Supplementary Data:

Discovery of azaindolin-2-one as a dual inhibitor of GSK3β and tau aggregation with potential neuroprotective activity

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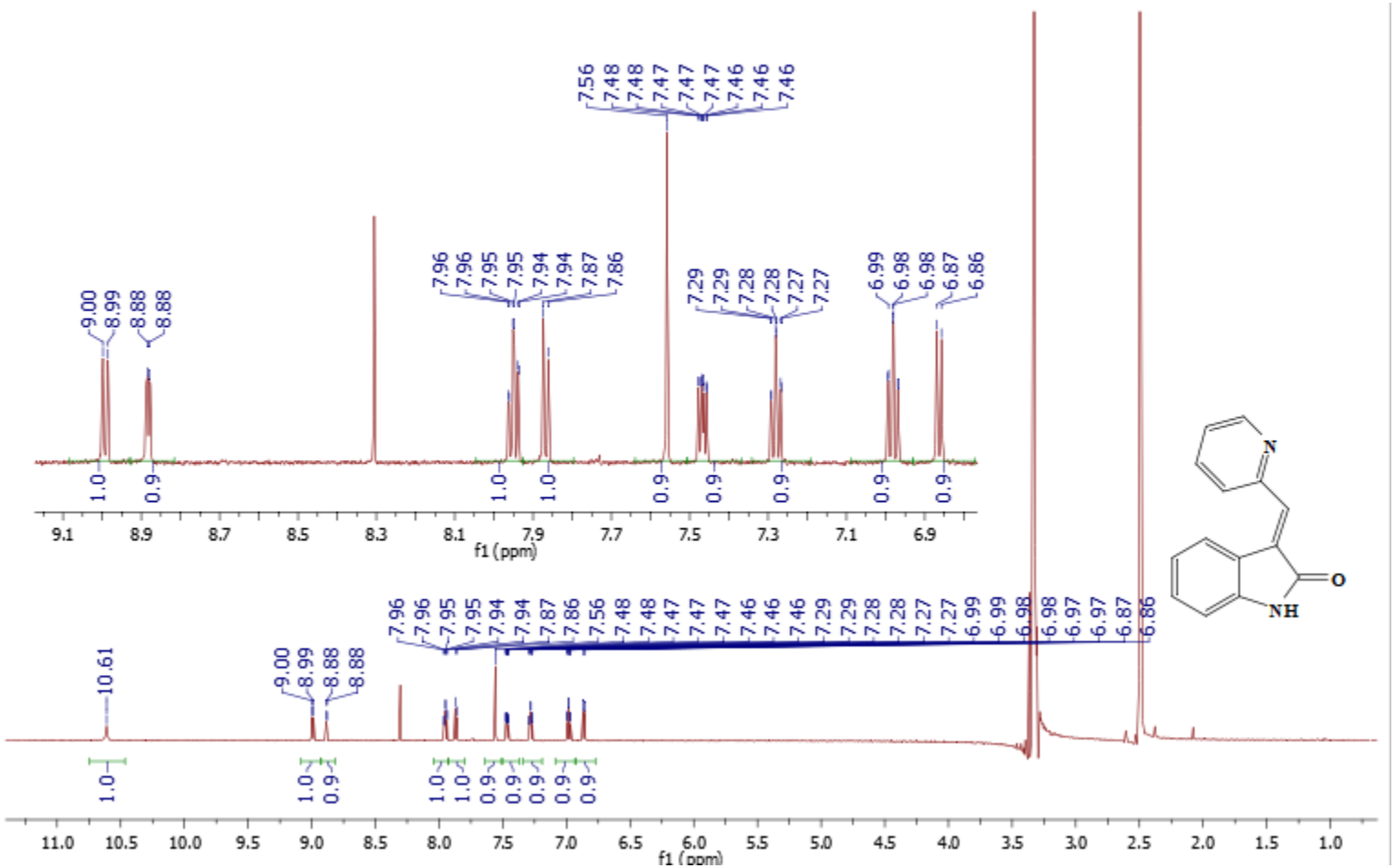


Figure S1. ^{1}H-NMR spectrum of compound **(*E*)-2a** (600MHz, DMSO-*d*6)

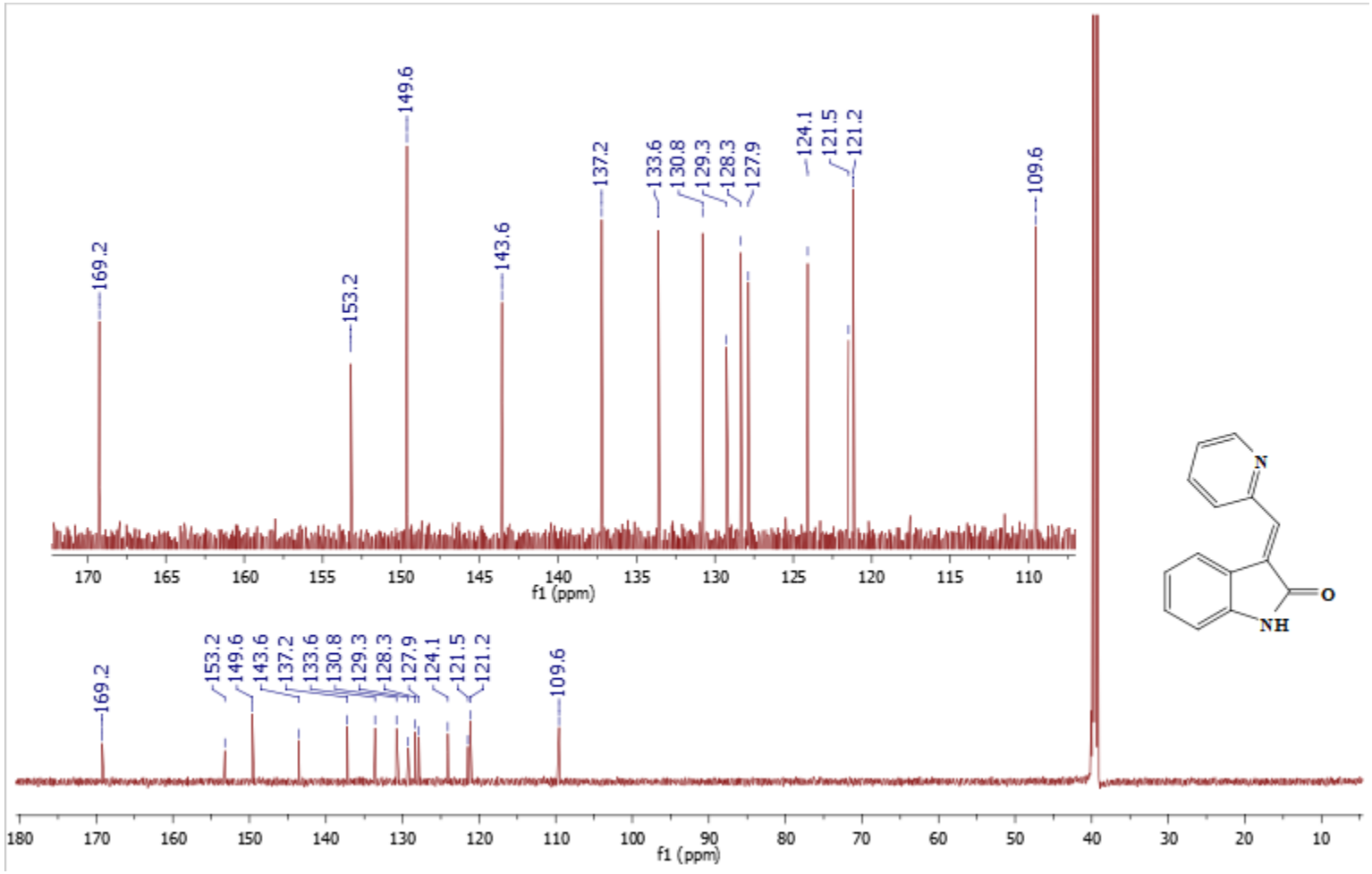


Figure S2. ^{13}C-NMR spectrum of compound **(*E*)-2a** (150MHz, DMSO-*d*6)

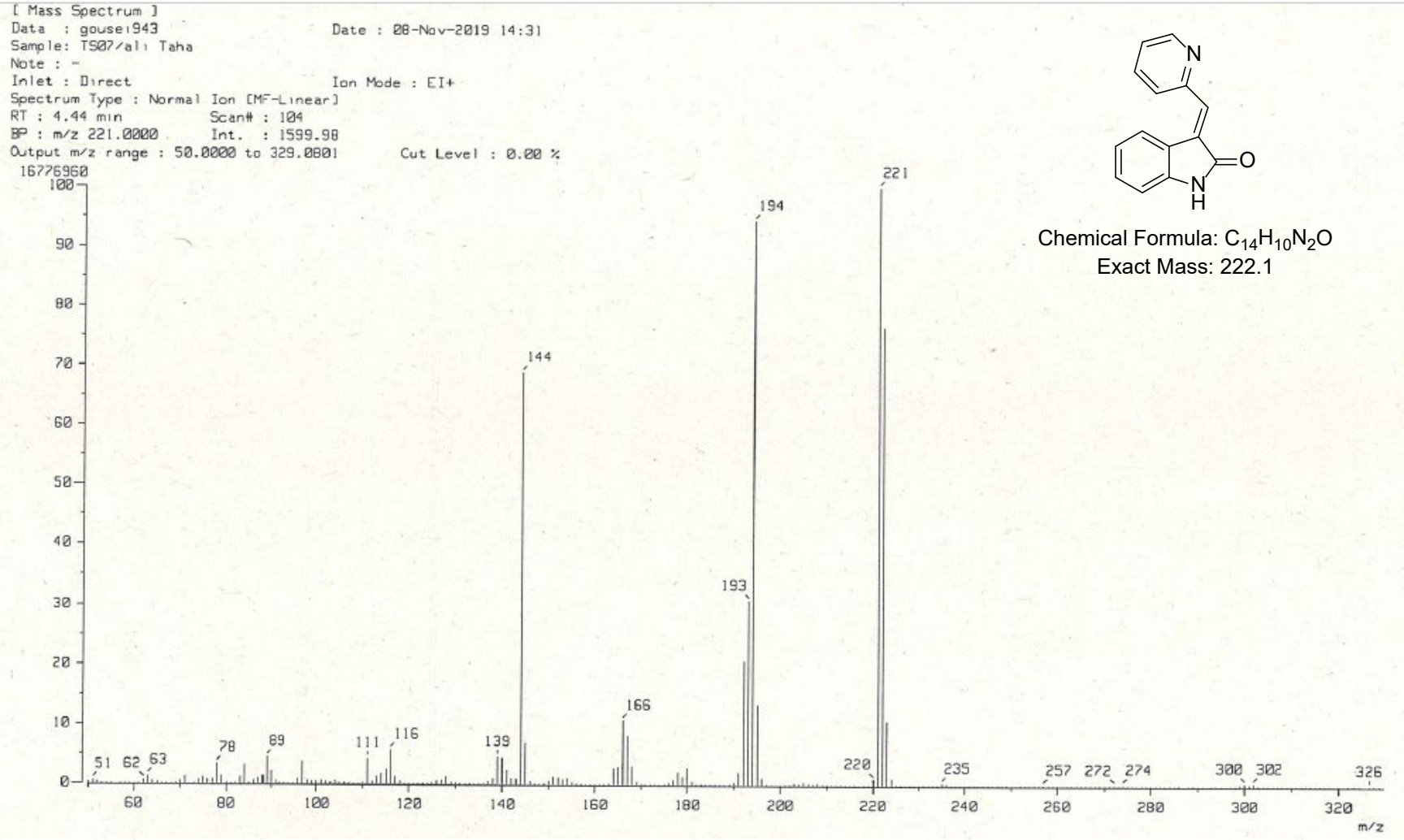


Figure S3. MS (EI+) of compound **(*E*)-2a**

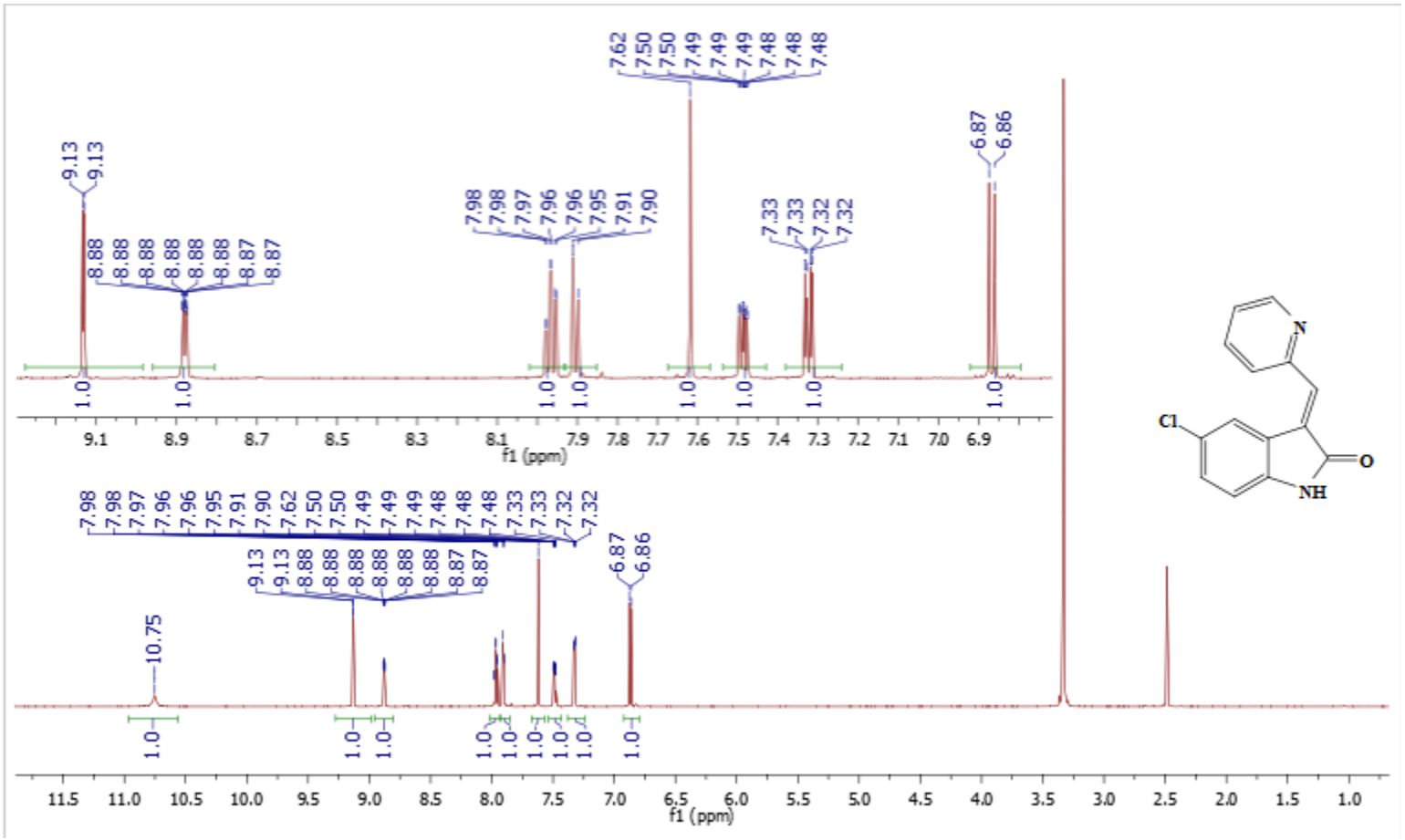


Figure S4. [1]H-NMR spectrum of compound **(*E*)-2b** (600MHz, DMSO-*d*6)

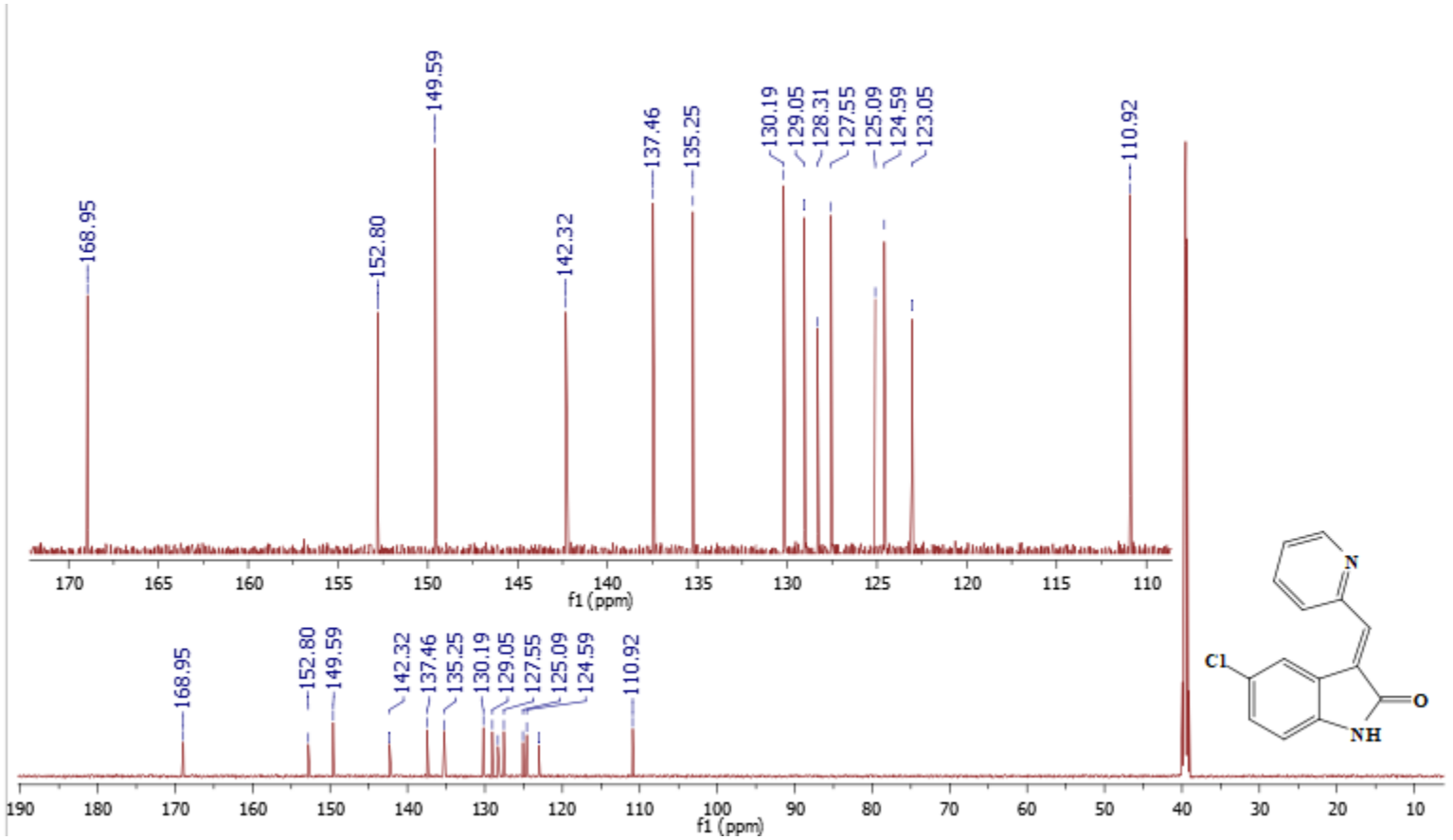


Figure S5. ^{13}C-NMR spectrum of compound **(*E*)-2b** (150MHz, DMSO-*d*6)

