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Synthesis of 1,3,4-oxadiazole and imidazo[1,2-*a*]pyridine based molecular hybrids and their *in vitro* antituberculosis and cytotoxicity studies

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A library of novel 1,3,4-oxadiazole substituted imidazo[1,2-*a*]pyridine based molecular hybrids have been synthesized and evaluated against *Mycobacterium tuberculosis* H37Rv. Out of 59 compounds synthesized, ten compounds show activity in the range of 3.125-12.5 μM. Compound **8p** is found to be most active with MIC_{99} value of 3.125-6.25 μM. Further, these ten compounds have also been tested for their toxicity against THP-1 cell line and are found to be non-toxic with TC_{50} value in the range of (10 - >50 μM) concentration.

Keywords: 1,3,4-Oxadiazole, imidazo[1,2-*a*]pyridine, anti-mycobacterial activity, cytotoxicity studies

Tuberculosis (TB), a leading infectious airborne disease predominantly caused by *Mycobacterium tuberculosis*, is one of the major causes of death from a single infectious pathogen. It is well established that the morbidity and mortality rate of TB patient is relatively higher in HIV-infected individuals. As per 2017 WHO global TB report, TB caused 1.7 million deaths in 2016 which includes 0.4 million deaths among the people co-infected with HIV and approximately 10.4 million new clinical cases of TB were reported worldwide in 2016[1]. DOTS therapy is a complicated process, which requires a strict and 6-month lengthy regimen and it has suffered a huge setback due to the emergence of drug-resistant strains[2].

This situation has further aggravated due to ever increasing incident rates of multi drug-resistant (MDR), extensively drug-resistant (XDR) and totally drug-resistant (TDR) by *Mycobacterium tuberculosis*. There is an urgent need to identify novel drugs to control the spread of drug-resistant TB[3-6]. Heterocycles in general and imidazopyridine in particular has played a significant role in the field of drug developments[7-9]. Among these, imidazo[1,2-*a*]pyridine have potential biological applications such as anti-mycobacterial[10-12], anti-cancer[13,14], anti-viral[15], anti-microbial[16], and anti-HIV[17] activity. In addition, imidazopyridine derivative such as imidazo[1,2-*a*]pyridine amide has shown promising activity against MDR and XDR TB[18-21]. Recently, imidazo[1,2-*a*]pyridine based highly innovative drug molecule Q203 (Figure 1) has been reported to possess activity against both MDR and XDR TB[22] (Figure 1).

The 1,3,4-oxadiazoles is another class of heterocycle that has gained a lot of attention of medicinal chemist due to their wide range of biological activities[23,24], the most notable being antipyretic[25], analgesic and anti-inflammatory[26], antidepressant[27], antimicrobial and anti-HIV[28], anti-tubercular[29], antioxidant[30], central nervous system dpressant[31], anticonvulsive[32], antihypertensive[33], and anticancer activity[34], *etc*. In order to solve the menaces of drug resistance, a concept of molecular hybridization has gained importance in recent years[4, 6, 35]. The molecules developed using this concept are found to have more potency and effectiveness against resistant strains than the parent drugs[36].

Recently imidazo[1,2-*a*]pyridine was identified *via* High Throughput Screening (HTS) as a potent anti-tubercular molecule active against both replicating *Mtb* H37Rv and multi- and extensively drug-resistant (XDR) *Mtb* strains[12,18,22,37-39]. These efforts led to the identification of pre-clinical anti-TB candidate Q203 (Figure 1)[22].

Keeping these points in mind and as a part of our on-going work on the development of molecular hybrids[40-46], we designed new set of molecular hybrids having imidazo[1,2-*a*]pyridine and oxadiazole as

