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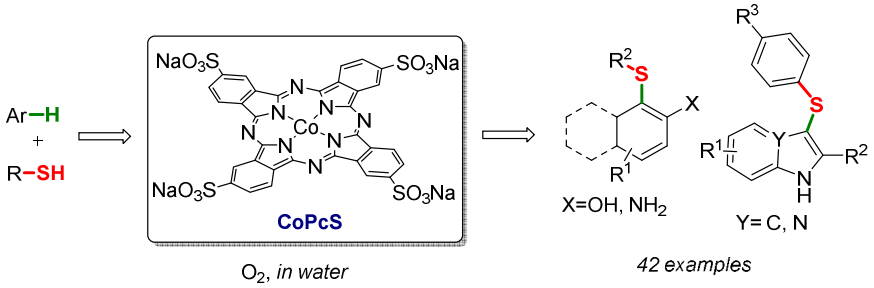
Cobalt-Catalyzed Aerobic Cross-dehydrogenative Coupling of C-H and Thiols in Water for C-S Formation

Xin Huang,[†] Yongqi Chen,[†] Shan Zhen,[†] Lijuan Song,[†] Mingqi Gao,[‡] Panke Zhang,[†] Heng Li,[†] Bingxin Yuan,*[,†] and Guanyu Yang[†]

[†]College of Chemistry and Molecular Engineering, Zhengzhou University, Henan, China 450001

[‡]China Tobacco Henan Industry Co., Ltd., Zhengzhou, Henan, China, 450001

Abstract: Organosulfides have great significance and value in synthetic and biological chemistry. To establish a versatile and green methodology for C-S bond generation, we successfully developed a new aerobic cross-dehydrogenative coupling of C-H and S-H to synthesize arylsulfides in water, utilizing CoPcS as the catalyst and O_2 as the oxidant. This protocol shows great tolerance of a wide range of substrates. A large variety of organosulfur compounds were produced in modest to excellent yields.



Introduction

Organosulfur compounds are attracting much interest from organic and medical chemists because of their abundance in nature and biological systems.[1] They are found to hold significant positions in living organisms as amino acids, peptides, protein crosslinking units, *etc*.[2] Antibiotics including penicillin and sulfa drugs have saved millions of lives in decades,[3] and noticeably, three of the five top selling drugs in 2015 were organosulfur compounds.[4] Due to the numerous biological applications and pharmaceutical value of organosulfur compounds, carbon-sulfur bond generation has become a primary focus in the synthesis of valuable chemical motifs.[5] The vast majority of synthetic methodologies for approaching C-S bond have been focused on transitional metal catalyzed cross-coupling of thiols and their derivatives with organohalides (Figure 1).[6] However, these methods are susceptible to the need for expensive and sensitive metal catalysts, harsh reaction conditions, extra additives, and producing toxic waste.

The upsurge in the concepts of green chemistry and atom economy led to the attempts of more practical and economical process for the C-S bond formation. Synthesis of aryl sulfide via C-H functionalization under metal-free[7] or transitional metal[8] catalyzed conditions with various sulfur sources such as disulfides, arylsulfonyl chlorides, sodium arylsulfinates, sulfinic acids and arylsulfonyl hydrazides, appears to be particularly appealing (Figure 1). In those protocols, such highly pre-functionalized sulfenylating reagents require several steps to prepare. Thus, the cross-dehydrogenative coupling of C-H bonds to form C-S bonds utilizing cheap and commercially available thiols as a sulfur source is of actual interest.[9]

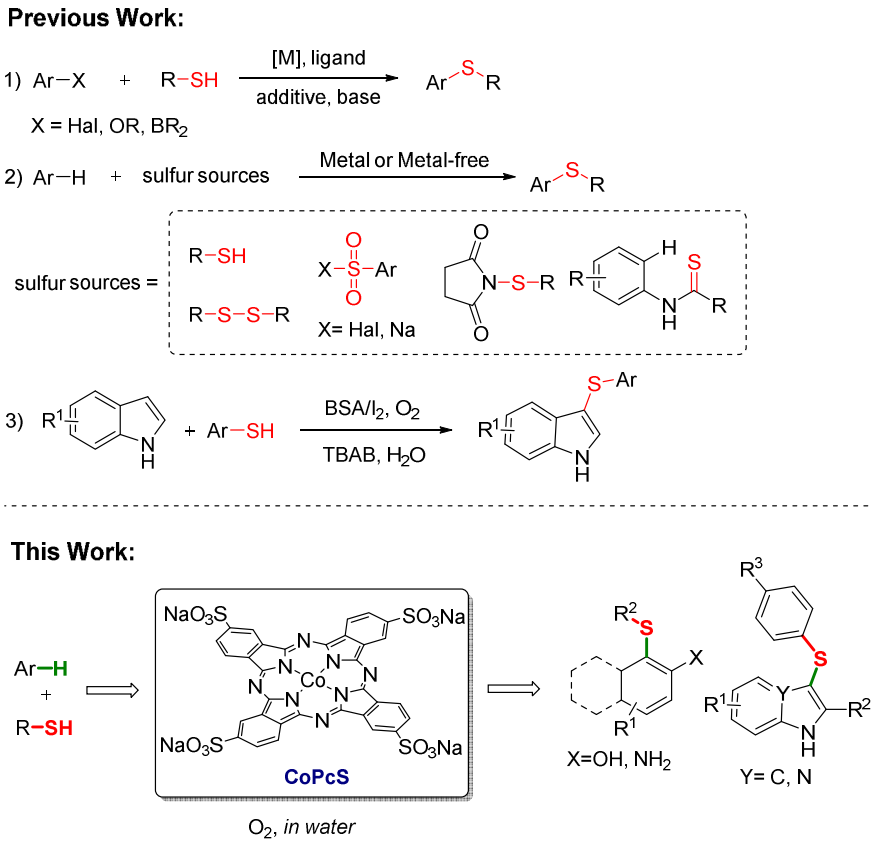


Figure 1. Synthetic Routes of Organosulfur Compounds.

O_2 has been regarded as the ideal oxidant owing to its low cost, environmental benignity, lack of toxic byproduct, and natural abundance. Surprisingly, only a few methods introduced the cross-coupling of C-H and S-H with O_2 as the sole oxidant.[10] For example, Fukuzawa et al developed the CuI/Bpy catalyzed oxidative coupling of benzoxazole and thiols under 1 atm O_2.[10g] Later, Deng and coworkers performed a I_2-catalyzed reaction of cyclohexanones with thiols to form 2-arylsulfanylphenol in the presence of O_2 as the sole oxidant.[10h] However, the main

problem is that most reactions were carried out in organic solvents, which are major sources of waste mass in chemical manufacturing.

From an economical and environmental point of view, water as solvent for organic synthesis has been significantly attractive in recent years. To the best of our knowledge, the cross-dehydrogenative coupling of C-H and S-H to achieve organosulfur compounds in water in the presence of O_2 was scarcely studied. The only work was reported by Sinha and coworkers, in which bovine serum albumin (BSA)-I_2 cocatalyzed the sulfenylation of indoles with thiolphenols in aqueous media using O_2 (Figure 1).[11] However, this novel synthetic method still suffers from several drawbacks, such as high loading of catalyst, relatively narrow substrate scopes, as well as the requirement of extra phase transfer catalyst TBAB.

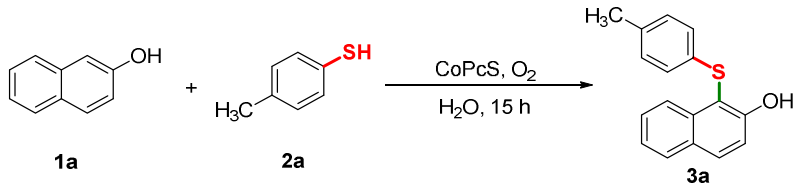
Cobalt(II) phthalocyanine-tetra-sodium sulfonate (CoPcS) with molecular oxygen is generally used to convert thiols to disulfides for petroleum treatment worldwidely,[12] while studies of its applications in catalytic synthesis lag far behind. Our group has devoted efforts to develop benign synthetic tools and promote the utilization of non-toxic aqueous media in organic synthesis. Recently, we reported the CoPcS-catalyzed aerobic oxidative coupling of amines and thiols to construct sulfenamides in water.[13] It is worth to mention that suitable solubility of CoPcS in water enables the usage of water as solvent, while tolerates the presence of aliphatic and aryl thiols well. From the perspective of green chemistry and industrial manufacturing, we designed a relatively versatile and environmental-friendly strategy to synthesize a large variety of aryl sulfides, via a Co-catalyzed oxidative coupling of C(sp^2)-H and thiols (Figure 1). By applying O_2 as the oxidant and water as the solvent, such cheap and commercially available Co catalyst offers a practical advantage for the synthesis of aryl sulfides.

