UNIVERSITÄT ROSTOCK

Synthesis of Substituted Dibenzothiophenes, Pyrazines, Quinoxalines, Flavones, Pyrimidines and Furans by Regioselective Palladium (0)-Catalyzed Cross-Coupling Reactions

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Affectionately Dedicated to

My dear Mother and Father

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IMRAN MALIK

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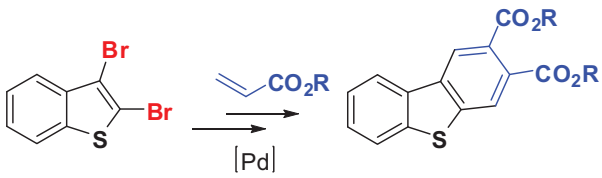

The palladium(0)-catalyzed Heck cross-coupling reactions of di- and tribromobenzothiophene provided functionalized dibenzothiophene by a domino ′twofold Heck / 6π-electrocyclization. The products were transformed by Pd/C-catalyzed oxidation to the corresponding dibenzothiophenes.

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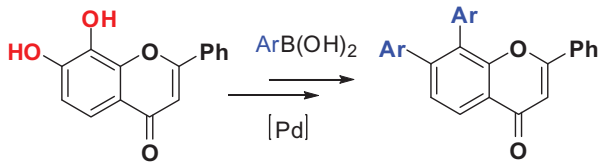

Suzuki-Miyaura cross coupling reactions of the bis(triflate) of 7,8-dihyroxyflavone was proceeded with different arylboronic acids to give mono- and diarylflavones with excellent site selectivity. The first attack occurred at the more electronically deficient and sterically less hindered position at C-7.

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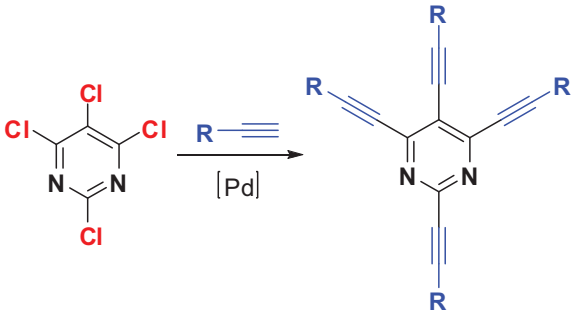

Sonogashira coupling reaction of 2,4,5,6-tetrachloropyrimidine yielded di-, tri-, and tetraalkynylpyrimidines with good site selectivity. Mixed Sonogashira / Suzuki products were also prepared. Most products showed excellent fluorescence properties.

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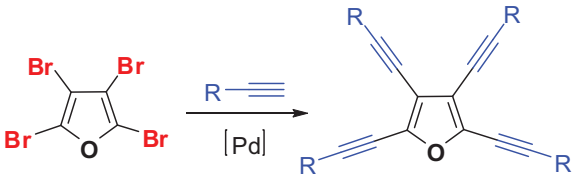

Sonogashira coupling reaction of 2,3,4,5-tetrabromofuran afforded di-, tri- and tetraalkynylfurans with excellent site selectivity. Mixed Sonogashira / Suzuki products were also obtained. Many derivatives showed excellent fluorescence properties.

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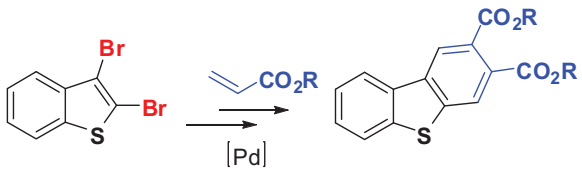
Task of this Thesis

Palladium catalyzed transformations have gained remarkable importance for C-C bond formation; these reactions are being used for the synthesis of a number of natural products, pharmaceutical drugs and advanced materials. The aim of this work is to enhance the scope of palladium catalyzed reactions. In recent years, site-selective palladium(0) catalyzed cross-coupling reactions of di- and trihalogenated molecules or the corresponding triflates have been studied. The Langer group has also greatly contributed to this. This paragraph outlines the tasks of this thesis. A more detailed introduction is given at the beginning of each individual chapter. I studied the site-selectivity of palladium catalyzed transformations of a number of di- and tribromides derived from hetero- and carbacycles. Reactions of bis(triflates) are also included. Site selective reactions of the substrates discussed in my thesis have not been previously studied by other research groups. In addition, I had the task to apply Heck reactions to substrates where these types of reactions have not been previously reported.

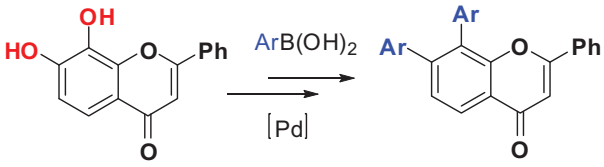
Although a diverse set of substrates were studied, the general topic of this thesis was to develope new applications of palladium(0)-catalyzed reactions to polyhalogenated substrates or their triflate analogues.

In continuation of related work in our group, I had the task to apply the concept of domino ′twofold Heck / 6π-electrocyclization′ reactions to di- and tribromo-benzothiophene. These reactions afforded functionalized dibenzothiophenes.

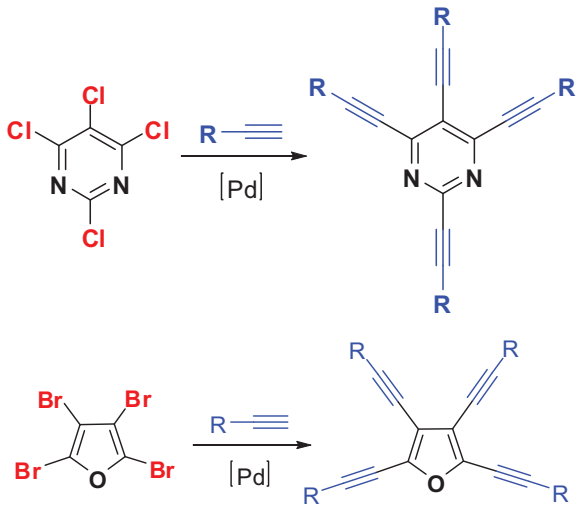


I also had the task to study domino ′twofold Heck / 6π-electrocyclization′ reactions of dichloropyrazine and dichloroquinoxaline. While Heck reactions were possible, the electrocyclizations failed.

Another task was to study regioselective Suzuki-Miyaura cross-coupling reactions of the bis-triflate of 7,8-dihydroxyflavone. These reactions afforded mono- and diarylflavones with good site selectivity.



The Sonogashira reaction is used as key step in the synthesis of many biological active compounds. My task was to study hitherto unknown Sonogashira coupling reactions of 2,4,5,6-tetrachloropyrimidine and of 2,3,4,5-tetrabromofuran. These reactions afforded the desired alkynylated heterocycles. Based on this, an important goal was to study the fluorescence properties.



A significant part of this dissertation has been published (see list of publications). A detailed introduction is given at the beginning of each individual chapter.

Efficient Synthesis of Functionalized Dibenzothiophenes by Domino Twofold Heck/6π-Electrocyclization Reaction of 2,3-Dibromobenzo-thiophene and 2,3,6-tribromobenzothiophene.

1.1 General Introduction

The Heck reaction was discovered by Heck in 1968 [1] and then developed by Mizoroki and Heck in the 1970's. It is the palladium catalyzed C-C coupling between aryl halides or vinyl halides with activated alkenes in the presence of palladium(0) catalyst and a base.[2] Palladium(II) acetate or Palladium(II) chloride in combination with different ligands, such as triphenyl phosphine (PPh_3), S-Phos, X-Phos, tricyclohexylphosphine (PCy_3), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), were used in this reaction. Phosphine ligands stabilize the palladium in its oxidation state zero state in the form of stable PdL_4 or PdL_3 species. There are many choices of base used in this reaction, such as triethylamine, diisoproylamine, potassium carbonate, sodium acetate.[3] The reactivity depends on the substituted olefins: more substituted olefins resulted slower reaction. However, electron poor olefins provided higher yields (electron withdrawing groups such as ester, ether, carboxylic acid, nitriles, located at the olefin). The type of leaving group also plays an important role. The reactivity order is I > Br > Cl.[4] The mechanism of the Heck reaction involves the oxidative addition, migratory insertion of the olefins and then β- hydride elimination.[5] The Heck reaction was widely used as a key step in the total synthesis of natural products, for the preparation of polymers, pharmaceuticals, and hydrocarbons.[6]

In a couple of years, Prof Langer's research group has extensively studied twofold Heck cross coupling reactions of 2,3-dibromobenzofuran (**a**),[7] 2,3-dibromothiophene (**b**),[8] 2,3-dibromo-N-methylindole (**c**),[9] 2,3-dibromofuran (**d**), 2,3-dibromoindenone (**e**),[10] 2,3-dibromo naphthaquinone (**f**).[11] (Figure.1). The electrocyclization and dehydrogenation of Heck products provided upon heating in the presence of Pd/C a variety of aromatized products.

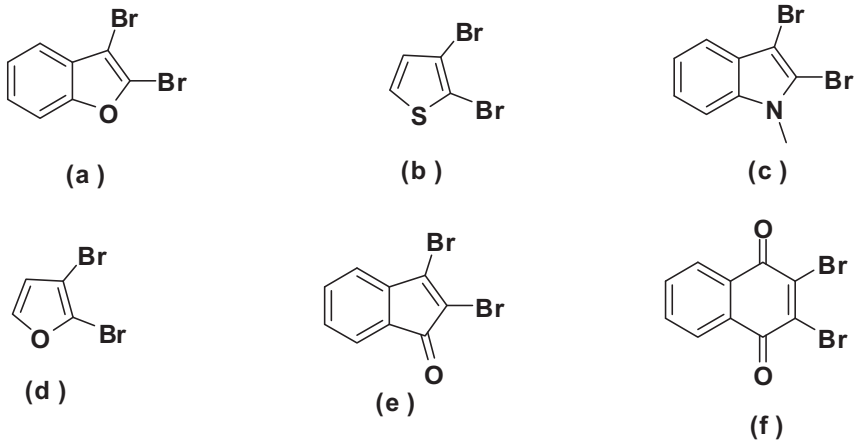


Figure 1. Heck Reaction Studies on vicinal dibromide in Prof Langer's Group.

1.2 Introduction

Benzothiophenes are found in drugs, such as raloxifene, zileuton and sertaconozole. Benzothiophenes are present in coffee beans and are used in many dyes, such as thioindigo and its derivatives. It is also used in crop protection; for example, Mobam is a potent insecticide, which inhibits the enzyme acetylcholinsterase. Dibenzothiophenes have never been reported as natural products, still, they can be obtained from coal tar. Among the various classes and numerous kinds of sulphur-containing organic compounds identified in fossil fuels, the most represented are dibenzothiophene (DBT), and its derivatives. Therefore, this compound can be considered to be the model substrate of organically bonded sulphur in fossil fuels.[12] However, they have shown substantial pharmacological properties, for example, antimicrobial,[13] antileishmanial,[14] antiprotozoal,[15] antidiabetic,[16] cytotoxic,[17] and genotoxic activity.[18] In addition, binding to the dopamine[19] to the estrogen receptor [20] and to neuroblastoma cells,[21] inhibition of human protein tyrosine phosphotase 1B,[22] and of MAOA[23] have been studied. Dibenzothiophene has been also used as a model S-heterocycle for studying desulfurization in a number of microorganisms, *Rhodococcus* sp. strain IGTS8 is a prototype sulfur-specific desulfurization bacterium.[24]

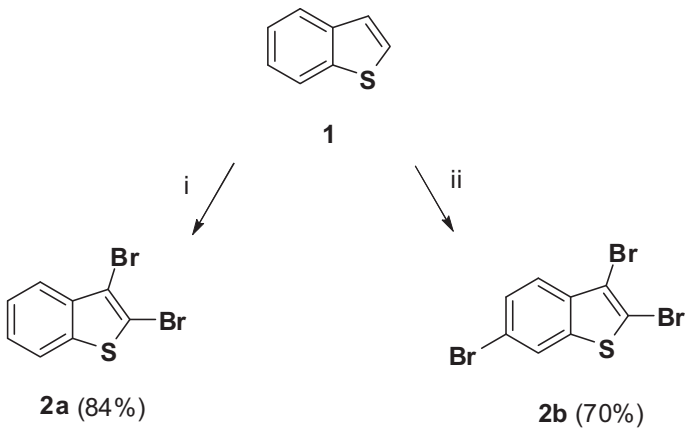
Presently and during recent years, polyhalogenated heterocycles have been shown to be regioselectively functionalized in palladium (0)-catalyzed cross-coupling reactions. To determine the regioselectivity in polyhalogenated compounds electronic and steric

parameters find key role by activation of single halogen atom.[25] Recently, Prof. P. Langer`s research group has reported the synthesis of aryl-substituted thiophenes, pyrroles, and selenophenes based on regioselective Suzuki reactions of tetrabromo-thiophene, tetrabromo-*N*-methylpyrrole, and tetrabromoselenophene, respectively.[26] Sonogashira, Negishi, and Stille coupling reactions of 2,3- and 2,6-dibromobenzofuran have been reported to regioselectively occur at position C-2.[27]

I have studied the Heck reactions of 2,3-dibromobenzothiophene and 2,3,6-tribromo-benzothiophene and subsequent 6π-electrocyclizations. Functionalized dibenzothiophene were efficiently prepared based on domino ′twofold Heck / 6π-electrocyclization′ reactions.[28]

1.3 Results and Discussion

The reaction of benzothiophene (**1**) with bromine (2.0 equiv.) and KOAc (2.0 equiv.) in CH_2Cl_2 (reflux, 18 h) resulted in the formation of 2,3-dibromobenzothiophene (**2a**) in 84% yield (Scheme 1). During optimization and scale-up of the reaction, I have found that more vigorous conditions (reflux, 18 h) were required to avoid the formation of mono-brominated by-products. I have also prepared, for the first time, 2,3,6-tribromobenzothiophene (**2b**) by using an excess of bromine (4.5 equiv) and KOAc (4.5 equiv) in CH_2Cl_2 (reflux, 24 h).



Scheme 1. Bromination of benzothiophene (**1**); *conditions*: *i*, Br_2 (2.0 equiv.), KOAc (2.0 equiv.) CH_2Cl_2, reflux, 18 h *ii*, Br_2 (4.5 equiv.), KOAc (4.5 equiv.), CH_2Cl_2, reflux, 24 h

The Heck reaction of **2a** with acrylates **3b,e** (2.5 equiv.) afforded the 2,3-di(alkenyl)benzothiophenes **4b,e** in good yields (Scheme 2, Table 1). The best yields were obtained when the reactions were carried out using $Pd(OAc)_2$ (5 mol%) and the biaryl monophosphine ligand $\mathbf{L_1}$ (10 mol%) which was recently developed by Buchwald and coworkers (Figure 2).[29] The reactions were carried out in DMF at 100 ˚C for 12 h. Heating of a xylene solution of **4b,e** in the presence of Pd/C resulted in the formation of dibenzothiophene **6b,e** in 79-81%.

The Heck reaction of **2a** with acrylates **3a,c,d**, carried out at 80-130 °C using several ligands (PCy_3, PPh_3) with $Pd(OAc)_2$, failed. I also tried different solvents such as N-methyl-2-pyrrolidone (NMP), acetonitrile (CH_3CN), dimethylsulfoxide (DMSO), dimethylacetamide (DMA), but no satisfactory results were obtained. Finally, I tried Buchwald ligands with palladium(II) acetate and DMF as solvent and obtained excellent results (For optimization, Table 2). The reaction of **2a** with acrylates **3a,c,d**, carried out at 130 °C and using biaryl monophosphine ligand $\mathbf{L_2}$, afforded the 1,2-dihydrodibenzothiophenes **5a,c,d** as a mixture of two isomers. Their formation can be explained by a domino ′twofold Heck / thermal 6π-electrocyclization′ cyclization and subsequent double bond migration. Heating of a xylene solution of crude **5a,c,d** in the presence of Pd/C resulted in the formation of dibenzothiophenes **6a,c,d** in 74-77% overall yields. The reaction of **2a** with chlorostyrene **3f** directly afforded dibenzothiophene **6f** (83%) in only one step.

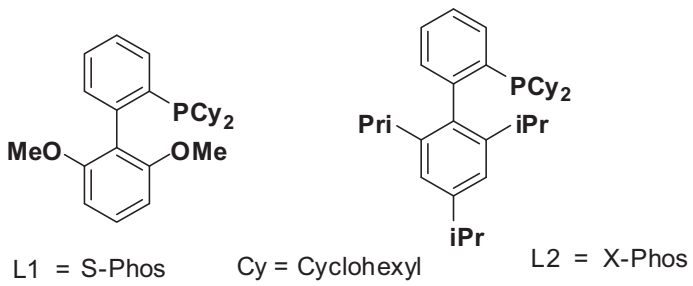
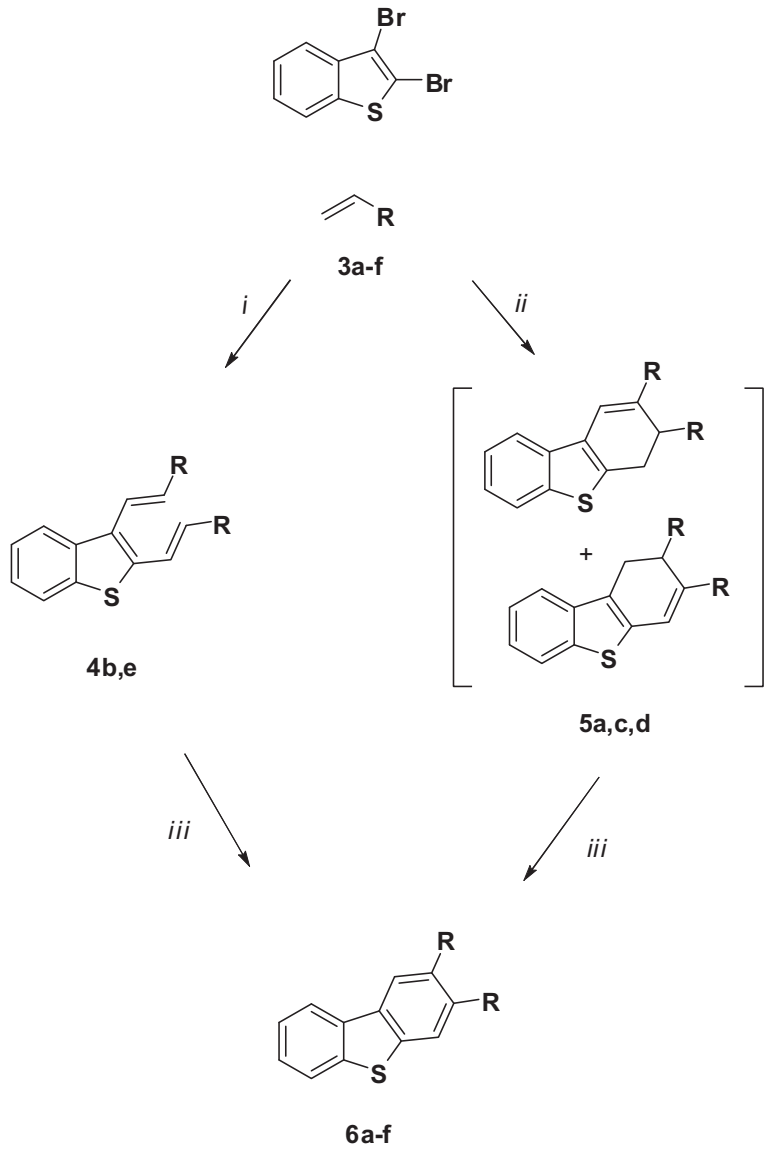


Figure 2. Biaryl monophosphine ligands developed by Buchwald and coworkers [29]



Scheme 2 Synthesis of **4b**,**e** and **6a**–**f**. *Reagents and conditions*:(*i*) $Pd(OAc)_2$ (5 mol-%), **L2** (10 mol-%), **3** (2.5equiv), Et_3N (8.0 equiv), DMF, 100 °C, 12 h; (*ii*) $Pd(OAc)_2$ (5 mol%), **L1** (10 mol-%), **3** (2.5 equiv), Et_3N, DMF, 130 °C, 48 h; (*iii*) Pd/C (10 mol-%), xylene, reflux, 48 h.

