

# Synthesis of Novel Thiazole Derivatives Bearing $\beta$ -Amino Acid and Aromatic Moieties as Promising Scaffolds for the Development of New Antibacterial and Antifungal Candidates Targeting Multidrug-Resistant Pathogens

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❖ NMR Spectra (1-9, all in DMSO-*d*<sub>6</sub>, Figures S1-S42)

❖ The list of fungal strains used for the study

3-(1-(4-Phenylaminophenyl)thioureido)propanoic acid (**1**)

Figure S1.  $^1\text{H}$  NMR of compound **1**.

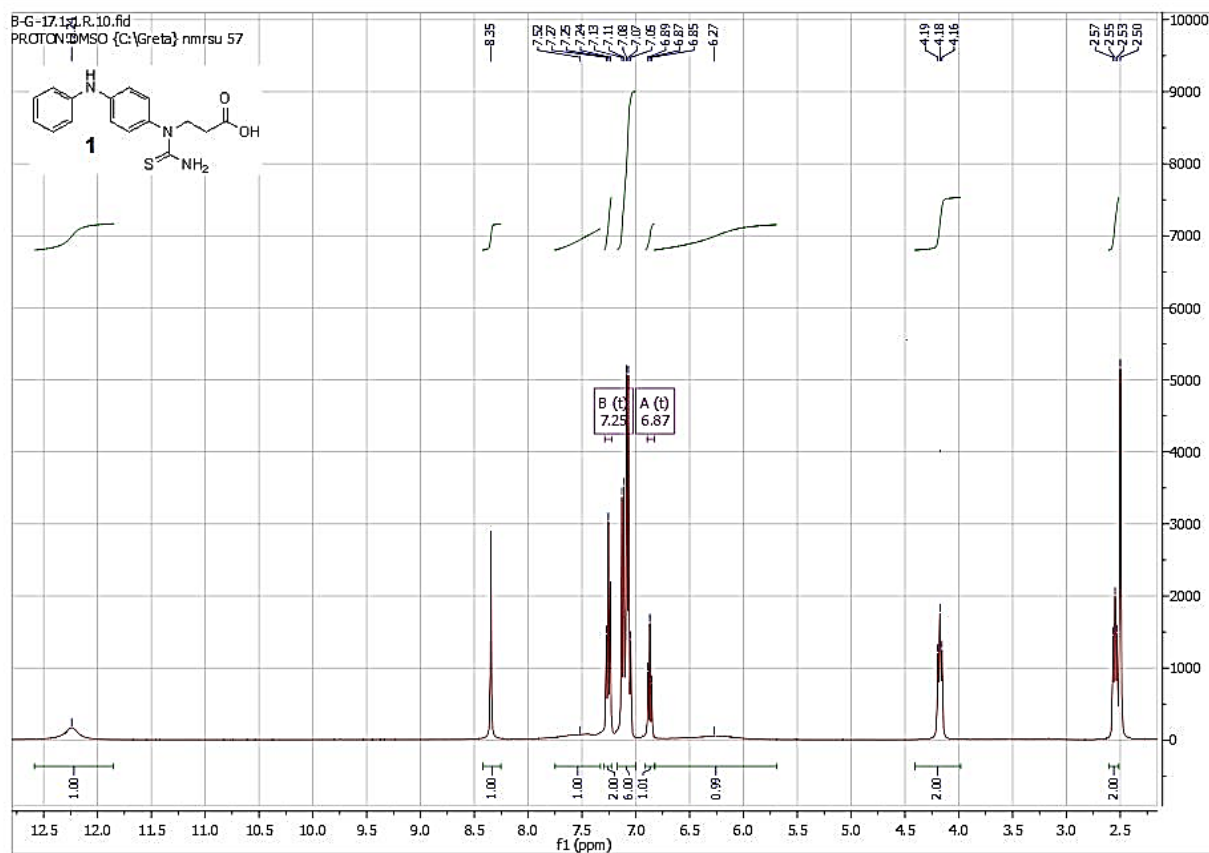
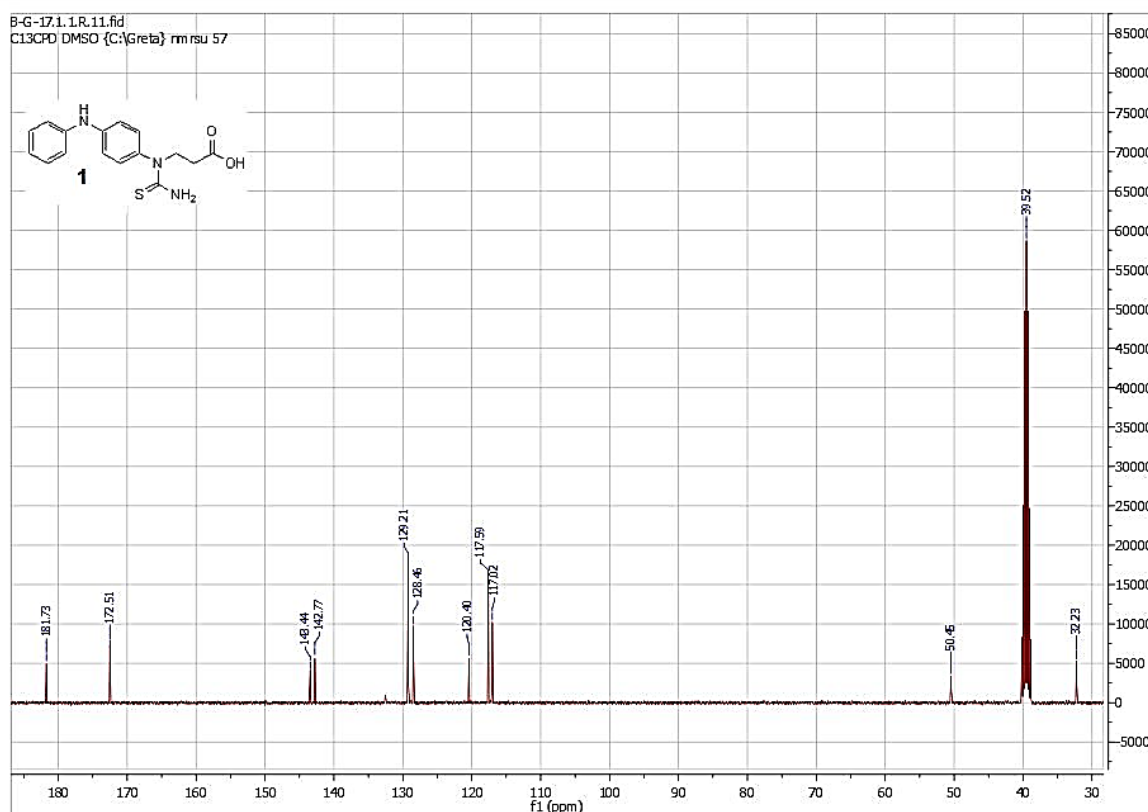


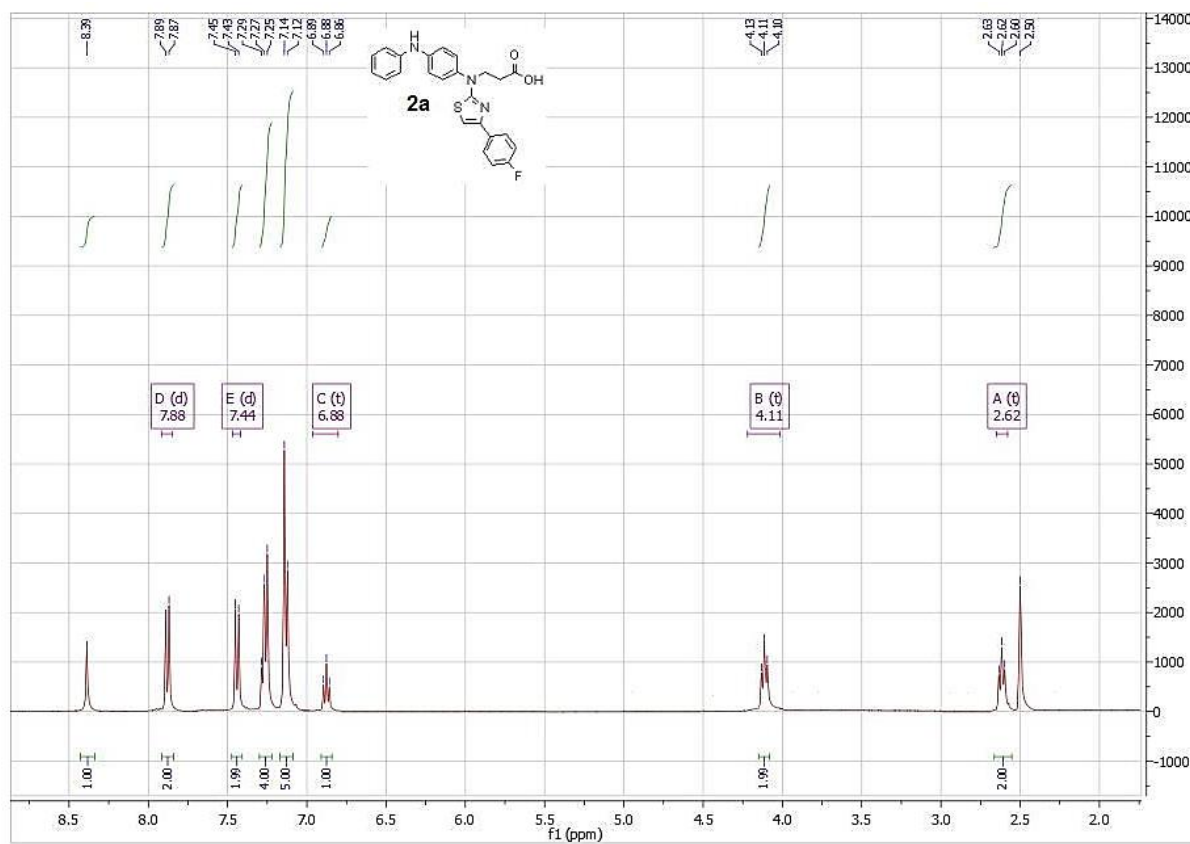
Figure S2:  $^{13}\text{C}$  NMR of compound **1**



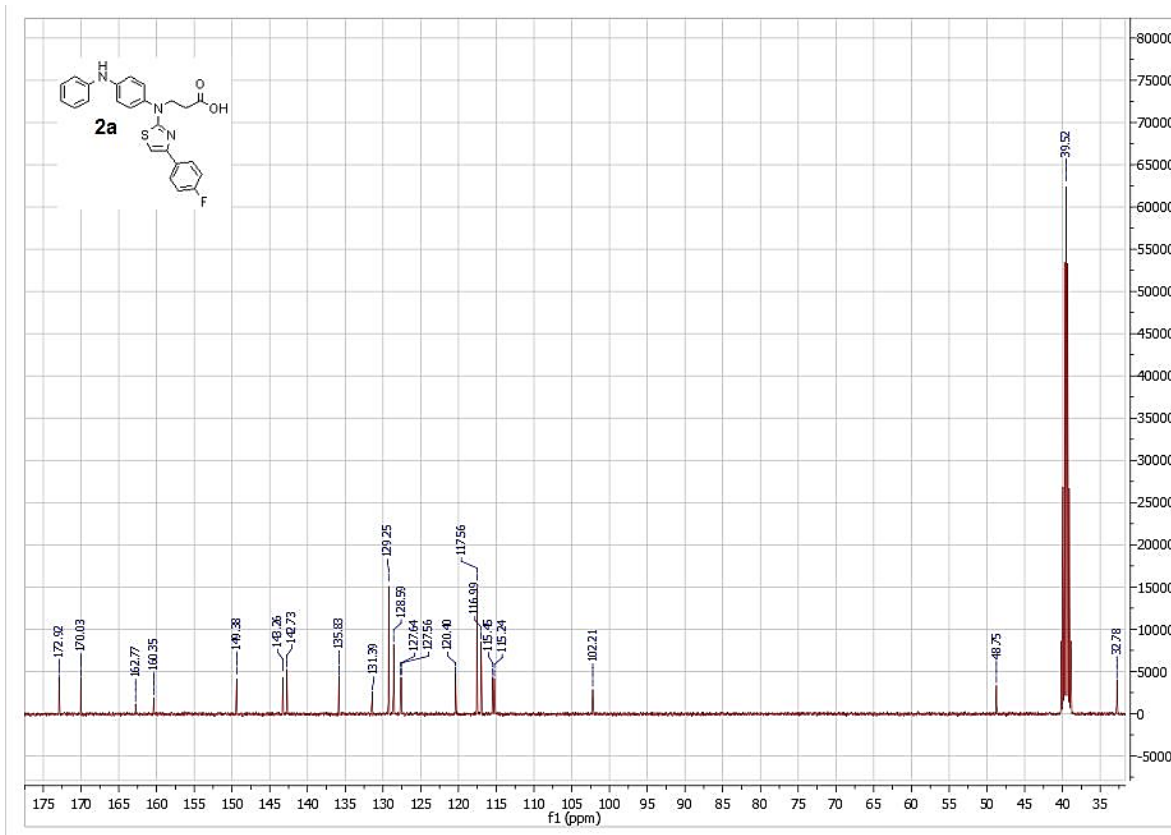
# **Synthesis of thiazoles 2-5**

**3-((4-(4-Fluorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanoic acid (2a):**

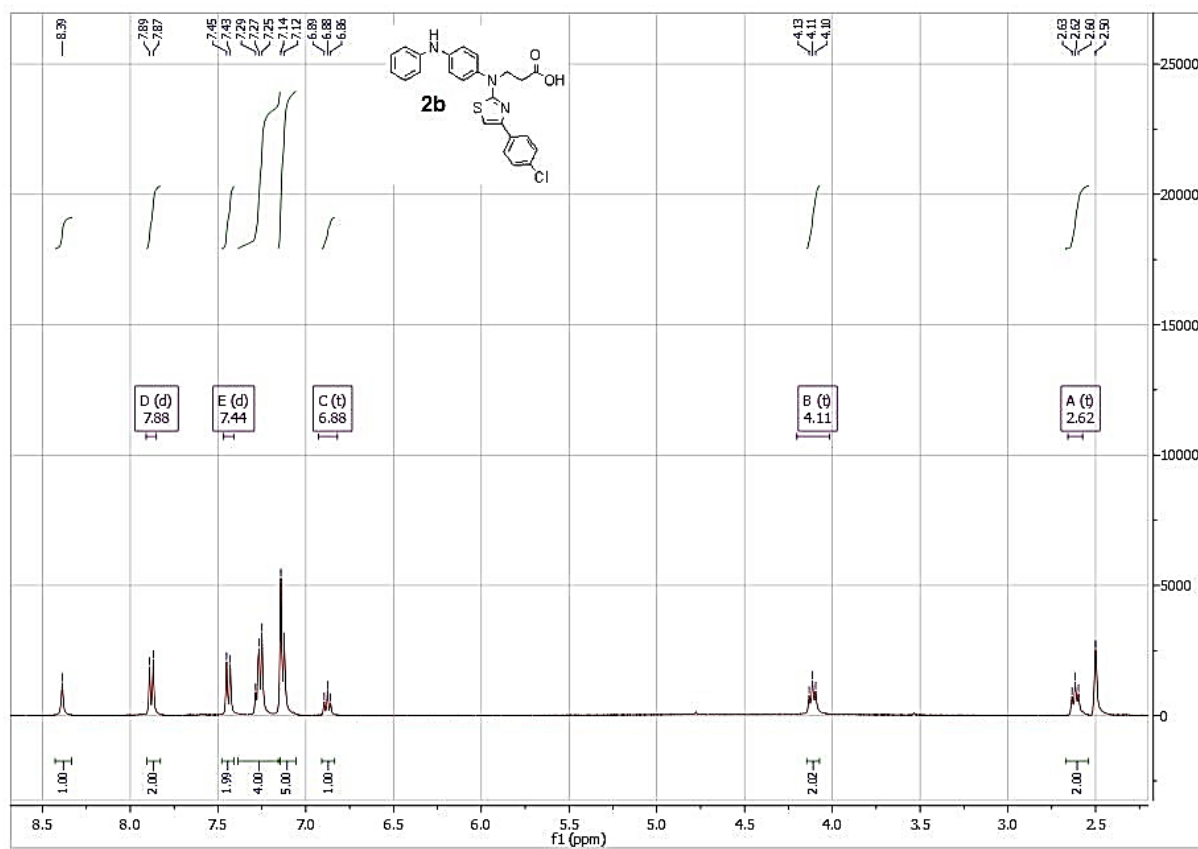
**Figure S3: <sup>1</sup>H NMR of compound 2a**



