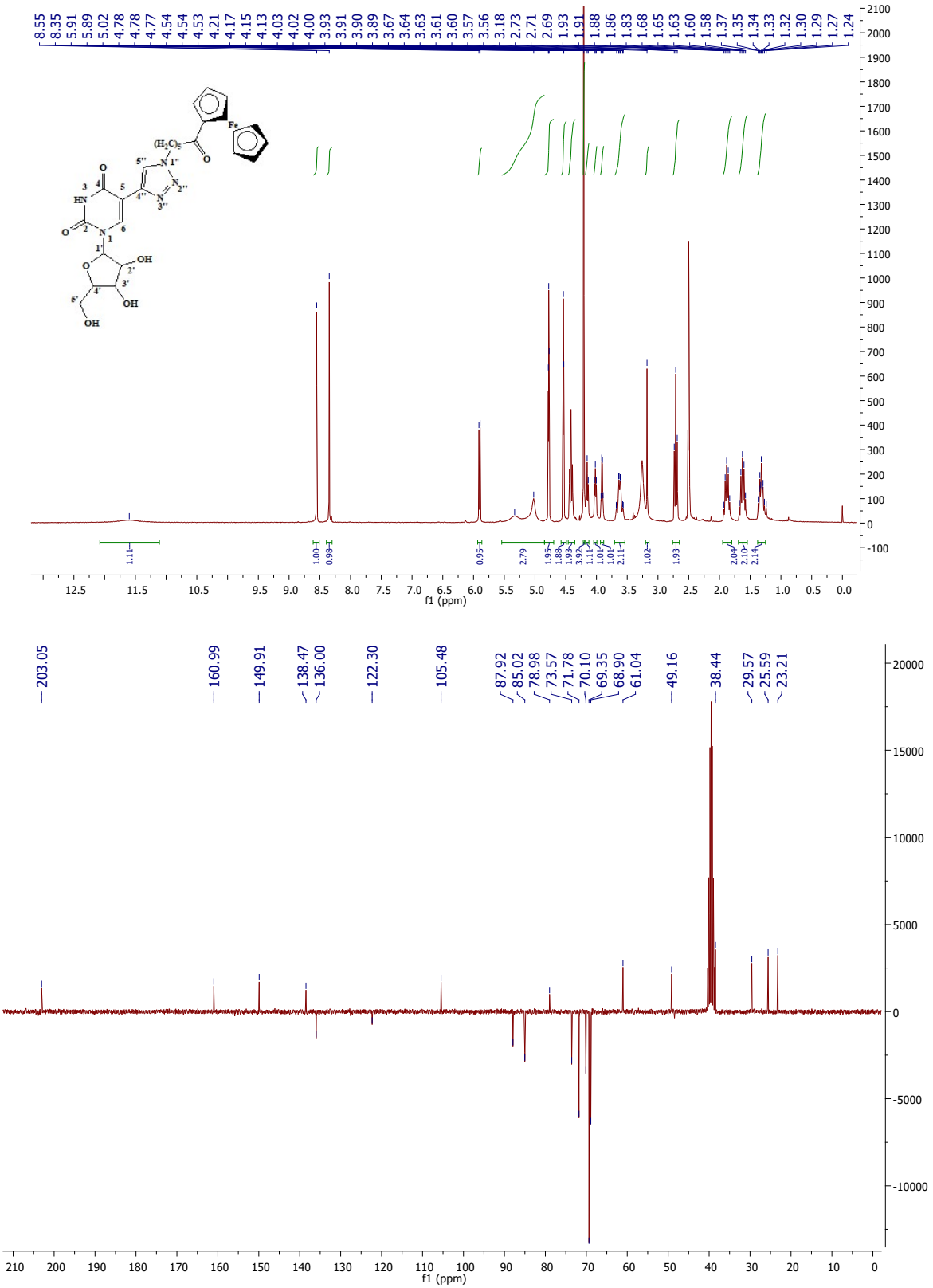


Figure S6. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **12**.

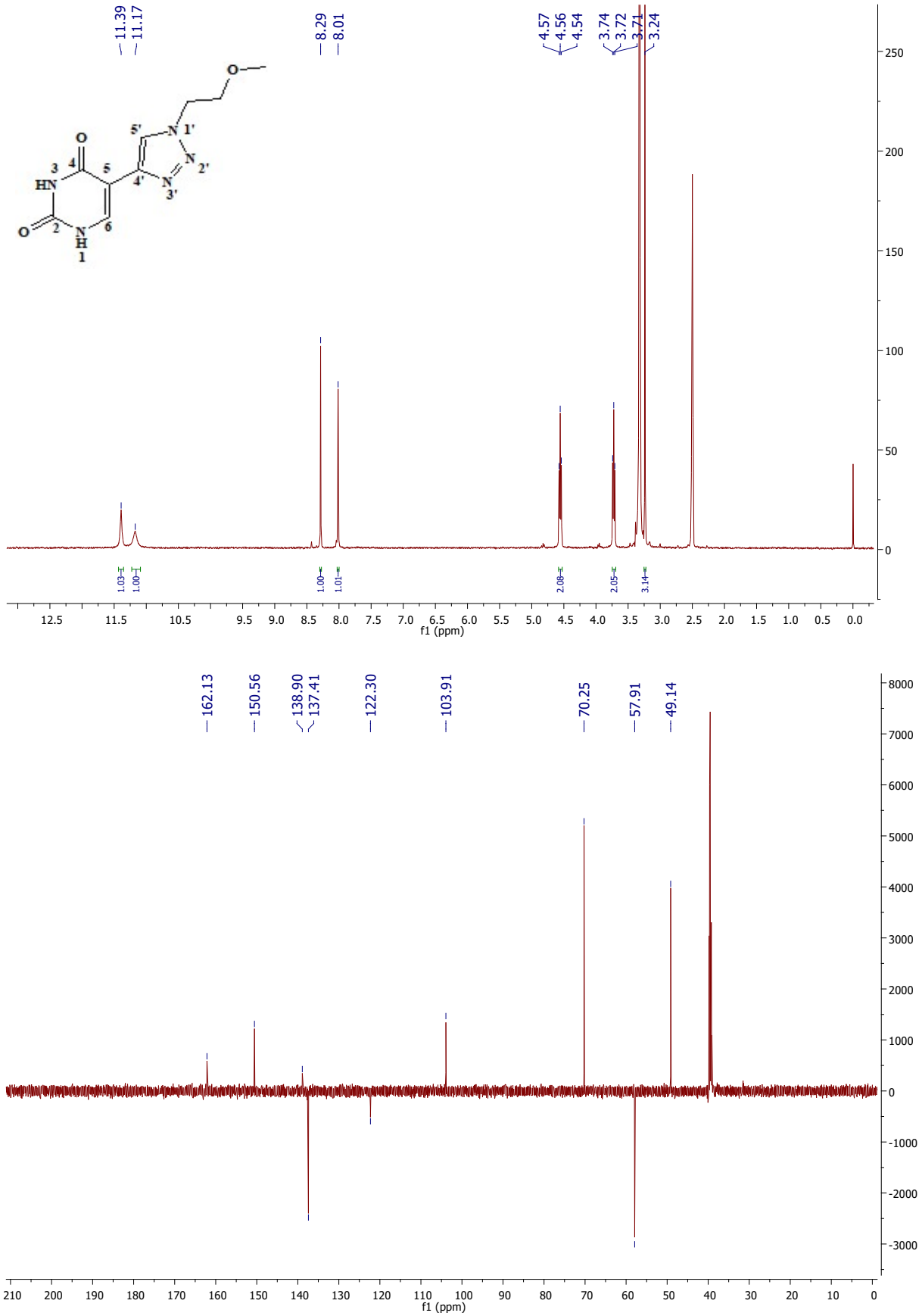


Figure S7. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **13**.

