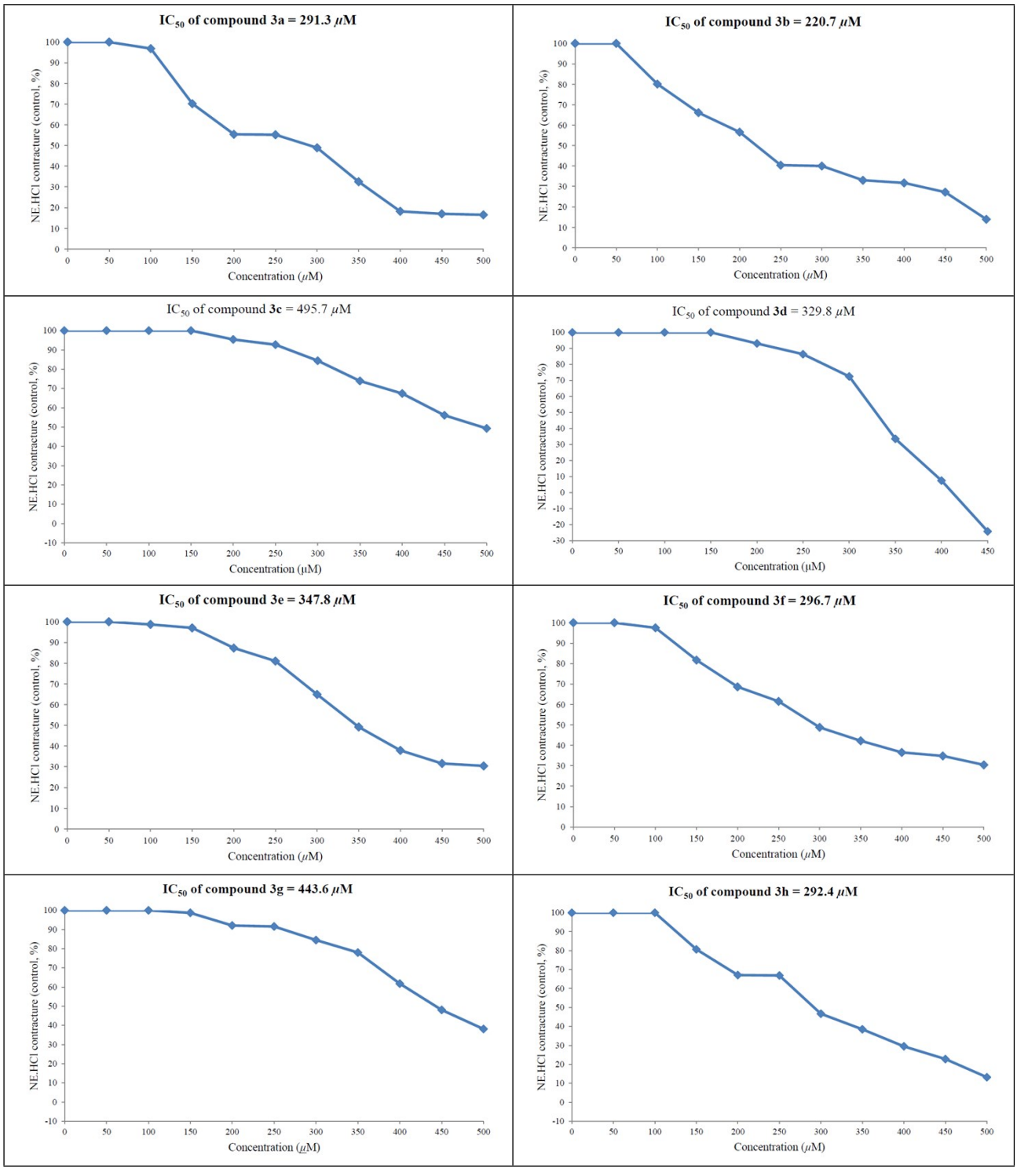
Electronic Supplementary Material (ESI) for New Journal of Chemistry.

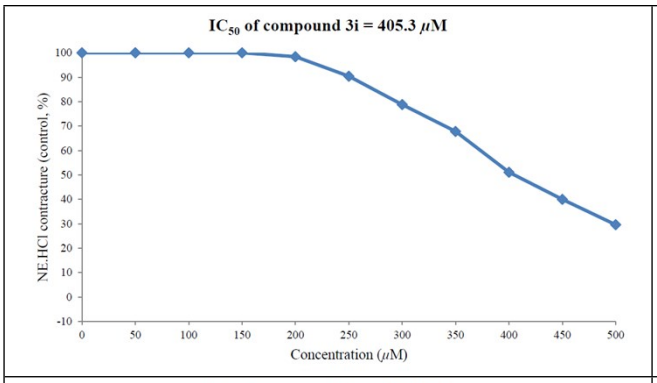
Supplementary material

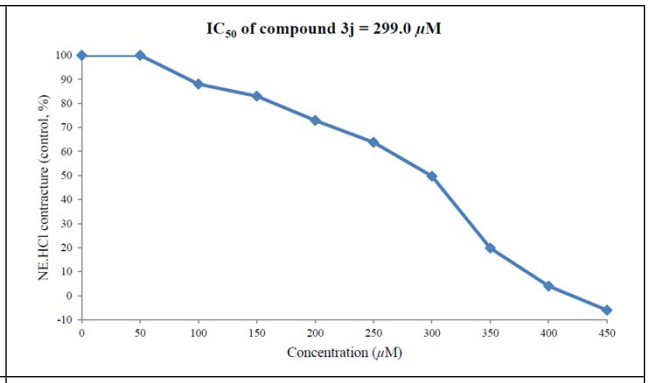
1. Vasodilation Activity Screening

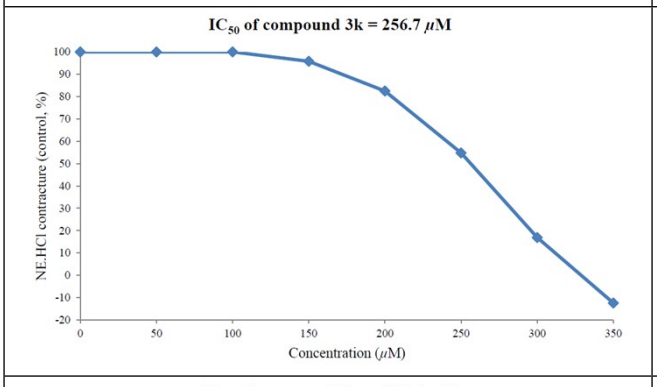
The vasodilation activity screening was undertaken by Pharmacology Department, National Research Centre, Egypt, according to the standard in vitro bioassay technique [1, 2] by testing the effects of the synthesized agents **3a-v** and compared with prazosin hydrochloride (α_1-AR antagonist) on isolated thoracic aortic rings of male Wistar rats (200–250 g) pre-contracted with norepinephrine hydrochloride. After light ether anesthesia, the rats were sacrificed by cervical dislocation. The aortae were immediately excised, freed of extraneous tissues, and prepared for isometric tension recording. Aorta was cut into (3–5 mm width) rings and each ring was placed in a vertical chamber "10 ml 5 jacketed automatic multi-chamber organ bath system (Model no. ML870B6/C, Panlab, Spain)" filled with Krebs solution composed of (in mM): NaCl, 118.0; KCl, 4.7; $NaHCO_3$, 25.0; $CaCl_2$, 1.8; NaH_2PO_4, 1.2; $MgSO_4$, 1.2; glucose, 11.0 and oxygenated with carbogen gas (95% O_2/5% CO_2) at 37 ± 0.5 °C. Each aortic ring was mounted between two stainless steel hooks passed through its lumen. The lower hook was fixed between two plates, while the upper one was attached to a force displacement transducer (Model no. MLT0201, Panlab, Spain) connected to an amplifier (PowerLab, AD Instruments Pty. Ltd.), which was connected to a computer. The Chart for windows (v 3.4) software was used to record and elaborate data. Preparations were stabilized under 2 g resting tension during 2 h, and then the contracture response to norepinephrine hydrochloride (10^{-6} M) was measured before and after exposure to increasing concentrations of the tested synthesized compounds (50, 100, 150, 200, 250, 300, 350, 400, 450 and 500 μM). The tested compounds were dissolved in dimethylsulfoxide (DMSO) as stock solution (10 ml of 0.005 M). Control experiments were performed in the presence of DMSO alone, at the same concentrations as those used with the derivatives tested, which demonstrated that the solvent did not affect the contractile response of isolated aorta. The observed vasodilation activity screening data for the synthesized compounds **3a-v** and prazosin hydrochloride are expressed as IC_{50} (μM) concentration necessary for 50% reduction of maximal norepinephrine hydrochloride induced contracture utilizing four different replicates. The standard deviation ±SD was calculated by SPSS-16.

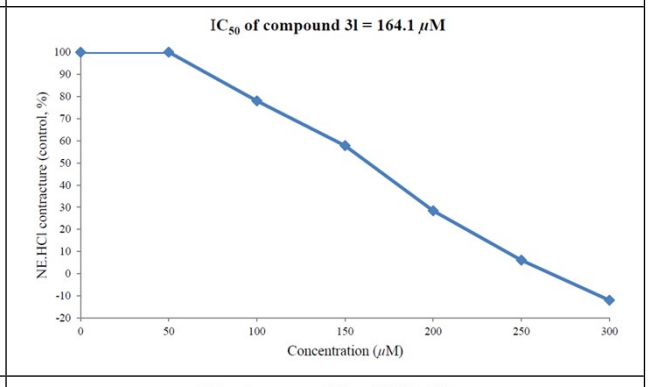
Table S1. Dose response curves the tested compounds

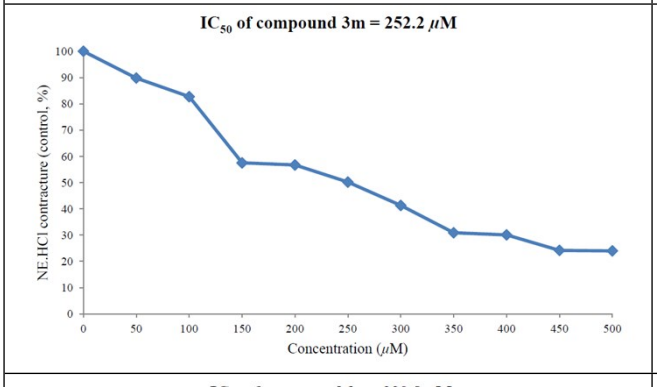


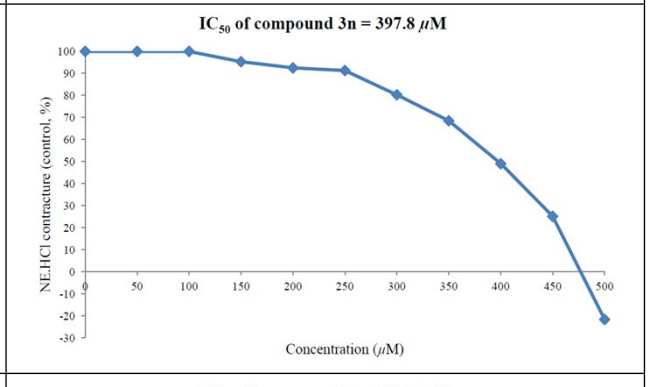

IC50 of compound 3i = 405.3 μM
NE.HCl contracture (control, %)
Concentration (μM)

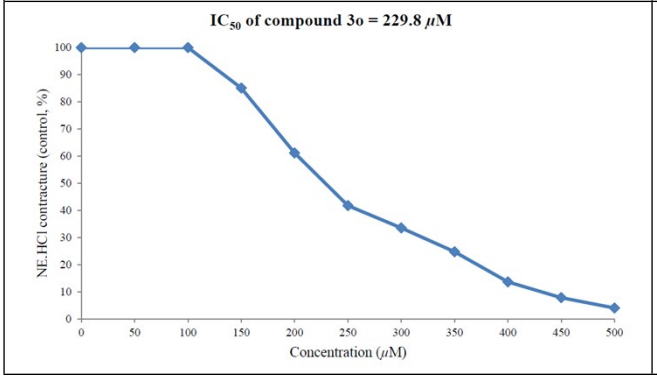

IC50 of compound 3j = 299.0 μM
NE.HCl contracture (control, %)
Concentration (μM)

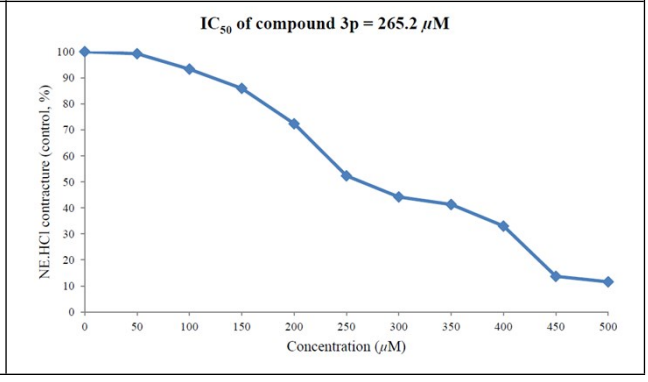

IC50 of compound 3k = 256.7 μM
NE.HCl contracture (control, %)
Concentration (μM)


IC50 of compound 3l = 164.1 μM
NE.HCl contracture (control, %)
Concentration (μM)


IC50 of compound 3m = 252.2 μM
NE.HCl contracture (control, %)
Concentration (μM)


IC50 of compound 3n = 397.8 μM
NE.HCl contracture (control, %)
Concentration (μM)


IC50 of compound 3o = 229.8 μM
NE.HCl contracture (control, %)
Concentration (μM)


IC50 of compound 3p = 265.2 μM
NE.HCl contracture (control, %)
Concentration (μM)

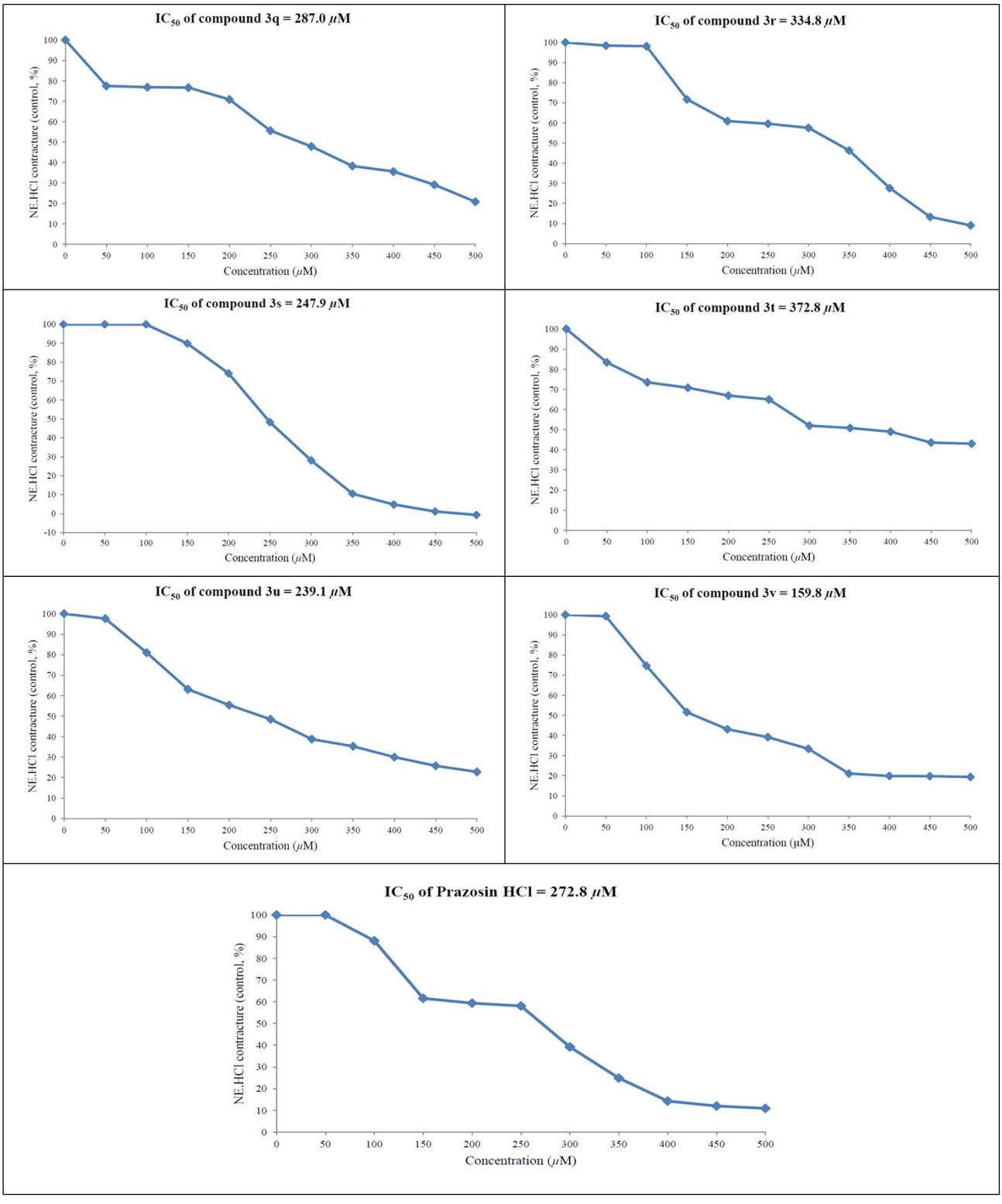

IC50 of compound 3q = 287.0 μM
IC50 of compound 3r = 334.8 μM
IC50 of compound 3s = 247.9 μM
IC50 of compound 3t = 372.8 μM
IC50 of compound 3u = 239.1 μM
IC50 of compound 3v = 159.8 μM
IC50 of Prazosin HCl = 272.8 μM
NE.HCl contracture (control, %)
Concentration (μM)

Table S2. Descriptor values for the test set compounds presented in the 2D-QSAR model.

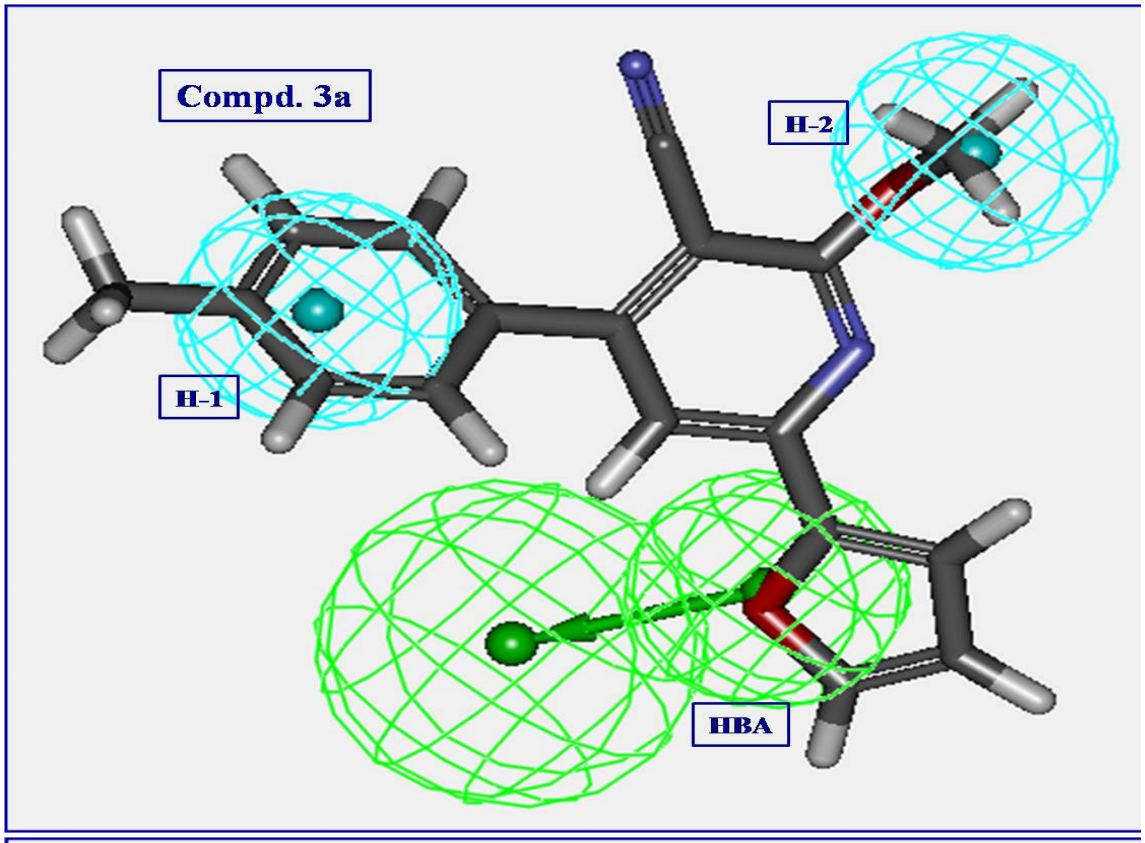
Entry	Compd.	D_1	D_2	D_3	D_4
1	**3k**	66.044	22445.4	2.1229	0.2
2	**3r**	65.9747	26751.7	2.0958	0.12766

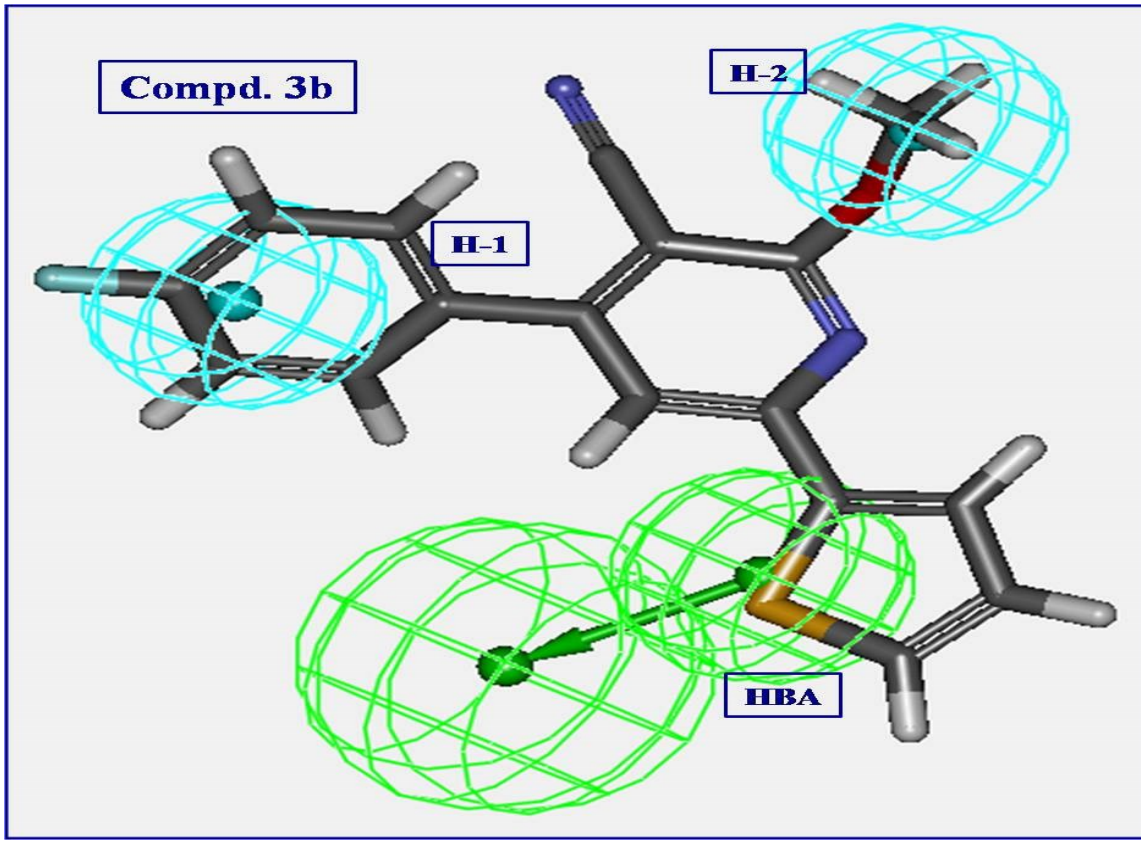
D_1 = Min. e-n attraction for bond H-C; D_2 = (1/6)X GAMMA polarizability (DIP); D_3 = Max. bonding contribution of one MO; D_3 = Relative number of double bonds.

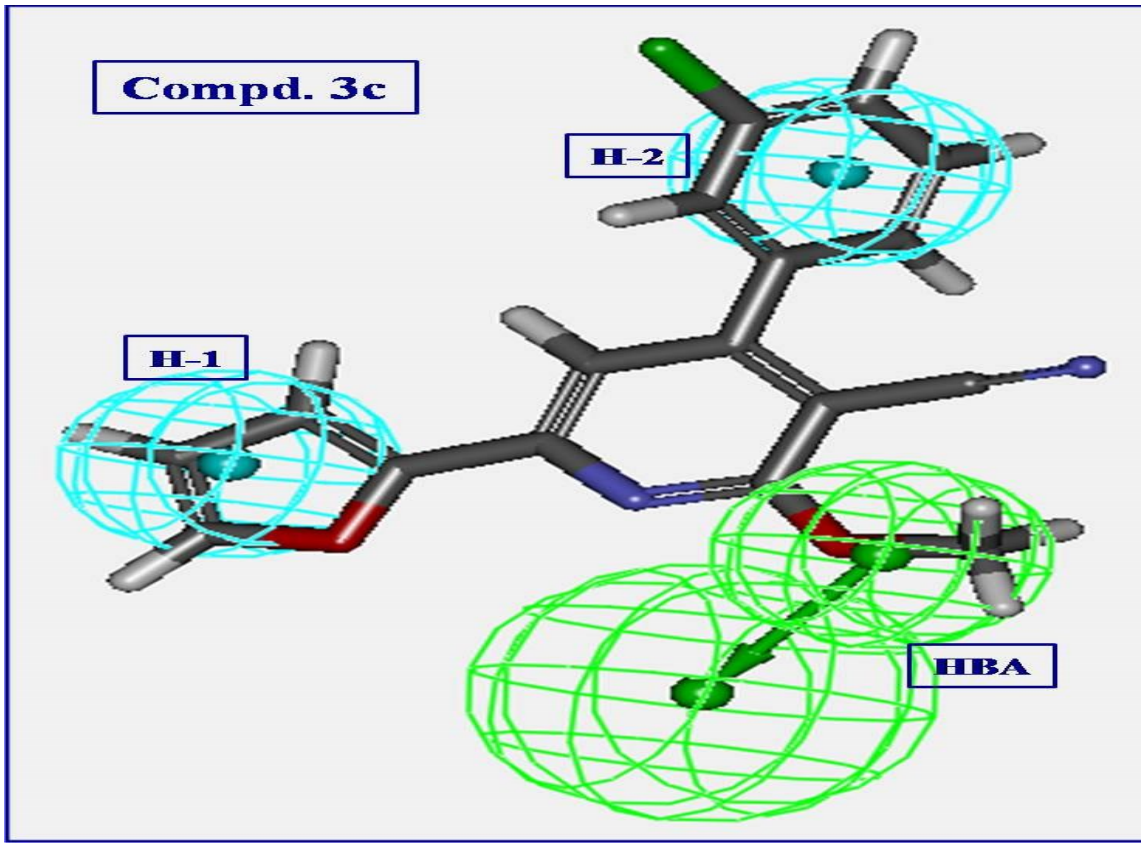
Table S3. Descriptor values for the training set compounds of the 2D-QSAR model.

