

Supplementary Information

Chromene-Dihydropyrimidinone and Xanthene-Dihydropyrimidinone hybrids: design, synthesis, and antibacterial and antibiofilm activities.

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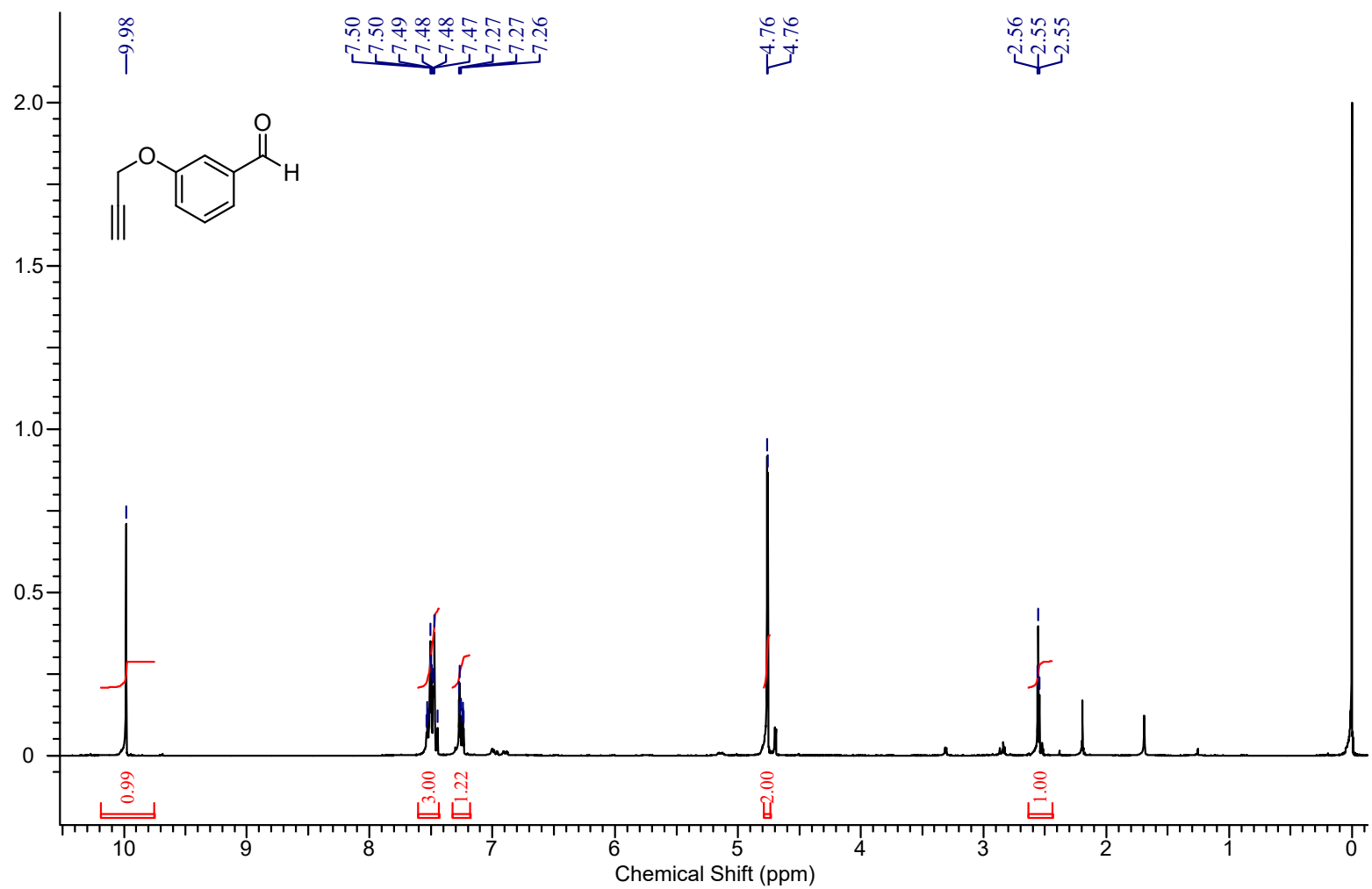


Figure S1: ¹H-NMR (300 MHz, CDCl₃) of 3a.

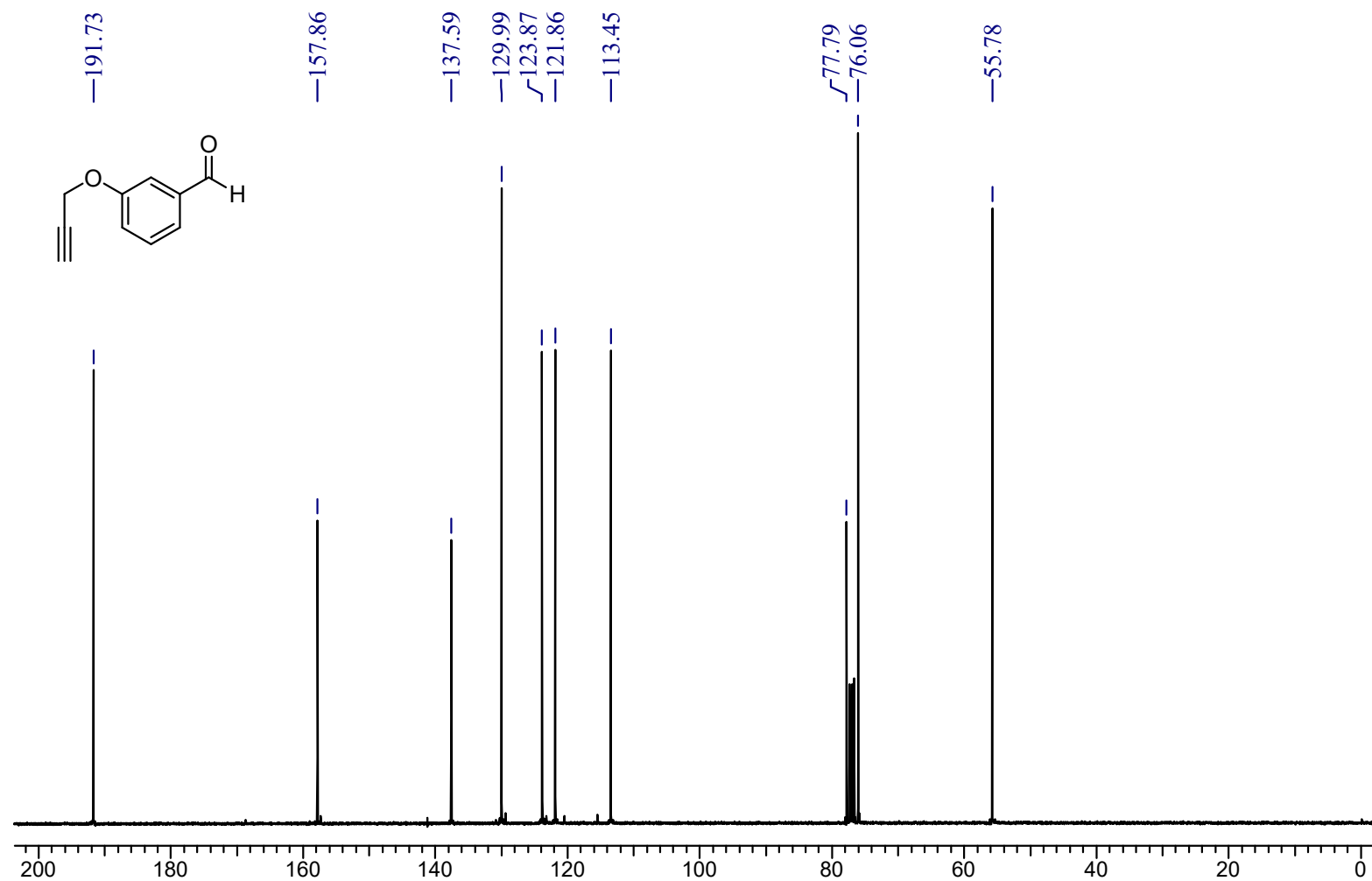


Figure S2: $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) of 3a.

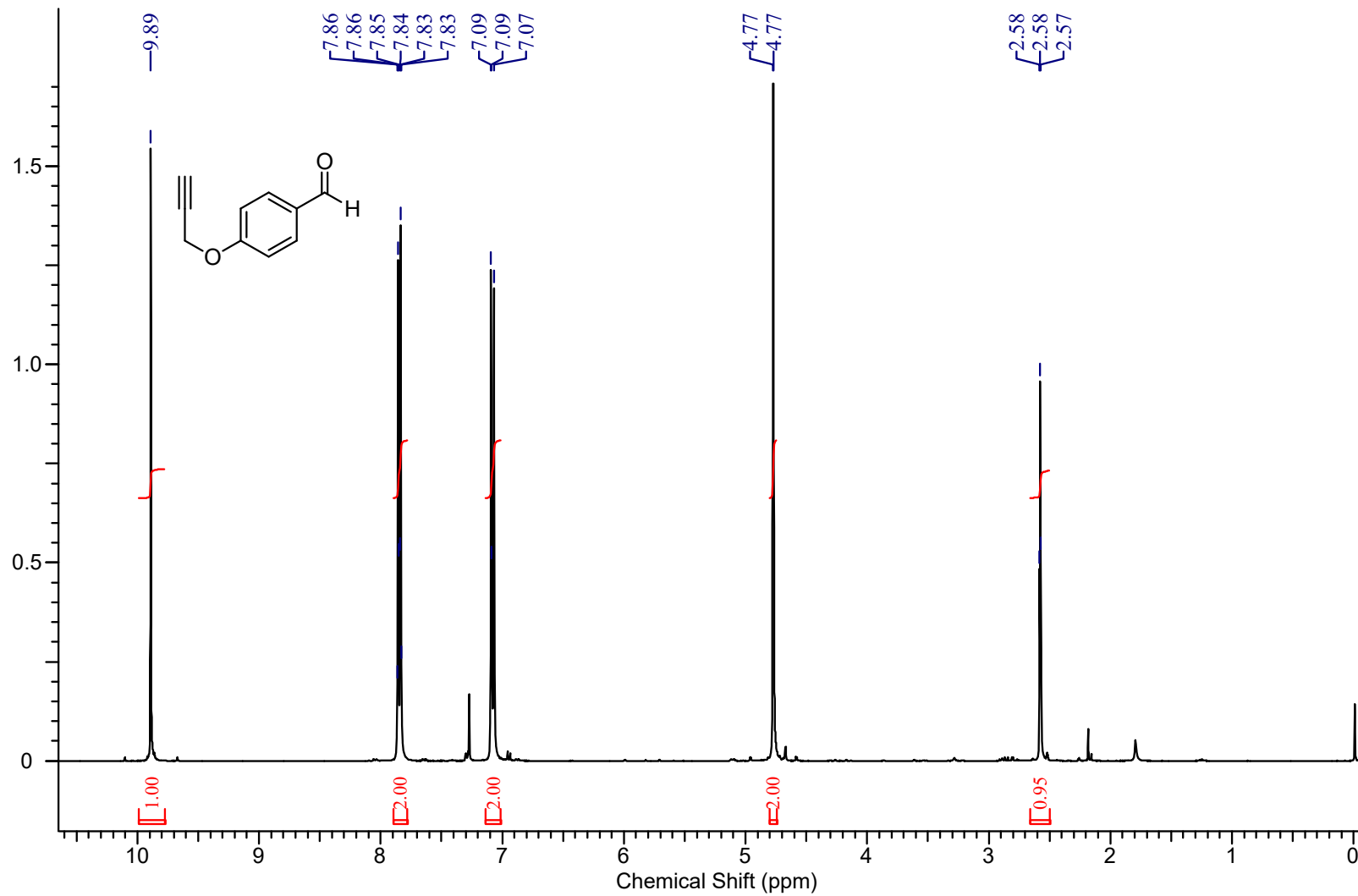


Figure S3: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 3b.

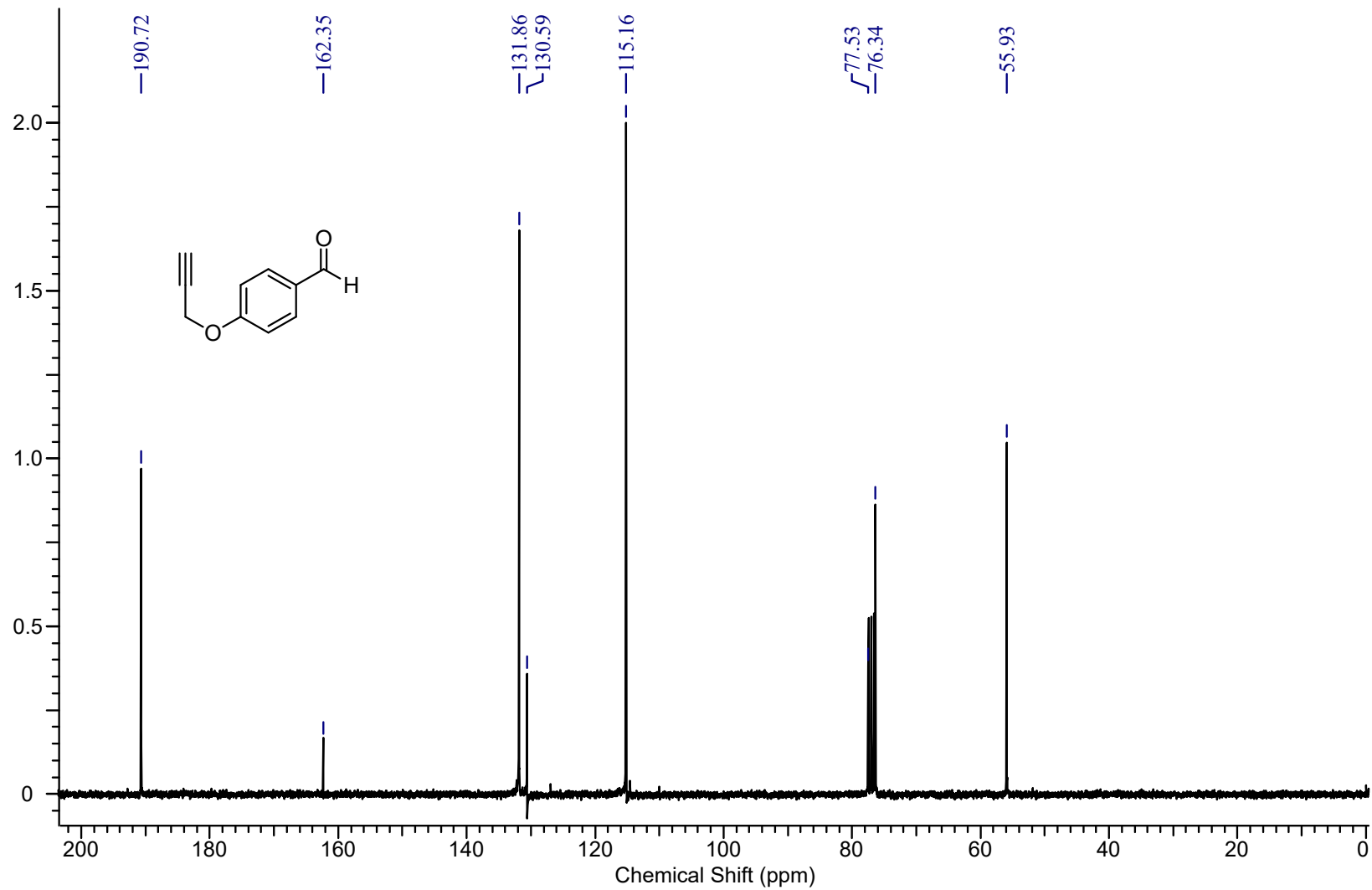


Figure S4: ^{13}C -NMR (75 MHz, CDCl_3) of 3b.

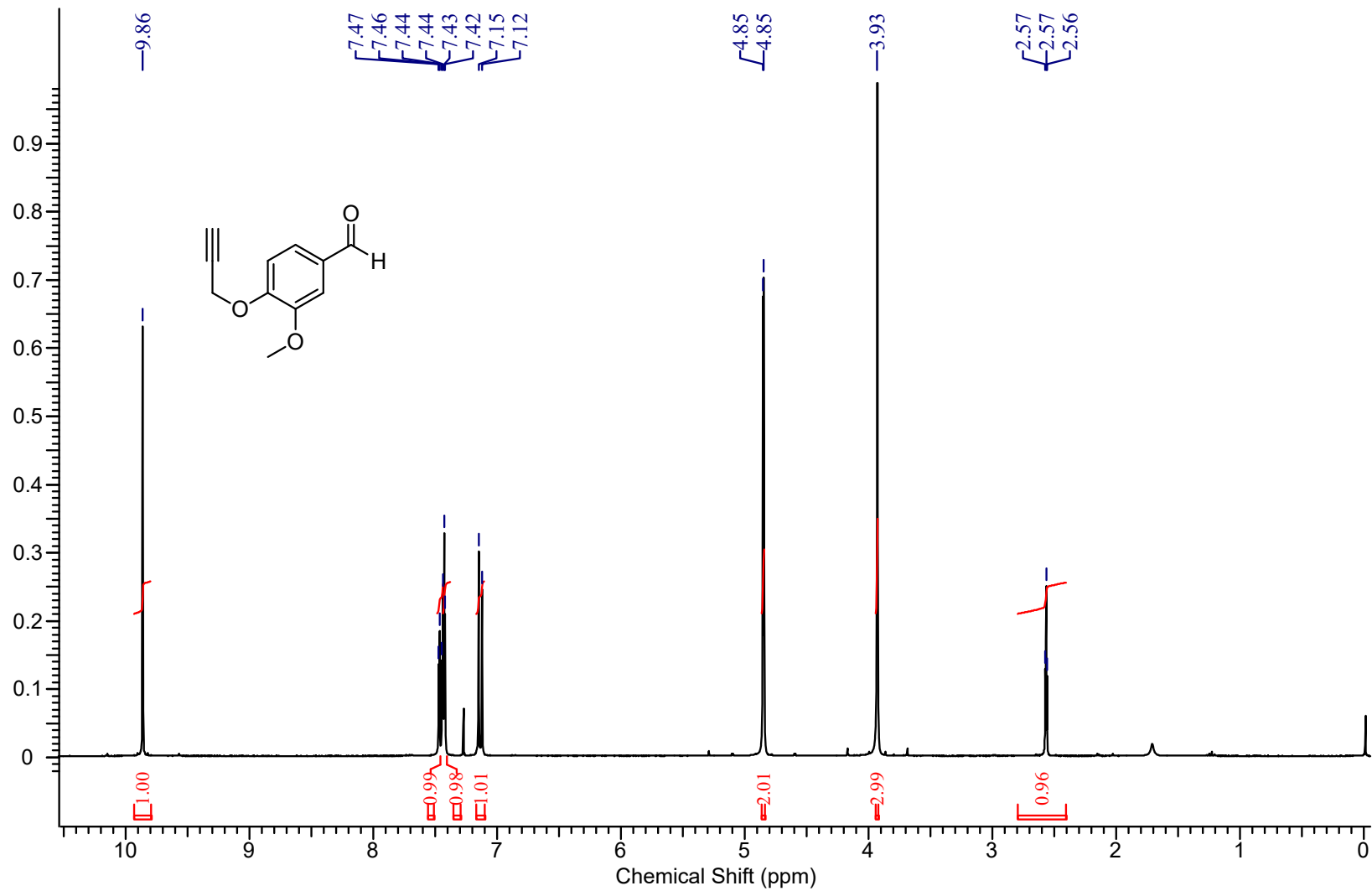


Figure S5: $^1\text{H-NMR}$ (300 MHz, CDCl_3) of 3c.

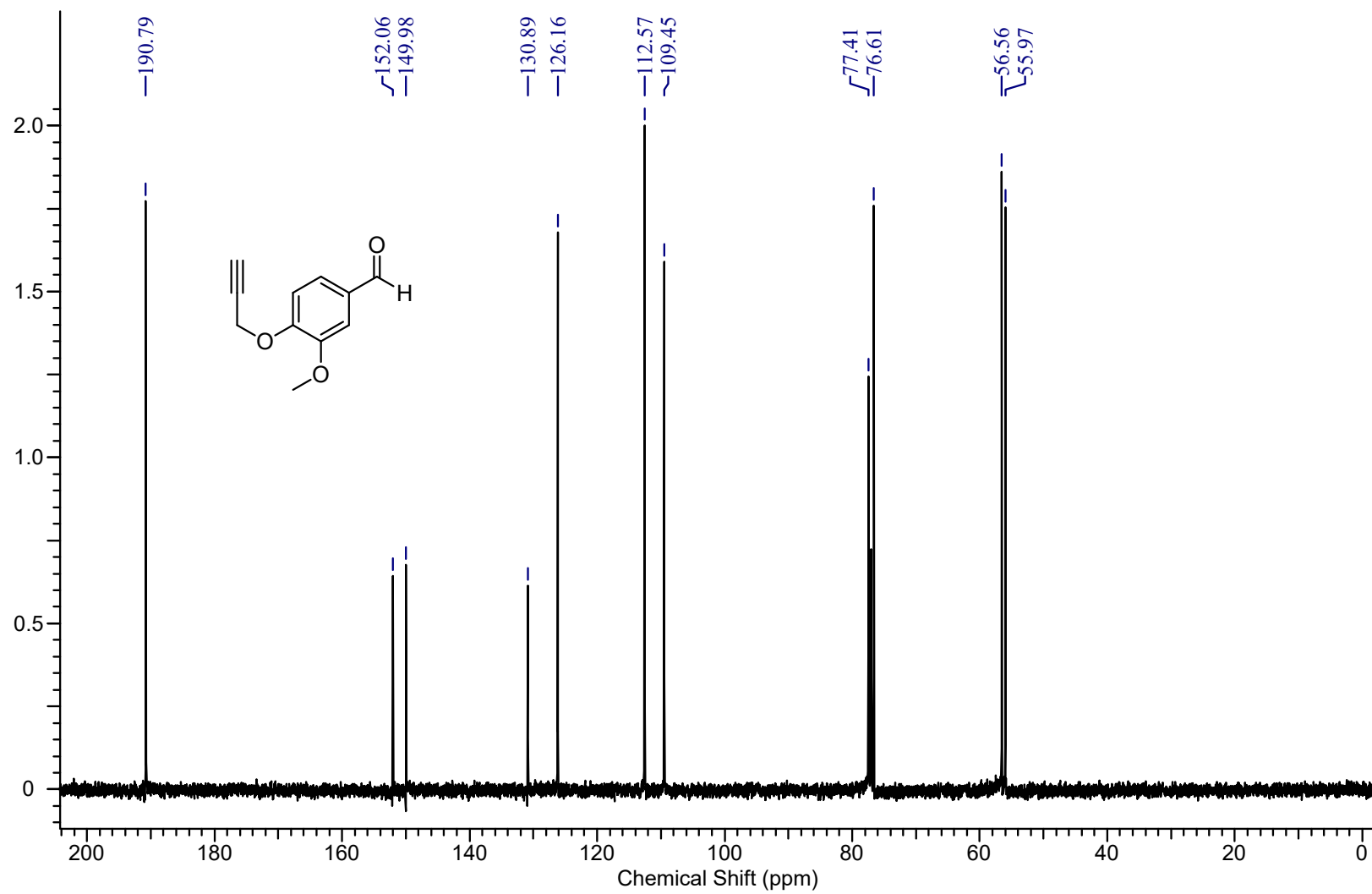


Figure S6: ^{13}C -NMR (75 MHz, CDCl_3) of 3c.

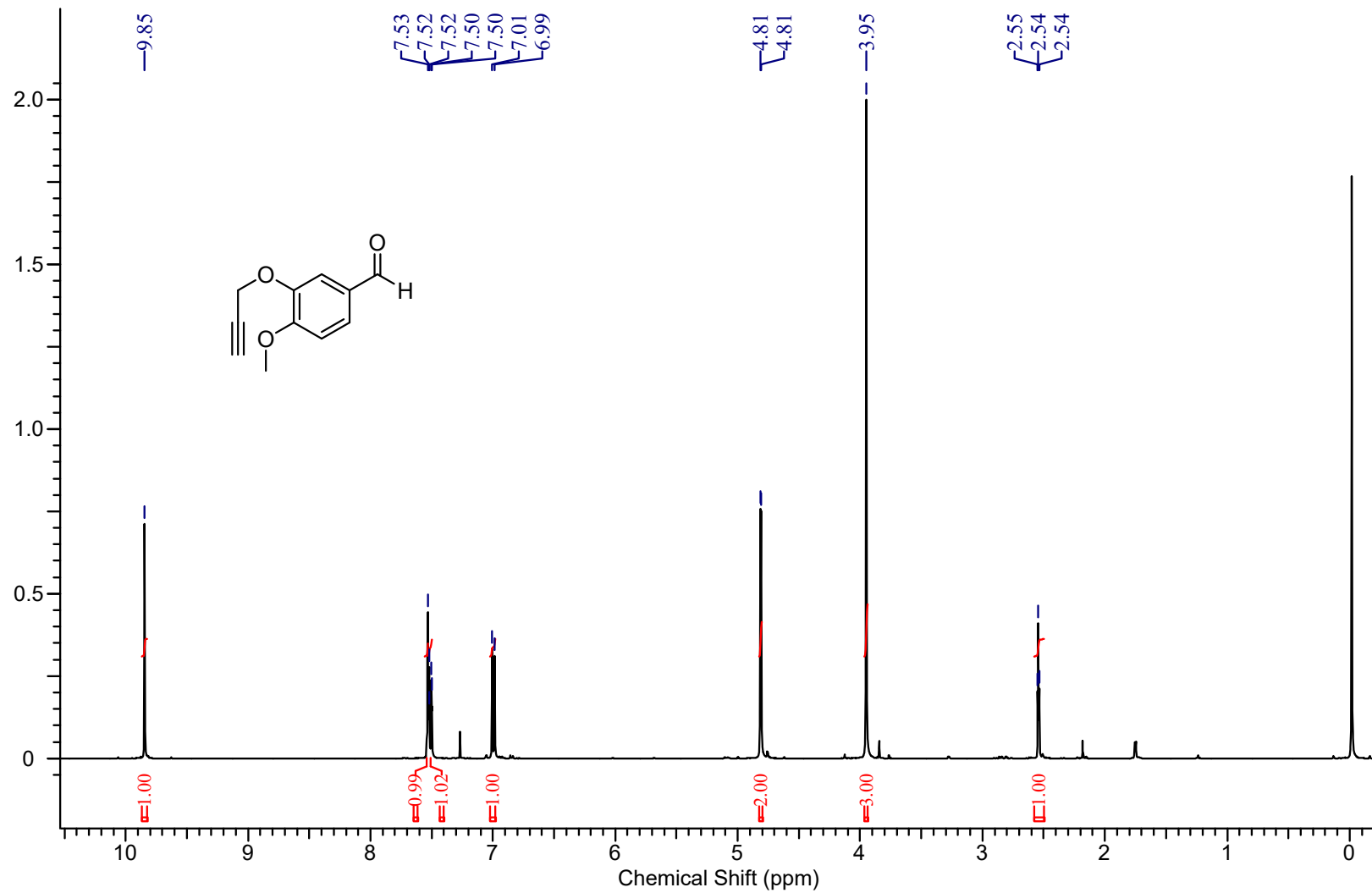


Figure S7: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 3d.

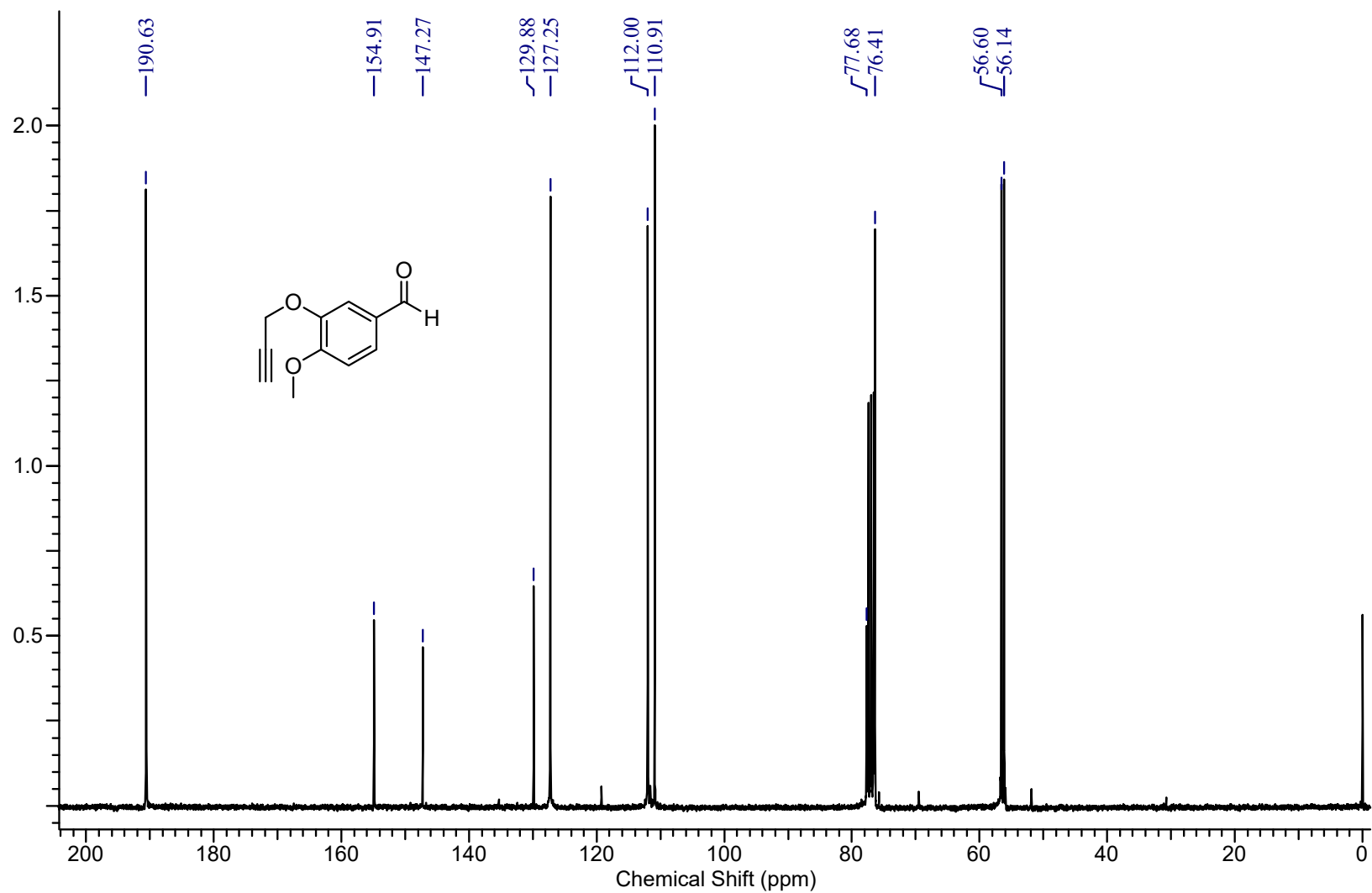


Figure S8: ^{13}C -NMR (75 MHz, CDCl_3) of 3d.

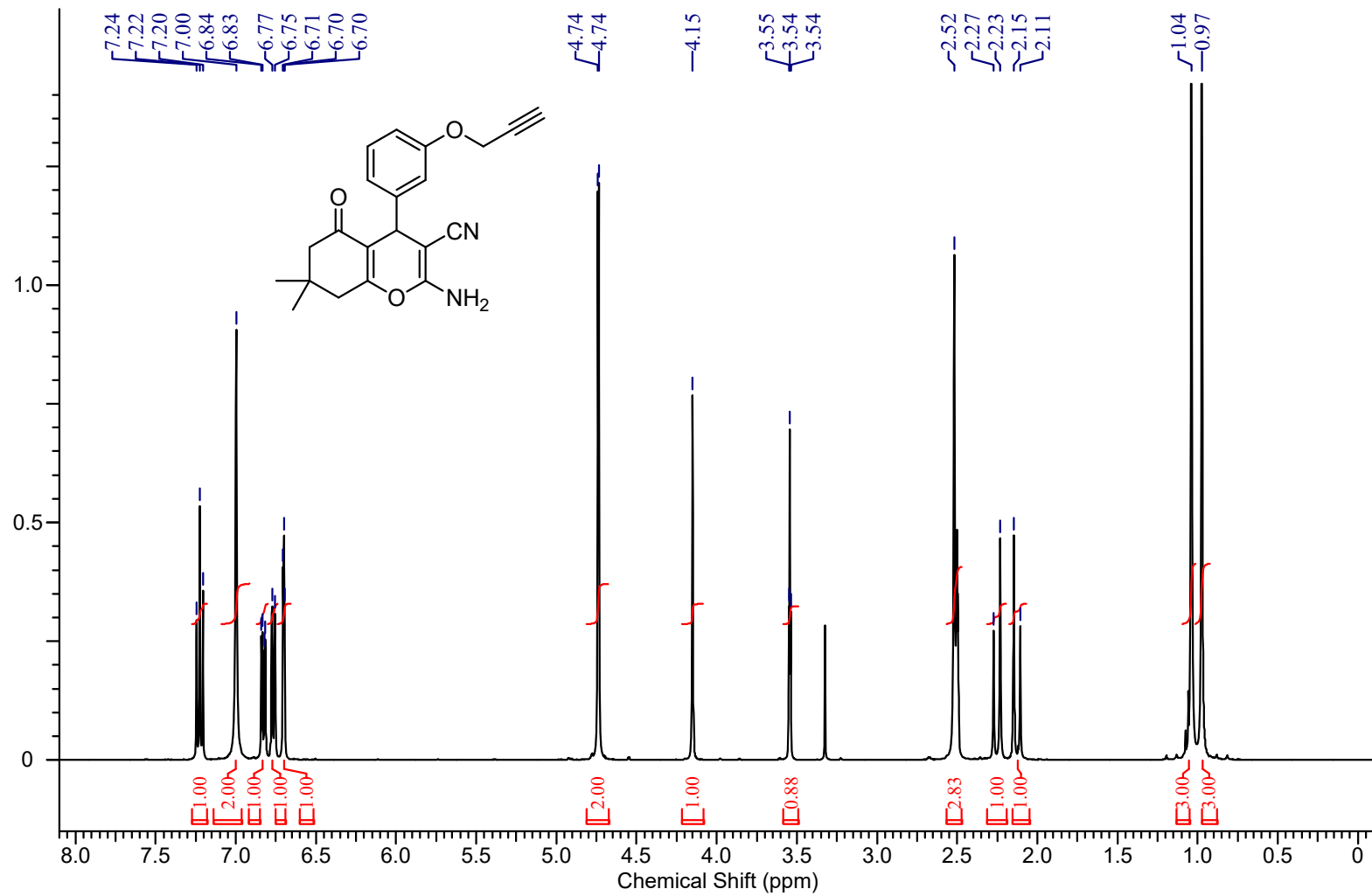


Figure S9: ¹H-NMR (400 MHz, DMSO-d₆) of 6a.

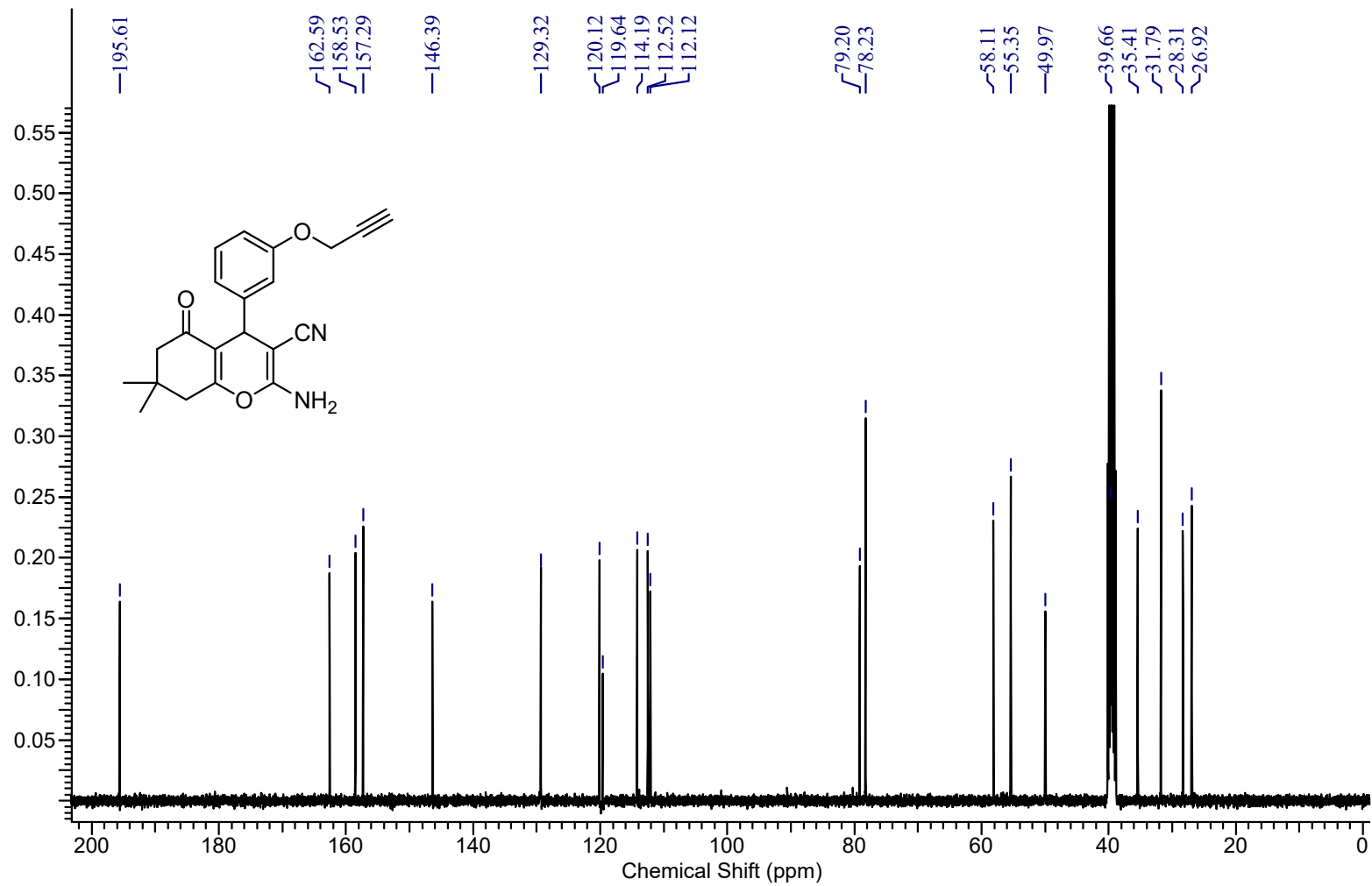


Figure S10: ^{13}C -NMR (100 MHz, DMSO-d_6) of 6a.

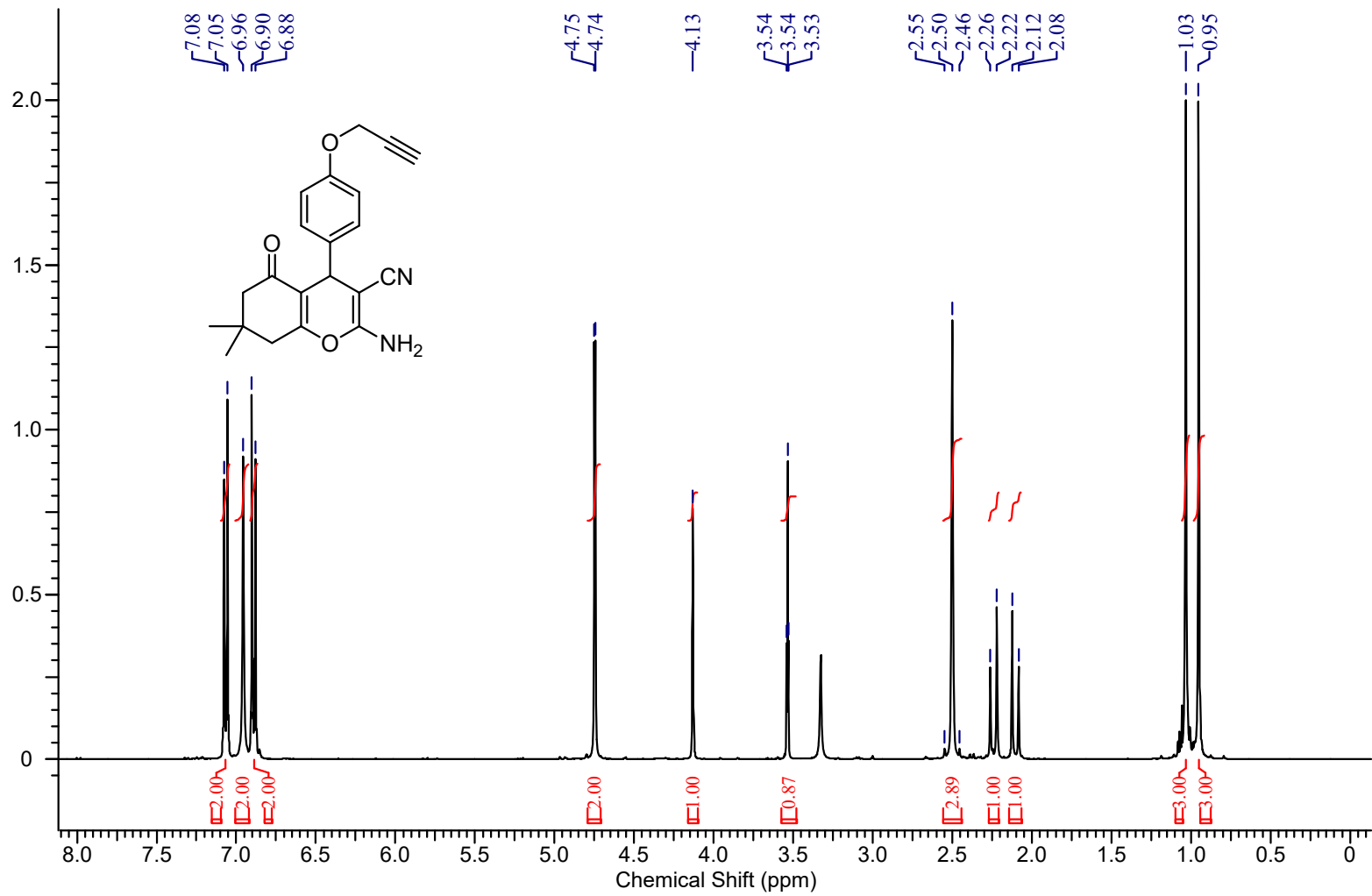


Figure S11: $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) of 6b.

