UNIVERSITÄT ROSTOCK

Synthesis of Substituted 1-Deazapurines *via* Pd/Cu Catalysed C-H Activation, Substituted Naphthyridines, Quinoxalines, and Trifluoromethyl-Substituted Arenes by Pd(0)-Catalysed Cross-Coupling Reactions

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Affectionately Dedicated to

My Family and My Teachers

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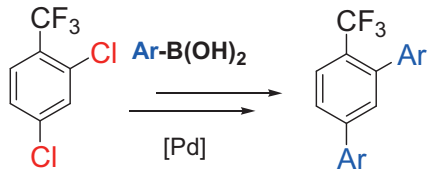
IFTIKHAR ALI

September 2011, Rostock, Germany

MAIN CONTENTS

Regioselective Palladium-Catalysed Cross-Coupling Reactions of 2,4-Dichloro-1-(trifluoromethyl)benzene



Suzuki-Miyaura cross-coupling reactions of 2,4-dichloro-1-(trifluoromethyl)benzene provided mono- and diarylated products. The first attack occurred at the less sterically hindered and the more electronically deficient position at C-4.

DETAILED CONTENTS

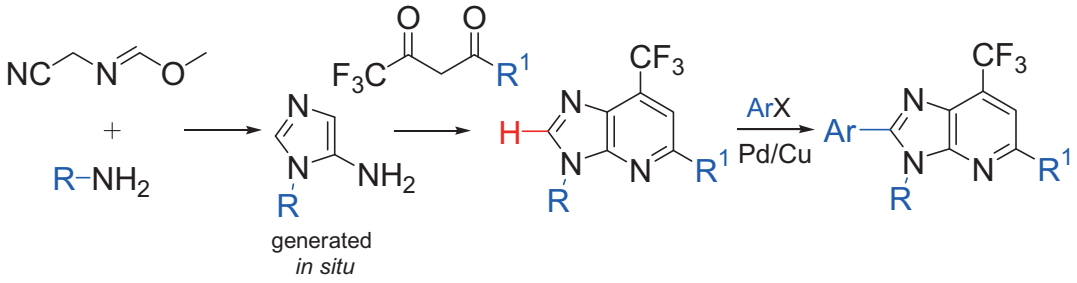
Summary of the Thesis

Aromatic organic compounds are ubiquitous in the modern society as medicines and functionalized materials. Heteroaromatic compounds have attracted considerable attention in these areas. Heterocycles are one of the most important organic structural motifs in a myriad of pharmaceutically active compounds and organic materials.

Therefore, the efficient synthesis of heterocycles and their derivatives has been a topic of great interest from the perspective of medicinal chemistry and organic synthesis. The simplest approach among the synthetic strategies is the arylation of heterocyclic C-H bonds. Palladium-catalyzed transformations possess an interesting and remarkable power for C-C bond formation.

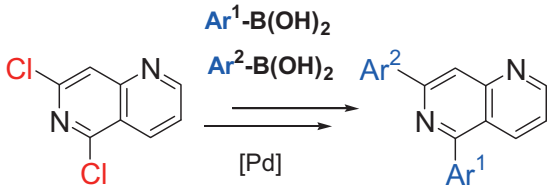
The aim of the present dissertation is to enhance the scope of palladium-catalyzed reactions. This paragraph outlines the tasks of this thesis. A more detailed introduction is given at the beginning of each chapter.

The first task was to synthesize 1-deazapurines from primary amines and 1,3-electrophilic reagents. After that Pd/Cu catalysed reactions afforded arylated products of 1-deazapurines by C-H bond activation.

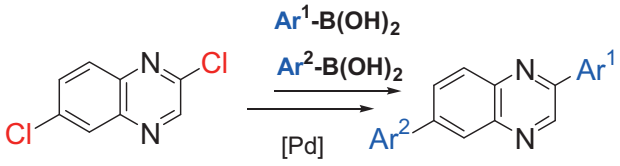


In Prof. Langer's research group, a number of di- and trihalogenated molecules or the corresponding triflates have already been studied with regard to the site-selectivities of Pd(0)-catalysed cross-coupling reactions.

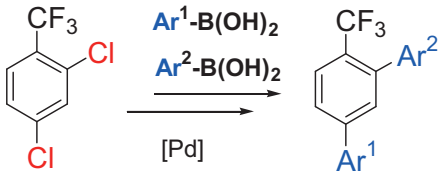
In continuation to that work, Pd(0)-catalysed reactions were carried out on 5,7-dichloro-1,6-naphthyridine. The reactions afforded mono- and diarylated naphthyridine derivatives.



Another task was to study the regioselective cross-coupling reactions of 2,6-dichloroquinoxaline. These reactions afforded mono- and diarylated quinoxaline derivatives with good site selectivity.



In addition, 2,4-dichloro-1-trifluoromethylbenzene was also studied for Pd(0)-catalysed cross coupling reactions. These reactions afforded the desired arylated products with good site selectivity.



1 Pd/Cu Catalysed Arylation of 1-Deazapurines *via* C-H Bond Activation

1.1 General Introduction

Heterocyclic compounds play a role of immense importance in human life because of their widespread applications, medicinal value in particular. Nitrogen heterocycles possess diverse medicinal potential that's why these compounds have received special attention in pharmaceutical chemistry.[1] Nitrogen-containing heterocycles are integral components of natural products, dyes, agrochemicals, and pharmaceuticals.[2]

Benzimidazoles are amongst the nitrogen containing pharmacologically active heterocyclic compounds.[3] Various compounds with benzimidazole motif possess a broad spectrum of biological activities including potent antifungal,[4] cytotoxic,[5] anticancer and antimetastatic (Tilomisole),[6] antitumor (TBZ),[7] anthelmintic (Albendazole (Abz), Mebendazole (Mbz)),[8] antiparasitic[9] and anti-HIV activity.[10]

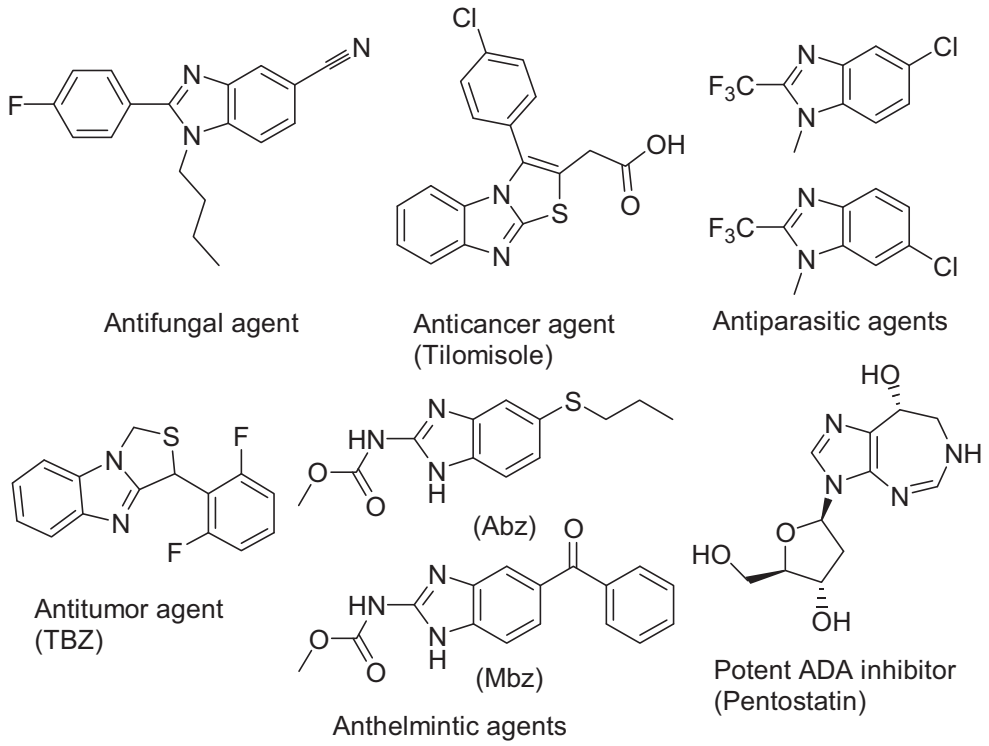
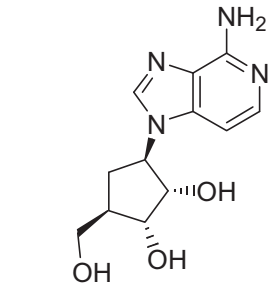


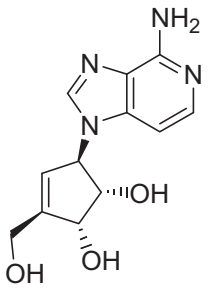
Figure 1. Pharmacologically relevant benzimidazole derivatives

Besides, vitamin-B12 contains a benzimidazole moiety.[11] Similarly, many commercially available drugs and pharmaceuticals contain a benzimidazole motif, such as Pradaxa, Astemizole, Omeprazol, Candesartan and Pentostatin.[12] Furthermore, benzimidazoles and related compounds act as corrosion inhibitors for metals and alloys.[13]

Purine and its derivatives are structural elements of therapeutic drug molecules. Many molecules with purine motif display a wide variety of interesting biological properties. Some of them are reported as adenosine receptor ligands,[14] modulators of multidrug resistance,[15] antiviral and antitumor agents,[16] antineoplastic agents,[17] and enzyme inhibitors.[18] For the finding of new biologically valuable agents, medicinal chemists and biochemists study structural modifications of naturally occurring nucleosides.[19] All such biological aspects are relevant for deazapurine derivatives. For example, carbocyclic nucleosides 3-deazaaristeromycin[20] and 3-deazaneplanocin[21] are noteworthy motifs among the 3-deazapurine derivatives that display biological activity.



(-)-3-deazaaristeromycin



(-)-3-deazaneplanocin

Figure 2. Pharmacologically relevant 3-deazapurine derivatives

7-Deazapurine nucleosides with frequent occurrence possess interesting biological properties. For example, a number of derivatives have been reported to show antiviral activities.[22]

1.2 Introduction

Imidazo[4,5-*b*]pyridine (commonly known as 1-deazapurine) is an important pharmacophore which leads to the synthesis of a number of biologically relevant targets. 1-Deazapurines constitute an important class of heterocyclic compounds which exhibit a broad spectrum of pharmacological properties.[23] 1-Deazapurine is a common structural motif found in numerous molecules that display antiviral, antifungal, antibacterial and antiproliferative activities. The potent biological activities and the prevalence of 1-desazapurines in both natural products and pharmaceuticals has inspired significant interest in the synthesis of these heterocycles.[24] 1-Deazapurine derivatives have been reported as potential phosphodiesterase inhibitors,[25] adenosine deaminase (ADA) inhibitors,[26] GPR4 receptor antagonists,[27] aurora-kinase inhibitors (CCT 129202), AT1 receptor (L-158,809) and AT1 antagonist[28] (Figure 3).

Some derivatives are reported to exhibit antitumor, anti-HIV-1, cytotoxic and adenosine-deaminase inhibition activities[29] along with in vivo activity against mouse leukemia.[30] Additionally, imidazo[4,5-*b*]pyridin-2-ones have been reported as nonsteroidal anti-inflammatory and analgesic agents[31] (Figure 3) with antidepressant, antiphlogistic, cardiotonic, hypotensive, antiarrhythmic and antisecretory biological activities.[32] Furthermore, 1-deazapurine derivatives are also considered as candidates for components of unnatural base pairs that are expected to develop novel functional biopolymers.[33]

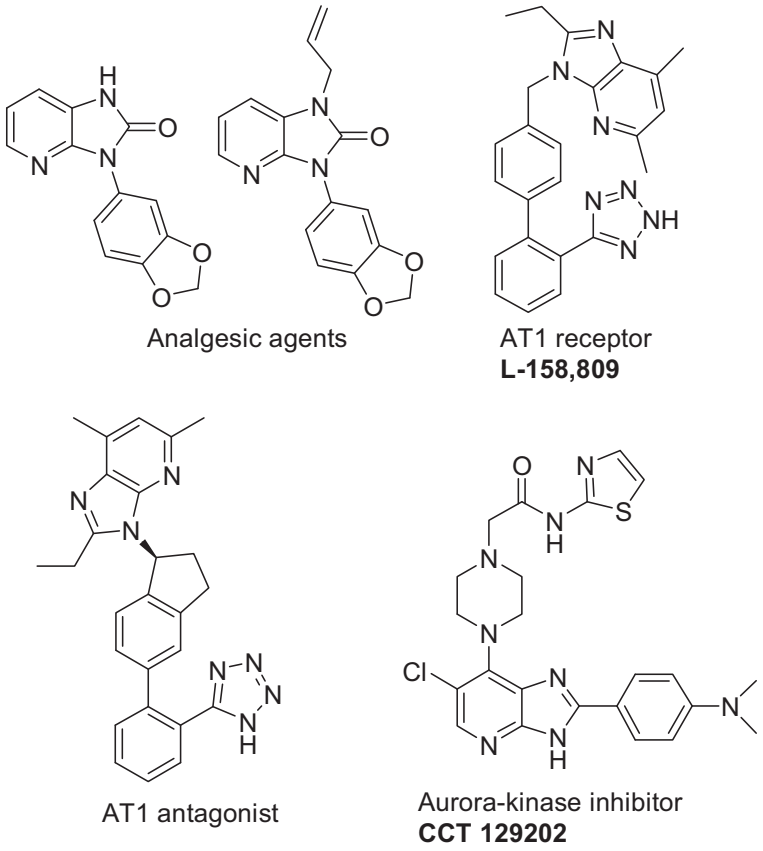


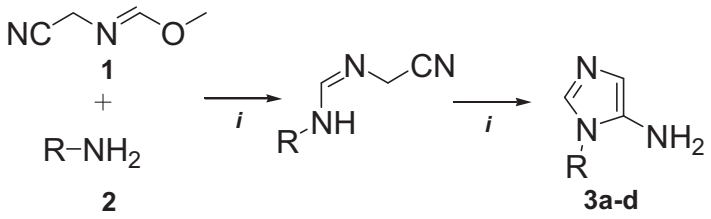
Figure 3. Pharmacologically relevant imidazo[4,5-*b*]pyridines (1-deazapurines)

C-H bond activation is an important area of organometallic chemistry that provides improved protocols in synthetic organic chemistry. In recent years, direct C-H activation reactions have received prominent attention[34] as an alternative method to cross-coupling reactions with the use of organometallics. Direct C-H arylation of arenes and heterocycles has been achieved by using, e.g., Rh,[35] Ru,[36] or Pd[37] catalysis using different bases and many types of aryl halides. I have studied the Pd/Cu catalysed arylation reactions of 1-deazapurine.

Direct C-H arylation of 1-deazapurine to the 2-position by diverse aryl halides was achieved with Pd catalysis in the presence of CuI and Cs_2CO_3, following a procedure[38] already reported.

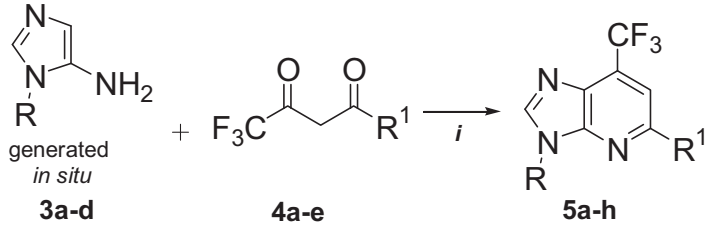
1.3 Results and Discussion

5-Aminoimidazoles **3a-d** were generated *in situ* by reaction of methyl *N*-(cyanomethyl)formimidate (**1**) with primary amines (**2a-d**) in continuous argon supply and subsequent cyclization (Scheme 1).



Scheme 1. Synthesis of 5-aminoimidazoles **3a-d** (generated *in situ*). Reagents and conditions: (i) CH_2Cl_2, Argon, Reflux, 2h.

The *in situ* generated imidazoles **3a-d** were treated with an equivalent amount of 1,3-electrophilic reagents (**4a-e**) and the reactions afforded the corresponding substituted imidazo[4,5-b]pyridines (1-deazapurines) **5a-h** in good yields. The best yield was obtained when the primary amine **2a** and the electrophilic reagent **4c** were reacted. (Scheme 2, Table 1).



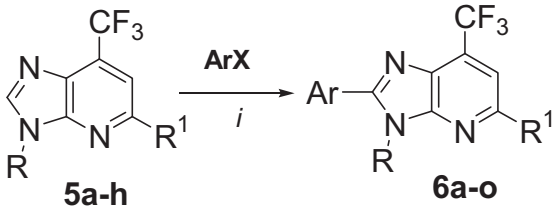
Scheme 2. Synthesis of substituted 3H-imidazo[4,5b]pyridines **5a-h**. Reagents and conditions: (i) CH_2Cl_2, argon, reflux, 5 h.

Table 1. Synthesis of **5a-h**

5	2, 3	4	R	R^1	% (**5**) [a]
a	**a**	**a**	4-(MeO)$C_6H_4CH_2$	CF_3	51
b	**a**	**b**	4-(MeO)$C_6H_4CH_2$	CH_3	65
c	**a**	**c**	4-(MeO)$C_6H_4CH_2$	2-Furyl	98
d	**b**	**d**	*t*-Bu	2-Thienyl	71
e	**b**	**b**	*t*-Bu	CH_3	69
f	**b**	**e**	*t*-Bu	C_6H_5	77
g	**c**	**e**	*c*-Hex	C_6H_5	70
h	**d**	**d**	$PhCH_2CH_2$	2-Thienyl	75

[a]Yields of isolated products.

The substituted 3H-imidazo(4,5-*b*)pyridines (**5a-h**) were treated with 2 mmol of aryl halides (**ArX**). The reactions were set up in the presence of argon and were carried out in DMF at 150 ^{0}C for different time periods. The corresponding arylated products **6a-o** were obtained in good yields (Scheme 3, Table 2).



Scheme 3. Synthesis of arylated 3H-imidazo[4,5-*b*]pyridines **6a-o**. Reagents and conditions: (i) $Pd(OAc)_2$ (5 mol%), CuI (3 equiv.), Cs_2CO_3 (2.5 equiv.), **ArX** (2 equiv.), DMF, Argon, 150 ^{0}C.

The reactions of electron poor aryl halides (containing F, CF_3) afforded the corresponding products in low yields, while electron rich aryl halides (containing Me, Et) afforded the corresponding products in higher yields.

The reactions of 3*H*-imidazo[4,5-*b*]pyridines **5b** with 4-iodotoluene and **5h** with phenylbromide resulted in the products **6b** and **6j**, respectively, in the best yields (Scheme 3, Table 2).

Table 2. Synthesis of **6a-n**.

Entry	6	5	R	R^1	ArX	t (h)	% (6)[a]
1	**a**	**a**	4-(MeO)$C_6H_4CH_2$	CF_3	4-MeC_6H_4I	50	42
2	**b**	**b**	4-(MeO)$C_6H_4CH_2$	CH_3	4-MeC_6H_4I	30	93
3	**c**	**c**	4-(MeO)$C_6H_4CH_2$	2-Furyl	4-MeC_6H_4I	30	69
4	**d**	**d**	*t*-Bu	2-Thienyl	4-MeC_6H_4I	48	59
5	**e**	**f**	*t*-Bu	C_6H_5	4-MeC_6H_4I	60	31
6	**f**	**e**	*t*-Bu	CH_3	2,4-$(Me_2)C_6H_3I$	56	50
7	**g**	**e**	*t*-Bu	CH_3	4-EtC_6H_4I	30	50
8	**h**	**c**	4-(MeO)$C_6H_4CH_2$	2-Furyl	C_6H_5Br	48	58
9	**i**	**d**	*t*-Bu	2-Thienyl	C_6H_5Br	30	47
10	**j**	**h**	$PhCH_2CH_2$	2-Thienyl	C_6H_5Br	57	83
11	**k**	**g**	*c*-Hex	C_6H_5	2-FC_6H_4Br	40	43
12	**l**	**f**	*t*-Bu	C_6H_5	2-FC_6H_4Br	60	25
13	**m**	**e**	*t*-Bu	CH_3	3-$(CF_3)C_6H_4Br$	56	20
14	**n**	**g**	*c*-Hex	C_6H_5	4-$(CF_3)C_6H_4Cl$	30	31
15	**o**	**f**	*t*-Bu	C_6H_5	4-EtC_6H_4I	30	63

[a] Yields of isolated products.

The structures of all products were established by spectroscopic methods. The structures of **6a** (Figure 4) and **6b** (Figure 5) were independently confirmed by 2D NMR correlations using HMBC, HSQC and NOESY. The chemical shift values of the carbon atoms were assigned with the help of HSQC experiments.

In the HMBC spectrum of **6a**, the aromatic protons at δ = 7.73 showed a strong correlation with C-2 (133.4). In the NOESY spectrum of **6a**, the aromatic protons (δ = 7.73) showed an interaction with the methylene protons (δ = 5.65) attached with the carbon resonating at δ = 47.1. The clear correlations and information from 2D NMR studies on **6a** (Figure 4) and **6b** (Figure 5) unambiguously confirmed that the 4-MeC_6H_4 moiety is attached to carbon atom C-2.

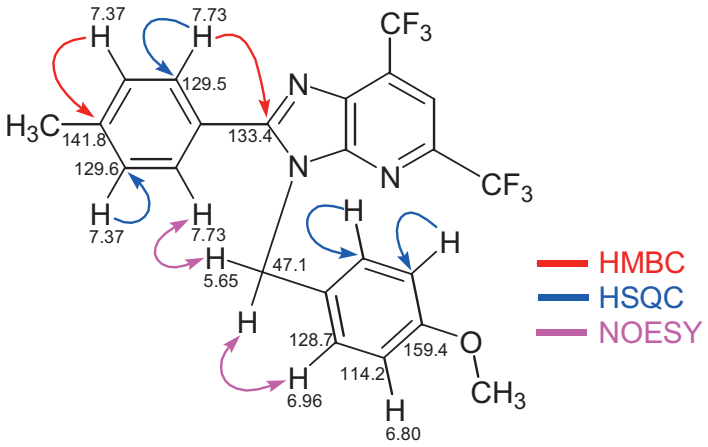


Figure 4. 2D-NMR correlations (HMBC, HSQC and NOESY) of **6a**.

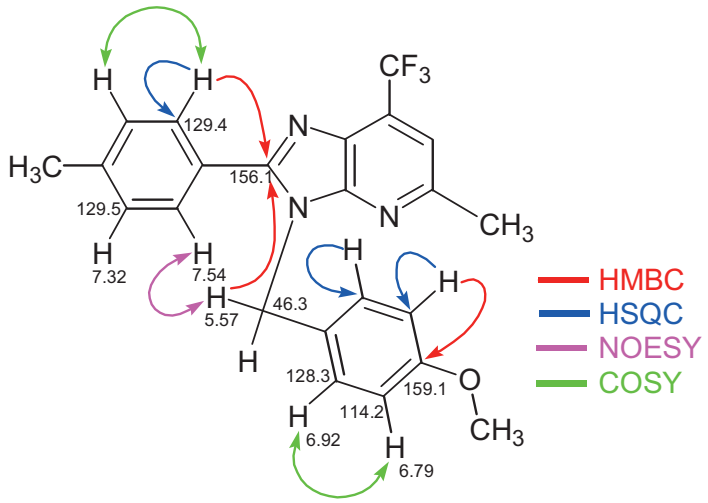
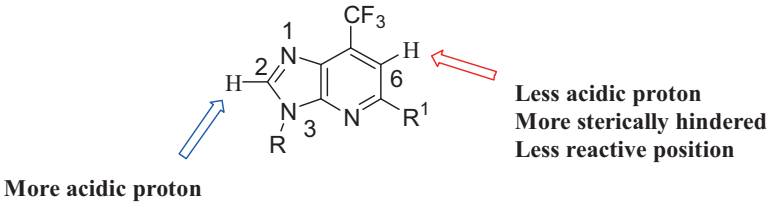


Figure 5. 2D-NMR correlations (HMBC, HSQC, NOESY and COSY) of **6b**.

The C-H bond at position **2** is more reactive because the proton is more acidic. The proton at C-6 is less acidic and is more sterically hindered. In conclusion, Pd/Cu easily activates the C-H bond at position 2, hence arylation takes place at C-2 (Scheme 4).



Scheme 4: Possible explanation for the C-H activation reactions of **5**

1.4 Conclusion

I have successfully synthesized derivatives of 3*H*-imidazo[4,5-*b*]pyridines (1-deazapurines) by the methodology of C-H bond activation following a procedure already reported. But this is the first time to synthesize arylated products of 3*H*-imidazo[4,5-*b*]pyridines.

In conclusion, a general Pd-catalyzed arylation of purines with aryl iodides by C-H activation in position **2** was developed by using Cs_2CO_3 and CuI as additives. Though the reaction conditions are rather harsh, the method can be efficiently applied in the synthesis of diverse 2-aryl-1-deazapurines.

2 Regioselective Palladium(0)-Catalysed Cross-Coupling Reactions of 5,7-Dichloro-1,6-naphthyridine.

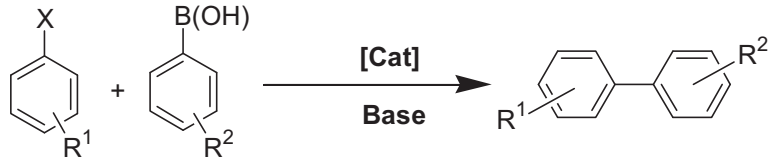
2.1 General Introduction

Pd-catalysed cross-coupling reactions with their tremendous enabling ability are modern, marvelous and powerful synthetic tools for the formation of highly substituted heterocycles[39] with their key role in total synthesis.[40] The regioselectivity of polyhalogenated heterocycles in Pd-catalysed cross-coupling reactions has been broadly studied and can provide a versatile and feasible way for the design and synthesis of libraries containing highly functionalized substituents in specific positions of a heterocyclic scaffold.[41]

The Suzuki-Miyaura reaction is a palladium-catalyzed cross-coupling of aryl halides (or pseudo halides) with organoboron reagents and is undoubtedly a most powerful, essential and versatile platform for catalytic transformations in organic chemistry. The Suzuki-Miyaura cross-coupling reaction has become one of the most widely utilized method for the formation of $C_{(sp2)}$-$C_{(sp2)}$ bonds because of its mild reaction conditions and its compatibility with a broad range of functional groups. The Suzuki-Miyaura reaction is currently a fundamental and interesting reaction for the preparation of diversified biaryls, which have a myriad of applications of worth in polymer, agricultural, agrochemical, pharmaceutical and material chemistry. Biaryls are present in a wide variety of compounds such as natural products, advanced materials, liquid crystals and more importantly ligand molecular probes for biological processes. Mostly, arylboronic acids are used as nucleophilic organoboron reagents in Suzuki-Miyaura reactions.[42]

In 1979, the seminal paper of Miyaura, Yamada, and Suzuki laid the basis for the Suzuki-Miyaura reaction which now emerged as an extremely powerful and valuable method for C-C bond formation by cross coupling of aryl bromides, iodides, chlorides and triflates with boronic acids. The reactivity order is ArI >ArBr>ArOTf>>ArCl.[43]

The Suzuki-Miyaura reaction has proven to be a practical way to generate C-C bonds by coupling an organic halide with an organoboron molecule, in the presence of a palladium catalyst (Scheme 5). The reaction proceeds in a basic medium, thus a boronate is the substrate involved in the substitution of the halide from the Pd(II) complex.



Scheme 5. Suzuki-Miyaura coupling reaction

The Suzuki-Miyaura reaction involes three steps in its mechanism. Firstly, oxidative addition of RX to Pd(0) takes place to form organopalladium halides. Then, in the transmetalation step, the halide is substituted by the organic R′ group of the organoboron species that provides a diorganopalladium complex, finally, in the reductive elimination, the C-C bond is formed, regenerating the catalyst (Figure 6).

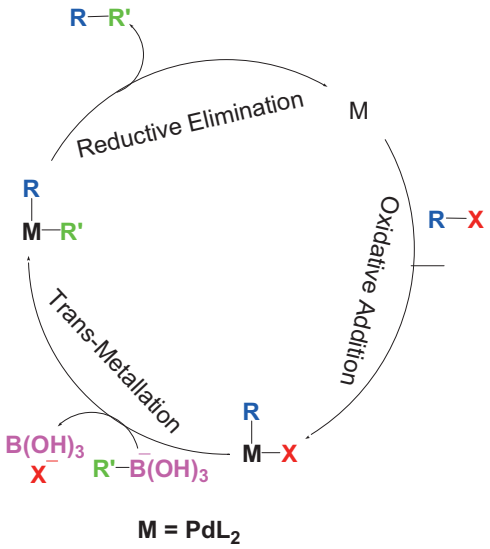


Figure 6. Simplified mechanism

The reaction proceeds in basic medium and a variety of bases can be used in this reaction, e.g. K_3PO_4, K_2CO_3, and Cs_2CO_3, which enhances the rate of transmetallation by increasing the nucleophilicity of the organoboran species by formation of an organoborate. The process can occur with a mono or dicoordinated Pd complex, with phosphines as the most common ligands, e.g. $Pd(OAc)_2$ together with phosphine ligands (such as PPh_3, PCy_3, SPhos and XPhos), $Pd(PPh_3)_2Cl_2$, or Pd $(PPh_3)_4$.[44]

Prof. Peter Langer's research group has carried out site-selective Suzuki-Miyaura reactions of polyhalogenated heteroaromatic and aromatic compounds or their triflates in a couple of years.

In this context, regioselective Suzuki-Miyaura reactions of tribromopyrazoles (**a**),[45] 2,3,4-tribromothiophene (**b**),[46] 2,3,5-tribromothiophene (**c**),[47] 2,3-dibromobenzofuran (**d**),[48] 1,2-dibromo-3,5-difluorobenzene (**e**),[49] 1,4-dibromo-2-fluorobenzene (**f**),[50] 2,4,5,6-tetrachloropyrimidine (**g**),[51] and tetrabromobenzoquinone (**h**)[52] have already been reported (Figure 7).

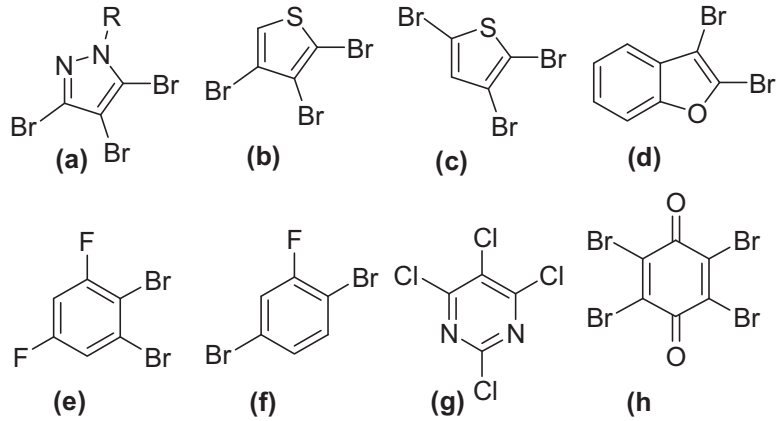


Figure 7. Suzuki-Miyaura reactions of vicinal halides studied in Prof. Langer's group

The Langer group has also reported regioselective Suzuki-Miyaura cross coupling reactions of several substrates containing triflate groups, such as bis(triflates) of dimethyl 4-fluoro-3,5-dihydroxphthalate (**i**),[53] 3,4-dihydroxbenzoate (**j**),[54] phenyl 1,4-dihydroxnaphthoate (**k**),[55] 2,4-bis(hydroxy)di- phenylsulfone (**l**),[56] 1,2-dihydroxyanthraquinone (**m**),[57] and methyl-2,5-dihydroxbenzoate (**n**)[58] (Figure 8). All substrates mentioned hereby proceeded with excellent site-selectivities.

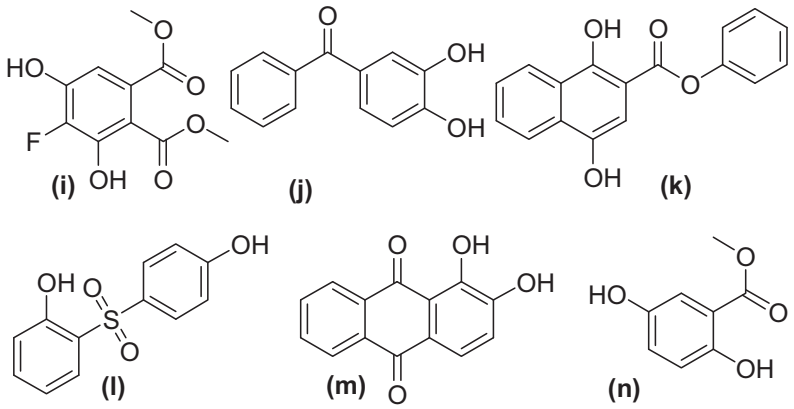


Figure 8. Dihydroxy substrates which were transformed into their triflates and subsequently reacted in Suzuki reractions (Langer group)

2.2 Introduction

Naphthyridines are nitrogen containing heterocycles in which two pyridine rings, each ring with one nitrogen atom, are joined through two adjacent carbon atoms. Arnold Reissert, in 1893, obtained the first derivative (1,8-naphthyridine) of the new heterocyclic system and suggested the common name naphthyridine to such heterocycles. Naphthyridines are also known as "pyridinopyridines" and "benzodiazines". There are generally six isomeric possible structures for naphthyridine heterocycles: 1,5- (**1**), 1,6- (**2**), 1,7- (**3**), 1,8- (**4**), 2,6- (**5**) and 2,7- naphthyridine (**6**) (Figure 9).

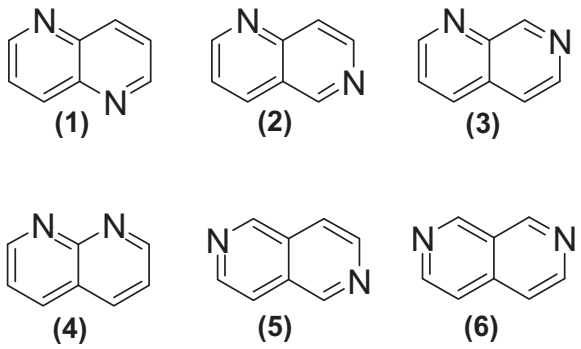


Figure 9. Isomeric structures of naphthyridine

In the literature some other terms have also been found, such as, "isonaphthyridine" [for 1,5-naphthyridine (**1**)], "benzodiazines", "pyridopyridines", "2,5-naphthyridine" [for 1,6-naphthyridine (**2**)], and "copyrin(e)" or copurine [for 2,7-naphthyridine (**6**)]. In 1927 the 1,5- and 1,8-naphthyridines were described as the first representatives of unsubstituted naphthyridines. The other isomers, 1,6-, 1,7- and 2,7-naphthyridines, were prepared in 1958 and 2,6-naphthyridine was synthesized in 1965.[59]

Pyridines and pyrido-fused derivatives, e.g. naphthyridines, are considered to be very interesting for their chemical reactivity and biological properties and these heterocycles possess wide range of pharmaceutical and agrochemical applications. Various naphthyridine derivatives exhibit a wide spectrum of biological activity such as bactericidal, fungicidal, antitumor, anti-inflammatory and carcinostatic. On behalf of such biological properties, naphthyridines have received considerable attention over the past years. The compounds incorporating naphthyridine motif have been reported useful in the treatment of cardiac arrhythmia, hypertention, rheumatoid arthritis, hyperlipidemia and mycocardial infarction.[60] 1,8-Naphthyridines have been reported to possess a wide range of biological activities such as antibacterial,[61] antitumor,[62] neurotoxic,[63] neuroprotective,[64] anticonvulsant and cardiac[65] activities (Figure 10).

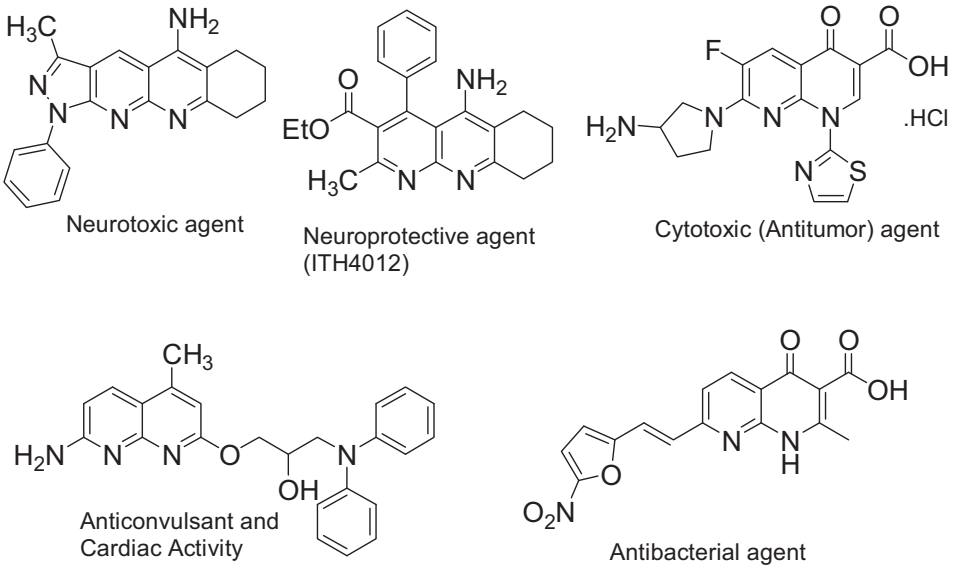


Figure 10. Pharmacologically relevant 1,8-naphthyridine derivatives.

Additionally several other naphthyridine derivatives exhibit inhibition of protein kinase D (PKD),[66] and acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE),[67] and some naphthyridine moieties act as transient receptor potential vanilloid (TRPV1) antagonist[68] (Figure 11).

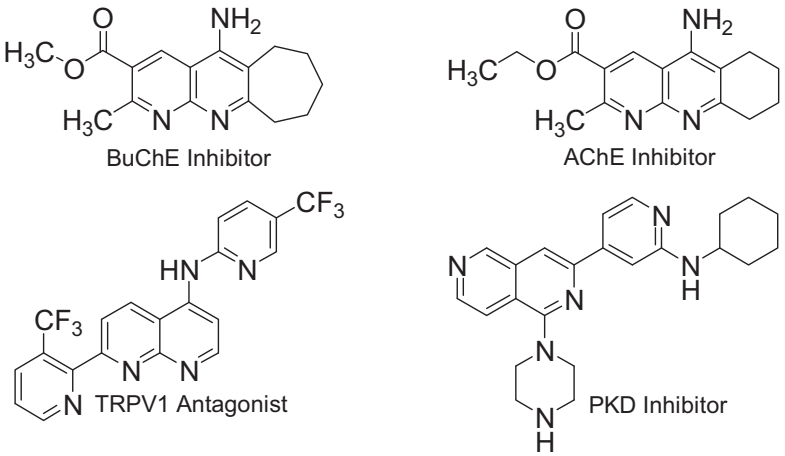


Figure 11. Naphthyridine inhibitors and antagonists

1,6-Naphthyridine derivatives also exhibit interesting biological properties, such as activity as antinociceptive agents,[69] HIV-1 integrase inhibitors,[70] and anti-human cytomegalovirus (HCMV) agents.[71]

Some other compounds with 1,6-naphthyridine motif have been reported for the inhibition of fibroblast growth factor receptors (FGFR). Fibroblast growth factors are major factors for some tumors and angiogenesis is essential for the growth and survival of solid tumors. The inhibition of FGFR tyrosine kinases is considered to be an effective strategy to prevent this inappropriate vascularisation[72] (Figure 12).

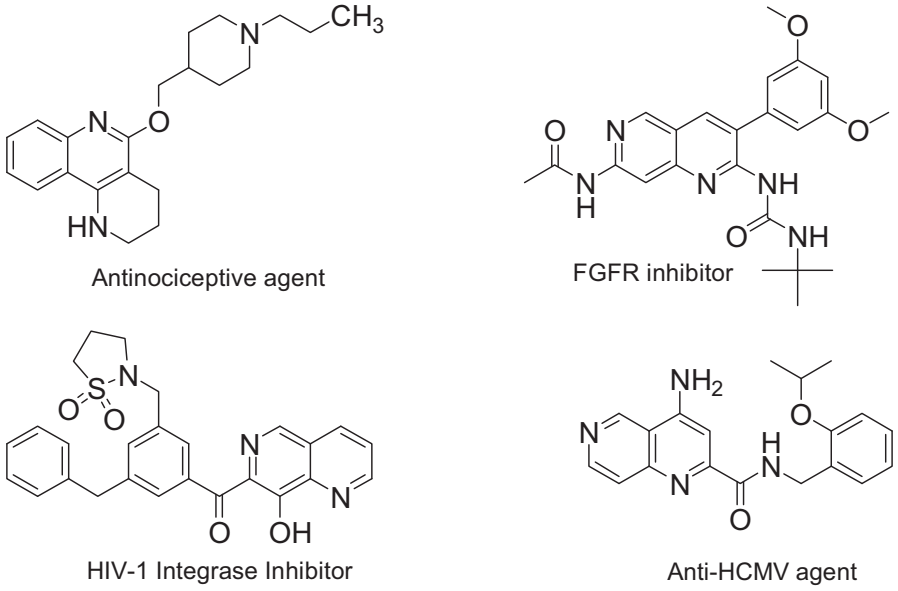
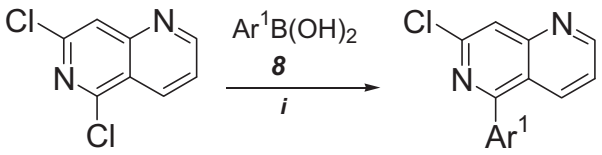


Figure 12. Pharmacologically relevant 1,6-naphthyridine derivatives

2.3 Results and Discussion

The commercially available 5,7-dichloro-1,6-naphthyridine (**7**) was studied for site-selective Suzuki-Miyaura cross-coupling reactions. The reactions of **7** with arylboronic acids **8a-l** (1.3 equiv.) afforded the 5-aryl-7-chloronaphthyridines **9a-l** in 33-96% yield (Scheme 6, Table 3).