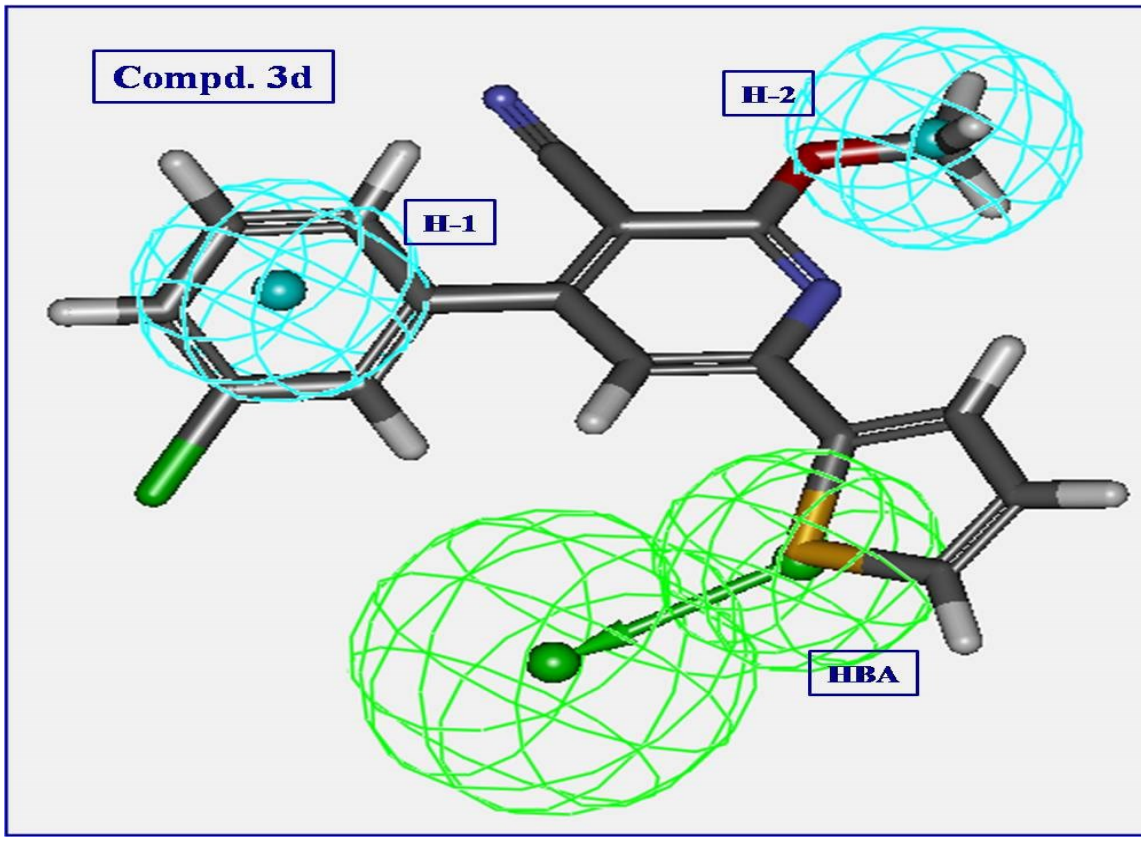
Entry	Compd.	D_1	D_2	D_3	D_4
1	**3a**	66.0758	20365.2	2.1136	0.13158
2	**3b**	67.1792	18536	2.0439	0.14286
3	**3c**	66.0375	19204.3	2.0547	0.14286
4	**3d**	67.086	16035.6	2.0221	0.14286
5	**3e**	65.9986	17108.5	2.1324	0.14286
6	**3f**	66.9087	18526.4	2.0224	0.14286
7	**3g**	66.045	19210	2.0754	0.12821
8	**3h**	66.8966	16714.5	2.0767	0.12821
9	**3i**	66.1015	18964.7	2.1307	0.11628
10	**3j**	67.1195	18322.7	2.0076	0.11628
11	**3l**	67.1802	23410.2	2.0066	0.2
12	**3m**	65.9366	23006.2	2.1408	0.15
13	**3n**	65.944	20737.5	2.1076	0.15
14	**3o**	66.474	26095.8	2.0839	0.13636
15	**3p**	66.1563	21913.8	2.0955	0.13953
16	**3q**	65.9516	23030.5	2.0877	0.13953
17	**3s**	65.9536	25348.6	2.1397	0.13043
18	**3t**	65.9763	23867	2.0729	0.13043
19	**3u**	66.0608	25428.7	2.1421	0.11905
20	**3v**	66.9048	26261.6	2.1267	0.11905

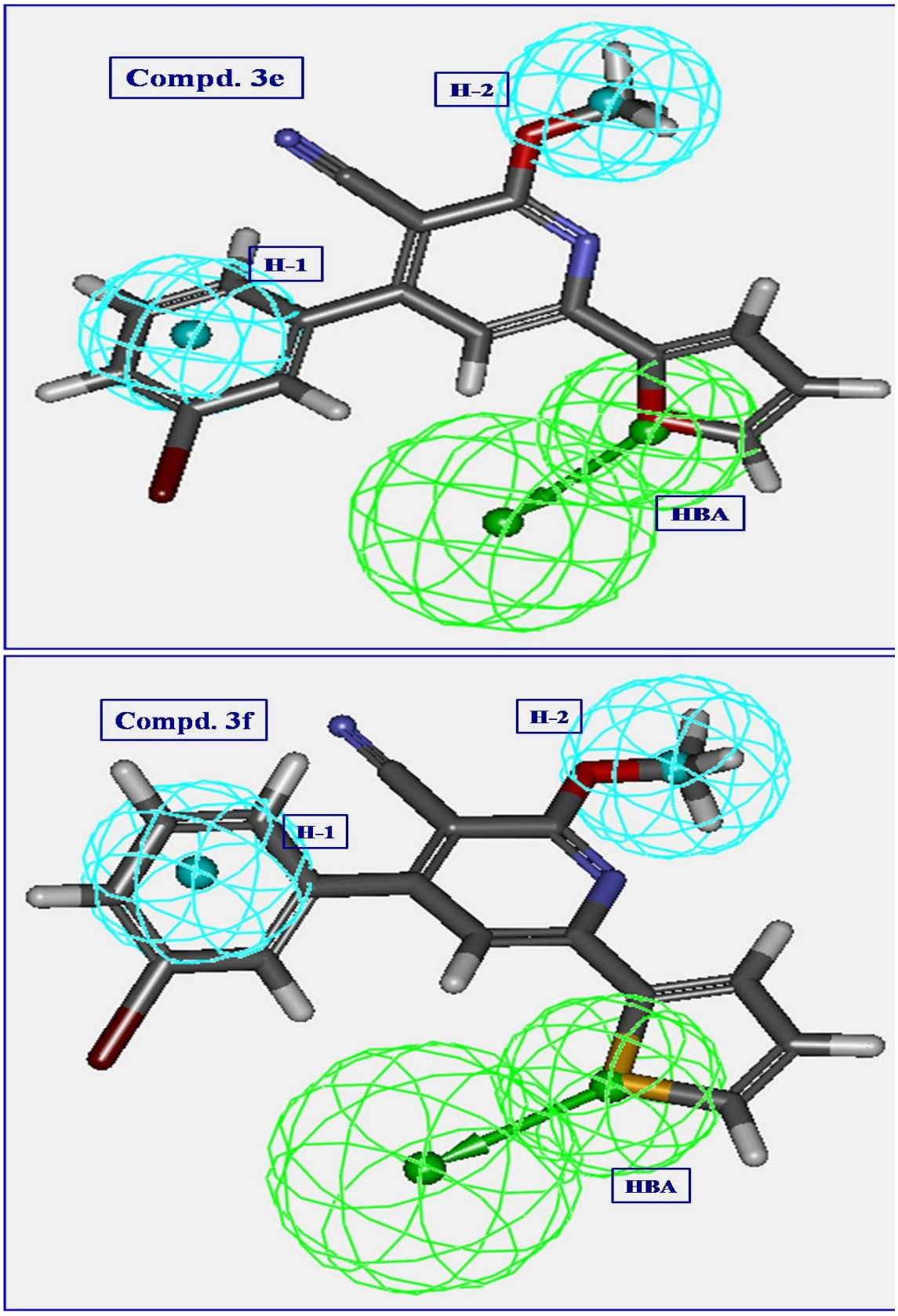
D_1 = Min. e-n attraction for bond H-C; D_2 = (1/6)X GAMMA polarizability (DIP); D_3 = Max. bonding contribution of one MO; D_3 = Relative number of double bonds.

