

Synthesis and Antimicrobial Activity of Oxazolone, Imidazolone and Triazine Derivatives Containing Benzothiophene

Gadada Naganagowda, Patchanita Thamyongkit, and Amorn Petsom*

Research Center for Bioorganic Chemistry (RCBC), Department of Chemistry, Faculty of Science,
Chulalongkorn University, Bangkok, Thailand.

*E-mail: ngchula.pdf@gmail.com, amorn.p@chula.ac.th

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ABSTRACT. 3-Chloro-1-benzothiophene-2-carbonylchloride (**1**) was allowed to react with glycine to give 3-chloro-1-benzothiophen-2-yl-carbonylaminoacetic acid (**2**). Various aldehydes were treated with compound (**2**) in acetic anhydride to get 1,3-oxazol-5-ones (**3a-d**). These oxazolones were treated with aromatic amines or hydrazides to get various imidazol-4-ones (**4a-h** or **5a**) separately. Oxazolones was also treated with aromatic hydrazine, through which expansion of five membered oxazole ring to six member triazine ring occurs to yield 1,2,4-triazin-6-ones (**6a-h**). The structures of all the synthesized compounds were confirmed by spectral data and were screened for antibacterial and antifungal activities

Key words: Benzothiophene, Imidazol-5-ones, 1,2,4-triazine-6-ones, Antimicrobial activity

INTRODUCTION

The exploitation of a simple molecule with different functionalities for the synthesis of heterocycles is a worthwhile contribution in the chemistry of heterocycles. The heterocyclic compounds containing nitrogen or sulfur are very interesting because of their physico-chemical properties with relevance to the design of new drugs and new materials, especially those relating to molecular conductors and magnets.¹ Imidazolone and triazines are a representative class of heterocyclic compounds with a wide variety of interesting properties which are used in medicine and agriculture.² It has been associated with diverse pharmacological activities such as hypertension and inhibition of platelets,³ anti-leukemic,⁴ anti-inflammatory⁵ and potent neuroprotective⁶ agents. The benzothiophene nucleus is associated with diverse pharmacological activities such as nervous system depressing,⁷ analgesic,⁸ herbicidal,⁹ muscle relaxant¹⁰ and tranquilizing¹¹ activities. The synthesis of compounds incorporating oxazolones, imidazolone and triazine moieties has been attracting widespread attention due to their diverse pharmacological properties such as antimicrobial, antiinflammatory, analgesic and antitumor activities.¹²⁻¹⁶

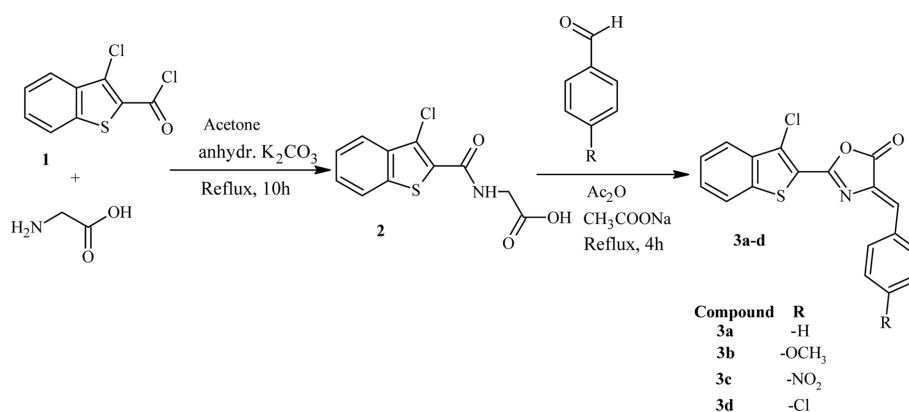
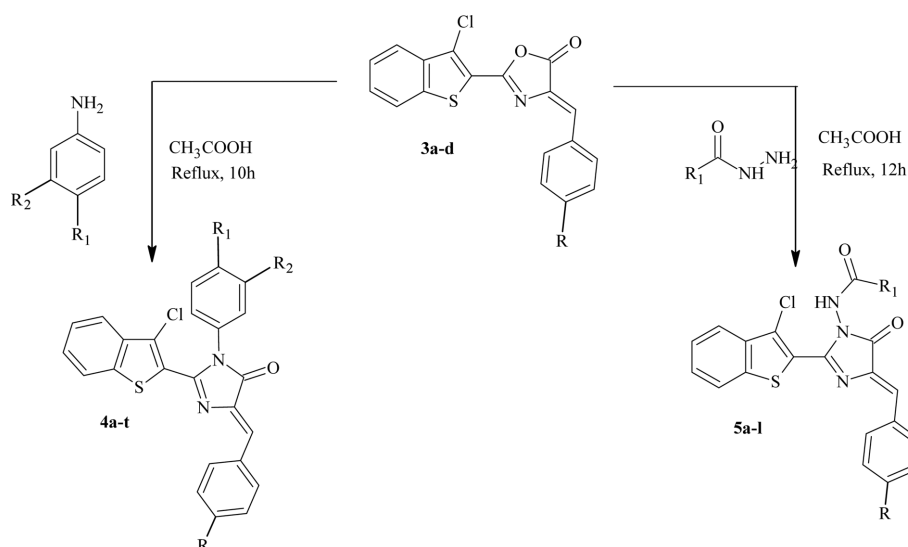
In view of these biological activities, it was planned to develop novel heterocyclic compounds containing oxazolones, imidazolone and triazine moiety at 2-position of benzothiophene ring. Encouraged by the importance of imidazolone and triazines rings in various pharmacolog-

ical lead molecules, we thought of incorporating these moieties to our base materials for research i.e, 3-chloro-1-benzothiophene-2-carbonylchloride at 2-position in order to get pharmacological lead molecules. This study work was done through the synthesis of oxazolone intermediate.

RESULTS AND DISCUSSION

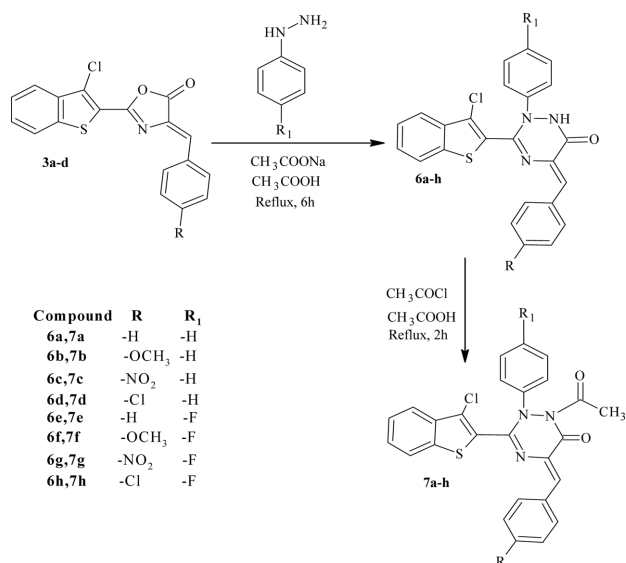
3-Chloro-1-benzothiophene-2-carbonyl chloride¹⁷ (**1**) was treated with glycine in dry acetone in the presence of K₂CO₃ to get acylated product **2**. ¹H-NMR spectrum of compound **2** exhibited signals at δ 12.79, 8.95 and 3.28 ppm due to -OH, -CONH and -CH₂ protons and a multiplet in between δ 7.98 and 7.85 ppm due to four aromatic protons. The required oxazolone **3a** was synthesized by the cyclization of compound **2** in the presence of acetic anhydride followed by condensation with benzaldehyde. Absence of -OH and -NH broad singlets signals in its ¹H-NMR spectrum and molecular ion peak at *m/z* 339.79 in its mass spectrum was confirmed for its formation of compound **3a** (Scheme 1).

Oxazolone **3a** was treated with 3-chloro-4-fluoroaniline in glacial acetic acid to get imidazol-4-one **4a** (Scheme 2). Compound **4a** exhibited IR peaks at 1650 and 1593 cm⁻¹ due to C=O and C=N stretching absorption frequencies, respectively. ¹H-NMR spectrum of compound **4a** exhibited a multiplet in between δ 8.01 to 7.71 ppm due to thirteen aromatic, and C=CH protons and molecular ion


Scheme 1. Synthesis of oxazol-5-ones **3a-d**.


