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Iodine-Catalyzed Cross Dehydrogenative Coupling Reaction: A Regioselective Sulfenylation of Imidazoheterocycles Using Dimethyl Sulfoxide as an Oxidant

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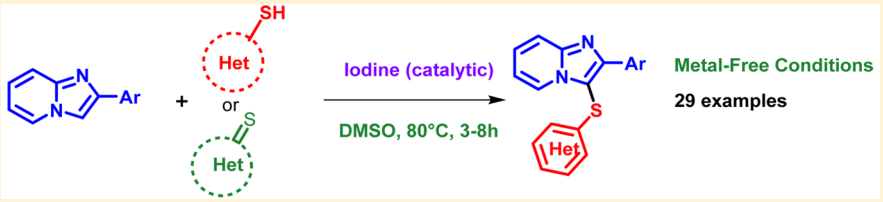
Supporting Information



ABSTRACT: A regioselective formation of C−S bonds has been achieved using a cross dehydrogenative coupling (CDC) protocol using iodine as a catalyst and dimethyl sulfoxide as an oxidant under green chemistry conditions. This strategy employs the reaction of easily available heterocyclic thiols or thiones with imidazoheterocycles. This protocol provides an efficient, mild, and inexpensive method for sulfenylation of imidazoheterocycles with a diverse range of heterocyclic thiols and heterocyclic thiones.

INTRODUCTION

Introduction of a sulfur moiety into organic molecules is one of the fundamental and major areas of research in organic synthesis because of the presence of sulfur-containing organic moieties in a variety of biologically and medicinally active molecules.[1] Among a variety of reactions, a C−H functionalization approach using a cross dehydrogenative coupling (CDC) strategy is becoming more attractive as it offers shorter synthetic routes and atom economical and environmentally benign protocols.[2] However, adopting a C−H functionalization strategy for the formation of C−S bonds is a challenge as sulfur-containing compounds are more prone to oxidation.[3] The reaction using DMSO as an oxidant is attractive as it leads to a few interesting transformations.[4] The greater interest in using DMSO as an oxidant is also due to environmental concerns.[4]

Among a plethora of sulfur-containing compounds, imidazo[1,2-*a*]pyridines are ubiquitous structural motifs that exhibit a broad range of biological activity and serve as building blocks for the construction of various pharmaceutically active compounds.[5] Sulfenylation of imidazo[1,2-*a*]pyridine derivatives has attracted attention in recent years.[6−13] Sulfenylation at C3 of imidazo[1,2-*a*]pyridines is accomplished using copper,[6,7] hypervalent iodine reagents,[8] strong acidic conditions,[9] ionic liquids,[10] or silica-supported $CeCl_3{\cdot}7H_2O$/NaI,[11] NCS,[12] ArSCl derivatives,[13] and iodine derivatives.[14] Most of these methods are useful for sulfenylation of imidazo[1,2-*a*]pyridines using nonheterocyclic thiols. To the best of our knowledge, there have been limited reports about the sulfenylation of imidazopyridiene heterocycles using heterocyclic thiols.[7]

Heterocyclic thiols and thiones are easily available or accessible structural blocks, and hence, the development of efficient functionalization strategies using heterocyclic thiols and thiones as precursors can lead to efficient routes for synthesizing a variety of biologically active compounds (Figure 1).[1] Surprisingly, the methods available for the sulfenylation using heterocyclic thiols and thiones are scanty,[7] and to the best of our knowledge, there are no metal-free conditions methods available. Sulfenylation of heterocyclic thiol and thione compounds is a challenging task, whereas a similar reaction with an aliphatic or carbocyclic thiol is facile (Scheme 1).[6−14] DMSO is an environmentally benign, sustainable oxidant[2a] and is used as a solvent in many chemical transformations and in industry, as well.[2a] As a continuation of our effort on metal-free reactions,[15] herein we describe our recent progress in using DMSO as an oxidant as well as a solvent in the presence of a catalytic amount of iodine, which led to a convenient method for the sulfenylation of imidazoheterocycles under mild and transition metal-free reaction conditions.

RESULTS AND DISCUSSION

Optimization of Reaction Conditions. Optimization studies were conducted using 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) and 1-phenyl-1*H*-tetrazole-5-thiol (**2a**) as model substrates in the presence of 20 mol % iodine. The solvent screening studies indicated that DMSO is the most suitable solvent, which resulted in the formation of product **3a** in 90% yield, whereas other solvents such as DMF, DMA, acetonitrile, EtoAc, and toluene were not suitable under the reaction conditions (entries 1 and 2, Table 1; also see the

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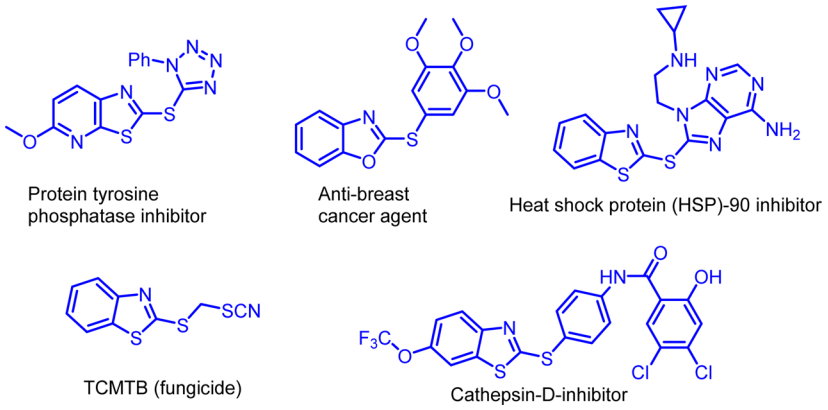
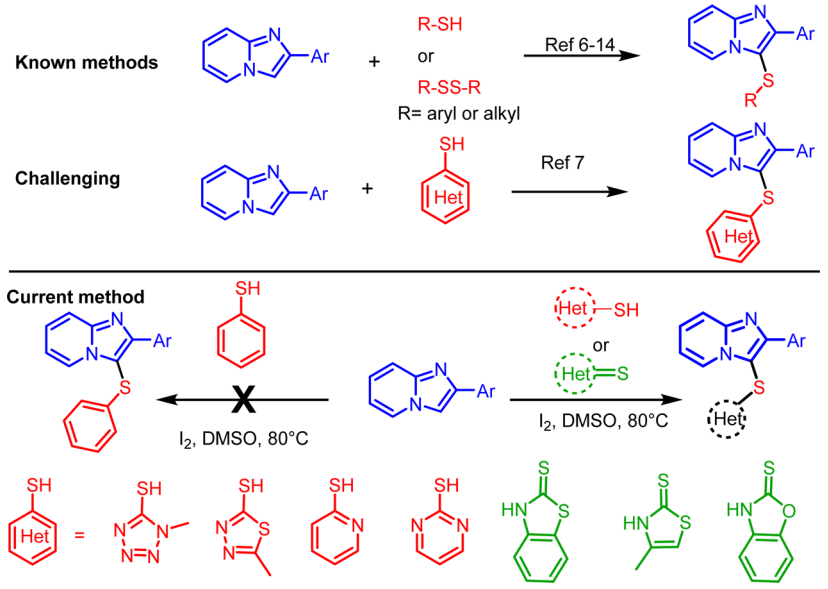


Figure 1. Pharmaceutically active heterocyclic sulfides.

