A Catalyst System, Copper/*N*-Methoxy-1*H*-pyrrole-2-carboxamide, for the Synthesis of Phenothiazines in Poly(ethylene glycol)

Manna Huang,[a] Jianying Hou,[a] Ruiqiao Yang,[b] Liting Zhang,[a] Xinhai Zhu,*[a] Yiqian Wan*[a]

[a] School of Chemistry and Chemical Engineering, Sun Yat-sen University, Guangzhou 510275, P. R. of China
Fax +86(20)84113610; E-mail: ceswyq@mail.sysu.edu.cn

[b] Hunan College for Preschool Education, Changde 415000, P. R. of China

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Abstract: A copper/*N*-methoxy-1*H*-pyrrole-2-carboxamide catalyst system has been established for the preparation of phenothiazines in good yields by two routes, starting from 2-iodoanilines and 2-bromobenzenethiol and from aryl *ortho*-dihalides and *o*-aminobenzenethiols, by conducting the reaction at 90 °C in poly(ethylene glycol)-100 (PEG-100). In addition, the catalyst system was useful for promoting direct arylation of various aryl amines, aliphatic amines, and aqueous ammonia. The simple experimental operation, low loading of catalyst system together with the use of green solvent, makes it attractive for the versatile syntheses of phenothiazines and various amines.

Key words: copper, homogeneous catalysis, amination, green chemistry, heterocycles

Phenothiazine was first prepared by Bernthsenin in 1883 to elucidate the structure of Lauth's violet and methylene blue.[1] Since then, the phenothiazine family has played an important role in both human medicine and the materials field. Phenothiazines represent the largest and oldest group of antipsychotic compounds in clinical medicine. In particular, they largely revolutionized the practice of psychiatric medicine, a process that is now continuing with the introduction of the newer atypical antipsychotics such as risperidone and olanzapine.[2] Chlorpromazine and prochlorperazine can be viewed as the prototypes of the many phenothiazines, and their congeners exert a significant influence on many organ systems of the body at once as cholinesterases inhibitors,[3] histamine H1 antagonists,[4] antitubercular agents,[5] lipid peroxidation inhibitors,[6] and so on.[5a,7] They have also been successfully employed in the materials field as a high-affinity selective heparin sensor,[8] molecular wires,[9] organic dyes,[10] electrogenerated chemiluminescence materials,[11] a chemosensor for the selective fluorescent detection of flavins,[12] and for their other electronic properties.[13] Given the significance of phenothiazines, many classical methods have been established to construct their core moiety: (1) In the cyclization of diphenyl sulfides, which is by far the most important method, the central step involves a Smiles rearrangement; however, many factors that govern the reaction, including steric hindrance, electrophilicity, the acidity of the acylamino group that attacks the aromatic nucleus and the nature of the base, often reduce its applications.[14] (2) The cyclization of diphenylamines with sulfur is substantially improved by using iodine as catalyst; however, it suffers from certain disadvantages, including a high temperature requirement and difficulty in separating the regioisomers.[15] (3) There are also many other methods, such as cyclization with benzoquinones,[16] cyclization of 2-aminothiophenols with cyclohexane-1,3-diones,[17] reductive cyclization of 2-nitrodiphenyl sulfides with triethyl phosphite,[18] and thermal cyclization of aryl azides with 1,2,3-benzothiadiazole.[19] Moreover, the functionalization of phenothiazine is also an important route to many phenothiazine's derivatives, but it is often hindered by poor regioselectivity.[11,13,20]

More recently, the application of transition-metal-catalyzed reactions to synthesize phenothiazines has attracted much attention. In 2008, Jorgensen[21] reported a palladium-catalyzed three-component approach to phenothiazines by way of formatting one C–S and two C–N bonds with or without microwave irradiation. In 2010, Ma[22] established the first copper-catalyzed coupling protocol using L-proline as a ligand to obtain phenothiazine derivatives from 2-iodoanilines and 2-bromobenzenethiols, in which finely tuning the temperature and reaction time of the C–S and C–N coupling, respectively, is crucial. Thereafter, in 2012, Zeng[23] reported a ligand-free protocol with high loading of copper (i.e., up to 30 mol%) as a catalyst to prepare the phenothiazines from aryl *ortho*-dihalides and *o*-aminobenzenethiols. At the same time, a simple one-pot method has been developed through a copper-catalyzed rearrangement of 2-aminobenzothiazoles.[24] However, the necessity of high temperature and long periods of time might be problematic for some types of substrates. Therefore, the development of an efficient copper-catalyzed protocol to provide phenothiazine and its derivatives in mild conditions and in a shorter reaction time is highly desirable. Herein, we report a novel catalyst system, copper/*N*-methoxy-1*H*-pyrrole-2-carboxamide, with which, phenothiazines were prepared from examples of both Ma's[22] and Zeng's[23] starting materials in good yields by direct carbon–heteroatom coupling at 90 °C for 15 hours (Scheme 1).

As part of our ongoing research interest in copper-catalyzed C–N coupling reactions, we envisioned that the ligand **L0** (Figure 1), which was previously identified as a high-performance ligand for a copper-catalyzed Ullmann-type C–N coupling reaction in water,[25] might also function in the synthesis of phenothiazines according to Ma's

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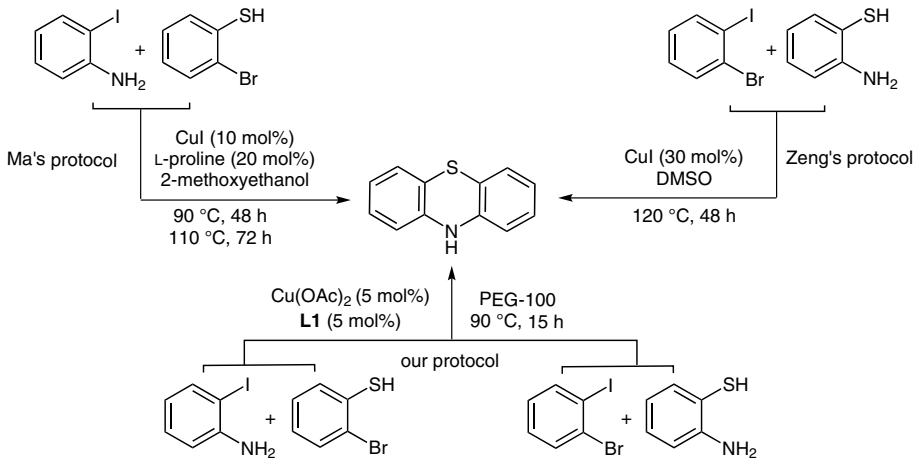