Compound	R	R ₁	R ₂	Compound	R	R ₁
4a	-H	-F	-Cl	5a	-H	
4b	-OCH ₃	-F	-Cl	5b	-OCH ₃	
4c	-NO ₂	-F	-Cl	5c	-NO ₂	
4d	-Cl	-F	-Cl	5d	-Cl	
4e	-H	-F	-	5e	-H	
4f	-OCH ₃	-F	-	5f	-OCH ₃	
4g	-NO ₂	-F	-	5g	-NO ₂	
4h	-Cl	-F	-	5h	-Cl	
4i	-H	-COCH ₃	-	5i	-H	
4j	-OCH ₃	-COCH ₃	-	5j	-OCH ₃	
4k	-NO ₂	-COCH ₃	-	5k	-NO ₂	
4l	-Cl	-COCH ₃	-	5l	-Cl	
4m	-H	-CH ₃	-	-	-	-
4n	-OCH ₃	-CH ₃	-	-	-	-
4o	-NO ₂	-CH ₃	-	-	-	-
4p	-Cl	-CH ₃	-	-	-	-
4q	-H	-NO ₂	-	-	-	-
4r	-OCH ₃	-NO ₂	-	-	-	-
4s	-NO ₂	-NO ₂	-	-	-	-

Scheme 2. Synthesis of imidazol-4-ones **4a-t** and **5a-l**.



Scheme 3. Synthesis of 1,2,4-triazine-6-ones **6a-h** and **7a-h**.

peak at m/z 467.34 in its mass spectrum which confirmed for its formation. Similarly, compounds **4b-t** were prepared. Oxazolones **3a-d** was refluxed with hydrazide in acetic acid to afford imidazol-4-ones **5a-i**. In confirmation, compound **5a** exhibited peaks at 3262, 1642 and 1591 cm^{-1} due to N-H, C=O and C=N stretching absorption frequencies, respectively. $^1\text{H-NMR}$ spectrum of compound **5a** exhibited a multiplet in the region δ 8.19-7.34 ppm due to fourteen aromatic and C=CH protons. Finally, compound **5a** exhibited a molecular ion peak at m/z 548.40 in its mass spectrum.

Oxazolones **3a-d** was treated with substituted phenyl hydrazine in the presence of sodium acetate in glacial acetic acid. The expansion of five member oxazole ring to six member triazine ring occurs to yield 1,2,4-triazine-6-ones **6a-h**. Singlet at δ 9.12 ppm due to NH proton of compound **6a** in its $^1\text{H-NMR}$ spectrum. Acetylation of compounds **6a-h** with acetyl chloride resulted in the formation of compounds **7a-h**. Singlet at δ 2.44 ppm due to three protons of $-\text{CH}_3$ group was appeared in compound **7a** (Scheme 3).

BIOLOGICAL EVALUATION

Antibacterial activity

A Cup plate method using Hi-Media agar medium was employed to study the antibacterial activity of the synthesized compounds against two Gram-positive bacteria, *Staphylococcus aureus*-ATCC 25923, and *Bacillus subtilis*-ATCC 6633 and Gram-negative bacteria, *Pseudomo-*

Table 1. Antibacterial activity of the tested compounds

Compound	Zone of inhibition (mm)			
	Gram positive bacteria		Gram negative bacteria	
	<i>S. aureus</i>	<i>B. subtilis</i>	<i>P. aeruginosa</i>	<i>E. coli</i>
2	13	14	14	14
3a	12	15	13	14
3c	11	15	13	13
3d	14	15	15	11
4c	10	14	15	11
4d	15	13	13	15
4f	13	15	15	13
4h	15	13	11	12
4j	14	12	12	11
4l	15	13	13	15
4n	14	15	15	13
4p	16	15	11	15
4s	15	15	15	11
5b	13	12	12	13
5d	15	15	15	11
5e	13	14	12	14
5j	13	16	12	15
6a	14	12	10	11
6d	15	15	15	11
6g	14	14	14	12
7a	16	13	15	15
7d	15	15	13	13
7g	13	11	11	11
Control (DMF)	00	00	00	00
Chloramphenicol	24	25	20	22
Streptomycin	23	21	18	20

nas aeruginosa-ATCC 10145 and *Escherichia coli*-ATCC 35218. Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water is done as per the standard procedure.¹⁸ Each test compound (50 mg) was dissolved in dimethyl formamide (50 mL, 1000 $\mu\text{g}/\text{mL}$) to obtain a sample solution. Sample volume for all the compounds was fixed at 0.1 mL. The cups were made by scooping out agar medium with a sterilized cork borer in a petri dish, which was previously inoculated with the microorganisms. The solution of each test compound (0.1 mL) was added to the cups and petri dishes, and was subsequently incubated at 37 °C for 48 h. Chloramphenicol and streptomycin were used as reference drugs and dimethyl formamide as a control. The zone of inhibition produced by each compound was measured in mm. As shown in the Table 1, the tested compounds showed slight to moderate antibacterial activity compared to standard drugs against each microorganism.

Table 2. Antifungal activity of the tested compounds

Compound	Zone of inhibition (mm)		
	<i>C. albicans</i>	<i>C. pannical</i>	<i>A. niger</i>
2	15	14	13
3a	14	13	14
3c	16	12	11
3d	12	11	12
4c	13	16	15
4d	14	16	14
4f	14	11	15
4h	15	12	12
4j	12	10	15
4l	11	15	14
4n	12	13	12
4p	13	12	11
4s	14	11	15
5b	14	16	13
5d	13	16	15
5e	14	16	11
5j	15	14	11
6a	14	15	12
6d	12	12	12
6g	12	15	12
7a	14	14	14
7d	11	12	11
7g	11	11	13
Control(DMF)	00	00	00
Griseofulvin	23	24	22

Antifungal activity

The antifungal activity of the synthesized compounds was tested against three different fungi, *i.e.* *Candida albicans*, *Cryosporium pannical*, and *Aspergillus niger* by a filter paper disc technique.¹⁹ The concentration of test compounds was 1000 µg/mL. After treatment for 48 h the zone of inhibition produced by each compound was measured in mm. Griseofulvin was used as the standard antifungal agent and dimethyl formamide as a control. The results of antifungal activity are depicted in Table 2. Tested compounds showed slight to moderate antifungal activity.

EXPERIMENTAL

All chemicals were analytical grade, purchased from commercial suppliers and used as received without further purification. Melting points were determined in open capillary and were uncorrected. FT-IR spectra were recorded on a Nicolet Fourier Transform Infrared Spectrophotometer: Impact 410 (Nicolet Instrument Technologies, Inc. WI, USA). Infrared spectra were recorded

between 400 cm⁻¹ to 4,000 cm⁻¹ in transmittance mode. ¹H-NMR and ¹³C-NMR were obtained in DMSO-*d*₆ at 400 MHz for ¹H nuclei and 100 MHz for ¹³C nuclei (Varian Company, USA). All chemical shifts were reported in parts per million (ppm) using residual proton or carbon signal in deuterated solvents as internal references. Mass spectra were obtained using matrix-assisted laser desorption ionization mass spectrometry (MALDI-TOF) by using dithranol as a matrix. Elemental analysis (C, H, N and S) was performed on Perkin Elmer 2400 analyzer. The purity of the compound was checked by TLC on silica gel and further purification was performed through column chromatography (silica gel, 60-120 mesh).

Preparation of 3-chloro-1-benzothiophene-2-carbonylchloride (1)

Compound **1** was prepared according to the literature procedure,¹⁷ mp. 112-114 °C (Lit. mp. 110-112 °C).

Preparation of 2-(3-chlorobenzo[b]thiophene-2-carboxamido)acetic acid (2)

A mixture of compound **1** (2.31 g, 0.01 mol) and glycine (0.75 g, 0.01 mol) in acetone (30 mL) in the presence of K₂CO₃ was refluxed for 10 h. After the completion of the reaction (TLC-monitoring), the reaction mixture was cooled down to room temperature and then poured into cold water. The precipitate was filtered, dried and recrystallized from toluene to get pure compound **2**.

Yield 77%; mp 215-217 °C; IR ν (cm⁻¹): 3320 (OH), 3130 (NH), 1650 (C=O); ¹H-NMR δ (ppm): 12.79 (s, 1H, OH), 8.95 (s, 1H, CONH), 7.98-7.85 (m, 4H, Ar-CH), 3.28 (s, 2H, CH₂); ¹³C-NMR δ (ppm): 161.5, 172.4, 141.1, 135.2, 129.4, 126.7, 124.5, 124.2, 122.8, 40.2, 33.6; MS, m/z: 269.70 (M⁺). Anal. Calcd. for C₁₁H₈ClNO₃S: C, 48.99; H, 2.99; N, 5.19; S, 11.89; found: C, 48.97; H, 2.95; N, 5.15; S, 11.83%.

General procedure for synthesis of compounds 3a-d

Exemplary detail for 4-benzylidene-2-(3-chlorobenzo [b]thiophen-2-yl)oxazol-5(4H)-one (3a): A mixture of benzaldehyde (2.65 g, 2.59 mL, 0.025 mol) and {(3-chloro-1-benzothiophen-2-yl)carbonyl}amino}acetic acid **2** (6.74 g, 0.025 mol) freshly fused sodium acetate (2.05 g, 0.025 mol) and acetic anhydride (7.65 g, 7.56 mL, 0.075 mol) was refluxed for 4 h. Alcohol (40 mL) was added to the reaction mixture while still warm and the mixture left overnight in refrigerator. The precipitate was filtered, washed successively with hot water, alcohol and benzene. Recrystallized from 1,4-dioxane to get **3a**. Compounds **3b-d** was

prepared in same manner.