Table 1. Synthesis of **4b,e** and **6a-f**

3,4,6	R	% (**4**) [a]	% (**6**) [a]
a	CO_2Et	- [b]	76
b	CO_2nBu	71	81
c	CO_2iBu	- [b]	74
d	CO_2nHex	- [b]	77
e	Ph	85	79
f	4-ClC_6H_4	- [b]	83 [c]

[a] Yields of isolated products based on **2a**.

[b] Experiment was not carried out.

[c] Product was directly formed from **2a** in one step.

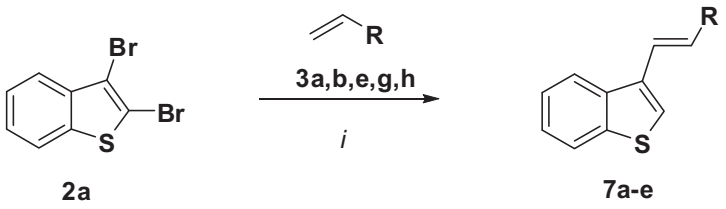
Table 2. Optimization of the reaction condition for Heck products

Entry	Conditions	Temp [°C]	(**4b**) [a] %	(**4e**) [a] %	(**5a**) [a] %	(**5c**) [a] %	(**6f**) [a] %
1	PPh_3(10 mol-%), $Pd(OAc)_2$ (5 mol-%), CH_3CN	80	- [b]	- [c]	- [b]	- [c]	- [b]
2	PPh_3(10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	100	22	31	- [b]	- [c]	62
3	PCy_3(10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	120	- [b]	- [c]	- [d]	- [d]	47
4	$N(CH_2CH_2OH)_3$, $Pd(OAc)_2$ (5 mol-%)	100	- [c]	- [b]	- [b]	- [c]	- [b]
5	$Pd(PPh_3)_4$ (10mol-%), DMF, K_2CO_3	120	- [b]	- [c]	- [b]	- [b]	20
6	L2 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	100	71	85	- [c]	- [c]	83
7	L1 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	130	- [c]	- [c]	- [d]	- [d]	- [c]

[a] isolated yield; [b] No Conversion; [c] Experiment was not carried out; [d] isomeric mixture.

According to the literature, the Sonogashira, Suzuki and Stille reactions of **2a** regioselectively occurred at carbon atom C-2.[27a] Surprisingly, I have found that the Heck reaction of **2a** with one equivalent of alkenes **3a,b,g,e,h** afforded the 3-(alkenyl)benzothiophenes **7a-e** (Scheme 3, Table 3). The best yield (81%) was obtained when **7a** was reacted with ethyl acrylate (**3a**) using $Pd(OAc)_2$ (5 mol-%) in combination with biaryl monophosphine ligand **L1** (10 mol-%). The employment of $Pd(OAc)_2$ in the presence of PPh_3 or PCy_3 did not give good yields. The reaction was carried out in DMF at 130 °C for 24 hours. Other solvents, such as N-methyl-2-pyrrolidone (NMP) and acetonitrile (CH_3CN), proved to be less successful in terms of yield (For Optimization of mono Heck products, Table 4).

The formation of products **7** can be explained by Heck reaction, which occurs at carbon atom C-3, and reduction of the bromide function located at carbon C-2. In case of benzofuran and indole, carbon atom C-2 is much more electron deficient than C-3. This effect is less pronounced in case of benzothiophene and the rate of the oxidative addition at C-2 and C-3 should be not too much different. A reduction of carbon C-2 in the first step is unlikely because the 2,3-dialkenylbenzothiophenes **4b,e** are cleanly formed without any reduction. Therefore, the reason for the formation of products **7** remains unclear at present.



Scheme 3. Synthesis of **7a-e**. Conditions: *i*, $Pd(OAc)_2$ (2.5-5 mol-%), $\mathbf{L_1}$ (for **7a,b,d**) or $\mathbf{L_2}$ (for **7c,e**) (5-10 mol-%), **3** (1.25 equiv.), NEt_3, DMF, 130 ˚C, 24 h.

Table 3. Synthesis of **7a-e**

3	**7**	R	% (**7**) [a]
a	a	CO_2Et	81
b	b	CO_2nBu	65
g	c	CN	51
e	d	Ph	74
h	e	4-MeC_6H_4	76

[a] Yields of isolated products

Table 4. Optimization of the reaction condition for **7a,c,e**

Entry	Conditions	Temp [°C]	(**7a**) [a] %	(**7c**) [a] %	(**7e**) [a] %
1	PPh_3(10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	80	- [b]	- [b]	- [c]
2	PCy_3(10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	90	- [b]	- [b]	- [c]
3	$N(CH_2CH_2OH)_3$, $Pd(OAc)_2$ (5 mol-%)	100	- [b]	- [b]	- [b]
4	PCy_3(10 mol-%), $Pd(OAc)_2$ (5 mol-%), NMP, K_2CO_3	120	17	22	42
5	L2 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	130	61	51	76
6	L1 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF	130	81	47	56

[a] isolated yield; [b] No Conversion;

[c] Experiment was not carried out

The structures of all products were established by spectroscopic methods.The structure of **7d** was idependently confirmed by X-ray crystal structure analysis (Figure 2).[30] The X-ray structure shows that the phenyl group, the alkenyl unit and the benzothiophene moiety are in plane.

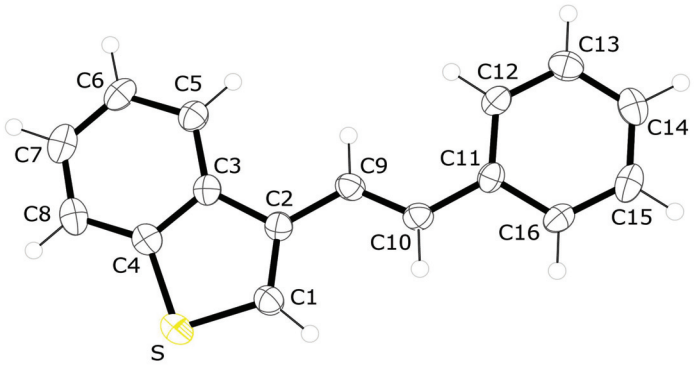
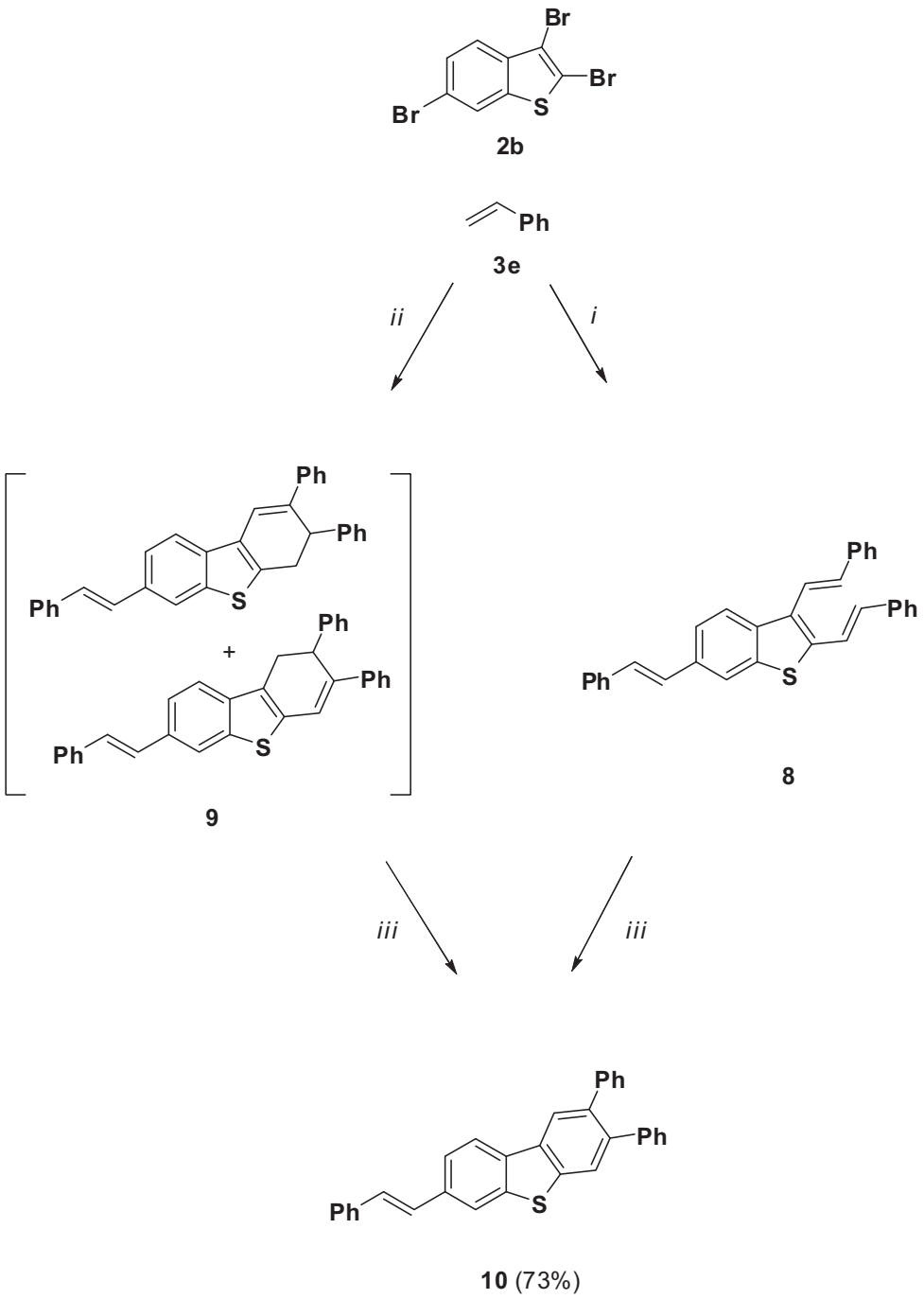


Figure 3. Molecular structure of **7d**



Scheme 4. Synthesis of **8**,**9** and **10**. *Conditions*: *i*, $Pd(OAc)_2$ (5 mol-%), $\mathbf{L_1}$ (10 mol-%), **3** (3.75 equiv.), NEt_3 (8.0 equiv.), DMF, 100 ˚C, 12 h; *ii*, $Pd(OAc)_2$ (5 mol-%), $\mathbf{L_1}$ (10 mol-%), **3** (3.75equiv.), NEt_3, DMF, 130 ˚C, 48 h; *iii*, Pd/C (10 mol-%), xylene, reflux, 48 h.

The Heck reaction of 2,3,6-tribromobenzothiophene (**2b**) with styrene (**3e**) afforded the 2,3,6-tri(alkenyl)benzothiophenes **8** (Scheme 4). The reaction was carried out in DMF at 100 ˚C for 12 h using $Pd(OAc)_2$/$\mathbf{L_1}$ as the catalyst. The $Pd(OAc)_2$/$\mathbf{L_1}$-catalyzed reaction of **2b** with **3e**, carried out at 130 °C, afforded **9** as a mixture of two isomers. Heating of a xylene solution of **8** and **9**, in the presence of Pd/C, afforded the 2,3-diphenyl-7-styryldibenzothiophenes **10.**

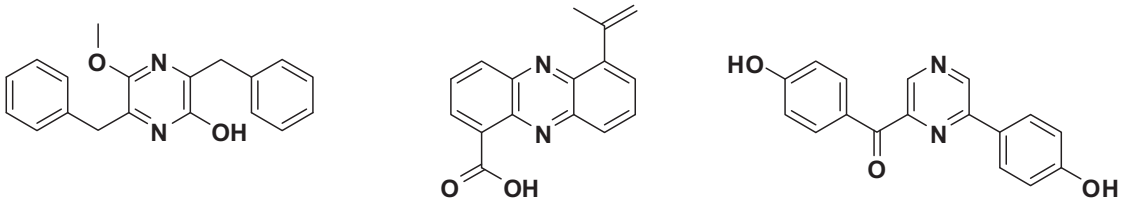
1.4 Conclusion

I have synthesized 2,3-di(alkenyl)benzothiophenes and dibenzothiophene by the first Heck reactions of 2,3-dibromobenzothiophene. I have obtained mono-Heck products along with reduction of carbon atom C-2, when 2,3-dibromobenzothiophene was treated with one equivalent of different alkenes. In addition, I was successful to prepare 2,3,6-tribromobenzothiophenes which were subsequently treated with styrenes to give 2,3-diphenyl-7-styryl-dibenzothiophenes in good yield. The functionalized dibenzo-thiophenes were formed by domino ′twofold Heck / 6π-electrocyclization′ reactions.

Synthesis of 2,3-Disubstituted Pyrazines and Quinoxalines by Heck Cross-Coupling Reactions of 2,3-Dichloropyrazine and 2,3-Dichloroquinoxaline

2.1 Introduction

Pyrazine and quinoxaline (benzopyrazine) are heterocyclic compounds which have significant biological and physical importance in organic chemistry. They are found in various natural products. Examples include various simple alkyl-substituted pyrazine derivatives,[31] botryllazines A and B,[32] or 2,5-bis(3-indolylmethyl)pyrazine.[33] Different types of quinoxaline analogues have been prepared which show antibiotic activity. Quinoxaline antibiotics of bicyclic octadepsipeptide are potent inhibitors of RNA synthesis and quinoxaline antibiotics of echinomycin analogues show remarkable cytotoxicity against human tumor cell lines.[34] Antimicrobial activity has been reported also for naturally occurring phenazines (isolated from marine actinomycete).[35] Pteridines (isolated from *Drosophila*) represent nucleobase-type natural products which are also pharmacologically active (e. g inhibition of tRNA-guanine transglycosylase).[36,37] A pyrazine derivative has been isolated from the mushroom *Albatrellus confluens* and promotes melanin synthesis by B 16 melanoma cells.[38] The cephalostatins and ritterazines show a strong cytotoxic and cancerostatic activity.[39]



Melanin synthesis promotor (pyrazine derivative)

Saphenic acid (phenezine)

Botryllazine B

Figure 4. Some examples of pyrazine natural products

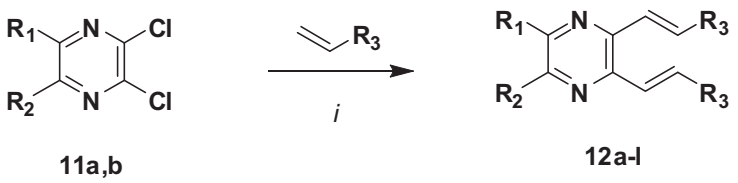
Some pyrazine derivatives, formed by reaction of 2,3-dichloropyrazine with DBU, show fluorescence properties.[40] 2,3-Dichloropyrazine and 2,3-dichloroquinoxaline represent useful building blocks for the synthesis of substituted and annulated pyrazines and quinoxalines. Condensed heterocycles have been prepared by cyclization of 2,3-dichloropyrazine with 2-aminobenzenethiol,[41] 2-aminophenol,[42] 3-hydroxy-1*H*-pyridine-2-thione,[43] 3-amino-6-methoxy-1*H*-pyridine-2-thione,[44] 2-amino-benzeneselenol,[45] and pyrid-2-yl-acetonitrile.[46] Open-chained pyrazines have been prepared by reaction of 2,3-dichloropyrazine with one equivalent of different enolates,[47] two equivalents of thiols,[48] and DMAP.[49] Transition metal-catalyzed reactions of 2,3-dichloropyrazine have only scarcely been reported. 2,3-Diarylpyrazines and 2,3-di(alkynyl)pyrazines have been recently prepared by Suzuki [50] and Sonogashira reactions, respectively.[51] In my thesis, I have studied the first Heck reactions of 2,3-dichloropyrazine and -quinoxaline.[52, 53] These reactions provide, depending on the reaction conditions, a convenient approach to 2,3-dialkenyl-, 2-alkenyl-3-alkyl-, and 2,3-dialkylpyrazines and their quinoxaline derivatives.

2.2 Results and Discussion

The reaction of 2,3-dichloropyrazine (**11a**) with ethyl acrylate (**3a**), in the presence of $Pd(OAc)_2$ (5 mol-%) and L2 (10 mol-%), afforded the 2,3-dialkenylpyrazine **12a** in 83% yield (Scheme 5, Table 5). The employment of $Pd(PPh_3)_4$ was less successful in terms of yield. The best yields were obtained when 5 mol-% of the catalyst, 10 mol-% of the ligand and a slight excess of the alkene (2.5 equiv) were employed and when the reaction mixture was stirred at 90 °C for 48 h. Partial hydrogenation was observed when the reaction was carried out at higher temperature. On the other hand, the yields also decreased when the temperature was decreased, due to lower conversion of the starting material (entry 1-6, Table 6).

The $Pd(OAc)_2$-catalyzed reaction of **11a** with styrenes **3e,f,h-j**, in the presence of L2 or L1, gave the 2,3-dialkenylpyrazines **12b-f** in 64-82% yields. The reaction of 2,3-dichloroquinoxaline (**11b**) with **3e, i, j, m** afforded the 2,3-dialkenylquinoxalines **12g-l** in

67-83% yields. The synthesis of the quinoxaline derivatives had to be carried out at 120 instead of 90 °C to obtain good yields.



11a,b **12a-l**

Scheme 5. Synthesis of 2,3-di(alkenyl)pyrazines and quinoxalines **12a-l**. Conditions: *i*, **3a,e,f,h-m** (2.5 equiv.), $Pd(OAc)_2$ (5 mol-%), L2 (for **12a,b,e-l**) or L1 (for **12c,d**) (10 mol-%), NEt_3, DMF, 90 ˚C.