The reaction conditions were systematically optimized for derivatives **9a-l** (Table 6). Both electron-poor and electron-rich arylboronic acids could be successfully employed. The best yields were obtained using the solvent system 1,4-dioxane / toluene (1:1), $Pd(PPh_3)_4$ (5 mol%) as the catalyst and 2M K_2CO_3 as the base. The reactions were carried out at 70 °C for 8 h (entry 12, Table 6). The reactions carried out at temperatures higher than 70 °C afforded a mixture of products. Therefore, the optimized conditions given in entry 12 allowed to prepare 5-aryl-7-chloronaphthyridines **9a-l** in good yields (Scheme 6, Table 3).



7 **9a-l**

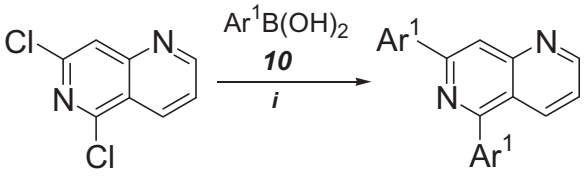
Scheme 6. Synthesis of **9a-l**. Reagents and conditions: (i) **7** (1 equiv), Ar^1-$B(OH)_2$ (1.3 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (1 mL), 1,4-dioxane / toluene (1:1), 70 ^{0}C, 8 h.

Table 3: Synthesis of **9a-l**.

Entry	**8, 9**	Ar^1	% [a] (**9**)
1	**a**	4-MeC_6H_4	70
2	**b**	3,5-$Me_2C_6H_3$	80
3	**c**	2-$(MeO)C_6H_4$	74
4	**d**	4-FC_6H_4	54
5	**e**	2,3,4-$(MeO)_3C_6H_2$	67
6	**f**	2,3-$(MeO)_2C_6H_3$	96
7	**g**	2-MeC_6H_4	70
8	**h**	4-ClC_6H_4	33
9	**i**	4-$(CF_3)C_6H_4$	65
10	**j**	4-$(MeO)C_6H_4$	79
11	**k**	4-$(Et)C_6H_4$	79
12	**l**	4-(*t*Bu)C_6H_4	67

[a]Yields of isolated products.

The Suzuki-Miyaura reactions of 5,7-dichloro-1,6-naphthyridine **7** with 2.5 equiv. of arylboronic acids **10a-i** gave 5,7-diaryl-1,6-naphthyridines **11a-i** in good yields. The best yields were obtained using 2.5 equiv. of the arylboronic acid, 5 mol% of $Pd(PPh_3)_4$ and 2 mL of 2M K_2CO_3 as base (1,4-Dioxane, 110 ^{0}C, 12 h). The reactions could be successfully carried out with both electron-rich and electron-poor arylboronic acids. The reaction of **7** with arylboronic acid **10c** afforded product **11c** in excellent yield (Scheme 7, Table 4).



7 **11a-i**

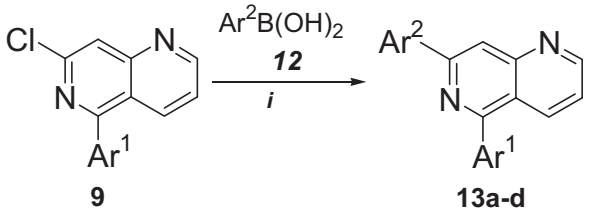
Scheme 7. Synthesis of **11a-i**. Reagents and conditions: (i) **7** (1 equiv), Ar^1-$B(OH)_2$ (2.5 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (2 mL), 1,4-dioxane, 110 ^{0}C, 12 h.

Table 4: Synthesis of **11a-i**.

Entry	**10, 11**	Ar^1	% [a] **(11)**
1	**a**	2-(MeO)C_6H_4	71
2	**b**	4-MeC_6H_4	74
3	**c**	3,5-$Me_2C_6H_3$	94
4	**d**	4-(Et)C_6H_4	67
5	**e**	4-(*t*Bu)C_6H_4	79
6	**f**	2,3,4-$(MeO)_3C_6H_2$	49
7	**g**	4-$(CF_3)C_6H_4$	64
8	**h**	3-FC_6H_4	74
9	**i**	4-(MeO)C_6H_4	73

[a] Yields of isolated products.

The Suzuki-Miyaura reactions of 5-aryl-7-chloronaphthyridines **9e,f** in with 1.3 equiv. of arylboronic acids **12a-d** afforded disubstituted products **13a-d** in good yields. The reaction of **9e** with arylboronic acid **12a** afforded the product **13a** in excellent yield (Scheme 8, Table 5).



9 **13a-d**

Scheme 8. Synthesis of **13a-d**. Reagents and conditions: (i) **9** (1 equiv), Ar^2-$B(OH)_2$ (1.3 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), 110 ^{0}C, 8 h.

Table 5: Synthesis of **13a-d**.

Entry	**12, 13**	**9**	Ar^1	Ar^2	% [a] (**13**)
1	**a**	**e**	2,3,4- $(MeO)_3C_6H_2$	3,5-$Me_2C_6H_3$	89
2	**b**	**e**	2,3,4- $(MeO)_3C_6H_2$	4-MeC_6H_4	64
3	**c**	**e**	2,3,4- $(MeO)_3C_6H_2$	4-(*t*Bu)C_6H_4	54
4	**d**	**f**	2,3-$(MeO)_2C_6H_3$	2-MeC_6H_4	47

[a] Yields of isolated products.

Table 6. Reaction conditions optimization for **s**ynthesis of **9a**

Entry	Solvent	Base	Temp.	Time	**9a**
1	1,4-Dioxane	2 equiv. K_3PO_4	80 °C	6h	mixture
2	1,4-Dioxane	2M K_2CO_3	100 °C	6h	mixture
3	THF	2M K_2CO_3	80 °C	6h	mixture
4	THF	2 equiv. K_3PO_4	80 °C	6h	mixture
5	Toluene	2 equiv. K_3PO_4	70 °C	6h	mixture
6	Toluene	2M K_2CO_3	80 °C	6h	mixture
7	Toluene	2 equiv. Cs_2CO_3	65 °C	6h	mixture
8	THF	2 equiv. Cs_2CO_3	70 °C	6h	mixture
9	DME	2M K_2CO_3	65 °C	10h	49
10	1,4-Dioxane	2M K_2CO_3	65 °C	6h	No Reaction
11	DMF	2M K_2CO_3	100 °C	6h	mixture
12	**1,4-Dioxane:Toluene (1:1)**	**2M K_2CO_3**	**70 °C**	**8h**	**70**

[a] $Pd(PPh_3)_4$ was used as catalyst in all reactions.

The structures of all products were established by NMR, MS and IR data. The structures of **9f** (Figure 13) and **11c** (Figure 14) were independently confirmed by X-ray crystallography.

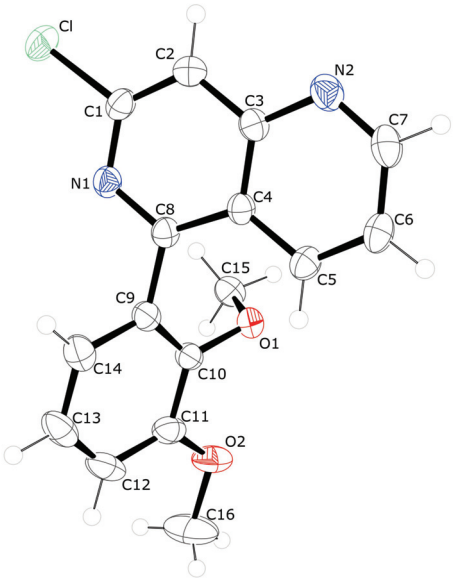


Figure 13. ORTEP view of the crystal structure of **9f**

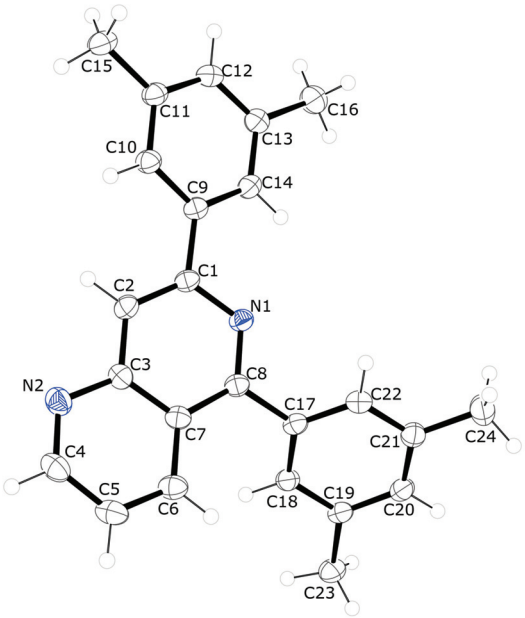
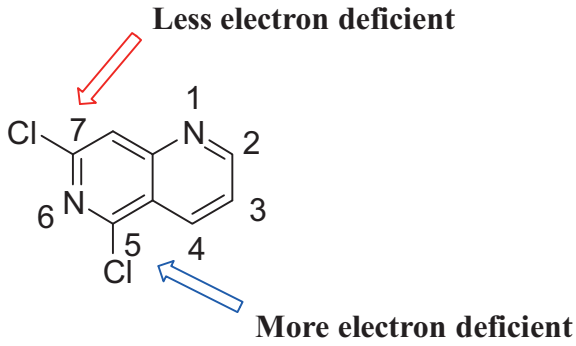


Figure 14. ORTEP view of the crystal structure of **11c**

The site-selective synthesis of **9a-l** could be explained on the basis of steric and electronic effects. The ^{1}H NMR chemical shift of the molecules in which the halide is replaced by a hydrogen usually gives a good possibility to estimate the electronic character and the site-selectivity of Pd catalyzed cross-coupling reactions of polyhalogenated substrates.[100c] The position C-5 (^{1}H NMR, 9.15 ppm) is more electron deficient as compared to position C-7 (^{1}H NMR, 8.45 ppm). Therefore, the first attack takes place at position at C-5.



Scheme 9: Possible explanation for the site-selectivity of cross-coupling reactions of **7**

2.4 Conclusion

I have successfully synthesized derivatives of 5,7-dichloro-1,6-naphthyridine by site-selective Suzuki-Miyaura cross-coupling reactions. The monoarylated products were isolated with good site-selectivity, employing electron-rich and electron-poor arylboronic acids.

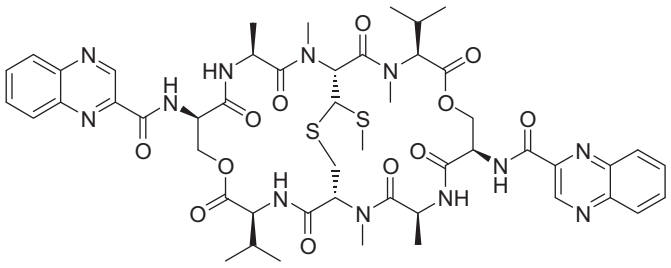
In conclusion, a general Pd(0)-catalyzed arylation of 5,7-dichloro-1,6-naphthyridine with a number of arylboronic acids was achieved by Suzuki-Miyaura reactions. The first attack occurred at position **5** which is more electron-deficient and less sterically hindered.

3 Regioselective Palladium(0)-Catalysed Cross-Coupling Reactions of 2,6-Dichloroquinoxaline

3.1 Introduction

Quinoxaline is a benzo-fused six-membered nitrogen containing heterocycle containing benzene ring and pyrazine ring. Quinoxaline is related to naphthalene but with less aromaticity. Quinoxalines are also called as benzopyrazines.[73] Different quinoxaline derivatives show a broad spectrum of biological activities including antibacterial and antifungal,[74] antihistamic, antioxidant and antiinflammatory,[75] antimicobacterial,[76] antiamoebic,[77] antiproliferative,[78] fungicidal and algicidal,[79] antimalarial and antileishmanial,[80] cytotoxic,[81] anticancer,[82] anti HIV and anti HCV,[83] anti-tuberculosis,[84] potent and selective class III tyrosine kinase inhibitory,[85] and potential influenza NS1A protein inhibitory activity.[86]

Certain quinoxaline antibiotics of octadepsipeptide type have been reported as antibacterial, antitumor and potent inhibitors of RNA synthesis; examples are echinomycine and triostin A[87] (Figure 15).



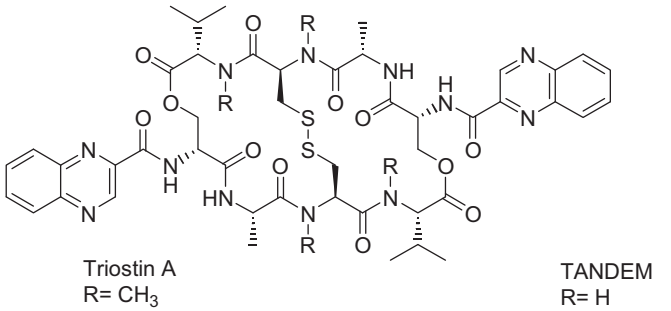
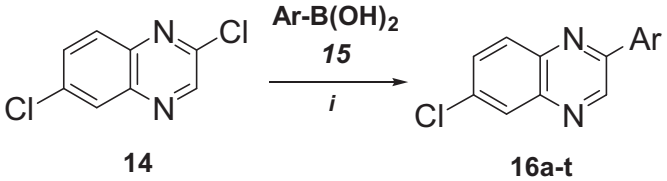


Figure 15. Quinoxaline antibiotics

Furthermore, some derivatives are reported as high-performance thermoplastics[88] and some other quinoxaline derivatives display bipolar characters that are reported as potential emissive and electron-transport moieties, hence they act as potential building blocks for the synthesis of organic semiconductors.[89]

3.2 Results and discussion

Pd-catalysed cross-coupling reactions are powerful tools for the formation of highly substituted heterocycles. The commercially available 2,6-dichloroquinoxaline (**14**) was studied for site-selective Suzuki-Miyaura cross-coupling reactions. The reactions of **14** with arylboronic acids **15a-t** (1.3 equiv.) afforded the 2-aryl-6-chloroquinoxalines **16a-t** in 23-97% yield. The reaction conditions were systematically optimized for derivatives **16a-t** (Table 6) in order to isolate the products in better yields. Both electron-poor and electron-rich arylboronic acids could be successfully employed. In case of arylboronic acids **15d,l,r,t**, the yields were low because of their lower reactivity as compared to **14**. The best yields were observed using THF as the solvent, $Pd(PPh_3)_4$ (5 mol%) as the catalyst and K_3PO_4 (2 equiv) as the base. The reactions were carried out at 90 °C for 8 h in a sealed tube (entry 6, Table 10). The reactions of highly reactive electron-rich arylboronic acids, carried out in THF, were carried out for 4 h at 85 °C (entry 3, Table 10). The reactions carried out in toluene or 1,4-dioxane needed higher temperature and afforded the products in lower yield (entry 6, Table 10). Therefore, the optimized conditions given in entry 6 allowed to prepare 2-aryl-6-chloroquinoxalines **16a-t** in good yields (Scheme 10, Table 7).



14 **16a-t**

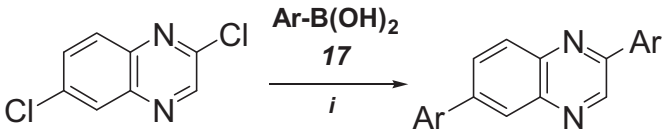
Scheme 10. Synthesis of **16a-t**. Reagents and conditions: (i) **14** (1 equiv), **15** (1.3 equiv), $Pd(PPh_3)_4$ (5 mol%), K_3PO_4 (2 equiv), THF (8 mL), 90 ^{0}C, 8 h.

Table 7: Synthesis of **16a-t**.

15, 16	Ar[1]	% [a] **(16)**
a	2-MeC_6H_4	77
b	3-MeC_6H_4	67
c	4-MeC_6H_4	75
d	2,6-$Me_2C_6H_3$	37
e	3,5-$Me_2C_6H_3$	90
f	2,4,6-$Me_3C_6H_2$	96
g	2-$(MeO)C_6H_4$	72
h	4-$(MeO)C_6H_4$	63
i	2,3-$(MeO)_2C_6H_3$	65
j	2,6-$(MeO)_2C_6H_3$	97
k	2,3,4-$(MeO)_3C_6H_2$	53
l	3-FC_6H_4	23
m	4-FC_6H_4	62
n	2-C_4H_3S	45
o	4-$(Et)C_6H_4$	96
p	4-(tBu)C_6H_4	77
q	4-$(CF_3)C_6H_4$	52
r	4-$(Vinyl)C_6H_4$	30
s	2-ClC_6H_4	78
t	3-ClC_6H_4	25

[a] Yields of isolated products.

The Suzuki-Miyaura reactions of 2,6-dichloroquinoxaline (**14**) with 2.5 equiv. of arylboronic acids **17a-f** gave 2,6-diarylquinoxalines **18a-f** in good yields. The best yields were obtained using 2.5 equiv. of the arylboronic acid, 5 mol% of $Pd(PPh_3)_4$ and 2 mL of 2M K_2CO_3 as the base (1,4-dioxane, 120 ^{0}C, 12 h). The reaction of **14** with arylboronic acid **17c** afforded product **18c** in optimal yield (Scheme 11, Table 8).



14 **18a-f**

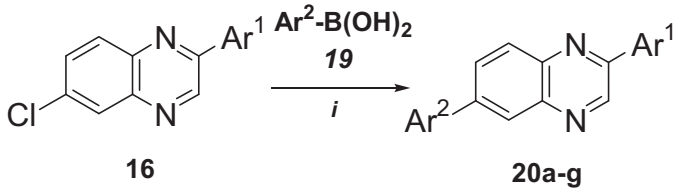
Scheme 11. Synthesis of **18a-f**. Reagents and conditions: (i) **14** (1 equiv), **17** (2.5 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (2 mL), 1,4-Dioxane (8 mL), 120 ^{0}C, 12 h.

Table 8: Synthesis of **18a-f**.

17, 18	Ar	% [a] (**18**)
a	2-MeC_6H_4	64
b	4-$(Me)C_6H_4$	51
c	3,5-$Me_2C_6H_3$	94
d	2-$(MeO)C_6H_4$	49
e	4-$(Et)C_6H_4$	47
f	4-$(tBu)C_6H_4$	26

[a] Yields of isolated products.

The Suzuki-Miyaura reactions of 2-aryl-6-chloroquinoxalines **16c,h,m-o** with 1.3 equiv. of arylboronic acids **19a-g** afforded disubstituted products **20a-g** in good yields. The reactions were carried out in 1,4-dioxane using $Pd(PPh_3)_4$ (5 mol%) and 2M K_2CO_3 (1 mL) at 120 ^{0}C for 8 h. The reaction of **16n** with arylboronic acid **19f** afforded product **20f** in 91% yield (Scheme 12, Table 9).



Scheme 12. Synthesis of **20a-g**. Reagents and conditions: (i) **16** (1 equiv), **19** (1.3 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (1 mL), 1,4-dioxane, 120 ^{0}C, 8 h.

Table 9: Synthesis of **20a-g**.

19, 20	**16**	Ar^1	Ar^2	% [a] (**20**)
a	**c**	4-MeC_6H_4	3,5-$Me_2C_6H_3$	70
b	**c**	4-MeC_6H_4	4-(*t*Bu)C_6H_4	78
c	**c**	4-MeC_6H_4	2-(MeO)C_6H_4	47
d	**h**	4-(MeO)C_6H_4	4-FC_6H_4	76
e	**m**	4-FC_6H_4	3,5-$Me_2C_6H_3$	63
f	**n**	2-C_4H_3S	3,5-$Me_2C_6H_3$	91
g	**o**	4-(Et)C_6H_4	4-MeC_6H_4	54

[a] Yields of isolated products.

Table 10. Reaction conditions optimization for synthesis of **3**.

Entry	Solvent	Catalyst	Temp. (°C)	Time (h)	**3**c (%)
1	1,4-Dioxane	$(PPh_3)_4Pd$	85	3	No reaction
2	1,4-Dioxane	$(PPh_3)_4Pd$	110	6	69
3	THF	$(PPh_3)_4Pd$	85	4	71
4	Toluene	$(PPh_3)_4Pd$	85	4	29
5	Toluene	$(PPh_3)_4Pd$	110	6	66
6	**THF**	**$(PPh_3)_4Pd$**	**90**	**8**	**75**

[a] 2 equiv. K_3PO_4 was used as base in each reaction

The structures of all products were established by NMR, MS and IR data. The structures of **16g** (Figure 16) and **20e** (Figure 17) were independently confirmed by X-ray crystallography.

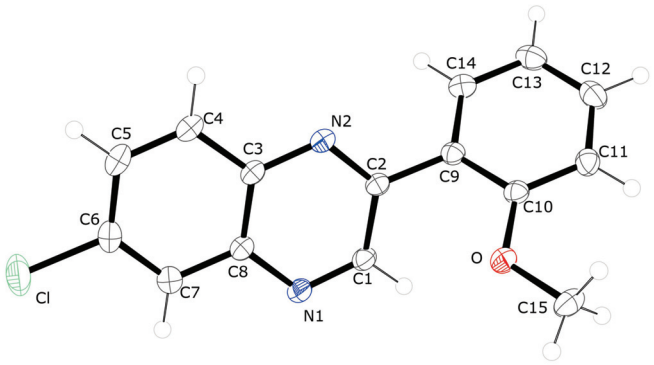


Figure 16. ORTEP view of the crystal structure of **16g**

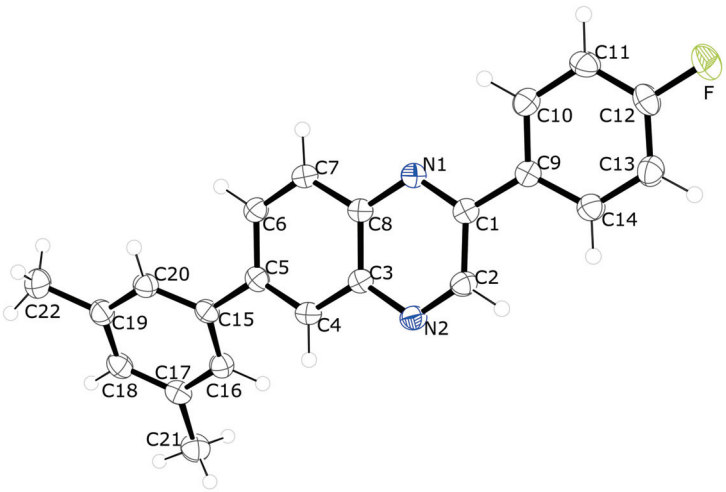
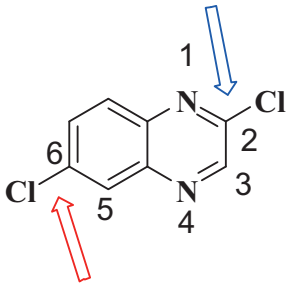


Figure 17. ORTEP view of the crystal structure of **20e**

The monoarylated products **16a-t** were synthesised by Suzuki-Miyaura reactions in good yield. The position 2 of 2,6-dichloroquinoxaline (**14**) is more electron-deficient as compared to position 6. The products were obtained with good site-selectivity.

More electron deficient



Less electron deficient

Scheme 13: Possible explanation for the site-selectivity of cross-coupling reactions of **14**

3.3 Conclusion

In conclusion, the Pd(0)-catalyzed Suzuki-Miyaura cross-coupling reactions of 2,6-dichloroquinoxaline (**14**) have been successfully carried out with good site-selectivity. The mono- and diarylated products were obtained in good yield. The first attack occurred at position C-2 that is more electron deficient as compared to position C-6.

4 Regioselective Palladium(0)-Catalysed Cross-Coupling Reactions of 2,4-Dichloro-1-(trifluoromethyl)benzene

4.1 Introduction

The trifluoromethyl (CF_3) group is a significant structural motif in many pharmaceutically relevant molecules[90] and with a wide range of important and interesting applications in organic, material, medicinal, and agricultural chemistry, due to its unique physical, chemical, and biological properties.[91]

Various compounds with CF_3 motif have been reported to exhibit biologically interesting properties such as antimalarial agents;[92] malaria which is still a worldwide problem of public health, affecting 300 million people and causing about 2.5 million deaths annually, mainly among children less than 5 years old[93] (Figure 18).

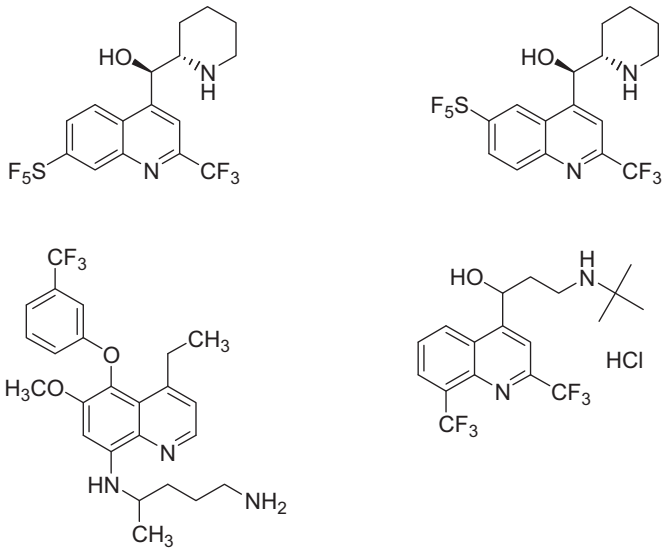


Figure 18. Antimalarial agents containing a CF_3 motif

Some more compounds with CF_3 motif act as potential antituberculosis agents (mafloquine),[94] antiviral agents,[95] in vitro androgen receptor antagonists and in vivo antiandrogenic agents,[96] amebicidal and trichomonacidal agents.[97]

Some other compounds with CF_3 moiety, such as JNJ-1930942, have also been reported as positive allosteric modulator of the α_7 nicotinic acetylcholine receptor (nAChR) which is a potential therapeutic target for the treatment of cognitive deficits associated with schizophrenia, Alzheimer's disease, Parkinson's disease, and attention-deficit/hyperactivity disorder.[98] , boxidine is the most effective, nonsteroidal, nonestrogenic and potent hypocholesteremic agent that is reported to inhibit the biosynthesis of cholesterol and it lowers the serum sterol level[99] (Figure 19).

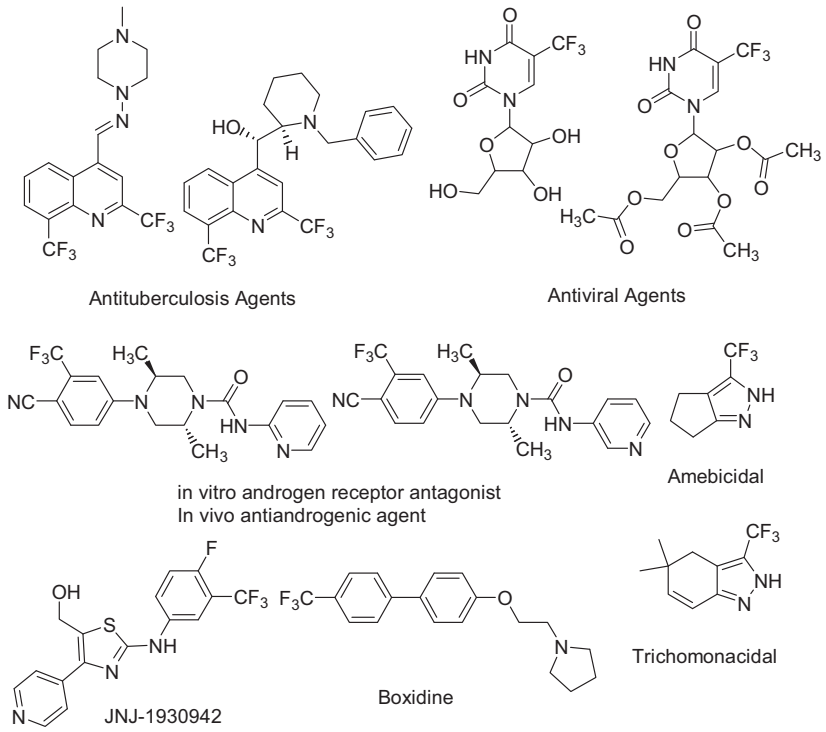
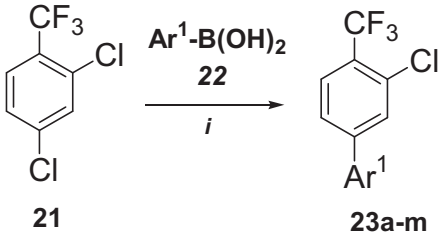


Figure 19. Pharmacologically relevant CF_3 motif containing compounds

4.2 Results and Discussion

The Suzuki-Miyaura cross-coupling reactions of commercially available 2,4-dichloro-1-(trifluoromethyl)benzene **21** with 1.3 equiv. of arylboronic acids **22a-m** afforded the biphenyls **23a-m** in moderate to good yields (Scheme 14, Table 11) with excellent site-selectivity.

The best yields were obtained using 1.3 equiv. of the arylboronic acid, $Pd(PPh_3)_4$ (0.05 equiv.) as the catalyst and 2M K_2CO_3 as the base (1,4-dioxane, 80 ^{0}C, 6 h). The formation of the opposite regioisomers was not observed.



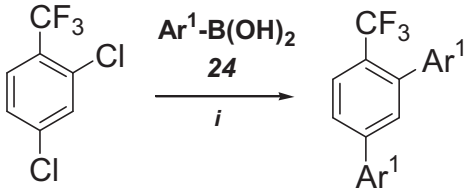
Scheme 14. Synthesis of **23a-m**. Reagents and conditions: (i) **21** (1 equiv), **22** (1.3 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (1 mL), 1,4-dioxane, 80 ^{0}C, 6 h.

Table 11: Synthesis of **23a-m**

22,23	Ar^1	% [a] (**23**)
a	2-MeC_6H_4	93
b	3-MeC_6H_4	95
c	4-MeC_6H_4	97
d	2,6-$Me_2C_6H_3$	36
e	3,5-$Me_2C_6H_3$	72
f	4-EtC_6H_4	49
g	2-$(MeO)C_6H_4$	56
h	2,3-$(MeO)_2C_6H_3$	74
i	2,3,4-$(MeO)_3C_6H_2$	60
j	2-ClC_6H_4	47
k	4-FC_6H_4	46
l	4-$(CF_3)C_6H_4$	35
m	3-$(CF_3)C_6H_4$	32

[a] Yields of isolated products.

The Suzuki-Miyaura reactions of 2,4-dichloro-1-(trifluoromethyl)benzene **21** with 2.5 equiv. of arylboronic acids **24a-d** gave 2,4-diaryl-1-(trifluoromethyl)benzene derivatives **25a-d** in good yields. The reactions were carried out at 110 ^{0}C in 1,4-dioxane using 2.5 equiv. of the arylboronic acid, 5 mol% of $Pd(PPh_3)_4$ and 2 mL of 2M K_2CO_3 as base. (Scheme 15, Table 12).



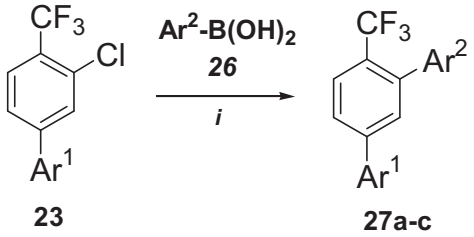
Scheme 15. Synthesis of **25a-d**. Reagents and conditions: (i) **21** (1 equiv), Ar^1-$B(OH)_2$ (2.5 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (2 mL), 1,4-Dioxane (8 mL), 110 ^{0}C, 8 h.

Table 12: Synthesis of **25a-c**

24, 25	Ar^1	% [a] (**25**)
a	2-MeC_6H_4	57
b	3-MeC_6H_4	39
c	4-MeC_6H_4	60
d	4-FC_6H_4	49

[a] Yields of isolated products.

The Suzuki-Miyaura reactions of 3-chloro-4'-methyl-4-(trifluoromethyl)biphenyl **23c** with 1.3 equiv. of arylboronic acids **26a-d** afforded unsymmetrical disubstituted products **27a-d** in moderate to good yields. The reactions were carried out in 1,4-dioxane using $Pd(PPh_3)_4$ (5 mol%) and 2M K_2CO_3 (1 mL) at 110 ^{0}C for 8 h (Scheme 16, Table 13).



Scheme 16. Synthesis of **27a-c**. Reagents and conditions: (i) **23c** (1 equiv), Ar^2-$B(OH)_2$ (1.3 equiv), $Pd(PPh_3)_4$ (5 mol%), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), 110 ^{0}C, 8 h.

Table 13: Synthesis of **27a-c**

26,27	**23**	Ar^1	Ar^2	% [a] (**27**)
a	**c**	4-MeC_6H_4	4-FC_6H_4	25
b	**c**	4-MeC_6H_4	4-$(MeO)C_6H_4$	59
c	**c**	4-MeC_6H_4	3,5-$Me_2C_6H_3$	64
d	**c**	4-MeC_6H_4	4-EtC_6H_4	40

[a] Yields of isolated products.

The structures of all products were established by NMR, MS and IR data. The structure of **23c** (Figure 20) was independently confirmed by X-ray crystallography.

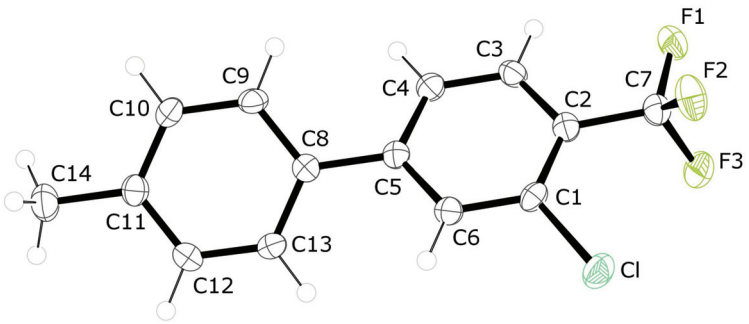
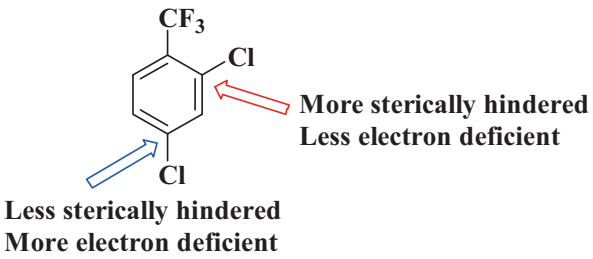


Figure 20. ORTEP view of the crystal structure of **23c**

The site-selective formation of **23a-m** can be explained by steric and electronic reasons. Generally, the first attack of palladium(0)-catalyzed cross-coupling reactions favours the more electron-deficient and less sterically hindered position.[100] The position at C-4 of 2,4-dichloro-1-(trifluoromethyl)benzene **21** is sterically less hindered and more electron deficient as compared to position 2 which is located nearby the CF_3 moiety (Scheme 17).



Scheme 17: Possible explanation for the site-selectivity of cross-coupling reactions of **21**

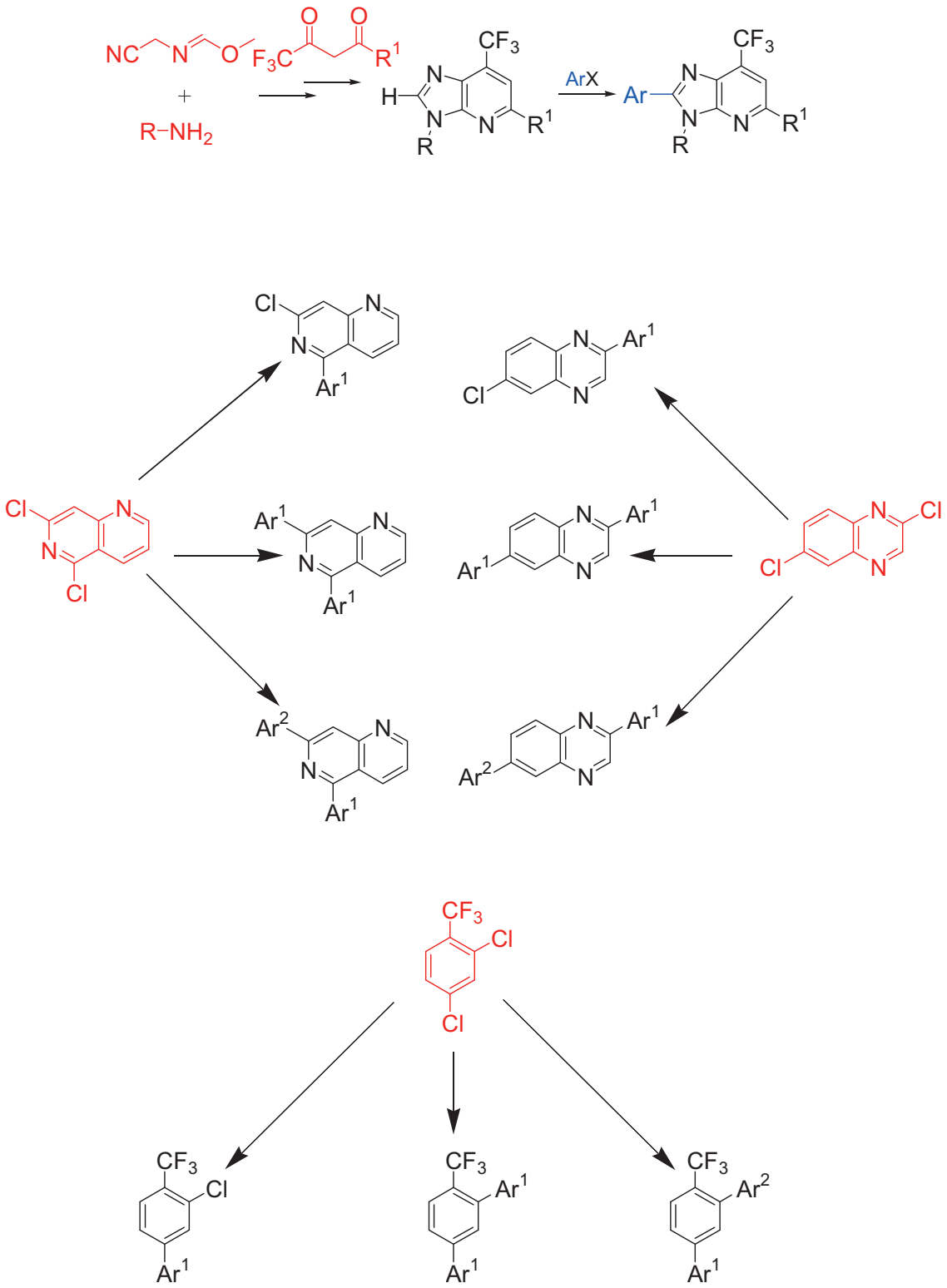
4.3 Conclusion

In conclusion, I have synthesised mono- and diarylated (both symmetrical and unsymmetrical) products *via* site-selective Suzuki-Miyaura cross-coupling reactions.

5 Abstract

The Pd/Cu catalyzed reactions of 3*H*-imidazo[4,5-*b*]pyridines (1-deazapurines) *via* C-H bond activation provided arylated 1-deazapurines. The arylation took place at position 2 of the 1-deazapurines. Pd(0)-catalysed Suzuki-Miyaura cross coupling reactions of 5,7-dichloro-1,6-naphthyridine, 2,6-dichloroquinoxaline and 2,4-dichloro-1-(trifluoromethyl)benzene with different arylboronic acids afforded aryl-substituted naphthyridines, quinoxalines and trifluoromethyl-substituted di- and terphenyls with excellent site-selectivity. The first attack occurred at the more electronically deficient and sterically less hindered position.

Die Pd / Cu-katalysierten Reaktionen von 3*H*-Imidazo[4,5-b]pyridinen (1-Desazapurinen) via C-H-Aktivierung lieferte arylierte 1-Deazapurine. Die Arylierung fand an Position 2 des 1-Desazapurins statt. Suzuki-Miyaura-Kupplungen von 5,7-Dichlor-1,6-naphthyridin, 2,6-Dichlorchinoxalin und 2,4-Dichlor-1-(trifluormethyl)benzol mit verschiedenen Arylboronsäuren ergab arylsubstituierte Naphthyridine, Chinoxaline, Trifluormethyl-substituierte Biphenyle und Terphenyle mit ausgezeichneter Regioselektivität. Der erste Angriff erfolgte an der elektronisch ärmeren und sterisch weniger gehinderten Position.



General Scheme. Palladium-catalyzed reactions developed in this thesis.

6 Experimental Section

6.1 General: Equipment, chemicals and work technique

^{1}H NMR Spectroscopy:

Bruker: AM 250, Bruker ARX 300, Bruker ARX 500; δ = 0.00 ppm for Tetramethylsilane; δ = 7.26 ppm for (CDCl3); Characterization of the signal fragmentations: s = singlet, d = doublet, dd = double of doublet, t = triplet, q = quartet, m = multiplet, br = broadly. All coupling constants are indicated as (*J*). 2D NMR techniques (NOESY, COSY, HSQC, and HMBC) were used for the confirmation of structure.

