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Synthesis of Pyridobenzazepines Using a One-Pot Rh/Pd-Catalyzed Process

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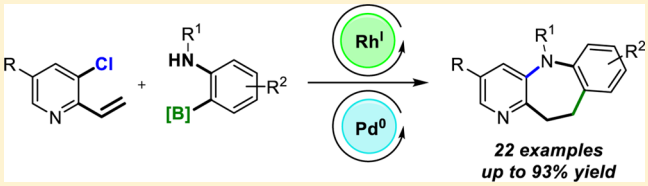
Supporting Information

ABSTRACT: In recent years, our group has been developing multicatalytic reactions for the synthesis of biologically relevant heterocyclic compounds. An efficient dual-metal catalyzed reaction of electron-deficient *o*-chlorovinylpyridines with *o*-aminophenylboronic esters to access pyridobenzazepines is described. Combining a Rh^{I}-catalyzed arylation followed by a Pd^{0}-catalyzed C−N coupling, in a one-pot procedure, provides a simplified method to access heterocycles without workup and purification after each step. The substrate scope encompasses a variety of *N*-H and *N*-alkylated pyridobenzazepine variants with yields up to 93%.



INTRODUCTION

Multicatalytic reactions offer an alternative to traditional step-by-step sequences and can reduce the amount of time, effort, and solvent used to construct useful products. Our objective is to learn about the compatibility of different catalysts and substrates in multicatalytic scenarios. This knowledge could be of use for others interested in developing new multicatalytic reactions. One variant uses several substrates and catalysts in a multicomponent-multicatayst reaction, $(MC)^2R$. Our group has applied this approach in various syntheses of heterocyclic scaffolds including dihydroquinolinones, oxindoles, and fully substituted triazoles.[1−4] Ideally, all the starting materials, reagents, and catalysts are added simultaneously, and the building blocks will react in a productive sequential manner under the same reaction conditions. To ensure successful application of this strategy, orthogonal reactivity of the metals and "time resolution" of the individual steps are necessary.[5]

In recent years, our group has synthesized functionalized seven-membered fused heterocyclic rings using dual-metal catalyzed processes to combine readily available vinylpyridines and *ortho*-functionalized phenylboronic acids. Recently, we reported a method for the synthesis of pyridobenzoxepines (Scheme 1a).[6] The analogous nitrogen-containing dibenzazepine is prevalent in many pharmaceutically relevant compounds, used as tricyclic antidepressants, and was recently reengineered as an anticancer agent, which exhibited efficacy on xenograft models of EFGR-driven cancer (Figure 1).[7−10]

Although the core structure of these tricyclic motifs is readily available, substituted analogues are difficult to access. Diversity in scaffolds is typically obtained by electrophilic aromatic substitution, which is often low-yielding and with limited control over site selectivity. Additionally, there are relatively few *de novo* syntheses of these structures.[11−15]

We recently reported the synthesis of the *N*-arylated pyridobenzazepine motif using a Rh/Pd-catalyzed $(MC)^2R$ (Scheme 1b).[16] These complex products could be obtained in high yields from vinylpyridines, *o*-chlorophenylboronic acids, and anilines by combining a Rh-catalyzed arylation reaction and two Pd-catalyzed C−N bond-forming reactions in one pot. The *N*-alkylated analogues could also be accessed by adopting a one-pot, two-step procedure where the Rh-catalyzed arylation was allowed to take place before the components for the Pd-catalyzed C−N bond forming reactions were added. While this protocol allowed for the synthesis of several *N*-alkylated products in moderate yields, we were interested in pursuing a more expedient procedure to access these highly valuable targets.

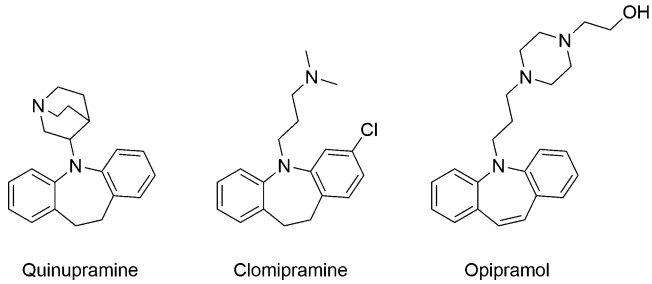


Figure 1. Examples of drugs that contain the dibenzazepine motif.

We herein report that *N*-alkylated as well as *N*-H pyridobenzazepine motifs can be synthesized by coupling *o*-aminophenylboronic esters to *o*-chlorovinylpyridines with a new approach using Rh-catalyzed 1,4-arylation followed by a Pd-catalyzed C−N coupling between a secondary amine and an aryl chloride (Scheme 1c). Compared to the arylated analogues, *N*-alkylated analogues are more relevant in pharmacophores, and the *N*-H motifs can be further derivatized at the secondary amine.[17] Furthermore, the products can be obtained using a one-step protocol compared to the previous two-step protocol,

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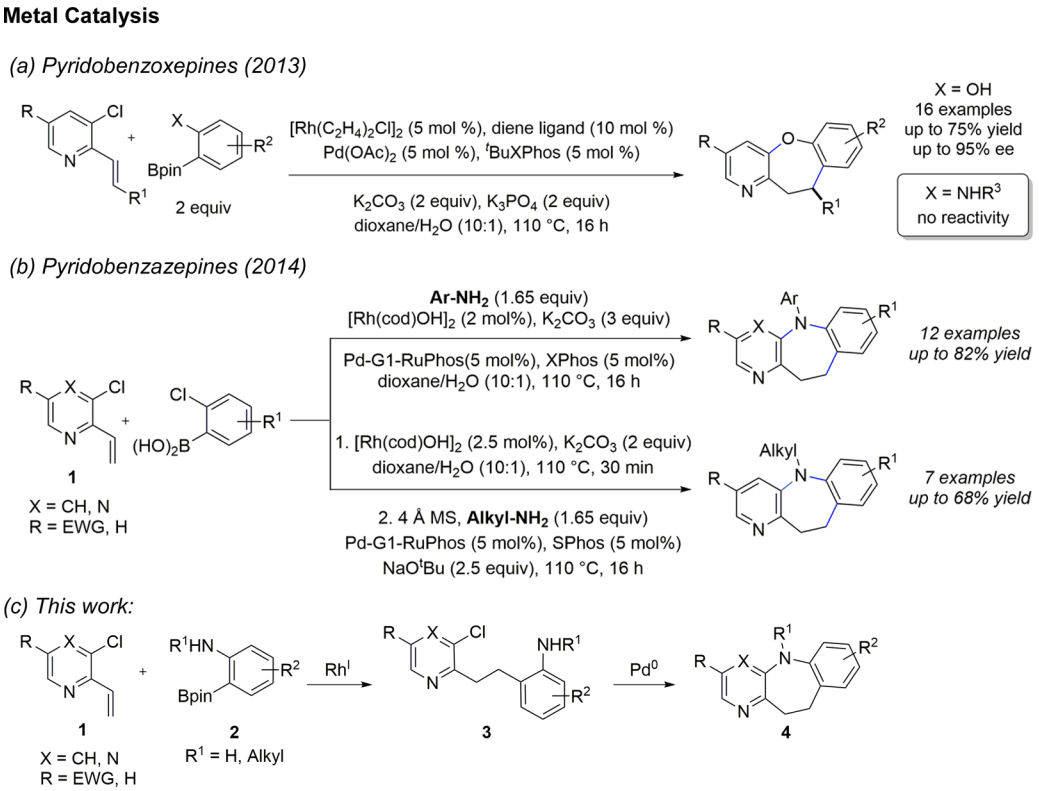
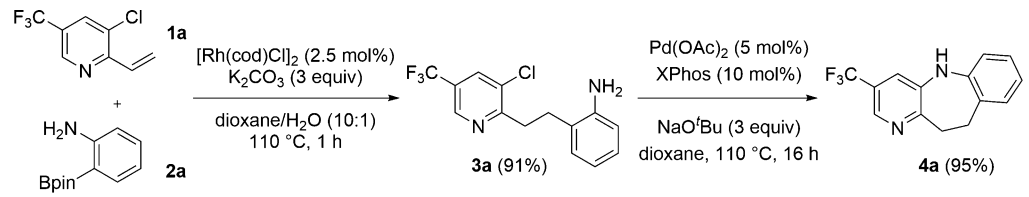
Scheme 1. Previous Approaches to Seven-Membered Heterocycles with Dual-Metal Catalysis



Scheme 2. Synthesis of Pyridobenzazepines



and the yields obtained were generally higher than the previous method, making this method advantageous for the synthesis of these motifs.

RESULTS AND DISCUSSION

To access *N*-H pyridobenzazepines, we used the Rh^{I}-catalyzed arylation with $[Rh(cod)Cl]_2$ as the catalyst and K_2CO_3 as the base. This process afforded 91% yield of intermediate **3a**, which was subjected to the Pd^{0}-catalyzed C−N bond formation using $Pd(OAc)_2$ with XPhos as the ligand and NaO^{t}Bu as the base. A 95% yield of the desired product **4a** was isolated (Scheme 2). Although the two steps can be telescoped in a one-pot, two-step procedure, molecular sieves had to be added to attain comparable yields. Consequently, a convenient one-pot procedure with a single addition of all the reagents at the start of the reaction is more desirable. However, simply combining the reagents from these individual steps gave a poor yield of **4a** (Table 1, entry 1), though switching the base to KOH showed an improvement in yield (Table 1, entry 2).[18] Changing the ligand to ^{t}BuBrettPhos did not improve the yield (Table 1, entry 3). Bidentate ligands such as Josiphos or Xantphos also fared worse (Table 1, entries 4 and 5). A variety of Buchwald precatalysts and ligands were screened (Figure 2). Changing the palladium source to Pd-G1-XPhos improved the yield (Table 1, entry 6), although the G2 and G3 versions of the same catalyst gave poorer yields under these conditions (Table 1, entries 7 and 8). A survey of bases showed that KOH afforded the highest isolated yield of 87% (Table 1, entry 9). Running the reaction without an excess of the XPhos ligand gave lower yields (Table 1, entry 10).