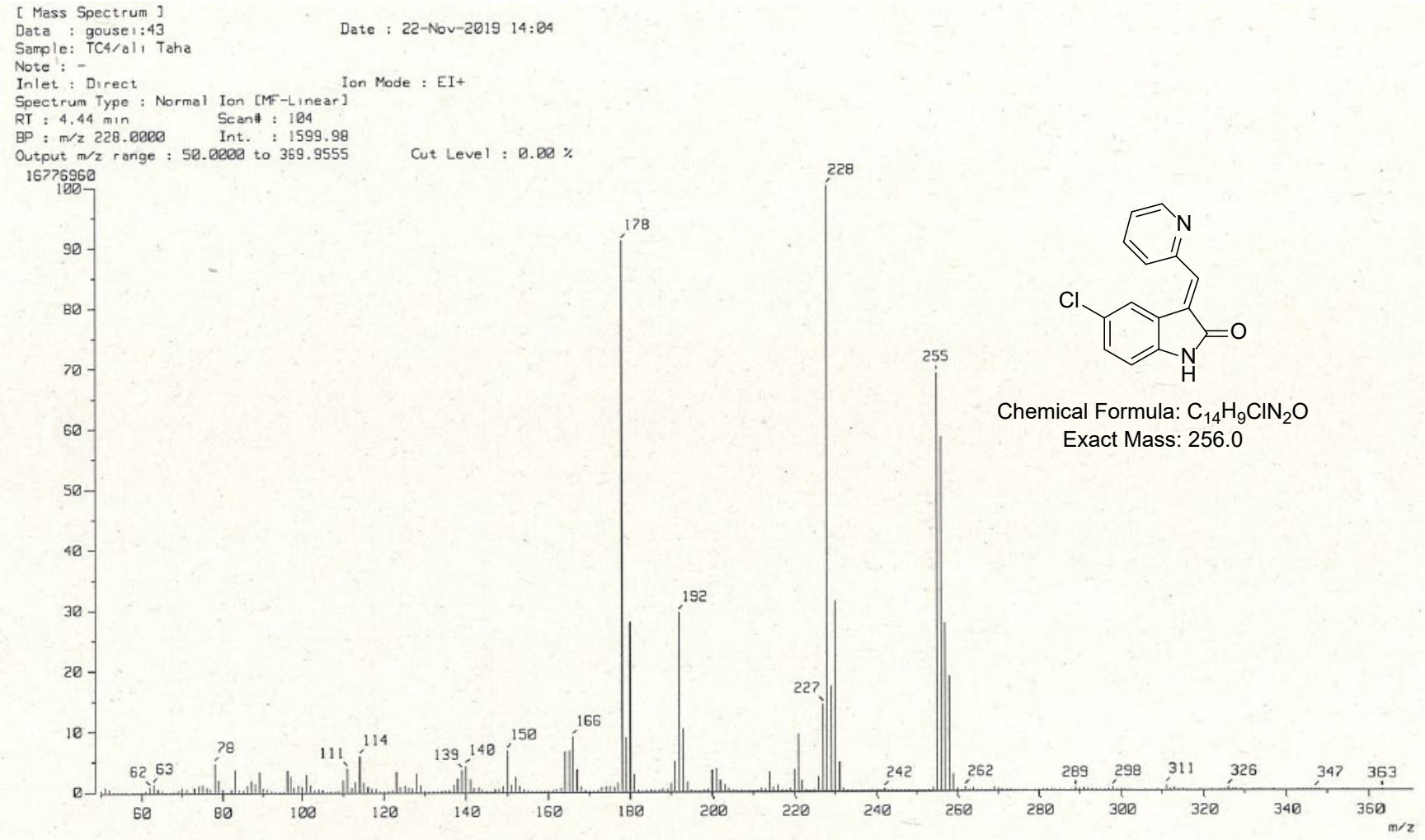


Figure S6. MS (EI+) of compound **(*E*)-2b**

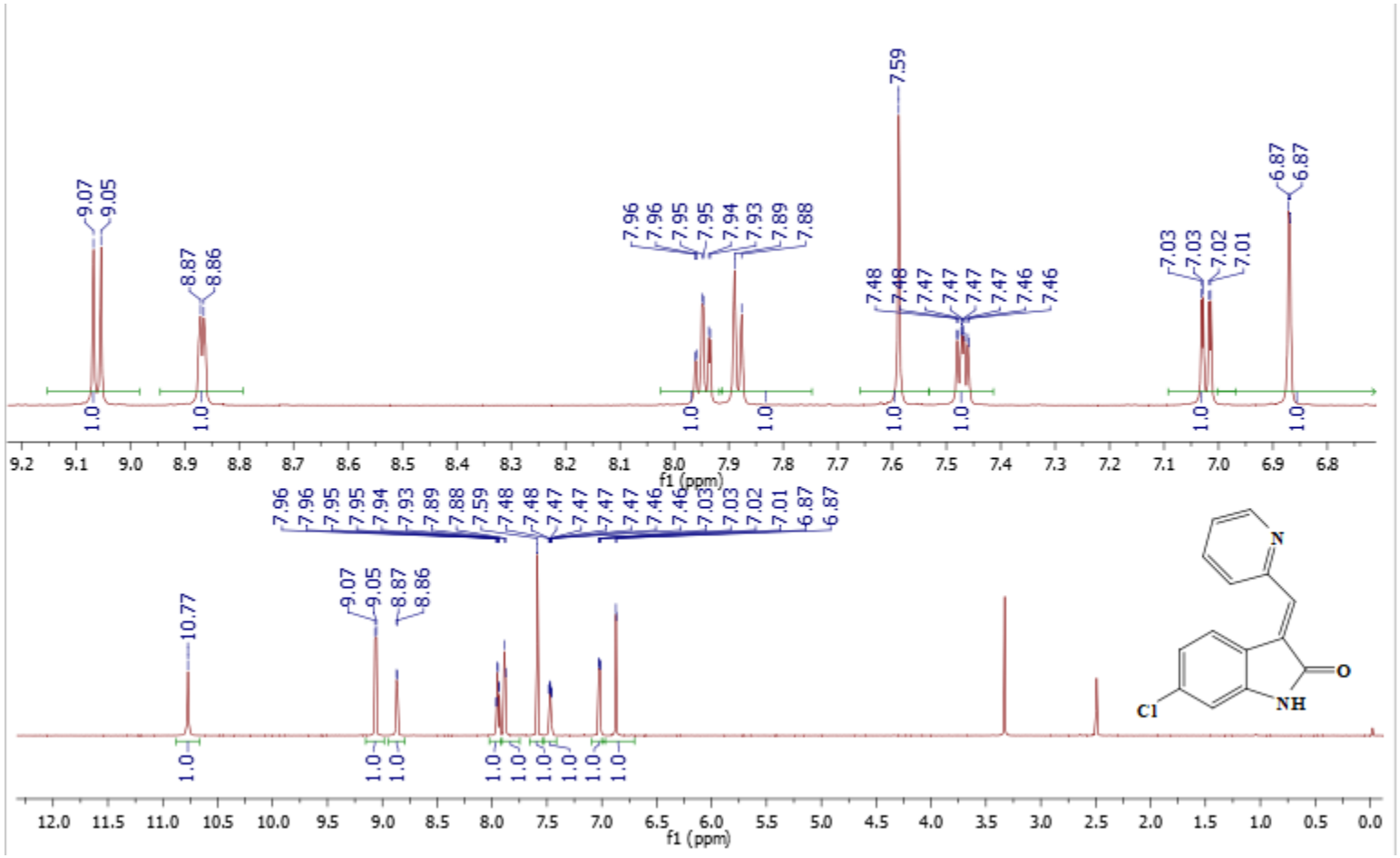


Figure S7. [1]H-NMR spectrum of compound **(*E*)-2c** (600MHz, DMSO-*d*6)

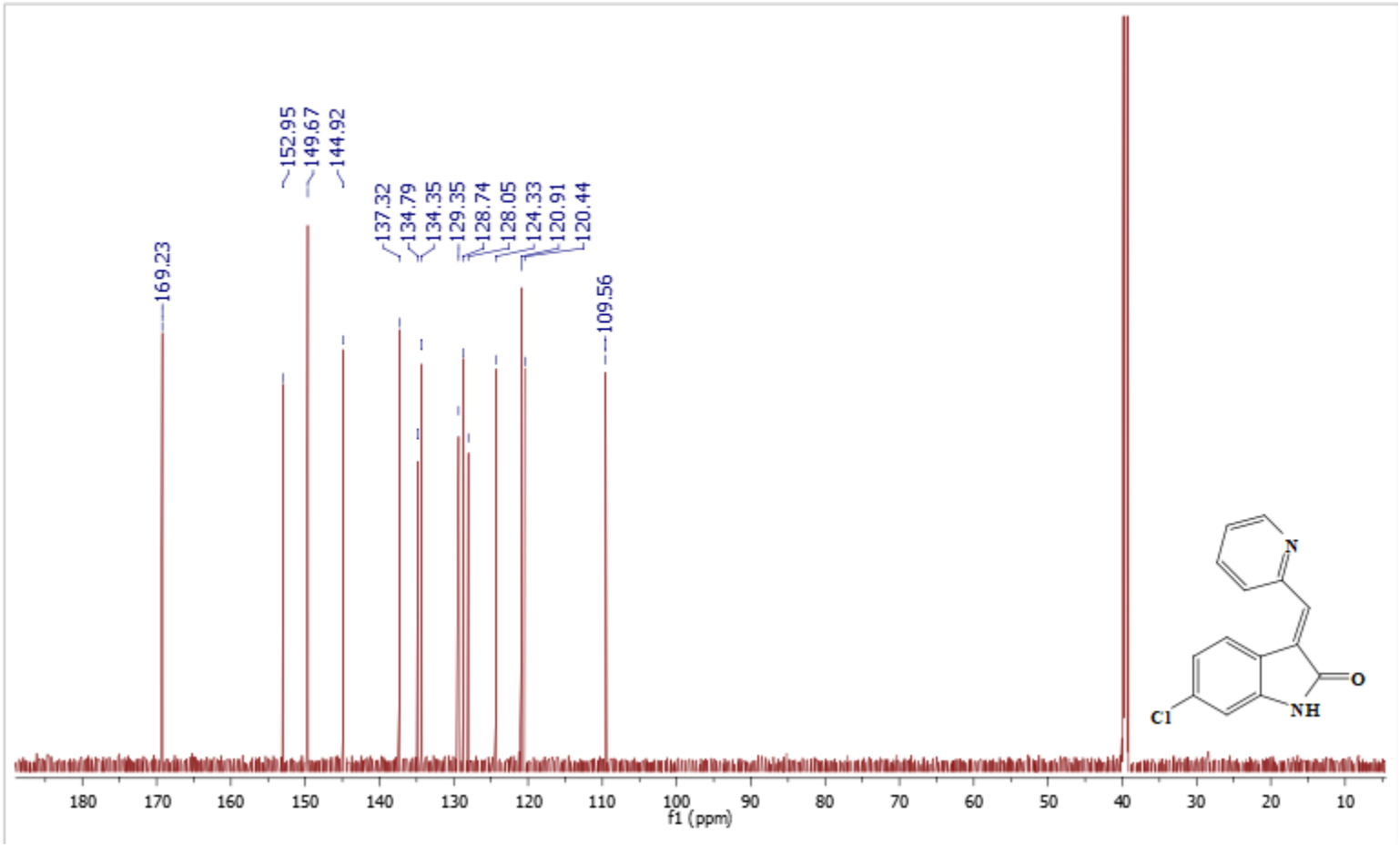


Figure S8. ^{13}C-NMR spectrum of compound **(*E*)-2c** (150MHz, DMSO-*d*6)

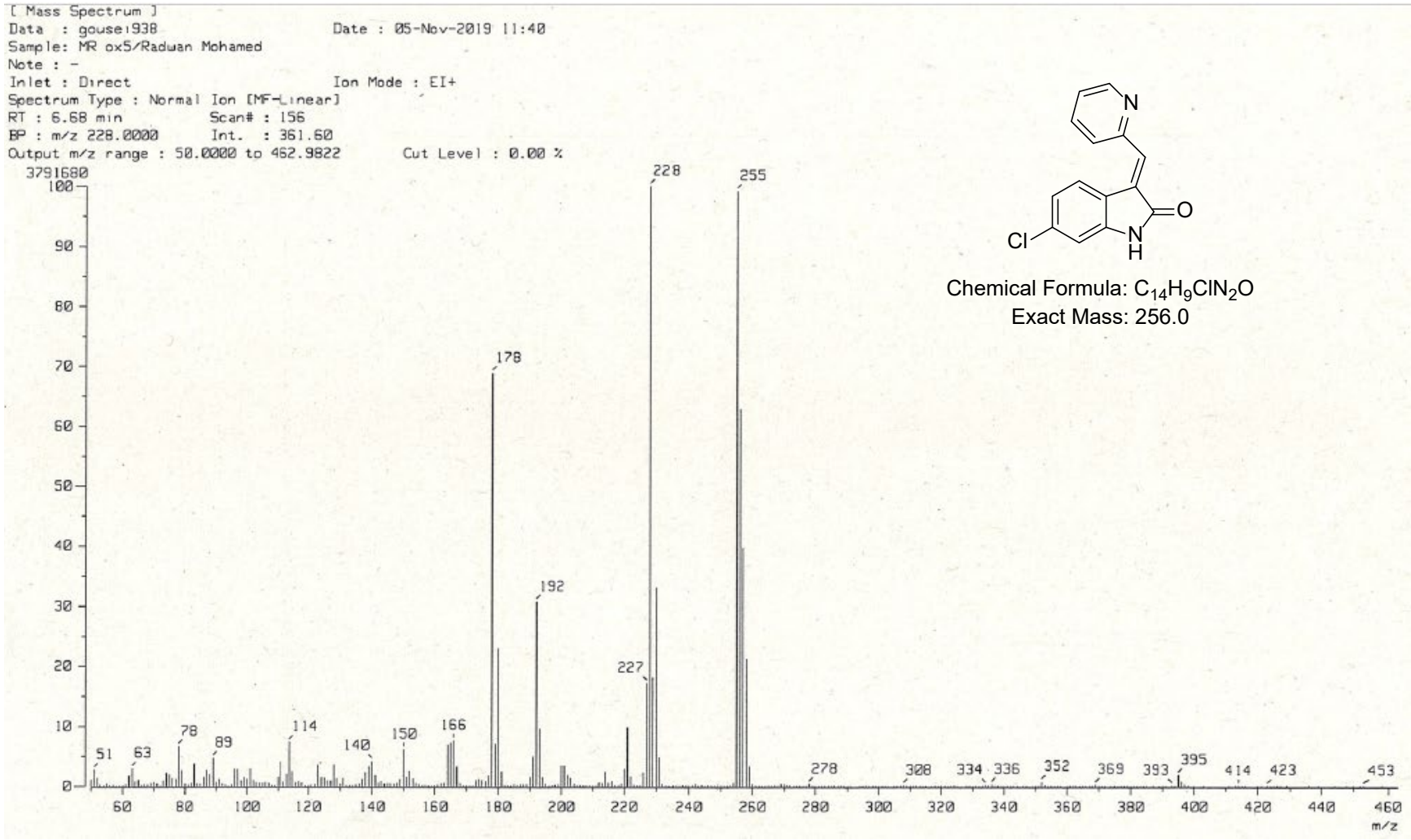


Figure S9. MS (EI+) of compound **(*E*)-2c**

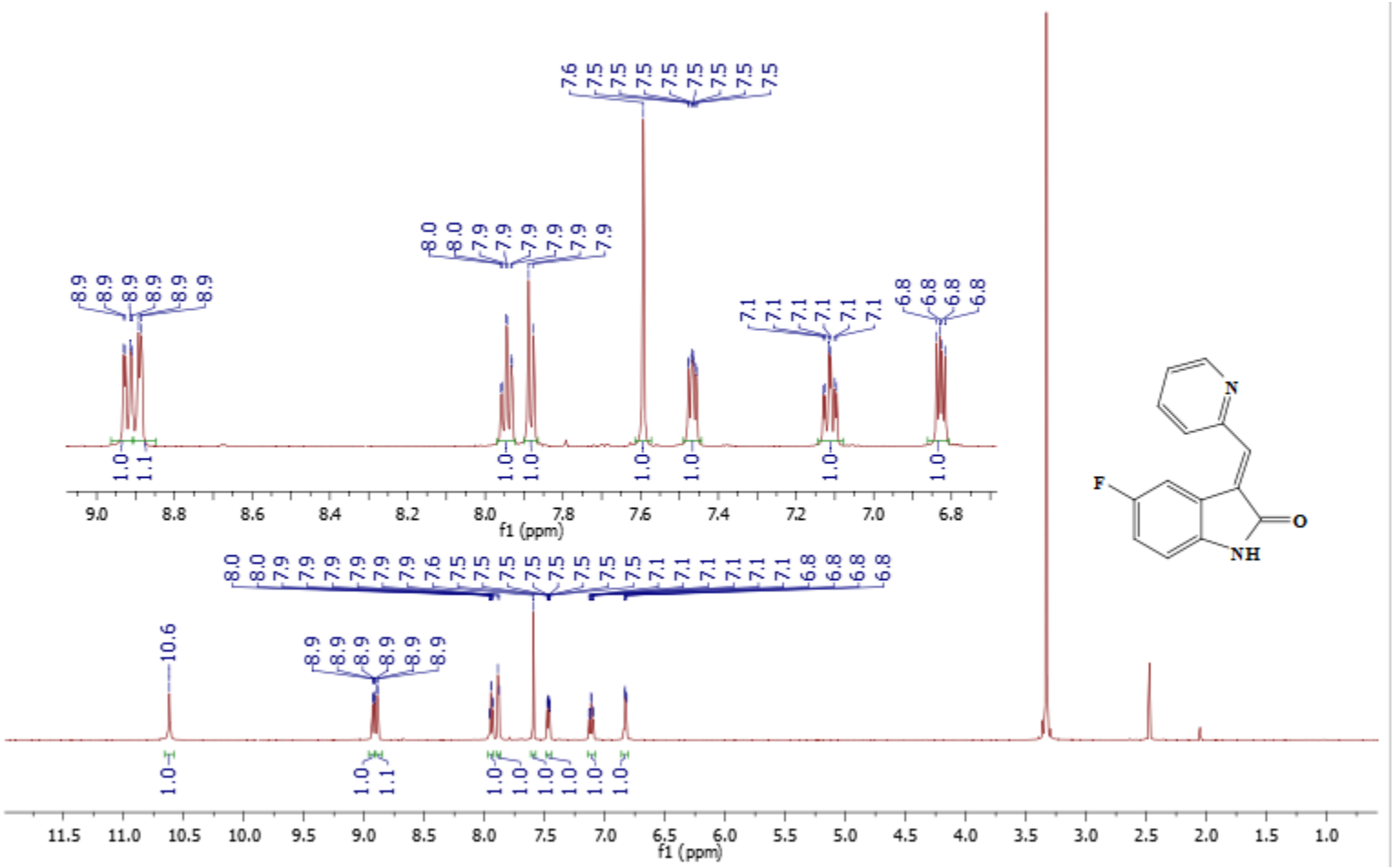


Figure S10. ^{1}H-NMR spectrum of compound **(*E*)-2d** (600MHz, DMSO-*d*6)

