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One-Pot Synthesis of Aminated Benzo-Fused Heterocycles and N-Substituted Dibenzothiophenes via Copper-Catalyzed Ullmann Type Reaction

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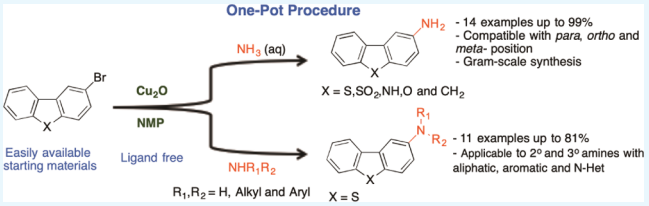
ABSTRACT: We report here a direct and effective method to synthesize a primary amine of several polycyclic aromatic compounds. This reaction has been achieved through copper (I)-catalyzed Ullmann C−N coupling. Furthermore, this strategy allows the synthesis of new N-substituted dibenzothiophene derivatives through the coupling of 2-bromodibenzothiophene with various ranges of primary and secondary amines. The use of inexpensive catalysts, aqueous ammonia as the convenient source of ammonia and ligand free, makes this protocol environmentally and economically favorable for the synthesis of these compounds.



INTRODUCTION

Benzo-fused five-membered heterocycles compounds are key structural components in natural products and synthetic compounds. These materials have a variety of applications including pharmaceuticals, photoactive compounds, and conducting polymers.[1] Among them, primary amines of dibenzothiophene, dibenzofuran, and carbazole have been explored as potential antimicrobial agents.[2] Several synthetic methods of these compounds were developed (Scheme 1a). For example, Gilman reported the synthesis of 2-aminodibenzothiophene through the synthesis of nitroarene, followed by reduction using Raney nickel as a catalyst.[3] Additionally, 2-aminodibenzothiophene and 2-aminodibenzofuran were synthesized through electrophilic amination, however, it required the synthesis of the organometallic starting material aryl lithium.[4] Recently, Uchida's group synthesized primary amines of dibenzothiophene, dibenzofuran, and carbazole through the synthesis of the starting material acetyl arenes.[5] These above methodologies require multiple steps, which are neither economically nor environmentally favorable. Therefore, amination of benzo-fused heteroaromatic compounds with a single step is in demand.

Transition metals have emerged as powerful materials that allow the direct formation of carbon-nitrogen bonds from aryl halides and ammonia.[6] Copper-catalyzed Ullmann type reaction has been extensively applied for the synthesis of a wide range of organic compounds including bioactive molecules because of the low cost of the catalyst, environmental benignity, and high turnover.[7] However, the traditional methods of Ullmann-type reaction require (1) harsh conditions such as high temperature (up to 200 °C), (2) the presence of ligand, which is environmentally and economically unfavorable, and (3) the presence of strong electron-withdrawing groups in aryl halides.[8] Development of Ullmann coupling reaction with milder conditions has been achieved in the coupling of aryl halides with ammonia that tolerates the synthesis of aniline derivatives with an electron-donating group as well as an electron-withdrawing group.[9] Nevertheless, few examples have been reported on the amination of halobenzene-fused heteroaromatic compounds. For example, Scalone and co-workers[10] performed the amination for coupling a variety of N- and S-containing heterocycle bromides utilizing the Ullman reaction in the absence of a ligand; however, this method was limited to the synthesis of primary amine and requires the use of an anhydrous solvent, an inert atmosphere, and gaseous ammonia as the source of amine, which are inconvenient to handle. For this reason, we herein wish to report a simple and convenient method in the room atmosphere through the copper (I)-catalyzed Ullmann C−N coupling and under ligand-free conditions, for the amination of benzo-fused heterocycles from readily available heteroaryl bromides and aqueous ammonia (Scheme 1b). This reaction not only enables the synthesis of primary amines but also applicable to the synthesis of secondary and tertiary amines.

RESULTS AND DISCUSSION

We initiated our investigation by the optimization of the reaction conditions to synthesize 2-aminodibenzothiophene

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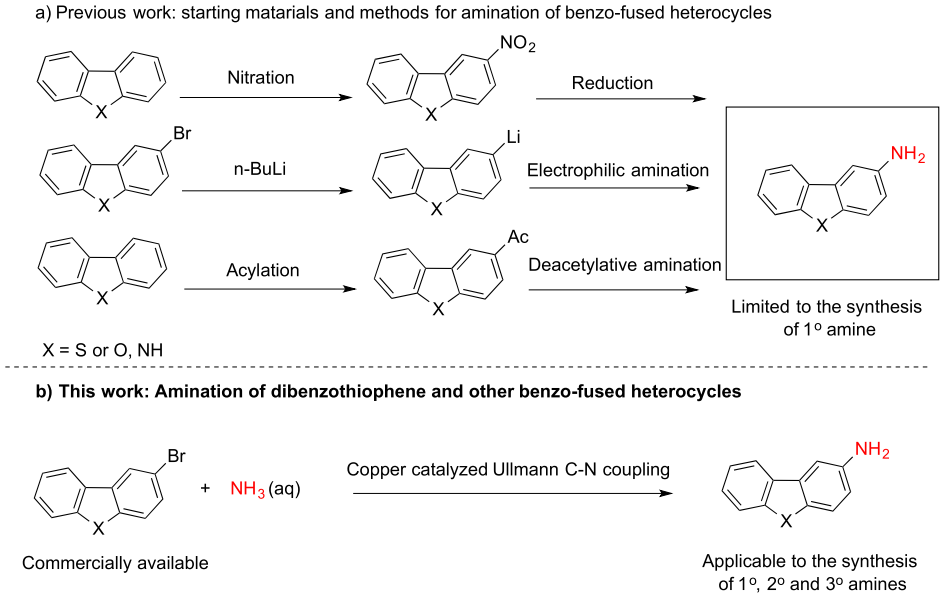
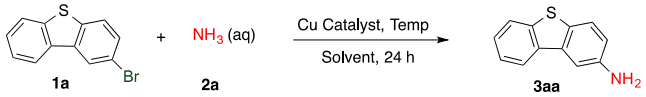
Scheme 1. Approaches for the Amination of Benzo-Fused Heterocycles



