Synthesis of functionalized Pyridines and Quinolines by Palladium-Catalyzed Cross-Coupling Reactions

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Declaration

I hereby declare that this thesis has been written without any assistance from third parties. Furthermore, I confirm that no sources have been used in the preparation of this thesis other than those indicated in the thesis itself.

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Rodisnel Perdomo Rivera

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Abstract

This thesis deals with the functionalization of pentahalogenated pyridines and dihalogenated quinolines through palladium catalyzed cross coupling reactions. This includes the synthesis, chemo-selective arylation and alkynylation of 4-bromo-2,3,5-trichloro-6-iodopyridine using Suzuki-Miyaura and Sonogashira reactions. Synthesized pentaalkynylated pyridines show strong fluorescence and were consequently analysed by UV/Vis- and fluorescence spectroscopy.

The chemo-selective arylation of 4,6-dihalogenated-2-(trifluoromethyl) quinoline by Suzuki-Miyaura reaction was studied. Obtained derivatives were evaluated for their potential to inhibit ecto-5'-nucleotidase for both human and rat.

Besides, the synthesis of indolo [2,3-*c*] quinolines was studied by sequential chemo-selective Suzuki-Miyaura reaction followed by double C-N coupling starting from 3-bromo-4-iodoquinoline.

Zusammenfassung

Die vorliegende Arbeit beschäftigt sich mit der Funktionalisierung von pentahalogenierten Pyridinen und dihalogenierten Chinolinen mittels Palladium katalysierter Kupplungsreaktionen. Dabei wurde eine Synthesemethode für 4-Brom-2,3,4-trichlor-6-iodpyridin entwickelt und diese Verbindung in chemoselektiven Arylierungen sowie Alkinylierung mittels Suzuki-Miyaura- bzw. Sonogashira-reaktionen eingesetzt. Die erhaltenden pentaalkinylierten Verbindugnen zeigen eine starke Fluoreszenz und wurden folglich mittels UV/Vis und Fluoreszenzspektroskopie näher untersucht.

Weiterhin wurden chemoselektive Arylierungen an zweifach halogenierten 2-(Trifluomethyl)-chinolinen durch Suzuki-Miyaura Reaktionen untersucht. Diese Verbindungen wurden zusätzlich bezüglich ihrer Inhibierungsaktivität hinsichtlich ecto-5‘-Nukleotidase untersucht.

Eine Darstellung von Indol[2,3-*c*]chinolinen unter Anwendung chemoselective Suzuki-Miyaura Reaktion und anschließender doppelte C-N Kupplung gelang ausgehend von 3-Brom-4-iodchinolin und bildet den Abschluss dieser Arbeit.

List of Abbreviations

Anal. calcd.	Elemental Analysis
Ar	Aryl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
calcd	Calculated
DCM/CH_2Cl_2	Dichloromethane
DEPT	Distortionless Enhancement by Polarisation Transfer
DMAC	Dimethylacetamide
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
dppf	1,1'- Bis(diphenylphosphino)ferrocene
ε	Extinction coefficient
EI	Electron Ionization
ESI	Electrospray Ionization
Et	Ethyl
Equiv.	Equivalent
GC	Gas chromatography
h	Hour
Hetar	Heteroayl
HRMS	High Resolution Mass Spectroscopy
Hz	Hertz
IR	Infrared spectroscopy
*i*Pr	Isopropyl
J	Coupling constant
Me	Methyl
mp	Melting point
MS	Mass Spectrometry
NEt_3	Triethylamine
NMR	Nuclear magnetic resonance
*n*Pr	*n*-Propyl
OMe	Methoxy
ORTEP	Oak Ridge Thermal Ellipsoid Plot
ppm	Parts per million

PCy_3	Tricyclohexylphosphine
[Pd]	Palladium complex
Ph	Phenyl
PPh_3	Triphenylphosphine
$PtBu_3 \cdot HBF_4$	Tri-*tert*-butylphosphonium tetrafluoroborate
DIPA/ $HN(iPr)_2$	Di-*iso*propylamine
R	Organic moiety
R_f	Retention factor
rt	Room temperature
SPhos	2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
UV/Vis	Ultraviolet and visible absorption spectroscopy
XPhos	2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl
λ	Wavelength
ϕ	Fluorescence quantum yield

Contents

1. Introduction

The synthesis of new molecular entities is of special interest for the development of many areas of research ranging from materials science to biological or pharmaceutical science. Therefore, the development of more efficient and economical synthetic methods is a priority of organic chemistry today. In this sense it is increasingly important to decrease the number of synthetic steps, the quantity of starting materials required and the formation of side-products.[1] Catalysis has proven to be very efficient for the development of reactions with high selectivity and high atom economy.

Catalysis is a phenomenon known since ancient times. Nowadays it plays a fundamental role in the manufacture of the vast majority of chemicals used by our society. In 1835 Berzelius recognized the effect of catalysts and was the first to propose the term catalysis. The first and still valid definition comes from Wilhelm Ostwald: "Catalysis is the acceleration of a slow chemical process by the presence of a foreign substance". Later he could specify it even more: "A catalyst is any substance that, without appearing in the final product of a chemical reaction, its speed changes".[2]

Presently, most of industrial chemical processes are based on catalysis. The replacement of classical stoichiometric methodologies with cleaner catalytic alternatives is promoted by a growing environmental awareness to reduce a waste production. Even today, more than 90 % of the chemical products are based on at least one catalytic step. For example, most of modern petrochemical technologies are catalytic one-step processes with high atom utilization.[3,4]

Cross-coupling reactions catalyzed by transition metals represent one of the most famous methodologies in modern organic chemistry and is becoming an indispensable tool for the synthetic organic chemist.[5] In recent years the application of this methodologies in the synthesis of drugs or products with potential biological activity[6] and new materials[7] is very common.

To carry out this type of couplings, a broad spectrum of transition metals has been used, in which undoubtedly, palladium is one of the most used metals in recent years due to the high catalytic activity of the complexes formed by this metal. In addition, Palladium-catalyzed cross-couplings reactions allows the control of the region-selectivity,[8] chemo-selectivity[9] and the possibility for multiple coupling reactions.[10]

Palladium catalysts offer a broad functional group tolerance, low toxicity and low sensitivity to air and moisture.[11]

The great variety of reactions of coupling C-C and C-Het bonds catalyzed by palladium has caused that, in the last century, an enormous quantity of publications in international scientific journals has appeared. In 2010, the importance of these processes in all areas of science was rewarded with the Nobel Prize in Chemistry to three representative researchers in this field: Richard F. Heck, Ei-ichi Negishi and Akira Suzuki.[12]

Until now, a wide range of palladium-catalyzed cross-coupling reactions for the formation of carbon-carbon bonds have been established. Figure 1 shows the most commonly utilized cross-couplings in organic synthesis.

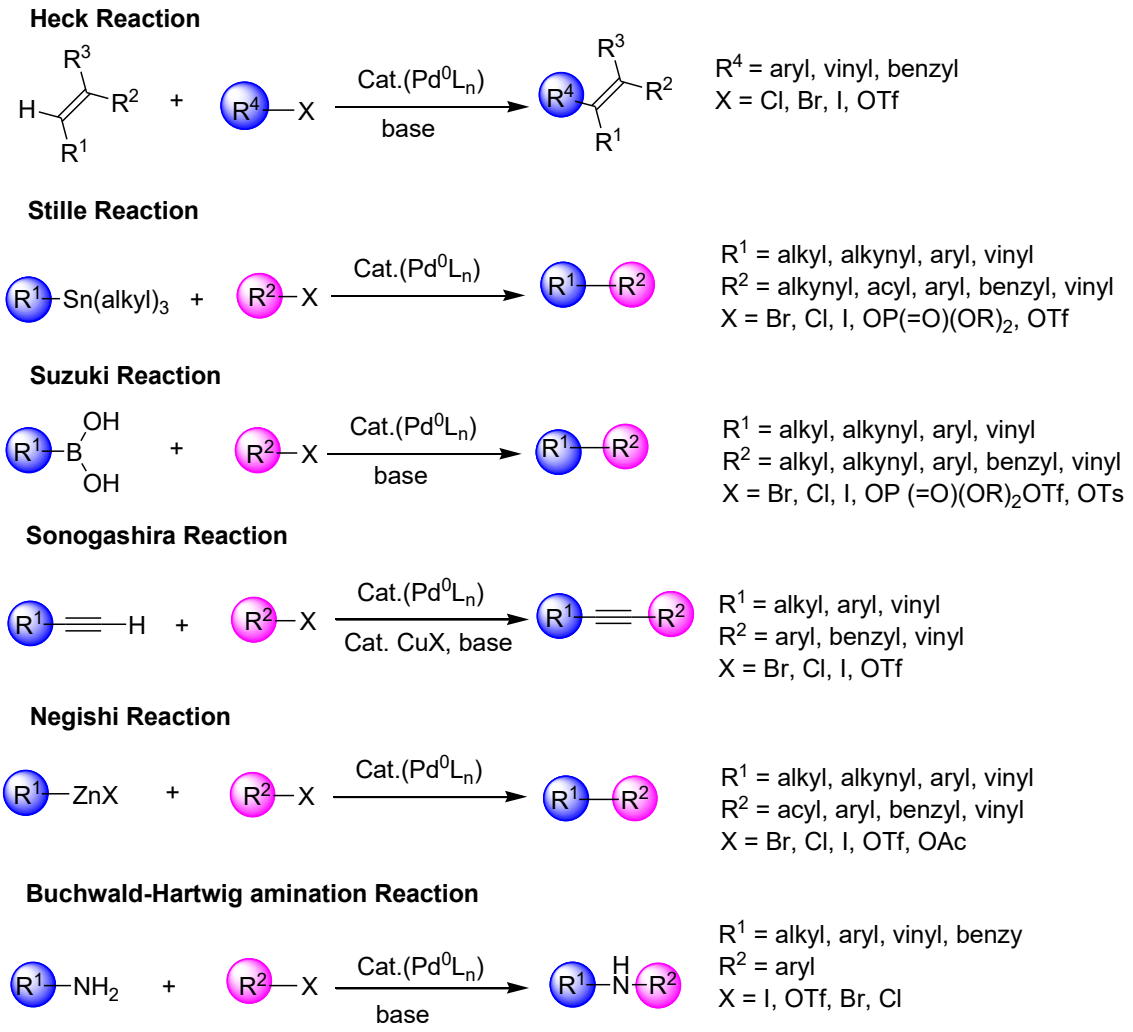


Figure 1. Prominent palladium-catalyzed cross-coupling reactions in organic synthesis.[13, 14]

Mechanistically, these reactions are very similar except for the Heck reaction. A general mechanism is shown in Figure 2.[15]

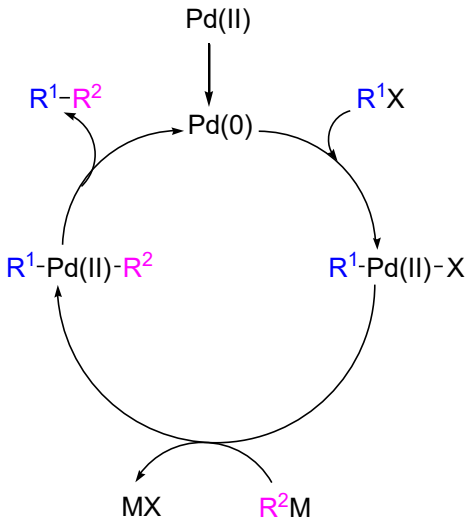


Figure 2: General mechanism of the cross-coupling reaction

Generally palladium-catalyzed coupling processes starts from a Pd(0) complex. However, as a source of palladium, Pd(0) or Pd(II) complexes can be used. The Pd(II) complexes are usually more stable than those of Pd(0).

The active species of palladium(0) is formed in situ either by dissociation of ligands derived from a complex of Pd(0) or by reduction of a Pd(II) precursor. Historically, reduction has often been effected by phosphines such as PPh_3 which generates the palladium(0) complex in addition to oxidized phosphorus by-products .[16-20] Afterwards, the oxidative addition of the organic electrophile R^1-X onto the Pd(0) can occur by different ways: associative bimolecular process (S_N2 reaction), radicalic or Ionic.

Due to the different strength of the C-X bond, iodides react faster than bromides, which in turn react faster than chlorides. Aryl fluorides are generally not reactive. In the case of aryl chlorides and -bromides, the oxidative addition is the rate limiting step.

The resulting organopalladium(II) complex then reacts in the transmetallation step with an organometallic compound. The result is a diorganopalladium(II) complex. When highly reactive aryl halides (e.g. iodides) are used, transmetallation is rate-limiting. Subsequently, reductive elimination of the desired organic coupling product is produced and the palladium(0) catalyst is regenerated (reductive elimination).

1.1. Suzuki-Miyaura Reaction

In 1979 N. Miyaura, A. Suzuki and co-worker were the first to describe a procedure about palladium-catalyzed cross-coupling reactions of aryl- or alkenyl halides or -triflates in the presence of organoboranes, organoboronic acids as well as organoboronic esters (cf. Figure 1, 3).[21] This popular method is universally known as Suzuki-Myaura reaction. In recent years, many papers and patents regarding the Suzuki-Myaura reaction were reported to improve site-selectivity, chemo-selectivity, low catalyst loading, expansion of substrates scope and applications of greener process-conditions (green solvent, low catalyst loading, recycling of catalyst, low temperature, minimizing side-products).[22, 23]

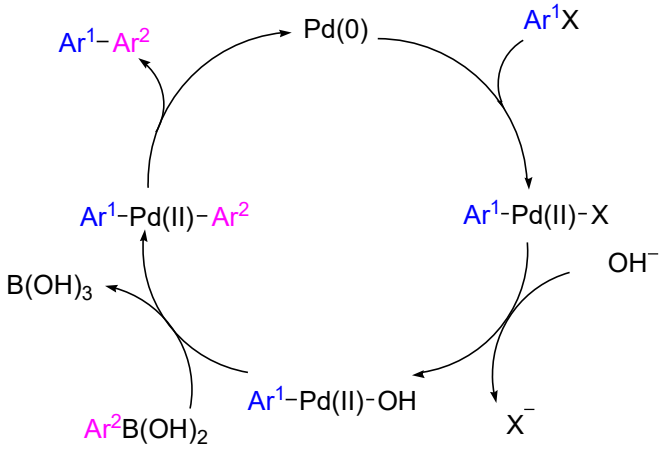


Figure 3. Possible reaction mechanism for Suzuki-Miyaura coupling

1.2. Sonogashira Cross-Coupling Reactions

The Sonogashira reaction was discovered in 1975 based on preliminary studies carried out independently by the groups of Cassar[24], Heck[25] and Sonogashira[26]. This reaction consists of a coupling of terminal alkynes with activated sp^2-carbons (halides or pseudohalides), using a palladium catalyst and a copper(I) co-catalyst (cf. Figure 1).

The mechanism of the Sonogashira reaction is based on a Cu/Pd transmetallation process in the presence of amines, consisting of two independent catalytic cycles. The cycle I contains typical oxidation addition, transmetallation and reductive elimination processes and cycle II results in the formation of the alkynyl copper reagent required for the transmetallation of cycle I (Figure 4).

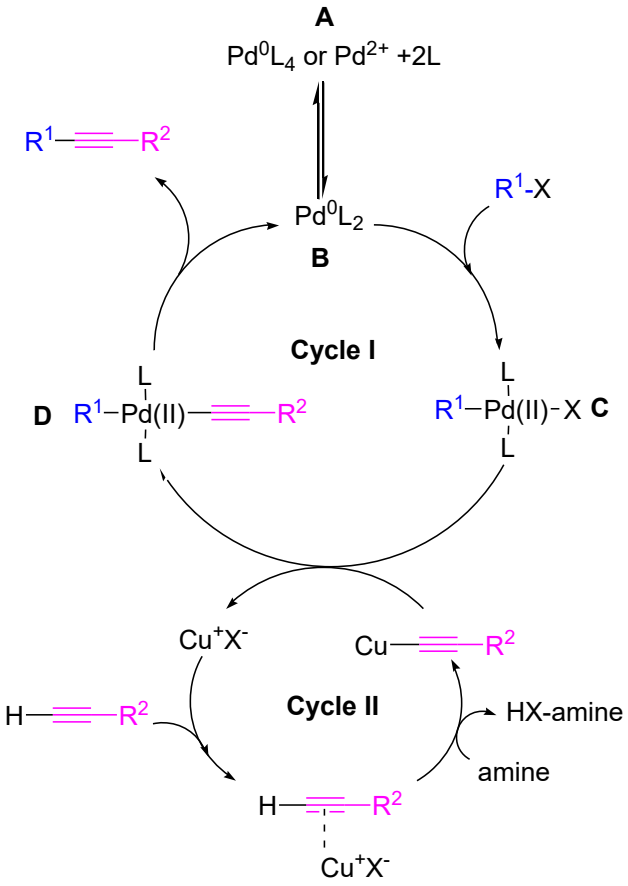


Figure 4. Proposed mechanism for the Sonogashira reaction.[27]

The efficiency of Sonogashira reactions are influenced by the steric and electronic effects of the employed alkyne and organic electrophile utilized as well as the bases, solvents and catalyst systems used.

1.3. Buchwald-Hartwig amination reaction

In 1994 the groups of Stephen L. Buchwald and John F. Hartwig independently developed the Buchwald-Hartwig amination reactions.[28] This important reaction is based on the formation of C-N bonds by Pd-catalyzed cross-coupling of amines with aryl halides. The efficiency demonstrated by the Buchwald-Hartwig amination reactions in the synthesis of aryl amines, mainly replaced conventional methods such as the Goldberg reaction, nucleophilic aromatic substitution and reductive amination.

After intensive studies with different ligand systems, different catalytic cycles for Buchwald-Hartwig reactions have been proposed. However, a catalytic cycle which has been recently suggested by Buchwald[29] for dialkylbiaryl phosphines is depicted in

Figure 5. After the formation of the catalytic species Pd^0L_n (n commonly = 2; sometimes n = 1; L = tertiary phosphines) follows an oxidative addition of the aryl halide to Pd^0L_n and subsequent coordination of the amine to the resulting palladium(II) intermediate. Base deprotonates the amine and the arylamine product are formed by reductive elimination and the catalyst is regenerated.

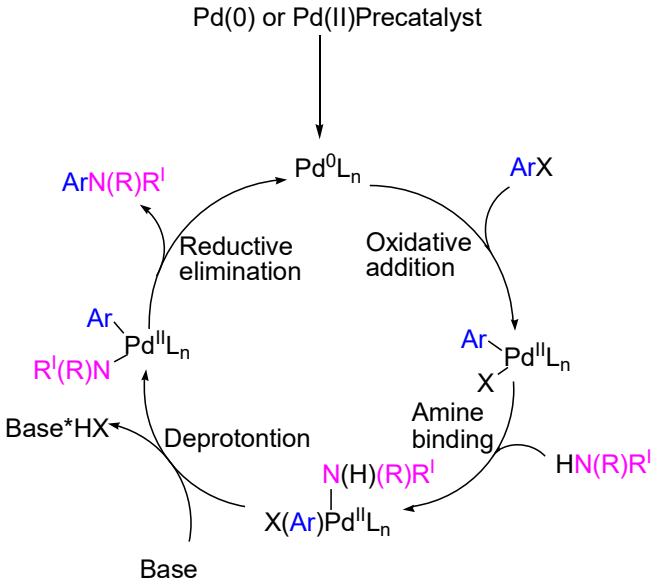


Figure 5. Catalytic cycle for palladium-catalyzed amination

It is important to point out that if amines possess β-hydrogen atoms, the $[PdL_nAr((NCH_2R)R^I)]$ complex may undergo a β-hydride elimination reaction to generate an imine as side-product (Figure 6).

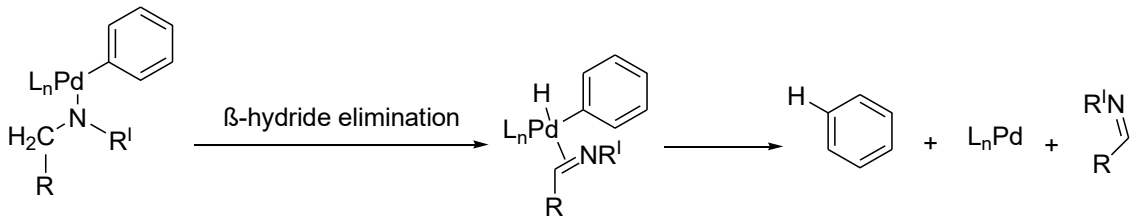


Figure 6. β-hydride elimination in Buchwald-Hartwig amination.

$Pd(OAc)_2$ and $Pd_2(dba)_3$ are common precursors which have been used for Buchwald-Hartwig reactions.

1.4. Purpose and scope of the present work

Palladium-catalyzed cross-coupling reactions have a growing impact on the development of new pharmaceuticals and materials. The application of these methods for the selective functionalization of polyhalogenated nitrogen heterocycles is increasingly attractive to synthetic chemists. Although aryl chlorides have the advantage of being cheaper and more widely available than the corresponding bromides and iodides.[30] These last ones, have the advantage of being much more reactive especially in Suzuki-Miyaura and Sonogashira reactions. Therefore, the presence of the different halogens in the same heterocycle makes selective reactions possible at specific positions with good yields.

In this work, simple pentahalogenated pyridine precursors will be studied for use in chemo-selective functionalization through Suzuki-Miyaura and Sonogashira reactions. In addition, selective arylation of 4,6-dihalogenated-2- (trifluoromethyl) quinoline will be developed and tested for their biological activity against ecto-5'-nucleotidase enzymes. Finally, the synthesis of indolo[2,3-*c*]quinolines will be studied by sequential chemo-selective Suzuki-Miyaura reaction followed by double C-N coupling starting from 3-bromo-4-iodoquinoline.

2. Synthesis of Functionalized Pyridines by Chemoselective Suzuki-Miyaura and Sonogashira Reactions.

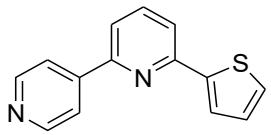
2.1. Chemoselective Suzuki-Miyaura Reaction of 4-bromo-2,3,5-trichloro-6-iodopyridine

2.1.1. Introduction

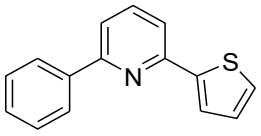
Pyridine was discovered in 1849 by the Scottish chemist Thomas Anderson as one of the constituents of bone oil.[31] In the following years it was found to be a part of many compounds related to life, such as Nicotinic acid (Vitamin B3), Pyridoxine (Vitamin B6), and NAD, to mention a few examples.

Pyridine derivatives are associated with diverse pharmacological properties such as antimicrobial,[32, 33] anticancer,[34] anticonvulsant,[35] and anti-HlV[36] activities. In the pharmaceutical industry, pyridine forms the nucleus of over 7000 existing drugs.[37]

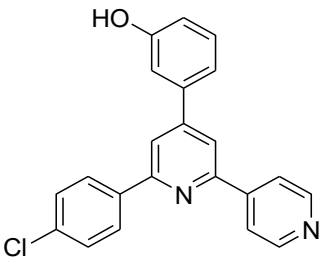
Naturally, such diversity in biological properties of pyridine derivatives attracted attention of synthetic and pharmaceutical chemists. In 2008 Eung-Seok Lee and co-workers synthesized 2,6-diaryl-substituted pyridines by modified Kröhnke procedure, which showed moderate cytotoxicity against several human cancer cell lines.[38] Four years later the same research group synthesized 2,4,6-triaryl –substituted pyridines which showed better cytotoxicity against several human cancer cell lines than the previous series of compounds mentioned above.[39] Hence, polysubstitution of pyridine could offer a range of compounds with potential high biological activity against cancer cells.



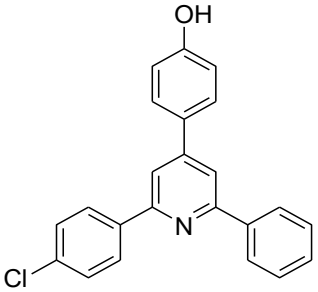
2-(pyridin-4-yl)-6-(thiophen-2-yl)pyridine



2-phenyl-6-(thiophen-2-yl)pyridine



2-(4-chlorophenyl)-4-(3-hydroxyphenyl)
-6-(pyridin-4-yl)pyridine



2-(4-chlorophenyl)-4-(4-hydroxyphenyl)
-6-(phenyl)pyridine

Figure 1. Arylated pyridines synthesized by the research group of Eung-Seok Lee with cytotoxicity against several human cancer cell lines.

Currently there is a wide variety of procedures that describe the synthesis of polyfunctionalized pyridines. Most of these are limited by the number of synthetic steps required. For example, despite being the first to synthesize the pentaarylpyridine with five different aryl groups, the procedure reported by Schmitt *et al* needed 13 steps to achieve the final product.[40] Another factor that limits many of new methods reported is the low variability of functional groups introduced to the pyridine ring, as is the case of the procedures described by Yamaguchi and co-workers[41,42] and Nishiwaki and co-workers.[43]

Site-selective Suzuki-Miyaura reactions of pentahalogenated pyridines provide a convenient method for the selective synthesis of highly functionalized pyridines, due to the broad range of functional groups and facile synthetic accessibility of boronic acids.

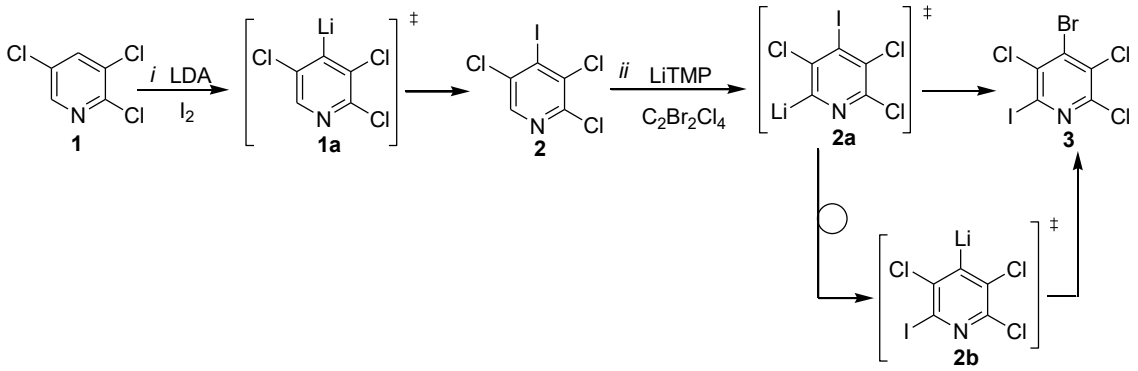
In this sense, my research group has accumulated a great experience in synthesizing highly functionalized pyridines by site-selective Suzuki-Miyaura reaction, using polyhalogenated pyridine as starting materials.[44] However, in case of pentachloropyridine electron density distribution of the pyridine core changed by introduction of arylrings in position 2 and 6, limiting the selectivity at position 4. Hence, selective arylation was impeded to access tri- and tetraarylated pyridines.

All these results led me to think that 4-bromo-2,3,5-trichloro-6-iodopyridine is an interesting starting material to explore the chemoselectivity in Suzuki-Miyaura reaction. The presence of bromine and iodine atoms as better leaving groups than chlorine, allows changing the regioselectivity of the cross-coupling reaction at the pyridine nucleus as compared to pentachloropyridine. Therefore, 4-bromo-2,3,5-trichloro-6-iodopyridine might guarantee a better selectivity, fundamentally at positions 6 and 4, giving rise to the formation of new molecules by the successive introduction of aryl substituents to the nucleus of the pyridine.

2.1.2. Synthesis of 4-bromo-2,3,5-trichloro-6-iodopyridine

For the synthesis of the novel starting material 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (Scheme 1), only 2 reaction steps are required, starting from commercially available 2,3,5-trichloropyridine, adapting a procedure described by Bobbio *et al.*.[45] First, lithiation of 2,3,5-trichloropyridine occurred selectively at position 4. Further treatment with iodine produced 2,3,5-trichloro-4-iodopyridine **2** in 75% yield. In the second

reaction step, deprotonation of 2,3,5-trichloro-4-iodopyridine **2** was performed with the base lithium 2,2,6,6-tetramethylpiperidide (LiTMP). It is important to note that initially generated 6-lithiated species **2a** instantaneously metamorphosed by migration of the heavy halogen to the less basic 4-lithiated isomer **2b**. Finally lithiated species **2b** was quenched by the addition of 1,2-dibromotetrachloroethane giving 4-bromo-2,3,5-trichloro-6-iodopyridine **3** in 77 % yield.



Scheme 2. Synthesis of starting material **3**. *i:* 1) **1**(1.0 equiv.), LDA (1.0 equiv.), THF, -78 °C, 2 h; 2) I_2 (1.2 equiv.), THF, -78 °C, 2 h. *ii:* 1) **2** (1.0 equiv.), LiTMP (1.0 equiv.), THF, -100 °C, 2 h; 2) $C_2Br_2Cl_4$ (3.3 equiv.), THF, -78 °C, 2 h.

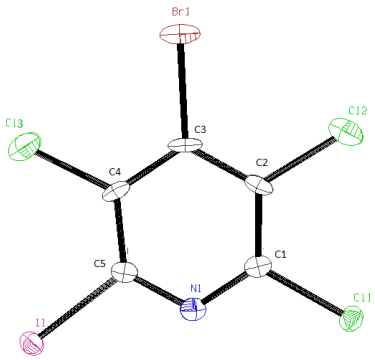


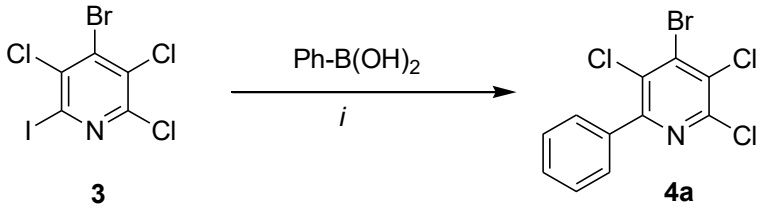
Figure 2. Single crystal structure of compound **3**.

^{1}H-NMR spectroscopic analysis allowed to observe that the only signal in the form of a singlet that previously appeared at 8.22 ppm for the proton belonging to compound **2**, disappeared for new starting material **3**. The analysis of the ^{13}C-NMR and DEPT spectra allowed identifying that the carbon signal that appeared as CH at 144.3 ppm for compound **2**, appeared in the starting material **3** as quaternary carbon at 138.9 ppm. The spectrum of GC/MS and HR-MS corroborated the presence of bromide as substituent

and later the structure of starting material **3** was confirmed by X-ray crystallographic analysis (Figure 2). IR and Elemental Analysis were also analyzed.

2.1.3. Chemoselective monoarylation to position 6

Having in hand 4-bromo-2,3,5-trichloro-6-iodopyridine **3** as a starting material, I started to search for suitable conditions for the monoarylation, using $Pd(PPh_3)_4$ (5 mol%) as a catalyst, K_3PO_4 (1.1 equiv) as base, phenylboronic acid (1.1 equiv.) in the presence of toluene as solvent at 100 °C for a period of 22 h. Although the desired compound **4a** was obtained with only 40 % yield (Scheme 2, Table 1, entry 1), these conditions served as a reference for the optimization process. The best yield was obtained when the amount of arylboronic acid was increased to 1.5 equivalents and a solvent mixture of toluene, water and ethanol was employed (entry 3). It is noteworthy, that the use of a more active catalyst system based on $Pd(OAc)_2$ and PCy_3 led to the formation of corresponding diarylated pyridine, exclusively (entry 4).



3 **4a**

Scheme 2. Optimization for the synthesis of **4a**. Conditions: *i*, **3** (1.0 equiv.), $PhB(OH)_2$, Pd -species, ligand, K_3PO_4 , solvent, 100 °C, 22 h.

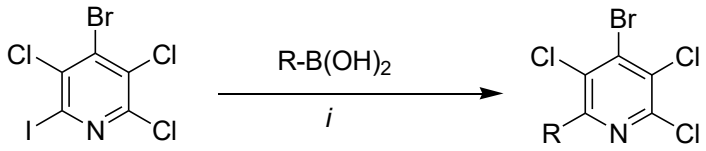
Table 1. Optimization for Synthesis of **4a**.

Entry	Pd source (mol%)	Ligand (mol%)	Base (equiv.)	Solvent	$PhB(OH)_2$ (equiv.)	4a (%)[a]
1	$Pd(PPh_3)_4$ (5)	-	K_3PO_4 (1.1)	Toluene	1.1	40
2	$Pd(PPh_3)_4$ (5)	-	K_3PO_4 (1.5)	Toluene	1.5	60
3	$Pd(PPh_3)_4$ (5)	-	K_3PO_4 (1.5)	Toluene/H_2O/ EtOH (6:1:1)	1.5	78
4	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4 (1.1)	Toluene	1.1	-

[a] Yield of isolated products.

Using optimized conditions a range of 4-bromo-2,3,5-trichloro-6-arylpyridines **4a-k** was synthesized in 60 – 86 % yield (Scheme 3, Table 2). Electron donating as well as electron withdrawing groups resulted in high yields (products **4a-g**, and **4i**). However, reaction of arylboronic acids bearing a trifluoromethyl, cyano or chloro substituent led to a decrease in yield (products **4h, 4j** and **4k**). In all the cases, the reactions were developed with high selectivity at position 6, since a reaction at another position was not observed.

Sterical hindrance by a methoxy group might have a negligible effect on the reaction outcome as emphasized by the synthesis of compounds **4c**, **4e** and **4i**. In particular the highest yield was obtained for compound **4i**, consisting of an *ortho*-methoxy group.



3 **4a-k**

Scheme 3. Synthesis of **4a-k**. Reaction conditions *i*: **3** (1.0 equiv.), R-B(OH)$_2$ (1.5 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (5 mol%), Toluene/EtOH/H_2O (6:1:1), 22 h, 100 °C.

Table 1. Chemoselective synthesis of monoarylated pyridines **4a-k**.

Compound	R	4 [%][a]
a	C_6H_5	78
b	4-MeC_6H_4	83
c	4-(MeO)C_6H_4	73
d	4-FC_6H_4	73
e	3-(MeO)C_6H_4	77
f	2-thienyl	81
g	3-(NO_2)C_6H_4	78
h	4-$CF_3C_6H_4$	60
i	2-(MeO)C_6H_4	86
j	4-(CN)C_6H_4	60
k	4-ClC_6H_4	69

[a] Yield of isolated products.

As expected, the monoarylation of 4-bromo-2,3,5-trichloro-6-iodopyridine **3**, allowed to achieve singinificantly higher yields than coresponding homologs synthesized by Ehlers *et al*. using Pentachloropyridine as starting material.[46] These excellent results are due to the fact that iodine in position 6 of the starting material **3** is a better leaving group than chlorine in pentachloropyridine.

The structure of compounds **4k** was independently confirmed by X-Ray diffraction analysis (Figure 3). The aryl group attached to the pyridine moiety of this compound is twisted out of plane and shows a torsion angle of 48.08° (N1-C5-C32-C33).

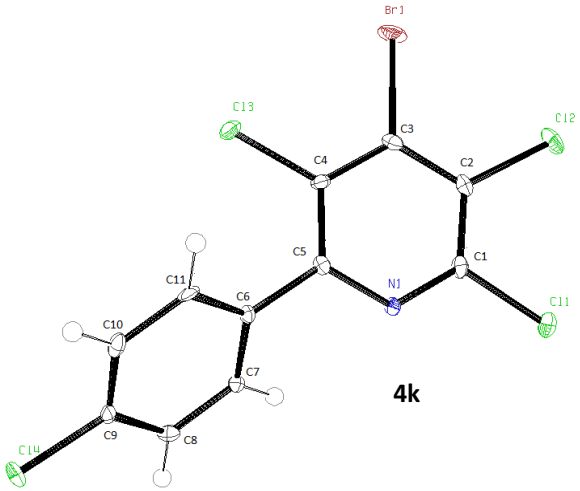
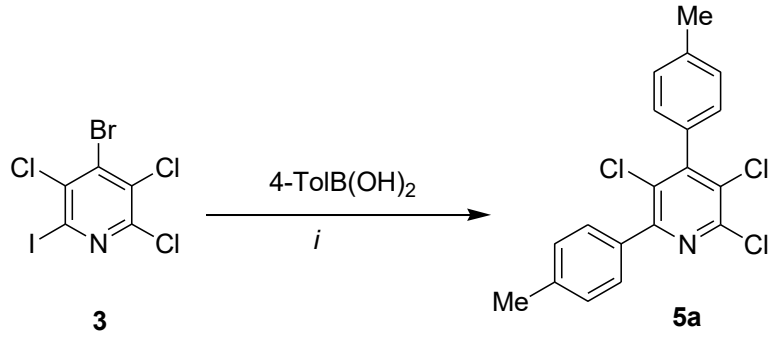


Figure 3: Single crystal structure of compound **4k**, nitrogen atoms blue, chlorine atoms green and bromine atom brown.

2.1.4. Chemoselective diarylation at positions 6 and 4.

Knowing that in a previous investigation Reimann *et al*.[44] employed pentachloropyridine as starting material and achieved selective diarylation at positions 2 and 6 of the pyridine nucleus. I assumed that 4-bromo-2,3,5-trichloro-6-iodopyridine **3** could also be an ideal substrate for chemoselective synthesis of 4,6-diarylpyridines (Scheme 4), giving access to regioisomeric 2,4-arylated pyridines.



3 5a

Scheme 4. Optimization for the synthesis of **5a**. Conditions: *i*, **3** (1.0 equiv.), 4-TolB(OH)$_2$, Pd -species (5 mol%), ligand (10 mol%), K_3PO_4, toluene/water/*n*-butanol (6:1:1), T °C, time h.

Table 2. Optimization for the synthesis of **5a**.

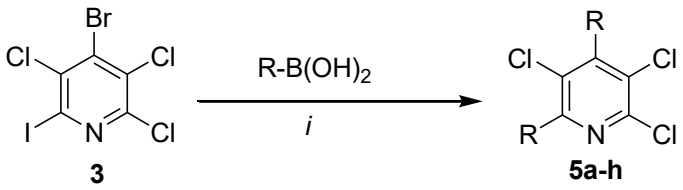
Entry	Pd source (mol%)	Ligand (mol%)	Base (equiv.)	4-TolB(OH)$_2$ (equiv.)	T (°C)	time (h)	5a (%)[a]
1	$Pd(PPh_3)_4$ (5)	-	K_3PO_4 (2.5)	2.5	100	19	50
2	$Pd(PPh_3)_4$ (5)	-	K_3PO_4 (2.5)	2.5	130	31	59
3	$Pd(PPh_3)_4$ (5)	-	K_3PO_4 (3.0)	3.0	130	31	62
4	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4 (2.0)	2.0	100	19	75
5	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4 (2.1)	2.1	100	19	81
6	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4 (2.5)	2.5	100	19	67
7	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4 (3.0)	3.0	100	19	58
8	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4 (3.5)	3.5	100	19	38

[a] Yield of isolated products

In the previous study I have already recognized PCy_3 might a good ligand for the diarylation of compound **3**. Hence, for the optimization of this reaction I selected $Pd(PPh_3)_4$ and $Pd(OAc)_2/PCy_3$ as catalyst (table 3). As expected, the best conditions for this chemoselective diarylation was when $Pd(OAc)_2$ (5 mol%) and PCy_3 was employed in the presence of K_3PO_4 (2.1 equiv) as base, *p*-Tolylboronic acid (2.1 equiv), toluene / water / *n*-butanol as solvent mixture at 100 °C, for a period of 19 h (entry 5). Increase in temperature, time, amount of base or corresponding arylboronic acid did not improve the yield.

The reaction of **3** with various arylboronic acids, using my optimized conditions (Table 3, entry 5), afforded 2,3,5-trichloro-6,4-diarylpyridines **5a-h** (Table 4) in moderate to very good yields (34-81 %). Compounds **5g** and **5h** were obtained in moderate yields, which can be explained by the formation of substantial amounts of triarylated side-products using electron-poor arylboronic acids, which might electronically activate the monoarylated intermediate and diarylated products for further coupling.

The presence of two methyl groups in *meta* position of the aryl ring in compound **5e** is evidence that substituents in this position do not represent an impediment for this double coupling.



3 **5a-h**

Scheme 5. Synthesis of **5a-h**. Reaction conditions *i*: **3** (1.0 equiv.), R-B(OH)$_2$ (2.1 equiv.), K_3PO_4 (2.1 equiv.), Pd(OAc)$_2$ (5 mol%), PCy_3 (10 mol%), Toluene/*n*BuOH/H_2O (6:1:1), 19 h, 100 °C.

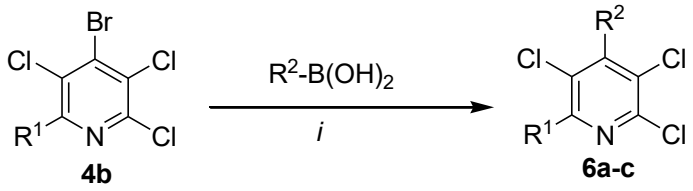
Table 3. Synthesis of 4,6-diarylated pyridines **5a-h**.

Compound	R	5 [%][a]
a	4-MeC_6H_4	81
b	4-ClC_6H_4	77
c	4-(MeO)C_6H_4	54
d	4-(CN)C_6H_4	66
e	3,5-(Me)$_2C_6H_4$	72
f	4-EtC_6H_4	58
g	3-ClC_6H_4	34
h	4-$CF_3C_6H_4$	35

[a] Yield of isolated products

2.1.5. Chemoselective arylation at positions 6 and 4 in a two-step procedure

For the chemoselective synthesis of the diarylated pyridines **6a-c** (Scheme 6, table 5) having two different aryl substituents, the same conditions described for the monoarylation were used in each of the two required reaction steps. First, compound **4b** (table 2) was synthesized, which was used for the next step by reaction with 1.5 equivalents of the respective arylboronic acid. The yields of **6a-c** are not affected by the nature of the substituents employed. However, separation problems from corresponding triarylated side products are mainly the reason for the moderate isolated yields.



Scheme 6. Synthesis of **6a-c**. Reaction conditions *i*: **4b** (1.0 equiv.), R^2-$B(OH)_2$ (1.5 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (5 mol%), Toluene/*n*BuOH/H_2O (6:1:1), 19 h, 100 °C.

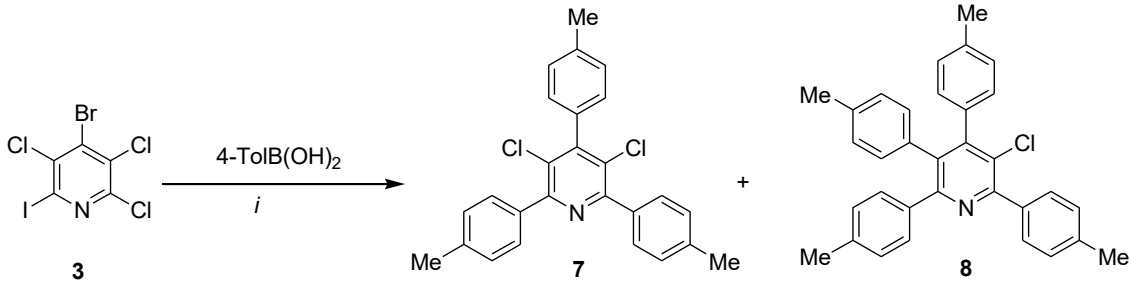
Table 4. Synthesis of 4,6-diarylated pyridines **6a-c**.

Compound	R^1	R^2	6 [%][a]
a	4-MeC_6H_4	4-$(CN)C_6H_4$	50
b	4-MeC_6H_4	3-$(NO_2)C_6H_4$	55
c	4-MeC_6H_4	3-$(MeO)C_6H_4$	48

[a] Yield of isolated products

2.1.6. Chemoselective triarylation at positions 6, 4 and 2

The selective synthesis of triarylated pyridine **7** in a single reaction step, starting from starting material **3**, was developed in the presence of $Pd(OAc)_2$ using PCy_3 or SPhos as a ligand, modifying the amount of 4-tolylboronic acid and the temperature in a solvent mixture consisting of toluene/water/*n*-butanol. Unfortunately, in spite of up to 100 % conversion of the starting material **3**, I obtained an inseparable mixture by column chromatography of the expected 3,5-dichloro-2,4,6-triarylpyridine **7** and tetraarylated 3-chloro-2,4,5,6-tetraarylpyridine **8** (Scheme 7, Table 6). The presence of both compounds in the mixture was confirmed by GC-MS analysis.



Scheme 7. Optimization for the synthesis of **7** (mixtures**7**+**8**): Conditions: *i*, **3** (0.26 mmol), 4-TolB(OH)$_2$, Pd -species (5 mol%), ligand (10 mol%), K_3PO_4 (3 equiv.), toluene/water/*n*-butanol (6:1:1), T °C, 19 h.

Table 6. Optimization of triple coupling reaction (Mixtures **7**/**8**)

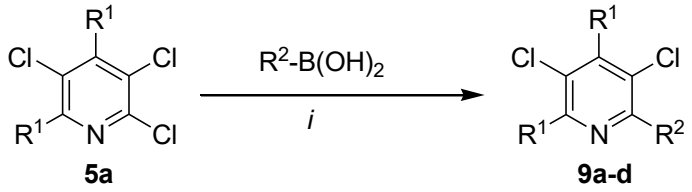
Entry	Pd source (mol%)	Ligands (mol%)	4-TolB(OH)$_2$ (equiv.)	T (°C)	Conversion [%]
1	Pd (OAc)$_2$ (5)	PCy_3 (10)	2.5	100	91
2	Pd (OAc)$_2$ (5)	PCy_3 (10)	3.0	100	95
3	Pd (OAc)$_2$ (5)	PCy_3 (10)	3.5	100	99
4	Pd (OAc)$_2$ (5)	PCy_3 (10)	4.0	100	100
5	Pd (OAc)$_2$ (5)	PCy_3 (10)	4.5	100	100
6	Pd (OAc)$_2$ (5)	SPhos (10)	3.2	100	100
7	Pd (OAc)$_2$ (5)	SPhos (10)	3.0	100	100
8	Pd (OAc)$_2$ (5)	SPhos (10)	3.2	70	84

The conversion was determined from isolated amount of starting material after the reaction.

2.1.7. Chemoselective triarylation at positions 6, 4 and 2 in a two-step procedure

To overcome the separation problems presented in the previous section, I explored the possibility of achieving the synthesis of 2,4,6-triarylated pyridines **9** in a stepwise procedure, starting from synthesized product **5**. To my delight, I obtained triarylated priridines **9a-d** (Scheme 8, Table 7), starting from **5a,** using Pd(PPh$_3$)$_4$ as catalyst in the presence of 1.2 equivalents of the respective arylboronic acids for 20 hours at 100 °C. The difficulties associated with the process of separation by column chromatography

were the main reason of obtained moderate yields, independently from the substitution pattern of the employed arylboronic acid.



Scheme 8. Synthesis of **9a-d**. Reaction conditions *i*: **5a** (1.0 equiv.), R^2-$B(OH)_2$ (1.2 equiv.), K_3PO_4 (1.2 equiv.), $Pd(PPh_3)_4$ (5 mol%), Toluene, 20 h, 100 °C.

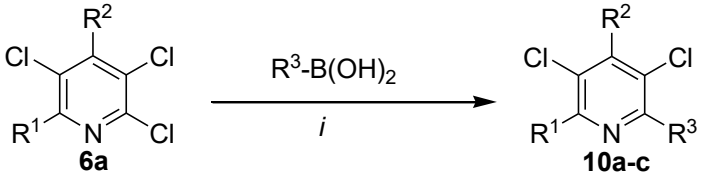
Table 7. Synthesis of triarylated pyridines **9a-d**.

Compound	R^1	R^2	9 [%][a]
a	4-MeC_6H_4	4-(MeO)C_6H_4	57
b	4-MeC_6H_4	2-(MeO)C_6H_4	49
c	4-MeC_6H_4	4-FC_6H_4	38
d	4-MeC_6H_4	4-ClC_6H_4	50

[a] Yield of isolated products

2.1.8. Chemoselective triarylation at positions 6, 4 and 2 in a three-step procedure

Encouraged by the successful synthesis of compounds **9a-d**, I studied the synthesis of triarylated pyridines, starting from compound **6a**. These triarylated pyridines **10a-c**, composed of three different aryl substituents and were isolated in good yields ranging from 61-77 %.



Scheme 9. Synthesis of **10a-c**. Reaction conditions *i*: **6a** (1.0 equiv.), R^3-$B(OH)_2$ (1.2 equiv.), K_3PO_4 (1.2 equiv.), $Pd(PPh_3)_4$ (5 mol%), Toluene, 20 h, 100 °C.

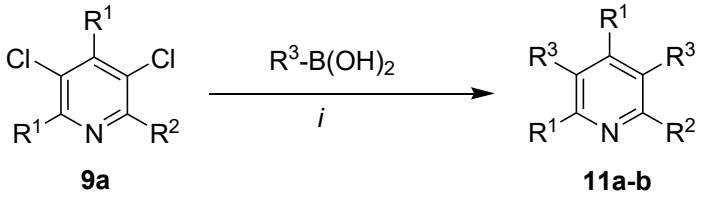
Table 8. Synthesis of triarylated pyridines **10a-c**.

Compound	R^1	R^2	R^3	10 [%][a]
a	4-MeC_6H_4	4-$(CN)C_6H_4$	4-($MeO)C_6H_4$	63
b	4-MeC_6H_4	4-$(CN)C_6H_4$	4-ClC_6H_4	77
c	4-MeC_6H_4	4-$(CN)C_6H_4$	4-$CF_3C_6H_4$	61

[a] Yield of isolated products

2.1.9. Chemoselective pentaarylation of 4-Bromo-2,3,5-trichloro-6-iodopyridine

Finally, with compounds **6**, **9** and **10** in hand, I decided to study the synthesis of pentaarylpyridines, using the reaction conditions previously reported by my research group.[46] The reaction of triarylated pyridine **9a** with phenylboronic acid and 4-*tert*-butylphenylboronic acid respectively, allowed the synthesis of **11a-b** with very good yields (Scheme 10, table 9).



9a **11a-b**

Scheme 10. Synthesis of **11a-b**. Reaction conditions *i*: **9a** (1.0 equiv.), R^3-$B(OH)_2$ (4.0 equiv.), K_3PO_4 (4.0 equiv.), $PdCl_2(CH_3CN)_2$ (5 mol%), SPhos (10 mol%), Toluene, 20 h, 100 °C.

Table 9. Synthesis of Pentaarylpyridines **11a,b**

Compound	R^1	R^2	R^3	11[%][a]
a	4-MeC_6H_4	4-$(MeO)C_6H_4$	C_6H_5	99
b	4-MeC_6H_4	4-$(MeO)C_6H_4$	4-*t*BuC_6H_4	80

[a] Yield of isolated products

The structure of compound **11a** was independently confirmed by X-Ray diffraction analysis (Figure 4). The aryl groups attached to the pyridine moiety of this compound are twisted out of plane provoking a propeller-type orientation. The aryl substituent located in *para* position shows a torsion angle of 60.74° (C2-C3-C19-C24). The aryl moieties attached *ortho* or *meta* to the pyridine core are less twisted by 48.15° and

50.43° (N1-C1-C6-C11 and N1-C5-C32-C33) as well as 58.02° and 63.45° (C1-C2-C13-C18 and C5-C4-C26-C27), respectively.

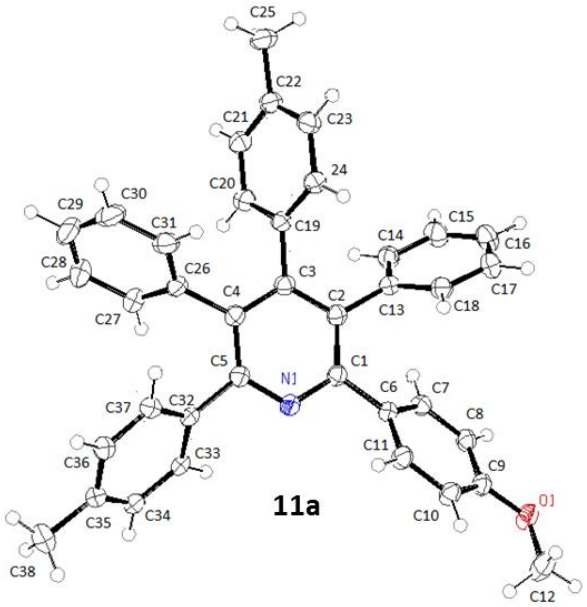
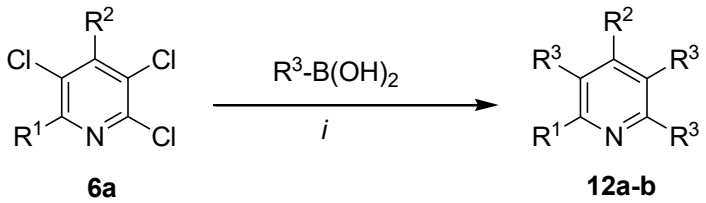


Figure 4: Single crystal structure of compound **11a**, oxygen atoms red, and nitrogen atoms blue.

Likewise, pentaarylpyridines **12a** and **12b** constituting of three different aryl substituents were synthesized with good yields starting from product **6a** (Scheme 11, Table 10).



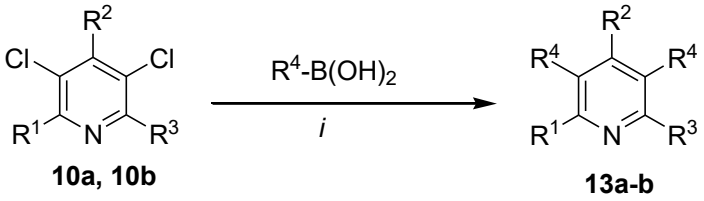
Scheme 11. Synthesis of **12a-b**. Reaction conditions *i*: **6a** (1.0 equiv.), R^3-$B(OH)_2$ (6.0 equiv.), K_3PO_4 (6.0 equiv.), $PdCl_2(CH_3CN)_2$ (5 mol%), SPhos (10 mol%), Toluene, 20 h, 100 °C.

Table 10. Synthesis of Pentaarylpyridines **12a-b**

Compound	R^1	R^2	R^3	12 [%][a]
a	4-MeC_6H_4	4-$(CN)C_6H_4$	4-$(MeO)C_6H_4$	93
b	4-MeC_6H_4	4-$(CN)C_6H_4$	4-*t*BuC_6H_4	75

[a] Yield of isolated products

Finally, pyridines **13a** and **13b**, which consist of four different aryl substituents, were obtained by arylation of positions 3 and 5 from compounds **10a** and **10b**, respectively (Scheme 12, Table 11). The moderate yield of product **13b** may be due to the formation of secondary products by reaction of the arylboronic acid with the arylchloride moiety in position 2 of the starting material **10b**.



Scheme 12. Synthesis of **13a-b**. Reaction conditions *i*: **10a** or **10b** (1.0 equiv.), R^4-$B(OH)_2$ (4.5 equiv.), K_3PO_4 (4.5 equiv.), $PdCl_2(CH_3CN)_2$ (5 mol%), SPhos (10 mol%), Toluene, 20 h, 100 °C.

Table 11. Synthesis of Pentaarylpyridines **13a-b**.

Compound	R^1	R^2	R^3	R^4	13 [%][a]
a	4-MeC_6H_4	4-$(CN)C_6H_4$	4-$(MeO)C_6H_4$	C_6H_5	90
b	4-MeC_6H_4	4-$(CN)C_6H_4$	4-ClC_6H_4	4-$(MeO)C_6H_4$	50

[a] Yield of isolated products

2.1.10. Conclusion

In conclusion, I was able to synthesize novel 4-bromo-2,3,5-trichloro-6-iodopyridine **3** as starting material, which allowed the development of an efficient method for the synthesis of aryl-substituted pyridines, using Suzuki-Miyaura reactions. The pentaarylpyridines were synthesized in very good yields by this methodology and shows very good functional group tolerance.

2.2. Chemoselective Sonogashira reactions of 4-bromo-2,3,5-trichloro-6-iodopyridine

2.2.1. Introduction

The Sonogashira reaction has become one of the most important and widely used methods for preparing alkyl and arylacetylenes due to their relatively simple implementation and good tolerance to functional groups.[47,48] This reaction have been part of key steps towards the synthesis of a wide variety of natural products such as the synthesis of Terbinafine,[49] as an antifungal medication and the chemoselective synthesis of Altinicline,[50] a medication for the treatment of Parkinson's disease (figure 5).

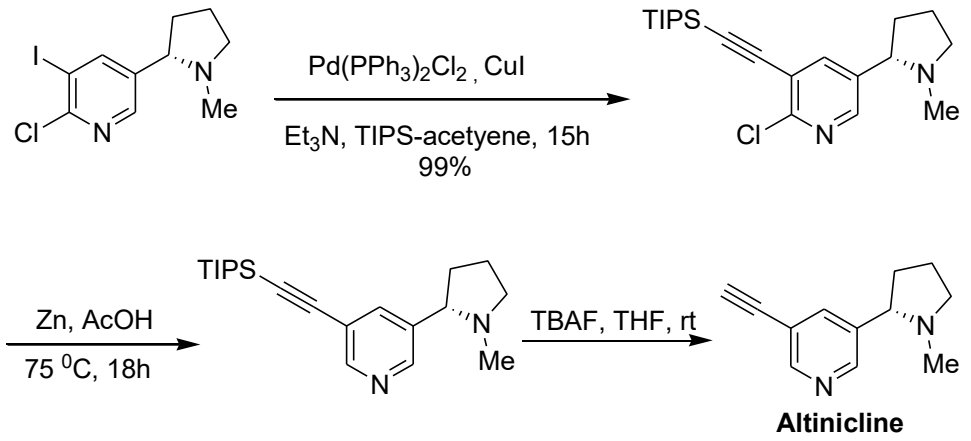


Figure 5. Synthesis of Altinicline

The synthesis of polyalkynylated compounds such as polyalkynylated derivatives of thiophenes,[51] pyrroles,[52] cyclobutadienes,[53] ferrocenes[54] and pyrimidines,[55] has gained a lot of research interests, due to their particular optical and electronic properties.