Table 5. Synthesis of **12a-l**

11	**3**	**12**	R^1	R^2	R^3	% (**12**) [a]	T [°C]
a	a	a	H	H	CO_2Et	83	90
a	e	b	H	H	Ph	82	90
a	i	c	H	H	4-(MeO)C_6H_4	78 [b]	90
a	h	d	H	H	4-MeC_6H_4	82 [b]	90
a	f	e	H	H	4-ClC_6H_4	66	90
a	j	f	H	H	4-(*t*BuO)C_6H_4	64	90
b	k	g	–(CH=CH)$_2$–		CO_2Me	78	120
b	l	h	–(CH=CH)$_2$–		*c*Hex	67	120
b	e	i	–(CH=CH)$_2$–		Ph	72	120
b	j	j	–(CH=CH)$_2$–		4-(*t*BuO)C_6H_4	67	120
b	i	k	–(CH=CH)$_2$–		4-(MeO)C_6H_4	83	120
b	m	l	–(CH=CH)$_2$–		4-*t*BuC_6H_4	69	120

[a] Yield of isolated products;

[b] L1 instead of L2 was used

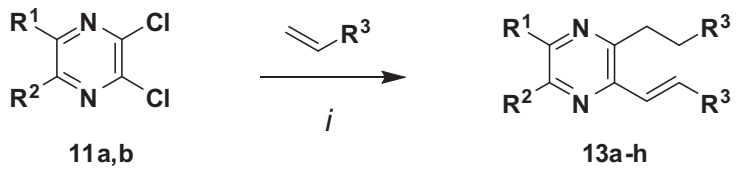
Table 6. Optimization of the reaction condition for **12a,b,g,h**

Entry	T [°C]	% (**12a**) [a]	% (**12b**) [a]	% (**12g**) [a]	% (**12h**) [a]
1	70	- [b]	- [b]	- [b]	- [c]
2	80	52	48	- [b]	- [c]
3	90	83	82	- [b]	- [b]
4	100	- [c]	- [c]	- [b]	- [b]
5	110	- [c]	- [c]	59	36
6	120	- [c]	- [c]	78	67

Reaction condition: L 2 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), DMF

[a] isolated yield; [b] No Conversion; [c] Experiment was not carried out

The $Pd(OAc)_2$-catalyzed reaction of 2,3-dichloropyrazine (**11a**) with acrylates **3a-d,k,n,o** (2.5 equiv.), carried out at 110 rather than 90 °C, afforded the 2-alkenyl-3-alkylpyrazines **13a-g** in 69-83% yield (Scheme 6, Table 7). The formation of products **13a-g** can be explained by partial reduction of the in situ formed 2,3-dialkenylpyrazines. The reaction of 2,3-dichloroquinoxaline (**11b**) with *tert*-butyl acrylate (**3n**), carried out at 130 ˚C , gave 2-alkenyl-3-alkylquinoxaline **13h**.



Scheme 6. Synthesis of 2-alkenyl-3-alkyl-pyrazines and quinoxalines **13a-h**. *Conditions*: *i*,: **3a-d, k, n, o** (2.5 equiv.), $Pd(OAc)_2$ (5 mol-%), L2 (10 mol-%), NEt_3, DMF, 110 ˚C, 48 h (for **13a-g**), 24 h (for **13h**)

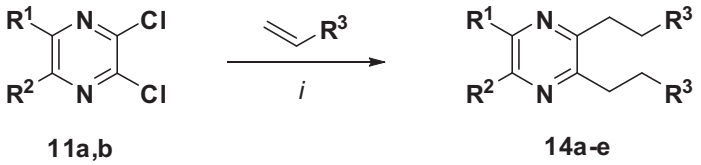
Table 7. Synthesis of **13a-h**

11	**3**	**13**	R^1	R^2	R^3	% (**13**) [a]	*T* [°C]
a	k	a	H	H	CO_2Me	78	110
a	a	b	H	H	CO_2Et	71	110
a	b	c	H	H	CO_2nBu	74	110
a	c	d	H	H	CO_2iBu	75	110
a	n	e	H	H	CO_2tBu	83	110
a	d	f	H	H	CO_2nHex	79	110
a	o	g	H	H	CO_2R [b]	69	110
b	n	h	$-(CH=CH)_2-$		CO_2tBu	75	130

[a] Yield of isolated products;

[b] $R = CH_2CH(Et)(CH_2)_3CH_3$

The $Pd(OAc)_2$-catalyzed reaction of **11a** with 2.5 equiv. of acrylates **3b,c,n**, carried out at 140 °C, afforded the 2,3-dialkylpyrazines **14a-c** in good yields (Scheme 7, Table 8). The formation of products **14a-c** can be explained by complete reduction, due to the high temperature. The reaction of **11b** with **3o** and **3n**, carried out at 150 °C, afforded the 2,3-dialkylquinoxalines **14d** and **14e**, respectively.



11a,b **14a-e**

Scheme 7. Synthesis of 2,3-dialkyl-pyrazines and quinoxalines **14a-e**. *Conditions*: *i*: **3b,c,n,o** (2.5 equiv.), $Pd(OAc)_2$ (5 mol-%), L2 (10 mol-%), NEt_3, DMF, 140 ˚C, 48 h (for **14a-c**), 150 ˚C 24 h (for **14d,e**).

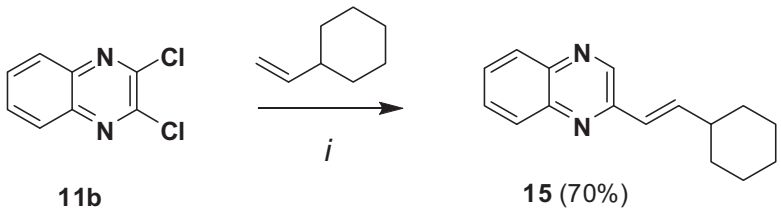
Table 8. Synthesis of **14a-e**

11	**3**	**14**	R^1	R^2	R^3	% (**14**) [a]	*T* [°C]
a	b	a	H	H	CO_2nBu	69	140
a	c	b	H	H	CO_2iBu	76	140
a	n	c	H	H	CO_2tBu	70	140
b	o	d	–(CH=CH)$_2$–		CO_2R [b]	69	150
b	n	e	–(CH=CH)$_2$–		CO_2tBu	77	150

[a] Yield of isolated products;

[b] R = $CH_2CH(Et)(CH_2)_3CH_3$

The $Pd(OAc)_2$-catalyzed reaction of **11b** with 1.25 rather than 2.5 equiv. of **3l**, carried out at 120 °C, afforded the 2-alkenylquinoxaline **15** in 70% yield (Scheme 8). The formation of product **15** can be explained by partial reduction of the in situ formed 2-chloro-3-alkenylquinoxaline.



11b **15** (70%)

Scheme 8. *Conditions*: *i*, Pd $(OAc)_2$ (5 mol-%), **L2** (10 mol-%), 3l (1.25 equiv.) NEt_3, DMF, 120 ˚C, 48 h.

2.3 Conclusion

I have synthesised 2,3-dialkenyl-, 2-alkenyl-3-alkyl-, and 2,3-dialkylpyrazines and their quinoxaline derivatives based on Heck cross-coupling reactions of 2,3-dichloropyrazine and quinoxaline. An increase of the reaction temperature results in partial or complete hydrogenation of the double bond. Electrocyclization reactions of the 2,3-dialkenylpyrazines and –quinoxalines proved to be unsuccessful (no conversion).

Synthesis of 7,8-Diarylflavones by Site-Selective Suzuki-Miyaura Cross Coupling Reactions of the Bis(triflate) of 7,8-Dihydroxyflavone

3.1 General Introduction

The Suzuki-Miyaura reaction has become a most significant synthetic process for the construction of C-C bonds. Among the various cross coupling reactions, the Suzuki-Miyaura reaction is widely used to prepare compounds which are pharmacological active and used in pharmaceutical industries.[54] The reactions involve, for example, the palladium catalyzed cross coupling between organoboron compounds and aryl halides. The scope of the reaction is not restricted to aryl derivatives, but includes also alkyl, alkenyl and alkynyl compounds. The reaction also works well with triflates (the OH group is converted into OTf with triflic anhydride); thus, phenolic compounds can be arylated by this method. Boronic esters, boranes or boronic acids can be used. Among the halides, the relative reactivity is I > OTf > Br > Cl.[55]

The mechanism of the Suzuki reaction involes three steps.The first step is the oxidative addition of organic halides to Pd(0) to form organopalladium halides. In the second step, a transmetallation with the boronic acid provides a diorganopalladium complex, which undergoes reductive elimination and regeneration of the palladium catalyst. Different types of bases are used in this reaction, e.g. potassium carbonate, potassium phosphate and cesium carbonate, which enhance the rate of the transmetalation by increasing the nucleophilicity of the organoboran compound by formation of an organoborate.[54,56] Several catalysts are used for this reaction, e.g. $Pd(OAc)_2$ together with phosphine ligands (such as PPh_3, PCy_3, SPhos and XPhos), $Pd(PPh_3)_2Cl_2$, or Pd $(PPh_3)_4$.[57]

Suzuki-Miyaura reactions have prominent applications in various fields. For example, non-linear optical (NLO) materials were prepared.[58] Terphenyls can be synthesized which are structural elements in liquid crystals and fluorescent compounds.[59] Poly(2,7-

carbazole) derivatives, which are active components in photovoltaic devices, have been also prepared by Suzuki-Miyaura reactions.[60]

In a couple of years, Prof. Peter Langer's research group has studied site-selective Suzuki-Miyaura reactions of polyhalogenated heteroaromatic and aromatic compounds or their triflates. In this context, regioselective Suzuki-Miyaura reactions of 2,3-dibromobenzofuran (**a**),[61] tribromopyrazoles (**b**),[62] 2,4,5,6-tetrachloropyrimidine (**c**),[63] tetrabromobenzoquinone (**d**),[64] 1,2-dibromo-3,5-difluorobenzene (**e**),[65] 1,4-dibromo-2-fluorobenzene (**f**),[66] 2,3,4-tribromothiophene (**g**),[67] and 2,3,5-tribromothiophene (**h**)[68] were reported (Figure 5).

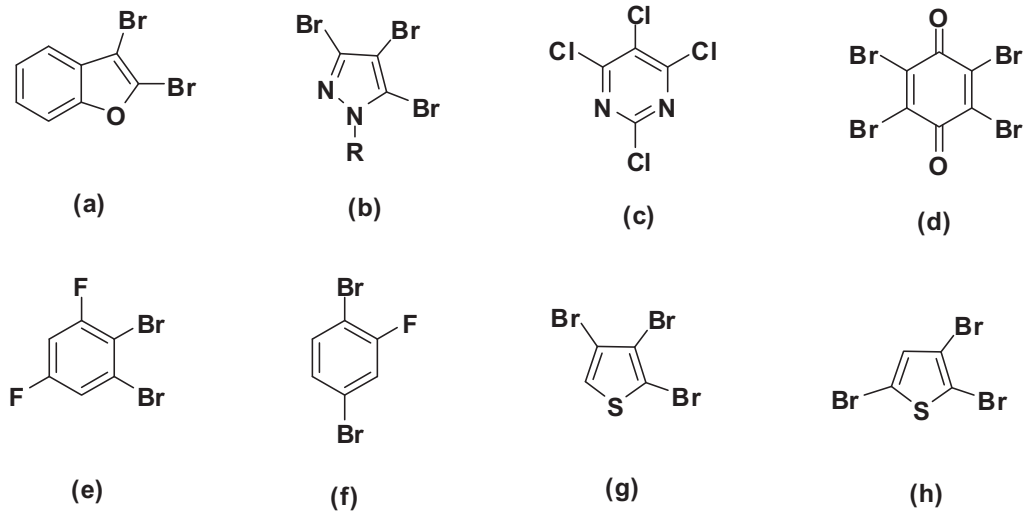


Figure 5. Suzuki reactions of vicinal halides studied in Prof. Langer's group

The Suzuki Miyaura reaction also provided excellent results for dihydroxylated substrates. Their OH groups were converted into OTf groups by using triflic anhydride and subsequently the site-selctivity of Suzuki reactions was studied. The Langer group reported regioselective Suzuki-Miyaura cross coupling reactions of the bis(triflates) of dimethyl 4-fluoro-3,5-dihydroxphthalate (**i**),[69] phenyl 1,4-dihydroxnaphthoate (**j**),[70] methyl-2,5-dihydroxbenzoate (**k**),[71] 3,4-dihydroxbenzoate (**l**),[72] 2,4-bis(hydroxy)di-phenylsulfone (**m**)[73] and 1,2-dihydroxyanthraquinone (**n**)[74] (Figure 6). All mentioned substrates proceeded with excellent site-selectivities.

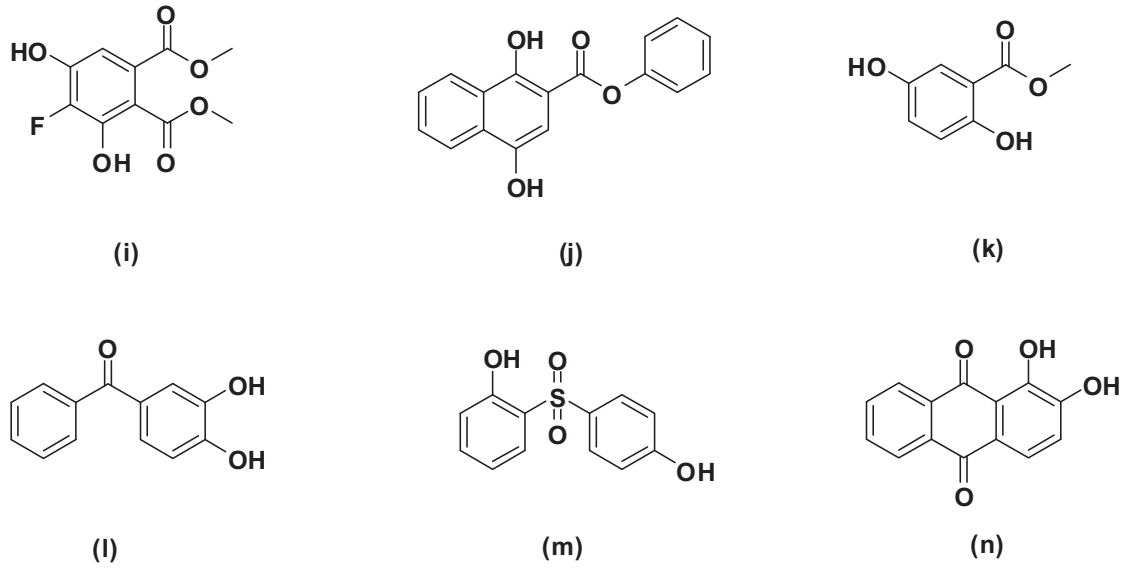


Figure 6. Suzuki Reaction Studies on Dihydroxy substrate in Prof. Langer's Group

3.2 Introduction to Flavones

Flavonoids are polyphenolic secondary metabolites that are widely distributed in higher plants. Flavones and flavonols are two major classes of flavonoids. Flavonols are present in fruits and vegetables, they have a 3-hydroxyflavone backbone.[75] Flavonols are potent inhibitors of CYP3A4, an enzyme which is responsible for the metabolism of many pharmaceutical drugs in the body.[76] Flavones are present in flowers, leaves and fruits of living plants as flavonoid glycosides. They have a 2-phenyl-1-benzopyran-4-one backbone. The difference between flavones and flavonols is the OH group located at C-3 position; flavonols have an OH group at C-3, while flavones have no OH group at C-3.[77] Flavones are of considerable pharmacological relevance and are widespread in nature as plant metabolites. Examples include various simple natural products, such as Chrysin, Apigenin, Luteolin, Scutellarein, or Wogonin, which have shown CYP2C9 inhibition (Figure 7).[77,78] Several flavones show activity against neurological disorders. Recently, Keqiang Ye and co-workers have revealed the fact that 7,8-dihydroxyflavone acts as a selective TrKB (tyrosine kinase receptor B) agonist, which is a powerful therapeutic tool for the treatment of various neurological diseases.[79] Many studies have shown that chrysin has anti-inflammation, anti-cancer and anti-oxidation, and anti-HIV effects.[80]

Natural anti-oxidant tangeretin shows significant protective effects against Parkinson's disease.[81]

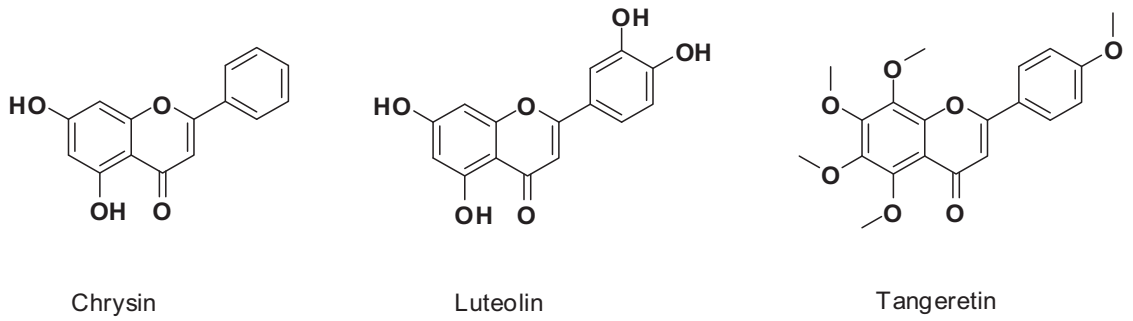


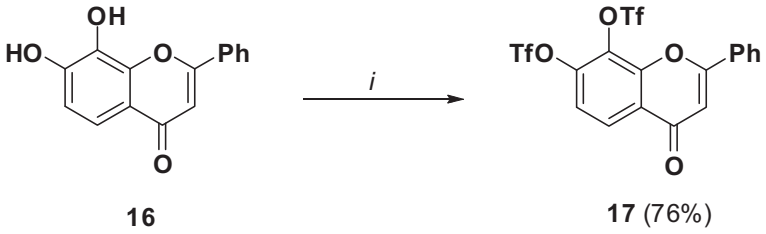
Figure 7. Some examples of natural product Flavones.

7,8-Dihydroxyflavone was synthesized starting from 2,3,4-trihydroxyacetophenone and benzoyl chloride in two steps via Baker-Venkatarama rearrangement.[82] It was also prepared by reaction of 2-fluorobenzoyl chloride, followed by cyclization of the intermediate benzophenone in the presence of sodium carbonate.[83] A new annellated 1,4-benzodioxane was prepared by reaction of 7,8-dihydroxyflavone with ethyl 2,3-dibromo-propanoate.[84] Despite the great pharmacological importance of flavones, only a few applications of palladium catalyzed cross coupling reactions to flavone-derived halides or triflates have been reported.[85] Suzuki reactions of halogenated flavones have been reported. [86] In my thesis, I have transformed the OH group of 7,8-dihydroxyflavone into triflates and then applied Suzuki reactions which proceed with excellent site-selectivity.

