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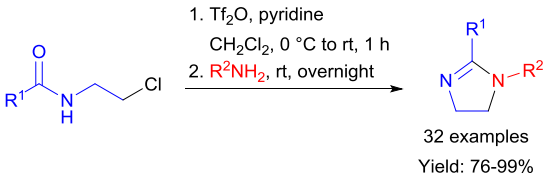

One-pot triflic anhydride-mediated synthesis of 1,2-disubstituted 2-imidazolines from *N*-(2-haloethyl)amides and amines

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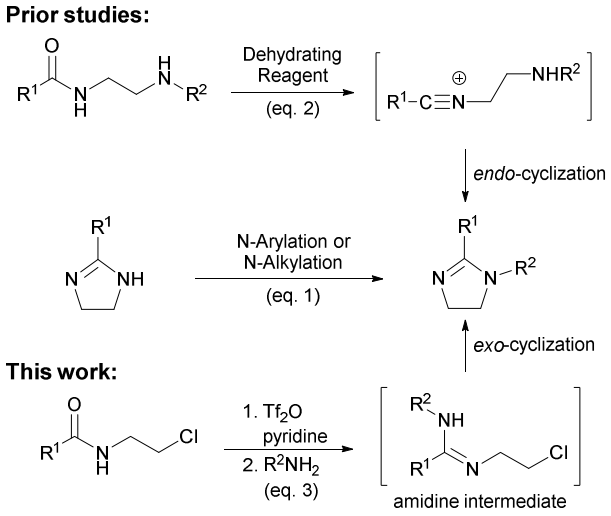
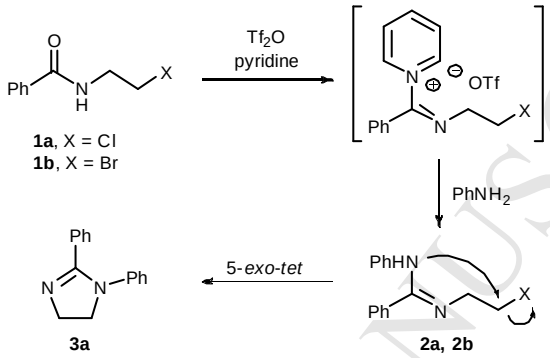
2-Imidazolines are valuable compounds in medicinal chemistry due to their array of pharmacological activities.[1] Correspondingly, interest in this scaffold has resulted in numerous methods for its preparation.[2] The synthesis of 1,2-disubstituted 2-imidazolines in particular commonly involves initial synthesis of the core 2-imidazoline scaffold followed by N-H functionalization through treatment with activated alkylating reagents or via metal-mediated coupling reactions with aryl halides (e.g. eq. 1).[3] Alternatively, 1,2-disubstituted 2-imidazolines may be constructed through intramolecular *endo*-cyclization of *N*-(2-aminoethyl)amides, wherein the tethered amino groups are pre-functionalized with carbon substituents (eq. 2).[4] Reactions of this type typically rely on the use of phosphorus dehydrating reagents such as trimethylsilyl polyphosphate (PPSE)[5] and the Hendrickson reagent,[6] and these reactions may be promoted by microwave heating.[7] A complementary yet less frequently encountered strategy for 1,2-disubstituted 2-imidazoline formation under milder conditions involves intramolecular *exo*-cyclization by a nucleophilic amidine (e.g. eq. 3).[8] One major advantage of performing the *exo*-cyclization over the abovementioned *endo*-cyclization is that the substituted amino group does not need to be incorporated prior to conversion of the amide functionality. Therefore, the *exo*-cyclization strategy presents an opportunity to access the desired 1,2-disubstituted 2-imidazoline scaffold through reduced synthetic effort.



The amidine moiety is a basic functionality that is generated through a variety of methods, including dehydration of amides followed by introduction of an amine. Common reagents for amidine synthesis via amide dehydration include $SOCl_2$, PCl_5, arylsulfonyl chlorides, and trifluoromethanesulfonic anhydride (Tf_2O).[9] Among these, Tf_2O has emerged as a stalwart reagent[10] for the preparation of amidines, as its use results in the generation of nonreactive triflate ions which are compatible with amines introduced subsequent to dehydration. Thus, isolation of the dehydration intermediates or removal of generated acids, as is necessary when using $SOCl_2$ or PCl_5, is not required, making Tf_2O a suitable reagent for use in one-pot multicomponent reactions. Consequently, Tf_2O has been innovatively used in many recent syntheses of amidine-containing molecules[11] including imidazolinium salts.[12] Herein, we report an operationally simple one-pot synthesis of 1,2-disubstituted 2-imidazolines via a Tf_2O-mediated reaction of *N*-(2-haloethyl)amides and primary amines.

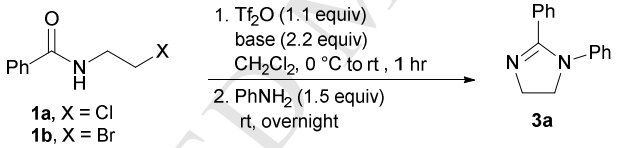
We initially envisioned the synthesis of 1,2-disubstituted 2-imidazolines to occur via the intramolecular 5-*exo*-*tet* cyclization of a halogen-tethered amidine. As such, the synthesis of haloamidine **2** was targeted, which we planned to generate from *N*-(2-haloethyl)amide **1** (Scheme 1). Chloroamide **1a** was synthesized by benzoylation of commercially available 2-chloroethylamine·HCl. Successive treatment of **1a** with Tf_2O and pyridine followed by aniline rapidly resulted in the generation of **2a** (as monitored by TLC). To our delight, subsequent intramolecular cyclization then proceeded in the same reaction flask to provide the desired 2-imidazoline **3a** in 94% yield (table 1, condition 1). The reaction yield was increased to 98% when performed on a multigram scale (table 1, condition 2). A similar yield of **3a** was obtained when analogous bromoamide **1b** was prepared and used in the reaction (table 1, condition 3). Other pyridine bases were screened in the reaction, which resulted in reduced product yields (table 1,

conditions 4-6). The Hendrickson reagent, also called the "POP" reagent, is generated from Tf_2O and Ph_3PO and has been previously used for the synthesis of 2-imidazolines bearing electron poor nitrogen substituents (e.g. tosyl). Use of the Hendrickson reagent failed to provide good yields of **3a** (condition 7), which is consistent with reports of the reagent working poorly in the presence of electron rich amines.[6g] These initial results led us to pursue the use of *N*-(2-chloroethyl)amides for the syntheses of additional 2-imidazolines under optimized reaction parameters (condition 1).



Scheme 1. One-pot Synthesis of 2-Imidazolines.