^{13}C NMR Spectroscopy:

Bruker: AM 250, (62.9 MHz); Bruker: ARX 300, (75 MHz), Bruker: ARX 500, (125 MHz) Ref: 29.84 ± 0.01 ppm and 206.26 ± 0.13 ppm δ = 77.00 ppm for CDCl3. The multiplicity of the carbon atoms was determined by the DEPT 135 and APT technique (APT = Attached Proton Test) and quoted as CH_3, CH_2, CH and C for primary, secondary, tertiary and quaternary carbon atoms. Characterization of the signal fragmentations: quart = quartet the multiplicity of the signals was determined by the DEPT recording technology and/or the APT recording technology.

Mass Spectroscopy:

AMD MS40, Varian MAT CH 7, MAT 731 (EI, 70 eV), Intecta AMD 402 (EI, 70 eV and CI), Finnigan MAT 95 (CI, 200 eV).

High Resolution mass spectroscopy:

Finnigan MAT 95 or Varian MAT 311; Bruker FT
CIR, AMD 402 (AMD Intectra).

Infrared spectroscopy (IR):

Bruker IFS 66 (FT IR), Nicolet 205 FT IR; Nicolet Protege 460, Nicolet 360 Smart Orbit (ATR); KBr, KAP, Nujol, and ATR; Peaks are given following assignments: w = weak, m = medium, s = strong, br = broad.

Elemental Analysis

LECO CHNS-932, Thermoquest Flash EA 1112.

X-ray crystal structure analysis:

Crystallographic data were collected on a Bruker X8Apex, Diffractometer with CCD-Kamera (MoKa und Graphit Monochromator, = 0.71073 Å). The structures were solved by direct methods using SHELXS-97 and refined against *F*2 on all data by full matrix least-squares with SHELXL-97.

Melting points:

Micro heating table HMK 67/1825 Kuestner (Büchi apparatus).

Column chromatography:

Chromatography was performed over Merck silica gel 60 (0,063 -0,200 mm, 70 - 230 mesh) as normal and/or over mesh silica gel 60 (0,040 - 0,063 mm, 200 -400 mesh) as Flash Chromatography. All solvent were distilled before use.

Thin Layer Chromatography (TLC):

Merck DC finished foils silica gel 60 F254 on aluminum foil and Macherey finished foils Alugram® Sil G/UV254. Detection under UV light with 254 nm and/or 366 nm without dipping reagent, as well as with anisaldehyde sulfuric acid reagent (1 mL anisaldehyde consisting in 100 mL stock solution of 85% methanol, 14% acetic acid and 1% sulfuric acid).

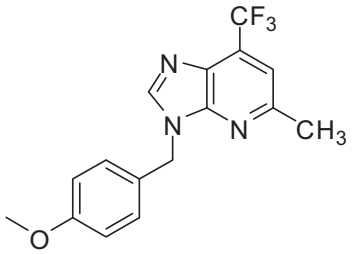
6.2 Pd/Cu Catalysed Arylation of 1-deazapurines *via* C-H Bond Activation

General Procedure for the Synthesis of Compounds 5a-h: To a Schlenk flask, CH_2Cl_2, the primary amine (**2a-d**), and methyl *N*-(cyanomethyl)-formimidate (**1**) were added under an argon atmosphere at r.t. The reaction mixture was refluxed for 2 h and after that, the mixture was cooled down to r.t., and then to 0°C using an ice bath. Afterwards, the 1,3-electrophilic reagent (**4a-e**) was added, and the mixture continued to stir at the same temperature for 15–20 min and was then refluxed for 5 h. The solvent was evaporated to dryness, and the residue was purified by column chromatography (*n*-heptane – EtOAc), to give **5a-h** as solid products.

3-(4-Methoxybenzyl)-5,7-bis(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5a):

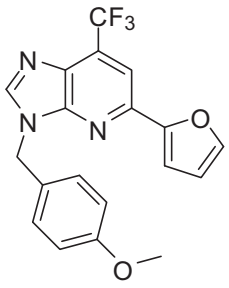
Starting with CH_2Cl_2 (6 mL), **1** (0.47 mL; 5.33 mmol), **2a** (0.68 mL, 5.33 mmol), **4a** (0.74 mL, 5.33 mmol), **5a** was isolated as yellowish solid (1.018 g, 51%); m.p. 108-110 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.72 (s, 3H, OCH_3), 5.40 (s, 2H, -CH_2-), 6.82 (d, ^3J = 8.7 Hz, 2H, ArH), 7.26 (d, ^3J = 8.7 Hz, 2H, ArH), 7.80 (s, 1H), 8.22 (s, 1H). ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 47.6 (-CH_2-), 55.3 (OCH_3), 111.5 (q, $^3J_{CF}$ = 4.40 Hz, CH), 114.6 (2CH), 121.8 (q, $^1J_{CF}$ = 274.0 Hz, CF_3), 125.4 (q, $^1J_{CF}$ = 274.0 Hz, CF_3), 126.41 (C), 129.5 (C, q, $^2J_{CF}$ = 35.2 Hz), 129.9 (2CH), 133.37 (C), 142.8 (q, $^2J_{CF}$ = 35.7 Hz, C), 148.0 (C), 148.1 (CH), 160.04 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -66.10 ($ArCF_3$), -62.13 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 3011 (w), 2958 (w), 2934 (m), 2912 (w), 2839 (w), 1611 (w), 1585 (w), 1513 (m), 1489 (w), 1464 (w), 1455 (w), 1441 (w), 1407 (w), 1390 (w), 1381 (w), 1352 (w), 1327 (w), 1306 (w), 1271 (s), 1255 (s), 1191 (m), 1174 (s), 1129 (s), 1109 (w), 1098 (w), 1033 (m), 964 (w), 940 (w), 940 (w), 921 (w), 903 (w), 880 (s), 842 (w), 833 (w), 804 (w), 759 (w), 748 (w), 728 (w), 709 (w), 681 (w), 666 (w), 655 (m), 632 (w), 597 (w), 564 (w); GC-MS (EI, 70 eV): m/z (%): 375 (M^+, 60), 360 (4), 340 (1), 312 (1), 360 (4), 178 (2), 121 (100), 91 (4), 78 (6) 51 (1). HRMS (EI): calcd for $C_{16}H_{11}F_6N_3O$ [M^+]: 375.08008; found: 375.080093.

3-(4-Methoxybenzyl)-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5b):



Starting with CH_2Cl_2 (6 mL), **1** (0.56 mL, 6.23 mmol), **2a** (0.81 mL, 6.23 mmol), **4b** (0.75 mL, 6.23 mmol), **5b** was isolated as brown solid (1.3 g, 65%); m.p. 95-97 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.64 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 5.31 (s, 2H, -CH2-), 6.78 (d, ^3J = 8.6 Hz, 2H, ArH), 7.18 (d, ^3J = 8.6 Hz, 2H, ArH), 7.24 (s, 1H), 7.95 (s, 1H). ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 19.2 (CH_3), 46.8 (-CH_2-), 55.3 (OCH_3), 114.3 (q, $^3J_{CF}$ = 4.40 Hz, CH), 114.4 (2CH), 122.9 (CF_3, q, $^1J_{CF}$ = 273.44 Hz), 127.5 (C), 128.6 (C, q, $^2J_{CF}$ = 34.11 Hz), 129.1 (C), 129.5 (2CH), 144.6 (CH), 148.0 (C), 154.2 (C), 159.7 (C). ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.17 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 3031 (w), 2956 (w), 2918 (m), 2842 (w), 1782 (w), 1741 (w), 1679 (w), 1613 (m), 1595 (w), 1585 (w), 1562 (w), 1555 (w), 1510 (m), 1495 (w), 1484 (w), 1465 (w), 1443 (w), 1433 (w), 1420 (w), 1397 (m), 1385 (m), 1363 (s), 1289 (s), 1272 (w), 1242 (m), 1231 (m), 1206 (w), 1184 (w), 1178 (w), 1165 (w), 1152 (m), 1123 (s), 1104 (s), 1027 (m), 976 (w), 963 (w), 928 (w), 915 (w), 895 (m), 871 (m), 843 (w), 827 (w), 817 (m), 793 (w), 762 (m), 725 (w), 716 (m), 675 (m), 667 (w), 636 (m), 623 (w), 566 (s), 537 (m); GC-MS (EI, 70 eV): m/z (%): 321 (M^+, 68), 306 (9), 214 (1), 151 (1), 121 (100), 106 (1), 91 (4), 77 (6), 65 (1), 51 (1); HRMS (EI): calcd for $C_{16}H_{14}F_3N_3O$ [M^+]: 321.10835; found: 321.108154

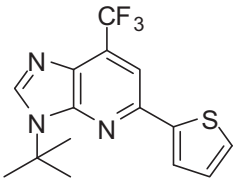
5-(Furan-2-yl)-3-(4-methoxybenzyl)-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5c):



Starting with CH_2Cl_2 (6 mL), **1** (0.28 mL, 3.12 mmol), **2a** (0.41 mL, 3.12 mmol), **4c** (0.46 mL, 3.12 mmol), **5c** was isolated as yellowish solid (0.992 g, 98); m.p. 144-146 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.71 (s, 3H, OCH_3), 5.36 (s, 2H, -CH_2-), 6.50 (dd, J = 1.70 Hz, J = 3.40 Hz, 1H, CH_{furyl}), 6.80 (d, ^3J = 8.6 Hz, 2H, ArH), 7.09-7.11 (m, 1H, CH_{furyl}), 7.25 (d, J = 8.6 Hz, 2H, ArH), 7.50-7.52 (m, 1H, CH_{furyl}), 7.85 (s, 1H, ArH), 8.01 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 47.0 (-CH_2-), 55.3 (OCH_3), 109.3 (CH_{furyl}), 110.3 (q, $^3J_{CF}$ = 4.40 Hz, CH), 112.3 (CH_{furyl}), 114.5 (2CH), 122.7 (CF_3, q, $^1J_{CF}$ = 273.45 Hz), 127.3 (C), 129.2 (q, $^2J_{CF}$ = 34.11 Hz, C), 129.6

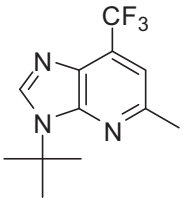
(2CH), 130.1 (C), 143.7 (CH_{furyl}), 145.5 (CH), 148.2 (C), 153.2 (C), 159.8 (2C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.32 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3120 (w), 3065 (m), 3013 (w), 2942 (w), 2912 (w), 2838 (w), 1613 (m), 1586 (w), 1513 (s), 1493 (m), 1464 (w), 1454 (w), 1440 (w), 1425 (w), 1396 (m), 1386 (w), 1360 (s), 1313 (w), 1305 (m), 1287 (w), 1261 (w), 1243 (s), 1226 (w), 1201 (m), 1169 (s), 1153 (m), 1127 (s), 1098 (m), 1070 (w), 1031 (s), 1005 (m), 962 (s), 943 (w), 932 (w), 912 (m), 885 (w), 873 (w), 863 (m), 846 (w), 835 (w), 821 (m), 777 (m), 744 (s), 714 (w), 682 (w), 666 (m), 632 (s), 595 (m), 534 (m); GC-MS (EI, 70 eV): m/z (%): 373 (M^+, 61), 358 (1), 224 (4), 207 (1), 173 (2), 150 (1), 121 (100), 91 (3), 77 (6), 51 (1); HRMS (ESI) calcd for $C_{19}H_{14}F_3N_3O_2$ $[M+H]^+$: 374.11109 found 374.1108.

3-tert-Butyl-5-(thiophen-2-yl)-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5d):



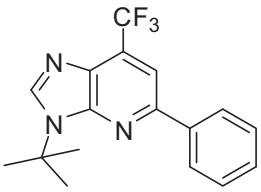
Starting with CH_2Cl_2 (6 mL), **1** (0.55 mL, 6.15 mmol), **2b** (0.65 mL, 6.15 mmol), **4d** (1.37 g, 6.15 equiv.), **5d** was isolated as pink solid (1.42 g, 71%); m.p. 143-145 °C. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.83 (s, 9H, $3CH_3$), 7.20 (dd, J = 3.78 Hz, J = 1.13 Hz, 1H, $CH_{thienyl}$), 7.69 (d, ^3J = 5.0 Hz, 1H, $CH_{thienyl}$), 7.02 (d, ^3J = 3.7 Hz, 1H, $CH_{thienyl}$), 8.12 (s, 1H, ArH), 8.62 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, DMSO-d_6): δ = 28.4 ($3CH_3$), 57.5 (C), 109.1 (q, $^3J_{CF}$ = 4.40 Hz, CH), 122.8 (q, $^1J_{CF}$ = 273.99 Hz, CF_3), 126.3 (CH), 127.3 (q, $^2J_{CF}$ = 33.56 Hz, C), 128.7 (CH), 130.8 (C), 143.9 (C), 145.4 (CH), 146.2 (2C), 147.9 (C); ^{19}F NMR (282.40 MHz, DMSO-d_6): δ = -60.85 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3125 (m), 3071 (w), 2976 (m), 2916 (w), 2874 (w), 1597 (s), 1540 (s), 1511 (w), 1482 (s), 1471 (m), 1433 (m), 1409 (w), 1388 (s), 1370 (s), 1350 (m), 1338 (m), 1303 (s), 1281 (w), 1264 (m), 1247 (m), 1224 (s), 1175 (s), 1149 (m), 1132 (s), 1082 (w), 1074 (w), 1063 (w), 1029 (w), 1020 (w), 931 (s), 900 (m), 872 (s), 846 (m), 826 (s), 818 (w), 791 (m), 770 (w), 749 (w), 723 (m), 702 (s), 666 (w), 658 (m), 647 (m), 635 (s), 618 (w), 611 (w), 589 (w), 570 (w), 554 (m), 530 (m); GC-MS (EI, 70 eV): m/z (%): 325 (M^+, 31), 269 (100), 250 (2), 224 (2), 205 (1), 146 (1), 57 (1), 41 (2), 29 (1); HRMS (ESI) calcd for $C_{15}H_{15}F_3N_3S$ $[M+H]^+$: 326.09333 found 326.09362.

3-tert-Butyl-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5e):



Starting with CH_2Cl_2 (6 mL), **1** (0.69 mL, 7.78 mmol), **2b** (0.82 mL, 7.78 mmol), **4b** (0.94 mL, 7.78 mmol), **5e** was isolated as white solid (1.38 g, 69%); m.p. 100-102 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.77 (s, 9H, $3CH_3$), 2.64 (s, 3H, CH_3), 7.21 (s, 1H, ArH), 8.10 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 24.7 (CH_3), 29.1 ($3CH_3$), 57.5 (C), 113.6 (q, $^3J_{CF}$ = 4.12 Hz, CH), 122.9 (q, $^1J_{CF}$ = 273.74 Hz, CF_3), 128.1 (q, $^2J_{CF}$ = 33.42 Hz, C), 130.3 (C), 142.9 (CH), 148.4 (C), 152.8 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.23 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3119 (s), 2984 (m), 2922 (s), 2877 (w), 2854 (w), 1813 (w), 1731 (w), 1673 (w), 1596 (s), 1478 (s), 1464 (w), 1435 (w), 1401 (w), 1382 (m), 1371 (m), 1359 (m), 1336 (s), 1302 (w), 1282 (w), 1264 (m), 1228 (s), 1220 (w), 1197 (w), 1164 (m), 1125 (s), 1077 (m), 1031 (m), 997 (w), 968 (m), 934 (w), 910 (m), 892 (s), 863 (s), 834 (w), 809 (m), 758 (w), 724 (s), 680 (m), 669 (m), 638 (s), 627 (w), 563 (m), 547 (w), 533 (w); GC-MS (EI, 70 eV): m/z (%): 257 (M^+, 28), 242 (3), 201 (100), 182 (10), 154 (2), 132 (8), 105 (1), 78 (1), 57 (3), 41 (4), 29 (2); HRMS (ESI) calcd for $C_{12}H_{15}F_3N_3$ $[M+H]^+$: 258.12126 found 258.12141.

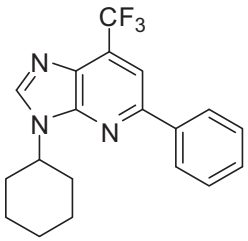
3-tert-Butyl-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5f):



Starting with CH_2Cl_2 (6 mL), **1** (0.84 mL, 9.4 mmol), **2b** (0.99 mL, 9.4 mmol), **4e** (2.03 g, 9.4 equiv.), **5f** was isolated as white solid (2.32 g, 77%); m.p. 130-132 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.84 (s, 9H, $3CH_3$), 7.35-7.47 (m, 3H, ArH), 7.85 (s, 1H, ArH), 8.03 (d, ^3J = 8.3 Hz, 2H, ArH), 8.19 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 29.2 ($3CH_3$), 57.8 (C), 111.1 (q, $^3J_{CF}$ = 4.12 Hz, CH), 122.9 (CF_3, q, $^1J_{CF}$ = 274.02 Hz), 127.0 (2CH), 128.8 (q, $^2J_{CF}$ = 33.42 Hz, C), 128.9 (2CH), 129.2 (CH), 131.5 (C), 138.6 (C), 143.9 (CH), 148.8 (C), 151.7 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.24 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3117 (m), 3089 (w), 3027 (w), 2979 (m), 2912 (w), 2882 (w), 1812 (w), 1737 (w), 1603 (m), 1580 (w), 1536 (w), 1490 (s), 1476 (s), 1441 (m), 1373 (s), 1339 (m), 1291 (m), 1259 (s), 1228 (s), 1182 (w), 1172 (w), 1163 (w), 1147 (w), 1130 (s), 1085 (w), 1062 (m), 1027 (m), 1001 (w), 969 (w), 943 (s), 910 (w), 869 (s), 835 (w), 821 (m), 790 (w), 767 (s), 726 (s), 687 (s), 672 (w), 665 (m), 647 (m), 635 (m),

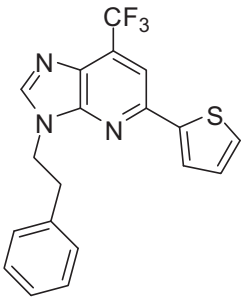
620 (s), 555 (m), 531 (w); GC-MS (EI, 70 eV): m/z (%): 319 (M^+, 22), 300 (1), 264 (17), 263 (100), 242 (2), 215 (1), 193 (2), 158 (1), 140 (2), 57 (1), 41 (1); HRMS (ESI) calcd for $C_{17}H_{17}F_3N_3$ $[M+H]^+$: 320.13691 found 320.13715.

3-Cyclohexyl-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5g):



Starting with CH_2Cl_2 (6 mL), **1** (0.52 mL, 5.79 mmol), **2c** (0.66 mL, 5.79 mmol), **4e** (1.25 g, 5.79 equiv.), **5g** was isolated as reddish solid (1.4 g, 70%); m.p. 120-122 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.31-2.04 (m, 8H, 4-CH_2-), 2.27-2.33 (m, 2H, -CH_2-), 4.68-4.78 (m, 1H, CH), 7.45-7.58 (m, 3H, ArH), 7.94 (s, 1H, ArH), 8.10-8.14 (m, 2H, ArH), 8.27 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 25.3 (CH_2), 25.6 ($2CH_2$), 33.3 ($2CH_2$), 54.5 (CH), 111.7 (q, $^3J_{CF}$ = 4.40 Hz, CH), 122.9 (q, $^1J_{CF}$ = 273.45 Hz, CF_3), 127.2 (2CH), 128.93 (2CH), 128.94 (q, $^2J_{CF}$ = 34.1 Hz, C) 129.3 (CH), 130.5 (C), 138.6 (C), 143.9 (CH), 148.2 (C), 152.5 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.21 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3102 (w), 3075 (w), 3027 (w), 3039 (w), 2938 (m), 2922 (m), 2857 (w), 1781 (w), 1748 (w), 1603 (w), 1493 (m), 1478 (m), 1456 (w), 1450 (w), 1399 (w), 1387 (m), 1377 (s), 1346 (w), 1310 (m), 1288 (m), 1265 (s), 1207 (s), 1147 (m), 1140 (w), 1124 (s), 1010 (w), 1084 (w), 1068 (w), 1054 (w), 1029 (w), 1001 (w), 994 (w), 985 (w), 966 (w), 941 (m), 918 (w), 890 (m), 873 (s), 852 (w), 838 (w), 821 (m), 790 (w), 765 (s), 714 (m), 689 (s), 672 (w), 664 (w), 634 (m), 620 (w), 615 (m), 576 (w), 532 (m); GC-MS (EI, 70 eV): m/z (%): 345 (M^+, 33), 290 (8), 276 (4), 263 (100), 244 (3), 140 (1), 102 (1), 77 (1), 55 (2), 41 (2); HRMS (ESI) calcd. for $C_{19}H_{19}F_3N_3$ $[M+H]^+$: 346.15256 found 346.15311.

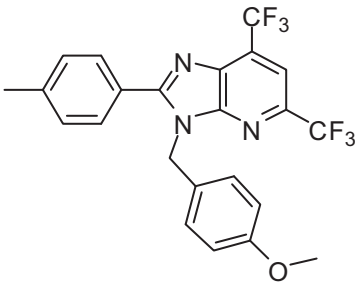
3-Phenethyl-5-(thiophen-2-yl)-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5h):



Starting with CH_2Cl_2 (6 mL), **1** (0.48 mL, 5.36 mmol), **2d** (0.68 mL, 5.36 mmol), **4d** (1.2 g, 5.36 equiv.), **5h** was isolated as light brown solid (1.5 g, 75%); m.p. 99-101 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.19 (t, J = 7.17, 2H, -CH_2-), 4.51 (t, J = 7.17, 2H, -CH_2-), 7.04-7.09 (m, 3H, ArH), 7.12-7.25 (m, 3H, ArH), 7.37 (d, J = 5.0 Hz, 1H, $CH_{thienyl}$), 7.61 (d, J = 3.5 Hz, 1H, $CH_{thienyl}$), 7.75 (s, 1H, ArH), 7.81 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 36.1 (-CH_2-), 45.7 (-CH_2-), 110.5 (q, $^3J_{CF}$ = 4.40 Hz, CH), 122.7 (q, $^1J_{CF}$ = 273.45 Hz, CF_3), 125.5 (CH), 127.1 (CH), 128.2 (CH), 128.3 (CH) 128.7 (2CH), 128.9 (2CH), 129.6 (q, $^2J_{CF}$ = 34.11 Hz, C), 137.3 (C), 144.0 (C), 145.6 (CH), 147.9 (C), 148.3 (2C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.27 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3103 (w), 3084 (w), 3031 (w), 2942 (w), 2869 (w), 1769 (w), 1596 (s), 1538 (m), 1496 (m), 1476 (w), 1454 (w), 1431 (s), 1397 (m), 1375 (s), 1349 (m), 1306 (w), 1298 (w), 1276 (m), 1261 (s), 1202 (s), 1123 (s), 1102 (m), 1027 (m), 1003 (w), 934 (m), 907 (w), 889 (w), 867 (s), 847 (w), 827 (m), 772 (w), 737 (m), 693 (s), 655 (m), 632 (m), 615 (w), 590 (w), 566 (w), 535 (w); GC-MS (EI, 70 eV): m/z (%): 373 (M^+, 30), 354 (2), 269 (100), 208 (2), 104 (5), 91 (4), 77 (2), 65 (1); HRMS (ESI) calcd for $C_{19}H_{15}F_3N_3S$ $[M+H]^+$: 374.09333 found 374.0932.

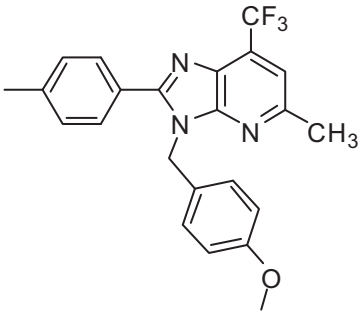
General Procedure for the Synthesis of Compounds 6a-o: DMF (6 mL) was added to an argon-purged pressure tube containing 3*H*-midazo[4,5-b]pyridine **5a-h** (1 mmol), $Pd(OAc)_2$ (0.05 mmol, 5 mol %), CuI (3 mmol), aryl halide (2 mmol), and Cs_2CO_3 (2.5 mmol). The reaction mixture was stirred at 150 °C for 30-60 h and, after cooling to r.t., the solvent was evaporated under reduced pressure. The products were isolated and purified by column chromatography (gradient elution n-heptane/ethyl acetate, ethyl acetate/isopropanol).

3-(4-Methoxybenzyl)-2-p-tolyl-5,7-bis(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6a):



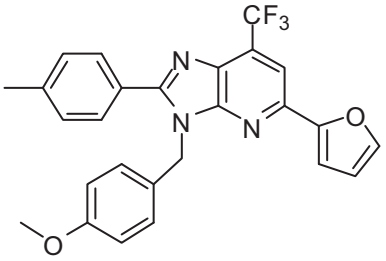
Starting with **5a** (0.25 g, 0.67 mmol), **ArX** (4-MeC_6H_4I) (0.145 g, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.382 g, 3 equiv.), Cs_2CO_3 (0.544 g, 2.5 equiv.), DMF (6 mL), reaction time 50 h, **6a** was isolated as brownish solid (0.132 g, 42%); mp 106–108 °C; ^{1}H NMR (250.12 MHz, DMSO-d_6): δ = 2.40 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 5.65 (s, 2H, -CH_2-), 6.80 (d, ^3J = 8.82 Hz, 2H, ArH), 6.96 (d, ^3J = 8.82 Hz, 2H, ArH), 7.37 (d, ^3J = 8.19 Hz, 2H, ArH), 7.73 (d, ^3J = 8.19 Hz, 2H, ArH), 8.11 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 21.5 (CH_3), 47.1 (-CH_2-), 55.2 (OCH_3), 111.6 (CH), 114.2 (2CH), 121.9 (q, $^1J_{CF}$ = 274.2 Hz, CF_3), 125.8 (C), 126.3 (q, $^1J_{CF}$ = 274.2 Hz, CF_3), 127.5 (C), 128.2 (q, $^2J_{CF}$ = 34.8 Hz, C), 128.7 (2CH), 129.5 (2CH), 129.6 (2CH), 129.9 (C), 133.4 (C), 141.7 (q, $^2J_{CF}$ = 35.7 Hz, C), 141.8 (C), 150.1 (C), 159.4 (C); ^{19}F NMR (282.40 MHz, DMSO-d_6): δ = -64.38 ($ArCF_3$), -60.52 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2962 (w), 2926 (w), 2844 (w), 1613 (m), 1586 (w), 1513 (s), 1466 (s), 1417 (m), 1376 (w), 1361 (w), 1322 (w), 1274 (s), 1249 (m), 1228 (m), 1176 (w), 1161 (w), 1130 (s), 1107 (m), 1087 (w), 1034 (m), 1018 (w), 993 (m), 948 (m), 920 (w), 886 (s), 843 (w), 826 (m), 809 (w), 776 (w), 732 (s), 710 (w), 671 (s), 626 (w), 573 (w), 536 (m); GC-MS (EI, 70 eV): m/z (%): 465 (M^+, 31), 446 (1), 232 (1), 121 (100), 77 (4); HRMS (EI) calcd for $C_{23}H_{17}F_6N_3O$ [M^+]: 466.13486 found 466.13458.

3-(4-Methoxybenzyl)-5-methyl-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6b):



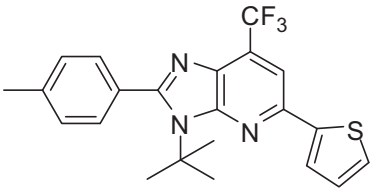
Starting with **5b** (0.2 g, 0.62 mmol), **ArX** (4-MeC_6H_4I) (0.27 g, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.353 g, 3 equiv.), Cs_2CO_3 (0.5 g, 2.5 equiv.), DMF (6 mL), reaction time 30 h, **6b** was isolated as deep brown solid (0.237 g, 93%); mp 114–116 °C; ^{1}H NMR (250.13 MHz, DMSO-d_6): δ = 2.36 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 5.57 (s, 2H, -CH_2-), 6.79 (d, ^3J = 8.75 Hz, 2H, ArH), 6.92 (d, ^3J = 8.75 Hz, 2H, ArH), 7.32 (d, ^3J = 8.00 Hz, 2H, ArH), 7.54 (s, 1H, ArH), 7.66 (d, ^3J = 8.12 Hz, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 21.4 (CH_3), 24.5 (CH_3), 46.3 (-CH_2-), 55.2 (OCH_3), 114.2 (2CH), 114.4 (q, $^3J_{CF}$ = 4.12 Hz, CH), 123.0 (q, $^1J_{CF}$ = 273.74 Hz, CF_3), 126.7 (C), 127.7 (q, $^2J_{CF}$ = 33.42 Hz, C), 128.3 (2CH), 128.8 (C), 129.1 (C), 129.4 (2CH), 129.5 (2CH), 140.7 (C), 149.9 (C), 153.3 (C), 156.1 (C), 159.1 (C); ^{19}F NMR (300.13 MHz, $CDCl_3$): δ = -61.83 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 3038 (w), 3009 (w), 2957 (w), 2921 (m), 2839 (w), 1613 (m), 1597 (w), 1584 (w), 1511 (s), 1468 (m), 1449 (m), 1426 (w), 1407 (m), 1388 (m), 1372 (w), 1362 (w), 1300 (m), 1279 (m), 1261 (w), 1245 (s), 1225 (w), 1190 (w), 1175 (w), 1162 (m), 1124 (s), 1097 (m), 1031 (s), 961 (w), 927 (w), 896 (s), 871 (s), 834 (w), 820 (s), 802 (w), 776 (m), 749 (w), 730 (s), 719 (s), 708 (w), 695 (w), 679 (s), 665 (w), 648 (m), 638 (w), 629 (w), 621 (w), 592 (s), 555 (m), 535 (w); GC-MS (EI, 70 eV): m/z (%): 411 (M^+, 49), 392 (1), 290 (2), 270 (1), 206 (1), 161 (1), 121 (100), 77 (4); HRMS (ESI) calcd for $C_{23}H_{20}F_3N_3O$ [M + H]$^+$: 412.16312 found 412.16302.

5-(Furan-2-yl)-3-(4-methoxybenzyl)-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6c):



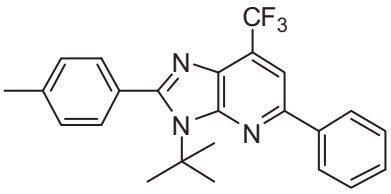
Starting with **5c** (0.2 g, 0.54 mmol), **ArX** (4-MeC_6H_4I) (0.235 g, 2 equiv.), $Pd(OAc)_2$ (0.006 g, 0.05 equiv.), CuI (0.308 g, 3 equiv.), Cs_2CO_3 (0.439 g, 2.5 equiv.), DMF (6 mL), reaction time 30 h, **6c** was isolated as brown solid (0.171 g, 69%); mp 98–100 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 3.68 (s, 3H, OCH_3), 5.48 (s, 2H, -CH_2-), 6.49 (dd, J = 1.70 Hz, J = 3.40 Hz, 1H, CH_{furyl}), 6.71 (d, ^3J = 8.87 Hz, 2H, ArH), 7.01 (d, ^3J = 8.87 Hz, 2H, ArH), 7.04-7.06 (m, 1H, CH_{furyl}), 7.21 (d, ^3J = 8.31 Hz, 2H, ArH), 7.48-7.50 (m, 1H, CH_{furyl}), 7.54 (d, ^3J = 8.31 Hz, 2H, ArH), 7.85 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 21.5 (CH_3), 46.6 (-CH_2-), 55.2 (OCH_3), 108.9 (CH_{furyl}), 112.3 (CH_{furyl}), 114.1 (2CH), 122.9 (CF_3, q, $^1J_{CF}$ = 272.37 Hz), 124.0 (CH), 126.6 (C), 128.3 (q, $^2J_{CF}$ = 34.33 Hz, C), 128.6 (CH), 128.7 (2CH), 129.4 (CH), 129.5 (2CH), 137.9 (C), 140.9 (CH_{furyl}), 143.5 (C), 144.1 (C), 150.2 (C), 152.4 (C), 153.5 (C), 155.2 (C), 159.2 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.97 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3033 (w), 2998 (w), 2956 (w), 2929 (w), 2873 (w), 2837 (w), 1809 (w), 1731 (w), 1698 (m), 1612 (s), 1586 (w), 1513 (s), 1496 (w), 1463 (s), 1455 (s), 1416 (m), 1406 (m), 1371 (m), 1270 (w), 1246 (s), 1165 (m), 1134 (s), 1095 (w), 1030 (w), 1019 (w), 944 (w), 912 (w), 878 (w), 821 (s), 767 (w), 732 (m), 677 (w), 664 (m), 638 (w), 622 (w), 590 (w), 561 (w), 533 (w); GC-MS (EI, 70 eV): m/z (%): 463 (M^+, 50), 444 (1), 342 (3), 121 (100), 116 (2), 91 (2), 77 (4); HRMS (EI) calcd for $C_{26}H_{20}F_3N_3O_2$ $[M]^+$: 463.15021 found 463.151076.

3-tert-Butyl-5-(thiophen-2-yl)-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6d):



Starting with **5d** (0.2 g, 0.62 mmol), **ArX** (4-MeC_6H_4I) (0.27 g, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.353 g, 3 equiv.), Cs_2CO_3 (0.504 g, 2.5 equiv.), DMF (6 mL), reaction time 48 h, **6d** was isolated as light brown solid (0.15 g, 59%); mp 190–192 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.66 (s, 9H, $3CH_3$), 2.35 (s, 3H, CH_3), 7.06-7.09 (d, ^3J = 3.59 Hz, 1H, $CH_{thienyl}$), 7.14-7.19 (m, 2H, ArH), 7.31-7.35 (m, 2H, ArH), 7.54 (d, ^3J = 3.78 Hz, 1H, $CH_{thienyl}$), 7.58 (dd, J = 3.78 Hz, J = 1.13 Hz, 1H, $CH_{thienyl}$), 7.74 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 21.5 (CH_3), 31.0 ($3CH_3$), 61.2 (C), 109.8 (q, $^3J_{CF}$ = 4.40 Hz, CH), 122.9 (q, $^1J_{CF}$ = 273.99 Hz, CF_3), 125.7 (CH), 127.7 (CH), 128.0 (q, $^2J_{CF}$ = 34.11 Hz, C), 128.3 (CH), 128.6 (2CH), 129.7 (2CH), 131.4 (C), 139.8 (C), 143.5 (C), 145.0 (C), 146.1 (C), 146.7 (C), 150.1 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.98 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3094 (w), 3069 (w), 3022 (w), 2980 (w), 2960 (w), 2919 (w), 2871 (w), 1618 (w), 1606 (w), 1589 (m), 1548 (w), 1536 (w), 1510 (w), 1504 (w), 1467 (s), 1429 (m), 1390 (w), 1381 (s), 1351 (m), 1334 (w), 1304 (w), 1276 (m), 1257 (m), 1248 (w), 1226 (w), 1218 (w), 1183 (w), 1170 (w), 1155 (w), 1137 (s), 1126 (m), 1072 (w), 1063 (w), 1053 (m), 1026 (w), 1015 (w), 950 (w), 945 (w), 906 (w), 875 (w), 864 (m), 849 (w), 827 (w), 817 (m), 798 (w), 761 (w), 750 (w), 727 (s), 709 (w), 682 (m), 665 (s), 628 (m), 616 (w), 602 (w), 575 (w), 535 (m); GC-MS (EI, 70 eV): m/z (%): 415 (M^+, 8), 359 (100), 338 (3), 196 (1), 146 (2), 118 (2), 91 (1), 57 (1), 41 (2), 29 (1); HRMS (ESI) calcd for $C_{22}H_{21}F_3N_3S$ $[M+H]^+$: 416.14028 found 416.14085.

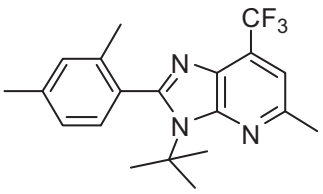
3-tert-Butyl-5-phenyl-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6e):



Starting with **5f** (0.2 g, 0.62 mmol), **ArX** (4-MeC_6H_4I) (0.27 g, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.353 g, 3 equiv.), Cs_2CO_3 (0.504 g, 2.5 equiv.), DMF (6 mL), reaction time 60 h, **6e** was isolated as light brown solid (0.079 g, 31%); mp 239–240 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 (s, 9H, $3CH_3$), 2.35 (s, 3H, CH_3), 7.16-7.19 (m, 2H, ArH), 7.32-7.40 (m, 3H, ArH), 7.43-

7.48 (m, 2H, ArH), 7.86 (s, 1H, ArH), 8.03-8.07 (m, 2H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 21.5 (CH_3), 31.1 ($3CH_3$), 60.9 (C), 111.1 (q, $^3J_{CF}$ = 4.40 Hz, CH), 123.1 (q, $^1J_{CF}$ = 273.45 Hz, CF_3), 126.9 (2CH), 127.9 (q, $^2J_{CF}$ = 33.56 Hz, C), 128.6 (2CH), 128.9 (2CH), 129.1 (CH), 129.6 (2CH), 131.6 (2C), 138.9 (2C), 139.8 (2C), 150.7 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.63 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 3028 (w), 2982 (w), 2922 (m), 2853 (w), 1698 (w), 1658 (m), 1619 (w), 1593 (m), 1498 (w), 1469 (m), 1461 (m), 1381 (s), 1331 (w), 1318 (w), 1302 (w), 1276 (m), 1247 (s), 1184 (w), 1175 (w), 1147 (w), 1128 (s), 1113 (w), 1082 (w), 1070 (w), 1056 (w), 1017 (w), 973 (w), 959 (m), 947 (w), 923 (w), 907 (w), 877 (s), 853 (w), 828 (w), 819 (m), 794 (w), 777 (m), 733 (m), 727 (w), 701 (m), 694 (w), 680 (w), 666 (w), 635 (w), 626 (s), 604 (w), 575 (w), 534 (w); GC-MS (EI, 70 eV): m/z (%): 409 (M^+, 8), 353 (100), 215 (1), 139 (1), 116 (2), 57 (1), 41 (2), 29 (1); HRMS (ESI) calcd for $C_{24}H_{23}F_3N_3$ $[M+H]^+$: 410.18386 found 410.18447.

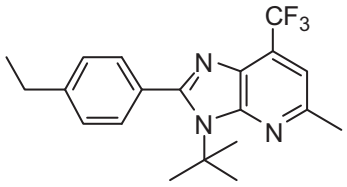
3-tert-Butyl-2-(2,4-dimethylphenyl)-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6f):



Starting with **5e** (0.2 g, 0.78 mmol), **ArX** (2,4-$Me_2C_6H_3I$) (0.23 mL, 2 equiv.), $Pd(OAc)_2$ (0.009 g, 0.05 equiv.), CuI (0.445 g, 3 equiv.), Cs_2CO_3 (0.634 g, 2.5 equiv.), DMF (6 mL), reaction time 56 h, **6f** was isolated as light grey gummy solid (0.14 g, 50%); ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.60 (s, 9H, $3CH_3$), 2.26 (s, 6H, $2CH_3$), 2.64 (s, 3H, CH_3), 7.00-7.02 (m, 3H, ArH), 7.20 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 21.2 ($2CH_3$), 24.7 (CH_3), 30.8 ($3CH_3$), 60.6 (C), 113.4 (q, $^3J_{CF}$ = 4.40 Hz, CH), 123.1 (q, $^1J_{CF}$ = 273.45 Hz, CF_3), 127.3 (q, $^2J_{CF}$ = 33.01 Hz, C), 127.6 (CH), 129.2 (C), 131.0 (CH), 134.7 (2C), 137.4 (CH), 150.3 (C), 151.7 (2C), 156.2 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.78 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2968 (w), 2922 (m), 2861 (w), 1737 (w), 1604 (w), 1589 (m), 1495 (w), 1476 (w), 1457 (m), 1386 (s), 1365 (s), 1329 (m), 1309 (w), 1274 (m), 1253 (m), 1224 (s), 1210 (w), 1155 (w), 1128 (s), 1074 (m), 1049 (m), 1016 (m), 997 (w), 933 (w), 906 (s), 866 (w), 852 (s), 800 (w), 727 (s), 715 (w), 683 (m), 662 (m), 626 (w), 612 (m), 557 (w), 537 (w); GC-MS (EI,

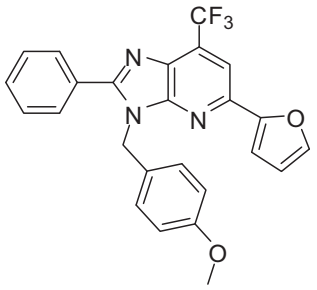
70 eV): m/z (%): 361 (M^+, 8), 305 (100), 285 (4), 270 (1), 132 (2), 116 (3), 77 (1), 57 (1), 41 (1); HRMS (ESI) calcd for $C_{20}H_{23}F_3N_3$ $[M+H]^+$: 362.18386 found 362.18417.