3.3 Results and discussion

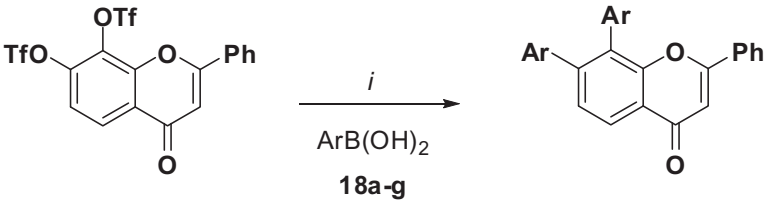
Commercially available 7,8-dihydroxyflavone (**16**) was transformed to its bis(triflate) **17** in 76% yield (Scheme 9) by using triflic anhydride (2.4 equiv) and pyridine (4 equiv). The addition of triflic anhydride was performed at -78 °C. The Suzuki-Miyaura reaction of **17** with arylboronic acids **18a-g** (2.6 equiv.) afforded the 7,8-diarylflavones **19a-g** in 59-74% yield (Scheme 10, Table 9). The reaction conditions were systematically optimized for derivatives **19a,c,e** (Table 10). Both electron-poor and electron-rich arylboronic acids could be successfully employed. The best yields were obtained using $Pd(PPh_3)_4$ (5 mol-%) as the catalyst and K_3PO_4 (4.0 equiv.) as the base. The reactions were carried out in 1,4-dioxane at 100 °C for 4 h (entry 4).The yields dropped when

$Pd(PPh_3)_2Cl_2$ (5 mol-%) or $Pd(OAc)_2$ (5 mol-%) in the presence of L2 or $P(OEt)_2Ph$ (10mol-%) were employed (entries 1-3). Therefore, the optimized condition given in entry allowed to prepare diarylflavones in good yields.



16 **17** (76%)

Scheme 9. Synthesis of **17**. *Reagents and conditions:* (*i*) **16** (1.0 equiv), Tf_2O (2.4 equiv), pyridine (4.0 equiv), CH_2Cl_2, -78 → 0 °C, 4h.



17 **19a-g**

Scheme 10. Synthesis of **19a-g**. *Reagents and conditions:* (*i*), **17** (1.0 equiv), **18a-g** (2.6 equiv), $Pd(PPh_3)_4$ (5 mol-%), K_3PO_4 (4.0 equiv), 1,4-dioxane, 100 °C, 4 h.

Table 9. Synthesis of **19a-g.**

18,19	R	% (**19**) [a]
a	4-EtC_6H_4	70
b	4-*t*BuC_6H_4	59
c	4-ClC_6H_4	72
d	4-FC_6H_4	62
e	4-$(MeO)C_6H_4$	68
f	4-MeC_6H_4	74
g	3,5-$Me_2C_6H_3$	71

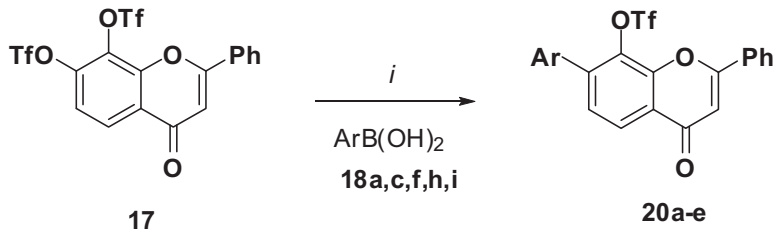
[a] Yields of isolated products

Table 10. Optimization of the reaction condition for **19a,c,e**

Entry	Conditions	Temp [°C]	(**19a**) [a] %	(**19c**) [a] %	(**19e**) [a] %
1	$P(OEt)_2Ph$(10mol-%), $Pd(OAc)_2$ (5 mol-%), K_3PO_4	90	32	26	35
2	$Pd(PPh_3)_2Cl_2$(5mol-%), K_3PO_4	100	39	41	44
3	L2 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), K_3PO_4	90	30	34	27
4	$Pd(PPh_3)_4$ (5mol-%), K_3PO_4	100	70	72	68

[a] Yields of isolated products

The Suzuki-Miyaura reaction of **17** with arylboronic acids **18a,c,f,h,i** (1.0 equiv.) afforded the 7-aryl-8-trifluorosulfonyloxy-flavones **20a-e** in 66-76% yield with very good site-selectivity (Scheme 11, Table 11). During the optimization, it proved to be important to use exactly 1.0 equiv. of the arylboronic acid and to carry out the reaction at 70 instead of 100 °C. Both electron-poor and electron-rich arylboronic acids were successfully used. The reaction conditions were systematically optimized for derivatives **20a,d** (Table 12). The best yields were obtained using $Pd(PPh_3)_4$ (5 mol-%) as the catalyst and K_3PO_4 (1.5 equiv.) as the base. The reactions were carried out in 1,4-dioxane at 70 °C for 4 h (entry 3, Table 12). The yields were observed lower when $Pd(PPh_3)_2Cl_2$ (5 mol-%) or $Pd(OAc)_2$ (5 mol-%) in the presence of L2 (10mol-%) were employed (entry 1-2).



Scheme 11. Synthesis of **20a-e**. *Reagents and conditions: i;* **17** (1.0 equiv.), **18a,c,f,h,i** (1.0 equiv), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (5 mol %), 1,4-dioxane, 70 °C, 4 h.

Table 11. Synthesis of **20a-e**

18	**20**	R	% (**20**) [a]
a	a	4-EtC_6H_4	72
c	b	4-ClC_6H_4	66
f	c	4-MeC_6H_4	76
h	d	4-(CF_3)C_6H_4	69
i	e	4-(HC=CH_2)C_6H_4	74

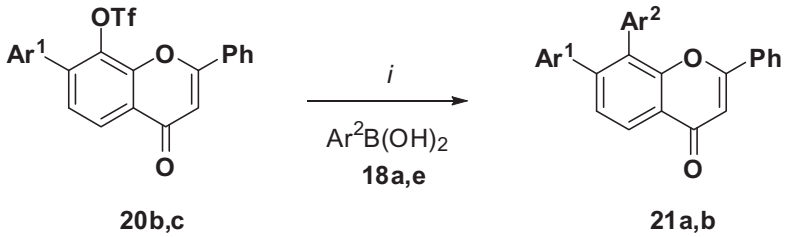
[a] Yields of isolated products

Table 12. Optimization of the reaction condition for **20a,d**

Entry	Conditions	Temp [°C]	(**20a**) [a] %	(**20d**) [a] %
1	$Pd(PPh_3)_2Cl_2$(5mol-%), K_3PO_4, Dioxane	70	55	42
2	L2 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), K_3PO_4, Dioxane	70	33	19
3	$Pd(PPh_3)_4$(5mol-%), K_3PO_4, Dioxane	70	72	69

[a] Yields of isolated products

The Suzuki-Miyaura reaction of **20c** and **20b** with arylboronic acids **18a** and **18e** (1.3 equiv.) afforded the 7,8-diarylflavones **21a** and **21b**, respectively (Scheme 12, Table 13). The reactions were carried out at 100 °C.



Scheme 12. Synthesis of **21a,b**. *Reagents and conditions:* (*i*) **20b,c** (1.0 equiv), **18a,e** (1.3 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (5 mol %), 1,4-Dioxane, 100 °C, 4h.

Table 13. Synthesis of 7,8-diarylflavones **21a,b**

18	**20**	**21**	Ar^1	Ar^2	% (**21**) [a]
a	c	a	4-MeC_6H_4	4-EtC_6H_4	66
e	b	b	4-ClC_6H_4	4-$(MeO)C_6H_4$	73

[a] Yields of isolated products

All products were characterized by spectroscopic methods. The constitutions of products **20a-e** and **21a,b** were proved by 2D NMR experiments (HMBC, NOESY). The structure of **19f** was independently confirmed by X-ray crystal structure analysis (Figure 8).[87] Inspection of the X-ray structure shows that the flavone unit (including the phenyl group located at C2) in plane. The other two phenyl groups are twisted out of plane, due to steric reasons.

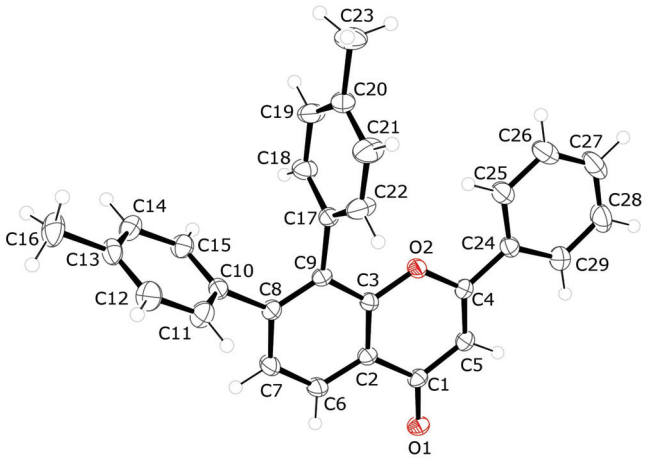


Figure 8. Molecular structure of **19f**

The structure of **20a** was confirmed by 2D-NMR correlation using HMQC, HMBC and NOESY. The chemical shift values of the carbon atoms were assigned with the help of an HMQC experiment, δ = 8.18 (125.4, C-5), 7.44 (127.4, C-6). In the HMBC spectrum, the aromatic proton of C-6 showed a strong coupling with C-5 (125.4), C-7 (131.6), C-1′ (135.1). In the NOESY spectrum, aromatic proton (δ = 7.44, C-6) showed an interaction

with proton 5-H (δ = 8.18). These information show that the 4-(Et)C_6H_4 moiety is attached to carbon atom C-7 (Figure 9).

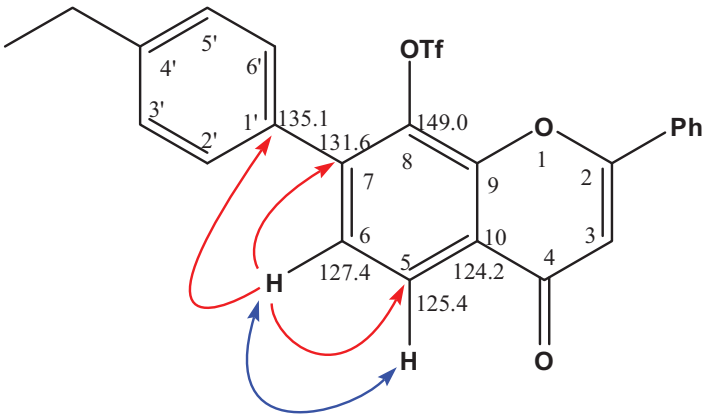


Figure 9. **HMBC** and **NOESY** correlations of **20a**

The site-selective formation of **20a-e** can be explained by steric and by electronic reasons. The first attack of palladium(0)-catalyzed cross-coupling reactions generally occurrs at the more electronical deficient and sterically less hindered position. Position 7 of **17** is sterically less hindered than position 8. In addition, position 7 (located *meta* to the ether oxygen atom and *para* to the carbonyl group) is considerably more electron-deficient than position 1 (located *ortho* to the ether oxygen atom and *meta* to the carbonyl group).

3.4 Conclusion

I have synthesized 7,8-diarylflavones by Suzuki-Miyaura reactions of the bis(triflate) of 7,8-dihydroxyflavone. The first attack proceeded with very good site-selectivity at position 7.

Regioselective Sonogashira Cross-Coupling Reactions of 2,4,5,6-Tetrachloropyrimidine and Fluorescence Properties of Bis-, Tris-, and Tetrakis(arylethynyl)pyrimidines

4.1 General Introduction

The Sonogashira reaction was developed in 1975. It is the coupling reaction between aryl or alkenyl halides or triflates and terminal alkynes. Two catalysts, palladium(0) and co-catalyst copper(I), are used in this reaction. The reaction requires a basic medium in order to deprotonate the alkyne. Several bases are used, such as triethylamine, diethylamine and *N,N*-diisopropylamine. Diisopropylamine and DMF are often used as solvents.[88]

The reactivity depends on the type of the aryl or alkenyl halides; the reactivity order is vinyl iodide > vinyl bromide > vinyl chloride > aryl iodide > aryl bromide > aryl chloride.[89] A possible drawback of the Sonogashira reaction is the in situ generation of a copper acetylide which may produce homocoupling products (diynes) along with the desired products. For Sonogashira reactions copper and ligand free variants have been developed.[90] The Sonogarshira reaction is the key step in several total syntheses of natural products photophysical materials.[91] In recent years, Professor Langer's research group has studied regioselective Sonogashira coupling reactions of N-methylpyrrole (**a**),[92] tetrabromoselenophene (**b**)[93] and phenyl-1,4-dihydroxynaphthoate (**c**) (Figure 10).[94]

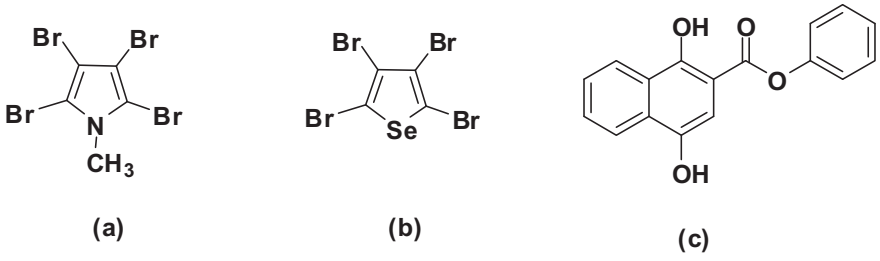


Figure 10. Substrates for Sonogashira reactions studied in Prof. Langer's group

4.2 Introduction

The chemistry of pyrimidine and its derivatives has been intensively studied, due to their pharmacological and physical properties. Pyrimidine derivatives, including uracil, thymine, cytosine, adenine, and guanine, are fundamental building blocks for deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Vitamin B1 (thiamine) is a well-known example of a naturally occurring pyrimidine that is encountered in our daily lives. Synthetic pyrimidine-containing compounds are being used in pharmaceutical industry as potent drugs. Pyrimethamine and trimethoprim are two prominent pyrimidine-containing chemotherapeutics. Trimethoprim is widely used as a general systemic antibacterial agent in combination with sulfamethoxazole. Pyrimethamine is used as anti-malarial and anti-protozoal drug in combination with sulfadiazine.[95] Multiple pharmacological studies for pyrimidine derivatives have shown significant importance and have made pyrimidine to a core structure which is important for analgesic, anti-hypertensive, anti-pyretic, anti-inflammatory, anti-neoplastics, anti-bacterials, anti-protozoal, anti-fungal, anti-viral and anti-folate drugs. They also play a role as pesticides, herbicides, and plant growth regulators.[96] Recent studies have shown that bicyclic pyrimidine nucleoside analogues are potent and selective inhibitors of Varicella Zoster Virus (VZV) replication.[97] Tao Wang reported some derivatives of pyrimidine which were identified as potent inhibitors of TrK kinase which play a critical role in cell signaling and cancer related processes.[98] Movassaghi reported a single step synthesis of pyrimidine derivative by cycloisomerization of amides and nitriles.[99] One-pot syntheses of aryl-substituted pyrimidines were performed through a coupling-isomerization sequence with subsequent cyclocondensation-aromatization with pyrimidium salts.[100]

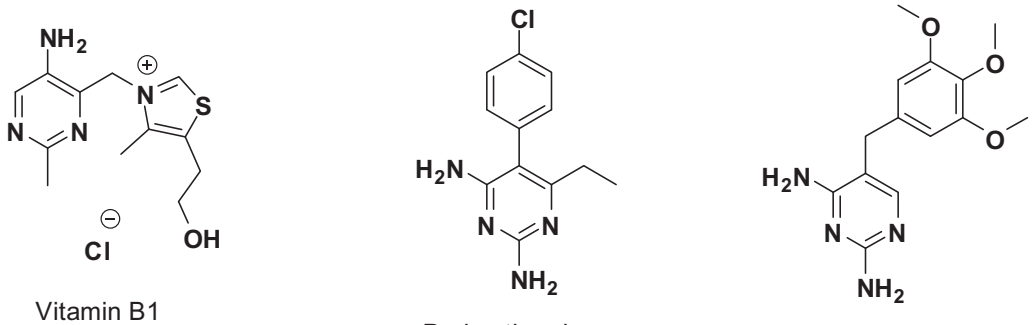


Figure 11. Some common examples of pyrimidine derivatives.

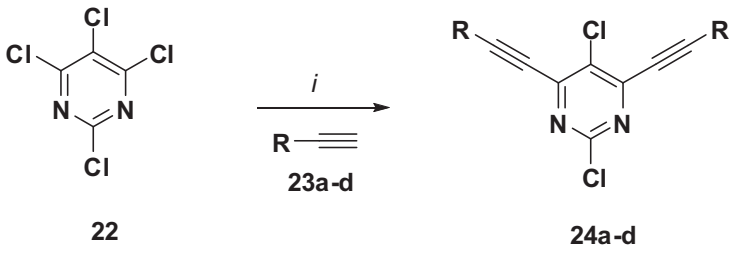
Monohalogenated pyrimidines have been used in Negishi and Suzuki coupling reactions.[101] Sonogashira, Negishi and Suzuki reactions of 2,4,6-trichloropyrimidine have been reported.[102] Recently, Suzuki-Miyaura coupling reactions of 2,4,5,6-tetachloro-pyrimidine have been studied by our group.[103]

Light emitting materials are applied in biological and material sciences. Conjugated organic systems have significant applications in various fields, such as LC (liquid crystals), FET (field effect transistors), OLED (organic light emitting devices), photovoltaic cells, and 3D-optical memory devices.[104] When any heterocyclic moiety, such as pyridine, pyrazine, pyrimidine, is introduced into extended π-systems, it often brings extraordinary electronic and optical changes. These changes may result in liquid crystalline and fluorescence properties.[105] In this chapter, I have synthesized and optimized the reaction conditions to achieve convenient synthesis of Sonogashira products of bis-, tris- and tetrakis(arylethynyl)pyrimidines and studied their UV-Vis and fluorescence properties.

4.3 Results and Discussion

The Sonogashira reaction of commercially available 2,4,5,6-tetrachloropyrimidine (**22**) with different substituted aryl acetylenes **23a-d** (2.4 equiv) afforded the 4,6-bis(arylethynyl)pyrimidines **24a-d** (Scheme 13, Table 14) in 73-91% yields. Different reaction conditions were optimized for derivatives **24a,c** (Table 15) . During optimization $Pd(PPh_3)_4$ (10mol-%), $Pd(OAc)_2$ (5 mol-%) in the presence of PCy_3 (10 mol-%) were initially employed, but no satisfactory results were obtained.The progress of reactions were monitored at lower temperature (20-60°C), as higher temperature increases the chances for tri-alkynylated products. $Pd(PPh_3)_2Cl_2$ (10 mol-%) was found to be the best catalyst. Several solvents were tried, but several of them did not work well, while good yields were obtained when DIPA was used (entry 1-5, Table 15). Almost all bis-Sonogashira products were obtained in good to excellent yields.

The structure of **24c** was independently confirmed by X-ray crystal structure analysis (Figure 12). Analysis of the structure shows that all three aryl groups are in one plane.



