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TBAB Catalyzed Csp^3–N Bond Formation by Coupling Pyridotriazoles with Anilines: A New Route to (2-Pyridyl)alkylamines

Diana Lamaa,[a] Hsin-Ping Lin,[a] Tourin Bzeih,[a] Pascal Retailleau,[b] Mouad Alami,[a]* and Abdallah Hamze.[a]*

Abstract. A new metal-free procedure allowing a Csp^3-N bond formation through coupling of pyridotriazoles and weakly nucleophilic anilines has been developed. This sustainable reaction shows high tolerance towards functional groups (ketones, free alcohols) leading to 2-picolylamines derivatives. The key to our success is the use of a catalytic amount of TBAB and water as a co-solvent leading to the formation of pyridyl-alkylamines derivatives. As this coupling tolerates the presence of Csp^2-Br bond on both partner of the reaction, this allowed us to perform a sequential one-pot reaction between functionalized triazolopyridines and anilines followed by a second coupling with *N*-tosylhydrazones leading to the formation of Csp^3-N and Csp^2-Csp^2 bonds.

Keywords: diazo compounds, metal-free, Csp^3-N bond formation, synthetic methods, nitrogen heterocycles

Introduction

Products that contain a Csp^3-nitrogen bond constitute a fascinating group of compounds with a large degree of structural diversity. Also, nitrogen heterocycles represent the most significant structural components of FDA approved drugs. Among them, pyridine nuclei are ubiquitous scaffolds that occupy a central role in many therapeutic compounds.[1] Figure 1 shows representative examples of bioactive molecules containing (2-Pyridyl)alkylamines motif with various pharmacological properties.[2, 3] Introduction of nitrogen atom into therapeutically active small molecules led to drastically change in the physicochemical and biological properties.[4] The typical example is the ampicillin, which differs from penicillin G (benzylpenicillin) by the presence of a benzylic amine. This change permits a broadened spectrum of activity and increases the acid-stability of ampicillin in comparison to penicillin G.[5]

The development of efficient methodologies for Csp^3–N bond formation is of paramount importance for academic research, as well as for chemical industries.[6] The most common route for the preparation of α-branched amines is the reductive amination of imino C=N bonds which are not always easy to synthesize and have limited stability.[7]

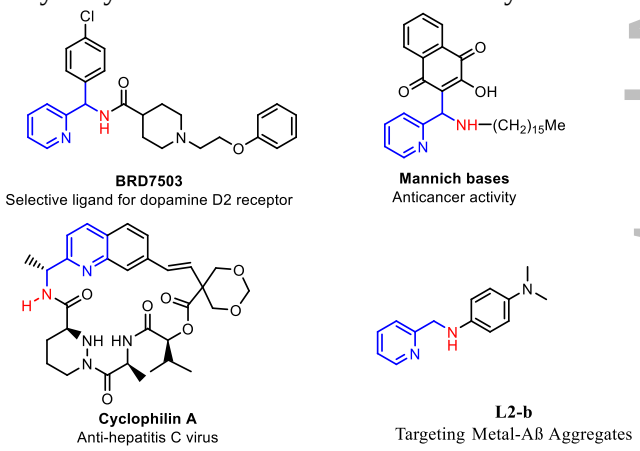

Figure 1. (2-Pyridyl)alkylamines-containing bioactive molecules.

Therefore, we have recently reported a copper-catalyzed reaction inducing Csp^3–N bond formation utilizing *N*-tosylhydrazones as coupling partners (Scheme 1a).[8]. This methodology works well for hydrazones derived from acetophenone, but was totally inefficient for hydrazone derived from 2-acetylpyridine, as the only isolated product was the pyridotriazole derivative (Scheme 1b). The formation of the latter compound can be explained by intramolecular cyclization of the diazo intermediate generated in situ on the nitrogen atom of the pyridine nucleus.

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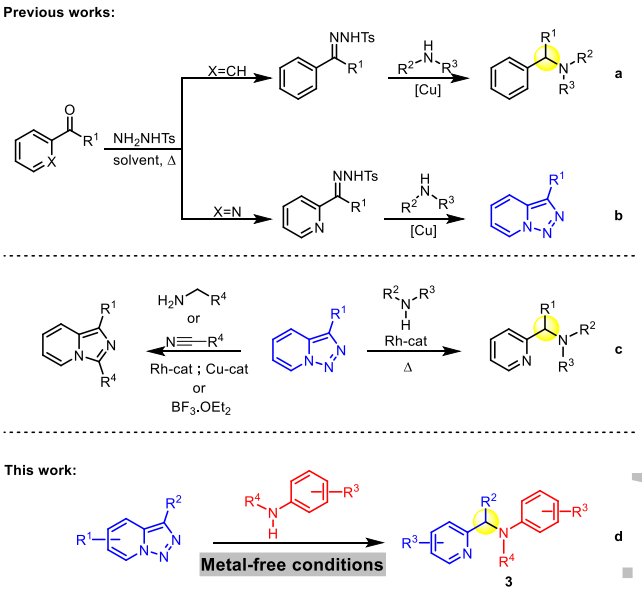
In recent years, the 1,2,3-triazole ring has emerged as a new partner of metal-catalyzed cross-coupling reactions.[9-11] It has been proved that *N*-fused-triazoles exist in an equilibrium between their closed and their opened form.[12] However, the opened form could be trapped with a metal to form the metallo-carbene, which plays the role of the reactive species in many transformations.[11] Consequently, triazolopyridine moiety has been employed as a precursor of rhodium,[13] or copper[14] carbenes in a wide range of organic transformations affording nitrogen-containing heterocyclic compounds such as imidazopyridines or indolizine (Scheme 1c).[10] However, metal-free transformations describing the pyridotriazole's ring-opening were barely reported in the literature. In this context, Adimurthy *et al* have reported the synthesis of imidazopyridines derivatives from benzotriazoles and nitriles in the presence of $BF_3.OEt_2$ (Scheme 1c).[15] Recently, Dong et al investigated the use of other acidic conditions in the synthesis of pyridopyrroloindolizine starting from azaindoles and pyridotriazoles.[16]

In connection with our interest in diazo chemistry,[17, 18] we envisaged the use of the emerging, economical, and eco-friendly metal-free conditions replacing the expensive and rare metal Rh catalysts in the formation of Csp^3–N bond from pyridotriazole derivatives. Herein, we wish to report a sustainable and practical transformation of 1,2,3-pyridotriazole into 2-picolylamines derivatives using metal-free conditions (Figure 1d). Highlighted features of this methodology include (a) easily available pyridotriazole derivatives from aldehydes, ketone or benzophenones; (b) transition-metal, and base-free coupling leading to the formation of C-N bond with the respect of sustainable approach that limits the use of expensive noble metals; (c) chemoselectivity and functional-group compatibility; (d) water tolerance; (e) development of sequential Csp^3-N and Csp^2-Csp^2 bonds formation in a one-pot manner.



Scheme 1. a and c, Metal catalyzed C–N bond formation through metallo-carbene species. b, In-situ rearrangement of the triazole from its corresponding *N*-tosylhydrazone. d, Metal-free formation of Csp^3–N bond from pyridotriazoles and amines.

Results and Discussion

To begin, the cross-coupling reaction of pyridotriazole **1a** and *p*-anisidine **2a** was chosen as a model to explore the reaction conditions (Table 1). During this study, a screening of various reaction parameters (solvent, temperature, and copper source) was carried out (for more details, see the Supporting Information part). Reaction development commenced by examining commercially available copper(II) acetylacetonate as the catalyst source (entries 1-6). The combination of $Cu(acac)_2$ and K_2CO_3 as the base in dioxane at 130 °C led to the formation of the desired product but in a low 25% yield (Table 1, entry 1). Other copper(I) or (II) sources were tested and no improvement of the yield was observed. In addition, similar or lower yields were obtained when different solvents were used such as toluene, PhF, and DCE (SI part). Notably, the efficiency of this transformations was significantly affected by the nature of the base. Thus, compound **3a** was not detected when using a strong base such as LiOtBu (entry 2). Following these results, we decided to carry out the coupling in the absence of base, which improved the reaction efficiency to provide the desired 2-picolylamine **3a** in 31% yield (Table 1, entry 3). Rising the temperature up to 150 °C increased slightly the yield to 38% (entry 4). The use of tetrabutylammonium bromide (TBAB 0.1 equiv) or H_2O (25 equiv) as additives also enhanced the reaction efficiency (Table 1, entries 5 and 6). Gratifyingly, we found that combining TBAB and H_2O efficiently promoted the reaction and afforded the desired compound **3a** in a good 82% yield (Table 1, entry 7). To our great surprise, further investigation of the reaction conditions showed that the cross-coupling could even take place in metal-free conditions with a moderate yield of 68% (Table 1, entry 9). Encouraged by these results, we decided to optimize the metal-free process. Rising the temperature up to 165 °C increased the yield to 79% (Table 1, entry 10). Fine-tuning of the reaction conditions led us to find that the use of 0.2 equivalent of TBAB instead of 0.1 equivalent boosted the yield to 92% (Table 1, entry 11). In addition, comparing different PTCs (cf, entries 12 and 13 *vs* 11) showed that the use of TBAB is the optimal for this transformation. Carrying out the reaction in water showed a lower yield due to the low solubility of the reagents in the reaction medium (Table 1, entry 14). Control experiment demonstrated that the TBAB was vital for this transformation (cf, entry 15 vs 16), as no desired product was detected in its absence, and that addition of water was very important (cf, entry 11 vs 15).