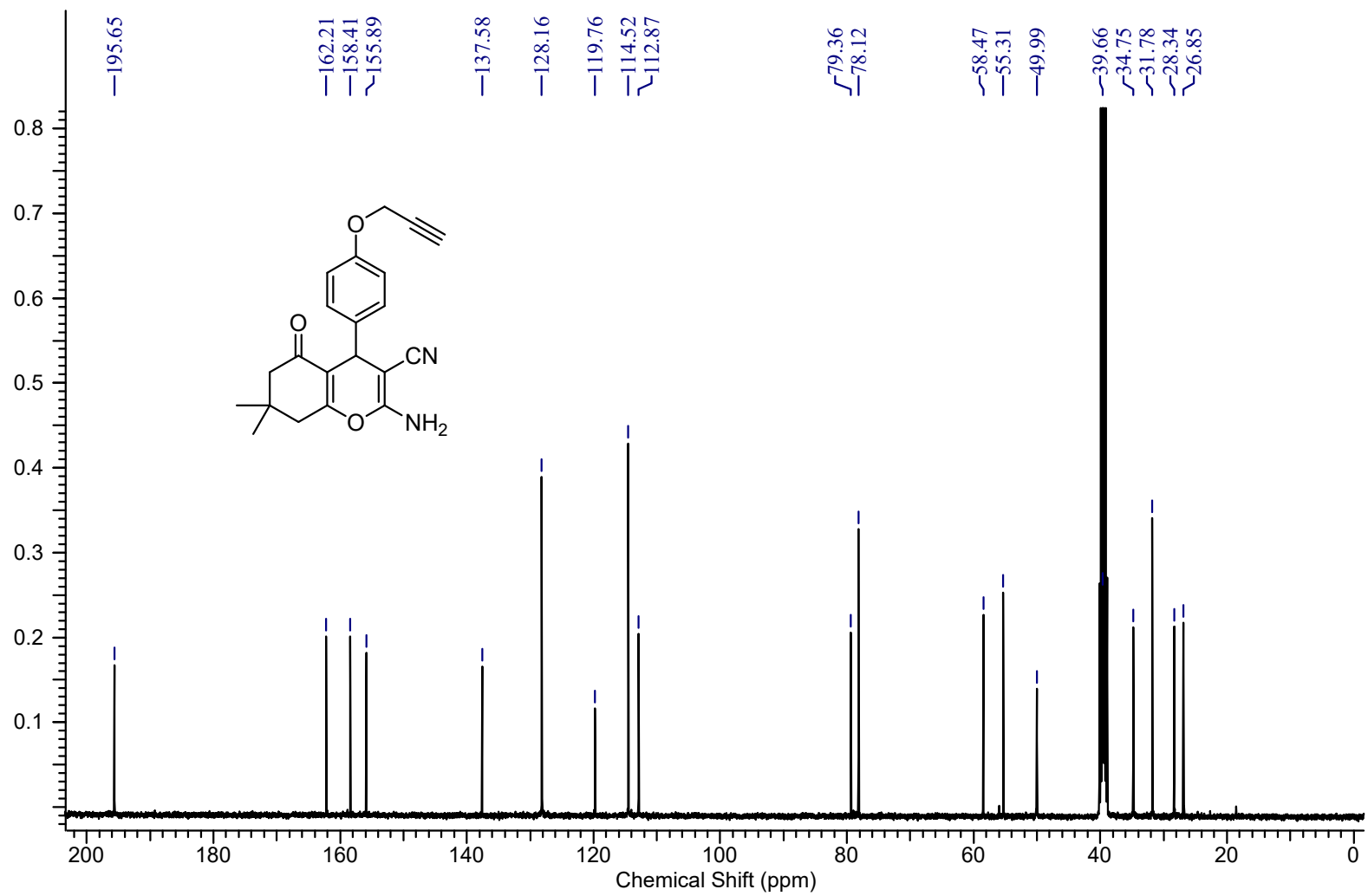


Figure S12: ¹³C-NMR (100 MHz, DMSO-d₆) of 6b.

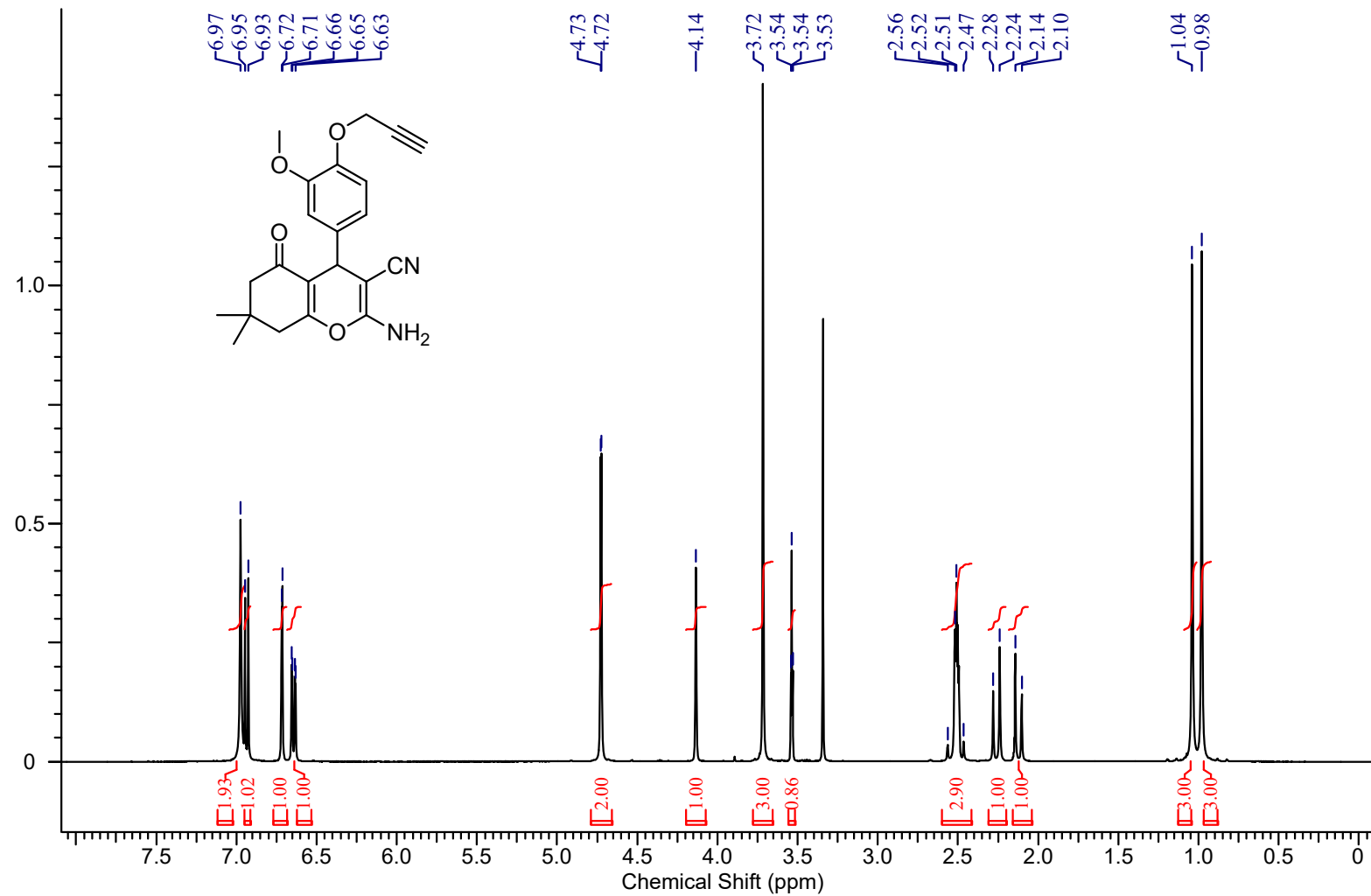


Figure S13: ¹H-NMR (400 MHz, DMSO-d₆) of 6c.

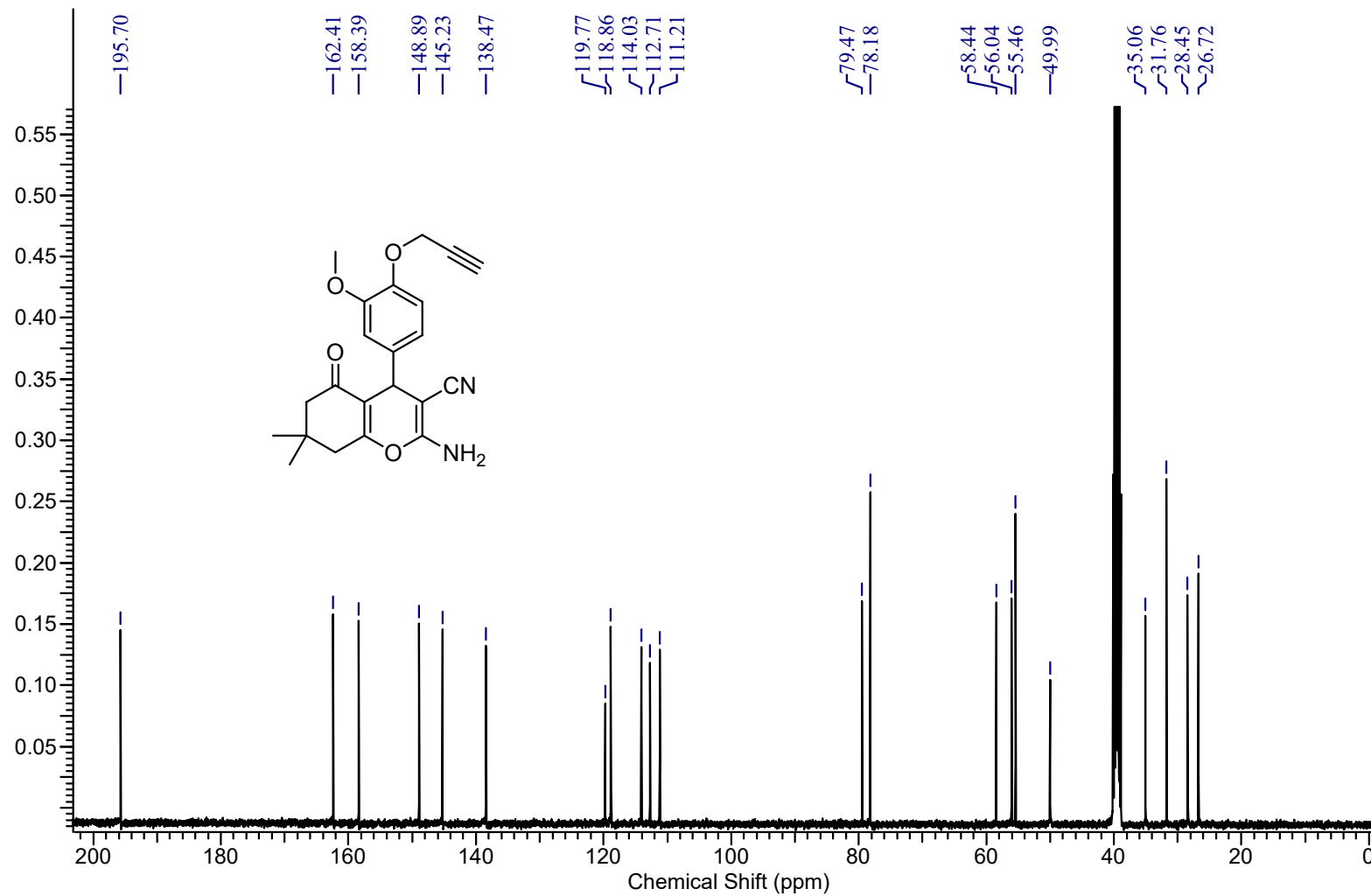


Figure S14: ^{13}C -NMR (100 MHz, DMSO-d_6) of 6c.

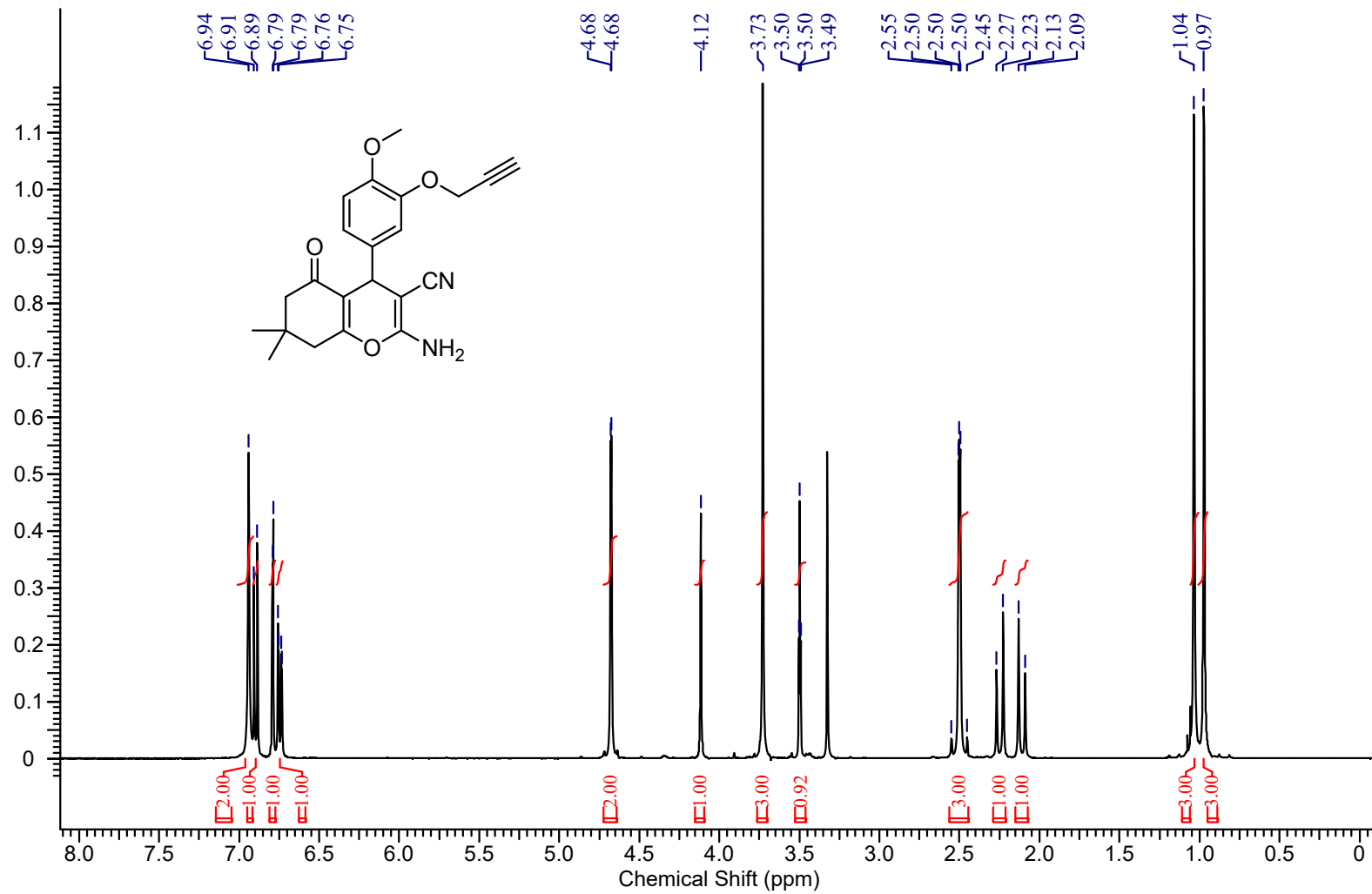


Figure S15: $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) of 6d.

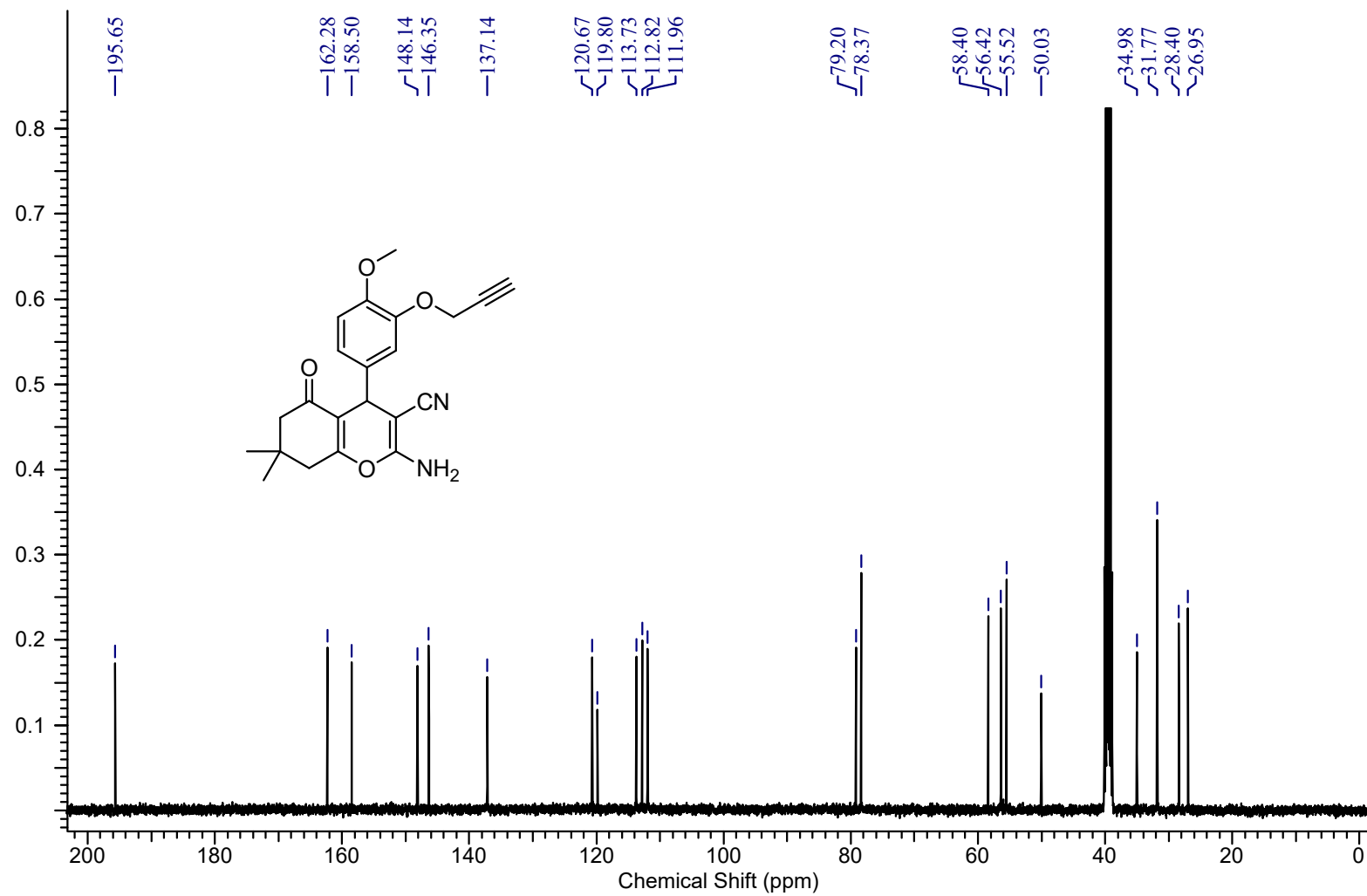


Figure S16: ^{13}C -NMR (100 MHz, DMSO-d_6) of 6d.

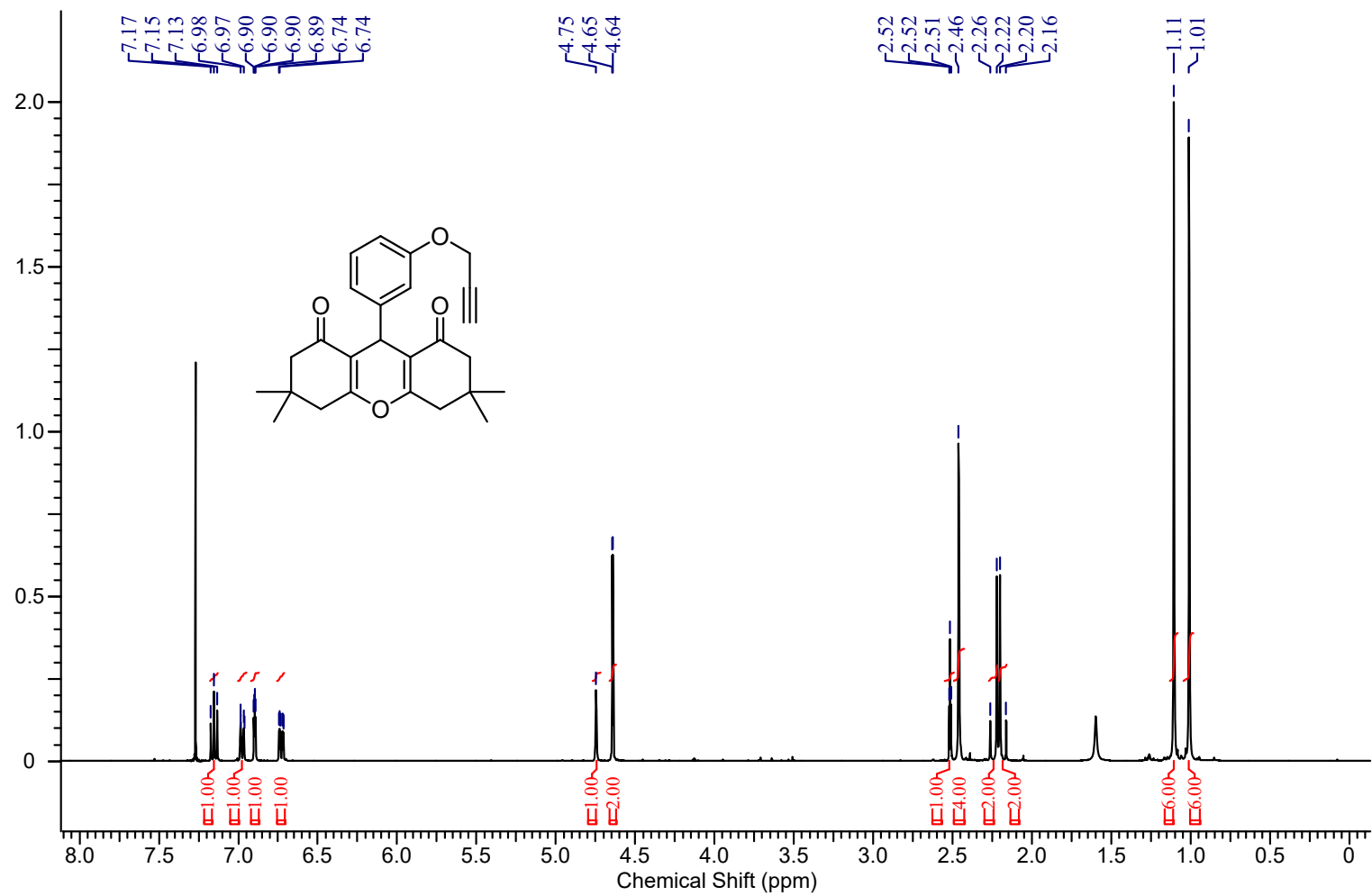


Figure S17: ¹H-NMR (400 MHz, CDCl₃) of 8a.

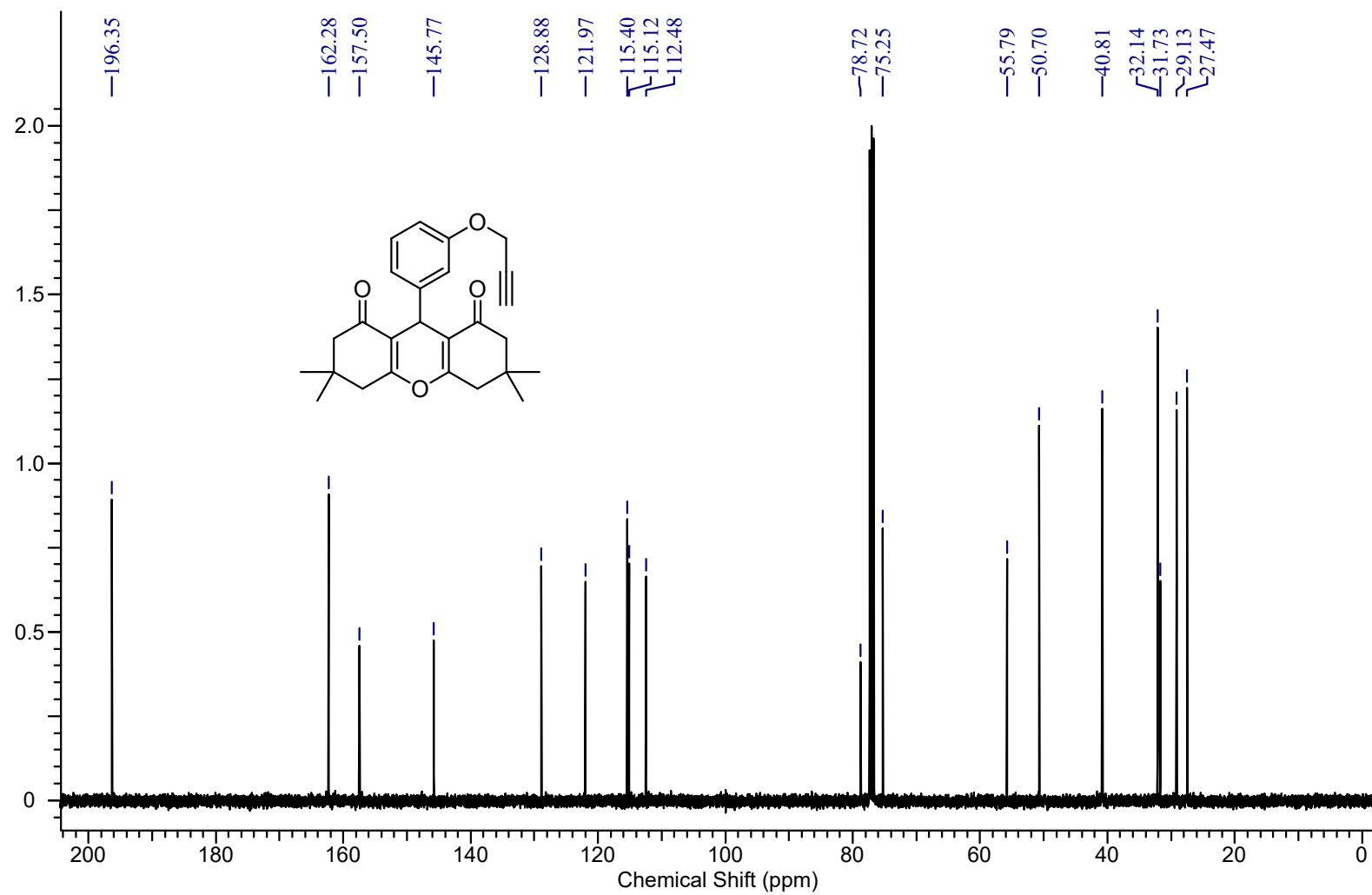


Figure S18: ^{13}C -NMR (100 MHz, CDCl_3) of 8a.

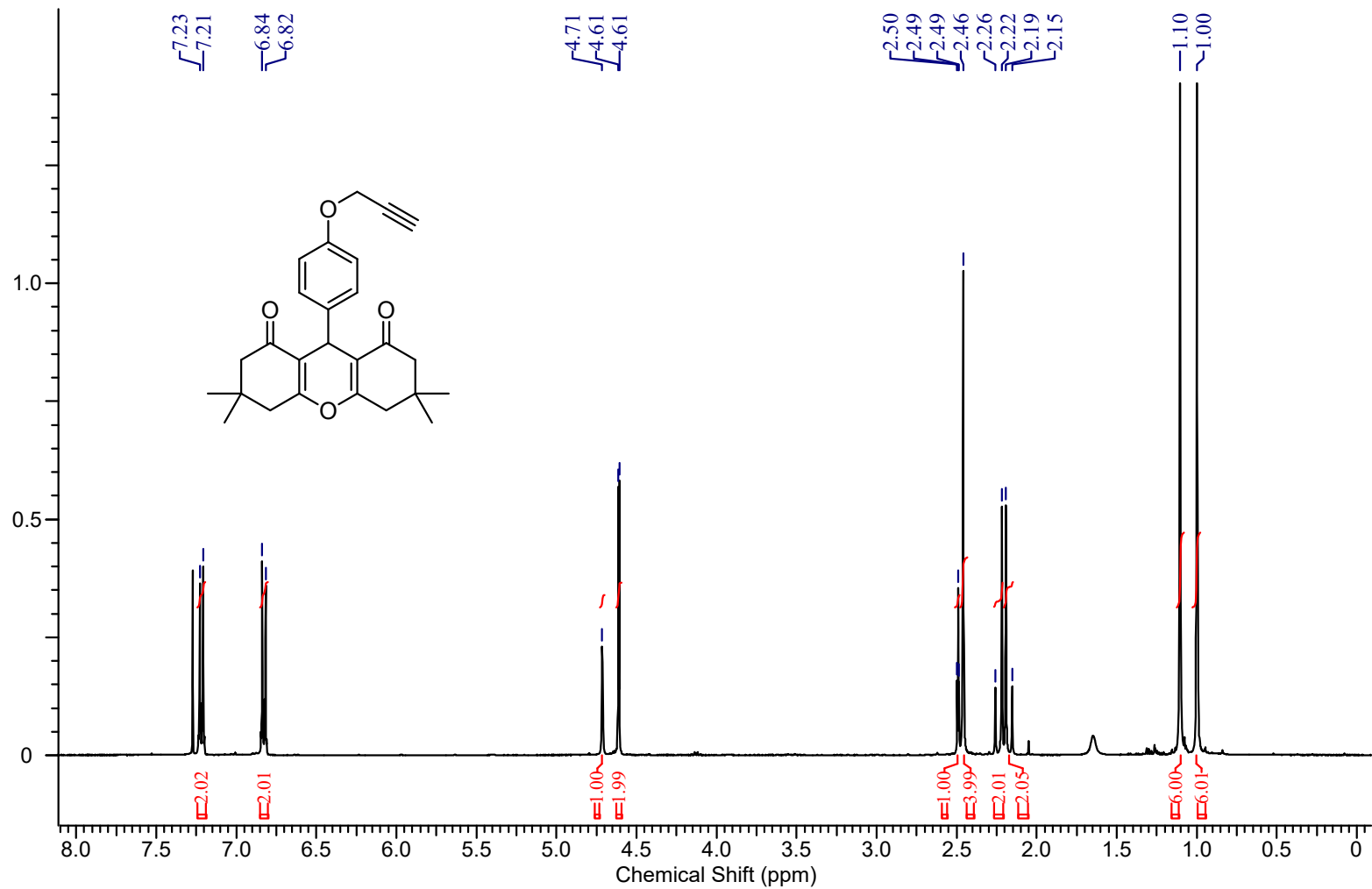


Figure S19: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 8b.

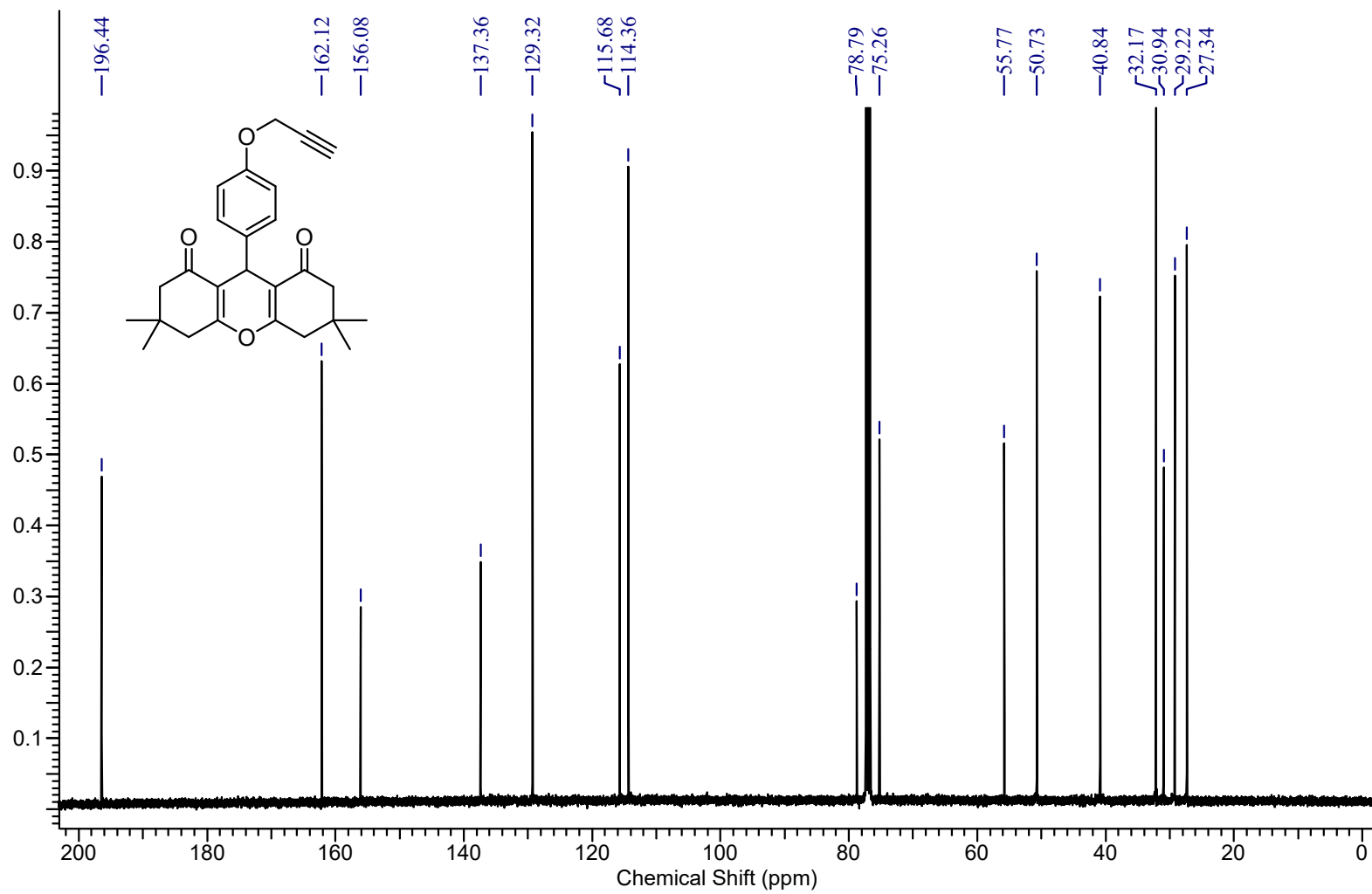


Figure S20: ^{13}C -NMR (100 MHz, CDCl_3) of 8b.

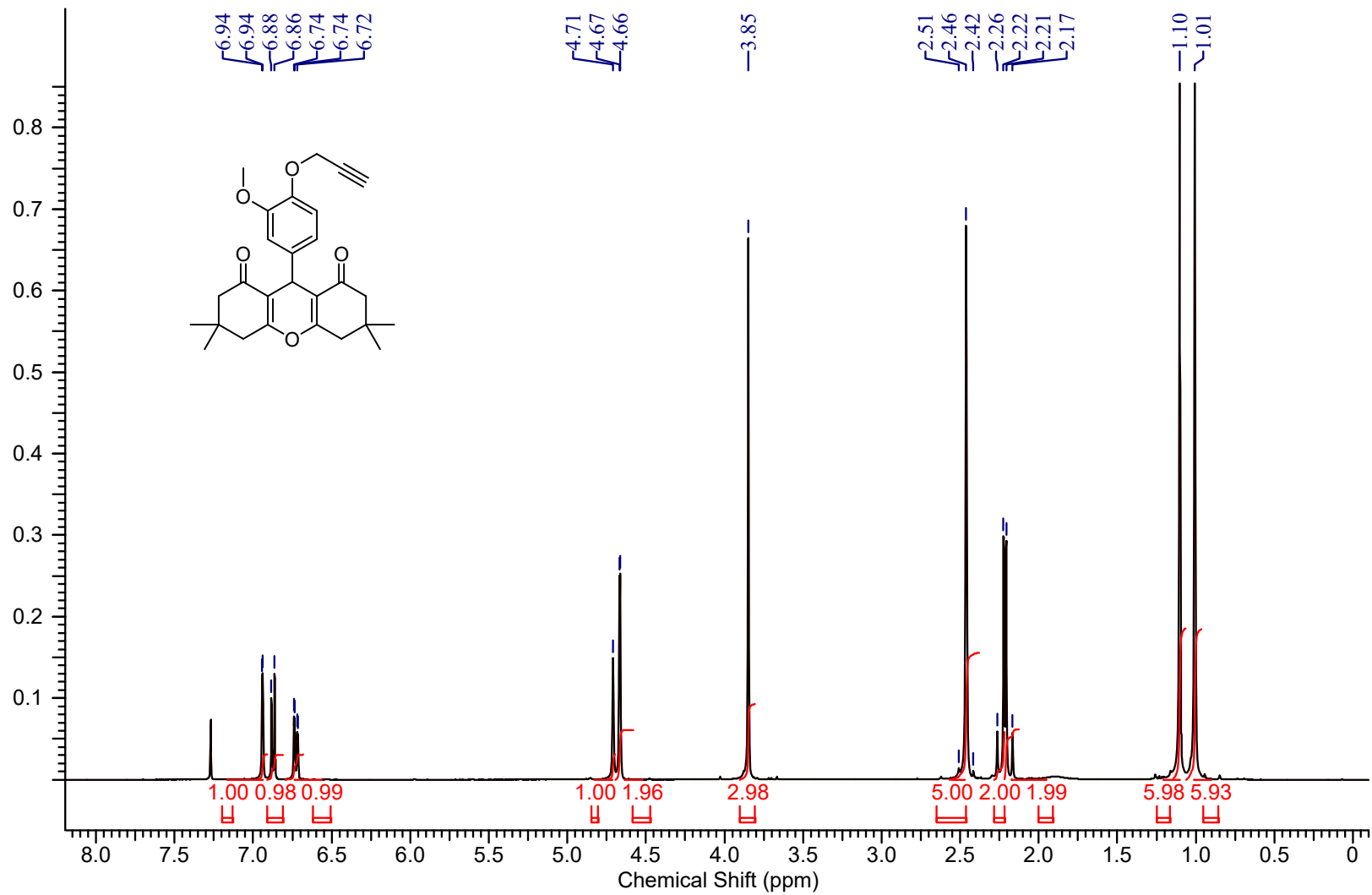


Figure S21: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 8c.

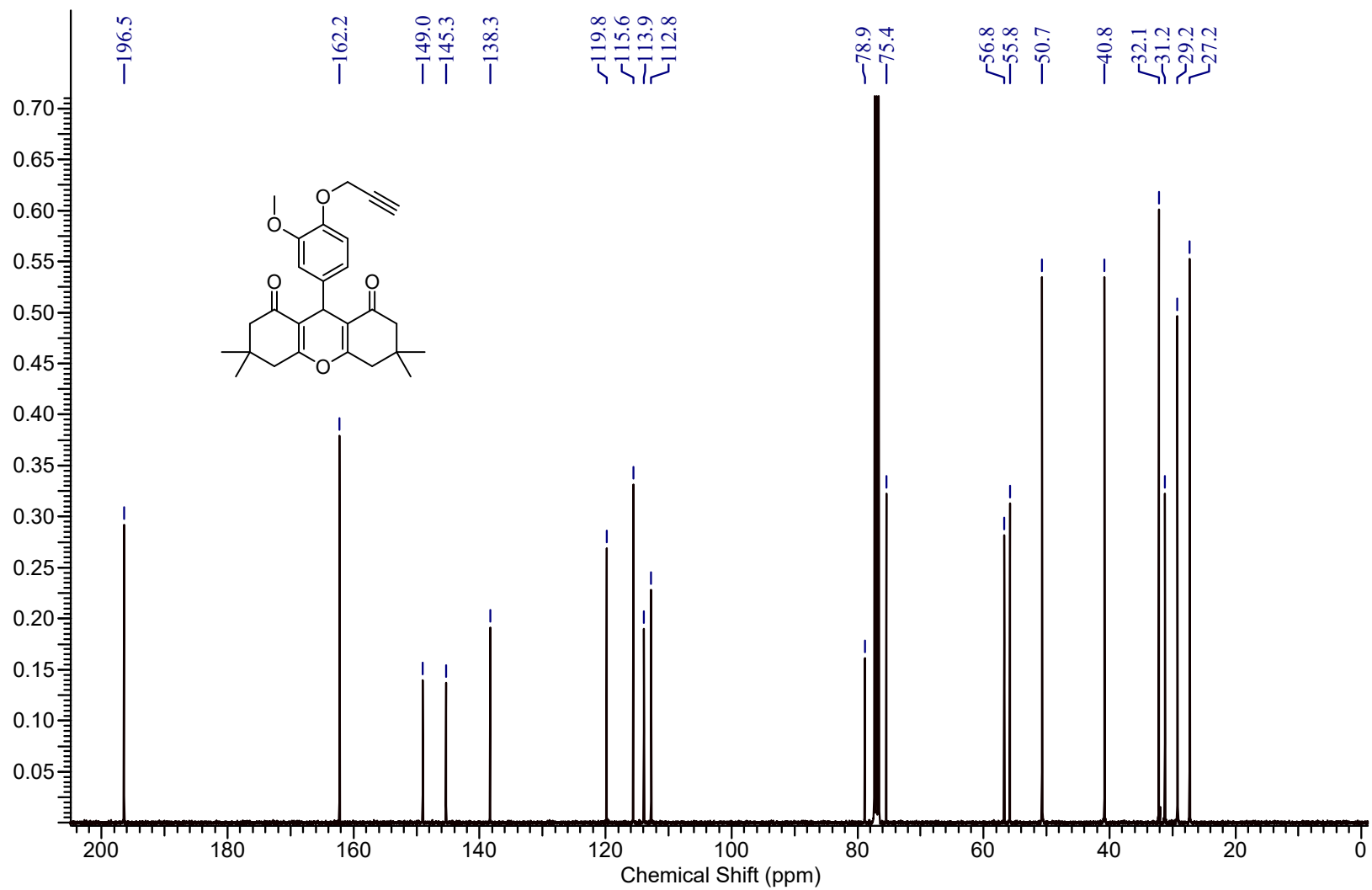


Figure S22: ^{13}C -NMR (100 MHz, CDCl_3) of 8c.

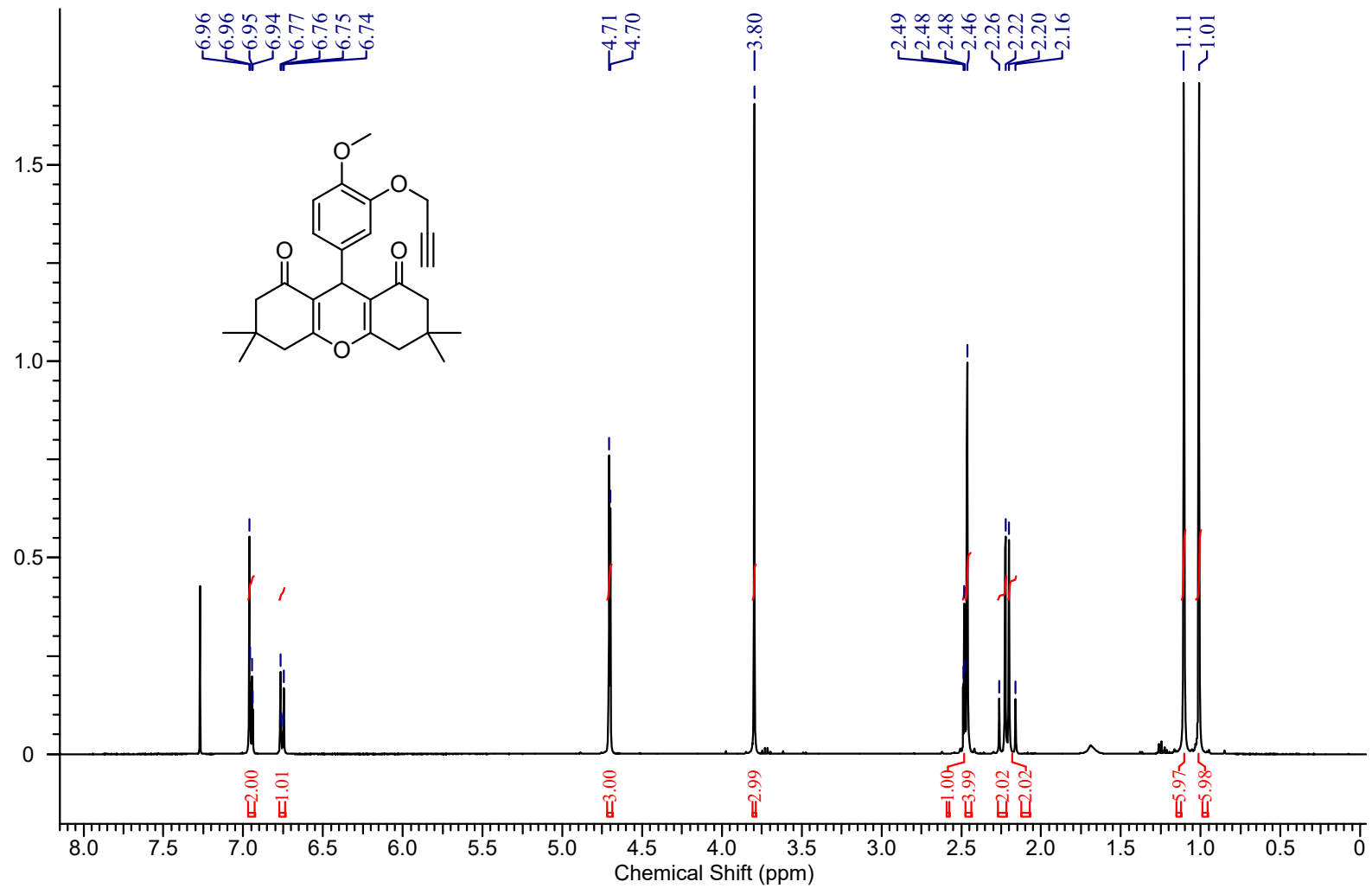


Figure S23: ¹H-NMR (400 MHz, CDCl₃) of 8d.