Scheme 13. Synthesis of **24a – d**: conditions and reagents: **22**(1.0 equiv), **23a – d** (2.4 equiv), CuI (5 mol-%), $Pd(PPh_3)_2Cl_2$ (10 mol-%), DIPA , 55°C, 2 h.

Table 14. Synthesis of **24a-d.**

23,24	R	% (**24**) [a]
a	4-*t*BuC_6H_4	76
b	Ph	73
c	3-(MeO)C_6H_4	81
d	6-(MeO)$C_{10}H_6$	91

[a] Yields of isolated products

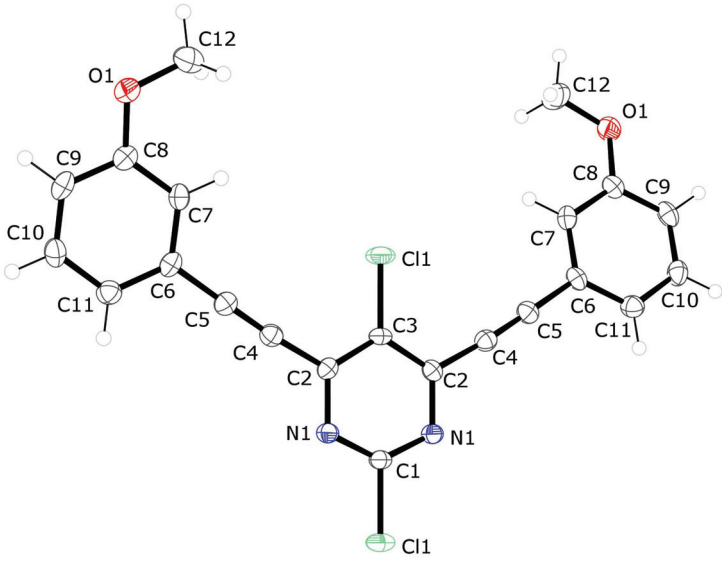


Figure 12. Molecular structure of **24c**

Table 15. Optimization of the reaction condition for **24a,c**

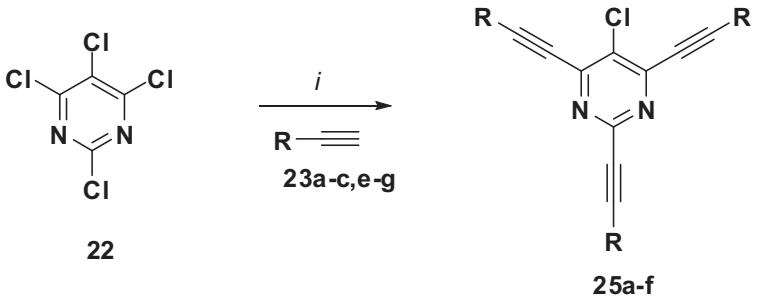
Entry	Conditions	Temp [°C]	Time (h)	(**24a**) [a] %	(**24c**) [a] %
1	PCy_3(10mol-%), $Pd(OAc)_2$ (5 mol-%), CuI, Toluene, Et_3N	50	6	- [b]	- [c]
2	PCy_3(10 mol-%), $Pd(OAc)_2$ (5 mol-%), CuI, Xylene, Et_3N	60	6	- [b]	- [c]
3	$Pd(PPh_3)_4$ (10mol-%), CuI, DMF, CS_2CO_3	60	4	31	26
4	L2 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), CuI, DMF, Et_3N	60	4	23	19
5	$Pd(PPh_3)_2Cl_2$(10mol-%), CuI, DIPA	55	2	76	81

[a] Yields of isolated products

[b] No Conversion

[c] Experiment was not carried out

The Sonogashira reaction of **22** with the substituted acetylenes **23a-c, e-g** (3.6 equiv.) afforded the tris(arylethynyl)pyrimidines **25a-f** (Scheme 14, Table 16) in 68-84 % yield.



Scheme 14. Synthesis of **25a–f**: conditions and reagents **22**(1.0 equiv), **23a–c, e-g** (3.6 equiv), CuI (5 mol-%), $Pd(PPh_3)_2Cl_2$ (10 mol-%), DIPA, 70°C, 2 h.

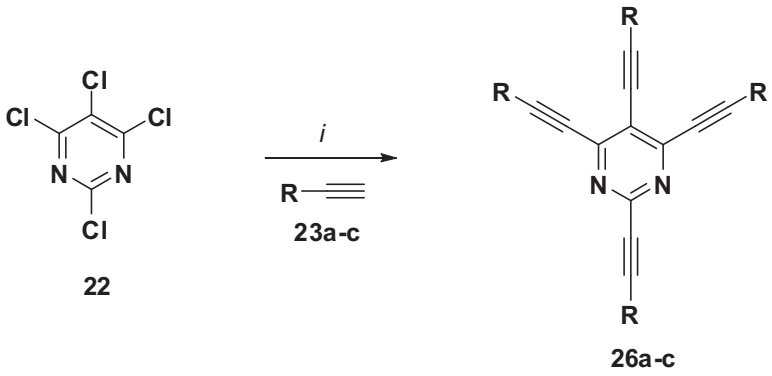
Table 16. Synthesis of **25a-f.**

23, 25	R	% (**25**) [a]
a, a	4-*t*BuC_6H_4	80
b, b	Ph	71
c, c	3-(MeO)C_6H_4	77
e, d	4-(Me)C_6H_4	84
f, e	C_7H_{11}	68
g, f	C_5H_7	69

[a] Yields of isolated products

For the synthesis of tetrakis(arylethynyl)pyrimidines the previously applied reaction conditions did not give tetra-alkynylated product. The reaction conditions were optimized for derivatives **26a,c** (Table 18). Unsuccessful attempts were made to improve the yield by varying solvents (DMF, DMA, toluene, xylene) with DIPA, triethylamine and cesium carbonate. During the optimization, $Pd(OAc)_2$ was used in the presence of various ligands such as PCy_3, PPh_3, L1, L2, but no satisfactory results were obtained. In fact, L1, L2 ligands provided the product, but the yields were very low. The effects of the base and of the solvent were evaluated and progress of reactions were observed (70-120 °C, 14-18 h) (entry 1-6, Table 18).The best yields were obtained when $Pd(PPh_3)_2Cl_2$ (10 mol-%) was used as catalyst, in dioxane with DIPA at 85°C for 16 h (entry 7, Table 18). Therefore, the optimized condition given in entry 6 allowed to prepare tetra-alkynylated product in good yields.

The Sonogashira coupling of **22** with **23a-c,** carried out at 85 °C for 16 hours and using the base DIPA (3 mL) and the solvent dioxane (7 mL), afforded **26a-c** (Scheme 15, Table 17) in 73-79% yields. It was concluded that the optimal conditons for the synthesis of tetra-alkynylated products include a combination of DIPA and dioxane, a temperature of 85 °C and longer reaction time (16-18 hours).



Scheme 15. Synthesis of **26a-c**: conditions and reagents **22** (1.0 equiv), **23a-c** (6.0 equiv), CuI (5 mol-%) $Pd(PPh_3)_2Cl_2$ (10 mol-%), DIPA (3 mL), Dioxane (7 mL), 85°C,16 h.

Table 17: Synthesis of **26a-c.**

23, 26	R	% (**26**) [a]
a	4-*t*BuC_6H_4	76
b	Ph	73
c	3-(MeO)C_6H_4	79

[a] Yields of isolated products

Table 18. Optimization of the reaction condition for **26a,c**

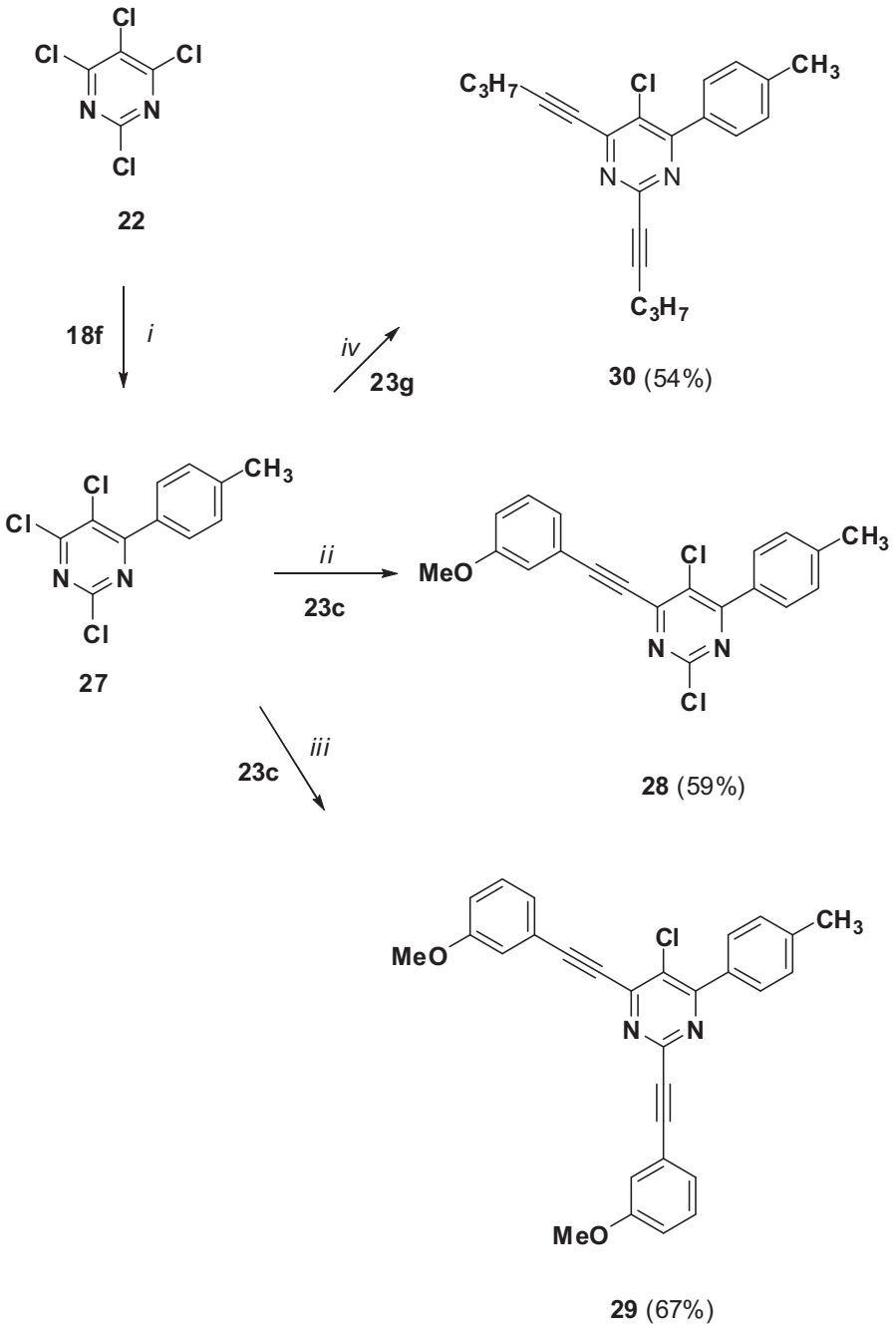
Entry	Conditions	Temp [°C]	(**26a**) [a] %	(**26c**) [a] %
1	$Pd(PPh_3)_2Cl_2$ (10mol-%), CuI, DIPA	70	- [b]	- [b]
2	PPh_3 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), CuI, DMA	120	- [b]	- [b]
3	PPh_3 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), CuI, Toluene	90	- [b]	- [c]
4	PCy_3 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), CuI, Xylene	100	- [b]	- [c]
5	$Pd(PPh_3)_4$ (10 mol-%), CuI, DMF,	120	- [b]	- [b]
6	L2 (10 mol-%), $Pd(OAc)_2$ (5 mol-%), CuI, DMF	100	23	19
7	$Pd(PPh_3)_2Cl_2$ (10mol-%), CuI, DIPA, Dioxane	85	76	79

[a] Yields of isolated products

[b] No Conversion

[c] Experiment was not carried out

The Suzuki-Miyaura reaction of 2,4,5,6-tetrachloropyrimidine (**22**) with 4-methylphenyl-boronic acid (**18f**) (1.0 equiv.), using 5 mol-% of $Pd(PPh_3)_2Cl_2$ at 60 °C for 2 hours, afforded product **27** in 76% yield. The Sonogashira reaction of **27** with 3-ethynylanisole (**23c**, 1 equiv.) yielded **28** in 59% yield. The reaction of **27** with 2 equiv. of **23c** afforded product **29** in 67% yields. The same reaction conditions applied with 1-pentyne (**23g**) afforded product **30** in 54% yields. During the optimization of the reaction conditions, the temperature played an important role. The mono-Sonogashira reaction of **22** and **27** was best carried out at 55 °C, while the bis-Sonogashira reactions of **27** had to be carried out at 70 °C.



Scheme 16. Synthesis of **27-30**: conditions : (i) **22** (1.0 equiv), 4-Methylphenylboronic acid (**18f**) (1.0 equiv) $Pd(PPh_3)_2Cl_2$ (5 mol-%), K_2CO_3 (2M, 1mL), Dioxane, 60 °C, 2 h (ii) **23c** (1.0 equiv), CuI (5 mol-%), $Pd(PPh_3)_2Cl_2$ (10 mol-%), DIPA (5 mL), 55 °C, 2 h. (iii) **23c** (2.0 equiv) CuI (5 mol-%), $Pd(PPh_3)_2Cl_2$ (10 mol-%), DIPA (5 mL), 70°C, 3 h. (iv) **23g** (2.0 equiv), CuI (5 mol-%), $Pd(PPh_3)_2Cl_2$ (10 mol-%), DIPA , 70°C, 3 h.

The structures of products **28** and **29** were independently confirmed by X-ray crystal structure analyses (Figures 13 and 14). The aryl groups attached to the alkyne unit are in plane. In contrast, the aryl moities of the biaryl uni are twisted out of plane, due to steric reasons.

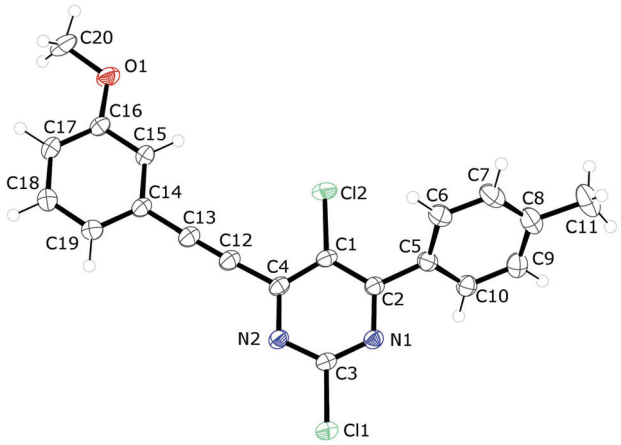


Figure 13. Molecular structure of **28**

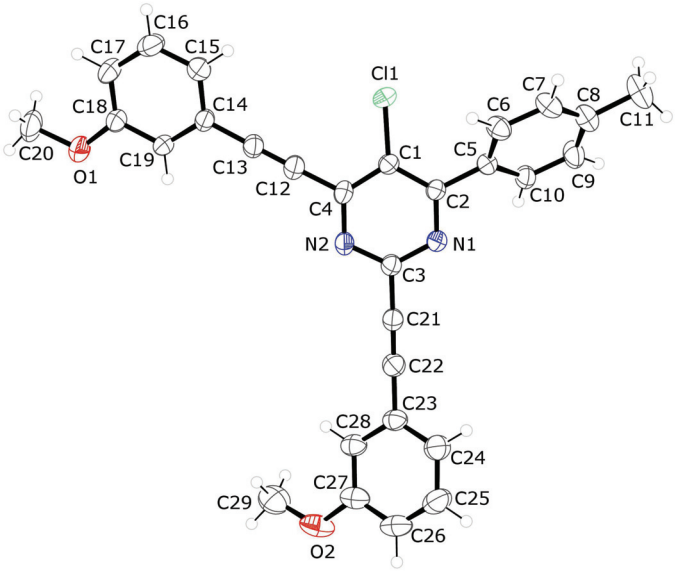


Figure 14. Molecular structure of **29**

The UV/Vis and fluorescence spectroscopic data of various pyrimidine derivatives, measured in chloroform at 25 °C, are summarized in Table 19. All the compounds collected in Table 19 contain a pyrimidine core; their absorption wavelengths (λ_{abs}) are in the UV region (297–371 nm) and their emission wavelengths (λ_{em}) (fluorescence) are in the UV or blue region (395–470 nm). Pyrimidines containing methoxy-substituted aryl groups exhibit absorptions and emissions in the range of λ_{abs}= 301–367 nm and λ_{em} = 426–470 nm, respectively. For *tert*-butyl derivatives, the absorptions and emissions are in the range of λ_{abs} = 325–371 nm and λ_{em} = 426–440 nm.

Table 19. Absorption and emission spectroscopic data for compounds in chloroform solution (10^{-4}–10^{-7}) at 25 °C.