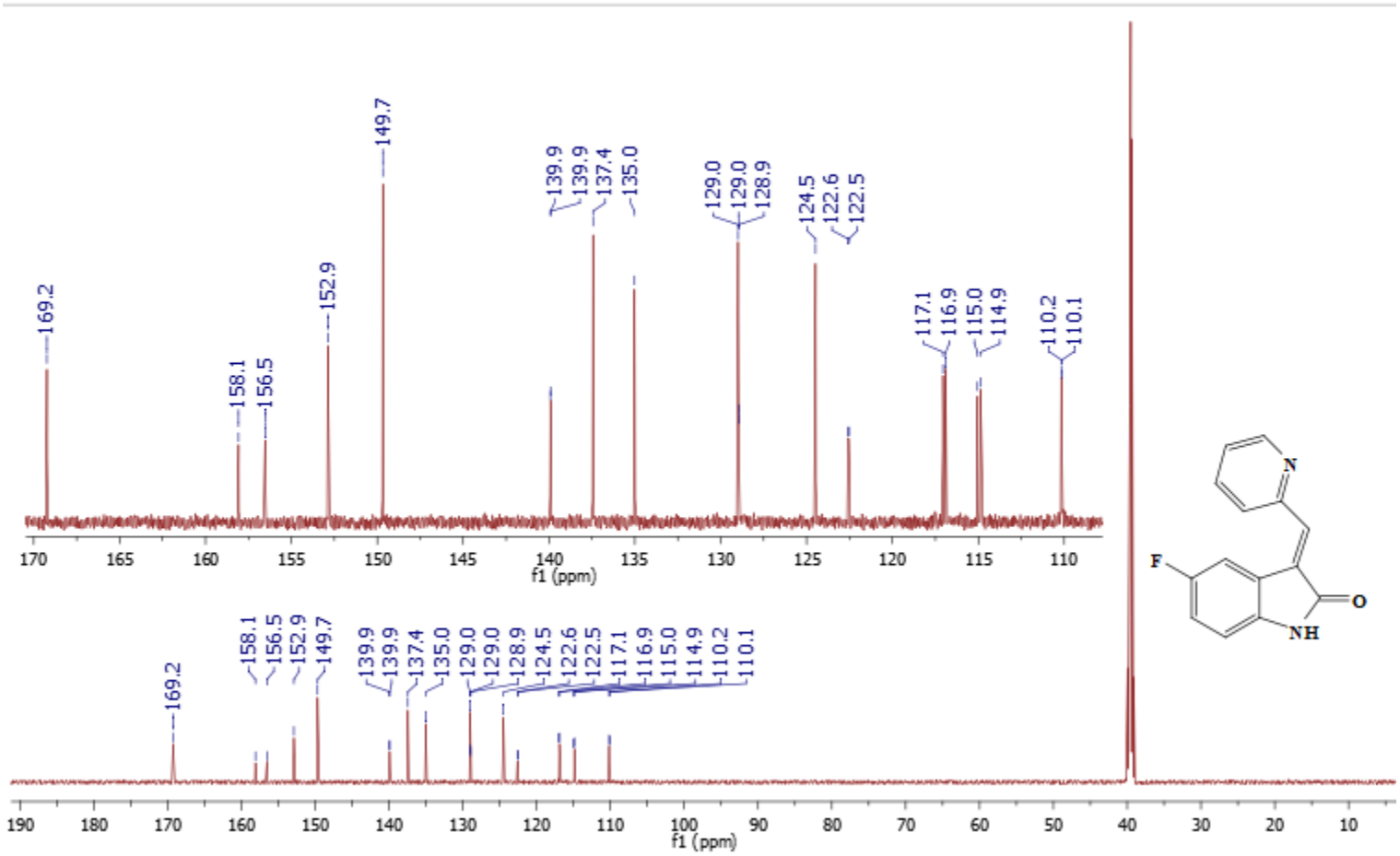


Figure S11. ^{13}C-NMR spectrum of compound **(*E*)-2d** (150MHz, DMSO-*d*6)

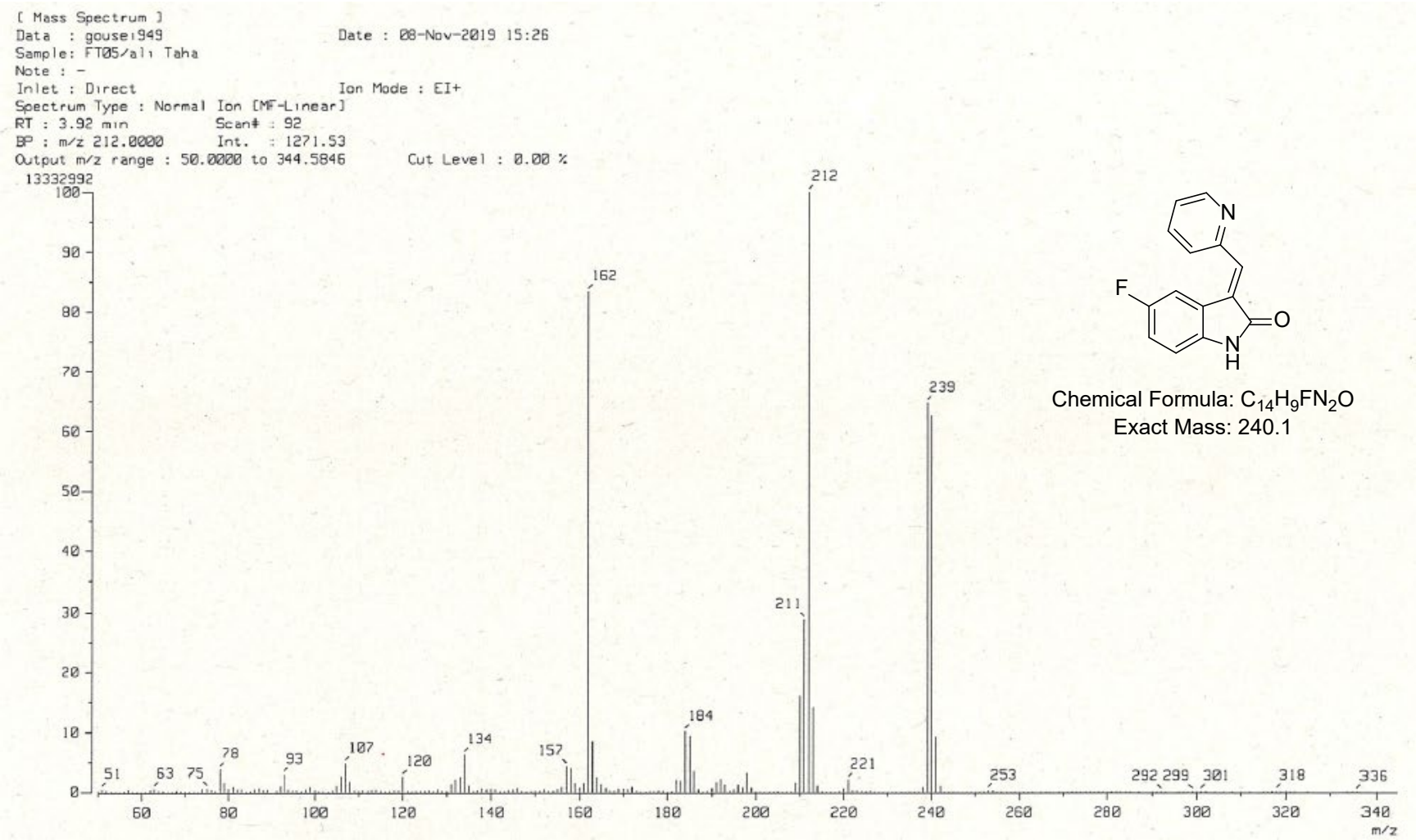


Figure S12. MS (EI+) of compound **(*E*)-2d**

[Elemental Composition]

Page: 1

Data : gousei:02

Date : 18-Nov-2019 16:17

Sample: FT05/ali Taha

Note : -

Inlet : Direct

Ion Mode : EI+

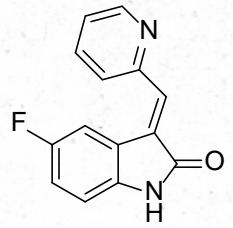
RT : 0.42 min

Scan#: 13

Elements : C 100/0, H 100/0, O 2/0, N 3/1, F 2/0

Mass Tolerance : 10mmu

Unsaturation (U.S.) : -0.5 - 150.0



Chemical Formula: $C_{14}H_9FN_2O$

Exact Mass: 240.0699

Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
240.0675	68.4	-5.1 / -1.2	15.0	C 17 H 8 N 2
		-40.7 / -9.8	10.5	C 13 H 10 O 2 N 3
		-9.8 / -2.4	11.0	C 14 H 9 O N 2 F
		+21.1 / +5.1	11.5	C 15 H 8 N F 2
		-14.6 / -3.5	7.0	C 11 H 10 O 2 N 2 F 2
		+37.8 / +9.1	7.5	C 10 H 8 O 2 N 3 F 2

Figure S13. HRMS (EI+) of compound **(*E*)-2d**

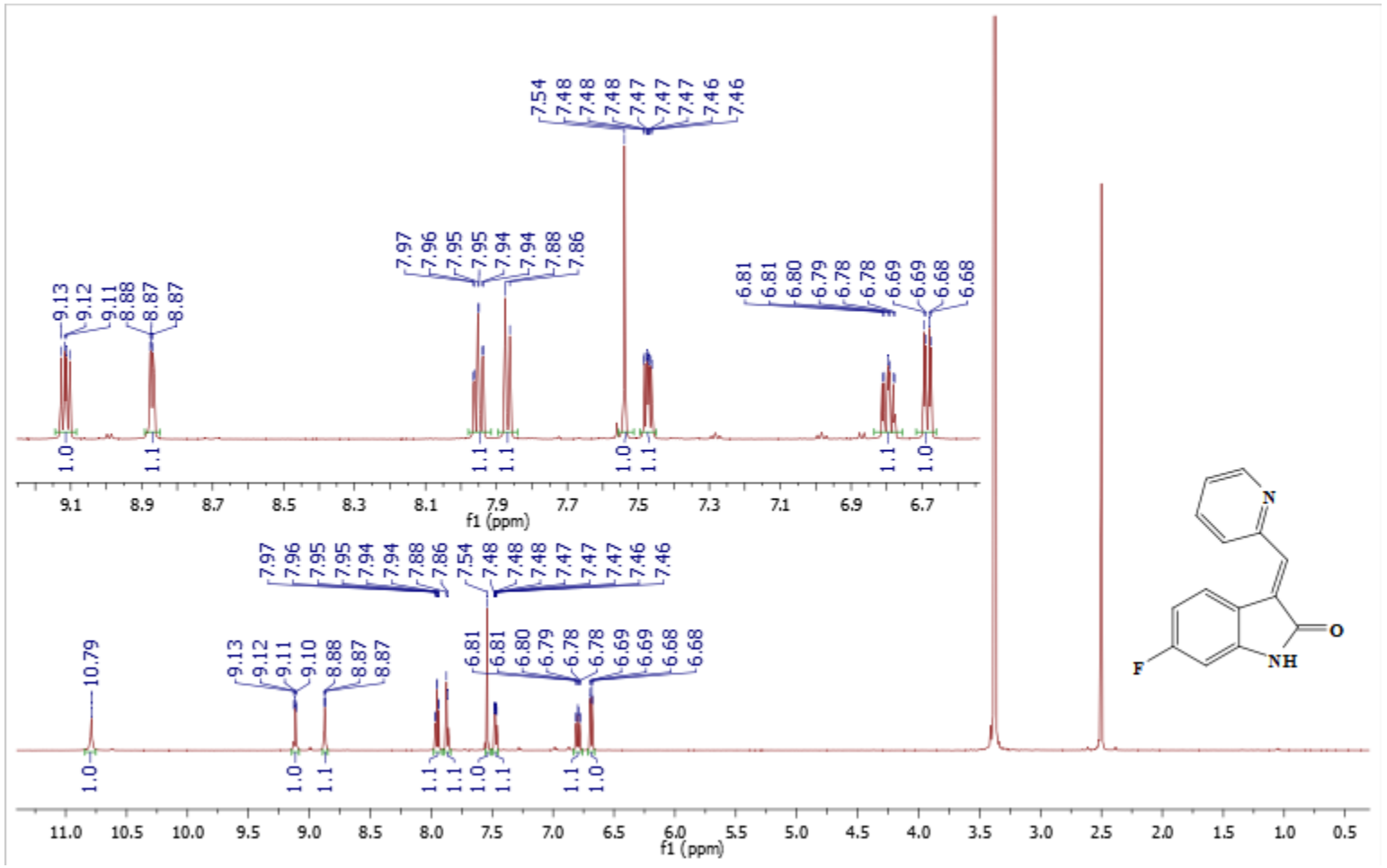


Figure S14. [1]H-NMR spectrum of compound **(*E*)-2e** (600MHz, DMSO-*d*6)

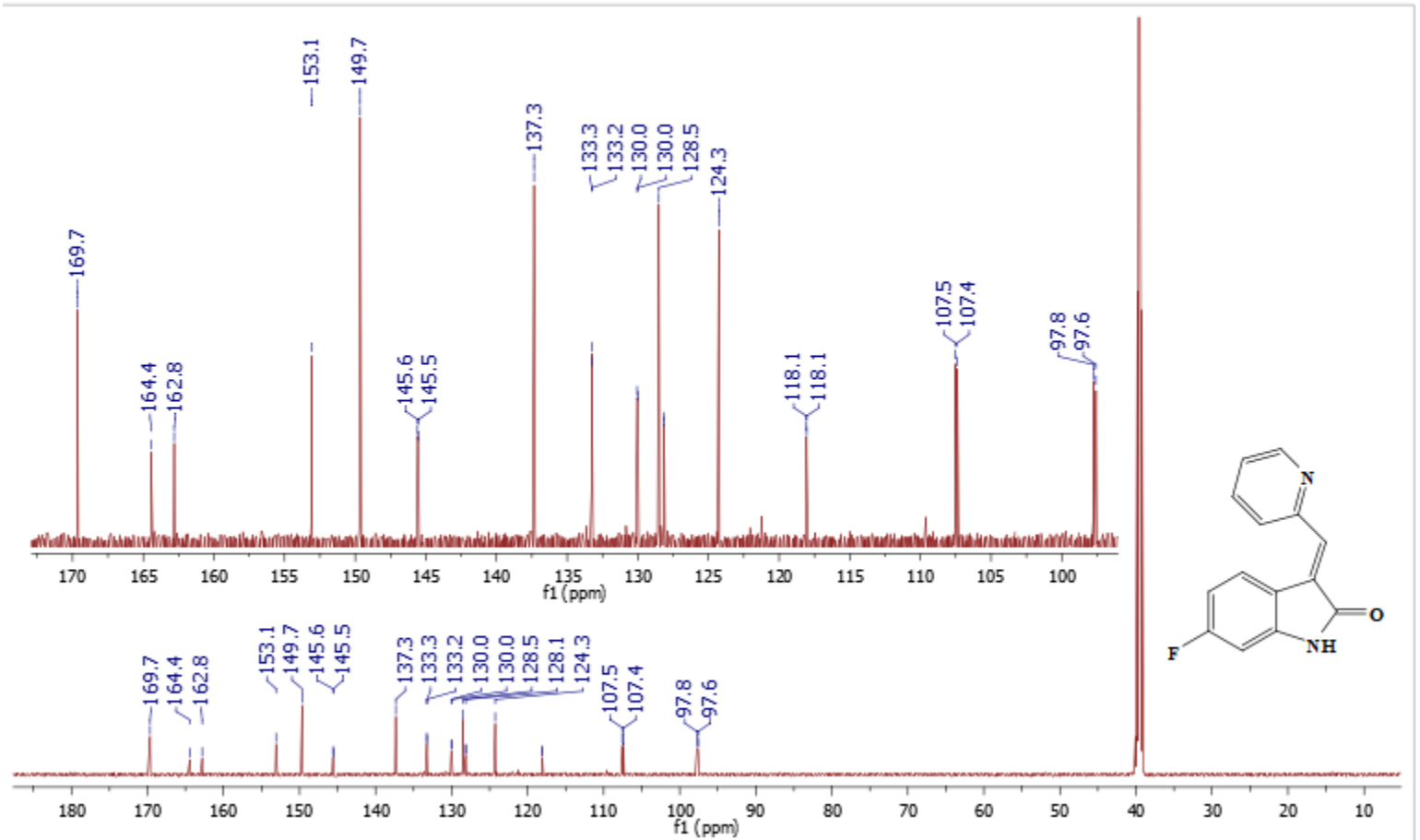


Figure S15. ^{13}C-NMR spectrum of compound **(*E*)-2e** (150MHz, DMSO-*d*6)