A screen of other bulky monophosphine ligands such as tBuXPhos, SPhos, and RuPhos demonstrated that XPhos was the best ligand for this domino reaction (Table 1, entries 11−14). This result is in alignment with reports from Buchwald on the efficiency of the XPhos ligand for the coupling of primary amines.[19] When we ran experiments with a mixed ligand system (Table 1, entries 15 and 16), slightly better yields were obtained. Finally, as a control study, running the reaction without palladium and ligand gave a >95% yield of **3a** (Table 1, entry 17), showing that C−N bond formation occurs via palladium catalysis and not through an S_NAr mechanism. Due to the similarity of the results of the mixed vs single ligand system (Table 1, entry 9 and 15), we examined the substrate scope using a single ligand to simplify the system (Table 2). However, it became apparent that using substrates other than **2a** gave much poorer yields in all cases. Similarly, running the reactions with Pd-G1-RuPhos and excess RuPhos ligand gave

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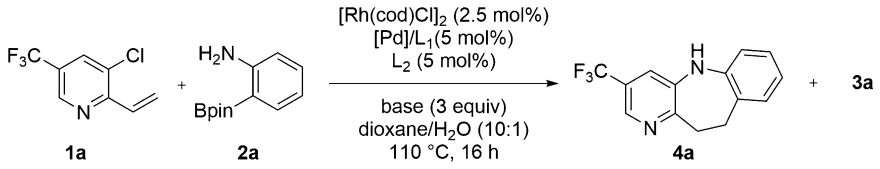
Table 1. Optimization of Domino Reaction of *N*-H Pyridobenzazepine[a]



entry	[Pd]/L_1	L_2	base	yield of **4a**[c] (%)	yield of **3a**[c] (%)
1[b]	$Pd(OAc)_2$	XPhos	K_2CO_3	13	
2[b]	$Pd(OAc)_2$	XPhos	KOH	72	
3[b]	$Pd(OAc)_2$	tBuBrettPhos	KOH	66	
4[b]	$Pd(OAc)_2$	Josiphos	KOH	36	
5[b]	$Pd(OAc)_2$	Xantphos	KOH	52	
6	Pd-G1-XPhos	XPhos	K_2CO_3	58	
7	Pd-G2-XPhos	XPhos	K_2CO_3	10	
8	Pd-G3-XPhos	XPhos	K_2CO_3	18	
9	Pd-G1-XPhos	XPhos	KOH	89 (87)	
10	Pd-G1-XPhos		KOH	63	
11	Pd-G1-tBuXPhos	tBuXPhos	K_2CO_3	6	12
12	Pd-G1-SPhos	SPhos	K_2CO_3	26	
13	Pd-G1-RuPhos	RuPhos	K_2CO_3	65	
14	Pd-G1-RuPhos	RuPhos	KOH	70 (75)	
15	Pd-G1-RuPhos	XPhos	KOH	93 (90)	
16	Pd-G1-XPhos	RuPhos	KOH	90	
17			KOH		>95

[a] **1a** (1.0 equiv, 0.2 mmol), **2a** (1.5 equiv). [b] 15 mol % $\mathbf{L_2}$ used. [c] ^{1}H NMR yields with *p*-nitroacetophenone as the internal standard with isolated yields in parentheses.

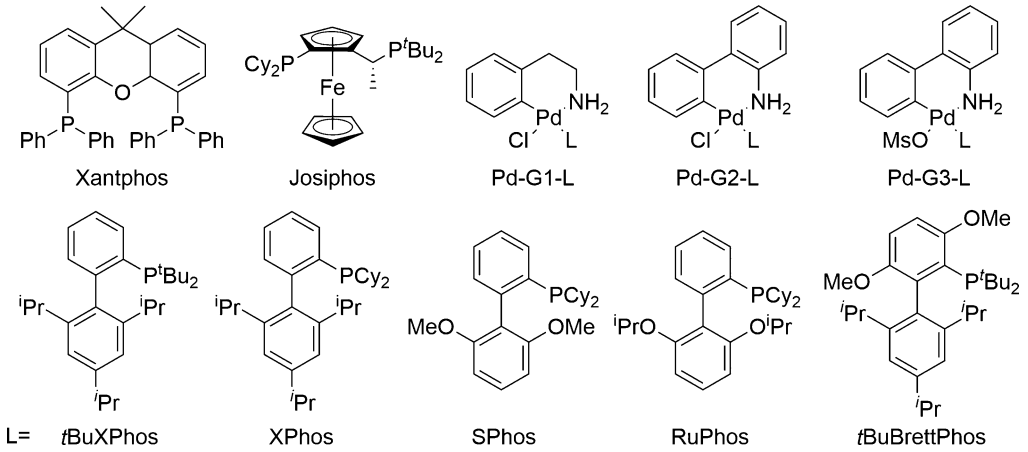


Figure 2. Buchwald palladacycle precatalysts and various ligands.

equally poor yields of the cyclized product. Hence, we settled on the mixed ligand system.

Based on our previous work with vinylpyrazines in multicatalytic reactions, we envisioned that these substrates would work well in the present reaction.[20] When we subjected *o*-chlorovinylpyrazine **1b** and **2a** to the domino catalysis conditions, **4c** was isolated in excellent yield. Running the reaction in the absence of the palladium gave none of the cyclization product, showing that cyclization did not occur through a base-mediated reaction. In place of the CF_3 group, vinylpyridines with Ms **1c** or CN **1d** were tolerated in the reaction to give **4d** and **4e** respectively.

In the absence of an electron-withdrawing R group on the vinylpyridine (i.e., R = CH_3 or H), the desired transformation failed to occur. Halides were tolerated on the ring (**4f,g**); however, the yield was much lower with a chloro on the aniline ring, possibly due to competing oxidative addition to the Pd catalyst. Electron-donating groups (**4h,i**) worked well, but an electron-withdrawing cyano group (**4j**) fared much worse.

Next, we wanted to explore the conditions for synthesizing *N*-alkylated pyridobenzazepines. We optimized the conditions for the synthesis of *N*-alkylated pyridobenzazepines using an *N*-benzylated derivative **2b** as the standard substrate. When reacting **1a** with **2b**, we found that $[Rh(cod)Cl]_2$, K_2CO_3, and Pd-G1-RuPhos with excess RuPhos ligand in a 10:1 mixture of 1,4-dioxane and H_2O gave an 85% yield of **4b** (Table 3, entry 1). This outcome is in line with reports from Buchwald on the high efficiency of RuPhos for the coupling of secondary amines.[19] $[Rh(cod)OH]_2$ gave comparable yields, while $[Rh(C_2H_4)_2Cl]_2$ gave lower yields (Table 3, entries 2 and 3). It was found that K_2CO_3 was the optimal base. The use of other

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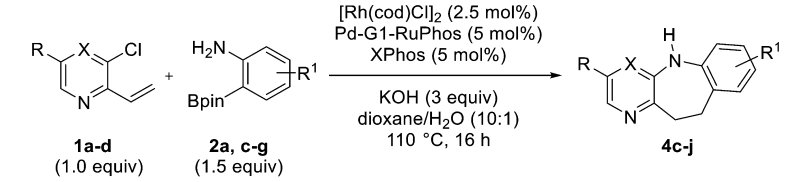
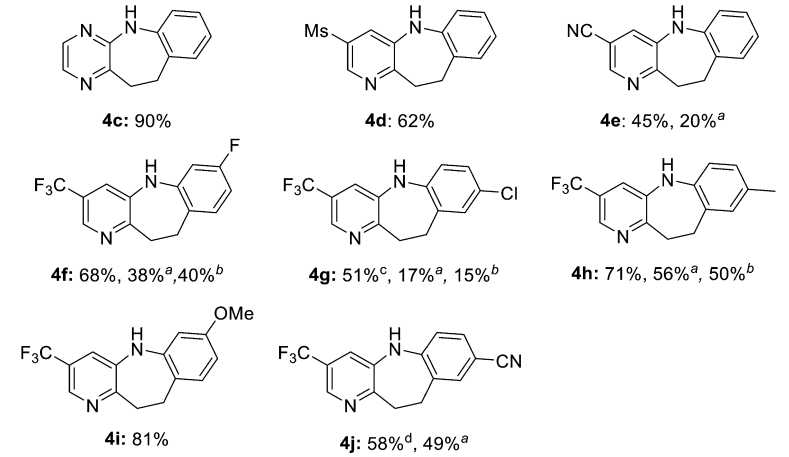
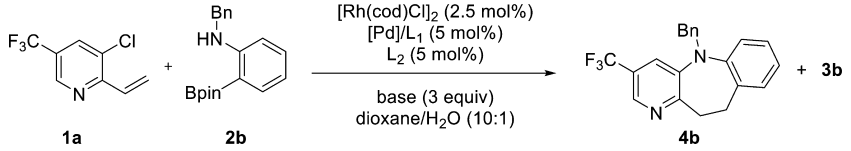
Table 2. Scope of *N*-H Pyridobenzazepines





[a]Pd-G1-XPhos instead of Pd-G1-RuPhos. [b]RuPhos instead of XPhos. [c]Uncyclized intermediate was isolated in 35% yield. [d]Uncyclized intermediate was isolated in 20% yield.

Table 3. Optimization of One-Pot Domino Reaction of *N*-Benzylated Pyridobenzazepine[a]



entry	[Pd]/L_1	L_2	base	yield of **4b**[b] (%)	yield of **3b**[b] (%)
1	**Pd-G1-RuPhos**	**RuPhos**	**K_2CO_3**	**85 (80)**	
2[c]	Pd-G1-RuPhos	RuPhos	K_2CO_3	79 (71)	
3[d]	Pd-G1-RuPhos	RuPhos	K_2CO_3	2	8
4	Pd-G1-RuPhos	RuPhos	KOH	42	
5	Pd-G1-RuPhos	RuPhos	$CsCO_3$	13	30
6	Pd-G1-XPhos	XPhos	K_2CO_3	60	30
7[e]	Pd-G1-RuPhos	RuPhos	K_2CO_3	75	
8[f]	Pd-G1-RuPhos	RuPhos	K_2CO_3	8	60
9[e]	$Pd(OAc)_2$	RuPhos	K_2CO_3	86 (81)	
10[g]	Pd-G1-RuPhos	RuPhos	K_2CO_3		60
11[h]	Pd-G1-RuPhos	RuPhos	K_2CO_3	59	
12[i]	Pd-G1-RuPhos	RuPhos	K_2CO_3	9	
13[j]	Pd-G1-RuPhos	RuPhos	K_2CO_3	18	
14[k]	Pd-G1-RuPhos	RuPhos	K_2CO_3	9	40
15[l]	Pd-G1-RuPhos	RuPhos	K_2CO_3	11	12

[a]**1a** (1.0 equiv, 0.3 mmol), **2a** (1.5 equiv), 0.1 M in dioxane, 110 °C, 16 h. [b]^{1}H NMR yields with *p*-nitroacetophenone as the internal standard with isolated yields in parentheses. [c][Rh(cod)OH]$_2$ instead of [Rh(cod)Cl]$_2$. [d][Rh(C_2H_4)$_2$Cl]$_2$ instead of [Rh(cod)Cl]$_2$. [e]10 mol % of L_2 used. [f]2.5 mol % of [Pd]/L_1 used. [g]Run at 100 °C. [h]Run at 120 °C. [i]Run at 0.05 M. [j]Run at 0.2 M. [k]Dioxane/H_2O = 10:0.5. [l]MeOH instead of H_2O.

inorganic bases such as KOH or Cs_2CO_3 fared poorly under otherwise identical conditions (Table 3, entries 4 and 5).