Results and Discussion

The optimization of reaction conditions were carried out by using 2-naphthol **1a** and 4-methylbenzenethiol **2a** as substrates in the presence of CoPcS, O_2 and H_2O at 100 ^oC for 15 h. We initiated our investigation by screening the ratio of thiol **2a** against naphthol **1a** (Table 1, Entry 1-3). The raising ratio of **2a** increases the yield from 55% to 82% (Entry 1-2). However, with 5 equiv **2a** present, the yield of target product **3a** decreased slightly (Entry 3). We continued to examine the amount of catalyst by varying the loading from 10 mol% to 1 mol%, and 5 mol%

turned out to be the optimal amount (Entry 2, 4, 5). When the template reaction was conducted in air, the yield of **3a** decreased to 58% (Entry 5). The temperature study was carried out, and the yield decreased along with the lowering of temperature from 100 °C to 60 °C (Entry 4, 6, 7). The concentration of reagents shows evident effect on the reaction. By lowering the volume of water from 12 mL to 2 mL, the yield increased up to 94% (4, 8-10). Further decreasing the amount of solvent to 1 mL led to slightly lower yield of **3a** (Entry 11). A control experiment without CoPcS gave no product (Entry 10), stating the necessity of CoPcS as the catalyst.

Table 1. Optimization of the Reaction Conditions.[a)]



1a **2a** **3a**

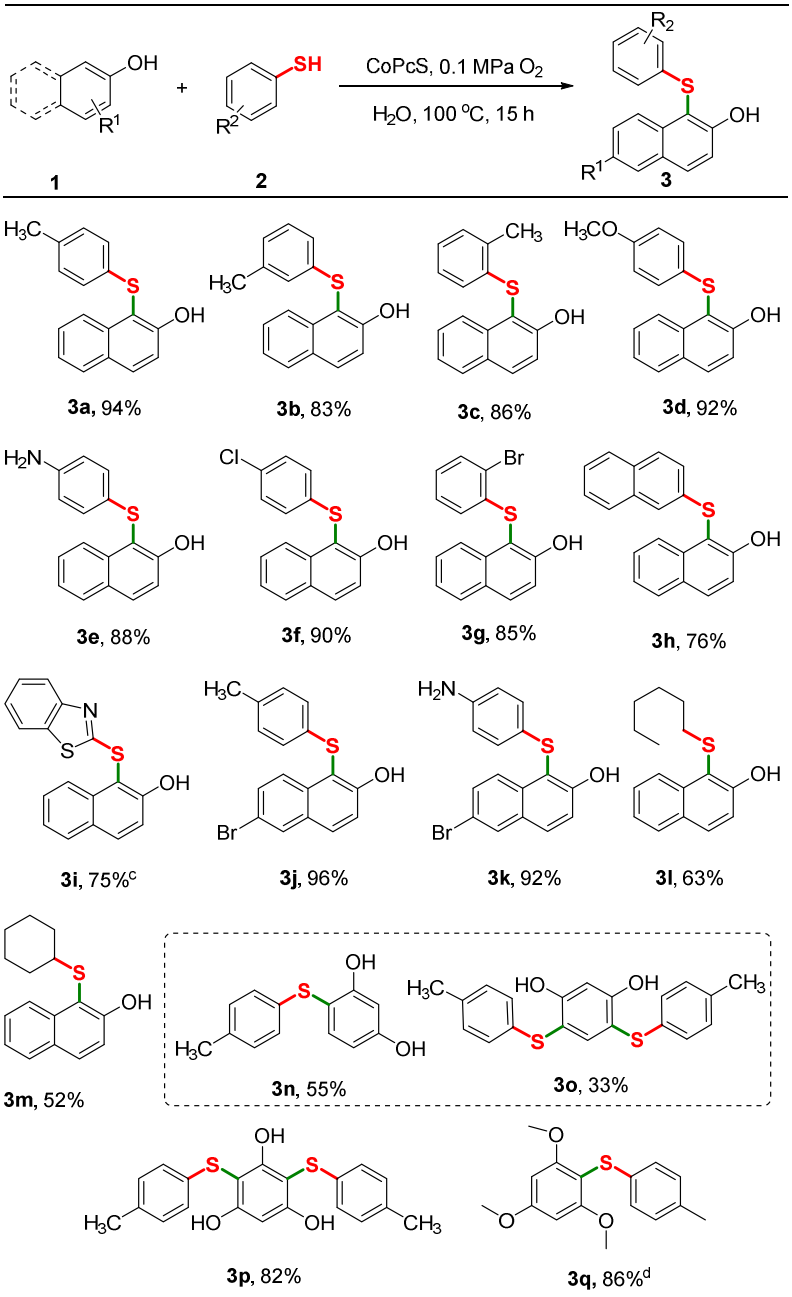
Entry	Ratio[b)]	[Co] (mol%)	T (°C)	H_2O (mL)	Yield (%)[c)]
1	1.5	10	100	12	55
2	3	10	100	12	82
3	5	10	100	12	74
4	3	5	100	12	84(58[d)])
5	3	1	100	12	67
6	3	5	80	12	53
7	3	5	60	12	47
8	3	5	100	8	84
9	3	5	100	4	90
10	3	5	100	2	**94**(0[e)])
11	3	5	100	1	92

[a)] Reaction condition: 0.5 mmol **1a**, 15 h, O_2 balloon. [b)] Ratio of **2a** .against **1a**. [c)] Isolated yields. [d)] In air. [e)] No catalyst.

With the optimum reaction condition in hand, we focused on the issues of synthetic scope and functional group compatibility. The sulfenylation reaction was further studied over 2-naphthol **1**, and a large variety of aryl thiols **2** were tested (Table 2). The coupling of **1** and **2** tolerates a wide range of common substituents. Aryl thiols bearing electron-donating groups (**2a-e**), such as methyl, methoxy, or amino, and electron-withdrawing groups (**2f**, **2g**), such as chloro, or bromo, successfully furnished the desired products **3a-g** in modest to excellent yields. However, substrates with π-electron withdrawing groups, such as nitro or nitrile, gave no product.

Aryl thiols **2a-c** with a methyl group at *ortho*-, *meta*- or *para*-position were tested and gave the desired arylsulfides **3a-c** in similar yields, showing no significant substituent effects. The substrate scope could be extended to naphthyl and heteroaromatic thiols. Naphthalene-2-thiol with an extended π-framework led to the target product **3h** in 76% yield, while 2-mercaptobenzothiazole containing a heteroaromatic ring resulted in the corresponding product **3i** in 75% yield. Reactions of 2-naphthol bearing bromo substituent occurred to form the corresponding C-S bonds in excellent yields as well (**3j** and **3k**). Alkyl thiols, such as 1-hexanethiol **2l** and cyclohexanethiol **2m** furnished target products **3l** and **3m** in lower yields. Reactivity of diphenol and trisphenol with thiols were studied by utilizing resorcinol and phloroglucinol as substrates. The coupling of resorcinol and 4-methylbenzenethiol gave a mixture of monosubstituted product **3n** (55%) and disubstituted product **3o** (33%). Phloroglucinol **2p** as a substrate led to the formation of disulfenylated compound **3p**. Three equivalents of 1,3,5-trimethoxybenzene **2q** over thiol produced monosulfenylated product **3q**. Phenols were explored as well, unfortunately, no product was formed.