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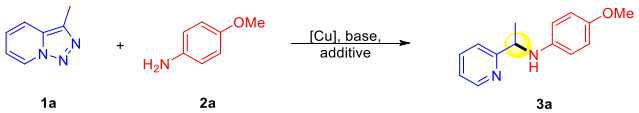
Table 1. Optimization of the reaction conditions.[a]



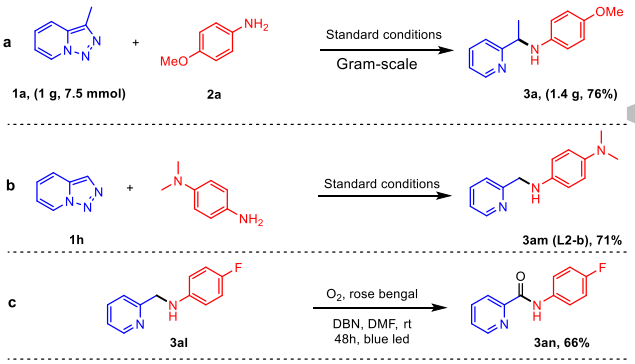
1a 2a 3a

Entry	catalyst	solvent	base	additive	T (°C)	t (h)	Yield (%)
1	$Cu(acac)_2$	dioxane	K_2CO_3	-	130	24	25
2	$Cu(acac)_2$	dioxane	LiO*t*Bu	-	130	24	-
3	$Cu(acac)_2$	dioxane	-	-	130	24	31
4	$Cu(acac)_2$	dioxane	-	-	150	24	38
5[b]	$Cu(acac)_2$	dioxane	-	**TBAB**	150	24	48
6[c]	$Cu(acac)_2$	dioxane	-	**H_2O**	150	24	46
7[b,c]	$Cu(acac)_2$	dioxane	-	**TBAB + H_2O**	150	24	82
8[d,c]	$Cu(acac)_2$	dioxane	-	**TBAB + H_2O**	130	24	45
9[b,c]	-	dioxane	-	TBAB + H_2O	150	12	68
10[b,c]	-	dioxane	-	TBAB + H_2O	165	12	79
11[d]	-	dioxane	-	**TBAB + H_2O**	**165**	**12**	**92**
12[d]	-	dioxane	-	TBAI + H_2O	165	12	65
13[d]	-	dioxane	-	TBAC + H_2O	165	12	59
14[d]	-	H_2O	-	TBAB	165	12	45
15[d]	-	dioxane	-	TBAB	165	12	58
16	-	dioxane	-	H_2O	165	12	0
17[d,e]	-	dioxane	-	**TBAB + H_2O**	**165**	**12**	**60**

[a] Reaction Conditions: substrate (**1a**, 0.5 mmol), aniline (**2a**, 2 equiv), [Cu] catalyst (0.1 equiv), base (2.2 equiv) in 5 mL of dioxane in a sealed tube. [b] TBAB (0.1 equiv) was used as additive. [c] H_2O (25 equiv) was used as additive, the use of 25 equiv was found to be the optimal. [d] TBAX (0.2 equiv) and H_2O (25 equiv) were used as additives. [e] 1 equivalent of aniline was used.

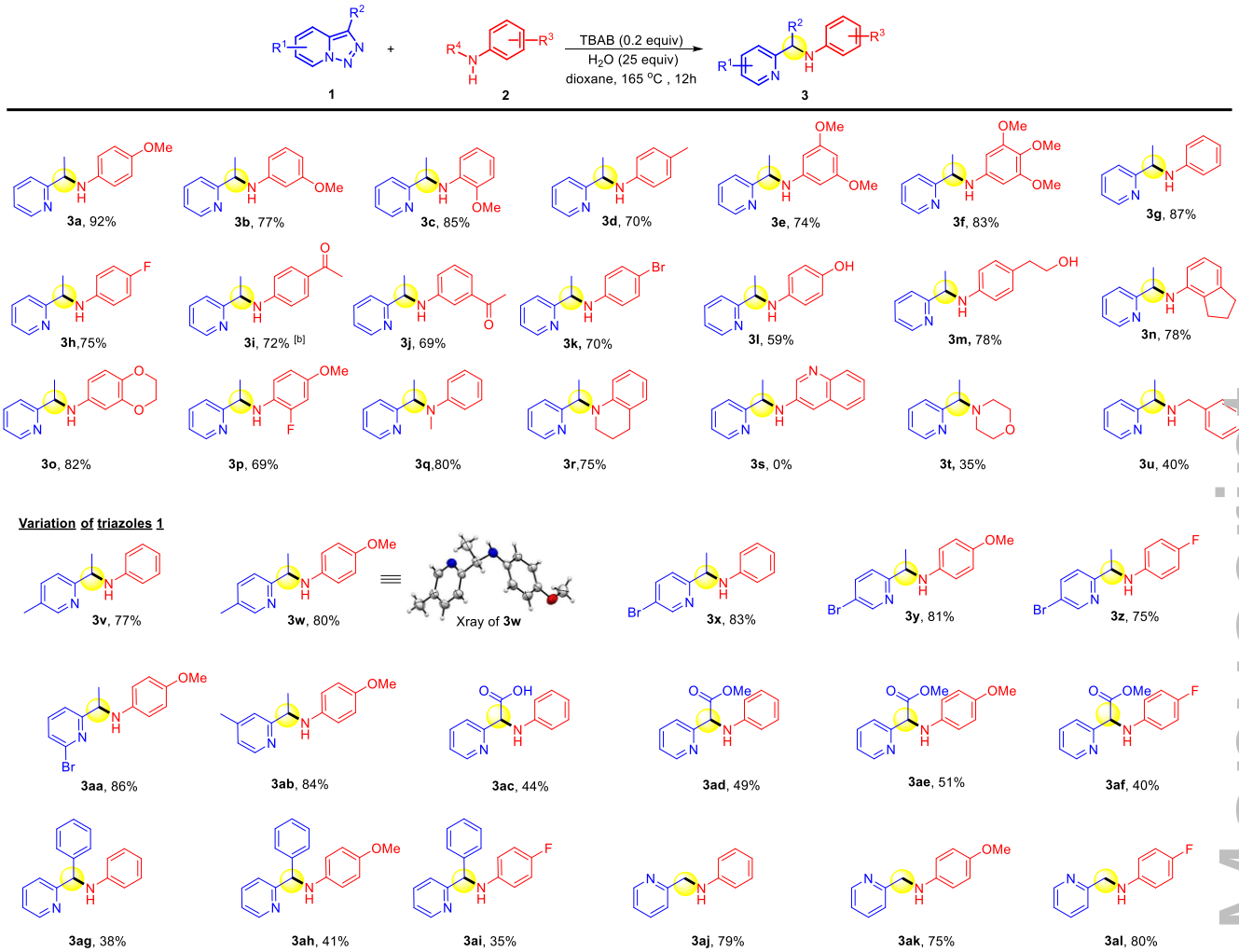
With the optimized conditions in hand, we investigated the substrate scope using different pyridotriazoles **1** and a series of anilines **2**. As presented in Table 2, the reaction worked efficiently affording the coupling products, in good to high yields. Both electron-donating and electron-withdrawing groups on the aniline ring underwent reaction to afford the desired products in good to high yields (compounds **3a-f**, **3h**, **3i**). Also, the reaction proceeds successfully with different substituents at various positions in the anilines (**3b**, **3e-f**, **3j**, **3p**), including bulky methoxy group at the *ortho* position (**3c**). It is noteworthy that the coupling tolerates the bromine substitution on aniline (compound **3k**), enabling later additional derivatizations through metal-catalyzed cross-coupling. Next, we examined the selectivity issue (NH vs OH), and the coupling was conducted in the presence of anilines having a free OH group (phenol or 2-phenylethanol), interestingly, we discovered that the reaction showed a high selectivity leading to an exclusive C-N bond formation (compound **3l-m**). Furthermore, bicyclic anilines also underwent the reaction forming the corresponding products (compounds **3n-o**). Coupling a secondary aniline constitutes a challenging issue, since the steric hindrance around the nitrogen center could affect its reactivity. We were pleased to find that the methylaniline and the tetrahydroquinoline reacted smoothly to give the corresponding products in good yields (compounds **3q-r**). Encouraged by these results, we further examined the substrate scope with respect to the second partner of the coupling reaction, the pyridotriazole. To our satisfaction, a variety of triazoles were used successfully, and the desired products were obtained in good yield (Table 2). The structure of the product **3w** was confirmed by single crystal X-ray diffraction.[19] It should be noted that halides (Br, F) are conserved in the reactions and provide potential points for further modifications (compounds **3x-aa**). Moreover, pyridotriazoles bearing different substituents at the C3 poisition conducted the reaction successfully. Thus, 3-methylcarboxylate-pyridotriazole afforded the carboxylic acid derivative (**3ac**) issued from the ester's hydrolysis after 12 h, however reducing the reaction time to 6h furnished the corresponding ester compounds in moderate yields (**3ad-af**). Readily available 3-phenyl-pyridotriazoles furnished the corresponding compounds in moderate yield (**3ag-ai**). Moreover, we performed the coupling with triazoles derived from 2-pyridine carboxaldehyde (compounds **3aj-al**) showing a further utility of this process.

Next, to demonstrate the robustness of this method, we conducted a gram-scale synthesis of compound **3a** in 76% yield (Scheme 2). Moreover, we have demonstrated the utility of our methodology by synthesizing **3am (L2-b)** from the triazolopyridine **1h** by a single step route with a 71% yield. **L2-b** is a metal chelating agent could generate nontoxic amyloid species and reduce toxicity linked to Aβ oligomers in vivo.[3, 20] In addition, we studied the late stage modification of compound **3al** by synthesizing the amide directly from the corresponding amine using the conditions reported recently by Das' group.[21] Thus compound **3al** underwent successfully a visible-light-mediated metal-free α-oxygenation to afford the amide **3an** with a 66% yield (Scheme 2c).



Scheme 2. Applications of the methodology and transformation. a. Gram-scale reaction of **3a**; b. Synthesis of **L2-b,** an Aβ oligomers metal-chelator; c. metal-free α oxygenation of amine **3al** to amide.

Table 2. Substrate scope of 1,2,3-pyridotriazoles with anilines.[a]



[a] Reaction conditions: substrate (**1**, 0.5 mmol), aniline (**2**, 2 equiv), TBAB (0.2 equiv), H_2O (25 equiv) in 5 ml of dioxane in a sealed tube. [b] 1 equiv of TBAB was employed.