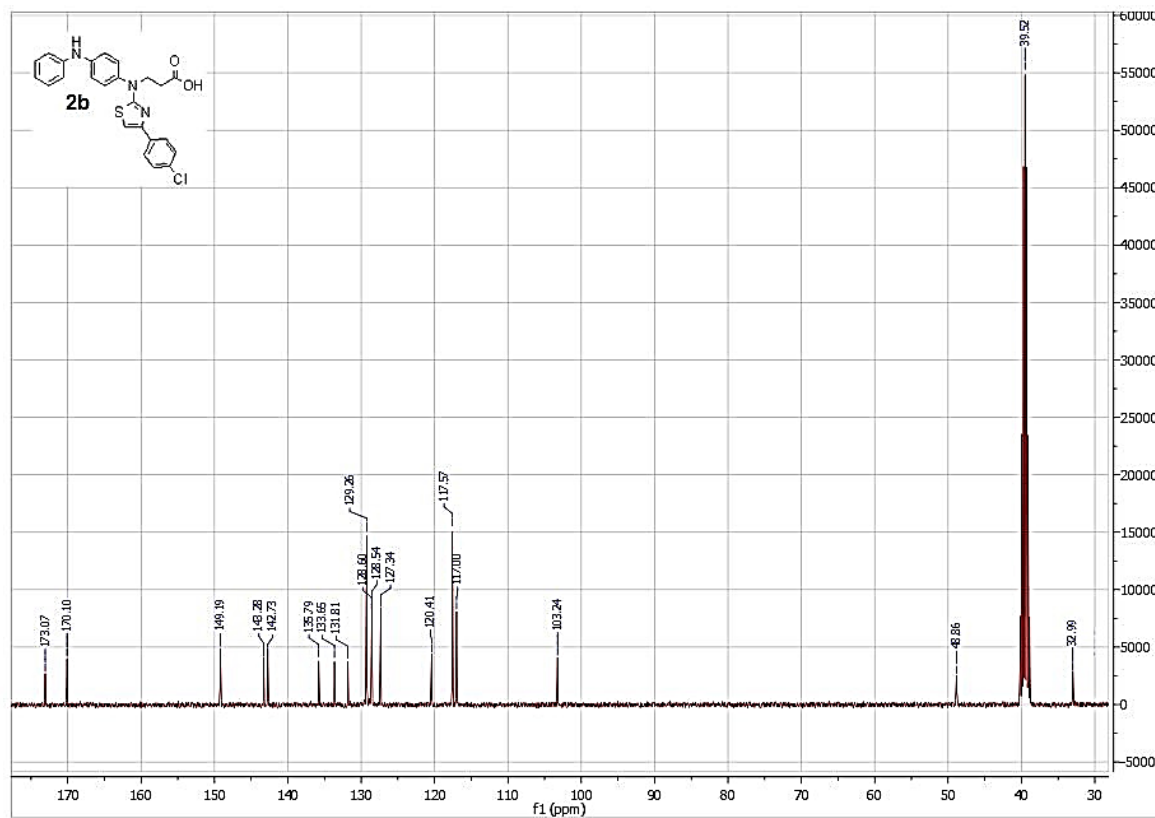
**Figure S4: <sup>13</sup>C NMR of compound 2a**



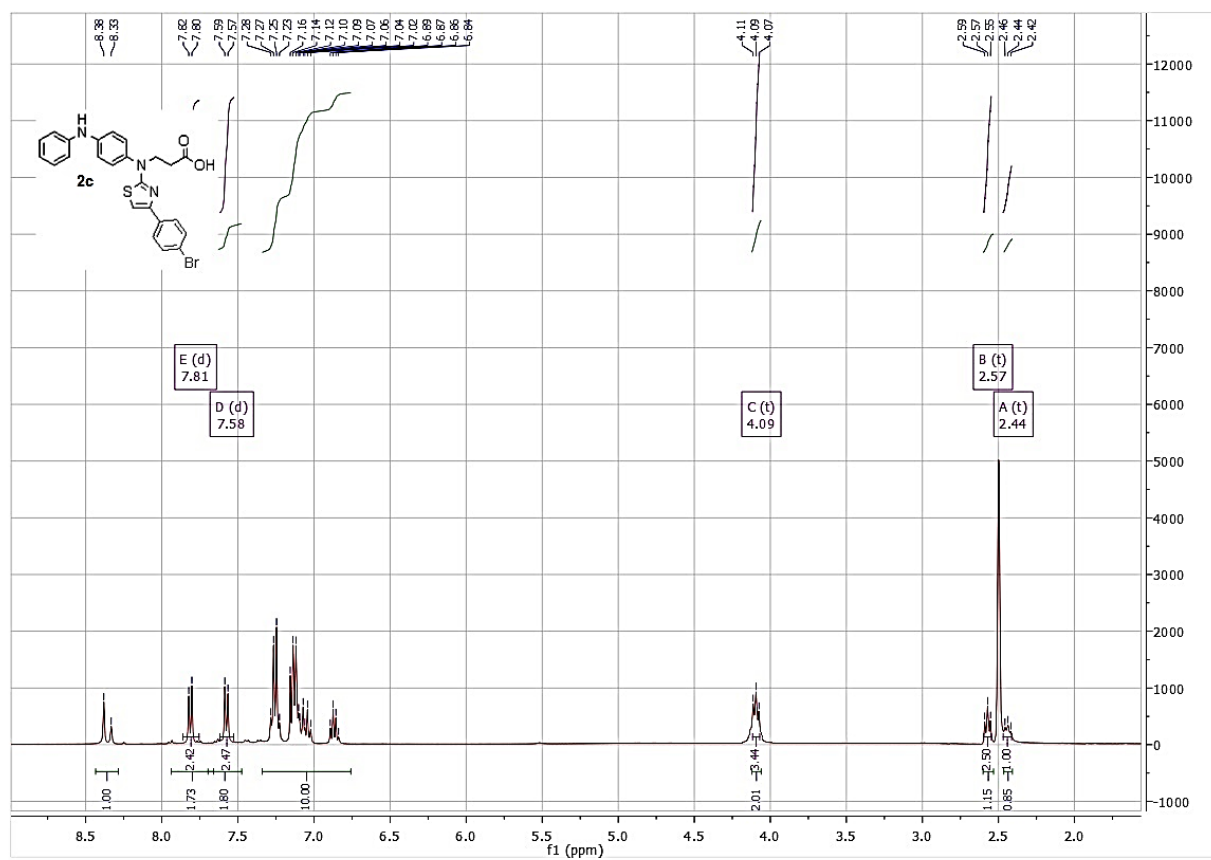
3-((4-(4-Chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanoic acid (**2b**):  
**Figure S5:**  $^1\text{H}$  NMR of compound **2b**



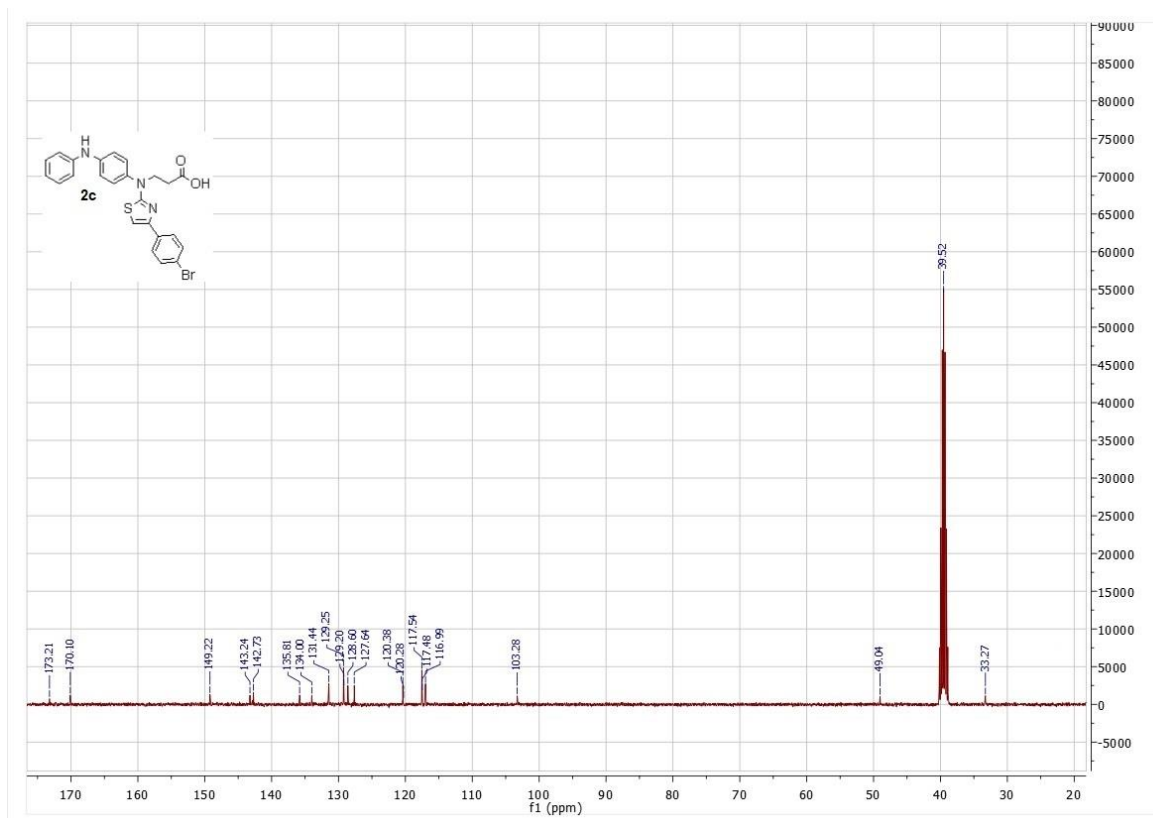
**Figure S6:**  $^{13}\text{C}$  NMR of compound **2b**



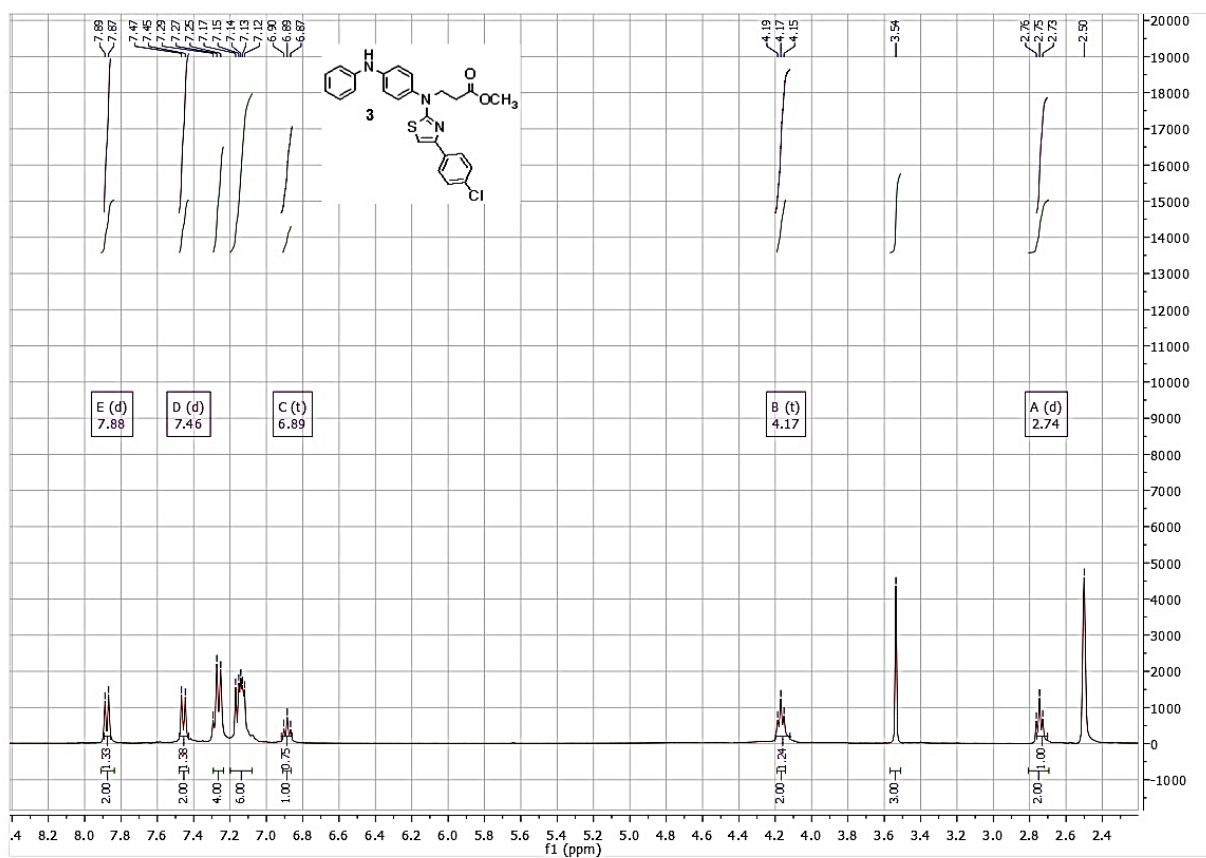
3-((4-(4-Bromophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanoic acid (**2c**):  
**Figure S7:**  $^1\text{H}$  NMR of compound **2c**



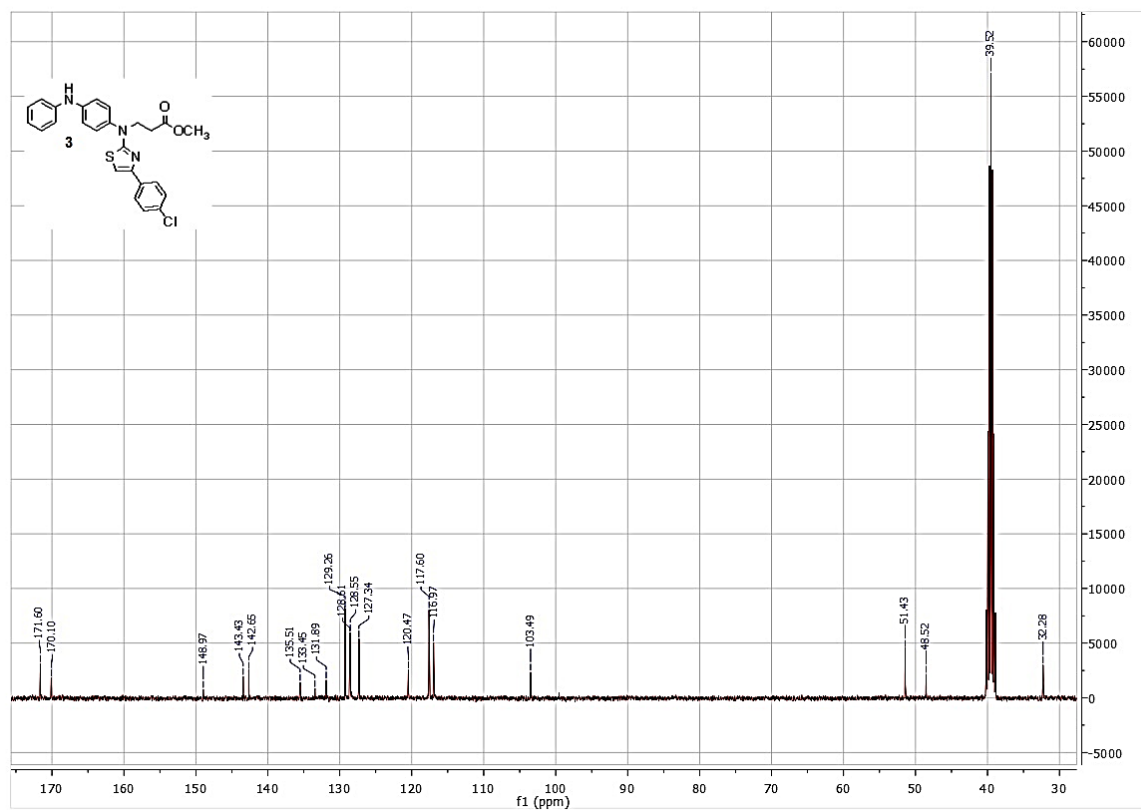
**Figure S8:**  $^{13}\text{C}$  NMR of compound **2c**



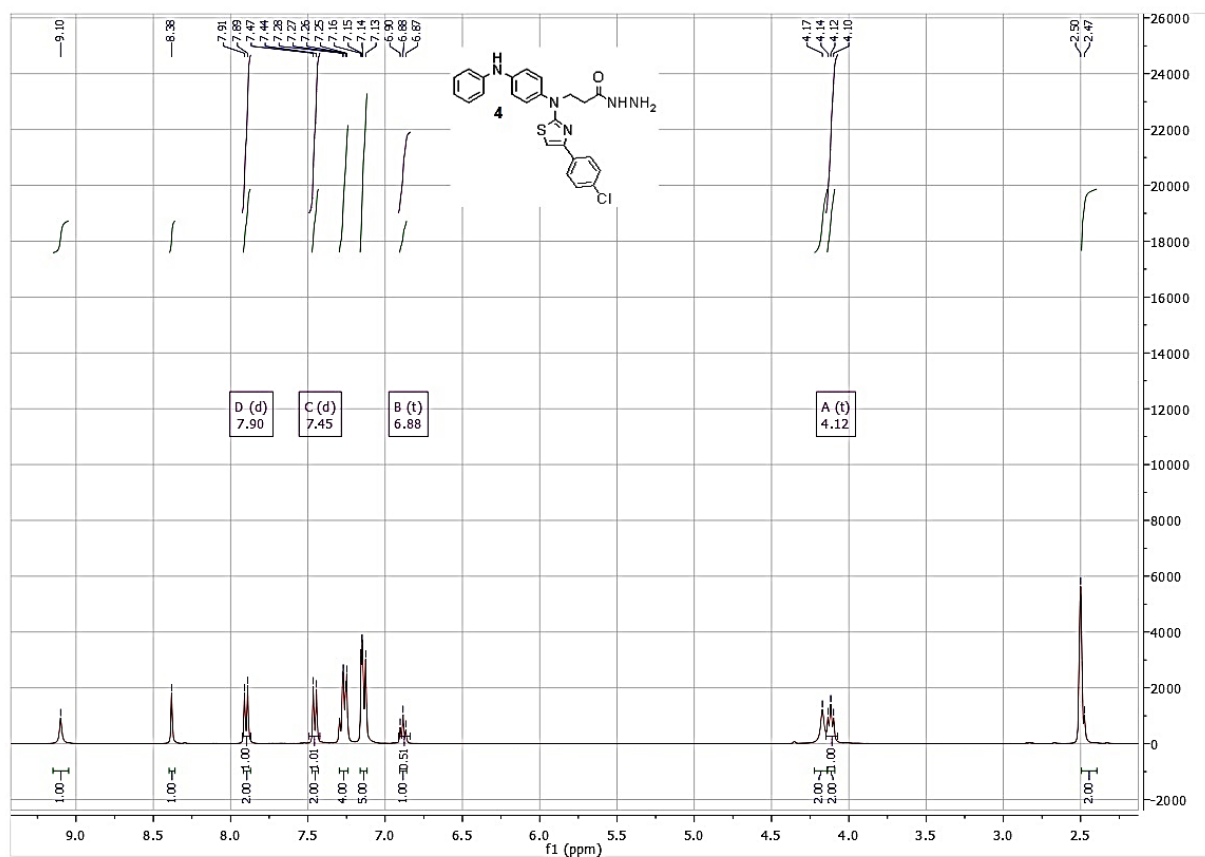
Methyl 3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanoate (**3**)  
**Figure S9:**  $^1\text{H}$  NMR of compound **3**



