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ARTICLE

Thionyl chloride-mediated synthesis of 2-azaindolizine sulfur-bridged dimers by C—H bond direct chalcogenation of imidazo[1,5-*a*]pyridines

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Abstract

Thionyl chloride-mediated chalcogenation of imidazo[1,5-*a*]pyridine serves as a new protocol for the synthesis of rare bisimidazopyridyl sulfides. This method provides the new route to synthesis of 2-azaindolizine sulfur-bridged dimers called chalcogenide under metal-free, elemental sulfur-free conditions without the use of polar solvents in regio-selective manner, at room temperature with the simple operational procedure.

KEYWORDS

bis-imidazopyridyl sulfides, C—H activation, C—H chalcogenations, chlorination, thionyl chloride

1 | INTRODUCTION

Imidazo[1,5-*a*]pyridines are an important class of the heterocyclic compound due to widespread applications in medicinal chemistry and material science.[1] The imidazo[1,5-*a*]pyridines have been investigated as organic light-emitting diodes,[2] organic thin-layer field effect transistors,[3] precursors of *N*-heterocyclic carbenes,[4] and for their biological activity.[5] Also, the metal complexes of imidazo[1,5-*a*]pyridines were reported in the literature and imidazo[1,5-*a*]pyridine derivative explored for their applications in medicinal chemistry and material science. Similarly, diaryl chalogenide are an important class of the heterocyclic compounds known for their applications in medicinal chemistry and material science.[6]

Due to the importance of substituted imidazo[1,5-*a*]pyridine number of publications exploring C—H functionalization methods reported in recent years. In 2013, Patil et al. developed metal-free protocol for methylthiolation of imidazo heterocycles[1,2-*a*]pyridines using dimethyl sulfoxide (DMSO)/$POCl_3$ complex.[7] The room temperature C3 thiolation catalyzed by *N*-chlorosuccinimide was reported by Chitrakar Ravi et al.[8] Deng et al. developed metal-free thiocarbomylation of imidazopyridine using carbomyl chloride and elemental sulfur.[9]

Glover et al. synthesized the bis-imidazopyridyl sulfides (Figure 1) from imidazo[1,5-*a*]pyridine using sulfural chloride in diethyl ether.[10] Shibahara et al. reported formation of the rare bis-imidazopyridyl sulfides during synthesis of imidazo[1,5-*a*]pyridine by iodine-mediated oxidative desulfurization-promoted cyclization of *N*-2-pyridylmethyl thioamides along with desired product.[11] Further Shibahara et al. developed the copper(I) thiophenecarboxylate (CuTC)-catalyzed protocol for the synthesis of bis-imidazopyridyl sulfides from *N*-2-pyridylmethyl thioamides using in DMSO (Figure 1) in moderate to good yield and reported DMSO is a crucial solvent for reaction.[12] Recently, Abdul Shakoor et al.

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developed method for the iodine-mediated synthesis of bis-imidazopyridyl sulfides using Na_2S as chalcogenating agent[13] and very recently Lu-Lu Tian et al. optimized the copper-catalyzed method for synthesis of sulfur-bridged imidazopyridines using isothiocynate as sulfur source.[14] Due to the importance of diaryl chalcogenides in the field of pharmaceuticals as well as in material science[6] many chalcogenation methods were reported in the literature.[15–18] These methods commonly utilized aryl chalcogenols and chalcogenolates in association with aryl halides. Chan-Lam coupling has also been used through oxidative cross-coupling reaction aryl-substituted chalocogenolates or chalocogenols with phenyl boronic acid.[19] They have used elemental sulfur reacted with arenes in thermal condition and have required very high temperature 230°C. The product was obtained in a stoichiometric ratio of diaryl sulfides along with hydrogen sulfides.[20] Some of the researchers have recently reported the few methods for the preparation of sulfides in association with simple electrophile or nucleophile with elemental sulfur. The literature for C—H chalcogenation although high yielding, employs metal catalysts and requires high temperatures, polar solvents like DMSO.[12] This prompted us to explore the new method by using simplified reaction conditions.

2 | RESULTS AND DISCUSSION

As a part of our interest toward synthesis of heterocyclic compounds and explore their biological activities, we are attracted toward imidazo[1,5-*a*]pyridines. During our studies, we have developed two methods for 1-chlorination of imidazo[1,5-*a*] pyridines and chalcogenation of imidazo[1,5-*a*]pyridines through C—H activation by using a common reagent thionyl chloride. Herein, we report operationally simple, metal-free, elemental sulfur-free, room temperature method for the synthesis of bis-imidazopyridyl sulfides. Thionyl chloride serves both as catalyst and chalcogenating agent for bis-imidazopyridyl sulfide formation. This is an important reagent for the synthesis of carbon-sulfur bond, which makes them convenient reagent for chemical synthesis.