Scheme 1. Approaches for the Sulfenylation of Imidazo[1,2-*a*]pyridines



Supporting Information). Using aq HI (55% in water, 20 mol %) as an acid additive, the desired product **3a** was obtained in 78% yield (entry 3), whereas aq HBr (55% in water, 20 mol %) did not afford the expected product (entry 4, Table 1). In addition, increasing or decreasing the amounts of **1a**, **2a**, or iodine was not helpful (entries 5−8, Table 1). The reaction proceeded well under an argon or oxygen atmosphere (entries 9 and 10, Table 1; also see page 4 of the Supporting Information). The reaction did not proceed in the absence of iodine or DMSO (entries 11 and 12, Table 1). With these screening studies, further investigation was continued using **1a** (1 equiv), **2a** (1.1 equiv), and iodine (20 mol %) in DMSO (1 mL) at 80 °C.

After the optimal reaction conditions had been established, the scope of the reaction was explored. The reaction of 1-phenyl-1*H*-tetrazole-5-thiol (**2a**) with imidazo[1,2-*a*]pyridine derivatives (**1**) having different substituents on the phenyl ring has been examined (Scheme 2). The reaction of thiol **2a** proceeded smoothly with imidazo[1,2-*a*]pyridine derivatives having methyl, naphthyl, or halogen substitution at the C3 and C4 positions of the phenyl group (**3b**−**3g**). The reaction of **2a** with imidazo[1,2-*a*]pyridine derivatives substituted with thiophene or furan at the C2 position of imidazo[1,2-*a*]pyridine furnished the corresponding sulfenylated products **3h** and **3i** in 71 and 80% yields, respectively. The reactions of thiol **2a** with imidazo[1,2-*a*]pyridines bearing substituents at positions 3 and 5−8 were examined. The imidazo[1,2-*a*]pyridine derivatives with methyl substitution at positions C7 and C8 were found to be more reactive and furnished the corresponding sulfenylated products **3j** and **3k**, respectively (86 and 86% yields, respectively), whereas the reaction of an imidazo[1,2-*a*]pyridine derivative with methyl substitution at the C5 position led to the sulfenylated product **3l** in 75% yield. Halogen substitution at the C6 position of imidazo[1,2-*a*]pyridine has no bearing on the outcome of the reaction and furnished products **3m** and **3n** in 78 and 83% yields, respectively. 3-Methylimidazo[1,2-*a*]pyridine, in which the C3 position is blocked, failed to furnish C2-sulfenylated product **3o** (Scheme 2). The regioselectivity observed in this reaction at the C3 position is due to the higher electron density at the C3 position of imidazo[1,2-*a*]pyridine heterocycles.[7,12,14a]

After the reactions of a variety of imidazo[1,2-*a*]pyridine derivatives (**1**) with 1-phenyl-1*H*-tetrazole-5-thiol (**2a**) had been explored, further investigation was undertaken using a variety of heterocyclic thiols (**2**) with **1a**, and results are presented in Scheme 3. From these reactions, it was found that a variety of heterocyclic thiols (**2**) can successfully react with **1a** to afford the corresponding sulfenylated products. The reaction

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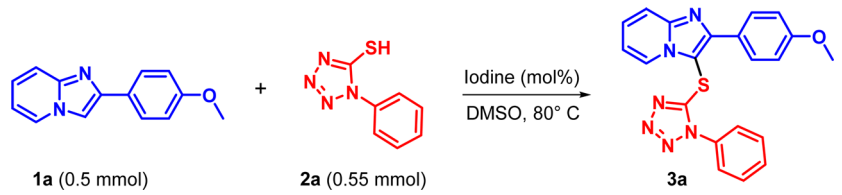
Table 1. Optimization of Reaction Conditions[a]



1a (0.5 mmol) + **2a** (0.55 mmol) → **3a**

entry	catalyst or additive (mol %)	solvent	time (h)	isolated yield (%)[b]
1	I_2 (20)	DMSO	8	90
2	I_2 (20)	solvents	24	trace[c]
3	55% aq HI (20)	DMSO	12	78
4	55% aq HBr (20)	DMSO	12	not detected
5	I_2 (20)	DMSO	8	90[d]
6	I_2 (20)	DMSO	8	86[e]
7	I_2 (10)	DMSO	16	82
8	I_2 (30)	DMSO	4	90
9	I_2 (20)	DMSO	10	90[f]
10	I_2 (20)	DMSO	8	91[g]
11	none	DMSO	12	not detected
12	I_2 (20)	none	12	not detected

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.55 mmol), and catalyst (0.1 mmol) in 1 mL of DMSO at 80 °C for 8 h. [b]Isolated yield. [c]Solvents = DMF, DMA, CH_3CN, EtOAc, and toluene. [d]One equivalent of **1a** and 1.5 equiv of **2a**. [e]One and one-half equivalents of **1a** and 1 equiv of **2a**. [f]Reaction under an argon atmosphere. [g]Reaction under an oxygen atmosphere.

of **1a** with heterocyclic thiols such as 1-methyl-1*H*-tetrazole-5-thiol and 5-methyl-1,3,4-thiadiazole-2-thiol proceeded well, furnishing their corresponding sulfenylated products **4a** and **4b**, respectively in excellent yields (93 and 81%, respectively). Although pyridine-2-thiol and pyrimidine-2-thiol underwent sulfenylation with **1a** to form **4c** and **4d**, respectively, in good to moderate yields (79 and 54%, respectively), these reactions required a stoichiometric amount of iodine to produce good yields of the products (Scheme 3). It is appropriate and noteworthy to mention that thiophenol under the standard reaction conditions was found to be less reactive and a trace amount sulfenylated product **4e** was obtained (Scheme 3). The scope of the sulfenylation reaction was further extended to a heterocyclic thione such as benzo[*d*]thiazole-2(3*H*)-thione, which can function as a surrogate thiol. Thus, the reaction of benzo[*d*]thiazole-2(3*H*)-thione under optimal reaction conditions afforded the expected sufenylated product **4f** in low yield (41%). However, the yield of **4f** increased to 90% with the use of a stoichiometric amount of iodine. Similarly, benzo[*d*]-thiazole-2(3*H*)-thione derivatives such as 5-methoxybenzo[*d*]-thiazole-2(3*H*)-thione, 4-methylthiazole-2(3*H*)-thione, and benzo[*d*]oxazole-2(3*H*)-thione successfully participated in the CDC reaction to afford **4g**–**4i**, respectively, in good to excellent yields [80, 86, and 65%, respectively (Scheme 3)].

The scope of this reaction was further extended to the imidazo[2,1-*b*]thiazole and pyrimidine derivatives (Scheme 4). 6-(4-Methoxyphenyl)imidazo[2,1-*b*]thiazole was successfully sulfenylated with phenyl-1*H*-tetrazole-5-thiol and 5-methyl-1,3,4-thiadiazole-2-thiol to form **5a** and **5b**, respectively, in excellent yields under the optimal reaction conditions (86 and 83%, respectively). Similarly, pyridine-2-thiol underwent a smooth sufenylation with 6-(4-methoxyphenyl)imidazo[2,1-*b*]thiazole to afford product **5c** in 84% yield. Thiones such as benzo[*d*]thiazole-2(3*H*)-thione and 4-methylthiazole-2(3*H*)-thione successfully coupled with 6-(4-methoxyphenyl)imidazo-[2,1-*b*]thiazole to afford **5d** and **5e**, respectively, in excellent yields with a stoichiometric amount of iodine [88 and 90%, respectively (Scheme 4)]. Similarly, 2-(4-methoxyphenyl)-imidazo[1,2-*a*]pyrimidine was successfully sulfenylated with thiol **2a** to furnish **6** in excellent yield [89% (Scheme 4)].