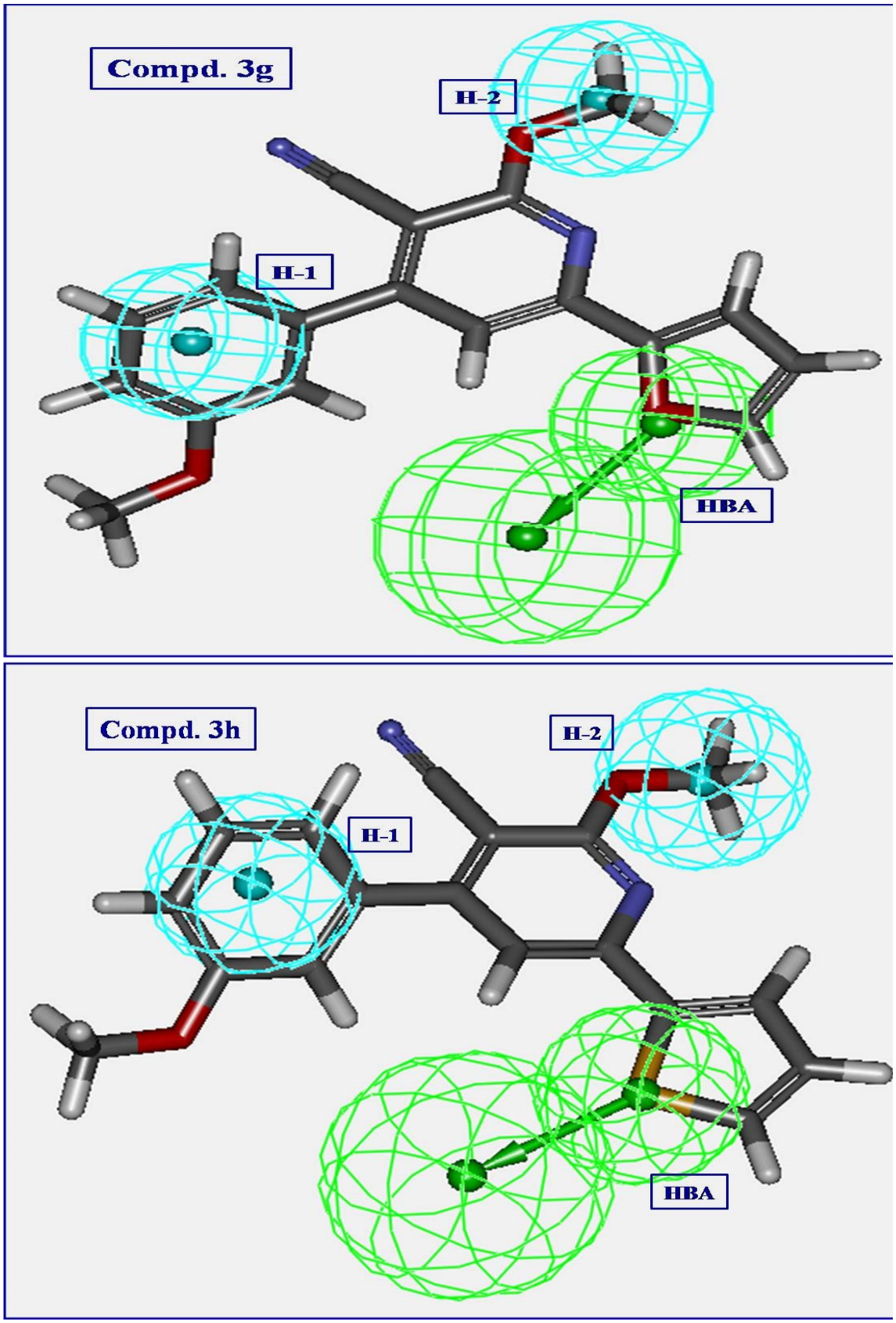

Compd. 3a
H-2
H-1
HBA

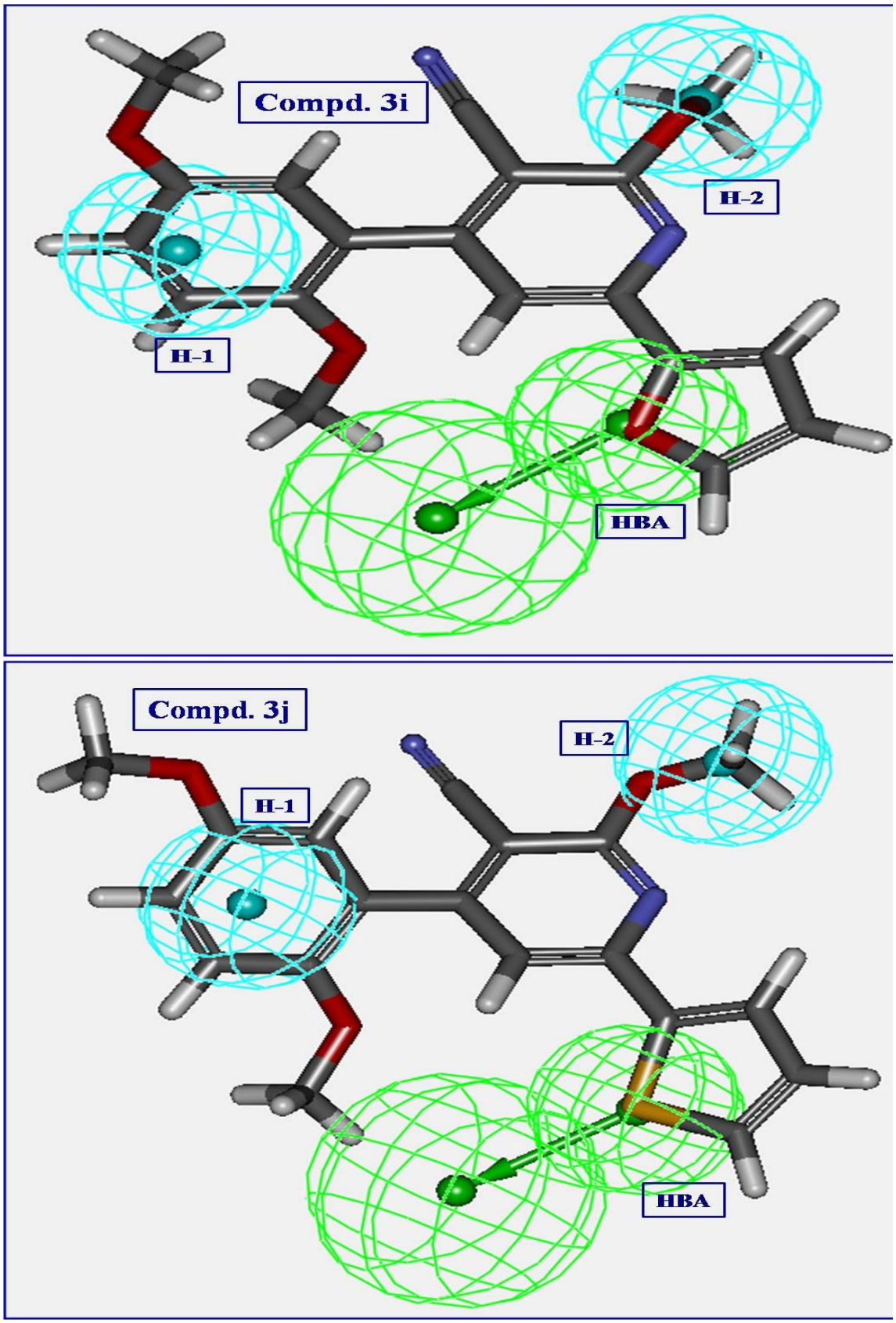

Compd. 3b
H-2
H-1
HBA

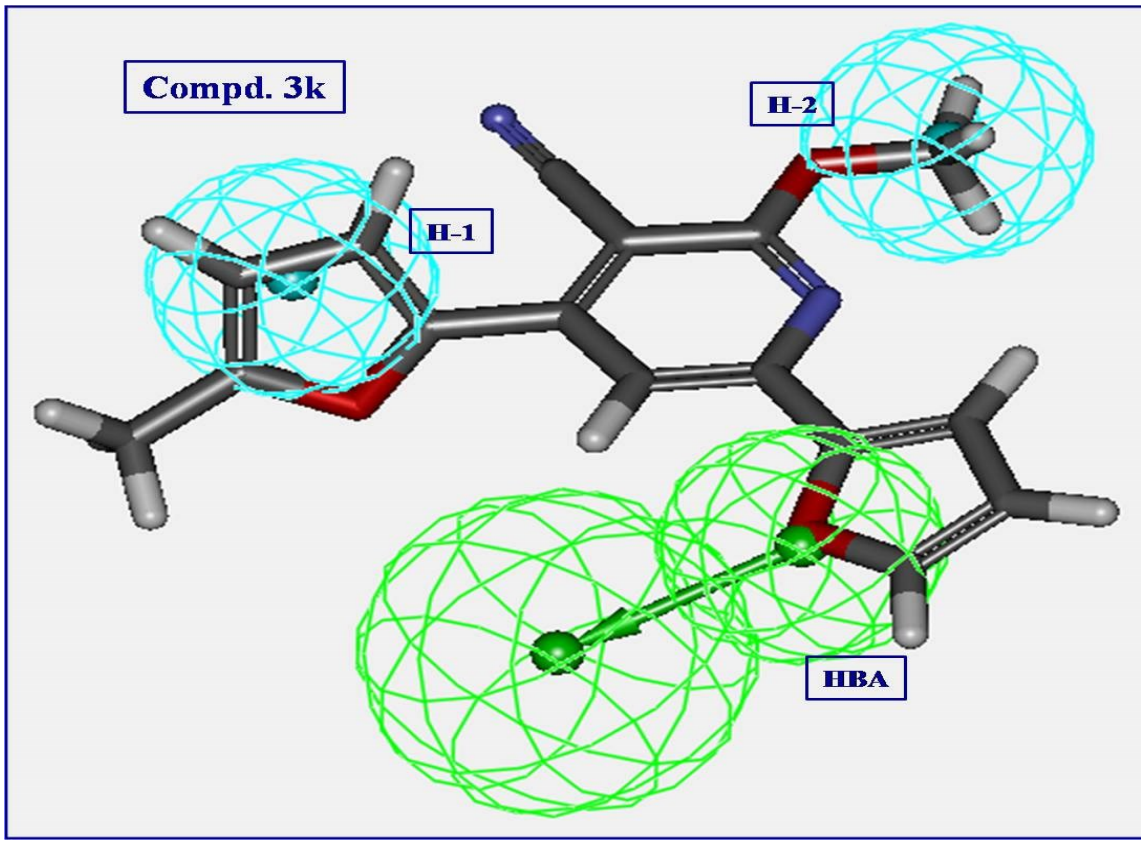

Compd. 3c
H-2
H-1
HBA

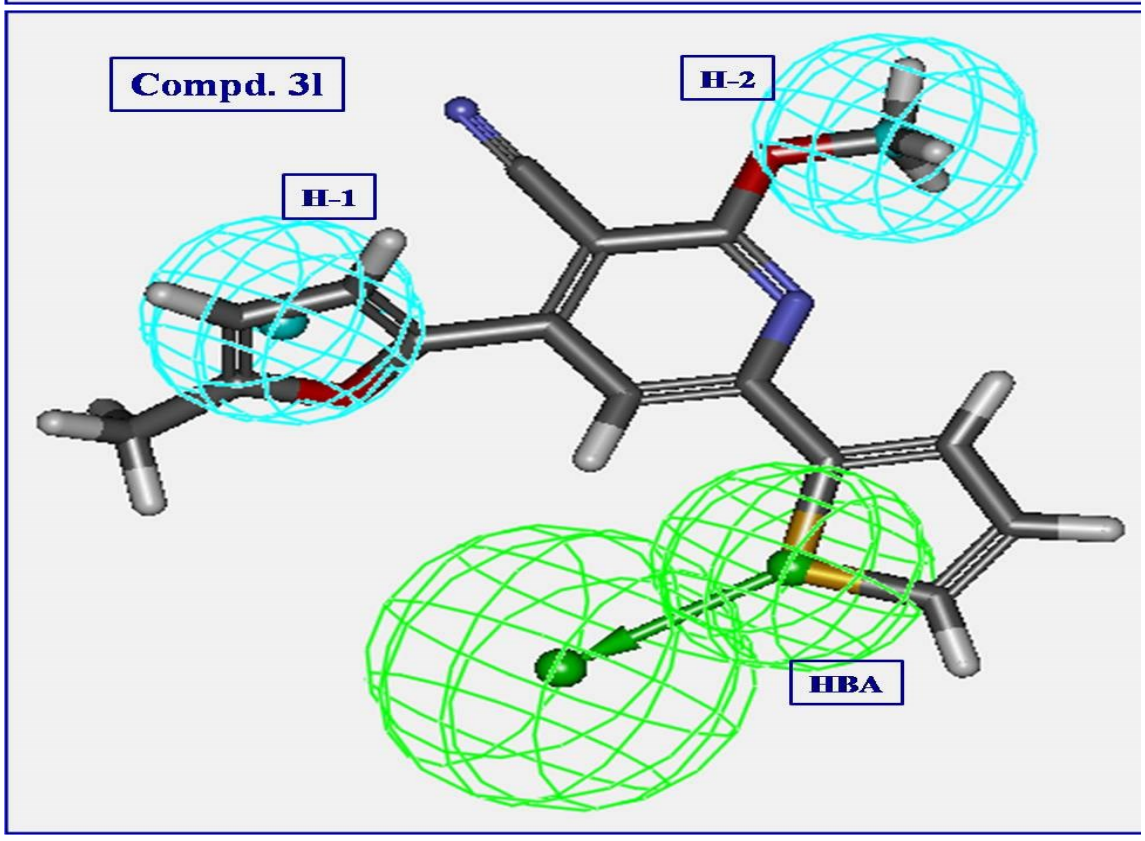

Compd. 3d
H-2
H-1
HBA

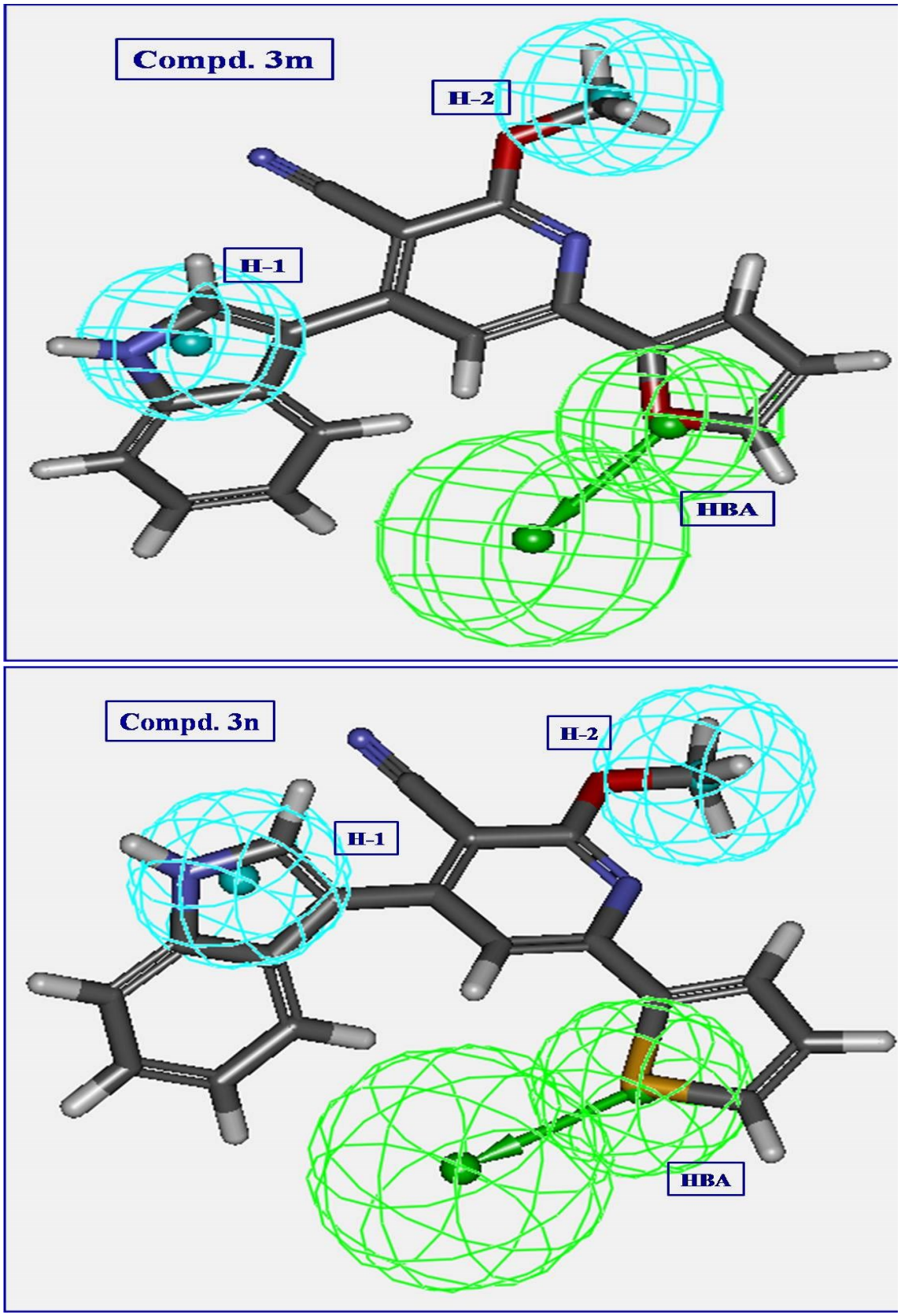

Compd. 3e
H-2
H-1
HBA
Compd. 3f
H-2
H-1
HBA

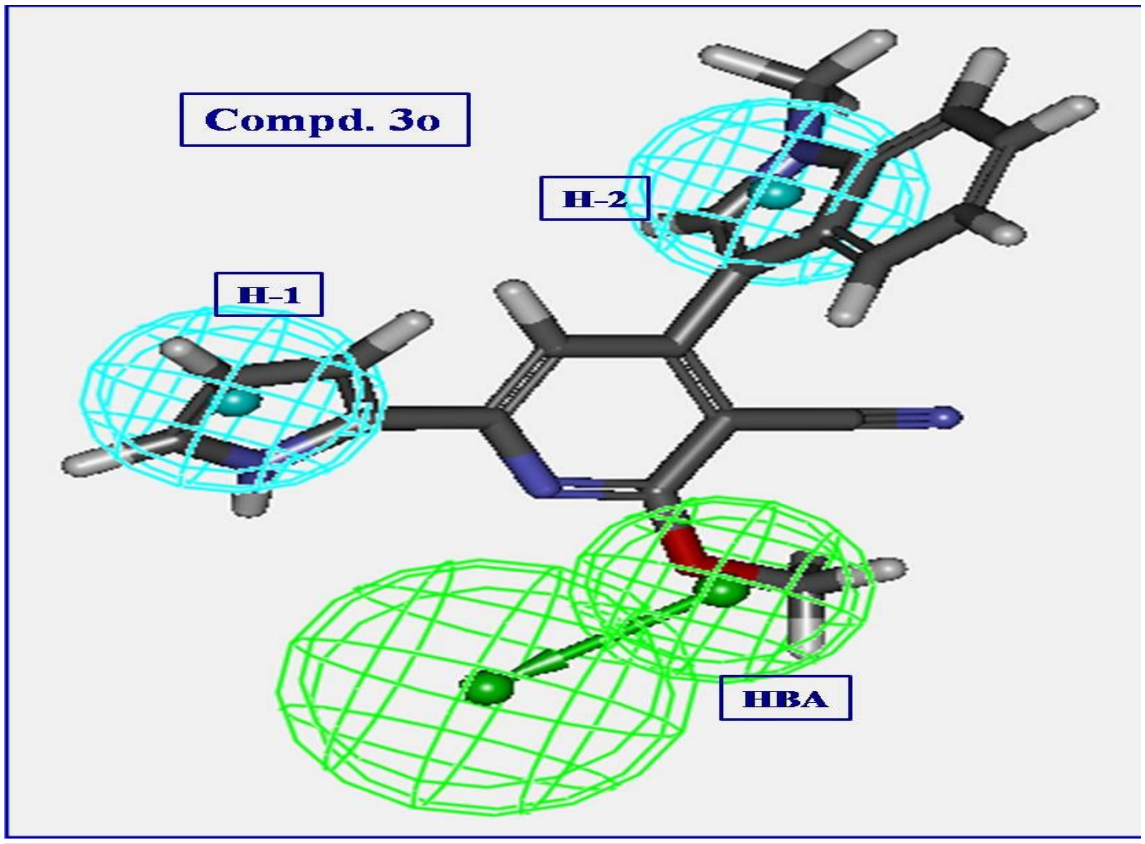

Compd. 3g
H-2
H-1
HBA
Compd. 3h
H-2
H-1
HBA

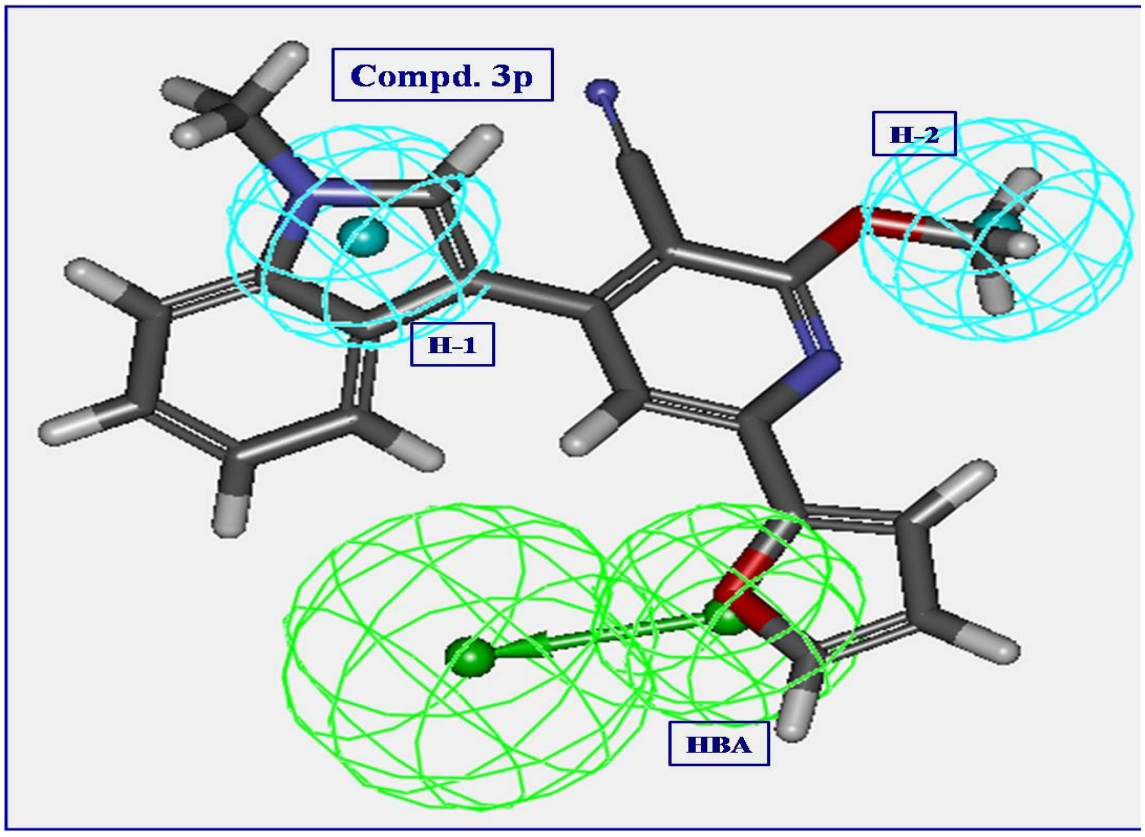

Compd. 3i
H-2
H-1
HBA
Compd. 3j
H-2
H-1
HBA

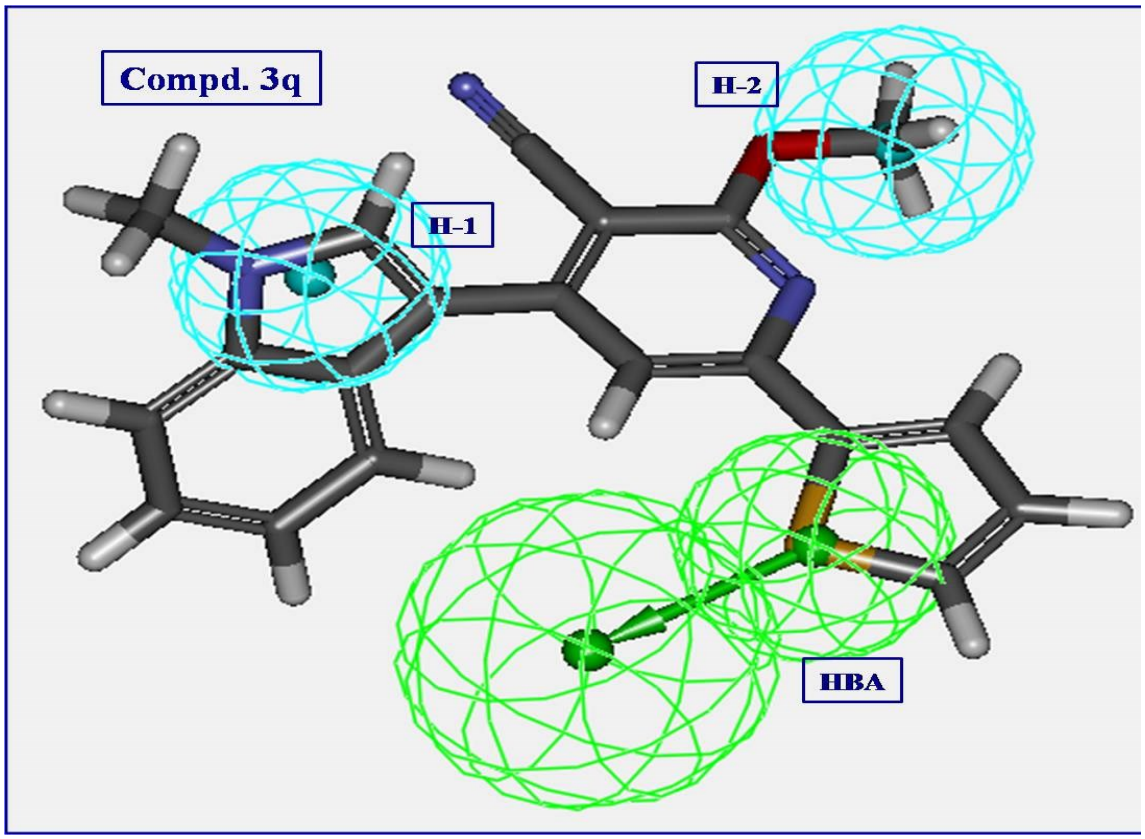

Compd. 3k
H-2
H-1
HBA

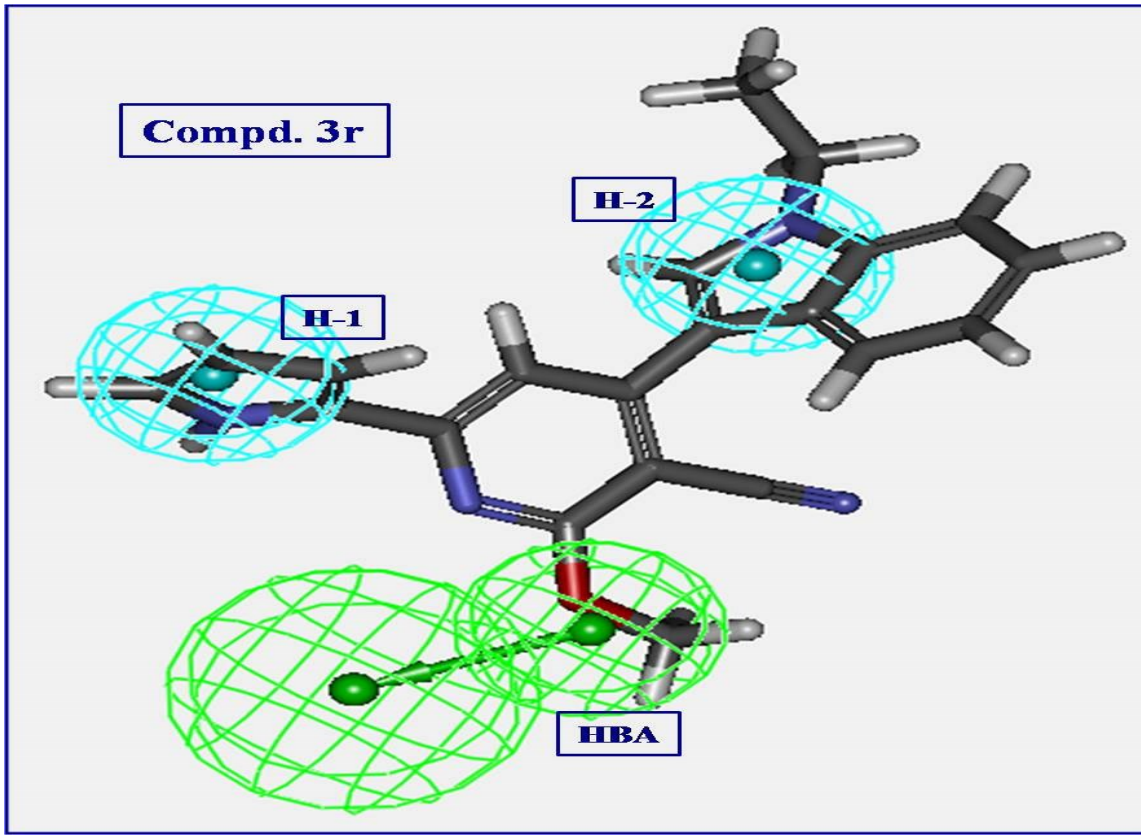

Compd. 3l
H-2
H-1
HBA

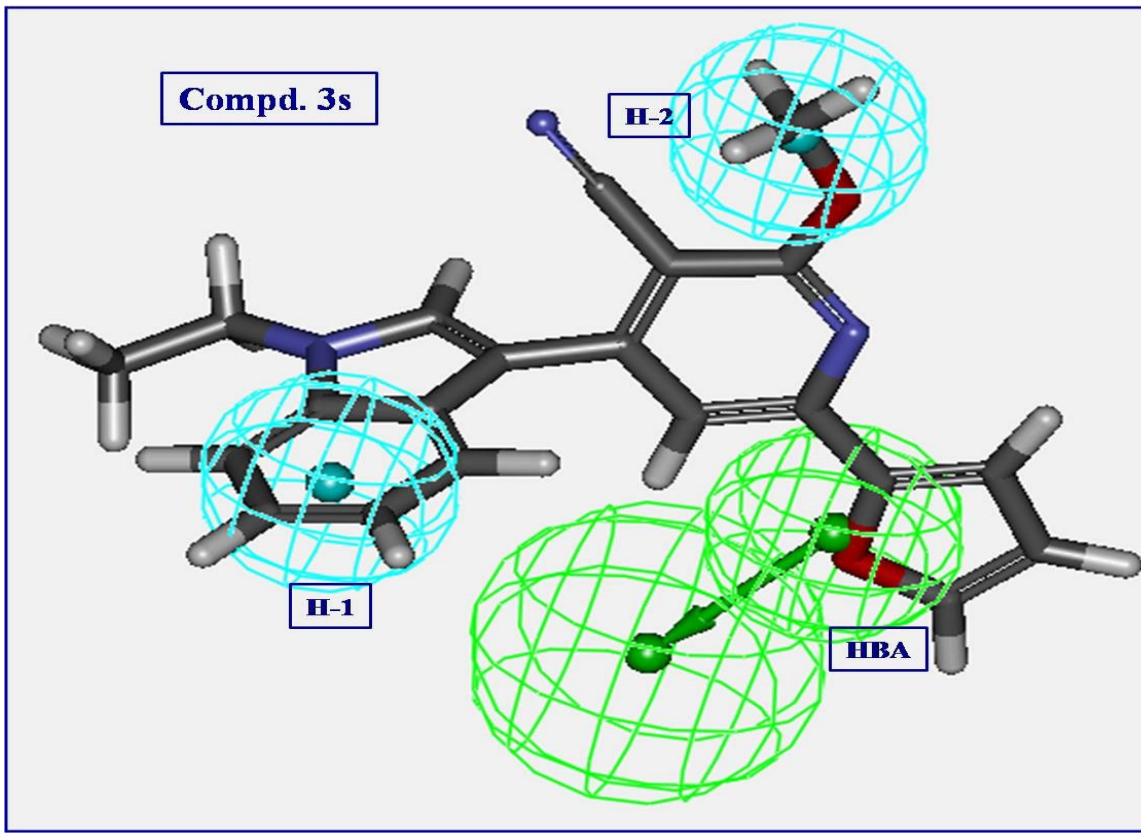

Compd. 3m
H-2
H-1
HBA
Compd. 3n
H-2
H-1
HBA

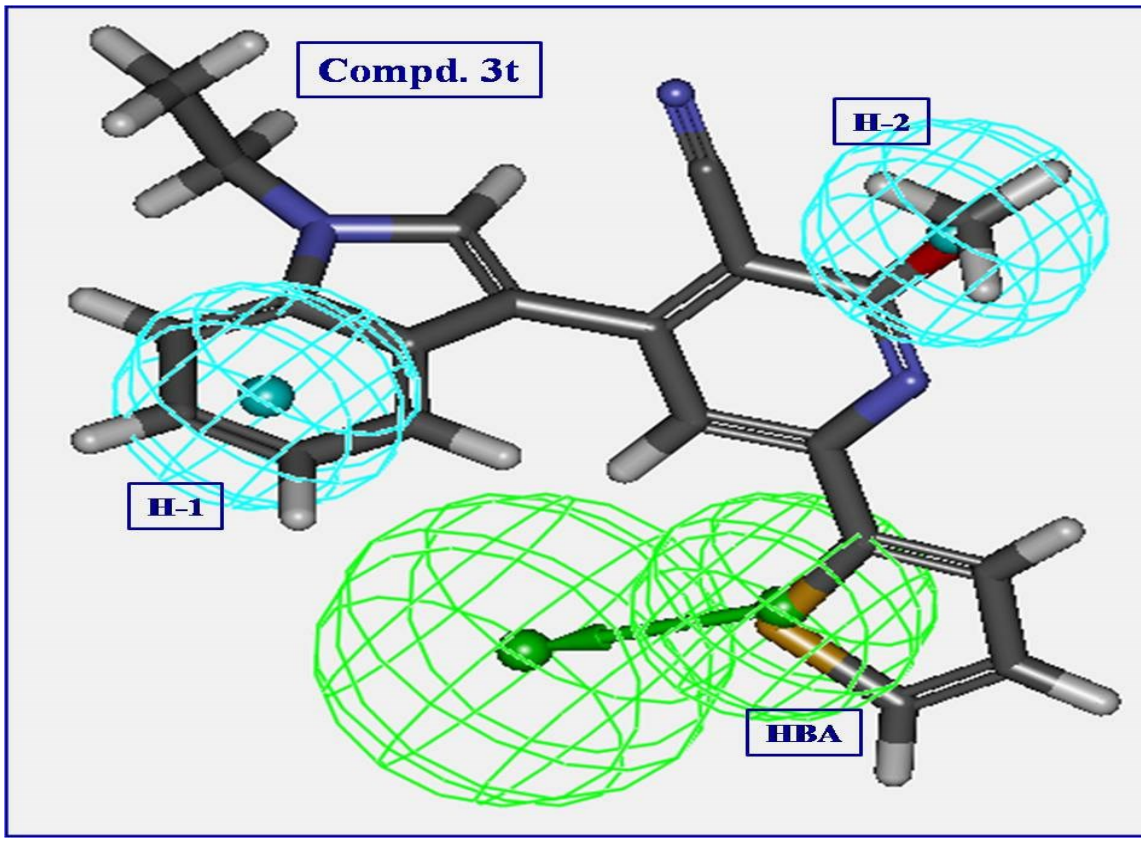

Compd. 3o
H-2
H-1
HBA


Compd. 3p
H-2
H-1
HBA


Compd. 3q
H-2
H-1
HBA


Compd. 3r
H-2
H-1
HBA


Compd. 3s
H-2
H-1
HBA


Compd. 3t
H-2
H-1
HBA

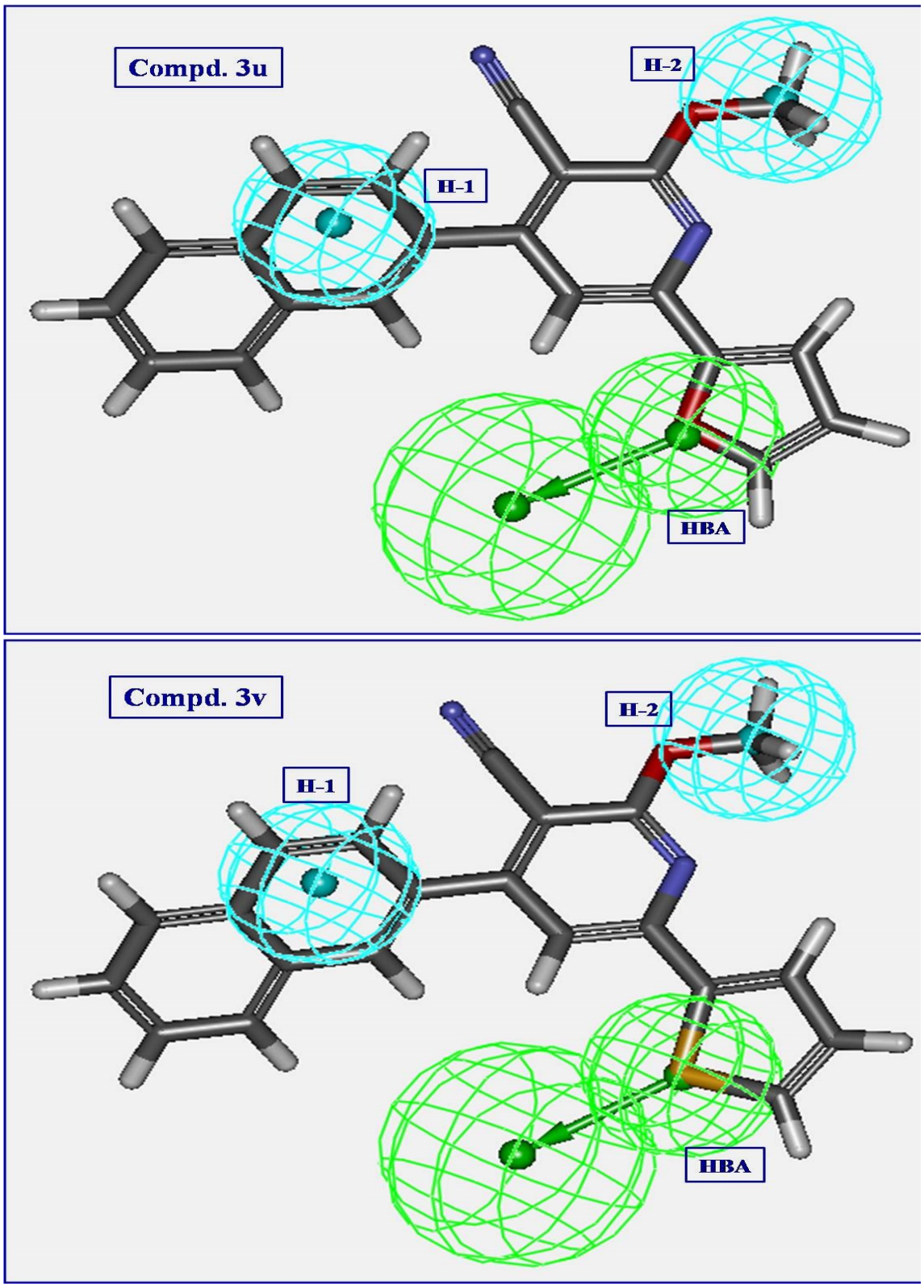


Fig. S1. 3D-pharmacophore model mapped on the tested compounds **3a-v**.

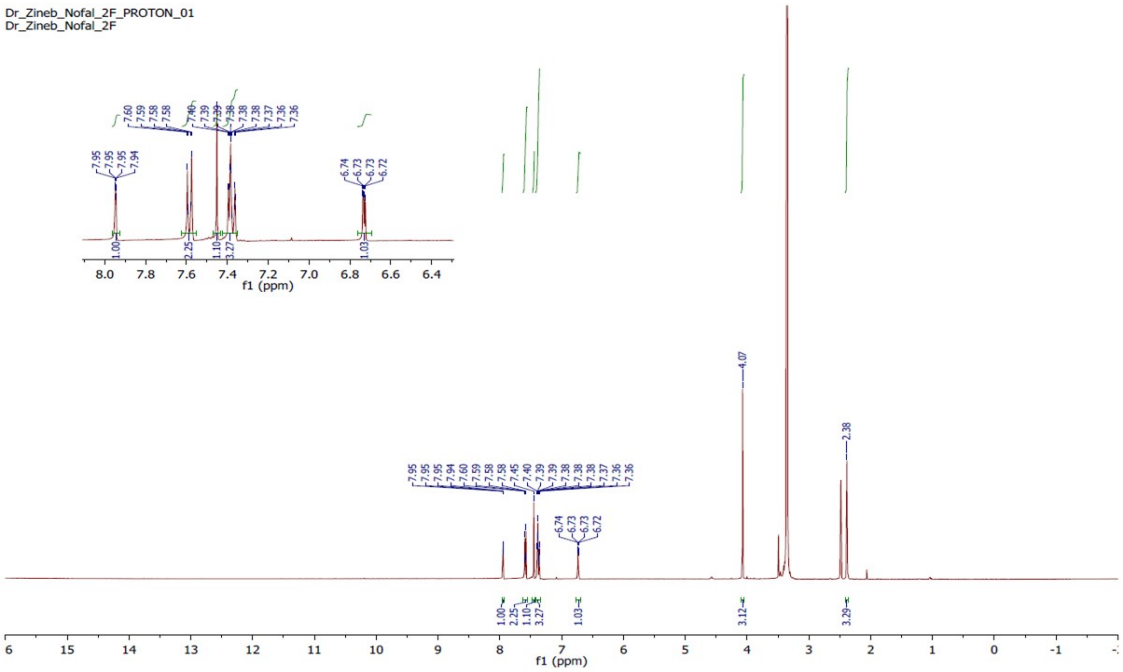


Figure S2. ^{1}H NMR spectrum of compound **3a**.

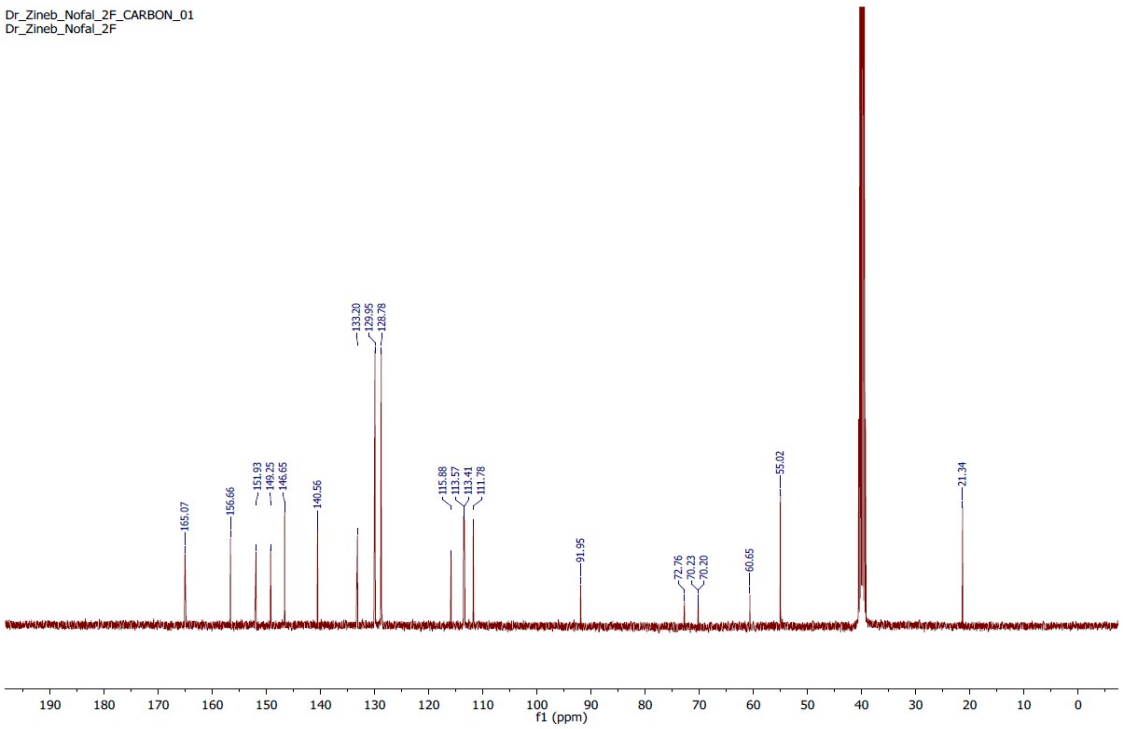


Figure S3. ^{13}C NMR spectrum of compound **3a**.

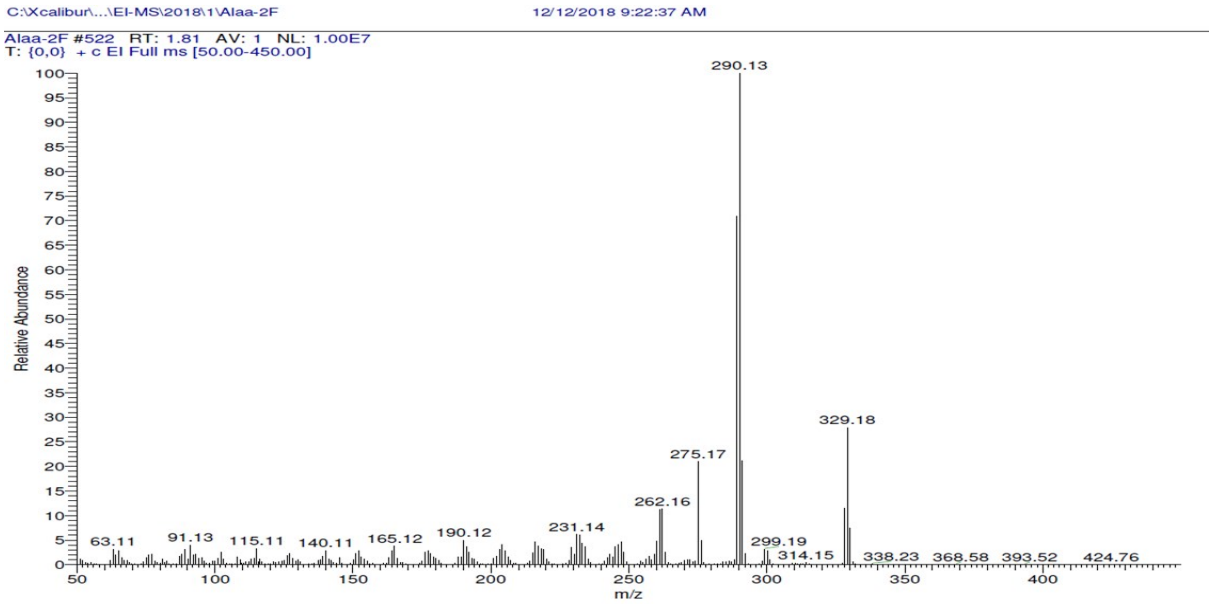


Figure S4. Mass spectrum of compound **3a**.

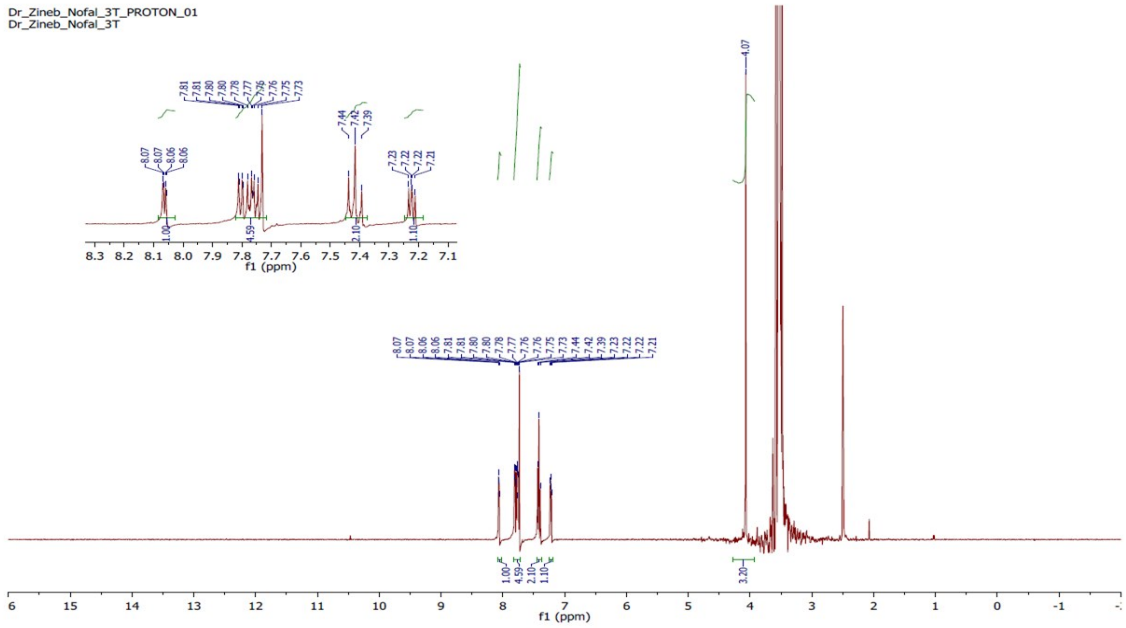


Figure S5. [1]H NMR spectrum of compound **3b**.

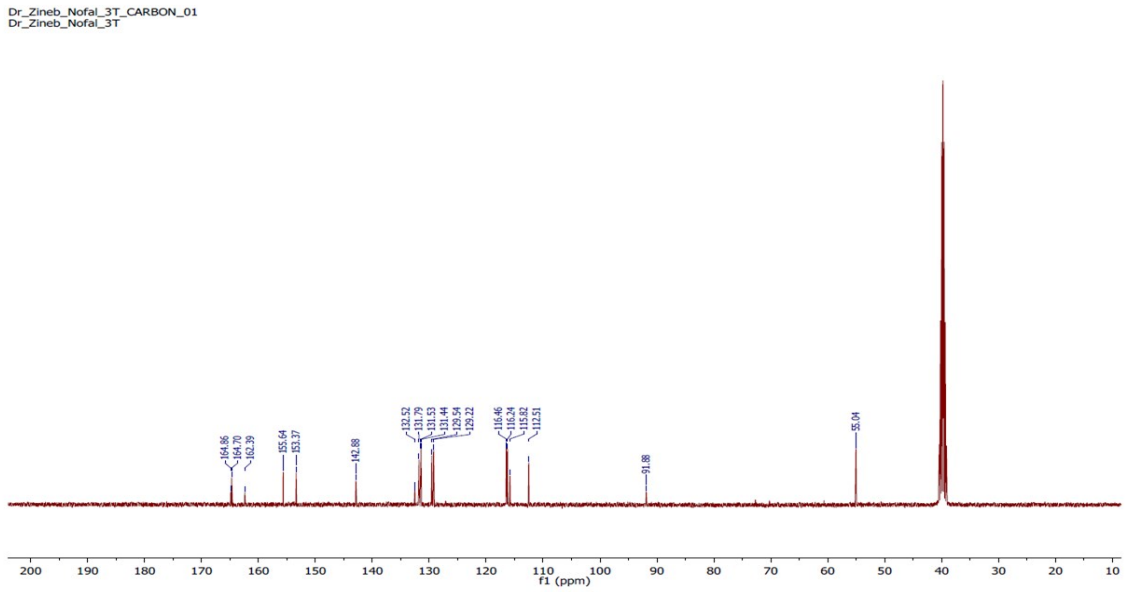


Figure S6. ^{13}C NMR spectrum of compound **3b**.

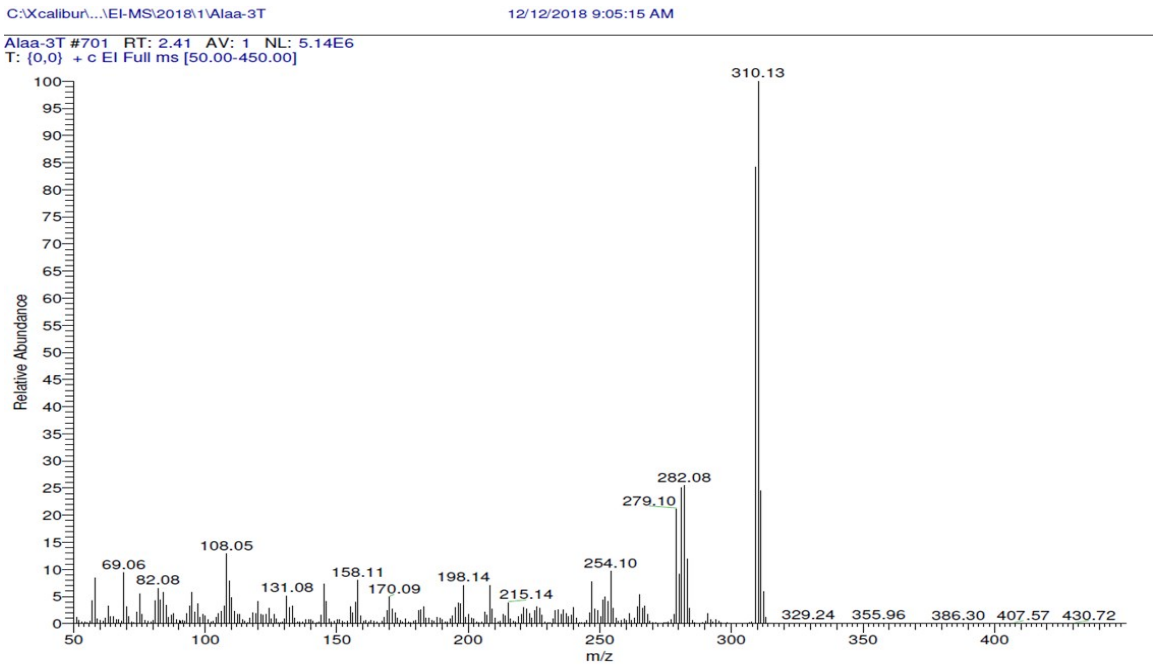


Figure S7. Mass spectrum of compound **3b**.

