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Metal-Free Thiocyanation of Imidazoheterocycles through Visible Light Photoredox Catalysis

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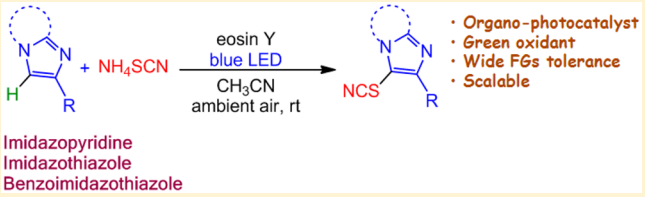
Supporting Information

ABSTRACT: A visible light mediated, metal-free process for the thiocyanation of imidazoheterocycles has been developed using eosin Y as a photoredox catalyst under ambient air at room temperature. A library of 3-(thiocyanato)imidazo[1,2-*a*]pyridines with broad functionalities have been synthesized in high yields. This methodology is also applicable for the selenocyanation of imidazo[1,2-*a*]pyridine.



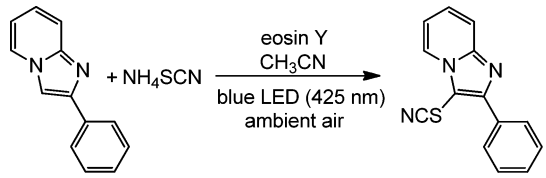
INTRODUCTION

Visible light driven photoredox processes have received much attention as a powerful tool to develop sustainable synthetic processes.[1] Metal complexes, mainly ruthenium and iridium, are commonly employed as efficient visible light photocatalysts.[2] Despite the excellent photophysical properties of ruthenium and iridium polypyridyl complexes in visible light photocatalysis, these are expensive and toxic.[3] Organic dyes are used as an attractive alternative to the transition-metal complexes in photoredox catalysis.[4] These are typically less expensive, less toxic, and easy to handle.[5] Particularly, eosin Y has been widely used as an organo-photocatalyst in synthetic transformations.[6]

The thiocyanation reaction is one of the most useful carbon−sulfur bond-forming reactions.[7] Organic thiocyanates usually serve as the synthetic precursors that can be conveniently converted into various sulfur-containing derivatives.[8] On the other hand, thiocyanates are the building blocks of many heterocyclic compounds that show a wide range of biological activities and also consist in many natural products.[9] Therefore, several methods have been developed for the thiocyanation of arenes and other heterocycles.[10]

In the past few years, much attention has been drawn on the imidazopyridine scaffolds because of their wide range of biological activities, for example, antiviral, antimicrobial, antitumor, anti-inflammatory, antiparasitic, hypnotic, etc.[11] Some marketed drugs like alpidem, zolpidem, necopidem, saripidem, zolimidine, etc., contain this scaffold. This moiety is also very useful in material sciences.[12] Consequently, various methods for the synthesis and functionalization of imidazoheterocycles have been reported.[13] Recently, we have also accounted a number of efficient methods for the synthesis[14] and functionalization[15] of imidazo[1,2-*a*]pyridine derivatives from readily available starting materials. The pharmacological activity of imidazopyridine derivatives is reliant on the nature of substituents at different positions. Incorporation of sulfur functionalities in azaheterocycles could impart marked biological properties.[16] Very recently, Li et al.[10f] reported a visible light mediated C-3 thiocyanation of indole derivatives using rose bengal as the photocatalyst. However, there is no report for the thiocyanation of imidazo[1,2-*a*]pyridine derivatives. On the basis of our experiences on functionalization of imidazopyridines, we envisaged that the thiocyanation of imidazopyridines could be carried out following a C(sp^2)-H functionalization strategy. Herein, we report a direct and environmentally benign method for the thiocyanation of imidazopyridines using eosin Y as a photoredox catalyst under ambient air at room temperature (Scheme 1).

Scheme 1. Thiocyanation of Imidazopyridine



RESULTS AND DISCUSSION

We started our investigation taking 2-phenylimidazo[1,2-*a*]pyridine (**1a**) as the model substrate to find a suitable reaction condition, as summarized in Table 1. Initially, the reaction was carried out employing 3 equiv of NH_4SCN as the thiocyanating agent and eosin Y (5 mol %) as the photocatalyst in DMSO under open air in the presence of blue LED light. The 2-phenyl-3-thiocyanatoimidazo[1,2-*a*]pyridine (**2a**) was obtained in 59% yield after 3 h (Table 1, entry 1). Inspired by the initial result, the effect of other solvents such as DMF, CH_3CN, THF, methanol, and chloroform were tested (Table 1, entries 2−6), and the best result (93%) was obtained in CH_3CN (Table 1, entry 3). Other photocatalysts such as rose bengal and $Ru(bpy)_3Cl_2·6H_2O$ were also tested (Table 1, entries 7 and 8), but both of them gave lower yields. No