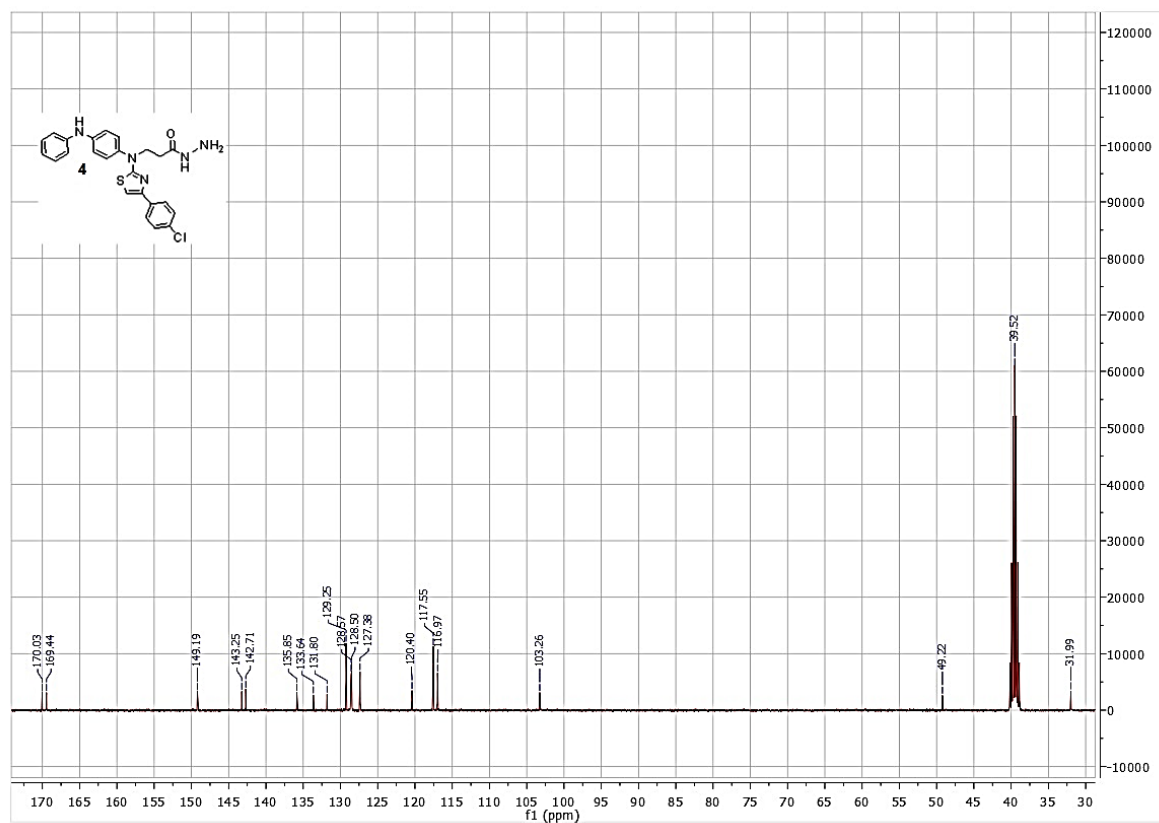
**Figure S10:**  $^{13}\text{C}$  NMR of compound **3**



3-((4-(4-Chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanehydrazide (**4**)  
**Figure S11:**  $^1\text{H}$  NMR of compound **4**

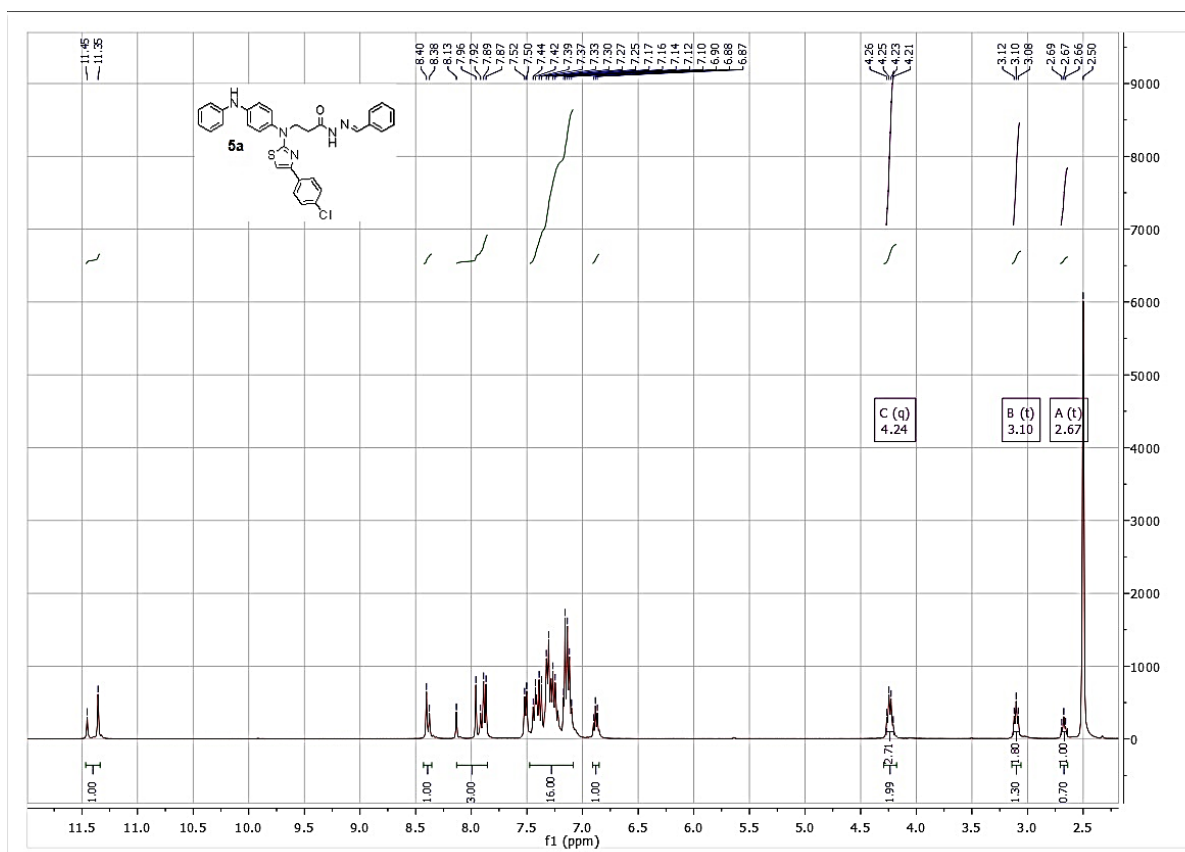


**Figure S12:**  $^{13}\text{C}$  NMR of compound **4**

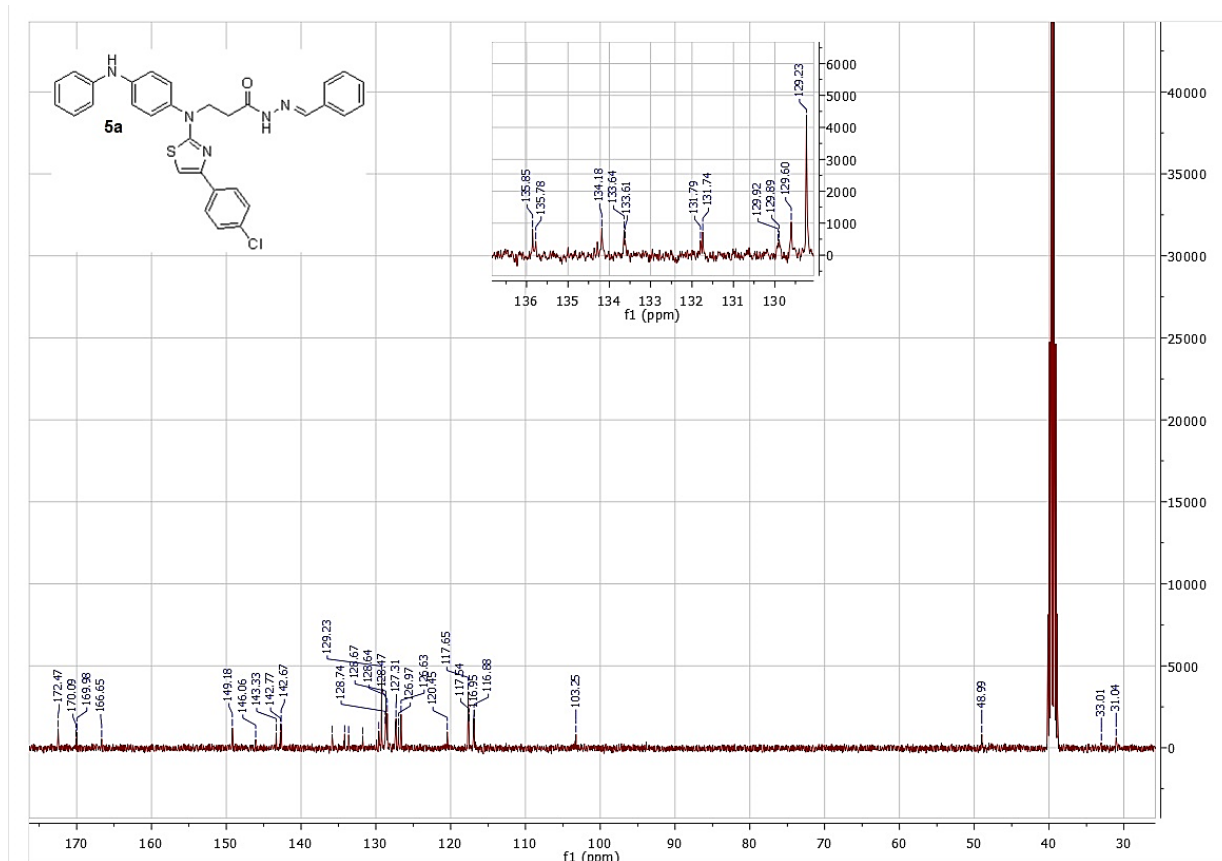


*N*-benzylidene-3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanehydrazide (**5a**)