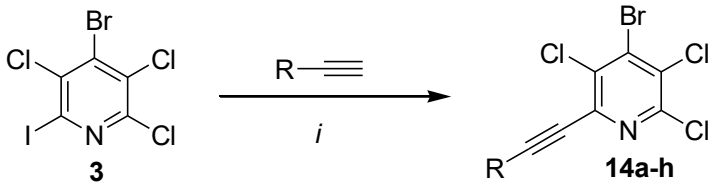
The synthesis of polyalkynylated pyridines has been an objective of special interest in my research group studying the synthesis of pentaalkynylpyridines[56] using pentachloropyridine as starting material, as well as the synthesis of 2,3,5,6–tetraalkynylpyridines[57] from 2,3,5,6-tetrachloropyridine. Despite the fact that electron deficient positions 2, 4 and 6 of pentachloropyridine ought to show a higher reactivity than positions 3 and 5, a site-selective Sonogashira reaction has not been possible,

because the nucleus of pyridine is significantly activated by introducing alkynyl substituents, facilitating further Sonogashira coupling reactions.

It can be expected that use of 4-bromo-2,3,5-trichloro-6-iodopyridine as starting material, allows the successive introduction of alkynyl substituents through chemoselective Sonogashira reactions, giving rise to new molecules with good emission properties including high quantum yields.

2.2.2. Chemoselective monoalkynylation at position 6

In order to find suitable conditions, for selective monoalkynylation on 4-bromo-2,3,5-trichloro-6-iodopyridine **3** by Sonogashira cross coupling reactions, I firstly studied the reaction using standard condition ($PdCl_2(PPh_3)_2$ 5 mol%, CuI (5 mol%) in NEt_3 with 1.1 equiv. of Phenylacetylene at room temperature).TLC analysis verified a significant part of starting material had been converted into a new product after 4 hours. After 19 hours had elapsed, the starting material was converted almost quantitatively and the desired product **14a** was isolated in 90 % yield and high chemoselectivity. As product **14a** was obtained in high yield and excellent chemoselectivity, I started to analyze the feasibility of these reaction conditions using various acetylenes (Scheme 13, Table 12). The best yields were obtained when arylalkynes with electron-donating groups were used (**14a-c**), while electron withdrawing groups led to diminished yields.



Scheme 13. Synthesis of **14a-h**. Reaction Conditions *i:* **3** (1.0 equiv.), acetylene (1.1 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (5 mol%), NEt_3, rt., 19 h.

Table 12. Synthesis of **14a-h**

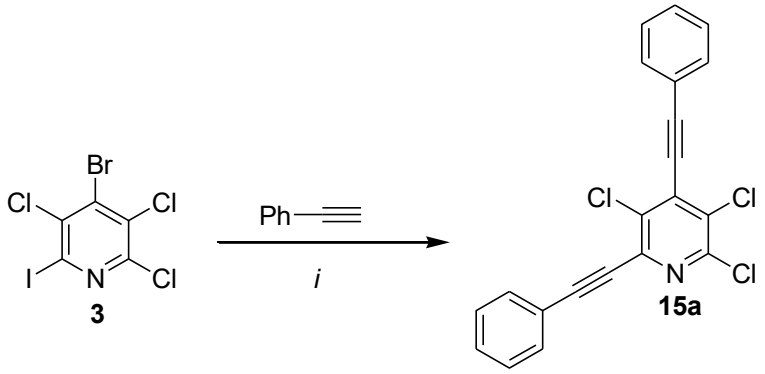
Compound	R	14 [%][a]
a	C_6H_5	90
b	4-*t*BuC_6H_4	92
c	4-(MeO)C_6H_4	86
d	4-FC_6H_4	45
e	*n*Pr	56
f	3-Pyridyl	35
g	4-*n*PrC_6H_4	73
h	Cyclopentyl	80

[a] Yield of isolated products

2.2.3. Chemoselective dialkynylation at positions 6 and 4

In the following, the chemoselectivity of Sonogashira reactions of 4-bromo-2,3,5-trichloro-6-iodopyridine **3** for a double Sonogashira coupling was studied. After some experimentation, using phenylacetylene as a model alkyne, it was found that best results were obtained using 1,4-dioxane as a solvent and diisopropylamine as a base at 80 °C for 20 h. in the presence of 5 mol% of $Pd(PPh_3)_4$ and 5 mol% of copper (I) iodide (entry 1, Scheme 14, Table 13).

It is important to note that when the reaction was carried out at lower temperatures, the yields decreased dramatically, giving substantial amounts of monoalkynylated coupling product. Similarly, the yield decreased, when HN(*i*Pr)$_2$ was exchanged by NEt_3.



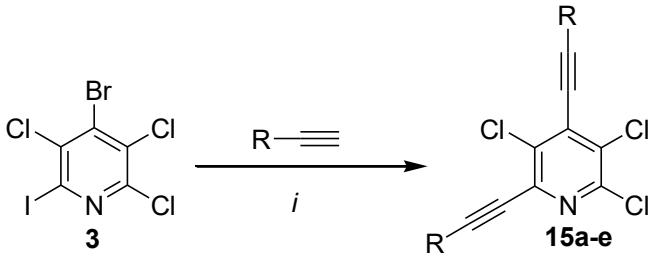
Scheme 14. Synthesis of **15a**. Optimization. *Conditions i:* **3** (1.0 equiv.), phenylacetylene (2.1 equiv.), $Pd(PPh_3)_4$ (5 mol%), CuI (5 mol%), 1,4-dioxane, Base, 20 h.

Table 13. Optimization for the synthesis of **15a**

Entry	Temperature (°C)	Base	15a [%][a]
1	80	$HN(iPr)_2$	61
2	40	$HN(iPr)_2$	0[b]
3	60	$HN(iPr)_2$	25
4	70	$HN(iPr)_2$	46
5	80	NEt_3	45

[a] Yield of isolated products; [b]only formation of coumpound **14a** was observed.

Using optimized conditions, the reaction of **3** with differently substituted alkynes afforded 2,3,5-trichloro-4,6-dialkynyl- pyridines **15a-e** in 51-67 % yield and very good chemoselectivity. Obtained yields were not affected significantly by the nature of the substituents of employed arylacetylene (Scheme 15, Table 14).



Scheme 15. Synthesis of **15a-e**. Reaction conditions: *i*, **3** (1.0 equiv.), acetylene (2.1 equiv.), $Pd(PPh_3)_4$ (5 mol%), CuI (5 mol%), $HN(iPr)_2$, 1,4-dioxane, 80 °C, 20 h.

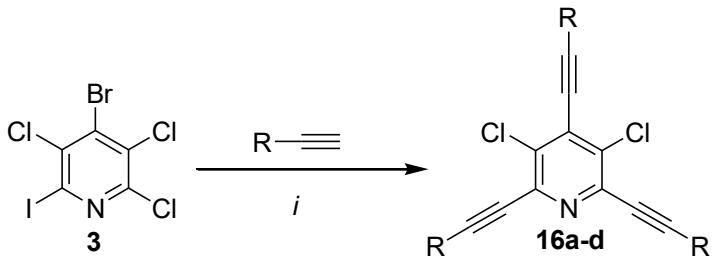
Table 14. Synthesis of **15a-e**

Compound	R	15 [%][a]
a	C_6H_5	61
b	4-*t*BuC_6H_4	67
c	4-(MeO)C_6H_4	51
d	4-*n*PrC_6H_4	63
e	4-FC_6H_4	54

[a] Yield of isolated products

2.2.4. Chemoselective trialkynylation at position 6, 4 and 2

Encouraged by the results achieved during the synthesis of dialkynylated products **15**, I decided to use the same conditions for chemoselective synthesis of 3,5-dichloro-2,4,6-trialkynyl-substituted pyridines **16a-d**, but logically employing increased amount of the alkyne. When 3.5 equivalents of phenylacetylene were used, the synthesis of 3,5-dichloro-2,4,6-tris (phenylethynyl) pyridine **16a** was achieved with a 55 % yield, but the formation of small quantities of additional side-products perhaps derived from tetra- and/or pentaalkynylation, were observed by TLC. Thus in another attempt, I reduced the amount of phenylacetylene to 3.1 equivalents, achieving an improved yield of 60 % of the desired product. Using these developed conditions several trialkynylated pyridines were synthesized with yields in a range of 44-60 % with good chemoselectivity (Scheme 16, Table 15).



Scheme 16. Synthesis of **16a-d**. Reaction conditions: *i*, **3** (1.0 equiv.), acetylene (3.1 equiv.), $Pd(PPh_3)_4$ (5 mol%), CuI (5 mol%), HN(*i*Pr)$_2$, 1,4-dioxane, 80 °C, 20 h.

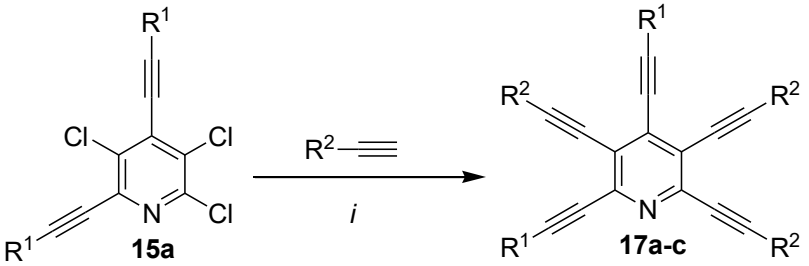
Table 15. Synthesis of **16a-d**

Compound	R	16 [%][a]
a	C_6H_5	60
b	4-FC_6H_4	44
c	4-$(MeO)C_6H_4$	58
d	4-MeC_6H_4	58

[a] Yield of isolated products

2.2.5. Chemoselective pentaalkynylation of 4-Bromo-2,3,5-trichloro-6-iodopyridine

For the synthesis of the pentaalkynyl pyridines **17a-c** (Scheme 17, Table 16), which contain two different alkynyl substituents in their composition, 2,3,5-trichloro-4,6-bis (phenylethynyl)pyridine **15a** was converted with 5.0 equivalents of three different acetylenes, under the conditions described by Ehlers *et al.*[56] All desired products were obtained in high yields ranging from 84-96 %.



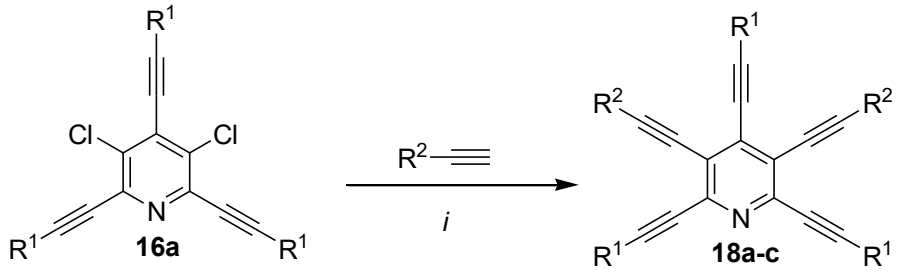
Scheme 17. Synthesis of **17a-c**. Reaction conditions: *i*, **15a** (1.0 equiv.), acetylene (5.0 equiv.), $Pd(CH_3CN)_2Cl_2$ (5 mol%), CuI (5 mol%), XPhos (10 mol%), $HN(iPr)_2$, 1,4-dioxane, 80 °C, 18 h.

Table 16. Synthesis of **17a-c**

Compound	R^1	R^2	17 [%][a]
a	C_6H_5	4-$(MeO)C_6H_4$	94
b	C_6H_5	4-FC_6H_4	96
c	C_6H_5	4-$tBuC_6H_4$	84

[a] Yield of isolated products

Finally, 3,5-dichloro-2,4,6-tris(phenylethynyl)pyridine **16a** was used to obtain pentaalkynylpyridines **18a-c** with very good yields (Scheme 18, Table 17).



Scheme 18. Synthesis of **18a-c**. Reaction conditions: *i*, **16a** (1.0 equiv.), acetylene (4.0 equiv.), $Pd(CH_3CN)_2Cl_2$ (5 mol%), CuI (5 mol%), XPhos (10 mol%), $HN(iPr)_2$, 1,4-dioxane, 80 °C, 18 h.

Table 17. Synthesis of **18a-c**

Compound	R^1	R^2	18 [%][a]
a	C_6H_5	4-(MeO)C_6H_4	95
b	C_6H_5	4-FC_6H_4	97
c	C_6H_5	4-*t*BuC_6H_4	65

[a] Yield of isolated products

2.2.6. Absorption and Fluorescence Properties

The 6 non-symmetrical pentaalkynylpyridines synthesizeds **17a-c** and **18a-c** were investigated by UV-VIS and fluorescence analysis in dichloromethane (Figure 6). Table 18 summarizes the corresponding spectral data of all analyzed compounds. The UV-VIS absorption spectra of the compounds exhibit four absorption bands around 324, 344, 382, and 418 nm. The absorption band of the compounds **17a** and **18a** containing (4-methoxyphenyl)ethynyl substituents, are slightly red-shifted, presumably due to the positive mesomeric effect of the methoxy group. The compounds **17b** and **18b**, containing fluoride as electron withdrawing groups, showed absorption bands shifted to shorter wavelengths.

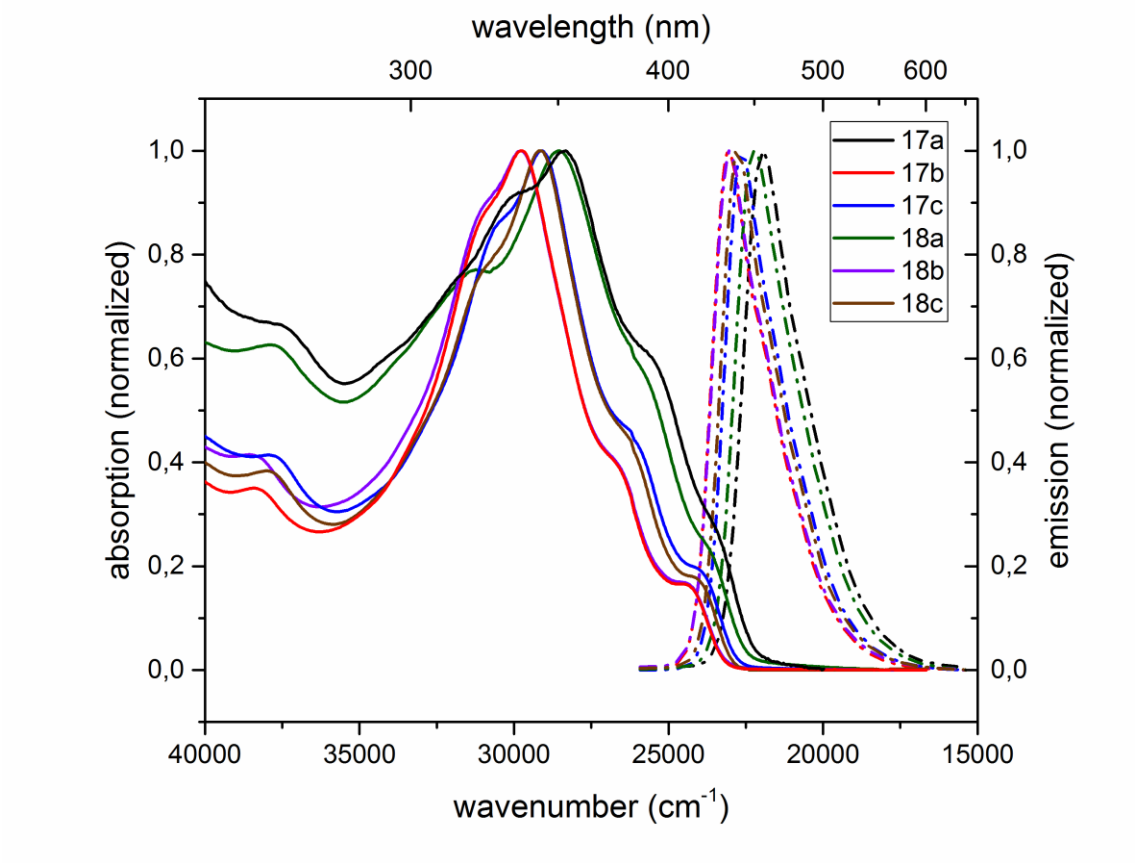


Figure 6. Normalized absorption and emission spectra of compounds **17a-c** and **18a-c** measured in dichloromethane.

The fluorescence spectra were measured in dichloromethane at an excitation wavelength of 370 nm. The fluorescence quantum yields were determined by comparison to the standard quinine hemisulfate salt monohydrate in H_2SO_4 (0.05M) which exhibits a fluorescence yield of 52 %.[58] All emission spectra have their maximum around 440 nm. Derivatives **17a** and **18a** containing (4-methoxyphenyl)ethynyl substituents, exhibits a slight red-shift of 456 and 451 nm respectively, while **18b**, containing (4-fluorophenyl)ethynyl substituents, showed the most blue-shifted emission 434 nm. All derivatives showed very good quantum yields, while compounds **17c** and **18c** which contain (4-*tert*-butylphenyl)ethynyl) as substituents, exhibited the highest quantum yield in 54,7 % and 54.6 % respectively.

Table 18. Absorption and emission spectroscopic data of **17a-c, 18a-c** and **PPEP**.

Comp.	λ_{1abs} (nm)	log ε λ_{1abs}	λ_{2abs} (nm)	log ε λ_{2abs}	λ_{3abs} (nm)	log ε λ_{3abs}	λ_{4abs} (nm)	log ε λ_{4abs}	λ_{em} (nm)	ϕ_{fluo} (%)
17a	335	4.85	353	4.88	390	4.67	425	4.34	456	49.2
17b	324	4.88	336	4.93	375	4.52	409	4.15	434	53.4
17c	327	4.93	344	5.00	382	4.66	418	4.27	442	54.7
18a	319	4.79	350	4.90	382	4.70	420	4.31	451	49.8
18b	324	4.84	336	4.89	375	4.49	413	4.09	434	48.2
18c	322	4.83	343	4.94	382	4.58	416	4.17	440	54.6
PPEP	-	-	338	5.04	376	4.66	421	4.15	477	55.0

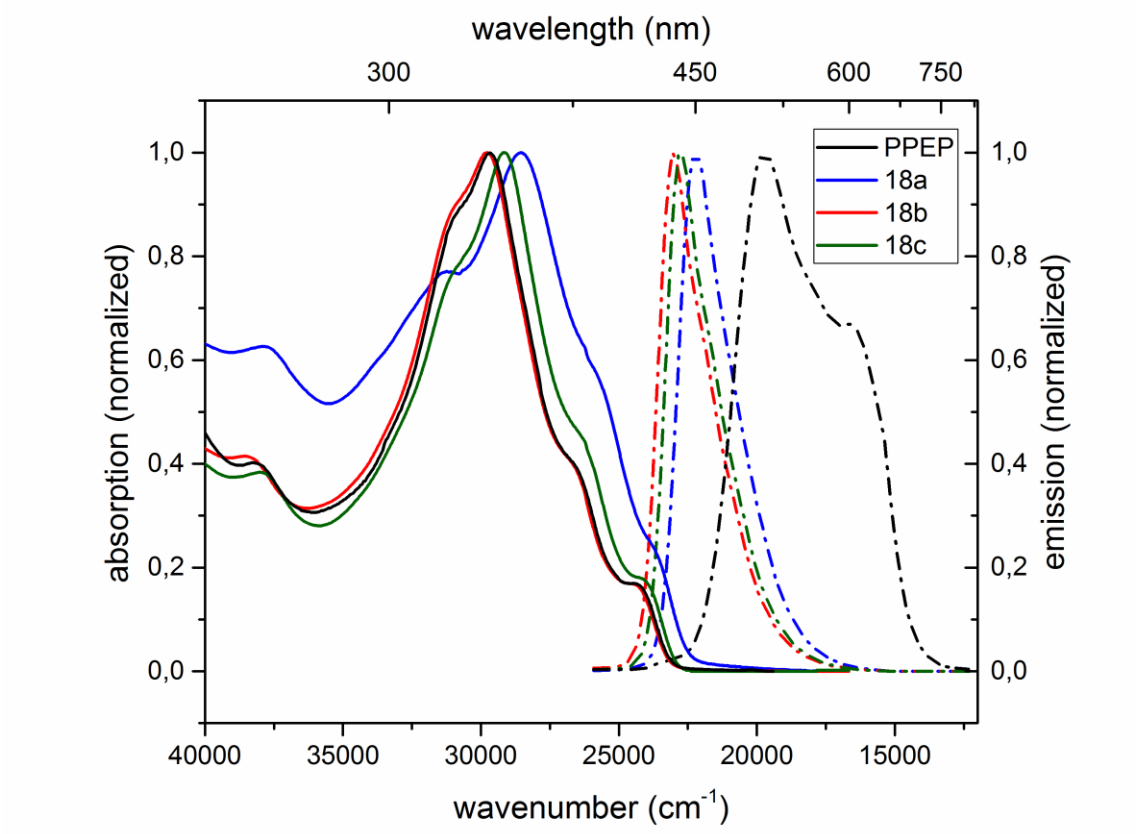


Figure 7. Comparison of normalized absorption and emission spectra of compounds **18a-c** with penta(phenylethynyl)pyridine **PPEP**.

In order to analyze the impact of substituents in 3- and 5-position of the pyridine core on Absorption and Fluorescence properties, I compared the absorption and emission

spectra of synthesized non-symmetrical pentaalkynylpyridines **18a-c** with already reported penta(phenylethynyl)pyridine **PPEP** (Figure 7).[56]

The UV-Vis spectra showed a great similarity between the compared compounds, especially between **PPEP** and **18b**. However, a great difference was observed betwen emission spectra of **PPEP** and pentaalkynylpyridines **18a-c**. While the non-symmetrical pentaalkynylpyridines **18a-c** exhibited emission bands around 440 nm, the compound **PPEP** exhibited a red-shifted band with maximum at 477 nm containing a shoulder at around 600 nm. However, determined quantum yields are in the same range.

2.2.7. Conclusion

Chemoselective Sonogashira reactions were successfully applied using 4-bromo-2,3,5-trichloro-6-iodopyridine in order to synthesize polyalkynylated pyridines. For the first time, selective synthesis is achieved at position 6 for a simple coupling, in positions 4 and 6 for double coupling and at positions 2,4,6 for triple coupling of pentahalogenated pyridines. In addition, pentaalkynyl pyridines with two different substituents around the pyridine nucleus were synthesized for the first time with very good yields. Furthermore, absorption and fluorescence properties of the non-symmetrical pentaalkynylpyridines **17a-c** and **18a-c** were studied. All compounds exhibit very good quantum yields, similar to already reported penta(phenylethynyl)pyridine **PPEP**.

3. Functionalization of Dihalogenated Quinolines

3.1. Chemoselective reactions of Suzuki-Miyaura on 4,6-dihalogenated-2-(trifluoromethyl)quinoline

3.1.1. Introduction

Quinolines derivatives are an important class of heterocycles that exhibit a wide range of biological activities. The quinolines are found as structural key elements in various natural products, especially in alkaloids, and used for the construction of many synthetic compounds with diverse pharmacological properties,[59, 60] such as antiasthmatic, anti-inflammatory and antimalarial activity,[61] anti-cancer[62] and antibiotic activity.[63]

2-Trifluoromethyl quinolines are important derivatives of quinolines, which constitute privileged scaffolds of many pharmaceutical products studied.[64] For example, Mefloquine (Figure 8, **A**) is a commercialized antiprotozoal drug that is used in the treatment of malaria.[65] Quinoline-based compound **B** (Figure 6), targets DNA topoisomerase IV, and DNA gyrase and can be used as antituberculosis agents.[66]

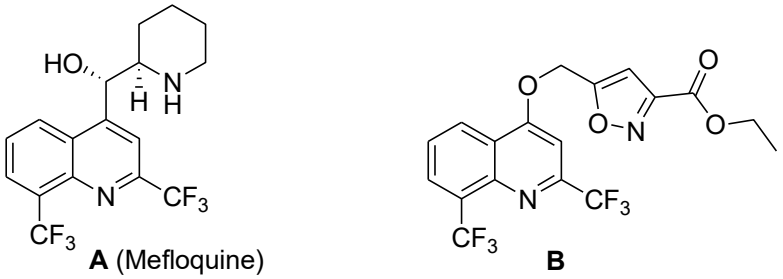


Figure 8. 2-(trifluromethyl) quinoline derivatives with important biological activity.

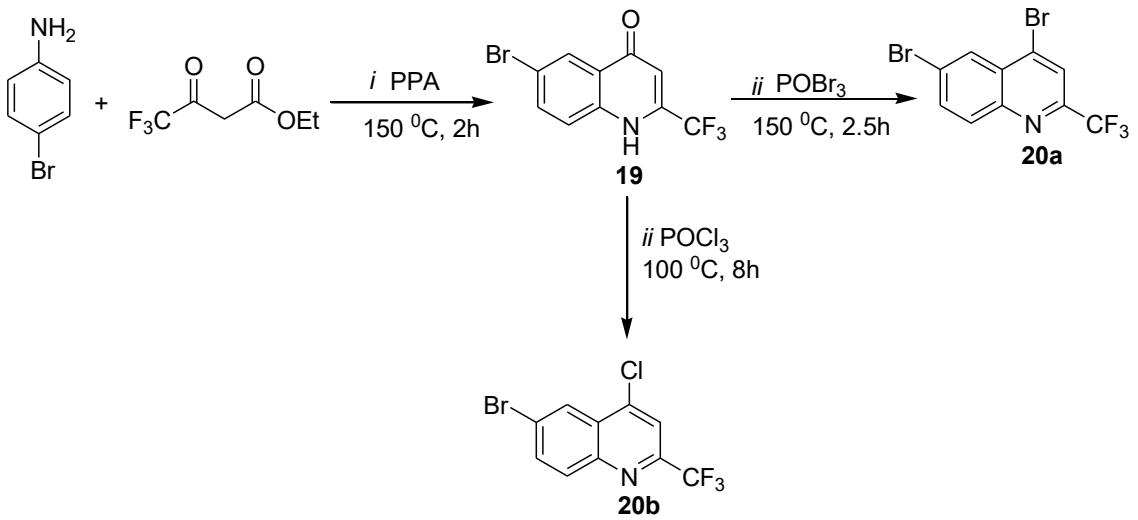
Based on the wide spectrum biological activity of trifluoromethylated quinolines huge interest arouse by synthetic chemists for new and efficient methods for the synthesis of such derivatives.[67] For example; Uneyama *et al*. reported a one-pot synthesis of 2-trifluoromethyl quinolines by rhodium(I)-catalyzed cyclization of *N*-aryl trifluoroacetimidoyl chlorides with alkynes.[68a] Wu and co-workers developed a copper(I)-catalyzed coupling reaction and subsequent cyclization to construct 4-substituted 2-trifluoromethylated quinolines.[68b]

Arylated quinoline derivatives are accessable through palladium-catalyzed cross-coupling reactions, starting from respective halogenated pyridines.[69, 70, 71]

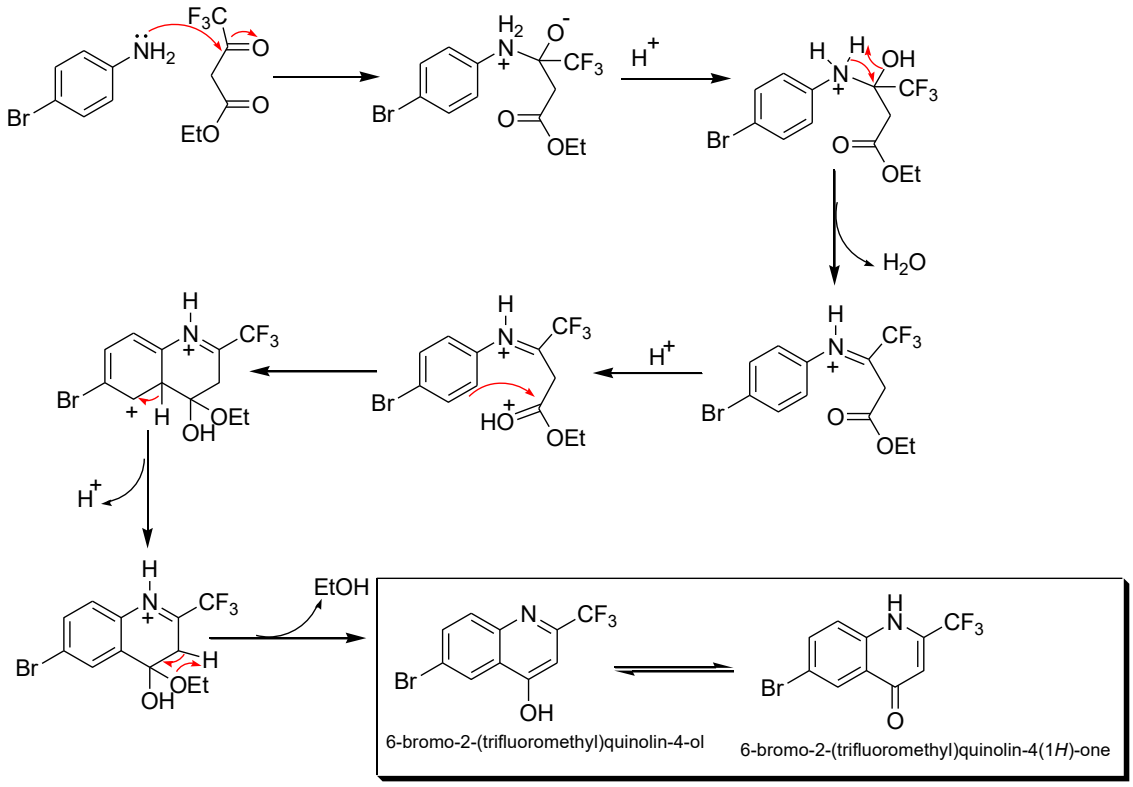
Recently, Professor Langer's research group reported the synthesis of 3,4,8-triarylated 2-(Trifluoromethyl) quinolines through selective Suzuki-Miyaura cross-coupling reactions. These synthesized compounds showed potent activity as nucleotide pyrophosphatase (NPPs) inhibitors.[72] Diarylation of 2-(trifluoromethyl) quinolines at positions 4 and 6 have not been described so far. The selective Suzuki-Miyaura reaction of 4,6-dihalogenated-2-(trifluoromethyl)quinoline allows access to novel quinolines derivatives that could have interesting biological activity, too.

3.1.2. Synthesis of 4,6- dihalogenated-2-(trifluoromethyl)quinoline

For the synthesis of 4,6-dibromo-2-(trifluoromethyl)quinoline **20a** and 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** as starting materials, I followed a two-step reaction procedure described by M. Schlosser *et al.*[73] In the first step, *p*-bromoaniline reacted with Ethyl-4,4,4-trifluoroacetoacetate affording 6-bromo-2-(trifluoromethyl) quinoline-4(1*H*)-one **19** in 78 % yield (Scheme 19). Intermediate **19** was then treated with phosphorus oxybromide or phosphorus oxychloride to obtain the corresponding 4,6-dibromo-2-(trifluoromethyl)quinoline **20a** and 6-bromo-4-chloro-2-(trifluoromethyl) quinoline **20b** in 80 % and 65 % yield, respectively. The first reaction step mentioned above corresponds to a modified mechanism of the Combes quinoline synthesis as shown in Scheme 20.[74]



Scheme 19. Synthesis path to **20a** and **20b**



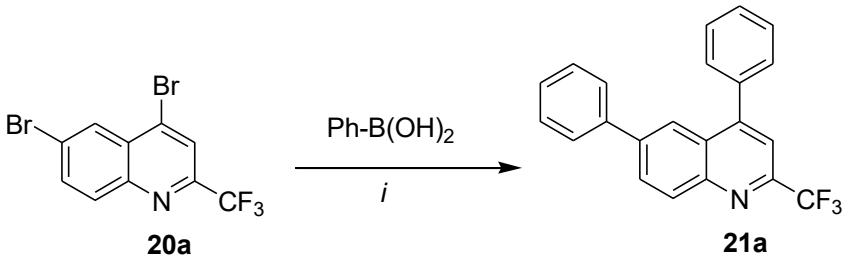
Scheme 20. Combes synthesis for 6-bromo-2-(trifluoromethyl) quinolin-4(1*H*)-one

First, a 1,2-condensation reaction between the β-ketone and the aniline gives a Schiff base under 2,3-dehydration. The reaction occurs preferentially on β-ketone, because it has a higher electrophilic character than β-ketoester, due to β-ketone is directly bonded to an electron withdrawing group as -CF_3. This is followed by protonation of the ester, resulting in an electrophilic aromatic substitution. Concentrated sulfuric acid was used in the classic synthesis as the dehydrogenation reagent.[75] However, polyphosphoric acid provide milder and more effective dehydrogenations and cyclizations.[76] Finally, the carboxyl group is protonated, whereby a proton shift between the two vicinal hydroxyl groups can occur. It comes to the elimination of ethanol, which results in the formation of the quinoline-4-ol. By tautomerism, the enol rearranges into the preferred keto form. The starting material for the following syntheses was obtained by the reaction with the corresponding phosphorus oxyhalide (Scheme 19).

3.1.3. Suzuki-Miyaura reactions on 4,6-dibromo-2-(trifluoromethyl) quinoline

3.1.3.1. Diarylation on 4,6-dibromo-2-(trifluoromethyl)quinoline

After the successful synthesis of 4,6-dibromo-2-(trifluoromethyl)quinoline **20a** as starting material. I started the optimization process looking for the most suitable conditions to carry out the diarylation by twofold Suzuki-Miyaura reactions. Based on the experiences of our research group,[77,78] I converted starting material **20a** with 2.6 equivalents of $PhB(OH)_2$, in presence of 5 mol% of $Pd(PPh_3)_4$ as catalyst, 2.6 equivalents of K_3PO_4 as base, using toluene as solvent at 100 °C for 8 hours. The desired product **21a** was synthesized in moderate 56 % yield. The use of another catalyst system, comprised of $Pd(OAc)_2$ (5 mol%)/$P(Cy)_3$ (10 mol%) gave the increased yield of 78 % (Scheme 21, Table 19, entry 2). A change of base and solvent or reduction of the amount of the catalytic system did not give any benefit.



Scheme 21. Optimization for the synthesis of **21a**. Conditions: *i*, **20a** (1.0 equiv.), $PhB(OH)_2$ (2.6 equiv.), base (2.6 equiv.), Pd-source, ligand, Solvent, 100 °C, 8h.

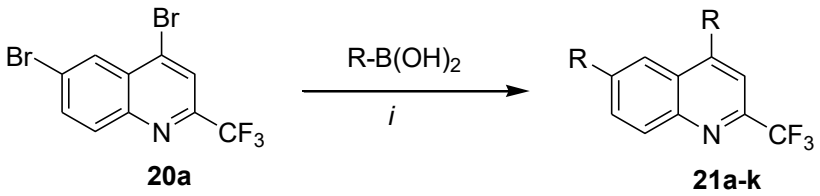
Table 19. Optimization for the synthesis of **21a**.

Entry	Pd source (mol%)	Ligand (mol%)	Base	Solvent (4 mL)	21a [%][a]
1	$Pd(PPh_3)_4$ (5)	-	K_3PO_4	toluene	56
2	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4	toluene	78
3	$Pd(OAc)_2$ (5)	PCy_3 (10)	Cs_2CO_3	toluene	50
4	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4	1,4-dioxane	46
5	$Pd(OAc)_2$ (2.5)	PCy_3 (5)	K_3PO_4	toluene	71

[a] Yield of isolated product.

The reaction of 4,6-dibromo-2-(trifluoromethyl)quinoline **20a** with different arylboronic acids, under optimized conditions, allowed the synthesis of nine different 4,6-diarylated

quinolines **21a-k** in yields between 35 % - 88 % (table 20). In general, good yields were obtained for the compounds derived from electron rich and electron poor arylboronic acids. However, yields were not very good for the synthesis of **21c** and **21i**. The moderate yields of **21c** can be explained by the formation of substantial amounts of side-products by further coupling on the C-Cl moiety of the aryl substituent. The sterically hindered 2,6-substituted- as well as 3-thienylboronic acid, did not react under these reaction conditions.



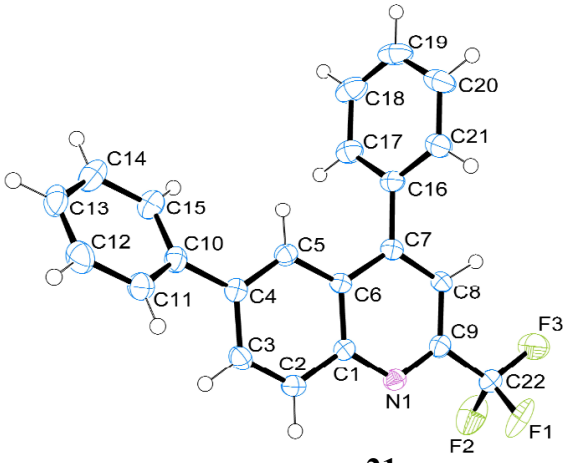
Scheme 22. Synthesis of **21a-j**. Reaction conditions *i*: **20a** (1.0 equiv.), R-B(OH)$_2$ (2.6 equiv.), K_3PO_4 (2.6 equiv.), $Pd(OAc)_2$ (5 mol%), PCy_3(10) (10 mol%), Toluene, 8 h, 100 °C.

Table 20. Synthesis of 4,6-diarylated quinolines **21a-k**.

Compound	R	21 [%][a]
a	C_6H_5	78
b	4-MeC_6H_4	86
c	4-ClC_6H_4	35
d	4-(MeO)C_6H_4	59
e	4-(CF_3O)C_6H_4	77
f	3-thienyl	Traces
g	3-FC_6H_4	47
h	2-MeC_6H_4	73
i	4-FC_6H_4	38
j	4-$CF_3C_6H_4$	88
k	2,6-$(Me)_2C_6H_3$	Traces

[a] Yield of isolated products.

The structure of compounds **21a** was independently confirmed by X-Ray diffraction analysis (Figure 9). The aryl groups attached to the 2-(trifluoromethyl)quinoline moiety of this compound are twisted out of plane. The aryl substituent located in position 4 shows a torsion angle of 60.04° (C8-C7-C16-C21) and the aryl substituent located in position 6 is less twisted 38.34° (C5-C4-C10-C15).

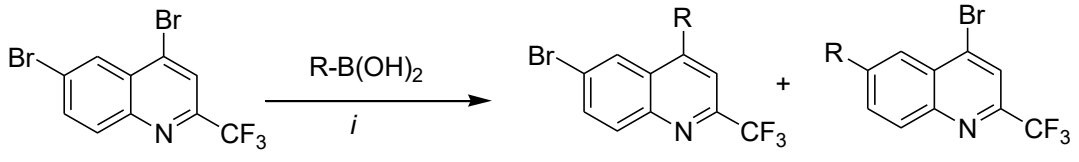


21a

Figure 9. Single crystal structure of compound **21a**

3.1.3.2. Site-Selective monoarylation on 4,6-dibromo-2-(trifluoromethyl) quinoline

I envisioned that **20a** might also be an ideal substrate for site selective arylation by Suzuki–Miyaura reactions. Despite testing different reaction conditions using only 1.0 equivalent of the respective arylboronic acids. In all cases inseparable mixtures of both 4- and 6-monoarylated isomers were isolated in ratios of 8:1 up 9:1, corroborated by ^{19}F-NMR and GC-MS analysis (Scheme 23, table 21).



20a **22a-b**

Scheme 23. Site-selective synthesis of **22a-b**. Conditions: *i*, **20a** (1.0 equiv.), R-B(OH)$_2$ (1.0 equiv.), Pd-species (5 mol%), ligand (10 mol%), K_3PO_4 (2.6 equiv.), solvent, 8 h.

Table 21. Employed reaction conditions for the synthesis of 22a-b

Entry	R	Solvent	T [°C]	Pd source (mol %)	Ligand (mol %)	22a-b [%][a]
1	C_6H_5	toluene	100	$Pd(OAc)_2$ (5)	PCy_3 (10)	0
2	C_6H_5	toluene	50	$Pd(OAc)_2$ (5)	PCy_3 (10)	0
3	C_6H_5	toluene	100	$Pd(PPh_3)_4$ (5)	-	46
4	C_6H_5	toluene	50	$Pd(PPh_3)_4$ (5)	-	17
5	C_6H_5	toluene/H_2O	100	$Pd(PPh_3)_4$ (5)	-	56
6	4-MeC_6H_4	toluene	100	$Pd(PPh_3)_4$ (5)	-	49

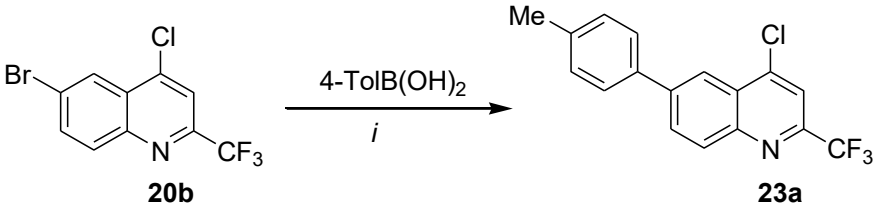
[a] In all cases the yields obtained were mixtures of monoarylated isomers.

3.1.4. Suzuki-Miyaura reaction of 6-bromo-4-chloro-2-(trifluoromethyl) quinoline

3.1.4.1. Chemoselective monoarylation in position 6

In order to overcome the inconvenience for the selective arylation of starting material **20a**. I decided to take advantage of the differences in reactivity of bromine as the better leaving group with respect to chlorine in Suzuki-Miyaura reactions. Hence, I studied the reactivity of 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** as new starting material in chemoselective Suzuki-Miyaura reactions.

Initially, the reaction of **20b** with 1.2 equivalents of 4-$TolB(OH)_2$ as model arylboronic acid in the presence of 5 mol% of $Pd(PPh_3)_4$ as a catalyst, 2.6 equivalents of K_3PO_4 as a base and a mixture of toluene/water as solvent at 80 °C for 8 hours was studied and allowed the synthesis of the desired product **23a** in 69 % yield. The yield was slightly improved to 72 %, when $Pd(OAc)_2$ in the presence of PCy_3 as a ligand was used as catalytic system (Scheme 24, table 22).



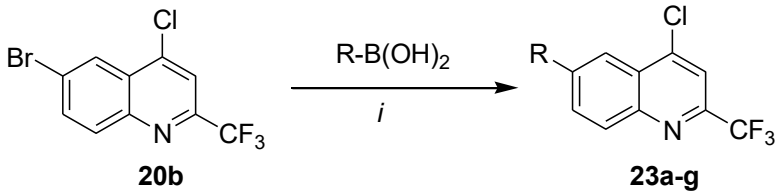
Scheme 24. Optimization for the synthesis of **23a**. Reaction conditions *i*: **20b** (1.0 equiv.), 4-TolB(OH)$_2$ (1.2 equiv.), K_3PO_4 (2.6 equiv.), Pd-species (5 mol%), Toluene/H_2O (4:1), 8 h, 80 °C.

Table 22. Optimization for the chemoselective synthesis of **23a**.

Entry	Pd source (mol %)	Ligand (mol %)	9a [%][a]
1	$Pd(PPh_3)_4$ (5)	-	69
2	$Pd(OAc)_2$ (5)	PCy_3 (10)	72

[a] Yield of isolated products.

Using the developed method I was able to isolate 6-arylated-4-chloroquinolines **23a-g** in good yields (72 % - 55 %) and high chemoselectivity (Scheme 25, Table 23). Obtained yields were not affected significantly by the nature of the substituents of employed arylboronic acids.



Scheme 25. Synthesis of **23a-g**. Reaction conditions *i*: **20b** (1.0 equiv.), R-B(OH)$_2$ (1.2 equiv.), K_3PO_4 (2.6 equiv.), $Pd(OAc)_2$ (5 mol%), PCy_3 (10 mol%), Toluene/H_2O (4:1), 8 h, 80 °C.

Table 23. Chemoselective synthesis of **23a-g**

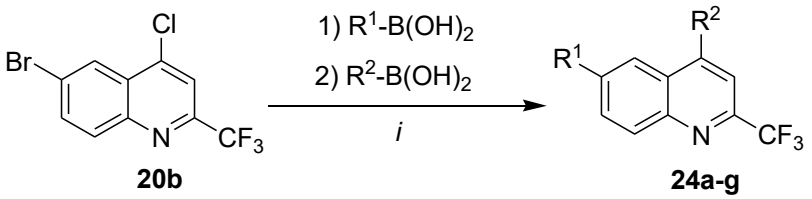
Compound	R	23 [%][a]
a	4-MeC_6H_4	72
b	3-$CF_3C_6H_4$	63
c	4-$(MeO)C_6H_4$	66
d	3,5-$(Me)_2C_6H_3$	58
e	2-MeC_6H_4	66
f	3-FC_6H_4	55
g	4-$(EtO)C_6H_4$	61

[a] Yield of isolated products.

3.1.4.2. Non-symmetrical diarylation on 6-bromo-4-chloro-2-(trifluoromethyl) quinoline

Motivated by the successful synthesis of **23a-g**, I thought that 6-bromo-4-chloro-2-(trifluoromethyl) quinoline **20b** could be an ideal substrate for non-symmetrical diarylation. The one-pot two-step reaction of **20b** with two different arylboronic acids was next studied. The reaction of **20b** with 1.2 equivalents of an arylboronic acid for 8 hours at 80 °C and subsequent addition of a second arylboronic acid (1.2 equiv.) for another 8 hours to 100 °C afforded the 2-(trifluoromethyl)-4,6-diarylquinolines **24a-g** containing two different aryl groups in moderate to good yields (Scheme 26, Table 24).

It is important to note that with this procedure (one-pot two-step reaction) the compound **24a** was obtained in a good 62 % yield (Entry 1, Table 24). It is noteworthy, when the reaction was started from the pure compound **23a** following the same conditions of the last step for the one-pot reaction, the yield of **24a** was only 32 %.



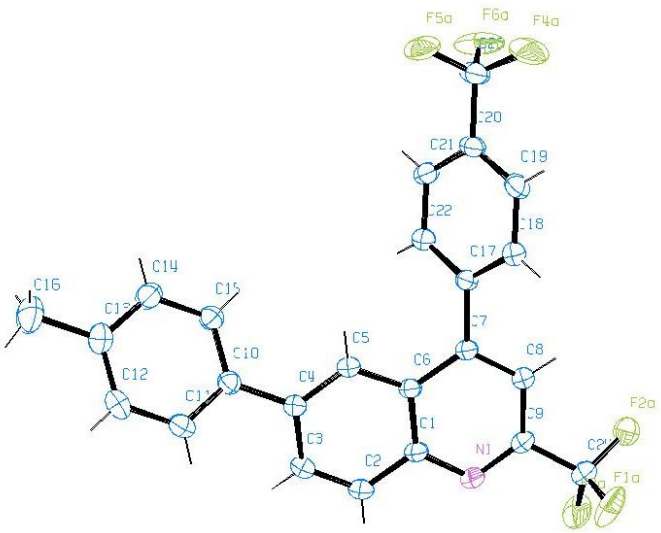
Scheme 26. Synthesis of **24a-g**. Reaction conditions *i*: 1) **20b** (1.0 equiv.), R^1-$B(OH)_2$ (1.2 equiv.), K_3PO_4 (2.6 equiv.), $Pd(OAc)_2$ (5 mol%), PCy_3 (10 mol%), Toluene/H_2O (4:1), 8 h, 80 °C; 2) R^2-$B(OH)_2$ (1.2 equiv.), 100 °C, 8 h.

Table 24. Non-symmetrical synthesis of 24a-g

Compound	R^1	R^2	24 [%][a]
a	4-MeC_6H_4	4-$(MeO)C_6H_4$	62
b	4-MeC_6H_4	4-$(EtO)C_6H_4$	59
c	4-MeC_6H_4	4-$CF_3C_6H_4$	57
d	4-MeC_6H_4	4-ClC_6H_4	46
e	4-$(MeO)C_6H_4$	4-MeC_6H_4	46
f	4-$(MeO)C_6H_4$	4-$CF_3C_6H_4$	46
g	4-$(MeO)C_6H_4$	C_6H_5	56

[a] Yield of isolated products.

All products were characterized by ^1H and ^{13}C NMR spectroscopy, IR spectroscopy and mass spectrometry. Moreover, the structure of compounds **24c** was independently confirmed by X-Ray diffraction analysis (Figure 10). The aryl groups attached to the 2-(trifluoromethyl)quinoline of this compound are twisted out of plane. The aryl substituent located in position 4 shows a torsion angle of 52.00° (C8-C7-C17-C18). The aryl substituent located in position 6 is less twisted by 27.40° (C5-C4-C10-C15).



24c

Figure 10. Single crystal structure of compound **24c**

3.1.5. Biological studies

3.1.5.1. Ecto-nucleotidases (ecto-5′-nucleotidase)

Ecto-nucleotidases are a family of nucleotide metabolizing enzymes that are expressed on the plasma membrane. Ecto-5′-nucleotidase (e5′NT), a membrane-bound glycoprotein, is a particular member of this group, which is responsible for the hydrolysis of extracellular mononucleotides, such as adenosine monophosphate (AMP) into adenosine.[79] At the same time, the extracellular level of adenosine regulates the activation of adrenergic receptors stimulating different cell signaling pathways. This results in the control of various physiological functions, such as vasodilation, angiogenesis, as well as regulation of cell growth and differentiation.[80-83] An abnormal expression of the e5′NT leads to malfunctions of these physiological processes. Interestingly an over-expression of e5′NT, which results in elevated levels of extracellular adenosine, has been found in various types of cancer.[84] The high levels of adenosine has been correlated with tumor proliferation, metastasis and angiogenesis by the activation of adenosine receptors.[85] For this reason selective inhibitors of e5'NT that reduce the hydrolysis of extracellular nucleotides and in this way the concentration of adenosine, could be promissory as a new therapeutic alternative against cancer. Various ADP analogs[86] and some non-nucleotide derived inhibitors, such as sulphonamides, anthraquinones, polyoxometallates, methylxanthines and sulfonic acids, have been reported as inhibitors of e5'NT.[87,88] Some quinolines derivatives have been shown potent activity as nucleotide pyrophosphatase (NPPs) inhibitors,[72] a related enzymatic

family, and therefore could be promising structures for the synthesis of new inhibitors of e5'NT.

3.1.5.2. Selective inhibition study of ecto-5'-nucleotidases (e5'NT)

The studies were accomplished in the Centre for Advanced Drug Research, COMSATS Institute of Information Technology, Abbottabad, Pakistan, as a part of a cooperation project.

All synthesized compounds (arylated-2- (trifluoromethyl) quinolines derivatives, **21a-j; 23a-g and 24a-g**) were studied for their potential to inhibit ecto-5'-nucleotidase, both human and rat source. Most derivatives showed selective inhibition on human ecto-5'-nucleotidases (*h*-e5'NT) at 100μM (Table 25). However, none of the derivatives was found to act as inhibitor of *r*-e5'NT at the same concentration.

In the series of 4,6-diarylated quinolines **21a-j**, the compound **21d** which contains a methoxy group in position 4 of the aryl substituents was the most potent inhibitor of h-e5'NT with an inhibitory value of IC50 ± SEM= 1.13±0.02 μM. The compound **21g**, containing a 3-fluoroaryl substituent, also resulted in strong inhibition at *h*-e5'NT (IC_{50} ± SEM= 1.19±0.03μM). The compound **21h**, possessing a *ortho*-tolyl groups, exhibited a lower inhibitory activity (IC_{50} ± SEM= 2.21±0.17 μM) as compared to **21d.** In case of derivative **21a** containing two phenyl rings, showed a reduced inhibitory response (IC50 ± SEM= 15.3±1.16 μM). Derivative **21e**, possessing trifluoromethoxy group located at position 4 of the phenyl rings, showed no inhibitory activity on *h*-e5'NT.

The bioactivity on 6-arylated-4-chloroquinolines **23a-g** was also studied. The compound **23f** containing a 3-fluoroaryl substituent showed the best inhibition of *h*-e5'NT with IC50 ± SEM= 1.78±0.08 μM. Again, the presence of the methoxy group at position 4 of the aryl substituent (**compound 23c**), showed a good inhibition on *h*-e5'NT with IC50 ± SEM = 2.41 ± 0.11μM. However the presence of the ethoxy group at position 4 of the aryl substituent (**derivative 23g**), resulted in loss of the inhibitory effect, with IC_{50} ± SEM= 25.9±2.83 μM. Derivative **23a**, possessing methyl group located at position 4 of the phenyl ring, showed no inhibitory activity on *h*-e5'NT.

Finally, 4,6-diarylated 2-(trifluoromethyl)quinolines **24a-g** were evaluated. This study identified that derivative **24f**, containing a 4-methoxphenyl substituent in position 6 and a 4-trifluoromethylphenyl substituent in position 4, as the best inhibitor of *h*-e5'NT with

IC50 ± SEM= 2.24±0.14 µM. For derivatives **24a** and **24e**, the combined presence of electron donating groups as methyl and methoxy resulted in loss of inhibitory activity.

Table 25. *In vitro* ecto-5'-nucleotidase (*h*-e5'NT and *r*-e5'NT) inhibitory activities

Sr. No.	Codes	*h*-e5'NT	*r*-e5'NT
		IC_{50}±SEM (µM)	
1	**19**	2.04±0.13	>100
2	**20a**	3.82±0.14	>100
3	**20b**	1.72±0.05	>100
4	**21a**	15.3±1.16	>100
5	**21c**	5.52±0.76	>100
6	**21d**	1.13±0.02	>100
7	**21e**	>100	>100
8	**21g**	1.19±0.03	>100
9	**21h**	2.21±0.17	>100
10	**21i**	5.79±0.98	>100
11	**21j**	13.1±1.07	>100
12	**23a**	>100	>100
13	**23b**	21.5±2.07	>100
14	**23c**	2.41±0.11	>100
15	**23d**	12.3±0.91	>100
16	**23e**	3.82±0.14	>100
17	**23f**	1.78±0.07	>100
18	**23g**	25.9±2.89	>100
19	**24a**	>100	>100
20	**24b**	23.7±2.34	>100
21	**24c**	9.93±0.89	>100
22	**24d**	8.03±0.99	>100
23	**24e**	>100	>100
24	**24f**	2.24±0.14	>100
25	**24g**	8.46±0.92	>100
Sulfamic acid		42.1±5.8	77.3±7.0

IC_{50} is the concentration at which 50% of the enzyme activity was inhibited. All the values were expressed as IC_{50}±SEM (standard error of mean) n=3.

3.1.5.3. Molecular docking

The calculations were accomplished in the Centre for Advanced Drug Research, COMSATS Institute of Information Technology, Abbottabad, Pakistan using FlexX utility of LeadIT v2.1.8 software from BioSolveIT GmbH, Germany.

In order to determine the most probable binding interactions between the compound with the highest inhibitory activity **21d** and the *h*-e5'NT enzyme, molecular docking

studies were carried out. This study revealed that the oxygen atom of the methoxy group and the fluorine atoms of the tri-fluoromethyl group are responsible for making two hydrogen bonds with amino acid groups within the active site (Figure 11). One hydrogen bond was formed by the fluorine atom with ASN499 and the other hydrogen bond was formed between the oxygen and the amino group of ARG354. The four rings of compound 21d and the amino acid residues PHE417 and PHE500 were coupled through eight π-π stacked interactions. In addition, the benzene ring adjacent to the methoxy group and amino acid residues PRO498 formed one π-alkyl interaction.

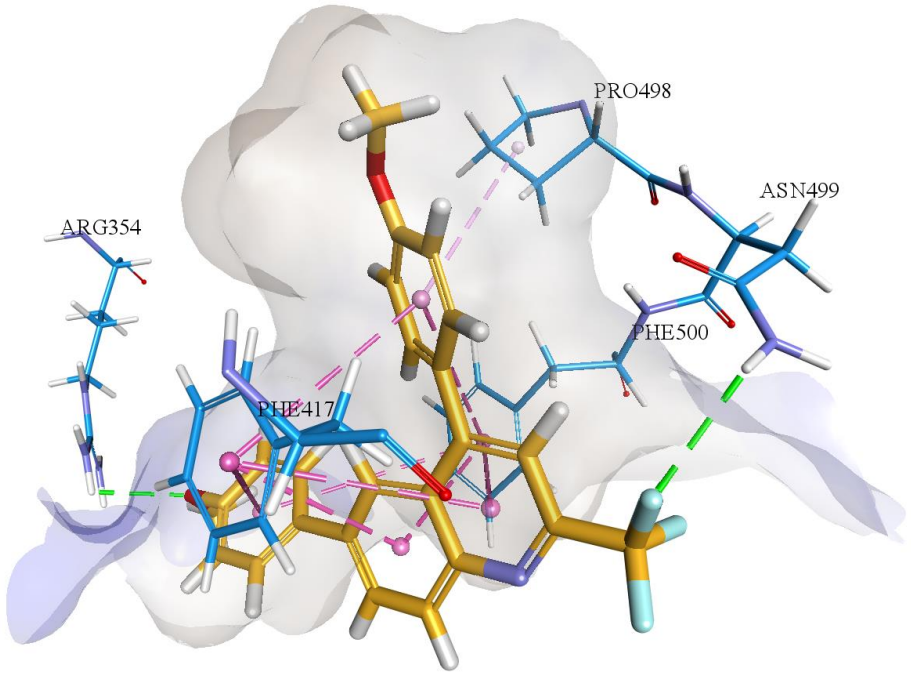


Figure 11. Probable binding interactions between compound **21d** with amino acid residues of *h*-e5'NT. Hydrogen bonding interaction is shown as green dashed lines and π-π interactions as pink dashed lines.