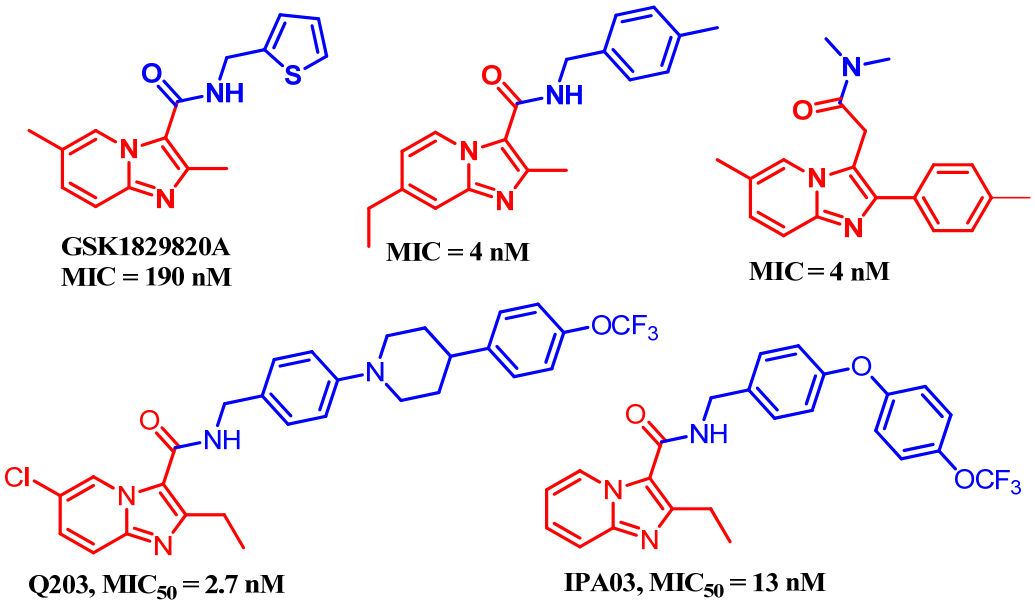


Figure 1 — Potent derivatives containing imidazo[1,2-*a*]pyridines scaffolds

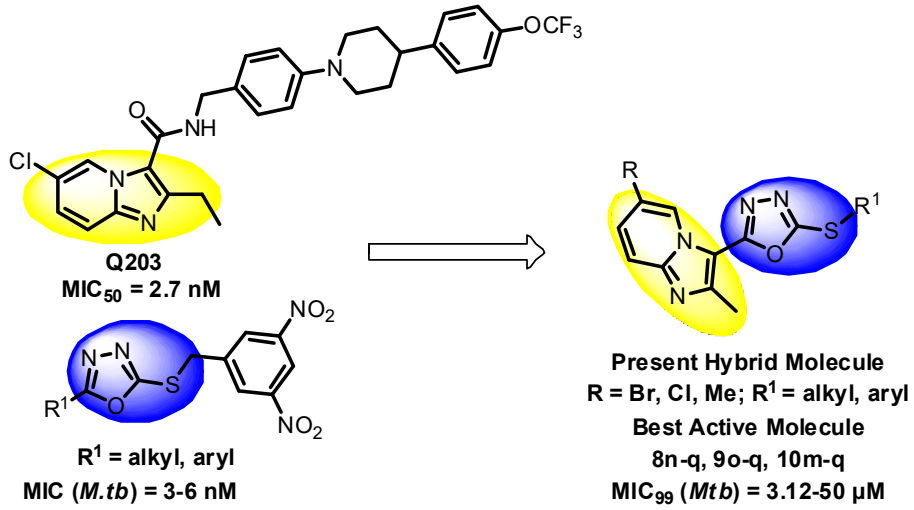


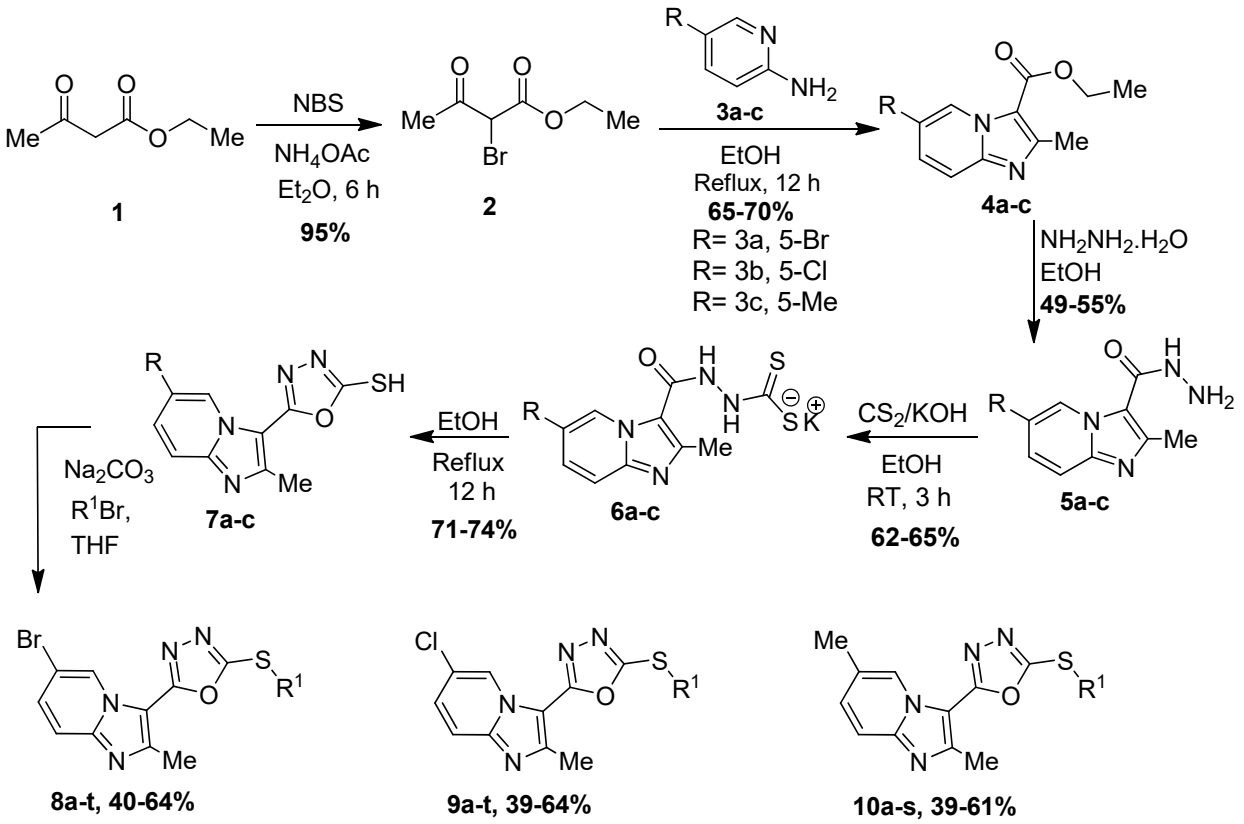
Figure 2 — Design strategy for the synthesis of 1,3,4-oxadiazole-imidazo[1,2-*a*]pyridine hybrids

active pharmacophores and evaluated them for anti-tuberculosis activity (Figure 2).

Results and Discussion

Chemistry

The 1,3,4-oxadiazole substituted imidazo[1,2-*a*] pyridine hybrids were synthesized as outlined in Scheme I. In the first step, ethyl acetoacetate (**1**) was added to the mixture of ammonium acetate and recrystallized *N*-bromosuccinimide. The reaction mixture was stirred at RT for 12 h to give intermediate (**2**)[47]. The intermediate **2** was then reacted with 2-aminopyridines (**3a-c**) and the reaction mixture was refluxed for 12 h to give compounds (**4a-c**)[45] Afterwards, compounds (**4a-c**) were refluxed with hydrazine hydrate in EtOH for 12 h to give compounds (**5a-c**)[45]. A solution of KOH in EtOH was taken and compounds (**5a-c**) were added to it in an ice bath. To the above solution, carbon disulfide was added in small portions with constant stirring. The reaction mixture was agitated continuously for a period of 3 h to give compounds (**6a-c**). The compounds (**6a-c**) were dissolved in EtOH and the reaction mixture was refluxed for 10-



1 **2** **4a-c** **5a-c** **6a-c** **7a-c**

8a-t, 40-64% **9a-t, 39-64%** **10a-s, 39-61%**

8a, R^1 = benzyl
8b, R^1 = 4-nitro benzyl
8c, R^1 = 4-bromo benzyl
8d, R^1 = 4-floro benzyl
8e, R^1 = 2-nitro benzyl
8f, R^1 = 2,5-difluorobenzyl
8g, R^1 = 2,3,4,5,6-pentafluorobenzyl
8h, R^1 = 4-cyanobenzyl
8i, R^1 = methyl 4-methylbenzoate
8j, R^1 = 1-methyl naphthalene
8k, R^1= ethyl
8l, R^1 = propyl
8m, R^1 = butyl
8n, R^1 = 3-methylbutyl
8o, R^1 = pentyl
8p, R^1 = hexyl
8q, R^1 = heptyl
8r, R^1 = octyl
8s, R^1 = geranyl
8t, R^1 = prop-1-yne

9a, R^1 = benzyl
9b, R^1 = 4-nitro benzyl
9c, R^1 = 4-bromo benzyl
9d, R^1 = 4-floro benzyl
9e, R^1 = 2-nitro benzyl
9f, R^1 = 2,5-difluorobenzyl
9g, R^1 = 2,3,4,5,6-pentafluorobenzyl
9h, R^1 = 4-cyanobenzyl
9i, R^1 = methyl 4-methylbenzoate
9j, R^1 = acetophenone
9k, R^1 = ethyl
9l, R^1 = propyl
9m, R^1 = butyl
9n, R^1 = 3-methylbutyl
9o, R^1 = pentyl
9p, R^1 = hexyl
9q, R^1 = heptyl
9r, R^1 = octyl
9s, R^1 = geranyl
9t, R^1 = prop-1-yne

10a, R^1 = benzyl
10b, R^1= 4-nitro benzyl
10c, R^1 = 4-bromo benzyl
10d, R^1 = 4-floro benzyl
10e, R^1 = 2-nitro benzyl
10f, R^1 = 2,5-difluorobenzyl
10g, R^1 = 1-methyl naphthalene
10h, R^1 = 4-cyanobenzyl
10i, R^1 = methyl 4-methylbenzoate
10j, R^1 = ethyl
10k, R^1 = propyl
10l, R^1 = butyl
10m, R^1 = 3-methylbutyl
10n, R^1 = pentyl
10o, R^1 = hexyl
10p, R^1 = heptyl
10q, R^1 = octyl
10r, R^1 = geranyl
10s, R^1 = prop-1-yne

Scheme I — Synthetic pathway of substituted 2-(benzylthio/alkylthio)-5-(2-methyl imidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole

12 h to give compounds (**7a-c**). To a solution of compounds (**7a-c**) in tetrahydrofuran were added substituted benzyl bromides or alkyl halides with Na_2CO_3 and the reaction mixture was stirred for 12h at RT to give compounds (**8a-t, 9a-t, 10a-s**) in moderate to good yield (Scheme I).

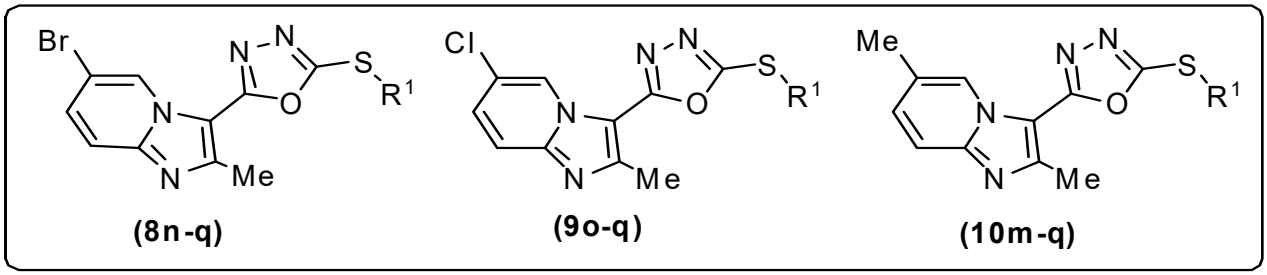
All the compounds were purified using silica gel column chromatography and characterized spectroscopically. The synthesized compounds were well characterized by using ^{1}H NMR, ^{13}C NMR and mass spectral techniques (See SI). Finally, the molecular structure was established by single crystal X-Ray diffraction analysis of **10b** (Figure 3). The spectral data matches with respect to compounds.

Figure 3 — Single crystal structure of 10b (CCDC no: 1860485)

In vitro Antibacterial Activity

All the synthesized compounds were screened against H37Rv strain of TB. These compounds were grouped in three different categories (**8a-8t, 9a-9t, 10a-10s**) based on substitution at C-6 position of imidazo[1,2-*a*]pyridine. While substitution at sulphur attached to benzoxazole was varied systematically in all the cases. The first group of compounds **8a-t** imidazo[1,2-*a*]pyridine has Br at C-6 position, while the second group **9a-t** has Cl at C-6 position & in third group **10a-t** has methyl group at C-6 position of imidazo[1,2-*a*]pyridine. Among all the tested compounds most of the compounds were found to be inactive up to 50 μM concentration except compounds **8n-8q** (MIC_{99} = 3.12-12.5 μM), **9o-9q** (MIC_{99} = 12.5 μM) and **10m-10q** (MIC_{99} = 12.5-50 μM). Structural analysis revealed that all these compounds (**8n-8q**) have alkyl group with chain length from butyl to heptyl and the activity was in the range of 3.12-12.5 μM with compound **8p** being most active (MIC_{99} = 3.12-6.25 μM). But when Br was replaced by Cl/methyl (compound **8a-t**) compounds having C_4-C_7 alkyl chain attached to 'S' the activity drops to 12.5-25 μM. In our activity assays, isoniazid control displayed MIC_{99} value of 0.39 μM in concordance with previous reports[44] (Table I).