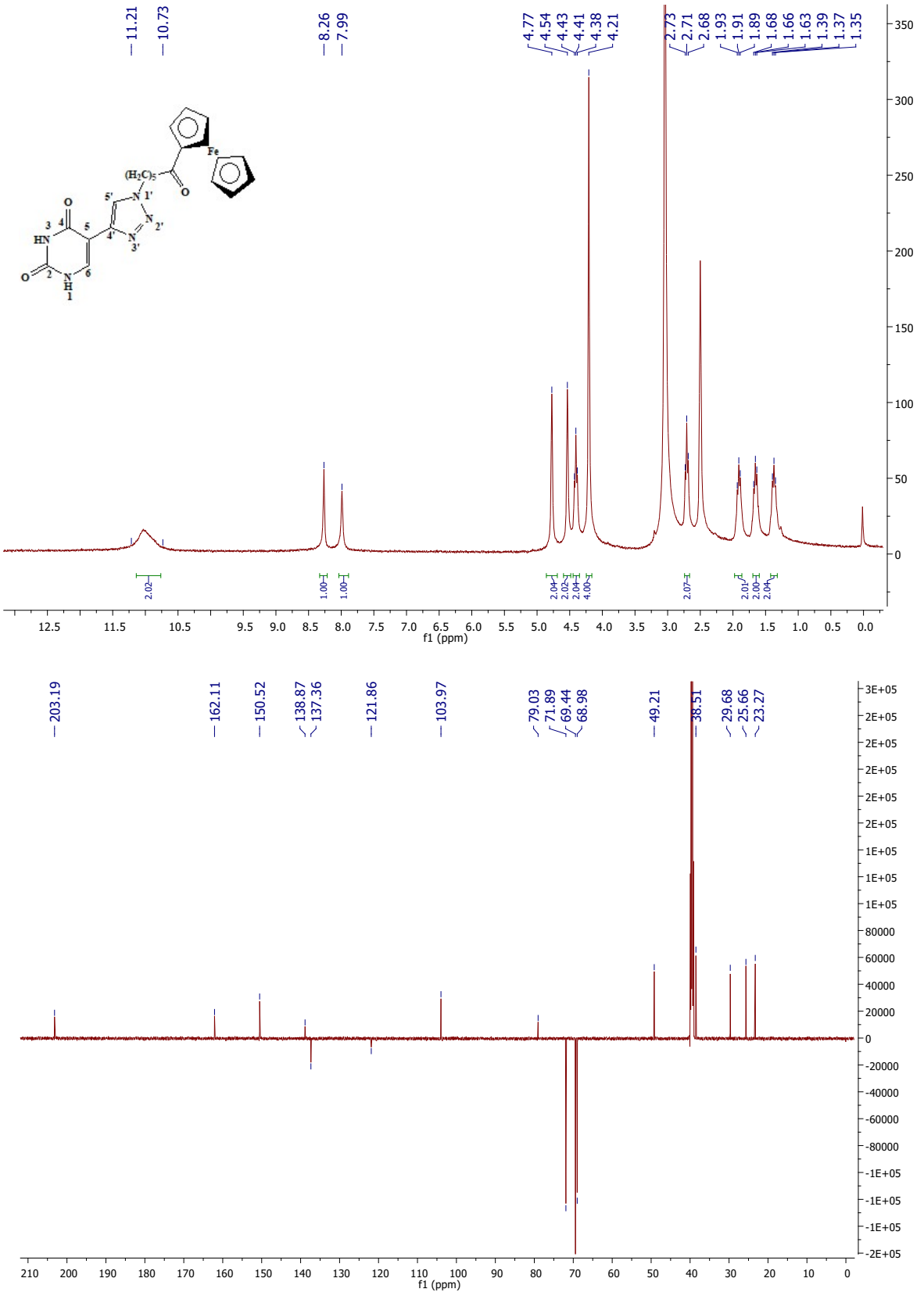


Figure S8. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **14**.

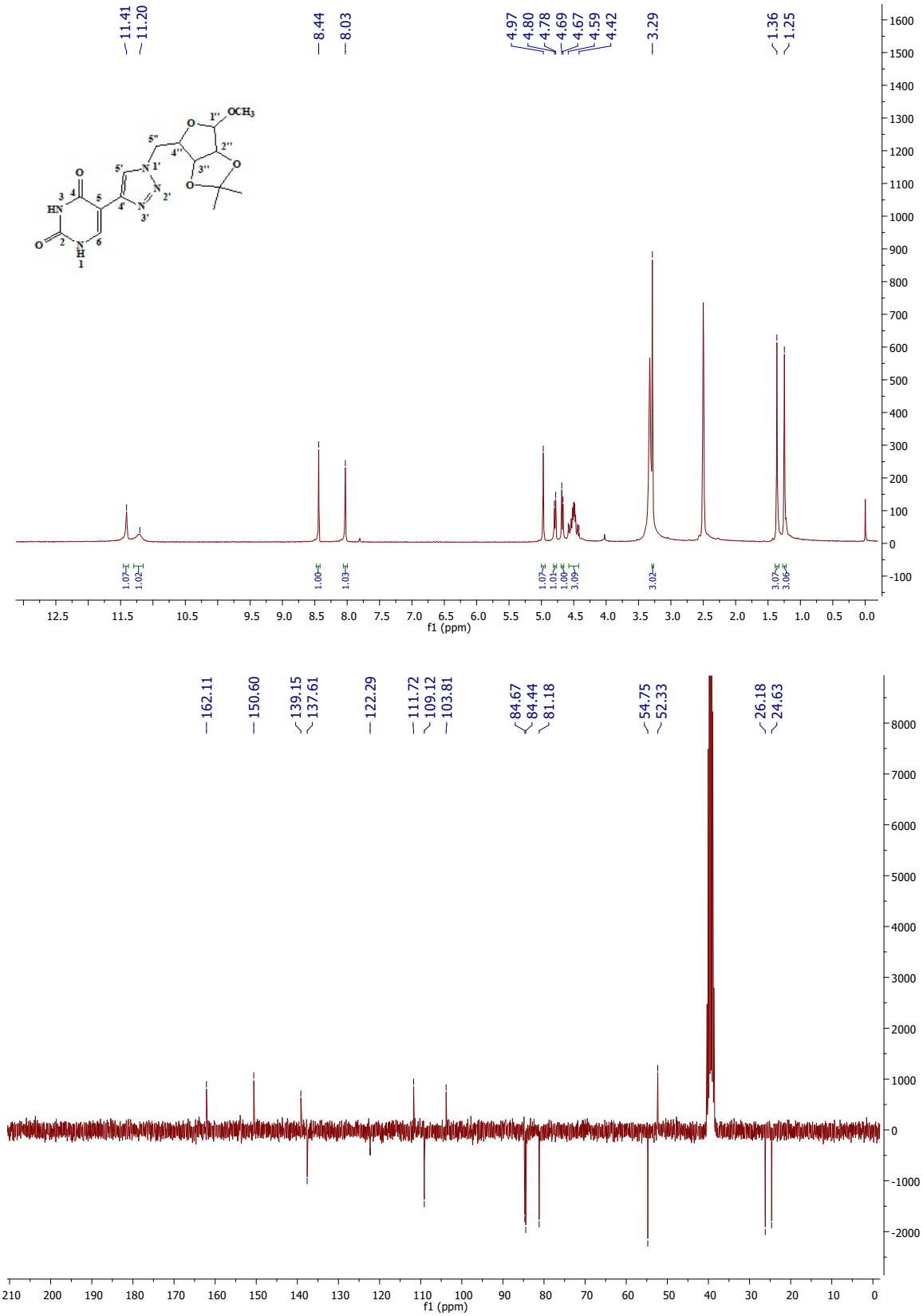


Figure S9. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **16**.

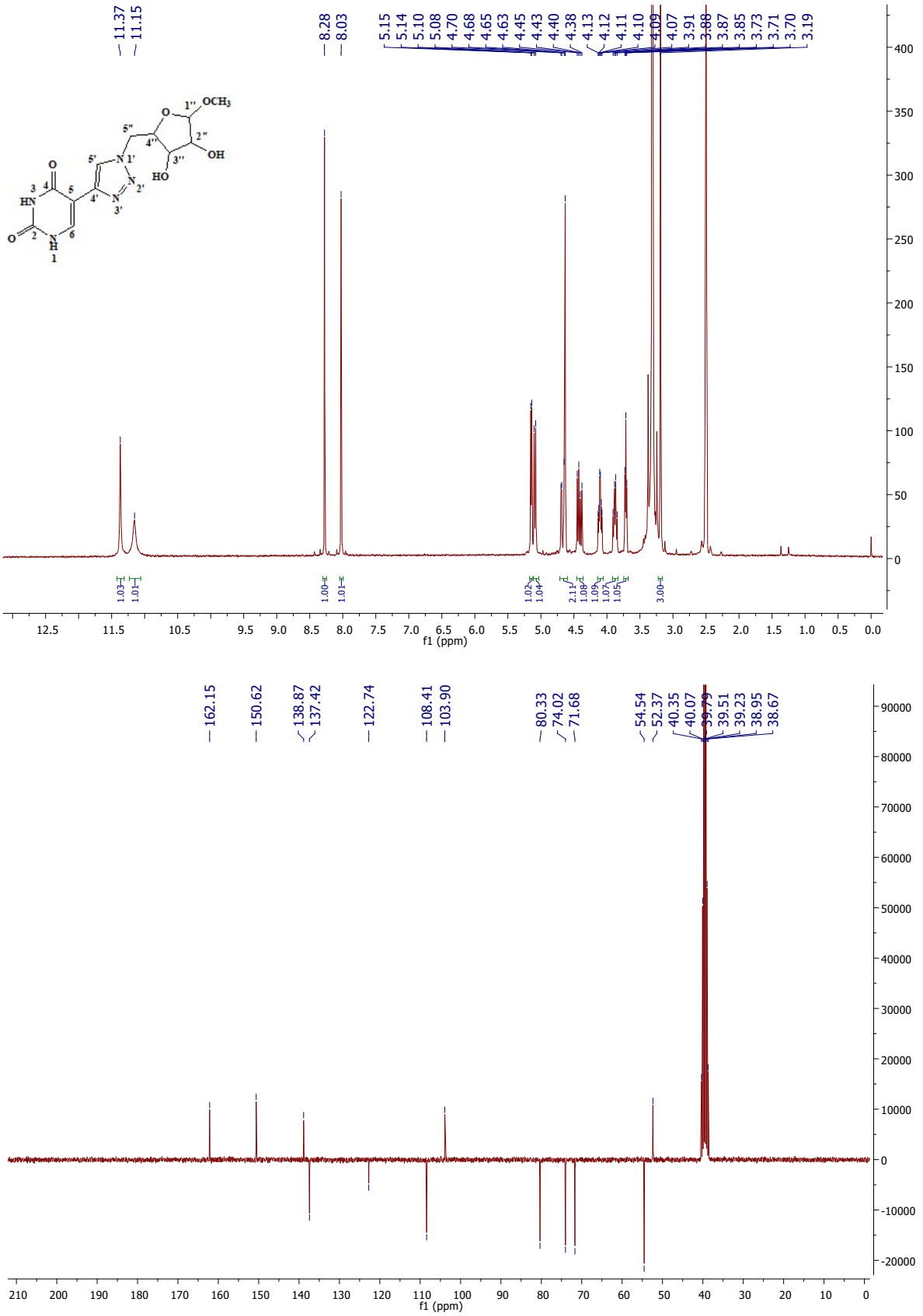


Figure S10. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **17**.