3.1.6. Conclusion

I described a simple method for the synthesis of mono, di and non-symmetrical diarylated -2-(trifluoromethyl) quinolines based on chemo-selective Suzuki-Miyaura reactions. This reaction was highly selective when applied to 6-bromo-4-chloro-2-(trifluoromethyl) quinoline as starting material, while application on 4,6-dibromo-2-(trifluoromethyl) quinoline gave mixtures of regioisomers. Furthermore, synthesized compounds were evaluated for their potential to inhibit ecto-5'-nucleotidase, both

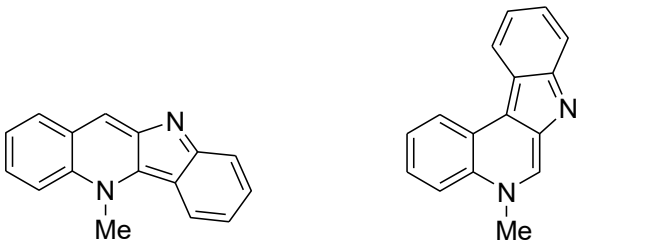
human and rat source. None of the compounds showed inhibitory activity on rat ecto-5'-nucleotidase (*r*-e5'NT). The majority of this series of compound exhibited selective inhibitory activity on *h*-e5'NT enzyme. The compound **21d** was found to be most active against human ecto-5'-nucleotidase (*h*-e5'NT). These newly synthesized classes of compounds can be used to develop novel drug candidates against cancer.

3.2. Synthesis of 7-substituted 7*H*-indolo[2,3-*c*]quinolines

3.2.1. Introduction

During the last 30 years the derivatives of the indoloquinoline alkaloids have attracted considerable attention[89] due to their wide range of biological activities, such as antimalarial,[90] anticancer, antimicrobial,[91] and antiplasmodial[92] to name a few.

The Cryptolepine (5-methyl-5*H*-indolo[3,2-*b*]quinoline) (**C**) is a derivative of the indoloquinoline of great biological importance which has been isolated from Cryptolepis sanguinolenta. The decoction of this plant has been used in traditional medicine against malaria, hypertension, hepatitis, and inflammation in West and Central Africa.[93] The ability of this molecule to inhibit DNA replication, transcription, and topoisomerase activities, has made it a promising anticancer agents in modern health.[94] Similarly, the isomer isoneocryptolepine (5-methyl-5*H*-indolo [2,3-c]quinoline) (**D**), although it has never been found in nature, was synthesized and showed much better selectivity (cytotoxicity / antiplasmodial activity ratio) than (**C**), which makes it a reference compound to evaluate the potential antiplasmodial activity of indoloquinolines.



Cryptolepine (C) **Isoneocryptolepine (D)**

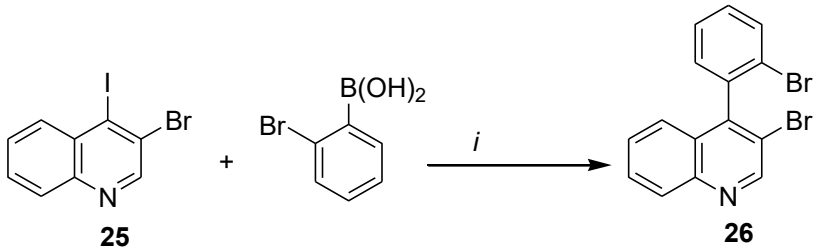
Figure 12. Indoloquinoline derivatives with antiplasmodial activity.

To expand the molecular library of pharmaceutically active compounds, many procedures have been developed for the synthesis of indoloquinolines derivatives in recent years.[95-98] For example, Wang reported an efficient iron-promoted synthesis of *6H*-indolo[2,3-*b*]quinolines by the reaction of aminophenyl alcohols and indoles.[99] Maes and co-workers developed an efficient synthetic route for 5-methyl-*5H*-indolo[2,3-*c*]quinoline and its *7H*-indolo[2,3-*c*]quinoline skeleton by combination of a selective Buchwald–Hartwig amination with a regioselective Pd catalyzed intramolecular arylation reaction starting from 3-bromoquinoline and 2-bromoaniline.[100,101] Wang and Li established a fascinating Rh(III)-catalyzed synthetic method for 6-(2-pyridinyl/2-pyrimidinyl)-*6H*-indolo[2,3-*b*]quinolines from indoles and isoxazoles.[102]

Despite the potentially high biological and pharmacological activity of these alkaloid derivatives only few reports can be found on the synthesis of 7-substituted 7*H*-indolo[2,3-*c*]quinolines. Therefore, it would be interesting to investigate the synthesis of new compounds of this family and the scope of palladium catalyzed reactions, through sequential chemoselective Suzuki-Miyaura reaction on 3-bromo-4-iodoquinoline followed by double Buchwald-Hartwig amination.

3.2.2. Synthesis of 3-bromo-4-(2-bromophenyl)quinoline

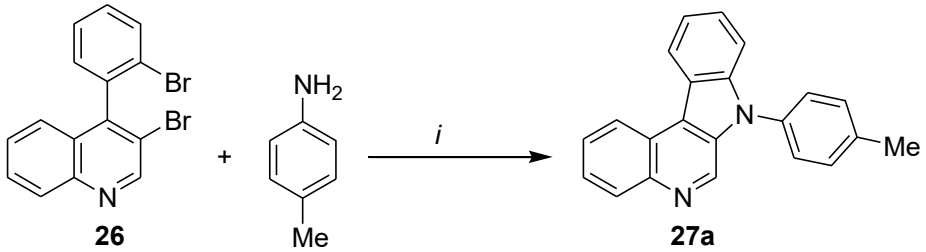
Initially, 3-bromo-4-iodoquinoline **25** was prepared according to a three-step procedure reported by Bogányi *et al.*[103] Subsequently, a chemoselective Suzuki-Miyaura reaction on compound **25** was carried out with 2-bromophenylboronic acid (Scheme 27). The Suzuki-Miyaura reaction proceeded selectively to position 4 corresponding to the break of the C-I bond of 3-bromo-4-iodoquinoline **25**, allowing access to desired product 3-bromo-4-(2-bromophenyl)quinoline **26** in 61 % yield. The good selectivity of this reaction is due to the fact that position 4 is less electron rich than position 3 and the iodine atom is a better leaving group than the bromine atom.



Scheme 27. Synthesis of **26**. Reaction conditions *i*: **25** (1.0 equiv.), 2-BrAr-$B(OH)_2$ (1.4 equiv.), Na_2CO_3 (2.0 equiv.), $Pd(PPh_3)_4$ (5 mol%), DMF/H_2O (10:1), 100 °C, 24 h.

3.2.3. Double Buchwald-Hartwig amination reactions on 3-bromo-4-(2-bromophenyl)quinoline

In order to find the most suitable conditions for the double C-N coupling of 3-bromo-4-(2-bromophenyl)quinoline, *p*-toluidine was selected as the model amine. Initially, the double Buchwald-Hartwig amination was studied by variation of ligands, using $Pd_2(dba)_3$ (5 mol%) as palladium precursor, NaO*t*Bu (2.4 equiv.) as base in presence of toluene as solvent at 100 °C for 24 hours (Entry 1-4, Table 26). Although the reactions proceeded with 100 % conversion, very low yields were obtained from the desired compound. An increase in temperature using xylene as solvent did not offer any improvement. However, the use of KO*t*Bu as a base allowed increasing the yield of compound **27a** to 94 % (Entry 6, Table 26).



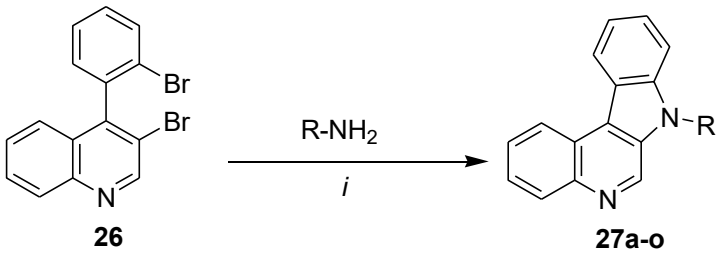
Scheme 28. Optimization for the synthesis of **27a**. Reaction conditions *i*: **26** (1.0 equiv.), Tol-NH_2 (1.5 equiv.), base (2.4 equiv.), $Pd_2(dba)_3$ (5 mol%), ligand, solvent, 24 h.

Table 26. Optimization for the synthesis of 27a

Entry	Ligand (mol%)	Base	T (°C)	Solvent	27a [%][a]
1	P*t*Bu$_3$·HBF$_4$ (10)	NaO*t*Bu	100	Toluene	Traces
2	BINAP (5)	NaO*t*Bu	100	Toluene	15
3	BINAP (10)	NaO*t*Bu	100	Toluene	28
4	dppf (10)	NaO*t*Bu	100	Toluene	11
5	BINAP (10)	NaO*t*Bu	140	Xylene	19
6	BINAP (10)	KO*t*Bu	100	Toluene	94

[a] Yield of isolated products.

With optimized conditions in hand, I studied the scope of the cyclization reaction of **26** with different amines. The employment of various anilines or benzyl amines afforded the corresponding products **27a-m** in good to excellent yields (Table 27). However, this method failed when it was applied for aliphatic amines **27n** and **27o**. Only very low yields of the desired products were obtained. With further optimization, I found that a temperature increase to 140 °C using xylene as the solvent allowed the synthesis of products **27n** and **27o** in very good yields.



26 **27a-o**

Scheme 29. Synthesis of **27a-o**. Reaction conditions *i*: **26** (1.0 equiv.), R-NH$_2$ (1.5 equiv.), KO*t*Bu (2.4 equiv.), Pd$_2$(dba)$_3$ (5 mol%), BINAP (10 mol%), toluene, 100 °C, 24 h.

Table 27. Synthesis of 27a-o

Compound	R	27 [%][a]
a	4-MeC_6H_4	94
b	4-$(MeO)C_6H_4$	95
c	4-FC_6H_4	95
d	4-ClC_6H_4	80
e	4-EtC_6H_4	90
f	4-$(EtO)C_6H_4$	76
g	C_6H_5	88
h	3,5-$(MeO)_2C_6H_3$	96
i	3,4-$(MeO)_2C_6H_3$	90
j	4-$MeC_6H_4CH_2$	92
k	4-$(MeO)C_6H_4CH_2$	71
l	4-$FC_6H_4CH_2$	89
m	Cyclopentyl	91
n	nC_6H_{13}	85[b]
o	nC_4H_9	88[b]

[a] Yield of isolated products; [b] Xylene (mixture of isomers) was used instead of toluene at 140°C.

3.2.4. Conclusion

I described an efficient and convenient procedure for the synthesis of 7-substituted 7*H*-indolo[2,3-*c*]quinolines based on chemoselective Suzuki-Miyaura reaction followed by double C-N coupling. The Suzuki-Miyaura reaction of the 2-bromophenylboronic acid with 3-bromo-4-(2-bromophenyl)quinoline proceeded with good site-selectivity in favour of positions 4. For the double C-N coupling reaction excellent yields were obtained, although for employment of *n*-butylamine and *n*-hexylamine higher temperatures were required.

4. Summary

In the present work, chemoselective cross-coupling reactions of Suszuki and Sonogashira on 4-bromo-2,3,5-trichloro-6-iodopyridine were successfully developed. After optimized conditions, it was possible to synthesize 35 new derivatives of aryl-substituted pyridines and 23 of alkynyl-substituted pyridines in good yields.

The non-symmetrical pentaalkynyl pyridines synthesized were evaluated for their optical properties UV/Vis and fluorescence spectroscopy. These compounds generally exhibited high quantum yields. Compounds **17c** and **18c** which contain (4-*tert*-butylphenyl) ethynyl) as substituents, were those with the highest quantum yield with 54.7 % and 54.6 % respectively.

In another study, the selective Suzuki-Miyaura reaction of 4,6-dibromo-2-(trifluoromethyl) quinoline was investigated. Initially, this starting material allowed the synthesis of nine new 4,6-diarylated quinolines derivatives with good yields. However, selective arylation only led to the synthesis of inseparable mixtures of both 4- and 6-monoarylated isomers. This problem was solved when 6-bromo-4-chloro-2-(trifluoromethyl) quinoline was used as the starting material. In this context, the bromine as the best leaving group with respect to chlorine, allowed the selective arylation to position 6 of 2- (trifluoromethyl) quinoline. In addition, 7 non-symmetrical diarylated derivatives were isolated. All products were evaluated for their potential to inhibit ecto-5'-nucleotidase, both human and rat source. The majority of this series of compound exhibited good selective inhibitory activity on human ecto-5'-nucleotidase. None of the derivatives showed activity against rat ecto-5'-nucleotidase. The compound **21d** was the most active against human ecto-5'-nucleotidase (h-e5'NT) with an inhibitory value of IC50 ± SEM= 1.13±0.02 μM.

Finally a series of 7-substituted 7*H* indolo [2,3-*c*] quinolines was obtained in very good yields by sequential chemoselective Suzuki-Miyaura reaction followed by double C-N coupling on 3-bromo-4-iodoquinoline as selected starting material.

Appendix

5. Experimental Section

5.1. Materials and Methods

5.1.1. General Remarks

All coupling reactions were carried out in oven-dried pressure tubes under argon atmosphere (Argon 4.6). Solvents for reactions were dried and distilled by standard methods or purchased in extra dry quality from Acros whenever exclusion of water was necessary. Solvents for liquid chromatography and extraction were always distilled prior to use (*n*-heptane, EtOAc, DCM). All employed chemicals, if not otherwise stated, were purchased from commercial sources and used without further purification.

5.1.2. Methods for Compound Characterization and Analysis

^{1}H-NMR-Spectroscopy: Bruker AVANCE 250 (250 MHz), Bruker AVANCE 300 (300 MHz), Bruker AVANCE 500 (500 MHz). The NMR spectra presented in this work were recorded in $CDCl_3$ solution except for some cases in which it was used DMSO-*d6*. All chemical shifts are given in ppm. All coupling constants are indicated as *J*. References: The spectra were calibrated according to the solvent signals: 7.27 ppm for $CDCl_3$, 2.54 ppm for DMSO-*d6*. Peak characterization: s = singlet, brs = broad singlet, d = doublet, brd = broad doublet, dpt = dublet of pseudo triplet, t = triplet, pt = pseudo triplet, dd = doublet of doublets, ddd = double doublet doublet, q = quartet, quin = quintet, m = multiplet.

^{13}C NMR-Spectroscopy: Bruker AVANCE 250 (250 MHz), Bruker AVANCE 300 (300 MHz), Bruker AVANCE 500 (500 MHz). The NMR spectra presented in this work were recorded in $CDCl_3$ solution except for some cases in which it was used DMSO-*d6*. All chemical shifts are given in ppm. All coupling constants are indicated as *J*. References: The spectra were calibrated according to the solvent signals: 77.00 ppm for $CDCl_3$, 39.5 ppm for DMSO-*d6*. Peak characterization: d = doublet, q = quartet. DEPT method was used for determining the presence of primary, secondary, tertiary and quaternary carbon atoms.

^{19}F NMR-Spectroscopy: Bruker AVANCE 300 (282 MHz). All chemical shifts are given in ppm.

Mass spectrometry (MS): Finnigan MAT 95 XP (electron ionization EI, 70 eV); 6890 N/5973 (Agilent), 6210 Time-of-Flight LC/MS (Agilent); Gas Chromatography MS (GCMS): Agilent HP-5890 with an Agilent HP-5973 Mass Selective Detector (EI) and HP-5 capillary column using helium carrier gas. Only the measurements with an average deviation from the theoretical mass of ±2 mDa were accounted as correct. High resolution MS [HR-MS (ESI)]: Agilent 1969 A TOF. Only the measurements with an average deviation from the theoretical mass of ±2 mDa were accounted as correct.

Infrared spectroscopy (IR): Nicolet 550 FT-IR spectrometer with ATR sampling technique for solids as well as liquids. Signal characterization: w = weak, m = medium, s = strong.

X-ray crystallography: Data were collected on a Bruker Kappa APEX II Duo diffractometer. The structure was solved by direct methods and refined by full-matrix least squares procedures on F2 with the SHELXTL software package (G. M. Sheldrick, Acta Crystallogr. 2008, A64, 112.); XP (Bruker AXS) was used for graphical representation.

UV/Vis spectroscopy: Lambda 5 (Perkin Elmer) and Analytic Jena Specord 50 UV/VIS spectrometer in Dichloromethane.

Fluorescence spectroscopy: Varian Cary Eclipse spectrometer in Dichloromethane. Quantum yield was determined using quinine hemisulfate salt monohydrate in 0.05M H_2SO_4 as standard.[58]

Elemental analysis (EA): C/H/N – Microanalysator TruSpec CHNS (Leco);

Melting point determination (mp): Micro-Hot-Stage GalenTM III Cambridge Instruments. The melting points have not been corrected.

Thin layer chromatography (TLC): Merck Silica 60 F254 on aluminum tin foil from Macherey–Nagel. Detection with UV light at 254 nm and/or 366 nm without dipping reagent.

Column chromatography: Separation on Fluka silica gel 60 (0.063–0.200 mm, 70 – 320 mesh); Eluents were distilled before use.

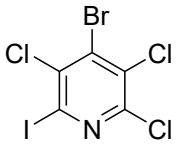
5.2. General Procedures and Product Characterizations

2,3,5-trichloro-4-iodopyridine (**2**) was prepared according to procedure described by Bobbio *et al.*[45]

Synthesis of the starting material 4-bromo-2,3,5-trichloro-6-iodopyridine (3):

An oven-dried 100 ml Schlenk-Flask was charged with 3 ml *n*-butyllithium/hexane-Solution (2.5 M). The hexane was removed under reduced pressure and 7.5 ml of dry THF was added. The resulting solution was cooled down to – 40 °C for 15 minutes and 2,2,6,6-Tetramethylpiperidine (7.41 mmol, 1.25 ml) was slowly added. Afterwards it was allowed to warm to 0 °C (icebath) and stirred for 30 minutes at this temperature. The mixture was again cooled to - 78 °C and stirred for 30 minutes at this temperature. In another Schlenk-Flask a solution of 2,3,5-trichloro-4-iodopyridine (3.73 mmol, 1.15 g) in 4 ml THF was prepared and added slowly to the LiTMP solution at - 100 °C . The reaction mixture was stirred for 2 h. During this time a suspension appears. In a third Schlenk-Flask a solution of 1,2-dibromotetrachloroethane (11.24 mmol, 3.66 g) in 11.5 ml THF was prepared and cooled to - 78 °C. The reaction mixture was transferred into the solution of 1,2-dibromotetrachloroethane by funnel and was stirred for additional 2 hours at - 78 °C. The mixture was allowed to warm to room temperature overnight. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/dichloromethane (10/1) as eluent.

4-bromo-2,3,5-trichloro-6-iodopyridine (3):



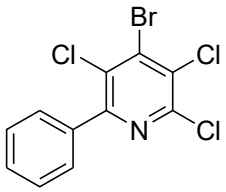
According to the procedure described above **3** was isolated as colorless crystalline solid; yield: 1.118 g (77 %); mp. 172 - 173 °C. **^{13}C-NMR** (62.9 MHz, $CDCl_3$): δ = 146.2 (C_{Hetar}), 138.9 (C_{Hetar}), 134.0 (C_{Hetar}), 132.7 (C_{Hetar}), 115.0 (C_{Hetar}). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2922 (m), 2794 (m), 2691 (m), 2598 (m), 2371 (m), 2275 (m), 2082 (m), 1797 (m), 1514 (m), 1481 (s), 1367 (m), 1307 (m), 1288 (s), 1257 (s), 1209 (s), 1144 (m), 1065 (s), 1001 (m), 958 (m), 880 (m), 808 (m), 754 (s), 717 (s), 628 (s), 599 (s), 564 (m), 545 (s). **MS** (EI, 70 eV): m/z (%) = 391 (M^+, 17), 389 (M^+, 65), 387 (M^+, 100), 385 (M^+, 48), 264 (12), 262 (42), 260 (65), 258 (34), 183 (12), 181 (40), 179 (38), 146 (13), 144 (21), 127 (77), 120 (12), 118

(16), 111 (17), 109 (47), 74 (23), 47 (11). **HR-MS** (EI): m/z = calcd. for C_5NBrCl_3I ($M+H^+$) 384.73189; found: 384.73204; calcd. for $C_5NBrCl_2{}^{37}ClI$ ($M+H^+$) 386.72894 found 386.72920; calcd. for $C_5N^{81}BrCl_3I$ ($M+H^+$) 386.72984; found 386.72920; calcd. for $C_5NBrCl^{37}Cl_2I$ ($M+H^+$) 388.72599; found 388.72642; calcd. for $C_5N^{81}BrCl_2{}^{37}ClI$ ($M+H^+$) 388.72689 ; found 388.72642; calcd. for $C_5N^{81}BrCl^{37}Cl_2I$ ($M+H^+$) 390.72394; found 390.72389; calcd. for $C_5NBr^{37}Cl_3I$ ($M+H^+$) 390.72304; found 390.72389. Anal. calcd. for C_5NBrCl_3I: C, 15.51; N, 3.62; found: C, 15.65; N, 3.71.

General procedure for the synthesis of compounds 4a–k:

An oven-dried, argon-flushed sealable glass tube was charged with 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg), $Pd(PPh_3)_4$ (5 mol%, 17.3 mg), the appropriate arylboronic acid (0.45 mmol) and K_3PO_4 (0.45 mmol, 95.53 mg) followed by a mixture of toluene/ water/ ethanol (6:1:1, 4 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 19 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/dichloromethane as eluent.

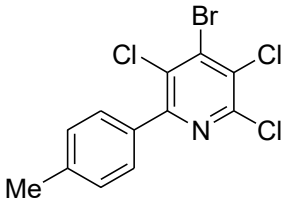
4-bromo-2,3,5-trichloro-6-phenylpyridine (4a):



4a was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and phenylboronic acid (0.45 mmol, 54.9 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 79 mg (78 %). mp. 111-112 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.67 - 7.69 (m, 2H, CH_{Ar}), 7.47-7.49 (m, 3H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 154.9 ($C_{Ar/Hetar}$), 146.9 ($C_{Ar/Hetar}$), 137.0 ($C_{Ar/Hetar}$), 136.7 (C_{Ar}), 131.0 ($C_{Ar/Hetar}$), 130.7 ($C_{Ar/Hetar}$), 129.7 ($2CH_{Ar}$), 129.4 ($2CH_{Ar}$), 128.2 (CH_{Ar}). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2960 (w), 2922 (w), 2852 (w), 2321 (w), 1801 (w), 1760 (w), 1598 (w), 1527 (m), 1481 (s), 1443 (m), 1368 (s), 1321 (s), 1304 (m), 1291 (s), 1276 (s), 1261 (s), 1196 (s), 1160 (m), 1077 (m), 1059 (m), 1001 (m), 964 (w), 883 (m), 804 (w), 765 (s), 736 (s), 704 (s), 690 (s), 652 (m), 617 (w), 599 (s), 559 (m). **MS** (EI, 70 eV): m/z (%) = 341 (M^+, 17), 339 (M^+, 63), 338 (M^+, 13), 337 (M^+, 100), 335 (M^+, 51), 304 (37), 303 (11), 302 (82), 300 (51), 223 (45), 222 (13), 221 (71), 186 (16), 185 (18), 160 (17), 151 (37), 150 (11),

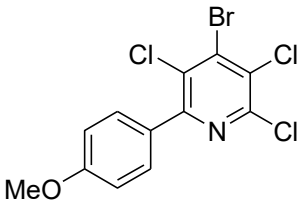
120 (18), 118 (23), 111 (10), 110 (11), 80 (10), 51 (11). **HR-MS** (ESI): m/z = calcd. for $C_{11}H_5BrCl_3N$ ($M+H^+$) 335.87437; found: 335.87405; calcd. for $C_{11}H_5BrCl_2{}^{37}ClN$ ($M+H^+$) 337.87191; found 337.87132; calcd. for $C_{11}H_5{}^{81}BrCl_3N$ ($M+H^+$) 337.87191; found 337.87132; calcd. for $C_{11}H_5BrCl^{37}Cl_2N$ ($M+H^+$) 339.86925; found 339.86946; calcd. for $C_{11}H_5{}^{81}BrCl_2{}^{37}ClN$ ($M+H^+$) 339.86925; found 339.86946. Anal. calcd. for $C_{11}H_5BrCl_3N$: C, 39.15; H, 1.49; N, 4.15 found: C, 39.22; H, 1.60; N, 4.19

4-bromo-2,3,5-trichloro-6-*p*-tolylpyridine (4b):



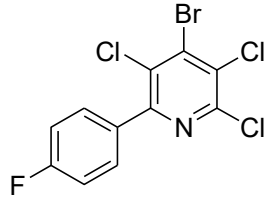
4b was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 4-methylphenylboronic acid (0.45 mmol, 61.2 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 87 mg (83 %). mp. 113 - 114 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.57 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.26 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 2.40 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 154.9 ($C_{Ar/Hetar}$), 146.8 ($C_{Ar/Hetar}$), 140.0 ($C_{Ar/Heta}$), 140.0 (C_{Ar}), 136.9 (C_{Ar}), 133.9 ($C_{Ar/Hetar}$), 130.6 ($C_{Ar/Hetar}$), 129.3 ($2CH_{Ar}$), 128.9 ($2CH_{Ar}$), 21.4 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2912 (m), 2853 (m), 2726 (w), 2677 (w), 2633 (w), 1908 (w), 1612 (m), 1576 (w), 1533 (m), 1513 (m), 1480 (s), 1436 (m), 1372 (s), 1323 (s), 1298 (s), 1275 (s), 1262 (s), 1197 (s), 1185 (s), 1159 (m), 1059 (m), 1022 (m), 963 (w), 884 (m), 820 (s), 799 (m), 760 (s), 749 (s), 717 (s), 672 (s), 659 (m), 603 (s), 566 (s), 559 (s), 540 (s). **MS** (EI, 70 eV): m/z (%) = 355 (M^+, 16), 354 (M^+, 13), 353 (M^+, 66), 352 (M^+, 30), 351 (M^+, 100), 350 (M^+, 29), 349 (M^+, 52), 348 (M^+, 13), 318 (15), 316 (29), 314 (19), 237 (10), 235 (17), 200 (12), 164 (20), 118 (12). **HR-MS** (ESI): m/z = calcd. for $C_{12}H_7NBrCl_3$ ($M+H^+$) 348.88220; found: 348.88204; calcd. for $C_{12}H_7NBrCl_2{}^{37}Cl$ ($M+H^+$) 350.87925, found 350.87956; calcd. for $C_{12}H_7N^{81}BrCl_3$ ($M+H^+$) 350.88015, foud 350.87956; calcd. for $C_{12}H_7NBr^{37}Cl_2Cl$ ($M+H^+$) 352.87630, found 352.87636; calcd. for $C_{12}H_7N_{81}Br^{37}ClCl_2$ ($M+H^+$) 352.87720, found 352.87636. Anal. calcd. for $C_{12}H_7NBrCl_3$: C, 41.01; H, 2.01; N, 3.99 found: C, 41.19; H, 2.16; N, 4.09.

4-bromo-2,3,5-trichloro-6-(4-methoxyphenyl)pyridine (4c):



4c was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 4-methoxyphenylboronic acid (0.45 mmol, 68.4 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 80 mg (73 %). mp. 143 - 144 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.70 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 7.00 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 3.88 (s, 3H, OCH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 161.1 (*C*-OCH_3), 154.8 ($C_{Ar/Hetar}$), 146.9 ($C_{Ar/Hetar}$), 137.2 (C_{Ar}), 131.3 ($2CH_{Ar}$), 130.6 ($C_{Ar/Hetar}$), 130.5 ($C_{Ar/Hetar}$), 129.3 ($C_{Ar/Hetar}$), 113.9 ($2CH_{Ar}$), 55.7 (OCH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3051 (w), 3018 (w), 2964 (m), 2923 (m), 2841 (m), 1858 (w), 1606 (s), 1578 (w), 1511 (s), 1481 (s), 1437 (m), 1371 (s), 1326 (s), 1303 (s), 1286 (s), 1279 (s), 1255 (s), 1199 (s), 1176 (s), 1113 (m), 1105 (s), 1061 (s), 1030 (s), 1010 (s), 954 (m), 883 (m), 828 (s), 799 (s), 764 (s), 752 (s), 671 (s), 658 (m), 627 (m), 602 (s), 572 (s), 559 (s). **MS** (EI, 70 eV): m/z (%) = 371 (M^+, 17), 370 (M^+, 8), 369 (M^+, 65), 368 (M^+, 14), 367 (M^+, 100), 365 (M^+, 52), 354 (5), 352 (7), 326 (11), 324 (16), 322 (8), 317 (5), 289 (10), 287 (6), 253 (5), 251 (7), 210 (7), 208 (11), 181 (5), 138 (7), 118 (5). **HR-MS** (ESI): m/z = calcd. for $C_{12}H_7ONBrCl_3$ ($M+H^+$) 364.87711; found: 364.87736; calcd. for $C_{12}H_7ONBrCl_2{}^{37}Cl$ ($M+H^+$) 366.87416; found 366.87499; calcd. for $C_{12}H_7ON^{81}BrCl_3$ ($M+H^+$) 366.87506; found 366.87499; calcd. for $C_{12}H_7ON^{81}BrCl_2{}^{37}Cl$ ($M+H^+$) 368.87211; found 368.87229; calcd. for $C_{12}H_7ONBrCl^{37}Cl_2$ ($M+H^+$) 368.87121; found 368.87229; calcd. for $C_{12}H_7ON^{81}BrCl^{37}Cl_2$ ($M+H^+$) 370.86916; found 370.86951; calcd. for $C1_2H_7ONBr^{37}Cl_3$ ($M+H^+$) 370.86826; found 370.86951. Anal. calcd. for $C_{12}H_7BrCl_3NO$: C, 39.22; H, 1.92; N, 3.81 found: C, 39.35; H, 2.01; N, 4.02.

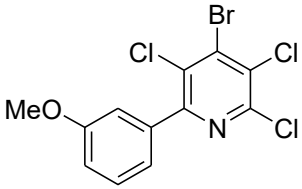
4-bromo-2,3,5-trichloro-6-(4-fluorophenyl)pyridine (4d):



4d was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 4-fluorophenylboronic acid (0.45 mmol, 63.0 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 78 mg (73 %). mp. 148 - 149 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.67-7.74 (m, 2H, CH_{Ar}), 7.13 - 7.21 (m, 2H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$):

δ = 163.5 (d, ^{1}J = 250.6 Hz, C_{Ar}-F), 153.8 (C_{Hetar}), 147.0 (C_{Hetar}), 137.1 (C_{Hetar}), 132.7 (d, ^{4}J = 3.3 Hz, C_{Ar}), 131.5 (d, ^{3}J = 8.5 Hz, $2CH_{Ar}$), 131.1 (C_{Hetar}), 130.6 (C_{Hetar}), 115.3 (d, ^{2}J = 21.9 Hz, $2CH_{Ar}$). **^{19}F-NMR** (282 MHz, $CDCl_3$): δ = -110.49. **IR** (ATR, cm^{-1}): ṽ = 3111 (w), 3063 (m), 2923 (m), 2853 (w), 1775 (w), 1603 (s), 1514 (s), 1483 (s), 1413 (w), 1381 (s), 1371 (s), 1323 (s), 1308 (s), 1296 (s), 1277 (s), 1262 (s), 1227 (s), 1201 (s), 1162 (s), 1101 (s), 1062 (s), 962 (m), 888 (m), 837 (s), 815 (s), 765 (s), 752 (s), 672 (s), 659 (s), 602 (s), 568 (s), 561 (s), 548 (m). **MS** (EI, 70 eV): m/z (%) = 359 (M^+, 17), 358 (M^+, 8), 357 (M^+, 61), 356 (M^+, 12), 355 (M^+, 100), 353 (M^+, 50), 322 (20), 320 (44), 318 (26), 241 (29), 240 (8), 239 (46), 204 (10), 178 (13), 169 (22), 120 (13), 118 (16). **HR-MS** (ESI): m/z = calcd. for $C_{11}H_4NBrCl_3F$ ($M+H^+$) 352.85712, found: 352.85730; calcd. for $C_{11}H_4NBrCl_2{}^{37}ClF$ ($M+H^+$) 354.85417; found 354.85455; calcd. for $C_{11}H_4N^{81}BrCl_3F$ ($M+H^+$) 354.85508, found 354.85455; calcd. for $C_{11}H_4N^{81}BrCl_2{}^{37}ClF$ ($M+H^+$) 356.85213; found 356.85190; calcd. for $C_{11}H_4NBrCl^{37}Cl_2F$ ($M+H^+$) 356.85122; found 356.85190; calcd. for $C_{11}H_4N^{81}BrCl^{37}Cl_2F$ ($M+H^+$) 358.84918; found 358.84890; calcd. for $C_{11}H_4NBr^{37}Cl_3F$ ($M+H^+$) 358.84827; found 358.84890. Anal. calcd. for $C_{11}H_4BrCl_3FN$: C, 37.17; H, 1.13; N, 3.94 found: C, 37.14; H, 1.23; N, 4.16.

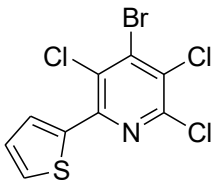
4-bromo-2,3,5-trichloro-6-(3-methoxyphenyl)pyridine (4e):



4e was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 3-methoxyphenylboronic acid (0.45 mmol, 68.4 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 85 mg (77 %). mp. 128 - 129 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 7.40 (pt, ^{3}J = 7.9 Hz, ^{3}J = 7.8 Hz, 1H, CH_{Ar}), 7.25 (ddd, ^{3}J = 6.67 Hz, ^{4}J = 1.6 Hz, ^{4}J = 1.0 Hz, 1H, CH_{Ar}), 7.18 (dd, ^{4}J = 2.6 Hz, ^{4}J = 1.6 Hz, 1H, CH_{Ar}), 7.02 (ddd, ^{3}J = 8.2 Hz, ^{4}J = 2.6 Hz, ^{4}J = 1.0 Hz, 1H, CH_{Ar}), 3.87 (s, 3H, OCH_3). **^{13}C-NMR** (63 MHz, $CDCl_3$): δ = 159.3 (*C*-OCH_3), 154.8 ($C_{Ar/Hetar}$), 146.9 ($C_{Ar/Hetar}$), 137.9 (C_{Ar}), 137.0 ($C_{Ar/Hetar}$), 131.1 ($C_{Ar/Hetar}$), 130.8 ($C_{Ar/Hetar}$), 129.3 (CH_{Ar}), 121.7 (CH_{Ar}), 115.5 (CH_{Ar}), 114.8 (CH_{Ar}), 55.4 (OCH_3). **IR** (ATR, cm^{-1}): ṽ = 3061 (w), 3001 (m), 2962 (m), 2939 (m), 2835 (m), 1790 (w), 1745 (w), 1593 (s), 1526 (m), 1487 (s), 1466 (s), 1372 (s), 1320 (s), 1300 (s), 1283 (s), 1265 (s), 1231 (vs), 1200 (s), 1185 (s), 1161 (s), 1076 (s), 1067 (s), 1030 (s), 993 (s), 926 (s), 873 (s), 833 (m), 795 (s), 761

(s), 749 (s), 702 (s), 689 (s), 658 (m), 602 (s), 553 (s). **MS** (EI, 70 eV): m/z (%) = 371 (M^+, 18), 370 (M^+, 19), 369 (M^+, 65), 368 (M^+, 61), 367 (M^+, 100), 366 (M^+, 79), 365 (M^+, 51), 364 (M^+, 37), 341, 340 (14), 339 (15), 338 (23), 337 (20), 336 (13), 302 (18), 300 (12), 289 (10), 223 (10), 221 (15), 210 (13), 208 (18), 138 (10), 118 (10). **HR-MS** (ESI): m/z = calcd. for $C_{12}H_7ONBrCl_3$ ($M+H^+$) 364.87711, found: 364.87699; calcd. for $C_{12}H_7ONBrCl_2{}^{37}Cl$ ($M+H^+$) 366.87416; found 366.87451; calcd. for $C_{12}H_7ON^{81}BrCl_3$ ($M+H^+$) 366.87506, found 366.87451; calcd. for $C_{12}H_7ON^{81}BrCl_2{}^{37}Cl$ ($M+H^+$) 368.87211; found 368.87179; calcd. for $C_{12}H_7ONBrCl^{37}Cl_2$ ($M+H^+$) 368.87121; found 368.87179; calcd. for $C_{12}H_7ON^{81}BrCl^{37}Cl_2$ ($M+H^+$) 370.86916, found 370.86922; calcd. for $C_{12}H_7ONBr^{37}Cl_3$ ($M+H^+$) 370.86826; found 370.86922. Anal. calcd. for $C_{12}H_7BrCl_3NO$: C, 39.22; H, 1.92; N, 3.81 found: C, 39.40; H, 2.03; N, 3.99.

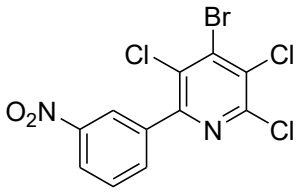
4-bromo-2,3,5-trichloro-6-(thiophen-2-yl)pyridine (4f):



4f was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 2-Thienylboronic acid (0.45 mmol, 57.6 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 83 mg (81 %). mp. 98 - 99 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 8.08 (dd, ^4J = 3.0 Hz, ^4J = 1.3 Hz, 1H, CH_{Hetar}), 7.69 (dd, ^3J = 5.1 Hz, ^4J = 1.3 Hz, 1H, CH_{Hetar}), 7.40 (dd, ^3J = 5.1 Hz, ^4J = 3.0 Hz, 1H, CH_{Hetar}). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 149.5 (C_{Hetar}), 146.6(C_{Hetar}), 137.4(C_{Hetar}), 137.1(C_{Hetar}), 130.2(C_{Hetar}), 129.7(C_{Hetar}), 128.8 (CH_{Hetar}), 128.7(CH_{Hetar}), 125.2(CH_{Hetar}). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3145 (w), 3095 (w), 2957 (w), 2923 (w), 1793 (w), 1518 (m), 1493 (m), 1475 (m), 1413 (m), 1337 (s), 1300 (s), 1284 (s), 1262 (m), 1192 (s), 1177 (m), 1081 (s), 1054 (m), 927 (m), 890 (m), 810 (s), 790 (s), 751 (s), 735 (s), 686 (s), 663 (s), 648 (s), 608 (s), 596 (s), 585 (s). **MS** (EI, 70 eV): m/z (%) = 347 (M^+, 19), 346 (M^+, 9), 345 (M^+, 70), 344 (M^+, 15), 343 (M^+, 100), 341 (M^+, 49), 310 (19), 308 (40), 306 (24), 229 (13), 227 (19), 157 (12), 118 (12), 45 (12). **HR-MS** (ESI): m/z = calcd. for $C_9H_3NBrCl_3S$ ($M+H^+$) 340.82297; found 340.82284; calcd. for $C_9H_3N^{81}BrCl_3S$ ($M+H^+$) 342.82092; found 342.82059; calcd. for $C_9H_3NBrCl_2{}^{37}ClS$ ($M+H^+$) 342.82002; found 342.82059; calcd. for $C_9H_3N^{81}BrCl_2{}^{37}ClS$ ($M+H^+$) 344.81797; found 344.81780; calcd. for $C_9H_3NBrCl^{37}Cl_2S$ ($M+H^+$) 344.81707; found 344.81780; calcd. for $C_9H_3N^{81}BrCl^{37}Cl_2S$ ($M+H^+$) 346.81502; found 346.81466;

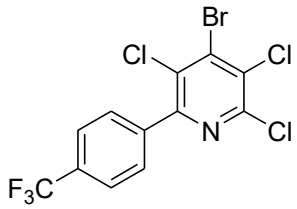
calcd. for $C_9H_3NBr^{37}Cl_3S$ ($M+H^+$) 346.81412; found 346.81466. Anal. calcd. for $C_9H_3BrCl_3NS$: C, 31.47; H, 0.88; N, 4.08 found: C, 31.60; H, 1.20; N, 4.29.

4-bromo-2,3,5-trichloro-6-(3-nitrophenyl)pyridine (4g):



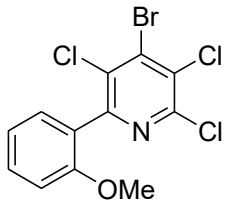
4g was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 3-nitrophenylboronic acid (0.45 mmol, 75.1 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 89 mg (78 %). mp. 166 - 167 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 8.60 (pt, ^4J = 1.7 Hz, 1H, CH_{Ar}), 8.34 (ddd, ^3J = 8.3 Hz, ^4J = 2.3 Hz, ^4J = 1.1 Hz, 1H, CH_{Ar}), 8.05 (ddd, ^3J = 7.8 Hz, ^4J = 1.7 Hz, ^4J = 1.1 Hz, 1H, CH_{Ar}), 7.68 (pt, ^3J = 8.0 Hz, 1H, CH_{Ar}). **^{13}C-NMR** (63 MHz, $CDCl_3$): δ = 152.0 ($C_{Ar/Hetar}$), 148.0 ($C_{Ar/Hetar}$), 147.5 (C_{Ar}), 138.0 (C_{Ar}), 137.5 ($C_{Ar/Hetar}$), 135.4 (CH_{Ar}), 132.4 ($C_{Ar/Hetar}$), 130.9 ($C_{Ar/Hetar}$), 129.4 (CH_{Ar}), 124.7 (CH_{Ar}), 124.5 (CH_{Ar}). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3102 (m), 3077 (m), 2961 (w), 2924 (w), 2858 (w), 1810 (w), 1746 (w), 1580 (w), 1536 (s), 1525 (s), 1494 (s), 1479 (s), 1369 (m), 1351 (s), 1327 (s), 1313 (s), 1304 (s), 1294 (s), 1272 (s), 1259 (s), 1201 (s), 1174 (m), 1095 (m), 1082 (s), 1066 (s), 1002 (m), 904 (s), 855 (s), 806 (s), 783 (s), 757 (m), 728 (s), 685 (s), 669 (s), 651 (m), 603 (s), 564 (s). **MS** (EI, 70 eV): m/z (%) = 386 (M^+, 19), 385 (M^+, 10), 384 (M^+, 66), 383 (M^+, 14), 382 (M^+, 100), 380 (M^+, 54), 340 (12), 338 (46), 337 (10), 336 (70), 334 (35), 324 (10), 301 (16), 299 (10), 257 (27), 255 (26), 220 (15), 187 (11), 185 (32), 118 (11). **HR-MS** (ESI): m/z = calcd. for $C_{11}H_4O_2N_2BrCl_3$ ($M+H^+$) 379.85162; found: 379.85154; calcd. for $C_{11}H_4O_2N_2BrCl_2{}^{37}Cl$ ($M+H^+$) 381.84867; found 381.84911; calcd. for $C_{11}H_4O_2N_2{}^{81}BrCl_3$ ($M+H^+$) 381.84958; found 381.84911; calcd. for $C_{11}H_4O_2N_2BrCl^{37}Cl_2$ ($M+H^+$) 383.84572; found 383.84618; calcd. for $C_{11}H_4O_2N_2{}^{81}BrCl_2{}^{37}Cl$ ($M+H^+$) 383.84663; found 383.84618; calcd. for $C_{11}H_4O_2N_2Br^{37}Cl_3$ ($M+H^+$) 385.81277, found 385.84350; calcd. for $C_{11}H_4O_2N_2{}^{81}BrCl^{37}Cl_2$ ($M+H^+$) 385.84368; found 385.84350. Anal. calcd. for $C_{11}H_4BrCl_3N_2O_2$: C, 34.55; H, 1.05; N, 7.33 found: C, 34.36; H, 1.15; N, 7.19.

4-bromo-2,3,5-trichloro-6-(4-(trifluoromethyl)phenyl)pyridine (4h):



4h was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 4-(trifluoromethyl)phenylboronic acid (0.45 mmol, 85.5 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 73 mg (60 %). mp. 123 - 124 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 7.82 (d, ^{3}J = 8.5 Hz, 2H, CH_{Ar}), 7.75 (d, ^{3}J = 8.5 Hz, 2H, CH_{Ar}). **^{13}C-NMR** (63 MHz, $CDCl_3$): δ = 153.3 ($C_{Ar/Hetar}$), 147.3 ($C_{Ar/Hetar}$), 140.0 (q, ^{5}J = 1.1 Hz, C_{Ar}), 137.3 ($C_{Ar/Hetar}$), 132.0 ($C_{Ar/Hetar}$), 131.6 (q, ^{2}J = 32.7 Hz, (C_{Ar}), 130.9 ($C_{Ar/Hetar}$), 129.8 ($2CH_{Ar}$), 125.3 (q, ^{3}J = 3.7 Hz, $2CH_{Ar}$), 123.8 (q, ^{1}J = 272.8 Hz, CF_3). **^{19}F-NMR** (235 MHz, $CDCl_3$): δ = - 62.89 ($ArCF_3$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3118 (w), 2939 (w), 2641 (w), 1805 (w), 1621 (m), 1581 (w), 1532 (m), 1489 (s), 1409 (m), 1325 (s), 1307 (s), 1283 (s), 1263 (s), 1200 (s), 1163 (s), 1105 (s), 1069 (s), 1061 (s), 1018 (s), 970 (s), 956 (s), 883 (m), 844 (s), 789 (s), 764 (s), 738 (s), 704 (s), 631 (s), 619 (s), 581 (s), 562 (s). **MS** (EI, 70 eV): m/z (%) = 409 (M^+, 17), 408 (M^+, 9), 407 (M^+, 63), 406 (M^+, 14), 405 (M^+, 100), 404 (M^+, 7), 403 (M^+, 53), 386 (8), 372 (33), 371 (10), 370 (74), 368 (47), 291 (41), 290 (14), 289 (64), 257 (12), 255 (18), 254 (19), 253 (13), 228 (19), 219 (24), 218 (14), 200 (11), 193 (14), 185 (12), 169 (11), 155 (17), 153 (18), 145 (11), 123 (12), 122 (11), 121 (10), 75 (17), 74 (10), 69 (18). **HR-MS** (EI): m/z = calcd. for $C_{12}H_4NBrCl_3F_3$ $[M]^+$: 402.85393; found: 402.85369; calcd. for $C_{12}H_4NBrCl_2\ ^{37}ClF_3$: 404.85098; found 404.85134; calcd. for $C_{12}H_4N^{81}BrCl_2\ ^{37}ClF_3$: 406.84893; found 406.84873. Anal. calcd. for $C_{12}H_4BrCl_3F_3N$: C 35.55, H 0.99, N 3.45; found: C 35.75, H 1.03, N 3.36.

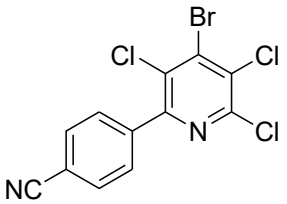
4-bromo-2,3,5-trichloro-6-(2-methoxyphenyl)pyridine (4i):



4i was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 2-methoxyphenylboronic acid (0.45 mmol, 68.4 mg) and was purified via column chromatography (heptane/dichloromethane). Pink solid; yield: 94 mg (86 %). mp. 123 - 124 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 7.37-7.48 (m, 1H, CH_{Ar}), 7.27 (dd, ^{3}J = 7.0 Hz, ^{4}J = 2.1 Hz, 1H, CH_{Ar}), 6.97-7.09 (m, 2H, CH_{Ar}), 3.81 (s, 3H, OCH_3). **^{13}C-NMR** (63 MHz, $CDCl_3$): δ = 156.6 (*C*-OCH_3), 153.9 ($C_{Ar/Hetar}$),

146.6 ($C_{Ar/Hetar}$), 135.9 ($C_{Ar/Hetar}$), 133.0 ($C_{Ar/Hetar}$), 131.1 (CH), 131.0 ($C_{Ar/Hetar}$), 130.1 (CH), 126.5 (C_{Ar}), 120.7 (CH_{Ar}), 111.0 (CH_{Ar}), 55.5 (OCH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3001 (w), 2960 (w), 2942 (w), 2922 (w), 2841 (w), 1601 (m), 1531 (w), 1488 (s), 1462 (s), 1437 (m) , 1372 (s), 1327 (m), 1281 (s), 1260 (s), 1240 (s), 1167 (m), 1097 (s), 1062 (s), 1041 (s), 1016 (s), 942 (w), 884 (w), 796 (s), 779 (m), 760 (s), 733 (s), 696 (s), 655 (m), 613 (m), 604 (s), 572 (s), 561 (s), 528 (m). **MS** (EI, 70 eV): m/z (%) = 369 (M^+, 15), 367 (M^+, 23), 365 (M^+, 12), 334 (46), 333 (15), 332 (100), 331 (13), 330 (64), 317 (10), 304 (21), 302 (21), 273 (11), 271 (12), 253 (37), 252 (12), 251 (57), 225 (11), 223 (27), 222 (10), 221 (22), 216 (16), 210 (15), 208 (20), 201 (11), 188 (11), 187 (13), 185 (12), 151 (15), 147 (12), 138 (18), 120 (14), 118 (20), 111 (11), 63 (12), 62 (6), 39 (8). **HR-MS** (EI): m/z = calcd. for $C_{12}H_7ONBrCl_3$ $[M]^+$: 364.87711; found: 364.87695; calcd. for $C_{12}H_7ONBrCl_2{}^{37}Cl$: 366.87416; found 366.87456; calcd. for $C_{12}H_7ON\ {}^{81}BrCl_2{}^{37}Cl$: 368.87211; found 368.87198. Anal. calcd. for $C_{12}H_7BrCl_3NO$: C 39.22, H 1.92, N 3.81; found: C 39.52, H 2.45, N 3.46.

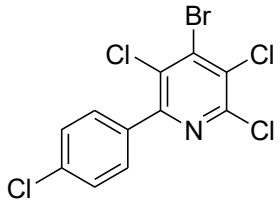
4-bromo-2,3,5-trichloro-6-(4-cyanophenyl)pyridine (4j):



4j was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 4-cyanophenylboronic acid (0.45 mmol, 66.1 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 64 mg (60 %). mp. 195 - 196 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 7.74-7.84 (m, 4H, CH_{Ar}). **^{13}C-NMR** (63 MHz, $CDCl_3$): δ = 152.6 ($C_{Ar/Hetar}$), 147.4 ($C_{Ar/Hetar}$), 140.7 ($C_{Ar/Hetar}$), 137.5 ($C_{Ar/Hetar}$), 132.3 ($C_{Ar/Hetar}$), 132.0 ($2CH_{Ar}$), 130.9 ($C_{Ar/Hetar}$), 130.2 ($2CH_{Ar}$), 118.2 (C≡N), 113.5 (C_{Ar}). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3102 (w), 3082 (w), 3053 (w), 2959 (w), 2922 (w), 2853 (w), 2227 (m), 1937 (w), 1525 (m), 1480 (m), 1370 (s), 1326 (s), 1302 (s), 1287 (m), 1273 (m), 1262 (s), 1199 (m), 1179 (m), 1063 (m), 1021 (m), 972 (w), 884 (m), 844 (s), 805 (m), 753 (s), 663 (m), 653 (s), 604 (s), 550 (m), 541 (s). **MS** (EI, 70 eV): m/z (%) = 366 (M^+, 17), 365 (M^+, 9), 364 (M^+, 64), 363 (M^+, 14), 362 (M^+, 100), 361 (M^+, 8), 360 (M^+, 52), 329 (36), 328 (12), 327 (79), 325 (50), 248 (39), 247 (13), 246 (61), 212 (10), 211 (20), 210 (21), 187 (10), 185 (28), 176 (38), 163 (10), 155 (14), 153 (15), 150 (12), 124 (12), 123 (19) 122 (11), 120 (34), 118 (49), 110 (10), 99 (15), 92 (12), 76 (10), 75 (19), 74 (12). **HR-MS** (EI): m/z = calcd. for $C_{12}H_4N_2BrCl_3$ $[M]^+$: 359.86180; found: 359.86197;

calcd. for $C_{12}H_4N_2{}^{81}BrCl_3$: 361.85975; found 361.85963; calcd. for $C_{12}H_4N_2{}^{81}BrCl_2{}^{37}Cl$: 363.85680; found 363.85706; calcd. for $C_{12}H_4N_2{}^{81}BrCl^{37}Cl_2$: 365.85385; found 365.85453. Anal. calcd. for $C_{12}H_4BrCl_3N_2$: C 39.77, H 1.11, N 7.73; found: C 40.24, H 1.36, N 7.39.

4-bromo-2,3,5-trichloro-6-(4-chlorophenyl)pyridine (4k):



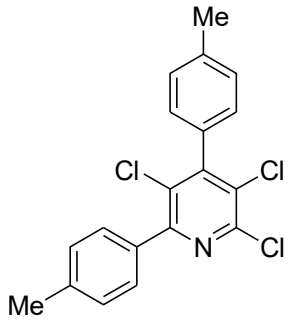
4k was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.3 mmol, 115.9 mg) and 4-chlorophenylboronic acid (0.45 mmol, 70.4 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 77 mg (69 %). mp. 161 - 162 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 7.65 (d, ^3J = 8.56 Hz, 2H, CH_{Ar}), 7.46 (d, ^3J = 8.56 Hz, 2H, CH_{Ar}). **^{13}C-NMR** (63 MHz, $CDCl_3$): δ = 153.6 ($C_{Ar/Hetar}$), 147.1 ($C_{Ar/Hetar}$), 137.2 ($C_{Ar/Hetar}$), 136.0 (C_{Ar}), 135.0 ($C_{Ar/Hetar}$), 131.3 ($C_{Ar/Hetar}$), 130.8 ($2CH_{Ar}$), 130.7 (C_{Ar}), 128.5 ($2CH_{Ar}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2957 (w), 1911 (w), 1594 (m), 1523 (w), 1496 (m), 1481 (s), 1371 (s), 1325 (s), 1308 (s), 1293 (s), 1260 (s), 1201 (m), 1182 (m), 1090 (m), 1059 (m), 1016 (s), 964 (m), 885 (m), 833 (s), 779 (s), 751 (s), 737 (s), 715 (m), 658 (m), 639 (s), 625 (m), 603 (s), 534 (m). **MS** (EI, 70 eV): m/z (%) = 377 (M^+, 6), 375 (M^+, 32), 374 (M^+, 10), 373 (M^+, 83), 372 (M^+, 13), 371 (M^+, 100), 370 (M^+, 6), 369 (M^+, 45), 338 (31), 336 (49), 334 (26), 259 (17), 257 (54), 256 (10), 255 (57), 222 (10), 221 (10), 220 (15), 219 (12), 196 (12), 194 (12), 187 (14), 185 (41), 169 (11), 168 (15), 155 (12), 153 (12), 150 (12), 123 (14), 120 (25), 118 (33), 111 (13), 110 (12), 109 (10), 99 (12), 98 (17), 97 (20), 85 (10), 75 (20), 74 (14), 50 (10). **HR-MS** (EI): m/z = calcd. for $C_{11}H_4NBrCl_4$ $[M]^+$: 368.82757; found: 368.82764; calcd. for $C_{11}H_4NBrCl_3{}^{37}Cl$: 370.82462; found 370.82506; calcd. for $C_{11}H_4N$ $^{81}BrCl_3{}^{37}Cl$: 372.82258; found 372.82230; calcd. for $C_{11}H_4N{}^{81}BrCl_2{}^{37}Cl_2$: 374.81963; found 374.81961. Anal. calcd. for $C_{11}H_4BrCl_4N$: C 35.53, H 1.08, N 3.77; found: C 35.67, H 1.18, N 3.76.

General procedure for the Synthesis of compounds 5a–h

An oven-dried, argon-flushed sealable glass tube was charged with 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg), $Pd(OAc)_2$ (5 mol%, 2.9 mg), PCy_3 (10 mol%, 7.24 mg), the appropriate arylboronic acid (0.55 mmol) and K_3PO_4

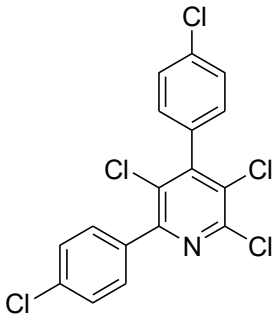
(0.55 mmol, 115.12 mg) followed by a mixture of toluene/water/*n*-butanol (6:1:1, 4 mL). The tube was sealed with a Teflon valve and stirred at 100 °C for 19 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/dichloromethane as eluent.

