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Synthesis of novel imidazopyridine-oxadiazole molecular hybrids by a regioselective sulfenylation of imidazo[1,2-*a*]pyridines with 1,3,4-oxadiazole-2-thiols using I_2-$FeCl_3$ catalytic system and O_2/air as co-oxidant

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Dedicated to Prof. Sambasivarao Kotha on his 65th Birth Anniversary

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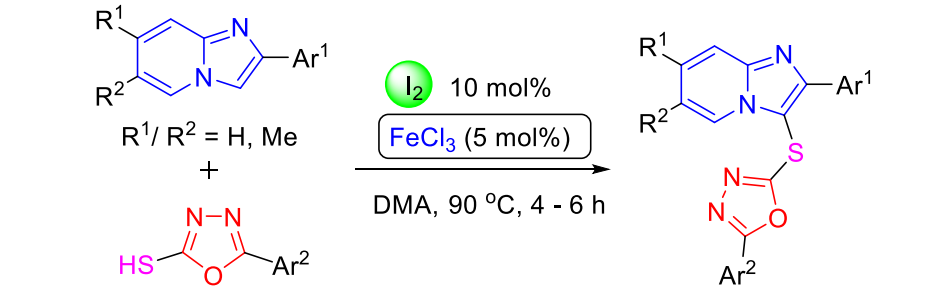
Abstract

Imidazo[1,2-a]pyridine and 1,3,4-oxadiazole are privileged scaffolds in medicinal chemistry owing to their diverse biological as well as pharmacological properties. They also have wide applications in material chemistry due to their interesting photophysical properties. Combining these two scaffolds through a thioether linkage leads to novel imidazopyridine-oxadiazole hybrids. This has been achieved by a regioselective C-3 sulfenylation of imidazo[1,2-a]pyridines with 1,3,4-oxadiazole-2-thiols using I_2-$FeCl_3$ as an efficient catalytic system and aerial oxygen as co-oxidant. This protocol provides a general, mild, efficient and atom-economic method for C-3 sulfenylation of imidazo[1,2-a]pyridines with 1,3,4-oxadiazole-2-thiols, a class of heterocyclic thiols not being used in such reactions.



Keywords: Sulfenylation, 2-arylimidazo[1,2-a]pyridine, 5-aryl-1,3,4-oxadiazole-2-thiols, iodine-catalyzed, molecular hybrids

Introduction

Imidazo[1,2-a]pyridine is an important fused heterocycle which has enormous applications in the field of medicinal chemistry,[1,2] material chemistry,[3,4] and in organometallics.[5,6] The C-3 functionalized imidazo-pyridine compounds exhibit variety of pharmacological activities such as anticancer,[7,8] antiviral,[9] anti-inflammatory,[10] anti-TB9,[11] anti-HIV,[12] antibacterial,[13] antiepileptic,[14] cytotoxicity, etc. Imidazo[1,2-a]pyridine functionalized at C-3 position has been found in many commercially available drugs such as alpidem (anxiolytic agent), minodronic acid (antiosteoporosis), zolpidem (treatment of insomnia), saripidem (sedative and anxiolytic), necopidem (sedative and anxiolytic), and DS-1 (GABA receptor antagonist) (Figure 1). Imidazo[1,2-a]pyridine skeleton is also found in natural products with diverse biological activities.[1] Imidazo[1,2-a]pyridine derived conjugates such as 2-(2′-hydroxyphenyl)imidazo[1,2-a]pyridine and its derivatives show unique optical properties.[3,4]

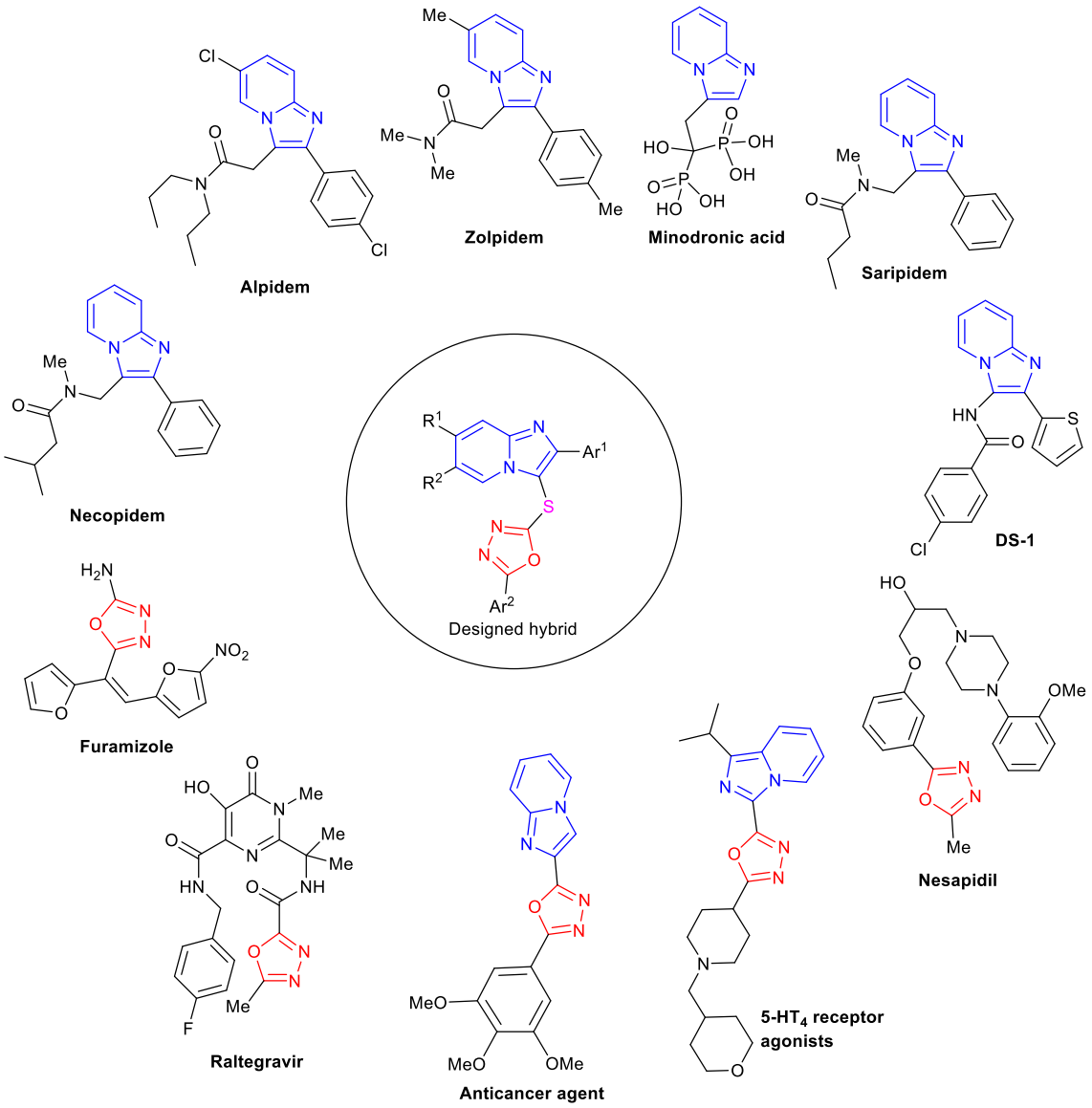


Figure 1. Examples of commercial drugs containing C-3 functionalized imidazo[1,2-*a*]pyridines and C-2 functionalized 1,3,4-oxadiazoles.

