Synthesis, Molecular docking and biological investigations of new pyrazolone chalcones

Ahmed A. Noser[1*], Maha M. Salem[2], Mohamed H. Baren [1] Adel I Selim [1], Esraa M. ElSafty[1], Hamada S.A. Mandour [1]

S1. Materials and Instrumentations

Unless otherwise stated, all reagents of analytical grade were purchased from Sigma-Aldrich and were used without further purification. All melting points were measured without corrections on a Gallenkamp melting point apparatus. The Fourier transform infrared spectroscopy (FTIR) spectra were recorded on a Perkin-Elmer FTIR 1430 spectrophotometer using KBr disk technique. The ^{1}H nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AC spectrometer (400 MHz) at 25 ^{o}C in DMSO-*d6* with TMS as an internal standard, and chemical shifts are reported in parts per million as d values; ^{13}C NMR was set at 101 MHz. Elemental analyses for C, H and N were also carried out and the values were found to be within ±0.4% of the theoretical ones unless otherwise indicated. Reaction progress was monitored by thin layer chromatography.

S2. *in-silico* studies

Using molecular docking experiments, the binding mechanisms of azo pyrazolones to the target protein YAP/TEAD were evaluated. target's crystal structures were provided by the RCSB protein data (PDB: #3KYS) (https://www.rcsb.org/structure/3KYS) . The enzyme-ligand interaction was investigated using Molegro Virtual Docker (2008) (http://molexus.io/molegro-virtual-docker/) . YAP/TEAD protein intermolecular interactions with azo pyrazolones were visualized using the Discovery Studio 3.5 software (https://discover.3ds.com/discovery-studio-visualizer-download). To estimate ADMET features, the web application SwissADME (http://www.swissadme.ch/) was employed.