3aa. The coupling of the substrate, 2-bromodibenzothiophene (**1a**), with aqueous ammonia solution (**2a**) was carried out with 10 mol % of Cu_2O and dimethyl sulfoxide (DMSO) at 100 °C. The desired product **3aa** was obtained in a moderate yield 47% within 24 h (Table 1, entry 1). Increasing the amount of copper loading to 20 mol % improved the reaction yield (entry 2). Increasing the temperature further improved the yield (entry 3). Other solvents were screened such as dimethylformamide (DMF) and *N*-methyl pyrrolidinone (NMP) (entries 4 and 5). NMP was found to be more effective providing the desired product in superior yield (entry 5). Also, the effects of different copper catalysts, such as CuI, CuCl, $Cu(OAc)_2$, and Cu powder, were examined (entries 6–9). We found that Cu_2O was more effective than both CuI and CuCl, while $Cu(OAc)_2$ and Cu powders produced none of the desired product.

Table 1. Optimization of Reaction Conditions[a]

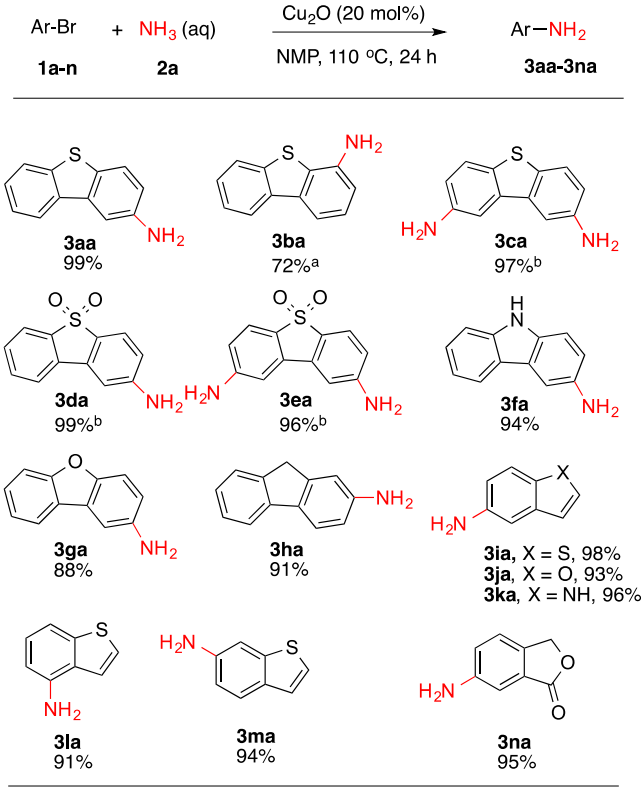


entry	catalyst	solvent	temp	yield (%)[b]
1	Cu_2O[c]	DMSO	100	47
2	Cu_2O	DMSO	100	64
3	Cu_2O	DMSO	110	73
4	Cu_2O	DMF	110	59
5	Cu_2O	NMP	110	99
6	CuI	NMP	110	66
7	CuCl	NMP	110	54
8	$Cu(OAc)_2$	NMP	110	0
9	Cu	NMP	110	0

[a]Reaction conditions: **1a**: (0.38 mmol), aqueous ammonia (1 mL), copper catalyst (20 mol %), solvent (1 mL), temperature for 24 h, and in a sealed tube. [b]Isolated yield. [c](Cu_2O: 10 mol %).

With these optimized reaction conditions, we explored the scope of this methodology. Because dibenzothiophene has emerged as an important structure in drug discovery,[11] bromodibenzothiophenes are explored using this catalysis system (Scheme 2). The amination of 4-bromodibenzothiophene **1b** afforded the desired product **3ba** in 71% yield after 48 h with a slight increase of temperature and copper loading. Also, 2,8 dibromodibenzothiophene was successfully converted to **3ca** in 97% yield after 48 h. Interestingly, the corresponding dioxide of bromodibenzothiophenes was also transformed after 48 h into the desired amines (**3da**–**3ea**) in excellent yield.

Scheme 2. Substrate Scope for the Reaction with Ammonia



[a]The reaction was conduct at 120 °C 48 h and 40 mol % of Cu_2O was used. [b]The reaction was conducted for 48 h.