Scheme 1 Different protocols of phenothiazine synthesis

strategy. However, the outcome was poor, affording mainly 2-[(2-bromophenyl)thio]aniline from 2-iodoaniline and 2-bromobenzenethiol together with trace of the target compound. Increasing the quantity of the ligand and CuI afforded more of the desired compound but with increase of much more unidentified side-reactions. Considering the different coordinative ability of O and N, we tried to design a novel ligand **L1** and its analogues using O instead of N-atom from **L0** to alleviate the side-reactions and to develop a more effective method for the synthesis of phenothiazine. It should be significant to test this idea because only **L4**, as a ligand, showed some indication for copper-catalyzed formation of highly substituted pyrazoles among these alkoxycarbamides to our knowledge.[26]

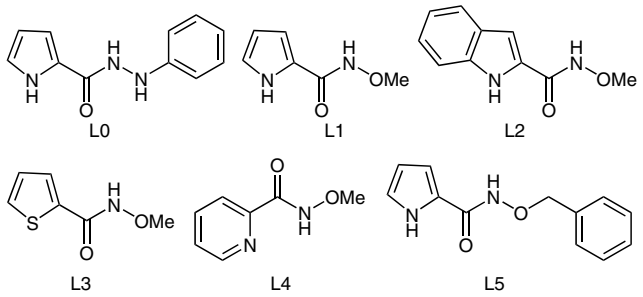


Figure 1 Ligands used in the reaction

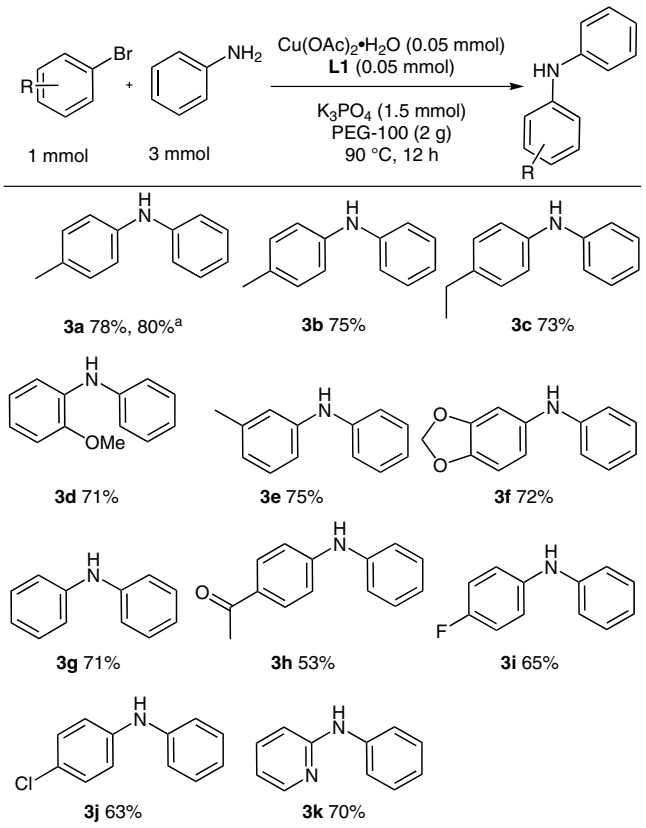
Moreover, poly(ethylene glycol)s (PEGs) are known to be nontoxic, recyclable, thermally stable, and inexpensive media for the use as phase-transfer catalysts (PTCs) and co-solvent, especially, they have ever been applicable in biomedical protocols.[27] Many types of organic reactions, such as substitution, oxidation, reduction, palladium- or copper-catalyzed coupling, etc., have been successfully performed in PEGs. Further work would no doubt continue using functional PEGs in polymer-supported syntheses and in recyclable catalyst procedures.[28] Hence, the benign nature and potent catalytic ability of PEGs made it an ideal media for us to explore our catalyst system in more detail.

As a starting point, **L1** and its analogues (Figure 1) have been synthesized and tested as ligands to establish a general copper-catalyzed C–N coupling protocol. Fortunately, the target compound was obtained in 68% normalized GC yield from 4-bromoanisole and aniline in 2-methoxyethanol with **L1**/$Cu(OAc)_2$ as catalyst, which encouraged us to optimize the reaction conditions. The optimized reaction condition consisting of $Cu(OAc)_2$ (5 mol%)/**L1** (5 mol%) and K_3PO_4 (150 mol%) with aniline (300 mol%) in PEG-100 at 90 °C for 12 hours was developed. It should be noted that **L1** was chosen to be an ultimate ligand due to its commercial availability although **L5** assumed the similar ability to **L1**. Besides, low loading of **L1** demonstrated some advantages over those previously reported by us[25,29] for copper-catalyzed C–N coupling.

Further, a variety of functionalized aryl halides were aminated using anilines (Scheme 2) or aliphatic amines (Scheme 3). The N-arylation of anilines with most aryl bromides, whether they are electron-rich, electron-neutral, or electron-poor, provided the desired products in good to excellent yields. It should be noted that even for *ortho*- and *meta*-substituted aryl bromides (Scheme 2, **3d**–**f**), the reaction afforded the desired products in high yields similar to the reactions *para*-substituted aryl bromides (Scheme 2, **3a**–**c**). These characteristics, especially the reduced steric *ortho*-effect, would accommodate itself to the development of an efficient synthetic route to phenothiazines according to Ma's[22] or Zeng's[23] strategy.

It was intriguing that the N-arylation of aqueous ammonia directly to primary amine afforded only a 58% yield due to the further arylation of the product under this experimental condition. However, as illustrated in Scheme 4, high yields of primary amines were otherwise readily provided under almost the same conditions, only using **L2** instead of **L1**.