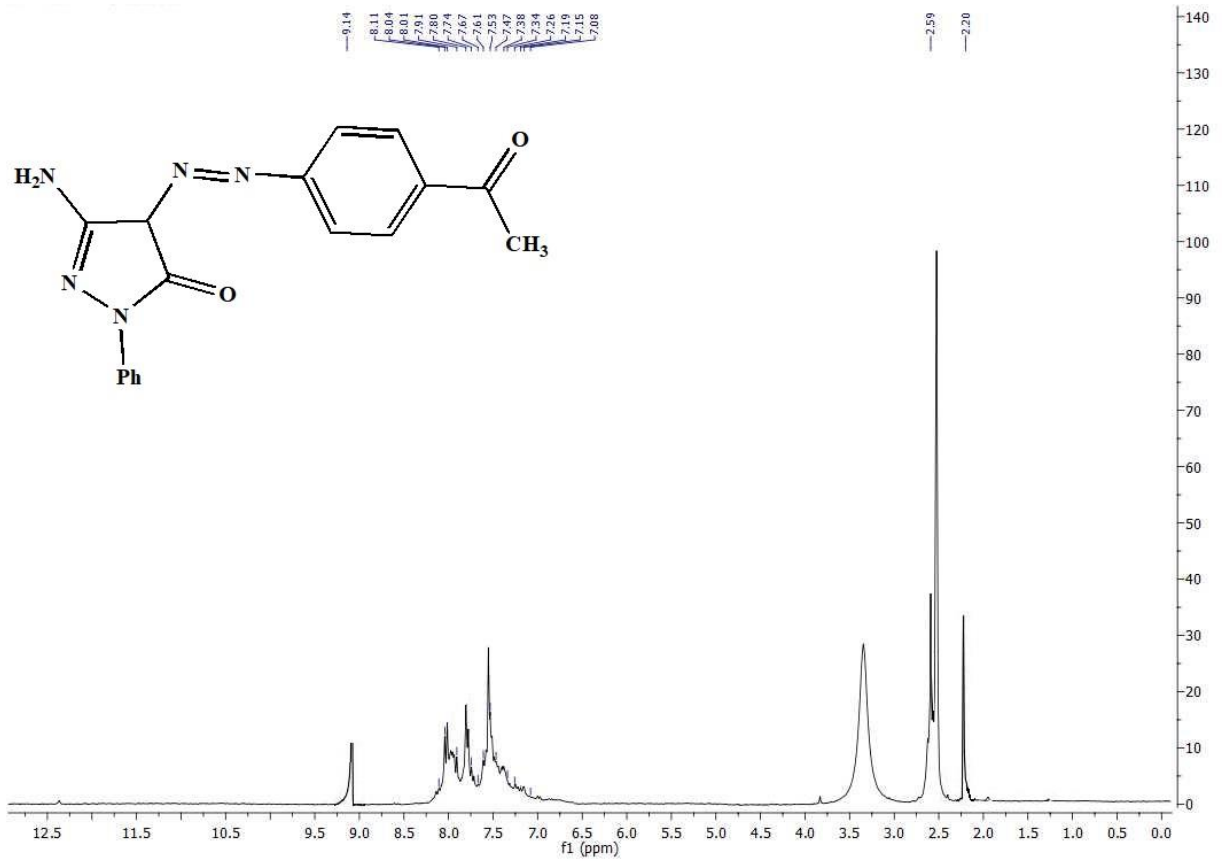

Fig. S1[1]H-NMR spectrum of compound **2**

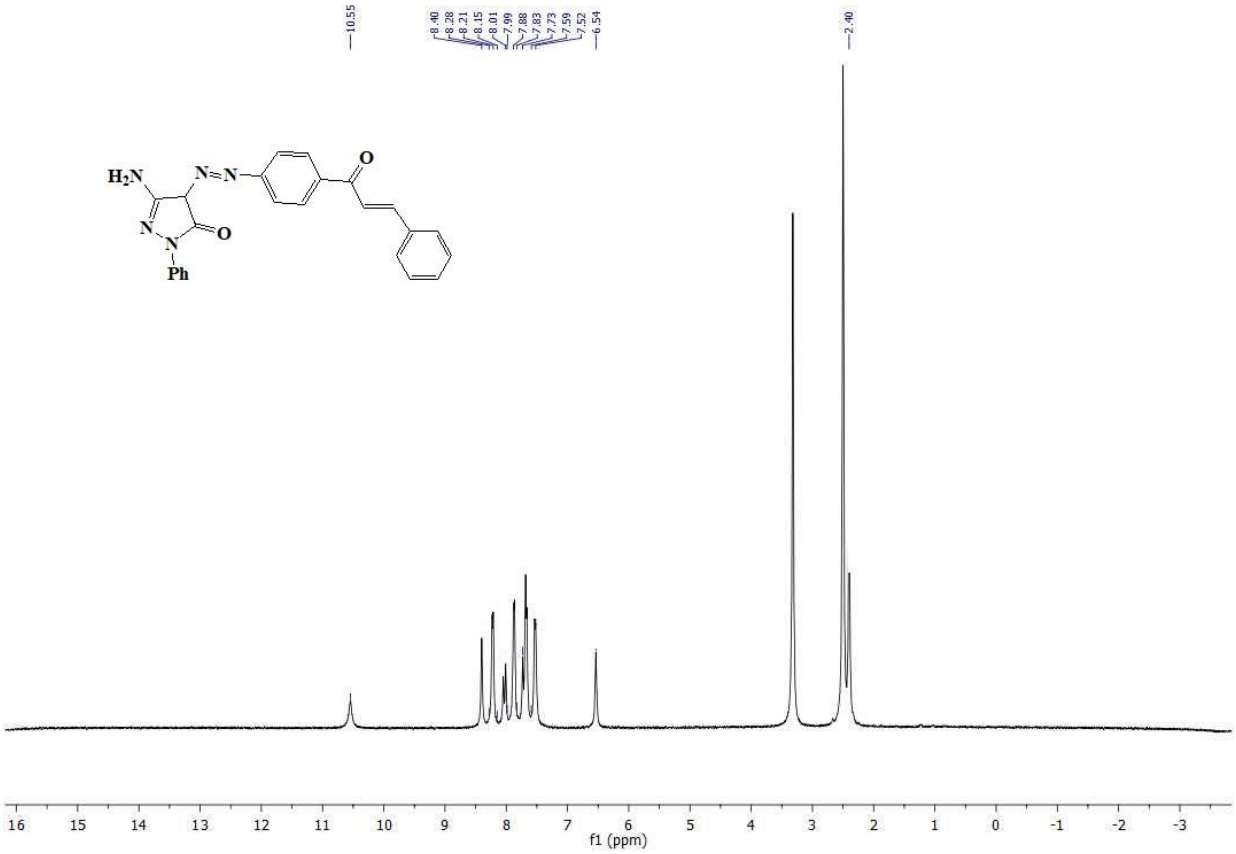

Fig. S2 ^{1}H-NMR spectrum of **compound 3a**