Table I — *In vitro* antimycobacterial activity and cytotoxicity of the 1,3,4-oxadiazole and imidazo[1,2-*a*]pyridine hybrids



S. No	Entry	MIC_{99}(μM)	TC_{50} values (μM)
1	**8n**	6.25-12.5	>50
2	**8o**	6.25-12.5	>50
3	**8p**	3.12-6.25	25
4	**8q**	12.5	>50
5	**9o**	12.5	>50
6	**9p**	12.5	>50
7	**9q**	12.5	>50
8	**10m**	25-50	-
9	**10n**	12.5	10
10	**10o**	12.5-25	10
11	**10p**	25	-
12	**10q**	12.5	>50
13	**Isoniazid**	0.39	-

Experimental Section

Instrumentation and Chemicals

All the chemicals were purchased from Sigma-Aldrich and were used without further purification. Progress of the reactions was monitored by thin layer chromatography (Merck Kiesel 60 F254, 0.2 mm thickness) and the compounds were purified by silica gel column chromatography. IR spectra were recorded on Perkin-Elmer FT-IR spectrophotometer using KBr pellets and the values were expressed in cm^{-1}. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on Jeol ECX spectrospin instrument using $CDCl_3$ or DMSO-d_6 as solvent with TMS as internal reference. The chemical shift values were expressed on δ scale and the coupling constant (*J*) in Hz. Melting points were recorded on EZ-Melt automated melting point apparatus, Stanford Research Systems and are uncorrected. Mass data were recorded in Jeol-Accu TOF JMS-T100LC and micromass LCT mass spectrometer/Data system Spectrometer/Data system.

Typical procedure for the synthesis of ethyl 2-bromo-3-oxobutanoate, 2[45]: Ethyl acetoacetate (10 g, 76.8 mmol) was taken in diethyl ether (200 mL) and ammonium acetate (17.7 g, 230.5 mmol) and recrystallized *N*-bromosuccinimide (13.6 g, 76.8 mmol) were added. The reaction mixture was stirred at RT for 12 h. After completion of the reaction, as evident from TLC, the reaction mixture was washed with water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to get the desired compound (**2**).

Typical procedure for the synthesis of substituted ethyl 2-methylimidazo[1,2-*a*]pyridine-3-carboxylate, 4a-c[45]: A solution of ethyl 2-bromo-3-oxobutanoate (47.8 mmol) in EtOH (200 mL) was added to a solution of substituted 2-aminopyridine (**3a-c,** 47.8 mmol). The mixture was stirred at reflux temperature for 12 h. After completion of the reaction, the solvent was removed from the reaction mixture. The resulting dark residue was dissolved in EtOAc and washed with water. The organic phase was washed with brine solution, dried over Na_2SO_4, and concentrated in vacuum to get a solid product. The crude residue was purified by flash column chromatography (*n*-hexane/EtOAc = 4:1) to give substituted ethyl 2-methylimidazo[1,2-*a*]pyridine-3-carboxylate (**4a-c**).

Typical procedure for the synthesis of substituted 2-methylimidazo[1,2-*a*]pyridine-3-carbohydrazide, 5a-c[46]: To a solution of substituted ethyl 2-methylimidaz[1,2-*a*]pyridine-3-carboxylate (**4a-c,** 33.6 mmol) in EtOH (200 mL) and hydrazine hydrate (134.4 mmol) was added to drop-wise and refluxed for 12 h. After cooling, the resulting precipitate was filtered, washed with EtOH and dried under vacuum to get substituted 2-methylimidazo[1,2-*a*]pyridine-3-carbohydrazide (**5a-c**).

Typical procedure for the synthesis of substituted potassium 2-(2-methylimidazo[1,2-*a*]pyridine-3-carbonyl)hydrazinecarbodithioate, 6a-c[46]: Substituted 2-methylimidazo[1,2-*a*]pyridine-3-carbohydrazide (**5a-c**, 18.6 mmol) was added slowly to KOH solution (27.9 mmol) in 120 mL EtOH in an ice bath. To the above solution, carbon disulfide (37.2 mmol) was added in small portions with constant stirring. The reaction mixture was agitated continuously for a period of 3 h. It was then diluted with anhydrous ether. The precipitated substituted potassium 2-(2-methylimidazo[1,2-*a*]pyridine-3-carbonyl) hydrazinecarbodithioate (**6a-c**) was collected by filtration. The precipitate was further washed with anhydrous ether (100 mL) and dried under vacuum. The potassium salt thus obtained was used in the next step without further purification.

Typical procedure for the synthesis of substituted 5-(2-methylimidazole[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole-2-thiol, 7a-c[46]: Compound (**6a-c**) was dissolved in EtOH (120 mL) and the reaction mixture was refluxed for 10-12 h. The progress of the reaction was monitored by TLC until completion. The solvent was evaporated, and the residue was acidified with 10% HCl. The precipitate was collected by filtration, washed with water and dried. The products substituted 5-(2-methylimidazole[1,2-a]pyridin-3-yl)-1,3,4-oxadiazole-2-thiol (**7a-c**) was obtained in good yield.

Typical procedure for the synthesis of substituted 2-(benzylthio/alkylthio)-5-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole, 8a-t, 9a-t, 10a-s[46]: To a solution of compound (7a-c) substituted 5-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole-2-thiol (1.50 mmol) in tetrahydrofuran (20 mL), substituted benzyl bromides or alkyl halide (1.50 mmol) and Na_2CO_3 (4.51 mmol) were added and the reaction mixture was stirred for 12 h at RT. The reaction mixture was poured into ice-water, and the resulting solid was filtered off, washed with water, and dried over Na_2SO_4. The crude residue was purified by flash column chromatography (*n*-

hexane/EtOAc) to give substituted 2-(benzylthio/alkylthio)-5-(2-methylimidazo[1,2-a] pyridin-3-yl)-1,3,4-oxadiazole (**8a-t, 9a-t, 10a-s**).

Characterization of compounds

2-(Benzylthio)-5-(6-bromo-2-methylimidazo[1,2-a] pyridin-3-yl)-1,3,4-oxadiazole, 8a: White solid, Yield 41%. m.p. 172-174°C. IR (Film): 3064, 3003, 2360, 1957, 1708, 1631, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.56 (s, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.48-7.44 (m, 3H), 7.37-7.30 (m, 3H), 4.54 (s, 2H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.38, 158.94, 148.74, 145.17, 135.44, 130.62, 129.05, 128.83, 128.16, 127.84, 117.24, 108.68, 107.68, 36.97, 15.46; HRMS Calcd for $C_{17}H_{13}BrN_4OS$: *m/z* 400.0008. Found: 401.0082 $(M + H)^+$, 403.0062 $(MH+2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((4-nitrobenzyl)thio)-1,3,4-oxadiazole, 8b: White solid, Yield 43%. m.p. 178-180°C. IR (Film): 3082, 2926, 2852, 2453, 2360, 1938, 1739, 1629, 1600 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.53 (s, 1H), 8.23-8.21 (m, 2H), 7.71-7.69 (m, 2H), 7.56 (d, *J* = 9.9 Hz, 1H), 7.49-7.46 (m, 1H), 4.60 (s, 2H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.65, 159.17, 148.99, 147.64, 143.24, 130.79, 130.05, 127.81, 123.97, 117.33, 108.80, 35.74, 15.52; HRMS Calcd for $C_{17}H_{12}BrN_5O_3S$: *m/z* 444.9844. Found: 445.9933. $(M + H)^+$, 447.9914 $(MH+2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((4-bromobenzyl)thio)-1,3,4-oxadiazole, 8c: White solid, Yield 50%. m.p. 190-192°C. IR (Film): 3064, 3001, 2922, 2852, 2360, 1950, 1793, 1741, 1627, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.48-7.44 (m, 3H), 7.37 (d, *J* = 8.4 Hz, 2H), 4.48 (s, 2H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.96, 159.04, 148.84, 145.21, 134.66, 131.91, 130.74, 130.66, 127.81, 122.19, 117.26, 108.70, 107.66, 36.18, 15.47; HRMS Calcd for $C_{17}H_{12}Br_2N_4OS$: *m/z* 477.9083. Found: 478.9156 $(M + H)^+$, 480.9137 $(MH+2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((4-fluorobenzyl)thio)-1,3,4-oxadiazole, 8d: White solid, Yield 46%. m.p. 162-164°C. IR (Film): 3088, 3066 3005, 2954, 2922, 1801, 1629, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.54 (s, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.48-7.45 (m, 3H), 7.04 (t, *J* = 8.4 Hz, 2H), 4.51 (s, 2H), 2.70 (s, 3H); HRMS Calcd for $C_{17}H_{12}BrFN_4OS$: *m/z* 417.9882. Found: 418.9956 $(M + H)^+$, 420.9935 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((2-nitrobenzyl)thio)-1,3,4-oxadiazole, 8e: White solid, Yield 43%. m.p. 204-206°C. IR (Film): 3032, 1629, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.53 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 8.7 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 1H), 4.89 (s, 2H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.81, 159.18, 148.99, 147.68, 145.24 134.03, 133.06, 132.52, 130.65, 129.47, 127.78, 125.75, 117.33, 108.71, 107.57, 34.62, 15.49; HRMS Calcd for $C_{17}H_{12}BrN_5O_3S$: *m/z* 444.9846. Found: 445.9918 $(M + H)^+$, 447.9900 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((2,5-difluorobenzyl)thio)-1,3,4-oxadiazole, 8f: White solid, Yield 55%. m.p. 166-168°C IR (Film): 3055, 2993, 2918, 2850, 1707, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.55 (s, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.46 (dd, *J* = 9.5, 2.3 Hz, 1H), 7.34-7.29 (m, 1H), 7.08-6.95 (m, 2H), 4.53 (s, 2H), 2.70 (s, 3H); HRMS Calcd for $C_{17}H_{11}BrF_2N_4OS$: *m/z* 435.9805. Found: 436.9879 $(M + H)^+$, 438.9859 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(((perfluorophenyl)methyl)thio)-1,3,4-oxa diazole, 8g: White solid, Yield 45%. m.p. 132-134°C. IR (Film): 3033, 2955, 2921, 2852, 1654, 1597 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 7.57 (d, *J* = 9.9 Hz, 1H), 7.48 (dd, *J* = 9.5, 2.3 Hz, 1H), 4.59 (s, 2H), 2.73 (s, 3H); HRMS Calcd for $C_{17}H_8BrF_5N_4OS$: *m/z* 489.9522. Found: 490.9598 $(M + H)^+$, 492.9579 $(MH + 2)^+$.

