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


# New *N*-(3'-acetyl-8-nitro-2,3-dihydro-1*H*,3'*H*-spiro[quinoline-4,2'-[1,3,4]thiadiazol]-5'-yl) acetamides Induced Cell death in MCF-7 cells via G2/M Phase Cell Cycle Arrest

Selvaraj Shyamsivappan[a,b], Raju Vivek[c], Thangaraj Suresh[a], Palanivel Naveen[b], Adhigaman Kaviyarasu[a], Sundarasamy Amsaveni[a], Shunmuganarayanan Athimoolam[d], Palathurai Subramaniam Mohan[a,*]

[a]*School of Chemical Sciences, Bharathiar University, Coimbatore-641046, Tamil Nadu, India.*
[b]*Department of Chemistry, Dr. N.G.P. Arts and Science College, Coimbatore-641048, Tamil Nadu, India.*
[c]*Cancer Research Program (CRP), Bio-Nano Therapeutics Research Laboratory, School of Life Sciences, Department of Zoology, Bharathiar University, Coimbatore-641046, Tamil Nadu, India.*
[d]*Department of Physics, Anna University, Nagercoil, Tamil Nadu, India*

## Crystal Data

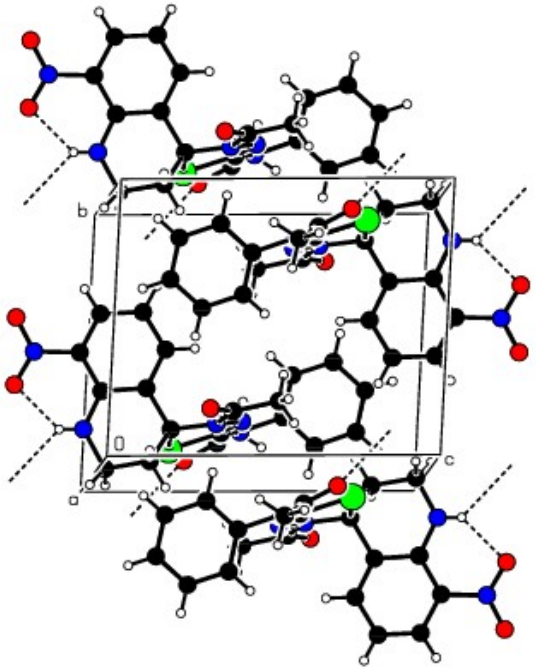


**Figure S1**. Packing of the molecules showed flat aggregation along ab-plane in the monoclinic unit cell is seen down along *a*-axis. The dashed lines are indicating the hydrogen bonds.

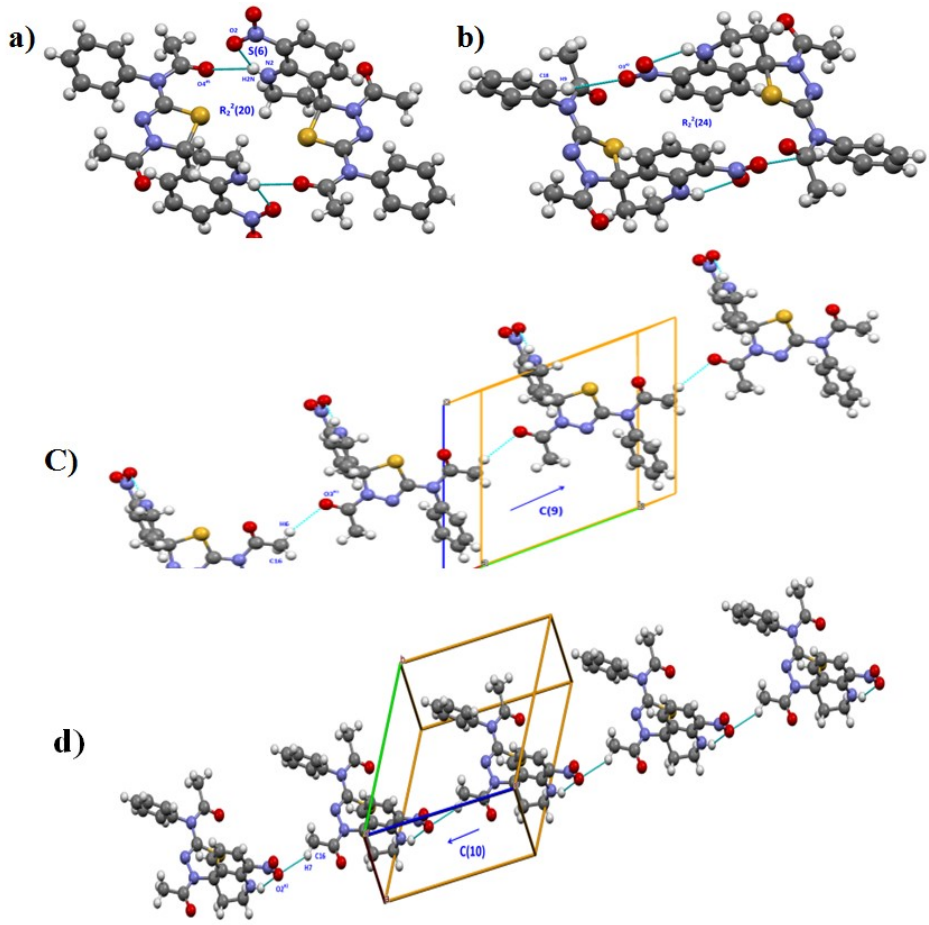


**Figure S2.** a & b shows the ring motifs; c & d shows the chain motifs. The dashed lines are indicating the hydrogen bonds.

**Table S1**. Geometry of hydrogen bonds (Å,°)

| D-H···A | D(D-H) | d(H···A) | D(D···A) | <(DHA) |
|---|---|---|---|---|
| C16-H6···O3$^{\#1}$ | 0.96 | 2.63 | 3.549(8) | 161 |
| C16-H7···O2$^{\#2}$ | 0.96 | 2.56 | 3.166(8) | 121 |
| C18-H9···O3$^{\#3}$ | 0.93 | 2.64 | 3.336(9) | 133 |
| C20-H13···O2$^{\#4}$ | 0.96 | 2.53 | 3.379(8) | 148 |
| C21-H16···O3 | 0.97 | 2.42 | 2.956(6) | 115 |
| N2-H2N···O2 | 0.77(4) | 2.03(4) | 2.625(7) | 133(3) |
| N2-H2N···O4$^{\#5}$ | 0.77(4) | 2.58(4) | 3.161(8) | 134(3) |

Symmetry transformation used to produce equivalent atoms:

#1 x, y+1, z; #2 x, y+1, z-1; #3 -x+2, -y+1, -z+1; #4x, y, z-1; #5 -x+2, -y+1, -z+2;

**Table S2**. Crystallographic details of the compound **4a, 4c,** and **4d**

| | 4a | 4c | 4d |
|---|---|---|---|
| Empirical formula | $C_{14}H_{15}N_5O_4S$ | $C_{16}H_{19}N_5O_4S$ | $C_{20}H_{19}N_5O_4S$ |
| Formula weight | 349.37 | 377.42 | 425.46 |
| Temperature | 293(2) K | 293 (2) K | 293 (2) K |
| Wavelength | 0.71073 Å | 0.71073 Å | 0.71073 Å |
| Crystal system | Tetragonal | Monoclinic | Triclinic |
| Space group | I 41/a | C 2/c | P -1 |
| Unit cell dimensions | a = 18.03(3) Å | a = 26.46(4) Å; α = 90°. | a = 8.80(2) Å α= 65.16(5)°. |
| | b = 18.028 Å | b = 6.552(10) Å; β = 94.62(2)°. | b = 11.28(3) Å β= 87.05(7)°. |
| | c = 20.39(4) Å | c = 20.28(3) Å; γ = 90°. | c = 11.33(3) Å γ = 84.17(7)°. |
| Volume | 6627(26) $Å^3$ | 3504(9) $Å^3$ | 1015(5) $Å^3$ |
| Z | 16 | 8 | 2 |
| Density (calculated) | 1.401 $Mg/m^3$ | 1.431 $Mg/m^3$ | 1.392 $Mg/m^3$ |
| Absorption coefficient | 0.225 $mm^{-1}$ | 0.218 $mm^{-1}$ | 0.197 $mm^{-1}$ |
| F(000) | 2912 | 1584 | 444 |
| Theta range for data collection | 2.259 to 24.998° | 2.439 to 25.000° | 2.147 to 24.999° |
| Index ranges | -21≤ h ≤ 20, -21≤ k ≤ 18, -24≤ l≤24 | -31 ≤ h ≤ 31, -7 ≤ k ≤ 7, -24 ≤ l ≤ 24 | -10 ≤ h ≤ 10, -13 ≤ k ≤ 13, -13 ≤ 1 ≤ 13 |
| Reflection collected | 28469 | 14309 | 19566 |
| Independent reflections | 2922 [R(int) = 0.0503] | 3080 [R(int) = 0.0550] | 3591 [R(int) = 0.0811] |
| Completeness to theta=25.242° | 97.20 % | 97.00 % | 97.50 % |
| Refinement method | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ |
| Data/ restraints/ parameters | 2922/ 0/ 219 | 3080/ 4/ 257 | 3591/ 0/ 277 |
| Goodness of fit on F2 | 1.078 | 1.035 | 1.11 |
| Final R indices [1.2sigma (I)] | R1 = 0.0440, wR2 = 0.1151 | R1=0.0529, wR2 = 0.1307 | R1 = 0.0643, wR2 = 0.1540 |
| R indices (all data) | R1= 0.0539, wR2= 0.1224 | R1= 0.0821, wR2= 0.1463 | R1= 0.0996, wR2= 0.1712 |
| Extinction coefficient | n/a | n/a | n/a |
| Largest diff. peak and hole | 0.409 and -0.368 $e.Å^{-3}$ | 0.337 and 0.611 $e.Å^{-3}$ | 0.796 and -0.302 $e.Å^{-3}$ |
| CCDC No. | 19800335 | 1946891 | 1980306 |

**Table S3**. Crystallographic details of the compound **4f** and **4i**

| | **4f** | **4i** |
|---|---|---|
| Empirical formula | $C_{16}H_{19}N_5O_4S$ | $C_{14}H_{24}ClN_5O_4S$ |
| Formula weight | 377.42 | 1531.21 |
| Temperature | 293(2) K | 292 (2) K |
| Wavelength | 0.71073 Å | 0.71073 Å |

| | | |
|---|---|---|
| Crystal system | Monoclinic | Triclinic |
| Space group | C2/c | P-1 |
| Unit cell dimensions | a = 26.56(4) Å | a = 12.294(7) Å= 104.620(9)°. |
| | b= 7.133(12) Å = 95.72(2)°. | b = 16.369 (7) Å= 105.192(12)°. |
| | c= 19.18(3) Å | c = 18.699(10) Å = 100.914(9)°. |
| Volume | 3615(10)Å$^3$ | 3380(3)Å$^3$ |
| Z | 8 | 8 |
| Density (calculated) | 1.387 Mg/m$^3$ | 1.505 Mg/m$^3$ |
| Absorption coefficient | 0.212 mm$^{-1}$ | 0.380 mm$^{-1}$ |
| F(000) | 1584 | 1576 |
| Theta range for data collection | 2.505 to 24.997°. | 2.171 to 25.000°. |
| Index ranges | -31 ≤ h ≤ 31, -8 ≤ k≤ 8, -22 ≤ l≤ 22 | -14 ≤ h ≤ 14, -19 ≤ k ≤ 18, -22 ≤ l ≤ 22 |
| Reflection collected | 16162 | 65269 |
| Independent reflections | 3190 [R(int) = 0.0823] | 11902 [R(int) = 0.0644] |
| Completeness to theta=25.242° | 97.10% | 97.20% |
| Refinement method | Full-matrix least-squares on F$^2$ | Full-matrix least-squares on F$^2$ |
| Data/ restraints/ parameters | 3190 / 0 / 239 | 11902 / 0 / 909 |
| Goodness of fit on F2 | 1.042 | 1.037 |
| Final R indices [1.2sigma (I)] | R1 = 0.0581, wR2 = 0.1298 | R1 = 0.0552, wR2 = 0.1387 |
| R indices (all data) | R1 = 0.1023, wR2 = 0.1482 | R1 = 0.0831, wR2 = 0.1550 |
| Extinction coefficient | n/a | n/a |
| Largest diff. peak and hole | 0.334 and -0.254 e.Å-$^3$ | 1.112 and -0.402 e.Å$^{-3}$ |
| CCDC No. | 1980370 | 1980267 |

