Supporting Information

Synthesis and Evaluation of Topoisomerase I Inhibitors Possessing the 5,13-Dihydro-6*H*-benzo[6,7]indolo[3,2-*c*]quinolin-6-one Scaffold

Tsutomu Fukuda,[a,*] Yuri Matsuo,[a] Fuyuki Matsuoka,[a] Naoki Yoshioka,[a] Gen Onodera,[a] Masanari Kimura,[a] Fumito Ishibashi,[b] and Masatomo Iwao[a]

[a] *Division of Chemistry and Materials Science, Graduate School of Engineering, Nagasaki University, 1-14 Bunkyo-machi, Nagasaki 852-8521, Japan*
[b] *Division of Marine Life Science and Biochemistry, Graduate School of Fisheries and Environmental Sciences, Nagasaki University, 1-14 Bunkyo-machi, Nagasaki 852-8521, Japan*

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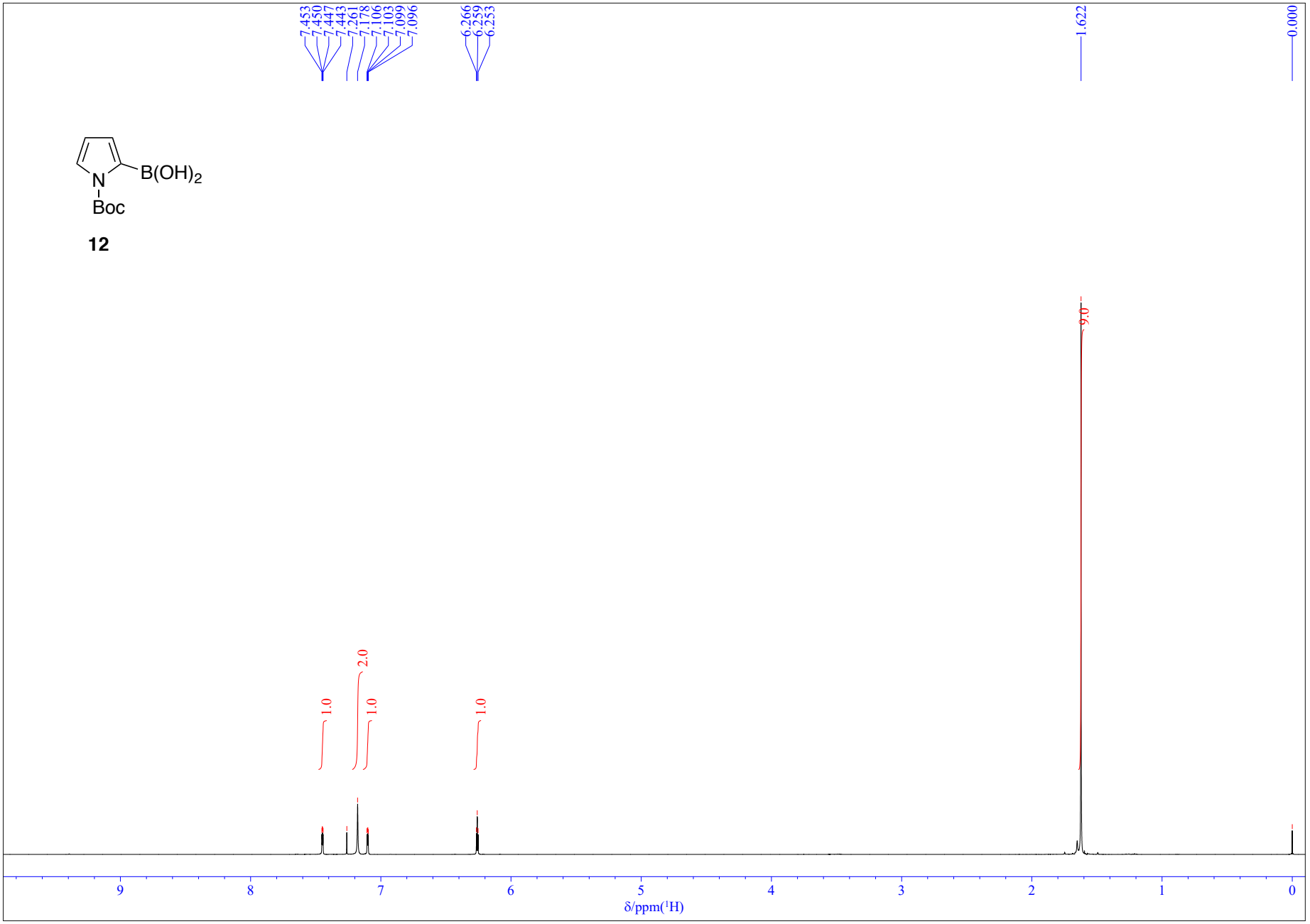

Figure S1. ^{1}H NMR spectrum of compound **12** (500 MHz, $CDCl_3$).

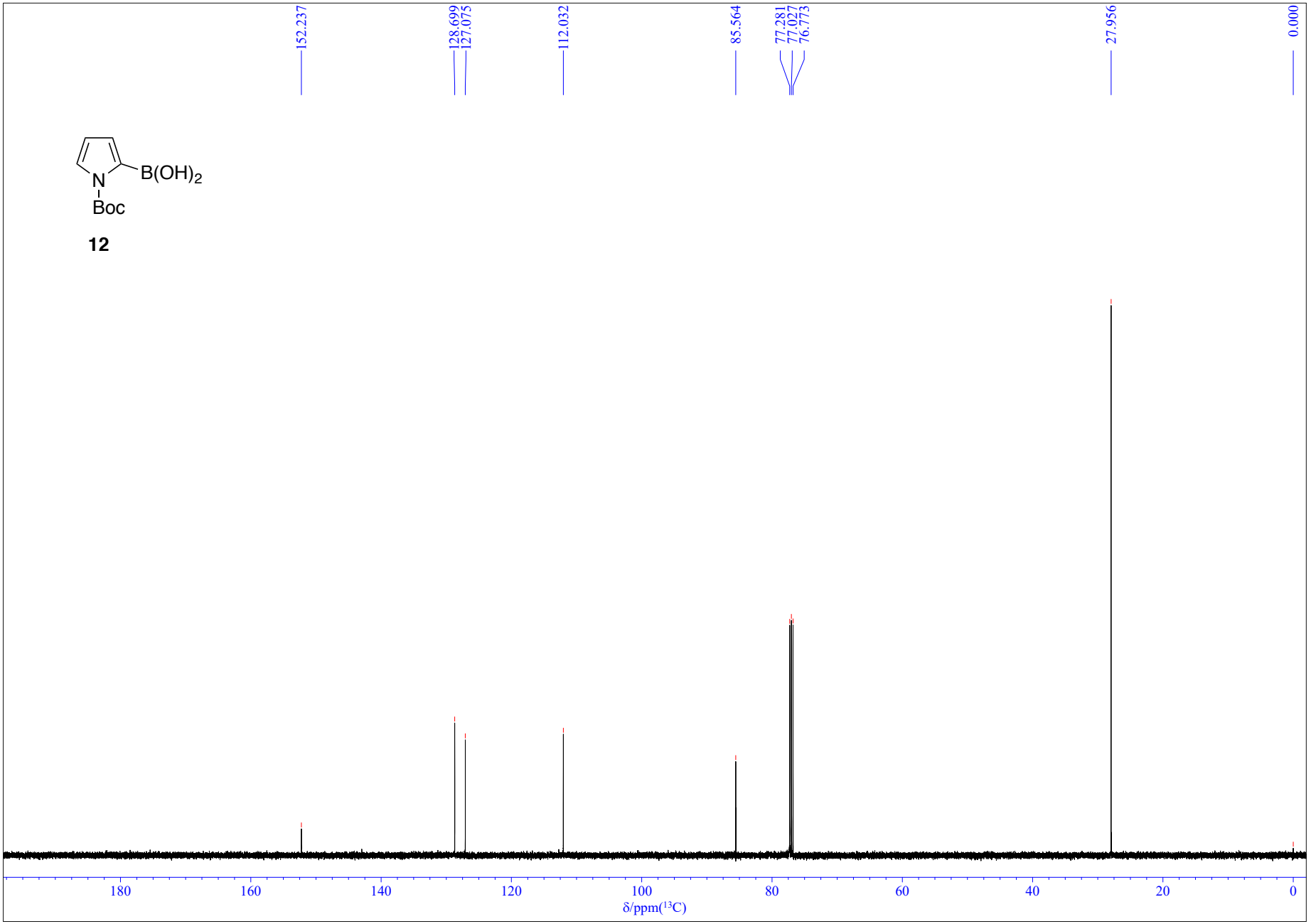

Figure S2. ^{13}C NMR spectrum of compound **12** (126 MHz, $CDCl_3$).

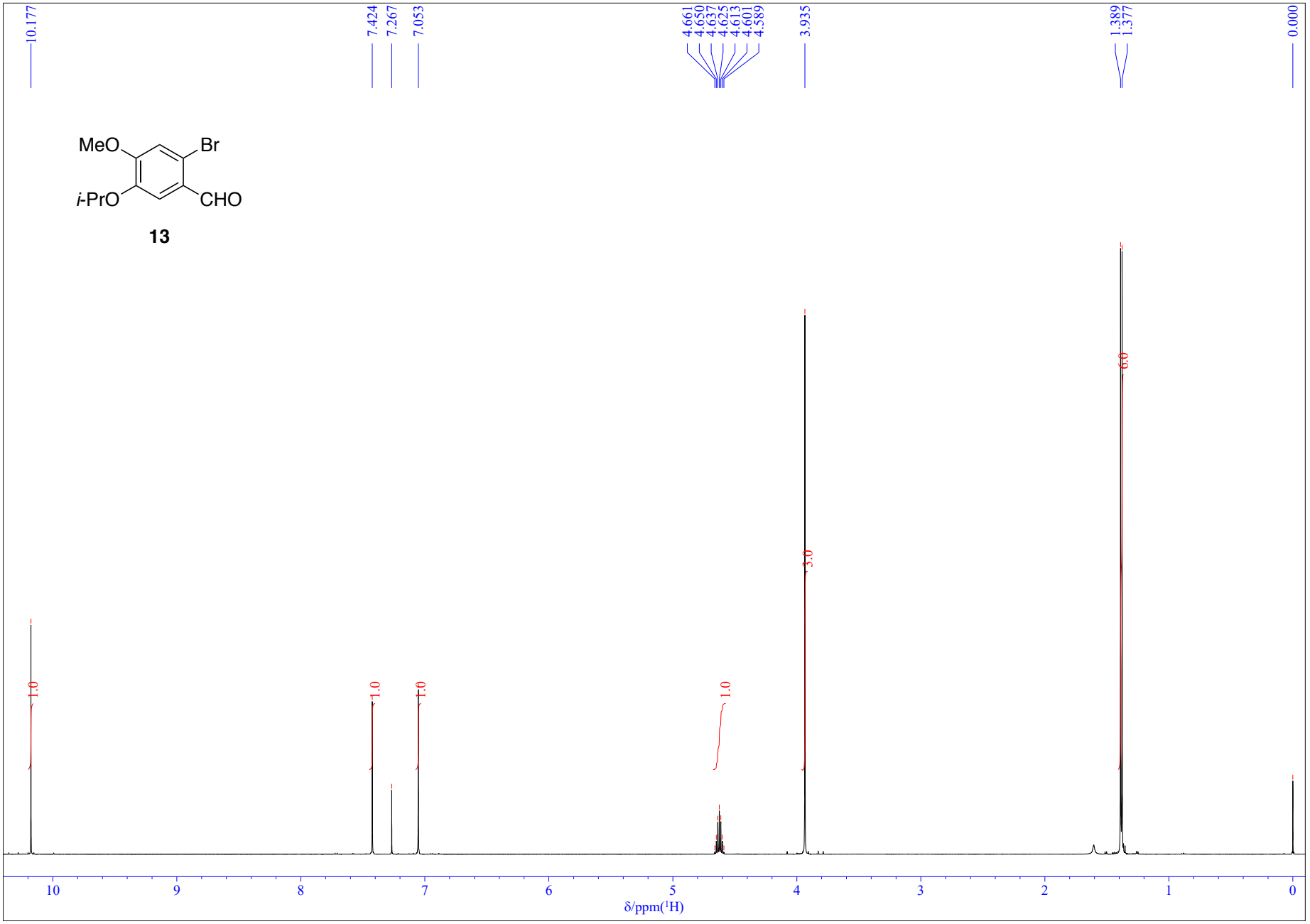

Figure S3. ^{1}H NMR spectrum of compound **13** (500 MHz, $CDCl_3$).

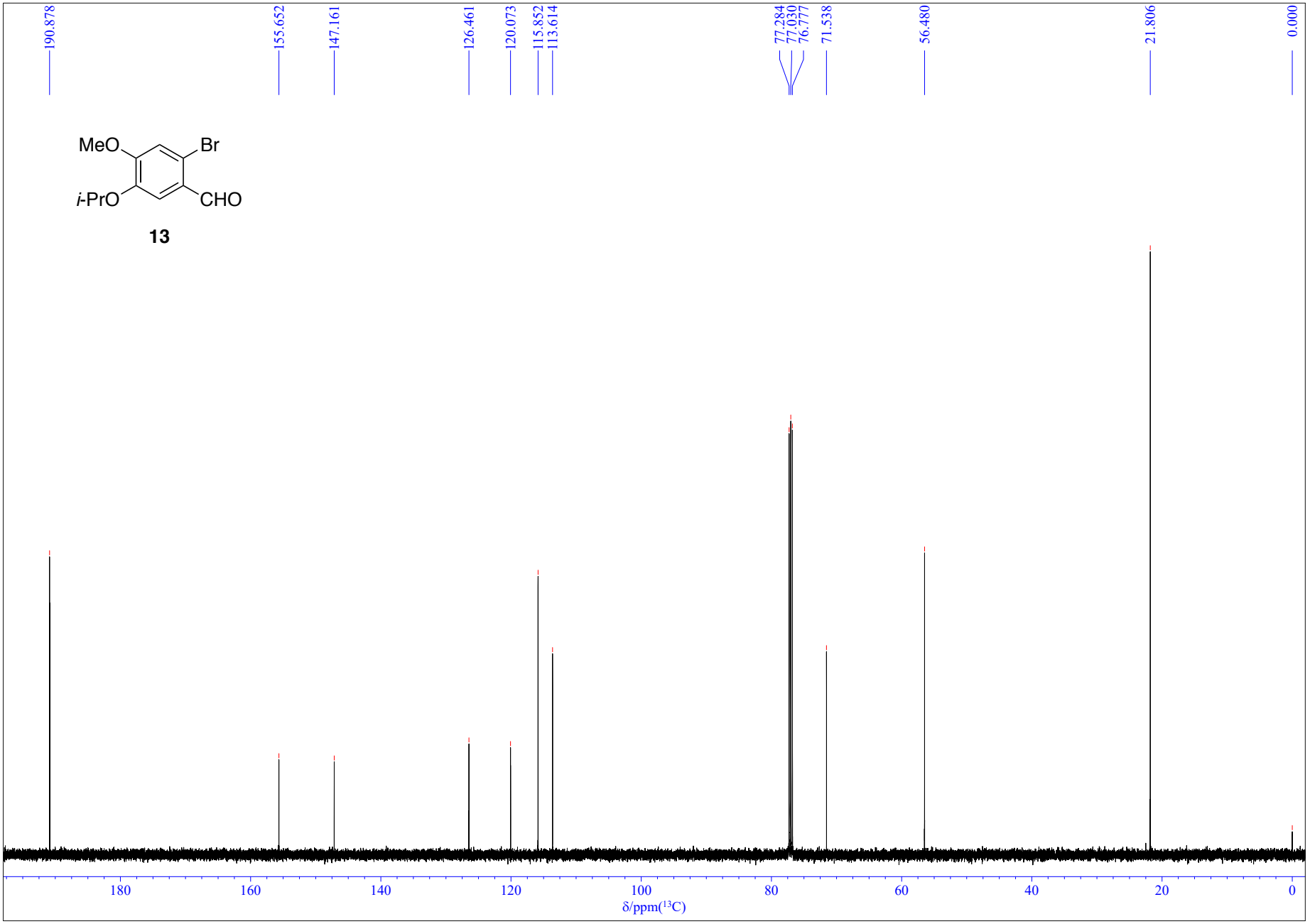

Figure S4. ^{13}C NMR spectrum of compound **13** (126 MHz, $CDCl_3$).

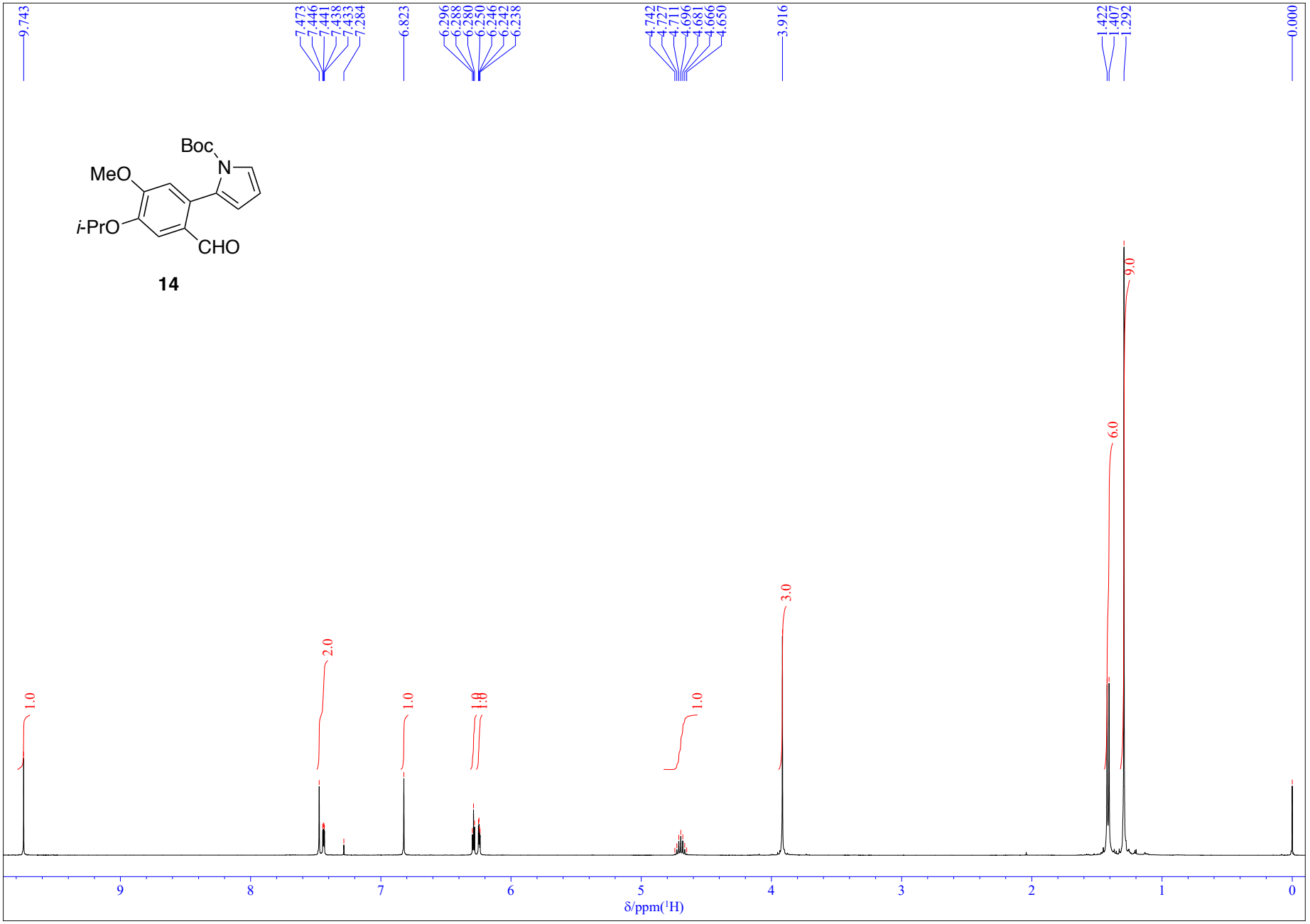

Figure S5. ^{1}H NMR spectrum of compound **14** (400 MHz, $CDCl_3$).

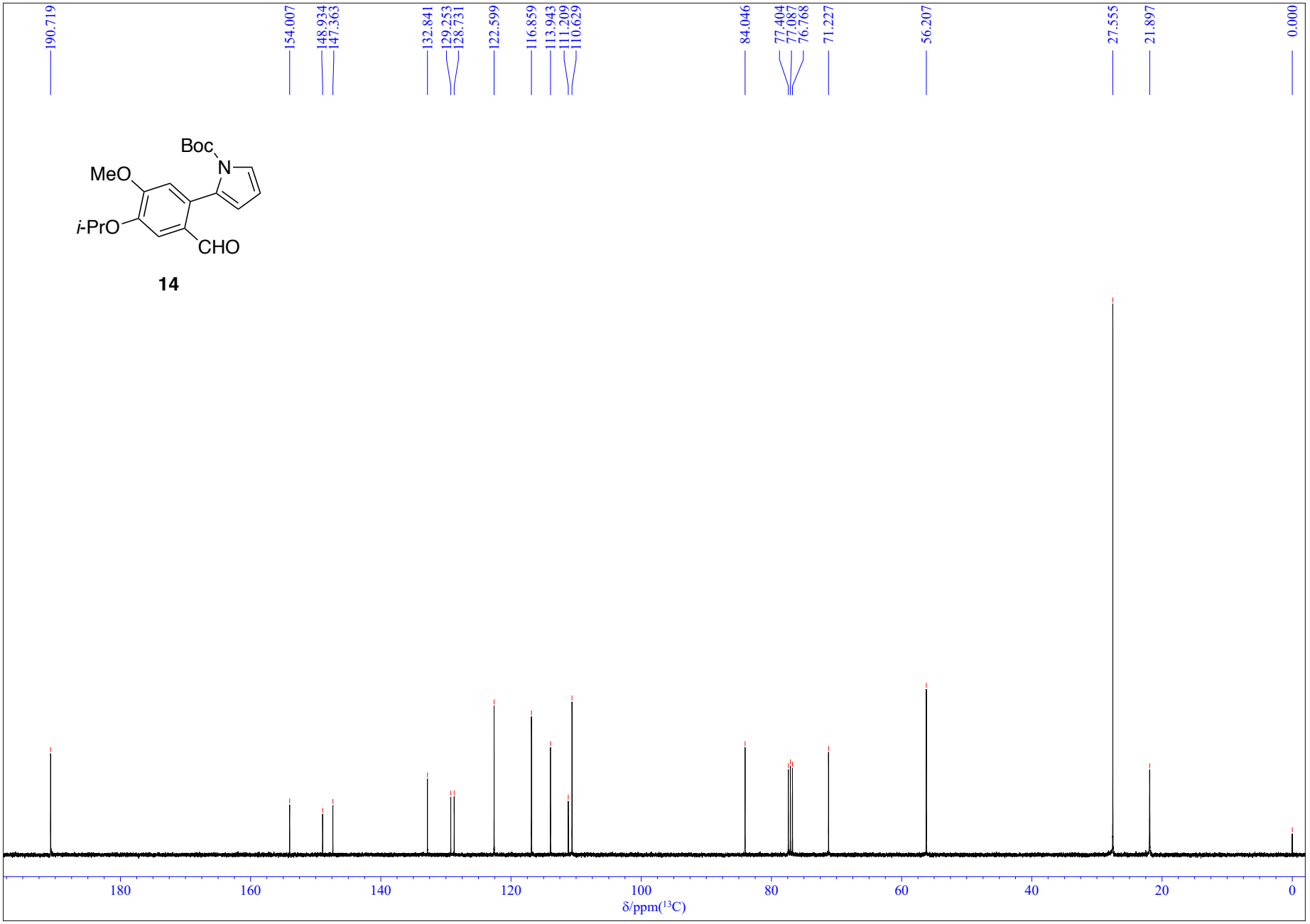

Figure S6. ^{13}C NMR spectrum of compound **14** (100 MHz, $CDCl_3$).

