Supplementary materials

Novel Thiazolidine-2,4-Dione-Trimethoxybenzene-Thiazole Hybrids as Human Topoisomerases Inhibitors

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Fig. S39. ^{13}C-NMR spectrum of 2-iodo-N-(4-phenylthiazol-2-yl)acetamide (**6b**).

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Fig. S50. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzlidene)thiazolidine-2,4-dion-3-yl)-N-(4-phenylthiazole-2-yl)acetamide (**7b**).

Fig. S51. ^{13}C-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzlidene)thiazolidine-2,4-dion-3-yl)-N-(4-phenylthiazole-2-yl)acetamide (**7b**).

Fig. S52. ^{1}H-NMR spectrum of (Z)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-methylphenyl)thiazol-2-yl)acetamide (**7c**).

Fig. S53. ^{13}C-NMR spectrum of (Z)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-methylphenyl)thiazol-2-yl)acetamide (**7c**).

Fig. S54. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-chlorophenyl)thiazol-2-yl)acetamide (**7d**).

Fig. S55. ^{13}C-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-chlorophenyl)thiazol-2-yl)acetamide (**7d**).

Fig. S56. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-bromophenyl)thiazol-2-yl)acetamide **(7e)**.

Fig. S57. ^{13}C-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-bromophenyl)thiazol-2-yl)acetamide (**7e**).

Fig. S58. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(benzo[*d*]thiazol-2-yl)acetamide (**7f**).

3) 2D-schematic representation of ligand-protein interactions. All the plots were calculated using LIGPLOT (Wallace A C, Laskowski R A & Thornton J M (1995). LIGPLOT: A program to generate schematic diagrams of protein-ligand interactions. *Prot. Eng.*, 8, 127-134.). Figures S59-S64 are relative to hTopo I; Figures S65-S70 are relative to hTopo II.

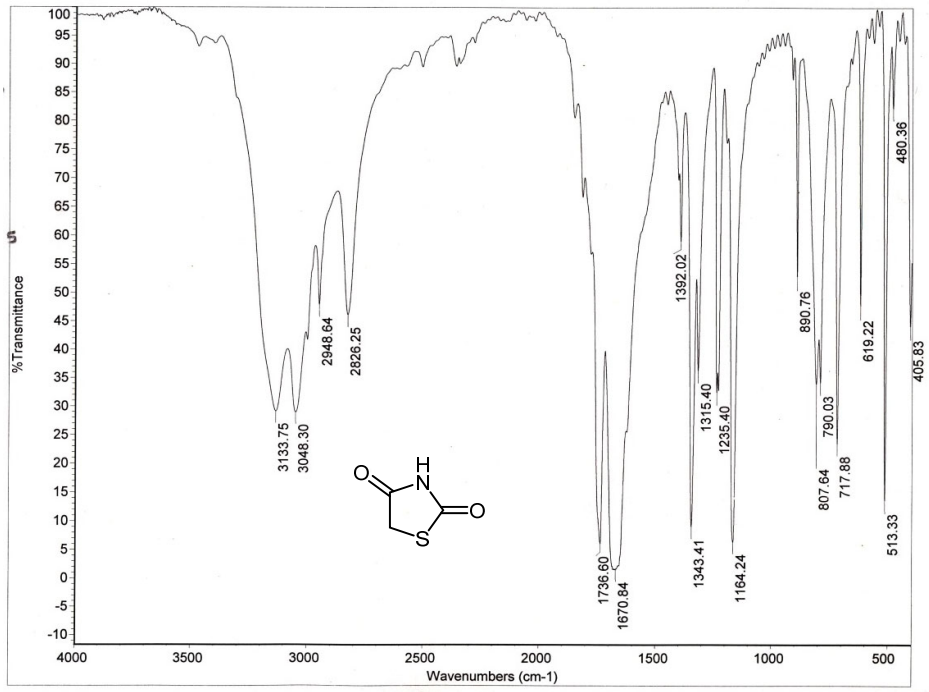


Fig. S1. IR spectrum of 1,3-thiazolidine-2,4-dione (**1**).

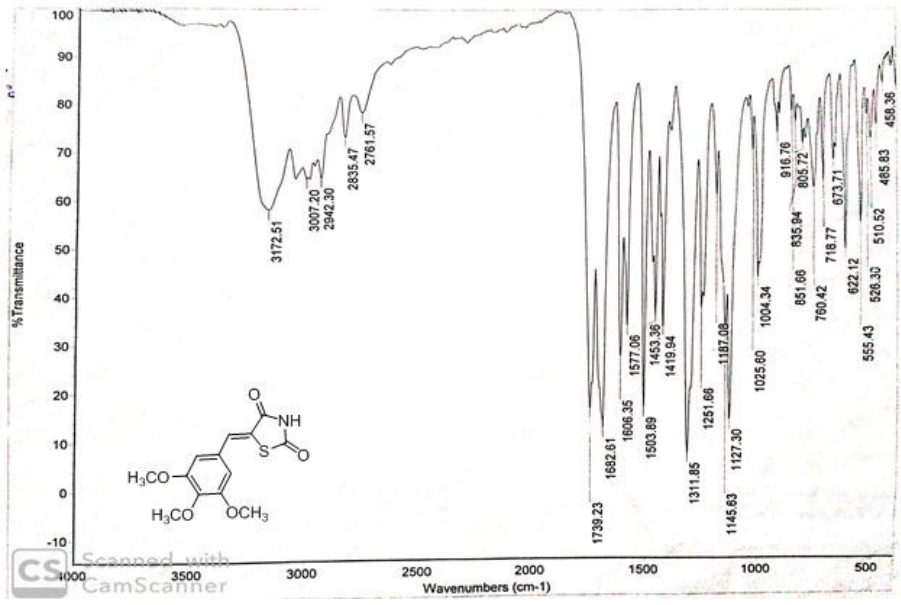


Fig. S2. IR spectrum of (*Z*)-5-(3,4,5-Trimethoxybenzylidene)thiazolidine-2,4-dione (**2**).

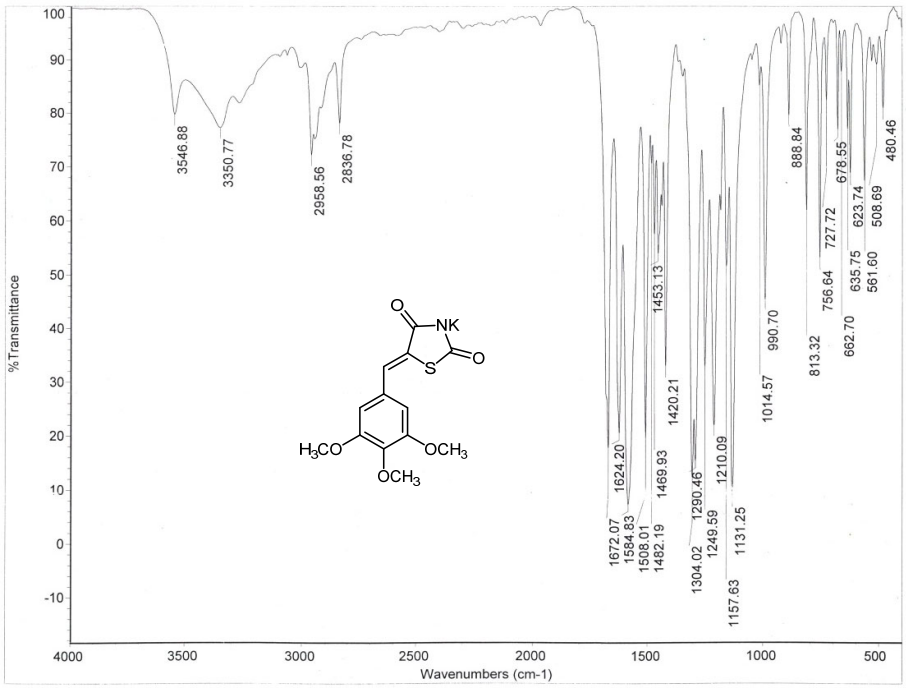


Fig. S3. IR spectrum of potassium (Z)-5-(3,4,5-Trimethoxybenzylidene)thiazolidine-2,4-dion-3-ide (**3**).

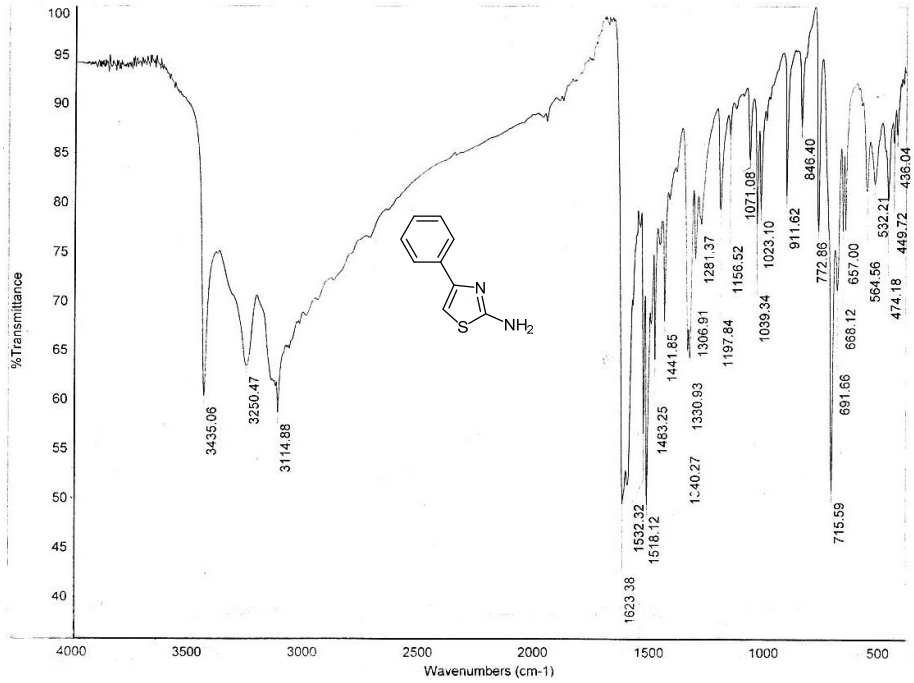


Fig. S4. IR spectrum of 2-amino-4-phenylthiazole (**4b**).

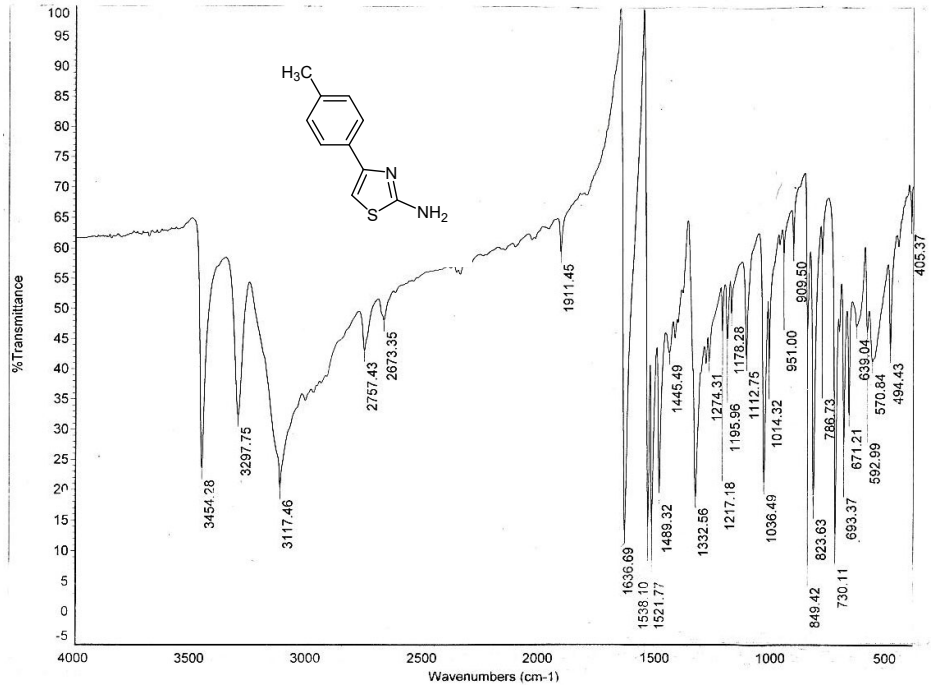


Fig. S5. IR spectrum of 2-amino-4-(4-methylphenyl)thiazole (**4c**).

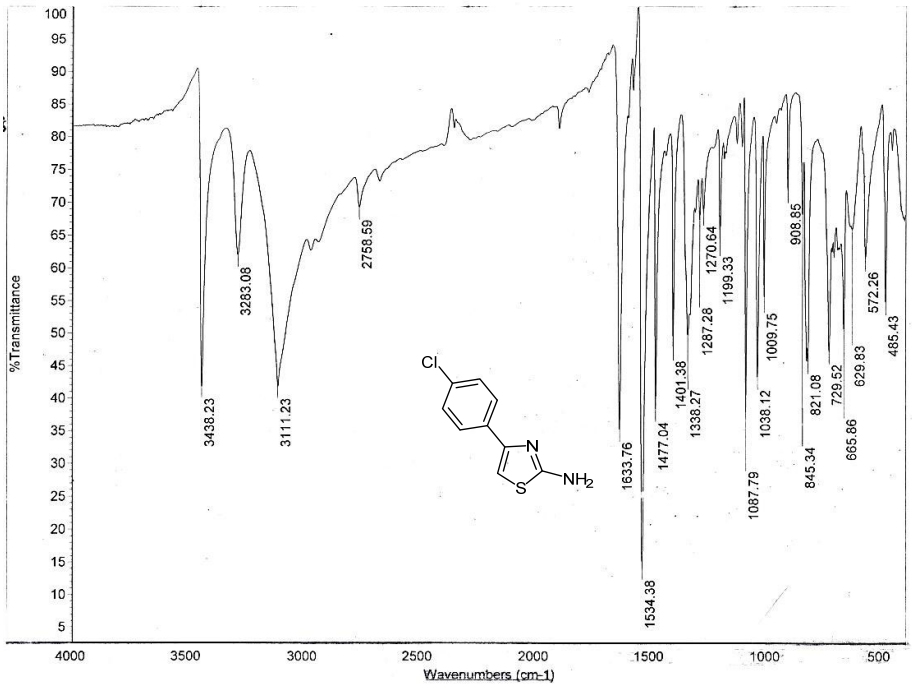


Fig. S6. IR spectrum of 2-amino-4-(4-chlorolphenyl)thiazole (**4d**).

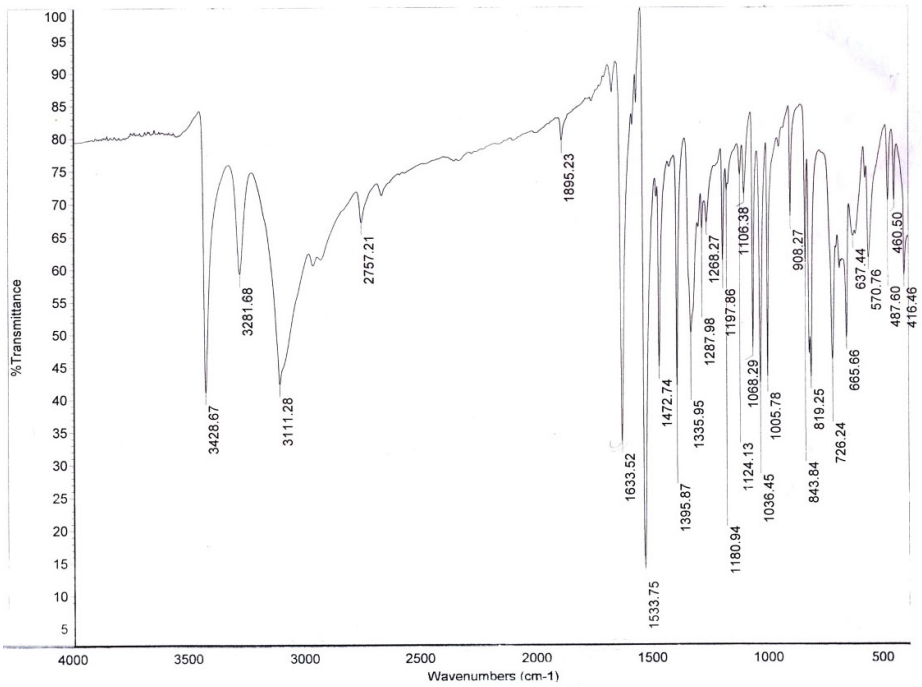


Fig. S7. IR spectrum of 2-amino-4-(4-bromolphenyl)thiazole (**4e**).

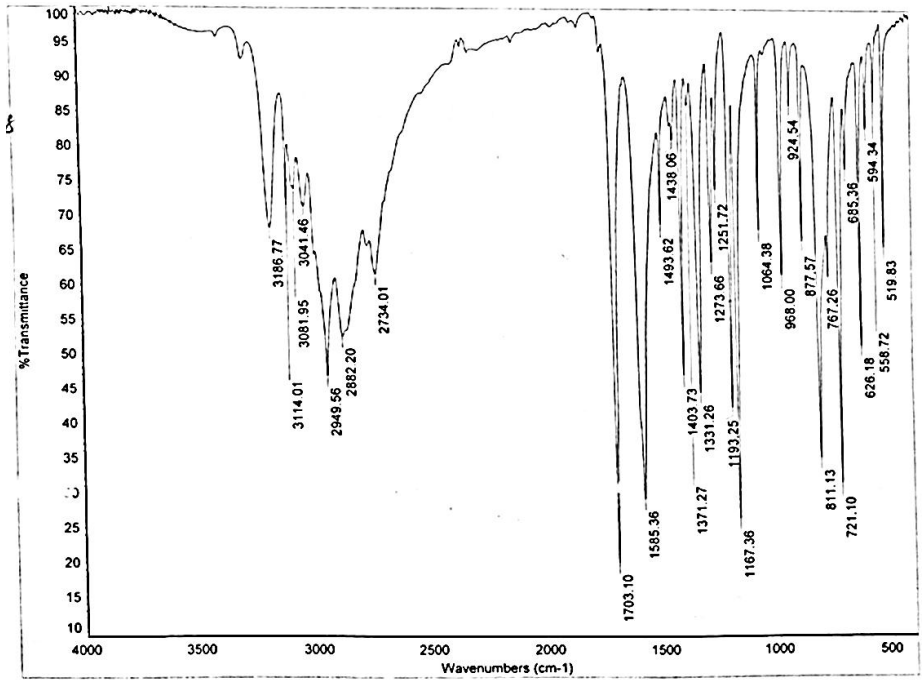


Fig. S8. IR spectrum of 2-chloro-N-(thiazol-2-yl)acetamide (**5a**).

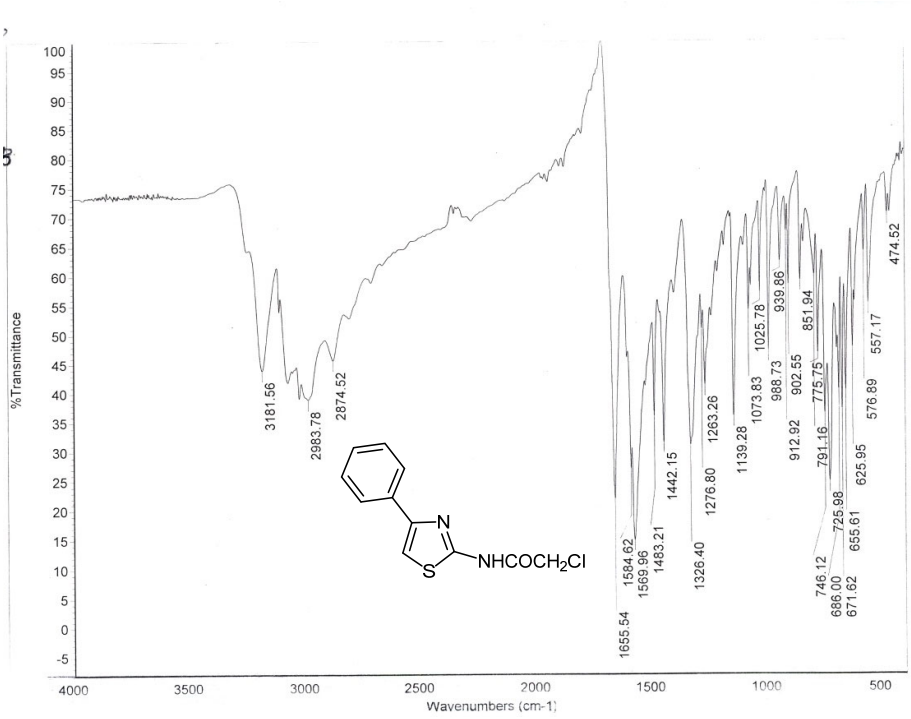


Fig. S9. IR spectrum of 2-chloro-N-(4-phenylthiazol-2-yl)acetamide (**5b**).