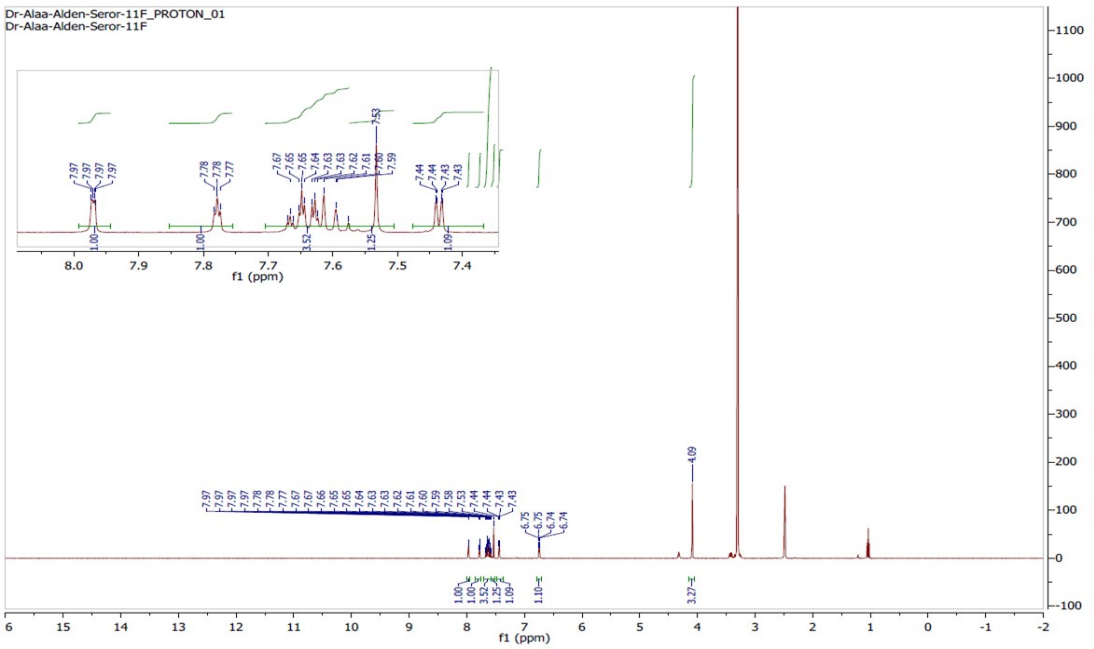


Figure S8. [1]H NMR spectrum of compound **3c**.

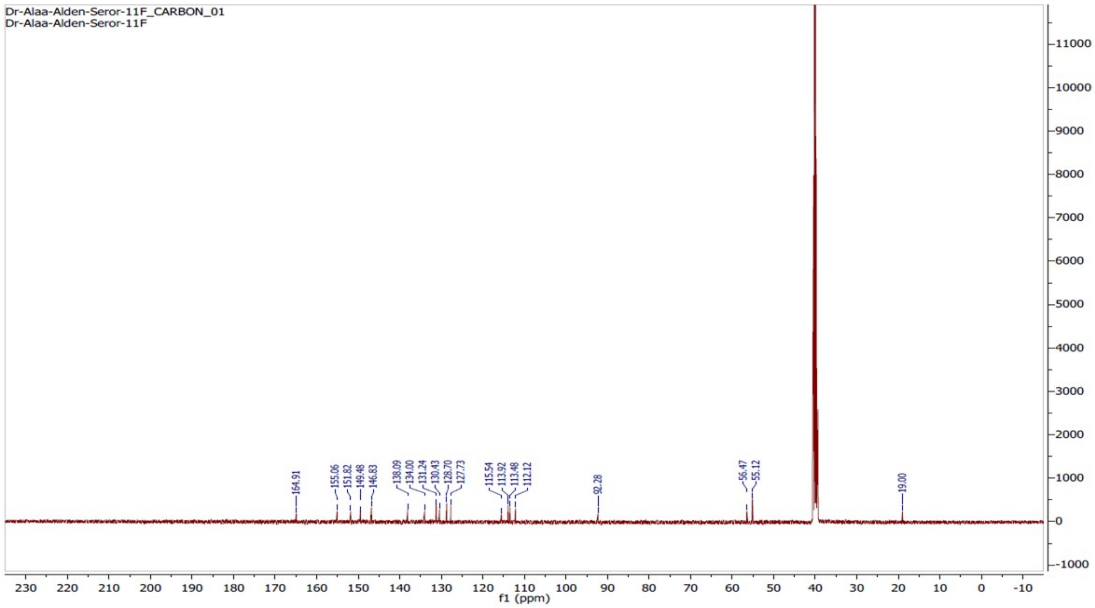


Figure S9. [13]C NMR spectrum of compound **3c**.

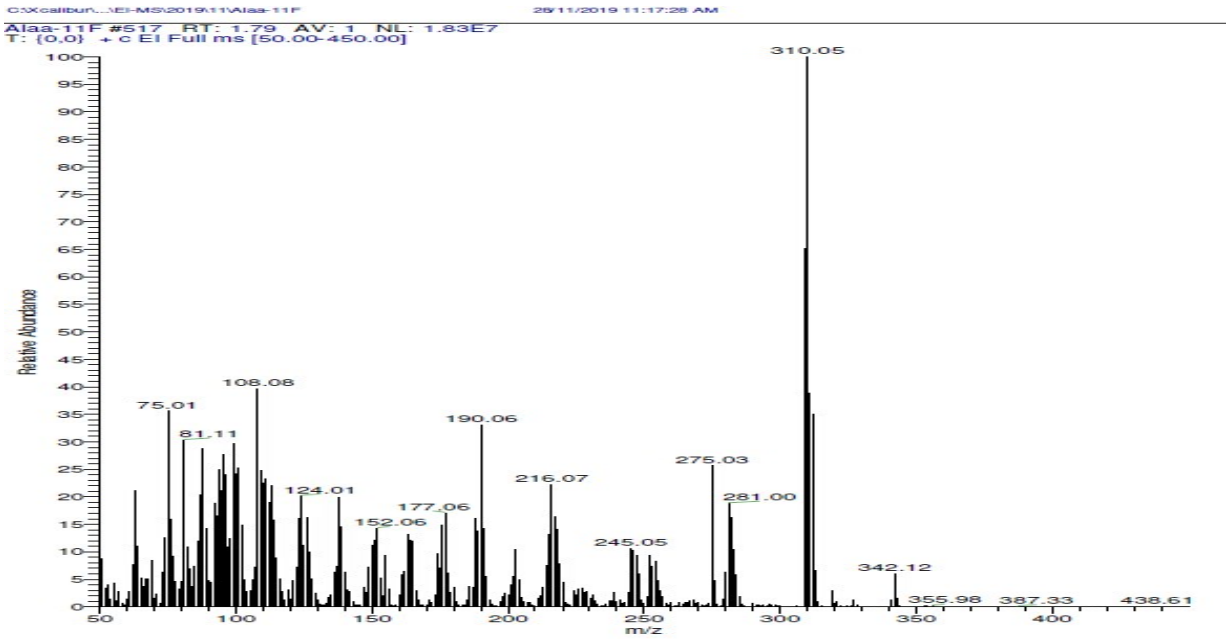


Figure S10. Mass spectrum of compound **3c**.

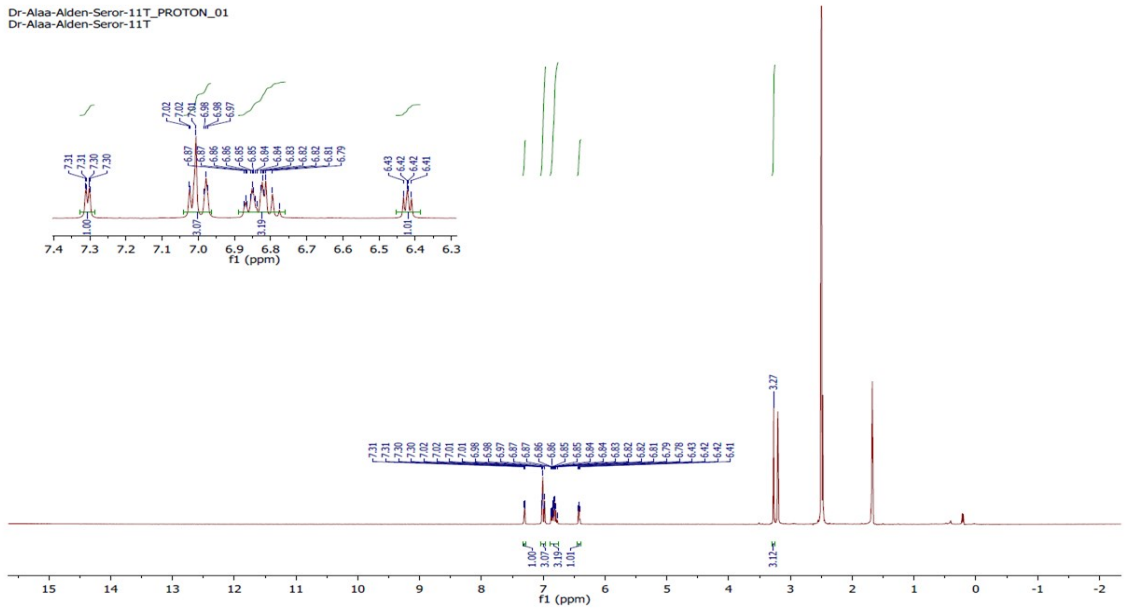


Figure S11. ^{1}H NMR spectrum of compound **3d**.

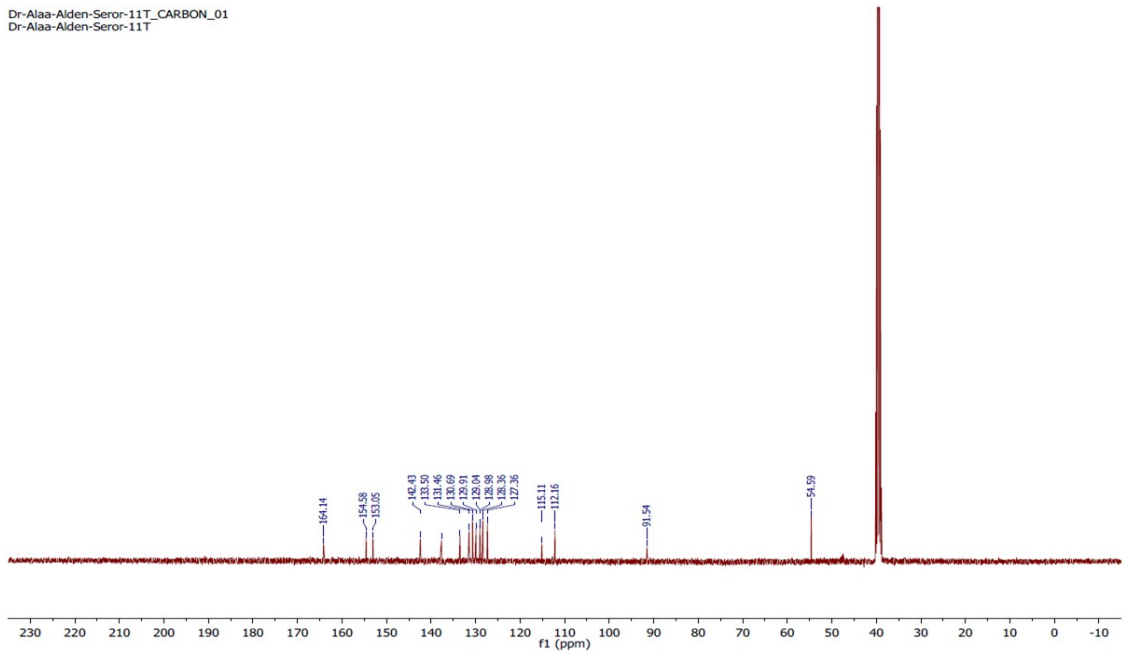


Figure S12. ^{13}C NMR spectrum of compound **3d**.

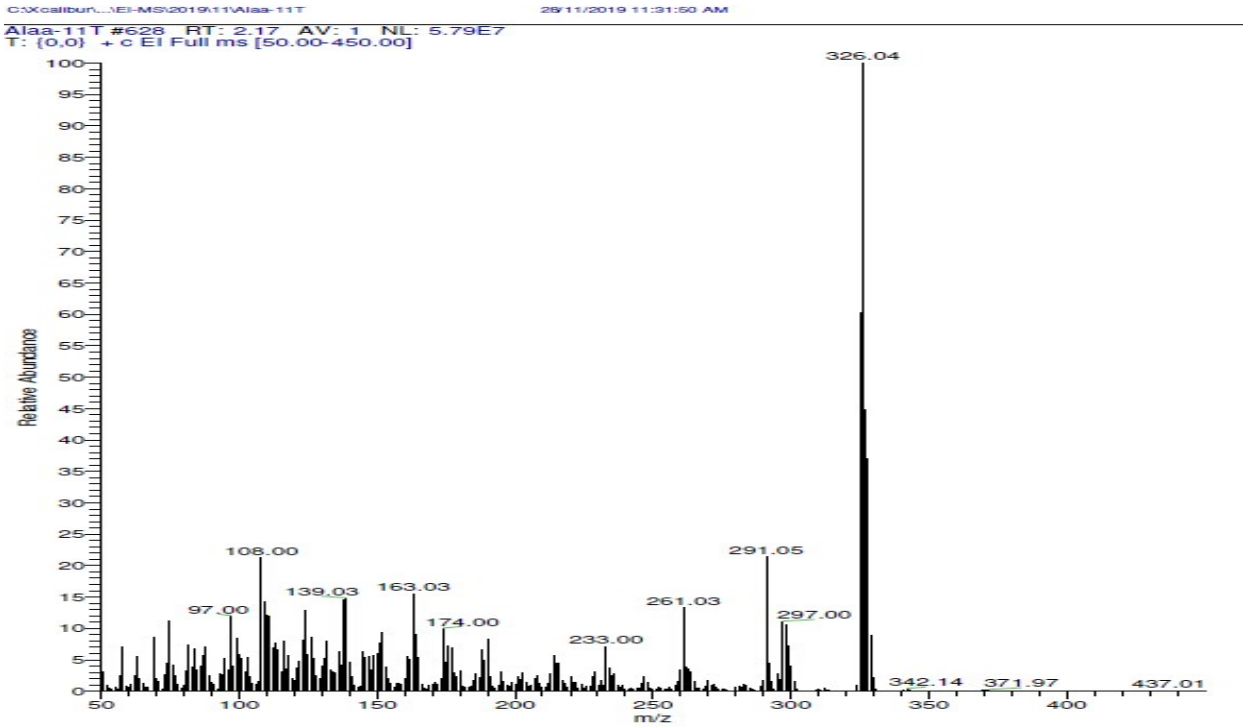


Figure S13. Mass spectrum of compound **3d**.

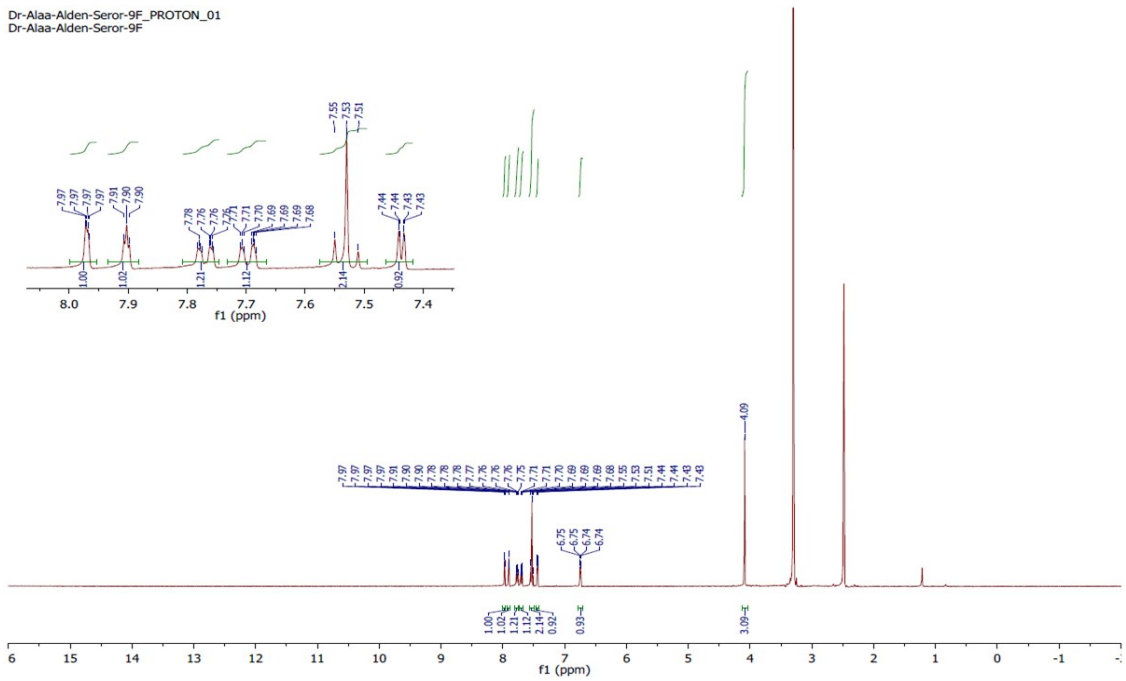


Figure S14. ^{1}H NMR spectrum of compound **3e**.

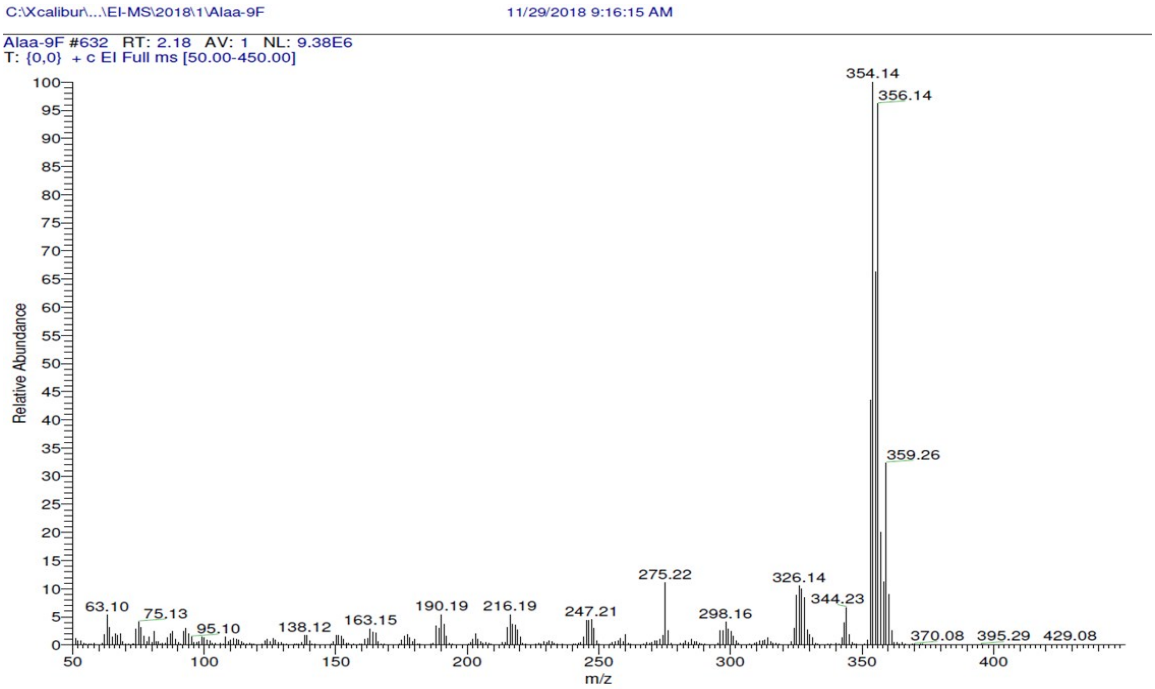


Figure S15. Mass spectrum of compound **3e**.

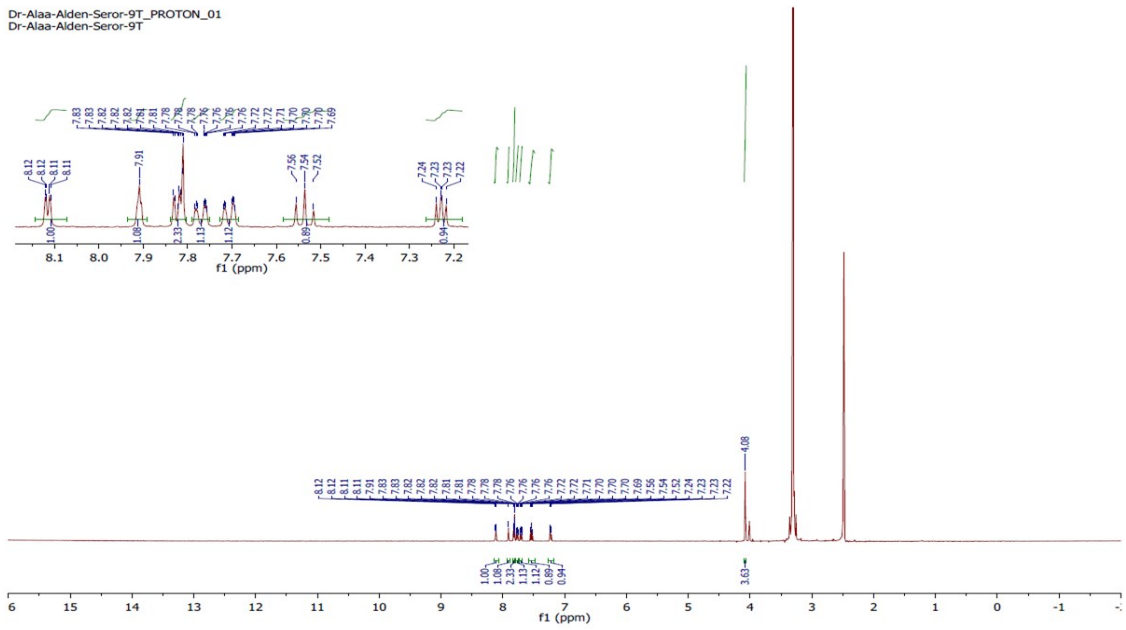


Figure S16. ^{1}H NMR spectrum of compound **3f.**

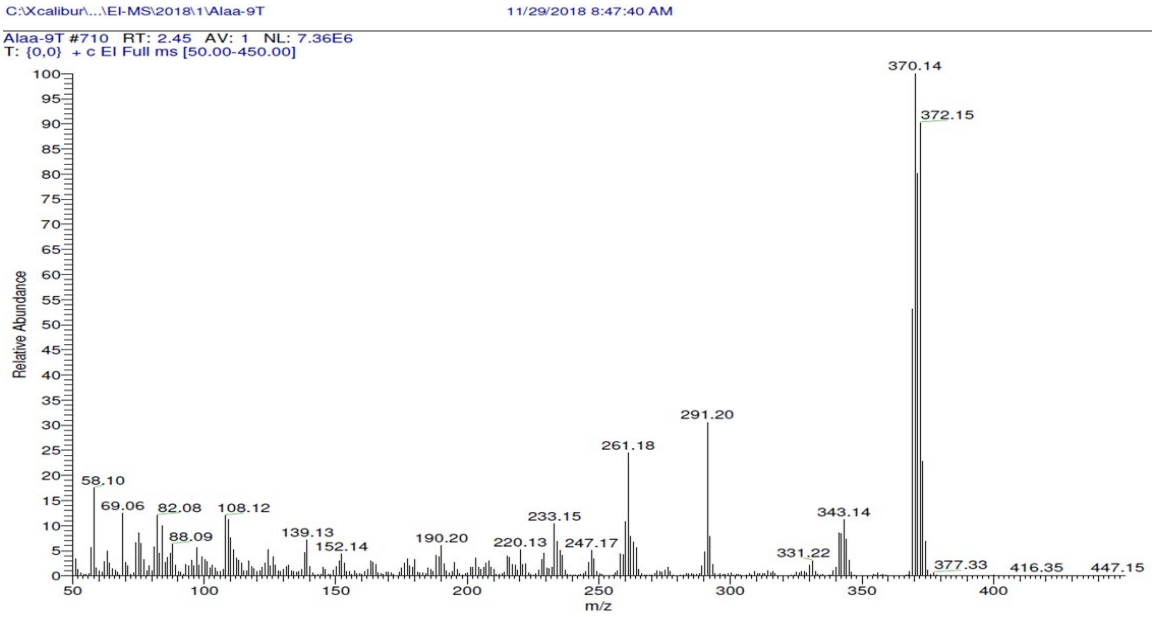


Figure S17. Mass spectrum of compound **3f**.

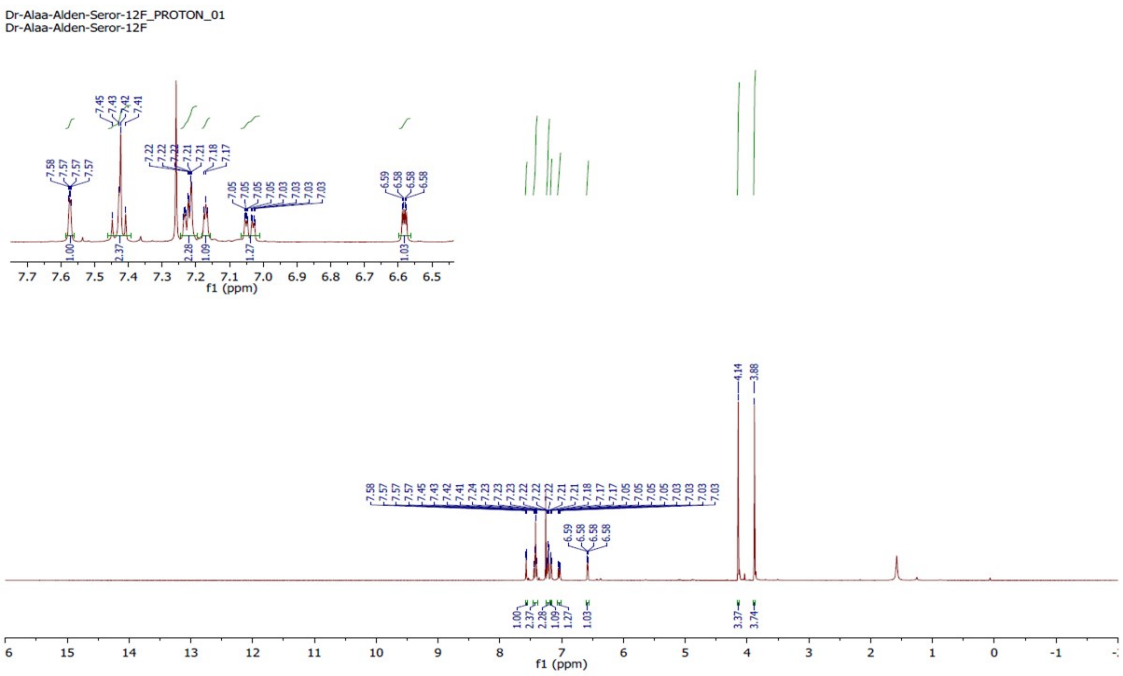


Figure S18. ^{1}H NMR spectrum of compound **3g**.

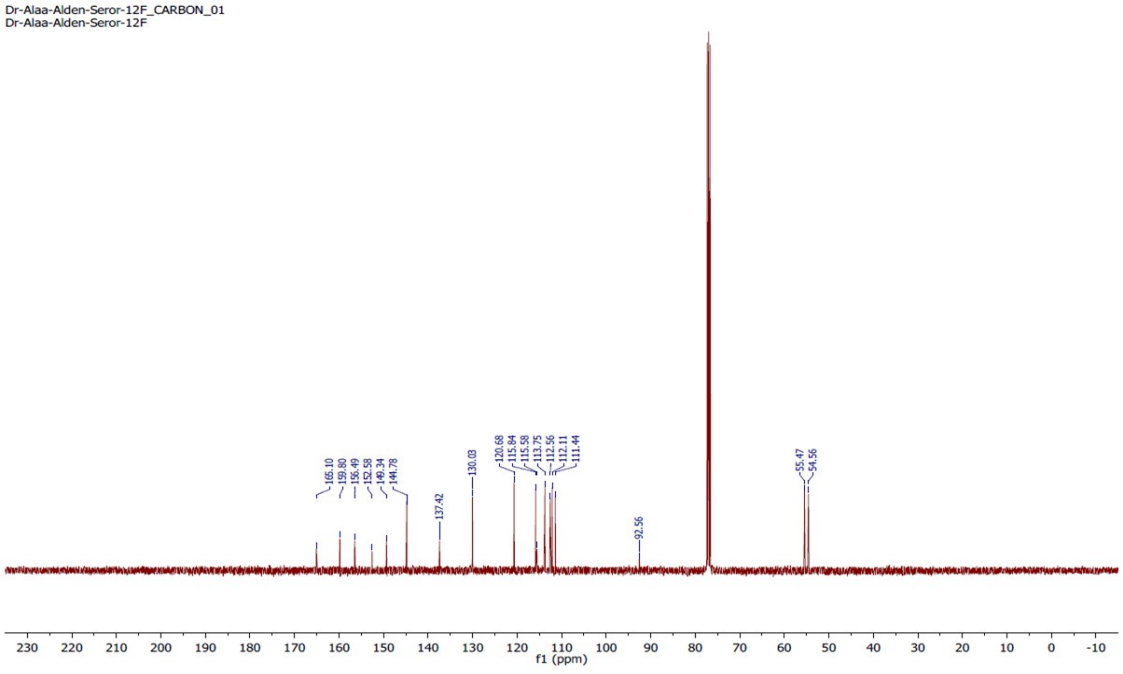


Figure S19. ^{13}C NMR spectrum of compound **3g**.