**Figure S13:**  $^1\text{H}$  NMR of compound **5a**

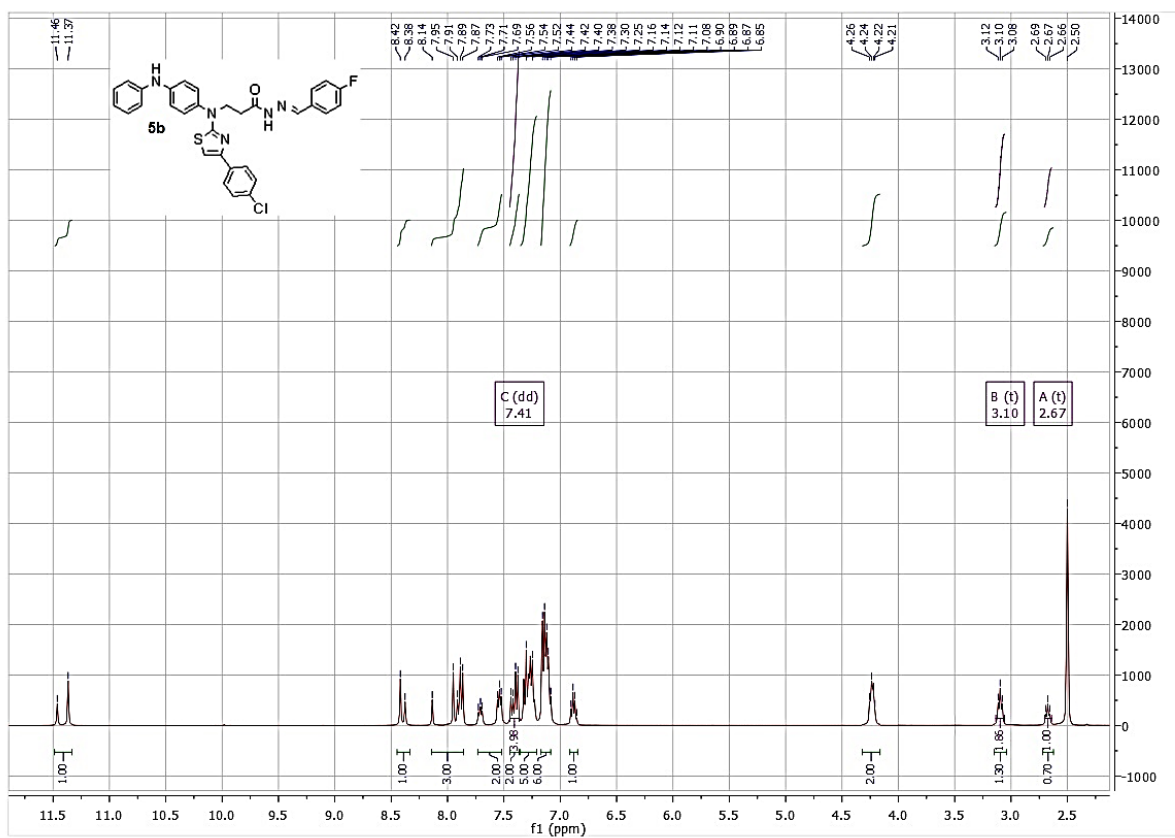


**Figure S14:**  $^{13}\text{C}$  NMR of compound **5a**

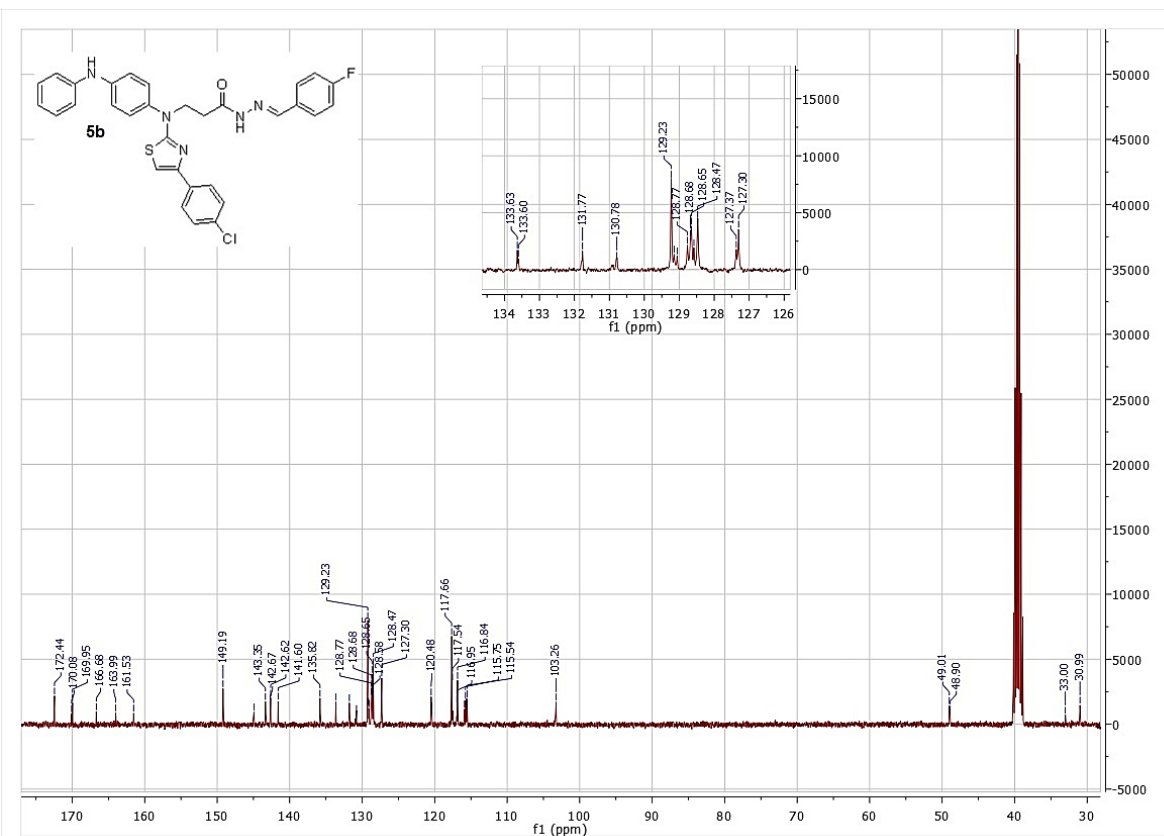




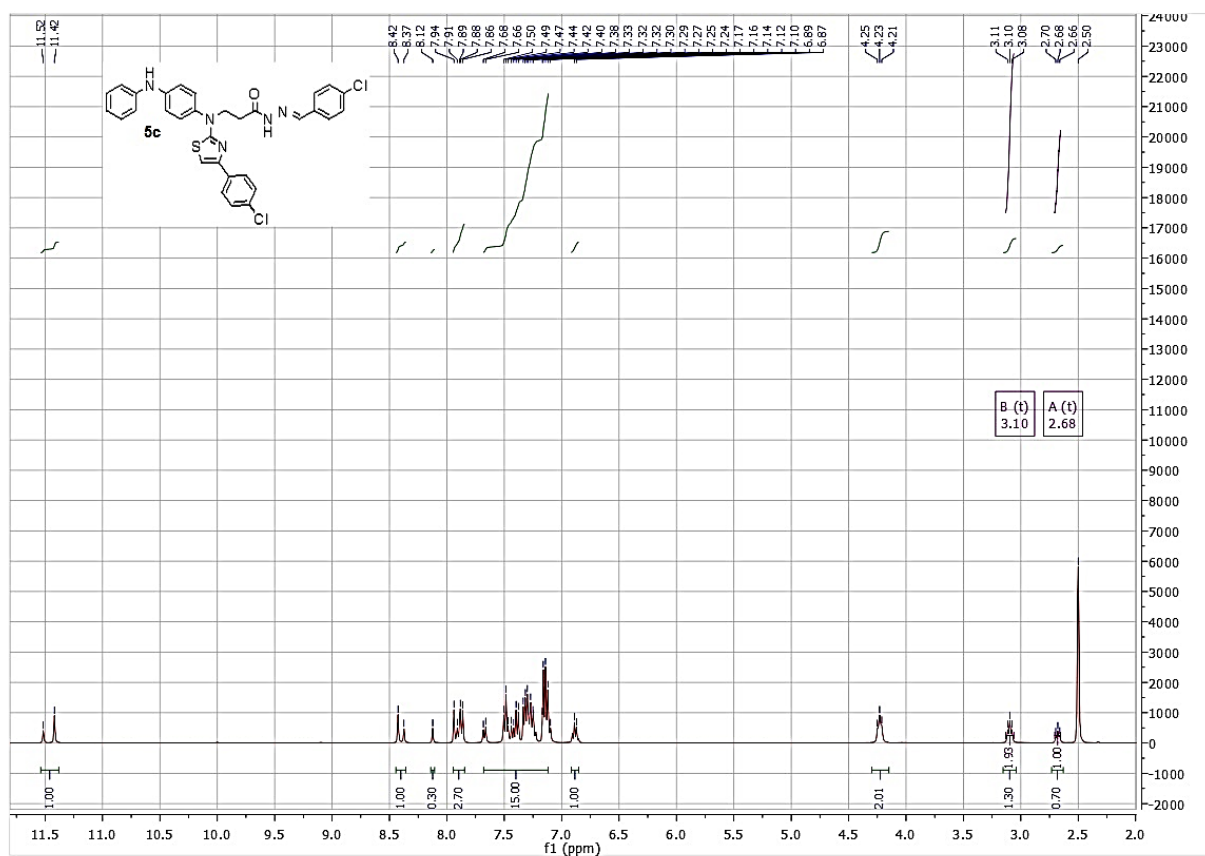
3-((4-(4-Chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)-N'-(4-fluorobenzylidene)propanehydrazide (**5b**)  
**Figure S15:**  $^1\text{H}$  NMR of compound **5b**



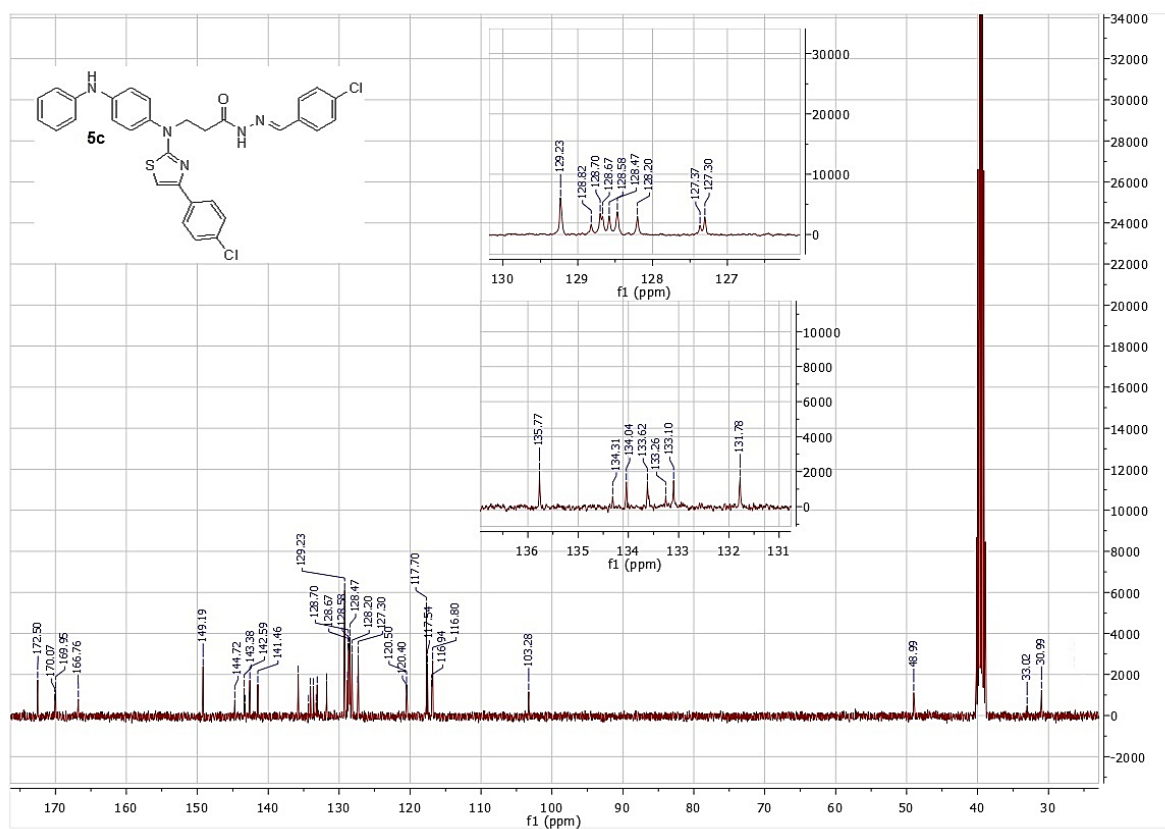
**Figure S16:**  $^{13}\text{C}$  NMR of compound **5b**



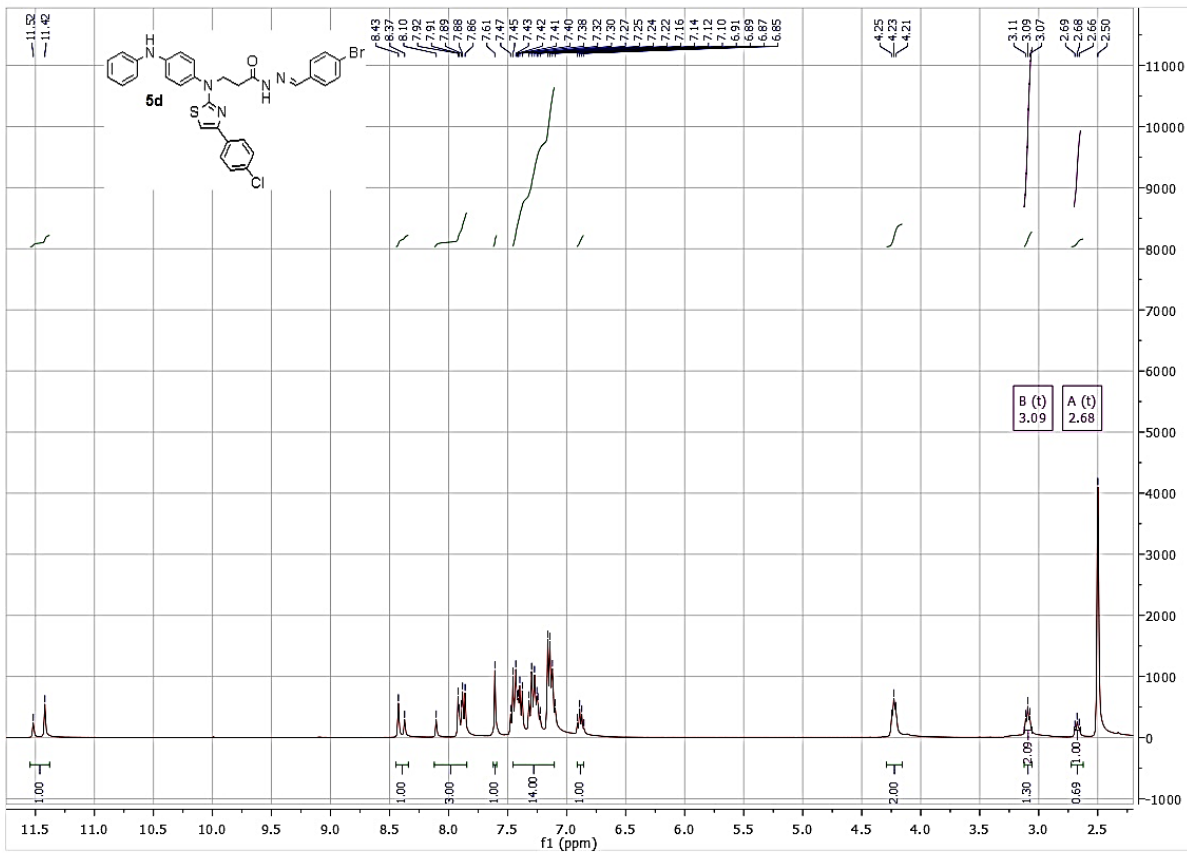
3-((4-(4-Chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)-N'-(4-chlorobenzylidene)propanehydrazide (**5c**)  
**Figure S17:**  $^1\text{H}$  NMR of compound **5c**



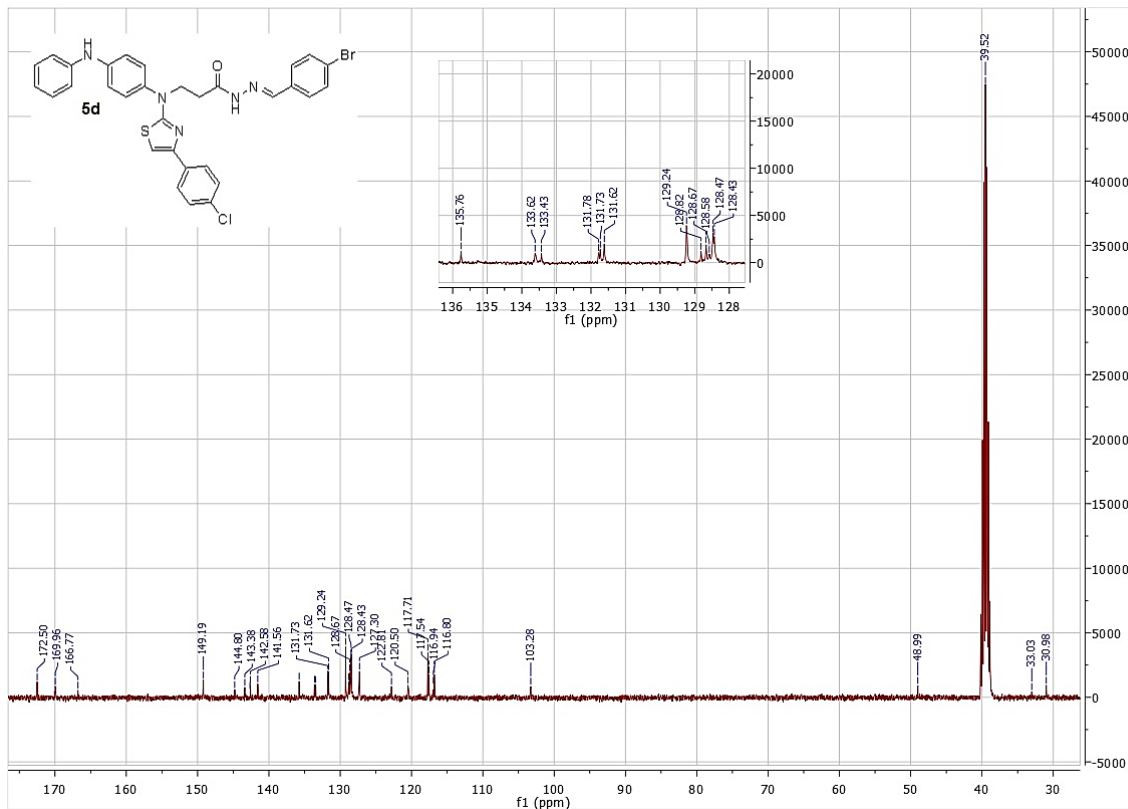
**Figure S18:**  $^{13}\text{C}$  NMR of compound **5c**



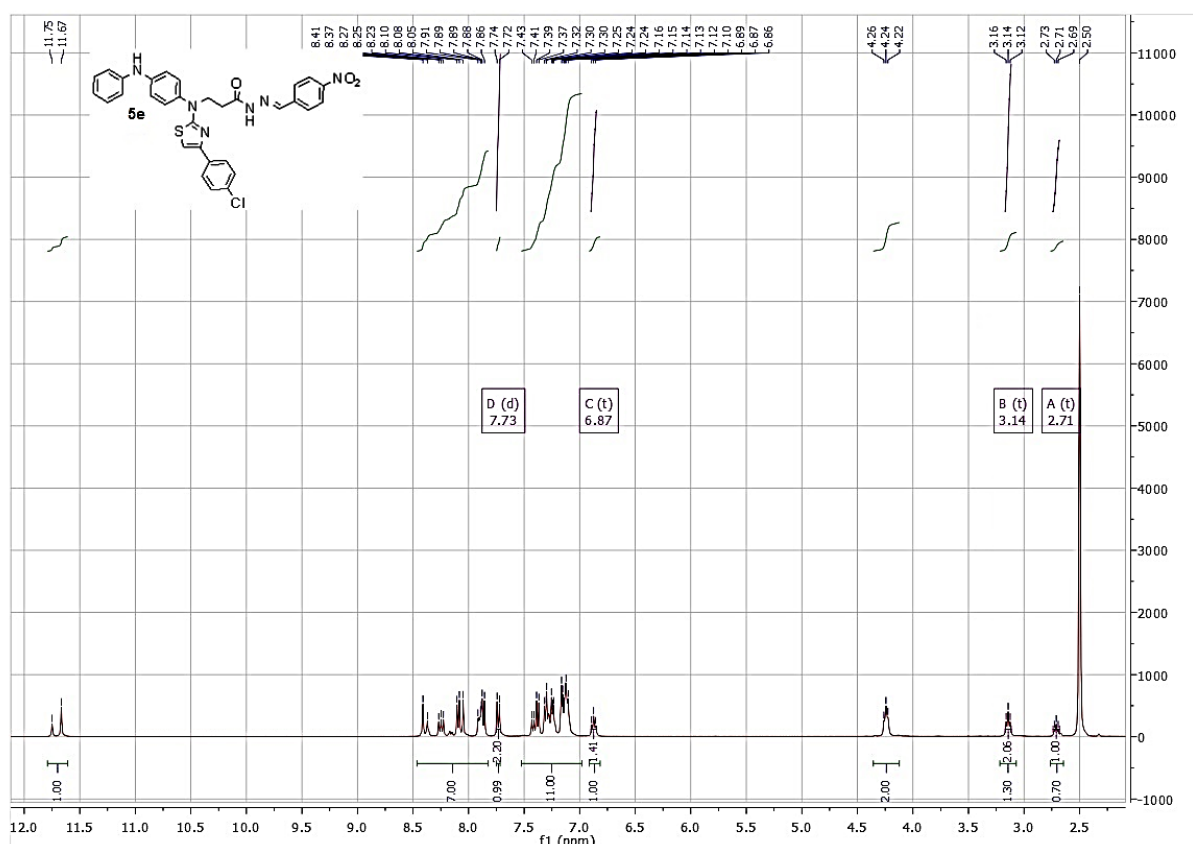
**Figure S19:**  $^1\text{H}$  NMR of compound **5d**