Yield 61%; mp 245-247 °C; IR ν (cm⁻¹): 1642 (C=O), 1595 (C=N); ¹H-NMR δ (ppm): 8.12-7.22 (m, 10H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 165.9, 164, 135.2, 131.6, 131.6, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 112.3; MS, m/z: 339.79 (M⁺). Anal. Calcd. for C₁₈H₁₀ClNO₂S: C, 63.62; H, 2.97; N, 4.12; S, 9.44; found: C, 63.58; H, 2.93; N, 4.09; S, 9.40%.

(3-Chlorobenzof[b]thiophen-2-yl)-4-(4-methoxybenzylidene)oxazol-5(4H)-one (3b): Yield 70%; mp 258-260 °C; IR ν (cm⁻¹): 1640 (C=O), 1597 (C=N); ¹H-NMR δ (ppm): 7.98-6.94 (m, 9H, Ar-CH and C=CH), 3.79 (s, 3H, OCH₃); ¹³C-NMR δ (ppm): 165.4, 164.5, 159.8, 131.6, 131.6, 130.2, 130.2, 114.2, 127.5, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 114.2, 112.3, 55.4; MS, m/z: 369.82 (M⁺). Anal. Calcd. for C₁₉H₁₂ClNO₃S: C, 61.71; H, 3.27; N, 3.79; S, 8.67; found: C, 61.69; H, 3.25; N, 3.75; S, 8.62%.

2-(3-Chlorobenzof[b]thiophen-2-yl)-4-(4-nitrobenzylidene)oxazol-5(4H)-one (3c): Yield 65%; mp 262-264 °C; IR ν (cm⁻¹): 1645 (C=O), 1607 (C=N); ¹H-NMR δ (ppm): 7.92-6.91 (m, 9H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 165.3, 164.3, 147.1, 141.3, 131.6, 131.6, 129.0, 129.0, 126.7, 125.9, 124.4, 124.3, 123.8, 122.8, 122, 119.9, 112.3, 23.8; MS, m/z: 384.79 (M⁺). Anal. Calcd. for C₁₈H₉ClN₂O₄S: C, 56.18; H, 2.36; N, 7.28; S, 8.33; found: C, 56.13; H, 2.31; N, 7.25; S, 8.30%.

(3-Chlorobenzof[b]thiophen-2-yl)-4-(4-chlorobenzylidene)oxazol-5(4H)-one (3d): Yield 63%; mp 265-267 °C; IR ν (cm⁻¹): 1635 (C=O), 1610 (C=N); ¹H-NMR δ (ppm): 8.02-7.12 (m, 9H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 165.1, 164.5, 133.5, 133.3, 131.6, 131.6, 129.0, 129.0, 128.7, 128.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 112.3; MS, m/z: 374.24 (M⁺). Anal. Calcd. for C₁₈H₉Cl₂NO₂S: C, 57.77; H, 2.42; N, 3.74; S, 8.57; found: C, 57.71; H, 2.40; N, 3.70; S, 8.52%.

General procedure for synthesis of compounds 4a-t

Exemplary detail for 4-benzylidene-1-(3-chloro-4-fluorophenyl)-2-(3-chlorobenzof[b]thiophen-2-yl)-1H-imidazol-5(4H)-one (4a): A mixture of compound 3a (3.39 g, 0.01 mol) in glacial acetic acid (10 mL) and 3-chloro-4-fluoroaniline (1.46 g, 0.01 mol) was refluxed for 10 h. The reaction mixture was allowed to cool down to room temperature, and then poured into ice cooled water with constant stirring. The precipitate was filtered, washed with water, dried and recrystallized from ethanol to get compound 4a. Compounds 4b-t were prepared in similar methodology.

Yield 55%; mp 270-272 °C; IR ν (cm⁻¹): 1650 (C=O), 1593 (C=N); ¹H-NMR δ (ppm): 8.01-7.71 (m, 13H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 169.3, 164.1, 154.4, 135.2, 131.6, 130.3, 129.7, 128.6, 128.6, 128.5, 128.5, 128.2, 127.9, 126.7, 125.9, 124.4, 124.3, 123.6, 122.8, 122, 120.9, 119.9, 114.6, 113.6; MS, m/z: 467.34 (M⁺). Anal. calcd. for C₂₄H₁₃Cl₂FN₂OS: C, 61.68; H, 2.80; N, 5.99; S, 6.86; found: C, 61.65; H, 2.77; N, 5.94; S, 6.81%.

(3-Chloro-4-fluorophenyl)-2-(3-chlorobenzof[b]thiophen-2-yl)-4-(4-methoxybenzylidene)-1H-imidazol-5(4H)-one (4b): Yield 59%; mp 269-271 °C; IR ν (cm⁻¹): 1651 (C=O), 1595 (C=N), 1070 (C-F); ¹H-NMR δ (ppm): 8.09-7.45 (m, 12H, Ar-CH and C=CH), 3.73 (s, 3H, OCH₃); ¹³C-NMR δ (ppm): 169.2, 164.3, 159.8, 154.4, 131.6, 130.3, 130.2, 130.2, 129.7, 128.2, 127.5, 126.7, 125.9, 124.4, 124.3, 123.6, 122.8, 122, 120.9, 119.9, 114.3, 114.1, 114.1, 113.3, 55.5; MS, m/z: 497.36 (M⁺). Anal. calcd. for C₂₅H₁₅Cl₂FN₂O₂S: C, 60.37; H, 3.04; N, 5.63; S, 6.45; found: C, 60.31; H, 3.00; N, 5.61; S, 6.40%.

(3-Chloro-4-fluorophenyl)-2-(3-chlorobenzof[b]thiophen-2-yl)-4-(4-nitrobenzylidene)-1H-imidazol-5(4H)-one (4c): Yield 61%; mp 266-268 °C; IR ν (cm⁻¹): 1648 (C=O), 1591 (C=N); ¹H-NMR δ (ppm): 7.99-6.98 (m, 12H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 169.6, 164.7, 154.4, 147.1, 141.3, 131.6, 130.3, 129.7, 129.0, 129.0, 128.2, 126.7, 125.9, 124.4, 124.3, 123.8, 123.8, 123.6, 122.8, 122, 120.9, 119.9, 114.1, 113.2; MS, m/z: 512.33 (M⁺). Anal. calcd. for C₂₄H₁₂Cl₂FN₃O₃S: C, 56.26; H, 2.36; N, 8.20; S, 6.26; found: C, 56.21; H, 2.31; N, 8.17; S, 6.21%.

(3-Chloro-4-fluorophenyl)-2-(3-chlorobenzof[b]thiophen-2-yl)-4-(4-chlorobenzylidene)-1H-imidazol-5(4H)-one (4d): Yield 62%; mp 259-261 °C; IR ν (cm⁻¹): 1649 (C=O), 1602 (C=N), 1070 (C-Cl); ¹H-NMR δ (ppm): 8.10-7.01 (m, 12H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 169.5, 164.0, 154.2, 133.5, 133.3, 131.6, 130.3, 129.7, 129.0, 129.0, 128.7, 128.7, 128.2, 126.7, 125.9, 124.4, 124.2, 123.6, 122.8, 122, 120.9, 119.9, 114.1, 113.1; MS, m/z: 501.78 (M⁺). Anal. calcd. for C₂₄H₁₂Cl₃FN₂OS: C, 57.45; H, 2.41; N, 5.58; S, 6.39; found: C, 57.40; H, 2.36; N, 5.55; S, 6.36%.

Benzylidene-2-(3-chlorobenzof[b]thiophen-2-yl)-1-(4-fluorophenyl)-1H-imidazol-5(4H)-one (4e): Yield 68%; mp 258-260 °C; IR ν (cm⁻¹): 1653 (C=O), 1599 (C=N); ¹H-NMR δ (ppm): 8.21-7.72 (m, 14H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 169.9, 164.2, 162.3, 135.2, 133.4, 131.6, 130.3, 130.1, 130.1, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 115.1, 115.1, 114.2; MS, m/z: 432.89 (M⁺). Anal. calcd. for C₂₄H₁₄ClFN₂OS: C, 66.59; H, 3.26; N, 6.47; S, 7.41;

found: C, 66.55; H, 3.23; N, 6.45; S, 7.38%.