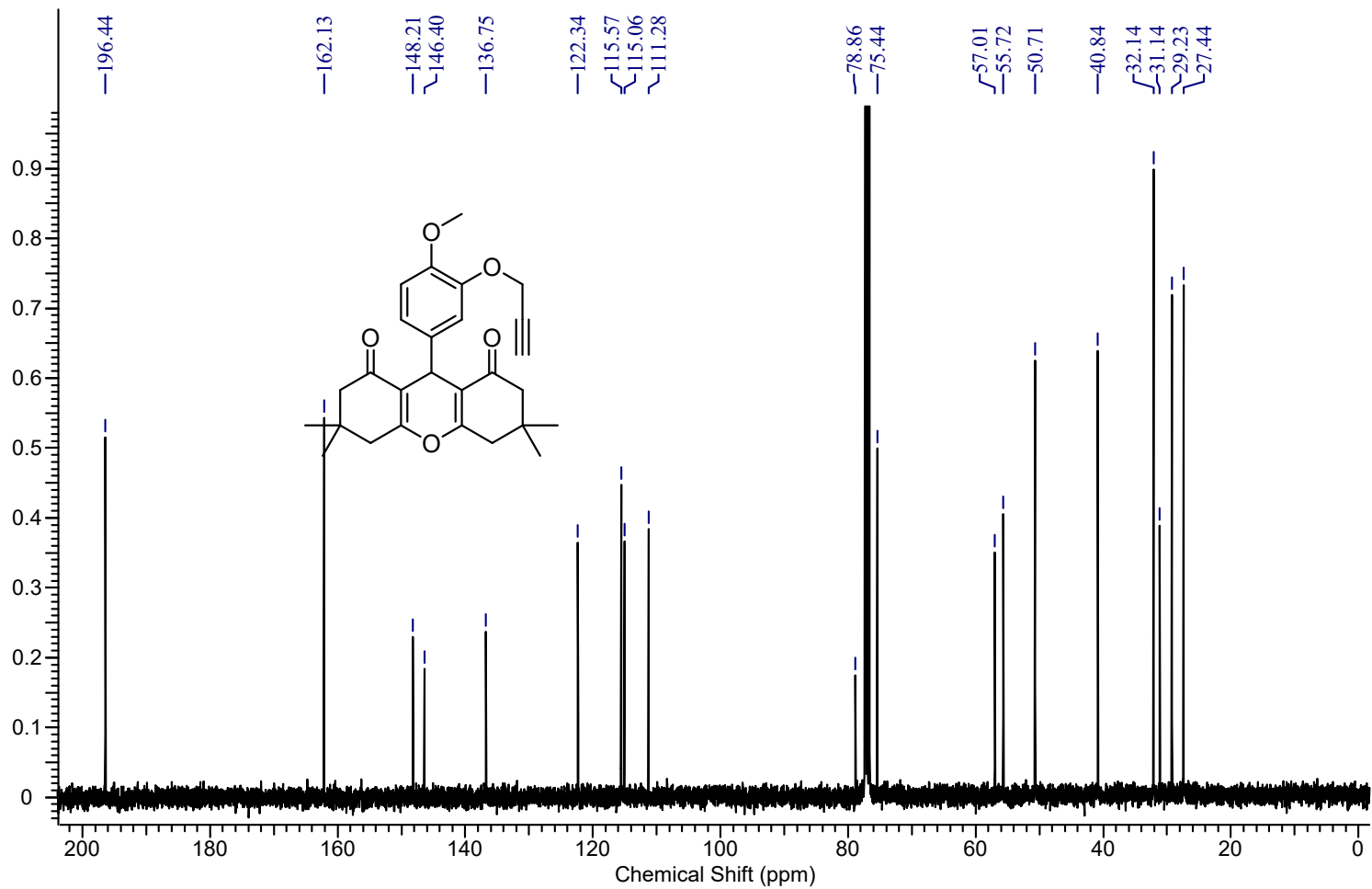


Figure S24: ^{13}C -NMR (100 MHz, CDCl_3) of 8d.

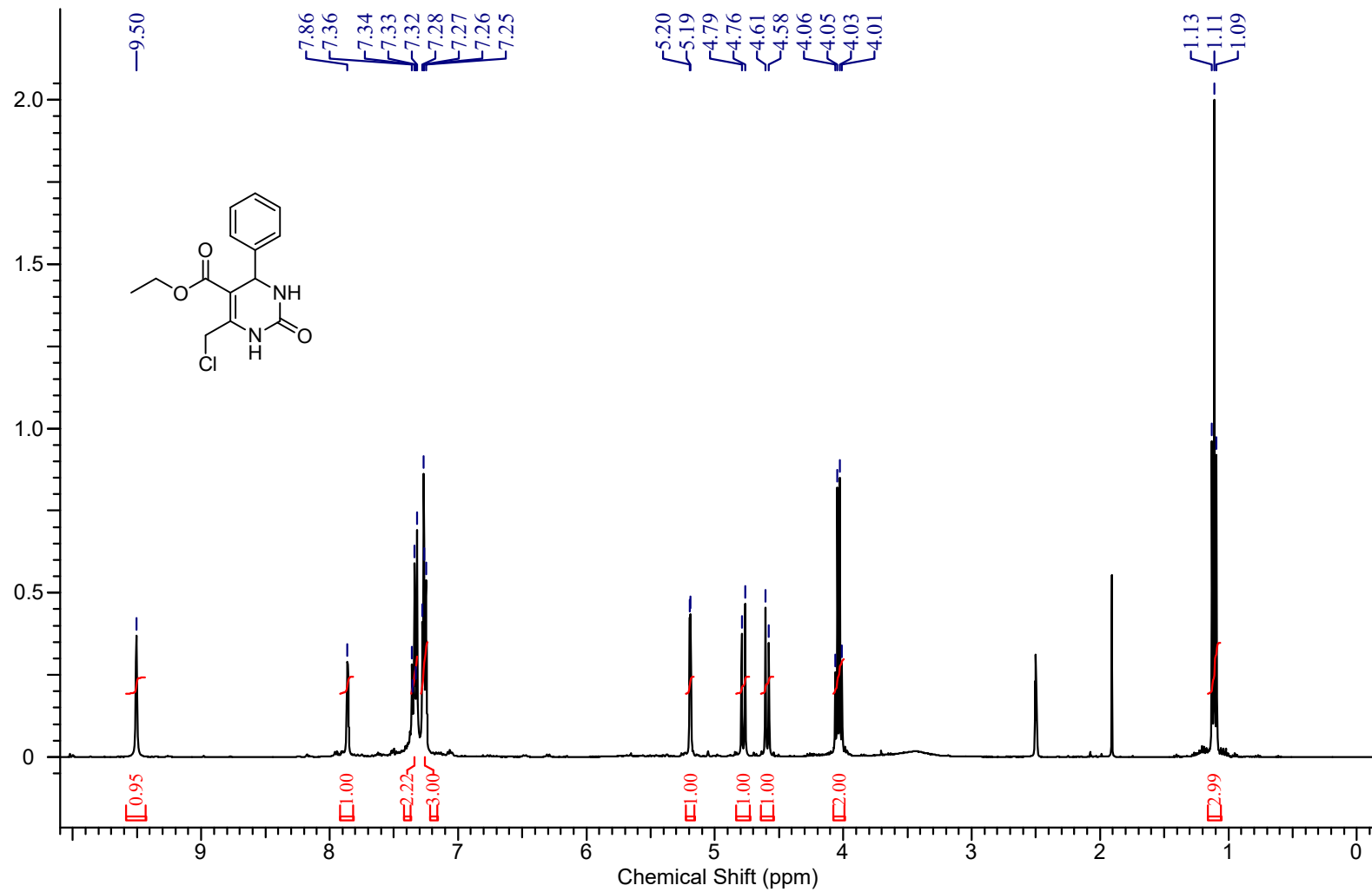


Figure S25: ¹H-NMR (400 MHz, DMSO-d₆) of 12a.

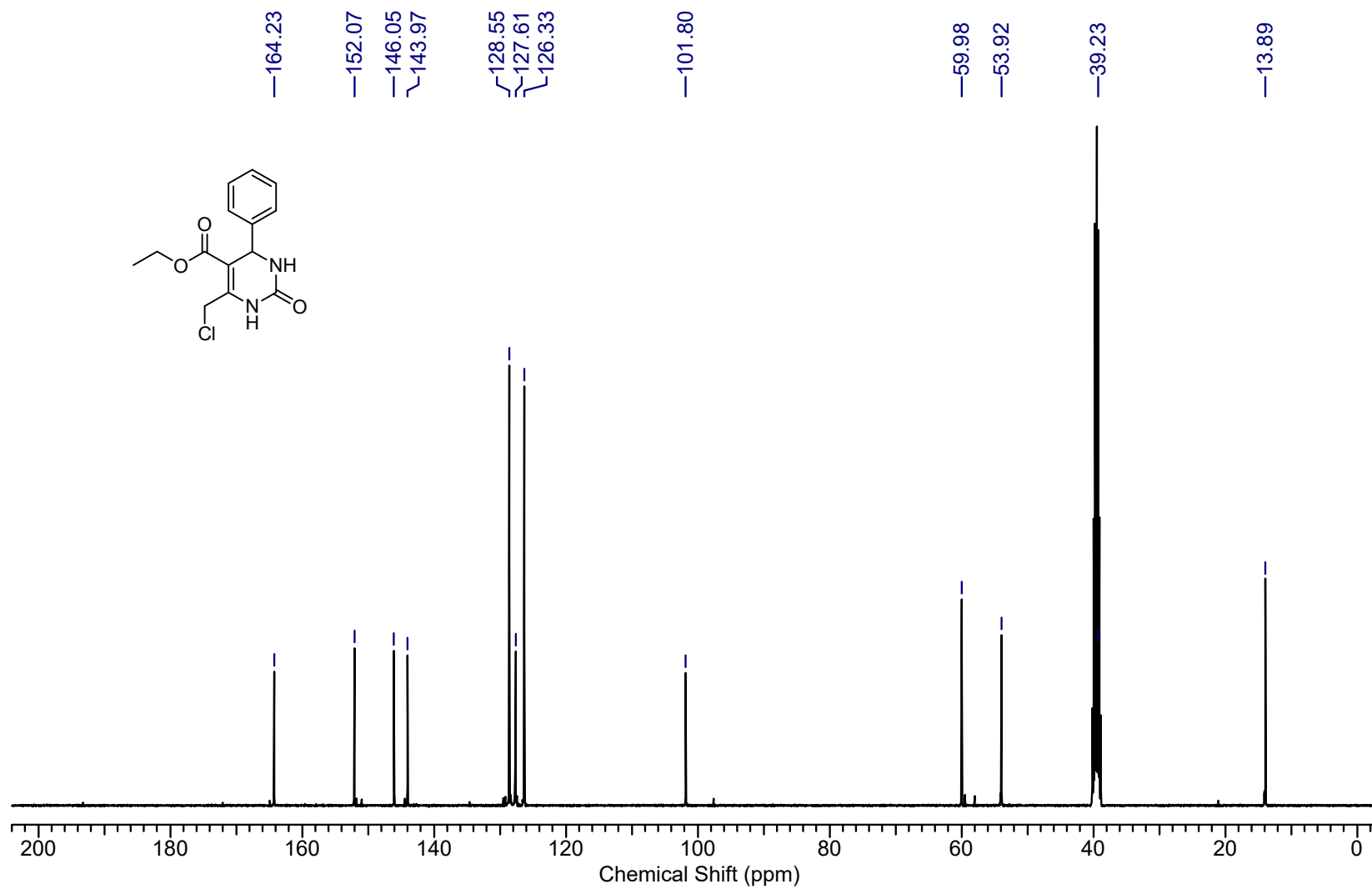


Figure S26: ^{13}C -NMR (100 MHz, DMSO-d_6) of 12a.

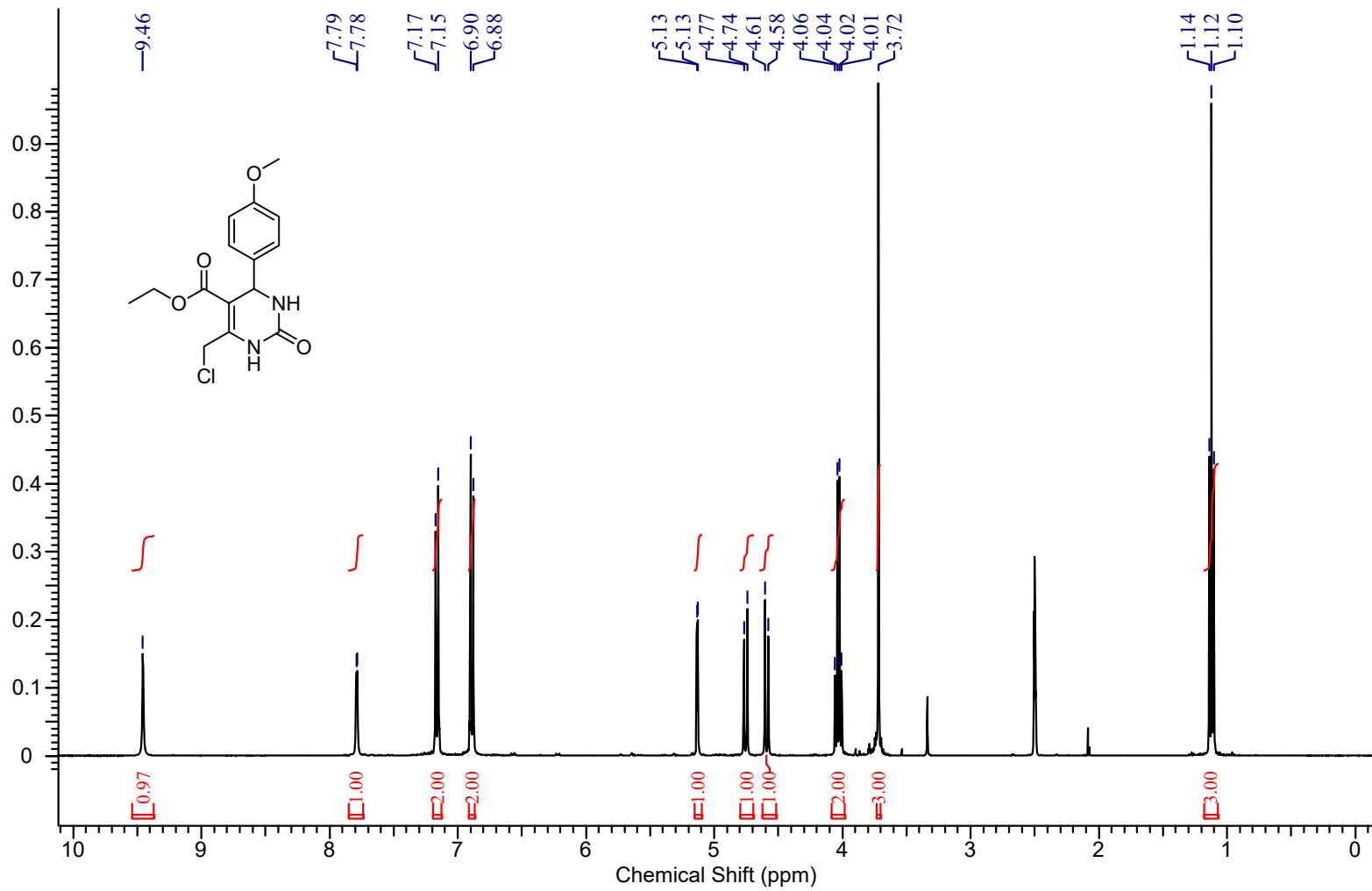


Figure S27: $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) of 12b.

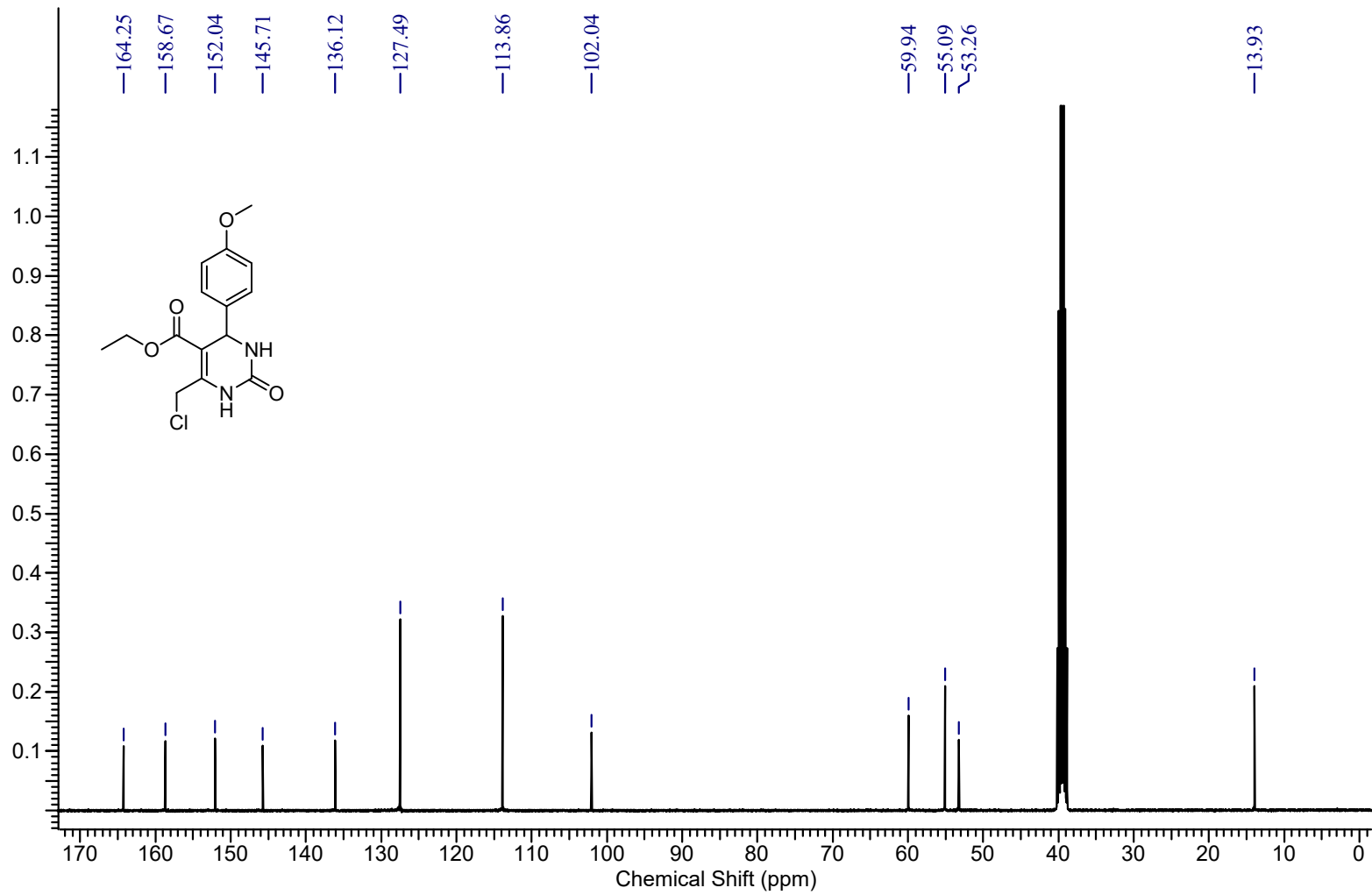


Figure S28: ^{13}C -NMR (100 MHz, DMSO-d_6) of 12b.

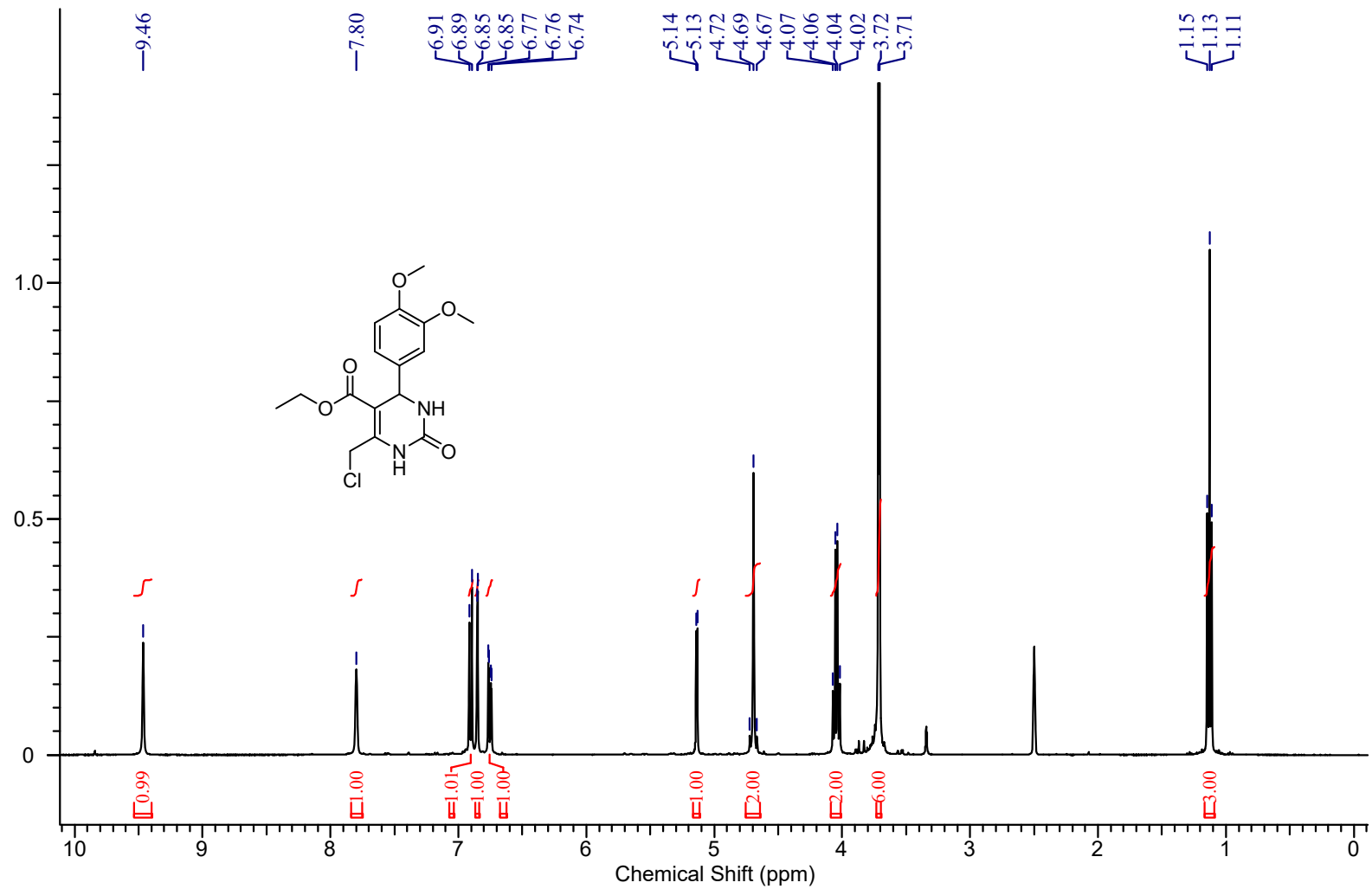


Figure S29: ¹H-NMR (400 MHz, DMSO-d₆) of 12c.

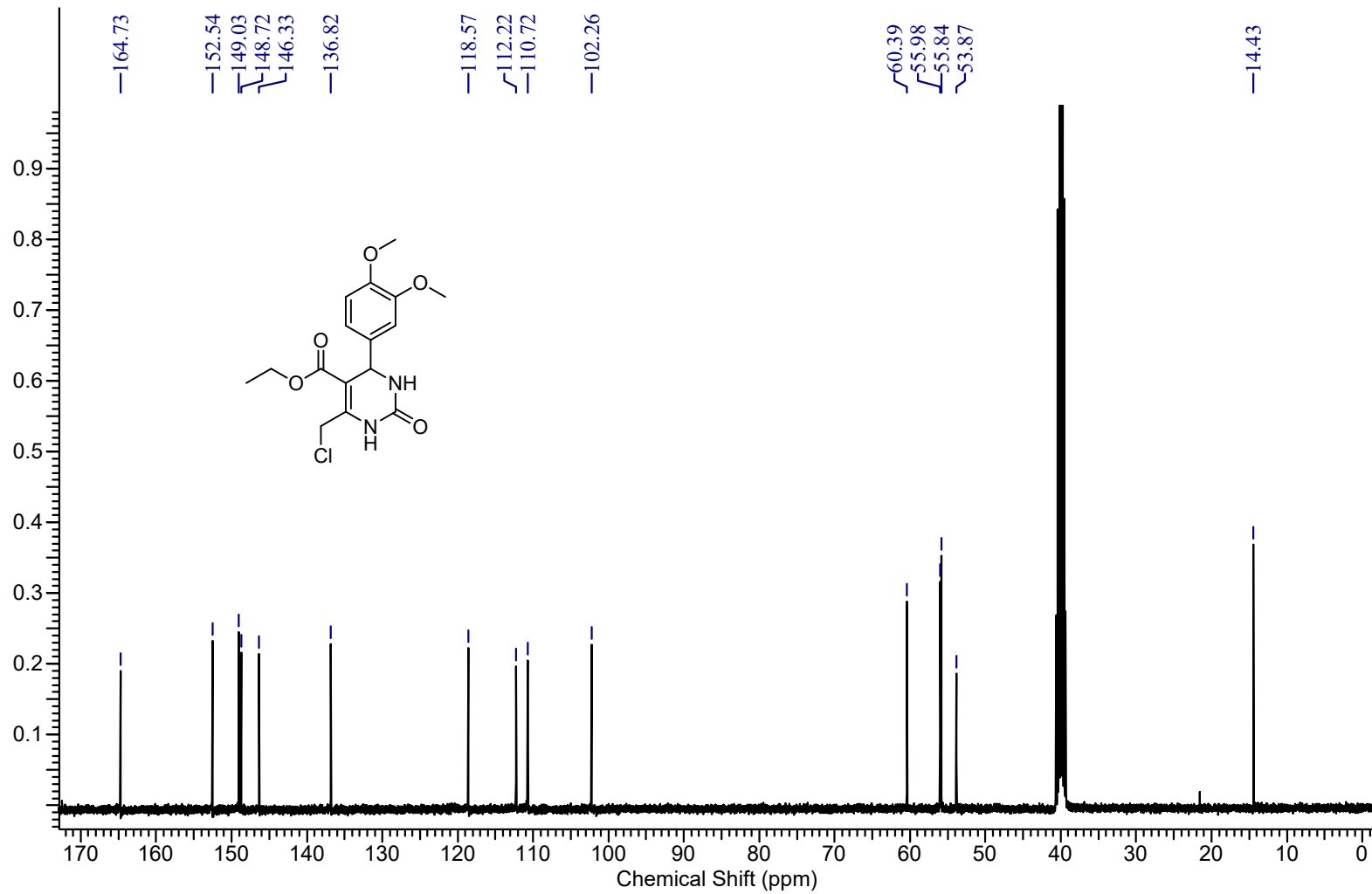


Figure S30: ^{13}C -NMR (100 MHz, DMSO-d_6) of 12c.

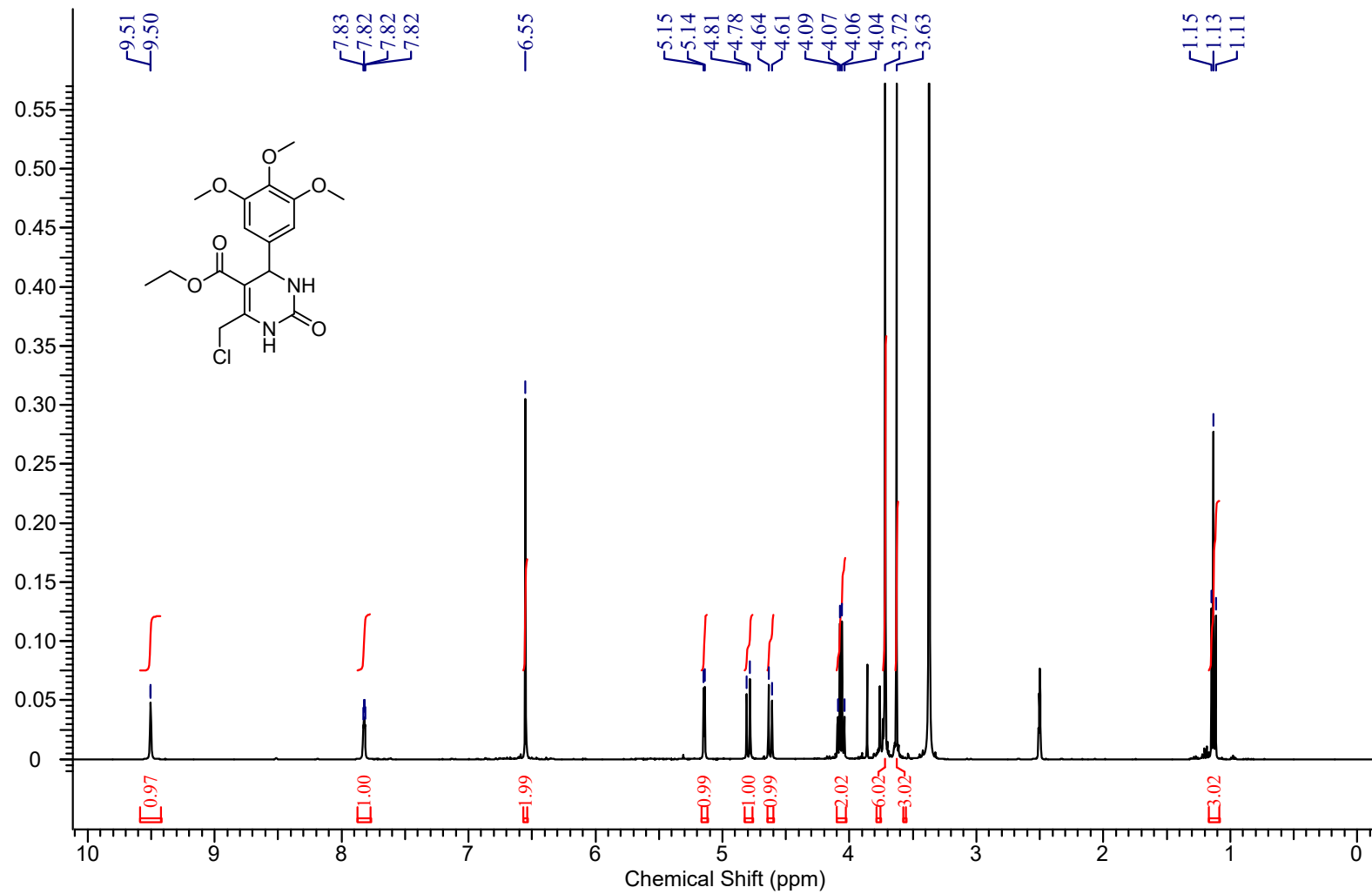


Figure S31: ¹H-NMR (400 MHz, DMSO-d₆) of 12d.

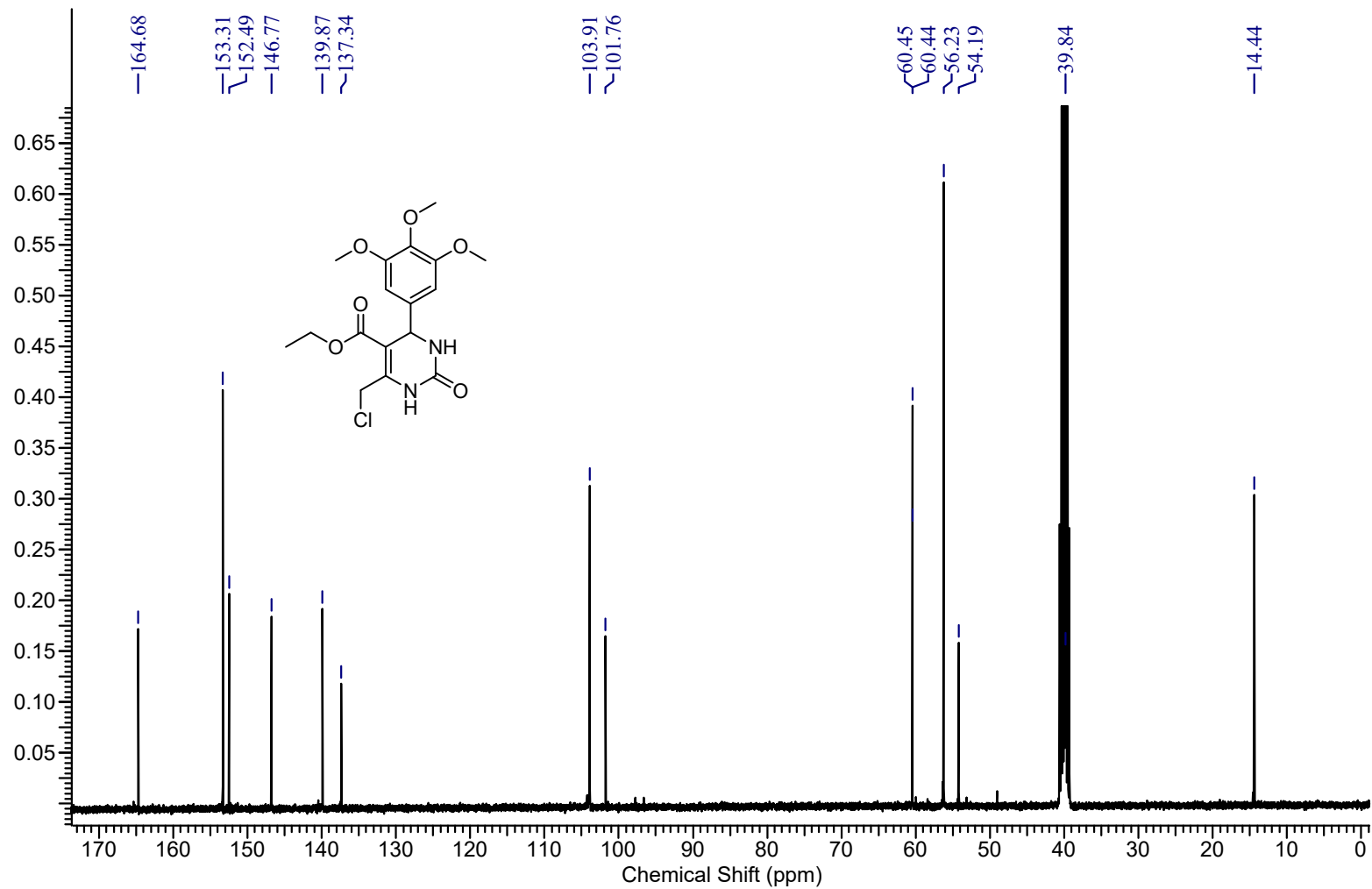


Figure S32: ^{13}C -NMR (100 MHz, DMSO-d_6) of 12d.

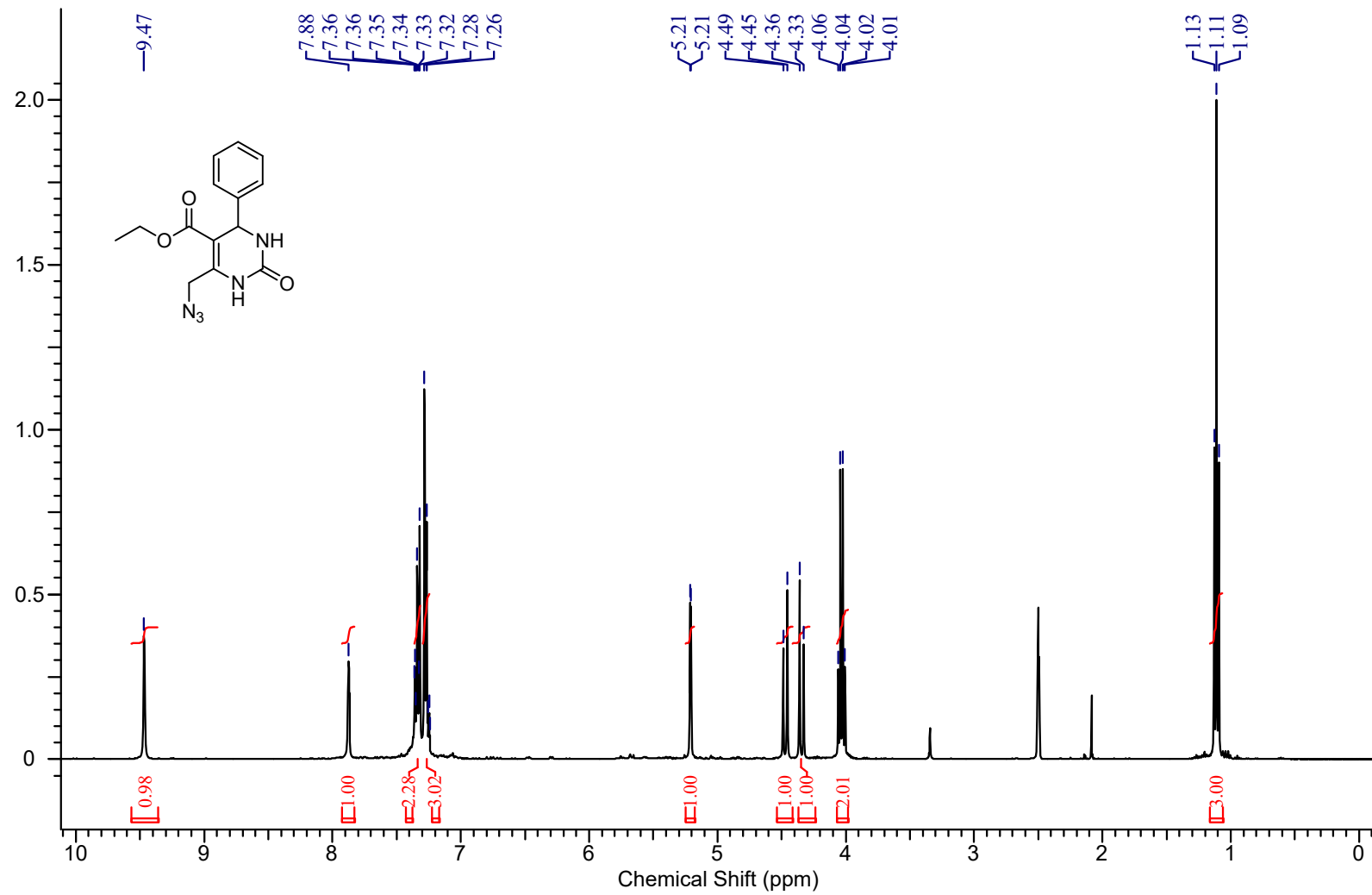


Figure S33: ¹H-NMR (400 MHz, DMSO-d₆) of 14a.

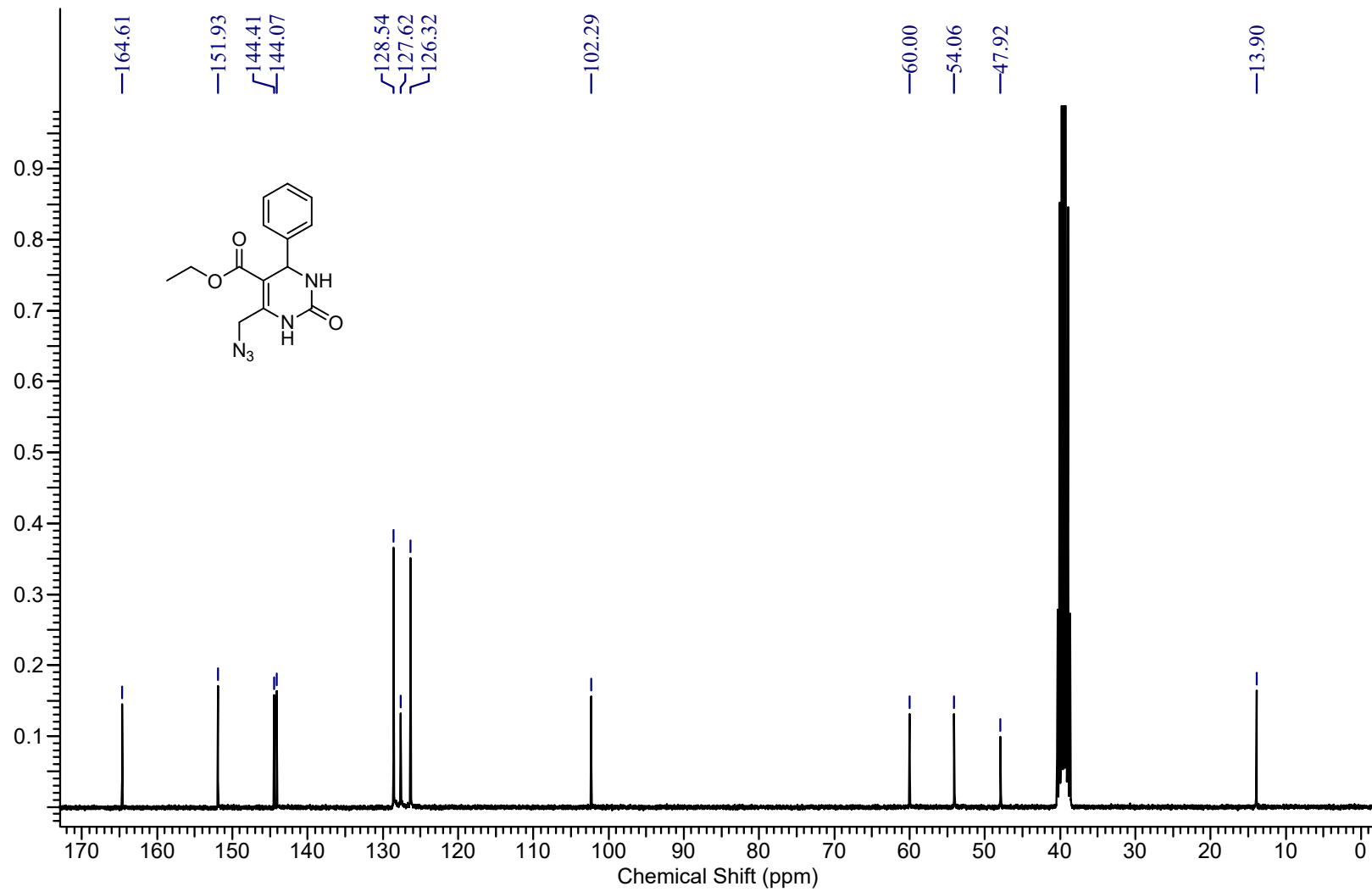


Figure S34: ^{13}C -NMR (100 MHz, DMSO-d_6) of 14a.