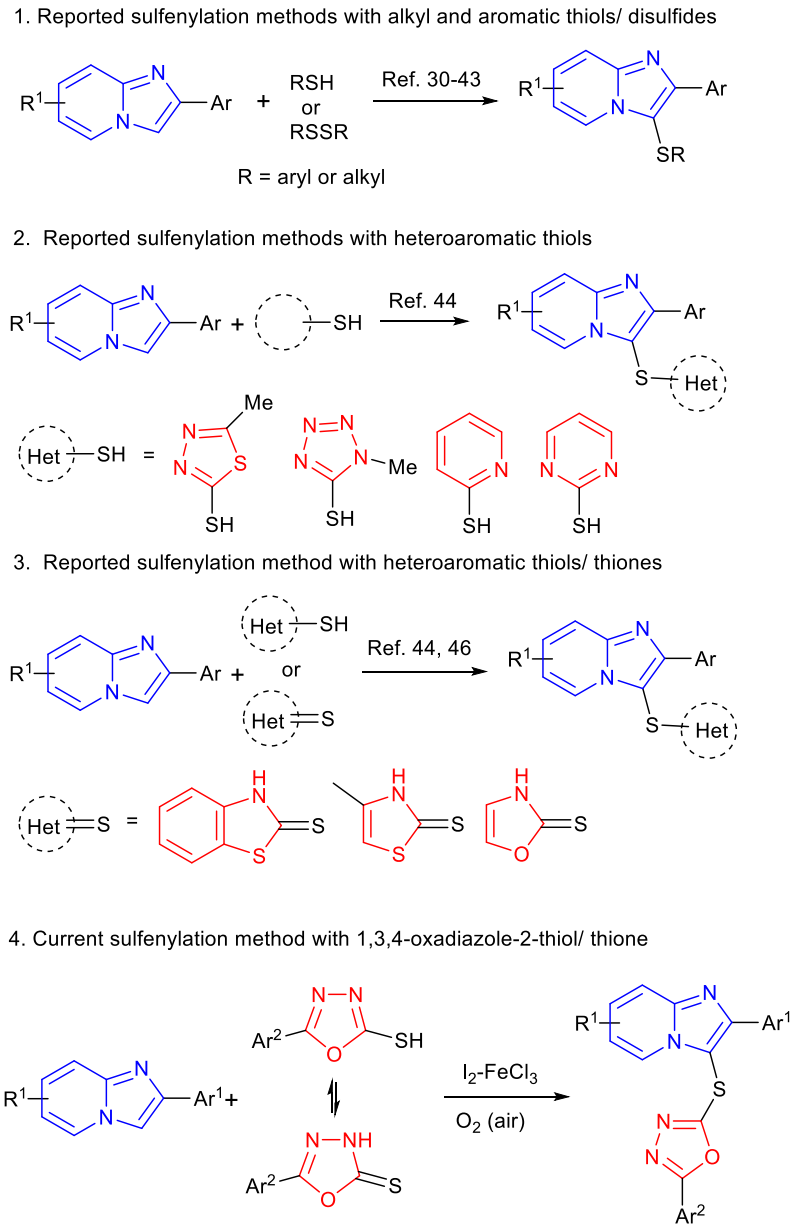
Like imidazo[1,2-a]pyridine, 1,3,4-oxadiazole is also a privileged scaffold and displays diverse biological activities such as anti-cancer,[15] antimicrobial, anti-inflammatory, etc.[16] The 1,3,4-oxadiazole skeleton is found in several commercially available drugs such as furamizole (antimicrobial), raltegravir (antiviral) and nesapidil (antihypertensive) (Figure 1). Many 1,3,4-oxadiazole derivatives are known for their herbicidal, insecticidal and fungicidal activities, and act as plant protection agents.[17] Oxadiazoles are considered as amide and ester bio isosteres.[18] Oxadiazole is capable of mimicking any local pair of amino acids in any secondary structure hence used as universal peptidomimetics.[19] Oxadiazoles also find use in materials development. The 1,2-diazole unit in oxadiazoles acts as an electron withdrawing group hence used in various types of conducting systems.[20] Oxadiazole derivatives have potential applications in organic light emitting diodes, laser dyes, optical brighteners and scintillators.[21]

Molecular hybridization is the quickest possible way to conjugate two different scaffolds which can drastically alter the properties of individual components and also can open up new avenues of pharmacological properties or material characteristics.[22] The development of molecular hybrid drugs with two or more pharmacophores can potentially overcome drug resistance. It can also reduce the side effects through multiple mechanisms of action. We have developed oxadiazole-urea hybrids as RECQL5 helicase inhibitors and anticancer agents having excellent cell permeability and cytotoxicity.[23] Very recently, we have reported the synthesis of thioether linked indole-oxadiazole molecular hybrids (MHs) and also shown their promising anti-proliferative activities against human breast carcinoma MCF-7 cell line.[24]

Bio-active MHs of imidazo[1,2-a]pyridine and 1,3,4-oxadiazole are not very uncommon. A series of imidazopyridine-oxadiazole hybrids have been reported for 5-HT_4 receptor partial agonist activity which can be useful in the treatment of Alzheimer's disease.[25] The imidazopyridine-oxadiazole hybrids have also been shown as anticancer agents.[26] Sometimes, a thioether linkage is critical for the bioactivities of many pharmacophores.[27] Imidazo[1,2-a]pyridine MHs linked at C-3 by a thioether to aryl and heteroaryl systems are also being reported with various biological activities.[28] The C-3 position in imidazo[1,2-a]pyridines is comparatively electron rich. Therefore, reaction with reactive electrophiles or radicals normally occurs at this position.[29]

Aryl or alkyl sulfenylated at C-3 of imidazo[1,2-a]pyridine have been achieved using commonly used sulfenylating agents (Scheme 1; entry 1) such as disulfides,[30] thiols,[31] sulfenyl chlorides,[32] sulfinates,[33] and sulfonyl hydrazines.[34] Phenyliodine bis(trifluoroacetate)-promoted oxidative intermolecular C–S cross-coupling of imidazopyridines with aryl thiols gave 3-arylsulfenylated imidazo[1,2-a]pyridines.[35] The direct sulfenylation of 2-aryl substitutituted imidazo[1,2-a]-pyridine with aryl and alkyl thiols in the presence of N-chlorosuccinimide (NCS) produced 2-aryl-3-(aryl/alkylthio)imidazo[1,2-a]pyridines.[36] Sulfenylation of imidazo[1,2-a]pyridines at C-3 with aryl thiols by using the flavin-iodine dual catalytic system in an aerobic environment gave good yield of products.[37] Synthesis of thiolated imidazo[1,2-a]pyridines at C-3 position with arylthiols was catalyzed by potassium iodide and TBHP as stoichiometric oxidant.[38]

Thioarylations of imidazo[1,2-a]pyridines with diaryl disulphide (Scheme 1; entry 1) have been performed using transition metal catalysts.[39] Iodine-mediated sulfenylation at C-3 of imidazo[1,2-a]pyridines has been reported using sodium arylsulfenates-I_2/PPh_3 which goes via disulphide intermediate.[40] Both substituted imidazo[1,2-a]pyridines and substituted disulfides under NH_4I-catalyzed C–H bond chalcogenation provided the desired C-3 sulfenylated products.[41] The oxidative sulfurization of imidazo[1,2-a]pyridine derivatives with diaryl disulfides using N-bromosuccinimide was also realized.[42] The C-3 sulfenylation of imidazo[1,2-a]pyridine with diphenyl disulphide was catalyzed by CuI-BF_3.OEt_2.[43]



Scheme 1. C-3 Sulfenylation methods for imidazo[1,2-a]pyridines.

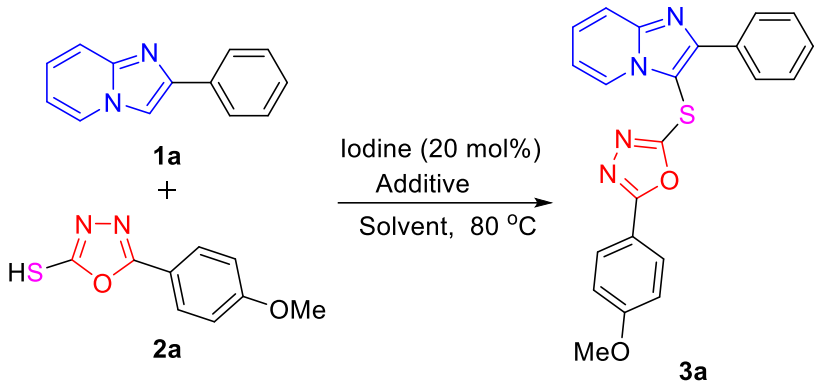
Most of the reported methods for 3-sulfenylation of imidazo[1,2-*a*]pyridine mentioned above mainly utilized arylthiols or disulfides. Sulfenylation with heterocyclic thiol compounds is a challenging task. The methods available for the sulfenylation using heteroaromatic thiols are rare (Scheme 1; entry 2).[44] Heteroaromatic thiol which remain equilibrium between tautomeric thione and thiol changes the reactivity pattern of thiol group compared to simple heteroaryl or aryl thiols.[45] The only report wherein both heteroaromatic thiols and thiones engaged in C-3 sulfenylation of imidazo[1,2-a]pyridine used I_2 as catalyst and DMSO as oxidant (Scheme 1; entry 3).[46] To the best of our knowledge, sulfenylation of imidazo[1,2-a]pyridine using using 1,3,4-oxadiazole-2-thiol has not been reported. Herein, we report a direct synthesis of imidazo[1,2-a]pyridine-1,3,4-oxadiazole MHs by C-3 sulfenylation of imidazo[1,2-*a*]pyridine with 5-aryl-1,3,4-oxadiazole-2-thiols/thiones for the first time using iodine-$FeCl_3$ as a non-toxic, inexpensive catalyst system and aerial oxygen as benign oxidant (Scheme 1; entry 4).

Results and Discussion

To prepare molecular hybrids of imidazo[1,2-a]pyridine and 1,3,4-oxadiazole connected the former at C-3 and the later at C-2 through a thioether linkage, it was essential to establish the conditions for C-3 sulfenylation of imidazo[1,2-a]pyridine with 1,3,4-oxadiazole-2-thiol. To optimize the reaction conditions, the reaction between 2-phenylimidazo[1,2-a]pyridine **1a** and 5-(4-methoxy)phenyl-1,3,4-oxadiazole-2-thiol **2a** was chosen as the model reaction (Table 1). When the reaction between stoichiometric amount of **1a** and **2a** was performed following the reported procedure[46] using 20 mol % iodine in DMSO (both as oxidant and solvent) at 80 °C for 8 h indeed gave the desired molecular hybrid **3a** albeit in low yield (Table 1, entry 1). The yield did not improve even when the reaction time or temperature (90 °C) was increased. The yield was not affected much when performed by using 20 mol % of iodine, DMSO (2 equivalent) and CH_3CN as solvent (Table 1, entry 2). Using stoichiometric amount of iodine, the yield of **3a** was improved to 65% but associated with the formation of a good amount of unidentified polar byproduct and the decomposition of thiol was also observed (Table 1, entry 3). Use of 20 mol % of iodine and different co-oxidants such as TBHP, H_2O_2, $K_2S_2O_8$ in CH_3CN also did not improve the yield of **3a** (Table 1, entries 4-6) to acceptable level. Copper salts have reported for positive effect in sulfenylation reactions.[44] Several copper salts such as $Cu(acac)_2$, $Cu(NO_3)_2$ and CuBr were screened as co-catalyst along with I_2 (Table 1, entries 7-9) without any beneficial effect.