(3-Chlorobenzof[b]thiophen-2-yl)-1-(4-fluorophenyl)-4-(4-methoxybenzylidene)-1H-imidazol-5(4H)-one (4f): Yield 67%; mp 302-304 °C; IR ν (cm⁻¹): 1653 (C=O), 1602 (C=N); ¹H-NMR δ (ppm): 8.14-6.99 (m, 13H, Ar-CH and C=CH), 3.81 (s, 3H, OCH₃); ¹³C-NMR δ (ppm): 169.3, 164.8, 162.2, 159.8, 133.4, 131.6, 130.3, 130.2, 130.2, 130.1, 130.1, 127.5, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 115.7, 115.7, 114.6, 114.1, 114.1, 55.3; MS, m/z: 462.92 (M⁺). Anal. calcd. for C₂₅H₁₆ClFN₂O₂S: C, 64.86; H, 3.48; N, 6.05; S, 6.93; found: C, 64.82; H, 3.44; N, 6.04; S, 6.90%.

(3-Chlorobenzof[b]thiophen-2-yl)-1-(4-fluorophenyl)-4-(4-nitrobenzylidene)-1H-imidazol-5(4H)-one (4g): Yield 71%; mp 291-293 °C; IR ν (cm⁻¹): 1643 (C=O), 1603 (C=N); ¹H-NMR δ (ppm): 8.09-7.03 (m, 13H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 169.6, 164.3, 162.9, 147.1, 141.3, 133.4, 131.6, 130.3, 130.1, 130.1, 129.0, 129.0, 126.7, 125.9, 124.4, 124.3, 123.8, 123.8, 122.8, 122.1, 119.4, 115.1, 115.1, 114.2; MS, m/z: 477.80 (M⁺). Anal. calcd. for C₂₄H₁₃ClFN₃O₃S: C, 60.32; H, 2.74; N, 8.79; S, 6.71; found: C, 60.30; H, 2.70; N, 8.72; S, 6.68%.

(3-Chlorobenzof[b]thiophen-2-yl)-4-(4-chlorobenzylidene)-1-(4-fluorophenyl)-1H-imidazol-5(4H)-one (4h): Yield 72%; mp 297-299 °C; IR ν (cm⁻¹): 1644 (C=O), 1598 (C=N); ¹H-NMR δ (ppm): 8.12-7.12 (m, 13H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 169.3, 164.3, 162.2, 133.5, 133.4, 133.3, 131.6, 130.3, 130.1, 130.1, 129.0, 129.0, 128.7, 128.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122.2, 119.3, 115.1, 115.1, 114.1; MS, m/z: 467.30 (M⁺). Anal. calcd. for C₂₄H₁₃Cl₂FN₂O₂S: C, 61.68; H, 2.80; N, 5.99; S, 6.86; found: C, 61.65; H, 2.78; N, 5.97; S, 6.82%.

(4-Acetylphenyl)-4-benzylidene-2-(3-chlorobenzof[b]thiophen-2-yl)-1H-imidazol-5(4H)-one (4i): Yield 69%; mp 303-305 °C; IR ν (cm⁻¹): 1646 (C=O), 1589 (C=N); ¹H-NMR δ (ppm): 8.21-6.99 (m, 14H, Ar-CH and C=CH), 2.50 (s, 3H, COCH₃); ¹³C-NMR δ (ppm): 197.3, 169.2, 164.3, 142.2, 136.6, 135.2, 131.6, 130.3, 129.0, 129.0, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 125.9, 124.4, 124.3, 124.3, 124.3, 122.8, 122, 119.2, 114.3, 26.4; MS, m/z: 456.94 (M⁺). Anal. calcd. for C₂₆H₁₇ClN₂O₂S: C, 68.34; H, 3.75; N, 6.13; S, 7.02; found: C, 68.30; H, 3.70; N, 6.04; S, 7.00%.

(4-Acetylphenyl)-2-(3-chlorobenzof[b]thiophen-2-yl)-4-(4-methoxybenzylidene)-1H-imidazol-5(4H)-one (4j): Yield 67%; mp 320-322 °C; IR ν (cm⁻¹): 1648 (C=O), 1597 (C=N); ¹H-NMR δ (ppm): 8.24-7.39 (m, 13H, Ar-CH and C=CH), 3.85 (s, 3H, OCH₃), 2.50 (s, 3H, COCH₃); ¹³C-NMR δ (ppm): 197.0, 169.8, 164, 159.8, 142.2, 136.6, 131.6,

130.3, 130.2, 130.2, 129.0, 129.0, 127.5, 126.7, 125.9, 124.4, 124.4, 124.3, 124.3, 122.8, 122, 119.9, 114.1, 114.1, 114.1, 55.2, 26.3; MS, m/z: 486.96 (M⁺). Anal. calcd. for C₂₇H₁₉ClN₂O₃S: C, 66.59; H, 3.93; N, 5.75; S, 6.58; found: C, 66.56; H, 3.90; N, 5.70; S, 6.53%.

(4-Acetylphenyl)-2-(3-chlorobenzof[b]thiophen-2-yl)-4-(4-nitrobenzylidene)-1H-imidazol-5(4H)-one (4k): Yield 64%; mp 295-297 °C; IR ν (cm⁻¹): 1646 (C=O), 1599 (C=N); ¹H-NMR δ (ppm): 8.13-7.69 (m, 13H, Ar-CH and C=CH), 2.69 (s, 3H, COCH₃); ¹³C-NMR δ (ppm): 197.7, 169.5, 164.3, 147.1, 142.2, 141.3, 136.6, 131.6, 130.3, 129.0, 129.0, 129.0, 126.7, 125.9, 124.4, 124.3, 124.3, 124.3, 123.8, 123.8, 122.8, 122.2, 119.2, 114.3, 26.1; MS, m/z: 501.70 (M⁺). Anal. calcd. for C₂₆H₁₆ClN₃O₄S: C, 62.21; H, 3.21; N, 8.37; S, 6.39; found: C, 62.16; H, 2.18; N, 8.35; S, 6.35%.

(4-Acetylphenyl)-2-(3-chlorobenzof[b]thiophen-2-yl)-4-(4-chlorobenzylidene)-1H-imidazol-5(4H)-one (4l): Yield 63%; mp 283-285 °C; IR ν (cm⁻¹): 1649 (C=O), 1605 (C=N); ¹H-NMR δ (ppm): 7.29-8.03 (m, 13H, Ar-CH and C=CH), 2.62 (s, 3H, OCH₃); ¹³C-NMR δ (ppm): 197.4, 169.3, 164.2, 142.2, 136.6, 133.5, 131.6, 130.3, 129.0, 129.0, 129.0, 129.0, 128.7, 128.7, 126.7, 125.9, 124.3, 124.3, 124.3, 122.8, 122, 119.9, 114.6, 26.3; MS, m/z: 491.38 (M⁺). Anal. calcd. for C₂₆H₁₆Cl₂N₂O₂S: C, 63.55; H, 3.28; N, 5.70; S, 6.53; found: C, 63.50; H, 3.26; N, 5.68; S, 6.50%.

Benzylidene-2-(3-chlorobenzof[b]thiophen-2-yl)-1-p-tolyl-1H-imidazol-5(4H)-one (4m): Yield 55%; mp 288-290 °C; IR ν (cm⁻¹): 1653 (C=O), 1607 (C=N); ¹H-NMR δ (ppm): 8.12-6.99 (m, 14H, Ar-CH and C=CH), 2.34 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 169.3, 164.2, 136.1, 135.1, 134.8, 131.6, 130.3, 129.2, 129.2, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 114.6, 21.5; MS, m/z: 428.90 (M⁺). Anal. calcd. for C₂₅H₁₇ClN₂O₂S: C, 70.00; H, 3.99; N, 6.53; S, 7.48; found: C, 69.89; H, 3.97; N, 6.48; S, 7.44%.

(3-Chlorobenzof[b]thiophen-2-yl)-4-(4-methoxybenzylidene)-1-p-tolyl-1H-imidazol-5(4H)-one (4n): Yield 59%; mp 297-299 °C; IR ν (cm⁻¹): 1652 (C=O), 1595 (C=N); ¹H-NMR δ (ppm): 8.27-7.64 (m, 13H, Ar-CH and C=CH), 3.79 (s, 3H, OCH₃), 2.31 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 169.5, 164.8, 159.3, 136.8, 134.8, 131.6, 130.3, 130.2, 130.2, 129.2, 129.2, 128.5, 128.5, 127.5, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 114.6, 114.1, 114.1, 55.4, 21.8; MS, m/z: 458.94 (M⁺). Anal. calcd. for C₂₆H₁₉ClN₂O₂S: C, 68.04; H, 4.17; N, 6.10; S, 6.99; found: C, 68.00; H, 4.12; N, 6.05; S, 6.94%.