Subsequently, based on the results obtained above, notably, on the fact that the coupling tolerated the presence of bromine substituent, we were curious to carry out a new coupling reaction on the compound **3k** in one-pot reaction fashion (Scheme 3). These types of transformations allow us to access rapidly to complex structures in attractive ecological and economical ways. Thus, limiting the waste and time of the purification of intermediates. Consequently, we envisaged creating first a Csp^3–N bond by reacting triazolopyridine and 4-bromoaniline (**2k**), followed by a new C–C bond by using a compatible Barluenga type cross-coupling reaction.[22]

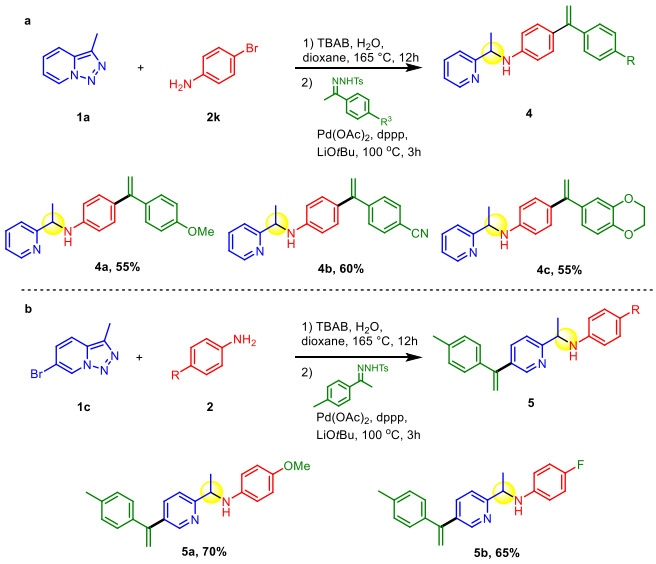
The coupling between intermediate **3k** and the *N*-tosylhydrazone was carried in the presence of $Pd(OAc)_2$ as the catalyst, the bidentate ligand dppp and LiOt-Bu as the base.[18] Gratifyingly, The reaction took place even in the presence of water, and TBAB from the first step affording the compound **4a** in 55 % yield (Scheme 3a). Remarkably, tosylhydrazones bearing electron-withdrawing group or heterocycles underwent efficiently the reaction affording the corresponding compound **4b** and **4c** in acceptable yields.

Next, we wondered if this one-pot reaction tolerates the use of bromopyridotriazole **1c** as the coupling partner. Again, we demonstrated the feasibility of the coupling by synthesizing 2,5-substituted pyridines **5a** and **5b** in good overall yields (Scheme 3b).

To gain insight into the reaction mechanism, we conducted control experiments (Scheme 4a-e). We examined the reactivity of the TBAB with pyridotriazole without the addition of the aniline. Thus, under the standard conditions, the formation of the benzylbromide intermediate **6** was confirmed by ^{1}H NMR analysis of the crude reaction mixture.[23] Addition of *para*-anisidine to the reaction medium conducted to the formation of compound **3a**. In addition, benzyl bromide **7** underwent the reaction with *p*-anisidine to afford the compound **3ai** proving that benzylbromide intermediate could work with aniline to give the final product (Scheme 4a-b). Performing the reaction in the presence of deuterated water afforded the compound **D-3d**. A D-incorporation at α position of the amine was observed; it was also accompanied by an H/D exchange on aniline's aromatic ring on *ortho* position due to the heating of the anilinium hydrobromide formed in situ

in the presence of D_2O (Scheme 4c).[24] These experiments clearly indicate the important role of TBAB and water for the reaction progression (cf. Table 1).

Pyridotriazole **1** is thermally subjected to tautomerization giving a diazo-compound **A** generated in situ from the pyridotriazole **1** upon heating,[25] which normally decomposes giving the carbene species.[26]



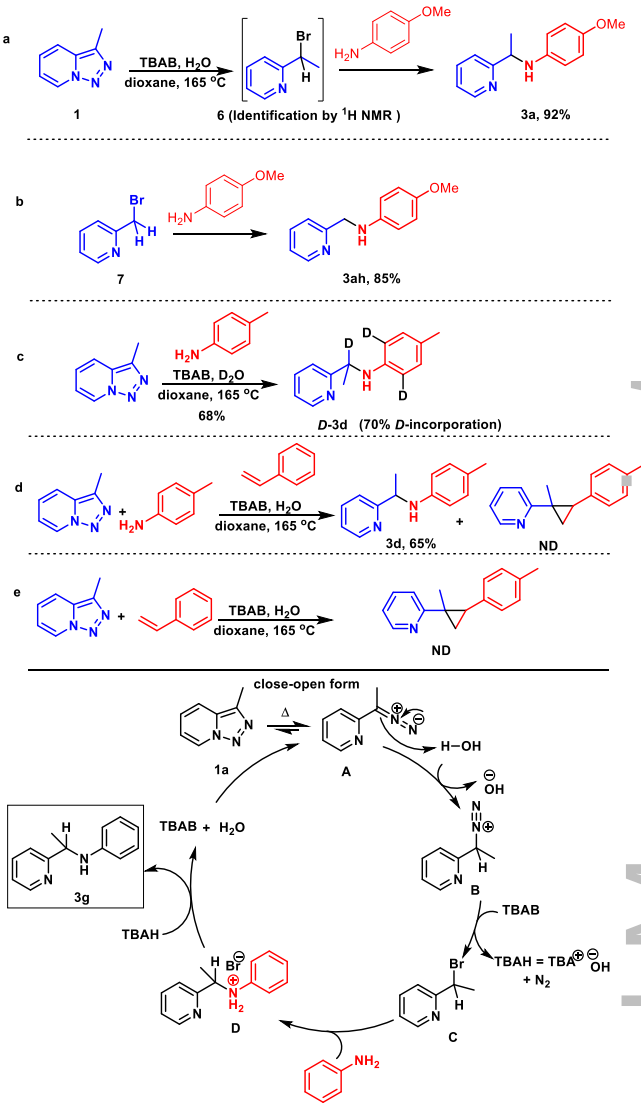
Scheme 3. Scope of One-Pot, Reaction of triazopyridines with anilines and *N*-tosylhydrazones with formation of C*sp*^{3}-N and C*sp*^{2}-C*sp*^{2} bonds.[a]

No cyclopropane product (2-(1-methyl-2-(*p*-tolyl)cyclopropyl)pyridine) was detected when styrene was added into the reaction in the presence or absence of aniline, indicating that no carbene intermediate was generated during the course of the reaction (Scheme 4d-e). Accordingly, the diazo compound **A** could react with water giving rise to the intermediate **B**. The electrophilic carbon bearing the diazo was then attacked by the nucleophilic bromine[27] of the TBAB forming the benzyl bromide intermediate **C** and lead to the N_2 release and formation of tetrabutylammonium hydroxide (TBAH)**.** Next, intermediate **C** was further attacked by the aniline affording the coupling product **D**.

Finally, **D** undergoes a deprotonation process in the presence of TBAH to afford the corresponding pyridyl-alkylamine **3**.

Conclusion

In summary, we have performed a metal-free reaction between pyridotriazoles, and a wide variety of commercially available anilines. This new process catalyzed by TBAB permits the formation of C*sp*^{3}–N bond affording a variety of α-branched arylamines. This methodology features a wide substrates scope, chemoselectivity, functional groups tolerance, and scalability. Moreover, additional coupling in a one-pot reaction could be conducted with the formation of C*sp*^{3}-N and C*sp*^{2}-C*sp*^{2} bonds affording access to a molecular diversity.



Scheme 4. Control experiments, and proposed mechanism.

Experimental Section

General procedure for the synthesis of α-branched amines.

0.5 mmol of pyridyltriazole , 1 mmol of aniline, 0.1 mmol of TBAB, 12.5 mmol (0.2 ml, 25 equiv) of H_2O in 5 ml of dioxane were placed in a sealed tube under argon. The mixture was allowed to stir at 165 °C for 12h. After cooled the solvent was removed under reduced pressure and the crude mixture was purified on flash column using a gradient of petroleum ether and ethyl acetate.

4-Methoxy-*N*-(1-(pyridin-2-yl)ethyl)aniline (3a)[28]. Column chromatography on silica gel afforded 105 mg of the desired compound **3a** as a brown solid (0.46 mmol, yield 92%). m.p. = 73-75 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.59 (td, *J* = 7.5, 1.8 Hz, 1H), 7.33 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.12 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 6.70 (d, *J* = 9.0 Hz, 2H), 6.52 (d, *J* = 9.0 Hz, 2H), 4.54 (q, *J* = 6.7 Hz, 1H), 3.69 (s, 3H), 1.52 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (75 MHz) δ 164.2 (Cq), 152.1 (Cq), 149.3 (CH), 141.4 (Cq), 136.9 (CH), 122.0 (CH), 120.5 (CH), 114.9 (4 CH), 55.8 (OCH_3), 55.7 (CH), 23.4 (CH_3). IR (ν, cm^{-1}) 3416,

3043, 2880, 1613, 1520, 1503, 1478, 1110. HRMS (ESI) for $C_{14}H_{17}N_2O$ $[M+H]^+$: calcd 229.1341, found 229.1336.

3-Methoxy-*N*-(1-(pyridin-2-yl)ethyl)aniline (3b). Column chromatography on silica gel afforded 88 mg of the desired compound **3b** as a brown solid (0.385 mmol, yield 77%). m.p. = 70-72 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (ddd, *J* = 4.7, 1.7, 1.0 Hz, 1H), 7.61 (td, *J* = 7.7, 1.7 Hz, 1H), 7.34 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.14 (ddd, *J* =7.7, 4.7, 1.0 Hz, 1H), 7.02 (t, *J* = 8.1 Hz, 1H), 6.26 – 6.16 (m, 2H), 6.12 (t, *J* = 2.3 Hz, 1H), 4.61 (q, *J* = 6.7 Hz, 1H), 4.50 (s, 1H), 3.70 (s, 3H), 1.54 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9 (Cq), 160.8 (C), 149.4 (CH), 148.6 (Cq), 137.0 (CH), 130.0 (CH), 122.1 (CH), 120.5 (CH), 106.6 (CH), 102.8 (CH), 99.5 (CH), 55.1 (CH), 54.8 (OCH_3), 23.3 (CH_3). IR (ν, cm^{-1}) 3421, 3050, 2867, 1625, 1543, 1501, 1460, 1180. HRMS (ESI) for $C_{14}H_{17}N_2O$ $[M+H]^+$: calcd 229.1341, found 229.1335.

