Electronic Supplementary Material (ESI) for RSC Advances.

Pyrrolizine/indolizine-bearing (un)substituted isoindole moiety: design, synthesis, antiproliferative and MDR reversal activities and in silico studies.

Amr L. AbdelSamad[a], Mohammed T. El-Saadi[b,c], Ahmed M. Gouda[b], Asmaa M. AboulMagd[a*]

[a] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Nahda University in Beni-Suef (NUB), Beni-Suef 62513, Egypt.

[b] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Beni-Suef University, Beni-Suef 62514, Egypt.

[c] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Sinai University-Kantra Branch, Ismaillia, Egypt.

[*] Corresponding author email: asmaa.aboulmaged@nub.edu.eg

Supplementary data

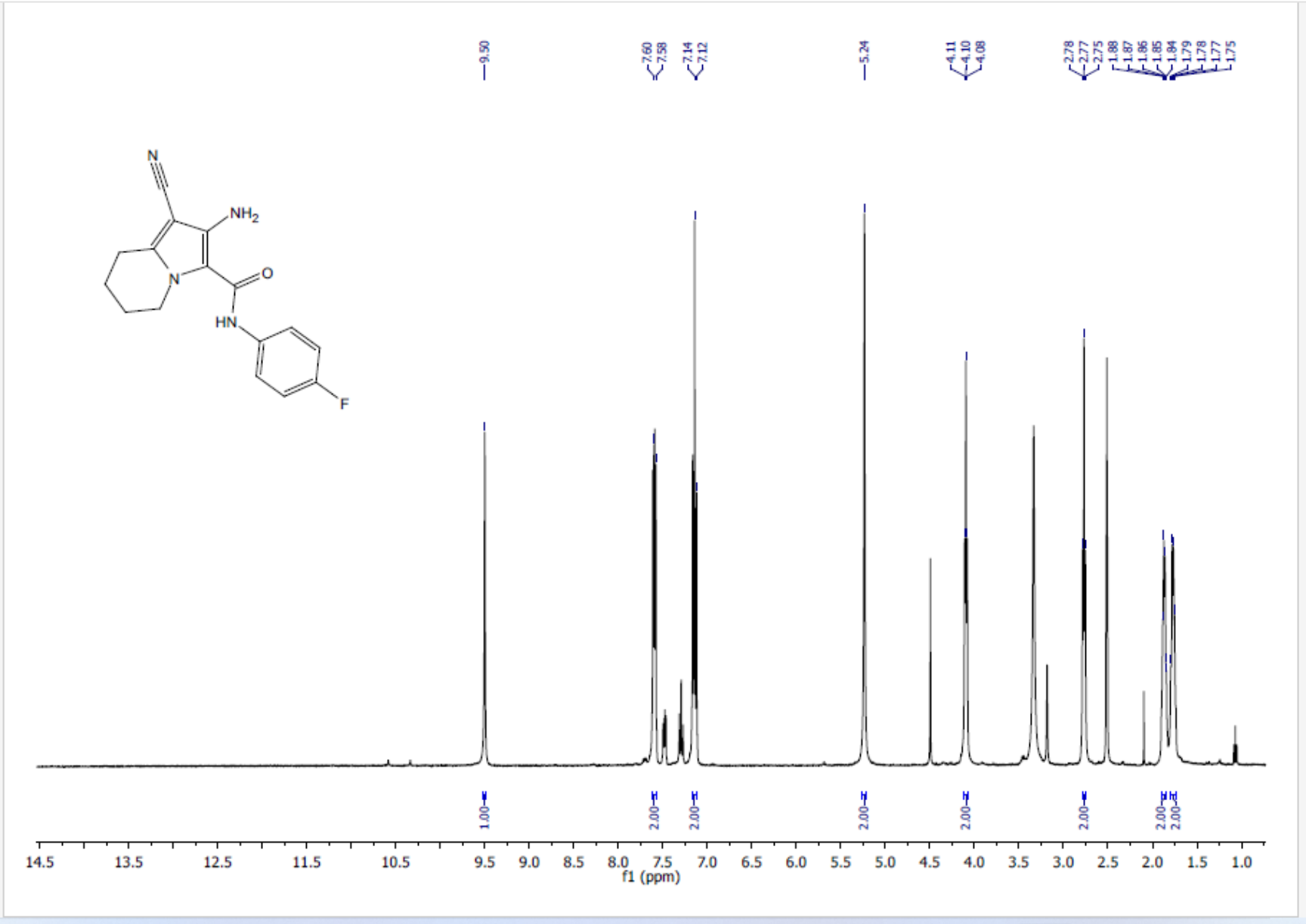


Fig.1. ^{1}H NMR of intermediate 5i (400 MHz, DMSO-d_6)

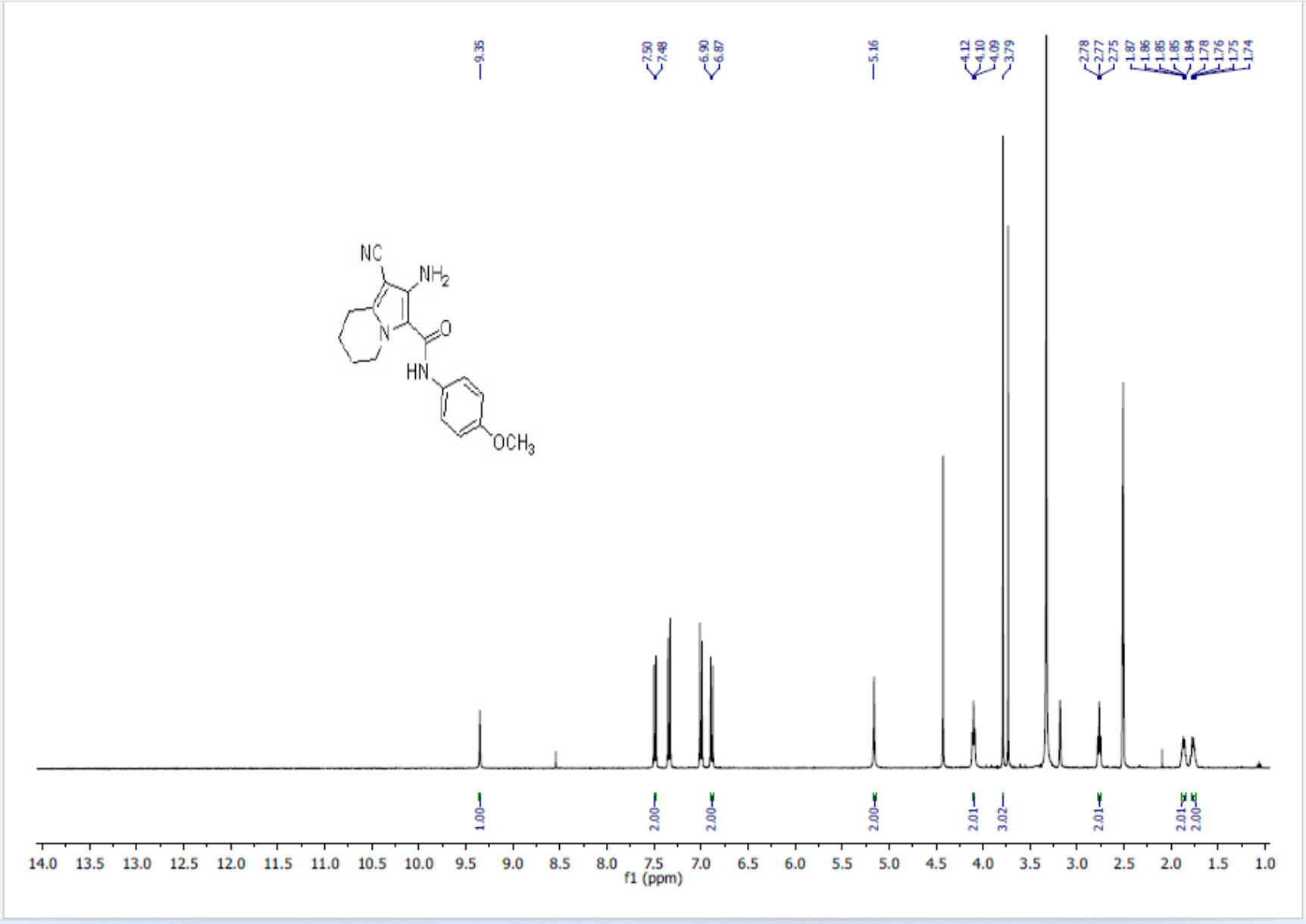


Fig.2. ^{1}H NMR of intermediate 5j (400 MHz, DMSO-d_6)

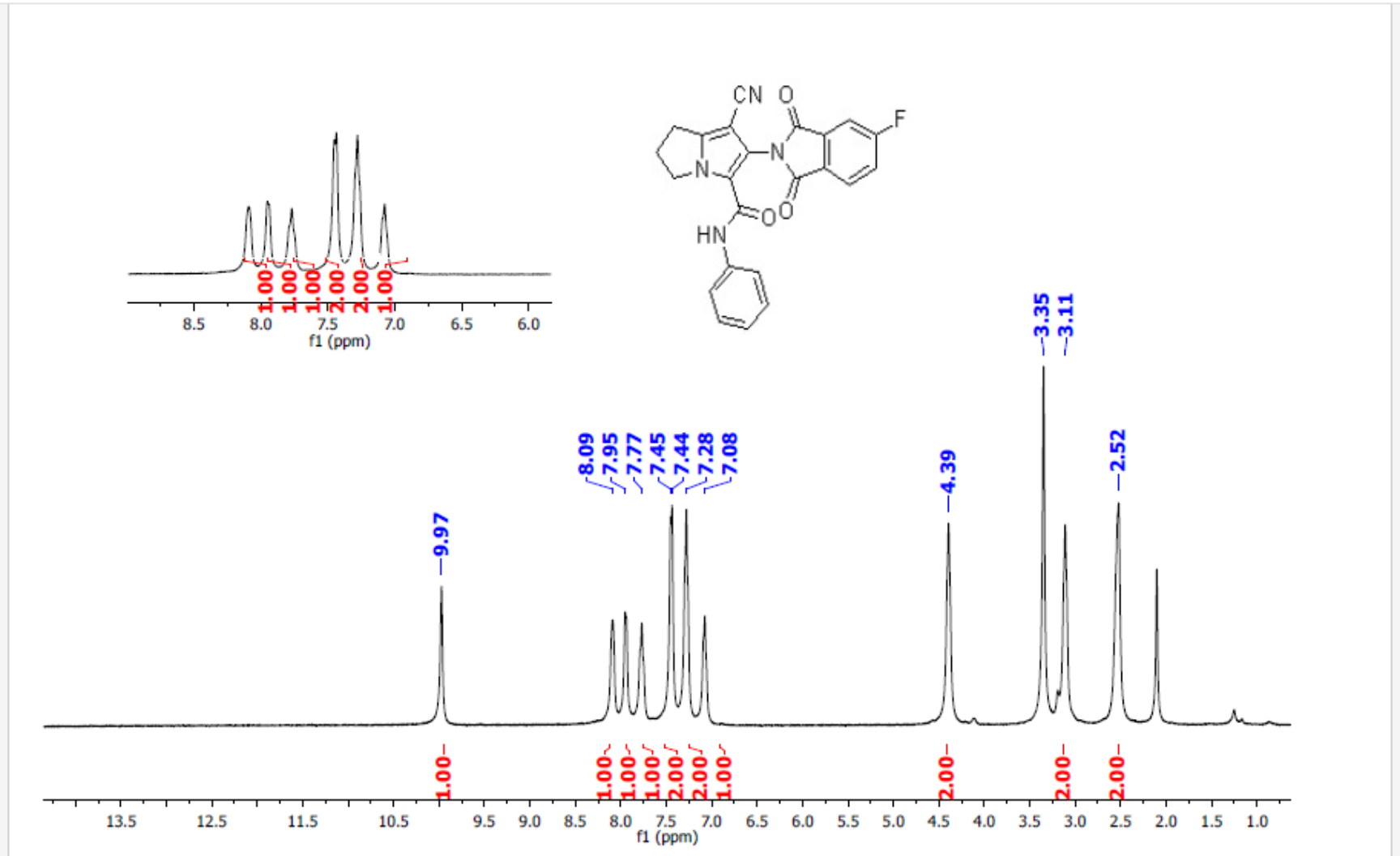


Fig.3. ^{1}H NMR of compound 6a (400 MHz, DMSO-d_6)

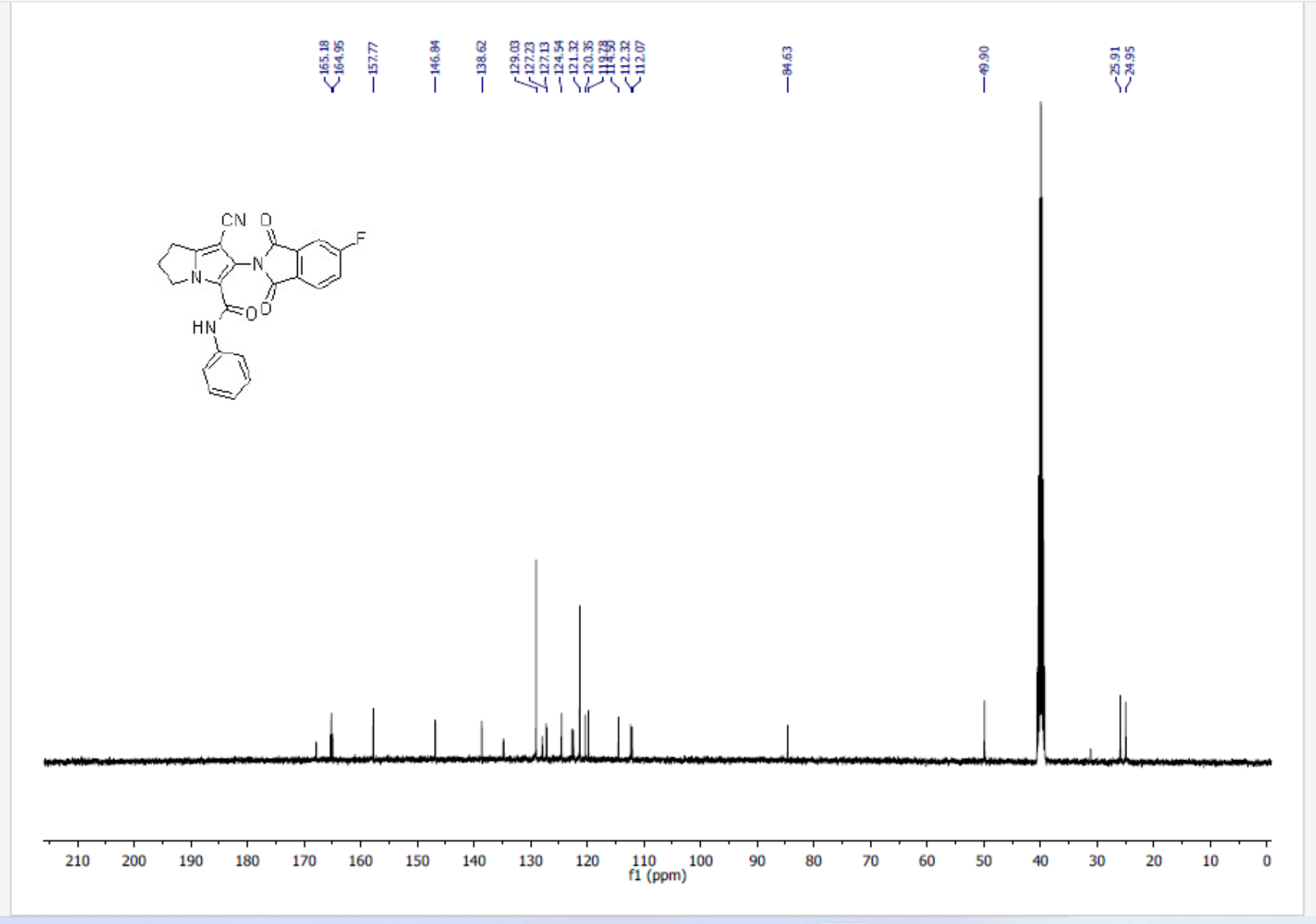


Fig.5. ^{13}C NMR of compound 6a (100 MHz, DMSO-d_6)

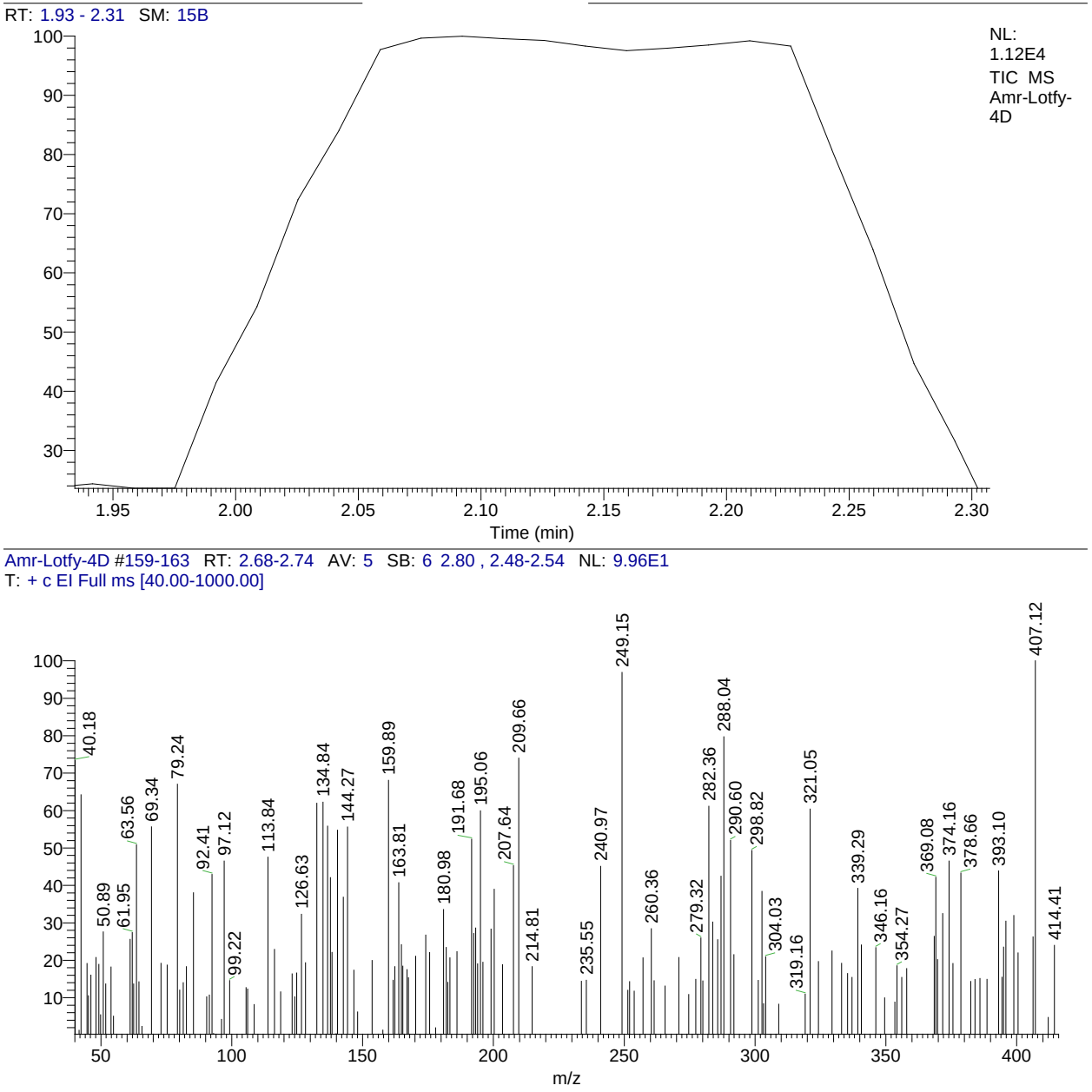


Fig.4. Mass spectra of compound 6a

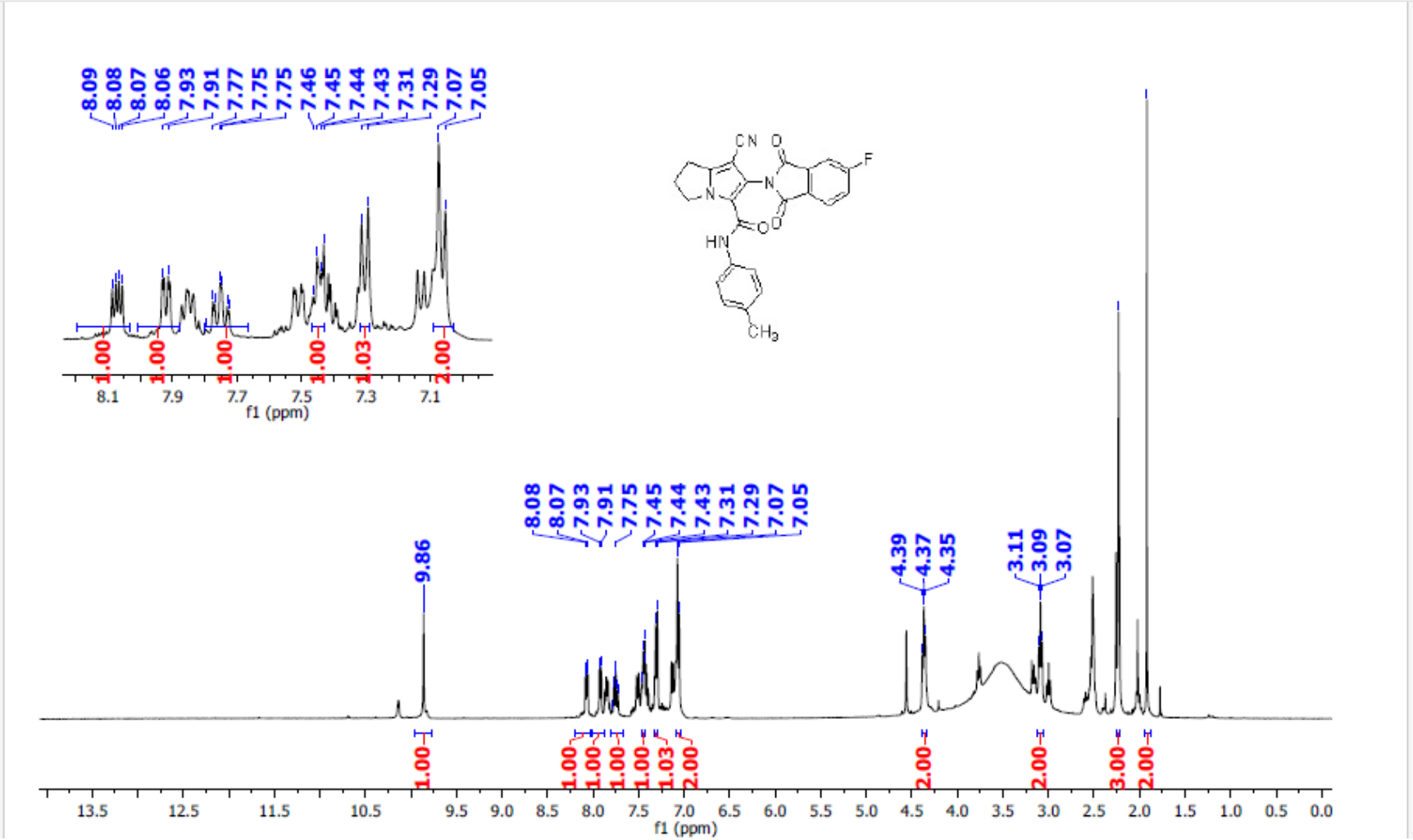


Fig.5. ^{1}H NMR of compound 6b (400 MHz, DMSO-d_6)

