Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Diclofenac derivatives as concomitant inhibitors of cholinesterase, monoamine oxidase, cyclooxygenase-2 and 5-lipoxygenase for the treatment of Alzheimer's disease: Synthesis, pharmacology, toxicity and docking studies

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Docking studies

In compound **11,** chlorine of dichlorobenzene moiety forms conventional H-bond with Gln192 and two halogen interactions each with Leu352 and Ser353. Ser353 also forms H-bond with NH group next to dichlorobenzene. Benzene ring next to NH group shows π-alkyl interaction with Arg513 and Val523. This Val523 is also show π-alkyl interaction with triazole ring and dichlorobenzene attached with triazole ring, this dichlorobenzene also shows show π-alkyl interaction with Leu352. Benzene ring of benzene sulfonamide shows π-alkyl interaction with Leu531. Sulfur of sulfonamide moiety form two π-sulfur bond each with Tyr348 and Tyr385 (**Figure S-1a**).

In compound **15** chlorines of dichlorobenzene moiety shows halogen interaction with Pro191 and Gly354. NH moiety next to carbonyl carbon form conventional H-bond with Gln192 and benzene ring next to NH functionality form π-lone pair interaction with Leu352. SO_2 of sulfonamide moiety form conventional H-bond Arg120 (**Figure S-1b**).

In compound **21** chlorine of dichlorobenzene moiety form conventional H-bond with Arg120 and sulfur moiety next to triazole ring show π-sulfur interaction with His90. Benzene of dichlorobenzene part next to NH shows two π-π T-shaped interactions with Tyr385 and Tyr387 respectively and amide π-stacked interaction with Gly526 and Ala527 while π-sulfur interaction with Met522 (**Figure S-1c**).

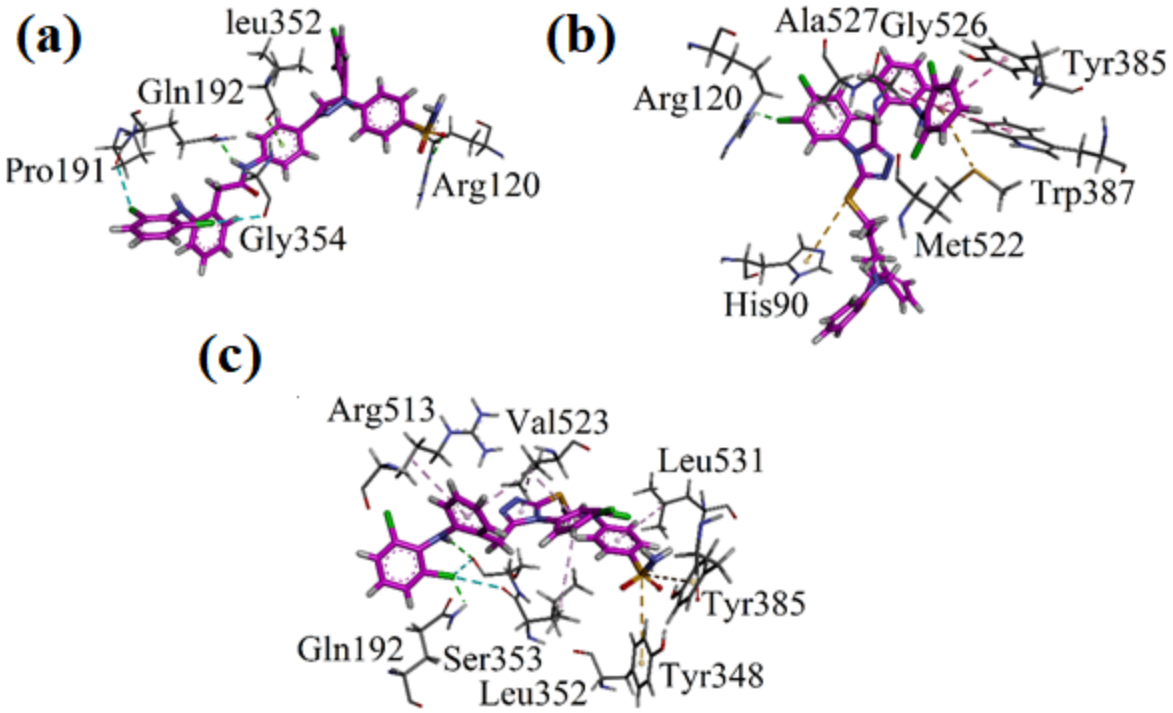

Figure S-1: 3-D docking interactions of synthesized compounds **11** (**a**), **15** (**b**) and **21**(**c**) with COX-2 (PDB ID = 1CX2) active site

Representative ^{1}H and ^{13}C NMR Spectrum

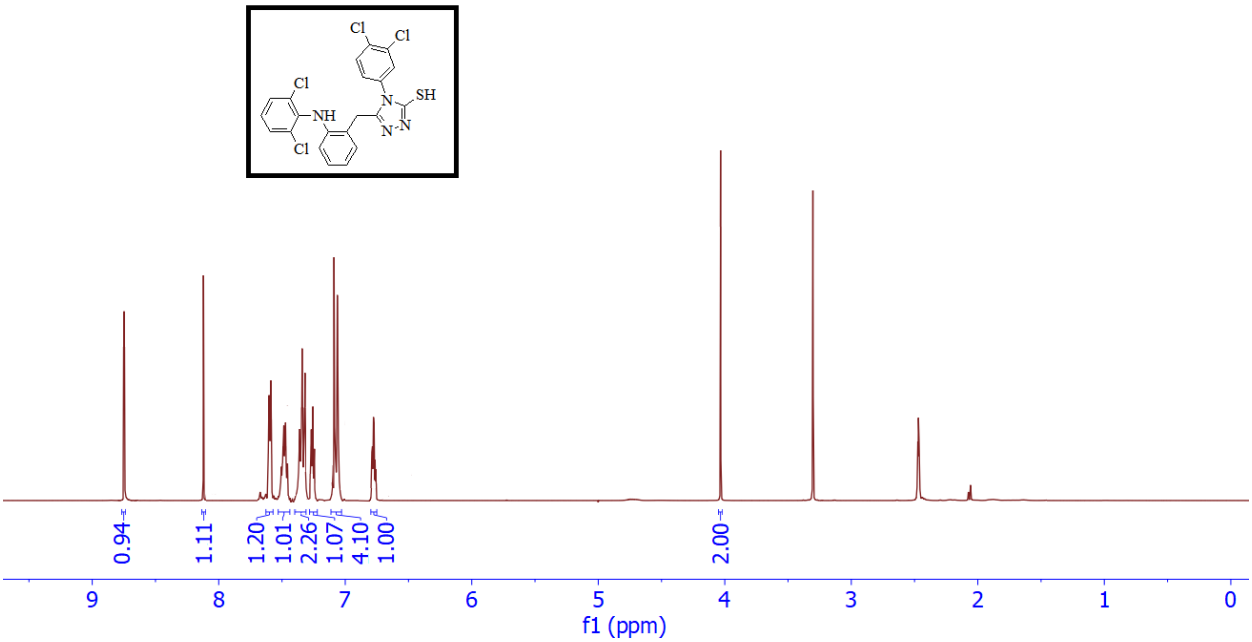

Figure S-2. ^{1}H NMR spectra of compound **12** (DMSO-d_6, 400 MHz)

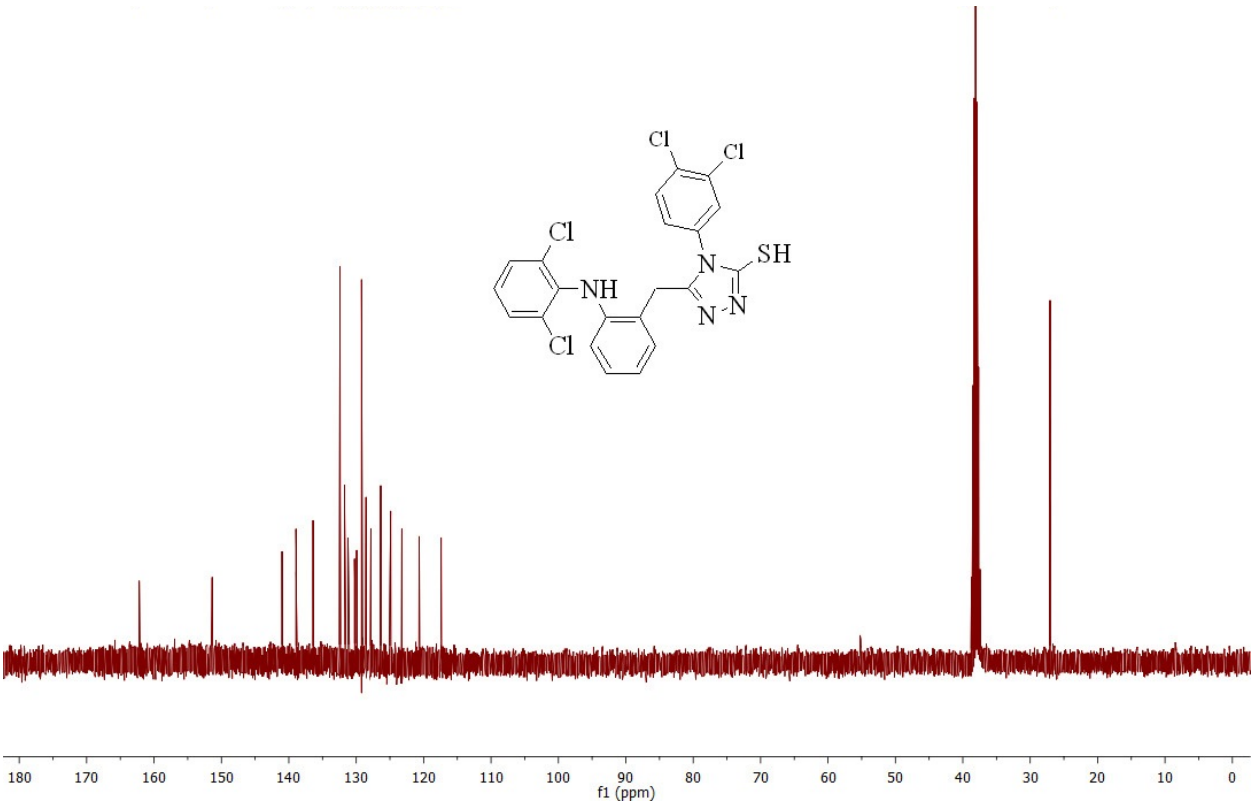

Figure S-3. ^{13}C NMR spectra of compound **12** (DMSO-d_6, 100 MHz)