2-Methoxy-*N*-(1-(pyridin-2-yl)ethyl)aniline (3c). Column chromatography on silica gel afforded 97 mg of the desired compound **3c** as a light brown oil (0.425 mmol, yield 85%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.59 (td, *J* = 7.7, 1.8 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.13 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 6.76 (td, *J* = 6.7, 5.6, 1.5 Hz, 1H), 6.70 (dd, *J* = 7.7, 1.5 Hz, 1H), 6.62 (td, *J* = 7.7, 1.6 Hz, 1H), 6.36 (dd, *J* = 7.7, 1.6 Hz, 1H), 4.87 (s, 1H), 4.61 (q, *J* = 6.8 Hz, 1H), 3.89 (s, 3H), 1.59 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5(Cq), 149.3(CH), 146.8(Cq), 137.1(Cq), 136.9(CH), 121.9(CH), 121.2(CH), 120.1(CH), 116.6(CH), 111.0(CH), 109.4(CH), 55.5(OCH_3), 54.9 (CH), 23.4 (CH_3). IR (ν, cm^{-1}) 3420, 3013, 2876, 1599, 1540, 1507, 1486, 1190. HRMS (ESI) for $C_{14}H_{17}N_2O$ $[M+H]^+$: calcd 229.1341, found 229.1342.

4-Methyl-*N*-(1-(pyridin-2-yl)ethyl)aniline (3d). Column chromatography on silica gel afforded 74 mg of the desired compound **3d** as a colerless oil (0.35 mmol, yield 70%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 – 8.52 (m, 1H), 7.60 (tt, *J* = 7.8, 1.3 Hz, 1H), 7.35 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.13 (ddt, *J* = 7.2, 4.9, 1.1 Hz, 1H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.49 (d, *J* = 8.1 Hz, 2H), 4.60 (q, *J* = 6.7 Hz, 1H), 4.32 (s, 1H), 2.20 (s, 3H), 1.54 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2 (Cq), 149.3(CH), 144.9 (Cq), 136.9(CH), 129.7 (2CH), 126.6 (Cq), 122.0 (CH), 120.4 (CH), 113.7 (2CH), 55.1 (CH), 23.3 (CH_3), 20.4 (CH). IR (ν, cm^{-1}) 3421, 3061, 2891, 1603, 1555, 1502, 1488. HRMS (ESI) for $C_{14}H_{17}N_2$ $[M+H]^+$: calcd 213.1392, found 213.1388.

3,5-Dimethoxy-*N*-(1-(pyridin-2-yl)ethyl)aniline (3e). Column chromatography on silica gel afforded 95 mg of the desired compound **3e** as a brown solid (0.37 mmol, yield 74%). m.p. = 83-85 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 7.61 (tt, *J* = 7.6, 1.4 Hz, 1H), 7.33 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.13 (ddt, *J* = 7.3, 4.9, 1.2 Hz, 1H), 5.83 (t, *J* = 2.1 Hz, 1H), 5.76 (d, *J* = 2.2 Hz, 2H), 4.60 (q, *J* = 6.8 Hz, 1H), 4.52 (s, 1H), 3.68 (s, 6H), 1.53 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8(Cq), 161.7(Cq), 149.4(CH), 149.1(Cq), 136.9(CH), 122.1(CH), 120.5(CH), 92.4(2CH), 90.1(CH), 55.2(2OCH_3), 54.7(CH), 23.2(CH_3). IR (ν, cm^{-1}) 3413, 3032, 2890, 1602, 1524, 1498, 1440, 1199. HRMS (ESI) for $C_{15}H_{19}N_2O_2$ $[M+H]^+$: calcd 259.1447, found 259.1454.

3,4,5-Trimethoxy-*N*-(1-(pyridin-2-yl)ethyl)aniline (3f). Column chromatography on silica gel afforded 119 mg of the desired compound **3f** as a brown oil (0.415 mmol, yield 83%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 – 8.51 (m, 1H), 7.64 (td, *J* = 7.6, 1.8 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.16 (dd, *J* = 7.5, 4.9 Hz, 1H), 5.80 (s, 2H), 4.58 (q, *J* = 6.7 Hz, 1H), 3.72 (s, 9H), 1.54 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2 (Cq), 153.9 (Cq), 149.3(CH), 144.0 (Cq), 137.1 (CH), 122.2 (CH), 120.5 (CH), 91.2 (2CH), 61.2 (CH_3), 56.0(2 CH_3), 55.4 (CH), 23.32 (CH_3). IR (ν, cm^{-1}) 3422, 3080, 2912, 1624, 1509, 1489, 1430, 1187. HRMS (ESI) for $C_{16}H_{21}N_2O_3$ $[M+H]^+$: calcd 289.1552, found 289.1553.

***N*-(1-(Pyridin-2-yl)ethyl)aniline (3g)[29].** Column chromatography on silica gel afforded 86 mg of the desired compound **3g** as a colorless oil (0.435 mmol, yield 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.61 (td, *J* = 7.8, 1.7 Hz, 1H), 7.35 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.13 (m, 3H), 6.66 (t, *J* = 7.4, 1H), 6.57 (d, *J* = 7.4, 2H), 4.63 (q, *J* = 6.7 Hz, 1H), 4.46 (s, 1H), 1.55 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz) δ 164.0 (Cq), 149.4 (CH), 147.2 (Cq), 137.0 (CH), 129.3 (2CH), 122.1 (CH), 120.4 (CH), 117.5 (CH), 113.5 (2CH), 54.9, 23.34. IR (ν, cm^{-1}) 3407, 3051, 2869, 1603, 1570, 1503, 1473. HRMS (ESI) for $C_{13}H_{15}N_2$ $[M+H]^+$: calcd 199.1235, found 199.1238.

4-Fluoro-*N*-(1-(pyridin-2-yl)ethyl)aniline (3h). Column chromatography on silica gel afforded 81 mg of the desired compound **3h** as colorless oil (0.375 mmol, yield 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (dt, *J* = 4.8, 1.2 Hz, 1H), 7.60 (td, *J* = 7.7, 1.2 Hz, 1H), 7.31 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.14 (ddt, *J* = 7.6, 4.8, 1.2 Hz, 1H), 6.86 – 6.71 (m, 2H), 6.55 – 6.41 (m, 2H), 4.54 (q, *J* = 6.7 Hz, 1H), 4.36 (s, 1H), 1.52 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz) δ 163.8 (Cq), 155.9 (Cq, d, *J* = 234.9 Hz), 149.5 (CH), 143.6 (Cq), 137.0 (CH), 122.2 (CH), 120.5 (CH), 115.7 (CH, d, *J* = 22.3 Hz), 114.4 (CH, d, *J* = 7.3 Hz), 55.5 (CH), 23.3 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$) δ -130.58. IR (ν, cm^{-1}) 3422, 3058, 2898, 1601, 1578, 1501, 1474. HRMS (ESI) for $C_{13}H_{14}N_2F$ $[M+H]^+$: calcd 217.1141, found 217.1143.

1-(4-((1-(Pyridin-2-yl)ethyl)amino)phenyl)ethan-1-one (3i). Column chromatography on silica gel afforded 86 mg of the desired compound **3i** as a light brown solid (0.36 mmol, yield 72%). m.p. = 120-122 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.8, 1.7 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 2H), 7.64 (td, *J* = 7.6, 1.7 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.18 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.55 (d, *J* = 8.7 Hz, 2H), 5.20 (d, *J* = 6.5 Hz, 1H), 4.71 (p, *J* = 6.5 Hz, 1H), 2.46 (s, 3H), 1.57 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.5 (C=O), 162.6 (Cq), 151.1 (Cq), 149.5 (CH), 137.10 (CH), 130.9 (2 CH), 126.9 (Cq), 122.4 (CH), 120.5 (CH), 112.2 (2CH), 54.1 (CH), 26.1 (CH_3), 23.0 (CH_3). IR (ν, cm^{-1}) 3325, 2971, 1652, 1599, 1528, 1474, 1277. HRMS (ESI) for $C_{15}H_{17}N_2O$ $[M+H]^+$: calcd 241.1341, found 241.1332.

1-(3-((1-(Pyridin-2-yl)ethyl)amino)phenyl)ethan-1-one (3j). Column chromatography on silica gel afforded 83 mg of the desired compound **3j** as a light brown solid (0.345 mmol, yield 69%). m.p. = 63-65 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 – 8.50 (m, 1H), 7.62 (td, *J* = 7.6, 1.6 Hz, 1H), 7.32 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.25 – 7.10 (m, 4H), 6.74 (ddd, *J* = 7.4, 2.3, 1.2 Hz, 1H), 4.89 – 4.55 (m, 2H), 2.50 (d, *J* = 0.8 Hz, 3H), 1.55 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6(Cq), 163.2(Cq), 149.4(CH), 147.4(Cq), 138.1(Cq), 136.9(CH), 129.4(CH), 122.2(CH), 120.6(C), 118.1(CH), 117.7(CH), 112.6(CH), 54.5(CH), 26.7(CH_3), 23.1(CH_3). IR (ν, cm^{-1}) 3330, 2954, 1663, 1598, 1524, 1482, 1270. HRMS (ESI) for $C_{15}H_{17}N_2O$ $[M+H]^+$: calcd 241.1341, found 241.1347.

4-Bromo-*N*-(1-(pyridin-2-yl)ethyl)aniline (3k). Column chromatography on silica gel afforded 97 mg of the desired compound **3k** as a colorless oil(0.35 mmol, yield 70%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 4.6, 1.2 Hz, 1H), 7.62 (td, *J* = 7.7, 1.2 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.22 – 7.12 (m, 3H), 6.44 (d, *J* = 8.3 Hz, 2H), 4.56 (q, *J* = 6.8 Hz, 1H), 1.53 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4 (C), 149.5 (CH), 146.2 (C), 137.0 (CH), 132.0 (2CH), 122.3 (CH), 120.5 (CH), 115.1 (2CH), 109.1 (C), 54.8 (CH), 23.2 (CH_3). IR (ν, cm^{-1}) 3300, 2969, 1593, 1571, 1498, 1434.HRMS (ESI) for $C_{13}H_{14}N_2Br$ $[M+H]^+$: calcd 277.0340, found 277.0333.