Table 2. Substrate Scopes of Naphthol with Thiophenol.[a, b)]

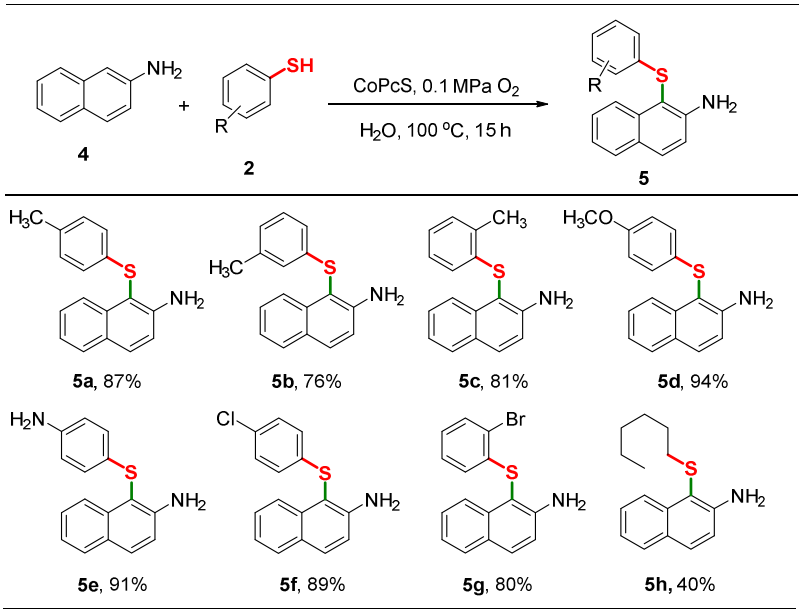


[a] Reaction condition: 0.5 mmol **1**, 1.5 mmol **2**, 5 mol% CoPcS, O_2 balloon, 2 mL H_2O, 100 °C, 15 h. [b] Isolated yields. [c] 0.6 mmol 2-benzothiazolethiol. [d] Solvent: DMSO, 1.5 mmol **1**, 0.5 mmol **2**.

The possibility of constructing C-S bond by using naphthylamine as substrate was explored as well (Table 3). Aryl thiols bearing electron-donating groups, such as methyl, methoxy, or amino, and electron-withdrawing groups, such as chloro, or bromo, produced the desired products **5a-g** in good to excellent yields. Similar to the results in Table 2, aryl thiols **2a-c** with a methyl group at *ortho*-, *meta*- or *para*-position led to the target products **5a-c** in comparable yields. 1-Hexanethiol

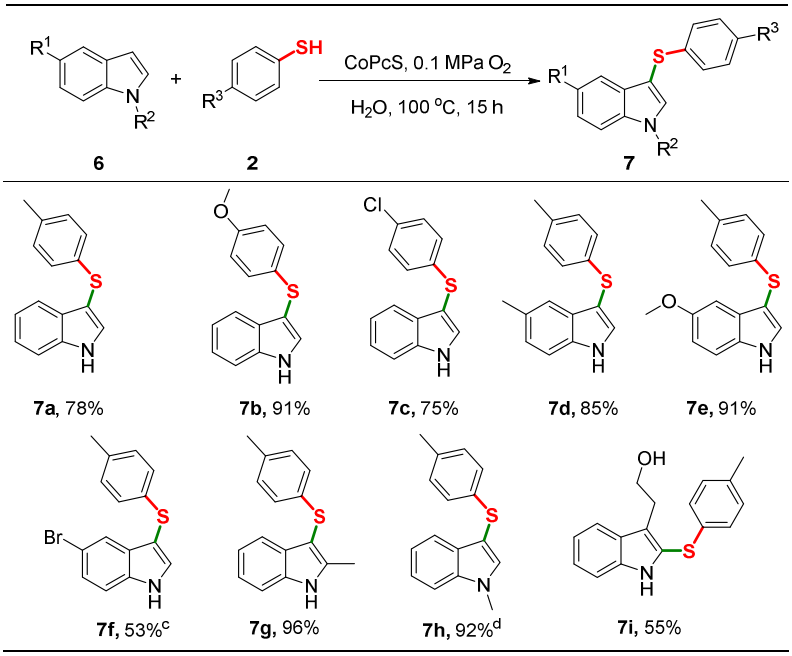
gave product **5h** in 40% yield.

Table 3. Substrate Scopes of Naphthylamine with Thiophenol.[a, b)]



[a)] Reaction condition： 0.5 mmol **4**, 1.5 mmol **2**, 5 mol% CoPcS, O_2 balloon, 2 mL H_2O, 100 °C, 15 h. [b)] Isolated yields.

Table 4. Substrate Scopes of Indole with Thiophenol.[a, b)]



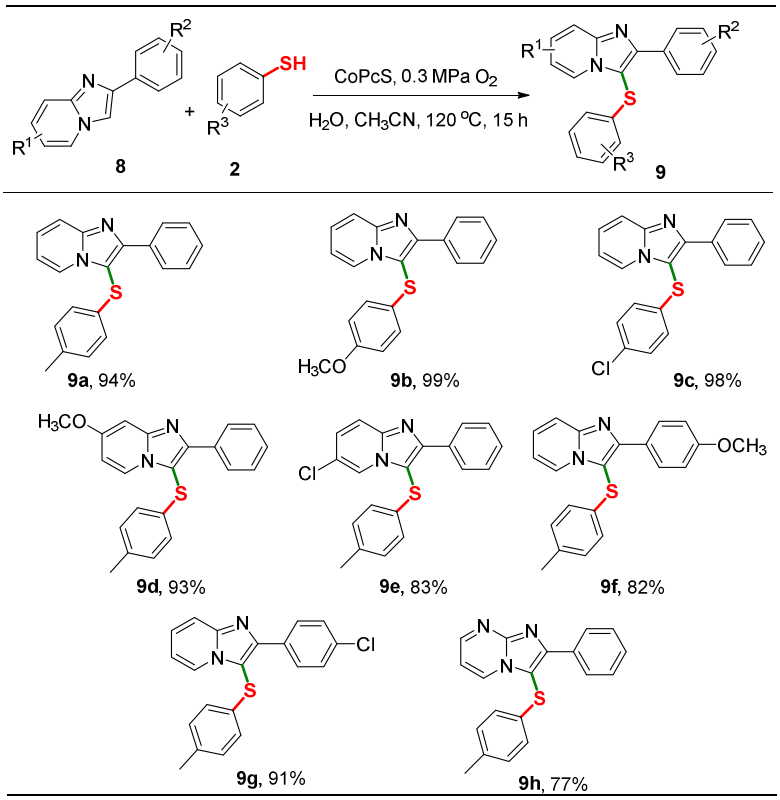
[a)] Reaction condition: 0.5 mmol **6**, 1.5 mmol **2**, 5 mol% CoPcS, O_2 balloon, 2 mL H_2O, 100 °C, 15 h. [b)] Isolated yields. [c)] Solvent: DMSO. [d)] Solvent: DMSO, 1.5 mmol **6**, 0.5 mmol **2**.

We also assessed the scope with respect to various indoles, as shown in Table 4. Indoles

reacted with arylthiols to give the desired products **7a-i** in modest to excellent yields. The results demonstrated that either indoles or thiols bearing electron-donating groups on the aryl rings are favored (**7a-f**). The catalytic system also allowed the direct sulfenylation of 2-methylindoline and N-methylindole occurring on 3-position of indole, forming **7g** and **7h** in 96% and 92% yields, respectively. The reaction of C-3 substituted indole with thiol led to C-2 sulfenylindole **7i**.

As an endeavor to expand the scopes, the reactivity of 2-phenylimidazo[1,2-a]pyridine was investigated (Table 5). The desired products were synthesized in good to excellent yields (**9a-g**), generally. Thiolphenols with electron-donating and electron-withdrawing substituents (methyl, methoxy, chloro) on 4-position of the aryl ring were well tolerated (**9a-c**). 2-Phenylimidazo[1,2-a]pyridines bearing methoxy group on 7-position and chloro group on 6-position furnished the target products (**9d, 9e**) in 93% and 83% yields, respectively, while substrates containing methoxy and chloro substituents on the phenyl ring led to **9f** and **9g** in 82% and 91% yields, respectively. The reaction worked with imidazo[1,2-a]pyrimidine as well, giving product **9h**.