Table 1. Optimization of Reaction Conditions



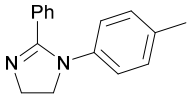
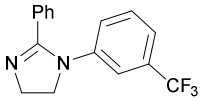
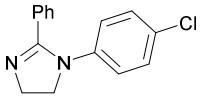
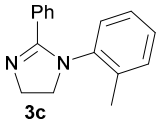
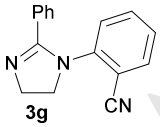
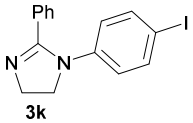
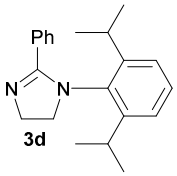
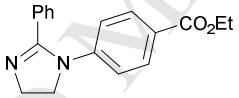
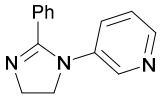
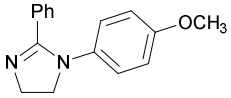
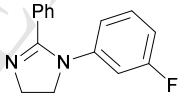
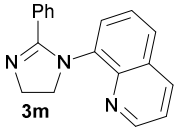
conditions[a]	amide	base	yield (%)[b]
1	1a	pyridine	94
2[c]	1a	pyridine	98
3	1b	pyridine	97
4	1a	2-chloropyridine	72
5	1a	2-fluoropyridine	39
6	1a	4-(dimethylamino)pyridine	0
7[d]	1a	pyridine	trace

[a]Reaction conditions: amide **1a** or **1b** (2 mmol), base (4.4 mmol), Tf_2O (2.2 mmol), CH_2Cl_2 (6 mL), 0 °C to rt, then $PhNH_2$ (3 mmol), rt, overnight. [b]Yield of isolated product. [c]Reaction performed on 10 mmol scale. [d]Reaction conditions: Tf_2O (1 mmol), Ph_3PO (2 mmol), CH_2Cl_2, 0 °C, 30 min, then **1a** (0.8 mmol), pyridine (1 mmol), rt, 1 hr, then $PhNH_2$, rt, overnight.

Exploration of the reaction scope initiated with the synthesis of 1,2-diaryl 2-imidazolines, which were prepared through the introduction of a variety of commercially available aryl amines. Treatment of **1a** with Tf_2O and pyridine followed by exposure to an appropriate aniline derivative led to the formation of corresponding 2-phenyl-2-imidazolines in high yields (Table 2). Alkyl-substituted anilines were readily incorporated into 2-

imidazolines (entries 1-3), including sterically bulky diisopropylaniline (entry 3). Anilines decorated with electron donating (entry 4) and electron withdrawing substituents (entries 5-7) were readily introduced in high yields. 2-Imidazolines comprising halogenated aniline units were also successfully prepared in high yields (entries 8-10). Finally, the reaction allowed for the introduction of heteroaromatic substituents, as demonstrated through the use of 3-aminopyridine (entry 11) and 8-aminoquinoline (entry 12).

Table 2. Reaction Scope varying *N*-Aryl Substituents through Addition of Aryl Amines

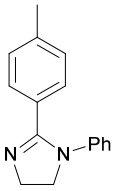
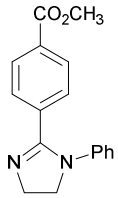
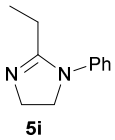
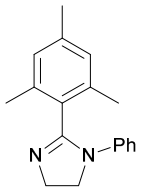
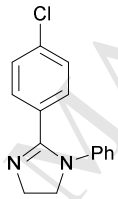
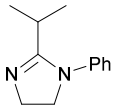
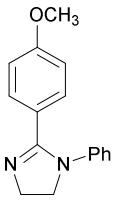
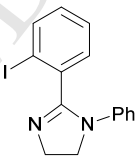
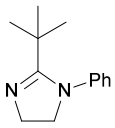
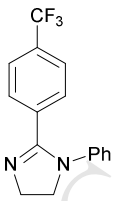
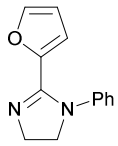
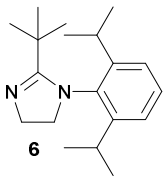
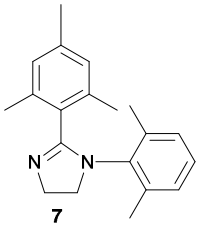
entry	2-imidazoline	yield (%)[b]	entry	2-imidazoline	yield (%)[b]	entry	2-imidazoline	yield (%)[b]
1	 **3b**	80	5	 **3f**	95	9	 **3j**	93
2	 **3c**	88	6	 **3g**	99	10	 **3k**	94
3	 **3d**	90	7	 **3h**	97	11	 **3l**	89
4	 **3e**	83	8	 **3i**	88	12	 **3m**	88

[a]Conditions: **1a** (1.0 equiv), pyridine (2.2 equiv), Tf_2O (1.1 equiv), CH_2Cl_2, 0 °C to rt, 1 hr, then aryl amine (1.5 equiv), rt, overnight. [b]Yield of isolated product.

The reaction also proved useful for the synthesis of 2-imidazolines bearing diverse C2 substituents. 2-Imidazolines of this type were synthesized from corresponding *N*-(2-chloroethyl)amides **4a-k**, which were readily prepared from 2-chloroethylamine·HCl through treatment with an appropriate acid chloride under basic conditions or via DIC coupling with an appropriate carboxylic acid. The amides were submitted to ring formation conditions with aniline as the nucleophilic amine to generate the corresponding *N*-phenyl-2-imidazolines in moderate to high yields (Table 3). Electron rich benzamides were transformed into the corresponding 2-imidazolines in excellent yields (entries 1-3). Electron withdrawing C2 substituents were tolerated in the reaction, albeit 2-imidazolines were

formed in slightly lower yields (entries 4-5). Haloarene-substituted and heteroatom-substituted 2-imidazolines were also prepared in moderate to good yields (entries 6-7 and 8, respectively). Alkanamides were efficiently transformed into C2-alkyl substituted 2-imidazolines (entries 9-11) with slight drops in reaction yield being observed with increasing alkyl branching. Lastly, the ability to incorporate multiple bulky substituents was explored through the synthesis of compounds **6** and **7**, which were afforded in good to high yields.

Table 3. Reaction Scope varying the C2-Substituent in Reaction with Aniline

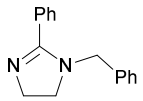
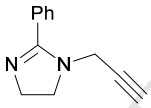
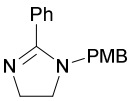
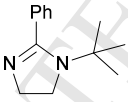
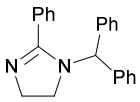
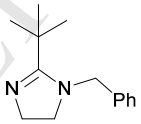
entry	2-imidazoline	yield (%)[b]	entry	2-imidazoline	yield (%)[b]	entry	2-imidazoline	yield (%)[b]
1	 **5a**	98	5	 **5e**	81	9	 **5i**	99
2	 **5b**	96	6	 **5f**	83	10	 **5j**	98
3	 **5c**	94	7	 **5g**	77	11	 **5k**	96
4	 **5d**	80	8	 **5h**	78	12[c]	 **6**	96
						13[d]	 **7**	86

[a]Conditions: *N*-(2-chloroethyl)amide (1.0 equiv), pyridine (2.2 equiv), Tf_2O (1.1 equiv), CH_2Cl_2, 0 °C to rt, 1 hr, then aniline (1.5 equiv), rt, overnight. [b]Yield of isolated product. [c]2,6-Diisopropylaniline used instead of aniline. [d]2,6-Dimethylaniline used instead of aniline.