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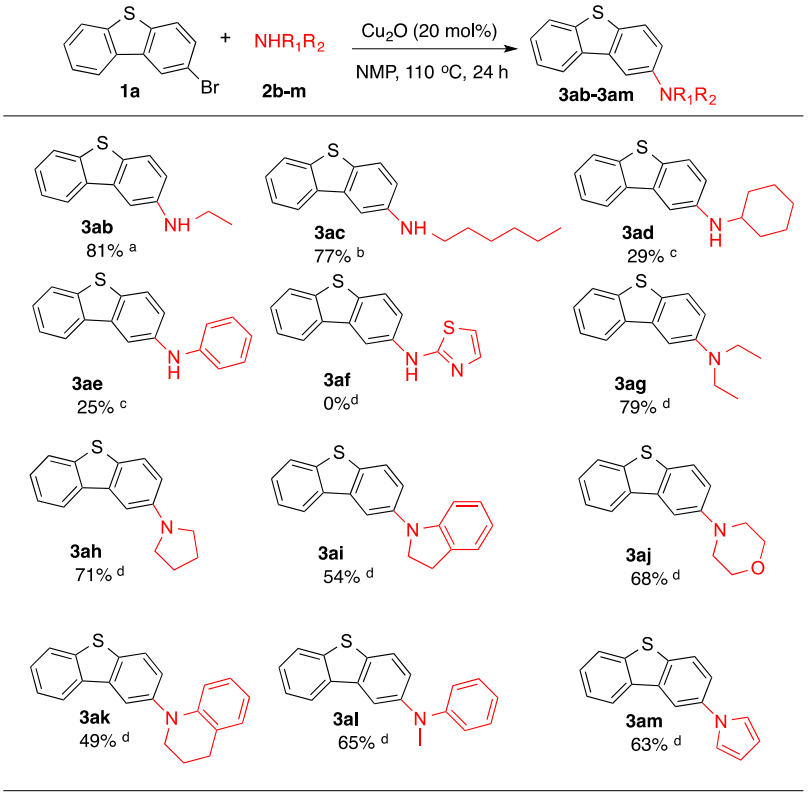
Scheme 3. Substrate Scope for the Reaction of 1a with Variety of Amines



[a]The reaction was conducted for 48 h, [b]2.0 equiv of Cs_2CO_3 was used. [c]1 equiv of NaO^{t}Bu was used. [d]2.0 equiv of NaO^{t}Bu was used.

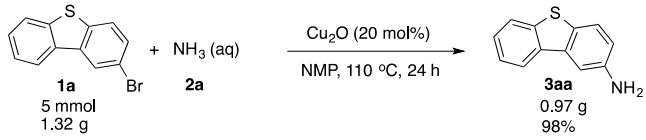
Bromo polyheteroaryls such as bromocarbazole, dibenzofuran, and fluorenone reacted smoothly under the specified conditions to form the corresponding amines in excellent yield (**3fa**−**3ha**). This reaction also worked well with bromo bicyclic heteroaryl derivatives regardless of the position of bromine (entries **3ia**−**3na**).

Next, we explored the substrate scope of this methodology by coupling 2-bromodibenzothiophene **1a** with a variety of amines (**2b**−**m**). As shown in Scheme 3, it was found that coupling **1a** with 30% aqueous ethylamine **2b** under our optimized conditions provided *N*-ethylamine **3ab** in 81% yield after 48 h. While the coupling with higher molecular weight primary amines such as hexylamine **2c** required the presence of Cs_2CO_3 to afford the desired product **3ac** in 79% isolated yield.

Coupling with bulky alkyl amine and aromatic amine (**2d**−**2e**) was also found to be compatible with these reaction conditions although were less reactive (**3ad**−**3ae**) and required the use of NaO^{t}Bu. Nevertheless, no reaction was observed when **1a** was coupled with 2-aminothiazole **2f**. The reaction of the secondary aliphatic amine, diethylamine **2g**, proceeded smoothly in the presence of NaO^{t}Bu to form the desired product **3ag** in 79%. N-containing heterocyclic compounds can be also coupled in this reaction (**3ah**−**3ak**). Interestingly, even the coupling with poorly nucleophilic amines such as *N*-methylaniline **2l** and pyrrole **2m** was accomplished in 65−63% yield, respectively (**3al**−**3am**).

To examine the scalability of this method, a gram-scale amination of compound **1a** was carried out (Scheme 4). The desired product **3aa** was obtained in 98% yield, which demonstrated the practicality of this procedure.

Scheme 4. Gram-Scale Amination of 1a



To further investigate the transforming application of this protocol, sulfonamide, the building block of many biological active compounds,[12] could be synthesized by the reaction of primary amine and benzenesulfonic chloride. Dibenzothiophene bearing the sulfonamide **5** (Scheme 5) was prepared rapidly at room temperature by reaction of compound **3aa** with benzene sulfonyl chloride **4** following the literature procedure.[13]

Based on our experimental results and literature precedents,[14] we propose a plausible mechanism for this Ullmann C−N coupling reaction as depicted in Scheme 6. Initially, the nucleophile is activated through the coordination to the copper (I) atom to form active species **I**. Next, species **I** reacts with 2-bromodibenzothiophene to produce the Cu (III) intermediate **II** via oxidative addition. Finally, the reductive elimination of **II** leads to C−N bond formation and regeneration of the Cu(I) catalyst.