**Table S4**. Crystallographic details of the compound **4h** and **4k**

| | **4h** | **4k** |
|---|---|---|
| Empirical formula | $C_{21}H_{21}N_5O_4S$ | $C_{16}H_{18}ClN_5O_4S$ |
| Formula weight | 439.49 | 410.85 |
| Temperature | 293(2) K | 293(2) K |
| Wavelength | 0.71073 Å | 0.71073 Å |
| Crystal system | Monoclinic | Monoclinic |
| Space group | P 21/n | C 2/c |
| Unit cell dimensions | a = 9.726(17) Å | a = 26.56(3) Å |
| | b = 11.07(2) Å; □ = 99.75(3)° | b = 6.708(6) Å □ = 93.285(17)°. |
| | c = 20.74(3) Å | c = 20.85(2) Å |
| Volume | 2200(7) Å$^3$ | 3709(6) Å$^3$ |
| Z | 4 | 8 |
| Density (calculated) | 1.327 Mg/m$^3$ | 1.472 Mg/m$^3$ |
| Absorption coefficient | 0.184 mm$^{-1}$ | 0.352 mm$^{-1}$ |
| F(000) | 920 | 1704 |
| Theta range for data collection | 2.092 to 24.999°. | 2.418 to 25.000°. |

| | | |
|---|---|---|
| Index ranges | -10 ≤ h ≤ 11, -13 ≤ k ≤ 13, -24 ≤ l ≤ 24 | -31 ≤ h ≤ 31, -7 ≤ k ≤ 7, -24 ≤ l ≤ 21 |
| Reflection collected | 16122 | 12115 |
| Independent reflections | 3880 [R(int) = 0.0357] | 3255 [R(int) = 0.0412] |
| Completeness to theta=25.242° | 97.40% | 97.10% |
| Refinement method | Full-matrix least-squares on F2 | Full-matrix least-squares on F2 |
| Data/ restraints/ parameters | 3880 / 0 / 283 | 3255 / 0 / 250 |
| Goodness of fit on F2 | 1.067 | 1.055 |
| Final R indices [1.2sigma (I)] | $R_1$ = 0.0436, $wR_2$ = 0.1073 | $R_1$ = 0.0578, $wR_2$ = 0.1422 |
| R indices (all data) | $R_1$ = 0.0559, $wR_2$ = 0.1136 | $R_1$ = 0.0791, $wR_2$ = 0.1553 |
| Extinction coefficient | n/a | n/a |
| Largest diff. peak and hole | 0.254 and -0.175 e.Å$^{-3}$ | 0.588 and -0.471 e.Å$^{-3}$ |
| CCDC No. | 1980270 | 1980268 |

## UV-Visible and Fluorescence Studies

The absorption spectrum of the compound **4a** showed intense bands at 282 and 436 nm in DMSO solvent. Further, the fluorescence spectrum of the compounds **4a** was recorded and the emission wavelength observed at 560 nm (Figure S3).

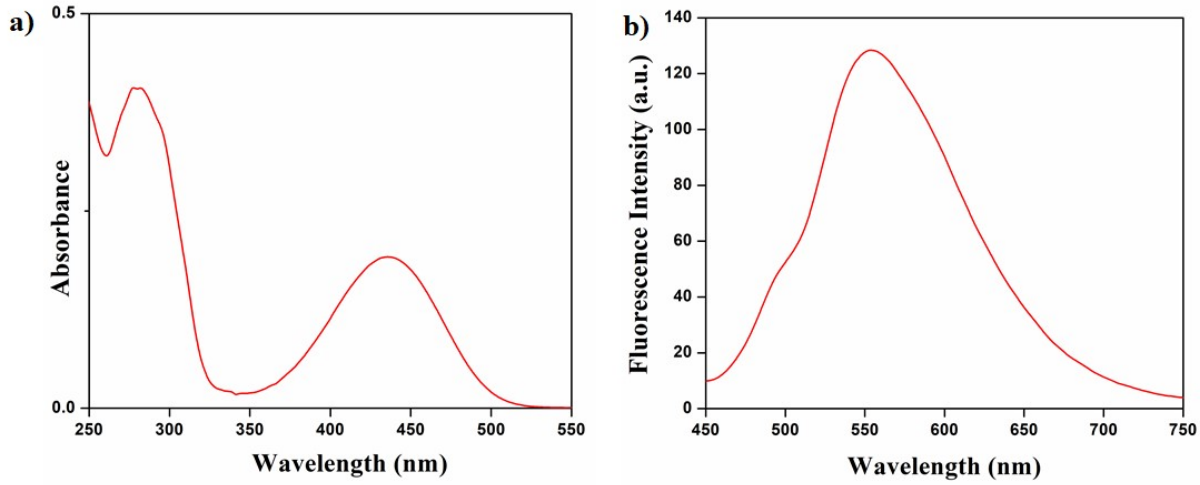


**Figure S3**. a) Absorption spectrum of the compound **4a** ($2\times10^{-4}$ M, $\lambda_{ex}$= 282 and 436 nm) in DMSO. b) Fluorescence spectrum of the compounds **4a** ($2\times10^{-4}$ M, $\lambda_{ex}$= 560 nm) in DMSO.