The synthesis of *N*-alkyl-substituted 2-imidazolines was also explored using our protocol. Dehydration of amide **1a** followed by introduction of alkyl amines resulted in the generation of *N*-alkyl-2-imidazolines in good yields (Table 4). In general, *N*-alkyl-2-imidazolines were prepared in reduced yields compared to *N*-aryl-2-

imidazolines. Benzylamine and substituted benzylamines were readily introduced without issue (entries 1-3). The benzyl substituents represent handles that may be readily removed. Similarly, the installation of propargylamine was tolerated (entry 4). However, no 2-imidazoline product was obtained when *tert*-butyl amine was used in the reaction (entry 5). This result was surprising, especially since diphenylmethanamine was so readily incorporated into the 2-imidazoline scaffold (entry 3). We reasoned that the *tert*-butyl amine was too bulky to approach the reactive imidoyl intermediate generated from dehydration of the amide. Previous studies have demonstrated that dehydration of amides with Tf_2O and less basic 2-fluoropyridine leads to the generation of nitrilium ions.[13] We postulated that a nitrilium ion would be better positioned to accept the bulky nucleophile during 2-imidazoline formation. Indeed, the use of 2-fluoropyridine instead of pyridine resulted in the synthesis of **8e** in 25% yield (data not shown). The yield was further increased to 79% by using 2-fluoropyridine and increasing the temperature of the reaction (reflux, entry 6). Lastly, 2-imidazoline **9** was prepared from the corresponding alkanamide to demonstrate the ability to incorporate alkyl substituents at both the N1 and C2 positions (entry 7).

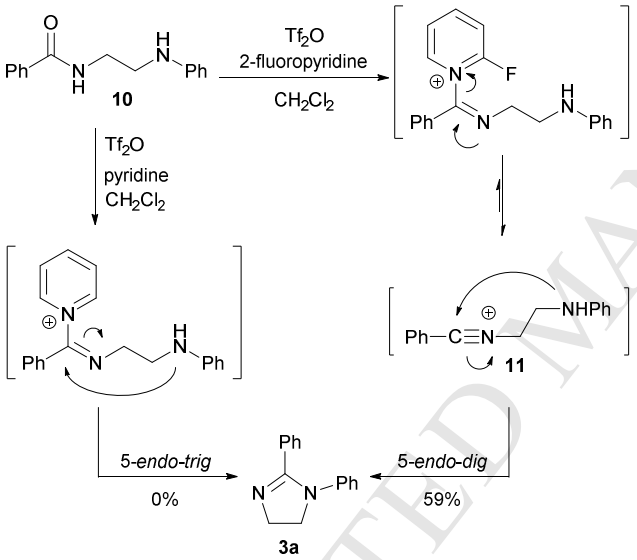
Table 4. Scope of *N*-Alkyl 2-Imidazoline Synthesis

entry	2-imidazoline	yield (%)[b]	entry	2-imidazoline	yield (%)[b]
1	 **8a**	76	4	 **8d**	77
2	 **8b**	77	5	 **8e**	0
			6[c]		79
3	 **8c**	81	7[d]	 **9**	97

[a]Conditions: **1a** (1.0 equiv), pyridine (2.2 equiv), Tf_2O (1.1 equiv), CH_2Cl_2, 0 °C to rt, 1 hr, then amine (1.5 equiv), rt, overnight. [b]Yield of isolated product. [c]Conditions: **1a** (1.0 equiv), 2-fluoropyridine (2.2 equiv), Tf_2O (1.1 equiv), CH_2Cl_2, 0 °C to rt, 1 hr, then $^tBuNH_2$ (1.5 equiv), reflux, overnight. [d]*N*-(2-chloroethyl)-2,2-dimethylpropanamide used as amide.

The reaction is believed to proceed through a haloamidine intermediate (e.g. **2**), which would undergo a 5-*exo*-*tet* cyclization to furnish the 2-imidazoline product (Scheme 1). However, as many known 2-imidazaoline syntheses proceed via intramolecular attack by an amine through an *endo*-cyclization process (e.g. eq. 2), we sought to determine whether such a cyclization was possible under our reaction conditions (Scheme 2). To test the

plausible 5-*endo-trig* cyclization, amino amide **10** was prepared[4d] and treated with Tf_2O and pyridine. The reaction produced no 2-imidazoline product after stirring at room temperature overnight, indicating that our product yields are primarily representative of reactions proceeding via 5-*exo-tet* cyclization. While the 5-*endo-trig* cyclization was unsuccessful, we anticipated that a related *5-endo-dig* cyclization would afford the desired 2-imidazoline product. Thus, compound **10** was submitted to similar reaction conditions employed for the synthesis of **8e**, wherein 2-fluoropyridine was used as a substitute for pyridine, and the reaction provided **3a** in 59% yield. The formation of 2-imidazoline product after the switch from pyridine to 2-fluoropyridine likely resulted from of the reaction proceeding through a nitrilium intermediate (**11**), which allows for a favorable 5-*endo-dig* cyclization.



Scheme 2. 2-Imidazoline Formation via *endo* Cyclization.

In conclusion, we report here the efficient synthesis of 1,2-disubstituted 2-imidazolines via a one-pot two-step reaction of halogen-tethered amides with Tf_2O and pyridine followed by addition of a primary amine. The reaction is tolerant of a variety of functional groups and provides diverse 1,2-disubstituted 2-imidazolines in high yields.

Experimental

General

Reactions were carried out in flame-dried glassware under nitrogen atmosphere. All reactions were magnetically stirred and monitored by TLC on EMD Millipore silica gel $60F_{254}$ pre-coated glass plates using either UV light (254 nm) or basic aqueous $KMnO_4$ stain to visualize the compounds. Column chromatography was carried out on

SiliaFlash P60 (230 – 400 mesh) silica gel supplied by SiliCycle. Infrared spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer. Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectra were recorded at the Max T. Rogers NMR facility of Michigan State University on a Varian Inova-500 spectrometer and an Agilent DDR2 500 MHz spectrometer and at the Lumigen Instrument Center of Wayne State University on a Bruker 700 MHz spectometer. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The residual solvent peak was used as a reference value.[14] High resolution mass spectra were recorded at the Lumigen Instrument Center of Wayne State University on a Waters LCT Premium XE spectrometer. Melting points were obtained using a Mel-Temp capillary melting point apparatus and are uncorrected. CH_2Cl_2 was distilled under N_2 from CaH_2; all other solvents were used without additional purification. All other chemicals, unless otherwise noted, were purchased from commercial vendors and were used without additional purification.

General procedure for *N*-(2-haloethyl)amide synthesis. To a mixture of either 2-chloroethylamine·HCl or 2-bromoethylamine·HBr and TEA in anhydrous CH_2Cl_2, cooled to 0 °C in an ice bath, was added dropwise an appropriate acid chloride or acid anhydride followed by 4-DMAP (for the indicted compounds). The ice bath was removed and the reaction stirred under N_2 atmosphere until complete, as determined by TLC. The reaction was washed successively with 1 M HCl, saturated $NaHCO_3$, and brine before being dried (Na_2SO_4) and concentrated. The crude product was then purified either by crystallization or silica gel chromatography.

***N*-(2-chloroethyl)benzamide (1a)** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (3.480 g, 30.0 mmol), TEA (4.19 mL, 30.0 mmol), benzoyl chloride (4.18 mL, 36.0 mmol) and CH_2Cl_2 (150 mL). The reaction stirred for 4 h and was washed and dried as described previously. The filtrate was concentrated and purified via crystallization from EtOAc and hexanes to afford 5.070 g (92% yield) of the title compound as a white solid (m.p. = 100 - 104 °C). The NMR spectral data[15,16] and melting point data (lit. m.p. = 105 - 106 °C)[17] are consistent with those reported in the literature.