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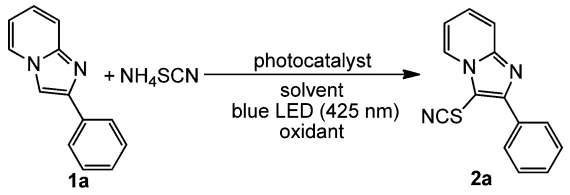
Table 1. Optimization of the Reaction Parameters[a]



entry	photocatalyst	solvent	oxidant	yield (%)
1	eosin Y	DMSO	air	59
2	eosin Y	DMF	air	62
3	eosin Y	CH_3CN	air	93
4	eosin Y	THF	air	34
5	eosin Y	methanol	air	11
6	eosin Y	chloroform	air	8
7	rose bengal	CH_3CN	air	40
8	$Ru(bpy)_3Cl_2·6H_2O$	CH_3CN	air	21
9		CH_3CN	air	
10[b]	eosin Y	CH_3CN		trace
11[c]	eosin Y	CH_3CN	air	71
12[d]	eosin Y	CH_3CN	air	46
13[e]	eosin Y	CH_3CN	air	84

[a]Reaction conditions (unless otherwise specified): **1a** (0.5 mmol), NH_4SCN (1.5 mmol), photocatalyst (5 mol %), solvent (2 mL), 3 h, rt. [b]In an inert atmosphere. [c]NH_4SCN (2 equiv) was used. [d]KSCN (1.5 mmol) was used. [e]Reaction performed in green LED (4 W) irradiation for 12 h.

formation of product was seen in absence of any photocatalyst (Table 1, entry 9). Only a trace amount of product was formed in an inert atmosphere (Table 1, entry 10). Furthermore, the yield of the reaction was decreased when 2 equiv of NH_4SCN was used (Table 1, entry 11). Moreover, a lower amount of the desired product was obtained on replacing NH_4SCN by KSCN (Table 1, entry 12). A decrease in yield (84%) was obtained when green LED (4 W) was used instead of blue LED even after 12 h (Table 1, entry 13). Finally, the optimized reaction conditions were obtained using 3 equiv NH_4SCN and 5 mol % of eosin Y in CH_3CN under blue LED irradiation in ambient air, affording the optimum 93% yield of the desired thiocyanated product within 3 h (Table 1, entry 3).

With the optimized reaction conditions in hand, we then varied imidazo[1,2-*a*]pyridines to show the generality of this methodology. As shown in Scheme 2, first we varied the substituents in the C-2 position of the imidazo[1,2-*a*]pyridines. The imidazopyridine moiety having −Me and −OMe substituted phenyl rings at the C-2 position produced the C-3 thiocyanated products in excellent yields (**2b** and **2c**). 3-NO_2 phenyl substituted imidazopyridine furnished the product in excellent yield (**2d**). Halogens are also well tolerated under the present reaction conditions (**2e** and **2f**). Imidazopyridines bearing −CN and −OH functionalities also afforded the desired products in moderate to good yields (**2g** and **2h**). It is notable that the marketed drug zolimidine reacted well to give the thiocyanated product which might show better bioactivity (**2i**). The naphthyl substituted substrate also worked well (**2j**). Moreover, heteroaryl substituted imidazopyridine was tested (**2k**). In addition, $-CF_3$ as well as aliphatic substituted imidazopyridines was found to very effective for thiocyanation (**2l** and **2m**). Interestingly, 2,3-unsubstituted imidazopyridine regioselectively produced the C-3 thiocyanated product in moderate yield (**2n**).

Next, we turned our attention to other imidazopyridines bearing substituents on the pyridine rings as shown in Scheme 3. Methyl substituted imidazopyridines gave the product with good yields (**2o** and **2p**). Imidazopyridine having other substituents like −CN, −Cl, and −Br furnished the desired thiocyanated products in moderate yields (**2q**−**2s**).

The present protocol is also applicable to other imidazoheterocycles like imidazo[2,1-*b*]thiazole and benzo[*d*]imidazo-[2,1-*b*]thiazole (Scheme 4). To our delight, the corresponding monothiocyanated products were obtained with excellent yields. The structure of **4b** was confirmed by X-ray analysis.[17] However, other simple imidazoles such as imidazole, *N*-methylimidazole, and 1,2 dimethylimidazole were unreacted under the present reaction conditions.

The gram-scale reaction was also performed in the usual laboratory setup (Scheme 5). The reaction afforded the thiocyanated derivative in excellent yield (89%). This result clearly demonstrated the practical applicability of this protocol for the thiocyanation of imidazopyridines.

