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

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3-Chloro-1-benzothiophene-2-carbonyl chloride **1** was reacted with glycine in acetone to give 3-chloro-1-benzothiophen-2-yl-carbonylaminoacetic acid **2**. Various aldehydes on treatment with compound **2** in acetic anhydride to gave 1,3-oxazol-5-ones **3a-d**. These oxazolones was treated with aromatic amines or hydrazides to get various imidazol-4-ones **4a-t** or **5a-l**. Oxazolones **3a-d** was also treated with aromatic hydrazines, expansion of five member 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 had been screened for antibacterial activity.

Key Words : Benzothiophene, Imidazol-5-ones, 1,2,4-Triazine-6-ones, Antimicrobial activity

Introduction

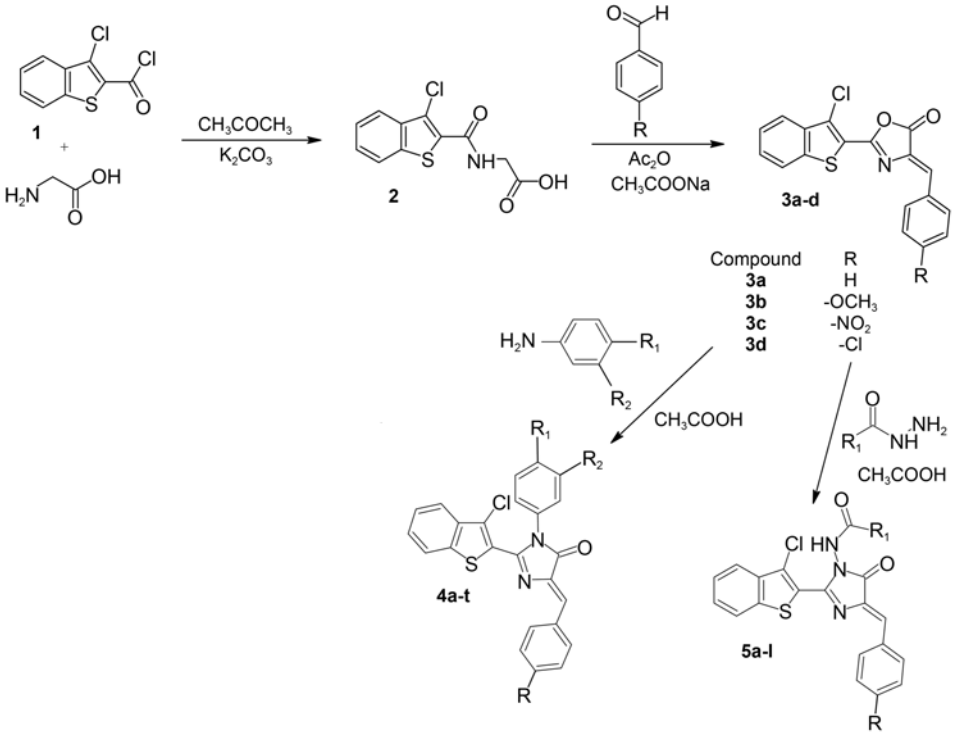
The exploitation of a simple molecule with different functionalities for the synthesis of heterocycles is a worthwhile contribution in the chemistry of heterocycles. The nitrogen and sulfur heterocyclic system families are very interesting because of their physico-chemical properties with relevance to 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*-inflammatory[5] and potent neuroprotective[6] agents. The benzothiophene nucleus is associated with diverse pharmacological activities such as nervous system depressing,[7] analgesic,[8] herbicidal,[9] muscle relaxant[10] and tranquilizing[11] 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, anti-inflammatory, analgesic and antitumor activities.[12-16] We were interested in the synthesis of benzothiophene coupled heterocycles at 2-position and in exploration of their biological investigation. In this manuscript, we report the preparation of oxazolones, imidazolones and triazines from benzothiophene moiety.