2,3,5-trichloro-4,6-di-*p*-tolylpyridine (5a):



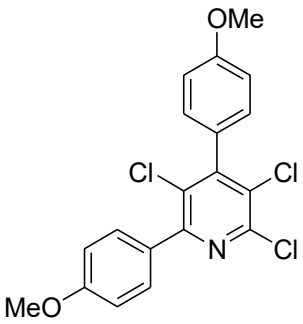
5a was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and *p*-tolylboronic acid (0.55 mmol, 74.8 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 76 mg (81 %). mp. 121 - 122 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.65 (d, ^3J = 8.2 Hz, 2H, CH_{Ar}), 7.35 (d, ^3J = 8.0 Hz, 2H, CH_{Ar}), 7.29 (d, ^3J = 8.0 Hz, 2H, CH_{Ar}), 7.19 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 2.46 (s, 3H, CH_3), 2.43 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 154.9 ($C_{Ar/Hetar}$), 150.9 ($C_{Ar/Hetar}$), 147.1($C_{Ar/Hetar}$), 139.5 ($C_{Ar/Hetar}$), 139.1 ($C_{Ar/Hetar}$), 134.1 ($C_{Ar/Hetar}$), 133.0 ($C_{Ar/Hetar}$), 129.4 ($4CH_{Ar}$), 129.0 ($2C_{Ar/Hetar}$), 128.8 ($2CH_{Ar}$), 128.3($2CH_{Ar}$), 21.5 (CH_3), 21.4 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3038 (w), 2920 (m), 2853 (m), 1908 (w), 1614 (m), 1575 (w), 1513 (m), 1500 (s), 1450 (m), 1373 (s), 1316 (m), 1295 (s), 1267 (s), 1205 (m), 1191 (s), 1168 (m), 1043 (s), 1022 (m), 965 (m), 875 (m), 836 (m), 819 (s), 793 (m), 767 (s), 758 (s), 729 (s), 719 (s), 670 (s), 643 (m), 618 (s), 610 (m), 580 (m), 563 (s). **MS** (EI, 70 eV): m/z (%) = 366 (M^+, 7), 365 (M^+, 34), 364 (M^+, 24), 363 (M^+, 97), 362 (M^+, 33), 361 (M^+, 100), 360 (M^+, 13), 328 (32), 327 (11), 326 (50), 255 (9), 254 (11), 241 (7), 240 (14), 91 (8). **HR-MS** (ESI): m/z = calcd. for $C_{19}H_{14}Cl_3N$ ($M+H^+$) 361.01863, found: 361.01827. Anal. calcd. for $C_{19}H_{14}Cl_3N$: C, 62.92; H, 3.89; N, 3.86 found: C, 62.89; H, 3.82; N, 3.95.

2,3,5-trichloro-4,6-bis(4-chlorophenyl)pyridine (5b):



5b was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 4-chlorophenylboronic acid (0.55 mmol, 86.0 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 80 mg (77 %). mp. 143 - 144 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.70 (d, ^{3}J = 8.6 Hz, 2H, CH_{Ar}), 7.53 (d, ^{3}J = 8.5 Hz, 2H, CH_{Ar}), 7.46 (d, ^{3}J = 8.6 Hz, 2H, CH_{Ar}), 7.23 (d, ^{3}J = 8.5 Hz, 2H, CH_{Ar}). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 153.7 ($C_{Ar/Hetar}$), 149.9 ($C_{Ar/Hetar}$), 147.5 ($C_{Ar/Hetar}$), 135.8 ($C_{Ar/Hetar}$), 135.4 ($C_{Ar/Hetar}$), 135.0 ($C_{Ar/Hetar}$), 133.8 ($C_{Ar/Hetar}$), 130.9 ($2CH_{Ar}$), 129.9 ($2CH_{Ar}$), 129.5 ($C_{Ar/Hetar}$), 129.2 ($2CH_{Ar}$), 128.7 ($C_{Ar/Hetar}$), 128.5 ($2CH_{Ar}$). **IR** (ATR, cm^{-1}): ṽ = 3094 (w), 3068 (w), 2953 (w), 2922 (m), 2852 (m), 1781 (w), 1732 (w), 1593 (m), 1535 (w), 1486 (s), 1402 (m), 1367 (s), 1307 (m), 1286 (s), 1259 (s), 1180 (m), 1166 (m), 1091 (s), 1041 (s), 1016 (s), 962 (m), 895 (w), 831 (s), 812 (s), 767 (s), 744 (s), 729 (s), 696 (m), 650 (s), 634 (s), 612 (s), 541 (m). **MS** (EI, 70 eV): m/z (%) = 407 (M^+, 21), 406 (M^+, 12), 405 (M^+, 65), 404 (M^+, 19), 403 (M^+, 100), 402 (M^+, 13), 401 (M^+, 63), 370 (26), 369 (11), 368 (54), 366 (42), 333 (14), 331 (15), 297 (15), 296 (15), 295 (21), 263 (12), 261 (38), 225 (22), 196 (15), 194 (22), 185 (13), 184 (15), 149 (18), 148 (27), 135 (11), 130 (24), 99 (15), 75 (14). **HR-MS** (ESI): m/z = calcd. for $C_{17}H_8Cl_5N$ ($M+H^+$) 401.91721, found: 401.91763; calcd. for $C_{17}H_8Cl_4{}^{35}ClN$: 403.91436, found: 403.9144; calcd. for $C_{17}H_8Cl_3{}^{35}Cl_2N$: 405.91156; found 405.91234. Anal. calcd. for $C_{17}H_8Cl_5N$: C, 50.60; H, 2.00; N, 3.47 found: C, 50.74; H, 2.28; N, 3.54.

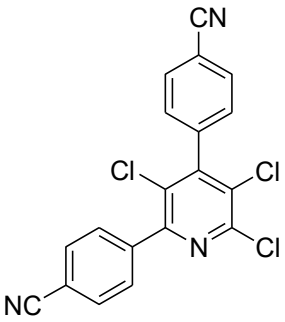
2,3,5-trichloro-4,6-bis(4-methoxyphenyl)pyridine (5c):



5c was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 4-methoxyphenylboronic acid (0.55 mmol, 83.6 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 55 mg (54 %). mp. 122 - 123 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.74 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 7.23 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 7.06 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 6.99 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 3.89 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3). **^{13}C-NMR**

(75 MHz, $CDCl_3$): δ = 160.5 (*C*-OCH_3), 160.0 (*C*-OCH_3), 154.4 ($C_{Ar/Hetar}$), 150.6 ($C_{Ar/Hetar}$), 147.1($C_{Ar/Hetar}$), 131.1 ($2CH_{Ar}$), 129.9 ($2CH_{Ar}$), 129.4 ($C_{Ar/Hetar}$), 129.0 ($C_{Ar/Hetar}$), 128.9 ($C_{Ar/Hetar}$), 128.1 ($C_{Ar/Hetar}$), 114.0 ($2CH_{Ar}$), 113.5($2CH_{Ar}$), 55.35 (OCH_3), 55.27 (OCH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 3010 (w), 2957 (w), 2933 (w), 2838 (w), 1603 (s), 1576 (w), 1507 (s), 1497 (s), 1461 (m), 1453 (m), 1370 (s), 1357 (m), 1295 (s), 1271 (m), 1245 (s), 1176 (s), 1115 (m), 1048 (m), 1026 (s), 966 (w), 876 (w), 839 (s), 833 (s), 826 (s), 794 (s), 760 (m), 739 (s), 641 (m), 616 (m), 608 (m), 576 (s), 529 (m). **MS** (EI, 70 eV): m/z (%) = 398 (M^+, 7), 397 (M^+, 32), 396 (M^+, 21), 395 (M^+, 96), 394 (M^+, 22), 393 (M^+, 100), 352 (8), 350 (8), 315 (7), 272 (7), 237 (8), 202 (8), 201 (13), 197 (9), 196 (11), 176 (7), 175 (11), 124 (7), 123 (7). **HR-MS** (EI): m/z = calcd. for $C_{19}H_{14}O_2NCl_3$ $[M]^+$: 393.00846; found: 393.00705; calcd. for $C_{19}H_{14}O_2NCl_2{}^{37}Cl$: 395.00551; found 395.00537; calcd. for $C_{19}H_{14}O_2NCl^{37}Cl_2$: 397.00256; found 397.00288. Anal. calcd. for $C_{19}H_{14}Cl_3NO_2$: C 57.82, H 3.58, N 3.55; found: C 58.08, H 3.69, N 3.49.

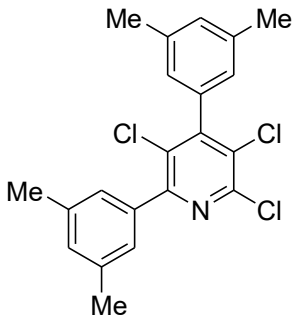
2,3,5-trichloro-4,6-bis(4-cyanophenyl)pyridine (5d):



5d was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 4-cyanophenylboronic acid (0.55 mmol, 80.8 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 65 mg (66 %). mp. 232 - 233 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.88-7.84 (m, 4H, $4CH_{Ar}$), 7.79 (d, ^3J = 8.3 Hz, 2H, CH_{Ar}), 7.43 (d, ^3J = 8.4 Hz, 2H, CH_{Ar}). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 152.9 ($C_{Ar/Hetar}$), 149.3 ($C_{Ar/Hetar}$), 148.1 ($C_{Ar/Hetar}$), 140.5 ($C_{Ar/Hetar}$), 139.5 ($C_{Ar/Hetar}$), 132.7 ($2CH_{Ar}$), 132.0 ($2CH_{Ar}$), 130.3 ($2CH_{Ar}$), 130.0 ($C_{Ar/Hetar}$), 129.4 ($2CH_{Ar}$), 128.3 ($C_{Ar/Hetar}$), 118.2 (C≡N), 118.0 (C≡N), 113.6 (C_{Ar}), 113.4(C_{Ar}). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3101 (w), 3072 (w), 3055 (w), 2954 w), 2921 (m), 2851 (w), 2227 (m), 1814 (w), 1732 (w), 1608 (w), 1540 (m), 1497 (m), 1405 (m), 1370 (s), 1358 (s), 1325 (m), 1308 (m), 1293 (s), 1267 (s), 1181 (m), 1163 (m), 1099 (m), 1044 (s), 1018 (m), 968 (m), 878 (m), 845 (s), 832 (s), 767 (s), 749 (s), 738 (s), 726 (m), 673 (s), 662 (s), 650 (s), 637 (s), 619 (s), 610 (m), 564 (s), 551 (s). **MS** (EI, 70 eV): m/z (%) = 388 (M^+, 6), 387 (M^+, 31), 386 (M^+, 19), 385 (M^+, 93), 384 (M^+, 22), 383 (M^+, 95), 352 (12), 351 (14), 350 (63), 349 (22), 348 (100), 313 (15), 286 (15), 278 (25), 277 (49), 252 (17), 251 (19), 250

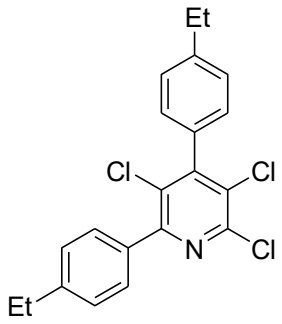
(22), 224 (12), 187 (15), 185 (35), 176 (10), 175 (11), 174 (11), 161 (14), 156 (15), 150 (11), 143 (12), 138 (12), 126 (10), 125 (13), 112 (11), 102 (11), 100 (10), 99 (15), 76 (11), 75 (18). **HR-MS** (EI): m/z = calcd. for $C_{19}H_8N_3Cl_3$ $[M]^+$: 382.97783; found: 382.97752; calcd. for $C_{19}H_8N_3Cl_2{}^{37}Cl$: 384.97488; found 384.97485; calcd. for $C_{19}H_8N_3Cl{}^{37}Cl_2$: 386.97193; found 386.97304. Anal. calcd. for $C_{19}H_8Cl_3N_3$: C 59.33, H 2.10, N 10.92; found: C 59.36, H 2.44, N 10.50.

2,3,5-trichloro-4,6-bis(3,5-dimethylphenyl)pyridine (5e):



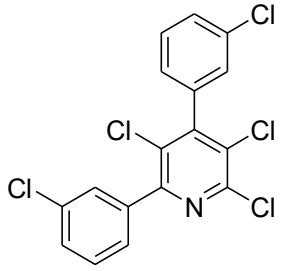
5e was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 3,5-dimethylphenylboronic acid (0.55 mmol, 82.5 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 72 mg (72 %). mp. 120 - 121 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.31 (s, 2H, CH_{Ar}), 7.13 (s, 1H, CH_{Ar}), 7.10 (s, 1H, CH_{Ar}), 6.89 (s, 2H, CH_{Ar}), 2.41 (s, 6H, $2CH_3$), 2.39 (s, 6H, $2CH_3$). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 155.3 ($C_{Ar/Hetar}$), 151.2 ($C_{Ar/Hetar}$), 147.0 ($C_{Ar/Hetar}$), 138.3 ($2C_{Ar/Hetar}$), 137.7 ($2C_{Ar/Hetar}$), 136.9 ($C_{Ar/Hetar}$), 135.8 ($C_{Ar/Hetar}$), 131.0 (CH_{Ar}), 130.7 (CH_{Ar}), 129.0 ($C_{Ar/Hetar}$), 128.9 ($C_{Ar/Hetar}$), 127.1 ($2CH_{Ar}$), 125.8 ($2CH_{Ar}$), 21.4 ($2CH_3$), 21.3 ($2CH_3$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3003 (w), 2953 (w), 2915 (w), 2858 (w), 1605 (m), 1541 (m), 1434 (m), 1372 (s), 1300 (s), 1291 (s), 1264 (m), 1229 (m), 1204 (m), 1164 (w), 1078 (m), 1041 (m), 1013 (m), 996 (m), 899 (m), 882 (w), 850 (s), 770 (m), 709 (s), 691 (m), 654 (m), 625 (m), 535 (m). **MS** (EI, 70 eV): m/z (%) = 394 (M^+, 7), 393 (M^+, 32), 392 (M^+, 25), 391 (M^+, 96), 390 (M^+, 35), 389 (M^+, 100), 388 (M^+, 12), 356 (38), 355 (15), 354 (59), 268 (13), 169 (12), 152 (11), 151 (9), 133 (17), 77 (10). **HR-MS** (EI): m/z = calcd. for $C_{21}H_{18}NCl_3$ $[M]^+$: 389.04993; found: 389.04979; calcd. for $C_{21}H_{18}NCl_2{}^{37}Cl$: 391.04698; found 391.04716; calcd. for $C_{21}H_{18}NCl{}^{37}Cl_2$: 393.04403; found 393.04448. Anal. calcd. for $C_{21}H_{18}Cl_3N$: C 64.55, H 4.64, N 3.58; found: C 64.34, H 4.58, N 3.38.

2,3,5-trichloro-4,6-bis(4-ethylphenyl)pyridine (5f):



5f was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 4-ethylphenylboronic acid (0.55 mmol, 82.5 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 59 mg (58 %). mp. 93 - 94 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.68 (d, ^{3}J = 8.1 Hz, 2H, CH_{Ar}), 7.37 (d, ^{3}J = 8.1 Hz, 2H, CH_{Ar}), 7.32 (d, ^{3}J = 8.1 Hz, 2H, CH_{Ar}), 7.21 (d, ^{3}J = 8.1 Hz, 2H, CH_{Ar}), 2.81-2.69 (m, 4H, $2CH_2CH_3$), 1.33 (t, ^{3}J = 6.7 Hz, 3H, CH_2CH_3), 1.29 (t, ^{3}J = 6.7 Hz, 3H, CH_2CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 154.9 ($C_{Ar/Hetar}$), 150.9 ($C_{Ar/Hetar}$), 147.1 ($C_{Ar/Hetar}$), 145.7 ($C_{Ar/Hetar}$), 145.1 ($C_{Ar/Hetar}$), 134.4 ($C_{Ar/Hetar}$), 133.1 ($C_{Ar/Hetar}$), 129.5 (2CH), 129.0 ($C_{Ar/Hetar}$), 128.9 ($C_{Ar/Hetar}$), 128.3 ($2CH_{Ar}$), 128.1 ($2CH_{Ar}$), 127.7 ($2CH_{Ar}$), 28.7 (CH_2CH_3), 28.6 (CH_2CH_3), 15.4 (CH_2CH_3), 15.1(CH_2CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2963 (m), 2929 (m), 2871 (w), 1610 (m), 1571 (w), 1539 (m), 1501 (m), 1464 (m), 1370 (s), 1303 (s), 1271 (s), 1186 (m), 1167 (w), 1099 (m), 1063 (w), 1043 (s), 968 (w), 876 (w), 851 (m), 829 (s), 767 (m), 738 (m), 716 (m), 668 (s), 619 (m), 578 (s), 537 (m). **MS** (EI, 70 eV): m/z (%) = 394 (M^+, 8), 393 (M^+, 32), 392 (M^+, 31), 391 (M^+, 99), 390 (M^+, 49), 389 (M^+, 100), 388 (28), 378 (20), 377 (13), 376 (58), 375 (16), 374 (61), 253 (10), 240 (9), 188 (11), 187 (11), 181 (13), 180 (36), 179 (40), 144 (10), 127 (12), 126 (11), 119 (12), 105 (14). **HR-MS** (EI): m/z = calcd. for $C_{21}H_{18}NCl_3$ $[M]^+$: 389.04993; found: 389.04880; calcd. for $C_{21}H_{18}NCl_2{}^{37}Cl$: 391.04698; found 391.04634; calcd. for $C_{21}H_{18}NCl^{37}Cl_2$: 393.04403; found 393.04394. Anal. calcd. for $C_{21}H_{18}Cl_3N$: C 64.55, H 4.64, N 3.58; found: C 65.00, H 4.99, N 3.30.

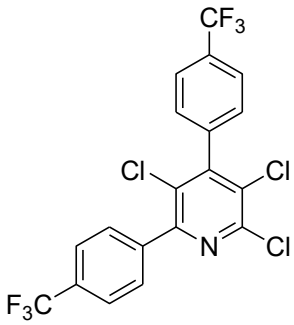
2,3,5-trichloro-4,6-bis(3-chlorophenyl)pyridine (5g):



5g was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 3-chlorophenylboronic acid (0.55 mmol, 86.0 mg) and was purified via column chromatography (heptane/dichloromethane). Oil colorless; yield: 35 mg (34 %). Rf (10 % ethyl acetate/ heptan) = 0.52. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.73 (d, ^{4}J = 1.8 Hz, 1H, CH_{Ar}), 7.63 (pdt, ^{3}J = 6.8, ^{4}J = 1.8 Hz, 1H, CH_{Ar}),

7.50-7.46 (m, 2H, CH_{Ar}), 7.35-7.45 (m, 2H, CH_{Ar}), 7.27-7.31 (m, 1H, CH_{Ar}), 7.14 - 7.21 (m, 1H, CH_{Ar}). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 153.5 ($C_{Ar/Hetar}$), 149.6 ($C_{Ar/Hetar}$), 147.6 ($C_{Ar/Hetar}$), 138.2 ($C_{Ar/Hetar}$), 137.0 ($C_{Ar/Hetar}$), 134.8 ($C_{Ar/Hetar}$), 134.2 ($C_{Ar/Hetar}$), 130.2 (CH_{Ar}), 129.7 ($C_{Ar/Hetar}$), 129.6 (CH_{Ar}), 129.6 (CH_{Ar}), 129.5 (CH_{Ar}), 129.5 (CH_{Ar}), 128.8 ($C_{Ar/Hetar}$), 128.5 (CH_{Ar}), 127.7 (CH_{Ar}), 126.6 (CH_{Ar}). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 2922 (w), 2852 (w), 1807 (w), 1762 (w), 1699 (w), 1596 (w), 1539 (w), 1472 (m), 1419 (w), 1366 (s), 1287 (s), 1256 (m), 1206 (m), 1113 (m), 1095 (m), 1048 (s), 9981 (w), 974 (w), 896 (m), 790 (m), 757 (s), 705 (s), 692 (s), 660 (m), 635 (w), 608 (m), 535 (m). **MS** (EI, 70 eV): m/z (%) = 407 (M^+, 21), 406 (M^+, 12), 405 (M^+, 65), 404 (M^+, 19), 403 (M^+, 100), 402 (M^+, 12), 401 (M^+, 62), 370 (35), 369 (15), 368 (72), 367 (13), 366 (56), 333 (15), 331 (15), 298 (11), 297 (18), 296 (16), 295 (23), 263 (12), 261 (40), 225 (25), 200 (10), 196 (15), 194 (21), 185 (12), 184 (12), 166 (13), 165 (12), 149 (20), 148 (29), 135 (10), 130 (13), 123 (10), 117 (10), 111 (10), 99 (17), 75 (18). **HR-MS** (EI): m/z = calcd. for $C_{17}H_8NCl_5$ $[M]^+$: 400.90939; found: 400.90909; calcd. for $C_{17}H_8NCl_4{}^{37}Cl$: 402.90644; found 402.90615; calcd. for $C_{17}H_8NCl_3{}^{37}Cl_2$: 404.90349; found 404.90354. Anal. calcd. for $C_{17}H_8Cl_5N$: C 50.60, H 2.00, N 3.47; found: C 50.97, H 2.48, N 3.07.

2,3,5-trichloro-4,6-bis(4-(trifluoromethyl)phenyl)pyridine (5h):



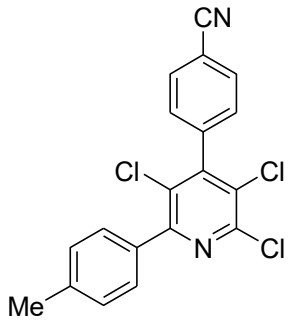
5h was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 4-(trifluoromethyl)phenylboronic acid (0.55 mmol, 104.5 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 43 mg (35 %). mp. 156 - 157 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.88 (d, ^3J = 8.3 Hz, 2H, CH_{Ar}), 7.83 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.76 (d, ^3J = 8.3 Hz, 2H, CH_{Ar}), 7.44 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 153.6 ($C_{Ar/Hetar}$), 149.7 ($C_{Ar/Hetar}$), 147.9 ($C_{Ar/Hetar}$), 139.9 ($C_{Ar/Hetar}$), 138.8 ($C_{Ar/Hetar}$), 131.5 (q, ^2J = 32.7 Hz, $2C_{Ar}$), 130.0 ($2CH_{Ar}$), 129.9 (C_{Ar}), 129.0 ($2CH_{Ar}$), 128.6 (C_{Ar}), 125.9 (q, ^3J = 3.7 Hz, $2CH_{Ar}$), 125.3 (q, ^3J = 3.7 Hz, $2CH_{Ar}$), 123.9 (q, ^1J = 272.3 Hz, CF_3), 123.8 (q, ^1J = 272.3 Hz, CF_3). **^{19}F-NMR** (282 MHz, $CDCl_3$): δ = -62.83 ($ArCF_3$), -62.85 ($ArCF_3$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3072 (w), 2925 (w), 2853 (w), 1580 (w), 1524 (w), 1508 (w), 1408 (m), 1380 (w), 1319 (s), 1296 (m), 1277 (m), 1189

(w), 1161 (m), 1107 (s), 1063 (s), 1018 (m), 981 (w), 909 (w), 880 (w), 841 (m), 827 (m), 776 (m), 705 (m), 679 (w), 644 (w), 630 (m), 621 (m), 612 (m), 593 (m). **MS** (EI, 70 eV): m/z (%) = 473 (M^+, 27), 472 (M^+, 18), 471 (M^+, 83), 470 (M^+, 19), 469 (M^+, 85), 452 (12), 450 (13), 438 (11), 437 (14), 436 (66), 435 (22), 434 (100), 400 (10), 364 (10), 363 (14), 344 (13), 329 (12), 295 (21), 294 (12), 228 (18), 193 (13), 145 (12), 75 (11), 69 (18). **HR-MS** (EI): m/z = calcd. for $C_{19}H_8NCl_3F_6$ $[M]^+$: 468.96210; found: 468.96243; calcd. for $C_{19}H_8NCl_2{}^{37}ClF_6$: 470.95915; found 470.95954; calcd. for $C_{19}H_8NCl^{37}Cl_2F_6$: 472.95620; found 472.95697. Anal. calcd. for $C_{19}H_8Cl_3F_6N$: C 48.49, H 1.71, N 2.98; found: C 48.43, H 1.98, N 2.82.

General procedure for the synthesis of compounds 6a–c

An oven-dried, argon-flushed sealable glass tube was charged with 4-bromo-2,3,5-trichloro-6-*p*-tolylpyridine **4b** (0.29 mmol, 100 mg), $Pd(PPh_3)_4$ (5 mol%, 16.5 mg), the appropriate arylboronic acid (0.43 mmol) and K_3PO_4 (0.43 mmol, 91 mg) followed by a mixture of toluene/water/*n*-butanol (6:1:1, 4 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 20 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/ethyl acetate as eluent.

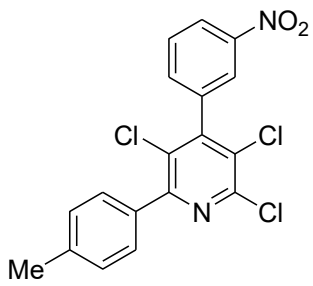
2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine (6a):



6a was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-*p*-tolylpyridine **4b** (0.29 mmol, 100 mg) and 4-cyanophenylboronic acid (0.43 mmol, 63.2 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 53 mg (50 %). mp. 191 - 192 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.85 (d, ^3J = 8.6 Hz, 2H, CH_{Ar}), 7.65 (d, ^3J = 8.2 Hz, 2H, CH_{Ar}), 7.43 (d, ^3J = 8.6 Hz, 2H, CH_{Ar}), 7.30 (d, ^3J = 7.9 Hz, 2H, CH_{Ar}), 2.43 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 155.3 ($C_{Ar/Hetar}$), 148.8 ($C_{Ar/Hetar}$), 147.5 ($C_{Ar/Hetar}$), 140.2 ($C_{Ar/Hetar}$), 139.9 ($C_{Ar/Hetar}$), 133.5 ($C_{Ar/Hetar}$), 132.6 ($2CH_{Ar}$), 129.5 ($2CH_{Ar}$), 129.4 ($2CH_{Ar}$), 128.9 ($2CH_{Ar}$), 128.0 ($C_{Ar/Hetar}$), 122,2 ($C_{Ar/Hetar}$), 118.2 (C≡N), 113.3 ($C_{Ar/Hetar}$), 21.4 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3092 (w), 3043 (w), 2955 (w), 2923 (w), 2855 (w), 2228 (m), 1572 (w), 1539 (w), 1497 (m), 1451 (w), 1366 (s), 1296 (s), 1266 (s), 1202 (m), 1184 (m), 1165 (w), 1096

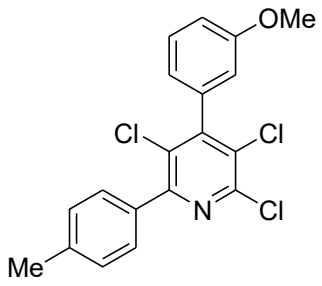
(w), 1043 (s), 970 (w), 958 (w), 877 (w), 823 (s), 766 (m), 738 (m), 680 (s), 667 (m), 646 (m), 619 (w), 572 (s), 554 (m). **MS** (EI, 70 eV): m/z (%) = 377 (M^+, 7), 376 (M^+, 31), 375 (M^+, 24), 374 (M^+, 96), 373 (M^+, 34), 372 (M^+, 100), 371 (14), 339 (29), 338 (12), 337 (45), 301 (10), 266 (19), 265 (24), 240 (10), 238 (10), 185 (11), 150 (10), 133 (15), 91 (18). **HR-MS** (EI): m/z = calcd. for $C_{19}H_{11}N_2Cl_3$ $[M]^+$: 371.99823; found: 371.99710; calcd. for $C_{19}H_{11}N_2Cl_2{}^{37}Cl$: 373.99528; found 373.99417; calcd. for $C_{19}H_{81}N_2Cl^{37}Cl_2$: 375.99233; found 375.99208. Anal. calcd. for $C_{19}H_{11}Cl_3N_2$: C 61.07, H 2.97, N 7.50; found: C 61.33, H 3.24, N 7.34.

2,3,5-trichloro-4-(3-nitrophenyl)-6-*p*-tolylpyridine (6b):



6b was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-*p*-tolylpyridine **4b** (0.29 mmol, 100 mg) and 3-nitrophenylboronic acid (0.43 mmol, 71.8 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 62 mg (55 %). mp. 113 - 114 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 8.38 (ddd, ^3J = 8.2 Hz, ^4J = 2.3 Hz, ^4J = 1.2 Hz, 1H, CH_{Ar}), 8.22 (pt, ^4J = 1.8 Hz, 1H, CH_{Ar}), 7.75 (pt, ^3J = 7.9 Hz, 1H, CH_{Ar}), 7.67-7.63 (m, 3H, CH_{Ar}), 7.30 (d, ^3J = 7.9 Hz, 2H, CH_{Ar}), 2.43 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 155.5 ($C_{Ar/Hetar}$), 148.4 ($C_{Ar/Hetar}$), 148.1 ($C_{Ar/Hetar}$), 147.5 ($C_{Ar/Hetar}$), 139.9 ($C_{Ar/Hetar}$), 137.1 ($C_{Ar/Hetar}$), 134.7 (CH_{Ar}), 133.5 ($C_{Ar/Hetar}$), 129.9 (CH_{Ar}), 129.4 (CH_{Ar}), 128.9 (CH_{Ar}), 128.5 ($C_{Ar/Hetar}$), 128.3 ($C_{Ar/Hetar}$), 124.1 (CH_{Ar}), 123.9 (CH_{Ar}), 21.4 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3082 (w), 3033 (w), 2922 (w), 2855 (w), 1581 (w), 1528 (s), 1512 (m), 1480 (w), 1453 (w), 1373 (m), 1345 (s), 1313 (w), 1295 (m), 1268 (m), 1204 (w), 1186 (w), 1165 (w), 1049 (m), 1002 (w), 931 (w), 899 (m), 825 (m), 811 (m), 768 (w), 730 (m), 702 (s), 691(s), 668 (m), 570 (m), 533 (w). **MS** (EI, 70 eV): m/z (%) = 397 (M^+, 6), 396 (M^+, 33), 395 (M^+, 20), 394 (M^+, 97), 393 (M^+, 24), 392 (M^+, 100), 348 (25), 346 (26), 311 (13), 276 (19), 275 (13), 274 (10), 261 (10), 241 (18), 240 (30), 238 (20), 214 (11), 213 (16), 155 (14), 138 (13), 120 (27), 106 (17), 91 (17). **HR-MS** (ESI): m/z = calcd. for $C_{18}H_{11}Cl_3N_2O_2$ ($[M+H]^+$): 392.99589, found: 392.99597, calcd. for $C_{18}H_{11}Cl_2{}^{37}ClN_2O_2$: 394.99315, found 394.99326, calcd. for $C_{18}H_{11}Cl^{37}Cl_2N_2O_2$: 396.99061, found 396.99107. Anal. calcd. for $C_{18}H_{11}Cl_3N_2O_2$: C 54.92, H 2.82, N 7.12; found: C 55.04, H 3.27, N 6.86.

2,3,5-trichloro-4-(3-methoxyphenyl)-6-*p*-tolylpyridine (6c):



6c was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-*p*-tolylpyridine **4b** (0.29 mmol, 100 mg) and 3-methoxyphenylboronic acid (0.43 mmol, 65.3 mg) and was purified via column chromatography (heptane/dichloromethane). Colorless viscous oil; yield: 51 mg (48 %). *Rf* = 0.73 (Heptan/ EA 4:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.66 (d, ^{3}J = 8.2 Hz, 2H, CH_{Ar}), 7.45 (dd, ^{3}J = 7.96 Hz, ^{3}J = 7.96 Hz, 1H, CH_{Ar}), 7.29 (d, ^{3}J = 8.2 Hz, 2H, CH_{Ar}), 7.03 (ddd, ^{3}J = 8.4 Hz, ^{4}J = 2.6 Hz, ^{5}J = 0.9 Hz, 1H, CH_{Ar}), 6.83-6.88 (m, 1H, CH_{Ar}), 6.82 (dd, ^{4}J = 2.6 Hz, ^{4}J = 1.7 Hz, 1H, CH_{Ar}), 3.87 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3), **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 159.7 (*C*-OCH_3), 154.9 ($C_{Ar/Hetar}$), 150.7 ($C_{Ar/Hetar}$), 147.1 ($C_{Ar/Hetar}$), 139.5 ($C_{Ar/Hetar}$), 137.0 ($C_{Ar/Hetar}$), 134.0 ($C_{Ar/Hetar}$), 129.9 ($2CH_{Ar}$), 129.4 ($2CH_{Ar}$), 128.8 (CH_{Ar}), 128.8 ($2C_{Ar/Hetar}$), 120.5 (CH_{Ar}), 114.5 (CH_{Ar}), 114.0 (CH_{Ar}), 55.3 (OCH_3), 21.4 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3033 (v), 2921 (w), 2853 (w), 1610 (m), 1579 (m), 1541 (m), 1510 (m), 1485 (m), 1453 (m), 1373 (s), 1314 (m), 1286 (s), 1269 (s), 1237 (s), 1203 (m), 1148 (m), 1053 (s), 1034 (s), 1020 (m), 994 (w), 907 (m), 877 (m), 822 (s), 770 (m), 750 (s), 712 (s), 634 (m), 576 (m), 491 (m), 481 (m), 408 (w). **MS** (EI, 70 eV): m/z (%) = 382 (M^+, 7), 381 (M^+, 33), 380 (M^+, 32), 379 (M^+, 100), 378 (M^+, 57), 377 (M^+, 99), 376 (37), 350 (5), 349 (9), 348 (8), 347 (9), 312 (6), 264 (7), 228 (9), 227 (9), 91 (5), 63 (5), 39 (5). **HR-MS (ESI)**: m/z = calcd. for $C_{19}H_{14}Cl_3NO$ ($M+H^+$) 378.02137; found 378.02176; calcd. for $C_{19}H_{14}Cl_2{}^{37}ClNO$ ($M+H^+$) 380.01864; found 380.01903; calcd. for $C_{19}H_{14}Cl^{37}Cl_2NO$ ($M+H^+$) 382.01611; found 382.01658; calcd. for $C_{19}H_{14}Cl_3NO$ ($M+Na^+$) 400.00332; found 400.00353; calcd. for $C_{19}H_{14}Cl_2{}^{37}ClNO$ ($M+H^+$) 402.00059; found 402.00064. Anal. calcd. for $C_{19}H_{14}Cl_3NO$: C 60.26, H 3.73, N 3.70; found: C 60.04, H 3.57, N 3.86.

General procedure for the synthesis of Triarylpyridine from 3 (mixtures 7/8)

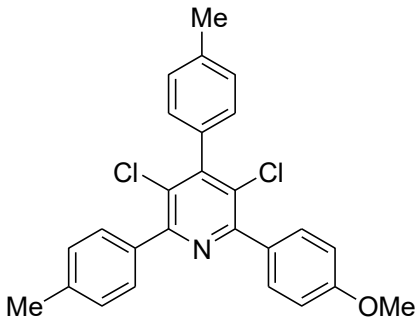
An oven-dried, argon-flushed sealable glass tube was charged with 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg), $Pd(OAc)_2$ (5 mol%, 2.9 mg), PCy_3 (10 mol%, 7.24 mg) or SPhos (10 mol%, 10.6 mg), the appropriate arylboronic acid (2.5-4.5 equivalent) and K_3PO_4 (0.77 mmol, 164.45 mg) followed by a mixture of

toluene/water/buthanol (6:1:1, 4 mL); The tube was sealed with a Teflon valve and stirred at 100 °C or 70 °C for 19 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography affording isomeric mixtures of 3,5-dichloro-2,4,6-tri-*p*-tolylpyridine **7** and 3-chloro-2,4,5,6-tetrakis-*p*-tolylpyridine **8** which could not be separated preparatively by column chromatography. The products were confirmed by GC-MS und HR-MS data.

General procedure for the synthesis of compounds 9a–d

An oven-dried, argon-flushed sealable glass tube was charged with 2,3,5-trichloro-4,6-di-*p*-tolylpyridine **5a** (0.28 mmol, 100 mg), $Pd(PPh_3)_4$ (5 mol%, 16 mg), the appropriate arylboronic acid (0.33 mmol) and K_3PO_4 (0.33 mmol, 70.3 mg) followed by anhydrous toluene (3 mL). The tube was sealed with a Teflon valve and stirred at 100 °C for 20 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/dichloromethane as eluent.

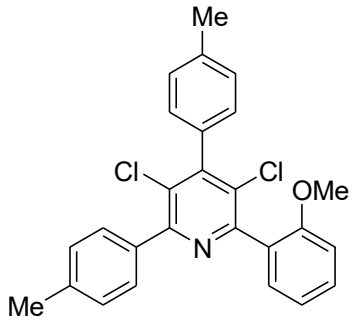
3,5-dichloro-2-(4-methoxyphenyl)-4,6-di-*p*-tolylpyridine (9a):



9a was synthesized according to general procedure using 2,3,5-trichloro-4,6-di-*p*-tolylpyridine **5a** (0.28 mmol, 100 mg) and 4-methoxyphenylboronic acid (0.33 mmol, 50.1 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 68 mg (57 %). mp. 137 - 138 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.79 (d, ^3J = 8.8 Hz, 2H, CH_{Ar}), 7.70 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.36 (d, ^3J = 7.9 Hz, 2H, CH_{Ar}), 7.30-7.23 (m, 4H, CH_{Ar}), 6.99 (d, ^3J = 8.8 Hz, 2H, CH_{Ar}), 3.87 (s, 3H, OCH_3), 2.47 (s, 3H, CH_3), 2.42 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 160.1 (*C*-OCH_3), 154.6 ($C_{Ar/Hetar}$), 154.2 ($C_{Ar/Hetar}$), 149.4 ($C_{Ar/Hetar}$), 138.8 ($C_{Ar/Hetar}$), 138.5 ($C_{Ar/Hetar}$), 135.6 ($C_{Ar/Hetar}$), 133.8 ($C_{Ar/Hetar}$), 131.1 (2CH), 130.8 ($C_{Ar/Hetar}$), 129.5 ($2CH_{Ar}$), 129.3 ($2CH_{Ar}$), 128.7 ($2CH_{Ar}$), 128.6 ($2CH_{Ar}$), 128.3 ($C_{Ar/Hetar}$), 128.2 ($C_{Ar/Hetar}$), 113.4 ($2CH_{Ar}$), 55.3 (OCH_3), 21.5 (CH_3), 21.4 (CH_3).

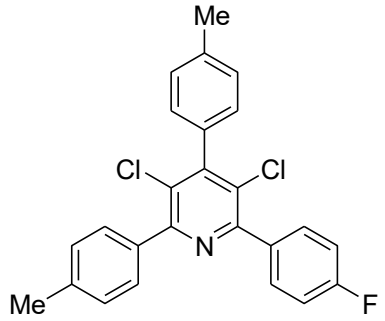
IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3034 (w), 3005 (w), 2956 (w), 2921 (w), 2836 (w), 1607 (m), 1504 (m), 1460 (w), 1453 (w), 1440 (w), 1362 (m), 1306 (w), 1249 (s), 1177 (m), 1155 (w), 1083 (m), 1037 (m), 1027 (m), 1008 (w), 968 (w), 877 (w), 837 (m), 819 (s), 792 (m), 778 (s), 756 (m), 737 (w), 722 (m), 673 (m), 643 (m), 621 (m), 602 (m), 578 (w), 539 (s), 531 (s). **MS** (EI, 70 eV): m/z (%) = 437 (M^+, 11), 436 (M^+, 17), 435 (M^+, 66), 434 (M^+, 28), 433 (M^+, 100), 400 (7), 399 (5), 398 (18), 202 (4). **HR-MS** (ESI): m/z = calcd. for $C_{26}H_{21}Cl_2NO$ ($[M+H]^+$): 434.1073, found: 434.10737, calcd. for $C_{26}H_{21}Cl^{37}ClN_2O$: 436.10493, found 436.10496, calcd. for $C_{26}H_{21}{}^{37}Cl_2N_2O$: 438.1033, found 438.10339. Anal. calcd. for $C_{26}H_{21}Cl_2NO$: C 71.89, H 4.87, N 3.22; found: C 71.67, H 5.03, N 2.96.

3,5-dichloro-2-(2-methoxyphenyl)-4,6-di-*p*-tolylpyridine (9b):



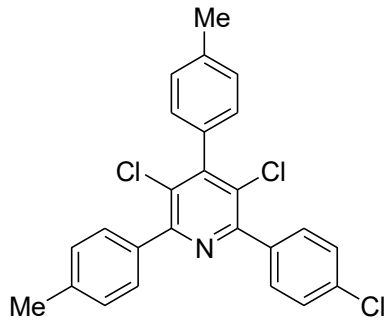
9b was synthesized according to general procedure using 2,3,5-trichloro-4,6-di-*p*-tolylpyridine **5a** (0.28 mmol, 100 mg) and 2-methoxyphenylboronic acid (0.33 mmol, 50.1 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 59 mg (49 %). mp. 106 - 107 °C.**^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.69 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.41 (d, ^3J = 7.4 Hz, 2H, CH_{Ar}), 7.35 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.28 (m, 4H, CH_{Ar}), 7.10-7.07 (m, 1H, CH_{Ar}), 7.00 (d, ^3J = 8.7 Hz, 1H, CH_{Ar}), 3.85 (s, 3H, OCH_3), 2.46 (s, 3H, CH_3), 2.41 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 156.9 (*C*-OCH_3), 154.8 ($2C_{Ar/Hetar}$), 153.8 ($C_{Ar/Hetar}$), 148.3 ($C_{Ar/Hetar}$), 138.6 ($C_{Ar/Hetar}$), 138.5 ($C_{Ar/Hetar}$), 135.6 ($C_{Ar/Hetar}$), 133.5 ($C_{Ar/Hetar}$), 130.6 (CH_{Ar}), 130.2 (CH_{Ar}), 129.6 ($2CH_{Ar}$), 129.2 ($2CH_{Ar}$), 128.8 ($2CH_{Ar}$), 128.7 ($2CH_{Ar}$), 128.1 ($2C_{Ar/Hetar}$), 120.6 (CH_{Ar}), 110.9 (CH_{Ar}), 55.6 (OCH_3), 21.4 (CH_3), 21.3 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3029 (w), 2919 (w), 2839 (w), 1603 (m), 1583 (w), 1506 (m), 1493 (m), 1455 (w), 1365 (s), 1305 (w), 1276 (m), 1246 (s), 1184 (m), 1157 (m), 1083 (m), 1021 (m), 967 (w), 878 (w), 818 (m), 785 (m), 746 (s), 729 (s), 687 (m), 668 (w), 584 (w), 548 (w), 536 (m). **MS** (EI, 70 eV): m/z (%) = 435 (M^+, 13), 434 (M^+, 11), 433 (M^+, 20), 432 (8), 401 (19), 400 (76), 399 (61), 398 (100), 368 (16), 363 (13), 215 (8), 202 (8), 158 (9). **HR-MS** (EI): m/z = calcd. for $C_{26}H_{21}ONCl_2$ $[M]^+$: 433.09947; found: 433.09878; calcd. for $C_{26}H_{21}ONCl^{37}Cl$: 435.09652; found 435.09638. Anal. calcd. for $C_{26}H_{21}Cl_2NO$: C 71.89, H 4.87, N 3.22; found: C 71.78, H 4.83, N 3.00.

3,5-dichloro-2-(4-fluorophenyl)-4,6-di-*p*-tolylpyridine (9c):



9c was synthesized according to general procedure using 2,3,5-trichloro-4,6-di-*p*-tolylpyridine **5a** (0.28 mmol, 100 mg) and 4-fluorophenylboronic acid (0.33 mmol, 46.2 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 44 mg (38 %). mp. 152 - 153 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.81 (dd, ^{3}J = 8.9 Hz, ^{4}J = 2.27 Hz, 2H, CH_{Ar}), 7.70 (d, ^{3}J = 8.2 Hz, 2H CH_{Ar}), 7.37 (d, ^{3}J = 7.9 Hz, 2H, CH_{Ar}), 7.30 (d, ^{3}J = 7.9 Hz, 2H, CH_{Ar}), 7.25 (d, ^{3}J = 8.1 Hz, 2H, CH_{Ar}), 7.16 (pt, ^{3}J = 8.8 Hz, 2H, CH_{Ar}), 2.47 (s, 3H, CH_3), 2.43 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 163.1 (d, ^{1}J = 249.8 Hz, (C_{Ar}-F)), 154.9 ($C_{Ar/Hetar}$), 153.57 ($C_{Ar/Hetar}$), 149.5 ($C_{Ar/Hetar}$), 138.9 ($C_{Ar/Hetar}$), 138.6 ($C_{Ar/Hetar}$), 135.3 ($C_{Ar/Hetar}$), 134.4 (d, ^{4}J = 3.66 Hz, C_{Ar}), 133.5 ($C_{Ar/Hetar}$), 131.7 (d, ^{3}J = 8.24 Hz, 2CH), 129.5 ($2CH_{Ar}$), 129.3 ($2CH_{Ar}$), 128.8 ($C_{Ar/Hetar}$), 128.7 ($2CH_{Ar}$), 128.5 ($2CH_{Ar}$), 128.4 ($C_{Ar/Hetar}$), 115 (d, ^{2}J = 22.0 Hz, $2CH_{Ar}$), 21.4 (CH_3), 21.4 (CH_3). **^{19}F-NMR** (282 MHz, $CDCl_3$): δ = - 112.42. **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3033 (w), 2922 (w), 2864 (w), 1898 (w), 1603 (m), 1574 (w), 1545 (w), 1502 (s), 1450 (w), 1361 (s), 1309 (m), 1297 (m), 1277 (w), 1226 (m), 1185 (m), 1155 (s), 1079 (m), 1031 (m), 1013 (m), 968 (w), 875 (m), 819 (s), 806 (m), 778 (s), 758 (m), 734 (m), 715 (m), 676 (m), 659 (m), 620 (w), 599 (m), 561 (w). **MS** (EI, 70 eV): m/z (%) = 425 (M^+, 13), 424 (M^+, 18), 423 (M^+, 76), 422 (M^+, 33), 421 (M^+, 100), 406 (6), 388 (22), 387 (17), 386 (69), 350 (6), 234 (6), 233 (8). **HR-MS** (EI): m/z = calcd. for $C_{25}H_{18}NCl_2F$ $[M]^+$: 421.07948; found: 421.07922; calcd. for $C_{25}H_{18}NCl^{37}ClF$: 423.07653; found 423.07657. Anal. calcd. for $C_{25}H_{18}Cl_2FN$: C 71.10, H 4.30, N 3.32; found: C 71.26, H 4.19, N 3.25.

3,5-dichloro-2-(4-chlorophenyl)-4,6-di-*p*-tolylpyridine (9d):



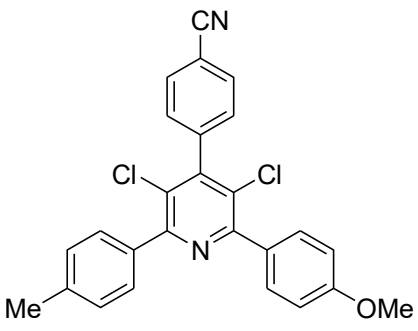
9d was synthesized according to general procedure using 2,3,5-trichloro-4,6-di-*p*-tolylpyridine **5a** (0.28 mmol, 100 mg) and 4-chlorophenylboronic acid (0.33 mmol, 51.6 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 60 mg (50 %). mp. 163 - 164 °C. **^{1}H-NMR**

(300 MHz, $CDCl_3$): δ = 7.76 (d, ^3J = 9.1 Hz, 2H, CH_{Ar}), 7.70 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.45 (d, ^3J = 8.7 Hz, 2H, CH_{Ar}), 7.37 (d, ^3J = 7.9 Hz, 2H, CH_{Ar}), 7.30 (d, ^3J = 7.9 Hz, 2H, CH_{Ar}), 7.25 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 2.47 (s, 3H, CH_3), 2.43 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 154.9 ($C_{Ar/Hetar}$), 153.4 ($C_{Ar/Hetar}$), 149.6 ($C_{Ar/Hetar}$), 139.0 ($C_{Ar/Hetar}$), 138.7 ($C_{Ar/Hetar}$), 136.7 ($C_{Ar/Hetar}$), 135.3 ($C_{Ar/Hetar}$), 134.9 ($C_{Ar/Hetar}$), 133.4 ($C_{Ar/Hetar}$), 131.1 ($2CH_{Ar}$), 129.5 ($2CH_{Ar}$), 129.3 ($2CH_{Ar}$), 129.0 ($C_{Ar/Hetar}$), 128.8 ($2CH_{Ar}$), 128.5 ($2CH_{Ar}$), 128.4 ($C_{Ar/Hetar}$), 128.2 ($2CH_{Ar}$), 21.5 (CH_3), 21.4 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3132 (w), 3090 (w), 3056 (w), 3032 (w), 2919 (w), 2864 (w), 1908 (w), 1595 (w), 1543 (w) 1488 (m), 1447 (w), 1361 (s), 1308 (w), 1298 (w), 1278 (w), 1186 (m), 1153 (m), 1076 (m), 1031 (w), 1010 (m), 968 (w), 948 (w), 872 (m), 818 (s), 777 (s), 763 (s), 734 (s), 713 (m), 686 (w), 651 (m), 620 (w), 584 (w), 562 (m). **MS** (EI, 70 eV): m/z (%) = 442 (M^+, 8), 441 (M^+, 30), 440 (M^+, 26), 439 (M^+, 100), 438 (M^+, 31), 437 (M^+, 99), 406 (6), 405 (9), 404 (35), 403 (15), 402 (56), 215 (6.34), 213 (8), 158 (5). **HR-MS** (EI): m/z = calcd. for $C_{25}H_{18}NCl_3$ $[M]^+$: 437.04993; found: 437.04960; calcd. for $C_{25}H_{18}NCl_2{}^{37}Cl$: 439.04698; found 439.04679. Anal. calcd. for $C_{25}H_{18}Cl_3N$: C 68.43, H 4.13, N 3.19; found: C 68.42, H 4.11, N 3.18.

General procedure for the synthesis of compounds 10a–c

An oven-dried, argon-flushed sealable glass tube was charged with 2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine **6a** (0.27 mmol, 100 mg), $Pd(PPh_3)_4$ (5 mol%, 15.5 mg), the appropriate arylboronic acid (0.32 mmol) and K_3PO_4 (0.32 mmol, 68.4 mg) followed by anhydrous toluene (3 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 20 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/ethyl acetate as eluent.

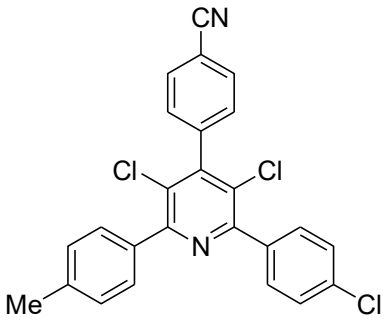
3,5-dichloro-2-(4-methoxyphenyl)-4-(4-cyanophenyl)-6-*p*-tolylpyridine (10a):



10a was synthesized according to general procedure using 2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine **6a** (0.27 mmol, 100 mg) and 4-methoxyphenylboronic acid (0.32 mmol, 48.6 mg)

and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 75 mg (63 %). mp. 187 - 188 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.84 (d, ^{3}J = 8.6 Hz, 2H, CH_{Ar}), 7.79 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 7.70 (d, ^{3}J = 8.2 Hz, 2H, CH_{Ar}), 7.48 (d, ^{3}J = 8.6 Hz, 2H, CH_{Ar}), 7.30 (d, ^{3}J = 7.9 Hz, 2H, CH_{Ar}), 7.00 (d, ^{3}J = 8.9 Hz, 2H, CH_{Ar}), 3.87 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 160.6 (*C*-OCH_3), 155.2 ($C_{Ar/Hetar}$), 154.8 ($C_{Ar/Hetar}$), 147.7 ($C_{Ar/Hetar}$), 141.4 ($C_{Ar/Hetar}$), 139.5 ($C_{Ar/Hetar}$), 135.2 ($C_{Ar/Hetar}$), 132.7 (2CH), 131.4 (2CH), 130.4 ($C_{Ar/Hetar}$), 130.1 ($2CH_{Ar}$), 129.7 ($2CH_{Ar}$), 129.0 ($2CH_{Ar}$), 127.5 ($C_{Ar/Hetar}$), 127.4 ($C_{Ar/Hetar}$), 118.7 (C≡N), 113.7 ($2CH_{Ar}$), 112.9 ($C_{Ar/Hetar}$), 55.6 (OCH_3), 21.6 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3039 (w), 2955 (w), 2923 (w), 2840 (w), 2232 (m), 1606 (m), 1576 (w), 1510 (m), 1498 (m), 1465 (w), 1441 (w), 1364 (s), 1304 (w), 1294 (m), 1281 (w), 1254 (s), 1175 (s), 1153 (m), 1080 (m), 1038 (w), 1014 (m), 971 (w), 876 (m), 846 (m), 830 (s), 791 (m), 781 (s), 745 (m), 724 (m), 663 (m), 619 (w), 601 (w), 557 (s). **MS** (EI, 70 eV): m/z (%) = 448 (M^+, 12), 447 (M^+, 19), 446 (M^+, 67), 445 (M^+, 31) 444 (M^+, 100), 409 (16), 393 (5), 366 (6), 330 (7), 329 (7), 316 (5), 240 (8), 222 (6), 214 (9). **HR-MS** (EI): m/z = calcd. for $C_{26}H_{18}ON_2Cl_2$ $[M]^+$: 444.07907; found: 444.07896; calcd. for $C_{26}H_{18}ON_2Cl^{37}Cl$: 446.07612; found 446.07673. Anal. calcd. for $C_{26}H_{18}Cl_2N_2O$: C 70.12, H 4.07, N 6.29; found: C 69.91, H 4.20, N 6.49.

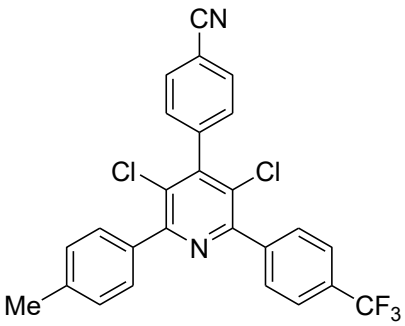
3,5-dichloro-2-(4-chlorophenyl)-4-(4-cyanophenyl)-6-*p*-tolylpyridine (10b):



10b was synthesized according to general procedure using 2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine **6a** (0.27 mmol, 100 mg) and 4-chlorophenylboronic acid (0.32 mmol, 50.0 mg) and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 92 mg (77 %). mp. 164 - 165 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.85 (d, ^{3}J = 8.5 Hz, 2H, CH_{Ar}), 7.76 (d, ^{3}J = 8.6 Hz, 2H, CH_{Ar}), 7.69 (d, ^{3}J = 8.2 Hz, 2H, CH_{Ar}), 7.48 (d, ^{3}J = 8.5 Hz, 2H, CH_{Ar}), 7.45 (d, ^{3}J = 8.6 Hz, 2H, CH_{Ar}), 7.30 (d, ^{3}J = 8.0 Hz, 2H, CH_{Ar}), 2.43 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 155.3 ($C_{Ar/Hetar}$), 153.7 ($C_{Ar/Hetar}$), 147.6 ($C_{Ar/Hetar}$), 140.8 ($C_{Ar/Hetar}$), 139.4 ($C_{Ar/Hetar}$), 136.1 ($C_{Ar/Hetar}$), 135.3 ($C_{Ar/Hetar}$), 134.7 ($C_{Ar/Hetar}$), 132.5 ($2CH_{Ar}$), 130.9 ($2CH_{Ar}$), 129.7 ($2CH_{Ar}$), 129.4 ($2CH_{Ar}$), 128.8 ($2CH_{Ar}$), 128.3 ($2CH_{Ar}$), 128.0 (C_{Ar}), 127.4 (C_{Ar}), 118,3 (C≡N), 112.9 (C_{Ar}), 21.4 (CH_3). **IR**

(ATR, cm^{-1}): $\tilde{\nu}$ = 3071 (w), 3056 (w), 3041 (w), 2956 (w), 2922 (w), 2853 (w), 1597 (w), 1511 (w), 1489 (m), 1449 (w), 1364 (s), 1308 (w), 1297 (w), 1269 (w), 1184 (w), 1155 (m), 1095 (m), 1080 (m), 1044 (w), 1011 (m), 973 (w), 905 (m), 875 (m), 829 (m), 818 (s), 781 (m), 729 (s), 654 (m), 619 (m), 573 (m), 553 (s). **MS** (EI, 70 eV): m/z (%) = 453 (M^+, 8), 452 (M^+, 34), 451 (M^+, 29), 450 (M^+, 99), 449 (M^+, 35), 448 (M^+, 100), 447 (8), 416 (11), 415 (36), 414 (18), 413 (55), 377 (11), 342 (9), 341 (9), 261 (19), 241 (11), 240 (20), 238 (11), 225 (21), 171 (10), 170 (13), 157 (14), 91 (12). **HR-MS** (EI): m/z = calcd. for $C_{25}H_{15}N_2Cl_3$ $[M]^+$: 448.02953; found: 448.02876; calcd. for $C_{25}H_{15}N_2Cl_2{}^{37}Cl$: 450.02658; found 450.02618; calcd. for $C_{25}H_{15}N_2Cl^{37}Cl_2$: 452.02363; found 452.02238. Anal. calcd. for $C_{25}H_{15}Cl_3N_2$: C 66.76, H 3.36, N 6.23; found: C 66.90, H 3.41 , N 6.09.