3-tert-Butyl-2-(4-ethylphenyl)-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6g):



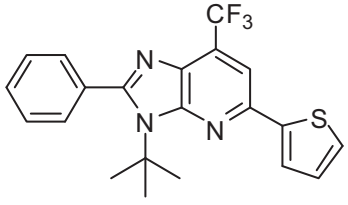
Starting with **5e** (0.2 g, 0.78 mmol), **ArX** (4-EtC_6H_4I) (0.23 mL, 2 equiv.), $Pd(OAc)_2$ (0.009 g, 0.05 equiv.), CuI (0.445 g, 3 equiv.), Cs_2CO_3 (0.634 g, 2.5 equiv.), DMF (6 mL), reaction time 30 h, **6g** was isolated as light brown gummy solid (0.14 g, 50%); ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.13-1.20 (m, 12H, 4CH_3), 1.58 (s, 3H, CH_3), 2.50-2.56 (m, 2H, -CH_2-), 7.13-7.17 (m, 3H, ArH), 7.40 (d, ^3J = 8.18 Hz, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 15.6 (CH_3), 24.8 (CH_3), 28.6 (-CH_2-), 30.9 (3CH_3), 60.7 (C), 113.5 (q, $^3J_{CF}$ = 4.58 Hz, CH), 123.2 (q, $^1J_{CF}$ = 273.74 Hz, CF_3), 126.9 (2CH), 127.4 (q, $^2J_{CF}$ = 33.36 Hz, C), 128.3 (2CH), 132.3 (C), 138.6 (C), 143.1 (C), 145.9 (C), 151.8 (C), 155.5 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.74 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3023 (w), 2964 (s), 2929 (m), 2872 (w), 2725 (w), 2632 (w), 2300 (w), 2228 (w), 1905 (w), 1788 (w), 1737 (w), 1659 (w), 1592 (m), 1499 (s), 1462 (s), 1410 (w), 1386 (s), 1365 (s), 1327 (m), 1306 (m), 1268 (w), 1228 (s), 1169 (w), 1158 (w), 1136 (s), 1072 (m), 1049 (w), 1019 (m), 1006 (w), 979 (w), 965 (w), 933 (w), 898 (s), 871 (m), 846 (w), 831 (w), 819 (s), 783 (w), 765 (w), 732 (m), 703 (w), 685 (m), 669 (w), 646 (w), 634 (w), 615 (w), 690 (m), 554 (w); GC-MS (EI, 70 eV): m/z (%): 361 (M^+, 11), 305 (100), 290 (58), 284 (5), 270 (3), 250 (1), 132 (1), 102 (1), 89 (2), 77 (1), 57 (2), 41 (2), 29 (1); HRMS calcd for $C_{20}H_{23}F_3N_3$ $[M+H]^+$: 362.18386 found 362.18395.

5-(Furan-2-yl)-3-(4-methoxybenzyl)-2-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6h):



Starting with **5c** (0.2 g, 0.62 mmol), **ArX** (C_6H_5Br) (0.13 mL, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.353 g, 3 equiv.), Cs_2CO_3 (0.504 g, 2.5 equiv.), DMF (6 mL), reaction time 48 h, **6h** was isolated as brown solid (0.162 g, 58%); mp 103–105 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.67 (s, 3H, OCH_3), 5.48 (s, 2H, -CH_2-), 6.49 (dd, J = 1.89 Hz, J = 3.40 Hz, 1H, CH_{furyl}), 6.72 (d, ^3J = 8.69 Hz, 2H, ArH), 7.03 (d, ^3J = 8.88 Hz, 1H, CH_{furyl}), 7.26 (d, ^3J = 8.69 Hz, 1H, CH_{furyl}), 7.37 (d, ^3J = 7.92 Hz, 2H, ArH), 7.44 (m, 1H, ArH), 7.61-7.66 (m, 2H, ArH), 7.73 (d, ^3J = 8.50 Hz, 2H, ArH), 7.86 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 46.7 (-CH_2-), 55.2 (OCH_3), 107.8 (CH_{furyl}), 111.4 (CH_{furyl}), 114.3 (2CH), 121.7 (q, $^1J_{CF}$ = 274.55 Hz, CF_3), 124.1 (CH), 126.4 (C), 127.9 (2CH), 128.6 (q, $^3J_{CF}$ = 4.40 Hz, CH), 128.8 (2CH), 129.6 (2CH), 130.3 (C), 130.6 (CH), 143.6 (CH_{furyl}), 144.3 (C), 152.8 (C), 153.5 (C), 154.9 (C), 156.9 (C), 159.2 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.98 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 3001 (w), 2959 (w), 2934 (w), 2912 (w), 2837 (w), 1722 (w), 1708 (w), 1693 (w), 1681 (w), 1611 (m), 1513 (s), 1466 (s), 1452 (w), 1441 (w), 1414 (m), 1376 (m), 1301 (w), 1267 (w), 1246 (s), 1214 (w), 1165 (w), 1134 (s), 1095 (w), 1027 (m), 945 (w), 919 (w), 903 (w), 880 (w), 821 (w), 789 (w), 780 (m), 696 (s), 664 (w), 609 (w), 565 (w), 535 (w); GC-MS (EI, 70 eV): m/z (%): 449 (M^+, 39), 328 (3), 121 (100), 105 (17), 77 (13), 39 (1); HRMS (ESI) calcd for $C_{25}H_{19}F_3N_3O_2$ $[M+H]^+$: 450.10370 found 450.10288.

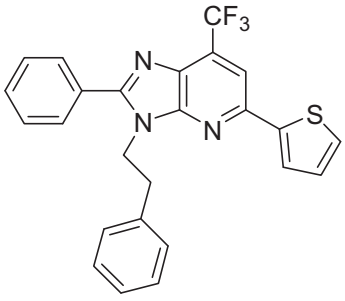
3-tert-Butyl-2-phenyl-5-(thiophen-2-yl)-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6i):



Starting with **5d** (0.2 g, 0.62 mmol), **ArX** (C_6H_5Br) (0.13 mL, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.353 g, 3 equiv.), Cs_2CO_3 (0.504 g, 2.5 equiv.), DMF (6 mL), reaction time 30 h, **6i** was isolated as yellow solid (0.117 g, 47%); mp 208–210 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.65 (s, 9H, $3CH_3$), 7.0 (dd, J = 3.78 Hz, J = 1.32 Hz, 1H, $CH_{thienyl}$), 7.27 (d, ^3J = 3.78 Hz, 1H, $CH_{thienyl}$), 7.36 (d, ^3J =

7.36 Hz, 2H, ArH), 7.55 (d, ^{3}J = 3.97 Hz, 1H, $CH_{thienyl}$), 7.58 (m, 1H, ArH), 7.63 (d, ^{3}J = 7.18 Hz, 2H, ArH), 7.45 (q, $^{4}J_{HF}$ = 1.89 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 30.9 ($3CH_3$), 61.1 (C), 109.7 (q, $^{3}J_{CF}$ = 4.40 Hz, CH), 122.9 (q, $^{1}J_{CF}$ = 273.99 Hz, CF_3), 124.7 (CH), 125.8 (CH), 126.1 (q, $^{2}J_{CF}$ = 34.66 Hz, C), 127.9 (2CH), 128.3 (CH), 128.9 (CH), 129.8 (2CH), 134.6 (C), 144.1 (C), 145.0 (C), 146.5 (C), 150.2 (C), 156.7 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.00 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3082 (w), 2979 (w), 2923 (w), 2871 (w), 1588 (m), 1536 (m), 1515 (w), 1559 (m), 1444 (m), 1430 (m), 1382 (s), 1367 (w), 1351 (w), 1332 (w), 1305 (m), 1277 (m), 1256 (s), 1227 (w), 1215 (w), 1165 (s), 1156 (m), 1121 (s), 1073 (m), 1063 (m), 1035 (w), 1027 (w), 1017 (w), 999 (w), 973 (w), 949 (m), 920 (w), 906 (w), 876 (w), 867 (m), 860 (w), 850 (w), 828 (w), 789 (w), 773 (m), 753 (m), 735 (w), 723 (m), 699 (s), 688 (w), 666 (m), 640 (w), 621 (w), 613 (w), 596 (w), 589 (w), 569 (w), 537 (w); GC-MS (EI, 70 eV): m/z (%): 401 (M^+, 20), 345 (100), 324 (2), 215 (2), 146 (1), 77 (1), 41 (2); HRMS (ESI) calcd for $C_{21}H_{19}F_3N_3S$ $[M+H]^+$: 402.12463 found 402.12507.

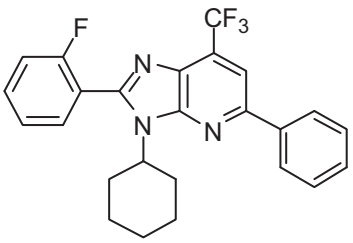
3-Phenethyl-2-phenyl-5-(thiophen-2-yl)-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6j):



Starting with **5h** (0.2 g, 0.54 mmol), **ArX** (C_6H_5Br) (0.12 mL, 2 equiv.), $Pd(OAc)_2$ (0.006 g, 0.05 equiv.), CuI (0.308 g, 3 equiv.), Cs_2CO_3 (0.439 g, 2.5 equiv.), DMF (6 mL), reaction time 57 h, **6j** was isolated as bright yellow solid (0.199 g, 83%); mp 137–139 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.14 (t, *J* = 6.99, 2H, $-CH_2-$), 4.57 (t, *J* = 7.55, 2H, $-CH_2-$), 6.99 (d, *J* = 8.12 Hz, 2H, ArH), 7.12-7.16 (m, 2H, ArH), 7.28-7.44 (m, 5H, ArH), 7.51-7.59 (m, 2H, ArH), 7.63 (d, *J* = 7.18 Hz, 2H, ArH), 7.76 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 35.6 ($-CH_2-$), 45.6 ($-CH_2-$), 110.3 (q, $^{3}J_{CF}$ = 4.12 Hz, CH), 122.8 (q, $^{1}J_{CF}$ = 274.00 Hz, CF_3), 124.2 (CH), 125.8 (2CH), 126.0 (CH), 126.9 (CH), 127.9 (CH), 128.3 (q, $^{2}J_{CF}$ = 33.88 Hz, C), 128.7 (CH), 128.8 (3CH), 129.0 (CH), 129.3 (CH), 129.5 (C), 130.4 (CH), 134.2 (C), 137.4 (C), 143.4 (C), 146.6 (C), 149.8 (C), 156.5 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.99 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3025 (w), 2960 (s), 2927 (m), 2868 (w), 1907 (w), 1732 (w), 1600 (m), 1544 (m),

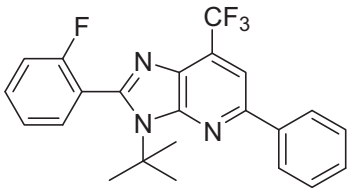
1496 (m), 1467 (w), 1453 (w), 1443 (w), 1418 (w), 1384 (s), 1367 (w), 1339 (w), 1329 (w), 1309 (w), 1271 (m), 1250 (m), 1228 (w), 1155 (w), 1125 (s), 1099 (w), 1073 (w), 1049 (w), 1029 (w), 1020 (w), 1004 (w), 959 (w), 942 (w), 929 (w), 898 (w), 868 (m), 846 (w), 833 (w), 809 (s), 779 (w), 755 (m), 739 (w), 696 (w), 684 (m), 666 (w), 618 (w), 609 (w), 586 (w), 558 (m), 532 (w); GC-MS (EI, 70 eV): m/z (%): 449 (M^+, 26), 358 (2), 345 (100), 324 (1), 242 (1), 208 (2), 186 (1), 146 (1), 105 (1), 91 (1), 77 (2); HRMS (ESI) calcd for $C_{25}H_{19}F_3N_3S$ $[M+H]^+$: 450.12463 found 450.12452.

3-Cyclohexyl-2-(2-fluorophenyl)-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6k):



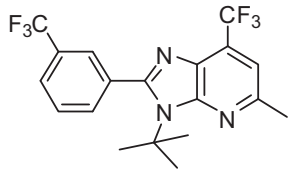
Starting with **5g** (0.2 g, 0.58 mmol), **ArX** (2-FC_6H_4Br) (0.13 mL, 2 equiv.), $Pd(OAc)_2$ (0.006 g, 0.05 equiv.), CuI (0.331 g, 3 equiv.), Cs_2CO_3 (0.471 g, 2.5 equiv.), DMF (6 mL), reaction time 40 h, **6k** was isolated as light brown solid (0.11 g, 43%); mp 188–190 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.17-1.39 (m, 4H, 2-CH_2-), 1.66-1.86 (m, 4H, 2-CH_2-), 2.70-2.82 (m, 2H, -CH_2-), 3.97-4.05 (m, 1H, CH), 7.13-7.19 (m, 1H, ArH), 7.23-7.28 (m, 1H, ArH), 7.33-7.51 (m, 4H, ArH), 7.57-7.63 (m, 1H, ArH), 7.85 (s, 1H, ArH), 8.01-8.05 (m, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 25.3 (-CH_2-), 26.1 (2-CH_2-), 30.9 (2-CH_2-), 58.4 (CH), 111.2 (q, $^3J_{CF}$ = 4.58 Hz, CH), 115.9 (d, $^2J_{CF}$ = 21.06 Hz, CH), 118.5 (d, $^2J_{CF}$ = 15.11 Hz, C), 123.1 (q, $^1J_{CF}$ = 274.20 Hz, CF_3), 124.9 (d, $^3J_{CF}$ = 3.66 Hz, CH), 127.0 (2CH), 128.5 (q, $^2J_{CF}$ = 33.87 Hz, C), 128.9 (2CH), 129.2 (CH), 130.8 (q, $^3J_{CF}$ = 1.83 Hz, C), 132.6 (q, $^3J_{CF}$ = 2.29 Hz, CH), 138.8 (C), 149.6 (C), 151.6 (C), 151.9 (C), 158.3 (C), 162.3 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -112.63 (ArF), -61.96 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2922 (m), 2850 (m), 1616 (w), 1606 (w), 1591 (w), 1506 (w), 1480 (m), 1446 (s), 1416 (m), 1386 (s), 1355 (w), 1319 (m), 1281 (s), 1252 (s), 1224 (w), 1211 (m), 1194 (w), 1187 (w), 1154 (s), 1137 (s), 1124 (s), 1109 (w), 1097 (w), 1076 (m), 1028 (w), 996 (w), 962 (m), 923 (w), 883 (m), 876 (s), 851 (w), 834 (m), 798 (m), 772 (s), 740 (m), 710 (w), 695 (s), 675 (w), 661 (m), 617 (m), 562 (w), 537 (w); GC-MS (EI, 70 eV): m/z (%): 439 (M^+, 20), 420 (4), 370 (5), 357 (100), 336 (3), 158 (1), 140 (1), 102 (1), 41 (1); HRMS (ESI) calcd for $C_{25}H_{22}F_4N_3$ $[M+H]^+$: 440.17444 found 440.17533.

3-tert-Butyl-2-(2-fluorophenyl)-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6l):



Starting with **5f** (0.2 g, 0.63 mmol), **ArX** (2-FC_6H_4Br) (0.13 mL, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.359 g, 3 equiv.), Cs_2CO_3 (0.511 g, 2.5 equiv.), DMF (6 mL), reaction time 60 h, **6l** was isolated as yellow solid (0.065 g, 25%); mp 156–158 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.71 (s, 9H, $3CH_3$), 7.06-7.22 (m, 3H, ArH), 7.37-7.49 (m, 4H, ArH), 7.88 (s, 1H, ArH), 8.06 (d, ^3J = 8.49 Hz, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 30.1 ($3CH_3$), 61.1 (C), 111.2 (q, $^3J_{CF}$ = 4.58 Hz, CH), 115.5 (d, $^2J_{CF}$ = 21.06 Hz, CH), 123.0 (q, $^1J_{CF}$ = 274.20 Hz, CF_3), 123.2 (d, $^2J_{CF}$ = 16.02 Hz, C), 124.1 (d, $^3J_{CF}$ = 3.66 Hz, CH), 127.0 (2CH), 128.5 (q, $^2J_{CF}$ = 33.88 Hz, C), 128.9 (2CH), 129.1 (CH), 130.5 (q, $^3J_{CF}$ = 1.83 Hz, C), 131.6 (d, $^3J_{CF}$ = 2.29 Hz, CH), 131.9 (d, $^3J_{CF}$ = 7.78 Hz, CH), 138.8 (C), 150.5 (C), 150.9 (C), 151.1 (C), 158.5 (C), 162.5 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -111.97 (ArF), -61.90 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3466 (w), 3057 (w), 2980 (w), 1737 (w), 1621 (w), 1580 (w), 1513 (w), 1474 (w), 1455 (m), 1448 (w), 1379 (s), 1366 (w), 1337 (w), 1320 (w), 1273 (w), 1255 (m), 1169 (s), 1153 (m), 1136 (w), 1113 (m), 1102 (w), 1067 (w), 1053 (m), 1035 (w), 1022 (w), 1000 (w), 983 (w), 960 (m), 948 (w), 933 (w), 919 (w), 883 (m), 867 (m), 818 (w), 798 (w), 768 (s), 747 (m), 732 (w), 687 (s), 672 (w), 620 (m), 602 (w), 591 (w), 529 (w); GC-MS (EI, 70 eV): m/z (%): 413 (M^+, 13), 357 (100), 336 (4), 236 (1), 215 (1), 189 (3), 140 (2), 121 (1), 57 (1), 41 (1); HRMS (ESI) calcd for $C_{23}H_{20}F_4N_3$ $[M+H]^+$: 414.15879 found 414.15857.

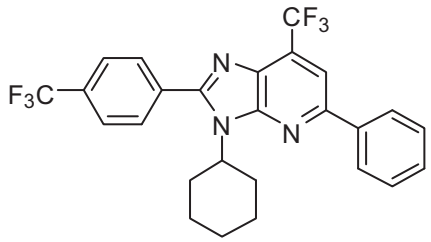
3-tert-Butyl-5-methyl-7-(trifluoromethyl)-2-(3-(trifluoromethyl)phenyl)-3H-imidazo[4,5-b]pyridine (6m):



Starting with **5e** (0.2 g, 0.78 mmol), **ArX** (3-$(CF_3)C_6H_4Br$) (0.22 mL, 2 equiv.), $Pd(OAc)_2$ (0.009 g, 0.05 equiv.), CuI (0.445 g, 3 equiv.), Cs_2CO_3 (0.634 g, 2.5 equiv.), DMF (6 mL), reaction time 56 h, **6m** was isolated as deep brown gummy solid (0.062 g, 20%); ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.60 (s, 9H, $3CH_3$), 2.67 (s, 3H, CH_3), 7.26 (s, 1H, ArH), 7.48-7.75 (m, 4H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 24.8 (CH_3), 31.0

(3CH_3), 60.9 (C), 113.9 (q, $^3J_{CF}$ = 4.40 Hz, CH), 122.9 (q, $^1J_{CF}$ = 273.45 Hz, CF_3), 123.7 (q, $^1J_{CF}$ = 272.35 Hz, CF_3), 126.4 (q, $^3J_{CF}$ = 3.85 Hz, CH), 126.8 (q, $^3J_{CF}$ = 3.85 Hz, CH), 127.8 (q, $^2J_{CF}$ = 32.56 Hz, C), 128.6 (CH), 129.5 (C), 130.5 (q, $^2J_{CF}$ = 32.46 Hz, C), 133.2 (CH), 135.7 (C), 150.1 (C), 152.6 (C), 153.7 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.77 ($ArCF_3$), -62.01 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2961 (w), 2926 (m), 2855 (w), 1728 (w), 1591 (w), 1477 (w), 1468 (w), 1433 (w), 1389 (m), 1368 (m), 1335 (w), 1318 (m), 1304 (m), 1274 (m), 1229 (m), 1162 (m), 1127 (s), 1094 (w), 1072 (m), 1032 (w), 1003 (w), 984 (w), 933 (w), 901 (m), 970 (w), 853 (w), 808 (m), 742 (w), 729 (w), 706 (s), 697 (w), 666 (w), 651 (w), 628 (w), 586 (w), 536 (w); GC-MS (EI, 70 eV): m/z (%): 401 (M^+, 3), 382 (2), 345 (100), 326 (4), 172 (3), 152 (1), 145 (1), 146 (1), 57 (2), 41 (2), 29 (1); HRMS (ESI) calcd for $C_{19}H_{17}F_6N_3$ $[M+H]^+$: 402.13994 found 402.1395.

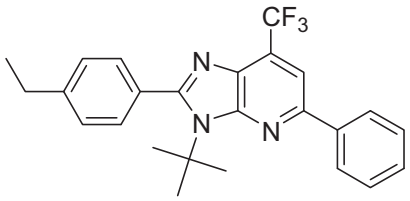
3-Cyclohexyl-5-phenyl-7-(trifluoromethyl)-2-(4-(trifluoromethyl)phenyl)-3H-imidazo[4,5-b]pyridine (6n):



Starting with **5g** (0.25 g, 0.73 mmol), **ArX** (4-(CF_3)C_6H_4Br) (0.19 mL, 2 equiv.), $Pd(OAc)_2$ (0.008 g, 0.05 equiv.), CuI (0.413 g, 3 equiv.), Cs_2CO_3 (0.589 g, 2.5 equiv.), DMF (6 mL), reaction time 30 h, **6n** was isolated as light yellow solid (0.11 g, 31%); mp 225–227 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.15-1.40 (m, 4H, 2-CH_2-), 1.86-1.96 (m, 4H, 2-CH_2-), 2.75-2.93 (m, 2H, -CH_2-), 4.22-4.33 (m, 1H, CH), 7.35-7.41 (m, 1H, ArH), 7.43-7.51 (m, 2H, ArH), 7.73-7.79 (m, 4H, ArH), 7.87 (s, 1H, ArH), 8.02-8.10 (m, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 25.2 (-CH_2-), 26.00 (2-CH_2-), 31.12 (2-CH_2-), 58.05 (CH), 111.54 (q, $^3J_{CF}$ = 4.58 Hz, CH), 123.4 (q, $^1J_{CF}$ = 274.20 Hz, 2CF_3), 125.87 (q, $^3J_{CF}$ = 4.12 Hz, 2CH), 126.9 (2CH), 128.9 (2CH), 129.3 (CH), 130.1 (2CH), 132.3 (q, $^2J_{CF}$ = 32.96 Hz, 2C), 133.7 (C), 138.6 (2C), 151.8 (C), 153.1 (C), 155.0 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.87 ($ArCF_3$), -62.06 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2945 (m), 2858 (m), 1621 (w), 1592 (w), 1469 (w), 1446 (w), 1426 (m), 1406 (w), 1385 (s), 1381 (s), 1351 (w), 1317 (s), 1276 (m), 1255 (m), 1227 (w), 1173 (m), 1153 (m), 1129 (s), 1104 (m), 1078 (w), 1062 (m), 1029 (w), 1015 (m), 994 (w), 962 (m), 922 (w), 891 (w), 881 (s), 854 (s), 822 (w), 785 (w), 770 (s), 754 (w), 742 (w), 713 (m), 692

(s), 675 (w), 666 (w), 620 (s), 596 (m), 556 (w); GC-MS (EI, 70 eV): m/z (%): 489 (M^+, 16), 470 (3), 434 (2), 408 (24), 407 (100), 344 (1), 236 (1), 140 (1), 55 (2), 41 (2); HRMS (EI) calcd for $C_{26}H_{21}F_6N_3$ [M^+] : 489.16342 found 489.163581.

3-tert-Butyl-2-(4-ethylphenyl)-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6o):

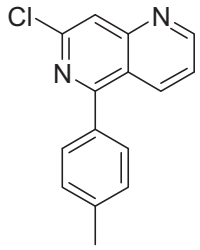


Starting with **5f** (0.2 g, 0.63 mmol), **ArX** (4-EtC_6H_4Br) (0.18 mL, 2 equiv.), $Pd(OAc)_2$ (0.007 g, 0.05 equiv.), CuI (0.359 g, 3 equiv.), Cs_2CO_3 (0.512 g, 2.5 equiv.), DMF (6 mL), reaction time 30 h, **6o** was isolated as brown solid (0.168 g, 63%); mp 227–229 °C; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.55 Hz, 3H, CH_3), 1.69 (s, 9H, $3CH_3$), 2.65 (q, J = 15.11, J = 7.55 Hz, 2H, -CH_2-), 7.20 (d, ^3J = 8.31 Hz, 2H, ArH), 7.36 (d, ^3J = 8.12 Hz, 2H, ArH), 7.39-7.49 (m, 3H, ArH), 7.86 (s, 1H, ArH), 8.05 (d, ^3J = 8.12 Hz, 2H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 15.6 (CH_3), 28.9 (-CH_2-), 31.1 ($3CH_3$), 60.9 (C), 110.9 (q, $^3J_{CF}$ = 4.40 Hz, CH), 123.1 (q, $^1J_{CF}$ = 273.99 Hz, CF_3), 126.9 (2CH), 127.5 (2CH), 127.5 (q, $^2J_{CF}$ = 33.56 Hz, C), 128.9 (2CH), 129.0 (CH), 129.7 (2CH), 131.9 (C), 139.0 (C), 146.1 (C), 150.6 (2C), 150.7 (C), 157.3 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -61.83 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3086 (w), 2967 (s), 2872 (w), 1915 (w), 1737 (w), 1619 (w), 1598 (w), 1500 (w), 1463 (m), 1378 (s), 1316 (w), 1285 (w), 1255 (m), 1204 (w), 1176 (m), 1153 (w), 1127 (s), 1083 (w), 1055 (w), 1016 (w), 1000 (w), 958 (m), 930 (w), 877 (m), 839 (m), 794 (w), 773 (m), 729 (w), 691 (s), 666 (w), 626 (m), 579 (w), 547 (w); GC-MS (EI, 70 eV): m/z (%): 423 (M^+, 9), 368 (23), 367 (100), 352 (34), 331 (3), 282 (1), 189 (2), 140 (2), 116 (8), 89 (2), 77 (2), 57 (8), 41 (8), 29 (4); HRMS (ESI) calcd for $C_{25}H_{25}F_3N_3$ [M+H]$^+$: 424.19951 found 424.19997.

6.3 Regioselective Palladium-Catalysed Cross-Coupling Reactions of 5,7-dichloro-1,6-naphthyridine.

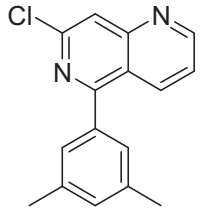
General procedure for synthesis of 9a-l: A 1,4-dioxane / toluene (1:1) solution (8 mL) of **7** (1.0 mmol), arylboronic acid **8** (1.3 equiv.), 2M K_2CO_3 (1 mL), and $Pd(PPh_3)_4$ (5 mol%) was heated at 70 °C for 8 h. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution *n*-heptane/ethyl acetate).

7-Chloro-5-p-tolyl-1,6-naphthyridine (9a):



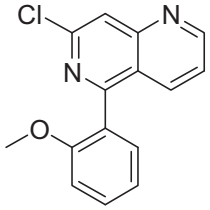
Starting with **7** (0.199 g, 1 mmol), **8a** (0.176 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 8 mL), **9a** was isolated as white solid (0.178 g, 70%); mp 138–141 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 7.25 (d, ^3J = 8.31 Hz, 2H, ArH), 7.37 (dd, J = 8.69 Hz, J = 4.16 Hz, 1H, ArH), 7.48 (d, ^3J = 8.12 Hz, 2H, ArH), 7.84 (s, 1H, ArH), 8.31-8.35 (m, 1H, ArH), 8.95 (dd, J = 4.34 Hz, J = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 (CH_3), 120.2 (CH), 120.8 (C), 122.2 (CH), 129.3 (2CH), 130.0 (2CH), 134.3 (C), 136.2 (CH), 139.8 (C), 148.3 (C), 152.9 (C), 155.2 (CH), 162.1 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3129 (w), 3021 (w), 2862 (w), 1914 (w), 1738 (w), 1610 (w), 1549 (s), 1466 (w), 1378 (w), 1340 (m), 1294 (m), 1182 (m), 1163 (m), 1112 (m), 1068 (s), 1043 (m), 1022 (w), 970 (m), 950 (w), 880 (m), 867 (s), 858 (s), 828 (s), 813 (s), 782 (s), 768 (m), 725 (m), 696 (w), 642 (w), 603 (m), 588 (m), 566 (w); GC-MS (EI, 70 eV): *m/z* (%): 254 (M^+, 100), 253 (73), 239 (87), 217 (42), 203 (30), 190 (23), 177 (8), 127 (8), 108 (11), 96 (13), 75 (13), 63 (12), 51 (10), 39 (9); HRMS (ESI) calcd for $C_{15}H_{12}ClN_2$ $[M+H]^+$: 255.06835 found 255.06841.

7-Chloro-5-(3,5-dimethylphenyl)-1,6-naphthyridine (9b):



Starting with **7** (0.199 g, 1 mmol), **8b** (0.194 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 8 mL), **9b** was isolated as light yellow solid (0.214 g, 80%); mp 155–159 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 2.30 (s, 6H, $2CH_3$), 7.05 (s, 1H, ArH), 7.16 (s, 2H, ArH), 7.34 (dd, *J* = 8.51 Hz, *J* = 4.10 Hz, 1H, ArH), 7.84 (s, 1H, ArH), 8.29-8.34 (m, 1H, ArH), 8.94 (dd, *J* = 4.26 Hz, *J* = 1.73 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.3 ($2CH_3$), 120.3 (CH), 120.8 (C), 122.2 (CH), 127.8 (2CH), 131.2 (CH), 136.3 (CH), 136.9 (C), 138.2 (2C), 148.2 (C), 152.8 (C), 155.2 (CH), 162.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3073 (w), 2953 (w), 2860 (w), 2726 (w), 1597 (m), 1552 (s), 1519 (w), 1494 (w), 1462 (m), 1429 (m), 1343 (m), 1298 (s), 1240 (w), 1164 (m), 1096 (w), 1076 (s), 1038 (w), 1015 (w), 975 (m), 904 (m), 879 (m), 849 (s), 822 (m), 782 (w), 772 (m), 709 (m), 678 (w), 609 (w), 601 (m), 589 (w), 540 (w); GC-MS (EI, 70 eV): *m/z* (%): 268 (M^+, 75), 255 (32), 253 (100), 231 (19), 217 (26), 190 (13), 163 (4), 139 (3), 127 (4), 115 (8), 102 (8), 95 (8), 77 (9), 63 (7), 51 (7), 39 (6); HRMS (ESI) calcd for $C_{16}H_{14}ClN_2$ $[M+H]^+$: 269.084 found 269.08434.

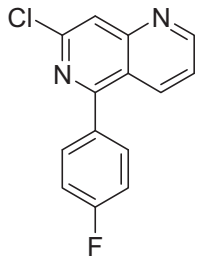
7-Chloro-5-(2-methoxyphenyl)-1,6-naphthyridine (9c):



Starting with **7** (0.1 g, 0.5 mmol), **8c** (0.099 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 4 mL), **9c** was isolated as white solid (0.1 g, 74%); mp 159–161 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.62 (s, 3H, OCH_3), 6.97 (d, ^3J = 8.50 Hz, 1H, ArH), 7.05 (dt, *J* = 7.55 Hz, *J* = 0.94 Hz, 1H, ArH), 7.31-7.37 (m, 2H, ArH), 7.39-7.45 (m, 1H, ArH), 7.91-7.97 (m, 2H, ArH), 8.97 (dd, *J* = 4.16 Hz, *J* = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.5 (OCH_3), 111.1 (CH), 120.8 (CH), 121.1 (CH), 122.0 (C), 122.1 (CH), 126.3 (C), 131.1 (CH), 131.5 (CH), 136.7 (CH), 148.4 (C), 152.0 (C), 155.2 (CH), 156.8 (C), 160.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3322 (br), 2989 (w), 2830 (w), 1603 (m), 1582 (w), 1553 (m), 1492 (w), 1432 (m), 1372 (m), 1347 (w), 1303 (m), 1285 (w), 1238 (m), 1165 (w), 1110 (m), 1065 (w), 1020 (s), 936 (w), 858 (m), 789 (w), 746 (s), 699 (w), 627 (m), 601 (m), 567 (w), 528 (w); GC-MS (EI, 70 eV): *m/z* (%): 270 (M^+, 70), 269 (76), 253 (69), 241 (36), 234 (100), 203 (62), 191 (17), 176

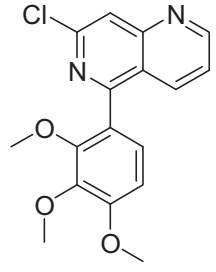
(24), 165 (62), 151 (16), 102 (28), 100 (11), 88 (17), 82 (13), 75 (28), 63 (23), 51 (16), 39 (14), 29 (1); HRMS (ESI) calcd for $C_{15}H_{12}ClN_2O$ $[M+H]^+$: 271.06327 found 271.06347.

7-Chloro-5-(4-fluorophenyl)-1,6-naphthyridine (9d):



Starting with **7** (0.1 g, 0.5 mmol), **8d** (0.09 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 4 mL), **9d** was isolated as white solid (0.07 g, 54%); mp 162–164 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.16-7.21 (m, 2H, ArH), 7.41 (dd, *J* = 8.69 Hz, *J* = 4.34 Hz, 1H, ArH), 7.60-7.65 (m, 2H, ArH), 7.92 (s, 1H, ArH), 8.30-8.34 (m, 1H, ArH), 9.02 (dd, *J* = 4.16 Hz, *J* = 1.51 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 115.9 (2CH, d, $^2J_{CF}$ = 22.01 Hz), 120.7 (CH), 122.5 (CH), 122.6 (C), 132.1 (2CH, d, $^3J_{CF}$ = 8.25 Hz), 133.2 (C, d, $^4J_{CF}$ = 3.30 Hz), 135.8 (CH), 148.4 (C), 152.9 (C), 155.4 (CH), 160.8 (C), 163.7 (C, d, $^1J_{CF}$ = 250.34 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -111.04 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3116 (w), 3054 (w), 1895 (w), 1597 (m), 1577 (w), 1562 (m), 1507 (s), 1434 (w), 1381 (w), 1367 (m), 1327 (m), 1295 (w), 1220 (s), 1173 (w), 1155 (m), 1093 (w), 1043 (w), 1013 (w), 968 (m), 881 (m), 833 (s), 801 (w), 771 (m), 729 (m), 694 (w), 634 (w), 602 (w), 586 (w), 575 (m), 528 (s); GC-MS (EI, 70 eV): *m/z* (%): 258 (M^+, 100), 257 (89), 221 (55), 195 (22), 169 (12), 144 (3), 131 (4), 111 (12), 98 (10), 75 (20), 62 (6), 57 (5), 50 (7), 39 (2), 31 (1); HRMS (ESI) calcd for $C_{14}H_9ClFN_2$ $[M+H]^+$: 259.04328 found 259.04323.

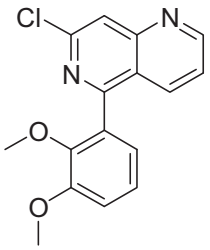
7-Chloro-5-(2,3,4-trimethoxyphenyl)-1,6-naphthyridine (9e):



Starting with **7** (0.199 g, 1 mmol), **8e** (0.276 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 8 mL), **9e** was isolated as white solid (0.221 g, 67%); mp 140 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.53 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.77 (d, *J* = 8.50 Hz, 1H, ArH), 7.09 (d, *J* = 8.50 Hz, 1H, ArH), 7.35 (dd, *J* = 8.50 Hz, *J* = 4.16 Hz, 1H, ArH), 7.91 (s, 1H, ArH), 8.03-8.07 (m, 1H, ArH), 8.97 (dd, *J* = 4.16 Hz, *J* = 1.70 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 56.2 (OCH_3), 61.1 (OCH_3), 61.6 (OCH_3), 107.8 (CH), 120.7 (CH), 121.9 (C), 122.2 (CH), 124.3 (C), 125.9 (CH), 136.8 (CH), 142.1 (C), 148.3 (C), 151.6

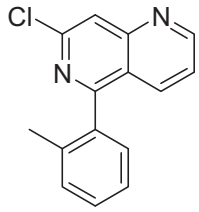
(C), 152.2 (C), 155.1 (C), 155.3 (CH), 159.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3005 (w), 2955 (w), 2839 (w), 1601 (m), 1555 (s), 1494 (m), 1469 (m), 1435 (w), 1373 (m), 1300 (s), 1225 (m), 1165 (w), 1100 (s), 1072 (s), 1023 (m), 976 (m), 924 (w), 877 (m), 799 (w), 770 (m), 719 (w), 646 (w), 597 (m), 559 (w); GC-MS (EI, 70 eV): *m/z* (%): 330 (M^+, 100), 329 (49), 313 (53), 294 (90), 279 (84), 268 (28), 257 (22), 251 (21), 241 (12), 229 (54), 215 (40), 165 (50), 139 (27), 87 (15), 75 (18), 63 (12), 51 (10); HRMS (ESI) calcd for $C_{17}H_{16}ClN_2O_3$ $[M+H]^+$: 331.0844 found 331.08454.

7-Chloro-5-(2,3-dimethoxyphenyl)-1,6-naphthyridine (9f):



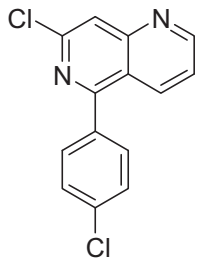
Starting with **7** (0.199 g, 1 mmol), **8f** (0.24 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 8 mL), **9f** was isolated as white solid (0.288 g, 96%); mp 133–135 °C. ^1H NMR (250.13 MHz, $CDCl_3$): δ = 3.52 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.98-7.08 (m, 2H, ArH), 7.16-7.26 (m, 1H, ArH), 7.37 (dd, *J* = 8.51 Hz, *J* = 4.10 Hz, 1H, ArH), 7.97 (s, 1H, ArH), 8.05-8.10 (m, 1H, ArH), 9.01 (dd, *J* = 4.26 Hz, *J* = 1.73 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.9 (OCH_3), 61.4 (OCH_3), 113.6 (CH), 120.9 (CH), 121.8 (C), 122.3 (CH), 122.8 (CH), 124.6 (CH), 131.7 (C), 136.8 (CH), 146.8 (C), 148.1 (C), 151.9 (C), 152.7 (C), 155.4 (CH), 159.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3345 (m), 3333 (m), 2999 (w), 2838 (w), 1603 (w), 1556 (m), 1468 (s), 1427 (m), 1370 (w), 1259 (s), 1209 (m), 1168 (w), 1107 (w), 1087 (s), 1031 (m), 982 (s), 878 (w), 859 (m), 795 (m), 749 (s), 696 (m), 588 (w), 559 (w), 541 (w), 531 (w); MS GC-MS (EI, 70 eV): *m/z* (%): 300 (M^+, 76), 299 (64), 285 (62), 283 (100), 271 (33), 264 (30), 257 (20), 246 (14), 239 (33), 229 (14), 221 (26), 213 (29), 193 (22), 177 (25), 165 (67), 152 (27), 125 (12), 102 (14), 99 (10), 89 (19), 77 (11), 75 (22), 63 (17), 51 (18), 39 (10); HRMS (ESI) calcd for $C_{16}H_{14}ClN_2O_2$ $[M+H]^+$: 301.07383 found 301.07366.

7-Chloro-5-o-tolyl-1,6-naphthyridine (9g):



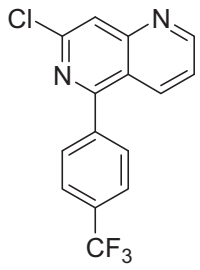
Starting with **7** (0.199 g, 1 mmol), **8g** (0.176 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 8 mL), **9g** was isolated as brown solid (0.18 g, 70%); mp 105–107 °C. ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 1.99 (s, 3H, CH_3), 7.19-7.34 (m, 5H, ArH), 7.81-7.90 (m, 2H, ArH), 8.96 (dd, *J* = 4.26 Hz, *J* = 1.89 Hz, 1H, ArH); ^{13}C NMR (250.13 MHz, $CDCl_3$), δ = 19.8 (CH_3), 120.7 (CH), 121.6 (C), 122.5 (CH), 125.8 (CH), 129.3 (CH), 129.7 (CH), 130.6 (CH), 135.9 (CH), 136.3 (C), 148.2 (C), 152.3 (C), 155.5 (CH), 156.3 (C), 162.8 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 2992 (w), 2858 (w), 1600 (m), 1556 (s), 1479 (w), 1368 (m), 1303 (s), 1207 (w), 1143 (w), 1087 (w), 1063 (m), 1034 (m), 972 (m), 959 (w), 864 (s), 795 (w), 768 (s), 736 (m), 706 (w), 635 (w), 603 (m), 536 (w); GC-MS (EI, 70 eV): *m/z* (%): *m/z* (%): 254 (M^+, 30), 253 (100), 217 (21), 190 (14), 139 (2), 126 (2), 115 (1), 108 (9), 89 (3), 75 (4), 63 (5), 51 (4), 39 (4); HRMS (ESI) calcd for $C_{15}H_{12}ClN_2$ $[M+H]^+$: 255.06835 found 255.06796.

7-Chloro-5-(4-chlorophenyl)-1,6-naphthyridine (9h):



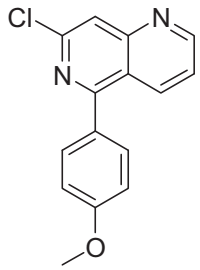
Starting with **7** (0.1 g, 0.5 mmol), **8h** (0.1 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 4 mL), **9h** was isolated as light yellow solid (0.045 g, 33%); mp 150–152 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.39-7.48 (m, 3H, ArH), 7.55-7.59 (m, 2H, ArH), 7.92 (s, 1H, ArH), 8.28-8.32 (m, 1H, ArH), 9.01 (dd, *J* = 3.97 Hz, *J* = 1.32 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 120.7 (C), 120.9 (CH), 122.6 (CH), 128.9 (2CH), 131.4 (2CH), 135.5 (C), 135.6 (CH), 136.1 (C), 148.5 (C), 152.9 (C), 155.5 (CH), 160.6 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 2923 (w), 2852 (w), 1602 (m), 1563 (w), 1551 (m), 1464 (m), 1402 (w), 1304 (m), 1264 (m), 1169 (w), 1102 (w), 1074 (s), 1013 (m), 966 (m), 875 (m), 852 (w), 835 (s), 794 (w), 771 (s), 745 (m), 706 (w), 635 (w), 603 (m), 586 (m), 541 (w); GC-MS (EI, 70 eV): *m/z* (%): 274 (M^+, 100), 273 (69), 239 (74), 203 (43), 176 (22), 150 (11), 137 (8), 119 (10), 111 (7), 101 (16), 99 (7), 88 (12), 75 (30), 51 (11), 39 (4); HRMS (ESI) calcd for $C_{14}H_9Cl_2N_2$ $[M+H]^+$: 275.01373 found 275.01322.