Furthermore, the scope of the reaction was extended for selenocyanation of imidazopyridines (Scheme 6). Intriguingly, the selenocyanated product **5a** was obtained in moderate yield. The SCN group of the imidazopyridine was also converted to SCF_3 (**6a**), which is a key functionality of many agrochemical and pharmaceutical products.[18]

Few controlled experiments were performed to get a better understanding on the probable mechanistic path, as shown in Scheme 7. The thiocyanation reaction did not proceed in the presence of radical scavenger TEMPO (entry 1), which indicates that the reaction possibly proceeds through a radical pathway. The reaction was also carried out in the dark (entry 2), but the reaction did not proceed at all, which strongly supports the radical mechanism. Furthermore, the reaction was performed in the presence of DABCO (entry 3). The reaction proceeded with equal ease, which thereby indicates that singlet oxygen is not involved in the reaction.[6g]

On the basis of the controlled experiments shown in Scheme 7, and the literature reports,[6a,b,10f] a plausible mechanistic path has been outlined in Scheme 8. Initially, eosin Y is being photoexcited in the presence of blue LED light. The thiocyanate anion is being oxidized to thiocyanate radical by the SET mechanism from anion to photoactivated eosin Y via a reductive quenching cycle. The resulting thiocyanate radical interacts with **1a** to produce the radical intermediate **B**. Subsequently, **B** is oxidized to the intermediate **C**, which affords the product **2a** via deprotonation. Aerobic oxygen probably plays a crucial role to complete the photoredox cycle by oxidation of the eosin Y radical anion to the ground state.

CONCLUSIONS

In summary, we have developed a visible light driven eosin Y catalyzed protocol for the C-3 thiocyanation of imidazoheterocycles at room temperature. The present method shows broad substrates scope applicability and a wide range of functional groups tolerance. Most importantly, this method is scalable and air is used as the sole green oxidant. To the best of our knowledge, this is the first report of the C-3 thiocyanation of imidazopyridines. This transformation is also applicable for the selenocyanation of imidazopyridine. We believe this protocol will gain much importance in organic synthesis, medicinal chemistry, and material science as a powerful and economical route for the thiocyanation and selenocyanation of imidazoheterocycles.

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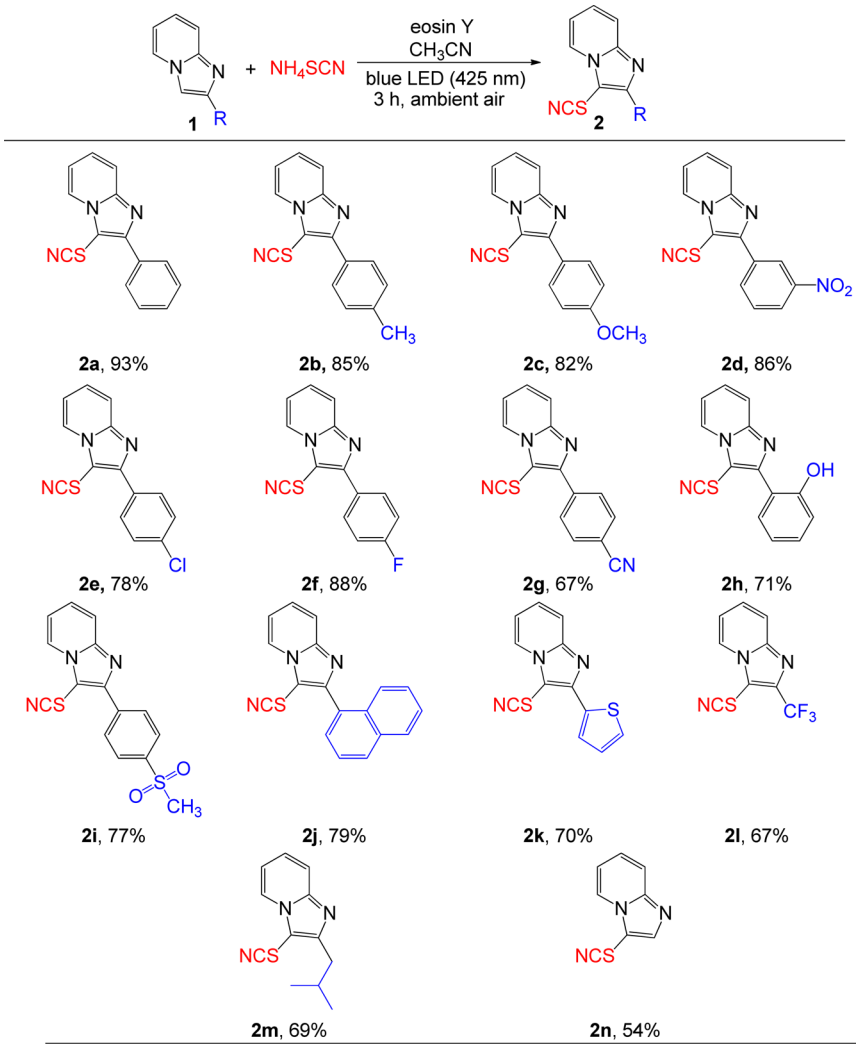
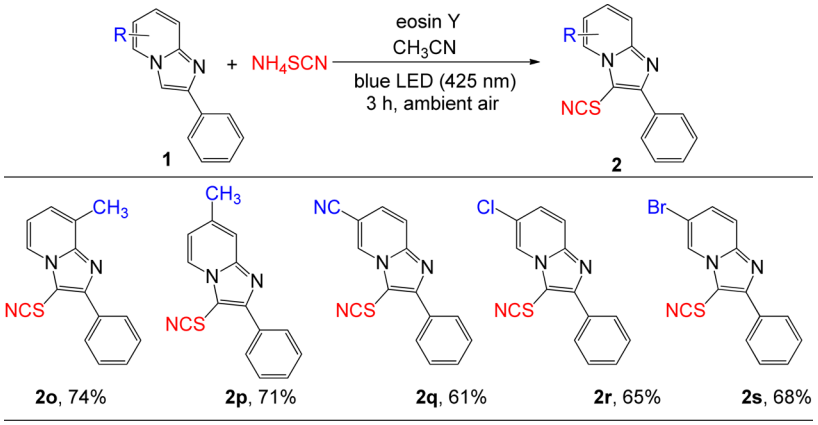
Scheme 2. Scope of Substrates: Variation of C-2 Substituents on the Imidazo[1,2-*a*]pyridines[a]