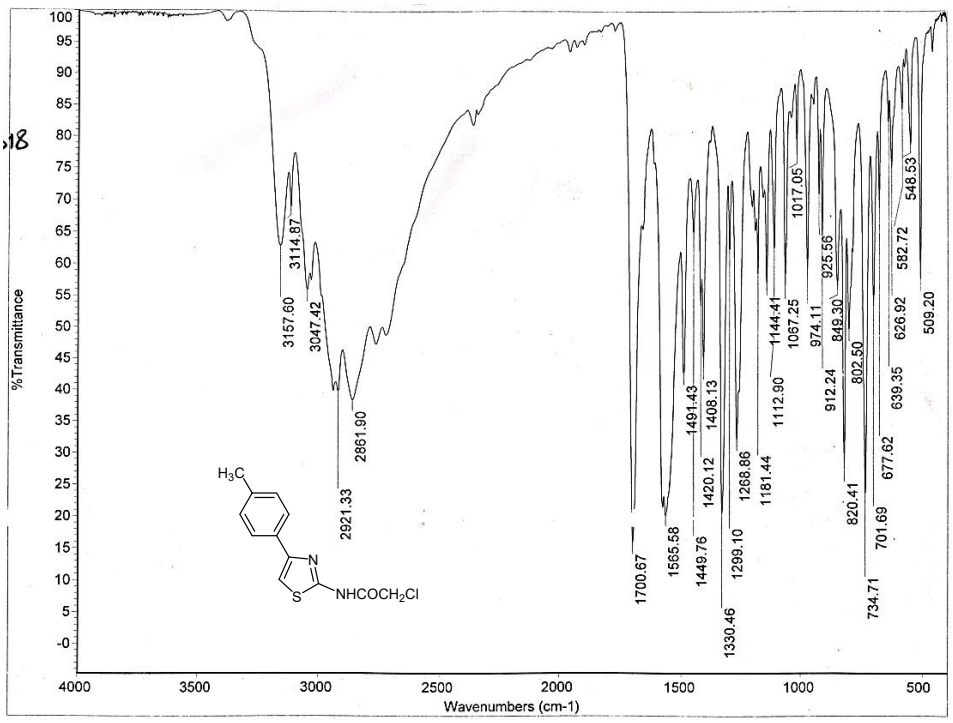


Fig. S10. IR spectrum of 2-chloro-N-(4-methylphenylthiazol-2-yl)acetamide (**5c**).

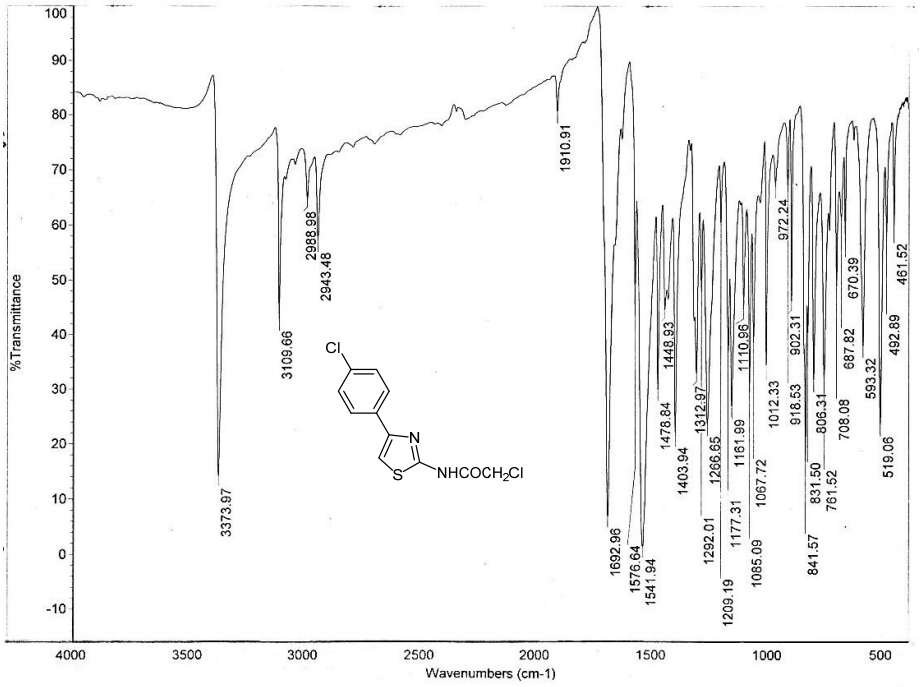


Fig. S11. IR spectrum of 2-chloro-N-(4-chlorophenylthiazol-2-yl)acetamide (**5d**).

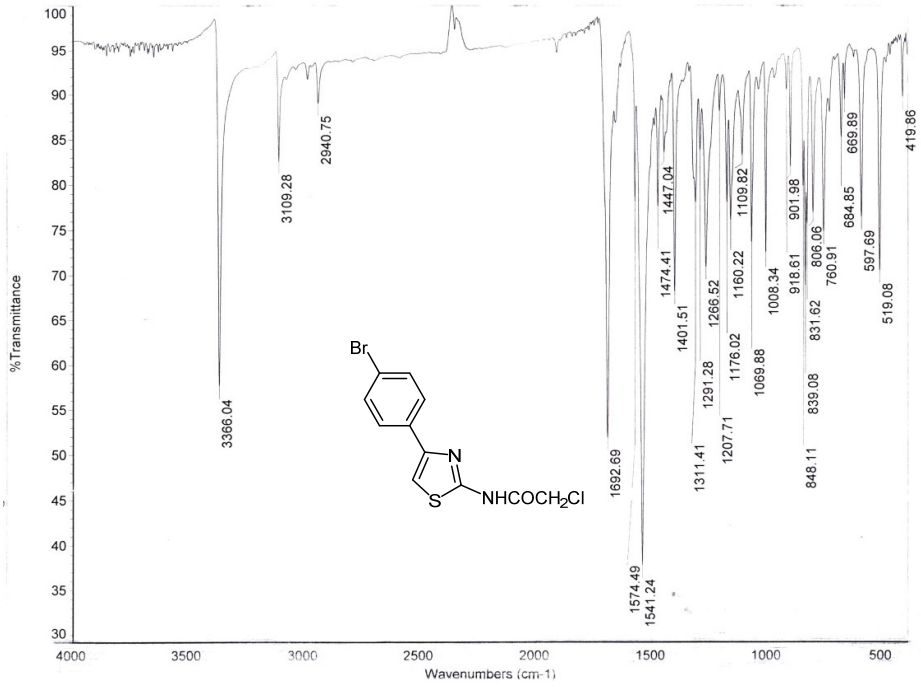


Fig. S12. IR spectrum of 2-chloro-N-(4-bromophenylthiazol-2-yl)acetamide (**5e**).

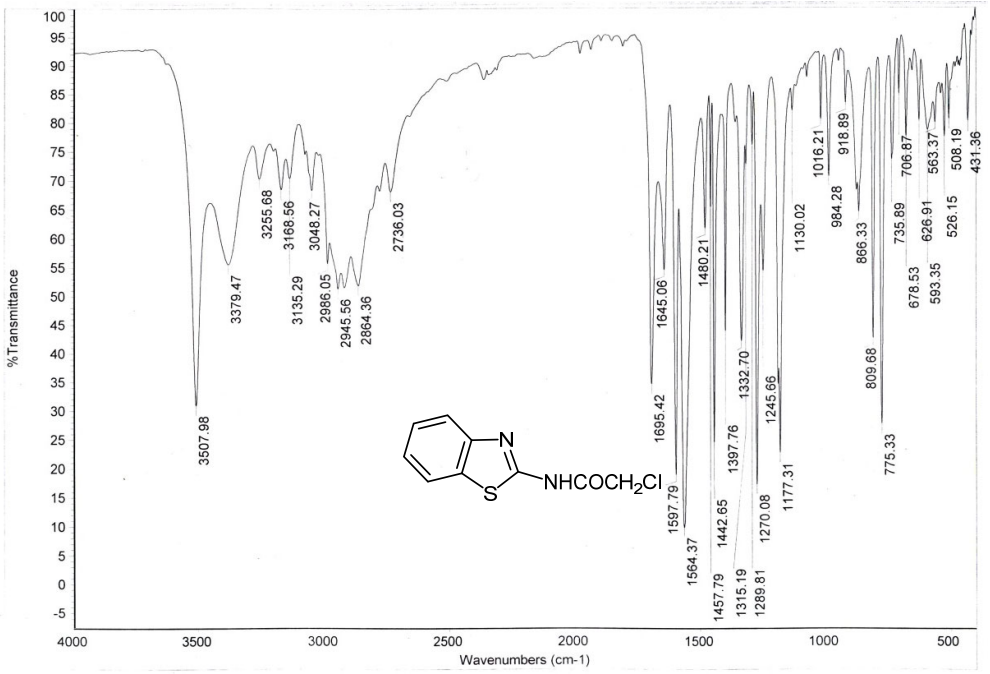


Fig. S13. IR spectrum of 2-chloro-N-(benzo[*d*] thiazol-2-yl)acetamide (**5f**).

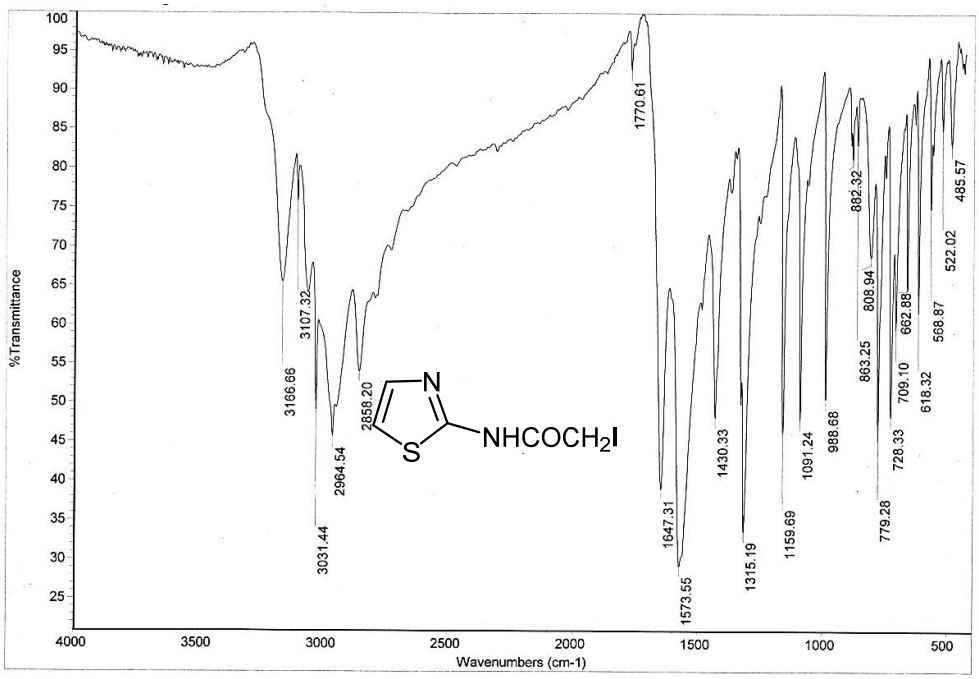


Fig. S14. IR spectrum of 2-iodo-N-(thiazol-2-yl)acetamide (**6a**).

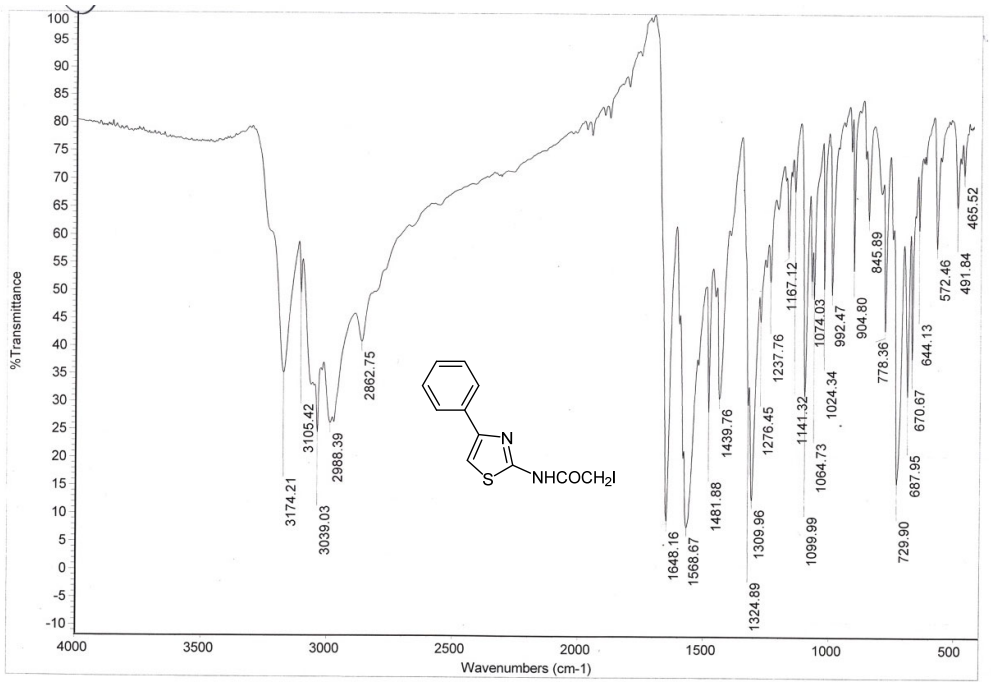


Fig. S15. IR spectrum of 2-iodo-N-(4-phenylthiazol-2-yl)acetamide (**6b**).

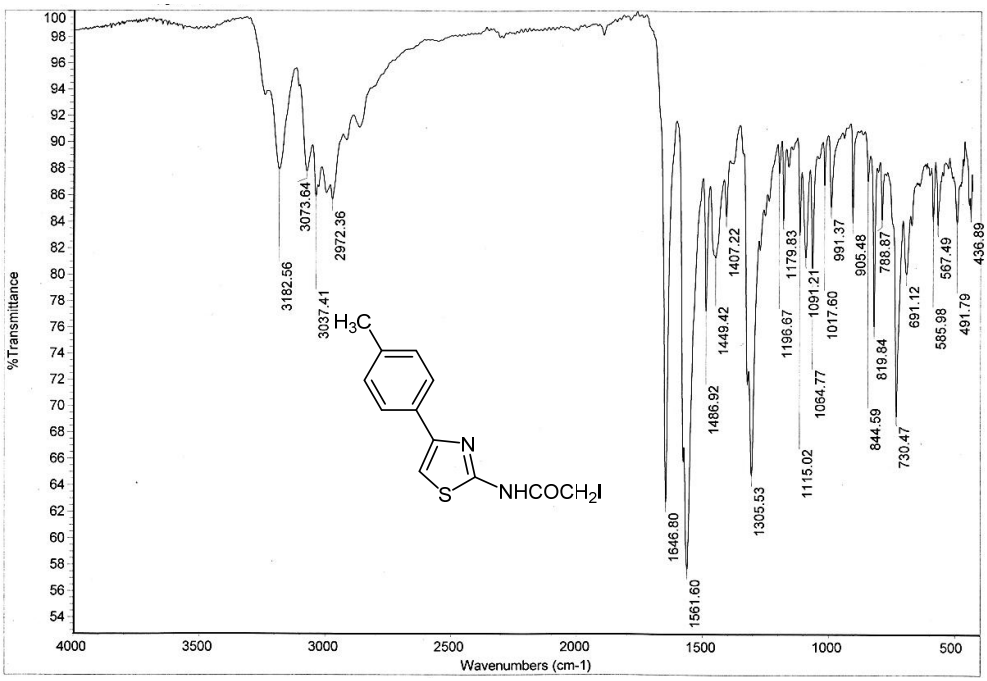


Fig. S16. IR spectrum of 2-iodo-N-(4-methyl phenylthiazol-2-yl)acetamide (**6c**).

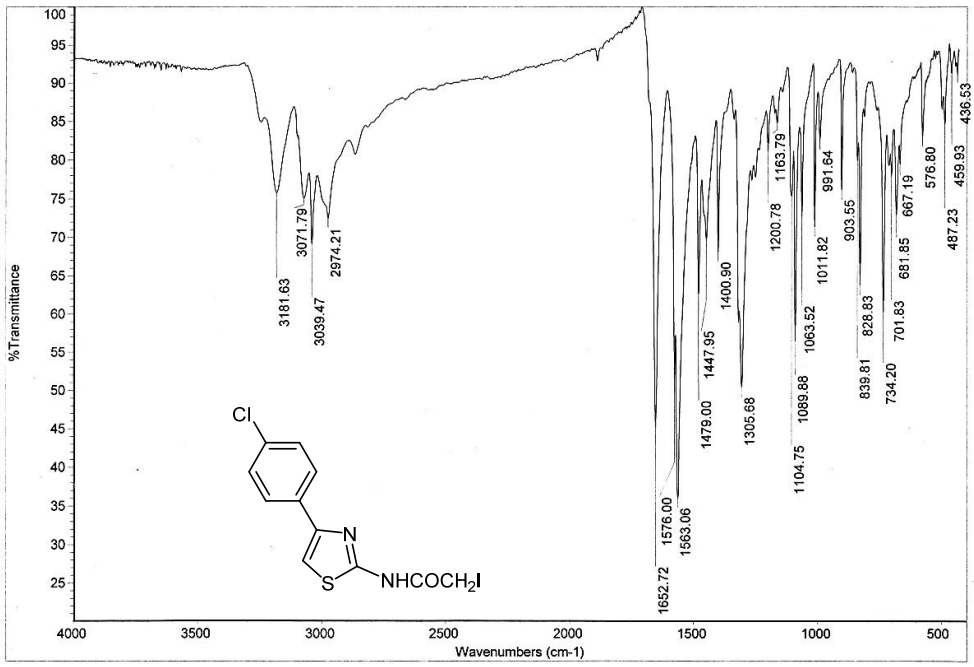


Fig. S17. IR spectrum of 2-iodo -N-(4-chlorophenylthiazol-2-yl)acetamide (**6d**).

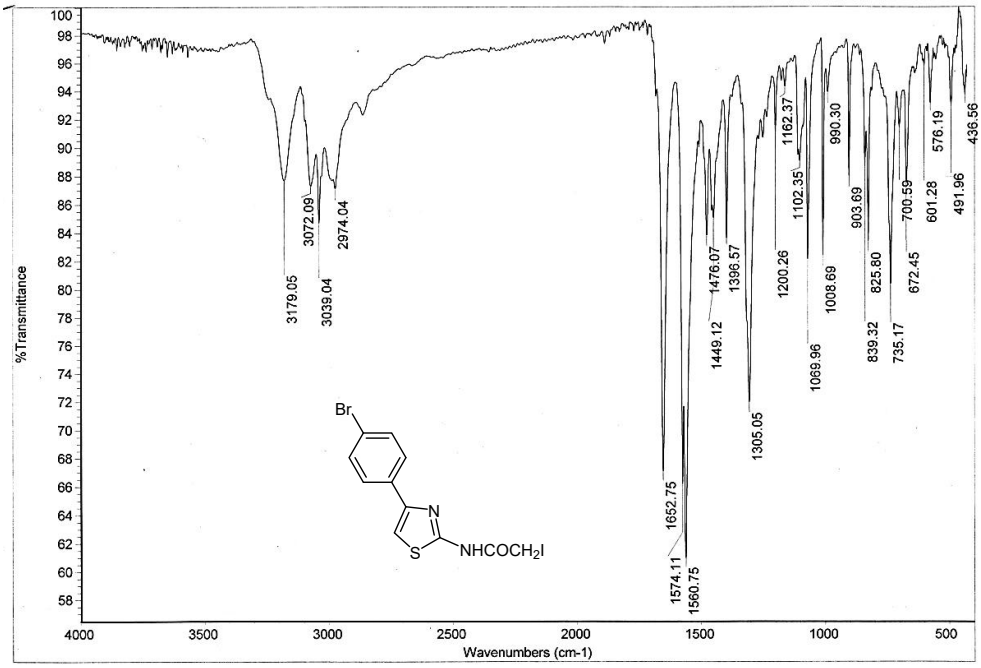


Fig. S18. IR spectrum of 2-iodo -N-(4-bromophenylthiazol-2-yl)acetamide (**6e**).