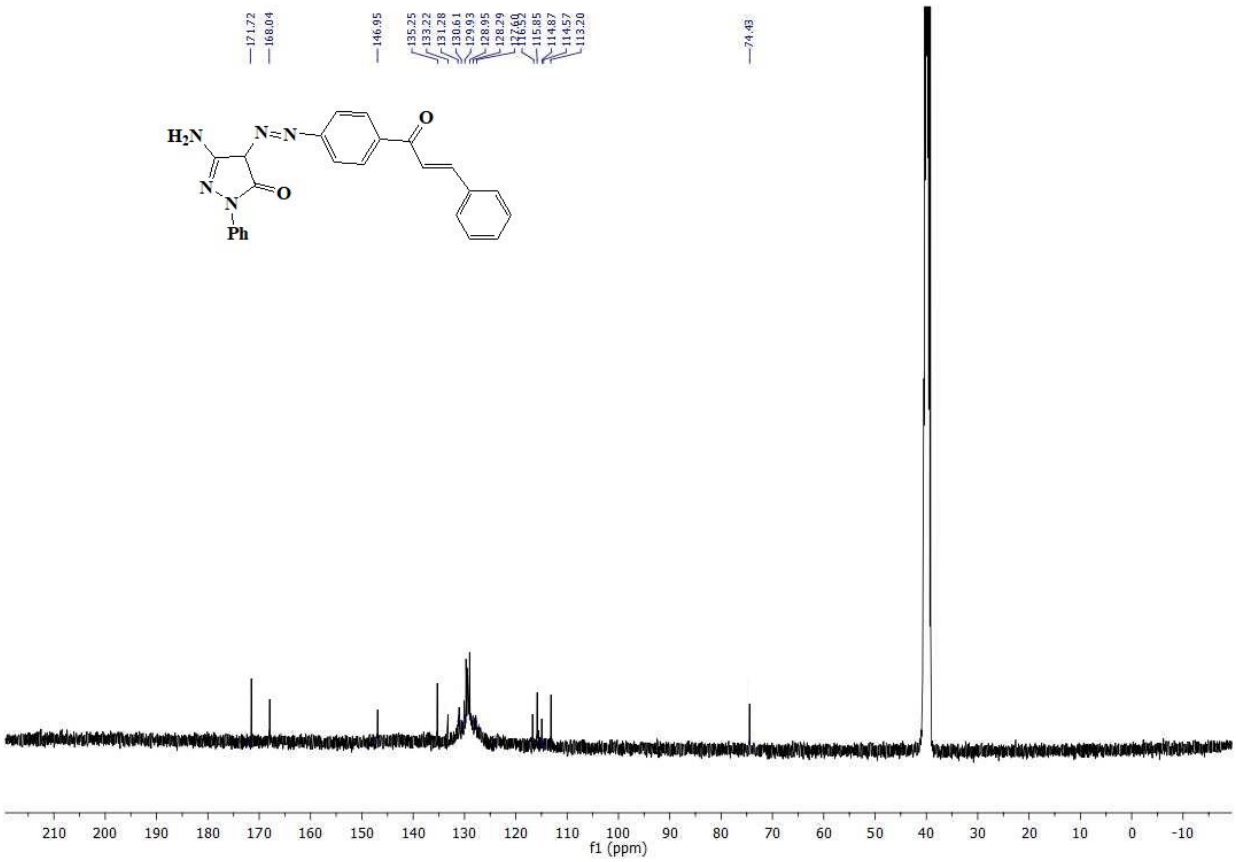

Fig. S3 ^{13}C-NMR spectrum of **compound 3a**

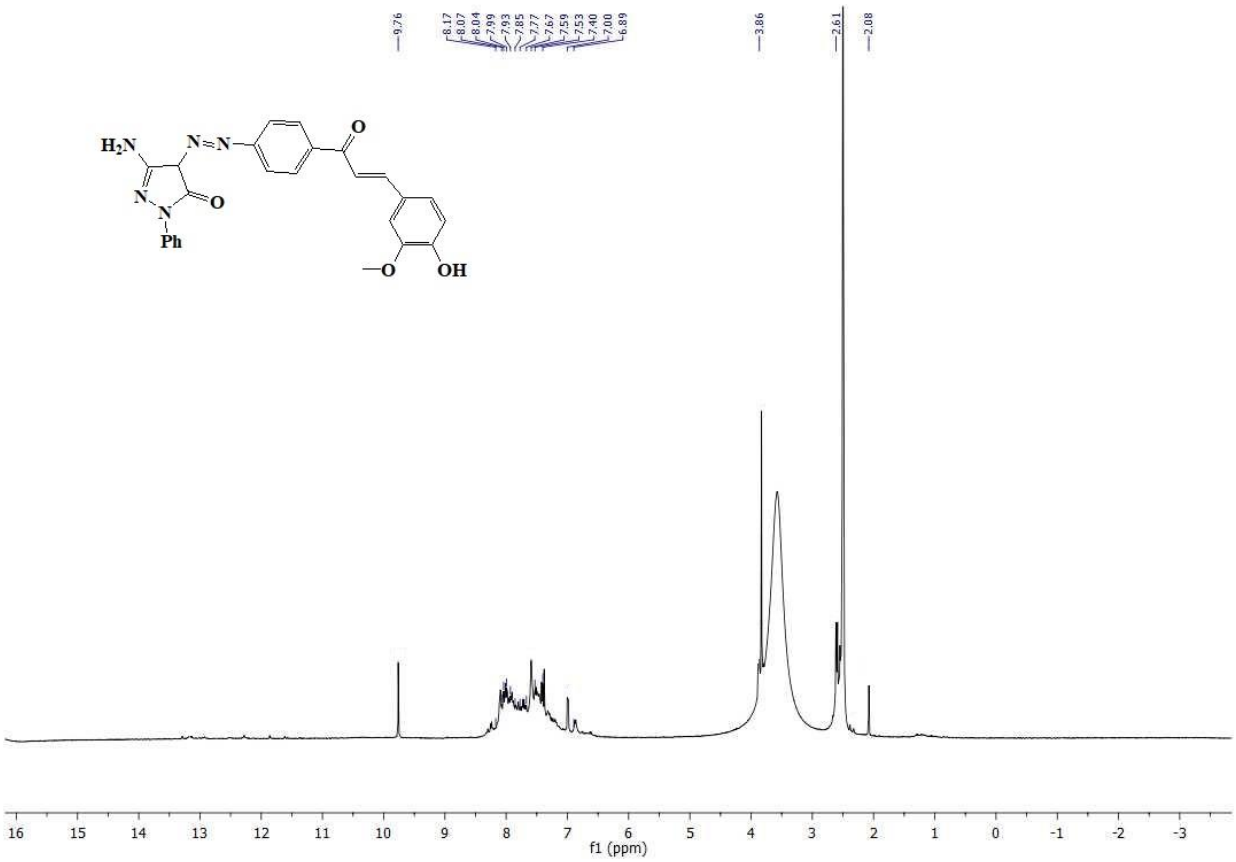

Fig. S4 ^{1}H-NMR spectrum of **compound 3b**