Product	**$\lambda 4_{abs}$** [nm]	**Log ε**	**$\lambda 5_{em}$** [nm]	**Stokes Shift** [nm]
24a	371	3.86	426	55
24b	354	3.35	395	41
24c	367	3.74	470	103
	$\lambda 2_{abs}$ [nm]	**Log ε**	**$\lambda 4_{em}$** [nm]	
25b	312	4.25	406	94
25c	301	3.73	426	125
26a	325	4.01	440	115
26b	316	4.32	426	110
26c	302	4.11	438	136
29	297	4.19	405	108

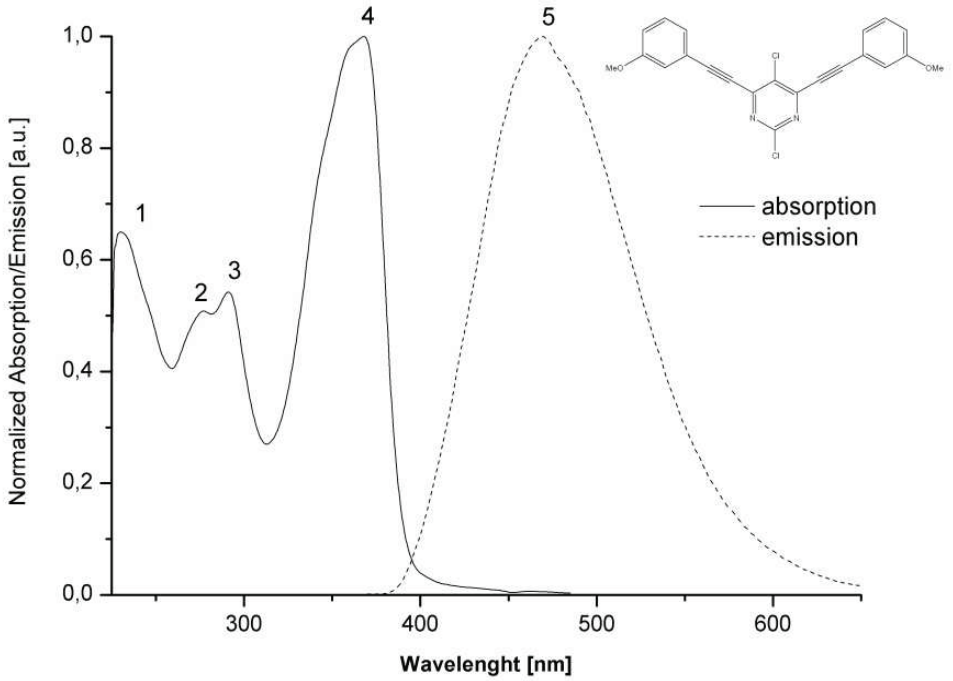


Figure 15. Absorption and emission spectra of compound **24c**

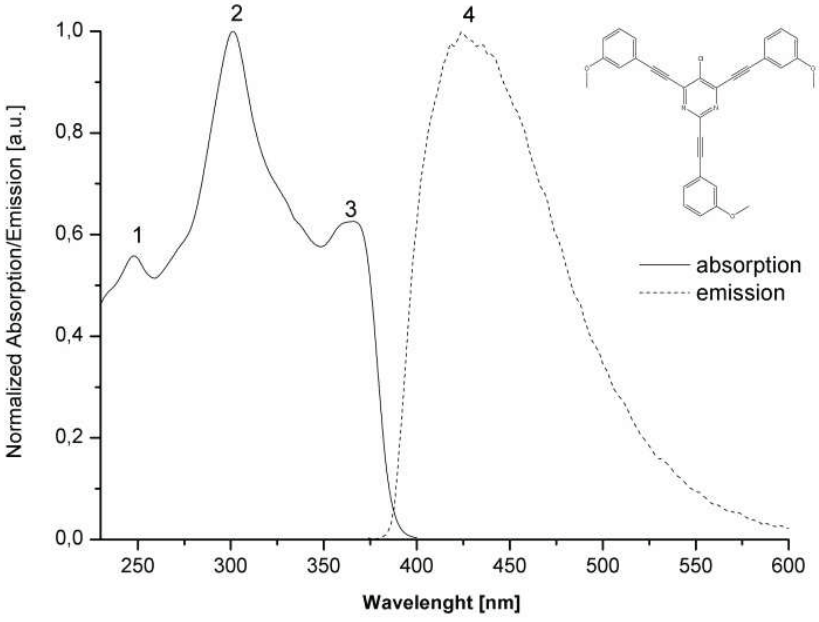


Figure 16. Absorption and emission spectra of compound **25c**

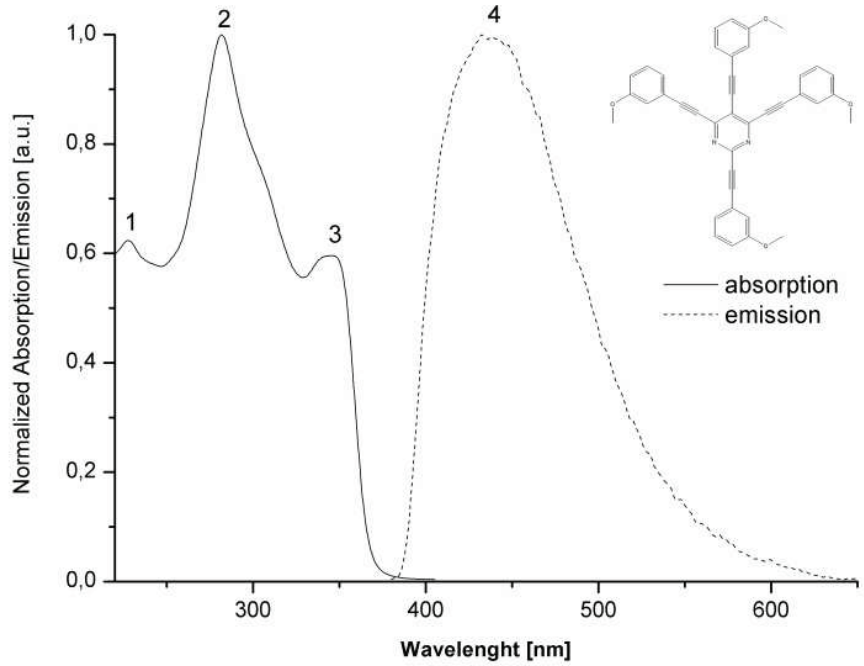


Figure 17. Absorption and emission spectra of compound **26c**

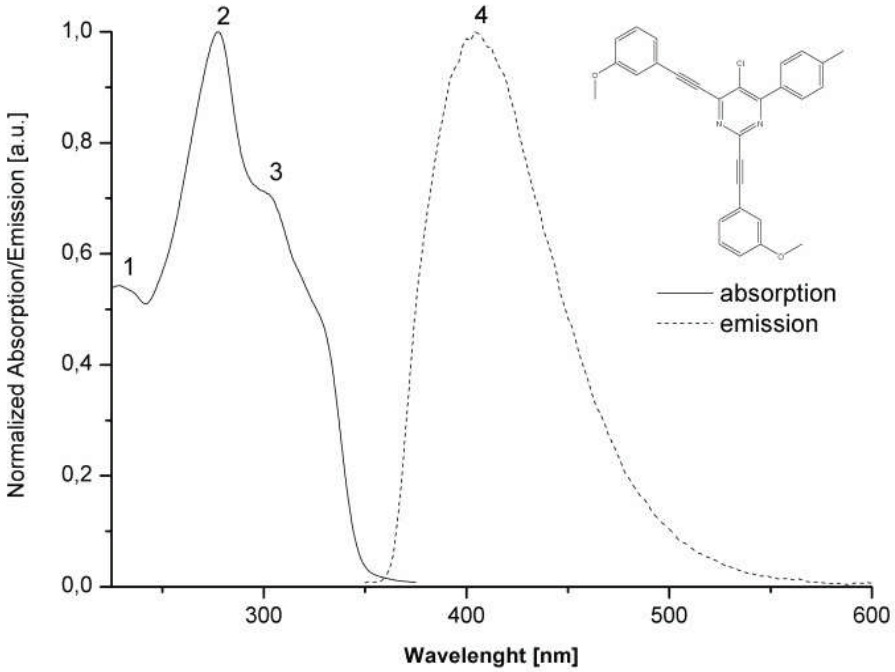


Figure 18. Absorption and emission spectra of compound **29**

The symmetrical Sonogashira products **24a** and **24b** exhibit absorptions $\lambda_{abs,\ max}$ = 298, 272 nm and emissions $\lambda_{em,\ max}$ = 426, 395 nm; the stokes shift is 55 and 41 nm, respectively. Compound **24c** showed absorptions $\lambda_{abs,\ max}$ = 276 nm and emissions $\lambda_{em,\ max}$ 470 nm; the stokes shift is 103 nm. A larger Stokes shift often corresponds to better overall fluorescence properties. Thus, compound **24c** has been found to possess the best fluorescence properties as compared to **24a** and **24b**. In this context, the presence of the strong electron donating group of **24c** plays an important role. In case of unsymmetrical Sonogashira products, compound **25c** shows a higher Stokes shift (125 nm), while **25b** shows a relatively small Stokes shift (94 nm). The same phenomenon can be observed for tetrakis(arylethynl)pyrimidines **26a-c**. While compound **26c** shows a higher Stokes shift (136 nm), **26a** and **26b** show smaller Stokes shifts. The mixed Suzuki-Sonogashira product **29** shows a Stokes shift of 108 nm.

4.4 Conclusion

I have synthesized bis-, tris-, and tetrakis(arylethynyl)pyrimidines by Sonogashira reactions. The fluorescence properties of the products have been studied.

Regioselective Sonogashira Coupling Reactions of 2,3,4,5-Tetrabromofuran and Fluorescence Properties of Bis-, Tris-, and Tetrakis(arylethynyl)furans

5.1 Introduction

Furan is an important five membered O-heterocycle which represents a versatile building block in synthetic organic chemistry. Substituted furans have attracted attention, due to their remarkable pharmacological and photo-physical properties.[106] Furan is widely found in many natural products, e.g. lophotoxin, pukalide, cembranolides, plakorsins A-C, rosefuran, kallolide, adociacetylene B, XH-14, perillene and dendrolasin.[107] Furan derivative ranitidine (brand name Zantac) is used in the treatment of peptic ulcer and gastroesophegeal reflux disease. Nitrofurantoin is used for the treatment of urinary tract infections and nifuroxazide is suggested for colitis and diarrhea treatment.[108] Much research efforts revealed the biological significance of furan derivatives, which have also shown anti-inflammatory, anti-tuberculosis, anti-cancer, and anti-fungal activities.[109]

Various methodologies have been developed for the synthesis of furans. In fact, furans have been used as a key precursor in the synthesis of many biologically active compounds. Furans can be synthesized by cyclodehydrations of 1,4 diketones,[110] condensations of α–halocarbonyl compounds with 1,3 dicarbonyl compounds,[111] cyclizations of β,γ–epoxyketones,[112] cyclodehydrations of γ–hydroxyl–α,β-unsaturated ketones,[113] heteroannulation reactions along with transition metal catalyzed cyclizations,[114] Feist-Benary cyclocondensations of different phosphoranes with α-haloketones,[115] base-mediated cyclizations of allenylalcohols and epoxides,[116] [3+2] annulations of alkynes with aldehydes,[117] and cyclizations of 1,4-diones in the presence of catalytic amounts of p-toluensulfonic acid.[118] Furan derivatives not only have pharmacological properties, but also they have shown excellent photophysical properties, due to which furan has gained attention in material sciences. In recent research, 2,5-bis(phenylethynyl)furan,[119] furan-nucleoside analogues,[120] bis-furylethene derivatives [121]

and furopyrimidine derivatives [122] have been reported to show non-linear optical (NLO), fluorescence and photochromic properties.

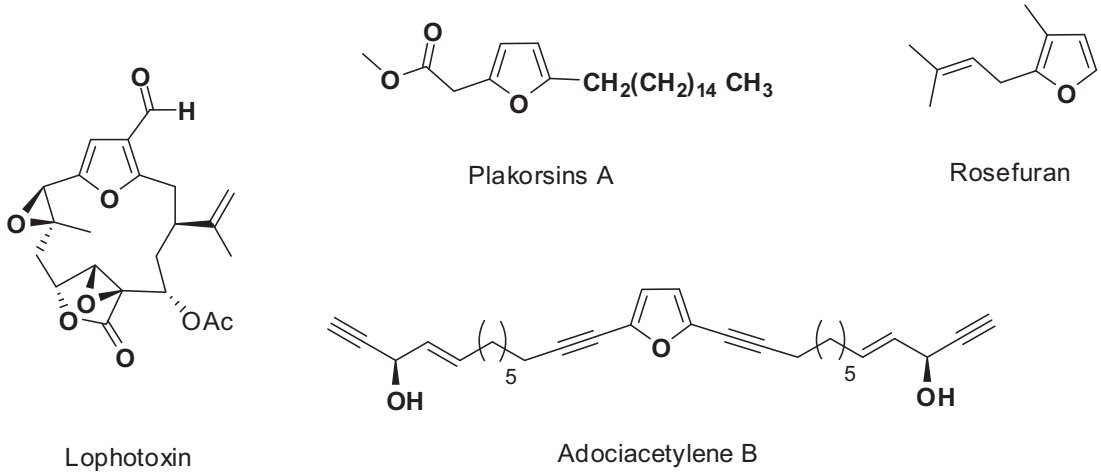
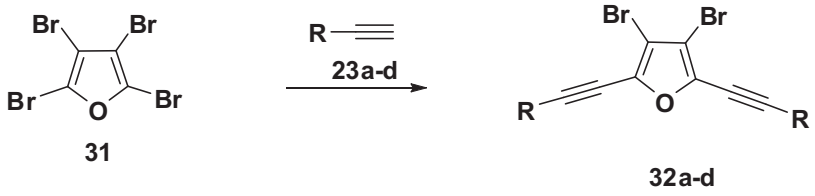


Figure 19. Some examples of furan natural products.

Sonogashira coupling reactions of 2,3-dibromofuran and 2,5-dibromofuran with site-selectivity in favour of position C-2 have been reported.[123] In my thesis, I have synthesized bis-, tris- and tetrakis(arylethnynl)furans by Sonogashira reactions of 2,3,4,5-tetrabromofuran. I have applied Suzuki reactions on bis-Sonogashira products and obtained the corresponding products. Most furan derivatives prepared in my thesis are fluorescence active.

5.2 Results and Discussion

The Sonogashira reaction of 2,3,4,5-tetrabromofuran (**31**) with different substituted alkynes (**23a-d**) (2.4 equiv) afforded 2,5-bis(arylethynyl)furans **32a-d** (Scheme 17, Table 20) in 71-81 % yield.



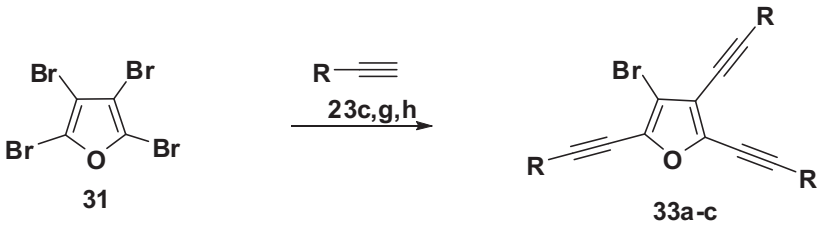
Scheme 17. Synthesis of **32a – d**: conditions and reagents: **31**(1.0 eq), **23a – d** (2.4 eq), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), DIPA (5mL) , 60°C, 2 h.

Table 20. Synthesis of **32a-d.**

23,32	R	% (**32**) [a]
a	4-tBuC_6H_4	78
b	Ph	71
c	3-(MeO)C_6H_4	81
d	6-(MeO)$C_{10}H_6$	76

[a] Yields of isolated products

The Sonogashira reaction of **31** with different substituted alkynes (**23c, g, h**) (3.6equiv) provided the 2,3,5-tris(arylethynyl)furans **33a-c** (Scheme 18, Table 21) in 64-77 % yield.



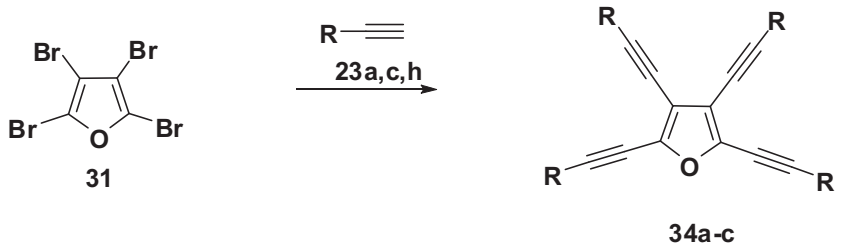
Scheme 18. Synthesis of **33a-c**: conditions and reagents **31**(1.0 eq), **23c,g,h** (3.6 eq), CuI (5 mol %) $Pd(PPh_3)_2Cl_2$ (10 mol %), DIPA (5mL), 60°C, 2 h.

Table 21. Synthesis of **33a-c**.

23,33	R	% (**33**) [a]
c a	3-(MeO)C_6H_4	77
h b	3-(Me)C_6H_4	73
g c	C_5H_7	64

[a] Yields of isolated products

The Sonogashira reaction of **31** with different substituted alkynes (**23a,c,h**) (4.8 equiv) afforded the 2,3,4,5-tetrakis(arylethynyl)furans **34a-c** (Scheme 19, Table 22) in 75-83 %.



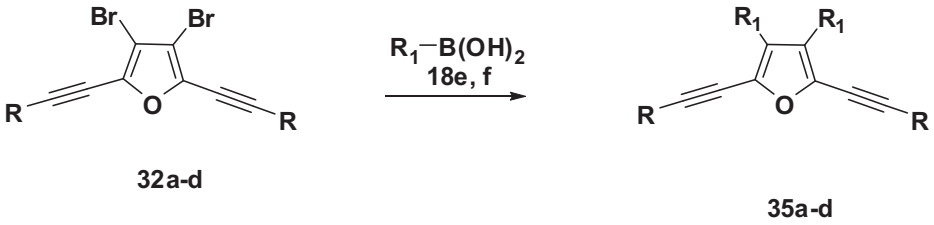
Scheme 19. Synthesis of **34a-c**: conditions and reagents: **31** (1.0 equiv), **23a,c,h** (4.8 equiv), CuI (5 mol-%) $Pd(PPh_3)_2Cl_2$ (10 mol-%), DIPA (5 mL), 75°C, 2 h.

Table 22. Synthesis of **34a-c.**

23,34	R	% (**34**) [a]
c, a	3-(MeO)C_6H_4	83
a, b	4-tBuC_6H_4	81
h, c	3-(Me)C_6H_4	75

[a] Yields of isolated products

The Suzuki-Miyaura reaction of 2,5-bis(arylethynyl)furans **32a-d** with 4-methoxy-phenylboronic acid (**18e**) and 4-methylphenylboronic acid (**18f**) resulted in the formation of **35a-d** (Scheme 20, Table 23) in good yields (69-79%).



32a-d

35a-d

Scheme 20. Synthesis of **35a-d**: conditions and reagents: **32a-d** (1.0 equiv), **18e,f** (2.0 equiv), $Pd(PPh_3)_2Cl_2$ (10 mol-%), K_2CO_3 (3equiv), Dioxane (5 mL), 70°C, 2 h.

Table 23. Synthesis of **35a-d.**

32, 35	**18**	R	R^1	% (**35**) [a]
a	e	4-tBuC_6H_4	4-(MeO)C_6H_4	76
b	e	Ph	4-(MeO)C_6H_4	69
c	e	3-(MeO)C_6H_4	4-(MeO)C_6H_4	79
d	f	6-(MeO)$C_{10}H_6$	4-(Me)C_6H_4	74

[a] Yields of isolated products

The structure of **35a** was confirmed by X-ray structure analysis (Figure 20). The aryl groups are twisted out of plane.