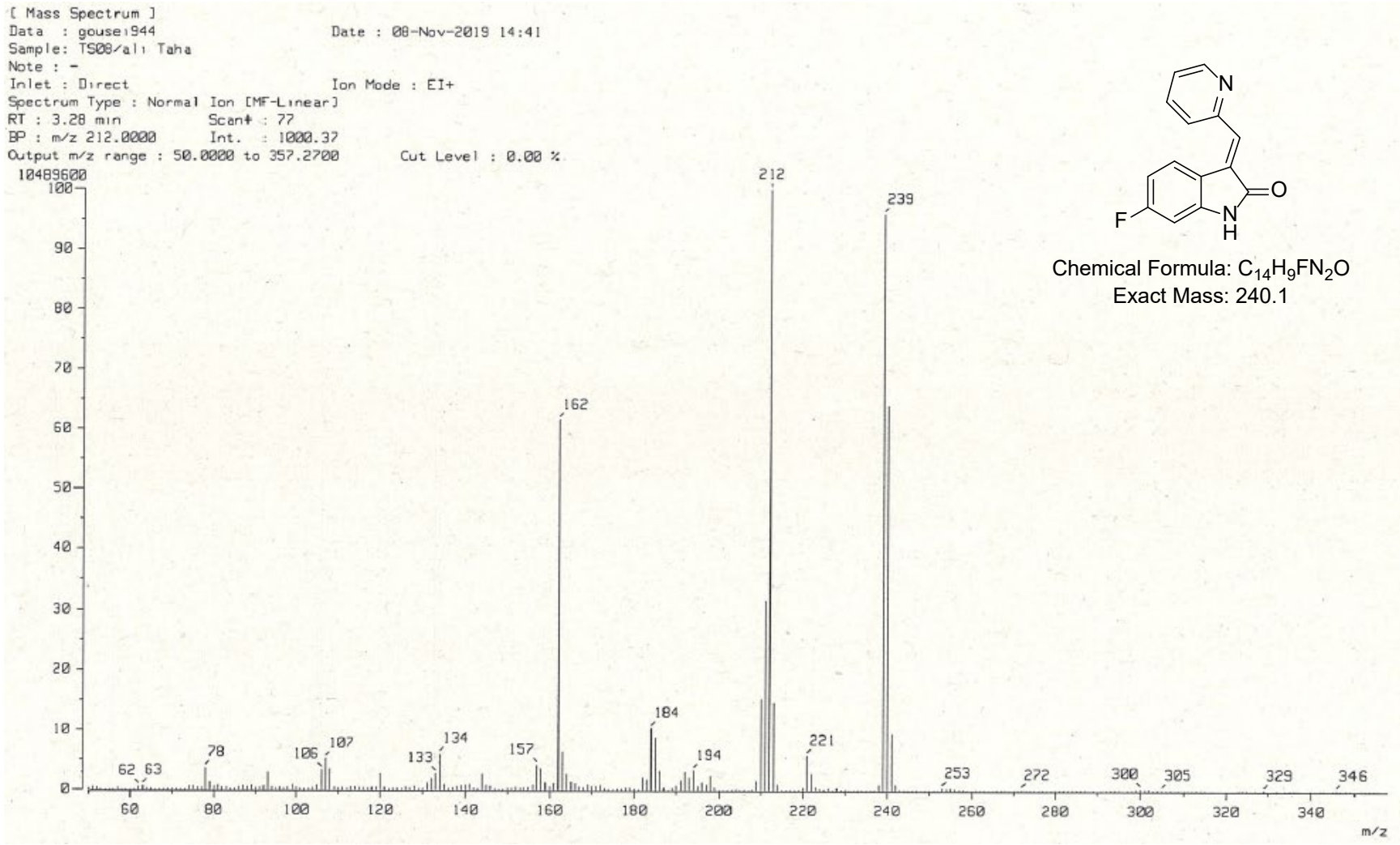


Figure S16. MS (EI+) of compound **(*E*)-2e**

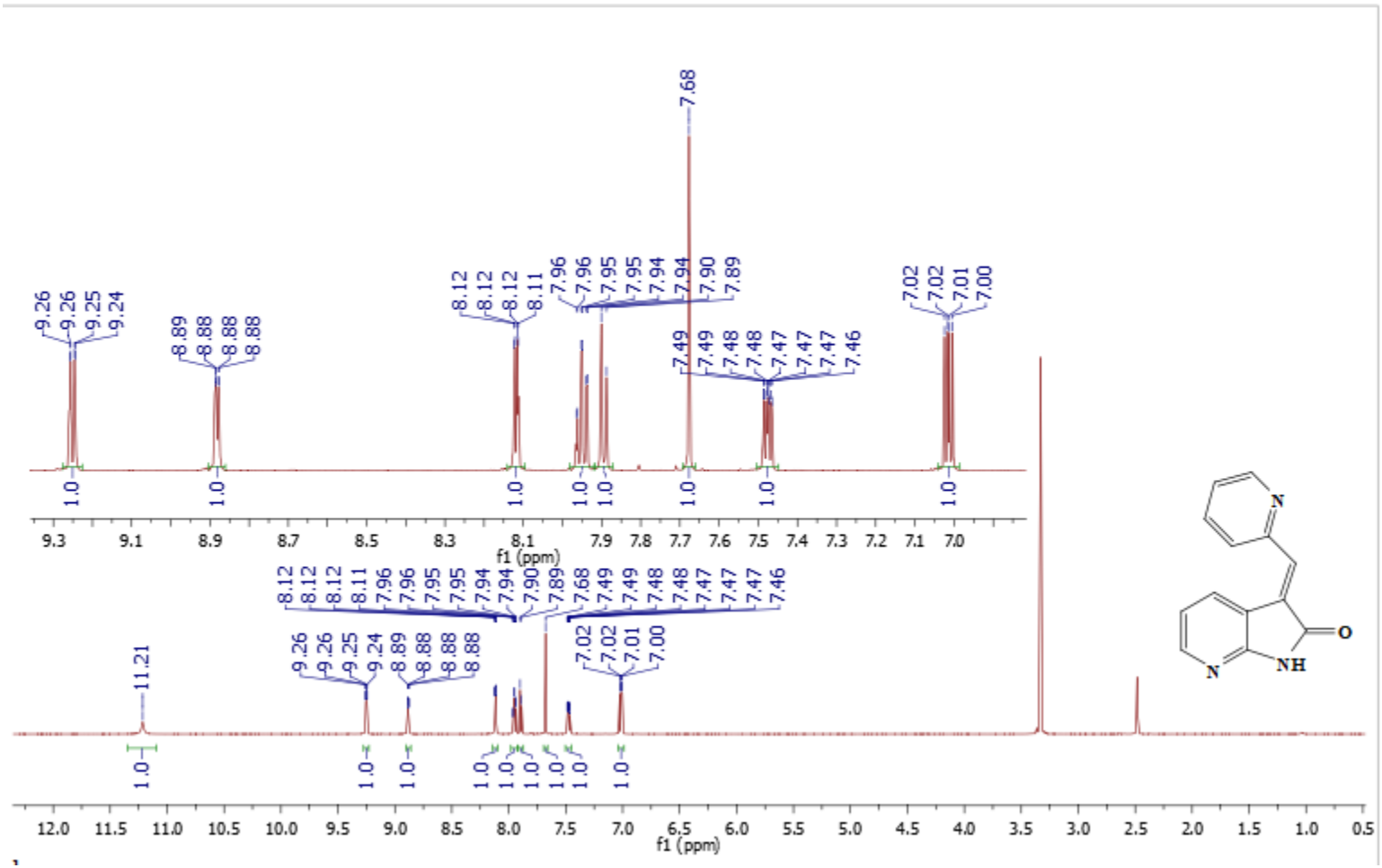


Figure S17. ^{1}H-NMR spectrum of compound **(*E*)-2f** (600MHz, DMSO-*d*6)

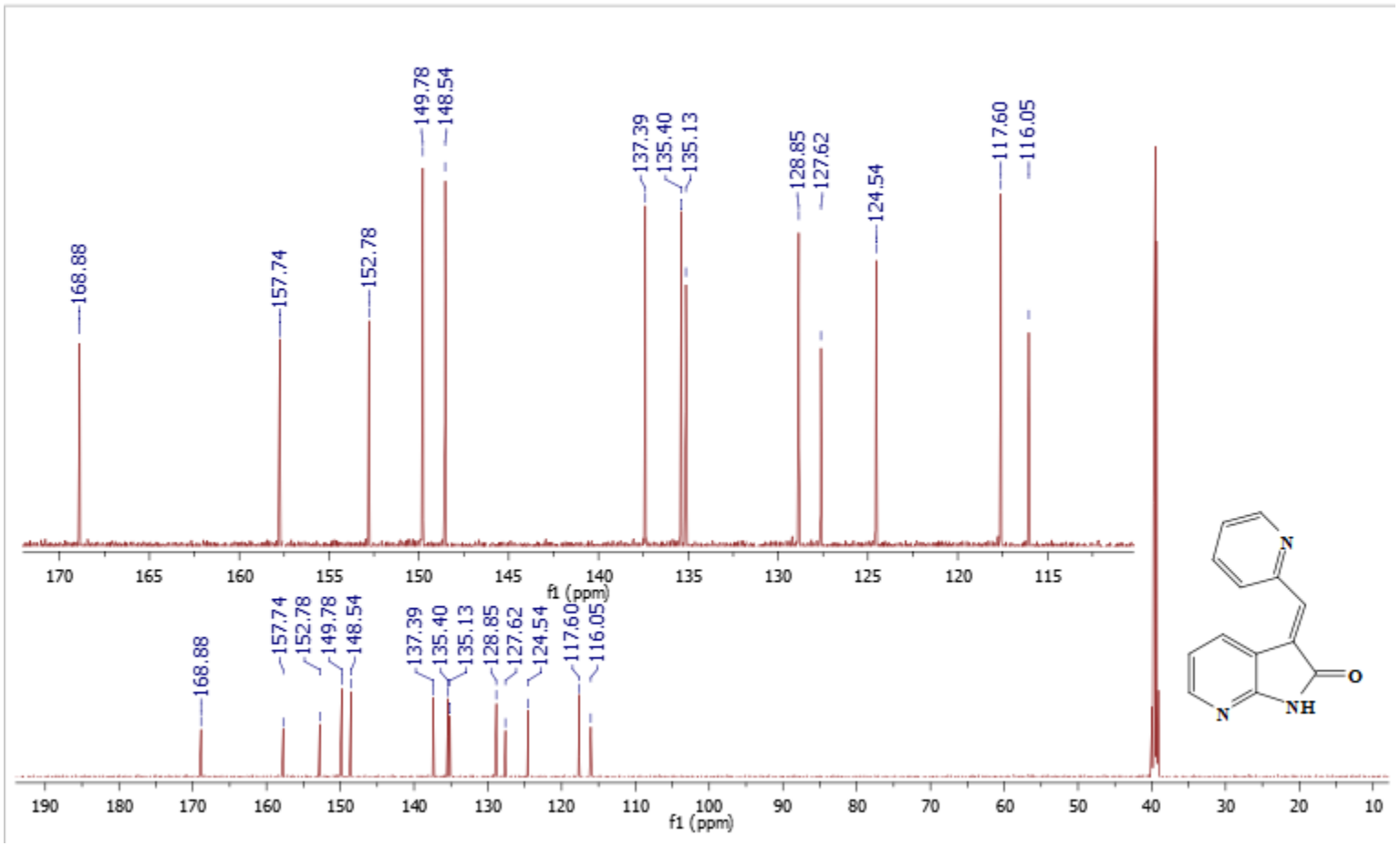


Figure S18. ^{13}C-NMR spectrum of compound **(*E*)-2f** (150MHz, DMSO-*d*6)

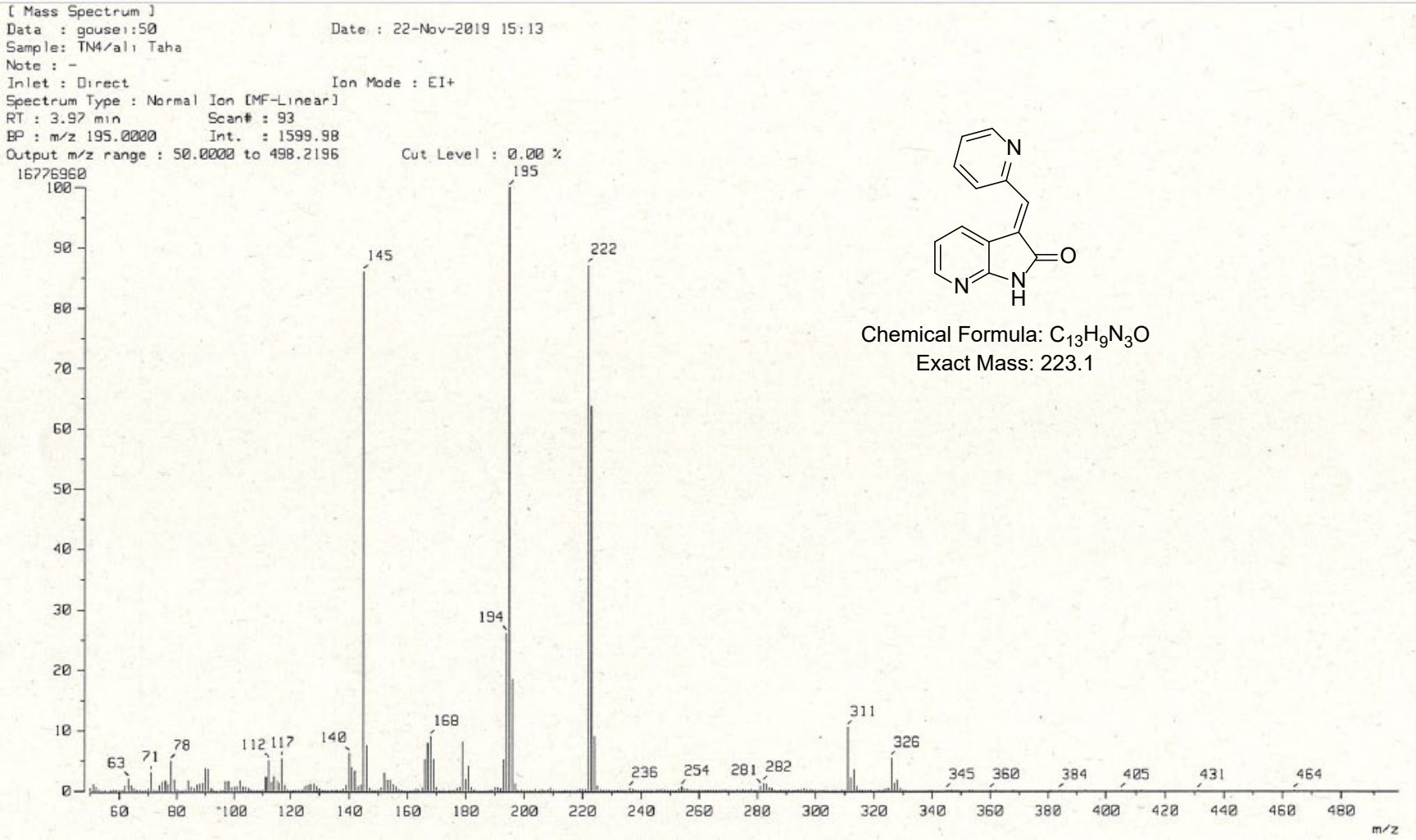


Figure S19. MS (EI+) of compound **(*E*)-2f**

[Elemental Composition]

Page: 1

Data : gousei:51

Date : 22-Nov-2019 15:23

Sample: TN4/ali Taha

Note : -

Inlet : Direct

Ion Mode : EI+

RT : 1.45 min

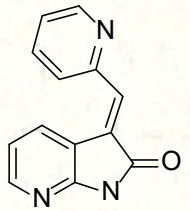
Scan#: 41

Elements : C 100/0, H 100/0, O 5/0, N 5/0

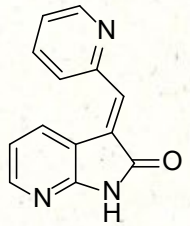
Mass Tolerance : 10mmu

Unsaturation (U.S.) : -0.5 - 150.0

Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
222.0647	59.1	-15.4 / -3.4	11.0	C 15 H 10 O 2
		+41.3 / +9.2	11.5	C 14 H 8 O 2 N
		+2.7 / +0.6	7.0	C 10 H 10 O 4 N 2
		-9.3 / -2.1	11.5	C 13 H 8 O N 3
		+8.8 / +2.0	7.5	C 8 H 8 O 3 N 5
223.0724	43.7	-15.7 / -3.5	10.5	C 15 H 11 O 2
		+40.7 / +9.1	11.0	C 14 H 9 O 2 N
		+2.3 / +0.5	6.5	C 10 H 11 O 4 N 2
		-9.7 / -2.2	11.0	C 13 H 9 O N 3
		+8.4 / +1.9	7.0	C 8 H 9 O 3 N 5