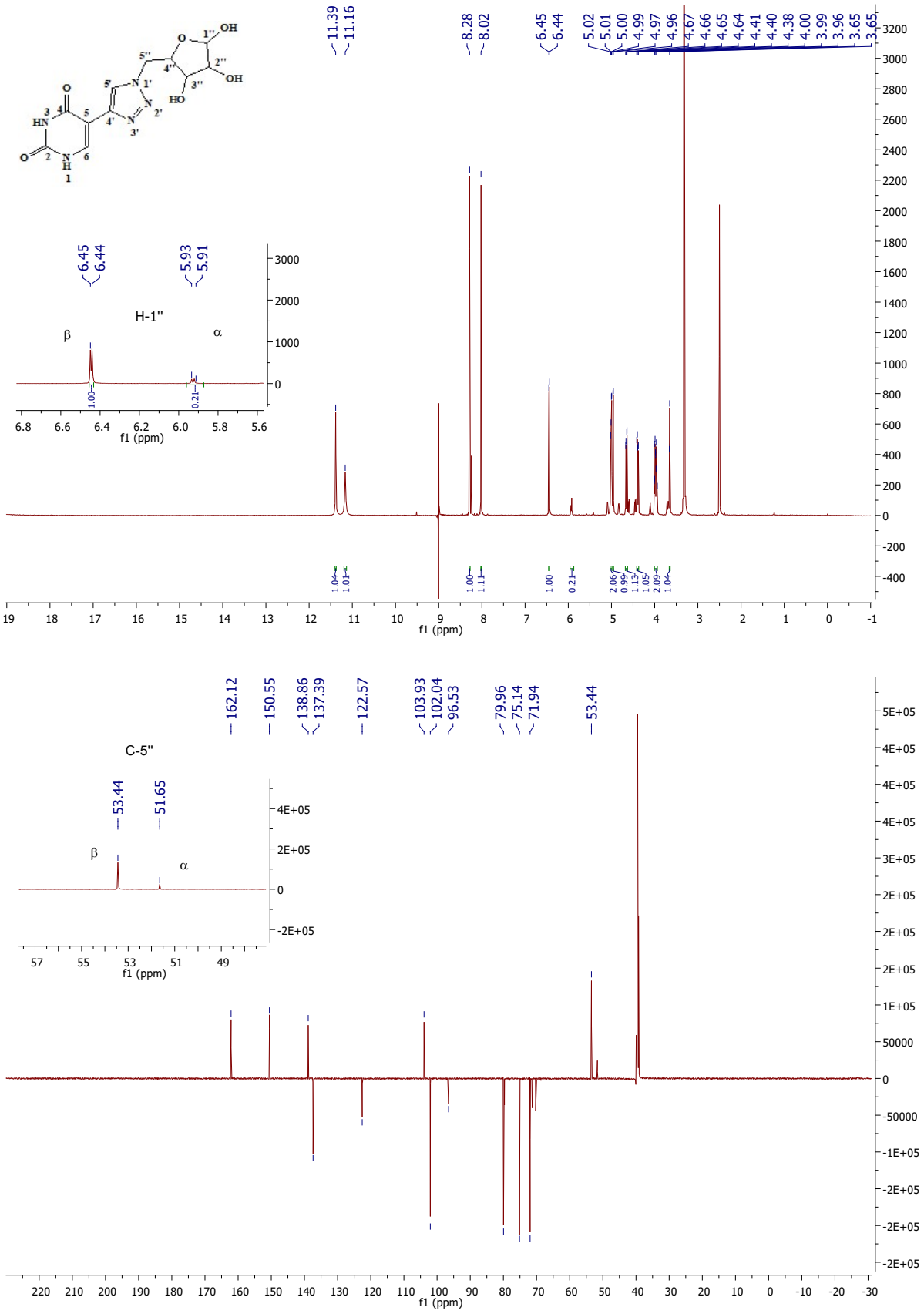


Figure S11. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **18**.

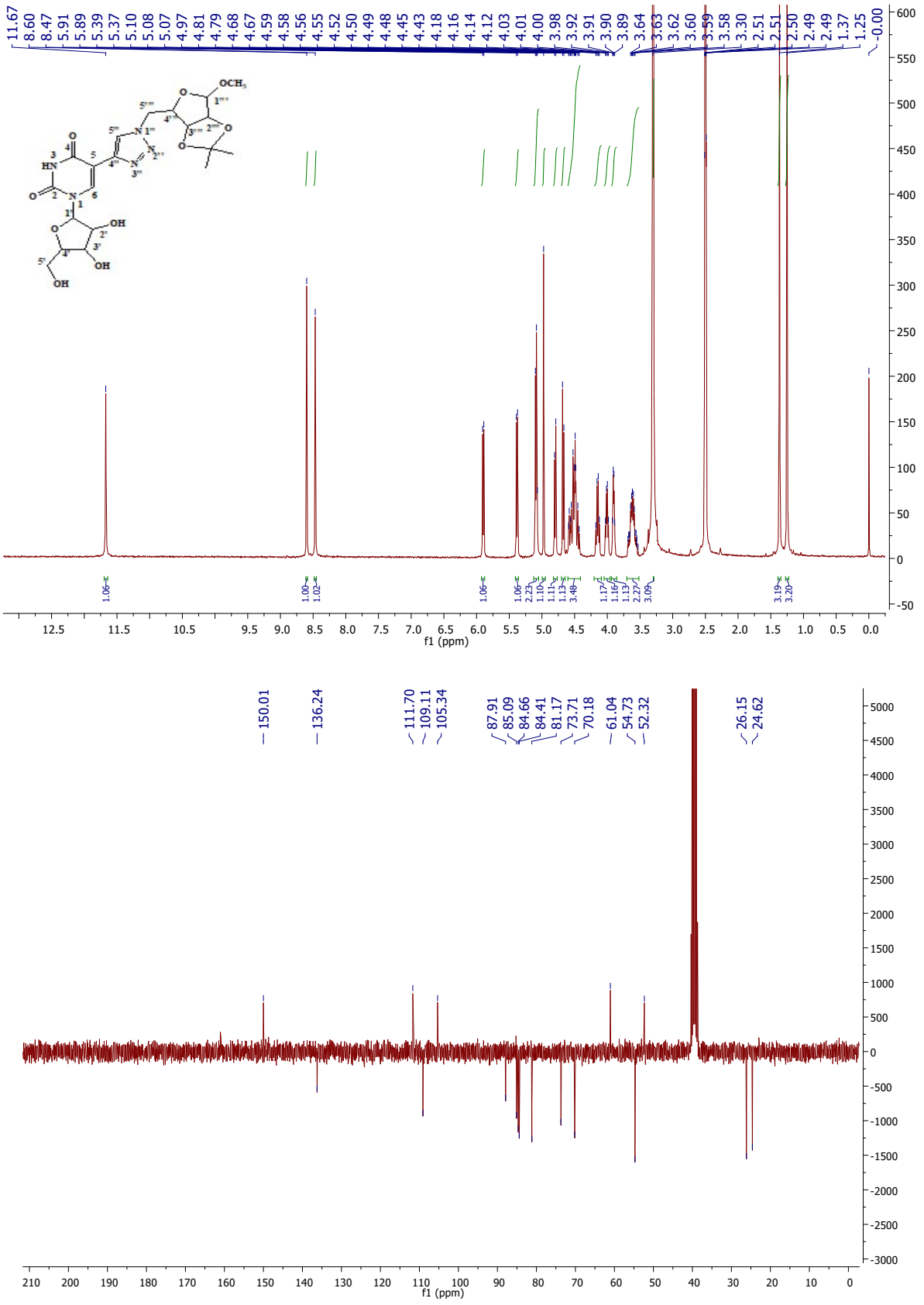


Figure S12. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **19**.