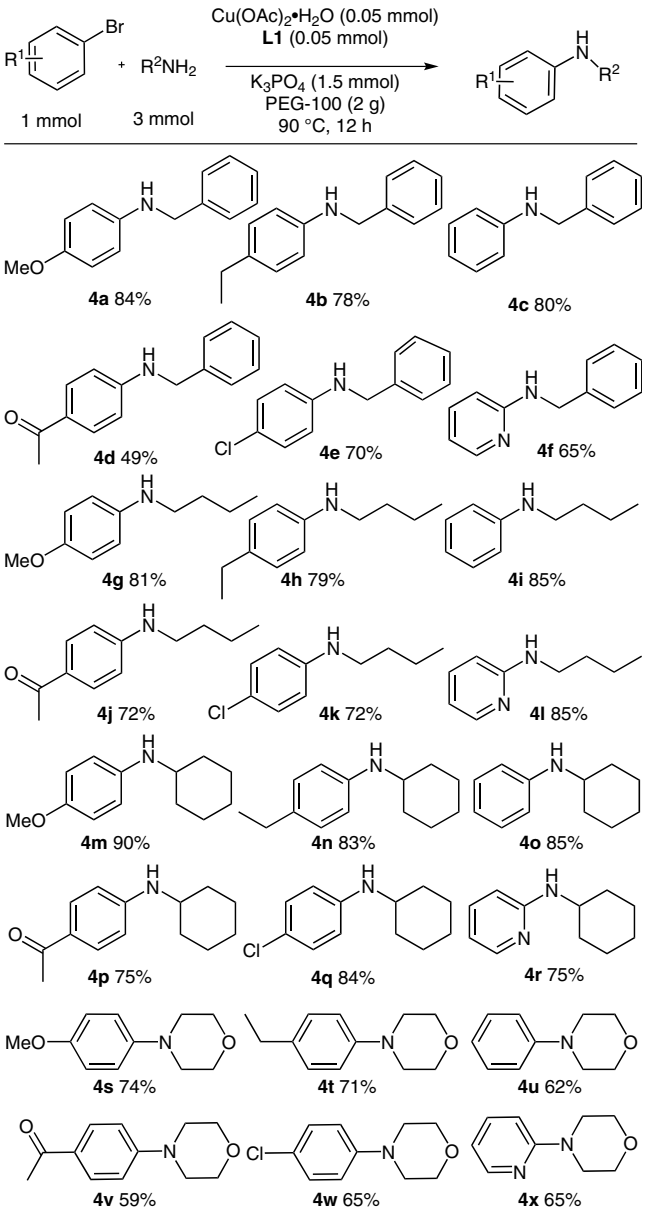
With favorable results in hand, it was reasonable for us to confront the syntheses of phenothiazines. As an applica-



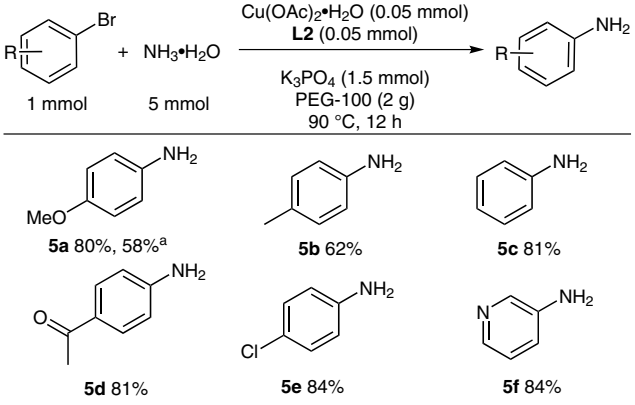
Scheme 2 Products and isolated yields for amination of aryl bromides with aniline. [a] 4-Iodoanisole was used.

tion of the optimized conditions to the protocol (Scheme 1), increasing the catalyst loading from 5 mol% to 10 mol% was rational because the reaction involved one C–S and one C–N bond formation. More interestingly, the replacement of the weak base (K_3PO_4) with a strong base (KOH) increased the yield of phenothiazine from 65% to 74% (Table 1, entry 3, method A). Inspired by the result of Zeng's,[23] the ligand-free protocol with CuI and $Cu(OAc)_2$ in PEG-100 was examined; however, only trace of phenothiazine was detected by TLC. Therefore, ligand **L1** was proved to be necessary for copper-catalyzed synthesis of phenothiazines in the green solvent, PEG-100. Hence, proceeding from these typical examples, phenothiazines with electron-rich and electron-poor substituents on the 3- or 4-position were obtained from examples of both Ma's[22] and Zeng's[23] starting materials in good yields at 90 °C for 15 hours (Table 1).

In conclusion, we have established a copper/*N*-methoxy-1*H*-pyrrole-2-carboxamide catalyst system that effectively promoted the reactions of either 2-iodoanilines and 2-bromobenzenethiol or aryl *ortho*-dihalides and *o*-aminobenzenethiols to phenothiazines in PEG-100. Moreover, the mild experimental conditions (90 °C, 15 h), the simple experimental operation (tuning the temperature and the reaction time stepwise is not necessary), and the low loading of the catalyst system (10 mol%), especially using a green solvent, PEG-100, make this approach useful for the versatile synthesis of phenothiazines from various starting materials. Furthermore, this protocol has also been con-

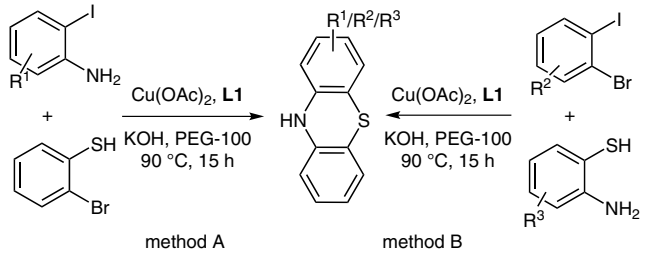


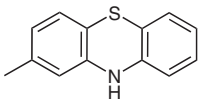
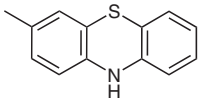
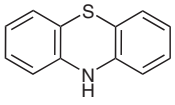
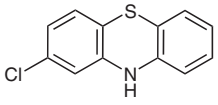
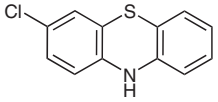
Scheme 3 Products and isolated yields for amination of aryl bromides with aliphatic amines



Scheme 4 Products and isolated yields for amination of aryl bromides with aqueous ammonia. [a] **L1** was used.