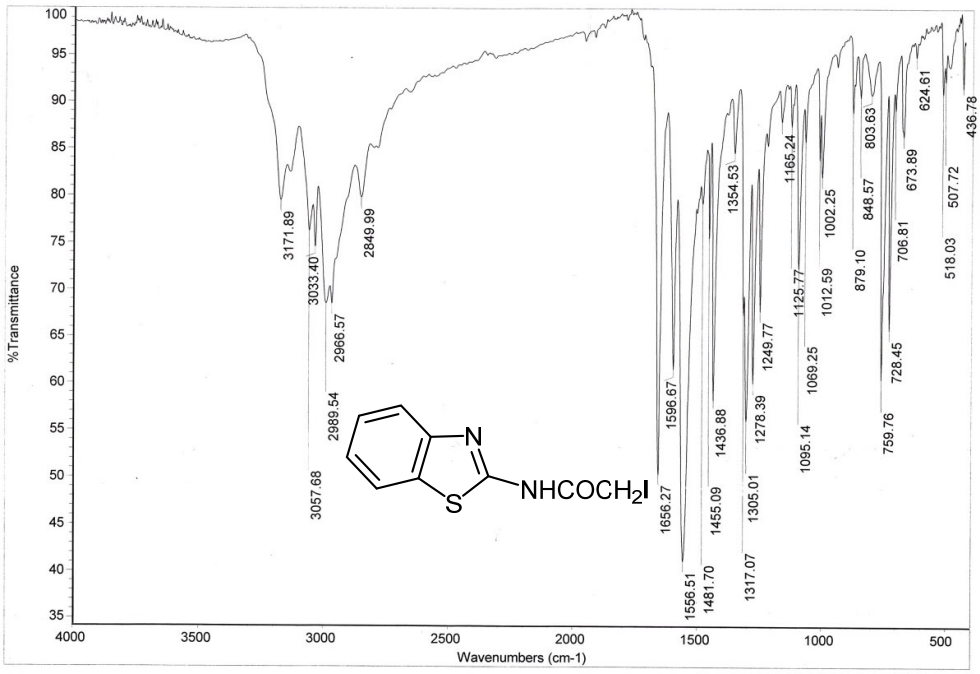


Fig. S19. IR spectrum of 2-iodo-N-(benzo[*d*]thiazol-2-yl)acetamide (**6f**).

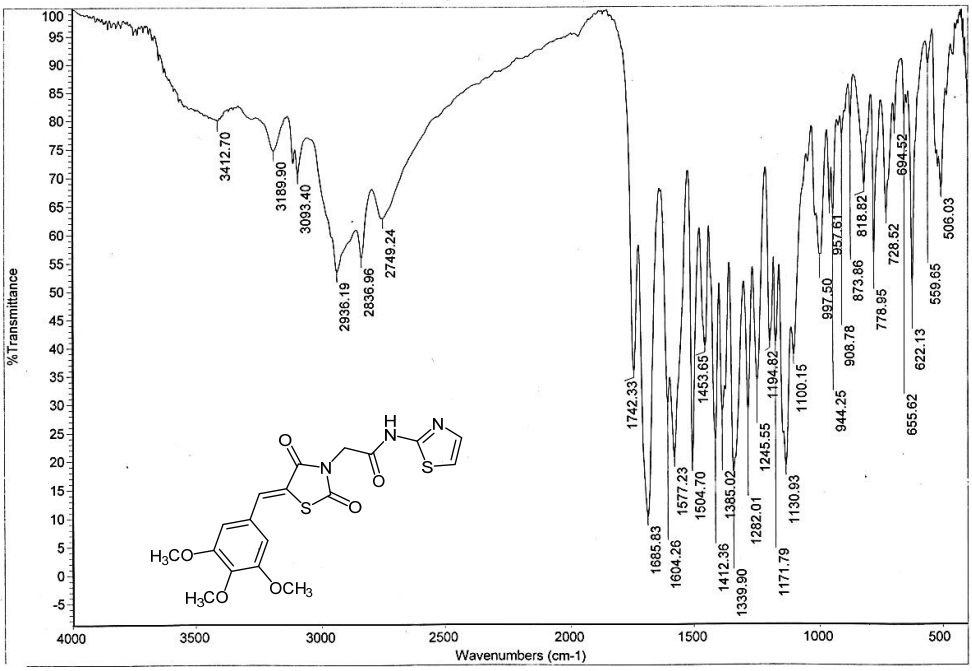


Fig. S20. IR spectrum of (Z)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(thiazol-2-yl)acetamide (**7a**).

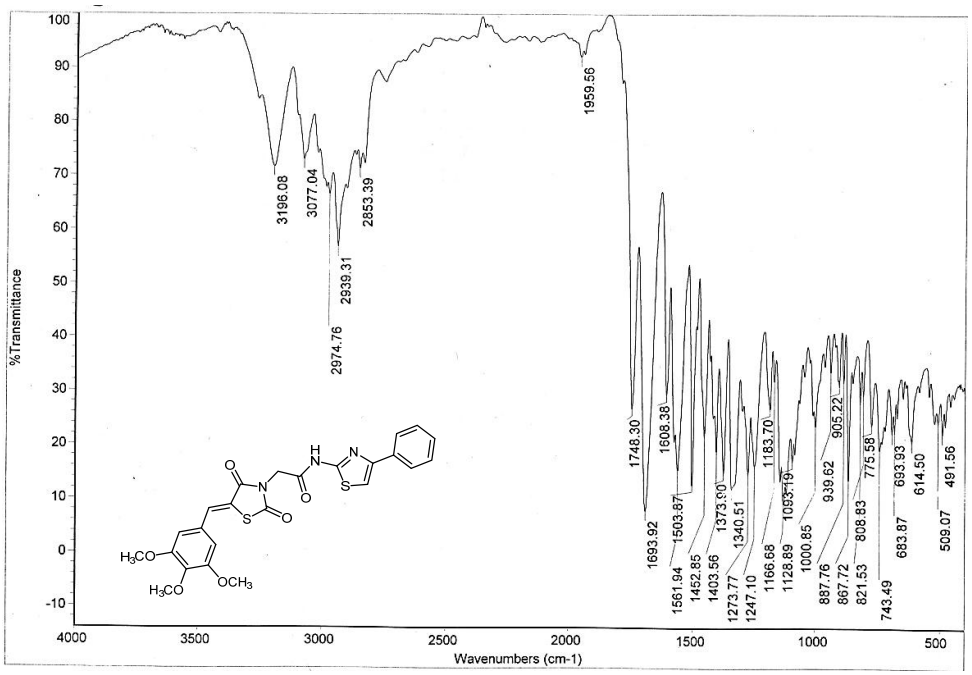


Fig. S21. IR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzlidene)thiazolidine-2,4-dion-3-yl)-N-(4-phenylthiazole-2-yl)acetamide (**7b**).

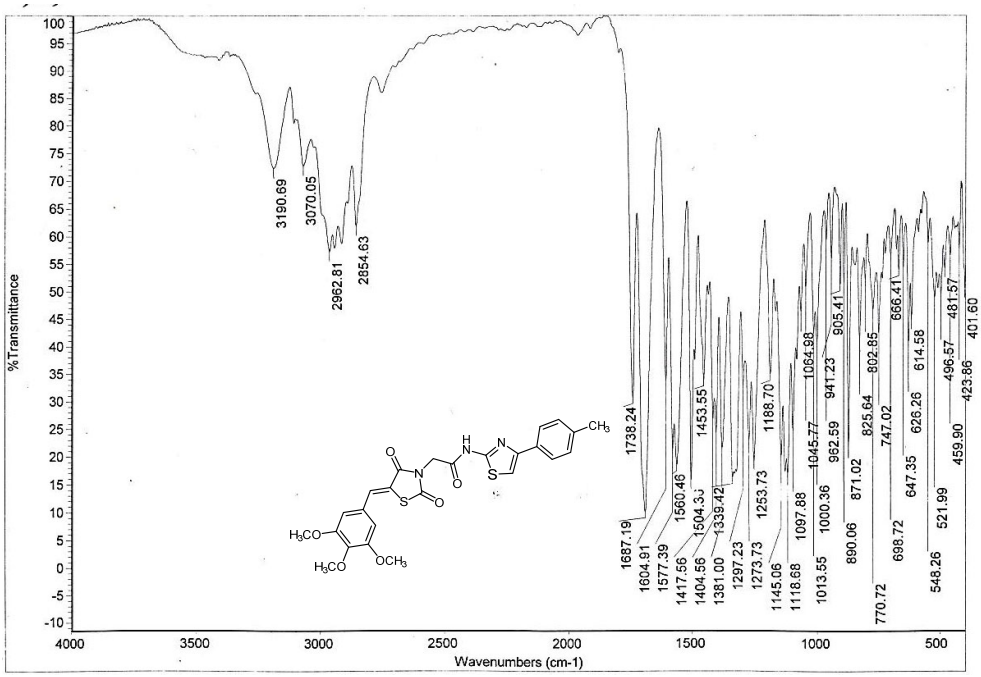


Fig. S22. IR spectrum of (Z)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-methylphenyl)thiazol-2-yl)acetamide (**7c**).

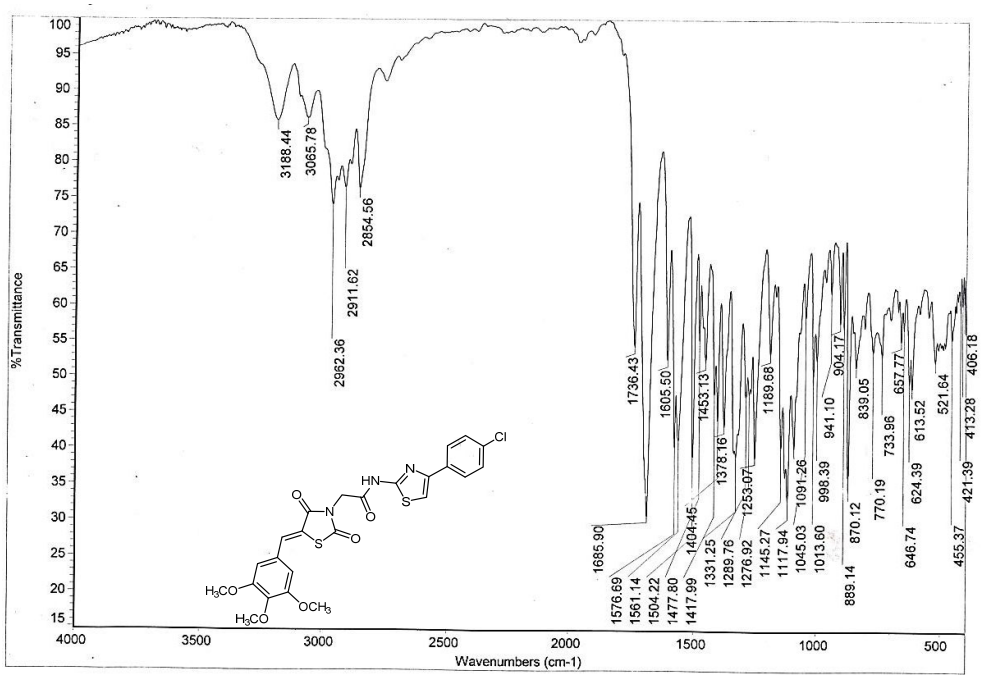


Fig. S23. IR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-chlorophenyl)thiazol-2-yl)acetamide (**7d**).

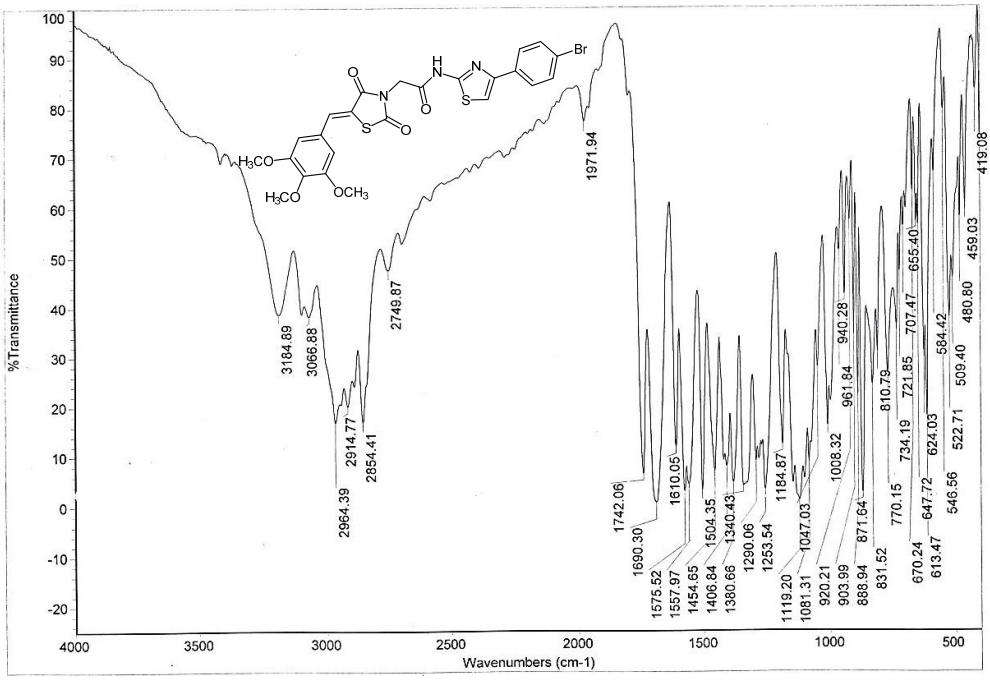


Fig. S24. IR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-bromophenyl)thiazol-2-yl)acetamide (**7e**).

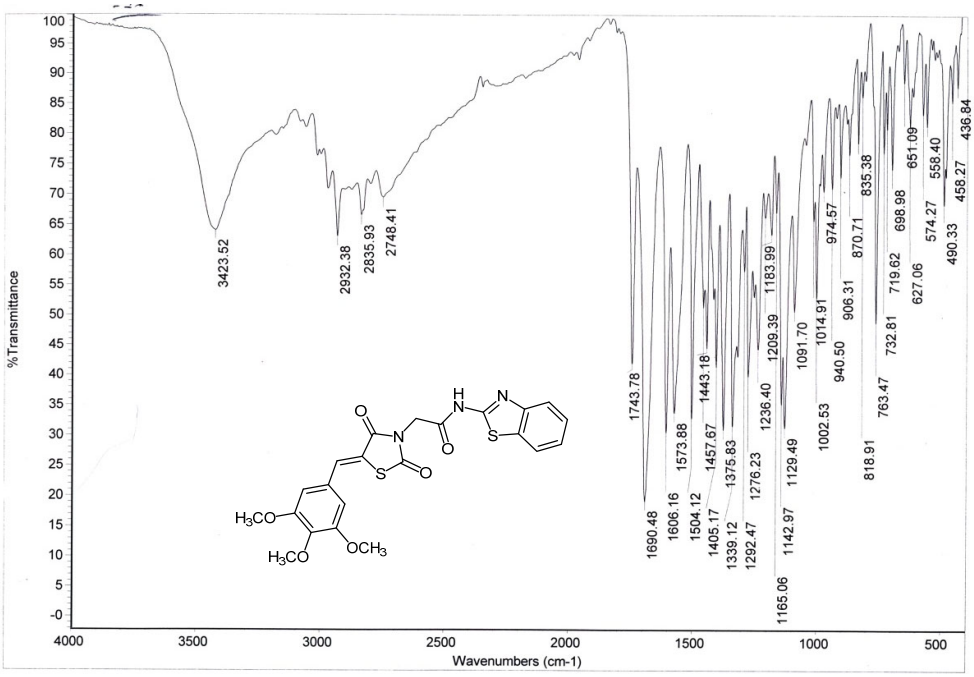


Fig. S25. IR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(benzo[*d*]thiazol-2-yl)acetamide (**7e**).

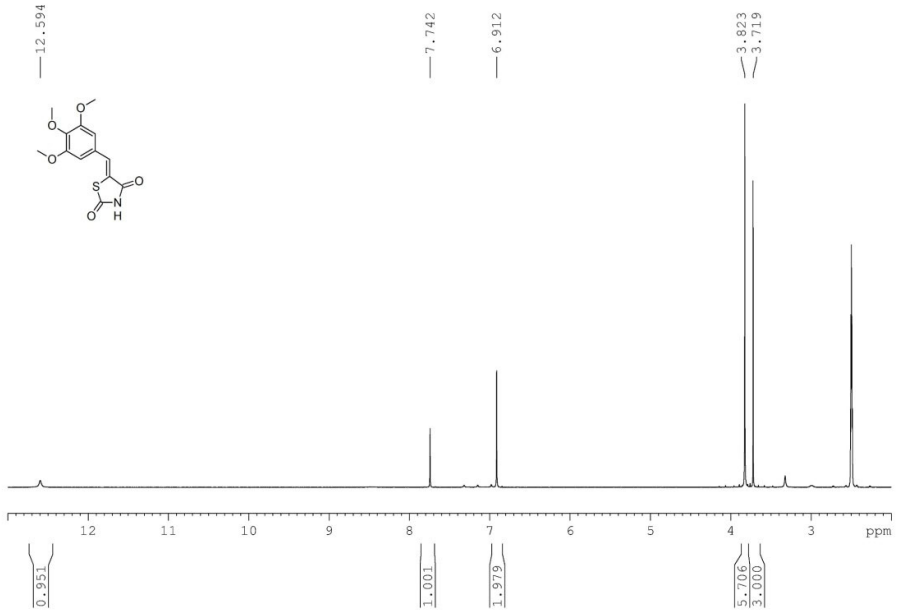


Fig. S26. ^{1}H-NMR spectrum of (*Z*)-5-(3,4,5-Trimethoxybenzylidene) thiazolidine-2,4-dione **(2).**

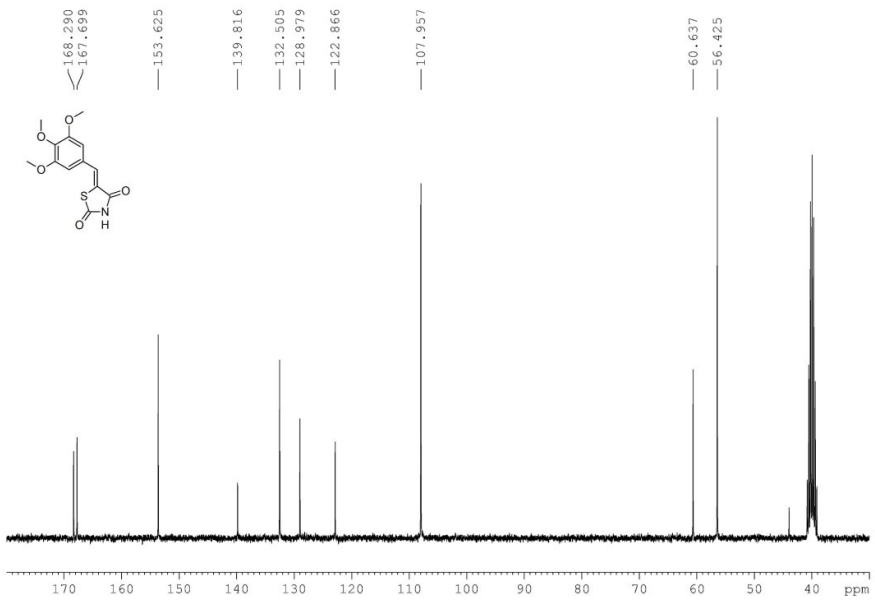


Fig. S27. ^{13}C-NMR spectrum of (*Z*)-5-(3,4,5-Trimethoxybenzylidene) thiazolidine-2,4-dione **(2).**

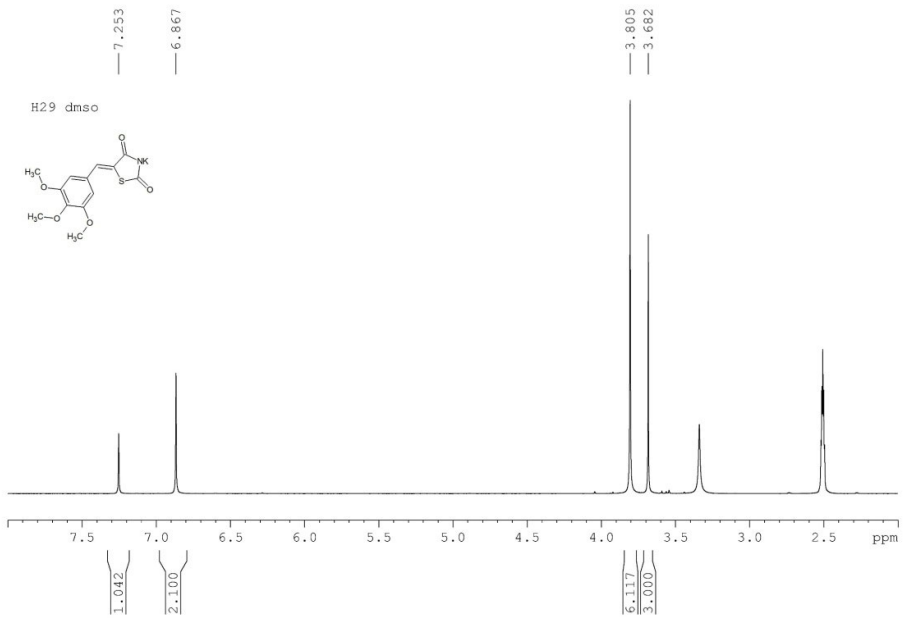


Fig. S28. ^{1}H-NMR spectrum of potassium (Z)-5-(3,4,5-Trimethoxybenzylidene)thiazolidine-2,4-dion-3-ide (**3**).