[a]Reaction conditions: Imidazo[1,2-*a*]pyridines **1** (0.5 mmol), NH_4SCN (1.5 mmol), eosin Y (5 mol %), CH_3CN (2 mL), blue LED, 3 h, rt, ambient air.

Scheme 3. Scope of Substrates: Variation of Substituents on Pyridine Ring[a]



[a]Reaction conditions: Imidazo[1,2-*a*]pyridines **1** (0.5 mmol), NH_4SCN (1.5 mmol), eosin Y (5 mol %), CH_3CN (2 mL), blue LED, 3 h, rt, ambient air.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in oven-dried 10 mL round-bottom flasks in open air. All solvents were dried and distilled before use. Commercial reagents were used without further purification unless otherwise noted. All the imidazoheterocycles were synthesized following the literature procedures.[14a,d] ^1H, $^{13}C\{^1H\}$, and

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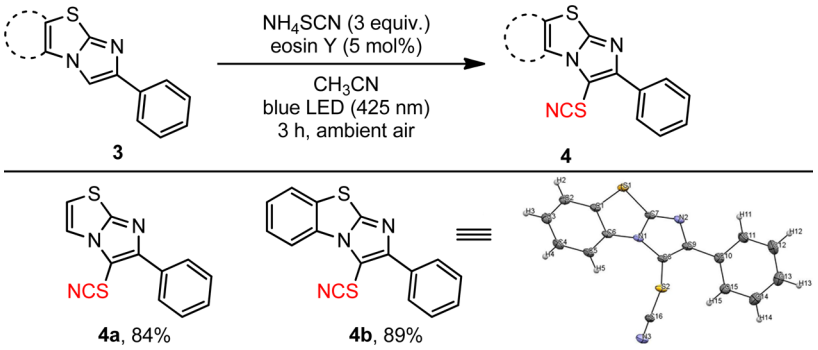
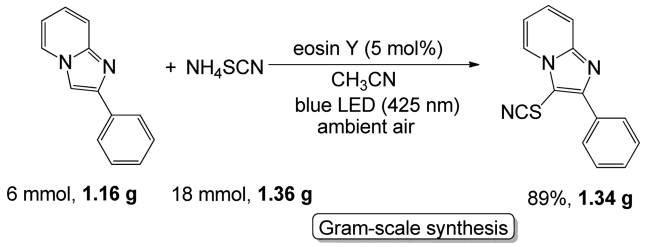
Scheme 4. Thiocyanation of Imidazoheterocycles

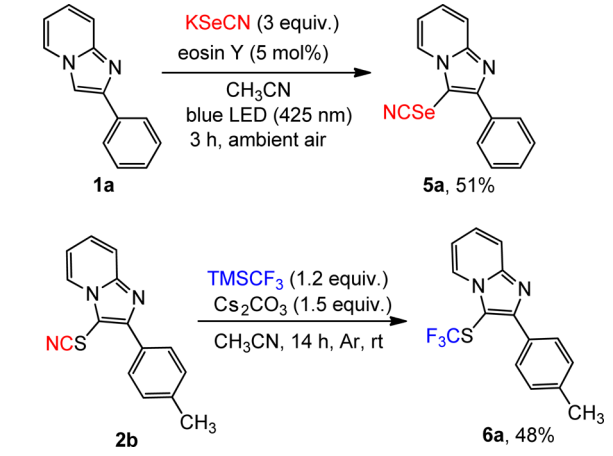


Scheme 5. Gram-Scale Reaction[a]



[a]Reaction conditions: Imidazo[1,2-*a*]pyridine **1a** (6 mmol), NH_4SCN (18 mmol), eosin Y (5 mol %), CH_3CN (20 mL), blue LED, 3 h, rt, ambient air.