The domino reaction did not give full conversion to **4b** using the combination of Pd-G1-XPhos with excess XPhos ligand (Table 3, entry 6). In analogy to the *N*-H case, the second- and third-generation Pd-XPhos palladacycles, with added XPhos, afforded negligible yields. Increasing the amount of excess ligand to 10 mol % or decreasing the palladium catalyst loading to 2.5 mol % significantly decreased the yield (Table 3, entries 7 and 8). We also wanted to determine if simple palladium sources could be used rather than the specialized precatalysts mentioned above. When the reaction was performed with the free ligand and $Pd(OAc)_2$, comparable yields (81%) to Pd-G1-RuPhos with an equivalent ligand loading (Table 3, entry 9) were obtained.[21] $PdCl_2$, Pd(dppf)Cl_2, Pd_2(dba)$_3$, or Pd-(PhCN)$_2Cl_2$ led to low yields and incomplete conversion to the desired product under otherwise standard conditions.

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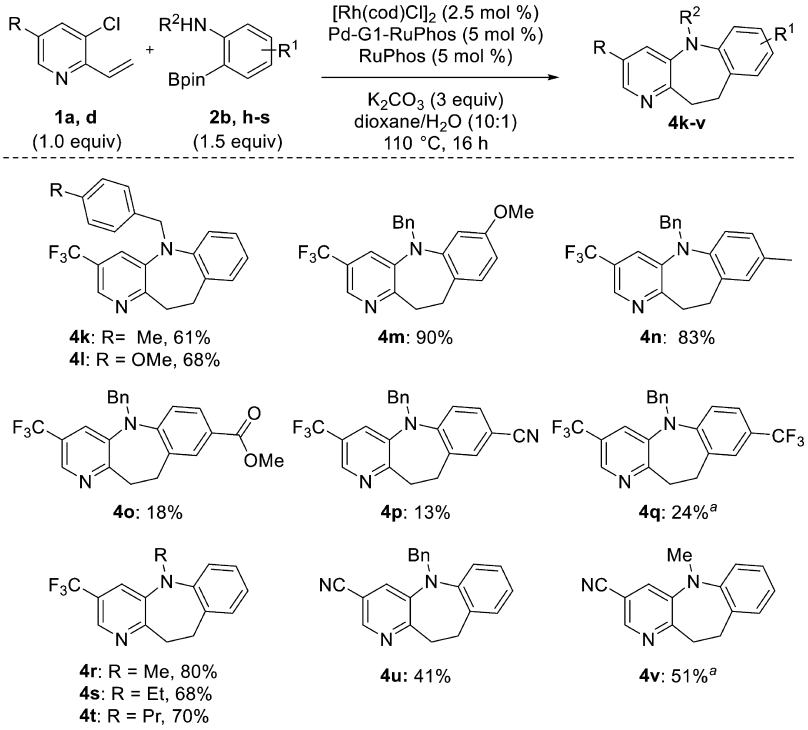
Table 4. Scope of *N*-Substituted Pyridobenzazepine



[a]KOH (3 equiv) used instead of K_2CO_3.

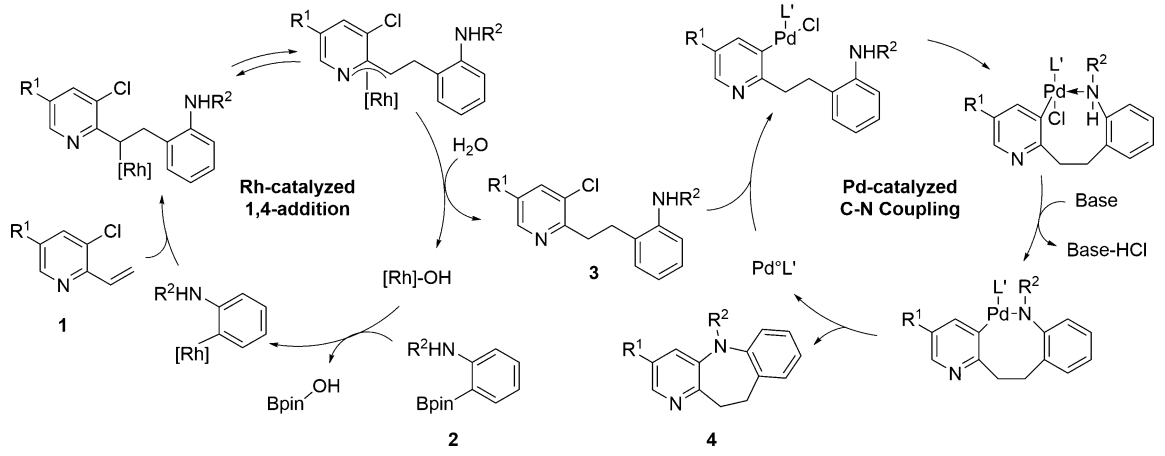


Figure 3. Proposed mechanism for the Rh/Pd-catalyzed formation of benzazepines.

When the temperature of the reaction was lowered to 100 °C, only 60% of intermediate **3b** and none of **4b** was observed (Table 3, entry 10). Running the reaction at 120 °C led to a lower yield of **4b** (Table 3, entry 11). A concentration of 0.1 M was found to be the optimal value, as reactions run at either 0.05 or 0.20 M proceeded in low yield (Table 3, entries 12 and 13). Halving the amount of water in the reaction led to lower yields of **3b** and incomplete conversion to **4b** (Table 3, entry 14). Using MeOH in place of H_2O led to incomplete conversion of **3b** to the desired product (Table 3, entry 15).

Hence, the best conditions used a combination of 2.5 mol % of $[Rh(cod)Cl]_2$, 3 equiv of K_2CO_3, and 5 mol % of Pd-G1-RuPhos precatalyst with 5 mol % excess RuPhos ligand in a 10:1 mixture of 1,4-dioxane and H_2O. With these optimized conditions, we studied the scope of the reaction (Table 4). Substrates bearing a *para* substituent on the *N*-benzyl group gave good yields of the desired products **4k,l**. Deborylation of **2** was the major side reaction when coupling the *N*-benzyl substrates to **1**. An analysis of the aniline component showed that electron-donating groups such as methoxy and methyl provided good yields (Table 4, **4m,n**). However, electron-withdrawing groups such as a methyl ester or cyano in that position generally gave lower yields of the product (Table 4, **4o−q**). Compounds **4o** and **4p** gave the intermediates in 71% and 80% yield, respectively. For **4q**, switching the base to KOH allowed for cyclization to the product, but 67% of the intermediate remained uncyclized. When the Rh-catalyzed step was run on its own, the intermediates could be obtained in good yields. The lowered yields for the Pd-catalyzed step could be due to the reduced nucleophilicity of the aniline. Alkyl chains of different lengths were incorporated in good yields (Table 4, **4r−t**) with around 15−20% of the dechlorinated

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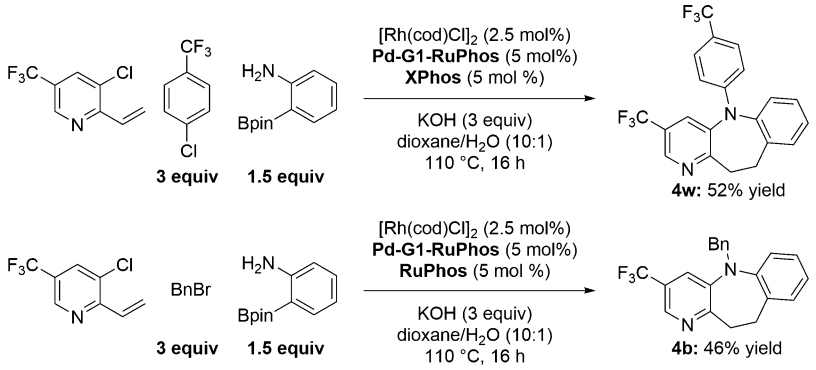
Scheme 3. Three-Component $(MC)^2R$



intermediate as the major side product. Bulky *N*-substituents on the aniline (i.e., *i*Pr) would lead to formation of the intermediate, without cyclizing, instead undergoing partial dechlorination.

We propose that the formation of the pyridobenzazepines occurs through a Rh-catalyzed 1,4-arylation followed by a Pd-catalyzed amination (Figure 3). First, $[Rh(cod)Cl]_2$ is converted to the more active [Rh]-OH species. [Rh]-OH then transmetalates with the 2-aminophenylboronic ester **2**, which reacts with the vinylpyridine **1** to give an aza-allylrhodium species. Protodemetalation gives intermediate **3**, and water regenerates [Rh]-OH. Oxidative addition of **3** to the Pd-catalyst occurs and the Pd coordinates to the aniline. In the presence of base, HCl is lost, and a reductive elimination gives rise to pyridobenzazepine **4**.

A limitation of the current process is that an electron-withdrawing substituent must be present in the 5 position of the vinylpyridine for the transformation to occur. This includes either a CF_3 or CN group. Subjecting **1d** with 2-(*N*-methylamino)phenylboronic acid pinacol ester gave moderate yields of **4v** along with 44% of unreacted vinylpyridine, using KOH. This reaction did not work with an unsubstituted vinylpyridine nor with a Ms or NO_2 group in the 5-position. Subjecting these unsuccessful substrates to the rhodium-catalyzed arylation conditions in the absence of palladium was also unsuccessful, leading only to deborylation of **2**. As an alternative strategy, we attempted to use a more electron-rich aminophenylboronic ester, but it was not found to be a viable solution to allow electron-neutral pyridines to react. When we attempted to react **1b** with **2b**, none of the *N*-substituted product was obtained. Instead, 40% yield of the intermediate was formed. It was re-subjected to the Pd-catalyzed conditions, but no reaction was observed.

Finally, we were also interested in seeing if we could extend this strategy to a three-component reaction (Scheme 3). We expected that compound **4a**, formed in situ from **1a** and **2a**, would undergo a second Pd-catalyzed C−N coupling with an external coupling partner. Using 3 equiv of an electron-deficient aryl chloride, we obtained 52% yield of the cyclized product **4w** under our standard domino reaction conditions. Using BnBr, Pd-G1-RuPhos, and XPhos gave **3b** (90% yield) exclusively as **4a** was not formed. We hypothesized that only cyclization of the secondary amine **3b** afforded **4b**. Hence, changing the excess ligand to RuPhos afforded **4b** in 46% yield (Scheme 3).