7-Chloro-5-(4-(trifluoromethyl)phenyl)-1,6-naphthyridine (9i):



Starting with **7** (0.1 g, 0.5 mmol), **8i** (0.123 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 4 mL), **9i** was isolated as white solid (0.1 g, 65%); mp 151–153 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.41 (dd, *J* = 8.69 Hz, *J* = 4.34 Hz, 1H, ArH), 7.73 (s, 4H, ArH), 7.93 (s, 1H, ArH), 8.26 (d, *J* = 8.50 Hz, 1H, ArH), 9.02 (dd, *J* = 4.16 Hz, *J* = 1.70 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 120.7 (C), 121.4 (CH), 122.7 (CH), 123.9 (CF_3, q, $^1J_{CF}$ = 271.25 Hz), 125.7 (2CH, q, $^3J_{CF}$ = 3.85 Hz), 130.5 (2CH), 131.6 (C, q, $^2J_{CF}$ = 32.46 Hz), 135.3 (CH), 140.5 (C), 148.5 (C), 152.8 (C), 155.6 (CH), 160.2 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.74 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3118 (w), 3053 (m), 2931 (w), 2849 (w), 1603 (m), 1555 (s), 1519 (w), 1470 (m), 1427 (w), 1410 (m), 1372 (w), 1322 (s), 1264 (w), 1176 (m), 1165 (m), 1107 (s), 1048 (w), 1062 (s), 1039 (w), 1016 (m), 971 (m), 880 (m), 841 (m), 771 (m), 723 (w), 660 (w), 618 (m), 606 (m), 571 (w), 542 (w); GC-MS (EI, 70 eV): *m/z* (%): 308 (M^+, 100), 307 (67), 271 (43), 239 (48), 203 (26), 177 (10), 126 (4), 102 (5), 88 (4), 75 (13), 51 (5), 39 (1); HRMS (ESI) calcd for $C_{15}H_9ClF_3N_2$ $[M+H]^+$: 309.04009 found 309.03998.

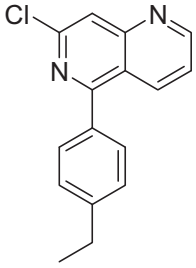
7-Chloro-5-(4-methoxyphenyl)-1,6-naphthyridine (9j):



Starting with **7** (0.1 g, 0.5 mmol), **8j** (0.099 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 4 mL), **9j** was isolated as white solid (0.126 g, 73%); mp 144–146 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 6.98 (d, ^3J = 8.89 Hz, 2H, ArH), 7.36 (dd, *J* = 8.69 Hz, *J* = 4.16 Hz, 1H, ArH), 7.56 (d, ^3J = 8.89 Hz, 2H, ArH), 7.84 (s, 1H, ArH), 8.35-8.38 (m, 1H, ArH), 8.97 (dd, *J* = 4.16 Hz, *J* = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.5 (OCH_3), 114.1 (2CH), 119.9 (CH), 120.7 (C), 122.2 (CH), 129.6 (C), 131.6 (2CH), 136.2 (CH), 148.3 (C), 152.9 (C), 155.1 (CH), 160.9 (C), 161.6 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3088 (w), 2974 (w), 2844 (w), 1600 (s), 1574 (w), 1513 (s), 1488 (w), 1467 (m), 1380 (m), 1339 (m), 1250 (s), 1174 (m), 1110 (w), 1068 (m), 1021 (s), 973 (w), 934 (w), 866 (m), 834 (s), 784 (m), 734 (w), 641 (w), 604 (w), 577 (m), 542 (w); GC-MS (EI, 70 eV): *m/z* (%): 270 (M^+, 100),

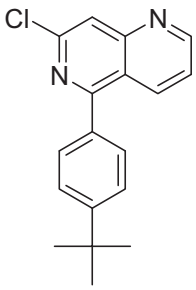
255 (16), 239 (46), 227 (34), 203 (14), 192 (27), 164 (26), 138 (8), 99 (3), 75 (13), 63 (12), 51 (6), 39 (5); HRMS (ESI) calcd for $C_{15}H_{12}ClN_2O$ $[M+H]^+$: 271.06327 found 271.06363.

7-Chloro-5-(4-ethylphenyl)-1,6-naphthyridine (9k):



Starting with **7** (0.1 g, 0.5 mmol), **8k** (0.097 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 4 mL), **9k** was isolated as light brown heavy oil (0.107 g, 79%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.19 (t, J = 7.55 Hz, 3H, CH_3), 2.64 (q, J = 7.37 Hz, J = 14.92 Hz, 2H, -CH_2-), 7.26 (d, ^3J = 7.93 Hz, 2H, ArH), 7.32 (dd, J = 8.69 Hz, J = 4.16 Hz, 1H, ArH), 7.49 (d, ^3J = 8.31 Hz, 2H, ArH), 7.83 (s, 1H, ArH), 8.32-8.35 (m, 1H, ArH), 8.93 (dd, J = 4.16 Hz, J = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 15.5 (CH_3), 28.8 (-CH_2-), 120.2 (CH), 120.7 (C), 122.2 (CH), 128.2 (2CH), 130.1 (2CH), 134.5 (C), 136.2 (CH), 146.1 (C), 148.4 (C), 152.9 (C), 155.2 (CH), 162.1 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3028 (w), 2962 (m), 2870 (w), 1914 (w), 1726 (w), 1599 (s), 1548 (s), 1513 (w), 1467 (m), 1427 (w), 1366 (m), 1342 (m), 1300 (m), 1284 (w), 1179 (m), 1074 (s), 1041 (w), 1019 (w), 970 (s), 879 (s), 857 (m), 838 (s), 769 (m), 707 (w), 661 (w), 641 (w), 618 (m), 602 (m), 573 (w), 554 (w), 531 (w); GC-MS (EI, 70 eV): *m/z* (%): 268 (M^+, 83), 267 (48), 253 (23), 239 (100), 216 (15), 190 (14), 151 (5), 126 (4), 108 (10), 89 (6), 77 (6), 75 (9), 63 (7), 39 (5); HRMS (ESI) calcd for $C_{16}H_{14}ClN_2$ $[M+H]^+$: 269.084 found 269.08427.

5-(4-tert-Butylphenyl)-7-chloro-1,6-naphthyridine (9l):

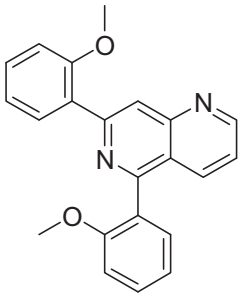


Starting with **7** (0.1 g, 0.5 mmol), **8l** (0.116 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane:Toluene (1:1, 4 mL), **9l** was isolated as white solid (0.1 g, 67%); mp 116–118 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.30 (s, 9H, 3CH_3), 7.36 (dd, J = 8.69 Hz, J = 4.16 Hz, 1H, ArH), 7.47 (d, ^3J = 8.69 Hz, 2H, ArH), 7.53 (d, ^3J = 8.69 Hz, 2H, ArH), 7.86 (s, 1H, ArH), 8.37-8.41 (m, 1H, ArH), 8.97 (dd, J = 4.16 Hz, J = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 31.3 (3CH_3), 34.8 (C), 120.2 (CH), 120.8 (C), 122.2 (CH), 125.7 (2CH), 129.9 (2CH), 134.3

(C), 136.3 (CH), 148.4 (C), 152.8 (C), 152.9 (C), 155.2 (CH), 162.1 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 2962 (m), 2867 (w), 1731 (w), 1600 (s), 1562 (s), 1548 (s), 1514 (w), 1467 (s), 1404 (w), 1362 (m), 1299 (m), 1264 (m), 1199 (w), 1165 (w), 1122 (m), 1070 (s), 1017 (w), 971 (m), 880 (m), 865 (m), 836 (s), 823 (w), 774 (m), 735 (w), 703 (w), 665 (w), 642 (w), 617 (m), 601 (s), 557 (w), 539 (m); GC-MS (EI, 70 eV): *m/z* (%): 296 (M^+, 32), 281 (100), 239 (12), 205 (6), 177 (4), 127 (4), 108 (7), 95 (4), 75 (4), 63 (2), 51 (2), 41 (9), 39 (4), 29 (1); HRMS (ESI) calcd for $C_{18}H_{18}ClN_2$ $[M+H]^+$: 297.1153 found 297.11525.

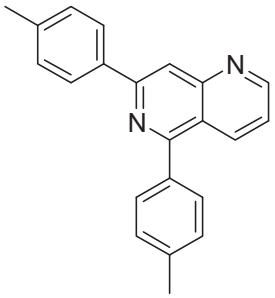
General procedure for the synthesis of 11a-i: A 1,4-dioxane solution (8 mL) of **7** (1.0 mmol), arylboronic acid **10** (2.5 equiv.), 2M K_2CO_3 (2 mL, 1 mL per cross-coupling), and $Pd(PPh_3)_4$ (5 mol%) was heated at 110 °C for 12 h in a pressure tube. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution *n*-heptane/ethyl acetate).

5,7-Bis(2-methoxyphenyl)-1,6-naphthyridine (11a):



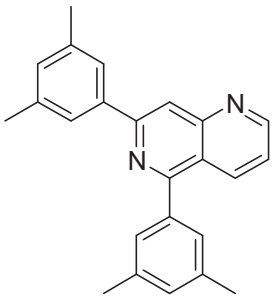
Starting with **7** (0.1 g, 0.5 mmol), **10a** (0.19 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11a** was isolated as light yellow solid (0.122 g, 71%); mp 156–158 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.62 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.95-7.09 (m, 4H, ArH), 7.27-7.33 (m, 2H, ArH), 7.37-7.46 (m, 2H, ArH), 7.92-7.96 (m, 1H, ArH), 8.01 (dd, *J* = 7.55 Hz, *J* = 1.70 Hz, 1H, ArH), 8.50 (s, 1H, ArH), 8.97 (dd, *J* = 4.34 Hz, *J* = 1.89 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.4 (OCH_3), 55.5 (OCH_3), 111.1 (CH), 111.3 (CH), 120.9 (CH), 121.1 (CH), 121.5 (CH), 121.6 (C), 121.9 (CH), 128.1 (C), 128.5 (C), 129.8 (CH), 130.4 (CH), 131.7 (CH), 131.8 (CH), 136.3 (CH), 150.9 (C), 152.1 (C), 154.2 (CH), 157.1 (C), 157.4 (C), 158.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3067 (w), 2922 (w), 2834 (w), 1597 (m), 1571 (m), 1518 (w), 1488 (m), 1392 (w), 1330 (m), 1280 (w), 1281 (s), 1235 (s), 1164 (m), 1125 (w), 1043 (w), 1015 (s), 966 (m), 880 (w), 188 (w), 771 (m), 751 (s), 705 (w), 655 (m), 585 (w), 574 (w), 558 (w), 541 (w), 533 (w); GC-MS (EI, 70 eV): *m/z* (%): 342 (M^+, 100), 341 (79), 311 (27), 297 (25), 281 (26), 237 (17), 180 (14), 164 (5), 134 (10), 94 (3), 77 (5), 75 (2), 63 (6), 51 (3), 39 (4); HRMS (ESI) calcd for $C_{22}H_{19}N_2O_2$ $[M+H]^+$: 343.1441 found 343.1446.

5,7-Di(p-tolyl)-1,6-naphthyridine (11b):



Starting with **7** (0.1 g, 0.5 mmol), **10b** (0.169 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11b** was isolated as light yellow solid (0.115 g, 74%); mp 112–114 °C. ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 7.21 (d, ^3J = 8.12 Hz, 2H, ArH), 7.25-7.29 (m, 3H, ArH), 7.58 (d, ^3J = 8.12 Hz, 2H, ArH), 8.07 (d, ^3J = 8.31 Hz, 2H, ArH), 8.19 (s, 1H, ArH), 8.30-8.34 (m, 1H, ArH), 8.92 (dd, J = 4.16 Hz, J = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.3 (CH_3), 21.4 (CH_3), 115.9 (CH), 120.7 (C), 121.5 (CH), 127.2 (2CH), 129.2 (2CH), 129.5 (2CH), 130.2 (2CH), 135.9 (CH), 136.0 (C), 139.0 (C), 139.1 (2C), 152.5 (C), 153.9 (C), 154.3 (CH), 160.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3128 (w), 3014 (w), 2917 (w), 2857 (w), 2730 (w), 1911 (w), 1599 (m), 1656 (s), 1513 (m), 1453 (w), 1384 (w), 1365 (m), 1296 (w), 1197 (w), 1181 (m), 1111 (w), 1031 (w), 968 (m), 877 (m), 860 (w), 817 (s), 786 (w), 766 (s), 721 (s), 657 (w), 618 (w), 588 (w), 577 (w), 567 (w); GC-MS (EI, 70 eV): *m/z* (%): 310 (M^+, 100), 309 (89), 295 (59), 266 (3), 217 (5), 190 (7), 147 (11), 115 (5), 91 (5), 65 (4), 51 (2), 39 (3); HRMS (ESI) calcd for $C_{22}H_{19}N_2$ $[M+H]^+$: 311.15482 found 311.15442.

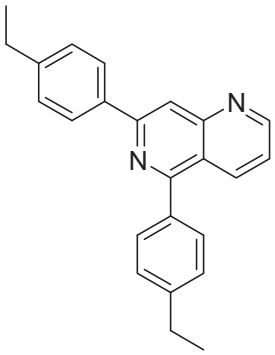
5,7-Bis(3,5-dimethylphenyl)-1,6-naphthyridine (11c):



Starting with **7** (0.1 g, 0.5 mmol), **10c** (0.186 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11c** was isolated as light yellow solid (0.16 g, 94%); mp 174–176 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.32 (s, 6H, $2CH_3$), 2.33 (s, 6H, $2CH_3$), 6.96 (s, 1H, ArH), 7.06 (s, 1H, ArH), 7.25-7.29 (m, 3H, ArH), 7.76 (s, 2H, ArH), 8.19 (s, 1H, ArH), 8.26-8.30 (m, 1H, ArH), 8.94 (dd, J = 4.34 Hz, J = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 ($2CH_3$), 21.5 ($2CH_3$), 116.7 (CH), 120.9 (C), 121.6 (CH), 125.2 (2CH), 127.9 (2CH), 130.7 (CH), 130.8 (CH), 135.9 (CH), 138.1 (2C), 138.3 (2C), 138.7 (C), 138.9 (2C), 154.3 (C), 154.4 (CH), 161.4 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3034 (w), 2913 (w), 2859 (w), 1596 (m), 1562 (m), 1494 (w), 1335 (w), 1310 (w), 1245 (w), 1176 (w), 1094 (w), 1083 (w), 1039 (m), 975 (w), 909 (w), 860 (m), 848

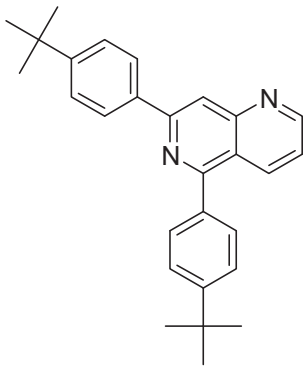
(s), 800 (w), 775 (m), 712 (m), 688 (s), 624 (w), 589 (w), 545 (w), 528 (w); GC-MS (EI, 70 eV): *m/z* (%): 338 (M^+, 100), 337 (83), 323 (76), 307 (6), 292 (3), 231 (3), 190 (3), 169 (6), 154 (12), 133 (3), 105 (1), 91 (1), 77 (3), 63 (1), 51 (1), 39 (2); HRMS (ESI) calcd for $C_{24}H_{23}N_2$ $[M+H]^+$: 339.18558 found 339.18594.

5,7-Di(p-tolyl)-1,6-naphthyridine (11d):



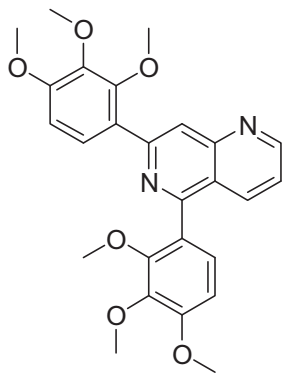
Starting with **7** (0.1 g, 0.5 mmol), **10d** (0.188 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11d** was isolated as brown solid (0.114 g, 67%); mp 90–92 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 4.53 Hz, 3H, CH_3), 1.23 (t, *J* = 4.34 Hz, 3H, CH_3), 2.59-2.71 (m, 4H, 2(-CH_2-)), 7.24 (d, ^3J = 8.31 Hz, 2H, ArH), 7.27-7.31 (m, 3H, ArH), 7.61 (d, ^3J = 8.31 Hz, 2H, ArH), 8.10 (d, ^3J = 8.31 Hz, 2H, ArH), 8.21 (s, 1H, ArH), 8.32-8.36 (m, 1H, ArH), 8.93 (dd, *J* = 4.16 Hz, *J* = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 15.5 (CH_3), 15.6 (CH_3), 28.7 (-CH_2-), 28.8 (-CH_2-), 115.9 (CH), 120.7 (C), 121.5 (CH), 127.3 (2CH), 128.0 (2CH), 128.3 (2CH), 130.3 (2CH), 135.9 (CH), 136.3 (C), 136.4 (C), 145.3 (C), 145.5 (C), 152.5 (C), 153.9 (C), 154.3 (CH), 160.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 3011 (w), 2961 (m), 2870 (w), 1914 (w), 1599 (s), 1582 (w), 1555 (s), 1513 (m), 1440 (w), 1420 (w), 1365 (m), 1327 (m), 1181 (m), 1116 (w), 1017 (w), 971 (m), 908 (w), 833 (s), 767 (m), 701 (w), 655 (w), 609 (w), 560 (w), 552 (w); GC-MS (EI, 70 eV): *m/z* (%): 338 (M^+, 100), 337 (63), 309 (70), 293 (10), 255 (1), 217 (3), 154 (16), 115 (2), 89 (2), 77 (2), 51 (1), 39 (1); HRMS (ESI) calcd for $C_{24}H_{23}N_2$ $[M+H]^+$: 339.18558 found 339.18577.

5,7-Bis(4-tert-butylphenyl)-1,6-naphthyridine (11e):



Starting with **7** (0.1 g, 0.5 mmol), **10e** (0.222 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11e** was isolated as light yellow solid (0.156 g, 79%); mp 125–127 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.28 (s, 9H, $3CH_3$), 1.32 (s, 9H, $3CH_3$), 7.28 (dd, J = 8.50 Hz, J = 4.34 Hz, 1H, ArH), 7.44 (d, ^3J = 8.69 Hz, 2H, ArH), 7.49 (d, ^3J = 8.50 Hz, 2H, ArH), 7.64 (d, ^3J = 8.69 Hz, 2H, ArH), 8.11 (d, ^3J = 8.69 Hz, 2H, ArH), 8.21 (s, 1H, ArH), 8.36-8.39 (m, 1H, ArH), 8.94 (dd, J = 4.34 Hz, J = 1.70 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 31.3 ($3CH_3$), 31.4 ($3CH_3$), 34.7 (C), 34.8 (C), 115.9 (CH), 120.7 (C), 121.5 (CH), 125.5 (2CH), 125.8 (2CH), 127.1 (2CH), 129.9 (2CH), 135.9 (CH), 136.2 (2C), 152.2 (C), 152.3 (C), 152.5 (C), 153.9 (C), 154.3 (CH), 160.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3037 (w), 2957 (s), 2865 (w), 1918 (w), 1602 (s), 1514 (w), 1468 (m), 1414 (w), 1363 (m), 1310 (w), 1200 (w), 1128 (w), 1052 (w), 1012 (w), 971 (m), 882 (m), 842 (s), 772 (m), 725 (m), 645 (w), 631 (w), 609 (w), 559 (s), 543 (w); GC-MS (EI, 70 eV): *m/z* (%): 394 (M^+, 64), 379 (100), 363 (21), 337 (16), 323 (4), 293 (3), 217 (1), 182 (13), 154 (16), 140 (1), 115 (1), 91 (1), 57 (3), 41 (7), 39 (1), 29 (1); HRMS (ESI) calcd for $C_{28}H_{31}N_2$ $[M+H]^+$: 395.24818 found 395.24873.

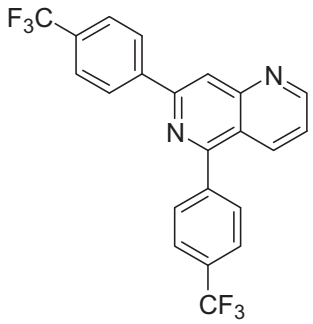
5,7-Bis(2,3,4-trimethoxyphenyl)-1,6-naphthyridine (11f):



Starting with **7** (0.1 g, 0.5 mmol), **10f** (0.265 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11f** was isolated as brown heavy oil (0.114 g, 49%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.51 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.72 (d, J = 8.88 Hz, 1H, ArH), 6.75 (d, J = 8.69 Hz, 1H, ArH), 7.14 (d, J = 8.50 Hz, 1H, ArH), 7.29 (dd, J = 8.31 Hz, J = 4.16 Hz, 1H, ArH), 7.69 (d, J = 8.69 Hz, 1H, ArH), 8.01-8.04 (m, 1H, ArH), 8.39 (s, 1H, ArH), 8.95 (dd, J = 4.34 Hz, J = 1.89 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 56.1 (OCH_3), 56.2 (OCH_3), 60.9 (OCH_3),

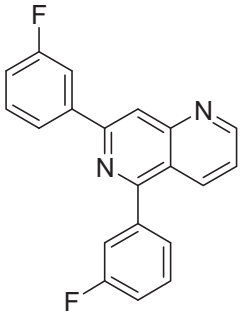
61.1 (2OCH_3), 61.5 (OCH_3), 107.6 (CH), 107.7 (CH), 120.7 (CH), 121.5 (C), 121.6 (CH), 125.8 (CH), 125.9 (C), 126.0 (CH), 126.6 (C), 136.3 (CH), 142.1 (C), 142.6 (C), 151.5 (C), 151.8 (C), 152.0 (C), 152.5 (C), 154.3 (C), 154.4 (CH), 154.5 (C), 158.4 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2934 (w), 2836 (w), 2568 (w), 2248 (w), 1594 (s), 1563 (m), 1494 (m), 1460 (s), 1410 (m), 1382 (w), 1366 (m), 1332 (m), 1287 (s), 1275 (m), 1224 (m), 1181 (w), 1130 (w), 1094 (s), 1080 (s), 1010 (m), 904 (m), 828 (w), 800 (m), 725 (s), 692 (w), 645 (w), 580 (w), 532 (m); GC-MS (EI, 70 eV): *m/z* (%): 462 (M^+, 100), 447 (54), 431 (23), 415 (11), 401 (15), 387 (12), 331 (6), 255 (8), 224 (24), 194 (20), 165 (15), 151 (20), 121 (15), 103 (15), 95 (21), 88 (10), 81 (3), 75 (3); HRMS (ESI) calcd for $C_{26}H_{27}N_2O_6$ $[M+H]^+$: 463.18636 found 463.18707.

5,7-Bis(4-(trifluoromethyl)phenyl)-1,6-naphthyridine (11g):



Starting with **7** (0.1 g, 0.5 mmol), **10g** (0.236 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11g** was isolated as white solid (0.135 g, 64%); mp 180 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.38 (dd, *J* = 8.50 Hz, *J* = 4.16 Hz, 1H, ArH), 7.64 (d, *J* = 8.12 Hz, 2H, ArH), 7.73-7.81 (m, 4H, ArH), 8.22-8.27 (m, 3H, ArH), 8.31 (s, 1H, ArH), 9.01 (d, *J* = 2.27 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 118.2 (CH), 121.2 (C), 122.7 (CH), 124.0 (CF_3, q, $^1J_{CF}$ = 272.37 Hz), 124.2 (CF_3, q, $^1J_{CF}$ = 271.91 Hz), 125.6 (2CH, q, $^3J_{CF}$ = 4.12 Hz), 125.8 (2CH, q, $^3J_{CF}$ = 3.66 Hz), 127.4 (2CH), 130.5 (2CH), 131.0 (C, q, $^2J_{CF}$ = 32.50 Hz), 131.3 (C, q, $^2J_{CF}$ = 32.96 Hz), 135.0 (CH), 141.8 (2C, q, $^5J_{CF}$ = 1.83 Hz), 152.2 (2C), 154.9 (CH), 159.7 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.59 ($ArCF_3$), -62.64 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3045 (w), 1931 (w), 1606 (m), 1566 (m), 1519 (w), 1422 (w), 1372 (w), 1320 (s), 1312 (s), 1207 (w), 1156 (m), 1102 (s), 1065 (s), 1013 (m), 985 (w), 885 (w), 843 (s), 820 (w), 770 (m), 686 (w), 647 (w), 626 (w), 619 (m), 589 (m), 527 (w); GC-MS (EI, 70 eV): *m/z* (%): 418 (M^+, 100), 417 (76), 350 (10), 279 (4), 199 (4), 175 (5), 150 (4), 125 (3), 99 (1), 75 (4), 51 (2), 39 (1); HRMS (ESI) calcd for $C_{22}H_{13}F_6N_2$ $[M+H]^+$: 419.09774 found 419.0984.

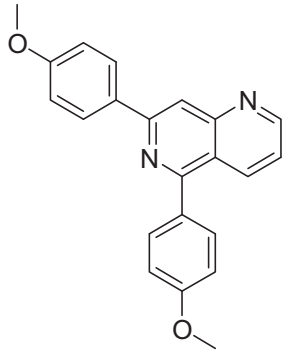
5,7-Bis(3-fluorophenyl)-1,6-naphthyridine (11h):



Starting with **7** (0.1 g, 0.5 mmol), **10h** (0.174 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11h** was isolated as white solid (0.119 g, 74%); mp 162–164 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 6.98-7.04 (m, 1H, ArH), 7.09-7.17 (m, 1H, ArH), 7.32-7.45 (m, 5H, ArH), 7.85-7.89 (m, 2H, ArH), 8.22 (s, 1H, ArH), 8.27-8.31 (m, 1H, ArH), 8.97 (dd, J = 4.16 Hz, J = 1.51 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 114.2 (CH, d, $^2J_{CF}$ = 22.89 Hz), 116.0 (CH, d, $^2J_{CF}$ = 21.06 Hz), 116.2 (CH, d, $^2J_{CF}$ = 21.06 Hz), 117.2 (CH, d, $^2J_{CF}$ = 22.43 Hz), 117.4 (CH), 120.9 (C), 122.3 (CH), 122.6 (CH, d, $^4J_{CF}$ = 2.75 Hz), 125.9 (CH, d, $^4J_{CF}$ = 2.75 Hz), 130.1 (CH, d, $^3J_{CF}$ = 8.24 Hz), 130.3 (CH, d, $^3J_{CF}$ = 8.24 Hz), 135.3 (CH), 140.6 (C, d, $^3J_{CF}$ = 7.32 Hz), 140.9 (C, d, $^3J_{CF}$ = 7.32 Hz), 152.3 (C), 152.4 (C, d, $^4J_{CF}$ = 2.29 Hz), 154.8 (CH), 159.5 (C, d, $^4J_{CF}$ = 2.29 Hz), 162.8 (C, d, $^1J_{CF}$ = 247.19 Hz), 163.4 (C, d, $^1J_{CF}$ = 245.36 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -112.32 (ArF), -112.64 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3071 (w), 2975 (w), 1926 (w), 1852 (w), 1765 (w), 1589 (m), 1561 (s), 1488 (m), 1442 (w), 1368 (m), 1287 (w), 1217 (m), 1163 (w), 1138 (m), 1038 (w), 968 (w), 940 (m), 882 (w), 872 (s), 812 (m), 773 (s), 717 (m), 678 (m), 661 (m), 622 (w), 580 (w), 567 (w); GC-MS (EI, 70 eV): *m/z* (%): 318 (M^+, 95), 317 (100), 290 (6), 269 (4), 221 (7), 195 (4), 125 (4), 112 (1), 95 (4), 75 (7), 51 (1), 39 (1); HRMS (ESI) calcd for $C_{20}H_{13}F_2N_2$ $[M+H]^+$: 319.10413 found 319.10403.

5,7-Bis(4-methoxyphenyl)-1,6-naphthyridine (11i):

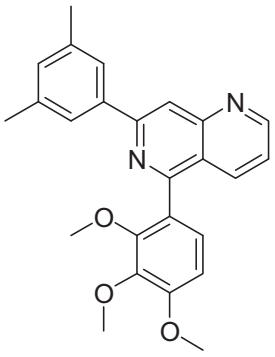
Starting with **7** (0.1 g, 0.5 mmol), **10i** (0.19 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **11i** was isolated as light yellow solid (0.126 g, 73%); mp 125–127 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.79 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.95 (d, ^3J = 8.88 Hz, 2H, ArH), 7.01 (d, ^3J = 8.88 Hz, 2H, ArH), 7.29 (dd, J = 8.50 Hz, J = 4.16 Hz, 1H, ArH), 7.66 (d, ^3J = 8.88 Hz, 2H, ArH), 8.13-8.16 (m, 3H, ArH), 8.34-8.37 (m,



1H, ArH), 8.93 (dd, J = 3.97 Hz, J = 1.32 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.3 (OCH_3), 55.4 (OCH_3), 113.9 (2CH), 114.2 (2CH), 115.0 (CH), 120.4 (C), 121.3 (CH), 128.6 (2CH), 131.4 (C), 131.6 (2CH), 135.9 (CH), 152.6 (2C), 153.5 (2C), 154.3 (CH), 160.4 (C), 160.6 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 2959 (w), 2916 (m), 2838 (w), 2551 (w), 2038 (w), 1727 (w), 1600 (s), 1579 (w), 1561 (w), 1511 (s), 1465 (m), 1388 (w), 1368 (m), 1304 (w), 1244 (s), 1195 (w), 1173 (s), 1113 (w), 1053 (w), 1023 (s), 969 (m), 879 (w), 826 (s), 787 (m), 765 (m), 714 (w), 657 (w), 617 (w), 604 (w), 581 (m), 552 (m), 529 (m); GC-MS (EI, 70 eV): *m/z* (%): 342 (M^+, 100), 341 (61), 311 (21), 299 (15), 255 (16), 229 (8), 203 (1), 171 (6), 134 (6), 114 (5), 101 (2), 89 (2), 76 (2), 63 (3), 39 (2); HRMS (ESI) calcd for $C_{22}H_{19}N_2O_2$ $[M+H]^+$: 343.1441 found 343.1441.

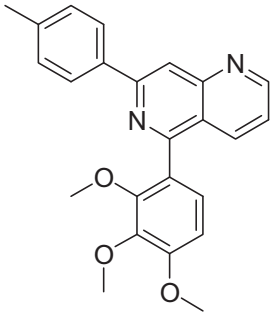
General procedure for the synthesis of 13a-d: A 1,4-dioxane solution (8 mL) of **9e,f** (1.0 equiv.), arylboronic acid **12** (1.3 equiv.), 2M K_2CO_3 (1 mL), and $Pd(PPh_3)_4$ (5 mol%) was heated at 110 °C for 8 h in a pressure tube. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution *n*-heptane/ethyl acetate).

7-(3,5-Dimethylphenyl)-5-(2,3,4-trimethoxyphenyl)-1,6-naphthyridine (13a):



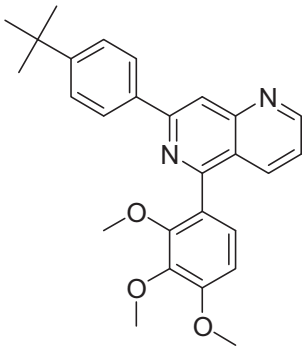
Starting with **9e** (0.1 g, 0.3 mmol), **12a** (0.058 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **13a** was isolated as light yellow solid (0.108 g, 89%); mp 141–143 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.34 (s, 6H, $2CH_3$), 3.52 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.80 (d, *J* = 8.50 Hz, 1H, ArH), 6.99 (s, 1H, ArH), 7.18 (d, *J* = 8.50 Hz, 1H, ArH), 7.31 (dd, *J* = 8.50 Hz, *J* = 4.16 Hz, 1H, ArH), 7.76 (s, 2H, ArH), 8.02-8.05 (m, 1H, ArH), 8.24 (s, 1H, ArH), 8.96 (dd, *J* = 4.16 Hz, *J* = 1.70 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 21.5 ($2CH_3$), 56.2 (OCH_3), 61.1 (OCH_3), 61.6 (OCH_3), 107.8 (CH), 117.1 (CH), 121.6 (CH), 121.9 (C), 125.2 (2CH), 125.9 (C), 126.1 (CH), 130.7 (CH), 136.5 (CH), 138.3 (2C), 139.1 (C), 142.1 (C), 151.7 (C), 151.8 (C), 154.4 (CH), 154.5 (C), 154.6 (C), 158.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2916 (w), 2839 (w), 1598 (m), 1562 (m), 1494 (w), 1460 (m), 1382 (w), 1366 (m), 1335 (w), 1279 (m), 1225 (m), 1164 (w), 1131 (w), 1094 (s), 1047 (w), 1034 (m), 1015 (w), 980 (m), 941 (w), 912 (w), 875 (m), 850 (m), 796 (w), 771 (m), 694 (w), 674 (m), 606 (w), 587 (w), 568 (w), 540 (w), 534 (w); GC-MS (EI, 70 eV): *m/z* (%): 400 (M^+, 74), 399 (60), 385 (100), 383 (36), 353 (23), 339 (25), 283 (8), 255 (15), 235 (23), 192 (9), 163 (5), 134 (23), 121 (10), 88 (2), 77 (3), 39 (1); HRMS (ESI) calcd for $C_{25}H_{25}N_2O_3$ $[M+H]^+$: 401.18597 found 401.18604.

7-p-Tolyl-5-(2,3,4-trimethoxyphenyl)-1,6-naphthyridine (13b):



Starting with **9e** (0.1 g, 0.3 mmol), **12b** (0.053 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **13b** was isolated as light brown solid (0.109 g, 64%); mp 137–139 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.34 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 6.77 (d, *J* = 8.69 Hz, 1H, ArH), 7.15 (d, *J* = 8.50 Hz, 1H, ArH), 7.23 (d, *J* = 7.93 Hz, 2H, ArH), 7.29 (dd, *J* = 8.50 Hz, *J* = 4.34 Hz, 1H, ArH), 8.01-8.07 (m, 3H, ArH), 8.23 (s, 1H, ArH), 8.95 (dd, *J* = 4.16 Hz, *J* = 1.70 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 21.3 (CH_3), 56.2 (OCH_3), 61.2 (OCH_3), 61.7 (OCH_3), 107.7 (CH), 116.4 (CH), 121.5 (CH), 121.9 (C), 125.9 (C), 126.0 (CH), 127.2 (2CH), 129.5 (2CH), 136.3 (C), 136.5 (CH), 139.0 (C), 142.2 (C), 151.7 (C), 151.9 (C), 154.1 (C), 154.5 (CH), 154.6 (C), 158.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 3016 (w), 2970 (w), 2839 (w), 1597 (m), 1513 (w), 1465 (m), 1408 (m), 1330 (w), 1291 (m), 1234 (m), 1129 (w), 1093 (s), 1053 (m), 1025 (w), 1012 (m), 986 (m), 927 (w), 871 (m), 819 (s), 743 (w), 686 (m), 642 (w), 564 (w), 557 (w), 531 (w); GC-MS (EI, 70 eV): *m/z* (%): 386 (M^+, 73), 385 (55), 371 (100), 355 (27), 339 (18), 325 (24), 295 (7), 269 (14), 221 (25), 186 (11), 142 (13), 128 (28), 91 (3), 75 (1), 51 (2), 39 (3); HRMS (ESI) calcd for $C_{24}H_{23}N_2O_3$ $[M+H]^+$: 387.17032 found 387.17041.

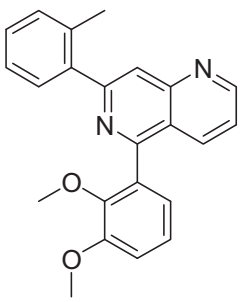
7-(4-tert-Butylphenyl)-5-(2,3,4-trimethoxyphenyl)-1,6-naphthyridine (13c):



Starting with **9e** (0.1 g, 0.3 mmol), **12c** (0.069 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **13c** was isolated as light yellow heavy oil (0.07 g, 54%). ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 1.29 (s, 9H, $3CH_3$), 3.53 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 6.77 (d, *J* = 8.67 Hz, 1H, ArH), 7.15 (d, *J* = 8.51 Hz, 1H, ArH), 7.27-7.32 (m, 1H, ArH), 7.45 (d, *J* = 8.51 Hz, 2H, ArH), 8.01-8.05 (m, 1H, ArH), 8.09 (d, *J* = 8.36 Hz, 2H, ArH), 8.25 (s, 1H, ArH), 8.95 (dd, *J* = 4.26 Hz, *J* = 1.73 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 31.3 ($3CH_3$), 34.7 (C), 56.2 (OCH_3), 61.1 (OCH_3), 61.7 (OCH_3), 107.7 (CH),

116.4 (CH), 121.5 (CH), 121.8 (C), 125.8 (2CH), 125.9 (C), 126.0 (CH), 127.0 (2CH), 136.2 (C), 136.5 (CH), 142.1 (C), 151.7 (C), 151.8 (C), 152.2 (C), 154.1 (C), 154.4 (CH), 154.6 (C), 158.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3053 (w), 2958 (m), 2866 (w), 1737 (w), 1601 (s), 1564 (m), 1513 (w), 1497 (m), 1462 (s), 1409 (m), 1366 (m), 1332 (w), 1270 (m), 1233 (m), 1178 (w), 1130 (w), 1094 (s), 1021 (w), 982 (m), 897 (w), 840 (m), 815 (w), 747 (w), 735 (w), 692 (m), 623 (w), 605 (w), 542 (w); GC-MS (EI, 70 eV): m/z (%): 428 (M^+, 62), 413 (100), 397 (25), 367 (20), 311 (12), 263 (8), 207 (19), 178 (12), 156 (10), 128 (29), 114 (22), 96 (4), 57 (13), 41 (13), 29 (6); HRMS (ESI) calcd for $C_{27}H_{29}N_2O_3$ $[M+H]^+$: 429.21727 found 429.21749.

5-(2,3-Dimethoxyphenyl)-7-o-tolyl-1,6-naphthyridine (13d):

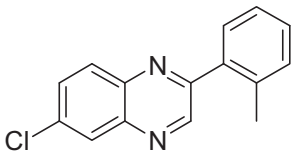


Starting with **9f** (0.1 g, 0.3 mmol), **12d** (0.053 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **13d** was isolated as light yellow heavy oil (0.06 g, 47%). ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 2.40 (s, 3H, CH_3), 3.43 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.98-7.04 (m, 2H, ArH), 7.13 (d, *J* = 7.88 Hz, 1H, ArH), 7.22-7.25 (m, 3H, ArH), 7.34 (dd, *J* = 8.51 Hz, *J* = 4.26 Hz, 1H, ArH), 7.49-7.53 (m, 1H, ArH), 7.97 (s, 1H, ArH), 8.05-8.09 (m, 1H, ArH), 8.98 (dd, *J* = 4.26 Hz, *J* = 1.73 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 20.6 (CH_3), 55.9 (OCH_3), 61.3 (OCH_3), 113.1 (CH), 120.9 (CH), 121.4 (C), 122.0 (CH), 123.2 (CH), 124.5 (CH), 125.9 (CH), 128.4 (CH), 130.1 (CH), 130.8 (CH), 133.1 (C), 136.2 (C), 136.7 (CH), 140.1 (C), 146.9 (C), 150.9 (C), 152.7 (C), 154.6 (CH), 156.8 (C), 158.7 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2929 (m), 2835 (w), 1601 (m), 1567 (s), 1463 (s), 1425 (m), 1366 (m), 1300 (w), 1260 (m), 1230 (w), 1205 (w), 1132 (w), 1075 (s), 1026 (w), 1002 (w), 984 (m), 904 (w), 884 (m), 791 (w), 766 (s), 728 (s), 703 (w), 677 (w), 652 (w), 613 (w), 587 (m), 572 (w); GC-MS (EI, 70 eV): *m/z* (%): 356 (M^+, 98), 355 (100), 339 (18), 325 (21), 309 (17), 269 (9), 242 (13), 219 (16), 154 (11), 140 (19), 121 (5), 102 (2), 99 (1), 89 (3), 75 (2), 63 (2), 51 (2), 39 (2); HRMS (ESI) calcd for $C_{23}H_{21}N_2O_2$ $[M+H]^+$: 357.161 found 357.16088.

6.4 Regioselective Palladium-Catalysed Cross-Coupling Reactions of 2,6-dichloroquinoxaline.

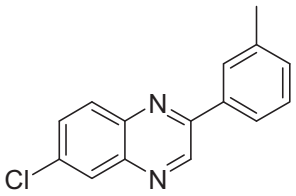
General procedure for synthesis of 16a-t: A THF solution (8 mL) of **14** (1.0 mmol), arylboronic acid **15** (1.3 equiv.), K_3PO_4 (2 equiv.), and $Pd(PPh_3)_4$ (5 mol%) was heated at 90 °C for 8 h. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution n-heptane/ethyl acetate).