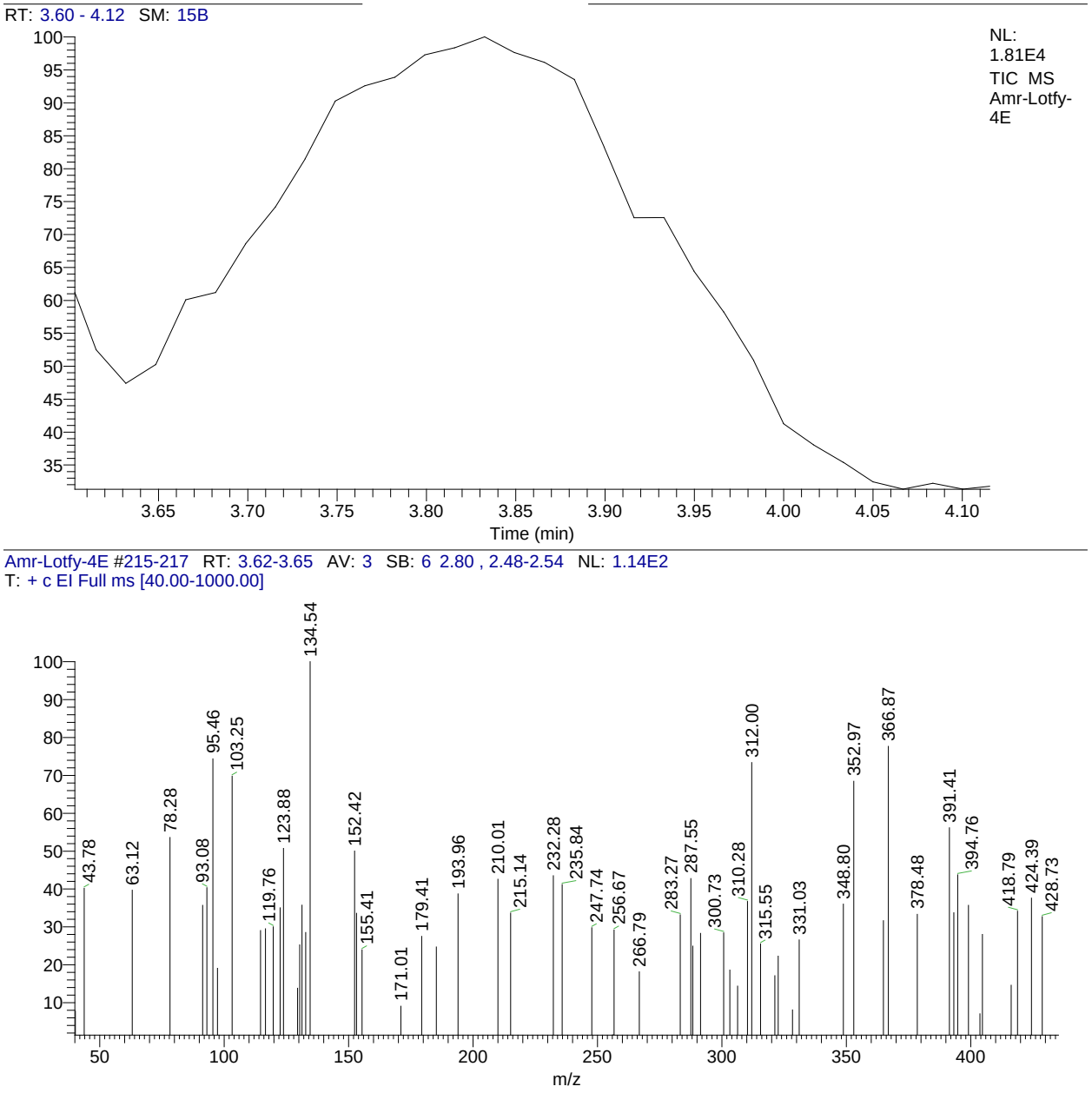


Fig.6. Mass spectra of compound 6b

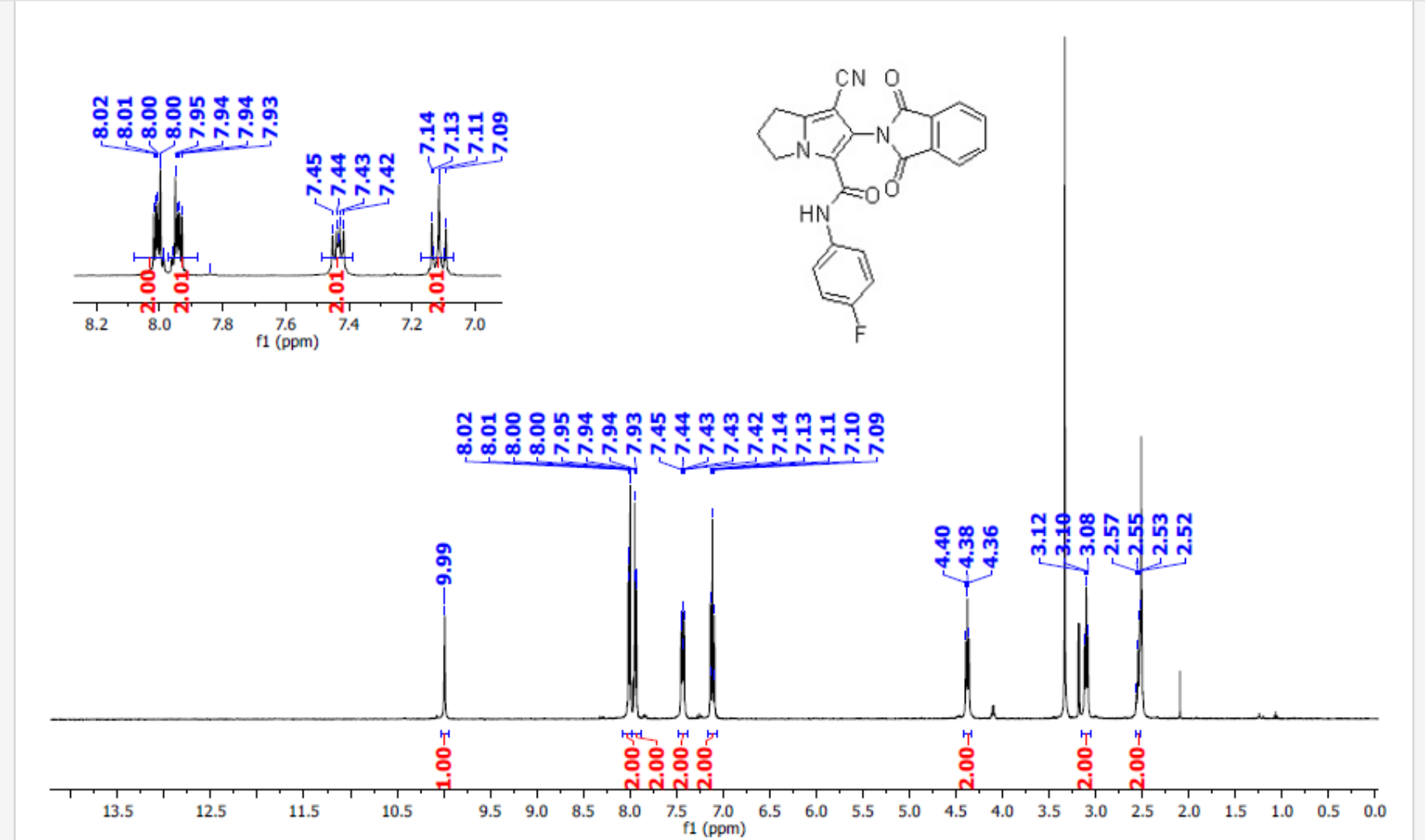


Fig.7. ^{1}H NMR of compound 6c (400 MHz, DMSO-d_6)

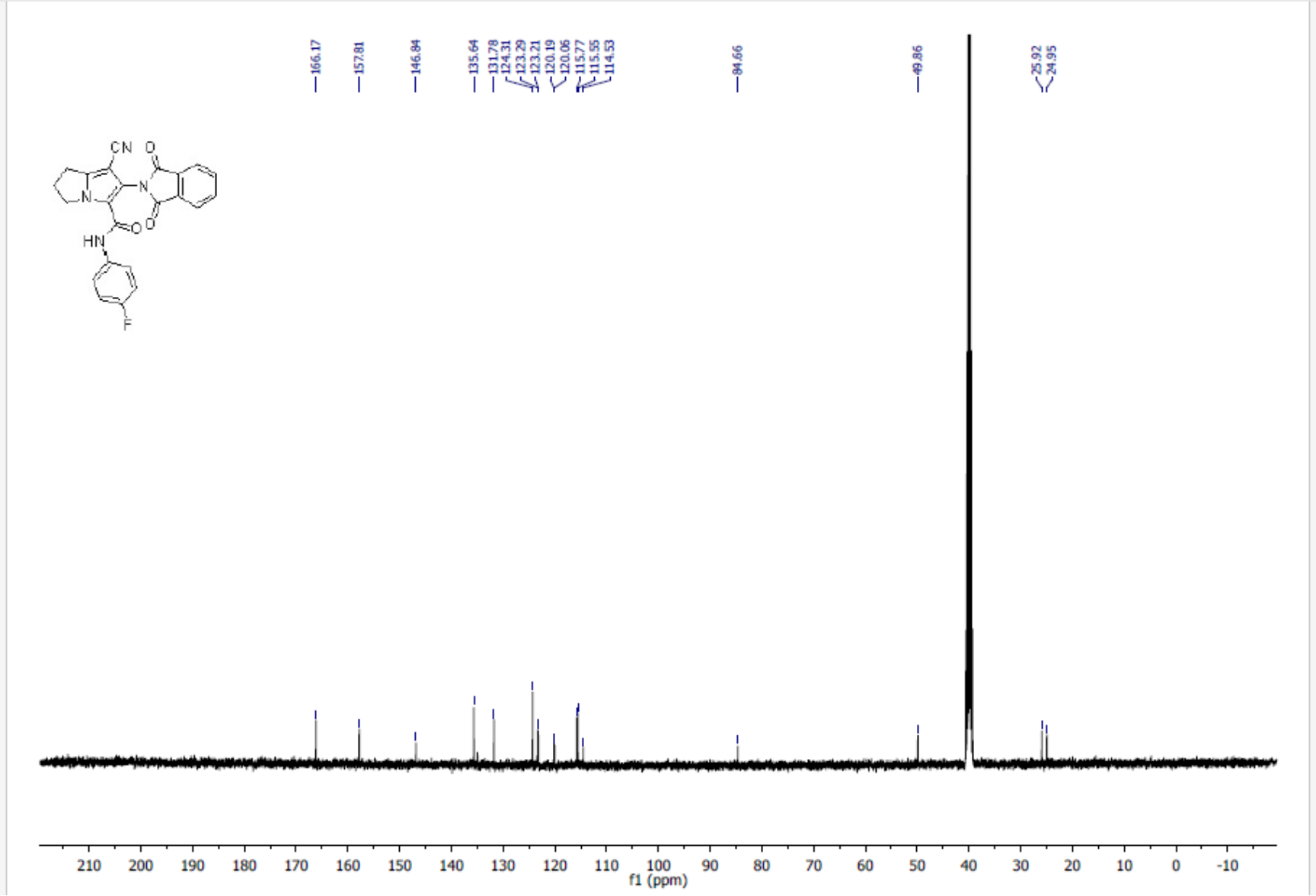


Fig.8. ^{13}C NMR of compound 6c (100 MHz, DMSO-d_6)

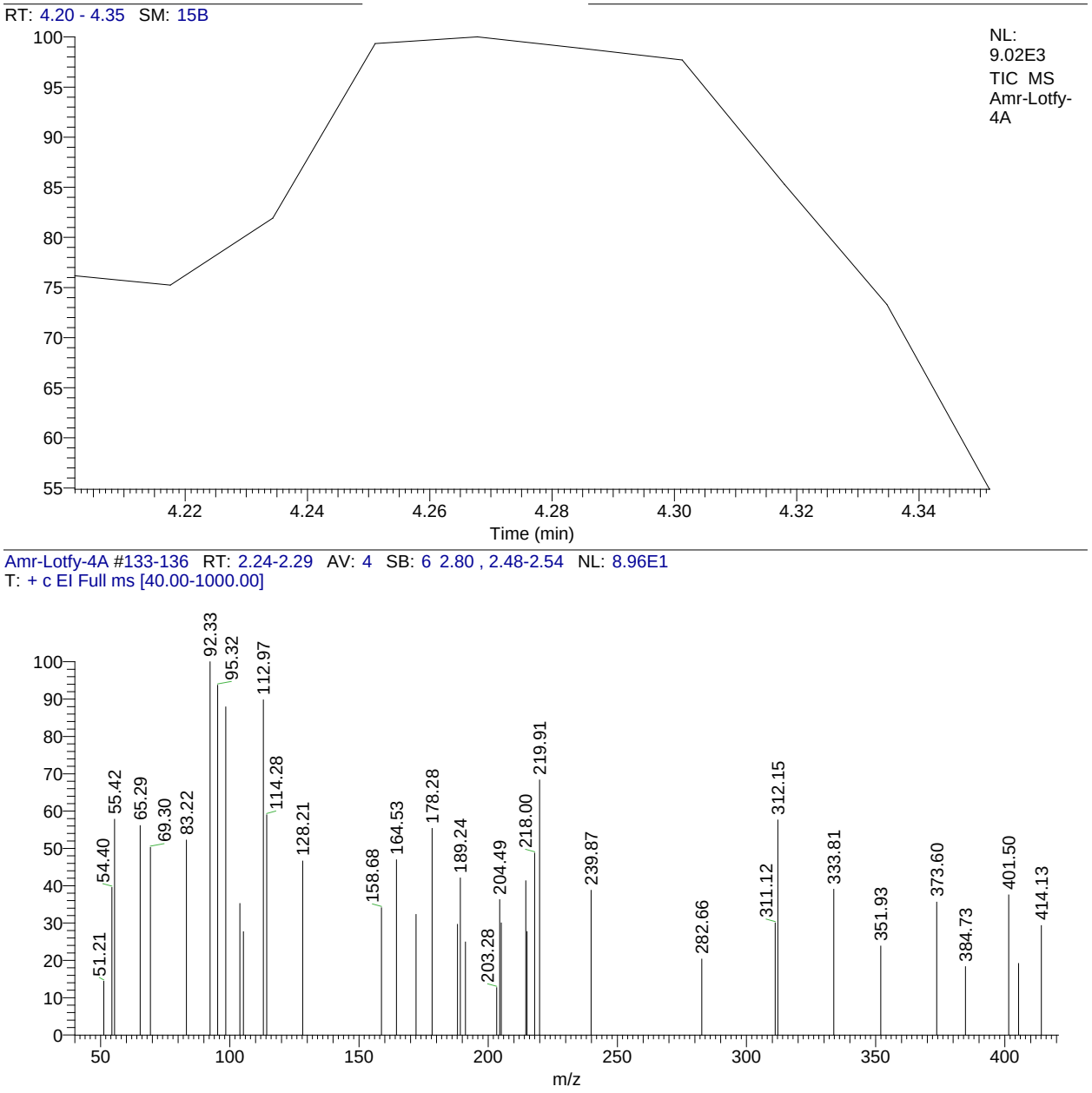


Fig.9. Mass spectra of compound 6c

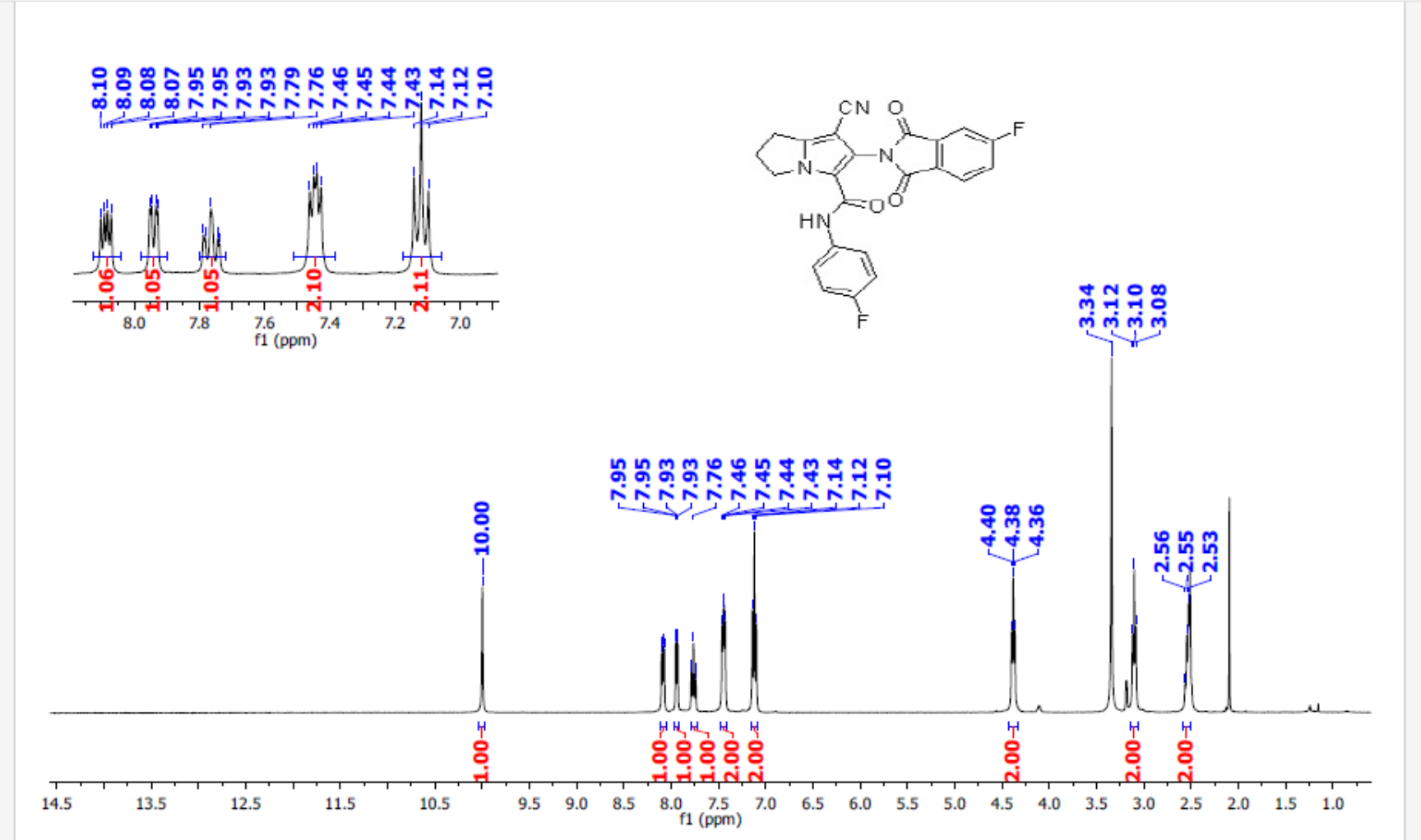


Fig.10. ^{1}H NMR of compound 6d (400 MHz, DMSO-d_6)