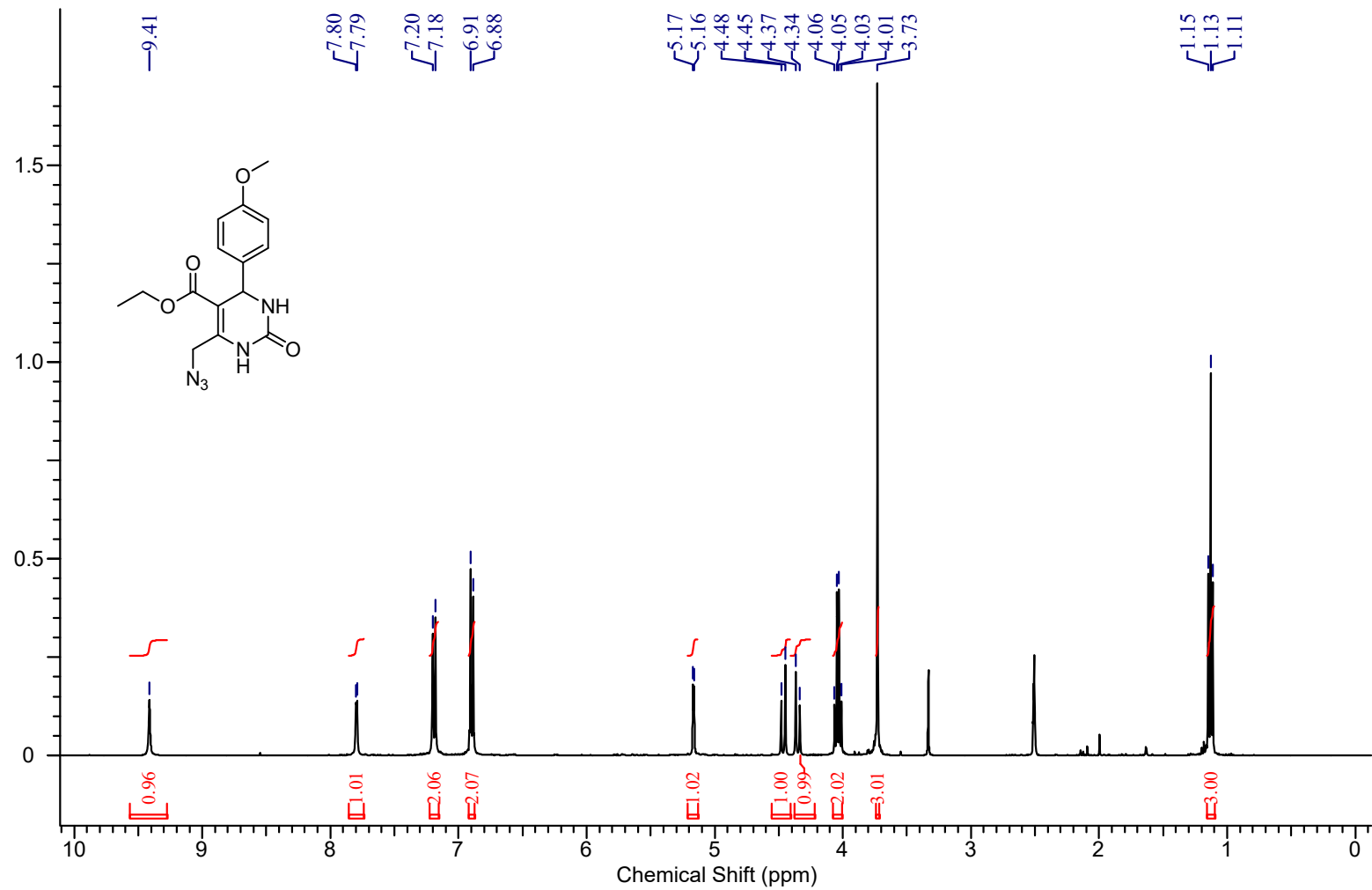


Figure S35: $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) of 14b.

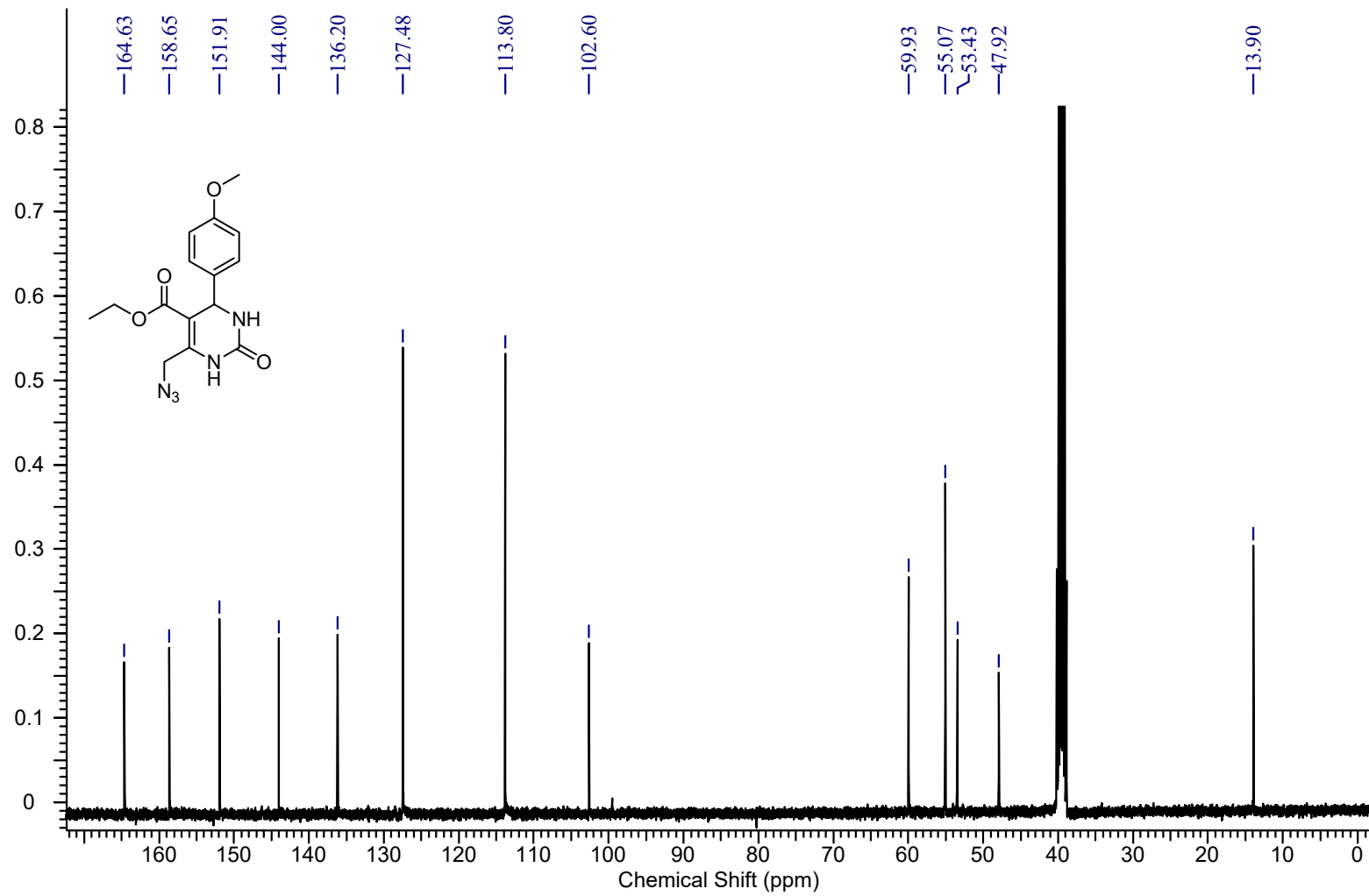


Figure S36: ^{13}C -NMR (100 MHz, DMSO-d_6) of 14b.

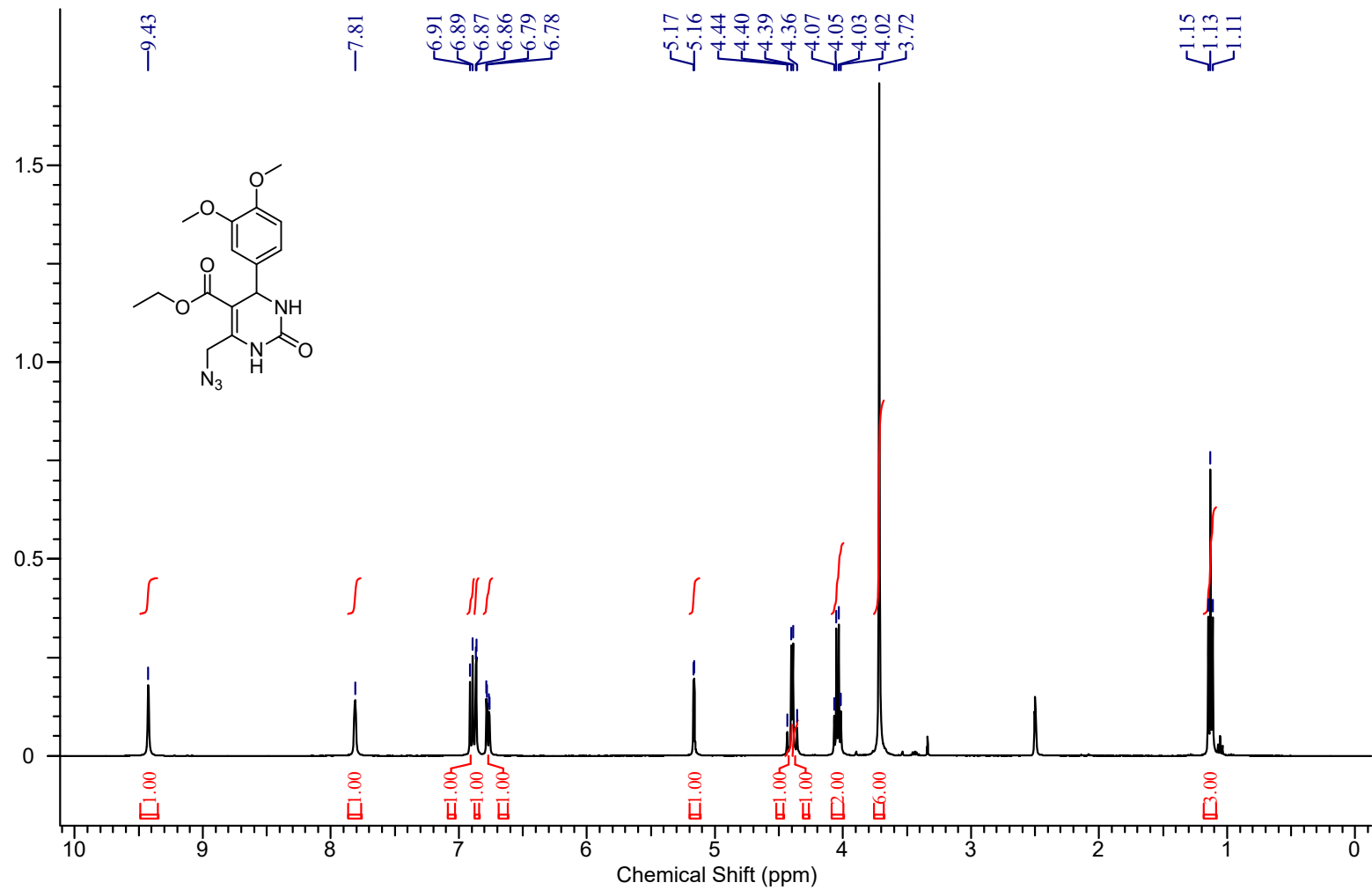


Figure S37: $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) of 14c.

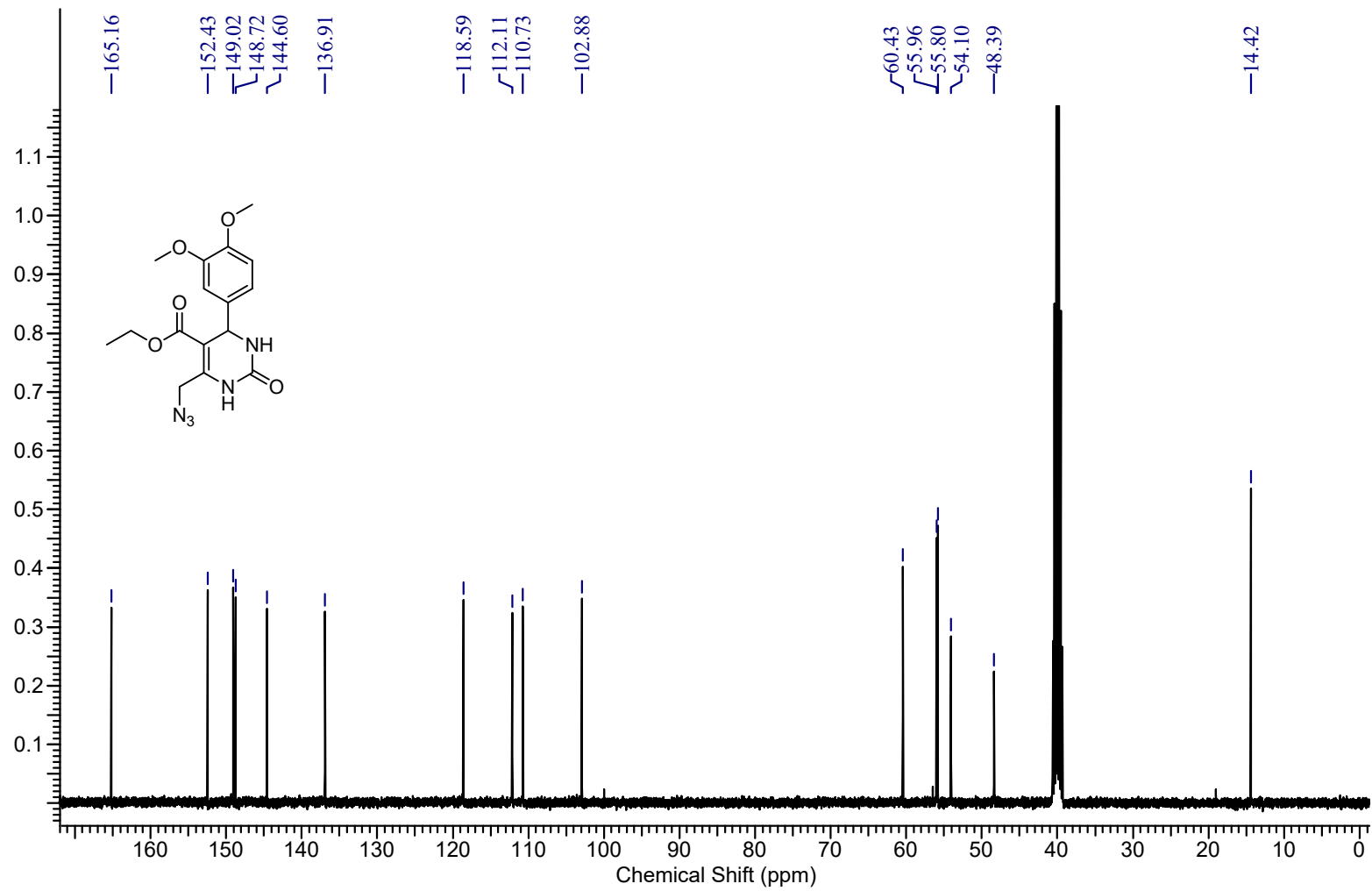


Figure S38: ^{13}C -NMR (100 MHz, DMSO-d_6) of 14c.

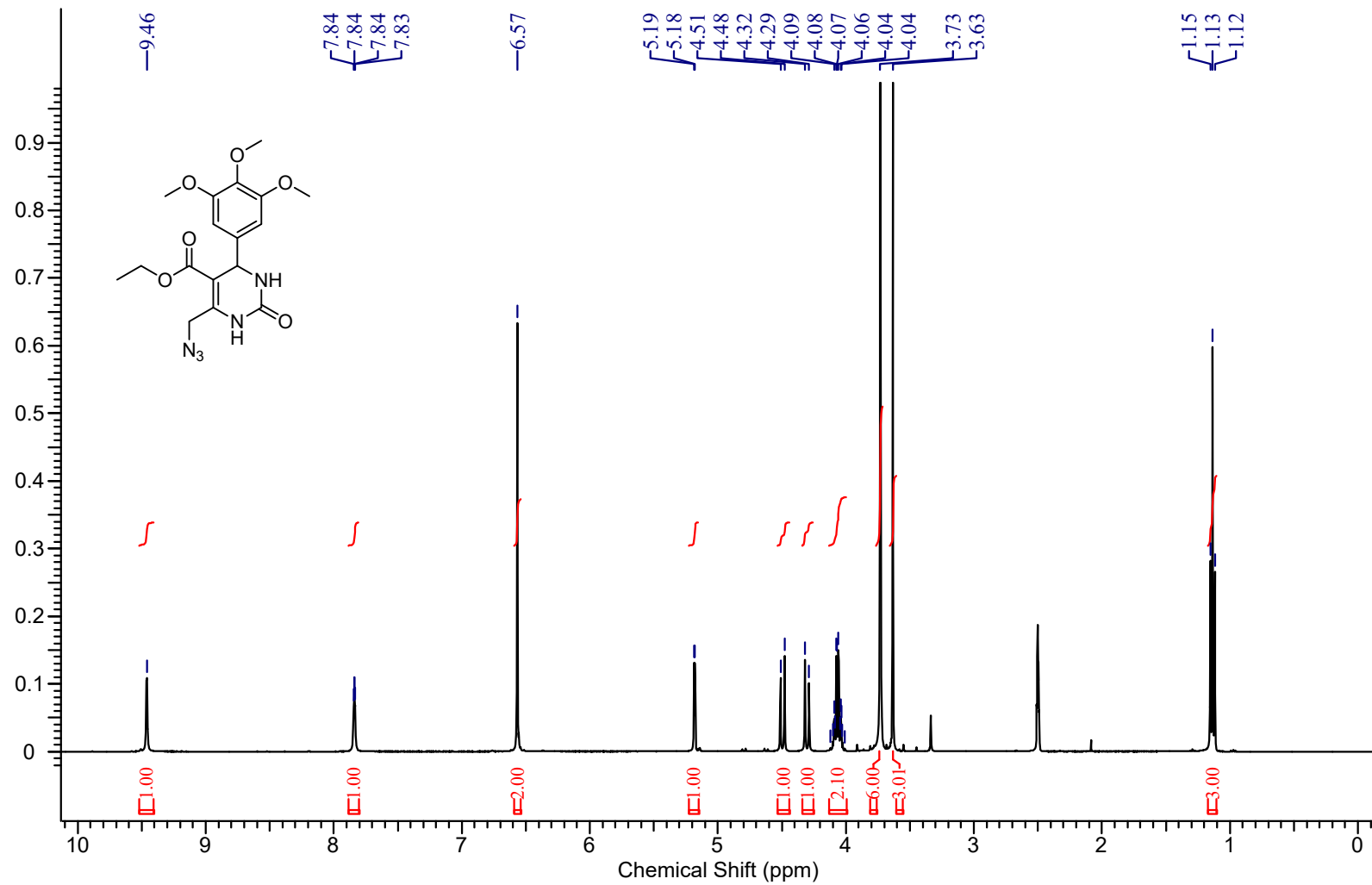


Figure S39: ¹H-NMR (400 MHz, DMSO-d₆) of 14d.

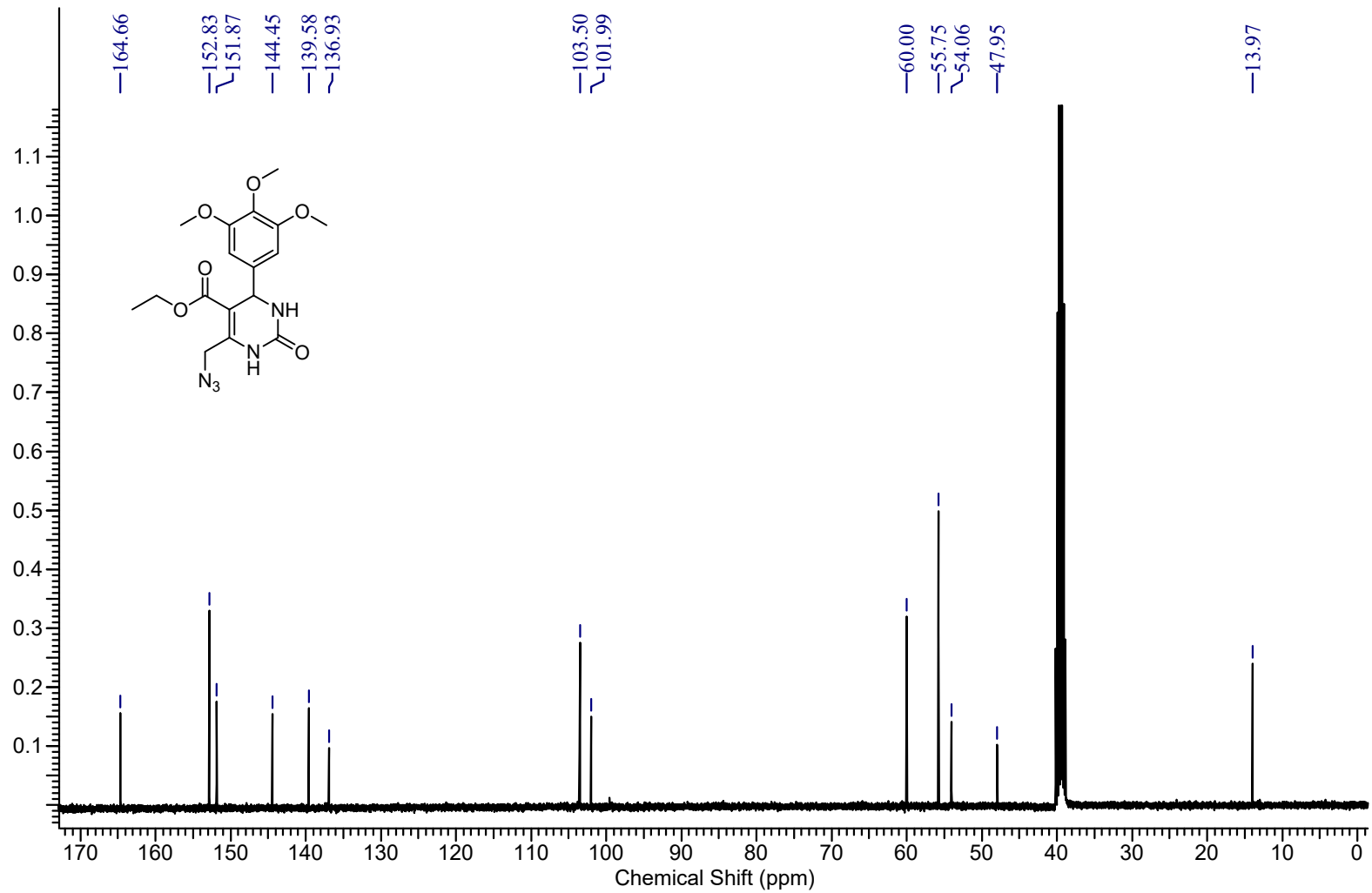


Figure S40: ^{13}C -NMR (100 MHz, DMSO-d_6) of 14d.

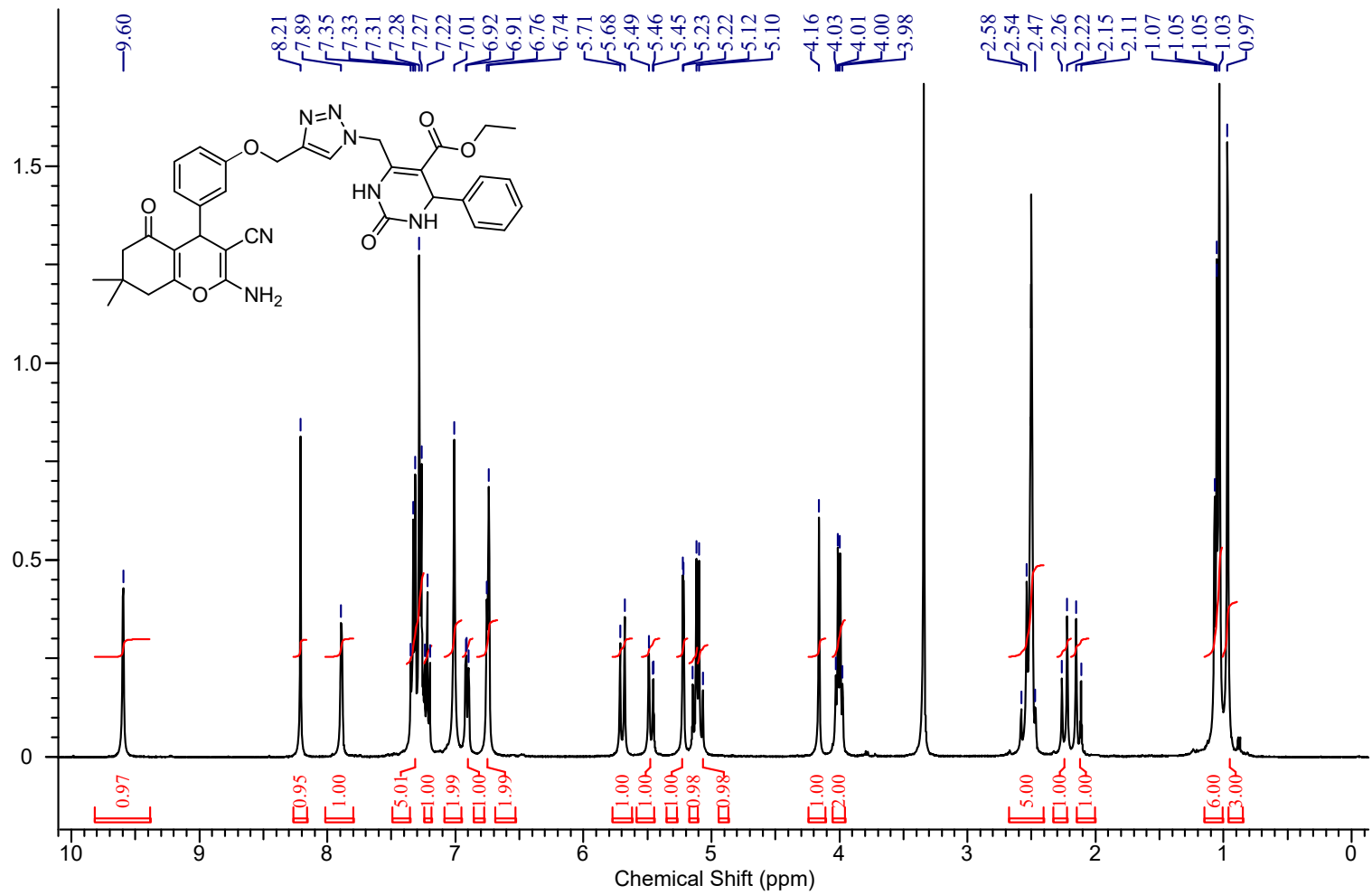


Figure S41: $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) of 15a.

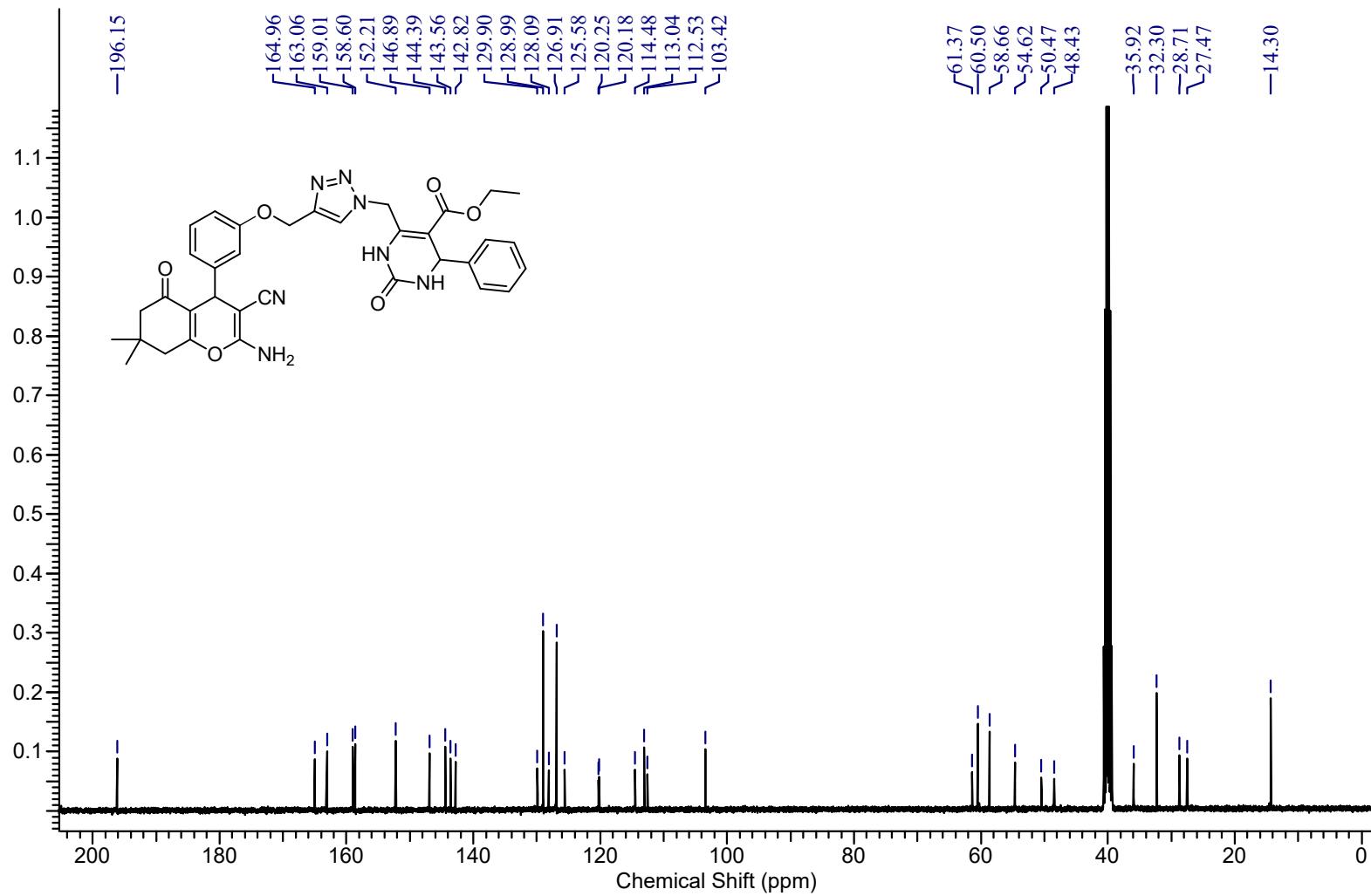


Figure S42: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15a.

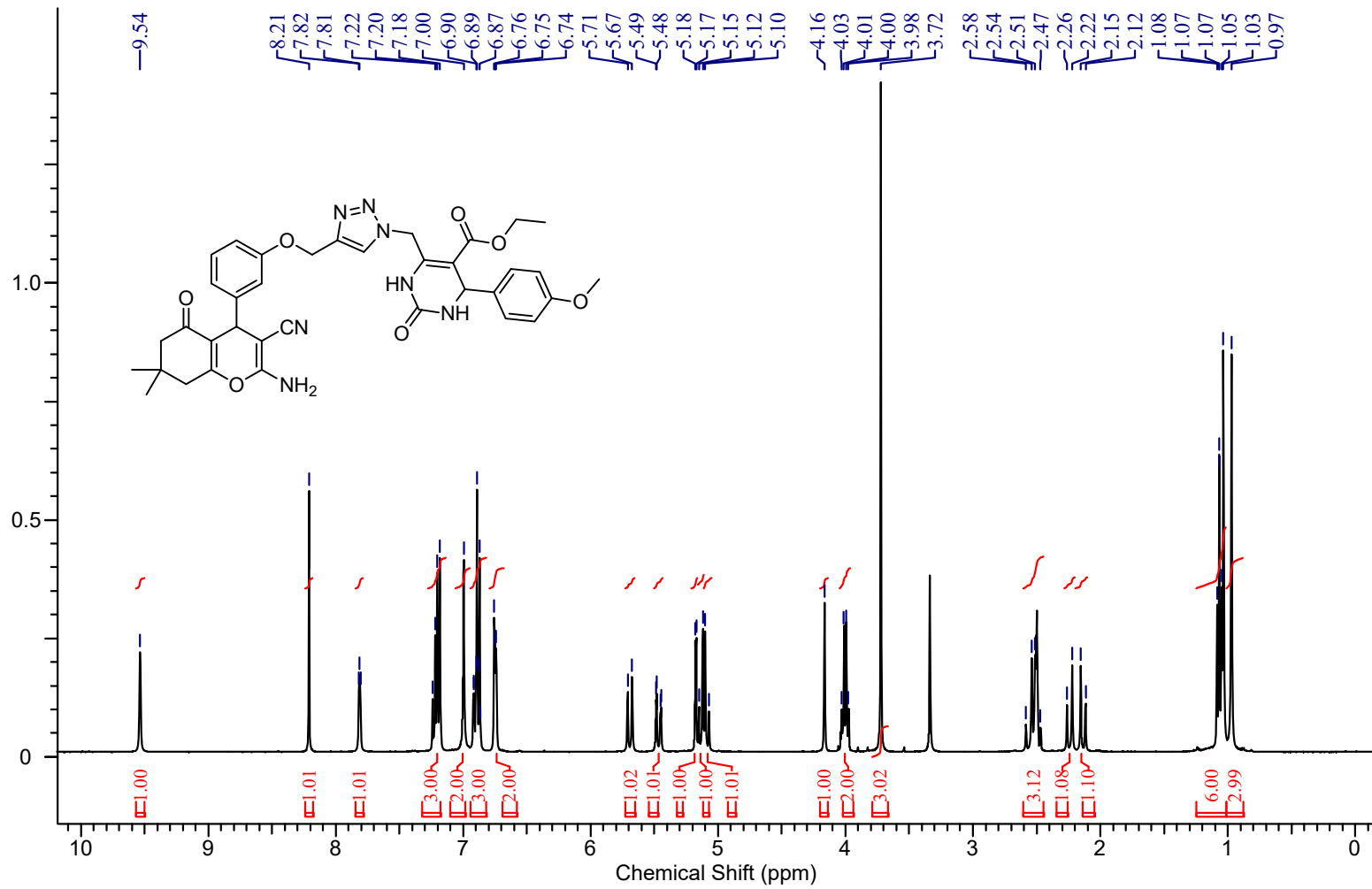


Figure S43: ¹H-NMR (400 MHz, DMSO-d₆) of 15b.

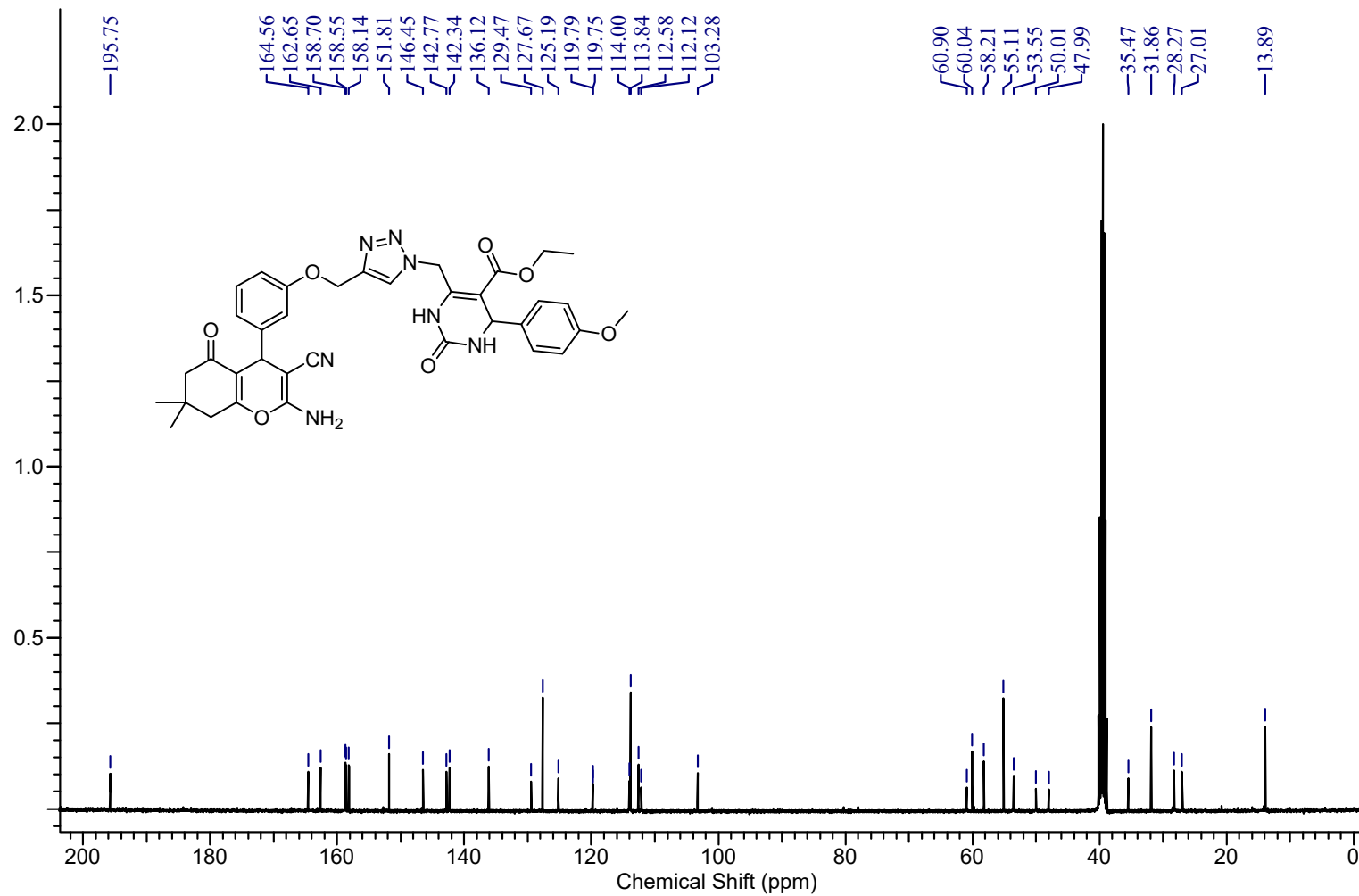


Figure S44: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15b.

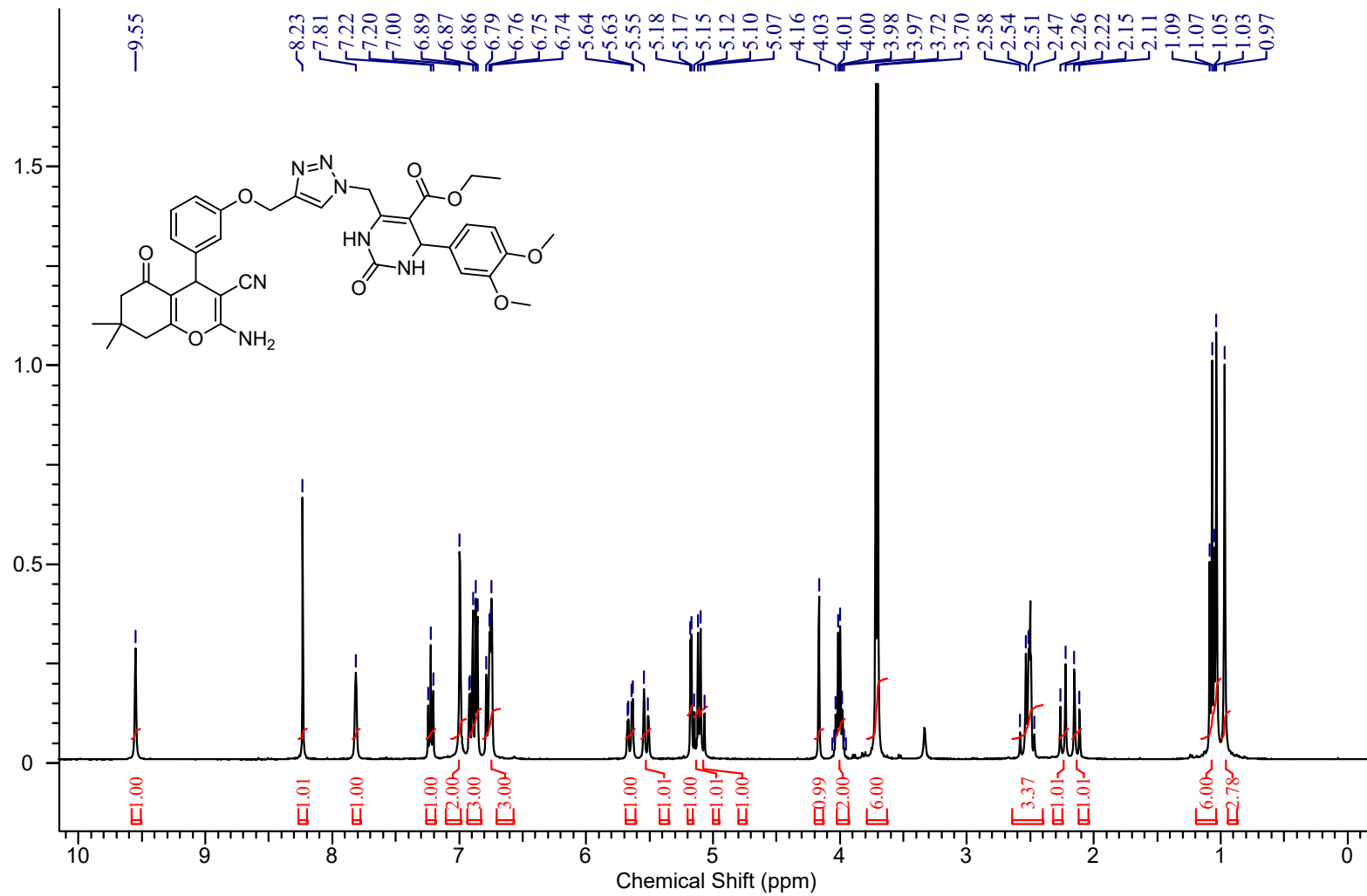


Figure S45: ¹H-NMR (400 MHz, DMSO-d₆) of 15c.

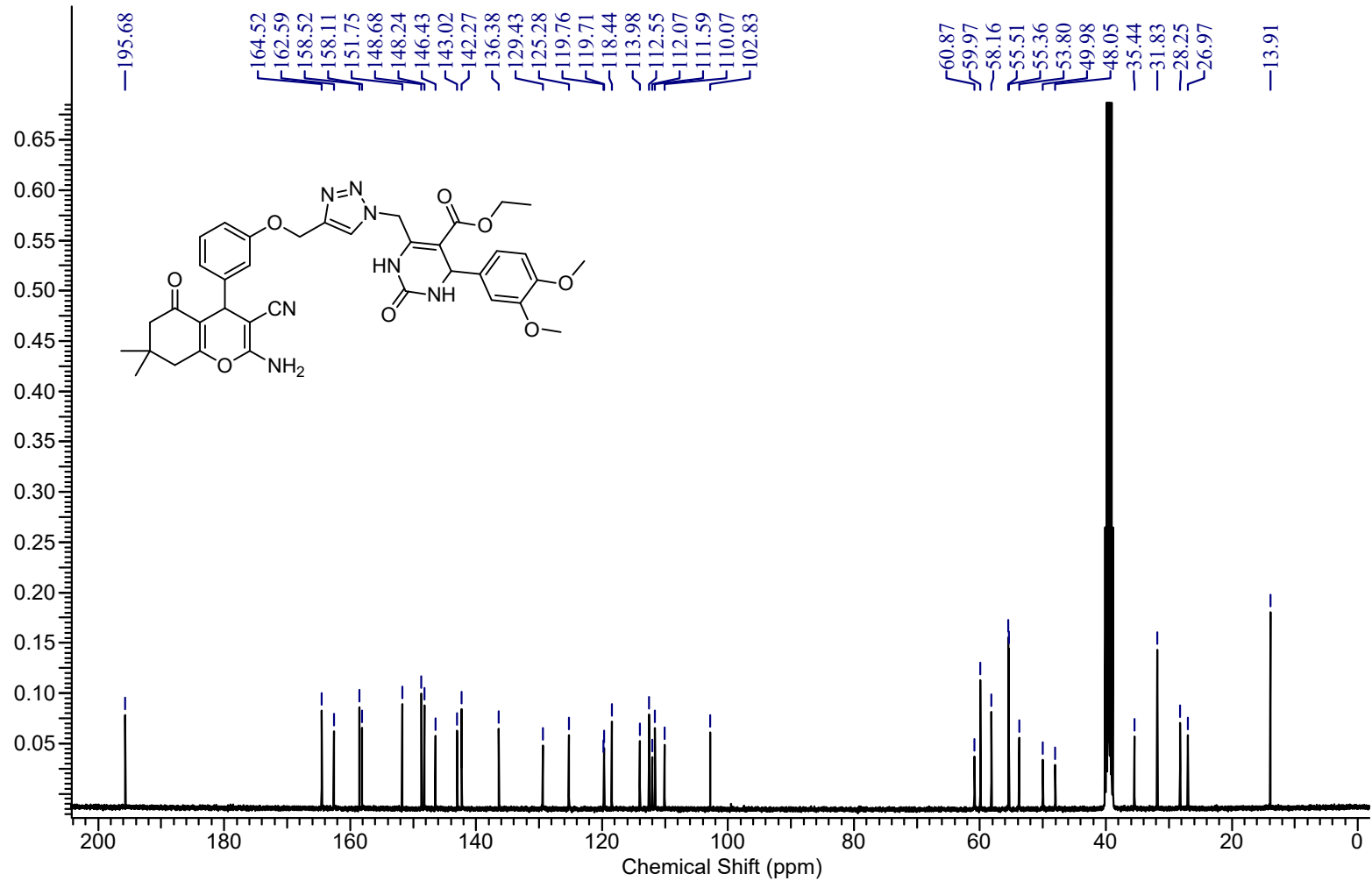


Figure S46: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15c.