To probe the mechanism, a few control experiments were conducted (Scheme 5). First, the reaction of **1a** and 1-phenyl-1*H*-tetrazole-5-thiol **2a** under the standard conditions in the presence of TEMPO proceeded well to form **3a** in 88% yield, indicating that the reaction is not proceeding through a radical mechanism (Scheme 5a). Further, a reaction of 1,2-bis(benzo-[*d*]thiazol-2-yl)disulfane with **1a** was performed, which proceeded well with a catalytic amount of iodine, furnishing the sulfenylated product **4f** in 86% yield. This experiment supports the idea that the reaction is proceeding through a disulfide intermediate (Scheme 5b), whereas benzo[*d*]thiazole-2(3*H*)-thione required a stoichiometric amount of iodine for sulfenylation [**4f** (Scheme 3)]. The reaction of **1a** with a stoichiometric amount of iodine led to an iodination at the C3 position of imidazo[1,2-*a*]pyridine in 59% yield [7 (Scheme 5c)].

3-Iodo-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**7**) in a reaction with thiol **2a** under optimal conditions furnished **3a** in 68% yield (Scheme 5d). The reaction of benzo[*d*]thiazole-2(3*H*)-thione or heterocyclic thiols under the optimal reaction conditions resulted in complete decomposition of the starting materials (Scheme 5e). The NMR study of the reaction of the thiol 1-methyl-1*H*-tetrazole-5-thiol under the optimal reaction conditions has shown the formation a disulfide intermediate (see the Supporting Information, NMR studies, experiment 1). Further, the NMR studies have also indicated that the reactions of thiol or thione with iodine and DMSO resulted in the complete decomposition of thiol or thione (see the Supporting Information, NMR studies, experiments 2 and 3). From these experiments, we believe that the reaction must be proceeding through the disulfide intermediate (Scheme 5).

On the basis of the literature precedence,[4a−d,14a] and control experiments, a plausible mechanism has been proposed (Scheme 6). Benzo[*d*]thiazole-2(3*H*)-thione (**I**) in the

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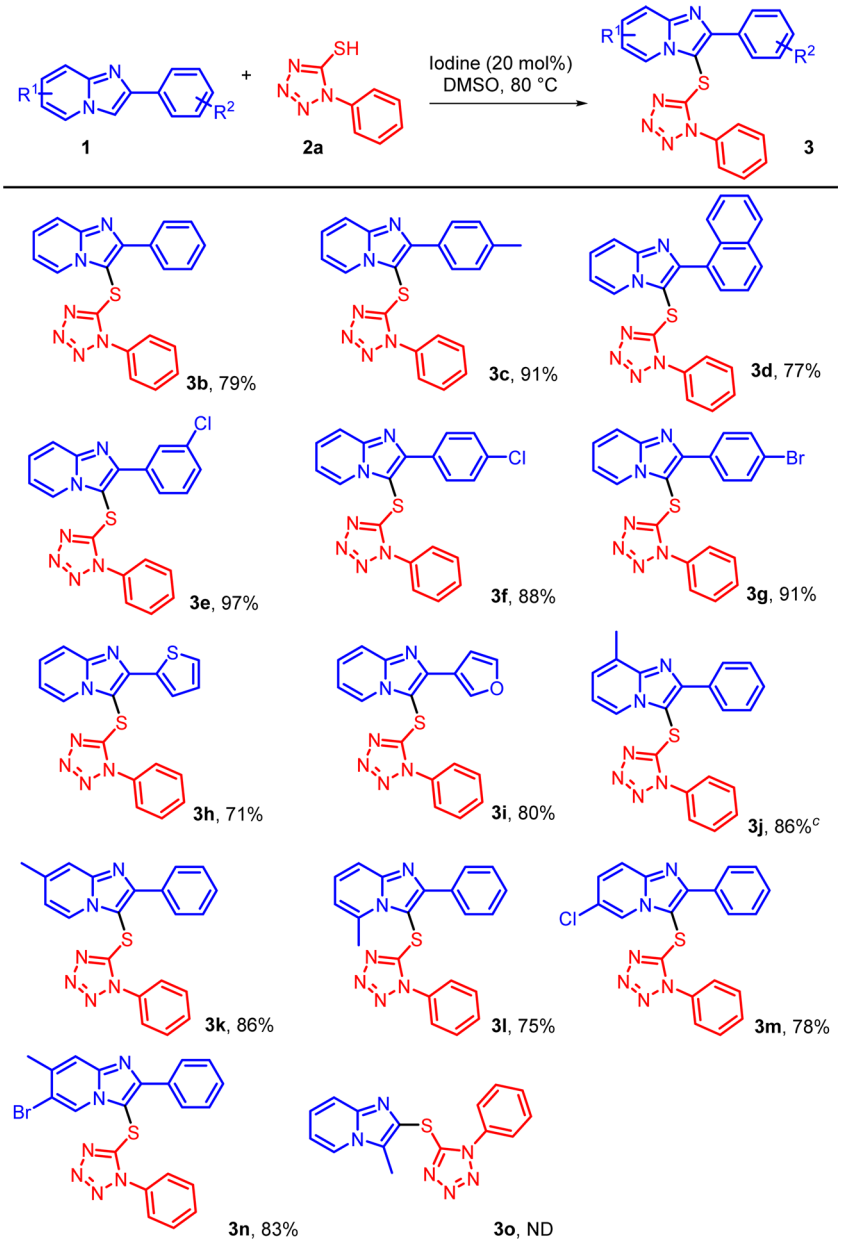
Scheme 2. Substrate Scope with 1-Phenyl-1*H*-tetrazole-5-thiol with Imidazo[1,2-*a*]pyridine Derivatives[a,b]



[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.55 mmol), and catalyst (0.1 mmol) in 1 mL of DMSO at 80 °C for 8 h. [b]Isolated yield. [c]Reaction performed on a gram scale.

presence of iodine, DMSO, and **1a** forms the intermediate 1,2-bis(benzo[*d*]thiazol-2-yl)disulfane (**II**). DMSO is known to react with HI to from a DMS:I_2 intermediate (**III**).[4d] The disulfide intermediate 1,2-bis(benzo[*d*]thiazol-2-yl)disulfane (**II**) reacts with the DMS:I_2 intermediate or I_2 to form intermediate **IV**, which contains a S–I bond. Further, the reaction of **IV** with **1a** furnishes **4f** and HI. In addition, HI reacts with DMSO, and cycles continue (Scheme 6). Benzo[*d*]thiazole-2(3*H*)-thione requires a stoichiometric amount of iodine (1 equiv) to drive the reaction rather than a catalytic amount, whereas 1,2-bis(benzo[*d*]thiazol-2-yl)-disulfane requires a catalytic amount of iodine (20 mol %). As benzo[*d*]thiazole-2(3*H*)-thione exists, predominantly, in thiol form, highly acidic conditions are required for converting thione to the corresponding thiol.[15f,g] Besides, iodine is required for the formation of 1,2-bis(benzo[*d*]thiazol-2-yl)-disulfane. The disulfide thus formed would react with **1a** in the presence of a catalytic amount of iodine to furnish the product **4f**.