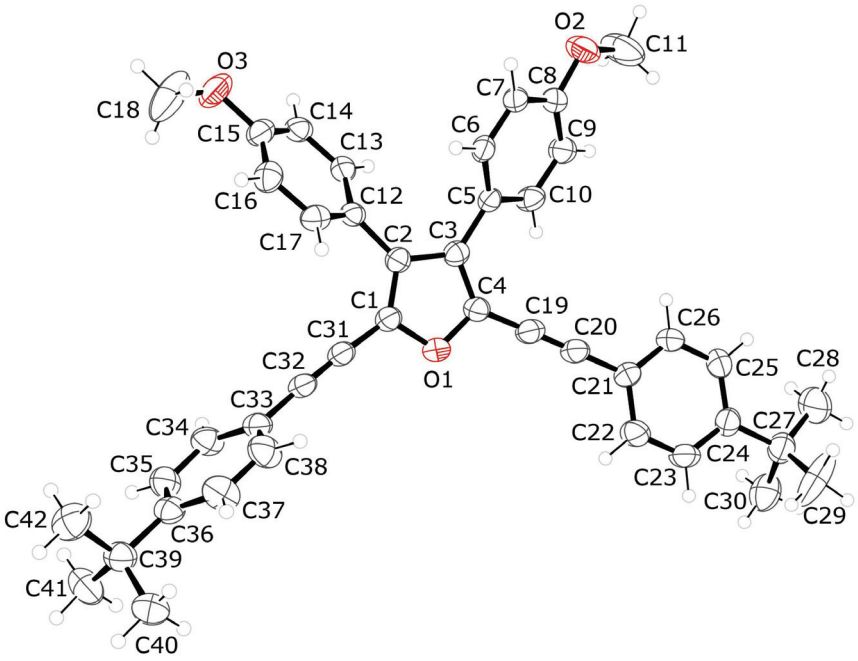


Figure 20. Molecular structure of **35a**

The UV/Vis and fluorescence spectroscopic data of various furan derivatives, measured in chloroform at 25 °C, are summerized in Table 24. All the compounds collected in Table 24 contain a furan core. Their absorption wavelengths (λ_{abs}) are in the UV region (303-374 nm) and their emission wavelengths (λ_{em}) (fluorescence) are in the UV or blue region (418-442 nm). Bis- and tris(arylethynyl)furans **32a-d** and **33a-c** did not show fluorescence. Tetrakis(arylethynyl)furan **34a-c** possess excellent fluorescence properties. All these compounds show high Stokes shift values (approx. 116-119 nm). Mixed Sonogashira-Suzuki products (**35a-d**) also show good fluorescence properties.

Table 24. Compounds in chloroform solution (10^{-4}–10^{-7}) at 25 °C.

Product	**$\lambda 1_{abs}$** [nm]	**Log ε**	**$\lambda 4_{em}$** [nm]	**Stokes Shift**[nm]
34a	309	3.83	425	116
34b	303	4.07	422	119
34c	304	4.16	420	116
35a	356	4.06	418	62
35b	355	4.25	420	65
35c	356	3.70	420	64
35d	374	3.47	442	68

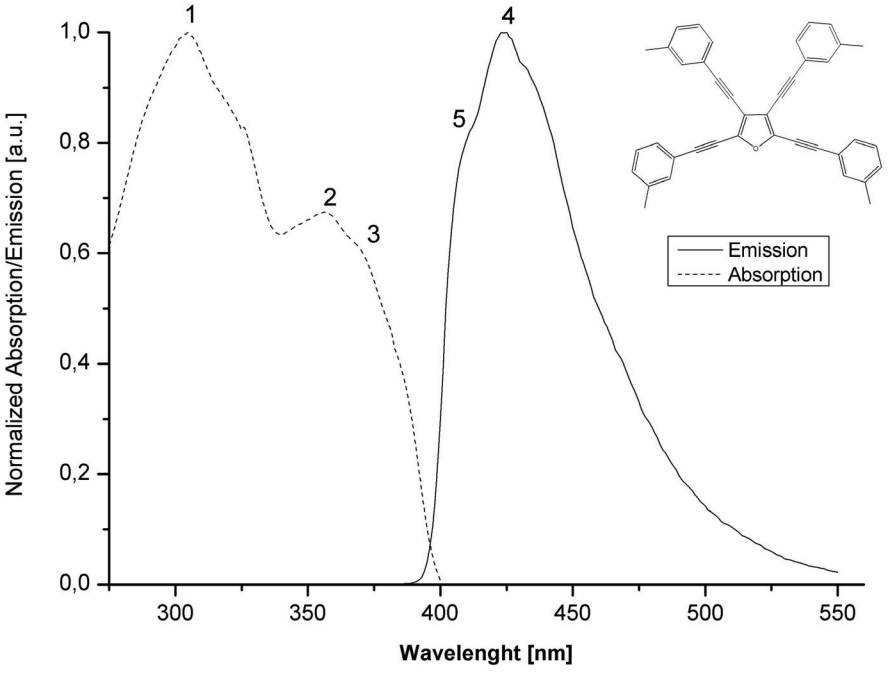


Figure 21. Absorption and emission spectra of compound **34c**

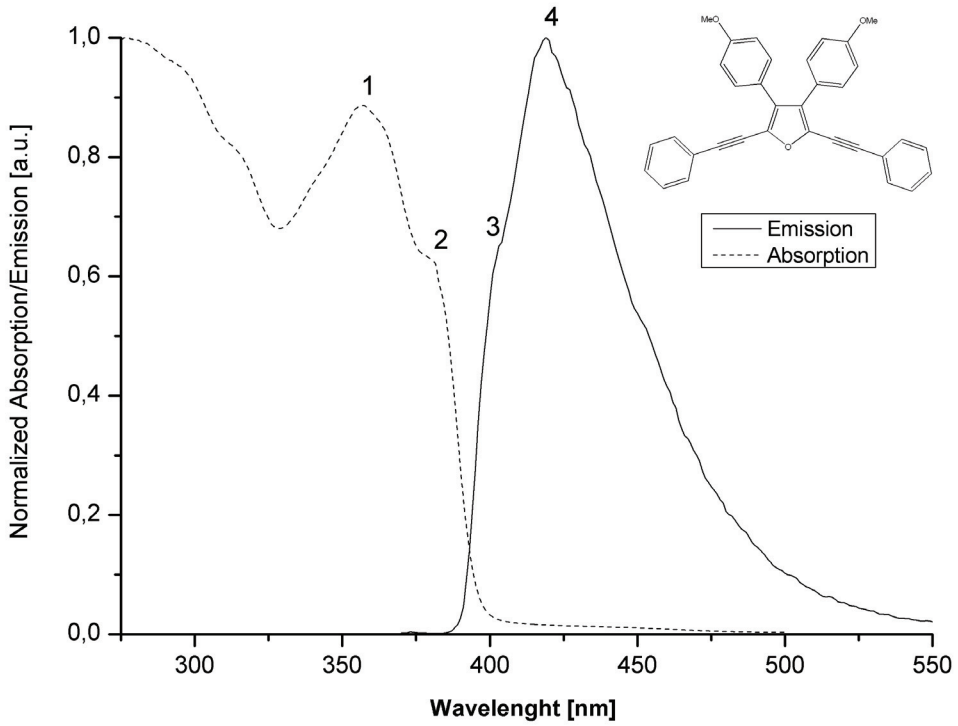


Figure 22. Absorption and emission spectra of compound **35b**

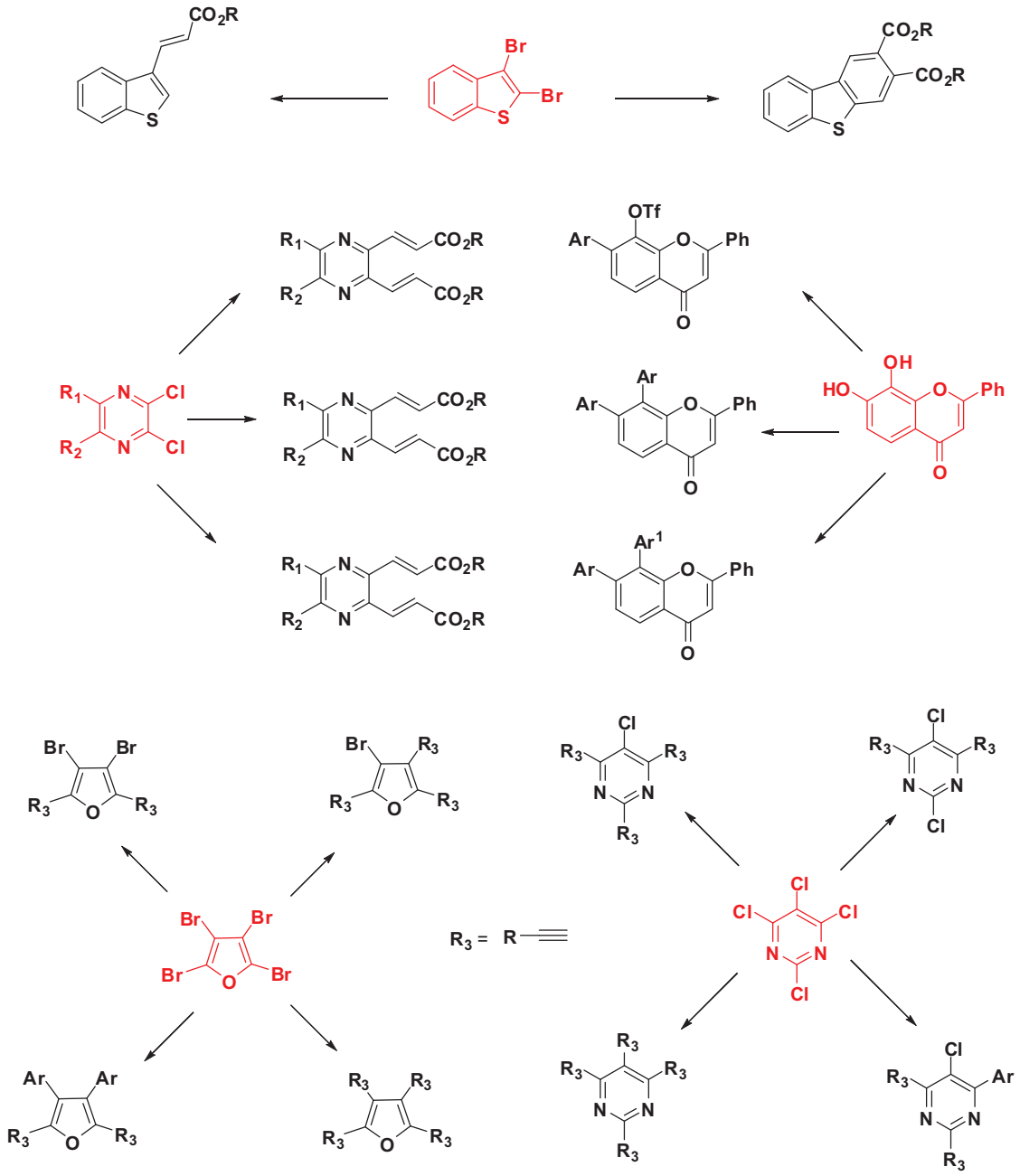
5.3 Conclusion

In conclusion, I have synthesized bis-, tris- and tetrakis(arylethynyl)furans by Sonogashira coupling reactions in good yields. Suzuki-Miyaura reactions of bis(aryethynyl)furans provided the corresponding products. Tetrakis(arylethynyl)furans show excellent fluorescence properties, while bis- and tris(arylethynyl)furan did not show a considerable fluorescence activity.

6 *Abstract*

The palladium(0)-catalyzed Heck cross coupling reactions of di- and tribromo benzothiophene provided functionalized dibenzothiophenes by domino twofold Heck / 6π-electrocyclization reactions. Heck cross coupling reactions of 2,3-dichloropyrazine and 2,3-dichloroquinoxaline provided 2,3-dialkenyl-, 2-alkenyl-3-alkyl- and 2,3-dialkylpyrazines and quinoxalines. The effect of the temperature on the product distribution was studied. Suzuki-Miyaura cross coupling reactions of the bis(triflate) of 7,8-dihyroxyflavone with different arylboronic acids afforded aryl-substituted flavones with excellent site-selectivity. The first attack occurred at the more electronically deficient and sterically less hindered position at C-7. Sonogashira coupling reactions of 2,4,5,6-tetrachloropyrimidine and 2,3,4,5-tetrabromofuran provided di-, tri- and tetra-alkynylated products. Mixed Sonogashira-Suzuki products were also prepared. Most derivatives show excellent fluorescence properties.

Palladium(0)-katalysierte Heck-Kupplungsreaktionen von Di- bzw. Tribrombenzo-thiophen lieferte funktionalisierte Dibrombenzothiophene durch Domino Heck / 6π-Elektrocyclisierungs Reaktionen. Heck-Reaktionen von 2,3-Dichlorpyrazin und 2,3-Dichlorchinoxalin lieferten 2,3-Dialkenyl-, 2-Alkenyl-3-alkyl- sowie 2,3-Dialkylpyrazine bzw. entsprechende Chinoxaline. Der Einfluss der Temperatur auf die Produktverteilung wurde für diese Reaktionen untersucht. Die Suzuki-Miyaura-Kupplungsreaktion des Bis(triflats) von 7,8-Dihydroxyflavon mit verschiedenen Arylboronsäuren ergab Arylflavone mit hervorragender Regioselektivität. Der Primärangriff erfolgte an der elektronenärmeren und weniger sterisch gehinderten Position C-7. Sonogashira Reaktionen von 2,4,5,6-Tetrachlorpyrimidin sowie 2,3,4,5-Tetrabromfuran lieferten entsprechende di-, tri- und tetraalkinyl-substituierte Produkte. Ebenso wurden gemischte Sonogashira-Suzuki-Produkte (mit einem Aryl- und einem Alkinylsubstituenten) synthetisiert. Die meisten der Derivate, die ausgehend von 2,4,5,6-Tetrachlorpyrimidin bzw. 2,3,4,5-Tetrabromfuran dargestellt wurden, zeigten exzellente Fluoreszen-zeigenschaften.



General Scheme. Palladium(0)-Catalyzed Reactions developed in this thesis.

7 *Experimental Section*

7.1 General: Equipment, chemicals and work technique

^{1}H NMR Spectroscopy:

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

^{13}C NMR Spectroscopy:

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

Mass Spectroscopy:

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

High Resolution mass spectroscopy:

Finnigan MAT 95 or Varian MAT 311; Bruker FT

CIR, AMD 402 (AMD Intectra).

Infrared spectroscopy (IR):

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

Elemental Analysis

LECO CHNS-932, Thermoquest Flash EA 1112.

X-ray crystal structure analysis:

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

Melting points:

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

Column chromatography:

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

Thin Layer Chromatography (TLC):

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

7.2 Synthesis of Functionalized Dibenzothiophenes by Domino ′Twofold Heck / 6π-Electrocyclization′ Reactions of 2, 3-Dibromobenzothiophene and 2,3,6-Tribromobenzothiophene.

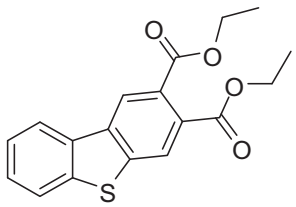
Synthesis of 2,3-Dibromobenzothiophene (2a); To a CH_2Cl_2 solution (50 mL) of benzo[*b*]thiophene (**1**, 5.00 g, 37.3 mmol) and KOAc (7.30 g, 74.6 mmol) was added Br_2 (3.8 mL, 74.6 mmol) at 20 °C, and the solution was heated under reflux for 24 h. To the solution was added a sat. solution of $Na_2S_2O_3$ and $NaHCO_3$. The organic and the aqueous layer were separated, and the latter was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash silica column chromatography (pure heptanes) to yield **2a** as a white solid (9.1 g, 84%).

Synthesis of 2,3,6-Tribromobenzothiophene (2b); To a CH_2Cl_2 solution (50 mL) of benzo[*b*]thiophene (**1**, 5.00 g, 37.3 mmol) and KOAc (16.5 g, 167.9 mmol) was added Br_2 (8.6 mL, 167.9 mmol) at 20 °C, and the solution was heated under reflux for 24 h. To the solution was added a sat. solution of $Na_2S_2O_3$ and $NaHCO_3$. The organic and the aqueous layer were separated, and the latter was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash silica column chromatography (pure heptanes) to yield **2b** as a white solid (9.7 g, 70%).

General procedure A for the synthesis of (6a-f); In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 2.5 mol% per Br atom) and dicyclohexyl-(2',6'-dimethoxybiphenyl-2-yl) phosphine (**L_1**) (41 mg, 10 mol%) in DMF (5 mL) was flushed with Ar and stirred at 20 °C to give a yellowish or brownish transparent solution. To the stirred solution were added the 2,3-dibromobenzothiophene (**2a**, 292 mg, 1.0 mmol), Et_3N (1.1 mL, 8.0 mmol), and the acrylate (1.25 equiv per Br). The reaction mixture was stirred at 100-130 °C for 12-48 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic

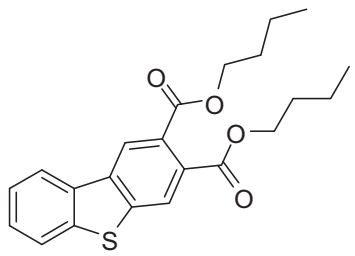
layers were washed with H_2O (3 × 20 mL), dried (Na_2SO_4), concentrated in vacuo, and passed through a column (silica gel). To a xylene solution (3 mL) of the crude product was added Pd/C (30 mg, 10 mol %). The solution was stirred under reflux for 48 h under argon atmosphere. The reaction mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes–EtOAc) to yield the product.

Diethyl Dibenzo [b,d]thiophene-2,3- dicarboxylate (6a);



Compound **6a** was prepared starting with **2a** (292 mg, 1.0 mmol) as an amorphous white solid (249 mg, 76%); m.p. 118–119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, 3H, J = 7.76 Hz, CH_3), 1.35 (t, 3H, J = 7.76 Hz, CH_3), 4.31–4.40 (m, 4H, 2 CH_2O), 7.41–7.48 (m, 2H, ArH), 7.79–7.82 (m, 1H, ArH), 8.12 (s, 1H, ArH), 8.13–8.15 (m, 1H, ArH), 8.43 (s, 1H, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.2 ($2CH_3$), 61.7, 61.8 (CH_2O), 122.3, 122.4, 123.0, 123.6, 125.1, 128.0 (CH), 128.5, 130.4, 134.4, 137.1, 140.7, 141.9 (C), 167.5, 167.7 (CO). IR (KBr): $\tilde{\nu}$ = 3053 (w), 2975 (w), 2931 (w), 2896 (w), 2867 (w), 1706 (s), 1632 (w), 1603 (w), 1540 (w), 1483 (w), 1469 (w), 1440 (m), 1366 (m), 1314 (m), 1247 (s), 1229 (s), 1098 (s), 1021 (s), 913 (w), 885 (w), 873 (w), 853 (w), 765 (s), 757 (s), 708 (s), 642 (w), 583 (w), 552 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 328 (40) $[M]^+$, 284 (06), 257 (54), 229 (19), 211 (58), 185 (100); HRMS (EI, 70 eV): *m/z* calcd for $C_{18}H_{16}O_4S$ $[M]^+$: 328.08715; found: 328.08765.