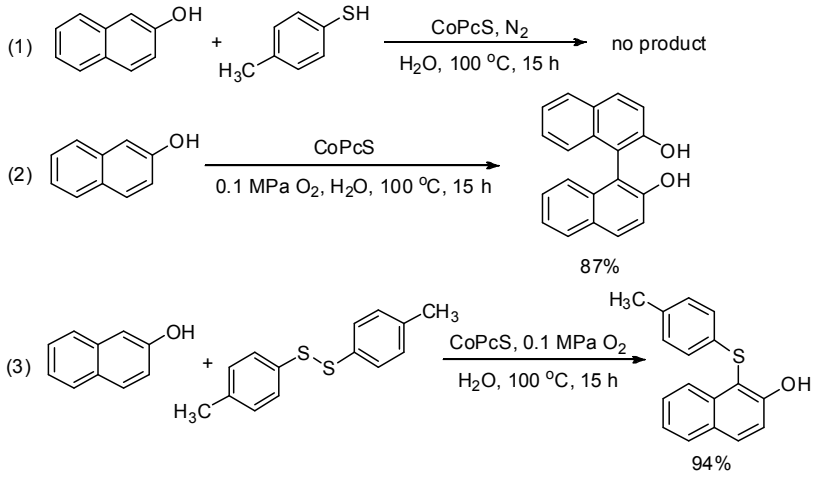
Table 5. Substrate Scopes of 2-Phenylimidazo[1,2-a]pyridine with Thiophenol.[a, b]



[a] Reaction condition: 0.5 mmol **8**, 1.5 mmol **2**, 5 mol% CoPcS, 0.3 MPa O_2, 2 mL H_2O/CH_3CN

(H_2O/CH_3CN = 5:1), 120 °C, 15 h. [b)] Isolated yields.

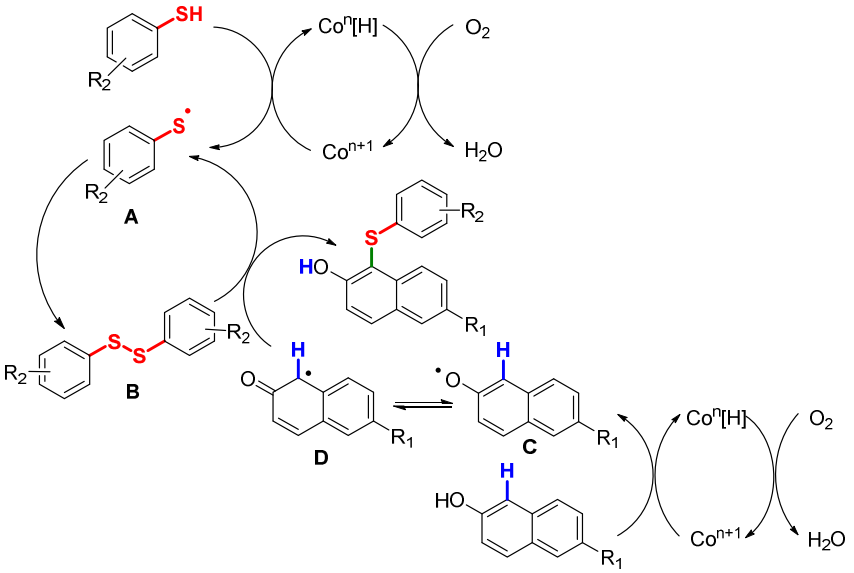
In order to gain sights into the reaction mechanism, a few control experiments were performed. As mentioned (Table 1, Entry 11), no product was formed in reaction of **1a** with **2a** in the absence of Co catalyst. On the other hand, the replacement of O_2 by air led to low yield (Table 1, Entry 4). Another control experiment was conducted under N_2, and no product was obtained (Scheme 1, Reaction 1). These observations state that CoPcS and O_2 are required in the catalytic oxidative crosscoupling. To obtain more insight into the reaction mechanism, we perfomed the homocoupling of **1a**, and 1,1'-Bi-2-naphthol was collected as the only product in 87% yield (Scheme 1, Reaction 2). This result might indicate that a radical on the 3-position of **1a** was created during the reaction and accomplished homocoupling to give 1,1'-Bi-2-naphthol. Furthermore, *p*-tolyl disulfide was applied to replace thiol, and successfully furnished the crosscoupling product **3a** in 94% yield (Scheme 1, Reaction 3). Drawing conclusion from this experimental evidence, disulfide might serves as an important intermediate and this protocol could adapt disulfide compounds as substrates to form C-S bonds as well.



Scheme 1. Experimental Evidence.

Based on the above observations, a plausible mechanism for the coupling of C-H bonds and thiols is proposed by taking naphthol as an example (Scheme 2). Initially, the interaction of Co(II) center with O_2 leads the formation of Co(III) complex.[14] O_2-activated Co(III) is capable of extracting one hydrogen atom from thiol molecule, resulting in a thiyl radical **A**.[13] Two thiyl radicals undergo homocoupling, leading to the disulfide intermediate **B**. On the other hand, Co(III) reacts with naphthol to form radical **C**. The naphthol radical **C** reacts with the disulfide

intermediate **B**, furnishing the desired product and releasing a thiol radical **A** to rejoin the catalytic cycle. Naphthylamines, indole and 2-phenylimidazo[1,2-a]pyridine[15] went under similar radical-mediated reaction mechanism.



Scheme 2. Proposed Reaction Mechanism.

In summary, we developed an efficient and benign Co-catalyzed cross-dehydrogenative coupling of C-H bonds and thiols. Our methodology is able to complete the C-S bond formation in water with molecular oxygen as the sole oxidant while avoid the use of toxic solvents. This strategy shows great tolerance of various substrates and substituents, providing an economical and valuable tool for synthetic chemistry and industrial manufacturing.

Experimental Section

General Information:

All materials and catalysts were purchased from general merchant. ^{1}H NMR and ^{13}C NMR spectra were recorded at a Bruker Avance III HD spectrometer (Bremen, Germany) at 600 MHz(400 MHz) for ^{1}H NMR and 150 MHz(100 MHz) for ^{13}C NMR with $CDCl_3$, d_6-DMSO or CD_2Cl_2 as the solvent and TMS as the internal standard. High resolution mass spectra (HRMS) were measured with an Agilent 1290-6540 Q-TOF (Santa Clara, USA). Low resolution mass spectra (LRMS) were recorded at an electron ionization (EI) conditions by using a Shimadzu GCMS-QP2010 Plus mass spectrometer (Kyoto, Japan). The melting points of the products were determined by an X-4 micro-melting point apparatus (Beijing, China).

Synthesis of Starting Materials

General Procedure: Synthesis of Starting Materials (Compounds 8a-8h).

Following a slightly modified literature procedure,[16] acetophenone (1.2mL, 10 mmol), pyridin-2-amine (1.1 g, 12 mmol), CuI (0.2 g, 1.0 mmol), and NMP (7 mL) were added to a 100 mL Schlenk tube armed with a magnetic stir bar. The tube was filled with air. The tube was placed in an oil bath at 100 °C with stirring for 12 h. The tube was cooled to room temperature, diluted with ethyl acetate, washed with brine, dried with Na_2SO_4, and concentrated on a rotovap. The residue was purified using column chromatography to give the product. Everything else is synthesized in the same way (**8a-8h**).