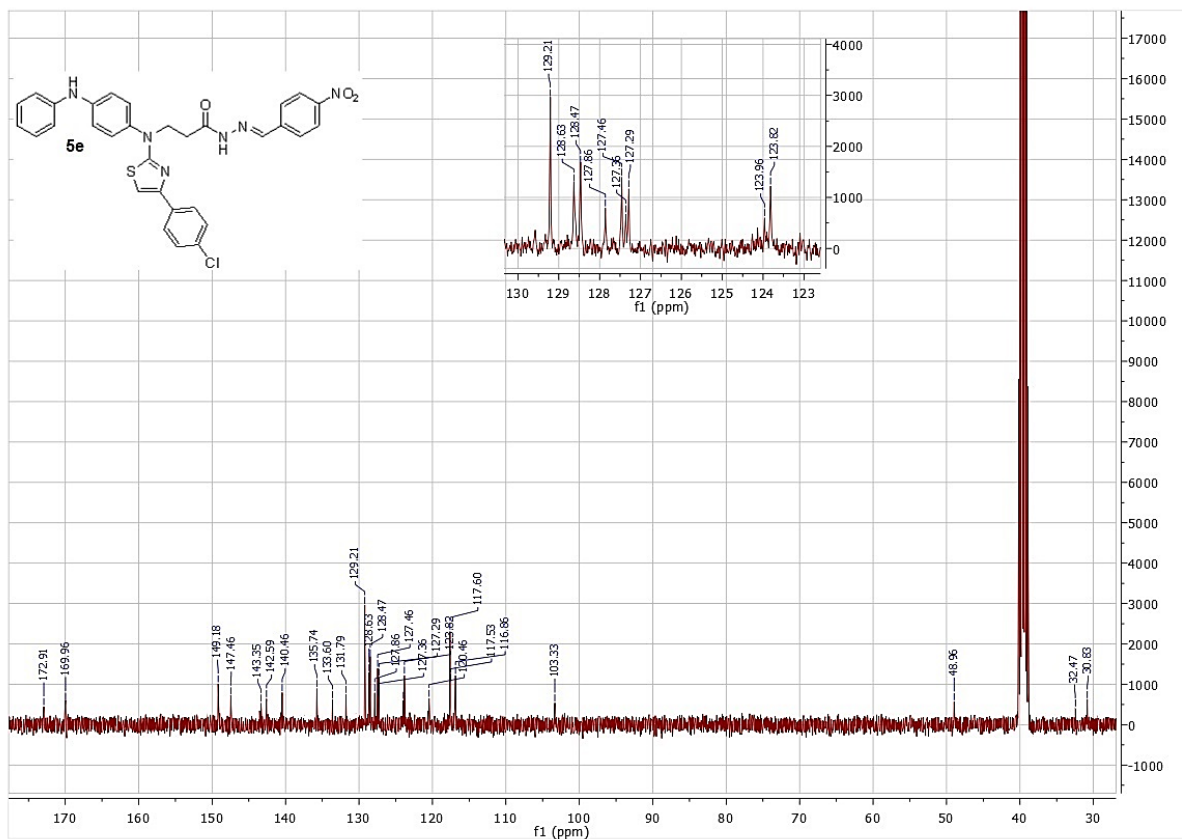
**Figure S20:**  $^{13}\text{C}$  NMR of compound **5d**



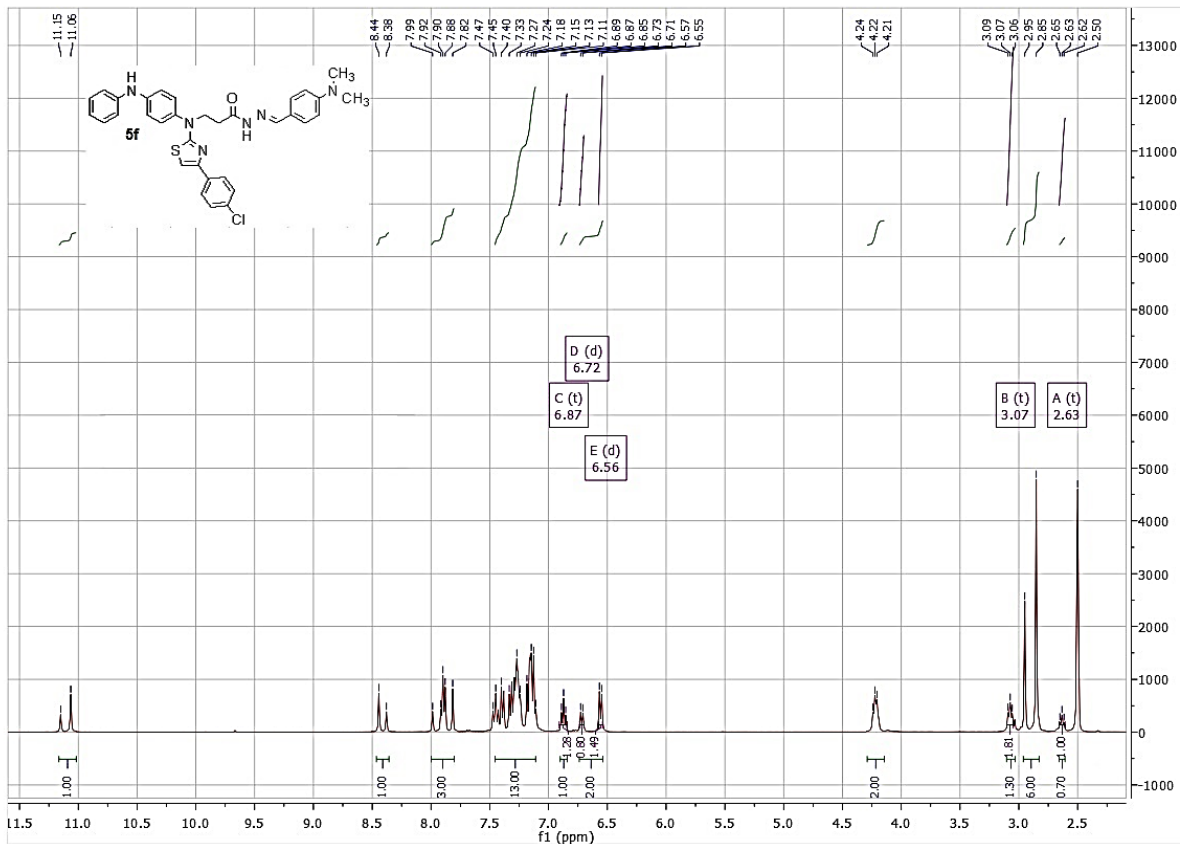
3-((4-(4-chlorophenyl)thiazol-2-yl)-N'-(4-nitrobenzylidene)-(4-(phenylamino)phenyl)amino)propanehydrazide (**5e**)  
**Figure S21:**  $^1\text{H}$  NMR of compound **5e**



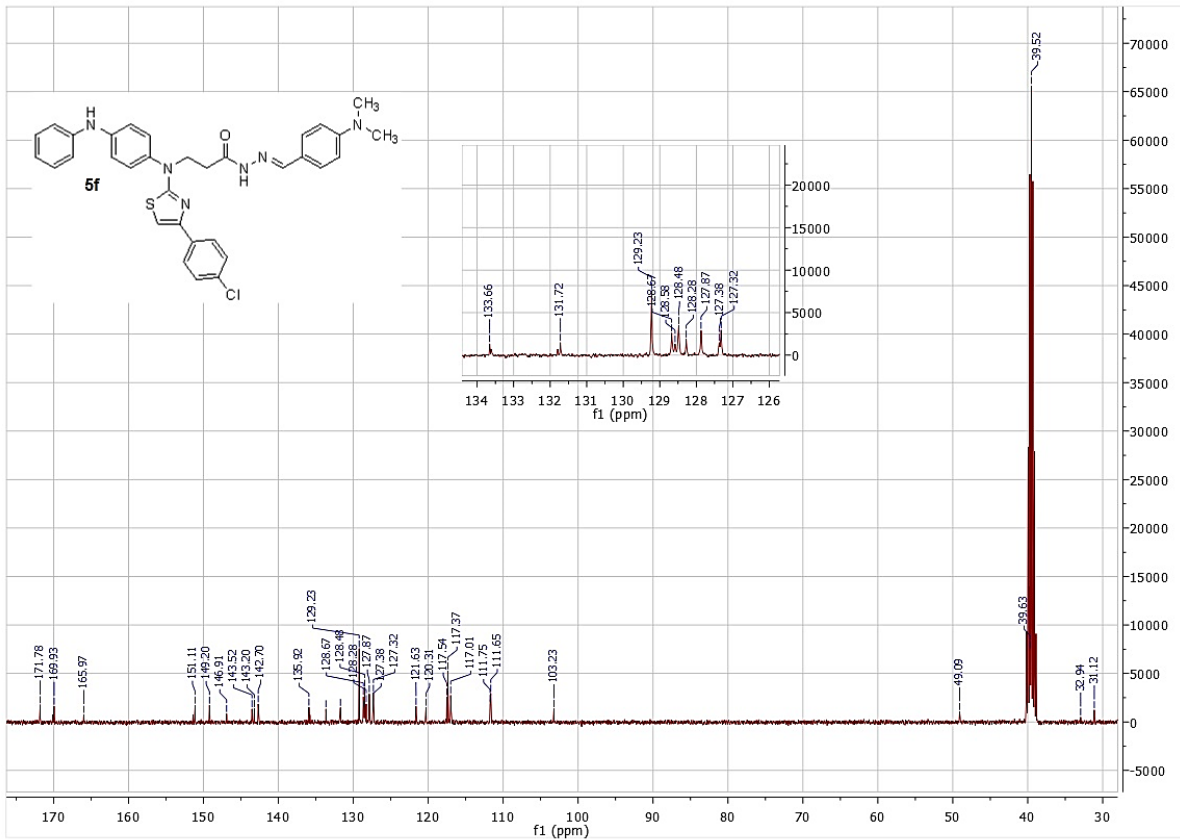
**Figure S22:**  $^{13}\text{C}$  NMR of compound **5e**



**Figure S23:** <sup>1</sup>H NMR of compound **5f**

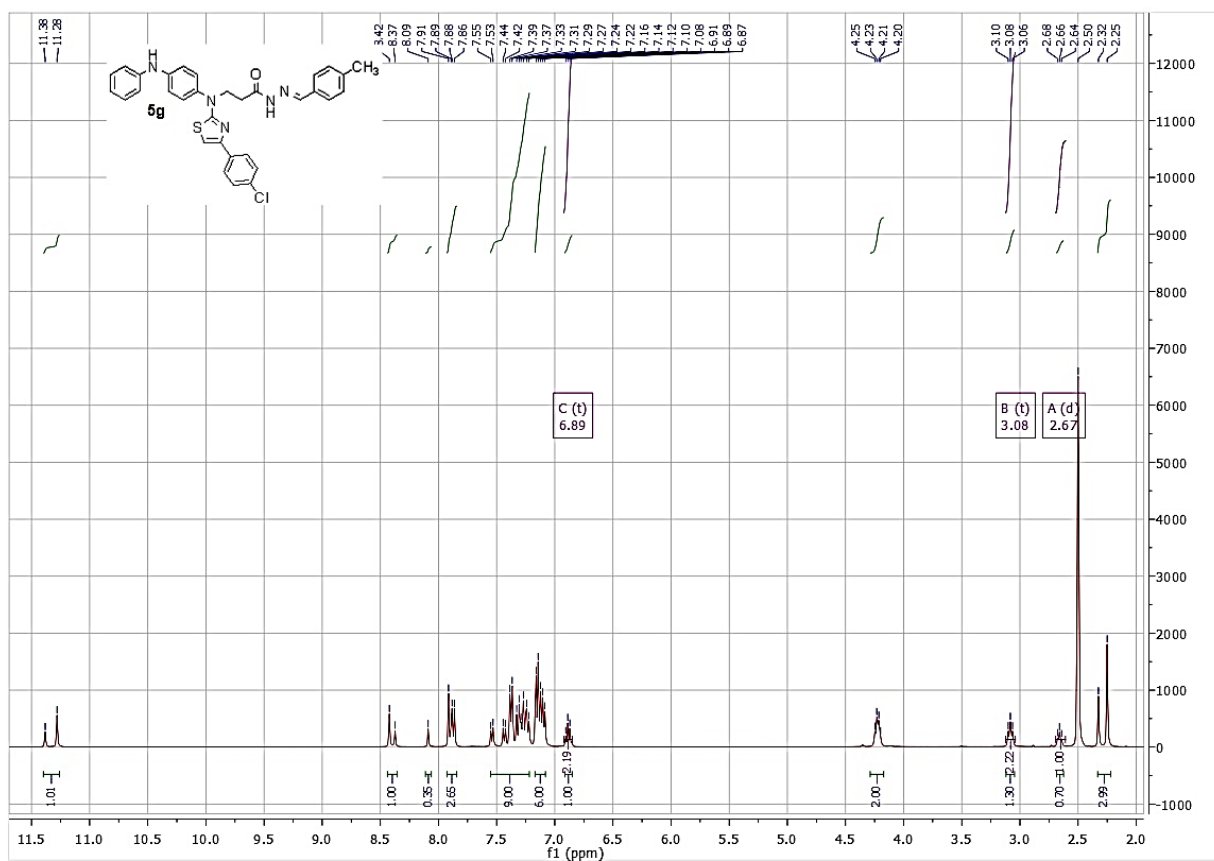


**Figure S24:**  $^{13}\text{C}$  NMR of compound **5f**

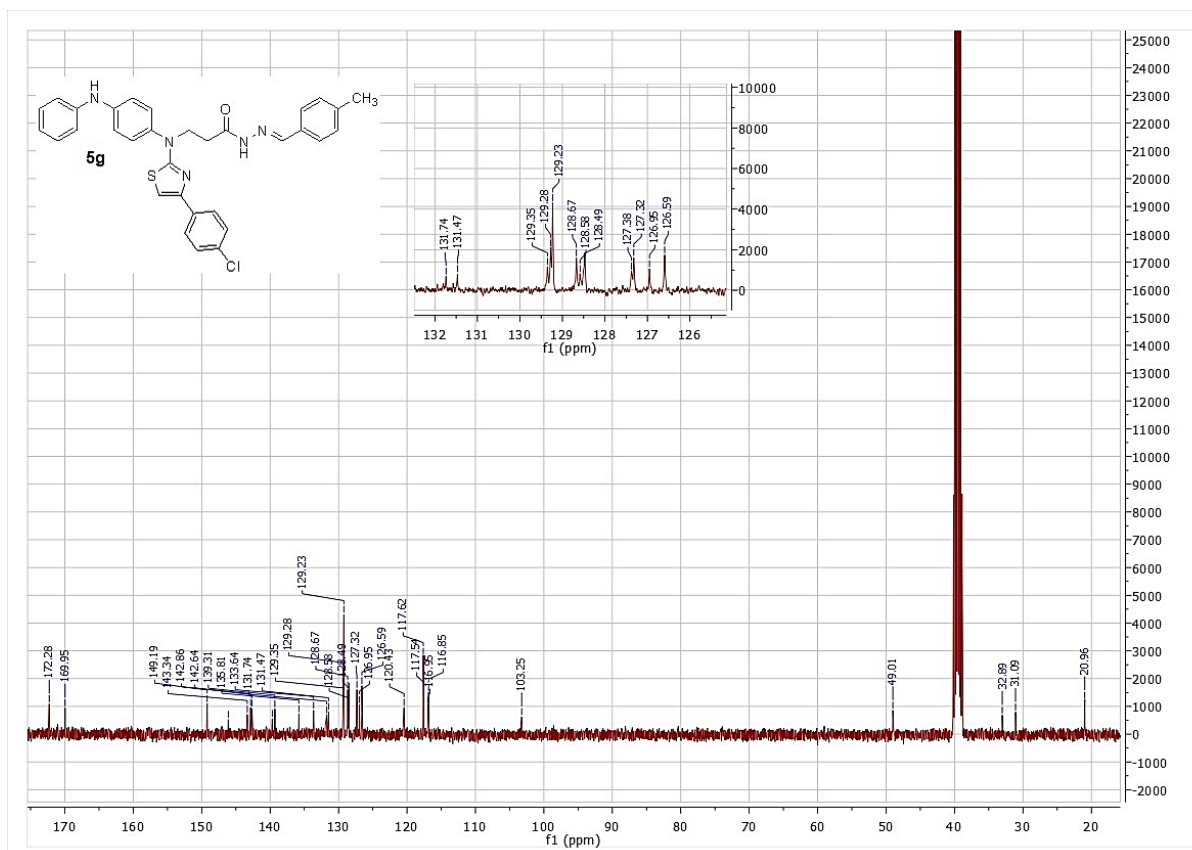


3-((4-(4-chlorophenyl)thiazol-2-yl)-N'-(4-methylbenzylidene)-(4-(phenylamino)phenyl)amino)propanehydrazide (**5g**)

**Figure S25:** <sup>1</sup>H NMR of compound **5g**



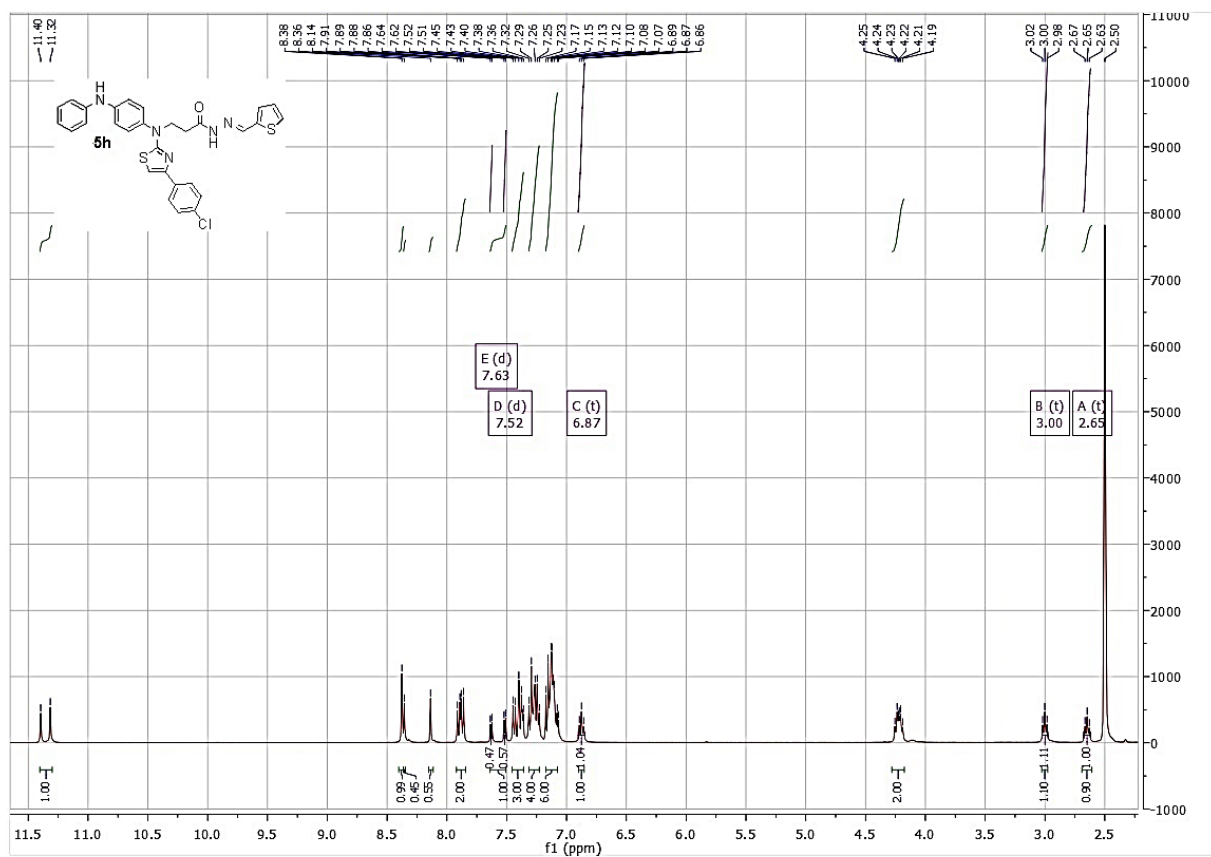
**Figure S26:** <sup>13</sup>C NMR of compound **5g**