Results and Discussion

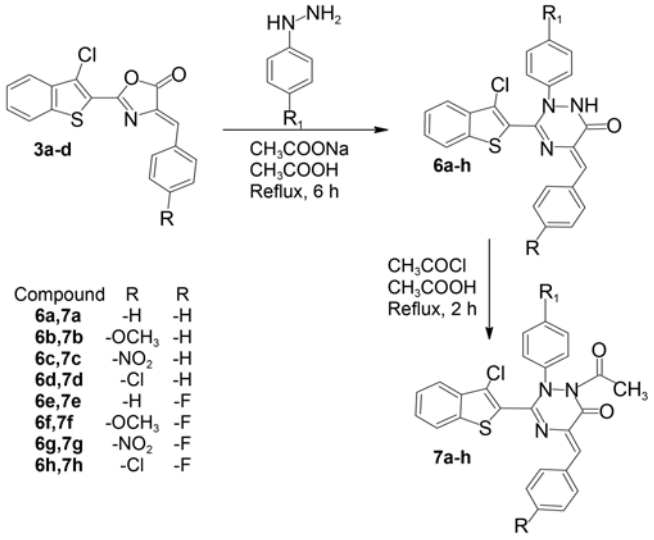
3-Chloro-1-benzothiophene-2-carbonyl chloride[17] **1** was treated with glycine in dry acetone in the presence of K_2CO_3 to get acylated product **2**. ^{1}H-NMR spectrum of compound **2** exhibited signals at 12.79, 8.95 and 3.28 δ ppm due to -OH, -CONH and -CH_2 protons and a multiplet in between 7.98 and 7.85 δ 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 ^{1}H-NMR spectrum and molecular ion peak at *m/z* 339.79 in its mass spectrum was confirmed for its formation of compound **3a**.

Compound **3a** was treated with 3-chloro-4-fluoroaniline in glacial acetic acid to get imidazol-4-one **4a**. Compound **4a** exhibited peaks at 1650 and 1593 cm^{-1} due to C=O and C=N stretching absorption frequencies, respectively. ^{1}H-NMR spectrum of compound **4a** exhibited a multiplet in between

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	-	-	-	-
4t	-Cl	-NO_2	-	-	-	-



Scheme 1. Synthesis of oxazol-5-ones **3a-d**, imidazol-4-ones **4a-t** and **5a-l**.



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

8.01 to 7.71 δ ppm due to thirteen aromatic, and C=CH protons and molecular ion peak at *m/z* 467.34 in its mass spectrum which confirmed for its formation. Similarly, compounds **4b-t** was prepared. Oxazolones **3a-d** was refluxed with hydrized in acetic acid to afforded 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}H-NMR spectrum of compound **5a** which exhibited a multiplet in the region 8.19-7.34 δ 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.

Oxazalones **3a-d** on treatment 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-triazin-6-ones **6a-h**. Singlet at 9.12 δ ppm due to NH proton of compound **6a** in its ^{1}H-NMR spectrum. Acetylation of compounds **6a-h** with acetyl chloride resulted in the formation of compounds **7a-h**. Singlet at 2.44 δ ppm due to three protons of -CH_3 group due to the formation of compound **7a**.

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, *Pseudomonas 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 μg/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 micro-organisms. The solution of each test compound (0.1 mL) was added to the cups and petri dishes and were 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

Table 1. Antibacterial activity of the tested compounds

Compound	Zone of inhibition (mm)			
	Gram positive bacteria		Gram negative bacteria	
	S. aureus	*B. subtilis*	*P. aeruginosa*	*E. coli*
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

Table 2. Antifungal activity of the tested compounds

Compound	Zone of inhibition (mm)		
	C. albicans	*C. pannical*	*A. niger*
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

each compound was measured in mm. As shown in the Table 1, the tested compounds showed slightly to moderate antibacterial activity compared to standard drugs against each microorganism.

Antifungal Activity. The antifungal activity of the synthesized compounds was tested against three different fungi, *i.e. Candida albicans*, *Crysosporium 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. ^{1}H-NMR and ^{13}C-NMR were obtained in DMSO-d_6 at 400 MHz for ^{1}H nuclei and 100 MHz for ^{13}C 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 240 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-carbonyl-chloride (1). Compound **1** was prepared according to the literature procedure,[17] mp 112-114 ºC (Lit. mp 110-112 ºC).