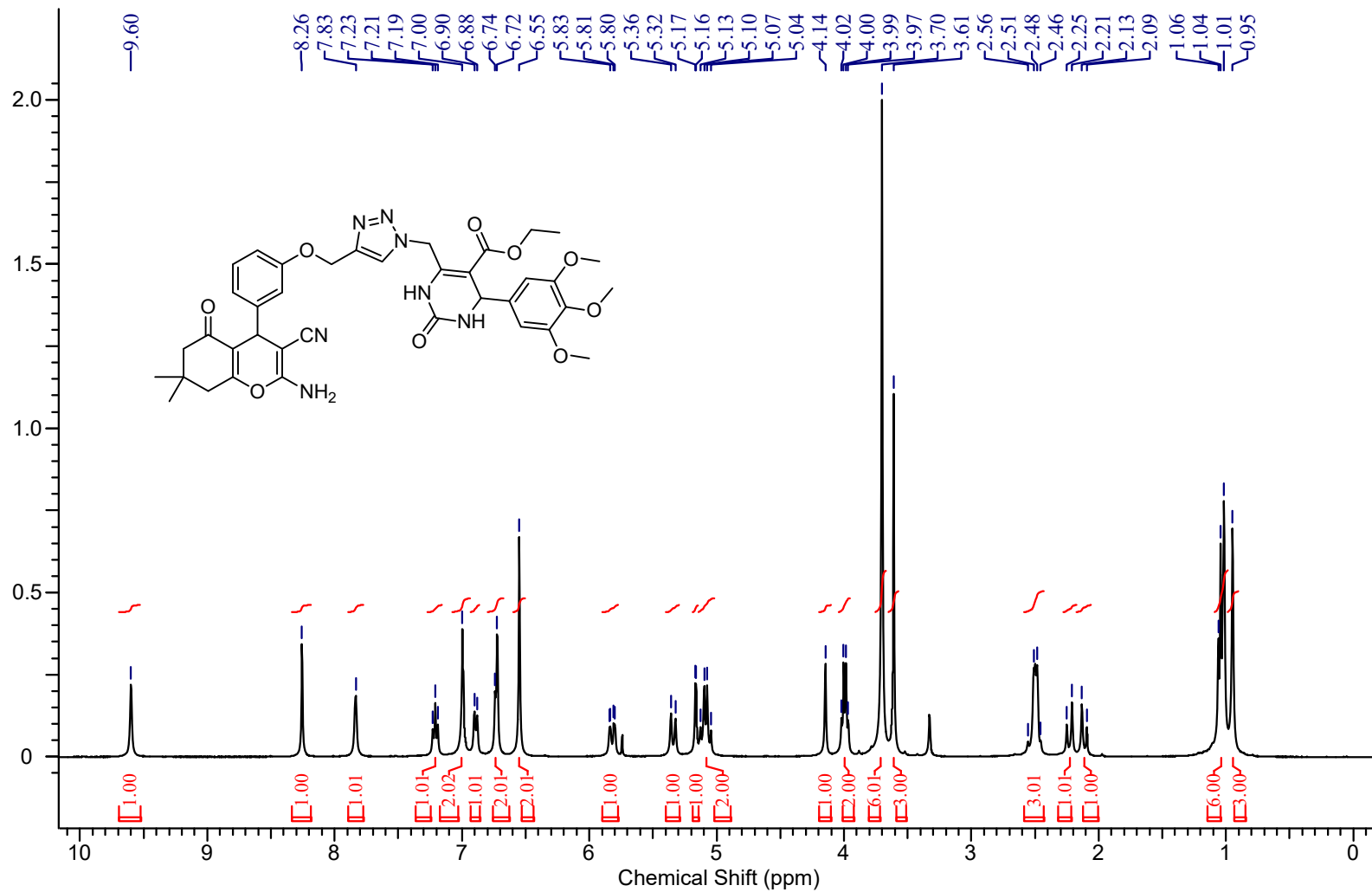


Figure S47: ¹H-NMR (400 MHz, DMSO-d₆) of 15d.

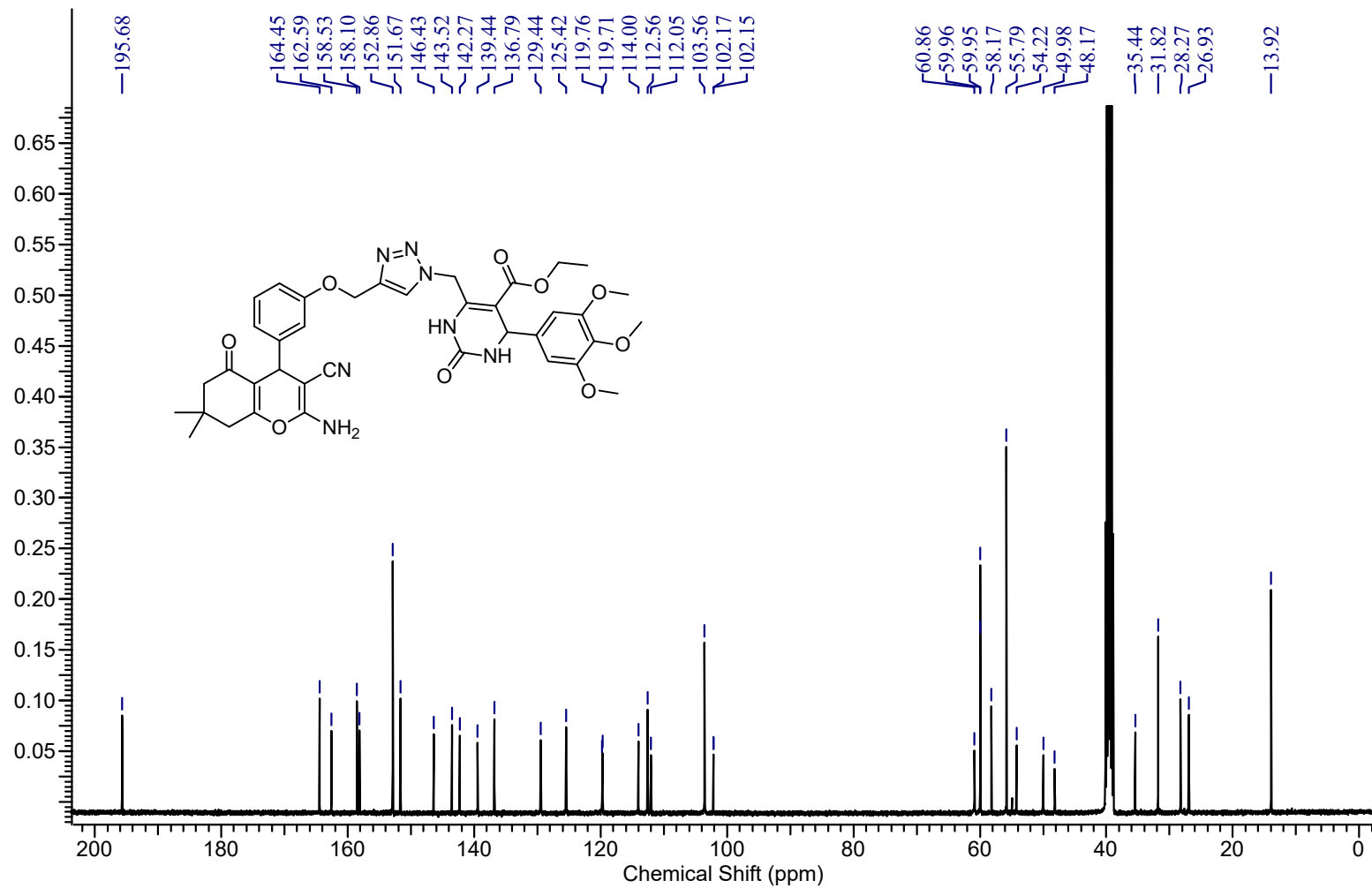


Figure S48: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15d.

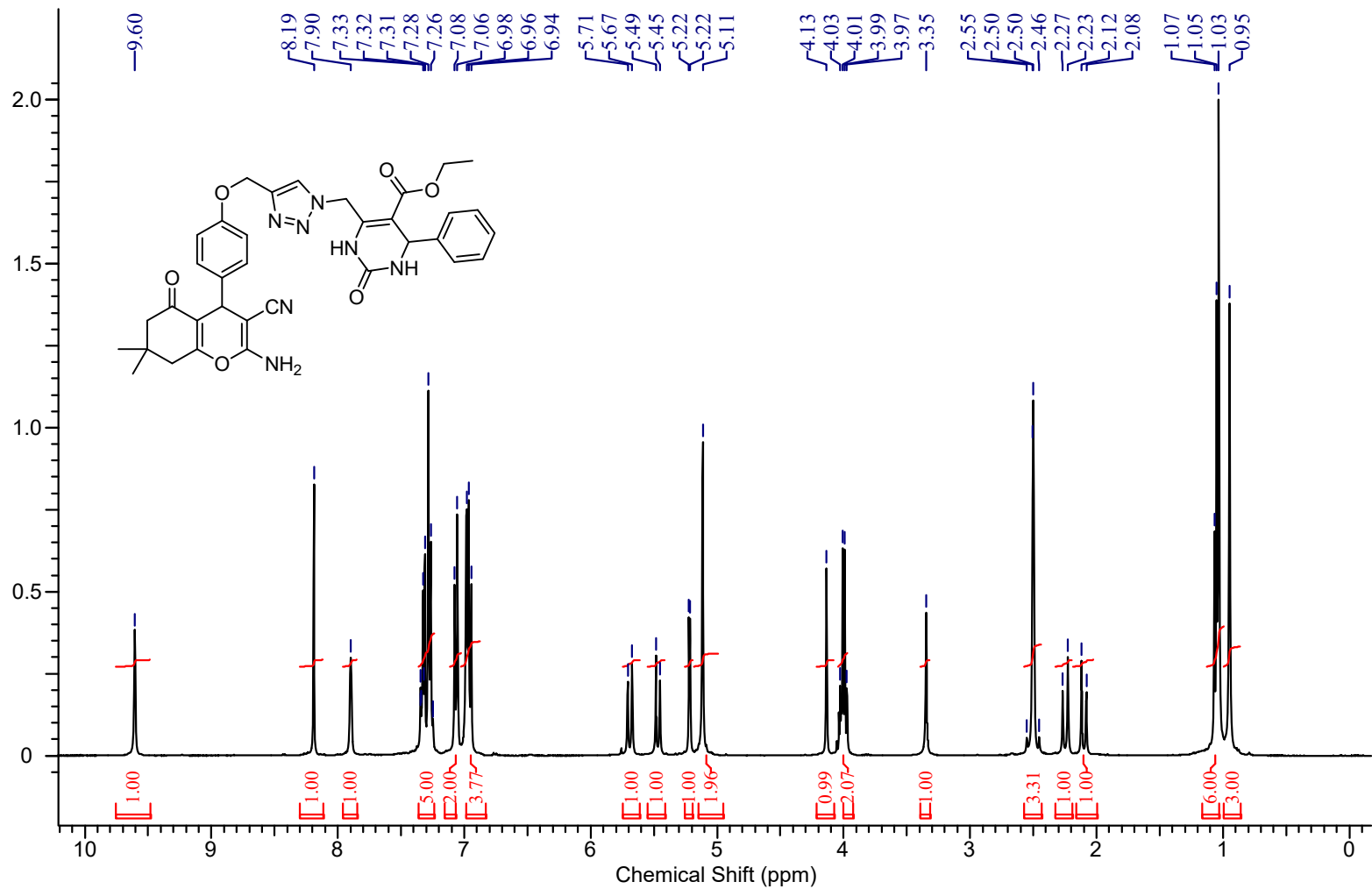


Figure S49: ¹H-NMR (400 MHz, DMSO-d₆) of 15e.

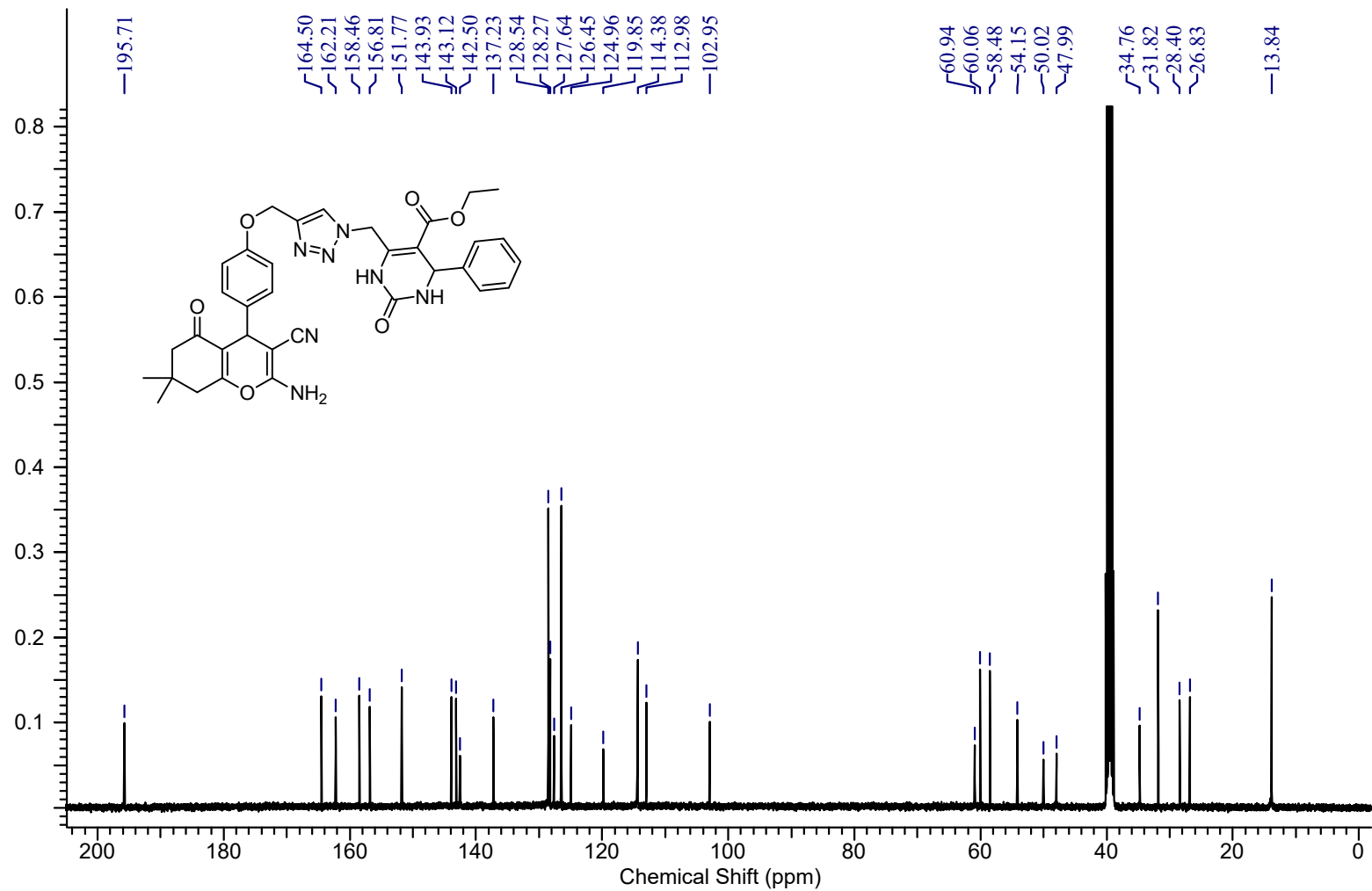


Figure S50: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15e.

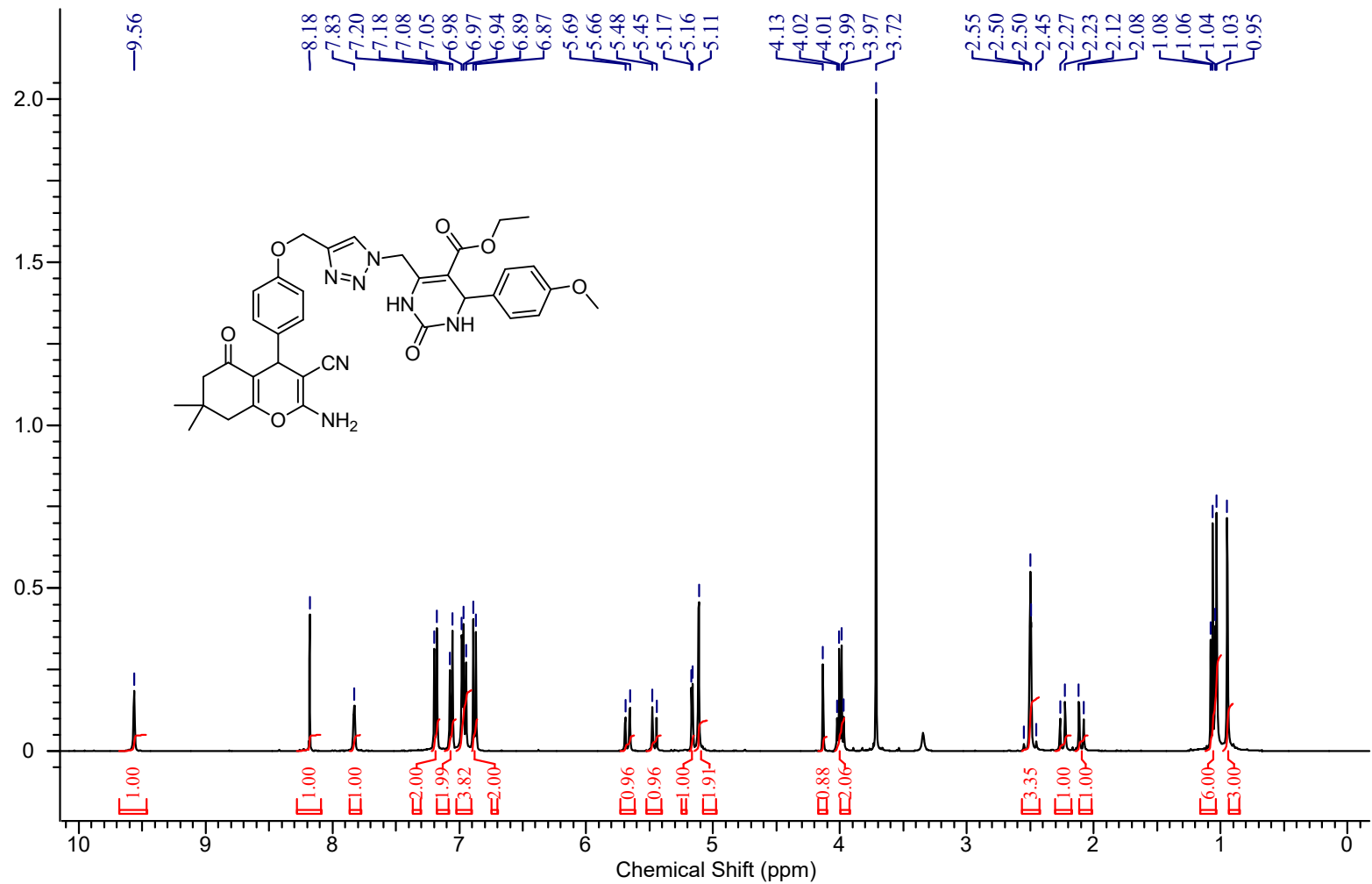


Figure S51: ¹H-NMR (400 MHz, DMSO-d₆) of 15f.

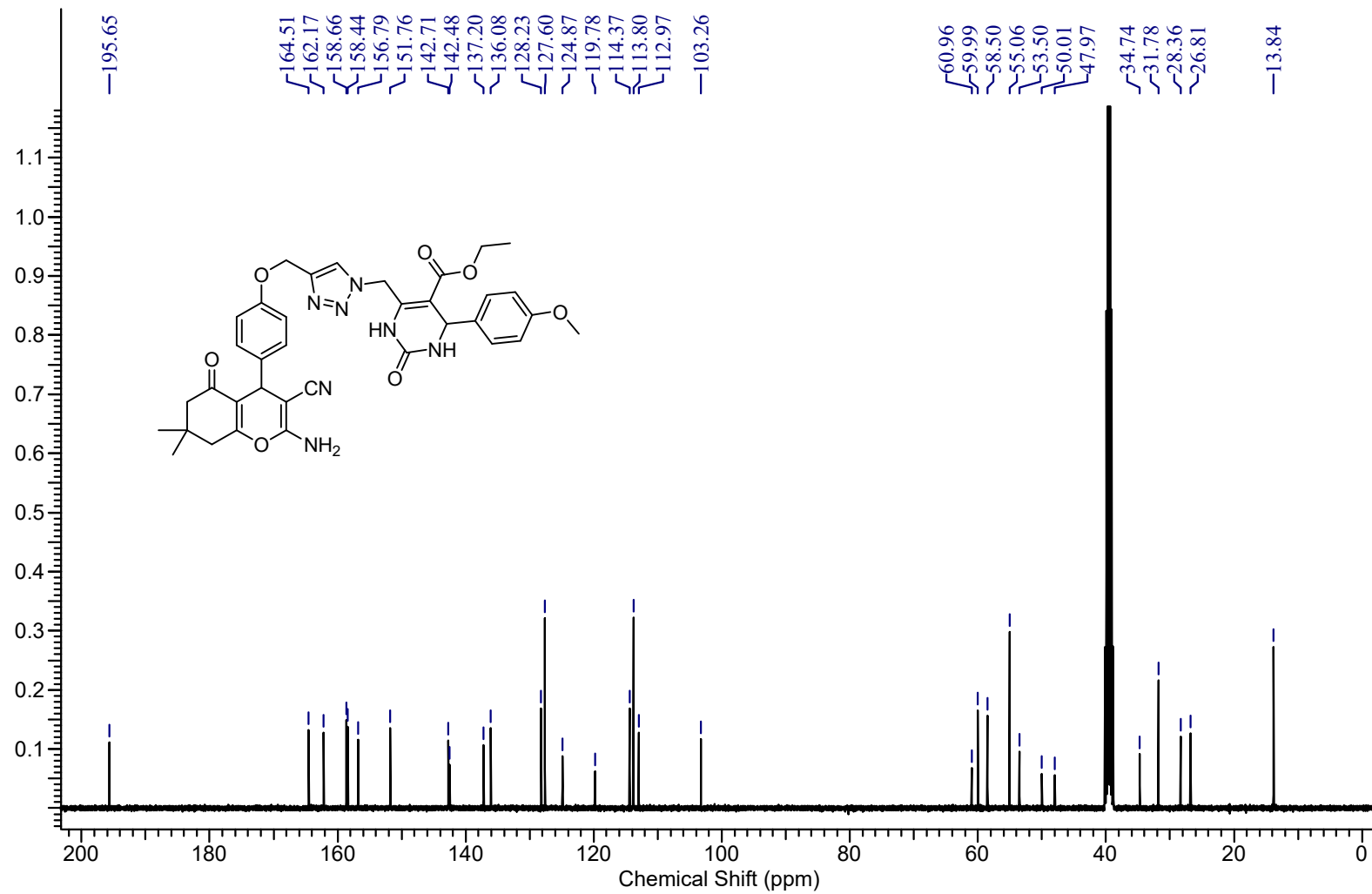


Figure S52: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15f.

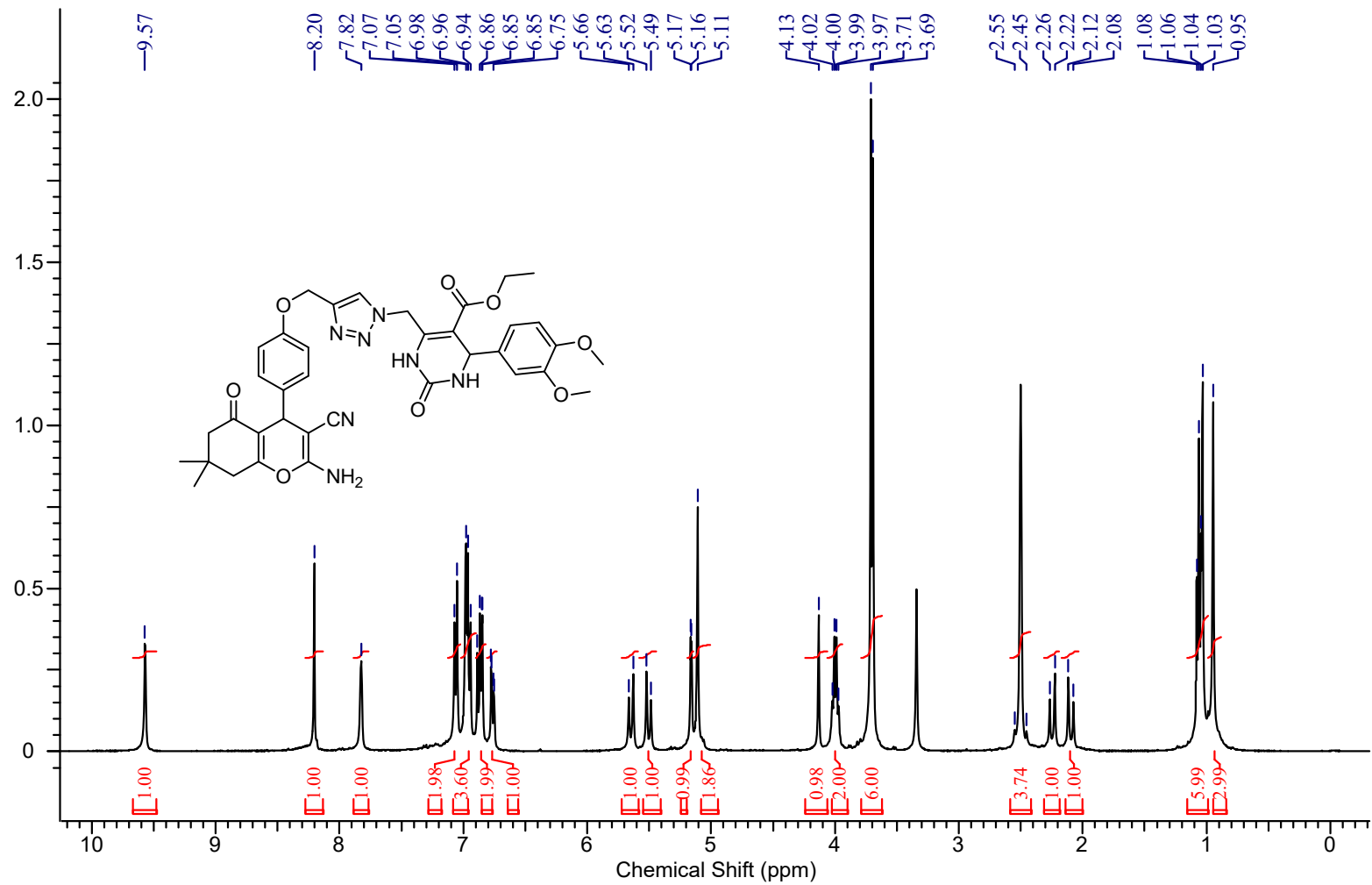


Figure S53: ¹H-NMR (400 MHz, DMSO-d₆) of 15g.

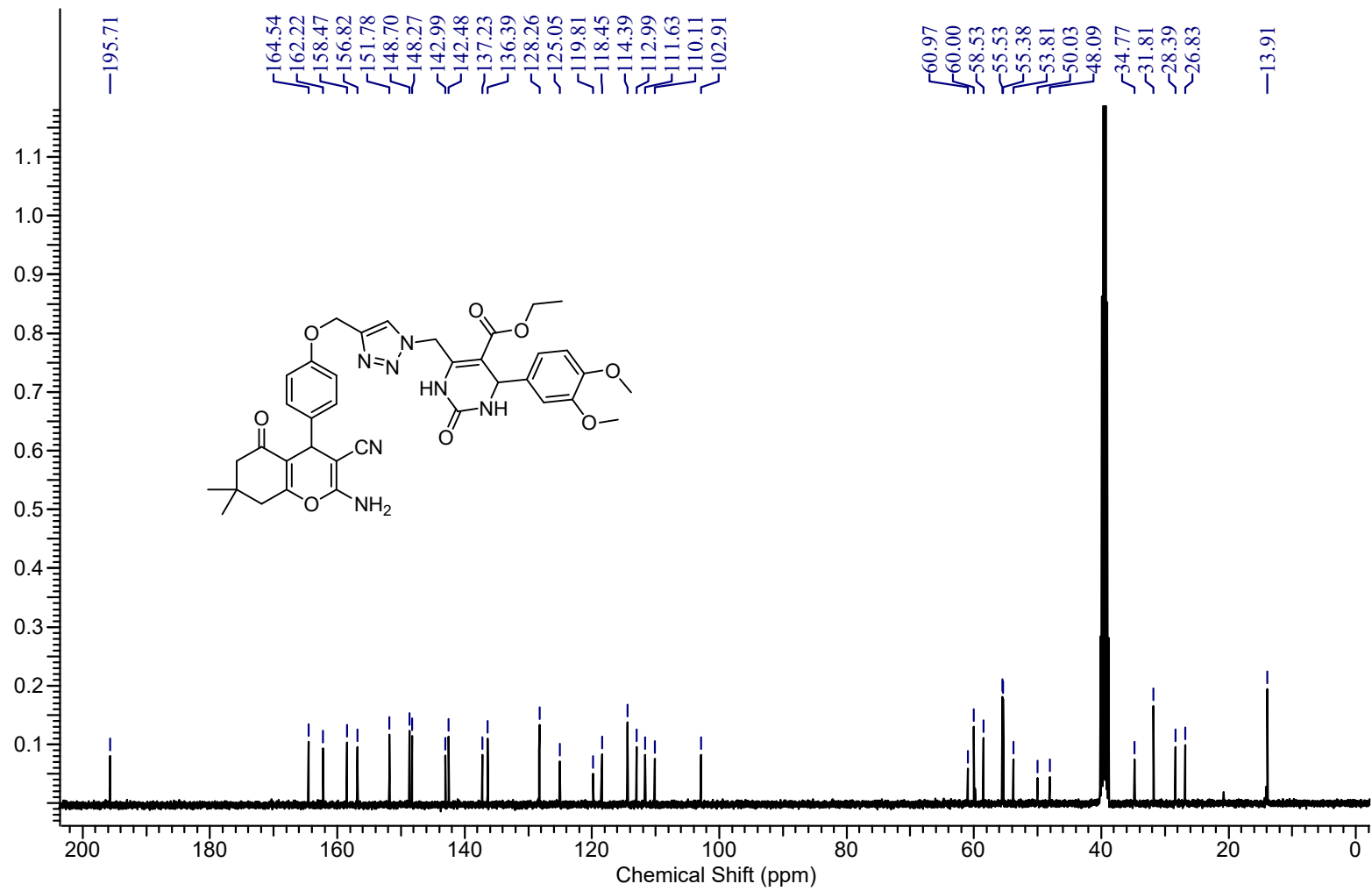


Figure S54: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15g.

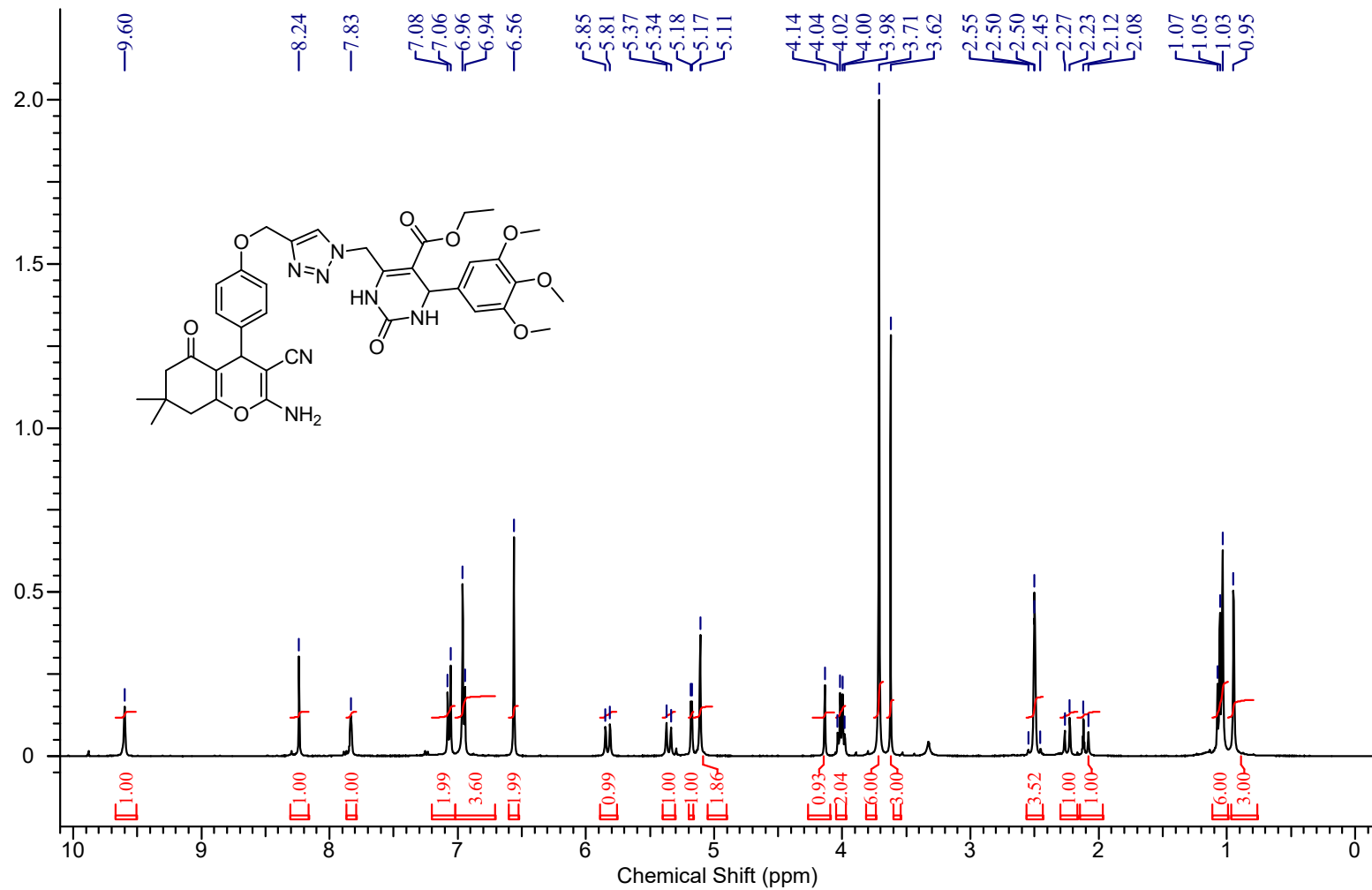


Figure S55: ¹H-NMR (400 MHz, DMSO-d₆) of 15h.

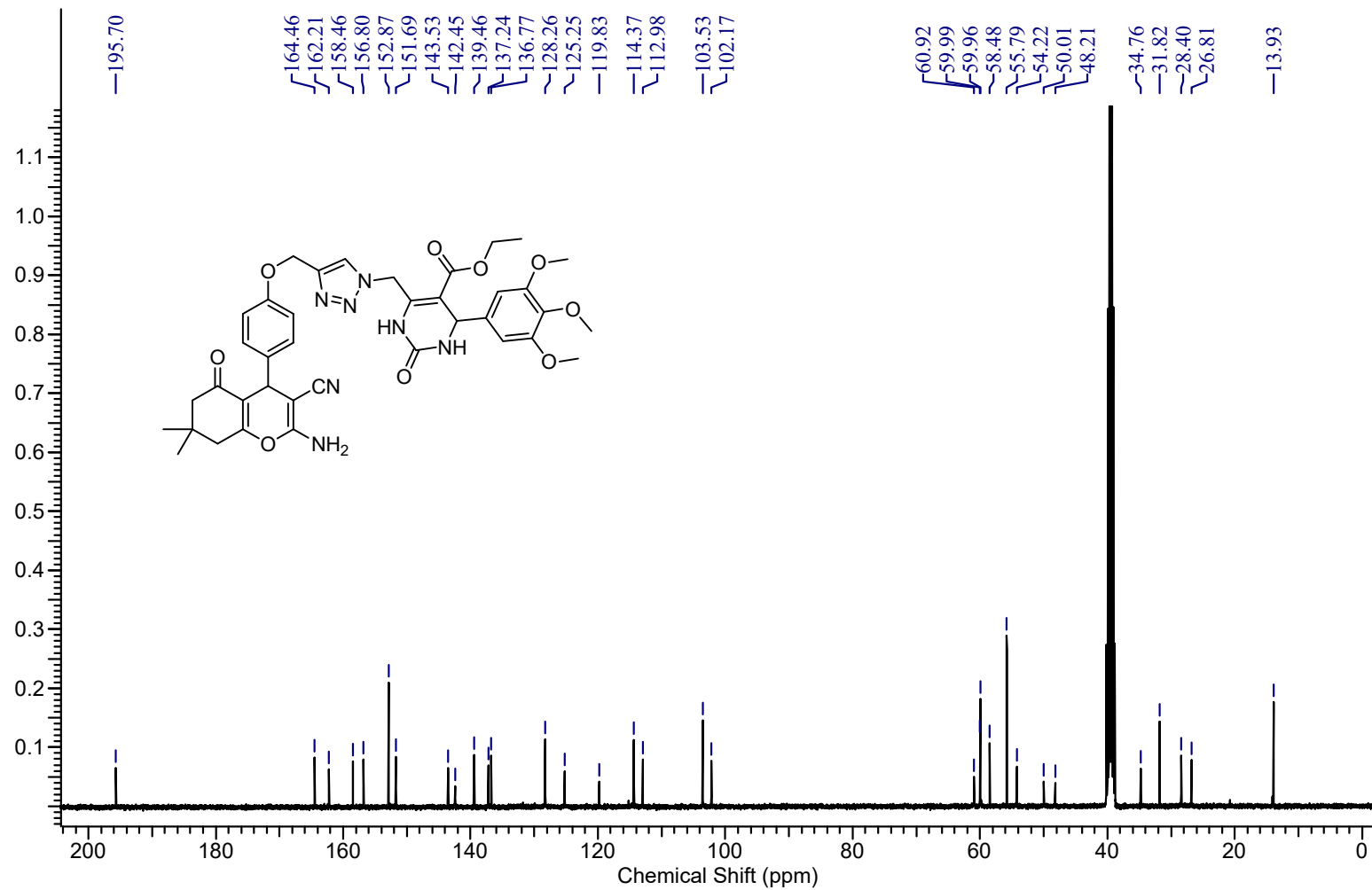


Figure S56: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15h.

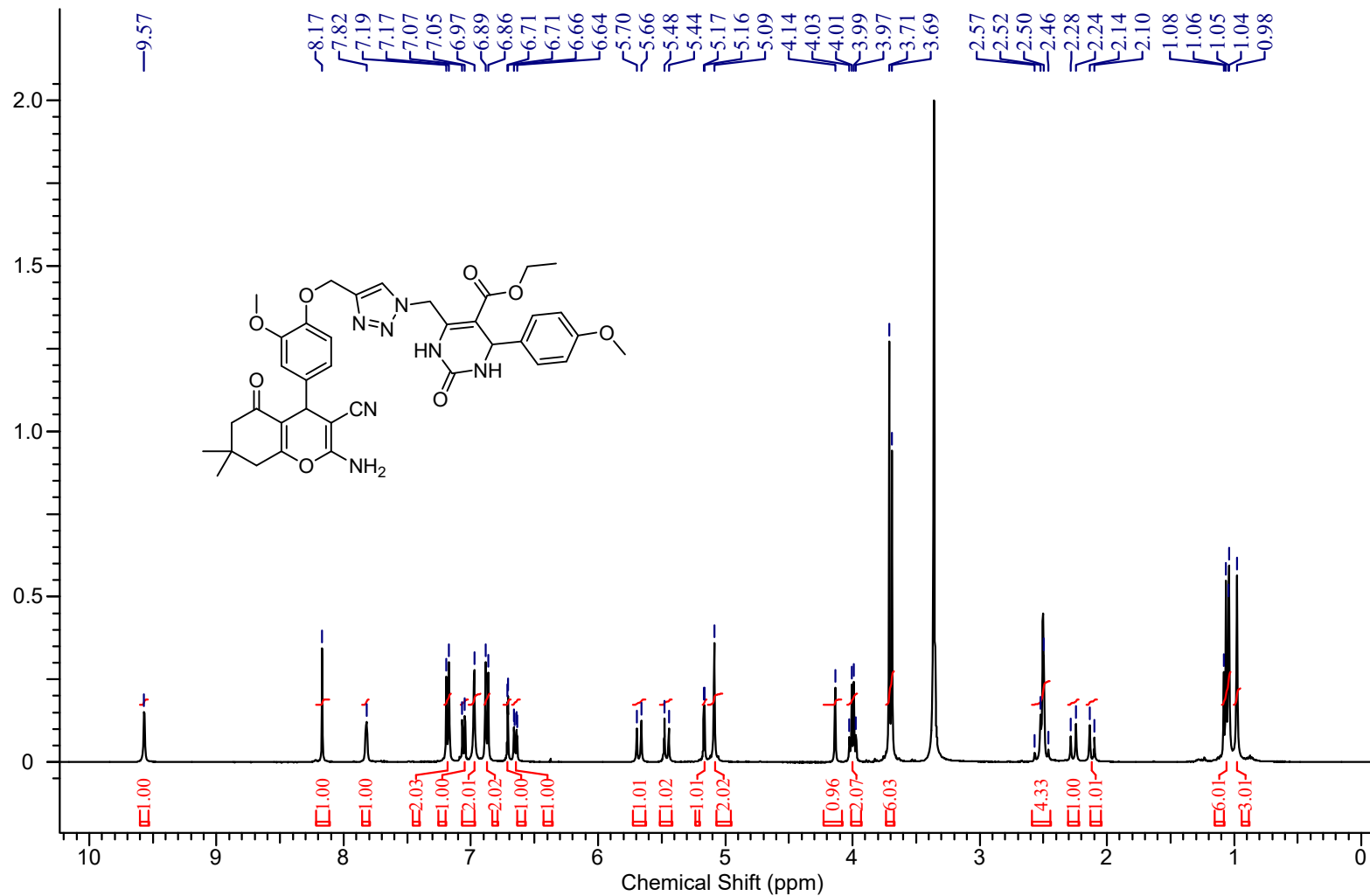


Figure S57: ¹H-NMR (400 MHz, DMSO-d₆) of 15i.