In summary, we have successfully developed a one-pot method that allows the direct amination of bromo polycyclic heteroatoms via a copper-catalyzed Ullmann C−N coupling reaction. Additionally, this catalyst system proved to be efficient not only for preparing primary amine but also secondary and tertiary amines with aliphatic, aromatic, and NH-containing heterocycles. We believe this catalysis system

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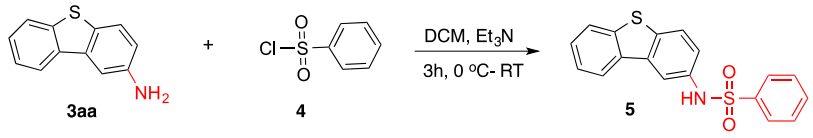
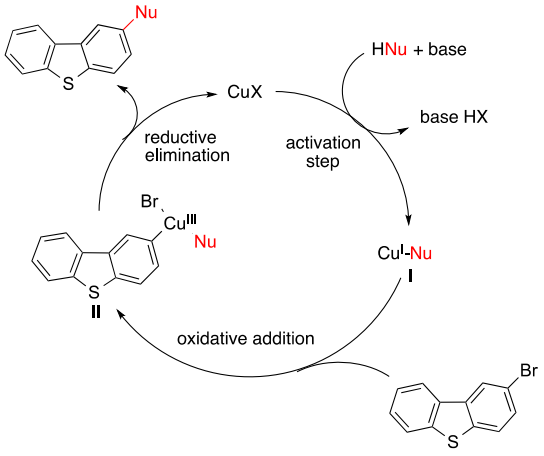
Scheme 5. Synthesis of Dibenzothiophene-Bearing Sulfonamide



Scheme 6. Plausible Catalytic Mechanism



should find wide utility for organic chemists and in the pharmaceutical industry. Applications of these compounds in medicinal chemistry are under investigation in our laboratory.

EXPERIMENTAL SECTION

General Information. All the bromo compounds were purchased from (Accela ChemBio and Ak Scientific) and used without further purification. Other reagents were purchased from sigma Aldrich, Across Organics, Oakwood Chemicals and were used without further purification. All the reactions were performed in Ace glass pressure tubes. Flash column chromatography was performed with silica gel (porosity 60 Å, particle size 63−200 μm, 70−230 mesh). Precoated aluminum gel plates (60A w/fluorescent indicator 254 nm) were used as thin layer chromatography plates and detected with UV light. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bucker Avance 400 MHz NMR spectrometer. Chemical shifts are reported in δ (ppm) values using TMS as an internal standard. High-resolution mass spectra (HRMS) were obtained on a Thermo-Fisher Exactive Orbitrap mass spectrometer using the atmospheric solid analysis probe (ASAP-MS) method.

General Experimental Procedures for the Synthesis of Primary Amines (3aa−3na). Bromo compounds **1** (100 mg, 1 equiv) were added into a pressure tube followed by Cu_2O (20 mol %), 1 mL ammonium hydroxide solution 28−30% w/w **2a**, and 1 mL NMP. The mixture was heated at 110 °C in an oil bath to the stated time in Scheme 2. Then, the mixture was cooled to room temperature and poured into ice water (4 mL) to obtain a solid precipitate. The precipitate formed was filtered and washed with water to afford the product. The product can be further purified by recrystallization with methanol or flash column chromatography (EtOAc/hexans = 3:7).

*Dibenzo[b,d]thiophene-2-amine (**3aa**).* Prepared using a general procedure, the reaction of bromo compound **1a** (0.38 mmol), Cu_2O (0.076 mmol), and **2a** (1 mL) and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3aa** (75 mg, 99%) as a white solid, mp 124−126 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07−8.05 (m, 1H), 7.84−7.82 (m, 1H), 7.64 (d, J = 8 Hz, 1H), 7.46−7.41 (m, 3H), 6.87 (d, J = 6.68 Hz, 1H), 3.67 (br, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.75, 140.47, 136.65, 135.32, 129.39, 126.53, 124.01, 123.31, 122.93, 121.50, 116.46, 107.17. HRMS (ASAP-MS) m/z: calcd for $C_{12}H_9N_1S$ [M + H]$^+$, 200.0522; found, 200.0528.

*Dibenzo[b,d]thiophen-4-amine (**3ba**).* Prepared using a general procedure, the reaction of bromo compound **1b** (0.38 mmol), Cu_2O (0.152 mmol), **2a** (1 mL) and NMP (1 mL) was carried out at 120 °C for 48 h to give the desired product **3ba** (54 mg, 71%) as a white solid, mp 108−110 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18−8.16 (m, 1H), 7.94−7.90 (m, 1H), 7.71 (d, J = 8 Hz, 1H), 7.51−7.49 (m, 2H), 7.37 (t, J = 7.72 Hz, 1H), 6.83 (d, J = 8 Hz, 1H), 3.90 (br, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl3): δ 141.04, 138.78, 136.81, 136.51, 126.69, 125.86, 125.70, 124.53, 123.04, 122.11, 112.61, 112.22; HRMS (ASAP-MS) m/z: calcd for $C_{12}H_9NS$[M + H]$^+$, 200.0528; found, 200.0528.

*Dibenzo[b,d]thiophene-2,8-diamine (**3ca**).* Prepared using a general procedure, the reaction of bromo compound **1c** (0.29 mmol), Cu_2O (0.058 mmol), **2a** (2 mL), and NMP (1 mL) was carried out at 110 °C for 48 h to give the desired product **3ca** (61 mg, 97%) as a white solid, mp 199−200 °C, ^{1}H NMR (400 MHz, CDCl3): δ 7.58 (d, J = 7.24 Hz, 2H), 7.36 (d, J = 4 Hz, 2H), 6.87 (dd, J = 1.6, 6.12 Hz, 2H), 3.78 (br, 4H). ^{13}C{^{1}H} NMR (100 MHz, CDCl3): δ 143.48, 136.38, 130.48, 123.43, 116.30, 107.08; HRMS (ASAP-MS) m/z: calcd for $C_{12}H_{10}N_2S$[M + H]$^+$, 215.0637; found, 215.0629.