CONCLUSION

In summary, we have reported a Rh/Pd-catalyzed two-component protocol to access *N*-alkylated or *N*-H pyridobenzazepines from easily accessible vinylpyridines and aminophenylboronic esters that affords up to 93% yield. It was also shown that a three-component $(MC)^2R$ could be performed under similar conditions to access both *N*-arylated and *N*-alkylated products in a one-pot procedure. These compounds are pharmaceutically relevant as many tricyclic scaffolds with the dibenzazepine motif contains an *N*-alkyl chain and *N*-H analogues can be further functionalized. Furthermore, the compounds presented are all novel and could show interesting biological reactivity. With our previously reported $(MC)^2R$ conditions to access *N*-aryl pyridobenzazepines, we now offer a suite of modular and efficient methods to access these diverse and highly functionalized heterocyclic structures.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under an argon atmosphere in oven- or flame-dried flasks or vials with magnetic stirring. Organic solutions were concentrated using a rotary evaporator at 30−45 °C under reduced pressure unless otherwise stated. Analytical TLC was performed on silica gel plates (0.2 mm, 60 Å pore size). Visualization was done under a 254 nm UV light source and by immersion in potassium permanganate solution. Flash chromatography was performed employing 230−400 mesh silica gel. All reagents, catalysts, and ligands were purchased from commercial sources and used without further purification. Prior to use, THF were distilled over Na/benzophenone, while 1,2-dichloroethane and propionitrile were distilled over CaH_2. Reagent-grade 1,4-dioxane was used straight from the bottle. ^1H, ^{13}C, and ^{19}F NMR were recorded at 25 °C in $CDCl_3$ on a Varian Mercury 400 MHz, 500 MHz, or Bruker Avance III 400 MHz spectrometer. ^1H spectra were referenced to residual protium resonances relative to Me_4Si ($CHCl_3$ δ 7.26). ^{13}C spectra were referenced to solvent carbon resonances ($CDCl_3$ δ 77.16). Chemical shifts are reported in parts per million (ppm) and coupling constants as scalar values in hertz. Data for ^1H NMR are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, tt = triplet of triplets, qd = quartet of doublets, m = multiplet), coupling constant (J, Hz), and integration. High-resolution mass spectra (HRMS) were obtained from an SI2Micromass 70S-250 spectrometer operating at 70 eV in EI mode, or an AB/Sciex QStar spectrometer operating in positive ESI mode. Mass analyzer type is TOF. FTIR spectra were recorded using an ATR method unless otherwise stated.

General Procedure for Benzylation. *N-(4-Methylbenzyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline* (**2h**). In an oven-dried scintillation vial with a stir bar were added 2-aminoboronic acid pinacol ester **2a** (138 mg, 1.5 mmol, 1 equiv) and 4-tolualdehyde (396 mg, 1.8 mmol, 1.2 equiv) and the mixture dissolved in anhydrous MeOH (1.5 mL) for 4 h. $NaBH_4$ (68 mg, 1.8 mmol, 1.2 equiv) was added portionwise, and the reaction was allowed to stir for 1 h. The reaction was partitioned in a 1:1 mixture of EtOAc (25 mL) and distilled water (25 mL). The organic layer was collected, the aqueous

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layer was extracted with EtOAc (25 mL × 2), and the organic layers were combined. The organic layers were washed with saturated NaCl solution and then dried over $MgSO_4$. The mixture was concentrated in vacuo and then purified by column chromatography (1% EtOAc in hexanes) to obtain 110 mg (23% yield, mp = 62−63 °C) of the desired product as a clear colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (dd, J = 7.3, 1.8 Hz, 1H), 7.26 (d, J = 7.9 Hz, 4H), 7.14 (d, J = 7.8 Hz, 2H), 6.63 (t, J = 7.4 Hz, 1H), 6.53 (d, J = 8.3 Hz, 1H), 6.33 (s, 1H), 4.36 (s, 2H), 2.34 (s, 3H), 1.32 (s, 12H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 154.4, 137.0, 136.7, 136.3, 133.1, 129.3, 129.1, 127.5, 126.8, 117.5, 115.6, 112.8, 109.8, 83.5, 48.1, 47.2, 24.9, 21.1. FT-IR: 3422, 2977, 2927, 1694, 1578, 1515, 1455, 1356, 1323, 1265, 1142, 1088, 1040, 962, 861, 835, 801, 752, 673, 657 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{20}H_{27}BNO_2$ 324.2129, found 324.2135.

*N-(4-Methoxybenzyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (**2i**).* Compound **2a** (138 mg, 1.5 mmol, 1 equiv) and 4-anisaldehyde (449 mg, 1.8 mmol, 1.2 equiv) were used. The crude mixture was purified by column chromatography (5% EtOAc in hexanes) to obtain 220 mg (43% yield, mp = 69−70 °C) of the product as a clear yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ7.65 (dd, J = 7.4, 1.6 Hz, 1H), 7.32−7.26 (m, 3H), 7.25 (ddd, J = 8.4, 7.2, 1.8 Hz, 1H), 6.91−6.85 (m, 2H), 6.63 (td, J = 7.3, 0.9 Hz, 1H), 6.55−6.50 (m, 1H), 6.28 (s, 1H), 4.33 (d, J = 3.3 Hz, 2H), 3.81 (s, 3H), 1.33 (s, 12H). ^{13}C NMR (500 MHz, $CDCl_3$: δ 158.5, 154.4, 137.0, 133.1, 131.8, 128.1, 115.6, 113.9, 109.8, 83.5, 55.3, 46.9, 24.9. FT-IR: 3415, 2927, 2846, 1605, 1578, 1513, 1457, 1358, 1325, 2346, 1144, 1010, 862, 828, 755, 659 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{20}H_{27}BNO_3$ 340.2079, found 340.2084.

General Procedure for Borylation of *o*-Halo N-Substituted Anilines. *N-Benzyl-5-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (**2j**).* In a flame-dried 3 dram vial that was purged with argon, *N*-benzyl-2-bromo-5-methoxyaniline (291 mg, 1 mmol, 1 equiv) was dissolved in dry 1,4-dioxane (4 mL). Et_3N (0.43 mL, 4 mmol, 4 equiv) and Pd(dppf)Cl_2 (43 mg, 0.1 mmol, 10 mol %) were added. Pinacolborane (0.44 mL, 3 mmol, 3 equiv) was added dropwise under argon. The crude mixture was purified by column chromatography (5% EtOAc in hexanes) to obtain the desired product (237 mg, mp = 89−91 °C) as a clear colorless solid in 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 8.2 Hz, 1H), 7.33−7.20 (m, 4H), 7.21−7.12 (m, 1H), 6.32 (s, 1H), 6.13 (dd, J = 8.3, 2.3 Hz, 1H), 5.96 (d, J = 2.2 Hz, 1H), 4.30 (d, J = 5.2 Hz, 2H), 3.64 (s, 3H), 1.23 (s, 12H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 144.5, 138.8, 138.5, 132.0, 128.7, 127.3, 127.3, 118.9, 112.3, 106.5, 48.0, 21.5. FT-IR: 3413, 2986, 2920, 1605, 1570, 1450, 1261, 1201, 1093, 1053, 860, 800, 735, 697, 660 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{20}H_{27}BNO_3$ 340.2079, found 340.2084.

*N-Benzyl-4-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (**2k**).* *N*-Benzyl-2-bromo-4-methylaniline (275 mg, 1 mmol, 1 equiv) was used. The crude mixture was purified by column chromatography (5% EtOAc in hexanes) to obtain the desired product (242 mg, mp = 74−75 °C) as pale yellow solid in 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.6 (d, J = 7.5 Hz, 1H), 7.4−7.3 (m, 4H), 7.3 (t, J = 7.2 Hz, 1H), 6.5 (d, J = 7.5 Hz, 1H), 6.4 (s, 1H), 6.3 (s, 1H), 4.4 (s, 2H), 2.3 (s, 3H), 1.3 (s, 12H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 154.6, 143.5, 139.9, 137.1, 134.8, 128.5, 127.0, 126.8, 117.0, 110.5, 83.4, 47.5, 24.9, 22.2. FT-IR: 3423, 2977, 2919, 2867, 1614, 1571, 1450, 1350, 1313, 1261, 1093, 1053, 963, 860, 801, 735, 697, 657 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{20}H_{27}BNO_2$ 324.2129, found 324.2135.

*Methyl 4-(Benzylamino)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (**2l**).* Methyl 4-(benzylamino)-3-iodobenzoate (367 mg, 1 mmol, 1 equiv) was used. The crude mixture was purified by column chromatography (5% EtOAc in hexanes) to obtain the desired product (315 mg, mp = 105−107 °C) as a pink solid in 86% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, J = 2.2 Hz, 1H), 7.91 (dd, J = 8.8, 2.3 Hz, 1H), 7.34 (d, J = 4.4 Hz, 4H), 7.28 (s, 1H), 6.83 (d, J = 5.8 Hz, 1H), 6.49 (d, J = 8.8 Hz, 1H), 4.45 (d, J = 5.5 Hz, 2H), 3.84 (s, 3H), 1.33 (s, 12H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 167.3, 157.5, 139.5, 138.7, 134.9, 128.6, 127.1, 126.8, 117.1, 83.9, 77.3, 77.0, 76.7, 47.1, 24.9, 14.2. FT-IR: 3396, 2979, 2940, 2858, 1705, 1605, 1480, 1527, 1424, 1371, 1325, 1294, 1249, 1140, 1113, 1053, 983, 852, 774, 732, 698, 662 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{21}H_{27}BNO_4$ 368.2028, found 368.2033.

*N-Benzyl-4-cyano-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (**2m**).* 4-(Benzylamino)-3-bromobenzonitrile (286 mg, 1 mmol, 1 equiv) was used. The crude mixture was purified by column chromatography (5% EtOAc in hexanes) to obtain 274 mg (82% yield, mp = 68−69 °C) of the product as a pink solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96−7.87 (m, 1H), 7.44 (ddd, J = 8.7, 2.1, 0.5 Hz, 1H), 7.39−7.28 (m, 1H), 6.87 (s, 1H), 6.47 (d, J = 8.7 Hz, 1H), 4.43 (d, J = 5.6 Hz, 2H), 1.33 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.6, 141.7, 138.2, 136.6, 128.7, 127.3, 126.7, 120.4, 109.7, 97.8, 84.3, 47.0, 24.9. FT-IR: 3395, 2979, 2214, 1604, 1580, 1524, 1452, 1421, 1392, 1367, 1329, 1281, 1194, 1139, 1056, 965, 898, 852, 817, 735, 696, 669 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{20}H_{24}BN_2O_2$ 335.1925, found 335.1931.