(3-Chlorobenzof[b]thiophen-2-yl)-4-(4-nitrobenzylidene)-1-p-tolyl-1H-imidazol-5(4H)-one (4o): Yield 57%; mp

289-291 °C; IR ν (cm^{-1}): 1654 (C=O), 1603 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.09-7.69 (m, 13H, Ar-CH and C=CH), 2.32 (s, 3H, CH_3); $^{13}\text{C-NMR}$ δ (ppm): 169.6, 164.3, 147.2, 141.3, 136.8, 134.8, 131.6, 130.3, 129.2, 129.2, 129.0, 129.0, 128.5, 128.5, 126.7, 125.9, 124.4, 124.3, 123.8, 123.8, 122.8, 122, 119.9, 114.2, 21.9; MS, m/z : 474.90 (M^+). Anal. calcd. for $\text{C}_{25}\text{H}_{16}\text{ClN}_3\text{O}_3\text{S}$: C, 63.36; H, 3.40; N, 8.87; S, 6.77; found: C, 63.31; H, 3.33; N, 8.82; S, 6.71%.

(3-Chlorobenzob[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)-1-*p*-tolyl-1H-imidazol-5(4H)-one (4p): Yield 69%; mp 321-323 °C; IR ν (cm^{-1}): 1639 (C=O), 1604 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.19-7.54 (m, 13H, Ar-CH and C=CH), 2.41 (s, 3H, CH_3); $^{13}\text{C-NMR}$ δ (ppm): 169.4, 164.7, 136.8, 134.3, 133.5, 133.3, 131.6, 130.3, 129.2, 129.2, 129.0, 129.0, 128.7, 128.7, 128.5, 128.5, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 114.1, 21.2; MS, m/z : 463.33 (M^+). Anal. calcd. for $\text{C}_{25}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}_3\text{S}$: C, 64.80; H, 3.48; N, 6.05; S, 6.92; found: C, 64.78; H, 3.42; N, 6.01; S, 6.89%.

Benzylidene-2-(3-chlorobenzob[*b*]thiophen-2-yl)-1-(4-nitrophenyl)-1H-imidazol-5(4H)-one (4q): Yield 61%; mp 310-312 °C; IR ν (cm^{-1}): 1642 (C=O), 1597 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.28-7.49 (m, 14H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 169.1, 164.5, 143.3, 143.5, 135.2, 131.6, 130.3, 129.2, 129.2, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 125.9, 124.4, 124.3, 124.1, 124.1, 122.8, 122, 119.2, 114.2; MS, m/z : 459.90 (M^+). Anal. calcd. for $\text{C}_{24}\text{H}_{14}\text{ClFN}_3\text{O}_3\text{S}$: C, 62.68; H, 3.07; N, 9.14; S, 6.97; found: C, 62.65; H, 3.02; N, 9.05; S, 6.90%.

(3-Chlorobenzob[*b*]thiophen-2-yl)-4-(4-methoxybenzylidene)-1-(4-nitrophenyl)-1H-imidazol-5(4H)-one (4r): Yield 72%; mp 312-314 °C; IR ν (cm^{-1}): 1644 (C=O), 1593 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.21-7.32 (m, 13H, Ar-CH and C=CH), 3.85 (s, 3H, OCH_3); $^{13}\text{C-NMR}$ δ (ppm): 169.7, 164.0, 159.5, 143.9, 143.5, 131.6, 130.3, 130.2, 130.2, 129.2, 129.2, 127.5, 126.7, 125.9, 124.4, 124.3, 124.1, 124.1, 122.8, 122, 119.9, 114.6, 114.2, 114.2, 55.1; MS (M^+): 489.93 (M^+). Anal. calcd. for $\text{C}_{25}\text{H}_{16}\text{ClFN}_3\text{O}_4\text{S}$: C, 61.29; H, 3.29; N, 8.58; S, 6.54; found: C, 61.20; H, 3.21; N, 8.51; S, 6.50%.

(3-Chlorobenzob[*b*]thiophen-2-yl)-4-(4-nitrobenzylidene)-1-(4-nitrophenyl)-1H-imidazol-5(4H)-one (4s): Yield 70%; mp 309-311 °C; IR ν (cm^{-1}): 1645 (C=O), 1604 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.32-7.03 (m, 13H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 169.2, 164.2, 147.1, 143.5, 143.5, 141.3, 131.6, 130.3, 129.2, 129.2, 129.0, 129.0, 126.7, 125.9, 124.4, 124.3, 124.1, 124.1, 123.8, 123.8, 122.8, 122, 119.5, 114.3; MS, m/z : 492.90 (M^+). Anal. calcd. for $\text{C}_{24}\text{H}_{13}\text{ClN}_4\text{O}_5\text{S}$: C, 57.09; H, 2.60; N, 11.10; S, 6.35; found: C, 57.04; H, 2.57; N, 11.07; S, 6.34%.

(3-Chlorobenzob[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)-

1-(4-nitrophenyl)-1H-imidazol-5(4H)-one (4t): Yield 60%; mp 279-281 °C; IR ν (cm^{-1}): 1647 (C=O), 1597 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.12-7.91 (m, 13H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 169.3, 164.3, 143.5, 143.5, 133.5, 133.3, 131.6, 130.3, 129.2, 129.2, 129.0, 129.0, 128.7, 128.7, 126.7, 125.9, 124.4, 124.3, 124.1, 124.1, 122.8, 122.3, 119.6, 114.5; MS, m/z : 494.35 (M^+). Anal. calcd. for $\text{C}_{24}\text{H}_{13}\text{Cl}_2\text{N}_3\text{O}_3\text{S}$: C, 58.31; H, 2.65; N, 8.50; S, 6.49; found: C, 58.27; H, 2.60; N, 8.49; S, 6.46%.

General procedure for synthesis of compounds 5a-I

Exemplary detail for 4-benzylidene-2-(3-chloro-1-benzothiothiophene-2-yl)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]-3-chlorobenzothiothiophene-2-carboxamide (5a): A mixture of compound **3a** (3.39 g, 0.01 mol) and 3-chloro-benzothiothiophene-2-carbohydrazide (2.26 g, 0.01 mol) in glacial acetic acid (10 mL) was refluxed for 12 h. After the completion of the reaction mixture (TLC-monitoring). The reaction mixture was allowed to cool down to room temperature and poured into ice cooled water with constant stirring. The resulting precipitate was filtered washed with water, dried and purified through column chromatography by using petroleum ether and ethyl acetate (60:40) as an eluent to afford pure compound **5a**. Compounds **5b-I** were prepared in similar methodology.

Yield 55%; mp 279-281 °C; IR ν (cm^{-1}): 3262 (N-H), 1642 (C=O), 1591 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.70 (s, 1H, NH), 8.19-7.34 (m, 14H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.5, 164.3, 160.6, 135.9, 141.6, 135.2, 133.4, 131.6, 130.3, 129.9, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 126.7, 125.9, 124.4, 124.4, 124.3, 124.3, 122.8, 122.8, 122, 119.9, 114.2; MS, m/z : 548.40 (M^+). Anal. calcd. for $\text{C}_{27}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_2\text{S}_2$: C, 59.13; H, 2.76; N, 7.66; S, 11.69; found: C, 59.10; H, 2.72; N, 7.62; S, 11.63%.

Chloro-N-[2-(3-chloro-1-benzob[*b*]thiophen-2-yl)-4-(4-methoxybenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]benzob[*b*]thiophene-2-carboxamide (5b): Yield 55%; mp 319-321 °C; IR ν (cm^{-1}): 3263 (N-H), 1644 (C=O), 1589 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.65 (s, 1H, NH), 8.22-7.79 (m, 13H, Ar-CH and C=CH), 3.73 (s, 3H, OCH_3); $^{13}\text{C-NMR}$ δ (ppm): 166.2, 164.7, 160.6, 159.8, 141.6, 135.9, 133.4, 131.6, 130.3, 130.2, 130.2, 129.9, 127.5, 126.7, 126.7, 125.9, 124.4, 124.4, 124.3, 124.3, 122.8, 122.8, 122.0, 119.9, 114.6, 114.2, 55.4; MS, m/z : 578.40 (M^+). Anal. calcd. for $\text{C}_{28}\text{H}_{17}\text{Cl}_2\text{N}_3\text{O}_3\text{S}_2$: C, 58.13; H, 2.96; N, 7.26; S, 11.09; found: C, 58.12; H, 2.90; N, 7.23; S, 11.03%.

Chloro-N-[2-(3-chloro-1-benzob[*b*]thiophen-2-yl)-4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]benzob[*b*]thiophene-2-carboxamide (5c): Yield 63%; mp 296-298 °C; IR ν (cm^{-1}): 3265 (N-H), 1643 (C=O), 1598

(C=N); $^1\text{H-NMR}$ δ (ppm): 13.45 (s, 1H, NH), 8.88-7.09 (m, 13H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.1, 164.1, 160.6, 147.1, 141.6, 141.3, 135.9, 133.4, 131.6, 130.3, 129.9, 129.0, 129.0, 126.7, 126.7, 125.9, 124.4, 124.4, 124.3, 124.3, 123.8, 123.8, 122.8, 122.8, 122, 119.3, 114.3; MS, m/z: 593.40 (M^+). Anal. calcd. for $\text{C}_{27}\text{H}_{14}\text{Cl}_2\text{N}_4\text{O}_4\text{S}_2$: C, 54.64; H, 2.38; N, 9.44; S, 10.81; found: C, 54.60; H, 2.35; N, 9.40; S, 10.78%.