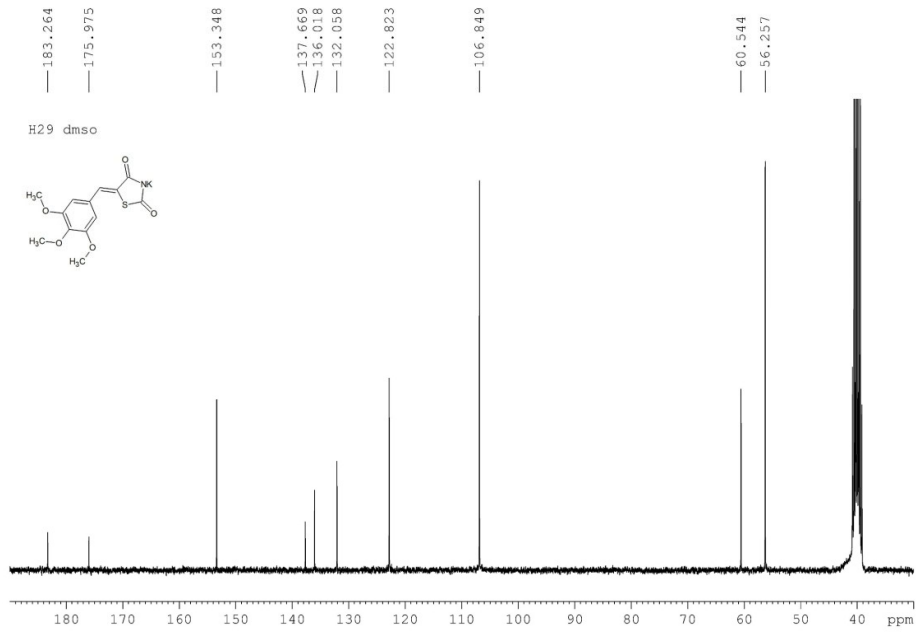


Fig. S29. ^{13}C-NMR spectrum of potassium (Z)-5-(3,4,5-Trimethoxybenzylidene)thiazolidine-2,4-dion-3-ide (**3**).

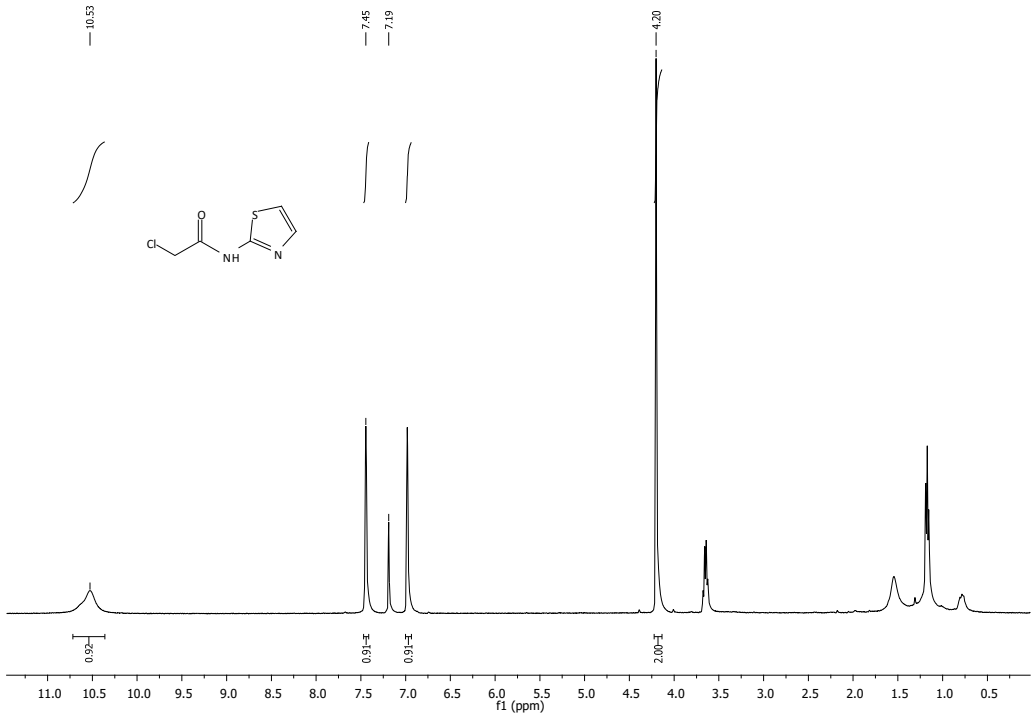


Fig. S30. ^{1}H-NMR spectrum of 2-chloro-N-(thiazol-2-yl)acetamide (**5a**). $CDCl_3$

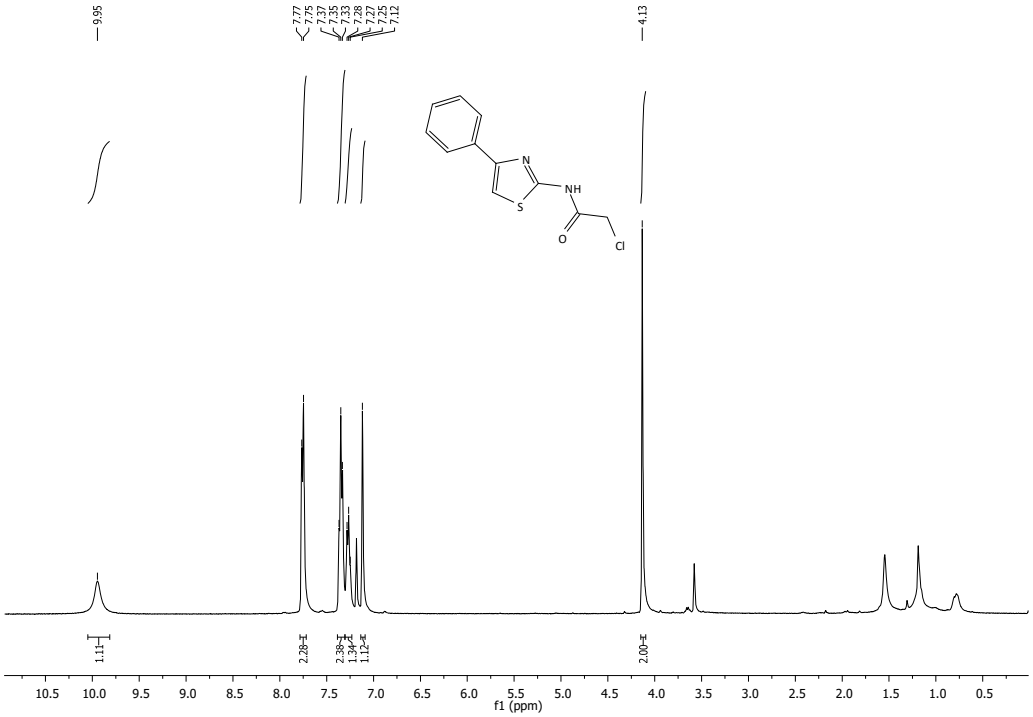


Fig. S31. ^{1}H-NMR spectrum of 2-chloro-N-(4-phenylthiazol-2-yl)acetamide (**5b**).

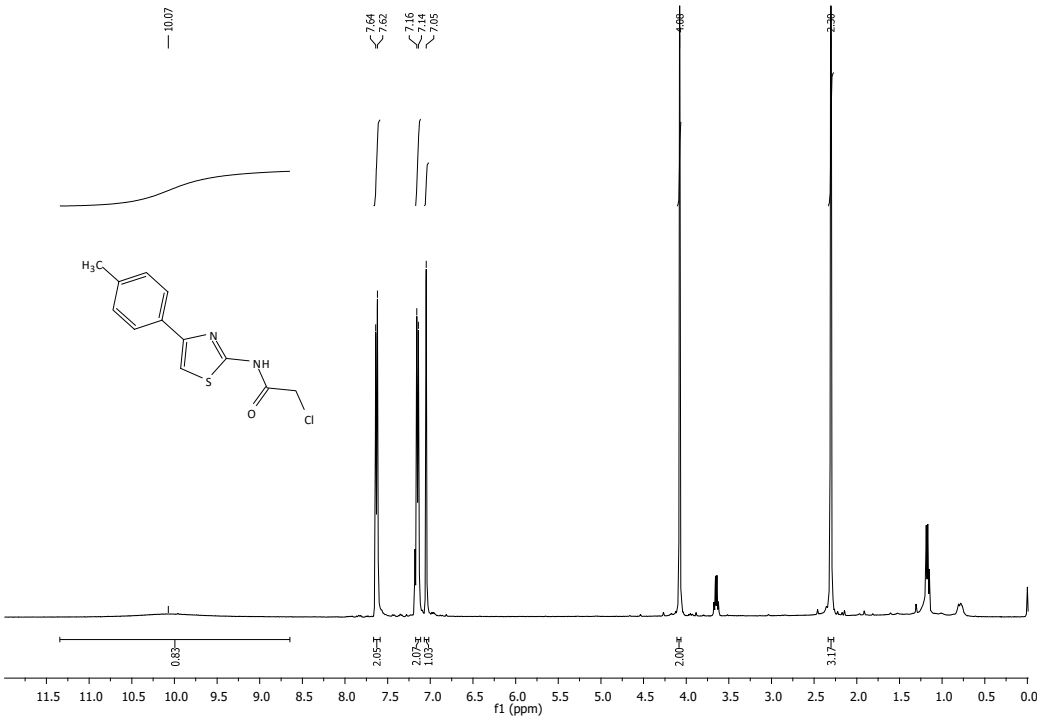


Fig. S32. ^{1}H-NMR spectrum ($CDCl_3$) of 2-chloro-N-(4-methylphenylthiazol-2-yl)acetamide (**5c**).

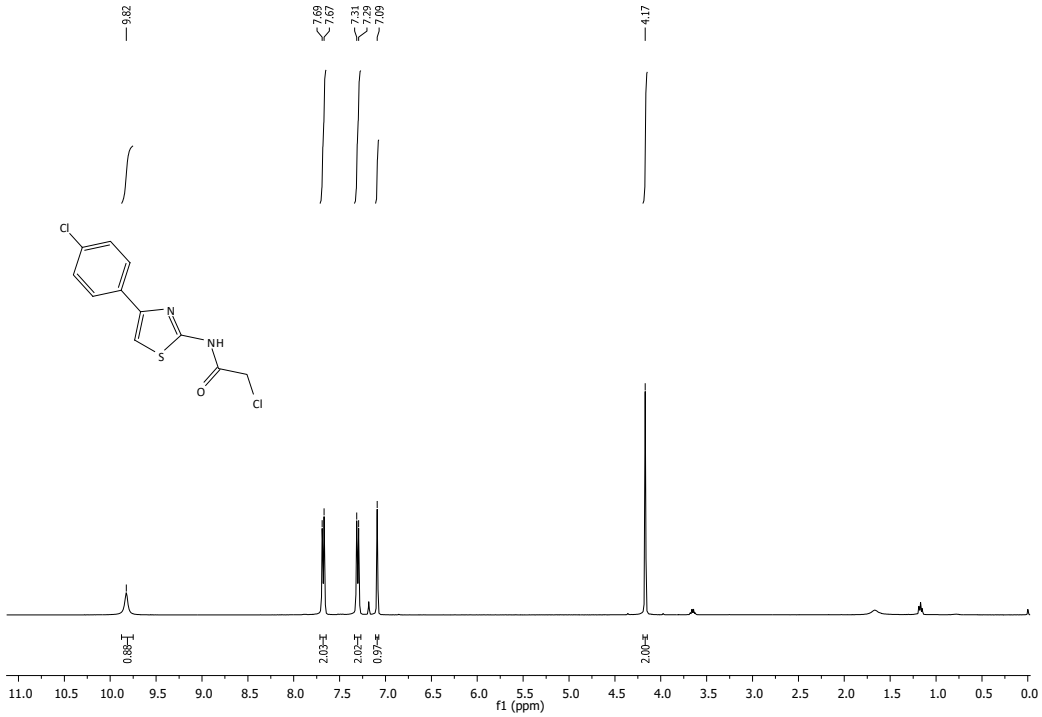


Fig.S33. ^{1}H-NMR spectrum ($CDCl_3$) of 2-chloro-N-(4-chlorophenylthiazol-2-yl)acetamide (**5d**).

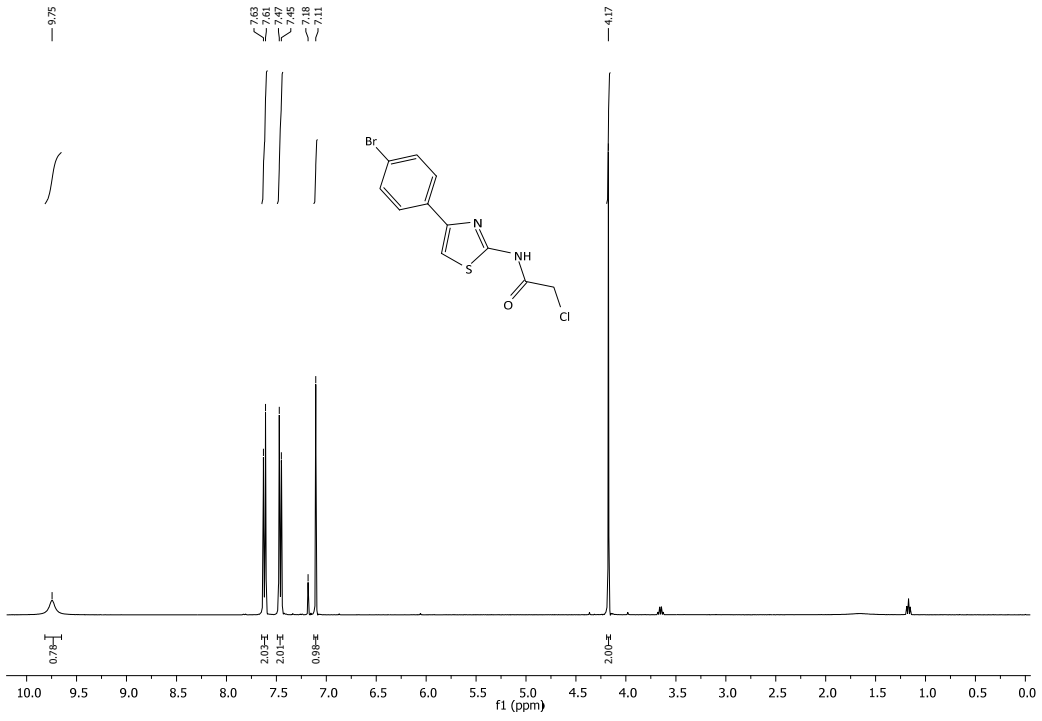


Fig. S34. ^{1}H-NMR spectrum ($CDCl_3$) of 2-chloro -N-(4-bromophenylthiazol-2-yl)acetamide (**5e**).

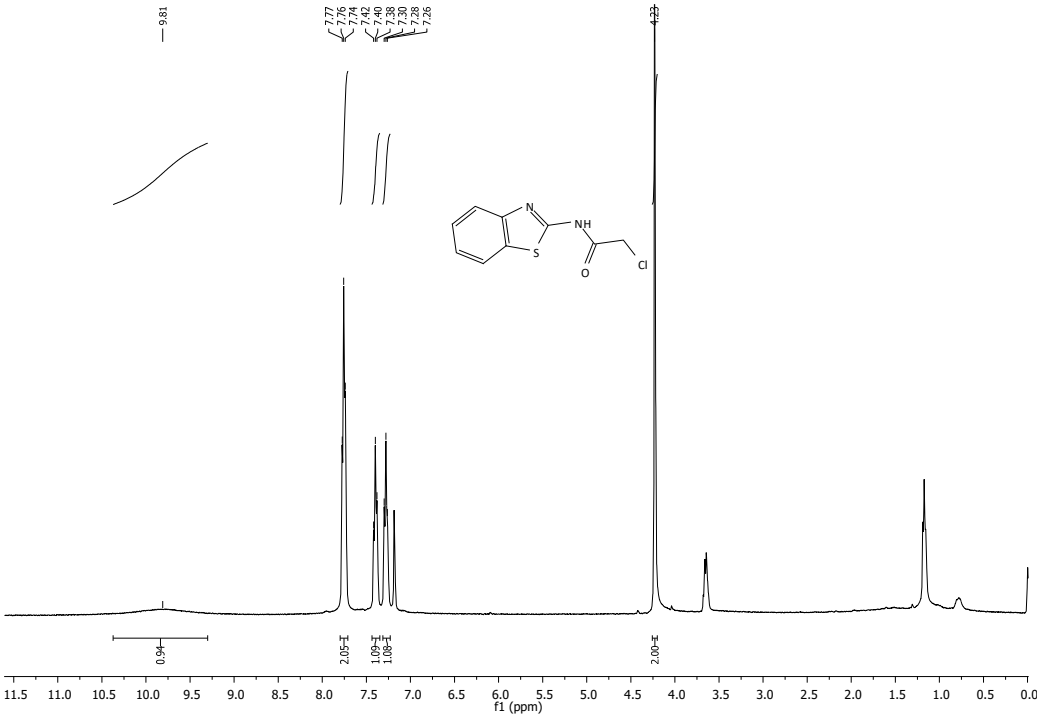


Fig. S35. ^{1}H-NMR spectrum ($CDCl_3$) of 2-chloro-N-(benzo[*d*]thiazol-2-yl)acetamide (**5f**).