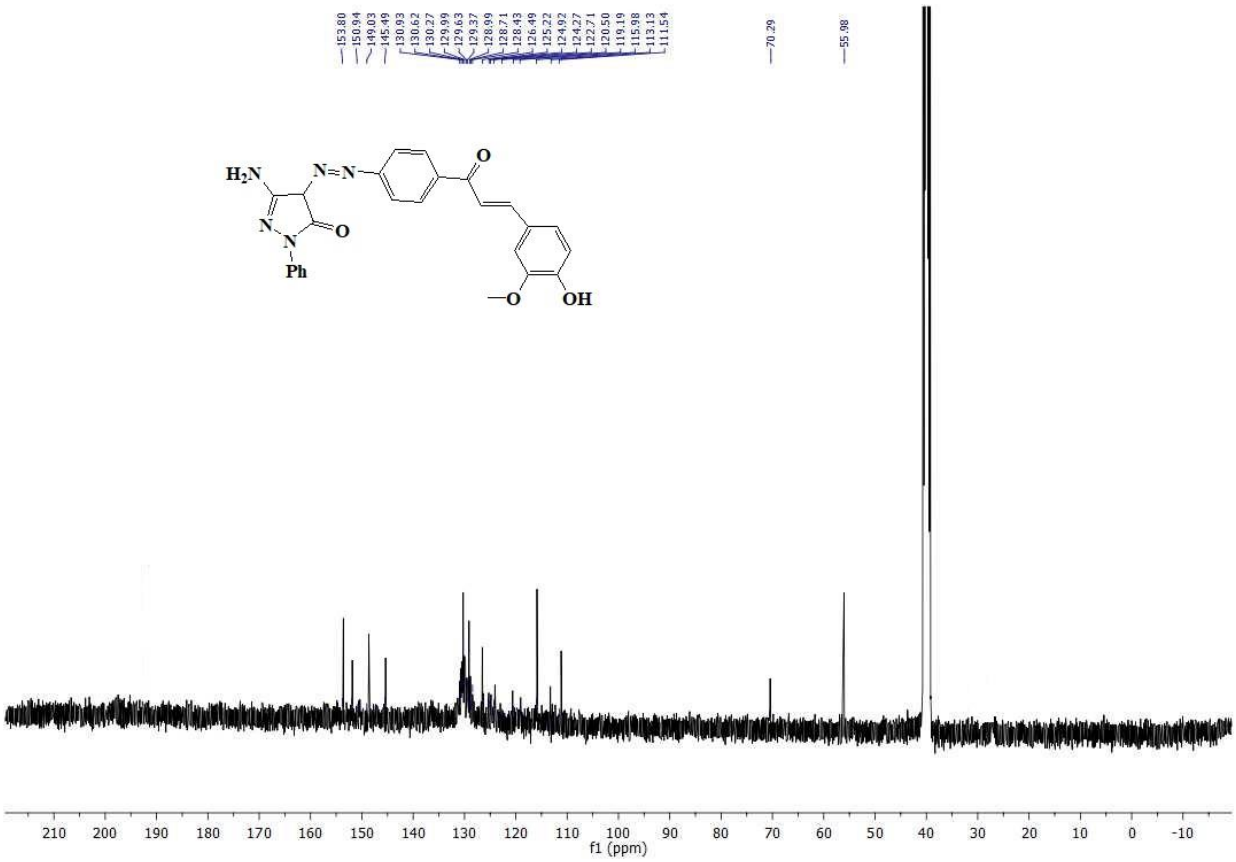

Fig. S5 ^{13}C-NMR spectrum of **compound 3b**

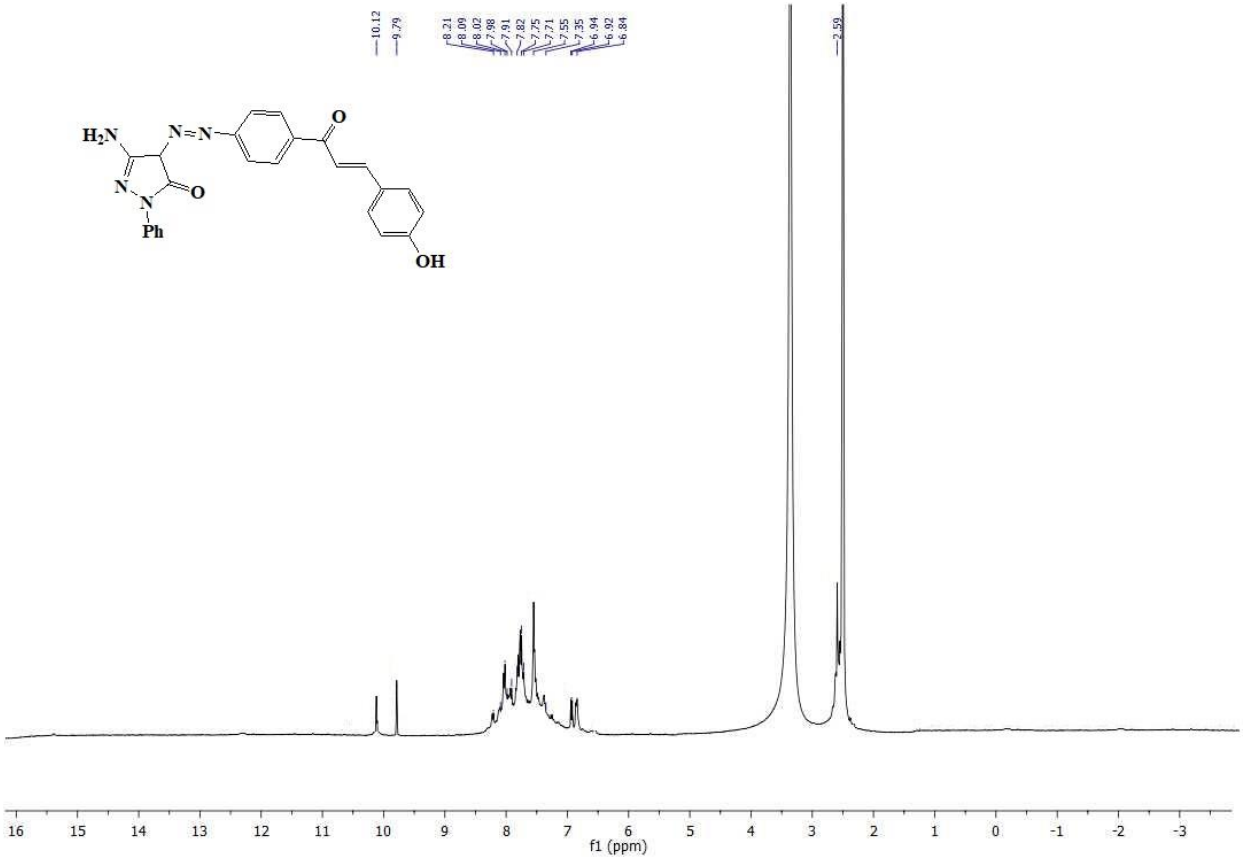

Fig. S6 ^{1}H-NMR spectrum of **compound 3c**