*N-Benzyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-trifluoromethylaniline (**2n**).* Methyl 4-(benzylamino)-3-iodobenzoate (367 mg, 1 mmol, 1 equiv) was used. The crude mixture was purified by column chromatography (5% EtOAc in hexanes) to obtain the desired product (279 mg, mp = 72−73 °C) as a white solid in 74% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, J = 2.1 Hz, 1H), 7.43 (dd, J = 8.5, 2.1 Hz, 1H), 7.35 (d, J = 1.0 Hz, 1H), 7.34 (s, 2H), 7.37−7.28 (m, 1H), 6.71 (s, 1H), 6.51 (d, J = 8.7 Hz, 1H), 4.43 (d, J = 4.1 Hz, 2H), 1.34 (s, 12H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.3, 138.8, 134.3 (q, $J_{(C-F)}$ = 3.8 Hz), 129.9 (q, $J_{(C-F)}$ = 3.6 Hz), 128.6, 127.1, 126.8, 125.1 (q, $J_{(C-F)}$ = 270.4 Hz), 117.3 (q, $J_{(C-F)}$ = 32.4 Hz), 109.2, 84.0, 47.1, 24.9. ^{19}F NMR (500 MHz, $CDCl_3$): δ 60.95. FT-IR: 3416, 2980, 1617, 1588, 1533, 1453, 1373, 1319, 1266, 1169, 1143, 1108, 1078, 963, 850, 818, 731, 697, 680 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{20}H_{24}BF_3NO_2$ 378.1847, found 378.1852.

General Procedure for the Synthesis of *N*-Alkylated *o*-Anilineboronic Acid Pinacol Esters. *N-Methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (**2o**).* In a flame-dried round-bottomed flask equipped with a stirbar was dissolved 2-aminoboronic acid pinacol ester, **2a**, (1.0 g, 6 mmol, 2 equiv) in dry THF (6 mL) under argon and then the mixture cooled to −40 °C. *n*-BuLi (2.5 M in hexanes, 1.2 mL, 1 equiv) was added dropwise, and the solution was stirred for 30 min. The solution was further cooled to −78 °C, and MeI (188 μL, 3 mmol, 1 equiv) was added dropwise. This was stirred for 12 h with warming to room temperature. The reaction was quenched by the addition of water (4 mL), and the organic layer was separated. The aqueous layer was extracted with EtOAc (50 mL × 3), and then the organic layer was washed with $NaHCO_3$, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The compound was isolated by column chromatography (5% EtOAc/hexanes) to obtain the desired product (643 mg) as a clear colorless oil in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 7.3 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 6.63 (t, J = 7.3 Hz, 1H), 6.55 (d, J = 8.3 Hz, 1H), 5.79 (s, 1H), 2.85 (s, 3H), 1.33 (s, 12H). ^{13}C NMR (500 MHz, $CDCl_3$-insert): δ 155.4, 137.1, 133.2, 115.4, 108.9, 83.5, 30.2, 24.9. FT-IR: 3433, 2979, 2934, 2810, 1606, 1582, 1524, 1467, 1430, 1358, 1325, 1273, 1173, 1143, 1106, 1086, 1049, 1034, 964, 837, 756, 677, 662 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{13}H_{21}BNO_2$ 234.1660, found 234.1665.

*N-Propyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (**2q**).* 1-Iodopropane (291 μL, 3 mmol, 1 equiv) was added. The compound was isolated by column chromatography (5% EtOAc/hexanes) to obtain the desired product (705 mg) as a clear colorless oil in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, J = 7.3, 1.8 Hz, 1H), 7.32 (ddd, J = 8.6, 7.2, 1.8 Hz, 1H), 6.63 (td, J = 7.3, 1.0 Hz, 1H), 6.58 (d, J = 8.3 Hz, 1H), 5.90 (s, br 1H), 3.13 (t, J = 6.8 Hz, 2H), 1.71 (h, J = 7.2 Hz, 2H), 1.36 (s, 12H), 1.05 (t, J = 7.4 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 154.8, 137.1, 133.1, 115.2, 109.4, 83.4, 45.1, 25.0, 22.4, 11.7. FT-IR: 3414, 2967, 2925, 2858, 1605, 1579, 1521, 1455, 1356, 1323, 1264, 1104, 1060, 1039, 962, 864, 753, 674, 658 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{15}H_{24}BNO_2$ 262.1973, found 262.1978.

*2-(2-(3-Chloro-5-(trifluoromethyl)pyridin-2-yl)ethyl)aniline (**3a**).* In a 2 dram vial equipped with a stir bar were added 3-chloro-5-

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trifluoro-2-vinylpyridine **1a** (42 mg, 0.2 mmol), 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **2a** (66 mg, 0.3 mmol, 1.5 equiv), $[Rh(cod)Cl]_2$ (2.5 mg, 0.01 mmol, 0.05 equiv), and KOH (34 mg, 0.06 mmol, 3.0 equiv). The product was isolated by column chromatography (15% EtOAc/hexanes) as a colorless solid (38 mg, mp = 57−62 °C) in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (s, 1H), 7.89 (d, J = 2.0 Hz, 1H), 7.15−7.00 (m, 2H), 6.83−6.64 (m, 2H), 3.86 (s, 2H), 3.41−3.20 (m, 2H), 3.05−2.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6 (q, $J_{(C-F)}$ = 1.4 Hz), 144.4, 144.0 (q, $J_{(C-F)}$ = 4.2 Hz), 133.8 (q, $J_{(C-F)}$ = 3.6 Hz), 131.3, 129.7, 129.3, 127.5, 125.7 (q, $J_{(C-F)}$ = 33.6 Hz), 122.8 (q, $J_{(C-F)}$ = 272.6 Hz), 118.8, 115.8, 34.9, 29.4. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.17. IR (NaCl, thin film): 3387, 3337, 3225, 3067, 3024, 2930, 2862, 1605, 1497, 1456, 1397, 1323, 1175, 1132, 1092, 1059, 916, 750 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{14}H_{13}ClF_3N_2$ 301.0719, found 301.0723.

General Procedure 1 for the Synthesis of *N*-H Benzazepines. *3-(Trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]azepine (**4a**).* In a 2 dram vial equipped with a stir bar were added 3-chloro-5-trifluoro-2-vinylpyridine **1a** (42 mg, 0.2 mmol), 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **2a** (66 mg, 0.3 mmol, 1.5 equiv), $[Rh(cod)Cl]_2$ (2.5 mg, 0.01 mmol, 0.05 equiv), Pd-G1-RuPhos (7.4 mg, 0.01 mmol, 0.05 equiv), XPhos (7.1 mg, 0.01 mmol, 0.05 equiv), and KOH (34 mg, 0.06 mmol, 3.0 equiv). The vial was flushed with argon gas. Then 1,4-dioxane (0.2 mL, 0.1 M) was added followed by distilled H_2O (0.02 mL). The vial was sealed with a Teflon screw cap, and then the seal was wrapped with Teflon tape. The mixture was placed into a 110 °C oil bath and heated for 16 h. Upon cooling to room temperature, the reaction mixture was partitioned between EtOAc (25 mL) and water (10 mL). The organic layer was kept, and the aqueous layer was extracted again with EtOAc (25 mL × 2). The organic fractions were combined, washed with saturated NaCl (1 M solution, dried over anhydrous $MgSO_4$), and concentrated in vacuo. NMR yields were obtained using *p*-nitroacetophenone as an internal standard. The product was isolated by column chromatography (10−50% EtOAc/hexanes) as a white solid (48 mg, mp 125−128 °C) in 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 0.9 Hz, 1H), 7.27−7.21 (m, 1H), 7.14 (ddd, J = 9.3, 7.5, 1.6 Hz, 2H), 6.91 (td, J = 7.4, 1.2 Hz, 1H), 6.81 (d, J = 7.8 Hz, 1H), 6.01 (s, 1H), 3.40−3.33 (m, 2H), 3.17−3.10 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.0 (q, $J_{(C-F)}$ = 1.4 Hz), 141.0, 138.6, 135.6 (q, $J_{(C-F)}$ = 4.2 Hz), 130.5, 129.8, 127.3, 125.2 (q, $J_{(C-F)}$ = 32.7 Hz), 123.7 (q, $J_{(C-F)}$ = 272.4 Hz), 121.4, 121.0 (q, $J_{(C-F)}$= 3.7 Hz), 118.5, 38.5, 32.5. ^{19}F NMR (564 MHz, $CDCl_3$): δ −62.39. IR (NaCl, neat): 3300, 3232, 3206, 3139, 3121, 3043, 2962, 2925, 2854, 2359, 2346, 1544, 1438, 1495, 1468, 1442, 1418, 1343, 1238, 1126, 1095, 968, 750, 668 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{14}H_{12}F_3N_2$ 265.0947, found 265.0953.

General Procedure 2 for the Synthesis of N-Substituted Pyridobenzazepines. *5-Benzyl-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]azepine (**4b**).* In a 2 dram vial equipped with a stir bar were added 3-chloro-5-trifluoro-2-vinylpyridine **1a** (42 mg, 0.2 mmol), *N*-benzyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **2b** (92 mg, 0.3 mmol, 1.5 equiv), $[Rh(cod)Cl]_2$ (2.5 mg, 0.01 mmol, 0.05 equiv), Pd-G1-RuPhos (8.2 mg, 0.01 mmol, 0.05 equiv), RuPhos (4.7 mg, 0.01 mmol, 0.05 equiv), and K_2CO_3 (84 mg, 0.6 mmol, 3.0 equiv). The vial was flushed with argon gas. Then 1,4-dioxane (0.2 mL, 0.1 M) was added followed by distilled H_2O (0.02 mL). The vial was sealed with a Teflon screw cap, and then the seal was wrapped with Teflon tape. The mixture was placed into a 110 °C oil bath and heated for 16 h. Upon cooling to room temperature, the reaction mixture was partitioned between EtOAc (25 mL) and water (10 mL). The organic layer was kept, and the aqueous layer was extracted again with EtOAc (25 mL × 3). The organic fractions were combined, washed with saturated NaCl solution, dried over anhydrous $MgSO_4$, and concentrated in vacuo. NMR yields were obtained using *p*-nitroacetophenone as an internal standard. The product was isolated by column chromatography (5% EtOAc in hexanes) as a peach crystal in 81% yield (57 mg, mp = 60−63 °C). Three-component procedure: In a 2 dram vial equipped with a stir bar were added **1a** (42 mg, 0.2 mmol, 1 equiv), **2a** (66 mg, 0.3 mmol, 1.5 equiv), $[Rh(cod)Cl]_2$ (2.5 mg, 0.01 mmol, 0.05 equiv), Pd-G1-RuPhos (8.2 mg, 0.01 mmol, 0.05 equiv), RuPhos (4.7 mg, 0.01 mmol, 0.05 equiv), and KOH (34 mg, 0.06 mmol, 3.0 equiv). The vial was flushed with argon gas. Then 1,4-dioxane (2 mL, 0.1 M) was added followed by distilled H_2O (0.2 mL) and benzyl bromide (71 μL, 0.6 mmol, 3 equiv). The vial was sealed with a Teflon screw cap, and then the seal was wrapped with Teflon tape. The mixture was placed into a 110 °C oil bath and heated for 16 h. Upon cooling to room temperature, the reaction mixture was partitioned between EtOAc (25 mL) and water (10 mL). The organic layer was kept, and the aqueous layer was extracted again with EtOAc (25 mL × 2). The organic fractions were combined, washed with saturated NaCl (1 M solution, dried over anhydrous $MgSO_4$), and concentrated in vacuo. The product was isolated using column chromatography (5% EtOAc in hexanes) to give the desired compound (33 mg, mp = 60−62 °C) as a peach crystalline solid in 46% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (s, 1H), 7.47 (s, 1H), 7.36 (s, 1H), 7.35 (s, 1H), 7.27 (t, J = 7.6 Hz, 2H), 7.23−7.15 (m, 4H), 7.08−7.01 (m, 1H), 4.96 (s, 2H), 3.44−3.37 (m, 2H), 3.36−3.29 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.8 (q, $J_{(C-F)}$ = 1.4 Hz), 148.0, 143.0, 137.6 (q, $J_{(C-F)}$ = 4.2 Hz), 136.64, 136.61, 128.8, 128.6, 128.0, 127.5, 127.0, 124.7, 124.1 (q, $J_{(C-F)}$ = 32.7 Hz), 123.5 (q, $J_{(C-F)}$ = 272.4 Hz), 122.6 (q, $J_{(C-F)}$ = 3.5 Hz), 121.5, 117.1, 55.7, 37.5, 29.9. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.32. FT-IR (NaCl, neat): 3065, 3033, 2924, 2853, 1602, 1494, 1456, 1416, 1335, 1324, 1228, 1122, 1099, 942, 908, 761, 739, 698, 643 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{21}H_{18}F_3N_2$ 355.1422, found 355.1427.