During our initial studies, exploring the thionyl chloride mediated chalcogenation of imidazo[1,5-*a*]pyridines, the reaction of (**3a**) using 3 eq. of thionyl chloride in dichloromethane at 25–30°C for 16 hr. produces 1-chloroimidazo [1,5-*a*]pyridines (**4a**) along with sulfur bridged imidazo[1,5-*a*]pyridine dimer (**5a**). The structure of both the compounds was in full agreement with spectral data. The key starting material, that is, imidazo [1,5-*a*]pyridines (**3a-e**) synthesized as per the reaction sequence is depicted in Scheme 1, starting from commercially available pyridin-2-ylmethanamine **1.** Pyridin-2-ylmethanamine **1** on reaction with substituted benzoyl chloride at 0–10°C in the presence of triethylamine produces *N*-(pyridin-2-ylmethyl)benzamide derivatives **2a-e** in 38 to 95% yield. Further **2a-e** on refluxing in $POCl_3$ for 4–6 hr produces imidazo [1,5-*a*]pyridines (**3a-e**) in 37–96% yield.

We have directed our chemistry efforts for the selective synthesis of sulfur-bridged imidazo[1,5-*a*]pyridine dimer (**5**), as a part of optimization (Table 1) we have carried out reaction in different solvents (Dichloromethane, Acetonitrile, 1,4-dioxane, Toluene, THF), different temperatures (0–40°C), and using different ratios of the thionyl chloride (0.5–10 eq.). On using the 2 (eq.) of thionyl chloride in dichloromethane (DCM) at 40°C yield 1-chloroimidazo[1,5-*a*] pyridines in good to excellent yield (up to 95%, Table 1, entry 13). By using an equivalent or lower concentration of thionyl chloride at 40°C, we observed the formation of

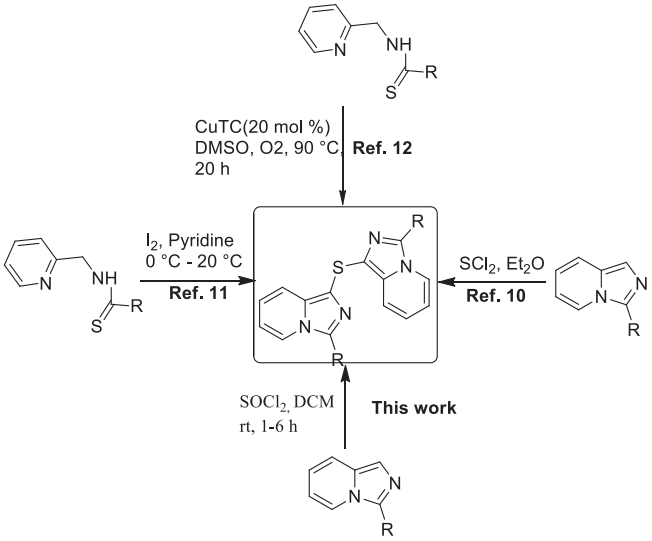
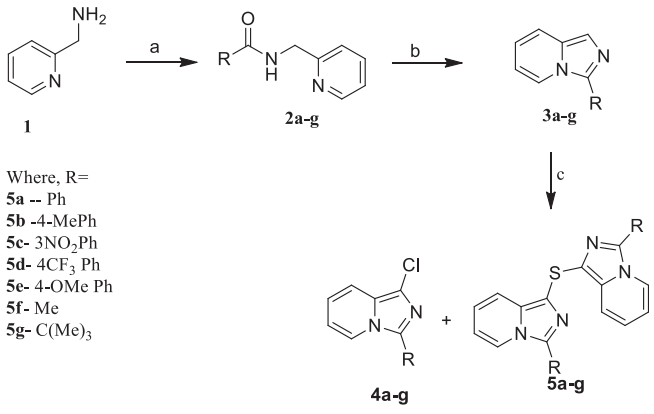
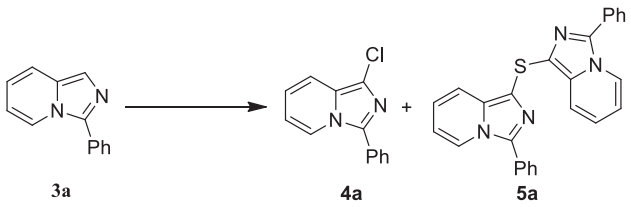


FIGURE 1 Approaches to synthesis of 2-azaindolizine sulfur-bridged dimers



SCHEME 1 Protocol for synthesis of 1-chloroimidazo [1,5-*a*] pyridines (**4**) and sulfur bridged imidazo[1,5-*a*]pyridine dimer (**5**). Reagents and Conditions: (a) RCOCl, TEA, dichloromethane, 0°C to 10°C, 1–2 hr; (b) POCl3, reflux, 4–6 hr; (c) SOCl2, dichloromethane, 25–30°C, 16 hr