4-((1-(Pyridin-2-yl)ethyl)amino)phenol (3l). Column chromatography on silica gel afforded 63 mg of the desired compound **3l** as a black solid (0.295 mmol, yield 59%). m.p. = 139-141 °C. ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.58 – 8.45 (m, 1H), 7.73 – 7.59 (m, 1H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.24 – 7.09 (m, 1H), 6.56 (d, *J* = 8.5 Hz, 2H), 6.45 (d, *J* = 8.5 Hz, 2H), 4.50 (q, *J* = 6.8 Hz, 1H), 1.45 (d, *J* = 6.7 Hz,

3H). ^{13}C NMR (75 MHz, Acetone-d_6) δ 149.8 (CH), 148.8 (Cq), 142.0 (2Cq), 137.3 (CH), 122.5 (CH), 120.9 (CH), 116.4 (CH), 115.4 (CH), 56.3 (CH), 23.3 (CH_3). IR (ν, cm^{-1}) 3402, 2974, 1584, 1562, 1495, 1420. HRMS (ESI) for $C_{13}H_{15}N_2O$ $[M+H]^+$: calcd 215.1184, found 215.1180.

2-(4-((1-(Pyridin-2-yl)ethyl)amino)phenyl)ethan-1-ol (3m). Column chromatography on silica gel afforded 94 mg of the desired compound **3m** as a brown solid (0.39 mmol, yield 78%). m.p. = 93-95 °C. ^{1}H NMR (300 MHz, Acetone-*d6*) δ 8.52 (d, *J* = 3.8 Hz, 1H), 7.67 (td, *J* = 7.7, 1.7 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.18 (dd, *J* = 7.3, 4.8 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 2H), 6.50 (d, *J* = 8.4 Hz, 2H), 5.32 (d, *J* = 5.2 Hz, 1H), 4.62 – 4.53 (m, 1H), 3.62 (dt, *J* = 12.6, 6.4 Hz, 2H), 3.48 (t, *J* = 5.4 Hz, 1H), 2.61 (t, *J* = 7.2 Hz, 2H), 1.48 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, Acetone-*d6*) δ 165.9 (Cq), 150.0 (CH), 147.2 (Cq), 137.5 (CH), 130.3 (2CH), 128.2 (Cq), 122.7 (CH), 120.9 (CH), 114.1 (2CH), 64.5 (CH_2), 55.7 (CH), 39.6 (CH_2), 23.3 (CH_3). HRMS (ESI) for $C_{15}H_{19}N_2O$ $[M+H]^+$: calcd 243.1497, found 243.1492.

***N*-(1-(Pyridin-2-yl)ethyl)-2,3-dihydro-1H-inden-4-amine (3n).** Column chromatography on silica gel afforded 93 mg of the desired compound **3n** as a brown oil (0.39 mmol, yield 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.57 (td, *J* = 7.7, 1.8 Hz, 1H), 7.36 – 7.28 (m, 1H), 7.10 (ddt, *J* = 7.2, 4.9, 1.1 Hz, 1H), 6.91 (t, *J* = 7.7 Hz, 1H), 6.59 (d, *J* = 7.4 Hz, 1H), 6.22 (d, *J* = 8.0 Hz, 1H), 4.64 (q, *J* = 6.7 Hz, 1H), 4.23 (s, 1H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.77 (t, *J* = 7.4 Hz, 2H), 2.10 (p, *J* = 7.4 Hz, 2H), 1.55 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0(Cq), 149.2(CH), 144.8(Cq), 143.3(Cq), 136.8(CH), 128.3(Cq), 127.4(CH), 121.9(CH), 120.2(CH), 113.6(CH), 108.4(CH), 54.7(CH), 33.4(CH_2), 29.5(CH_2), 24.5(CH_2), 23.3(CH_3). IR (ν, cm^{-1}) 3340, 3072, 2891, 1603, 1559 1501, 1466. HRMS (ESI) for $C_{16}H_{19}N_2$ $[M+H]^+$: calcd 239.1548, found 239.1541.

***N*-(1-(Pyridin-2-yl)ethyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-amine (3o).** Column chromatography on silica gel afforded 104 mg of the desired compound **3o** as brown solid (0.41 mmol, yield 82%). m.p. = 96-98 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.60 (td, *J* = 7.7, 1.8 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.12 (dd, *J* = 7.7, 5.0 Hz, 1H), 6.63 (d, *J* = 9.4 Hz, 1H), 6.14 – 6.08 (m, 2H), 4.50 (q, *J* = 6.7 Hz, 1H), 4.20 – 4.08 (m, 4H), 1.50 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1 (Cq), 149.4 (CH) , 144.0 (Cq), 142.2 (Cq), 136.9 (CH), 135.7 (Cq), 122.0 (CH), 120.5 (CH), 117.6 (CH), 107.4 (CH), 102.3 (CH), 64.8 (CH_2), 64.2 (CH_2), 55.5 (CH), 23.3 (CH_3). IR (ν, cm^{-1}) 3325, 2970, 2869, 1592, 1506, 1453, 1217. HRMS (ESI) for $C_{15}H_{17}N_2O_2$ $[M+H]^+$: calcd 257.1290, found 257.1282.

2-Fluoro-4-methoxy-*N*-(1-(pyridin-2-yl)ethyl)aniline (3p). Column chromatography on silica gel afforded 85 mg of the desired compound **3p** as a light brown solid (0.345 mmol, yield 69%). m.p. = 113-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.62 (td, *J* = 7.7, 1.7 Hz, 1H), 7.31 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.15 (ddd, *J* = 7.7, 4.9, 1.0 Hz, 1H), 6.75 (t, *J* = 9.1 Hz, 1H), 6.36 (dd, *J* = 13.4, 2.6 Hz, 1H), 6.25 (ddd, *J* = 8.9, 2.6, 1.2 Hz, 1H), 4.51 (q, *J* = 6.7 Hz, 1H), 4.30 (s,1H), 3.76 (s, 3H), 1.52 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.63 (C), 153.53 (d, *J* = 243.6 Hz, C), 149.48 (CH), 142.38 (d, *J* = 9.2 Hz, C), 139.51 (d, *J* = 11.1 Hz, C), 122.21, 120.51, 115.97 (d, *J* = 2.8 Hz, CH), 108.73 (d, *J* = 2.6 Hz, CH), 102.62 (d, *J* = 22.0 Hz, CH), 57.59 (OCH_3), 55.41 (CH), 23.26 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$) δ -136.12. IR (ν, cm^{-1}) 3358, 3020, 2914, 1588, 1543, 1504, 1462, 1180. HRMS (ESI) for $C_{14}H_{16}N_2OF$ $[M+H]^+$: calcd 247.1247, found 247.1251.

***N*-Methyl-*N*-(1-(pyridin-2-yl)ethyl)aniline (3q).** Column chromatography on silica gel afforded 85 mg of the desired compound **3q** as a colorless oil (0.4 mmol, yield 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 – 8.57 (m, 1H), 7.59 (td, *J* = 7.7, 1.9 Hz, 1H), 7.29 – 7.18 (m, 3H), 7.14 (dd, *J* = 7.5, 4.9 Hz, 1H), 6.87 – 6.79 (m, 2H), 6.72 (ddd, *J* = 8.3, 6.7, 1.1 Hz, 1H), 5.13 (q, *J* = 6.9 Hz, 1H), 2.80 (s, 3H), 1.63 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5(Cq), 150.1(Cq), 149.2(CH), 136.6(CH), 129.3(2CH), 121.9(CH), 121.6(2CH), 116.9(CH), 113.2 (CH), 59.1(CH), 32.4(CH_3), 16.3(CH_3). IR (ν, cm^{-1}) 3064, 2878, 1589, 1555, 1506, 1487. HRMS (ESI) for $C_{14}H_{17}N_2$ $[M+H]^+$: calcd 213.1392, found 213.1397.

1-(1-(Pyridin-2-yl)ethyl)-1,2,3,4-tetrahydroquinoline (3r)[30]. Column chromatography on silica gel afforded 89 mg of the desired compound **3r** as a colorless oil (0.375 mmol, yield 75%). ^{1}H NMR (300 MHz, , $CDCl_3$) δ 8.61 (d, *J* = 5.0 Hz, 1H), 7.60 (td, *J* = 7.6, 1.8 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.15 (dd, *J* = 7.6, 5.0 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 2H), 6.60 (q, *J* = 7.8, 7.3 Hz, 2H), 5.12 (q, *J* = 7.0 Hz, 1H), 3.34 (ddd, *J* = 12.3, 8.3, 4.2 Hz, 1H), 3.19 (dt, *J* = 11.2, 5.0 Hz, 1H), 2.80 (t, *J* = 6.5 Hz, 2H), 1.94 (tq, *J* = 12.9, 7.6, 5.8 Hz, 2H), 1.68 (d, *J* = 7.0 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7 (C), 149.3 (CH), 145.5 (C), 136.6 (CH), 129.3 (CH), 127.2 (CH), 123.1 (C), 121.9 (CH), 121.4 (CH), 115.9 (CH), 111.1 (CH), 57.7 (CH), 43.4 (CH_2), 28.6 (CH_2), 22.6 (CH_2), 16.2 (CH_3). IR (ν, cm^{-1}) 3052, 2912, 1579, 1502, 1499, 1487. HRMS (ESI) for $C_{16}H_{19}N_2$ $[M+H]^+$: calcd 238.1548, found 239.1543.

4-(1-(pyridin-2-yl)ethyl)morpholine (3t). Column chromatography on silica gel afforded 34 mg of the desired compound **3s** as a light yellow oil (0.175 mmol, yield 35%). ^{1}H NMR (300 MHz, MeOD) δ 8.51 (d, *J* = 4.9 Hz, 1H), 7.85 (t, *J* = 7.7 Hz, 1H), 7.60 – 7.51 (m, 1H), 7.38 – 7.27 (m, 1H), 3.71 (t, *J*= 4.7 Hz, 4H) 3.55 (q, *J* = 6.8 Hz, 1H), 2.67 – 2.53 (m, 2H), 2.46-2.33 (m, 2H), 1.42 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, MeOD).δ 158.26 (C), 149.5 (CH), 138.8(CH), 123.9(CH), 123.7(CH), 67.9 (2CH_2), 67.7(CH), 52.3(2CH_2), 18.7(CH_3). IR (ν, cm^{-1}) 3152, 3066, 2888, 1560, 1505, 1488, 1201. HRMS (ESI) for $C_{11}H_{17}N_2O$ $[M+H]^+$: calcd 193.1341, found 193.1338.