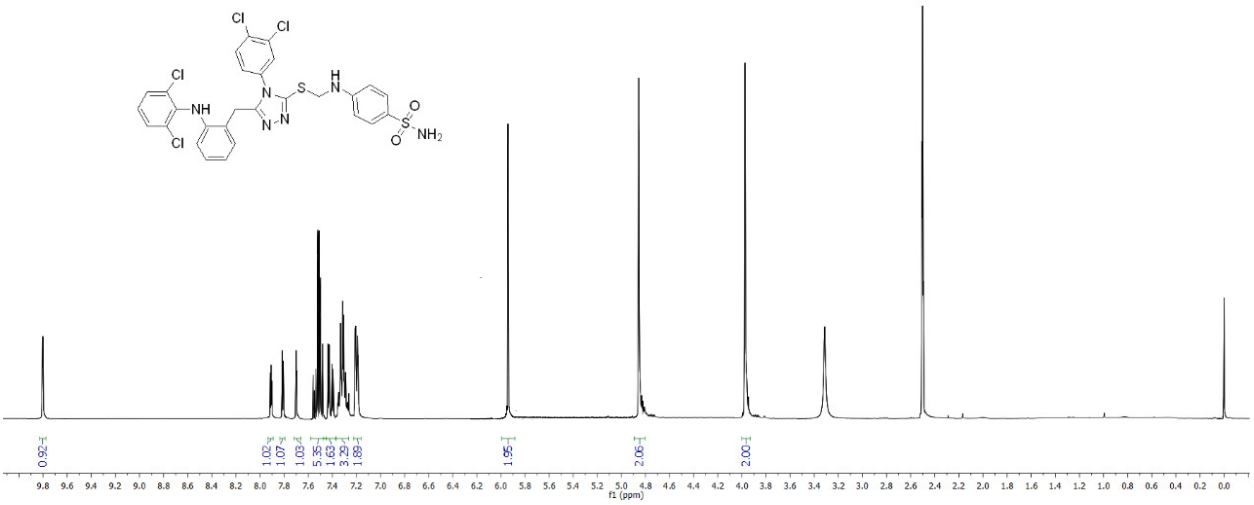

Figure S-4. ^{1}H NMR spectra of compound **15** (DMSO-d_6, 400 MHz)

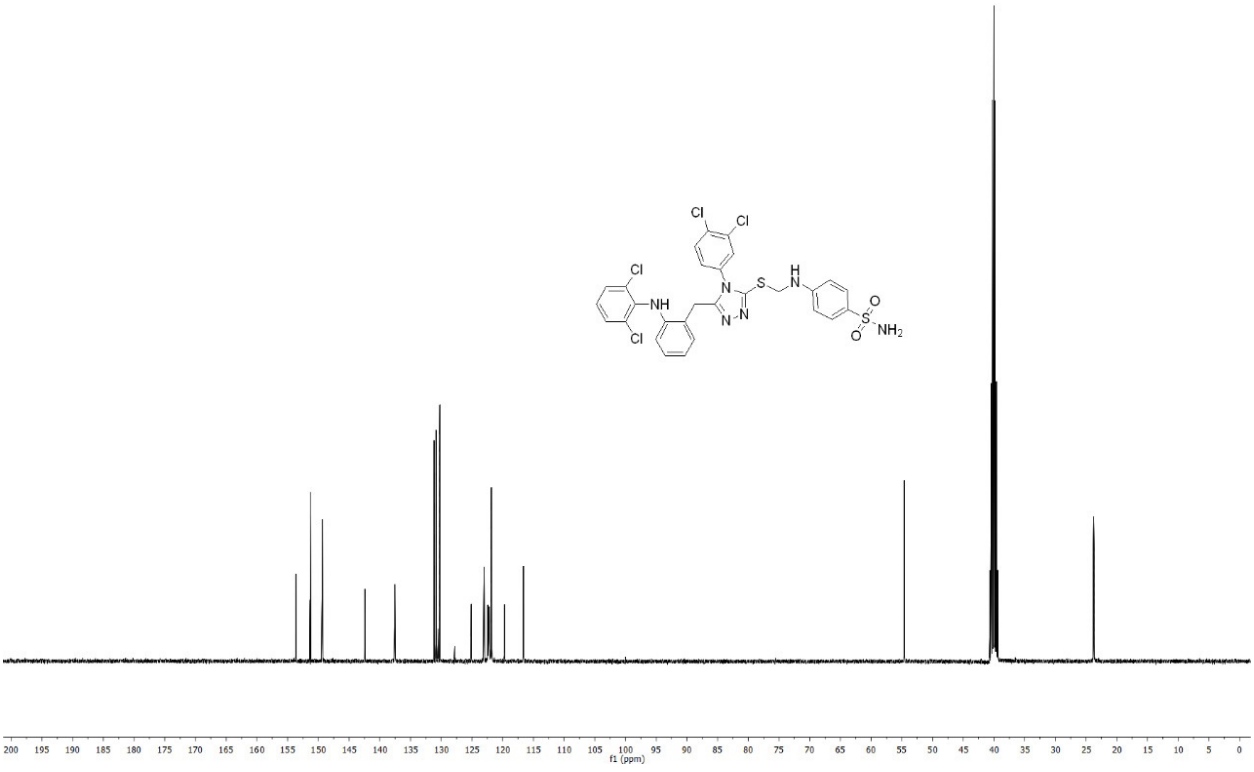

Figure S-5. ^{13}C NMR spectra of compound **15** (DMSO-d6, 100 MHz)

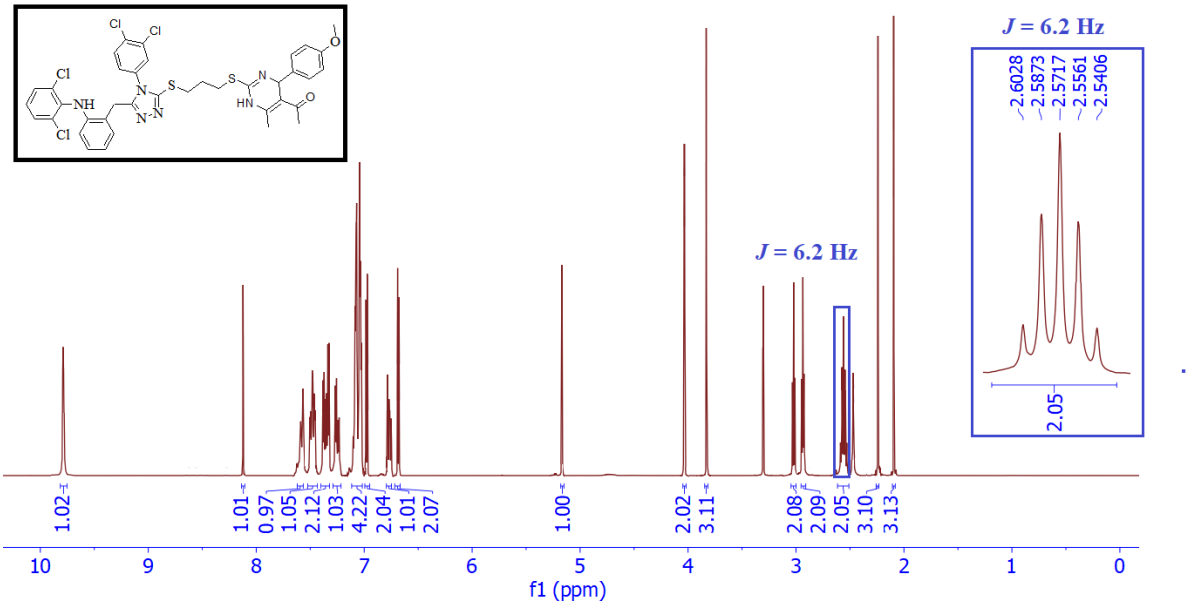

Figure S-6. ^{1}H NMR spectra of compound **26** (DMSO-d_6, 400 MHz)