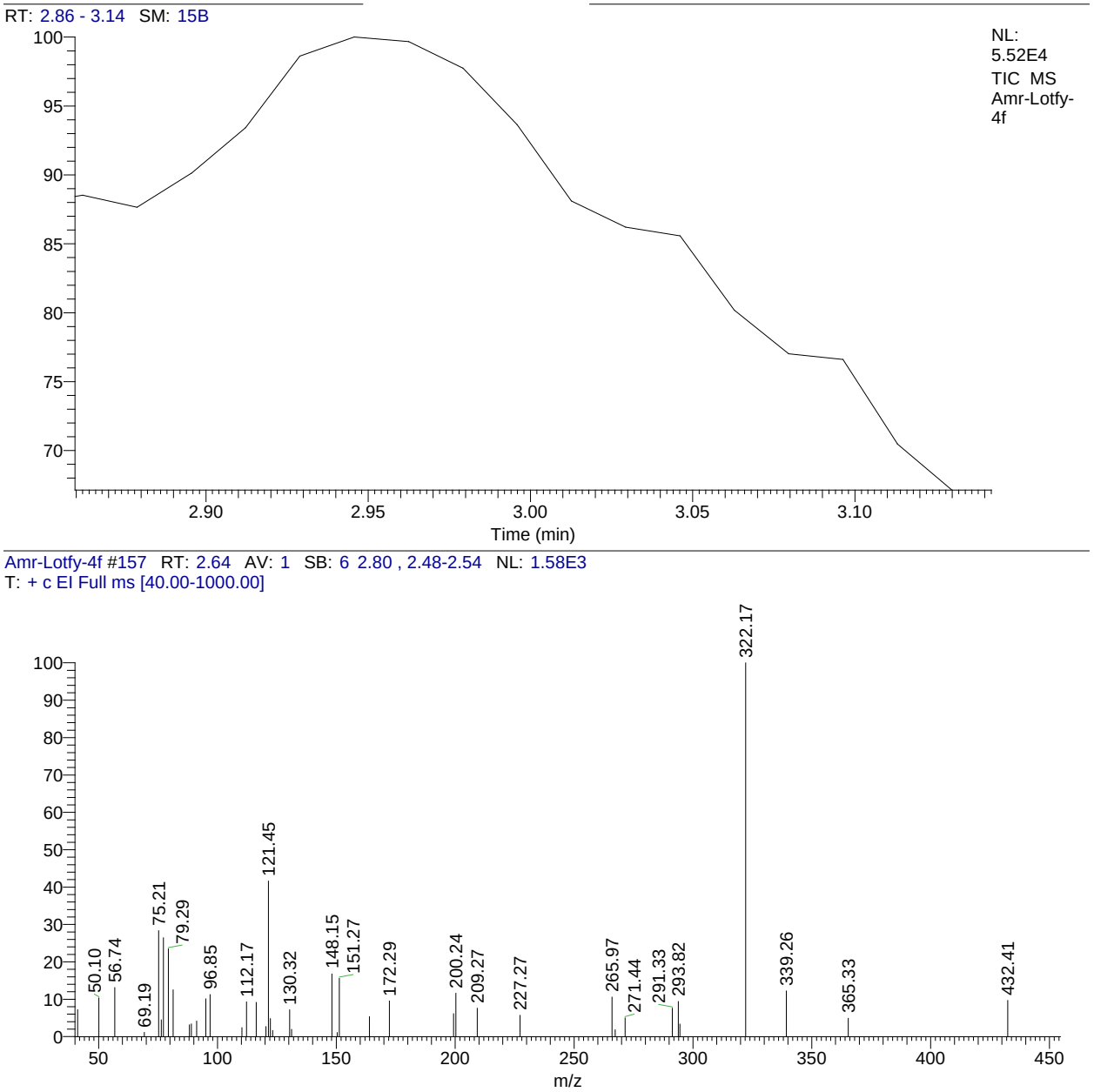


Fig.11. Mass spectra of compound 6d

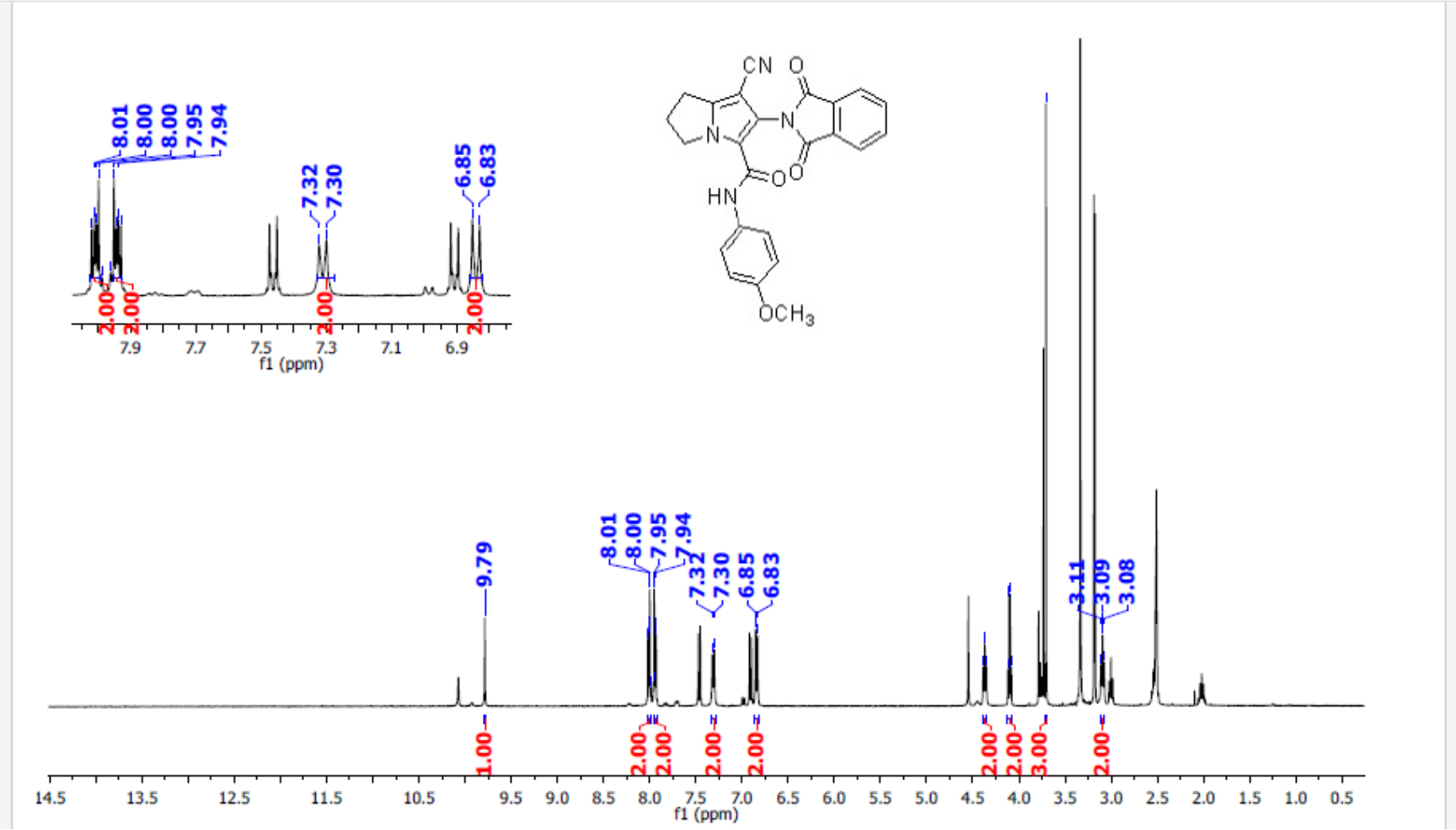


Fig.12. ^{1}H NMR of compound 6e (400 MHz, DMSO-d_6)

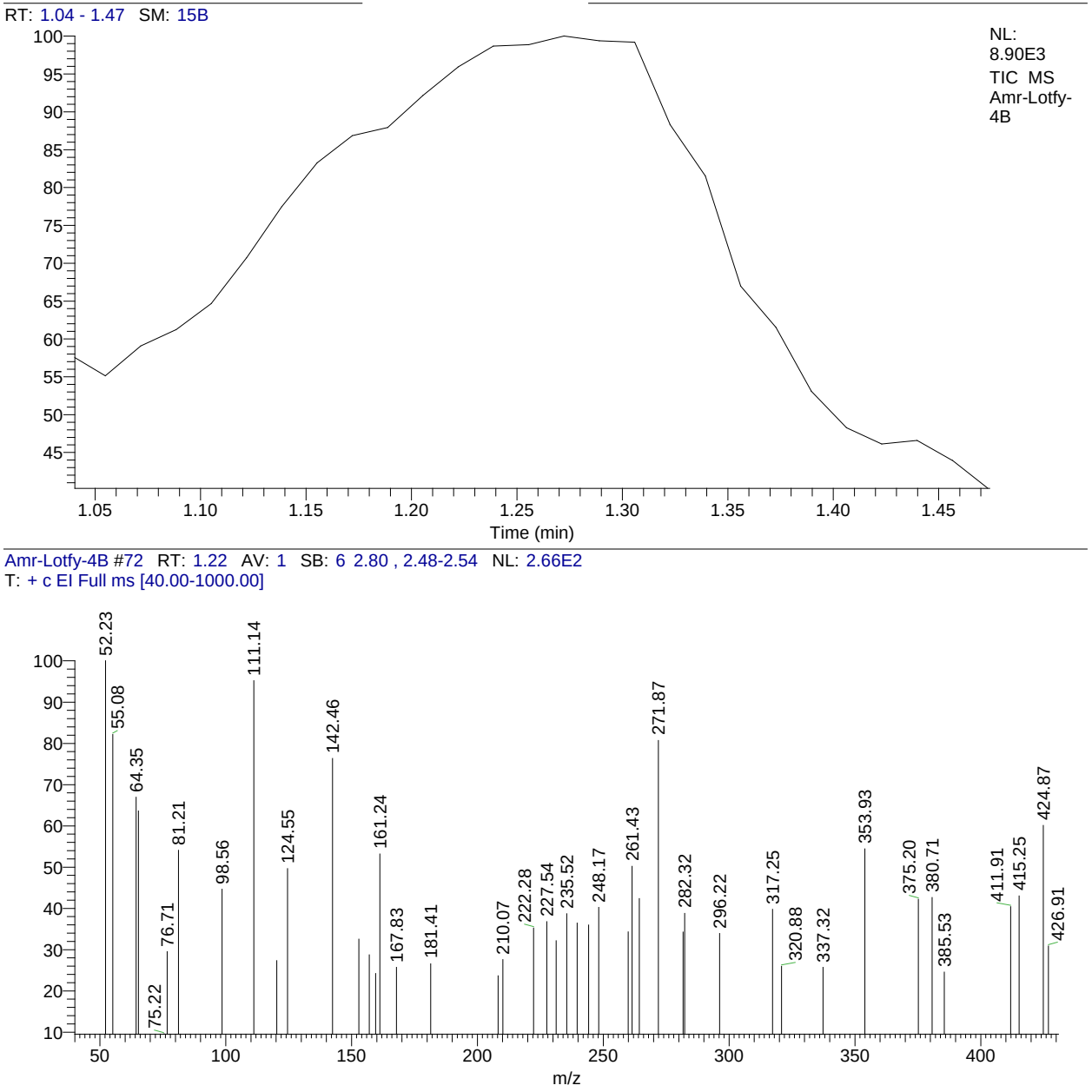


Fig.13. Mass spectra of compound 6e

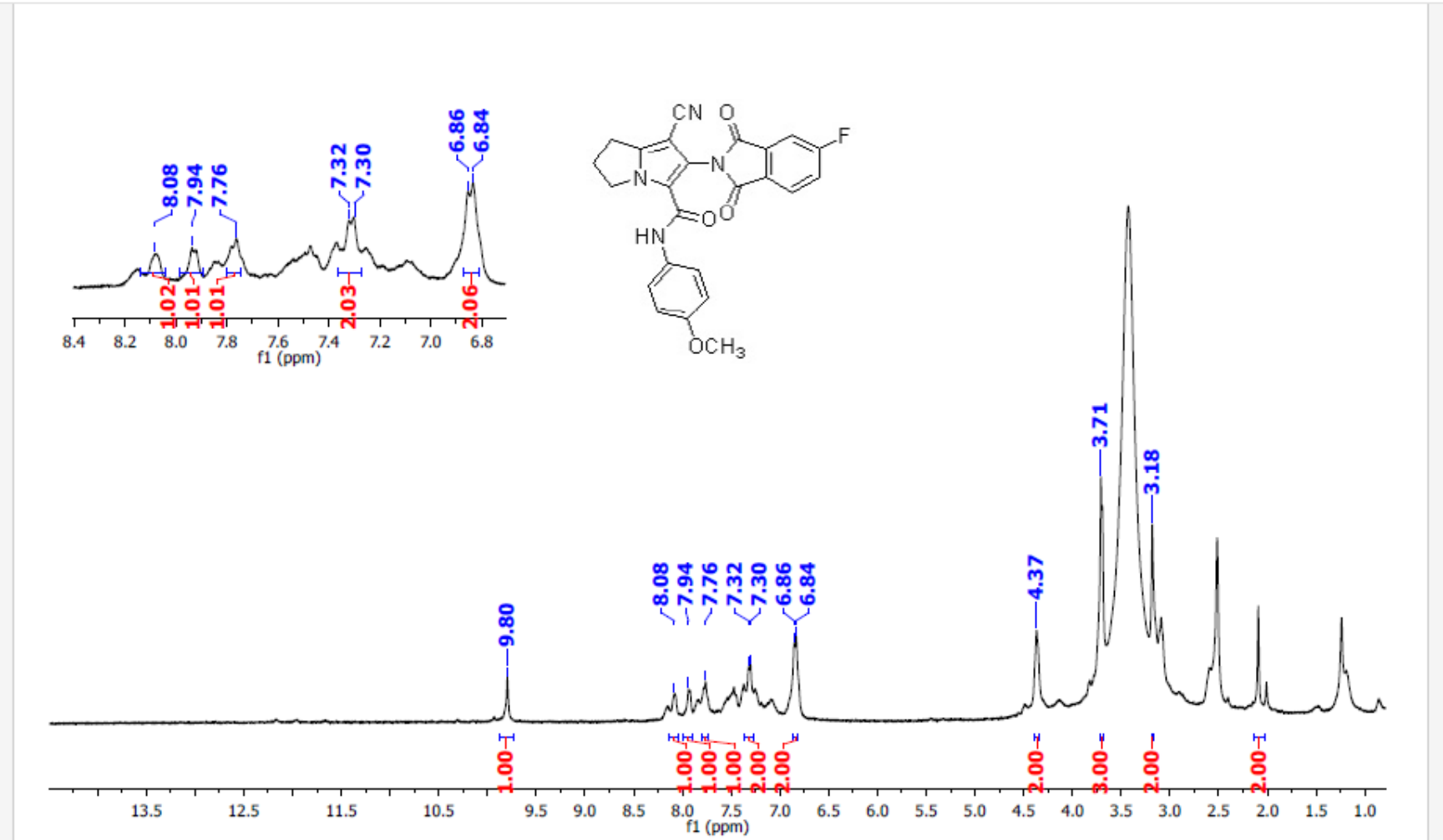


Fig.14. ^{1}H NMR of compound 6f (400 MHz, DMSO-d_6)

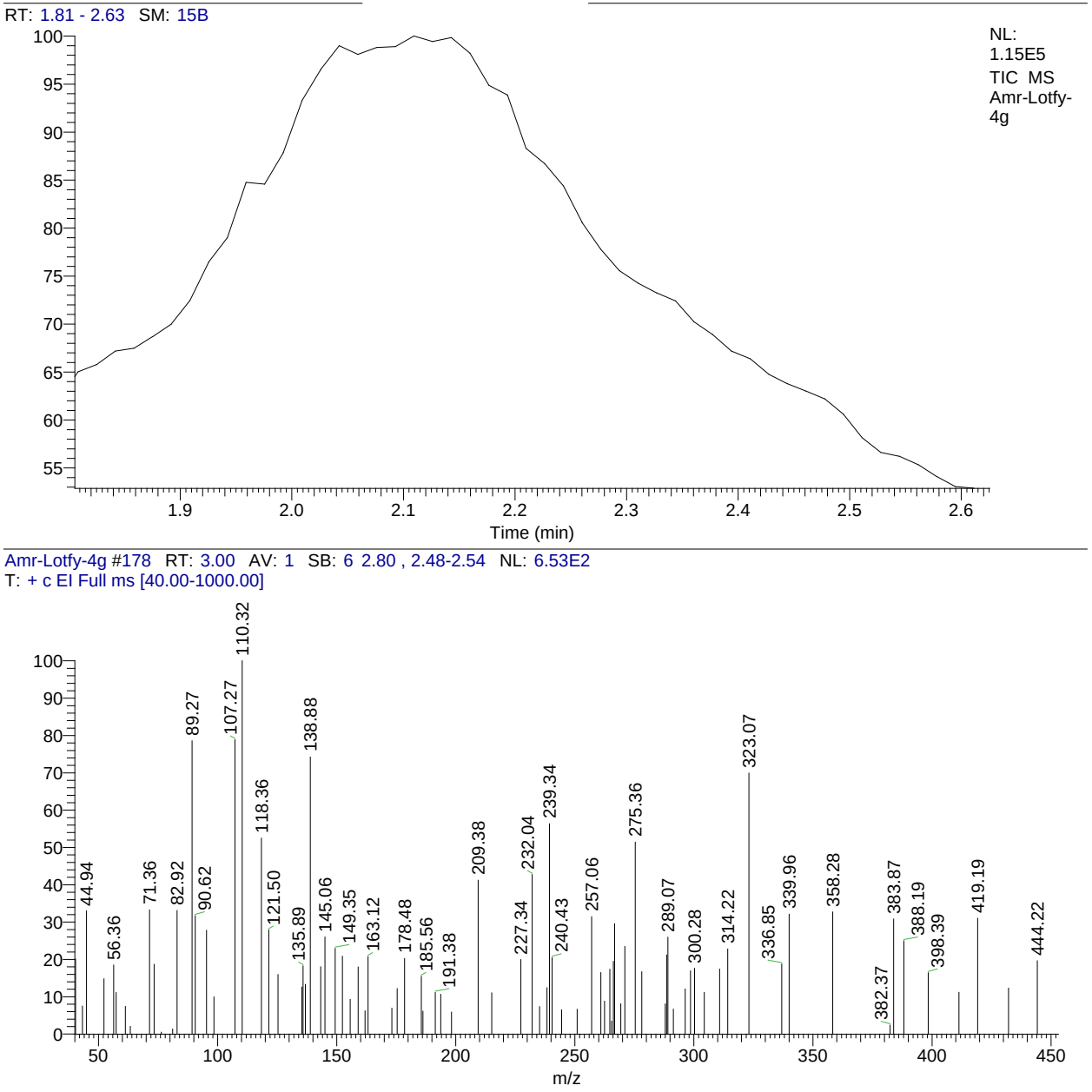


Fig.15. Mass spectra of compound 6f

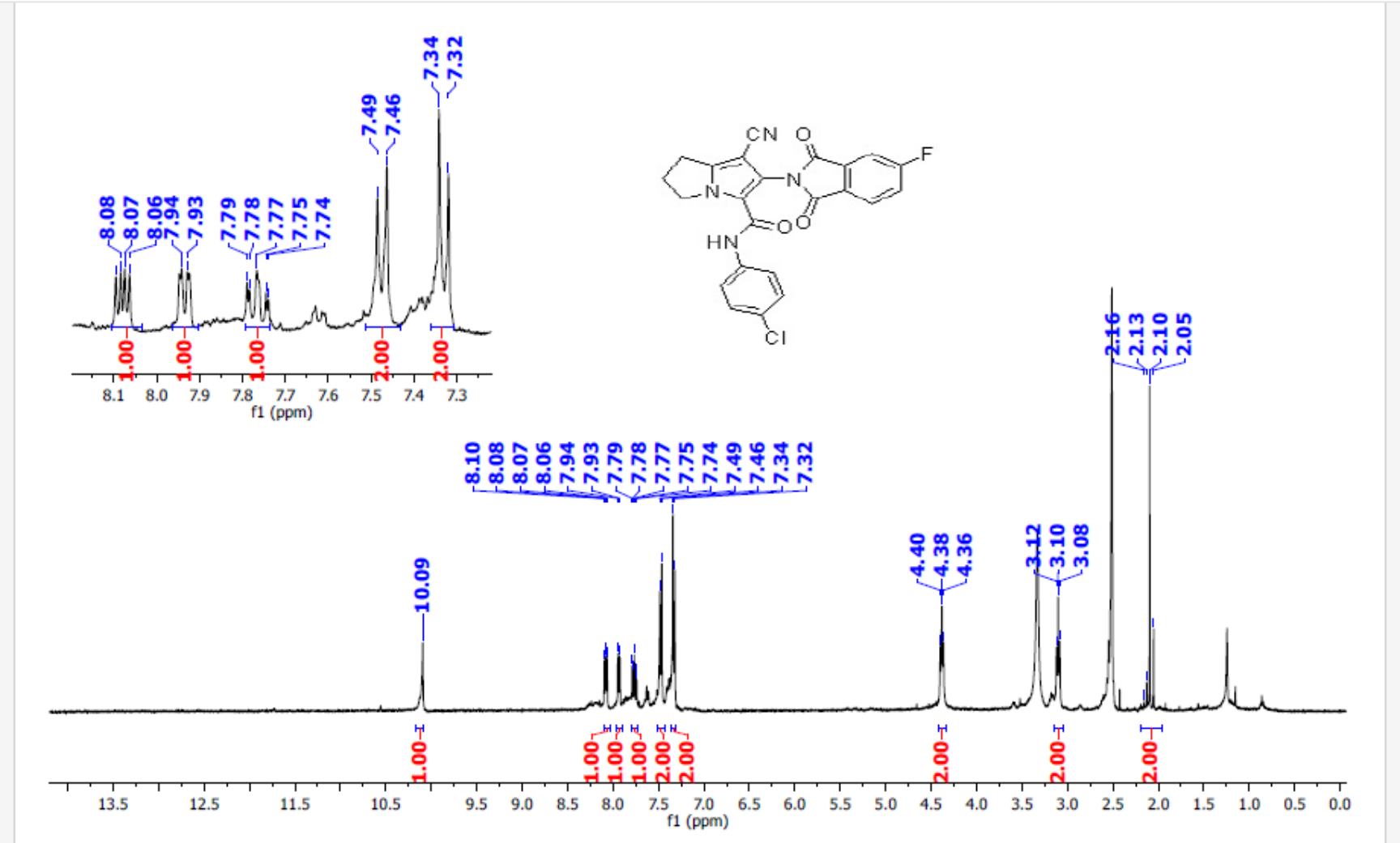


Fig.16. ^{1}H NMR of compound 6g (400 MHz, DMSO-d_6)

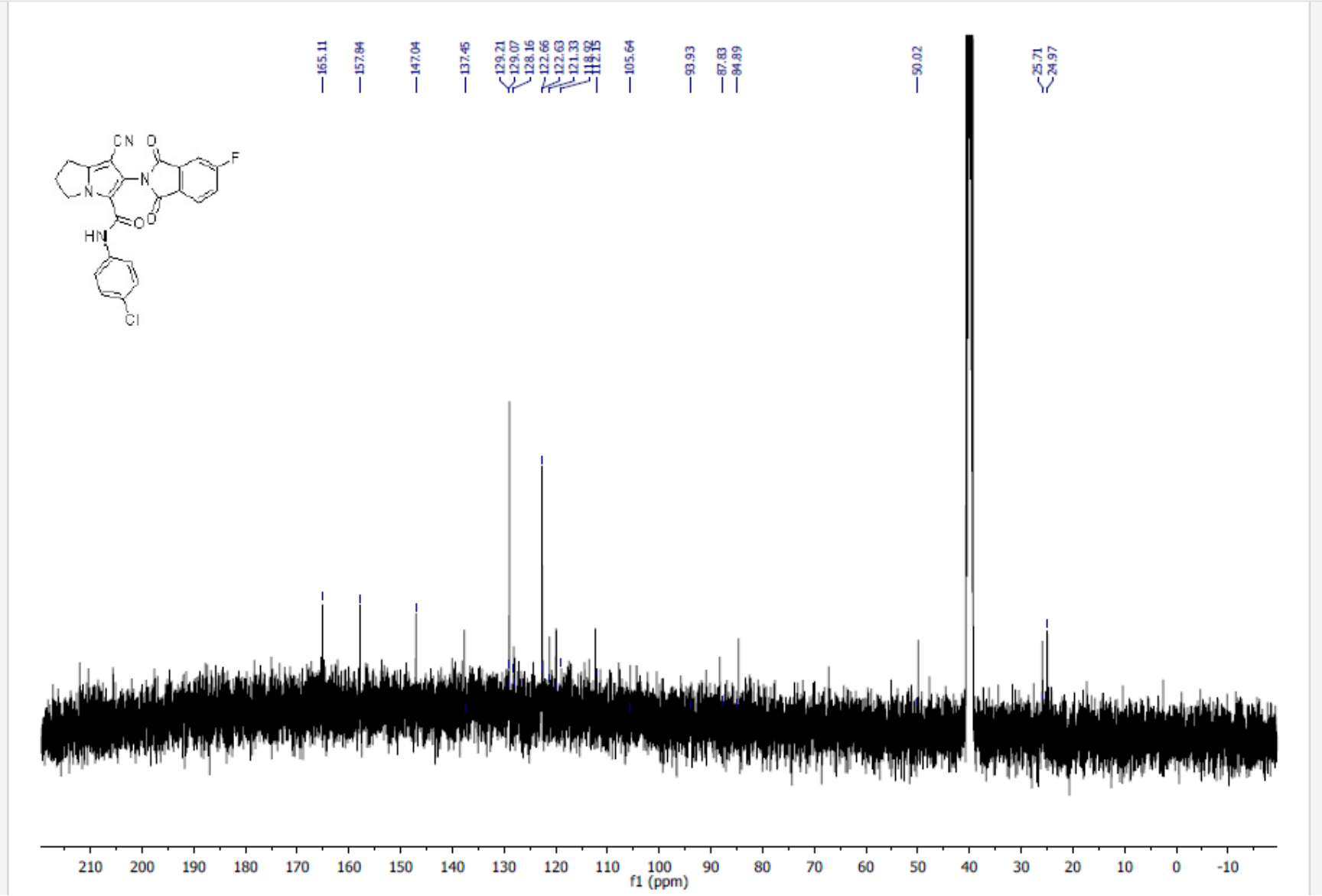


Fig.17. ^{13}C NMR of compound 6g (100 MHz, DMSO-*d*$_6$)