Chloro-N-[2-(3-chloro-1-benzothiophen-2-yl)-4-(4-chlorobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]benzothiophene-2-carboxamide (5d): Yield 60%; mp 297-299 °C; IR ν (cm^{-1}): 3269 (N-H), 1664 (C=O), 1601 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.09 (s, 1H, NH), 8.32-7.43 (m, 13H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.3, 164.3, 160.6, 141.6, 135.9, 133.5, 133.4, 133.3, 131.6, 130.3, 129.0, 129.9, 129.0, 128.7, 128.7, 126.7, 126.7, 125.9, 124.4, 124.4, 124.3, 124.3, 122.8, 122.8, 122, 119.2, 114.9; MS, m/z: 582.90 (M^+). Anal. calcd. for $\text{C}_{27}\text{H}_{14}\text{Cl}_3\text{N}_3\text{O}_2\text{S}_2$: C, 55.63; H, 2.42; N, 7.21; S, 11.00; found: C, 55.60; H, 2.39; N, 7.16; S, 10.96.

N-[4-benzylidene-2-(3-chloro-1-benzo[b]thiophen-2-yl)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]benzo[b]furan-2-carboxamide (5e): Yield 55%; mp 309-311 °C; IR ν (cm^{-1}): 3273 (N-H), 1662 (C=O), 1608 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.41 (s, 1H, NH), 8.13-7.79 (m, 14H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.2, 164, 157.2, 157.1, 150.0, 135.2, 131.6, 130.3, 128.6, 128.6, 128.5, 128.5, 127.9, 126.9, 125.9, 126.7, 124.7, 124.4, 124.3, 123.3, 122.8, 122, 120.9, 119.4, 114.4, 111.3, 108.7; MS, m/z: 497.92 (M^+). Anal. calcd. for $\text{C}_{27}\text{H}_{16}\text{ClN}_3\text{O}_3\text{S}$: C, 65.12; H, 3.24; N, 8.44; S, 6.44; found: C, 65.09; H, 3.20; N, 8.40; S, 6.40%.

N-[2-(3-chloro-1-benzothiophen-2-yl)-4-(4-methoxybenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]benzofuran-2-carboxamide (5f): Yield 56%; mp 279-291 °C; IR ν (cm^{-1}): 3273 (N-H), 1649 (C=O), 1599 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.54 (s, 1H, NH), 7.99-7.14 (m, 13H, Ar-CH and C=CH), 3.74 (s, 3H, OCH_3); $^{13}\text{C-NMR}$ δ (ppm): 166.8, 164.3, 159.2, 157.2, 157.1, 150.0, 131.6, 130.3, 130.2, 130.2, 127.5, 126.9, 126.7, 125.9, 124.7, 124.4, 124.3, 123.3, 122.8, 122, 120.9, 119.9, 114.2, 114.2, 108.9, 111.1, 114.2, 55.5; MS, m/z: 527.90 (M^+). Anal. calcd. for $\text{C}_{28}\text{H}_{18}\text{ClN}_3\text{O}_4\text{S}$: C, 64.70; H, 3.44; N, 7.96; S, 6.07; found: C, 64.67; H, 3.40; N, 7.91; S, 6.00%.

N-[2-(3-chloro-1-benzo[b]thiophen-2-yl)-4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]benzo[b]benzo[b]furan-2-carboxamide (5g): Yield 51%; mp 291-293 °C; IR ν (cm^{-1}): 3272 (N-H), 1648 (C=O), 1591 (C=N);

$^1\text{H-NMR}$ δ (ppm): 13.44 (s, 1H, NH), 8.32-7.69 (m, 13H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.3, 164.8, 157.1, 157.1, 150.0, 147.1, 141.3, 131.6, 130.3, 129.0, 129.0, 126.9, 126.7, 125.9, 124.7, 124.4, 124.3, 123.3, 123.8, 123.8, 122.8, 122, 120.9, 119.9, 114.1, 111.2, 108.7; MS, m/z: 542.90 (M^+). Anal. calcd. for $\text{C}_{27}\text{H}_{15}\text{ClN}_4\text{O}_5\text{S}$: C, 59.73; H, 2.78; N, 10.32; S, 5.91; found: C, 59.70; H, 2.74; N, 10.39; S, 5.89%.

N-[2-(3-chloro-1-benzothiophen-2-yl)-4-(4-chlorobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]benzo[b]furan-2-carboxamide (5h): Yield 53%; mp 296-298 °C; IR ν (cm^{-1}): 3279 (N-H), 1663 (C=O), 1596 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.49 (s, 1H, NH), 8.17-7.79 (m, 13H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.7, 164.2, 157.1, 157.1, 130.3, 150.0, 133.5, 133.3, 131.6, 129.0, 129.0, 128.7, 128.7, 126.9, 126.7, 125.9, 124.7, 124.4, 124.3, 123.3, 122.8, 122, 120.9, 119.9, 114.6, 111.3, 108.5; MS, m/z: 532.35 (M^+). Anal. calcd. for $\text{C}_{27}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_3\text{S}$: C, 60.91; H, 2.84; N, 7.89; S, 6.02; found: C, 60.89; H, 2.80; N, 7.85; S, 6.00%.

N-[4-benzylidene-2-(3-chloro-1-benzothiophen-2-yl)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]pyridine-4-carboxamide (5i): Yield 59%; mp 289-291 °C; IR ν (cm^{-1}): 3268 (N-H), 1666 (C=O), 1593 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.47 (s, 1H, NH), 8.09-7.29 (m, 14H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.7, 164.2, 164.3, 149.7, 149.7, 140.8, 135.2, 131.6, 130.3, 128.5, 128.5, 128.6, 128.6, 127.9, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 121.7, 121.5, 119.3, 114.2; MS, m/z: 458.90 (M^+). Anal. calcd. for $\text{C}_{24}\text{H}_{15}\text{ClN}_4\text{O}_2\text{S}$: C, 62.81; H, 3.29; N, 12.21; S, 6.99; found: C, 62.78; H, 3.26; N, 12.17; S, 6.95%.

N-[2-(3-chloro-1-benzothiophen-2-yl)-4-(4-methoxybenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]pyridine-4-carboxamide (5j): Yield 59%; mp 271-273 °C; IR ν (cm^{-1}): 3270 (N-H), 1663 (C=O), 1557 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.19 (s, 1H, NH), 8.19-7.27 (m, 13H, Ar-CH and C=CH), 3.74 (s, 3H, OCH_3); $^{13}\text{C-NMR}$ δ (ppm): 166.6, 164.3, 164.2, 159.8, 149.7, 149.7, 140.8, 131.6, 130.3, 130.2, 130.2, 127.5, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 121.7, 121.7, 119.9, 114.6, 114.2, 114.2, 56.8; MS, m/z: 488.90 (M^+). Anal. calcd. for $\text{C}_{25}\text{H}_{17}\text{ClN}_4\text{O}_3\text{S}$: C, 61.41; H, 3.50; N, 11.46; S, 6.56; found: C, 61.38; H, 3.48; N, 11.42; S, 6.54%.

N-[2-(3-chloro-1-benzothiophen-2-yl)-4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]pyridine-4-carboxamide (5k): Yield 67%; mp 271-273 °C; IR ν (cm^{-1}): 3273 (N-H), 1655 (C=O), 1610 (C=N); $^1\text{H-NMR}$ δ (ppm): 13.68 (s, 1H, NH), 8.27-7.38 (m, 13H, Ar-CH and C=CH); $^{13}\text{C-NMR}$ δ (ppm): 166.8, 164.2, 164.3, 149.7, 149.7,

147.1, 141.3, 140.8, 131.6, 130.3, 129.0, 129.0, 126.7, 125.9, 124.4, 124.3, 123.8, 123.8, 122.8, 122.2, 121.7, 121.1, 119.9, 114.2; MS, m/z: 503.90 (M^+). Anal. calcd. for $C_{24}H_{14}ClN_5O_4S$: C, 57.20; H, 2.80; N, 13.90; S, 6.36; found: C, 57.17; H, 2.78; N, 13.88; S, 6.33%.

***N*-[2-(3-chloro-1-benzothiophen-2-yl)-4-(4-chlorobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]pyridine-4-carboxamide (5l)**: Yield 57%; mp 274-276 °C; IR ν (cm^{-1}): 3277 (NH), 1668 (C=O), 1612 (C=N); 1H -NMR δ (ppm): 13.43 (s, 1H, NH), 8.31-7.59 (m, 13H, Ar-CH and C=CH); ^{13}C -NMR δ (ppm): 166.4, 164.3, 164.3, 149.2, 149.7, 140.8, 133.5, 133.3, 131.6, 130.3, 129.0, 129.0, 128.7, 128.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 121.7, 121.7, 119.6, 114.3; MS, m/z: 493 (M^+). Anal. calcd. for $C_{24}H_{14}Cl_2N_4O_2S$: C, 58.43; H, 2.86; N, 11.36; S, 6.50; found: C, 58.40; H, 2.82; N, 11.32; S, 6.47%.

