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Palladium-Catalyzed Domino Double *N*-Arylations (Inter- and Intramolecular) of 1,2-Diamino(hetero)arenes with *o*,*o*′-Dihalo(hetero)arenes for the Synthesis of Phenazines and Pyridoquinoxalines

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Keywords: Medicinal chemistry / Nitrogen heterocycles / Domino reactions / Palladium / Arenes / Oxidation

Domino reactions for the synthesis of phenazines have been developed that start from 1,2-diaminoarenes and 1,2-dihaloarenes and proceed through palladium-catalyzed double *N*-arylations (inter- and intramolecular) followed by an in situ oxidation. A variety of functional groups, which include base-sensitive groups, were well tolerated under the optimized reaction conditions to afford phenazines in good to excellent yields. The protocol was extended to the synthesis of pyridoquinoxalines by employing either *o*-phenylenediamines and 2,3-dihalopyridines or 1,2-diaminopyridines and 1,2-dihaloarenes.

Introduction

Natural and synthetic phenazines display a wide spectrum of biological properties that include antibacterial, antitricholonal, antimalerial, and antitumor activities.[1] The mode of action for phenazines is proposed to involve the intercalation into duplex DNA or the generation of toxic anionic radicals that are involved in redox cycling. Fluorescent phenazine derivatives that demonstrate photosensitizing activity in photodynamic therapy (PDT)[2] and bis(triazolyl) phenazine derivatives that exhibit metal-ion sensor properties in aqueous solution[3] have also been synthesized. A majority of the methods to synthesize phenazines involve generating the fused tricyclic skeleton through the construction of the central heterocyclic ring. An early approach, which employs a Wohl–Aue procedure, involves heating aniline and nitrobenzene above 200 °C to yield phenazines in moderate yields along with the formation of a significant amount of byproduct.[4] Methods to prepare phenazine-*N*-oxide and phenazine-*N*,*N*′-dioxide are also known, and upon deoxygenation these compounds afford phenazines in moderate yields.[5] The condensation of *o*-phenylenediamines with *ortho*-benzoquinones, generated in situ from the corresponding catechols, has been an important route that directly leads to phenazines.[6] A widely used approach based on this preparation is followed by an intramolecular reductive or oxidative cyclization of the appropriate *ortho*-substituted diphenylamines in the presence or absence of a metal catalyst. Although reductive cyclizations of *o*-nitro-,[7] *o*,*o*′-dinitro-,[8] and *o*-nitro-*o*′-fluorodiarylamines[9] have been reported to obtain phenazines with limited substitution patterns, an oxidative cyclization was effected on *o*,*o*′-diaminodiarylamines[10] under harsh condition to yield phenazines. The palladium-catalyzed intramolecular *N*-arylation of *o*-amino-*o*′-bromodiarylamines, performed in multiple steps, has also been realized.[11] Recently, phenazines were prepared in good yields under acidic or basic conditions from *o*-nitrosodiphenylamine.[12] Very recently, the palladium[13] or copper-catalyzed[14] homocoupling of 2-halogenoanilines was reported to yield symmetrically substituted phenazines. A general structure–activity relationship analysis is difficult to derive from the literature, as a large number of diverse targets have been used to evaluate biological activity. This is likely because there is not an adequate, concise, general approach to synthesize phenazines.[1]

The palladium-catalyzed C–N bond forming reaction between (hetero)arylamines and (hetero)aryl halides has found wide applications in the synthesis of pharmaceutical drugs, natural products, and compounds that are useful for materials science.[15] However, reports describing tandem C–N bond formation through a reaction between 1,2-diamino(hetero)arenes and 1,2-dihalo(hetero)arenes are scarce.[16] Since the early 1900s, Hinsberg's reaction with 1,2-diaminoarenes and activated 1,2-dihaloheteroarenes (1,2-dichloroquinoxaline or 1,2-dichloropyrazine) at or above 150 °C has been used to prepare dihydrodiazacenes in good yields.[17] Recently, it has been demonstrated that tandem *N*,*N*′-arylations of 1,4-disubstituted 2,3-diaminonaphthalene with activated 1,2-dichloroquinoxaline are not successful under Hinsberg's conditions. Subsequently, Bunz