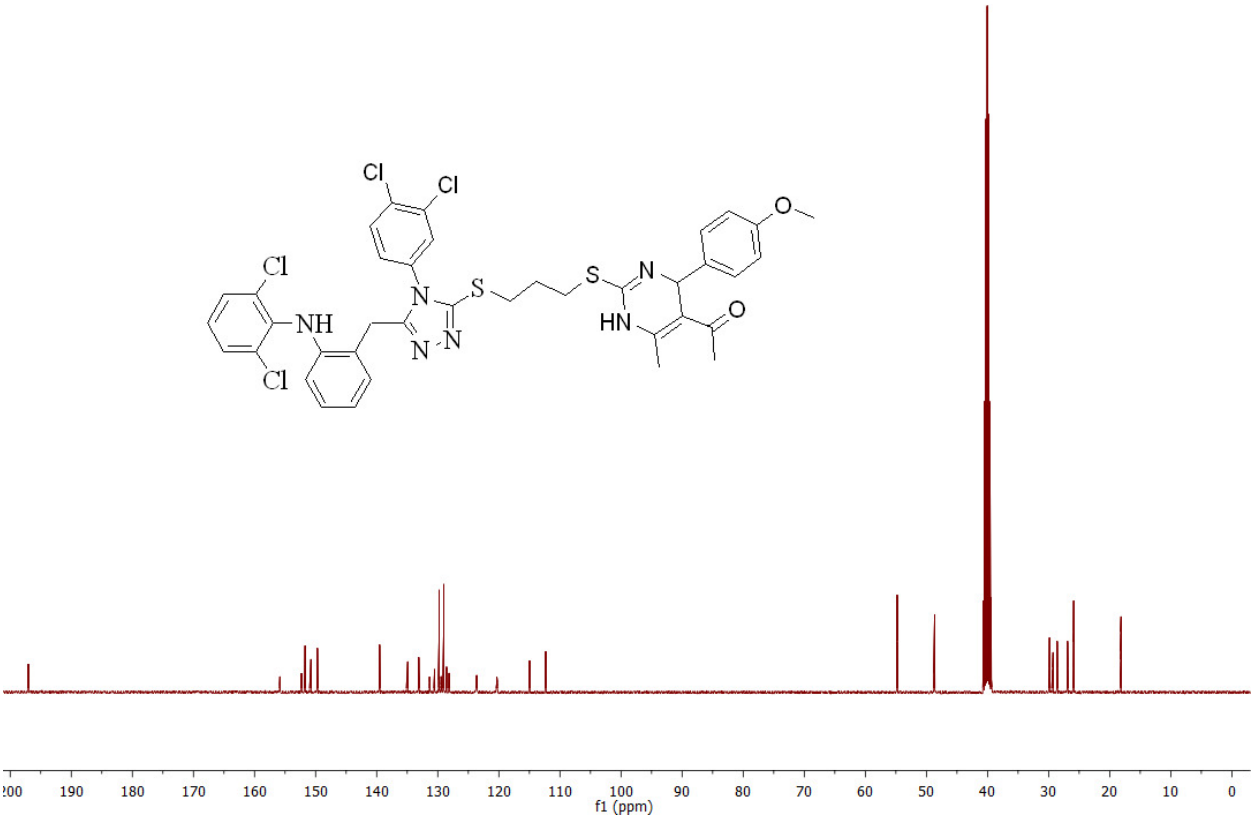

Figure S-7. ^{13}C NMR spectra of compound **26** (DMSO-d_6, 100 MHz)

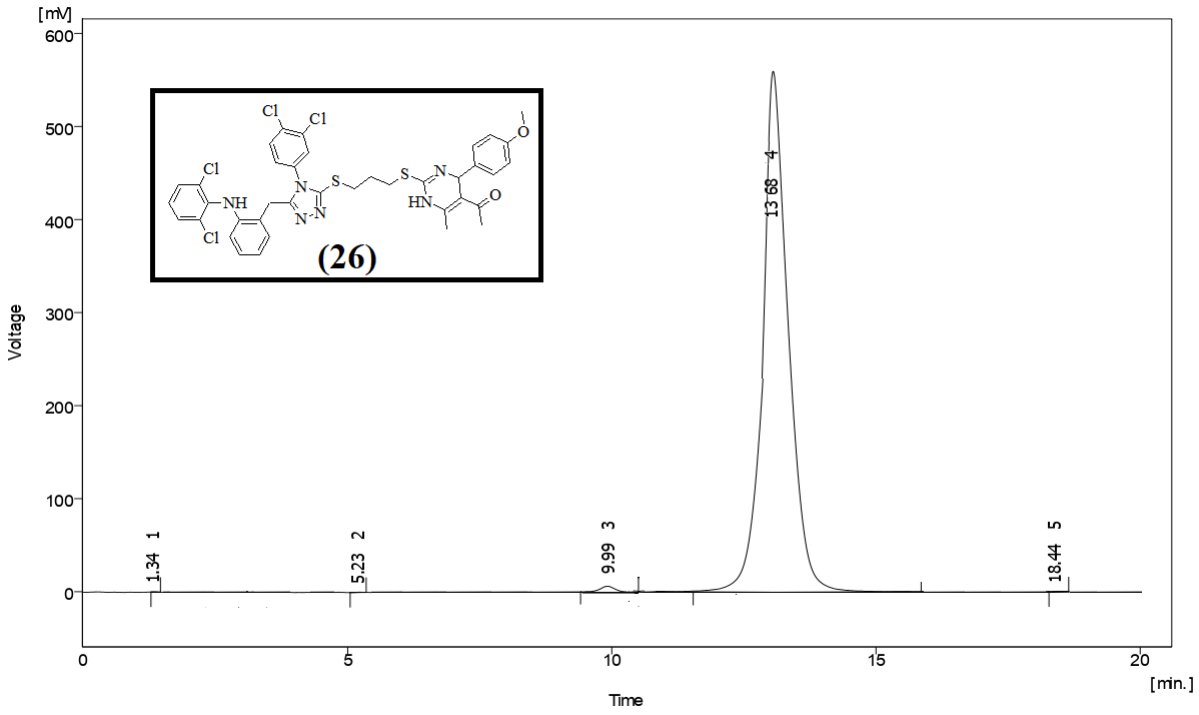

Figure S-8. HPLC chromatogram of compound **26**

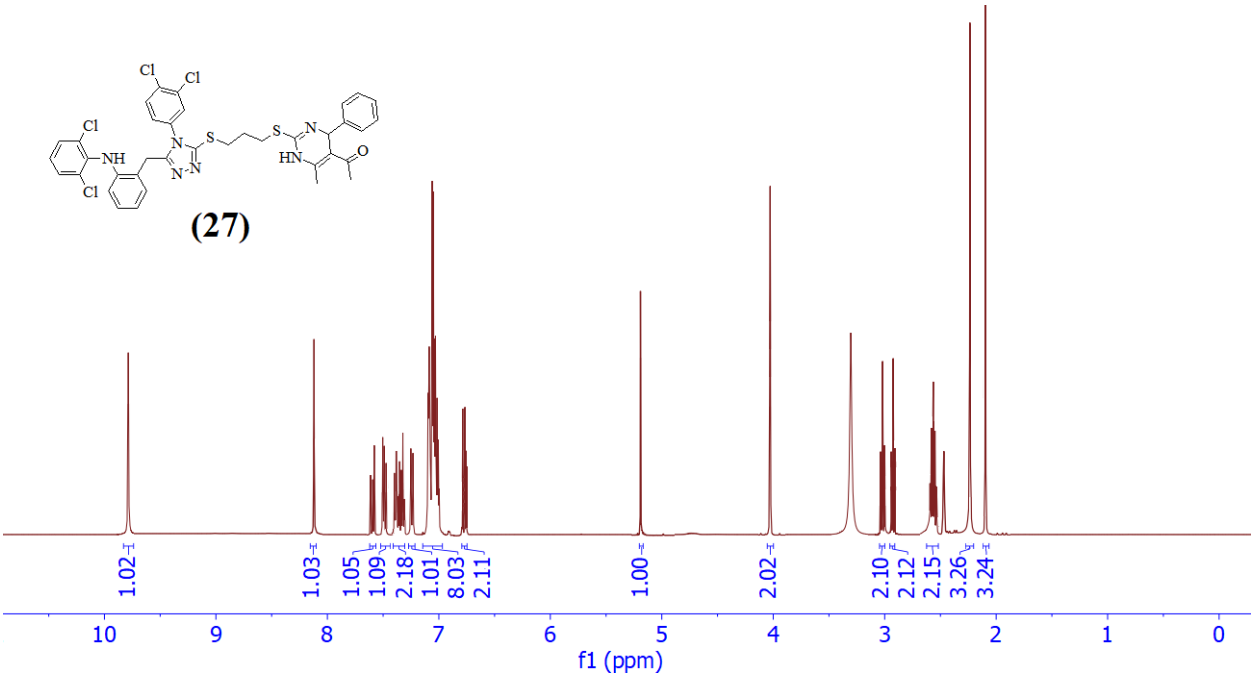

Figure S-9. ^{1}H NMR spectra of compound **27** (DMSO-d_6, 400 MHz)