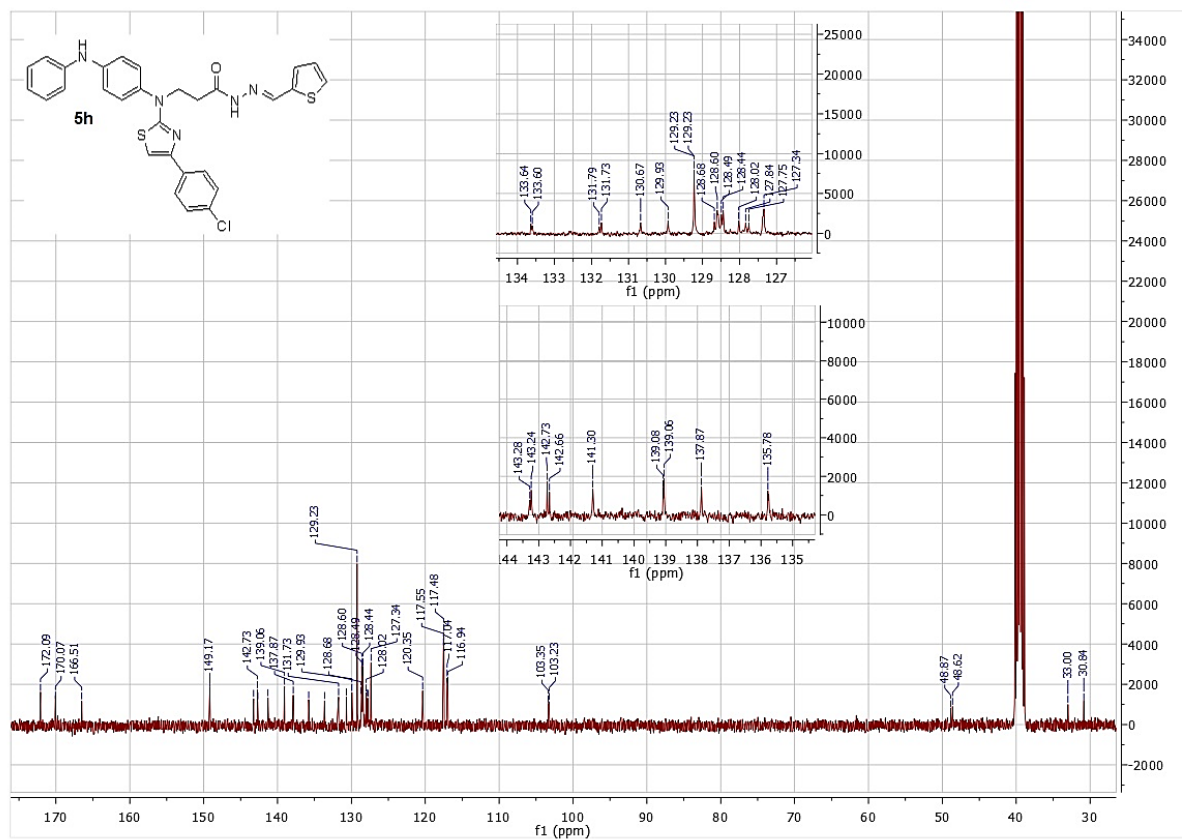


3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)-N'-(thiophen-2-ylmethylene)propanehydrazide (**5h**)

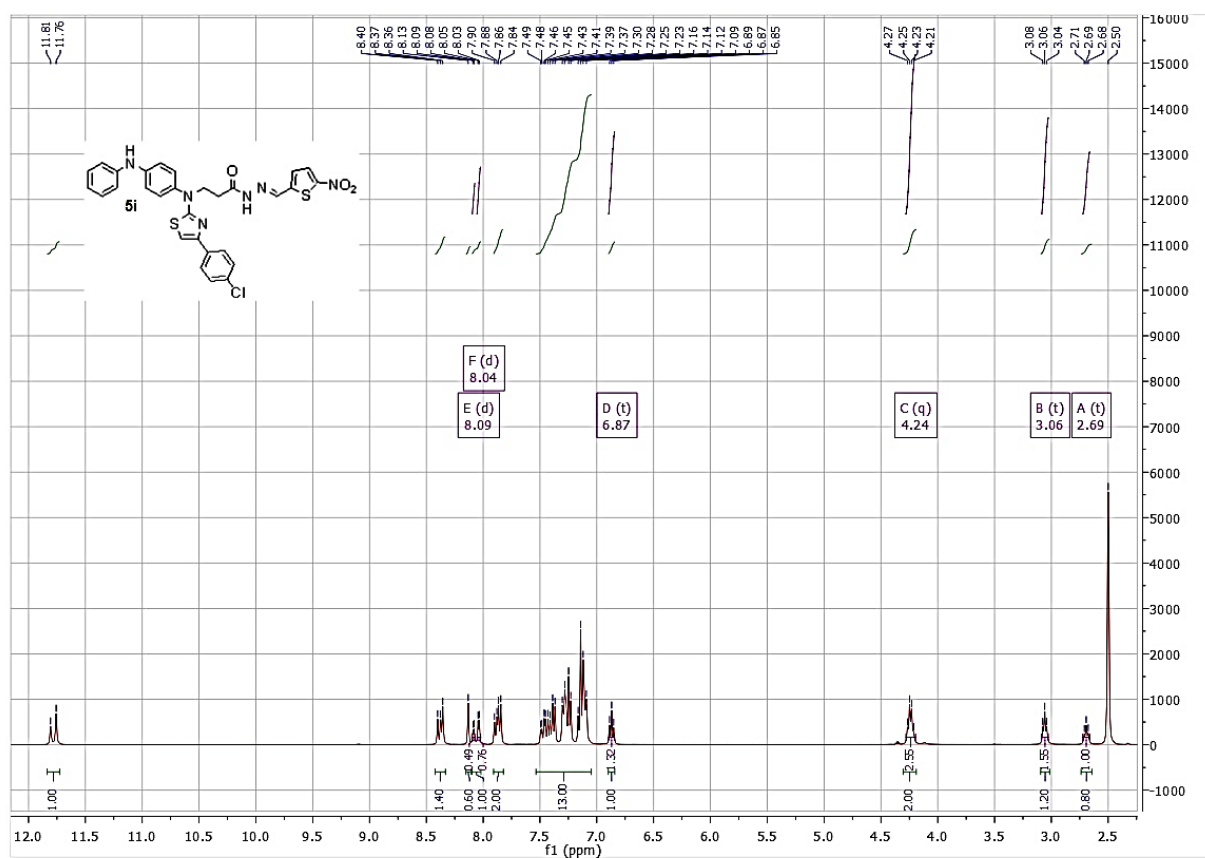
**Figure S27:** <sup>1</sup>H NMR of compound **5h**



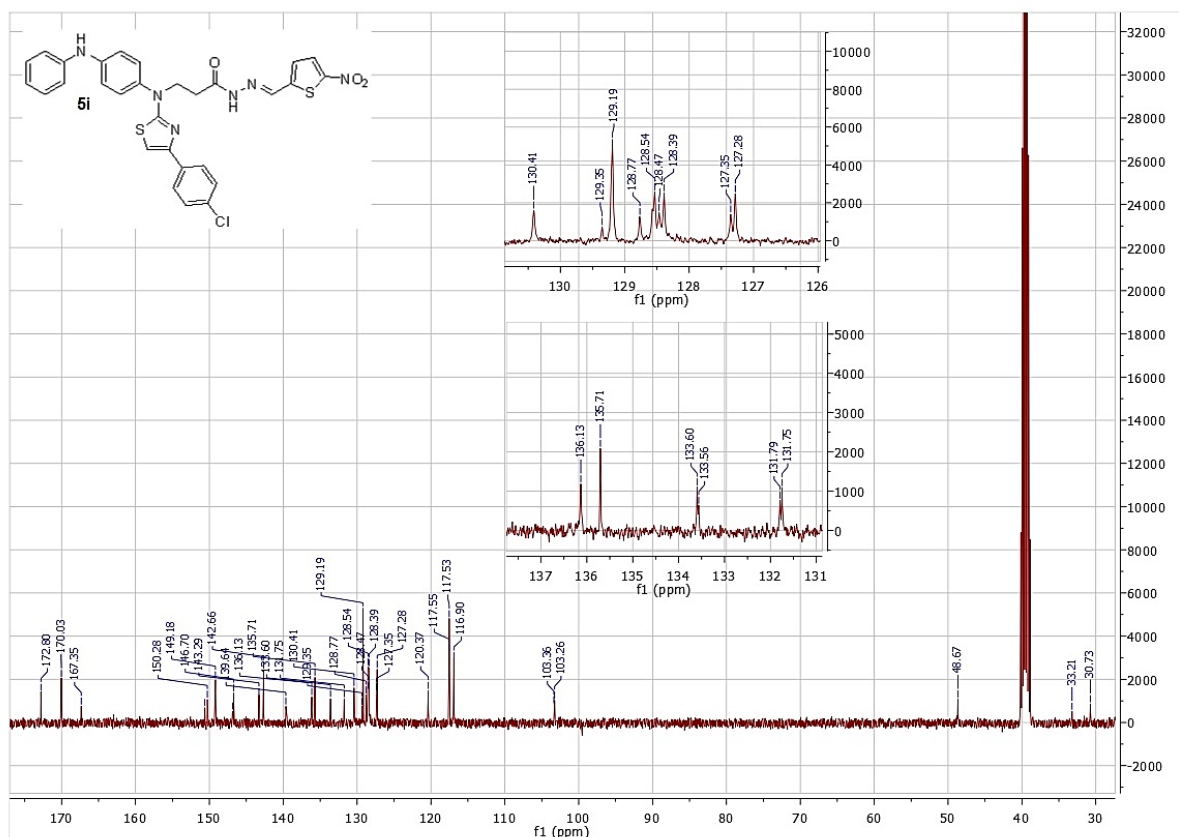
**Figure S28:** <sup>13</sup>C NMR of compound **5h**



3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)-N'-((5-nitrothiophen-2-yl)methylene)propanehydrazide (**5i**)  
**Figure S29:**  $^1\text{H}$  NMR of compound **5i**