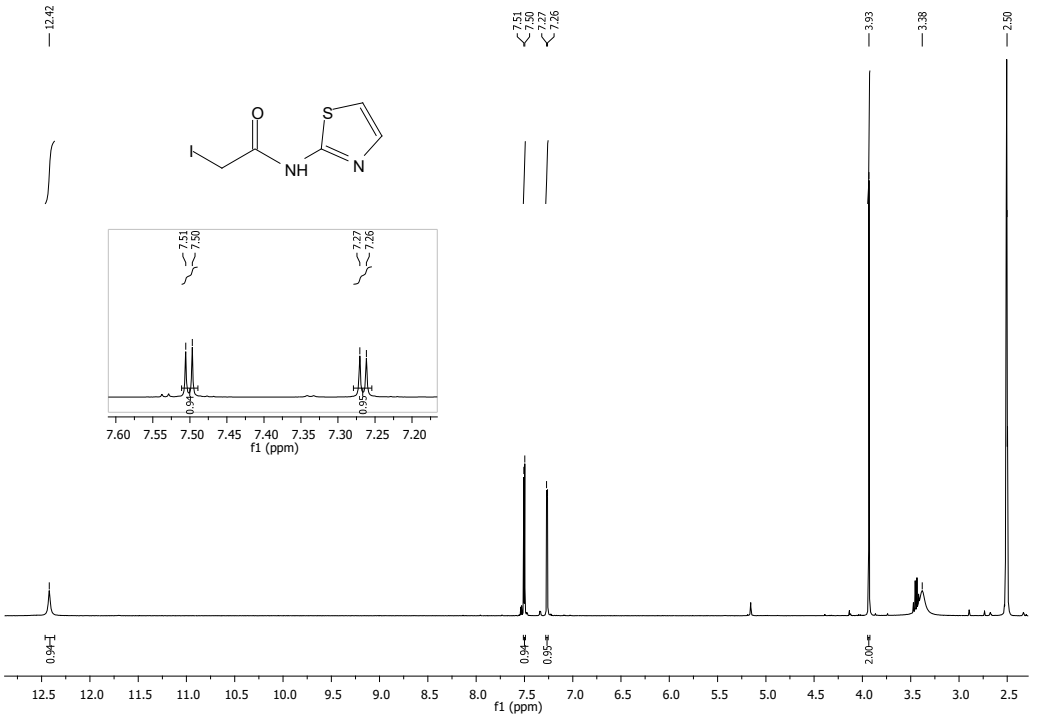


Fig. S36. ^{1}H-NMR spectrum of 2-iodo-N-(thiazol-2-yl)acetamide (**6a**).

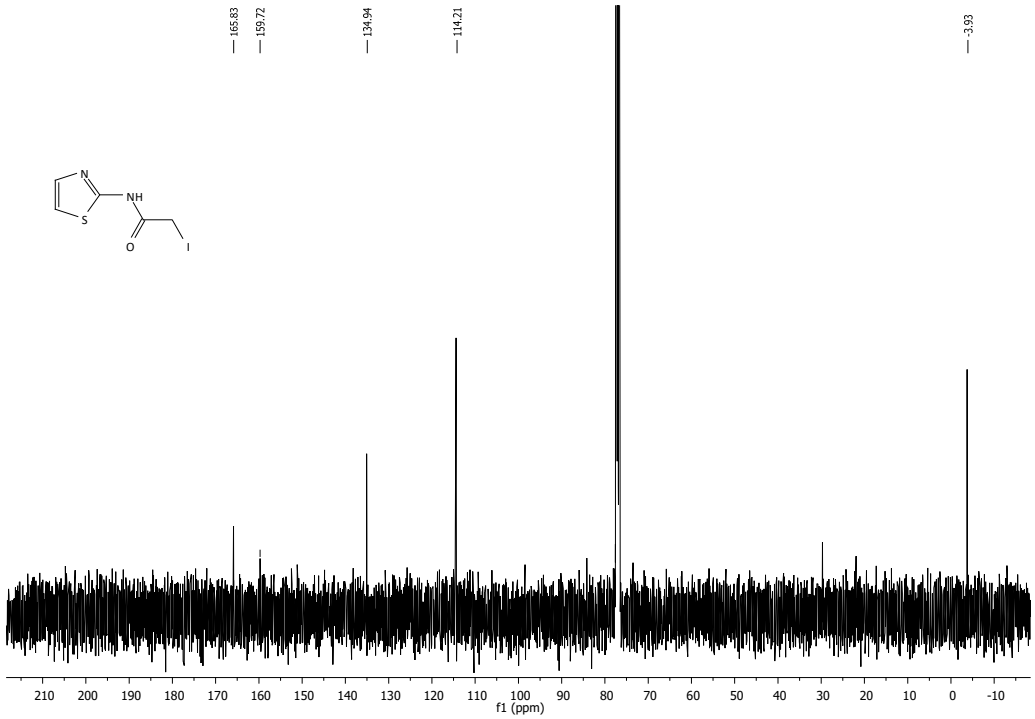


Fig. S37. ^{13}C-NMR spectrum ($CDCl_3$) of 2-iodo-N-(thiazol-2-yl)acetamide (**6a**).

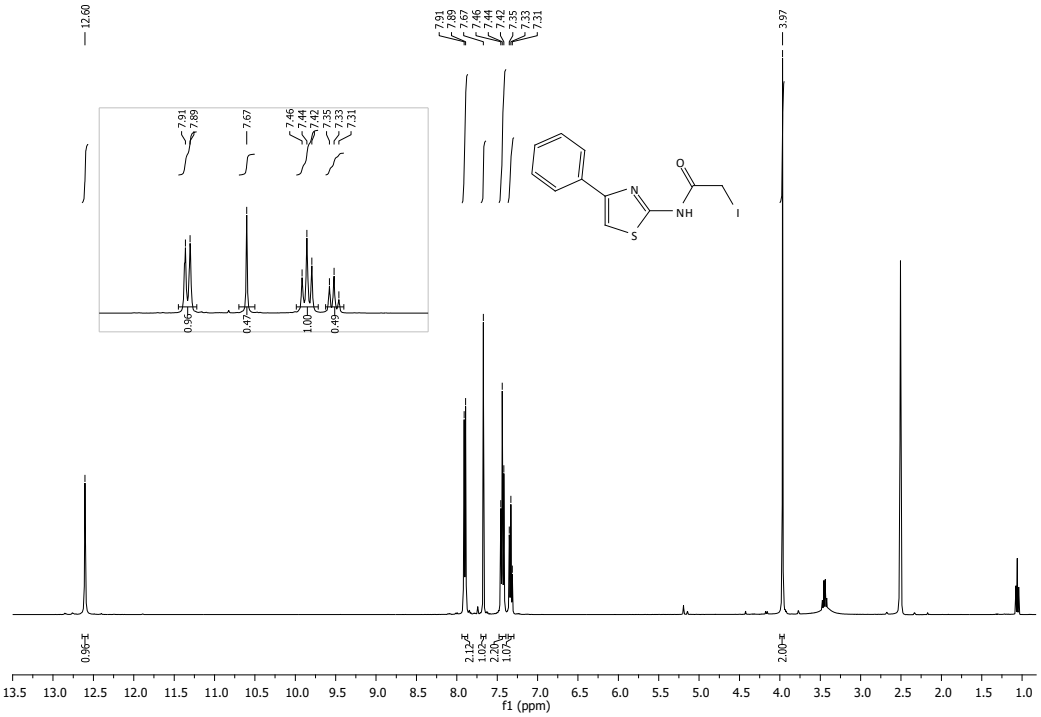


Fig. S38. ^{1}H-NMR spectrum of 2-iodo-N-(4-phenylthiazol-2-yl)acetamide (**6b**).

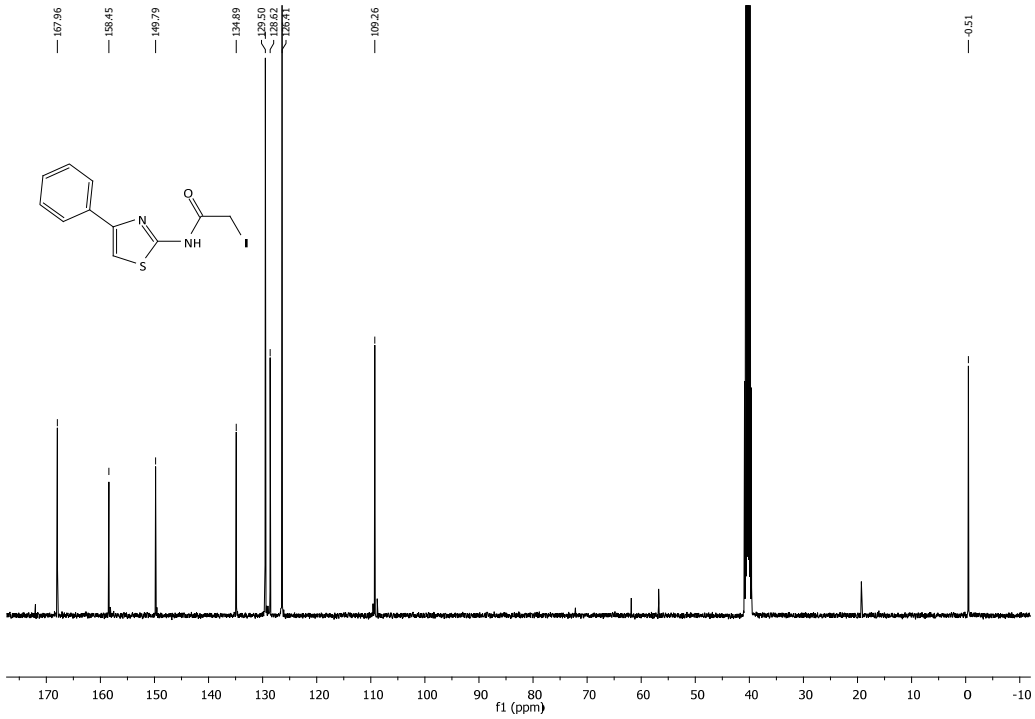


Fig. S39. ^{13}C-NMR spectrum of 2-iodo-N-(4-phenylthiazol-2-yl)acetamide (**6b**).

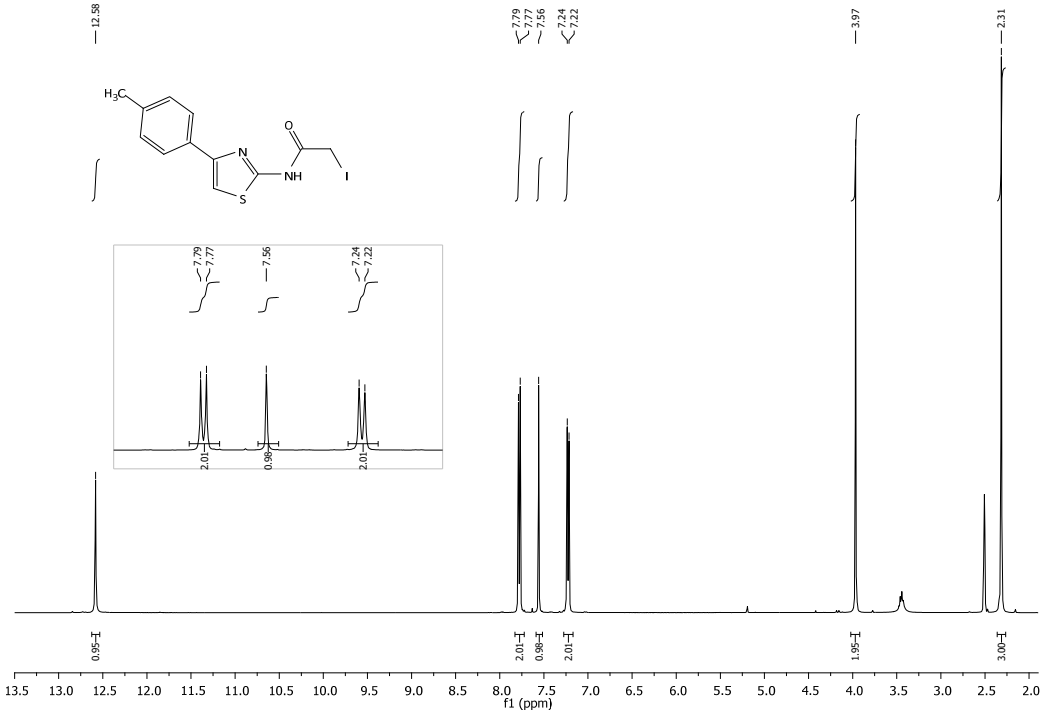


Fig. S40. ^{1}H-NMR spectrum of 2-iodo-N-(4-methylphenylthiazol-2-yl)acetamide (**6c**).

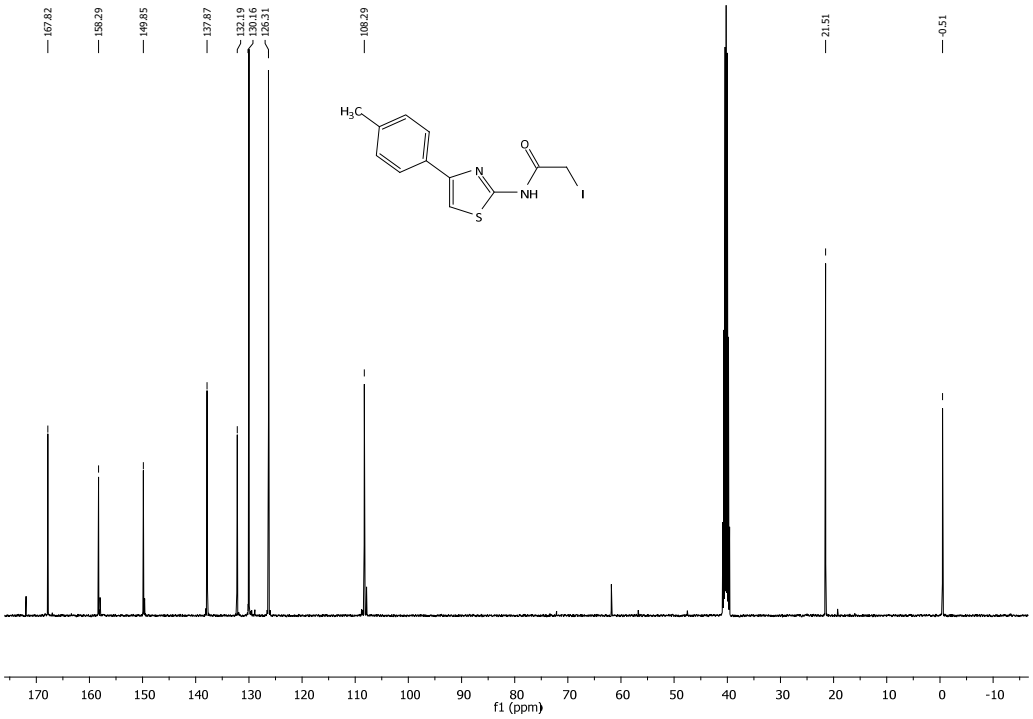


Fig. S41. ^{13}C-NMR spectrum of 2-iodo-N-(4-methyl phenylthiazol-2-yl)acetamide (**6c**).

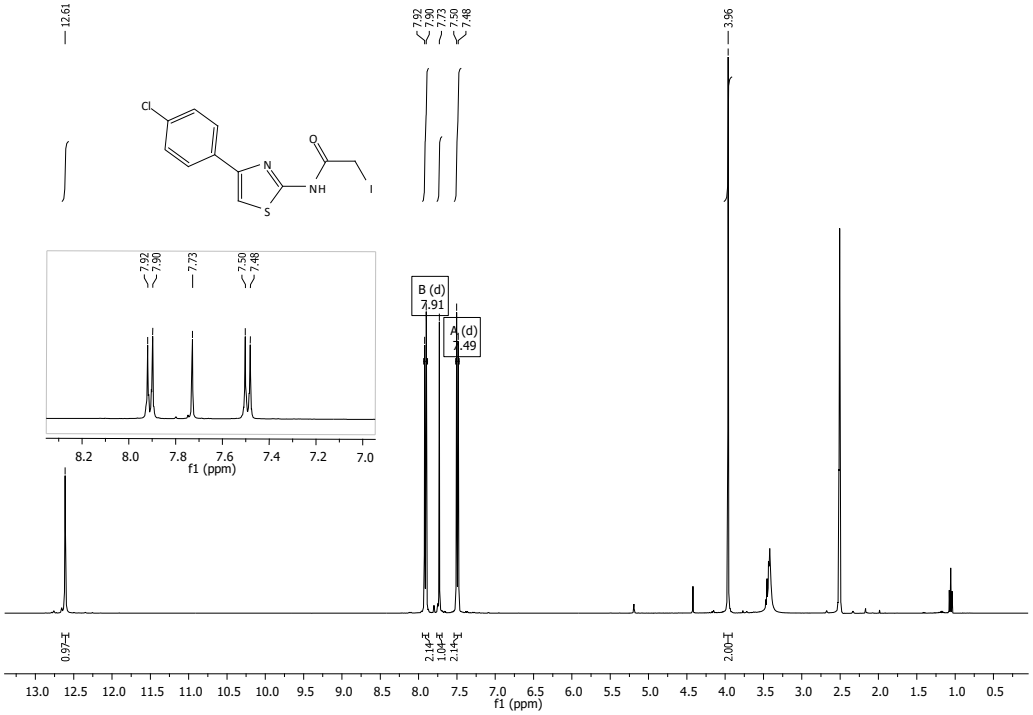


Fig. S42. ^{1}H-NMR spectrum of 2-iodo-N-(4-chlorophenylthiazol-2-yl)acetamide (**6d**).

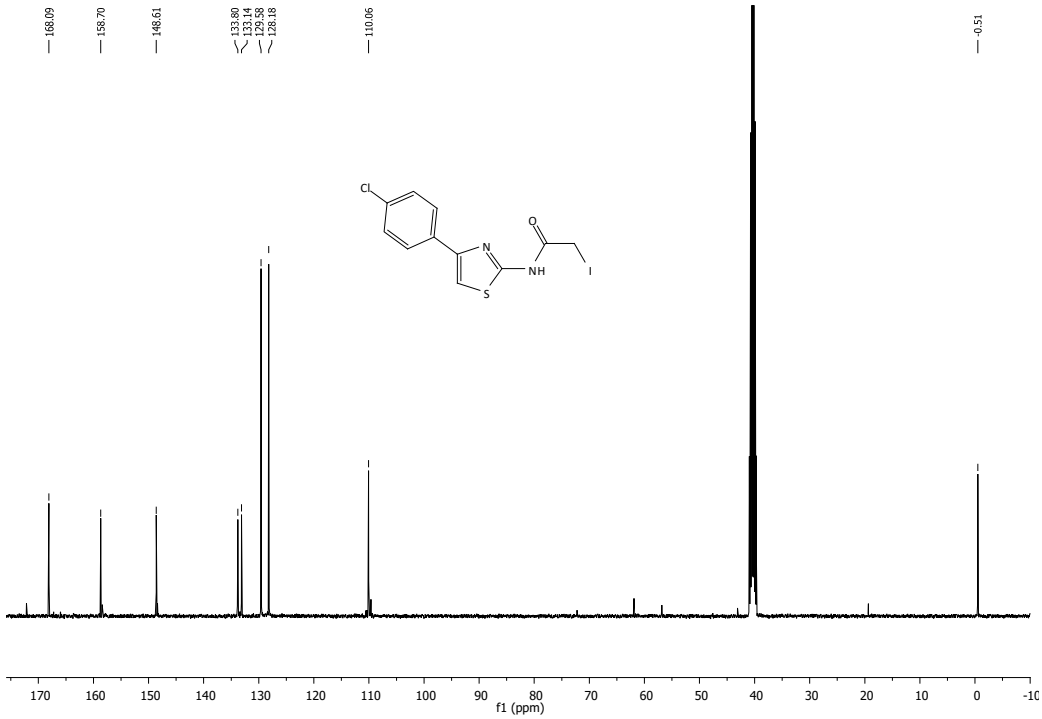


Fig. S43. ^{13}C-NMR spectrum of 2-iodo-N-(4-chlorophenylthiazol-2-yl)acetamide (**6d**).