TABLE 1 Optimization of reaction parameter



Sr. no.	Solvent	Mole ratio of $SOCl_2$	Temperature (°C)	Reaction time (hr)	(% conversion)[d] 4	5
1	Dichloromethane[b]	0.5 eq.	25	16	16.54	53.37
2	Dichloromethane	1.0 eq.	25	16	19.94	59.10
3	Dichloromethane	2.0	25	16	29.06	62.98
4	Dichloromethane	3.0	25	16	30.20	62.71
5	Dichloromethane	5.0	25	16	32.65	60.01
6	Dichloromethane	10.0	25	16	35.43	58.94
7	Neat	10.0	25	16	30.61	61.24
8	Acetonitrile	2.0	25	8	32.86	66.64
9	1,4-dioxane	2.0	25	10	30.09	64.18
10	THF[b]	2.0	25	16	14.88	52.28
11	Toluene	2.0	25	16	35.20	55.31
12	Dichloromethane	1.0	40	16	20.05	60.23
13	Dichloromethane	2.0	40	6	**95.2**[c]	0
14	Dichloromethane	3.0	40	6	90.8[c]	0
15	Dichloromethane	5.0	40	6	85.3[c]	0
16	Dichloromethane	2.0	0	6	0[a]	0[a]
17	Dichloromethane[b]	2.0	5	16	1.92	16.94
18	Dichloromethane[b]	2.0	15	16	41.97	34.69
19	THF[b]	2.0	5	16	Traces	0
20	THF	2.0	10–15	12	23.69	76.51

[a]No reaction and only starting material isolated.
[b]Incomplete reaction.
[c]Isolated yield.
[d]By liquid chromatography–mass spectrometry.

both the bis-imidazopyridyl sulfides of imidazo[1,5-*a*]pyridines along with 1-chloroimidazo[1,5-*a*]pyridines (Table 1, entry 12). On using excess thionyl chloride in DCM or as neat at 40°C the selectively 1-chloro-imidazo[1,5-*a*]pyridines formed and isolated in good yields (Condition c, Supporting information, Table 1). However, the reaction at room temperature produces both the products (**4a** and **5a**) in mentioned ratio (entry 1–11), even the reaction in neat thionyl chloride produces both the products **5a** and **4a** in 2:1 ratio (entry 7). The reaction also proceeds in Toluene, Acetonitrile, 1,4-dioxane, THF, and no effects of solvent polarity is observed on the ratio of products which remain almost same. The reaction in dichloromethane on using thionyl chloride (0.5 and 1 eq.) produces both the products in the ration 3:1; however, reaction is incomplete. On using 2 equivalent of thionyl chloride in dichloromethane at 5°C, the ratio of products is improved to ~9:1; however, 80% of the starting material remains unreacted (entry 17). These results indicate that the optimal condition is reaction in dichloromethane with 2 equivalent thionyl chloride at 25°C.

Having established the optimal condition, we went on to the substrate scope of the reaction on different imidazo [1, 5-*a*]pyridine and to our pleasure, utmost of the tested substrates gave the 2-azaindolizine sulfur-bridged dimers

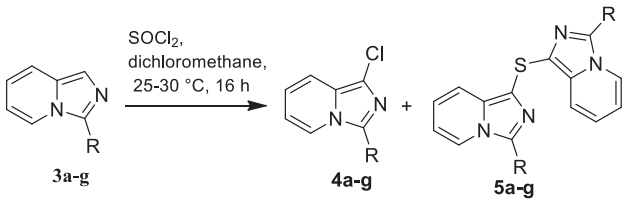
under this condition (Table 2). The 3-Arylimidazo[1,5-*a*]pyridine with electron donating (Me and OMe) and electron withdrawing (NO_2, CF_3) were well tolerated and corresponding products were isolated in moderate good yield (Table 2, entry 1–5). The electron donating groups on the aryl ring gave slightly higher yields of the products (**5a**, **5b**, **5e**) as compared to the aryl rings with electron withdrawing substituents (**5c** and **5d**). However, the 3-alkylimidazo[1,5-*a*]pyridine gives the low yield of product as compared to the 3 arylimidazo[1,5-a]pyridines (entry 5 and 6). The 3-methylimidazo[1,5-*a*]pyridine **3f** gave lower yield of the product (**4f**: 6%, **5f**: 13%, Table 2, entry 5) as most of the starting material **3f** degraded under reaction condition.