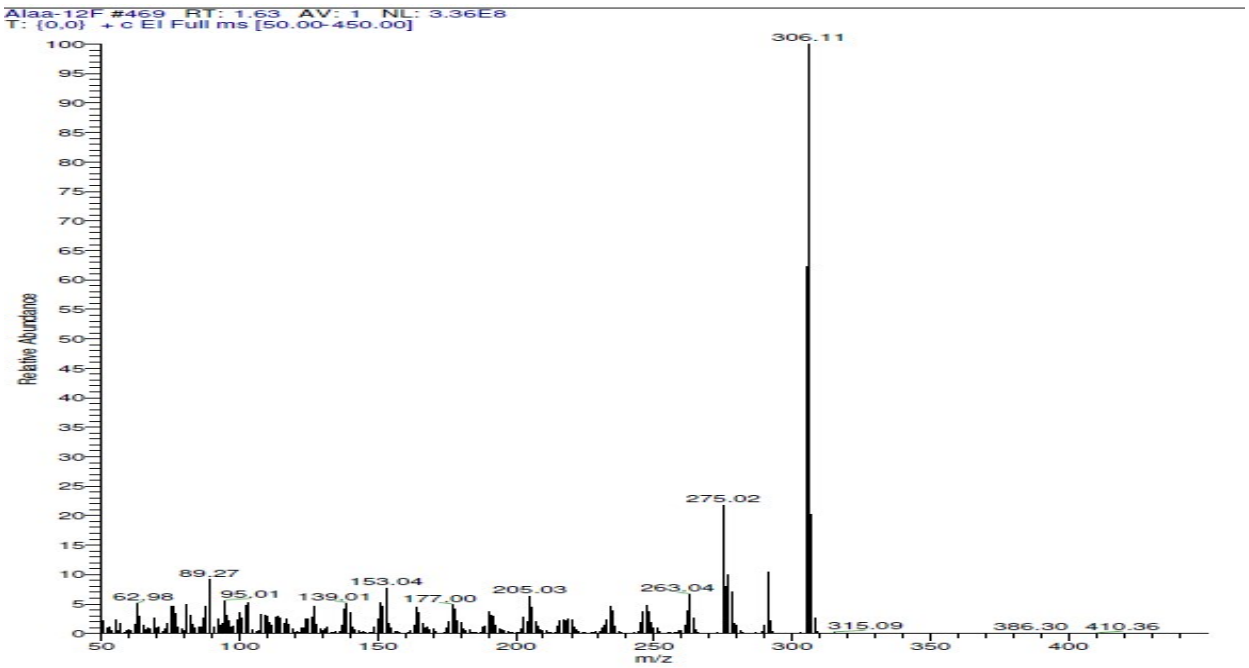


Figure S20. Mass spectrum of compound **3g**.

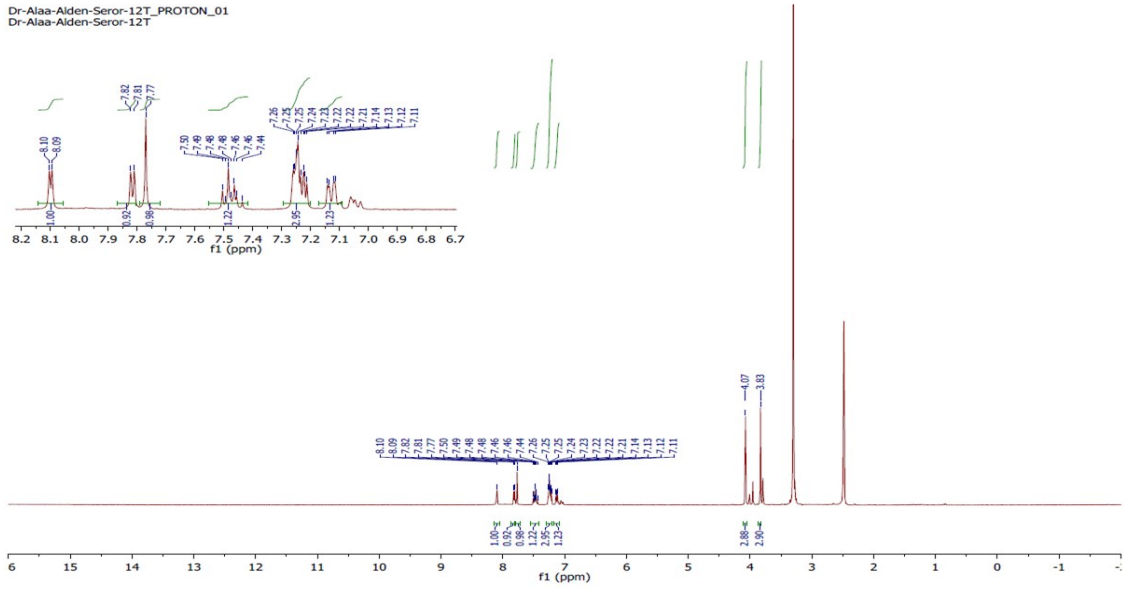


Figure S21. ^{1}H NMR spectrum of compound **3h**.

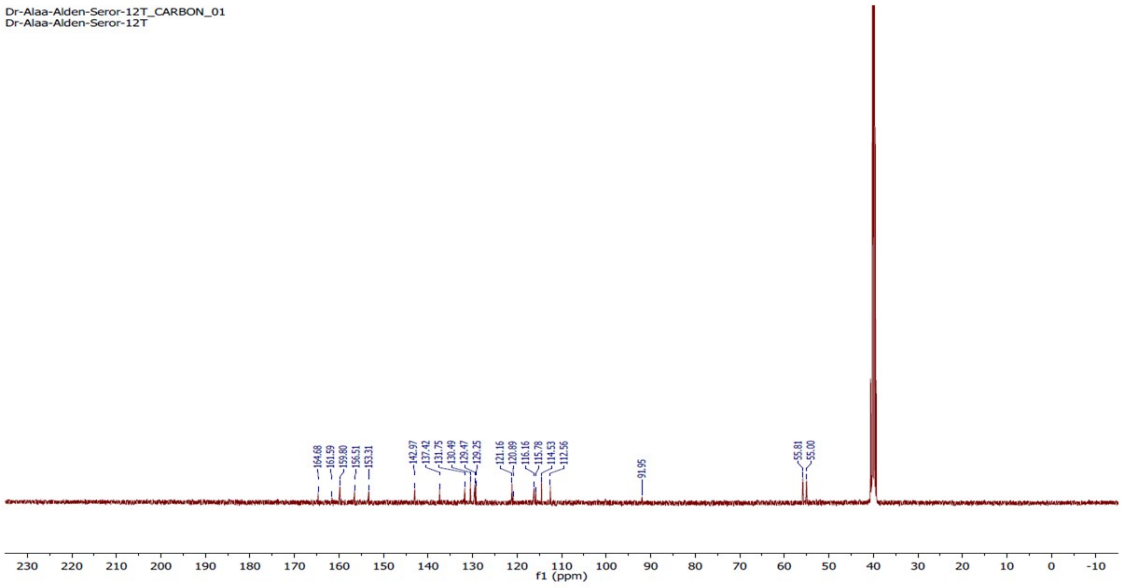


Figure S22. ^{13}C NMR spectrum of compound **3h**.

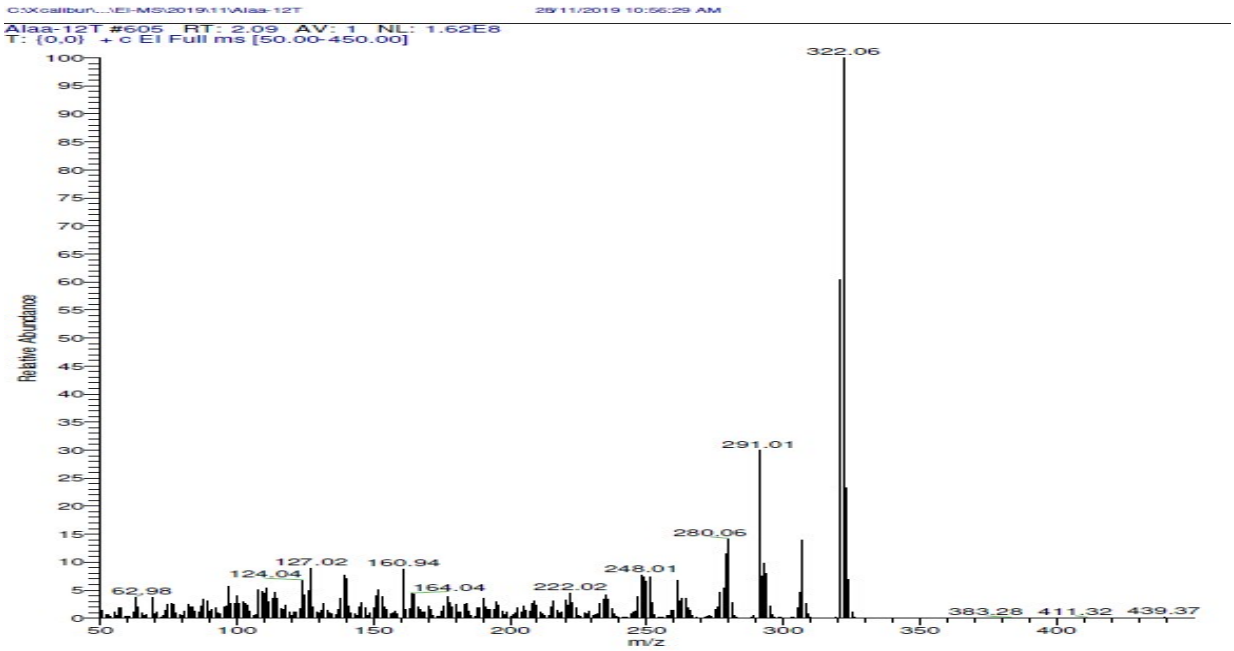


Figure S23. Mass spectrum of compound **3h**.

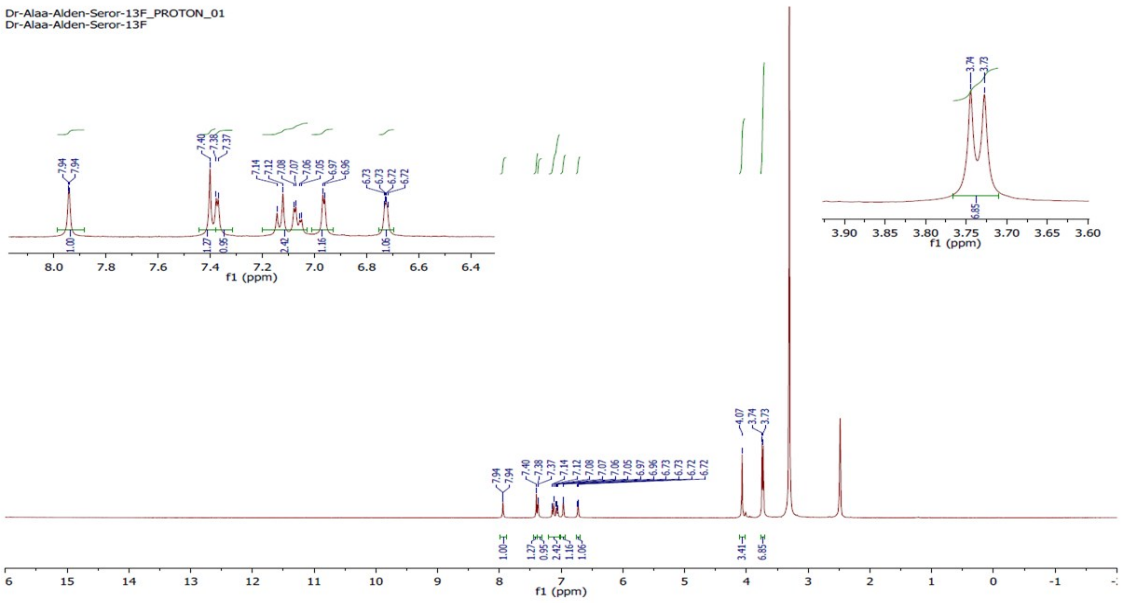


Figure S24. ^{1}H NMR spectrum of compound **3i**.

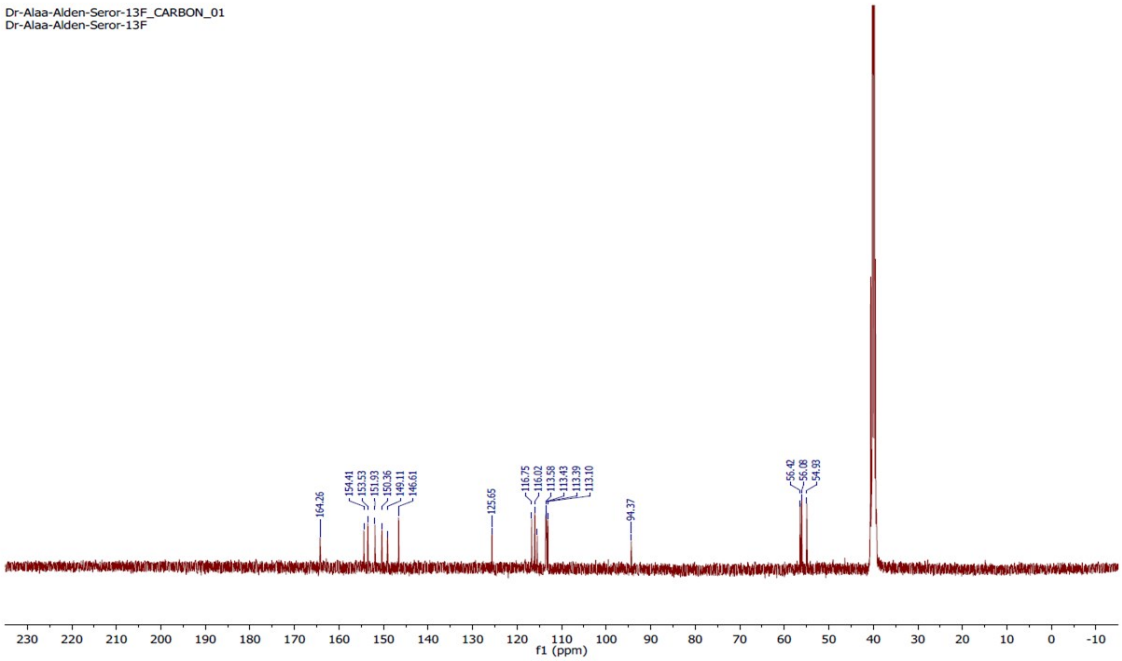


Figure S25. ^{13}C NMR spectrum of compound **3i**.

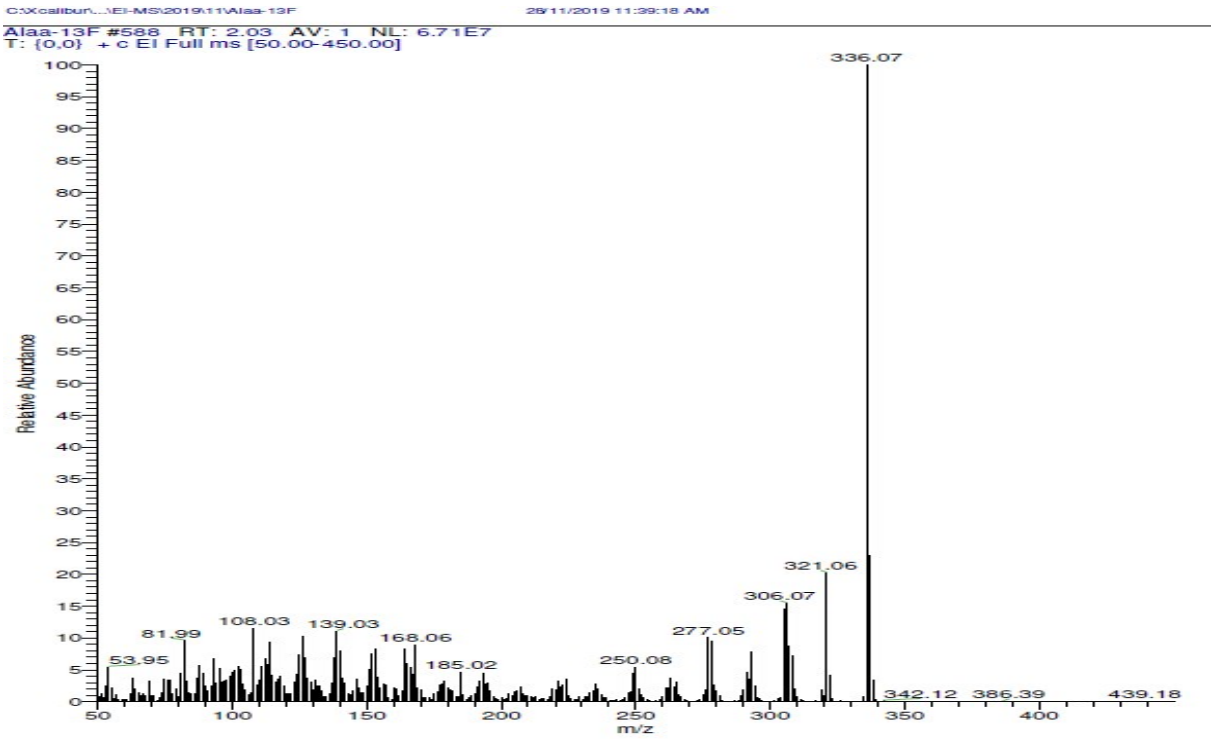


Figure S26. Mass spectrum of compound **3i**.

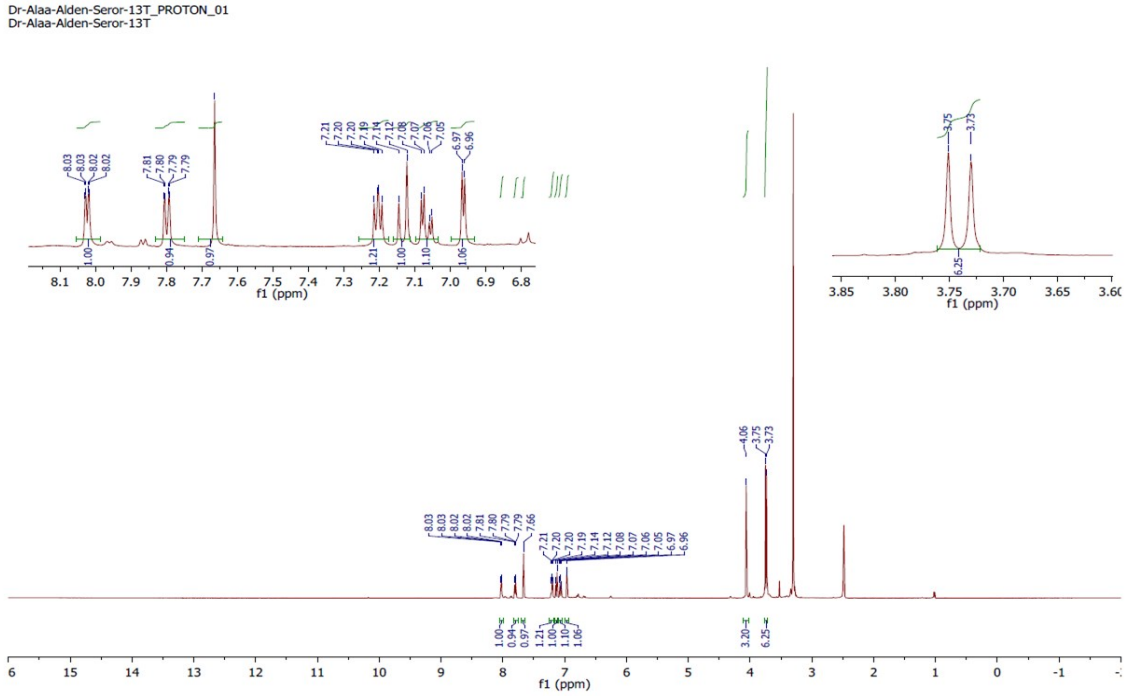


Figure S27. ^{1}H NMR spectrum of compound **3j**.

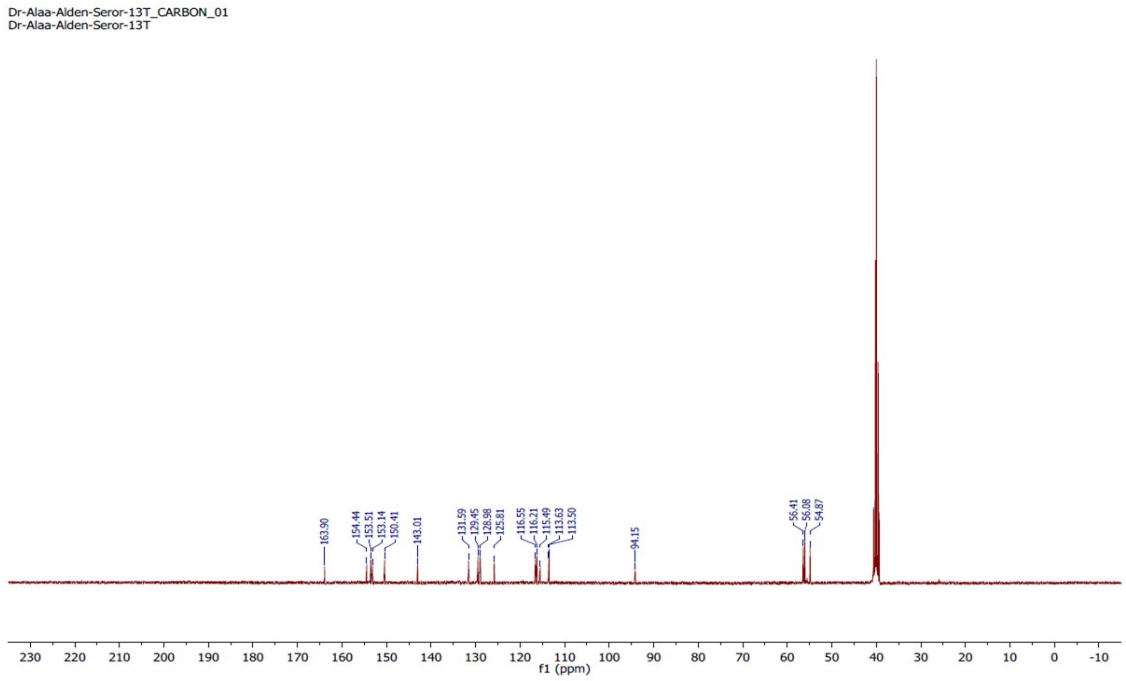


Figure S28. ^{13}C NMR spectrum of compound **3j**.

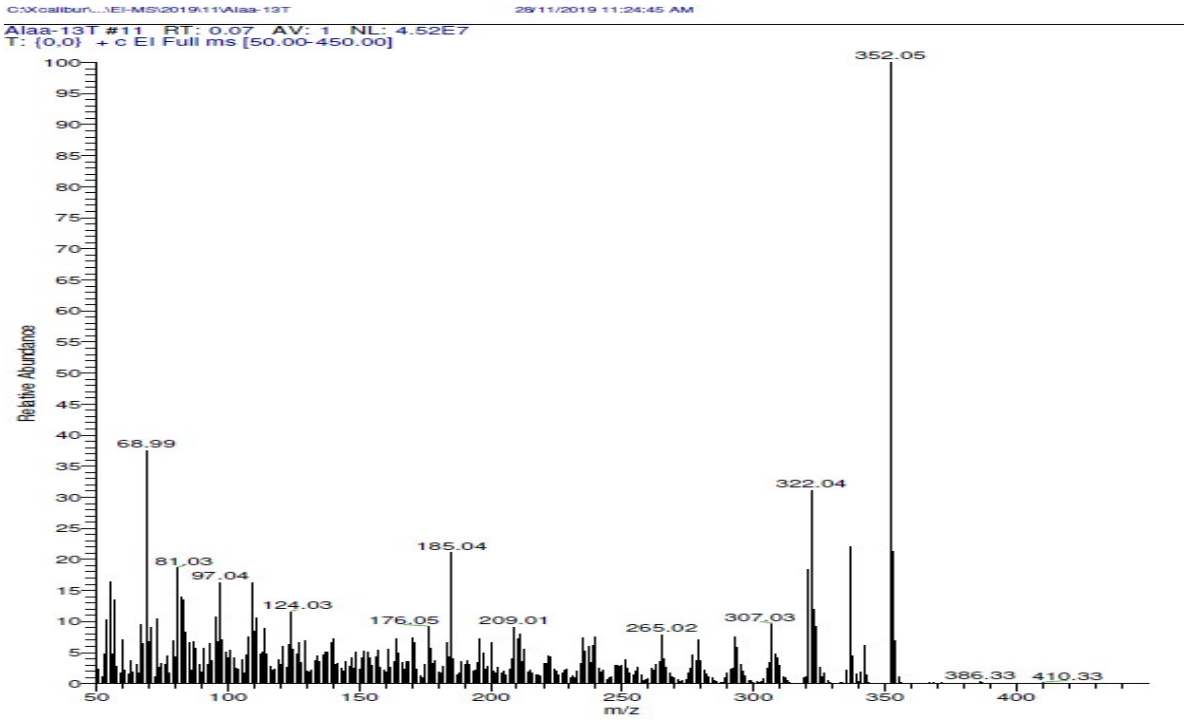


Figure S29. Mass spectrum of compound **3j**.

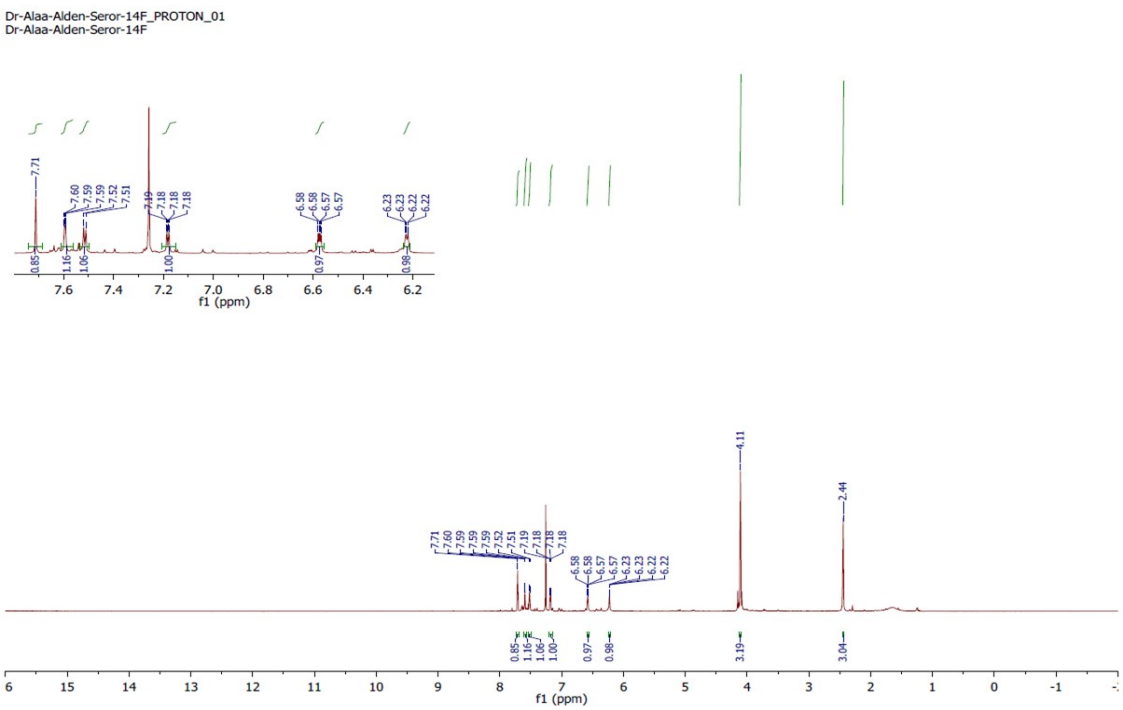


Figure S30. [1]H NMR spectrum of compound **3k**.

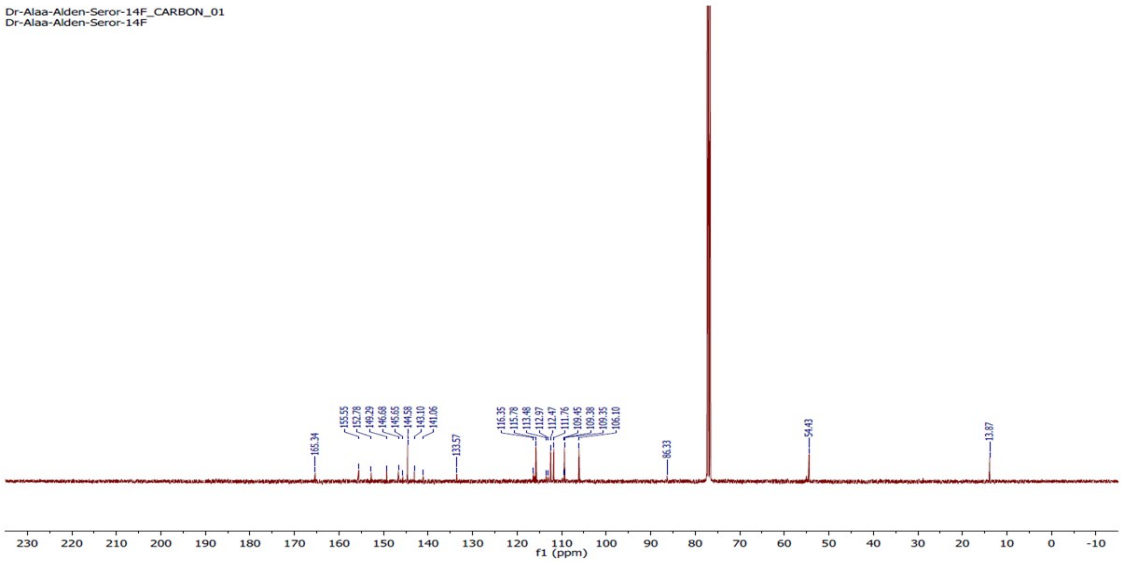


Figure S31. [13]C NMR spectrum of compound **3k**.