## Spectral Data

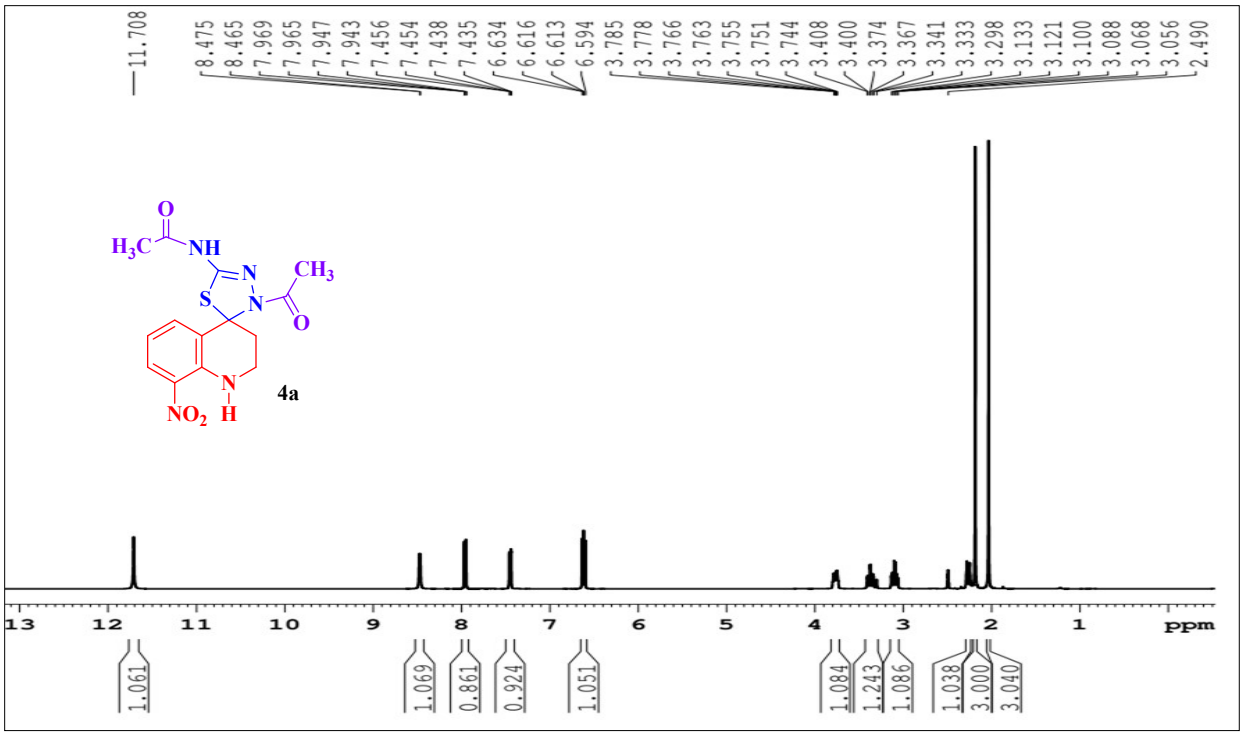


**Figure S4. $^{1}$H NMR spectrum of compound 4a**

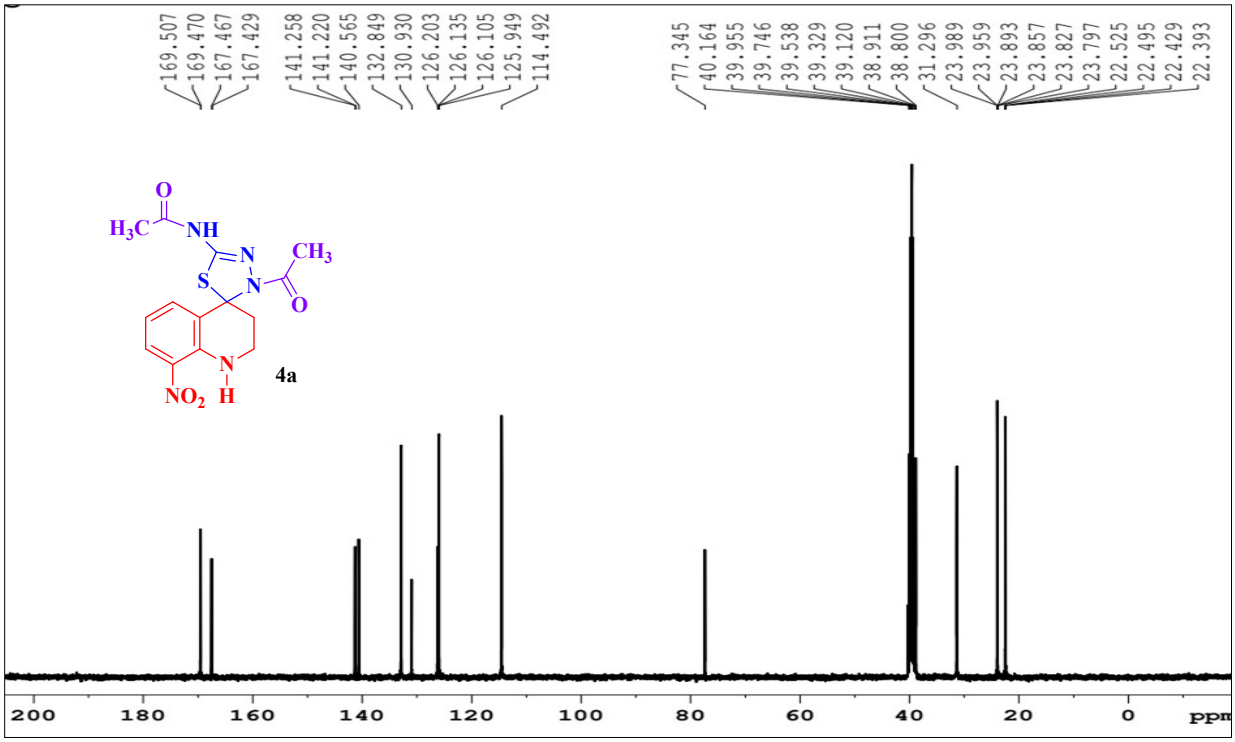


**Figure S5. $^{13}$C spectrum of compound 4a**

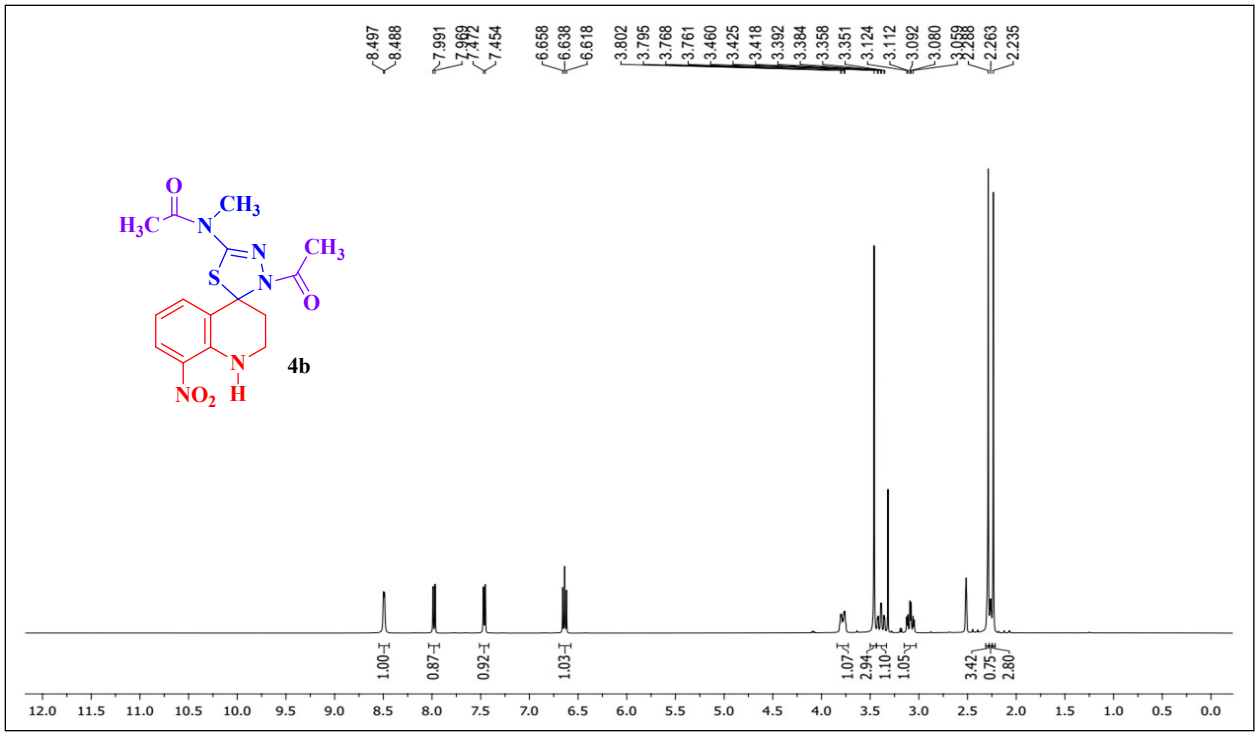


**Figure S6. $^{1}$H NMR spectrum of compound 4b**

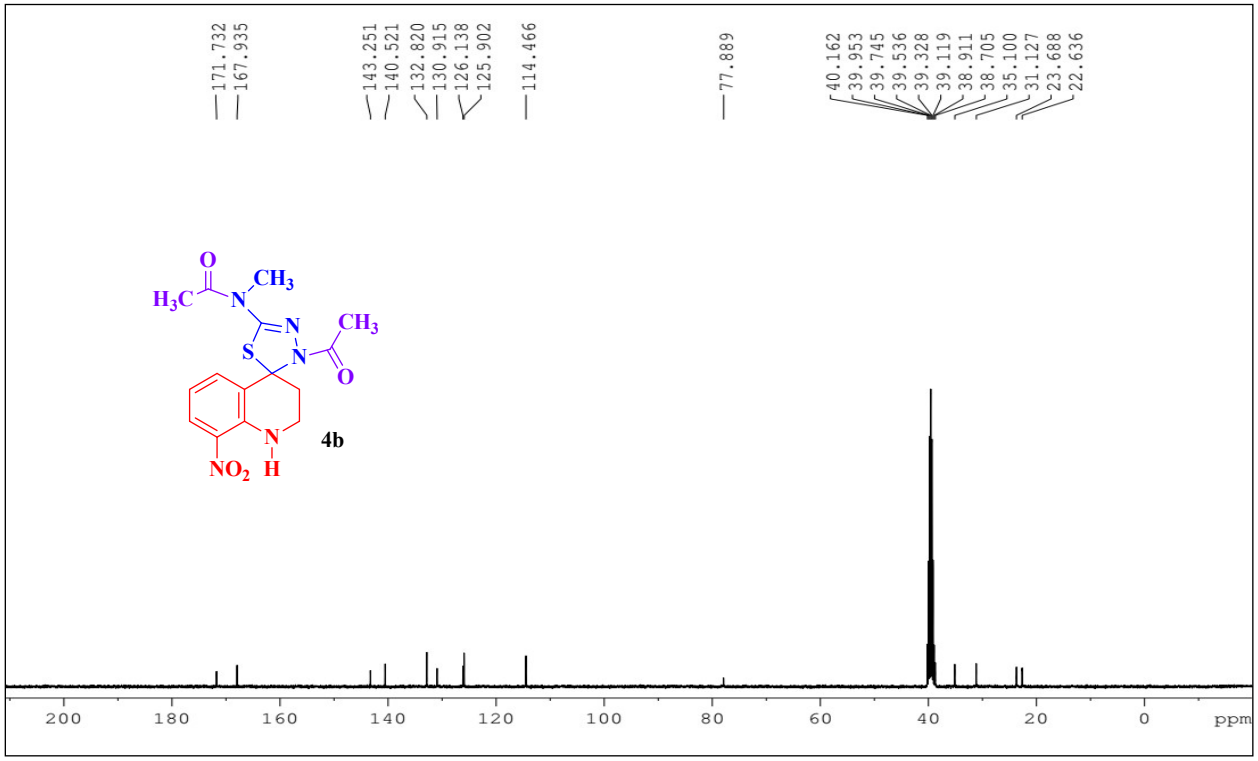