Due to the importance of C—H chalcogenation reaction, we were curious and interested to develop the method for selective chalcogenation on imidazo[1,5-*a*]pyridines. For these purposes, we have carried out several experiments to develop this method and also carried out the optimization part (Table 1). At ambient temperature (25–30°C), we observed the formation of the bis-imidazopyridyl sulfides of imidazo[1,5-*a*]pyridine in a ratio of maximum 4:1 to with 1-chloroimidazopyridine. Starting materials remained unreacted when reaction was performed at lower temperature (0, 5, 10–15 and −78°C). Also, we studied the concentration of the thionyl chloride but the ratio of the product remains unaltered in neat the reaction with the neat thionyl chloride also. The most common observation during the reaction is first the formation of the bis-imidazopyridyl sulfides of the imidazopyridine along with the unreacted starting materials with the time starting material was consumed and the formation of both the products in the mentioned ratio was observed. To confirm our observations, we carried out the control experiment on the isolated bis-imidazopyridyl sulfides (**5a**) by using 1.2 eq. thionyl chloride in dichloromethane room temperature but we observed only unreacted **5a** on thin layer chromatography (TLC) after 24 hr stirring but upon heating at 40°C and we found the bis-imidazopyridyl sulfides are converted to the 1-choloroimidazo[1,5-*a*]pyridine (**4a**) in 8 hr. Also, we have performed the reaction on **6** using 1.2 eq. of $SOCl_2$ in DCM at 0–40°C, at 0–5°C no reaction after 8.0 hr stirring, at room temperature ~30% of product **4a** formation was observed along with unreacted **6** but upon heating at 40°C for 3 hr complete conversion of the **6** to **4a** is observed. This experiment gives an evidence that chlorination may occur through the C—H chalcogenation. On the basis of the literature reports and our observations, a plausible mechanism is proposed for the formation of the bis-imidazopyridyl sulfides **5** (Figure 2). Initially, imidazo[1,5-*a*]pyridine 1,1′-sulfinylbis (3-phenylimidazo[1,5-a]pyridine) **6** is generated from 3-phenylimidazo[1,5-a]pyridine **3a** on treatment with thionyl chloride. Which on further treatment with thionyl chloride underwent deoxygenation with evolution of chlorine and sulfur dioxide to produce **5a** (Path A). Alternatively **6** on reaction with thionyl chloride yields **4a** with evolution of SO_2 (Path B) (Figure 2).

To confirm the structure of bis-imidazopyridyl sulfides (**5a**), we have carried out the oxidation on bis-imidazopyridyl sulfides/ thiodimer to their corresponding sulfoxide (**6**) and sulfone (**7**) derivatives using *m*-CPBA. We have isolated both sulfoxide and sulfone and confirmed by using mass spectra and ^{1}H NMR (Scheme 3).

To check the applicability of this method, we have performed this reaction on a gram scale and we have successfully isolated the 1-chloro-3-phenylimidazo[1,5-*a*]pyridine and bis(3-phenylimidazo[1,5-*a*]pyridin-1-yl)sulfane from 3-phenylimidazo[1,5-*a*]pyridine in a ratio of 1:3 and the overall atom economy of the reaction is 99% (Scheme 4).

TABLE 2 $SOCl_2$ mediated synthesis of 2-azaindolizine sulfur-bridged dimers



Where, R=
5a -- Ph
5b -4-MePh
5c- 3NO_2Ph
5d- 4CF_3 Ph
5e- 4-OMe Ph
5f- Me
5g- C(Me)$_3$

Entry	Substrate	Yield of 4 (%)	Yield of 5 (%)
1	3a	30.2	69.0
2	3b	31.2	66.4
3	3c	21.9	18.8
4	3d	28.8	56.8
5	3e	21.7	59.4
6	3f	6.2	13.5
7	3g	26.2	33.4

3 | PLAUSIBLE MECHANISM

3.1 | Experimental

3.1.1 | General methods

All commercial chemicals and solvents are of reagent grade and were used without further purification. The thin layer chromatography was performed on Merck pre-coated silica gel 60 F_{254} plates, with visualization under UV light. ^{1}H NMR and ^{13}C NMR spectra were recorded