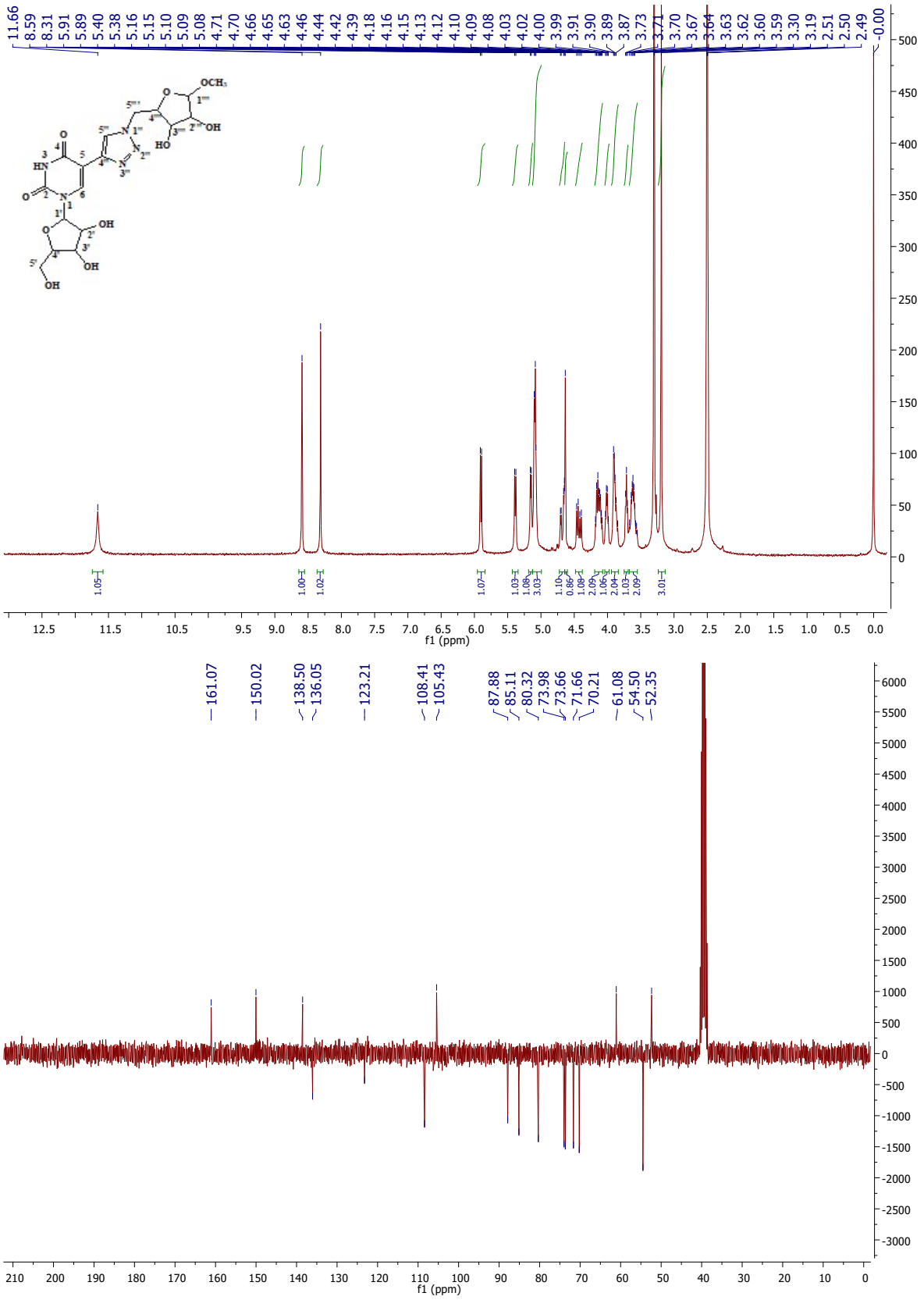
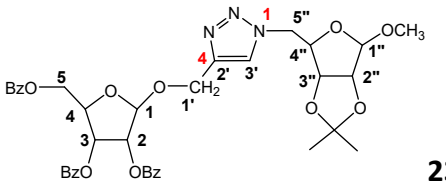


Figure S13. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR spectra (75 MHz, APT, DMSO-d_6) of compound **20**.



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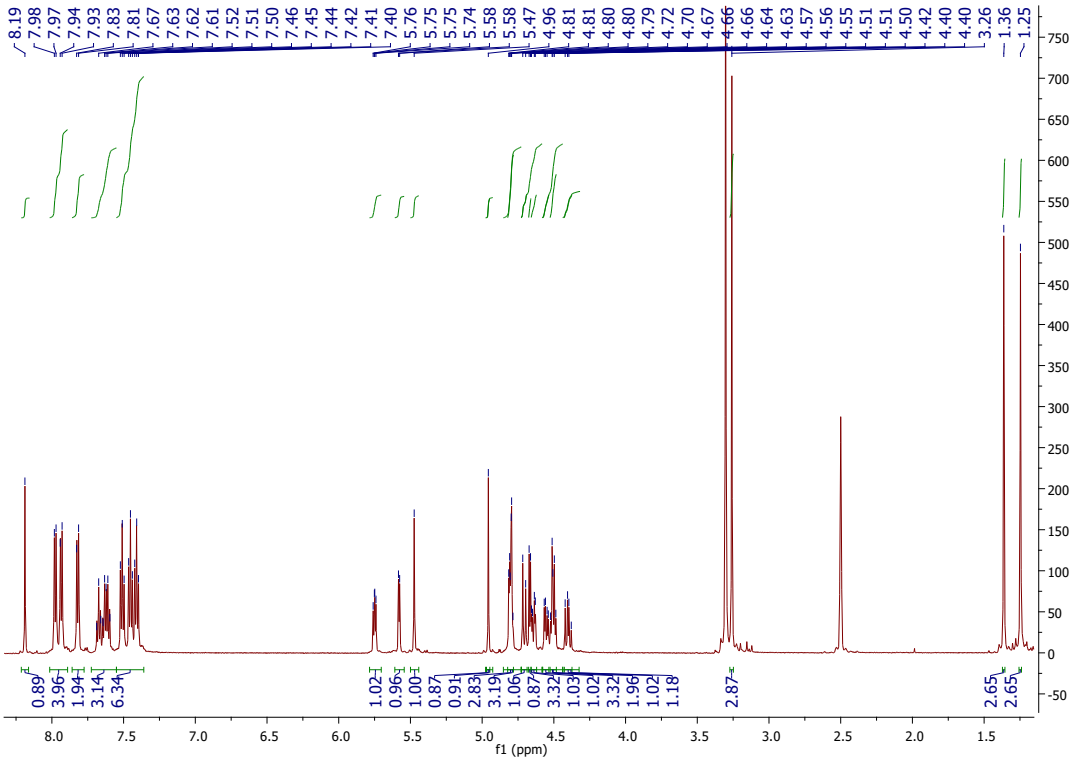


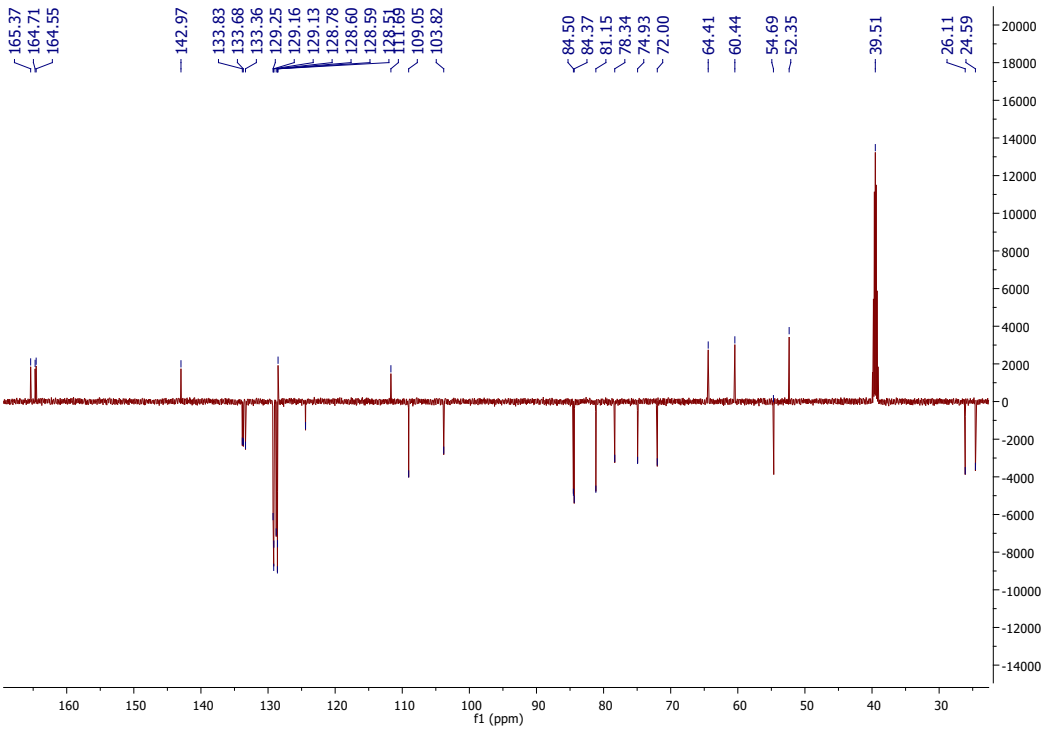
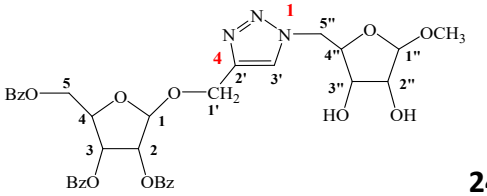


Figure S14. ^{1}H NMR (600 MHz, DMSO-d_6) and ^{13}C NMR (151 MHz, APT, DMSO-d_6) spectra of compound **23**.