Preparation of 2-(3-Chlorobenzo[*b*]thiophene-2-carboxamido)aceticacid (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 K_2CO_3 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 ºC; IR ν (cm^{-1}): 3320 (OH), 3130 (NH), 1650 (C=O); ^{1}H-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,

CH_2); ^{13}C-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 $C_{11}H_8ClNO_3S$: 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(4*H*)-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 ºC; IR ν (cm^{-1}): 1642 (C=O), 1595 (C=N); ^{1}H-NMR δ (ppm): 8.12-7.22 (m, 10H, Ar-CH and C=CH); ^{13}C-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 $C_{18}H_{10}ClNO_2S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-methoxybenzylidene)oxazol-5(4*H*)-one (3b): Yield 70%; mp 258-260 ºC; IR ν (cm^{-1}): 1640 (C=O), 1597 (C=N); ^{1}H-NMR δ (ppm): 7.98-6.94 (m, 9H, Ar-CH and C=CH), 3.79 (s, 3H, OCH_3); ^{13}C-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 $C_{19}H_{12}ClNO_3S$: 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-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-nitrobenzylidene)oxazol-5(4*H*)-one (3c): Yield 65%; mp 262-264 ºC; IR ν (cm^{-1}): 1645 (C=O), 1607 (C=N); ^{1}H-NMR δ (ppm): 7.92-6.91 (m, 9H, Ar-CH and C=CH); ^{13}C-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 $C_{18}H_9ClN_2O_4S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)oxazol-5(4*H*)-one (3d). Yield 63%; mp 265-267 ºC; IR ν (cm^{-1}): 1635 (C=O), 1610 (C=N); ^{1}H-NMR δ (ppm): 8.02-7.12 (m, 9H, Ar-CH and C=CH); ^{13}C-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 $C_{18}H_9Cl_2NO_2S$: 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-chlorobenzo[b]thiophen-2-yl)-1*H*-imidazol-5(4*H*)-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 ºC; IR ν (cm^{-1}): 1650 (C=O), 1593 (C=N); ^{1}H-NMR δ (ppm): 8.01-7.71 (m, 13H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{13}Cl_2FN_2OS$: C, 61.68; H, 2.80; N, 5.99; S, 6.86; found: C, 61.65; H, 2.77; N, 5.94; H, 6.81%.

1-(3-Chloro-4-fluorophenyl)-2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-(4-methoxybenzylidene)-1*H*-imidazol-5(4*H*)-one (4b): Yield 59%; mp 269-271 ºC; IR ν (cm^{-1}): 1651 (C=O), 1595 (C=N), 1070 (C-F); ^{1}H-NMR δ (ppm): 8.09-7.45 (m, 12H, Ar-CH and C=CH), 3.73 (s, 3H, OCH_3); ^{13}C-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 $C_{25}H_{15}Cl_2FN_2O_2S$: 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%.

1-(3-Chloro-4-fluorophenyl)-2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-(4-nitrobenzylidene)-1*H*-imidazol-5(4*H*)-one (4c): Yield 61%; mp 266-268 ºC; IR ν (cm^{-1}): 1648 (C=O), 1591 (C=N); ^{1}H-NMR δ (ppm): 7.99-6.98 (m, 12H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{12}Cl_2FN_3O_3S$: 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%.

1-(3-Chloro-4-fluorophenyl)-2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)-1*H*-imidazol-5(4*H*)-one (4d): Yield 62%; mp 259-261 ºC; IR ν (cm^{-1}): 1649 (C=O), 1602 (C=N), 1070 (C-Cl); ^{1}H-NMR δ (ppm): 8.10-7.01 (m, 12H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{12}Cl_3FN_2OS$: 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%.

4-Benzylidene-2-(3-chlorobenzo[*b*]thiophen-2-yl)-1-(4-fluorophenyl)-1*H*-imidazol-5(4*H*)-one (4e): Yield 68%; mp 258-260 ºC; IR ν (cm^{-1}): 1653 (C=O), 1599 (C=N); ^{1}H-NMR δ (ppm): 8.21-7.72 (m, 14H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{14}ClFN_2OS$: 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%.