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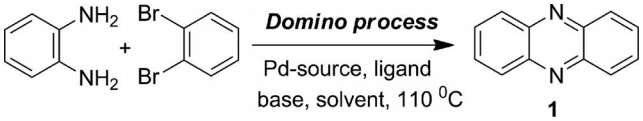
et al. demonstrated that successful coupling could be achieved by a tandem intra- or intermolecular *N*-arylation that employs Pd-ligand catalysts.[18]

Earlier, we demonstrated that a one-pot palladium-catalyzed *N*-arylation of 1,2-dihalopyridines followed by an intramolecular C–H arylation gave various substituted carbolines.[19] Herein, we report a one-pot synthesis of phenazines that employs readily available 1,2-diaminoarenes and unactivated 1,2-dihaloarenes and proceeds through palladium-catalyzed domino inter- and intramolecular *N*-arylations followed by an oxidation. Furthermore, an extension of this protocol is also described to synthesize pyridoquinoxalines by utilizing either *o*-phenylenediamines and 2,3-dihalopyridines or 1,2-diaminopyridines and 1,2-dihaloarenes.

Results and Discussion

Initially, a one-pot domino approach was investigated that involved *o*-phenylenediamine and 1,2-dibromobenzene as the two coupling partners to prepare phenazine. Heating *o*-phenylenediamine and 1,2-dibromobenzene in the presence of 10 mol-% $Pd(OAc)_2$, 20 mol-% PPh_3, and 2.2 equiv. of the strong base NaO*t*Bu or 3.3 equiv. of the weak base Cs_2CO_3 at 110 °C in toluene produced phenazine in only a detectable amount (see Table 1, Entries 1 and 2). Changing the ligand from PPh_3 to PCy_3 (Cy = cyclohexyl) resulted in a significant conversion to afford phenazine (**1**)[7a] in 30% yield (see Table 1, Entry 3). Next, we investigated the effects of a few other ligands commonly used in the *N*-arylation reactions of arylamines (typically 10 mol-% of the ligand was used; see Table 1, Entries 4–8). Among them, 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (S-Phos) and 2,2′-bis(diphenylphospino)-1,1′-binapthyl (BINAP) had comparable effects in the presence of 3.3 equiv. of Cs_2CO_3 to enable the formation of **1** in 89 and 88% yields, respectively. Evidently, when the reaction presented in Entry 8 was carried out for only 4 h, phenazine (**1**) and the *N*-monoarylated product *N*1-(2-bromophenyl)benzene-1,2-diamine [**1(i)**],[20] (see Supporting Information) were isolated in 30 and 45% yield, respectively. Remarkably, the formation of *N*-monoarylated product **1(i)** suggests that the reaction follows a domino reaction pathway. Employing the S-Phos ligand produced similar result in the presence of NaO*t*Bu to give **1** in 85% yield, whereas BINAP produced inferior results and furnished **1** in 51% yield (see Table 1, Entries 9 and 10). Furthermore, the yield of **1** was lower when S-Phos was used in the presence of K_3PO_4 or K_2CO_3 (see Table 1, Entries 11 and 12). Although replacing $Pd(OAc)_2$ with $Pd_2(dba)_3$ (dba = dibenzylideneacetone) was detrimental (see Table 1, Entry 13), the formation of **1** was not observed when $PdCl_2$ was employed in the reaction (see Table 1, Entry 14). A solvent other than toluene had a significant impact on the outcome of the reaction as reflected in Entries 15–17. A lower catalyst loading [5 mol-% $Pd(OAc)_2$ and 5 mol-% of either S-Phos or BINAP] resulted in significantly lower yields of phenazine (**1**) along with the formation of the *N*-monoarylated product in varying yields (see Table 1, Entries 18 and 19). The reduced yield of the phenazine as a result of the lower catalyst loadings may be explained by the oxidation of dihydrophenazine into phenazine, which could lead to the reductive poisoning of some of the palladium catalyst.[18]

Table 1. Optimization study for the synthesis of phenazine (**1**).[a]