***N*-(2-bromoethyl)benzamide (1b)** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-bromoethylamine HBr (4.099 g, 20.0 mmol), TEA (5.6 mL, 40 mmol), CH_2Cl_2 (100 mL), benzoic anhydride (4.525 g, 20.0 mmol), and DMAP (0.125 g, 1.02 mmol). The reaction stirred for 3 h and was washed and dried as described previously. The filtrate was concentrated and purified via crystallization from EtOAc and hexanes to afford 1.012 g (22% yield) of the title compound as a white solid (m.p. = 106 - 108 °C). ^{1}H NMR (500 MHz,

$CDCl_3$) δ 3.60 (t, *J* = 5.8 Hz, 2H), 3.88 (q, *J* = 5.8 Hz, 2H), 6.61 (broad s, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.77 – 7.81 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 134.1, 131.7, 128.6, 127.0, 41.5, 32.7; IR (neat) 3305, 3065, 1634, 1542, 1302, 1175 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_9H_{11}BrNO$ [M+H], 228.0024; found, 228.0021. The melting point data is consistent with the literature value (lit. m.p. = 104 - 105 °C).[18]

***N*-(2-chloroethyl)-4-methylbenzamide (4a)** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (1.162 g, 10.0 mmol), TEA (2.80 mL, 20.1 mmol), 4-methylbenzoyl chloride (1.32 g, 9.98 mmol) and CH_2Cl_2 (50 mL). The reaction stirred for 3 h and was washed and dried as described previously. The filtrate was concentrated and purified via crystallization from EtOAc and hexanes to afford 1.130 g (57% yield) of the title compound as a white solid (m.p. = 122 - 125 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.71 (t, *J* = 5.2 Hz, 2H), 3.78 (q, *J* = 5.6 Hz, 2H), 6.69 (broad s, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6, 142.2, 131.1, 129.2, 126.9, 44.1, 41.6, 21.4; IR (neat) 3321, 1643, 1540, 1505, 1252, 1183 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{10}H_{13}ClNO$ [M+H], 198.0686; found, 198.0680.

***N*-(2-chloroethyl)-2,4,6-trimethylbenzamide (4b)** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (1.168 g, 10.1 mmol), TEA (2.80 mL, 20.1 mmol), 2,4,6-trimethylbenzoyl chloride (1.70 mL, 10 mmol) and CH_2Cl_2 (50 mL). The reaction stirred for 4 h and was washed and dried as described previously. The filtrate was concentrated and purified via crystallization from EtOAc and hexanes to afford 0.873 g (38% yield) of the title compound as a white solid (m.p. = 120 - 122 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27 (s, 9H), 3.70 – 3.76 (m, 4H), 6.19 (broad s, 1H), 6.83 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 138.5, 134.4, 134.1, 128.2, 43.9, 41.3, 21.0, 19.0; IR (neat) 3235, 3062, 2859, 1631, 1611, 1547, 1447, 1312, 1186 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{12}H_{17}ClNO$ [M+H], 226.0999; found, 226.0994.

***N*-(2-chloroethyl)-4-methoxybenzamide (4c)** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (2.322 g, 20.0 mmol), TEA (5.60 mL, 40.2 mmol), 4-methoxybenzoyl chloride (3.578 g, 21.0 mmol) and CH_2Cl_2 (50 mL). The reaction stirred for 4 h and was washed and dried as described previously. The filtrate was concentrated and purified by silica gel chromatography (50% to 100% EtOAc in hexanes as eluent) to afford 1.427 g (33% yield) of the title compound as a white solid (m.p. = 129 - 131 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (t, *J* = 5.2 Hz, 2H), 3.76 (q, *J* = 5.7 Hz, 2H), 3.83 (s, 3H),

6.67 (broad s, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.75 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 162.3, 128.8, 126.2, 113.7, 55.4, 44.1, 41.6; IR (neat) 3283, 3018, 1634, 1607, 1500, 1256, 1185 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{10}H_{13}ClNO_2$ [M+H], 214.0635; found, 214.0634.

***N*-(2-chloroethyl)-4-trifluoromethylbenzamide (4d)** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (2.342 g, 20.2 mmol), TEA (5.60 mL, 40.1 mmol), 4-(trifluoromethyl)benzoyl chloride (2.97 mL, 20.0 mmol) and CH_2Cl_2 (100 mL). The reaction stirred for 3 h and was washed and dried as described previously. The filtrate was purified via crystallization from EtOAc and hexanes afford 2.597 g (52% yield) of the title compound as a white solid (m.p. = 101 - 105 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (t, *J* = 5.5 Hz, 2H), 3.81 (q, *J* = 5.3 Hz, 2H), 6.76 (broad s, 1H) 7.69 (d, *J* = 8.1 Hz, 2H), 7.89 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 137.3, 133.4 (q, $^2J_{C\text{-}F}$ = 32 Hz), 127.5, 125.7 (q, $^3J_{C\text{-}F}$ = 4 Hz), 123.6 (q, $^1J_{C\text{-}F}$ = 273 Hz), 43.8, 41.8; IR (neat) 3236, 3070, 1630, 1563, 1323, 1156, 1121, 1066 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{10}H_{10}ClF_3NO$ [M+H], 252.0403; found, 252.0397.

Methyl 4-[(2-chloroethyl)carbamoyl]benzoate (4e) To a solution of monomethyl terephthalate (0.993 g, 5.51 mmol), 2-chloroethylamine HCl (0.576 g, 4.97 mmol), TEA (0.70 mL, 5.0 mmol), and N-hydroxysuccinimide (0.576 g, 5.00 mmol) in CH_2Cl_2 (6.5 mL), cooled in an ice bath, was added dropwise diisopropyl carbodiimide (0.97 mL, 6.3 mmol). The ice bath was removed and the reaction stirred under N_2 atmosphere overnight. The reaction mixture was washed successively with aqueous 1.0 M HCl solution and brine before being dried (Na_2SO_4) and concentrated. Purification via silica gel chromatography (40% to 50% EtOAc in hexanes as eluent) afforded 0.564 g (47% yield) of the title compound as a white solid (m.p. = 116 - 118 °C). The NMR spectral data and melting point data (lit. m.p. = 123 °C) are consistent with those reported in the literature.[19]

***N*-(2-chloroethyl)-4-chlorobenzamide (4f)** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (1.161 g, 10.0 mmol), TEA (2.80 mL, 20.1 mmol), 4-chlorobenzoyl chloride (1.747 g, 9.98 mmol) and CH_2Cl_2 (50 mL). The reaction stirred for 4 h and was washed and dried as described previously. The filtrate was concentrated and purified by silica gel chromatography (50% to 100% EtOAc in hexanes as eluent) to afford 1.226 g (56% yield) of the title compound as a white solid (m.p. = 107 - 108 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71 (t, *J* = 5.1 Hz, 2H), 3.77 (q, *J* = 5.7 Hz, 2H), 6.76 (broad s, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 138.0, 132.3, 128.8, 128.4, 43.9,

41.7; IR (neat) 3296, 3077, 1626, 1599, 1546, 1488, 1326, 1093 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_9H_{10}Cl_2NO$ [M+H], 218.0139; found, 218.0136.