Table 1 Copper-Catalyzed Formation of Phenothiazines[a]



Entry	Product	Method	Yield (%)[b]
1	 **6a**	A B	46 74
2	 **6b**	A	73
3	 **6c**	A B	74 (65)[c] 64
4	 **6d**	A B	58 55
5	 **6e**	A	57

[a] Reaction conditions: aniline (1 mmol) and 2-bromobenzenethiol (1.2 mmol) (method A) or aryl halide (1 mmol) and 2-aminobenzenethiol (1.2 mmol) (method B), $Cu(OAc)_2 \cdot H_2O$ (10 mol%), **L1** (10 mol%), KOH (4 mmol), PEG-100 (2 g), 90 °C, 15 h, under N_2 atmosphere.
[b] Isolated yield.
[c] K_3PO_4 was used instead of KOH.

firmed to be efficient for the preparation of a variety of amines from broad substrates, including a range of electron-rich, electron-neutral or electron-poor, and even *ortho*-substituted aryl bromides, as well as various amines including aryl amines, aliphatic amines, secondary amines, and aqueous ammonia.

All starting materials and reagents are commercially available and used as received. Petroleum ether (PE) used refers to the fraction boiling in the 60–90 °C range. Most reactions were carried out in a preheated oil bath in vials (size: 10 mL) sealed with a septum. Flash column chromatography was performed with silica gel (200–300 mesh). TLC was carried out with Merck silica gel GF_{254} plates. The known products **3**–**5** were characterized by NMR and MS data and compared with the previously reported data (see Supporting Information). ^{1}H NMR and ^{13}C NMR spectra were recorded at r.t. on a Bruker Avance III 400 instrument or a Mercury-Plus 300 instrument with TMS as an internal reference. LC/MS was run on a LCMS-2010A. GC/MS was run on a Finnigan Voyager with an electron impact (70 eV) mass selective detector and an innowax 30 m × 0.25 mm × 0.25 μm capillary a polar column. GC-MS method: initial temperature: 50 °C, initial time: 3 min; ramp: 20 °C/min; final temperature: 250 °C, final time: 2 min. EI mass spectra were recorded on the Thermo DSQ mass spectrometer. Elemental analyses were carried out with a Vario EL series analyzer and have errors of ± 0.4% for CHN elements. Melting points were determined on a WRS-1B digital melting point apparatus and are not corrected. IR spectra were recorded on a Thermo 330 FT-IR spectrophotometer.

***N*-Methoxy-1*H*-pyrrole-2-carboxamide (L1)**
[CAS Reg. No.: 890122-55-1]

To a 10 mL sealed vial equipped with a magnetic stir bar were added 2-(trichloroacetyl)pyrrole (1070 mg, 5 mmol), methoxyammonium chloride (625 mg, 7.5 mmol), and Et_3N (2.5 mL). The reaction mixture was stirred in an oil bath preheated to 80 °C for 12 h. After allowing the mixture to cool to r.t., it was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using EtOAc–PE (1:1) as eluent to afford **L1**; yield: 50 mg (78%); yellow solid; mp 97–99 °C.

IR (KBr): 3217, 3152, 3003, 2938, 2804, 2737, 2677, 2491, 1599, 1528, 1469, 1443, 1403, 1344, 1279, 1204, 1189, 1150, 1096, 1040, 963, 933, 838, 752, 609, 571 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.63 (br s, 1 H, NH), 6.82–6.76 (m, 1 H, ArH), 6.72–6.67 (m, 1 H, ArH), 6.08–6.00 (m, 1 H, ArH), 3.69 (s, 3 H, OCH_3).

^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6): δ = 160.8, 122.9, 122.4, 111.6, 109.5, 64.3.

MS (ESI+): m/z = 141 ($[M + H]^+$).

***N*-Methoxy-1*H*-indole-2-carboxamide (L2)**
[CAS Reg. No.: 96680-12-5]

To a 100 mL round-bottomed flask equipped with a magnetic stir bar were added indole-2-carboxylic acid (805 mg, 5 mmol), methoxyammonium chloride (625 mg, 7.5 mmol), (dimethylaminopropyl)carbodiimide hydrochloride (1440 mg, 7.5 mmol), 4-dimethylaminopyridine (1830 mg, 15 mmol), and CH_2Cl_2 (50 mL). The reaction mixture was stirred at r.t. overnight. After concentrating the mixture in vacuo, the residue was purified by flash column chromatography on silica gel using CH_2Cl_2–MeOH (40:1) as eluent to afford **L2**; yield: 776 mg (82%); white solid; mp 144–145 °C.

IR (KBr): 3416, 3297, 3199, 2995, 2939, 2875, 1624, 1565, 1523, 1496, 1433, 1361, 1342, 1320, 1290, 1222, 1188, 1122, 1048, 980, 932, 855, 834, 777, 747, 735, 652, 543, 434 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78 (br s, 1 H, NH), 7.65 (d, J = 8.0 Hz, 1 H, ArH), 7.45 (d, J = 8.3 Hz, 1 H, ArH), 7.33–7.28 (m, 1 H, ArH), 7.14 (t, J = 7.5 Hz, 1 H, ArH), 7.07 (s, 1 H, ArH), 3.92 (s, 3 H, OCH_3).

^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6): δ = 160.8, 136.7, 128.2, 127.4, 124.2, 121.9, 120.3, 112.2, 104.3, 64.4.

MS (ESI+): m/z = 213 ($[M + Na]^+$).

***N*-Methoxy-1*H*-thiophene-2-carboxamide (L3)**
[CAS Reg. No.: 103185-33-7]

To a 100 mL round-bottomed flask equipped with a magnetic stir bar were added thiophene-2-carboxylic acid (720 mg, 5 mmol), methoxyammonium chloride (625 mg, 7.5 mmol), (dimethylaminopropyl)carbodiimide hydrochloride (1440 mg, 7.5 mmol), 4-dimethylaminopyridine (1830 mg, 15 mmol), and CH_2Cl_2 (50 mL). The reaction mixture was stirred at r.t. overnight. After concentrating the mixture in vacuo, the residue was purified by flash column chro-

matography on silica gel using CH_2Cl_2–MeOH (40:1) as eluent to afford **L3**; yield: 428 mg (50%); white solid; mp 60–61 °C.

IR (KBr): 3210, 3108, 3054, 2975, 2933, 2896, 2811, 1628, 1533, 1502, 1436, 1417, 1352, 1310, 1249, 1143, 1080, 1060, 1014, 936, 827, 739, 715, 661, 605, 552 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.25 (br s, 1 H, NH), 7.72 (s, 1 H, ArH), 7.56 (d, *J* = 4.9 Hz, 1 H, ArH), 7.12 (t, *J* = 4.2 Hz, 1 H, ArH), 3.88 (s, 3 H, OCH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.5, 135.2, 131.0, 129.5, 127.8, 64.4.