General procedure for synthesis of compounds 6a-h

Exemplary detail for 5-benzylidene-3-(3-chloro-1-benzothiophen-2-yl)-2-phenyl-1,2,4-triazin-6(5H)-one (6a): A mixture of compound **3a** (3.39 g, 0.01 mol), phenyl hydrazine (1.08 g, 0.96 mL, 0.01 mol) and sodium acetate (0.2 g) in glacial acetic acid (10 mL) was refluxed for 6 h. The completion of the reaction was monitored through TLC. After completion of the reaction, the reaction mixture was cooled down to room temperature and poured into crushed ice with vigorous stirring. The precipitate was filtered, washed with water, dried and purified through column chromatography by using n-hexane and ethyl acetate (70:30) as an eluent to get pure compound **6a**. Compounds **6b-h** were prepared in similar manner.

Yield 55%; mp 230-232 °C; IR ν (cm^{-1}): 3280 (N-H), 1653 (C=O), 1609 (C=N); 1H -NMR δ (ppm): 9.12 (s, 1H, NH), 8.34-7.19 (m, 15H, Ar-CH and C=CH); ^{13}C -NMR δ (ppm): 165.3, 164.2, 136.1, 135.2, 134.5, 131.6, 129.2, 129.2, 128.6, 128.5, 128.5, 128.6, 127.9, 126.7, 125.9, 124.4, 124.3, 123.9, 123.9, 122.8, 122.8, 122.4, 119.3, 114.2; MS, m/z: 429.90 (M^+). Anal. calcd. for $C_{24}H_{16}ClN_3OS$: C, 67.05; H, 3.75; N, 9.77; S, 7.46; found: C, 67.01; H, 3.71; N, 9.72; S, 7.43%.

(3-Chloro-1-benzothiophen-2-yl)-5-(4-methoxybenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (6b): Yield 61%; mp 245-247 °C; IR ν (cm^{-1}): 3285 (N-H), 1657 (C=O), 1607 (C=N); 1H -NMR δ (ppm): 9.10 (s, 1H, NH), 8.44-7.76 (m, 14H, Ar-CH and C=CH), 3.68 (s, 3H, OCH₃); ^{13}C -NMR δ (ppm): 165.5, 164.2, 159.5, 136.2, 134.5, 131.6, 130.2, 130.2, 129.2, 129.2, 127.5, 126.7, 125.9, 124.4, 124.3, 123.9, 123.9, 122.8, 122, 119.9, 114.6,

114.1, 114.1, 55.1; MS, m/z: 459.91 (M^+). Anal. calcd. for $C_{25}H_{18}ClN_3O_2S$: C, 65.28; H, 3.94; N, 9.14; S, 6.97; found: C, 65.22; H, 3.92; N, 9.10; S, 6.93%.

(3-Chloro-1-benzothiophen-2-yl)-5-(4-nitrobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (6c): Yield 55%; mp 312-315 °C; IR ν (cm^{-1}): 3273 (N-H), 1653 (C=O), 1600 (C=N); 1H -NMR δ (ppm): 8.99 (s, 1H, NH), 8.14-7.69 (m, 14H, Ar-CH and C=CH); ^{13}C -NMR δ (ppm): 165.5, 164.2, 147.1, 141.2, 136.2, 131.6, 129.2, 129.2, 129.0, 129.0, 126.7, 125.9, 124.4, 124.3, 123.9, 123.9, 123.8, 123.8, 122.8, 122.8, 122, 119.9, 114.2; MS, m/z: 474.90 (M^+). Anal. calcd. for $C_{24}H_{15}ClN_4O_3S$: C, 60.70; H, 3.18; N, 11.80; S, 6.75; found: C, 60.68; H, 3.14; N, 11.78; S, 6.74%.

(3-Chloro-1-benzothiophen-2-yl)-5-(4-chlorobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (6d): Yield 63%; mp 265-267 °C; IR ν (cm^{-1}): 3270 (N-H), 1649 (C=O), 1612 (C=N); 1H -NMR δ (ppm): 9.13 (s, 1H, NH), 8.09-7.68 (m, 14H, Ar-CH and C=CH); ^{13}C -NMR δ (ppm): 165.1, 164.7, 136.1, 134.1, 133.3, 131.6, 133.5, 129.2, 129.2, 129.0, 129.0, 128.7, 128.7, 126.7, 125.9, 124.4, 124.3, 123.9, 123.9, 122.8, 122.8, 122, 119.9, 114.2; MS, m/z: 464.36 (M^+). Anal. calcd. for $C_{24}H_{15}Cl_2N_3OS$: C, 62.08; H, 3.26; N, 9.05; S, 6.91; found: C, 62.03; H, 3.23; N, 9.01; S, 6.89%.

Benzylidene-3-(3-chloro-1-benzothiophen-2-yl)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5H)-one (6e): Yield 58%; mp 299-302 °C; IR ν (cm^{-1}): 3278 (N-H), 1647 (C=O), 1605 (C=N); 1H -NMR δ (ppm): 9.21 (s, 1H, NH), 8.34-7.69 (m, 14H, Ar-CH and C=CH); ^{13}C -NMR δ (ppm): 165.9, 164.8, 157.1, 135.2, 134.5, 131.8, 131.6, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 116.0, 116.3, 114.2; MS, m/z: 447.90 (M^+). Anal. calcd. for $C_{24}H_{15}ClFN_3OS$: C, 64.36; H, 3.38; N, 9.38; S, 7.16; found: C, 64.32; H, 3.35; N, 9.34; S, 7.12%.

(3-Chlorobenzothiophen-2-yl)-2-(4-fluorophenyl)-5-(4-methoxybenzylidene)-1,2-dihydro-1,2,4-triazin-6(5H)-one (6f): Yield 49%; mp 319-321 °C; IR ν (cm^{-1}): 3275 (N-H), 1660 (C=O), 1603 (C=N); 1H -NMR δ (ppm): 9.31 (s, 1H, NH), 8.33-8.03 (m, 13H, Ar-CH and C=CH), 3.69 (s, 3H, OCH₃); ^{13}C -NMR δ (ppm): 165.2, 164.1, 159.7, 157.7, 134.5, 131.8, 131.6, 130.2, 130.2, 127.5, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 116.0, 116.0, 114.6, 114.1, 114.1, 55.5; MS, m/z: 477.90 (M^+). Anal. calcd. for $C_{25}H_{17}ClFN_3O_2S$: C, 62.83; H, 3.59; N, 8.79; S, 6.71; found: C, 62.80; H, 3.55; N, 8.75; S, 6.69%.

(3-Chlorobenzothiophen-2-yl)-2-(4-fluorophenyl)-5-(4-nitrobenzylidene)-1,2-dihydro-1,2,4-triazin-6(5H)-

one (6g): Yield 51%; mp 321-323 °C; IR ν (cm⁻¹): 3281 (N-H), 1661 (C=O), 1604 (C=N); ¹H-NMR δ (ppm): 9.21 (s, 1H, NH), 8.21-7.59 (m, 13H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 165.2, 164.8, 157.7, 147.1, 141.3, 134.5, 131.8, 131.6, 129.0, 129.0, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 123.8, 123.8, 122.8, 122, 119.9, 116.2, 116.2, 114.2; MS, m/z: 492.90 (M⁺). Anal. calcd. for C₂₄H₁₄ClFN₄O₃S: C, 58.48; H, 2.86; N, 11.37; S, 6.51; found: C, 58.44; H, 2.83; N, 11.32; S, 6.49%.

(3-Chlorobenzob[thiophen-2-yl]-5-(4-chlorobenzylidene)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5H)-one (6h): Yield 57%; mp 309-311 °C; IR ν (cm⁻¹): 3282 (N-H), 1654 (C=O), 1605 (C=N); ¹H-NMR δ (ppm): 9.09 (s, 1H, NH), 8.19-7.37 (m, 13H, Ar-CH and C=CH); ¹³C-NMR δ (ppm): 165.3, 164.3, 157.2, 147.5, 141.3, 134.5, 131.8, 131.6, 129.0, 129.0, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 123.8, 123.8, 122.8, 122, 119.9, 116.3, 116.3, 114.4; MS, m/z: 482.35 (M⁺). Anal. calcd. for C₂₄H₁₄Cl₂FN₃OS: C, 59.76; H, 2.93; N, 8.71; S, 6.65; found: C, 59.72; H, 2.90; N, 8.68; S, 6.60%.