3,5-dichloro-2-(4-(trifluoromethyl)phenyl)-4-(4-cyanophenyl)-6-*p*-tolylpyridine (10c):



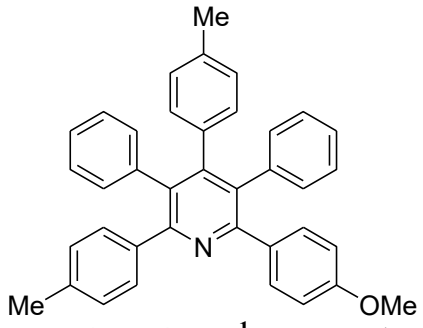
10c was synthesized according to general procedure using 2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine **6a** (0.27 mmol, 100 mg) and 4-(trifluoromethyl)phenylboronic acid (0.32 mmol, 60.8 mg) and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 79 mg (61 %). mp. 187 - 188 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.92 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.86 (d, ^3J = 8.5 Hz, 2H, CH_{Ar}), 7.75 (d, ^3J = 8.2 Hz, 2H, CH_{Ar}), 7.70 (d, ^3J = 8.2 Hz, 2H, CH_{Ar}), 7.50 (d, ^3J = 8.5 Hz, 2H, CH_{Ar}), 7.31 (d, ^3J = 7.9 Hz, 2H, CH_{Ar}), 2.44 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 155.5 ($C_{Ar/Hetar}$), 153.5 ($C_{Ar/Hetar}$), 147.8 ($C_{Ar/Hetar}$), 141.2 ($C_{Ar/Hetar}$), 140.6 ($C_{Ar/Hetar}$), 139.6 ($C_{Ar/Hetar}$), 134.6 ($C_{Ar/Hetar}$), 132.6 ($2CH_{Ar}$), 131.1 (q, ^2J = 32.5 Hz, C_{Ar}), 130.0 ($2CH_{Ar}$), 129.8 ($2CH_{Ar}$), 129.5 ($2CH_{Ar}$), 128.9 ($2CH_{Ar}$), 128.6 ($C_{Ar/Hetar}$), 127.6 ($C_{Ar/Hetar}$), 125.1 (q, ^3J = 3.85 Hz, $2CH_{Ar}$), 123.9 (q, ^1J = 272.35 Hz, CF_3), 118.3 (C≡N), 113.0 (C_{Ar}), 21.4 (CH_3). **^{19}F-NMR** (282 MHz, $CDCl_3$): δ = -62.73 ($ArCF_3$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3044 (w), 2919 (w), 2858 (w), 2229 (w), 1811 (w), 1611 (w), 1581 (w), 1524 (w), 1452 (w), 1411 (w), 1369 (m), 1354 (m), 1322 (s), 1272 (w), 1187 (w), 1166 (m), 1123 (s), 1111 (s), 1088 (m), 1065 (s), 1018 (m), 960 (w), 877 (m), 854 (m), 845 (m), 828 (s), 780 (m), 742 (m), 724 (m), 699 (m), 649 (m), 619 (m), 594 (m), 550 (m). **MS** (EI, 70 eV): m/z (%) = 486 (M^+,

13), 485 (M^+, 19), 484 (M^+, 68), 483 (M^+, 35), 482 (M^+, 100), 481 (14), 449 (19), 448 (16), 447 (52), 295 (6), 240 (6). **HR-MS** (ESI): m/z = calcd. for $C_{26}H_{15}Cl_2F_3N_2$ ($[M+H]^+$): 483.06371, found: 483.06374, calcd. for $C_{26}H_{15}Cl^{37}ClF_3N_2$: 485.06132, found 485.06241. Anal. calcd. for $C_{26}H_{15}Cl_2F_3N_2$: C 64.61, H 3.13, N 5.80; found: C 64.45, H 3.07, N 5.47.

General procedure for the synthesis of compounds 11a–b

An oven-dried, argon-flushed sealable glass tube was charged with 3,5-dichloro-2-(4-methoxyphenyl)-4,6-di-*p*-tolylpyridine **9a** (0.23 mmol, 100 mg), $PdCl_2(CH_3CN)_2$ (5 mol%, 3.0 mg), SPhos (10 mol%, 9.5 mg), the appropriate arylboronic acid (0.92 mmol) and K_3PO_4 (0.92 mmol, 195.5 mg) followed by anhydrous toluene (3 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 20 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/dichloromethane as eluent.

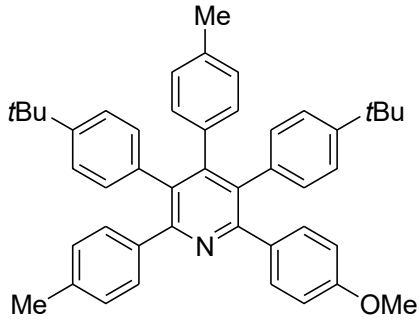
2-(4-methoxyphenyl)-3,5-diphenyl-4,6-di-*p*-tolylpyridine (11a):



11a was synthesized according to general procedure using 3,5-dichloro-2-(4-methoxyphenyl)-4,6-di-*p*-tolylpyridine **9a** (0.23 mmol, 100 mg) and phenylboronic acid (0.92 mmol, 112.2 mg) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 118 mg (99 %). mp. 242 - 243 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.37 (d, ^3J = 8.8 Hz, 2H, CH_{Ar}), 7.33 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.06 - 6.99 (m, 8H, CH_{Ar}), 6.97–6.89 (m, 4H, CH_{Ar}), 6.75-6.70 (m, 4H, CH_{Ar}), 6.65 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 3.77 (s, 3H, OCH_3), 2.29 (s, 3H, CH_3), 2.14 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 158.9 ($C_{Ar/Hetar}$), 156.1 ($C_{Ar/Hetar}$), 155.7 ($C_{Ar/Hetar}$), 150.2 ($C_{Ar/Hetar}$), 138.9 ($C_{Ar/Hetar}$), 138.9 ($C_{Ar/Hetar}$), 138.2 ($C_{Ar/Hetar}$), 136.9 ($C_{Ar/Hetar}$), 135.5 ($C_{Ar/Hetar}$), 135.2 ($C_{Ar/Hetar}$), 133.5 ($C_{Ar/Hetar}$),133.1 ($C_{Ar/Hetar}$), 133.1 ($C_{Ar/Hetar}$), 131.6 ($2CH_{Ar}$), 131.3 ($2CH_{Ar}$), 130.3 ($2CH_{Ar}$), 130.1 ($2CH_{Ar}$), 128.2 ($2CH_{Ar}$), 127.6 ($2CH_{Ar}$), 127.4 ($2CH_{Ar}$), 127.3 ($2CH_{Ar}$), 126.0 ($2CH_{Ar}$), 125.9 ($2CH_{Ar}$), 112.9 ($2CH_{Ar}$), 55.1 (OCH_3), 21.2 (CH_3), 21.1 (CH_3). **IR** (ATR, cm^{-1}):

$\tilde{\nu}$ = 3054 (w), 3029 (w), 2949 (w), 2917 (w), 2866 (w), 1603 (m), 1578 (w), 1504 (m), 1444 (m), 1389 (m), 1353 (w), 1329 (w), 1297 (w), 1272 (w), 1245 (s), 1173 (m), 1042 (m), 1029 (m), 1006 (w), 963 (w), 880 (w), 818 (s), 796 (m), 764 (m), 697 (s), 657 (m), 620 (w), 594 (w), 555 (m), 537 (m). **MS** (EI, 70 eV): m/z (%) = 518 (M^+, 21), 517 (71), 516 (100), 472 (10), 236 (7), 220 (5), 213 (6), 207 (8), 201 (7), 191 (6), 189 (7), 165 (6). **HR-MS** (ESI): m/z = calcd. for $C_{38}H_{31}NO$ ($[M+H]^+$): 518.24784, found: 518.24755. Anal. calcd. for $C_{38}H_{31}NO$: C 88.17, H 6.04, N 2.71; found: C 87.81, H 5.94, N 2.52.

3,5-bis(4-*tert*-butylphenyl)-2-(4-methoxyphenyl)-4,6-di-*p*-tolylpyridine (11b):



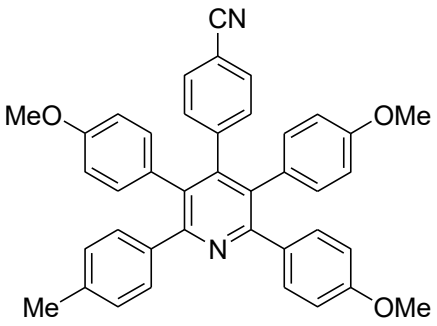
11b was synthesized according to general procedure using 3,5-dichloro-2-(4-methoxyphenyl)-4,6-di-*p*-tolylpyridine **9a** (0.23 mmol, 100 mg) and 4-*tert*-butylphenylboronic acid (0.92 mmol, 163.8 mg) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 116 mg (80 %). mp. 237 - 238 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.36 (d, ^3J = 8.9 Hz, 2H, CH_{Ar}), 7.32 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 7.03 (dd, ^3J = 8.5 Hz, ^3J = 8.4 Hz, 4H, CH_{Ar}), 6.97 (d, ^3J = 8.0 Hz, 2H CH_{Ar}), 6.81 (d, ^3J = 7.9 Hz, 4H, CH_{Ar}), 6.70 (d, ^3J = 8.7 Hz, 4H, CH_{Ar}), 6.60 (d, ^3J = 8.1 Hz, 2H, CH_{Ar}), 3.77 (s, 3H, OCH_3), 2.29 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 1.22 (s, 18H, CH_3 $_{tBu}$). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 158.7 ($C_{Ar/Hetar}$), 155.8 ($C_{Ar/Hetar}$), 155.5 ($C_{Ar/Hetar}$), 150.4 ($C_{Ar/Hetar}$), 148.9 ($C_{Ar/Hetar}$), 148.9 ($C_{Ar/Hetar}$), 136.7 ($C_{Ar/Hetar}$), 135.9 ($C_{Ar/Hetar}$), 135.8 ($C_{Ar/Hetar}$), 135.4 ($C_{Ar/Hetar}$), 135.1 ($C_{Ar/Hetar}$), 133.1 ($C_{Ar/Hetar}$), 133.1 ($C_{Ar/Hetar}$), 131.6 ($2CH_{Ar}$), 130.9 ($4CH_{Ar}$), 130.4 ($2CH_{Ar}$), 130.2 ($2CH_{Ar}$), 128.1 ($2CH_{Ar}$), 127.3 ($2CH_{Ar}$), 124.2 ($2CH_{Ar}$), 124.1 ($2CH_{Ar}$), 112.7 ($2CH_{Ar}$), 55.1 (OCH_3), 34.3 (2C $_{tBu}$), 31.3 ($6CH_3$ $_{tBu}$), 21.2 (CH_3), 20.9 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3028 (w), 2958 (m), 2903 (m), 2866 (m), 1609 (m), 1512 (m), 1500 (m), 1460 (m), 1443 (w), 1387 (m), 1361 (m),1297 (w), 1244 (s), 1178 (m), 1171 (m), 1110 (m), 1043 (m), 1031(m), 1020 (m), 1001 (w), 947 (w), 850 (m), 820 (s), 810 (m), 793 (m), 763 (m), 718 (m), 699 (w), 673 (m), 666 (m), 585 (m), 552 (m), 531 (m). **MS** (EI, 70 eV): m/z (%) = 630 (32), 629 (M^+, 88), 628 (100), 614 (7), 613 (7), 612 (12), 572 (9), 556 (8), 528 (3), 281 (5), 231 (7), 219 (6), 181 (12), 169 (11), 131 (16), 119 (14), 91 (18), 78 (6), 69 (50), 57 (9), 44 (20), 43 (6), 41 (13), 40 (44), 39 (10). **HR-MS** (ESI):

m/z = calcd. for $C_{46}H_{47}NO$ ($[M+H]^+$): 630.37304 found: 630.37286. Anal. calcd. for $C_{46}H_{47}NO$: C 87.72, H 7.52, N 2.22; found: C 87.52, H 7.50, N 2.15.

General procedure for the synthesis of 12a–b

An oven-dried, argon-flushed sealable glass tube was charged with 2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine **6a** (0.23 mmol, 85 mg), $PdCl_2(CH_3CN)_2$ (5 mol%, 3.0 mg), SPhos (10 mol%, 9.4 mg), the appropriate arylboronic acid (1.37 mmol) and K_3PO_4 (1.37 mmol, 291 mg) followed by anhydrous toluene (4 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 20 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/dichloromethane as eluent.

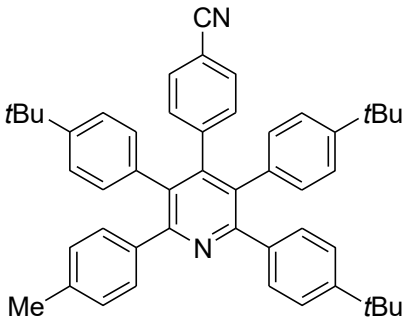
2,3,5-tris(4-methoxyphenyl)-4-(4-cyanophenyl)-6-*p*-tolylpyridine (12a):



12a was synthesized according to general procedure using 2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine **6a** (0.23 mmol, 85 mg) and 4-methoxyphenylboronic acid (1.37 mmol, 208.2 mg) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 124 mg (93 %). mp. 228 - 229 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.28 (d, ^3J = 8.9 Hz, 2H, CH_{Ar}), 7.23 (d, ^3J = 8.2 Hz, 2H, CH_{Ar}), 7.18 (d, ^3J = 8.5 Hz, 2H, CH_{Ar}), 6.93 (d, ^3J = 8.0 Hz, 2H, CH_{Ar}), 6.80 (d, ^3J = 8.5 Hz, 2H, CH_{Ar}), 6.70–6.63 (m, 6H, CH_{Ar}), 6.50 (dd, ^3J = 8.8, ^4J = 3.7 Hz, 4H, CH_{Ar}), 3.69 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 2.21 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 159.0 (*C*-OCH_3), 158.1 (*C*-OCH_3), 158.1 (*C*-OCH_3), 156.5 ($C_{Ar/Hetar}$), 156.0 ($C_{Ar/Hetar}$), 148.6 ($C_{Ar/Hetar}$), 144.2 ($C_{Ar/Hetar}$), 137.8 ($C_{Ar/Hetar}$), 137.2 ($C_{Ar/Hetar}$), 133.1 ($C_{Ar/Hetar}$), 132.2 ($4CH_{Ar}$), 131.9 ($C_{Ar/Hetar}$), 131.9 ($C_{Ar/Hetar}$), 131.5 ($2CH_{Ar}$), 131.2 ($2CH_{Ar}$), 130.9 ($2CH_{Ar}$), 130.2 ($C_{Ar/Hetar}$), 130.2 ($C_{Ar/Hetar}$), 130.1 ($2CH_{Ar}$), 128.3 ($2CH_{Ar}$), 118.9 (C≡N), 113.3 ($2CH_{Ar}$), 113.2 ($2CH_{Ar}$), 113.0 ($2CH_{Ar}$), 109.8 ($C_{Ar/Hetar}$), 55.2 (O*C*H_3), 55.0 (2O*C*H_3), 21.2 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2956 (w), 2931 (w), 2834 (w), 2224 (m), 1608 (m), 1576 (w), 1529 (w), 1513 (m), 1501 (m), 1460 (w), 1445 (w), 1390 (m), 1353 (w), 1299 (w), 1287 (m), 1243 (s), 1174 (s), 1109 (m), 1028 (m), 1016 (m), 951 (w),

852 (w), 843 (m), 823 (m), 805 (m), 761 (m), 732 (w), 683 (w), 671 (w), 655 (m), 632 (m), 558 (s), 535 (m). **MS** (EI, 70 eV): m/z (%) = 590 (7), 589 (26), 588 (M^+, 84), 587 (100), 543 (8), 294 (33), 253 (7), 234 (7), 233 (6), 223 (6), 218 (8), 207 (14), 201 (7), 152 (6), 73 (11). **HR-MS** (ESI): m/z = calcd. for $C_{40}H_{32}N_2O_3$ ($[M+H]^+$): 589.24857, found: 589.24799. Anal. calcd. for $C_{40}H_{32}N_2O_3$: C 81.61, H 5.48, N 4.76; found: C 81.22, H 5.49, N 4.48.

2,3,5-tris(4-*tert*-butylphenyl)-4-(4-cyanophenyl)-6-*p*-tolylpyridine (12b):

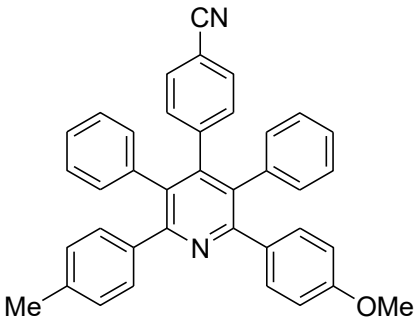


12b was synthesized according to general procedure using 2,3,5-trichloro-4-(4-cyanophenyl)-6-*p*-tolylpyridine **6a** (0.23 mmol, 85 mg) and 4-*tert*-butylphenylboronic acid (1.37 mmol, 243.9 mg) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 114 mg (75 %). mp. 256 - 257 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.33 (d, ^3J = 8.4 Hz, 4H, CH_{Ar}), 7.23-7.16 (m, 4H, CH_{Ar}), 7.07-6.97 (m, 6H, CH_{Ar}), 6.89 (d, ^3J = 8.5 Hz, 2H, CH_{Ar}), 6.78 (dd, ^3J = 8.5 Hz, ^3J = 8.5 Hz, 4H, CH_{Ar}), 2.30 (s, 3H, CH_3), 1.27 (s, 9H, CH_3 $_{tBu}$), 1.22 (s, 9H, CH_3 $_{tBu}$), 1.22 (s, 9H, CH_3 $_{tBu}$). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 156.5 ($C_{Ar/Hetar}$), 156.2 ($C_{Ar/Hetar}$), 150.2 ($C_{Ar/Hetar}$), 149.7 ($C_{Ar/Hetar}$), 149.7 ($C_{Ar/Hetar}$), 148.2 ($C_{Ar/Hetar}$), 144.1 ($C_{Ar/Hetar}$), 137.7 ($C_{Ar/Hetar}$), 137.6 ($C_{Ar/Hetar}$), 137.1 ($C_{Ar/Hetar}$), 134.9 ($C_{Ar/Hetar}$), 134.9 ($C_{Ar/Hetar}$), 132.6 ($C_{Ar/Hetar}$), 132.5 ($C_{Ar/Hetar}$), 131.3 ($2CH_{Ar}$), 130.8 ($2CH_{Ar}$), 130.8 ($2CH_{Ar}$), 130.5 ($2CH_{Ar}$), 130.1 ($2CH_{Ar}$), 129.8 ($2CH_{Ar}$), 128.2 ($2CH_{Ar}$), 124.6 ($2CH_{Ar}$), 124.5 ($2CH_{Ar}$), 124.3 ($2CH_{Ar}$), 118.9 (C≡N), 109.6 (C_{Ar}), 34.4 (C $_{tBu}$), 34.4 (C $_{tBu}$), 34.3 (C $_{tBu}$), 31.2 ($6CH_3$ $_{tBu}$), 31.2 ($3CH_3$ $_{tBu}$), 21.2 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3050(w), 2954 (m), 2904 (m), 2867 (m), 2225 (m), 1738 (w), 1682 (w), 1608 (w), 1533 (m), 1513 (m), 1496 (m), 1462 (m), 1362 (m), 1309 (w), 1270 (m), 1242 (m), 1202 (m), 1180 (m), 1109 (m), 1019 (m), 1002 (m), 972 (w), 884 (w), 852 (s), 831 (s), 820 (s), 809 (s),796 (m), 772 (m), 754 (m), 737 (w), 700 (m), 664 (m), 629 (m), 578 (s), 562 (m), 551 (s), 532 (m). **MS** (EI, 70 eV): m/z (%) = 666 (M^+, 63), 665 (100), 651 (5), 609 (7), 593 (5), 579 (6), 554 (5), 553 (9), 551 (11), 318 (23), 207 (6), 57 (59), 41(16). **HR-MS** (ESI): m/z = calcd. for $C_{49}H_{50}N_2$ ($[M+H]^+$): 667.40468, found: 667.40437. Anal. calcd. for $C_{49}H_{50}N_2$: C 88.24, H 7.56, N 4.20; found: C 88.17, H 7.27, N 3.89

General procedure for the synthesis of compounds 13a–b

An oven-dried, argon-flushed sealable glass tube was charged with the appropriate tri-arylated pyridine **10a** or **10b** (0.22 mmol, 100 mg), $PdCl_2(CH_3CN)_2$ (5 mol%, 2.9 mg), SPhos (10 mol%, 9.22 mg), the appropriate arylboronic acid (0.99 mmol) and K_3PO_4 (0.99 mmol, 191 mg) followed by anhydrous toluene (3 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 20 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/ethyl acetate as eluent.

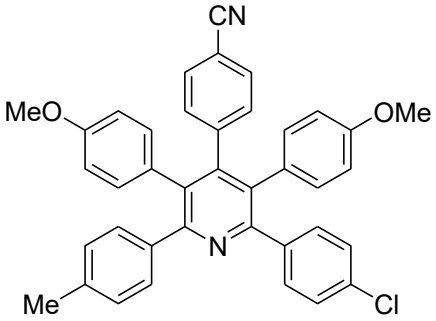
2-**(4-methoxyphenyl)-3,5-diphenyl-4-(4-cyanophenyl)-6-*p*-tolylpyridine (13a):**



13a was synthesized according to general procedure using 3,5-dichloro-2-(4-methoxyphenyl)-4-(4-cyanophenyl)-6-*p*-tolylpyridine **10a** (0.22 mmol, 100 mg), and phenylboronic acid (0.99 mmol, 120.7 mg) and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 107 mg (90 %). mp. 261 - 262 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.38 (d,^3J = 8.9 Hz, 2H, CH_{Ar}), 7.33 (d,^3J = 8.2 Hz, 2H, CH_{Ar}), 7.23 (d, ^3J = 8.5 Hz, 2H, CH_{Ar}), 7.08–7.04 (m, 6H, CH_{Ar}), 7.01 (d, ^3J = 8.4 Hz, 2H, CH_{Ar}), 6.94–6.84 (m, 6H, CH_{Ar}), 6.73 (d, ^3J = 8.9 Hz, 2H, CH_{Ar}), 3.77 (s, 3H, OCH_3), 2.30 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 159.1 (*C*-OCH_3), 156.4 ($C_{Ar/Hetar}$), 155.9($C_{Ar/Hetar}$), 148.3 ($C_{Ar/Hetar}$), 143.8 ($C_{Ar/Hetar}$), 138.0 ($C_{Ar/Hetar}$), 137.9 ($C_{Ar/Hetar}$), 137.5 ($C_{Ar/Hetar}$), 137.4 ($C_{Ar/Hetar}$), 132.9 ($C_{Ar/Hetar}$), 132.3 ($C_{Ar/Hetar}$), 132.3 ($C_{Ar/Hetar}$), 131.5 ($2CH_{Ar}$), 131.1 ($2CH_{Ar}$), 131.1 ($2CH_{Ar}$), 130.8 ($2CH_{Ar}$), 130.1 ($2CH_{Ar}$), 128.3 ($2CH_{Ar}$), 127.8 ($2CH_{Ar}$), 127.8 ($2CH_{Ar}$), 126.7 ($2CH_{Ar}$), 126.6 ($2CH_{Ar}$), 118.7 (C≡N), 113.0 ($2CH_{Ar}$), 109.9 (C_{Ar}), 55.1 (OCH_3), 21.2 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3045 (w), 3025 (w), 2951 (w), 2929 (w), 2905 (w), 2832 (w), 1602 (m), 1577 (w), 1534 (m), 1510 (m), 1503 (m), 1443 (w), 1389 (m), 1309 (w), 1295 (w), 1264 (w), 1244 (s), 1175 (m), 1157 (w), 1074 (w), 1024 (m), 1006 (w), 969 (w), 880 (w), 848 (m), 816 (m), 767 (m), 742 (m), 727 (m), 703 (s), 660 (m), 626 (w), 594 (w), 557 (m), 532 (m). **MS** (EI, 70 eV): m/z (%) = 529 (21), 528 (M^+, 71), 527 (100), 484 (8), 483 (12), 264 (8), 165

(5). **HR-MS** (ESI): m/z = calcd. for $C_{38}H_{28}N_2O$ ($[M+H]^+$): 529.22744, found: 529.22698. Anal. calcd. for $C_{38}H_{28}N_2O$: C 86.34, H 5.34, N 5.30; found: C 86.12, H 5.29, N 5.14.

2-(4-chlorophenyl)-3,5-bis(4-methoxyphenyl)-4-(4-cyanophenyl)-6-*p*-tolylpyridine (13b):

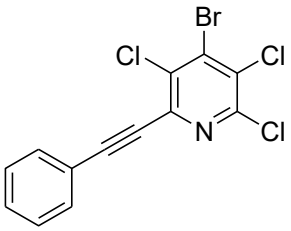


13b was synthesized according to general procedure using 3,5-dichloro-2-(4-chlorophenyl)-4-(4-cyanophenyl)-6-p-tolylpyridine **10b** (0.22 mmol, 100 mg), and 4-methoxyphenylboronic acid (0.99 mmol, 150.4 mg) and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 66 mg (50 %). mp. 246 - 247 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 7.35 (d, ^3J = 8.7 Hz, 2H, CH_{Ar}), 7.30 (d, ^3J = 8.2 Hz, 2H, CH_{Ar}), 7.27 (d, ^3J = 8.7 Hz, 2H, CH_{Ar}), 7.18 (d, ^3J = 8.7 Hz, 2H, CH_{Ar}), 7.03 (d, ^3J = 7.9 Hz, 2H, CH_{Ar}), 6.89 (d, ^3J = 8.5 Hz, 2H, CH_{Ar}), 6.75 (dd, ^3J = 8.8 Hz, ^3J = 8.8 Hz, 4H, CH_{Ar}), 6.59 (dd, ^3J = 8.8 Hz, ^3J = 8.9 Hz, 4H, CH_{Ar}), 3.73 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 2.30 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 158.3 (*C*-OCH_3), 158.2 ($C_{Ar/Hetar}$), 156.8 ($C_{Ar/Hetar}$), 155.3 ($C_{Ar/Hetar}$), 148.8 ($C_{Ar/Hetar}$), 143.9 ($C_{Ar/Hetar}$), 139.1 ($C_{Ar/Hetar}$), 137.5 ($C_{Ar/Hetar}$), 137.4 ($C_{Ar/Hetar}$), 133.6 ($C_{Ar/Hetar}$), 132.8 ($C_{Ar/Hetar}$), 132.4 ($C_{Ar/Hetar}$), 132.1 ($4CH_{Ar}$), 131.5 ($2CH_{Ar}$), 131.2 ($2CH_{Ar}$), 130.9 ($2CH_{Ar}$), 129.9 ($2CH_{Ar}$), 129.9 (C_{Ar}), 129.6 (C_{Ar}), 128.4 ($2CH_{Ar}$), 127.8 ($2CH_{Ar}$), 118.8 (C≡N), 113.4 ($2CH_{Ar}$), 113.3 ($2CH_{Ar}$), 110.0 (C_{Ar}), 55.0 ($2OCH_3$), 21.2 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2933 (w), 2837 (w), 1607 (m), 1533 (w), 1511 (m), 1488 (w), 1461 (w), 1387 (m), 1305 (w), 1288 (m), 1242 (s), 1174 (m), 1160 (w), 1089 (w), 1030 (m), 1020 (m), 1011 (m), 999 (w), 963 (w), 880 (w), 803 (m), 760 (w), 729 (s), 692 (w), 649 (m), 613 (w), 558 (m), 548 (w), 534 (w). **MS** (EI, 70 eV): m/z (%) = 595 (M^+, 11), 594 (M^+, 32), 593 (M^+, 58), 592 (M^+, 84), 591 (100), 547 (11), 297 (7), 296 (11), 227 (5), 220 (5), 207 (7), 199 (6), 190 (13), 178 (6), 164 (5), 163 (6). **HR-MS** (ESI): m/z = calcd. for $C_{39}H_{29}ClN_2O_2$ ($[M+H]^+$): 593.19903, found: 593.199, calcd. for $C_{39}H_{29}{}^{37}ClN_2O_2$: 595.19825, found 595.19807. Anal. calcd. for $C_{39}H_{29}ClN_2O_2$: C 78.98, H 4.93, N 4.72; found: C 78.78, H 4.59, N 4.84.

General procedure for the synthesis of compounds 14a–h

An oven-dried, argon-flushed sealable glass tube was charged with 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg), $Pd(PPh_3)_2Cl_2$ (0.013 mmol, 5 mol%), and CuI (0.013 mmol, 5 mol%). The solids were diluted with triethylamine (21.5 mmol, 3 mL). The solution was stirred at ambient temperature for ten minutes. Afterwards, 0.28 mmol of appropriate acetylene was added. The pressure tube was closed with a Teflon cap and the reaction mixture was stirred at room temperature for 19 h. Afterwards, the reaction mixture was diluted with distilled water and dichloromethane. The aqueous layer was extracted with dichloromethane (three times). The combined organic layers were dried with sodium sulfate, filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography using heptane/dichloromethane as eluent to purify the corresponding monoalkynylpyridines.

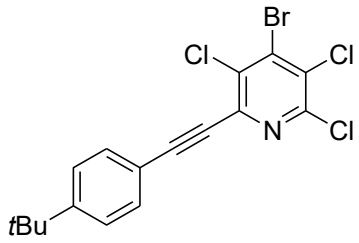
4-bromo-2,3,5-trichloro-6-(2-phenylethynyl)pyridine (14a):



14a was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and ethynylbenzene (0.28 mmol, 0.031 mL) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 84 mg (90 %). mp. 135 – 136 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.67 - 7.60 (m, 2H, CH_{Ar}), 7.48-7.37 (m, 3H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 147.1 ($C_{Ar/Hetar}$), 139.3 ($C_{Ar/Hetar}$), 135.8 ($C_{Ar/Hetar}$), 134.6 ($C_{Ar/Hetar}$), 132.4 ($2CH_{Ar}$), 131.6 ($C_{Ar/Hetar}$), 130.0 ($2CH_{Ar}$), 128.5 (CH_{Ar}), 121.1 (C_{Ar}), 97.3 (C≡C), 84.8 (C≡C). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 2954 (m), 2922 (m), 2220 (m), 1519 (s), 1492 (s), 1440 (m), 1386 (s), 1321 (s), 1269 (s), 1217 (s), 1080 (s), 916 (m), 820 (s), 755 (s), 686 (s), 677 (s), 641 (m), 557 (s), 549 (s), 530 (s). **MS** (EI, 70 eV): m/z (%) = 365 (M^+, 17), 363 (M^+, 63), 362 (14), 361 (M^+, 100), 359 (M^+, 52), 247 (15), 245 (24), 219 (10), 184 (24), 175 (32), 127 (10), 120 (12), 118 (18), 92 (16). **HR-MS** (EI): m/z = calcd. for $C_{13}H_5NBrCl_3$ $[M]^+$: 358.86655, found: 358.86609; calcd. for $C_{13}H_5NBrCl_2{}^{37}Cl$ $[M]^+$: 360.86360, found: 360.86361; calcd. For $C_{13}H_5NBrCl^{37}Cl_2$ $[M]^+$: 362.86065, found: 362.86092; calcd. For $C_{13}H_5N^{81}BrCl_2{}^{37}Cl$ $[M]^+$: 362.86155, found: 362.86092; calcd. For $C_{13}H_5N^{81}BrCl^{37}Cl_2$ $[M]^+$: 364.85860, found: 364.85840;

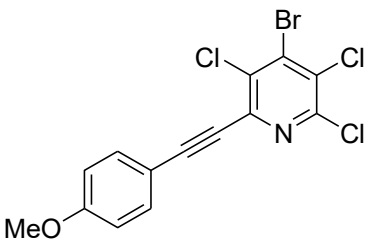
calcd. For $C_{13}H_5NBr^{37}Cl_3$ $[M]^+$: 364.85770, found: 364.85840; Anal. calcd. for $C_{13}H_5NBrCl_3$: C 43.20, H 1.39, N 3.88; found: C 43.11, H 1.24, N 3.94 .

2-(2-(4-*tert*-butylphenyl)ethynyl)-4-bromo-3,5,6-trichloropyridine (14b):



14b was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-*tert*-butyl-4-ethynylbenzene (0.28 mmol, 0.051 mL) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 100 mg (92 %). mp. 107 – 108 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.58 (d, ^3J = 8.6 Hz, 2H, CH_{Ar}), 7.43 (d, ^3J = 8.6 Hz, 2H, CH_{Ar}), 1.34 (s, 9H, CH_3 $_{tBu}$). **^{13}C-NMR** 75.0 MHz, $CDCl_3$): 153.7 ($C_{Ar/Hetar}$), 147.0 ($C_{Ar/Hetar}$), 139.6 ($C_{Ar/Hetar}$), 135.7 ($C_{Ar/Hetar}$), 134.5 ($C_{Ar/Hetar}$), 132.2 ($2CH_{Ar}$), 131.3 ($C_{Ar/Hetar}$), 125.6 ($2CH_{Ar}$), 118.0 (C_{Ar}), 97.9 (C≡C), 84.5 (C≡C), 35.0 (C $_{tBu}$), 31.1 ($3CH_3$ $_{tBu}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2963 (m), 2905 (m), 2215 (m), 1515 (m), 1483 (s), 1462 (m), 1383 (s), 1319 (s), 1289 (s), 1271 (s), 1214 (s), 1196 (m), 1081 (s), 998 (m), 945 (m), 895 (m), 843 (s), 835 (s), 819 (s), 766 (s), 738 (s), 705 (s), 693 (s), 644 (m), 614 (s), 564 (s). **MS** (EI, 70 eV): m/z (%) = 421 (M^+, 5), 419 (M^+, 19), 418 (6), 417 (M^+, 29), 415 (M^+, 14), 406 (17), 405 (11), 404 (64), 403 (19), 402 (100), 401 (13), 400 (50), 376 (10), 374 (13), 188 (10), 41 (11). **HR-MS** (ESI): m/z = calcd. for $C_{17}H_{13}BrCl_3N$ $[M+Na]^+$: 437.91892, found: 437.91832; calcd. for $C_{17}H_{13}BrCl_2{}^{37}ClN$ $[M+Na]^+$: 439.91597, found: 439.91607; calcd. for $C_{17}H_{13}{}^{81}BrCl_3N$ $[M+Na]^+$: 439.91687, found: 439.91607, calcd. for $C_{17}H_{13}{}^{81}BrCl_2{}^{37}Cl_2N$ $[M+Na]^+$: 441.91392, found: 441.91327; calcd. for $C_{17}H_{13}BrCl^{37}Cl_2N$ $[M+Na]^+$: 441.91302, found: 441.91327; calcd. for $C_{17}H_{13}Br^{37}Cl_3N$ $[M+Na]^+$: 443.91007, found: 443.91174; calcd. for $C_{17}H_{13}{}^{81}BrCl^{37}Cl_2N$ $[M+Na]^+$: 443.91097, found: 443.91174. Anal. calcd. for $C_{17}H_{13}BrCl_3N$: C 48.90, H 3.14, N 3.35; found: C 48.81, H 3.21, N 3.26.

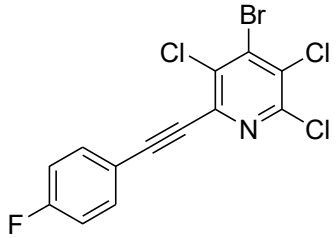
4-bromo-2,3,5-trichloro-6-(2-(4-methoxyphenyl)ethynyl)pyridine, (14c):



14c was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-methoxybenzene (0.28 mmol, 0.036 mL) and was purified via column chromatography

(heptane/dichloromethane). White solid; yield: 86 mg (86 %). mp. 132 - 133 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.57 (d, ^{3}J = 8.88 Hz, 2H, CH_{Ar}), 6.90 (d, ^{3}J = 8.88 Hz, 2H, CH_{Ar}), 3.84 (s, 3H, OCH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 161.0 ($C_{Ar/Hetar}$), 146.9 ($C_{Ar/Hetar}$), 139.6 ($C_{Ar/Hetar}$), 135.5 ($C_{Ar/Hetar}$), 134.1 ($C_{Ar/Hetar}$), 134.1 ($2CH_{Ar}$), 130.9 ($C_{Ar/Hetar}$), 114.2 ($2CH_{Ar}$), 113.0 (C_{Ar}), 98.0 (C≡C), 84.2 (C≡C), 55.3 (OCH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2922 (w), 2849 (w), 2201 (m), 1602 (m), 1517 (s), 1509 (s), 1442 (m), 1320 (m), 1272 (s), 1251 (s), 1167 (s), 1077 (m), 1020 (s), 955 (m), 829 (s), 788 (s), 735 (s), 666 (m), 549 (s), 535 (s). **MS** (EI, 70 eV): m/z (%) = 395 (M^+, 17), 394 (10), 393 (M^+, 63), 392 (15), 391 (M^+, 100), 390 (7), 389 (M^+, 52), 378 (16), 376 (25), 374 (13), 348 (11), 234 (30), 232 (43), 205 (12), 171 (12), 162 (21), 120 (11), 118 (14), 114 (15). **HR-MS** (ESI): m/z = calcd. for $C_{14}H_7BrCl_3NO$ $[M+H]^+$: 389.88494, found: 389.88518; calcd. for $C_{14}H_7{}^{81}BrCl_3NO$ $[M+H]^+$: 391.88289, found: 391.88293; calcd. for $C_{14}H_7{}^{81}BrCl_2{}^{37}ClNO$ $[M+H]^+$: 393.87994, found: 393.88035; calcd. for $C_{14}H_7{}^{81}BrCl^{37}Cl_2NO$ $[M+H]^+$: 395.87699, found 395.87740. Anal. calcd. for $C_{14}H_7BrCl_3NO$: C 42.95, H 1.80, N 3.58; found: C 42.90, H 1.88, N 3.56.

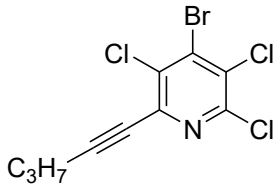
4-bromo-2,3,5-trichloro-6-(2-(4-fluorophenyl)ethynyl)pyridine (14d):



14d was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-fluorobenzene (0.28 mmol, 0.032 mL) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 44 mg (45 %). mp. 136 - 137 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.67 - 7.60 (m, 2H, CH_{Ar}), 7.14 - 7.06 (m, 2H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 163.0 (d, $^{1}J_{C-F}$ = 255.7 Hz, C_{Ar}), 147.2 ($C_{Ar/Hetar}$), 139.2 ($C_{Ar/Hetar}$), 135.8 ($C_{Ar/Hetar}$), 134.5 ($C_{Ar/Hetar}$), 134.5 (d, $^{3}J_{C-F}$ = 8.8 Hz, $2CH_{Ar}$), 131.7 ($C_{Ar/Hetar}$), 117.2 (d, $^{4}J_{C-F}$ = 3.5 Hz, C_{Ar}), 116.0 (d, $^{2}J_{C-F}$ = 22.3 Hz, $2CH_{Ar}$), 96.1 (C≡C), 84.6 (d, $^{5}J_{C-F}$ = 1.6 Hz, C≡C). **^{19}F -NMR** (282 MHz, CDCl3): δ = - 107.48 (s). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 2921 (m), 2215 (m), 1597 (m), 1505 (s), 1484 (s), 1386 (s), 1320 (s), 1282 (s), 1231 (s), 1220 (s), 1213 (s), 1155 (s), 1072 (s), 1014 (m), 915 (m), 834 (s), 796 (s), 735 (s), 666 (m), 529 (s). **MS** (EI, 70 eV): m/z (%) = 383 (M^+, 17), 382 (9), 381 (M^+, 65), 380 (14), 379 (M^+, 100), 377 (M^+, 50), 265 (10), 263 (16), 202 (14), 193 (18), 118 (11). **HR-MS** (EI): m/z = calcd. for $C_{13}H_4NBrCl_3F$ $[M]^+$: 376.85712, found: 376.85662; calcd. for

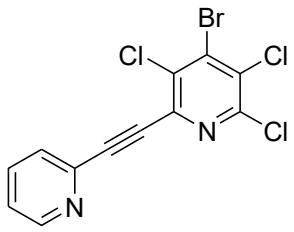
$C_{13}H_4NBrCl_2{}^{37}ClF$ $[M]^+$: 378.85417, found: 378.8535; calcd. for $C_{13}H_4N^{81}BrCl_3F$: 378.85508, found: 378.85435; calcd. for $C_{13}H_4N^{81}BrCl_2{}^{37}ClF$ $[M]^+$: 380.85213, foud: 380.85190; calcd. for $C_{13}H_4NBrCl^{37}Cl_2F$ $[M]^+$: 380.85122, found: 380.85190; calcd. for $C_{13}H_4N^{81}BrCl^{37}Cl_2F$ $[M]^+$: 382.84918, found: 382.84917; calcd. for $C_{13}H_4NBr^{37}Cl_3F$: 382.84827, found: 382.84917. Anal. calcd. for $C_{13}H_4NBrCl_3$: C 41.15, H 1.06, N 3.69; found: C 41.10, H 1.11, N 3.60.

4-bromo-2,3,5-trichloro-6-(pent-1-ynyl)pyridine (14e):



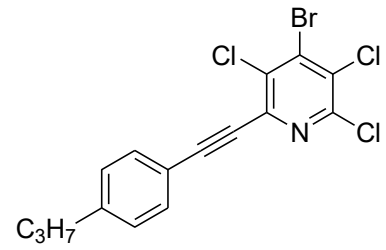
14e was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-pentyne (0.28 mmol, 0.028 mL) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 47.4 mg (56 %). mp. 52 - 53 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 2.51 (t, ^3J = 7.0 Hz, 2H, CH_2), 1.77 - 1.62 (m, 2H, CH_2), 1.08 (t, ^3J = 7.4 Hz, 3H, CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 146.8 ($C_{Ar}/_{Hetar}$), 139.6 ($C_{Ar}/_{Hetar}$), 135.6 ($C_{Ar}/_{Hetar}$), 134.4 ($C_{Ar}/_{Hetar}$), 131.1 ($C_{Ar}/_{Hetar}$), 100.1 (2C≡C), 21.6 (CH_2), 21.5 (CH_2), 13.5 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2964 (m), 2874 (m), 2229 (s), 1514 (m), 1483 (s), 1425 (m), 1376 (s), 1317 (s), 1288 (s), 1254 (s), 1203 (s), 1088 (m), 862 (m), 774 (s), 738 (m), 682 (s), 553 (s). **MS** (EI, 70 eV): m/z (%) = 331 (M^+, 9), 329 (M^+, 33), 328 (15), 327 (M^+, 51), 326 (18), 325 (M^+, 27), 324 (8), 316 (17), 314 (64), 313 (10), 312 (10), 310 (52), 301 (22), 300 (21), 299 (34), 233 (10), 231 (11), 184 (21), 182 (30), 155 (13), 122 (10), 121 (20), 120 (24), 118 (29), 115 (10), 111 (12), 99 (11), 86 (14), 85 (15), 29 (10). **HR-MS** (EI): m/z = calcd. for $C_{10}H_7NBrCl_3$ $[M]^+$: 324.88220, found: 324.88151; calcd. for $C_{10}H_7NBrCl_2{}^{37}Cl$ $[M]^+$: 326.87925, found: 326.87936; calcd. for $C_{10}H_7N^{81}BrCl_3$ $[M]^+$: 326.88015, found: 326.87936; calcd. for $C_{10}H_7N^{81}BrCl_2{}^{37}Cl$ $[M]^+$: 328.87720, found: 328.87681; calcd. for $C_{10}H_7NBrCl^{37}Cl_2$ $[M]^+$: 328.87720, found: 328.87681; calcd. for $C_{10}H_7N^{81}BrCl^{37}Cl_2$ $[M]^+$: 330.87425, found: 330.87411; calcd. for $C_{10}H_7NBr^{37}Cl_3$ $[M]^+$: 330.87335, found: 330.87411. Anal. calcd. for $C_{10}H_7NBrCl_3$: C 36.68, H 2.15, N 4.28; found: C 36.59, H 2.12, N 4.25.

2-(2-(4-bromo-3,5,6-trichloropyridin-2-yl)ethynyl)pyridine, (14f):



14f was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 2-ethynylpyridine (0.28 mmol, 0.028 mL) and was purified via column chromatography (heptane/ dichloromethane). Yellow solid; yield: 32 mg (35 %). mp. 189 – 190 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 8.69 (ddd, ^{3}J = 4.9 Hz, ^{4}J = 1.7 Hz, ^{5}J = 1.1 Hz, 1H, Hetar), 7.80 - 7.69 (m, 1H, Hetar), 7.65 (dpt, ^{3}J = 7.8 Hz, ^{5}J = 1.1 Hz, 1H, Hetar), 7.34 (ddd, ^{3}J = 7.5 Hz, ^{4}J = 4.9 Hz, ^{5}J = 1.4 Hz, 1H, Hetar). **^{13}C-NMR** (75.0 MHz, CDCl3): δ = 150.4 (CH_{Hetar}), 147.3 (C_{Hetar}), 141.6 (C_{Hetar}), 138.5 (C_{Hetar}), 136.4 (CH_{Hetar}), 135.9 (C_{Hetar}), 135.3 (C_{Hetar}), 132.6 (C_{Hetar}), 128.3 (CH_{Hetar}), 124.2 (CH_{Hetar}), 94.8 (C≡C), 83.5 (C≡C). **IR** (ATR, cm^{-1}): ṽ = 3076 (w), 2954 (w), 2850 (m), 2205 (w), 1582 (m), 1488 (s), 1464 (s), 1431 (s), 1378 (s), 1317 (s), 1287 (s), 1273 (s), 1243 (m), 1190 (s), 1083 (s), 991 (s), 965 (m), 885 (m), 828 (s), 773 (s), 764 (s), 732 (s), 689 (s), 567 (s), 538 (s). **MS** (EI, 70 eV): m/z (%) = 364 (M^+, 65), 363 (15), 362 (M^+, 100), 361 (10), 360 (M^+, 53), 329 (7), 327 (15), 248 (11), 246 (17), 220 (11), 211 (13), 185 (18), 176 (17), 155 (12), 153 (11), 123 (18), 120 (21), 118 (29), 78 (10), 75 (11), 52 (11), 51 (19), 50 (11). **HR-MS** (EI): m/z = calcd. for $C_{12}H_4N_2BrCl_3$ $[M]^+$: 359.86180, found: 359.86149; calcd. for $C_{12}H_4N_2BrCl_2{}^{37}Cl$ $[M]^+$: 361.85885, found: 361.85894; calcd. for $C_{12}H_4N_2{}^{81}BrCl_3$ $[M]^+$: 361.85975, found: 361.85894; calcd. for $C_{12}H_4N_2BrCl^{37}Cl_2$ $[M]^+$: 363.85590, found: 363.85626; calcd. for $C_{12}H_4N_2{}^{81}BrCl_2{}^{37}Cl$ $[M]^+$: 363.85680, found: 363.85626. Anal. calcd. for $C_{12}H_4N_2BrCl_3$: C 39.77, H 1.11, N 7.73; found: C 39.84, H 1.17, N 7.68.

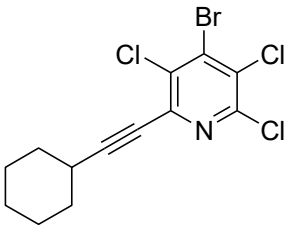
4-bromo-2,3,5-trichloro-6-(2-(4-propylphenyl)ethynyl)pyridine (14g);



14g was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-propylbenzene (0.28 mmol, 0.044 mL) and was purified via column chromatography (heptane/ dichloromethane). Yellow solid; yield: 76 mg (73 %). mp. 66 – 67 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.56 (d, ^{3}J = 8.12 Hz, 2H, CH_{Ar}), 7.21 (d, ^{3}J = 8.0 Hz, 2H, CH_{Ar}), 2.63 (t, ^{3}J = 7.36 Hz, 2H,

CH_2), 1.67 (m, 2H, CH_2), 0.96 (t, ^3J = 7.37 Hz, 3H, CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 147.0 ($C_{Ar/Hetar}$), 145.3 ($C_{Ar/Hetar}$), 139.5 ($C_{Ar/Hetar}$), 135.7 ($C_{Ar/Hetar}$), 134.4 ($C_{Ar/Hetar}$), 132.3 ($2CH_{Ar}$), 131.3 (C_{Ar}), 128.7 ($2CH_{Ar}$), 118.2 (C_{Ar}), 97.7 (C≡C), 84.5 (C≡C), 38.1 (CH_2), 24.2 (CH_2), 13.7 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2865 (w), 2206 (m), 1520 (m), 1481 (s), 1389 (s), 1319 (s), 1269 (s), 1211 (m), 1186 (m), 1078 (m), 945 (w), 822 (s), 795 (m), 735 (s), 658 (m), 550 (s), 536 (s). **MS** (EI, 70 eV): m/z (%) = 407 (M^+, 6), 405 (M^+, 27), 404 (7), 403 (M^+, 42), 401 (M^+, 22), 378 (17), 377 (10), 376 (63), 375 (15), 374 (100), 373 (9), 372 (52), 260 (15), 258 (23), 197 (17), 188 (35), 140 (19), 118 (10). **HR-MS** (EI): m/z = calcd. for $C_{16}H_{11}NBrCl_3$ $[M]^+$: 400.91350, found: 400.91283; calcd. for $C_{16}H_{11}NBrCl_2{}^{37}Cl$ $[M]^+$: 402.91055, found 402.91065; calcd. for $C_{16}H_{11}N$ $^{81}BrCl_2{}^{37}Cl$ $[M]^+$: 404.90850, found 404.908338; calcd. for $C_{16}H_{11}N{}^{81}BrCl{}^{37}Cl_2$ $[M]^+$: 406.90555; found 406.90612. Anal. calcd. for $C_{16}H_{11}NBrCl_3$: C 47.62, H 2.75, N 3.47; found: C 47.58, H 2.78, N 3.50.

4-bromo-2,3,5-trichloro-6-(2-cyclohexylethynyl)pyridine (14h):

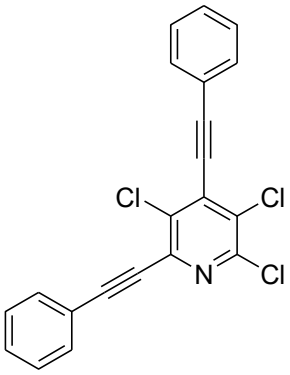


14h was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and ethynylcyclohexane (0.28 mmol, 0.037 mL) and was purified via column chromatography (heptane/ dichloromethane). White solid; yield: 76 mg (80 %). mp. 77 – 78 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 2.78 - 269 (m, 1H, CH), 1.94 – 1.86 (m, 2H, CH_2), 1.82 - 173 (m, 2H, CH_2), 1.68 – 1.39 (m, 6H, $3CH_2$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 146.7 ($C_{Ar/Hetar}$), 139.8 ($C_{Ar/Hetar}$), 135.5 ($C_{Ar/Hetar}$), 134.5 ($C_{Ar/Hetar}$), 130.9 ($C_{Ar/Hetar}$), 104.1 (2C≡C), 31.8 ($2CH_2$), 29.8 (CH), 25.8 (CH_2), 24.6 ($2CH_2$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2941 (w), 2924 (s), 2848 (s), 2218 (s), 1520 (m), 1487 (m), 1375 (s), 1319 (s), 1288 (m), 1205 (s), 1091 (w), 891 (w), 770 (m), 739 (w), 692 (s), 567 (m), 554 (m). **MS** (EI, 70 eV): m/z (%) = 368 (M^+, 14), 367 (26), 366 (M^+, 19), 341 (20), 340 (66), 339 (31), 338 (100), 336 (52), 312 (27), 299 (21), 286 (20), 195 (22), 120 (24), 118 (31), 93 (20), 91 (21), 82 (22), 80 (30), 79 (24), 77 (21), 67 (65), 41 (52), 39 (36). **HR-MS** (ESI): m/z = calcd. for $C_{13}H_{11}NBrCl_2{}^{37}Cl$ $[M+H]^+$: 366.91055; found: 366.91024; calcd. for $C_{13}H_{11}NBrCl{}^{37}Cl_2$ $[M+H]^+$: 368.90760 found 368.90775. Anal. calcd. for $C_{13}H_{11}BrCl_3N$: C 42.49, H 3.02, N 3.81; found: C 42.38, H 3.18, N 3.78

General procedure for the synthesis of compounds 15a–e

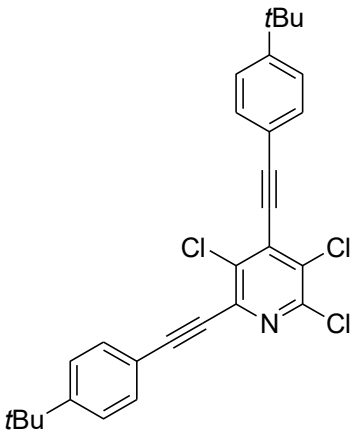
An oven-dried, argon-flushed sealable glass tube was charged with 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg), $Pd(PPh_3)_4$ (0.013 mmol, 5 mol%) and CuI (0.013 mmol, 5 mol%). The solids were diluted with 5 ml of dry 1,4-dioxane and diisopropylamine (14.3 mmol, 2 mL). The solution was stirred at ambient temperature for ten minutes. Afterwards, 0.54 mmol of appropriate acetylene was added. The pressure tube was closed with a Teflon cap and the reaction mixture was stirred at 80 °C. After 20 h the reaction was cooled to room temperature and diluted with distilled water and dichloromethane. The aqueous layer was extracted with dichloromethane (three times). The combined organic layers were dried with sodium sulfate, filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography using heptane/dichloromethane as eluent to purify the corresponding dialkynylpyridines.

2,3,5-trichloro-4,6-bis(2-phenylethynyl)pyridine (15a):



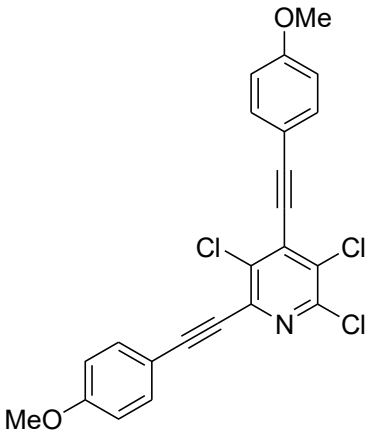
15a was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynylbenzene (0.54 mmol, 0.059 mL) and was purified via column chromatography (heptane/ dichloromethane). Yellow solid; yield: 60 mg (61 %). mp. 171 - 172 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.69 - 7.64 (m, 4H, CH_{Ar}), 7.51 - 7.36 (m, 6H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 147.1 ($C_{Ar/Hetar}$), 139.2 ($C_{Ar/Hetar}$), 133.9 ($C_{Ar/Hetar}$), 133.6 ($C_{Ar/Hetar}$), 132.3 ($2CH_{Ar}$), 130.8 ($C_{Ar/Hetar}$), 130.4 ($2CH_{Ar}$), 129.8 ($2CH_{Ar}$), 128.6 ($2CH_{Ar}$), 128.5 ($2CH_{Ar}$), 121.4 (C_{Ar}), 121.2 (C_{Ar}), 106.1 (C≡C), 96.8 (C≡C), 84.7 (C≡C), 82.1 (C≡C). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2924 (w), 2212 (m), 1531 (m), 1498 (m), 1290 (s), 1259 (m), 1184 (w), 1095 (m), 1067 (m), 912 (m), 804 (m), 749 (s), 679 (s), 527 (m). **MS** (EI, 70 eV): m/z (%) = 385 (M^+, 33), 384 (22), 383 (M^+, 99), 382 (24), 381 (M^+, 100), 311 (12), 275 (19), 250 (8), 192 (6), 184 (6). **HR-MS** (EI): m/z = calcd. for $C_{21}H_{10}NCl_2{}^{37}Cl$ $[M]^+$: 382.98438; found: 382.98430; calcd. for $C_{21}H_{10}NCl^{37}Cl_2$ $[M]^+$: 384.98143 found: 384.98196. Anal. calcd. for $C_{21}H_{10}Cl_3N$: C 65.91, H 2.63, N 3.66; found: C 65.82, H 2.67, N 3.73.

2,4-bis(2-(4-*tert*-butylphenyl)ethynyl)-3,5,6-trichloropyridine (15b);



15b was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-*tert*-butyl-4-ethynylbenzene (0.54 mmol, 0.097 mL) and was purified via column chromatography (heptane/dichloromethane). Yellow solid; yield: 85 mg (67 %). mp. 159 – 160 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.61 - 7.58 (m, 4H, CH_{Ar}), 7.47 - 7.41 (m, 4H, CH_{Ar}), 1.36 (s, 9H, CH_3 $_{tBu}$), 1.35 (s, 9H, CH_3 $_{tBu}$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 154.1 (C_{Ar}), 153.4 (C_{Ar}), 146.9 ($C_{Ar/Hetar}$), 139.4 ($C_{Ar/Hetar}$), 133.8 ($C_{Ar/Hetar}$), 133.7 ($C_{Ar/Hetar}$), 132.1 (4CH), 130.4 ($C_{Ar/Hetar}$), 125.7 (2CH), 125.5 (2CH), 118.3 (C_{Ar}), 118.2 (C_{Ar}), 106.5 (C≡C), 97.3 (C≡C), 84.4 (C≡C), 81.8 (C≡C), 35.0 (C $_{tBu}$), 34.9 (C $_{tBu}$), 31.1 (6CH_3 $_{tBu}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2958 (m), 2927 (w), 2213 (m), 1528 (m), 1405 (w), 1383 (m), 1289 (s), 1198 (w), 1107 (w), 1017 (w), 829 (s), 720 (m), 558 (s). **MS** (EI, 70 eV): m/z (%) = 497 (M^+, 15), 496 (14), 495 (M^+, 48), 494 (14), 493 (M^+, 47), 483 (7), 482 (29), 481 (24), 480 (100), 479 (26), 479 (26), 478 (99), 231 (10). **HR-MS** (ESI): m/z = calcd. for $C_{29}H_{26}NCl_3$ $[M+H]^+$: 494.12036; found: 494.12; calcd. for $C_{29}H_{10}NCl_2{}^{37}Cl$ $[M+H]^+$: 496.11788 found: 496.11732; calcd. for $C_{29}H_{10}NCl^{37}Cl_2$ $[M+H]^+$: 498.11576 found: 498.11535. Anal. calcd. for $C_{29}H_{26}Cl_3N$: C 70.38, H 5.30, N 2.83; found: C 70.46, H 5.22, N 2.80.