Chemical Formula: $C_{13}H_8N_3O$
Exact Mass: 222.0667



Chemical Formula: $C_{13}H_9N_3O$
Exact Mass: 223.0746

Figure S20. HRMS (EI+) of compound **(*E*)-2f**

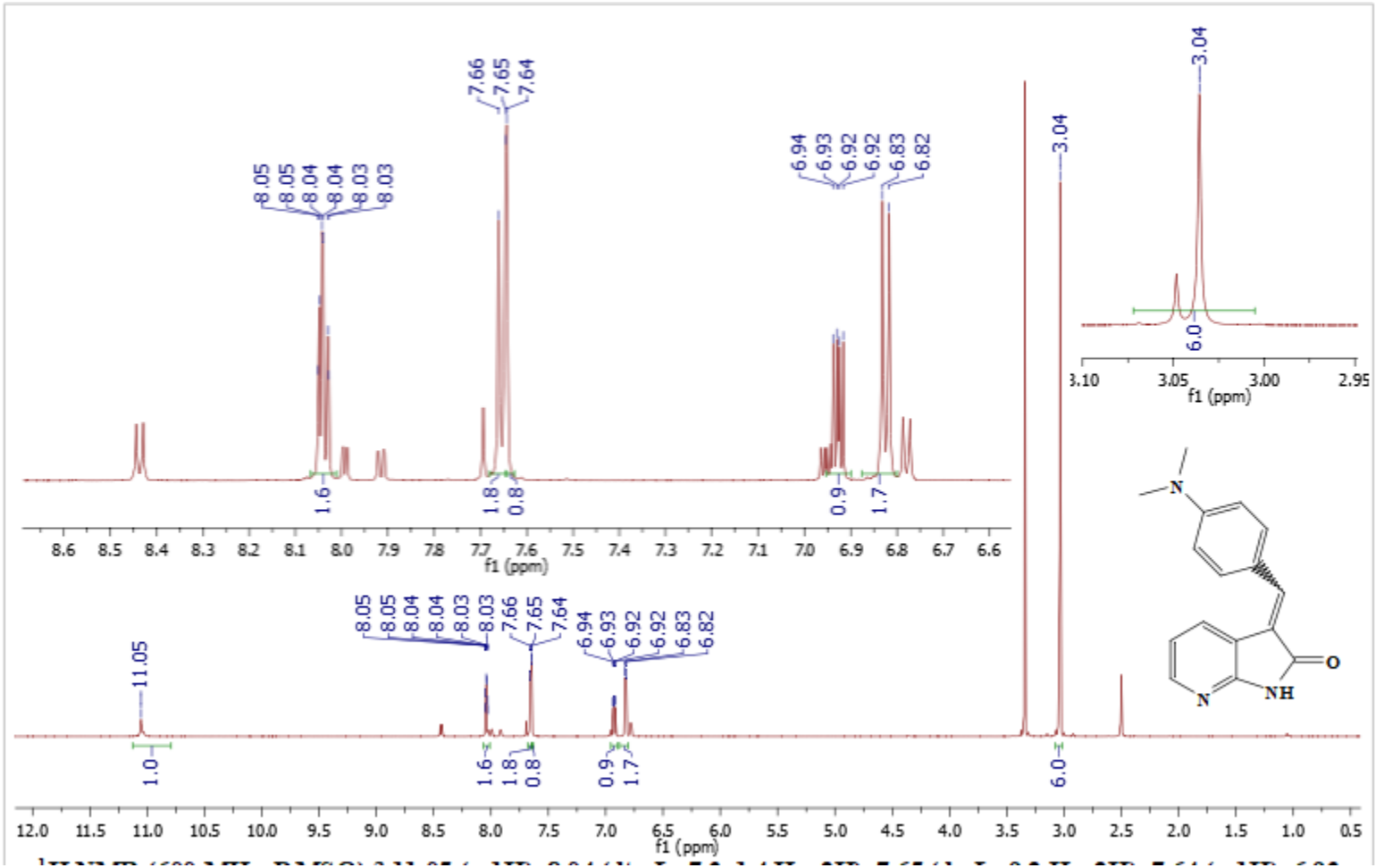


Figure S21. [1]H-NMR spectrum of compound **(*E*/*Z*)-3a** (600MHz, DMSO-*d*6)

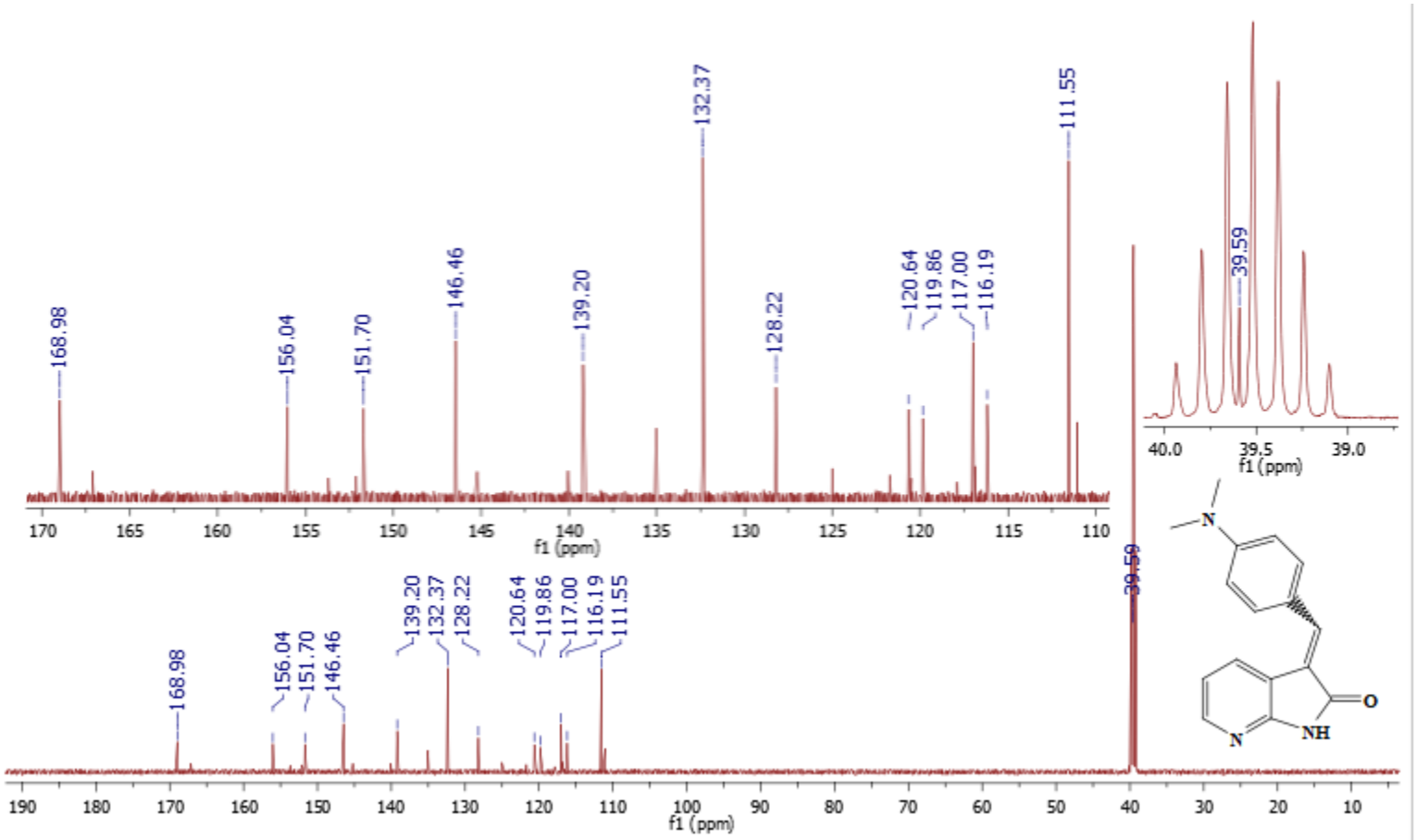


Figure S22. ^{13}C-NMR spectrum of compound **(*E*/*Z*)-3a** (150MHz, DMSO-*d*6)

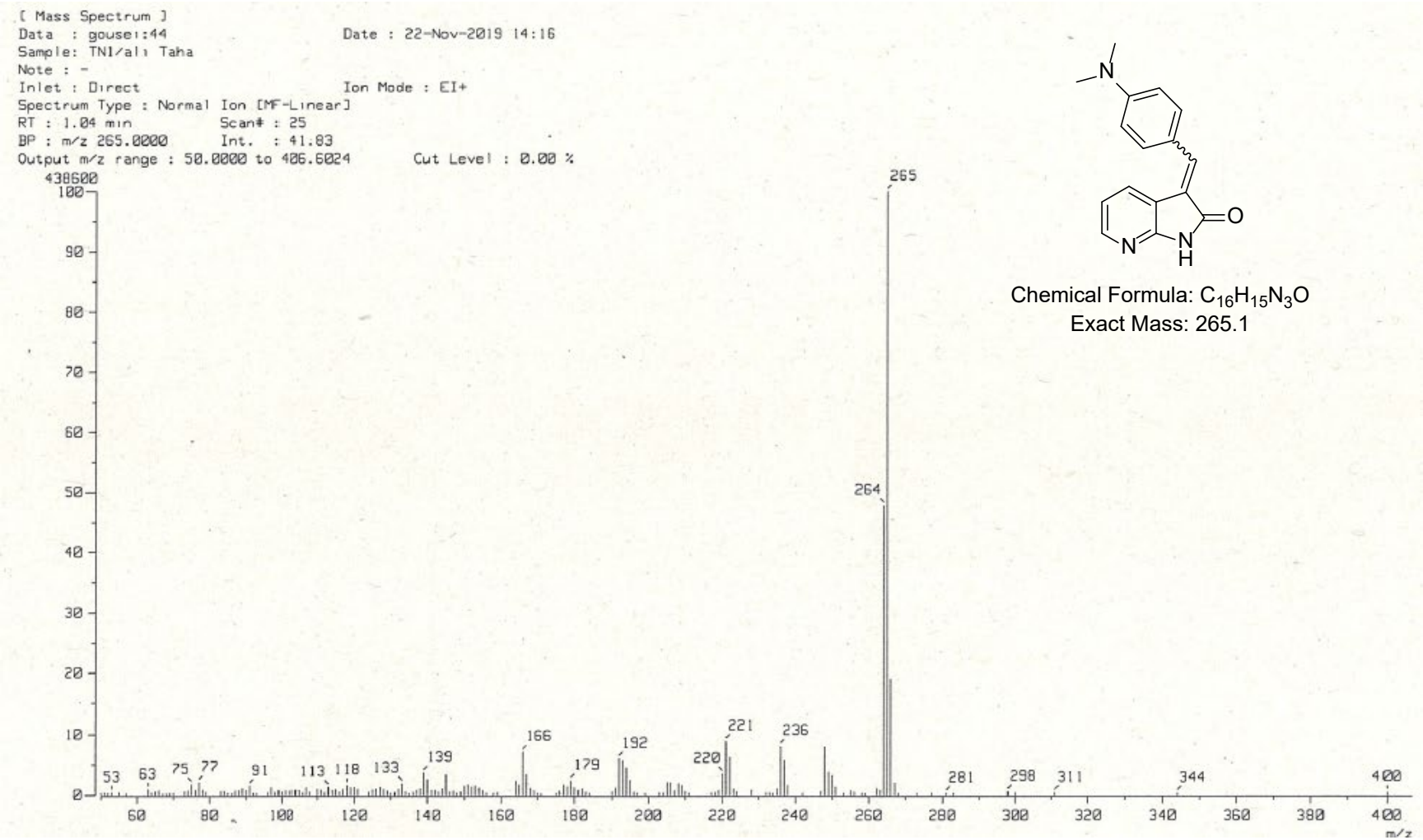


Figure S23. MS (EI+) of compound **(*E*/*Z*)-3a**

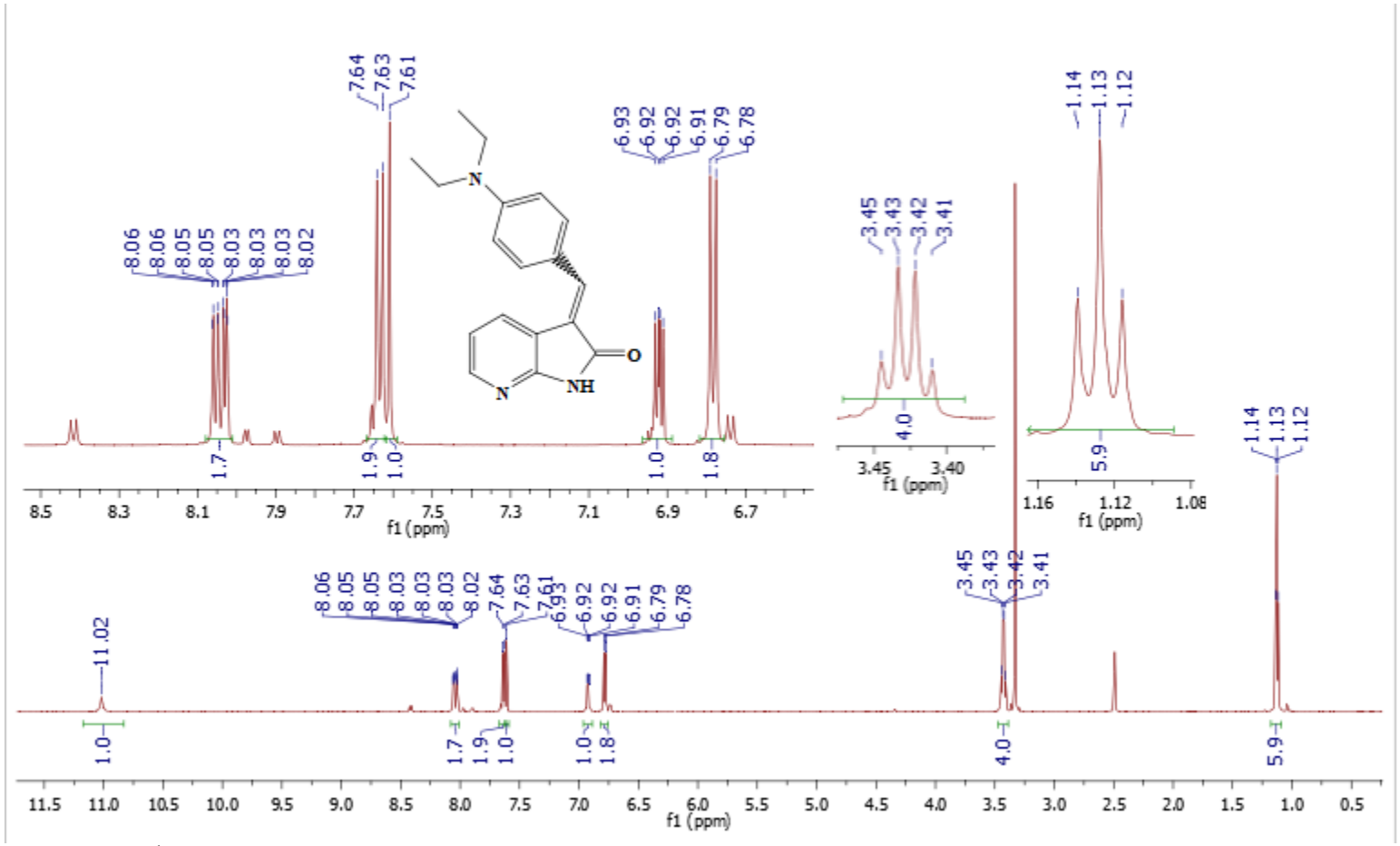


Figure S24. [1]H-NMR spectrum of compound **(*E*/*Z*)-3b** (600MHz, DMSO-*d*6)

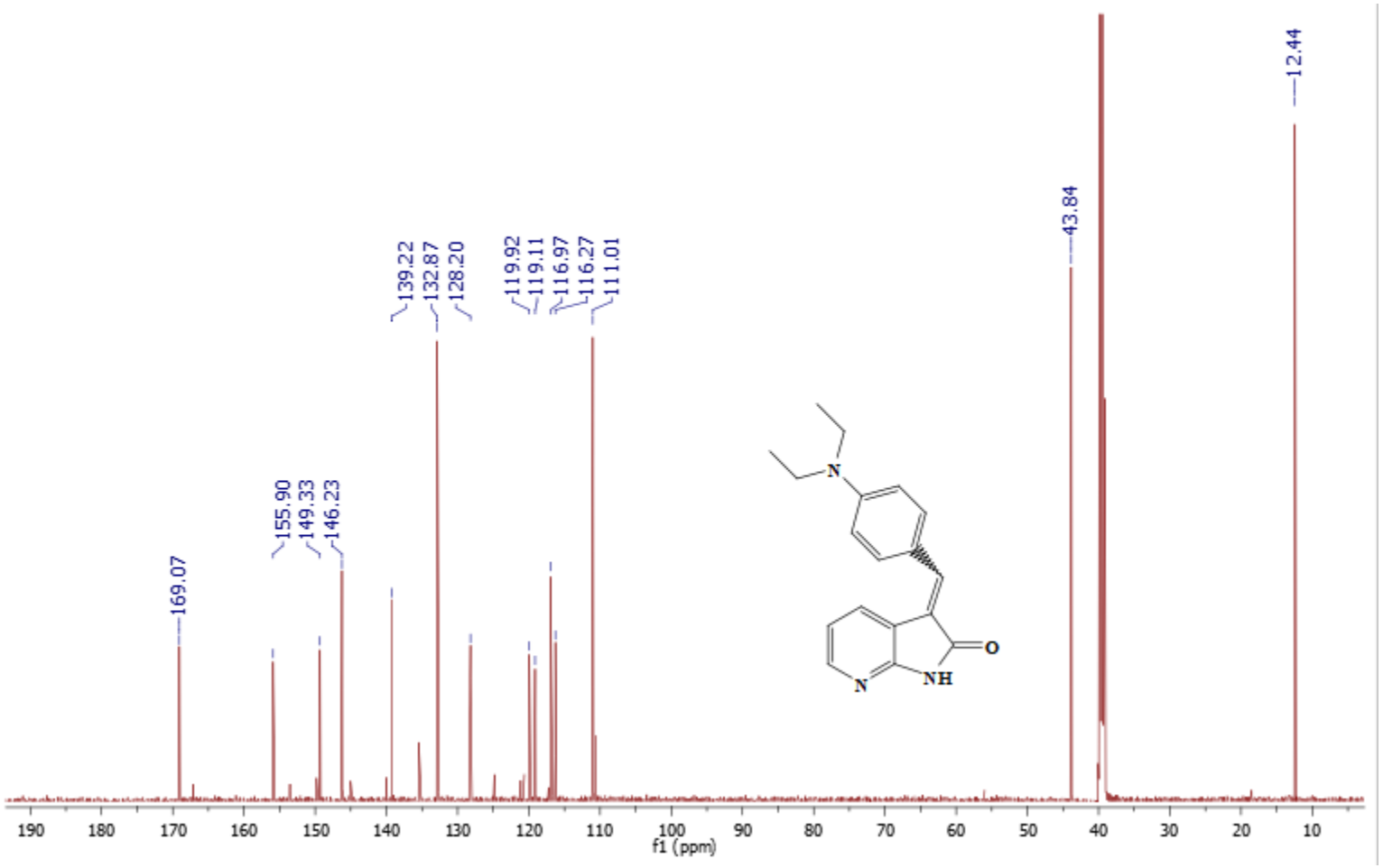


Figure S25. ^{13}C-NMR spectrum of compound **(*E*/*Z*)-3b** (150MHz, DMSO-*d*6)