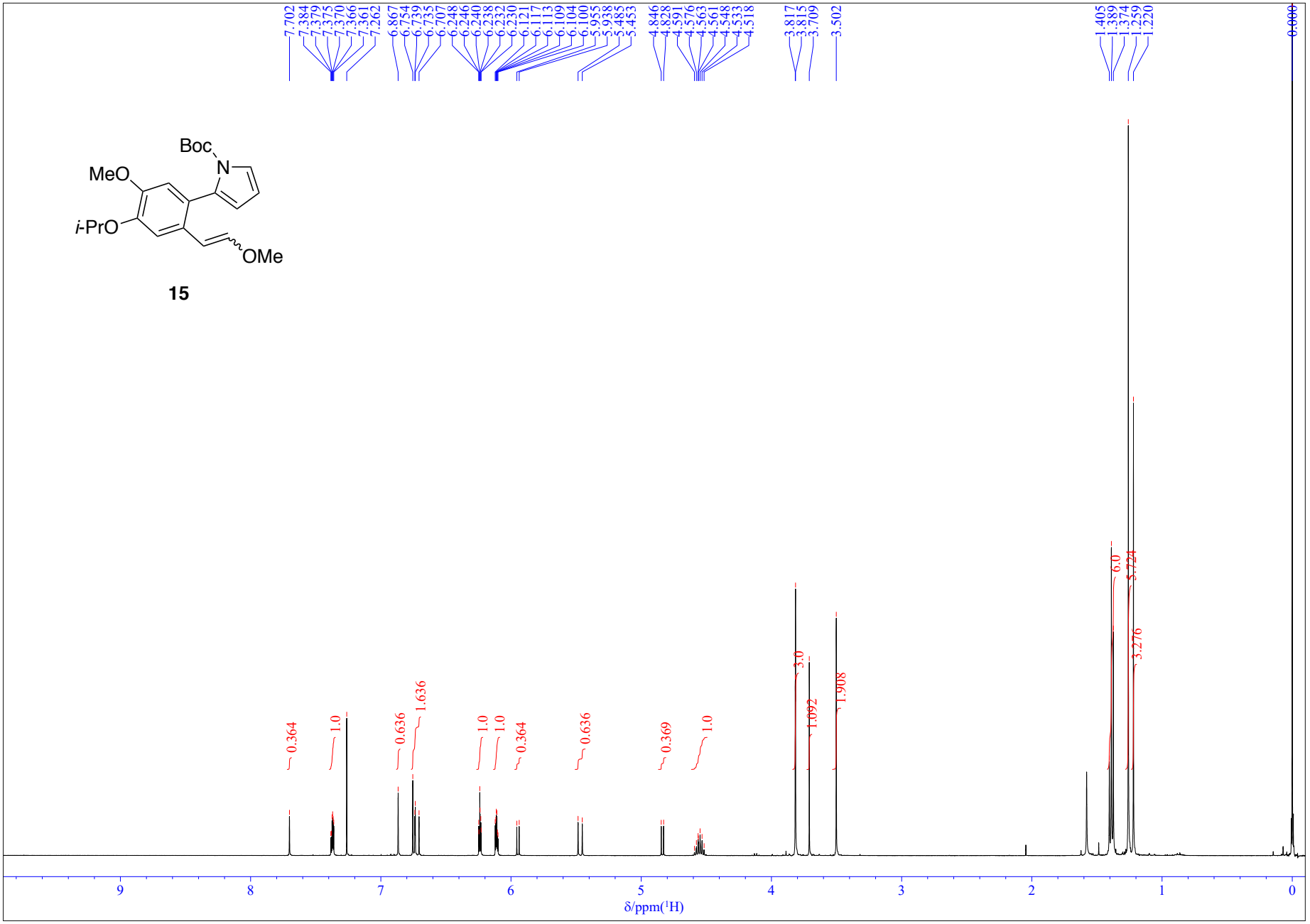

Figure S7. ^{1}H NMR spectrum of compound **15** (400 MHz, $CDCl_3$).

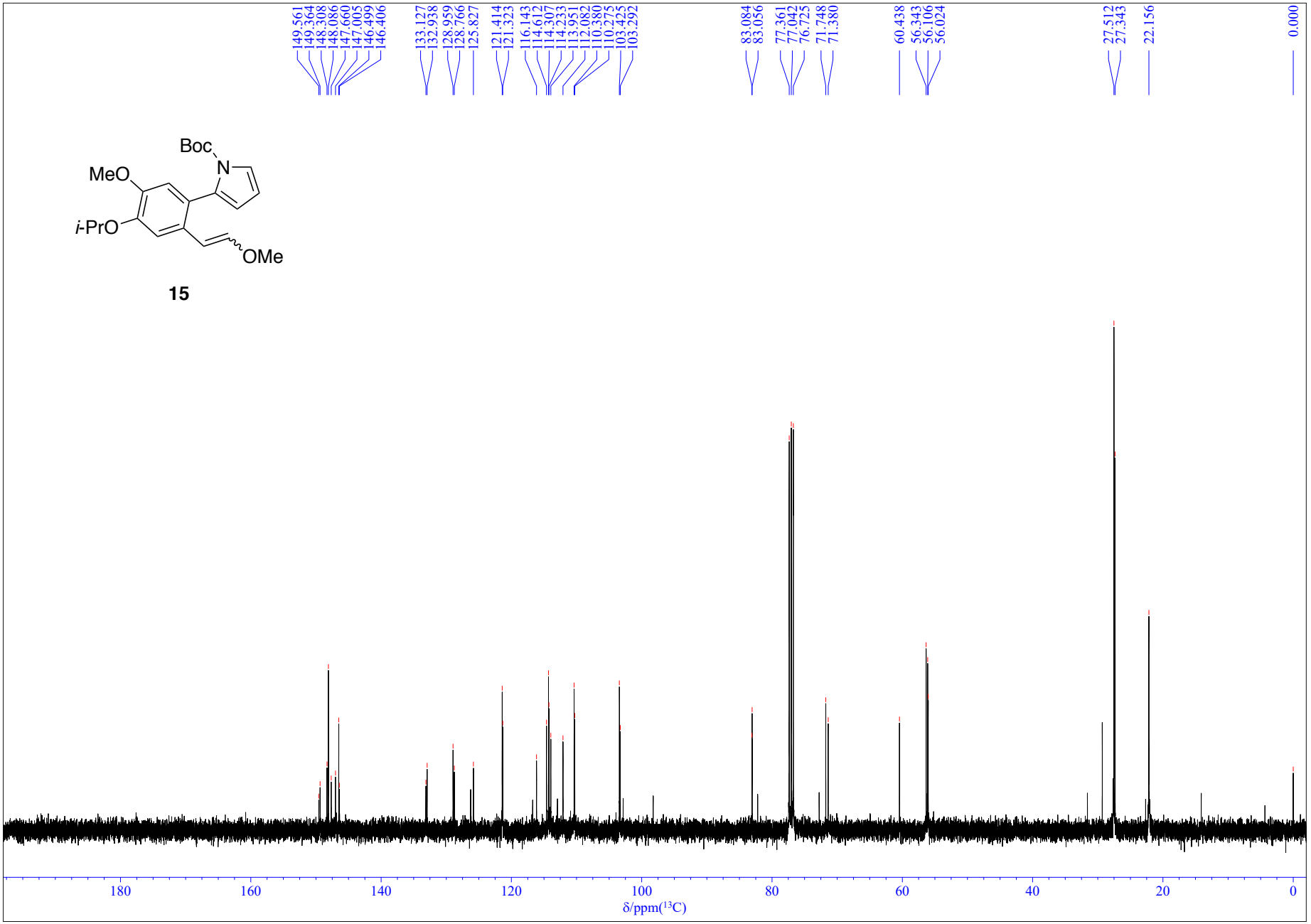

Figure S8. ^{13}C NMR spectrum of compound **15** (100 MHz, $CDCl_3$).

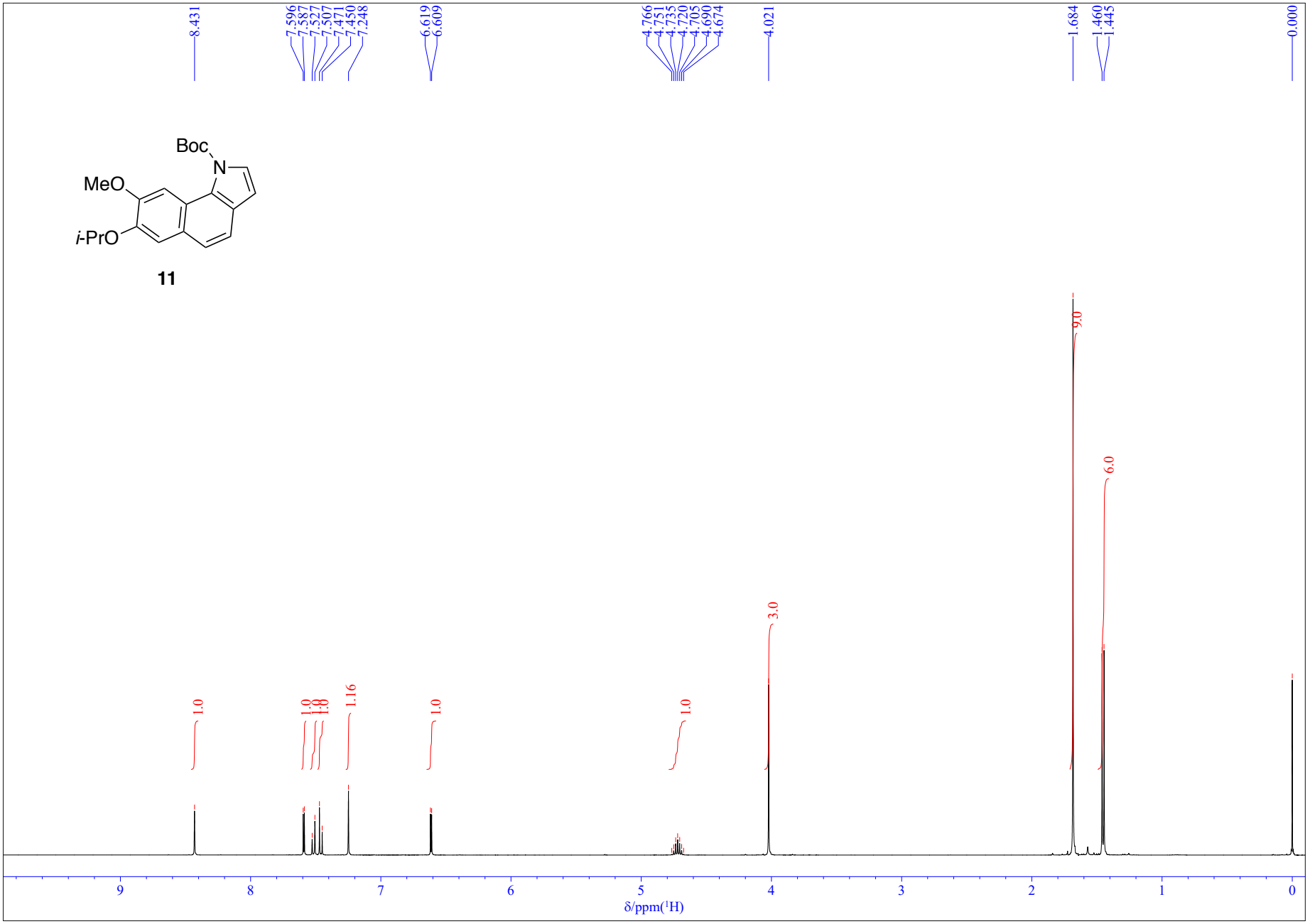

Figure S9. ^{1}H NMR spectrum of compound **11** (400 MHz, $CDCl_3$).

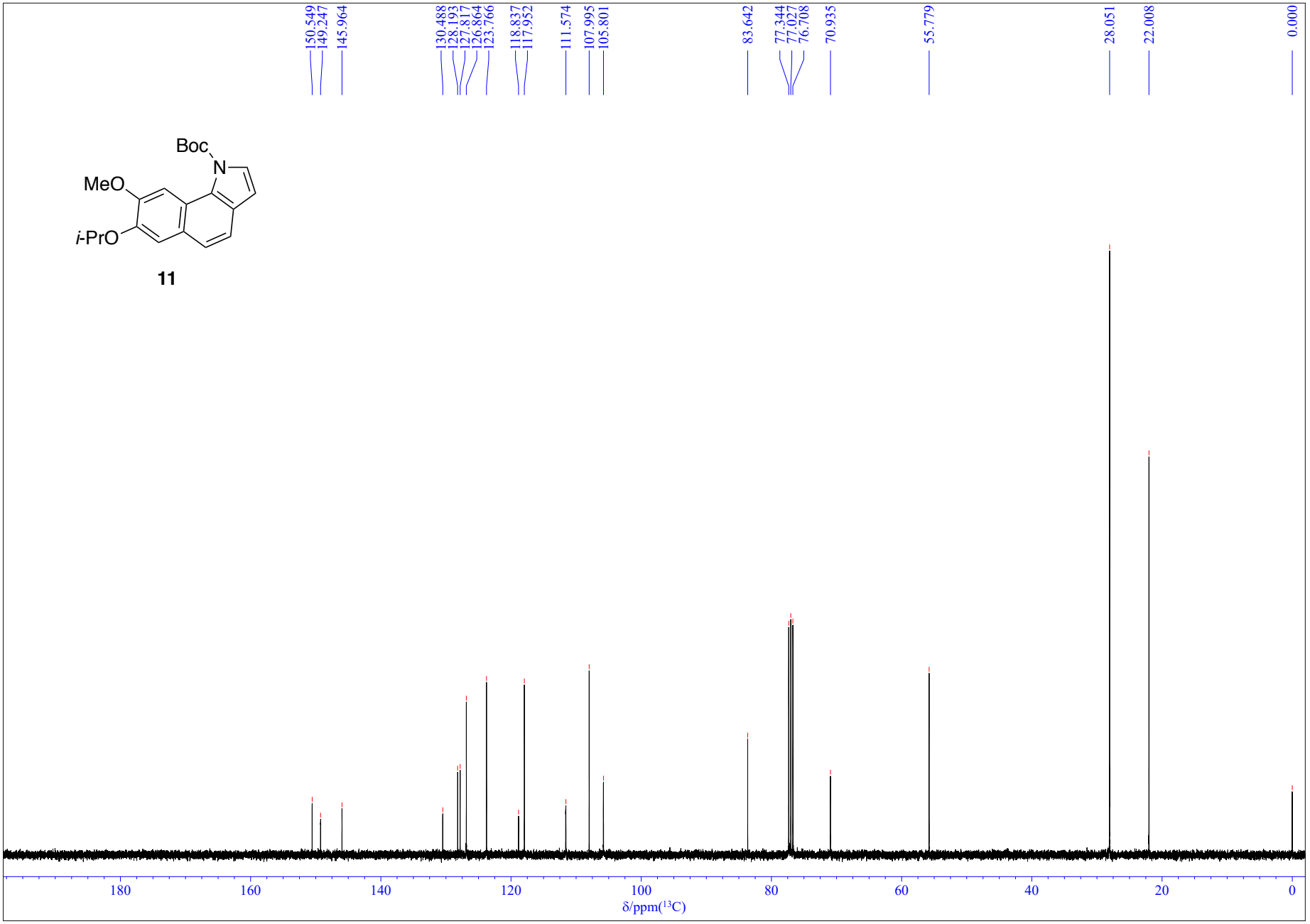

Figure S10. ^{13}C NMR spectrum of compound **11** (100 MHz, $CDCl_3$).

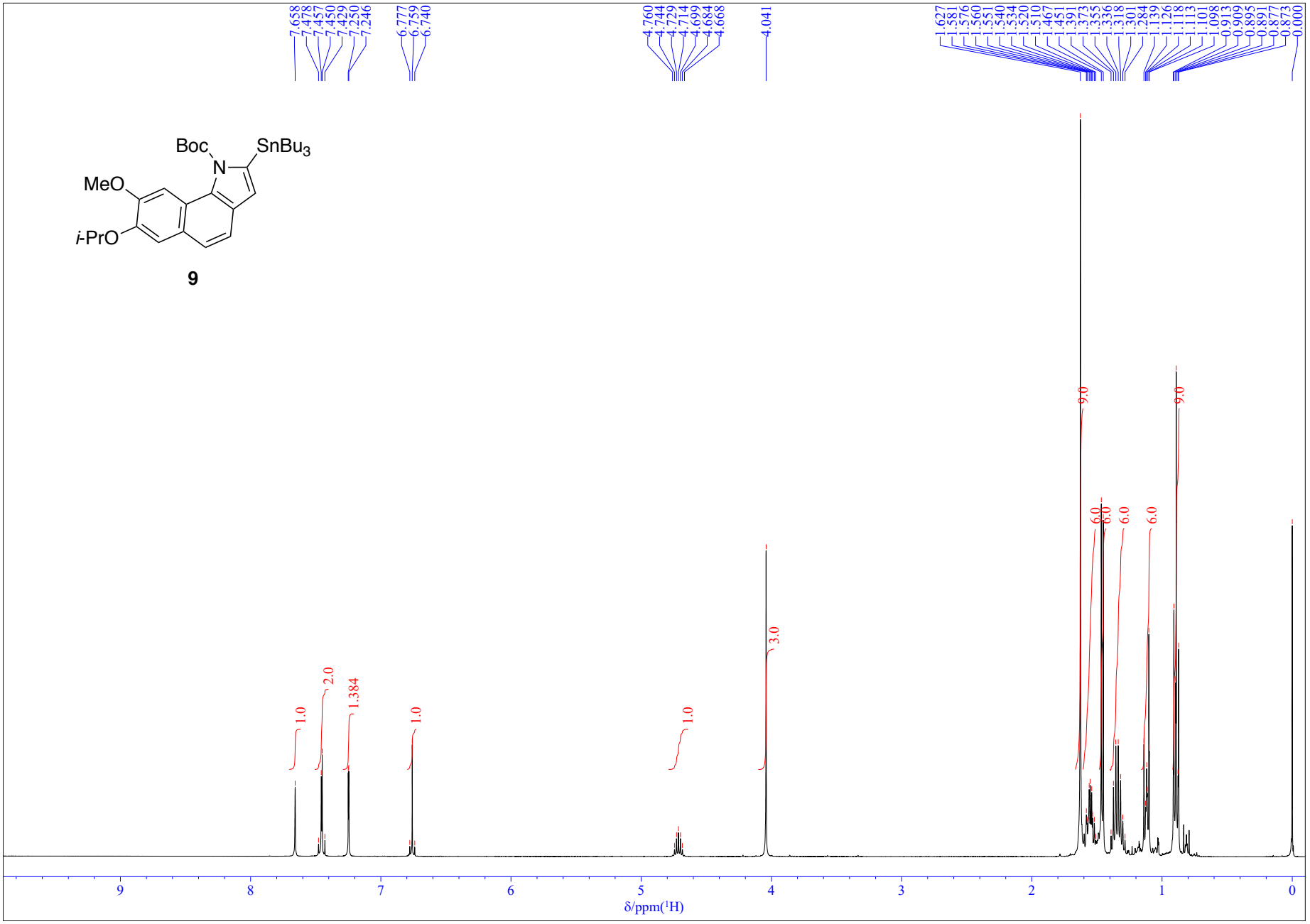

Figure S11. ^{1}H NMR spectrum of compound **9** (400 MHz, $CDCl_3$).

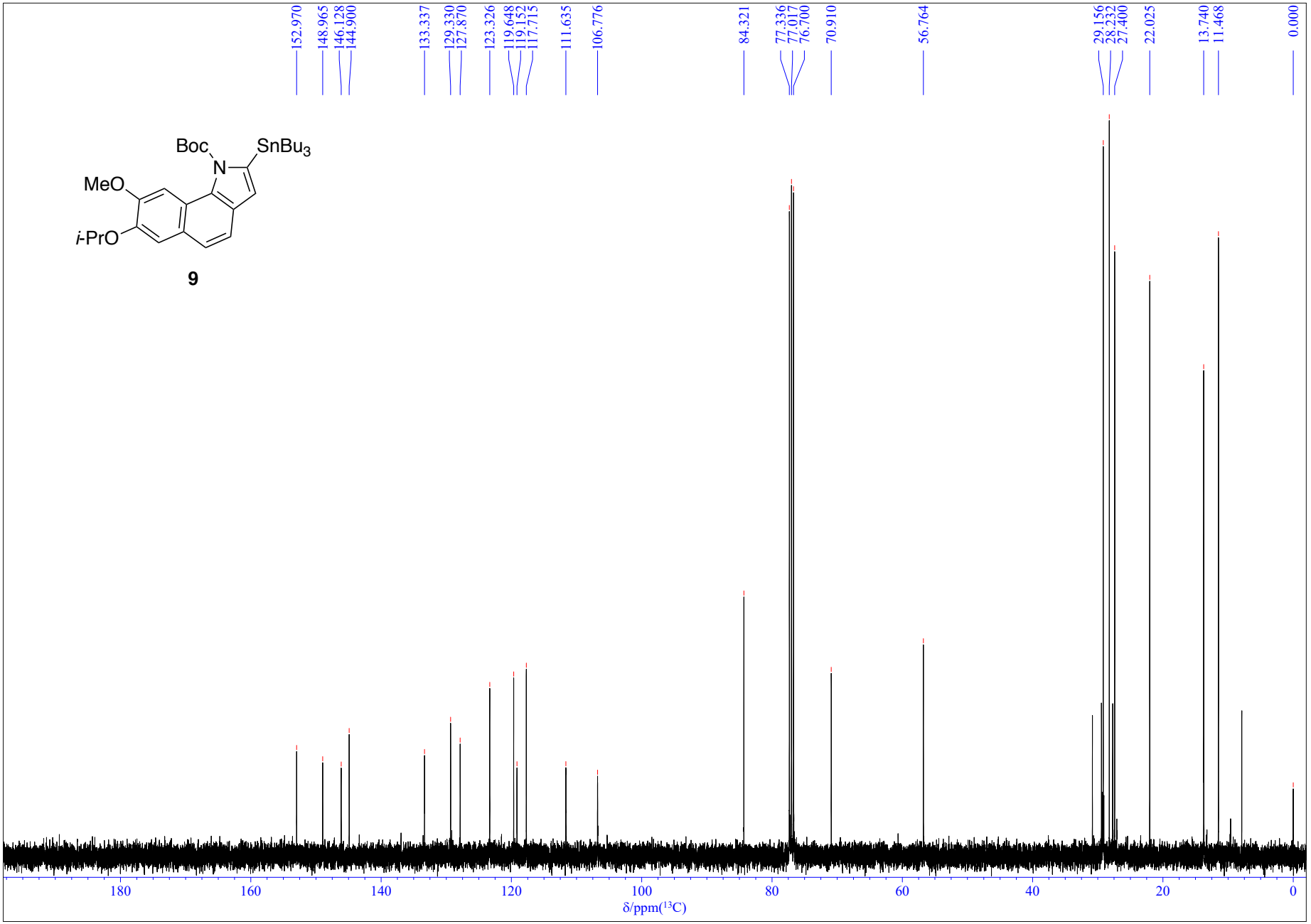

Figure S12. ^{13}C NMR spectrum of compound **9** (100 MHz, $CDCl_3$).

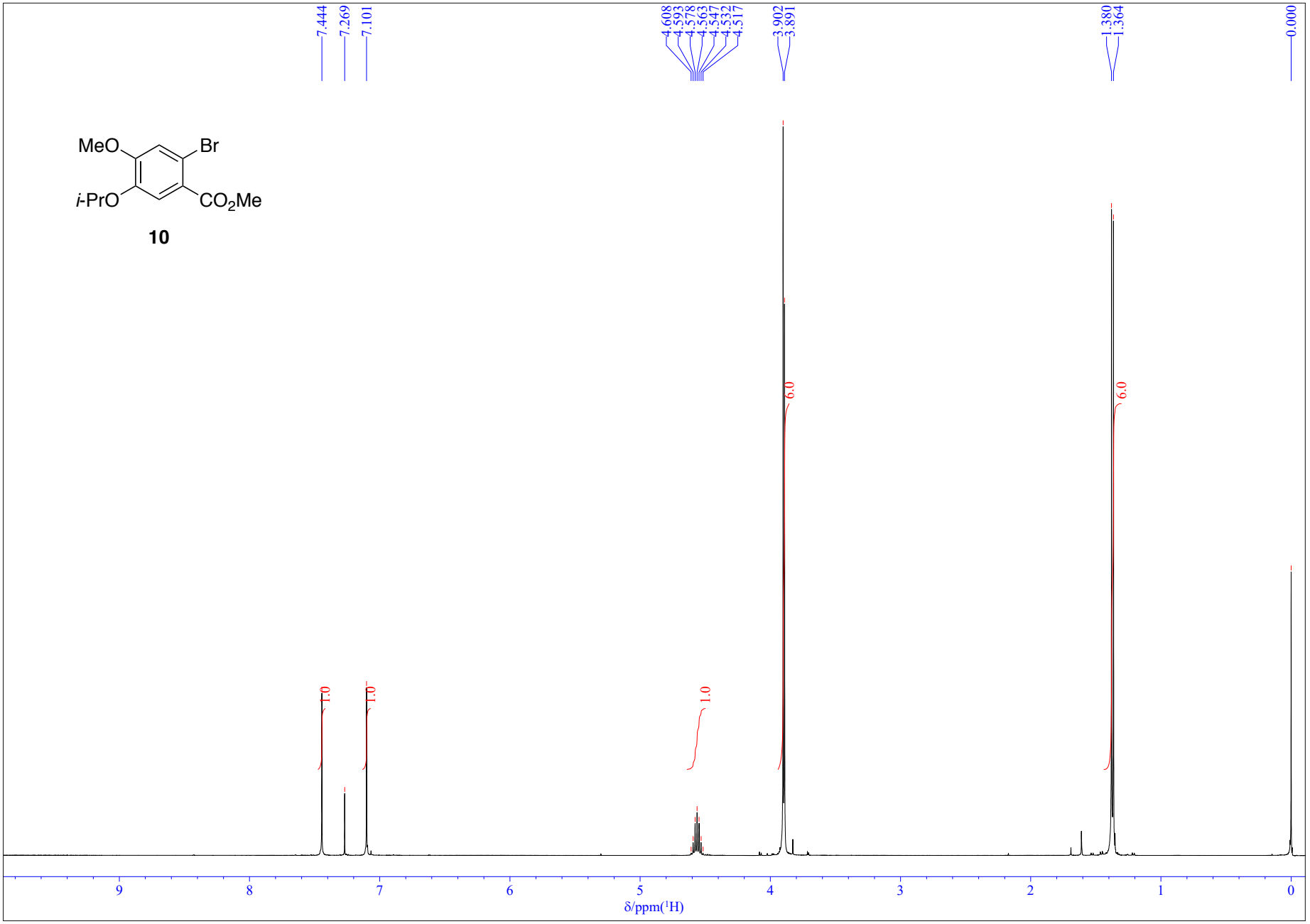

Figure S13. ^{1}H NMR spectrum of compound **10** (400 MHz, $CDCl_3$).