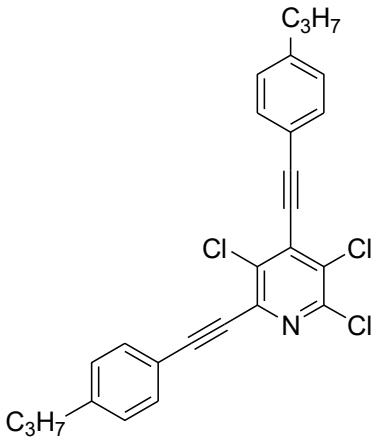
2,3,5-trichloro-4,6-bis(2-(4-methoxyphenyl)ethynyl)pyridine, (15c):



15c was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-methoxybenzene (0.54 mmol, 0.070 mL) and was purified via column chromatography (heptane/dichloromethane). Yellow solid; yield: 58 mg (51 %). mp. 157 - 158 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.62-7.58 (m, 4H, CH_{Ar}), 6.96-6.90 (m, 4H, CH_{Ar}), 3.87 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 161.3 (C_{Ar}),

160.9 (C_{Ar}), 146.9 ($C_{Ar/Hetar}$), 139.4 ($C_{Ar/Hetar}$), 134.1 ($2CH_{Ar}$), 134.0 ($2CH_{Ar}$), 133.8 ($C_{Ar/Hetar}$), 133.3 ($C_{Ar/Hetar}$), 129.8 ($C_{Ar/Hetar}$), 114.3 ($2CH_{Ar}$), 114.2 ($2CH_{Ar}$), 113.4 (C_{Ar}), 113.2 (C_{Ar}), 106.8 (C≡C), 97.3 (C≡C), 84.1 (C≡C), 81.7 (C≡C), 55.4 (OCH_3), 55.4 (OCH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2922 (w), 2837 (w), 2205 (m), 1602 (m), 1529 (s), 1513 (s), 1436 (w), 1289 (s), 1248 (s), 1167 (s), 1105 (m), 825 (s), 759 (m), 531 (m), 505 (m). **MS** (EI, 70 eV): m/z (%) = 445 (M^+, 35), 444 (24), 443 (M^+, 98), 442 (26), 441 (M^+, 100), 428 (14), 426 (14), 285 (11), 221 (12)**. HR-MS** (EI): m/z = calcd. for $C_{23}H_{14}O_2NCl_3$ $[M]^+$: 441.00846; found: 441.00754; calcd. for $C_{23}H_{14}O_2NCl_2{}^{37}Cl$ $[M]^+$: 443.00551 found: 443.00431; calcd. for $C_{23}H_{14}O_2NCl{}^{37}Cl_2$ $[M]^+$: 445.00256 found: 445.00323. Anal. calcd. for $C_{23}H_{14}Cl_3NO_2$: C 62.40, H 3.19, N 3.16; found: C 62.51, H 3.26, N 3.19.

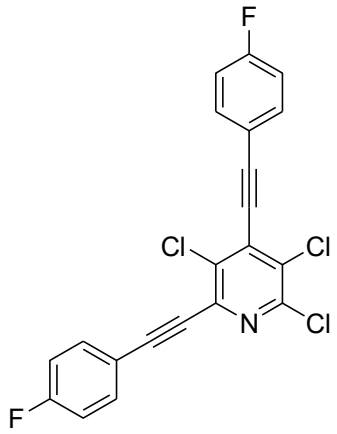
2,3,5-trichloro-4,6-bis(2-(4-propylphenyl)ethynyl)pyridine (15d):



15d was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-propylbenzene (0.54 mmol, 0.085 mL) and was purified via column chromatography (heptane/dichloromethane). Yellow solid; yield: 76 mg (63 %). mp. 65 - 66 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.57 (dd, ^3J = 8.20 Hz, ^4J = 2.52 Hz, 4H, CH_{Ar}), 7.26 - 7.19 (m, 4H, CH_{Ar}), 2.68 - 2.60 (m, 4H, $2CH_2$), 1.71 - 1.59 (m, 4H, $2CH_2$), 0.99 - 0.84 (m, 6H, $2CH_3$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 146.9 ($C_{Ar/Hetar}$), 145.7 (C_{Ar}), 145.1 (C_{Ar}), 139.3 ($C_{Ar/Hetar}$), 133.7 ($C_{Ar/Hetar}$), 133.7 ($C_{Ar/Hetar}$), 132.3 ($2CH_{Ar}$), 132.3 ($2CH_{Ar}$), 130.4 ($C_{Ar/Hetar}$), 128.8 ($2CH_{Ar}$), 128.7 ($2CH_{Ar}$), 118.5 (C_{Ar}), 118.4 (C_{Ar}), 106.6(C≡C), 97.3 (C≡C), 84.4 (C≡C), 81.9 (C≡C), 38.1 (CH_2), 38.1 (CH_2), 24.3 (CH_2), 24.3 (CH_2), 13.7 (CH_3), 13.7 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2925 (m), 2865 (m), 2211 (m), 1529 (s), 1493 (m), 1463 (m), 1382 (s), 1290 (s), 1215 (m), 1179 (m), 1090 (w), 912 (m), 837 (m), 812 (s), 773 (m), 557 (s), 529 (s). **MS** (EI, 70 eV): m/z (%) = 469 (35), 468 (29), 467 (M^+, 97), 466 (27), 465 (M^+, 100), 440 (33), 439 (21), 438 (86), 437 (22), 436 (88), 409 (22), 407 (27), 301 (10), 204 (24), 203 (26). **HR-MS** (EI): m/z = calcd. for $C_{27}H_{22}NCl_3$ $[M]^+$: 465.08123; found: 465.08073; calcd. for

$C_{27}H_{22}NCl_2{}^{37}Cl$ $[M]^+$: 467.07828 found: 467.07898. Anal. calcd. for $C_{27}H_{22}Cl_3N$: C 69.47, H 4.75, N 3.00; found: C 69.56, H 4.65, N 2.92.

2,3,5-trichloro-4,6-bis(2-(4-fluorophenyl)ethynyl)pyridine (15e):



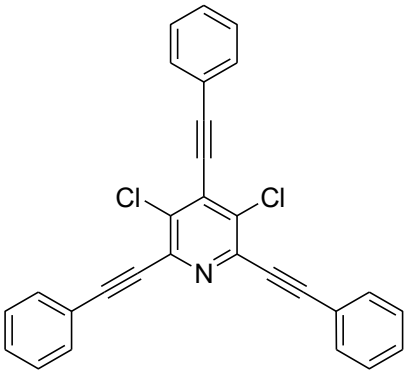
15e was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-fluorobenzene (0.54 mmol, 0.062 mL) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 58 mg (54 %). mp. 198 - 199 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.69 - 7.62 (m, 4H, CH_{Ar}), 7.17 - 7.06 (m, 4H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 163.8 (d, $^1J_{CF}$ = 253.64 Hz, C_{Ar}), 163.5 (d, $^1J_{CF}$ = 253.50 Hz, C_{Ar}), 147.2 ($C_{Ar/Hetar}$), 139.1 ($C_{Ar/Hetar}$), 134.5 (d, $^3J_{CF}$ = 8.20 Hz, $2CH_{Ar}$), 134.5 (d, $^3J_{CF}$ = 8.20 Hz, $2CH_{Ar}$), 133.8 ($C_{Ar/Hetar}$), 133.4 ($C_{Ar/Hetar}$), 130.8 ($C_{Ar/Hetar}$), 117.5 (d, $^4J_{CF}$ = 3.30 Hz, C_{Ar}), 117.3 (d, $^4J_{CF}$ = 3.85 Hz, C_{Ar}), 116.2 (d, $^2J_{CF}$ = 22.56 Hz, $2CH_{Ar}$), 115.9 (d, $^2J_{CF}$ = 22.01 Hz, $2CH_{Ar}$), 105.0 (C≡C), 95.8 (C≡C), 84.3 (d, $^5J_{CF}$ = 1.10 Hz, C≡C), 81.9 (d,$^5J_{CF}$ = 1.60 Hz, C≡C). **^{19}F** -NMR (282 MHz, $CDCl_3$): δ = -106.87 (s, 1F, Ar), -107.81 (s, 1F, Ar). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3073 (w), 2921 (m), 2215 (m), 1598 (m), 1513 (m), 1387 (m), 1290 (s), 1227 (s), 1154 (s), 1093 (m), 914 (m), 830 (s), 768 (m), 551 (w), 528 (s), 497 (m). **MS** (EI, 70 eV): m/z (%) = 421 (M^+, 32), 420 (22), 419 (M^+, 100), 418 (24), 417 (M^+, 97), 347 (17), 311 (17), 286 (11), 209 (13), 202 (11), 143 (9)**.** **HR-MS** (EI): m/z = calcd. for $C_{21}H_8NCl_3F_2$ $[M]^+$: 416.96849; found: 416.96951; calcd. for $C_{21}H_8NCl_2{}^{37}ClF_2$ $[M]^+$: 418.96554 found: 418.96601; calcd. for $C_{21}H_8NCl^{37}Cl_2F_2$ $[M]^+$: 420.96259 found: 420.96335. Anal. calcd. for $C_{21}H_8Cl_3F_2N$: C 60.25, H 1.93, N 3.35; found: C 60.36, H 2.01, N 3.40.

General procedure for the synthesis of compounds 16a–d

An oven-dried, argon-flushed sealable glass tube was charged with 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg), $Pd(PPh_3)_4$ (0.013 mmol, 5 mol%) and CuI (0.013 mmol, 5 mol%). The solids were diluted with 5 ml of dry 1,4-dioxane and diisopropylamine (14.3 mmol, 2 mL). The solution was stirred at ambient temperature for ten minutes. Afterwards, 0.80 mmol of appropriate acetylene was added. The

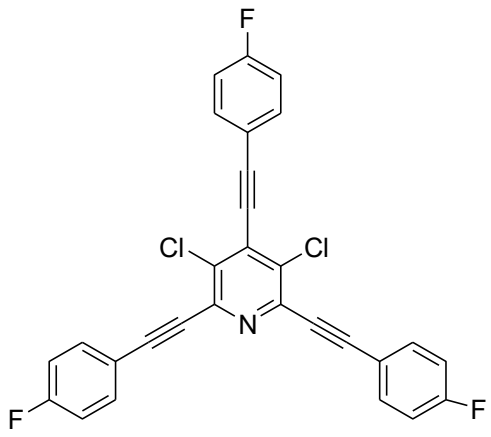
pressure tube was closed with a Teflon cap and the reaction mixture was stirred at 80 °C. After 20 h the reaction was cooled to room temperature and diluted with distilled water and dichloromethane. The aqueous layer was extracted with dichloromethane (three times). The combined organic layers were dried with sodium sulfate, filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography using heptane/dichloromethane as eluent to purify the corresponding trialkynylpyridines.

3,5-dichloro-2,4,6-tris(2-phenylethynyl)pyridine (16a):



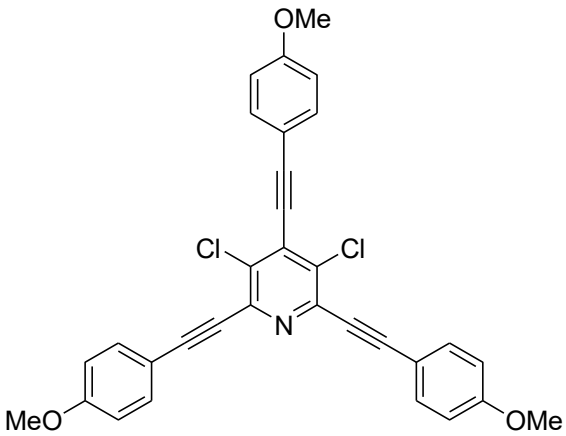
16a was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynylbenzene (0.80 mmol, 0.088 mL) and was purified via column chromatography (heptane/ dichloromethane). Yellow solid; yield: 69 mg (60 %). mp. 151 - 152 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.71 - 7.63 (m, 6H, CH_{Ar}), 7.48 - 7.36 (m, 9H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 140.4 ($C_{Ar/Hetar}$), 133.9 ($C_{Ar/Hetar}$), 132.3 ($6CH_{Ar}$), 131.9 ($C_{Ar/Hetar}$), 130.2 (CH_{Ar}), 129.6 ($2CH_{Ar}$), 128.6 ($2CH_{Ar}$), 128.5 ($4CH_{Ar}$), 121.7 (C_{Ar}), 121.4 (C_{Ar}), 105.3 (C≡C), 95.8 (C≡C), 85.3 (C≡C), 81.9 (C≡C). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3048 (w), 2955 (w), 2216 (m), 1529 (m), 1369 (m) 1264 (m), 1212 (m), 1097 (m), 1025 (m), 973 (m), 916 (w), 751 (s), 688 (s), 485 (m), 472 (m). **MS** (EI, 70 eV): m/z (%) = 451 (12), 450 (21), 449 (M^+, 66), 448 (32), 447 (M^+, 100), 376 (7), 375 (14), 250 (15)**. HR-MS** (EI): m/z = calcd. for $C_{29}H_{15}NCl_2$ $[M]^+$: 447.05761; found: 447.05671; calcd. for $C_{29}H_{15}NCl^{37}Cl$ $[M]^+$: 449.05466 found: 449.05489. Anal. calcd. for $C_{29}H_{15}Cl_2N$: C 77.69, H 3.37, N 3.12; found: C 77.73, H 3.48, N 3.21.

3,5-dichloro-2,4,6-tris(2-(4-fluorophenyl)ethynyl)pyridine (16b):



16b was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-fluorobenzene (0.80 mmol, 0.092 mL) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 57 mg (44 %). mp. 182 - 183 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.70 - 7.56 (m, 6H, CH_{Ar}), 7.15 - 7.06 (m, 6H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 163.7 (d, $^{1}J_{CF}$ = 253.09 Hz, C_{Ar}), 163.4 (d, $^{1}J_{CF}$ = 252.00 Hz, C_{Ar}), 140.3 ($C_{Ar/Hetar}$), 134.5 (d, $^{3}J_{CF}$ = 8.80 Hz, 2 or 4 CH_{Ar}), 134.4 (d, $^{3}J_{CF}$ = 8.80 Hz, 2 or 4 CH_{Ar}), 133.8 ($C_{Ar/Hetar}$), 131.8 ($C_{Ar/Hetar}$), 117.7 (d, $^{4}J_{CF}$ = 3.30 Hz, C_{Ar}), 117.5 (d, $^{4}J_{CF}$ = 3.85 Hz, C_{Ar}), 116.1 (d, $^{2}J_{CF}$ = 22.01 Hz, $2CH_{Ar}$), 115.9 (d, $^{2}J_{CF}$ = 22.01 Hz, $4CH_{Ar}$), 104.4 (C≡C), 94.8 (C≡C), 84.9 (d, $^{5}J_{CF}$ = 1.10 Hz, C≡C), 81.7 (d, $^{5}J_{CF}$ = 1.10 Hz, C≡C). **^{19}F** -NMR (282 MHz, $CDCl_3$): δ = - 107.24 (s, 1F, Ar), - 108.20 (s, 2F, Ar). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 1599 (m), 1535 (m), 1509 (s), 1403 (w), 1372 (m), 1227 (s), 1154 (s), 1091 (m), 961 (w), 829 (s), 772 (m), 527 (m), 461 (m). **MS** (EI, 70 eV): m/z (%) = 505 (14), 504 (20), 503 (M^+, 69), 502 (34), 501 (M^+, 100), 429 (10), 286 (21), 251 (10), 143 (9)**. HR-MS** (EI): m/z = calcd. for $C_{29}H_{12}NCl_2F_3$ $[M]^+$: 501.02934; found: 501.02880; calcd. for $C_{29}H_{12}NCl^{37}ClF_3$ $[M]^+$: 503.02639 found: 503.02697. Anal. calcd. for $C_{29}H_{12}Cl_2F_3N$: C 69.34, H 2.41, N 2.79; found: C 69.43, H 2.36, N 2.70.

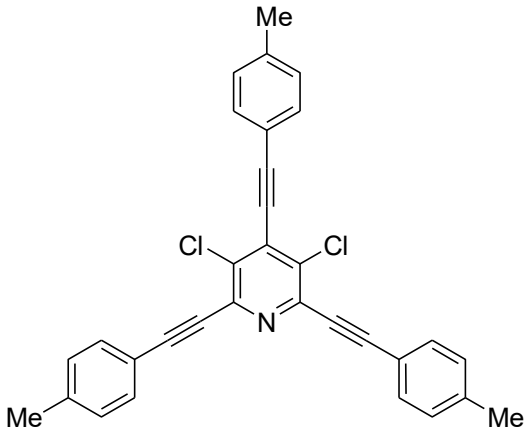
3,5-dichloro-2,4,6-tris(2-(4-methoxyphenyl)ethynyl)pyridine (16c):



16c was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-methoxybenzene (0.80 mmol, 0.104 mL) and was purified via column chromatography (heptane/dichloromethane). Yellow solid; yield: 80 mg (58 %). mp. 143 –

144 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.63 - 7.58 (m, 6H, CH_{Ar}), 6.96 - 6.89 (m, 6H, CH_{Ar}), 3.87 (s, 3H, OCH_3), 3.85 (s, 6H, $2OCH_3$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 161.1 (C_{Ar}), 160.6 (C_{Ar}), 140.4 ($C_{Ar/Hetar}$), 134.0 (CH_{Ar}), 133.9 (CH_{Ar}), 132.9 ($C_{Ar/Hetar}$), 131.9 ($C_{Ar/Hetar}$) , 114.3 (CH_{Ar}), 114.1 (CH_{Ar}), 113.8 (C_{Ar}), 113.5 (C_{Ar}), 105.8 (C≡C), 96.0 (C≡C), 84.6 (C≡C), 81.5 (C≡C), 55.4 (OCH_3), 55.3 ($2OCH_3$). **IR** (ATR, cm^{-1}): ṽ = 3070 (w), 2919 (m), 2838 (w), 1602 (m), 1507 (s), 1439 (m), 1373 (m), 1290 (m), 1247 (s), 1168 (m), 1020 (m), 830 (s), 766 (m), 569 (m), 487 (m). **MS** (EI, 70 eV): m/z (%) = 541 (14), 540 (22), 539 (M^+, 69), 538 (33), 537 (M^+, 100), 522 (9), 169 (2)**.** **HR-MS** (EI): m/z = calcd. for $C_{32}H_{21}O_3NCl_2$ $[M]^+$: 537.08930; found: 537.08800; calcd. for $C_{32}H_{21}O_3NCl^{37}Cl$ $[M]^+$: 539.08635 found: 539.08608. Anal. calcd. for $C_{32}H_{21}Cl_2NO_3$: C 71.38, H 3.93, N 2.60; found: C 71.50, H 4.04, N 2.62.

3,5-dichloro-2,4,6-tris(2-*p*-tolylethynyl)pyridine (16d):

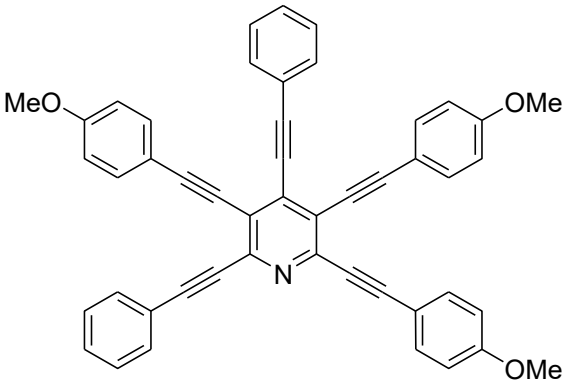


16d was synthesized according to general procedure using 4-bromo-2,3,5-trichloro-6-iodopyridine **3** (0.26 mmol, 100 mg) and 1-ethynyl-4-methylbenzene (0.80 mmol, 0.101 mL) and was purified via column chromatography (heptane/dichloromethane). Yellow solid; yield: 74 mg (58 %). mp. 177 - 178 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.58 - 7.54 (m, 6H, CH_{Ar}), 7.25 - 7.19 (m, 6H, CH_{Ar}), 2.42 (s, 3H, CH_3), 2.40 (s, 6H, $2CH_3$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 140.7 ($C_{Ar/Hetar}$), 140.4 (C_{Ar}) 139.9 (C_{Ar}), 133.5 ($C_{Ar/Hetar}$), 132.2 ($2CH_{Ar}$), 131.9 ($C_{Ar/Hetar}$), 129.3 (CH_{Ar}), 129.2 (CH_{Ar}), 118.6 (C_{Ar}), 118.4 (C_{Ar}), 105.7 (C≡C), 96.1 (C≡C), 84.9 (C≡C), 81.7 (C≡C), 21.7 (CH_3), 21.7 ($2CH_3$). **IR** (ATR, cm^{-1}): ṽ = 3026 (w), 2956 (w), 2853 (w), 2212 (m), 1536 (m), 1369 (m), 1262 (w), 1209 (m), 1177 (m), 1093 (m), 833 (w), 809 (s), 764 (m), 526 (s), 459 (m), 422 (m); **MS** (EI, 70 eV): m/z (%) = 493 (18), 492 (M^+, 27), 491 (80), 490 (M^+, 40), 489 (100), 403 (7), 402 (9), 135 (7). **HR-MS** (ESI): m/z = calcd. for $C_{32}H_{21}NCl_2$ $[M+H]^+$: 490.11238; found: 490.11211; calcd. for $C_{32}H_{21}NCl^{37}Cl$ $[M+H]^+$: 492.11025 found: 492.11011. Anal. calcd. for $C_{32}H_{21}Cl_2N$: C 78.37, H 4.32, N 2.86; found: C 78.48, H 4.19, N 2.80.

General procedure for the synthesis of compounds 17a–c

An oven-dried, argon-flushed sealable glass tube was charged with 2,3,5-trichloro-4,6-bis(2-phenylethynyl)pyridine **15a** (0.21 mmol, 80 mg), $Pd(CH_3CN)_2Cl_2$ (0.0105 mmol, 5 mol%), XPhos (0.010 mmol, 10 mol%) and CuI (0.0105 mmol, 5 mol%). The solids were diluted with 7 ml of dry 1,4-dioxane and diisopropylamine (28.7 mmol, 4 mL). The solution was stirred at ambient temperature for ten minutes. Afterwards, 1.05 mmol of appropriate acetylene was added. The pressure tube was closed with a Teflon cap and the reaction mixture was stirred at 80 °C. After 18 h the reaction was cooled to room temperature and diluted with distilled water and dichloromethane. The aqueous layer was extracted with dichloromethane (three times). The combined organic layers were dried with sodium sulfate, filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography using heptane/dichloromethane as eluent to purify the corresponding pentaalkynylpyridines.

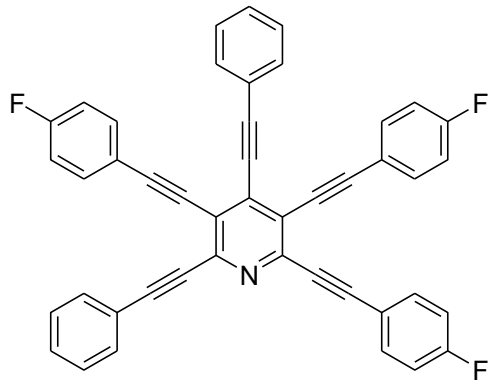
2,3,5-tris(2-(4-methoxyphenyl)ethynyl)-4,6-bis(2-phenylethynyl)pyridine (17a):



17a was synthesized according to general procedure using 2,3,5-trichloro-4,6-bis(2-phenylethynyl)pyridine **15a** (0.21 mmol, 80 mg) and 1-ethynyl-4-methoxybenzene (1.05 mmol, 0.139 mL) and was purified via column chromatography (heptane/ dichloromethane). Yellow solid; yield: 132 mg (94 %). mp. 185 – 186 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.68 - 7.65 (m, 4H, CH_{Ar}), 7.62 - 7.56 (m, 6H, CH_{Ar}), 7.43 - 7.35 (m, 6H, CH_{Ar}), 6.93 - 6.89 (m, 6H, CH_{Ar}), 3.86 (brs, 9H, $3OCH_3$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 160.5 (C_{Ar}), 160.4 ($2C_{Ar}$), 143.0 (C_{Ar}), 142.6 ($C_{Ar/Hetar}$), 134.6 ($C_{Ar/Hetar}$), 133.8 ($2CH_{Ar}$), 133.3 ($4CH_{Ar}$), 132.2 ($2CH_{Ar}$), 132.1 ($2CH_{Ar}$), 129.5 (CH_{Ar}), 129.2 (CH_{Ar}), 128.6 ($2CH_{Ar}$), 128.4 ($2CH_{Ar}$), 122.9 (C_{Ar}), 122.8 ($C_{Ar/Hetar}$), 122.5 (C_{Ar}), 122.4 (C_{Ar}), 114.9 (C_{Ar}), 114.9 (C_{Ar}), 114.3 (C_{Ar}), 114.2 ($4CH_{Ar}$), 114.1 ($2CH_{Ar}$), 102.1 (C≡C), 101.3 (2C≡C), 95.3 (C≡C), 94.6 (C≡C), 88.0 (C≡C), 87.1 (C≡C), 85.8 (C≡C), 84.7 (C≡C), 84.6 (C≡C), 55.4 ($2OCH_3$), 55.3 (OCH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3050 (w), 2929 (w), 2834 (w), 2200 (m), 1602 (m), 1507 (s), 1459 (m), 1398 (m), 1246 (s), 1166

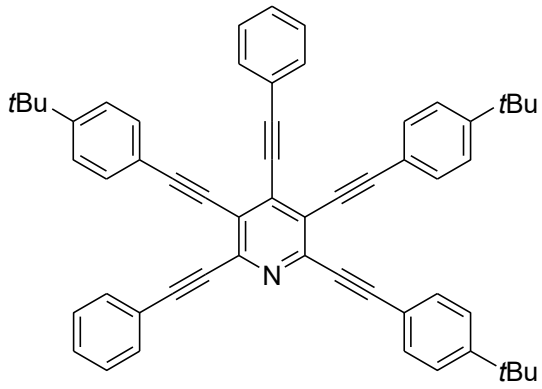
(s), 1106 (m), 1025 (s), 976 (m), 827 (s), 806 (m), 752 (s), 686 (s), 592 (m), 529 (s), 496 (m). **MS** (EI, 70 eV): m/z (%) = 669 (M^+, 37), 335 (7), 151 (17), 44 (100), 43 (10), 40 (24). **HR-MS** (EI): m/z = calcd. for $C_{48}H_{31}O_3N$ $[M]^+$: 669.22985; found: 669.22890. Anal. calcd. for $C_{48}H_{31}N\,O_3$: C 86.08, H 4.67, N 2.09; found: C 86.24, H 4.51, N 2.01.

2,3,5-tris(2-(4-fluorophenyl)ethynyl)-4,6-bis(2-phenylethynyl)pyridine (17b):



17b was synthesized according to general procedure using 2,3,5-trichloro-4,6-bis(2-phenylethynyl)pyridine **15a** (0.21 mmol, 80 mg) and 1-ethynyl-4-fluorobenzene (1.05 mmol, 0.120 mL) and was purified via column chromatography (heptane/dichloromethane). Brown solid; yield: 127 mg (96 %). mp 213 – 214 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.64 - 7.55 (m, 10H, CH_{Ar}), 7.47 - 7.34 (m, 6H, CH_{Ar}), 7.10 - 7.03 (m, 6H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 163.2 (d, $^1J_{CF}$ = 252.00 Hz, C_{Ar}), 163.1 (d, $^1J_{CF}$ = 252.00 Hz, $2C_{Ar}$), 143.4 (C_{Ar}), 143.1 ($C_{Ar/Hetar}$), 135.3 ($C_{Ar/Hetar}$), 134.2 (d, $^3J_{CF}$ = 8.80 Hz, $2CH_{Ar}$), 133.7 (d, $^3J_{CF}$ = 8.80 Hz, $2CH_{Ar}$), 133.7 (d, $^3J_{CF}$ = 8.80 Hz, $2CH_{Ar}$), 132.2 ($2CH_{Ar}$), 132.0 ($2CH_{Ar}$), 129.8 (CH_{Ar}), 129.5 (CH_{Ar}), 128.6 ($2CH_{Ar}$), 128.5 ($2CH_{Ar}$), 122.7 ($C_{Ar/Hetar}$), 122.5 (C_{Ar}), 122.2 (C_{Ar}), 122.1 ($C_{Ar/Hetar}$), 118.8 (d, $^4J_{CF}$ = 3.30 Hz, C_{Ar}), 118.8 (d, $^4J_{CF}$ = 3.30 Hz, C_{Ar}), 118.2 (d, $^4J_{CF}$ = 3.30 Hz, C_{Ar}), 115.9 (d, $^2J_{CF}$ = 22.01 Hz, $2CH_{Ar}$), 115.9 (d, $^2J_{CF}$ = 22.5 Hz, $2CH_{Ar}$), 115.9 (d, $^2J_{CF}$ = 22.01 Hz, $2CH_{Ar}$), 102.8 (C≡C), 100.1 (C≡C), 99.9 (C≡C), 95.2 (C≡C), 93.9 (C≡C), 87.7 (C≡C), 87.5 (d, $^5J_{CF}$ = 1.65 Hz, C≡C), 85.4 (C≡C), 85.1 (d, $^5J_{CF}$ = 1.65 Hz, C≡C), 85.1 (d, $^5J_{CF}$ = 1.65 Hz, C≡C). **^{19}F** -NMR (282 MHz, $CDCl_3$): δ = - 108.56 (s, 1F, Ar), - 108.88 (s, F, Ar), - 108.98 (s, F, Ar). **IR** (ATR, cm^{-1}): ṽ = 3064 (w), 3046 (w), 1598 (w), 1503 (m), 1400 (w), 1215 (m), 1150 (m), 976 (m), 827 (s), 782 (m), 750 (s), 685 (s), 629 (m), 589 (m), 524 (s), 448 (m). **MS** (EI, 70 eV): m/z (%) = 633 (M^+, 100), 632 (10), 316 (6), 44 (15), 40 (18)**. HR-MS** (EI): m/z = calcd. for $C_{45}H_{22}NF_3$ $[M]^+$: 633.16989; found: 633.16885. Anal. calcd. for $C_{45}H_{22}F_3N$: C 85.30, H 3.50, N 2.21; found: C 85.41, H 3.54, N 2.11.

2,3,5-tris(2-(4-*tert*-butylphenyl)ethynyl)-4,6-bis(2-phenylethynyl)pyridine (17c):



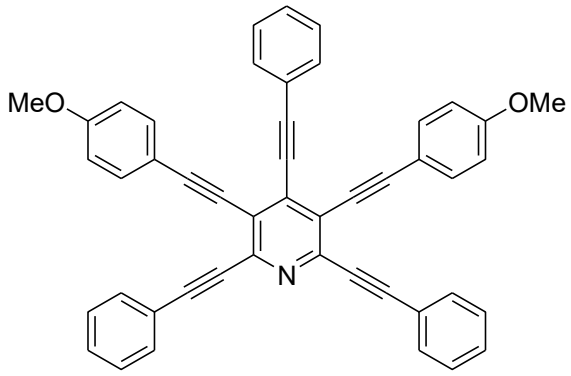
17c was synthesized according to general procedure using 2,3,5-trichloro-4,6-bis(2-phenylethynyl)pyridine **15a** (0.21 mmol, 80 mg) and 1-*tert*-butyl-4-ethynylbenzene (1.05 mmol, 0.189 mL) and was purified via column chromatography (heptane/ dichloromethane). Brown solid; yield: 132 mg (84 %). mp. 90 – 91 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.71 - 7.67 (m, 4H, CH_{Ar}), 7.64 - 7.58 (m, 6H, CH_{Ar}), 7.44 - 7.39 (m, 12H, CH_{Ar}), 1.38 (s, 9H, CH_3 $_{tBu}$), 1.37 (s, 18H, CH_3 $_{tBu}$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 152.8 (C_{Ar}), 152.6 (C_{Ar}), 152.6 (C_{Ar}), 143.3 ($C_{Ar/Hetar}$), 143.0 ($C_{Ar/Hetar}$), 135.1($C_{Ar/Hetar}$), 132.3 ($2CH_{Ar}$), 132.2 ($2CH_{Ar}$), 132.1 ($2CH_{Ar}$), 131.6 ($2CH_{Ar}$), 131.6 ($2CH_{Ar}$), 129.5 (CH_{Ar}), 129.3 (CH_{Ar}), 128.6 ($2CH_{Ar}$), 128.4 ($2CH_{Ar}$), 125.6 ($4CH_{Ar}$), 125.5 ($2CH_{Ar}$), 122.9 ($C_{Ar/Hetar}$), 122.9 ($C_{Ar/Hetar}$), 122.5 (C_{Ar}), 122.3 (C_{Ar}), 119.9 (C_{Ar}), 119.8 (C_{Ar}), 119.2 (C_{Ar}), 102.4 (C≡C), 101.4 (C≡C), 101.4 (C≡C), 95.4 (C≡C), 94.8 (C≡C), 87.9 (C≡C), 87.5 (C≡C), 85.7 (C≡C), 85.1 (C≡C), 85.0 (C≡C), 34.9 (3C $_{tBu}$), 31.2 (9CH_3 $_{tBu}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 2958 (m), 2865 (w), 2207 (m), 1598 (w), 1502 (s), 1400 (s), 1362 (m), 1266 (m), 1106 (m), 1024 (w), 828 (s), 753 (s), 727 (m), 686 (s), 557 (s), 528 (m). **MS** (EI, 70 eV): m/z (%) = 747 (M^+, 100), 732 (9), 359 (11), 358 (13), 44 (43), 40 (38)**. HR-MS** (EI): m/z = calcd. for $C_{57}H_{49}N$ $[M]^+$: 747.38595; found: 747.38531. Anal. calcd. for $C_{57}H_{49}N$: C 91.52, H 6.60, N 1.87; found: C 91.56, H 6.63, N 1.80.

General procedure for the synthesis of compounds 18a–c

An oven-dried, argon-flushed sealable glass tube was charged with 3,5-dichloro-2,4,6-tris(2-phenylethynyl)pyridine **16a** (0.18 mmol, 80 mg), $Pd(CH_3CN)_2Cl_2$ (0.0089 mmol, 5 mol%), Xphos (0.018 mmol, 10 mol%) and CuI (0.0089 mmol, 5 mol%). The solids were diluted with 5 mL of dry 1,4-dioxane and diisopropylamine (21.5 mmol, 3 mL). The solution was stirred at ambient temperature for ten minutes. Afterwards, 0.71 mmol of appropriate acetylene was added. The pressure tube was closed with a Teflon cap and the reaction mixture was stirred at 80 °C. After 18 h the reaction was cooled to room

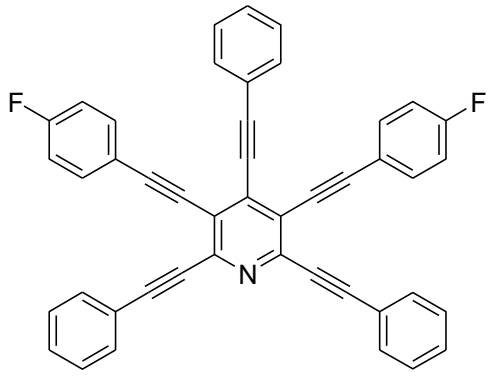
temperature and diluted with distilled water and dichloromethane. The aqueous layer was extracted with dichloromethane (three times). The combined organic layers were dried with sodium sulfate, filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography using heptane/dichloromethane as eluent to purify the corresponding pentaalkynylpyridines.

3,5-bis(2-(4-methoxyphenyl)ethynyl)-2,4,6-tris(2-phenylethynyl)pyridine, (18a):



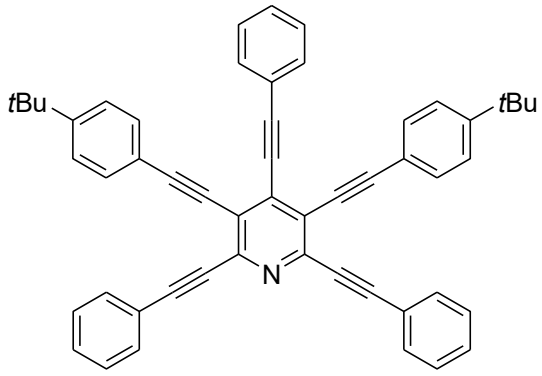
18a was synthesized according to general procedure using 3,5-dichloro-2,4,6-tris(2-phenylethynyl)pyridine **16a** (0.18 mmol, 80 mg) and 1-ethynyl-4-methoxybenzene (0.71 mmol, 0.092 mL) and was purified via column chromatography (heptane/ dichloromethane). Brown solid; yield: 108 mg (95 %). mp. 199 - 200 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.69 - 7.66 (m, 6H, CH_{Ar}), 7.58 (d, ^{3}J = 8.88 Hz, 4H, CH_{Ar}), 7.44 - 7.37 (m, 9H, CH_{Ar}), 6.91 (d, 4H, ^{3}J = 8.88 Hz, CH_{Ar}), 3.86 (s, 6H, OCH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 160.4 (C_{Ar}), 142.7 ($C_{Ar/Hetar}$) , 134.7 ($C_{Ar/Hetar}$), 133.4 (CH_{Ar}), 132.2 (CH_{Ar}), 132.1 (CH_{Ar}), 129.6 (CH_{Ar}), 129.3 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 123.2 ($C_{Ar/Hetar}$), 122.5 (C_{Ar}), 122.3 (C_{Ar}), 114.9 (C_{Ar}), 114.2 (CH_{Ar}), 102.3 (C≡C), 101.6 (C≡C), 94.7 (C≡C), 87.9 (C≡C), 85.7 (C≡C), 84.5 (C≡C), 55.4 ($2OCH_3$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3050 (w), 2930 (w), 2200 (m), 1602 (m), 1502 (s), 1440 (m), 1289 (m), 1244 (s) 1167 (s), 1105 (m), 1025 (m), 827 (s), 805 (m), 754 (s), 687 (s), 645 (m), 596 (m), 528 (s), 409 (m); **MS** (EI, 70 eV): m/z (%) = 639 (M^+, 100), 319 (8), 275 (8), 44 (21), 40 (20). **HR-MS** (EI): m/z = calcd. for $C_{47}H_{29}O_2N$ $[M]^+$: 639.21928; found: 639.21803. Anal. calcd. for $C_{47}H_{29}NO_2$: C 88.24, H 4.57, N 2.19; found: C 88.19, H 4.45, N 2.18.

3,5-bis(2-(4-fluorophenyl)ethynyl)-2,4,6-tris(2-phenylethynyl)pyridine, **(18b):**



18b was synthesized according to general procedure using 3,5-dichloro-2,4,6-tris(2-phenylethynyl)pyridine **16a** (0.18 mmol, 80 mg) and 1-ethynyl-4-fluorobenzene (0.71 mmol, 0.081 mL) and was purified via column chromatography (heptane/ dichloromethane). Brown solid; yield: 107 mg (97 %). mp. 205 - 206 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.67 - 7.57 (m, 10H, CH_{Ar}), 7.46 - 7.35 (m, 9H, CH_{Ar}), 7.12 - 7.04 (m, 4H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 163.1 (d, $^{1}J_{CF}$ = 250.89 Hz, C_{Ar}), 143.4 ($C_{Ar/Hetar}$), 133.8 (d, $^{3}J_{CF}$ = 8.25 Hz, CH_{Ar}), 132.2 (CH_{Ar}), 132.0 (CH_{Ar}), 129.8 (CH_{Ar}), 129.5 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (CH_{Ar}), 122.7 (C_{Ar}), 122.2 (C_{Ar},) 122.1 (C_{Ar}), 118.9 (d, $^{4}J_{CF}$ = 3.30 Hz, C_{Ar}), 118.9 (C_{Ar}), 115.9 (d, $^{2}J_{CF}$ = 22.56 Hz, CH_{Ar}), 102.7 (C≡C), 100.1 (C≡C), 95.2 (C≡C), 87.7 (C≡C), 85.4 (C≡C), 85.2 (d, $^{5}J_{CF}$ = 1.10 Hz, C≡C). **^{19}F** - NMR (282 MHz, $CDCl_3$): δ = -108.02 (s). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3104 (w), 3062 (w), 2923 (w), 2205 (m), 1597 (m), 1501 (s), 1400 (m), 1222 (m), 1151 (m), 1069 (w), 921 (w), 828 (s), 755 (s), 688 (s), 596 (m), 525 (s), 448 (m). **MS** (EI, 70 eV): m/z (%) = 615 (M^+ 100), 614 (10), 308 (6), 44 (5), 40 (15)**. HR-MS** (EI): m/z = calcd. for $C_{45}H_{23}NF_2$ $[M]^+$: 615.17931; found: 615.17888. Anal. calcd. for $C_{45}H_{23}F_2N$: C 87.79, H 3.77, N 2.28; found: C 87.72, H 3.64, N 2.40.

3,5-bis(2-(4-*tert*-butylphenyl)ethynyl)-2,4,6-tris(2-phenylethynyl)pyridine, (18c):



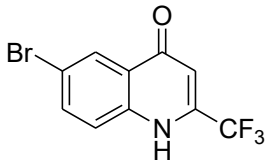
18c was synthesized according to general procedure using 3,5-dichloro-2,4,6-tris(2-phenylethynyl)pyridine **16a** (0.18 mmol, 80 mg) and 1-*tert*-butyl-4-ethynylbenzene (0.71 mmol, 0.128 mL) and was purified via column chromatography (heptane/ dichloromethane). Yellow solid; yield: 80 mg (65 %). mp. 226 – 227 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.70 - 7.67 (m, 6H, CH_{Ar}), 7.59 (d, ^{3}J = 8.69 H_Z, 4H, CH_{Ar}), 7.44 - 7.39 (m, 13H, CH_{Ar}), 1.36 (s, 18H, CH_3

$_{t\text{Bu}}$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 152.7 (C_{Ar}), 143.1 ($C_{Ar/Hetar}$), 135.2 ($C_{Ar/Hetar}$), 132.3 (CH_{Ar}), 132.2 (CH_{Ar}), 131.6 (CH_{Ar}), 129.6 (CH_{Ar}), 129.3 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 125.6 (CH_{Ar}), 123.1 ($C_{Ar/Hetar}$), 122.4 (C_{Ar}), 122.3 (C_{Ar}), 119.8 (C_{Ar}), 102.6 (C≡C), 101.5 (C≡C), 94.9 (C≡C), 87.9 (C≡C), 85.6 (C≡C), 84.9 (C≡C), 34.9 (*C* $_{t\text{Bu}}$), 31.2 (CH_3 $_{t\text{Bu}}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 2951 (w), 2864 (w), 2201 (m), 1500 (m), 1442 (w), 1397 (m), 1266 (w), 1215 (w), 1107 (w), 829 (m), 751 (s), 687 (s), 558 (m), 527 (m). **MS** (EI, 70 eV): m/z (%) = 691 (M^+, 100), 677 (7), 676 (12), 331 (11), 330 (14), 44 (13), 40 (49)**. HR-MS** (EI): m/z = calcd. for $C_{53}H_{41}N$ $[M]^+$: 691.32335; found: 691.32469. Anal. calcd. for $C_{53}H_{41}N$: C 92.00, H 5.97, N 2.02; found: C 92.12, H 5.81, N 2.16.

Procedure for the synthesis of 6-bromo-2-(trifluoromethyl)quinolin-4(1*H*)-one (19)

An oven-dried round-bottom flask (250 mL) was charged with polyphosphoric acid (0.8 g/mmol of aniline) and ethyl-4,4,4- trifluoroacetoacetate (1 equiv.; 23.25 mmol, 4.28 g). The mixture was warmed to 75 °C under stirring for 5 minutes. The agitated solution was charged with 4-bromoanilin (1 equiv.; 23.25 mmol, 4 g) and the reaction mixture was warmed to 150 °C under stirring for two hours. After the reaction mixture is cooled to room temperature, NaOH solution (10 %) was added which lead to precipitation of a white solid and more NaOH solution (10 %) was added until the solid was solved again. The solution was filtered and afterwards acidified with HCl solution (10 %) until the white solid precipitates again. The Precipitate was filtered off and dried.

6-bromo-2-(trifluoromethyl)quinolin-4(1*H*)-one (19):



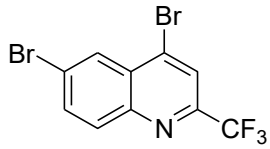
According to the procedure described above **19** was isolated as white solid; yield: 5.34 g (78 %); mp. 277 – 279 °C. **^{1}H-NMR** (300 MHz, DMSO-d_6): δ = 8.28 (d, 1H, ^4J = 2.46 Hz, $CH_{Ar/Hetar}$), 7.90 (brs, 2H, $CH_{Ar/Hetar}$), 7.06 (s, 1H, $CH_{Ar/Hetar}$), 3.92 (s, 1H, NH). **^{13}C-NMR** (75 MHz, DMSO-d_6): δ = 164.5 (C=O), 146.4 (q, ^2J = 34.66 Hz, *C*-CF_3), 145.4 (C_{Ar}), 134.5 ($CH_{Ar/Hetar}$), 129.6 ($CH_{Ar/Hetar}$), 124.7 ($CH_{Ar/Hetar}$), 123.2 (C_{Ar}), 121.2 (q, ^1J = 275.65 Hz, CF_3), 119.8 (C_{Ar}), 101.7(q, ^3J = 4.13 Hz, *C*H-C-CF_3); **^{19}F-NMR** (300 MHz, DMSO-d_6): δ = -66.62 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3253 (w), 3072 (m), 2956 (m), 1633 (w), 1554 (s), 1508 (s), 1468 (s), 1419 (m), 1356 (m), 1298 (s),

1279 (s), 1194 (s), 1192 (s), 1149 (s), 1134 (s), 1109 (s), 1092 (s), 1059 (m), 889 (m), 862 (s), 854 (s), 827 (s), 723 (s), 710 (m), 621 (m), 555 (s), 538 (s); **MS** (EI, 70 eV): m/z (%) = 291 (M^+, 100), 274 (6), 272 (7), 245 (13), 243 (19), 224 (16), 222 (24), 196 (8), 194 (9), 184 (18), 164 (10), 115 (11), 88 (17), 87 (13), 75 (15), 69 (27), 63 (19), 50 (10); **HR-MS** (ESI): m/z = calcd. for $C_{10}H_5BrF_3NO$ $[M+H]^+$: 291.95794, found 291.95858, calcd. for $C_{10}H_5{}^{81}BrF_3NO$ $[M+H]^+$: 293.95595 found: 293.9566,; Anal. calcd. for $C_{10}H_5BrF_3NO$: C 40.84, H 2.40, N 4.76; found: C 40.53, H 2.44, N 4.58.

Procedure for the synthesis of 4,6-dibromo-2-(trifluoromethyl)quinoline (20a)

An oven-dried round-bottom flask (250 mL) was charged with phosphorous oxybromide (1.1 equiv.; 4.994 mmol, 1.4306 g) and was warmed to 75 °C under stirring for 5 minutes. Afterwards, quinolinone **19** (1 equiv.; 4.543 mmol, 1.3260 g) was added in one portion and the mixture was warmed to 150 °C under stirring for 2.5 h. Afterwards, it was cooled the reaction mixture to room temperature, ice-water was added carefully and the mixture was made basic by addition of NaOH solution (10 %). The Solids were filtered off and dried.

4,6-dibromo-2-(trifluoromethyl)quinoline (20a):



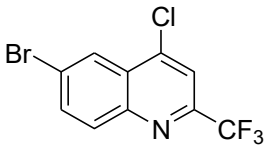
According to the procedure described above **20a** was isolated as yellow solid; yield: 1.282 g (80 %); mp. 123 – 124 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.44 (d, 1H, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 8.10 (d, 1H ^3J = 9.06 Hz, $CH_{Ar/Hetar}$), 8.04 (s, 1H, $CH_{Ar/Hetar}$), 7.95 (dd, 1H, ^3J = 9.06 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 147.9 (q, ^2J = 35.76 Hz, *C*-CF_3), 146.2 (C_{Ar}), 135.4 ($CH_{Ar/Hetar}$), 134.5 (C_{Ar}), 132.2 ($CH_{Ar/Hetar}$), 129.6 (C_{Ar}), 129.1 ($CH_{Ar/Hetar}$), 125.0 (q, ^1J = 274.89 Hz, CF_3), 124.8 (C_{Ar}), 121.8 (q, ^3J = 2.29 Hz, *C*H-C-CF_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.60 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3064 (w), 2980 (w), 1954 (w), 1603 (w), 1579 (w), 1450 (m), 1394 (w), 1335 (m), 1313 (m), 1257 (w), 1191 (m), 1140 (s), 1093 (s), 1065 (s), 885 (m), 874 (s), 870 (s), 825 (s), 768 (m), 706 (m), 681 (s), 594 (m), 530 (m); **MS** (EI, 70 eV): m/z (%) = 355 (M^+, 100), 353 (M^+, 54), 276 (12), 274 (12), 207 (14), 205 (14), 126 (12), 100 (30), 99 (28), 74 (18), 69 (10); **HR-MS** (ESI): m/z = calcd. for $C_{10}H_4NBr_2F_3$ $[M]^+$: 352.86571, found: 352.86595, calcd. for $C_{10}H_4NBr\,{}^{81}BrF_3$: 354.86366, found 354.86414, calcd. for

$C_{10}H_4N^{81}Br_2F_3$: 356.86162, found 356.86181; Anal. calcd. for $C_{10}H_4NBr_2F_3$: C 33.84 , H 1.14, N 3.95; found: C 34.10, H 0.95, N 4.04.

Procedure for the synthesis of 6-bromo-4-chloro-2-(trifluoromethyl)quinoline (20b)

An oven-dried round-bottom flask (250 mL) was charged with phosphorous oxychloride (1.1 equiv.; 67.639 mmol, 6.19 mL) and warmed to 75 °C under stirring for 5 minutes. Afterwards, quinolinone **19** (1 equiv.; 61.49 mmol, 17.959 g) was added in one portion and the mixture was warmed to 100 °C under stirring for 8 h. Afterwards, the mixture was cooled to room temperature, ice-water was added carefully and the mixture was made basic by addition of NaOH solution (10 %). The Solids were filtered off and dried.

6-bromo-4-chloro-2-(trifluoromethyl)quinoline (20b):

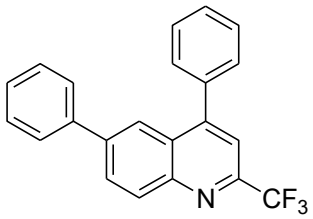


According to the procedure described above **20b** was isolated as yellow solid; yield: 12.8 g (65 %); mp. 97 – 98 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.46 (d, 1H, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 8.11 (d, 1H, ^3J = 8.88 Hz, $CH_{Ar/Hetar}$), 7.95 (dd, 1H, ^3J = 8.88 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.85 (s, 1H, $CH_{Ar/Hetar}$). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 148.0 (q, ^2J = 35.5 Hz, *C*-CF_3), 146.5 (C_{Ar}), 143.5 (C_{Ar}), 135.4 ($CH_{Ar/Hetar}$), 132.1 ($CH_{Ar/Hetar}$), 128.1 (C_{Ar}), 126.5 ($CH_{Ar/Hetar}$), 124.5 (C_{Ar}), 120.8 (q, ^1J = 275.38 Hz, CF_3), 118.0 (q, ^3J = 2.20 Hz, *C*H-C-CF_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.71 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3061 (w), 2980 (w), 1741 (w), 1605 (w), 1578 (w), 1452 (m), 1398 (w), 1340 (m), 1308 (w), 1257 (w), 1191 (m), 1138 (s), 1093 (s), 1066 (m), 987 (m), 887 (m), 876 (m), 870 (s), 837 (s), 775 (m), 694 (s), 617 (m), 598 (m), 530 (m); **MS** (EI, 70 eV): m/z (%) = 311 (M^+, 100), 310 (9), 309 (M^+, 83), 242 (25), 240 (19), 230 (13), 180 (11), 13 (7), 161 (22), 126 (7), 100 (12), 99 (21), 74 (11); **HR-MS** (EI): m/z = calcd. for $C_{10}H_4NBrClF_3$ $[M]^+$: 308.91623; found: 308.91614; calcd. for $C_{10}H_4N^{18}BrClF_3$: 310.91418; found 310.91411; calcd. for $C_{10}H_4N$ $^{81}Br^{37}ClF_3$ 312.91123; found 312.91158; Anal. calcd. for $C_{10}H_4NBrClF_3$: C 38.68, H 1.30, N 4.51; found: C 38.98, H1.10, N 4.60.

General procedure for the synthesis of compounds 21a–k

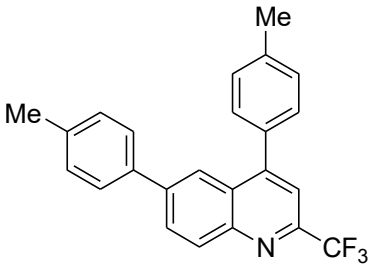
An oven-dried, argon-flushed sealable glass tube was charged with 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg), Palladium (II) acetate (5 mol%, 5.6 mg), Tricyclohexylphosphine (10 mol%, 14.2 mg), the appropriate boronic acid (1.3 mmol) and K_3PO_4 (1.3 mmol, 276.0 mg) followed by anhydrous toluene (4.0 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 8 h. The cooled reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography (heptane/dichlormethan).

2-(trifluoromethyl)-4,6-diphenylquinoline (21a):



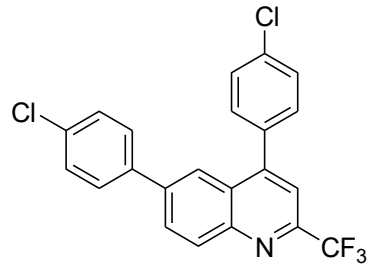
21a was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and phenylboronic acid (1.3 mmol, 158.5 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 136 mg (78 %); mp. 164 - 165 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.38 (d, 1H, ^3J = 8.7 Hz, $CH_{Ar/Hetar}$), 8.18 (d, 1H, ^4J = 1.9 Hz, $CH_{Ar/Hetar}$), 8.10 (dd, 1H, ^3J = 8.8, ^4J = 2.0 Hz, $CH_{Ar/Hetar}$), 7.72 (s, 1H, $CH_{Ar/Hetar}$), 7.55 - 7.66 (m, 7H, $7CH_{Ar}$), 7.37-7.52 (m, 3H, $3CH_{Ar}$). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 150.9 ($C_{Ar/Hetar}$), 147.3(q, ^2J = 34.4 Hz, *C*-CF_3), 147.2 (C_{Ar}), 141.4 (C_{Ar}), 139.9 (C_{Ar}), 137.1 (C_{Ar}), 130.9 (CH), 130.4 (CH), 129.5 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.1 (CH), 127.6 (C_{Ar}), 127.5 (CH), 121.7 (q, ^1J = 275.4 Hz, CF_3), 123.4 (CH), 117.4 (q, ^3J = 2.2 Hz, *C*H-C-CF_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): -67.40 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3062 (w), 2849 (w), 1620 (w), 1576 (w), 1464 (m), 1444 (w), 1389 (m), 1367 (m), 1311 (w), 1279 (w), 1261 (s), 1184 (s), 1176 (s), 1130 (s), 1092 (s), 1020 (m), 885 (s), 758 (s), 712 (s), 696 (s), 623 (s), 600 (m), 582 (m), 528 (m); **MS** (EI, 70 eV): m/z (%) = 349 (M^+, 100), 348 (18), 328 (10), 278 (9), 252 (10), 202 (8), 77 (6); **HR-MS** (EI): m/z = calcd for $C_{22}H_{14}NF_3$ $[M]^+$: 349.10729; found: 349.10652; Anal. calcd. for $C_{22}H_{14}NF_3$: C 75.64, H 4.04, N 4.01; found: C 75.87, H 4.10, N 3.62.