2-(3-Chlorobenzo[b]thiophen-2-yl)-1-(4-fluorophenyl)-4-(4-methoxybenzylidene)-1*H*-imidazol-5(4*H*)-one (4f):

Yield 67%; mp 302-304 ºC; IR ν (cm^{-1}): 1653 (C=O), 1602 (C=N); ^{1}H-NMR δ (ppm): 8.14-6.99 (m, 13H, Ar-CH and C=CH), 3.81 (s, 3H, OCH_3); ^{13}C-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 $C_{25}H_{16}ClFN_2O_2S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-1-(4-fluorophenyl)-4-(4-nitrobenzylidene)-1*H*-imidazol-5(4*H*)-one (4g): Yield 71%; mp 291-293 ºC; IR ν (cm^{-1}): 1643 (C=O), 1603 (C=N); ^{1}H-NMR δ (ppm): 8.09-7.03 (m, 13H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{13}ClFN_3O_3S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)-1-(4-fluorophenyl)-1*H*-imidazol-5(4*H*)-one (4h): Yield 72%; mp 297-299 ºC; IR ν (cm^{-1}): 1644 (C=O), 1598 (C=N); ^{1}H-NMR δ (ppm): 8.12-7.12 (m, 13H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{13}Cl_2FN_2OS$: 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%.

1-(4-Acetylphenyl)-4-benzylidene-2-(3-chlorobenzo[*b*]-thiophen-2-yl)-1*H*-imidazol-5(4*H*)-one (4i): Yield 69%; mp 303-305 ºC; IR ν (cm^{-1}): 1646 (C=O), 1589 (C=N); ^{1}H-NMR δ (ppm): 8.21-6.99 (m, 14H, Ar-CH and C=CH), 2.50 (s, 3H, $COCH_3$); ^{13}C-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 $C_{26}H_{17}ClN_2O_2S$: 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%.

1-(4-Acetylphenyl)-2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-(4-methoxybenzylidene)-1*H*-imidazol-5(4*H*)-one (4j): Yield 67%; mp 320-322 ºC; IR ν (cm^{-1}): 1648 (C=O), 1597 (C=N); ^{1}H-NMR δ (ppm): 8.24-7.39 (m, 13H, Ar-CH and C=CH), 3.85 (s, 3H, OCH_3), 2.50 (s, 3H, $COCH_3$); ^{13}C-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 $C_{27}H_{19}ClN_2O_3S$: 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%.

1-(4-Acetylphenyl)-2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-(4-nitrobenzylidene)-1*H*-imidazol-5(4*H*)-one (4k): Yield 64%; mp 295-297 ºC; IR ν (cm^{-1}): 1646 (C=O), 1599 (C=N); ^{1}H-NMR δ (ppm): 8.13-7.69 (m, 13H, Ar-CH and C=CH), 2.69 (s, 3H, $COCH_3$); ^{13}C-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, 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 $C_{26}H_{16}ClN_3O_4S$: 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%.

1-(4-Acetylphenyl)-2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)-1*H*-imidazol-5(4*H*)-one (4l): Yield 63%; mp 283-285 ºC; IR ν (cm^{-1}): 1649 (C=O), 1605 (C=N); ^{1}H-NMR δ (ppm): 7.29-8.03 (m, 13H, Ar-CH and C=CH), 2.62 (s, 3H, OCH_3); ^{13}C-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 $C_{26}H_{16}Cl_2N_2O_2S$: 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%.

4-Benzylidene-2-(3-chlorobenzo[b]thiophen-2-yl)-1-*p*-tolyl-1*H*-imidazol-5(4*H*)-one (4m): Yield 55%; mp 288-290 ºC; IR ν (cm^{-1}): 1653 (C=O), 1607 (C=N); ^{1}H-NMR δ (ppm): 8.12-6.99 (m, 14H, Ar-CH and C=CH), 2.34 (s, 3H, CH_3); ^{13}C-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 $C_{25}H_{17}ClN_2OS$: 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%.