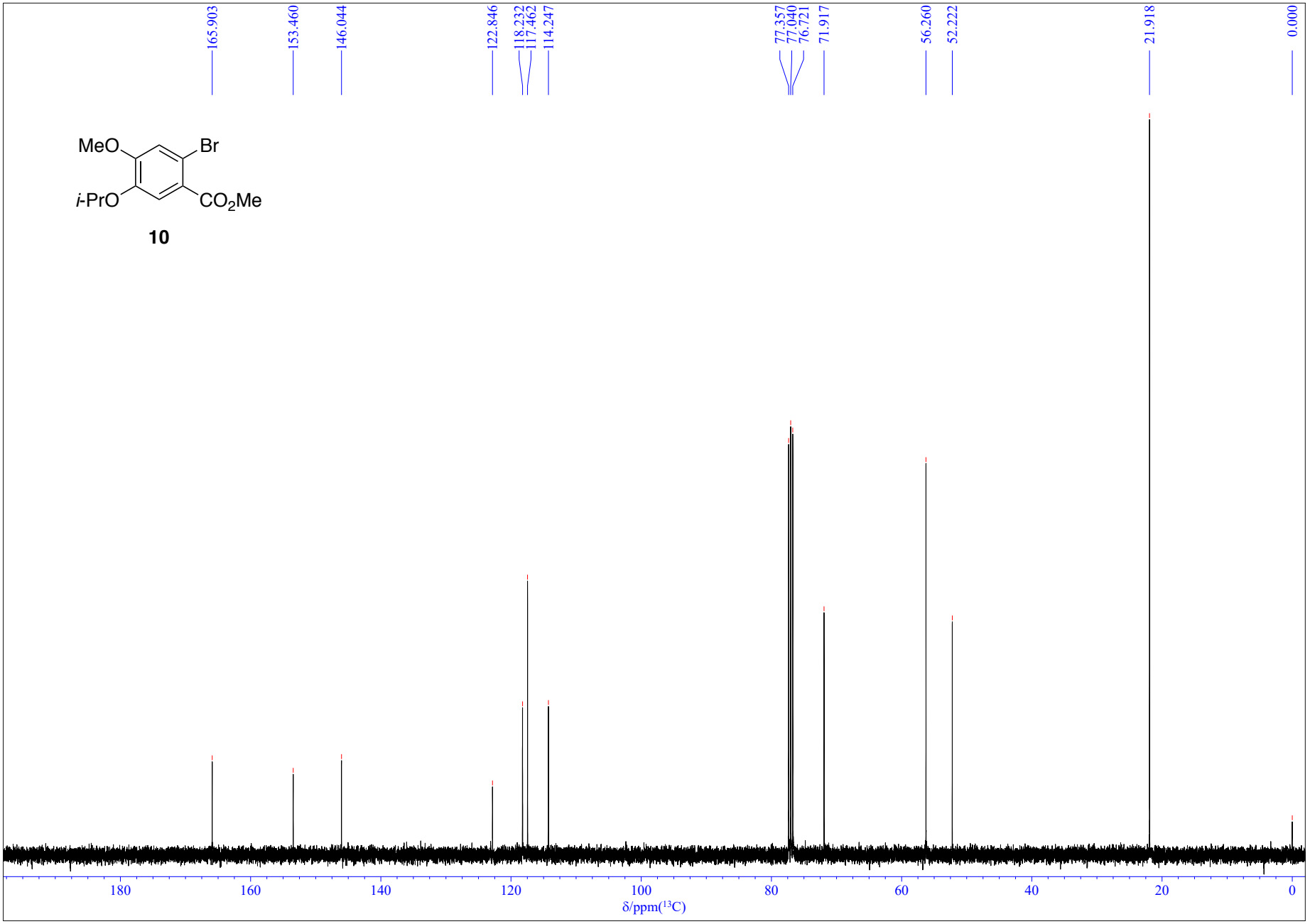

Figure S14. ^{13}C NMR spectrum of compound **10** (100 MHz, $CDCl_3$).

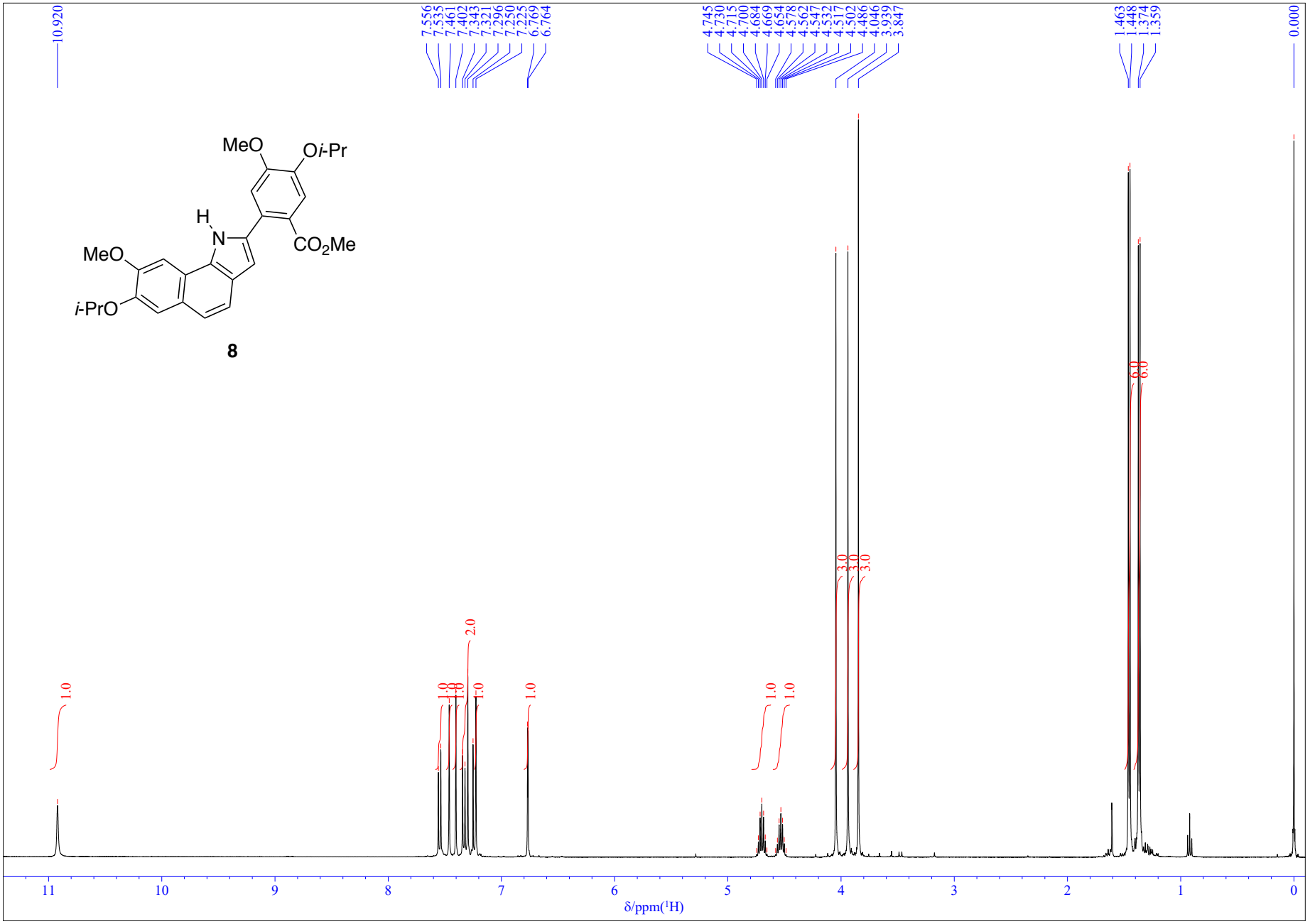

Figure S15. ^{1}H NMR spectrum of compound **8** (400 MHz, $CDCl_3$).

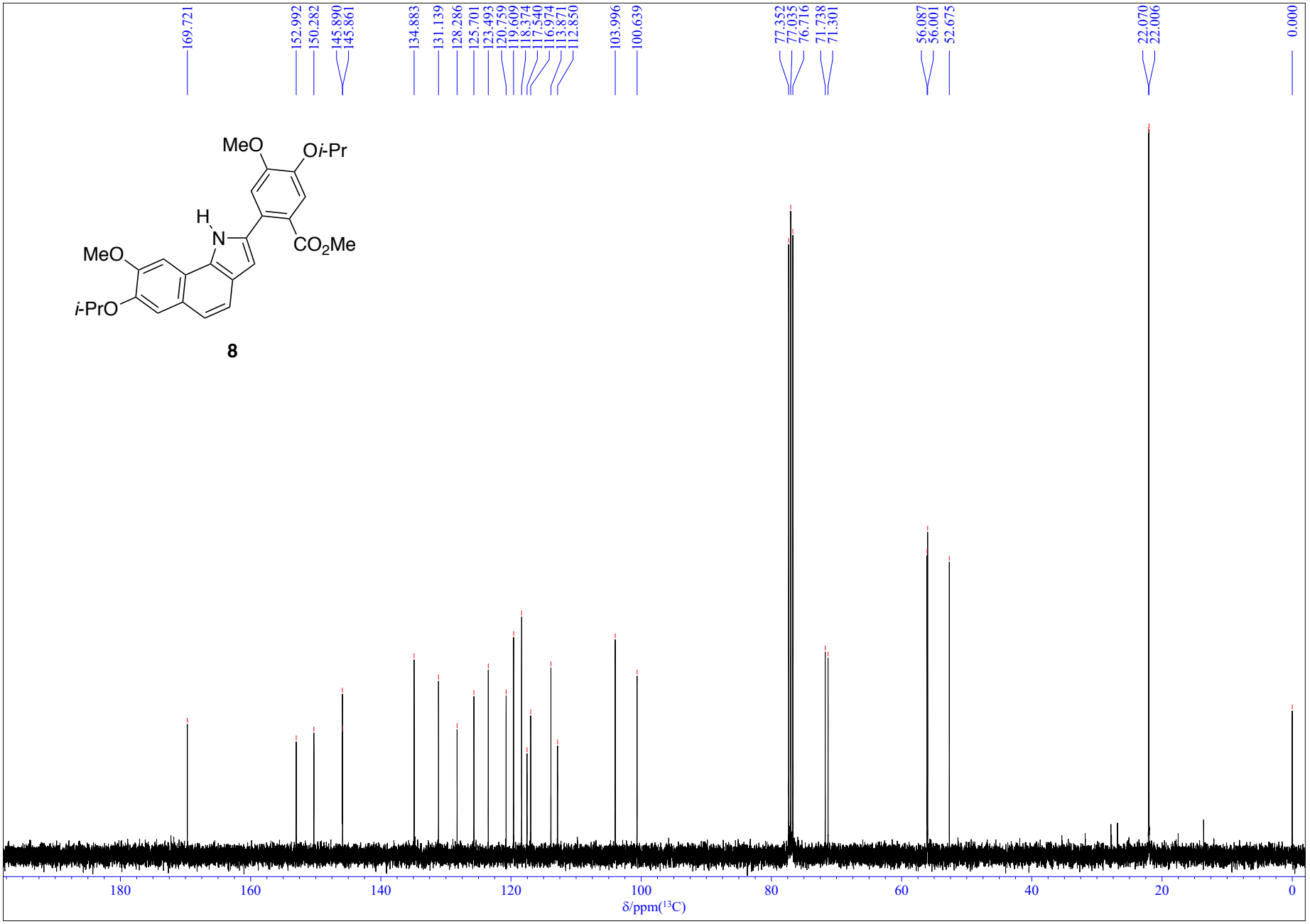

Figure S16. ^{13}C NMR spectrum of compound **8** (100 MHz, $CDCl_3$).

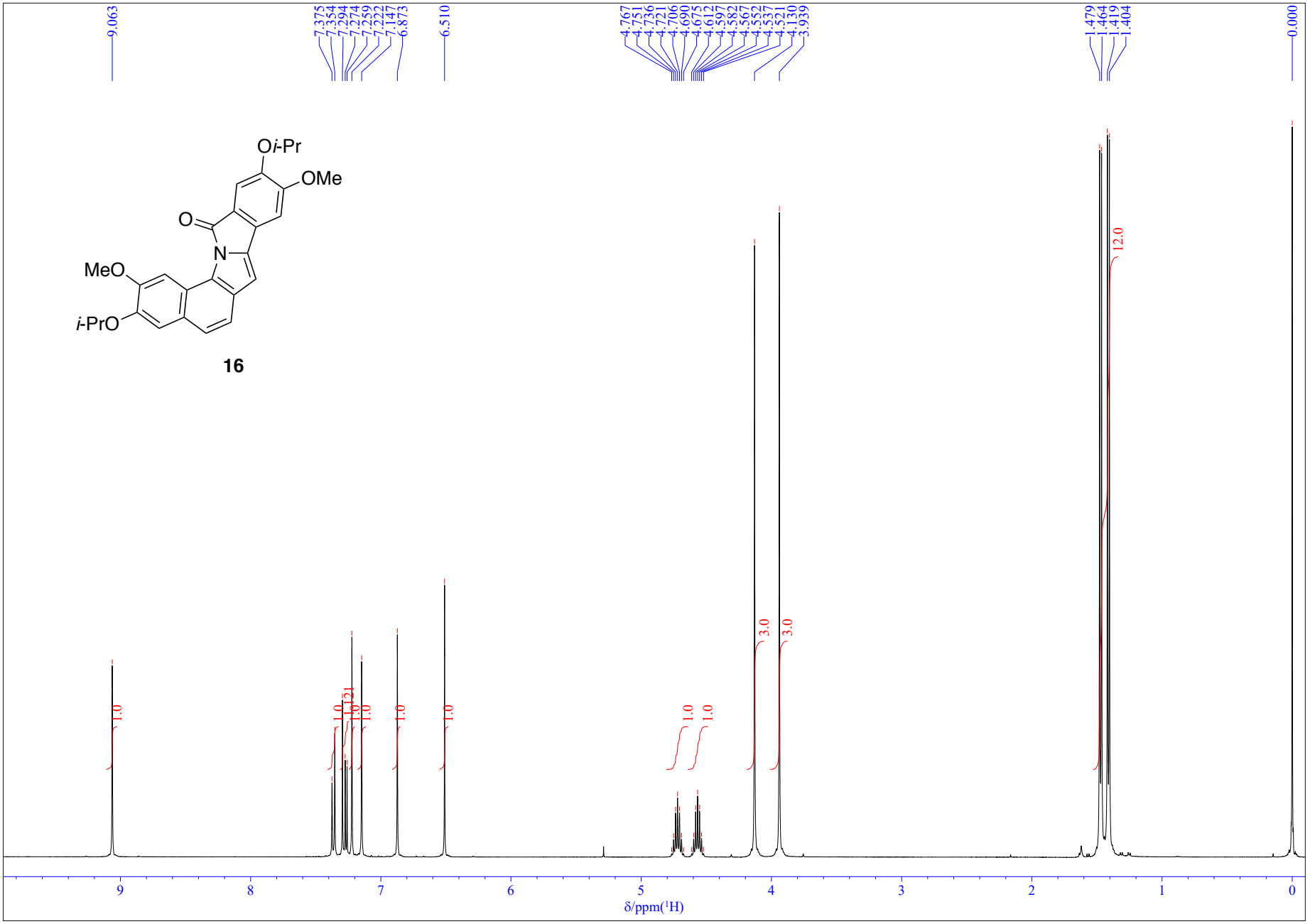

Figure S17. ^{1}H NMR spectrum of compound **16** (400 MHz, $CDCl_3$).

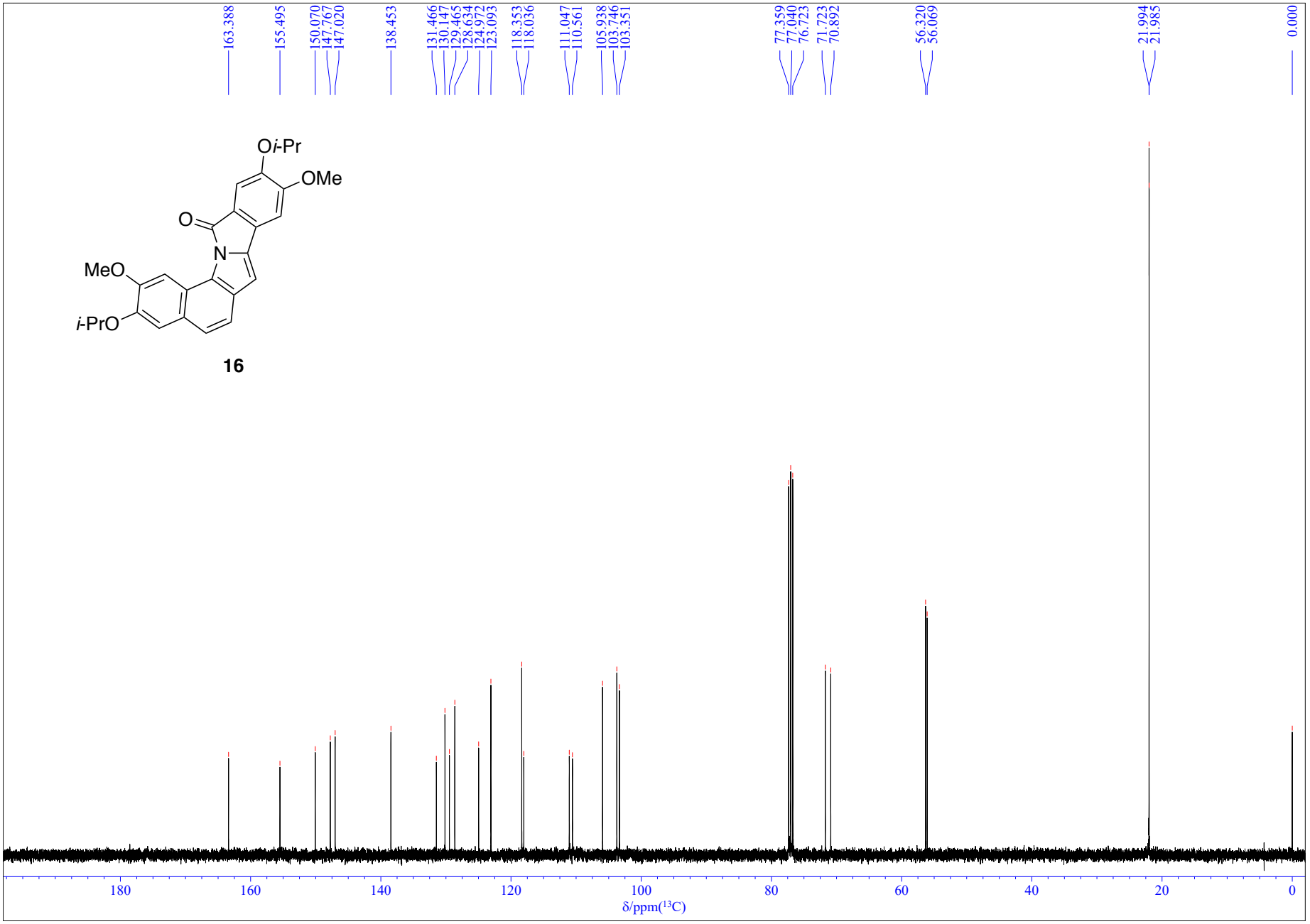

Figure S18. ^{13}C NMR spectrum of compound **16** (100 MHz, $CDCl_3$).

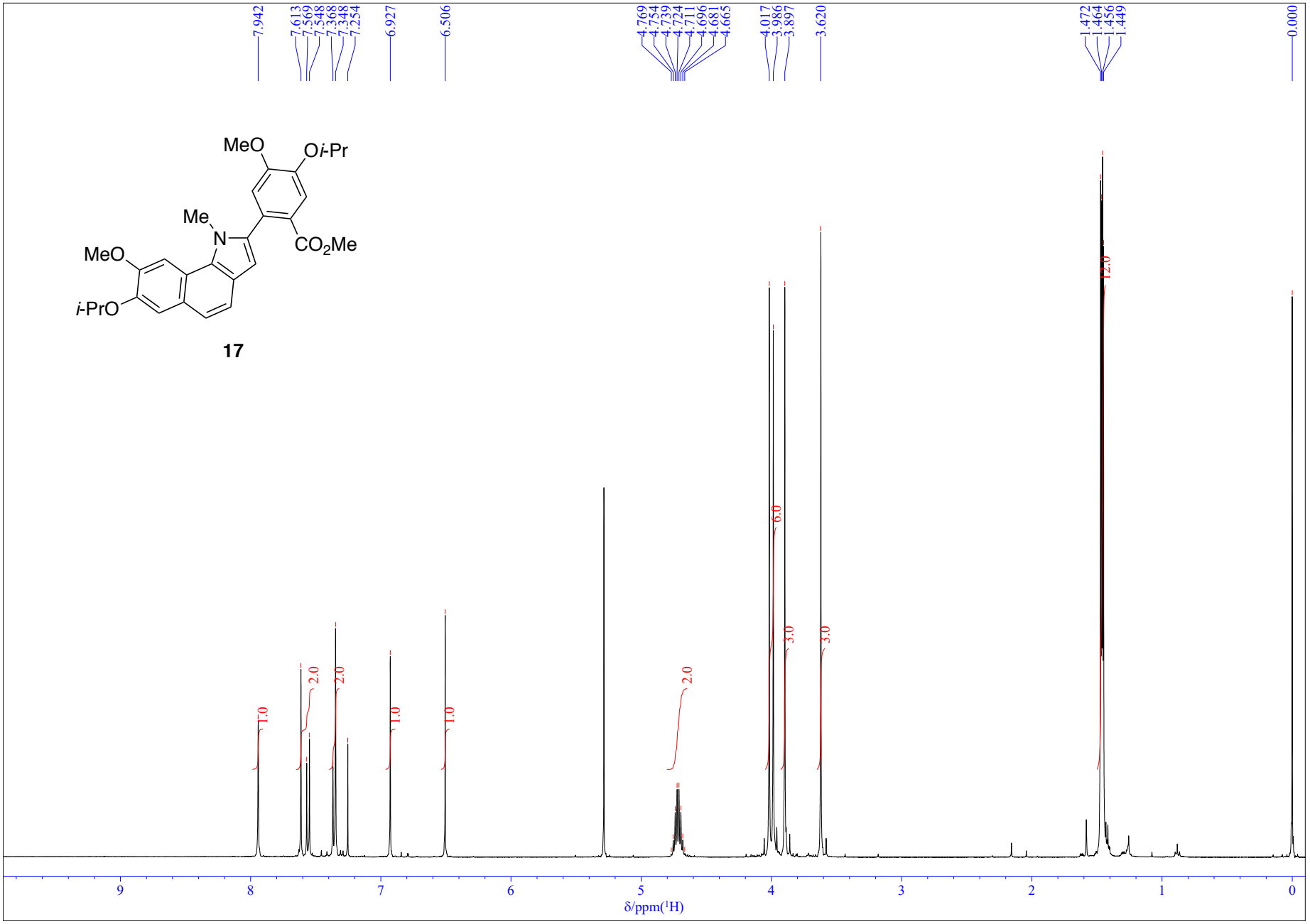

Figure S19. ^{1}H NMR spectrum of compound **17** (400 MHz, $CDCl_3$).

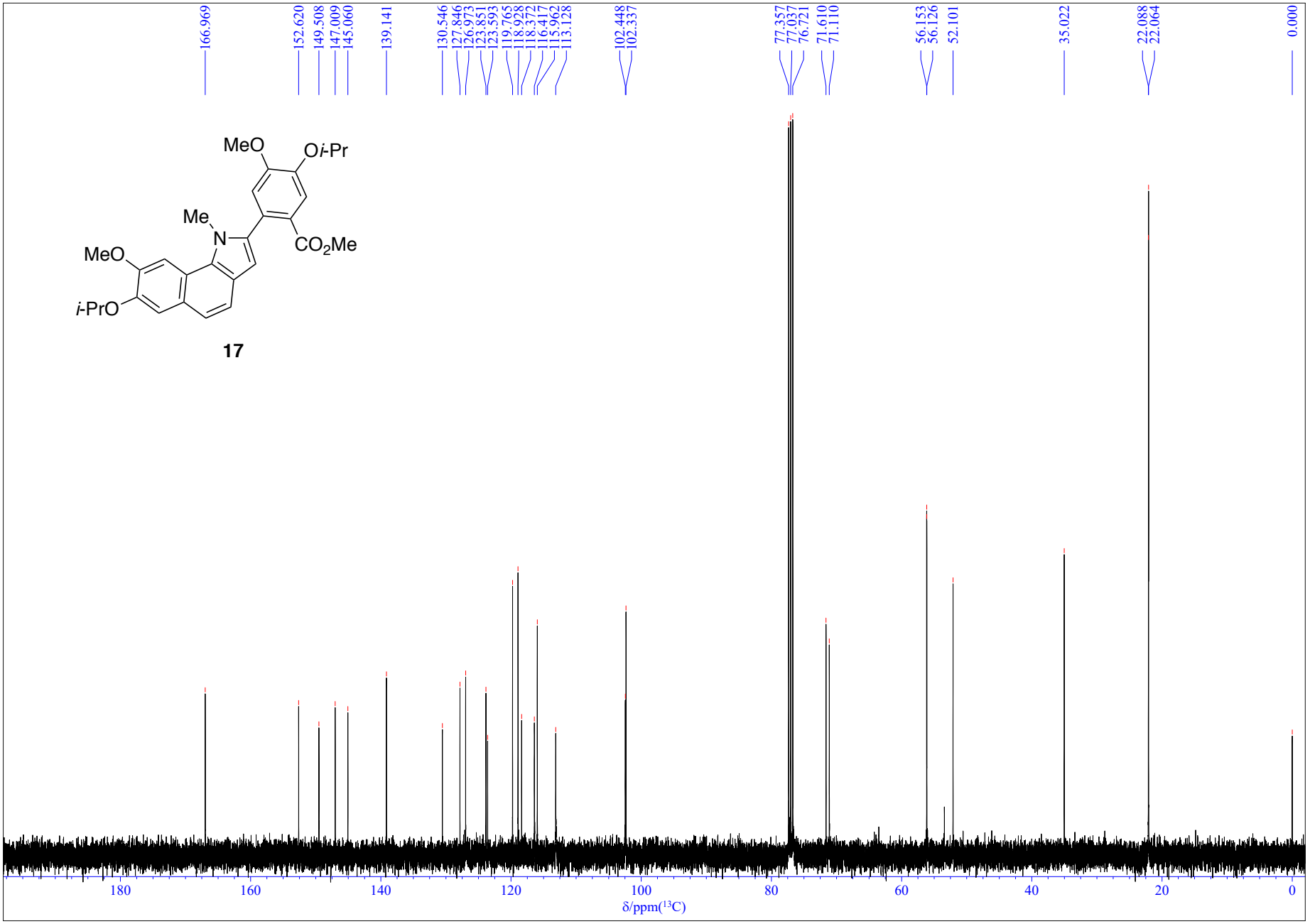

Figure S20. ^{13}C NMR spectrum of compound **17** (100 MHz, $CDCl_3$).