■ CONCLUSION

In conclusion, we have developed a simple synthetic approach for regioselective sulfenylation of imidazoheterocycles using iodine as a catalyst and DMSO as an oxidant. To the best our knowledge, this is the first report of sulfenylation of imidazoheterocycles with heterocyclic thiols or thiones under metal-free conditions. A diverse range of heterocyclic thiols and heterocyclic thiones successfully coupled to imidazoheterocycles through the CDC reaction. The described transformation is highly practical as the starting materials and reagents used are readily available. Iodine and DMSO are

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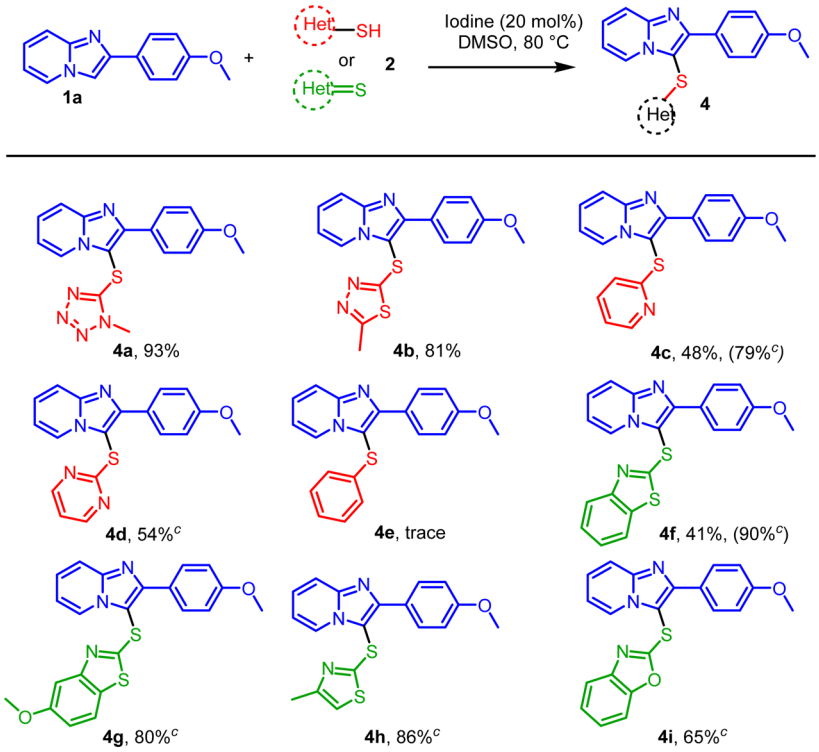
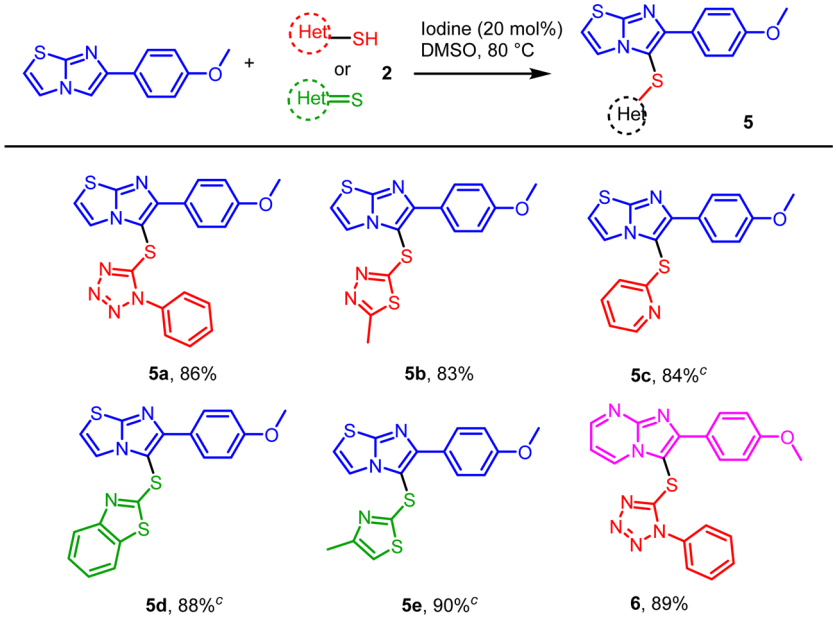
Scheme 3. Substrate Scope with Heterocyclic Thiols (2) with 2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridine[a,b]



[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.55 mmol), and catalyst (0.1 mmol) in 1 mL of DMSO at 80 °C for 8 h. [b]Isolated yield. [c]One equivalent of iodine used, at 80 °C for 3 h.

Scheme 4. Substrate Scope with 6-(4-Methoxyphenyl)imidazo[2,1-*b*]thiazole and Heterocyclic Thiols and Thiones[a,b]



[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.55 mmol), and catalyst (0.1 mmol) in 1 mL of DMSO at 80 °C for 8 h. [b]Isolated yield. [c]One equivalent of iodine used, at 80 °C for 3 h.

inexpensive and are a green sustainable catalyst and a green sustainable oxidant, respectively.

EXPERIMENTAL SECTION

General Information. NMR spectra were recorded on a 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6. Tetramethylsilane (TMS; δ 0.00) for ^{1}H NMR in $CDCl_3$ and a residual nondeuterated solvent peak (δ 2.50) in DMSO-d_6 served as internal standards. The solvent signal ($CDCl_3$, δ 77.00; DMSO-d_6, δ 39.5) was used as an internal standard for ^{13}C NMR. IR spectra were recorded using an FT-IR spectrometer. Mass spectra were recorded with a Q-TOF mass spectrometer (HRMS). Flash column chromatography was performed by packing glass columns with commercial silica gel 230−400 mesh

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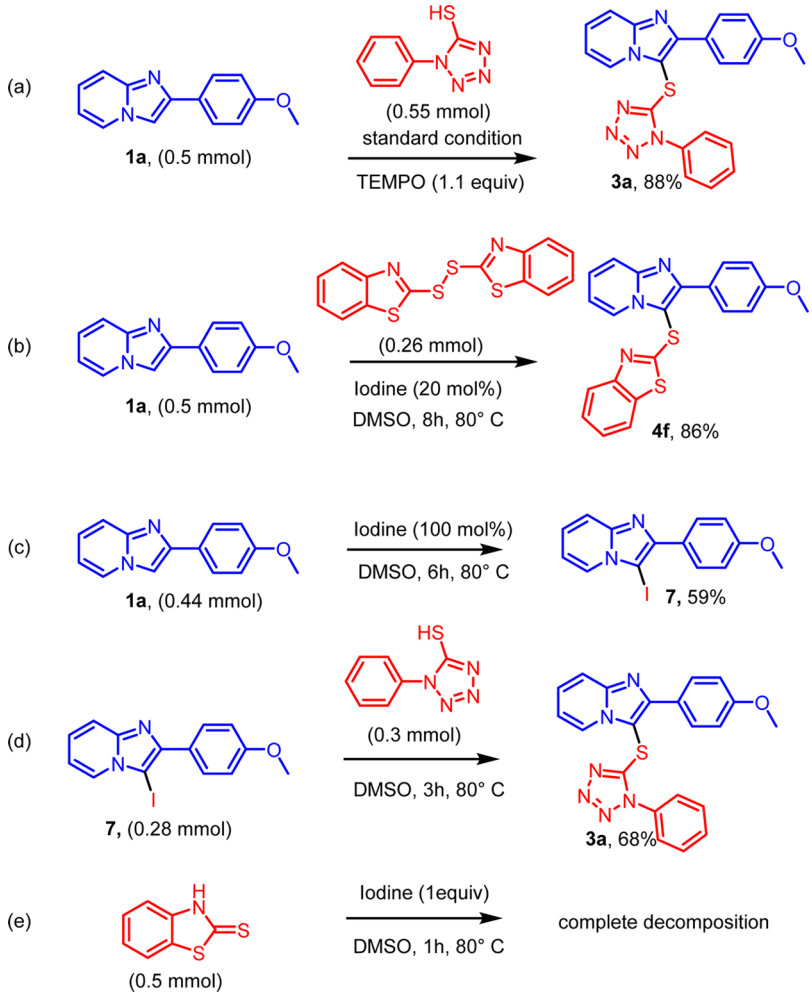
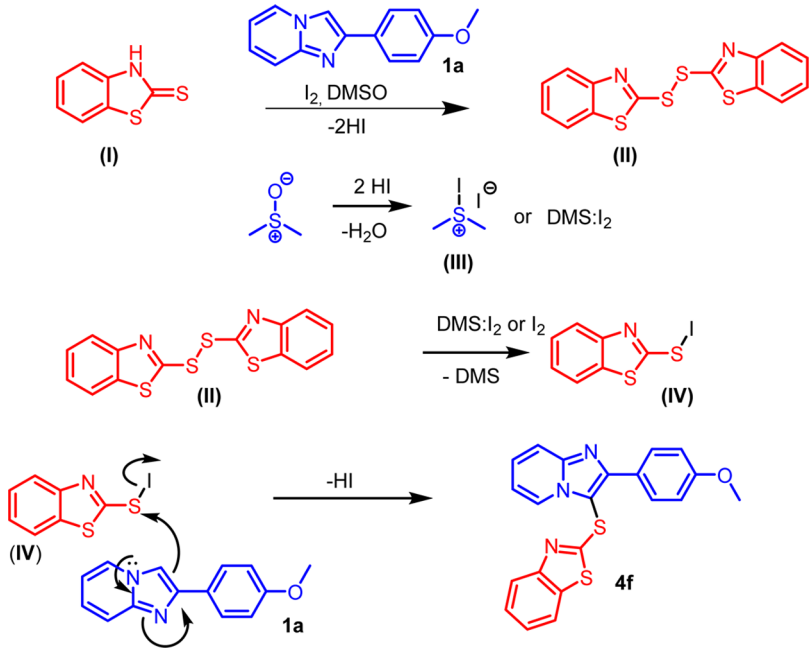
Scheme 5. Control Experiments