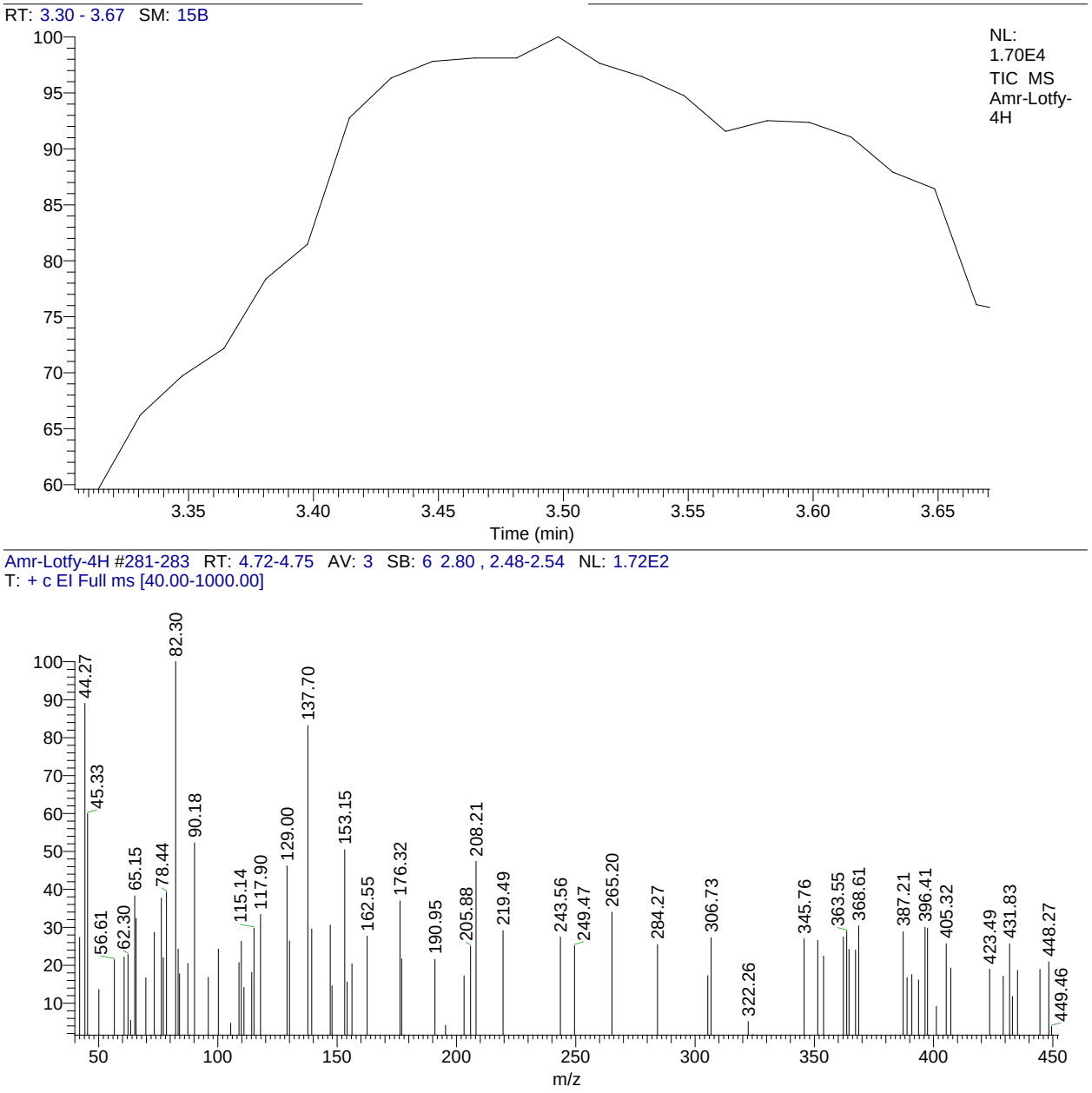


Fig.18. Mass spectra of compound 6g

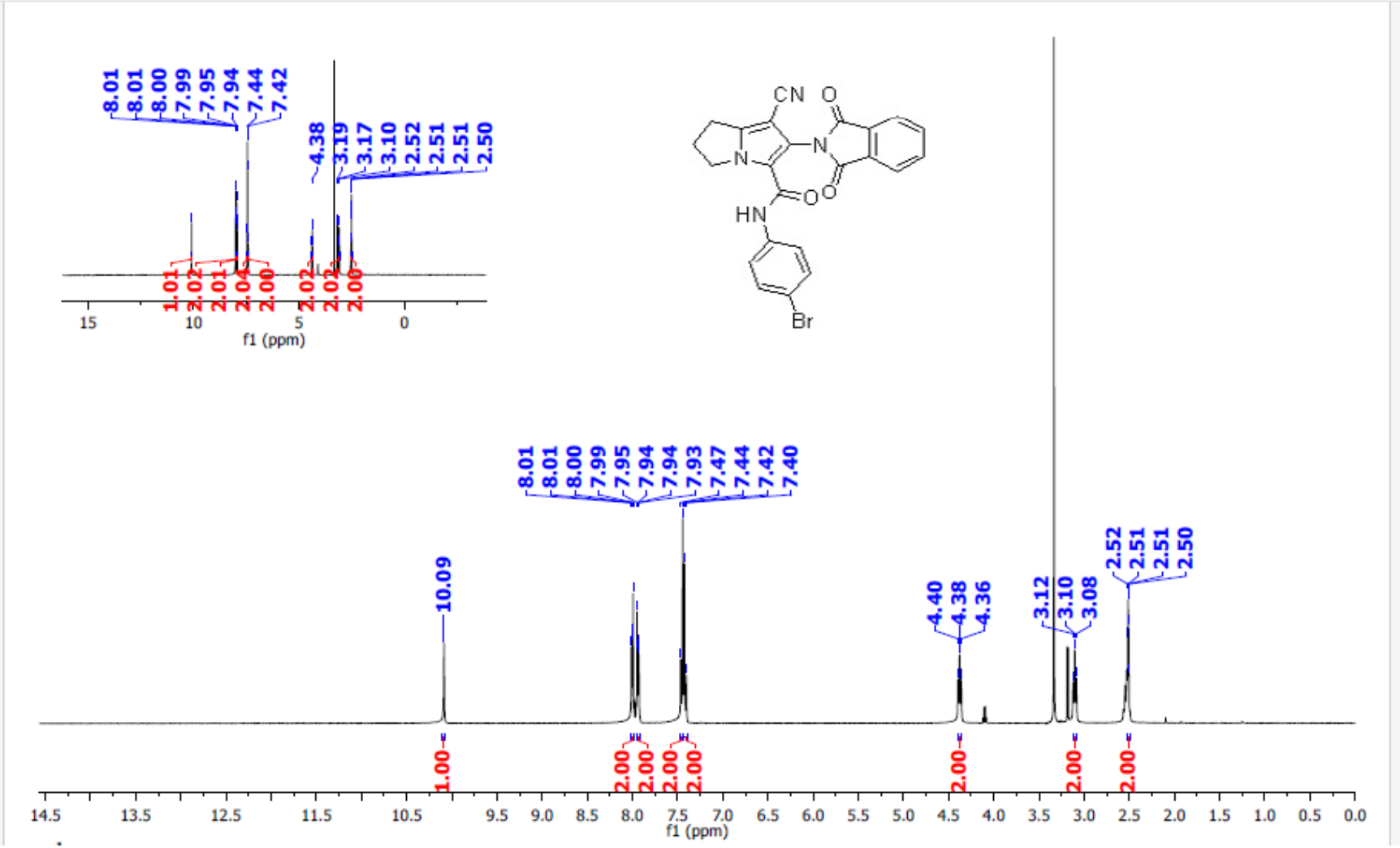


Fig.19. ^{1}H NMR of compound 6h (400 MHz, DMSO-d_6)

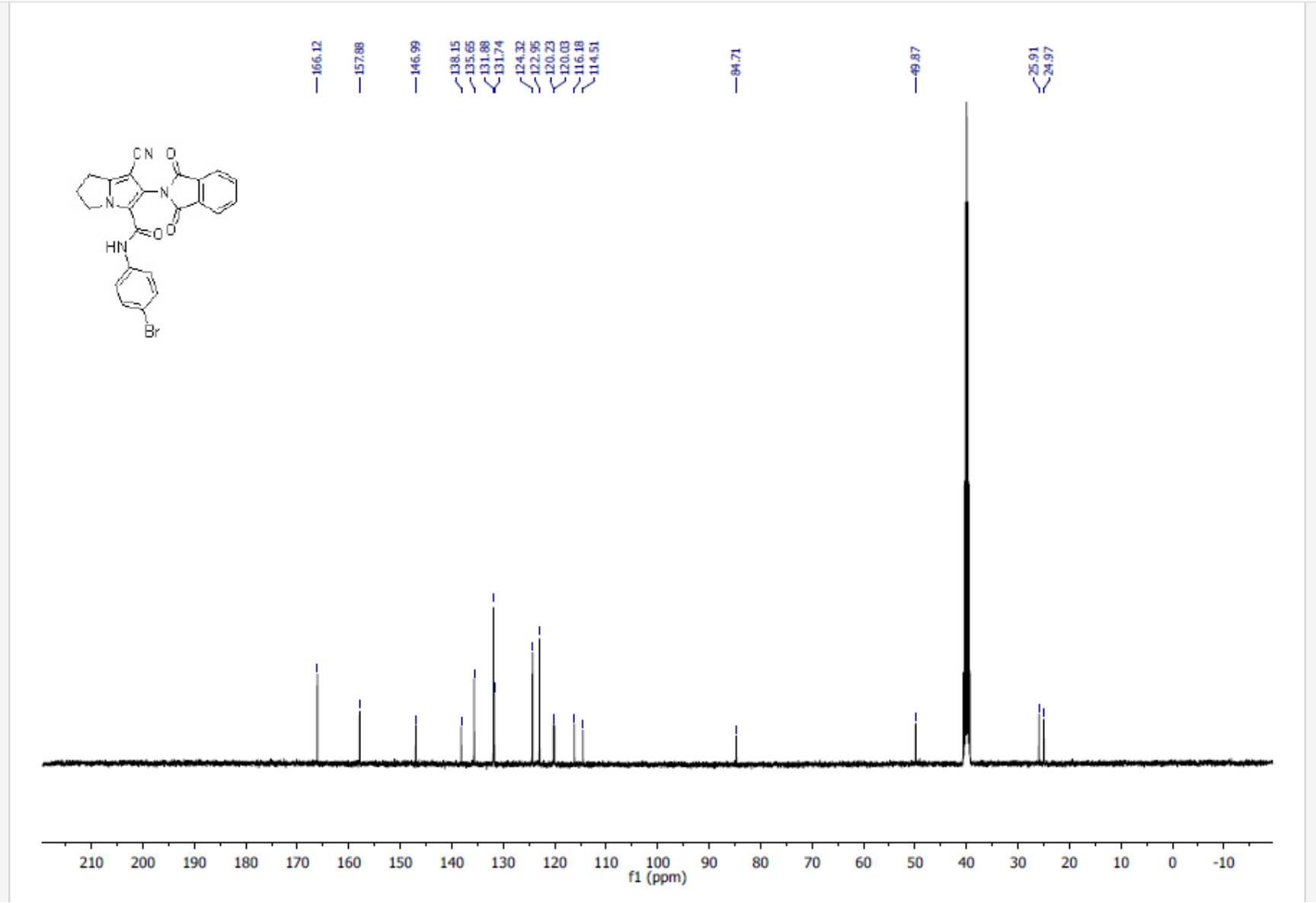


Fig.20. ^{13}C NMR of compound 6h (100 MHz, DMSO-d_6)

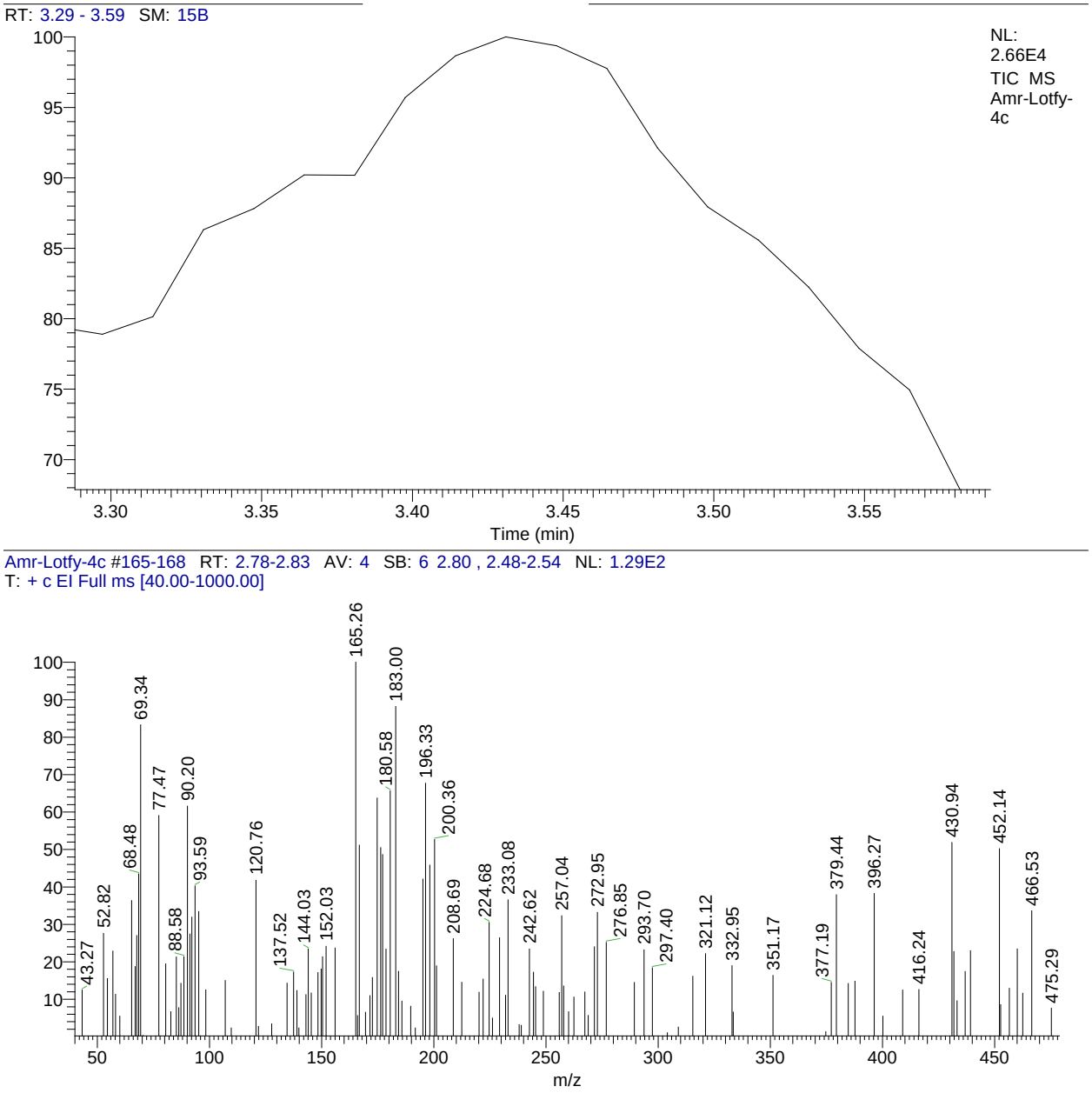


Fig.21. Mass spectra of compound 6h

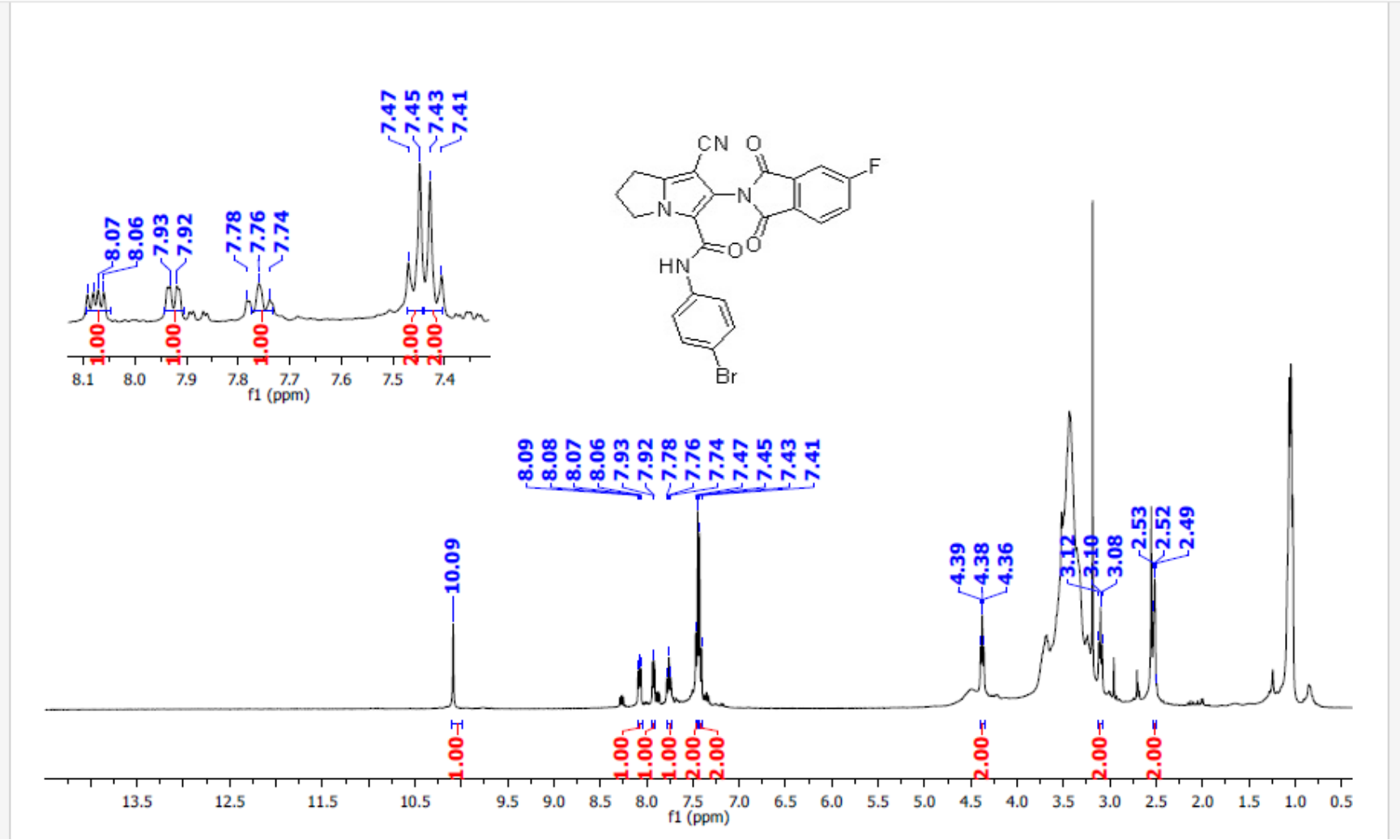


Fig.22. ^{1}H NMR of compound 6i (400 MHz, DMSO-d_6)

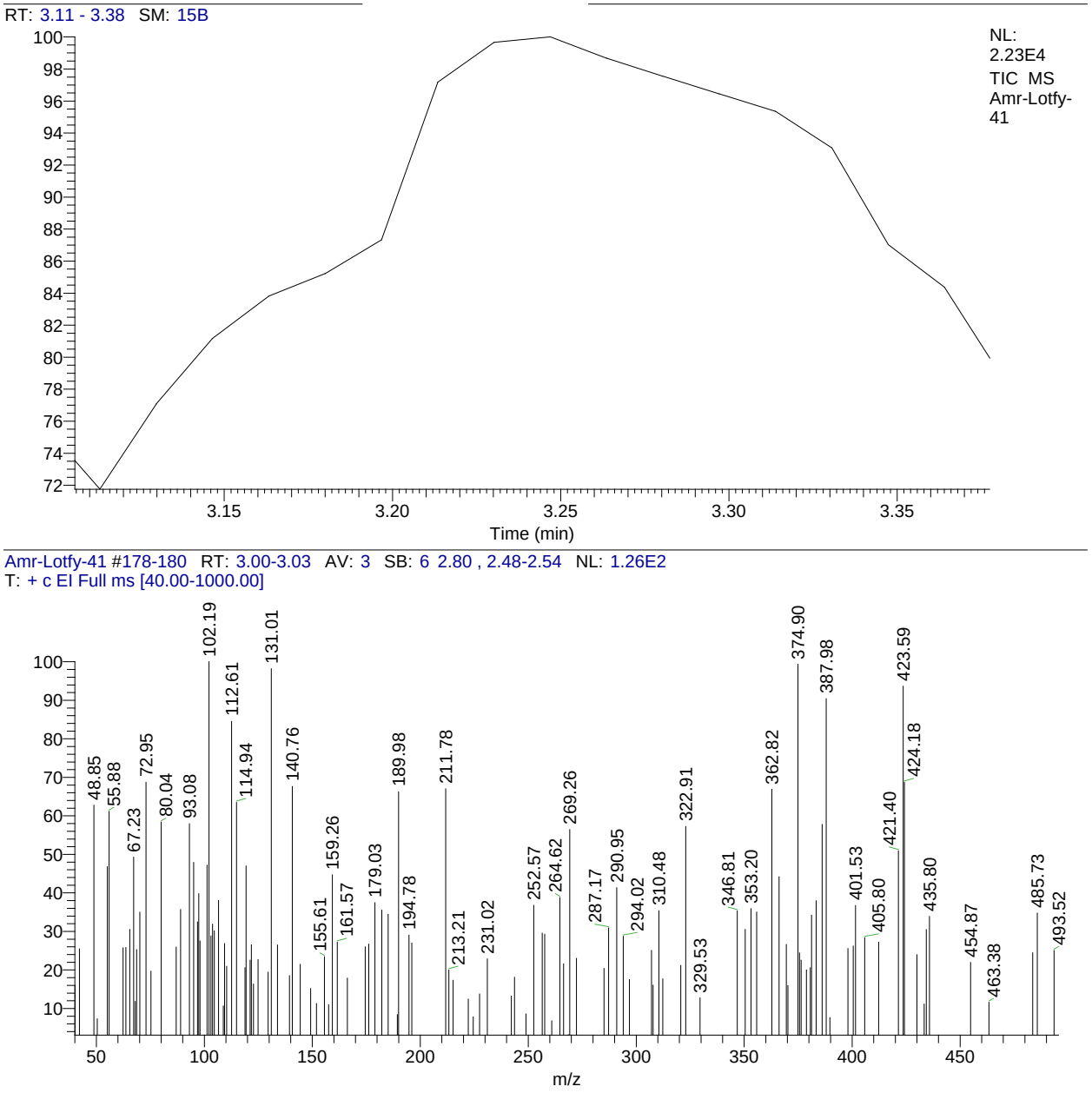


Fig.23. Mass spectra of compound 6i

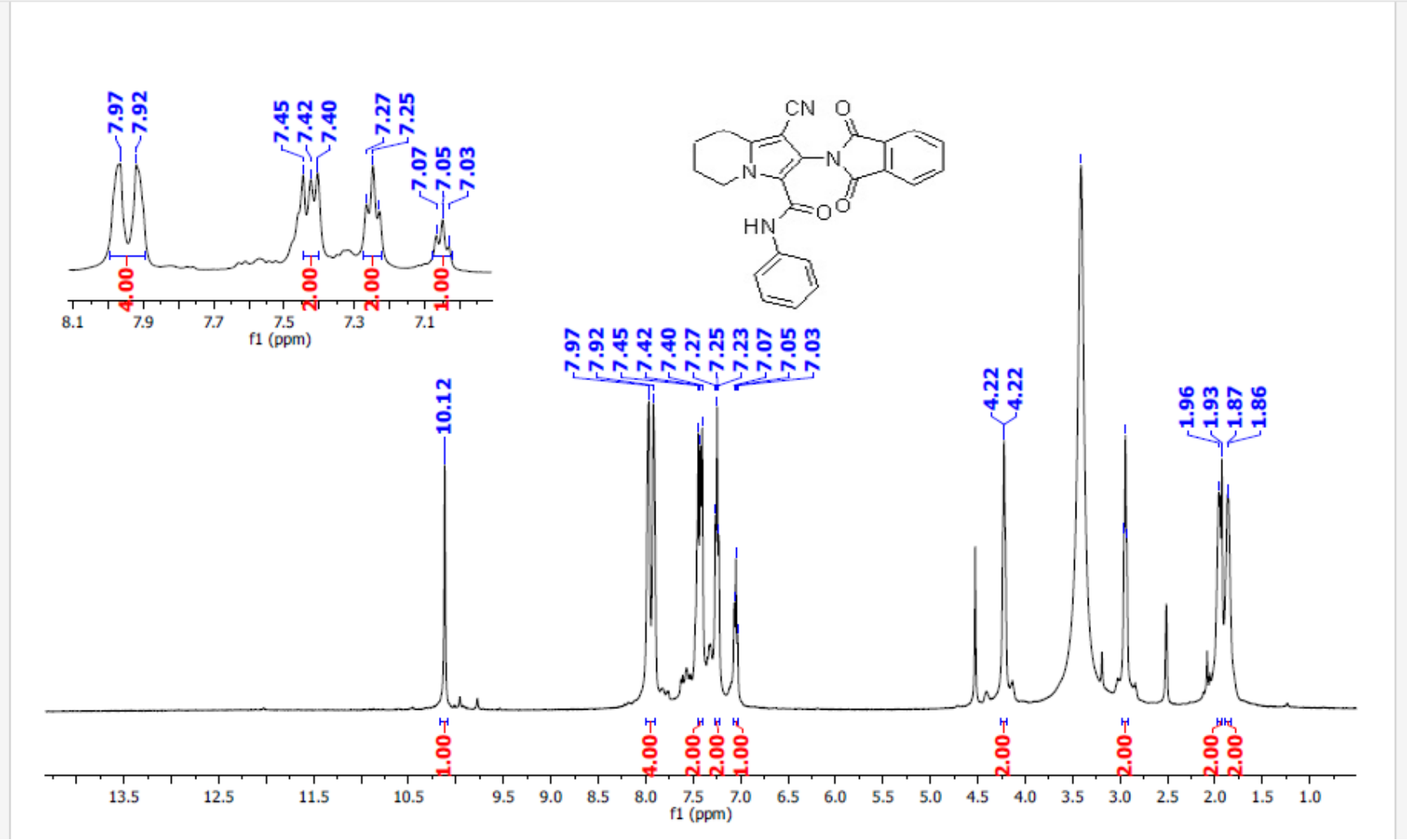


Fig.24. ^{1}H NMR of compound 6j (400 MHz, DMSO-d_6)