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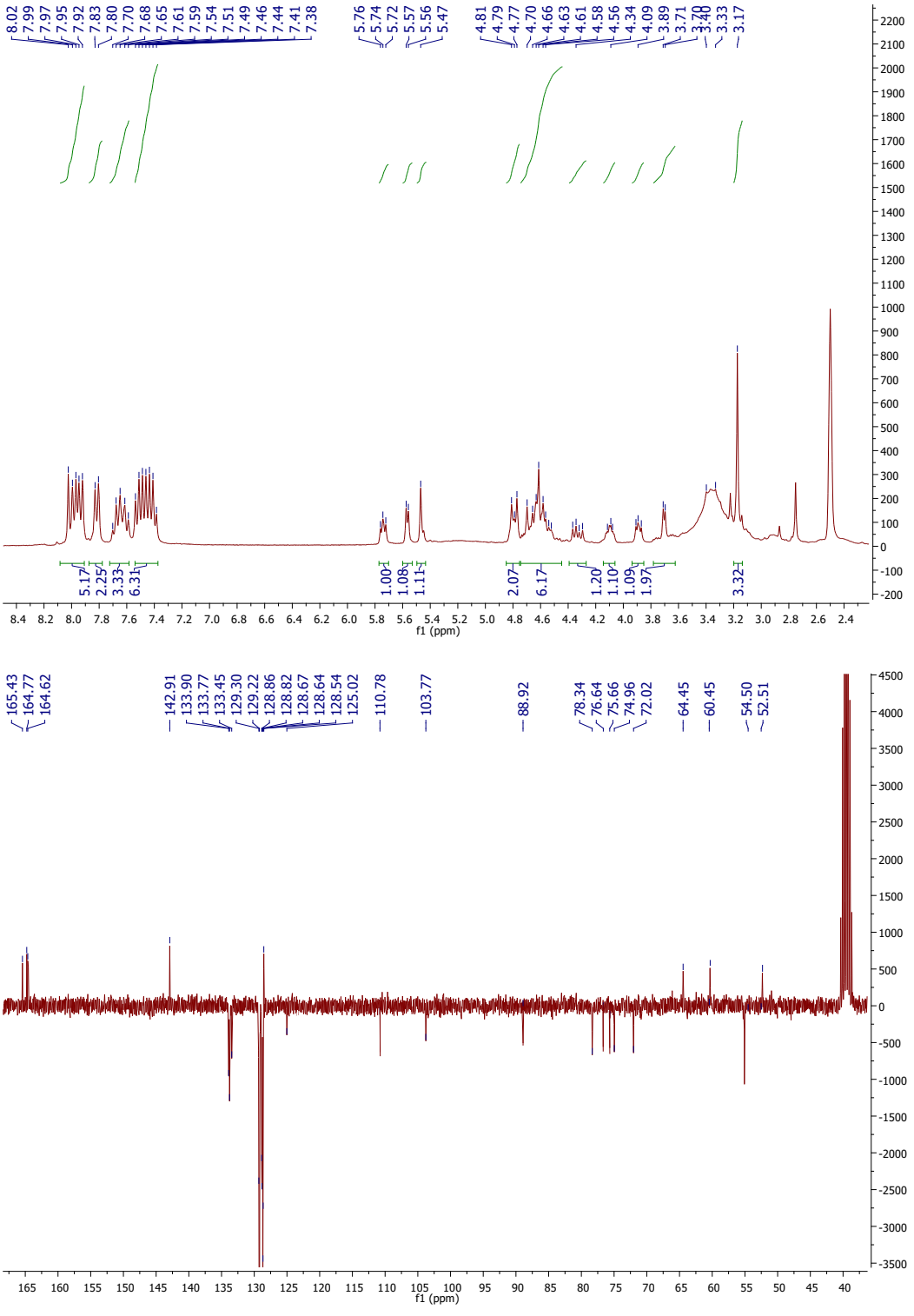
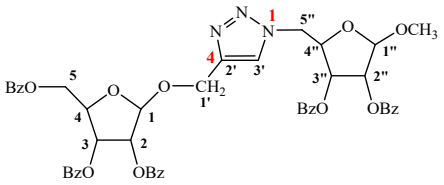


Figure S15. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, APT, DMSO-d_6) spectra of compound **24**.



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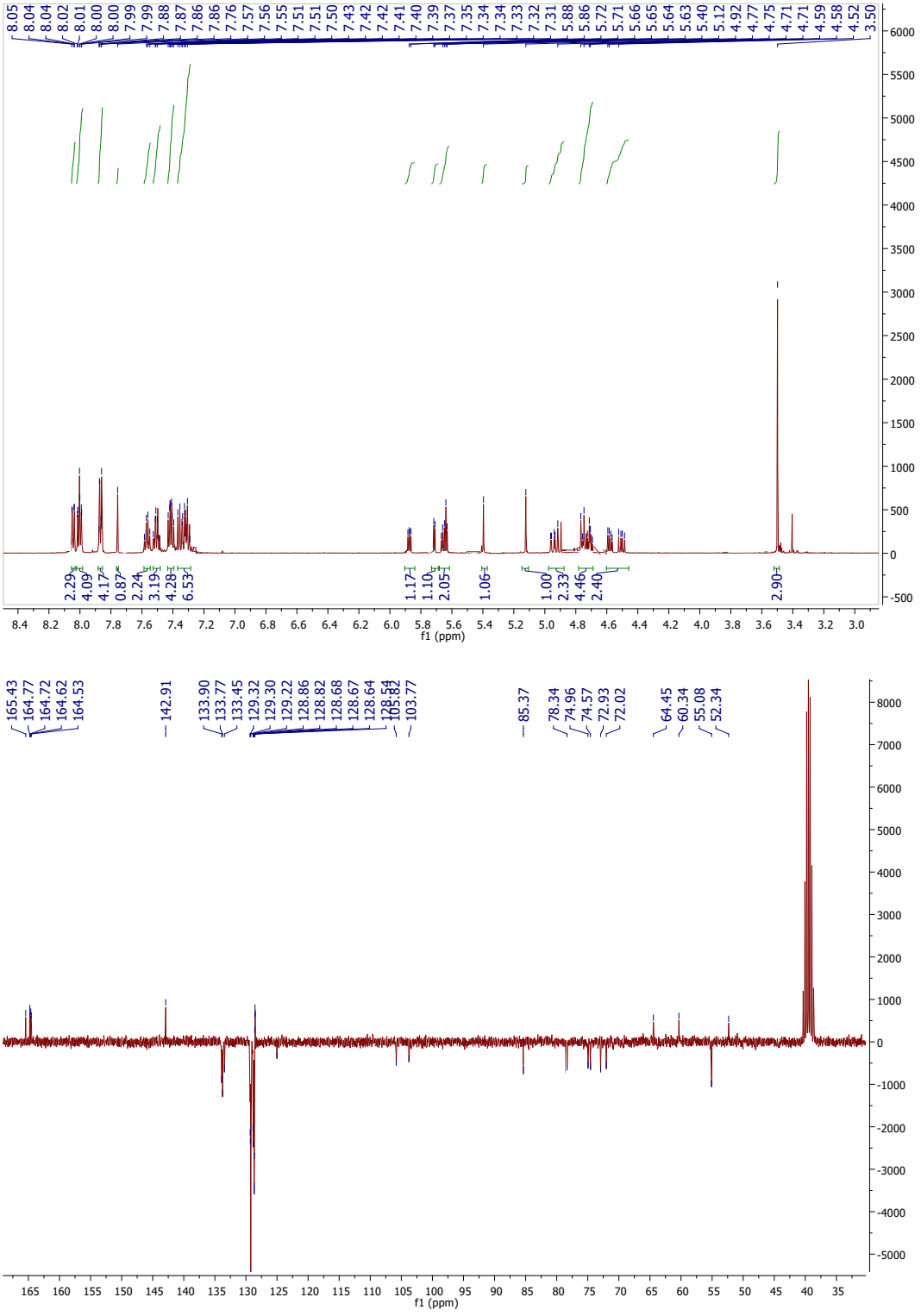

Figure 16. ^{1}H NMR (600 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, APT, DMSO-d_6) spectra of compound **25**.