*Dibenzo[b,d]thiophen-2-amine,5,5-dioxide (**3da**).* Prepared using a general procedure, the reaction of bromo compound **1d** (0.33 mmol), Cu_2O (0.067 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 48 h to give the desired product **3da** (78 mg, 99%) as a white solid, mp 278−280 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.91 (d, J = 8 Hz, 1H), 7.84 (d, J = 7.4 Hz, 1H), 7.73 (td, J = 6.44, 1.12 Hz, 1H), 7.59 (td, J = 6.6 Hz, 0.96 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 1.96 Hz, 1H) 6.69 (dd, J = 6.4, 2.04 Hz, 1H), 6.28 (s, 2H), ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 154.84, 139.12, 134.34, 133.32, 131.68, 130.89, 123.83, 122.99, 122.19, 121.86, 114.85, 105.50; HRMS (ASAP-MS) m/z: calcd for $C_{12}H_9NSO_2$[M + H]$^+$, 232.0427; found, 232.0420.

*Dibenzo[b,d]thiophene-2,8-diamine, 5,5-dioxide (**3ea**).* Prepared using a general procedure, the reaction of bromo compound **1e** (0.33 mmol), Cu_2O (0.067 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 48 h to give the desired product **3ea** (63 mg, 96%) as a white solid, mp > 300 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.42 (d, J = 8 Hz, 2H), 6.88 (d, J = 2 Hz, 2H), 6.63 (dd, J = 8, 2 Hz, 2H) 6.16 (s, 4H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 154.26, 133.65, 124.98, 123.17, 114.38, 104.91; HRMS (ASAP-MS) m/z: calcd for $C_{12}H_{10}N_2O_2S$[M + H]$^+$, 247.0551; found, 247.0536.

*9H-Carbazol-2-amine (**3fa**).* Prepared using a general procedure, the reaction of bromo compound **1f** (0.40

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mmol), Cu_2O (0.081 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3fa** (70 mg, 94%) as a black solid, mp 247−249 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.69 (s, 1H), 7.89 (d, J = 8 Hz, 1H), 7.35 (d, J = 8 Hz, 1H), 7.27 (td, J = 5.96, 1.12 Hz, 1H), 7.23 (d, J = 1.52 Hz, 1H), 7.18 (d, J = 8 Hz, 1H), 7.03 (t, J = 8 Hz, 1H), 6.76 (dd, J = 1, 8 Hz, 1H), 4.67 (br, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 141.61, 140.64, 133.31, 125.27, 123.53, 122.69, 120.25, 117.92, 115.71, 111.58, 111.14, 104.14; HRMS (ASAP-MS) m/z: calcd for $C_{12}H_{10}N_2$ [M + H]$^+$, 183.0917; found, 183.0912.

Dibenzo[b,d]furan-2-amine (***3ga***). Prepared using a general procedure, the reaction of bromo compound **1g** (0.40 mmol), Cu_2O (0.080 mmol), and **2a** (1 mL) and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ga** (65 mg, 88%) as a white solid, mp 126−128 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 7.68 Hz, 1H), 7.53 (d, J = 8.16, 1H), 7.44 (t, J = 6 Hz, 1H), 7.72 (d, J = 8.64 Hz, 1H) 7.31 (t, J = 8 Hz, 1H), 7.26 (d, J = 2.32 Hz, 1H), 6.85 (dd, J = 2.40, 6.24 Hz, 1H) 3.52 (br, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): 156.76, 150.38, 142.00, 126.92, 124.88, 124.30, 122.22, 120.54, 115.76, 111.93, 111.62, 106.00; HRMS (ASAP-MS) m/z: calcd for $C_{12}H_9NO$ [M + H]$^+$, 184.0757; found, 184.0757.

9H-Fluoren-2-amine (***3ha***). Prepared using a general procedure, the reaction of bromo compound **1h** (0.41 mmol), Cu_2O (0.081 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ha** (67 mg, 91%) as a light yellow solid, mp 125−127 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 7.52 Hz, 1H), 7.59 (d, J = 8.04 Hz, 1H), 7.48 (d, J = 7.4 Hz, 1H) 7.33 (t, J = 7.32, 1H), 7.20 (t, J = 7.36 Hz, 1H), 6.90 (s, 1H), 6.73 (d, J = 8 Hz, 1H) 3.83 (s, 2H) 3.83 (br, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.69, 145.15, 142.29, 142.14, 133.05, 126.65, 125.11, 124.77, 120.64, 118.61, 114.06, 111.89, 36.85; HRMS (ASAP-MS) m/z: calcd for $C_{13}H_{11}N$ [M + H]$^+$, 182.0964; found, 182.0958.

Benzo[b]thiophen-5-amine (***3ia***). Prepared using a general procedure, the reaction of bromo compound **1i** (0.46 mmol), Cu_2O (0.093 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ia** (69 mg, 98%) as a red solid, mp 69−70 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.48 Hz, 1H), 7.40 (d, J = 5.40 Hz, 1H),7.16 (d, J = 5.52 Hz, 1H), 7.12 (s, 1H), 6.80 (d, J = 8 Hz, 1H) 3.40 (br, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.50, 140.87, 130.48, 127.10, 123.05, 122.96, 114.88, 108.32; HRMS (ASAP-MS) m/z: calcd for C_8H_7NS[M + H]$^+$, 150.0372; found, 150.0372.