Entry	Metal source	Ligand	Base	Solvent	% Yield
1	$Pd(OAc)_2$	PPh_3	NaO*t*Bu	toluene	trace
2	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	toluene	trace
3	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	toluene	30
4	$Pd(OAc)_2$	DPEPhos[b]	Cs_2CO_3	toluene	trace
5	$Pd(OAc)_2$	Xantphos[b]	Cs_2CO_3	toluene	20
6	$Pd(OAc)_2$	DPPF	Cs_2CO_3	toluene	0
7	$Pd(OAc)_2$	S-Phos	Cs_2CO_3	toluene	89
8	$Pd(OAc)_2$	BINAP	Cs_2CO_3	toluene	88
9	$Pd(OAc)_2$	S-Phos	NaO*t*Bu	toluene	85
10	$Pd(OAc)_2$	BINAP	NaO*t*Bu	toluene	51
11	$Pd(OAc)_2$	S-Phos	K_3PO_4	toluene	63
12	$Pd(OAc)_2$	S-Phos	K_2CO_3	toluene	30
13[c]	$Pd_2(dba)_3$	S-Phos	Cs_2CO_3	toluene	65
14	$PdCl_2$	S-Phos	Cs_2CO_3	toluene	0
15	$Pd(OAc)_2$	S-Phos	Cs_2CO_3	dioxane	60
16	$Pd(OAc)_2$	S-Phos	Cs_2CO_3	*o*-Xyl[b]	58
17	$Pd(OAc)_2$	S-Phos	Cs_2CO_3	DMA[b]	40
18[d]	$Pd(OAc)_2$	S-Phos	Cs_2CO_3	toluene	35
19[e]	$Pd(OAc)_2$	BINAP	Cs_2CO_3	toluene	45

[a] Diamine (0.50 mmol), dibromobenzene (0.50 mmol), $Pd(OAc)_2$ (0.05 mmol), ligand (0.05 mmol), base (1.10 or 1.65 mmol), solvent (250 mM), 110 °C, 16 h. [b] DPEPhos = (oxydi-2,1-phenylene)-bis(diphenylphosphine), Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, *o*-Xyl = *o*-xylene, DMA = *N*,*N*-dimethylacetamide. [c] Employed 5 mol-% $Pd_2(dba)_3$. [d] Employed 5 mol-% $Pd(OAc)_2$ and 5 mol-% S-Phos. [e] Used 5 mol-% $Pd(OAc)_2$ and 5 mol-% BINAP.

With the optimized conditions [$Pd(OAc)_2$ (10 mol-%), S-Phos (10 mol-%), Cs_2CO_3 (3.3 equiv.), toluene (250 mM), 110 °C, 16 h] in hand, we next examined the scope of substrates that were commercially available. 4-Methoxy-*o*-phenylenediamine was treated with 1,2-dibromobenzene under the optimized conditions to yield phenazine **2**[11b] in 78% yield (see Table 2, Entry 1).

It is noteworthy that Beifuss et al. published a report based on the synthesis of compound **2** through various methods, wherein compound **2** was best obtained in three steps with an overall 44% yield.[11b] Also, methyl 3,4-diaminobenzoate afforded phenazine **3**[21] in 85% yield, which indicated that the ester group tolerated the mild reaction conditions (see Table 2, Entry 2). However, an electron-deficient *o*-phenylenediamine such as 4-trifluoromethyl-*o*-phenylenediamine underwent a less effective reaction with 1,2-dibromobenzene to afford phenazine **4** in 45% yield (see Table 2, Entry 3). Similarly, *o*-phenylenediamine derivatives were treated with 1,2-dibromo-4,5-(methylenedioxy)benzene under the optimized conditions to obtain phenazines