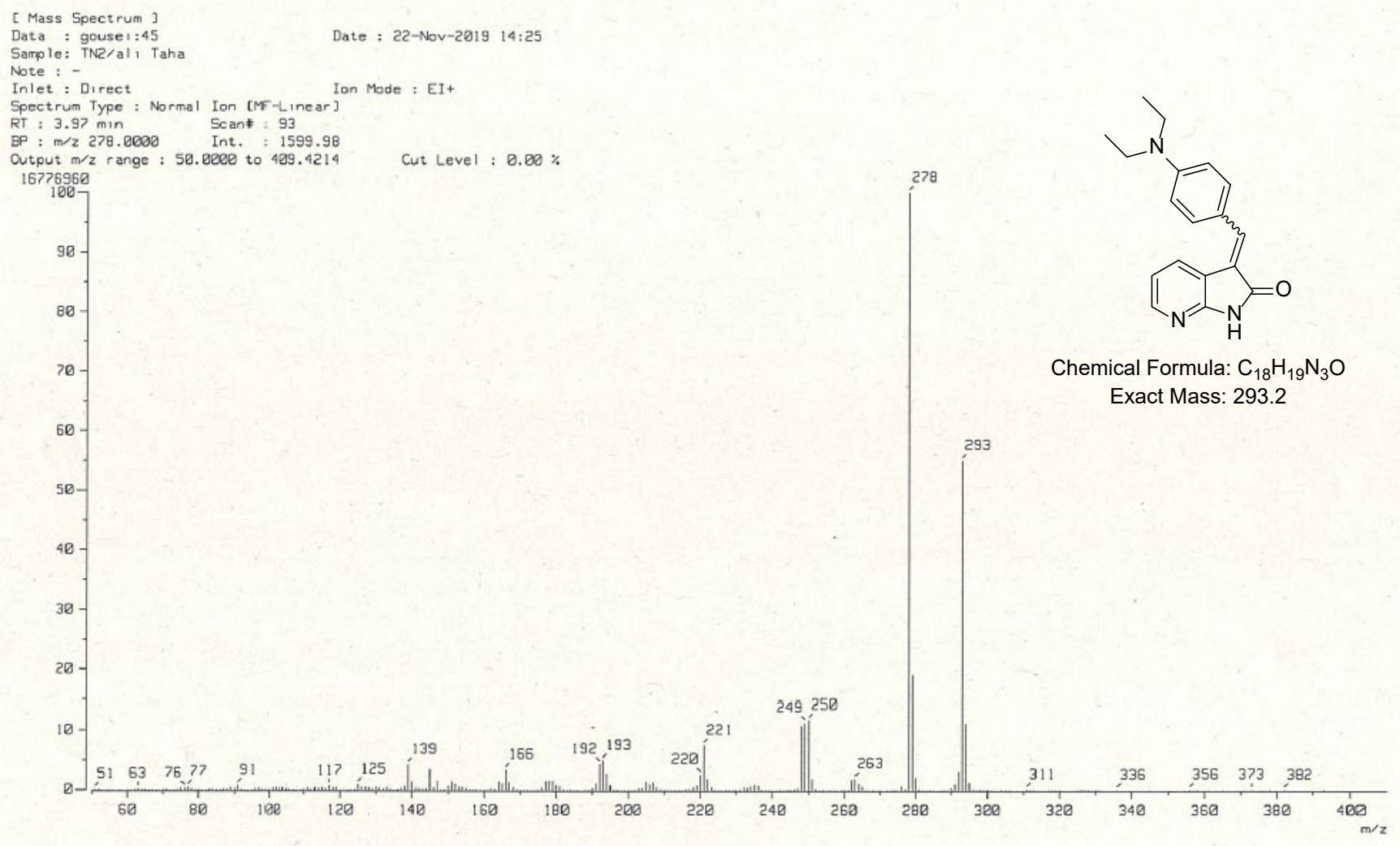


Figure S26. MS (EI+) of compound **(*E*/*Z*)-3b**

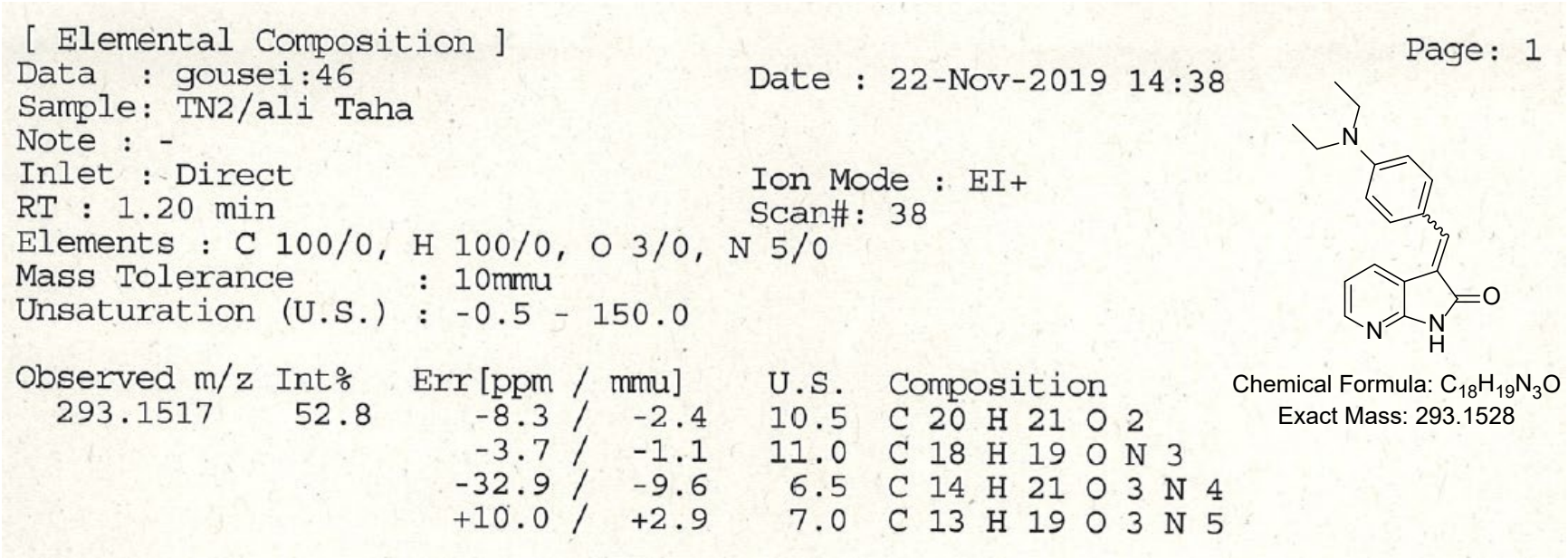


Figure S27. HRMS (EI+) of compound ***(E/Z)*-3b**

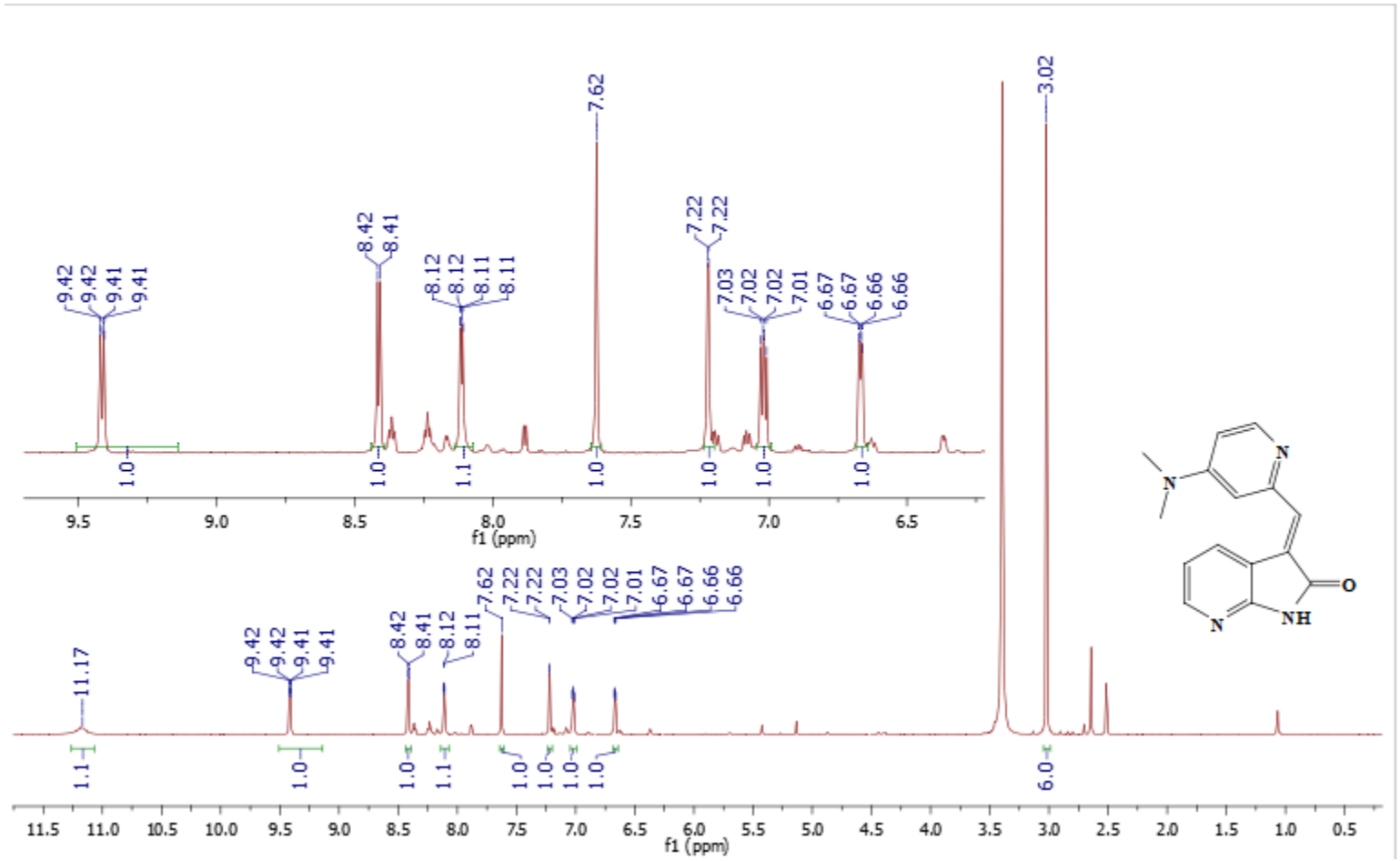


Figure S28. [1]H-NMR spectrum of compound **(*E*)-3c** (600MHz, DMSO-*d*6)

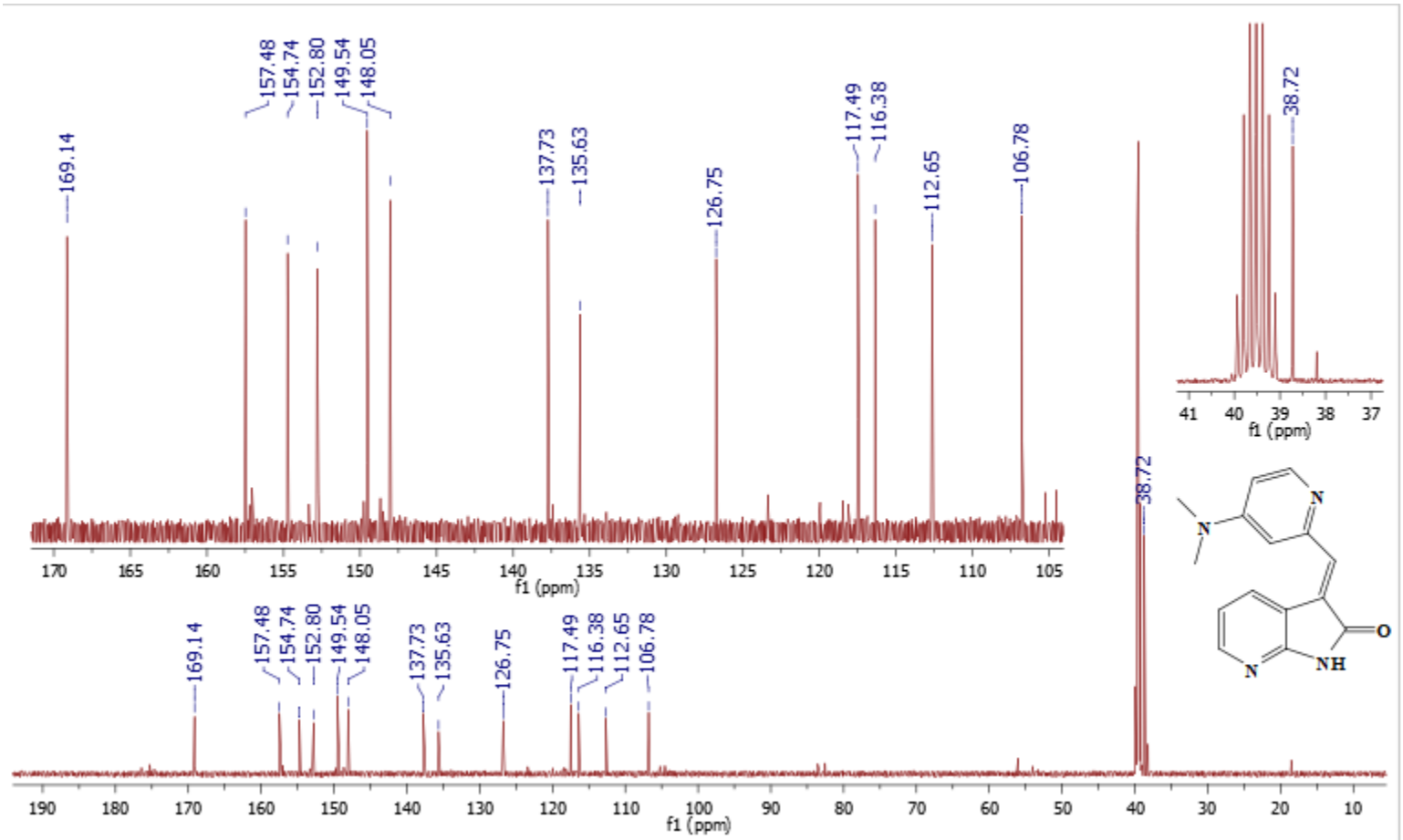


Figure S29. ^{13}C-NMR spectrum of compound **(*E*)-3c** (150MHz, DMSO-*d*6)

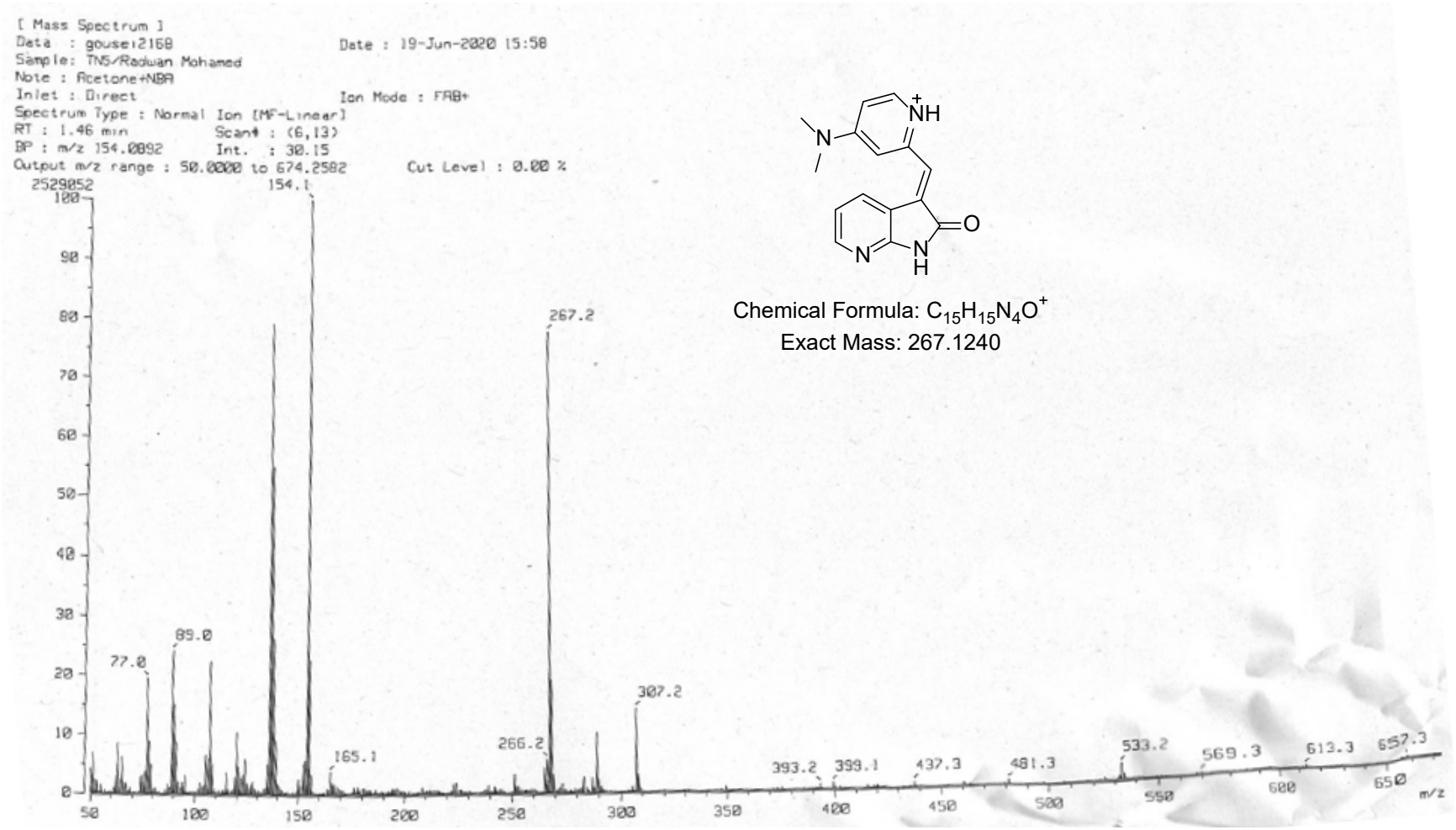
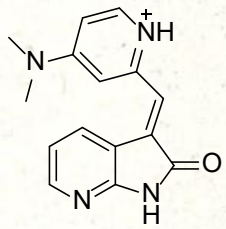


Figure S30. MS (FAB+) of compound ***(E)*-3c**

[Elemental Composition]
Data : gousei2169
Sample: TN5/Radwan Mohamed
Note : Acetone+NBA
Inlet : Direct
RT : 5.13 min
Elements : C 200/0, H 200/0, O 5/0, N 8/0
Mass Tolerance : 20ppm, 10mmu if m/z < 500, 20mmu if m/z > 1000
Unsaturation (U.S.) : -0.5 - 100.0

Date : 19-Jun-2020 16:03
Ion Mode : FAB+
Scan#: (19,24)

Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
267.1268	100.0	+35.4 / +9.5	14.5	C 21 H 15
		+13.4 / +3.6	5.5	C 14 H 19 O 5
		+3.4 / +0.9	10.0	C 17 H 17 O 2 N
		-28.6 / -7.7	5.5	C 13 H 19 O 4 N 2
		+18.4 / +4.9	6.0	C 12 H 17 O 4 N 3
		+8.4 / +2.2	10.5	C 15 H 15 O N 4
		-23.6 / -6.3	6.0	C 11 H 17 O 3 N 5
		-33.6 / -9.0	10.5	C 14 H 15 N 6
		+23.5 / +6.3	6.5	C 10 H 15 O 3 N 6
		+13.4 / +3.6	11.0	C 13 H 13 N 7
		-8.6 / -2.3	2.0	C 6 H 17 O 5 N 7
		-18.6 / -5.0	6.5	C 9 H 15 O 2 N 8