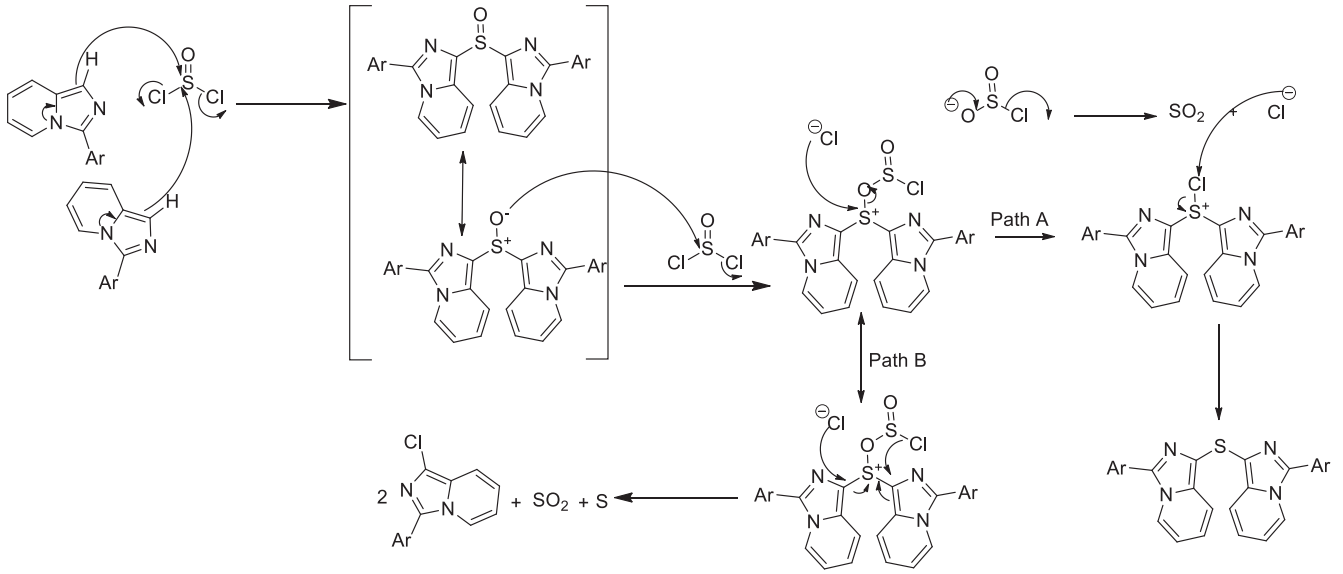
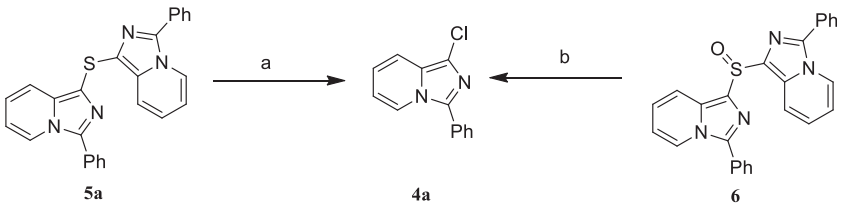


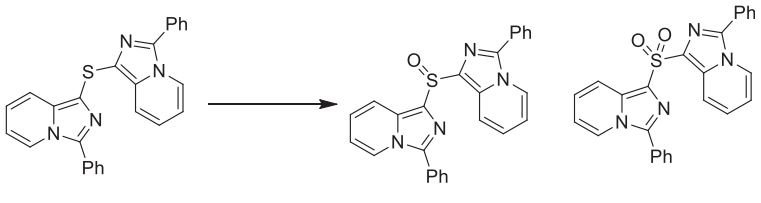
FIGURE 2 Plausible mechanism for synthesis of 2-azaindolizine sulfur-bridged dimers from imidazo[1,5-*a*]pyridine

SCHEME 2 Synthesis of 1-chloroimidazopyridne from bisimidazopyridyl sulfide



Reagents and Conditions: a) $SOCl_2$, DCM, 40 °C, 8 hr; b) $SOCl_2$, DCM, 40 °C, 3 hr

SCHEME 3 Oxidation of bisimidazopyridyl sulfide

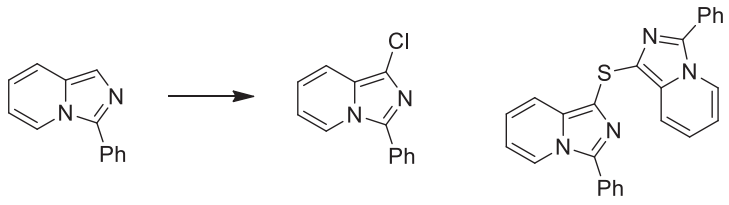


Reagents and Conditions. *m*-CPBA, dichloromethane, 0 °C, 0.5 h.

with Bruker 400, 500, 100 MHz AVANCE instrument and *J* values are in Hertz and chemical shifts (δ) are reported in ppm relative to internal tetramethylsilane. Mass spectral data were obtained on a Bruker Daltonics spectrometer using an electrospray ionization quadrapole-time of flight analysis. Melting points are recorded on Lab India melting point apparatus and are uncorrected.