Typical Procedure for the products

General Procedure 1: A 25 mL Schlenk flask was charged with 2-Naphthol (0.5 mmol), thiophenols (1.5 mmol), CoPcS (22.4 mg, 0.025 mmol), H_2O (2 mL), 0.1 MPa O_2, and then the resulting mixture was stirred at 100 ^oC. After 15 h, the reaction mixture was extracted with ethyl acetate (3 × 10 mL), and then dried over anhydrous sodium sulfate and filtered. After evaporation of the solvent under vacuum, the residue was subjected to flash column chromatography on silica gel to afford products **3a**-**3q.**

General Procedure 2: A 25 mL Schlenk flask was charged with 2-Naphthylamine (0.5 mmol), thiophenols (1.5 mmol), CoPcS (22.4 mg, 0.025 mmol), H_2O (2 mL), 0.1 MPa O_2, and then the resulting mixture was stirred at 100 ^oC. After 15 h, the reaction mixture was extracted with ethyl acetate (3 × 10 mL), and then dried over anhydrous sodium sulfate and filtered. After evaporation of the solvent under vacuum, the residue was subjected to flash column chromatography on silica gel to afford products **5a**-**5h.**

General Procedure 3: A 25 mL Schlenk flask was charged with 1-*H*-indole (0.5 mmol), thiophenols (1.5 mmol), CoPcS (22.4 mg, 0.025 mmol), H_2O (2 mL), 0.1 MPa O_2, and then the resulting mixture was stirred at 100 ^oC. After 15 h, the reaction mixture was extracted with ethyl acetate (3 × 10 mL), and then dried over anhydrous sodium sulfate and filtered. After evaporation of the solvent under vacuum, the residue was subjected to flash column chromatography on silica gel to afford products **7a**-**7i.**

General Procedure 4: A 25 mL Schlenk flask was charged with 2-phenylimidazo[1,2-a]pyridine (0.5 mmol), thiophenols (1.5 mmol), CoPcS (22.4 mg, 0.025 mmol), H_2O/CH_3CN(5:1)(2 mL), 0.1

MPa O_2, and then the resulting mixture was stirred at 120 °C. After 15 h, the reaction mixture was extracted with ethyl acetate (3 × 10 mL), and then dried over anhydrous sodium sulfate and filtered. After evaporation of the solvent under vacuum, the residue was subjected to flash column chromatography on silica gel to afford products **9a**-**9h.**

(3a) 1-(p-Tolylthio)naphthalen-2-ol.[17] Yellow solid (125.0 mg, 94% yield) (hexane as eluent), mp: 78-80 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.22 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 9.0 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.49-7.46 (m, 1H), 7.36-7.31 (m, 2H), 7.21 (s, 1H), 7.00-6.93 (m, 4H), 2.23 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$), δ = 156.9, 135.8, 135.5, 132.7, 131.8, 130.0, 129.5, 128.6, 127.9, 126.7, 124.8, 123.8, 116.9, 108.7, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{14}OS$ 266; Found 266.

(3b)1-(m-Tolylthio)naphthalen-2-ol. Yellow solid (110.4 mg, 83% yield) (hexane as eluent), mp: 87-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.50-7.46 (m, 1H), 7.37-7.32 (m, 2H), 7.18 (s, 1H), 7.05-7.01 (m, 1H), 6.70 (s, 2H), 6.77 (d, J = 7.7 Hz, 1H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 158.4, 140.5, 136.9, 136.5, 134.2, 130.9, 130.5, 130.0, 129.3, 128.4, 128.3, 126.2, 125.3, 124.9, 118.3, 109.7, 22.8. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}OS$ 267.0838; Found 267.0823.

(3c) 1-(o-Tolylthio)naphthalen-2-ol.[17] Yellow solid (114.4 mg, 86% yield) (hexane as eluent), mp: 67-69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.48-7.45 (m, 1H), 7.38-7.33 (m, 2H), 7.17 (d, J = 7.4 Hz, 1H), 7.07 (s, 1H), 7.01-6.98 (m, 1H), 6.86-6.82 (m, 1H), 6.37 (d, J = 7.8 Hz, 1H), 2.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 158.6, 137.0, 136.6, 135.8, 134.2, 131.7, 131.0, 130.0, 129.4, 128.2, 126.9, 126.2, 126.1, 125.3, 118.4, 108.7, 21.5. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{14}OS$ 266; Found 266.

(3d) 1-((4-Methoxyphenyl)thio)naphthalen-2-ol.[17] Yellow solid (129.7 mg, 92% yield) (hexane as eluent), mp: 71-73 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.49-7.45 (m, 1H), 7.35-7.29 (m, 3H), 7.02 (d, J = 8.8 Hz, 2H), 6.69 (d, J = 8.8 Hz, 2H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 157.4, 155.6, 134.3, 131.5, 128.4, 127.7, 127.5, 126.8, 124.9, 123.7, 122.7, 115.8, 113.9, 54.2. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{14}O_2S$ 282; Found 282.

(3e) 1-((4-aminophenyl)thio)naphthalen-2-ol. Light red solid (117.5 mg, 88% yield) (hexane: EtOAc = 2:1 as eluent), mp: 177-179 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.93 (s, 1H), 8.38 (d, J = 8.5 Hz, 1H), 7.87-7.81 (m, 2H), 7.51-7.47 (m, 1H), 7.33-7.26 (m, 2H), 6.93 (d, J = 8.6 Hz, 2H), 6.42 (d, J

= 8.6 Hz, 2H), 5.06 (s, 2H). ^{13}C NMR (100 MHz, DMSO), δ = 159.4, 149.3, 137.6, 133.0, 132.1, 130.5, 130.2, 129.1, 126.4, 124.9, 123.1, 120.3, 116.4, 113.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{14}NOS$ 268.0791; Found 268.0796.

(3f) 1-((4-Chlorophenyl)thio)naphthalen-2-ol.[17] Yellow solid (128.7 mg, 90% yield) (hexane: EtOAc = 30:1 as eluent), mp: 90-92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.49-7.46 (m, 1H), 7.37-7.31 (m, 2H), 7.11-7.09 (m, 3H), 6.92 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 158.5, 136.7, 135.4, 134.6, 133.3, 131.0, 130.8, 130.1, 129.6, 129.1, 125.9, 125.5, 118.4, 109.1. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{11}ClOS$ 286; Found 286.

(3g) 1-((2-bromophenyl)thio)naphthalen-2-ol.[18] Colorless solid (280 mg, 85% yield) (hexane: EtOAc = 30:1 as eluent), mp: 69-71 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.11 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.49-7.47 (m, 1H), 7.44-7.41 (m, 1H), 7.33-7.30 (m, 2H), 7.04 (s, 1H), 6.87-6.82 (m, 2H), 6.32-6.30 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$), δ = 157.4, 136.6, 135.4, 133.4, 133.0, 129.6, 128.7, 128.3, 128.0, 126.9, 126.4, 124.6, 124.2, 121.1, 117.2, 107.2. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{11}BrOS$ 330; Found 330.

(3h) 1-(Naphthalen-2-ylthio)naphthalen-2-ol.[7c] White solid (114.8 mg, 76% yield) (hexane as eluent), mp: 91-93 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (d, *J* = 8.5 Hz, 1H), 7.94 (d, *J* = 8.9 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.72-7.70 (m, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.57-7.54 (m, 1H), 7.49-7.45 (m, 1H), 7.42 (s, 1H), 7.39-7.36 (m, 4H), 7.22 (s, 1H), 7.19-7.17 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 157.1, 135.5, 133.7, 132.9, 132.8, 131.7, 129.6, 128.9, 128.6, 128.0, 127.7, 127.0, 126.6, 125.7, 124.7, 124.7, 124.6, 123.9, 116.9, 108.1. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{20}H_{14}OS$ 302; Found 302.

(3i) 1-(benzo[d]thiazol-2-ylthio)naphthalen-2-ol.[20] Yellow solid (115.9 mg, 75% yield) (hexane: EtOAc = 10:1 as eluent), mp: 210-212 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.9 Hz, 1H), 7.89-7.84 (m, 2H), 7.58-7.53 (m, 1H), 7.48-7.35 (m, 4H), 7.21-7.17 (m, 1H) . ^{13}C NMR (100 MHz, $CDCl_3$), δ = 168.3, 157.8, 155.9, 135.4, 135.0, 134.4, 129.6, 128.7, 128.5, 126.2, 124.5, 124.4, 124.1, 121.9, 120.9, 117.8, 106.8. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{11}NOS_2$ 309; Found 309.