2-(trifluoromethyl)-4,6-di-*p*-tolylquinoline (21b):



21b was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 4-methylphenylboronic acid (1.3 mmol, 176.7 mg) and was purified via column chromatography (heptane/dichloromethane). Yellow solid; yield: 163 mg (86 %); mp. 126 – 127 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.36 (d,1H, ^{3}J = 8.7 Hz, $CH_{Ar/Hetar}$), 8.20 (d, 1H, ^{4}J = 1.9 Hz, $CH_{Ar/Hetar}$), 8.09 (dd, 1H, ^{3}J = 8.7, ^{4}J = 2.0 Hz, $CH_{Ar/Hetar}$), 7.70 (s, 1H, $CH_{Ar/Hetar}$), 7.54 (d, 2H, ^{3}J = 8.1 Hz, $2CH_{Ar}$), 7.49 (d, 2H, ^{3}J = 8.1 Hz, $2CH_{Ar}$), 7.40 (d, 2H, ^{3}J = 7.8 Hz, $2CH_{Ar}$), 7.29 (d, 2H, ^{3}J = 7.9 Hz, $2CH_{Ar}$), 2.51 (s, 3H, CH_3), 2.42 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 150.9 ($C_{Ar/Hetar}$), 147.2 (q, ^{2}J = 34.4 Hz, *C*-CF_3), 147.08 (C_{Ar}), 141.2 (C_{Ar}), 139.1 (C_{Ar}), 138.0 (C_{Ar}), 137.1 (C_{Ar}), 134.3 (C_{Ar}), 130.8 (CH), 130.2 (CH), 129.7 (CH), 129.6 (CH), 129.4 (CH), 127.7 (C_{Ar}), 127.3 (CH), 123.1(CH), 121.7 (q, ^{1}J = 275.4 Hz, CF_3), 117.3 (q, ^{3}J = 2.2 Hz, *C*H-C-CF_3), 21.3 (CH_3), 21.1 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = - 67.40 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3034 (w), 2920 (w), 2854 (w), 1612 (w), 1570 (w), 1460 (m), 1362 (m), 1311 (w), 1279 (m), 1259 (s), 1213 (w), 1178 (s), 1126 (s), 1093 (s), 1018 (m), 968 (m), 895 (s), 883 (s), 852 (m), 812 (s), 791 (s), 725 (s), 698 (s), 677 (m), 608 (m), 581 (m), 559 (m), 544 (m); **MS** (EI, 70 eV): m/z (%) = 377 (M^+, 100), 362 (7), 91 (5)**; HR-MS** (EI): m/z = calcd. for $C_{24}H_{18}NF_3$ $[M]^+$: 377.13859; found: 377.13836; Anal. calcd. for $C_{24}H_{18}NF_3$: C 76.38, H 4.81, N 3.71; found: C 76.50, H 4.68, N 3.46.

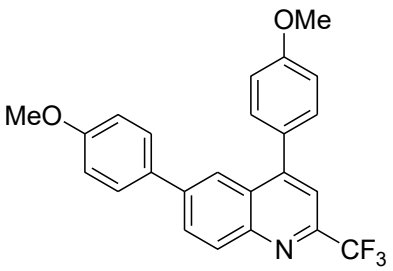
4,6-bis(4-chlorophenyl-2-(trifluoromethyl)quinoline (21c):



21c was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 4-chlorophenylboronic acid (1.3 mmol, 203.3 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 74.0 mg (35 %); mp. 172 - 173 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.38 (d, 1H, ^{3}J = 9.4 Hz, $CH_{Ar/Hetar}$), 8.06 (m, 2H, $CH_{Ar/Hetar}$), 7.68 (s, 1H, $CH_{Ar/Hetar}$), 7.61 - 7.43 (m, 8H, $8CH_{Ar}$). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 149.6 ($C_{Ar/Hetar}$), 147.6 (q,

^{2}J = 34.9 Hz, *C*-CF_3), 147.2 (C_{Ar}), 140.4 (C_{Ar}), 135.5 (C_{Ar}), 135.4 (C_{Ar}), 134.5 (C_{Ar}), 131.3 (CH), 130.8 (CH), 130.2 (CH), 129.3 (CH), 129.0 ($_{CAr}$), 128.7 (CH), 128.2 (CH), 127.4 (C_{Ar}), 122.9 (CH), 121.5 (q, ^{1}J = 275.4 Hz, CF_3), 117.5 (q, ^{3}J = 3.3 Hz, *C*H-C-CF_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.46 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 2850 (w), 1630 (w), 1593 (w), 1568 (w), 1458 (m), 1387 (m), 1360 (m), 1304 (w), 1259 (s), 1188 (m), 1176 (s), 1136 (s), 1088 (s), 1012 (s), 969 (m), 893 (m), 822 (s), 793 (s), 694 (m), 631 (m), 606 (m), 534 (m); **MS** (EI, 70 eV): m/z (%) = 417 (M^+, 100), 382 (5), 362 (6), 346 (8), 327 (8), 277 (14)**; HR-MS** (EI): m/z = calcd for $C_{22}H_{12}NCl_2F_3$ $[M]^+$: 417.02934, found: 417.02832, calcd for $C_{22}H_{12}NCl$ $^{37}ClF_3$ $[M]^+$: 419.02639; found: 419.02608; Anal. calcd. for $C_{22}H_{12}NCl_2F_3$: C 63.18, H 2.89, N 3.35; found: C 63.07, H 2.87, N 3.14.

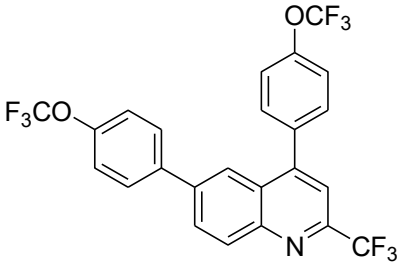
2-(trifluoromethyl)-4,6-bis(4-methoxyphenyl)quinoline (21d):



21d was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 4-methoxyphenylboronic acid (1.3 mmol, 197.5 mg) and was purified via column chromatography (heptane/dichloromethane). Yellow solid; yield: 121.0 mg (59 %); mp. 107 - 108 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.33 (d, 1H, ^{3}J = 8.9 Hz, $CH_{Ar/Hetar}$), 8.17 (d, 1H, ^{4}J = 1.9 Hz, $CH_{Ar/Hetar}$), 8.06 (dd, 1H, ^{3}J = 8.9 Hz, ^{4}J = 2.1 Hz, $CH_{Ar/Hetar}$), 7.67 (s, 1H, $CH_{Ar/Hetar}$), 7.58 (d, 2H, ^{3}J = 8.9 Hz, $2CH_{Ar}$), 7.53 (d, 2H, ^{3}J = 8.9 Hz, CH_{Ar}), 7.12 (d, 2H, ^{3}J = 8.9 Hz, $2CH_{Ar}$), 7.01 (d, 2H, ^{3}J = 8.9 Hz, $2CH_{Ar}$), 3.93 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 160.3 (*C*-OCH_3), 159.8 (*C*-OCH_3), 150.4 ($C_{Ar/Hetar}$), 147.0 (q, ^{2}J = 34.4 Hz, *C*-CF_3), 146.9 (C_{Ar}), 140.73 (C_{Ar}), 132.4 (C_{Ar}), 130.8 (CH), 130.8 (CH), 129.9 (CH), 129.5 (C_{Ar}), 128.6 (CH), 127.8 (C_{Ar}), 121.7 (q, ^{1}J = 275.4 Hz, CF_3), 122.6 (CH), 117.2 (q, ^{3}J = 1.7 Hz, *C*H-C-CF_3), 114.5 (CH), 114.4 (CH), 55.4 (O*C*H_3), 55.4 (O*C*H_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.39 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 2933 (w), 2841(w), 1608 (m), 1574 (m), 1516 (m), 1458 (m), 1385 (w), 1327 (w), 1290 (m), 1250 (s), 1174 (s), 1119 (s), 1095 (s), 1026 (s), 980 (w), 891 (m), 824 (s), 814 (s), 787 (m), 768 (w), 698 (m), 631 (w), 609 (w), 555 (m); **MS** (EI, 70 eV): m/z (%) = 409 (M^+, 100), 394 (19); **HR-MS** (EI): m/z = calcd for

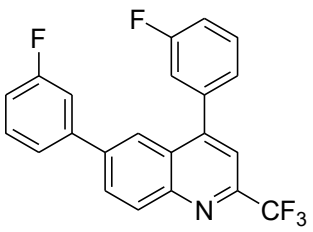
$C_{24}H_{18}O_2NF_3$ $[M]^+$: 409.12841; found: 409.12942; Anal. calcd. for $C_{24}H_{18}O_2NF_3$: C 70.41, H 4.43, N 3.42; found: C 70.39, H 4.48, N 3.22.

2-(trifluoromethyl)-4,6-bis(4-(trifluoromethoxy)phenyl)quinolone (21e):



21e was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 4-(trifluoromethoxy)phenylboronic acid (1.3 mmol, 267.7 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 200.0 mg (77 %); mp. 135 - 136 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): 8.40 (d, 1H, ^3J = 9.25 Hz, $CH_{Ar/Hetar}$), 8.07 (m, 2H, $2CH_{Ar/Hetar}$), 7.71 (s,1H, $CH_{Ar/Hetar}$), 7.64 (m, 4H, $4CH_{Ar}$), 7.47 (d, 2H, ^3J = 7.9 Hz, $2CH_{Ar}$), 7.35 (d, 2H, ^3J = 7.9 Hz, $2CH_{Ar}$). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 149.9 (q, ^3J = 1.9 Hz, *C*-OCF_3), 149.5 ($C_{Ar/Hetar}$), 149.4 (q, ^3J = 1.9 Hz, *C*-OCF_3), 147.7 (q, ^2J = 34.7 Hz, *C*-CF_3), 147.2 (C_{Ar}), 140.4 (C_{Ar}), 138.5 (C_{Ar}), 135.5 (C_{Ar}), 131.4 (CH), 131.0(CH), 130.3 (CH), 128.9 (CH), 127.4 (C_{Ar}), 123.1 (CH), 121.5 (CH), 121.5 (q, ^1J = 275.4 Hz, CF_3), 121.4 (CH), 120.5 (q, ^1J = 258.3 Hz, $2OCF_3$), 117.7 (q, ^3J = 1.7 Hz, *C*H-C-CF_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.51 ($ArCF_3$); -57.82 ($ArCF_3$); -57.69 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3086 (w), 2924 (w), 1608 (w), 1581 (w), 1514 (w), 1497 (m), 1462 (w), 1389 (w), 1319 (w), 1281 (m), 1254 (s), 1211 (s), 1180 (s), 1149 (s), 1130 (s), 1093 (s), 1016 (m), 981 (m), 947 (m), 893 (m), 829 (s), 810 (m), 791 (m), 685 (m), 631 (m), 606 (m), 559 (m), 543 (m); **MS** (EI, 70 eV): m/z (%) = 517 (M^+, 100), 448 (5), 432 (6), 69 (28); **HR-MS** (EI): m/z = calcd. for $C_{24}H_{12}O_2NF_9$ $[M]^+$: 517.07188; found: 517.07260; Anal. calcd. for $C_{24}H_{12}O_2NF_9$: C 55.72, H 2.34, N 2.71; found: C 56.08, H 2.31, N 2.59.

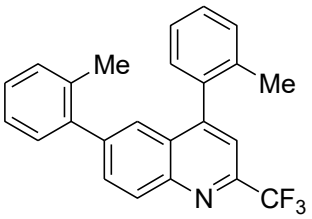
2-(trifluoromethyl)-4,6-bis(3-fluorophenyl)quinoline (21g):



21g was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 3-fluorophenylboronic acid (1.3 mmol, 181.9 mg) and was purified via column chromatography (heptane/dichloromethane).White solid; yield: 91.0 mg (47 %); mp. 109 – 110 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.40 (dd, 1H, ^3J = 8.31 Hz,

^4J = 1.13 Hz $CH_{Ar/Hetar}$), 8.09 (m, 2H, $CH_{Ar/Hetar}$), 7.72 (s, 1H, $CH_{Ar/Hetar}$), 7.60 (m, 1H, CH_{Ar}), 7.50–7.26 (m, 6 H, 6CH_{Ar}), 7.11 (m, 1 H, CH_{Ar}). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 164.7 (d, ^1J = 246.5 Hz, C_{Ar}), 161.6 (d, ^1J = 248.1 Hz, C_{Ar}), 149.6 ($C_{Ar/Hetar}$), 147.6 (q, ^2J = 34.7 Hz, *C*-CF_3), 147.3 (C_{Ar}), 142.1 (d, ^3J = 7.70 Hz, C_{Ar}), 140.4 (C_{Ar}), 139.02 (d, ^3J = 7.70 Hz, C_{Ar}), 131.3 (CH), 130.7 (d, ^3J = 4.95 Hz, C_{Ar}), 130.6 (d, ^3J = 4.95 Hz, C_{Ar}), 130.3 (CH), 127.3 (C_{Ar}), 125.2 (d, ^4J = 3.30 Hz, C_{Ar}), 123.3 (CH), 123.2 (d, ^4J = 3.30 Hz, C_{Ar}), 121.5 (q, ^1J = 275.4 Hz, CF_3), 117.6 (q, ^3J = 1.93 Hz, *C*H-C-CF_3), 116.6 (d, ^2J = 22.56 Hz, C_{Ar}), 116.2 (d, ^2J = 21.46 Hz, C_{Ar}), 115.1 (d, ^2J = 21.46 Hz, C_{Ar}), 114.5 d, ^2J = 22.01 Hz, C_{Ar}); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -112.24 (ArF); -111.52 (ArF); - 67.49 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 2924 (w), 2852 (w), 1614 (w), 1506 (m), 1470 (m), 1441 (m), 1383 (m), 1323 (m), 1279 (m), 1267 (s), 1180 (s), 1163 (s), 1136 (s), 1120 (s), 1093 (s), 997 (m), 970 (w), 910 (m), 885 (m), 835 (m), 798 (s), 783 (s), 768 (m), 712 (s), 673 (s), 611 (m), 538 (w); **MS** (EI, 70 eV): m/z (%) = 385 (M^+, 100), 364 (12), 316 (6), 314 (6), 220 (6); **HR-MS** (EI): m/z = calcd. for $C_{22}H_{12}NF_5$ $[M]^+$: 385.08844; found: 385.08814; Anal. calcd. for $C_{22}H_{12}NF_5$: C 68.57, H 3.14, N 3.63; found: C 68.56, H 3.042, N 3.24.

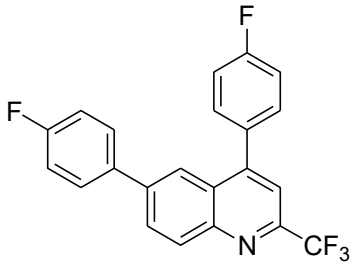
2-(trifluoromethyl)-4,6-di*o*-tolylquinoline (21h):



21h was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 2-methylphenylboronic acid (1.3 mmol, 176.7 mg) and was purified via column chromatography (heptane/dichloromethane).White solid; yield: 138.0 mg (73 %); mp. 153 - 154 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.25 (d, 1H, ^3J = 8.7 Hz, $CH_{Ar/Hetar}$), 7.72 (dd, 1H, ^3J = 8.67 Hz, ^4J = 1.89 Hz, $CH_{Ar/Hetar}$), 7.55 (s, 1H, $CH_{Ar/Hetar}$), 7.40 (d, 1H, ^4J = 1.9 Hz, $CH_{Ar/Hetar}$), 7.32 - 7.11 (m, 8H, 8CH_{Ar}), 2.13 (s, 3H, CH_3), 1.98 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 151.0 ($C_{Ar/Hetar}$), 147.5 (q, ^2J = 34.4 Hz, *C*-CF_3), 146.5 (C_{Ar}), 142.4 (C_{Ar}), 140.6 (C_{Ar}), 136.5 (C_{Ar}), 135.8 (C_{Ar}), 135.4 (C_{Ar}), 132.6 (CH), 130.5 (CH), 130.4 (CH), 130.1 (CH), 129.8 (CH), 129.4 (CH), 128.9 (CH), 127.9 (CH), 127.8 (C_{Ar}), 121.7 (q, ^1J = 275.4 Hz, CF_3), 125.9 (CH), 125.7 (CH), 117.5 (q, ^3J = 1.7 Hz, *C*H-C-CF_3), 20.4 (CH_3), 19.9 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.35 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2924 (w), 2864 (w), 1610 (w), 1572 (w), 1454 (w), 1367 (w), 1319 (w), 1288 (w), 1259 (m), 1227 (w), 1182 (s),

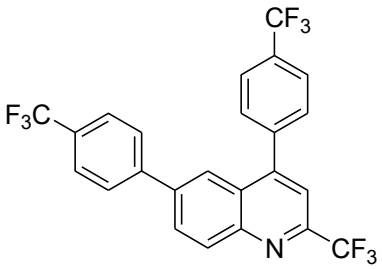
1146 (s), 1134 (s), 1090 (s), 1024 (w), 899 (m), 841 (m), 791 (w), 731 (m), 725 (m), 690 (m), 608 (m), 555 (w); **MS** (EI, 70 eV): m/z (%) = 377 (M^+, 100), 376 (45), 362 (18), 308 (8), 286 (5), 284 (7), 216 (5), 91 (6); **HR-MS** (EI): m/z = calcd. for $C_{24}H_{18}NF_3$ $[M]^+$: 377.13859; found: 377.13809; Anal. calcd. for $C_{24}H_{18}NF_3$: C 76.38, H 4.81, N 3.71; found: C 76.14, H 4.79, N 3.64.

2-(trifluoromethyl)-4,6-bis(4-fluorophenyl)quinoline (21i):



21i was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 4-fluorophenylboronic acid (1.3 mmol, 181.9 mg) and was purified via column chromatography (heptane/dichloromethane).White solid; yield: 73.0 mg (38 %); mp. 173 – 174 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.26 (brd, 1H, ^3J = 9,4 Hz, $CH_{Ar/Hetar}$), 7.97 - 7.93 (m, 2H, $2CH_{Ar/Hetar}$), 7.58 (s, 1H, $CH_{Ar/Hetar}$), 7.48 (m, 4H, $4CH_{Ar}$); 7.23 - 7.16 (m, 2H, $2CH_{Ar}$), 7.10 - 7.03 (m, 2H, $2CH_{Ar}$). **^{13}C-NMR** ($CDCl_3$, 75, 46 MHz): δ = 163.3 (d, ^1J = 249.8 Hz, CF), 162.9 (d, ^1J = 248.14 Hz, CF), 149.8 ($C_{Ar/Hetar}$), 147.2 (q, ^2J = 34.4 Hz, C-CF_3), 147.1 (C_{Ar}), 140.6 (C_{Ar}), 135.9 (d, ^4J = 3.30 Hz, C_{Ar}), 133.0 (d, ^4J = 3.30 Hz, C_{Ar}), 131.3 (d, ^3J = 8.25 Hz 2(C_{Ar})), 131.2 (CH), 130.3 (CH), 129.2 (d, ^3J = 8.25 Hz, 2(C_{Ar})), 127.6 (C_{Ar}), 122.9 (CH), 121.6 (q, ^1J = 275.4 Hz, CF_3), 117.6 (q, ^3J = 1.7 Hz, *C*H-C-CF_3), 116.1 (d, ^2J = 22.01 Hz, 2 (C_{Ar})), 116.0 (d, ^2J = 21.46 Hz, 2 (C_{Ar})); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -113.88 (ArF); -111.83 (ArF), -67.45 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 2920 (w), 2850 (w), 1605 (m), 1512 (m), 1462 (m), 1387 (m), 1325 (w), 1261 (m), 1221 (s), 1178 (m), 1170 (m), 1159 (s), 1130 (s), 1095 (s), 982 (m), 960 (w), 895 (m), 847 (m), 825 (s), 820 (s), 806 (s), 789 (m), 775 (m), 698 (m), 677 (m), 606 (m), 557 (s), 551 (s); **MS** (EI, 70 eV): m/z (%) = 385 (M^+, 100), 364 (10), 314 (7), 220 (5), 95 (2); **HR-MS** (EI): m/z = calcd for $C_{22}H_{12}NF_5$ $[M]^+$: 385.08844; found: 385.08803; Anal. calcd. for $C_{22}H_{12}NF_5$: C 68.57, H 3.14, N 3.63; found: C 68.71, H 3.09, N 3.44.

2-(trifluoromethyl)-4,6-bis(4-(trifluoromethyl)phenyl)quinoline (21j):



21j was synthesized according to general procedure using 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg) and 4-(trifluoromethyl)phenylboronic acid (1.3 mmol, 246.9 mg) and was purified via column chromatography (heptane/dichloromethane).White solid; yield: 214.0 mg (88 %); mp. 138 - 139 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.43 (d, 1H, ^{3}J = 8.9 Hz, $CH_{Ar/Hetar}$), 8.12 (dd, 1H, ^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $CH_{Ar/Hetar}$), 8.06 (d, 1H, ^{4}J = 1.70 Hz, $CH_{Ar/Hetar}$), 7.89 (s, 1H, $CH_{Ar/Hetar}$), 7.87 (s, 1H, CH_{Ar}), 7.77 - 7.70 (m, 7H, $7CH_{Ar}$). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 149.5 ($C_{Ar/Hetar}$), 147.9 (q, ^{2}J = 34.9 Hz, *C*-CF_3), 147.4 (C_{Ar}), 143.3 (C_{Ar}), 140.5 (C_{Ar}), 131.5 (q, ^{2}J = 32.74 Hz, C_{Ar}) 131.5 (C_{Ar}), 130.4 (q, ^{2}J = 32.74 Hz, C_{Ar}), 130.4 (CH), 129.9 (CH), 127.6 (q, ^{1}J = 272.35 Hz, C_{Ar}), 127.9(CH), 127.2 (C_{Ar}), 126.1 (CH), 126.1 (q, ^{3}J = 3.58 Hz, C_{Ar}), 126.0 (q, ^{3}J = 3.58 Hz, C_{Ar}), 123.5 (CH), 121.5 (q, ^{1}J = 275.4 Hz, CF_3), 120.4 (q, ^{1}J = 272.35 Hz, C_{Ar}), 117.7 (q, ^{3}J = 1.7 Hz, *C*H-C-CF_3), **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.53 ($ArCF_3$), -62.72 ($ArCF_3$), -62.64 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3062 (w), 2929 (w), 1620 (w), 1464 (w), 1406 (w), 1321 (s), 1165 (s), 1141 (s), 1126 (s), 1109 (s), 1093 (s), 1065 (s), 1016 (s), 845 (m), 827 (s), 775 (w), 652 (w), 617 (m), 584 (w), 530 (w); **MS** (EI, 70 eV): m/z (%) = 485 (M^+, 100), 466 (13), 416 (10), 396 (11), 346 (6), 69 (6); **HR-MS** (EI): m/z = calcd. for $C_{24}H_{12}NF_9$ $[M]^+$: 485.08205; found: 485.08163; Anal. calcd. for $C_{24}H_{12}NF_9$: C 59.39, H 2.49, N 2.89; found: C 59.95, H 2.73, N 2.69.

General procedure for the synthesis of compounds 22a-b (Regioisomeric Mixtures)

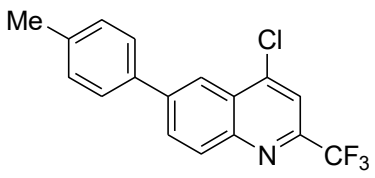
An oven-dried and argon-flushed pressure tube was charged with 2-trifluoromethyl-4,6-dibromoquinoline **20a** (0.5 mmol, 177.5 mg), Pd source (5 mol%), ligand (10 mol%), the appropriate boronic acid (1.0 equiv.; 0.5 mmol) and K_3PO_4 (2.6 equiv.; 1.3 mmol) followed by toluene (5.0 mL) or toluene/H_2O (4:1) ; The tube was sealed with a Teflon valve and the reaction mixture was stirred at 100 or 50 °C for 8 h. The cooled reaction mixture was diluted with water and extracted with DCM. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under vacuum. The residue was purified by column chromatography (heptane/dichlormethan). In all cases

were isolated inseparable mixtures of both 4- and 6-monoarylated isomers, in rtios of 8:1up 9:1, corroborated by ^{19}F-NMR and GC-MS analysis.

General procedure for the synthesis of compounds 23a-g

An oven-dried and argon-flushed pressure tube was charged with 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg), palladium(II) acetate (5 mol%, 5.6 mg), tricyclohexylphosphine (10 mol%, 14.2 mg), the appropriate boronic acid (1.2 equiv.; 0.6 mmol) and K_3PO_4 (2.6 equiv.; 1.3 mmol) followed by toluene (4.0 mL) and water (1 mL); The tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 8 h. The cooled reaction mixture was diluted with water and extracted with DCM. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under vacuum. The residue was purified by column chromatography (heptane/dichlormethan).

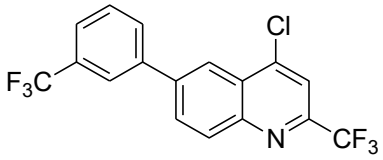
4-Chloro-2-(trifluoromethyl)-6-*p*-tolylquinoline (23a):



23a was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) and 4-methylphenylboronic acid (0.6 mmol, 81.6 mg) and was purified via column chromatography (heptane/dichloromethane).White solid; yield: (72 %) 116.0 mg); mp. 105 – 106 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.43 (d, 1H, ^4J = 1.89 Hz, $CH_{Ar/Hetar}$), 8.29 (d, 1H, ^3J = 8.69 Hz, $CH_{Ar/Hetar}$), 8.13 (dd, 1H, ^3J = 8.88 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.84 (s, 1H, $CH_{Ar/Hetar}$), 7.66 (d, 2H, ^3J = 8.12 Hz, CH_{Ar}), 7.35 (d, 2H, ^3J = 7.74 Hz, $2CH_{Ar}$), 2.46 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 147.2 (q, ^2J = 35.2 Hz, *C*-CF_3), 147.2 ($C_{Ar/Hetar}$), 144.4 (C_{Ar}), 142.4 (C_{Ar}), 138.6 (C_{Ar}), 136.4 (C_{Ar}), 131.3(CH), 130.9 (CH), 129.9 (CH), 127.4 (CH), 127.3 (C_{Ar}), 121.1 (CH), 121.1 (q, ^1J = 275.38 Hz, CF_3), 117.5 (q, ^3J = 2.20 Hz, *C*H-C-CF_3), 21.2 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.48 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3027 (w), 2922 (w), 1589 (w), 1570 (w), 1493 (m), 1462 (m), 1381 (w), 1348 (s), 1321 (m), 1250 (m), 1184 (s), 1173 (s), 1138 (s), 1115 (s), 1095 (s), 897 (m), 851 (s), 812 (s), 773 (m), 719 (w), 700 (s), 600 (m), 536 (m); **MS** (EI, 70 eV): m/z (%) = 321 (M^+, 100), 320 (31), 300 (8), 216 (7), 214 (8), 189 (10), 69 (18); **HR-MS** (EI): m/z = calcd. for $C_{17}H_{11}NClF_3$ $[M]^+$:

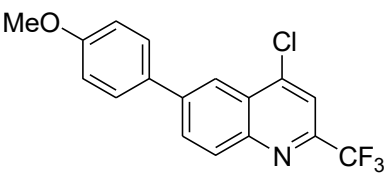
321.05266; found: 321.05217; calcd. for $C_{17}H_{11}N\,^{37}ClF_3$: 323.04971; found 323.04977; Anal. calcd. for $C_{17}H_{11}NClF_3$: C 63.46, H 3.45, N 4.35; found: C 63.86, H 3.33, N 4.28.

4-Chloro-2-(trifluoromethyl)-6-(3-(trifluoromethyl)phenylquinoline (23b):



23b was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) and 3-(trifluoromethyl)phenylboronic acid (0.6 mmol, 114.0 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 119.0 mg (63 %); mp. 130 – 131 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.48 (d, 1H, ^4J = 1.89 Hz, $CH_{Ar/Hetar}$), 8.36 (d, 1H, ^3J = 8.69 Hz, $CH_{Ar/Hetar}$), 8.13 (dd, 1H, ^3J = 8.88 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.79–7.88 (m, 5H, $CH_{Ar/Hetar,}$ $5CH_{Ar}$). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 147.6 ($C_{Ar/Hetar}$), 147.5 (q, ^2J = 35.1 Hz, *C*-CF_3), 144.8 ($C_{Ar/Hetar),}$ 142.9 ($C_{Ar/Hetar}$), 141.0 (C_{Ar}), 131.4 (CH), 131.1 (CH), 130.1 (q, ^2J = 32.96 Hz, C_{Ar}), 128.0 (CH), 127.3 (C_{Ar}), 126.1 (q, ^3J = 3.66 Hz, 2(C_{Ar})), 124.1 (q, ^1J = 276.95 Hz, C_{Ar}), 122.3 (CH), 120.9 (q, ^1J = 275.57 Hz, CF_3), 117.8 (q, ^3J = 2.29 Hz, *C*H-C-CF_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.62 ($ArCF_3$), -62.61 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3093 (w), 2935 (w), 1619 (w), 1583 (w), 1558 (w), 1462 (w), 1402 (w), 1335 (s) 1325 (s), 1252 (m), 1173 (s), 1147 (s), 1113 (s), 1093 (s), 1070 (s), 1012 (s), 951 (m), 897 (m), 847 (m), 820 (s), 770 (m), 739 (m), 694 (s), 625 (m), 592 (m), 536 (w); **MS** (EI, 70 eV): m/z (%) = 375 (M^+, 100), 356 (10), 371 (12), 201 (7), 69 (14); **HR-MS** (EI): m/z = calcd. for $C_{17}H_8NClF_6$ $[M]^+$: 375.02440; found: 375.02417; calcd. for $C_{17}H_8N^{37}ClF_6$: 377.02145; found 377.02160; Anal. calcd. for $C_{17}H_8NClF_6$: C 54.35, H 2.15, N 3.73; found: C 54.78, H 2.03, N 3.54.

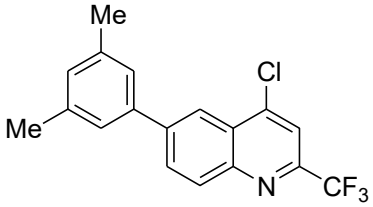
4-chloro-2-(trifluoromethyl)-6-(4-methoxyphenyl)quinoline (23c):



23c was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) and 4-methoxyphenylboronic acid (0.6 mmol, 91.2 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 111.0 mg (66 %); mp. 121 – 122 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.38 (d, 1H, ^4J = 1.89 Hz, $CH_{Ar/Hetar}$), 8.27 (d, 1H, ^3J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.11 (dd, 1H,

^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.83 (s, 1H, $CH_{Ar/Hetar}$), 7.73 - 7.80 (m, 2H, $2CH_{Ar}$), 7.09-7.04 (m, 2H, $2CH_{Ar}$), 3.90 (s, 3H, OCH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 160.2 (*C*OCH_3), 147.0 (q, ^{2}J = 35.2 Hz, *C*-CF_3), 146.9 ($C_{Ar/Hetar}$), 144.3 ($C_{Ar/Hetar}$), 142.1 ($C_{Ar/Hetar}$), 131.7 (C_{Ar}), 131.2 (CH), 130.9 (CH), 128.7 (CH), 127.4 (C_{Ar}), 121.1 (q, ^{1}J = 275.38 Hz, CF_3), 120.6 (CH), 117.5 (q, ^{3}J = 2.20 Hz *C*H-C-CF_3), 114.6 (CH), 55.4 (OCH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.47 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3036 (w), 2960 (w), 2937 (w), 2841 (w), 1608 (m), 1520 (w), 1464 (m), 1417 (w), 1371 (w), 1358 (s), 1303 (w), 1247 (s), 1188 (s), 1173 (s), 1153 (s), 1115 (s), 1093 (s) 1039 (m), 1022 (s), 897 (m), 864 (s), 852 (s), 825 (s), 816 (s), 773 (m), 729 (w), 700 (s), 648 (m), 576 (m), 544 (m); **MS** (EI, 70 eV): m/z (%) = 337 (M^+, 100), 322 (30), 296 (11), 295 (7), 294 (38), 268 (8), 239 (7), 190 (8), 188 (7), 164 (8), 69 (13); **HR-MS** (EI): m/z = calcd. for $C_{17}H_{11}ONClF_3$ $[M]^+$: 337.04758; found: 337.04760; calcd. for $C_{17}H_{11}ON^{37}Cl_1F_3$: 339.04463; found 339.04487; Anal. calcd. for $C_{17}H_{11}ONClF_3$: C 60.46, H 3.28, N 4.15; found: C 60.73, H 3.27, N 4.00.

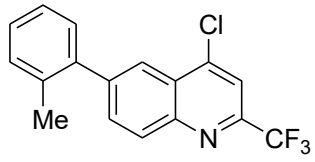
4-chloro-2-(trifluoromethyl)-6-(3,5-dimethylphenyl)quinoline (23d):



23d was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) and 3,5-dimethylphenylboronic acid (0.6 mmol, 90.0 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 98.0 mg (58 %); mp. 121 – 122 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.43 (d, 1H, ^{4}J = 1.89 Hz, $CH_{Ar/Hetar}$), 8.29 (d, 1H, ^{3}J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.13 (dd, 1H, ^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.85 (s, 1H, $CH_{Ar/Hetar}$), 7.36 (s, 2H, $2CH_{Ar}$), 7.11 (s, 1H), 2.45 (s, 6H, 2 CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 147.2 (q, ^{2}J = 35.2 Hz, *C*-CF_3), 147.2 ($C_{Ar/Hetar}$), 144.5 ($C_{Ar/Hetar}$), 142.8 ($C_{Ar/Hetar}$), 139.3 (C_{Ar}), 138.8 (C_{Ar}), 131.6 (CH), 130.8 (CH), 130.2 (CH), 127.3 (C_{Ar}), 121.1 (q, ^{1}J = 275.38 Hz, CF_3), 125.5 (CH), 121.4 (CH), 117.5 (q, ^{3}J = 2.20 Hz, *C*H-C-CF_3), 21.4 (2(CH_3)); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.49 $ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3091 (w), 2914 (w), 2859 (w), 1460 (m), 1348 (s), 1329 (m), 1306 (s), 1252 (m), 1184 (s), 1169 (s), 1132 (s), 1095 (s), 849 (s), 825 (s), 754 (m), 712 (w), 696 (s), 648 (m), 598 (m), 569 (m), 528 (m); **MS** (EI, 70 eV): m/z (%) = 335 (M^+, 100), 334 (13), 320 (20), 300 (10), 285 (6), 214 (11), 69 (13); **HR-MS** (EI): m/z = calcd. for $C_{18}H_{13}NClF_3$ $[M]^+$: 335.06831; found:

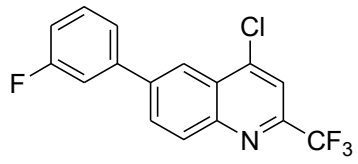
335. 06803; calcd for $C_{18}H_{13}N\,^{37}ClF_3$: 337.06536; found 337.06571; Anal. calcd. for $C_{18}H_{13}NClF_3$: C 64.39, H 3.90, N 4.17; found: C 64.53, H 3.94, N 4.03.

4-chloro-2-(trifluoromethyl)-6-*o*-tolylquinoline (23e):



23e was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) and 2-methylphenylboronic acid (0.6 mmol, 81.6 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 106.0 mg (66 %); mp. 98 – 99 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.31 (d, 1H, ^3J = 8.7 Hz, $CH_{Ar/Hetar}$), 8.26 (d, 1H, ^4J = 1.70 Hz, $CH_{Ar/Hetar}$), 7.90 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$); 7.87 (s, 1H, $CH_{Ar/Hetar}$), 7.39 – 7.33 (m, 4H, $4CH_{Ar}$), 2.34 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 147.6 (q, ^2J = 35.2 Hz, *C*-CF_3), 147.0 ($C_{Ar/Hetar}$), 144.54 ($C_{Ar/Hetar}$), 143.7 ($C_{Ar/Hetar}$), 140.2 (C_{Ar}), 135.4 (C_{Ar}), 133.6 (CH), 130.7 (CH), 130.2 (CH), 129.9 (CH), 28.3 (CH), 126.9 (C_{Ar}), 121.1 (q, ^1J = 275.38 Hz, CF_3), 126.2 (CH), 123.9 (CH), 117.5 (q, ^3J = 2.20 Hz, *C*H-C-CF_3), 20.5 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.51 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 3016 (w), 2976 (w), 1583 (w), 1572 (w), 1487 (m), 1460 (m), 1379 (w), 1344 (s), 1321 (m), 1250 (m), 1184 (s), 1171 (s), 1151 (s), 1126 (s), 1117 (s), 1093 (s), 895 (s), 862 (s), 847 (s), 814 (m), 754 (s), 723 (s), 696 (s), 685 (s), 654 (m), 611 (m), 554 (m), 532 (m); **MS** (EI, 70 eV): m/z (%) = 321 (M^+, 100), 320 (80), 306 (17), 302 (16), 300 (28), 286 (11), 285 (10), 266 (6), 265 (9), 216 (11), 214 (21), 189 (14), 69 (29); **HR-MS** (EI): m/z = calcd. for $C_{17}H_{11}NClF_3$ $[M]^+$: 321.05266; found: 321.05193; calcd for $C_{17}H_{11}N^{37}ClF_3$: 323.04971; found 323.04963; Anal. calcd. for $C_{17}H_{11}NClF_3$: C 63.46, H 3.45, N 4.35; found: C 63.54, H 3.41, N 4.13.

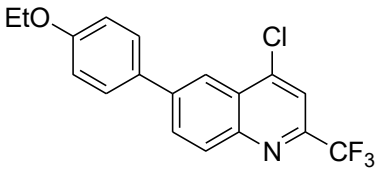
4-chloro-2-(trifluoromethyl)-6-(3-fluorophenyl)quinoline (23f):



23f was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) and 3-fluorophenylboronic acid (0.6 mmol, 84.0 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 90.0 mg (55 %); mp. 96 – 97 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.44 (d, 1H, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 8.32 (d, 1H, ^3J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.10 (dd, 1H, ^3J = 8.88 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$),

7.86 (s, 1H, $CH_{Ar/Hetar}$), 7.56 – 7.43 (m, 3H, $3CH_{Ar}$), 7.20 - 7.13 (m, 1H, CH_{Ar}). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 163.3 (d, ^1J = 247.04 Hz, C_{Ar}), 147.8 (q, ^2J = 35.2 Hz, *C*-CF_3), 147.5 ($C_{Ar/Hetar}$), 144.7 ($C_{Ar/Hetar}$), 141.6 (d, ^3J = 7.7 Hz, C_{Ar}), 141.2 (d, ^4J = 2.20 Hz, C_{Ar}), 140.1 (C_{Ar}), 131.2 (CH), 131.1 (CH), 130.7 (d, ^3J = 8.25 Hz, C_{Ar}), 127.3 (C_{Ar}), 120.9 (q, ^1J = 275.38 Hz, CF_3), 121.8 (CH), 117.7 (q, ^3J = 2.20 Hz, *C*H-C-CF_3), 115.4 (d, ^2J = 22.01 Hz, C_{Ar}), 114.6 (d, ^2J = 22.01 Hz, C_{Ar}); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.58 ($ArCF_3$), -112.06 (ArCF); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2926 (w), 2850 (w), 1606 (w), 1508 (m), 1470 (m), 1344 (s), 1311 (m), 1259 (m), 1190 (s), 1174 (s), 1153 (s), 1126 (s), 1093 (s), 974 (m), 964 (m), 893 (m), 860 (s), 835 (s), 783 (s), 771 (s), 698 (s), 685 (s), 650 (s), 581 (m), 527 (m); **MS** (EI, 70 eV): m/z (%) = 325 (M^+, 100), 221 (16), 194 (7), 69 (16); **HR-MS** (EI): m/z = calcd for $C_{16}H_8NClF_4$ $[M]^+$: 325.02759; found: 325.02749; calcd for $C_{16}H_8N\,^{37}ClF_4$: 327.02464; found 327.02498; Anal. calcd. for $C_{16}H_8NClF_4$: C 59.00, H 2.48, N 4.30; found: C 59.11, H 2.34, N 4.13.

4-chloro-6-(4-ethoxyphenyl)-2-(trifluoromethyl)quinoline (23g):



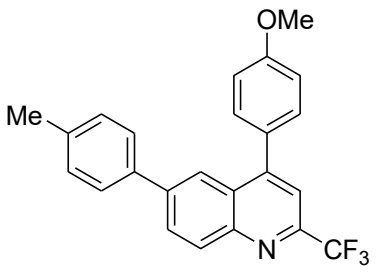
23g was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) and 4-ethoxyphenylboronic acid (0.6 mmol, 99.6 mg) and was purified via column chromatography (heptane/dichloromethane). White solid; yield: 107.0 mg (61 %); mp. 138 – 139 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.38 (d, 1H, ^4J = 1.70 Hz, $CH_{Ar/Hetar}$), 8.27 (d, 1H, ^3J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.11 (dd, 1H, ^3J = 8.88 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.83 (s, 1H, $CH_{Ar/Hetar}$), 8.70 (d, 2H, ^3J = 8.88 Hz, $2CH_{Ar}$), 7.06 (d, 2H, ^3J = 8.69 Hz, $2CH_{Ar}$), 4.13 (q, 2H, ^3J = 6.99 Hz, CH_2), 1.48 (t, 3H, ^3J = 6.99 Hz, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 159.6 (*C*-OC_2H_5), 147.0 (q, ^2J = 35.2 Hz, *C*-CF_3), 146.9 ($C_{Ar/Hetar}$), 144.3 ($C_{Ar/Hetar}$), 142.1 ($C_{Ar/Hetar}$), 131.5 (C_{Ar}), 131.2 (CH), 130.9 (CH), 128.7 (CH), 127.4 (C_{Ar}), 121.1 (q, ^1J = 275.38 Hz, CF_3), 120.5 (CH), 117.5 (q, ^3J = 2.20 Hz, *C*H-C-CF_3), 115.1 (CH), 63.6 (CH_2), 14.8 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.47 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2983 (w), 2929 (w), 2885 (w), 1606 (m), 1518 (w), 1462 (m), 1419 (w), 1394 (w), 1354 (s), 1325 (m), 1309 (w), 1244 (s), 1188 (m), 1182 (s), 1167 (s), 1140 (s), 1117 (s), 1097 (s), 1047 (s), 899 (m), 874 (s), 835 (s), 827 (s), 810 (s), 779 (m), 729 (m), 700 (s), 683 (s), 650 (m), 559 (m), 527 (m); **MS** (EI, 70 eV): m/z (%) = 351 (M^+, 57), 325 (33), 324 (23), 323 (100), 322

(14), 294 (12), 239 (7), 219 (8), 190 (9), 189 (6), 164 (7), 163 (7), 69 (7), 29 (28); **HR-MS** (EI): m/z = calcd. for $C_{18}H_{13}ONClF_3$ $[M]^+$: 351.06323; found: 351.06317; calcd for $C_{18}H_{13}ON\,^{37}Cl_1F_3$: 353.06028; found 353.06093; Anal. calcd. $C_{18}H_{13}ONClF_3$: C 61.46, H 3.73, N 3.98; found: C 61.57, H 3.74, N 3.76.

General procedure for the synthesis of compounds 24a–g

An oven-dried and argon-flushed pressure tube was charged with 6-bromo-4chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg), palladium(II) acetate (5 mol%, 5.6 mg), tricyclohexylphosphine (10 mol%, 14.2 mg), the corresponding 4-methylphenylboronic acid or 4-methoxyphenylboronic acid (1.2 equiv.; 0.6 mmol) and K_3PO_4 (2.6 equiv.; 1.3 mmol) followed by toluene (4.0 mL) and water (1 mL); The tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 8 h. Afterwards the appropriate second boronic acid (1.2 equiv.; 0.6 mmol) was added. The tube was sealed with a Teflon valve again and stirred at 100 °C for 8 h. The cooled reaction mixture was diluted with water and extracted with DCM. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under vacuum. The residue was purified by column chromatography (heptane/dichlormethan).

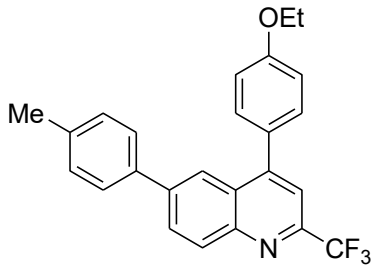
2-(trifluoromethyl)-4-(4-methoxyphenyl)-6-*p*-tolylquinoline (24a):



24a was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) with 4-methylphenylboronic acid (0.6 mmol, 81.6 mg) and later it was added 4-methoxyphenylboronic acid (0.6 mmol, 91.2 mg) as second boronic acid. The compound **24a** was purified via column chromatography (heptane/dichloromethane). White solid; yield: 121.0 mg (62 %); mp. 104 – 105 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.32 (d, 1H, ^3J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.18 (d, 1H, ^4J = 1.89 Hz, $CH_{Ar/Hetar}$), 8.05 (dd, 1H, ^3J = 8.88 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.65 (s, 1H, $CH_{Ar/Hetar}$), 7.49 - 7.53 (m, 4H, $4CH_{Ar}$), 7.26 (d, 2H, ^3J = 9.06 Hz, $2CH_{Ar}$), 7.06 - 7.10 (m, 2H, $2CH_{Ar}$), 3.90 (s, 3H, OCH_3), 2.39 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 160.3 (*C*-OCH_3), 150.6 ($C_{Ar/Hetar}$), 147.1 ($C_{Ar/Hetar}$), 147.0 (q, ^2J = 34.4 Hz, *C*-CF_3), 141.1 (C_{Ar}), 138.1 (C_{Ar}), 137.1 (C_{Ar}), 130.8 (CH), 130.2 (CH), 129.7 (CH), 129.5 (C_{Ar}), 127.8 (C_{Ar}), 127.3 (CH), 123.1 (CH), 121.7

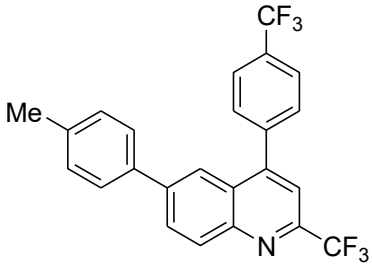
(q, ^{1}J = 275.10 Hz, CF_3), 117.2 (q, ^{3}J = 2.20 Hz, *C*H-C-CF_3), 114.4 (CH), 55.4 (OCH_3), 21.1 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.38 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3016 (w), 2947 (w), 2920 (w), 2843 (w), 1608 (m), 1514 (m), 1469 (m), 1387 (s), 1300 (m) 1265 (s), 1250 (s), 1174 (s), 1122 (s), 1093 (s), 1038 (s) 1028 (s), 893 (s), 835 (s), 814 (s), 787 (s), 721 (m), 698 (s), 642 (m), 608 (m), 571 (s), 554 (m), 527 (m); **MS** (EI, 70 eV): m/z (%) = 393 (M^+, 100), 378 (6), 91(4); **HR-MS** (EI): m/z = calcd. for $C_{24}H_{18}ONF_3$ $[M]^+$: 393.13350; found: 393.13322; Anal. calcd. for $C_{24}H_{18}ONF_3$: C 73.27, H 4.61, N 3.56; found: C 73.39, H 4.77, N 3.17.

4-(4-ethoxyphenyl)-2-(trifluoromethyl)-6-*p*-tolylquinoline (24b):



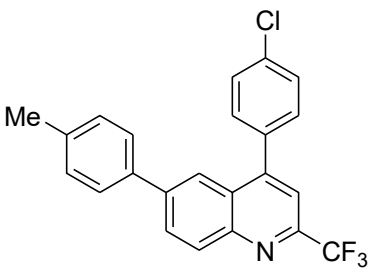
24b was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) with 4-methylphenylboronic acid (0.6 mmol, 81.6 mg) and later it was added 4-ethoxyphenylboronic acid (0.6 mmol, 99.6 mg) as second boronic acid. The compound **24b** was purified via column chromatography (heptane/dichloromethane). White solid; yield: 120.0 mg (59 %); mp. 92 – 93 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.24 (d, 1H, ^{3}J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.11 (d, 1H, ^{4}J = 1.51 Hz, $CH_{Ar/Hetar}$), 7.98 (dd, 1H, ^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.57 (s, 1H, $CH_{Ar/Hetar}$), 7.43 (m, 4H, $4CH_{Ar}$), 7.18 (d, 2H, ^{3}J = 8.12 Hz, $2CH_{Ar}$), 7.00 (d, 2H, ^{3}J = 8.50 Hz, $2CH_{Ar}$), 4.06 (q, 2H, ^{3}J = 6.99 Hz, CH_2), 2.32 (s, 3H, CH_3), 1.40 (t, 3H, ^{3}J = 6.99 Hz, OCH_2-*CH_3*). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 159.7 (*C*-OC_2H_5), 150.7 ($C_{Ar/Hetar}$), 147.2 (q, ^{2}J = 34.4 Hz, *C*-CF_3), 147.2 ($C_{Ar/Hetar}$), 141.1 (C_{Ar}), 138.1 (C_{Ar}), 137.1 (C_{Ar}), 130.8 (CH), 130.1 (CH), 129.7 (CH), 129.3 (C_{Ar}), 127.8 (C_{Ar}), 127.3 (CH), 123.1 (CH), 121.8 (q, ^{1}J = 275.39 Hz, CF_3), 117.2 (q, ^{3}J = 1.83 Hz, *C*H-C-CF_3), 114.9 (CH), 63.7 (CH_2), 21.1 (CH_3), 14.8(OCH_2-*CH_3*); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.40 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3031(w), 2980 (w), 2929 (w), 2899 (w), 1608 (m), 1514 (m), 1460 (m), 1385 (m), 1296 (m), 1261 (s), 1254 (s), 1176 (s), 1128 (s), 1117 (s), 1093 (s), 1039 (m), 1018 (m), 897 (m), 833 (s), 804 (s), 781 (s), 733 (m), 704 (m), 646 (w), 600 (s), 575 (m), 528 (m); **MS** (EI, 70 eV): m/z (%) = 407 (M^+, 100), 380 (14), 379 (56), 378 (18), 334 (5), 264 (5), 91 (5), 29 (20); **HR-MS** (EI): m/z = calcd. for $C_{25}H_{20}ONF_3$ $[M]^+$: 407.14915; found: 407.14909; Anal. calcd. for $C_{25}H_{20}ONF_3$: C 73.70, H 4.95, N 3.44; found : C 73.56, H 4.93, N 3.53.

2-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-6-*p*-tolylquinoline (24c):



24c was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) with 4-methylphenylboronic acid (0.6 mmol, 81.6 mg) and later it was added 4-(trifluoromethyl)phenylboronic acid (0.6 mmol, 114.0 mg) as second boronic acid. The compound **24c** was purified via column chromatography (heptane/dichloromethane). White solid; yield: 122.0 mg (57 %); mp. 139 – 140 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.38(d, 1H, ^{3}J = 8.7 Hz, $CH_{Ar/Hetar}$), 8.12 (dd, 1H, ^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $CH_{Ar/Hetar}$), 8.03 (d, 1H, ^{4}J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.87 (d, 2H, ^{3}J = 8.50 Hz, $2CH_{Ar}$), 7.69-7.72 (m, 3H, $3CH_{Ar}$), 7.52 (d, 2H, ^{3}J = 8.0 Hz, $2CH_{Ar}$), 7.30 (d, 2H, ^{3}J = 8.0 Hz, $2CH_{Ar}$), 2.42 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 149.1 ($C_{Ar/Hetar}$), 147.2 (q, ^{2}J = 34.4 Hz, *C*-CF_3), 147,0 ($C_{Ar/Hetar}$), 141.9 ($C_{Ar/Hetar}$), 140.8 (C_{Ar}), 138.4 (C_{Ar}), 136.8 (C_{Ar}), 131.7 (q, ^{2}J = 32.46 Hz, C_{Ar}), 131.0 (CH), 10.7 (CH), 129.9 (CH), 129.8 (CH), 127.4 (CH), 127.2 (C_{Ar}), 125.9 (q, ^{3}J = 3.58 Hz, C_{Ar}), 123.9 (q, ^{1}J = 272.35 Hz, C_{Ar}), 122.4 (CH), 121.6 (q, ^{1}J = 275.38 Hz, CF_3), 117.4 (q, ^{3}J = 2.20 Hz, *C*H-C-CF_3), 21.1 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.42 ($ArCF_3$), -62.67 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 3026 (w), 2920 (w), 2852 (w), 1618 (w), 1462 (m), 1406 (w), 1387 (m), 1363 (w), 1323 (s), 1263 (m), 1180 (s), 1157 (m), 1128 (s), 1119 (s), 1109 (s), 1093 (s), 1065 (s), 1016 (m), 847 (s), 837 (s), 816 (s), 783 (m), 766 (m), 710 (m), 677 (m), 652 (m), 617 (m), 596 (m), 552 (m), 540 (m); **MS** (EI, 70 eV): m/z (%) = 431 (M^+, 100), 430 (19), 412 (7), 91 (5), 69 (7); **HR-MS** (EI): m/z = calcd. for $C_{24}H_{15}NF_6$ $[M]^+$: 431.11032; found: 431.11042; Anal. calcd. for $C_{24}H_{15}NF_6$: C 66.82, H 3.50, N 3.25; found: C 66.60, H 3.24, N 3.68.

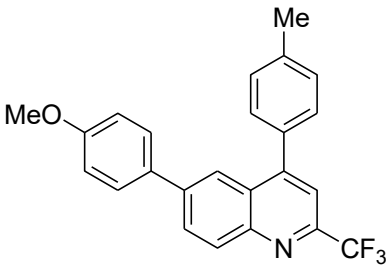
4-(4-chlorophenyl)-2-(trifluoromethyl)-6-*p*-tolylquinoline (24d):



24d was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) with 4-methylphenylboronic acid (0.6 mmol, 81.6 mg) and later it was added 4-chlorophenylboronic acid (0.6 mmol, 93.8 mg) as second

boronic acid. The compound **24d** was purified via column chromatography (heptane/dichloromethane). White solid; yield: 91.0 mg (46 %); mp. 156 – 157 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.36 (d, 1H, ^3J = 8.7 Hz, $CH_{Ar/Hetar}$), 8.08 - 8.12 (m, 2H, $2CH_{Ar/Hetar}$), 7.67 (s, 1H, $CH_{Ar/Hetar}$), 7.59 - 7.51 (m, 6H, $6CH_{Ar}$), 7.30 (d, 2H, ^3J = 8.12 Hz, $2CH_{Ar}$), 2.43 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 149.5 ($C_{Ar/Hetar}$), 147.2 (q, ^2J = 34.7 Hz, *C*-CF_3), 147.0 ($C_{Ar/Hetar}$), 141.6 (C_{Ar}), 138.3 (C_{Ar}), 136.9 (C_{Ar}), 135.6 (C_{Ar}), 135.4 (C_{Ar}), 130.9 (CH), 130.8 (CH), 1130.5 (CH), 129.8 (CH), 129.2 (CH), 127.4 (C_{Ar}), 127.3 (CH), 122.6 (CH), 121.6 (q, ^1J = 275.38 Hz, CF_3), 117.3 (q, ^3J = 2.20 Hz, *C*H-C-CF_3), 21.1 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.39 ($ArCF_3$); **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 3030 (w), 2920 (w), 1595 (m), 1570 (w), 1489 (m), 1460 (m), 1387 (m), 1325 (m), 1257 (m), 1182 (s), 1126 (s), 1088 (s), 895 (s), 831 (s), 816 (s), 779 (m), 729 (m), 667 (m), 606 (m), 540 (m); **MS** (EI, 70 eV): m/z (%) = 397 (M^+, 100), 396 (15), 91 (7), 69 (4); **HR-MS** (EI): m/z = calcd. for $C_{23}H_{15}NClF_3$ $[M]^+$: 397.08396; found: 397.08374; calcd. for $C_{23}H_{15}N^{37}ClF_3$: 399.08101; found 399.08155; Anal. calcd. for $C_{23}H_{15}NClF_3$: C 69.44, H 3.80, N 3.52; found: C 69.80, H 3.95, N 3.43.

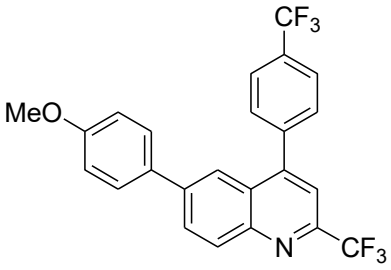
2-(trifluoromethyl)-6-(4-methoxyphenyl)-4-*p*-tolylquinoline (24e):



24e was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) with 4-methoxyphenylboronic acid (0.6 mmol, 91.2 mg) and later it was added 4-methylphenylboronic acid (0.6 mmol, 81.6 mg) as second boronic acid. The compound **24e** was purified via column chromatography (heptane/dichloromethane). White solid; yield: 90.0 mg (46 %); mp. 130 - 131 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.34 (d, 1H, ^3J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.16 (d, 1H, ^4J = 1.89 Hz, $CH_{Ar/Hetar}$); 8.06 (dd, 1H, ^3J = 8.88 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.68 (s, 1H, $CH_{Ar/Hetar}$), 7.58 (d, 2H, ^3J = 8.88 Hz, $2CH_{Ar}$), 7.49 (d, 2H, ^3J = 7.96 Hz, $2CH_{Ar}$), 7.40 (d, 2H, ^3J = 7.93 Hz, $2CH_{Ar}$), 7.01 (d, 2H, ^3J = 8.88 Hz, $2CH_{Ar}$), 3.87 (s, 3H, OCH_3), 2.50 (s, 3H, CH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 159.8 (*C*-OCH_3), 150.8 ($C_{Ar/Hetar}$), 147.0 (q, ^2J = 34.4 Hz, *C*-CF_3), 146.9 ($C_{Ar/Hetar}$), 140.8 (C_{Ar}), 139.1 (C_{Ar}), 134.0 (C_{Ar}), 132.4 (C_{Ar}), 130.8 (CH), 130.0 (CH), 129.6 (CH), 129.4 (CH), 128.5 (CH), 127.8 (C_{Ar}), 122.6

(CH), 121.7 (q, ^{1}J = 275.38 Hz, CF_3), 117.3 (q, ^{3}J = 2.20 Hz, *C*H-C-CF_3), 114.5 (CH), 55.4 (OCH_3), 21.3 (CH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.36 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3055 (w), 2997 (w), 2928 (w), 2839 (w), 1605 (s), 1524 (m), 1495 (s), 1460 (m), 1387 (m) 1327 (m), 1259 (s) 1248 (s), 1180 (s), 1120 (s), 1095 (s), 1039 (m), 1022 (m), 897 (m), 847 (m), 816 (s), 785 (m), 723 (m), 698 (m), 636 (m), 608 (m), 575 (m), 554 (m), 540 (m); **MS** (EI, 70 eV): m/z (%) = 394 (25), 393 (M^+, 100), 378 (20), 334 (4), 308 (3), 284 (5), 264 (5), 214 (2), 189 (2), 139 (2), 91(2), 69 (3), 65 (2), 39 (2); **HR-MS** (EI): m/z = calcd. for $C_{24}H_{18}ONF_3$ $[M]^+$: 393.13350; found: 393.13351; Anal. calcd. for $C_{24}H_{18}ONF_3$: C 73.27, H 4.61, N 3.56; found: C 73.62, H 4.73, N 3.61.