4-(((5-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)methyl)benzo nitrile, 8h: White solid, Yield 49%. m.p. 160-162°C. IR (Film): 3286, 3033 2231, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.53 (s, 1H), 7.67-7.63 (m, 4H), 7.55 (d, *J* = 9.9 Hz, 1H), 7.48 (d, *J* = 9.9 Hz, 1H), 4.56 (s, 2H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.48, 159.16, 148.90, 145.22, 141.22, 132.49, 130.73, 129.82, 127.74, 118.34, 117.26, 111.94, 108.76, 107.43, 36.03, 15.46; HRMS Calcd for $C_{18}H_{12}BrN_5OS$: *m/z* 424.9938. Found: 426.0011 $(M + H)^+$, 427.9992 $(MH + 2)^+$.

Methyl-4-(((5-(6-bromo-2-methylimidazo[1,2-*a*] pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio) methyl)

benzoate, 8i: White solid, Yield 40%. m.p. 195-197°C. IR (Film): 2922, 1724, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.54 (s, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.55 (t, *J* = 8.7 Hz, 3H), 7.46 (dd, *J* = 9.1, 2.3 Hz, 1H), 4.57 (s, 2H), 3.90 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.48, 161.85, 159.03, 148.79, 145.17, 140.70, 130.65, 130.02, 129.86, 129.05, 127.78, 117.22, 108.70, 107.54, 52.16, 36.39, 15.42; HRMS Calcd for $C_{19}H_{15}BrN_4O_3S$: *m/z* 458.0043. Found: 459.0116 $(M + H)^+$, 461.0097 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((naphthalen-1-ylmethyl)thio)-1,3,4-oxa diazol, 8j: White solid, Yield 47%. m.p. 159-161°C. IR (Film): 3062, 3003, 1627, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.56 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 6.8 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.55-7.51 (m, 2H), 7.47-7.41 (m, 2H), 5.04 (s, 2H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.59, 158.93, 148.80, 145.17, 133.91, 131.13, 130.60, 130.48, 129.39, 129.05, 128.38, 127.83, 126.77, 126.13, 125.35, 123.17, 117.24, 108.68, 107.74, 35.06, 15.44; HRMS Calcd for $C_{21}H_{15}BrN_4OS$: *m/z* 450.0145. Found: 451.0218 $(M + H)^+$, 453.0200 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(ethylthio)-1,3,4-oxadiazole, 8k: White solid, Yield 60%. m.p. 164-166°C. IR (Film): 3060, 2998, 2924, 2857, 1629, 1599 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.55 (s, 1H), 7.53 (d, *J* = 9.1 Hz, 1H), 7.44 (d, *J* = 9.1 Hz, 1H), 3.33 (q, *J* = 7.3 Hz, 2H), 2.72 (s, 3H), 1.53 (t, *J* = 7.3Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.94, 158.77, 148.63, 145.17, 130.53, 127.85, 117.24, 108.63, 107.84, 27.24, 15.45, 14.73; HRMS Calcd for $C_{12}H_{11}BrN_4OS$: *m/z* 337.9836. Found: 338.9908 $(M + H)^+$, 340.9888 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(propylthio)-1,3,4-oxadiazole, 8l: White solid, Yield 61%. m.p. 144-146°C. IR (Film): 3062, 3000, 2959, 2925, 2866, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 7.54 (d, *J* = 9.6 Hz, 1H), 7.45 (dd, *J* = 9.1, 2.7, Hz, 1H), 3.31 (t, *J* = 7.1 Hz, 2H), 2.74 (s, 3H), 1.96-1.87 (m, 2H), 1.11 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.20, 158.74, 148.60, 145.17, 130.52, 127.86, 117.24, 108.63, 107.78, 34.71, 22.79, 15.43, 13.14; HRMS Calcd for $C_{13}H_{13}BrN_4OS$: *m/z* 351.9993. Found: 353.0065 $(M + H)^+$, 355.0044 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(butylthio)-1,3,4-oxadiazole, 8m: white solid, Yield 64%. m.p. 130-132°C. IR (Film): 3027, 2923, 2855, 2319, 1743, 1600 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 7.55 (d, *J* = 10.0 Hz, 1H), 7.46 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.33 (t, *J* = 7.5 Hz, 2H), 2.74 (s, 3H), 1.90-1.83 (m, 2H), 1.57-1.48 (m, 2H), 0.98 (t, *J* = 7.3Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.23, 158.74, 148.60, 145.17, 130.52, 127.86, 117.24, 108.62, 107.78, 32.53, 31.34, 21.76, 15.46, 13.47; HRMS Calcd for $C_{14}H_{15}BrN_4OS$: *m/z* 366.0149. Found: 367.0198 $(M + H)^+$, 369.0198 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-a]pyridin-3-yl)-5-(isopentylthio)-1,3,4-oxadiazole, 8n: White solid, Yield 60%. m.p. 96-98°C. IR (Film): 3063, 3002, 2955, 2870, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 7.55 (d, *J* = 9.6 Hz, 1H), 7.46 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.33 (t, *J* =6.8 Hz, 3H), 2.74 (s, 3H), 1.79-1.73 (m, 2H), 0.98 (d, *J* = 6.4Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.16, 158.72, 148.58, 145.14, 130.49, 127.83, 117.22, 108.61, 107.76, 38.11, 30.94, 27.45, 22.10, 15.46; HRMS Calcd for $C_{15}H_{17}BrN_4OS$: *m/z* 380.0306. Found: 381.0354 $(M + H)^+$, 383.0354 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(pentylthio)-1,3,4-oxadiazole, 8o: White solid, Yield 61%. m.p. 102-104°C. IR (Film): 3078, 3025, 2921, 2850, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.46 (dd, *J* = 9.4, 1.8 Hz, 1H), 3.33 (t, *J* = 7.5 Hz, 2H), 2.74 (s, 3H), 1.92-1.85 (m, 2H), 1.51-1.34 (m, 4H), 0.93 (t, *J* = 7.3Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.25, 158.75, 148.61, 145.18, 130.54, 127.89, 117.26, 108.64, 107.81, 32.83, 30.37, 29.06, 22.11, 15.48, 13.88; HRMS Calcd for $C_{15}H_{17}BrN_4OS$: *m/z* 380.0301. Found: 381.0374 $(M + H)^+$, 383.0353 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(hexylthio)-1,3,4-oxadiazole, 8p: White solid, Yield 42%. m.p. 78-80°C. IR (Film): 3069, 3007, 2919, 2855, 1713, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 7.55 (d, *J* = 9.9 Hz, 1H), 7.47-7.45 (m, 1H), 3.32 (t, *J* = 7.6 Hz, 2H), 2.74 (s, 3H), 1.91-1.84 (m, 2H), 1.53-1.46 (m, 2H), 1.36-1.21 (m, 4H), 0.92-0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.25, 158.74, 148.61, 145.12, 130.54, 127.88, 117.26, 108.64, 107.79, 32.84, 31.18, 29.30, 28.29, 22.48, 15.48, 13.97; HRMS Calcd for $C_{16}H_{19}BrN_4OS$: *m/z* 394.0461. Found: 395.0534 $(M + H)^+$, 397.0515 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(heptylthio)-1, 3,4-oxadiazole, 8q: White solid, Yield 42%. m.p. 77-79°C. IR (Film): 3086, 2924, 2855, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.45 (dd, *J* = 8.9, 1.8 Hz, 1H), 3.32 (t, *J* = 7.5 Hz, 2H), 2.74 (s, 3H), 1.91-1.84 (m, 2H), 1.67 (s, 2H), 1.52-1.45 (m, 2H), 1.37-1.25 (m, 4H), 0.89 (t, *J* = 6.4Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.00, 158.74, 148.62, 145.36, 130.55, 127.90, 117.27, 108.65, 107.76, 32.88, 31.63, 29.37, 28.69, 28.60, 22.53, 15.47, 14.01; HRMS Calcd for $C_{17}H_{21}BrN_4OS$: *m/z* 408.0619. Found: 409.0694 $(M + H)^+$, 411.0674 $(MH+2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(octylthio)-1,3, 4-oxadiazole, 8r: White solid, Yield 42%. m.p. 88-90°C. IR (Film): 3026, 2923, 2852, 2319, 1704, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.46 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.32 (t, *J* = 7.1 Hz, 2H), 2.74 (s, 3H), 1.91-1.84 (m, 2H), 1.52-1.45 (m, 2H), 1.37-1.28 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.24, 158.75, 148.61, 145.18, 130.52, 127.89, 117.26, 108.62, 107.80, 32.87, 31.72, 29.36, 29.09, 28.98, 28.63, 22.58, 15.43, 14.04; HRMS Calcd for $C_{18}H_{23}BrN_4OS$: *m/z* 422.0776. Found: 423.0826 $(M + H)^+$, 425.0807 $(MH + 2)^+$.