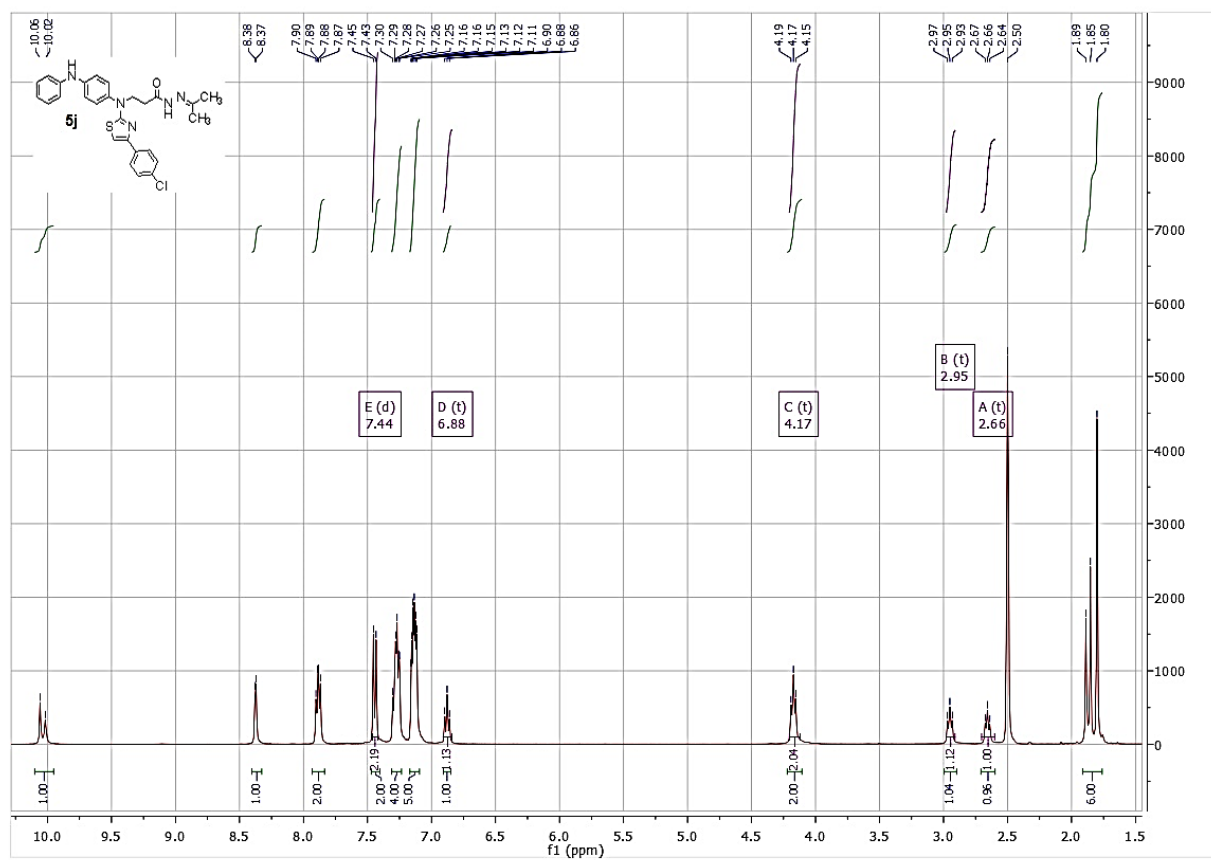


**Figure S30:**  $^{13}\text{C}$  NMR of compound **5i**

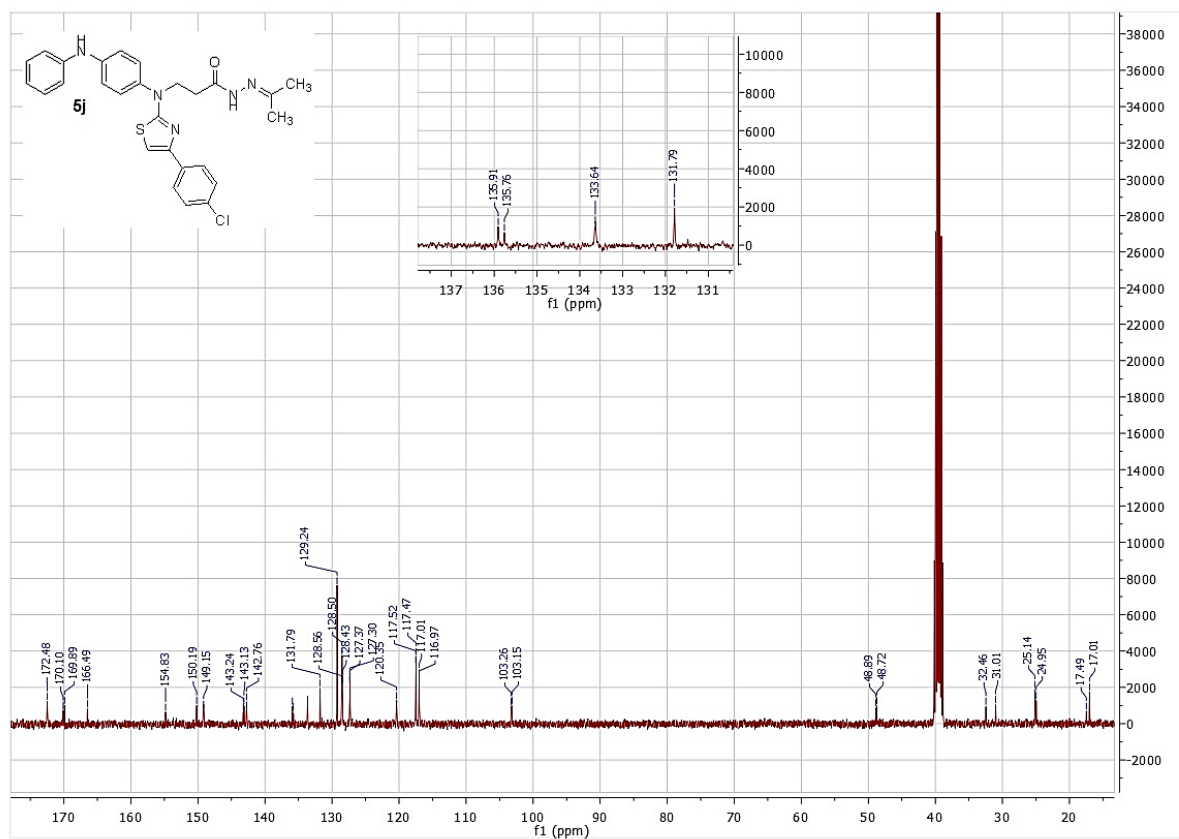




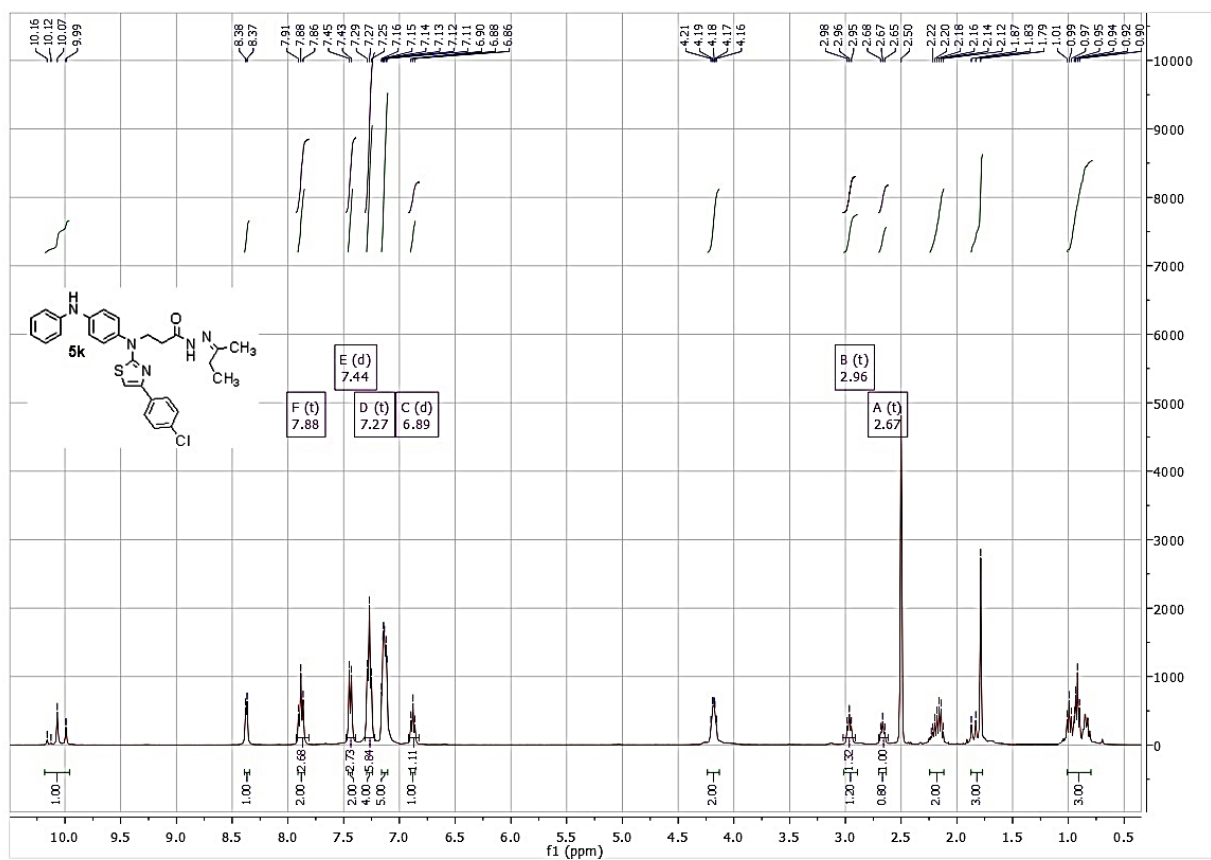
3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)-N'-(propan-2-ylidene)propanehydrazide (**5j**)  
**Figure S31**  $^1\text{H}$  NMR of compound **5j**



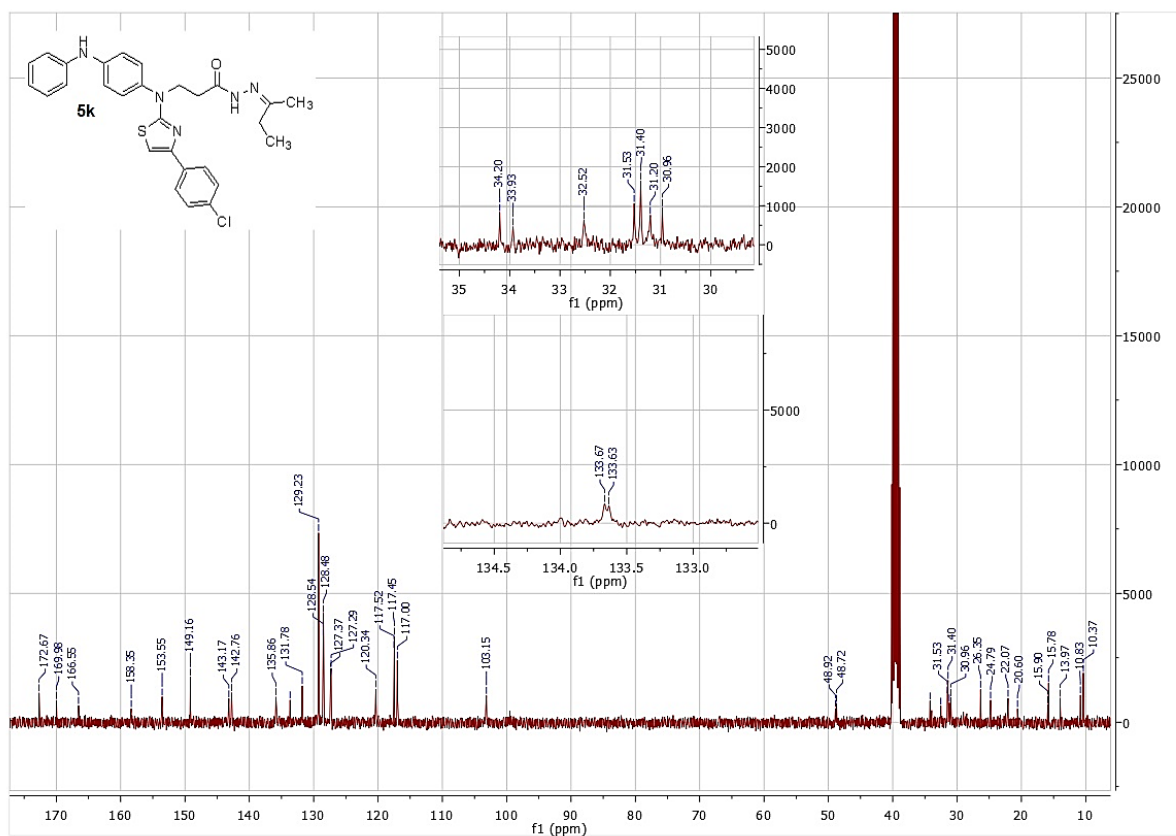
**Figure S32:**  $^{13}\text{C}$  NMR of compound **5j**



*N'*-(butan-2-ylidene)-3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanehydrazide (**5k**)  
**Figure S33:** <sup>1</sup>H NMR of compound **5k**



**Figure S34:** <sup>13</sup>C NMR of compound **5k**



## Synthesis of azoles 6-9

3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)-1-(3,5-dimethyl-1H-pyrazol-1-yl)propan-1-one (**6**)

Figure S35: <sup>1</sup>H NMR of compound **6**

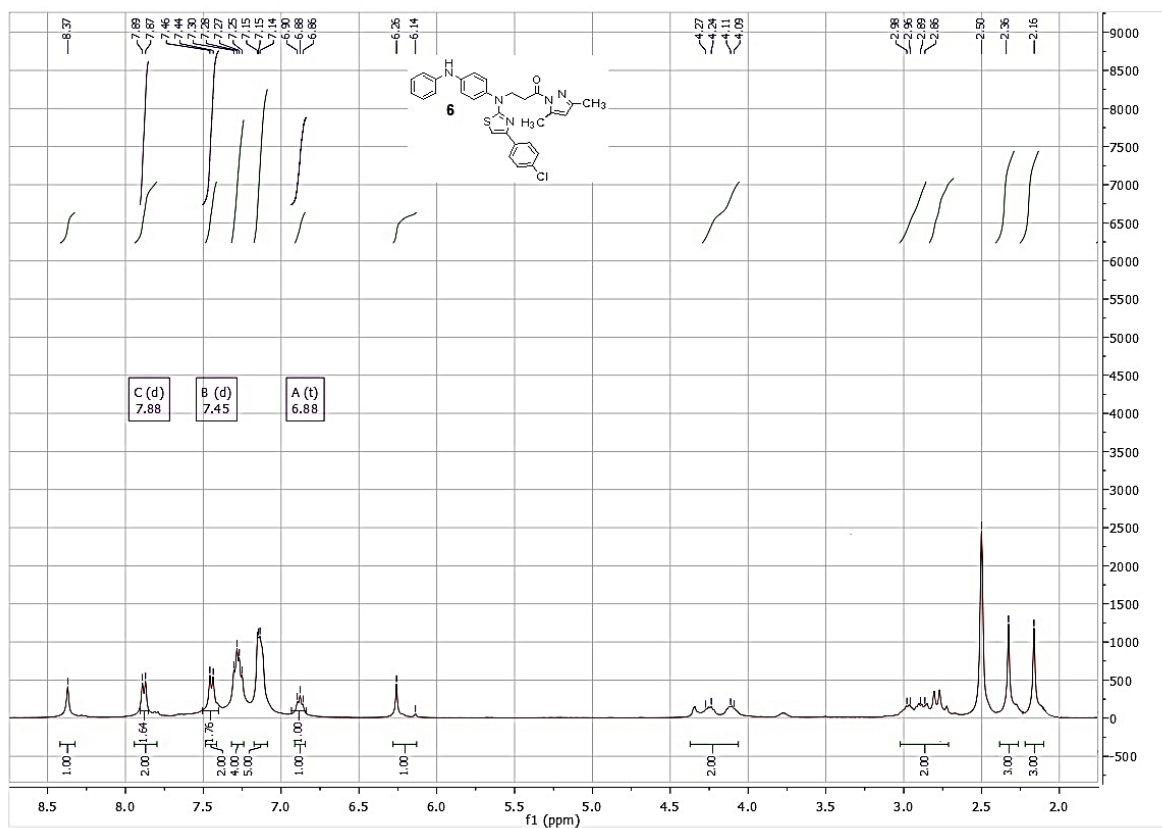
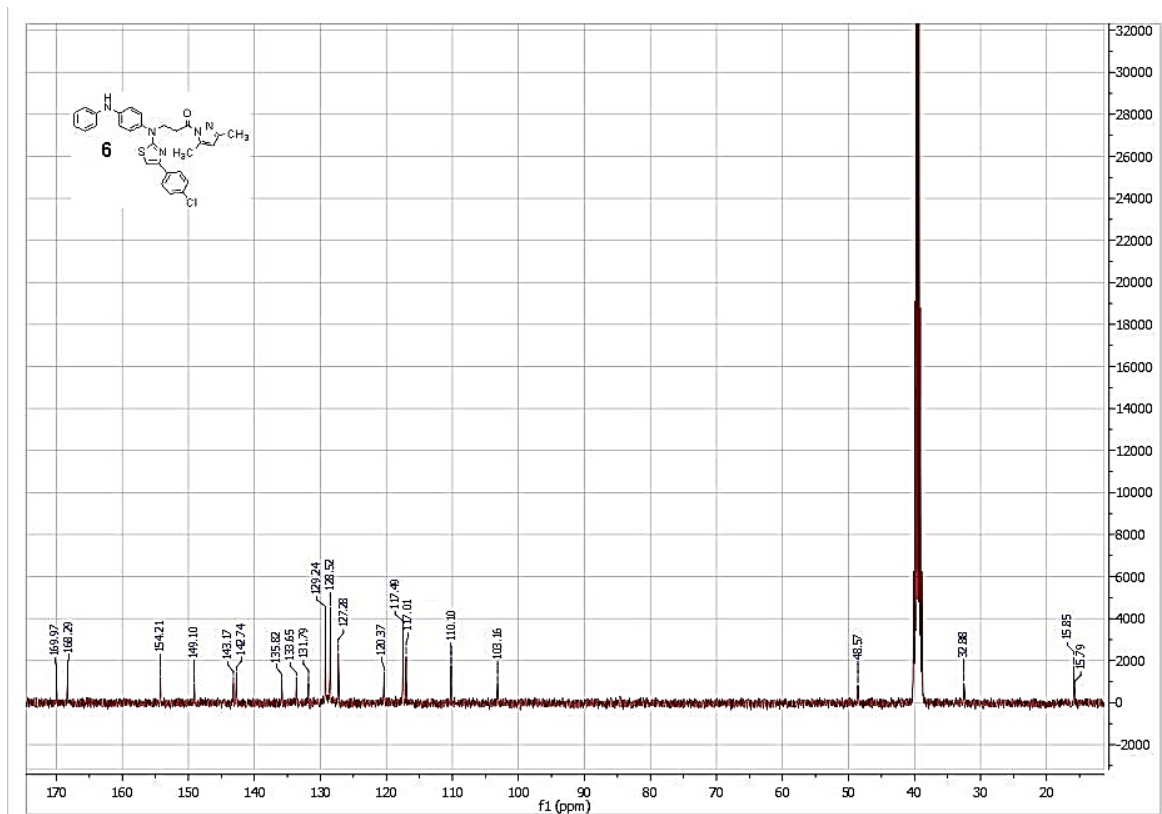
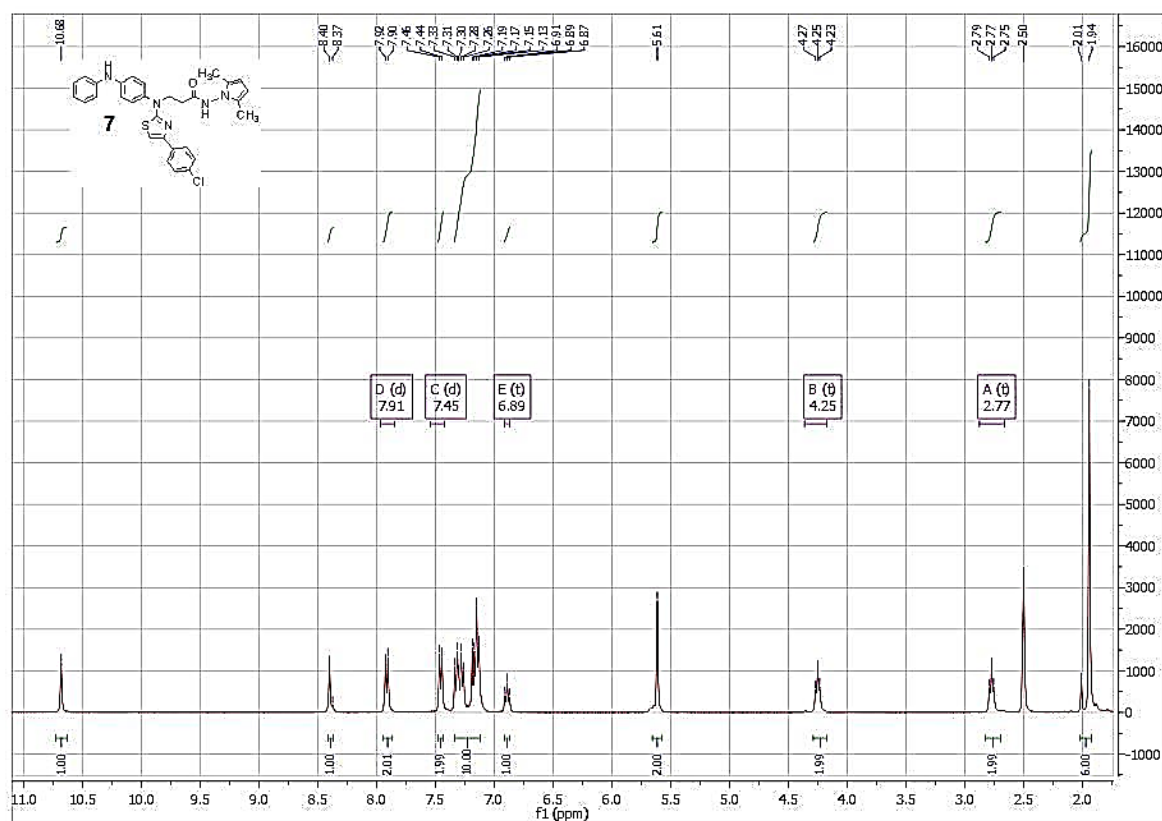