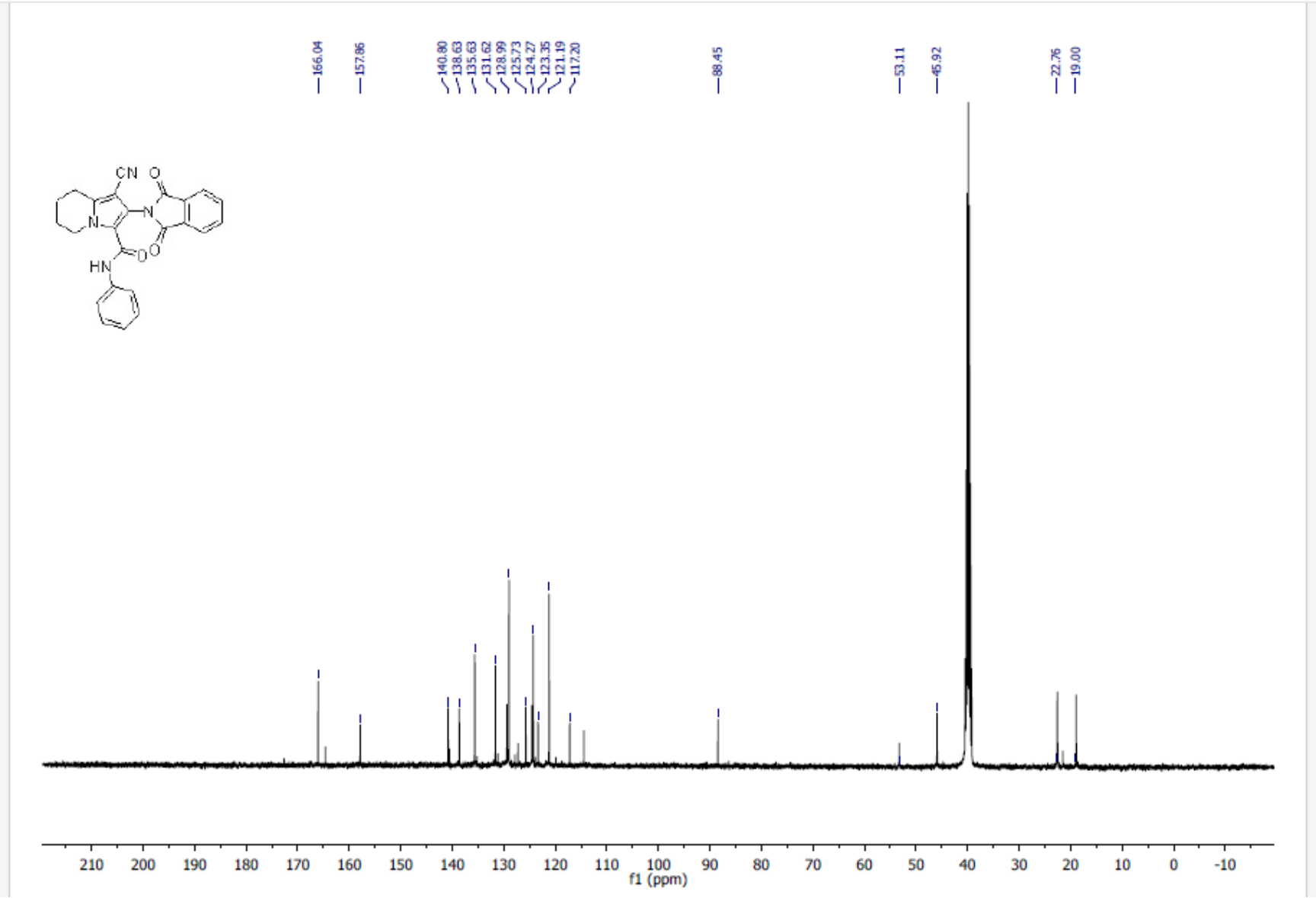


Fig.25. ^{13}C NMR of compound 6j (100 MHz, DMSO-d_6)

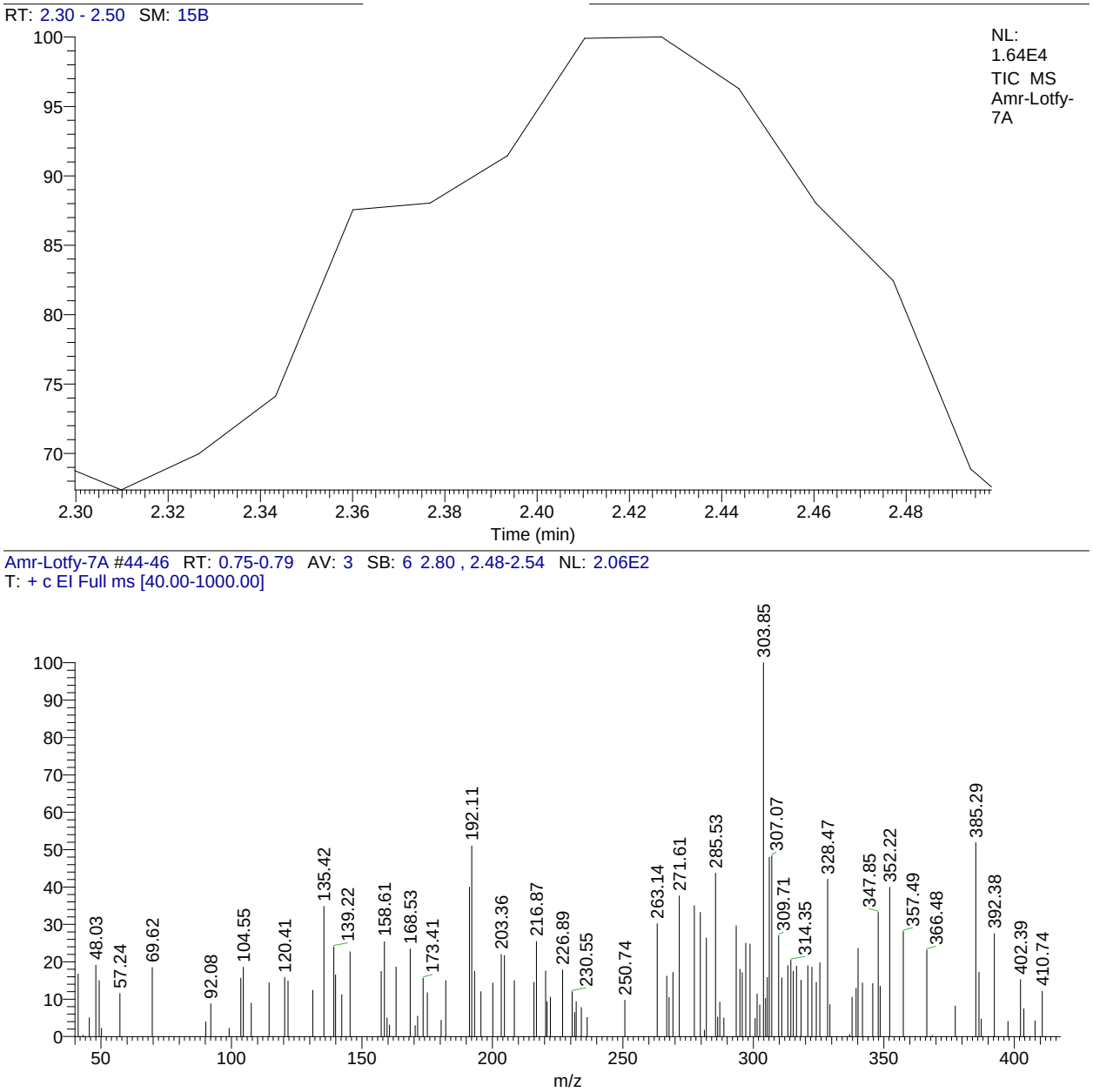


Fig.26. Mass spectra of compound 6j

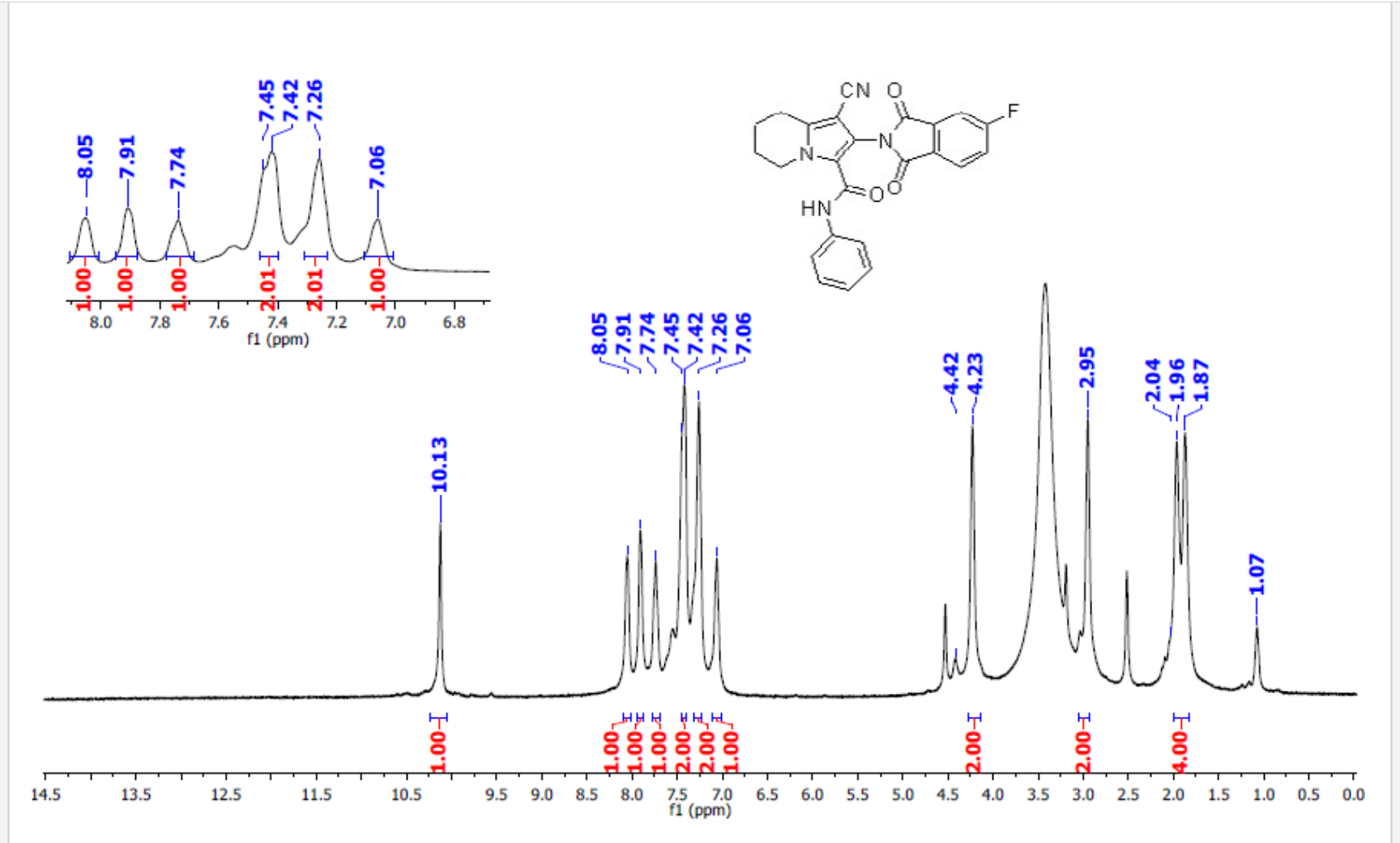


Fig.27. ^{1}H NMR of compound 6k (400 MHz, DMSO-d_6)

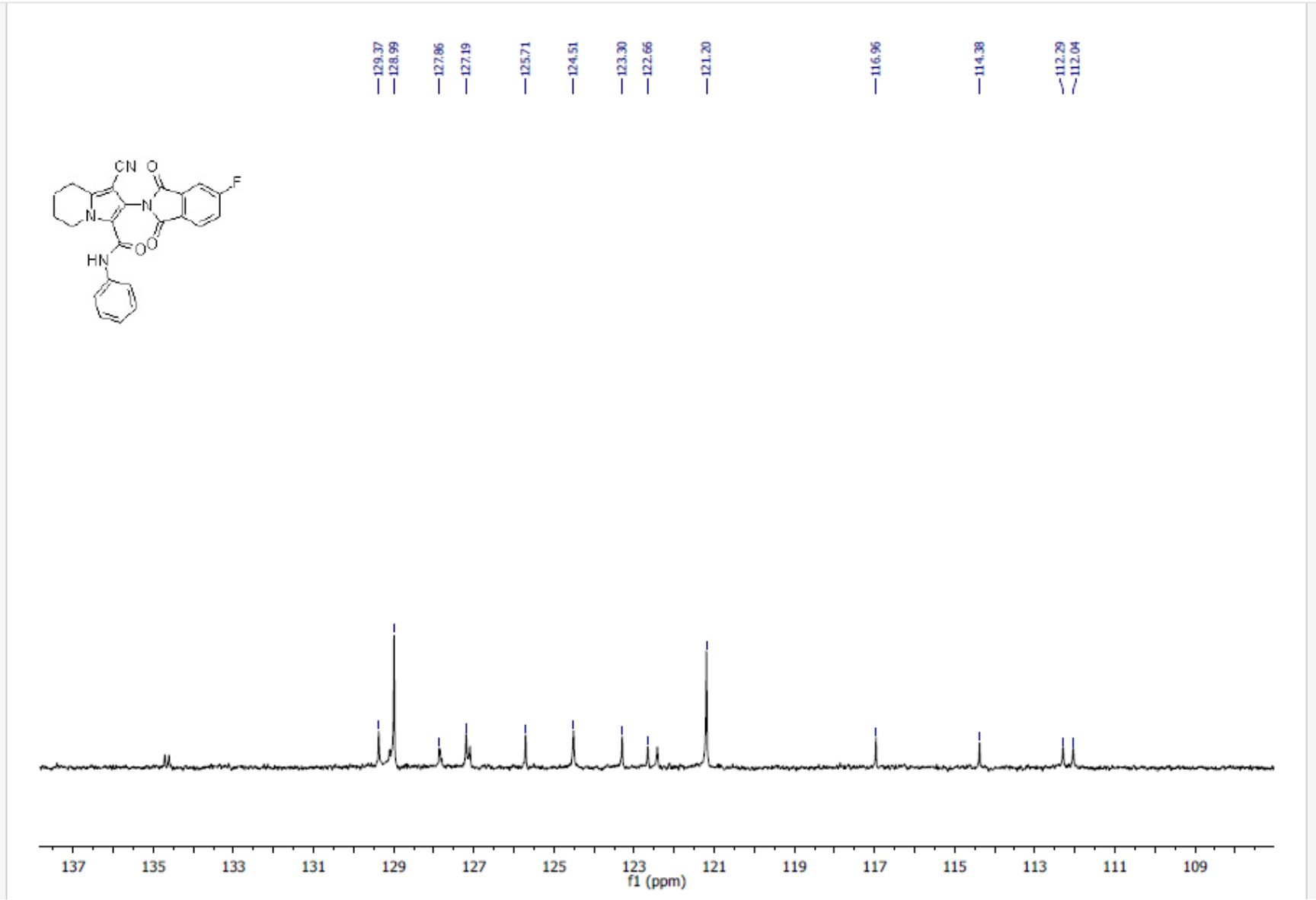


Fig.28. ^{13}C NMR of compound 6k (100 MHz, DMSO-d_6)

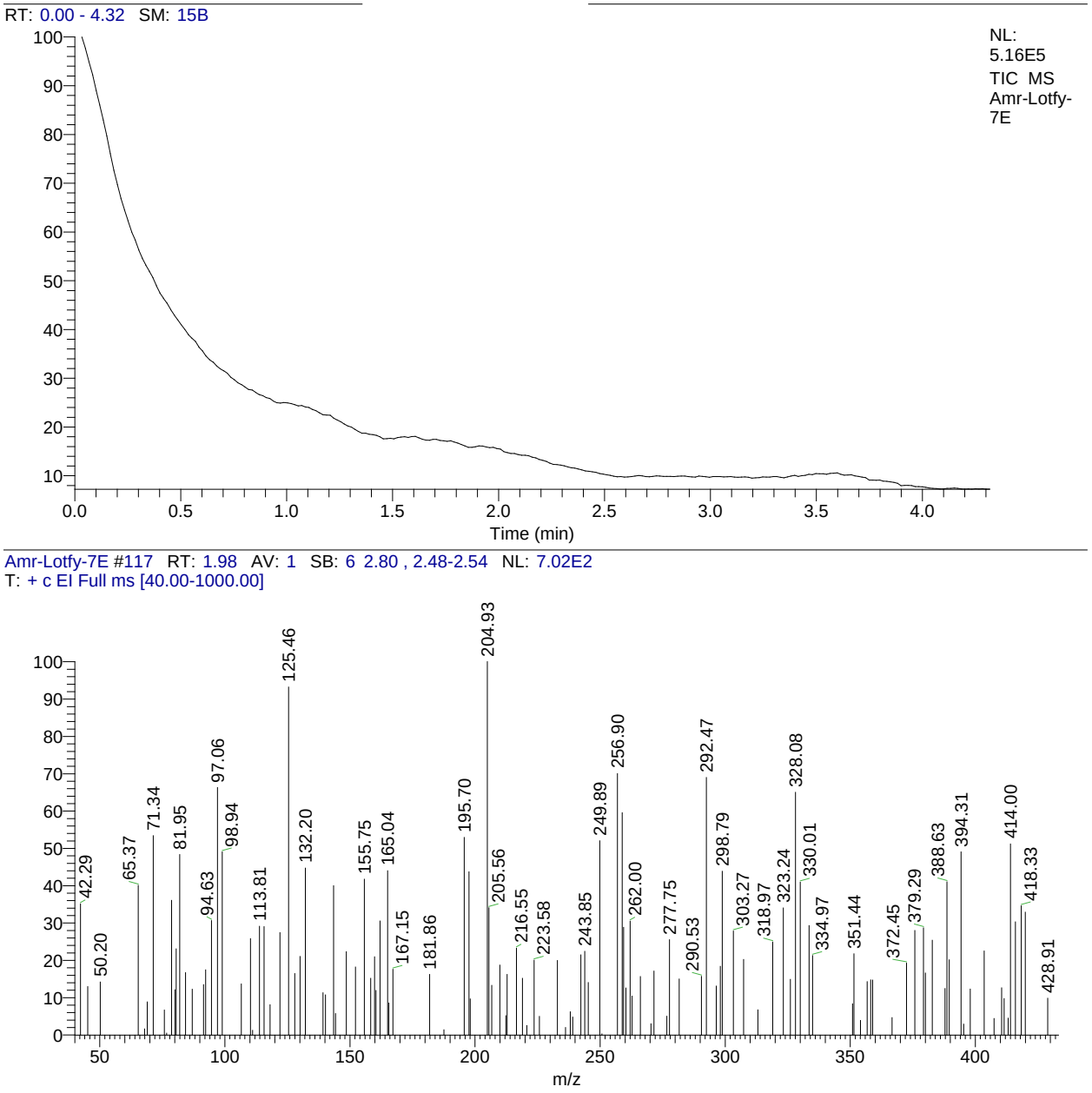


Fig.29. Mass spectra of compound 6k

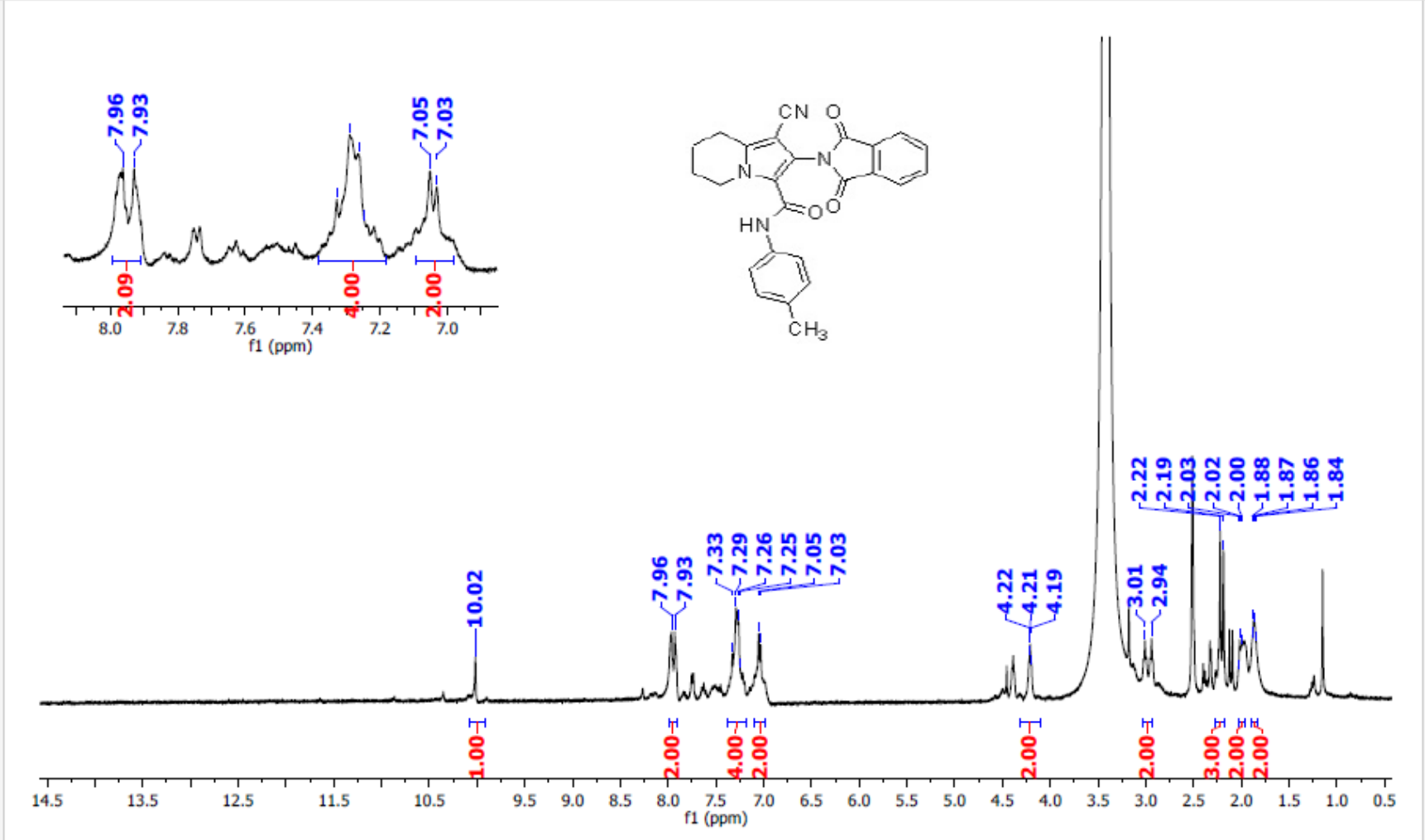


Fig.30. ^{1}H NMR of compound 6l (400 MHz, DMSO-d_6)