MS (ESI+): *m*/*z* = 196 ($[M + Na]^+$).

N-Methoxypicolinamide (L4)
[CAS Reg. No.: 79081-08-6]

To a 100 mL round-bottomed flask equipped with a magnetic stir bar were added picolinic acid (615 mg, 5 mmol), methoxyammonium chloride (625 mg, 7.5 mmol), (dimethylaminopropyl)carbodiimide hydrochloride (1440 mg, 7.5 mmol), 4-dimethylaminopyridine (1830 mg, 15 mmol), and CH_2Cl_2 (50 mL). The reaction mixture was stirred at r.t. overnight. After concentrating the mixture in vacuo, the residue was purified by flash column chromatography on silica gel using CH_2Cl_2–MeOH (50:1) as eluent to afford **L4**; yield: 663 mg (87%); pale yellow solid; mp 35–36 °C.

IR (KBr): 3258, 2980, 2939, 2816, 1676, 1589, 1570, 1487, 1464, 1435, 1285, 1243, 1169, 1149, 1090, 1052, 1037, 998, 942, 891, 817, 751, 701, 621 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 10.44 (s, 1 H, NH), 8.51–8.41 (m, 1 H, ArH), 8.16–8.07 (m, 1 H, ArH), 7.84–7.76 (m, 1 H, ArH), 7.44–7.33 (m, 1 H, ArH), 3.86 (s, 3 H, OCH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.9, 149.0, 148.2, 137.5, 126.7, 122.4, 64.6.

MS (ESI+): *m*/*z* = 153 ($[M + H]^+$).

***N*-(Benzyloxy)-1*H*-pyrrole-2-carboxamide (L5)**
To a 10 mL sealed vial equipped with a magnetic stir bar were added 2-(trichloroacetyl)pyrrole (1070 mg, 5 mmol), benzylhydroxylamine hydrochloride (1200 mg, 7.5 mmol), and Et_3N (2.5 mL). The reaction mixture was stirred in an oil bath preheated to 80 °C for 10 h. After allowing the mixture to cool to r.t., it was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using CH_2Cl_2–MeOH (50:1) as eluent to afford **L5**; yield: 800 mg (74%); pale yellow solid; mp 102–104 °C.

IR (KBr): 3377, 3166, 2978, 1635, 1511, 1450, 1443, 1405, 1325, 1119, 1089, 1044, 1016, 964, 853, 828, 743, 695, 676, 593 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.81 (br s, 1 H, NH), 8.67 (s, 1 H, ArH), 7.45–7.34 (m, 5 H, ArH), 6.98–6.93 (m, 1 H, ArH), 6.68 (s, 1 H, ArH), 6.26–6.19 (m, 1 H, ArH), 4.99 (s, 2 H, OCH_2).

^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6): δ = 160.7, 135.8, 129.2, 128.4, 128.3, 123.1, 122.1, 111.6, 109.3, 78.3.

MS (EI, 70 eV): *m*/*z* (%) = 216 (6, $[M^+]$), 94 (26, $[C_4H_4CO^+]$), 91 (100, $[C_7H_7^+]$).

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.70; H, 5.60; N, 12.95.

Amines 3a–k and 4a–x; General Procedure A (GP A)
To a 10 mL sealed vial equipped with a magnetic stir bar were added $Cu(OAc)_2 \cdot H_2O$ (10 mg, 0.05 mmol), **L1** (7 mg, 0.05 mmol), aryl bromide (1.0 mmol), amine (3.0 mmol), K_3PO_4 (318 mg, 1.5 mmol), and PEG-100 (2.0 g). The reaction mixture was stirred in an oil bath preheated to 90 °C for 12 h. After allowing the mixture to cool to r.t., it was extracted with EtOAc (3 × 25 mL) and the combined organic phases were washed with H_2O (20 mL), brine (70 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to afford the desired product.

4-Methoxy-*N*-phenylaniline (3a)
[CAS Reg. No.: 1208-86-2]

According to GP A, 4-bromoanisole (187 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:20) as eluent to afford **3a**; yield: 155 mg (78%); white solid; mp 105–106 °C.

4-Methyl-*N*-phenylaniline (3b)
[CAS Reg. No.: 620-84-8]

According to GP A, 1-bromo-4-methylbenzene (171 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **3b**; yield: 137 mg (75%); white solid; mp 87–88 °C.

4-Ethyl-*N*-phenylaniline (3c)
[CAS Reg. No.: 32804-22-1]

According to GP A, 1-bromo-4-ethylbenzene (185 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C, 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **3c**; yield: 143 mg (73%); white solid; mp 86–87 °C.

2-Methoxy-*N*-phenylaniline (3d)
[CAS Reg. No.: 1207-92-7]

According to GP A, 2-bromoanisole (87 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **3d**; yield: 141 mg (71%); colorless oil.

3-Methoxy-*N*-phenylaniline (3e)
[CAS Reg. No.: 101-16-6]

According to GP A, 2-bromoanisole (187 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **3e**; yield: 149 mg (75%); colorless oil.

***N*-Phenylbenzo[*d*][1,3]dioxol-5-amine (3f)**
[CAS Reg. No.: 222640-45-1]

According to GP A, 5-bromobenzo[*d*][1,3]dioxole (201 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:20) as eluent to afford **3f**; yield: 153 mg (72%); colorless oil.

Diphenylamine (3g)
[CAS Reg. No.: 122-39-4]

According to GP A, bromobenene (157 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAC–PE (1:40) as eluent to afford **3g**; yield: 120 mg (71%); pale yellow solid.

1-[4-(Phenylamino)phenyl]ethanone (3h)
[CAS Reg. No.: 23600-83-1]

According to GP A, 1-(4-bromophenyl)ethanone (199 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:5) as eluent to afford **3h**; yield: 112 mg (53%); yellow solid; mp 112–114 °C.

4-Fluoro-*N*-phenylaniline (3i)
[CAS Reg. No.: 330-83-6]

According to GP A, 1-bromo-4-fluorobenzene (185 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **3i**; yield: 122 mg (65%); pale yellow solid; mp 36–37 °C.

4-Chloro-*N*-phenylaniline (3j)
[CAS Reg. No.: 1205-71-6]

According to GP A, 1-bromo-4-chlorobenzene (191.5 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **3j**; yield: 128 mg (63%); pale yellow solid; mp 64–65 °C.