(3j) 6-Bromo-1-(p-tolylthio)naphthalen-2-ol.[17] White solid (165.1 mg, 96% yield) (hexane as eluent), mp: 117-119 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 9.0 Hz, 1H), 7.92 (s, 1H), 7.76

(d, *J* = 8.9 Hz, 1H), 7.53-7.50 (m, 1H), 7.32 (d, *J* = 9.0 Hz, 1H), 7.21 (s, 1H), 6.98-6.90 (m, 4H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 157.1, 136.2, 134.1, 131.6, 131.3, 131.1, 130.6, 130.5, 130.1, 126.8, 126.7, 118.0, 117.7, 109.2. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{13}BrOS$ 344; Found 344.

***(3k) 1-((4-aminophenyl)thio)-6-bromonaphthalen-2-ol*.** Light red solid, (158.7 mg, 92% yield) (hexane: EtOAc = 2:1 as eluent), mp: 162-164 °C. ^{1}H NMR (600 MHz, DMSO) δ = 10.20 (s, 1H), 8.35 (d, *J* = 9.0 Hz, 1H), 8.10 (d, *J* = 2.1 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.62-7.60 (m, 1H), 7.350-7.34 (m, 1H), 6.98-6.95 (m, 2H), 6.48-6.46 (m, 2H), 5.12 (s, 2H). ^{13}C NMR (150 MHz, DMSO), δ = 158.4, 148.0, 134.9, 130.9, 130.8, 130.5, 130.4, 130.3, 127.5, 121.4, 120.2, 116.5, 115.0, 112.5. HRMS (ESI-TOF) m/z: $[M+H]^+$Calcd for $C_{16}H_{13}BrNOS$ 345.9896; Found 345.9895.

***(3l) 1-(hexylthio)naphthalen-2-ol*.** Yellow oil (80.0 mg, 63% yield) (hexane: EtOAc = 5:1 as eluent). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8.5 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 2H), 7.54 (t, *J* = 8.1 Hz, 1H), 7.40 (s, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 8.9 Hz, 1H), 2.67 (t, *J* = 8.5 Hz, 2H), 1.56 - 1.49 (m, 2H), 1.36 - 1.30 (m, 2H), 1.25 - 1.19 (m, 4H), 0.84 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 156.4, 135.4, 131.5, 129.4, 128.7, 127.5, 124.7, 123.5, 116.4, 111.4, 36.0, 31.4, 30.0, 28.6, 22.6, 14.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{21}OS$ 261.1308; Found 261.1312.

***(3m) 1-(cyclohexylthio)naphthalen-2-ol.*[19]** Yellow oil (67.0 mg, 52% yield) (hexane: EtOAc = 5:1 as eluent). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8.5 Hz, 1H), 7.77-7.74 (m, 2H), 7.53 (t, *J* = 8.1 Hz, 1H), 7.44 (s, 1H), 7.35-7.32 (m, 1H), 7.26 (d, *J* = 8.9 Hz, 1H), 2.92-2.87 (m, 1H), 1.90 (d, *J* = 13.3 Hz, 2H), 1.71-1.69 (m, 2H), 1.53 (s, 1H), 1.42-1.39 (m, 2H), 1.18-1.17 (m, 3H) . ^{13}C NMR (100 MHz, $CDCl_3$), δ = 156.8, 136.0, 131.5, 129.4, 128.6, 127.4, 125.0, 123.4, 116.4, 110.4, 48.4, 33.9, 26.2, 25.6. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{18}OS$ 258; Found 258.

***(3n) 4-(p-tolylthio)benzene-1,3-diol.*[7c]** White solid, (64.0 mg, 55% yield) (hexane: EtOAc = 20:1 as eluent), mp: 80-82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 (d, *J* = 8.4 Hz, 1H), 7.04-6.95 (m, 4H), 6.55 (d, *J* = 2.1 Hz, 1H), 6.46-6.43 (m, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 159.2, 158.4, 138.1, 136.0, 133.0, 130.0, 126.7, 109.2, 108.1, 102.4, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{13}H_{12}O_2S$ 232; Found 232.

(3o) 4,6-bis(p-tolylthio)benzene-1,3-diol. White solid, (58 mg, 33% yield) (hexane: EtOAc = 20:1 as eluent), mp: 108-110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.75 (s, 1H), 7.05-6.97 (m, 8H), 6.76 (s, 3H), 2.27 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 160.6, 145.0, 136.3, 132.4, 130.1, 127.0, 109.6,

102.1, 21.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}O_2S_2$ 355.0821; Found 355.0804.

(3p) 2,4-bis(p-tolylthio)benzene-1,3,5-triol. White solid (151.7 mg, 82% yield) (hexane: EtOAc = 20:1 as eluent), mp: 122-124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.02-6.89 (m, 11H), 6.42 (s, 1H), 2.26 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 161.0, 160.2, 136.6, 130.8, 130.2, 126.7, 95.7, 94.6, 21.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}O_3S_2$ 371.0770; Found 371.0772.

(3q) p-tolyl(2,4,6-trimethoxyphenyl)sulfane.[7c] White solid (124.0 mg, 86 % yield) (hexane: EtOAc = 10:1 as eluent), mp: 93-96^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.00 - 6.90 (m, 4H), 6.21 (s, 2H), 3.87 (s, 3H), 3.81 (s, 6H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, CDCl3) δ= 162.8, 162.5, 135.0, 134.1, 129.3, 126.0, 91.2, 56.3, 55.4, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{18}O_3S$ 290; Found 290.

(5a) 1-(p-tolylthio)naphthalen-2-amine.[17] Light red solid (115.3 mg, 87% yield) (hexane: EtOAc = 10:1 as eluent), mp: 115-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 8.5 Hz, 1H), 7.70 (t , *J* = 8.0 Hz, 2H), 7.43-7.39 (m, 1H), 7.26-7.22 (m, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.96-6.90 (m, 4H), 4.68 (s, 2H), 3.21 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$), δ = 148.4, 136.7, 134.9, 133.3, 131.7, 129.8, 128.5, 128.4, 127.8, 126.1, 124.4, 122.6, 117.7, 105.2, 21.0. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{15}NS$ 265; Found 265.

***(5b) 1-(m-tolylthio)naphthalen-2-amine*.** Light red solid (100.7 mg, 76% yield) (hexane: EtOAc = 10:1 as eluent), mp: 72-74 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 8.5 Hz, 1H), 7.73-7.69 (m, 2H), 7.43-7.40 (m, 1H), 7.25-7.23 (m, 1H), 7.02-6.99 (m, 2H), 6.89 (s, 1H), 6.85 (d, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 4.68 (s, 2H), 2.19 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$), δ = 148.5, 138.8, 136.8, 136.6, 131.8, 128.9, 128.4, 128.4, 127.8, 126.5, 126.1, 124.3, 122.9, 122.6, 117.7, 104.7, 21.5. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}NS$ 266.0998; Found 266.1009.

(5c) 1-(o-tolylthio)naphthalen-2-amine. Light red solid (107.3 mg, 81% yield) (hexane: EtOAc = 10:1 as eluent), mp: 105-107 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.19 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.42-7.39 (m, 1H), 7.26-7.24 (m, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.98-6.95 (m, 1H), 6.85-6.83 (m, 1H), 6.42 (d, *J* = 7.9 Hz, 1H), 4.66 (s, 2H), 2.54 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$), δ = 148.6, 136.7, 135.6, 134.9, 131.8, 130.1, 128.5, 128.4, 127.8, 126.5, 124.7, 124.3, 124.2, 122.6, 117.7, 103.9, 20.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}NS$ 266.0998; Found 266.1005.

(5d) 1-((4-methoxyphenyl)thio)naphthalen-2-amine.[17] Light red solid (132.1 mg, 94% yield) (hexane: EtOAc = 10:1 as eluent), mp: 104-106 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.31 (d, *J* = 8.5

Hz, 1H), 7.66 (d, *J* = 8.5 Hz, 2H), 7.42-7.39 (m, 1H), 7.23-7.20 (m, 1H), 6.98-6.92 (m, 3H), 6.66 (d, *J* = 8.8 Hz, 2H), 4.67 (s, 2H), 3.62 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$), δ = 157.9, 148.4, 136.7, 131.6, 128.5, 128.1, 127.8, 127.6, 124.4, 122.6, 117.8, 114.8, 106.2. 55.4. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{15}NOS$ 281; Found 281.