2-(3-Chlorobenzo[b]thiophen-2-yl)-4-(4-methoxybenzylidene)-1-*p*-tolyl-1*H*-imidazol-5(4*H*)-one (4n): Yield 59%; mp 297-299 ºC; IR ν (cm^{-1}): 1652 (C=O), 1595 (C=N); ^{1}H-NMR δ (ppm): 8.27-7.64 (m, 13H, Ar-CH and C=CH), 3.79 (s, 3H, OCH_3), 2.31 (s, 3H, CH_3); ^{13}C-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 $C_{26}H_{19}ClN_2O_2S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-nitrobenzylidene)-1-*p*-tolyl-1H-imidazol-5(4*H*)-one (4o): Yield 57%; mp 289-291 ºC; IR ν (cm^{-1}): 1654 (C=O), 1603 (C=N); ^{1}H-NMR δ (ppm): 8.09-7.69 (m, 13H, Ar-CH and C=CH), 2.32 (s, 3H, CH_3); ^{13}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 $C_{25}H_{16}ClN_3O_3S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)-1-*p*-tolyl-1H-imidazol-5(4*H*)-one (4p): Yield 69%; mp 321-323 ºC; IR ν (cm^{-1}): 1639 (C=O), 1604 (C=N); ^{1}H-NMR δ (ppm): 8.19-7.54 (m, 13H, Ar-CH and C=CH), 2.41 (s, 3H, CH_3); ^{13}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 $C_{25}H_{16}Cl_2N_2OS$: 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%.

4-Benzylidene-2-(3-chlorobenzo[*b*]thiophen-2-yl)-1-(4-nitrophenyl)-1*H*-imidazol-5(4*H*)-one (4q): Yield 61%; mp 310-312 ºC; IR ν (cm^{-1}): 1642 (C=O), 1597 (C=N); ^{1}H-

NMR δ (ppm): 8.28-7.49 (m, 14H, Ar-CH and C=CH); ^{13}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 $C_{24}H_{14}ClFN_3O_3S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-methoxybenzylidene)-1-(4-nitrophenyl)-1*H*-imidazol-5(4*H*)-one (4r): Yield 72%; mp 312-314 ºC; IR ν (cm^{-1}): 1644 (C=O), 1593 (C=N); ^{1}H-NMR δ (ppm): 8.21-7.32 (m, 13H, Ar-CH and C=CH), 3.85 (s, 3H, OCH_3); ^{13}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 $C_{25}H_{16}ClFN_3O_4S$: 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%.

2-(3-Chlorobenzo[b]thiophen-2-yl)-4-(4-nitrobenzylidene)-1-(4-nitrophenyl)-1*H*-imidazol-5(4*H*)-one (4s): Yield 70%; mp 309-311 ºC; IR ν (cm^{-1}): 1645 (C=O), 1604 (C=N); ^{1}H-NMR δ (ppm): 8.32-7.03 (m, 13H, Ar-CH and C=CH); ^{13}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 $C_{24}H_{13}ClN_4O_5S$: 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%.

2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-(4-chlorobenzylidene)-1-(4-nitrophenyl)-1*H*-imidazol-5(4*H*)-one (4t): Yield 60%; mp 279-281 ºC; IR ν (cm^{-1}): 1647 (C=O), 1597 (C=N); ^{1}H-NMR δ (ppm): 8.12-7.91 (m, 13H, Ar-CH and C=CH); ^{13}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 $C_{24}H_{13}Cl_2N_3O_3S$: 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-l.

Exemplary Detail for 4-benzylidene-2-(3-chloro-1-benzothiophen-2-yl)-5-oxo-4,5-dihydro-1*H*-imidazol-1-yl]-3-chlorobenzothiophene-2-carboxamide (5a): A mixture of compound **3a** (3.39 g, 0.01 mol) and 3-chloro-benzothiophene-2-carbohydrizide (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 ºC; IR ν (cm^{-1}): 3262 (N-H), 1642 (C=O), 1591 (C=N); ^{1}H-NMR δ (ppm): 13.70 (s, 1H, NH), 8.19-7.34 (m, 14H, Ar-CH and C=CH); ^{13}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 $C_{27}H_{15}Cl_2N_3O_2S_2$: 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%.