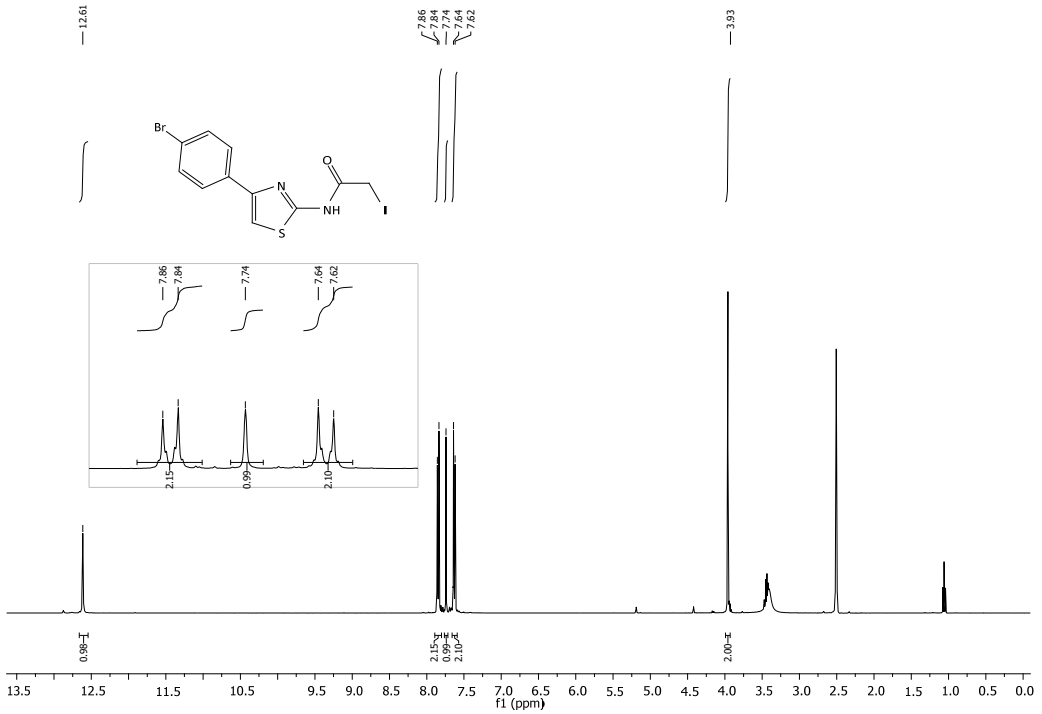


Fig. S44. ^{1}H-NMR spectrum of 2-iodo -N-(4-bromophenylthiazol-2-yl)acetamide (**6e**).

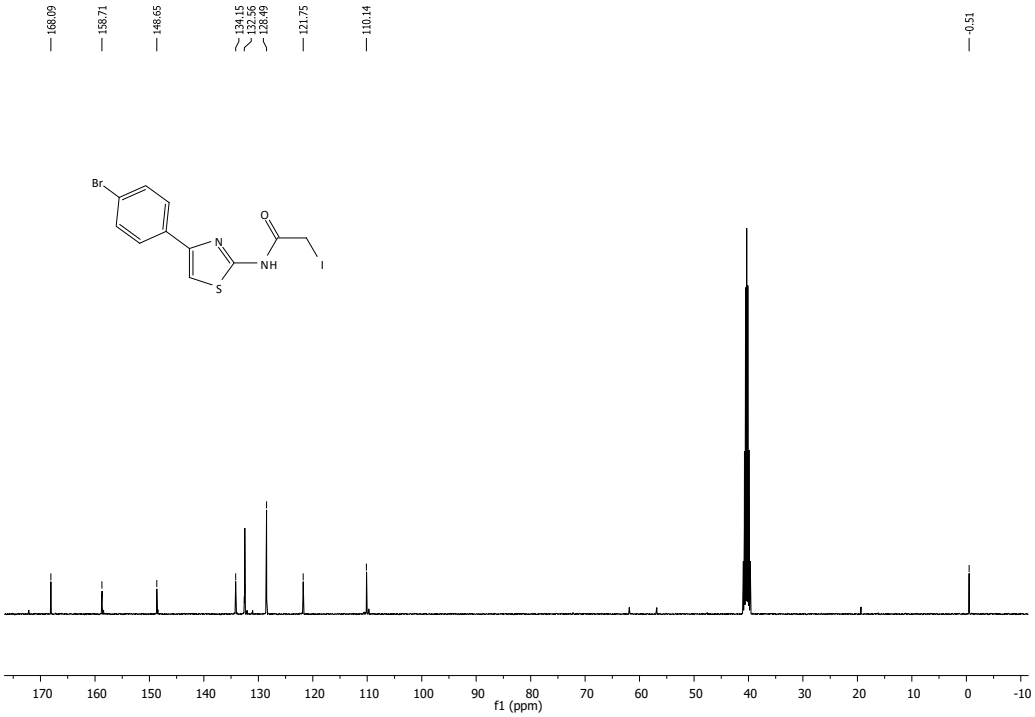


Fig. S45. ^{13}C-NMR spectrum of 2-iodo -N-(4-bromophenylthiazol-2-yl)acetamide (**6e**).

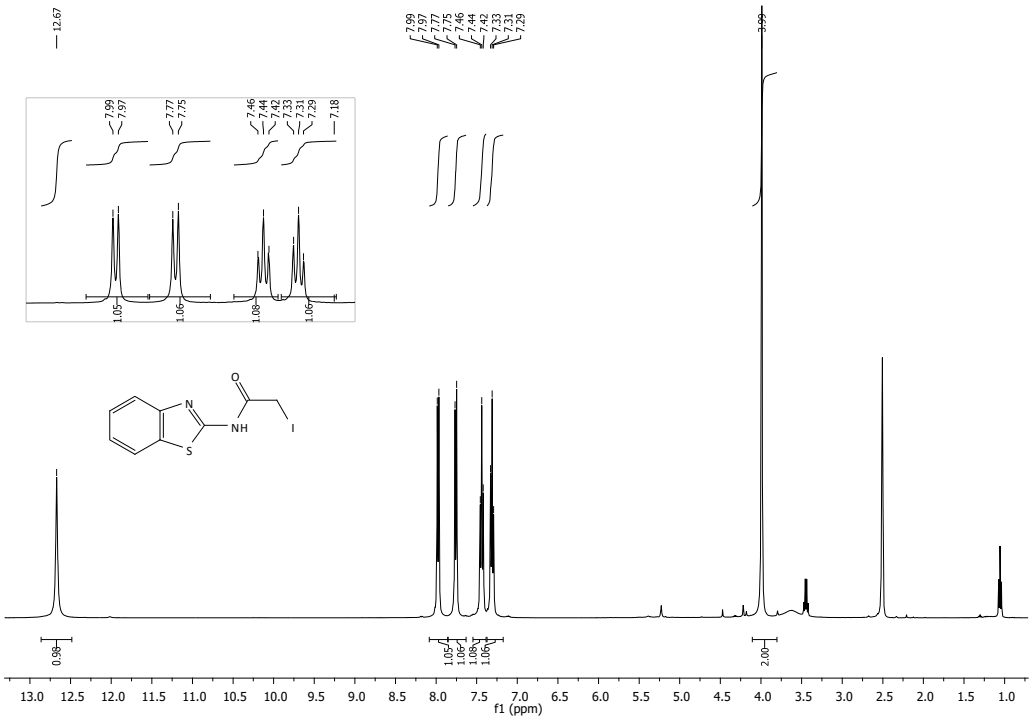


Fig. S46. ^{1}H-NMR spectrum of 2-iodo-N-(benzo[*d*]thiazol-2-yl)acetamide (**6f**).

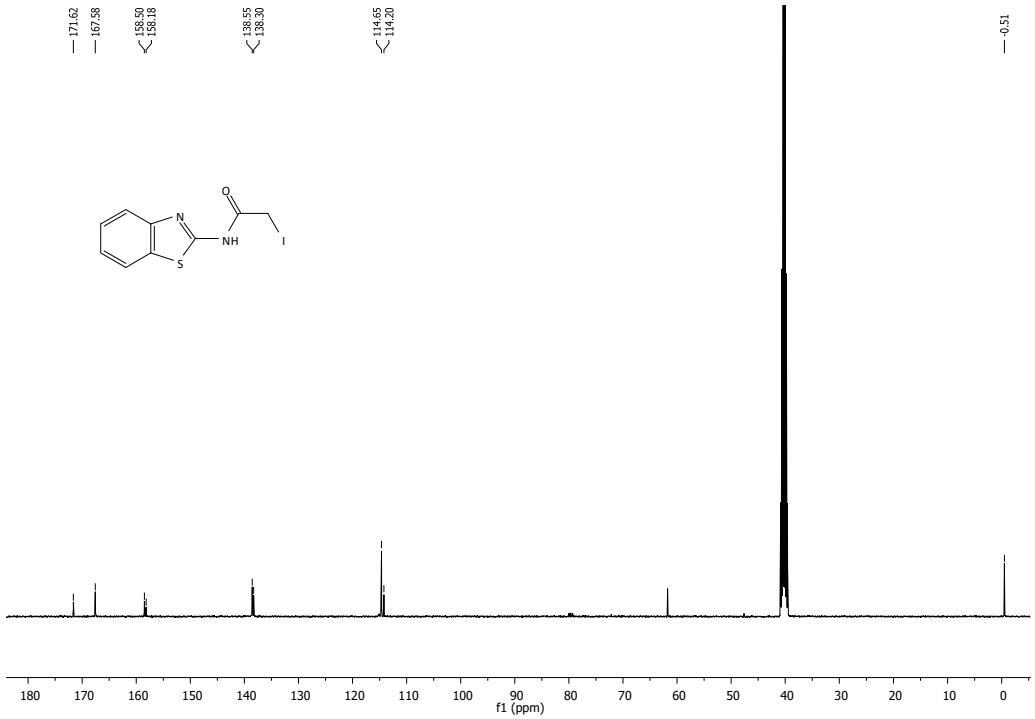


Fig. S47. ^{13}C-NMR spectrum of 2-iodo-N-(benzo[*d*]thiazol-2-yl)acetamide (**6f**).

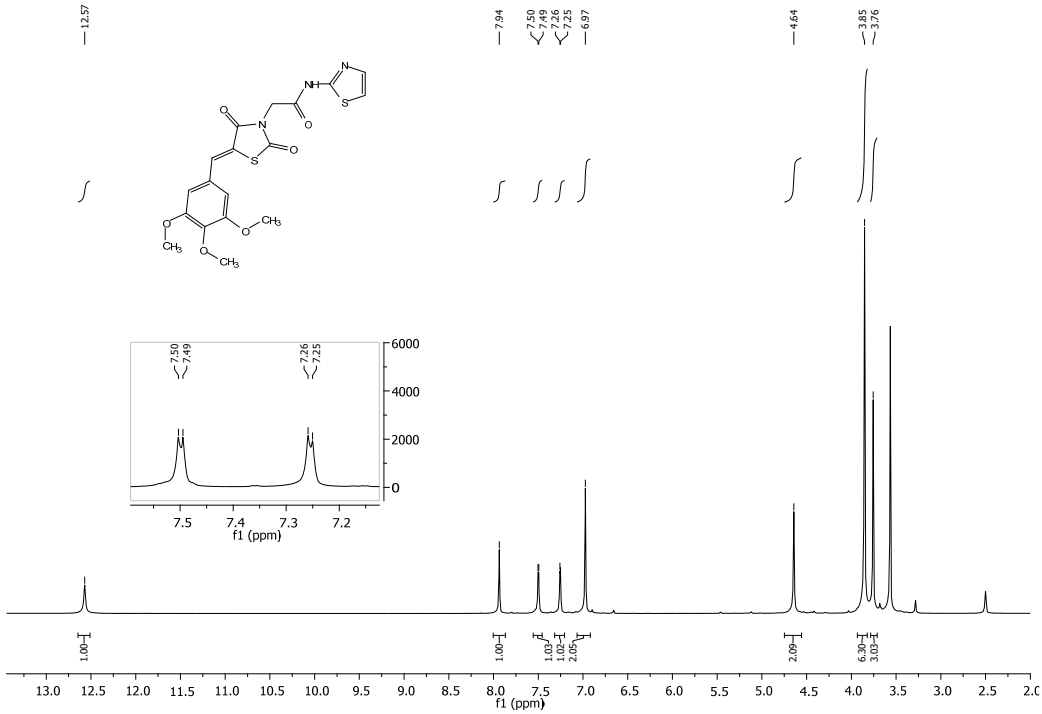


Fig. S48. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzlidene)thiazolidine-2,4-dion-3-yl)-N-(thiazole-2-yl)acetamide (**7a**).

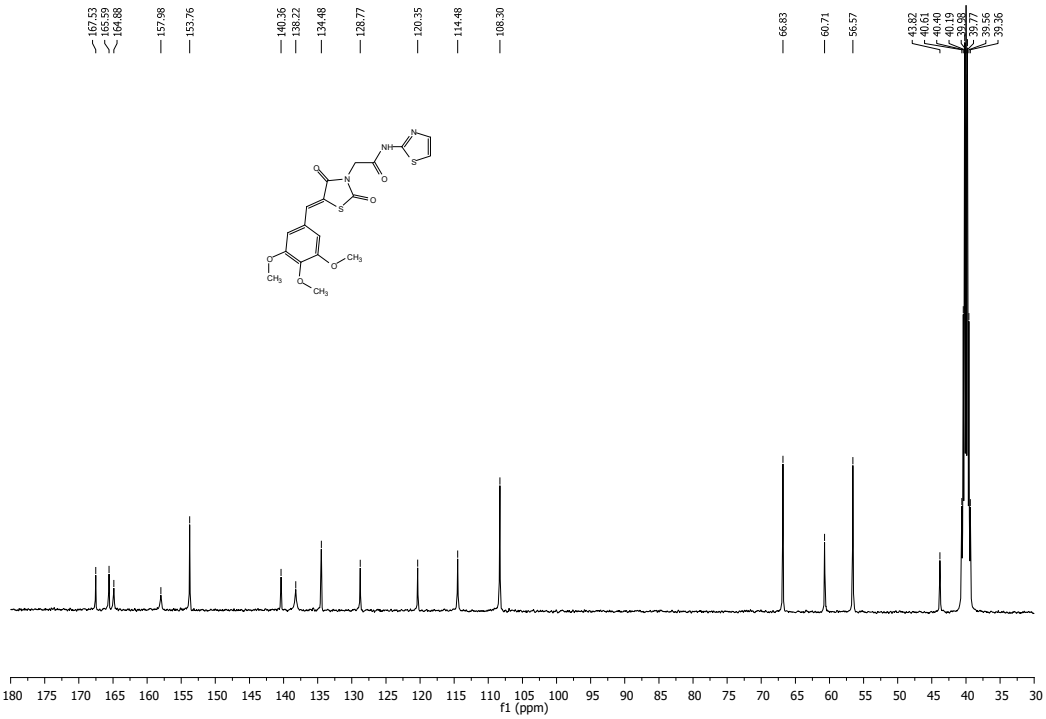


Fig. S49. ^{13}C-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzlidene)thiazolidine-2,4-dion-3-yl)-N-(thiazole-2-yl)acetamide (**7a**).

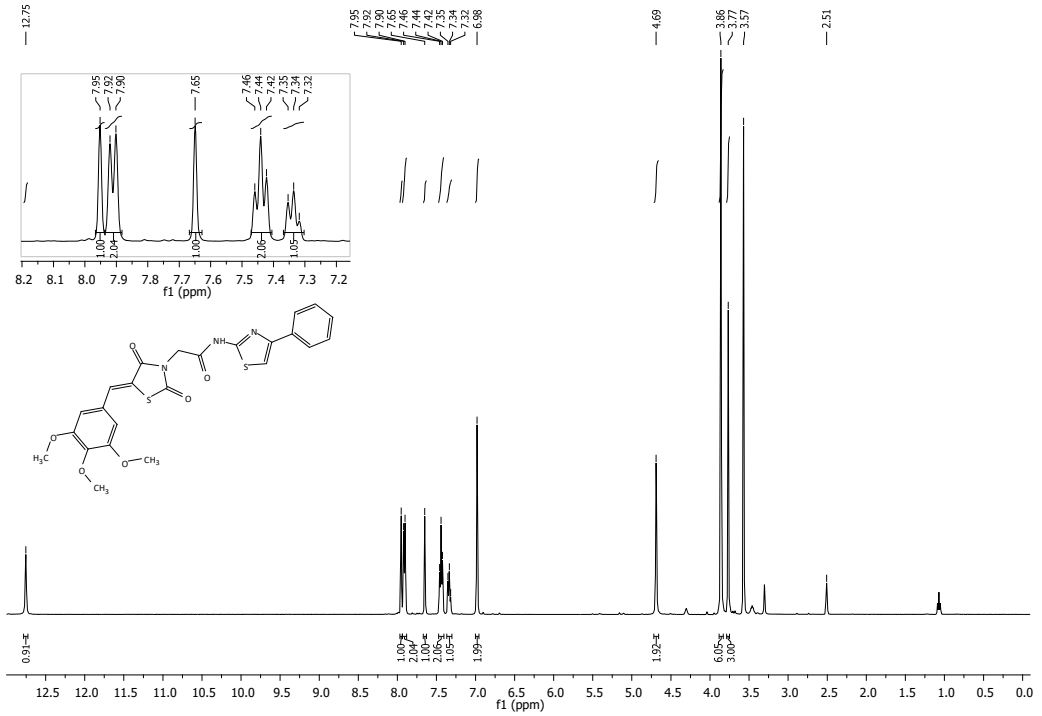


Fig. S50. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzlidene)thiazolidine-2,4-dion-3-yl)-N-(4-phenylthiazole-2-yl)acetamide (**7b**).

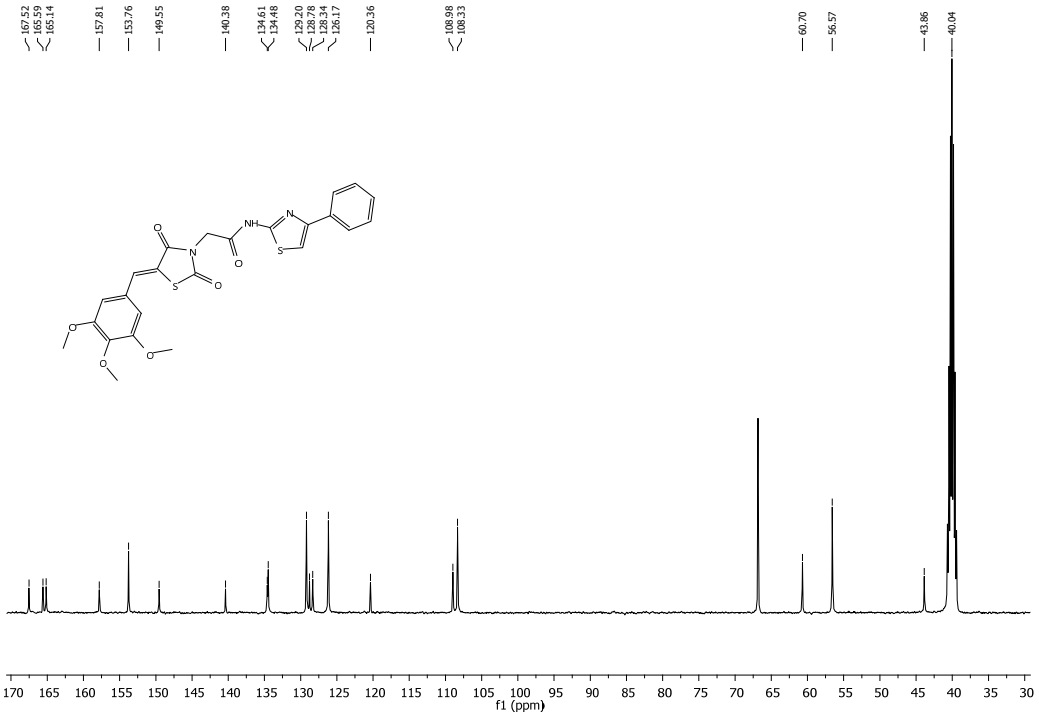


Fig. S51. ^{13}C-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzlidene)thiazolidine-2,4-dion-3-yl)-N-(4-phenylthiazole-2-yl)acetamide (**7b**).