General procedure for the synthesis bis (3-substitutedimidazo[1,5-a]pyridin-1-yl)sulfane and 1-chloro-3-phenylimidazo[1,5-a]pyridine (4a-g and 5a-g)

Thionyl chloride (2 mmol) was added to a solution of 3-substituted imidazo[1,5-*a*]pyridine (1 mmol) in dichloromethane (5 ml) and stirred resulting reaction



SCHEME 4 Gram scale synthesis of bisimidazopyridyl sulfide

Reagents and Conditions. $SOCl_2$, DCM, 25 - 30 °C, 16 h.

mixture at ambient temperature for 16 hr. Progress of the reaction was monitored by TLC. TLC shows two spots and starting material is consumed. Reaction mixture was quenched in ice cold water and the pH was adjusted to 9 with 30% aqueous sodium hydroxide solution. Extracted reaction mixture with dichloromethane (3 × 20 ml) and combined organic layers were washed with brine (25 ml). Dried organic layers over anhydrous sodium sulfate and filtered. Filtrate was concentrated on rotavapor under reduced pressure to get crude. Purification done on the combi-flash using 0–45% ethyl acetate in petroleum ether. The non-polar spot **4** eluted at 8–12% and the polar spot **5** eluted at 30–40% ethyl acetate in petroleum ether.

1-chloro-3-phenylimidazo[1,5-a]pyridine (4a)[21,22]

Off white solid; Yield: 712.0 mg, 30.22%; MP: 127–121°C; ^{1}H-NMR Spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.25 (1H, d, *J* = 7, H Ar), 7.80 (2H, d, *J* = 7.5, H Ar), 7.55 (2H, t, *J* = 7.5, H Ar), 7.49 (2H, t, *J* = 9, H Ar), 6.81(1H, t, *J* = 7, H Ar), 6.63 (1H, t, *J* = 6.5, H Ar); Mass Spectrum, *m/z*, (*I*rel, %): 166.7$[M]^+$ (100), 230.1$[M + 2H]^+$ (30).

1-chloro-3-(p-tolyl)imidazo[1,5-a]pyridine (4b)[22]

Off white solid; Yield: 72.8 mg, 31.2%; MP: 72–74°C; ^{1}H-NMR Spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.21 (1H, d, *J* = 7, H Ar), 7.658 (2H, d, *J* = 8, H Ar), 7.47 (1H, d, *J* = 9, H Ar), 7.35 (2H, d, *J* = 7.5, H Ar), 6.78 (1H, t, *J* = 6.5, H Ar), 6.61 (1H, t, *J* = 6.5, H Ar), 2.45 (3H, s, —CH_3); Mass Spectrum, *m/z*, (*I*rel, %): 243.3$[M]^+$(100), 244.1$[M + 2H]^+$(30).

1-chloro-3-(3-nitrophenyl)imidazo[1,5-a]pyridine (4c)

Orange solid; Yield: 50.2 mg, 21.9%; mp: 157–158°C; ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.68 (1H, s, H Ar), 8.26–8.24 (2H, m, H Ar), 8.21–8.10 (2H, m, H Ar), 7.79–7.66 (1H, m, H Ar), 7.04–6.93 (1H, m, H Ar), 6.93–6.74 (1H, m, H Ar); ^{13}C-NMR Spectrum (100 MHz, $CDCl_3$): 148.59, 136.5, 135.37, 134.37, 133.81, 131.54, 130.10, 123.22, 122.39, 121.14, 121.10, 119.55, 114.85; Mass Spectrum, *m/z*, (*I*rel, %): 274.3 $[M + H]^+$ (100).

1-chloro-3-(4-[trifluoromethyl]phenyl)imidazo[1,5-a] pyridine (4d)[22]

Off white solid; Yield: 65.0 mg, 28.8%; mp: 109–111°C; ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.27 (1H, dd, J = 8.0, 1.2, H, Ar), 7.94 (2H, d, J = 8.0, ArH), 7.79 (2H, d, J = 8.0, ArH), 7.53 (1H, d, *J* = 8.0, 4.0, ArH), 6.89–6.85 (1H, m, ArH), 6.84–6.69(1H, m, ArH); Mass Spectrum, *m/z*, (*I*rel, %): 298.8 $[M+ 2H]^+$ (30%).

1-chloro-3-(4-methoxyphenyl)imidazo[1,5-a] pyridine (4e)[22]

Off white solid; Yield: 65.0 mg, 21.7%; mp: 81–83°C; Mass Spectrum, *m/z*, (*I*rel, %): 258.9 $[M]^+$(100), 260.7 $[M+ 2H]^+$(30); high resolution mass spectrometry (HRMS): m/z 259.0601 calculated for $[C_{12}H_{11}N_2O + H]^+$ (259.0633).