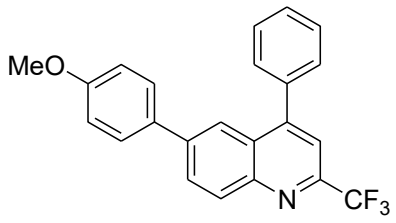
2-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-6-(4-methoxyphenyl)quinoline (24f):



24f was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) with 4-methoxyphenylboronic acid (0.6 mmol, 91.2 mg) and later it was added 4-(trifluoromethyl)phenylboronic acid (0.6 mmol, 114.0 mg) as second boronic acid. The compound **24f** was purified via column chromatography (heptane/dichloromethane). White solid; yield: 103.0 mg (46 %); mp. 127 – 128 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.36 (d, 1H, ^{3}J = 8.88 Hz, $CH_{Ar/Hetar}$), 8.10 (dd, 1H, ^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.99 (d, 1H, ^{4}J = 1.89 Hz, $CH_{Ar/Hetar}$), 7.87 (d, 2H, ^{3}J = 8.12 Hz, $2CH_{Ar}$), 7.72 (d, 2H, ^{3}J = 7.93 Hz, $2CH_{Ar}$), 7.68 (s, 1H, $CH_{Ar/Hetar}$), 7.57 (dd, 2H, ^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $2CH_{Ar}$); 7.02 (dd, 2H, ^{3}J = 8.88 Hz, ^{4}J = 2.08 Hz, $2CH_{Ar}$), 3.87 (s, 3H, OCH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 159.9 (*C*-OCH_3), 148.9 ($C_{Ar/Hetar}$), 147.0 (q, ^{2}J = 34.4 Hz, *C*-CF_3), 146.9 ($C_{Ar/Hetar}$), 141.5 ($C_{Ar/Hetar}$), 140.9 (C_{Ar}), 132.0 (C_{Ar}), 131.2 (q, ^{2}J = 33.01 Hz, C_{Ar}), 131.0 (CH), 130.5 (CH), 129.9 (CH), 128.6 (CH), 128.1 (q, ^{1}J = 272.35 Hz, C_{Ar}), 127.3 (C_{Ar}), 125.9 (q, ^{3}J = 3.85 Hz, C_{Ar}), 121.8 (CH), 121.6 (q, ^{1}J = 275.39 Hz, CF_3), 117.4 (q, ^{3}J = 1.65 Hz, *C*H-C-CF_3), 114.6 (CH), 55.4 (OCH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$): δ = -67.40 ($ArCF_3$), -62.65 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3001 (w), 2956 (w), 2835 (w), 1608 (m), 1587 (w), 1495 (s), 1464 (m), 1406 (w), 1323 (s), 1265 (m), 1171 (s), 1136 (s), 1111 (s), 1095 (s), 1065 (s), 1016 (m), 895 (m), 845 (m), 833 (s), 806 (s), 766 (m), 748 (m), 710 (s), 675 (m), 615 (s), 596 (m), 552 (m),

527 (m); **MS** (EI, 70 eV): m/z (%) = 447 (M^+, 100), 432 (20), 428 (7), 404 (6), 334 (9), 224 (5), 158 (5); **HR-MS** (EI): m/z = calcd. for $C_{24}H_{15}ONF_6$ $[M]^+$: 447.10523; found: 447.10491; Anal. calcd. for $C_{24}H_{15}ONF_6$: C 64.43, H 3.38, N 3.13; found: C 64.26, H 3.47, N 3.22.

2-(trifluoromethyl)-6-(4-methoxyphenyl)-4-phenylquinoline (24g):



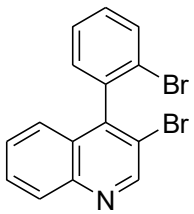
24g was synthesized according to general procedure using 6-bromo-4-chloro-2-(trifluoromethyl)quinoline **20b** (0.5 mmol, 155.3 mg) with 4-methoxyphenylboronic acid (0.6 mmol, 91.2 mg) and later it was added phenylboronic acid (0.6 mmol, 73.2 mg) as second boronic acid. The compound **24g** was purified via column chromatography (heptane/dichloromethane). White solid; yield: 106.0 mg (56 %); mp. 102 – 103 °C. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ = 8.35 (d, 1H, ^3J = 8.80 Hz, $CH_{Ar/Hetar}$); 8.12 (d, 1H, ^4J = 1.70 Hz, $CH_{Ar/Hetar}$); 8.07 (dd, 1H, ^3J = 8.69 Hz, ^4J = 2.08 Hz, $CH_{Ar/Hetar}$), 7.69 (s, 1H, $CH_{Ar/Hetar}$), 7.55 - 7.59 (m, 7H, $7CH_{Ar}$), 6.99 - 7.02 (m, 2H, $2CH_{Ar}$), 3.86 (s, 3H, OCH_3). **^{13}C-NMR** ($CDCl_3$, 75,46 MHz): δ = 159.8 (*C*-OCH_3), 150.7 ($C_{Ar/Hetar}$), 147.0 (q, ^2J = 34.4 Hz, *C*-CF_3), 146.9 ($C_{Ar/Hetar}$), 140.9 (C_{Ar}), 137.3 (C_{Ar}), 132.3 (C_{Ar}), 130.8 (CH), 130.1 (CH), 129.5 (CH), 129.0 (CH), 128.8 (CH), 128.6 (CH), 127.7 (C_{Ar}), 122.5 (CH), 121.7 (q, ^1J = 275.38 Hz, CF_3), 117.4 (q, ^3J = 1.65 Hz, *C*H-C-CF_3), 114.5 (CH), 55.4 (OCH_3); **^{19}F-NMR** (300 MHz, $CDCl_3$):δ = -67.36 ($ArCF_3$); **IR** (ATR, cm^{-1}): ṽ = 3039 (w), 2929 (w), 2833 (w), 1606 (m), 1500 (m), 1462 (m), 1365 (m), 1315 (w), 1240 (s), 1178 (s), 1165 (s), 1122 (s), 1117 (s), 1093 (s), 1039 (s), 1022 (m), 893 (m), 825 (s), 806 (s), 792 (m), 712 (s), 698 (s), 677 (m), 606 (m), 584 (m), 554 (m), 528 (m); **MS** (EI, 70 eV): m/z (%) = 379 (M^+, 100), 364 (25), 266 (8), 265 (5), 133 (7), 119 (6); **HR-MS** (EI): m/z = calcd. for $C_{23}H_{16}ONF_3$ $[M]^+$: 379.11785; found: 379.11721; Anal. calcd. for $C_{23}H_{16}ONF_3$: C 72.82, H 4.25, N 3.69; found: C 73.02, H 4.23, N 3.46.

3-bromo-4-iodoquinoline (25) was prepared according to a three-step procedure reported by Bogányi *et al*.[103]

Procedure for the synthesis of 3-bromo-4-(2-bromophenyl)quinoline (26)

An oven-dried, argon-flushed sealable glass tube was charged with 3-bromo-4-iodoquinoline **25** (0.3 mmol, 100 mg), $Pd(PPh_3)_4$ (5 mol%, 17.3 mg), 2-bromophenylboronic acid (0.42 mmol, 84.3 mg) and Na_2CO_3 (0.60 mmol, 63.5 mg) followed by a mixture of DMF/ water (10:1, 1.01 mL); The tube was sealed with a Teflon valve and stirred at 100 °C for 24 h. The cooled reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/ ethyl acetate as eluent.

3-bromo-4-(2-bromophenyl)quinoline (26):



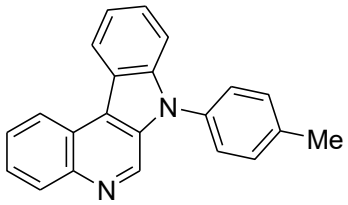
According to the procedure described above **26** was isolated as a white solid; yield: 66 mg (61 %); mp. 130 - 131 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.09 (s, 1H, CH_{Hetar}), 8.19 (d, ^3J = 8.50 Hz, 1H, $CH_{Ar/Hetar}$), 7.81 - 7.73 (m, 2H, $CH_{Ar/Hetar}$), 7.55 - 7.48 (m, 2H, $CH_{Ar/Hetar}$), 7.45 - 7.39 (m, 1H, CH_{Ar}), 7.33 (dd, ^3J = 8.50 Hz, ^4J = 0.76 Hz, 1H, CH_{Ar}), 7.25 (dd, ^3J = 7.55 Hz, ^4J = 1.70 Hz, 1H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 151.8 ($CH_{Ar/Hetar}$), 146.5 ($C_{Ar/Hetar}$), 146.5 ($C_{Ar/Hetar}$), 137.8 (C_{Ar}), 133.1 (CH_{Ar}), 130.7 (CH_{Ar}), 130.4 (CH_{Ar}), 129.7 (CH_{Ar}), 129.6 (CH_{Ar}), 128.2 ($C_{Ar/Hetar}$), 127.9 (CH_{Ar}), 127.7 (CH_{Ar}), 125.7 (CH_{Ar}), 122.9 (C_{Ar}), 118.8 ($C_{Ar/Hetar}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 1570 (m), 1467 (m), 1427 (m), 1104 (m), 1047 (m), 1025 (m), 918 (m), 759 (s), 728 (s) 709 (m), 604 (s), 595 (m). **MS** (EI, 70 eV): m/z (%) = 365 (M^+, 15), 363 (M^+, 30), 361 (M^+, 15), 284 (12), 282 (12), 204 (16), 203 (100), 202 (13), 176 (17), 175 (11). **HR-MS** (EI): m/z = calcd. for $C_{15}H_9Br_2N$ 360.90963 found: 360.90888; calcd. for $C_{15}H_9Br^{81}BrN$ 362.90758 found 362.90688 calcd. for $C_{15}H_9{}^{81}Br_2N$ 364.90553 found 364.90517.

General procedure for the Synthesis of tne compounds 27a-m

An oven-dried, argon-flushed sealable glass tube was charged with 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg), $Pd_2(dba)_3$ (5 mol%, 12.6 mg), *rac*-BINAP (10 mol%, 18.3 mg), the appropriate amine, (0.41 mmol) and KO*t*Bu (0.67 mmol, 74.2 mg) followed by toluene (3 mL). The tube was sealed with a Teflon valve and stirred at 100 °C for 24 h. The cooled reaction mixture was diluted with water

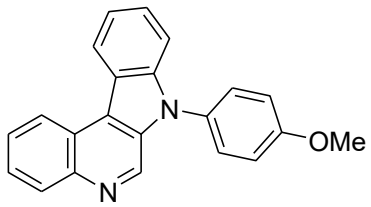
and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/ ethyl acetate as eluent.

7-*p*-tolyl-*7H*-indolo[2,3-*c*]quinoline (27a):



27a was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-methylaniline (0.41 mmol, 44.3 mg) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 80 mg (94 %); mp. 137 - 138 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.13 (s, 1H, CH_{Hetar}), 8.80 (dd, ^3J = 8.31 Hz, ^4J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 8.67 (d, ^3J = 7.93 Hz, 1H, $CH_{Ar/Hetar}$), 8.35 (dd, ^3J = 8.12 Hz, ^4J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 7.82 - 7.69 (m, 2H, $CH_{Ar/Hetar}$), 7.63 - 7.56 (m, 2H, CH_{Ar}), 7.52 - 7.46 (m, 5H, CH_{Ar}), 2.46 (s, 3H, CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 142.8 ($C_{Ar/Hetar}$), 141.1 ($C_{Ar/Hetar}$), 138.6 (C_{Ar}), 136.9 ($CH_{Ar/Hetar}$), 133.6 ($C_{Ar/Hetar}$), 133.6 (C_{Ar}), 130.8 ($2CH_{Ar}$), 130.0 ($CH_{Ar/Hetar}$), 127.4 ($CH_{Ar/Hetar}$), 127.3 ($CH_{Ar/Hetar}$), 127.2 ($2CH_{Ar}$), 126.0 ($CH_{Ar/Hetar}$), 124.6 ($C_{Ar/Hetar}$), 123.4 ($2CH_{Ar/Hetar}$), 122.1($C_{Ar/Hetar}$), 121.7 ($C_{Ar/Hetar}$), 121.4 ($CH_{Ar/Hetar}$),111.3 ($CH_{Ar/Hetar}$), 21.3 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3081 (w), 3035 (w), 2960 (w), 2918 (w), 2854 (w), 1606 (m), 1511 (s), 1454 (m), 1329 (s), 813 (m), 756 (s), 733 (s), 681 (m), 513 (m), 427 (s). **MS** (EI, 70 eV): m/z (%) = 309 (23), 308 (M^+, 100), 307 (19), 306 (6), 292 (6), 190 (6), 146 (6). **HR-MS** (EI): m/z = calcd. for $C_{22}H_{16}N_2$ 308.13080 found: 308.13063.

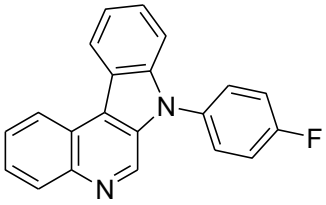
7-(4-methoxyphenyl)-*7H*-indolo[2,3-*c*]quinoline (27b):



27b was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-methoxyaniline (0.41 mmol, 50.9 mg) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 85 mg (95 %); mp 141 - 142 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.09 (s, 1H, CH_{Hetar}), 8.79 (dd, ^3J = 8.31Hz, ^4J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 8.66 (d, ^3J = 7.93 Hz, 1H, $CH_{Ar/Hetar}$), 8.34 (dd, ^3J = 8.50Hz, ^4J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 7.81 - 7.76 (m, 1H, $CH_{Ar/Hetar}$), 7.73 - 7.68 (m, 1H, $CH_{Ar/Hetar}$), 7.62 - 7.58 (m, 1H, $CH_{Ar/Hetar}$), 7.55 - 7.46 (m, 4H, CH_{Ar}),

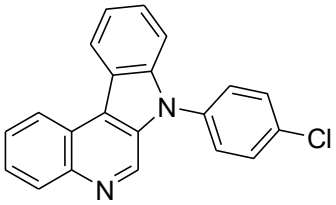
7.18 (d, ^{3}J = 9.06 Hz, 2H, CH_{Ar}), 3.96 (s, 3H, OCH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 159.6 (*C*-OCH_3), 142.9 ($C_{Ar/Hetar}$), 141.3 ($C_{Ar/Hetar}$), 137.0 ($CH_{Ar/Hetar}$), 133.8 ($C_{Ar/Hetar}$), 130.2 ($CH_{Ar/Hetar}$), 128.9 ($C_{Ar/Hetar}$), 128.7 ($2CH_{Ar}$), 127.3 ($CH_{Ar/Hetar}$), 127.2 ($CH_{Ar/Hetar}$), 125.9 ($CH_{Ar/Hetar}$), 124.6 (C_{Ar}), 123.3 ($CH_{Ar/Hetar}$), 123.3 ($CH_{Ar/Hetar}$), 122.0 ($C_{Ar/Hetar}$), 121.4 ($C_{Ar/Hetar}$), 121.2 ($CH_{Ar/Hetar}$), 115.3 ($2CH_{Ar}$), 111.2 ($CH_{Ar/Hetar}$), 55.7 (O*C*H_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3041 (w), 3002 (w), 2930 (w), 2835 (w), 1611 (m), 1510 (s), 1456 (m), 1239 (s), 1186 (m), 1031 (m), 821 (s), 757 (s), 735 (s), 427 (m). **MS** (EI, 70 eV): m/z (%) = 325 (24), 324 (M^+, 100), 309 (26), 280 (17), 279 (16), 140 (8). **HR-MS** (EI): m/z = calcd. for $C_{22}H_{16}ON_2$ 324.12571 found: 324.12608.

7-(4-fluorophenyl)-*7H*-indolo[2,3-*c*]quinoline (27c):



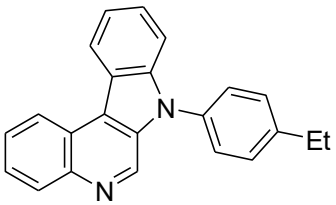
27c was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-fluoroaniline (0.41 mmol, 39.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 81 mg (95 %); mp. 119 - 120 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.09 (s, 1H, CH_{Hetar}), 8.79 (dd, ^{3}J = 8.12Hz, ^{4}J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 8.68 - 8.65 (m, 1H, $CH_{Ar/Hetar}$), 8.35 (dd, ^{3}J = 8.12Hz, ^{4}J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 7.82 - 7.69 (m, 2H, $CH_{Ar/Hetar}$), 7.64 - 7.57 (m, 3H, CH_{Ar}), 7.53 - 7.48 (m, 2H, CH_{Ar}), 7.42 - 7.34 (m, 2H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 162.3 (d, $^{1}J_{CF}$ = 249.24 Hz, *C*F), 143.1 ($C_{Ar/Hetar}$), 141.0 ($C_{Ar/Hetar}$), 136.6 ($CH_{Ar/Hetar}$), 133.6 ($C_{Ar/Hetar}$), 132.3 (d, $^{4}J_{CF}$ = 3.30 Hz, C_{Ar}), 130.16 ($CH_{Ar/Hetar}$), 129.4 ($CH_{Ar/Hetar}$), 129.2 ($CH_{Ar/Hetar}$), 127.5 ($2CH_{Ar/Hetar}$), 126.2 ($CH_{Ar/Hetar}$), 124.5 ($C_{Ar/Hetar}$), 123.4 (d, $^{3}J_{CF}$ = 8.25 Hz, $2CH_{Ar}$), 122.2 ($C_{Ar/Hetar}$), 121.8 ($C_{Ar/Hetar}$), 121.6 ($CH_{Ar/Hetar}$), 117.3 (d, $^{2}J_{CF}$ = 22.56 Hz, $2CH_{Ar}$), 110.9 ($CH_{Ar/Hetar}$). **^{19}F-NMR** (282 MHz, $CDCl_3$): δ = -111.98 (ArCF). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3039 (w), 2919 (w), 1613 (m), 1510 (s), 1453 (m), 1330 (m), 1219 (m), 1157 (m), 818 (m), 800 (m), 755 (m), 730 (s), 571 (m), 518 (m), 421 (m). **MS** (EI, 70 eV): m/z (%) = 313 (22), 312 (M^+, 100), 311 (31), 310 (9); 190 (6), 156 (7). **HR-MS** (EI): m/z = calcd. for $C_{21}H_{13}N_2F$ 312.10573 found: 312.10531.

7-(4-chlorophenyl)-*7H*-indolo[2,3-*c*]quinoline (27d):



27d was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-chloroaniline (0.41 mmol, 52.7 mg) and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 72 mg (80 %); mp. 143 - 144 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.11 (s, 1H, CH_{Hetar}), 8.79 (dd, ^{3}J = 8.51 Hz, ^{4}J = 1.10 Hz, 1H, $CH_{Ar/Hetar}$), 8.67 (d, ^{3}J = 7.88 Hz, 1H, $CH_{Ar/Hetar}$), 8.35 (dd, ^{3}J = 8.35 Hz, ^{4}J = 1.42 Hz, 1H, $CH_{Ar/Hetar}$), 7.83 - 7.72 (m, 2H, $CH_{Ar/Hetar}$), 7.70 - 7.64 (m, 2H, $CH_{Ar/Hetar}$), 7.62 - 7.48 (m, 5H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 143.0 ($C_{Ar/Hetar}$), 140.8 ($C_{Ar/Hetar}$), 136.5 ($CH_{Ar/Hetar}$), 134.9 (C_{Ar}), 134.3 ($C_{Ar/Hetar}$), 132.3 ($C_{Ar/Hetar}$), 130.5 ($2CH_{Ar}$), 130.1 ($CH_{Ar/Hetar}$), 128.7 ($2CH_{Ar}$), 127.6 ($CH_{Ar/Hetar}$), 127.5($CH_{Ar/Hetar}$), 126.3 ($CH_{Ar/Hetar}$), 124.4 ($C_{Ar/Hetar}$), 123.5 ($CH_{Ar/Hetar}$), 123.4 ($CH_{Ar/Hetar}$) 122.3 (C_{Ar}), 122.1 ($C_{Ar/Hetar}$), 121.7 ($CH_{Ar/Hetar}$), 110.9 ($CH_{Ar/Hetar}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 3051 (w), 2950 (w), 2916 (w), 1594 (m), 1495 (s), 1453 (m), 1375 (m), 1325 (m), 1092 (m), 1049 (m) 754 (s), 740 (s), 726 (s), 682 (m), 516 (m), 426 (m). **MS** (EI, 70 eV): m/z (%) = 330 (M^+, 32), 329 (29), 328 (M^+, 100), 327 (17), 292 (16), 190 (29), 188 (13), 164 (16), 163 (16), 111 (23), 75 (39). **HR-MS** (EI): m/z = calcd. for $C_{21}H_{13}N_2Cl$ 328.07618 found: 328.07671; calcd. for $C_{21}H_{13}N_2{}^{37}Cl$ 330.07323 found 330.07397.

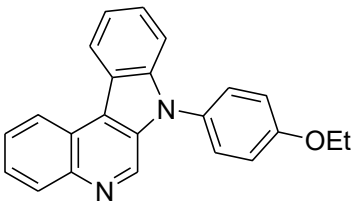
7-(4-ethylphenyl)-*7H*-indolo[2,3-*c*]quinoline (27e):



27e was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-ethylaniline (0.41 mmol, 51.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 80 mg (90 %); mp. 103 - 104 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.14 (s, 1H, CH_{Hetar}), 8.80 (dd, ^{3}J = 8.35 Hz, ^{4}J = 1.10 Hz, 1H, $CH_{Ar/Hetar}$), 8.67 (d, ^{3}J = 7.88 Hz, 1H, $CH_{Ar/Hetar}$), 8.36 (dd, ^{3}J = 8.51 Hz, ^{4}J = 1.42 Hz, 1H, $CH_{Ar/Hetar}$), 7.82 - 7.67 (m, 2H, $CH_{Ar/Hetar}$), 7.60 - 7.57 (m, 2H, $CH_{Ar/Hetar}$), 7.56 - 7.46 (m, 5H, CH_{Ar}), 2.85 (q, ^{3}J = 7.57 Hz, 2H, CH_2), 1.40 (t, ^{3}J = 7.57 Hz, 3H, CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 144.8 ($C_{Ar/Hetar}$), 142.9 ($C_{Ar/Hetar}$), 141.1 (C_{Ar}), 136.9 ($CH_{Ar/Hetar}$), 133.8 (C_{Ar}), 133.6 ($C_{Ar/Hetar}$), 130.0 ($CH_{Ar/Hetar}$), 129.6 ($2CH_{Ar/Hetar}$), 127.3

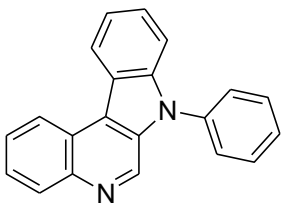
($CH_{Ar/Hetar}$), 127.3 ($CH_{Ar/Hetar}$), 127.2 ($2CH_{Ar}$), 126.0 ($CH_{Ar/Hetar}$), 124.6 ($C_{Ar/Hetar}$), 123.4 ($2CH_{Ar}$), 122.1 ($C_{Ar/Hetar}$), 121.7 ($C_{Ar/Hetar}$), 121.3 ($CH_{Ar/Hetar}$), 111.3 ($CH_{Ar/Hetar}$), 28.6 (*C*H_2), 15.5 (*C*H_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3047 (w), 2965 (w) 2926 (w), 2873 (w), 1607 (m), 1512 (m), 1454 (m), 1382 (m), 1331 (m), 1052 (m), 756 (m), 734 (s), 683 (m), 424 (m). **MS** (EI, 70 eV): m/z (%) = 323 (27), 322 (M^+, 100), 307 (37), 306 (14), 305 (15), 217 (13), 190 (15), 89 (14), 77 (10). **HR-MS** (EI): m/z = calcd. for $C_{23}H_{18}N_2$ 322.14645 found: 322.14655.

7-(4-ethoxyphenyl)-*7H*-indolo[2,3-*c*]quinoline (27f):



27f was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-ethoxyaniline (0.41 mmol, 53.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 71 mg (76 %); mp. 152 - 153 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.09 (s, 1H, CH_{Hetar}), 8.79 (dd, ^3J = 8.31 Hz, ^4J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 8.66 (d, ^3J = 7.93 Hz, 1H, $CH_{Ar/Hetar}$), 8.35 (dd, ^3J = 8.31 Hz, ^4J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 7.82 - 7.68 (m, 2H, $CH_{Ar/Hetar}$), 7.62 - 7.48 (m, 5H, CH_{Ar}), 7.17 (d, ^3J = 8.88 Hz, 2H, CH_{Ar}), 4.19 (q, ^3J = 7.0 Hz, 2H,CH_2), 1.53 (t, ^3J = 7.0 Hz, 3H,CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 159.0 (*C*-OC_2H_5), 142.7 ($C_{Ar/Hetar}$), 141.4 ($C_{Ar/Hetar}$), 136.9 ($CH_{Ar/Hetar}$), 133.8 ($C_{Ar/Hetar}$), 129.9 ($CH_{Ar/Hetar}$), 128.7 ($2CH_{Ar}$), 128.6 ($C_{Ar/Hetar}$), 127.4 ($CH_{Ar/Hetar}$), 127.3 ($CH_{Ar/Hetar}$), 126.0 ($CH_{Ar/Hetar}$), 124.6 (C_{Ar}), 123.4 ($CH_{Ar/Hetar}$), 123.3 ($CH_{Ar/Hetar}$), 121.9 ($C_{Ar/Hetar}$), 121.6 ($C_{Ar/Hetar}$), 121.3 ($CH_{Ar/Hetar}$), 115.8 ($2CH_{Ar}$), 111.2 ($CH_{Ar/Hetar}$), 63.9 (*C*H_2), 14.8 (*C*H_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 3038 (w), 2975 (w), 2874 (w), 1161 (m), 1509 (s), 1456 (m), 1393 (m), 1381 (m), 133 (m), 1231 (s), 1114 (m), 1045 (m), 923 (m), 816 (m), 755 (m), 734 (s), 526 (m), 425 (m). **MS** (EI, 70 eV): m/z (%) = 339 (23), 338 (M^+, 100), 310 (28), 309 (48), 281 (12), 280 (28), 279 (29), 29 (36). **HR-MS** (EI): m/z = calcd. for $C_{23}H_{18}ON_2$ 338.14136 found: 338.14116.

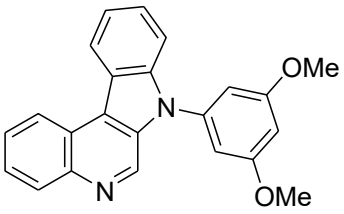
7-phenyl-*7H*-indolo[2,3-*c*]quinoline (27g):



27g was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and aniline (0.41 mmol, 38.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield:

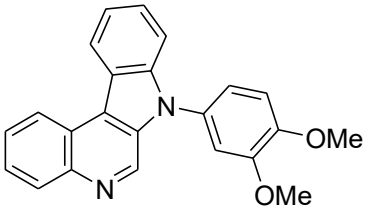
71 mg (88 %); mp 108 - 109 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.15 (s, 1H, CH_{Hetar}), 8.81 (dd, ^{3}J = 8.35 Hz, ^{4}J = 1.10 Hz, 1H, $CH_{Ar/Hetar}$) 8.68 (d, ^{3}J = 7.88 Hz, 1H, $CH_{Ar/Hetar}$), 8.36 (dd, ^{3}J = 8.04 Hz, ^{4}J = 0.95 Hz, 1H, $CH_{Ar/Hetar}$), 7.83 - 7.68 (m, 3H, $CH_{Ar/Hetar}$), 7.67 - 7.48 (m, 7H, CH_{Ar}). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 140.9 ($C_{Ar/Hetar}$), 136.9 ($CH_{Ar/Hetar}$), 136.3 ($C_{Ar/Hetar}$), 133.4 (C_{Ar}), 130.2 ($2CH_{Ar}$), 130.1 ($CH_{Ar/Hetar}$), 128.5 ($CH_{Ar/Hetar}$), 127.4 (4 CH_{Ar}), 126.1 ($CH_{Ar/Hetar}$), 124.5 ($C_{Ar/Hetar}$), 123.4 ($CH_{Ar/Hetar}$), 123.4 ($CH_{Ar/Hetar}$), 122.2 ($C_{Ar/Hetar}$), 121.9 ($C_{Ar/Hetar}$), 121.5 ($CH_{Ar/Hetar}$), 118.9 ($C_{Ar/Hetar}$), 111.2 ($CH_{Ar/Hetar}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3039 (w), 2921 (w), 2851 (w), 1593 (m), 1497 (m), 1449 (m), 1378 (m), 1330 (m), 756 (s), 734 (s), 702 (s), 678 (m), 607 (m), 513 (m), 426 (m). **MS** (EI, 70 eV): m/z (%) = 29 (24), 294 (M^+, 100), 293 (30), 292 (11), 190 (21), 163 (10), 77 (33), 51 (24). **HR-MS** (EI): m/z = calcd. for $C_{21}H_{14}N_2$ 294.11515 found: 294.11480.

7-(3,5-dimethoxyphenyl)-*7H*-indolo[2,3-*c*]quinoline (27h):



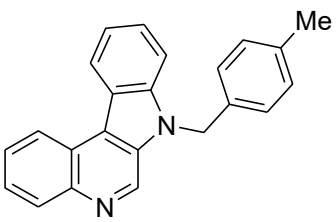
27h was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 3,5-dimethoxyaniline (0.41 mmol, 63.3 mg) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 94 mg (96 %); mp. 105 - 106 °C. **^{1}H-NMR** (250 MHz, $CDCl_3$): δ = 9.23 (s, 1H, CH_{Hetar}), 8.80 (dd, ^{3}J = 8.35 Hz, ^{4}J = 1.10 Hz, 1H, $CH_{Ar/Hetar}$), 8.67 (d, ^{3}J = 7.88 Hz, 1H, $CH_{Ar/Hetar}$), 8.38 (dd, ^{3}J = 8.04 Hz, ^{4}J = 0.95 Hz, 1H, $CH_{Ar/Hetar}$), 7.84 - 7.58 (m, 4H, $CH_{Ar/Hetar}$), 7.54 - 7.47 (m, 1H, $CH_{Ar/Hetar}$), 6.77 (d, ^{4}J = 2.36 Hz, 2H, $2CH_{Ar}$), 6.67 (t, ^{4}J = 2.36 Hz, 1H, CH_{Ar}), 3.88 (s, 6H, $2OCH_3$). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 161.9 ($2C$-OCH_3), 142.4 ($C_{Ar/Hetar}$), 140.9 ($C_{Ar/Hetar}$), 137.8 ($C_{Ar/Hetar}$), 136.6 ($CH_{Ar/Hetar}$), 133.2 ($C_{Ar/Hetar}$), 129.7 ($CH_{Ar/Hetar}$), 127.6 ($CH_{Ar/Hetar}$), 127.5 ($CH_{Ar/Hetar}$), 126.3 ($CH_{Ar/Hetar}$), 124.5($C_{Ar/Hetar}$), 123.4 ($CH_{Ar/Hetar}$), 123.4 ($CH_{Ar/Hetar}$), 122.2 ($C_{Ar/Hetar}$), 122.1 ($C_{Ar/Hetar}$), 121.6 ($CH_{Ar/Hetar}$), 111.5 ($CH_{Ar/Hetar}$), 105.5 ($2CH_{Ar}$), 100.6 (CH_{Ar}), 55.7 ($2OCH_3$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3048 (w), 3004 (w), 2933 (w), 2839 (w), 1591 (s), 1452 (m), 1426 (m), 1336 (m), 1284 (m), 1203 (m), 1156 (s), 1042 (m), 825 (m), 730 (s), 679 (m), 609 (m), 426 (m). **MS** (EI, 70 eV): m/z (%) = 355 (23), 354 (M^+, 100), 267 (11), 190 (11), 63 (9). **HR-MS** (EI): m/z = calcd. for $C_{23}H_{18}O_2N_2$ 354.13628 found: 354.13563.

7-(3,4-dimethoxyphenyl)-*7H*-indolo[2,3-*c*]quinoline (27i):



27i was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 3,4-dimethoxyaniline (0.41 mmol, 63.3 mg) and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 88 mg (90 %); mp. 122 - 123 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.13 (s, 1H, CH_{Hetar}), 8.79 (d, ^{3}J = 7.93 Hz, 1H, $CH_{Ar/Hetar}$), 8.67 (d, ^{3}J = 7.93 Hz, 1H, $CH_{Ar/Hetar}$), 8.34 (d, ^{3}J = 8.31 Hz, 1H, $CH_{Ar/Hetar}$), 7.81 - 7.68 (m, 2H, $CH_{Ar/Hetar}$), 7.63 - 7.47 (m, 3H, $CH_{Ar/Hetar}$), 7.19 (dd, ^{3}J = 8.50 Hz. ^{4}J = 2.27 Hz 1H, CH_{Ar}), 7.16 - 7.09 (m, 2H, CH_{Ar}), 4.04 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 150.1 (*C*-OCH_3), 149.2(*C*-OCH_3), 143.0 ($C_{Ar/Hetar}$), 141.3 ($C_{Ar/Hetar}$), 137.1 ($CH_{Ar/Hetar}$), 133.8 ($C_{Ar/Hetar}$), 130.2 ($CH_{Ar/Hetar}$), 129.0 (C_{Ar}), 127.3 ($CH_{Ar/Hetar}$), 127.3 ($CH_{Ar/Hetar}$), 125.9 ($CH_{Ar/Hetar}$), 124.5 ($C_{Ar/Hetar}$), 123.4 ($2CH_{Ar/Hetar}$), 122.0 ($C_{Ar/Hetar}$), 121.5 ($C_{Ar/Hetar}$), 121.3 ($CH_{Ar/Hetar}$), 119.9 (CH_{Ar}), 111.8 (CH_{Ar}), 111.2 (CH_{Ar}), 110.8 ($CH_{Ar/Hetar}$), 56.2 (O*C*H_3), 56.2 (O*C*H_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3047 (w), 2991 (w), 2957 (w), 2832 (w), 1512 (s), 1460 (m), 1326 (m), 1257 (s), 1238 (s), 1024 (s), 803 (m), 759 (s), 738 (m), 676 (m), 577 (m). **MS** (EI, 70 eV): m/z (%) = 355 (25), 354 (M^+, 100), 339 (12), 311 (11), 309 (10), 295 (12), 279 (11), 267 (14), 217 (16), 79 (11), 51 (14). **HR-MS** (EI): m/z = calcd. for $C_{23}H_{18}O_2N_2$ 354.13628 found: 354.13620.

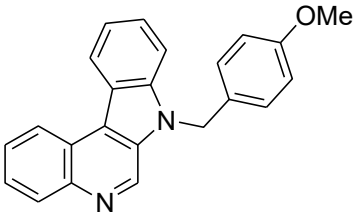
7-(4-methylbenzyl)-*7H*-indolo[2,3-*c*]quinoline (27j):



27j was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and *p*-Methylbenzylamine (0.41 mmol, 53.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). White solid; yield: 82 mg (92 %); mp. 176 - 177 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.22 (s, 1H, CH_{Hetar}), 8.76 (dd, ^{3}J = 8.31 Hz, ^{4}J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 8.64 (d, ^{3}J = 8.12 Hz, 1H, $CH_{Ar/Hetar}$), 8.33 (dd, ^{3}J = 8.31 Hz, ^{4}J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 7.80 - 7.67 (m, 2H, $CH_{Ar/Hetar}$), 7.62 - 7.59 (m, 2H, $CH_{Ar/Hetar}$), 7.50 - 7.43 (m, 1H, $CH_{Ar/Hetar}$), 7.09 (d, ^{3}J = 8.31 Hz, 2H, CH_{Ar}), 7.05 (d, ^{3}J = 8.50 Hz, 2H, CH_{Ar}), 5.71 (s, 2H, CH_2), 2.29 (s, 3H, CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 142.5 ($C_{Ar/Hetar}$), 140.5 ($C_{Ar/Hetar}$), 137.7 ($C_{Ar/Hetar}$), 136.1 ($CH_{Ar/Hetar}$), 133.3 (C_{Ar}), 133.0 ($CH_{Ar/Hetar}$), 130.0 (C_{Ar}), 129.6 ($2CH_{Ar}$), 127.3

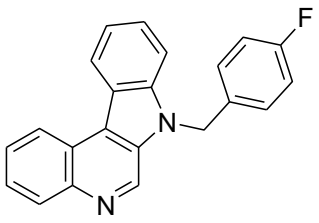
($CH_{Ar/Hetar}$), 127.2 ($CH_{Ar/Hetar}$), 126.3 ($2CH_{Ar}$), 125.9 ($CH_{Ar/Hetar}$), 124.6 ($C_{Ar/Hetar}$), 123.5 ($CH_{Ar/Hetar}$), 123.2 ($CH_{Ar/Hetar}$), 122.0 ($C_{Ar/Hetar}$), 121.5 ($C_{Ar/Hetar}$), 120.8 ($CH_{Ar/Hetar}$), 110.4 ($CH_{Ar/Hetar}$), 46.8 (CH_2), 21.0 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3051 (w), 3025 (w), 2918 (w), 2851 (w), 1612 (m), 1515 (m), 1330 (m), 757 (m), 745 (s), 734 (s), 677 (m), 604 (m), 593 (m), 514 (m), 426 (m). **MS** (EI, 70 eV): m/z (%) = 322 (M^+, 29), 218 (11), 217 (34), 216 (10), 190 (17), 105 (100), 103 (13), 79 (17), 77 (20). **HR-MS** (EI): m/z = calcd. for $C_{23}H_{18}N_2$ 322.14645 found: 322.14599.

7-(4-methoxybenzyl)-7*H*-indolo[2,3-*c*]quinoline (27k):



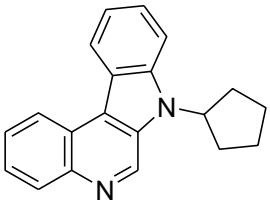
27k was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-methoxybenzylamine (0.41 mmol, 54.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 66 mg (71 %); mp. 132 - 133 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.23 (s, 1H, CH_{Hetar}), 8.74 (dd, ^3J = 8.31 Hz, ^4J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 8.63 (d, ^3J = 8.12 Hz, 1H, $CH_{Ar/Hetar}$), 8.33 (dd, ^3J = 8.12 Hz, ^4J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 7.79 - 7.66 (m, 2H, $CH_{Ar/Hetar}$), 7.62 - 7.59 (m, 2H, $CH_{Ar/Hetar}$), 7.50 - 7.42 (m, 1H, $CH_{Ar/Hetar}$), 7.10 (d, ^3J = 8.88 Hz, 2H, CH_{Ar}), 6.80 (d, ^3J = 8.88 Hz, 2H, CH_{Ar}), 5.68 (s, 2H, CH_2), 3.74 (s, 3H, OCH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 159.3 (C-OCH_3), 142.6 ($C_{Ar/Hetar}$), 140.4 ($C_{Ar/Hetar}$), 136.2 ($CH_{Ar/Hetar}$), 132.9 ($C_{Ar/Hetar}$), 130.1 ($CH_{Ar/Hetar}$), 128.4 ($C_{Ar/Hetar}$), 127.7 ($2CH_{Ar}$), 127.3 ($CH_{Ar/Hetar}$), 127.2 ($CH_{Ar/Hetar}$), 125.8 ($CH_{Ar/Hetar}$), 124.6 (C_{Ar}), 123.5 ($CH_{Ar/Hetar}$), 123.2 ($CH_{Ar/Hetar}$), 122.0 ($C_{Ar/Hetar}$), 121.4 ($C_{Ar/Hetar}$), 120.8 ($CH_{Ar/Hetar}$), 114.4 ($2CH_{Ar}$), 110.4 ($CH_{Ar/Hetar}$), 55.2 (OCH_3), 46.5 (CH_2). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3051 (w), 300 (w), 2935 (w), 2835 (w), 1612 (m), 1512 (s), 1470 (m), 1288 (m), 1243 (s), 1180 (m), 1038 (m), 760 (s), 727 (s), 606 (m), 424 (m). **MS** (EI, 70 eV): m/z (%) = 338 (M^+, 19), 217 (29), 190 (15), 121 (100), 78 (17), 77 (14). **HR-MS** (EI): m/z = calcd. for $C_{23}H_{18}ON_2$ 338.14136 found: 338.14124.

7-(4-fluorobenzyl)-*7H*-indolo[2,3-*c*]quinoline (27l):



27l was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and 4-fluorobenzylamine (0.41 mmol, 47.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 80 mg (89 %); mp. 129 - 130 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.20 (s, 1H, CH_{Hetar}), 8.75 (dd, ^{3}J = 8.31 Hz, ^{4}J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 8.64 (d, ^{3}J = 8.12 Hz, 1H, $CH_{Ar/Hetar}$), 8.33 (dd, ^{3}J = 8.12 Hz, ^{4}J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 7.80 - 7.70 (m, 2H, $CH_{Ar/Hetar}$), 7.68 - 7.56 (m, 2H, $CH_{Ar/Hetar}$), 7.50 - 7.45 (m, 1H, $CH_{Ar/Hetar}$), 7.14 - 7.09 (m, 2H, CH_{Ar}), 6.99 - 6.93 (m, 2H, CH_{Ar}), 5.72 (s, 2H, CH_2). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 162.3 (d, $^{1}J_{CF}$ = 246.49 Hz, CF), 142.7 ($C_{Ar/Hetar}$), 140.3 ($C_{Ar/Hetar}$), 135.9 ($CH_{Ar/Hetar}$), 132.9 ($C_{Ar/Hetar}$), 132.1 (d, $^{4}J_{CF}$ = 3.30 Hz, C_{Ar}), 130.1 ($CH_{Ar/Hetar}$), 128.0 (d, $^{3}J_{CF}$ = 8.25 Hz $2CH_{Ar}$), 127.4 ($CH_{Ar/Hetar}$), 127.3 ($CH_{Ar/Hetar}$), 126.0 ($CH_{Ar/Hetar}$), 124.6 (C_{Ar}), 123.6 ($CH_{Ar/Hetar}$), 123.2 ($CH_{Ar/Hetar}$), 122.1 ($C_{Ar/Hetar}$), 121.6 ($C_{Ar/Hetar}$), 121.0 ($CH_{Ar/Hetar}$), 115.9 (d, $^{2}J_{CF}$ = 22.01 Hz, $2CH_{Ar}$), 110.2 ($CH_{Ar/Hetar}$), 46.3 (CH_2). **^{19}F-NMR** (282 MHz, $CDCl_3$): δ = **-**114.13 (Ar-F). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3047 (w), 2928 (w), 1602 (m), 1507 (m), 1330 (m), 1217 (m), 1152 (m), 820 (m), 756 (s), 733 (s), 682 (m), 605 (m), 483 (m), 423 (m). **MS** (EI, 70 eV): m/z (%) = 326 (M^+, 26), 217 (24), 190 (12), 109 (100), 83 (16). **HR-MS** (EI): m/z = calcd. for $C_{22}H_{15}N_2F$ 326.12138 found: 326.12116.

7-cyclopentyl-*7H*-indolo[2,3-*c*]quinoline (27m):



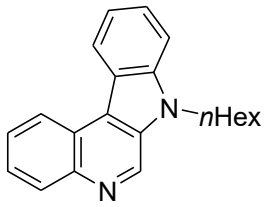
27m was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and cyclopentyl amine (0.41 mmol, 41.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 72 mg (91 %); mp. 56 - 57 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.39 (s, 1H, CH_{Hetar}), 8.77 (dd, ^{3}J = 8.31 Hz, ^{4}J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 8.65 (d, ^{3}J = 8.12 Hz, 1H, $CH_{Ar/Hetar}$), 8.33 (dd, ^{3}J = 8.31 Hz, ^{4}J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 7.78 - 7.60 (m, 4H, $CH_{Ar/Hetar}$), 7.44 (ddd, ^{3}J = 8.12 Hz, ^{3}J = 6.99 Hz, ^{4}J = 1.13 Hz, 1H, $CH_{Ar/Hetar}$), 5.39 (quin, ^{3}J = 9.06 Hz. 1H, $CH_{;alkyl}$), 2.51 - 2.41 (m, 2H, $CH_{2;alkyl}$), 2.38 - 2.29 (m, 2H, $CH_{2;alkyl}$), 2.26 - 2.13 (m, 2H, $CH_{2;alkyl}$), 2.01 - 1.87 (m, 2H, $CH_{2;alkyl}$). **^{13}C-NMR**

(75.0 MHz, $CDCl_3$): δ = 141.9 (C), 139.6 (C), 136.6 (CH), 132.3 (C), 129.9 (CH), 127.2 (CH), 126.7 (CH), 125.7 (CH), 124.8 (C), 123.7 (CH), 123.1 (CH), 122.2 (C), 121.6 (C), 120.4 (CH), 111.2 (CH), 56.2 ($CH_{;alkyl}$), 30.5 ($2CH_{2;alkyl}$), 25.4 ($2CH_{2;alkyl}$). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3049 (w), 2919 (s), 2850 (m), 1612 (m), 1512 (m), 1460 (m), 1331 (m), 1295 (m), 1165 (m), 760 (s), 746 (s), 685 (m), 610 (m), 427 (m). **MS** (EI, 70 eV): m/z (%) = 287 (14), 286 (M^+, 58), 257 (10), 219 (16), 218 (100), 217 (61), 216 (18), 191 (11), 190 (37), 189 (13), 188 (12), 164 (12), 163 (11), 69 (29), 41 (50), 39 (16). **HR-MS** (EI): m/z = calcd. for $C_{20}H_{18}N_2$ 286.14645 found: 286.14619.

General procedure for the Synthesis of tne compounds 27n-o

An oven-dried, argon-flushed sealable glass tube was charged with 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg), $Pd_2(dba)_3$ (5 mol%, 12.6 mg), *rac*-BINAP (10 mol%, 18.3 mg), the appropriate amine, (0.41 mmol) and KO*t*Bu (0.67 mmol, 74.2 mg) followed by xylene (isomeric mixture) (3 mL). The tube was sealed with a Teflon valve and stirred at 140 °C for 24 h. The cooled reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by column chromatography using heptane/ ethyl acetate as eluent.

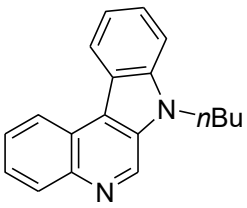
7-*n*-hexyl-*7H*-indolo[2,3-*c*]quinoline (27n):



27n was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and *n*-hexylamine (0.41 mmol, 55.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 71 mg (85 %); mp. 113 - 114 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = = 9.28 (s, 1H, CH_{Hetar}), 8.74 (dd, ^3J = 8.20 Hz, ^4J = 0.95 Hz, 1H, $CH_{Ar/Hetar}$), 8.61 (d, ^3J = 8.20 Hz, 1H, $CH_{Ar/Hetar}$), 8.33 (dd, ^3J = 8.20 Hz, ^4J = 0.95 Hz, 1H, $CH_{Ar/Hetar}$), 7.77 - 7.73 (m, 1H, $CH_{Ar/Hetar}$), 7.70 - 7.66 (m, 1H, $CH_{Ar/Hetar}$), 7.64 - 7.61(m, 2H, $CH_{Ar/Hetar}$), 7.46 - 7.43 (m, 1H, $CH_{Ar/Hetar}$), 4.54 (t, ^3J = 7.25 Hz, 2H, CH_2), 2.0 - 1.94 (m, 2H, CH_2), 1.36 - 1.25 (m, 6H,3CH_2), 0.86 (t, ^3J = 7.25 Hz, 3H, CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 142.5 (C), 140.1 (C), 136.1 (CH), 132.9 (C), 130.1 (CH), 127.2 (CH), 126.9 (CH), 125.6 (CH), 124.7 (C), 123.5 (CH), 123.2 (CH), 121.9 (C), 120.9 (C), 120.5 (CH), 110.2 (CH), 43.5 (CH_2), 31.5 (CH_2), 29.7 (CH_2), 26.9

(CH_2), 22.5 (CH_2), 13.9 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3053 (w), 2950 (m), 2923 (m), 2853 (m), 1613 (m), 1560 (m), 1513 (m), 1513 (m), 1459 (m), 1379 (m), 1331 (m), 755 (m), 743 (s), 730 (s), 602 (m), 422 (m). **MS** (EI, 70 eV): m/z (%) = 302 (M^+, 50), 232 (18), 231 (100), 217 (6), 190 (5), 176 (6). **HR-MS** (EI): m/z = calcd. for $C_{21}H_{22}N_2$ 302.17775 found: 302.17760.

7-*n*-butyl-*7H*-indolo[2,3-*c*]quinoline (27o):



27o was synthesized according to general procedure using 3-bromo-4-(2-bromophenyl)quinoline **26** (0.28 mmol, 100 mg) and *n*-butylamine (0.41 mmol, 55.0 µL) and was purified via column chromatography (heptane/ ethyl acetate). Yellow solid; yield: 66 mg (88 %); mp. 103 - 104 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 9.28 (s, 1H, CH_{Hetar}), 8.73 (dd, ^3J = 8.31 Hz, ^4J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 8.61 (d, ^3J = 8.12 Hz, 1H, $CH_{Ar/Hetar}$), 8.32 (dd, ^3J = 8.31 Hz, ^4J = 1.32 Hz, 1H, $CH_{Ar/Hetar}$), 7.78 - 7.67 (m, 2H, $CH_{Ar/Hetar}$), 7.66 - 7.60 (m, 2H, $CH_{Ar/Hetar}$), 7.47 - 7.41 (m, 1H, $CH_{Ar/Hetar}$), 4.55 (t, ^3J = 7.18 Hz, 2H, CH_2), 2.01 - 1.91 (m, 2H, CH_2), 1.48 - 1.36 (m, 2H, CH_2), 0.96 (t, ^3J = 7.36 Hz, 3H, CH_3). **^{13}C-NMR** (75.0 MHz, $CDCl_3$): δ = 142.6 (C), 140.6 (C), 136.2 (CH), 132.9 (C), 130.2 (CH), 127.1 (CH), 126.8 (CH), 125.6 (CH), 124.7 (C), 123.5 (CH), 123.2 (CH), 121.9 (C), 120.9 (C), 120.4 (CH), 110.1 (CH), 43.2 (CH_2), 31.8 (CH_2), 20.5 (CH_2), 13.8 (CH_3). **IR** (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2950 (w), 2926 (w), 2867 (w), 1613 (m), 1561 (m), 1513 (m), 1469 (m), 1437 (m), 1513 (m), 1469 (m), 1381 (m), 1348 (m), 1332 (s), 1293 (m), 1250 (m), 1151 (m), 757 (m), 742 (m), 729 (m),4223 (m). **MS** (EI, 70 eV): m/z (%) = 274 (M^+, 44), 232 (17), 231 (100), 217 (8), 190 (6), 176 (7). **HR-MS** (EI): m/z = calcd. for $C_{19}H_{18}N_2$ 274.14645 found: 274.14637.

5.3. Crystallographic Data

Crystal data and structure refinement for 4-bromo-2,3,5-trichloro-6-iodopyridine (3)	
	is_lo002n
Crystal data	
Chemical formula	$0.87(C_5BrCl_3IN)\cdot 0.13(C_5BrCl_4N)$
M_r	375.56
Crystal system, space group	Tetragonal, $P4_12_12$
Temperature (K)	123
a, c (Å)	5.4082 (3), 30.402 (2)
V (Å^3)	889.22 (12)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	8.52
Crystal size (mm)	0.16 × 0.09 × 0.04
Data collection	
Diffractometer	Bruker Apex Kappa-II-CCD-diffractometer
Absorption correction	Multi-scan (*SADABS*; Sheldrick, 2004)
T_{min}, T_{max}	0.564, 0.746
No. of measured, independent and observed [I > 2σ(I)] reflections	9706, 1470, 1318
R_{int}	0.063
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.735
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.048, 0.089, 1.28
No. of reflections	1470
No. of parameters	57
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.70, −1.10
Absolute structure	Refined as an inversion twin.
Absolute structure parameter	0.05 (4)

Crystal data and structure refinement for 4-bromo-2,3,5-trichloro-6-(4-chlorophenyl) pyridine (4k)	
	is_r25
Crystal data	
Chemical formula	$C_{11}H_4BrCl_4N$
M_r	371.86
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	123
a, b, c (Å)	3.8934 (2), 25.7303 (14), 12.1698 (7)
β (°)	95.006 (2)
V (Å^3)	1214.50 (11)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	4.24
Crystal size (mm)	0.99 × 0.02 × 0.02
Data collection	
Diffractometer	Bruker D8 QUEST diffractometer
Absorption correction	Multi-scan (*SADABS*; Sheldrick, 2004)
T_{min}, T_{max}	0.603, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	35706, 2924, 2436
R_{int}	0.243
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.661
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.055, 0.128, 1.10
No. of reflections	2924
No. of parameters	154
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.25, −0.97

Crystal data and structure refinement for 2-(4-methoxyphenyl)-3,5-diphenyl-4,6-di-*p*-tolylpyridine (11a)	
	is_r266
Crystal data	
Chemical formula	$C_{38}H_{31}NO$
M_r	517.64
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	123
a, b, c (Å)	9.9547 (5), 15.7621 (8), 18.305 (1)
β (°)	92.577 (3)
V (Å^3)	2869.3 (3)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.07
Crystal size (mm)	0.40 × 0.12 × 0.12
Data collection	
Diffractometer	Bruker Apex Kappa-II-CCD-diffractometer
Absorption correction	Multi-scan (*SADABS*; Sheldrick, 2004)
T_{min}, T_{max}	0.678, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	42507, 7621, 5721
R_{int}	0.045
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.682
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.046, 0.121, 1.02
No. of reflections	7621
No. of parameters	395
No. of restraints	45
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.30, −0.23

Crystal data and structure refinement for 2-(trifluoromethyl)-4,6-diphenylquinoline (21a)	
	is_rp3-1
Crystal data	
Chemical formula	$C_{22}H_{14}F_3N$
Mr	349.34
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	173
a, b, c (Å)	9.7957 (4), 6.7048 (2), 25.3358 (9)
β (°)	98.093 (2)
V (Å3)	1647.44 (10)
Z	4
Radiation type	Mo *K*α
μ (mm−1)	0.11
Crystal size (mm)	0.20 × 0.11 × 0.11
Data collection	
Diffractometer	Bruker-Nonius Apex X8-CCD-diffractometer
Absorption correction	Multi-scan (*SADABS*; Sheldrick, 2004)
Tmin, Tmax	0.709, 0.746
No. of measured, independent and observed [I > 2σ(I)] reflections	20385, 4151, 2804
Rint	0.050
(sin θ/λ)max (Å−1)	0.671
Refinement	
R[F2 > 2σ(F2)], wR(F2), S	0.060, 0.113, 1.10
No. of reflections	4151
No. of parameters	299
No. of restraints	19
H-atom treatment	H-atom parameters constrained
Δρmax, Δρmin (e Å−3)	0.29, −0.22

Crystal data and structure refinement for 2-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-6-*p*-tolylquinoline (24c)	
Identification code	is_rp413
Crystal data	
Chemical formula	C24H15F6N
M_r	431.37
Crystal system, space group	Triclinic, *P*
Temperature (K)	173
a, *b*, *c* (Å)	10.4516 (2), 12.8402 (3), 16.7333 (3)
α, β, γ (°)	106.412 (1), 94.990 (1), 112.592 (1)
V (Å^3)	1939.75 (7)
Z	4
Radiation type	Mo Kα
μ (mm−1)	0.13
Crystal size (mm)	0.44 × 0.25 × 0.23
Data collection	
Diffractometer	Bruker Apex Kappa II-CCD-diffractometer
Absorption correction	Multi-scan (SADABS; Sheldrick, 2004)
Tmin, Tmax	0.720, 0.746
No. of measured, independent and observed [I > 2σ(I)] reflections	58961, 11306, 8706
Rint	0.021
(sin θ/λ)max (Å−1)	0.703
Refinement	
R[F2 > 2σ(F2)], wR(F2), S	0.055, 0.158, 1.02
No. of reflections	11306
No. of parameters	636
No. of restraints	38
H-atom treatment	H-atom parameters constrained
Δρmax, Δρmin (e Å−3)	0.73, −0.41

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