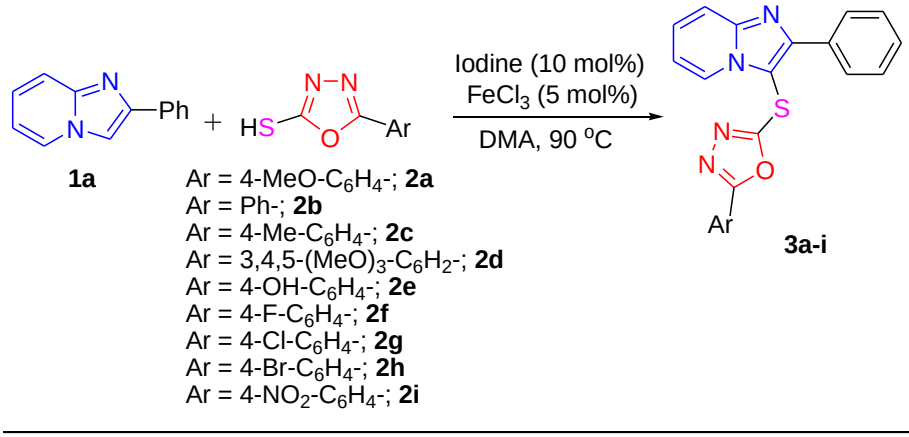
A Fe(III) salt/ I_2 catalyst system has been employed for sulfenylation of indole with aromatic thiols.[47] Iron salts are also relatively less toxic compared to many other metal salts and considered to be suitable for green and sustainable chemistry. This metal also possesses good redox properties and can liberate iodine on reaction with iodide salts.[48] Therefore, the sulfenylation reaction between imidazo[1,2-a]pyridine **1a** and 1,3,4-oxadiazole-2-thiol **2a** was performed in the presence of 5 mol % of $FeCl_3$ as co-catalyst in addition to 20 mol % of iodine as catalyst in acetonitrile at 80 °C. Gratifyingly, the yield of **3a** was increased to 86% (Table 1, entry 10). Other iron salts viz. $FeSO_4.7\ H_2O$ and $Fe(acac)_3$ also facilitated the reaction but the yield **3a** was less in comparison to $FeCl_3$ (Table 1, entries 11 & 12). We next turned our attention to select the best solvent for the reaction. Dichloroethane and DMSO (Table 1, entries 13 &14) gave similar result but the yield of **3a** was poor in 1,4-dioxane (Table 1, entry 15). The reaction did not proceed in water (Table 1, entry 16). Interestingly, when N,N-dimethylacetamide (DMA) was used as the solvent, the yield of **3a** was increased to 90% (Table1, entry 17). We optimized the reaction further in terms of catalyst loading and temperature. The iodine loading was decreased to 10 mol % and increasing the temperature to 90 ^oC for over 4 h, the yield was further improved to 92% (Table 1, entry 18). Further decrease in iodine quantity reduced the yield of **3a** (Table 1, entry 19). Iodine plays an important role in catalytic cycle and without it, little amount of product formation was observed (Table 1, entry 20). Therefore, the optimized reaction conditions is to use 1 equiv each of 2-phenylimidazo[1,2-a]pyridine **1a** and 5-(4-methoxy)phenyl-1,3,4-oxadiazole-2-thiol **2a**, 10 mol % iodine, 5 mol % $FeCl_3$ and DMA as solvent at 90 °C over 4 h which gave the desired MH product **3a** in 92% yield (Table 1, entry 18).

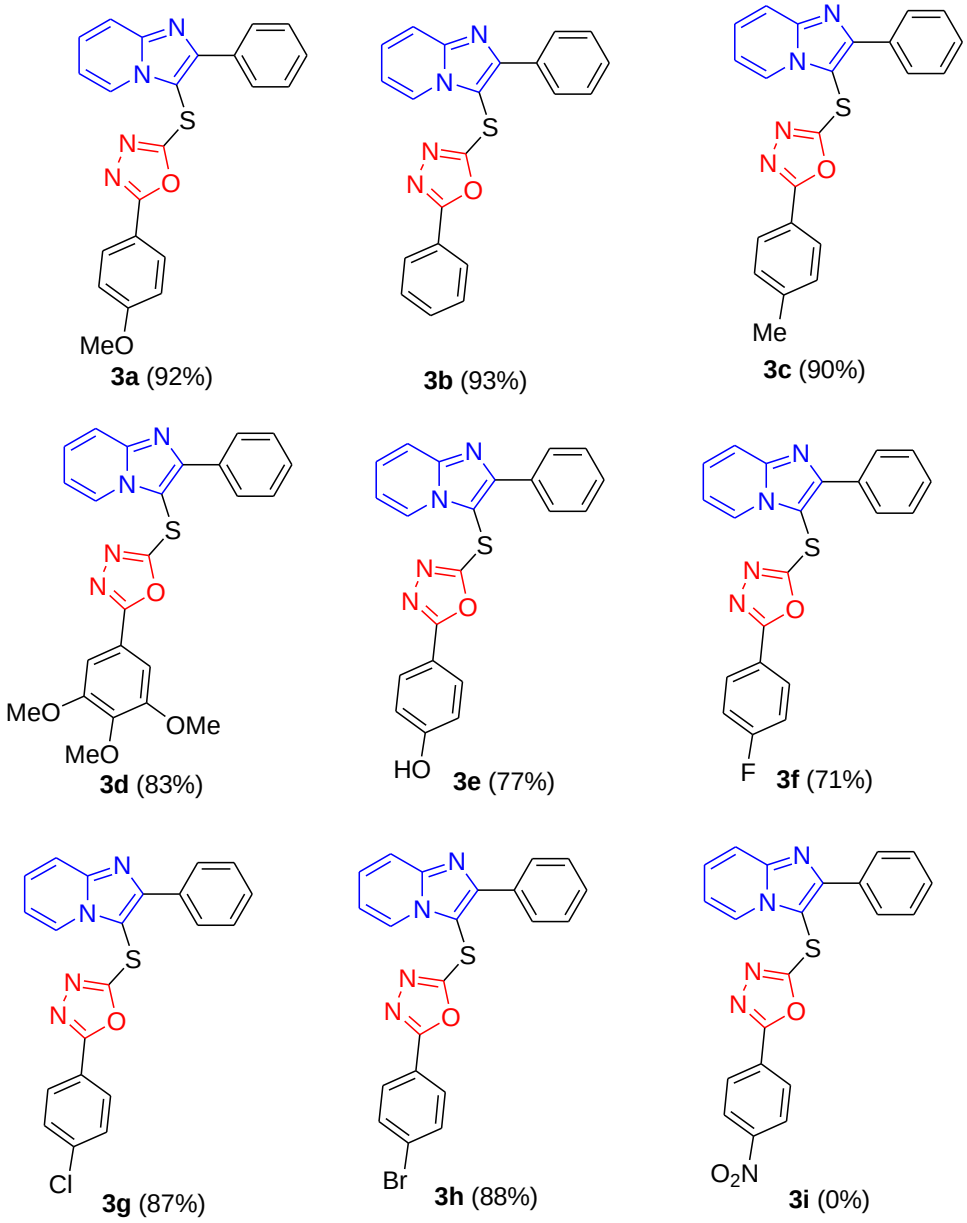
Table 1. Optimization of sulfenylation reaction



Entry	Additive	Solvent	Time	Yield[a,b]
1	____	DMSO	8 h	42%
2	DMSO (2 equiv)	CH_3CN	8 h	45%
3[c]	DMSO (2 equiv)	CH_3CN	8 h	65%
4	TBHP (2 equiv)	CH_3CN	4 h	61%
5	H_2O_2 (2 equiv)	CH_3CN	4 h	38%
6	$K_2S_2O_8$ (2 equiv)	CH_3CN	4 h	44%
7	$Cu(acac)_2$ (5 mol %)	CH_3CN	4 h	43%
8	$Cu(NO_3)_2.3H_2O$ (5 mol%)	CH_3CN	4 h	40%
9	CuBr (5 mol %)	CH_3CN	4 h	38%
10	$FeCl_3$ (5 mol %)	CH_3CN	4 h	86%
11	$FeSO_4.7H_2O$ (5 mol %)	CH_3CN	4 h	71%
12	$Fe(acac)_3$ (5 mol %)	CH_3CN	4 h	55%
13	$FeCl_3$ (5 mol%)	DCE	4 h	79%
14	$FeCl_3$ (5 mol %)	DMSO	4 h	80%
15	$FeCl_3$ (5 mol %)	1,4-dioxane	4 h	75%
16	$FeCl_3$ (5 mol %)	H_2O	4 h	N.R.
17	$FeCl_3$ (5 mol %)	DMA	4 h	90%
18[d]	$FeCl_3$ (5 mol %)	DMA	4 h	92%
19[e]	$FeCl_3$ (5 mol %)	DMA	4 h	81 %
20[f]	$FeCl_3$ (5 mol %)	DMA	4 h	26%

[a]Reaction Conditions: **1a** (0.2 mmol) and **2a** (0.2 mmol), iodine (20 mol %), additive, solvent (1.5 mL), 80 °C, 4 h; [b]Isolated yield; [c]Iodine (100 mol %); [d]Iodine (10 mol %) at 90 °C; [e]Iodine (5 mol %); [f]In absence of iodine.