1-Benzofuran-5-amine (***3ja***). Prepared using a general procedure, the reaction of bromo compound **1j** (0.50 mmol), Cu_2O (0.102 mmol), and **2a** (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ja** (63 mg, 93%) as a brownish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 2.12 Hz, 1H), 7.31 (d, J = 8.64 Hz, 1H), 6.89 (d, J = 2.24 Hz, 1H), 6.70 (dd, 6.64, 2.36 Hz, 1H), 6.63 (m, 1H), 3.61 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 149.56, 145.43, 141.98, 128.25, 113.60, 111.60, 106.12, 106.01. HRMS (ASAP-MS) m/z: calcd for C_8H_7NO[M + H]$^+$, 134.0606; found, 134.0613.

1H-Indol-5-amine (***3ka***). Prepared using a general procedure, the reaction of bromo compound **1k** (0.51 mmol), Cu_2O (0.102 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ka** (65 mg, 96%) as a brown solid. mp 131−132 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.56 (s, 1H), 7.12 (t, J = 4 Hz, 1H), 7.08 (d, J = 8 Hz, 1H) 6.67 (d, J = 2 Hz, 1H), 6.48 (dd, J = 8.4, 2.3 Hz, 1H), 6.12 (m, 1H) 4.48 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 141.43, 130.19, 128.97, 125.15, 112.26, 111.80, 103.65, 100.00. HRMS (ASAP-MS) m/z: calcd for $C_8H_8N_2$[M + H]$^+$, 133.0760; found, 133.0765.

Benzo[b]thiophen-4-amine (***3la***). Prepared using a general procedure, the reaction of bromo compound **1l** (0.46 mmol), Cu_2O (0.093 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3la** (64 mg, 91%) as a gray solid, mp 51−53 °C, ^{1}H NMR (400 MHz, CDCl3): δ 7.38−7.36 (m, 2H), 7.31−7.29 (m, 1H), 7.20 (t, J = 8 Hz, 1H) 6.67 (d, J = 8 Hz, 1H), 4.04 (br, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl3): δ 141.49, 141.12, 128.26, 125.45, 124.40, 119.27, 113.02, 108; HRMS (ASAP-MS) m/z: calcd for C_8H_7NS[M + H]$^+$, 150.0372; found, 150.0368.

Benzo[b]thiophen-6-amine (***3ma***). Prepared using a general procedure, the reaction of bromo compound **1m** (0.46 mmol), Cu_2O (0.093 mmol), **2a** (1 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ma** (66 mg, 94%) as a white solid. mp 114−115 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8 Hz, 1H), 7.18 (dd, J = 16, 4 Hz, 3H), 6.79 (d, J = 8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.69, 141.52, 132.46, 124.11, 123.51, 122.11, 114.52, 107.06. m/z: calcd for C_8H_7NS[M + H]$^+$, 150.0372; found, 150.0370.

6-Amino-1(3H)-Isobenzofuranone (***3na***). Prepared using a general procedure, the reaction of bromo compound **1n** (0.46 mmol), Cu_2O (0.093 mmol), and **2a** (1 mL) and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3na** (67 mg, 95%) as a white solid mp 195−197 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.43 (d, J = 8 Hz, 1H), 6.68 (d, J = 1.84 Hz, 1H) 6.66 (d, J = 1.88 Hz, 1H) 6.24 (s, 2H) 5.16 (s, 2H), ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) 171.28, 155.14, 150.61, 126.64, 115.21, 111.55, 104.92, 69.14. HRMS (ASAP-MS) m/z: calcd for $C_8H_7NO_2$[M + H]$^+$, 150.0550; found, 150.0560.

General Procedures for the Synthesis of N-Substituted Dibenzothiophenes 3ab−3am. 2-Bromodibenzothiophene **1a** (0.38 mmol) was added into a pressure tube followed by Cu_2O (0.076 mmol), the amine source **2b−m** (0.76 mmol), and 1 mL NMP. The mixture was heated at 110 °C in an oil bath to the stated time in Scheme 3. Then, the reaction was poured into ice water (4 mL) and extracted three times with ethyl acetate (20 mL). The organic phase was dried over Mg_2SO_4, filtered, and the solvent was removed under reduced pressure to provide the crude product. The crude product was purified by flash column chromatography (eluent: hexane/ethyl acetate: 9:1) to give the pure product.

N-Ethyldibenzo[b,d]thiophen-2-amine (***3ab***). Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), ethylamine (70% solution in water) **2b** (1 mL), and NMP (1 mL) was carried out at 110 °C for 48 h to give the desired product **3ab** as a colorless oil (70 mg, 81%), ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.22−8.20 (m, 1H), 7.92−7.90 (m, 1H), 7.65 (d, J = 8.64 Hz, 1H), 7.44−7.42 (m, 2H), 7.39 (d, J = 2.20 Hz, 1H), 6.87 (dd, J = 8.6, 2.28 Hz, 1H), 5.77 (br, 1H) 3.17 (q, J = 7.08 Hz, 2H), 1.24 (t, J = 7.12 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 147.61, 139.88, 136.57, 135.75, 126.88, 125.66, 124.58, 123.44, 122.18, 115.89, 102.91, 38.2133, 14.8329.

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HRMS (ASAP-MS) m/z: calcd for $C_{14}H_{13}NS$ $[M + H]^+$, 228.0835; found, 228.0841.