(E)-2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((3,7-dimethylocta-2,6-dien-1-yl)thio) -1,3,4-oxadiazole, 8s: Semi solid ,Yield 43%; IR (Film): 3080, 2922, 2853, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.51 (s, 1H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.39 (dd, *J* = 9.5, 2.3Hz, 1H), 5.39 (t, *J* = 6.8 Hz, 1H), 5.00-4.97 (m, 1H), 3.92 (d, *J* = 7.6 Hz, 2H), 2.67 (s, 3H), 2.04-1.94 (m, 4H), 1.70 (s, 3H), 1.60 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.08, 158.88, 145.23, 143.24, 139.28, 131.92, 130.58, 127.90, 123.50, 117.26, 116.95, 114.10, 108.70, 39.50, 31.02, 29.68, 26.25, 22.55, 16.33, 15.50; HRMS Calcd for $C_{20}H_{23}BrN_4OS$: *m/z* 446.0775. Found: 447.0849 $(M + H)^+$, 449.0830 $(MH + 2)^+$.

2-(6-Bromo-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(prop-2-yn-1-ylthio)-1,3,4-oxadiazole, 8t: White solid, Yield 57%. m.p. 158-160°C. IR (Film): 3159, 3078, 2954, 2919, 2850, 2104, 1922, 1695, 1628, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 7.56 (d, *J* = 9.9 Hz, 1H), 7.49-7.46 (m, 1H), 4.07 (d, *J* = 1.9 Hz, 2H), 2.75 (s, 3H), 2.37 (t, *J* = 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.05, 159.28, 148.98, 145.25, 130.69, 127.85, 117.26, 108.73, 107.64, 21.28, 15.49; HRMS Calcd for $C_{13}H_9BrN_4OS$: *m/z* 347.9680. Found: 348.9753 $(M + H)^+$, 350.9733 $(MH + 2)^+$.

2-(Benzylthio)-5-(6-chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole, 9a: White solid, Yield 63%. m.p. 157-159°C. IR (Film): 3066, 3006, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 7.48 (d, *J* = 6.8 Hz, 2H), 7.37-7.30 (m, 4H), 4.54 (s, 2H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.36, 158.95, 148.93, 145.08, 135.44, 129.06, 128.83, 128.45, 128.16, 125.76, 122.22, 116.95, 107.84, 36.97, 15.50; HRMS Calcd for $C_{17}H_{13}ClN_4OS$: *m/z* 356.0506. Found: 357.0578 $(M + H)^+$, 359.0554 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((4-nitrobenzyl)thio)-1,3,4oxadiazole, 9b: White solid, Yield 57%. m.p. 186-188°C. IR (Film): 3106, 2991, 1693, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.43 (s, 1H), 8.21 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 9.1 Hz, 1H), 7.39-7.36 (m, 1H), 4.60 (s, 2H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.38, 159.28, 149.14, 147.58, 145.18, 143.24, 130.05, 128.62, 125.70, 123.95, 122.33, 117.02, 107.62, 35.72, 15.53; HRMS Calcd for $C_{17}H_{12}ClN_5O_3S$: *m/z* 401.0364. Found: 402.0437 $(M + H)^+$, 404.0411 $(MH + 2)^+$.

2-((4-Bromobenzyl)thio)-5-(6-chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole, 9c: White solid, Yield 59%. m.p. 187-190°C. IR (Film): 3067, 3005, 1635, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 7.59 (d, *J* = 9.9 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H) 7.38-7.35 (m, 3H), 4.48 (s, 2H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.94, 159.05, 148.99, 145.10, 134.66, 131.91, 130.74, 128.50, 125.72, 122.25, 122.19, 116.96, 107.74, 36.18, 15.49; HRMS Calcd for $C_{17}H_{12}BrClN_4OS$: *m/z* 433.9615. Found: 434.9687 $(M + H)^+$, 436.9667 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((4-fluorobenzyl)thio)-1,3,4-oxadiazole, 9d: White solid, Yield 63%. m.p. 157-158°C. IR (Film): 3070, 3009, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.46 (s, 1H), 7.59 (d, *J* = 9.9 Hz, 1H), 7.48-7.45 (m, 2H), 7.37 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.04 (t, *J* = 8.4 Hz, 2H), 4.51 (s, 2H), 2.71 (s, 3H); HRMS Calcd for $C_{17}H_{12}ClFN_4OS$: *m/z* 374.0403. Found: 375.0477 $(M + H)^+$, 377.0451 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((2-nitrobenzyl)thio)-1,3,4-oxadiazole, 9e: White solid, Yield 60%. m.p. 199-201°C. IR (Film): 3085, 3026, 1634, 1600 cm[1]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.66-7.58 (m, 2H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.36 (dd, *J* = 9.1, 2.3 Hz, 1H), 4.89 (s, 2H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.70, 159.15, 149.10, 147.46, 145.09, 134.03, 133.06, 132.50, 129.45, 128.48, 125.74, 125.65, 122.24, 116.99, 107.69, 34.59, 15.50; HRMS Calcd for $C_{17}H_{12}ClN_5O_3S$: *m/z* 401.0346. Found: 402.0419 $(M + H)^+$, 404.0393 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((2,5-difluorobenzyl)thio)-1,3,4-oxadiazole, 9f: White solid, Yield 59%. m.p. 152-154°C. IR (Film): 3066, 3005, 1603 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.59 (d, *J* = 9.9 Hz, 1H), 7.37 (dd, *J* = 9.5, 2.3 Hz, 1H), 7.34-7.30 (m, 1H), 7.08-6.95 (m, 2H), 4.53 (s, 2H), 2.71 (s, 3H); HRMS Calcd for $C_{17}H_{11}ClF_2N_4OS$: *m/z* 392.0315. Found: 393.0388 $(M + H)^+$, 395.0363 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(((perfluorophenyl)methyl)thio)1,3,4-oxadiazole, 9g: White solid, Yield 56%. m.p. 149-151°C. IR (Film): 3036, 2926, 2854, 1655, 1599 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.39 (dd, *J* = 9.5, 2.3 Hz, 1H), 4.59 (s, 2H), 2.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.59, 159.58, 149.32, 146.49, 145.25, 143.99, 140.15, 138.88, 136.20, 128.71, 125.80, 122.40, 117,02, 109.72, 107.63, 24.10, 15.50; HRMS Calcd for $C_{17}H_8ClF_5N_4OS$: *m/z* 446.0027. Found: 447.0103 $(M + H)^+$, 449.0077 $(MH + 2)^+$.