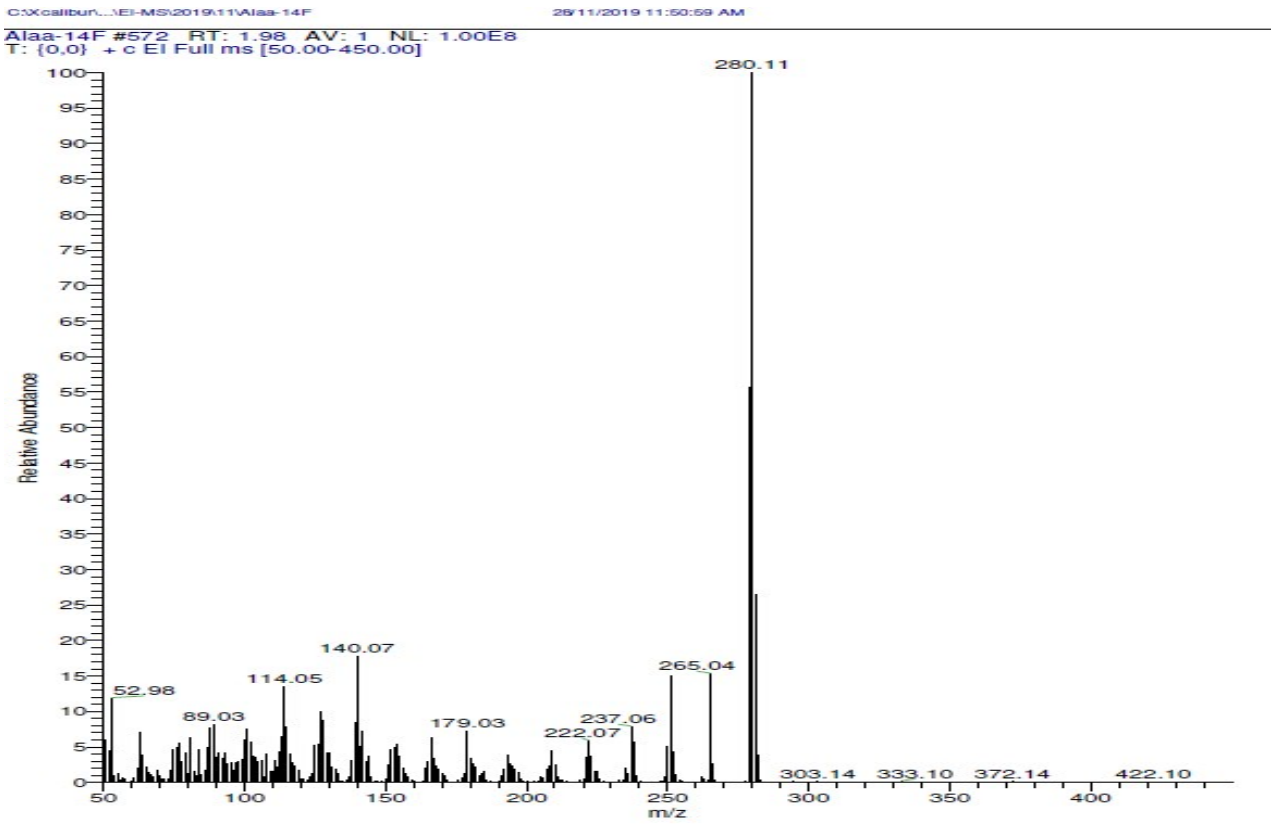


Figure S32. Mass spectrum of compound **3k**.

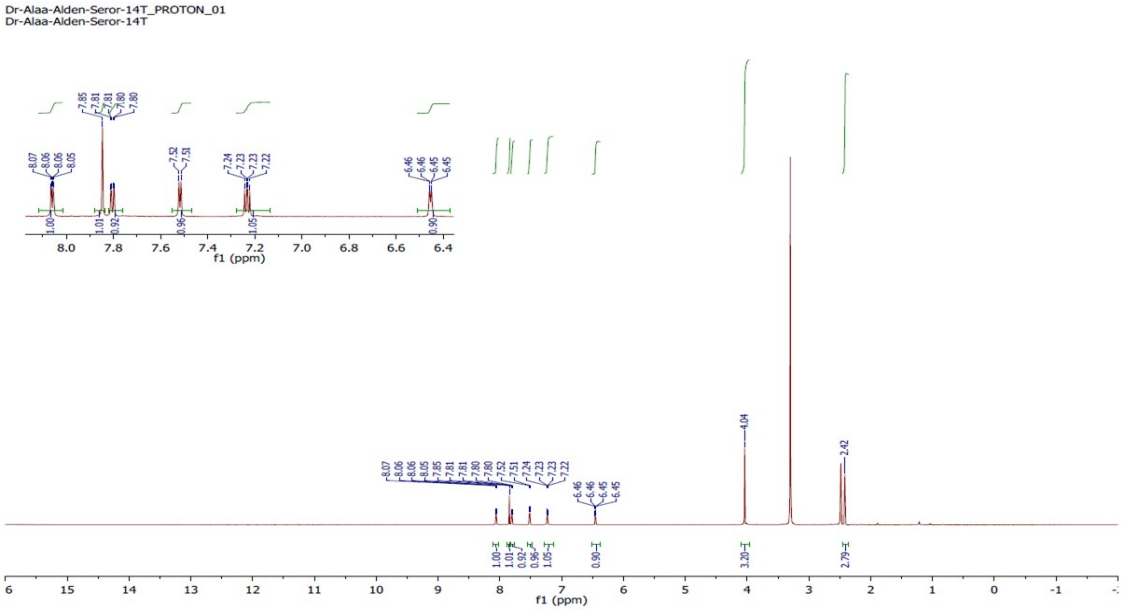


Figure S33. ^{1}H NMR spectrum of compound **3l**.

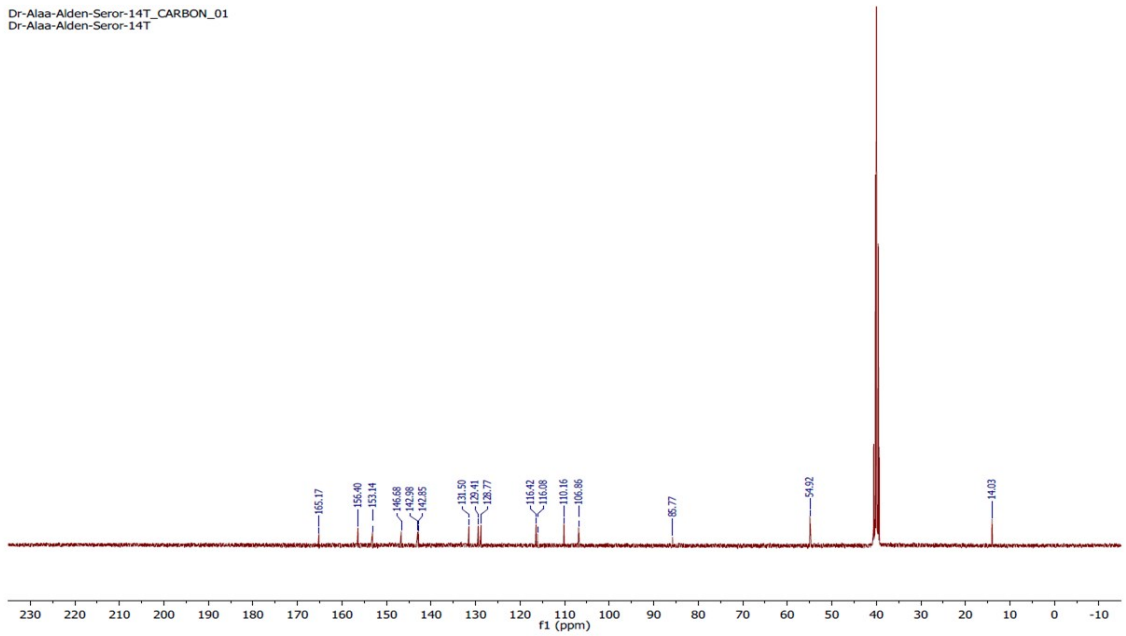


Figure S34. ^{13}C NMR spectrum of compound **3l**.

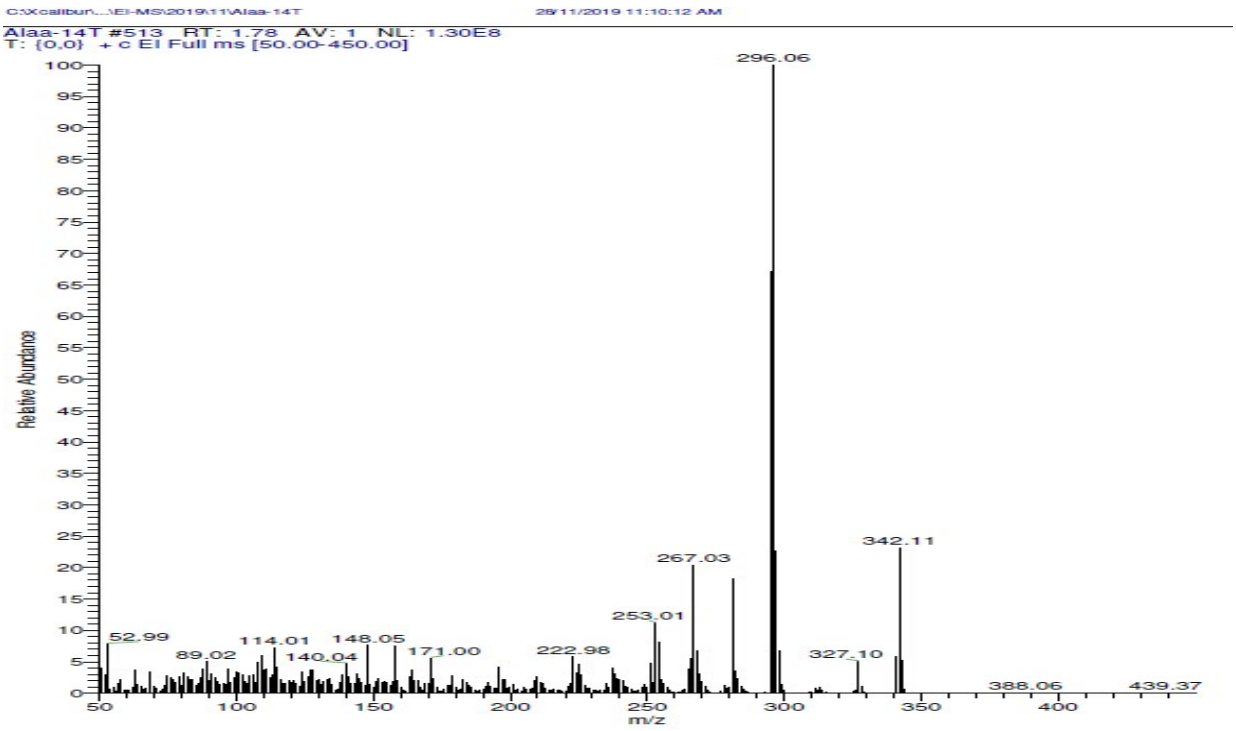


Figure S35. Mass spectrum of compound **3l**.

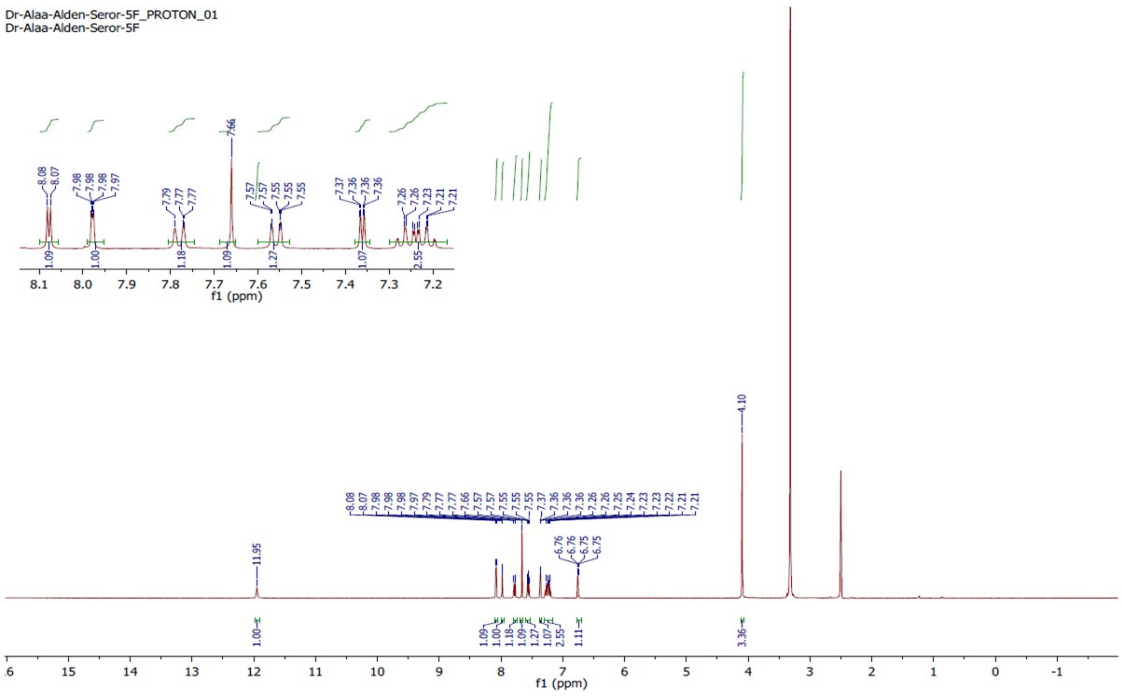


Figure S36. ^{1}H NMR spectrum of compound **3m**.

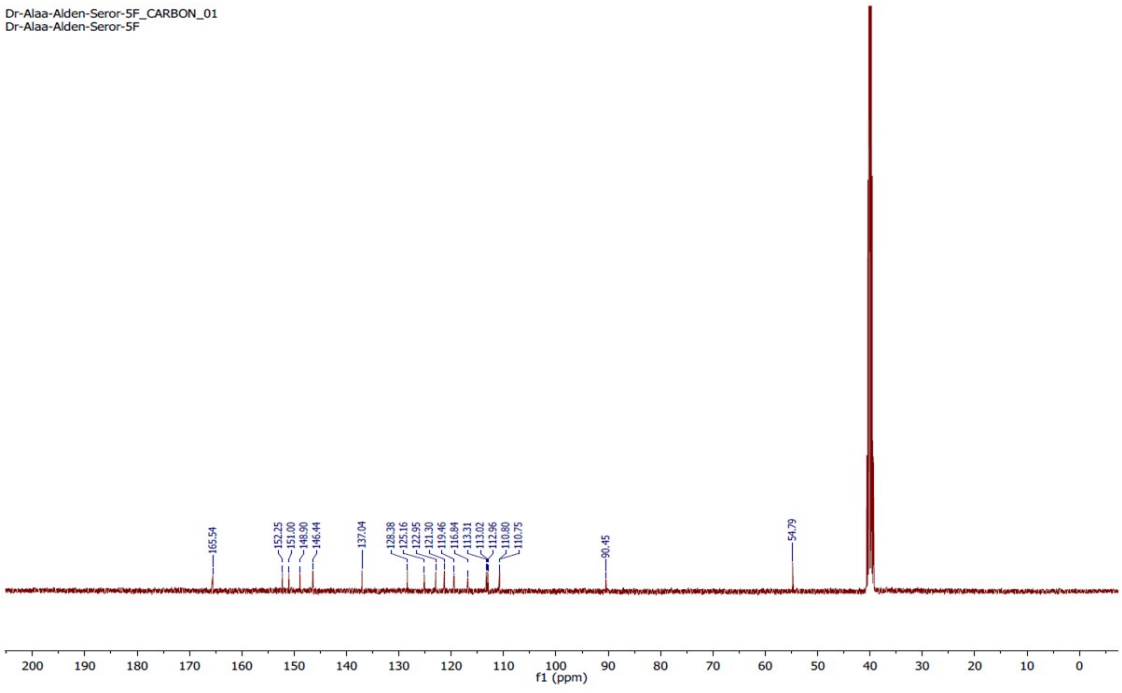


Figure S37. ^{13}C NMR spectrum of compound **3m**.

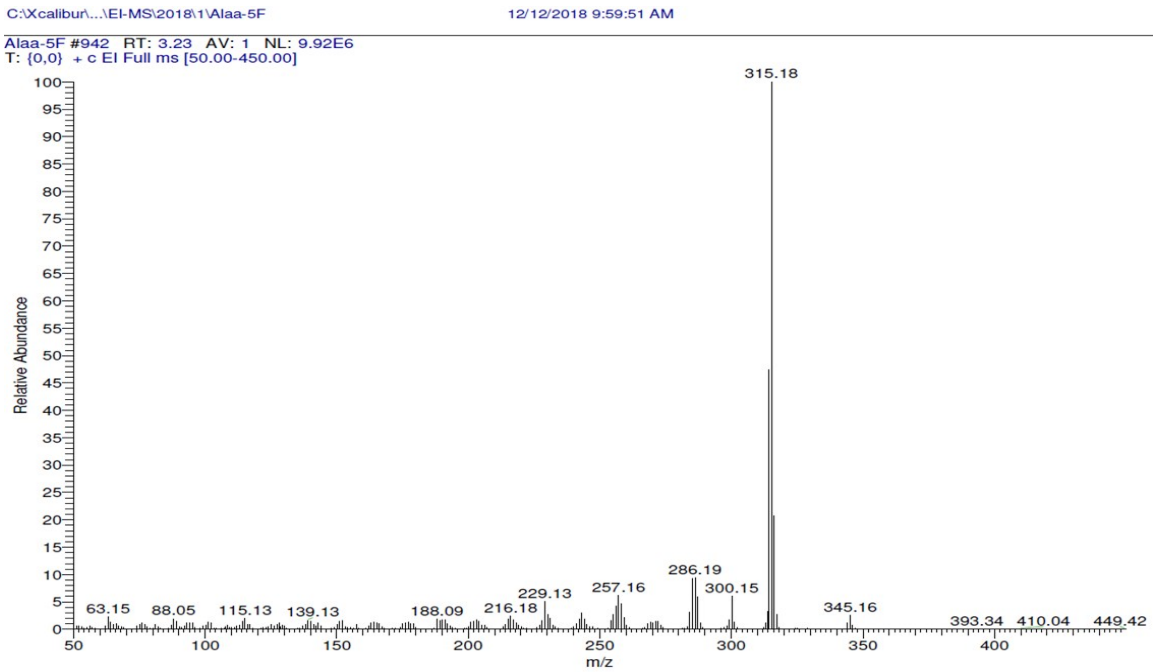


Figure S38. Mass spectrum of compound **3m**.

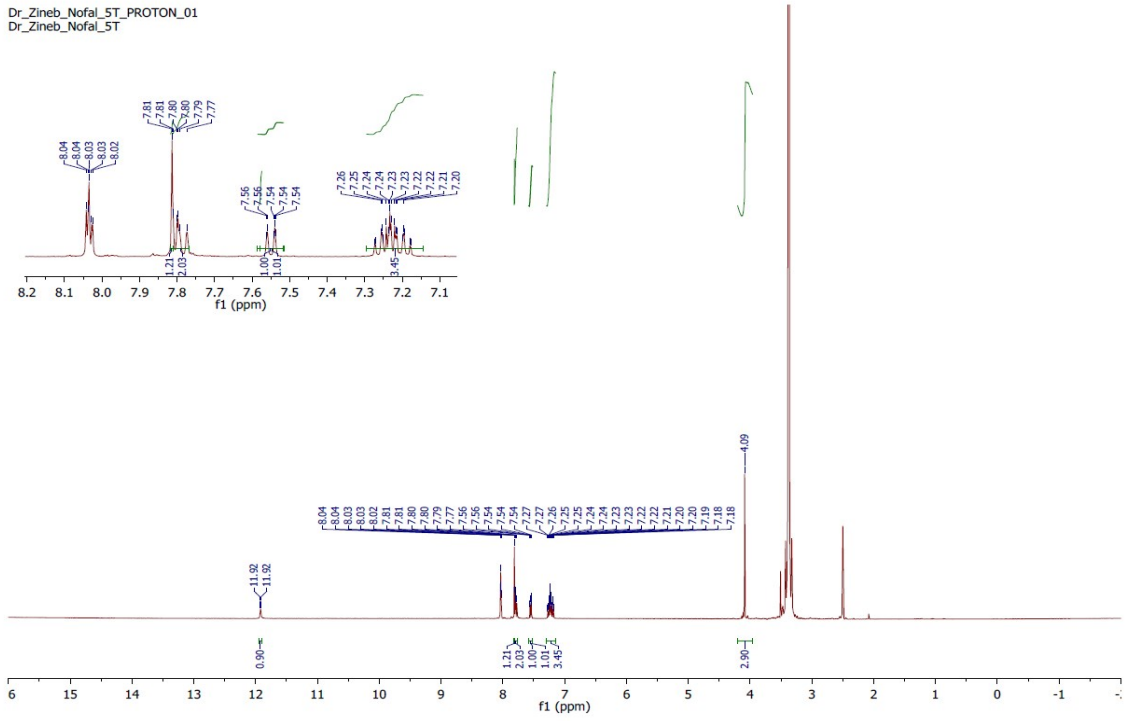


Figure S39. ^{1}H NMR spectrum of compound **3n**.

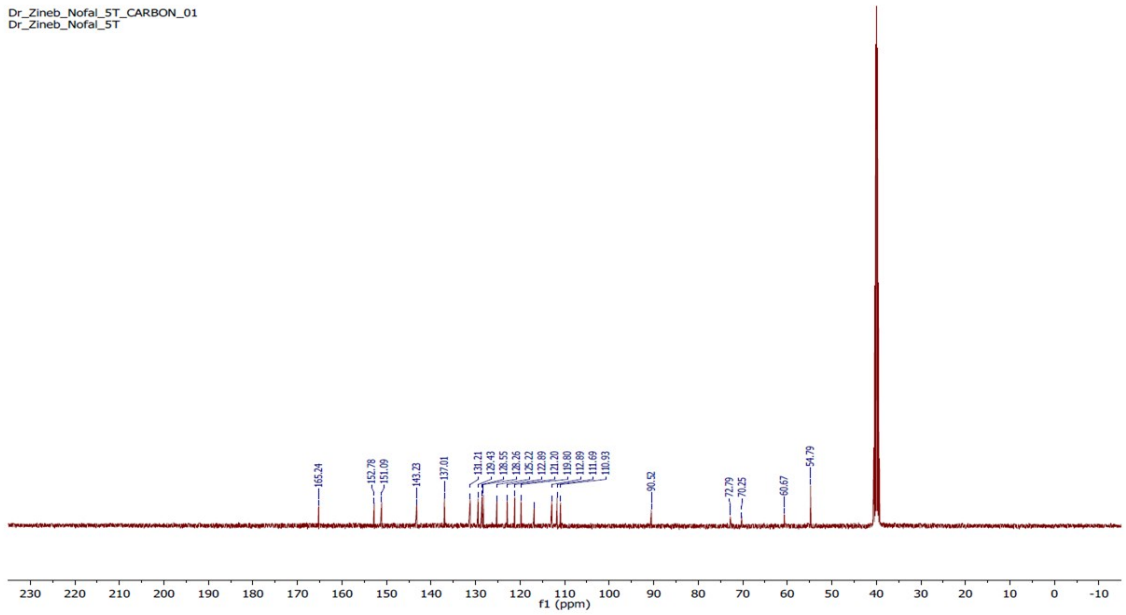


Figure S40. ^{13}C NMR spectrum of compound **3n**.

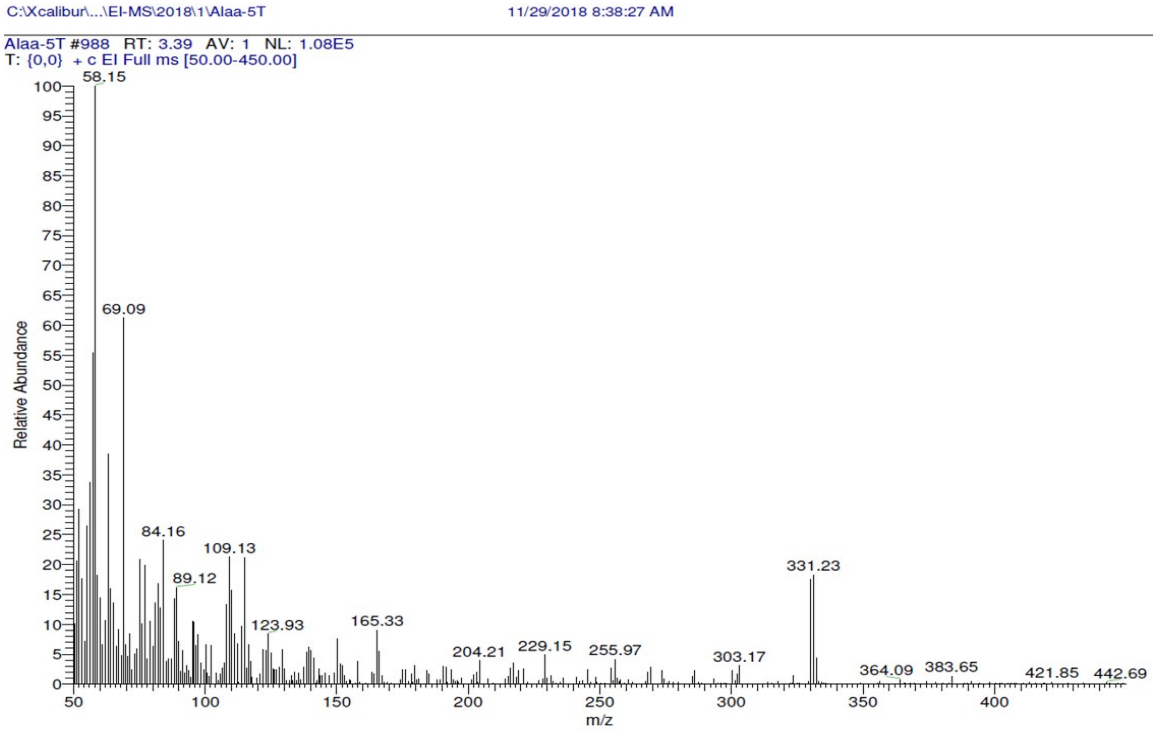


Figure S41. Mass spectrum of compound **3n**.

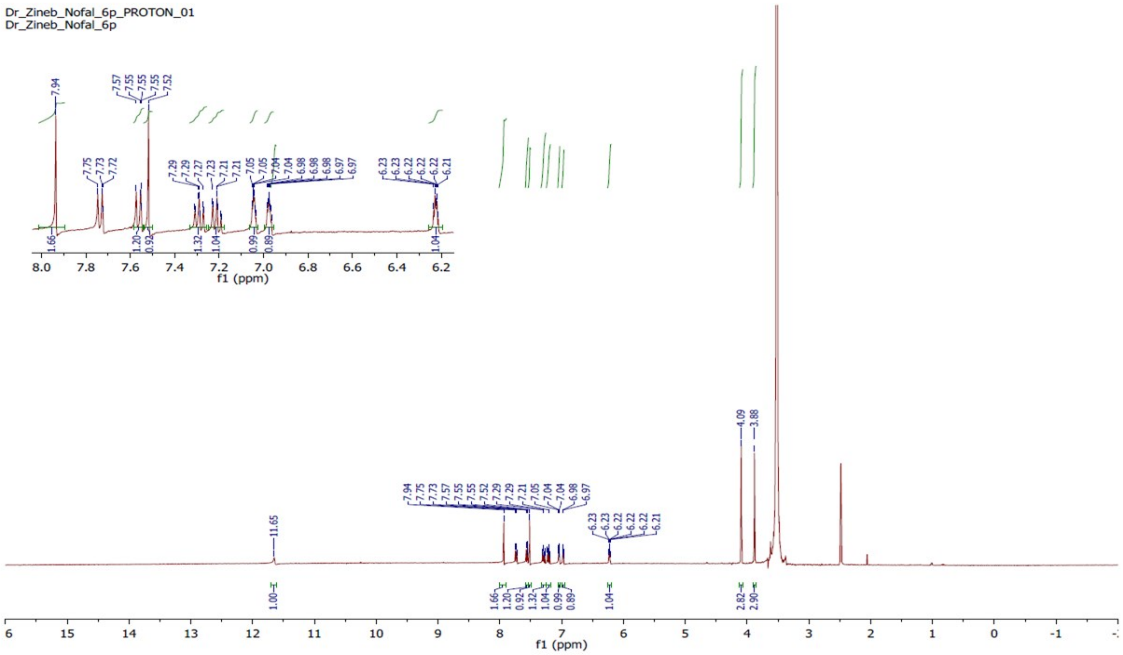


Figure S42. ^{1}H NMR spectrum of compound **3o**.

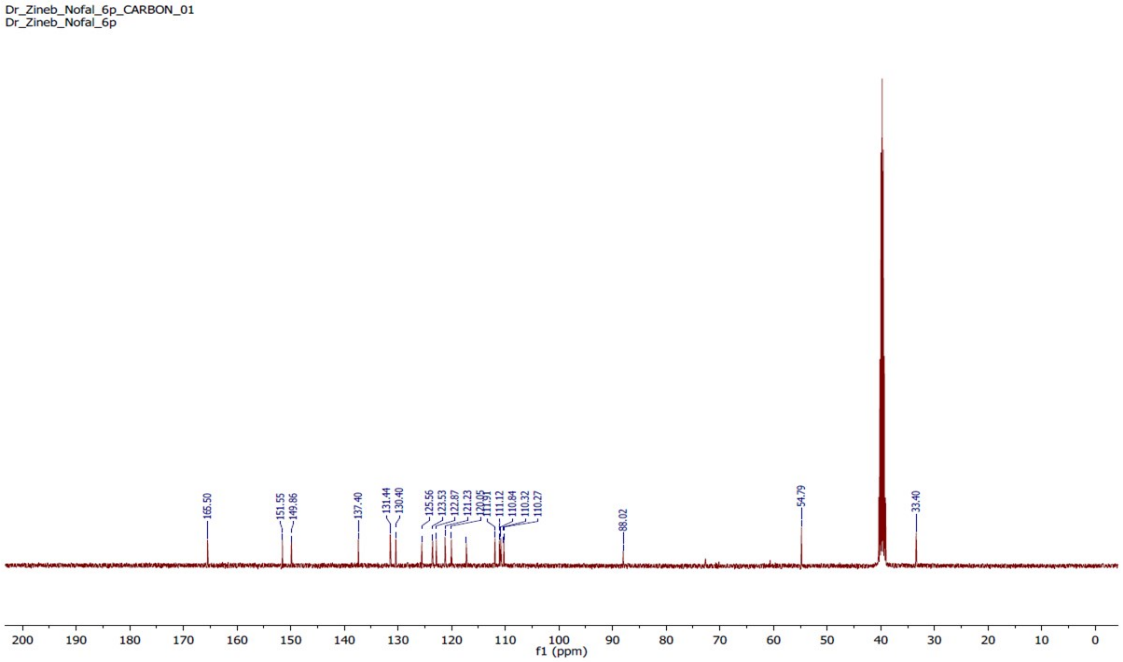


Figure S43. ^{13}C NMR spectrum of compound **3o**.