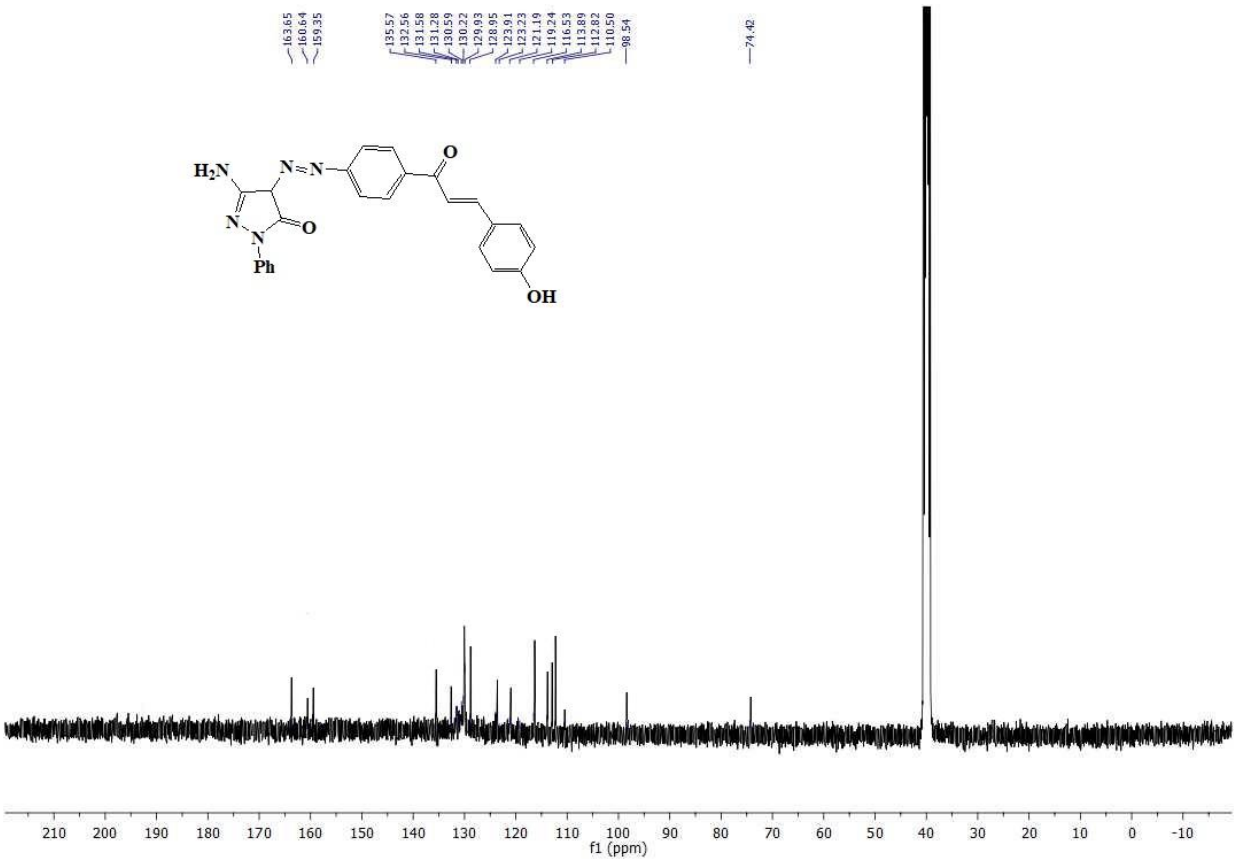

Fig. S7 ^{13}C-NMR spectrum of **compound 3c**

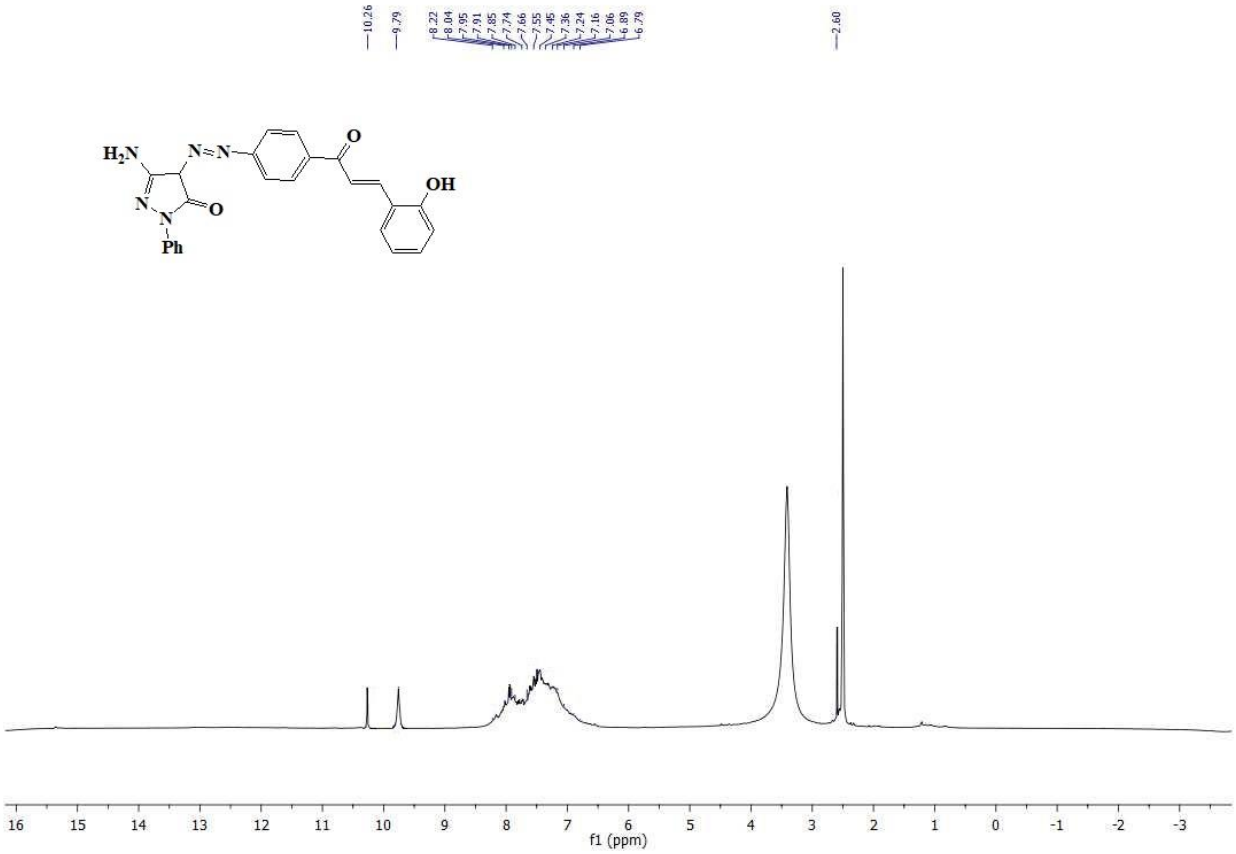

Fig. S8 ^{1}H-NMR spectrum of **compound 3d**