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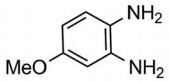
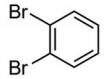
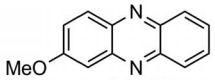
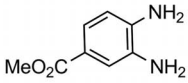
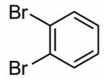
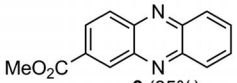
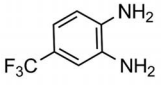
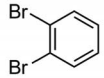
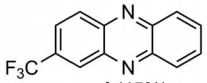
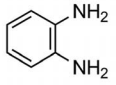
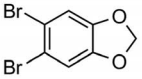
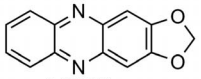
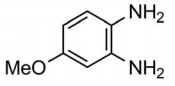
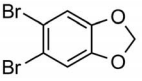
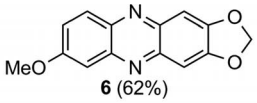
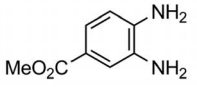
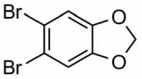
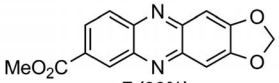
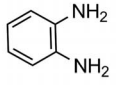
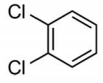
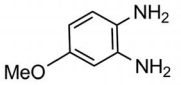
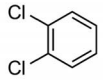
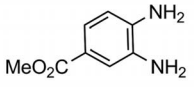
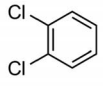
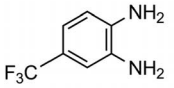
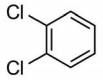
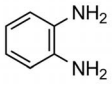
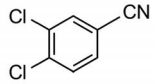
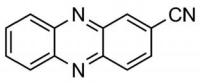
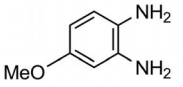
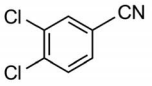
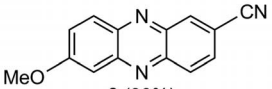
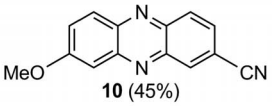
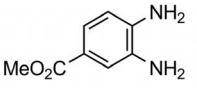
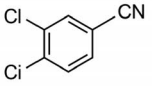
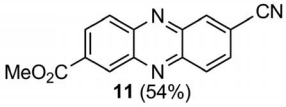
Table 2. Synthesis of various substituted phenazines.[a]

Entry	Diamine	Dihalo arene	Phenazine (%)
1			 **2** (78%)
2			 **3** (85%)
3			 **4** (45%)
4			 **5** (64%)
5			 **6** (62%)
6			 **7** (90%)
7			**1** (44%)
8			**2** (46%)
9			**3** (52%)
10			**4** (24%)
11			 **8** (62%)
12			 **9** (30%) +  **10** (45%)
13			 **11** (54%)

[a] Diamine (0.50 mmol), dibromobenzene (0.50 mmol), $Pd(OAc)_2$ (0.05 mmol), S-Phos (0.05 mmol), Cs_2CO_3 (1.65 mmol), solvent (250 mM), 110 °C, 16 h.

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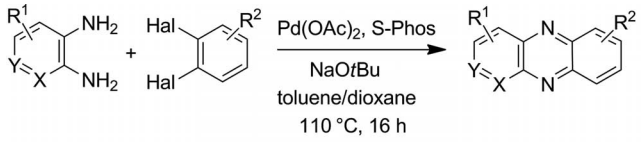
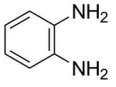
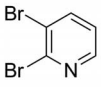
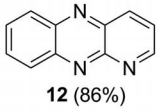
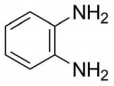
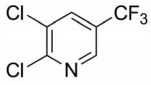
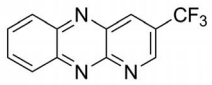
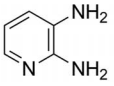
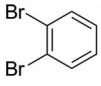
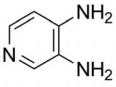
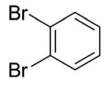
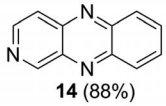
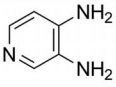
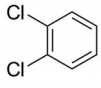
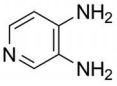
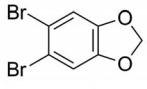
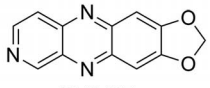
5–**7** in good to excellent yields (see Table 2, Entries 4–6). Gratifyingly, the *o*-phenylenediamines that were treated with 1,2-dichlorobenzene under the optimized conditions also furnished phenazines **1**–**4** in 24–52% yields (see Table 2, Entries 7–10). A similar trend was observed, but with reduced reactivity between the *o*-phenylenediamines and 1,2-dichlorobenzene. Furthermore, *o*-phenylenediamine underwent a reaction with 3,4-dichlorobenzonitrile under the one-pot domino reaction conditions to afford phenazine **8**[22] in 62% yield (see Table 2, Entry 11). Similarly, 4-methoxy-*o*-phenylenediamine gave a separable 3:2 mixture of regioisomeric phenazines **9** and **10** with a combined 75% yield (see Table 2, Entry 12). The reaction of methyl 3,4-diaminobenzoate and 3,4-dichlorobenzonitrile gave a crude product, which upon isolation provided phenazine **11**[22] in 54% yield (see Table 2, Entry 13).