N-benzyl-1-(pyridin-2-yl)ethan-1-amine (3u).[31] Column chromatography on silica gel afforded 42 mg of the desired compound 3t as a colorless oil (0.2 mmol, yield 40%). ^{1}H NMR (300 MHz, , $CDCl_3$) δ 8.58 (d, *J* = 4.9 Hz, 1H), 7.66 (dt, *J* = 7.4, 1.2, 1H), 7.37 – 7.28 (m, 5H), 7.25 – 7.13 (m, 2H), 3.93 (q, *J* = 6.7 Hz, 1H), 3.65 (s, 2H), 1.41 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4 (C), 149.4(CH), 140.5 (C), 136.7(CH), 128.5(2CH), 128.3(2CH), 127.0(CH), 122.1(CH), 121.4(CH), 58.8(CH), 51.8(CH_2), 23.0(CH_3). IR (ν, cm^{-1}) 3389, 3140, 3012, 2915, 1600, 1545, 1469. HRMS (ESI) for $C_{14}H_{17}N_2$ $[M+H]^+$: calcd 213.1392, found 213.1388.

***N*-(1-(5-Methylpyridin-2-yl)ethyl)aniline (3v).** Column chromatography on silica gel afforded 82 mg of the desired compound **3v** as a light brown solid (0.385 mmol, yield 77%). m.p. = 80-82 °C. ^{1}H NMR (300 MHz, , $CDCl_3$) δ 8.40 (d, *J* = 2.2 Hz, 1H), 7.41 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 2H), 6.65 (t, *J* = 7.7 Hz, 1H), 6.56 (d, *J* = 7.7 Hz, 2H), 4.59 (q, *J* = 6.7 Hz, 1H), 4.43 (s, 1H), 2.30 (s, 3H), 1.53 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1 (C), 149.7 (CH), 147.3 (C), 137.5 (CH), 131.4 (C), 129.2 (2CH), 119.9 (CH), 117.4 (CH), 113.5 (2CH), 54.5 (CH), 23.4 (CH_3), 18.2 (CH_3).). IR (ν, cm^{-1}) 3361, 3010, 2915, 1605, 1556, 1466. HRMS (ESI) for $C_{14}H_{17}N_2$ $[M+H]^+$: calcd 213.1392, found 213.1390.

4-Methoxy-*N*-(1-(5-methylpyridin-2-yl)ethyl)aniline (3w). Column chromatography on silica gel afforded 97 mg of the desired compound **3w** as a light yellow solid (0.4 mmol, yield 80%). m.p. = 111-113 °C. ^{1}H NMR (300 MHz, , $CDCl_3$) δ 8.38 (d, *J* = 1.9 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 6.70 (d, *J* = 8.9 Hz, 2H), 6.52 (d, *J* = 8.9 Hz, 2H), 4.51 (q, *J* = 6.7 Hz, 1H), 4.15 (s, 1H), 3.69 (s, 3H), 2.29 (s, 3H), 1.50 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3 (Cq), 152.1 (Cq), 149.7 (CH), 141.5 (Cq), 137.5 (CH), 131.4 (Cq), 120.0 (CH), 114.9 (4CH), 55.8 (OCH_3), 55.4 (CH), 23.4 (CH_3), 18.2 (CH3). IR (ν, cm^{-1}) 3340, 3000, 2926, 1602, 1511, 1442, 1295. HRMS

(ESI) for $C_{15}H_{19}N_2O$ $[M+H]^+$: calcd 243.1497, found 243.1488.

***N*-(1-(5-Bromopyridin-2-yl)ethyl)aniline (3x).** Column chromatography on silica gel afforded 115 mg of the desired compound **3x** as an yellow oil (0.415 mmol, yield 83%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (d, *J* = 2.4 Hz, 1H), 7.73 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.69 (t, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 4.58 (q, *J* = 6.8 Hz, 1H), 1.54 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9 (C), 150.5 (CH), 147.0 (C), 139.5 (CH), 129.4 (2CH), 121.8 (CH), 118.8 (C), 117.9 (CH), 113.6 (2CH), 54.6 (CH), 23.3 (CH_3). IR (ν, cm^{-1}) 3322, 3076, 2899, 1607, 1577, 1498. .HRMS (ESI) for $C_{13}H_{14}N_2Br$ $[M+H]^+$: calcd 277.0340, found 277.0348.

***N*-(1-(5-Bromopyridin-2-yl)ethyl)-4-methoxyaniline (3y).** Column chromatography on silica gel afforded 124 mg of the desired compound **3y** as a yellow oil (0.405 mmol, yield 81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.3 Hz, 1H), 7.71 (dt, *J* = 8.3, 2.3 Hz, 1H), 7.26 (d, *J* = 8.3 Hz, 1H), 6.71 (d, *J* = 8.9 Hz, 2H), 6.50 (d, *J* = 8.9 Hz, 2H), 4.50 (q, *J* = 6.7 Hz, 1H), 3.70 (s, 3H), 1.51 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1 (C), 152.4 (C), 150.5 (CH), 141.1 (C), 139.5 (CH), 121.9 (CH), 118.8 (C), 114.9 (4CH), 55.8 (OCH_3), 55.4 (CH), 23.3 (CH_3). IR (ν, cm^{-1}) 3401, 3055, 2901, 1602, 1589, 1533, 1484. 1276. HRMS (ESI) for $C_{14}H_{16}N_{2O}Br$ $[M+H]^+$: calcd 307.0446, found 307.0443.

***N*-(1-(5-Bromopyridin-2-yl)ethyl)-4-fluoroaniline (3z).** Column chromatography on silica gel afforded 110 mg of the desired compound **3z** as a colorless oil (0.375 mmol, yield 75%). ^{1}H NMR (300 MHz , $CDCl_3$) δ 8.56 (d, *J* = 4.8 Hz, 1H), 7.61 (td, *J* = 7.7, 1.8 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.23 (m, 2H), 7.14 (dd, *J* = 7.5, 5.0 Hz, 1H), 4.53 (q, *J* = 7.1 Hz, 1H), 1.71 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2 (C), 156.29 (C, d, *J* = 234.9 Hz), 149.8 (CH), 143.9 (2C), 122.6 (CH), 120.8 (CH), 116.09 (CH, d, *J* = 22.3 Hz), 114.81 (CH, d, *J* = 7.3 Hz), 55.8 (CH), 23.7 (CH3). ^{19}F NMR (376 MHz, $CDCl_3$) δ -127.57. IR (ν, cm^{-1}) 3371, 3103, 2945, 1609, 1525, 1503. HRMS (ESI) for $C_{13}H_{13}N_2BrF$ $[M+H]^+$: calcd 295.0246, found 295.0238.

***N*-(1-(6-bromopyridin-2-yl)ethyl)-4-methoxyaniline (3aa).** Column chromatography on silica gel afforded 132 mg of the desired compound **3aa** as a colorless oil (0.43 mmol, yield 86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (td, *J* = 7.9, 0.8 Hz, 1H), 7.35 – 7.28 (m, 2H), 6.71 (d, *J* = 9.0 Hz, 2H), 6.49 (d, *J* = 9.2 Hz, 2H), 4.51 (q, *J* = 6.7 Hz, 1H), 4.01 (s, 1H), 3.70 (s, 3H), 1.52 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4 (C), 152.4 (C), 141.8 (C), 141.1 (C), 139.2 (CH), 126.3 (CH), 119.1 (CH), 115.0 (2CH), 114.9 (2CH), 55.8 (OCH3), 55.5 (CH), 23.3 (CH3). IR (film) 3390, 2973, 2922, 1582, 1554, 1514, 1436, 1235. . HRMS (ESI) for $C_{14}H_{16}N_{2O}Br$ $[M+H]^+$: calcd 307.0446, found 307.0449.

4-methoxy-N-(1-(4-methylpyridin-2-yl)ethyl)aniline (3ab). Column chromatography on silica gel afforded 102 mg of the desired compound **3ab** as a colorless oil (0.42 mmol, yield 84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 5.0 Hz, 1H), 7.15 (s, 1H), 6.95 (d, *J* = 4.9 Hz, 1H), 6.70 (d, *J* = 9.0 Hz, 2H), 6.53 (d, *J* = 9.0 Hz, 2H), 4.50 (q, *J* = 6.7 Hz, 1H), 3.70 (s, 3H), 2.29 (s, 3H), 1.50 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1 (C), 152.1 (C), 149.1 (CH), 148.0 (C), 141.6 (C), 123.1 (CH), 121.3 (CH), 114.9 (4CH), 55.8 (OCH3), 55.7 (CH), 23.3 (CH3), 21.2 (CH3). IR (film) 3385, 2966, 2929, 1577, 1550, 1517, 1438, 1236. HRMS (ESI) for $C_{15}H_{19}N_2O$ $[M+H]^+$: calcd 243.1497, found 243.1498.

2-(phenylamino)-2-(pyridin-2-yl)acetic acid(3ac). Column chromatography on silica gel afforded 52 mg of the desired compound **3ac** as a light yellow oil (0.22 mmol, yield 44%). ^{1}H NMR (300 MHz, MeOD-d_4) δ 8.49 (d, *J* = 5.0 Hz, 1H), 7.82 – 7.71 (m, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 6.4 Hz, 1H), 7.11 – 6.99 (m, 2H), 6.65 – 6.51 (m, 3H), 4.44 (s, 1H). ^{13}C NMR (75 MHz, MeOD) δ 162.1 (CO), 149.5 (CH), 148.4 (C), 138.7 (CH), 137.2 (C), 129.9 (2CH), 123.5 (CH), 118.1 (CH), 113.9 (2CH), 66.0 (CH3).IR (film) 3376, 2998, 2977, 1582, 1567, 1530, 1444.HRMS (ESI) for $C_{13}H_{13}N_2O_2$[M+H]$^+$: calcd 229.0977, found 229.0969.