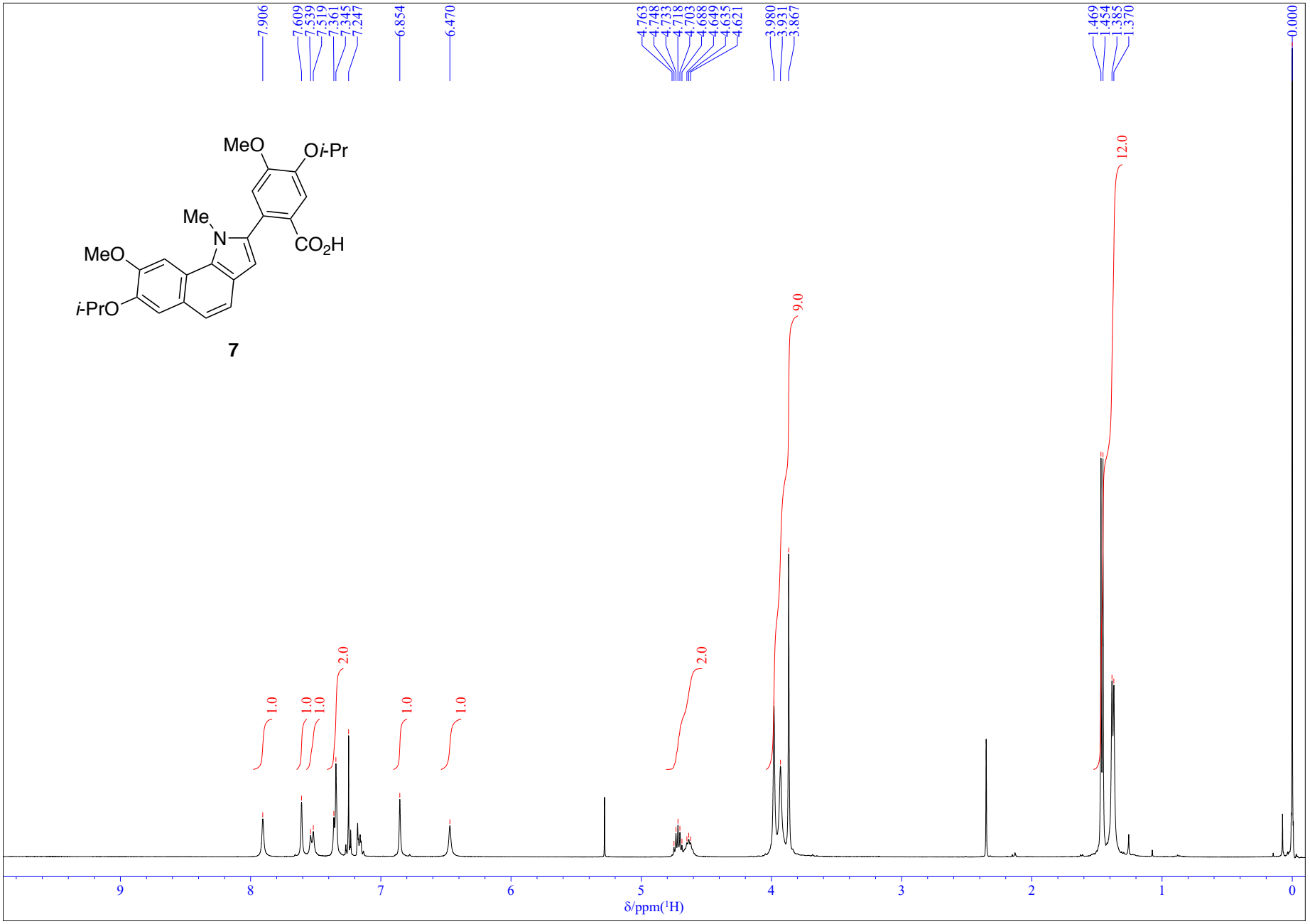

Figure S21. ^{1}H NMR spectrum of compound **7** (400 MHz, $CDCl_3$).

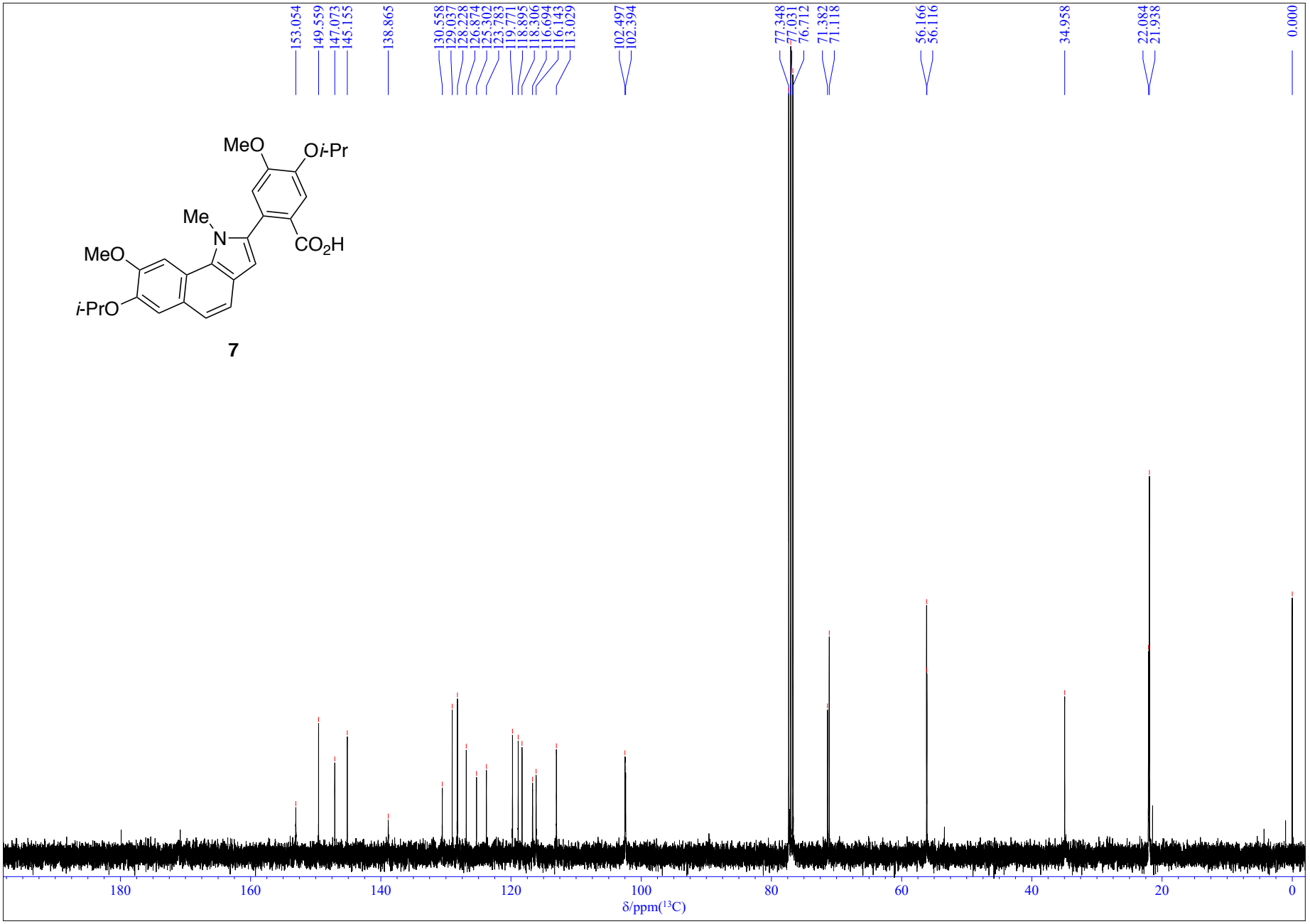

Figure S22. ^{13}C NMR spectrum of compound **7** (100 MHz, $CDCl_3$).

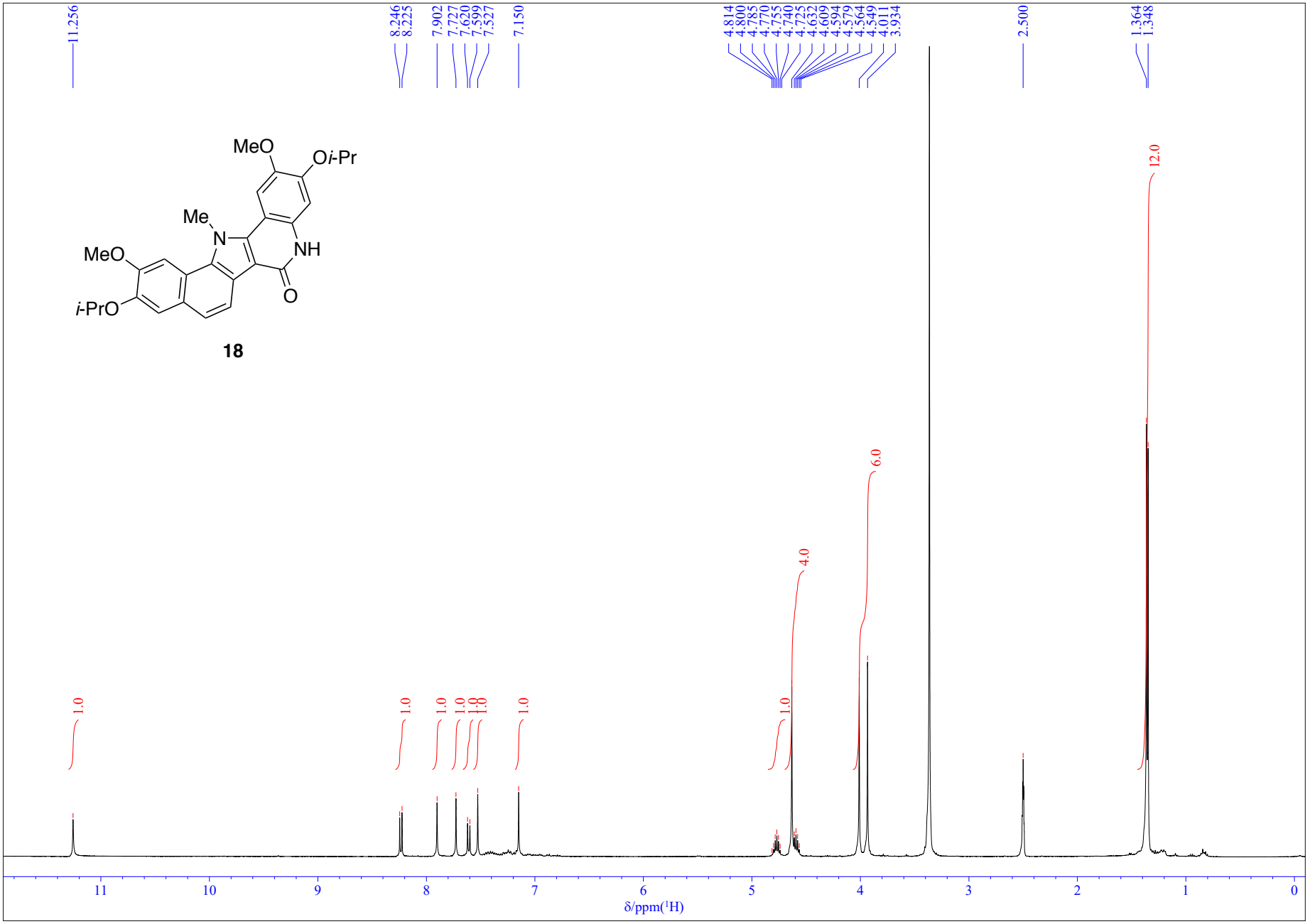

Figure S23. ^{1}H NMR spectrum of compound **18** (400 MHz, DMSO-d_6).

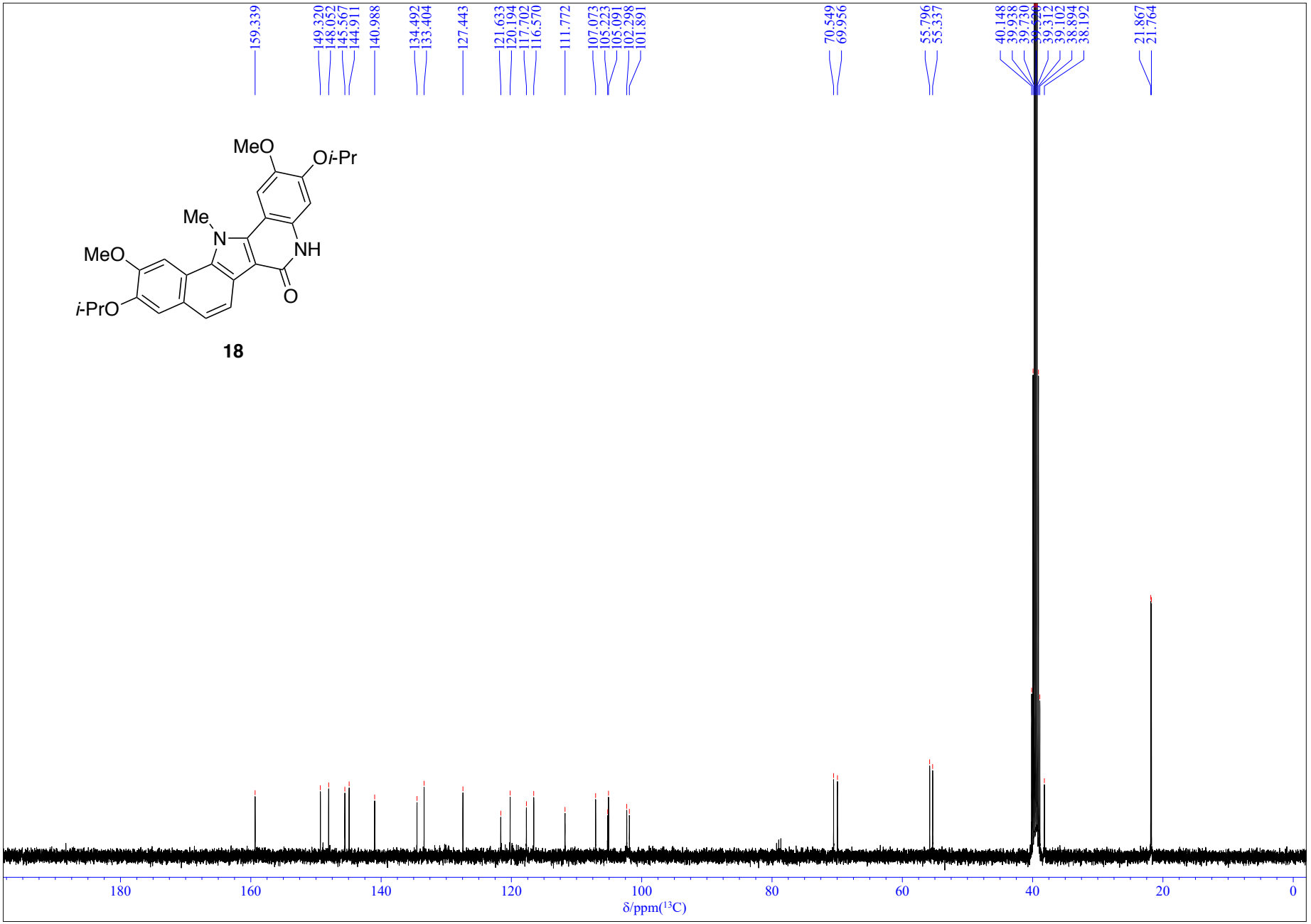

Figure S24. ^{13}C NMR spectrum of compound **18** (100 MHz, DMSO-d_6).

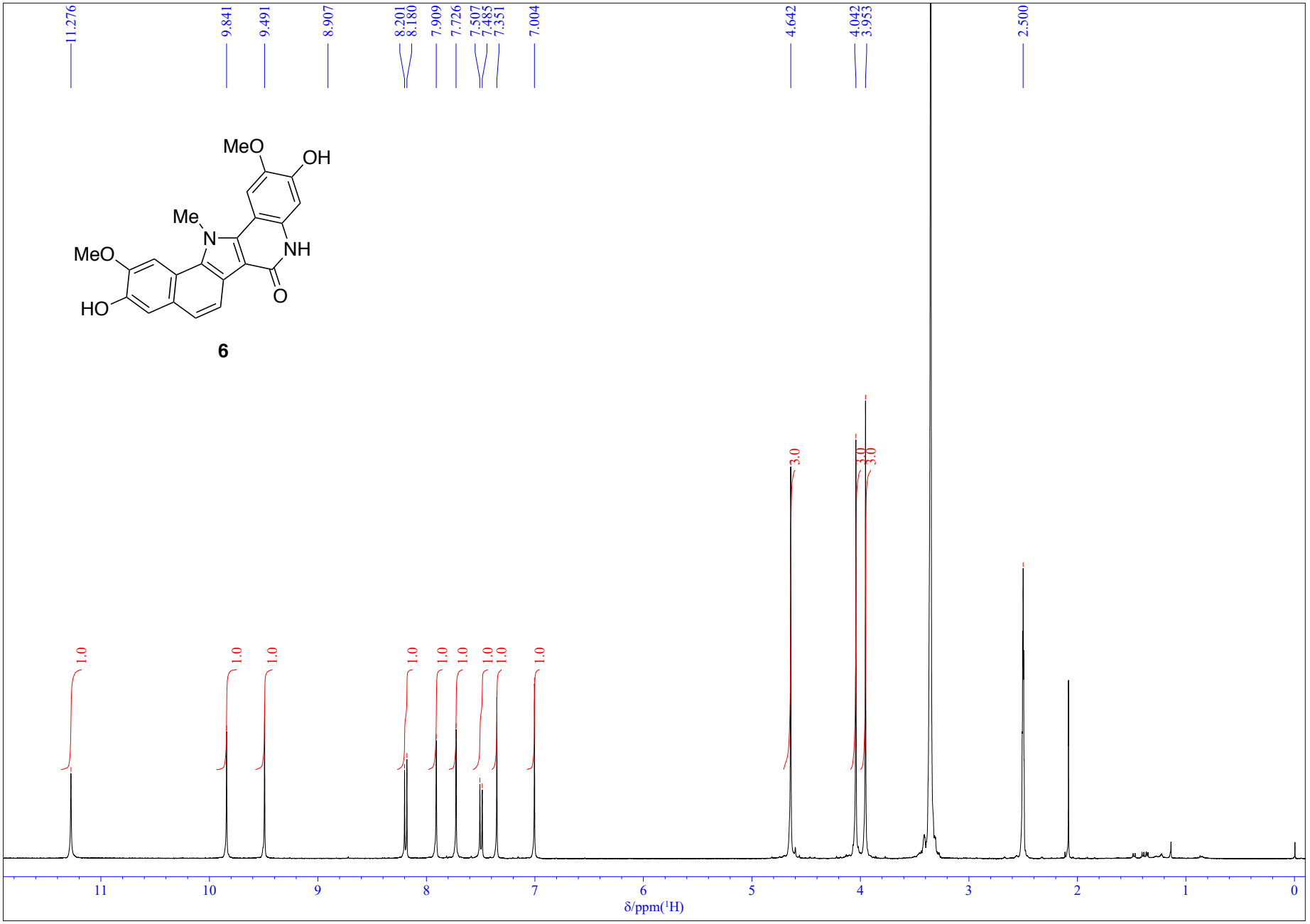

Figure S25. ^{1}H NMR spectrum of compound **6** (400 MHz, DMSO-d_6).

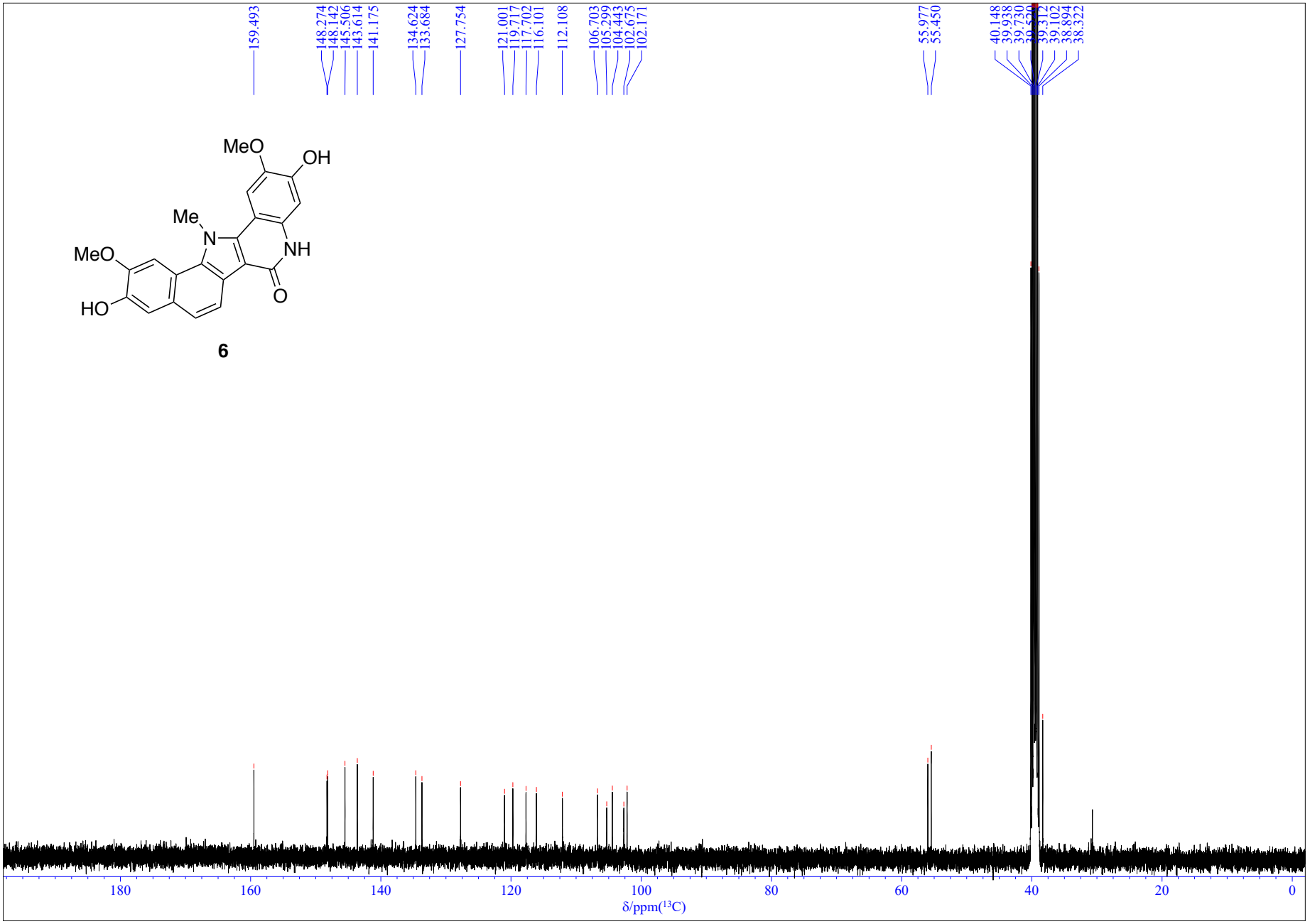

Figure S26. ^{13}C NMR spectrum of compound **6** (100 MHz, DMSO-d_6).