(5e) 1-((4-aminophenyl)thio)naphthalen-2-amine. Light red solid (121.0 mg, 91% yield) (hexane: EtOAc = 1:1 as eluent), mp: 112-114 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8.5 Hz, 1H), 7.69-7.67 (m, 2H), 7.44-7.41 (m, 1H), 7.24-7.22 (m, 1H),6.98 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.47 (d, *J* = 8.5 Hz, 2H), 4.70 (s, 2H), 3.51 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$), δ = 148.1, 144.5, 136.7, 131.3, 128.5, 128.4, 128.3, 127.6, 124.7, 124.5, 122.5, 117.7, 116.0, 107.0. HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{16}H_{14}N_2S$ 266.0881; Found 266.0878.

(5f) 1-((4-chlorophenyl)thio)naphthalen-2-amine.[17] Light red solid (126.8 mg, 89% yield) (hexane: EtOAc = 10:1 as eluent), mp: 120-122 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.20 (d, *J* = 8.5 Hz, 1H), 7.73-7.69 (m, 2H), 7.43-7.40 (m, 1H), 7.26-7.23 (m, 1H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 8.5 Hz, 2H), 4.67 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$), δ = 148.6, 136.5, 135.5, 132.2, 130.9, 129.1, 128.5, 128.5, 128.0, 127.2, 124.0, 122.8, 117.7, 104.1. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{12}ClNS$ 285; Found 285.

(5g) 1-((2-bromophenyl)thio)naphthalen-2-amine. Light red solid (131.6 mg, 80% yield) (hexane: EtOAc = 10:1 as eluent), mp: 114-116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.18 (d, *J* = 8.4 Hz, 1H), 7.79-7.72 (m, 2H), 7.54-7.52 (m, 1H), 7.45-7.41 (m, 1H), 7.29-7.24 (m, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.95-6.89 (m, 2H), 6.41-6.38 (m, 1H), 4,71 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 148.7, 137.6, 136.5, 132.8, 132.3, 128.5, 128.0, 127.8, 126.1, 125.9, 124.0, 122.8, 121.0, 117.7, 103.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{13}BrNS$ 329.9947; Found 329.9949.

(5h) 1-(hexylthio)naphthalen-2-amine. Yellow oil (52.0 mg, 40% yield) (hexane: EtOAc = 10:1 as eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 (d, J = 8.5 Hz, 1H), 7.63 - 7.52 (m, 2H), 7.50 - 7.46 (m, 1H), 7.26 - 7.22 (m, 1H), 6.92 (d, J = 8.7 Hz, 1H), 4.77 (s, 2H), 2.71 - 2.68 (m, 2H), 1.51 - 1.43 (m, 2H), 1.35 - 1.25 (m, 2H), 1.21 - 1.12 (m, 4H), 0.77 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.8, 136.5, 130.4, 128.5, 128.4, 127.2, 124.5, 122.2, 117.4, 109.1, 34.9, 31.5, 30.0, 28.7, 22.6, 14.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{22}NS$ 260.1467; Found 260.1469.

(7a) 3-(p-tolylthio)-1H-indole.[21] White solid (94.4 mg, 78% yield) (hexane: EtOAc = 30:1 as eluent), mp: 130-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.37

(d, *J* = 9.5 Hz, 2H), 7.23-7.21 (m, 1H), 7.16-7.12 (m, 1H), 7.03-6.94 (m, 4H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$), δ = 136.5, 135.5, 134.7, 130.5, 129.6, 129.1, 126.3, 123.0, 120.9, 119.7, 111.6, 103.4, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{15}H_{13}NS$ 239; Found 239.

(7b) 3-((4-methoxyphenyl)thio)-1H-indole.[21] White solid (115.0 mg, 91 % yield) (hexane: EtOAc = 10:1 as eluent), mp: 109-111^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 (s, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.41 - 7.34 (m, 2H), 7.26 - 7.19 (m, 1H), 7.17 - 7.10 (m, 3H), 6.73 - 6.69 (m, 2H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.8, 136.5, 130.1, 129.6, 129.0, 128.6, 123.0, 120.8, 119.7, 114.6, 111.6, 104.5, 55.4. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{15}H_{13}NOS$ 255; Found 255.

(7c) 3-((4-chlorophenyl)thio)-1H-indole.[21] White solid (97.0 mg, 75 % yield) (hexane: EtOAc = 10:1 as eluent), mp: 130-132^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.45 (s, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.50 (d, J = 2.6 Hz, 1H), 7.46 (d, J = 8.2 Hz, 1H), 7.30-7.19 (m, 1H), 7.17 – 7.15 (m, 1H), 7.13 - 7.10 (m, 2H), 7.03 - 6.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.8, 136.5, 130.7, 130.5, 128.8, 127.1, 123.2, 121.1, 119.5, 111.7. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{14}H_{10}ClNS$ 259; Found 259.

(7d) 5-methyl-3-(p-tolylthio)-1H-indole.[22] White solid (107.0 mg, 85 % yield) (hexane: EtOAc = 5:1 as eluent), mp: 125-127^{o}C. ^{1}H NMR (400 MHz, $CDCl^3$) δ = 8.26 (s, 1H), 7.40 (s, 2H), 7.30 (d, J = 8.3 Hz, 1H), 7.09 – 7.06 (m, 1H), 7.03 - 6.95 (m, 4H), 2.40 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 135.8, 134.8, 134.5, 130.8, 130.4, 129.5, 129.4, 126.0, 124.7, 119.2, 111.2, 102.5, 21.5, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{15}NS$ 253; Found 253.

(7e) 5-methoxy-3-(p-tolylthio)-1H-indole.[22] White solid (117.0 mg, 87 % yield) (hexane: EtOAc = 5:1 as eluent), mp: 73-75^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.29 (s, 1H), 7.31 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 7.05 (d, J = 2.4 Hz, 1H), 7.02 - 6.98 (m, 2H), 6.95 (d, J = 8.2 Hz, 2H), 6.89 – 6.86 (m, 1H), 3.74 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.1, 135.7, 134.7, 131.5, 131.4, 130.0, 129.6, 126.1, 113.5, 112.6, 102.6, 100.9, 55.9, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{15}NOS$ 269; Found 269.

(7f) 5-bromo-3-(p-tolylthio)-1H-indole.[22] Yellow solid (84.0 mg, 53 % yield) (hexane: EtOAc = 5:1 as eluent), mp: 127-129^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.43 (s, 1H), 7.80 - 7.70 (m, 1H), 7.46 (d, J = 2.6 Hz, 1H), 7.33 - 7.26 (m, 2H), 7.00 (s, 4H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 135.1, 135.0, 134.9, 131.7, 131.0, 129.6, 126.3, 126.1, 122.3, 114.4, 113.1, 103.4, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{15}H_{12}BrNS$ 317; Found 317.

(7g) 2-methyl-3-(p-tolylthio)-1H-indole.[22] White solid (121.0 mg, 96 % yield) (hexane: EtOAc = 5:1

as eluent), mp: 96-99°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (s, 1H), 7.54 (d, J = 7.7 Hz, 1H), 7.27 - 7.22 (m, 1H), 7.19 - 7.07 (m, 2H), 6.94 (s, 4H), 2.41 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.1, 135.8, 135.5, 134.4, 130.4, 129.6, 125.8, 122.2, 120.7, 119.0, 110.8, 99.7, 21.0, 12.2. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{15}NS$ 253; Found 253.

(7h) 1-methyl-3-(p-tolylthio)-1H-indole.[22] White solid (116.0 mg, 92 % yield) (hexane: EtOAc = 10:1 as eluent), mp: 123-125°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.61 (d, J = 7.9 Hz, 1H), 7.36 (d, J = 8.2 Hz, 1H), 7.31 - 7.24 (m, 2H), 7.18 - 7.11 (m, 1H), 7.01 (d, J = 8.3 Hz, 2H), 6.95 (d, J = 8.1 Hz, 2H), 3.81 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =137.5, 136.0, 134.9, 134.6, 129.9, 129.5, 126.1, 122.5, 120.5, 119.8, 109.7, 101.2, 33.2, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{16}H_{15}NS$ 253; Found 253.