4-(((5-(6-Chloro-2-methylimidazo[1,2-a]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)methyl) benzonitrile, 9h: White solid, Yield 62%. m.p. 178-180°C. IR (Film): 3091, 2925, 2360, 2229, 1604 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (s, 1H), 7.63-7.54 (m, 5H), 7.33 (dd, *J* = 9.5, 2.3 Hz, 1H), 4.52 (s, 2H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.46, 159.20, 149.08, 145.13, 141.22, 132.50, 129.84, 128.57, 125.66, 122.29, 118.34, 116.98, 111.97, 107.61, 36.04, 15.50; HRMS Calcd for $C_{18}H_{12}ClN_5OS$: *m/z* 381.0453. Found: 382.0526 $(M + H)^+$, 384.0501 $(MH + 2)^+$.

Methyl-4-(((5-(6-chloro-2-methylimidazo[1,2-*a*] pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio) methyl) benzoate, 9i: White solid, Yield 59%. m.p. 166-168°C. IR (Film): 2922, 1724, 1606 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.58 (t, *J* = 9.1 Hz, 3H), 7.37 (dd, *J* = 9.5, 2.3 Hz, 1H), 4.57 (s, 2H), 3.90 (s, 3H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.50, 161.84, 159.08, 149.00, 145.10, 140.71, 130.04, 129.87, 129.07, 128.50, 125.72, 122.24, 116.96, 107.72, 52.18, 36.39, 15.50; HRMS Calcd for $C_{19}H_{15}ClN_4O_3S$: *m/z* 414.0586. Found: 415.0659(M + H)$^+$, 417.0636 $(MH + 2)^+$.

2-((5-(6-Chloro-2-methylimidazo[1,2-a]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)-1-phenyl-ethanone, 9j: White solid, Yield 63%. m.p. 225-227°C. IR (Film): 3064, 3005, 2917, 1676, 1604 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.07 (d, *J* = 7.6 Hz, 2H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 9.1 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.38 (dd, *J* = 9.5, 2.3 Hz, 1H), 5.00 (s, 2H), 2.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.72, 162.24, 159.09, 149.11, 145.14, 134.81, 134.31, 129.00, 128.50, 125.73, 122.24, 117.01, 107.74, 41.52, 15.54; HRMS Calcd for $C_{18}H_{13}ClN_4O_2S$: *m/z* 384.0458. Found: 385.0536 $(M + H)^+$, 387.0509 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(ethylthio)-1,3,4-oxadiazole, 9k: White solid, Yield 39%. m.p. 151-153°C. IR (Film): 3068, 3008, 2926, 2859, 2361, 2336, 1895, 1744, 1603 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 7.36 (dd, *J* = 9.6, 1.4 Hz, 1H), 3.35 (q, *J* = 7.3 Hz, 2H), 2.74 (s, 3H), 1.56 (t, *J* = 7.1Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.89, 158.74, 148.73, 145.02, 128.35, 125.71, 122.15, 116.91, 107.89, 27.21, 15.46, 14.71; HRMS Calcd for $C_{12}H_{11}ClN_4OS$: *m/z* 294.0313. Found: 295.0385 $(M + H)^+$, 297.0357 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-a]pyridin-3-yl)-5-(propyl thio)-1,3,4-oxadiazole, 9l: White solid, Yield 45%. m.p. 145-147°C. IR (Film): 3066, 3002, 2958**,** 2866, 1599 cm-1; 1H NMR (400 MHz, CDCl3): δ 9.48 (s, 1H), 7.60 (d, *J* = 9.6 Hz, 1H), 7.37 (d, *J* = 9.1, Hz, 1H), 3.31 (t, *J* = 6.8 Hz, 2H) 2.75 (s, 3H), 1.96-1.85 (m, 2H), 1.11 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3): δ 163.15, 158.71, 148.70, 144.99, 128.36, 125.72, 122.16, 116.91, 108.15, 34.65, 22.75, 15.45, 13.13; HRMS Calcd for $C_{13}H_{13}ClN_4OS$: *m/z* 308.0474. Found: 309.0547 $(M + H)^+$, 311.0519 $(MH + 2)^+$.

2-(Butylthio)-5-(6-chloro-2-methylimidazo[1,2-*a*] pyridin-3-yl)-1,3,4-oxadiazole, 9m: White solid,

Yield 47%. m.p. 136-138°C. IR (Film): 3070, 3008, 2957, 2927, 2863, 1939, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.48 (s, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 7.36 (dd, *J* = 9.4, 2.3 Hz, 1H), 3.33 (t, *J* = 7.3 Hz, 2H), 2.74 (s, 3H), 1.90-1.83 (m, 2H), 1.57-1.48 (m, 2H), 0.98 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.22, 158.76, 148.76, 145.06, 128.39, 125.76, 122.21, 116.95, 108.03, 32.54, 31.34, 21.76, 15.47, 13.47; HRMS Calcd for $C_{14}H_{15}ClN_4OS$: *m/z* 322.0639. Found: 323.0712 $(M + H)^+$, 325.0684 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(isopentylthio)-1,3,4-oxadiazole, 9n: White solid, Yield 49%. m.p. 102-104°C. IR (Film): 3069, 3006, 2954, 2869, 1600 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.48 (s, 1H), 7.60 (d, *J* = 9.6 Hz, 1H), 7.36 (dd, *J* = 9.1, 1.8 Hz, 1H), 3.33 (t, *J* = 6.8 Hz, 2H), 2.74 (s, 3H), 1.82-1.75 (m, 3H), 0.98 (d, *J* = 6.4Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.17, 158.74, 148.74, 145.04, 128.38, 125.75, 122.19, 116.94, 107.94, 38.10, 30.94, 27.45, 22.10, 15.47; HRMS Calcd for $C_{15}H_{17}ClN_4OS$: *m/z* 336.0795. Found: 337.0867 $(M + H)^+$, 339.0842 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(pentylthio)-1,3,4-oxadiazole, 9o: White solid, Yield 48%. m.p. 112-114°C. IR (Film): 3086, 3030, 2970, 2924, 2852, 2362, 1944, 1791, 1716, 1631, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.49 (s, 1H), 7.60 (d, *J* = 9.9 Hz, 1H), 7.36 (dd, *J* = 9.5, 2.3Hz, 1H), 3.32 (t, *J* = 7.6 Hz, 2H), 2.75 (s, 3H), 1.92-1.85 (m, 2H), 1.51-1.34 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.22, 158.75, 148.76, 145.05, 128.39, 125.77, 122.18, 116.96, 107.98, 32.78, 30.73, 29.03, 22.12, 15.52, 13.91; HRMS Calcd for $C_{15}H_{17}ClN_4OS$: *m/z* 336.0819. Found: 337.0891 $(M + H)^+$, 339.0866 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(hexylthio)-1,3,4-oxadiazole, 9p: Brown solid, Yield 53%. m.p. 83-85°C. IR (Film): 3070, 3008, 2954, 2926, 2854, 1716, 1631, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.49 (s, 1H), 7.60 (d, *J* = 9.1 Hz, 1H), 7.37 (d, *J* = 9.6 Hz, 1H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.74 (s, 3H), 1.91-1.84 (m, 2H), 1.51-1.46 (m, 2H), 1.34-1.33 (m, 4H), 0.90 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.21, 158.74, 148.72, 145.03, 128.39, 125.76, 122.19, 116.94, 107.94, 32.82, 31.16, 29.28, 28.27, 22.46, 15.47, 13.95; HRMS Calcd for $C_{16}H_{19}ClN_4OS$: *m/z* 350.0934. Found: 351.1006 $(M + H)^+$, 353.0981 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(heptylthio)-1,3,4-oxadiazole, 9q: Brown solid, Yield 40%. m.p. 68-70°C. IR (Film): 3089, 2924, 2855, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.48 (s, 1H), 7.59 (d, *J* = 10.0 Hz, 1H), 7.36 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.74 (s, 3H), 1.91-1.84 (m, 2H), 1.52-1.45 (m, 2H), 1.39-1.25 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.21, 158.71, 148.71, 145.02, 128.39, 125.74, 122.19, 116.92, 107.93, 32.81, 31.60, 29.08, 28.66, 28.56, 22.51, 15.45, 14.00; HRMS Calcd for $C_{17}H_{21}ClN_4OS$: *m/z* 364.1125. Found: 365.1193 $(M + H)^+$.

2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(octylthio)-1,3,4-oxadiazole, 9r: Yellow solid, Yield 48%. m.p. 74-76°C. IR (Film): 3031, 2925, 2853, 1745, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.59 (d, *J* = 9.6 Hz, 1H), 7.36 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.74 (s, 3H), 1.91-1.84 (m, 2H),1.52-1.45 (m, 2H), 1.37-1.28 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.21, 158.74, 148.74, 145.05, 128.37, 125.76, 122.19, 116.95, 107.96, 32.85, 31.71, 29.34, 29.08, 28.97, 28.62, 22.57, 15.45, 14.03; HRMS Calcd for $C_{18}H_{23}ClN_4OS$: *m/z* 378.1281. Found: 379.1349 $(M + H)^+$, 381.1325 $(MH + 2)^+$.