Next, we turned our attention to the development of metal-catalyzed domino reactions that employ either *o*-phenylenediamines and 2,3-dihalopyridines or 1,2-diaminopyridines and 1,2-dihaloarenes for the synthesis of pyridoquinoxalines (see Table 3).[23] Disappointingly, we observed that the treatment of *o*-phenylenediamine with 2,3-dibromopyridine under the optimized conditions afforded pyrido[2,3-*b*]quinoxaline **12**[24] in <10% yield. Previously, we[19] and others[25] realized that palladium-catalyzed *N*-arylation reactions between anilines and 1,2-dihalopyridines could be best effected in the presence of a strong base (NaO*t*Bu). To our delight, *o*-phenylenediamine underwent a reaction with either 2,3-dibromopyridine or 2,3-dichloro-5-trifluoromethylpyridine under modified conditions [$Pd(OAc)_2$ (10 mol-%), S-Phos (10 mol-%), NaO*t*Bu (3.5 equiv.), toluene/dioxane (3:1, 250 mM), 110 °C, 16 h] to afford pyrido[2,3-*b*]quinoxalines **12**[24] and **13** in 86 and 30% yields, respectively (see Table 3, Entries 1 and 2). Subsequently, the reaction between 2,3- or 3,4-diaminopyridine and 1,2-dibromobenzene under the modified conditions gave **12** and pyrido[3,4-*b*]quinoxaline **14** in 52 and 88% yields, respectively (see Table 3, Entries 3 and 4). Pleasingly, when 3,4-diaminopyridine was treated with 1,2-dichlorobenzene, **14** was isolated in 70% yield (see Table 3, Entry 5). The reaction between 3,4-diaminopyridine and 1,2-dibromo-4,5-(methylenedioxy)benzene gave pyrido[3,4-*b*]-quinoxaline **15**, albeit in the low yield of 31% (see Table 3, Entry 6).

Table 3. Synthesis of pyridoquinoxalines.[a]



Entry	Diaminoarenes	Dihaloarenes	Pyridoquinoxalines (%)
1			 **12** (86%)
2			 **13** (30%)
3			**12** (52%)
4			 **14** (88%)
5			**14** (70%)
6			 **15** (31%)

[a] $Pd(OAc)_2$ (10 mol-%), S-Phos (10 mol-%), NaO*t*Bu (3.5 equiv.), toluene/dioxane (3:1, 250 mM), 110 °C, 16 h.

Conclusions

In summary, we have developed domino reactions for synthesis for phenazines by employing palladium-catalyzed double *N*-arylation reactions (inter- and intramolecular) and starting from readily available 1,2-diaminoarenes and 1,2-dihaloarenes. The protocol was extended to the synthesis of pyridoquinoxalines by utilizing *o*-phenylenediamines and 2,3-dihalopyridines or 1,2-diaminopyridines and 1,2-dihaloarenes. A variety of functional groups, which included base-sensitive groups, were tolerated under the optimized conditions to afford phenazines or pyridoqunioxalines in good to excellent yields. In so doing, we developed general metal-catalyzed domino inter- and intramolecular *N*-arylations of 1,2-diamino(hetero)arenes with 1,2-dihalo(hetero)arenes, which were largely unexplored previously. The present method may allow easy access to various substituted phenazines and pyridoquinoxalines for a general structure–activity relationship study.