***N*-(2-chloroethyl)-2-iodobenzamide (4g).** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (1.937 g, 16.7 mmol), TEA (2.20 mL, 15.7 mmol), 2-iodobenzoyl chloride (2.11 g, 9.3 mmol) and CH_2Cl_2 (50 mL). The reaction stirred overnight and was washed and dried as described previously. The filtrate was concentrated and purified by a silica plug (75% EtOAc in hexanes) followed by crystallization from EtOAc and hexanes to afford 1.248 g (43% yield) of the title compound as a white solid (m.p. = 96 - 100 °C). The NMR spectral data and melting point data (lit. m.p. = 102 - 104 °C) are consistent with those reported in the literature.[20]

***N*-(2-chloroethyl)furan-2-carboxamide (4h)**. Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (0.550 g, 4.74 mmol), TEA (1.20 mL, 8.59 mmol), 2-furoyl chloride (0.559 g, 4.28 mmol) and CH_2Cl_2 (10 mL). The reaction stirred overnight and was washed and dried as described previously. The filtrate was concentrated and purified by silica gel chromatography (50% EtOAc in hexanes) followed by crystallization from EtOAc and hexanes to afford 0.172 g (23% yield) of the title compound as a white needle-like solid (m.p. = 68 - 72 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (t, *J* = 5.5 Hz, 2H), 3.76 (q, *J* = 5.6 Hz, 2H), 6.49 (dd, *J* = 3.5, 1.7 Hz, 1H), 6.84 (broad s, 1H), 7.11 (dd, *J* = 3.4, 0.8 Hz, 1H), 7.44 (dd, *J* = 1.9, 0.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 147.5, 144.1, 114.6, 112.1, 43.8, 40.8; IR (neat) 3256, 2964, 1644, 1591, 1533, 1476, 1430, 1302, 1195 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_9ClNO_2$ [M+H], 174.0322; found, 174.0328.

***N*-(2-chloroethyl)propanamide (4i).** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (1.168 g, 10.1 mmol), TEA (2.80 mL, 20.1 mmol), propionic anhydride (1.30 mL, 10 mmol), 4-DMAP (0.114 g, 0.933 mmol), and CH_2Cl_2 (50 mL). The reaction stirred for 2 h and was washed and dried as described previously. The filtrate was concentrated and purified by silica gel chromatography (50% EtOAc in hexanes as eluent) to afford 0.684 g (50% yield) of the title compound as a colorless oil. The NMR spectral data is consistent with those reported in the literature.[21]

***N*-(2-chloroethyl)-2-methylpropanamide (4j).** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (2.325 g, 20.0 mmol), TEA (5.70 mL, 40.8 mmol), isobutyryl chloride (2.20 mL, 21.0 mmol), 4-DMAP (0.122 g, 1.00 mmol), and CH_2Cl_2 (50 mL). The reaction stirred overnight and was washed and dried as described previously. The filtrate was concentrated and purified by silica gel chromatography (50% to 100% EtOAc in hexanes as eluent) to afford 1.410 g (53% yield) of the title compound as a white solid (m.p. = 44 – 47 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.15 (d, *J* = 6.9 Hz, 6H), 2.38 (hept, *J* = 6.9 Hz, 1H), 3.55 – 3.63 (m, 4H), 6.00 (broad s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 44.1, 41.0, 35.5, 19.5; IR (neat) 3286, 2972, 1646, 1548, 1240 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_6H_{13}ClNO$ [M+H], 150.0686; found, 150.0680.

***N*-(2-chloroethyl)-2,2-dimethylpropanamide (4k).** Prepared according to the general procedure for *N*-(2-haloethyl)amide synthesis using 2-chloroethylamine hydrochloride (2.388 g, 20.6 mmol), TEA (5.60 mL, 40.2 mmol), trimethylacetyl chloride (2.50 mL, 20.4 mmol), 4-DMAP (0.070 g, 0.57 mmol) and CH_2Cl_2 (100 mL). The reaction stirred overnight and was washed and dried as described previously. The filtrate was concentrated and purified via crystallization from EtOAc and hexanes to afford 1.597 g (47% yield) of the title compound as white solid (m.p. = 61 – 64 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (s, 9H), 3.54 – 3.63 (m, 4H), 6.10 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 44.1, 41.1, 38.7, 27.5; IR (neat) 3347, 2971, 1640, 1527, 1206 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_{15}ClNO$ [M+H], 164.0842; found, 164.0834.

General procedure for 2-imidazoline synthesis. A solution of appropriate *N*-(2-haloethyl)amide (1 equiv.) in CH_2Cl_2 was cooled in an ice bath and treated successively with pyridine (2.2 equiv.) and triflic anhydride (1.1 equiv.). The ice bath was removed and the reaction stirred under N_2 atmosphere for 1 h. An appropriate primary amine (1.5 equiv.) was then added and the reaction stirred at room temperature overnight. The reaction was diluted with saturated $NaHCO_3$ solution and the biphasic mixture vigorously stirred for 30 min before being extracted with CH_2Cl_2 (x3). The pooled organic extracts were dried (Na_2SO_4) and concentrated, and the crude product was purified via silica gel chromatography. For larger scale reactions, azeotropic distillation of residual pyridine prior to performing silica gel chromatography was performed to simplify chromatographic separations.

1,2-Diphenyl-4,5-dihydro-1*H*-imidazole (3a). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (1.838 g, 10.0 mmol), CH_2Cl_2 (12 mL), pyridine (1.70 mL, 22 mmol), triflic anhydride (2.00 mL,

12 mmol), and aniline (1.37 mL, 15 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (2.185 g, 98%) as a solid (m.p. = 65 - 69 °C). The NMR spectral data[3b,4d,22] and melting point data (lit. m.p. = 72 - 76 °C)[20] are consistent with those reported in the literature.

2-Phenyl-1-(4-methylphenyl)-4,5-dihydro-1*H*-imidazole (3b). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.362 g, 1.97 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and *p*-toluidine (0.328 g, 3.06 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (96% EtOAc / 4% TEA as eluent) to afford the desired product (0.375 g, 80%) as an oil. The NMR spectral data is consistent with those reported in the literature.[3b,22]

2-Phenyl-1-(2-methylphenyl)-4,5-dihydro-1*H*-imidazole (3c). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.363 g, 1.98 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and *o*-toluidine (0.32 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.411 g, 88%) as a solid (m.p. = 88 – 90 °C). The NMR spectral data and melting point data (lit. m.p. = 86 °C) are consistent with those reported in the literature.[3b]

1-[2,6-di(propan-2-yl)phenyl]-2-phenyl-4,5-dihydro-1*H*-imidazole (3d). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.364 g, 1.98 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and 2,6-diisopropylaniline (0.57 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.548 g, 90%) as a solid (m.p. = 106 – 108 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.9 Hz, 6H), 3.24 (septet, *J* = 6.9 Hz, 2H), 3.79 (t, *J* = 10.3 Hz, 2H), 4.11 (t, *J* = 10.3 Hz, 2H), 7.09 (d, *J* = 7.7 Hz, 2H), 7.14 (dd, *J* = 8.2, 7.0 Hz, 2H), 7.21 – 7.27 (m, 2H), 7.41 (dd, *J* = 8.4, 1.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 147.3, 136.7, 130.3, 129.7, 128.4, 128.2, 127.7, 124.4, 55.4, 53.1, 27.9, 25.6, 23.2; IR (neat) 2962, 2863, 1598, 1570, 1449, 1391, 1265 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{21}H_{27}N_2$ [M+H], 307.2174; found, 307.2183.