**Figure S7. $^{13}$C spectrum of compound 4b**

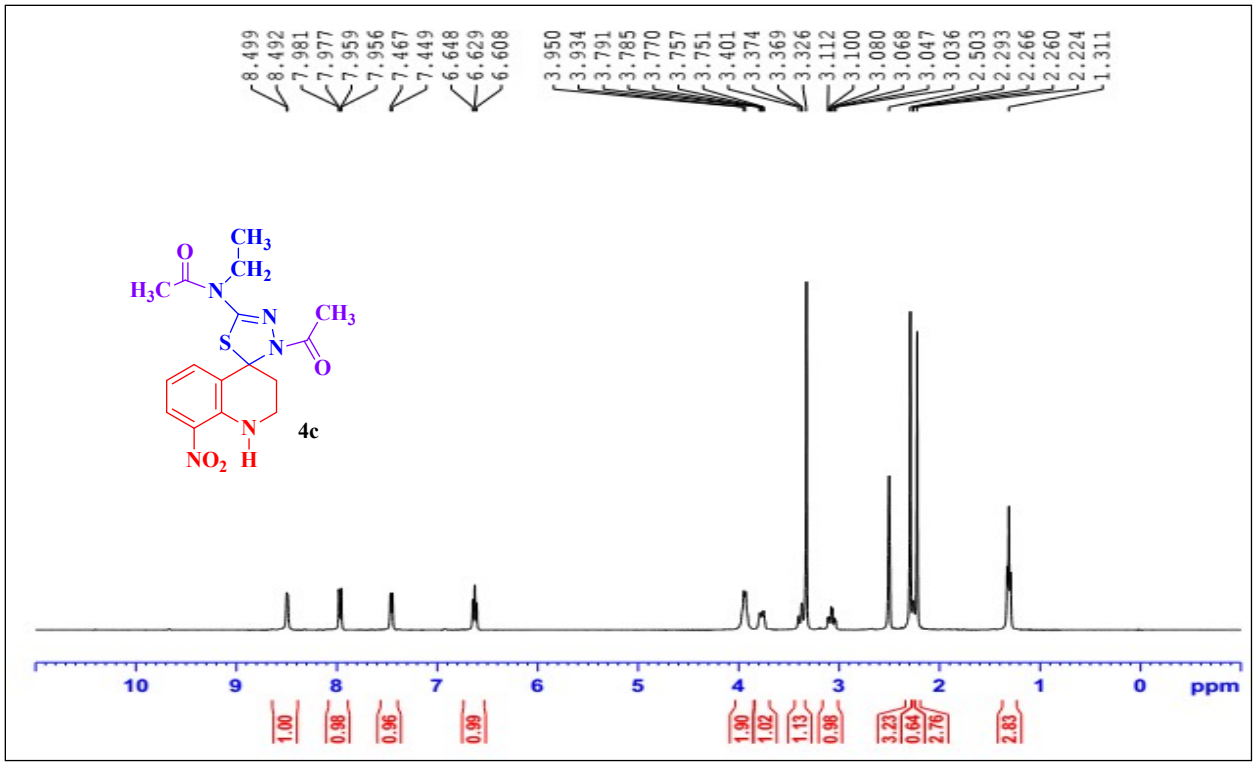


**Figure S8. $^{1}$H NMR spectrum of compound 4c**

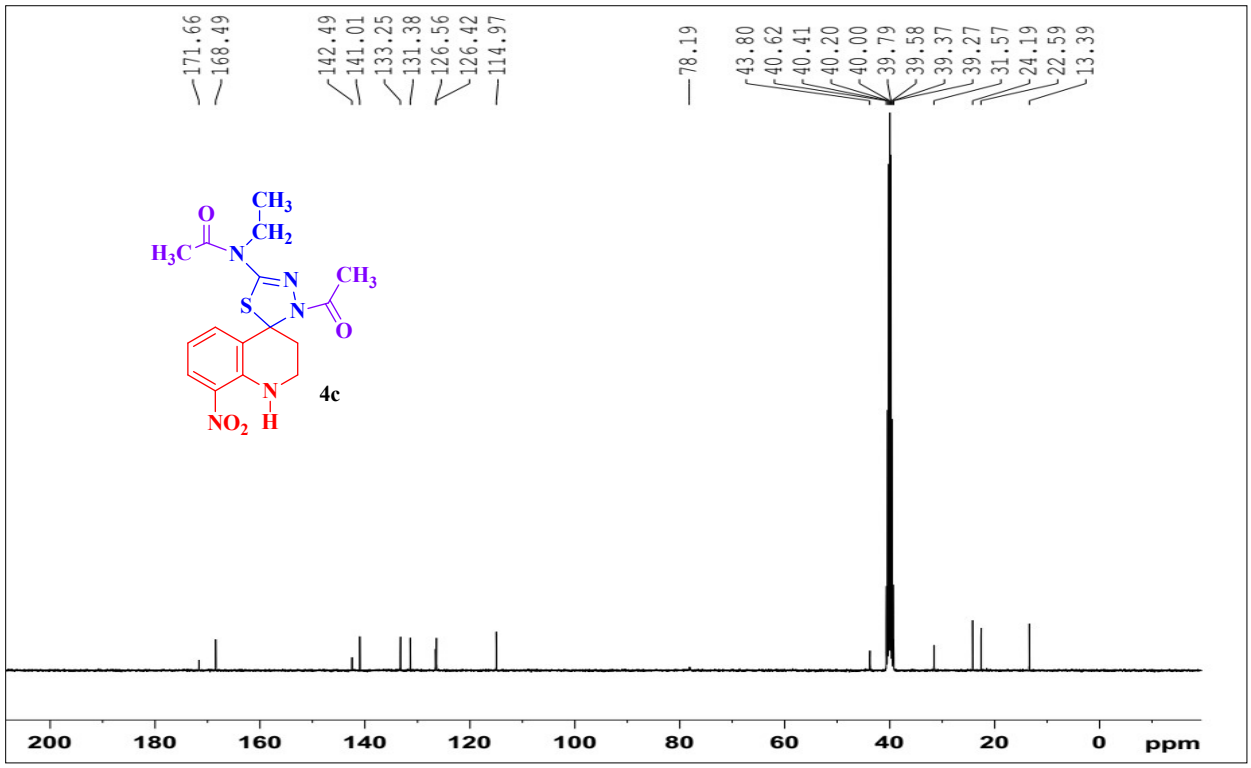


**Figure S9. $^{13}$C NMR spectrum of compound 4c**

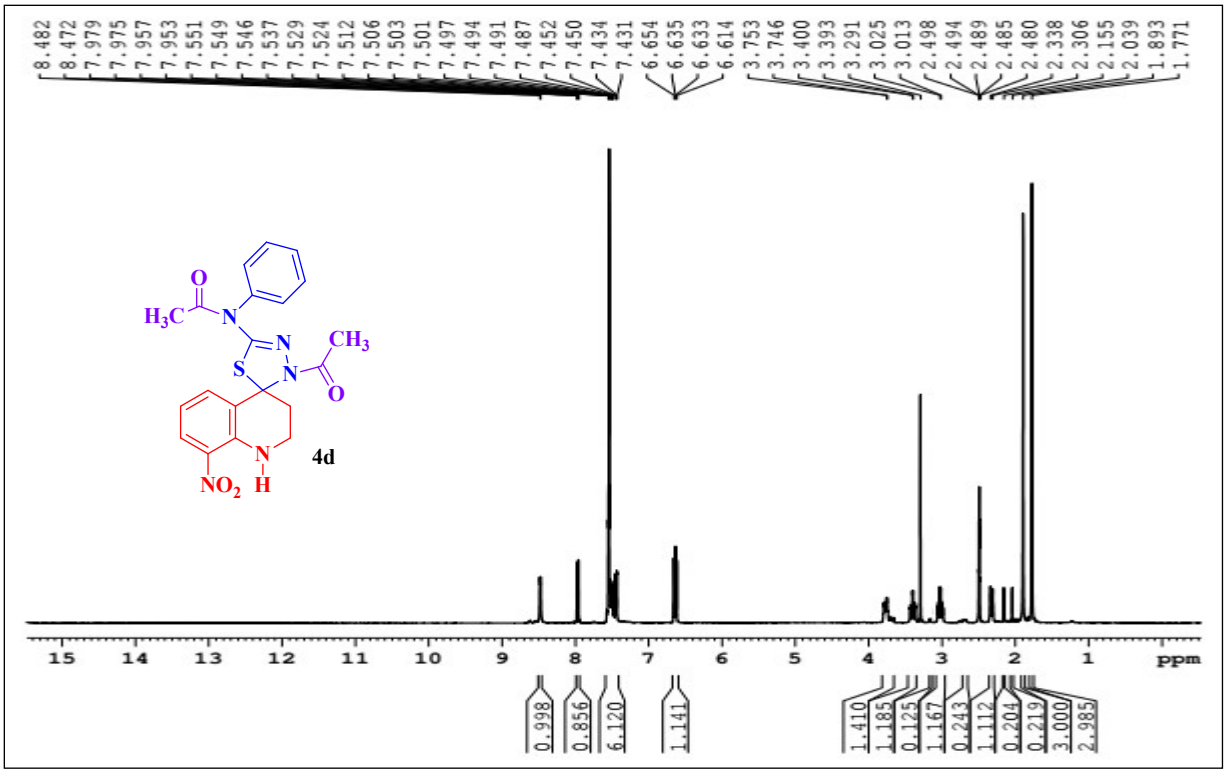


**Figure S10. $^{1}$H NMR spectrum of compound 4d**

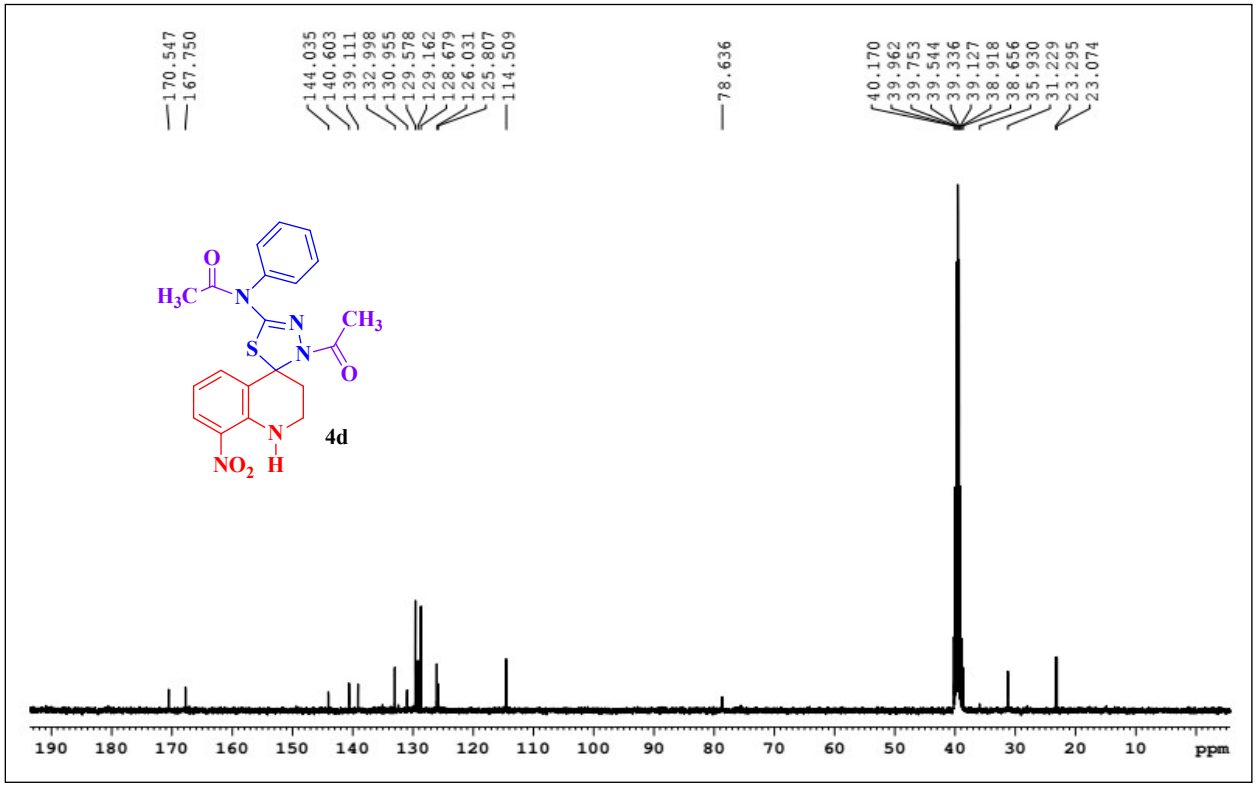


**Figure S11. $^{13}$C NMR spectrum of compound 4d**

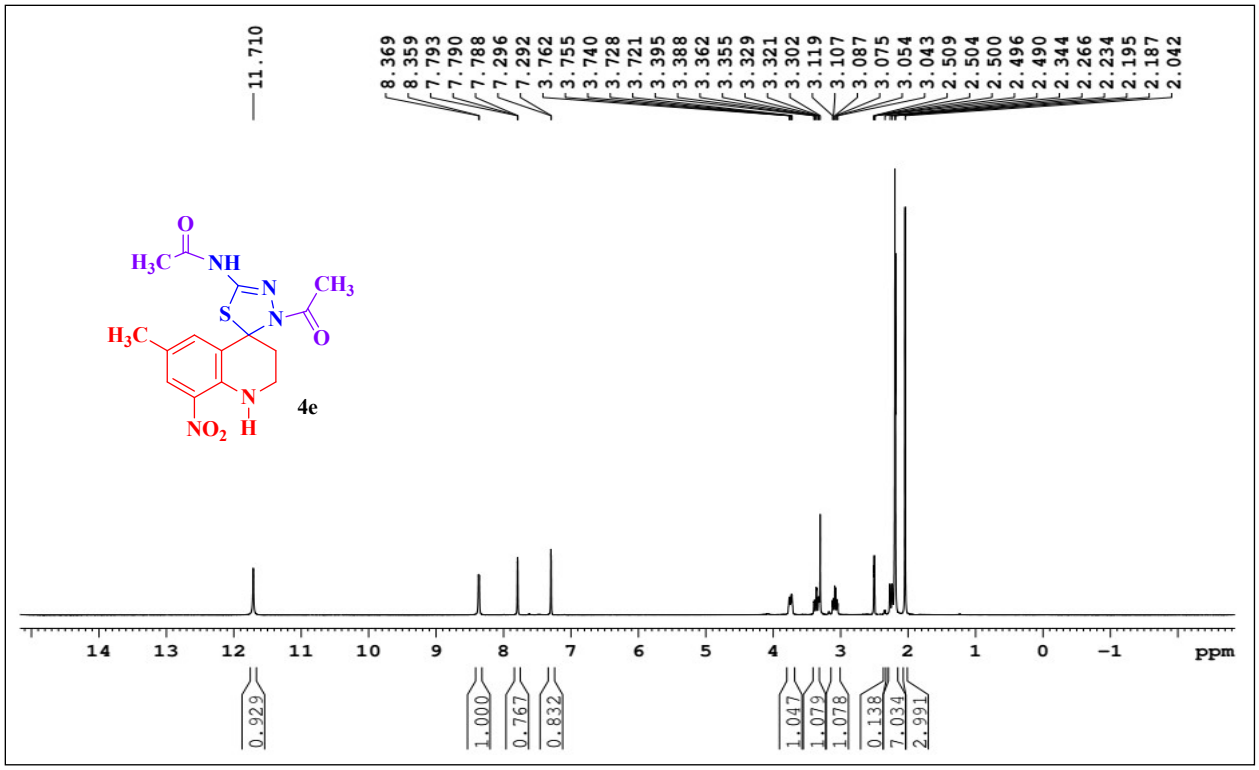