6-Chloro-2-o-tolylquinoxaline (16a):



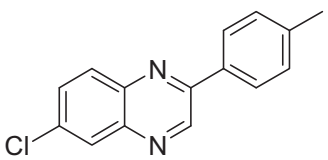
Starting with **14** (0.1 g, 0.5 mmol), **15a** (0.088 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16a** was isolated as white solid (0.098 g, 77%); mp 121-123 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.38 (s, 3H, CH_3), 7.25-7.36 (m, 3H, ArH), 7.44-7.48 (m, 1H, ArH), 7.65 (dd, *J* = 9.07 Hz, *J* = 2.26 Hz, 1H, ArH), 7.98-8.06 (m, 2H, ArH), 8.92 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 20.4 (CH_3), 126.4 (CH), 128.1 (CH), 129.6 (CH), 129.9 (CH), 130.8 (CH), 131.2 (CH), 131.3 (CH), 135.5 (C), 136.6 (C), 136.7 (C), 140.5 (C), 141.3 (C), 146.7 (CH), 155.1 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 3043 (w), 2986 (w), 2930 (w), 2746 (w), 1606 (m), 1568 (w), 1539 (m), 1445 (w), 1417 (w), 1385 (w), 1335 (w), 1268 (w), 1175 (m), 1124 (w), 1065 (m), 1037 (s), 960 (s), 936 (w), 901 (s), 870 (m), 827 (s), 785 (m), 754 (s), 726 (s), 701 (m), 679 (w), 639 (w), 579 (s), 553 (m), 540 (w), 528 (w); GC-MS (EI, 70 eV): m/z (%): 254 (M^+, 35), 253 (100), 218 (12), 190 (3), 165 (4), 127 (3), 116 (8), 110 (2), 100 (1), 90 (4), 75 (7), 63 (3), 39 (1); HRMS (EI) calcd for $C_{15}H_{12}ClN_2$ $[M+H]^+$: 255.06835 found 255.06869.

6-Chloro-2-m-tolylquinoxaline (16b):



Starting with **14** (0.1 g, 0.5 mmol), **15b** (0.088 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16b** was isolated as white solid (0.085 g, 67%); mp 125-127 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 7.26 (d, ^3J = 7.55 Hz, 1H, ArH), 7.37 (t, J = 7.74 Hz, 1H, ArH), 7.63 (dd, J = 8.88 Hz, J = 2.27 Hz, 1H, ArH), 7.87 (d, ^3J = 7.54 Hz, 1H, ArH), 7.92 (s, 1H, ArH), 7.98-8.02 (m, 2H, ArH), 9.22 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 20.5 (CH_3), 123.6 (CH), 127.0 (CH), 127.1 (CH), 128.1 (CH), 129.8 (CH), 130.22 (CH), 130.23 (CH), 134.1 (C), 135.3 (C), 138.0 (C), 139.8 (C), 140.8 (C), 143.3 (CH), 151.1 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3024 (w), 2960 (w), 2856 (w), 1952 (w), 1841 (w), 1711 (w), 1606 (w), 1588 (m), 1537 (m), 1494 (w), 1470 (w), 1453 (m), 1330 (w), 1314 (m), 1224 (w), 1169 (m), 1135 (m), 1060 (w), 996 (w), 962 (s), 923 (w), 912 (s), 869 (m), 831 (s), 789 (s), 738 (w), 692 (s), 673 (m), 643 (w), 617 (w), 585 (s), 547 (w), 529 (w); GC-MS (EI, 70 eV): m/z (%): 254 (M^+, 100), 239 (4), 227 (18), 219 (5), 192 (10), 165 (11), 127 (4), 110 (7), 91 (4), 75 (12), 51 (2), 39 (2); HRMS (EI) calcd for $C_{15}H_{11}ClN_2$ [M^+]: 254.06053 found 254.060317.

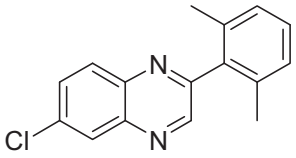
6-Chloro-2-p-tolylquinoxaline (16c):



Starting with **14** (0.1 g, 0.5 mmol), **15c** (0.088 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16c** was isolated as white solid (0.096 g, 75%); mp 136 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.38 (s, 3H, CH_3), 7.29 (d, ^3J = 7.93 Hz, 2H, ArH), 7.63 (dd, J = 9.06 Hz, J = 2.08 Hz, 1H, ArH), 7.97-8.02 (m, 4H, ArH), 9.22 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 (CH_3), 127.4 (2CH), 128.0 (CH), 129.9 (2CH), 130.7 (CH), 131.2 (CH), 133.52 (C), 134.94 (C), 140.7 (C), 140.8 (C), 141.7 (C), 144.1 (CH), 151.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2916 (w), 2854 (w), 2722 (w), 1607 (m), 1576 (w), 1536 (m), 1476 (m), 1413 (m), 1359 (w), 1315 (m), 1300 (w), 1260 (w), 1170 (s), 1136 (w), 1125 (w), 1064 (m), 1044 (m), 1018 (w), 958 (m), 918 (m), 890 (m), 813 (s), 778 (w), 712 (m), 642 (w), 629 (w), 569 (s), 544 (w); GC-MS (EI, 70 eV): m/z (%): 254 (M^+, 100), 227 (20), 192 (10), 165 (9), 116 (11), 100 (2) 89 (6), 75

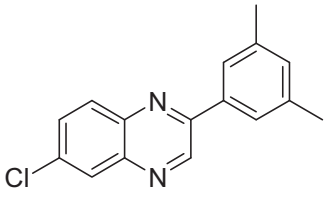
(10), 63 (3), 50 (2), 39 (1); HRMS (EI) calcd for $C_{15}H_{11}ClN_2$ [M^+]: 254.06053 found 254.060639.

6-Chloro-2-(2,6-dimethylphenyl)quinoxaline (16d):



Starting with **14** (0.1 g, 0.5 mmol), **15d** (0.097 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16d** was isolated as brownish heavy oil (0.050 g, 37%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.00 (s, 6H, $2CH_3$), 7.07-7.10 (m, 2H, ArH), 7.17-7.23 (m, 1H, ArH), 7.65 (dd, *J* = 8.88 Hz, *J* = 2.27 Hz, 1H, ArH), 7.98-8.08 (m, 2H, ArH), 8.72 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 20.4 ($2CH_3$), 128.1 (2CH), 128.3 (CH), 129.1 (CH), 130.8 (CH), 131.3 (CH), 135.7 (C), 136.3 (2C), 136.7 (C), 140.9 (C), 141.5 (C), 147.2 (CH), 155.7 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 3020 (w), 2919 (w), 2855 (w), 2735 (w), 2516 (w), 2392 (w), 2230 (w), 1932 (w), 1865 (w), 1748 (w), 1667 (w), 1602 (m), 1546 (m), 1505 (w), 1474 (s), 1451 (w), 1377 (w), 1293 (m), 1199 (w), 1169 (s), 1131 (w), 1091 (w), 1062 (m), 1042 (s), 1029 (w), 990 (w), 960 (m), 914 (w), 899 (s), 877 (w), 829 (s), 786 (w), 768 (s), 731 (m), 673 (m), 626 (m), 584 (s), 560 (w), 541 (m); GC-MS (EI, 70 eV): m/z (%): 268 (M^+, 39), 267 (100), 253 (6), 232 (6), 190 (2), 133 (3), 116 (3), 103 (6), 89 (2), 77 (4), 63 (2), 39 (1); HRMS (EI) calcd for $C_{16}H_{14}ClN_2$ [M+H]$^+$: 269.084 found 269.08432.

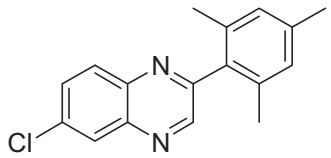
6-Chloro-2-(3,5-dimethylphenyl)quinoxaline (16e):



Starting with **14** (0.1 g, 0.5 mmol), **15e** (0.097 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16e** was isolated as white solid (0.12 g, 90%); mp 178-179 ^{o}C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.35 (s, 6H, $2CH_3$), 7.06 (s, 1H, ArH), 7.59 (dd, *J* = 8.88 Hz, *J* = 2.27 Hz, 1H, ArH), 7.66 (s, 2H, ArH), 7.95-7.99 (m, 2H, ArH), 9.17 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 ($2CH_3$), 125.3 (2CH), 128.0 (CH), 130.7 (CH), 131.2 (CH), 132.1 (CH), 134.9 (C), 136.3 (C), 138.8 (2C), 140.8 (C), 141.7 (C), 144.4 (CH), 152.2 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3042 (w), 3010 (w), 2916 (w), 2858 (w), 2735 (w), 1936 (w), 1880 (w), 1798 (w), 1755 (w), 1606 (m), 1573 (w), 1536 (m), 1494 (w), 1453 (w),

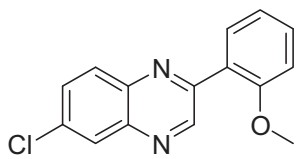
1416 (w), 1398 (w), 1371 (w), 1312 (m), 1258 (w), 1172 (s), 1119 (w), 1088 (m), 997 (m), 966 (m), 948 (w), 867 (m), 844 (w), 828 (s), 782 (m), 721 (w), 706 (s), 674 (m), 626 (m), 590 (m), 550 (w), 542 (m); GC-MS (EI, 70 eV): m/z (%): 268 (M^+, 100), 241 (13), 226 (4), 206 (4), 190 (6), 134 (3), 116 (13), 100 (2), 89 (2), 75 (8), 50 (1), 39 (1); HRMS (EI) calcd for $C_{16}H_{13}ClN_2$ [M^+]: 268.07618 found 268.076349.

6-Chloro-2-(2,4,6-trimethylphenyl)quinoxaline (16f):



Starting with **14** (0.12 g, 0.6 mmol), **15f** (0.165 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.035 g, 0.05 equiv.), K_3PO_4 (0.254 g, 2 equiv.), THF (4 mL), **16f** was isolated as yellowish solid (0.163 g, 96%); mp 100 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.97 (s, 6H, $2CH_3$), 2.25 (s, 3H, CH_3), 6.90 (s, 2H, ArH), 7.62 (dd, *J* = 8.88 Hz, *J* = 2.27 Hz, 1H, ArH), 7.96-8.06 (m, 2H, ArH), 8.70 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 19.2 ($2CH_3$), 20.1 (CH_3), 127.2 (CH), 127.8 (2CH), 129.7 (CH), 130.1 (CH), 132.9 (C), 134.5 (C), 135.1 (2C), 137.8 (C), 139.9 (C), 140.3 (C), 146.4 (CH), 154.8 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 3042 (m), 2964 (w), 2916 (m), 2854 (w), 1818 (w), 1727 (w), 1610 (m), 1567 (w), 1539 (m), 1470 (w), 1446 (m), 1417 (w), 1373 (m), 1330 (w), 1317 (w), 1295 (m), 1266 (w), 1222 (w), 1163 (m), 1125 (m), 1042 (m), 978 (w), 964 (m), 911 (w), 892 (s), 846 (s), 828 (s), 788 (s), 739 (w), 688 (m), 634 (w), 588 (m), 572 (m), 543 (m), 530 (w); GC-MS (EI, 70 eV): m/z (%): 282 (M^+, 40), 281 (100), 267 (9), 246 (4), 204 (1), 144 (2), 128 (2), 115 (5), 100 (1), 75 (4), 50 (1), 39 (1); HRMS (ESI) calcd for $C_{17}H_{16}ClN_2$ [M+H]$^+$: 283.09869 found 283.10003.

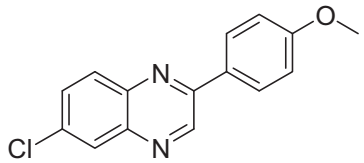
6-Chloro-2-(2-methoxyphenyl)quinoxaline (16g):



Starting with **14** (0.1 g, 0.5 mmol), **15g** (0.099 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16g** was isolated as white solid (0.097 g, 72%); mp 143 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.83 (s, 3H, OCH_3), 6.98 (d, ^3J = 8.31 Hz, 1H, ArH), 7.08 (dt, *J* = 7.55, *J* = 0.94 Hz, 1H, ArH), 7.38-7.44 (m, 1H, ArH), 7.61 (dd, *J* = 8.88 Hz, *J* = 2.46 Hz, 1H, ArH), 7.81 (dd, *J* = 7.55 Hz, *J* = 1.70 Hz, 1H, ArH), 7.98-8.03 (m, 2H, ArH), 9.27 (s, 1H, ArH); ^{13}C NMR (75.46 MHz,

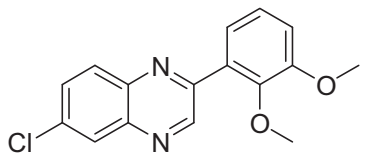
$CDCl_3$), δ = 54.6 (OCH_3), 110.4 (CH), 120.5 (CH), 125.1 (C), 126.9 (CH), 129.7 (2CH), 130.5 (CH), 130.7 (CH), 133.9 (C), 140.2 (C), 140.3 (C), 147.1 (CH), 151.3 (C), 156.4 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 2973 (w), 2838 (w), 1939 (w), 1754 (w), 1600 (s), 1544 (w), 1493 (m), 1459 (s), 1392 (w), 1296 (w), 1239 (s), 1173 (m), 1117 (m), 1060 (s), 1020 (m), 962 (m), 930 (m), 901 (m), 876 (m), 834 (s), 777 (w), 741 (s), 702 (m), 685 (w), 641 (m), 611 (w), 583 (m), 571 (w), 557 (w), 541 (w); GC-MS (EI, 70 eV): m/z (%): 270 (M^+, 100), 253 (55), 241 (48), 213 (17), 178 (14), 165 (27), 151 (8), 118 (11), 110 (14), 103 (9), 90 (11), 75 (24), 63 (11), 39 (4); HRMS (ESI) calcd for $C_{15}H_{12}ClN_2O$ $[M+H]^+$: 271.06327 found 271.06367.

6-Chloro-2-(4-methoxyphenyl)quinoxaline (16h):



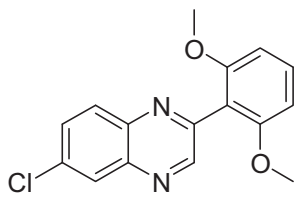
Starting with **14** (0.1 g, 0.5 mmol), **15h** (0.099 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16h** was isolated as yellowish white solid (0.086 g, 63%); mp 124-146 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 6.98 (d, ^3J = 9.07 Hz, 2H, ArH), 7.58 (dd, J = 9.07 Hz, J = 2.46 Hz, 1H, ArH), 7.92-7.98 (m, 2H, ArH), 8.06 (d, ^3J = 8.88 Hz, 2H, ArH), 9.18 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.4 (OCH_3), 114.6 (2CH), 128.0 (CH), 128.8 (C), 128.9 (2CH), 130.6 (CH), 131.1 (CH), 134.6 (C), 140.8 (C), 141.4 (C), 143.8 (CH), 151.5 (C), 161.6 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3048 (m), 3015 (w), 2930 (w), 2894 (w), 2039 (w), 1915 (w), 1882 (w), 1651 (w), 1604 (s), 1580 (w), 1519 (m), 1463 (w), 1398 (w), 1315 (s), 1269 (w), 1250 (s), 1183 (w), 1167 (s), 1114 (m), 1070 (w), 1024 (s), 955 (m), 921 (m), 898 (m), 823 (s), 783 (m), 727 (w), 689 (m), 633 (m), 570 (s), 545 (w); GC-MS (EI, 70 eV): m/z (%): 270 (M^+, 100), 255 (17), 243 (10), 227 (8), 200 (7), 192 (4), 133 (11), 110 (5), 90 (6), 75 (9), 63 (5), 39 (1); HRMS (EI) calcd for $C_{15}H_{11}ClN_2O$ [M^+]: 270.05544 found 270.055440.

6-Chloro-2-(2,3-dimethoxyphenyl)quinoxaline (16i):



Starting with **14** (0.12 g, 0.6 mmol), **15i** (0.142 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.035 g, 0.05 equiv.), K_3PO_4 (0.254 g, 2 equiv.), THF (4 mL), **16i** was isolated as white solid (0.118 g, 65%); mp 124 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.69 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 7.00 (dd, *J* = 8.12 Hz, 1.51 Hz, 1H, ArH), 7.15 (t, *J* = 7.93, 1H, ArH), 7.38 (dd, *J* = 7.74 Hz, *J* = 1.51 Hz, 1H, ArH), 7.62 (dd, *J* = 8.88 Hz, *J* = 2.27 Hz, 1H, ArH), 7.98-8.04 (m, 2H, ArH), 9.27 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 56.0 (OCH_3), 61.4 (OCH_3), 114.3 (CH), 122.7 (CH), 124.8 (CH), 128.0 (CH), 130.8 (CH), 130.9 (CH), 131.2 (C), 135.3 (C), 141.2 (C), 141.4 (C), 147.6 (C), 147.8 (CH), 151.9 (C), 153.1 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2996 (w), 2951 (m), 2840 (m), 1582 (m), 1542 (m), 1484 (m), 1466 (s), 1428 (m), 1397 (w), 1320 (m), 1266 (s), 1234 (m), 1185 (w), 1175 (m), 1138 (w), 1110 (m), 1086 (m), 1041 (s), 994 (s), 934 (m), 918 (m), 850 (m), 834 (s), 811 (w), 783 (m), 765 (m), 741 (s), 690 (m), 679 (m), 635 (w), 623 (m), 597 (s), 565 (w), 534 (m); GC-MS (EI, 70 eV): m/z (%): 300 (M^+, 100), 285 (47), 283 (91), 271 (34), 257 (23), 242 (13), 213 (11), 179 (18), 165 (26), 142 (6), 120 (7), 110 (13), 100 (7), 92 (5), 75 (20), 63 (6), 50 (6), 39 (2); HRMS (EI) calcd for $C_{16}H_{13}ClN_2O_2$ [M^+]: 300.06601 found 300.065686.

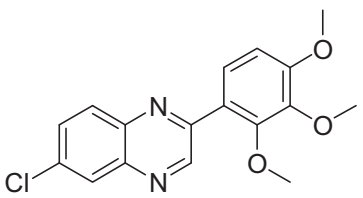
6-Chloro-2-(2,6-dimethoxyphenyl)quinoxaline (16j):



Starting with **14** (0.12 g, 0.5 mmol), **15j** (0.142 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.035 g, 0.05 equiv.), K_3PO_4 (0.254 g, 2 equiv.), THF (4 mL), **16j** was isolated as yellow solid (0.175 g, 97%); mp 135-137 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.78 (s, 6H, 2(OCH_3)), 6.93-6.94 (m, 2H, ArH), 7.40 (d, *J* = 2.83 Hz, 1H, ArH), 7.61 (dd, *J* = 8.88 Hz, *J* = 2.27 Hz, 1H, ArH), 7.98-8.02 (m, 2H, ArH), 9.29 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.9 (OCH_3), 56.3 (OCH_3), 113.0 (CH), 115.9 (CH), 117.5 (CH), 126.6 (C), 127.9 (CH), 130.7 (2CH), 135.1 (C), 141.1 (C), 141.3 (C), 148.0 (CH), 151.8 (C), 152.0 (C), 154.3 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 2985 (w), 2831 (w), 1621 (w), 1586 (m), 1538 (m), 1497 (s), 1464 (w), 1425 (m), 1394 (w), 1336 (w), 1304 (s), 1259 (m), 1225 (m), 1208 (m), 1181 (s), 1154 (m), 1060 (m), 1021 (s), 965 (m), 930

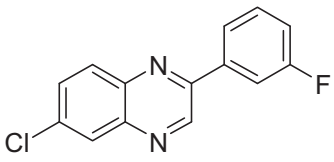
(w), 883 (m), 832 (s), 795 (s), 786 (m), 732 (s), 700 (m), 683 (w), 653 (w), 618 (w), 600 (w), 593 (w), 541 (w), 534 (w); GC-MS (EI, 70 eV): m/z (%): 300 (M^+, 100), 285 (64), 283 (88), 269 (14), 257 (12), 242 (16), 214 (7), 179 (13), 165 (24), 148 (13), 120 (7), 110 (11), 100 (5), 75 (14), 63 (5), 50 (4), 39 (1); HRMS (EI) calcd for $C_{16}H_{13}ClN_2O_2$ [M^+]: 300.06601 found 300.065903.

6-Chloro-2-(2,3,4-trimethoxyphenyl)quinoxaline (16k):



Starting with **14** (0.12 g, 0.6 mmol), **15k** (0.165 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.035 g, 0.05 equiv.), K_3PO_4 (0.254 g, 2 equiv.), THF (4 mL), **16k** was isolated as yellowish solid (0.105 g, 53%); mp 106-108 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 3.79 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.78 (d, ^3J = 8.69 Hz, 1H, ArH), 7.55-7.61 (m, 2H, ArH), 7.94-8.00 (m, 2H, ArH), 9.24 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 56.2 (OCH_3), 61.0 (OCH_3), 61.6 (OCH_3), 108.2 (CH), 123.8 (C), 125.9 (CH), 128.0 (CH), 130.6 (CH), 130.8 (CH), 134.9 (C), 141.1 (C), 141.2 (C), 142.3 (C), 147.6 (CH), 151.7 (C), 152.5 (C), 155.7 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3052 (w), 2943 (m), 2848 (w), 1601 (s), 1542 (m), 1494 (w), 1460 (m), 1433 (w), 1414 (s), 1335 (w), 1309 (m), 1280 (m), 1210 (m), 1210 (m), 1171 (m), 1133 (w), 1106 (s), 1087 (m), 1014 (s), 969 (m), 949 (w), 928 (m), 902 (m), 853 (m), 823 (m), 774 (s), 700 (w), 689 (w), 681 (w), 648 (m), 629 (w), 597 (m), 568 (w), 544 (m); GC-MS (EI, 70 eV): m/z (%): 330 (M^+, 100), 315 (51), 313 (40), 299 (12), 287 (14), 272 (15), 257 (13), 229 (12), 215 (15), 203 (10), 201 (26), 178 (10), 163 (14), 153 (11), 135 (8), 110 (6), 100 (7), 75 (10), 51 (2), 39 (6); HRMS (EI) calcd for $C_{17}H_{15}ClN_2O_3$ [M^+]: 330.07657 found 330.076374.

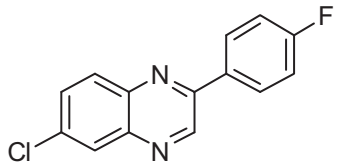
6-Chloro-2-(3-fluorophenyl)quinoxaline (16l):



Starting with **14** (0.1 g, 0.5 mmol), **15l** (0.09 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16l** was isolated as white solid (0.03 g, 23%); mp 172-173 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.13-7.19 (m, 1H, ArH), 7.43-7.50 (m, 1H, ArH), 7.67 (dd, J = 8.88 Hz, J = 2.27 Hz, 1H,

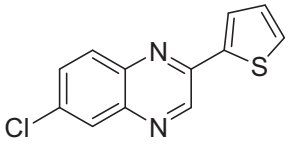
ArH), 7.85-7.89 (m, 2H, ArH), 8.00-8.05 (m, 2H, ArH), 9.23 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 113.5 (CH, d, $^2J_{CF}$ = 23.35 Hz), 116.4 (CH, d, $^2J_{CF}$ = 21.06 Hz), 122.0 (CH, d, $^4J_{CF}$ = 2.75 Hz), 127.1 (CH), 129.8 (CH, d, $^3J_{CF}$ = 8.24 Hz), 129.9 (CH), 130.6 (CH), 134.7 (C), 137.6 (C, d, $^3J_{CF}$ = 7.78 Hz), 139.7 (C), 141.0 (C), 142.8 (CH), 149.5 (C, d, $^4J_{CF}$ = 2.75 Hz), 162.4 (C, d, $^1J_{CF}$ = 247.19 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -111.56 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3087 (w), 3065 (w), 2923 (w), 2850 (w), 1953 (w), 1815 (w), 1704 (w), 1590 (m), 1495 (w), 1435 (m), 1402 (w), 1314 (m), 1203 (m), 1134 (w), 1066 (w), 1050 (w), 975 (s), 939 (w), 865 (s), 831 (s), 789 (s), 695 (s), 670 (s), 616 (w), 596 (m), 549 (w); GC-MS (EI, 70 eV): m/z (%): 258 (M^+, 100), 231 (31), 196 (21), 169 (4), 129 (4), 110 (15), 100 (4), 75 (23), 63 (1), 50 (4); HRMS (EI) calcd for $C_{14}H_8ClFN_2$ [M^+]: 258.03546 found 258.035713.

6-Chloro-2-(4-fluorophenyl)quinoxaline (16m):



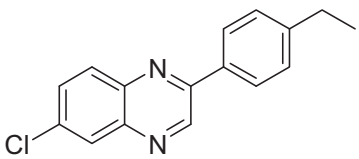
Starting with **14** (0.1 g, 0.5 mmol), **15m** (0.09 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16m** was isolated as yellowish white solid (0.08 g, 62%); mp 165-168 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.13-7.21 (m, 2H, ArH), 7.64 (dd, *J* = 9.07 Hz, *J* = 2.46 Hz, 1H, ArH), 7.96-8.02 (m, 2H, ArH), 8.07-8.14 (m, 2H, ArH), 9.20 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 116.3 (2CH, d, $^2J_{CF}$ = 21.52 Hz), 128.1 (CH), 129.5 (2CH, d, $^3J_{CF}$ = 8.70 Hz), 130.7 (CH), 131.4 (CH), 132.5 (C, d, $^4J_{CF}$ = 3.20 Hz), 135.3 (C), 140.7 (C), 141.7 (C), 143.7 (CH), 150.8 (C), 164.4 (C, d, $^1J_{CF}$ = 251.31 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -110.01 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 3012 (w), 2914 (w), 1600 (s), 1558 (w), 1514 (m), 1478 (m), 1445 (w), 1359 (w), 1305 (m), 1237 (s), 1162 (m), 1105 (w), 1047 (m), 1014 (w), 957 (m), 901 (m), 872 (m), 828 (s), 790 (m), 720 (m), 691 (m), 638 (w), 626 (w), 571 (s); GC-MS (EI, 70 eV): m/z (%): 258 (M^+, 100), 233 (11), 231 (33), 196 (20), 169 (5), 129 (5), 121 (8), 110 (13), 100 (4), 75 (22), 63 (1), 50 (4); HRMS (EI) calcd for $C_{14}H_8ClFN_2$ [M^+]: 258.03546 found 258.035593.

6-Chloro-2-(thiophen-2-yl)quinoxaline (16n):



Starting with **14** (0.1 g, 0.5 mmol), **15n** (0.082 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16n** was isolated as yellow solid (0.056 g, 45%); mp 154-156 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.11-7.14 (m, 1H, ArH), 7.48 (dd, *J* = 5.10 Hz, *J* = 1.13 Hz, 1H, ArH), 7.59 (dd, *J* = 8.88 Hz, *J* = 2.46 Hz, 1H, ArH), 7.77 (dd, *J* = 3.78 Hz, *J* = 1.13 Hz, 1H, ArH), 7.89-7.96 (m, 2H, ArH), 9.13 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 127.2 (CH), 128.1 (CH), 128.6 (CH), 130.2 (CH), 130.3 (CH), 131.4 (CH), 134.8 (C), 140.6 (C), 141.5 (C), 141.8 (C), 142.8 (CH), 147.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3095 (w), 3064 (w), 3011 (w), 2007 (w), 1941 (w), 1887 (w), 1746 (w), 1693 (w), 1593 (m), 1541 (s), 1474 (m), 1433 (w), 1414 (m), 1369 (w), 1311 (m), 1269 (w), 1176 (s), 1131 (m), 1062 (s), 1002 (s), 942 (s), 872 (m), 832 (s), 789 (m), 747 (w), 709 (s), 692 (w), 630 (w), 615 (w), 588 (s), 558 (m); GC-MS (EI, 70 eV): m/z (%): 246 (M^+, 100), 219 (29), 184 (12), 140 (10), 110 (11), 100 (3), 84 (2), 75 (12), 58 (3), 39 (2); HRMS (EI) calcd for $C_{12}H_7ClN_2S$ [M^+]: 246.00130 found 246.001467.

6-Chloro-2-(4-ethylphenyl)quinoxaline (16o):



Starting with **14** (0.1 g, 0.5 mmol), **15o** (0.098 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16o** was isolated as white solid (0.13 g, 96%); mp 104 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.21 (t, ^3J = 7.74 Hz, 3H, CH_3), 2.65 (q, *J* = 7.55 Hz, *J* = 15.12 Hz, 2H, -CH_2-), 7.29 (d, ^3J = 8.50 Hz, 2H, ArH), 7.59 (dd, *J* = 9.07 Hz, *J* = 2.27 Hz, 1H, ArH), 7.94-8.02 (m, 4H, ArH), 9.19 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 15.4 (CH_3), 28.8 (-CH_2-), 127.5 (2CH), 128.1 (CH), 128.8 (2CH), 130.8 (CH), 131.2 (CH), 133.8 (C), 134.9 (C), 140.8 (C), 141.7 (C), 144.1 (CH), 147.1 (C), 151.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 3039 (w), 2955 (m), 2865 (w), 1607 (s), 1537 (s), 1504 (w), 1477 (s), 1445 (w), 1416 (m), 1334 (w), 1313 (s), 1281 (m), 1225 (w), 1173 (s), 1127 (w), 1053 (s), 1014 (m), 957 (s), 922 (m), 998 (s), 871 (m), 825 (s), 805 (w), 782 (w), 750 (w), 720 (m), 689 (m), 660 (w), 641 (w), 628 (m), 582 (s), 569 (m), 540 (m); GC-MS (EI, 70 eV): m/z (%): 268 (M^+, 100), 255 (26), 253 (79), 226

(4), 190 (7), 163 (2), 116 (18), 110 (8), 89 (7), 84 (1), 75 (11), 63 (3), 51 (2), 39 (1); HRMS (EI) calcd for $C_{16}H_{13}ClN_2$ [M^+]: 268.07618 found 268.076421.

2-(4-tert-Butylphenyl)-6-chloroquinoxaline (16p):

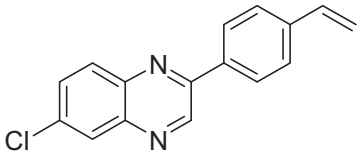
Starting with **14** (0.1 g, 0.5 mmol), **15p** (0.106 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16p** was isolated as white solid (0.115 g, 77%); mp 99-102 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.30 (s, 9H, $3CH_3$), 7.50 (d, ^3J = 8.69 Hz, 2H, ArH), 7.60 (dd, J = 9.07 Hz, J = 2.46 Hz, 1H, ArH), 7.95-8.04 (m, 4H, ArH), 9.21 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 31.2 ($3CH_3$), 34.9 (C), 126.2 (2CH), 127.3 (2CH), 128.1 (CH), 130.8 (CH), 131.2 (CH), 133.6 (C), 134.9 (C), 140.9 (C), 141.7 (C), 144.1 (CH), 151.9 (C), 153.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3093 (w), 3063 (w), 2955 (m), 2867 (w), 1601 (m), 1569 (w), 1537 (m), 1504 (w), 1474 (m), 1455 (w), 1404 (m), 1392 (w), 1360 (m), 1333 (w), 1316 (m), 1302 (w), 1270 (m), 1244 (w), 1200 (m), 1174 (m), 1147 (w), 1111 (w), 1093 (m), 1045 (m), 1012 (m), 975 (w), 957 (s), 920 (s), 897 (s), 879 (m), 841 (s), 826 (s), 799 (w), 739 (m), 694 (w), 672 (m), 660 (w), 640 (w), 623 (w), 577 (s), 539 (m); GC-MS (EI, 70 eV): m/z (%): 296 (M^+, 31), 281 (100), 265 (5), 253 (11), 218 (1), 203 (1), 163 (4), 140 (2), 116 (7), 110 (4), 75 (5), 39 (1); HRMS (EI) calcd for $C_{18}H_{17}ClN_2$ [M^+]: 296.10748 found 296.107517.

6-Chloro-2-(4-(trifluoromethyl)phenyl)quinoxaline (16q):

Starting with **14** (0.1 g, 0.5 mmol), **15q** (0.123 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16q** was isolated as white solid (0.081 g, 52%); mp 128-130 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.67 (dd, J = 8.88 Hz, J = 2.27 Hz, 1H, ArH), 7.75 (d, ^3J = 8.12 Hz, 2H, ArH), 8.01-8.06 (m, 2H, ArH), 8.23 (d, ^3J = 8.12 Hz, 2H, ArH), 9.26 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 123.9 (CF_3, q, $^1J_{CF}$ = 272.35 Hz), 126.1 (2CH, q, $^3J_{CF}$ = 3.30 Hz), 127.8 (2CH), 128.2 (CH), 132.2 (C, q, $^2J_{CF}$ = 32.46 Hz), 130.9 (CH), 131.7 (CH), 136.0 (C), 139.6 (C), 140.7 (C), 142.2 (C), 143.8 (CH), 150.3 (C); ^{19}F NMR

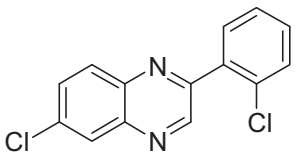
(282.40 MHz, $CDCl_3$): δ = -62.81 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3043 (w), 1928 (w), 1809 (w), 1617 (w), 1604 (m), 1538 (m), 1519 (w), 1478 (m), 1414 (m), 1326 (s), 1260 (w), 1195 (w), 1174 (w), 1157 (m), 1107 (s), 1068 (s), 1015 (m), 960 (m), 927 (m), 899 (m), 850 (m), 832 (s), 800 (w), 774 (w), 745 (w), 678 (w), 651 (m), 636 (w), 624 (w), 598 (s), 568 (m), 544 (w); GC-MS (EI, 70 eV): m/z (%): 308 (M^+, 100), 281 (24), 246 (9), 226 (8), 212 (2), 177 (4), 152 (6), 136 (2), 110 (17), 100 (4), 75 (20), 50 (3); HRMS (EI) calcd for $C_{15}H_8ClF_3N_2$ [M^+]: 308.03226 found 308.031777.

6-Chloro-2-(4-vinylphenyl)quinoxaline (16r):



Starting with **14** (0.1 g, 0.5 mmol), **15r** (0.096 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16r** was isolated as yellow solid (0.04 g, 30%); mp 113-115 °C. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 5.29 (d, *J* = 11.33 Hz, 1H, $-CH_2-$), 5.79 (d, *J* = 17.56 Hz, 1H, $-CH_2-$), 6.65-6.75 (m, 1H, -CH-), 7.49 (d, ^3J = 8.31 Hz, 2H, ArH), 7.61 (dd, *J* = 8.88 Hz, *J* = 2.27 Hz, 1H, ArH), 7.95-8.00 (m, 2H, ArH), 8.06 (d, ^3J = 8.50 Hz, 2H, ArH), 9.21 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 114.6 ($-CH_2-$), 125.9 (2CH), 126.6 (2CH), 127.0 (CH), 129.7 (CH), 130.3 (CH), 134.1 (C), 134.5 (C), 135.1 (CH), 138.6 (C), 139.8 (C), 140.7 (C), 142.9 (CH), 150.3 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3046 (w), 2921 (m), 2851 (w), 1606 (m), 1568 (w), 1536 (m), 1475 (m), 1445 (w), 1411 (m), 1333 (w), 1314 (m), 1210 (w), 1172 (s), 1132 (w), 1047 (m), 987 (w), 957 (m), 899 (m), 844 (w), 825 (s), 782 (w), 731 (m), 675 (w), 605 (w), 572 (s), 544 (w); GC-MS (EI, 70 eV): m/z (%): 266 (M^+, 100), 238 (14), 204 (10), 177 (3), 129 (12), 102 (8), 75 (11), 63 (2), 50 (2); HRMS (EI) calcd for $C_{16}H_{11}ClN_2$ [M^+]: 266.06053 found 266.060883.

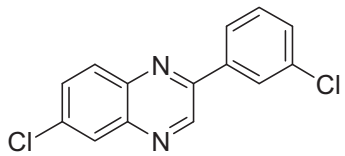
6-Chloro-2-(2-chlorophenyl)quinoxaline (16s):



Starting with **14** (0.12 g, 0.5 mmol), **15s** (0.121 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.035 g, 0.05 equiv.), K_3PO_4 (0.254 g, 2 equiv.), THF (4 mL), **16s** was isolated as white solid (0.129 g, 78%); mp 177 °C. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.34-7.40 (m, 2H, ArH), 7.44-7.49 (m, 1H, ArH), 7.62-7.68 (m, 2H, ArH), 8.00-8.07 (m, 2H, ArH), 9.13 (s, 1H, ArH); ^{13}C NMR

(75.46 MHz, $CDCl_3$), δ = 126.5 (CH), 127.2 (CH), 129.3 (CH), 129.8 (CH), 129.9 (CH), 130.3 (CH), 130.9 (CH), 131.5 (C), 134.9 (C), 135.1 (C), 139.8 (C), 140.6 (C), 145.9 (CH), 151.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3091 (w), 3047 (m), 2982 (w), 1921 (w), 1807 (w), 1621 (w), 1598 (s), 1543 (m), 1504 (w), 1476 (s), 1447 (w), 1429 (m), 1397 (w), 1356 (w), 1324 (w), 1311 (m), 1265 (w), 1248 (m), 1176 (s), 1147 (w), 1137 (m), 1093 (w), 1075 (m), 1040 (s), 1031 (w), 961 (s), 935 (s), 921 (w), 898 (s), 862 (w), 833 (s), 802 (w), 791 (m), 748 (s), 723 (m), 686 (m), 676 (m), 642 (w), 615 (w), 579 (m), 538 (m); GC-MS (EI, 70 eV): m/z (%): 274 (M^+, 100), 247 (20), 241 (30), 239 (93), 212 (21), 177 (31), 137 (18), 110 (20), 102 (12), 100 (9), 88 (2), 75 (36), 63 (2), 51 (4), 50 (7); HRMS (EI) calcd for $C_{14}H_8Cl_2N_2$ [M^+]: 274.00591 found 274.005460.

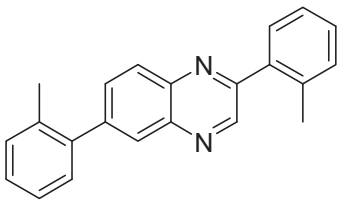
6-Chloro-2-(3-chlorophenyl)quinoxaline (16t):



Starting with **14** (0.1 g, 0.5 mmol), **15t** (0.1 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), K_3PO_4 (0.212 g, 2 equiv.), THF (4 mL), **16t** was isolated as white solid (0.035 g, 25%); mp 167 °C. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.41-7.43 (m, 2H, ArH), 7.65 (dd, *J* = 8.88 Hz, *J* = 2.27 Hz, 1H, ArH), 7.93-8.04 (m, 3H, ArH), 8.13-8.14 (m, 1H, ArH), 9.20 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 125.4 (CH), 127.6 (CH), 128.1 (CH), 130.4 (2CH), 130.9 (CH), 131.6 (CH), 135.4 (C), 135.7 (C), 138.1 (C), 140.7 (C), 142.0 (C), 143.7 (CH), 150.4 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3080 (w), 3048 (m), 1937 (w), 1822 (w), 1712 (w), 1602 (w), 1537 (m), 1475 (m), 1371 (w), 1311 (s), 1258 (w), 1175 (m), 1106 (w), 1065 (m), 1048 (w), 966 (s), 940 (m), 904 (m), 873 (w), 831 (m), 791 (s), 755 (m), 700 (s), 671 (m), 638 (w), 586 (m), 547 (w), 530 (w); GC-MS (EI, 70 eV): m/z (%): 275 (M^+, 17), 274 (100), 247 (18), 239 (26), 212 (21), 177 (23), 137 (14), 110 (18), 100 (6), 84 (2), 75 (28), 63 (2), 50 (6); HRMS (EI) calcd for $C_{14}H_8Cl_2N_2$ [M^+]: 274.00591 found 274.005347.

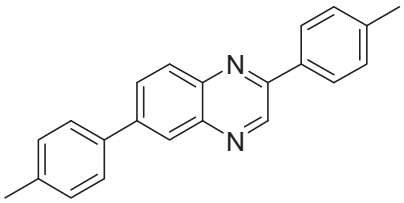
General procedure for the synthesis of 18a-f: A 1,4-dioxane solution (8 mL) of **14** (1.0 equiv.), arylboronic acid **17** (2.5 equiv.), 2M K_2CO_3 (2 mL), and $Pd(PPh_3)_4$ (5 mol%) was heated at 120 °C for 12 h. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution n-heptane/ethyl acetate).

2,6-Di(o-tolyl)quinoxaline (18a):



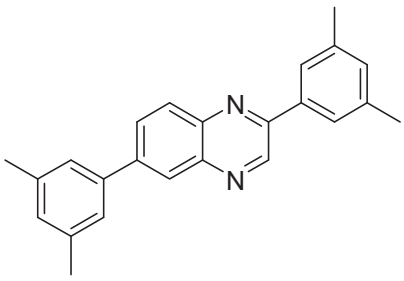
Starting with **14** (0.1 g, 0.5 mmol), **17a** (0.169 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **18a** was isolated as as white solid (0.1 g, 64%); mp 139 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.28 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 7.22-7.33 (m, 7H, ArH), 7.47-7.50 (m, 1H, ArH), 7.71 (dd, *J* = 8.69 Hz, *J* = 2.08 Hz, 1H, ArH), 8.02-8.12 (m, 2H, ArH), 8.95 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 20.4 (CH_3), 20.6 (CH_3), 126.1 (CH), 126.4 (CH), 128.0 (CH), 128.9 (CH), 129.1 (CH), 129.4 (CH), 129.9 (CH), 130.0 (CH), 130.6 (CH), 131.3 (CH), 132.2 (CH), 135.4 (C), 136.6 (C), 137.2 (C), 140.5 (C), 140.9 (C), 141.0 (C), 143.7 (C), 146.2 (CH), 154.9 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3092 (w), 3019 (w), 2921 (w), 2854 (w), 2735 (w), 1954 (w), 1822 (w), 1551 (w), 1567 (w), 1539 (m), 1494 (w), 1481 (m), 1434 (m), 1349 (w), 1314 (m), 1268 (w), 1164 (m), 1060 (m), 1029 (m), 977 (w), 961 (m), 848 (s), 791 (w), 757 (s), 728 (s), 705 (w), 666 (m), 626 (m), 600 (w), 564 (w), 546 (w), 535 (w); GC-MS (EI, 70 eV): *m/z* (%): 310 (M^+, 48), 309 (100), 190 (2), 165 (8), 153 (4), 115 (10), 89 (3), 75 (1), 65 (2), 51 (1), 39 (1); HRMS (ESI) calcd for $C_{22}H_{19}N_2$ $[M+H]^+$: 311.15428 found 311.15435.