***N*-Phenylpyridin-2-amine (3k)**
[CAS Reg. No.: 6631-37-4]

According to GP A, 2-bromopyridine (158 mg, 1.0 mmol) was treated with aniline (279 mg, 3.0 mmol) at 90 for 12 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as eluent to afford **3k**; yield: 120 mg (70%); white solid; mp 108–109 °C.

***N*-Benzyl-4-methoxyaniline (4a)**
[CAS Reg. No.: 17377-95-6]

According to GP A, 4-bromoanisole (187 mg, 1.0 mmol) was treated with benzylamine (321 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4a**; yield: 180 mg (84%); white solid; mp 50–51 °C.

***N*-Benzyl-4-ethylaniline (4b)**
[CAS Reg. No.: 109240-32-6]

According to GP A, 1-bromo-4-ethylbenzene (185 mg, 1.0 mmol) was treated with benzylamine (321 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4b**; yield: 165 mg (78%); colorless oil.

***N*-Benzylaniline (4c)**
[CAS Reg. No.: 103-32-2]

According to GP A, bromobenzene (157 mg, 1.0 mmol) was treated with benzylamine (321 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4c**; yield: 147 mg (80%); pale yellow solid; mp 38–40 °C.

1-[4-(Benzylamino)phenyl]ethanone (4d)
[CAS Reg. No.: 59852-82-3]

According to GP A, 1-(4-bromophenyl)ethanone (199 mg, 1.0 mmol) was treated with benzylamine (321 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:5) as eluent to afford **4d**; yield: 111 mg (49%); yellow solid; mp 88–90 °C.

***N*-Benzyl-4-chloroaniline (4e)**
[CAS Reg. No.: 2948-37-0]

According to GP A, 1-bromo-4-chlorobenzene (191.5 mg, 1.0 mmol) was treated with benzylamine (321 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:20) as eluent to afford **4e**; yield: 151 mg (70%); pale yellow solid; mp 46–47 °C.

***N*-Benzylpyridin-2-amine (4f)**
[CAS Reg. No.: 6935-27-9]

According to GP A, 2-bromopyridine (158 mg, 1.0 mmol) was treated with benzylamine (321 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:10) as eluent to afford **4f**; yield: 120 mg (65%); white solid; mp 96–98 °C.

***N*-Butyl-4-methoxylaniline (4g)**
[CAS Reg. No.: 61829-43-4]

According to GP A, 4-bromoanisole (187 mg, 1.0 mmol) was treated with butan-1-amine (219 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:20) as eluent to afford **4g**; yield: 145 mg (81%); colorless oil.

***N*-Butyl-4-ethylaniline (4h)**
According to GP A, 1-bromo-4-ethylbenzene (185 mg, 1.0 mmol) was treated with butan-1-amine (219 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4h**; yield: 140 mg (79%); colorless oil.

IR (KBr): 3413, 2960, 2929, 2869, 1867, 1618, 1581, 1520, 1479, 1409, 1376, 1317, 1263, 1183, 1143, 1085, 820, 531 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.02 (d, *J* = 8.5 Hz, 2 H, ArH), 6.59–6.53 (m, 2 H, ArH), 3.55 (br s, 1 H, NH), 3.15–3.05 (m, 2 H, CH_2), 2.55 (q, *J* = 7.6 Hz, 2 H, CH_2), 1.66–1.54 (m, 2 H, CH_2), 1.50–1.36 (m, 2 H, CH_2), 1.20 (t, *J* = 7.6 Hz, 3 H, CH_3), 0.96 (t, *J* = 7.3 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.0, 134.4, 129.9, 114.3, 45.4, 33.2, 29.3, 21.7, 17.4, 15.3.

MS (ESI+): *m*/*z* = 178 ($[M + H]^+$).

Anal. Calcd for $C_{12}H_{19}N{\cdot}0.05H_2O$: C, 80.89; H, 10.80; N, 7.86. Found: C, 80.84; H, 10.61; N, 7.82.

***N*-Butylaniline (4i)**
[CAS Reg. No.: 1126-78-9]

According to GP A, bromobenene (157 mg, 1.0 mmol) was treated with butan-1-amine (219 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4i**; yield: 126 mg (85%); colorless oil.

1-[4-(Butylamino)phenyl]ethanone (4j)
[CAS Reg. No.: 99433-24-6]

According to GP A, 1-(4-bromophenyl)ethanone (199 mg, 1.0 mmol) was treated with butan-1-amine (219 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:5) as eluent to afford **4j**; yield: 137 mg (72%); yellow solid; mp 70–71 °C.

***N*-Butyl-4-chloroaniline (4k)**
[CAS Reg. No.: 5441-81-6]

According to GP A, 1-bromo-4-chlorobenzene (191.5 mg, 1.0 mmol) was treated with butan-1-amine (219 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:20) as eluent to afford **4k**; yield: 132 mg (72%); colorless oil.

***N*-Butylpyridin-2-amine (4l)**
[CAS Reg. No.: 76293-30-6]

According to GP A, 2-bromopyridine (158 mg, 1.0 mmol) was treated with butan-1-amine (219 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as eluent to afford **4l**; yield: 127 mg (85%); pale yellow solid; mp 39–40 °C.

***N*-Cyclohexyl-4-methoxyaniline (4m)**
[CAS Reg. No.: 780-02-9]

According to GP A, 4-bromoanisole (187 mg, 1.0 mmol) was treated with cyclohexanamine (297 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel

using EtOAc–PE (1:20) as eluent to afford **4m**; yield: 185 mg (90%); white solid; mp 41–42 °C.

***N*-Cyclohexyl-4-ethylaniline (4n)**
[CAS Reg. No.: 801192-87-0]

According to GP A, 1-bromo-4-ethylbenzene (185 mg, 1.0 mmol) was treated with cyclohexanamine (297 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4n**; yield: 168 mg (83%); colorless oil.

***N*-Cyclohexylaniline (4o)**
[CAS Reg. No.: 1821-36-9]

According to GP A, bromobenene (157 mg, 1.0 mmol) was treated with cyclohexanamine (297 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4o**; yield: 148 mg (85%); colorless oil.

1-[4-(Cyclohexylamino)phenyl]ethanone (4p)
[CAS Reg. No.: 1056627-93-0]

According to GP A, 1-(4-bromophenyl)ethanone (199 mg, 1.0 mmol) was treated with cyclohexanamine (297 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:5) as eluent to afford **4p**; yield: 162 mg (75%); yellow solid; mp 113–114 °C.