*10,11-Dihydro-5H-benzo[b]pyrazino[2,3-f]azepine (**4c**).* Following procedure 1, 2-chloro-3-vinylpyrazine **1c** (28 mg, 0.2 mmol) and **2a** (66 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (15−25% EtOAc in hexanes) in 90% yield (35 mg, mp = 70−71 °C) as a pink solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, J = 2.6 Hz, 1H), 7.92 (d, J = 2.6 Hz, 1H), 7.16 (td, J = 7.7, 1.6 Hz, 1H), 7.14−7.12 (m, 1H), 7.08 (s, 1H), 6.93 (td, J = 7.4, 1.2 Hz, 1H), 6.88 (dd, J = 7.9, 1.1 Hz, 1H), 3.34−3.21 (m, 2H), 3.17−3.07 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 150.6, 142.6, 140.1, 139.7, 133.9, 130.2, 127.3, 121.8, 118.9, 37.5, 32.3. FT-IR: 3266, 3047, 2924, 2851, 1610, 1542, 1495, 1418, 1319, 1238, 1140, 947, 752 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{12}H_{12}N_3$ 198.1026, found 198.1031.

*3-Methylsulfonyl-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]azepine (**4d**).* Following procedure 1, 2-chloro-5-methylsulfonyl-2-vinylpyridine **1d** (43 mg, 0.2 mmol) and **2a** (66 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (30% EtOAc in hexanes) in 62% yield (34 mg, mp = 210−213 °C) as a pink solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, J = 1.9 Hz, 1H), 7.58 (d, J = 2.0 Hz, 1H), 7.22−7.08 (m, 2H), 6.92 (td, J = 7.4, 1.2 Hz, 1H), 6.85 (dd, J = 7.9, 1.1 Hz, 1H), 6.28 (s, 1H), 3.42−3.36 (m, 2H), 3.16−3.12 (m, 2H), 3.12 (s, 3H). ^{13}C NMR (500 MHz, $(CD_3)_2SO$): δ 152.4, 140.7, 139.1, 136.8, 135.0, 130.4, 129.8, 127.4, 122.5, 121.7, 118.7, 45.0, 38.8, 32.3. FT-IR: 3363, 2918, 1575, 1530, 1496, 1358, 1439, 1408, 1315, 1140, 910, 952, 753 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{14}H_{15}N_2O_2S$ 275.0849, found 275.0854.

*3-Cyano-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]azepine (**4e**).* Following procedure 1, 3-chloro-5-cyano-2-vinylpyridine **1d** (33 mg, 0.2 mmol) and **2a** (66 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (15% EtOAc in hexanes) in 45% yield (20 mg, mp = 179−171 °C) as a pink solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.2 (d, J = 1.7 Hz, 1H), 7.3 (d, J = 1.7 Hz, 1H), 7.2−7.1 (m, 2H), 6.9 (td, J = 7.4, 1.1 Hz, 1H), 6.8 (dd, J = 7.9, 1.0 Hz, 1H), 6.0 (s, 1H), 3.6−3.3 (m, 2H), 3.2−2.8 (m, 2H).^{13}C NMR (500 MHz, $CDCl_3$): δ 151.6, 141.3, 141.3, 140.5, 138.7, 130.5, 129.8, 129.3, 127.4, 126.2, 121.8, 118.7, 116.8, 107.7, 38.9, 32.3. FT-IR: 3368, 3293, 2020, 2930, 2845, 2233, 1600, 1582, 1532, 1492, 1457, 1410, 1329, 1248, 906, 729 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{14}H_{12}N_3$ 222.1026, found 222.1031.

*7-Fluoro-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4f**).* Following procedure 1, **1a** (42 mg, 0.2 mmol) and 2-amino-4-fluorophenylboronic acid pinacol ester **2c** (71 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (15% EtOAc in hexanes) in 68% yield (38 mg, mp =

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130−134 °C) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, J = 0.9 Hz, 1H), 7.27 (d, J = 1.3 Hz, 1H), 7.05 (dd, J = 8.4, 6.4 Hz, 1H), 6.59 (td, J = 8.2, 2.5 Hz, 1H), 6.54 (dd, J = 10.1, 2.5 Hz, 1H), 6.23 (s, 1H), 3.38−3.30 (m, 2H), 3.21−2.65 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 162.8, 160.8, 150.9 (apparent d, $J_{(C-F)}$ = 0.9 Hz), 142.0 (d, $J_{(C-F)}$ = 10.0 Hz), 138.2, 135.9 (q, $J_{(C-F)}$ = 4.0 Hz), 131.8 (d, $J_{(C-F)}$ = 9.4 Hz), 125.3 (q, $J_{(C-F)}$ = 33.0 Hz), 125.2, 125.2, 123.4 (q, $J_{(C-F)}$ = 272.4 Hz), 121.4 (q, $J_{(C-F)}$ = 3.6 Hz), 107.9 (d, $J_{(C-F)}$ = 20.9 Hz), 105.2 (d, $J_{(C-F)}$ = 25.0 Hz), 38.3, 31.9. ^{19}F NMR (500 MHz, $CDCl_3$): δ −62.3, −116.2 (q, J = 8.1, 6.9 Hz). FT-IR: 3316, 3228, 3165, 2962, 2913, 2868, 1617, 1559, 1502, 1468, 1422, 1341, 1241, 1162, 1138, 1093, 1002, 928, 892, 850, 804. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{14}H_{11}F_4N_2$ 283.0853, found 283.0866.

*8-Chloro-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4g**).* Following procedure 1, **1a** (33 mg, 0.2 mmol) and 2-amino-5-chlorophenylboronic acid pinacol ester **2d** (76 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (15% EtOAc in hexanes) in 51% yield (30 mg, mp = 164−165 °C) as a white solid which turns yellow immediately. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (q, J = 0.8 Hz, 1H), 7.24 (d, J = 1.5 Hz, 1H), 7.13−7.06 (m, 2H), 6.74 (d, J = 8.3 Hz, 1H), 6.07 (s, 1H), 3.41−3.24 (m, 2H), 3.19−2.85 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 150.53 (q, $J_{(C-F)}$ = 4.1 Hz), 139.6, 138.2, 136.0 (q, $J_{(C-F)}$ = 4.1 Hz), 131.3, 130.1, 127.1, 126.1, 125.2 (q, $J_{(C-F)}$ = 32.9 Hz), 123.4 (q, $J_{(C-F)}$ = 272.4 Hz), 121.1 (q, $J_{(C-F)}$ = 3.6 Hz), 119.7, 38.2, 32.3. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.3. FT-IR: 3310, 3235, 3129, 2950, 2929, 2859, 1656, 1607, 1547, 1492 1465, 1419, 1350, 1138, 1099, 968, 890, 817. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{14}H_{11}ClF_3N_2$ 299.0563, found 299.0562.

*8-Methyl-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4h**).* Following procedure 1, **1a** (42 mg, 0.2 mmol) and 2-amino-5-methylphenylboronic acid pinacol ester **2e** (71 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (15% EtOAc in hexanes) in 71% yield (40 mg, mp = 99−100 °C) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, J = 2.0, 0.9 Hz, 1H), 7.22 (d, J = 1.8 Hz, 1H), 7.01 (d, J = 7.6 Hz, 1H), 6.72 (ddd, J = 7.6, 1.7, 0.8 Hz, 1H), 6.63 (t, J = 1.1 Hz, 1H), 6.13 (s, 1H), 3.40−3.33 (m, 2H), 3.10−3.07 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 150.9 (q, $J_{(C-F)}$ = 1.4 Hz), 140.7, 138.7, 137.1, 135.4 (q, $J_{(C-F)}$ = 4.1 Hz), 130.4, 126.7, 125.1 (q, $J_{(C-F)}$ = 32.7 Hz), 123.5 (q, $J_{(C-F)}$ = 272.3 Hz), 122.2, 120.9 (q, $J_{(C-F)}$ = 3.6 Hz), 119.0, 38.7, 32.1, 20.9. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.3. FT-IR: 3311, 3132, 2926, 1629, 1547, 1505, 1468, 1420, 1347, 1241, 1162, 1141, 1117, 1096, 983, 902, 857, 798. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{15}H_{14}F_3N_2$ 279.1104, found 279.1110.

*7-Methoxy-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]-pyrido[2,3-f]azepine (**4i**).* Following procedure 1, **1a** (42 mg, 0.2 mmol and 2-amino-5-methylphenylboronic acid pinacol ester **2f** (71 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (10% EtOAc in hexanes) in 81% yield (48 mg, mp = 159−160 °C) as a beige solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (dd, J = 1.7, 0.8 Hz, 1H), 7.23 (d, J = 1.6 Hz, 1H), 7.01 (d, J = 8.3 Hz, 1H), 6.47 (dd, J = 8.3, 2.5 Hz, 1H), 6.36 (d, J = 2.5 Hz, 1H), 6.15 (s, 1H), 3.77 (s, 3H), 3.35−3.30 (m, 2H), 3.10−3.03 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 158.9, 151.1 (q, $J_{(C-F)}$ = 1.4 Hz), 141.8, 138.5, 135.7 (q, $J_{(C-F)}$ = 4.1 Hz), 131.4, 125.1 (q, $J_{(C-F)}$ = 32.7 Hz), 123.5 (q, $J_{(C-F)}$ = 272.3 Hz), 122.2, 121.0 (q, $J_{(C-F)}$ = 3.6 Hz), 106.6, 104.2, 55.3, 38.8, 31.8. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.3. FT-IR: 3367, 3310, 3217, 3123, 2956, 2923, 2850, 1620, 1595, 1556, 1508, 1468, 1423, 1347, 1244, 1165, 1120, 1096, 1044, 922, 905, 847, 798, 738. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{15}H_{14}F_3N_2O$ 295.1053, found 295.1063.