Experimental Section

General Methods: All reagents and solvents were purchased from commercial sources and used as received. All of the 1,2-diamino(hetero)arenes and 1,2-dihalo(hetero)arenes were purchased from commercial vendors. All palladium-catalyzed domino reactions were degassed and performed in screw-capped vials under argon. The ^1H and ^{13}C NMR spectroscopic data were recorded with a 400 MHz spectrometer and are reported in δ units. The samples were dissolved in $CDCl_3$, and the coupling constants (*J* values) are reported in Hz. Column chromatography was performed on silica gel (100–200 or 230–400 mesh). High resolution mass spectra (HRMS) were obtained with a Bruker-Maxis. All melting points were recorded with a melting point apparatus that was equipped with a calibrated thermometer. All new compounds were characterized by using melting point (for solids), ^1H and ^{13}C NMR, IR, and HRMS data.

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General Procedure for the Synthesis of Phenazines: In a screw-capped vial that was equipped with a rubber septum, a mixture of the *o*-phenylenediamine (0.5 mmol), the 1,2-dibromobenzene (0.5 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), S-Phos (20.5 mg, 0.05 mmol), and Cs_2CO_3 (537 mg, 1.65 mmol) in toluene (2 mL) was purged with argon for approximately 10 min and then heated at 110 °C for 16 h under argon. The reaction mixture was cooled to room temperature and then diluted with an excess amount of ethyl acetate. The obtained suspension was filtered through a Celite bed, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1 to 3:2) to give the phenazine.

***N*1-(2-Bromophenyl)benzene-1,2-diamine [1(i)]:**[20] Pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (dd, J = 7.9, 1.3 Hz, 1 H), 7.10 (m, 3 H), 6.84 (dd, J = 7.8, 1.2 Hz, 1 H), 6.79 (dt, J = 7.5, 1.3 Hz, 1 H), 6.67 (dt, J = 7.8, 1.4 Hz, 1 H), 6.58 (dd, J = 8.1, 1.4 Hz, 1 H), 5.73 (s, 1 H), 3.83 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.1, 143.0, 132.5, 128.3, 127.1, 127.0, 126.6, 119.5, 119.0, 116.0, 114.2, 110.2 ppm. HRMS: calcd. for $C_{12}H_{12}BrN_2$ [M + H]$^+$ 263.0184; found 263.0180. IR (Nujol): $\tilde{\nu}$ = 3456, 3375, 1275, 1260, 764, 749 cm^{-1}.

2-Methoxyphenazine (2):[11b] Yellow solid; m.p. 123–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, J = 8.4 Hz, 1 H), 8.17 (d, J = 9.5 Hz, 1 H), 8.10 (d, J = 9.5 Hz, 1 H), 7.74–7.84 (m, 2 H), 7.51 (dd, J = 9.5, 2.7 Hz, 1 H), 7.41 (d, J = 2.7 Hz, 1 H), 4.02 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3, 145.0, 143.3, 141.9, 140.7, 130.6, 130.4, 129.6, 129.0, 128.8, 126.4, 104.4, 55.9 ppm. HRMS: calcd. for $C_{13}H_{11}N_2O$ [M + H]$^+$ 211.0871; found 211.0871.

Methyl Phenazine-2-carboxylate (3):[21] Dark brown solid; m.p. 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.03 (d, J = 1.6 Hz, 1 H), 8.42 (dd, J = 9.0, 1.6 Hz, 1 H), 8.27–8.32 (m, 3 H), 7.88–7.94 (m, 2 H), 4.07 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2, 144.7, 144.3, 144.1, 142.5, 133.0, 131.7, 131.6, 131.0, 130.0, 129.9, 129.7, 129.3, 52.7 ppm. HRMS: calcd. for $C_{14}H_{11}N_2O_2$ [M + H]$^+$ 239.0821; found 239.0815. IR (KBr): $\tilde{\nu}$ = 1725, 1617, 1275, 1260, 764, 749 cm^{-1}.

2-(Trifluoromethyl)phenazine (4): Pale yellow solid; m.p. 170–172 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (s, 1 H), 8.39 (d, J = 9.1 Hz, 1 H), 8.27–8.30 (m, 2 H), 7.98 (dd, J = 9.1, 1.9 Hz, 1 H), 7.90–7.96 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5, 144.2, 143.7, 142.0, 132, 131.7, 131.6, 131.3, 131.2, 129.9, 129.8, 128.1, 128.0, 125.5, 124.9 (q, J = 275 Hz) ppm. HRMS: calcd. for $C_{13}H_8F_3N_2$ [M + H]$^+$ 249.0640; found 249.0631.