**Figure S12. $^{1}$H NMR spectrum of compound 4e**

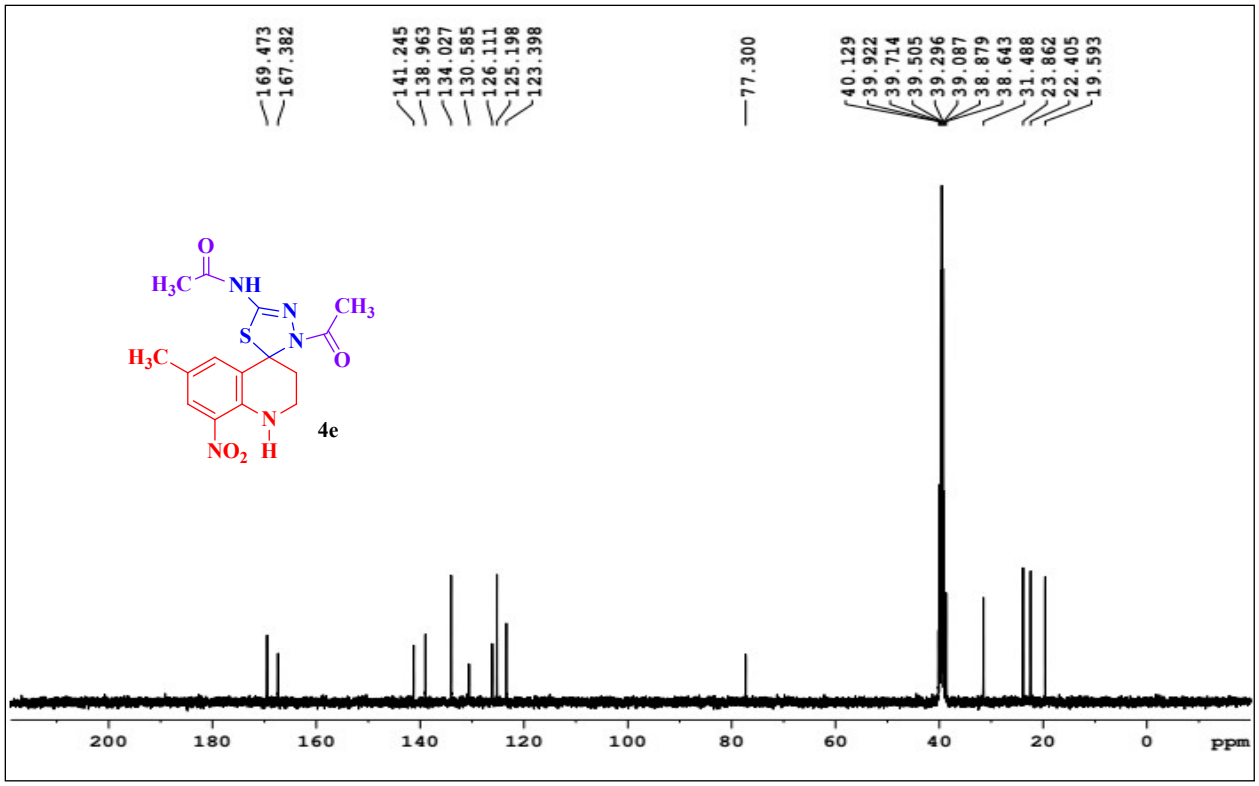


**Figure S13. $^{13}$C NMR spectrum of compound 4e**

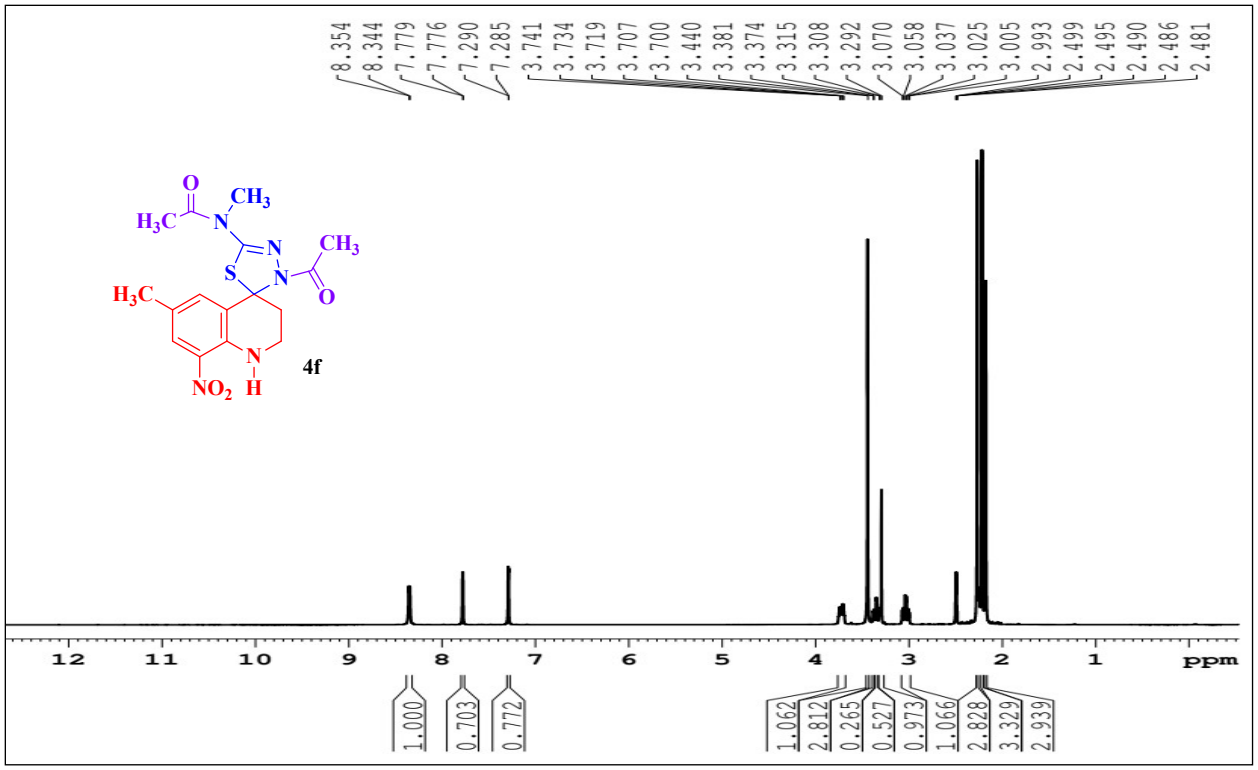


**Figure S14. $^{1}$H NMR spectrum of compound 4f**

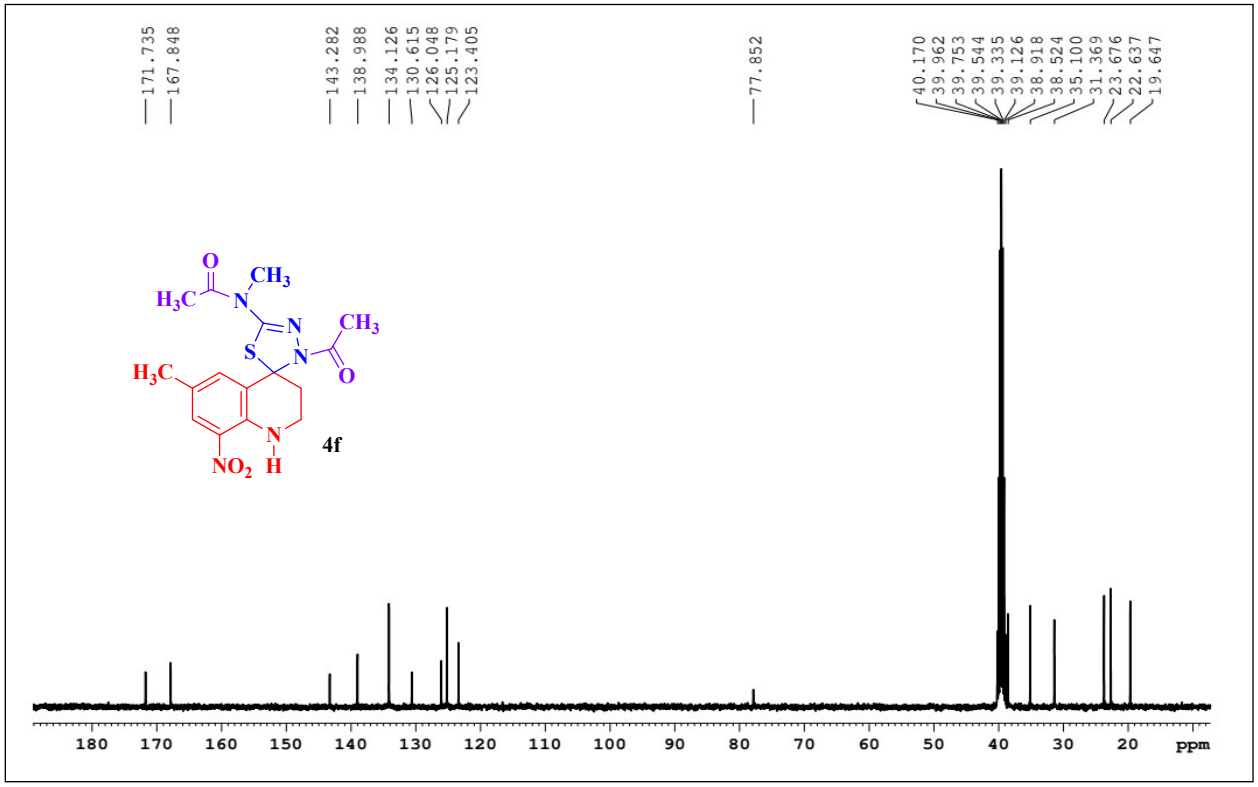


**Figure S15. $^{13}$C NMR spectrum of compound 4f**

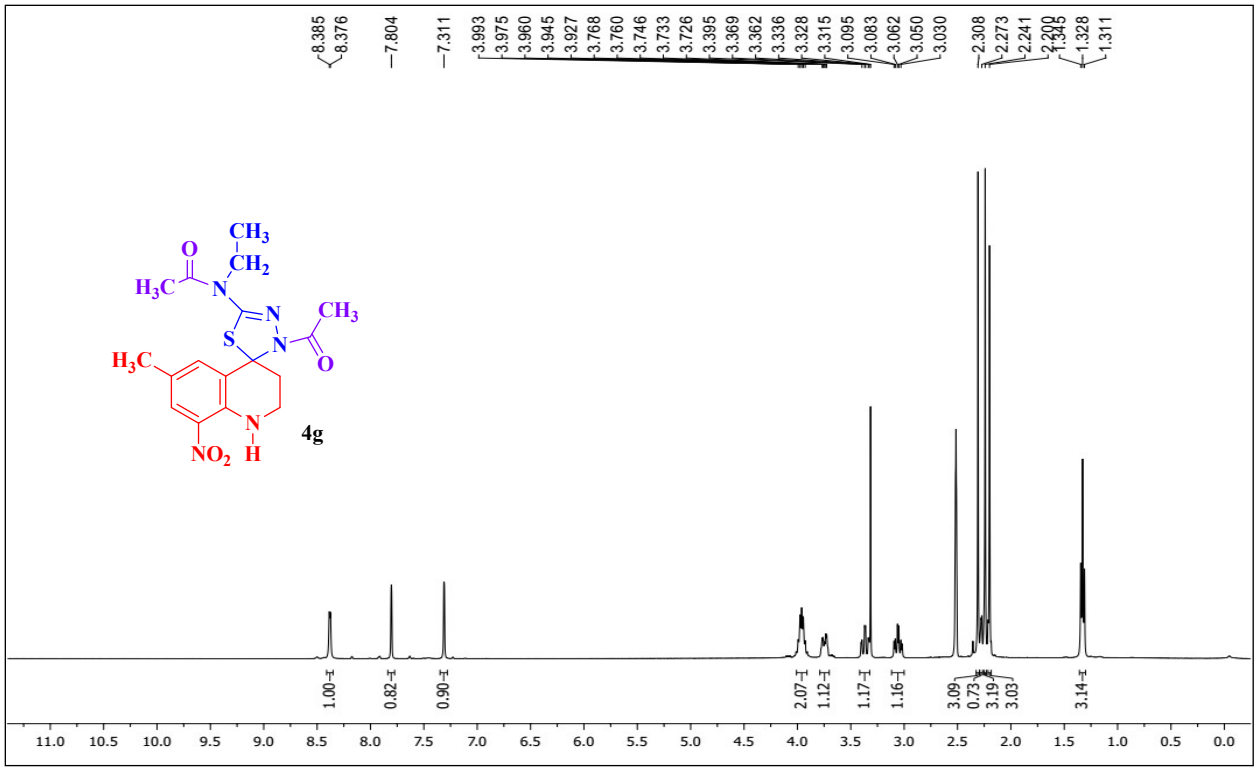