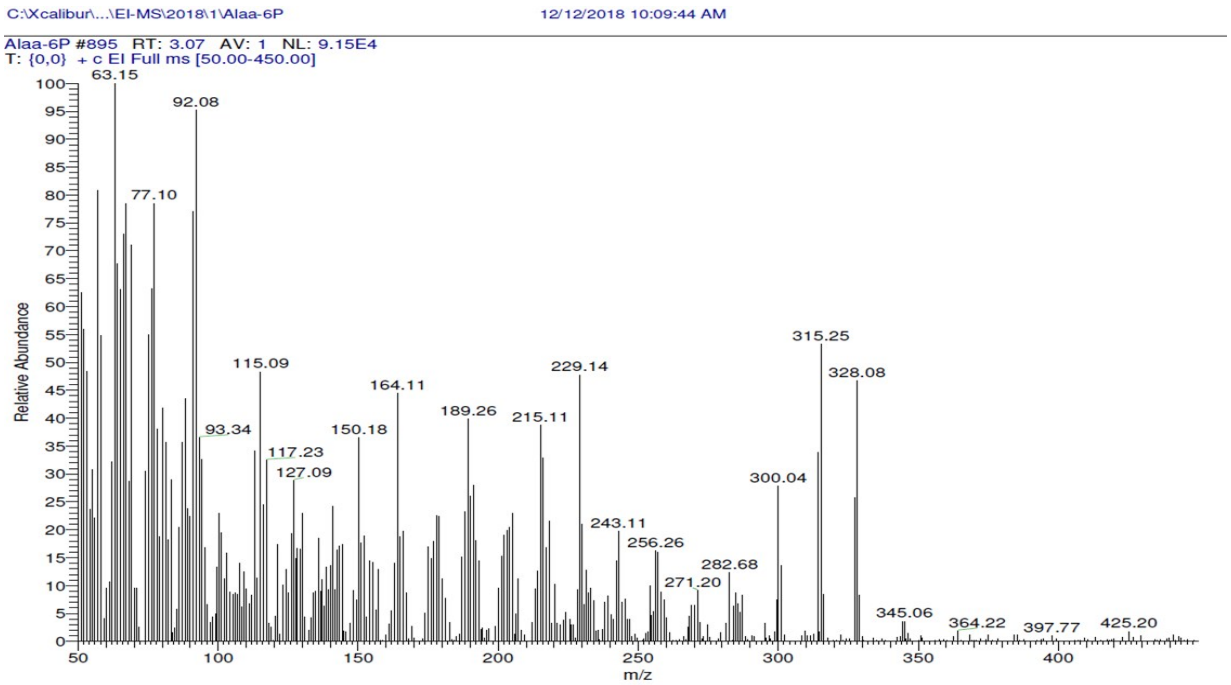


Figure S44. Mass spectrum of compound **3o**.

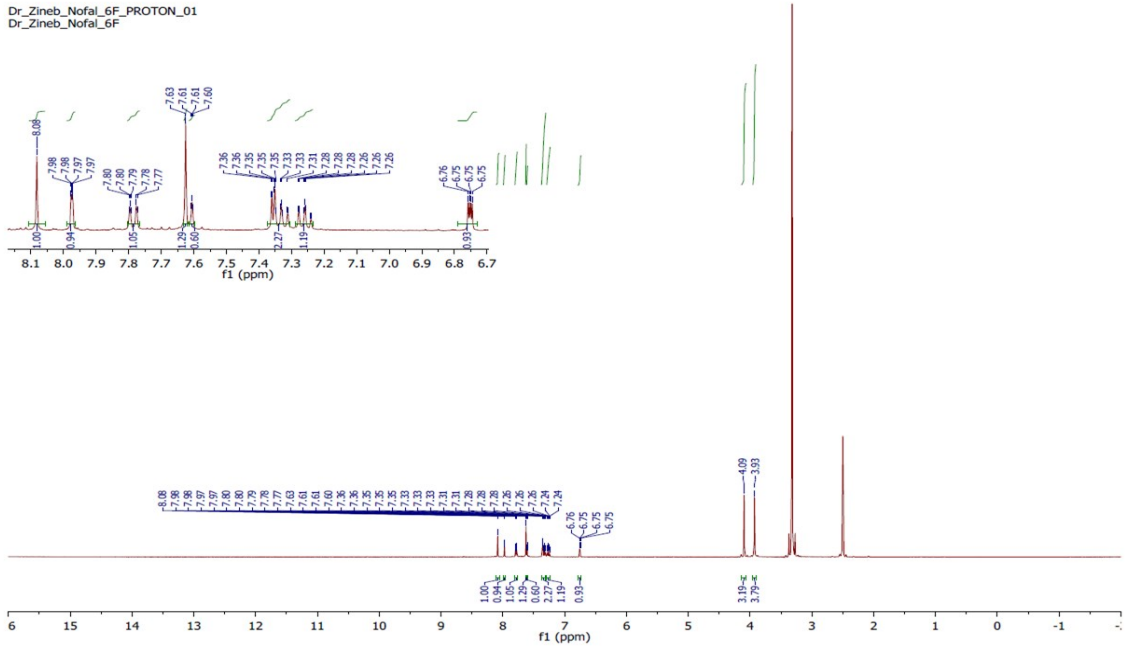


Figure S45. ^{1}H NMR spectrum of compound **3p**.

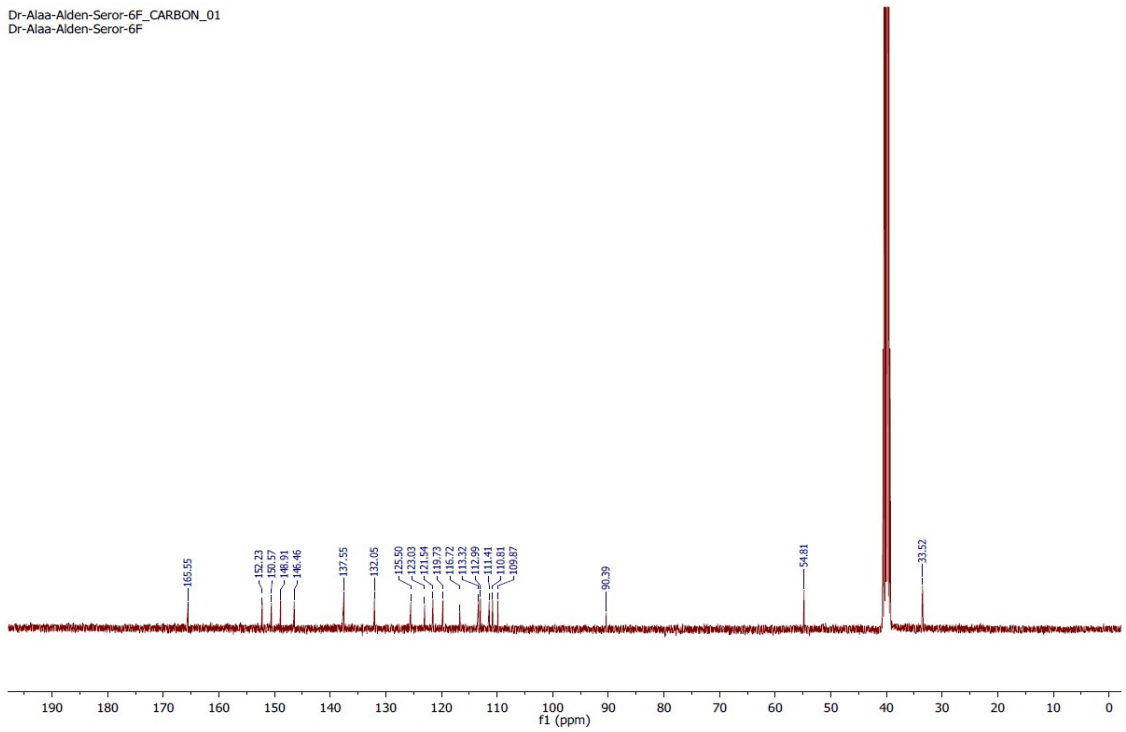


Figure S46. ^{13}C NMR spectrum of compound **3p**.

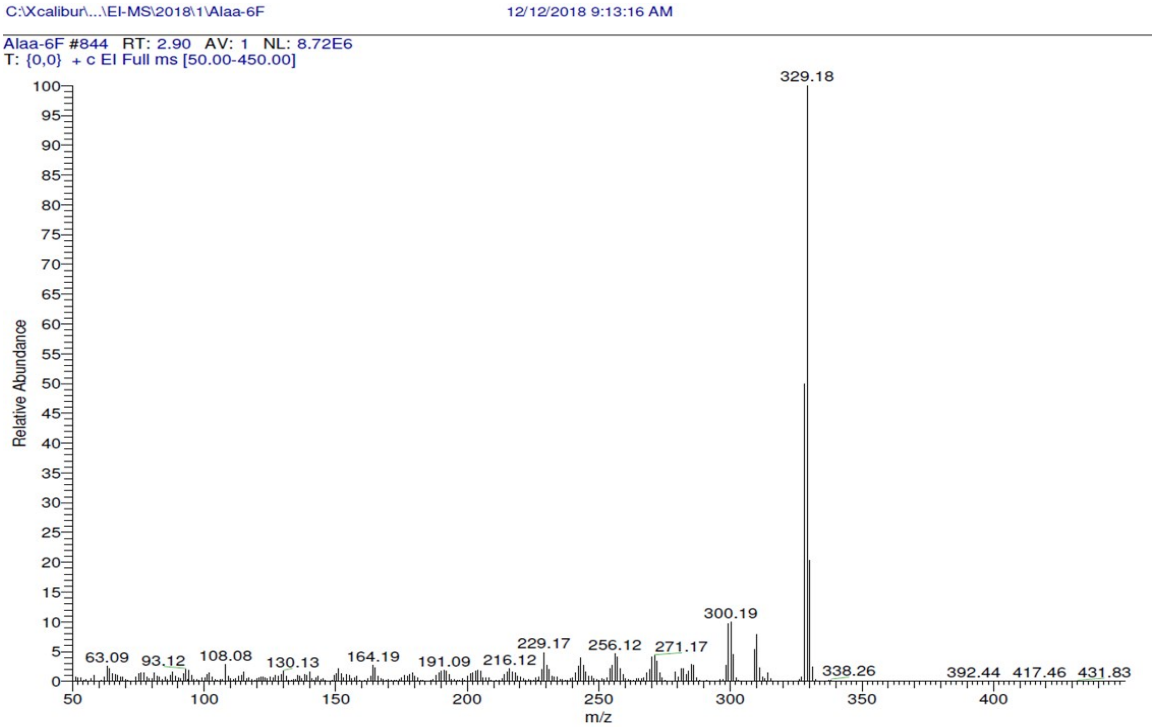


Figure S47. Mass spectrum of compound **3p**.

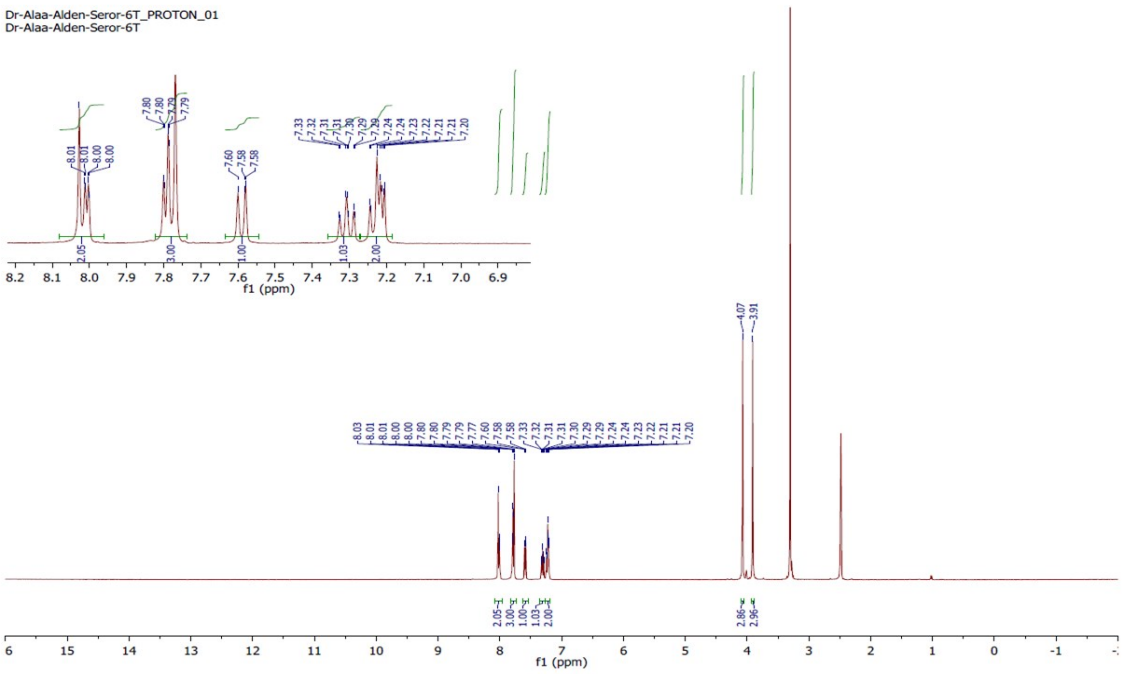


Figure S48. ^{1}H NMR spectrum of compound **3q**.

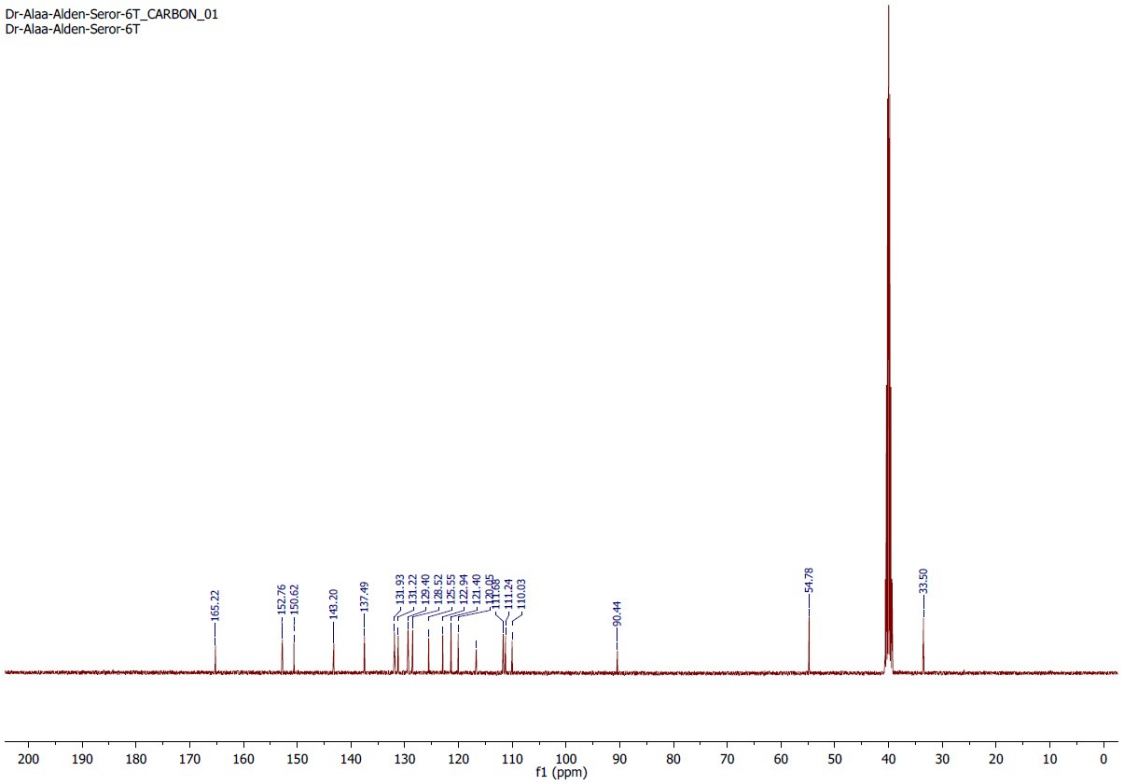


Figure S49. ^{13}C NMR spectrum of compound **3q**.

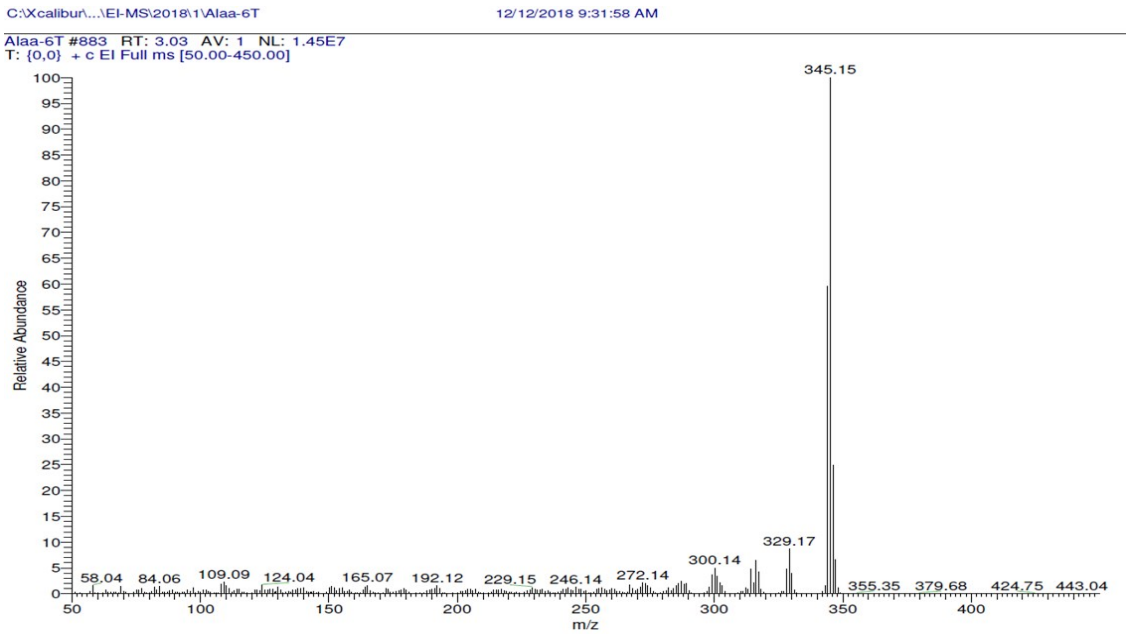


Figure S50. Mass spectrum of compound **3q**.

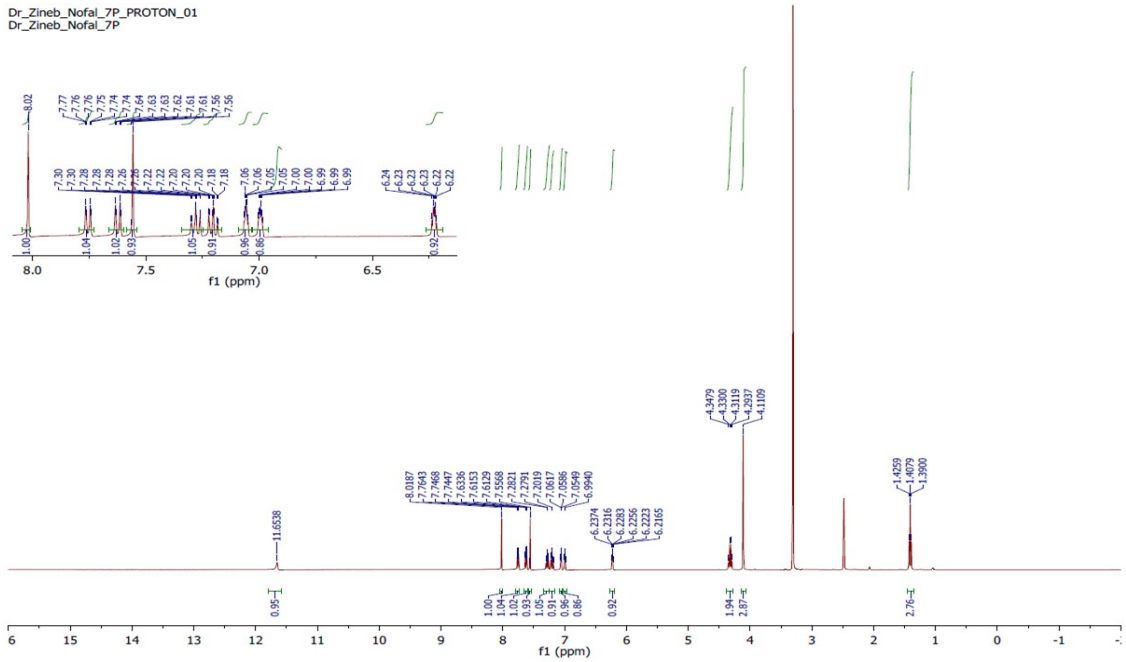


Figure S51. ^{1}H NMR spectrum of compound **3r**.

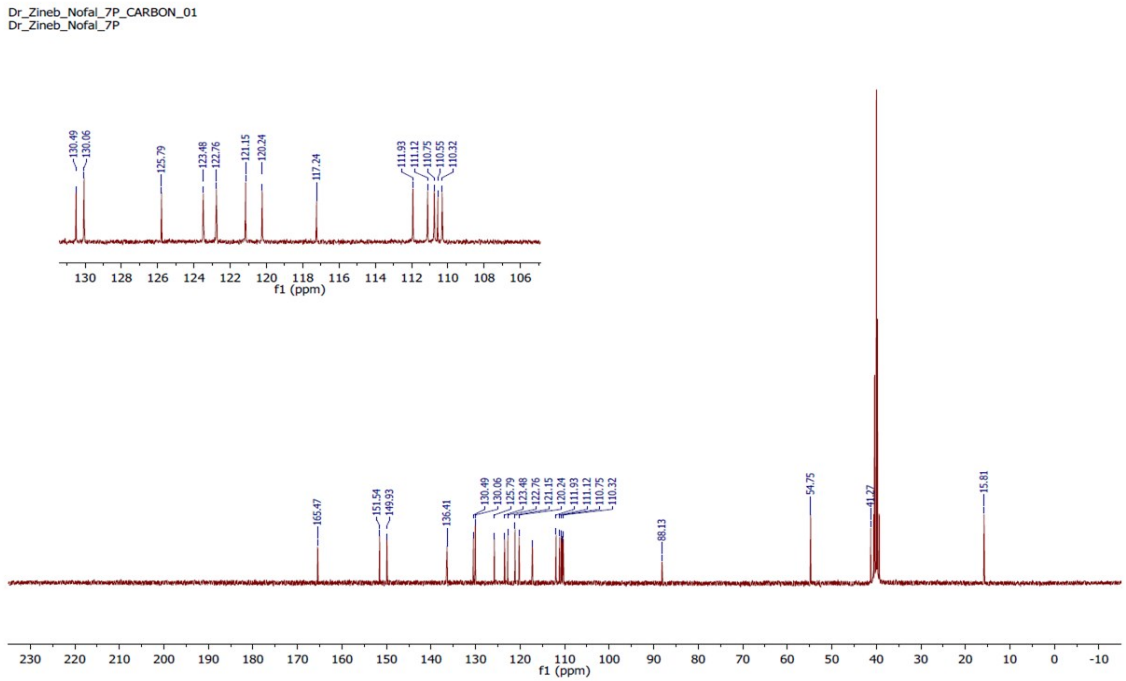


Figure S52. ^{13}C NMR spectrum of compound **3r**.

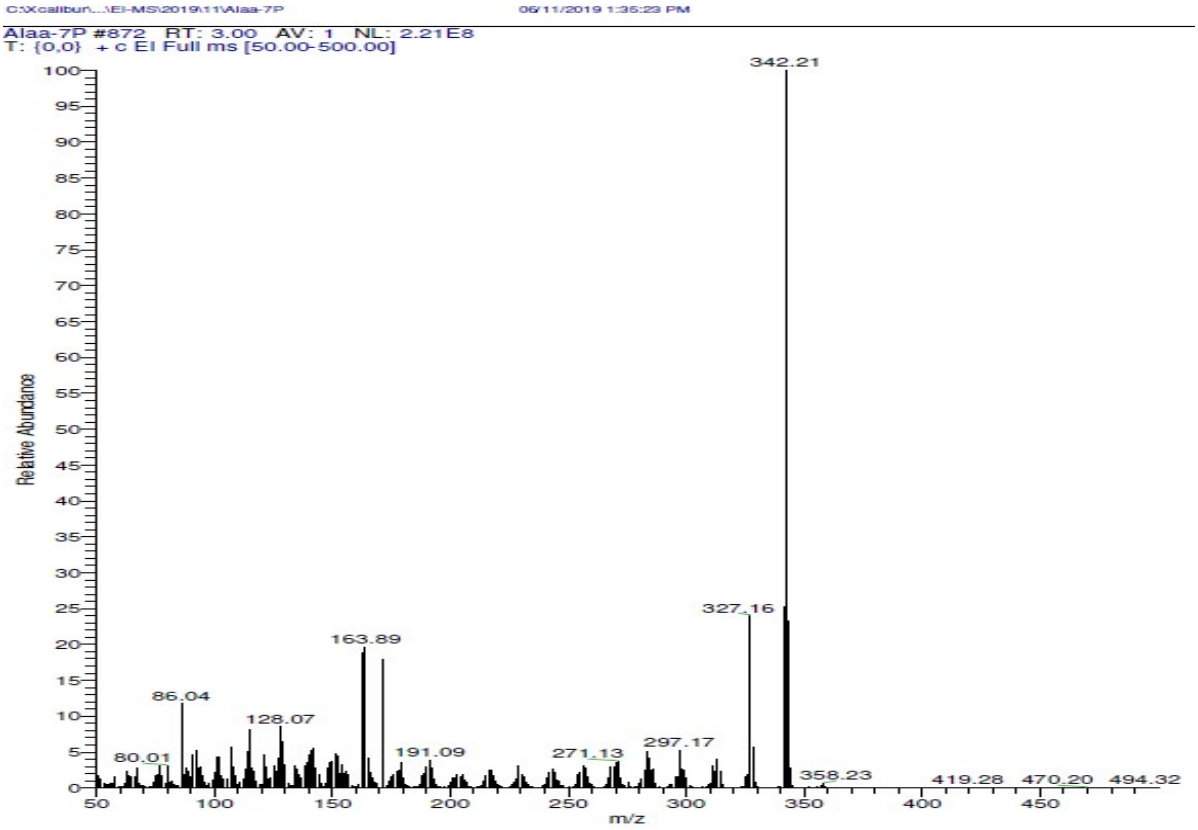


Figure S53. Mass spectrum of compound **3r**.

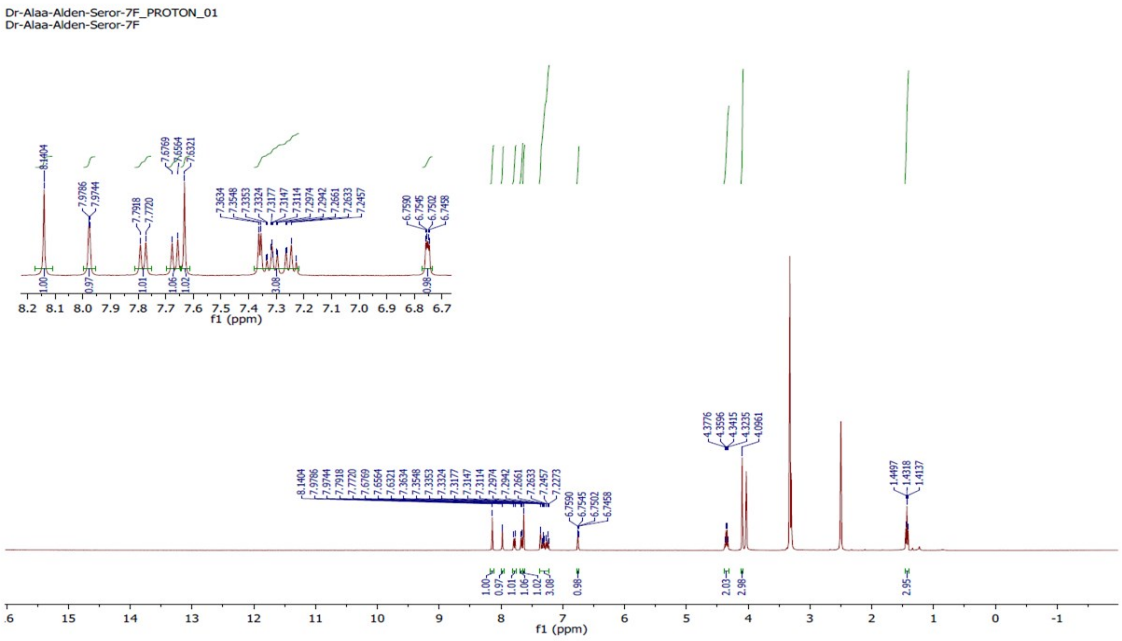


Figure S54. ^{1}H NMR spectrum of compound **3s**.