[1,3]Dioxolo[4,5-*b*]phenazine (5): Pale brown solid; m.p. 170–171 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (dd, J = 10, 2.6 Hz, 2 H), 7.75 (dd, J = 9.32, 2.6 Hz, 2 H), 7.39 (s, 2 H), 6.22 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.2, 142.8, 141.6, 129.2, 128.8, 103.2, 102.6 ppm. HRMS: calcd. for $C_{13}H_9N_2O_2$ [M + H]$^+$ 225.0664; found 225.0662.

7-Methoxy-[1,3]dioxolo[4,5-*b*]phenazine (6): Pale yellow solid; m.p. 252–254 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 9.3 Hz, 1 H), 7.41 (dd, J = 9.3, 2.7 Hz, 1 H), 7.33–7.36 (m, 3 H), 6.19 (s, 2 H), 3.99 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 152.1, 151.0, 143.1, 142.6, 140.8, 138.5, 129.8, 124.2, 104.6, 103.4, 102.9, 102.4, 55.7 ppm. HRMS: calcd. for $C_{14}H_{11}N_2O_3$ [M + H]$^+$ 255.0770; found 255.0760.

Methyl [1,3]Dioxolo[4,5-*b*]phenazine-7-carboxylate (7): Brown solid; m.p. 239–241 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (d, J = 1.5 Hz, 1 H), 8.31 (dd, J = 8.9, 1.7 Hz, 1 H), 8.16 (d, J = 4.7 Hz, 1 H), 7.41 (s, 1 H), 7.40 (s, 1 H), 6.26 (s, 2 H), 4.03 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 153.3, 152.7, 144.1,143.7, 143.2, 140.6, 132.0, 130.4, 129.1, 128.3, 103.3, 103.1, 102.9, 52.6 ppm. HRMS: calcd. for $C_{15}H_{11}N_2O_4$ [M + H]$^+$ 283.0719; found 283.0710. IR (KBr): $\tilde{\nu}$ = 2318, 1725, 1635, 1446, 1275, 1260, 1082, 764, 749 cm^{-1}.

Phenazine-2-carbonitrile (8):[22] Yellow solid; m.p. 212–214 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.67 (d, J = 1.3 Hz, 1 H), 8.34 (d, J = 8.9 Hz, 1 H), 8.25–8.29 (m, 2 H); 7.90–7.97 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.6, 144.4, 143.8, 141.8, 136.6, 132.4, 131.8, 131.5, 130.0, 129.8, 129.6, 118.0, 113.8 ppm. HRMS: calcd. for $C_{13}H_8N_3$ [M + H]$^+$ 206.0718; found 206.0709. IR (KBr): $\tilde{\nu}$ = 1635, 1446, 1275, 1260, 1083, 1020, 764, 750 cm^{-1}.

7-Methoxyphenazine-2-carbonitrile (9): Yellow solid; m.p. 190–194 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (d, J = 1.2 Hz, 1 H), 8.31 (d, J = 8.8 Hz, 1 H), 8.12 (d, J = 9.5 Hz, 1 H), 7.86 (dd, J = 8.8, 1.6 Hz, 1 H), 7.61 (dd, J = 9.5, 2.7 Hz, 1 H), 7.41 (d, J = 2.6 Hz, 1 H), 4.07 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3, 146.2, 142.3, 142.2, 141.8, 135.6, 131.4, 130.8, 128.7, 128.4, 118.2, 113.6, 104.4, 56.1 ppm. HRMS: calcd. for $C_{14}H_{10}N_3O$ [M + H]$^+$ 236.0824; found 236.0818.