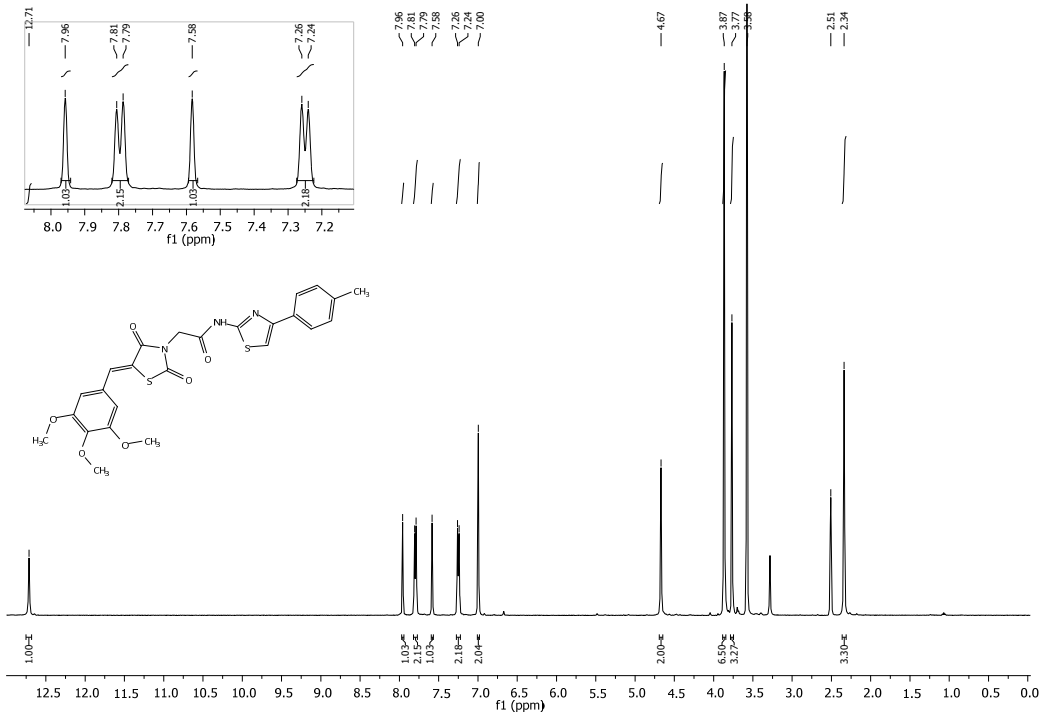


Fig. S52. ^{1}H-NMR spectrum of (Z)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-methylphenyl)thiazol-2-yl)acetamide (**7c**).

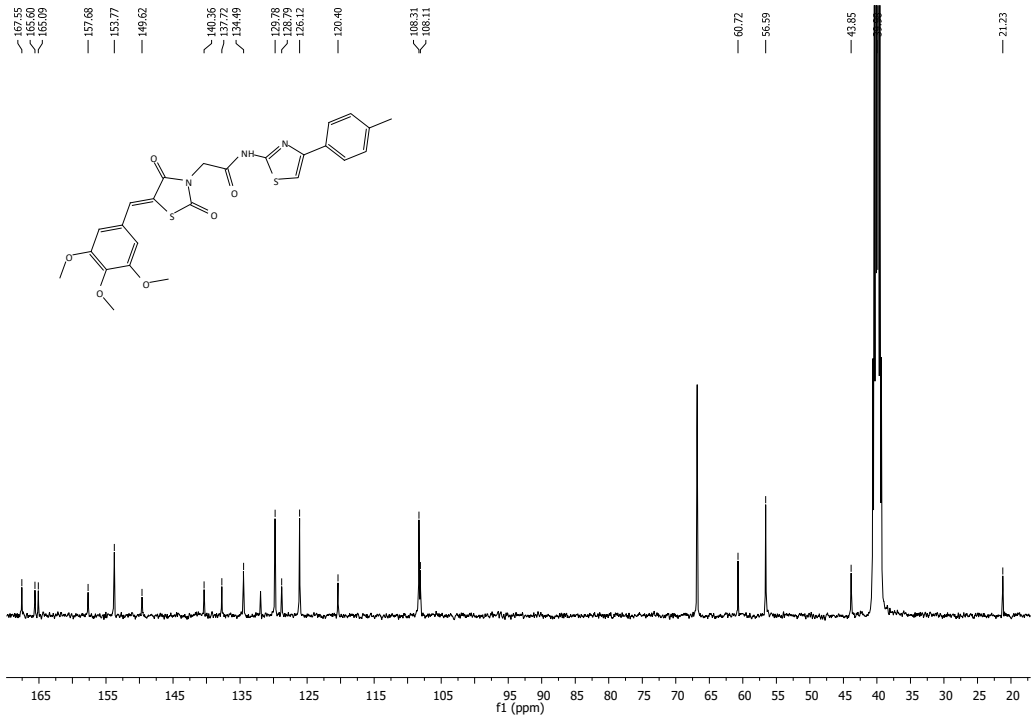


Fig. S53. ^{13}C-NMR spectrum of (Z)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-methylphenyl)thiazol-2-yl)acetamide (**7c**).

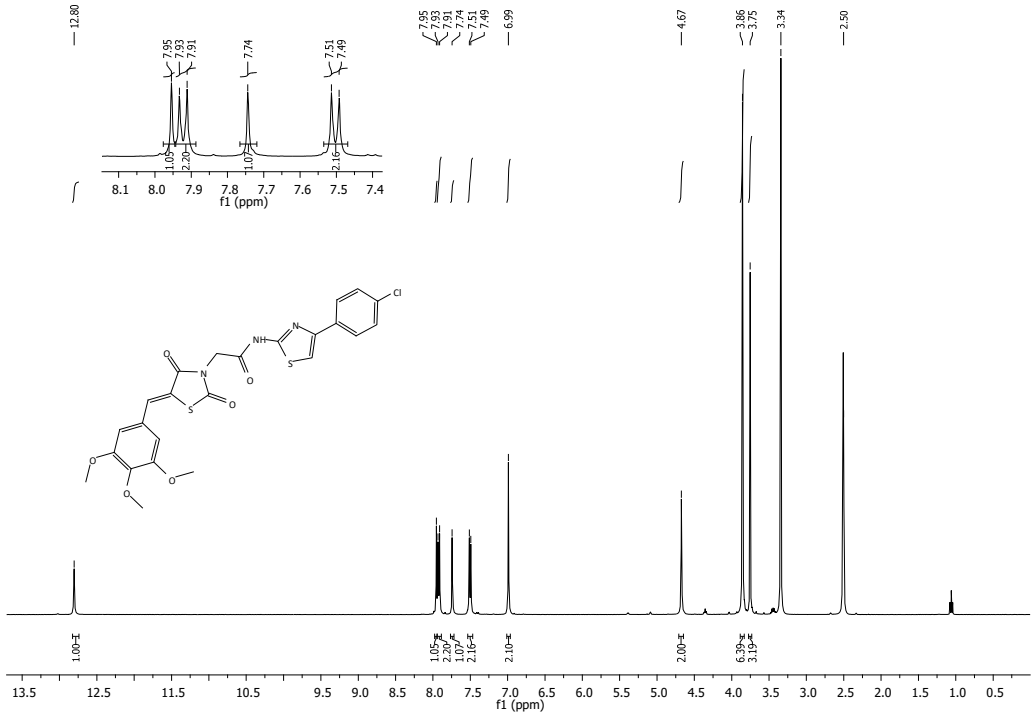


Fig. S54. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-chlorophenyl)thiazol-2-yl)acetamide (**7d**).

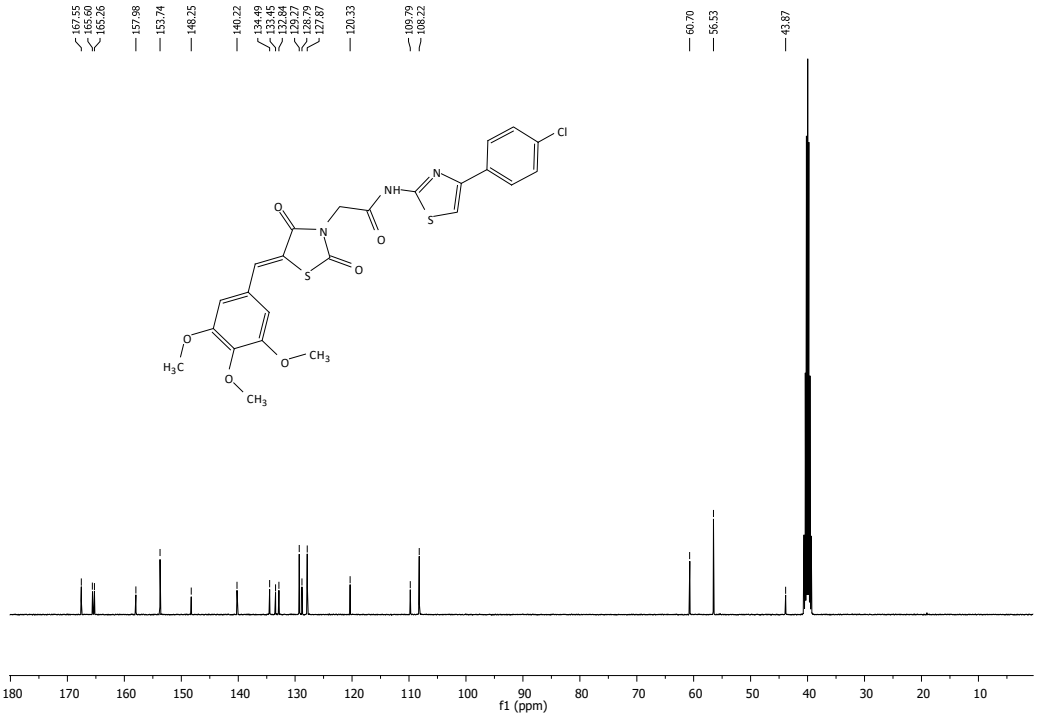


Fig. S55. ^{13}C-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-chlorophenyl)thiazol-2-yl)acetamide (**7d**).

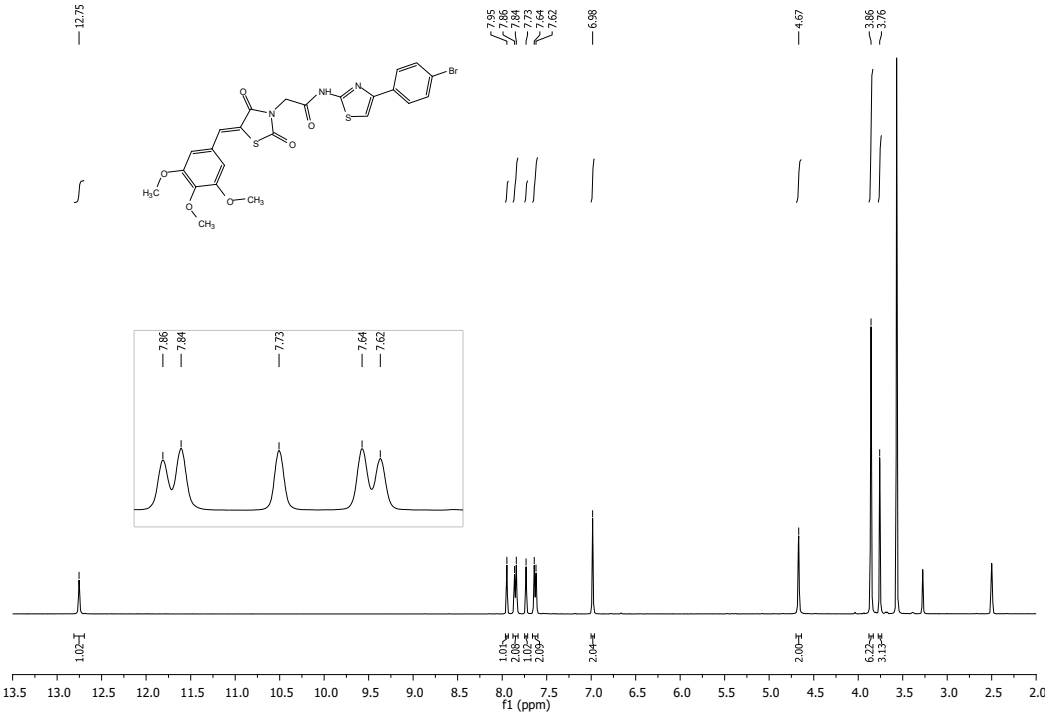


Fig. S56. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-bromophenyl)thiazol-2-yl)acetamide **(7e)**.

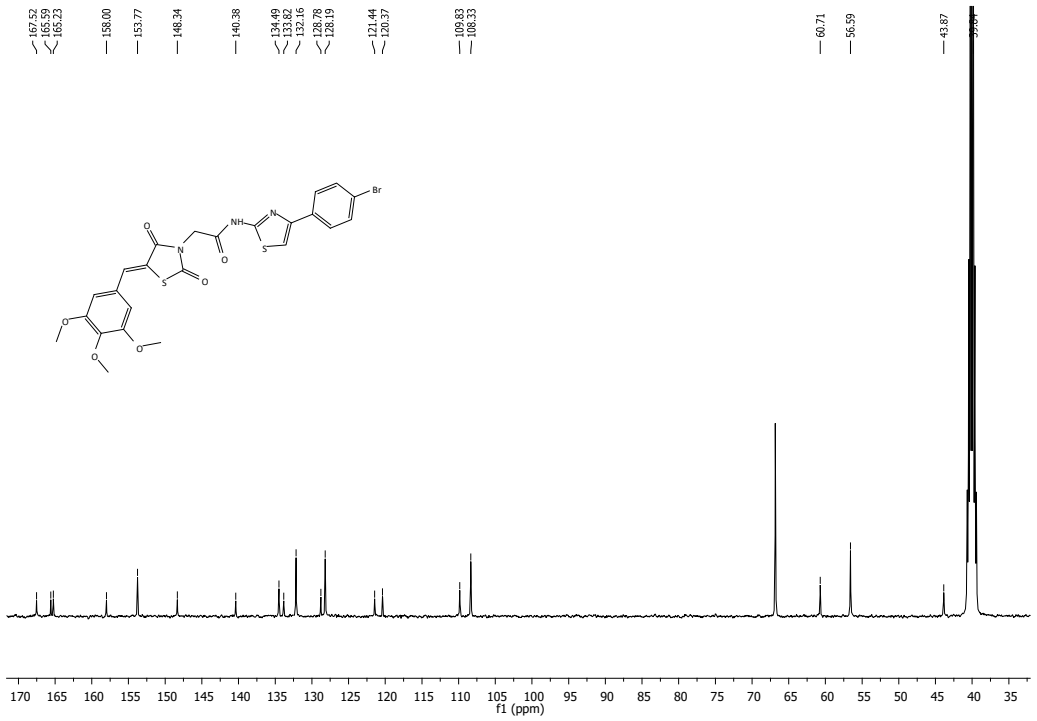


Fig. S57. ^{13}C-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(4-(4-bromophenyl)thiazol-2-yl)acetamide (**7e**).

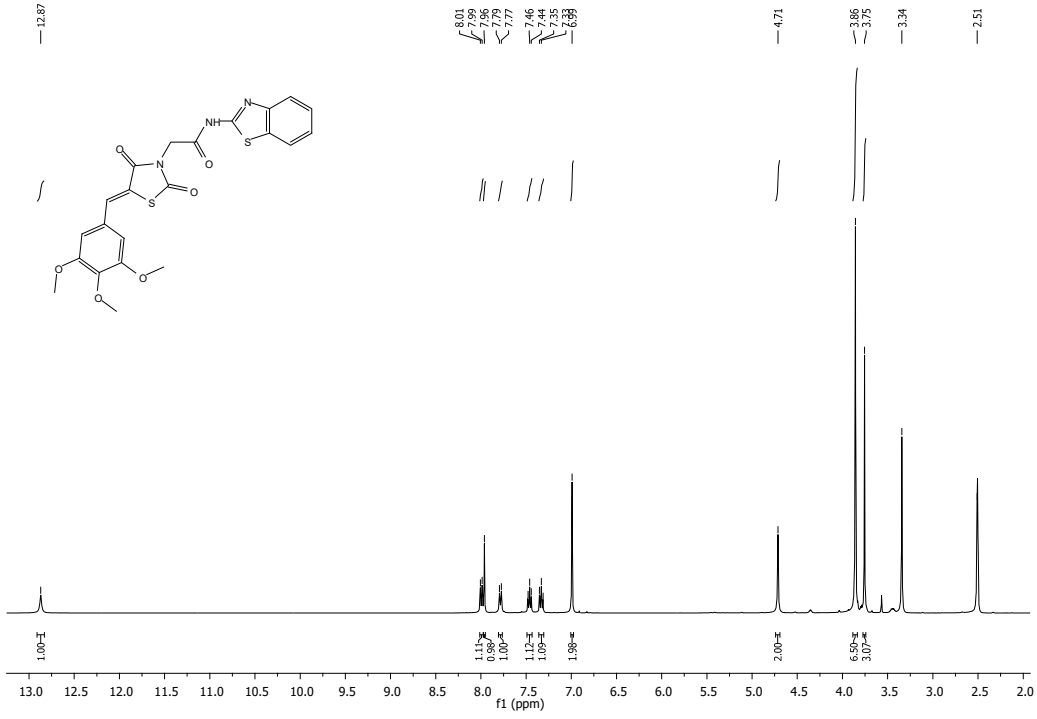


Fig. S58. ^{1}H-NMR spectrum of (*Z*)-2-(5-(3,4,5-trimethoxybenzylidene)thiazolidin-2,4-dion-3-yl)-N-(benzo[*d*]thiazol-2-yl)acetamide (**7f**).

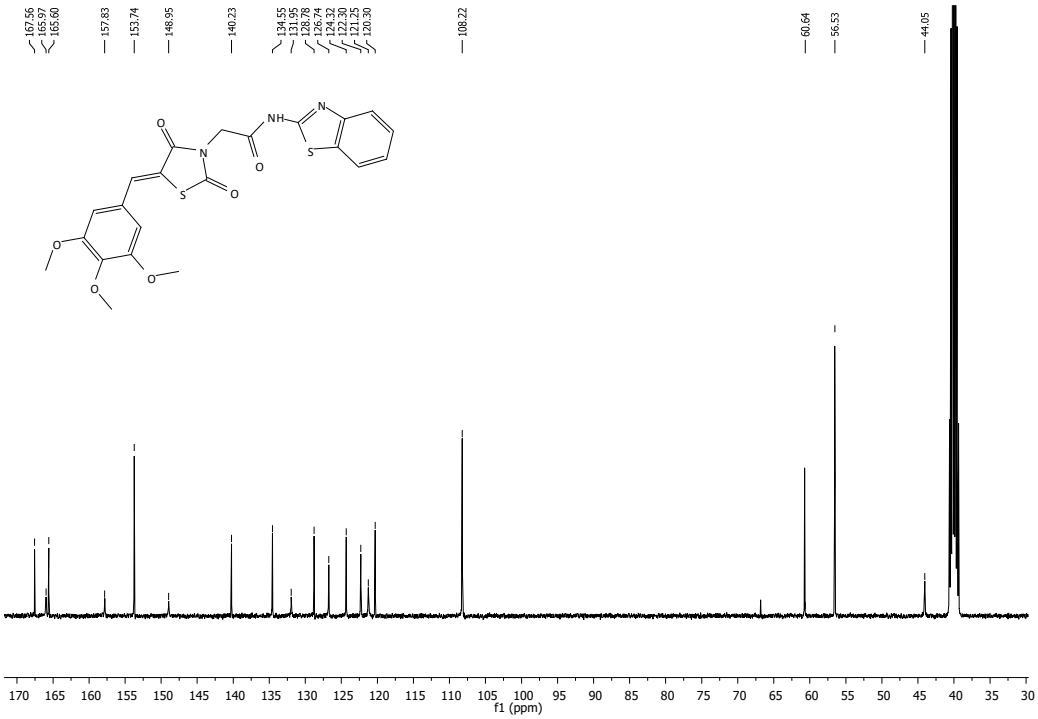
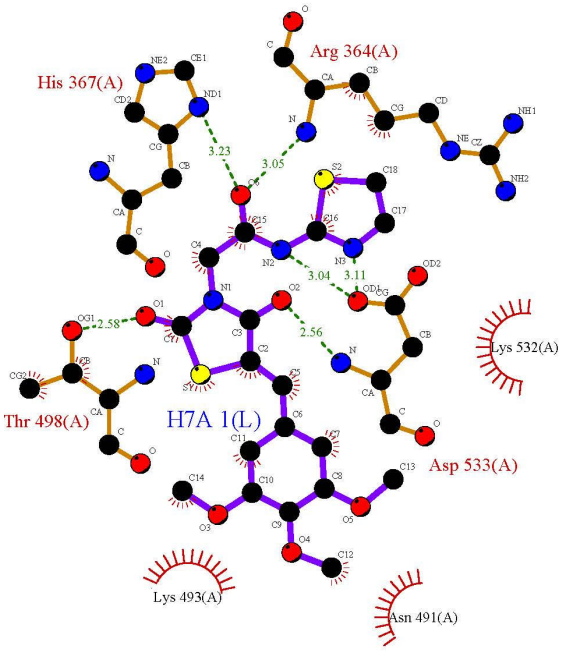

167.56
165.97
165.60
157.83
153.74
148.95
140.23
134.55
131.95
128.78
126.74
123.32
121.30
121.25
120.30
108.22
60.64
56.53
44.05
NH
N
S
O
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30
f1 (ppm)

Fig. S59.