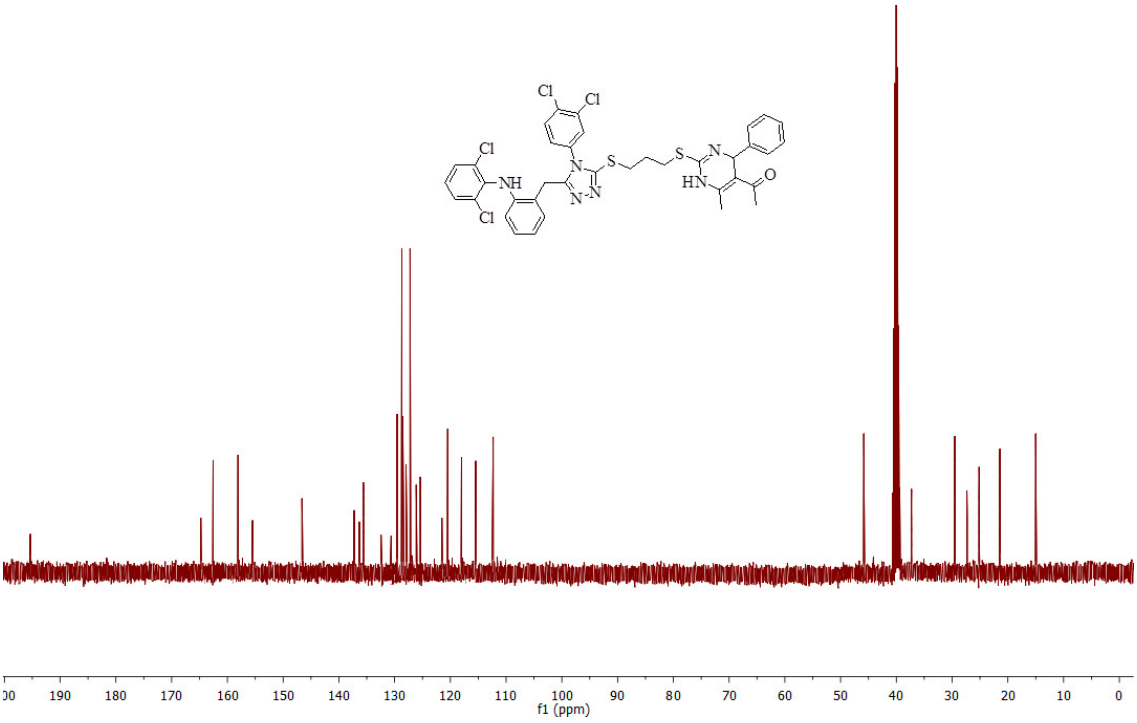

Figure S-10. ^{13}C NMR spectra of compound **27** (DMSO-d_6, 100 MHz)

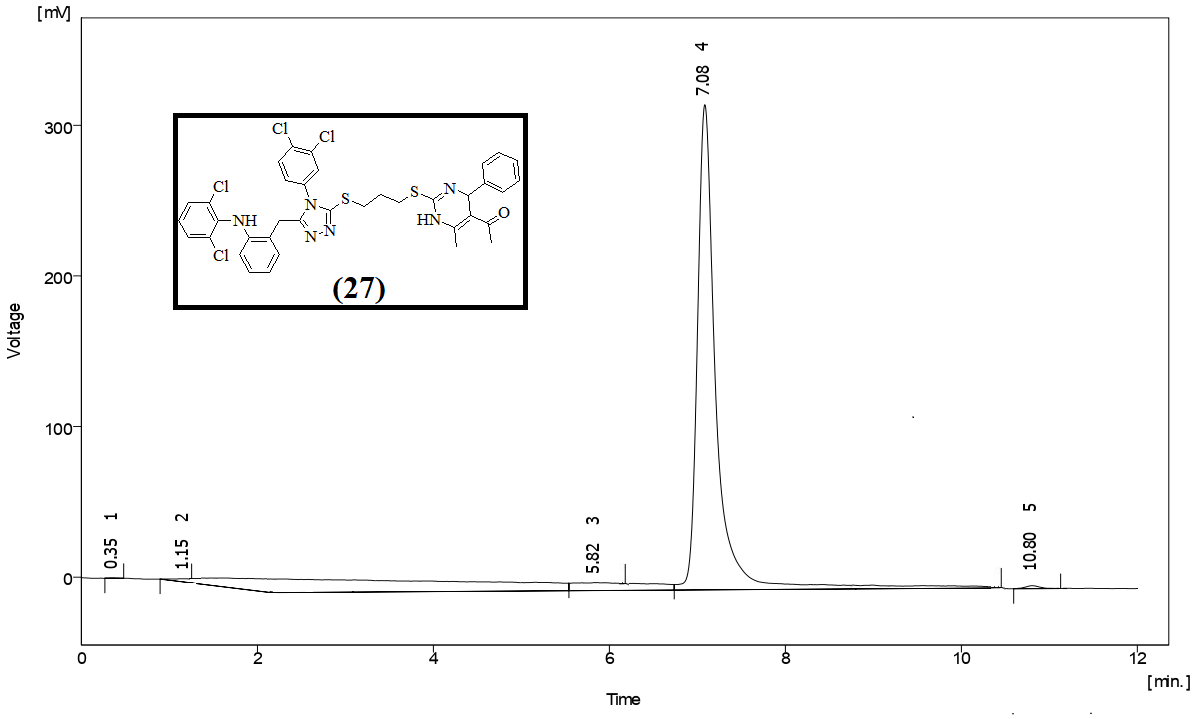

Figure S-11. HPLC chromatogram of compound **27**

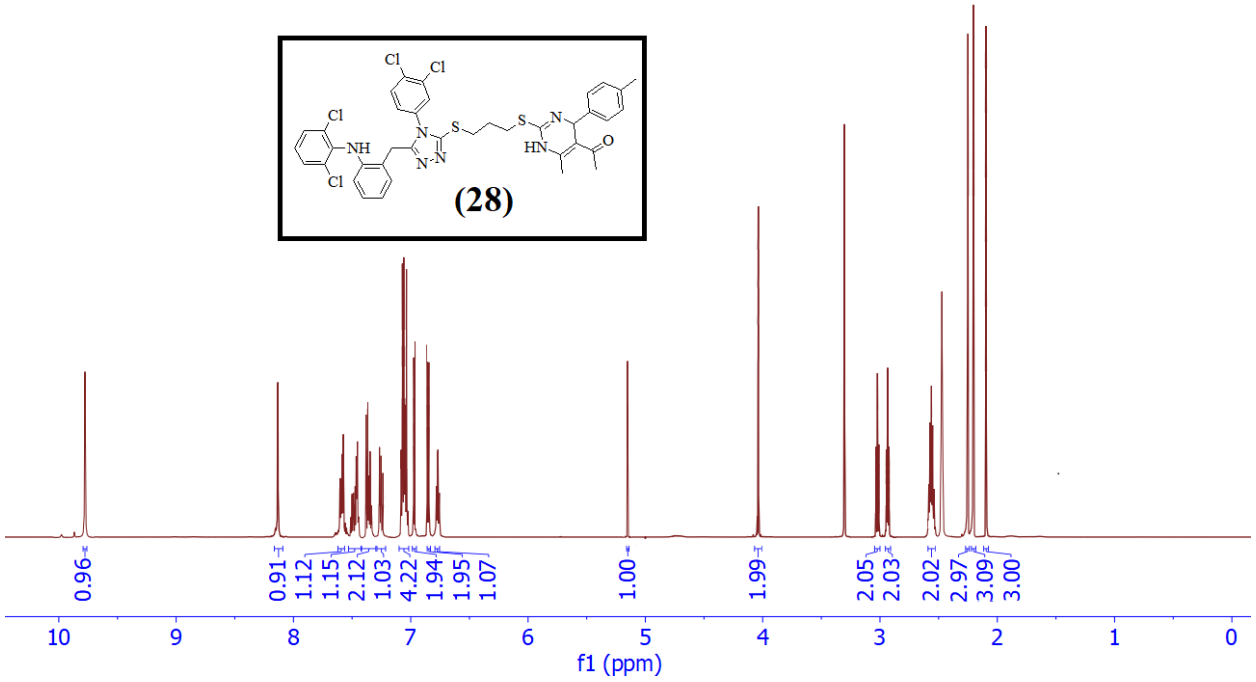

Figure S-12. ^{1}H NMR spectra of compound **28** (DMSO-d_6, 400 MHz)

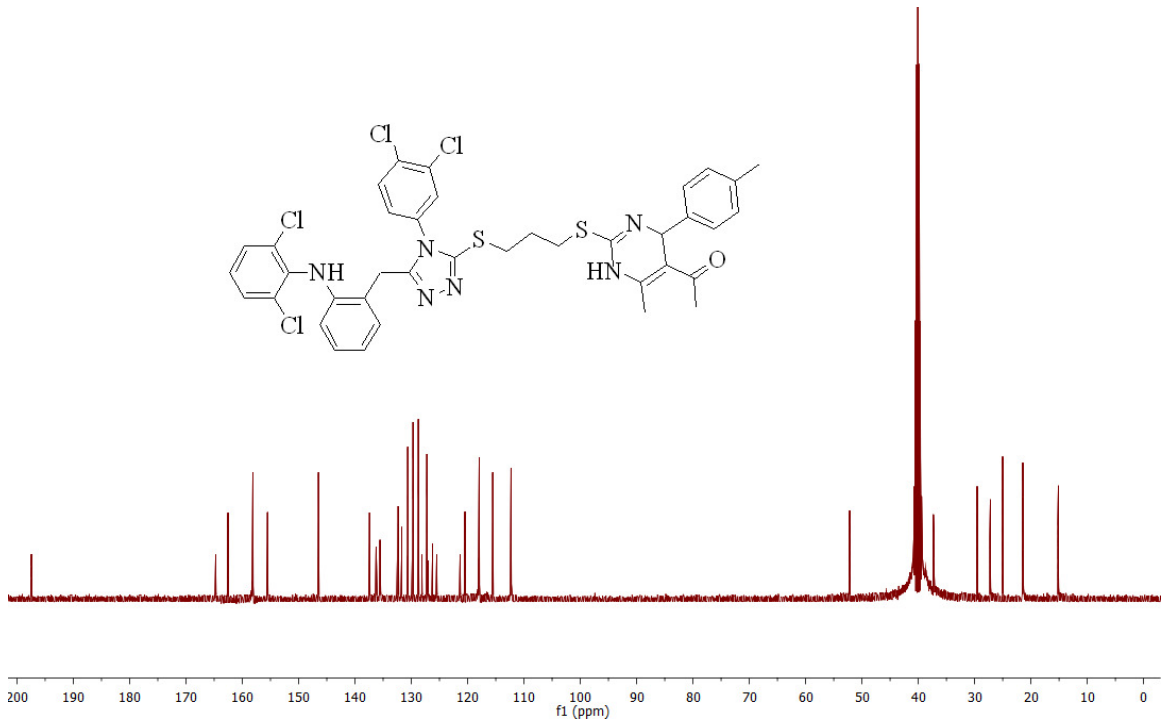

Figure S-13. ^{13}C NMR spectra of compound **28** (DMSO-d_6, 100 MHz)