2-Phenyl-1-(4-methoxyphenyl)-4,5-dihydro-1*H*-imidazole (3e). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.368 g, 2.00 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and *p*-anisidine (0.376 g, 3.05 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (1% to 4% TEA in EtOAc as eluent) to afford the desired product (0.421 g, 83%) as a solid (m.p. = 70 – 72 °C). The NMR spectral data[3b,22] and melting point data (lit. m.p. = 70 °C)[3b] are consistent with those reported in the literature.

2-Phenyl-1-(3-trifluoromethylphenyl)-4,5-dihydro-1*H*-imidazole (3f). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.370 g, 2.01 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and 3-(trifluoromethyl)aniline (0.37 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.557 g, 95%) as a solid (m.p. = 30 – 34 °C). The NMR spectral data is consistent with those reported in the literature.[3b]

2-(2-Phenyl-4,5-dihydro-1*H*-imidazol-1-yl)benzonitrile (3g). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.362 g, 1.97 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.38 mL, 2.2 mmol), and 2-aminobenzonitrile (0.362 g, 3.06 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.485 g, 99%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 – 4.12 (m, 4H), 7.34 (ddd, *J* = 7.9, 6.1, 2.3 Hz, 1H), 7.47 – 7.51 (m, 3H), 7.54 – 7.60 (m, 2H), 7.61 – 7.65 (m, 2H), 8.03 – 8.07 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5, 153.7, 146.7, 135.0, 133.1, 130.2, 128.7, 127.7, 127.2, 126.5, 125.2, 117.8, 53.4, 48.9; IR (neat) 3062, 2886, 2220, 1644, 1561, 1467, 1390 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{14}N_3$ [M+H], 248.1188; found, 248.1178.

1-(4-benzoic acid ethyl ester)-2-phenyl-4,5-dihydro-1*H*-imidazole (3h). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.365 g, 1.99 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and ethyl 4-aminobenzoate (0.495 g, 3.00 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.570 g, 97%) as an oil. The NMR spectral data is consistent with those reported in the literature.[3b]

2-Phenyl-1-(3-fluorophenyl)-4,5-dihydro-1*H*-imidazole (3i). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.316 g, 1.72 mmol), CH_2Cl_2 (6 mL), pyridine (0.29 mL, 3.8 mmol), triflic anhydride (0.33 mL, 2.0 mmol), and 3-fluoroaniline (0.25 mL, 2.6 mmol). Following workup, which was modified to include washing with 1 M NaOH solution instead of sat. $NaHCO_3$ solution, and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.363 g, 88%) as an oil. The NMR spectral data is consistent with those reported in the literature.[3b]

2-Phenyl-1-(4-chlorophenyl)-4,5-dihydro-1*H*-imidazole (3j). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.367 g, 2.00 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and 4-chloroaniline (0.381 g, 2.99 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.475 g, 93%) as a solid (m.p. = 94 – 96 °C). The NMR spectral data is consistent with those reported in the literature.[3b,22]

2-Phenyl-1-(4-iodophenyl)-4,5-dihydro-1*H*-imidazole (3k). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.363 g, 1.98 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.38 mL, 2.2 mmol), and 4-iodoaniline (0.656 g, 3.00 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.648 g, 94%) as a solid (m.p. = 130 – 132 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.98 – 4.11 (m, 4H), 6.52 (d, J = 8.8 Hz, 2H), 7.29 – 7.34 (m, 2H), 7.39 (tt, J = 7.4 Hz, 1.3 Hz, 1H), 7.42 – 7.50 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 142.7, 137.6, 130.8, 130.1, 128.5, 128.3, 123.9, 86.2, 53.6, 53.0; IR (neat) 3017, 2971, 1582, 1574, 1484, 1375, 1217 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{15}H_{14}IN_2$ [M+H], 349.0202; found, 349.0205.

3-(2-Phenyl-4,5-dihydro-1*H*-imidazol-2-yl)pyridine (3l). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.367 g, 2.00 mmol), CH_2Cl_2 (8 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and 3-aminopyridine (0.282 g, 3.00 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (1 – 5% TEA in EtOAc as eluent) to afford the desired product (0.397 g, 89%) as an oil. The NMR spectral data is consistent with those reported in the literature.[3b]

8-(2-Phenyl-4,5-dihydro-1*H*-imidazol-2-yl)quinoline (3m). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.366 g, 1.99 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride

(0.37 mL, 2.2 mmol), and 8-aminoquinoline (0.433 g, 3.00 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.477 g, 88%) as a solid (m.p. = 141 – 143 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.20 (s, 4H), 7.08 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.47 – 7.50 (m, 2H), 7.58 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.13 (dd, *J* = 8.2, 1.8 Hz, 1H), 8.95 (dd, *J* = 4.2, 1.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 149.7, 143.8, 141.9, 136.2, 131.2, 129.6, 129.3, 128.4, 127.8, 126.3, 126.1, 125.3, 121.5, 55.4, 54.1; IR (neat) 2925, 2861, 1593, 1492, 1368, 1272 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{18}H_{16}N_3$ [M+H], 274.1344; found, 274.1349.

2-(4-Methylphenyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5a). Prepared according to the general procedure for 2-imidazoline synthesis with **4a** (0.401 g, 2.03 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.470 g, 98%) as an oil. The NMR spectral data is consistent with those reported in the literature.[3b]

2-(2,4,6-Trimethylphenyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5b). Prepared according to the general procedure for 2-imidazoline synthesis with **4b** (0.440 g, 1.95 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.496 g, 96%) as a solid (m.p. = 152 – 154 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.13 (s, 6H), 2.28 (s, 3H), 3.96 – 4.09 (m, 4H), 6.59 (dt, *J* = 7.8, 1.1 Hz, 2H), 6.82 (s, 2H), 6.86 (tt, *J* = 7.5, 1.1 Hz, 1H), 7.05 – 7.10 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2, 140.7, 138.6, 136.1, 129.1, 128.6, 128.3, 121.7, 117.4, 52.5, 50.0, 21.2, 19.4; IR (neat) 3056, 2867, 1618, 1596, 1374, 1259 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{18}H_{21}N_2$ [M+H], 265.1705; found, 265.1715.

2-(4-Methoxyphenyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5c). Prepared according to the general procedure for 2-imidazoline synthesis with **4c** (0.429 g, 2.01 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.475 g, 94%) as a solid (m.p. = 74 – 76 °C). The NMR spectral data is consistent with those reported in the literature.[22]

2-(4-Trifluoromethylphenyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5d). Prepared according to the general procedure for 2-imidazoline synthesis with **4d** (0.500 g, 1.99 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.463 g, 80%) as a solid (m.p. = 75 – 77 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.05 – 4.09 (m, 4H), 6.78 (dd, *J* = 8.5, 1.0 Hz, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 7.16 – 7.21 (m, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 142.7, 134.7, 131.6 (q, $^2J_{C\text{-}F}$ = 33 Hz), 129.0, 128.9, 125.1 (q, $^3J_{C\text{-}F}$ = 4 Hz), 123.9, 123.8 (q, $^1J_{C\text{-}F}$ = 271 Hz), 122.8, 54.2, 53.3; IR (neat) 3059, 2861, 1549, 1492, 1321, 1108 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{14}F_3N_2$ [M+H], 291.1109; found, 291.1105.