Scheme 2. Synthesis of MHs from imidazo[1,2-a]pyridine **1a** and 5-aryl-1,3,4-oxadiazole-2-thiols **2a-i**.

With the optimized reaction procedure, the scope of reaction was explored between imidazo[1,2-a]pyridine **1a** and 5-aryl-1,3,4-oxadiazole-2-thiols **2a-i** having aryl groups with varying electronic substituents (Scheme 2). The MHs **3a**-**3h** were obtained in good to excellent yield (71-93%) and in all cases the C-3 sulfenylated regioisomer was formed exclusively. This is in accordance with the electron rich nature at C-3 of imidazo[1,2-a]pyridine where electrophilic attack takes place. Amongst the 5-aryl-1,3,4-oxadiazole-2-thiols, 5-phenyl-1,3,4-oxadiazole-2-thiol **2b** reacted with **1a** and the MH **3b** has been isolated in highest yield (93%). The reactions of 5-aryl-1,3,4-oxadiazole-2-thiols having aryl group bearing electron donating substituents like OMe and Me took place smoothly and corresponding MHs **3a** and **3c** (Figure 2) obtained in excellent yield. In case of thiols having aryl group such as 3,4,5-trimethoxyphenyl and 4-hydroxyphenyl, the reactions also occurred smoothly but took slightly longer reaction time (6-7 h) for completion providing MHs **3d** & **3e** in 83% and 77% yield, respectively. Reaction of 4-flurophenyl-1,3,4-oxadiazole-2-thiol **2f** with **1a** produced the MH **3f** in 71% yield. Whereas 4-chlrophenyl and 4-bromophenyl substituted thiols gave excellent yield of MHs **3g** in 87% and **3h** in 88%, respectively. Unfortunately, the reaction did not progress with 4-nitrophenyl-1,3,4-oxadiazole-2-thiol **2i**.

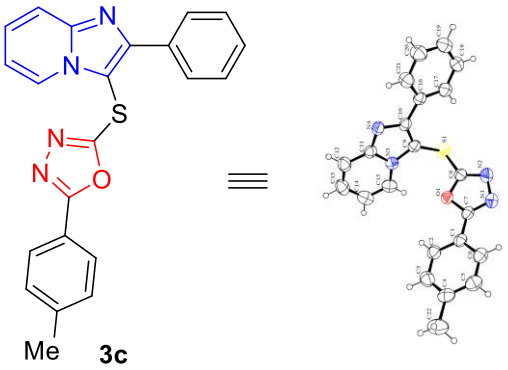


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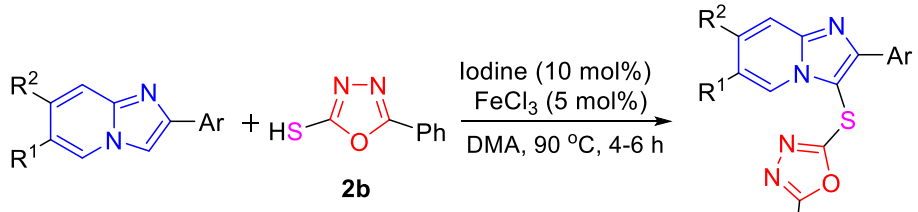
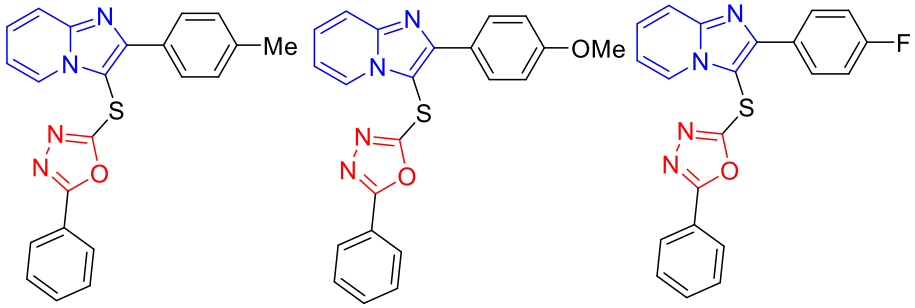
Figure 2. X-Ray crystal structure of **3c.**

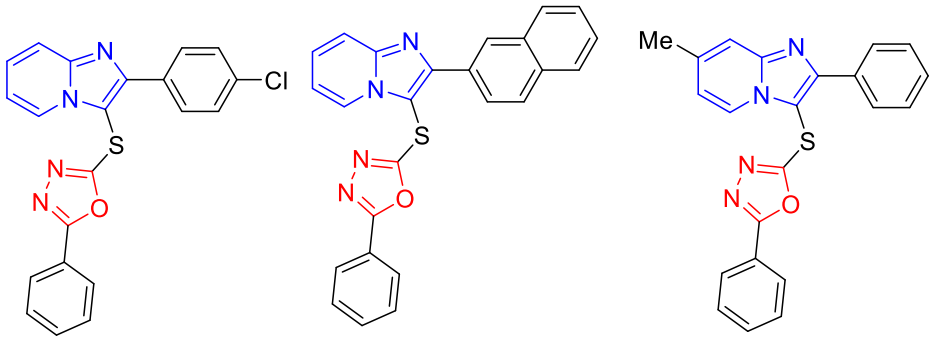
To find out the generality of the methodology, we next explored the reaction of 5-phenyl-1,3,4-oxadiazole-2-thiol **2b** with a few imidazo[1,2-*a*]pyridine **1** derivatives where the 2-aryl group in imidazole ring of imidazo[1,2-a]pyridine has substituents with varying electronic properties and in two cases the pyridine ring is substituted with a Me group at two different positions (Scheme 3). The reaction of thiol **2b** with imidazo[1,2-a]pyridine derivatives having 2-aryl groups such as 4-methylphenyl, 4-methoxyphenyl, 4-fluorophenyl, 4-chlorophenyl and naphth-2-yl smoothly reacted and produced the desired MHs **4a**-**4e** in good to excellent yield. Electron donating 4-methylphenyl and 4-methoxyphenyl groups furnished the MHs **4a** and **4b** with excellent yield 94% and 90%, respectively. Electron withdrawing substituents in the C-2 aryl group such 4-fluorophenyl influenced the reaction negatively with increase in reaction time to 6 h and the MH **4c** was obtained in 68% yield. 4-Chlorophenyl and naphth-2-yl substituent have performed well in the reaction and the corresponding MHs **4d** and **4e** were isolated in 81% and 88% yield, respectively. Imidazo[1,2-a]pyridine having methyl substituents either at C-6 or C-7 position of the pyridine ring and a phenyl substituent at C-2 of the imidazole ring reacted well with 5-phenyl-1,3,4-oxadiazole-2-thiol **2b**, and furnished the corresponding MHs **4f** and **4g** in 90% and 91% yield, respectively.



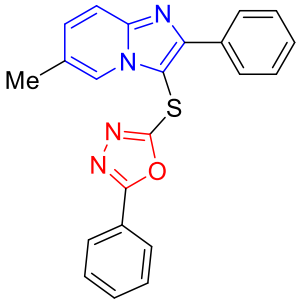
Ar = 4-Me-C_6H_4-, R^1,R^2 = H; **1b**
Ar = 4-MeO-C_6H_4-, R^1,R^2 = H; **1c**
Ar = 4-F-C_6H_4-, R^1,R^2 = H; **1d**
Ar = 4-Cl-C_6H_4-, R^1,R^2 = H; **1e**
Ar = 2-Napth-, R^1,R^2 = H; **1f**
Ar = Ph, R^1= H, R^2 = Me; **1g**
Ar = Ph, R^1= Me, R^2 = H; **1h**



4a (94%) **4b** (90%) **4c** (68%)