Scheme 6. A Tentative Reaction Mechanism



(commercial suppliers), and thin-layer chromatography was performed using silica gel GF-254. All catalysts, reagents, and reactants were procured from commercial suppliers. Dichloroethane solvent was distilled over calcium hydride, stored over molecular sieves, and used

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for all procedures. Other solvents, used for workup and chromatographic procedures, were purchased from commercial suppliers and used without any further purification.

Typical Experimental Procedure for Sulfenylation of Imidazoheterocycles. Imidazoheterocycles (0.5 mmol) and heterocyclic thiols (0.55 mmol) were dissolved in DMSO (1 mL) and added iodine (0.1 mmol) (addition of iodine for thiols is highly exothermic, and decomposition of thiol was observed). The reaction mixture was stirred at 80 °C for 3−8 h. After the reaction had reached completion (monitored by TLC), water (25 mL) and a dilute sodium thiosulfate solution (5 mL) were added and an extract product with ethyl acetate (3 × 20 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified on a silica gel column using 30−50% EtOAc/hexane to obtain the pure products.

*2-(4-Methoxyphenyl)-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo-[1,2-a]pyridine (**3a**).* Pale yellow oily liquid: yield 90% (180 mg); R_f = 0.2 (50% EtOAc/hexane); IR (neat) 3417, 2964, 2888, 2833, 1790, 1737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 6.8 Hz, 1H), 7.88 (d, J = 9.2 Hz, 2H), 7.66 (d, J = 8.8 Hz, 1H), 7.49−7.46 (m, 5H), 7.38−7.34 (m, 1H), 6.96−6.91 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 152.2, 151.4, 147.6, 133.0, 130.4, 129.9, 129.7, 127.4, 125.0, 124.6, 124.1, 117.5, 113.8, 113.4, 98.2, 55.2; HRESI-MS (m/z) calcd for $C_{21}H_{16}N_6OS$ (M^+ + H) 401.1185, found (M^+ + H) 401.1183.

*2-Phenyl-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo[1,2-a]-pyridine (**3b**).* White solid: mp 148−151 °C; yield 79% (146 mg); R_f = 0.2 (50% EtOAc/hexane); IR (KBr) 3051, 2921, 1944, 1676, 1631, 1595, 1529, 1493 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 6.8 Hz, 1H), 7.92−7.90 (m, 2H), 7.68 (d, J = 8.8 Hz, 1H), 7.46−7.45 (m, 5H), 7.41−7.34 (m, 4H), 6.96−6.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 151.2, 147.6, 132.9, 132.4, 130.4, 129.7, 128.8, 128.6, 128.3, 127.4, 124.7, 124.0, 117.7, 113.6, 99.1; HRESI-MS (m/z) calcd for $C_{20}H_{14}N_6S$ (M^+ + Na) 393.0898, found (M^+ + Na) 393.0897.

*3-[(1-Phenyl-1H-tetrazol-5-yl)thio]-2-(p-tolyl)imidazo[1,2-a]-pyridine (**3c**).* Pale yellow oily liquid: yield 91% (175 mg); R_f = 0.3 (50% EtOAc/hexane); IR (neat) 3020, 2964, 2873, 2831, 1800, 1729, 1674, 1596 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 6.8 Hz, 1H), 7.81 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.54−7.49 (m, 5H), 7.42−7.38 (m, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.01−6.96 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 151.4, 147.6, 138.9, 133.1, 130.5, 129.7, 129.7, 129.1, 128.6, 127.4, 124.7, 124.1, 117.8, 113.5, 98.8, 21.3; HRESI-MS (m/z) calcd for $C_{21}H_{16}N_6S$ (M^+ + H) 385.1235, found (M^+ + H) 385.1233.

*2-(Naphthalen-1-yl)-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo-[1,2-a]pyridine (**3d**).* Yellow viscous liquid: yield 77% (162 mg); R_f = 0.3 (50% EtOAc/hexane); IR (neat) 3056, 3012, 2957, 2929, 2854, 1939, 1731, 1632, 1594, 1494 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 6.8 Hz, 1H), 7.42−7.27 (m, 3H), 7.81 (d, J = 9.2 Hz, 1H), 7.54 (d, J = 6.8 Hz, 1H), 7.49−7.45 (m, 3H), 7.43−7.30 (m, 4H), 7.26−7.273 (m, 2H), 7.08 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 151.6, 147.9, 133.6, 1323.0, 132.0, 130.3, 130.2, 129.6, 129.3, 128.8, 128.1, 127.6, 126.4, 125.9, 125.9, 125.1, 124.9, 123.8, 118.1, 113.8, 102.2; HRESI-MS (m/z) calcd for $C_{24}H_{16}N_6S$ (M^+ + Na) 443.1055, found (M^+ + Na) 443.1057.

*2-(3-Chlorophenyl)-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo-[1,2-a]pyridine (**3e**).* White solid: mp 175−178 °C; yield 97% (196 mg); R_f = 0.2 (30% EtOAc/hexane); IR (KBr) 3075, 2252, 2202, 2088, 1631, 1594, 1564, 1491, 1444 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 6.8 Hz, 1H), 7.93 (d, J = 0.8 Hz, 1H), 7.83−7.80 (m, 1H), 7.68 (d, J = 9.2 Hz, 1H), 7.53−7.45 (m, 5H), 7.42−7.38 (m, 1H), 7.35−7.28 (m, 2H), 6.99 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 150.6, 147.6, 134.3, 134.3, 132.9, 130.6, 129.8, 129.6, 128.8, 128.5, 127.7, 126.7, 124.8, 124.1, 117.9, 113.9, 99.7; HRESI-MS (m/z) calcd for $C_{20}H_{13}ClN_6S$ (M^+ + Na) 427.0509, found (M^+ + Na) 427.0511.