1-chloro-3-methylimidazo[1,5-a]pyridine (4f)

Blackish solid; Yield: 5.5 mg, 6.2%; mp: decomposes at 60°C; ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.65 (1H, d, *J* = 6.8, ArH), 7.40 (1H, d, *J* = 9.2, ArH), 6.73 (1H, t, *J* = 9.2, ArH), 6.20 (1H, t, *J* = 6.4, ArH), 2.61 (3H, s, -CH_3); Mass Spectrum, *m/z*, (*I*rel, %): 166.7 $[M]^+$(100), 168.1$[M + 2H]^+$(30).

3-(tert-butyl)-1-chloroimidazo[1,5-a]pyridine (4g)

Brown solid; Yield: 125.3 mg, 26.2%; mp: 114–115°C; ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.00 (1H, d, *J* = 8.0, ArH), 7.40 (1H, d, *J* = 9.0, ArH), 6.68 (1H, q, *J* = 8.0, 4.0, ArH), 6.54 (1H, t, *J* = 8.0, ArH), 1.55 (9H, s, *tert-Bu*);13C-NMR (400 MHz, $CDCl_3$): 143.25, 122.76, 117.77(2C), 177.58(2C), 112.36, 33.0, 28.07(3C); Mass Spectrum, *m/z*, (*I*rel, %): 210.2 $[M+ 2H]^+$ (30%); HRMS: *m/z* 209.0836 calculated for $[C_{11}H_{14}ClN_2 + H]^+$(209.0836).

Bis(3-phenylimidazo[1,5-a]pyridin-1-yl)sulfane (5a)[11,12]

Brown solid; Yield: 1487.0 mg, 69.0%; mp: 173–177°C; ^{1}H-NMR Spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 8.45 (1H, d, *J* = 7, ArH), 8.03 (1H, d, *J* = 9, ArH), 7.81 (2H, d, *J* = 7.5, ArH), 7.59 (2H, t, *J* = 4.2, ArH), 7.54 (1H, t, *J* = 7, ArH), 7.15 (1H, t, *J* = 7.5, ArH), 6.89 (1H, t,

J = 3.9, ArH); Mass Spectrum, *m/z*, (*I*rel, %): 419.2[M + H]$^+$ (100).

bis(3-(p-tolyl)imidazo[1,5-a]pyridin-1-yl)sulfane (5b)[12]
Off white solid; Yield: 142.4 mg, 66.4%; mp: 161–164°C; ^{1}H-NMR Spectrum (500 MHz, $CDCl_3$), δ, ppm (J, Hz): 8.17 (2H, d, J = 7, ArH), 8.05 (2H, d, J = 9, ArH), 7.66 (4H, d, J = 8, ArH), 7.31 (4H, t, J = 7.5, ArH), 6.83 (2H, t, J = 7, ArH), 6.58 (2H, t, J = 6.5, ArH), 2.43 (6H, s, 2 × CH_3); Mass Spectrum, *m/z*, (*I*rel, %): 447.4[M]$^+$, 448.1 [M + 2H]$^+$.

Bis(3-(3-nitrophenyl)imidazo[1,5-a]pyridin-1-yl) sulfane (5c)
Orange solid; Yield: 40.0 mg, 18.8%; mp: 197–200°C ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (J, Hz): 8.70 (2H, s, ArH), 8.32–8.26 (4H, m, ArH), 8.22–8.10 (2H, m, ArH), 7.76 (2H, t, J = 8.0, ArH), 7.61–7.59 (2H, m, ArH), 6.93–6.84 (2H, m, ArH), 6.80–6.76 (2H, m, ArH); 13C-NMR (100 MHz, $CDCl_3$): 133.64(4C), 133.21(2C), 131.11 (4C), 127.37(2C), 123.33(2C), 121.84(2C), 120.94(2C), 120.07(2C), 117.97(2C), 115.13(2C); Mass Spectrum, *m/z*, (*I*rel, %): 509.6 [M+ H]$^+$. HRMS: *m/z* 531.0851 calculated for [$C_{26}H_{16}N_6O_4S$ + Na]$^+$(531.0846).

Bis(3-(4-[trifluoromethyl]phenyl)imidazo[1,5-a]pyridin-1-yl)sulfane (5d)[11,12]
Pale yellow solid; Yield: 120.0 mg, 56.8%; mp: 190–193°C; ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (J, Hz): 8.38 (2H, d, J = 8.0, ArH), 8.33(2H, d, J = 8.0, ArH), 7.97–7.93 (4H, m, ArH), 7.79–7.96 (4H, m, ArH), 6.96–6.89 (2H, m, ArH), 6.71–6.65 (2H, m, ArH); Mass Spectrum, *m/z*, (*I*rel, %): 555.62 [M+ H]$^+$. HRMS: *m/z* 577.0888 calculated for [$C_{28}H_{16}F_6N_4S$ + Na]$^+$(577.0892).