2-(4-Benzoic acid methyl ester)-1-phenyl-4,5-dihydro-1*H*-imidazole (5e). Prepared according to the general procedure for 2-imidazoline synthesis with **4e** (0.517 g, 2.14 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.40 mL, 2.4 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (2% to 4% TEA in EtOAc as eluent) to afford the desired product (0.485 g, 81%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.89 (s, 3H), 4.05 – 4.09 (m, 4H), 6.77 (dt, *J* = 8.0, 1.1 Hz, 2H), 7.00 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.14 – 7.18 (m, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.95 (d, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 161.9, 142.8, 135.5, 131.2, 129.4, 128.8, 128.6, 123.7, 122.7, 54.1, 53.3, 52.2; IR (neat) 2950, 2869, 1718, 1594, 1495, 1271 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{17}H_{17}N_2O_2$ [M+H], 281.1290; found, 281.1278.

2-(4-Chlorophenyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5f). Prepared according to the general procedure for 2-imidazoline synthesis with **4f** (0.223 g, 1.02 mmol), CH_2Cl_2 (3 mL), pyridine (0.18 mL, 2.2 mmol), triflic anhydride (0.19 mL, 1.1 mmol), and aniline (0.14 mL, 1.5 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.219 g, 83%) as an oil. The NMR spectral data is consistent with those reported in the literature.[3b]

2-(2-Iodophenyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5g). Prepared according to the general procedure for 2-imidazoline synthesis with **4g** (0.477 g, 1.54 mmol), CH_2Cl_2 (5 mL), pyridine (0.27 mL, 3.3 mmol), triflic anhydride (0.29 mL, 1.7 mmol), and aniline (0.21 mL, 2.3 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.416 g, 77%)

as a solid (m.p. = 119 – 122 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.05 – 4.08 (m, 4H), 6.62 – 6.67 (m, 2H), 6.90 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.04 – 7.12 (m, 3H), 7.36 (td, *J* = 7.4, 1.1 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.78 (dd, *J* = 8.0, 1.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 140.7, 139.4, 137.7, 130.7, 130.3, 128.6, 128.1, 122.3, 119.3, 96.4, 53.0, 51.4; IR (neat) 3063, 2846, 1618, 1597, 1577, 1496, 1375, 1269, 1137 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{15}H_{14}IN_2$ [M+H], 349.0202; found, 349.0218.

2-(2-furanyl)-4,5-dihydro-1-methyl-1*H*-imidazole (5h). Prepared according to the general procedure for 2-imidazoline synthesis with **4h** (0.180 g, 0.959 mmol), CH_2Cl_2 (3 mL), pyridine (0.19 mL, 2.3 mmol), triflic anhydride (0.19 mL, 1.1 mmol), and aniline (0.14 mL, 1.5 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.158 g, 78%) as a solid (m.p. = 54 – 59 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.90 – 3.97 (m, 2H), 4.03 – 4.09 (m, 2H), 6.31 (d, *J* = 1.3 Hz, 2H), 6.97 – 7.04 (m, 2H), 7.15 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.25 – 7.33 (m, 2H), 7.38 (t, *J* = 1.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 144.6, 143.9, 142.8, 129.0, 125.0, 124.1, 113.7, 111.0, 54.7, 53.2; IR (neat) 3111, 2863, 1624, 1549, 1482, 1279 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{13}H_{13}N_2O$ [M+H], 213.1028; found, 213.1022.

2-Ethyl-1-phenyl-4,5-dihydro-1*H*-imidazole (5i). Prepared according to the general procedure for 2-imidazoline synthesis with **4i** (0.272 g, 2.00 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (2% to 4% TEA in EtOAc as eluent) to afford the desired product (0.344 g, 99%) as a light yellow oil. The NMR spectral data is consistent with those reported in the literature.[23]

2-(1-Methylethyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5j). Prepared according to the general procedure for 2-imidazoline synthesis with **4j** (0.267 g, 1.78 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (96% EtOAc / 4% TEA as eluent) to afford the desired product (0.336 g, 98%) as an oil. The NMR spectral data is consistent with those reported in the literature.[23,24]

2-(1,1-Dimethylethyl)-1-phenyl-4,5-dihydro-1*H*-imidazole (5k). Prepared according to the general procedure for 2-imidazoline synthesis with **4k** (0.333 g, 2.03 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic

anhydride (0.37 mL, 2.2 mmol), and aniline (0.27 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.397 g, 96%) as a solid (m.p. = 87 – 90 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9H), 3.70 (ddd, *J* = 11.4, 9.0, 1.7 Hz, 2H), 3.81 (ddd, *J* = 9.6, 9.0, 1.8 Hz, 2H), 7.24 – 7.30 (m, 3H), 7.34 – 7.39 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 144.6, 129.4, 129.2, 127.2, 58.1, 52.2, 34.8, 29.6; IR (neat) 2974, 2869, 1585, 1486, 1177 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{13}H_{19}N_2$ [M+H], 203.1548; found, 203.1539.

2-(1,1-Dimethylethyl)-1-[2,6-di(propan-2-yl)phenyl]-4,5-dihydro-1*H*-imidazole (6). Prepared according to the general procedure for 2-imidazoline synthesis with **4k** (0.333 g, 2.03 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and 2,6-diisopropylaniline (0.57 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.561 g, 96%) as a solid (m.p. = 108 – 111 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.17 (d, *J* = 6.9 Hz, 6H), 1.27 (d, *J* = 6.9 Hz, 6H), 3.12 (sep, *J* = 7.5 Hz, 2H), 3.71 (t, *J* = 10.3 Hz, 2H), 3.91 (t, *J* = 10.3 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.7 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 172.1, 147.7, 136.7, 128.7, 124.2, 55.6, 50.2, 35.2, 29.5, 28.2, 26.5, 22.5; IR (neat) 2964, 2865, 1583, 1441, 1360, 1177 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{19}H_{31}N_2$ [M+H], 287.2487; found, 287.2486.

2-(2,4,6-Trimethylphenyl)-1-(2,6-dimethylphenyl)-4,5-dihydro-1*H*-imidazole (7). Prepared according to the general procedure for 2-imidazoline synthesis with **4b** (0.225 g, 1.00 mmol), CH_2Cl_2 (3 mL), pyridine (0.17 mL, 2.2 mmol), triflic anhydride (0.19 mL, 1.1 mmol), and 2,6-dimethylaniline (0.18 mL, 1.5 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.249 g, 86%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.16 (s, 3H), 2.19 (s, 6H), 2.21 (s, 6H), 3.82 (t, *J* = 10.2 Hz, 2H), 4.15 (t, *J* = 10.2 Hz, 2H), 6.66 (s, 2H), 6.92 (d, *J* = 7.2 Hz, 2H), 6.97 (dd, *J* = 8.5, 6.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 137.8, 137.4, 136.9, 136.5, 128.6, 128.3, 128.0, 126.6, 53.4, 51.4, 20.9, 20.8, 19.0; IR (neat) 2971, 2924, 1598, 1470, 1428, 1367, 1217 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{20}H_{25}N_2$ [M+H], 293.2018; found, 293.2025.