8-Methoxyphenazine-2-carbonitrile (10): Yellow solid; m.p. 251–253 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 1.2 Hz, 1 H), 8.26 (d, J = 8.9 Hz, 1 H), 8.13 (d, J = 9.5 Hz, 1 H), 7.91 (dd, J = 8.9, 1.76 Hz, 1 H), 7.60 (dd, J = 9.5, 2.7 Hz, 1 H), 7.42 (d, J = 2.6 Hz, 1 H), 4.07 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8, 146.5, 143.9, 142.0, 140.3, 136.5, 131.1, 130.6, 129.9, 128.1, 118.3, 112.1, 104.3, 56.1 ppm. HRMS: calcd. for $C_{14}H_{10}N_3O$ [M + H]$^+$ 236.0824; found 236.0812.

Methyl 7-Cyanophenazine-2-carboxylate (11):[22] Yellow solid; m.p. 242–245 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.03 (s, 1 H), 8.72 (d, J = 9.1 Hz, 1 H), 8.48 (d, J = 8.8 Hz, 1 H), 8.35–8.42 (m, 2 H), 7.98 (d, J = 8.8 Hz, 1 H), 4.08 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.5, 143.8, 142.7, 136.7, 133.3, 133.1, 132.9, 131.8, 131.6, 131.1, 130.7, 130.6, 130.3, 130.1, 52.9 ppm. HRMS: calcd. for $C_{15}H_{10}N_3O_2$ [M + H]$^+$ 264.0773; found 264.0763. IR (KBr): $\tilde{\nu}$ = 1725, 1621, 1446, 1275, 1260, 1083, 1020, 764, 750 cm^{-1}.

Pyrido[2,3-*b*]quinoxaline (12):[24] Dark brown solid; m.p. 145–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.37 (dd, J = 3.8, 1.9 Hz, 1 H), 8.62 (dd, J = 8.6, 1.9 Hz, 1 H), 8.39 (dd, J = 6.6, 3.4 Hz, 1 H), 8.29 (dd, J = 6.6, 3.4 Hz, 1 H), 7.91–7.95 (m, 2 H), 7.79 (dd, J = 8.6, 3.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.5, 149.5, 145.0, 144.2, 139.1, 138.5, 131.6, 131.4, 130.3, 129.4, 125.5 ppm. HRMS: calcd. for $C_{11}H_8N_3$ [M + H]$^+$ 182.0718; found 182.0718.

3-(Trifluoromethyl)pyrido[2,3-*b*]quinoxaline (13): Yellow solid; m.p. 115–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.52 (d, J = 2.4 Hz, 1 H), 8.93 (d, J = 1.2 Hz, 1 H), 8.31–8.44 (m, 2 H), 7.99–8.04 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.5, 150.0, 146.0, 145.0, 137.0, 136.9, 136.8, 133.0, 132.4, 130.4, 129.7, 128.9, 127.6, 127.5, 127.3, 126.3, 124.1 (q, J = 275 Hz), 121.4, 119.5, 117.4 ppm. HRMS: calcd. for $C_{12}H_7F_3N_3$ [M + H]$^+$ 250.0592; found 250.0589.

Pyrido[3,4-*b*]quinoxaline (14): Yellow solid; m.p. 171–173 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.81 (s, 1 H), 8.85 (d, J = 6.1 Hz, 1 H), 8.35 (d, J = 8.5 Hz, 1 H), 8.29 (d, J = 8.0 Hz, 1 H), 8.08 (d, J = 6.1 Hz, 1 H), 7.92–8.01 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 146.2, 145.6, 144.5, 144.3, 138.1, 132.9, 131.4, 130.5, 129.7, 121.1 ppm. HRMS: calcd. for $C_{11}H_8N_3$ [M + H]$^+$ 182.0718; found 182.0707.

[1,3]Dioxolo[4,5-*g*]pyrido[3,4-*b*]quinoxaline (15): Tan solid; m.p. 287–290 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.63 (s, 1 H), 8.76

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(d, J = 6.0 Hz, 1 H), 7.94 (d, J = 6.0 Hz, 1 H), 7.45 (s, 1 H), 7.41 (s, 1 H), 6.29 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 145.2, 136.6, 120.6, 103.6, 103.1, 103.0 ppm. HRMS: calcd. for $C_{12}H_8N_3O_2$ $[M + H]^+$ 226.0617; found 226.0608.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra for all new compounds are provided.

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