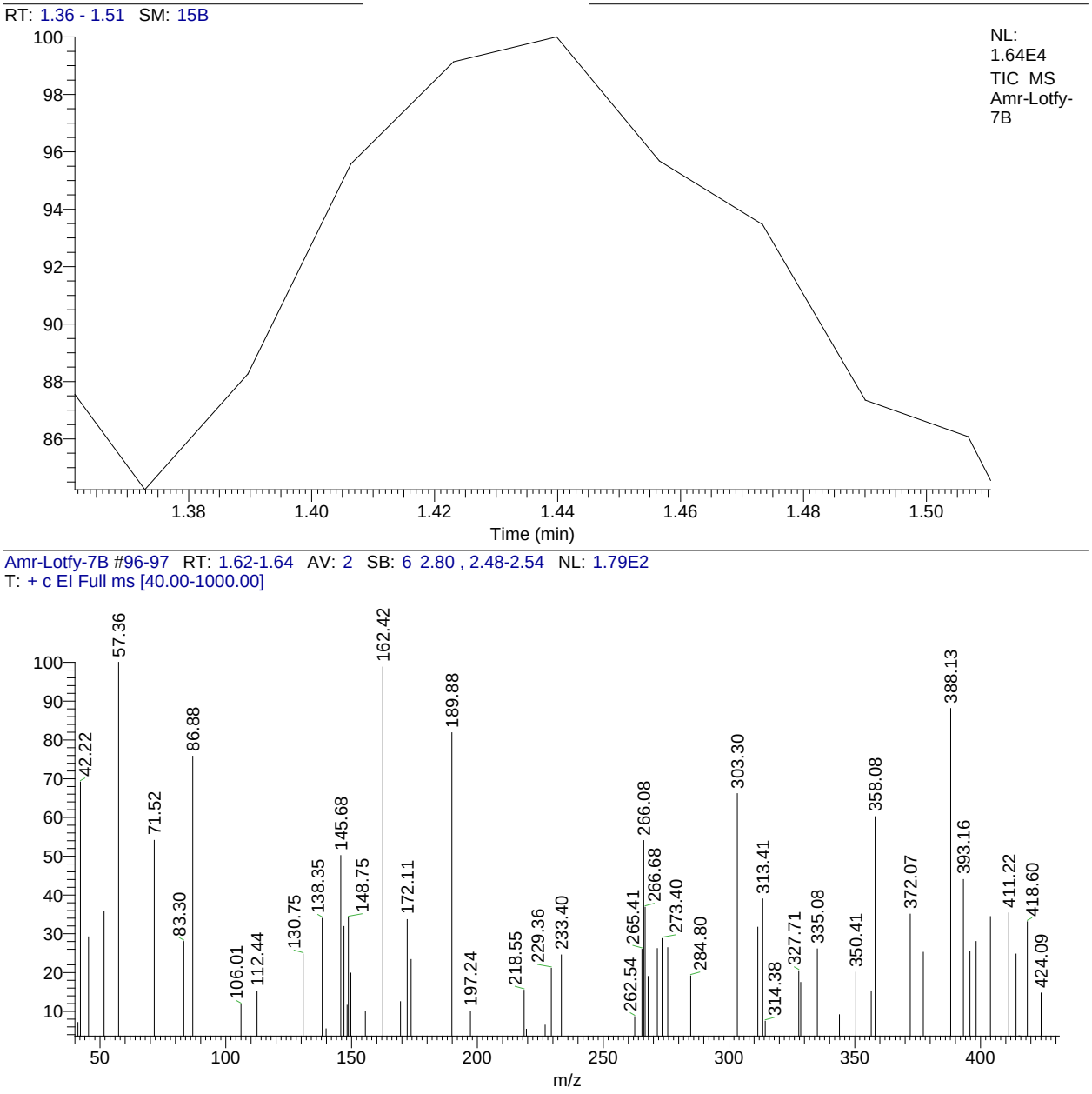


Fig.31. Mass spectra of compound 6l

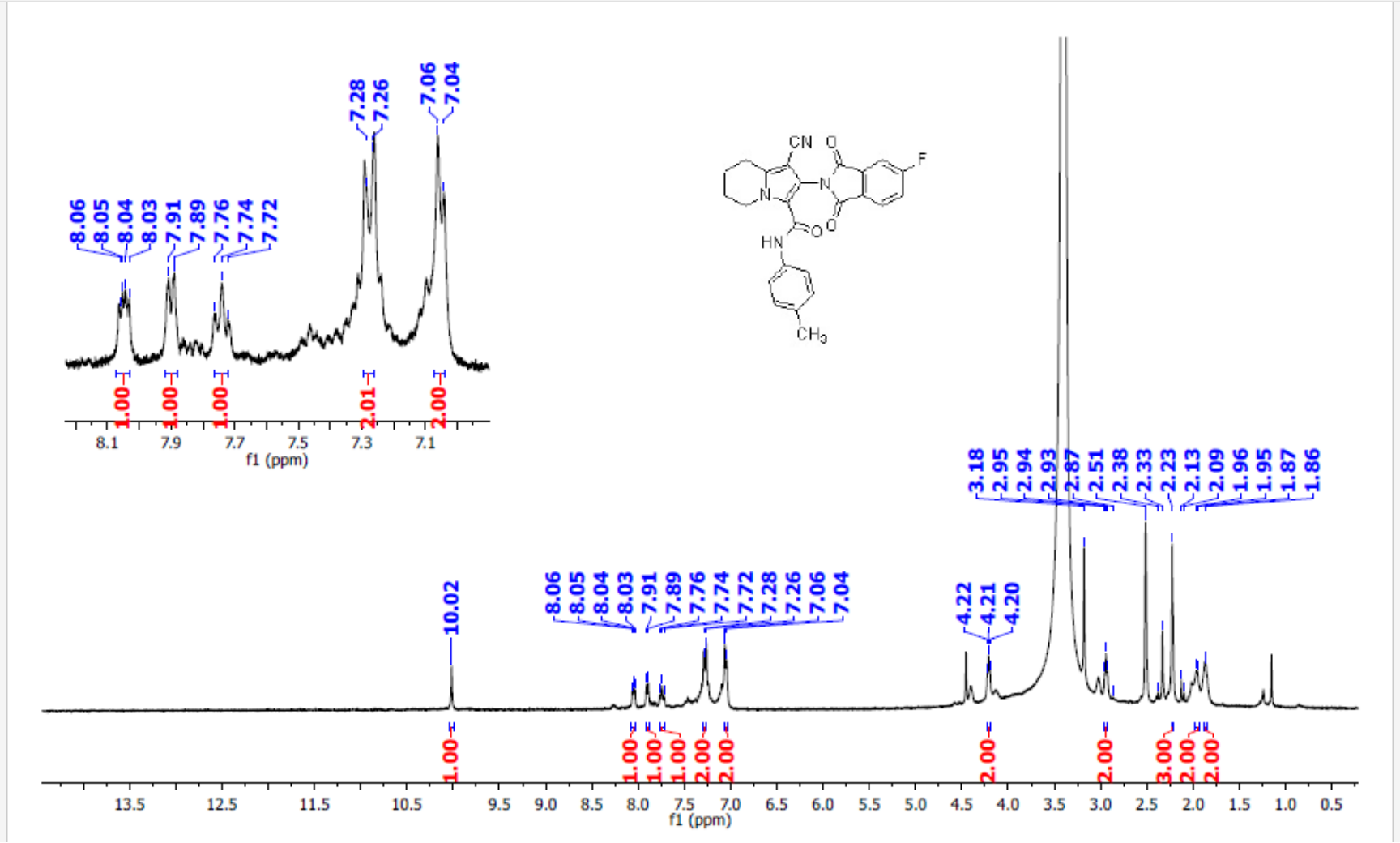


Fig.32. ^{1}H NMR of compound 6m (400 MHz, DMSO-d_6)

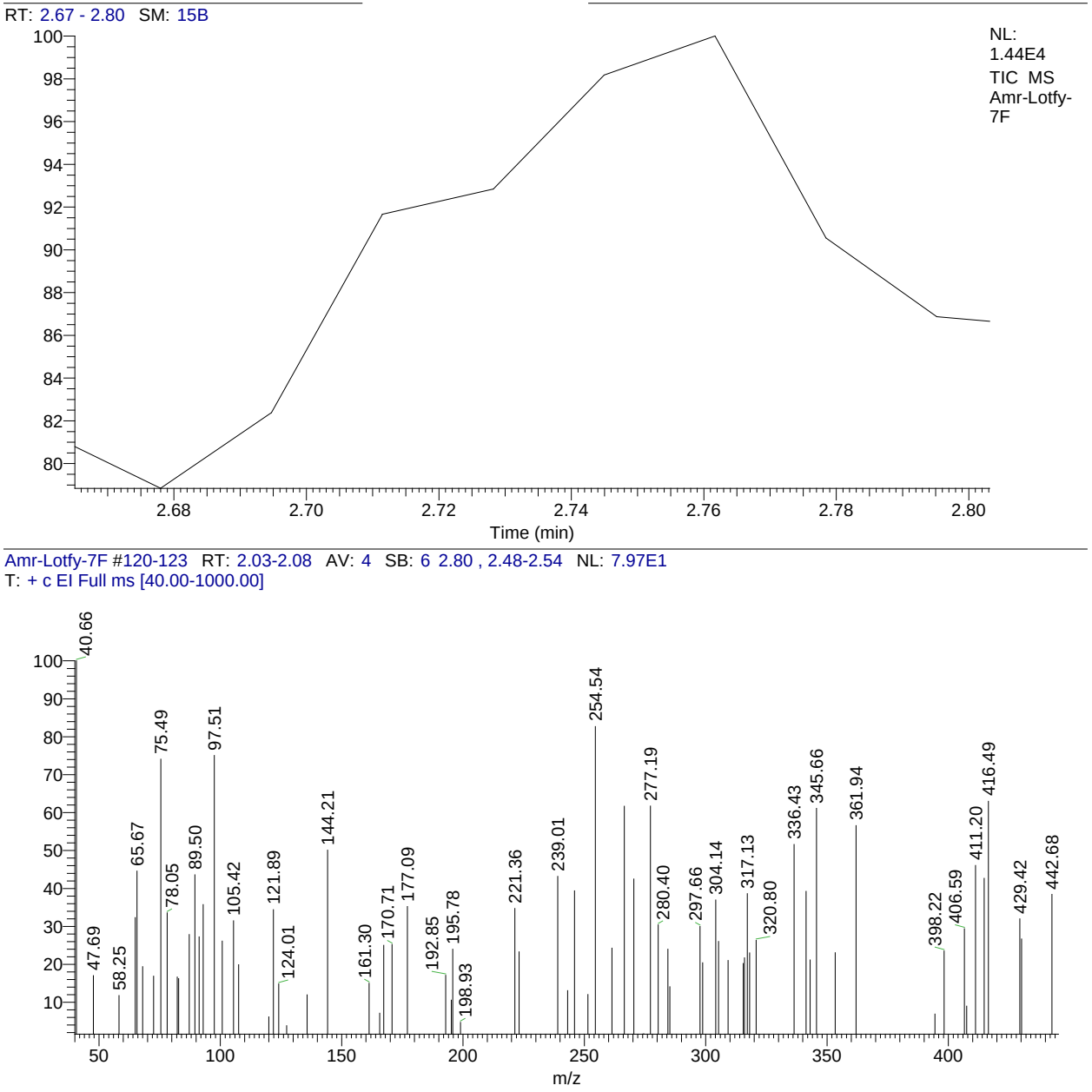


Fig.33. Mass spectra of compound 6m

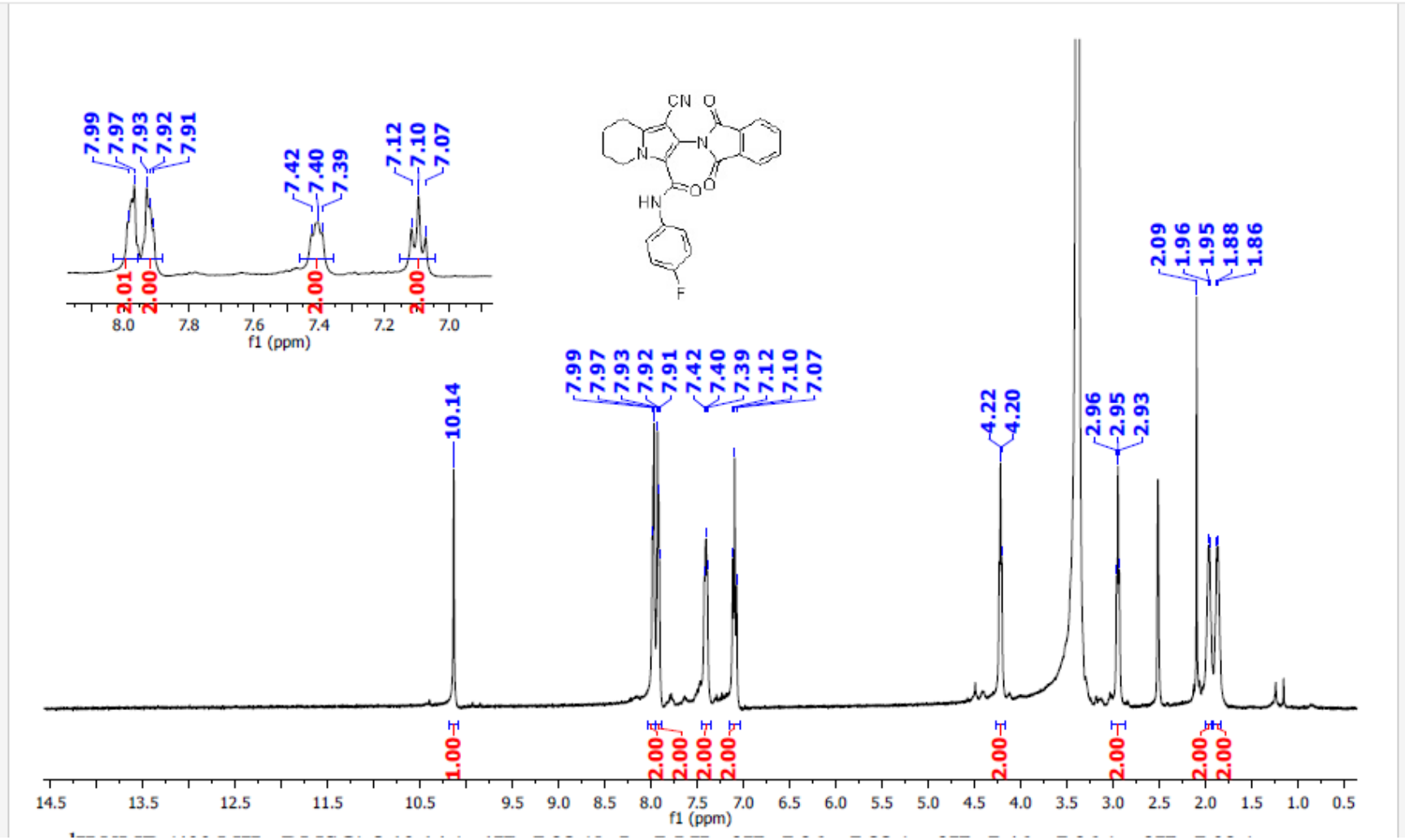


Fig.34. ^{1}H NMR of compound 6n (400 MHz, DMSO-d_6)

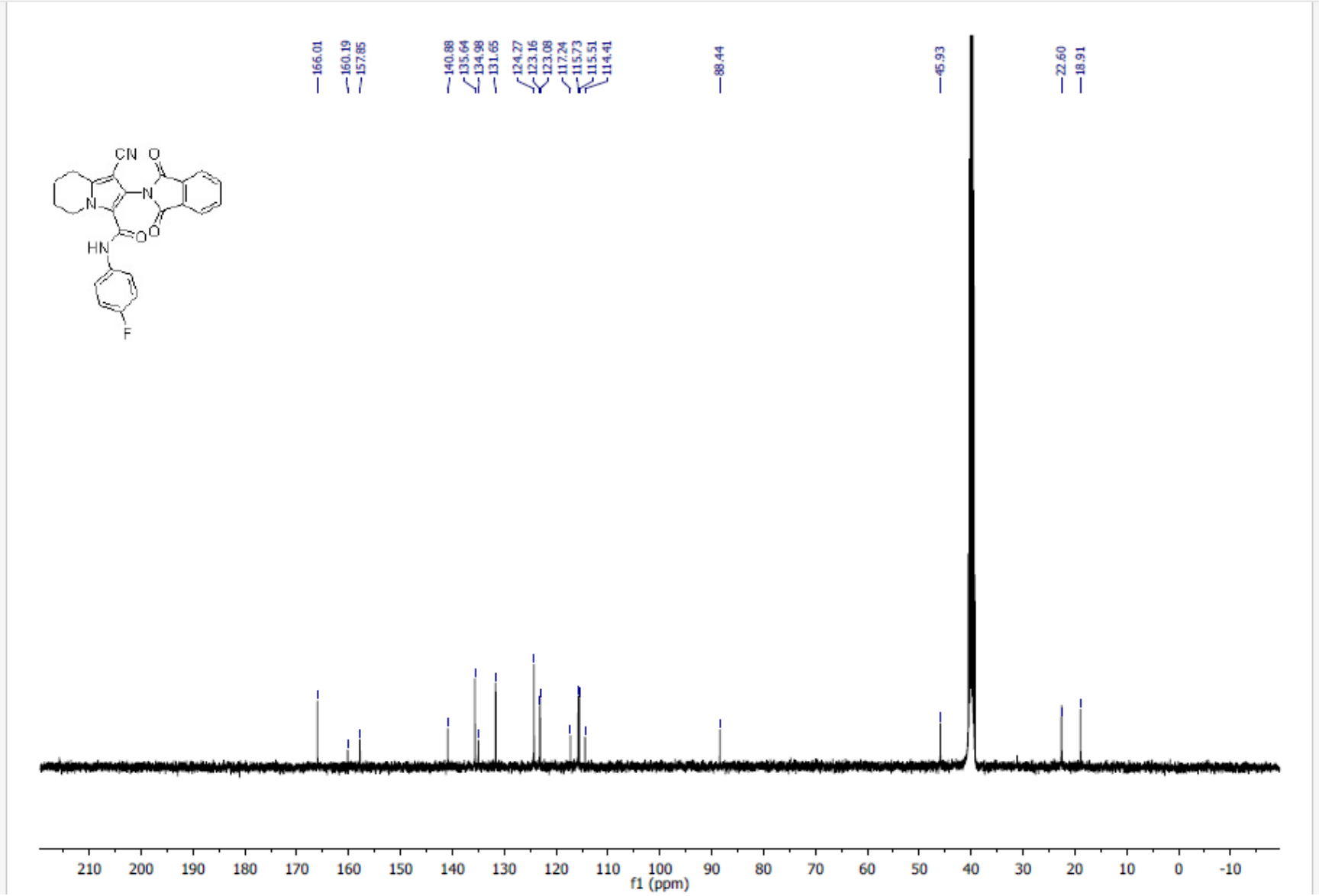


Fig.35. ^{13}C NMR of compound 6n (100 MHz, DMSO-d_6)