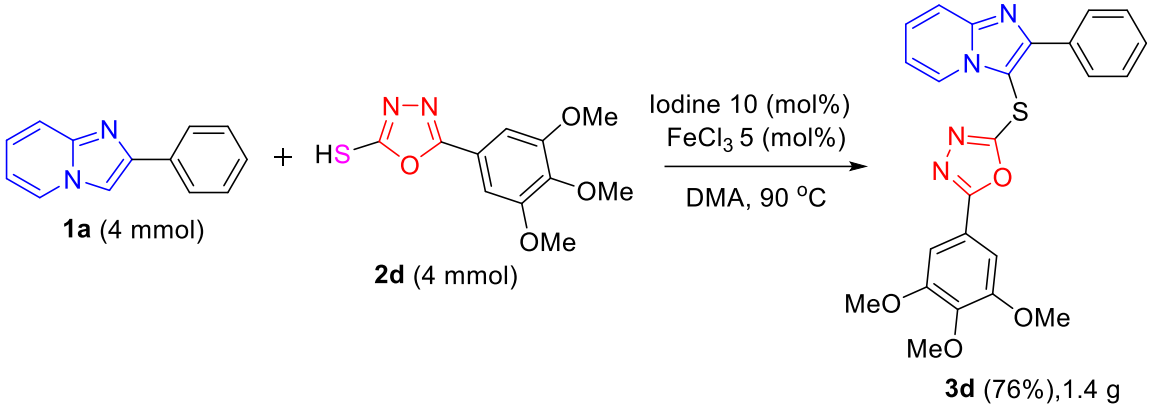
4d (81%) **4e** (88%) **4f** (90%)



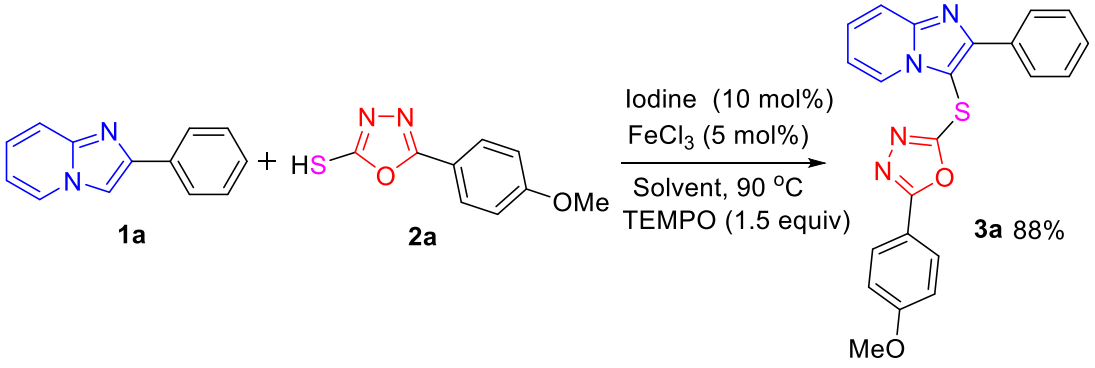
4g (91%)

Scheme 3. Synthesis of MHs from 5-phenyl-1,3,4-oxadiazole-2-thiol **2b** and imidazo[1,2-a]pyridine derivatives **1b-h**.

To show the utility of the methodology, **3d** was synthesised in gram scale (Scheme 4) using 4 mmol of imidazo[1,2-a]pyridine **1a** and 4 mmol of 5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole-2-thiol **2d** under the optimized conditions in 60 mL pressure tube (air atmosphere). After work-up, pure **3d** was obtained in 76% yield (1.4 g) just by simple filtration through a silica gel column. Therefore, this protocol can be used as a practical method for the synthesis of MHs made up of thioether linked imidazo[1,2-a]pyridine and 1,3,4-oxadiazole which might find use in medicinal chemistry and materials development.



Scheme 4. Gram scale synthesis.



Scheme 5. Control experiment in the presence of TEMPO.

The mechanism of sulfenylation of 2-arylimidazo[1,2-a]pyridines with alkyl/aryl thiols using iodine as catalyst have been explained via disulfide formation[46] or sulfenyl iodide.[50] From our earlier experience,[26] the formation of disulfide from 5-ary-1,3,4-oxadiazole-2-thiol could not be observed when treated with iodine even at elevated temperature. To get further insight into the reaction mechanism, the reaction of 2-phenylimidazo[1,2-a]pyridine **1a** and 5-methoxy-1,3,4-oxadiazole-2-thiol **2a** was performed under the standard conditions in the presence of 1.5 equiv of TEMPO as a radical inhibitor. Interestingly, the reaction proceeds well to form **3a** in 88% yields indicating that the reaction is not proceeding through a radical mechanism (Scheme 5). So, the most plausible mechanism of the reaction is presented in Figure 3. Molecular iodine reacts with 5-methoxy-1,3,4-oxadiazole-2-thiol **2a** to give sulfenyl iodide **A** and a molecule of HI. 2- Phenylimidazo[1,2-a]pyridine **1a** then undergoes an electrophilic substitution with the sulfenyl iodide **A** producing product **3a** and another molecule of HI. The HI molecules then oxidized by Fe(III) to give I_2 which then continues the catalytic cycle while Fe(II) undergoes oxidation by areal O_2 to give back Fe(III) and the process continues.

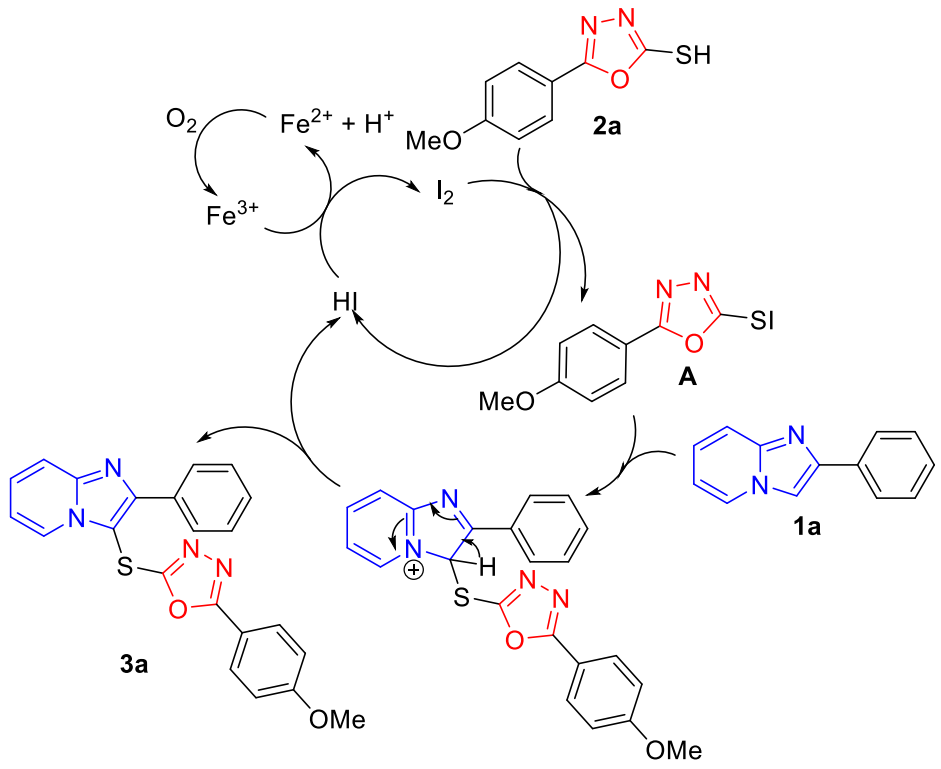


Figure 3. Plausible reaction mechanism.

Conclusions

In summary, we have developed a regioselective C-3 sulfenylation of 2-arylimidazo[1,2-a]pyridines with 5-aryl-1,3,4-oxadiazole-2-thiols for the synthesis of novel imidazopyridine-oxadiazole MHs using iodine-$FeCl_3$ catalyst system and aerial O_2 co-oxidant. To the best of our knowledge, this is the first report of sulfenylation of 2-arylimidazo[1,2-a]pyridines using 5-aryl-1,3,4-oxadiazole-2-thiols and also under such conditions. The MHs are interesting compounds and might find applications in medicinal chemistry and in materials development. The optimization of structures and evaluation of such properties are under active consideration.

Experimental Section

General. The reagents and chemicals were procured from Sigma Aldrich and Spectrochem (India) Ltd. (SRL), and used as such. TLC was examined on pre-coated aluminum plates (G/UV_{254}). The column chromatographic separation was conducted on silica gel (SRL; 230–400 mesh). ^1H and ^{13}C NMR spectra were recorded on Bruker spectrometers at operating ^1H frequencies of 300 MHz and ^{13}C frequencies of 75 MHz as mentioned in the individual spectrum. The spectra were referenced to residual protic solvent. The melting points were recorded in open-ended capillary tubes on a Digital melting-point apparatus (Buchi M560). Infrared (IR) spectroscopy was recorded using TENSOR II Bruker spectrophotometer. High Resolution Mass Spectrometric (HRMS) analysis was done using 6540 UHD Accurate-Mass Agilent Q-TOF LC/MS instrument. Single crystal X-ray crystallographic analysis was done using CrysAlisPRO, Oxford Diffraction /Agilent Technologies UK Ltd, Yarnton, England.