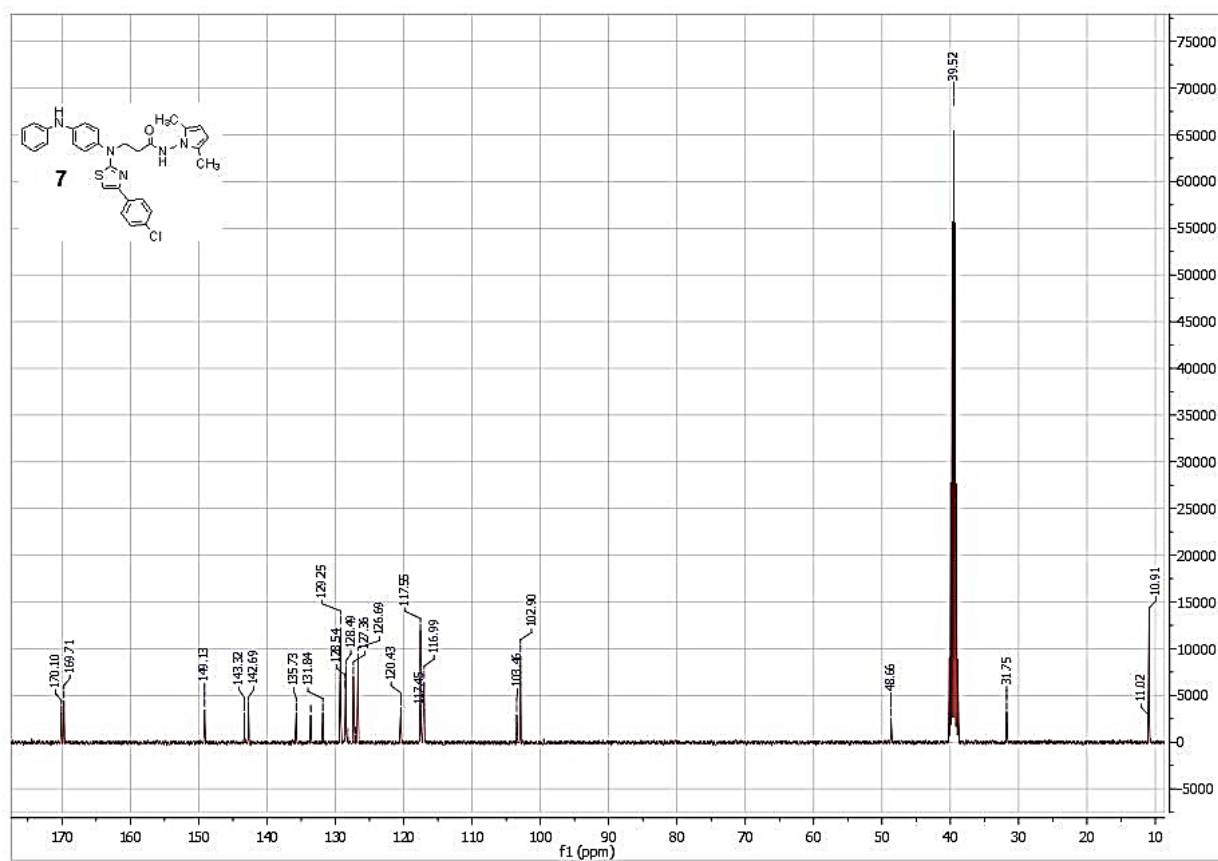
Figure S36: <sup>13</sup>C NMR of compound **6**



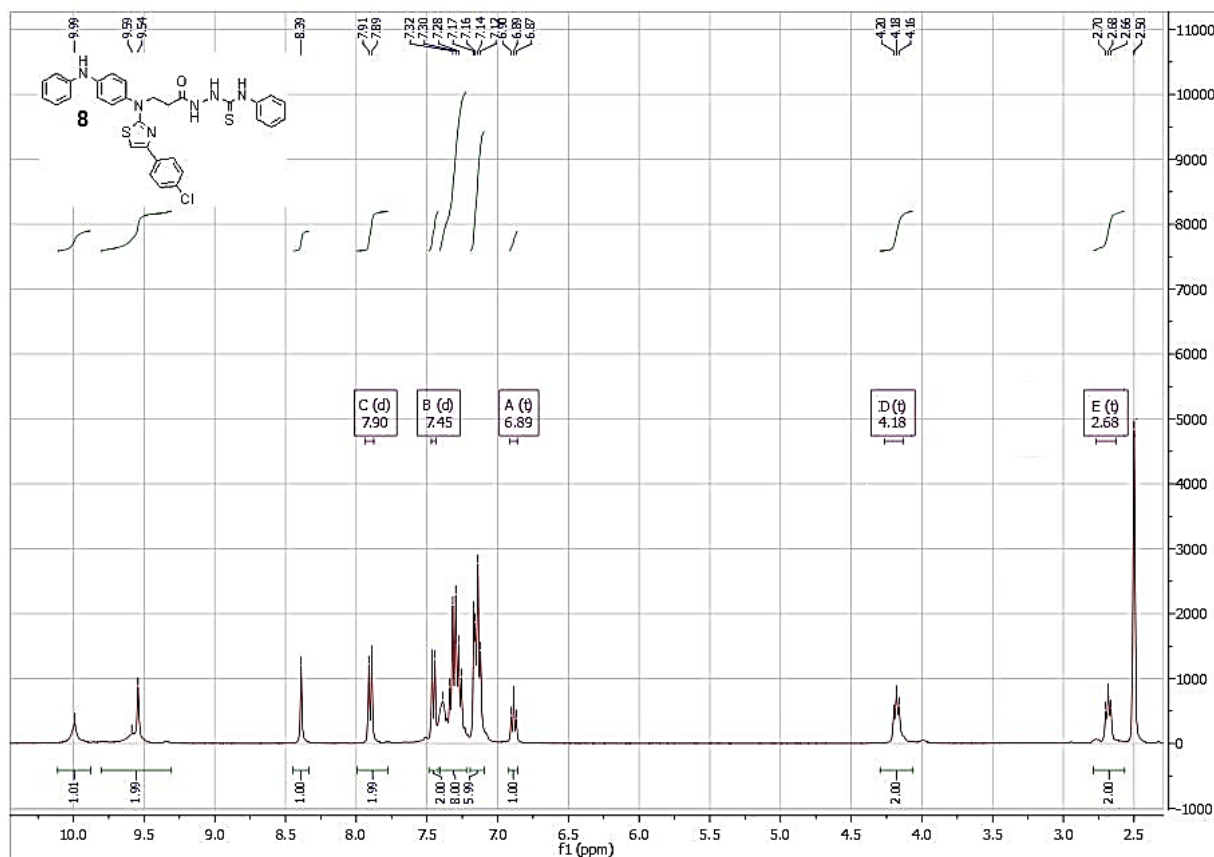
2-(3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)-N-(2,5-dimethyl-1H-pyrrol-1-yl)propanamide (**7**)  
**Figure S37:**  $^1\text{H}$  NMR of compound **7**



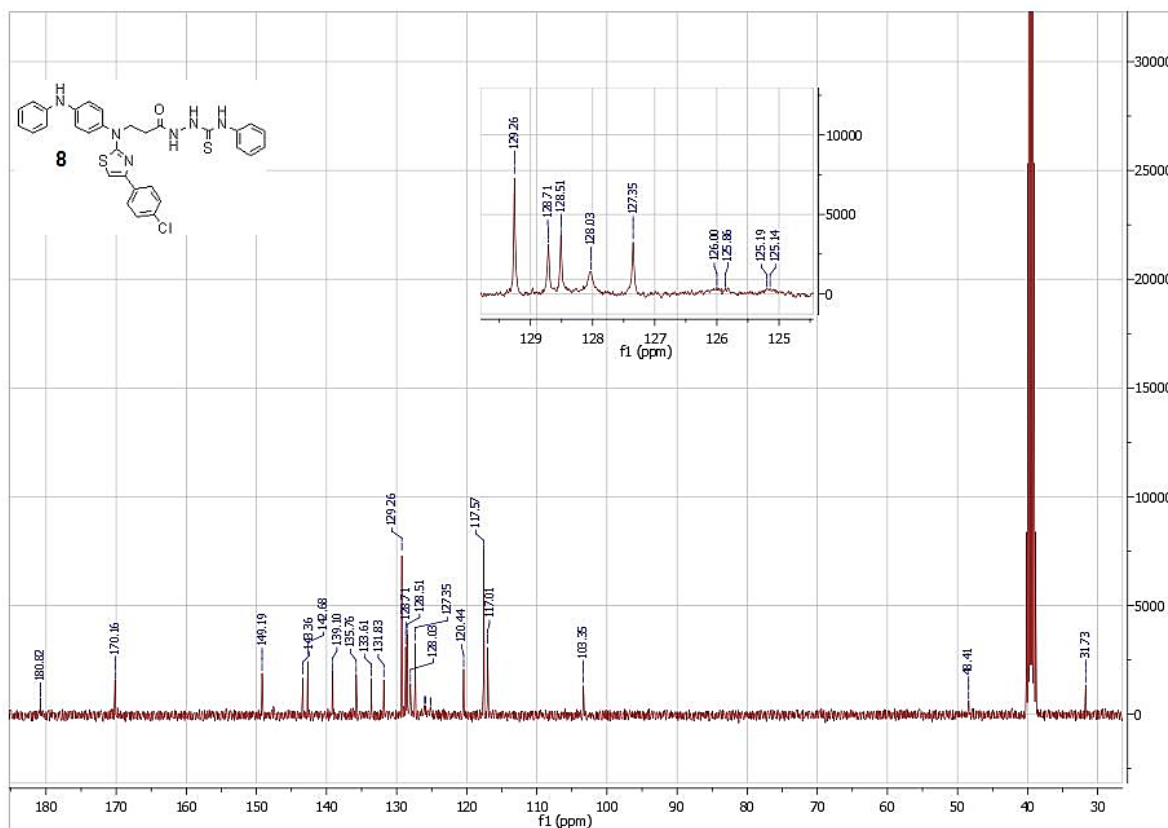
**Figure S38:**  $^{13}\text{C}$  NMR of compound **7**



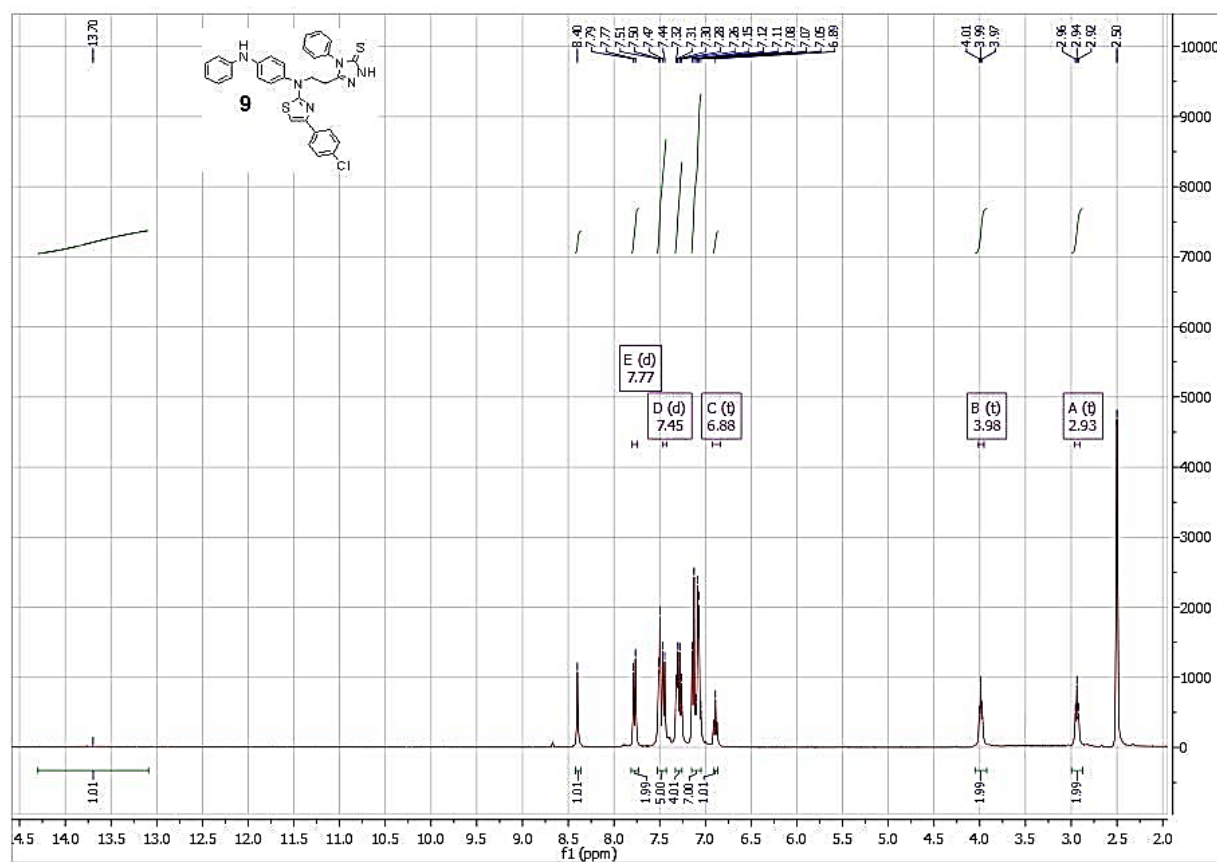
2-(3-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)propanoyl)-N-phenylhydrazine-1-carbothioamide (**8**)  
**Figure S39:**  $^1\text{H}$  NMR of compound **8**



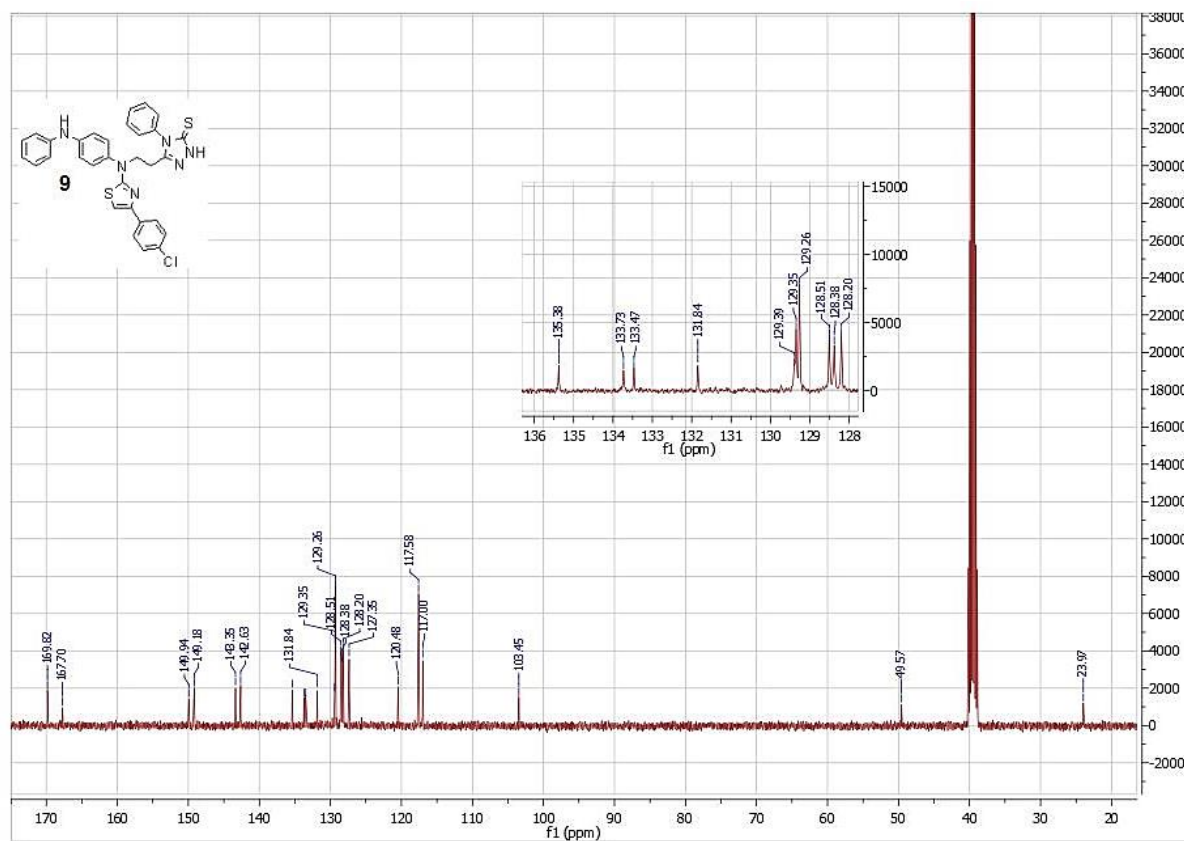
**Figure S40:**  $^{13}\text{C}$  NMR of compound **8**



5-(2-((4-(4-chlorophenyl)thiazol-2-yl)(4-(phenylamino)phenyl)amino)ethyl)-4-phenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**9**)  
**Figure S41:**  $^1\text{H}$  NMR of compound **9**



**Figure S42:**  $^{13}\text{C}$  NMR of compound **9**



**Table S1.** The list of fungal strains used for the study

<b>Fungi</b>	<b>Isolate number</b>	<b>Strain feature</b>	<b>Source</b>
<i>Aspergillus fumigatus</i>	731	Azole resistance, L98H, TR34	CDC
<i>Aspergillus fumigatus</i>	732	Azole resistance, F495I, L98H, S297T, TR34	CDC
<i>Aspergillus fumigatus</i>	2122	Pan-susceptible	Laboratory strain
<i>Candida auris</i>	381	Azole resistant	CDC
<i>Candida auris</i>	382	Azole resistant	CDC
<i>Candida auris</i>	383	Azole resistant	CDC
<i>Candida auris</i>	384	Azole resistant	CDC
<i>Candida duobushaemulonii</i>	389	Azole resistant	CDC
<i>Candida krusei</i>	397	Azole resistant	CDC
<i>Candida albicans</i>	1214	Azole resistant	Laboratory strain

**Abbreviations:** ATCC-American Type Culture Collection; CDC – Center for Disease Control.