*8-Cyano-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4j**).* Following procedure 1, **1a** (42 mg, 0.2 mmol) and 2-amino-5-cyanophenylboronic acid pinacol ester **2g** (73 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (10% EtOAc in hexanes) in 58% yield (33 mg, mp = 84−86 °C) as a off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.60−7.29 (m, 3H), 6.90 (d, J = 8.8 Hz, 1H), 6.84 (s, 1H), 3.44−3.30 (m, 2H), 3.19−2.99 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 151.5 (q, $J_{(C-F)}$ = 1.4 Hz), 144.9, 137.2, 137.1 (q, $J_{(C-F)}$ = 4.1 Hz), 134.8, 131.2, 128.9, 125.4 (q, $J_{(C-F)}$ = 33.0 Hz), 123.3 (q, $J_{(C-F)}$ = 272.4 Hz), 122.1 (q, $J_{(C-F)}$ = 3.5 Hz), 119.4, 118.7, 102.9, 38.0, 32.8. FT-IR: 3341, 3228, 3144, 3059, 2965, 2929, 2865, 2223, 1614, 1538, 1504, 1462, 1426, 1344, 1162, 1129, 1093, 965, 898, 825, 741. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{15}H_{11}F_3N_3$ 290.0900, found 290.0906.

*5-(4-Methylbenzyl)-3-(trifluoromethyl)-10,11-dihydro-5H-benzo-[b]pyrido[2,3-f]azepine (**4k**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2h** (97 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (5% EtOAc in hexanes) in 61% yield (45 mg, mp = 74−76 °C) as a clear colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28 (dd, J = 1.9, 1.0 Hz, 1H), 7.48 (d, J = 1.6 Hz, 1H), 7.29−7.24 (m, 2H), 7.23−7.19 (m, 1H), 7.19−7.14 (m, 2H), 7.06 (m, 1H), 6.82−6.78 (m, 1H), 4.92 (s, 2H), 3.45−3.36 (m, 2H), 3.36−3.26 (m, 2H), 2.28 (s, 3H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 158.8, 155.8 (q, $J_{(C-F)}$ = 1.3 Hz), 148.0, 143.0, 137.5 (q, $J_{(C-F)}$ = 4.1 Hz), 136.6, 129.3, 128.8, 128.6, 126.9, 124.6, 124.0 (q, $J_{(C-F)}$ = 32.5 Hz), 123.6 (q, $J_{(C-F)}$ = 272.4 Hz), 122.7 (q, $J_{(C-F)}$ = 3.5 Hz), 121.5, 114.0, 55.1, 55.0, 37.5, 29.9. ^{19}F NMR (377 MHz, CDCl3): δ −62.30. FT-IR: 2926, 2855, 1694, 1518, 1494, 1458, 1418, 1332, 1229, 1128, 1100, 946, 804, 754, 650, 621 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{22}H_{20}F_3N_2$ 369.1573, found 369.1575.

*5-(p-Methyoxybenzyl)-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]azepine (**4l**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2i** (102 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (5% EtOAc in hexanes) in 68% yield (52 mg) as a clear colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (t, J = 2.0, 1.0 Hz, 1H), 7.53−7.46 (m, 1H), 7.29−7.25 (m, 2H), 7.23−7.14 (m, 3H), 7.05 (ddd, J = 7.4, 6.2, 2.4 Hz, 1H), 6.82−6.78 (m, 2H), 4.90 (s, 2H), 3.74 (s, 3H), 3.46−3.37 (m, 2H), 3.37−3.26 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 158.8, 155.8 (q, $J_{(C-F)}$ = 1.4 Hz), 148.0, 143.0, 137.5 (q, $J_{(C-F)}$ = 4.2 Hz), 136.6, 129.3, 128.8, 128.6, 127.0, 124.6, 124.0 (q, $J_{(C-F)}$ = 32.5 Hz), 123.6 (q, $J_{(C-F)}$ = 272.5 Hz), 122.8 (q, $J_{(C-F)}$ = 3.5 Hz), 121.5, 114.0, 55.1, 55.0, 37.5, 29.9. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.29. FT-IR: 2925, 2853, 1612, 1513, 1494, 1458, 1430, 1417, 1331, 1250, 1171, 1147, 1127, 1100, 1035, 945, 890, 826, 755 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{22}H_{20}F_3N_2O$ 385.1522, found 385.1527.

*5-Benzyl-7-methoxy-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]azepine (**4m**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2j** (100 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (5% EtOAc in hexanes) in 90% yield (69 mg, mp = 107−109 °C) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (s, 2H), 7.47 (s, 1H), 7.38−7.33 (m, 2H), 7.30−7.24 (m, 2H), 7.22−7.16 (m, 1H), 7.10 (d, J = 8.3 Hz, 1H), 6.73 (dd, J = 2.5, 0.7 Hz, 1H), 6.59 (dd, J = 8.3, 2.5 Hz, 1H), 4.94 (s, 2H), 3.75 (s, 3H), 3.47−3.30 (m, 2H), 3.30−3.19 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 158.6, 156.3 (q, $J_{(C-F)}$ = 1.6 Hz), 148.7, 143.0, 137.9 (q, $J_{(C-F)}$ = 4.2 Hz), 136.6, 129.5, 128.6, 128.4, 128.0, 127.5, 124.0 (q, $J_{(C-F)}$ = 32.6 Hz), 123.5 (q, $J_{(C-F)}$ = 272.6 Hz), 122.9 (q, $J_{(C-F)}$ = 3.6 Hz), 109.4, 107.9, 55.6 55.4, 37.5, 29.2. ^{19}F NMR (500 MHz, $CDCl_3$): δ −62.28. FT-IR: 2923, 2858, 1724, 1610, 1507, 1436, 1327, 1252, 1219, 1166, 1128, 1080, 1018, 965, 840, 740, 699 cm^{-1}. HRMS (DART): m/z [M + H]$^+$ calcd for $C_{22}H_{20}F_3N_2O$ 385.1522, found 385.1527.

*5-Benzyl-8-methyl-3-(trifluoromethyl)-10,11-dihydro-5H-benzo-[b]pyrido[2,3-f]azepine (**4n**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2k** (97 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (5% EtOAc in hexanes) in 83% yield (61 mg, mp = 74−75 °C) as a clear colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.45 (s, 1H), 7.35 (d, J = 7.5 Hz, 2H), 7.30−7.24 (m, 3H), 7.19 (t, J = 7.1 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.99 (s, 1H), 6.87 (d, J = 7.6 Hz, 1H), 4.96 (s, 2H), 3.38 (q, 2H), 3.28 (m, 2H), 2.29 (s, 3H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.0 (q, $J_{(C-F)}$ = 1.5 Hz), 148.1, 142.9, 137.5 (q, $J_{(C-F)}$ = 4.2 Hz), 136.75, 136.73, 133.5, 129.1, 128.6, 128.6, 128.1, 127.7, 127.5, 127.2, 125.3, 124.7, 124.0 (q, $J_{(C-F)}$ = 32.5 Hz), 123.6 (q, $J_{(C-F)}$ = 272.7 Hz), 122.7, 122.6 (q, $J_{(C-F)}$ = 3.5 Hz), 122.5, 122.1, 117.8, 111.4, 55.6, 37.7, 29.5, 21.2.^{19}F NMR (400 MHz, $CDCl_3$): δ −62.38. FT-IR: 3043, 2925,

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2873, 1603, 1508, 1433, 1328, 1243, 1165, 1124, 1101, 1080, 1027, 957, 892, 740, 699 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{22}H_{20}F_3N_2$ 369.1573, found 369.1578.

*Methyl 5-Benzyl-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]-pyrido[2,3-f]azepine-8-carboxylate (**4o**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2l** (110 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (5% EtOAc in hexanes) in 18% yield (15 mg) as clear colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.34 (dd, J = 2.0, 1.0 Hz, 1H), 7.87 (s, 1H), 7.82 (dd, J = 8.4, 2.1 Hz, 1H), 7.53 (d, J = 1.9 Hz, 1H), 7.37−7.29 (m, 2H), 7.29−7.23 (m, 2H), 7.23−7.14 (m, 2H), 5.00 (s, 2H), 3.88 (s, 2H), 3.43 (q, J = 4.9, 4.3 Hz, 2H), 3.34 (dd, J = 7.5, 4.3 Hz, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 166.6, 156.5 (q, $J_{(C-F)}$ = 1.2 Hz), 151.2, 142.6, 138.6 (q, $J_{(C-F)}$ = 3.8 Hz), 136.1, 134.9, 130.9, 129.2, 128.7, 128.5, 127.9, 126.2, 125.4, 124.4 (q, $J_{(C-F)}$ = 33.2 Hz), 123.7 (q, $J_{(C-F)}$ = 3.4 Hz), 123.4 (q, $J_{(C-F)}$ = 272.6 Hz), 120.9, 56.0, 52.0, 36.6, 30.5. ^{19}F NMR (500 MHz, $CDCl_3$): −62.28. FT-IR: 2961, 2855, 1717, 1609, 1499, 1431, 1337, 1293, 1227, 1128, 945, 911, 777, 741, 701 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{23}H_{20}F_3N_2O_2$ 413.1471, found 413.1477.

*5-Benzyl-7-cyano-3-(trifluoromethyl)-10,11-dihydro-5H-benzo-[b]pyrido[2,3-f]azepine (**4p**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2m** (100 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (5% EtOAc in hexanes) in 13% yield (10 mg) as a clear colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.37 (dd, J = 2.0, 1.0 Hz, 1H), 7.55 (d, J = 1.9 Hz, 1H), 7.46 (d, J = 2.0 Hz, 1H), 7.42 (dd, J = 8.4, 2.1 Hz, 1H), 7.32−7.23 (m, 4H), 7.24−7.16 (m, 2H), 4.98 (s, 2H), 3.43 (dd, J = 8.3, 4.4 Hz, 2H), 3.33−3.22 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.6 (d, $J_{(C-F)}$ = 1.5 Hz), 150.7, 142.4, 139.3 (q, $J_{(C-F)}$ = 4.1 Hz), 135.6, 135.5, 133.4, 130.9, 128.8, 127.9, 124.7 (q, $J_{(C-F)}$ = 32.9 Hz), 124.3 (q, $J_{(C-F)}$ = 3.5 Hz), 123.3 (q, $J_{(C-F)}$ = 272.6 Hz), 121.6, 118.7, 106.9, 56.1, 35.9, 30.5. ^{19}F NMR (500 MHz, $CDCl_3$): δ −62.38. FT-IR: 3037, 2964, 2927, 2861, 2226, 1606, 1497, 1425, 1339, 1331, 1309, 1233, 1128, 1102, 947, 910, 834, 740, 699 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{22}H_{16}F_3N_3$ 380.1369, found 380.1375.