General procedure for synthesis 3a-h, 4a-g as exemplified for compound 3a. A solution of 2-arylimidazo[1,2-a]pyridine **1a** (48.5 mg, 0.25 mmol), 5-(4-methoxy)phenyl-1,3,4-oxadiazole-2-thiol **2a** (52.0 mg, 0.25 mmol), iodine (6.3 mg, 10 mol %) and $FeCl_3$ (2 mg, 5 mol %) in DMA (1 mL) was stirred at 90 °C for 4 h in a 15 mL teflon capped pressure tube. After completion of the reaction (monitored by TLC) resulting mixture was successively worked-up using aqueous solution of sodium thiosulfate pentahydrate-ethyl acetate. The organic phase was then dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude product was purified by silica gel column chromatography using petroleum ether and ethyl acetate (3:2) as the eluent to afford pure **3a** (91 mg, 92%).

2-(4-methoxyphenyl)-5-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-1,3,4-oxadiazole (3a). White solid (91 mg, 92% yield); mp 150.1 - 151.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.52 (d, *J* 6.9 Hz, 1 H), 8.18 (d, *J* 7.5 Hz, 2 H), 7.79 - 7.72 (m, 3 H), 7.53-7.37 (m, 4 H), 7.01 (t, *J* 6.9 Hz, 1 H), 6.91 (d, *J* 8.4 Hz, 2 H), 3.82 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6, 162.6, 159.5, 152.5, 147.7, 132.8, 129.0, 128.8, 128.6, 127.4, 124.7, 117.9, 115.6, 114.5, 113.7, 99.8, 55.4; IR (neat, ν_{max} cm^{-1}): 1608, 1479, 1264, 1016, 751, 692; HRMS (ESI): Calculated for $C_{22}H_{17}N_4O_2S$ [M + H$^+$] 401.1072, found 401.1078.

2-phenyl-5-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)-1,3,4-oxadiazole (3b). White crystalline solid (86 mg, 93% yield); mp 162.8 – 163.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.52 (d, *J* 6.6 Hz, 1 H), 8.17 (d, *J* 7.2 Hz, 2 H), 7.86 (d, *J* 6.9 Hz, 2 H), 7.76 (d, *J* 9.0 Hz, 1 H), 7.54 – 7.40 (m, 7 H), 7.04 (t, *J* 6.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.7, 160.3, 152.6, 147.8, 132.8, 132.0, 129.1, 128.8, 128.6, 127.5, 126.8, 124.7, 123.2, 118.0, 113.7, 99.5; IR (neat, ν_{max} cm^{-1}): 1470, 1342, 1166, 764, 692; HRMS (ESI): Calculated for $C_{21}H_{14}N_4OS$ [M + H$^+$]: 371.0961, found 371.0966.

2-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-5-(*p*-tolyl)-1,3,4-oxadiazole (3c). Off white crystalline solid (86 mg, 90% yield); mp 163.4 – 164.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.59 (d, *J* 6.6 Hz, 1 H), 8.21 (d, *J* 6.6 Hz, 2 H), 7.99 (d, *J* 8.7 Hz, 1 H), 7.74 (d, *J* 8.4 Hz, 2 H), 7.58-7.47 (m, 4 H), 7.25 (d, *J* 8.1 Hz, 2 H), 7.16 (t, *J* 6.6 Hz, 1 H), 2.39 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.8, 159.9, 152.5, 147.7, 142.7, 132.8, 129.8, 129.0, 128.8, 128.6, 127.5, 126.7, 124.7, 120.4, 117.9, 113.7, 99.7, 21.6; IR (neat, ν_{max} cm^{-1}): 1609, 1472, 1436, 1339, 1070, 731, 698; HRMS (ESI): Calculated for $C_{22}H_{17}N_4OS$ [M + H$^+$] 385.1123, found: 385.1125.

2-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole (3d). White solid (95 mg, 83% yield); mp 170.8 – 171.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.61 (d, *J* 6.6 Hz, 1 H), 8.23 (d, *J* 6.6 Hz, 2 H), 8.05 (d, *J* 8.7 Hz, 1 H), 7.62-7.48 (m, 4 H), 7.22 (t, *J* 6.6 Hz, 1 H), 7.07 (s, 2 H) 3.88 (s, 3 H), 3.84 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6, 160.0, 153.6, 152.5, 147.7, 141.4, 132.7, 129.1, 128.7, 128.5, 127.4, 124.8, 118.1, 118.0, 113.7, 104.0, 99.6, 61.0, 56.3; IR (neat, ν_{max} cm^{-1}): 1594, 1428, 1234, 739, 688; HRMS (ESI): Calculated for $C_{24}H_{21}N_4O_4S$ [M + H$^+$] 461.1283, found: 461.1284.

4-(5-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-1,3,4-oxadiazol-2-yl)phenol (3e). White solid powder (74 mg, 77% yield); mp 244.3 – 245.9 °C; ^{1}H NMR (300 MHz, DMSO- d_6) δ (ppm) 8.70 (d, *J* 6.0 Hz, 1 H), 8.29 (s, 1 H), 8.11 (d, *J* 6.6 Hz, 2 H), 7.80 (d, *J* 8.7 Hz, 1 H), 7.67 (d, *J* 7.8 Hz, 2 H), 7.58 – 7.44 (m, 4 H), 7.18 (t, *J* 6.0 Hz, 1 H), 6.89 (d, *J* 7.8 Hz, 2 H); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 166.5, 161.3, 159.8, 151.2, 147.4, 133.2, 129.4, 129.0, 128.9, 128.8, 128.5, 126.1, 117.7, 116.6, 114.4, 100.2, 79.6; IR (neat, ν_{max} cm^{-1}): 3008, 1610, 1480, 1234, 836, 735; HRMS (ESI): Calculated for $C_{21}H_{15}N_4O_2S$ [M + H$^+$] 387.0915, found: 387.0919.

2-(4-fluorophenyl)-5-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)-1,3,4-oxadiazole (3f).

Off White solid (68 mg, 71% yield); mp 170.6 – 171.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.57 (d, *J* 6.3 Hz, 1 H), 8.20 (d, *J* 7.2 Hz, 2 H), 7.99 (d, *J* 6.0 Hz, 1 H), 7.89 – 7.84 (m, 2 H), 7.58 -7.45 (m, 4 H), 7.16-7.11 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.8, 164.9 (d, $J_{C\text{-}F}$ 252.7 Hz), 160.4, 152.6, 147.7, 132.7, 128.9 (d, $J_{C\text{-}F}$ 33 Hz),

128.7, 128.6, 127.5, 124.7, 119.5, 118.0, 116.6, 116.3, 113.8, 99.4; IR (neat, ν_{max} cm^{-1}): 1603, 1464, 1225, 734, 616; HRMS (ESI): Calculated for $C_{21}H_{14}FN_4OS$ [M + H^+] 389.0872, found: 389.0878.

2-(4-chlorophenyl)-5-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-1,3,4-oxadiazole (3g). White crystalline solid (88 mg, 87% yield); mp 186.7 – 187.8 °C; ^{1}H NMR (300 MHz, DMSO- d_6) δ (ppm) 8.69 (d, *J* 6.6 Hz, 1 H), 8.11 (d, *J* 7.5 Hz, 2 H), 7.82 (t, *J* 8.7 Hz, 3 H), 7.61 (d, *J* 8.7 Hz, 2 H), 7.55 – 7.41 (m, 4 H), 7.17 (t, *J* 6.6 Hz, 1 H); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 165.5, 161.3, 151.4, 147.5, 137.3, 133.1, 130.1, 129.4, 129.0, 128.8, 128.6, 126.2, 122.3, 117.7, 114.4, 99.7; IR (neat, ν_{max} cm^{-1}): 1603, 1440, 1152, 752, 690; HRMS (ESI): Calculated for $C_{21}H_{14}ClN_4OS$ [M + H^+]: 405.0576, found: 405.0592.

2-(4-bromophenyl)-5-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-1,3,4-oxadiazole (3h). White solid (98 mg, 88% yield); mp 205.1 – 206.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.49 (d, *J* 6.9 Hz, 1 H), 8.16 (d, *J* 6.9 Hz, 2 H), 7.76-7.68 (m, 3 H), 7.58-7.39 (m, 6 H), 7.02 (t, *J* 6.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.9, 160.6, 152.7, 147.8, 132.7, 132.4, 129.1, 128.7, 128.6, 128.1, 127.5, 126.8, 124.7, 122.1, 118.0, 113.8, 99.2; IR (neat, ν_{max} cm^{-1}): 1629, 1472, 1338, 1071, 732, 691; HRMS (ESI): Calculated for $C_{21}H_{14}BrN_4OS$ [M + H^+]: 449.0071, found: 449.0065.

2-phenyl-5-((2-(*p*-tolyl)imidazo[1,2-*a*]pyridin-3-yl)thio)-1,3,4-oxadiazole (4a). Off white solid (90 mg, 94% yield); mp 174.1 – 175.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.50 (d, *J* 6.9 Hz, 1 H), 8.08 (d, *J* 7.8.1 Hz, 2 H), 8.84 (d, *J* 7.5 Hz, 2 H), 7.74 (d, *J* 9.0 Hz, 1 H), 7.51 – 7.30 (m, 6 H), 7.01 (t, *J* 6.9 Hz, 1 H), 2.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6, 160.4, 152.6, 147.7, 139.1, 132.0, 129.8, 129.3, 129.0, 128.6, 127.4, 126.8, 124.7, 123.2, 117.9, 113.6, 99.2, 21.4; IR (neat, ν_{max} cm^{-1}): 1632, 1549, 1342, 1068, 765, 692; HRMS (ESI): Calculated for $C_{22}H_{17}N_4OS$ [M + H^+]: 385.1123, found: 385.1127.