Methyl 2-(phenylamino)-2-(pyridin-2-yl)acetate (3ad). Column chromatography on silica gel afforded 59 mg of the desired compound **3ad** as a yellow oil (0.245 mmol, yield 49%).^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (dt, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.68 (td, *J* = 7.7, 1.8 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.28 – 7.20 (m, 1H), 7.15 (t, *J* = 8.0 Hz, 2H), 6.73 (t, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 7.7 Hz, 2H), 5.43 (s, 1H), 5.28 (s, 1H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9 (CO), 156.4(C), 149.6(CH), 146.1 (C), 137.2 (CH), 129.4 (2CH), 123.3 (CH), 122.1 (CH), 118.4 (CH), 113.6 (2CH), 62.4 (CH), 52.9 (OCH3). IR (film) 3249, 2988, 2976, 1720, 1572, 1567, 1535, 1440. HRMS (ESI) for $C_{14}H_{15}N_2O_2$[M+H]$^+$: calcd 243.1134, found 243.1139.

Methyl 2-((4-methoxyphenyl)amino)-2-(pyridin-2-yl)acetate (3ae). Column chromatography on silica gel afforded 69 mg of the desired compound **3ae** as a light yellow oil (0.255 mmol, yield 51%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (dt, *J* = 5.0, 1.9, 1.0 Hz, 1H), 7.67 (td, *J* = 7.7, 1.7 Hz, 1H), 7.47 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.22 (ddt, *J* = 7.1, 4.8, 1.1 Hz, 1H), 6.74 (d, *J* = 8.7 Hz, 2H), 6.62 (d, *J* = 8.9 Hz, 2H), 5.21 (s, 1H), 5.14 (s, 1H), 3.71 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0 (CO), 156.6 (C), 152.8 (C), 149.6 (CH), 140.2 (C), 137.1 (CH), 123.2 (CH), 122.2 (CH), 115.0 (4CH), 63.3 (CH), 55.7 (OCH3), 52.8 (OCH3). IR (film) 3236, 2990, 2976, 1722, 1569, 1550, 1535, 1449. HRMS (ESI) for $C_{15}H_{17}N_2O_3$[M+H]$^+$: calcd 273.1239, found 273.1245.

Methyl 2-((4-fluorophenyl)amino)-2-(pyridin-2-yl)acetate (3af). Column chromatography on silica gel afforded 52 mg of the desired compound **3af** as a yellow oil (0.2 mmol, yield 40%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.9 Hz, 1H), 7.68 (td, *J* = 7.5, 1.5 Hz, 1H), 7.46 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.30 – 7.21 (m, 1H), 6.91 – 6.80 (m, 2H), 6.64 – 6.52 (m, 2H), 5.33 (d, *J* = 7.2 Hz, 1H), 5.21 (d, *J* = 7.1 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8 (CO), 156.4 (d, *J* = 236.3 Hz), 156.1 (C), 149.6 (CH), 142.5 (C), 137.2 (CH), 123.4 (CH), 122.2 (CH), 115.90 (d, *J* = 22.5 Hz), 114.63 (d, *J* = 7.4 Hz), 62.9 (CH), 52.8 (OCH3). ^{19}F NMR (188 MHz, $CDCl_3$) δ -126.98. IR (film) 3256, 2991, 2975, 1725, 1601, 1567, 1544, 1451. HRMS (ESI) for $C_{14}H_{14}N_2O_2F$[M+H]$^+$: calcd 261.1039, found 261.1036.

***N*-(Phenyl(pyridin-2-yl)methyl)aniline (3ag)[32].** Column chromatography on silica gel afforded 49 mg of the desired compound **3ag** as a colorless oil (0.19 mmol, yield 38%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (d, *J* = 4.2 Hz, 1H), 7.67 (td, *J* = 7.7, 1.9 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.44 – 7.32 (m, 3H), 7.30 (d, *J* = 7.1 Hz, 1H), 7.24 – 7.12 (m, 3H), 6.77 – 6.64 (m, 3H), 5.63 (d, *J* = 4.6 Hz, 1H), 5.50 (d, *J* = 4.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0(Cq), 149.3(CH), 147.1(Cq), 142.6(Cq), 136.9(CH), 129.2(CH), 128.9(CH), 127.6(CH), 127.5(CH), 122.3(CH), 122.0(CH), 117.6(CH), 113.7(CH), 63.4(CH). IR (ν, cm^{-1}) 3398, 3061, 2888, 1606, 1599, 1576, 1533, 1498, 1474. HRMS (ESI) for $C_{18}H_{17}N_2$ $[M+H]^+$: calcd 261.1392, found 261.1394.

4-Methoxy-*N*-(phenyl(pyridin-2-yl)methyl)aniline (3ah)[32]. Column chromatography on silica gel afforded 60 mg of the desired compound **3ah** as a yellow oil (0.205 mmol, yield 41%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 – 8.53 (m, 1H), 7.61 (td, *J* = 7.8, 1.8 Hz, 1H), 7.45 (d, *J* = 7.1 Hz, 2H), 7.39 – 7.28 (m, 3H), 7.27 – 7.22 (m, 1H), 7.15 (dd, *J* = 7.4, 4.9 Hz, 1H), 6.71 (d, *J* = 8.9 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 5.51 (s, 1H), 5.13 (s, 1H), 3.70 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3 (C), 152.2(C), 149.3 (CH), 142.7 (C), 142.4 (CH), 141.4 (C), 136.9 (CH), 128.9 (2CH), 127.6 (CH), 127.5 (2CH), 122.2 (CH), 122.0 (CH), 114.9 (2CH), 114.9 (CH), 64.3 (CH), 55.8 (OCH_3). HRMS (ESI) for $C_{19}H_{19}N_2O$ $[M+H]^+$: calcd 291.1497, found 291.1494.

4-Fluoro-*N*-(phenyl(pyridin-2-yl)methyl)aniline (3ai). Column chromatography on silica gel afforded 49 mg of the desired compound **3ai** as a yellow oil (0.175 mmol, yield 35%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, *J* = 4.7 Hz, 1H), 7.63 (td, *J* = 7.7, 1.8 Hz, 1H), 7.47 (dd, *J* = 7.5, 1.8 Hz, 2H), 7.40 – 7.28 (m, 3H), 7.30 – 7.25 (m, 1H), 7.18 (dd, *J* = 7.5, 4.9 Hz, 1H), 6.88 – 6.80 (m, 2H), 6.61 – 6.53 (m, 2H), 5.53 (d, *J* = 3.6 Hz, 1H), 5.44 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8 (Cq), 155.9.5 (Cq, d, *J* = 234 Hz), 149.2(CH), 143.5 (Cq), 142.4 (Cq), 136.9 (CH), 129.0 (2CH), 127.7 (CH), 127.4 (2CH), 122.4(CH), 122.0 (CH), 115.66 (CH, d, *J* = 22.3 Hz), 114.53 (CH, d, *J* = 7.4 Hz), 63.9 (CH). ^{19}F NMR (188 MHz, $CDCl_3$) δ -128.09. . IR (ν, cm^{-1}) 3386, 3122, 2919, 1603, 1586, 1520, 1488. HRMS (ESI) for $C_{18}H_{16}N_2F$ $[M+H]^+$: calcd 279.1298, found 279.1298.

***N*-(Pyridin-2-ylmethyl)aniline (3aj)[33].** Column chromatography on silica gel afforded 73 mg of the desired compound **3aj** as a yellow oil (0.175 mmol, yield 79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 5.0, 1.6 Hz, 1H), 7.64 (tt, *J* = 7.7, 1.3 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.23 – 7.14 (m, 3H), 6.73 (td, *J* = 7.3, 1.3 Hz, 1H), 6.67 (dd, *J* = 7.4, 1.3 Hz, 2H), 4.47 (s, 2H), 4.31 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6 (C), 149.2 (CH), 147.9 (C), 136.7 (CH), 129.3 (2CH), 122.1 (CH), 121.6 (CH), 117.6 (CH), 113.1 (2CH), 49.3 (CH_2). IR (ν, cm^{-1}) 3330, 3120, 3010, 2920, 1610, 1544, 1477. HRMS (ESI) for $C_{12}H_{13}N_2$ $[M+H]^+$: calcd 185.1079, found 185.1080.

4-Methoxy-*N*-(pyridin-2-ylmethyl)aniline (3ak)[34]. Column chromatography on silica gel afforded 80 mg of the desired compound **3ak** as a yellow oil (0.375 mmol, yield 75%). ^{1}H NMR (300 MHz , $CDCl_3$) δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.63 (td, *J* = 7.7, 1.8 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.16 (dd, *J* = 7.3, 5.3 Hz, 1H), 6.78 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 4.41 (s, 2H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9(C), 152.3(C), 149.3(CH), 142.2(C), 136.6 (CH), 122.1 (CH), 121.7 (CH), 114.9 (2CH), 114.3 (2CH), 55.8 (CH_2), 50.3 (OCH_3). IR (ν, cm^{-1}) 3345 3111, 3009, 2918, 1599, 1533, 1456, 1209. HRMS (ESI) for $C_{13}H_{15}N_2O$ $[M+H]^+$: calcd 215.1184, found 215.1182.

4-Fluoro-*N*-(pyridin-2-ylmethyl)aniline (3al)[35]. Column chromatography on silica gel afforded 81 mg of the desired compound **3al** as a white solid (0.4 mmol, yield 80%). m.p. = 64-66 °C. ^{1}H NMR (300 MHz , $CDCl_3$) δ 8.58 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.64 (td, *J* = 7.7, 1.8 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.18 (dd, *J* = 7.5, 5.0 Hz, 1H), 6.94 – 6.83 (m, 2H), 6.65 – 6.52 (m, 2H), 4.69 (s, 1H), 4.41 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3(C), 156.05 (C, d, *J* = 235.0 Hz), 149.3 (CH), 144.4(C), 136.7(CH), 122.3 (CH), 121.7 (CH), 115.78 (CH, d, *J* = 22.3 Hz), 113.96 (CH, d, *J* = 7.4 Hz), 50.0 (CH2). ^{19}F NMR (188 MHz, $CDCl_3$) δ -127.99. IR (ν, cm^{-1}) 3280, 3133, 3003, 2899, 1605, 1587, 1520, 1488. HRMS (ESI) for $C_{12}H_{14}N_2F$ $[M+H]^+$: calcd 203.0985, found 203.0979.