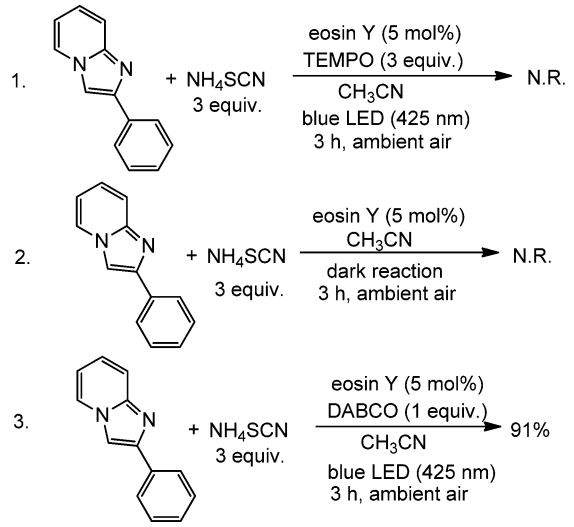
Scheme 6. Selenocyanation and Trifluoromethylthiolation of Imidazo[1,2-*a*]pyridine



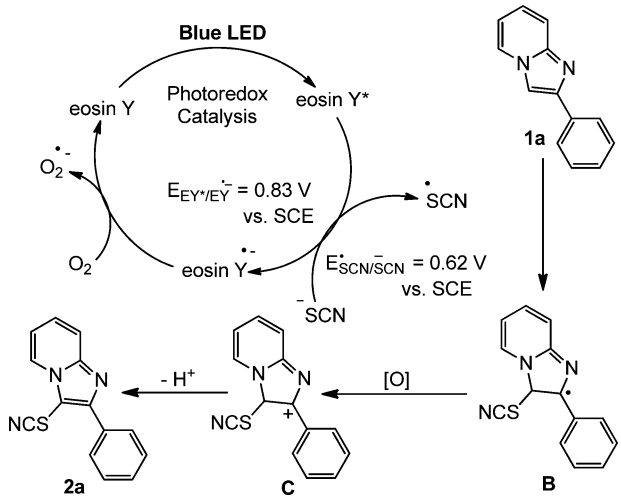
^{19}F NMR spectra were recorded using $CDCl_3$ and DMSO-d_6 solution at ambient temperature on a spectrometer operating at 400 MHz for ^1H, and proton-decoupled $^{13}C\{^1H\}$ NMR spectra were recorded at 100 and 376 MHz for ^{19}F NMR. The chemical shifts of all ^1H and $^{13}C\{^1H\}$ NMR spectra are referenced to the residual signal of $CDCl_3$ (δ 7.26 ppm for the ^1H NMR spectra and δ 77.16 ppm for the $^{13}C\{^1H\}$ NMR spectra) and DMSO-d_6 (δ 2.50 ppm for the ^1H NMR spectra and δ 39.50 ppm for the $^{13}C\{^1H\}$ NMR spectra). Coupling constant J was given in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, m = multiplet. TLC was monitored with aluminum backed silica gel 60 (HF_{254}) plates (0.25 mm) using various organic solvent mixtures. Column chromatography was performed with silica gel (60−120 mesh). X-ray single-crystal data were collected using a charge-coupled device (CCD) area detector.

Typical Experimental Procedure for the Synthesis of 2-Phenyl-3-thiocyanatoimidazo[1,2-*a*]pyridine (2a) (Table 1). An oven-dried 5 mL round-bottom flask was charged with 2-phenylimidazo[1,2-*a*]pyridine (**1a**) (0.5 mmol, 97 mg), ammonium thiocyanate (1.5 mmol, 114 mg), and eosin Y (5 mol %, 17 mg) in CH_3CN (2 mL), and the reaction mixture was stirred under blue LED irradiation for 3 h under ambient air. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with ethyl acetate. The organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get the crude residue, which was purified by column chromatography

Scheme 7. Controlled Experiments



Scheme 8. Probable Mechanism



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on silica gel (60−120 mesh) using petroleum ether:ethyl acetate = 9:1 as an eluent to afford the pure thiocyanated product (**2a**) (117 mg, 93%) as a red solid.

*2-Phenyl-3-thiocyanatoimidazo[1,2-a]pyridine (**2a**).* Red solid (117 mg, 93%), mp 110−112 °C. IR (KBr): 3070, 2349, 1639, 1452 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.47−8.46 (m, 1H), 8.06−8.04 (m, 2H), 7.81−7.79 (m, 1H), 7.54−7.50 (m, 4H), 7.15 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 153.1, 148.0, 131.9, 129.6, 128.9, 128.9, 128.2, 124.5, 118.4, 114.6, 108.2, 94.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{10}N_3S$: 252.0595; found: 252.0591.