*N-Hexyldibenzo[b,d]thiophen-2-amine (**3ac**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), hexyl amine **2c** (0.07 mL) and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ac** as a brown oil (83 mg, 77%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.22−8.20 (m, 1H), 7.92−7.90 (m, 1H), 7.64 (d, J = 8 Hz, 1H), 7.46−7.41 (m, 2H), 7.39 (d, J = 4 Hz, 1H), 6.89 (dd, J = 2.08, 6.56 Hz, 1H), 5.69 (s, 1H), 3.12 (q, J = 6.72 Hz, 2H), 1.65−1.58 (m, 2H), 1.43−1.39 (m, 2H), 1.31 (t, J = 3.71 Hz, 4H), 0.88 (t, J = 6.92, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 147.72, 139.92, 136.58, 135.78, 126.84, 125.55, 124.53, 123.40, 122.15, 115.81, 102.84, 43.74, 31.69, 29.15, 26.98, 22.65, 14.42; HRMS (ASAP-MS) m/z: calcd for $C_{18}H_21NS$ $[M + H]^+$, 284.1460; found, 284.1467.

*N-Cyclohexyldibenzo[b,d]thiophen-2-amine (**3ad**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), cyclohexyl amine **2d** (0.07 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ad** (31 mg, 29%) as a white solid, mp 256−258 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.22−8.20 (m, 1H), 7.92−7.90 (m, 1H), 7.62 (d, J = 8 Hz, 1H), 7.45−7.43 (m, 2H), 7.42 (d, J = 4 Hz, 1H), 6.87 (dd, J = 2.28, 6.48 Hz, 1H), 5.53 (d, J = 8.28 Hz, 1H), 1.90 (dd, J = 3.2, 9.48 Hz, 2H), 1.78−1.73 (m, 2H), 1.65−1.62 (m, 1H) 1.46−1.36 (m, 2H), 1.26−1.15 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 146.57, 139.86, 136.59, 135.72, 126.87, 125.23, 124.55, 123.51, 123.42, 122.20, 116.07, 103.44, 51.12, 33.06, 26.14, 25.08, HRMS (ASAP-MS) m/z: calcd for $C_{18}H_{19}NS$ $[M + H]^+$, 282.1303; found, 282.1311.

*N-Phenyldibenzo[b,d]thiophen-2-amine (**3ae**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), aniline **2e** (0.07 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ae** (26 mg, 25%) as a white solid, mp 270−273 °C ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.35 (s, 1H), 8.22−8.20 (m, 1H), 7.99−7.96 (m, 2H) 7.86 (d, J = 8.6 Hz, 1H), 7.49−7.46 (m, 2H), 7.30−7.25 (m, 3H), 7.19−7.12 (m, 2H) 6.85 (tt, J = 7.2, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 144.28, 141.49, 139.92, 136.44, 135.33, 130.1360, 129.75, 127.38, 124.95, 124.03, 123.54, 122.33, 120.08, 119.37, 116.82, 109.69; HRMS (ASAP-MS) m/z: calcd for $C_{18}H_{13}NS$ $[M + H]^+$, 276.0841; found, 276.0845.

*N,N-Diethyldibenzo[b,d]thiophen-2-amine (**3ag**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), diethylamine **2g** (0.05 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ag** (77 mg, 79%) as a yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.33−8.31 (m, 1H), 7.92−7.89 (m, 1H), 7.72 (d, J = 8.8 Hz, 1H), 7.54 (d, J = 2.6 Hz, 1H), 7.45−7.43 (m, 2H), 6.95 (dd, J = 8.9, 2.6 Hz, 1H), 3.45 (q, J = 7.0 Hz, 4H), 1.14 (t, J = 7.0 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 146.25, 139.94, 136.83, 135.82, 127.02, 125.46, 124.55, 123.74, 123.42, 122.43, 114.51, 104.44, 44.47, 12.8194; HRMS(ASAP-MS) m/z: calcd for $C_{16}H_{17}NS$ $[M + H]^+$, 256.1154; found, 256.1154.

*1-(Dibenzo[b,d]thiophen-2-yl)pyrrolidine (**3ah**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), pyrrolidine **2h** (0.05 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ah** (69 mg, 71%) as a light yellow solid, mp 189−191 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.40 (dd, J = 1.2, 6.96 Hz, 1H), 8.01(dd, J = 1.08, 6.96 Hz, 1H) 7.66 (dd, J = 0.80, 7.08 Hz, 1H), 7.56−7.48 (m, 2H), 7.43 (t, J = 7.88 Hz, 1H), 7.23 (d, J = 8 Hz, 1H), 3.13 (s, 4H), 2.013 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 148.53, 140.51, 138.52, 135.27, 128.34, 127.87, 126.33, 125.63, 124.97, 122.95, 117.56, 114.38, 51.46, 23.80; HRMS (ASAP-MS) m/z: calcd for $C_{16}H_{15}NS$ $[M + H]^+$, 254.0998; found, 254.0990.

*1-(Dibenzo[b,d]thiophen-2-yl)-2,3-dihydro-1H-indole (**3ai**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), indoline **2i** (0.09 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ai** (62 mg, 54%) as a white solid, mp 249−251 °C ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.36−8.33 (m, 1H), 8.09 (d, J = 2.04 Hz, 1H), 7.99−7.96 (m, 1H), 7.93 (d, J = 8.8 Hz, 1H) 7.51−7.46 (m, 3H), 7.19 (d, J = 8 Hz, 1H), 7.14 (d, J = 7.88 Hz, 1H), 7.06 (t, J = 7.68 Hz, 1H) 6.73 (t, J = 7.28 Hz, 1H), 4.02 (t, J = 8.44 Hz, 2H), 3.11 (t, J = 8.32 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ147.18, 141.85, 139.84, 136.47, 135.32, 131.66, 131.02, 127.61, 127.55, 125.58, 125.05, 123.90, 123.49, 122.60, 119.37, 118.88, 110.54, 107.83, 52.56, 27.96; HRMS (ASAP-MS) m/z: calcd for $C_{20}H_{15}NS$ $[M + H]^+$, 302.0998; found, 302.0998.