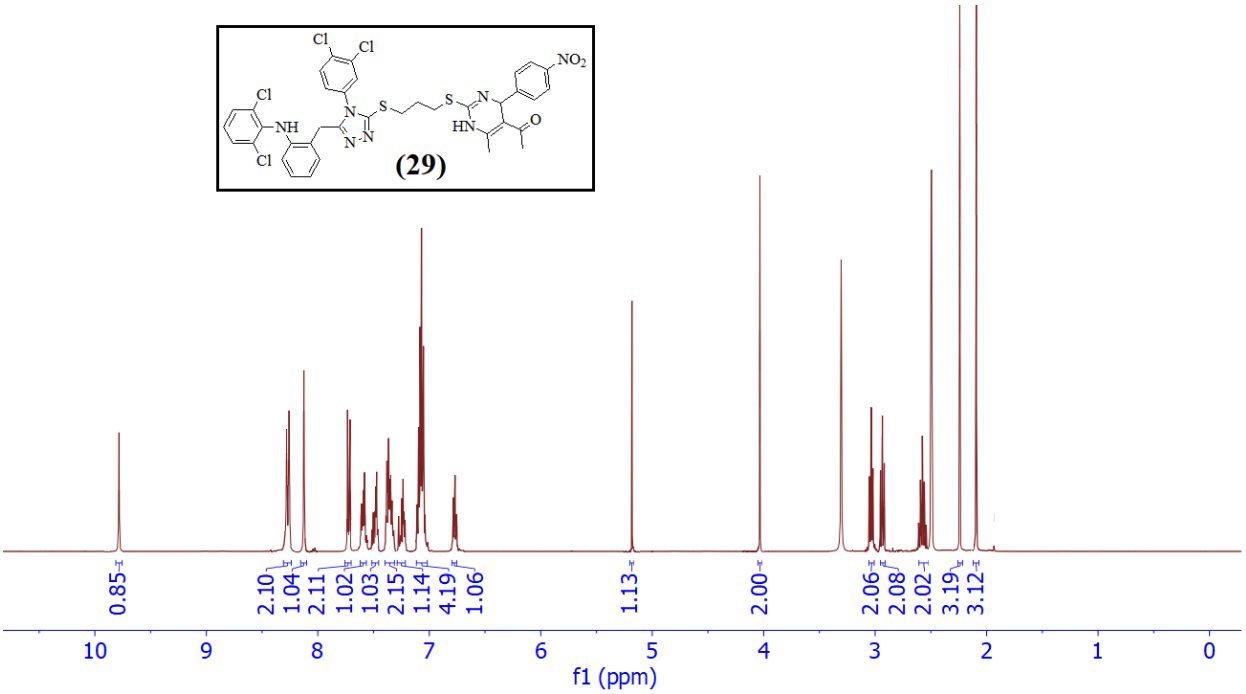

Figure S-14. ^{1}H NMR spectra of compound **29** (DMSO-d_6, 400 MHz)

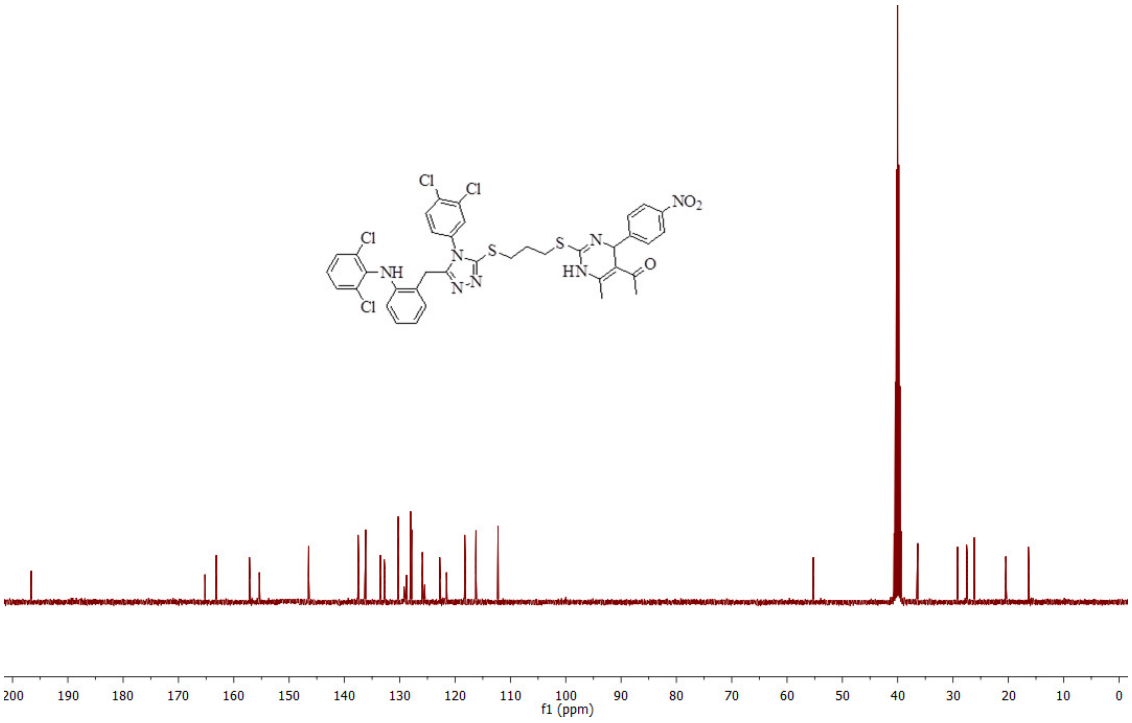

Figure S-15. ^{13}C NMR spectra of compound **29** (DMSO-d_6, 100 MHz)