2-((2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)thio)-5-phenyl-1,3,4-oxadiazole (4b). White crystalline solid (89 mg, 90% yield); mp 138.4 – 139.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.52 (d, *J* 6.6 Hz, 1 H), 8.17 (d, *J* 8.7 Hz, 2 H), 7.86 – 7.82 (m, 3 H), 7.50 – 7.40 (m, 4 H), 7.09 – 7.02 (m, 3 H), 3.86 (s, 3 H); ^{13}C NMR (75 MHz,$CDCl_3$) δ (ppm) 166.6, 160.5, 160.4, 152.4, 147.7, 132.0, 130.1, 129.0, 127.4, 126.8, 125.3, 124.6, 123.2, 117.7, 114.0, 113.5, 98.6, 55.3; IR (neat, ν_{max} cm^{-1}): 1606, 1539, 1469, 1246, 1027, 747, 689; HRMS (ESI): Calculated for $C_{22}H_{17}N_4O_2S$ [M + H^+]: 401.1072, found: 401.1077.

2-((2-(4-fluorophenyl)imidazo[1,2-*a*]pyridin-3-yl)thio)-5-phenyl-1,3,4-oxadiazole (4c). White solid (66 mg, 68% yield); mp 162.5 – 163.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.52 (d, *J* 6.6 Hz, 1 H), 8.18 (t, *J* 5.4 Hz, 2 H), 7.86 (d, *J* 7.5 Hz, 2 H), 7.75 (d, *J* 8.7 Hz, 1 H), 7.53 – 7.40 (m, 4 H), 7.20 (t, *J* 8.4 Hz, 2 H), 7.04 (t, *J* 6.6 Hz, 1 H); ^{13}C NMR (75 MHz,$CDCl_3$) δ (ppm) 166.7, 163.3 (d, $J_{C\text{-}F}$ 247.5 Hz), 160.2, 151.6, 147.7, 132.1, 130.6 (d, $J_{C\text{-}F}$ 8.2 Hz), 129.1, 128.9, 127.6, 126.8, 124.7, 123.1, 117.9, 115.8, 115.5 113.8, 99.3; IR (neat, ν_{max} cm^{-1}): 1602, 1468, 1224, 798, 693; HRMS (ESI): Calculated for $C_{21}H_{13}FN_4OS$ [M + H^+]: 389.0866, found: 389.0880

2-((2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)thio)-5-phenyl-1,3,4-oxadiazole (4d). White solid (82 mg, 81% yield); mp 187.8 – 188.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.52 (d, *J* 6.6 Hz, 1 H), 8.15 (d, *J* 8.4 Hz, 2 H), 7.86 (d, *J* 7.5 Hz, 2 H), 7.75 (d, *J* 9.0 Hz, 1 H), 7.51 – 7.41 (m, 6 H), 7.05 (t, *J* 6.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.7, 160.0, 151.3, 147.7, 135.1, 132.1, 131.3, 130.0, 129.1, 128.8, 127.7, 126.8, 124.7, 123.1, 118.0, 113.9, 99.7; IR (neat, ν_{max} cm^{-1}): 1555, 1347, 1184, 759, 679; HRMS (ESI): Calculated for $C_{21}H_{13}ClN_4OS$ [M + H^+]: 405.0571 , found: 405.0578.

2-((2-(naphthalen-2-yl)imidazo[1,2-*a*]pyridin-3-yl)thio)-5-phenyl-1,3,4-oxadiazole (4e). White solid (92 mg, 88% yield); mp 126.6 – 127.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.70 (s, 1 H), 8.56 (d, *J* 6.9 Hz, 1 H), 8.34 (d, *J* 7.5 Hz, 1 H), 7.97 (d, *J* 8.7 Hz, 2 H), 7.90 – 7.77 (m, 4 H), 7.53 – 7.50 (m, 2 H), 7.49 – 7.38 (m, 4 H), 7.05 (t, *J* 6.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.7, 160.2, 152.5, 147.8, 133.5, 133.3, 132.0, 130.2, 129.0, 128.7, 128.4, 128.2, 127.7, 127.6, 126.8, 126.7, 126.3, 126.0, 124.7, 123.2, 118.0, 113.8, 99.9; IR (neat, ν_{max} cm^{-1}): 1553, 1442, 1183, 748, 691; HRMS (ESI): Calculated for $C_{25}H_{17}N_4OS$ [M + H^+]: 421.1123, found: 421.1129.

2-((7-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-5-phenyl-1,3,4-oxadiazole (4f). White solid (86 mg, 90% yield); mp 211.4 – 212.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.37 (d, *J* 6.9 Hz, 1 H), 8.16 (d, *J* 7.8 Hz, 2 H), 7.85 (d, *J* 7.5 Hz, 2 H), 7.52-7.40 (m, 7 H), 6.85 (d, *J* 6.9 Hz, 1 H), 2.46 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6, 160.5, 152.6, 148.1, 138.8, 132.9, 132.0, 129.0, 128.9, 128.7, 128.5, 126.8, 123.8, 123.2, 116.5, 116.3, 98.6, 21.4; IR (neat, ν_{max} cm^{-1}): 1487, 1357, 1169, 770, 692; HRMS (ESI): Calculated for $C_{22}H_{16}N_4OS$ [M + H$^+$]: 385.1117, found: 385.1117.

2-((6-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)-5-phenyl-1,3,4-oxadiazole (4g). White solid (87 mg, 91% yield); mp 181.6 – 182.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.28 (s, 1 H), 8.16 (d, *J* 6.6 Hz, 2 H), 7.86 (d, *J* 6.9 Hz, 2 H), 7.65 (d, *J* 9.0 Hz, 1 H), 7.52 - 7.41 (m, 6 H), 7.28 – 7.24 (m, 1 H), 2.41 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6, 160.5, 152.4, 146.8, 132.9, 132.0, 130.5, 129.1, 128.9, 128.7, 128.5, 126.8, 123.7, 123.2, 122.5, 117.3, 98.9, 18.4; IR (neat, ν_{max} cm^{-1}): 1553, 1336, 1163, 772, 689; HRMS (ESI): Calculated for $C_{22}H_{16}N_4OS$ [M + H$^+$]:385.1117, found: 385.1117.

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Supplementary Material

Electronic Supplementary Information (ESI) available: Copy of ^{1}H and ^{13}C NMR spectra of products **3a-3h** and **4a-4g**, X-ray crystallographic data of compound **3c.**

References

1. Couty, F.; Evano, G.. In Comprehensive Heterocyclic Chemistry III; Katritzky, A. R.; Ramsden, C. A., Scriven, E. F. V.; Taylor, R. J. K., Eds.; Elsevier: Oxford, 2008; Vol. *11*, p 409−499.
2. Enguehard- Gueiffier, C.; Gueiffier, A. *Mini-Rev. Med. Chem.* **2007**, *7*, 888-899. http://dx.doi.org/10.2174/138955707781662645
3. Wan, J.; Zheng, C.-J.; Fung, M, -K.; Liu, X. – K.; Zheng, X, -H. *J. Mater. Chem.* **2012**, *22*, 4502-4510. https://doi.org/10.1039/C2JM14904D
4. Shono, H.; Ohkawa, T.; Tomoda, H.; Mutai, T.; Araki, K. *ACS Appl. Mater. Interfaces.* **2011**, *3*, 654-657. https://doi.org/10.1021/am200022z
5. John, A.; Shaikh, M.M.; Butcher, R. J.; Ghosh, P. *Dalton Trans.* **2010**, *39*, 7353-7363. https://doi.org/10.1039/C003174G
6. Song, G.; Zhang, Y.; Li, X. *Organometallics,* **2008**, *27*, 1936- 1943. https://doi.org/10.1021/om800109a
7. Guclu, D.; Kuzu, B.; Tozlu, I.; Taspinar, F.; Canpinar, H.; Taspinar, M.; Menges, N. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 2647-2651. https://doi.org/10.1016/j.bmcl.2018.06.033