(E)-2-(6-Chloro-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-((3,7-dimethylocta-2,6-dien-1-yl)thio)-1,3,4-oxadiazole, 9s: Semi solid, Yield 48%; IR (Film): 3088, 2964, 2922, 2854, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.51 (s, 1H), 7.64 (d, *J* = 9.1 Hz, 1H), 7.40 (dd, *J* = 9.6, 2.3 Hz, 1H), 5.51-5.44 (m, 1H), 5.06-5.03 (m, 1H), 4.00 (d, *J* = 7.6 Hz, 2H), 2.76 (s, 3H), 2.10-2.07 (m, 4H), 1.78 (d, *J* = 4.5 Hz, 3H), 1.67(s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.99, 158.81, 148.78, 145.06, 143.15, 131.96, 128.42, 125.78, 123.49, 122.20, 116.95, 110.02, 107.96, 39.49, 31.01, 26.24, 25.63, 17.68, 16.31, 15.51; HRMS Calcd for $C_{20}H_{23}ClN_4OS$: *m/z* 402.1277. Found: 403.1351 $(M + H)^+$, 405.1325 $(MH + 2)^+$.

2-(6-Chloro-2-methylimidazo[1,2-a]pyridin-3-yl)-5-(prop-2-yn-1-ylthio)-1,3,4-oxadiazole, 9t: White solid, Yield 64%. m.p. 154-156°C. IR (Film): 3165, 2108, 1631, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.38 (dd, *J* = 9.5, 2.3 Hz, 1H), 4.08 (d, *J* = 2.3 Hz, 2H), 2.76 (s, 3H), 2.37 (t, *J* = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.06, 159.33, 149.17, 145.19,

128.58, 125.78, 122.30, 117.00, 107.74, 73.09, 21.28, 15.55; HRMS Calcd for $C_{13}H_9ClN_4OS$: *m/z* 304.0185. Found: 305.0257 $(M + H)^+$, 307.0231 $(MH + 2)^+$.

2-(Benzylthio)-5-(2,6-dimethylimidazo[1,2-*a*] pyridin-3-yl)-1,3, 4-oxadiazole, 10a: Brown solid, Yield 50%. m.p. 143-145°C. IR (Film): 2922, 1610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.16 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.47 (d, *J* = 6.8 Hz, 2H), 7.37-7.28 (m, 3H), 7.26-7.23 (m, 1H), 4.53 (s, 2H), 2.69 (s, 3H), 2.42 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.70, 159.46, 148.06, 145.72, 135.51, 130.10, 129.00, 128.74, 128.03, 125.62, 123.75, 115.87, 106.89, 36.89, 18.28, 15.47; HRMS Calcd for $C_{18}H_{16}N_4OS$: *m/z* 336.1047. Found: 337.1119 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-((4-nitrobenzyl)thio)-1,3,4-oxadiazole, 10b: White solid, Yield 44%. m.p. 174-176°C. IR (Film): 3743, 2480, 1743, 1698, 1648, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.12 (s, 1H), 8.20 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 9.1 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.28-7.24 (m, 1H), 4.59 (s, 2H), 2.69 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.74, 159.83, 148.36, 147.49, 145.89, 143.39, 130.28 130.02, 125.61, 123.90, 116.00, 106.71, 35.67, 18.31, 15.56; HRMS Calcd for $C_{18}H_{15}N_5O_3S$: *m/z* 381.0906. Found: 382.0978 $(M + H)^+$.

2-((4-Bromobenzyl)thio)-5-(2,6-dimethylimidazo [1,2-*a*]pyri dine-3-yl)-1,3,4-oxadiazole, 10c: White solid, Yield 41%. m.p. 144-146°C. IR (Film): 3851, 3742, 2361, 2321, 1744, 1699, 1648, 1605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.14 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.27-7.23 (m, 1H), 4.47 (s, 2H), 2.68 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.36, 159.67, 148.26, 145.86, 134.80, 131.90, 130.75, 130.21, 125.68, 123.85, 122.13, 115.99, 106.89, 36.18, 18.33, 15.55; HRMS Calcd for $C_{18}H_{15}BrN_4OS$: *m/z* 414.0155. Found: 415.0226 $(M + H)^+$, 417.0208 $(MH + 2)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-((4-fluorobenzyl)thio)-1,3,4-oxadiazole, 10d: White solid, Yield 48%. m.p. 150-152°C. IR (Film): 3852, 3742, 2361, 1699, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.15 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.48-7.44 (m, 2H), 7.26-7.23 (m, 1H), 7.05-7.01 (m, 2H), 4.50 (s, 2H), 2.69 (s, 3H), 2.42 (s, 3H); HRMS Calcd for $C_{18}H_{15}FN_4OS$: *m/z* 354.0954. Found: 355.1027 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-((2-nitrobenzyl)thio)-1,3,4-oxadiazole, 10e: Brown solid, Yield 51%. m.p. 149-151°C. IR (Film): 3860, 3743, 3648, 3619, 2361, 2322, 1741, 1693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.13 (s, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.56-7.49 (m, 2H), 7.27-7.24 (m, 1H), 4.88 (s, 2H), 2.67 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.07, 159.76, 148.35, 147.48, 145.84, 133.99, 133.02, 132.62, 130.21, 129.39, 125.72, 125.58, 123.86, 116.01, 106.82, 34.55, 18.32, 15.54; HRMS Calcd for $C_{18}H_{15}N_5O_3S$: *m/z* 381.0898. Found: 382.0969 $(M + H)^+$.

2-((2,5-Difluorobenzyl)thio)-5-(2,6-dimethylimidazo [1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole, 10f: White solid, Yield 50%. m.p. 149-150°C. IR (Film): 3064, 3035, 2926, 1911, 1641, 1605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.16 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.35-7.31 (m, 1H), 7.27-7.24 (m, 1H), 7.08-6.95 (m, 2H), 4.52 (s, 2H), 2.69 (s, 3H), 2.43 (s, 3H); HRMS Calcd for $C_{18}H_{14}F_2N_4OS$: *m/z* 372.0856. Found: 373.0932 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-((naphthalen-1-ylmethyl)thio)-1,3,4-oxadiazole, 10g: White solid, Yield51%. m.p. 156-158°C. IR (Film): 3743, 3619, 3062, 3003, 2465, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 6.8 Hz, 1H), 7.62-7.51 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 1H) 7.25 (d, *J* = 8.4 Hz, 1H), 5.04 (s, 2H), 2.65 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.02, 159.55, 148.12, 145.77, 133.93, 131.18, 130.64, 130.23, 129.34, 129.04, 128.32, 126.76, 126.12, 125.71, 125.35, 123.88, 123.23, 115.94, 106.88, 35.07, 18.35, 15.46; HRMS Calcd for $C_{22}H_{18}N_4OS$: *m/z* 386.1202. Found: 387.1274 $(M + H)^+$.

4-(((5-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazo l-2-yl)thio)methyl)benzonitrile, 10h: White solid, Yield 58%. m.p. 164-166°C. IR (Film): 3859, 3741, 3698, 3676, 3647, 3617, 3082, 2992, 2353, 2318, 2219, 1706, 1646, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.13 (s, 1H), 7.64-7.62 (m, 4H), 7.56 (d, *J* = 9.1 Hz, 1H), 7.27-7.25 (m, 1H), 4.54 (s, 2H), 2.69 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 160.87, 159.65, 148.33, 145.90, 141.37, 132.50, 130.32, 129.85, 125.65, 123.95, 118.54, 116.02, 111.93, 36.05, 18.33, 15.56; HRMS Calcd for $C_{19}H_{15}N_5OS$: *m/z* 361.1009. Found: 362.1081 $(M + H)^+$.