2,6-Di(p-tolyl)quinoxaline (18b):



Starting with **14** (0.1 g, 0.5 mmol), **17b** (0.169 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **18b** was isolated as as white solid (0.08 g, 51%); mp 203-205 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.35 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 7.25 (d, ^3J = 7.93 Hz, 2H, ArH), 7.29 (d, ^3J = 7.93 Hz, 2H, ArH), 7.60 (d, ^3J = 8.12 Hz, 2H, ArH), 7.95 (dd, J = 8.69 Hz, J = 1.89 Hz, 1H, ArH), 8.03 (d, ^3J = 8.12 Hz, 2H, ArH), 8.08-8.21 (m, 2H, ArH), 9.24 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 21.2 (CH_3), 21.5 (CH_3), 126.1 (CH), 127.3 (2CH), 127.4 (2CH), 129.7 (CH), 129.80 (CH), 129.83 (2CH), 129.9 (2CH), 134.1 (C), 136.9 (C), 137.5 (C), 138.1 (C), 140.5 (C), 141.7 (C), 142.0 (C), 143.6 (CH), 151.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3020 (w), 2913 (w), 2856 (w), 2726 (w), 1614 (m), 1503 (w), 1402 (w), 1322 (w), 1275 (w), 1186 (w), 1167 (m), 1118 (w), 1054 (m), 975 (w), 931 (m), 849 (w), 816 (s), 723 (m), 691 (w), 606 (m), 587 (w), 554 (w); GC-MS (EI, 70 eV): m/z (%): 310 (M^+, 100), 295 (2), 268 (1), 166 (14), 139 (1), 116 (15), 91 (1), 63 (1); HRMS (EI) calcd for $C_{22}H_{18}N_2$ [M^+]: 310.14645 found 310.146793.

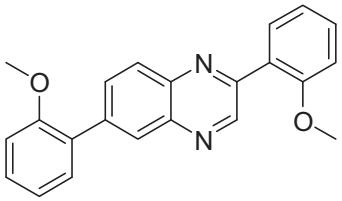
2,6-Bis(3,5-dimethylphenyl)quinoxaline (18c):



Starting with **14** (0.1 g, 0.5 mmol), **17c** (0.186 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **18c** was isolated as as yellow solid (0.16 g, 94%); mp 190-192 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.33 (s, 6H, $2CH_3$), 2.36 (s, 6H, $2CH_3$), 6.97 (s, 1H, ArH), 7.05 (s, 1H, ArH), 7.29 (s, 2H, ArH), 7.70 (s, 2H, ArH), 7.93 (dd, J = 8.69 Hz, J = 2.08 Hz, 1H, ArH), 8.01-8.19 (m, 2H, ArH), 9.20 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 20.4 ($4CH_3$), 124.3 (2CH), 124.4 (2CH), 125.4 (CH), 128.6 (CH), 128.7 (CH), 128.9 (CH), 130.8 (CH), 135.7 (C), 137.6 (2C), 137.7 (2C), 138.6 (C), 140.5 (C), 140.7 (C), 141.3 (C), 142.9 (CH), 150.8 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3012 (w), 2913 (m), 2854 (w), 2734 (w), 1597 (m), 1538 (w), 1435 (w), 1373 (w), 1316 (m), 1286 (w), 1217 (w), 1164 (m), 1087 (m), 1037 (m), 967 (m), 938 (w), 842 (s), 788 (m), 771 (w), 711 (m), 681 (s), 628 (m), 569

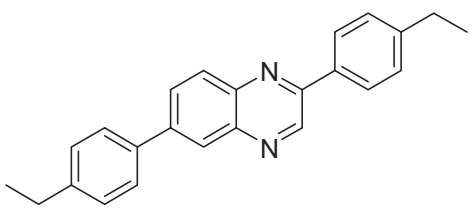
(w), 544 (w); GC-MS (EI, 70 eV): m/z (%): 338 (M^+, 100), 311 (2), 296 (1), 180 (7), 154 (2), 130 (8), 115 (4), 77 (1); HRMS (EI) calcd for $C_{24}H_{22}N_2$ [M^+]: 338.17775 found 338.177487.

2,6-Bis(2-methoxyphenyl)quinoxaline (18d):



Starting with **14** (0.1 g, 0.5 mmol), **17d** (0.19 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **18d** was isolated as yellow solid (0.085 g, 49%); mp 128-129 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.75 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 6.93-6.97 (m, 2H, ArH), 6.99-7.09 (m, 2H, ArH), 7.26-7.40 (m, 3H, ArH), 7.82 (dd, *J* = 7.55 Hz, *J* = 1.70 Hz, 1H, ArH), 7.89 (dd, *J* = 8.69 Hz, *J* = 2.08 Hz, 1H, ArH), 8.05-8.18 (m, 2H, ArH), 9.25 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.5 (OCH_3), 55.6 (OCH_3), 111.4 (CH), 111.5 (CH), 121.1 (CH), 121.5 (CH), 126.7 (C), 128.6 (CH), 129.0 (CH), 129.4 (C), 129.5 (CH), 131.1 (CH), 131.3 (CH), 131.6 (CH), 132.1 (CH), 140.0 (C), 140.9 (C), 141.8 (C), 147.3 (CH), 151.8 (C), 156.6 (C), 157.4 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 3024 (w), 2938 (w), 2838 (w), 1599 (m), 1489 (m), 1440 (w), 1336 (w), 1268 (m), 1233 (s), 1163 (m), 1116 (m), 1060 (m), 1039 (w), 1016 (s), 960 (m), 904 (m), 842 (w), 828 (m), 784 (m), 741 (s), 695 (w), 666 (m), 617 (m), 576 (m), 562 (w), 541 (w); GC-MS (EI, 70 eV): m/z (%): 342 (M^+, 100), 341 (58), 325 (48), 313 (29), 297 (10), 270 (4), 237 (19), 207 (3), 193 (4), 164 (6), 139 (15), 131 (7), 118 (8), 90 (4), 77 (3), 63 (3), 39 (1); HRMS (EI) calcd for $C_{22}H_{18}N_2O_2$ [M^+]: 342.13628 found 342.135862.

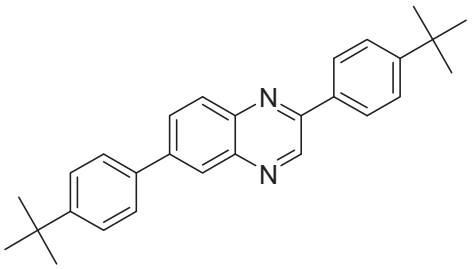
2,6-Bis(4-ethylphenyl)quinoxaline (18e):



Starting with **14** (0.1 g, 0.5 mmol), **17e** (0.188 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **18e** was isolated as white solid (0.08 g, 47%); mp 150 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.223 (t, ^3J = 7.18 Hz, 3H, CH_3), 1.224 (t, ^3J = 7.55 Hz, 3H, CH_3), 2.65 (q, *J* = 7.55 Hz, *J* = 15.12 Hz, 2H, -CH_2-), 2.67 (q, *J* = 7.55 Hz, *J* = 15.12 Hz, 2H, -CH_2-), 7.27 (d, ^3J = 8.50 Hz, 2H, ArH), 7.32 (d, ^3J = 8.50 Hz, 2H, ArH),

7.62 (d, ^3J = 8.31 Hz, 2H, ArH), 7.95 (dd, J = 8.68 Hz, J = 2.08 Hz, 1H, ArH), 8.05 (d, ^3J = 8.31 Hz, 2H, ArH), 8.08-8.21 (m, 2H, ArH), 9.23 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 15.4 (CH_3), 15.5 (CH_3), 28.6 (-CH_2-), 28.8 (-CH_2-), 126.1 (CH), 127.4 (2CH), 127.5 (2CH), 128.6 (2CH), 128.7 (2CH), 129.7 (CH), 129.8 (CH), 134.3 (C), 137.1 (C), 141.6 (C), 141.7 (C), 142.0 (C), 143.7 (CH), 144.4 (C), 146.7 (C), 151.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3025 (w), 2931 (w), 2874 (w), 1614 (m), 1513 (w), 1452 (m), 1300 (w), 1203 (w), 1165 (m), 1121 (w), 1057 (m), 1015 (m), 960 (m), 914 (w), 829 (s), 798 (w), 684 (w), 633 (w), 609 (m), 590 (w), 553 (w); GC-MS (EI, 70 eV): m/z (%): 338 (M^+, 100), 323 (55), 308 (13), 190 (2), 154 (13), 115 (5), 102 (1), 90 (1), 51 (1); HRMS (EI) calcd for $C_{24}H_{18}N_2$ [M^+]: 338.17775 found 338.177824.

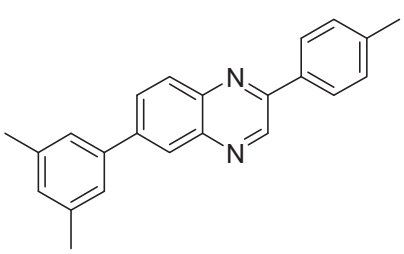
2,6-Bis(4-tert-butylphenyl)quinoxaline (18f):



Starting with **14** (0.1 g, 0.5 mmol), **17f** (0.223 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.029 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (4 mL), **18f** was isolated as white solid (0.052 g, 26%); mp 265-267 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.32 (s, 18H, 6CH_3), 7.47 (d, ^3J = 8.50 Hz, 2H, ArH), 7.52 (d, ^3J = 8.69 Hz, 2H, ArH), 7.65 (d, ^3J = 8.50 Hz, 2H, ArH), 7.97 (dd, J = 8.69 Hz, J = 2.08 Hz, 1H, ArH), 8.06 (d, ^3J = 8.50 Hz, 2H, ArH), 8.09-8.23 (m, 2H, ArH), 9.25 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 31.2 (3CH_3), 31.3 (3CH_3), 34.7 (C), 34.9 (C), 126.0 (2CH), 126.1 (CH), 126.2 (2CH), 127.1 (2CH), 127.2 (2CH), 129.7 (CH), 129.8 (CH), 134.1 (C), 136.8 (C), 141.6 (C), 141.7 (C), 141.9 (C), 143.7 (CH), 151.3 (C), 151.5 (C), 153.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3062 (w), 2964 (m), 2863 (w), 2707 (w), 1614 (m), 1504 (w), 1455 (m), 1361 (m), 1301 (w), 1265 (m), 1202 (w), 1138 (w), 1047 (m), 976 (w), 930 (m), 890 (m), 823 (s), 742 (w), 694 (w), 640 (w), 610 (m), 566 (s), 545 (w); GC-MS (EI, 70 eV): m/z (%): 394 (M^+, 63), 380 (31), 379 (100), 363 (10), 335 (3), 295 (2), 182 (11), 154 (10), 102 (1), 41 (3); HRMS (EI) calcd for $C_{28}H_{30}N_2$ [M^+]: 394.24035 found 394.240463.

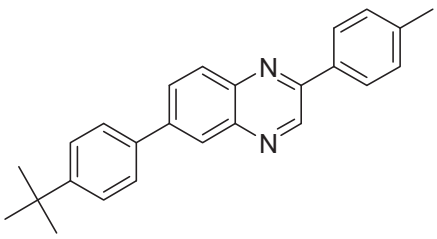
General procedure for the synthesis of 20a-g: A 1,4-dioxane solution (8 mL) of **16** (1.0 equiv.), arylboronic acid **19** (1.3 equiv.), 2M K_2CO_3 (2 mL), and $Pd(PPh_3)_4$ (5 mol%) was heated at 120 °C for 8 h. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution n-heptane/ethyl acetate).

6-(3,5-Dimethylphenyl)-2-p-tolylquinoxaline (20a):



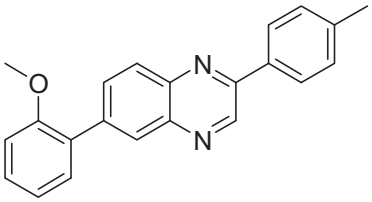
Starting with **16c** (0.05 g, 0.2 mmol), **19a** (0.039 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.012 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (3 mL), **20a** was isolated as light yellow solid (0.045 g, 70%); mp 168°C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.34 (s, 6H, $2CH_3$), 2.37 (s, 3H, CH_3), 6.99 (s, 1H, ArH), 7.28 (s, 1H, ArH), 7.30 (s, 3H, ArH), 7.95 (dd, J = 8.69 Hz, J = 2.08 Hz, 1H, ArH), 8.03 (d, ^3J = 8.12 Hz, 2H, ArH), 8.08 (d, ^3J = 8.69 Hz, 1H, ArH), 8.20 (d, J = 2.07 Hz, 1H, ArH), 9.23 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 ($3CH_3$), 125.4 (2CH), 126.4 (CH), 127.4 (2CH), 129.6 (CH), 129.7 (CH), 129.8 (2CH), 129.9 (CH), 134.0 (C), 138.6 (2C), 139.7 (C), 140.4 (C), 141.6 (C), 141.7 (C), 142.3 (C), 143.6 (CH), 151.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3030 (w), 2913 (m), 2727 (w), 1601 (m), 1555 (w), 1463 (w), 1427 (w), 1370 (w), 1276 (w), 1184 (w), 1164 (w), 1075 (w), 1049 (m), 960 (m), 929 (w), 881 (w), 818 (s), 776 (w), 717 (m), 682 (m), 640 (w), 624 (w), 614 (s), 569 (w), 555 (w), 536 (w); GC-MS (EI, 70 eV): *m/z* (%): 324 (M^+, 100), 309 (5), 297 (5), 180 (42), 162 (20), 130 (27), 115 (11), 77 (1), 65 (1), 63 (1); HRMS (ESI) calcd for $C_{23}H_{21}N_2$ $[M+H]^+$: 325.16993 found 325.17059.

6-(4-tert-Butylphenyl)-2-p-tolylquinoxaline (20b):



Starting with **16c** (0.05 g, 0.2 mmol), **19b** (0.046 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.012 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (3 mL), **20b** was isolated as light yellow solid (0.054 g, 78%); mp 185-187°C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.31 (s, 9H, $3CH_3$), 2.37 (s, 3H, CH_3), 7.28 (d, ^3J = 7.93 Hz, 2H, ArH), 7.46 (d, ^3J = 8.69 Hz, 2H, ArH), 7.65 (d, ^3J = 8.50 Hz, 2H, ArH), 7.95 (dd, J = 8.88 Hz, J = 1.89 Hz, 1H, ArH), 8.03 (d, ^3J = 8.31 Hz, 2H, ArH), 8.09 (d, J = 8.69 Hz, 1H, ArH), 8.22 (d, J = 1.51 Hz, 1H, ArH), 9.23 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 (CH_3), 31.3 ($3CH_3$), 34.7 (C), 126.0 (2CH), 126.1 (CH), 127.1 (2CH), 127.4 (2CH), 129.7 (CH), 129.8 (CH), 129.9 (2CH), 134.0 (C), 136.7 (2C), 140.4 (2C), 141.7 (C), 141.9 (C), 143.6 (CH), 151.3 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 3032 (w), 2902 (w), 2865 (w), 1916 (w), 1614 (m), 1514 (w), 1450 (m), 1397 (w), 1362 (m), 1269 (w), 1186 (w), 1166 (m), 1143 (w), 1109 (w), 1048 (w), 1009 (w), 958 (m), 925 (m), 889 (w), 842 (w), 819 (s), 740 (w), 718 (m), 687 (w), 672 (w), 628 (w), 606 (m), 564 (w), 558 (m), 547 (m); GC-MS (EI, 70 eV): *m/z* (%): 352 (M^+, 100), 309 (25), 297 (9), 178 (10), 152 (7), 141 (15), 65 (1), 39 (1); HRMS (ESI) calcd for $C_{25}H_{25}N_2$ $[M+H]^+$: 353.20123 found 353.20151.

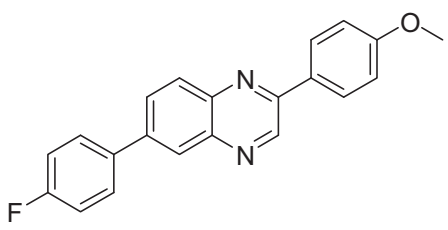
6-(2-Methoxyphenyl)-2-p-tolylquinoxaline (20c):



Starting with **16c** (0.05 g, 0.2 mmol), **19c** (0.04 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.012 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (3 mL), **20c** was isolated as light yellow solid (0.03 g, 47%); mp 125-127°C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.35 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 6.94-7.04 (m, 2H, ArH), 7.26-7.33 (m, 3H, ArH), 7.39 (dd, J = 7.55 Hz, J = 1.70 Hz, 1H, ArH), 7.91 (dd, J = 8.69 Hz, J = 1.89 Hz, 1H, ArH), 8.01-8.17 (m, 4H, ArH), 9.21 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 (CH_3), 55.6 (OCH_3), 111.4 (CH), 121.1 (CH), 127.4 (2CH), 128.6 (CH), 129.0 (CH), 129.3 (C), 129.5 (CH),), 129.9 (2CH),), 131.1 (CH),), 132.6 (CH), 134.1 (C), 139.9 (C), 140.4 (C), 141.4 (C), 141.5 (C), 143.3 (CH), 151.5 (C), 156.6 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 3002 (w), 1916

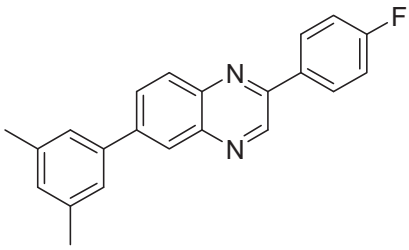
(w), 2834 (w), 1613 (w), 1567 (w), 1518 (w), 1464 (m), 1415 (w), 1322 (w), 1283 (w), 1243 (m), 1182 (w), 1119 (m), 1059 (w), 1025 (m), 977 (w), 932 (m), 900 (m), 833 (s), 823 (s), 754 (s), 716 (w), 636 (w), 616 (w), 609 (m), 576 (w), 543 (w); GC-MS (EI, 70 eV): *m/z* (%): 326 (M^+, 100), 311 (20), 284 (20), 182 (9), 163 (12), 139 (12), 131 (5), 115 (2), 102 (1), 63 (1), 39 (1); HRMS (ESI) calcd for $C_{22}H_{19}N_2O$ $[M+H]^+$: 327.14919 found 327.15004.

6-(4-Fluorophenyl)-2-(4-methoxyphenyl)quinoxaline (20d):



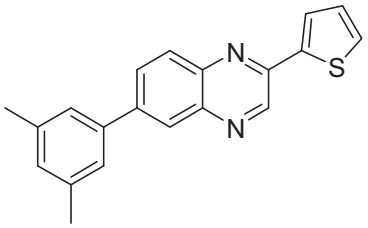
Starting with **16h** (0.08 g, 0.3 mmol), **19d** (0.054 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (3 mL), **20d** was isolated as white solid (0.074 g, 76%); mp 187-189 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 3.84 (s, 3H, OCH_3), 7.02 (d, ^3J = 9.07 Hz, 2H, ArH), 7.13 (t, J = 8.69 Hz, 2H, ArH), 7.62-7.69 (m, 2H, ArH), 7.90 (dd, J = 8.69 Hz, J = 2.08 Hz, 1H, ArH), 8.07-8.16 (m, 4H, ArH), 9.23 (s, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 55.5 (OCH_3), 114.6 (2CH), 116.0 (2CH, d, $^2J_{CF}$ = 22.01 Hz), 126.4 (CH), 128.9 (2CH), 129.1 (2CH, d, $^3J_{CF}$ = 8.25 Hz), 129.3 (C), 129.6 (CH), 129.8 (CH), 135.9 (C, d, $^4J_{CF}$ = 3.30 Hz), 140.8 (C), 141.4 (C), 141.6 (C), 143.6 (CH), 151.3 (C), 161.5 (C), 163.0 (C, d, $^1J_{CF}$ = 247.59 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -114.27 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3062 (w), 3014 (w), 2970 (w), 2843 (w), 1600 (m), 1545 (w), 1510 (m), 1454 (w), 1401 (w), 1306 (w), 1253 (m), 1226 (m), 1178 (w), 1115 (w), 1100 (w), 1027 (m), 960 (m), 902 (w), 890 (w), 826 (s), 785 (w), 720 (w), 696 (w), 640 (m), 631 (w), 589 (m), 554 (w), 534 (m); GC-MS (EI, 70 eV): m/z (%): 330 (M^+, 100), 315 (14), 287 (10), 260 (2), 195 (2), 170 (12), 120 (20), 103 (1), 90 (1), 75 (1), 65 (1), 63 (1); HRMS (EI) calcd for $C_{21}H_{15}FN_2O$ $[M^+]$: 330.11629 found 330.116150.

6-(3,5-Dimethylphenyl)-2-(4-fluorophenyl)quinoxaline (20e):



Starting with **16m** (0.07 g, 0.3 mmol), **19e** (0.058 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (3 mL), **20e** was isolated as white solid (0.055 g, 63%); mp 163-165 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.34 (s, 6H, $2CH_3$), 6.99 (s, 1H, ArH), 7.16 (t, J = 8.69 Hz, 2H, ArH), 7.29 (s, 2H, ArH), 7.95 (dd, J = 8.69 Hz, J = 1.89 Hz, 1H, ArH), 8.04-8.20 (m, 4H, ArH), 9.19 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 20.4 ($2CH_3$), 115.2 (2CH, d, $^2J_{CF}$ = 21.97 Hz), 124.4 (2CH), 125.4 (CH), 128.3 (CH), 128.5 (2CH, d, $^3J_{CF}$ = 8.24 Hz), 128.8 (CH), 129.2 (CH), 131.9 (C, d, $^4J_{CF}$ = 3.20 Hz), 137.6 (2C), 138.6 (C), 140.5 (C), 140.7 (C), 141.6 (C), 142.2 (CH), 149.3 (C), 163.2 (C, d, $^1J_{CF}$ = 250.85 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -110.61 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3339 (s), 2919 (w), 2859 (w), 2735 (w), 1599 (m), 1538 (w), 1469 (w), 1410 (w), 1343 (w), 1298 (w), 1264 (w), 1225 (m), 1142 (w), 1048 (m), 960 (m), 911 (w), 839 (m), 827 (s), 789 (w), 722 (m), 684 (m), 634 (w), 612 (s), 573 (w), 552 (w), 541 (w); GC-MS (EI, 70 eV): m/z (%): 328 (M^+, 100), 313 (3), 180 (13), 164 (3), 130 (9), 115 (5), 94 (1), 75 (1); HRMS (EI) calcd for $C_{22}H_{17}FN_2$ [M^+]: 328.13703 found 328.136677.

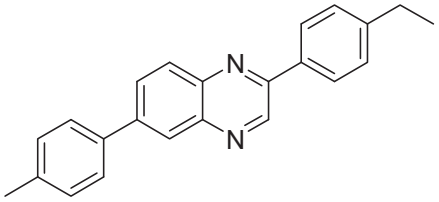
6-(3,5-Dimethylphenyl)-2-(thiophen-2-yl)quinoxaline (20f):



Starting with **16n** (0.05 g, 0.2 mmol), **19f** (0.039 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.012 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (3 mL), **20f** was isolated as yellow solid (0.058 g, 91%); mp 152^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 6.98 (s, 1H, ArH), 7.10-7.13 (m, 1H, ArH), 7.29 (s, 2H, ArH), 7.46 (dd, J = 5.10 Hz, J = 1.13 Hz, 1H, ArH), 7.77 (dd, J = 3.78 Hz, J = 1.13 Hz, 1H, ArH), 7.90-8.16 (m, 3H, ArH), 9.15 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 ($2CH_3$), 125.3 (2CH), 126.4 (CH), 126.8 (CH), 128.5 (CH), 129.2 (CH), 129.7 (CH), 129.8 (CH), 130.2 (CH), 138.6 (3C), 139.6 (C), 141.4 (C), 141.6 (C), 142.2 (C), 142.4 (CH), 147.0 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3106 (w), 3012 (w), 2913 (m), 2858 (w), 2722 (w), 1602 (m), 1573 (w), 1539 (m),

1454 (w), 1517 (m), 1371 (w), 1321 (m), 1238 (w), 1161 (w), 1132 (m), 1064 (w), 1006 (m), 935 (w), 919 (m), 891 (w), 819 (s), 786 (w), 775 (m), 750 (w), 703 (m), 682 (s), 625 (w), 615 (s), 606 (w), 561 (w), 537 (w); GC-MS (EI, 70 eV): *m/z* (%): 316 (M^+, 100), 301 (4), 180 (19), 158 (7), 130 (14), 115 (5), 69 (1), 63 (1), 57 (1); HRMS (ESI) calcd for $C_{20}H_{17}N_2S$ $[M+H]^+$: 317.11070 found 317.11119.

2-(4-Ethylphenyl)-6-p-tolylquinoxaline (20g):

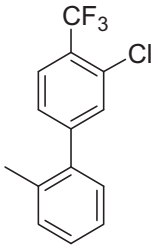


Starting with **16o** (0.07 g, 0.3 mmol), **19g** (0.053 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (3 mL), **20g** was isolated as yellowish solid (0.046 g, 54%); mp 152-154 ^oC. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.21 (t, ^3J = 7.55 Hz, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.65 (q, J = 7.73 Hz, J = 15.29 Hz, 2H, -CH_2-), 7.22 (d, ^3J = 7.74 Hz, 2H, ArH), 7.29 (d, ^3J = 8.31 Hz, 2H, ArH), 7.57 (d, ^3J = 8.12 Hz, 2H, ArH), 7.92 (dd, J = 8.69 Hz, J = 2.07 Hz, 1H, ArH), 8.02-8.18 (m, 4H, ArH), 9.21 (s, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 15.4 (CH_3), 21.2 (CH_3), 28.8 (-CH_2-), 126.1 (CH), 127.3 (2CH), 127.5 (2CH), 128.7 (2CH), 129.7 (2CH), 129.8 (2CH), 134.3 (C), 136.8 (C), 138.1 (C), 141.6 (C), 141.7 (C), 141.9 (C), 143.7 (CH), 146.7 (C), 151.5 (C); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3021 (w), 2962 (m), 2854 (w), 2729 (w), 1915 (w), 1822 (w), 1727 (w), 1613 (m), 1513 (w), 1452 (m), 1336 (w), 1276 (w), 1209 (w), 1165 (m), 1080 (w), 1015 (w), 960 (m), 932 (m), 894 (w), 835 (m), 817 (s), 788 (w), 722 (w), 665 (w), 608 (m), 588 (w), 554 (w), 542 (w); GC-MS (EI, 70 eV): m/z (%): 324 (M^+, 100), 309 (36), 254 (1), 166 (8), 154 (7), 116 (11), 103 (1), 91 (2), 77 (1), 51 (1); HRMS (EI) calcd for $C_{23}H_{20}N_2$ $[M^+]$: 324.16210 found 324.162056.

6.5 Regioselective Palladium-Catalysed Cross-Coupling Reactions of 2,4-Dichloro-1-(trifluoromethyl)benzene

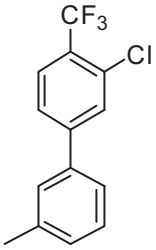
General procedure for the synthesis of 23a-m: A 1,4-dioxane solution (8 mL) of **21** (1.0 equiv.), arylboronic acid **22** (1.3 equiv.), 2M K_2CO_3 (1 mL per cross coupling), and $Pd(PPh_3)_4$ (5 mol%) was heated at 80 °C for 6 h. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution n-heptane/ethyl acetate).

3'-Chloro-2-methyl-4'-(trifluoromethyl)biphenyl (23a):



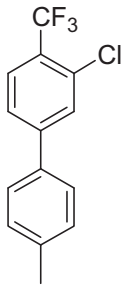
Starting with **21** (0.215 g, 1 mmol), **22a** (0.176 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23a** was isolated as colorless oil (0.251 g, 93%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.31 (s, 3H, CH_3), 7.21-7.24 (m, 1H), 7.28-7.37 (m, 4H), 7.52 (s, 1H, ArH), 7.76 (d, ^3J = 7.93 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 20.3 (CH_3), 123.1 (CF_3, q, $^1J_{CF}$ = 272.89 Hz), 126.1 (CH), 126.8 (C, q, $^2J_{CF}$ = 31.91 Hz), 127.3 (CH, q, $^3J_{CF}$ = 4.95 Hz), 127.6 (CH), 128.5 (CH), 129.4 (CH), 130.7 (CH), 132.1 (CH), 135.2 (2C), 139.1 (C), 147.2 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.27 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3214 (w), 3063 (w), 3021 (w), 2956 (w), 2926 (w), 2865 (w), 2741 (w), 1921 (w), 1804 (w), 1609 (m), 11602 (m), 1556 (m), 1504 (w), 1481 (w), 1455 (w), 1383 (m), 1312 (s), 1280 (w), 1248 (m), 1173 (m), 1126 (s), 1102 (s), 1054 (w), 1027 (s), 964 (w), 945 (w), 892 (m), 867 (w), 838 (s), 786 (w), 760 (s), 738 (m), 724 (m), 681 (m), 661 (w) , 641 (m), 599 (w), 594 (w) , 565 (w), 551 (w), 536 (w); GC-MS (EI, 70 eV): m/z (%): 270 (M^+, 100), 235 (11), 215 (27), 165 (80), 139 (3), 115 (3), 91 (3), 69 (5), 63 (3), 39 (2); HRMS (EI) calcd for $C_{14}H_{10}ClF_3$ [M^+]: 270.04176 found 270.042298.

3-Chloro-3'-methyl-4-(trifluoromethyl)biphenyl (23b):



Starting with **21** (0.215 g, 1 mmol), **22b** (0.176 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23b** was isolated as colorless oil (0.257 g, 95%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.48 (s, 3H, CH_3), 7.27-7.30 (m, 1H), 7.39-7.43 (m, 3H), 7.56-7.59 (m, 1H), 7.75-7.78 (m, 2H); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 (CH_3), 123.1 (CF_3, q, $^1J_{CF}$ = 272.83 Hz), 124.3 (CH), 125.2 (CH), 126.8 (C, q, $^2J_{CF}$ = 31.59 Hz), 127.8 (CH, q, $^3J_{CF}$ = 5.04 Hz), 127.9 (CH), 129.0 (CH), 129.6 (CH), 129.9 (CH), 132.6 (C, q, $^4J_{CF}$ = 2.29 Hz), 138.2 (C), 138.9 (2C), 146.3 (C);^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.19 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3214 (w), 3027 (w), 2952 (w), 2923 (w), 2864 (w), 2736 (w), 1922 (w), 1883 (w), 1853 (w), 1791 (w), 1698(w), 1674 (w), 1605 (m), 1557 (m), 1503 (m), 1480 (w), 1456 (w), 1427 (w), 1377 (m), 1312 (s), 1299 (w), 1273(w), 1254 (w), 1175 (m), 1126 (s), 1104 (s), 999 (w), 961 (w), 910 (w), 880 (m), 835 (s), 781 (s), 736 (m), 721 (w), 698 (m) , 684 (w), 633 (m), 596 (w) , 569 (w), 540 (w); GC-MS (EI, 70 eV): m/z (%): 270 (M^+, 100), 251 (5), 235 (12), 215 (9), 201 (6), 183 (2), 165 (33), 125 (1), 91 (2), 69 (2), 39 (1); HRMS (EI) calcd for $C_{14}H_{10}ClF_3$ [M^+]: 270.04176 found 270.041311.

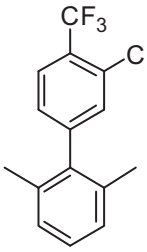
3-Chloro-4'-methyl-4-(trifluoromethyl)biphenyl (23c):



Starting with **21** (0.215 g, 1 mmol), **22c** (0.176 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23c** was isolated as white solid (0.262 g, 97%); mp 55-57 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.44 (s, 3H, CH_3), 7.31 (d, ^3J = 8.49 Hz, 2H, ArH), 7.50 (d, ^3J = 8.12 Hz, 2H, ArH), 7.56 (d, ^3J = 8.12 Hz, 1H, ArH), 7.74 (d, ^3J = 8.69 Hz, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.2 (CH_3), 123.1 (CF_3, q, $^1J_{CF}$ = 275.65 Hz), 124.9 (CH), 126.6 (C, q, $^2J_{CF}$ = 31.36 Hz), 127.0 (2CH), 127.9 (CH, q, $^3J_{CF}$ = 5.50 Hz), 129.6 (CH), 129.9 (2CH), 132.6 (C, q, $^3J_{CF}$ = 1.65 Hz), 135.4 (C), 138.9 (C), 146.1 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.19 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3070 (w), 3040 (w), 3029 (m), 2921 (m), 2858 (w), 2739 (w), 1916 (w), 1797 (w), 1769 (w), 1602 (s), 1551 (m), 1520 (w), 1489 (m), 1413 (w), 1379 (m), 1356 (w), 1313 (s), 1290 (w), 1270 (w), 1254 (w), 1214 (w), 1187 (w), 1171 (m), 1121 (s), 1105 (s),

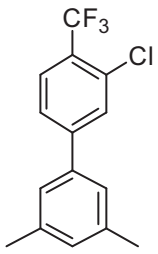
1040 (w), 1026 (m), 1014 (w), 959 (m), 904 (w), 887 (m), 845 (w), 836 (m), 808 (s), 785 (m), 740 (m), 717 (w), 676 (m), 643 (w), 624 (w), 588 (m), 561 (m), 547 (w); GC-MS (EI, 70 eV): m/z (%): 270 (M^+, 100), 235 (14), 215 (8), 165 (32), 139 (2), 99 (1), 87 (1), 75 (1), 63 (1), 51 (1), 39 (1); HRMS (EI) calcd for $C_{14}H_{10}ClF_3$ [M^+]: 270.04176 found 270.041119.

3'-Chloro-2,6-dimethyl-4'-(trifluoromethyl)biphenyl (23d):



Starting with **21** (0.215 g, 1 mmol), **22d** (0.194 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23d** was isolated as colorless oil (0.102 g, 36%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.95 (s, 6H, $2CH_3$), 7.03-7.15 (m, 4H, ArH), 7.25 (s, 1H, ArH), 7.66 (d, ^3J = 7.93 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 20.7 ($2CH_3$), 123.0 (CF_3, q, $^1J_{CF}$ = 272.83 Hz), 126.8 (C, q, $^2J_{CF}$ = 31.59 Hz), 127.60 (2CH), 127.64 (CH), 127.7 (CH, q, $^3J_{CF}$ = 5.49 Hz), 128.0 (CH), 132.0 (CH), 132.4 (C, q, $^3J_{CF}$ = 1.83 Hz), 135.5 (2C), 138.9 (C), 146.6 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.28 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 3022 (w), 2953 (w), 2923 (w), 2855 (w), 2739 (w), 1928 (w), 1858 (w), 1787 (w), 1607 (m), 1559 (m), 1500 (w), 1464 (m), 1445 (w), 1384 (m), 1312 (s), 1285 (w), 1251 (m), 1240 (w), 1173 (m), 1126 (s), 1101 (s), 1054 (w), 1028 (s), 988 (w), 964 (w), 919 (w), 889 (m), 834 (s), 769 (s), 758 (w),752 (w), 718 (m), 667 (m), 646 (m) , 595 (w), 566 (m), 553 (w); GC-MS (EI, 70 eV): m/z (%): 284 (M^+, 100), 269 (25), 249 (73), 234 (28), 180 (22), 165 (38), 152 (4), 139 (1), 105 (1), 89 (2), 39 (1); HRMS (EI) calcd for $C_{15}H_{12}ClF_3$ [M^+]: 284.05741 found 284.056674.

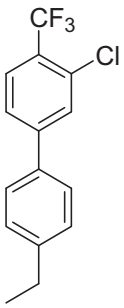
3-Chloro-3',5'-dimethyl-4-(trifluoromethyl)biphenyl (23e):



Starting with **21** (0.215 g, 1 mmol), **22e** (0.194 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23e** was isolated as colorless oil (0.204 g, 72%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.43 (s, 6H, $2CH_3$), 7.11 (s, 1H, ArH), 7.22 (s, 2H, ArH), 7.56 (d, ^3J = 8.49 Hz, 1H, ArH), 7.73-7.76 (m, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.3 ($2CH_3$), 123.1 (CF_3, q, $^1J_{CF}$ = 272.83 Hz), 125.1 (2CH), 125.2 (CH), 126.7 (C, q, $^2J_{CF}$ = 31.58 Hz), 127.7 (CH, q, $^3J_{CF}$ = 5.04 Hz), 129.9 (CH), 130.4 (CH),

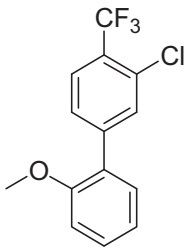
132.5 (C, q, $^{3}J_{CF}$ = 1.83 Hz), 138.2 (C), 138.7 (2C), 146.4 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.19 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3016 (w), 2922 (w), 2856 (w), 1602 (m), 1562 (w), 1554 (m), 1501 (w), 1493 (w), 1479 (w), 1467 (w), 1443 (w), 1432 (w), 1409 (w), 1379 (w), 1315 (s), 1264 (w), 1212 (w), 1177 (m), 1132 (s), 1108 (m), 1040 (w), 1026 (m), 997 (w), 963 (w), 895 (w), 885 (w), 853 (w), 831 (m), 775 (w), 723 (w), 698 (w), 667 (w), 661 (w), 636 (w), 540 (w); GC-MS (EI, 70 eV): m/z (%): 284 (M^+, 100), 269 (23), 249 (11), 234 (14), 165 (18), 152 (2), 105 (1), 51 (1); HRMS (EI) calcd for HRMS (EI) calcd for $C_{15}H_{12}ClF_3$ [M^+]: 284.05741 found 284.057528.

3-Chloro-4'-ethyl-4-(trifluoromethyl)biphenyl (23f):



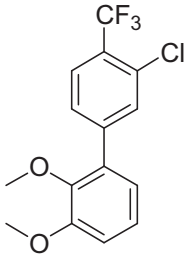
Starting with **21** (0.215 g, 1 mmol), **22f** (0.195 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23f** was isolated as colorless oil (0.14 g, 49%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.55 Hz, 3H, CH_3), 2.63 (q, *J* = 7.55 Hz, *J* = 15.11 Hz, 2H), 7.22 (d, ^{3}J = 8.50 Hz, 2H, ArH), 7.41-7.48 (m, 3H), 7.63-7.66 (m, 2H); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 15.5 (CH_3), 28.6 (-CH_2-), 123.1 (CF_3, q, $^{1}J_{CF}$ = 272.90 Hz), 124.9 (CH), 127.0 (C, q, $^{2}J_{CF}$ = 34.66 Hz), 127.1 (2CH), 127.9 (CH, q, $^{3}J_{CF}$ = 5.50 Hz), 128.7 (2CH), 129.7 (CH), 132.6 (C, q, $^{3}J_{CF}$ = 1.65 Hz), 135.6 (C), 145.2 (C), 146.1 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.19 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3026 (w), 2966 (w), 2932 (w), 2874 (m), 1907 (w), 1579 (w), 1605 (m), 1576 (w), 1552 (m), 1523 (w), 1488 (w), 1461 (w), 1455 (w), 1420 (m), 1382 (m), 1312 (s), 1293 (w), 1254 (w), 1175 (m), 1127 (s), 1103(s), 1059 (w), 1042 (w), 1025 (m), 1015 (m), 962 (w), 887 (m), 820 (s), 772 (w), 736 (m) , 699 (w), 674 (m), 644(w), 624 (w), 594 (m), 561 (m), 532 (w); GC-MS (EI, 70 eV): m/z (%): 284 (M^+, 50), 271 (32), 269 (100), 249 (4), 233 (7), 165 (19), 117 (1), 77 (1), 63 (1), 39 (1); HRMS (EI) calcd for $C_{15}H_{12}ClF_3$ [M^+]: 284.05741 found 284.056982.

3'-Chloro-2-methoxy-4'-(trifluoromethyl)biphenyl (23g):



Starting with **21** (0.215 g, 1 mmol), **22g** (0.198 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23g** was isolated as heavy oil (0.16 g, 56%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.75 (s, 3H, OCH_3), 6.91-6.99 (m, 2H, ArH), 7.21 (dd, J = 7.55 Hz, J = 1.89 Hz, 1H, ArH), 7.28-7.34 (m, 1H, ArH), 7.42-7.45 (m, 1H, ArH), 7.60-7.64 (m, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.5 (OCH_3), 111.4 (CH), 121.0 (CH), 123.1 (CF_3, q, $^1J_{CF}$ = 272.83 Hz), 126.5 (C, q, $^2J_{CF}$ = 31.59 Hz), 127.0 (CH, q, $^3J_{CF}$ = 5.49 Hz), 127.7 (CH, C), 130.0 (CH), 130.6 (CH), 131.7 (C, q, $^3J_{CF}$ = 1.83 Hz), 132.3 (CH), 143.7 (C), 156.4 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.25 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 3002 (w), 2941 (w), 2836 (w), 1605 (m), 1581 (w), 1555 (w), 1504 (m), 1482 (m), 1463 (m), 1435 (m), 1386 (m), 1311 (s), 1277 (w), 1251 (m), 1238 (m), 1175 (m), 1120 (s), 1103 (s), 1056 (w), 1025 (s), 1003 (w), 963 (w), 935 (w), 889 (m), 851 (w), 833 (m), 784 (m), 748 (s), 731 (w), 682 (m), 635 (m), 615 (w), 593 (w), 574 (w) , 566 (w), 554 (m); GC-MS (EI, 70 eV): m/z (%): 286 (M^+, 100), 267 (7), 251 (19), 236 (59), 217 (13), 202 (21), 152 (4), 139 (12), 118 (19), 99 (3), 87 (7), 39 (2); HRMS (EI) calcd for $C_{14}H_{10}ClF_3O$ [M^+]: 286.03688 found 286.036464.