*2-(4-Chlorophenyl)-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo-[1,2-a]pyridine (**3f**).* White solid: mp 170−172 °C; yield 88% (178 mg); R_f = 0.2 (30% EtOAc/hexane); IR (KBr) 3060, 2923, 2852, 2381, 2249, 2201, 1941, 1631, 1592, 1494, 1454 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 6.8 Hz, 1H), 7.86 (dd, J = 8.8, 2.0 Hz, 2H), 7.69 (d, J = 9.2 Hz, 1H), 7.57−7.378 (m, 6H), 7.36 (dd, J = 8.8, 2.0 Hz, 2H), 7.01−6.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 151.0, 147.7, 134.9, 133.0, 131.1, 130.6, 129.9, 129.8, 128.6, 127.7, 124.8, 124.2, 117.9, 113.8, 99.4; HRESI-MS (m/z) calcd for $C_{20}H_{13}ClN_6S$ (M^+ + Na) 427.0509, found (M^+ + Na) 427.0509.

*2-(4-Bromophenyl)-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo-[1,2-a]pyridine (**3g**).* White solid: mp 170−172 °C; yield 91% (204 mg); R_f = 0.2 (30% EtOAc/hexane); IR (KBr) 3062, 2922, 2851, 2200, 2115, 2042, 1993, 1943, 1745, 1630, 1590, 1493 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 6.8 Hz, 1H), 7.79 (d, J = 8.8 Hz, 2H), 7.68 (d, J = 8.8 Hz, 1H), 7.56−7.38 (m, 8H), 7.00−6.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2, 150.9, 147.7, 133.0, 131.5, 131.5, 130.6, 130.1, 129.8, 127.7, 124.8, 124.1, 123.3, 117.9, 113.8, 99.5; HRESI-MS (m/z) calcd for $C_{20}H_{13}BrN_6S$ (M^+ + Na) 471.0003, found (M^+ + Na) 471.0002.

*3-[(1-Phenyl-1H-tetrazol-5-yl)thio]-2-(thiophen-2-yl)imidazo[1,2-a]pyridine (**3h**).* White solid: mp 164−168 °C; yield 71% (134 mg); R_f = 0.3 (50% EtOAc/hexane); IR (KBr) 3122, 3060, 3032, 2923, 2852, 1961, 1630, 1590, 1490 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 6.8 Hz, 1H), 7.73 (dd, J = 3.6, 0.8 Hz, 1H), 7.63 (d, J = 9.2 Hz, 1H), 7.51−7.44 (m, 5H), 7.37−7.33 (m, 2H), 7.05−7.03 (m, 1H), 6.94−6.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 147.5, 147.0, 135.1, 132.9, 130.5, 129.7, 127.6, 127.3, 127.1, 124.5, 124.2, 117.4, 113.6, 97.8; HRESI-MS (m/z) calcd for $C_{18}H_{12}N_6S_2$ (M^+ + H) 377.0643, found (M^+ + H) 377.0645.

*2-(Furan-3-yl)-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo[1,2-a]-pyridine (**3i**).* White solid: mp 140−143 °C; yield 80% (144 mg); R_f = 0.2 (50% EtOAc/hexane); IR (KBr) 3094, 3035, 2921, 2853, 1956, 1629, 1590, 1493 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 6.8 Hz, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.52−7.46 (m, 6H), 7.40−7.35 (m, 1H), 6.99−6.94 (m, 2H), 6.47 (dd, J = 3.6, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 147.8, 147.5, 143.7, 143.4, 133.1, 130.5, 129.7, 127.6, 124.5, 124.3, 117.7, 113.8, 111.6, 110.6, 98.3; HRESI-MS (m/z) calcd for $C_{18}H_{12}N_6OS$ (M^+ + Na) 383.0691, found (M^+ + Na) 383.0696.

*2-(4-Methoxyphenyl)-8-methyl-3-[(1-phenyl-1H-tetrazol-5-yl)-thio]imidazo[1,2-a]pyridine (**3j**).* Yellow oily liquid: yield 86% (1.49 g); R_f = 0.2 (30% EtOAc/hexane); IR (neat) 3409, 3069, 2926, 2839, 1734, 1610, 1534, 1496 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 6.8 Hz, 1H), 7.89−7.86 (m, 2H), 7.48−7.45 (m, 5H), 7.14 (d, J = 7.2 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 6.84 (t, J = 6.8 Hz, 1H), 3.83 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 152.0, 151.6, 147.9, 133.1, 130.3, 130.0, 129.6, 127.7, 126.1, 125.4, 124.1, 122.3, 113.8, 113.4, 98.4, 55.2, 16.6; HRESI-MS (m/z) calcd for $C_{22}H_{18}N_6OS$ (M^+ + H) 415.1341, found (M^+ + H) 415.1343.

*2-(4-Methoxyphenyl)-7-methyl-3-[(1-phenyl-1H-tetrazol-5-yl)-thio]imidazo[1,2-a]pyridine (**3k**).* White solid: mp 180−183 °C; yield 86% (179 mg); R_f = 0.2 (50% EtOAc/hexane); IR (KBr) 3052, 2964, 2935, 2841, 2201, 1891, 1638, 1605, 1529 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 6.8 Hz, 1H), 7.86 (d, J = 7.2 Hz, 1H), 7.51−7.46 (m, 5H), 7.42 (s, 1H), 6.91 (d, J = 8.8 Hz, 2H), 6.78 (dd, J = 6.8, 1.2 Hz, 1H), 3.83 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 152.3, 151.5, 148.0, 138.7, 133.1, 130.4, 129.9, 129.7, 125.2, 124.1, 123.8, 116.2, 116.0, 113.8, 97.4, 55.2, 21.3; HRESI-MS (m/z) calcd for $C_{22}H_{18}N_6OS$ (M^+ + H) 415.1341, found (M^+ + H) 415.1342.

*2-(4-Methoxyphenyl)-5-methyl-3-[(1-phenyl-1H-tetrazol-5-yl)-thio]imidazo[1,2-a]pyridine (**3l**).* Yellow oily liquid: yield 75% (155 mg); R_f = 0.2 (50% EtOAc/hexane); IR (neat) 3397, 3143, 3066, 2934, 2837, 2548, 2048, 1636, 1609, 1534 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.70 (m, 2H), 7.59 (d, J = 8.8 Hz, 1H), 7.53−7.50 (m, 3H), 7.45−7.42 (m, 2H), 7.28−7.24 (m, 1H), 6.91−6.88 (m, 2H), 6.66 (d, J = 7.2 Hz, 1H), 3.83 (s, 3H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 155.2, 154.9, 149.4, 138.2, 133.2, 130.6, 130.4, 129.8, 127.6, 125.3, 124.0, 116.3, 115.5, 113.7, 99.0, 55.2, 20.4; HRESI-MS (m/z) calcd for $C_{22}H_{18}N_6OS$ (M^+ + H) 415.1341, found (M^+ + H) 415.1343.

*6-Chloro-2-(4-methoxyphenyl)-3-[(1-phenyl-1H-tetrazol-5-yl)-thio]imidazo[1,2-a]pyridine (**3m**).* White solid: mp 182−184 °C; yield 78% (169 mg); R_f = 0.3 (50% EtOAc/hexane); IR (KBr) 3121,

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3068, 2925, 2834, 2045, 1969, 1889, 1705, 1605, 1530, 1496, 1462 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.32−8.31 (m, 1H), 7.88 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 9.2 Hz, 1H), 7.54−7.48 (m, 5H), 7.33 (dd, J = 9.6, 2.0 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 153.0, 151.2, 146.0, 133.1, 130.6, 129.9, 129.8, 128.7, 124.7, 124.2, 122.7, 121.8, 118.0, 113.9, 99.3, 55.3; HRESI-MS (m/z) calcd for $C_{21}H_{15}ClN_6OS$ (M^+ + H) 435.0795, found (M^+ + H) 435.0798.