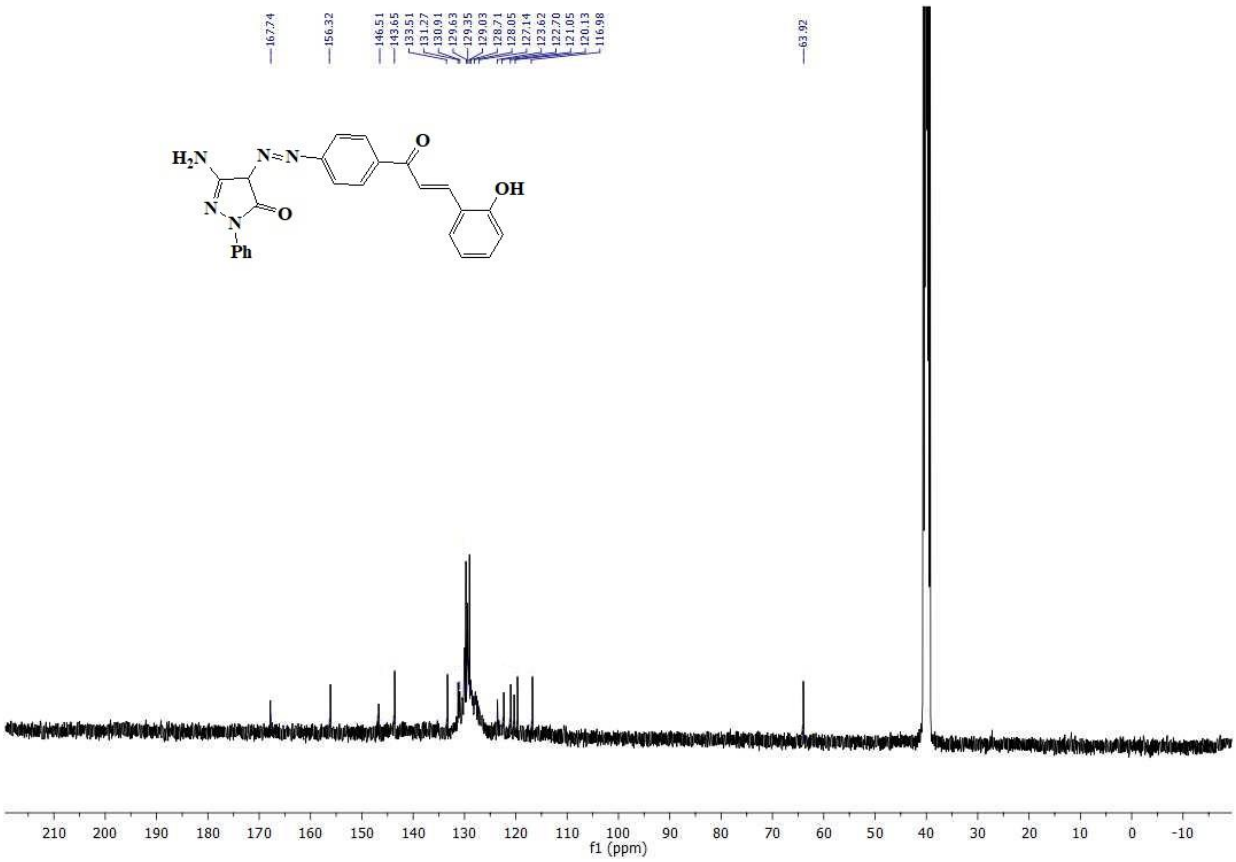

Fig. S9 ^{13}C-NMR spectrum of **compound 3d**

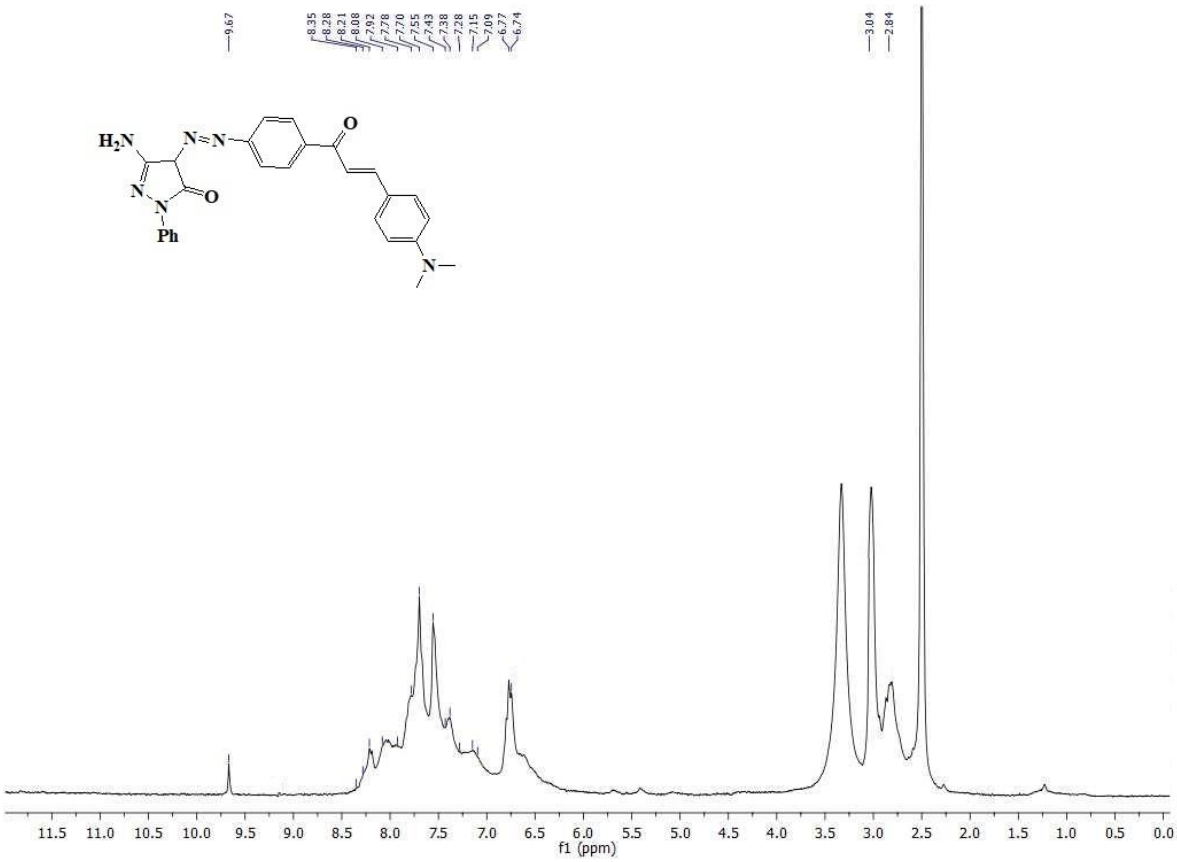

Fig. S10 ^{1}H-NMR spectrum of **compound 3e**