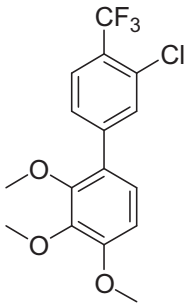
3'-Chloro-2,3-dimethoxy-4'-(trifluoromethyl)biphenyl (23h):



Starting with **21** (0.215 g, 1 mmol), **22h** (0.237 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23h** was isolated as colorless oil (0.235 g, 74%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.53 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.78-6.81 (m, 1H, ArH), 6.85 (dd, J = 8.31 Hz, J = 1.51 Hz, 1H, ArH, ArH), 6.98-7.03 (m, 1H, ArH), 7.42-7.45 (m, 1H, ArH), 7.59-7.61 (m, 2H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 55.9 (OCH_3), 60.8 (OCH_3), 112.9 (CH), 122.0 (CH), 123.1 (CF_3, q, $^1J_{CF}$ = 272.89 Hz), 124.5 (CH), 126.8 (C, q, $^2J_{CF}$ = 31.91 Hz), 127.2 (CH, q, $^3J_{CF}$ = 4.95 Hz), 127.6 (CH), 131.8 (C, q, $^3J_{CF}$ = 1.65 Hz), 132.1 (CH), 132.9 (C), 143.5 (C), 146.6 (C), 153.3 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.23 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3030 (w), 2966 (m), 2933 (w), 2874 (w), 1907 (w), 1606 (m), 1579 (w), 1516 (w), 1474 (m), 1415 (w), 1399 (m), 1377 (w), 1330 (s), 1283 (m), 1255 (m), 1167 (s), 1123 (s), 1087 (s), 1065 (w),

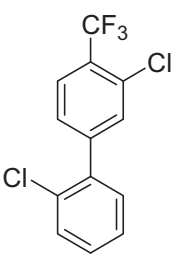
1029 (m), 1014 (m), 965 (w), 904 (m), 842 (w), 825 (s), 774 (w), 731 (w), 717 (m), 677 (w), 657 (m), 632 (m), 598 (m), 581 (w), 554 (m); GC-MS (EI, 70 eV): m/z (%): 316 (M^+, 100), 301 (17), 266 (92), 251 (12), 223 (10), 204 (8), 169 (6), 141 (2), 126 (2), 99 (1), 69 (3); HRMS (EI) calcd for $C_{15}H_{12}ClF_3O_2$ [M^+]: 316.04724 found 316.046783.

3'-Chloro-2,3,4-trimethoxy-4'-(trifluoromethyl)biphenyl (23i):



Starting with **21** (0.215 g, 1 mmol), **22i** (0.276 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23i** was isolated as colorless oil (0.207 g, 60%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.61 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 6.63 (d, J = 8.69 Hz, 1H, ArH), 6.89 (d, J = 8.69 Hz, 1H, ArH), 7.34 (d, J = 8.12 Hz, 1H, ArH), 7.56-7.59 (m, 2H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 55.9 (OCH_3), 60.9 (OCH_3), 61.1 (OCH_3), 107.7 (CH), 122.5 (CF_3, q, $^1J_{CF}$ = 272.89 Hz), 124.6 (CH), 125.6 (C), 126.2 (C, q, $^2J_{CF}$ = 31.36 Hz), 127.1 (CH, q, $^3J_{CF}$ = 5.50 Hz), 127.3 (CH), 131.8 (CH), 142.7 (C), 143.4 (C), 151.4 (C), 153.5 (C), 154.3 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.18 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2995 (w), 2938 (w), 2837 (w), 1740 (w), 1596 (s), 1552 (m), 1509 (m), 1484 (m), 1462 (m), 1434 (w), 1416 (m), 1378 (m), 1313 (w), 1304 (s), 1293 (w), 1257 (w), 1234 (m), 1211 (m), 1175 (s), 1127 (m), 1104 (s), 1084 (s), 1025 (w), 1009 (s), 927 (m), 883 (m), 838 (m), 794 (s), 759 (w), 737 (m), 697 (w), 689 (w), 654 (w), 621 (w), 603 (w) , 585 (w), 539 (w); GC-MS (EI, 70 eV): m/z (%): 346 (M^+, 100), 331 (16), 296 (31), 288 (19), 217 (29), 182 (6), 167 (2), 132 (1), 99 (2), 69 (2); HRMS (EI) calcd for $C_{16}H_{14}ClF_3O_3$ [M^+]: 346.05781 found 346.056833.

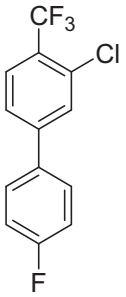
2,3'-Dichloro-4'-(trifluoromethyl)biphenyl (23j):



Starting with **21** (0.215 g, 1 mmol), **22j** (0.202 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23j** was isolated as colorless oil (0.135 g, 47%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.24-7.29 (m, 3H, ArH), 7.35-7.38 (m, 1H, ArH), 7.40-7.43 (m, 1H, ArH), 7.51 (s, 1H, ArH), 7.66 (d, ^3J = 8.12 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 122.9 (CF_3, q, $^1J_{CF}$ = 273.29 Hz), 128.0 (C, q, $^2J_{CF}$ = 33.42 Hz),

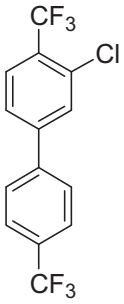
127.1 (CH), 127.2 (CH, q, $^{3}J_{CF}$ = 5.49 Hz), 127.8 (CH), 129.7 (CH), 130.2 (CH), 130.9 (CH), 132.0 (C, q, $^{3}J_{CF}$ = 1.83 Hz), 132.2 (C), 132.3 (CH), 137.7 (C), 144.3 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.40 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 2924 (w), 2854 (w), 1923 (w), 1807 (w), 1607 (m), 1569 (m), 1556 (w), 1503 (m), 1468 (m), 1435 (m), 1385 (m), 1311 (s), 1264 (w), 1244 (w), 1174 (m), 1125 (s), 1103 (m), 1077 (m), 1050 (w), 1037(s), 1027 (m), 981 (w), 962 (w), 947 (w), 891 (m), 865 (w), 834 (s), 756 (m), 749 (m) , 740 (w), 731 (w), 705(m), 671 (m), 636 (m), 598 (w), 562 (w) , 557(w), 542 (w); GC-MS (EI, 70 eV): m/z (%): 290 (M^+, 100), 271 (5), 255 (4), 235 (10), 220 (25), 201 (5), 186 (12), 170 (4), 150 (5), 123 (1), 99 (2), 50 (1); HRMS (EI) calcd for $C_{13}H_7Cl_2F_3$ [M^+]: 289.98714 found 289.987078.

3-Chloro-4'-fluoro-4-(trifluoromethyl)biphenyl (23k):



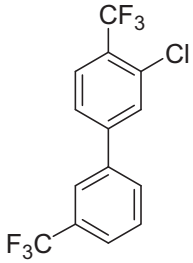
Starting with **21** (0.215 g, 1 mmol), **22k** (0.181 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23k** was isolated as white solid (0.127 g, 46%); mp 67-69 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.02-7.11 (m, 2H, ArH), 7.37-7.48 (m, 3H, ArH), 7.58 (s, 1H, ArH), 7.63 (d, ^{3}J = 8.31 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 116.2 (2CH, d, $^{2}J_{CF}$ = 22.01 Hz), 123.0 (CF_3, q, $^{1}J_{CF}$ = 272.90 Hz), 125.0 (CH), 128.0 (CH, q, $^{3}J_{CF}$ = 4.95 Hz), 128.9 (2CH, d, $^{3}J_{CF}$ = 8.25 Hz), 127.0 (C, q, $^{2}J_{CF}$ = 31.91 Hz), 129.8 (CH), 132.8 (C, q, $^{3}J_{CF}$ = 1.65 Hz), 134.4 (C, d, $^{4}J_{CF}$ = 3.30 Hz), 145.1 (C), 163.3 (CF, d, $^{1}J_{CF}$ = 249.24 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.28 ($ArCF_3$), -112.95 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3075 (w), 3049 (w), 2924 (w), 2856 (w), 1890 (w), 1605 (m), 1598 (m), 1561 (w), 1521 (w), 1495 (m), 1489 (m), 1421 (w), 1383 (m), 1313 (s), 1290 (w), 1232 (s), 1179 (w), 1160 (w), 1126 (s), 1105 (s), 1059(w), 1038 (w), 1024 (m), 1014 (w), 959 (w), 884 (m), 839 (w), 820 (s), 804 (m), 764 (w) , 738 (m), 712 (w), 701(w), 675 (m), 712 (w), 701 (w), 675 (m), 637 (w), 619 (w), 593 (m), 560 (m), 546 (w); GC-MS (EI, 70 eV): m/z (%): 274 (M^+, 100), 238 (4), 219 (15), 170 (19), 120 (1), 94 (3), 85 (1), 75 (2), 69 (1); HRMS (EI) calcd for $C_{13}H_7ClF_4$ [M^+]: 274.01669 found 274.016090.

3-Chloro-4,4'-bis(trifluoromethyl)biphenyl (23l):



Starting with **21** (0.215 g, 1 mmol), **22l** (0.246 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23l** was isolated as colorless oil (0.114 g, 35%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.47-7.50 (m, 1H, ArH), 7.59-7.72 (m, 6H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 122.8 (CF_3, q, $^1J_{CF}$ = 272.90 Hz), 124.0 (CF_3, q, $^1J_{CF}$ = 271.80 Hz), 125.4 (CH), 127.6 (2CH), 126.1 (2CH, q, $^3J_{CF}$ = 3.85 Hz), 128.2 (CH, q, $^3J_{CF}$ = 5.50 Hz), 130.1 (CH), 130.9 (2C, q, $^2J_{CF}$ = 32.46 Hz), 133.0 (C, q, $^3J_{CF}$ = 1.65 Hz), 141.8 (C), 144.6 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.45 ($ArCF_3$), -62.69 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2934 (w), 1924 (w), 1737 (w), 1607 (m), 1557 (m), 1492 (w), 1421 (w), 1381 (m), 1313 (s), 1257 (w), 1165 (w), 1105 (s), 1069 (s), 1038 (w), 1025 (m), 1014 (m), 964 (w), 956 (w), 890 (m), 850 (w), 824 (s), 771 (w), 742 (w), 732 (w), 693 (m), 653 (m), 625 (w), 598 (m), 558 (w), 543 (w); GC-MS (EI, 70 eV): m/z (%): 324 (M^+, 100), 305 (18), 274 (8), 220 (14), 170 (3), 144 (1), 112 (2), 99 (1), 75 (1), 69 (2); HRMS (EI) calcd for $C_{14}H_7ClF_6$ [M^+]: 324.01350 found 324.013171.

3-Chloro-3',4-bis(trifluoromethyl)biphenyl (23m):

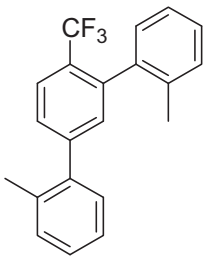


Starting with **21** (0.215 g, 1 mmol), **22a** (0.246 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (8 mL), **23a** was isolated as colorless oil (0.103 g, 32%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.49-7.61 (m, 3H, ArH), 7.64-7.74 (m, 4H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 122.8 (CF_3, q, $^1J_{CF}$ = 273.29 Hz), 123.9 (CF_3, q, $^1J_{CF}$ = 272.37 Hz), 123.9 (CH, q, $^3J_{CF}$ = 4.12 Hz), 124.7 (CH, q, $^3J_{CF}$ = 3.66 Hz), 125.3 (CH), 125.4 (CH, q, $^3J_{CF}$ = 3.66 Hz), 129.7 (CH), 130.0 (CH), 130.5 (CH), 131.5 (C, q, $^2J_{CF}$ = 32.04 Hz), 131.7 (C, q, $^2J_{CF}$ = 32.50 Hz), 133.1 (C, q, $^3J_{CF}$ = 1.83 Hz), 139.1 (C), 144.6 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -62.43 ($ArCF_3$), -62.72 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3071 (w), 3051 (w), 2926 (w), 1608 (m), 1565 (w), 1510 (w), 1503 (w), 1484 (w), 1443 (m), 1412 (w), 1385 (m), 1334 (m), 1314 (s), 1289 (w), 1267 (m), 1255 (m), 1167 (m), 1120 (s), 1104 (s), 1074 (m), 1049(m), 1026 (m), 1001 (w), 963 (w), 922 (w), 908 (w), 885 (m), 862 (m), 837 (m), 798 (s) , 782 (w), 762 (w), 695(s), 674 (w), 665 (w), 659 (w), 636 (w), 620 (w), 591 (w), 557 (w) , 544 (w);

GC-MS (EI, 70 eV): m/z (%): 324 (M^+, 100), 305 (15), 274 (6), 220 (13), 170 (3), 145 (1), 109 (1), 99 (1), 75 (1), 69 (2); HRMS (EI) calcd for $C_{14}H_7ClF_6$ [M^+]: 324.01350 found 324.013577.

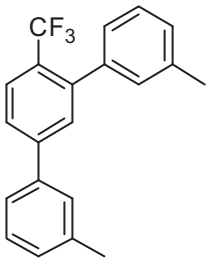
General procedure for the synthesis of 25a-d: A 1,4-Dioxane solution (8 mL) of **21** (1.0 equiv.), arylboronic acid **24** (2.5 equiv.), 2M K_2CO_3 (2 mL), and $Pd(PPh_3)_4$ (5 mol%) was heated at 110 °C for 8 h. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution n-heptane/ethyl acetate).

4-Trifluoromethyl-1,3-bis(2-methylphenyl)-benzene (25a):



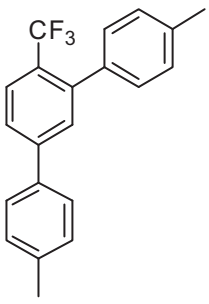
Starting with **21** (0.215 g, 1 mmol), **24a** (0.337 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (8 mL), **25a** was isolated as colorless oil (0.186 g, 57%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.01 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 7.09-7.19 (m, 9H), 7.34 (qd, J = 8.12 Hz, J = 0.94 Hz, 1H, ArH), 7.70 (d, ^3J = 7.93 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 20.1 (CH_3), 20.4 (CH_3), 124.2 (CF_3, q, $^1J_{CF}$ = 273.74 Hz), 124.9 (CH), 125.9 (CH), 126.0 (CH, q, $^3J_{CF}$ = 5.04 Hz), 127.2 (C, q, $^2J_{CF}$ = 29.76 Hz), 127.91 (CH), 127.98 (CH), 128.0 (CH), 129.5 (CH), 129.6 (2CH), 130.6 (CH), 132.4 (CH), 135.2 (C), 135.9 (C), 138.9 (C), 140.2 (C), 140.5 (C, q, $^4J_{CF}$ = 2.29 Hz), 145.1 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -58.80 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 3020 (w), 2953 (w), 2923 (w), 2858 (w), 2738 (w), 2620 (w), 2576 (w), 1917 (w), 1806 (w), 1727 (w), 1609 (m), 1601 (m), 1564 (m), 1507 (w), 1479 (m), 1455 (m), 1390 (m), 1310 (s), 1256 (w), 1168 (s), 1116 (s), 1070 (m), 1044 (w), 1030 (m), 1009 (m), 985 (w), 964 (w), 943 (w), 908 (s), 866 (w), 839 (s), 768 (m), 754 (s), 739 (m), 724 (s), 692 (m), 653 (m), 639 (m), 630 (m), 597 (m), 557 (m), 539 (m); GC-MS (EI, 70 eV): m/z (%): 326 (M^+, 100), 311 (9), 285 (5), 257 (19), 242 (10), 215 (7), 165 (12), 105 (2), 91 (3), 65 (1); HRMS (EI) calcd for $C_{21}H_{17}F_3$ [M^+]: 326.12769 found 326.127047.

4-Trifluoromethyl-1,3-bis(3-methylphenyl)-benzene (25b):



Starting with **21** (0.215 g, 1 mmol), **24b** (0.337 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (8 mL), **25b** was isolated as colorless oil (0.126 g, 39%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 7.05-7.14 (m, 4H), 7.19-7.35 (m, 4H), 7.46 (s, 1H), 7.54-7.58 (m, 1H), 7.69 (d, ^3J = 8.31 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.4 (CH_3), 21.5 (CH_3), 124.3 (CF_3, q, $^1J_{CF}$ = 273.74 Hz), 124.4 (CH), 125.7 (CH), 126.1 (CH), 126.5 (CH, q, $^3J_{CF}$ = 5.04 Hz), 127.1 (C, q, $^2J_{CF}$ = 30.21 Hz), 127.7 (CH), 128.0 (CH), 128.4 (CH), 128.8 (CH), 128.9 (CH), 129.7 (CH), 130.7 (CH), 137.4 (C), 138.6 (C), 139.4 (C), 139.9 (C), 141.9 (C, q, $^4J_{CF}$ = 1.83 Hz), 144.2 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -56.54 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3030 (m), 2922 (m), 2853 (w), 2732 (w), 1943 (w), 1876 (w), 1788 (w), 1726 (w), 1603 (m), 1585 (w), 1567 (m), 1479 (m), 1454 (w), 1379 (m), 1309 (s), 1267 (w), 1165 (m), 1117 (s), 1096 (w), 1078 (m), 1031 (s), 999 (w), 962 (w), 895 (w), 881 (w), 835 (m), 783 (s), 758 (w), 734 (w), 703 (s), 694 (w), 643 (m), 611 (w), 589 (m), 563 (w); GC-MS (EI, 70 eV): m/z (%): 326 (M^+, 100), 305 (11), 291 (5), 257 (3), 165 (3), 128 (1), 91 (1); HRMS (EI) calcd for $C_{21}H_{17}F_3$ [M^+]: 326.12769 found 326.127119.

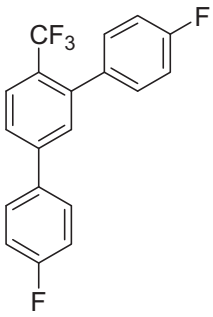
4-Trifluoromethyl-1,3-bis(4-methylphenyl)-benzene (25c):



Starting with **21** (0.215 g, 1 mmol), **24c** (0.337 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (8 mL), **25c** was isolated as colorless oil (0.196 g, 60%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.29 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 7.11-7.20 (m, 6H, ArH), 7.37-7.44 (m, 3H, ArH), 7.51-7.55 (m, 1H, ArH), 7.66 (d, ^3J = 8.12 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.2 (CH_3), 21.3 (CH_3), 124.4 (CF_3, q, $^1J_{CF}$ = 274.20 Hz), 125.4 (CH), 126.6 (CH, q, $^3J_{CF}$ = 5.49 Hz), 126.8 (CH), 127.0 (C, q, $^2J_{CF}$ = 30.21 Hz), 127.1 (2CH), 128.6 (CH), 128.89 (CH, q, $^5J_{CF}$ = 1.37 Hz),), 129.5 (CH), 129.7 (2CH), 130.6 (CH), 136.6 (C), 136.7 (C), 137.0 (C), 138.2 (C), 141.9 (C), 144.0 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -56.47 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3024 (w), 2921 (m), 2856 (w), 2732 (w), 2620 (w), 2590 (w), 1904

(m), 1798 (w), 1732 (w), 1652 (w), 1607 (s), 1578 (w), 1561 (w), 1515 (m), 1500 (w), 1490 (m), 1455 (w), 1417 (w), 1383 (m), 1348 (w), 1307 (s), 1281 (w), 1264 (w), 1211 (w), 1170 (s), 1118 (s), 1111 (s), 1075 (s), 1029 (s), 1008 (m), 963 (w), 945 (w), 901 (m), 841 (m), 809 (s), 801 (m), 779 (w), 758 (m), 738 (w), 720 (m), 698 (w), 679 (w), 653 (w), 641 (w), 626 (w), 606 (w), 586 (m), 565 (w), 540 (m); GC-MS (EI, 70 eV): m/z (%): 326 (M^+, 100), 286 (1), 257 (4), 215 (2), 165 (3), 91 (2); HRMS (EI) calcd for $C_{21}H_{17}F_3$ [M^+]: 326.12769 found 326.127380.

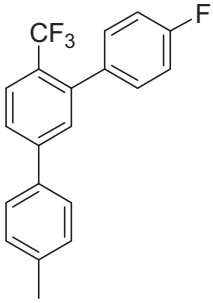
4-Trifluoromethyl-1,3-bis(4-fluorophenyl)-benzene (25d):



Starting with **21** (0.215 g, 1 mmol), **24d** (0.348 g, 2.5 equiv.), $Pd(PPh_3)_4$ (0.058 g, 0.05 equiv.), 2M K_2CO_3 (2 mL), 1,4-Dioxane (8 mL), **25d** was isolated as colorless oil (0.165 g, 49%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 6.99-7.09 (m, 4H, ArH), 7.24-7.28 (m, 2H, ArH), 7.39 (s, 1H, ArH), 7.48-7.57 (m, 3H, ArH), 7.71 (d, ^3J = 8.12 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 114.9 (2CH, d, $^2J_{CF}$ = 22.01 Hz), 116.0 (2CH, d, $^2J_{CF}$ = 21.46 Hz), 124.2 (CF_3, q, $^1J_{CF}$ = 273.45 Hz), 125.9 (CH), 126.8 (CH, q, $^3J_{CF}$ = 5.50 Hz), 127.4 (C, q, $^2J_{CF}$ = 30.26 Hz), 128.9 (2CH, d, $^3J_{CF}$ = 8.25 Hz), 130.6 (2CH), 130.7 (C, q, $^3J_{CF}$ = 1.65 Hz), 135.4 (C, d, $^4J_{CF}$ = 3.30 Hz), 135.6 (C, d, $^4J_{CF}$ = 3.30 Hz), 140.9 (C, q, $^3J_{CF}$ = 1.65 Hz), 143.2 (C), 162.6 (CF, d, $^1J_{CF}$ = 247.04 Hz), 163.1 (CF, d, $^1J_{CF}$ = 248.14 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -56.73 ($ArCF_3$), -113.77 (ArF), -114.50 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3046 (w), 2923 (w), 2854 (w), 1894 (w), 1608 (m), 1568 (w), 1511 (m), 1490 (m), 1405 (w), 1384 (w), 1309 (s), 1264 (w), 1224 (m), 1174 (w), 1117 (s), 1095 (w), 1076 (m), 1030 (m), 1010 (w), 961 (w), 903 (w), 822 (s), 790 (m), 721 (m), 679 (m), 635 (w), 621 (w), 605 (w), 585 (w), 563 (m), 542 (m); GC-MS (EI, 70 eV): *m/z* (%): 334 (M^+, 100), 313 (7), 264 (9), 244 (6), 219 (7), 167 (6), 122 (2), 75 (1); HRMS (EI) calcd for $C_{19}H_{11}F_5$ [M^+]: 334.07754 found 334.077305.

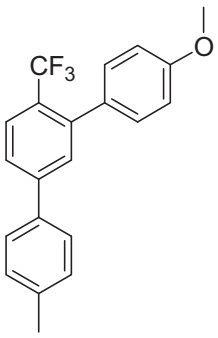
General procedure for the synthesis of 27a-d: A 1,4-dioxane solution (8 mL) of **23** (1.0 equiv.), arylboronic acid **26** (1.3 equiv.), 2M K_2CO_3 (1 mL), and $Pd(PPh_3)_4$ (5 mol%) was heated at 110 °C for 8 h. After cooling to room temperature, H_2O was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (gradient elution n-heptane/ethyl acetate).

1-(4'- Methylphenyl)-3-(4''-fluorophenyl)-4-trifluoromethylbenzene (27a):



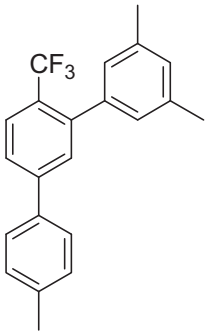
Starting with **23c** (0.12 g, 0.4 mmol), **26a** (0.072 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.023 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **27a** was isolated as colorless oil (0.037 g, 25%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 6.99-7.07 (m, 2H, ArH), 7.17-7.29 (m, 4H, ArH), 7.43-7.46 (m, 3H, ArH), 7.59 (d, ^3J = 8.31 Hz, 1H, ArH), 7.70 (d, ^3J = 8.12 Hz, 1H, ArH); ^{13}C NMR (75.46 MHz, $CDCl_3$), δ = 21.2 (CH_3), 114.8 (2CH, d, $^2J_{CF}$ = 21.46 Hz), 124.3 (CF_3, q, $^1J_{CF}$ = 273.45 Hz), 125.8 (CH), 126.7 (CH, q, $^3J_{CF}$ = 4.95 Hz), 127.1 (2CH), 127.5 (C, q, $^2J_{CF}$ = 30.81 Hz), 129.7 (2CH), 130.5 (CH), 130.7 (2CH, d, $^3J_{CF}$ = 8.25 Hz), 135.8 (C, d, $^4J_{CF}$ = 3.30 Hz), 136.4 (C), 140.8 (C, q, $^3J_{CF}$ = 2.20 Hz), 138.3 (C), 144.2 (C), 162.5 (CF, d, $^1J_{CF}$ = 247.04 Hz); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -56.64 ($ArCF_3$), -114.74 (ArF); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3028 (w), 2923 (w), 2859 (w), 2733 (w), 1901 (w), 1741 (w), 1606 (m), 1563 (w), 1512 (m), 1490 (m), 1417 (w), 1308 (s), 1282 (w), 1224 (m), 1172 (m), 1117 (s), 1076 (m), 1030 (m), 1010 (w), 962 (w), 837 (m), 810 (s), 783 (w), 741 (w), 702 (w), 639 (w), 624 (w), 587 (w), 564 (w), 542 (w); GC-MS (EI, 70 eV): *m/z* (%): 330 (M^+, 100), 289 (3), 261 (7), 246 (5), 220 (2), 183 (2), 165 (10), 144 (3), 109 (1), 91 (3), 89 (1), 75 (1), 63 (1), 51 (1), 39 (1); HRMS (EI) calcd for $C_{20}H_{14}F_4$ [M^+]: 330.10261 found 330.102661.

1-(4'- Methylphenyl)-3-(4''-methoxyphenyl)-4-trifluoromethylbenzene (27b):



Starting with **23c** (0.08 g, 0.3 mmol), **26b** (0.059 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **27b** was isolated as colorless oil (0.06 g, 59%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.31 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 6.86 (d, ^3J = 8.69 Hz, 2H, ArH), 7.15-7.24 (m, 4H, ArH), 7.39-7.44 (m, 3H, ArH), 7.52-7.55 (m, 1H, ArH), 7.68 (d, ^3J = 8.12 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.1 (CH_3), 55.3 (OCH_3), 113.3 (2CH), 124.4 (CF_3, q, $^1J_{CF}$ = 273.74 Hz), 125.3 (CH), 126.6 (CH, q, $^3J_{CF}$ = 5.49 Hz), 127.0 (C, q, $^2J_{CF}$ = 29.76 Hz), 127.1 (2CH), 129.7 (2CH), 130.2 (2CH, q, $^5J_{CF}$ = 1.37 Hz), 130.7 (CH), 132.3 (C), 136.5 (C), 138.2 (C), 141.6 (C, q, $^3J_{CF}$ = 1.83 Hz), 144.0 (C), 159.2 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -56.56 ($ArCF_3$); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3030 (w), 3000 (w), 2934 (w), 2836 (w), 1607 (m), 1562 (w), 1510 (m), 1463 (w), 1385 (w), 1307 (s), 1291 (w), 1243 (m), 1170 (m), 1116 (s), 1107 (s), 1076 (m), 1029 (s), 1004 (w), 962 (w), 930 (m), 809 (s), 762 (w), 679 (w), 624 (w), 606 (w), 587 (w), 573 (w), 545 (w); GC-MS (EI, 70 eV): *m/z* (%): 342 (M^+, 100), 279 (5), 264 (6), 249 (3), 233 (2), 215 (2), 171 (4), 124 (1), 91 (2), 65 (1), 39 (1); HRMS (EI) calcd for $C_{21}H_{17}F_3O$ [M^+]: 342.12260 found 342.122754.

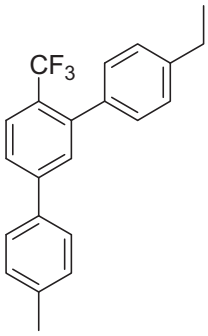
1-(4'- Methylphenyl)-3-(3'',5''-dimethylphenyl)-4-trifluoromethylbenzene (27c):



Starting with **23c** (0.08 g, 0.3 mmol), **26c** (0.058 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **27c** was isolated as colorless oil (0.065 g, 64%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.28 (s, 6H, $2CH_3$), 2.31 (s, 3H, CH_3), 6.92 (s, 2H, ArH), 6.96 (s, 1H, ArH), 7.17 (d, ^3J = 8.50 Hz, 2H, ArH), 7.42-7.45 (m, 3H, ArH), 7.53-7.56 (m, 1H, ArH), 7.68 (d, ^3J = 8.31 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 21.1 (CH_3), 21.3 ($2CH_3$), 124.4 (CF_3, q, $^1J_{CF}$ = 271.91 Hz), 125.3 (CH), 126.4 (C, q, $^2J_{CF}$ = 30.67 Hz), 126.6 (CH, q, $^3J_{CF}$ = 5.49 Hz), 126.8 (2CH, q, $^5J_{CF}$ = 1.37 Hz), 127.1 (2CH), 129.3 (CH), 129.7 (2CH), 130.5 (CH), 136.6 (C), 137.2 (2C), 138.2 (C), 139.9 (C), 142.1 (C, q, $^3J_{CF}$ = 1.83 Hz), 143.9 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -56.51 ($ArCF_3$); IR (ATR, cm^{-1}):

$\tilde{\nu}$ = 3023 (w), 2952 (w), 2919 (m), 2862 (w), 2735 (w), 1917 (w), 1598 (m), 1562 (w), 1470 (w), 1381 (w), 1307 (s), 1281 (m), 1192 (w), 1161 (m), 1119 (s), 1095 (w), 1027 (m), 964 (w), 900 (w), 858 (m), 811 (s), 772 (w), 717 (w), 704 (m), 659 (w), 646 (w), 633 (w), 589 (m), 541 (w); GC-MS (EI, 70 eV): *m/z* (%): 340 (M^+, 100), 305 (7), 271 (4), 256 (5), 239 (5), 170 (4), 162 (5), 141 (1), 127 (3), 105 (3), 91 (2), 77 (1), 65 (1), 51 (1), 39 (1); HRMS (EI) calcd for $C_{22}H_{19}F_3$ [M^+]: 340.14334 found 340.143000.

1-(4'-Methylphenyl)-3-(4''-ethylphenyl)-4-trifluoromethylbenzene (27d):



Starting with **23c** (0.08 g, 0.3 mmol), **26d** (0.059 g, 1.3 equiv.), $Pd(PPh_3)_4$ (0.017 g, 0.05 equiv.), 2M K_2CO_3 (1 mL), 1,4-Dioxane (4 mL), **27d** was isolated as colorless oil (0.04 g, 40%). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.55 Hz, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.63 (q, *J* = 7.74 Hz, *J* = 15.30 Hz, 2H, -CH_2-), 7.16-7.23 (m, 6H, ArH), 7.41-7.46 (m, 3H, ArH), 7.54-7.57 (m, 1H, ArH), 7.68 (d, ^3J = 8.31 Hz, 1H, ArH); ^{13}C NMR (62.89 MHz, $CDCl_3$), δ = 15.4 (CH_3), 21.1 (CH_3), 28.6 (-CH_2-), 124.4 (CF_3, q, $^1J_{CF}$ = 274.20 Hz), 125.3 (2CH), 126.6 (CH, q, $^3J_{CF}$ = 5.50 Hz), 127.1 (2CH), 127.3 (2CH), 128.5 (C), 128.9 (CH, q, $^4J_{CF}$ = 1.83 Hz), 129.6 (2CH), 126.9 (C, q, $^2J_{CF}$ = 30.21 Hz), 130.6 (CH), 136.5 (C), 137.3 (C), 141.9 (C, q, $^3J_{CF}$ = 1.83 Hz), 143.6 (C), 143.9 (C); ^{19}F NMR (282.40 MHz, $CDCl_3$): δ = -56.50 ($ArCF_3$); IR (ATR, cm^{-1}): IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3025 (w), 2928 (w), 2872 (w), 2731 (w), 2620 (w), 2431 (w), 2302 (w), 1905 (w), 1728 (w), 1665 (w), 1606 (m), 1514 (w), 1454 (w), 1384 (w), 1307 (s), 1265 (w), 1170 (m), 1112 (s), 1075 (m), 1029 (m), 1008 (w), 963 (w), 902 (w), 833 (w), 809 (s), 773 (w), 718 (w), 640 (w), 626 (w), 608 (w), 587 (w), 541 (w); GC-MS (EI, 70 eV): *m/z* (%): 340 (M^+, 98), 325 (100), 305 (5), 270 (6), 241 (4), 189 (2), 162 (14), 127 (3), 105 (4), 91 (4), 65 (2), 51 (1), 39 (1); HRMS (EI) calcd for $C_{22}H_{19}F_3$ [M^+]: 340.14334 found 340.142981.

Appendix: Crystal Data and Structure Refinement

Table 14. Crystal data and structure refinement for **9f.**

Identification code	**is_n15**	
Empirical formula	$C_{16}H_{13}ClN_2O_2$	
Formula weight	300.73	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 8.9306 (3) Å	α= 90.00°
	b = 24.0720 (7) Å	β= 105.2530 (10)°
	c = 13.6808 (4) Å	γ = 90.00°
Volume	2837.46 (15) $Å^3$	
Z	8	
Density (calculated)	1.408 Mg/m^3	
Absorption coefficient	0.28 mm^{-1}	
F(000)	1248	
Crystal size	0.38 x 0.27 x 0.17 mm	
Θ range for data collection	2.5° to 30.0°.	
Index ranges	$-12\leq h\leq 12$, $-32\leq k\leq 33$, $-14\leq l\leq 19$	
Reflections collected	32140	
Independent reflections	8276 [R(int) = 0.0254]	
Completeness to Θ = 30.00°	99.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.955 and 0.903	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6331 / 0 / 383	
Goodness-of-fit on F^2	1.040	
Final R indices [$F^2>2\sigma(F^2)$]	R1 = 0.0456, wR = 0.0981	
R indices (all data)	R1 = 0.0655, $wR(F^2)$ = 0.1063	
Largest diff. peak and hole	0.302 and -0.379 $e.Å^{-3}$	

Table 15. Crystal data and structure refinement for **11c**.

Identification code	**is_n10**	
Empirical formula	$C_{24}H_{22}N_2$	
Formula weight	338.44	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 15.4248 (5) Å	α= 90.00°
	b = 15.6793 (6) Å	β= 110.744 (2)°
	c = 16.1729 (6) Å	γ = 90.00°
Volume	3657.8 (2) $Å^3$	
Z	8	
Density (calculated)	1.229 Mg/m^3	
Absorption coefficient	0.07 mm^{-1}	
F(000)	1440	
Crystal size	0.54 x 0.25 x 0.22 mm	
Θ range for data collection	1.6° to 28.00°	
Index ranges	-18≤h≤20, -20≤k≤20, -21≤l≤21	
Reflections collected	36789	
Independent reflections	8834	
Completeness to Θ = 28.00°	99.9%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.984 and 0.962	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6452 / 0 / 477	
Goodness-of-fit on F^2	1.08	
Final R indices [$F^2>2\sigma(F^2)$]	R1 = 0.046, wR = 0.1292	
R indices (all data)	R1 = 0.0657, $wR(F^2)$ = 0.1400	
Largest diff. peak and hole	0.317 and -0.200 $e.Å^{-3}$	

Table 16. Crystal data and structure refinement for **16g**.

Identification code	**av_q3**	
Empirical formula	$C_{15}H_{11}ClN_2O$	
Formula weight	270.71	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 3.8558 (10) Å	α= 62.043 (10)°
	b = 13.376 (3 Å	β= 89.839 (11)°
	c = 13.951 (3) Å	γ = 84.563 (10)°
Volume	632.0 (3) $Å^3$	
Z	2	
Density (calculated)	1.423 Mg/m^3	
Absorption coefficient	0.29 mm^{-1}	
F(000)	280	
Crystal size	1.11 x 0.21 x 0.14 mm	
Θ range for data collection	1.7° to 30.0°	
Index ranges	-5≤h≤5, -18≤k≤18, -19≤l≤19	
Reflections collected	11308	
Independent reflections	3632	
Completeness to Θ = 30.0°	98.2%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.960 and 0.736	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3267 / 0 / 173	
Goodness-of-fit on F^2	1.040	
Final R indices [$F^2>2\sigma(F^2)$]	R1 = 0.0373, wR = 0.0979	
R indices (all data)	R1 = 0.0419, $wR(F^2)$ = 0.1011	
Largest diff. peak and hole	0.346 and -0.368 $e.Å^{-3}$	

Table 17. Crystal data and structure refinement for **20e**.

Identification code	**av_q19**	
Empirical formula	$C_{22}H_{17}FN_2$	
Formula weight	328.38	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.3626 (3) Å	α= 88.380 (2)°
	b = 11.8575 (4) Å	β= 85.796 (2)°
	c = 18.6843 (7) Å	γ = 88.122 (2)°
Volume	1625.37 (11) $Å^3$	
Z	4	
Density (calculated)	1.342 Mg/m^3	
Absorption coefficient	0.09 mm^{-1}	
F(000)	688	
Crystal size	0.30 x 0.12 x 0.05 mm	
Θ range for data collection	1.7° to 28.1°	
Index ranges	-9≤h≤9, -15≤k≤15, -24≤l≤24	
Reflections collected	36045	
Independent reflections	7929	
Completeness to Θ = 28.1°	99.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.996 and 0.974	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5345 / 0 / 455	
Goodness-of-fit on F^2	1.07	
Final R indices [F^2>2σ(F^2)]	R1 = 0.045, wR = 0.1128	
R indices (all data)	R1 = 0.0760, $wR(F^2)$ = 0.124	
Largest diff. peak and hole	0.27 and -0.23 $e.Å^{-3}$	

Table 18. Crystal data and structure refinement for **23c**.

Identification code	**av_a133a**	
Empirical formula	$C_{14}H_{10}ClF_3$	
Formula weight	270.67	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 9.3940 (7) Å	α= 97.508 (4)°
	b = 9.4551 (7) Å	β= 91.207 (4)°
	c = 13.7991 (9) Å	γ = 102.301 (4)°
Volume	1185.73 (15) $Å^3$	
Z	4	
Density (calculated)	1.516 Mg/m^3	
Absorption coefficient	0.34 mm^{-1}	
F(000)	552	
Crystal size	0.28 x 0.25 x 0.03 mm	
Θ range for data collection	5.5° to 64.9°	
Index ranges	-12≤h≤12, -12≤k≤12, -18≤l≤18	
Reflections collected	26270	
Independent reflections	6257	
Completeness to Θ = 28.1°	99.4%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.990 and 0.912	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3390 / 8 / 353	
Goodness-of-fit on F^2	0.97	
Final R indices [$F^2>2\sigma(F^2)$]	R1 = 0.041, wR = 0.1070	
R indices (all data)	R1 = 0.0929, $wR(F^2)$ = 0.121	
Largest diff. peak and hole	0.42 and -0.25 $e.Å^{-3}$	

Abbreviations

Ac	Acetyl
M^+	Molecular ion
calcd	Calculated
CI	Chemical Ionization
COSY	Correlation Spectroscopy
DEPT	Distortionless Enhancement by Polarization Transfer
HSQC	Heteronuclear Single Quantum Correlation
EI	Electron Impact
GC	Gas Chromatography
EI-MS	Electron Impact Mass Spectrum
HMBC	Heteronuclear Multiple Bond Correlation
HRMS	High Resolution Mass Spectrometry
IR	Infrared Spectroscopy
MS	Mass Spectrometry
mp	Melting point
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser and Exchange Spectroscopy
ORTEP	Oak Ridge Thermal Ellipsoid Plot
Ph	Phenyl
ppm	Parts per million
R_f	Retention factor
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Tetramethylsilane
Tol	Tolyl (p-MeC_6H_4)

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Erklärung / Daclaration

Hiermit erkläre ich, daß diese Arbeit bisher von mir weder an der Mathematisch-Naturwissenschaftlichen Fakultät der Universität Rostock noch einer anderen wissenschaftlichen Einrichtung zum Zwecke der Promotion eingereicht wurde. Ferner erkläre ich, dass ich diese Arbeit selbständig verfasst und keine anderen als die darin angegebenen Hilfsmittel benutzt habe.

I hereby declare that this work has so for neither submitted to the Faculty of Mathematics and Natural Sciences at the University of Rostock nor to any other scientific Institution for the purpose of doctorate. Further more, I declare that I have written this work by myself and that I have not used any other sources, other than mentioned earlier in this work.

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Publications

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[7] "Regioselective Palladium(0)-Catalysed cross-coupling reactions of 2,6-dichloroquinoxaline", **Ali, I.**; Villinger, A.; Langer, P. (*Synthesis* **2012**, accepted)

[8] "Regioselective Palladium(0)-Catalysed cross-coupling reactions of 2,4-dichloro-1-(trifluoromethyl)benzene", **Ali, I.**; Siyo, B.; Villinger, A.; Langer, P. (in preparation)

[9] "Pd/Cu Catalysed arylation of 1-deazapurines *via* C-H bond activation", **Ali, I.**; Iaroshenko, V. O.; Ostrovskyi, D.; Langer, P. (in preparation)