General procedure for synthesis of compounds 7a-h

Exemplary detail for 1-acetyl-5-benzylidene-3-(3-chloro-1-benzob[thiophen-2-yl]-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (7a): Compound **6a** (4.29 g, 0.01 mol) was treated with acetyl chloride (0.78 g, 0.70 mL, 0.01 mol) in glacial acetic acid (10 mL) was refluxed for 2 h at 45 °C. The reaction mixture was left to cool down to room temperature and the resulting precipitate was filtered off, washed several times with light petroleum ether, dried and then recrystallized from 1,4-dioxane. Purification by column chromatography [silica-gel, petroleum ether/ethyl acetate (95:05)] yielded pure **7a**. Compounds **7b-h** were prepared in similar methodology.

Yield 53%; mp 365-367 °C; IR ν (cm⁻¹): 1648 (C=O), 1603 (C=N); ¹H-NMR δ (ppm): 8.41-7.39 (m, 15H, Ar-CH and C=CH), 2.42 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 174.5, 164.3, 163.4, 136.2, 135.2, 134.5, 131.6, 129.2, 129.2, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 125.9, 124.4, 124.3, 123.9, 123.9, 122.8, 122.8, 122, 119.9, 114.3, 21.8; MS, m/z: 471.90 (M⁺). Anal. calcd. for C₂₆H₁₈ClN₃O₂S: C, 66.17; H, 3.84; N, 8.90; S, 6.79; found: C, 66.12; H, 3.80; N, 8.88; S, 6.75%.

Acetyl-3-(3-chloro-1-benzothiophen-2-yl)-5-(4-Methoxybenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (7b): Yield 49%; mp 373-375 °C; IR ν (cm⁻¹): 1652 (C=O), 1604 (C=N); ¹H-NMR δ (ppm): 8.09-7.38 (m, 14H, Ar-CH and C=CH), 3.69 (s, 3H, OCH₃), 2.45 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 174.8, 164.2, 163.9, 159.8, 136.2,

134.5, 131.6, 130.2, 130.2, 129.2, 129.2, 127.5, 126.7, 125.9, 124.4, 123.9, 123.9, 124.3, 122.8, 122.8, 122.3, 119.9, 114.6, 114.2, 114.1, 55.2, 21.6; MS, m/z: 501.98 (M⁺). Anal. calcd. for C₂₇H₂₀ClN₃O₃S: C, 64.60; H, 4.02; N, 8.37; S, 6.39; found: C, 64.57; H, 4.00; N, 8.33; S, 6.35%.

Acetyl-3-(3-chloro-1-benzothiophen-2-yl)-5-(4-nitrobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (7c): Yield 47%; mp 319-321 °C; IR ν (cm⁻¹): 1653 (C=O), 1606 (C=N); ¹H-NMR δ (ppm): 8.21-7.44 (m, 14H, Ar-CH and C=CH), 2.49 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 174.8, 164.3, 163.9, 147.1, 141.3, 136.2, 134.5, 131.6, 129.2, 129.2, 129.0, 129.0, 126.7, 125.9, 124.4, 124.3, 123.8, 123.7, 123.7, 123.8, 122.8, 122.8, 122.4, 119.9, 114.6, 21.1; MS, m/z: 516.95 (M⁺). Anal. calcd. for C₂₆H₁₇ClN₄O₄S: C, 60.41; H, 3.31; N, 10.84; S, 6.20; found: C, 60.35; H, 3.25; N, 10.80; S, 6.16%.

Acetyl-3-(3-chloro-1-benzothiophen-2-yl)-5-(4-chlorobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (7d): Yield 49%; mp 345-347 °C; IR ν (cm⁻¹): 1647 (C=O), 1607 (C=N); ¹H-NMR δ (ppm): 8.39-8.01 (m, 14H, Ar-CH and C=CH), 2.38 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 174.5, 164.4, 163.9, 136.2, 134.5, 133.5, 133.3, 131.6, 129.2, 129.2, 129.0, 129.0, 128.7, 128.7, 126.7, 125.9, 124.4, 124.3, 123.9, 123.9, 122.8, 122.8, 122, 119.9, 114.3, 21.8; MS, m/z: 506.40 (M⁺). Anal. calcd. for C₂₆H₁₇Cl₂N₃O₂S: C, 61.67; H, 3.38; N, 8.30; S, 6.33; found: C, 61.63; H, 3.35; N, 8.26; S, 6.30%.

Acetyl-5-benzylidene-3-(3-chloro-1-benzothiophen-2-yl)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5H)-one (7e): Yield 52%; mp 330-332 °C; IR ν (cm⁻¹): 1651 (C=O), 1598 (C=N); ¹H-NMR δ (ppm): 8.48-8.12 (m, 14H, Ar-CH and C=CH), 2.35 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 174.7, 164.6, 163.9, 157.7, 135.2, 134.5, 131.8, 131.6, 128.6, 128.6, 128.5, 128.5, 127.9, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 116.0, 116.0, 114.6, 21.5; MS, m/z: 489.92 (M⁺). Anal. calcd. for C₂₆H₁₇ClFN₃O₂S: C, 63.74; H, 3.50; N, 8.58; S, 6.54; found: C, 63.70; H, 3.48; N, 8.54; S, 6.51%.

Acetyl-3-(3-chlorobenzob[thiophen-2-yl]-2-(4-fluorophenyl)-5-(4-methoxybenzylidene)-1,2-dihydro-1,2,4-triazin-6(5H)-one (7f): Yield 51%; mp 335-337 °C; IR ν (cm⁻¹): 1650 (C=O), 1596 (C=N); ¹H-NMR δ (ppm): 8.09-7.87 (m, 13H, Ar-CH and C=CH), 3.73 (s, 3H, OCH₃), 2.48 (s, 3H, CH₃); ¹³C-NMR δ (ppm): 174.5, 164.0, 163.7, 159.3, 157.7, 134.5, 131.8, 131.6, 130.2, 130.2, 127.5, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 116.0, 116.0, 114.6, 114.1, 114.1, 55.6, 21.8; MS, m/z: 519.94 (M⁺). Anal. calcd. for C₂₇H₁₉ClFN₃O₃S: C, 62.37; H, 3.68; N, 8.08; S, 6.17; found: C, 62.35; H, 3.65; N, 8.02; S, 6.13%.

Acetyl-3-(3-chlorobenzothiofen-2-yl)-2-(4-fluorophenyl)-5-(4-nitrobenzylidene)-1,2-dihydro-1,2,4-triazin-6(5H)-one (7g): Yield 58%; mp 321-323 °C; IR ν (cm^{-1}): 1644 (C=O), 1589 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.03-7.29 (m, 13H, Ar-CH and C=CH), 2.47 (s, 3H, CH₃); $^{13}\text{C-NMR}$ δ (ppm): 174.6, 164.9, 163.9, 157.7, 147.1, 141.3, 134.5, 131.8, 131.6, 129.0, 129.0, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 123.5, 123.5, 122.8, 122, 119.9, 116.3, 116.3, 114.6, 21.6; MS, m/z: 534.94 (M⁺). Anal. calcd. for C₂₆H₁₆ClFN₄O₄S: C, 58.38; H, 3.01; N, 10.47; S, 5.99; found: C, 58.34; H, 3.00; N, 10.42; S, 5.93%.

1-Acetyl-3-(3-chlorobenzothiofen-2-yl)-5-(4-chlorobenzylidene)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5H)-one (7h): Yield 56%; mp 312-314 °C; IR ν (cm^{-1}): 1641 (C=O), 1607 (C=N); $^1\text{H-NMR}$ δ (ppm): 8.10-7.38 (m, 13H, Ar-CH and C=CH), 2.44 (s, 3H, CH₃); $^{13}\text{C-NMR}$ δ (ppm): 174.1, 164.8, 163.7, 157.7, 134.5, 133.5, 133.3, 131.8, 131.6, 129.0, 129.0, 128.7, 128.7, 126.7, 126.7, 126.7, 125.9, 124.4, 124.3, 122.8, 122, 119.9, 116.2, 116.2, 114.3, 21.5; MS, m/z: 524.39 (M⁺). Anal. calcd. for C₂₆H₁₆Cl₂FN₃O₂S: C, 59.55; H, 3.08; N, 8.01; S, 6.11; found: C, 59.50; H, 3.04; N, 8.00; S, 6.05%.

CONCLUSION

In conclusion, a new series of benzothiophene containing oxazolone, imidazolones and triazines derivatives were synthesized, fully characterized and evaluated for their antibacterial and antifungal activities. The newly synthesized heterocyclics exhibited moderate antibacterial activity against *S. aureus*, *B. subtilis*, *P. aeruginosa* and *E. coli* and significant antifungal activity against *C. albicans*, *C. parvula* and *A. niger*. It can be concluded that these classes of compounds certainly holds great promise as active leads in medicinal chemistry. A further study to acquire more information concerning pharmacological activity is in progress.

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