Chemical Formula: $C_{15}H_{15}N_4O^+$
Exact Mass: 267.1240

Figure S31. HRMS (FAB+) of compound **(*E*)-3c**

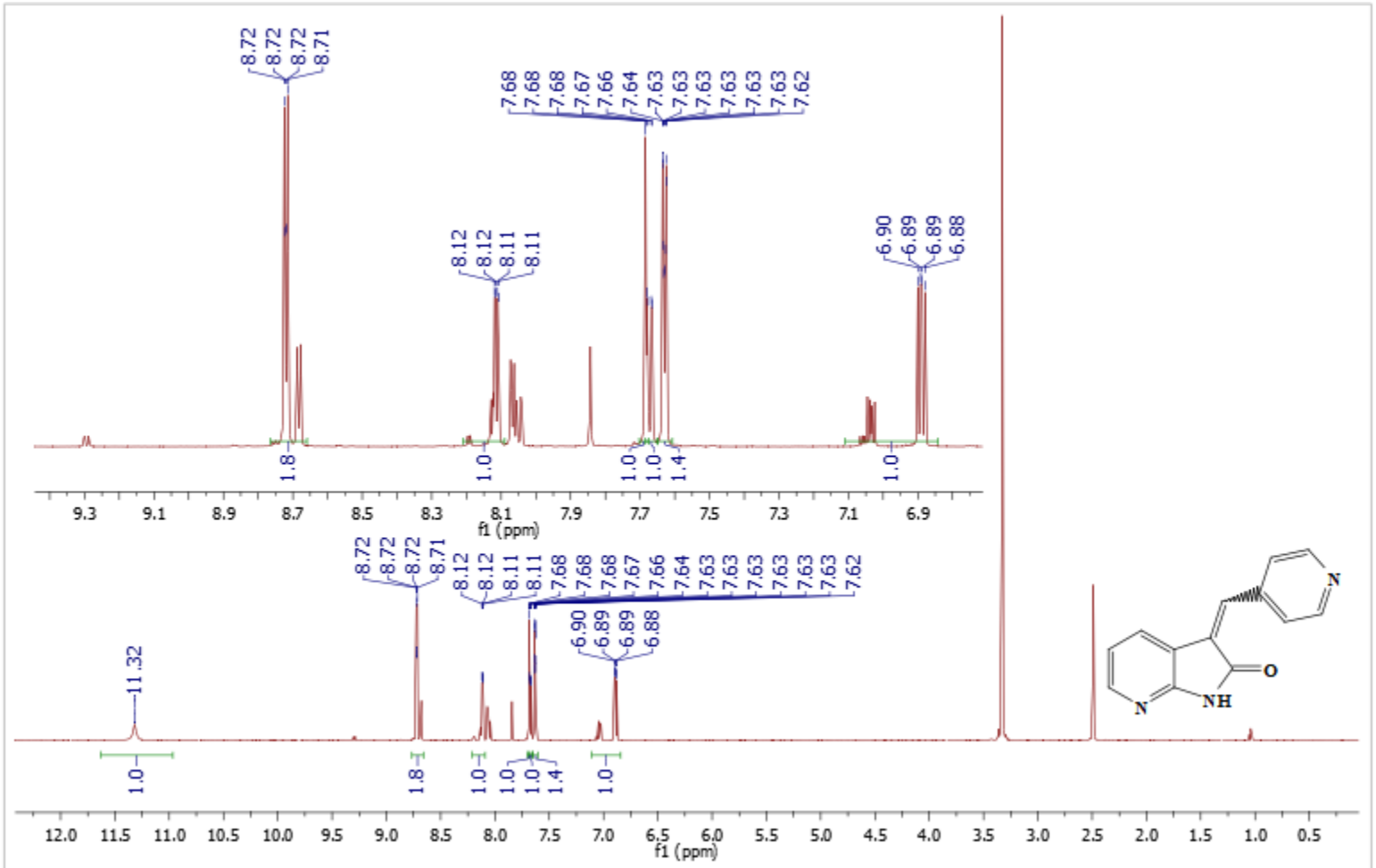


Figure S32. [1]H-NMR spectrum of compound **(*E*/*Z*)-3d** (600MHz, DMSO-*d*6)

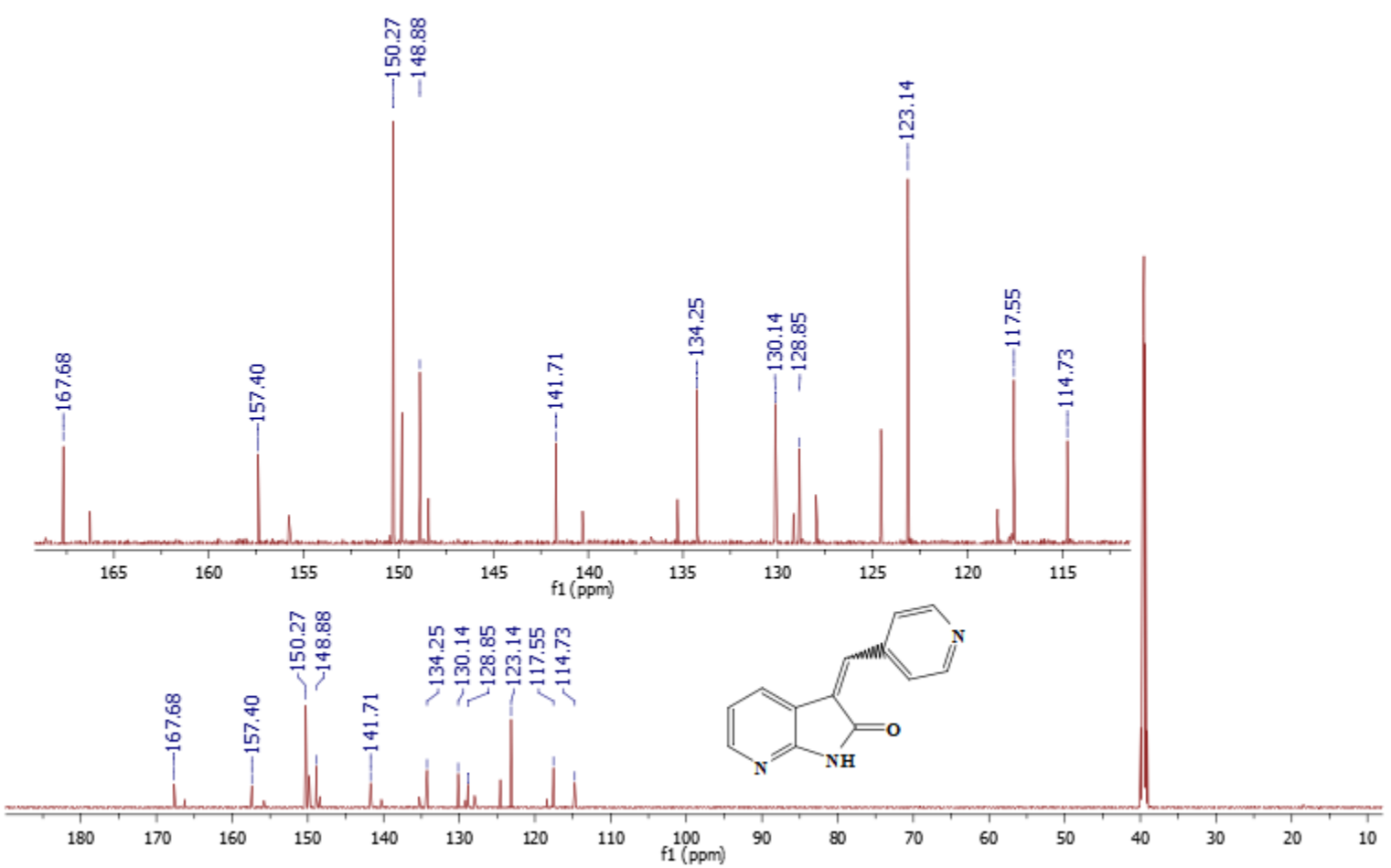


Figure S33. ^{13}C-NMR spectrum of compound **(*E*/*Z*)-3d** (150MHz, DMSO-*d*6)

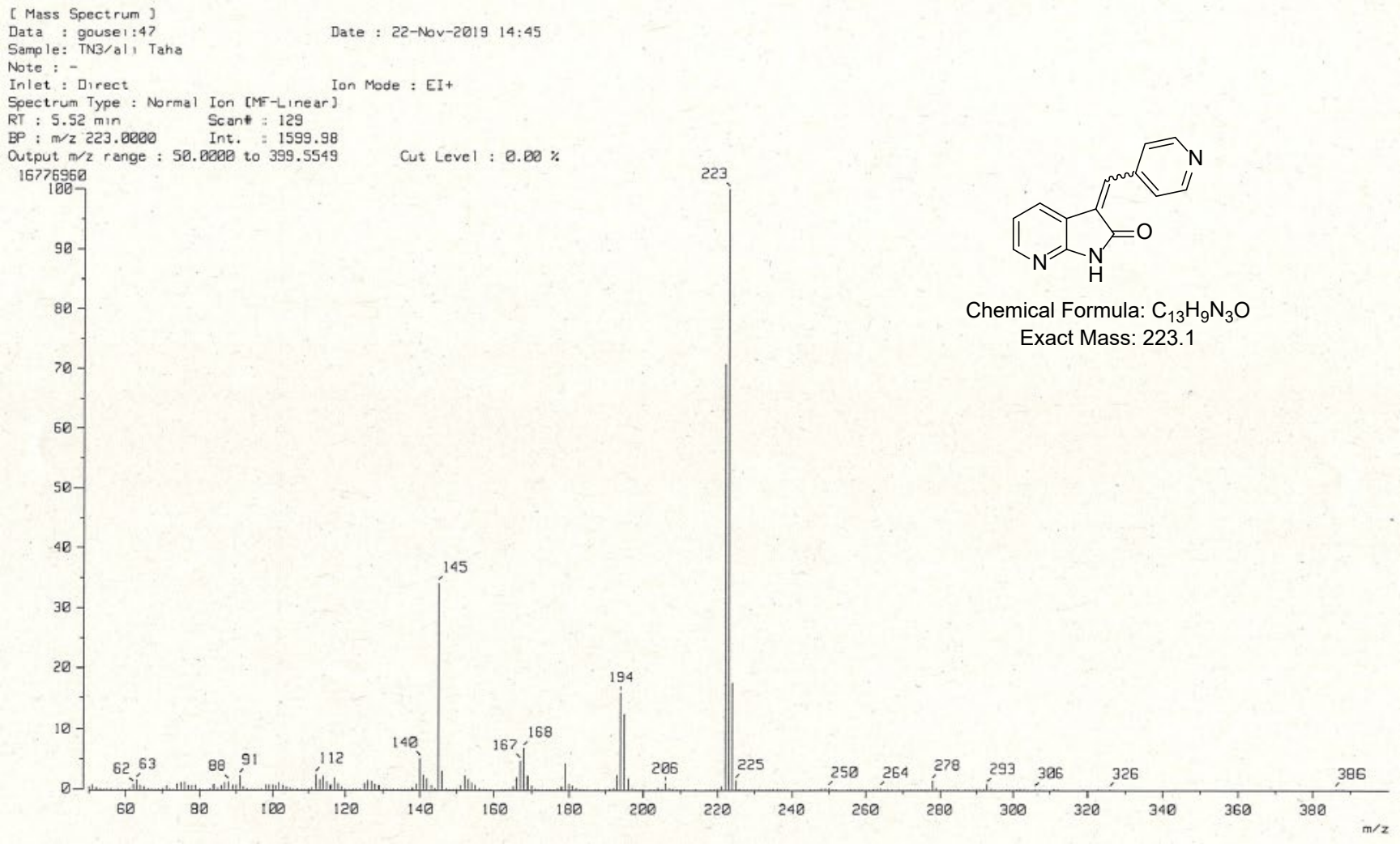


Figure S34. MS (EI+) of compound **(*E*/*Z*)-3d**

[Elemental Composition] Page: 1

Data : gousei:48 Date : 22-Nov-2019 14:56

Sample: TN3/ali Taha

Note : -

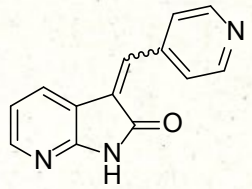
Inlet : Direct Ion Mode : EI+

RT : 0.87 min Scan#: 25

Elements : C 100/0, H 100/0, O 3/0, N 5/0

Mass Tolerance : 10mmu

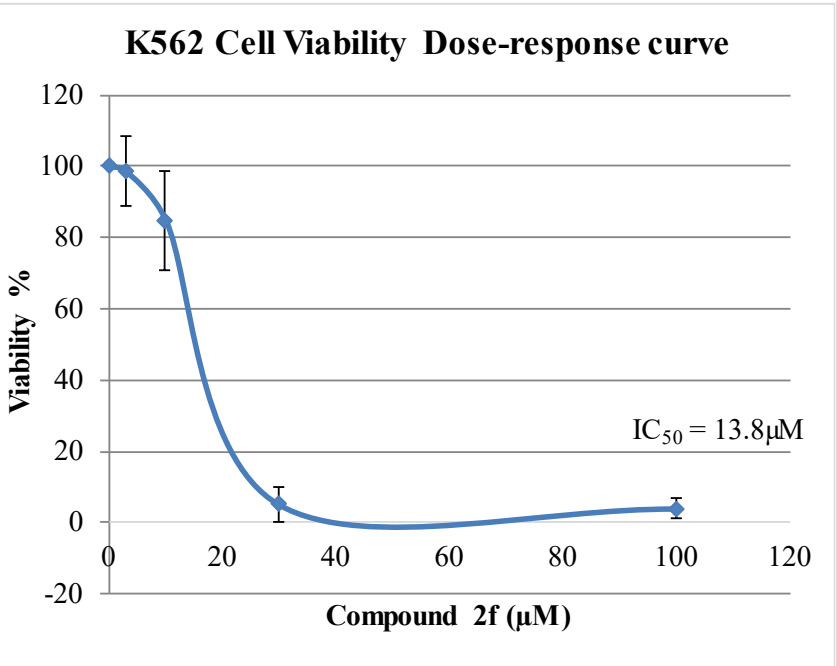
Unsaturation (U.S.) : -0.5 - 150.0



Chemical Formula: $C_{13}H_9N_3O$
Exact Mass: 223.0746

Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
223.0717	100.0	-18.8 / -4.2	10.5	C 15 H 11 O 2
		+37.5 / +8.4	11.0	C 14 H 9 O 2 N
		-12.8 / -2.9	11.0	C 13 H 9 O N 3
		+43.6 / +9.7	11.5	C 12 H 7 O N 4
		+5.2 / +1.2	7.0	C 8 H 9 O 3 N 5

Figure S35. HRMS (EI+) of compound **(*E*/*Z*)-3d**



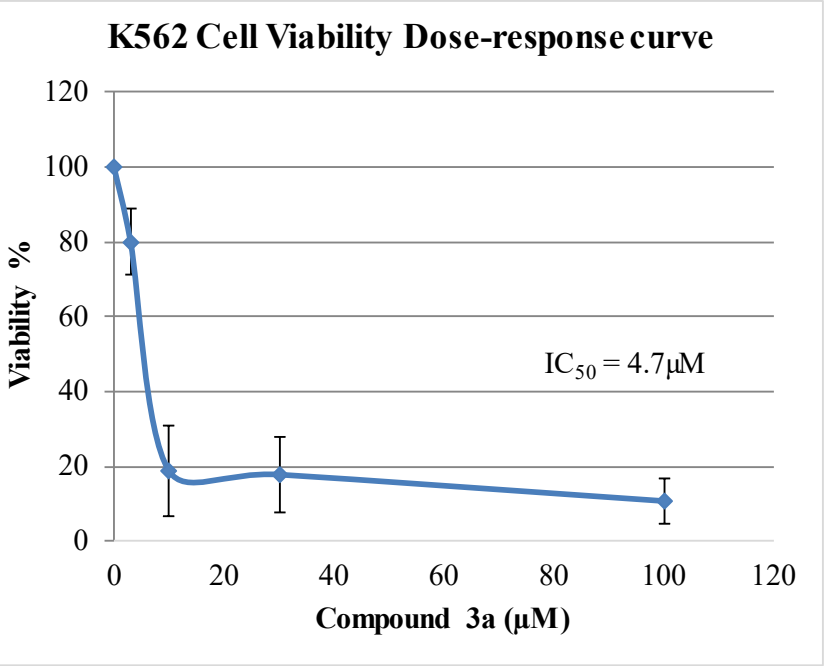


Figure S36. Cell viability Dose-response curve for inhibition of K562 cells. Data are given as mean ± SEM of n= 3 independent experiments, shown as percentage of control, DMSO (= 100%).