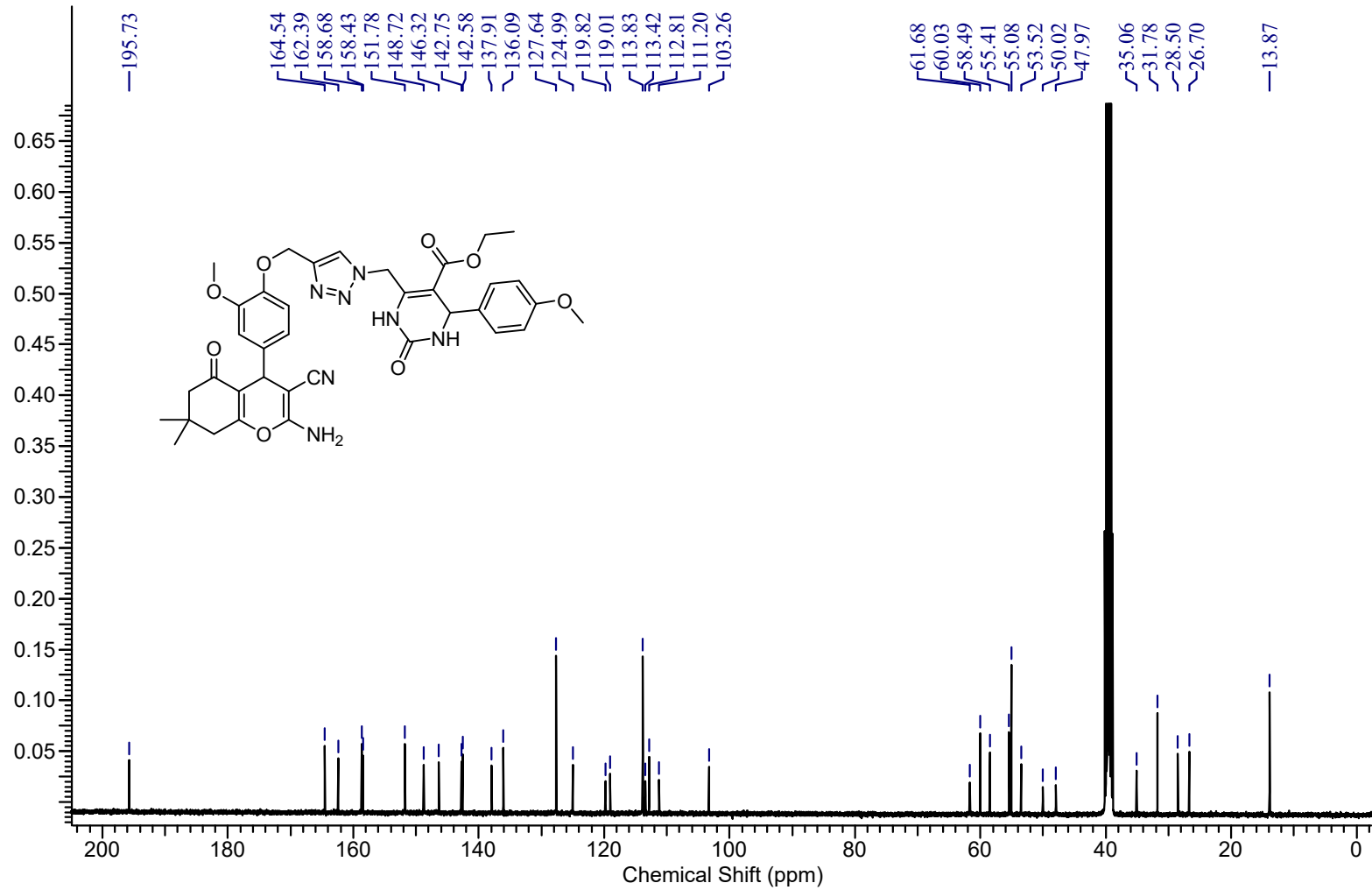


Figure S58: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15i.

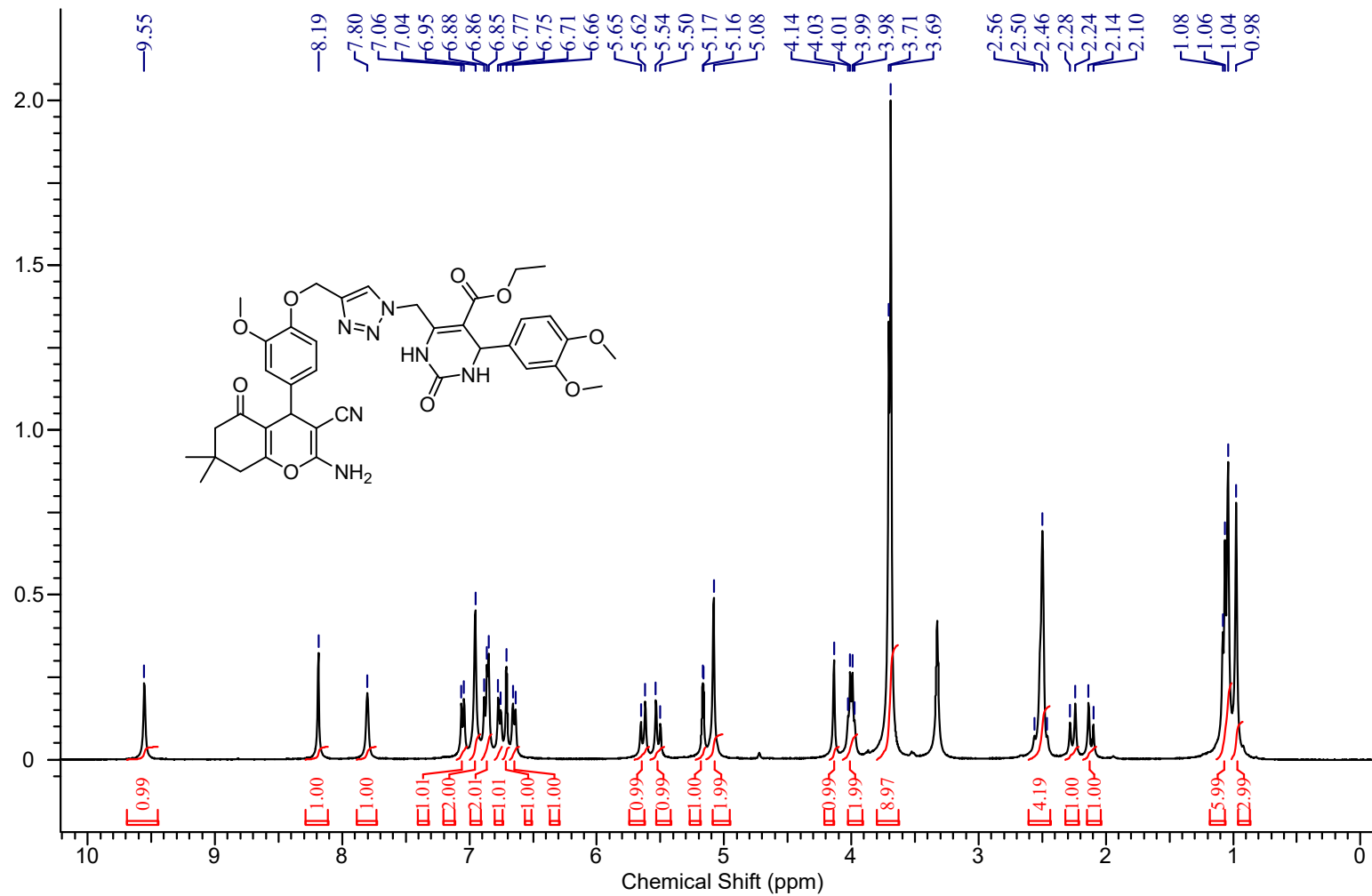


Figure S59: ¹H-NMR (400 MHz, DMSO-d₆) of 15j.

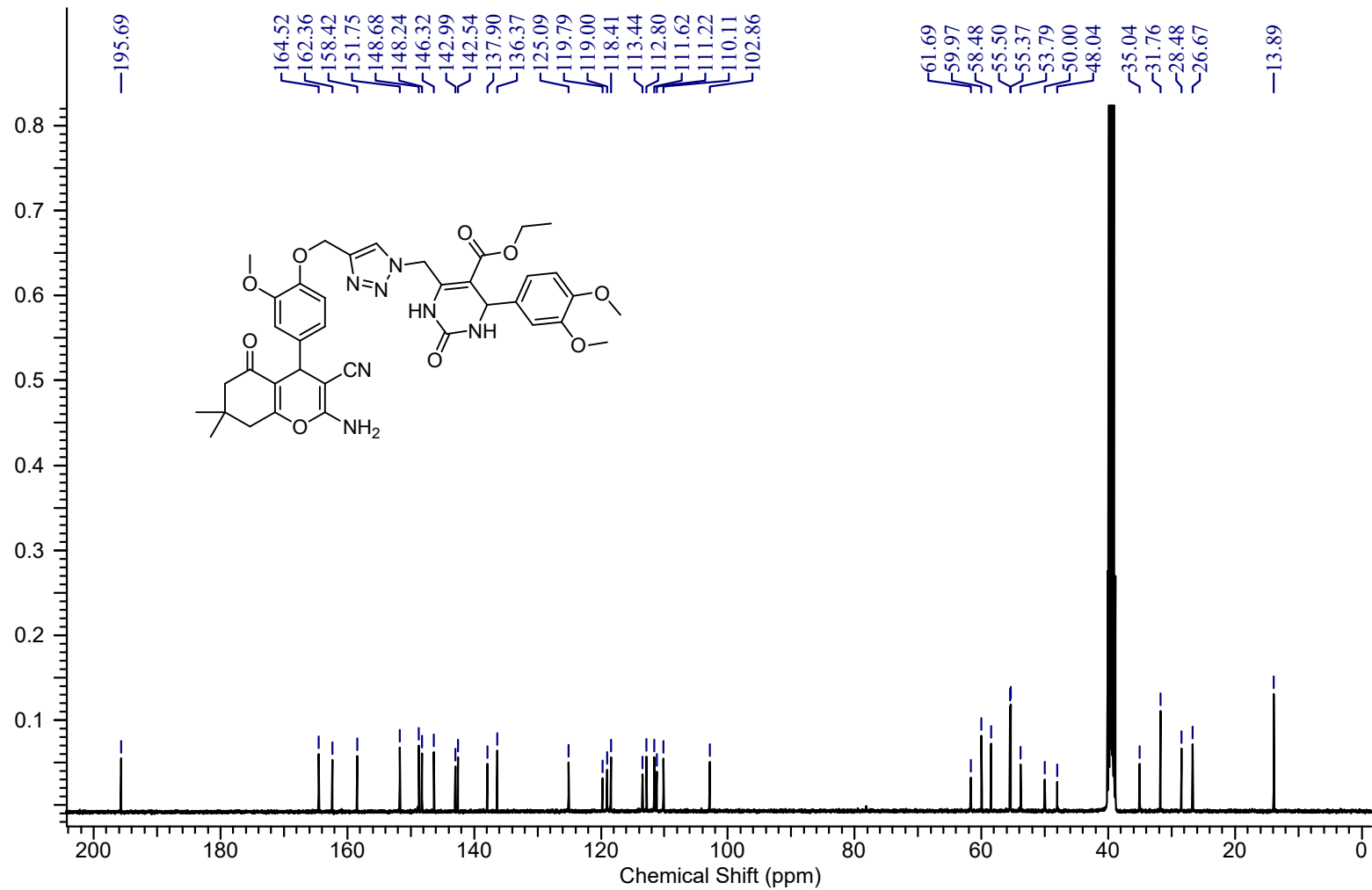


Figure S60: ^{13}C -NMR (100 MHz, DMSO-d_6) of 15j.

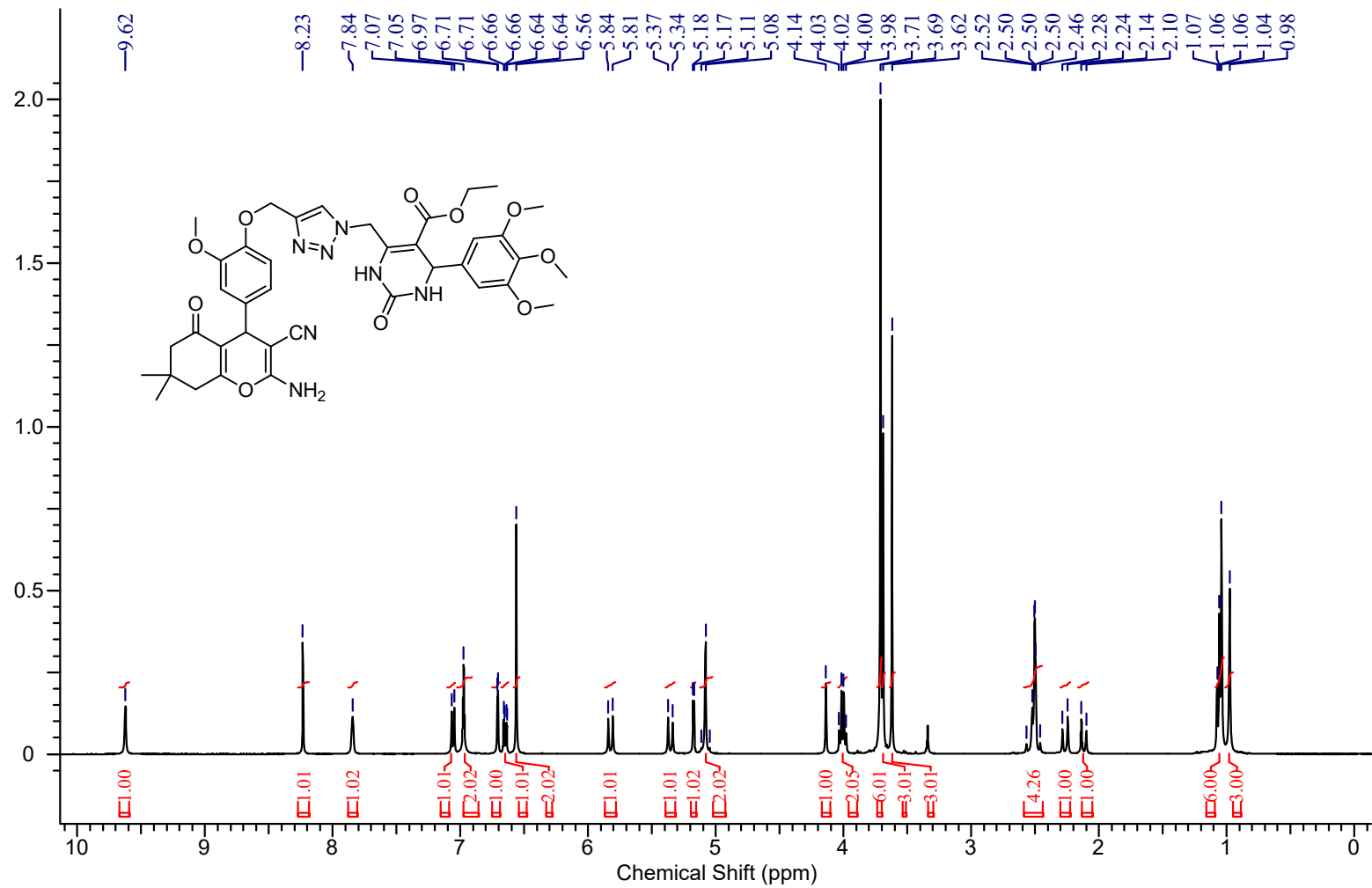


Figure S61: ¹H-NMR (400 MHz, DMSO-d₆) of 15k.

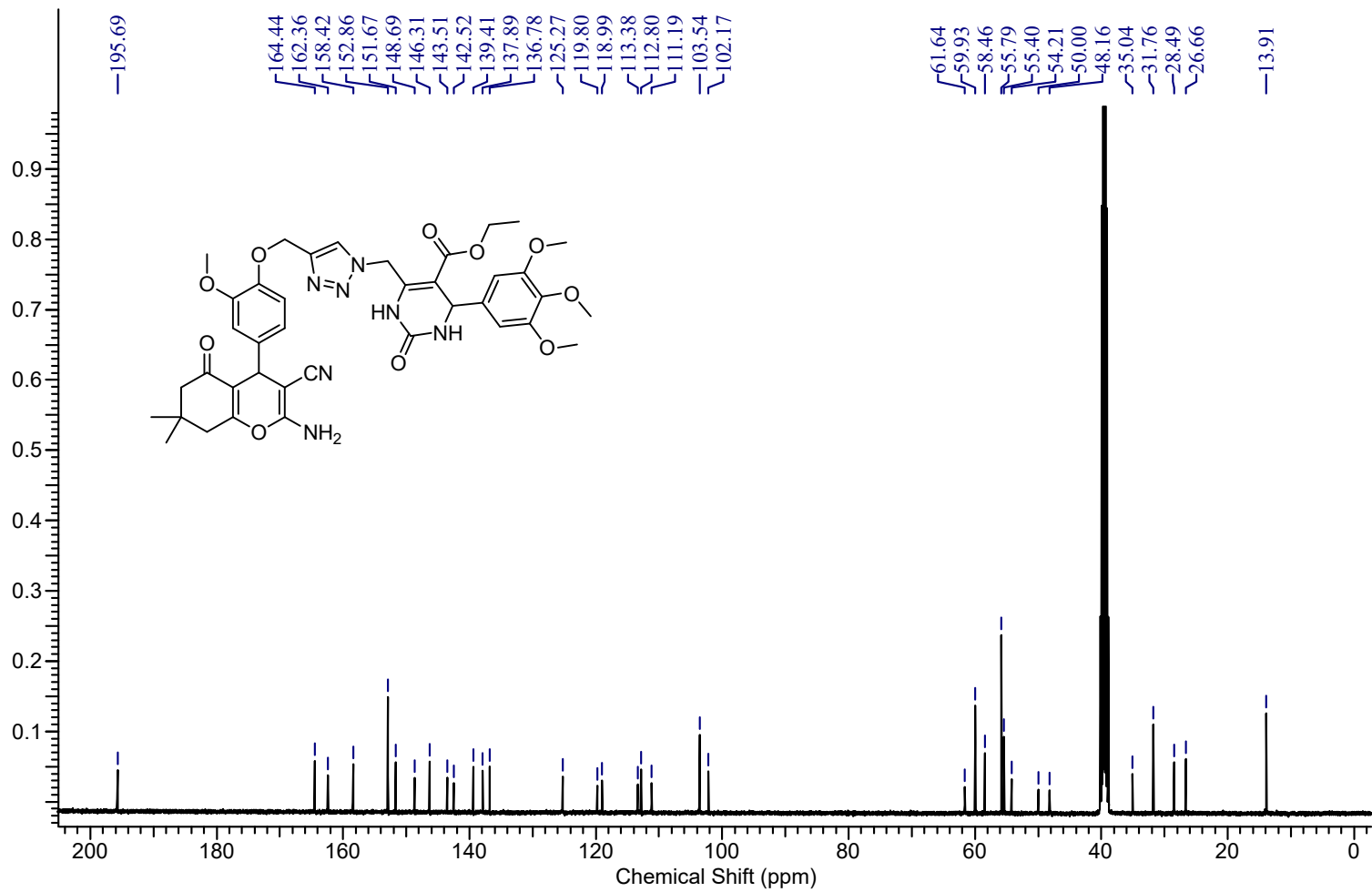


Figure S62: ¹³C-NMR (100 MHz, DMSO-d₆) of 15k.

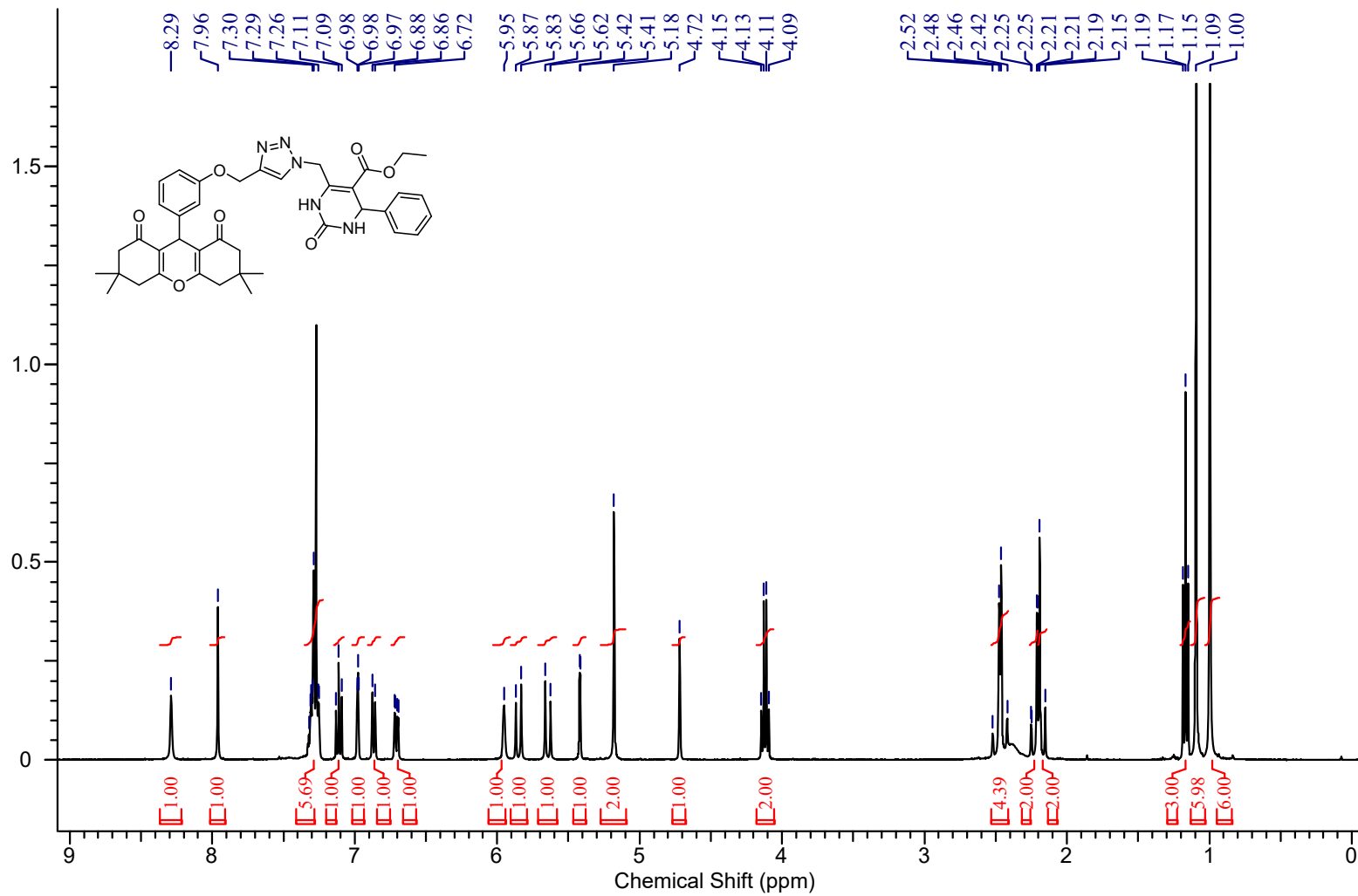


Figure S63: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 15I.

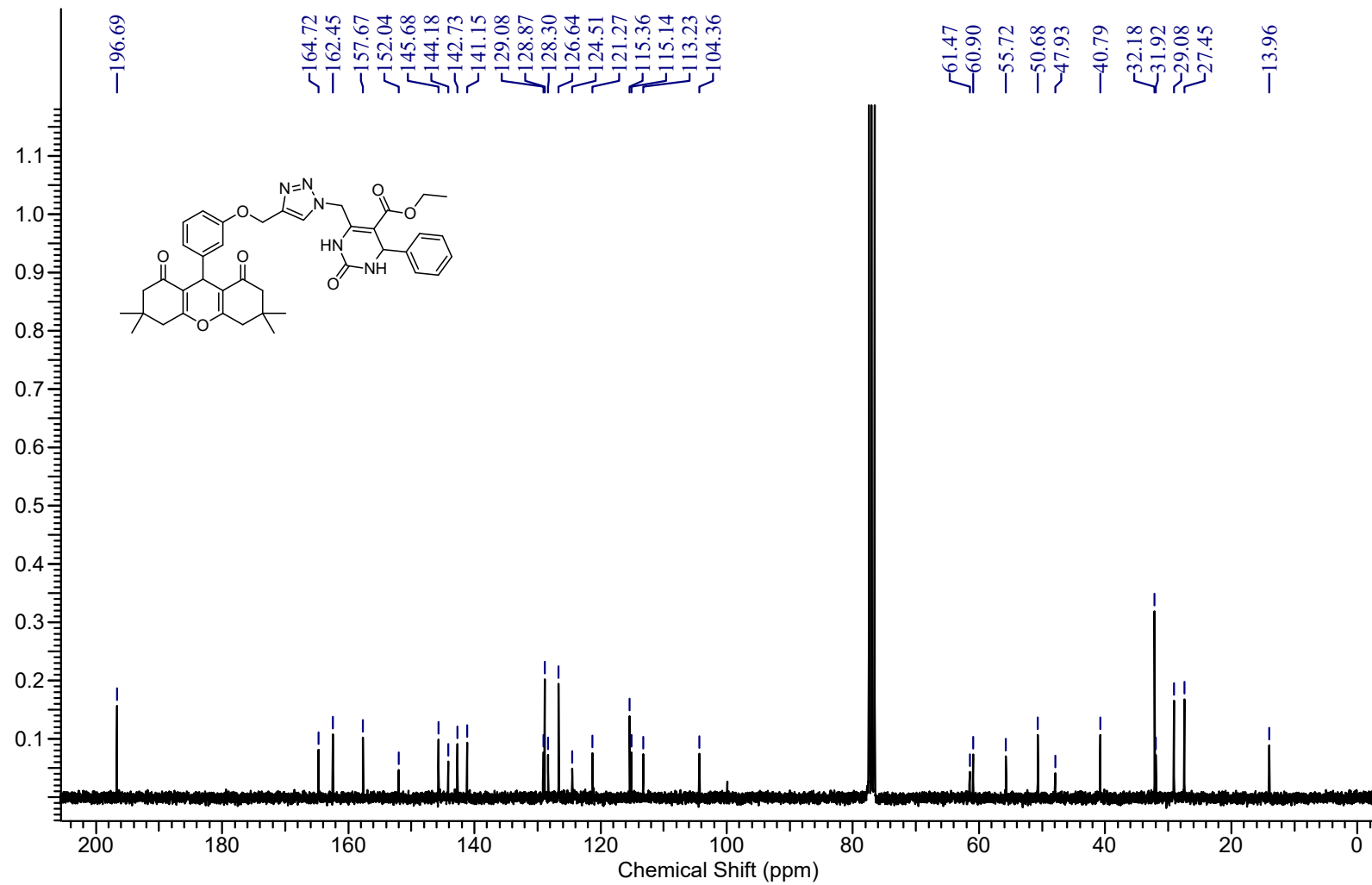


Figure S64: ¹³C-NMR (100 MHz, CDCl₃) of 15l.

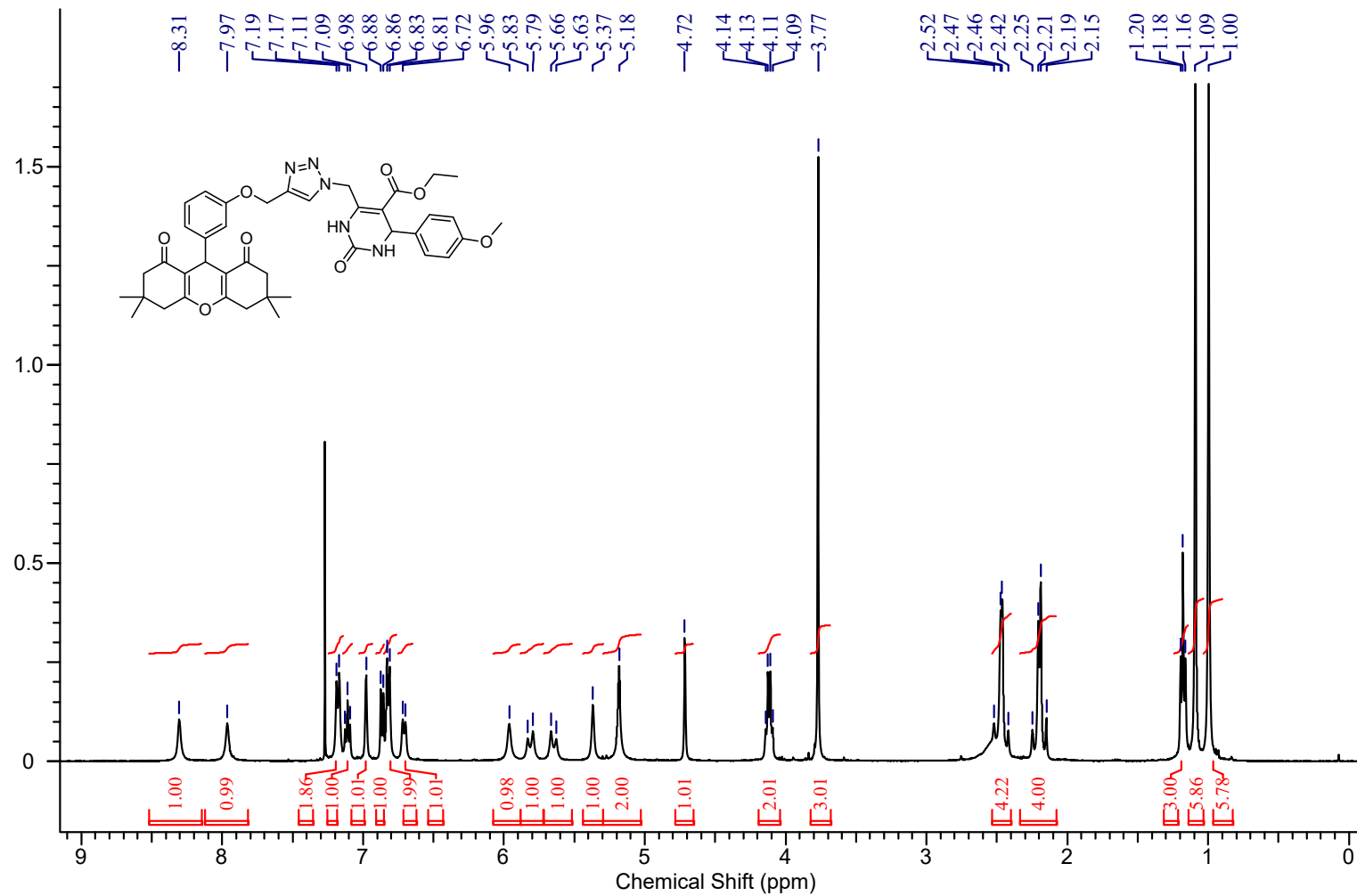


Figure S65: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 15m.

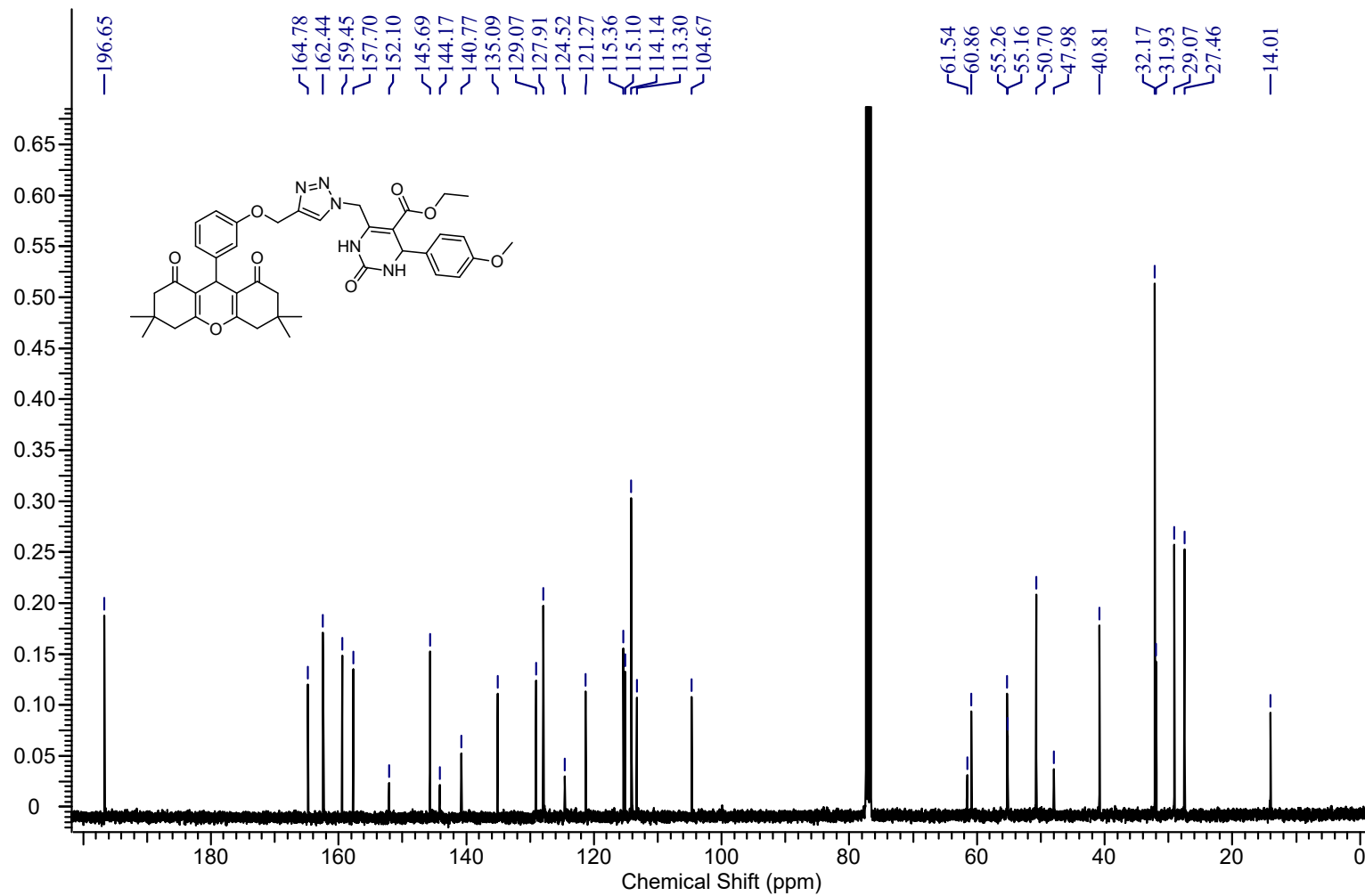


Figure S66: ^{13}C -NMR (100 MHz, CDCl_3) of 15m.

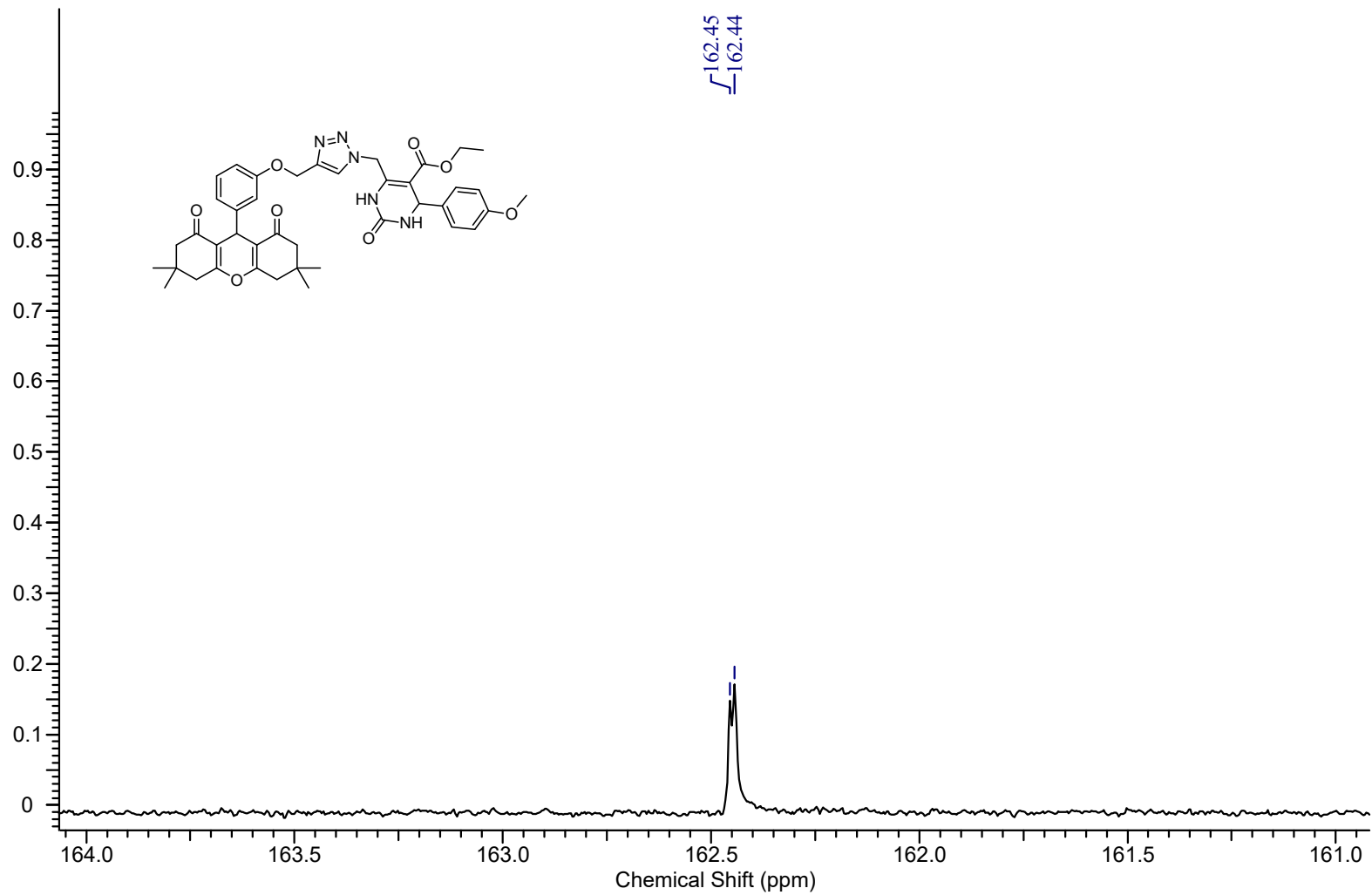


Figure S67: ¹³C-NMR (100 MHz, CDCl₃) of 15m (161.0 to 164.0 ppm)

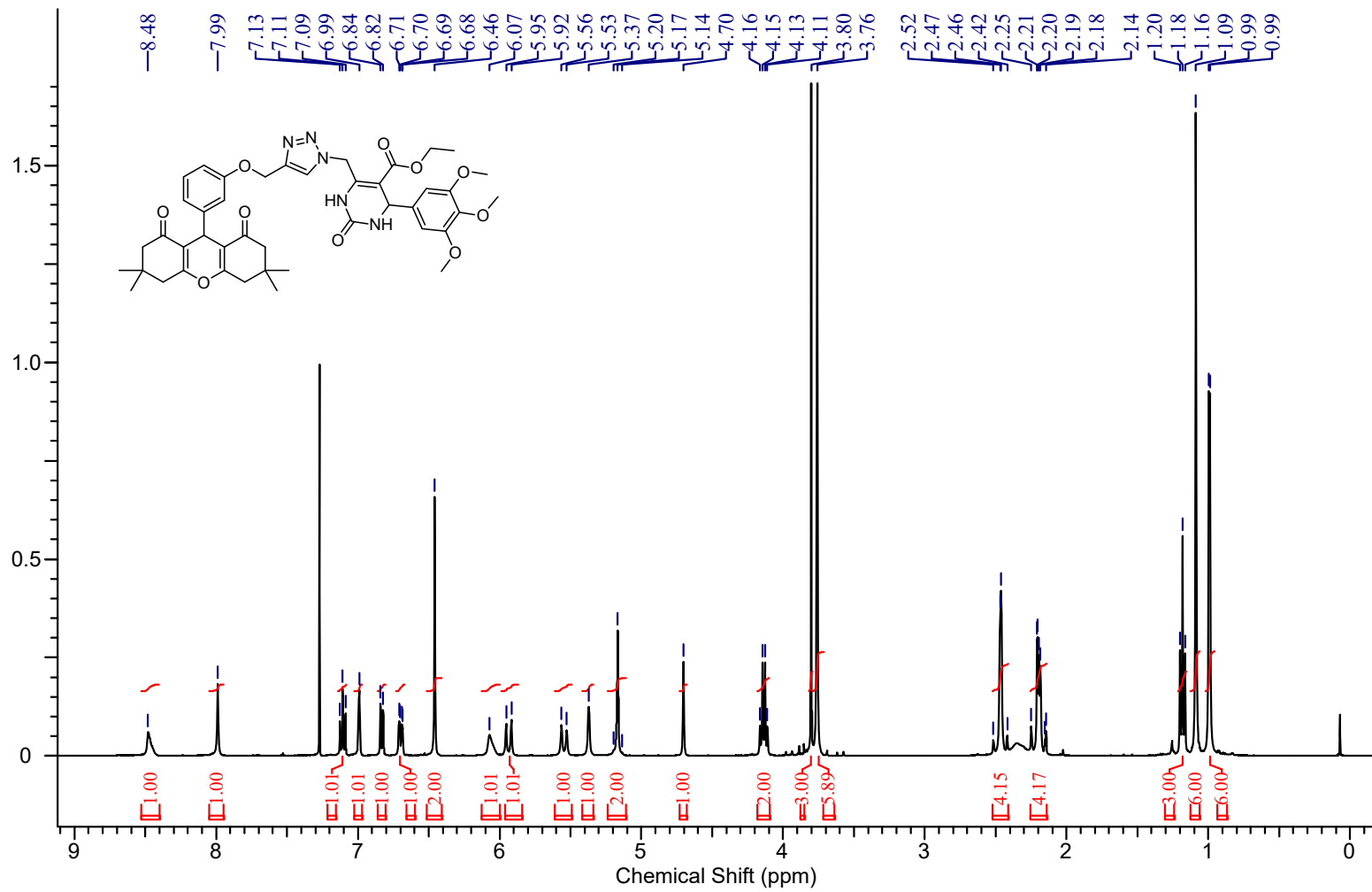


Figure S68: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 15n.

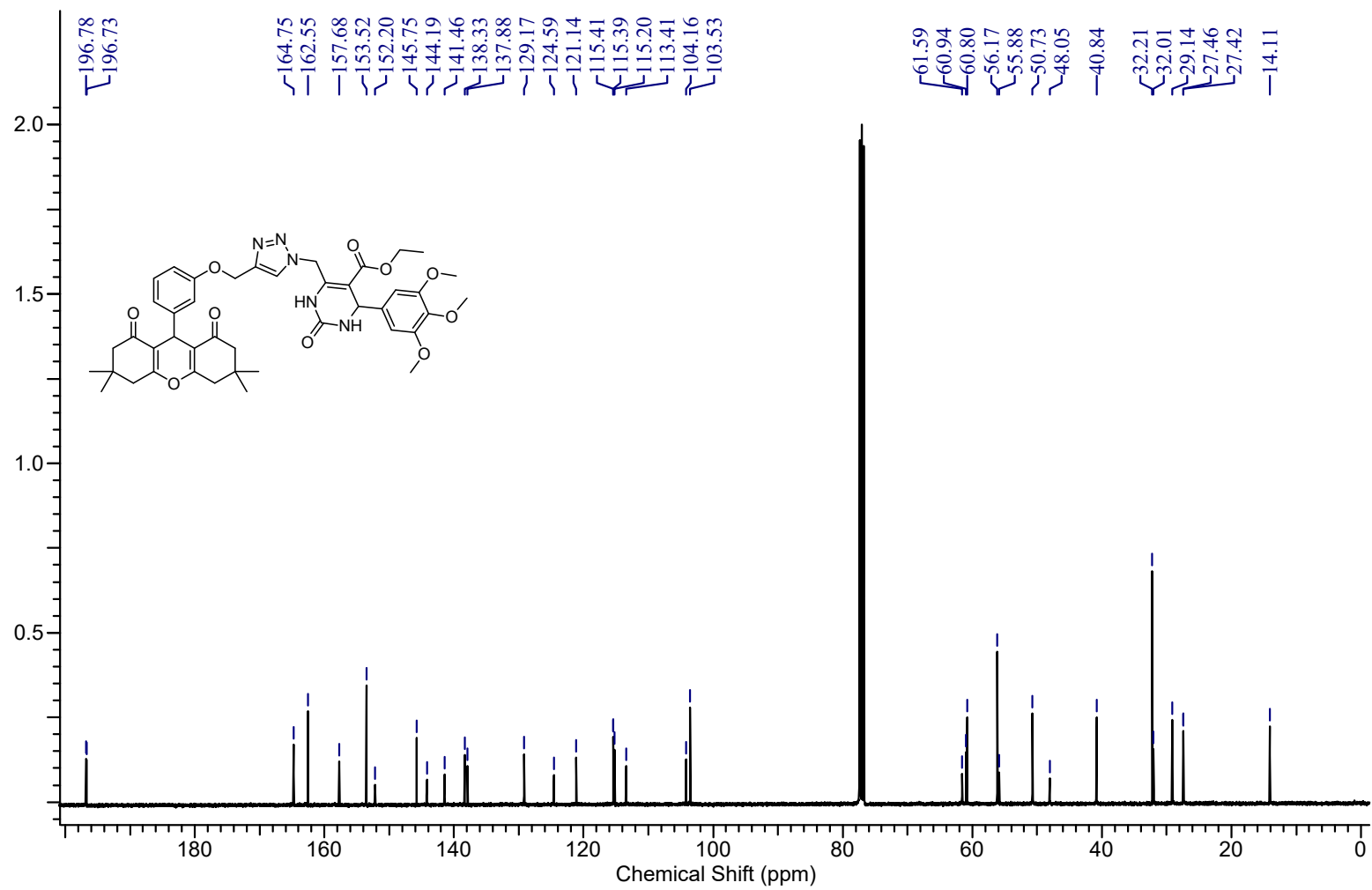


Figure S69: ^{13}C -NMR (100 MHz, CDCl_3) of 15n.