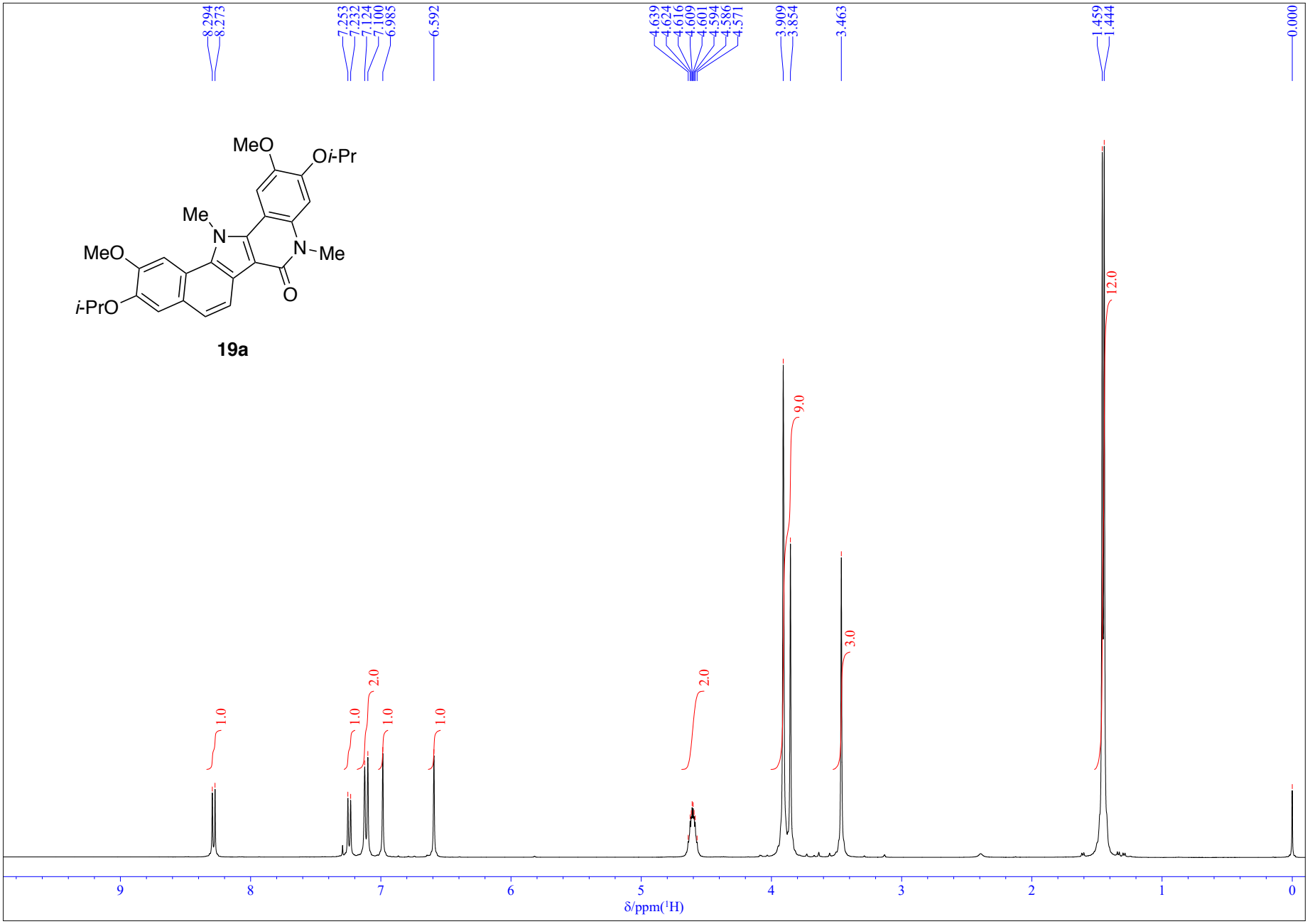

Figure S27. ^{1}H NMR spectrum of compound **19a** (400 MHz, $CDCl_3$).

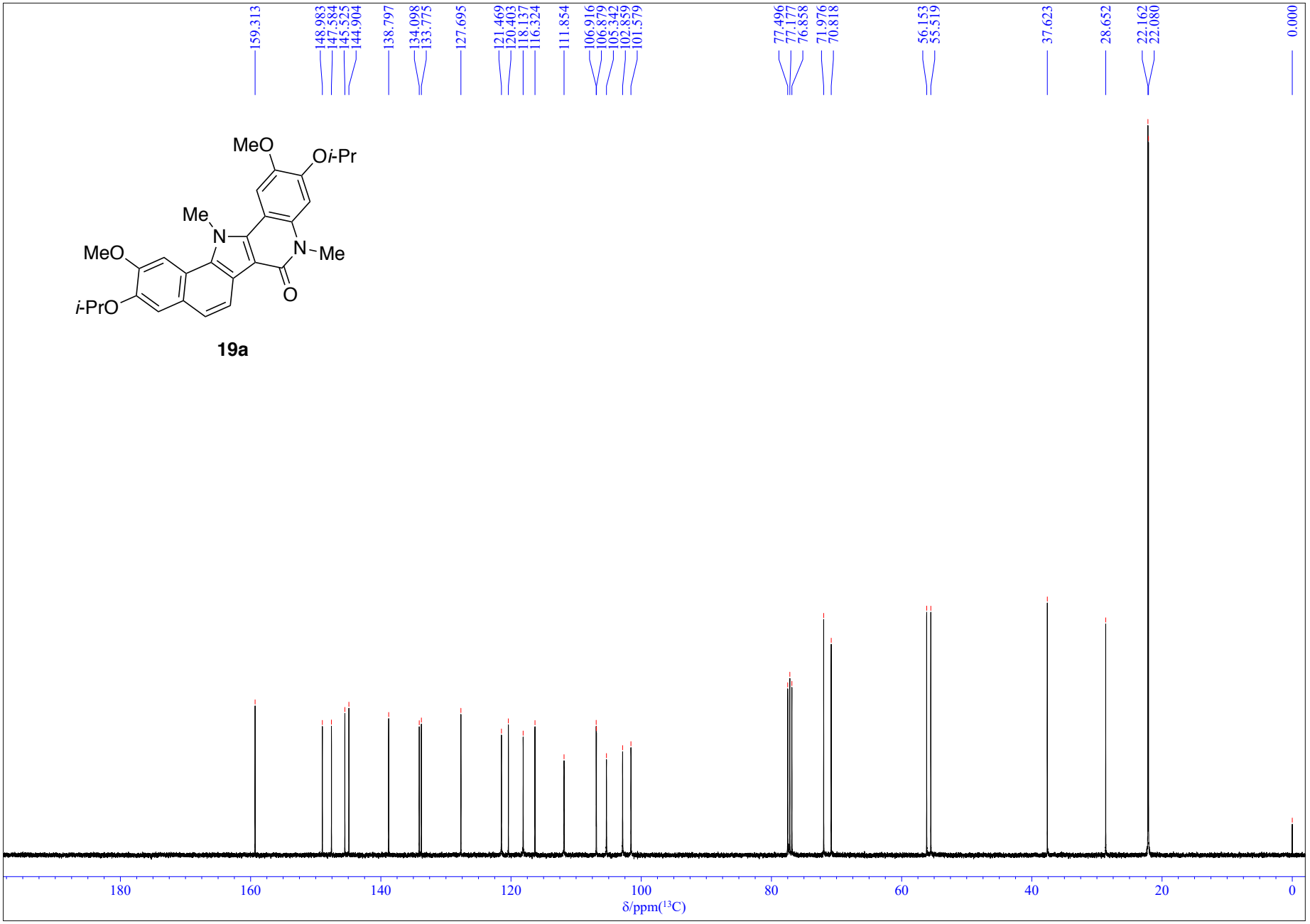

Figure S28. ^{13}C NMR spectrum of compound **19a** (100 MHz, $CDCl_3$).

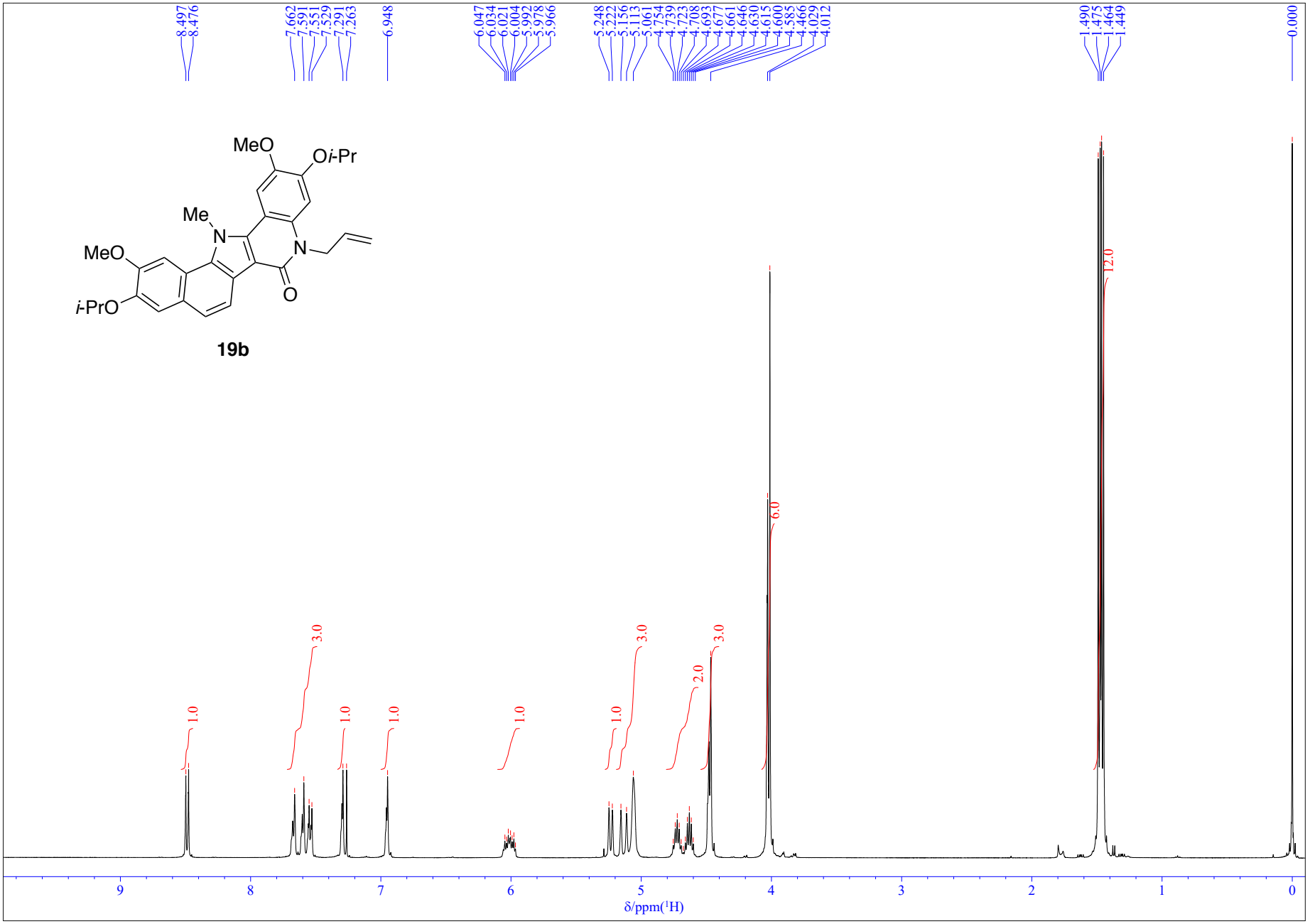

Figure S29. ^{1}H NMR spectrum of compound **19b** (400 MHz, $CDCl_3$).

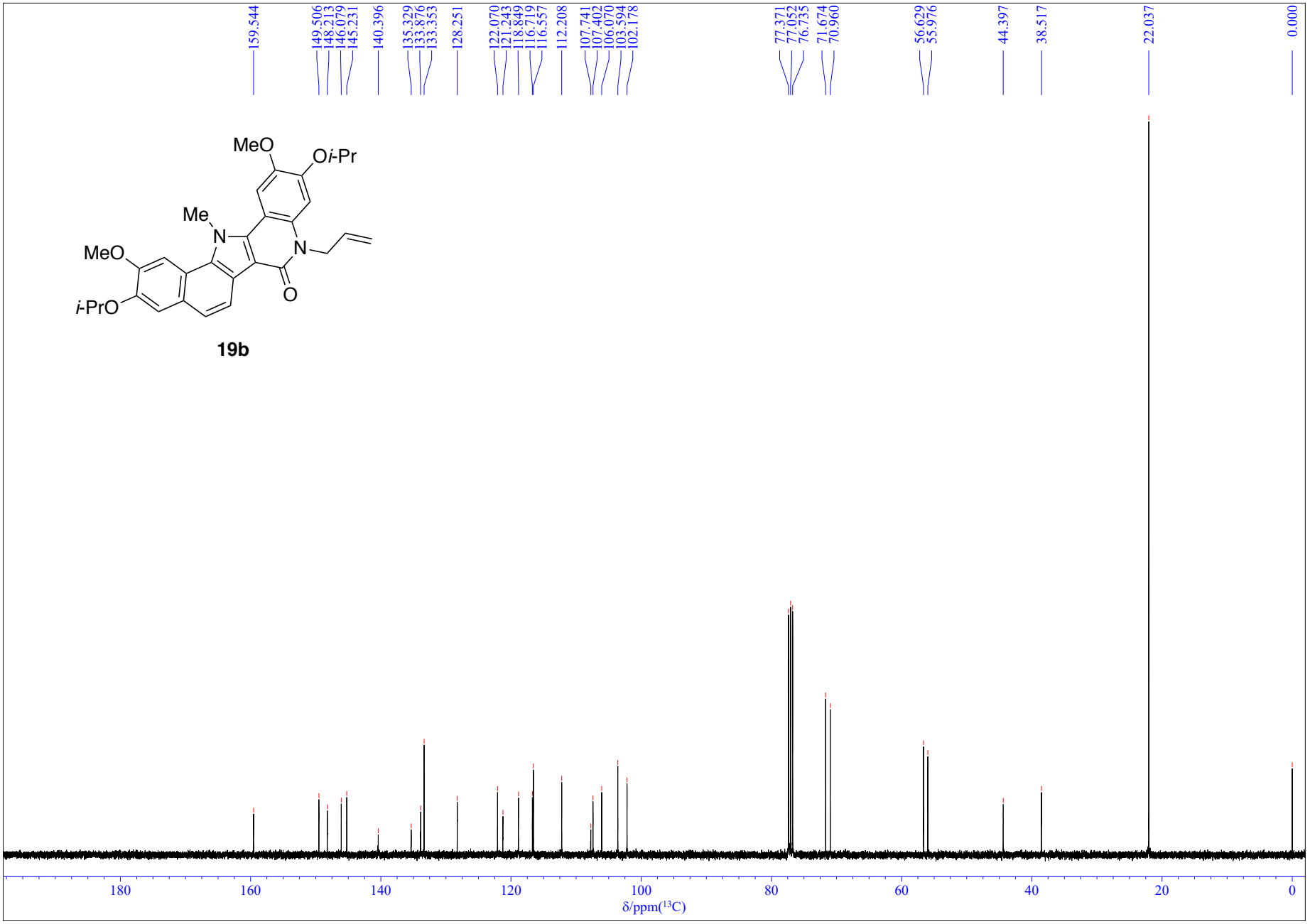

Figure S30. ^{13}C NMR spectrum of compound **19b** (100 MHz, $CDCl_3$).

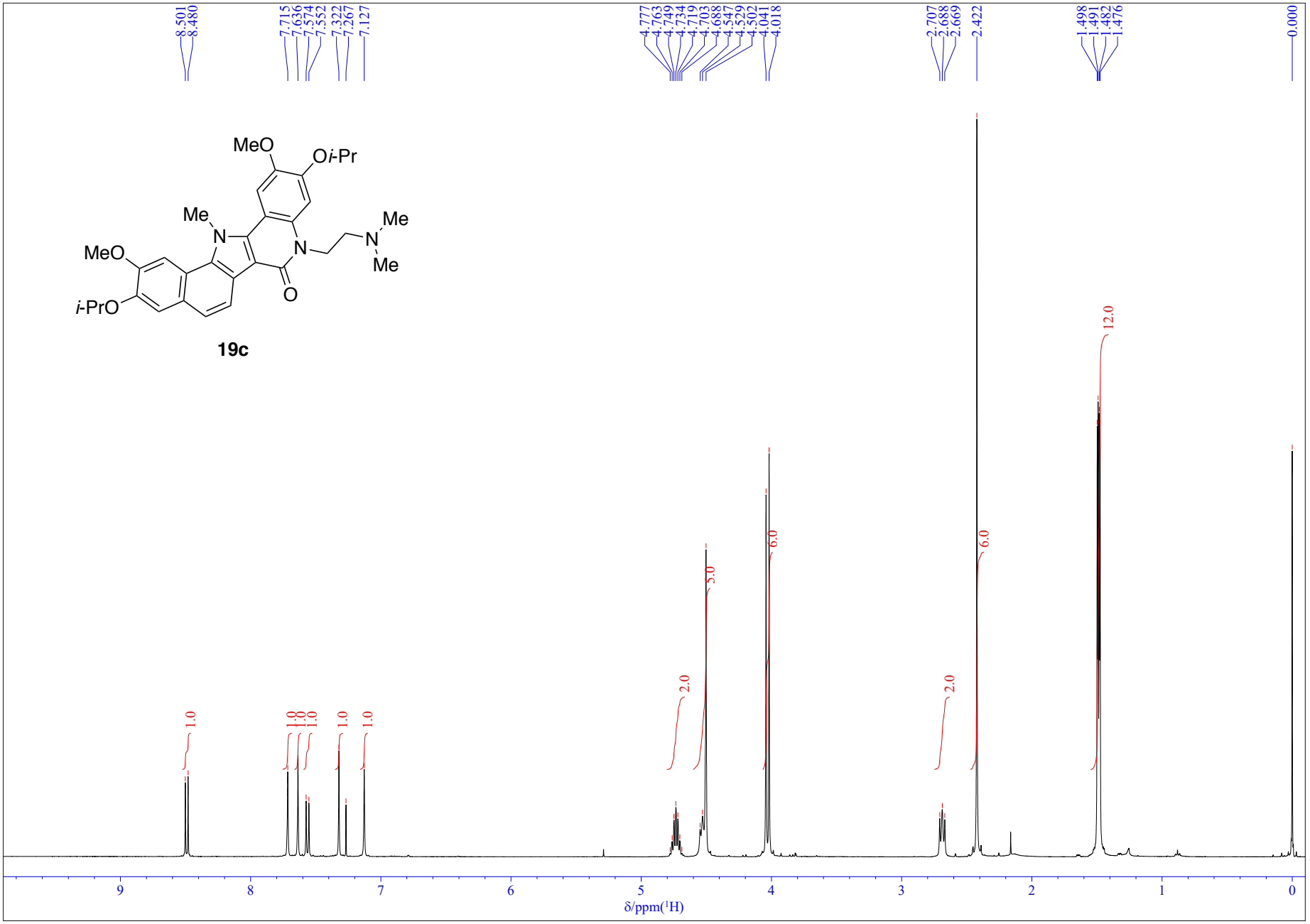

Figure S31. ^{1}H NMR spectrum of compound **19c** (400 MHz, $CDCl_3$).

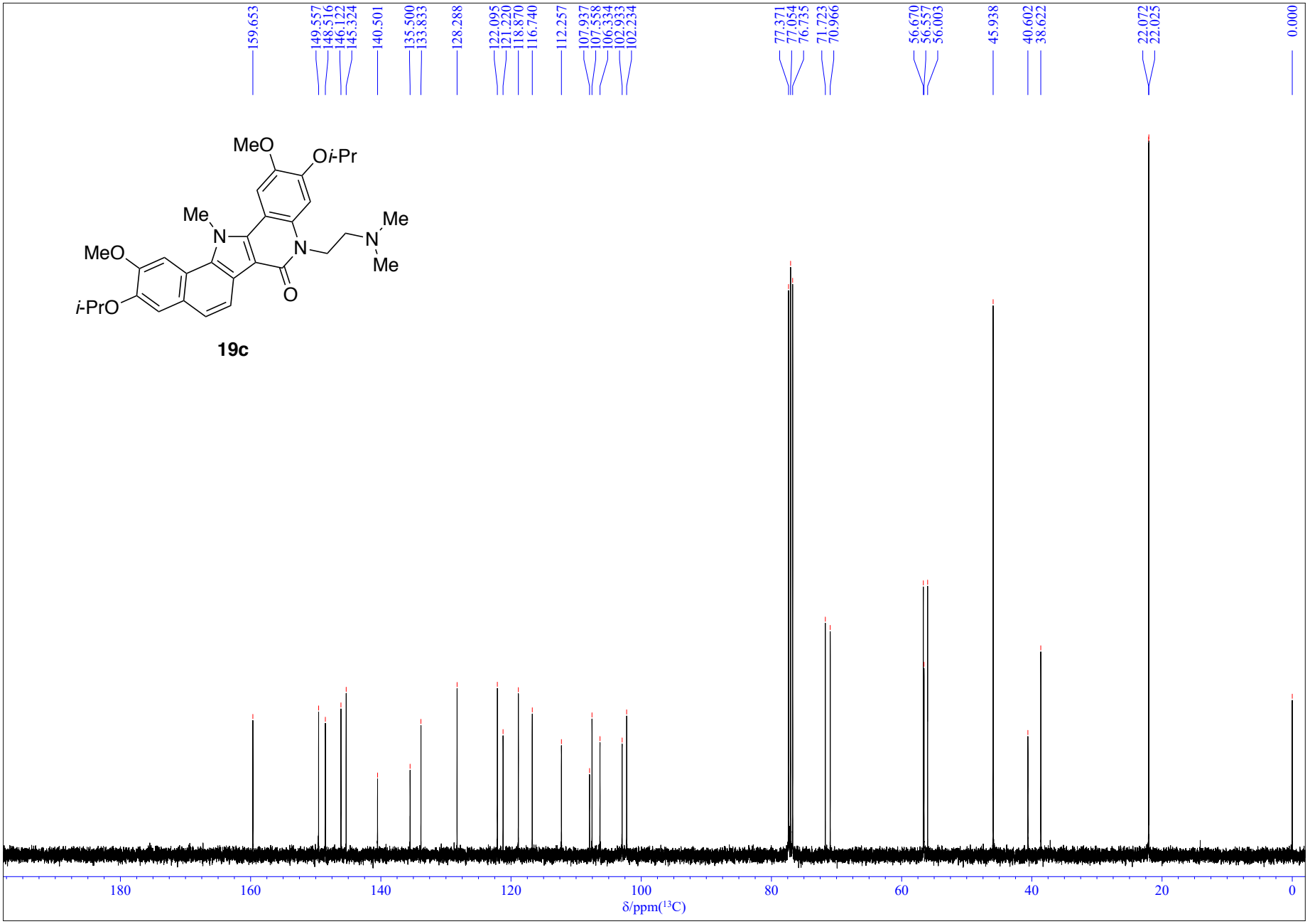

Figure S32. ^{13}C NMR spectrum of compound **19c** (100 MHz, $CDCl_3$).

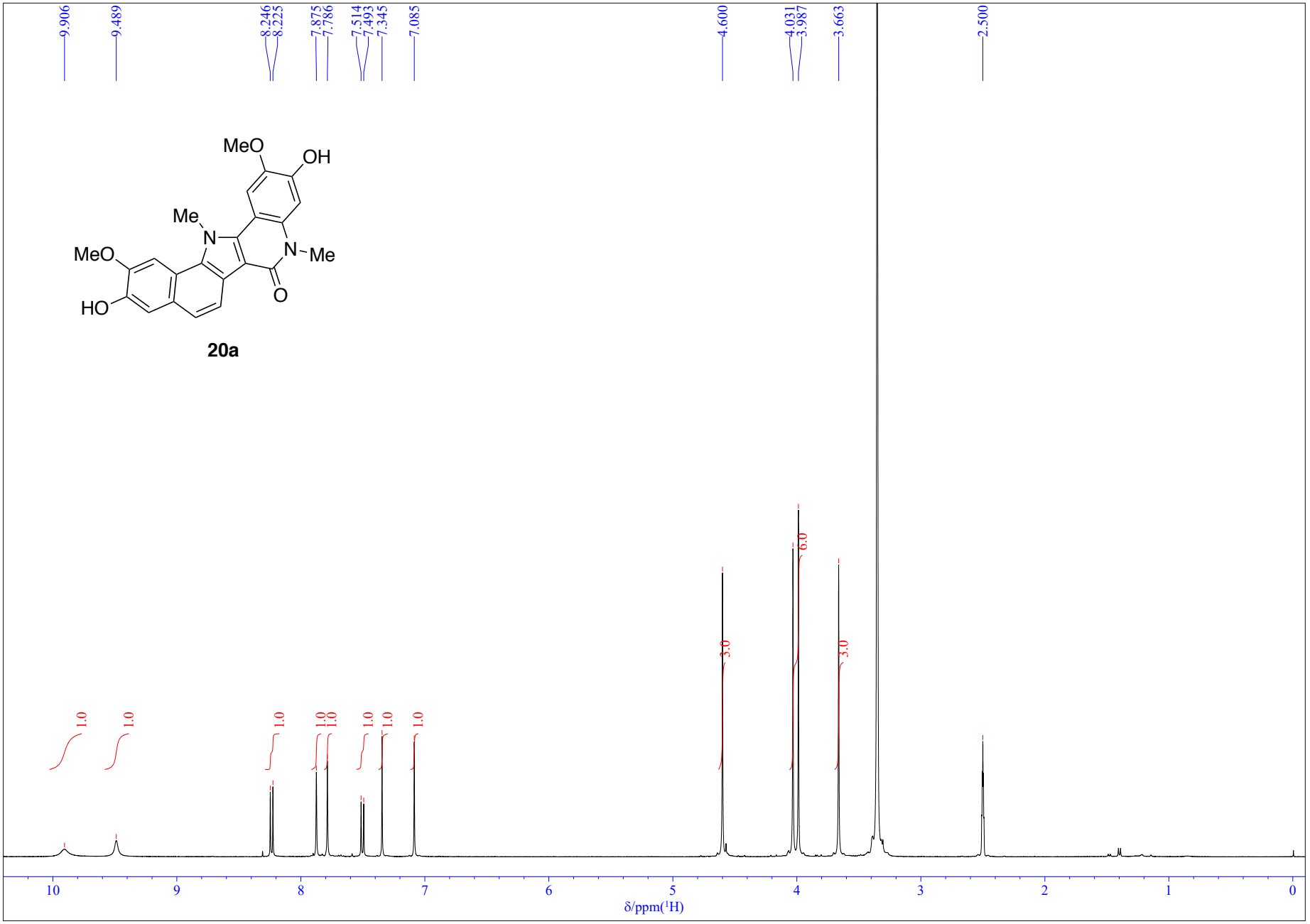

Figure S33. ^{1}H NMR spectrum of compound **20a** (400 MHz, DMSO-d_6).