Methyl-4-(((5-(2,6-dimethylimidazo[1,2-*a*] pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)methyl) benzoate, 10i: White solid, Yield 51%. m.p. 160-162°C. IR (Film): 3035, 2922, 2855, 1722, 1605 cm-^{1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.14 (s, 1H), 8.01 (d, *J* = 8.4 Hz, 2H), 7.58-7.54 (m, 3H), 7.27-7.23 (m, 1H), 4.56 (s, 2H), 3.90 (s, 3H) 2.68 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.51, 161.23, 159.65, 148.21, 145.81, 140.84, 130.19, 129.99, 129.05, 125.63, 115.93, 106.82, 52.15, 36.36, 18.29, 15.51; HRMS Calcd for $C_{20}H_{18}N_4O_3S$: *m/z* 394.1083. Found: 395.1155 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(ethylthio)-1,3,4-oxadiazole, 10j: White solid, Yield 53%. m.p. 100-102°C. IR (Film): 3329, 3087, 2968, 2926, 2863, 2361, 1606 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.17 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.24 (d, *J* = 7.3 Hz, 1H), 3.37-3.30 (m, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.55 (t, *J* = 7.3Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.29, 159.35, 147.97, 145.77, 130.06, 125.67, 123.73, 115.93, 107.02, 27.17, 18.32, 15.52, 14.76; HRMS Calcd for $C_{13}H_{14}N_4OS$: *m/z* 274.0874. Found: 275.0946 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(propylthio)-1,3,4-oxadiazole, 10k: White solid, Yield 39%. m.p. 109-111°C. IR (Film): 3327, 3083, 3014, 2960, 2924, 2866, 2359, 1602 cm-^{1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.17 (s, 1H), 7.55 (d, *J* = 8.7 Hz, 1H), 7.24 (d, *J* = 9.1 Hz, 1H), 3.29 (t, *J* = 7.8 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.96-1.87 (m, 2H), 1.10 (t, *J* = 8.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.53, 159.32, 148.06, 145.75, 130.05, 125.67, 123.72, 115.92, 106.82, 34.62, 22.80, 18.31, 15.50, 13.14; HRMS Calcd for $C_{14}H_{16}N_4OS$: *m/z* 288.1032. Found: 289.1104$(M + H)^+$.

2-(Butylthio)-5-(2,6-dimethylimidazo[1,2-*a*] pyridin-3-yl)-1,3,4-oxadiazole, 10l: White solid, Yield 43%. m.p. 98-100°C. IR (Film): 3326, 2957, 2926, 2862, 1606 cm-^{1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.24 (dd, *J* = 9.1, 1.3 Hz, 1H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H),1.90-1.82 (m, 2H), 1.57-1.48 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.60, 159.34, 147.95, 145.78, 130.08, 125.69, 123.76, 115.93, 107.06, 32.48, 31.37, 21.75, 18.31, 15.49, 13.48; HRMS Calcd for $C_{15}H_{18}N_4OS$: *m/z* 302.1186. Found: 303.1258 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(isopentylthio)-1,3,4-oxadiazole, 10m: White solid, Yield 52%. m.p. 112-114°C. IR (Film): 2933, 2860, 1598 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.18 (s, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.24 (d, *J* = 9.1 Hz, 1H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.78-1.74 (m, 3H), 0.98 (d, *J* = 6.4Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.56, 159.35, 147.98, 145.80, 130.06, 125.70, 123.74, 115.95, 107.06, 38.16, 30.91, 27.44, 22.10, 18.31, 15.51; HRMS Calcd for $C_{16}H_{20}N_4OS$: *m/z* 316.1338. Found: 317.1410 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(pentylthio)-1,3,4-oxadiazole, 10n: White solid, Yield 43%. m.p. 59-61°C. IR (Film): 3082, 3015, 2953, 2922, 2854, 1680, 1642, 1600 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.18 (s, 1H), 7.56 (d, *J* = 9.1 Hz, 1H), 7.24 (dd, *J* = 9.1, 1.5 Hz, 1H), 3.31 (t, *J* = 7.2 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.92-1.84 (m, 2H), 1.49 -1.37 (m, 4H), 0.93 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.60, 159.34, 147.95, 145.78, 130.07, 125.70, 123.75, 115.94, 107.06, 32.75, 30.72, 29.07, 22.11, 18.33, 15.52, 13.89; HRMS Calcd for $C_{16}H_{20}N_4OS$: *m/z* 316.1357. Found: 317.1450 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(hexylthio)-1,3,4-oxadiazole, 10o: White solid, Yield 43%. m.p. 64-66°C. IR (Film): 3328, 2921, 1605 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.18 (s, 1H), 7.56 (d, *J* = 8.7 Hz, 1H), 7.24 (d, *J* = 9.1 Hz, 1H), 3.31(t, *J* = 7.3 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.91-1.83 (m, 2H), 1.52-1.45 (m, 2H), 1.36-1.30 (m, 4H), 0.91-0.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.62, 159.34, 147.95, 145.79, 130.09, 125.71, 123.77, 115.94, 107.08, 32.80, 31.17, 29.34, 28.27, 22.46, 18.32, 15.50, 13.95; HRMS Calcd for $C_{17}H_{22}N_4OS$: *m/z* 330.1503. Found: 331.1575 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(heptylthio)-1,3,4-oxadiazole, 10p: White solid, Yield 43%. m.p. 63-65°C. IR (Film): 3085, 2925, 2856, 1604 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.56 (d, *J* = 9.1 Hz, 1H), 7.24 (d, *J* = 9.1 Hz, 1H), 3.31 (t, *J* = 7.5 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.91-1.83 (m, 2H), 1.50-1.44 (m, 2H), 1.35-1.25 (m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.62, 159.33, 147.94, 145.78, 130.09, 125.70, 123.76, 115.94, 107.07, 32.80, 31.61, 29.38, 28.68, 28.57, 22.52, 18.32, 15.50, 14.00; HRMS Calcd for $C_{18}H_{24}N_4OS$: *m/z* 344.1657. Found: 345.1729 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(octylthio)-1,3,4-oxadiazole, 10q: White solid, Yield 61%. m.p. 74-77°C. IR (Film): 2918, 2851, 1606 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.18 (s, 1H), 7.55 (d, *J* = 8.7 Hz, 1H), 7.24 (d, *J* = 9.1 Hz, 1H), 3.30 (t, *J* = 7.3 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.91-1.83 (m, 4H), 1.52-1.44 (m, 2H), 1.36-1.28 (s, 6H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.61, 159.33, 147.95, 145.79, 130.07, 125.70, 123.75, 115.94, 107.07, 32.80, 31.71, 29.38, 29.08, 28.97, 28.61, 22.57, 18.31, 15.50, 14.03; HRMS Calcd for $C_{19}H_{26}N_4OS$: *m/z* 358.1827. Found: 359.1911$(M + H)^+$.

(E)-2-(2,6-Dimethylimidazo[1,2-a]pyridin-3-yl)-5-((3,7-dimethylocta-2,6-dien-1-yl)thio)-1,3,4-oxadiazole, 10r: Semi solid, Yield 44%. m.p. 126-28°C. IR (Film): 3348, 3084, 2965, 2922, 2855, 1654, 1604 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.07 (s, 1H), 7.45 (d, *J* = 9.1 Hz, 1H), 7.14 (dd, *J* = 9.1, 1.5 Hz, 1H), 5.38 (t, *J* = 7.6 Hz, 1H), 4.96 (brs, 1H), 3.90 (d, *J* = 7.6 Hz, 2H), 2.64 (s, 3H), 2.33 (s, 3H), 2.01 - 1.98 (m, 4H), 1.68 (s, 3H), 1.58 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.23, 159.28, 147.88, 145.66, 142.82, 131.81, 129.97, 125.59, 123.64, 123.41, 117.01, 115.82, 106.95, 39.38, 30.88, 26.15, 25.54, 18.24, 17.59, 16.19, 15.43; HRMS Calcd for $C_{21}H_{26}N_4OS$: *m/z* 382.1834. Found: 383.1906 $(M + H)^+$.

2-(2,6-Dimethylimidazo[1,2-*a*]pyridin-3-yl)-5-(prop-2-yn-1-ylthio)-1,3,4-oxadiazole, 10s: White solid, Yield 56%. m.p. 163-165°C. IR (Film): 3222, 3146, 3036, 2924, 2855, 2355, 2319, 2105, 1741, 1642, 1603 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.18 (s, 1H), 7.56 (d, *J* = 9.1Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 4.06 (d, *J* = 2.3 Hz, 2H), 2.74 (s, 3H), 2.42 (s, 3H), 2.36 (t, *J* = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl3): δ 160.47, 159.92, 148.40, 145.91, 130.28, 125.74, 123.91, 115.99, 106.73, 21.25, 18.34, 15.57; HRMS Calcd for $C_{14}H_{12}N_4OS$: *m/z* 284.0735. Found: 285.0807$(M+H)^+$.

Conclusions

In summary, we have reported the synthesis and antimycobacterial activity evaluation of a series of 1,3,4-oxadiazole-imidazo[1,2-*a*]pyridine hybrids. The *in vitro* evaluation of ten out of fifty-nine molecular hybrids against Mycobacterium tuberculosis H37Rv strain, have shown activity in the range of 3.125-12.5 μM. Compound **8p** was found to be most active with MIC_{99} value of 3.125-6.250 μM. Further, these ten compounds were also tested for their *in vitro* toxicity against THP-1 cell line and were found to be non-toxic with TC_{50} value in the range of (10 - >50 μM) concentration.

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