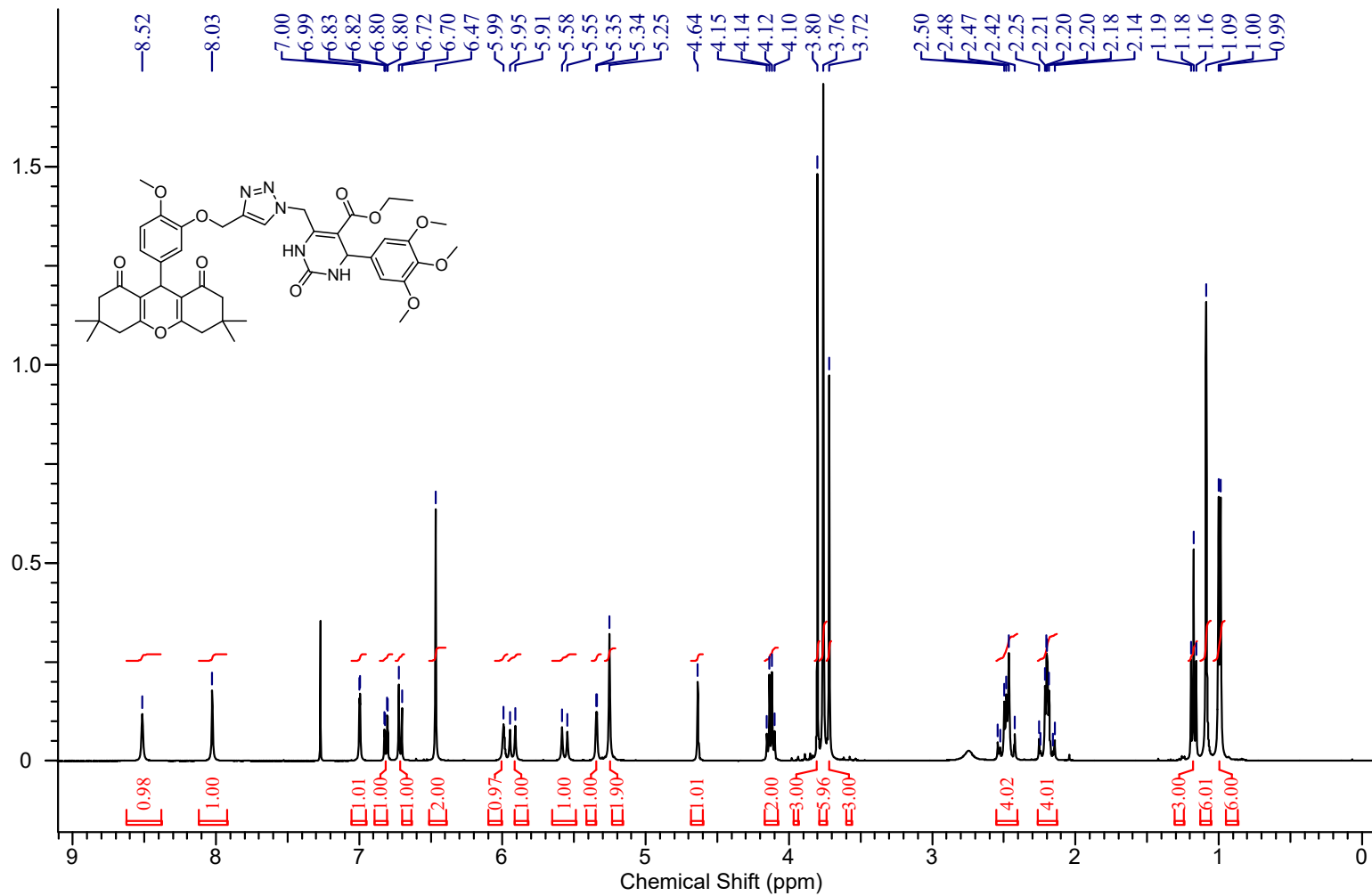


Figure S70: ¹H-NMR (400 MHz, CDCl₃) of 15o.

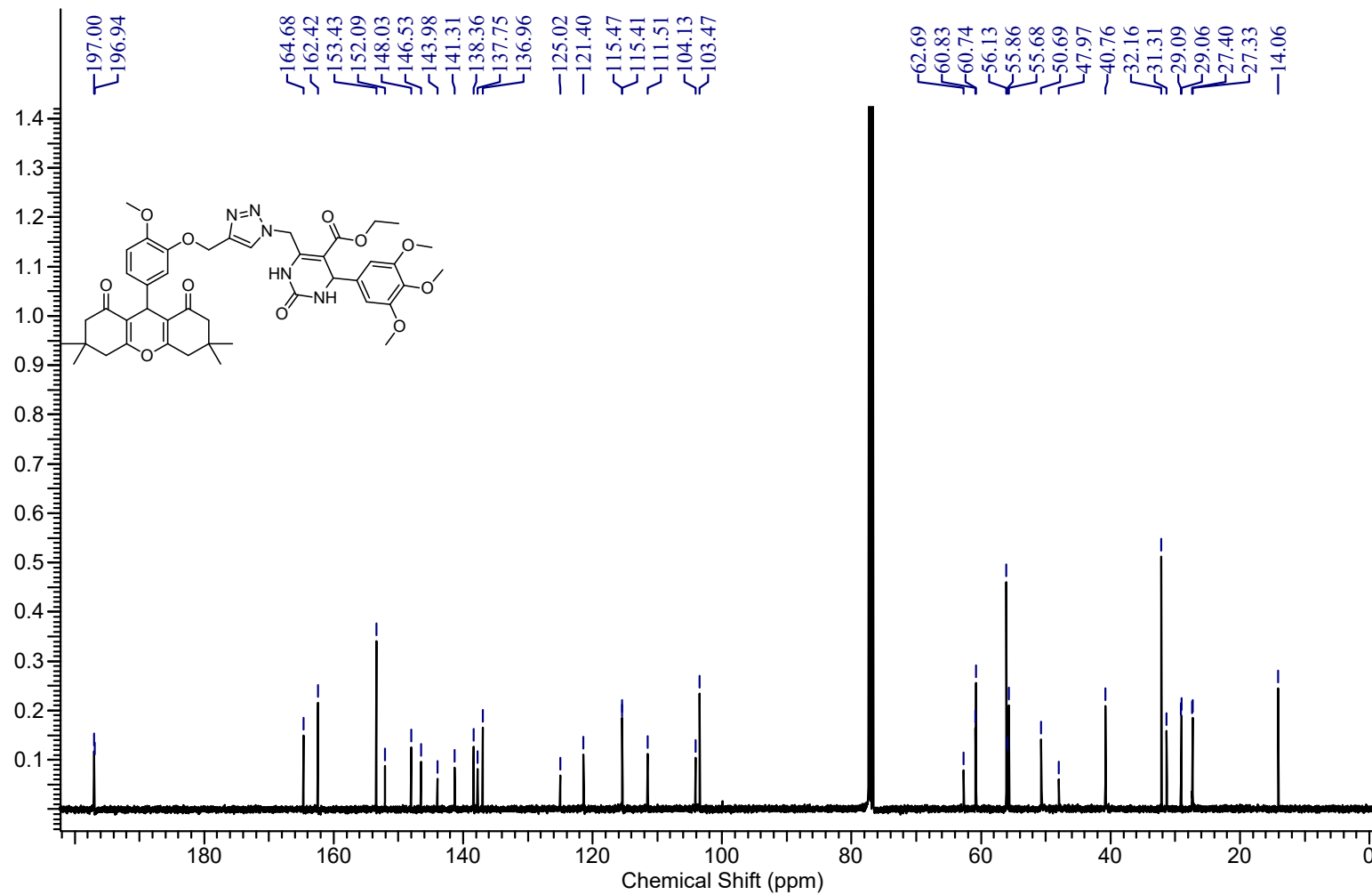


Figure S71: ^{13}C -NMR (100 MHz, CDCl_3) of 15o.

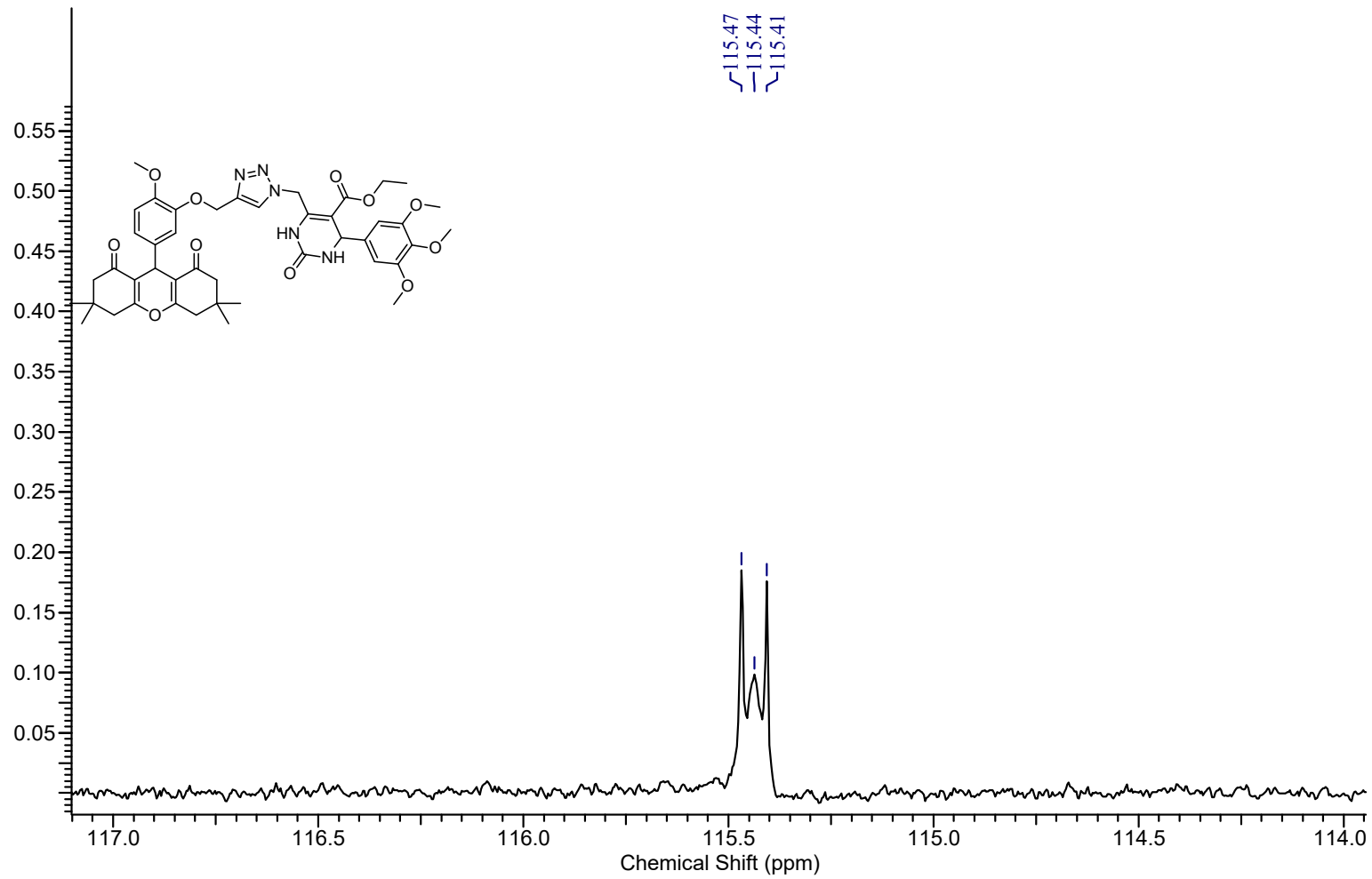


Figure S72: ¹³C-NMR (100 MHz, CDCl₃) of 15o (114.0 to 117.0 ppm).

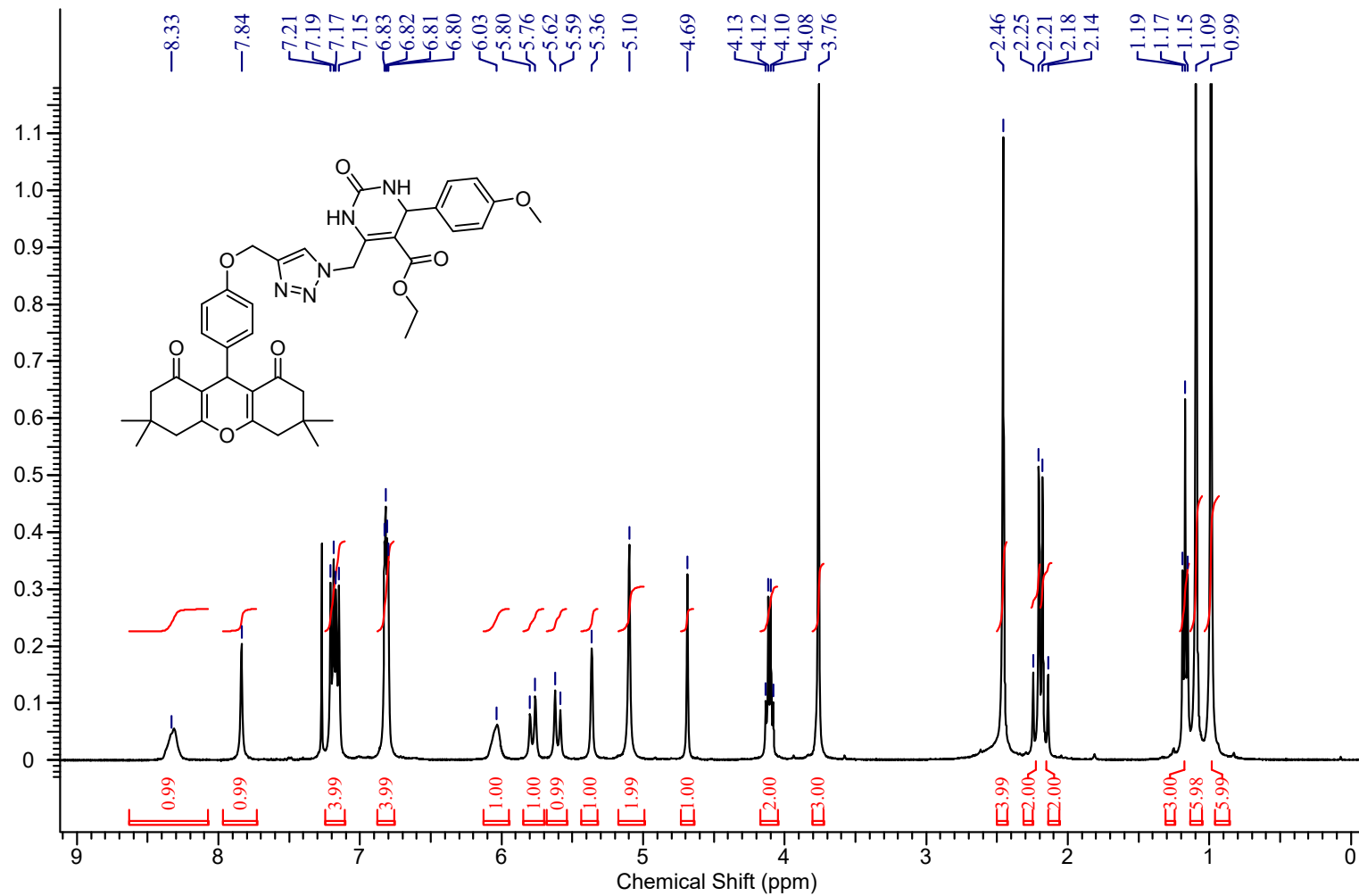


Figure S73: ¹H-NMR (400 MHz, CDCl₃) of 15p.

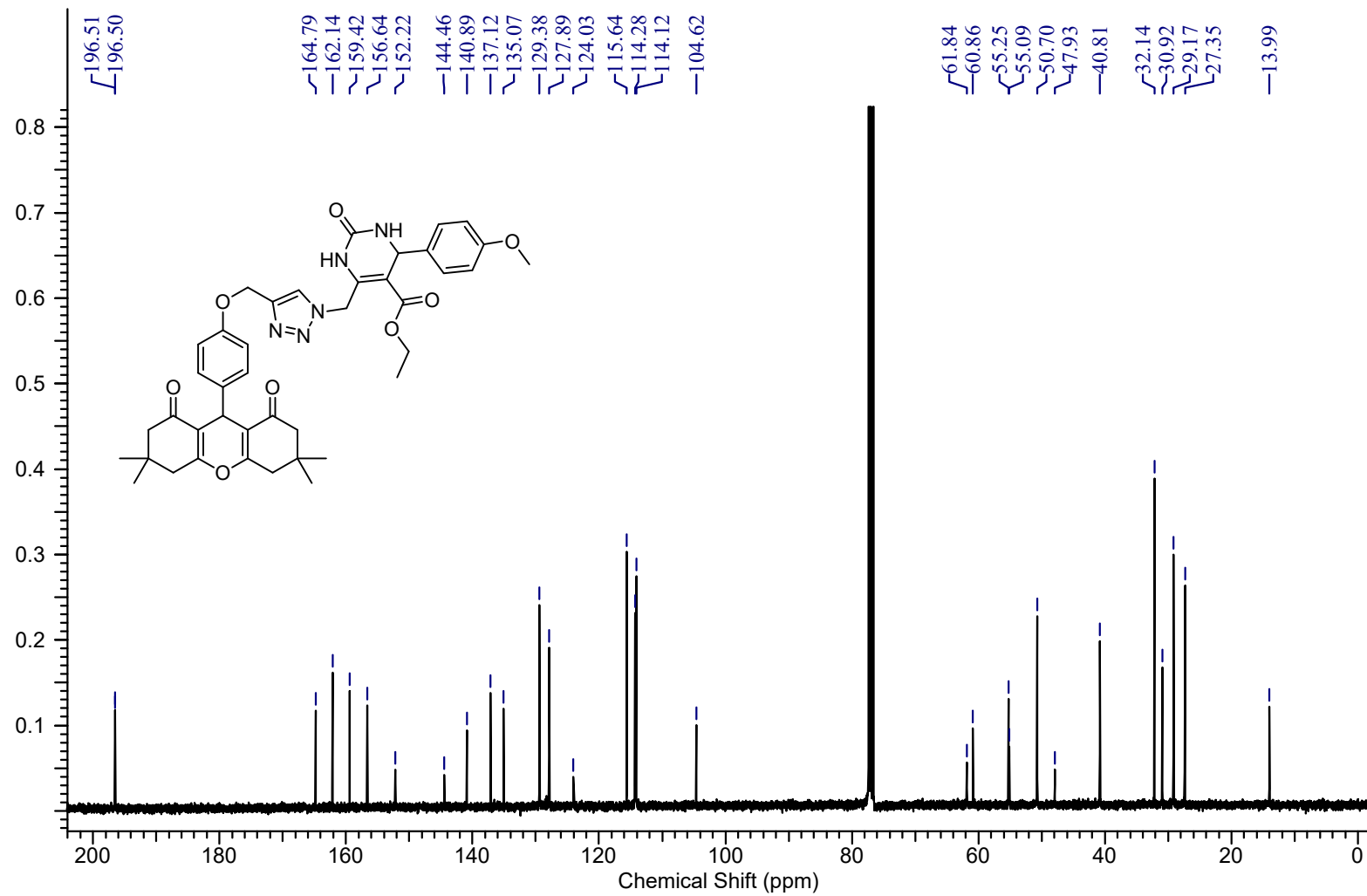


Figure S74: ^{13}C -NMR (100 MHz, CDCl_3) of 15p.

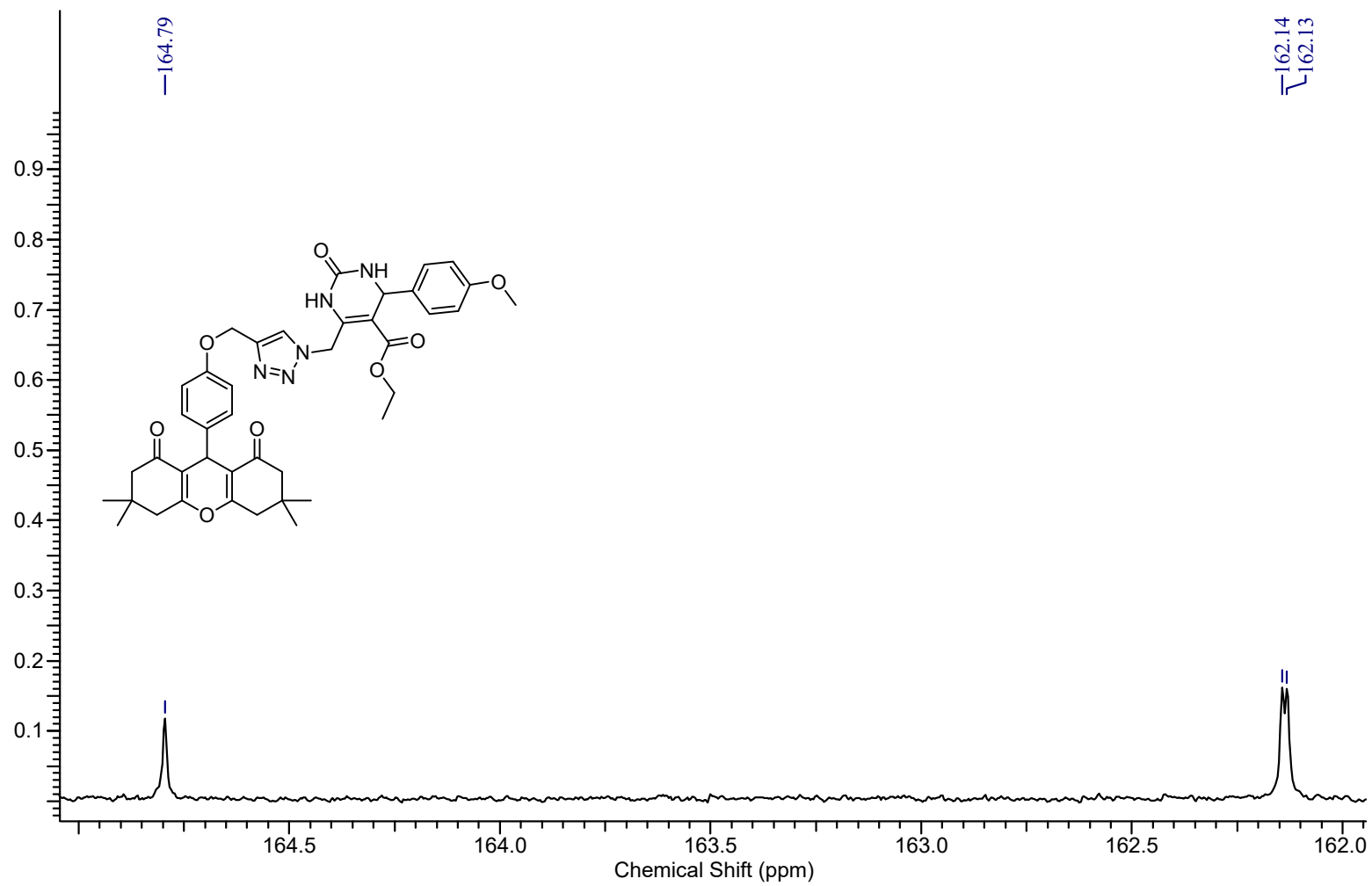


Figure S75: ¹³C-NMR (100 MHz, CDCl₃) of 15o (162.0 to 165.0 ppm).

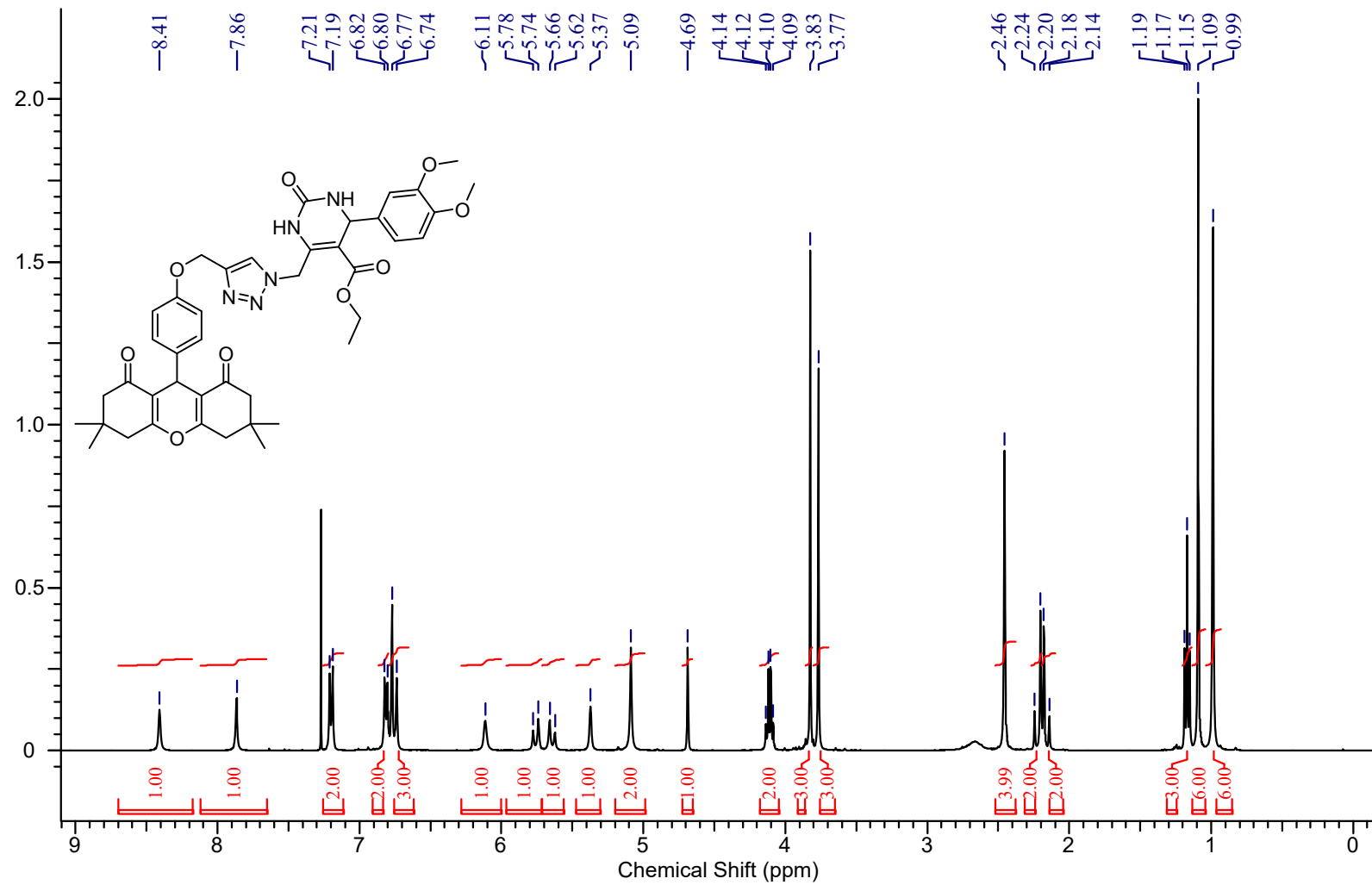


Figure S76: ¹H-NMR (400 MHz, CDCl₃) of 15q.

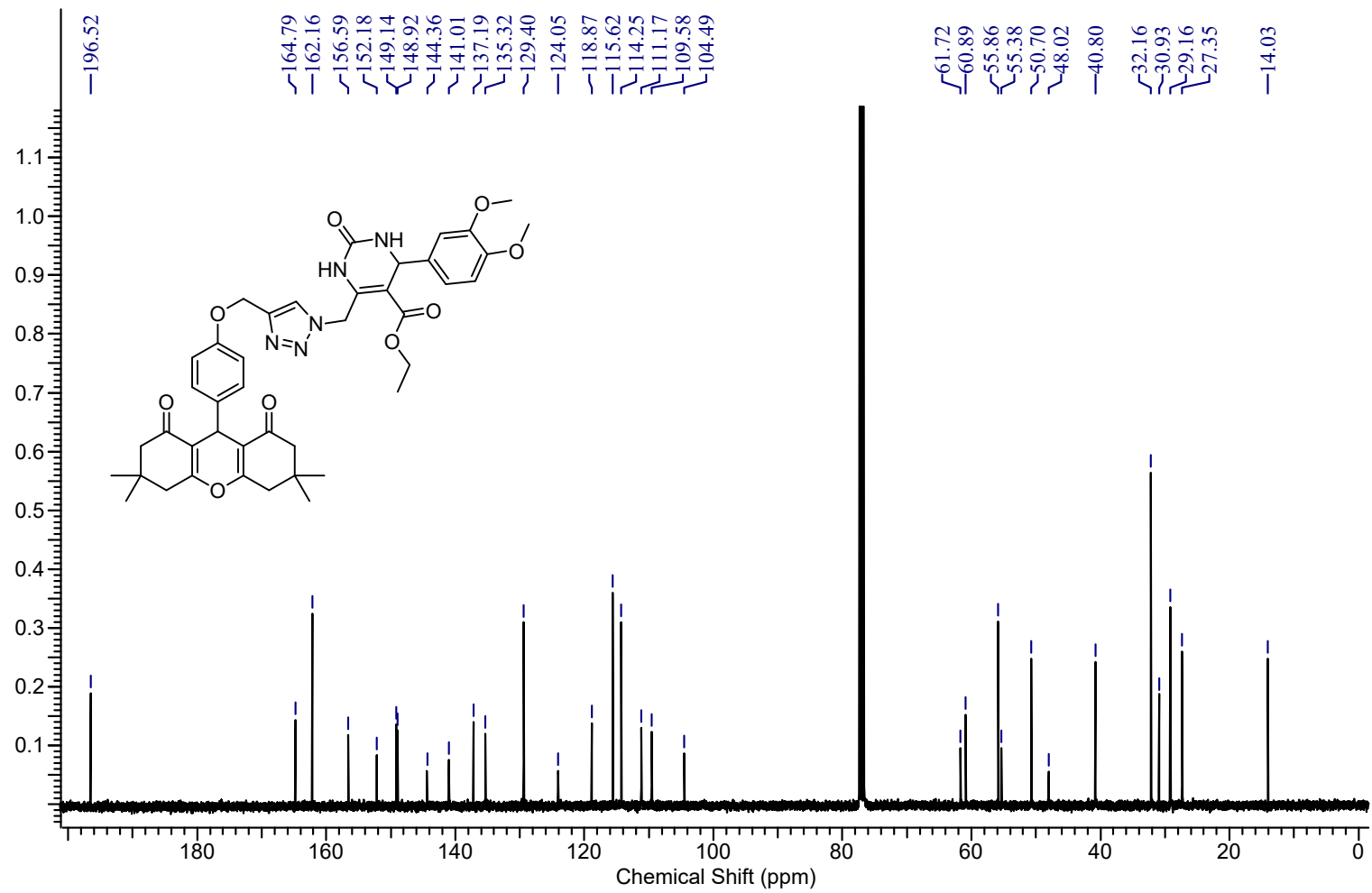


Figure S77: ^{13}C -NMR (100 MHz, CDCl_3) of 15q.

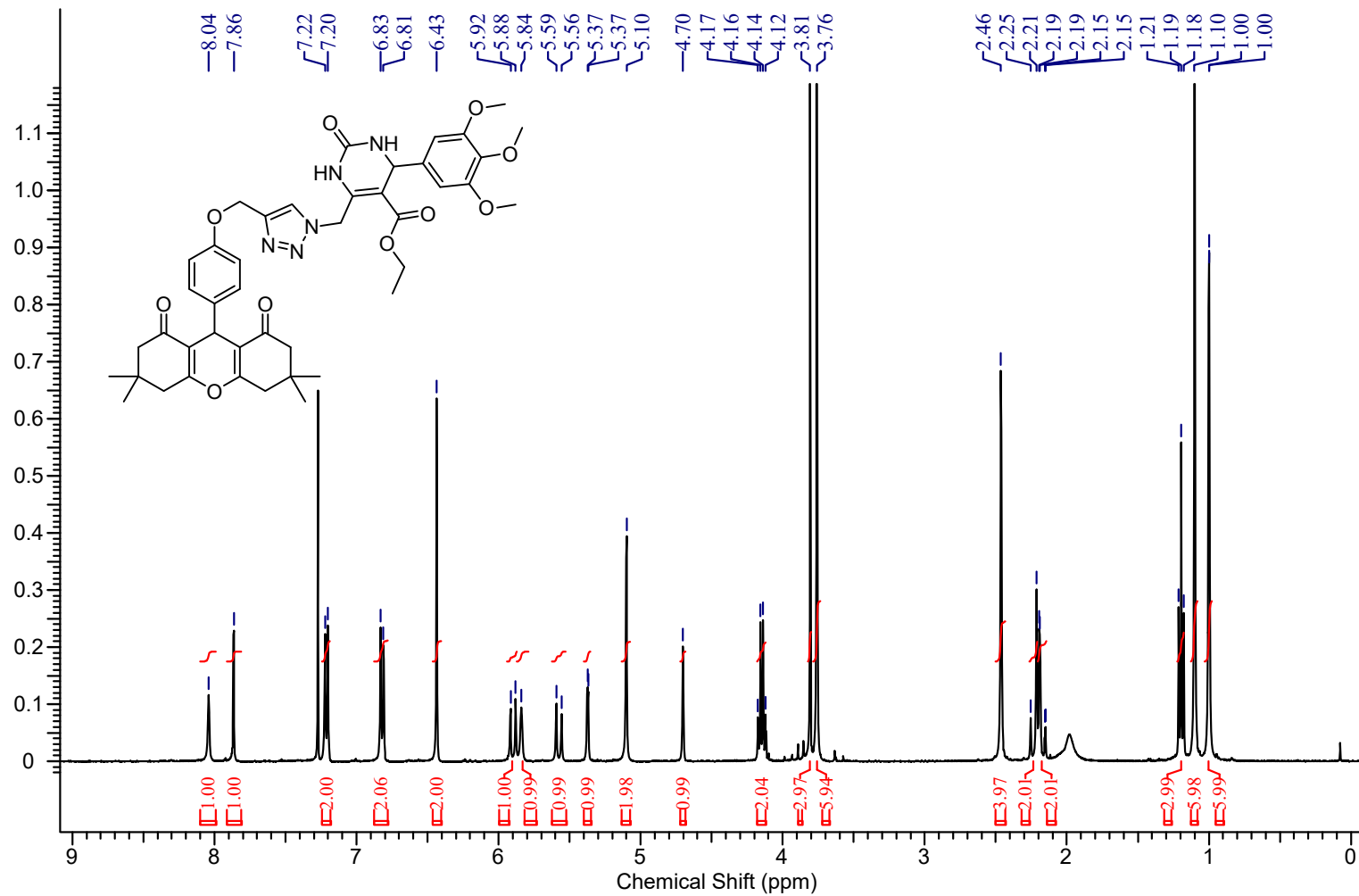


Figure S78: ¹H-NMR (400 MHz, CDCl₃) of 15r.

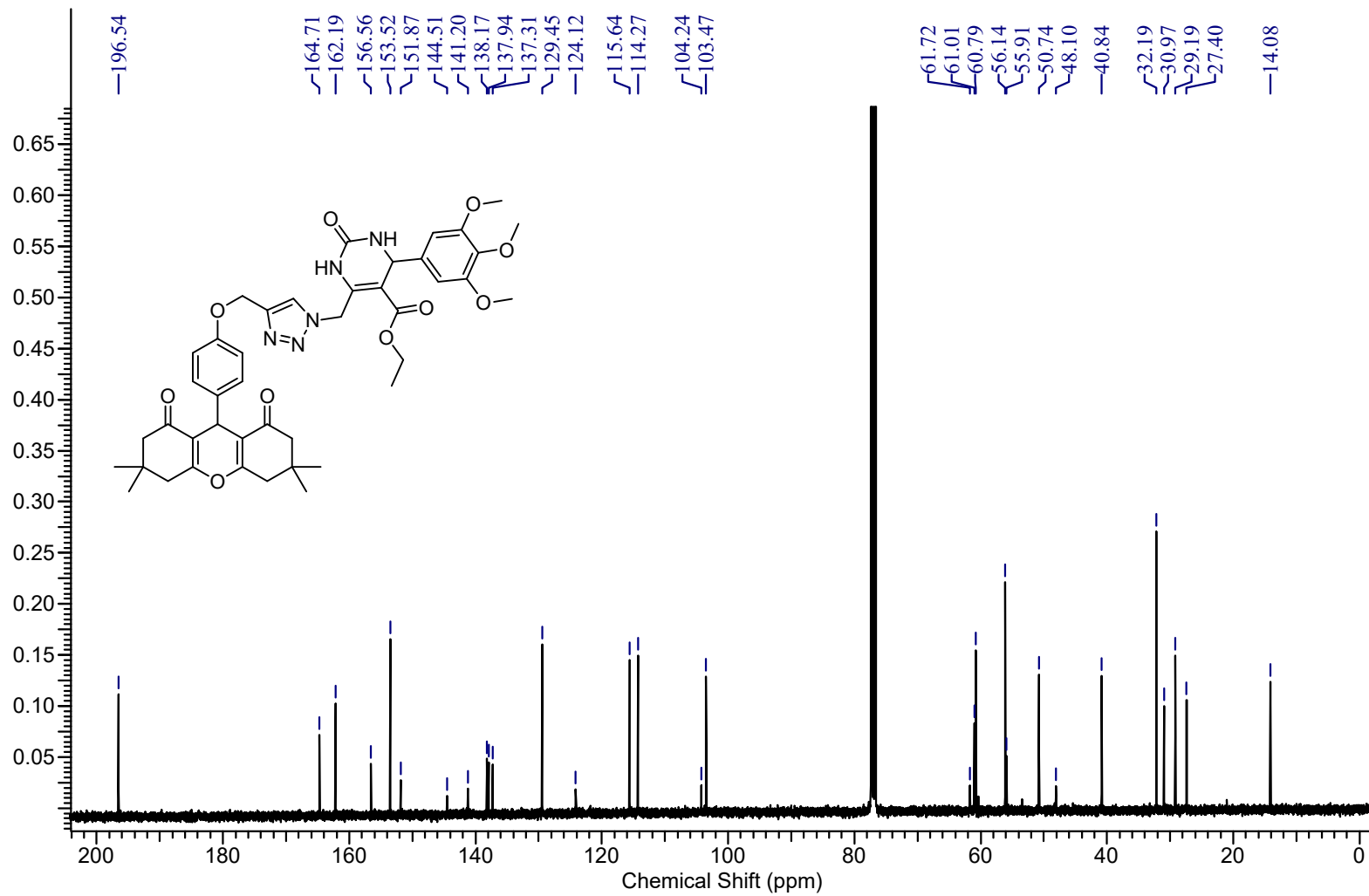


Figure S79: ^{13}C -NMR (100 MHz, CDCl_3) of 15r.

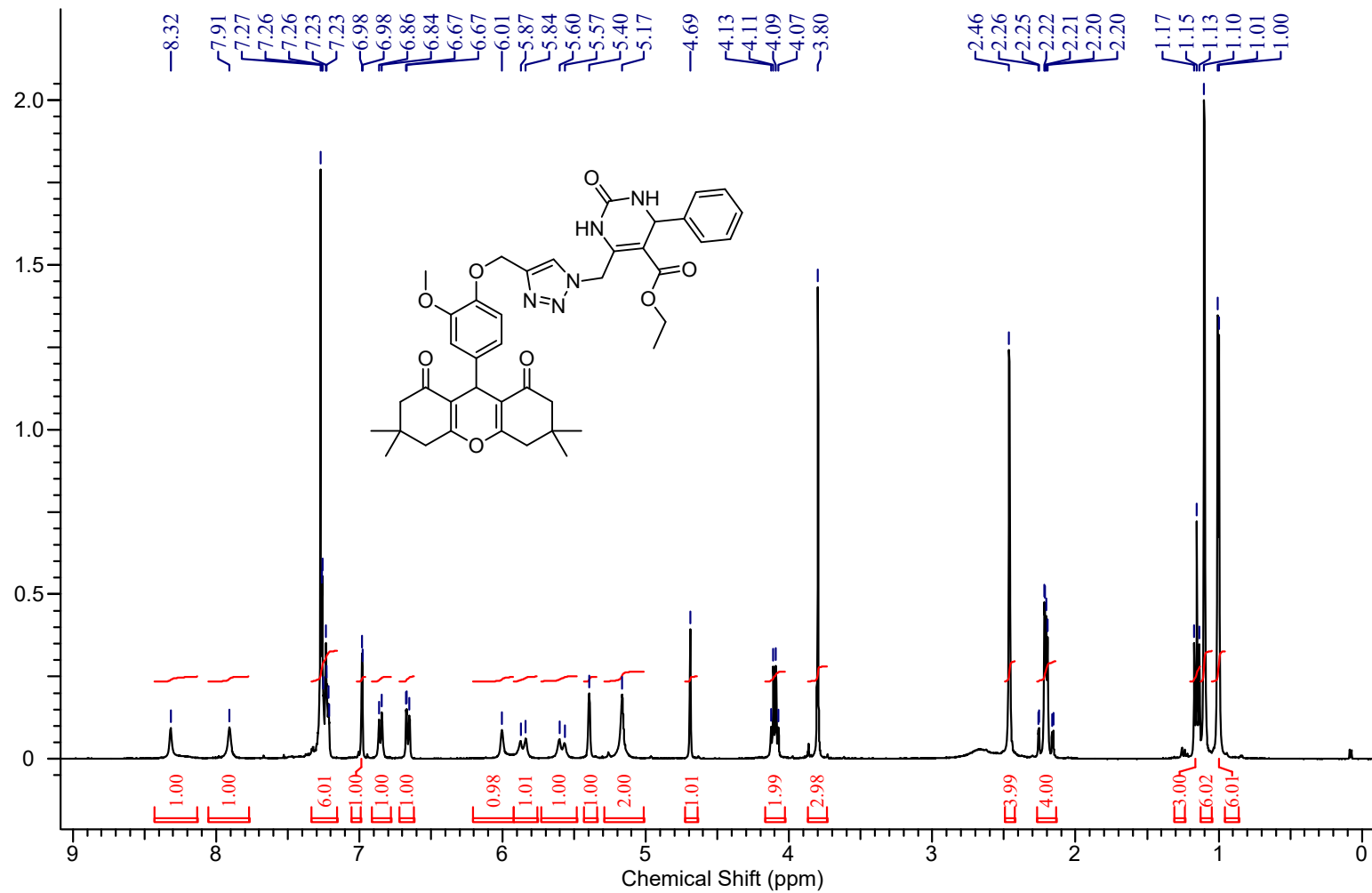


Figure S80: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 15s.