2-Phenyl-1-(phenylmethyl)-4,5-dihydro-1*H*-imidazole (8a). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.336 g, 1.83 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and benzylamine (0.33 mL, 3.0 mmol). Following workup and concentration, the residue was

purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.328 g, 76%) as an oil. The NMR spectral data is consistent with those reported in the literature.[25,26]

1-[(4-methoxyphenyl)methyl]-2-phenyl-4,5-dihydro-1*H*-imidazole (8b). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.364 g, 1.98 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and 4-methoxybenzylamine (0.39 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.405 g, 77%) as a light yellow solid (m.p. = 77 – 79 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.38 (t, *J* = 9.9 Hz, 2H), 3.81 (s, 3H), 3.91 (t, *J* = 9.9 Hz, 2H), 4.24 (s, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 7.38 – 7.45 (m, 3H), 7.56 – 7.63 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 158.9, 131.3, 129.9, 129.8, 128.44, 128.38, 128.1, 114.0, 55.3, 53.2, 52.4, 50.8; IR (neat) 2931, 2876, 1610, 1508, 1389, 1245, 1013 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{17}H_{19}N_2O$ [M+H], 267.1497; found, 267.1490.

2-Phenyl-1-(diphenylmethyl)-4,5-dihydro-1*H*-imidazole (8c). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.187 g, 1.02 mmol), CH_2Cl_2 (3 mL), pyridine (0.17 mL, 2.2 mmol), triflic anhydride (0.19 mL, 1.1 mmol), and diphenylmethanamine (0.27 mL, 1.5 mmol). A modified workup consisted of diluting the reaction mixture in EtOAc and washing with 1 M NaOH solution instead of sat. $NaHCO_3$ solution. Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.257 g, 81%) as a solid (m.p. = 107 – 110 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 3.47 (t, *J* = 10.3 Hz, 2H), 3.92 (t, *J* = 10.3 Hz, 2H), 6.10 (s, 1H), 7.13 (d, *J* = 7.5 Hz, 4H), 7.30 – 7.39 (m, 6H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 167.0, 138.7, 131.0, 128.9, 128.6, 128.29, 128.28, 127.8, 63.5, 50.5, 45.7; IR (neat) 3030, 2854, 1593, 1572, 1403, 1268 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{22}H_{21}N_2$ [M+H], 313.1705; found, 313.1693.

2-phenyl-1-(prop-2-yn-1-yl)-4,5-dihydro-1*H*-imidazole (8d). Prepared according to the general procedure for 2-imidazoline synthesis with **1a** (0.365 g, 1.99 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.37 mL, 2.2 mmol), and propargylamine (0.19 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.283 g, 77%) as a solid (m.p. = 57 – 58 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 2.24 (s, 1H), 3.60 (t, *J* = 9.8 Hz, 2H), 3.88 – 3.92 (m, 4H), 7.38 – 7.46 (m, 3 H), 7.55 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.7, 130.4, 129.6, 128.5,

128.0, 78.2, 72.9, 52.2, 50.1, 38.3; IR (neat) 3164, 2844, 2108, 1615, 1599, 1573 1379 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{12}H_{13}N_2$ [M+H], 185.1079; found, 185.1080.

1-(1,1-dimethylethyl)-2-phenyl-4,5-dihydro-1*H*-imidazole (8e). A solution of **1a** (0.375 g, 2.04 mmol) in CH_2Cl_2 (6 mL) was cooled in an ice bath and treated successively with 2-fluoropyridine (0.40 mL, 4.6 mmol) and triflic anhydride (0.39 mL, 2.3 mmol). The ice bath was removed and the reaction stirred under N_2 atmosphere for 1 h before *t*-butyl amine (0.32 mL, 3.0 mmol) was added. The reaction mixture then refluxed overnight. The reaction was diluted with saturated $NaHCO_3$ solution and the mixture was extracted with CH_2Cl_2 (x3). The pooled organic extracts were dried (Na_2SO_4) and concentrated, and the crude product was purified via silica gel chromatography (2% - 4% TEA in EtOAc as eluent) to afford the desired product (0.324 g, 79% yield) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.11 (s, 9H), 3.66 (t, *J* = 9.7 Hz, 2H), 3.80 (t, *J* = 9.9 Hz, 2H), 7.34 – 7.38 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 134.4, 129.1, 128.4, 127.9, 55.1, 50.8, 48.4, 29.7; IR (neat) 2966, 2917, 2849, 1612, 1584, 1275 cm^{-1} ; HRMS (ESI): *m/z* calcd for $C_{13}H_{19}N_2$ [M+H], 203.1548; found, 203.1552.

2-(1,1-Dimethylethyl)-2-(phenylmethyl)-4,5-dihydro-1*H*-imidazole (9) Prepared according to the general procedure for 2-imidazoline synthesis with **4k** (0.373 g, 2.28 mmol), CH_2Cl_2 (6 mL), pyridine (0.36 mL, 4.4 mmol), triflic anhydride (0.39 mL, 2.3 mmol), and benzylamine (0.33 mL, 3.0 mmol). Following workup and concentration, the residue was purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford the desired product (0.493 g, 97%) as an orange solid (m.p. = 69 – 72 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.20 (t, *J* = 10.0 Hz, 2H), 3.67 (t, *J* = 10.0 Hz, 2H), 4.52 (s, 2H), 7.24 – 7.37 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 137.7, 128.6, 127.4, 126.9, 52.7, 51.6, 51.0, 33.6, 28.8; IR (neat) 2974, 1589, 1454, 1277, 1166 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{14}H_{21}N_2$ [M+H], 217.1705; found, 217.1715.

***N*-[2-(phenylamino)ethyl]benzamide (10).** Prepared as a white solid (m.p. = 125 – 126 °C) according to a known protocol.[10] ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 3.37 (q, *J* = 6.1 Hz, 2H), 3.63 (q, *J* = 6.2 Hz, 2H), 5.13 (broad s, 1H), 6.57 (t, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 8.6 Hz, 2H), 7.09 (dd, *J* = 8.6, 7.2 Hz, 2H), 7.44 (dd, *J* = 8.3, 6.7 Hz, 2H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.88 – 7.99 (m, 3H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 167.9, 149.7, 135.8, 131.9, 129.8, 129.1, 128.0, 117.1, 113.1, 44.1, 40.0; IR (neat) 3362, 1631, 1600, 1577, 1519, 1270 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{15}H_{17}N_2O$ [M+H], 241.1341; found, 241.1332. The melting point data is consistent with the literature value (lit. m.p. = 127 °C).[4d]

Conversion of **10** to **3a**: A mixture of **10** (0.0726 g, 0.30 mmol) in CH_2Cl_2 (2 mL), cooled to 0 °C was treated with 2-fluoropyridine (0.06 mL, 0.70 mmol) and triflic anhydride (0.06 mL, 0.36 mmol). The ice bath was removed and the reaction stirred under nitrogen atmosphere at room temperature overnight. The reaction was worked up according to the general procedure for 2-imidazoline synthesis and purified by silica gel chromatography (98% EtOAc / 2% TEA as eluent) to afford desired product **3a** (0.040 g, 59%).

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Supplementary data

^{1}H and ^{13}C NMR spectra for all new compounds associated with this article can be found, in the online version at doi.xx.xxxx

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