***N*-Cyclohexyl-4-chloroaniline (4q)**
[CAS Reg. No.: 56506-61-7]

According to GP A, 1-bromo-4-chlorobenzene (191.5 mg, 1.0 mmol) was treated with cyclohexanamine (297 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:20) as eluent to afford **4q**; yield: 175 mg (84%); white solid; mp 43–44 °C.

***N*-Cyclohexylpyridin-2-amine (4r)**
[CAS Reg. No.: 15513-16-3]

According to GP A, 2-bromopyridine (158 mg, 1.0 mmol) was treated with cyclohexanamine (297 mg, 3.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as eluent to afford **4r**; yield: 128 mg (73%); white solid; 106–107 °C.

4-(4-Methoxyphenyl)morpholine (4s)
[CAS Reg. No.: 27347-14-4]

According to GP A, 4-bromoanisole (187 mg, 1.0 mmol) was treated with morpholine (261 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:10) as eluent to afford **4s**; yield: 143 mg (74%); white solid; mp 73–74 °C.

4-(4-Ethyphenyl)morpholine (4t)
[CAS Reg. No.: 1207717-24-5]

According to GP A, 1-bromo-4-ethylbenzene (185 mg, 1.0 mmol) was treated with morpholine (261 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:10) as eluent to afford **4t**; yield: 135 mg (71%); white solid; mp 58–59 °C.

4-Phenylmorpholine (4u)
[CAS Reg. No.: 92-53-5]

According to GP A, bromobenzene (157 mg, 1.0 mmol) was treated with morpholine (261 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:40) as eluent to afford **4u**; yield: 100 mg (62%); pale yellow solid; mp 51–52 °C.

1-(4-Morpholinophenyl)ethanone (4v)
[CAS Reg. No.: 39910-98-0]

According to GP A, 1-(4-bromophenyl)ethanone (199 mg, 1.0 mmol) was treated with morpholine (261 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:2) as eluent to afford **4v**; yield: 121 mg (59%); white solid; mp 97–98 °C.

4-(4-Chlorophenyl)morpholine (4w)
[CAS Reg. No.: 70291-67-7]

According to GP A, 1-bromo-4-chlorobenzene (191.5 mg, 1.0 mmol) was treated with morpholine (261 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:10) as eluent to afford **4w**; yield: 128 mg (65%); white solid; 74–76 °C.

4-(Pyridin-2-yl)morpholine (4x)
[CAS Reg. No.: 24255-25-2]

According to GP A, 2-bromopyridine (158 mg, 1.0 mmol) was treated with morpholine (261 mg, 3 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2–MeOH (100:1) as eluent to afford **4x**; yield: 100 mg (61%); colorless oil.

Anilines 5a–f; General Procedure B (GP B)
To a 10 mL sealed vial equipped with a magnetic stir bar were added $Cu(OAc)_2 \cdot H_2O$ (10 mg, 0.05 mmol), *N*-methoxy-1*H*-indole-2-carboxamide (9.5 mg, 0.05 mmol), aryl bromide (1.0 mmol), 28% aq ammonia (0.4 mL, 5.0 mmol), K_3PO_4 (318 mg, 1.5 mmol), and PEG-100 (2.0 g). The reaction mixture was stirred in an oil bath preheated to 90 °C for 12 h. After allowing the mixture to cool to r.t., it was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with H_2O (20 mL) and brine (70 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to afford the desired product.

4-Methoxyaniline (5a)
[CAS Reg. No.: 104-94-9]

According to GP B, 4-bromoanisole (187 mg, 1.0 mmol) was treated with 28% aq ammonia (0.4 mL, 5.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:5) as eluent to afford **5a**; yield: 98 mg (80%); white solid; mp 59–60 °C.

***p*-Toluidine (5b)**
[CAS Reg. No.: 106-49-0]

According to GP B, 1-bromo-4-methylbenzene (171 mg, 1.0 mmol) was treated with 28% aq ammonia (0.4 mL, 5.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as eluent to afford **5b**; yield: 66 mg (62%); white solid; mp 43–44 °C.

Aniline (5c)
[CAS Reg. No.: 62-53-3]

According to GP B, bromobenzene (157 mg, 1.0 mmol) was treated with 28% aq ammonia (0.4 mL, 5.0 mmol) 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as eluent to afford **5c**; yield: 75 mg (81%); colorless oil.

1-(4-Aminophenyl)ethanone (5d)
[CAS Reg. No.: 99-92-3]

According to GP B, 1-(4-bromophenyl)ethanone (199 mg, 1.0 mmol) was treated with 28% aq ammonia (0.4 mL, 5.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:2) as eluent to afford **5d**; yield: 109 mg (81%); white solid; mp 106–107 °C.

4-Chloroaniline (5e)
[CAS Reg. No.: 106-47-8]

According to GP B, 1-bromo-4-chlorobenzene (191.5 mg, 1.0 mmol) was treated with 28% aq ammonia (0.4 mL, 5.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:3) as eluent to afford **5e**; yield: 107 mg (84%); yellow solid; mp 70–71 °C.

Pyridin-3-amine (5f)
[CAS Reg. No.: 462-08-8]

According to GP B, 2-bromopyridine (158 mg, 1.0 mmol) was treated with 28% aq ammonia (0.4 mL, 5.0 mmol) at 90 °C for 12 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2–MeOH (20:1) as eluent to afford **5f**; yield: 107 mg (84%); yellow solid; 63–64 °C.

Phenothiazines 6a–e; General Procedure
Method A: To a 10 mL sealed vial equipped with a magnetic stir bar were added $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol), **L1** (14 mg, 0.1 mmol), aniline (1.0 mmol), 2-bromobenzenethiol (227 mg, 1.2 mmol), KOH (224 mg, 4.0 mmol), and PEG-100 (2.0 g). The reaction mixture was stirred in an oil bath preheated to 90 °C for 15 h. After allowing the mixture to cool to r.t., it was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with H_2O (40 mL) and brine (80 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to afford the desired product.

Method B: To a 10 mL sealed vial equipped with a magnetic stir bar were added $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol), **L1** (14 mg, 0.1 mmol), aryl halide (1.0 mmol), 2-aminobenzenethiol (1.2 mmol), KOH (224 mg, 4.0 mmol), and PEG-100 (2.0 g). The reaction mixture was stirred in an oil bath preheated to 90 °C for 15 h. After allowing the mixture to cool to r.t., it was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with H_2O (40 mL) and brine (80 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to afford the desired product.