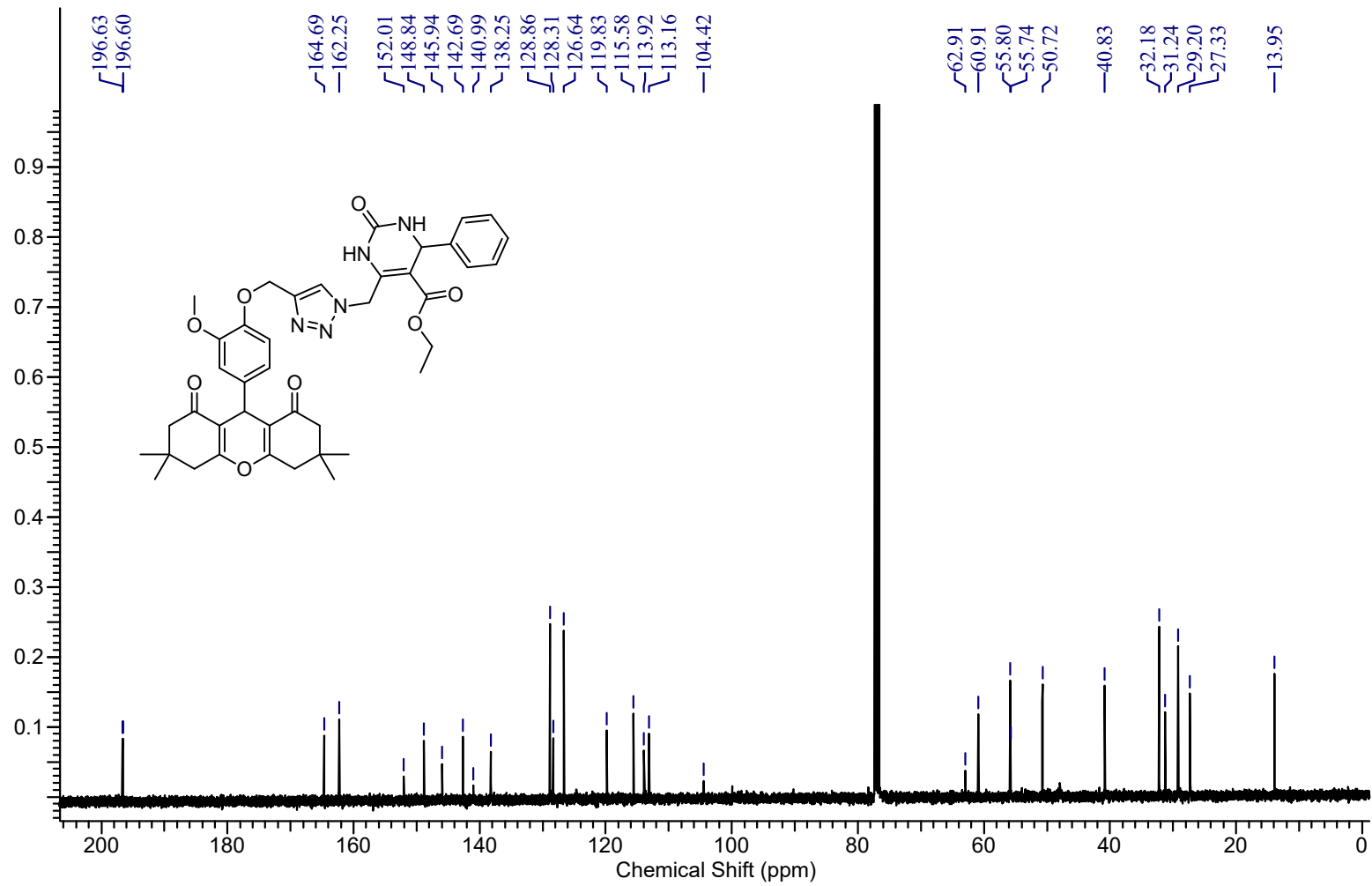


Figure S81: ^{13}C -NMR (100 MHz, CDCl_3) of 15s.

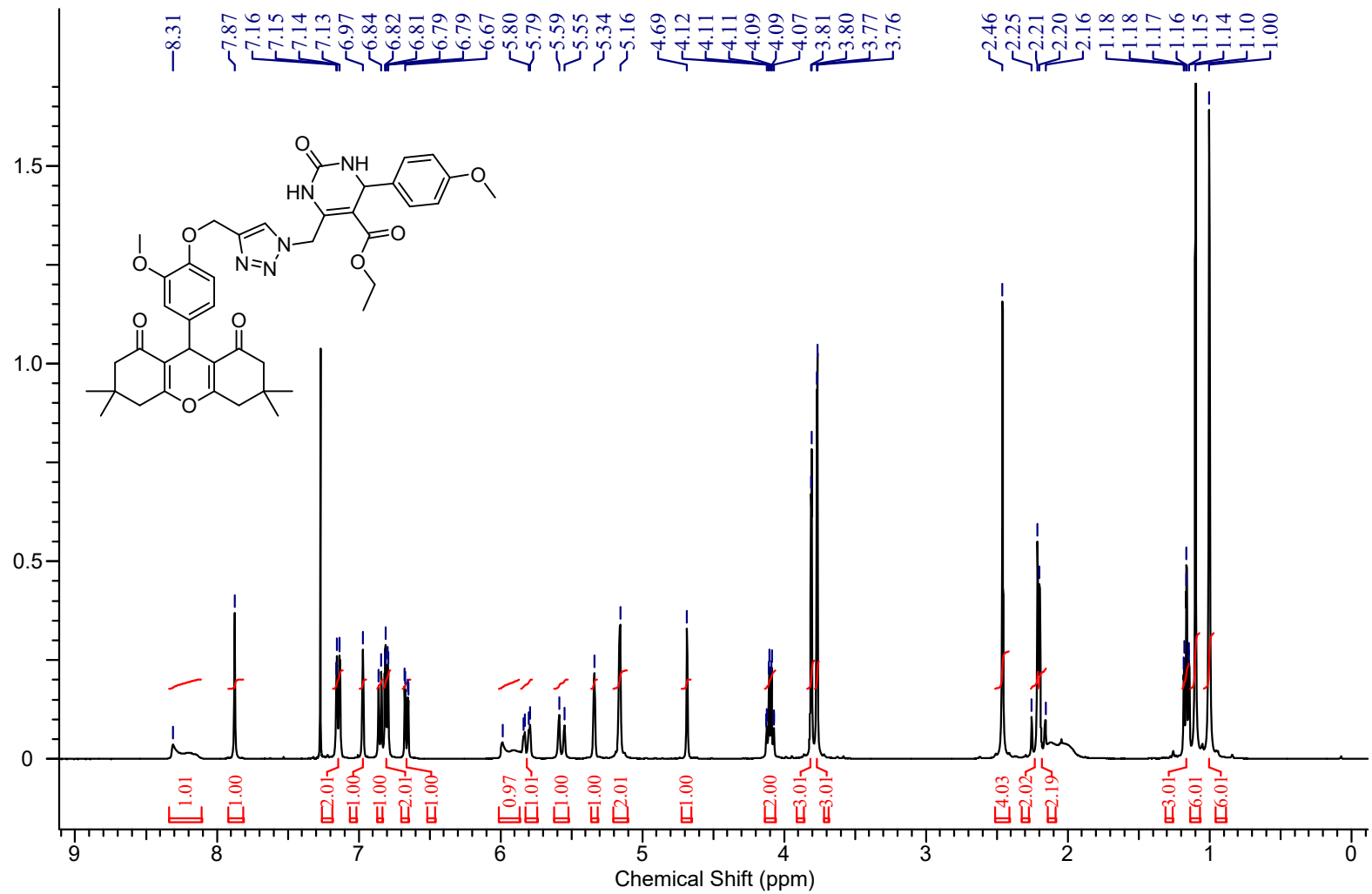


Figure S82: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 15t.

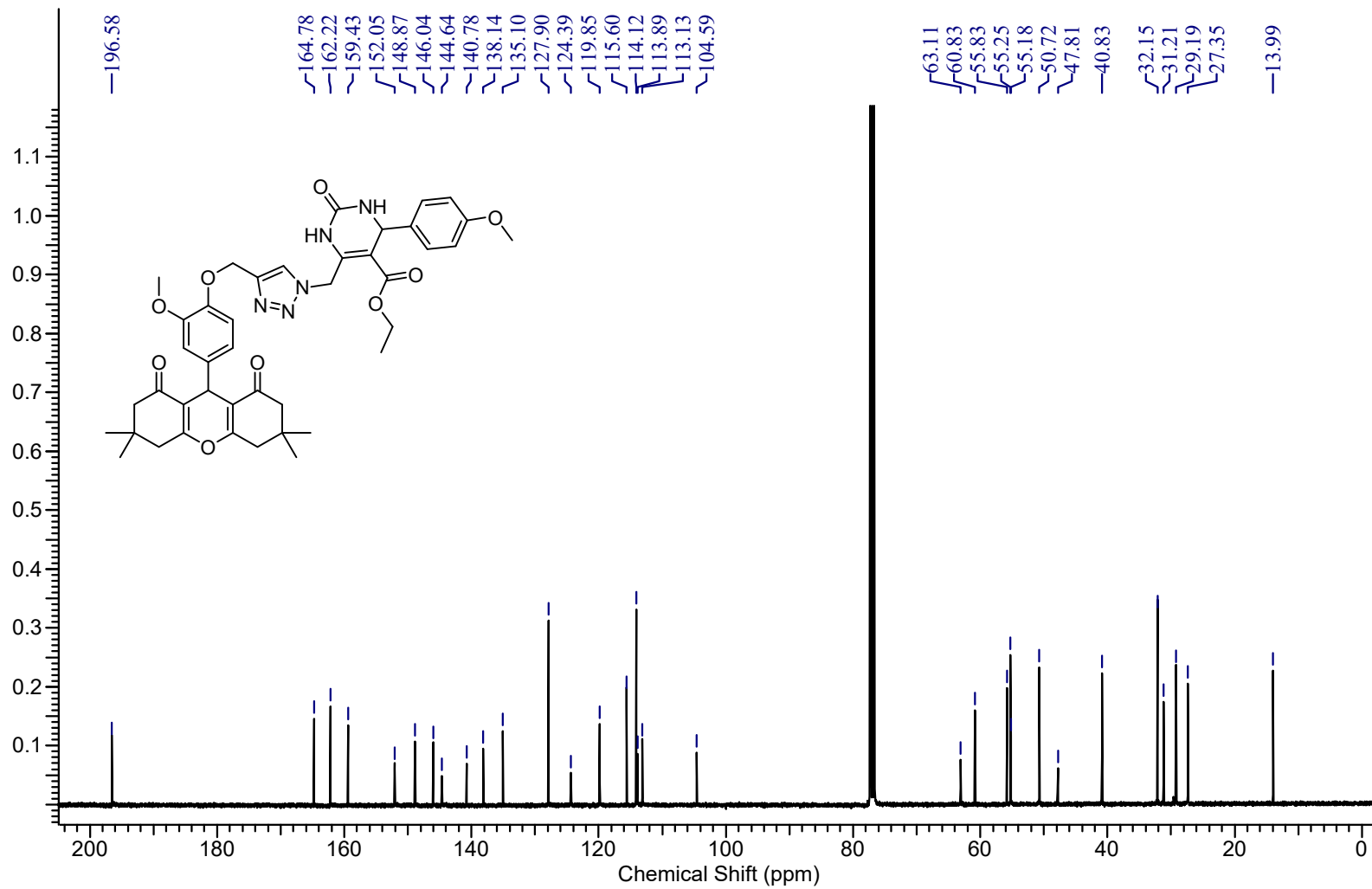


Figure S83: ¹³C-NMR (100 MHz, CDCl₃) of 15t.

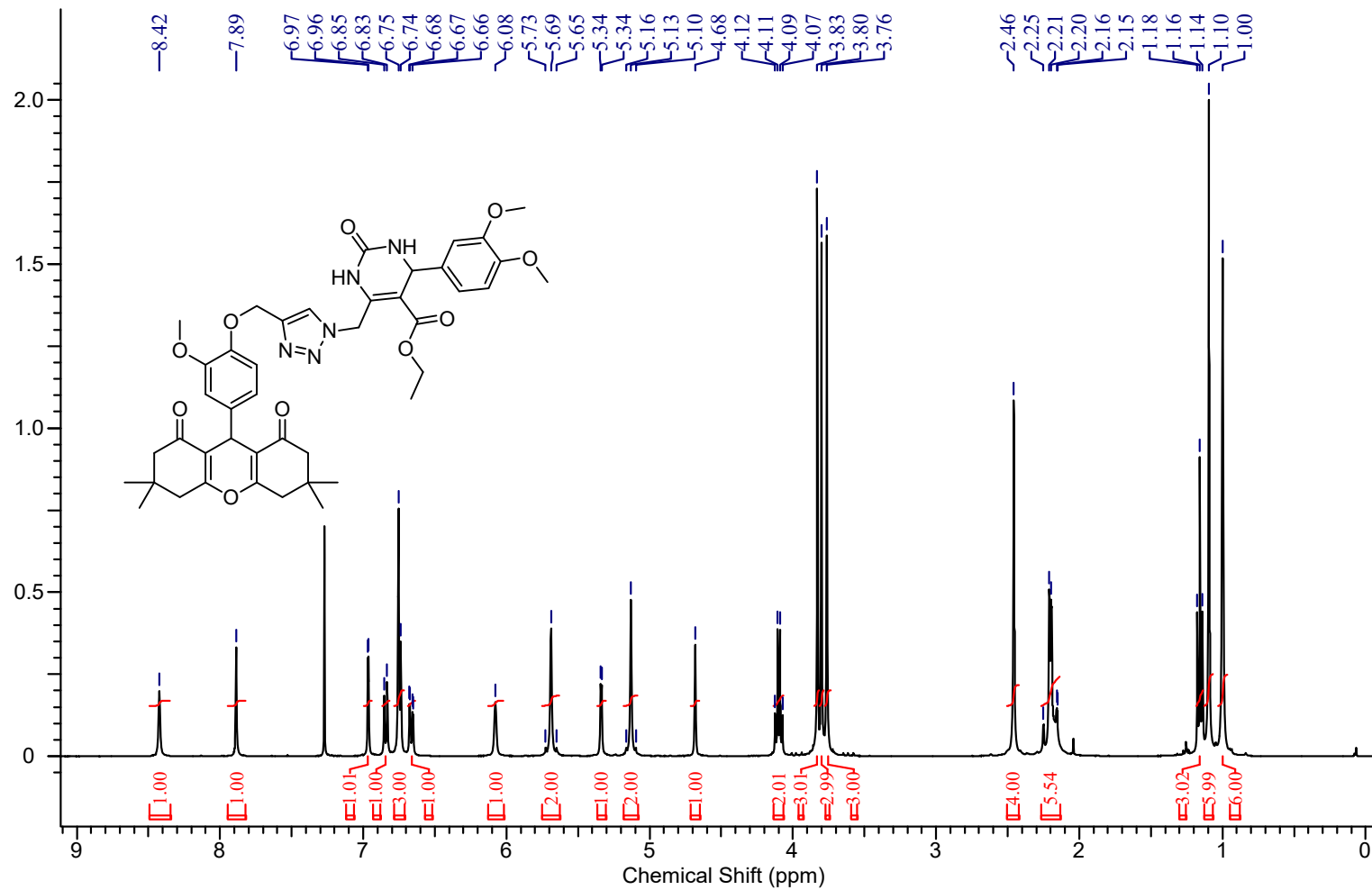


Figure S84: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 15u.

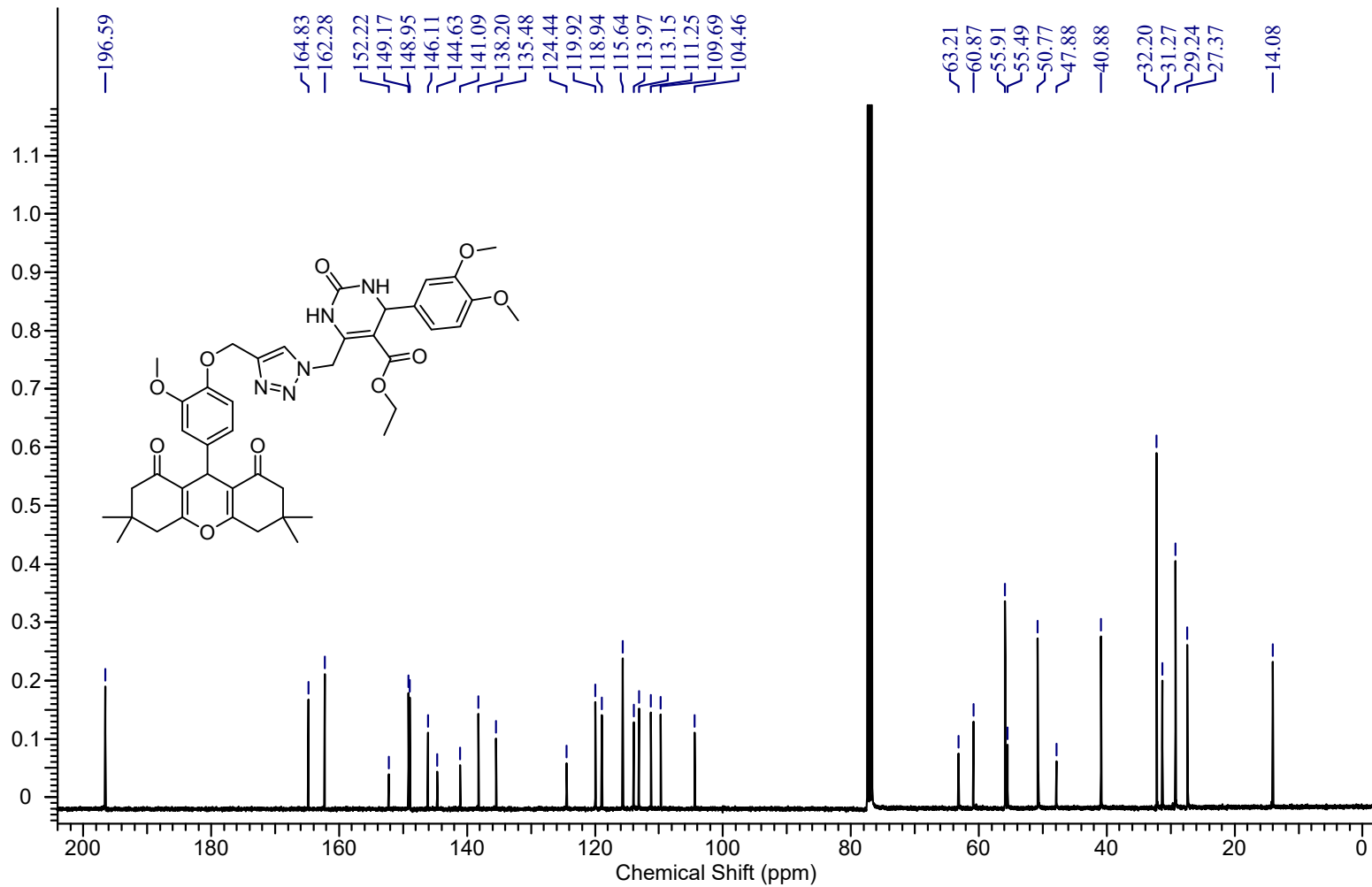


Figure S85: ^{13}C -NMR (100 MHz, CDCl_3) of 15u.

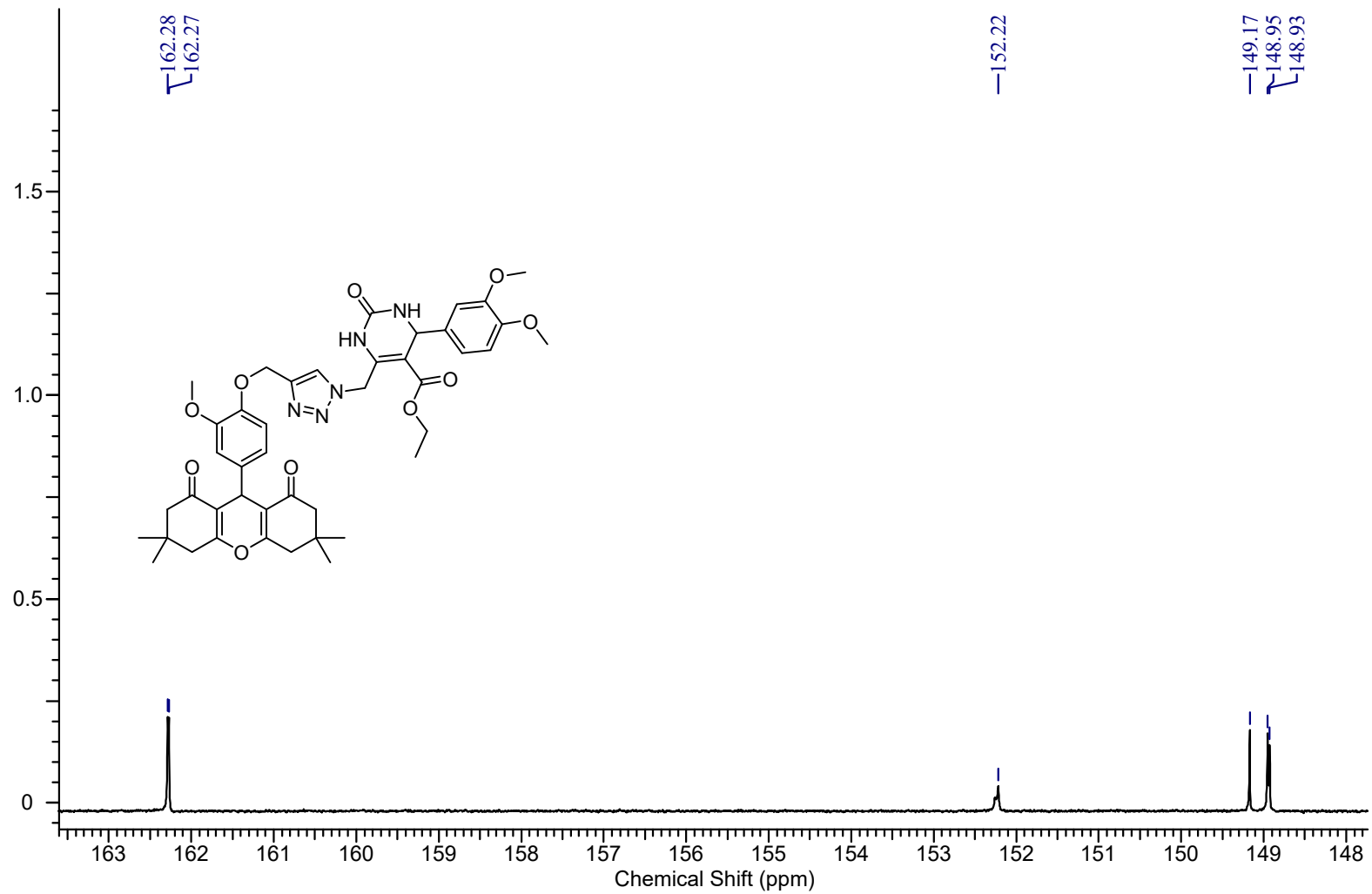


Figure S86: ¹H-NMR (400 MHz, CDCl₃) of 15u (148.0 to 163.0 ppm).

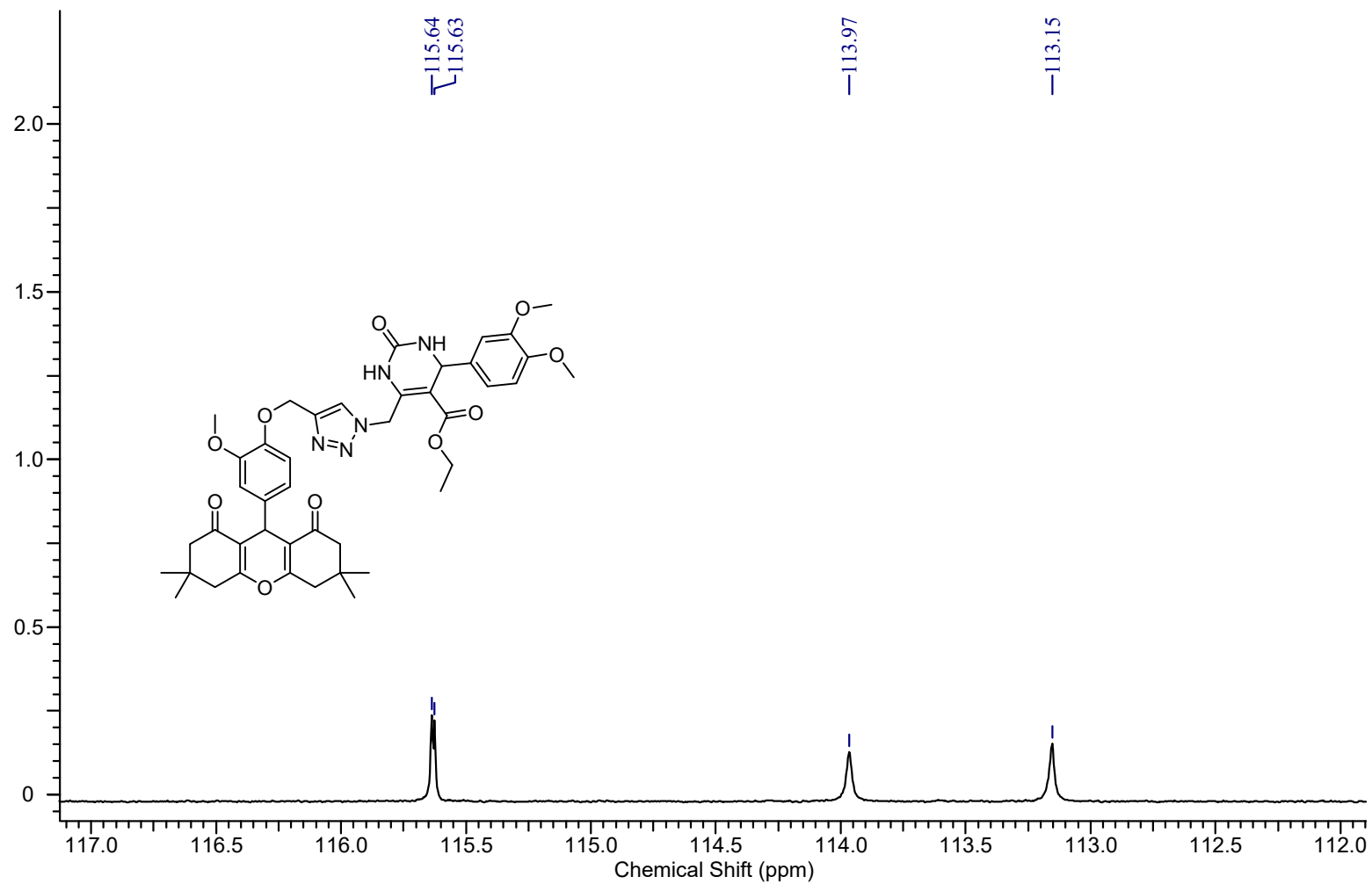


Figure S87: ¹H-NMR (400 MHz, CDCl₃) of 15u (112.0 to 117.0 ppm).

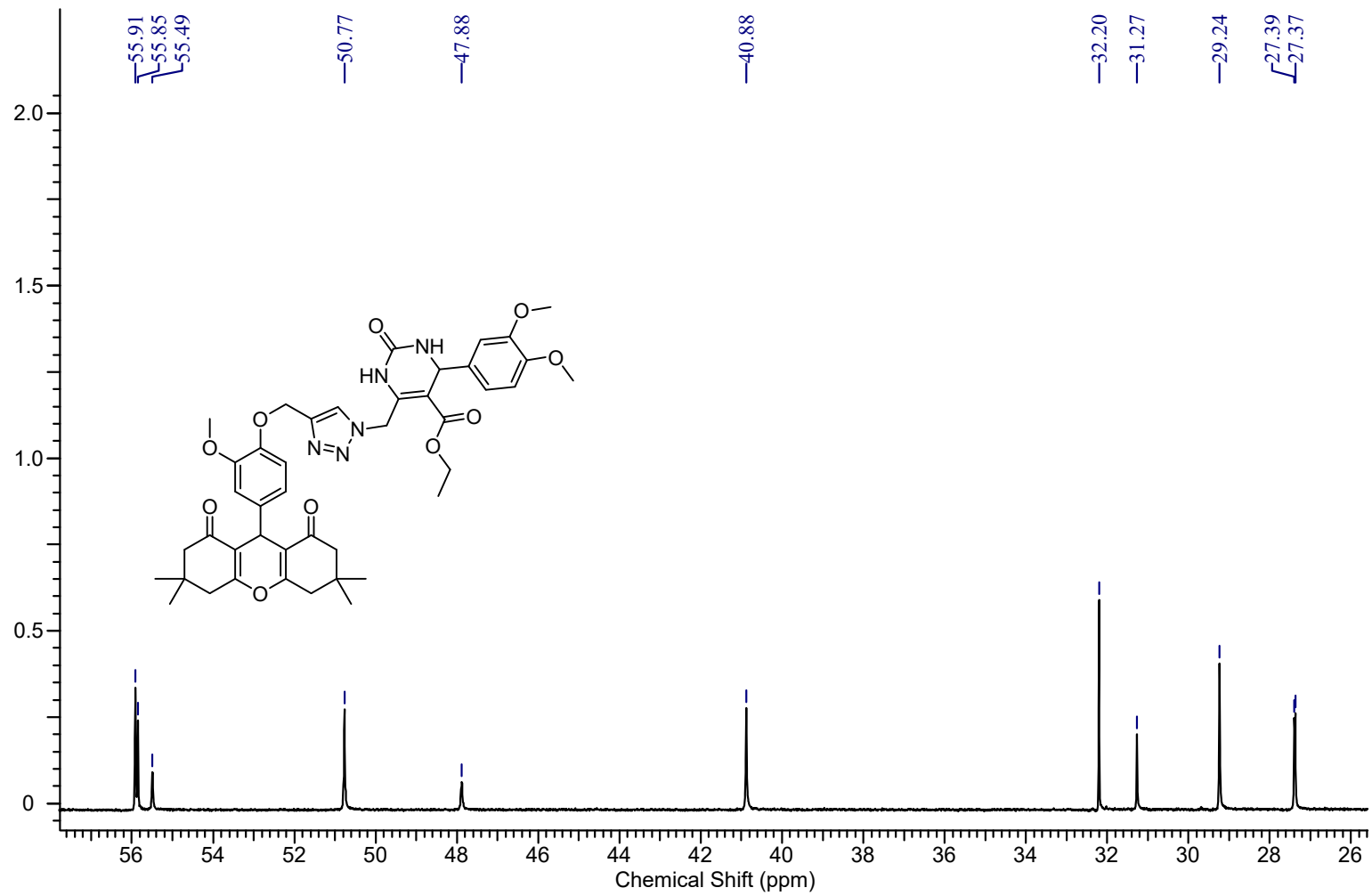


Figure S88: $^1\text{H-NMR}$ (400 MHz, CDCl_3) of 15u (26.0 to 57.0 ppm).

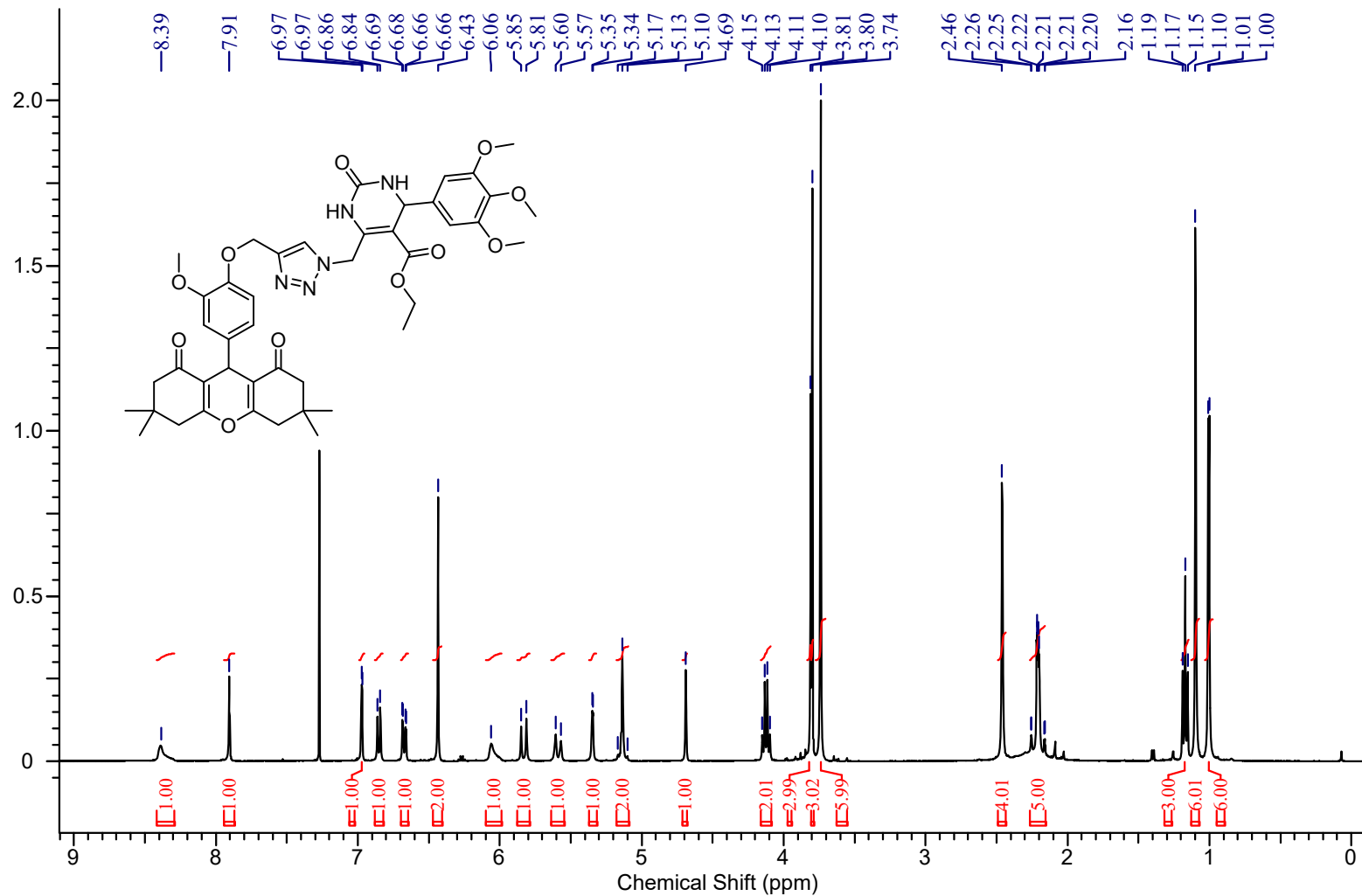


Figure S89: ¹H-NMR (400 MHz, CDCl₃) of 15v.

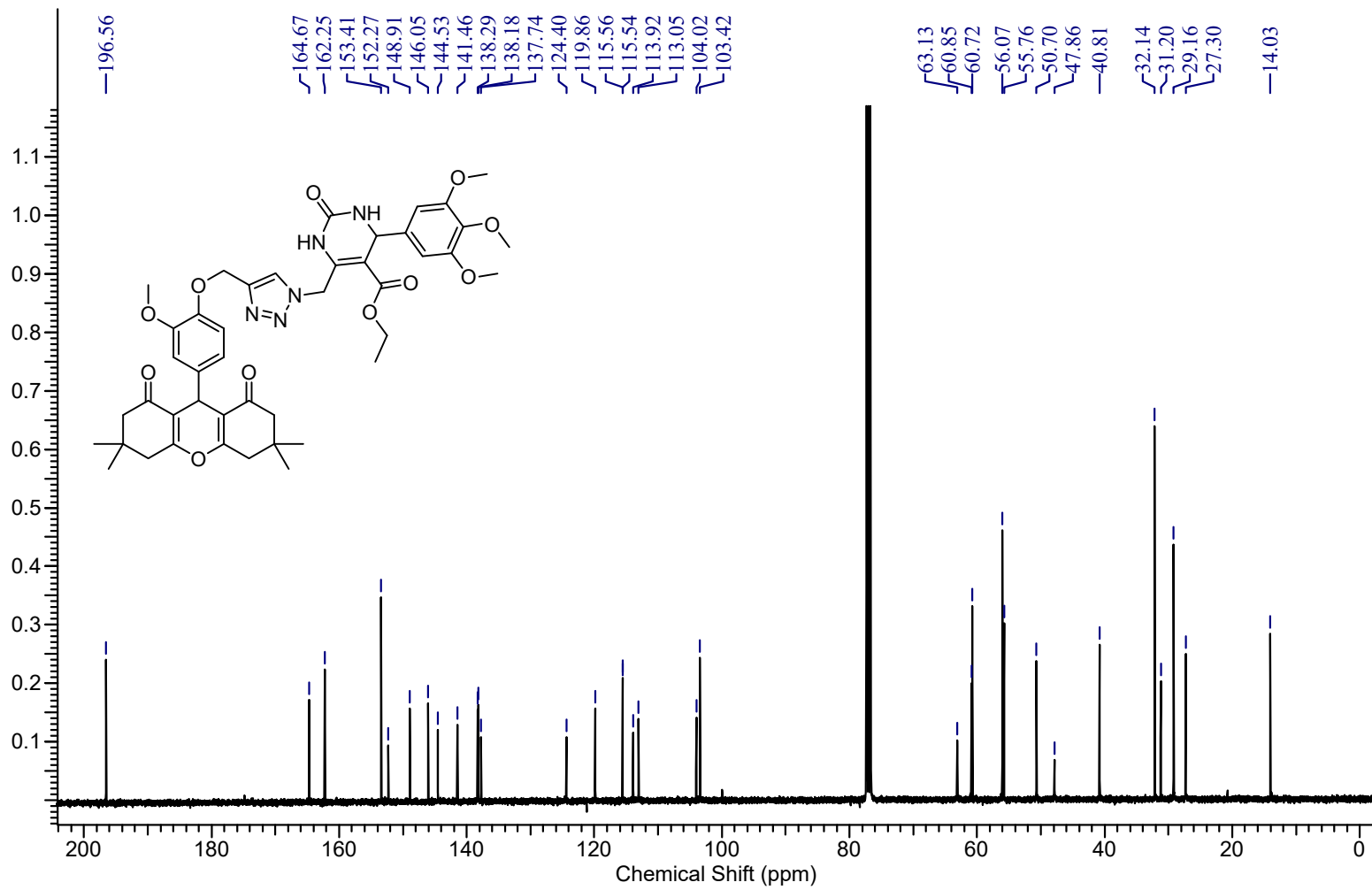


Figure S90: ^{13}C -NMR (100 MHz, CDCl_3) of 15v.

Table S1. Antibiofilm activity of chromene and xanthene derivatives against *S. aureus*. The results are reported in % of biofilm formation at 570 nm compared to the untreated control (100% of biofilm formation).

Compound	Concentration ($\mu\text{g mL}^{-1}$)							
	128	64	32	16	8	4	2	1
15a	46.37 \pm 7.75*	57.10 \pm 7.60*	72.13 \pm 8.68*	82.81 \pm 12.90	90.04 \pm 7.33	91.38 \pm 11.34	94.73 \pm 12.55	100.61 \pm 9.73
15b	50.38 \pm 5.19*	71.76 \pm 5.47*	88.86 \pm 11.15	90.11 \pm 11.75	98.40 \pm 6.01	100.39 \pm 7.57	100.19 \pm 10.72	114.84 \pm 14.10
15c	66.29 \pm 7.48*	97.09 \pm 6.66	103.19 \pm 7.59	110.17 \pm 12.69	110.68 \pm 7.43	105.80 \pm 5.67	110.38 \pm 7.20	106.20 \pm 8.34
15d	76.16 \pm 3.87*	81.32 \pm 7.83*	80.35 \pm 7.45*	103.59 \pm 6.85	109.83 \pm 3.21*	97.48 \pm 5.40	82.96 \pm 3.03*	78.79 \pm 4.46*
15e	65.54 \pm 6.61*	96.21 \pm 12.63	106.70 \pm 9.89	108.20 \pm 9.40	111.99 \pm 13.56	104.38 \pm 8.59	106.06 \pm 5.47	112.39 \pm 15.43
15f	63.89 \pm 9.22*	85.93 \pm 7.31*	93.58 \pm 12.17	95.15 \pm 8.24	93.71 \pm 11.50	92.11 \pm 12.05	93.05 \pm 1.55*	98.78 \pm 9.89
15g	79.15 \pm 8.59*	88.90 \pm 7.41*	99.57 \pm 3.72	104.45 \pm 13.15	95.06 \pm 7.28	92.68 \pm 7.58	98.79 \pm 3.15	108.32 \pm 8.01
15h	85.45 \pm 5.39*	88.63 \pm 9.69	95.40 \pm 10.25	107.73 \pm 9.24	101.00 \pm 5.97	103.15 \pm 10.80	95.60 \pm 6.65	91.92 \pm 8.24
15i	63.29 \pm 1.64*	74.19 \pm 6.71*	88.82 \pm 6.56*	94.85 \pm 4.41	95.90 \pm 5.23	99.91 \pm 7.65	96.78 \pm 9.95	105.47 \pm 10.10
15j	84.57 \pm 5.06*	89.05 \pm 2.46*	94.19 \pm 4.56	98.49 \pm 1.68	100.39 \pm 5.21	95.12 \pm 6.43	93.33 \pm 4.56	93.82 \pm 9.23
15k	79.13 \pm 0.99*	82.45 \pm 5.75*	93.46 \pm 6.76	95.81 \pm 11.60	97.23 \pm 3.48	98.28 \pm 5.52	96.38 \pm 2.08*	99.26 \pm 9.06
15l	58.21 \pm 7.54*	83.67 \pm 7.57*	94.92 \pm 5.87	109.66 \pm 10.46	115.50 \pm 2.21*	114.58 \pm 6.48*	108.90 \pm 2.17*	113.73 \pm 10.32
15m	56.32 \pm 7.78*	78.28 \pm 8.47*	86.31 \pm 8.68	100.58 \pm 4.95	105.67 \pm 5.92	99.28 \pm 9.87	102.03 \pm 5.67	101.10 \pm 9.11
15n	58.25 \pm 7.08*	72.65 \pm 3.90*	98.24 \pm 7.03	111.09 \pm 8.46	108.95 \pm 16.91	104.20 \pm 9.42	106.41 \pm 8.94	109.89 \pm 3.61*
15o	72.75 \pm 11.53*	94.53 \pm 8.34	102.88 \pm 3.99	107.06 \pm 4.11*	123.19 \pm 10.15*	125.86 \pm 16.83	128.31 \pm 20.30	112.80 \pm 0.66
15p	66.38 \pm 7.29*	81.78 \pm 8.16*	92.53 \pm 10.56	107.44 \pm 5.34	116.65 \pm 7.14*	116.10 \pm 8.13*	111.82 \pm 5.86*	123.08 \pm 11.85*
15q	54.19 \pm 8.46*	63.00 \pm 11.32*	69.72 \pm 7.74*	79.14 \pm 7.16*	87.23 \pm 8.11	86.24 \pm 6.98*	90.48 \pm 6.34	90.32 \pm 12.47
15r	71.01 \pm 10.46*	73.86 \pm 4.43*	99.84 \pm 7.08	106.88 \pm 7.38	107.16 \pm 9.26	101.83 \pm 6.30	102.49 \pm 1.34	102.24 \pm 1.49
15s	73.80 \pm 8.21*	88.58 \pm 8.85	91.59 \pm 9.14	96.09 \pm 7.89	99.42 \pm 4.48	101.18 \pm 8.74	103.24 \pm 8.76	122.70 \pm 8.60*
15t	76.65 \pm 5.99*	81.96 \pm 5.61*	98.70 \pm 8.86	103.19 \pm 7.03	110.63 \pm 10.96	111.57 \pm 9.44	107.43 \pm 11.63	110.11 \pm 10.22
15u	82.15 \pm 5.40*	94.10 \pm 2.04*	97.61 \pm 2.26	99.55 \pm 3.58	105.11 \pm 3.14*	101.54 \pm 2.32	98.16 \pm 5.74	97.28 \pm 4.69
15v	77.29 \pm 6.03*	97.70 \pm 10.79	99.60 \pm 11.40	103.19 \pm 3.87	103.10 \pm 8.90	100.60 \pm 14.78	102.28 \pm 4.54	106.41 \pm 7.02
Vancomycin	Concentration ($\mu\text{g mL}^{-1}$)							
	16	8	4	2	1	0.5	0.25	0.125
	9.55 \pm 1.46*	10.27 \pm 0.98*	12.88 \pm 4.80*	19.22 \pm 3.22*	23.77 \pm 1.80*	26.84 \pm 4.10*	38.13 \pm 3.93*	49.80 \pm 4.65*

* $p < 0.05$.