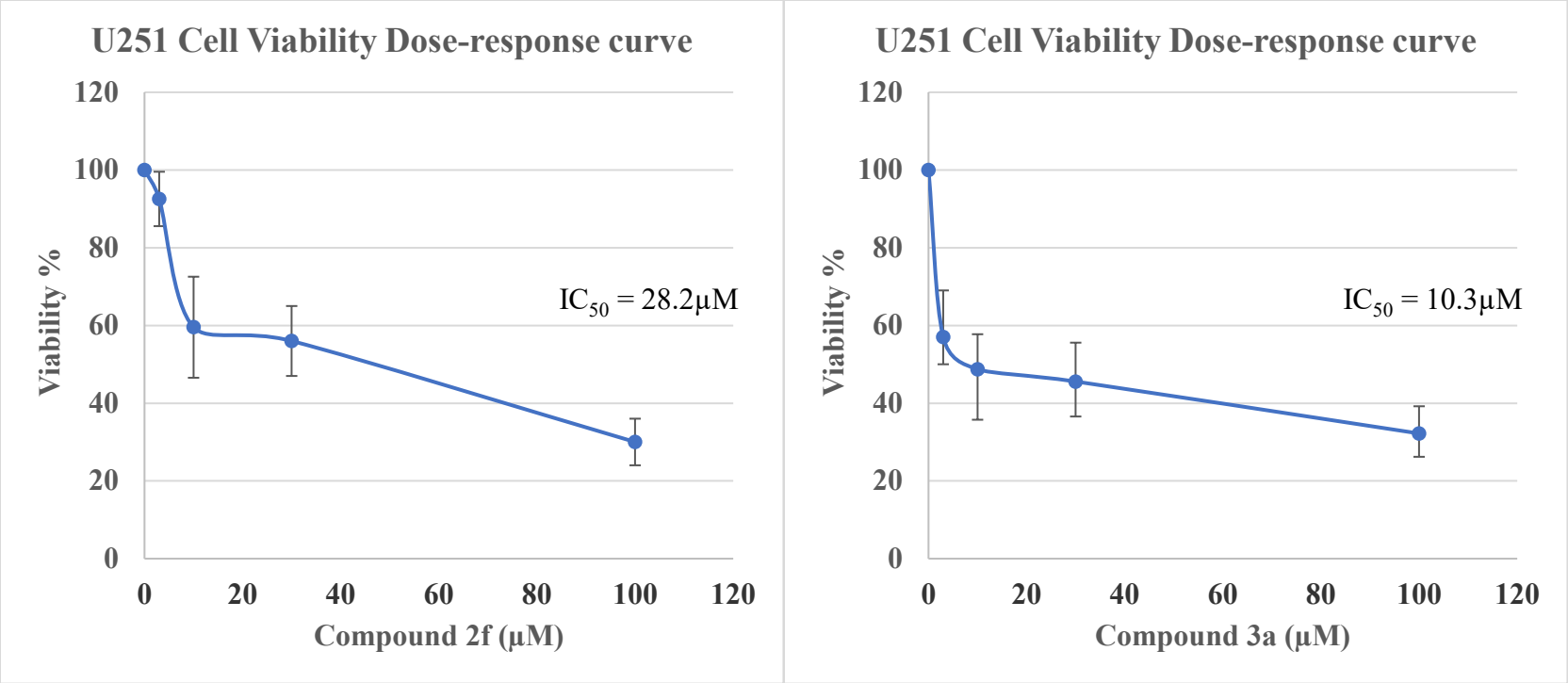


Figure S37. Cell viability Dose-response curve for inhibition of U251 cells. Data are given as mean ± SEM of n= 3 independent experiments, shown as percentage of control, DMSO (= 100%).

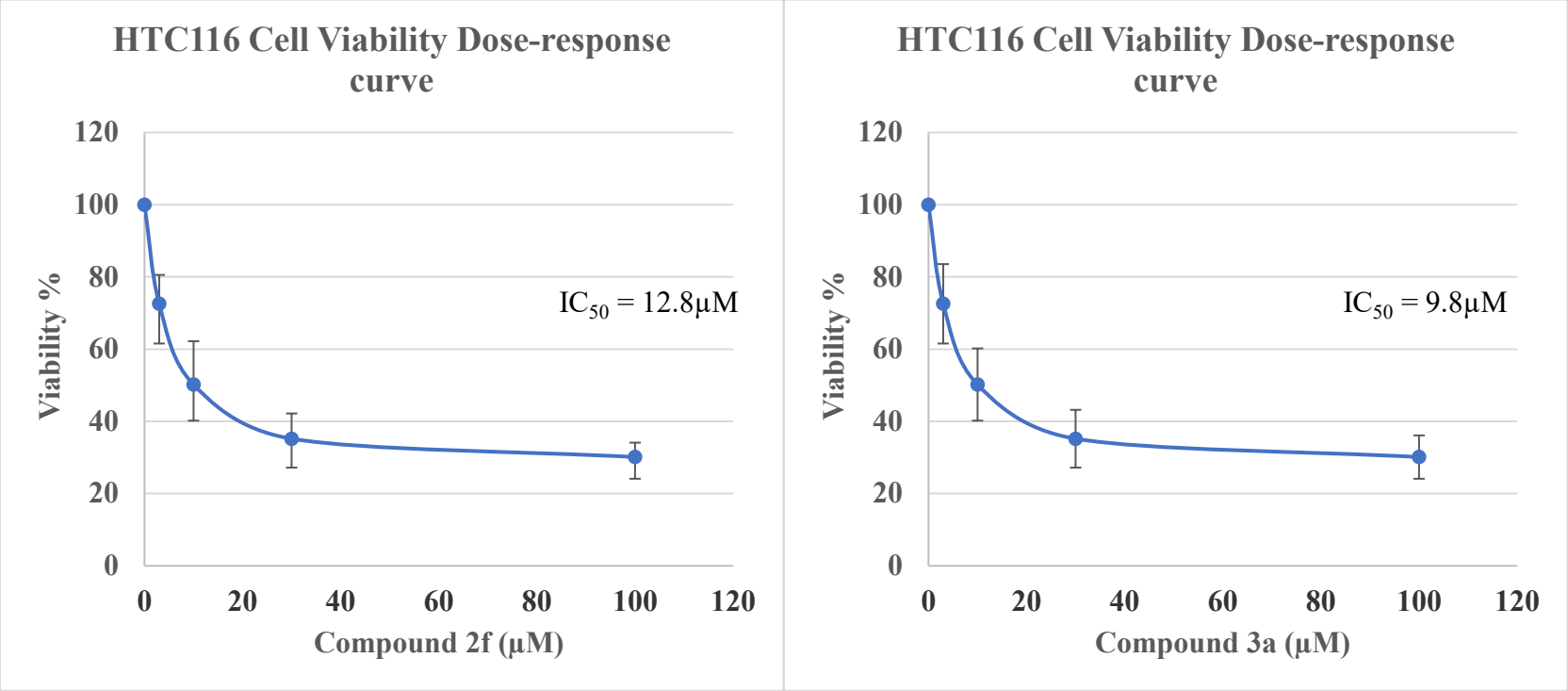


Figure S38. Cell viability Dose-response curve for inhibition of HTC116 cells. Data are given as mean ± SEM of n= 3 independent experiments, shown as percentage of control, DMSO (= 100%).

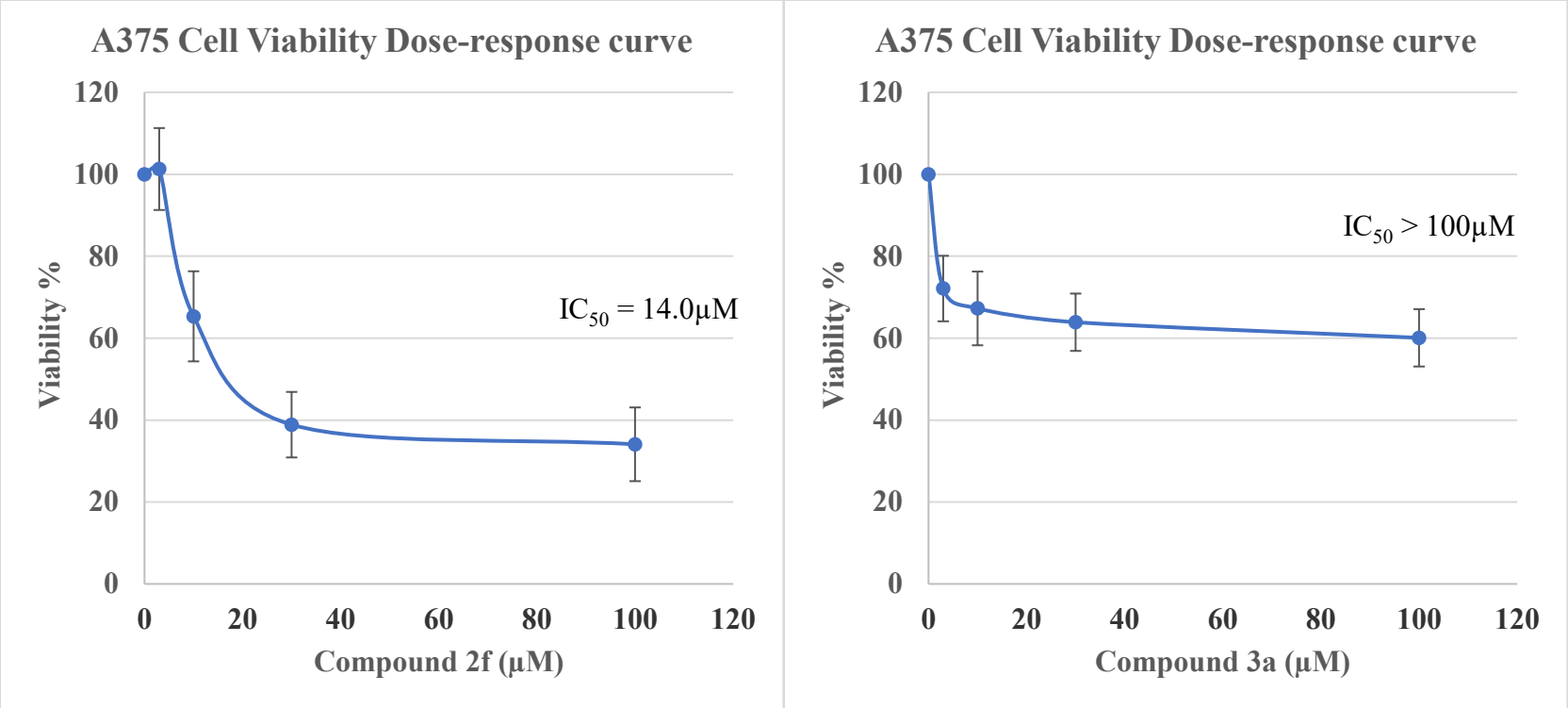


Figure S39. Cell viability Dose-response curve for inhibition of A375 cells. Data are given as mean ± SEM of n= 3 independent experiments, shown as percentage of control, DMSO (= 100%).

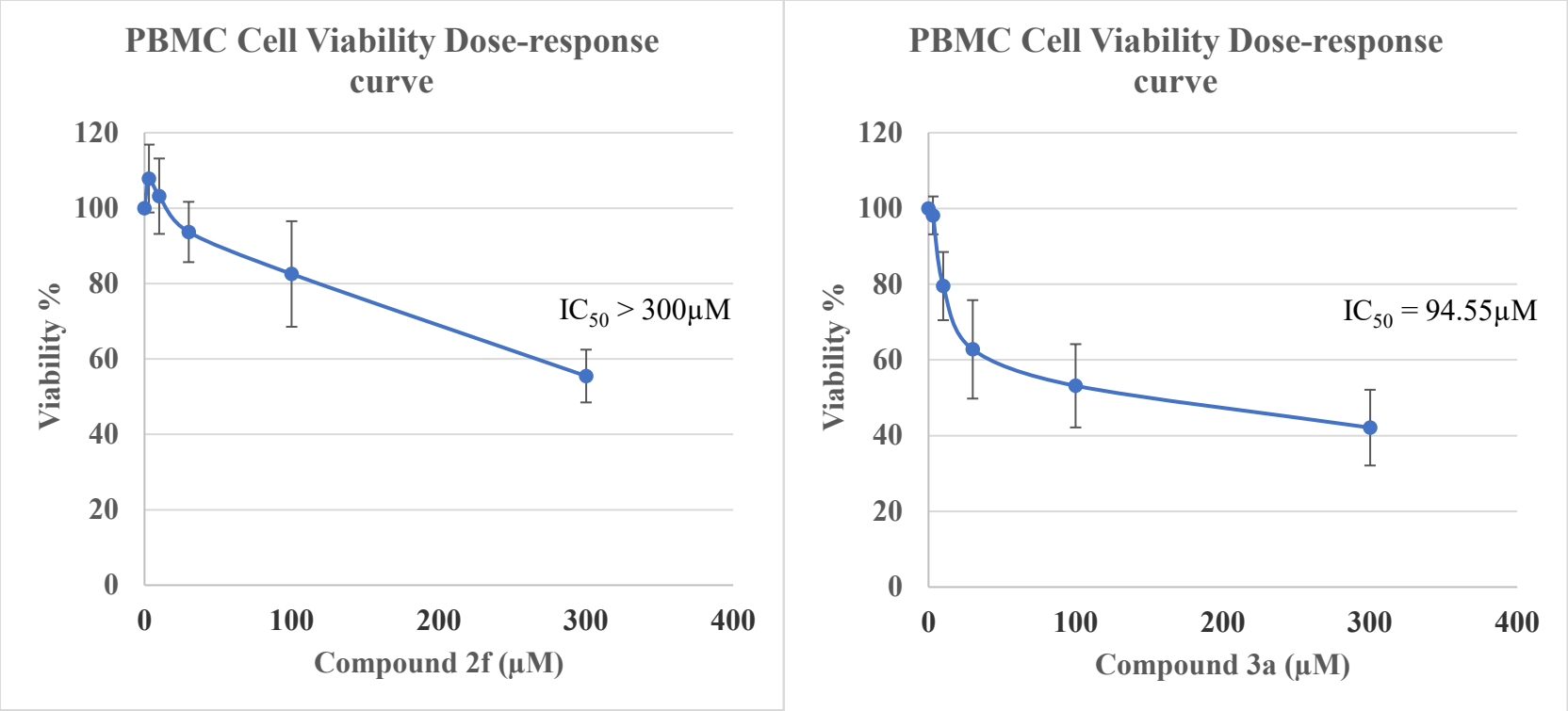


Figure S40. Cell viability Dose-response curve for inhibition of PBMC cells. Data are given as mean ± SEM of n= 3 independent experiments, shown as percentage of control, DMSO (= 100%).

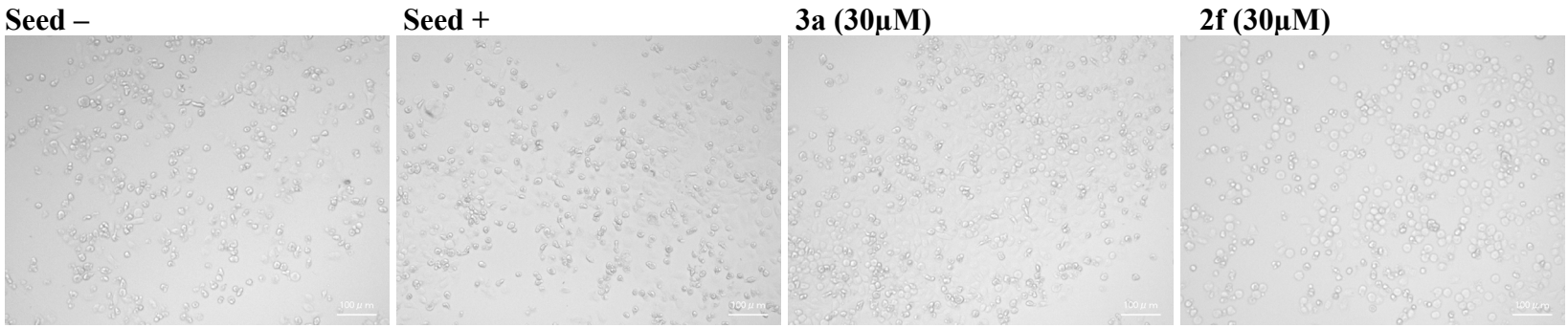


Figure S41. Effects of different concentrations of seed positive (seed +), **2f (30µM)** and **3a (30µM)** on Hela cell morphology photographed under an inverted microscope 24 hours after treatment compared to untreated Hela cells, seed negative (seed -).

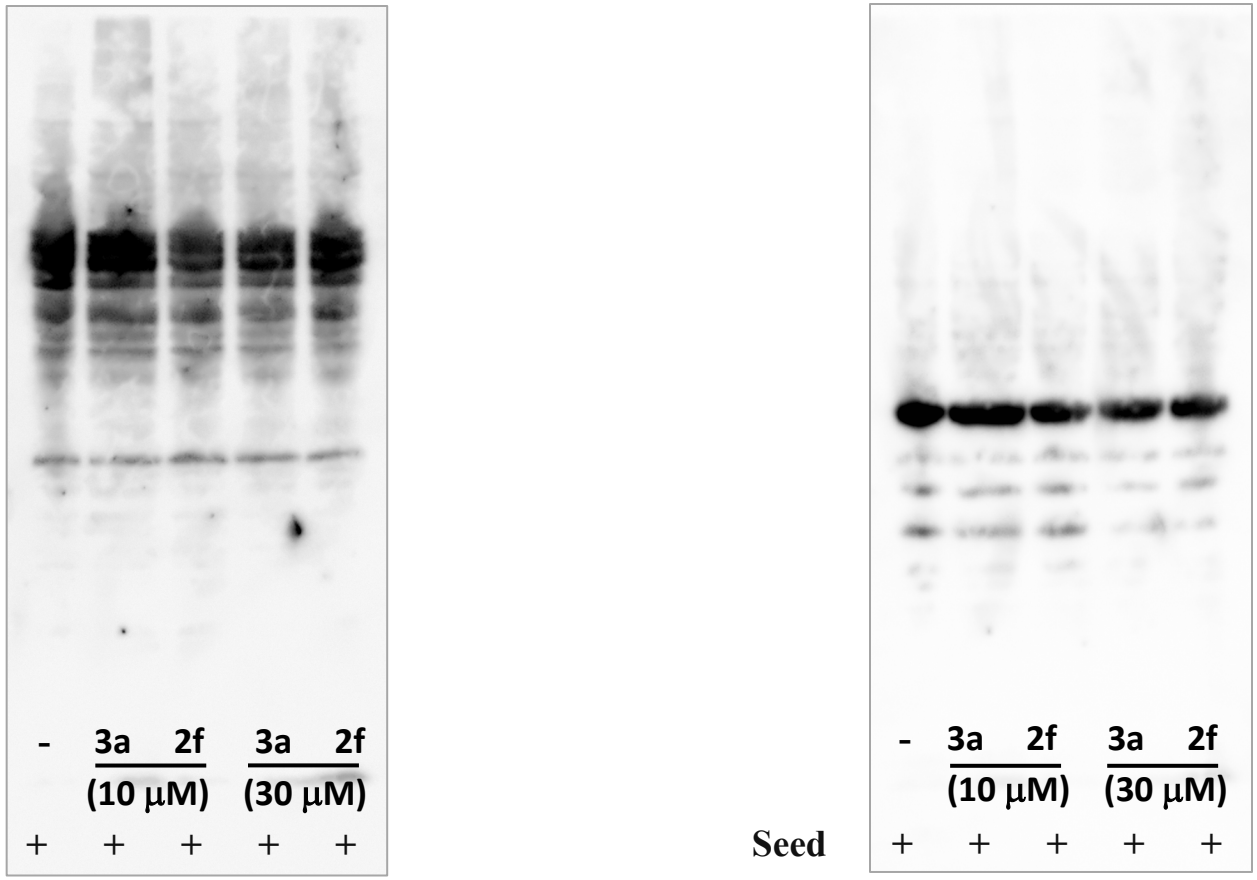


Figure S42. The whole gel of western blot analysis showing the effect of different concentrations of **3a (10μM)**, **2f (10μM) 3a (30μM)** and **2f (30μM)** on total tau proteins **(A),** using GAPDH as a reference **(B)** after 24 hours treatment compared to Hela cells, seed positive (seed +). The same membrane stained with anti-Tau in **(A)** and anti-GAPDH in **(B)**.