*6-Bromo-2-(4-methoxyphenyl)-7-methyl-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo[1,2-a]pyridine (**3n**).* White solid: mp 181−183 °C; yield 83% (205 mg); R_f = 0.2 (30% EtOAc/hexane); IR (KBr) 3049, 2921, 2831, 1604, 1576, 1529, 1487, 1462, 1380 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.80 (d, J = 8.8 Hz, 2H), 7.54−7.49 (m, 6H), 6.92−6.90 (m, 2H), 3.84 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 152.7, 151.5, 146.9, 138.4, 133.1, 130.5, 129.9, 129.8, 124.9, 124.7, 124.2, 116.8, 113.9, 112.3, 97.7, 55.3, 22.7; HRESI-MS (m/z) calcd for $C_{22}H_{17}BrN_6OS$ (M^+ + H) 493.0446, found (M^+ + H) 493.0444.

*2-(4-Methoxyphenyl)-3-[(1-methyl-1H-tetrazol-5-yl)thio]imidazo-[1,2-a]pyridine (**4a**).* White solid: mp 196−200 °C; yield 93% (156 mg); R_f = 0.3 (70% EtOAc/hexane); IR (KBr) 3089, 2973, 2931, 2844, 1946, 1900, 1604, 1570, 1529 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 6.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 2H), 7.70 (d, J = 8.8 Hz, 1H), 7.42−7.38 (m, 1H), 7.03−6.99 (m, 3H), 3.87 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 152.1, 150.1, 147.5, 130.2, 127.7, 125.0, 124.8, 117.6, 114.0, 113.7, 98.8, 55.3, 34.1; HRESI-MS (m/z) calcd for $C_{16}H_{14}N_6OS$ (M^+ + H) 339.1028, found (M^+ + H) 339.1033.

*2-{[2-(4-Methoxyphenyl)imidazo[1,2-a]pyridin-3-yl]thio}-5-methyl-1,3,4-thiadiazole (**4b**).* White solid: mp 160−162 °C; yield 81% (143 mg); R_f = 0.2 (70% EtOAc/hexane); IR (KBr) 3030, 2921, 2835, 2550, 2200, 1733, 1607, 1571, 1531 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 6.8 Hz, 1H), 8.16 (dd, J = 6.8, 2.0 Hz, 2H), 7.72 (d, J = 8.8 Hz, 1H), 7.42−7.38 (m, 1H), 7.02−6.97 (m, 3H), 3.87 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 166.4, 160.3, 151.1, 147.3, 129.6, 127.4, 125.0, 124.2, 117.5, 113.9, 113.6, 103.6, 55.2, 15.6; HRESI-MS (m/z) calcd for $C_{17}H_{14}N_4OS_2$ (M^+ + H) 355.0687, found (M^+ + H) 355.0688.

*2-(4-Methoxyphenyl)-3-(pyridin-2-ylthio)imidazo[1,2-a]pyridine (**4c**).* Yellow oil: yield 79% (132 mg); R_f = 0.2 (50% EtOAc/hexane); IR (neat) 3417, 2961, 2897, 2834, 1800, 1729, 1674, 1610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.43−8.41 (m, 1H), 8.28 (d, J = 6.8 Hz, 1H), 8.15 (d, J = 8.8 Hz, 2H), 7.72 (d, J = 8.8 Hz, 1H), 7.40−7.28 (m, 2H), 7.03−7.01 (m, 1H), 6.96−6.94 (m, 2H), 6.88−6.84 (m, 1H), 6.60 (dd, J = 8.4, 0.8 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 158.6, 151.2, 150.1, 147.2, 137.2, 129.6, 126.6, 125.7, 124.3, 120.8, 119.3, 117.3, 113.8, 112.9, 104.3, 55.2; HRESI-MS (m/z) calcd for $C_{19}H_{15}N_3OS$ (M^+ + H) 334.1014, found (M^+ + H) 334.1012.

*2-(4-Methoxyphenyl)-3-(pyrimidin-2-ylthio)imidazo[1,2-a]-pyridine (**4d**).* Brown solid: mp 172−175 °C; yield 54% (90 mg); R_f = 0.2 (70% EtOAc/hexane); IR (KBr) 3069, 3036, 2923, 2842, 1701, 1676, 1604, 1553, 1466 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 5.2 Hz, 2H), 8.22 (d, J = 6.4 Hz, 1H), 8.10−8.08 (m, 2H), 7.73 (d, J = 8.8 Hz, 1H), 7.36−7.32 (m, 1H), 7.02−6.95 (m, 3H), 6.86 (t, J = 6.8 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 159.9, 158.0, 151.0, 147.1, 129.9, 126.5, 126.0, 124.6, 117.8, 117.4, 113.7, 112.6, 104.2, 55.2; HRESI-MS (m/z) calcd for $C_{18}H_{14}N_4OS$ (M^+ + H) 335.0967, found (M^+ + H) 335.0965.

*2-{[2-(4-Methoxyphenyl)imidazo[1,2-a]pyridin-3-yl]thio}benzo-[d]thiazole (**4f**).* White solid: mp 184−186 °C; yield 90% (175 mg); R_f = 0.3 (50% EtOAc/hexane); IR (KBr) 3058, 3023, 2996, 2924, 2545, 1901, 1698, 1604, 1570, 1528 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 6.8 Hz, 1H), 8.19−8.16 (m, 2H), 7.88 (d, J = 8.4 Hz, 1H), 7.75 (dd, J = 9.2, 0.8 Hz, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.40−7.36 (m, 2H), 7.26−7.20 (m, 1H), 6.98−6.95 (m, 2H), 6.91−6.90 (m, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 1603, 154.5, 152.1, 147.6, 135.4, 129.7, 127.4, 126.2, 125.1, 124.5, 124.2, 121.9, 121.0, 117.6, 113.9, 113.5, 103.1, 55.2; HRESI-MS (m/z) calcd for $C_{21}H_{15}N_3OS_2$ (M^+ + H) 390.0735, found (M^+ + H) 390.0734.

*5-Methoxy-2-{[2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl]-thio}benzo[d]thiazole (**4g**).* White solid: mp 123−127 °C; yield 80% (168 mg); R_f = 0.2 (50% EtOAc/hexane); IR (KBr) 3113, 3054, 2956, 2926, 2828, 2194, 2046, 1678, 1601, 1529 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (dd, J = 6.8, 0.8 Hz, 1H), 8.18−8.16 (m, 2H), 7.76 (d, J = 9.2 Hz, 1H), 7.42−7.38 (m, 3H), 6.99−6.87 (m, 4H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 160.3, 159.0, 155.8, 152.2, 147.7, 129.7, 127.4, 127.2, 125.2, 124.3, 121.2, 117.6, 114.3, 114.0, 113.5, 104.9, 103.2, 55.6, 55.2; HRESI-MS (m/z) calcd for $C_{22}H_{17}N_3O_2S_2$ (M^+ + H) 420.0840, found (M^+ + H) 420.0841.

*2-{[2-(4-Methoxyphenyl)imidazo[1,2-a]pyridin-3-yl]thio}-4-methylthiazole (**4h**).* White solid: mp 117−119 °C; yield 86% (152 mg); R_f = 0.5 (50% EtOAc/hexane); IR (KBr) 3058, 3029, 2955, 2923, 2839, 1608, 1572, 1529, 1500, 1459 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, J = 6.8, 0.8 Hz, 1H), 8.16 (d, J = 8.8 Hz, 2H), 7.71 (dd, J = 8.8, 0.8 Hz, 1H), 7.37−7.33 (m, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.93−6.90 (m, 1H), 6.62 (d, J = 0.8 Hz, 1H), 3.83 (s, 3H), 2.37 (d, J = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 160.2, 154.3, 151.4, 147.3, 129.6, 127.1, 125.3, 124.3, 117.4, 114.3, 113.8, 113.2, 104.1, 55.2, 17.2; HRESI-MS (m/z) calcd for $C_{18}H_{15}N_3OS_2$ (M^+ + Na) 376.0554, found (M^+ + Na) 376.0550.