2-Methyl-10*H*-phenothiazine (6a)
[CAS Reg. No.: 5828-51-3]

According to method A, 2-iodo-5-methylaniline (233 mg, 1.0 mmol) was treated with 2-bromobenzenethiol (227 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6a**; yield: 97 mg (46%); white solid.

According to method B, 2-bromo-1-iodo-4-methylbenzene (297 mg, 1.0 mmol) was treated with 2-aminobenzenethiol (150 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6a**; yield: 157 mg (74%); white solid; mp 186–187 °C.

IR (KBr): 3336, 1592, 1567, 1470, 1431, 1377, 1311, 1281, 1258, 1176, 1151, 1123, 1033, 924, 862, 797, 739, 716, 677, 627, 581, 549, 531, 487, 427 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.47 (s, 1 H, NH), 6.99–6.91 (m, 1 H, ArH), 6.87 (dd, *J* = 7.6, 1.4 Hz, 1 H, ArH), 6.78–6.63 (m, 3 H, ArH), 6.56 (d, *J* = 7.7 Hz, 1 H, ArH), 6.49 (d, *J* = 0.7 Hz, 1 H, ArH), 2.14 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 144.0, 143.8, 138.7, 129.2, 128.0, 127.8, 124.3, 123.4, 118.5, 116.9, 116.2, 114.8, 22.5.

MS (70 eV, EI+): *m*/*z* (%) = 213 (100, $[M^+]$), 180 (80, $[C_{13}H_{10}N^+]$), 167 (32, $[C_{12}H_9N^+]$).

3-Methyl-10*H*-phenothiazine (6b)
[CAS Reg. No.: 3939-47-7]

According to method A, 2-iodo-4-methylaniline (233 mg, 1.0 mmol) was treated with 2-bromobenzenethiol (227 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6b**; yield: 155 mg (73%); white solid; mp 170–172 °C.

IR (KBr): 3337, 2915, 1605, 1577, 1501, 1475, 1430, 1309, 1264, 1245, 1140, 1124, 1033, 925, 885, 807, 738, 715, 685, 645, 569, 547, 527, 499, 423 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.43 (s, 1 H, NH), 7.00–6.83 (m, 2 H, ArH), 6.79–6.53 (m, 5 H, ArH), 2.11 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 143.0, 140.2, 131.3, 128.5, 128.0, 127.1, 126.8, 122.0, 117.0, 116.9, 114.9, 20.6.

MS (70 eV, EI+): *m*/*z* (%) = 213 (100, $[M^+]$), 180 (68, $[C_{13}H_{10}N^+]$).

10*H*-Phenothiazine (6c)
[CAS Reg. No.: 92-84-2]

According to method A, 2-iodoaniline (219 mg, 1.0 mmol) was treated with 2-bromobenzenethiol (227 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6c**; yield: 148 mg (74%); white solid.

According to method B, 1-bromo-2-iodobenzene (283 mg, 1.0 mmol) was treated with 2-aminobenzenethiol (150 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6c**; yield: 127 mg (64%); white solid; mp 183–184 °C.

IR (KBr): 3340, 3051, 1596, 1570, 1472, 1442, 1306, 1282, 1262, 1243, 1153, 1119, 1078, 1033, 924, 884, 858, 847, 737, 715, 685, 656, 552, 531, 493, 426 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 8.61 (br s, 1 H, NH), 7.07–6.90 (m, 4 H, ArH), 6.82–6.66 (m, 4 H, ArH).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 142.6, 128.0, 126.7, 122.2, 116.8, 114.9.

MS (70 eV, EI+): *m*/*z* (%) = 199 (100, $[M^+]$), 167 (38, $[C_{12}H_9N^+]$).

2-Chloro-10*H*-phenothiazine (6d)
[CAS Reg. No.: 92-39-7]

According to method A, 5-chloro-2-iodoaniline (253 mg, 1.0 mmol) was treated with 2-bromobenzenethiol (227 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6d**; yield: 134 mg (58%); white solid.

According to method B, 1-bromo-2-iodobenzene (283 mg, 1.0 mmol) was treated with 2-amino-4-chlorobenzenethiol (192 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6d**; yield: 129 mg (55%); white solid; mp 193–194 °C.

IR (KBr): 3334, 1593, 1567, 1467, 1429, 1369, 1302, 1274, 1241, 1154, 1122, 1094, 1031, 925, 850, 802, 745, 730, 673, 585, 552, 529, 478, 428 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.73 (s, 1 H, NH), 7.04–6.83 (m, 3 H, ArH), 6.80–6.71 (m, 2 H, ArH), 6.70–6.61 (m, 2 H, ArH).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 145.3, 142.9, 133.6, 129.6, 129.2, 128.1, 124.1, 123.0, 117.9, 117.4, 116.5, 115.6.

MS (70 eV, EI+): *m*/*z* (%) = 233 (75, $[M^+]$), 235 (25, $[M^+]$), 198 (100, $[C_{12}H_8NS^+]$).

3-Chloro-10*H*-phenothiazine (6e)
[CAS Reg. No.: 1207-99-4]

According to method A, 4-chloro-2-iodoaniline (253 mg, 1.0 mmol) was treated with 2-bromobenzenethiol (227 mg, 1.2 mmol) at 90 °C for 15 h. The crude product was purified by column chromatography on silica gel using EtOAc–PE (1:50) as eluent to afford **6e**; yield: 132 mg (57%); white solid; mp 198–200 °C.

IR (KBr): 3336, 1594, 1469, 1427, 1375, 1307, 1293, 1272, 1241, 1152, 1124, 1103, 1031, 928, 880, 853, 813, 745, 712, 671, 632, 565, 545, 503, 464, 445 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.70 (br s, 1 H, NH), 7.05–6.92 (m, 3 H, ArH), 6.89 (d, J = 7.5 Hz, 1 H, ArH), 6.74 (t, J = 7.3 Hz, 1 H, ArH), 6.64 (dd, J = 7.9, 4.1 Hz, 2 H, ArH).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 143.0, 142.5, 129.2, 128.6, 127.7, 126.8, 126.4, 123.4, 120.0, 117.0, 116.8, 116.0.

MS (70 eV, EI+): m/z (%) = 233 (100, [M^+]), 235 (33, [M^+]), 198 (78, [$C_{12}H_8NS^+$]).

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