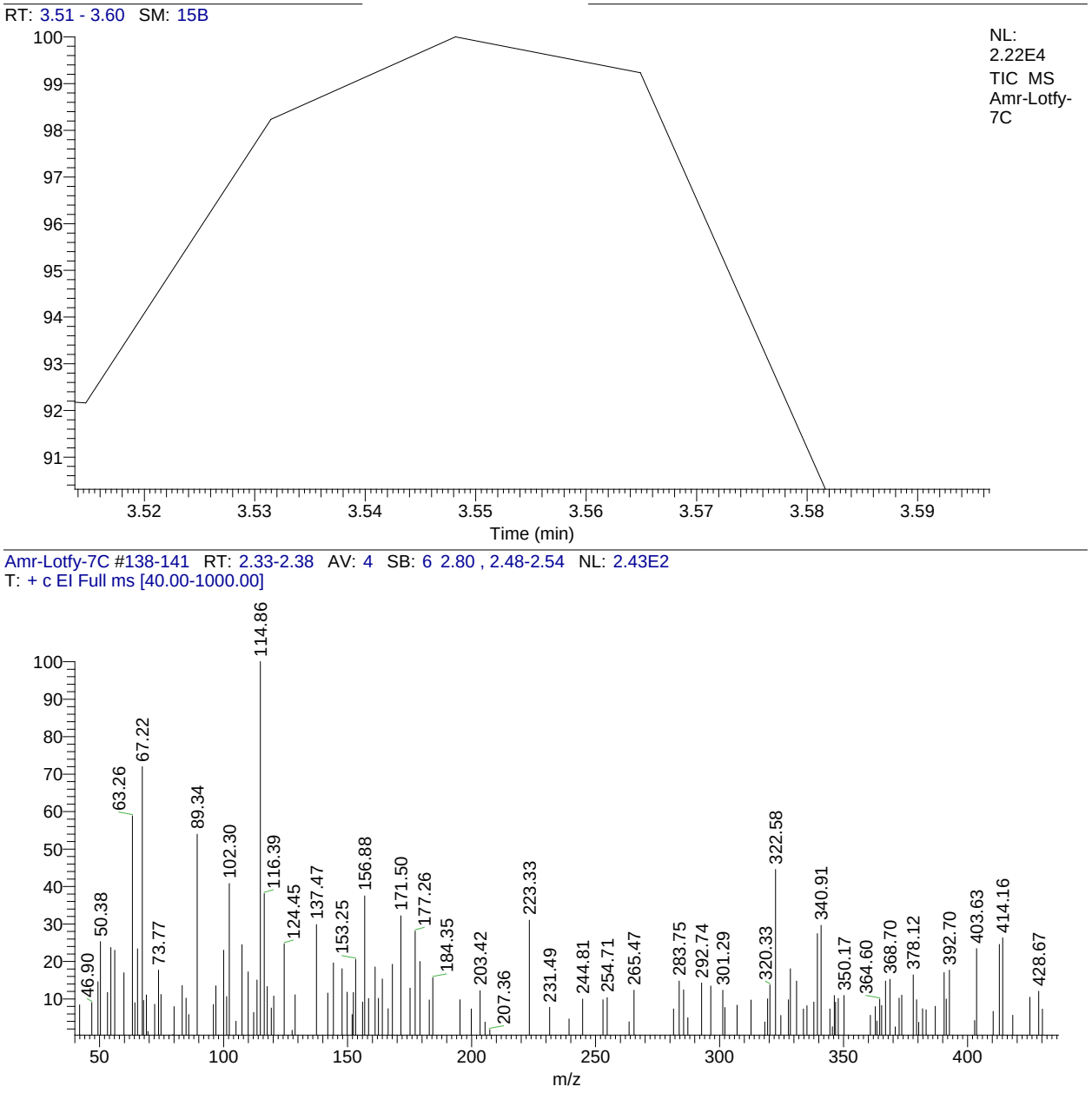


Fig.36. Mass spectra of compound 6n

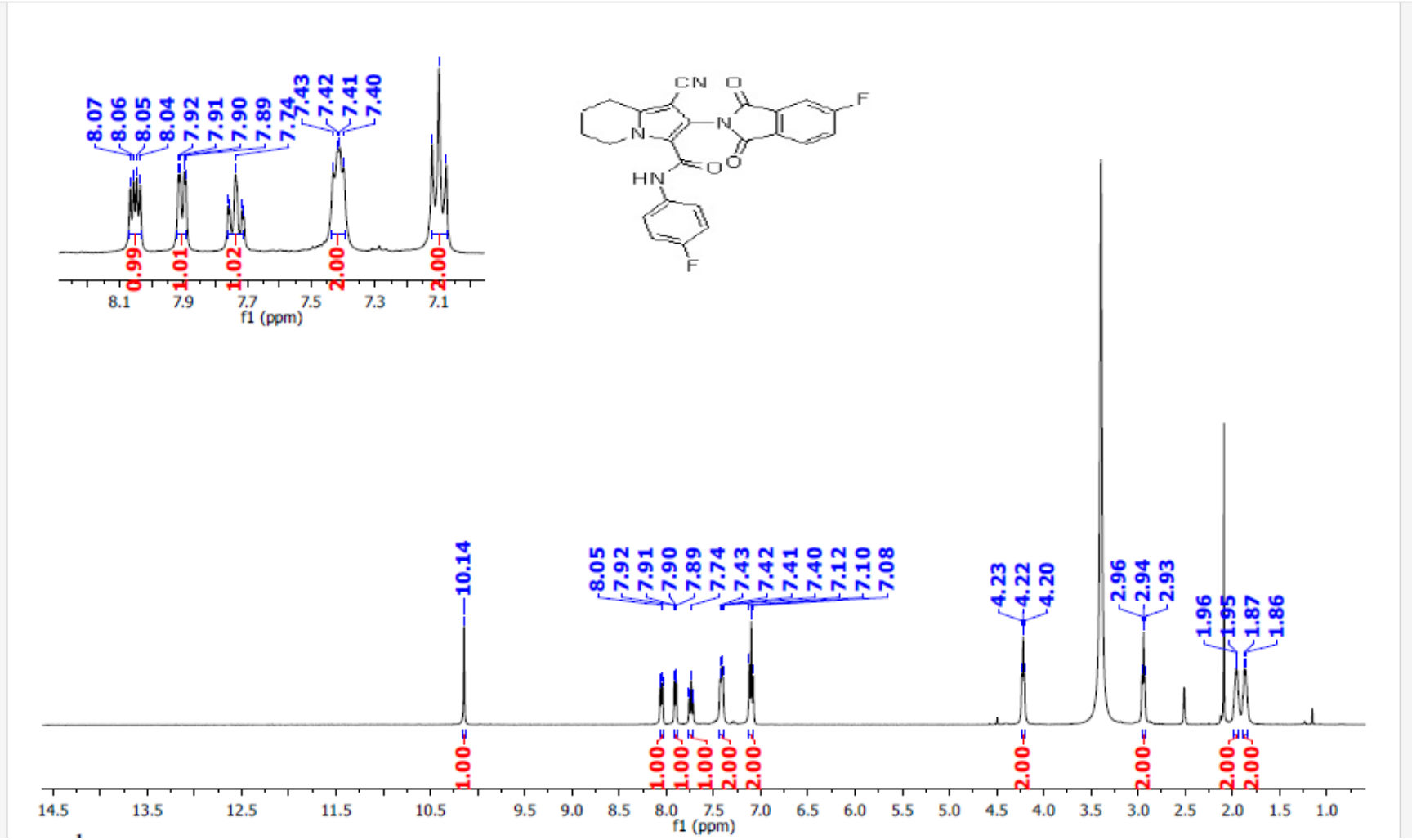


Fig.37. ^{1}H NMR of compound 6o (400 MHz, DMSO-d_6)

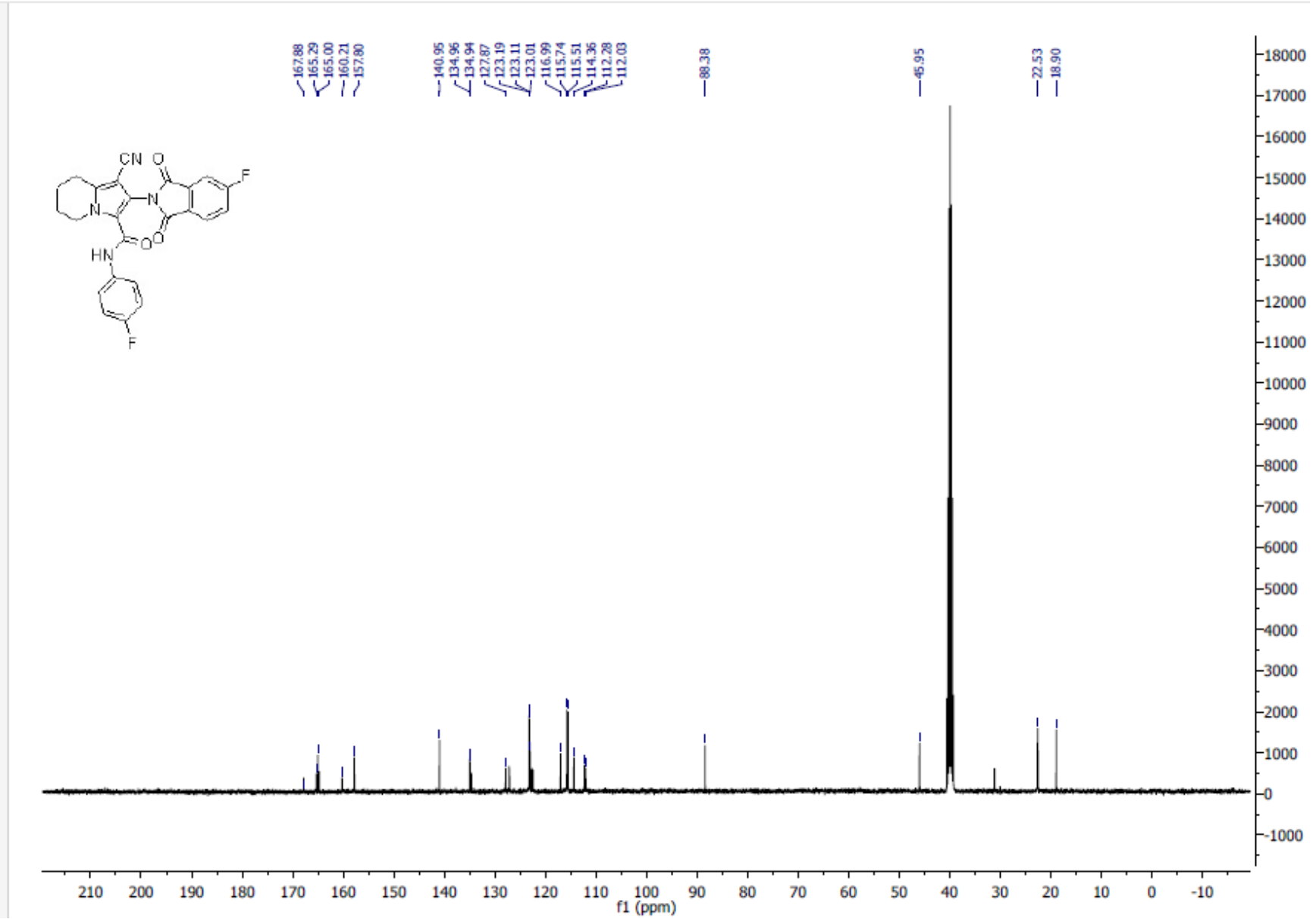


Fig.38. ^{13}C NMR of compound 6o (100 MHz, DMSO-d_6)

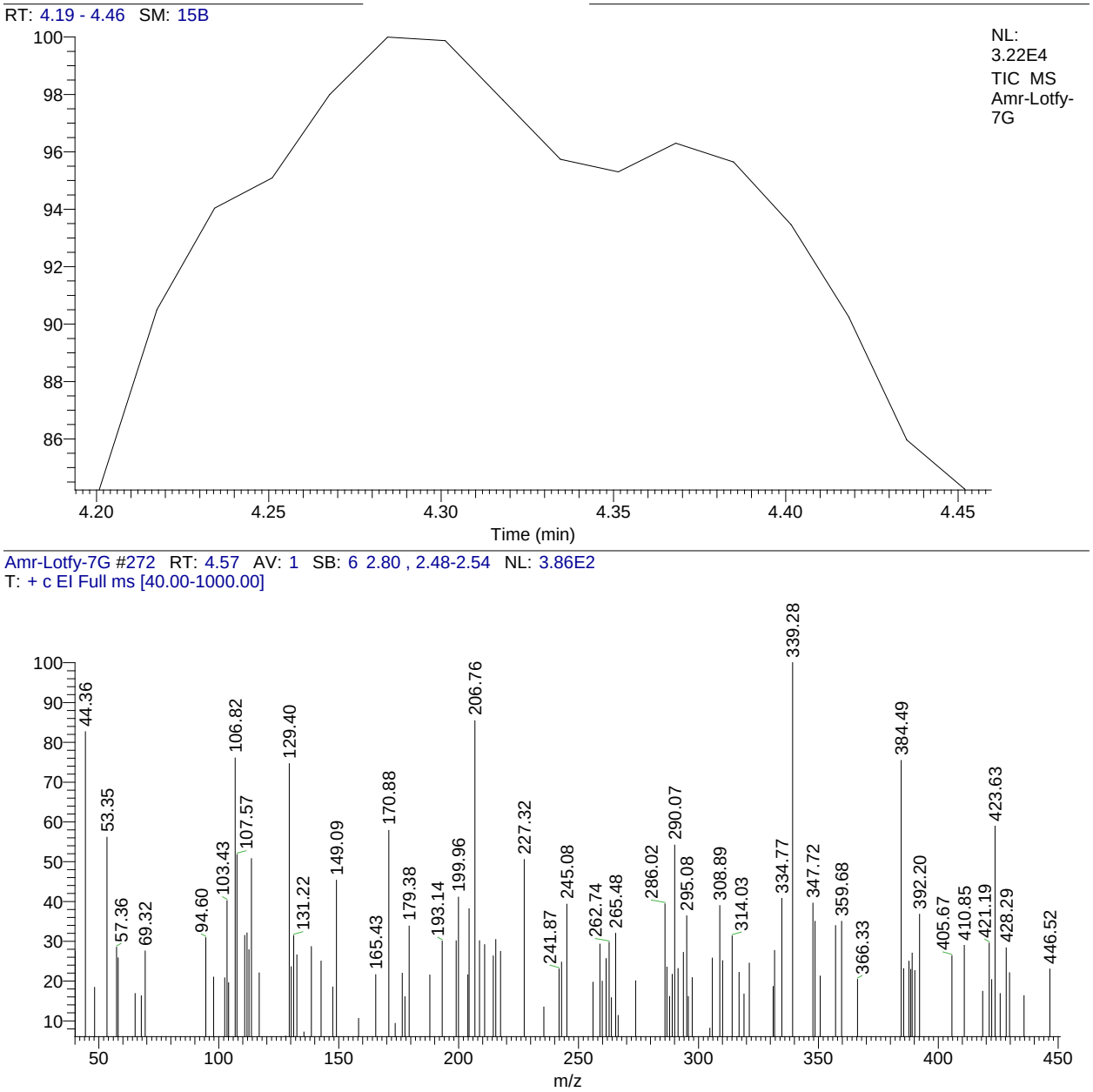


Fig.39. Mass spectra of compound 6o

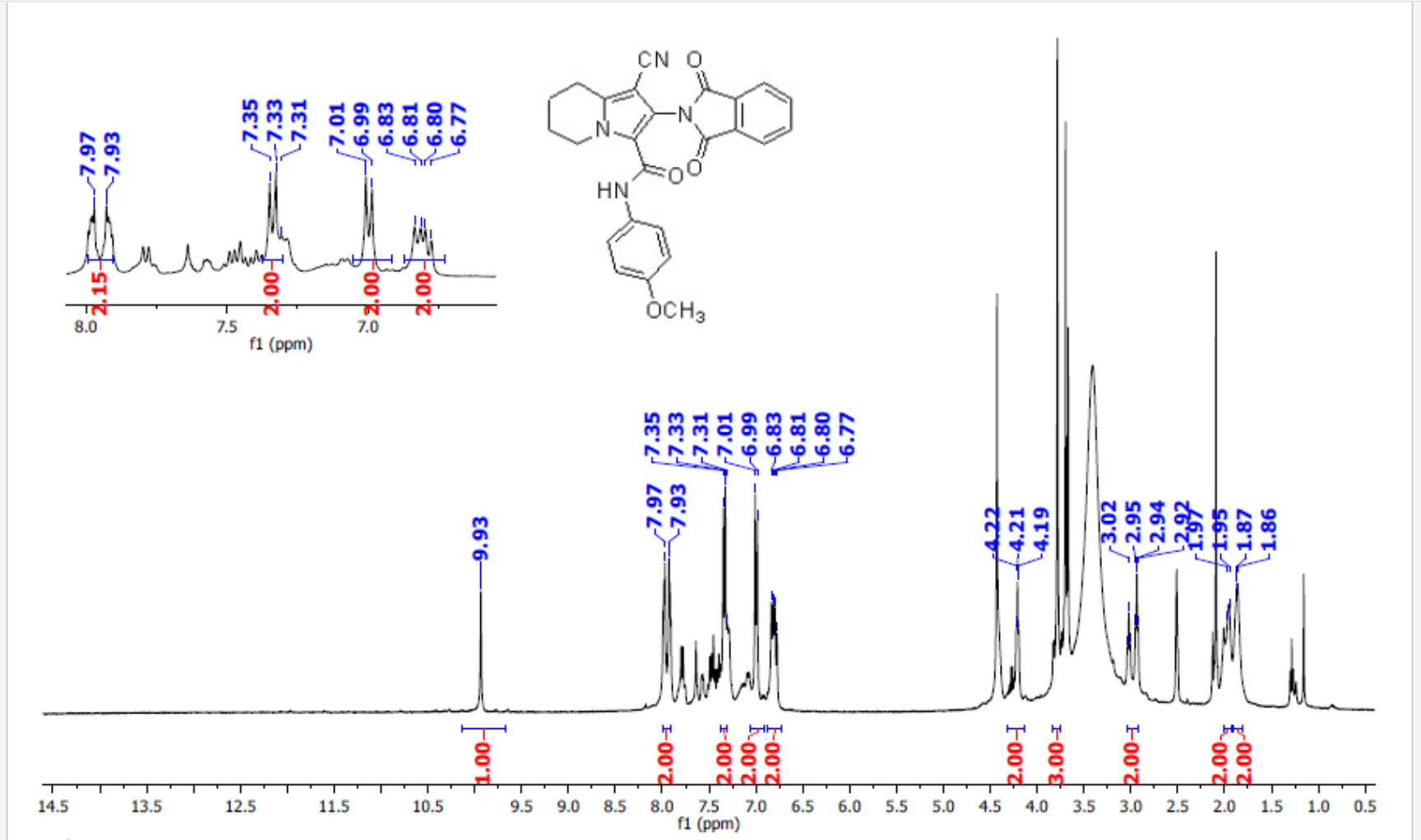


Fig.40. ^{1}H NMR of compound 6p (400 MHz, DMSO-d_6)

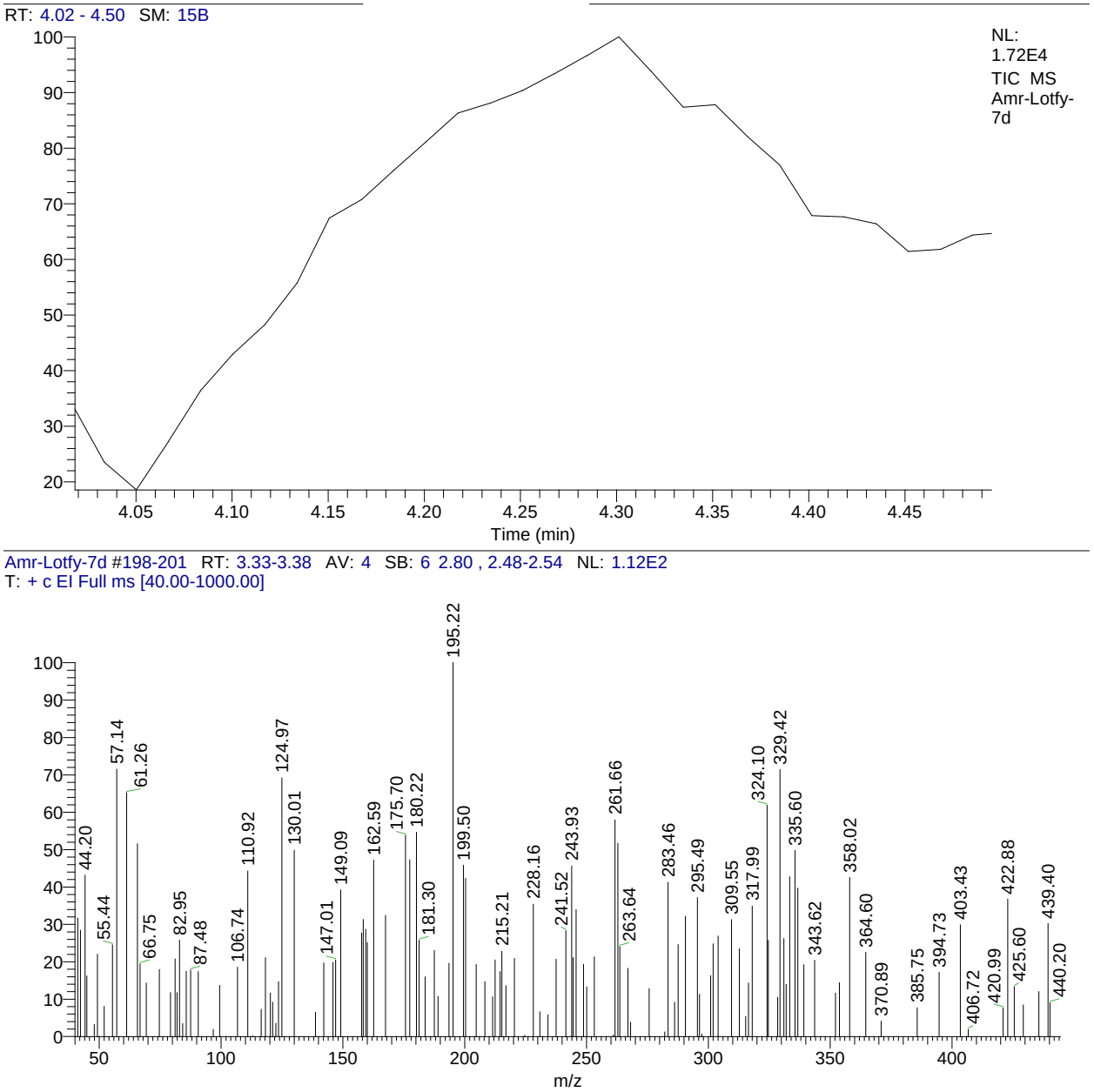


Fig.41. Mass spectra of compound 6p

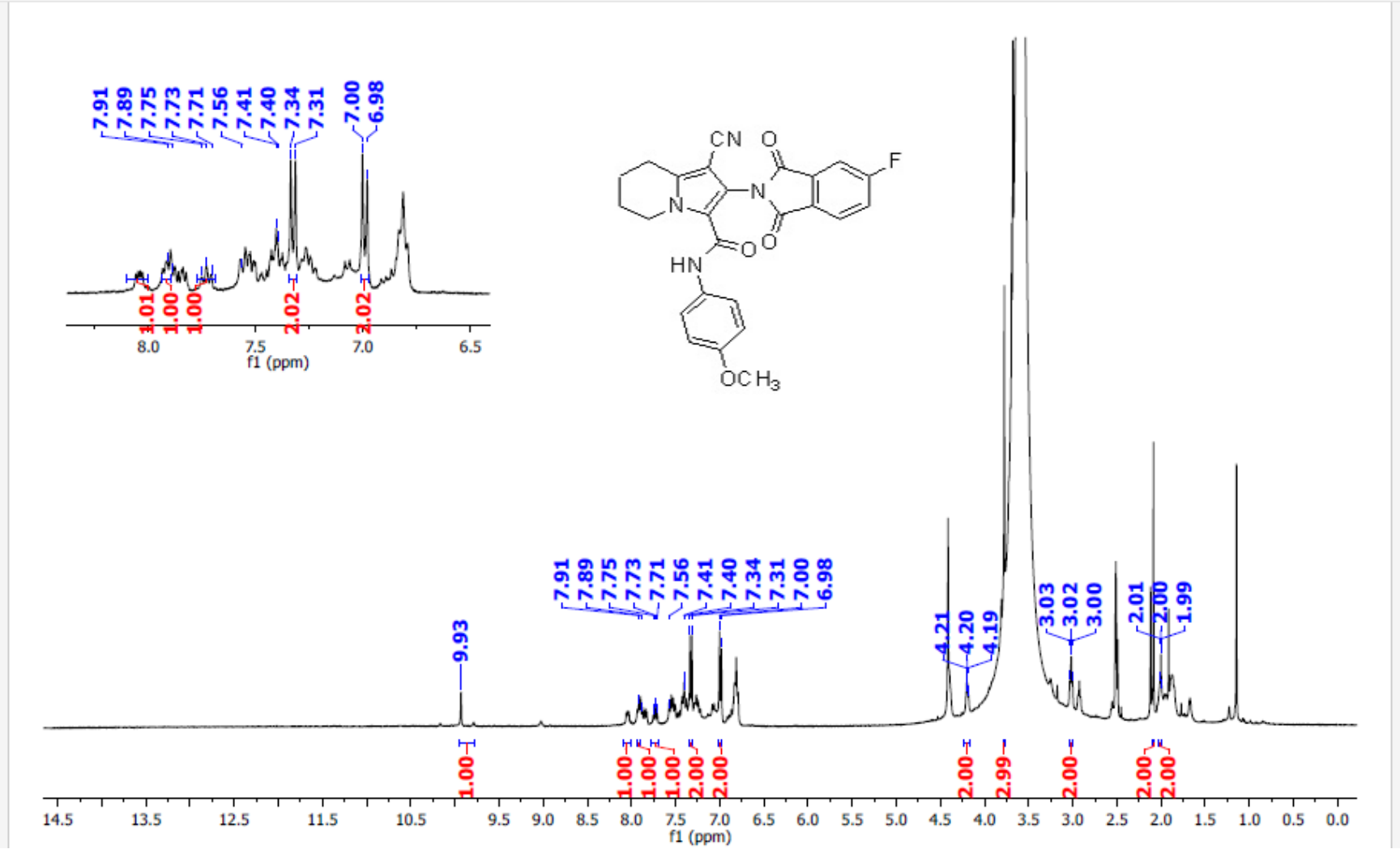


Fig.42. ^{1}H NMR of compound 6q (400 MHz, DMSO-d_6)