*3-Thiocyanato-2-(p-tolyl)imidazo[1,2-a]pyridine (**2b**).* Red solid (112 mg, 85%), mp 99−101 °C. IR (KBr): 3068, 2357, 1648, 1445 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (s, 1H), 7.97 (d, J = 7.6 Hz, 2H), 7.84−7.83 (m, 1H), 7.51 (s, 1H), 7.34 (d, J = 7.2 Hz, 2H), 7.17 (s, 1H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 152.1, 147.2, 140.1, 129.6, 128.8, 128.2, 124.6, 117.9, 114.9, 108.1, 95.1, 21.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3S$: 266.0752; found: 266.0745.

*2-(4-Methoxyphenyl)-3-thiocyanatoimidazo[1,2-a]pyridine (**2c**).* Yellow solid (115 mg, 82%), mp 102−104 °C. IR (KBr): 3081, 2352, 1627, 1459 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, J = 6.8 Hz, 1H), 8.02 (d, J = 8.8 Hz, 2H), 7.80 (d, J = 8.8 Hz, 1H), 7.48 (t, J = 8.0 Hz, 1H), 7.14 (t, J = 6.8 Hz, 1H), 7.05 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 160.9, 152.4, 147.5, 130.3, 128.5, 124.5, 123.8, 117.8, 114.6, 114.3, 108.1, 94.2, 55.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3OS$: 282.0701; found: 282.0696.

*2-(3-Nitrophenyl)-3-thiocyanatoimidazo[1,2-a]pyridine (**2d**).* Red solid (127 mg, 86%), mp 128−130 °C. IR (KBr): 3076, 2355, 1620, 1441, 1340, 1275 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 8.97−8.93 (m, 1H), 8.86−8.78 (m, 1H), 5.57 (d, J = 9.2 Hz, 1H), 8.36−8.31 (m, 1H), 7.94−7.85 (m, 2H), 7.67−7.63 (m, 1H), 7.42−7.32 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 148.0, 146.7, 134.1, 132.2, 130.5, 128.8, 125.5, 123.7, 122.4, 120.8, 117.5, 115.0, 110.0, 99.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_9N_4O_2S$: 297.0446; found: 297.0443.

*2-(4-Chlorophenyl)-3-thiocyanatoimidazo[1,2-a]pyridine (**2e**).* White solid (112 mg, 78%), mp 109−111 °C. IR (KBr): 3041, 2359, 1635, 1475, 1278, 814 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 8.81 (d, J = 6.0 Hz, 1H), 8.09 (d, J = 7.6 Hz, 2H), 7.87 (d, J = 8.0 Hz, 1H), 7.72−7.65 (m, 3H), 7.39−7.38 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 147.3, 145.5, 134.4, 129.9, 129.9, 129.7, 128.9, 125.7, 116.5, 115.5, 109.8, 99.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_9ClN_3S$: 286.0206; found: 286.0201.

*2-(4-Fluorophenyl)-3-thiocyanatoimidazo[1,2-a]pyridine (**2f**).* Red solid (118 mg, 88%), mp 86−88 °C. IR (KBr): 3061, 2343, 1634, 1464, 1340 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.44−8.42 (m, 1H), 8.05−8.02 (m, 2H), 7.76 (d, J = 8.4 Hz, 1H), 7.50−7.46 (m, 1H), 7.21−7.13 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.6 (d, $J_{C\text{-}F}$ = 249 Hz), 151.1, 147.3, 130.8 (d, $J_{C\text{-}F}$ = 9 Hz), 128.8, 127.4, 124.5, 117.8, 115.9 (d, $J_{C\text{-}F}$ = 22 Hz), 114.9, 107.9, 95.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ − 110.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_9FN_3S$: 270.0501; found: 270.0494.

*4-(3-Thiocyanatoimidazo[1,2-a]pyridin-2-yl)benzonitrile (**2g**).* Red solid (92 mg, 67%), mp 142−144 °C. IR (KBr): 3076, 2360, 2221, 1463 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, J = 6.8 Hz, 1H), 8.22 (d, J = 8.0 Hz, 2H), 7.83−7.79 (m, 3H), 7.56−7.52 (m, 1H), 7.22−7.19 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.7, 148.1, 136.4, 132.6, 129.3, 128.7, 124.6, 118.7, 118.6, 115.2, 113.0, 107.5, 96.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_9N_4S$: 277.0548; found: 277.0547.

*2-(3-Thiocyanatoimidazo[1,2-a]pyridin-2-yl)phenol (**2h**).* Yellow solid (94 mg, 71%), mp 113−115 °C. IR (KBr): 3686, 3049, 2389, 1604, 1454 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.50−8.34 (m, 2H), 7.72−7.52 (m, 2H), 7.36−7.32 (m, 1H), 7.21−7.20 (m, 1H), 7.07−6.97 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 158.5, 150.7, 145.8, 131.6, 129.0, 127.9, 124.2, 119.3, 118.2, 117.4, 115.2, 114.8, 107.6, 93.6. HRMS-EI m/z: $[M]^+$ Calcd for $C_{14}H_9N_3OS$: 267.0466; found: 267.0466.