8. Kamal, A.; Kumar, G.B.; Nayak, V.L.; Reddy, V.S.; Shaik, A.B.; Rajender; Reddy, M.K. *Med. Chem. Commun.* **2015**, *6*, 606-612. https://doi.org/10.1039/C4MD00400K
9. Feng, S.; Hong, D.; Wang, B.; Zheng, X.; Miao, K.; Wang, L.; Yun, H.; Gao, L.; Zhao, S.; Shen, H.C.; *ACS Med. Chem. Lett.* **2015**, *6*, 359-362. https://doi.org/10.1021/acsmedchemlett.5b00008
10. Moraski, G. C.; Markely, L. D.; Carmer, J.; Hipskind, P.A.; Boshoff. H.; Bailey, M. A.; Alling, T.; Ollinger, J.; Parish, Tanya.; Miller, J. *ACS Med. Chem. Lett.* **2013**, *4*, 675-679. https://doi.org/10.1021/ml400088y
11. Gudmundsson, K. S.; Boggs, S. D.; Catalano, J. G.; Svolto, A.; Spaltenstein, A.; Thomson, M.; Wheelan, P.; Jenkinson, S. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6399-6403. https://doi.org/10.1016/j.bmcl.2009.09.056
12. Cheng, Y.; Moraski, G. C.; Carmer, J.; Miller, M. J.; Schorey, J. S. *PLoS One* **2014**, *9*, e87483. https://doi.org/10.1371/journal.pone.0087483
13. Ulloora, S.; Shabaraya, R.; Adhikari, A. V. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 3368-3372. https://doi.org/10.1016/j.bmcl.2013.03.086
14. Glomb, T.; Szymankiewicz, K.; Swiatek, P. *Molecules*, **2018**, *23*, 3361. https://doi.org/10.3390/molecules23123361
15. Khaliullah, H.; Ahsan, M. J.; Hedaitullah, M.; Khan, S.; Ahmed, B. *Mini-Rev. Med. Chem.* **2012**, *12*, 789-801. https://doi.org/10.2174/138955712801264800
16. Luczynski, M.; Kudelko, A. *Appl. Sci.* **2022**, *12*, 3756. https://doi.org/10.3390/app12083756
17. Kumari, S.; Carmona, A. V.; Tiwari, A. K.; Trippier, P. C. *J. Med. Chem.* **2020**, *63*, 122290-12358. https://doi.org/10.1021/acs.jmedchem.0c00530
18. Ko, E.; Liu, J.; Perez, L. M.; Lu, G.; Schaefer, A.; Burgess, K. *J. Am. Chem. Soc.* **2011**, *133*, 462-477. https://doi.org/10.1021/ja1071916
19. Wroblowska, M.; Kudelko, A.; Kuznik, N.; Laba, K.; Lapkowski, M. *J. Heterocycl. Chem.* **2017**, *54*, 1550. https://doi.org/10.1002/jhet.2743
20. Chidirala, S.; Ulla, H.; Valaboja, A.; Kiran, M. R.; Mohanty, M. E.; Satyanarayan, M. N.; Umesh, G.; Bhanuprakash, K.; Rao, V. J. *J. Org. Chem*. **2016**, *81*, 603- 614. https://doi.org/10.1021/acs.joc.5b02423
21. Taber, R. L.; Boyd, T. *J. Heterocycl. Chem.* **1972**, *9*, 393-394. https://doi.org/10.1002/jhet.5570090235
22. Ivasiv, V.; Albertini, C.; Goncalves, A. E.; Rossi, M.; Bolognesi, M. *Curr. Top. Med. Chem.* **2019**, *19*, 1694 - 1711. http://dx.doi.org/10.2174/1568026619666190619115735
23. Chakraborty, S.; Dutta, K.; Gupta, P.; Das, A.; Das, A.; Ghosh, S. K.; Patro, B. S. *J. Med. Chem*. **2021**, *64*, 1524-1544. https://doi.org/10.1021/acs.jmedchem.0c01692
24. Dutta, K.; Guha Majumdar, A.; Kushwah, N.; Wadawale, A. P.; Patro, B. S.; Ghosh, S. K. *J. Heterocycl. Chem.* **2022**, *50*, 0000. https://doi.org/10.1002/jhet.4549
25. Nirogi, R.; Mohammed, A. R.; Shinde, A. K.; Gagginapally, R. S.; Kancharala, D. M.; Meddekadi, V. R.; Bogaraju, N.; Ravella, S. R.; Singh, P.; Birangal, S. R.; Subramanian, R.; Palacharla, R. C.; Bendade, V.;

Muddana, N,; Jayarajan, P. *J. Med. Chem.* **2018**, *11*, 4993-5008. https://doi.org/10.1021/acs.jmedchem.8b00457
26. Sigalpalli, D. K; Kiranmai, G.; Devi, G. P.; Tokala, R.; Sana, S.; Tripura, C.; Jadhav, G. S.; Kadagathur, M.; Shankaraiah, N.; Nagesh, N.; Babu, B. N.; Tangellamudi, N. D. *Bioorg. Med. Chem.* **2021**, *43*, 116277. https://doi.org/10.1016/j.bmc.2021.116277
27. Kadam, P. R.; Bodke, Y. D.; Naik, M. D.; Nagaraja, O.; Manjunatha, B. *Results in Chemistry* **2022**, *4*, 100303. https://doi.org/10.1016/j.rechem.2022.100303
28. Chitrakar, R.; Sistla, R.; Vadithe, L. N.; Subbarayappa, A. *Bioorg. Med. Chem. Lett.* **2021**, *49*, 128307. https://doi.org/10.1016/j.bmcl.2021.128307
29. Ravi, C.; Adimurthy, S. *Chem. Rec*. **2017**, *17*, 1-21. https://doi.org/10.1002/tcr.201600146
30. Rafique, J.; Saba, S.; Rosario, A. R.; Braga, A. L. *Chem. Eur. J.* **2016**, *22*, 11854- 11862. https://doi.org/10.1002/chem.201600800
31. Cao, H.; Chen, L.; Liu, J.; Cai, H.; Deng, H.; Chen, G.; Yan, C.; Chen, Y. *RSC Adv.* **2015**, *5*, 22356-22360. https://doi.org/10.1039/C5RA01342A
32. Ravi, C.; Mohan, D. C.; Adimurthy, S. *Org. Biomol. Chem.* **2016**, *14*, 2282-2290. https://doi.org/10.1039/C5OB02475G
33. Huang, X.; Wang, S.; Li, B.; Wang, X.; Ge, Z.; Li, R. *RSC Adv.* **2015**, *5*, 22654-22657. https://doi.org/10.1039/C4RA17237J
34. Bagdi, A. K.; Mitra, S.; Ghosh, M.; Hajra, A. *Org. Biomol. Chem.* **2015**, *13*, 3314-3320. https://doi.org/10.1039/C5OB00033E
35. Hamdouchi, C.; Sanchez, C.; Ezquerra, J. *Synthesis*, **1998**, *867*. https://doi.org/10.1055/s-1998-2078
36. Ravi, C.; Mohan, D. C.; Adimurthy, S. *Org. Lett*. **2014**, *16*, 2978-2981. https://doi.org/10.1021/ol501117z
37. Iida, H.; Demizu, R.; Ohkado, R. *J. Org. Chem*. **2018**, *83*, 12291-12296. https://doi.org/10.1021/acs.joc.8b01878
38. Kong, D.; Wang, Q.; Huang, T.; Liang, M.; Lin, Q.; Wu, M. *Tetrahedron*, **2019**, *75*, 1457- 1463. https://doi.org/10.1016/j.tet.2019.01.059
39. Ge, W.; Zhu, X.; Wei, Y.; *Euro. J. Org. Chem.* **2013**, *2013*, 6015-6020. https://doi.org/10.1002/ejoc.201300905
40. Guo, Y.-J.; Lu, S.; Tian, L.-l.; Huang, E.-L.; Hao, X.-q.; Zhu, X.; Shao, T.; Song, M.-P. *J. Org. Chem*. **2018**, *83*, 338-349. https://doi.org/10.1021/acs.joc.7b02734
41. Bettanin, L.; Saba, S.; Doerner, C. V.; Franco, M. S.; Godoi, M.; Rafique, J.; Braga, A. L. *Tetrahedron*, **2018**, *74*, 3971-3980. https://doi.org/10.1016/j.tet.2018.05.084
42. Maddi, R. R.; Shirsat, P. K.; Kumar, S.; Meshram, H. M. *Chemistry Select*, **2017**, *2*, 1544-1547. https://doi.org/10.1002/slct.201601460
43. Mohan, D. C.; Rao, S. N.; Ravi, C.; Adimurthy, S. *Asian. J. Org. Chem.* **2014**, *3*, 609 – 613. https://doi.org/10.1002/ajoc.201402004
44. Zheng, Z.; Qi, D.; Shi, L. *Cat. Commun.* **2015**, *66*, 83-86. http://dx.doi.org/10.1016/j.catcom.2015.03.023

45. Karpenko, Y.; Omelyyanchik, L.; Panasenko, T. *Chem. Chem. Technol.* **2018**, *12*, 419- 428. https://doi.org/10.23939/chcht12.04.419
46. Siddaraju, Y.; Prabhu, K. R. *J. Org. Chem.* **2016**, *81*, 7838- 7846. https://doi.org/10.1021/acs.joc.6b01487
47. Yadav, J. S.; Reddy, B. V. S.; Reddy, Y. J.; Praneeth, K. *Synthesis* **2009**, *9*, 1520- 1524. https://doi.org/10.1055/s-0028-1088035
48. Ujwaldev, S. M.; Rohit, K. R.; Harry, N. A.; Anilkumar, G. *Tetrahedron Lett.* **2019,** *60*, 150950. https://doi.org/10.1016/j.tetlet.2019.150950
49. Tehri, P.; Aegurula, B.; Peddinti, R. K. *Tetrahedron Lett.* **2017**, *58*, 2062-2065. https://doi.org/10.1016/j.tetlet.2017.04.043
50. Rahaman, R.; Das, S.; Barman, P. *Green Chem*. **2018**, *20*, 141-147. https://doi.org/10.1039/C7GC02906C