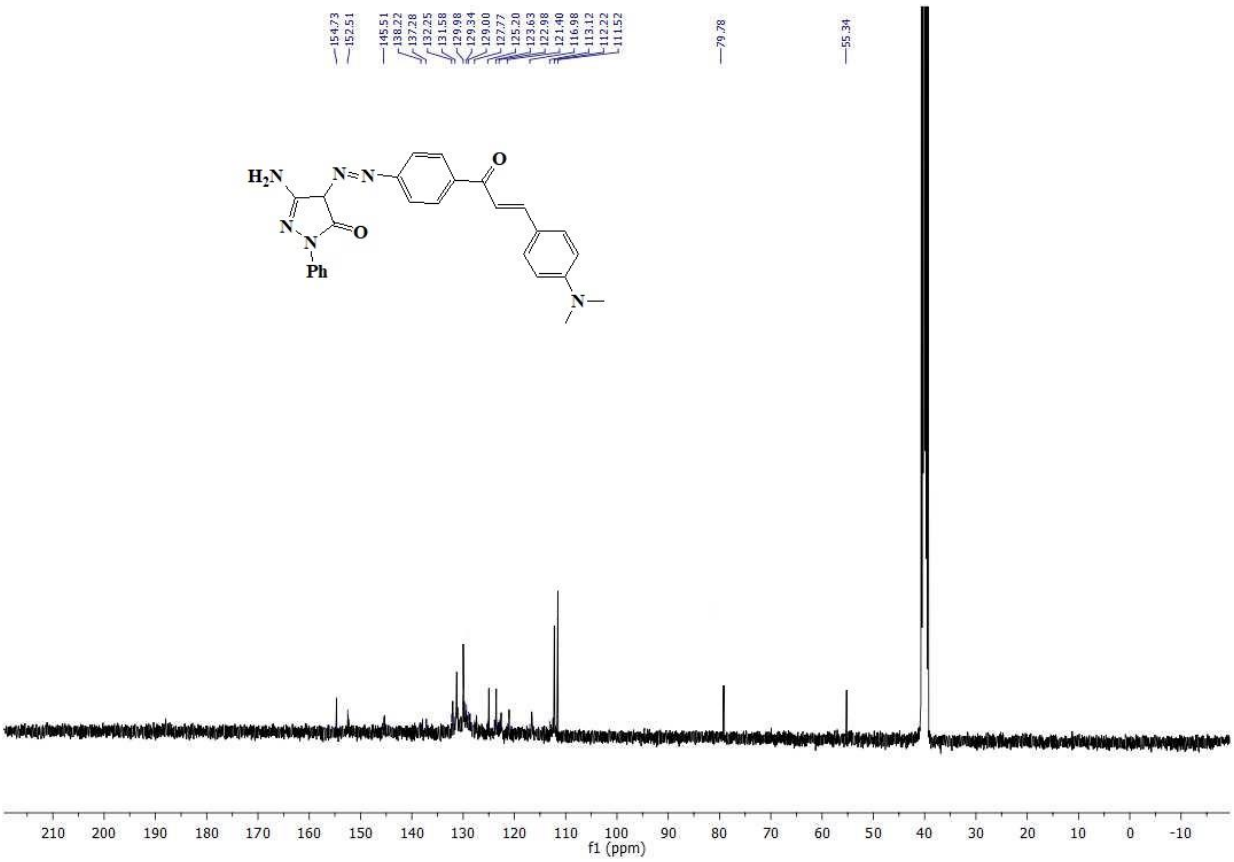

Fig. S11 ^{13}C-NMR spectrum of **compound 3e**

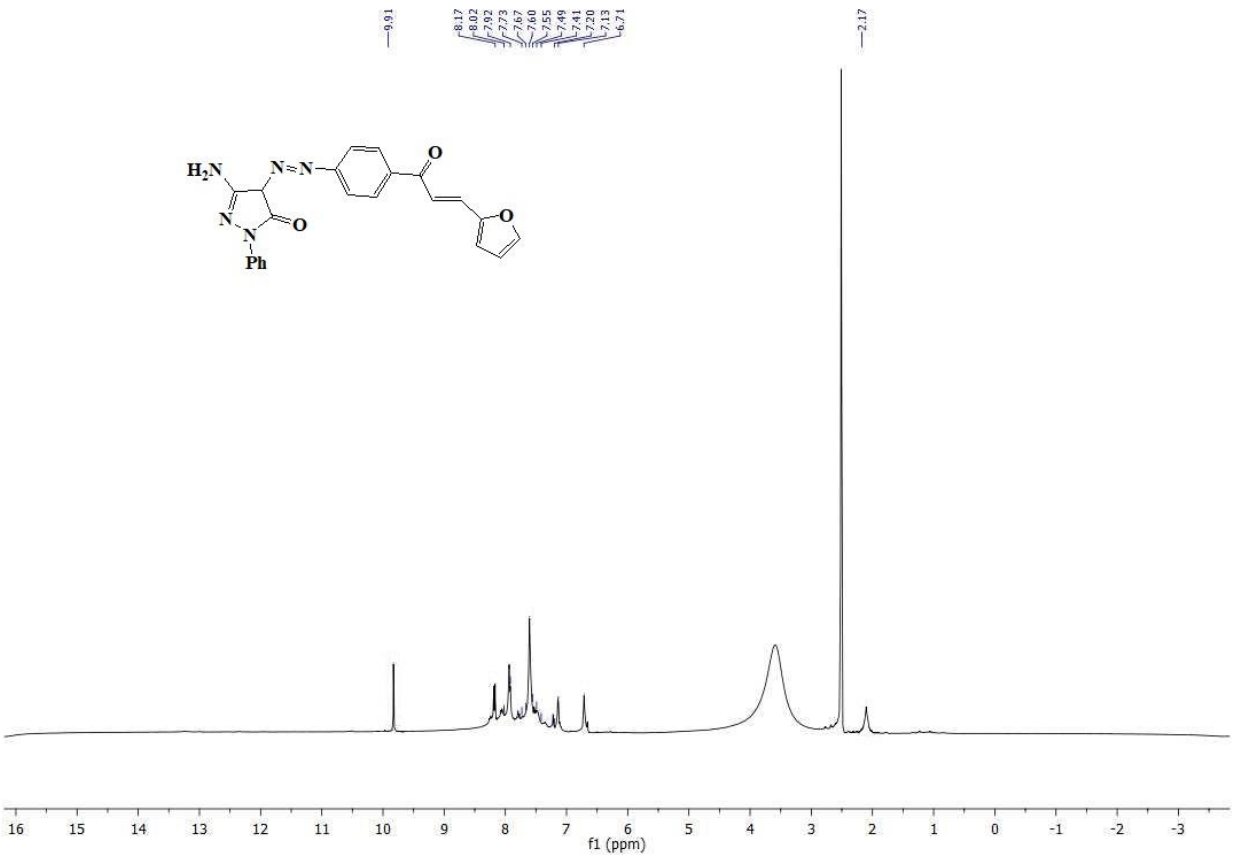

Fig. S12 ^{1}H-NMR spectrum of **compound 3f**