*N-Benzyl-3,7-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4q**).* Following procedure 2, **1a** (42 mg, 0.2 mmol), **2n** (113 mg, 0.6 mmol, 1.5 equiv), and KOH (50 mg, 0.6 mmol, 3 equiv) were added (KOH was used in place of K_2CO_3). The product was isolated by column chromatography (5% EtOAc in hexanes) in 24% yield (21 mg) as a clear colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, J = 0.9 Hz, 1H), 7.60 (d, J = 1.5 Hz, 1H), 7.52 (s, 1H), 7.48 (dd, J = 8.5, 1.9 Hz, 1H), 7.45−7.38 (m, 2H), 7.37−7.30 (m, 3H), 7.29−7.27 (m, 1H), 5.06 (s, 2H), 3.53−3.50 (m, 2H), 3.44−3.41 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.2 (d, $J_{(C-F)}$ = 1.4 Hz), 151.0−149.4 (q, 1.2), 142.6, 138.7 (q, $J_{(C-F)}$ = 4.1 Hz), 136.0, 135.8, 128.8, 128.0, 127.8, 126.3 (q, $J_{(C-F)}$ = 3.7 Hz), 125.9 (q, $J_{(C-F)}$ = 32.8 Hz), 124.4 (q, $J_{(C-F)}$ = 272.3 Hz), 124.4 (q, $J_{(C-F)}$ = 32.8 Hz), 124.0 (q, $J_{(C-F)}$ = 3.8 Hz), 124.0 (q, $J_{(C-F)}$ = 271.4 Hz), 123.6 (q, $J_{(C-F)}$ = 3.5 Hz), 121.3, 55.9, 36.4, 30.4. ^{19}F NMR (377 MHz, $CDCl_3$-insert): δ −62.1, −62.3. FTIR: 3032, 2926, 2865, 1613, 1597, 1435, 1417, 1323, 1229, 1110, 947, 911, 831, 829 735, 699, 701, 635. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{22}H_{17}F_6N_2$ 423.1290, found 423.1292.

*5-Methyl-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4r**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2o** (70 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (2−5% EtOAc in hexanes) in 80% yield (44 mg) as a clear colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.44 (s, 1H), 7.25−7.19 (m, 2H), 7.12−7.04 (m, 2H), 3.39−3.36 (m, 5H), 3.22 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 154.5 (q, $J_{(C-F)}$ = 1.4 Hz), 148.3, 144.0, 136.6 (q, $J_{(C-F)}$ = 4.2 Hz), 136.2, 128.6, 126.9, 124.4 (q, $J_{(C-F)}$ = 32.4 Hz), 124.2, 123.7 (q, $J_{(C-F)}$ = 272.8 Hz), 120.4, 120.3 (q, $J_{(C-F)}$ = 3.5 Hz), 40.1, 38.1, 29.9. ^{19}F NMR (500 MHz, $CDCl_3$): δ −62.14. FT-IR: 2929, 2812, 1603, 1564, 1495, 1457, 1434, 1413, 1336, 1283, 1116, 1099, 944, 889, 758, 634 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{15}H_{14}F_3N_2$ 279.1109, found 279.1109.

*5-Ethyl-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4s**).* Following procedure 2, **1a** (42 mg, 0.2 mmol) and **2p** (74 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (2−5% EtOAc in hexanes) in 68% yield (40 mg, mp = 74−75 °C) as a clear colorless solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, J = 1.0 Hz, 1H), 7.48 (d, J = 1.6 Hz, 1H), 7.23−7.19 (m, 2H), 7.11−7.05 (m, 2H), 3.80 (q, J = 7.0 Hz, 2H), 3.36 (m, 2H), 3.23 (m, 2H), 1.18 (t, J = 7.0 Hz, 3H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 155.8 (q, $J_{(C-F)}$ = 1.4 Hz), 147.3, 143.9, 137.3 (q, $J_{(C-F)}$ = 4.2), 137.4, 128.7, 123.68 (q, $J_{(C-F)}$ = 272.2 Hz), 126.9, 124.3 (q, $J_{(C-F)}$ = 32.7 Hz), 124.6, 122.1 (q, $J_{(C-F)}$ = 3.51 Hz), 121.6, 45.2, 37.4, 29.6, 13.5. ^{19}F NMR (500 MHz, $CDCl_3$): δ −62.13. FT-IR: 2964, 2916, 2846, 1609, 1494, 1458, 1424, 1333, 1234, 1146, 1134, 1104, 961, 901, 765 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{16}H_{16}F_3N_2$ 293.1266, found 293.1266.

*5-Propyl-3-(trifluoromethyl)-10,11-dihydro-5H-benzo[b]pyrido-[2,3-f]azepine (**4t**).* Following procedure 2, **1a** (42 mg, 0.2 mmol), **2q** (78 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (2−5% EtOAc in hexanes) in 70% yield (42 mg, mp = 55−56 °C) as a clear colorless solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, J = 0.6 Hz, 1H), 7.39 (d, J = 1.5 Hz, 1H), 7.14−7.06 (m, 2H), 7.03−6.92 (m, 2H), 3.60 (t, J = 6.9 Hz, 2H), 3.29−3.22 (m, 2H), 3.16−3.11 (m, 2H), 1.49 (h, J = 7.2 Hz, 2H), 0.81 (t, J = 7.4 Hz, 3H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 155.8 (q, $J_{(C-F)}$ = 1.4 Hz), 147.4, 144.0, 137.4 (q, $J_{(C-F)}$ = 4.2 Hz), 137.3, 128.8, 126.9, 124.6, 124.3 (q, $J_{(C-F)}$ = 32.4 Hz), 123.7 (q, $J_{(C-F)}$ = 272.9 Hz), 122.1 (q, $J_{(C-F)}$ = 3.5 Hz), 121.6, 52.5, 37.4, 29.6, 20.7, 11.6.^{19}F NMR (500 MHz, $CDCl_3$): δ −62.13. FT-IR: 2970, 2930, 2882, 2855, 1603, 1494, 1416, 1335, 1226, 1124, 1098, 957, 899, 755 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{17}H_{18}F_3N_2$ 307.1422, found 307.1422.

*5-Benzyl-3-cyano-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]-azepine (**4u**).* Following procedure 2, **1a** (33 mg, 0.2 mmol) and **2b** (92 mg, 0.3 mmol, 1.5 equiv) were added. The product was isolated by column chromatography (5% EtOAc in hexanes) in 41% yield (26 mg, mp = 146−148 °C) as a clear colorless solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.26 (d, J = 1.8 Hz, 1H), 7.44 (d, J = 1.8 Hz, 1H), 7.37−7.33 (m, 2H), 7.29 (t, J = 7.5 Hz, 2H), 7.24−7.14 (m, 4H), 7.09−7.04 (m, 1H), 4.94 (s, 2H), 3.43−3.36 (m, 2H), 3.36−3.28 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.4, 147.8, 143.2, 142.9, 136.8, 136.3, 128.8, 128.7, 127.8, 127.6, 127.2, 125.0, 121.7, 117.0, 106.8, 55.8, 38.2, 29.7. FT-IR: 3040, 2934, 2846, 2231, 1580, 1493, 1451, 1410, 1331, 1242, 1152, 1113, 961, 905, 762, 726, 697 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{21}H_{18}N_3$ 312.1495, found 312.1501.

*3-Cyano-5-methyl-10,11-dihydro-5H-benzo[b]pyrido[2,3-f]-azepine (**4v**).* Following procedure **2**, **1a** (33 mg, 0.2 mmol), **2o** (70 mg, 0.3 mmol, 1.5 equiv) and KOH (50 mg, 0.6 mmol, 3 equiv) were added (KOH was used in place of K_2CO_3). The product was isolated by column chromatography (5% EtOAc in hexanes) in 51% yield (24 mg, 122−123 °C) as clear colorless needles. ^1H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, J = 1.7 Hz, 1H), 7.45 (d, J = 1.8 Hz, 1H), 7.25−7.18 (m, 2H), 7.12−7.05 (m, 2H), 3.39−3.33 (m, 5H), 3.24−3.18 (m, 2H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 155.2, 148.0, 143.9, 142.2, 136.3, 128.5, 127.1, 125.7, 124.5, 120.7, 117.2, 107.1, 40.3, 38.6, 29.7. FT-IR: 2961, 2931, 2238, 1588, 1494, 1458, 1410, 1325, 1252, 1116, 989, 700 cm^{-1}. HRMS (DART): m/z $[M + H]^+$ calcd for $C_{15}H_{14}N_3$ 236.1183, found 236.1187.

*3-(Trifluoromethyl)-5-(4-(trifluoromethyl)phenyl)-10,11-dihydro-5H-benzo[b]pyrido[2,3- f]azepine (**4w**).* The substrates used were 3-chloro-5-(trifluoromethyl)-2-vinylpyridine (42 mg, 0.20 mmol, 1 equiv), 2-aminophenylboronic acid (66 mg, 0.3 mmol, 1.5 equiv), and 1-chloro-4-(trifluoromethyl)benzene (32 μL, 0.24 mmol, 1.2 equiv). The product was isolated using column chromatography (40% EtOAc/hexanes) to give the titled compound in 52% yield (21 mg, mp 155−158 °C) as a yellow crystalline solid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 (dd, J = 2.2, 1.0 Hz, 1H), 7.98 (d, J = 192.1 Hz, 1H), 7.52−7.33 (m, 6H), 6.67−6.54 (m, 2H), 3.29 (t, J = 6.8 Hz, 2H), 3.02 (dd, J = 7.6, 6.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.8 (q, $J_{(C-F)}$ = 1.1 Hz), 150.28 (q, J = 1.1 Hz), 144.4 (q, $J_{(C-F)}$ = 3.9 Hz), 142.4, 139.1, 138.1, 134.7 (q, $J_{(C-F)}$ = 3.5 Hz), 130.6, 129.4, 128.9, 128.0, 126.6 (q, $J_{(C-F)}$ = 3.7 Hz), 125.4 (q, $J_{(C-F)}$ = 33.3 Hz), 124.5 (q, $J_{(C-F)}$ = 270.7 Hz), 123.0 (q, $J_{(C-F)}$ = 272.6 Hz), 121.0 (q, $J_{(C-F)}$ = 32.8 Hz), 112.4, 35.3, 28.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ −61.51,

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−62.07. IR (NaCl, neat): 2930, 2859, 1605, 1518, 1410, 1321, 1165, 1138, 1117, 1069, 827, 756 cm-1. HRMS (DART): *m/z* cacld for $C_{21}H_{15}F_6N_2$ $(M+H)^+$ 409.1139, found 409.1142.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00568.

^1H, ^{13}C NMR for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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