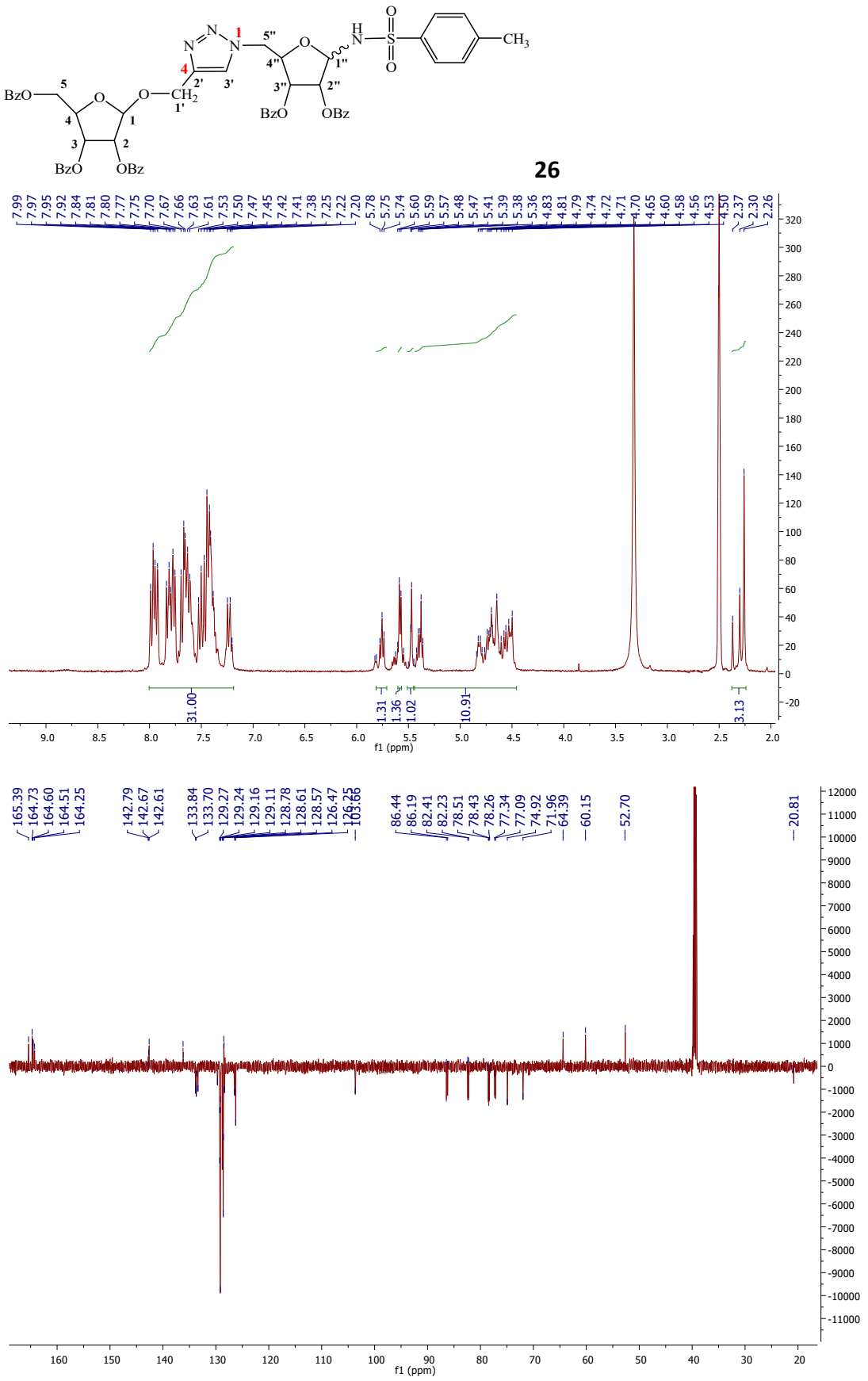

Figure S17. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (151 MHz, APT, DMSO-d_6) spectra of compound **26**.

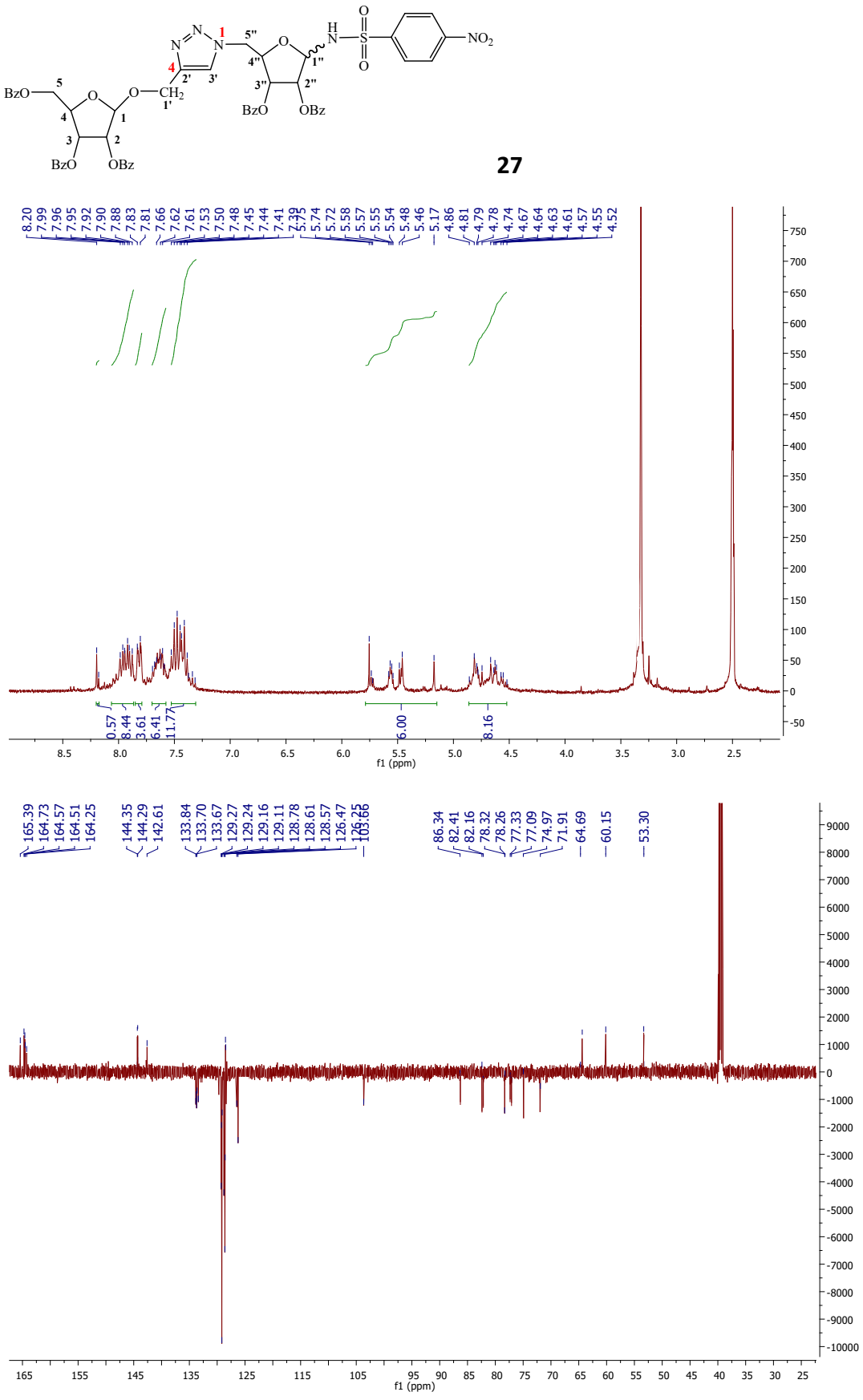

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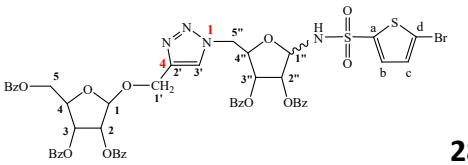
Figure S18. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, APT, DMSO-d_6) spectra of compound **27**.



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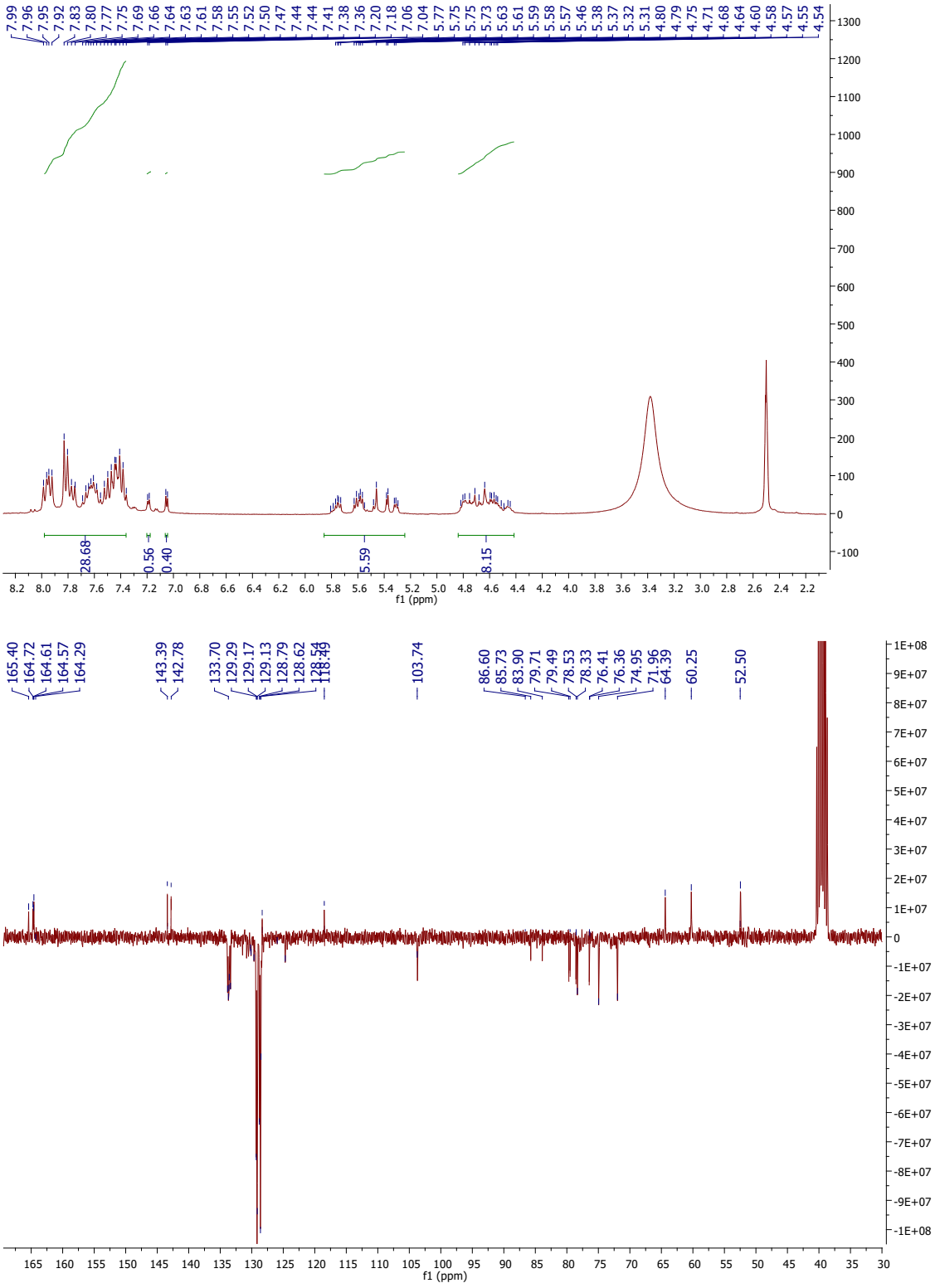
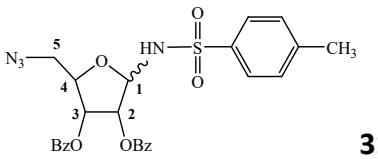


Figure S19. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (151 MHz, APT, DMSO-d_6) spectra of compound **28**.