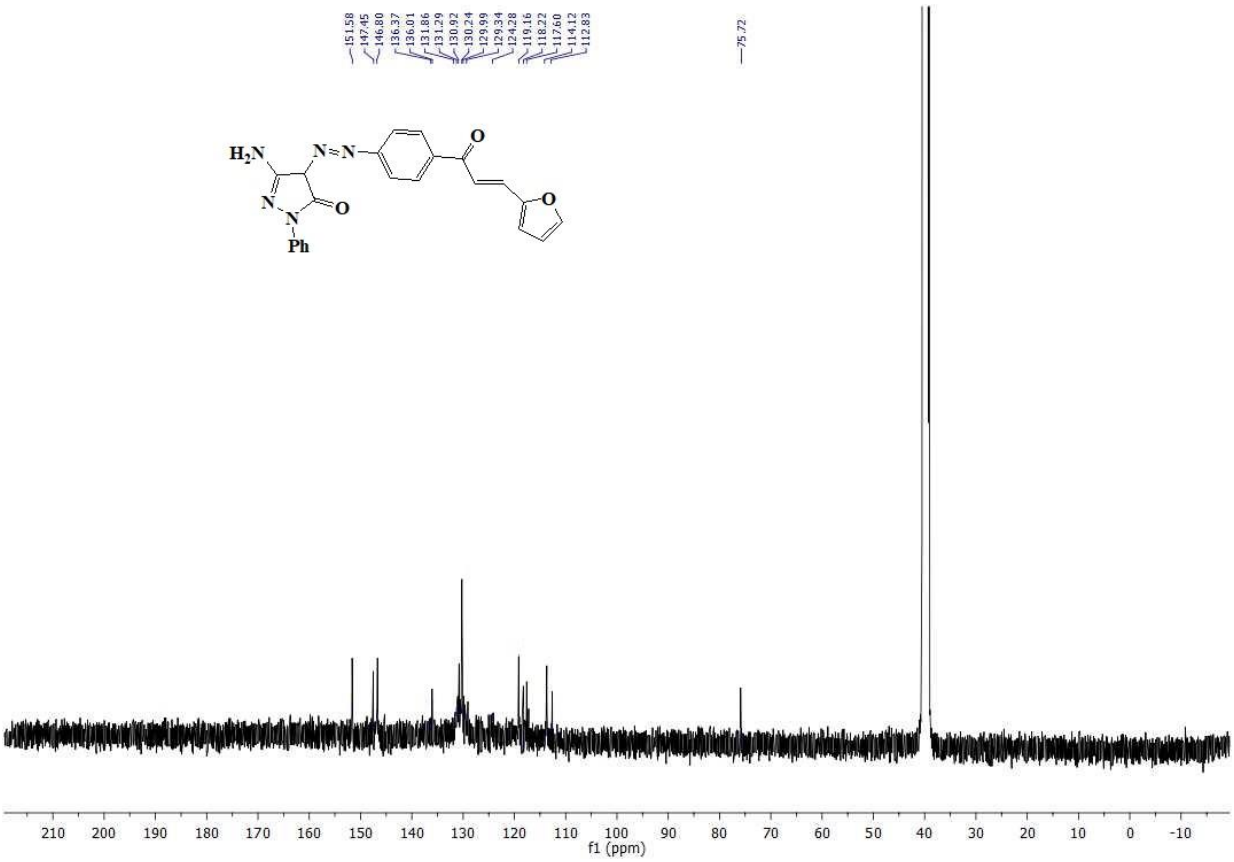

Fig. S13 ^{13}C-NMR spectrum of **compound 3f**

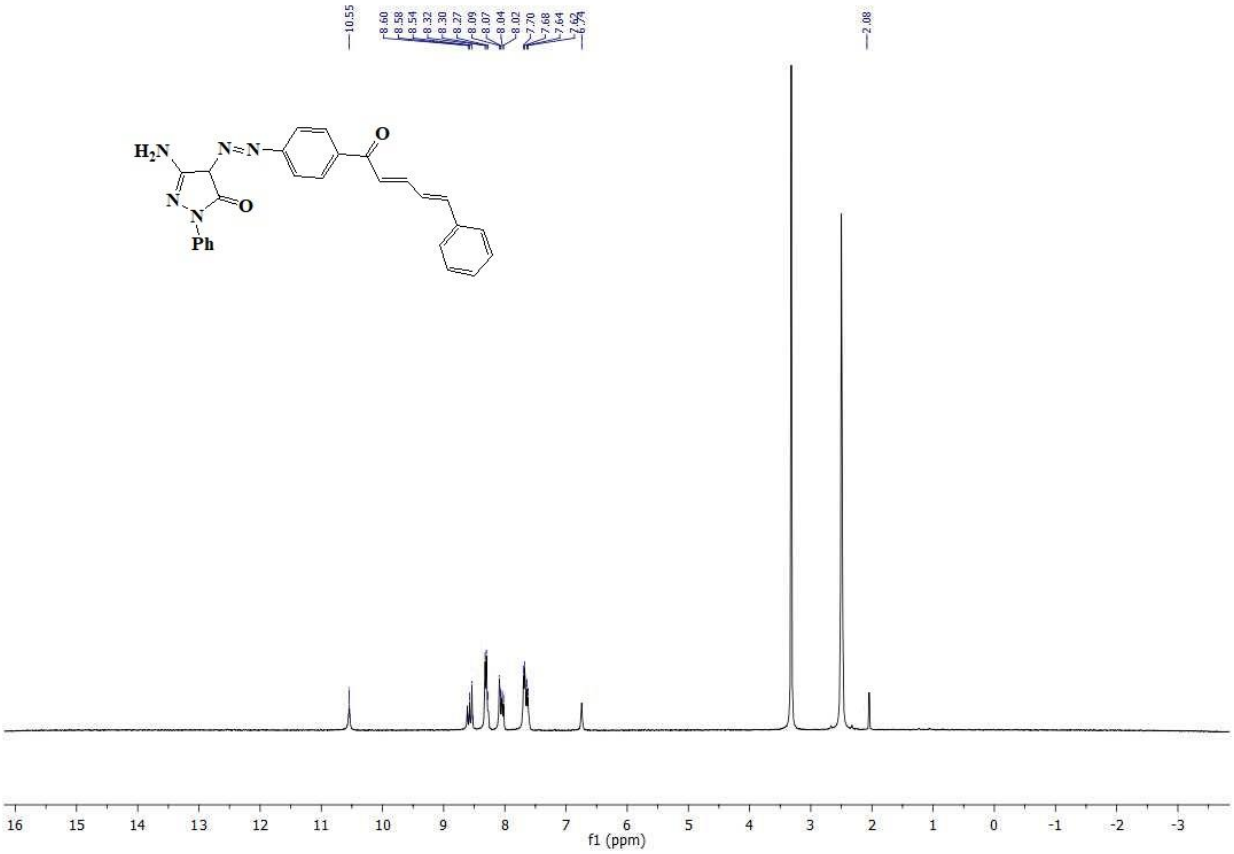

Fig. S14 ^{1}H-NMR spectrum of **compound 3g**