(7i) 2-(2-(p-tolylthio)-1H-indol-3-yl)ethanol. White solid (78.0 mg, 55 % yield) (hexane: EtOAc = 3 :1 as eluent), mp: 47-49°C. ^{1}H NMR (400 MHz, DMSO) δ = 11.40 (s, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.32 (d, J = 8.1 Hz, 1H), 7.17 – 7.13 (m, 1H), 7.09 (d, J = 8.2 Hz, 2H), 7.06 - 6.93 (m, 3H), 4.72 (s, 1H), 3.54 (t, J = 7.6 Hz, 2H), 2.98 (t, J = 7.6 Hz, 2H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 137.6, 135.7, 134.2, 130.3, 127.9, 127.1, 123.1, 122.5, 119.7, 119.5, 119.3, 111.8, 62.1, 29.2, 20.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}NOS$ 284.1104; Found 284.1107.

(9a) 2-phenyl-3-(p-tolylthio)imidazo[1,2-a]pyridine.[23] White solid (148.5mg, 94% yield) (hexane: EtOAc = 5:1 as eluent), mp: 140-142°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 6.8 Hz, 1H), 8.21 (d, *J* = 7.6 Hz, 2H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.43 (q, *J* = 7.4 Hz, 2H), 7.40-7.28 (m, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 2H), 6.85 (t, *J* = 6.8 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ=151.2, 147.0, 136.1, 133.4, 131.5, 130.2, 128.6, 128.4, 128.4, 126.6, 125.8, 124.6, 117.6, 113.0, 106.9, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{20}H_{16}N_2S$ 316 ; Found 316.

(9b) 3-((4-methoxyphenyl)thio)-2-phenylimidazo[1,2-a]pyridine.[23] White solid (164.3mg, 99% yield) (hexane: EtOAc= 5:1 as eluent), mp: 105-107°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.31-8.29 (m, 1H), 8.26-8.22 (m, 2H), 7.71-7.69 (m, 1H), 7.49-7.42 (m, 2H), 7.41-7.29 (m, 2H), 7.02-6.96 (m, 2H), 6.89-6.84 (m, 1H), 6.78-6.74 (m, 2H), 3.72 (s, 3H).^{13}C NMR (100MHz, $CDCl_3$) δ=158.6, 150.9, 146.9, 133.5, 128.5, 128.4, 128.4, 127.9, 126.5, 125.5, 124.5, 117.6, 115.2, 112.9, 107.8, 55.4. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{20}H_{16}N_2OS$ 332 ; Found 332.

(9c) 3-((4-chlorophenyl)thio)-2-phenylimidazo[1,2-a]pyridine.[23] White solid(164.6mg, 98% yield) (hexane: EtOAc= 5:1 as eluent), mp: 127-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25-8.21 (m, 1H),

8.20-8.16 (m, 2H), 7.75-7.71 (m,1H), 7.46-7.31 (m, 4H), 7.19-7.14 (m, 2H), 6.94-6.85 (m, 3H).^{13}C NMR (100MHz, $CDCl_3$) δ=151.7, 147.2, 133.8, 133.2, 132.1, 129.6, 128.8, 128.5, 128.3, 126.9, 124.3, 117.8, 113.3, 105.7. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{19}H_{13}ClN_2S$ 336 ; Found 336.

***(9d) 7-methoxy-2-phenyl-3-(p-tolylthio)imidazo[1,2-a]pyridine*.** White solid (160.9 mg, 93% yield) (hexane: EtOAc= 5:1 as eluent), mp: 65-66°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21-8.17 (m, 2H), 8.07 (d, *J* = 7.4 Hz, 1H), 7.44-7.33 (m, 3H), 7.02 (d, *J* = 8.0 Hz, 3H), 6.94-6.89 (m, 2H), 6.58-6.53 (m, 1H), 3.89 (s, 3H), 2.26 (s, 3H).^{13}C NMR (100MHz, $CDCl_3$) δ=159.5, 151.0, 148.5, 135.9, 133.5, 131.9, 130.2, 128.4, 128.1, 125.6, 124.9, 107.8, 105.3, 95.1, 55.7, 20.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{19}N_2OS$ 347.1213 ; Found 347.1217.

***(9e) 6-chloro-2-phenyl-3-(p-tolylthio)imidazo[1,2-a]pyridine.*[24]** White solid(145.3mg, 83% yield) (hexane: EtOAc= 5:1 as eluent), mp: 158-160°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 1.4 Hz, 1H), 8.22-8.17 (m, 2H), 7.65 (d, *J* = 9.4 Hz, 1H), 7.46-7.41 (m, 2H), 7.38-7.34 (m, 1H), 7.29-7.25 (m, 1H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 2H), 2.27 (s, 3H).^{13}C NMR (100MHz, $CDCl_3$) δ=151.9, 145.3, 136.4, 133.0, 130.9, 130.4, 128.8, 128.5, 128.3, 127.9, 125.9, 122.5, 121.5, 118.0, 107.9, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{20}H_{15}ClN_2S$ 350 ; Found 350.

***(9f) 2-(4-methoxyphenyl)-3-(p-tolylthio)imidazo[1,2-a]pyridine.*[25]** White solid (141.9 mg, 82% yield) (hexane: EtOAc= 5:1 as eluent), mp: 159-161°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24 (dd, *J* = 6.8, 0.7 Hz, 1H), 8.18 (d, *J* = 8.6 Hz, 2H), 7.68 (dd, *J* = 9.0, 0.6 Hz, 1H), 7.33-7.24 (m, 1H), 7.03-6.98 (m, 4H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.81 (t, *J* = 6.8 Hz, 1H), 3.82 (s, 3H), 2.24 (s, 3H).^{13}C NMR (100MHz, $CDCl_3$) δ=159.9, 151.1, 147.0, 135.9, 131.7, 130.2, 129.7, 126.5, 126.1, 125.7, 124.5, 117.4, 113.9, 112.9, 105.8, 55.3, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{21}H_{18}N_2OS$ 346 ; Found 346.

***(9g) 2-(4-chlorophenyl)-3-(p-tolylthio)imidazo[1,2-a]pyridine.*[25]** White solid (159.3 mg, 91% yield)(hexane: EtOAc= 5:1 as eluent), mp: 131-132°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 6.8 Hz, 1H), 8.22-8.15 (m, 2H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.43-7.37 (m, 2H), 7.36-7.29 (m,1H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.92-6.83 (m, 3H), 2.25 (s, 3H).^{13}C NMR (100MHz, $CDCl_3$) δ=149.9, 147.0, 136.2, 134.5, 131.9, 131.2, 130.3, 129.6, 128.7, 126.8, 125.8, 124.6, 117.6, 113.2, 107.0, 20.9. LRMS (EI) m/z: $[M]^+$ Calcd for $C_{20}H_{15}ClN_2S$ 350 ; Found 350.

***(9h) 2-phenyl-3-(p-tolylthio)imidazo[1,2-a]pyrimidine.*[25]** White solid(122.0mg, 77% yield)(hexane: EtOAc= 5:1 as eluent), mp: 144-146°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.64-8.62 (m, 1H), 8.52-8.49 (m, 1H), 8.37-8.33 (m, 2H), 7.48-7.37 (m, 3H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.94-6.89 (m, 3H), 2.26 (s,

3H). ^{13}C NMR (100MHz, $CDCl_3$) δ=152.5, 151.5, 149.9, 136.6, 132.8, 132.1, 130.5, 130.4, 129.1, 128.6, 128.5, 126.1, 109.3, 105.9, 20.9. LRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{15}N_3S$ 317; Found 317.

ASSOCIATED CONTENT

Supporting information

^{1}H and ^{13}C NMR spectra (PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: bxyuan@zzu.edu.cn

Notes

The authors declare no competing financial interest.

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