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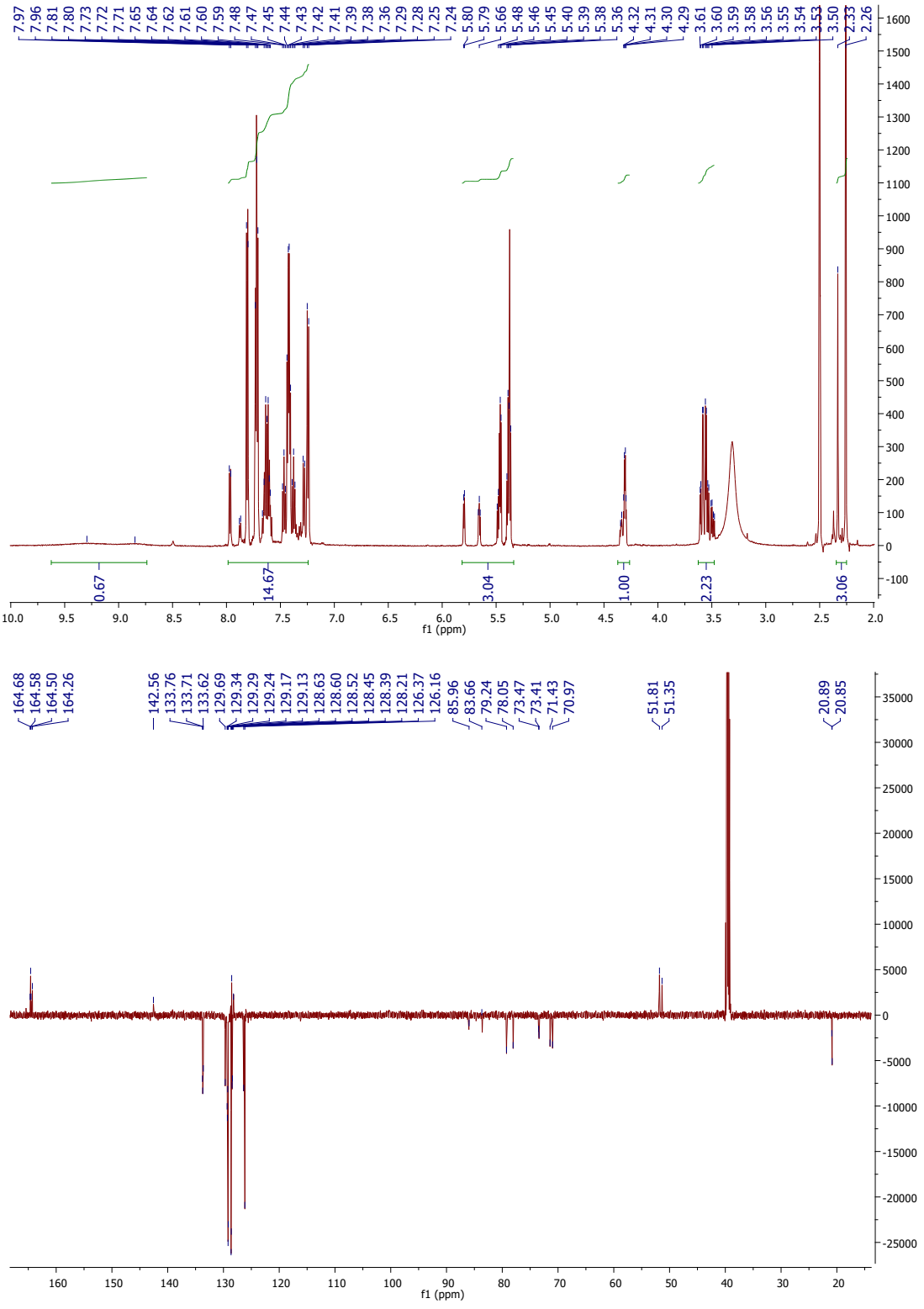
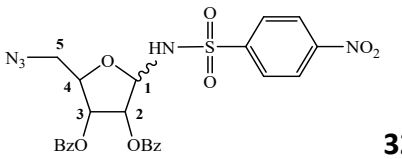


Figure S20. ^{1}H NMR (600 MHz, DMSO-d_6) and ^{13}C NMR (151 MHz, APT, DMSO-d_6) spectra of compound **31**.



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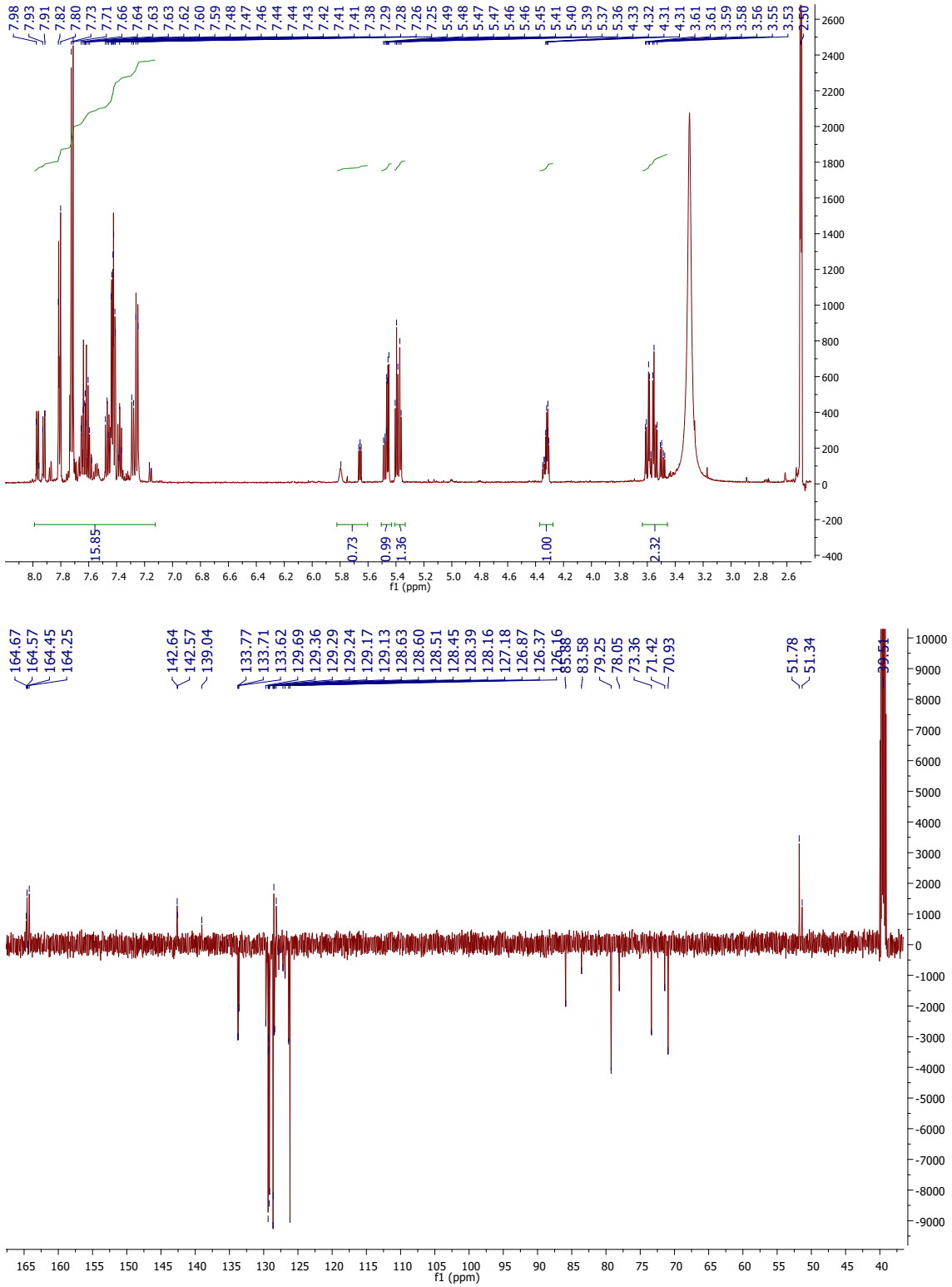
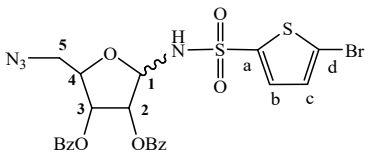


Figure S21. ^{1}H NMR (600 MHz, DMSO-d_6) and ^{13}C NMR (151 MHz, APT, DMSO-d_6) spectra of compound **32**.