Key

Ligand bond

Non-ligand bond

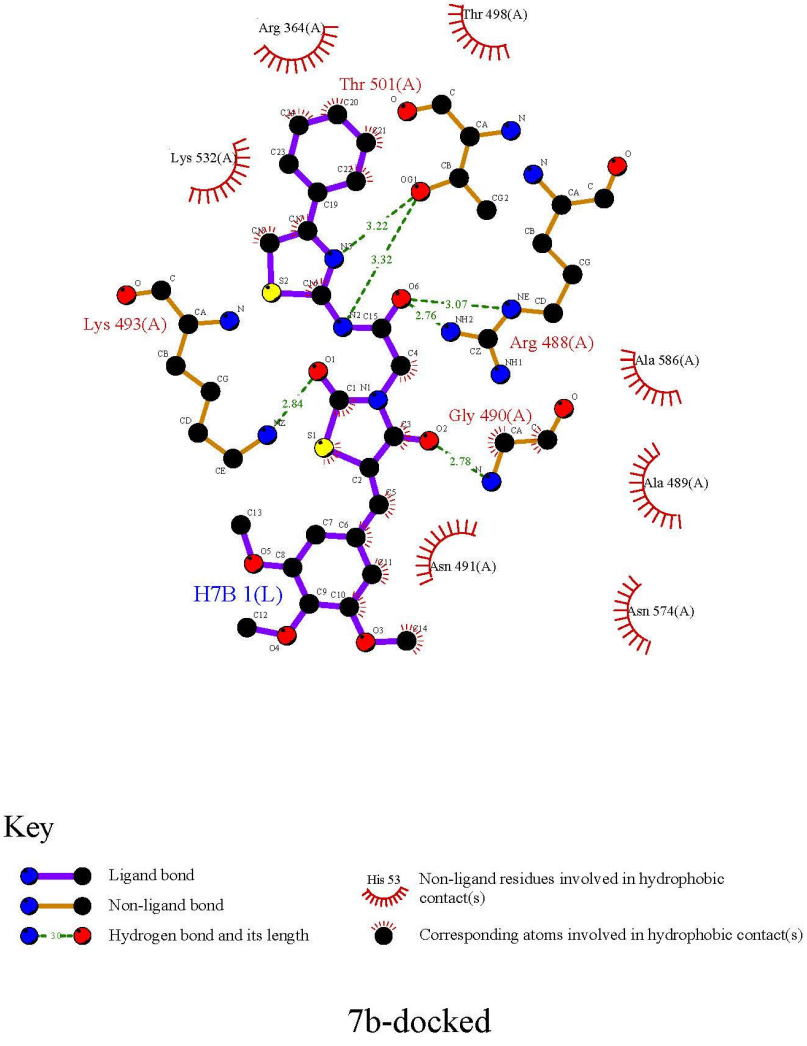
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

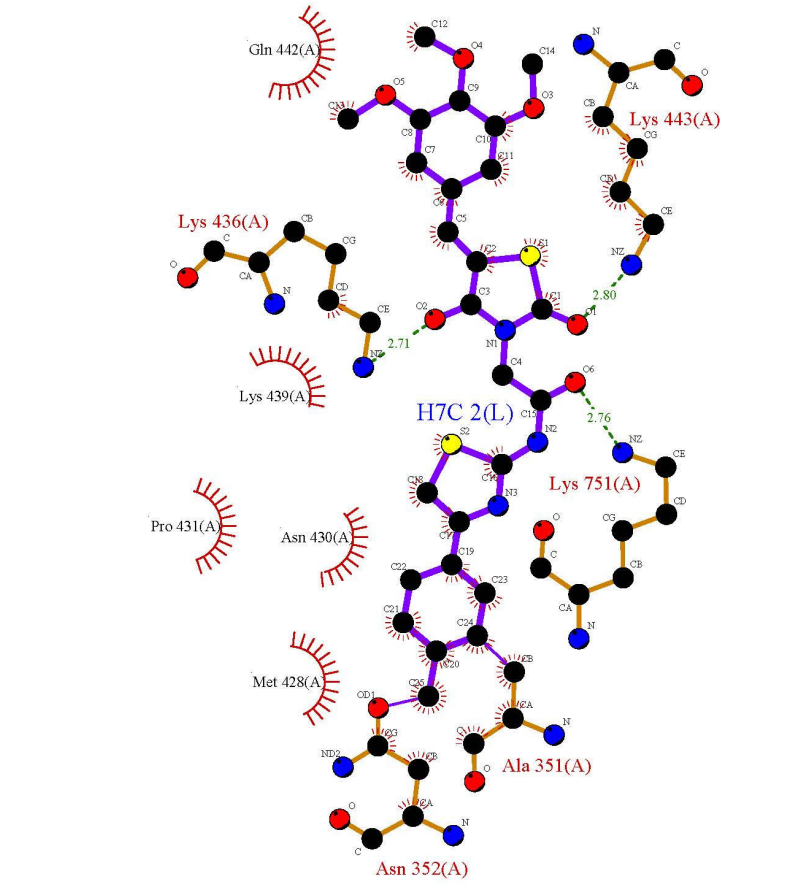
7a-docked

Fig. S60.



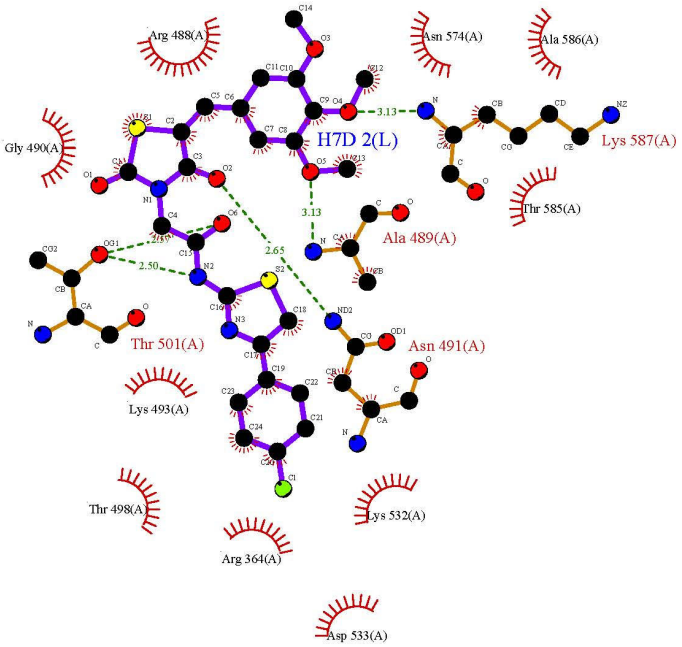
7b-docked

Fig. S61.



7c-minE

Fig. S62.



Key

Ligand bond

Non-ligand bond

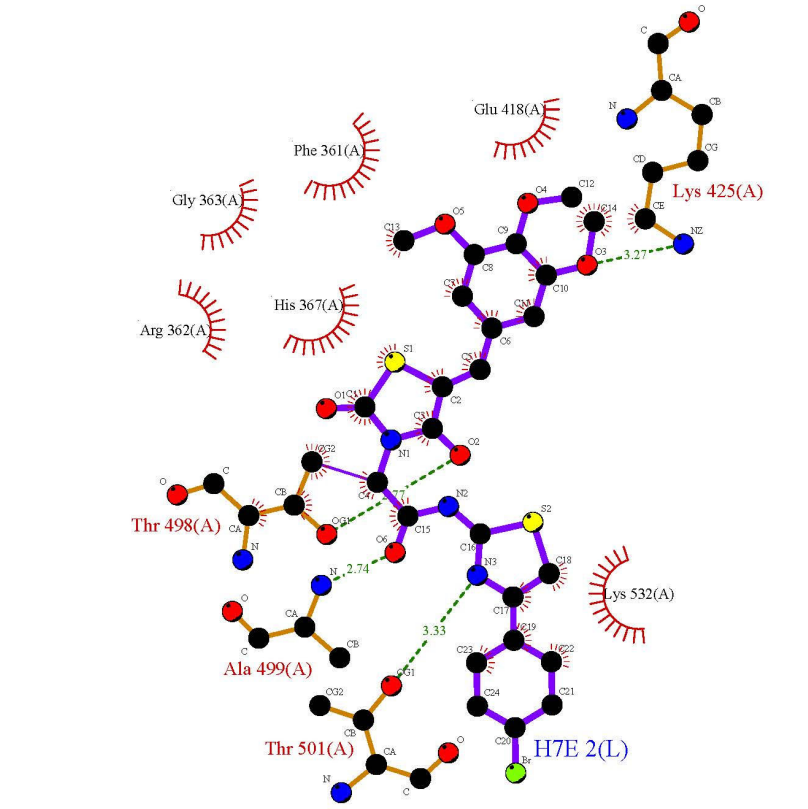
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

7d-minE

Fig. S63.



Key

Ligand bond

Non-ligand bond

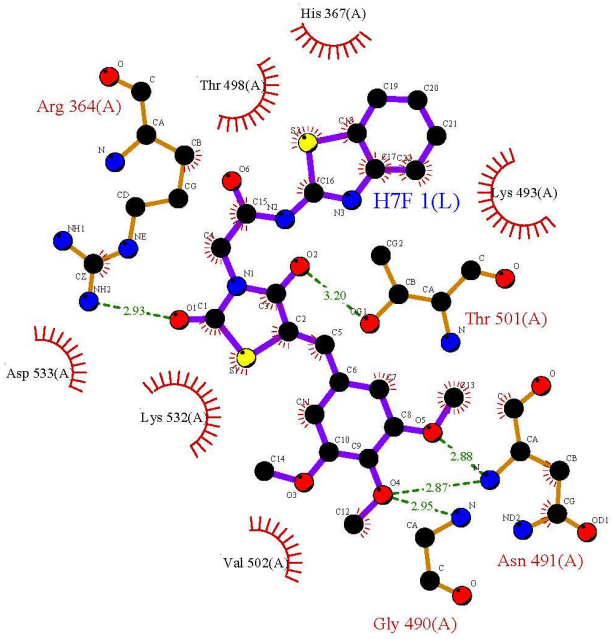
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

7e-minE

Fig. S64.



Key

Ligand bond

Non-ligand bond

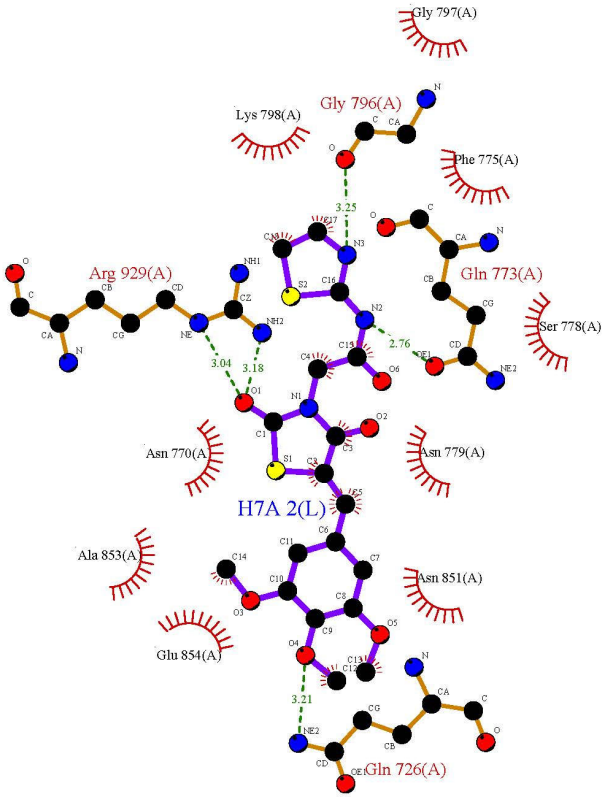
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

7f-maxpop

Fig. S65.



Key

Ligand bond

Non-ligand bond

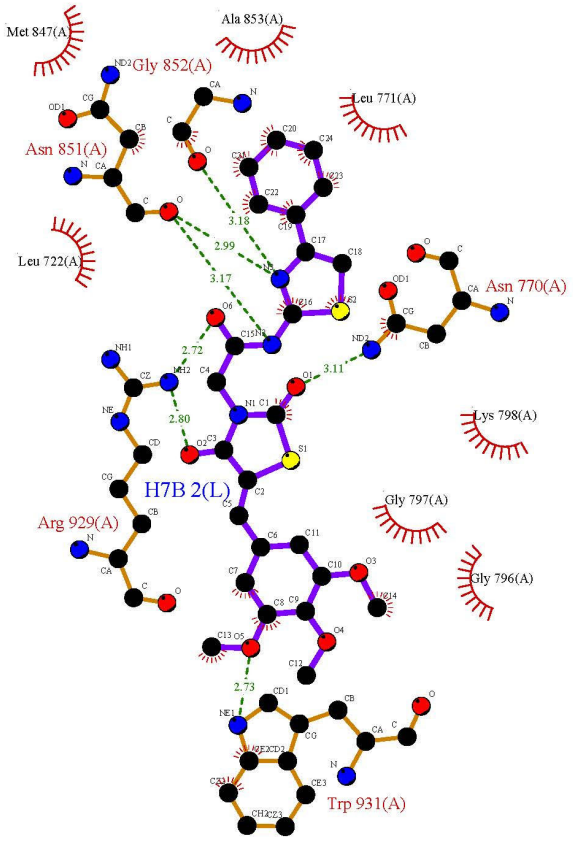
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

5gwk-7a

Fig. S66.



Key

Ligand bond

Non-ligand bond

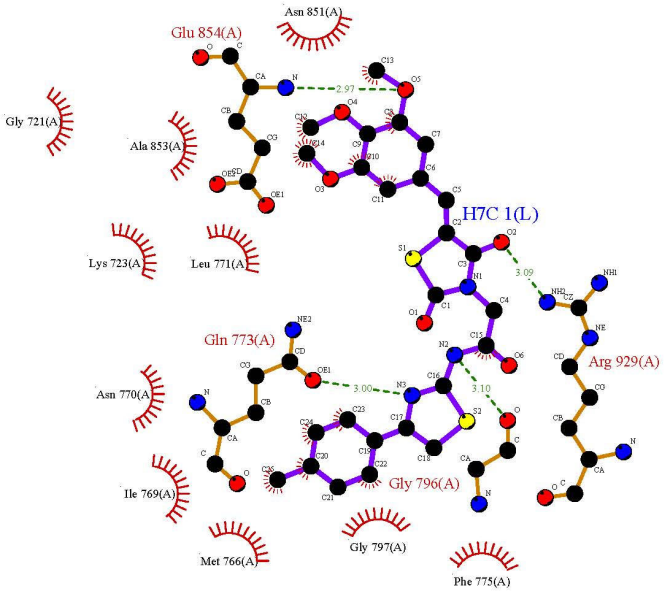
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

5gwk-7b

Fig. S67.



Key

Ligand bond

Non-ligand bond

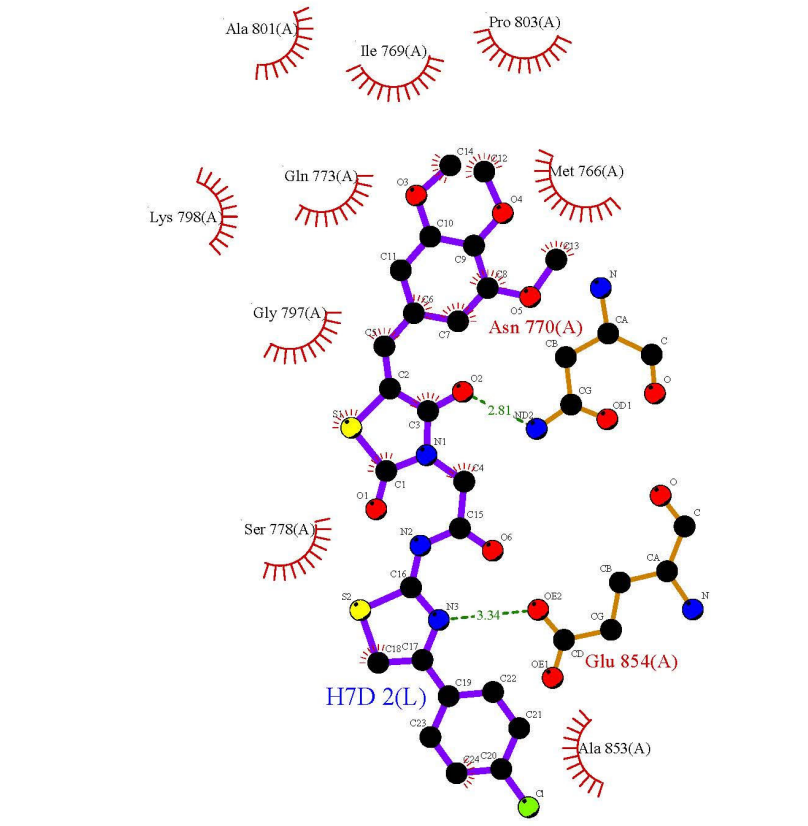
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

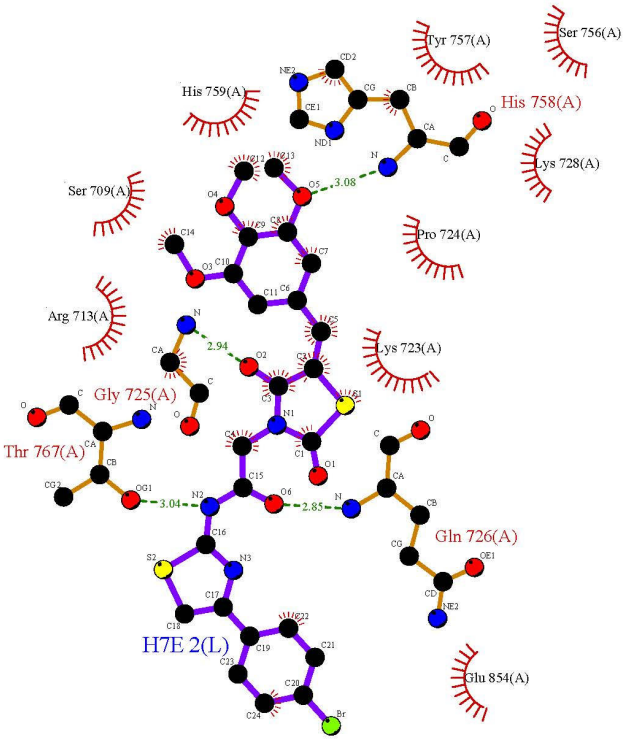
5gwk-7c

Fig. S68.



5gwk-7d

Fig. S69.



Key

Ligand bond

Non-ligand bond

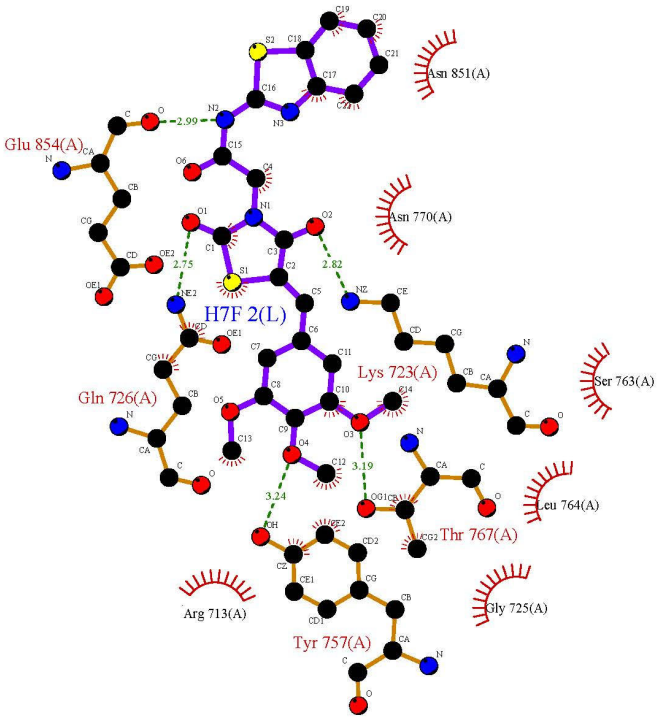
Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

5gwk-7e

Fig. S70.



Key

Ligand bond

Non-ligand bond

Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

5gwk-7f