**Figure S16. $^{1}$H NMR spectrum of compound 4g**

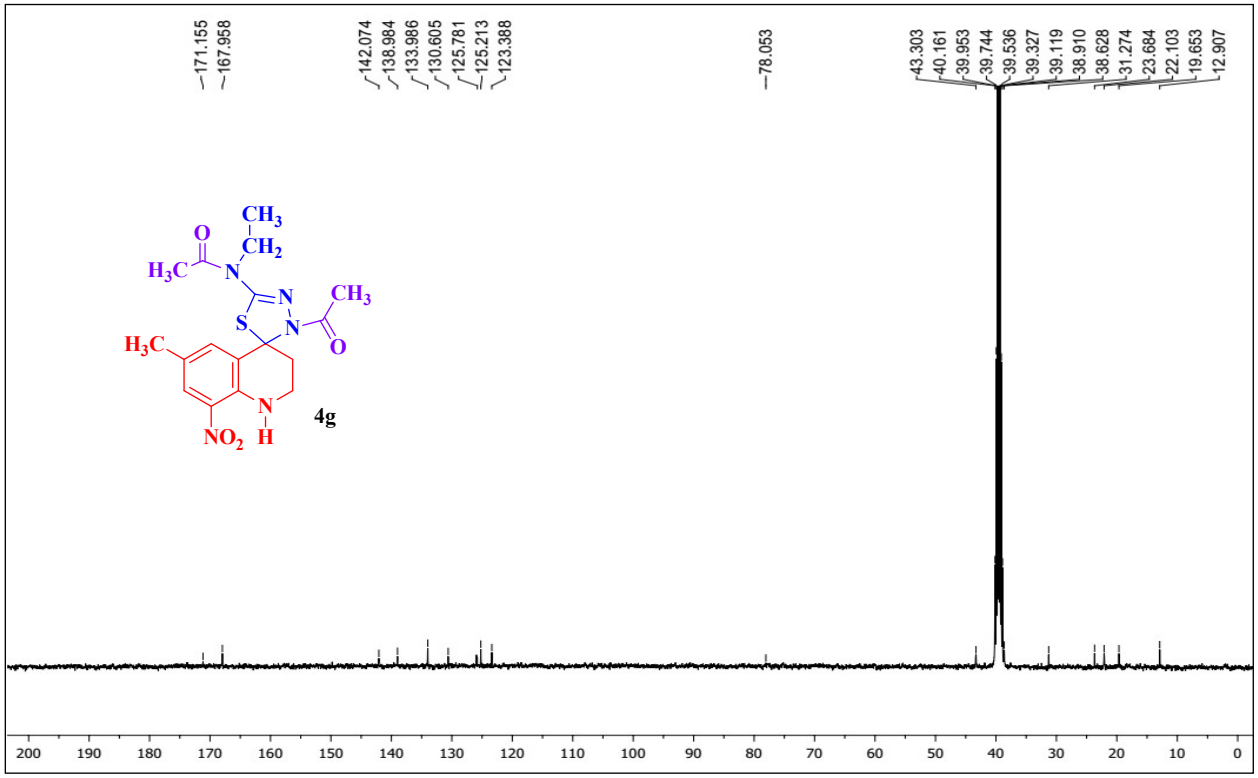


**Figure S17. $^{13}$C NMR spectrum of compound 4g**

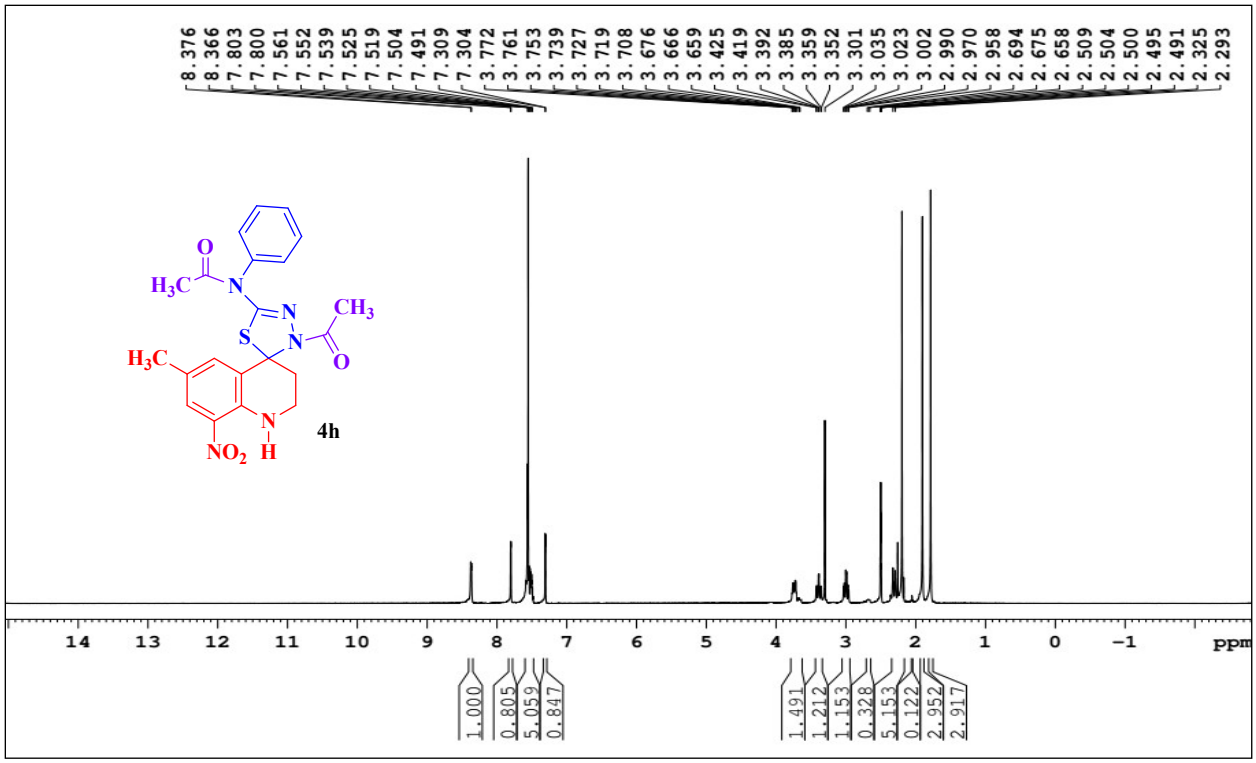


**Figure S18. $^{1}$H NMR spectrum of compound 4h**

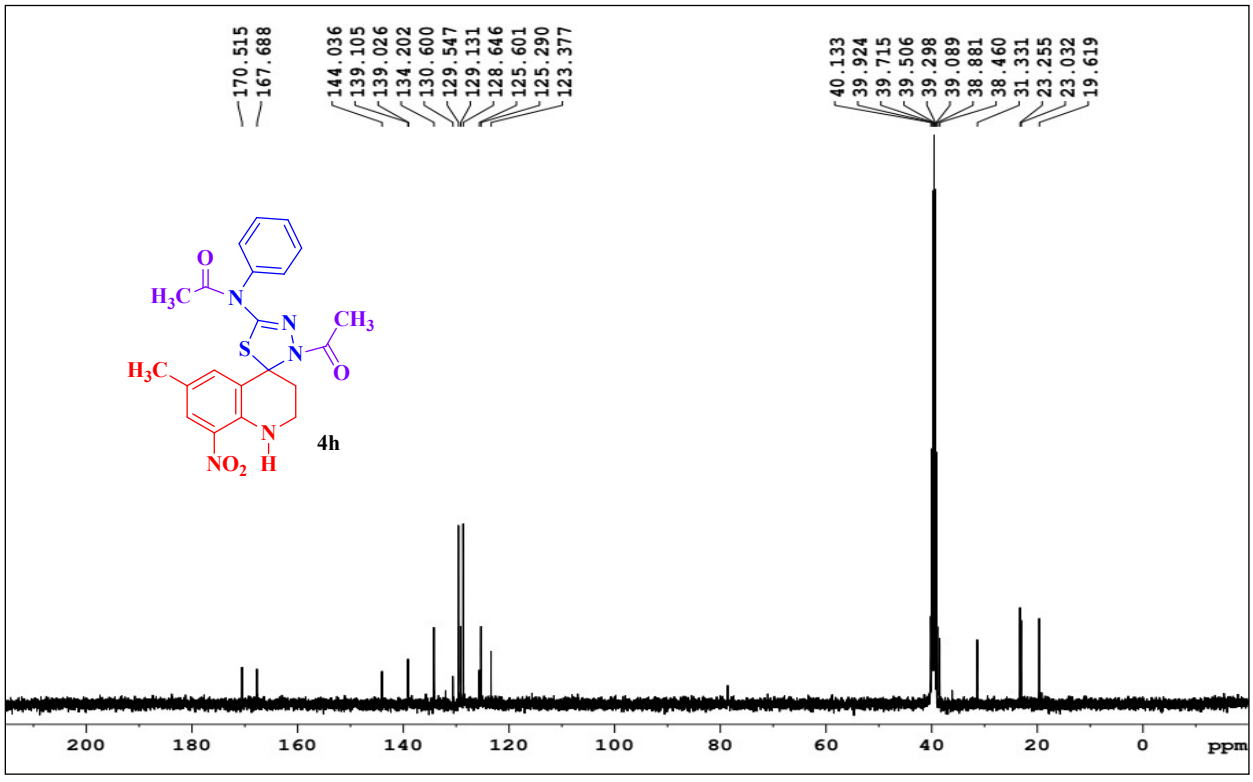


**Figure S19. $^{13}$C NMR spectrum of compound 4h**

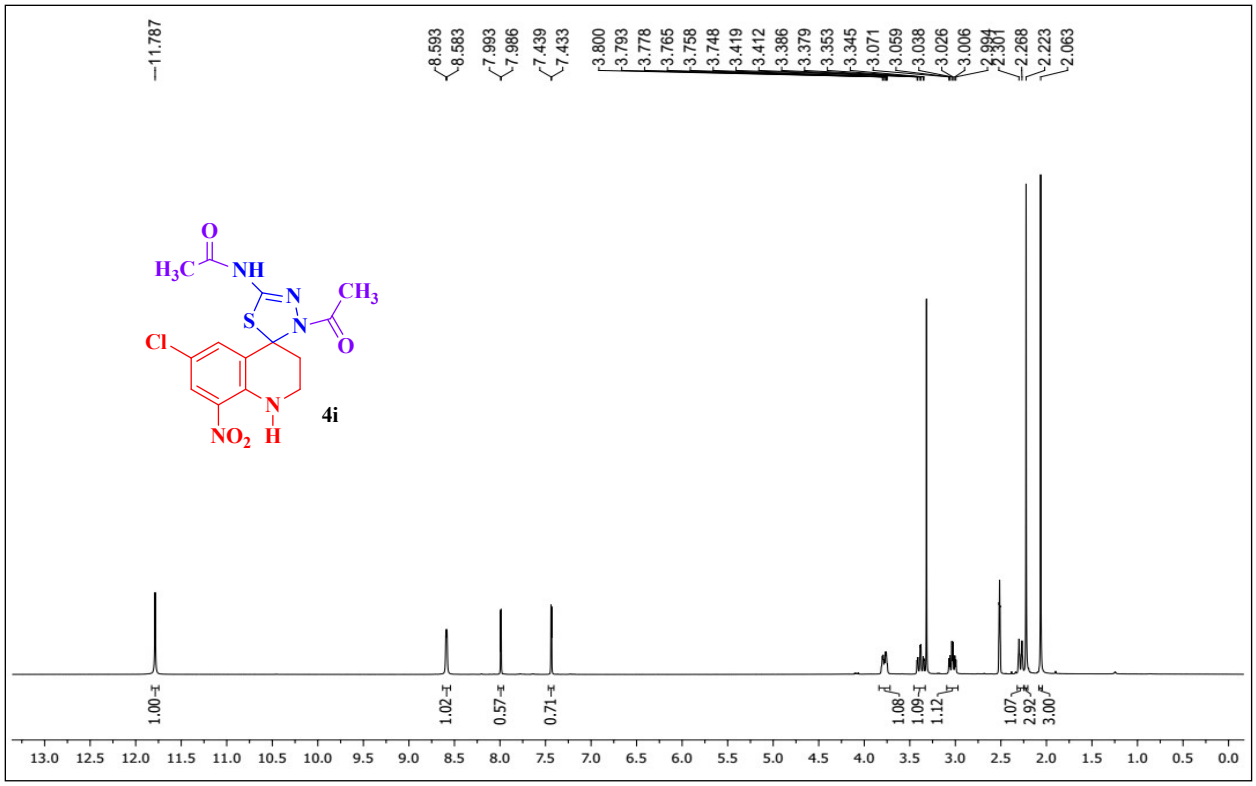