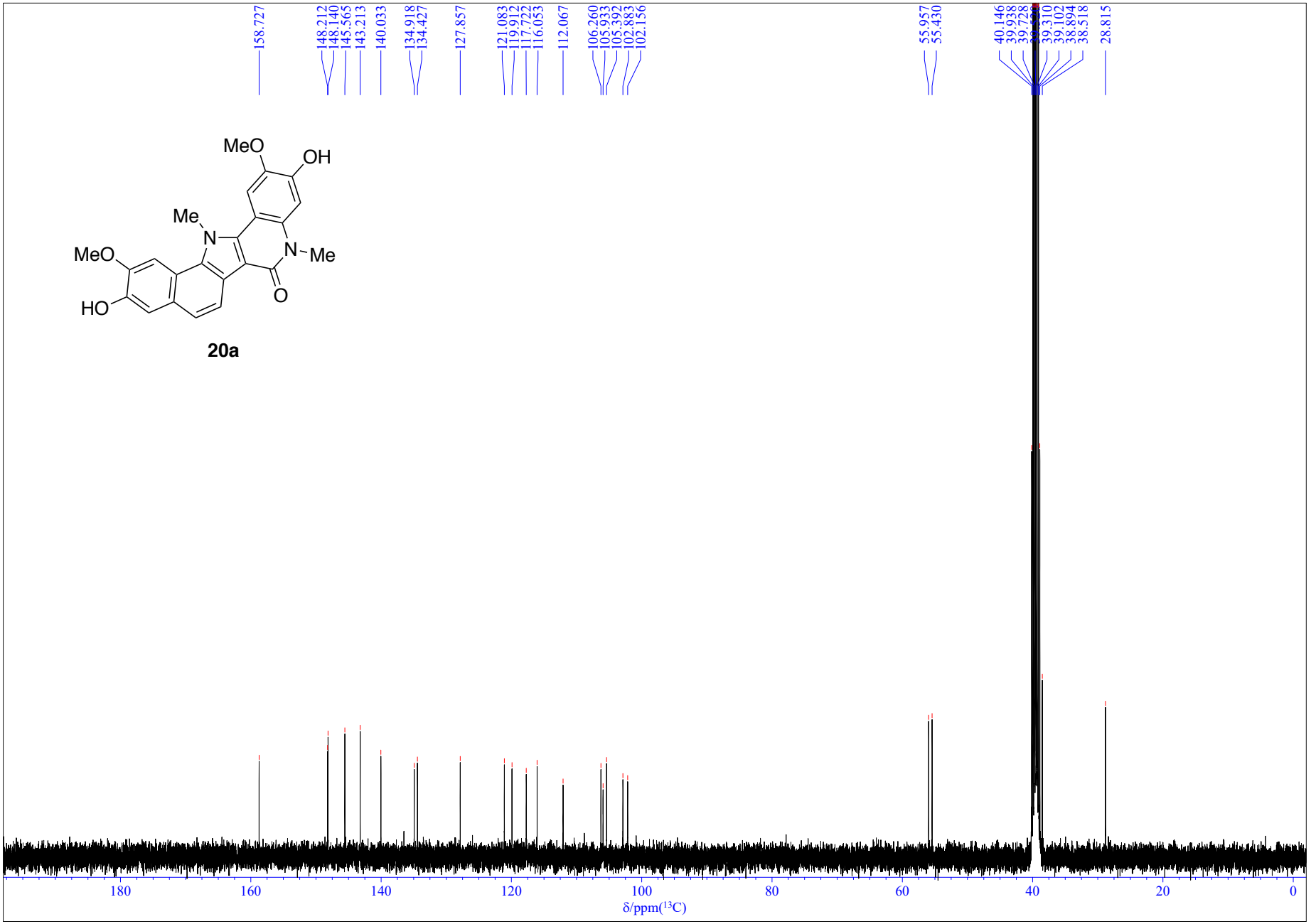

Figure S34. ^{13}C NMR spectrum of compound **20a** (100 MHz, DMSO-d_6).

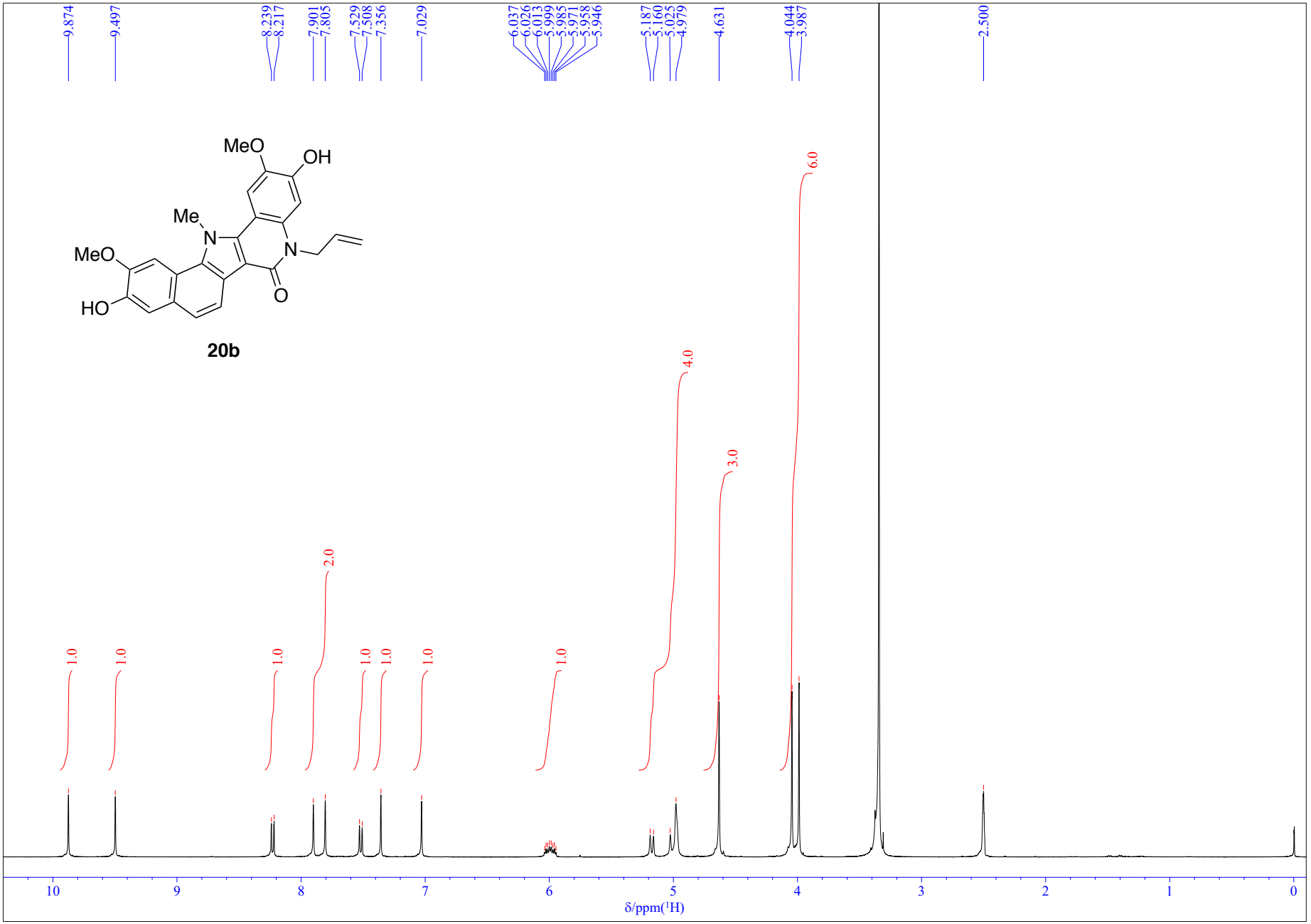

Figure S35. ^{1}H NMR spectrum of compound **20b** (400 MHz, DMSO-d_6).

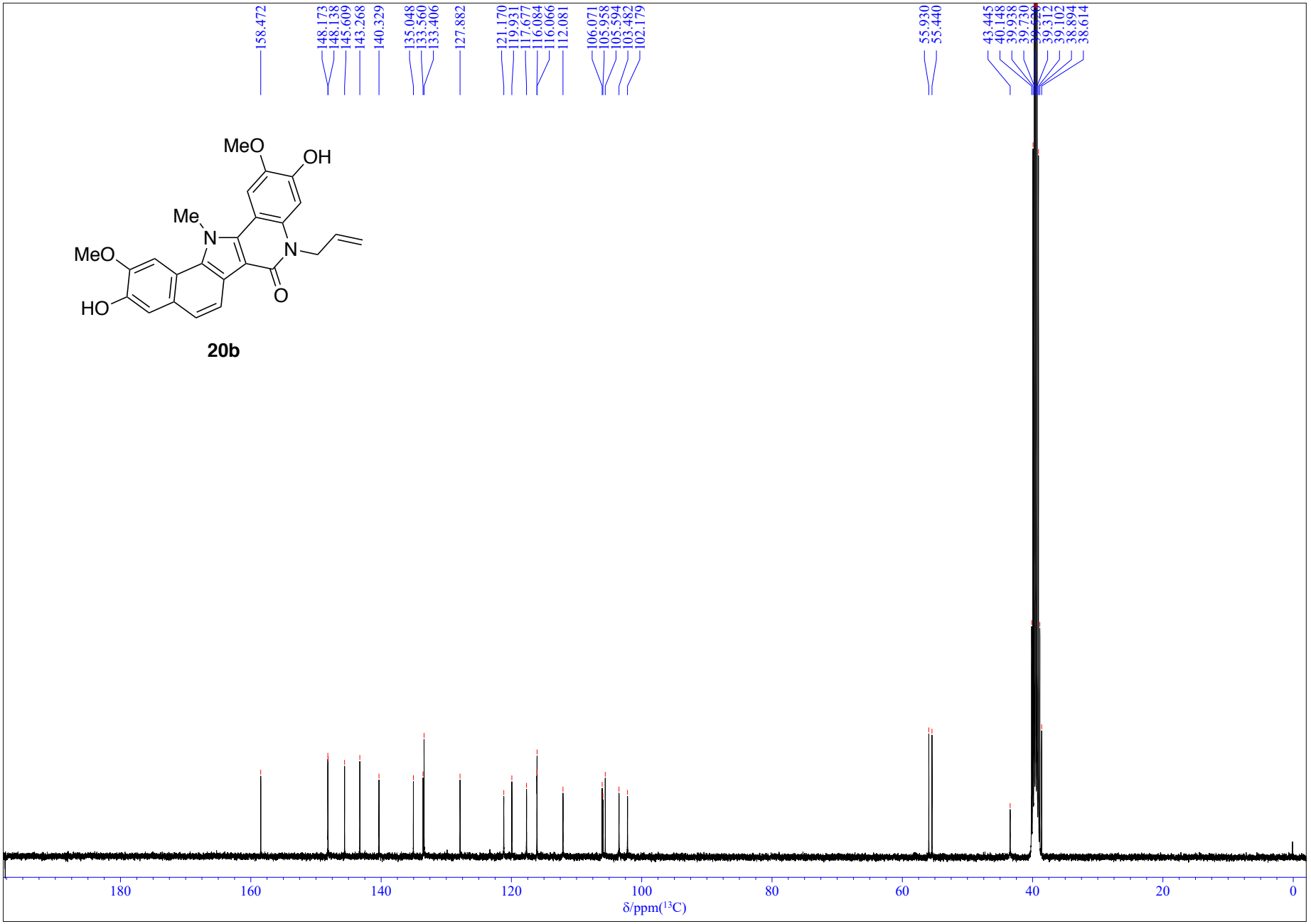

Figure S36. ^{13}C NMR spectrum of compound **20b** (100 MHz, DMSO-d_6).

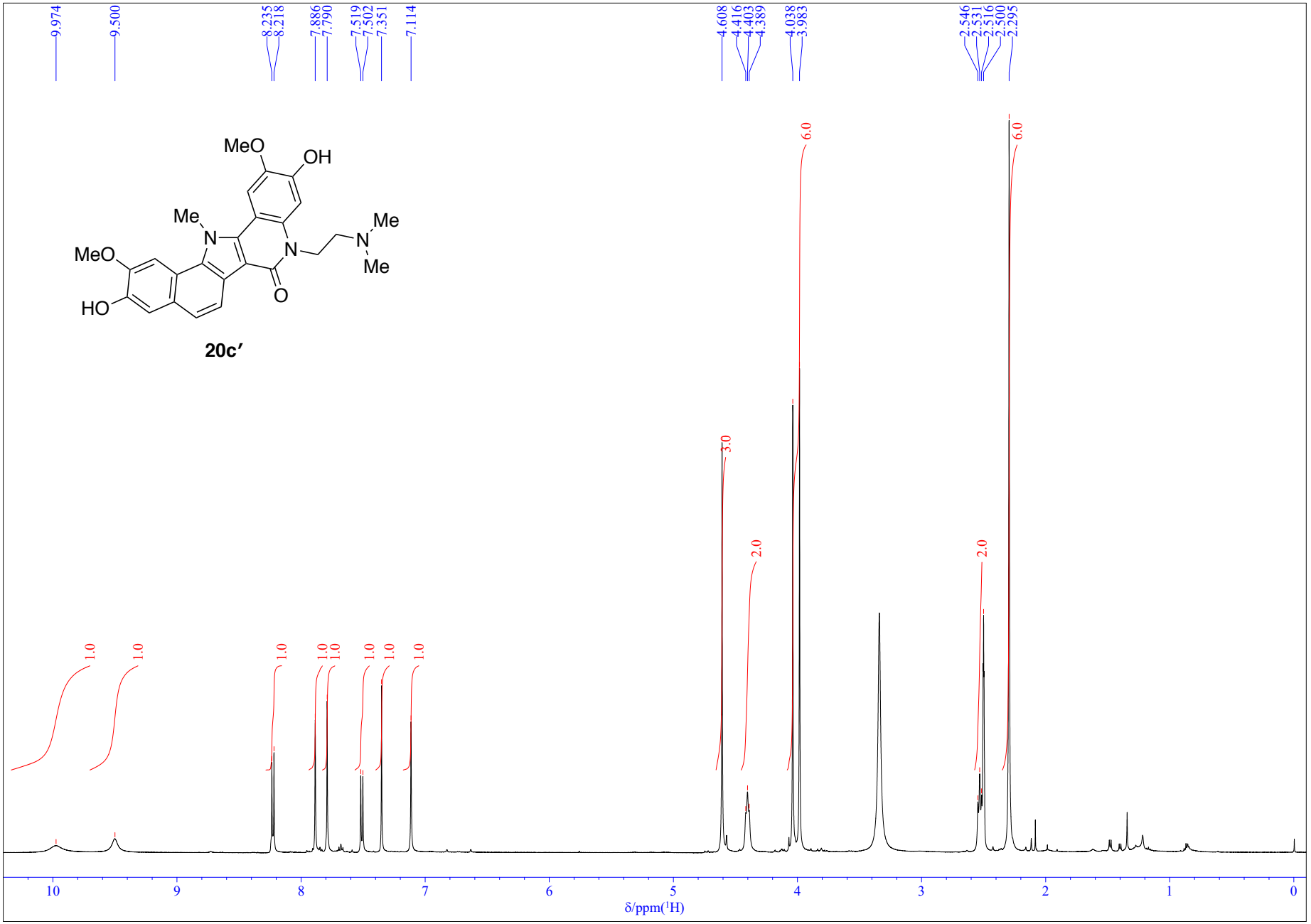

Figure S37. ^{1}H NMR spectrum of compound **20c′** (500 MHz, DMSO-d_6).

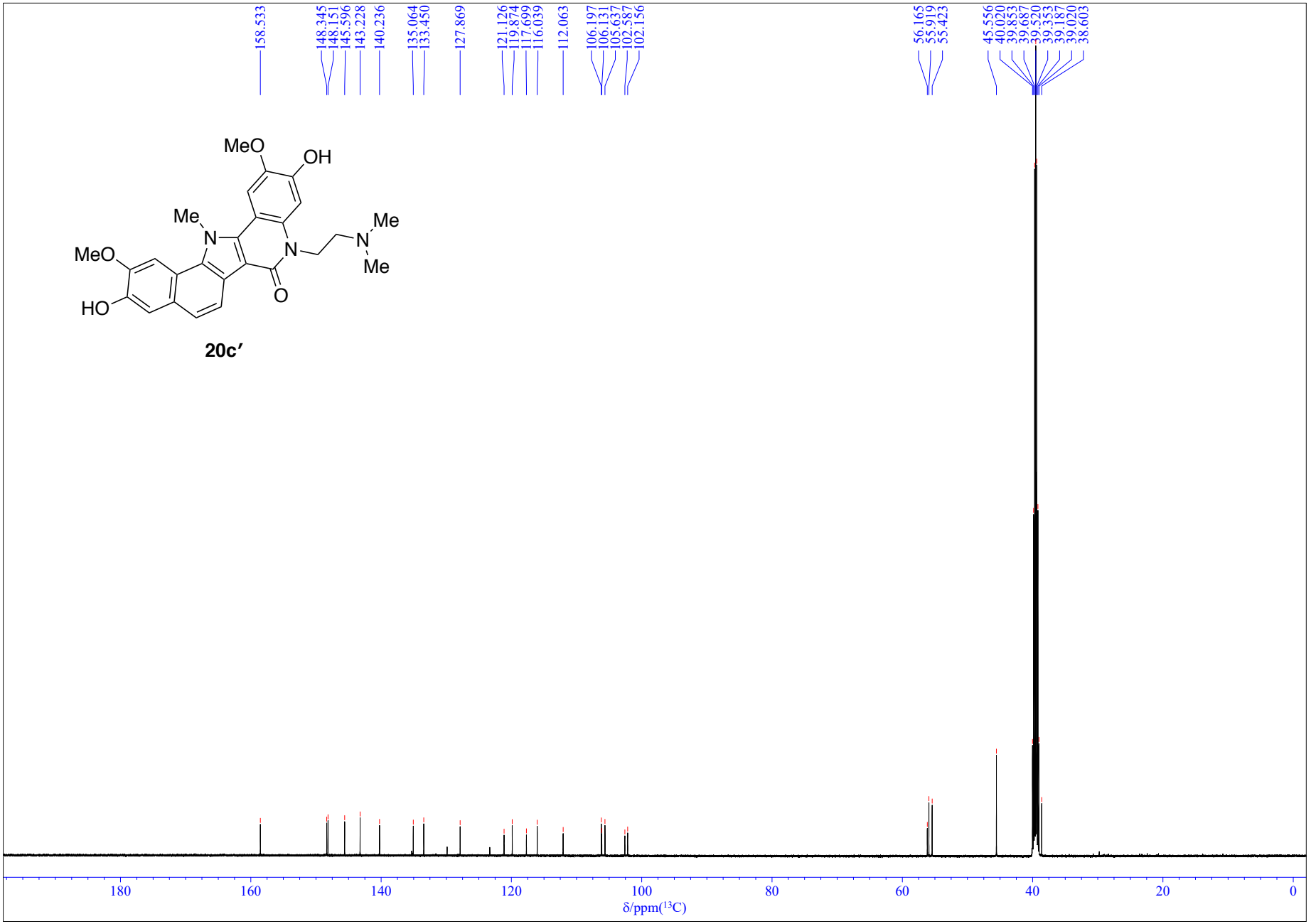

Figure S38. ^{13}C NMR spectrum of compound **20c**′ (126 MHz, DMSO-d_6).

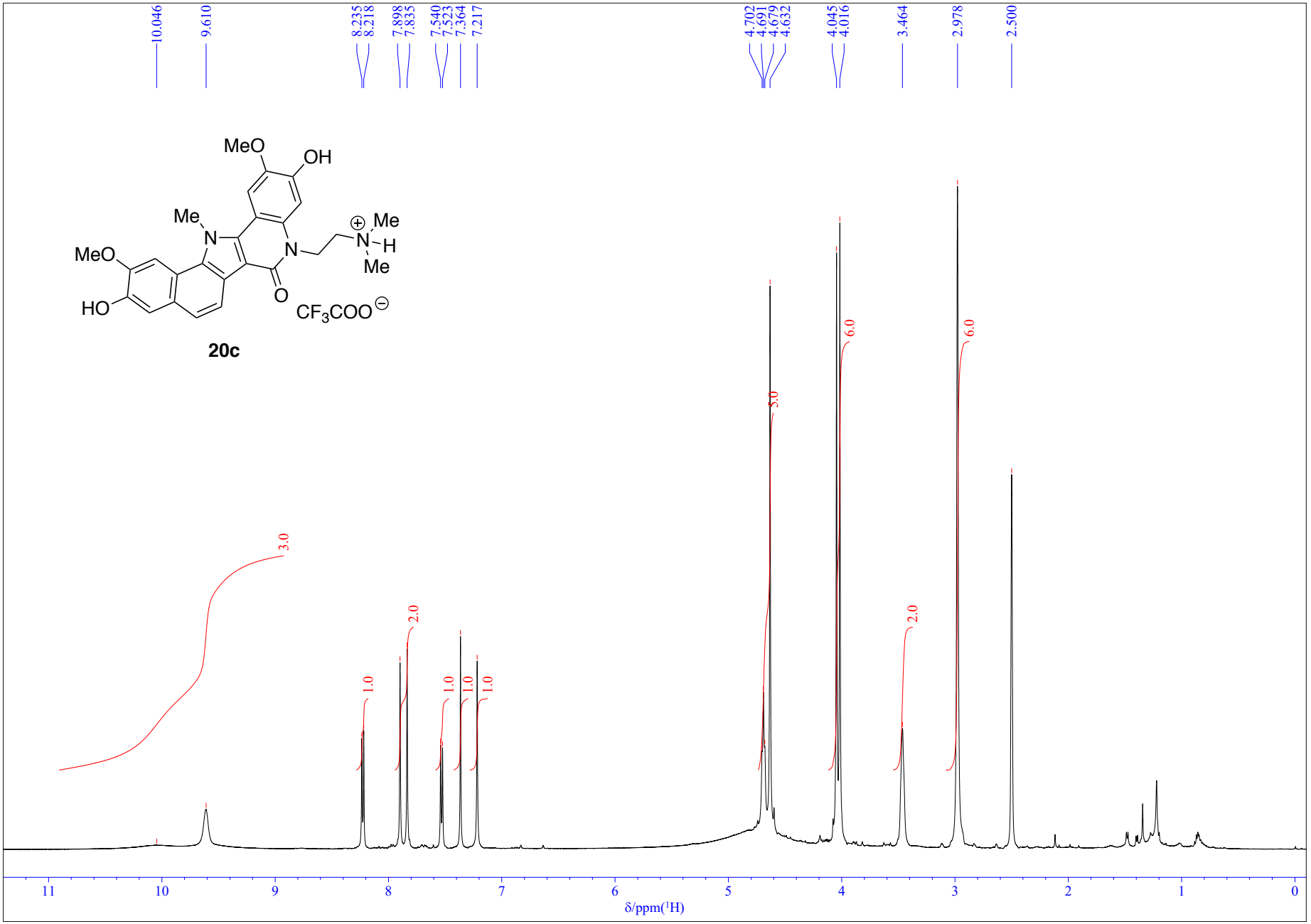

Figure S39. ^{1}H NMR spectrum of compound **20c** (500 MHz, DMSO-d_6).