*2-(4-(Methylsulfonyl)phenyl)-3-thiocyanatoimidazo[1,2-a]-pyridine (**2i**).* White solid (126 mg, 77%), mp 162−164 °C. IR (KBr): 3037, 2391, 1643, 1413, 1299, 1149 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 8.82 (d, J = 6.4 Hz, 1H), 8.36 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 8.8 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.38 (t, J = 6.8 Hz, 1H), 3.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 147.9, 146.7, 141.5, 136.8, 129.9, 129.4, 127.9, 126.1, 117.6, 115.8, 110.4, 100.4, 43.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3O_2S_2$: 330.0371; found: 330.0391.

*2-(Naphthalen-1-yl)-3-thiocyanatoimidazo[1,2-a]pyridine (**2j**).* Yellow solid (119 mg, 79%) mp 118−120 °C. IR (KBr): 3051, 2351, 1494 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, J = 6.4 Hz, 1H), 8.04−7.98 (m, 2H), 7.94−7.86 (m, 2H), 7.69 (d, J = 6.4 Hz, 1H), 7.63−7.59 (m, 1H), 7.53−7.51 (m, 3H), 7.19−7.16 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 153.1, 147.6, 133.7, 131.7, 130.1, 129.2, 128.7, 128.5, 128.4, 127.0, 126.3, 125.7, 125.1, 124.6, 118.2, 114.9, 108.1, 98.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{12}N_3S$: 302.0752; found: 302.0747.

*3-Thiocyanato-2-(thiophen-2-yl)imidazo[1,2-a]pyridine (**2k**).* Yellow solid (90 mg, 70%), mp 108−110 °C. IR (KBr): 3074, 2354, 1643, 1488 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.42−8.40 (m, 1H), 7.97−7.96 (m, 1H), 7.75−7.72 (m, 1H), 7.51−7.50 (m, 1H), 7.48−7.44 (m, 1H), 7.22−7.20 (m, 1H), 7.14−7.10 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.1, 148.0, 134.8, 128.4, 128.3, 128.2, 127.9, 124.3, 118.1, 114.6, 107.6, 93.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_8N_3S_2$: 258.0160; found: 258.0153.

*3-Thiocyanato-2-(trifluoromethyl)imidazo[1,2-a]pyridine (**2l**).* Red solid (81 mg, 67%), mp 92−94 °C. IR (KBr): 3043, 2397, 2165, 1529 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, J = 6.8 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.63−7.59 (m, 1H), 7.32−7.28 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 147.2, 142.1 (q, $J_{C\text{-}F}$ = 76 Hz), 129.3, 124.5, 120.5 (q, $J_{C\text{-}F}$ = 268 Hz), 116.3, 113.9, 106.4, 98.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ − 61.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_9H_5F_3N_3S$: 244.0156; found: 244.0150.

*2-Isobutyl-3-thiocyanatoimidazo[1,2-a]pyridine (**2m**).* Yellow liquid (80 mg, 69%), IR (KBr): 3071, 2362, 1430 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.90 (d, J = 6.8 Hz, 1H), 7.97−7.90 (m, 2H), 7.56−7.53 (m, 1H), 2.83 (d, J = 7.2 Hz, 2H), 2.26−2.19 (m, 1H), 0.97 (d, J = 6.8 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 147.6, 142.6, 132.6, 126.7, 116.8, 114.0, 109.4, 103.1, 34.3, 28.2, 22.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}N_3S$: 232.0908; found: 232.0905.

*3-Thiocyanatoimidazo[1,2-a]pyridine (**2n**).* Yellow liquid (47 mg, 54%). IR (KBr): 3058, 2344, 1449 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, J = 6.4 Hz, 1H), 8.02 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 6.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.0, 143.2, 127.6, 124.2, 118.7, 114.7, 107.9, 99.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_8H_6N_3S$: 176.0282; found: 176.0276.

*8-Methyl-2-phenyl-3-thiocyanatoimidazo[1,2-a]pyridine (**2o**).* Red solid (98 mg, 74%), mp 98−100 °C. IR (KBr): 3051, 2358, 1629, 1456 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 6.8 Hz, 1H), 8.06−8.04 (m, 2H), 7.55−7.51(m, 2H), 7.49−7.45 (m, 1H), 7.27−7.25 (m, 1H), 7.04 (t, J = 6.8 Hz, 1H), 2.70 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 152.4, 148.0, 132.0, 129.4, 129.0, 128.8, 128.5, 127.1, 122.2, 114.6, 108.2, 95.2, 16.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_3S$: 266.0752; found: 266.0744.