**Figure S20. $^{1}$H NMR spectrum of compound 4i**

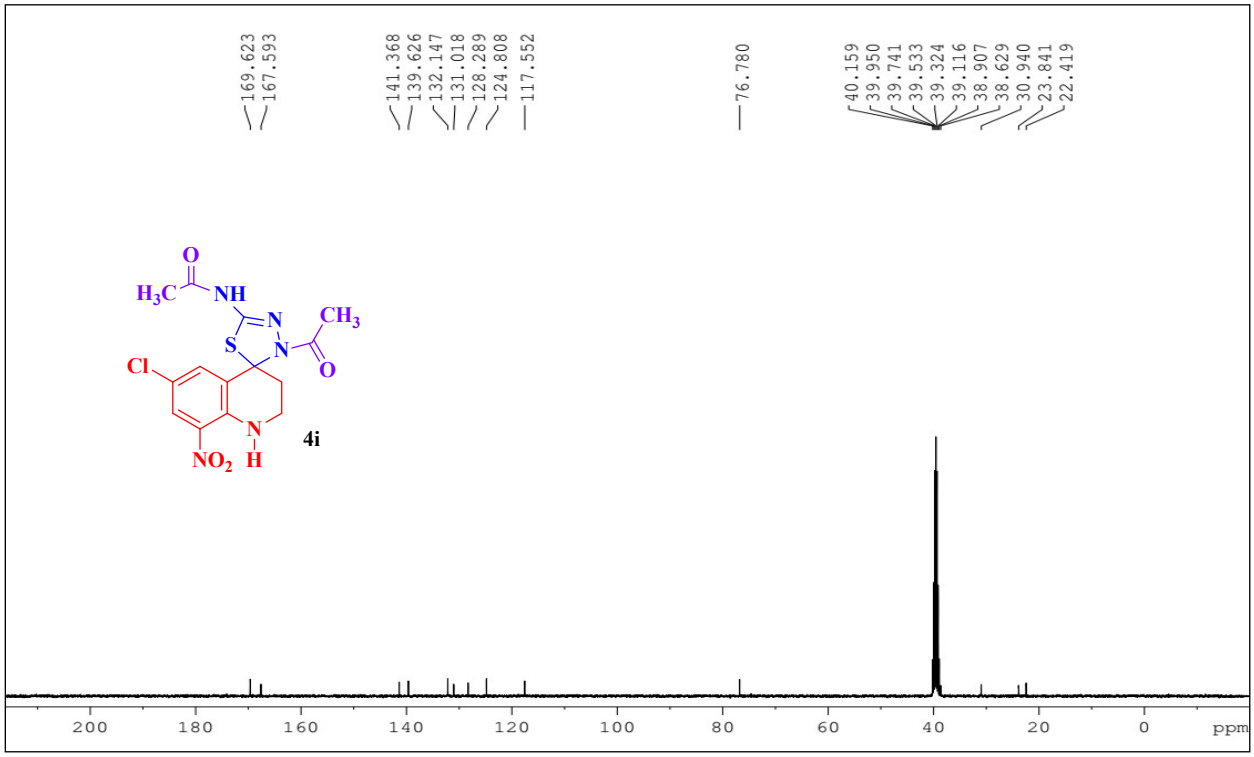


**Figure S21. $^{13}$C NMR spectrum of compound 4i**

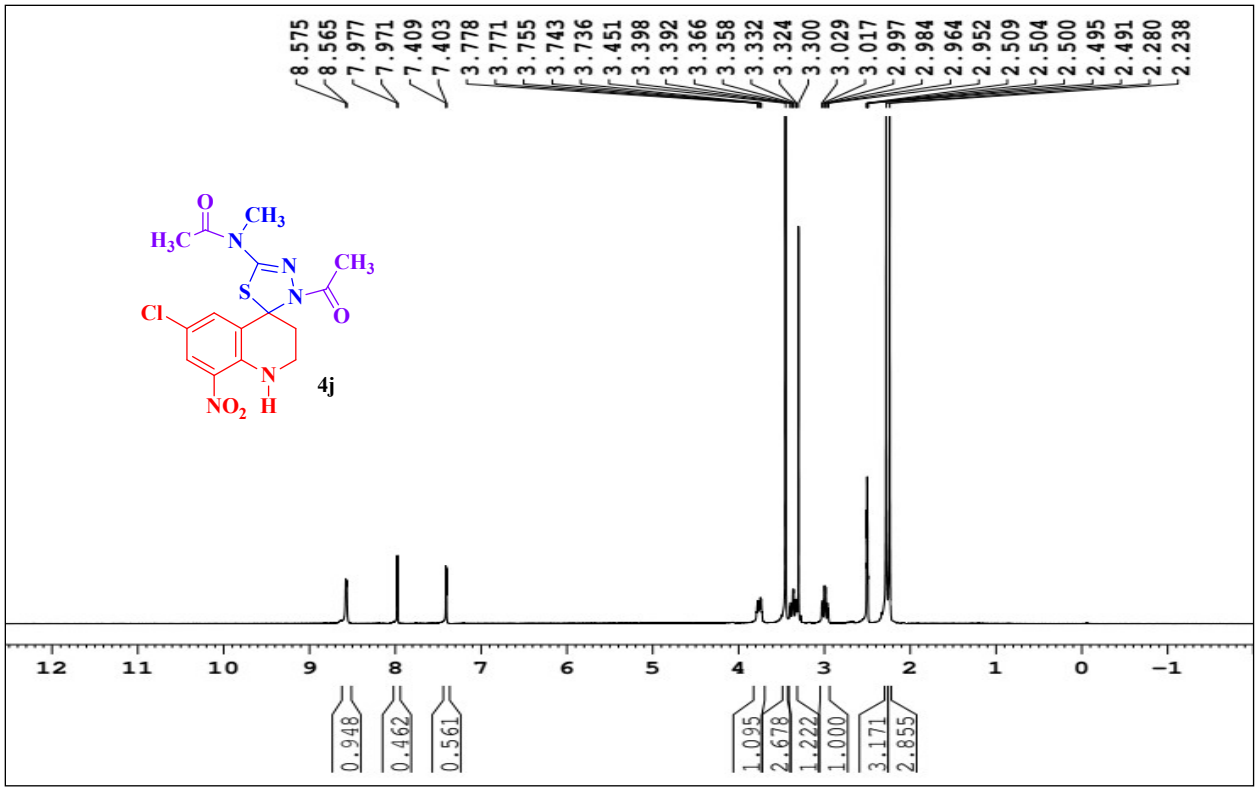


**Figure S22. $^{1}$H NMR spectrum of compound 4j**

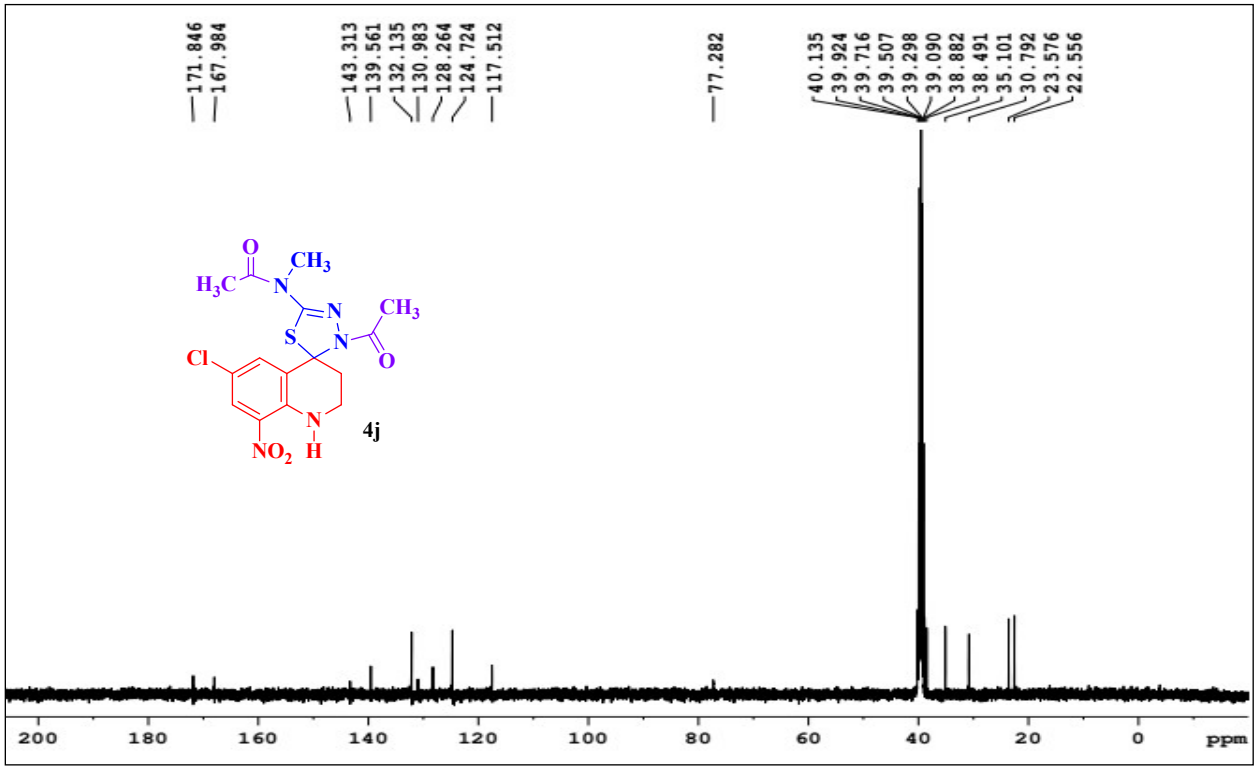


**Figure S23. $^{13}$C NMR spectrum of compound 4j**

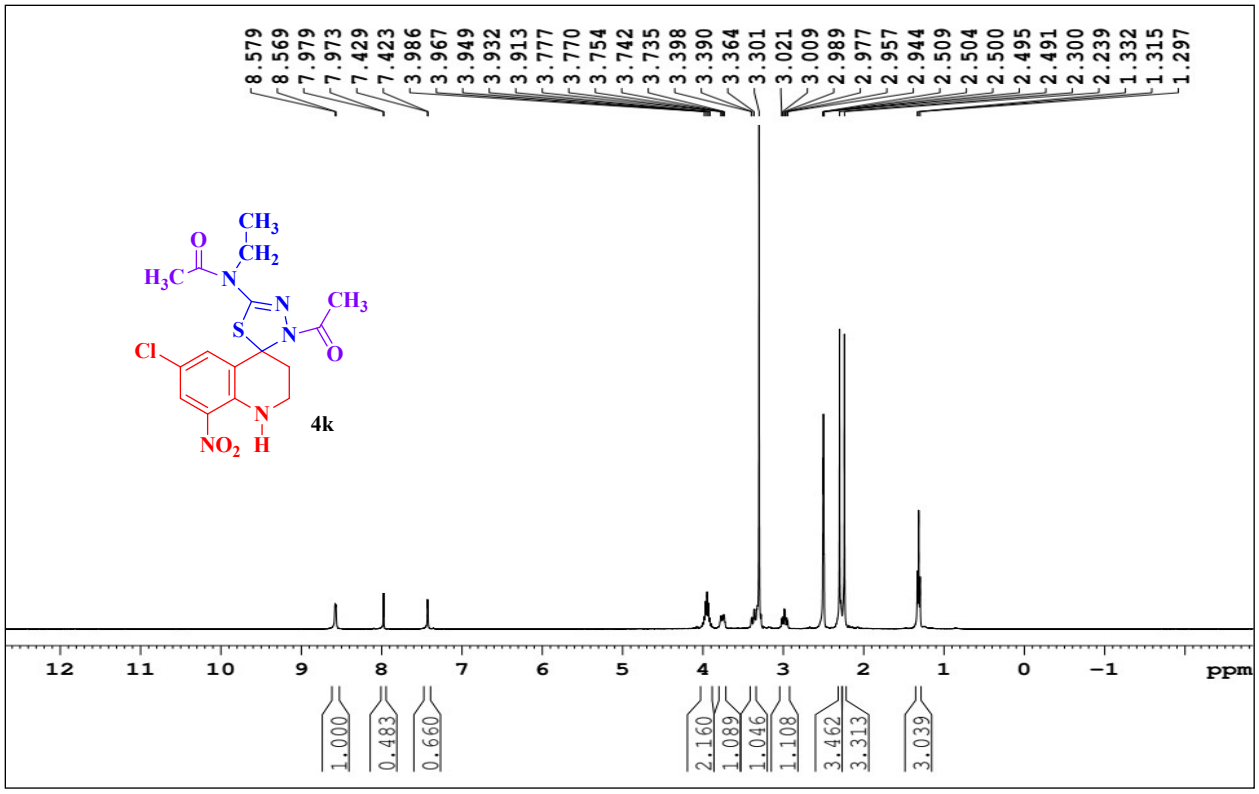