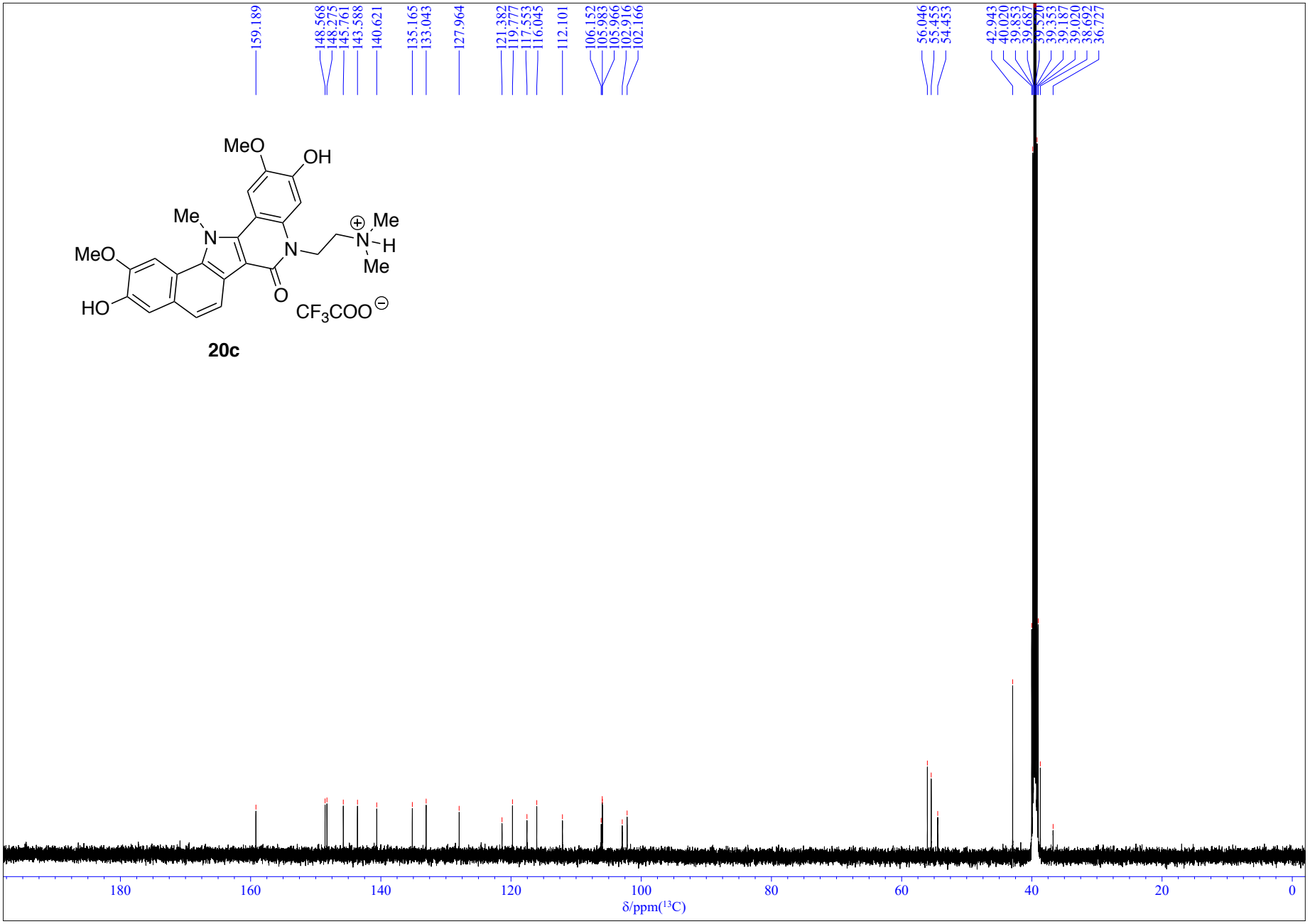

Figure S40. ^{13}C NMR spectrum of compound **20c** (126 MHz, DMSO-d_6).

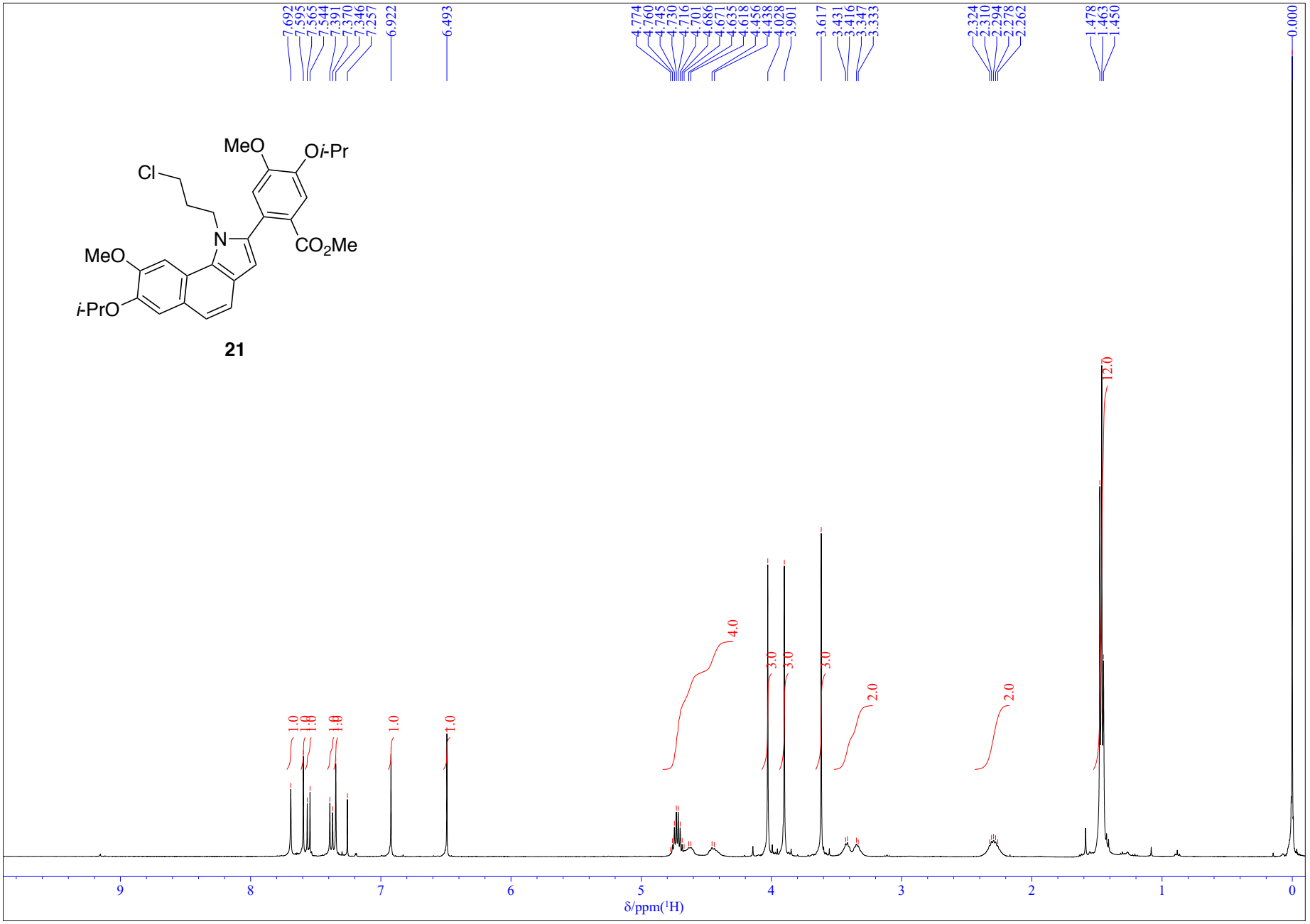

Figure S41. ^{1}H NMR spectrum of compound **21** (400 MHz, $CDCl_3$).

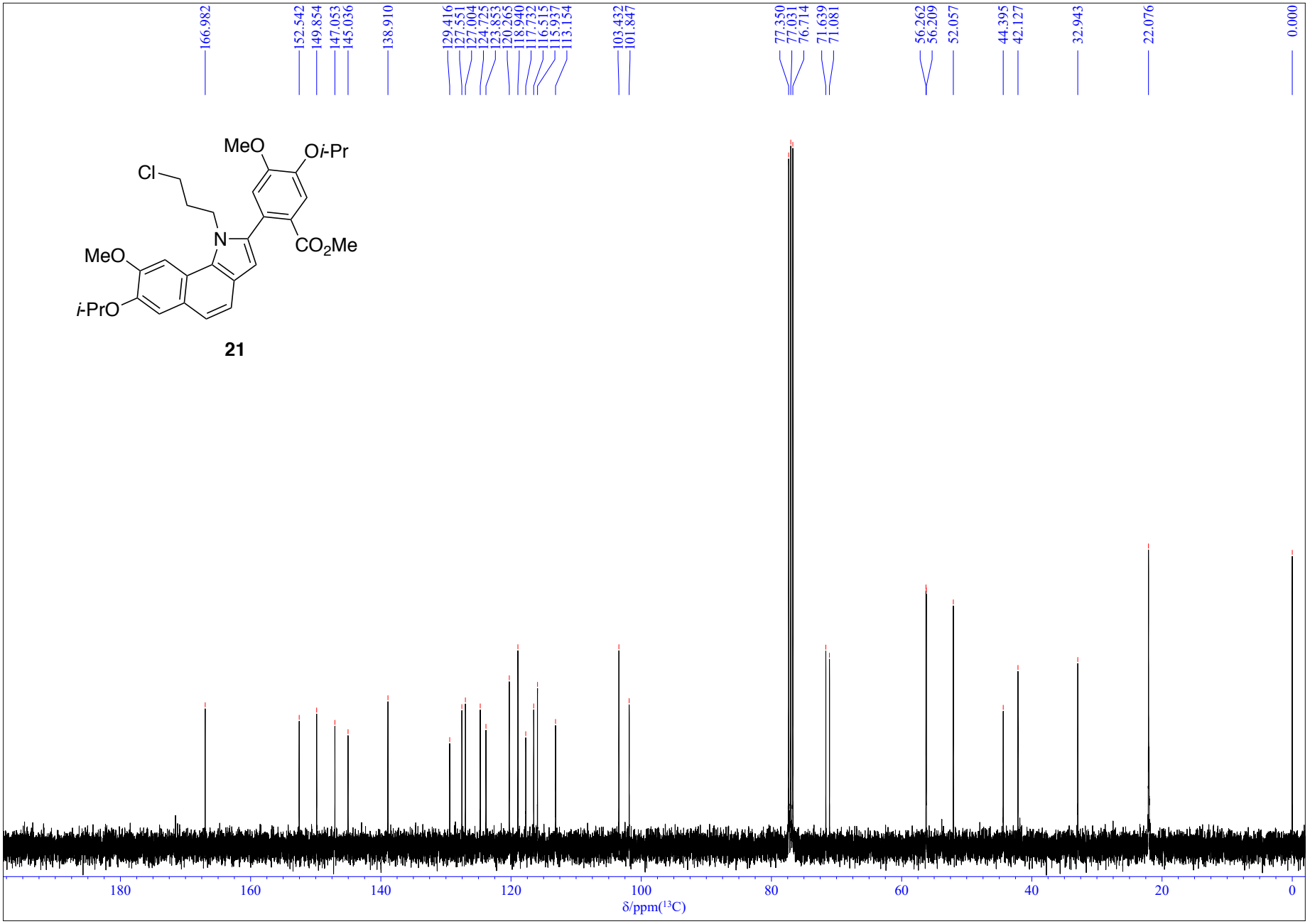

Figure S42. ^{13}C NMR spectrum of compound **21** (100 MHz, $CDCl_3$).

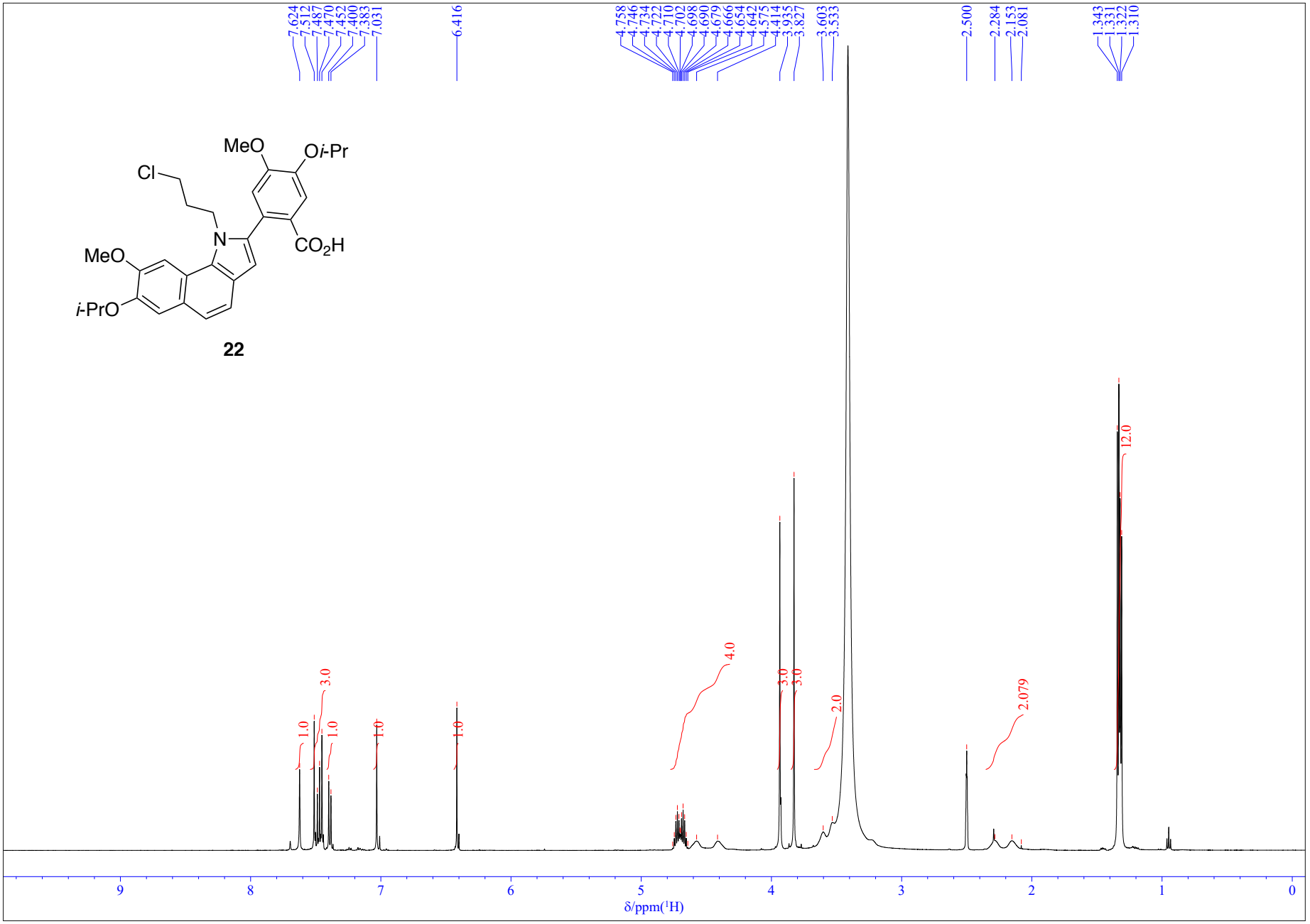

Figure S43. ^{1}H NMR spectrum of compound **22** (500 MHz, DMSO-d_6).

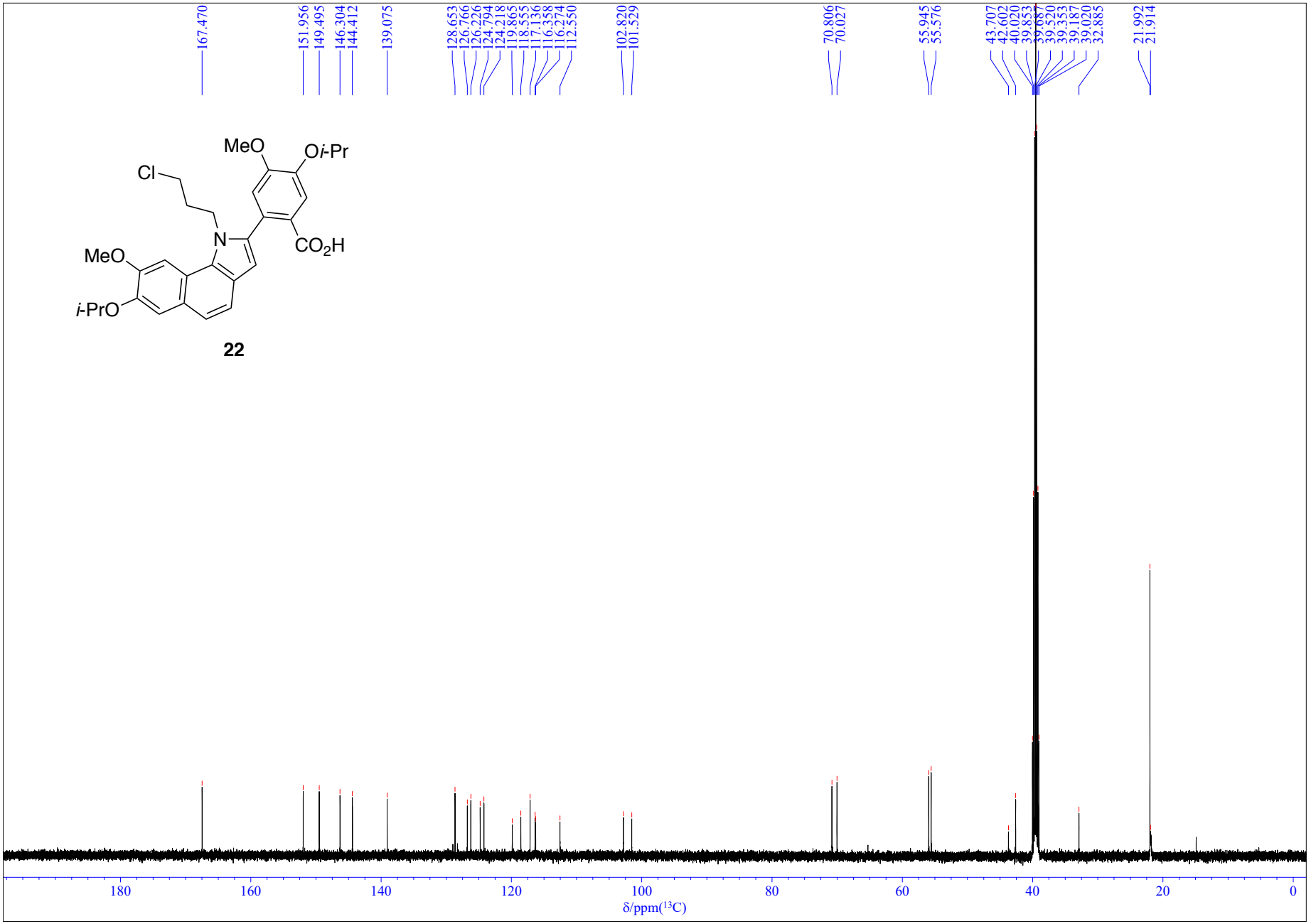

Figure S44. ^{13}C NMR spectrum of compound **22** (126 MHz, DMSO-d_6).

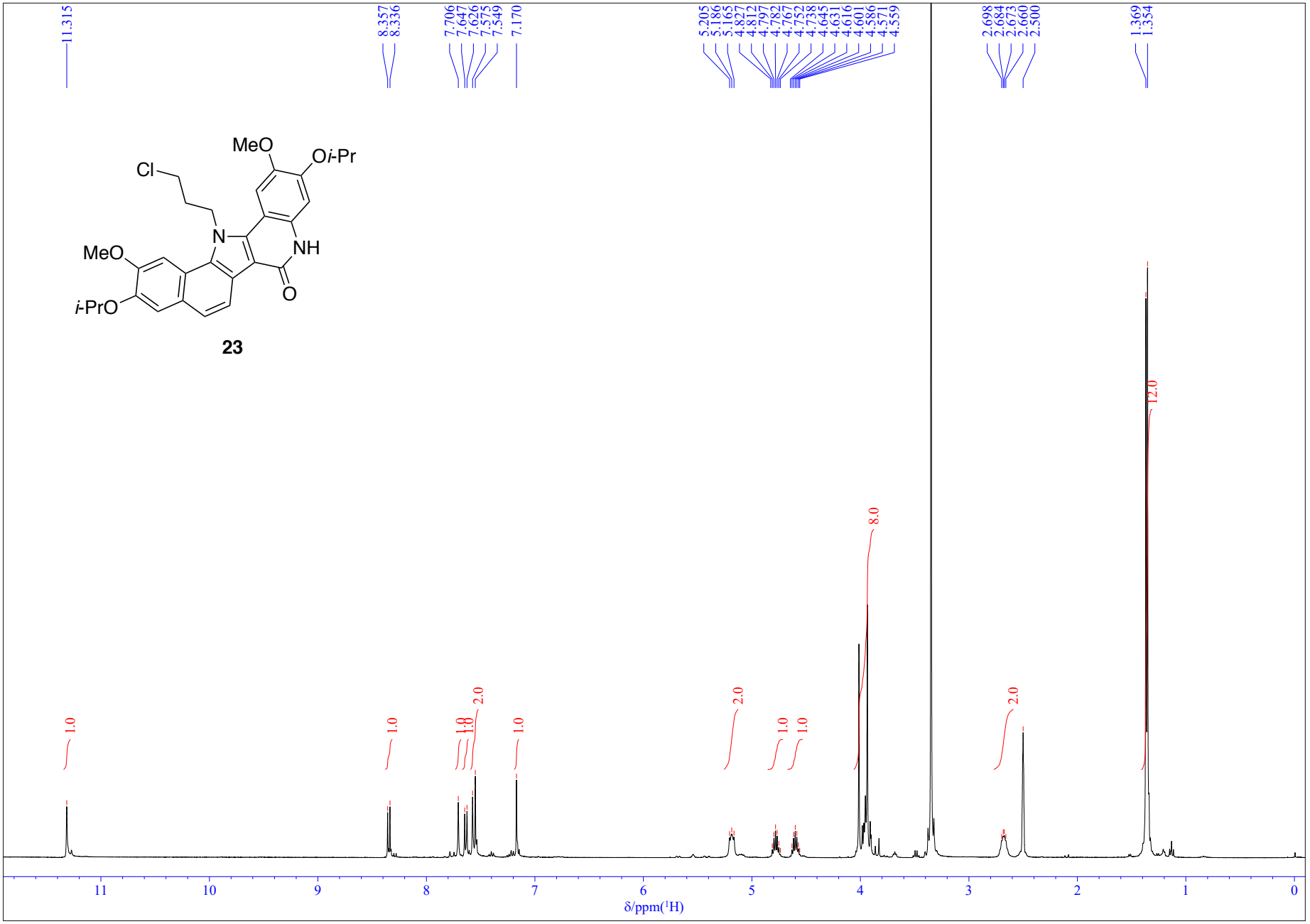

Figure S45. ^{1}H NMR spectrum of compound **23** (400 MHz, DMSO-d_6).

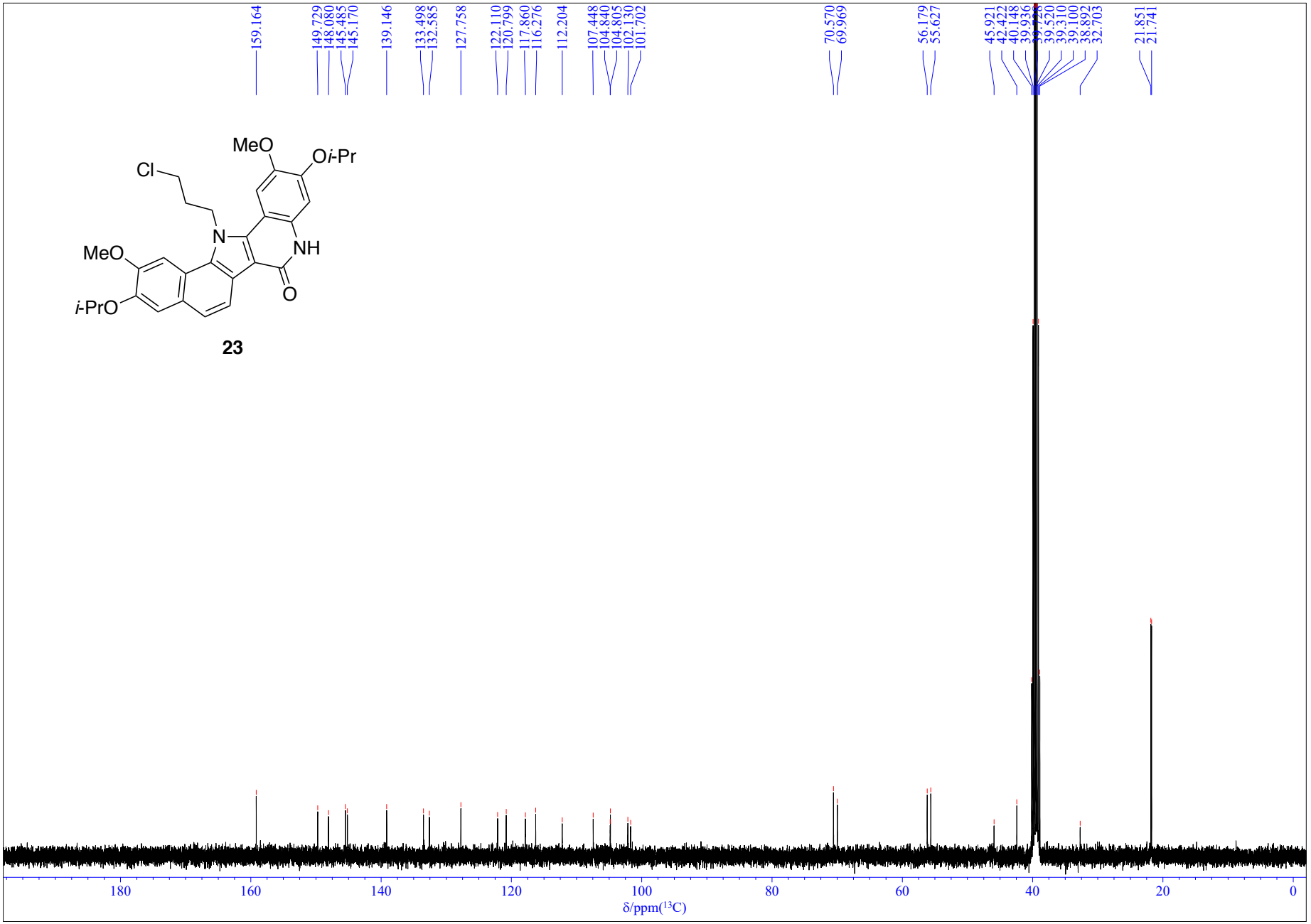

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Figure S46. ^{13}C NMR spectrum of compound **23** (100 MHz, DMSO-d_6).