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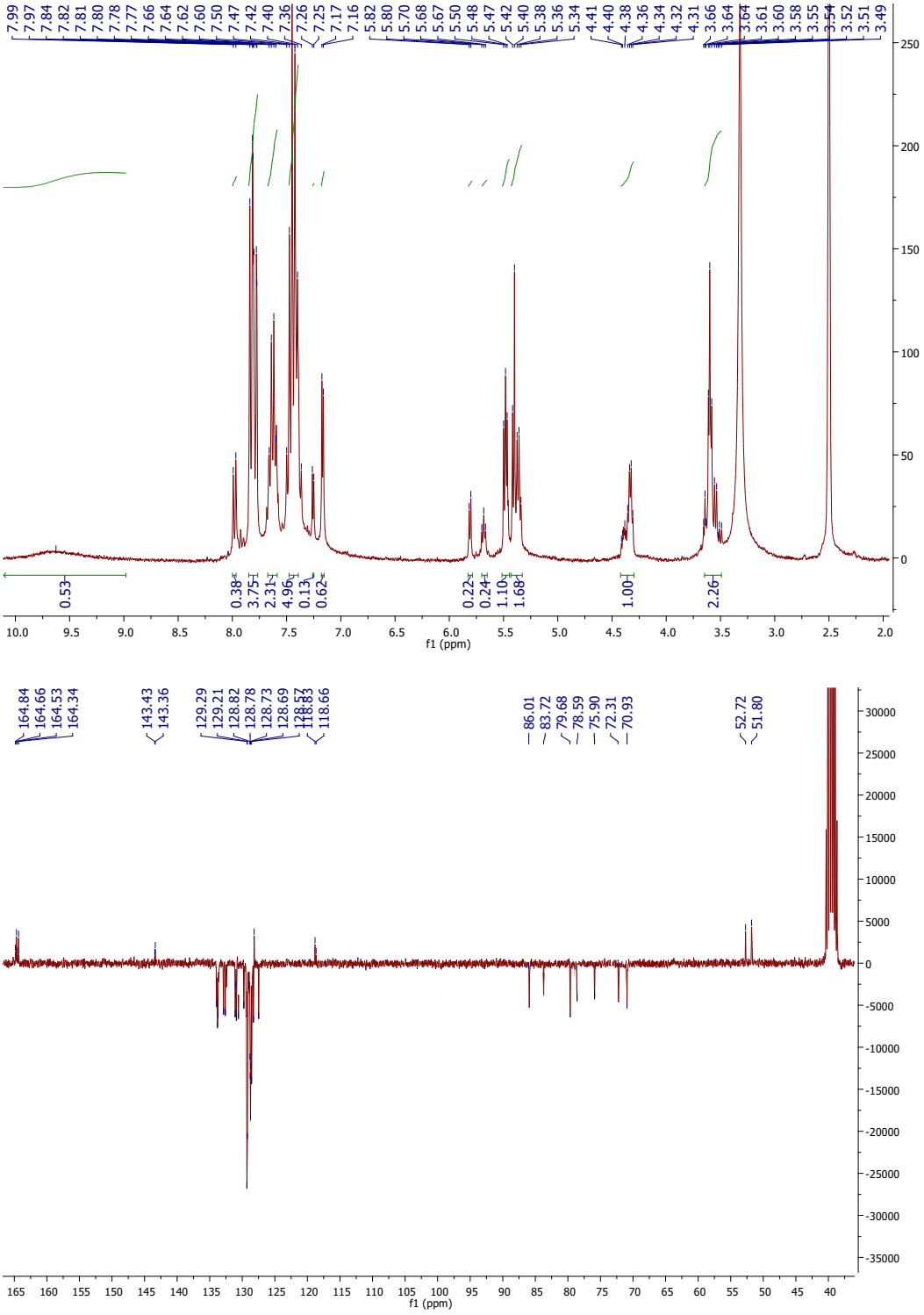

Figure S22. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, APT, DMSO-d_6) spectra of compound **33**.

Table S1 Sensitivity of human tumor and normal cells to *C*5–[1,2,3]triazolyl-flex-nucleoside analogs (**7**–**14**, **16**–**20**) expressed as **IC_{50}**[a] value and **SI** tumor selectivity indeks

						ICI_{50}/μM							
			SI		**SI**		**SI**		**SI**		**SI**		**SI**
Comp.	**MDCK**	**HeLa**		**Caco-2**		**NCI-H358**		**Raji**		**K562**		**HuT-78**	
7	>100	>100	-	>100	-	>100	-	>100	-	>100	-	71.8 ±4.3	1.4
8	>100	>100	-	>100	-	>100	-	>100	-	>100	-	56.8 ±2.1	1.8
9	>100	>100	-	>100	-	>100	-	>100	-	>100	-	67.2 ±14.1	1,5
10	>100	>100	-	>100	-	>100	-	>100	-	>100	-	57.3 ±5.8	1.8
11	>100	>100	-	>100	-	>100	-	100	-	94.3±12.0	-	63.7 ±10.2	1.6
12	>100	>100	-	>100	-	>100	-	**7.8± 4.6**	**12.8**	**4.0 ±0.6**	**25.0**	**14.3 ±5.6**	**7.0**
13	>100	>100	-	>100	-	>100	-	>100	-	>100	-	**17.4 ±5.8**	**5.8**
14	>100	>100	-	>100	-	>100	-	64.5 ±8.1	1.6	15.9 ±5.3	**6.3**	< 100	-
16	>100	>100	-	>100	-	>100	-	>100	-	>100	-	72.6 ±9.2	1.4
17	>100	>100	-	>100	-	>100	-	>100	-	97.5± 15.5	-	90.6 ±16.1	1.1
18	> 100	>100	-	6.7±1.0	-	> 100	-	> 100	-	61.3 ±11.8	1.6	> 100	-
19	>100	>100	-	>100	-	>100	-	> 100	-	> 100	-	70.5 ±5.2	1.3
20	>100	>100	-	>100	-	>100	-	> 100	-	> 100	-	71.8 ±1.6	1.4
5-FU	55±.8.7	8.2±1.9	6.7	5.9±0.7	9.3	≥50	-	> 100	-	9.8±1.1	5.6	> 100	-

[a]IC_{50} – Compound concentration that inhibited cell growth by 50 %. Data represents mean IC_{50} (μM) values ± standard deviation (SD) of three independent experiments. Exponentially growing cells were treated with compounds during 72 h. Cytotoxicity was analyzed using MTT survival assay. **5-FU**: 5-Fluorouracil.

Table 2. Sensitivity of human tumor and normal cells to investigated ribofuranoside conjugates (**23**–**28**), and 5-azido-ribosyl-sulfonamides (**31**–**33**) expressed as **IC_{50}**[a] value and **SI** tumor selectivity index.

						IC_{50}/µM							
			SI		**SI**		**SI**		**SI**		**SI**		**SI**
Comp.	**MDCK**	**HeLa**		**Caco-2**		**NCI-H358**		**Raji**		**K562**		**HuT-78**	
23	>100	>100	-	>100	-	>100	-	>100	-	>100	-	76.4 ±12.1	1.3
24	5.7 ±1.1	11.6 ±1.3	-	13.3 ±3.7	-	13.4 ±6.4	-	15.4 ±1.1	-	15.7 ±1.3	-	4.8 ±2.8	-
25	>100	>100	-	>100	-	>100	-	>100	-	>100	-	>100	-
26	> 100	71.9 ±11.1	-	80.6 ±4.2	-	> 100	**-**	**34.5 ±0.1**	2.9	**2.4 ±0.0**	**41.7**	**6.2 ±2.6**	**16.3**
27	86.1 ±8.7	>100	-	>100	-	25.2±0.2	**-**	**12.5 ±2.6**	**8.6**	**10.11 ±1.8**	**9.9**	**40.5 ±6.8**	2.5
28	>100	>100	-	>100	-	>100	-	-	-	>100		76.2 ±0.9	1.3
31	>100	>100	-	>100	-	>100	-	76.9 ±3.2	1.3	47.2 ±27.3	2.1	57.4 ±8.8	1.7
32	>100	>100	-	>100	-	>100	-	>100		52.7 ±18.2	-	93.9 ±16.0	-
33	>100	>100	-	>100	-	>100	**-**	**10.6 ±0.1**	**9.4**	**4.9 ±1.7**	**20.4**	**8.9 ±1.3**	**11.2**
5-FU	55±.8.7	8.2±1.9	6.7	5.9±0.7	9.3	≥50	-	>100	-	9.8±1.1	5.6	>100	-

[a]IC_{50} – Compound concentration that inhibited cell growth by 50 %. Data represents mean IC_{50} (µM) values ± standard deviation (SD) of three independent experiments. Exponentially growing cells were treated with compounds during 72 h. Cytotoxicity was analyzed using MTT survival assay. " – " not analysed; **5-FU**: 5-Fluorouracil.