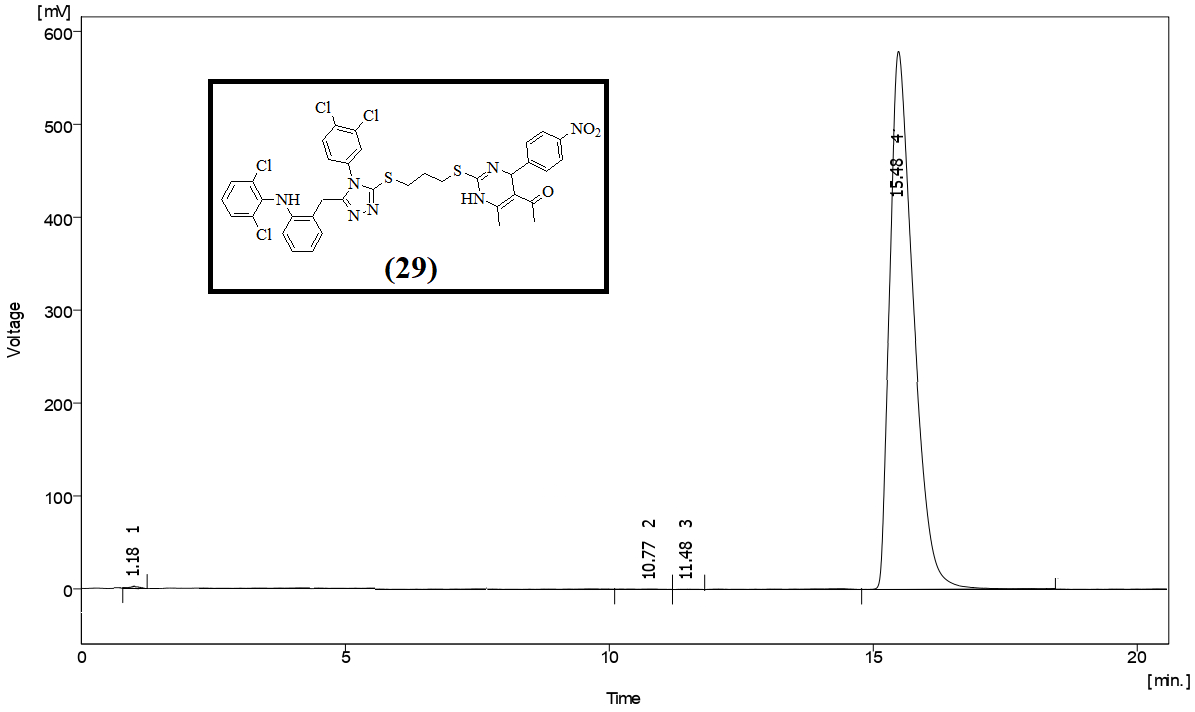

Figure S-16. HPLC chromatogram of compound **29**

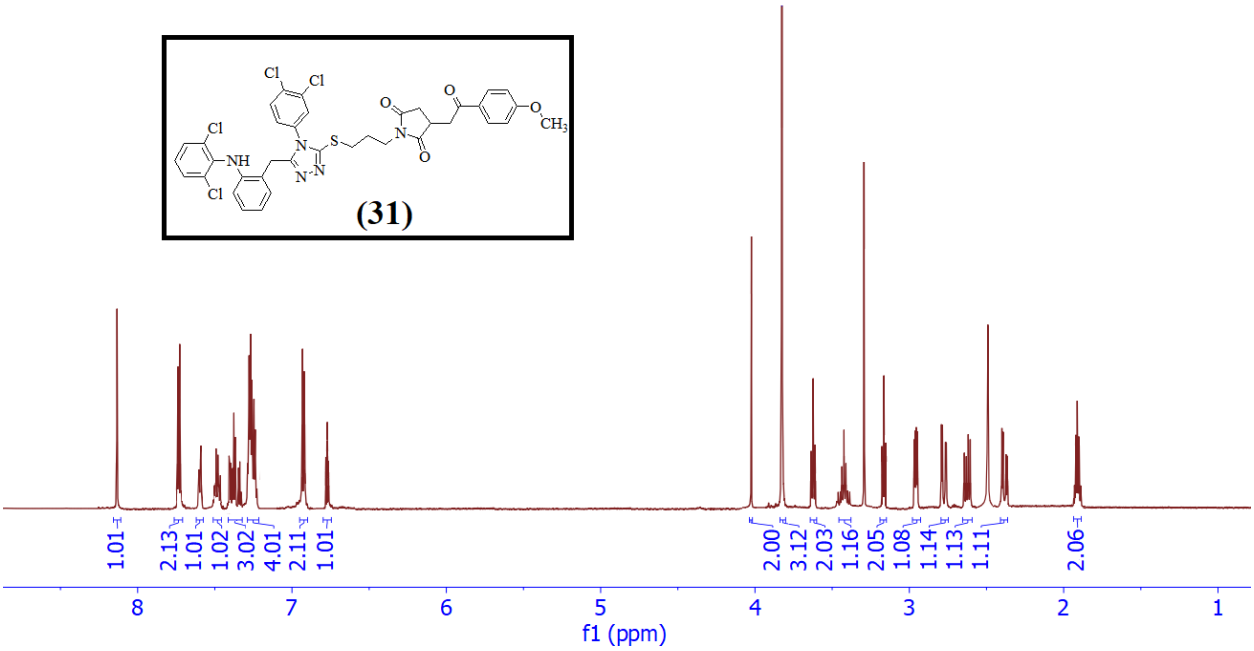

Figure S-17. ^{1}H NMR spectra of compound **31** (DMSO-d_6, 400 MHz)

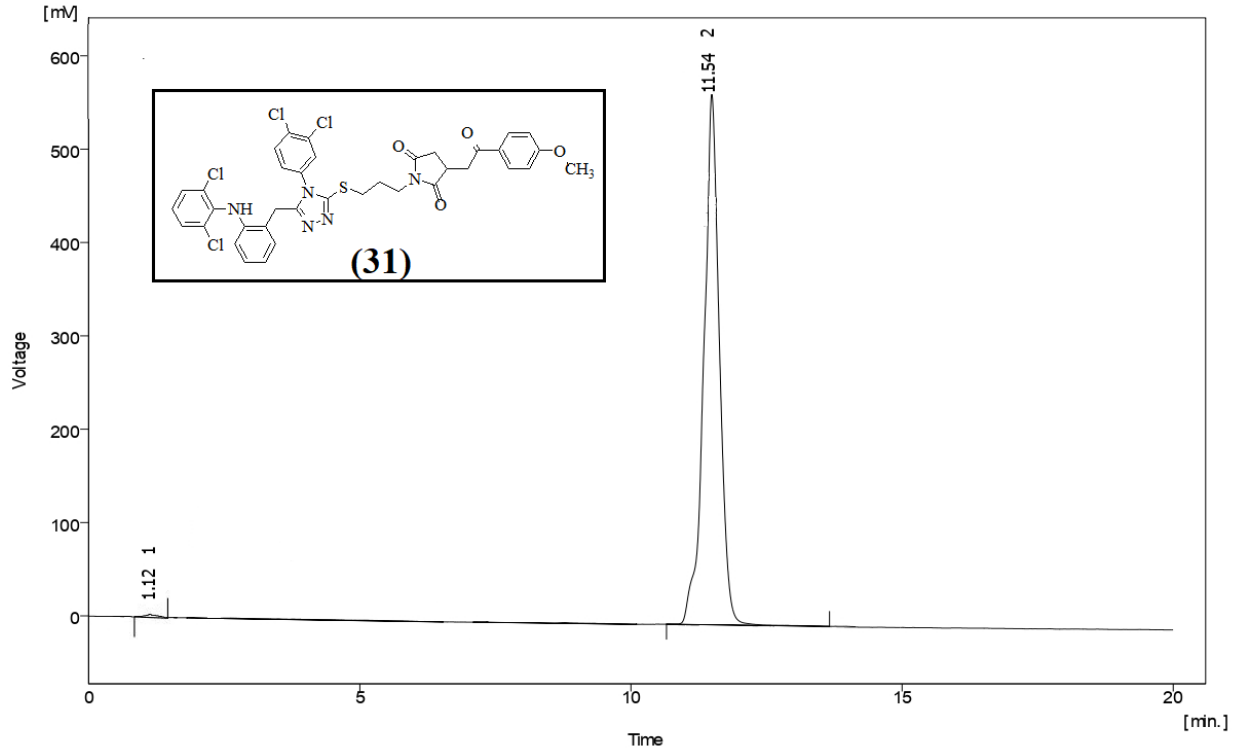

Figure S-18. HPLC chromatogram of compound **31**

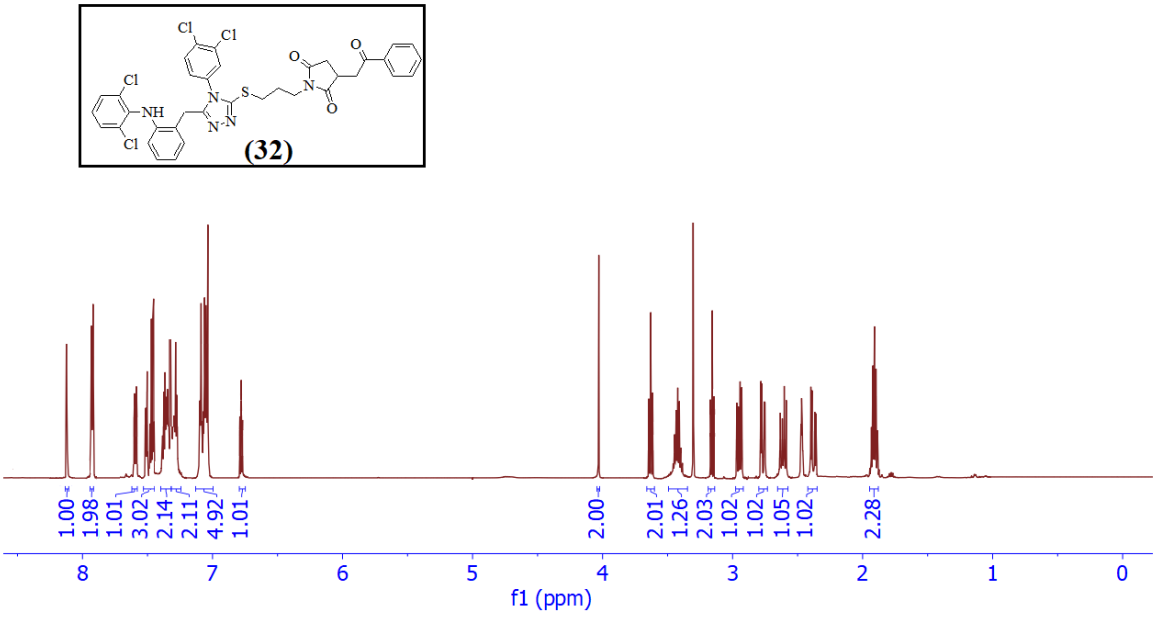

Figure S-19. ^{1}H NMR spectra of compound **32** (DMSO-d_6, 400 MHz)