3-Chloro-*N*-[2-(3-chloro-1-benzo[*b*]thiophen-2-yl)-4-(4-methoxybenzylidene)-5-oxo-4,5-dihydro-1*H*-imidazol-1-yl]benzo[b]thiophene-2-carboxamide (5b): Yield 55%; mp 319-321 ºC; IR ν (cm^{-1}): 3263 (N-H), 1644 (C=O), 1589 (C=N); ^{1}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}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 $C_{28}H_{17}Cl_2N_3O_3S_2$: 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%.

3-Chloro-*N*-[2-(3-chloro-1-benzo[*b*]thiophen-2-yl)-4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1*H*-imidazol-1-yl]benzo[*b*]thiophene-2-carboxamide (5c): Yield 63%; mp 296-298 ºC; IR ν (cm^{-1}): 3265 (N-H), 1643 (C=O), 1598 (C=N); ^{1}H-NMR δ (ppm): 13.45 (s, 1H, NH), 8.88-7.09 (m, 13H, Ar-CH and C=CH); ^{13}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 $C_{27}H_{14}Cl_2N_4O_4S_2$: 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%.

3-Chloro-*N*-[2-(3-chloro-1-benzothiophen-2-yl)-4-(4-chlorobenzylidene)-5-oxo-4,5-dihydro-1*H*-imidazol-1-yl]benzothiophene-2-carboxamide (5d): Yield 60%; mp 297-299 ºC; IR ν (cm^{-1}): 3269 (N-H), 1664 (C=O), 1601 (C=N); ^{1}H-NMR δ (ppm): 13.09 (s, 1H, NH), 8.32-7.43 (m, 13H, Ar-CH and C=CH); ^{13}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 $C_{27}H_{14}Cl_3N_3O_2S_2$: 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-1*H*-imidazol-1-yl]benzo[*b*]furan-2-carboxamide (5e):** Yield 55%; mp 309-311 ºC; IR ν (cm^{-1}): 3273 (N-H), 1662 (C=O), 1608 (C=N); ^{1}H-NMR δ (ppm): 13.41 (s, 1H, NH), 8.13-7.79 (m, 14H, Ar-CH and C=CH); ^{13}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 $C_{27}H_{16}ClN_3O_3S$: 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-1*H*-imidazol-1-yl]benzofuran-2-carboxamide (5f):** Yield 56%; mp 279-291 ºC; IR ν (cm^{-1}): 3273 (N-H), 1649 (C=O), 1599 (C=N); ^{1}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}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 $C_{28}H_{18}ClN_3O_4S$: 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-1*H*-imidazol-1-yl]benzo[*b*]benzo[*b*]furan-2-carboxamide (5g):** Yield 51%; mp 291-293 ºC; IR ν (cm^{-1}): 3272 (N-H), 1648 (C=O), 1591 (C=N); ^{1}H-NMR δ (ppm): 13.44 (s, 1H, NH), 8.32-7.69 (m, 13H, Ar-CH and C=CH); ^{13}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 $C_{27}H_{15}ClN_4O_5S$: 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-1*H*-imidazol-1-yl]benzo[*b*]furan-2-carboxamide (5h):** Yield 53%; mp 296-298 ºC; IR ν (cm^{-1}): 3279 (N-H), 1663 (C=O), 1596 (C=N); ^{1}H-NMR δ (ppm): 13.49 (s, 1H, NH), 8.17-7.79 (m, 13H, Ar-CH and C=CH); ^{13}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 $C_{27}H_{15}Cl_2N_3O_3S$: 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-1*H*-imidazol-1-yl]pyridine-4-carboxamide (5i):** Yield 59%; mp 289-291 ºC; IR ν (cm^{-1}): 3268 (N-H), 1666 (C=O), 1593 (C=N); ^{1}H-NMR δ (ppm): 13.47 (s, 1H, NH), 8.09-7.29 (m, 14H, Ar-CH and C=CH); ^{13}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 $C_{24}H_{15}ClN_4O_2S$: 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-1*H*-imidazol-1-yl]pyridine-4-carboxamide (5j):** Yield 59%; mp 271-273 ºC; IR ν (cm^{-1}): 3270 (N-H), 1663 (C=O), 1557 (C=N); ^{1}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}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 for $C_{25}H_{17}ClN_4O_3S$: 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-1*H*-imidazol-1-yl]pyridine-4-carboxamide (5k):** Yield 67%; mp 271-273 ºC; IR ν (cm^{-1}): 3273 (N-H), 1655 (C=O), 1610 (C=N); ^{1}H-NMR δ (ppm): 13.68 (s, 1H, NH), 8.27-7.38 (m, 13H, Ar-CH and C=CH); ^{13}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-1*H*-imidazol-1-yl]pyridine-4-carboxamide (5l):** Yield 57%; mp 274-276 ºC; IR ν (cm^{-1}): 3277 (NH), 1668 (C=O), 1612 (C=N); ^{1}H-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 $C_{24}H_{14}Cl2N_4O_2S$: 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-benzo[*b*]thiophen-2-yl)-2-phenyl-2,5-dihydro-1,2,4-triazin-6(5*H*)-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 elutent to get pure compound **6a**. Compounds **6b-h** were prepared in similar manner.