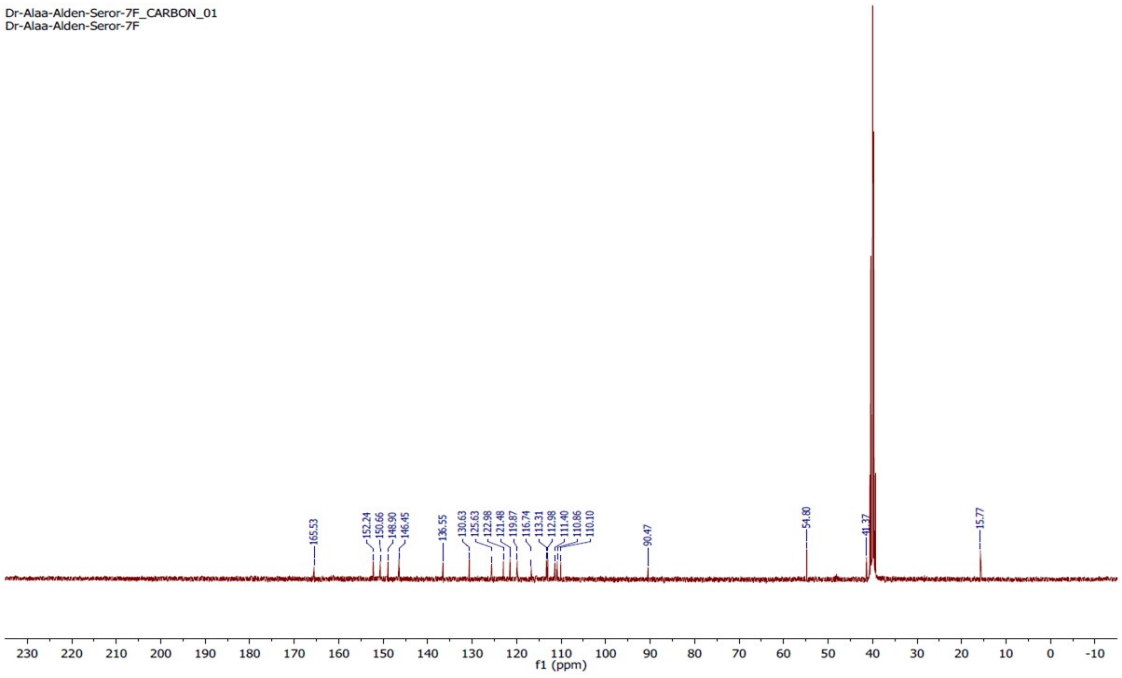


Figure S55. ^{13}C NMR spectrum of compound **3s**.

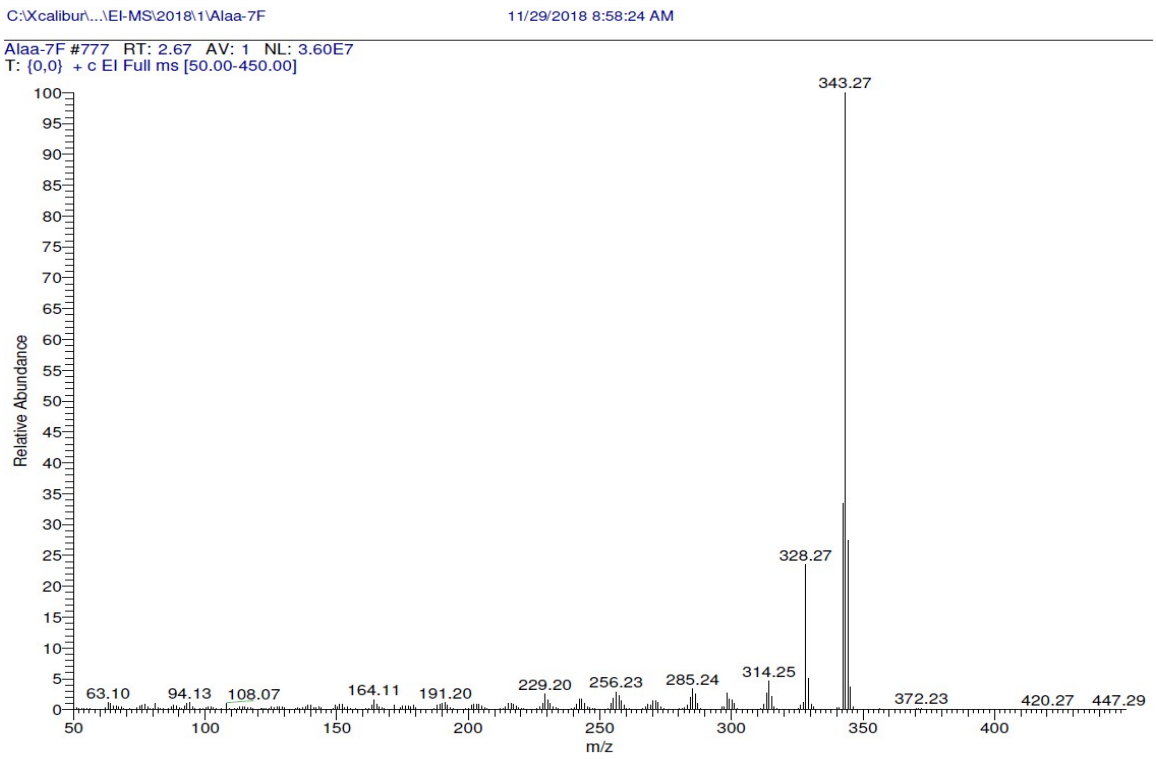


Figure S56. Mass spectrum of compound **3s**.

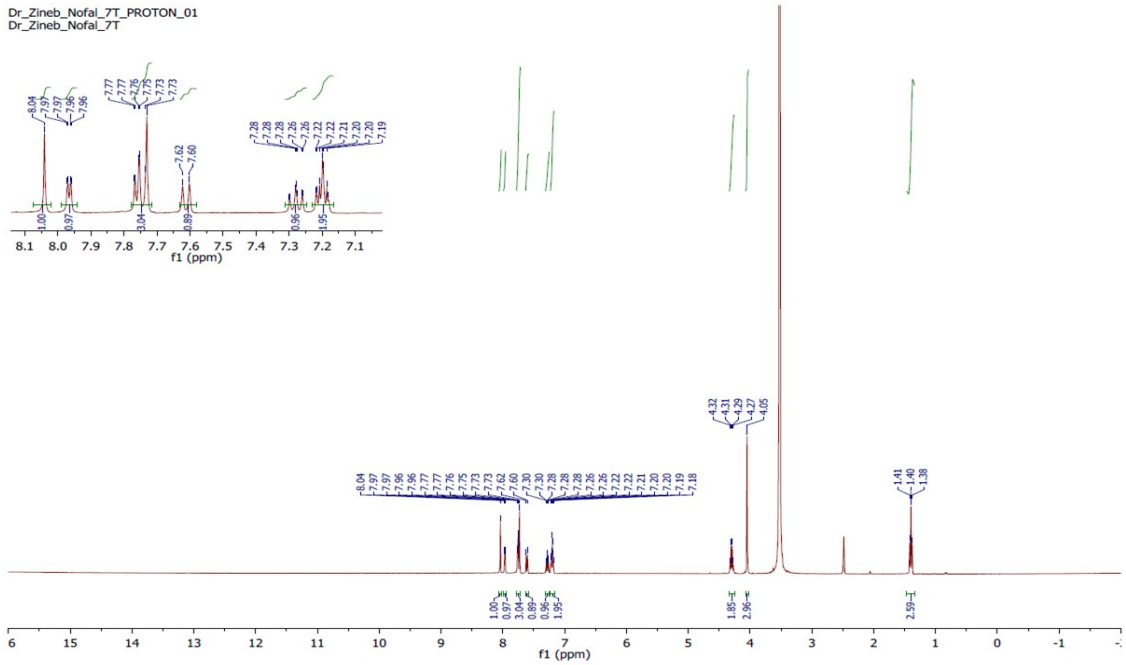


Figure S57. ^{1}H NMR spectrum of compound **3t**.

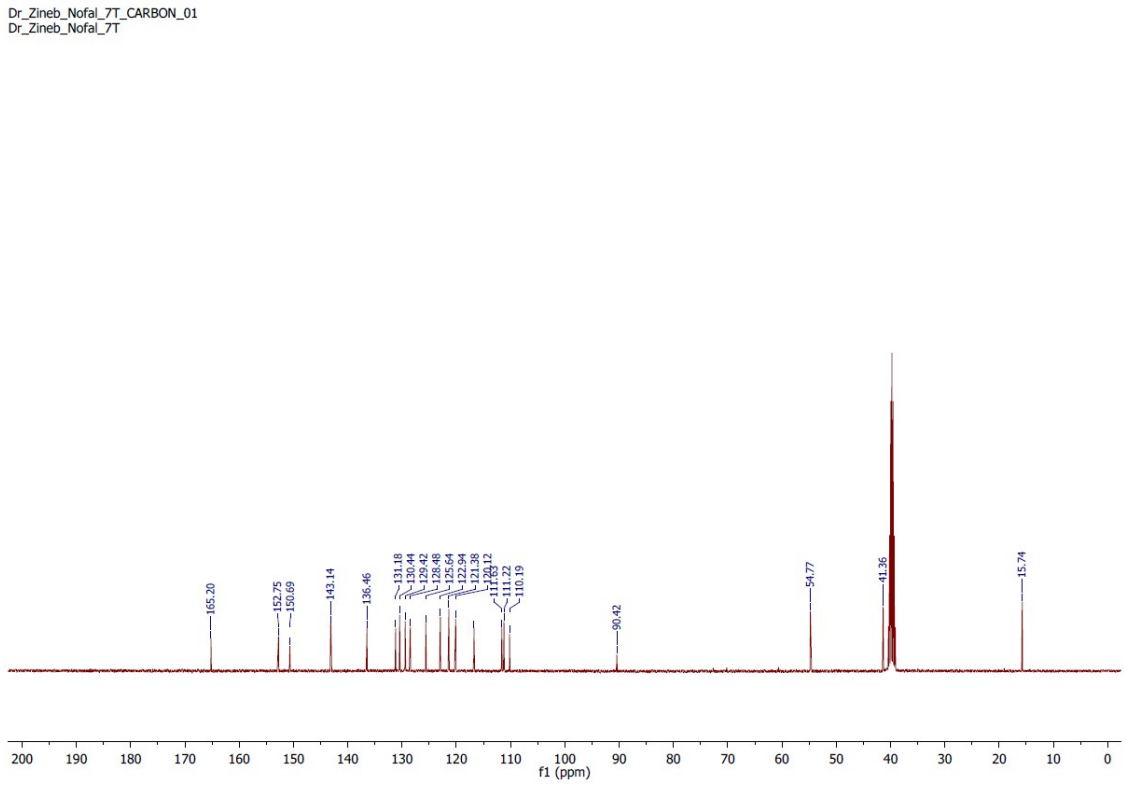


Figure S58. ^{13}C NMR spectrum of compound **3t**.

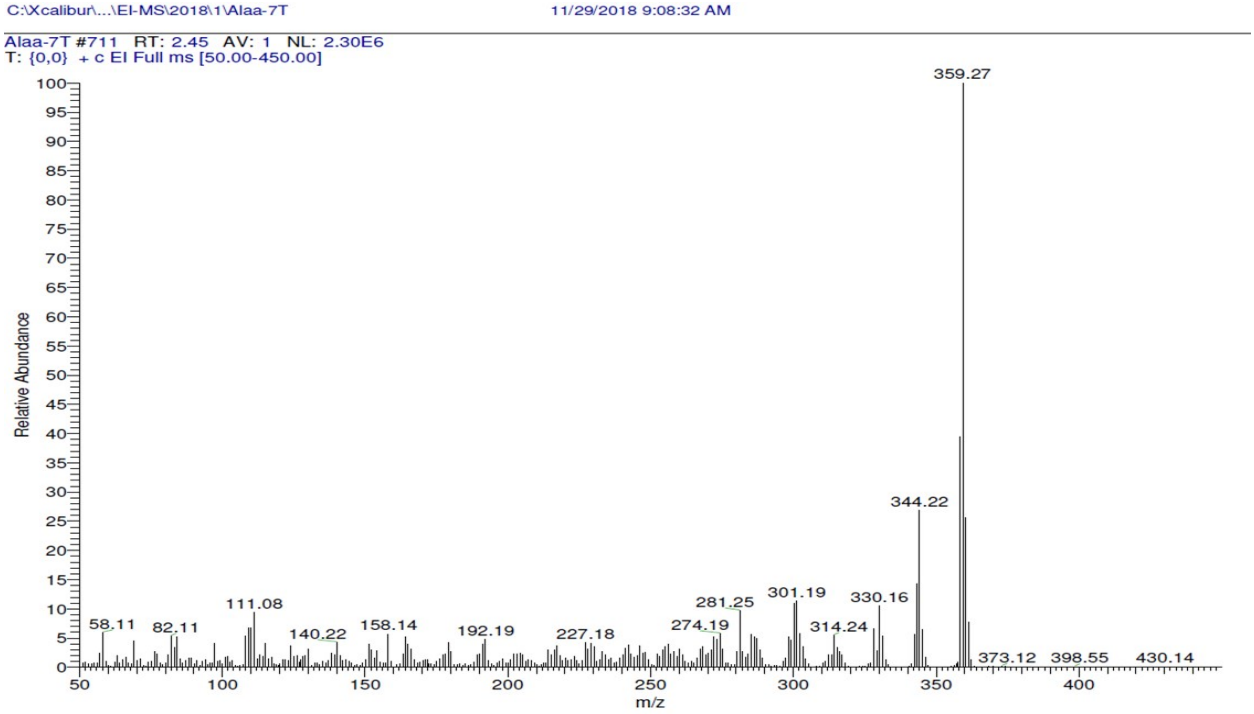


Figure S59. Mass spectrum of compound **3t**.

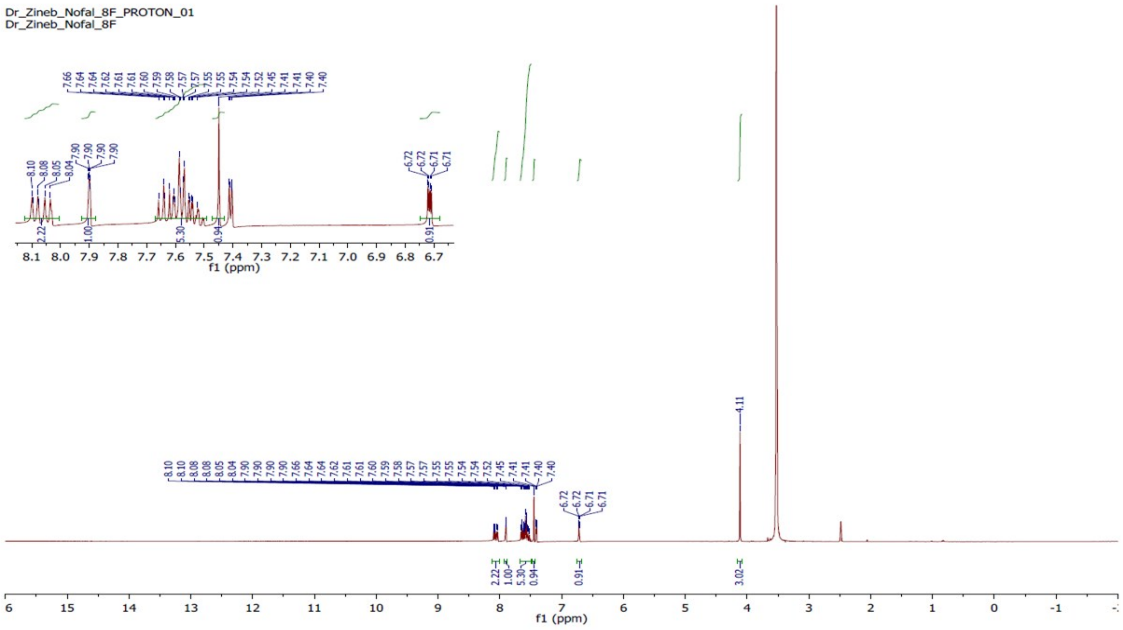


Figure S60. ^{1}H NMR spectrum of compound **3u**.

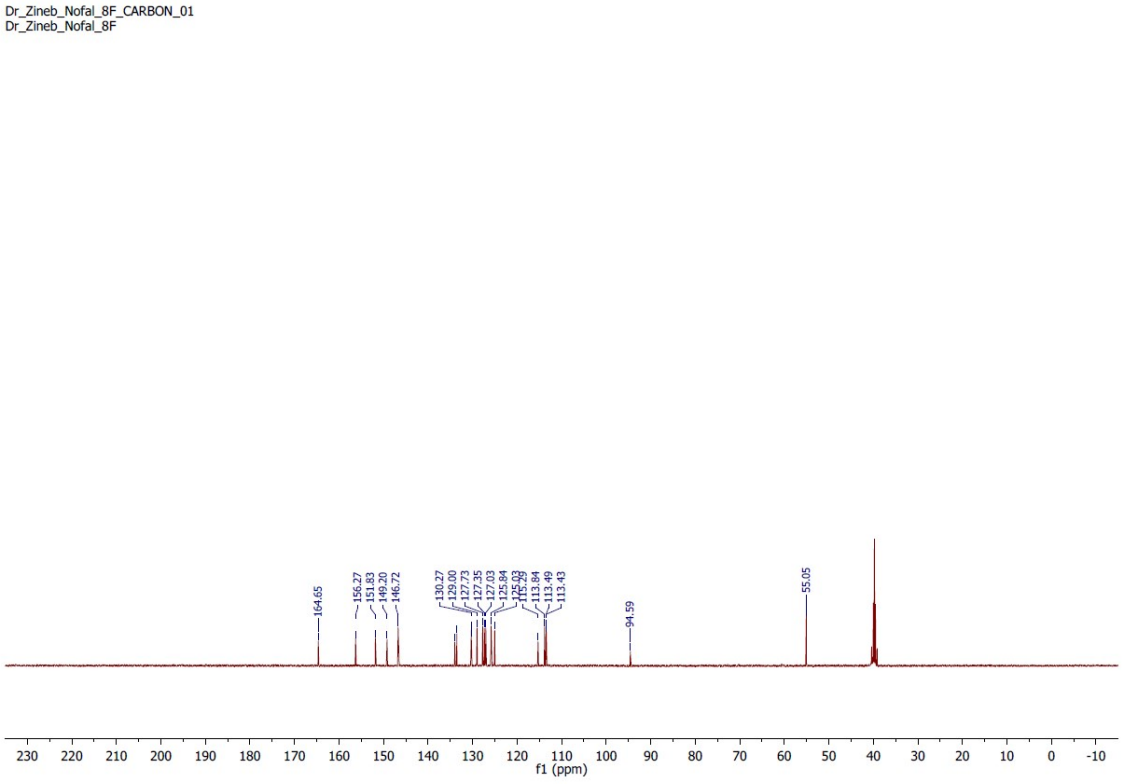


Figure S61. ^{13}C NMR spectrum of compound **3u**.

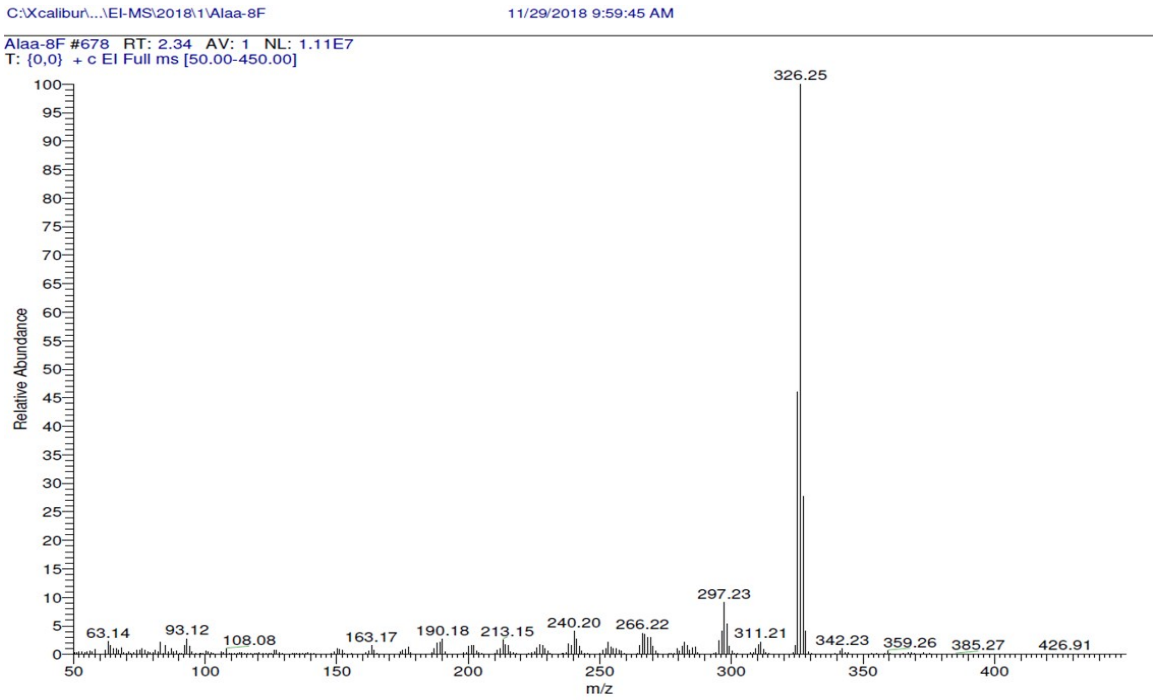


Figure S62. Mass spectrum of compound **3u**.

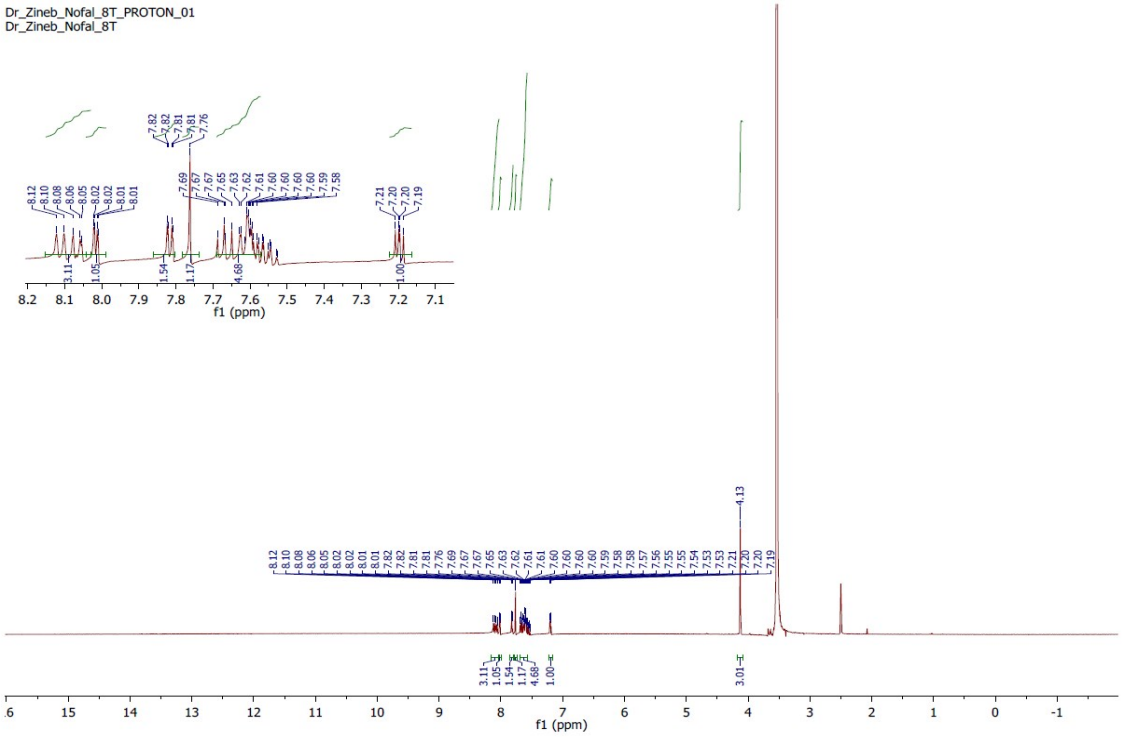


Figure S63. ^{1}H NMR spectrum of compound **3v**.

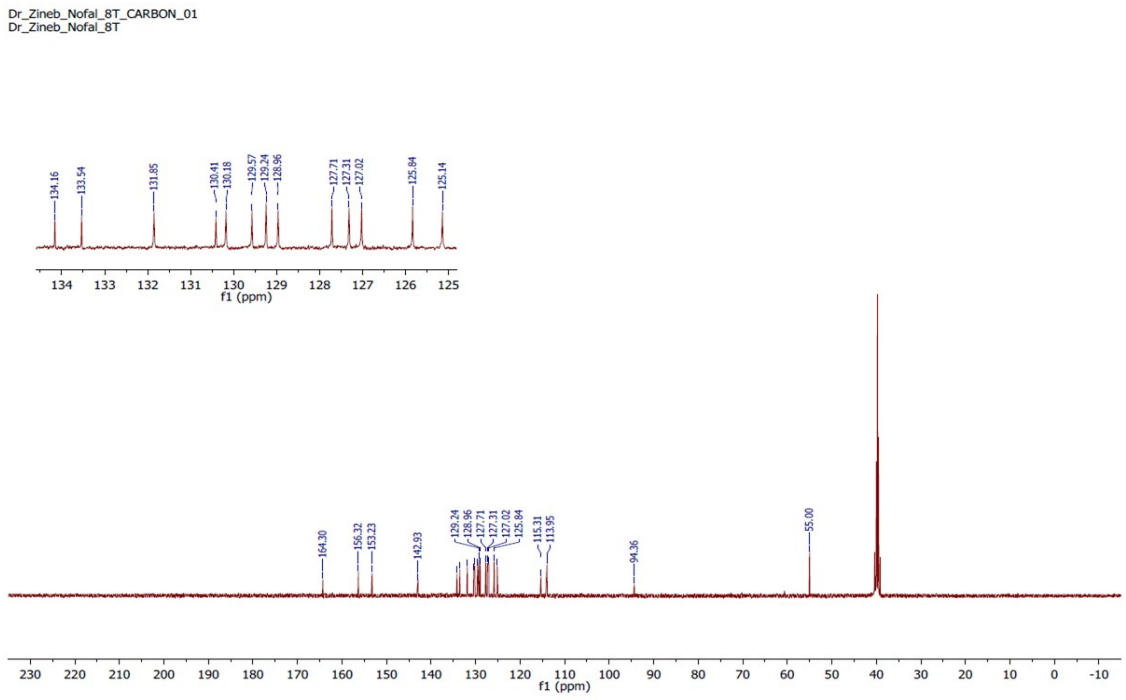


Figure S64. ^{13}C NMR spectrum of compound **3v**.

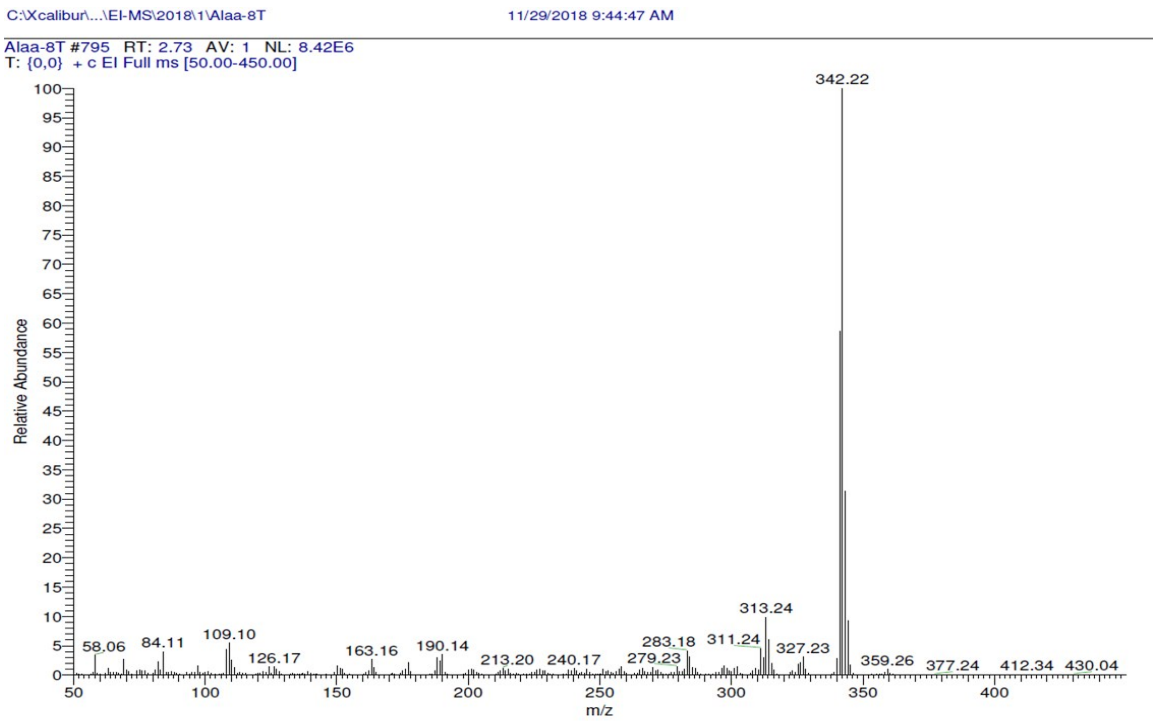


Figure S65. Mass spectrum of compound **3v**.

[1] M.N. Aziz, S.S. Panda, E.M. Shalaby, N.G. Fawzy, A.S. Girgis, Facile synthetic approach towards vasorelaxant active 4-hydroxyquinazoline-4-carboxamides, *RSC Adv*., **9** (2019) 28534-28540.

[2] N.M. Khalifa, A.M. Srour, S.S. AbdEl-Karim, D.O. Saleh, M. A. Al-Omar, Synthesis and 2D-QSAR study of active benzofuran-based vasodilators, *Molecules*, **22** (2017) 1820.