***N*^{1},*N*^{1}-Dimethyl-*N*^{4}-(pyridin-2-ylmethyl)benzene-1,4-diamine (3am)[3].** Column chromatography on silica gel afforded 80 mg of the desired compound **3am** as a light orange oil (0.355 mmol, yield 71%).^{1}H NMR (300 MHz , $CDCl_3$) δ 8.57 (d, *J* = 4.8 Hz, 1H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.16 (dd, *J* = 7.4, 5.0 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 2H), 6.65 (d, *J* = 8.4 Hz, 2H), 4.42 (s, 2H), 2.81 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4 (C), 149.2 (CH), 144.3 (C), 140.5 (C), 136.6 (CH), 122.0 (CH), 121.7 (CH), 115.9 (2CH), 114.6 (2CH), 50.5 (CH_2), 42.3 ($2NCH_3$). IR (ν, cm^{-1}) 3351, 3095, 3021, 2887, 1606, 1577, 1502, 1483. HRMS (ESI) for $C_{14}H_{18}N_3$ $[M+H]^+$: calcd 228.1501, found 228.1499.

***N*-(4-Fluorophenyl)picolinamide (3an)[36].** A 10 mL flask was charged with 0.20 mmol of **3al** and 0.006 mmol of rose bengal. After purging the flask with vacuum nitrogen, oxygen atmosphere was introtuced through an O_2 balloon. Finally dry DMF (0.7 mL) and dry DBN solution (0.3mmol, 1 mol/L in DMF) were added. The resulting mixture was stirred for 48 h under blue LED irradiation. The resulting mixture underwent an aqueous workup and was extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Column chromatography on silica gel afforded 26 mg of the desired compound **3ak** as a light brown solid (0.12 mmol, yield 66%). m.p. = 103-105 ºC ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.62 (d, *J* = 4.8 Hz, 1H), 8.30 (d, *J* = 7.8 Hz, 1H), 7.92 (td, *J* = 7.7, 1.6 Hz, 1H), 7.75 (dd, *J* = 9.0, 4.7 Hz, 2H), 7.49 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 7.08 (t, *J* = 8.7 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0(C), 159.5 (C, d, *J* = 249.4 Hz), 150.0 (C), 148.1 (CH), 137.8 (CH), 134.3(C), 126.6 (CH), 122.5 (CH), 121.47 (CH, d, *J* = 7.8 Hz), 115.8 (CH, d, *J* = 24.4 Hz). ^{19}F NMR (188 MHz, $CDCl_3$) δ -118.08. HRMS (ESI) for $C_{12}H_{10}N_2OF$ $[M+H]^+$: calcd 217.0777, found 217.0786.

4-(1-(4-Methoxyphenyl)vinyl)-*N*-(1-(pyridin-2-yl)ethyl)aniline (4a). Column chromatography on silica gel afforded 91 mg of the desired compound **4a** as a yellow oil (0.275 mmol, yield 55%). ^{1}H NMR (300 MHz , $CDCl_3$) δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.63 (td, *J* = 7.7, 1.9 Hz, 1H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.26 (d, *J* = 8.7 Hz, 2H), 7.19 – 7.08 (m, 3H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.52 (d, *J* = 8.6 Hz, 2H), 5.23 (d, *J* = 1.6 Hz, 1H), 5.15 (d, *J* = 1.6 Hz, 1H), 4.64 (q, *J* = 6.6 Hz, 1H), 3.81 (s, 3H), 1.56 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8(C), 159.2 (C), 149.3 (CH), 146.9 (C), 137.1(CH), 130.9 (C), 129.6 (2CH), 129.2 (2CH), 122.1(CH), 120.5 (CH), 113.5 (2CH), 113.0 (2CH), 110.4 (CH2), 55.4 (OCH_3), 54.8 (CH), 23.3 (CH_3). IR (ν, cm^{-1}) 3380, 3110, 2930, 1610, 1519, 1512, 1434, 1247. HRMS (ESI) for $C_{22}H_{23}N_2O$ $[M+H]^+$: calcd 331.1810, found 331.1812.

4-(1-(4-((1-(Pyridin-2-yl)ethyl)amino)phenyl)vinyl)benzonitrile (4b). Column chromatography on silica gel afforded 98 mg of the desired compound **4b** as a yellow oil (0.3 mmol, yield 60%). ^{1}H NMR (300 MHz , $CDCl_3$) δ 8.58 (dd, *J* = 4.8, 1.8 Hz, 1H), 7.68 – 7.55 (m, 3H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.20 – 7.12 (m, 1H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.53 (d, *J* = 8.6 Hz, 2H), 5.43 (s, 1H), 5.26 (s, 1H), 4.64 (q, *J* = 6.8 Hz, 1H), 1.56 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5 (CN), 149.4 (CH), 148.6 (Cq), 147.3 (Cq), 147.1 (Cq), 137.0 (CH), 132.0 (2 CH), 129.1 (4CH), 122.2 (CH), 120.4 (CH), 119.1 (Cq), 113.7 (CH_2), 113.1 (2CH), 111.1 (Cq), 54.7 (CH), 23.2 (CH_3). IR (ν, cm^{-1}) 3386, 3120, 2927, 1609, 1520, 1470. HRMS (ESI) for $C_{22}H_{20}N_3$ $[M+H]^+$: calcd 326.1657, found 326.1660.

4-(1-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)vinyl)-*N*-(1-(pyridin-2-yl)ethyl)aniline (4c). Column chromatography on silica gel afforded 98 mg of the desired compound **4c** as a yellow oil (0.275 mmol, yield 55%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 4.0, 0.7 Hz, 1H), 7.62 (td, *J* = 7.7, 1.3 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.15 – 7.10 (m, 3H), 6.86 (d, *J* = 1.4 Hz, 1H), 6.84 – 6.77 (m, 2H), 6.51 (d, *J* = 8.4 Hz, 2H), 5.22 (s, 1H), 5.15 (s, 1H), 4.67 – 4.60 (m, 1H)), 4.24 (s, 4H), 1.55 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9 (Cq), 149.4 (CH), 149.2 (Cq), 146.9 (Cq), 143.2 (Cq), 143.1 (Cq), 137.0 (CH), 135.8 (Cq), 130.6 (Cq), 129.3 (2CH), 122.1 (CH), 121.8 (CH), 120.5 (CH), 117.4 (CH), 116.8 (CH), 113.0 (2CH), 110.7 (CH_2), 64.6 (CH_2), 64.5 (CH_2), 54.8 (CH), 23.3 (CH_3). IR (ν, cm^{-1}) 3378, 3115, 2929, 1609, 1518, 1472. HRMS (ESI) for $C_{23}H_{23}N_2O_2$ $[M+H]^+$: calcd 359.1760, found 359.1761.

4-Methoxy-*N*-(1-(5-(1-(p-tolyl)vinyl)pyridin-2-yl)ethyl)aniline (5a). Column chromatography on silica gel afforded 120 mg of the desired compound **5a** as a brown oil (0.35 mmol, yield 70%). ^{1}H NMR (300 MHz , $CDCl_3$) δ 8.58 (d, *J* = 2.3 Hz, 1H), 7.55 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 6.57 (d, *J* = 8.8 Hz, 2H), 5.50 (s, 1H), 5.44 (s, 1H), 4.60 (q, *J* = 6.7 Hz, 1H), 3.71 (s, 3H), 2.37 (s, 3H), 1.57 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5 (C), 152.2 (C), 148.8 (CH), 146.8 (C), 141.5 (C), 138.1 (C), 137.7 (C), 136.5 (CH), 135.6 (C), 129.2 (2CH), 128.1 (2CH), 119.8 (CH), 115.0 (4CH), 114.8

(CH_2), 55.9 (OCH_3), 55.5 (CH), 23.4 (CH_3), 21.3 (CH_3). IR (ν, cm^{-1}) 3388, 3087, 2861, 1606, 1577, 1521, 1499. 1265. HRMS (ESI) for $C_{23}H_{25}N_2O$ $[M+H]^+$: calcd 345.1967, found 345.1955.

4-Fluoro-*N*-(1-(5-(1-(p-tolyl)vinyl)pyridin-2-yl)ethyl)aniline (5b). Column chromatography on silica gel afforded 108 mg of the desired compound **5b** as a brown oil (0.325 mmol, yield 65%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.2 Hz, 1H), 7.54 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.84 (dd, *J* = 9.8, 7.6 Hz, 2H), 6.56 – 6.48 (m, 2H), 5.51 (s, 1H), 5.44 (s, 1H), 4.58 (q, *J* = 6.7 Hz, 1H), 2.37 (s, 3H), 1.56 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0 (C), 155.9 (d, *J* = 235.1 Hz, C), 148.9 (CH), 146.7 (C), 143.6 (C), 138.1 (C), 137.7 (C), 136.5 (CH), 135.8 (C), 129.2 (2CH), 128.0 (2CH), 119.8 (CH), 115.7 (d, *J* = 22.3 Hz, 2CH), 114.9 (CH_2), 114.4 (d, *J* = 7.3 Hz, 2CH), 55.3 (CH), 23.3 (CH_3), 21.3 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$) δ -127.97. IR (ν, cm^{-1}) 3401, 3015, 2905, 1612, 1587, 1510, 1483. HRMS (ESI) for $C_{22}H_{22}N_2F$ $[M+H]^+$: calcd 333.1767, found 333.1770

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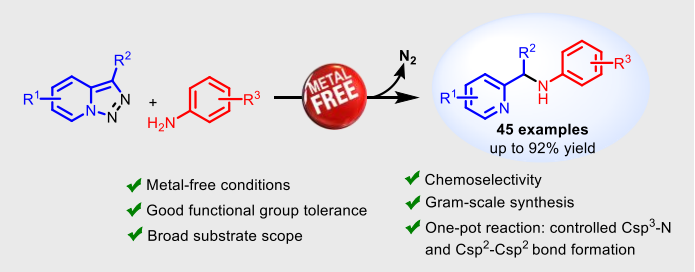

Synthetic Methods

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Metal-Free Csp^3–N Bond Formation by Coupling Pyridotriazoles with Anilines: A New Route to (2-Pyridyl)alkylamines

Pyridyl-alkylamines derivatives were prepared through a coupling of pyridotriazoles and nucleophilic amines using a catalytic amount of TBAB and water as a co-solvent. This metal-free coupling features broad functional groups tolerance, allowing the formation of Csp3-N and Csp2-Csp2 bonds in one pot-fashion affording access to a molecular diversity