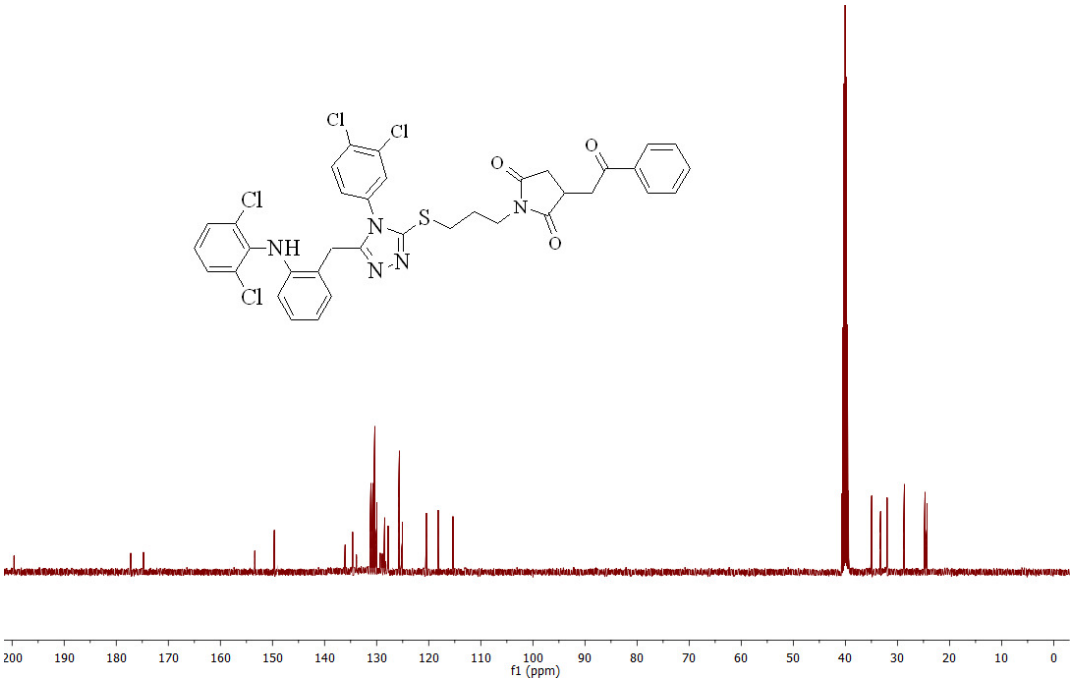

Figure S-20. ^{13}C NMR spectra of compound **32** (DMSO-d_6, 100 MHz)

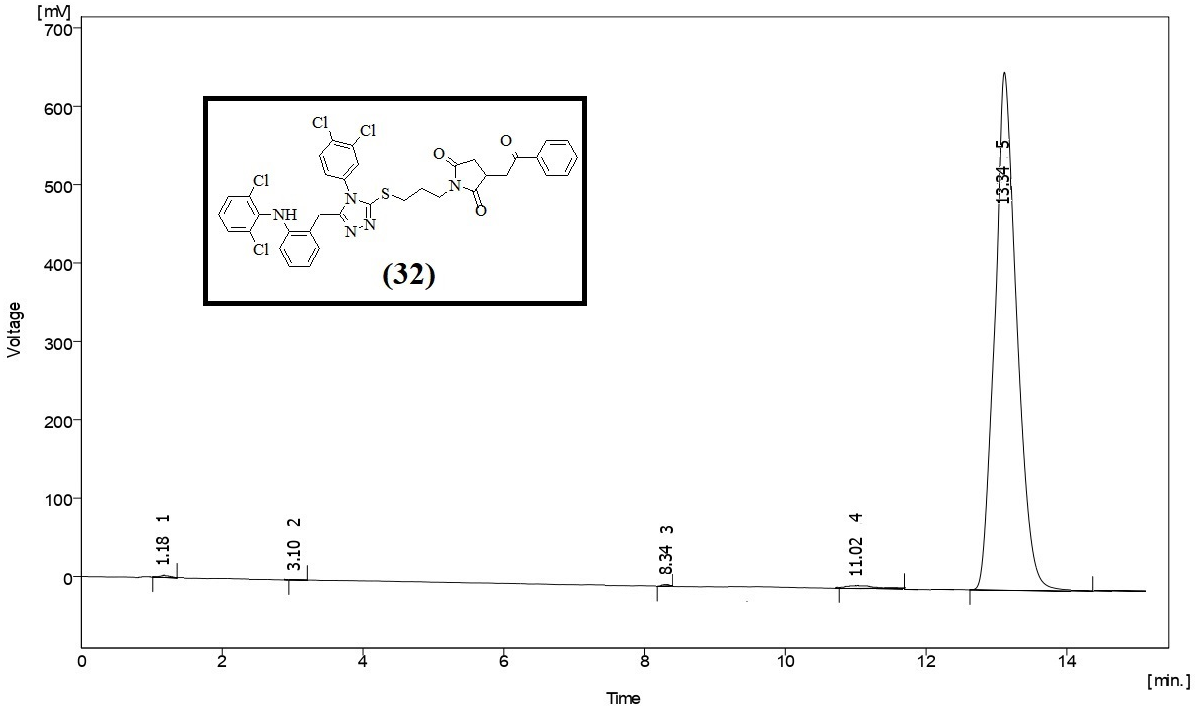

Figure S-21. HPLC chromatogram of compound **32**

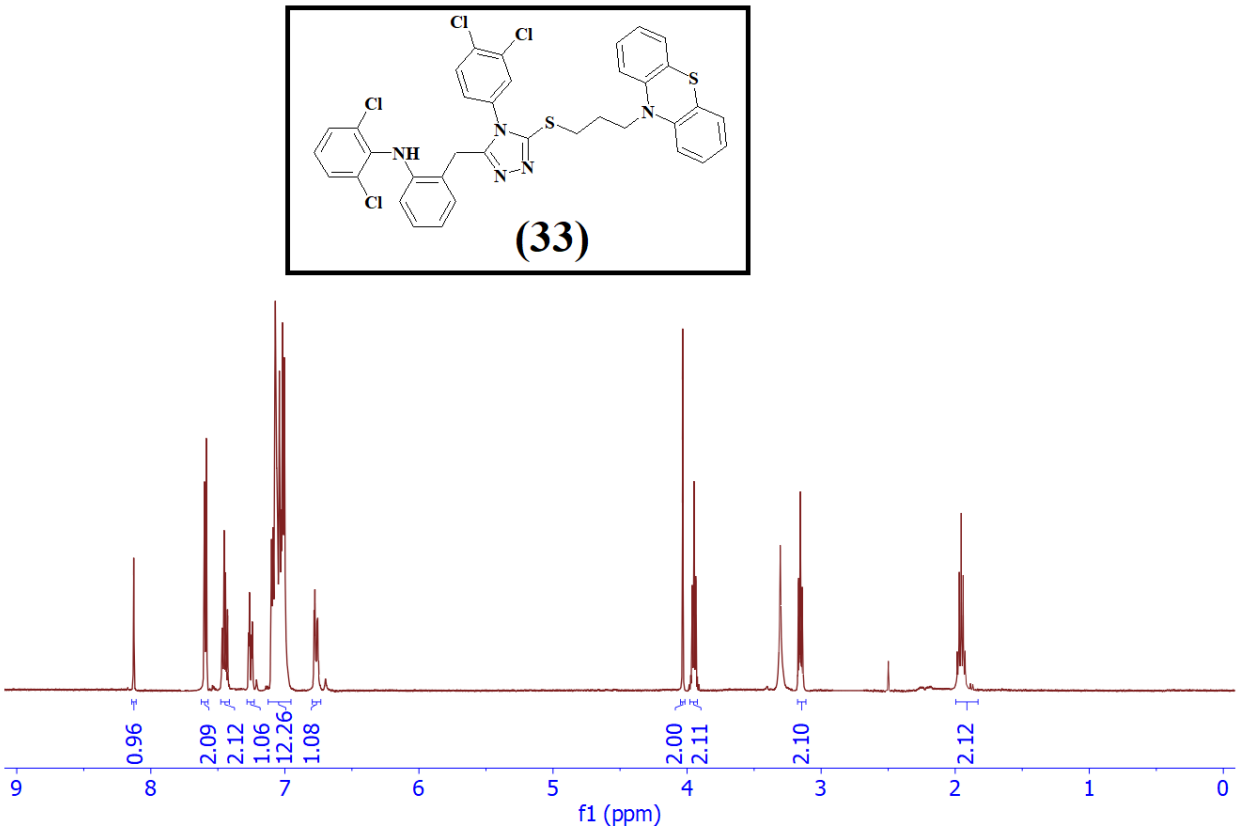

Figure S-22. ^{1}H NMR spectra of compound **33** (DMSO-d_6, 400 MHz)

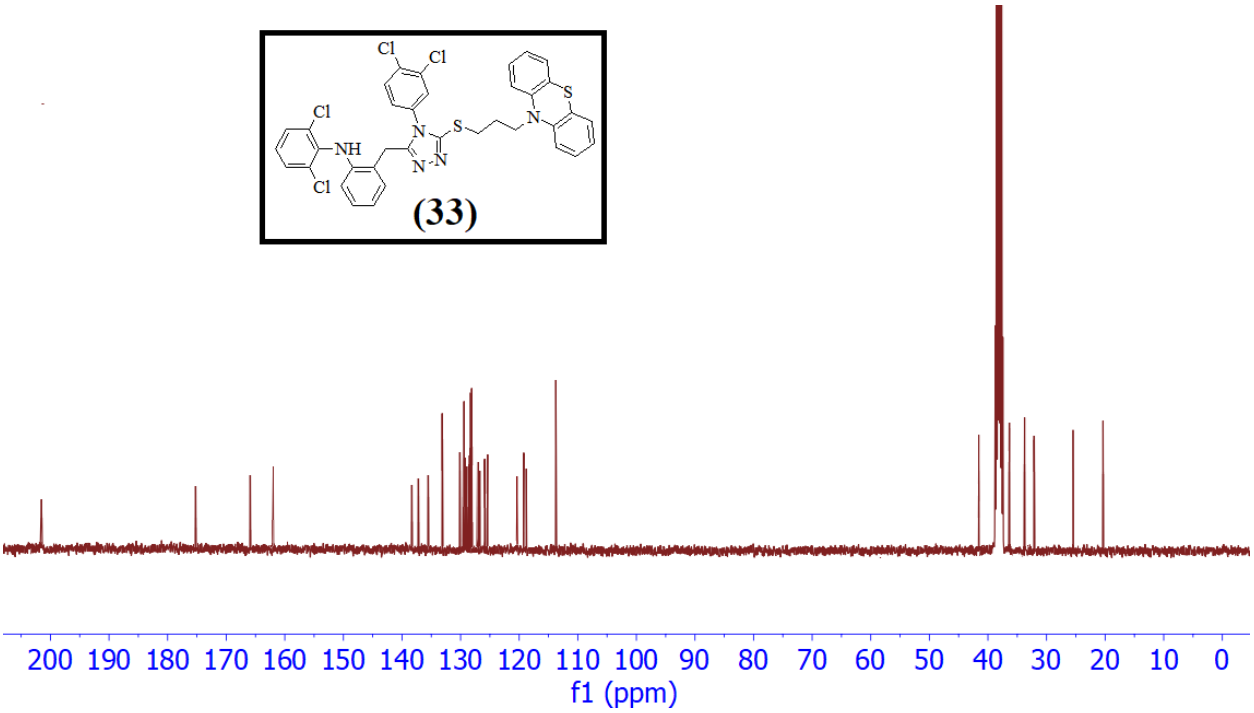

Figure S-23. ^{13}C NMR spectra of compound **33** (DMSO-d_6, 100 MHz)