*7-Methyl-2-phenyl-3-thiocyanatoimidazo[1,2-a]pyridine (**2p**).* Brown solid (94 mg, 71%), mp 104−106 °C. IR (KBr): 3078, 2348, 1654, 1431 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, J = 6.8 Hz, 1H), 8.03 (d, J = 7.2 Hz, 2H), 7.54−7.47 (m, 3H), 7.46−7.44 (m, 1H), 6.95 (d, J = 6.8 Hz, 1H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 153.0, 148.3, 139.8, 132.0, 129.4, 128.8, 128.8, 123.6, 117.1, 116.8, 108.3, 93.9, 21.5. HRMS (ESI-TOF): Calcd for $C_{15}H_{11}N_3S$ ($[M + H]$)$^+$: 266.0752; found: 266.0749.

*2-Phenyl-3-thiocyanatoimidazo[1,2-a]pyridine-6-carbonitrile (**2q**).* Red solid (84 mg, 61%), mp 132−134 °C. IR (KBr): 3062, 2351, 2237, 1629, 1429 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.85 (s, 1H), 8.07−8.04 (m, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.58−7.49 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.9, 147.3, 130.8, 130.3,

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130.2, 129.0, 128.9, 128.1, 119.3, 115.7, 107.1, 100.9, 97.4. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_9N_4S$: 277.0548; found: 277.0543.

6-Chloro-2-phenyl-3-thiocyanatoimidazo[1,2-a]pyridine (**2r**). Yellow solid (93 mg, 65%), mp 101−103 °C. IR (KBr): 3049, 2346, 1645, 1431 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.48 (s, 1H), 8.09−8.02 (m, 2H), 7.71 (d, *J* = 9.6 Hz, 1H), 7.56−7.51 (m, 2H), 7.50−7.46 (m, 1H), 7.45−7.42 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 153.7, 146.4, 131.6, 129.8, 129.6, 128.9, 128.8, 123.1, 122.5, 118.7, 107.7, 95.8. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_9ClN_3S$: 286.0206; found: 286.0204.

6-Bromo-2-phenyl-3-thiocyanatoimidazo[1,2-a]pyridine (**2s**). Brown solid (112 mg, 68%), mp 128−130 °C. IR (KBr): 3022, 2341, 2158, 1479 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.03 (d, *J* = 7.2 Hz, 2H), 7.65 (d, *J* = 9.2 Hz, 1H), 7.52−7.45 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 153.4, 146.3, 131.7, 131.4, 129.8, 128.9, 128.8, 124.7, 118.9, 109.4, 107.8, 95.6. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_9BrN_3S$: 329.9701; found: 329.9692.

6-Phenyl-5-thiocyanatoimidazo[2,1-b]thiazole (**4a**). White solid (108 mg, 84%), mp 124−126 °C. IR (KBr): 3120, 2354, 2158, 1438 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.2 Hz, 2H), 7.66−7.65 (m, 1H), 7.51−7.48 (m, 2H), 7.45−7.41 (m, 1H), 7.06 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.5, 153.4, 132.1, 129.2, 128.8, 128.2, 117.8, 114.8, 108.5, 95.9. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{12}H_8N_3S_2$ ($[M + H]$)$^+$: 258.0160; found: 258.0155.

2-Phenyl-3-thiocyanatobenzo[d]imidazo[2,1-b]thiazole (**4b**). White solid (137 mg, 89%), mp 152−154 °C. IR (KBr): 3070, 2352, 2156, 1479 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, *J* = 8.4 Hz, 1H), 7.99−7.97 (m, 2H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.59−7.55 (m, 1H), 7.54−7.50 (m, 2H), 7.47−7.42 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 155.6, 152.8, 132.9, 131.8, 130.2, 129.3, 128.8, 128.5, 127.0, 125.8, 124.6, 113.9, 108.9, 98.1. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{10}N_3S_2$ ($[M + H]$)$^+$: 308.0316; found: 308.0313.

2-Phenyl-3-selenocyanatoimidazo[1,2-a]pyridine (**5a**). Yellow solid (76 mg, 51%), mp 135−137 °C. IR (KBr): 3066, 2513, 1645 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.66−8.46 (m, 1H), 8.01−7.97 (m, 2H), 7.79−7.76 (m, 1H), 7.55−7.45 (m, 4H), 7.16−7.11 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 129.7, 129.4, 129.3, 129.1, 128.8, 128.6, 128.0, 126.9, 125.6, 118.2, 114.5, 98.9. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{10}N_3Se$: 300.0040; found: 300.0034.

2-(p-Tolyl)-3-((trifluoromethyl)thio)imidazo[1,2-a]pyridine (**6a**).[18b] White solid (63 mg, 48%), ^1H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 6.8 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 2H), 7.72−7.70 (m, 1H), 7.42−7.38 (m, 1H), 7.31−7.29 (m, 2H), 7.03−6.99 (m, 1H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.3, 148.1, 139.2, 129.8, 129.3, 128.7 (q, J_{C-F} = 313 Hz), 128.6, 127.8, 124.6, 117.9, 113.7, 98.7, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ − 43.23.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01369.

Data for compound **4b** (CIF)

Scanned copies of ^1H and ^{13}C NMR spectra of the synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

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