Yield 55%; mp 230-232 ºC; IR ν (cm^{-1}): 3280 (N-H), 1653 (C=O), 1609 (C=N); ^{1}H-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-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(4-methoxybenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (6b): Yield 61%; mp 245-247 ºC; IR ν (cm^{-1}): 3285 (N-H), 1657 (C=O), 1607 (C=N); ^{1}H-NMR δ (ppm): 9.10 (s, 1H, NH), 8.44-7.76 (m, 14H, Ar-CH and C=CH), 3.68 (s, 3H, OCH_3); ^{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-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(4-nitrobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (6c): Yield 55%; mp 312-315 ºC; IR ν (cm^{-1}): 3273 (N-H), 1653 (C=O), 1600 (C=N); ^{1}H-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-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(4-chlorobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (6d): Yield 63%; mp 265-267 ºC; IR ν (cm^{-1}): 3270 (N-H), 1649 (C=O), 1612 (C=N); ^{1}H-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%.

5-Benzylidene-3-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (6e): Yield 58%; mp 299-302 ºC; IR ν (cm^{-1}): 3278 (N-H), 1647 (C=O), 1605 (C=N); ^{1}H-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-(3-Chlorobenzo[*b*]thiophen-2-yl)-2-(4-fluorophenyl)-5-(4-methoxybenzylidene)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (6f): Yield 49%; mp 319-321 ºC; IR ν (cm^{-1}): 3275 (N-H), 1660 (C=O), 1603 (C=N); ^{1}H-NMR δ (ppm): 9.31 (s, 1H, NH), 8.33-8.03 (m, 13H, Ar-CH and C=CH), 3.69 (s, 3H, OCH_3); ^{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-(3-Chlorobenzo[*b*]thiophen-2-yl)-2-(4-fluorophenyl)-5-(4-nitrobenzylidene)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (6g): Yield 51%; mp 321-323 ºC; IR ν (cm^{-1}): 3281 (N-H), 1661 (C=O), 1604 (C=N); ^{1}H-NMR δ (ppm): 9.21 (s, 1H, NH), 8.21-7.59 (m, 13H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{14}ClFN_4O_3S$: 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-(3-Chlorobenzo[*b*]thiophen-2-yl)-5-(4-chlorobenzylidene)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (6h): Yield 57%; mp 309-311 ºC; IR ν (cm^{-1}): 3282 (N-H), 1654 (C=O), 1605 (C=N); ^{1}H-NMR δ (ppm): 9.09 (s, 1H, NH), 8.19-7.37 (m, 13H, Ar-CH and C=CH); ^{13}C-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 $C_{24}H_{14}Cl_2FN_3OS$: 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-benzo[*b*]thiophen-2-yl)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-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 ºC. 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 ºC; IR ν (cm^{-1}): 1648 (C=O), 1603 (C=N); ^{1}H-NMR δ (ppm): 8.41-7.39 (m, 15H, Ar-CH and C=CH), 2.42 (s, 3H, CH_3); ^{13}C-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 $C_{26}H_{18}ClN_3O_2S$: 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%.