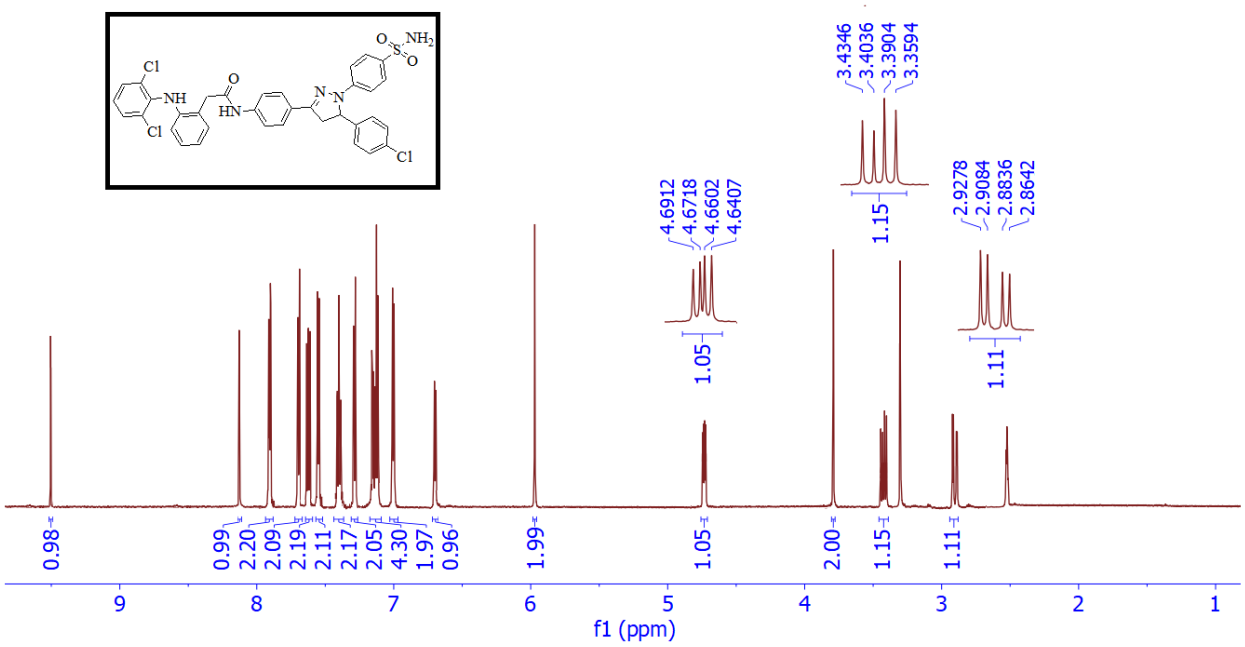

Figure S-24. ^{1}H NMR spectra of compound **39** (DMSO-d_6, 400 MHz)

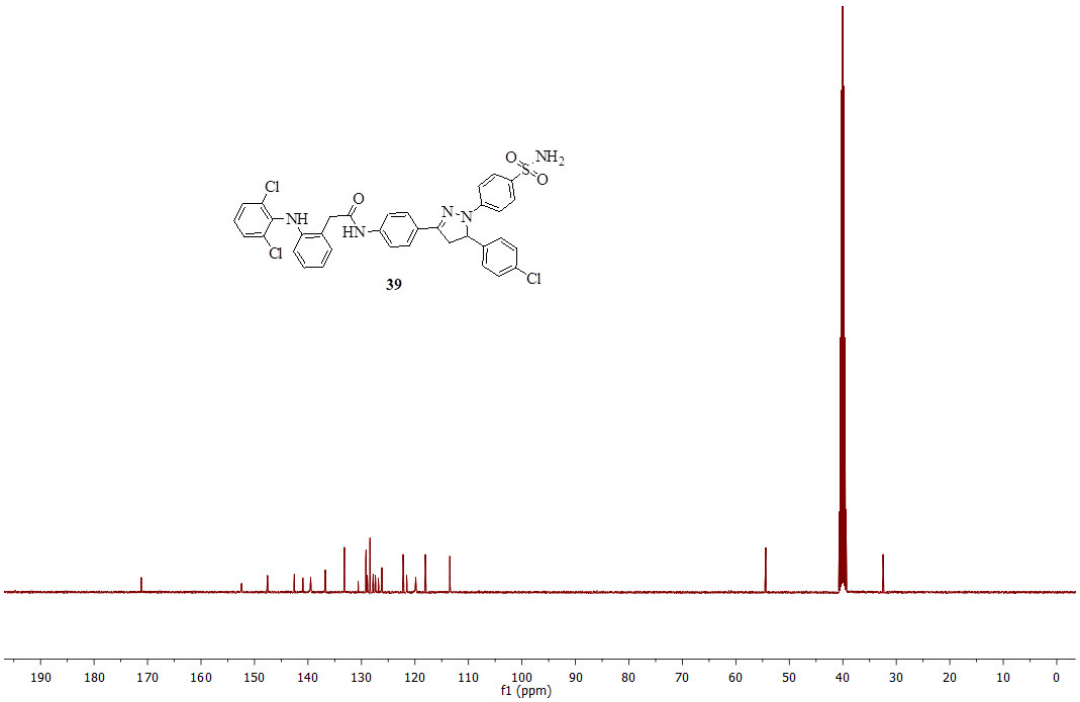

Figure S-25. ^{13}C NMR spectra of compound **39** (DMSO-d_6, 100 MHz)

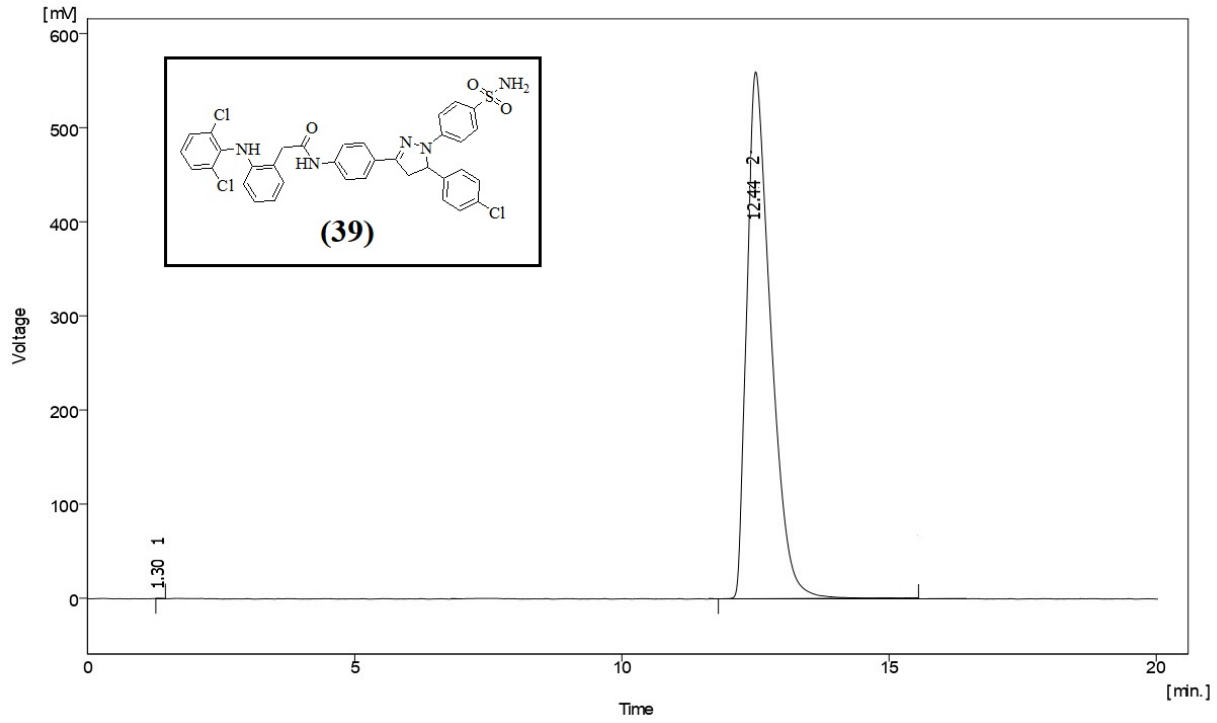

Figure S-26. HPLC chromatogram of compound **39**