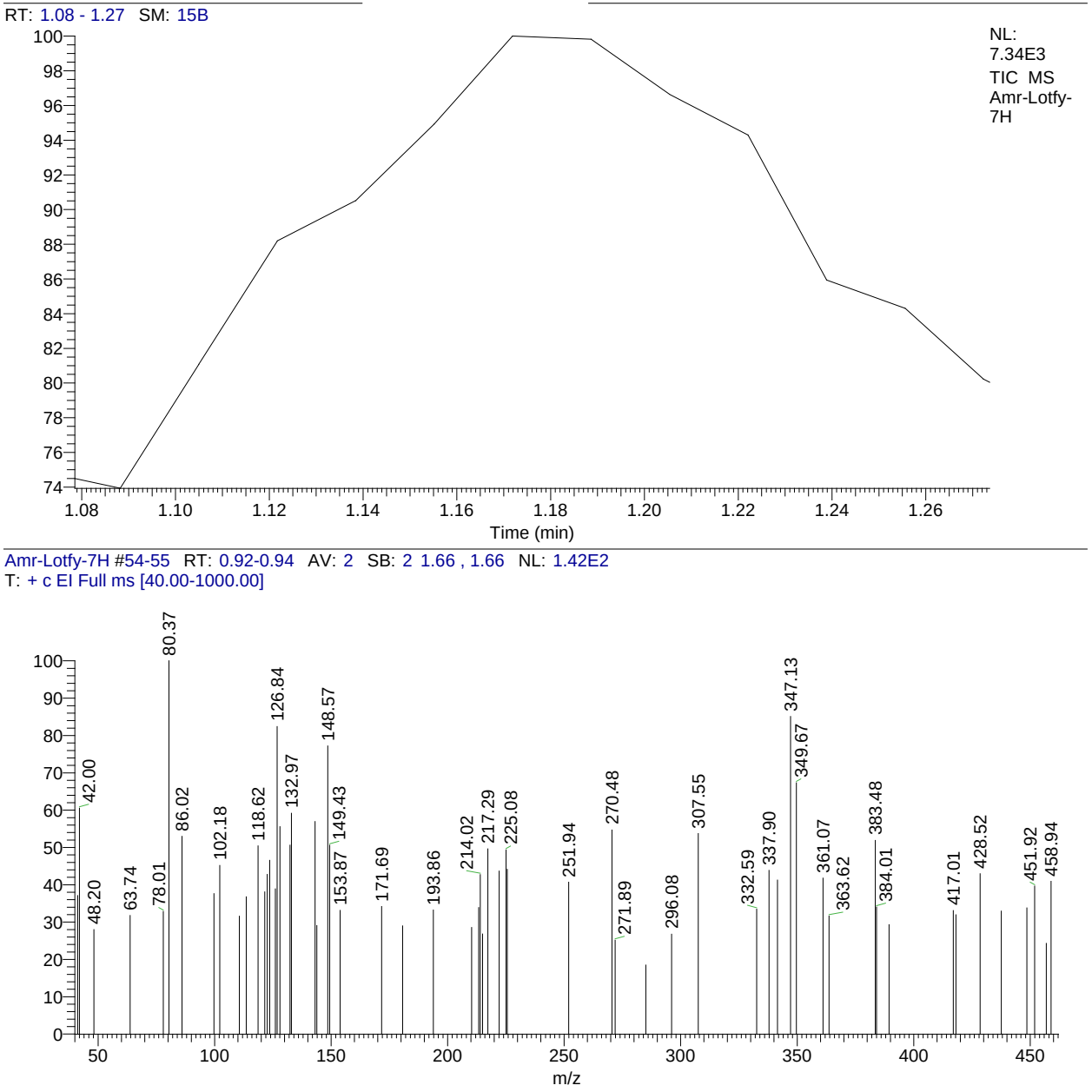
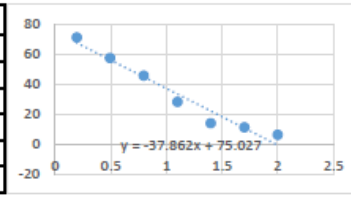


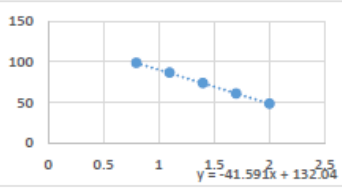
Fig.43. Mass spectra of compound 6q

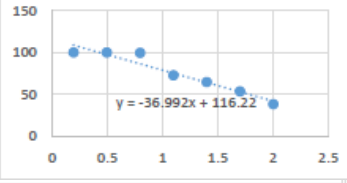
Raw data used to calculate the IC_{50} for compounds 6a-q against HePG-2, HCT-116, and MCF-7 cell lines

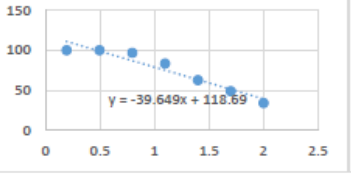
Conc. (µM)	log conc.	mean of % viability HePG-2	HCT-116	MCF-7
DOX				
100	2	6.3	7.1	6.2
50	1.698970004	11.2	13.9	10.9
25	1.397940009	14.1	18.7	14.3
12.5	1.096910013	28.3	31.4	26.9
6.25	0.795880017	45.8	47.9	41.5
3.125	0.494850022	57.6	60.5	58.4
1.56	0.193124598	71.2	73.8	69.1
6a				
100	2	48.9	53.4	50.1
50	1.698970004	61.2	71.8	66.5
25	1.397940009	73.8	89.1	81.9
12.5	1.096910013	87	99.3	98.3
6.25	0.795880017	98.6	100	100
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100
6b				
100	2	38.5	42.5	40.8
50	1.698970004	53.7	56.9	51.9
25	1.397940009	64.8	68.1	66.7
12.5	1.096910013	72.9	81.3	78.1
6.25	0.795880017	99.6	95.2	92.3
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100
6c				
100	2	34.2	35.1	37.5
50	1.698970004	48.7	51.6	54.2
25	1.397940009	62.8	59.3	64.1
12.5	1.096910013	83.6	72.9	73.8
6.25	0.795880017	97.1	96.7	99.6
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100
6d				
100	2	6.3	8.6	12.1
50	1.698970004	11.2	17.1	23.4
25	1.397940009	21.8	24.2	36.2
12.5	1.096910013	35.2	32.9	42.5
6.25	0.795880017	44.5	63.7	65
3.125	0.494850022	78.3	72.5	86.6
1.56	0.193124598	87.5	90.8	100
6e				
100	2	32.7	27.1	34.2
50	1.698970004	49	47.2	48.1
25	1.397940009	60.3	55.3	56.7
12.5	1.096910013	75.9	74	70.3
6.25	0.795880017	94.2	88.7	92.9
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100

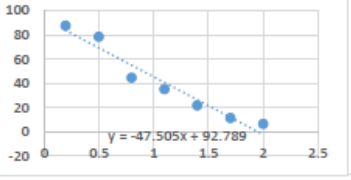
HePG-2

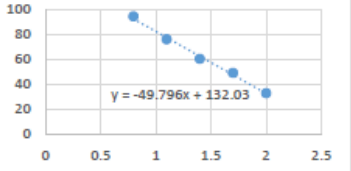




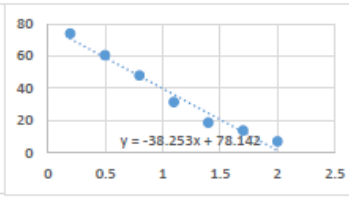


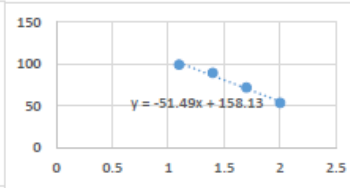


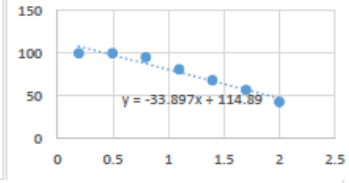


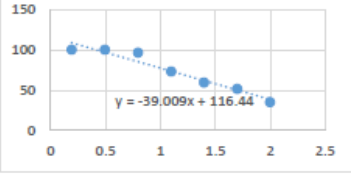


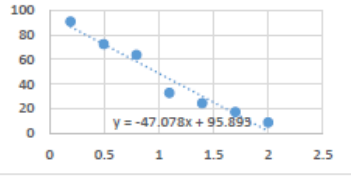
HCT-116

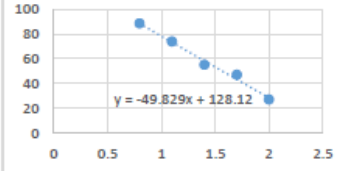




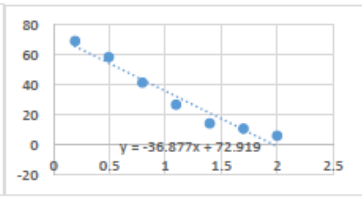


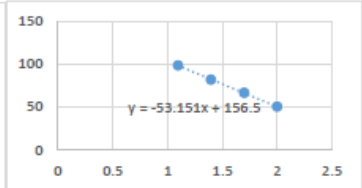


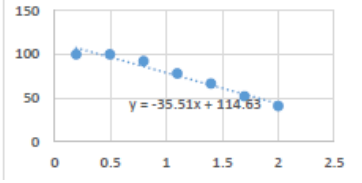


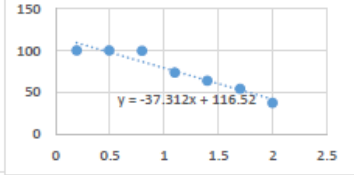


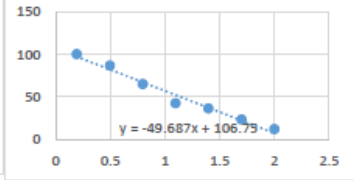
MCF-7

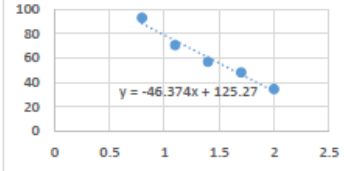




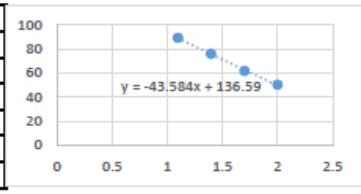


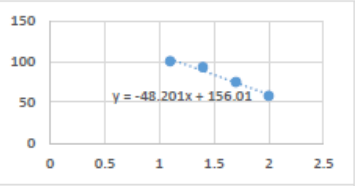


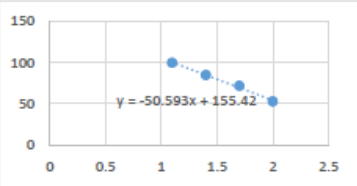




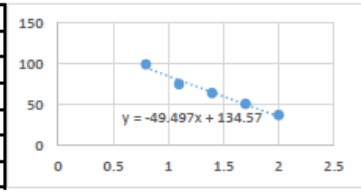
6f				
100	2	50.1	57.8	52.9
50	1.698970004	61.4	74.6	71.5
25	1.397940009	75.9	93.1	84.6
12.5	1.096910013	89	100	99.3
6.25	0.795880017	100	100	100
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100

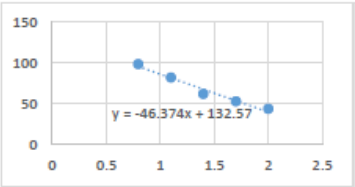


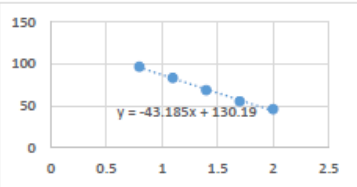




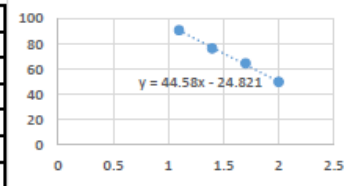
6g				
100	2	37.1	43.5	45.8
50	1.698970004	50.9	52.7	54.9
25	1.397940009	64.2	61.8	68.6
12.5	1.096910013	75.3	82.1	83.1
6.25	0.795880017	99.4	98.6	96.7
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100

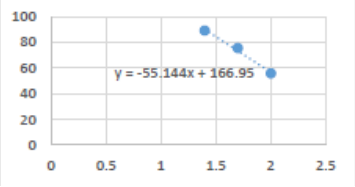


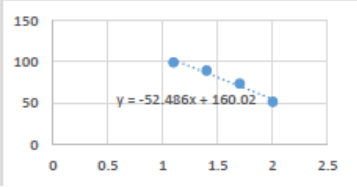




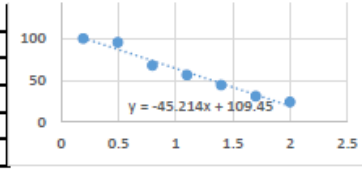
6h				
100	2	49.8	55.7	52.1
50	1.698970004	64.5	75.2	73.8
25	1.397940009	76.2	88.9	89.6
12.5	1.096910013	90.9	100	99.5
6.25	0.795880017	100	100	100
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100

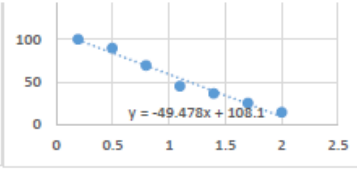


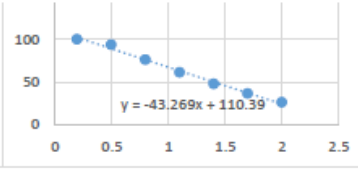




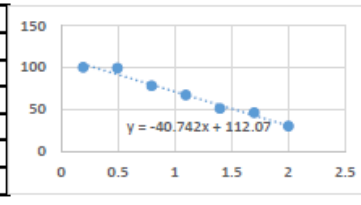
50	1.698970004	30.8	24.7	36.2
25	1.397940009	44.2	36.1	47.5
12.5	1.096910013	56.3	44.9	61.3
6.25	0.795880017	67.9	69.2	75.8
3.125	0.494850022	95.7	89.6	93.6
1.56	0.193124598	100	100	100

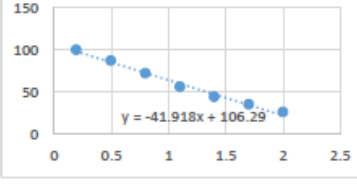


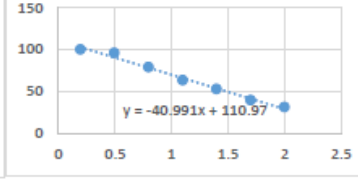




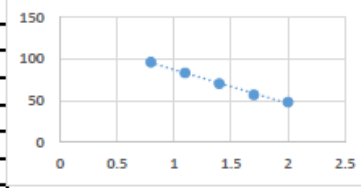
6j				
100	2	29.9	26.2	31.2
50	1.698970004	46.1	35.3	39.6
25	1.397940009	51.2	44.5	52.7
12.5	1.096910013	67.2	56.4	63.5
6.25	0.795880017	78	72.5	79.1
3.125	0.494850022	99.3	87.3	96
1.56	0.193124598	100	100	100

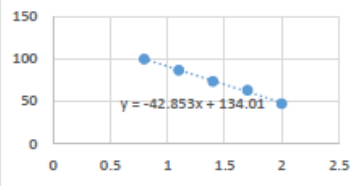


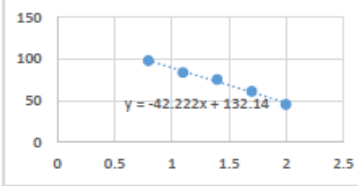




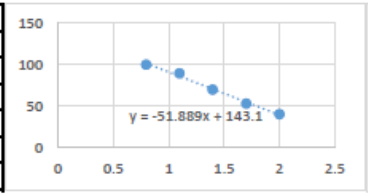
6k				
100	2	48.6	47.3	45.9
50	1.698970004	57.3	63	61.6
25	1.397940009	70.4	73.5	75.8
12.5	1.096910013	83.7	86.8	84.1
6.25	0.795880017	96.5	99.9	98.2
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100

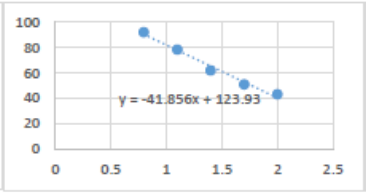


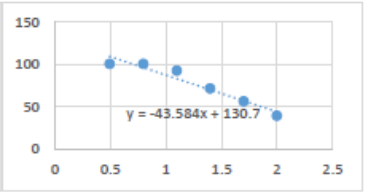




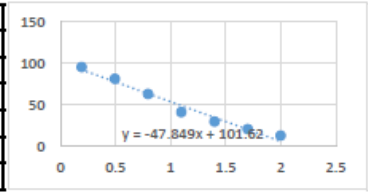
6l				
100	2	40.2	43.1	38.9
50	1.698970004	53.1	51	55.7
25	1.397940009	69.8	62.1	71.3
12.5	1.096910013	89.7	78.6	92.1
6.25	0.795880017	100	92.3	100
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100

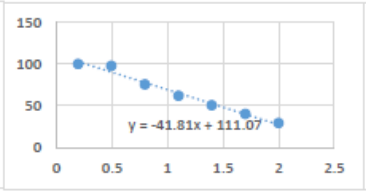


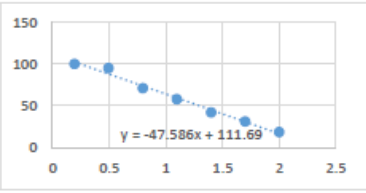




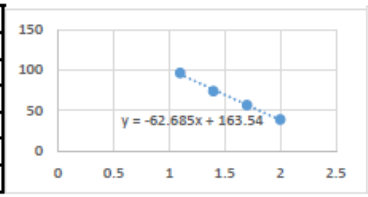
6m				
100	2	12.9	29.2	18.7
50	1.698970004	20.3	40.5	31.3
25	1.397940009	29.8	50.7	42.1
12.5	1.096910013	41	62.3	57.8
6.25	0.795880017	63.1	75.8	71.2
3.125	0.494850022	81.3	98	95.4
1.56	0.193124598	95.6	100	100

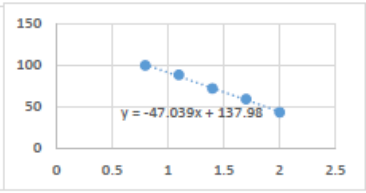


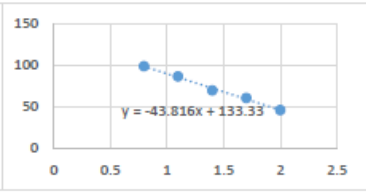




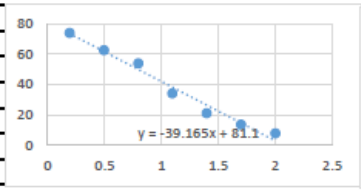
6n				
100	2	39	43.2	45.6
50	1.698970004	56.8	58.8	60.4
25	1.397940009	73.9	71.7	69.5
12.5	1.096910013	96.2	88	86.3
6.25	0.795880017	100	99.4	98.6
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100

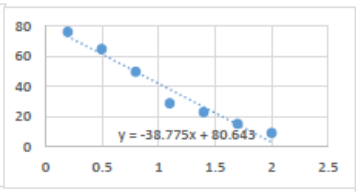


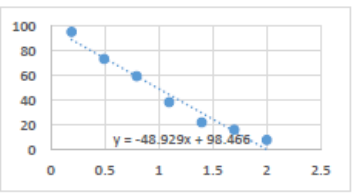




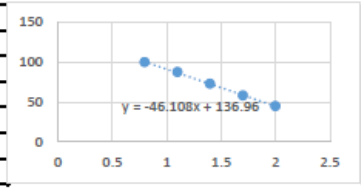
6o				
100	2	7.8	9.1	8.1
50	1.698970004	13.5	15.2	16.4
25	1.397940009	21	23	22.3
12.5	1.096910013	34	28.9	38.7
6.25	0.795880017	53.9	49.7	59.5
3.125	0.494850022	62.7	64.8	73.4
1.56	0.193124598	74.1	76.1	95.2

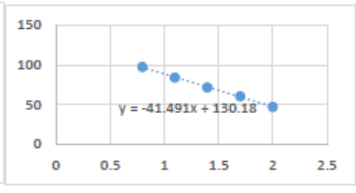


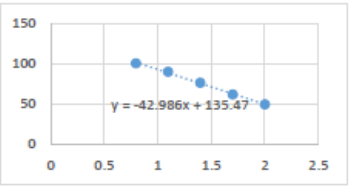




6p				
100	2	44.8	47.1	49.2
50	1.698970004	58.1	60.3	61.8
25	1.397940009	72.7	71.7	76.3
12.5	1.096910013	87.3	84.2	89.6
6.25	0.795880017	99.6	97.6	100
3.125	0.494850022	100	100	100
1.56	0.193124598	100	100	100







6q				
100	2	34.9	26.9	30.9
50	1.698970004	46.1	41.2	43.7
25	1.397940009	59	53.8	54.8
12.5	1.096910013	67.4	69.1	71.1
6.25	0.795880017	83.8	78.6	90.2
3.125	0.494850022	99.3	98.7	100
1.56	0.193124598	100	100	100