*2-{[2-(4-Methoxyphenyl)imidazo[1,2-a]pyridin-3-yl]thio}benzo-[d]oxazole (**4i**).* Pale yellow solid: mp 145−147 °C; yield 65% (121 mg); R_f = 0.3 (50% EtOAc/hexane); IR (KBr) 3094, 3030, 2927, 2832, 1892, 1609, 1538, 1502 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 6.8 Hz, 1H), 8.10 (d, J = 8.8 Hz, 2H), 7.73 (d, J = 8.8 Hz, 1H), 7.56−7.54 (m, 1H), 7.38−7.34 (m, 2H), 7.26−7.20 (m, 2H), 6.98 (d, J = 8.8 Hz, 2H), 6.94−6.90 (m, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 160.2, 152.1, 152.0, 147.6, 141.8, 130.0, 127.1, 125.3, 124.5, 119.2, 117.6, 113.9, 113.2, 110.2, 99.5, 55.2; HRESI-MS (m/z) calcd for $C_{21}H_{15}N_3O_2S$ (M^+ + H) 374.0963, found (M^+ + H) 374.0961.

*6-(4-Methoxyphenyl)-5-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo-[2,1-b]thiazole (**5a**).* White solid: mp 157−159 °C; yield 86% (175 mg); R_f = 0.5 (30% EtOAc/hexane); IR (KBr) 3101, 2920, 2848, 1607, 1527, 1452, 1386, 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78−7.75 (m, 2H), 7.54−7.42 (m, 6H), 6.91−6.86 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 153.6, 152.7, 151.5, 133.1, 130.5, 129.7, 129.2, 125.2, 124.2, 118.4, 113.8, 113.3, 99.4, 55.2; HRESI-MS (m/z) calcd for $C_{19}H_{14}N_6OS_2$ (M^+ + H) 407.0749, found (M^+ + H) 407.0747.

*6-(4-Methoxyphenyl)-5-[(5-methyl-1,3,4-thiadiazol-2-yl)thio]-imidazo[2,1-b]thiazole (**5b**).* White solid: mp 133−136 °C; yield 83% (149 mg); R_f = 0.2 (50% EtOAc/hexane); IR (KBr) 3126, 3098, 2958, 2925, 2838, 1611, 1535, 1467, 1435, 1391, 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03−8.01 (m, 2H), 7.56 (d, J = 4.4 Hz, 1H), 6.96−6.93 (m, 3H), 3.83 (s, 3H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 166.5, 159.9, 152.6, 152.3, 128.8, 125.2, 117.9, 113.9, 113.5, 104.5, 55.2, 15.6; HRESI-MS (m/z) calcd for $C_{15}H_{12}N_4OS_3$ (M^+ + H) 361.0252, found (M^+ + H) 361.0256.

*6-(4-Methoxyphenyl)-5-(pyridin-2-ylthio)imidazo[2,1-b]thiazole (**5c**).* Yellow oil: yield 84% (142 mg); R_f = 0.2 (50% EtOAc/hexane); IR (neat) 3110, 3046, 2930, 2835, 1609, 1571, 1530, 1435, 1415 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44−8.41 (m, 1H), 8.05−8.02 (m, 2H), 7.46−7.42 (m, 2H), 7.04−7.00 (m, 1H), 6.93−6.90 (m, 2H), 6.84 (d, J = 4.8 Hz, 1H), 6.77−6.75 (m, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 159.2, 152.6, 151.6, 150.0, 137.3, 128.7, 126.0, 120.5, 119.5, 118.1, 113.8, 112.7, 105.3, 55.2; HRESI-MS (m/z) calcd for $C_{17}H_{13}N_3OS_2$ (M^+ + H) 340.0578, found (M^+ + H) 340.0577.

*2-{[6-(4-Methoxyphenyl)imidazo[2,1-b]thiazol-5-yl]thio}benzo-[d]thiazole (**5d**).* Yellow oil: yield 88% (174 mg); R_f = 0.4 (50% EtOAc/hexane); IR (neat) 3132, 3110, 3061, 2997, 2960, 2835, 1610, 1531, 1464 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 8.0 Hz, 1H), 7.61−7.59 (m, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.42−7.38 (m, 1H), 7.27−7.22 (m, 1H), 6.93 (d, J = 9.2 Hz, 1H), 6.89 (d, J = 4.4 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 160.0, 154.5, 153.7, 152.6, 135.5, 128.9, 126.3, 125.4, 124.5, 122.0, 121.0, 117.9, 113.9, 113.4, 104.1, 55.2; HRESI-MS (m/z)

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calcd for $C_{19}H_{13}N_3OS_3$ (M^+ + H) 396.0299, found (M^+ + H) 396.0297.

*6-(4-Methoxyphenyl)-5-[(4-methylthiazol-2-yl)thio]imidazo[2,1-b]thiazole (**5e**).* Yellow oil: yield 90% (161 mg); R_f = 0.4 (50% EtOAc/hexane); IR (neat) 3416, 3108, 2957, 2926, 2835, 1610, 1529, 1464 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.8 Hz, 2H), 7.51−7.50 (m, 1H), 6.94 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 4.4 Hz, 1H), 6.67 (s, 1H), 3.82 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 159.8, 154.2, 152.8, 152.1, 128.8, 125.6, 118.0, 114.5, 113.8, 113.0, 105.1, 55.2, 17.2; HRESI-MS (m/z) calcd for $C_{16}H_{13}N_3OS_3$ (M^+ + H) 360.0299, found (M^+ + H) 360.0297.

*2-(4-Methoxyphenyl)-3-[(1-phenyl-1H-tetrazol-5-yl)thio]imidazo-[1,2-a]pyrimidine (**6**).* Pale yellow solid: mp 176−178 °C; yield 89% (178 mg); R_f = 0.2 (70% EtOAc/hexane); IR (neat) 3073, 3009, 2929, 2839, 1893, 1731, 1608, 1529, 1498 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (dd, J = 6.8, 2.0 Hz, 1H), 8.63 (dd, J = 4.0, 2.0 Hz, 1H), 7.95−7.52 (m, 2H), 7.53−7.46 (m, 5H), 7.00 (dd, J = 7.2, 4.8 Hz, 1H), 6.89−6.87 (m, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 153.2, 152.1, 150.9, 150.3, 132.9, 132.6, 130.6, 130.1, 129.8, 124.3, 124.1, 113.8, 109.5, 97.4, 55.2; HRESI-MS (m/z) calcd for $C_{20}H_{15}N_7OS$ (M^+ + Na) 424.0956, found (M^+ + Na) 424.0958.

*3-Iodo-2-(4-methoxyphenyl)imidazo[1,2-a]pyridine (**7**).* White solid: mp 130−132 °C; yield 59% (92 mg); R_f = 0.2 (30% EtOAc/hexane); IR (KBr) 3314, 3158, 2932, 2835, 2317, 1610, 1534, 1468 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 6.8 Hz, 1H), 8.03−8.00 (m, 2H), 7.59 (d, J = 9.2 Hz, 1H), 7.26−7.20 (m, 1H), 7.03−7.00 (m, 2H), 6.91−6.87 (m, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 148.0, 147.9, 129.7, 126.4, 126.1, 125.3, 117.3, 113.7, 112.9, 58.7, 55.3; HRESI-MS (m/z) calcd for $C_{14}H_{11}IN_2O$ (M^+ + H) 350.9994, found (M^+ + H) 350.9995.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01487.

Optimization data, the NMR study, and ^1H and ^{13}C NMR spectral data of all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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