Bis(3-(4-methoxyphenyl)imidazo[1,5-a]pyridin-1-yl) sulfane (5e)[11,12]
Dark brown solid; Yield: 190.0 mg, 59.4%; mp: 177–182°C; ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (J, Hz): 8.10 (2H, d, J = 7.2, ArH), 8.02 (2H, d, J = 9.2, ArH), 7.67 (4H, d, J = 8.8, ArH), 7.01 (4H, d, J = 8.8, ArH), 6.81–6.77 (2H, m, ArH), 6.54 (2H, t, J = 6.4, ArH), 3.89 (6H, s, 2 x CH_3); 13C-NMR (100 MHz, $CDCl_3$): 160.05(2C), 137.82(2C), 133.31(2C), 129.71(4C), 121.53(2C), 119.93(2C), 119.42(2C), 114.35(4C), 114.52 (2C), 55.38(2C); Mass Spectrum, *m/z*, (*I*rel, %): 479.6 [M+ H]$^+$. HRMS: *m/z* 501.1352 calculated for [$C_{28}H_{22}N_4O_2S$ + Na]$^+$(501.1356).

Bis(3-methylimidazo[1,5-a]pyridin-1-yl)sulfane (5f)
Black solid; Yield: 30.0 mg, 13.5%; mp: 61–63°C; ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (J, Hz): 7.91 (2H, d, J = 9.2, ArH), 7.62 (2H, d, J = 7.2, ArH), 6.80 (2H, t, J = 7.2, ArH), 6.40 (2H, t, J = 6.4, ArH), 2.61 (6H, s, 2 × CH_3); Mass Spectrum, *m/z*, (*I*rel, %): 295.6 [M + H]$^+$.

Bis(3-(tert-butyl)imidazo[1,5-a]pyridin-1-yl)sulfane (5g)
Dark Brown solid; Yield: 145.0 mg, 33.4%; mp: 163–166°C ^{1}H-NMR Spectrum (400 MHz, $CDCl_3$), δ, ppm (J, Hz): 7.98 (2H, q, J = 8.0, 4.0, ArH), 6.72 (1H, q, J = 8.0, ArH), 6.50 (1H, t, J = 8.0, ArH), 1.53 (9H, s, *tert. Bu*.); 13C-NMR (400 MHz, $CDCl_3$): 144.66, 133.45, 123.03, 120.49, 119.66, 118.32, 112.10, 33.5, 28.14 (3C); Mass Spectrum, *m/z*, (*I*rel, %): 379.6 [M+ H]$^+$. HRMS: *m/z* 401.1765 calculated for [$C_{22}H_{26}N_4S$ + Na]$^+$(401.1770).

1,1′-sulfinylbis(3-phenylimidazo[1,5-a]pyridine) (6)
Off white solid; Yield: 37.1 mg, 17.9%; mp: 144–149°C; ^{1}H-NMR Spectrum (400 MHz, DMSO-d_6), δ, ppm (J, Hz): 8.54 (2H, t, J = 7.2, ArH), 8.08 (2H, d, J = 9.2, ArH), 7.80 (2H, d, J = 6.8, ArH), 7.59–7.50 (6H, m, ArH), 7.21–7.17 (2H, m, ArH), 6.94 (2H, t, J = 6.8, ArH); Mass Spectrum, *m/z*, (*I*rel, %): 435.5 [M+ H]$^+$.

1,1′-sulfonylbis(3-phenylimidazo[1,5-a]pyridine) (7)
Off white solid; Yield: 71.2 mg, 33.02%; mp: 126–129°C; ^{1}H-NMR Spectrum (400 MHz, DMSO-d_6), δ, ppm (J, Hz): 8.54 (2H, d, J = 7.2, ArH), 8.26 (2H, d, J = 9.6, ArH), 7.78 (4H, dd, J = 8.0, 1.6, ArH), 7.60–7.52 (6H, m, ArH), 7.41–7.37 (2H, m, ArH), 7.02 (2H, t, J = 6.8, ArH); Mass Spectrum, *m/z*, (*I*rel, %): 451.5 [M+ H]$^+$.

4 | CONCLUSION

We have reported for first time the C—H chalcogenation of imidazo [1, 5-*a*] pyridines by using thionyl chloride. In this methodology, we have optimized the C—H chalcogenation at ambient temperature using the metal-free, elemental sulfur-free conditions without use of polar solvents. Control experiment on bis-imidazopyridyl sulfides (**5a**) and sulfoxide (**6**) to 1-chloro imidazo[1,5-*a*]pyridine shed some light that the chlorination occurs through the thiodimerization (bisimidazopyridyl sulfide) of imidazo[1,5-*a*]pyridines.

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