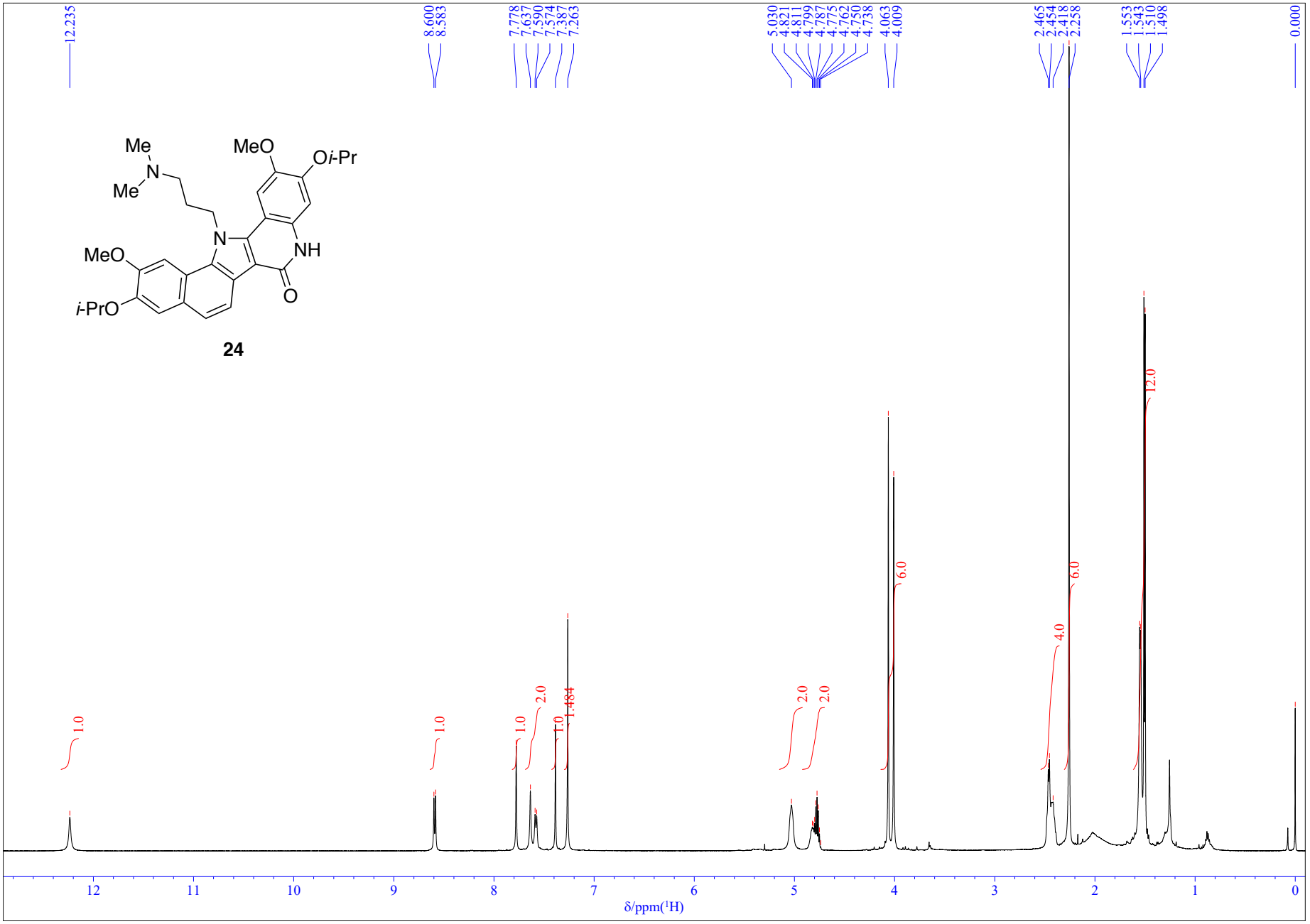

Figure S47. ^{1}H NMR spectrum of compound **24** (500 MHz, $CDCl_3$).

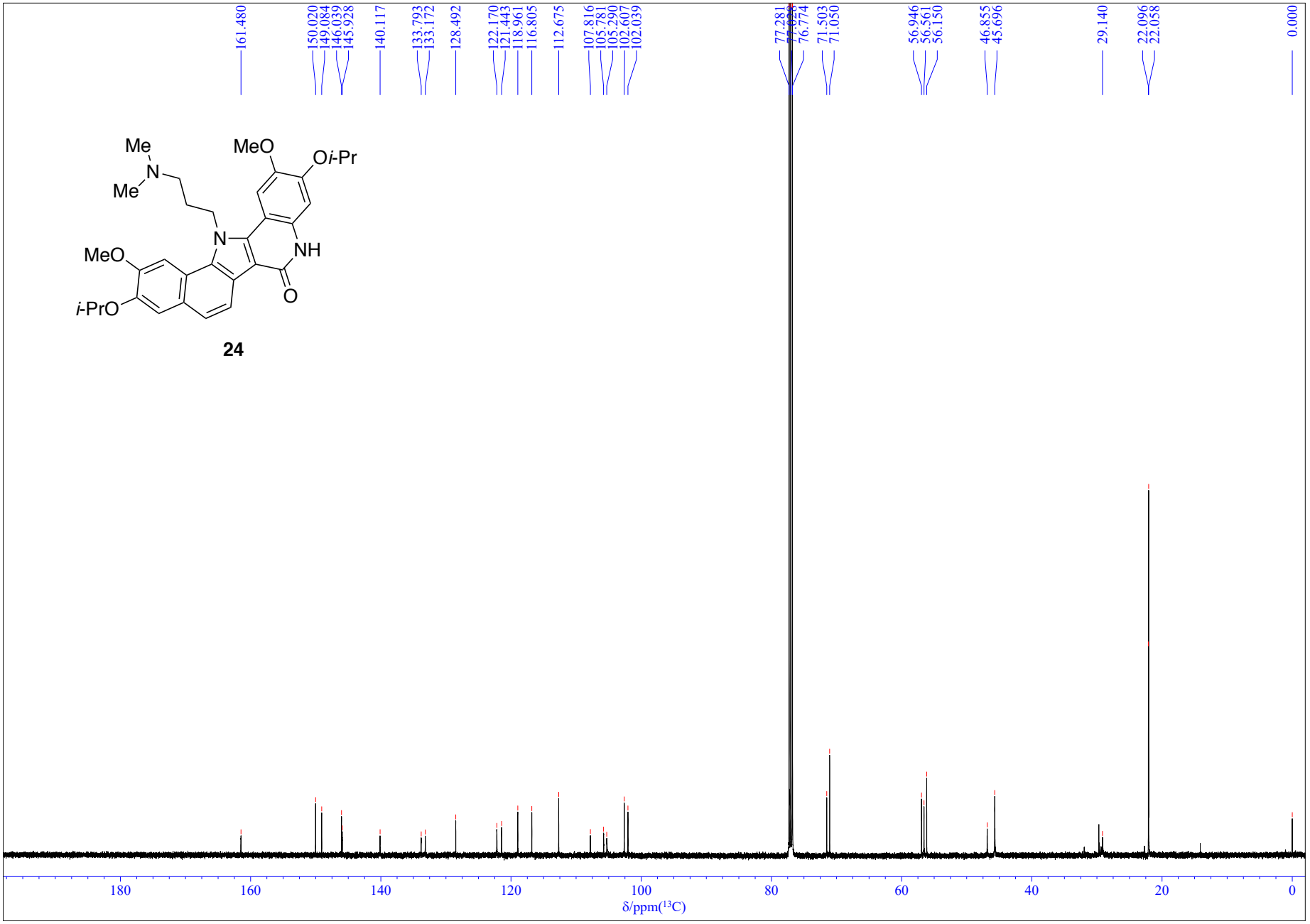

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Figure S48. ^{13}C NMR spectrum of compound **24** (126 MHz, $CDCl_3$).

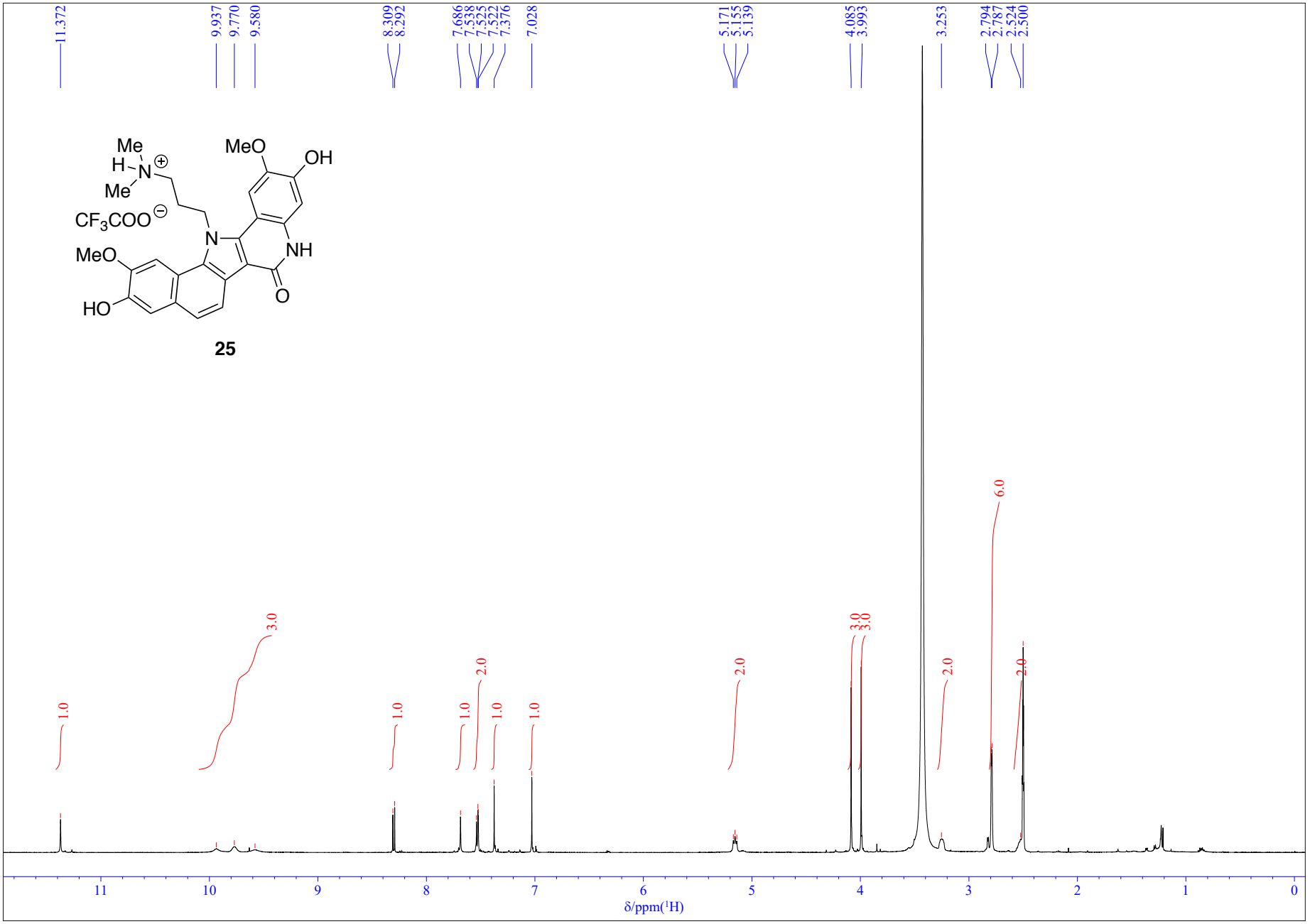


Figure S49. ^{1}H NMR spectrum of compound **25** (500 MHz, DMSO-d_6).

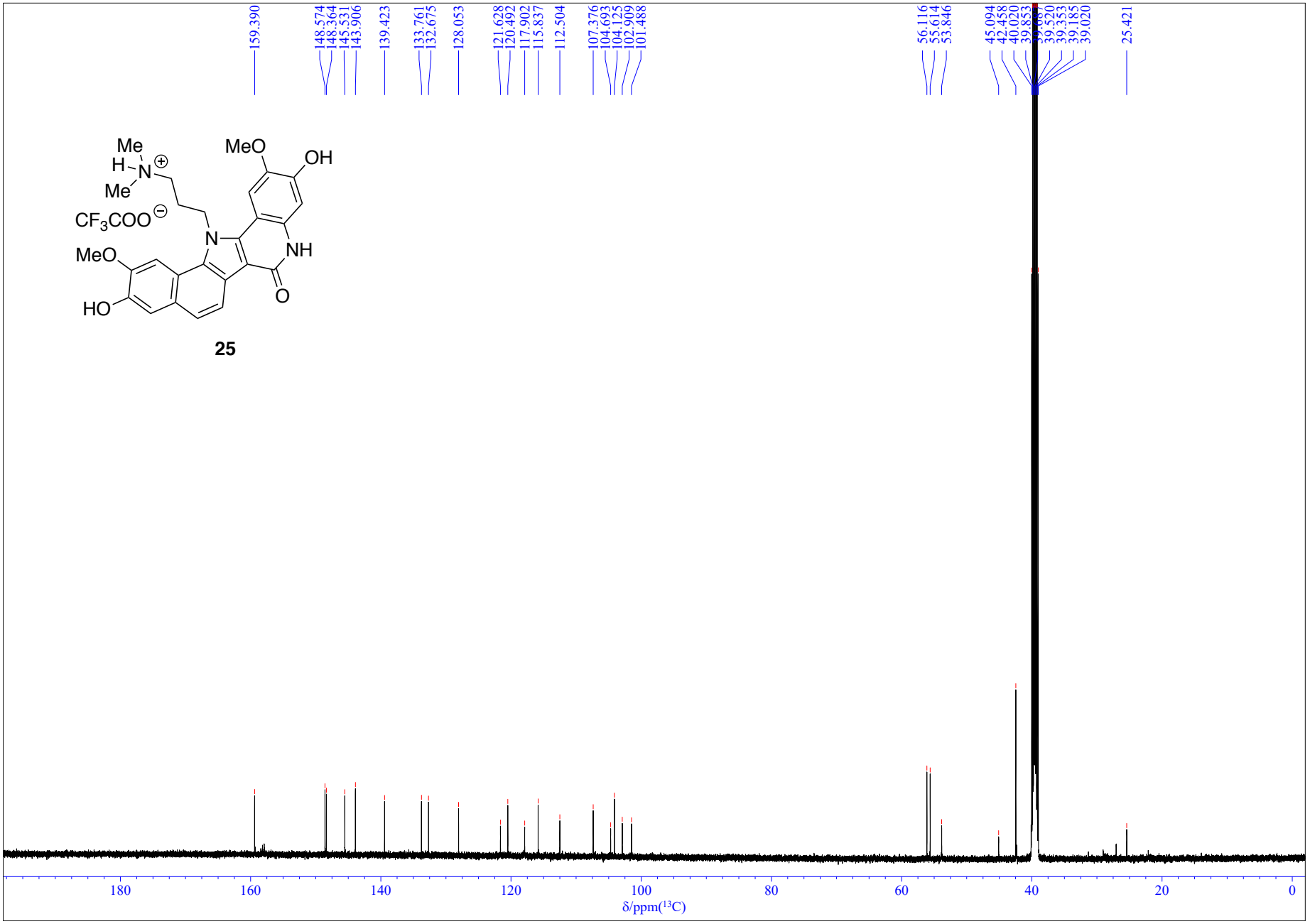
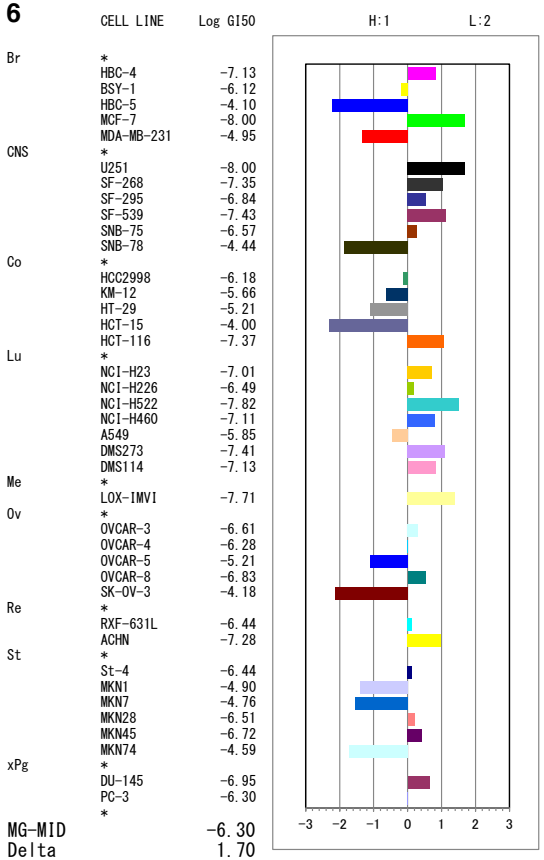


Figure S50. ^{13}C NMR spectrum of compound **25** (126 MHz, DMSO-d_6).

6

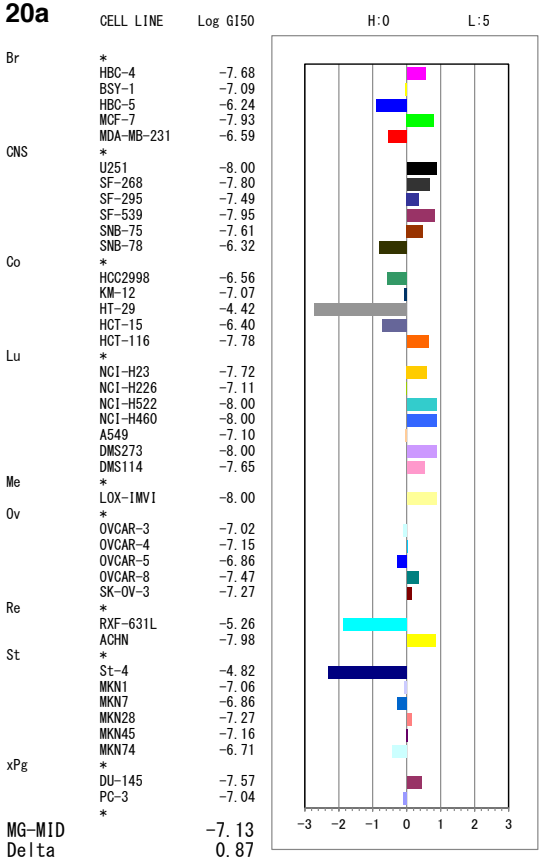


	CELL LINE	Log GI50
Br	*	
	HBC-4	-7.13
	BSY-1	-6.12
	HBC-5	-4.10
	MCF-7	-8.00
	MDA-MB-231	-4.95
CNS	*	
	U251	-8.00
	SF-268	-7.35
	SF-295	-6.84
	SF-539	-7.43
	SNB-75	-6.57
	SNB-78	-4.44
Co	*	
	HCC2998	-6.18
	KM-12	-5.66
	HT-29	-5.21
	HCT-15	-4.00
	HCT-116	-7.37
Lu	*	
	NCI-H23	-7.01
	NCI-H226	-6.49
	NCI-H522	-7.82
	NCI-H460	-7.11
	A549	-5.85
	DMS273	-7.41
	DMS114	-7.13
Me	*	
	LOX-IMVI	-7.71
Ov	*	
	OVCAR-3	-6.61
	OVCAR-4	-6.28
	OVCAR-5	-5.21
	OVCAR-8	-6.83
	SK-OV-3	-4.18
Re	*	
	RXF-631L	-6.44
	ACHN	-7.28
St	*	
	St-4	-6.44
	MKN1	-4.90
	MKN7	-4.76
	MKN28	-6.51
	MKN45	-6.72
	MKN74	-4.59
xPg	*	
	DU-145	-6.95
	PC-3	-6.30
	*	
MG-MID		-6.30
Delta		1.70
Range		4.00

Results of COMPARE:

Rank	Compounds	r	Molecular Targets / Drug Type
1	SN-38	0.85	DNA Topoisomerase I Inhibitors topoisomerase (I, II)
2	SN-38	0.84	DNA Topoisomerase I Inhibitors topoisomerase (I, II)
3	SN-38	0.825	DNA Topoisomerase I Inhibitors topoisomerase (I, II)

20a

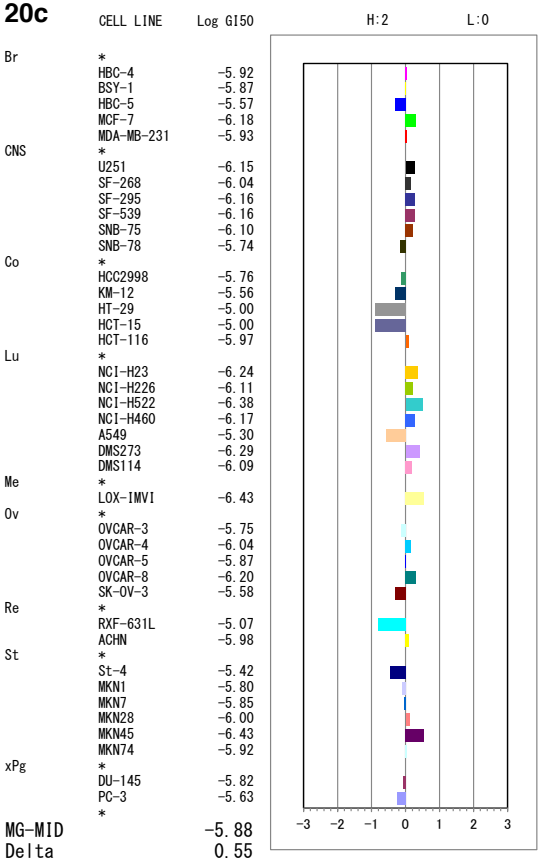


	CELL LINE	Log GI50
Br	*	
	HBC-4	-7.68
	BSY-1	-7.09
	HBC-5	-6.24
	MCF-7	-7.93
	MDA-MB-231	-6.59
CNS	*	
	U251	-8.00
	SF-268	-7.80
	SF-295	-7.49
	SF-539	-7.95
	SNB-75	-7.61
	SNB-78	-6.32
Co	*	
	HCC2998	-6.56
	KM-12	-7.07
	HT-29	-4.42
	HCT-15	-6.40
	HCT-116	-7.78
Lu	*	
	NCI-H23	-7.72
	NCI-H226	-7.11
	NCI-H522	-8.00
	NCI-H460	-8.00
	A549	-7.10
	DMS273	-8.00
	DMS114	-7.65
Me	*	
	LOX-IMVI	-8.00
Ov	*	
	OVCAR-3	-7.02
	OVCAR-4	-7.15
	OVCAR-5	-6.86
	OVCAR-8	-7.47
	SK-OV-3	-7.27
Re	*	
	RXF-631L	-5.26
	ACHN	-7.98
St	*	
	St-4	-4.82
	MKN1	-7.06
	MKN7	-6.86
	MKN28	-7.27
	MKN45	-7.16
	MKN74	-6.71
xPg	*	
	DU-145	-7.57
	PC-3	-7.04
	*	
MG-MID		-7.13
Delta		0.87
Range		3.58

Results of COMPARE:

Rank	Compounds	r	Molecular Targets / Drug Type
1	SN-38	0.732	DNA Topoisomerase I Inhibitors topoisomerase (I, II)
2	TAS-103	0.727	DNA Topoisomerase I, II Inhibitors DNA-Intercalating Drugs topoisomerase (I, II)
3	SN-38	0.718	DNA Topoisomerase I Inhibitors topoisomerase (I, II)

20c



	CELL LINE	Log GI50
Br	*	
	HBC-4	-5.92
	BSY-1	-5.87
	HBC-5	-5.57
	MCF-7	-6.18
	MDA-MB-231	-5.93
CNS	*	
	U251	-6.15
	SF-268	-6.04
	SF-295	-6.16
	SF-539	-6.16
	SNB-75	-6.10
	SNB-78	-5.74
Co	*	
	HCC2998	-5.76
	KM-12	-5.56
	HT-29	-5.00
	HCT-15	-5.00
	HCT-116	-5.97
Lu	*	
	NCI-H23	-6.24
	NCI-H226	-6.11
	NCI-H522	-6.38
	NCI-H460	-6.17
	A549	-5.30
	DMS273	-6.29
	DMS114	-6.09
Me	*	
	LOX-IMVI	-6.43
Ov	*	
	OVCAR-3	-5.75
	OVCAR-4	-6.04
	OVCAR-5	-5.87
	OVCAR-8	-6.20
	SK-OV-3	-5.58
Re	*	
	RXF-631L	-5.07
	ACHN	-5.98
St	*	
	St-4	-5.42
	MKN1	-5.80
	MKN7	-5.85
	MKN28	-6.00
	MKN45	-6.43
	MKN74	-5.92
xPg	*	
	DU-145	-5.82
	PC-3	-5.63
	*	
MG-MID		-5.88
Delta		0.55
Range		1.43

Results of COMPARE:

Rank	Compounds	r	Molecular Targets / Drug Type
1	SN-38	0.727	DNA Topoisomerase I Inhibitors DNA Topoisomerase II Inhibitors DNA Intercalater
2	SN-38	0.723	DNA Topoisomerase I Inhibitors DNA Topoisomerase II Inhibitors DNA Intercalater
3	Doxorubicin hydrochloride	0.709	DNA Topoisomerase II Inhibitor

Figure S51. Chemosensitivity patterns of BIQs **6**, **20a**, and **20c** against the JFCR39 panel and the results of COMPARE analyses. The mean graph shows the deviation of log GI_{50} value of each cell line from MG-MID. The correlation coefficient r (r = 0–1) shows the similarity of the chemosensitivity pattern of the tested compound to that of the known antitumor agent in the database.