**Figure S24. $^{1}$H NMR spectrum of compound 4k**

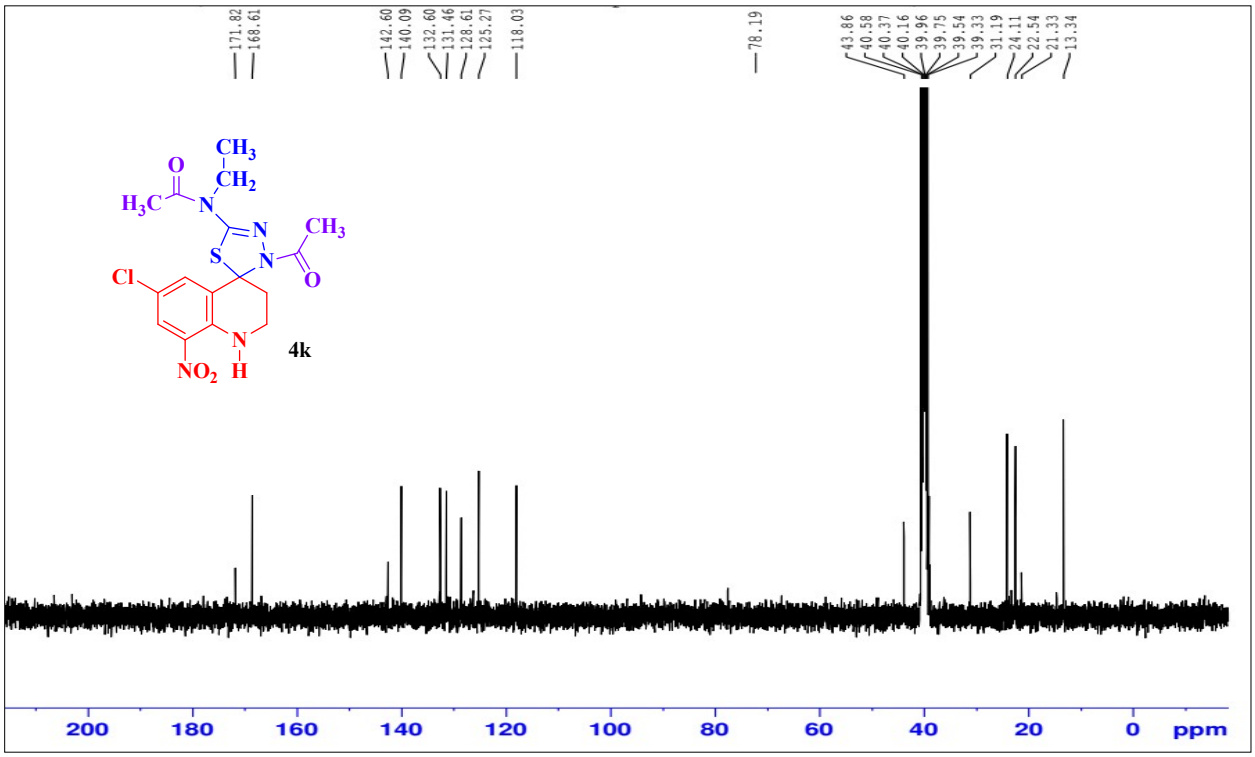


**Figure S25. $^{13}$C NMR spectrum of compound 4k**

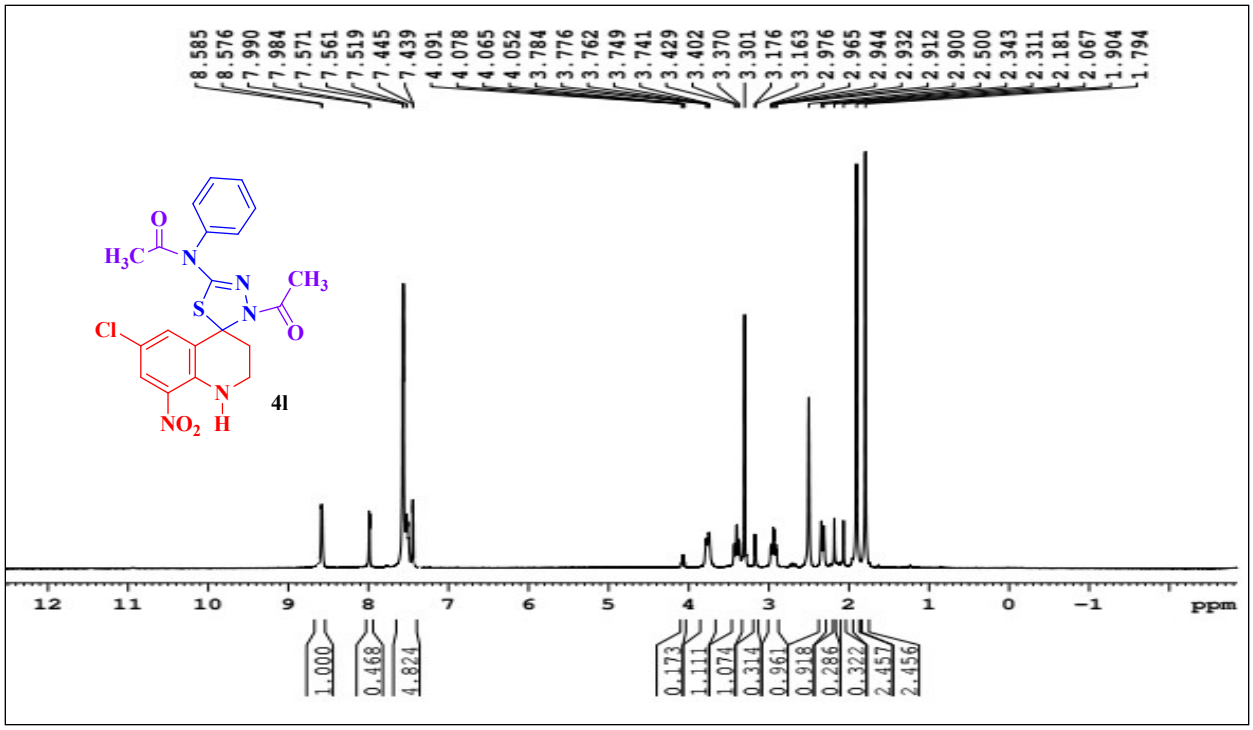


**Figure S26. $^{1}$H NMR spectrum of compound 4l**

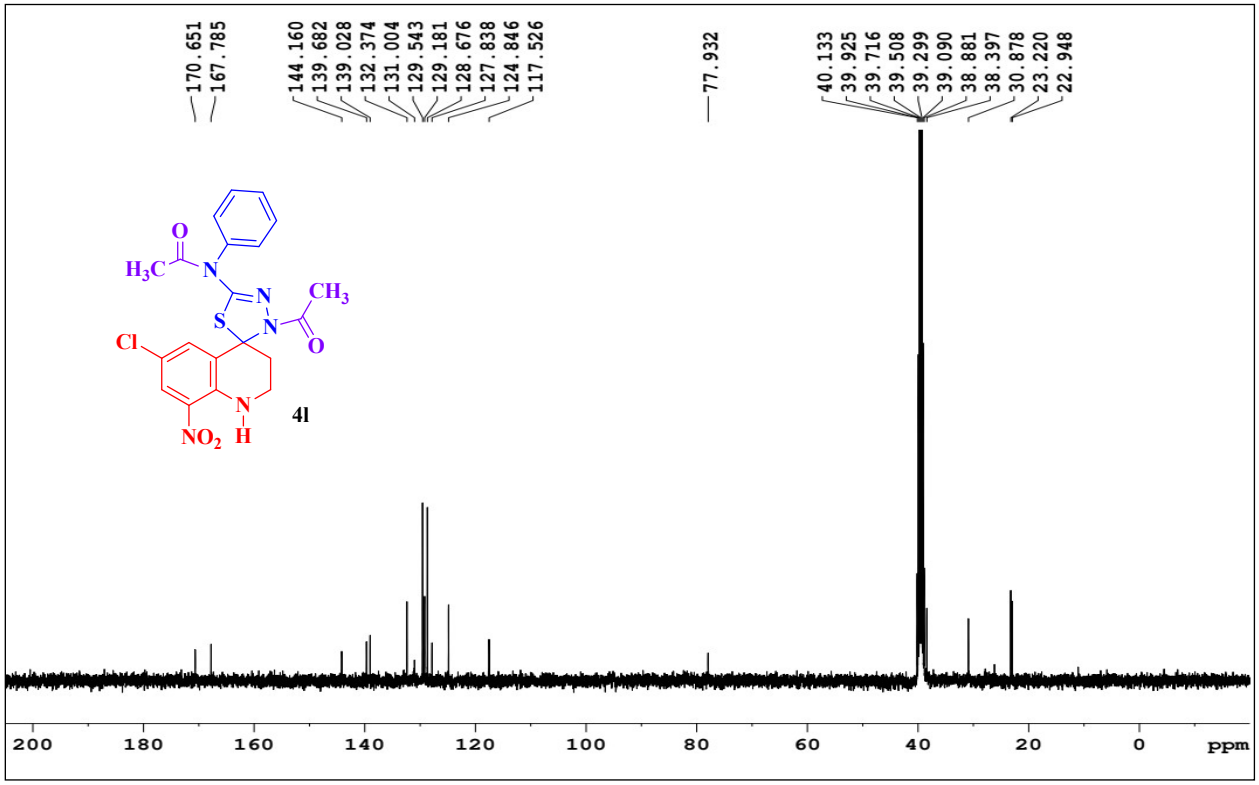


**Figure S27. $^{13}$C NMR spectrum of compound 4l**