1-Acetyl-3-(3-chloro-1-benzothiophen-2-yl)-5-(4-Methoxybenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (7b): Yield 49%; mp 373-375 ºC; IR ν (cm^{-1}): 1652 (C=O), 1604 (C=N); ^{1}H-NMR δ (ppm): 8.09-7.38 (m, 14H, Ar-CH and C=CH), 3.69 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3); ^{13}C-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 $C_{27}H_{20}ClN_3O_3S$: 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%.

1-Acetyl-3-(3-chloro-1-benzothiophen-2-yl)-5-(4-nitrobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (7c): Yield 47%; mp 319-321 ºC; IR ν (cm^{-1}): 1653 (C=O), 1606 (C=N); ^{1}H-NMR δ (ppm): 8.21-7.44 (m, 14H, Ar-CH and C=CH), 2.49 (s, 3H, CH_3); ^{13}C-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 $C_{26}H_{17}ClN_4O_4S$: 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%.

1-Acetyl-3-(3-chloro-1-benzothiophen-2-yl)-5-(4-chlorobenzylidene)-2-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (7d): Yield 49%; mp 345-347 ºC; IR ν (cm^{-1}): 1647 (C=O), 1607 (C=N); ^{1}H-NMR δ (ppm): 8.39-8.01 (m, 14H, Ar-CH and C=CH), 2.38 (s, 3H, CH_3); ^{13}C-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 $C_{26}H_{17}Cl_2N_3O_2S$: 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%.

1-Acetyl-5-benzylidene-3-(3-chloro-1-benzothiophen-2-yl)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (7e): Yield 52%; mp 330-332 ºC; IR ν (cm^{-1}): 1651

(C=O), 1598 (C=N); ^{1}H-NMR δ (ppm): 8.48-8.12 (m, 14H, Ar-CH and C=CH), 2.35 (s, 3H, CH_3); ^{13}C-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 $C_{26}H_{17}ClFN_3O_2S$: 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%.

1-Acetyl-3-(3-chlorobenzo[*b*]thiophen-2-yl)-2-(4-fluorophenyl)-5-(4-methoxybenzylidene)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (7f): Yield 51%; mp 335-337 ºC; IR ν (cm^{-1}): 1650 (C=O), 1596 (C=N); ^{1}H-NMR δ (ppm): 8.09-7.87 (m, 13H, Ar-CH and C=CH), 3.73 (s, 3H, OCH_3), 2.48 (s, 3H, CH_3); ^{13}C-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 $C_{27}H_{19}ClFN_3O_3S$: 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%.

1-Acetyl-3-(3-chlorobenzo[*b*]thiophen-2-yl)-2-(4-fluorophenyl)-5-(4-nitrobenzylidene)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (7g): Yield 58%; mp 321-323 ºC; IR ν (cm^{-1}): 1644 (C=O), 1589 (C=N); ^{1}H-NMR δ (ppm): 8.03-7.29 (m, 13H, Ar-CH and C=CH), 2.47 (s, 3H, CH_3); ^{13}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 $C_{26}H_{16}ClFN_4O_4S$: 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-chlorobenzo[b]thiophen-2-yl)-5-(4-chlorobenzylidene)-2-(4-fluorophenyl)-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (7h): Yield 56%; mp 312-314 ºC; IR ν (cm^{-1}): 1641 (C=O), 1607 (C=N); ^{1}H-NMR δ (ppm): 8.10-7.38 (m, 13H, Ar-CH and C=CH), 2.44 (s, 3H, CH_3); ^{13}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 $C_{26}H_{16}Cl_2FN_3O_2S$: 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 modarate antibacterial activity against *S. aureus*, *B. subtilis*, *P. aeruginosa* and *E. coli* and significant antifungal activity against *C. albicans*, *C. pannical* and *A. niger*. It can be concluded that these classes of compounds certainly holds great promise towards good active leads in medicinal chemistry. A further study to acquire more information concerning pharmacological activity is in progress.

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