*4-(Dibenzo[b,d]thiophen-2-yl)morpholine (**3aj**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), morpholine **2j** (0.06 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3aj** (70 mg, 68%) as a light yellow solid, mp 210−212 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38−8.36 (m, 1H), 7.94−7.97 (m, 1H), 7.88 (d, J = 4 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.49−7.46 (m, 2H), 7.23 (dd, J = 2.48, 4 Hz, 1H), 3.81 (t, J = 4.88 Hz, 4H), 3.24 (t, J = 4.72, 4H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 149.73, 139.90, 136.46, 135.74, 129.58, 127.25, 124.78, 123.62, 123.48, 123.56, 117.38, 108.14, 66.62, 49.65; HRMS (ASAP-MS) m/z: calcd for $C_{16}H_{15}NOS$ $[M + H]^+$, 270.0947; found, 270.0938.

*1-(Dibenzo[b,d]thiophen-2-yl)-1,2,3,4-tetrahydroquinoline (**3ak**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), tetrahydroquinoline **2k** (0.10 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3ak** (59 mg, 49%) as a white solid, mp 288−289 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.35−8.33 (m, 1H), 8.23 (d, J = 2.08 Hz, 1H), 8.03−7.98 (m, 2H), 7.54−7.46 (m, 2H), 7.41 (dd, J = 8.6, 2.16 Hz, 1H), 7.04 (dd, J = 7.4, 1.7 Hz, 1H), 6.65 (td, J = 7.3, 1.2 Hz, 1H) 6.57 (dd, J = 8.2, 1.2 Hz, 1H), 3.74−3.67 (m, 2H), 2.84 (t, J = 6.4 Hz, 2H), 2.04 (dd, J = 6.5, 5.0 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 145.81, 145.01, 139.78, 136.97, 135.35, 134.33, 129.76, 127.59, 126.81, 125.43, 125.11, 124.46, 124.31, 123.56, 122.72, 118.68, 118.43, 115.14, 51.33, 27.68, 22.76; HRMS (ASAP-MS) m/z: calcd for $C_{21}H_{17}NS$ $[M + H]^+$, 316.1154; found, 316.1156.

*1-(Dibenzo[b,d]thiophen-2-yl)pyrrole (**3al**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), *N*-methylaniline **2l** (0.08 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3al** (60 mg, 63%) as a light yellow solid, mp 241−242 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.61 (d, J = 2.2 Hz, 1H), 8.54−8.51, (m, 1H) 8.10 (d, J

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= 8.64 Hz, 1H), 8.05−8.03 (m, 1H), 7.77 (dd, J = 2.32, 6.32 Hz, 1H), 7.56−7.54 (m, 4H), 6.33 (t, J = 2.2 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 140.01, 138.06, 136.67, 135.45, 135.33, 127.93, 125.18, 124.50, 123.60, 123.10, 119.86, 119.55, 112.93, 110.95; HRMS (ASAP-MS) m/z: calcd for $C_{16}H_{11}NS$ $[M + H]^+$, 250.0685; found, 250.0678.

*N-Methyl-N-phenyldibenzo[b,d]thiophen-2-amine (**3am**).* Prepared using a general procedure, the reaction of 2-bromodibenzothiophene **1a** (0.38 mmol), Cu_2O (0.076 mmol), pyrrole **2m** (0.05 mL), and NMP (1 mL) was carried out at 110 °C for 24 h to give the desired product **3am** (72 mg, 65%) as a white solid, mp 276−278 °C, ^1H NMR (400 MHz, DMSO-d_6): δ 8.33−8.29 (m, 1H), 8.06 (d, J = 2.24, 1H), 8.03−7.96 (m, 1H) 7.90 (d, J = 8.6 Hz, 1H), 7.52−7.44 (m, 2H), 7.31−7.24 (m, 2H), 7.20 (dd, J = 8.7, 2.3 Hz, 1H), 6.99 (td, J = 7.9, 1.1 Hz, 2H) 6.90 (tt, J = 7.3, 1.1 Hz, 2H), 3.38 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 149.55, 146.72, 139.86, 136.81, 135.42, 132.47, 129.68, 127.48, 125.00, 124.03, 123.54, 122.85, 122.63, 120.8545, 119.1778, 114.9368, 40.9466; HRMS (ASAP-MS) m/z: calcd for $C_{19}H_{15}NS$ $[M + H]^+$, 290.0998; found, 290.1000.

*N-Dibenzothiophen-2-yl-benzenesulfonamide (**5**).* Prepared according to a literature procedure[13] to give the desired product **5** (130 mg, 76%) as a white solid mp > 300 °C, ^1H NMR (DMSO-d_6, 400 MHz, ppm): 10.47 (s, 1H), 8.17−8.15 (m, 1H), 8.01−7.98 (m, 2H), 7.88 (d, J = 8, 1 Hz, 1H), 7.81−7.79 (m, 2H), 7.60−7.48 (m, 5H), 7.22 (dd, J = 6.24, 2 Hz, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz, ppm): δ 139.80, 139.78, 135.96, 135.42, 134.89, 134.84, 133.40, 129.72, 127.86, 127.21, 125.32, 124.17, 123.65, 122.22, 121.26, 114.03. HRMS (ASAP-MS) m/z: calcd $C_{18}H_{13}NO_2S_2$ $[M + H]^+$, 340.0460; found, 340.0477.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c00414.

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

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Notes

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