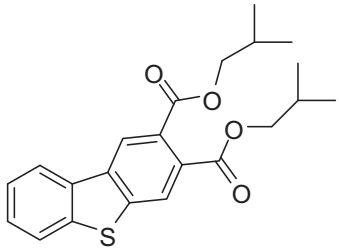
Dibutyl dibenzo[b,d]thiophene-2,3-dicarboxylate (6b):



Compound **6b** was prepared starting with **2a** (292 mg, 1.0 mmol) as a highly viscous oil (311 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, 3H, J = 7.3 Hz, CH_3), 0.92 (t, 3H, J = 7.4 Hz, CH_3), 1.34–1.47 (m, 4H), 1.64–1.74 (m, 4H), 4.28 (t, 2H, J = 6.7 Hz, OCH_2), 4.30 (t, 2H, J = 6.6Hz, OCH_2), 7.44–7.48 (m, 2H, ArH), 7.80-7.83(m, 1H, ArH), 8.13 (s, 1H, ArH), 8.15-8.17 (m, 1H, ArH), 8.43 (s, 1H, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.7 ($2CH_3$), 18.2, 29.6, 64.7 (CH_2), 121.3, 121.4, 122.0, 122.6, 124.0, 127.0 (CH), 127.5,

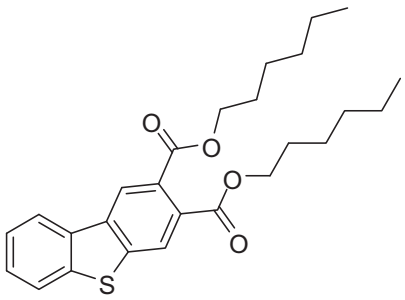
129.4, 133.4, 136.1, 139.7, 140.8 (C), 166.5, 166.8 (CO). IR (KBr): $\tilde{\nu}$ = 2957 (m), 1717 (s), 1459 (m), 1263 (s), 1119 (m), 1092 (m), 1018 (w), 760 (m), 731 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 384 (20) $[M]^+$, 328 (06), 311 (04), 272 (31), 255 (100), 228 (10), 211 (05), 171 (12). HRMS (EI, 70 eV): *m/z* calcd for $C_{22}H_{24}O_4S$ $[M]^+$: 384.13898; found: 384.139182.

Diisobutyl dibenzo[b,d]thiophene-2,3-dicarboxylate (6c);



Compound **6c** was prepared starting with **2a** (292 mg, 1.0 mmol) as highly viscous oil (284 mg, 74%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, 6H, *J* = 1.6 Hz, CH_3), 0.96 (d, 6H, *J* = 1.6 Hz, CH_3), 1.94–2.06 (m, 2H), 4.06 (d, 2H, *J* = 6.5 Hz, OCH_2), 4.08 (d, 2H, *J* = 6.7 Hz, OCH_2), 7.44–7.47 (m, 2H), 7.80–7.83 (m, 1H), 8.13 (s, 1 H, ArH), 8.15–8.16 (m, 1H), 8.43 (s, 1H, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 19.2 (CH_3), 71.9 (OCH_2), 27.7 122.3, 122.4, 123.0, 123.6, 125.0, 128.0 (CH), 128.6, 130.4, 134.4, 137.1, 140.7, 141.8 (C), 167.5, 167.8 (CO). IR (KBr): $\tilde{\nu}$ = 2959 (m), 2873 (w), 1717 (s), 1604 (w), 1468 (m), 1263 (s), 1120 (m), 1091 (m), 982 (m), 759 (m), 730 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 384 (20) $[M]^+$, 328 (06), 311 (02), 272 (56), 255 (100), 228 (11), 211 (05). 171 (12). HRMS (EI, 70 eV): *m/z* calcd for $C_{22}H_{24}O_4S$ $[M]^+$: 384.13898; found: 384.13901.

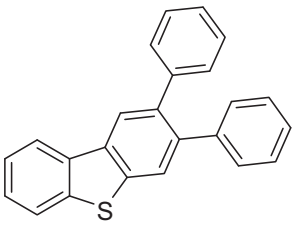
Dihexyl dibenzo[b,d]thiophene-2,3-dicarboxylate (6d);



Compound **6d** was prepared starting with **2a** (292 mg, 1.0 mmol) as highly viscous oil (338 mg, 77%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, 3H, *J* = 6.1 Hz, CH_3), 0.84 (t, 3H, *J* = 5.4 Hz, CH_3), 1.23–1.39 (m, 12H), 1.64–1.74 (m, 4H), 4.27(t, 2H, *J* = 6.8 Hz, OCH_2), 4.28 (t, 2H, *J* = 6.9 Hz, OCH_2), 7.43–7.46 (m, 2H), 7.79–7.82 (m, 1H), 8.12 (s, 1 H, ArH), 8.13–8.15 (m, 1H), 8.42 (s, 1H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 22.5, 25.6, 28.5, 31.5 (CH_2), 66.0 (OCH_2), 122.3, 122.4, 123.0, 123.6, 125.0, 128.0 (CH), 128.6, 130.4, 134.4, 137.1, 140.7, 141.9 (C),

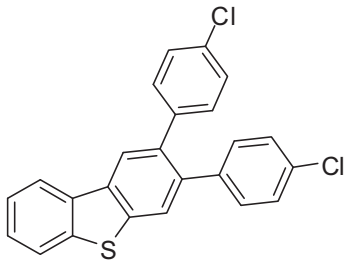
167.6, 167.8 (CO). IR (KBr): $\tilde{\nu}$ = 2953 (m), 2927 (m), 1718 (s), 1459 (w), 1263 (s), 1120 (m), 1092 (m), 760 (m), 729 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 440 (14) $[M]^+$, 356 (06), 272 (33), 255 (100), 228 (09), 182 (07). HRMS (EI, 70 eV): *m/z* calcd for $C_{26}H_{32}O_4S$ $[M]^+$: 440.20158; found: 440.20186.

2,3-Diphenyldibenzo[b,d]thiophene (6e);



Compound **6e** was prepared starting with **2b** (292 mg, 1.0 mmol) as a brownish semisolid (265 mg, 79%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.11–7.34 (m, 10H), 7.44–7.50 (m, 4H), 7.70 (d, 1H, *J* = 8.3 Hz, ArH), 7.89 (s, 1H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 120.7, 122.7, 123.6, 123.7, 126.5, 126.7 127.6, 128.6, 128.7, 128.8 (CH), 130.3, 133.8, 137.4, 139.1, 140.4 (C). IR (KBr): $\tilde{\nu}$ = 2926 (w), 2850 (w), 1665 (m), 1594 (m), 1446 (m), 1246 (m), 1107 (m), 958 (w), 746 (m), 691 (s), 595 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 336 (15) $[M]^+$, 321 (06), 302 (03), 261 (32), 184 (04), 167 (05). HRMS (EI, 70 eV): *m/z* calcd for $C_{24}H_{16}S$ $[M]^+$: 336.09672; found: 336.09660.

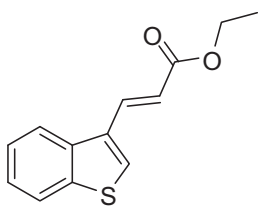
2,3-Bis(4-chlorophenyl)dibenzo[b,d]thiophene (6f);



Compound **6f** was prepared starting with **2b** (292 mg, 1.0 mmol) as a brown semisolid (336 mg, 83%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.24–7.43 (m, 10H), 7.60–7.93 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 121.3, 121.9, 122.2, 123.0, 124.4, 124.6, 124.9, 127.6, 127.7, 128.9 (CH), 133.3, 133.6, 133.8, 135.1, 135.9, 137.2, 137.7, 140.1, 140.5,142.5 (C). IR (KBr): $\tilde{\nu}$ =3058 (w), 1708 (s), 1587 (m), 1489 (m), 1421 (w), 1358 (w), 1219 (m), 1090 (m), 1012 (m), 828 (m), 756 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 404 (40) $[M]^+$, 384 (67), 368 (08), 351 (08), 334 (07), 307 (12), 266 (12), 224 (15), 202 (07), 161 (34). HRMS (EI, 70 eV): *m/z* calcd for $C_{24}H_{14}Cl_2S$ $[M]^+$: 404.01878; found: 404.01880.

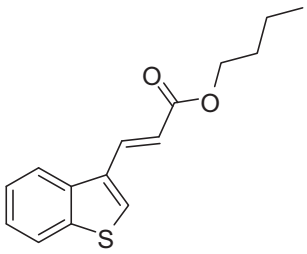
General Procedure B for the Synthesis of (7a-e); In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (06 mg, 0.025 mmol) and dicyclohexyl-(2',6'-dimethoxybiphenyl-2-yl) phosphine (**L1**, 21 mg, 0.05 mmol) in DMF (5 mL) was flushed with Ar and stirred at 20 °C to give a yellowish or brownish transparent solution. To the stirred solution were added the 2,3-dibromobenzothiophene (**2a**, 292 mg, 1.0 mmol), Et_3N (1.1 mL, 8.0 mmol), and the acrylate (1.25 mmol). The reaction mixture was stirred at 130 °C for 24 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with H_2O (3 × 20 mL), dried (Na_2SO_4), concentrated in vacuo, and passed through a column (flash silica gel, heptanes–EtOAc) to yield the product.

(E)-Ethyl 3-(benzo[b]thiophen-3-yl)acrylate (7a):



Compound **7a** was prepared starting with **2a** (292 mg, 1.0mmol) as a colorless viscous oil (188 mg, 81%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, 3H, J = 7.1 Hz, CH_3), 4.21 (q, 2H, J = 7.2, 14.3 Hz, OCH_2), 6.45 (d, 1H, J = 16.1 Hz), 7.25–7.40 (m, 2 H), 7.66 (s, 1H, ArH), 7.78–7.81 (m, 1H), 7.88 (d, 1H, J = 16.1 Hz), 7.91–7.95 (m, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.3 (CH_3), 60.5 (OCH_2), 118.7, 122.1, 123.0, 124.9, 125.0, 128.0 (CH), 131.6 (C), 136.3 (CH), 137.1, 140.5 (C), 167.1 (CO). IR (KBr): $\tilde{\nu}$ = 2978 (w), 1703 (s), 1627 (s), 1503 (w), 1368 (m), 1257 (m), 1158 (s), 1093 (w), 1043 (m), 971 (m), 731 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 232 (92) $[M]^+$, 217 (02), 204 (09), 187 (100), 175 (04), 160 (29) 147 (07) 115 (67). HRMS (EI, 70 eV): *m/z* calcd for $C_{13}H_{12}O_2S$ $[M]^+$: 232.05525; found: 232.05530.

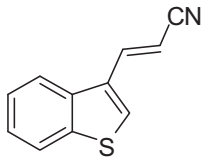
(E)-Butyl 3-(benzo[b]thiophen-3-yl)acrylate (7b):



Compound **7b** was prepared starting with **2a** (292 mg, 1.0mmol) as a colorless viscous oil (169 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, 3H, J = 7.4 Hz, CH_3), 1.30–1.42 (m, 2H), 1.57–1.69 (m, 2H), 4.16 (t, 2H, J = 6.7 Hz, OCH_2), 6.45 (d, 1H, J = 15.9 Hz), 7.25–7.41 (m, 2 H), 7.66 (s,

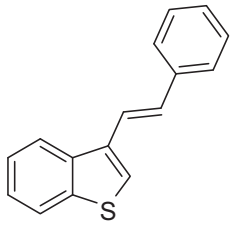
1H, ArH), 7.77–7.81 (m, 1H), 7.88 (d, 1H, J = 16.1 Hz), 7.91–7.95 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 (CH_3), 18.2, 29.7 (CH_2), 63.4 (OCH_2), 117.7, 121.1, 121.9, 123.9, 124.0, 126.9 (CH), 130.6 (C), 135.2 (CH), 136.1, 139.4 (C), 166.2 (CO). IR (KBr): $\tilde{\nu}$ = 2956 (m), 1719 (s), 1542 (w), 1459 (m), 1316 (m), 1262 (s), 1119 (m), 1092 (m), 1018 (w), 898 (w), 760 (m), 731 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 260 (90) $[M]^+$, 245 (14), 231 (20), 217 (40), 204 (27), 187 (100) 175 (18) 160 (29). HRMS (EI, 70 eV): *m/z* calcd for $C_{15}H_{16}O_2S$ $[M]^+$: 260.09110; found: 260.09136.

(E)-3-(Benzo[b]thiophen-3-yl)acrylonitrile (7c):



Compound **7c** was prepared starting with **2a** (292 mg, 1.0mmol) as light brown semisolid (94 mg, 51%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.63 (d, 1H, J = 16.3 Hz), 7.26–7.41 (m, 1 H), 7.49 (d, 1H, J = 16.2 Hz), 7.68–7.73 (m, 3H), 7.78–7.84 (m, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 96.9 (CH), 117.7 (C), 122.5, 124.8, 125.2, 127.0 (CH), 128.5 (C), 129.2 (CH), 138.1, 139.2 (C), 143.3 (CH). IR (KBr). $\tilde{\nu}$ = 2921 (m), 2213 (w), 1611 (m), 1457 (m), 1365 (w), 1107 (m), 952 (m), 745 (s), 618 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 260 (90) $[M]^+$, 185 (100), 158 (09), 140 (10), 126 (01), 114 (05). HRMS (EI, 70 eV): *m/z* calcd for $C_{11}H_7NS$ $[M]^+$: 185.02937; found: 185.02874.

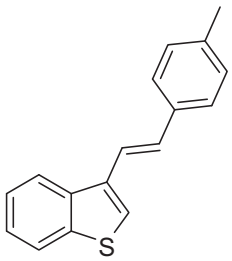
(E)-3-Styrylbenzo[b]thiophene (7d):



Compound **7d** was prepared starting with **2a** (292 mg, 1.0mmol) as a colorless crystalline solid (174 mg, 76%); m.p. 93–95 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.12–7.23 (m, 2 H), 7.28–7.36 (m, 5H), 7.46 (s, 1H, ArH), 7.46–7.49 (m, 2H, ArH), 7.77–7.83 (m, 1H, ArH), 7.91–7.94 (m, 1H, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 120.7, 121.8, 122.0, 123.0, 124.33, 124.6, 126.4, 127.7, 128.8, 130.3 (CH), 134.2, 137.4, 137.8, 140.5 (C). IR (KBr): $\tilde{\nu}$ = 2921 (s), 2851 (s), 1667 (m), 1598 (m), 1492 (m), 1454 (m), 1446 (m), 1434 (m), 1377 (w), 1365 (w), 1346 (w), 1260 (w), 1243 (w), 1204 (w), 1176 (w), 1156 (w), 1029 (w), 1019 (w), 948 (w), 907 (w), 887 (w), 864 (w), 757 (s), 748 (s), 730 (s), 696 (s), 623 (w), 591 (w), 555 (w), 538 (w) cm^{-1}. GC-MS (EI, 70

eV): *m/*z (%) = 236 (100) $[M]^+$, 221 (18), 202 (16), 189 (05), 117 (08). HRMS (EI, 70 eV): *m/z* calcd for $C_{16}H_{12}S$ $[M]^+$: 236.06542; found: 236.064490.

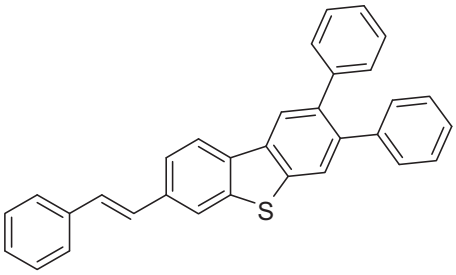
(E)-3-(4-Methylstyryl)benzo[b]thiophene (7e):



Compound **7e** was prepared starting with **2a** (292 mg, 1.0mmol) as a white crystalline solid (190 mg, 76%); m.p. 107–109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ =2.29 (s, 3H, CH_3), 7.11–7.38 (m, 6H), 6.88 (d, 1H, J = 16.0 Hz), 7.79 (d, 2H, J = 7.3 Hz), 7.92 (d, 2H, J = 7.2 Hz). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 21.3 (CH_3), 119.7, 121.4, 121.9, 123.0, 124.2, 124.5, 126.3, 129.4, 130.2 (CH), 134.3, 134.6, 137.6, 137.8, 140.5 (C). IR (KBr): $\tilde{\nu}$ = 2919 (m), 1642 (w), 1425 (m), 1234 (m), 1109 (w), 962 (m), 805 (s), 754 (s), 730 (s), 709 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 250 (75) $[M]^+$, 235 (100), 221 (06), 202 (11), 189 (04), 158 (02), 139 (02). HRMS (EI, 70 eV): *m/z* calcd for $C_{17}H_{14}S$ $[M]^+$: 250.08107; found: 250.08125.

Synthesis of (E)-2,3-Diphenyl-7-styryldibenzo[b,d]thiophene (10); In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 1.7 mol% per Br atom) and dicyclohexyl-(2',6'-dimethoxybiphenyl-2-yl) phosphine (**L1**, 41 mg, 0.10 mmol) in DMF (5 mL) was flushed with Ar and stirred at 20 °C to give a yellowish or brownish transparent solution. To the stirred solution were added the 2,3,6-tribromobenzothiophene (**2b**, 371 mg, 1.0 mmol), Et_3N (1.1 mL, 8.0 mmol), and the acrylate (1.25 equiv per Br). The reaction mixture was stirred at 130 °C for 48 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with H_2O (3 × 20 mL), dried (Na_2SO_4), concentrated in vacuo, and passed through a column (silica gel). To a xylene solution (3 mL) of the crude product was added Pd/C (30 mg, 10 mol %). The solution was stirred under reflux for 48 h under argon atmosphere. The reaction mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes–EtOAc) to yield the product.

(E)-2,3-Diphenyl-7-styryldibenzo[b,d]thiophene (10);

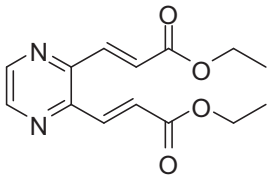


Compound **10** was prepared starting with **2b** (371 mg, 1.0 mmol) as a brownish semisolid (319 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.01–7.20 (m, 7H), 7.24–7.34 (m, 7H), 7.40–7.47 (m, 6H), 7.75–7.86 (m, 2H, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 120.7, 121.3, 122.1, 122.3, 122.9, 125.6, 126.5, 126.6, 127.5, 128.6, 128.7, 128.8 (CH), 129.7, 130.3 (C), 130.4 (CH), 137.3, 137.4, 137.4, 137.5, 139.9, 140.5, 141.2, 142.1 (C). IR (KBr): $\tilde{\nu}$ = 3054 (w), 3023 (w), 291 (w), 1681 (m), 1596 (m), 1493 (m), 1445 (m), 1178 (w), 1155 (w), 1072 (w), 1026 (w), 956 (s), 908 (w), 876 (w), 812 (w), 747 (s), 733 (s), 688 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 438 (19) $[M]^+$, 368 (31), 338 (100), 259 (20), 234 (16), 202 (10), 105 (15). HRMS (EI, 70 eV): *m/z* calcd for $C_{32}H_{22}S$ $[M]^+$: 438.14422; found: 438.144012.

7.3 Synthesis of 2,3-Disubstituted Pyrazines and Quinoxalines by Heck Cross-Coupling Reactions of 2,3-Dichloropyrazine and 2,3-Dichloroquinoxaline.

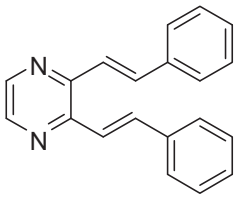
General procedure for the two-fold Heck cross-coupling reactions; In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 2.5 mol% per Cl) and dicyclohexyl (2',4',6'-triisopropylbiphenyl-2-yl)phosphine (Xphos) (47 mg, 0.10 mmol) in DMF (5 mL) was purged with Ar and stirred at 20 °C to get a yellowish or brownish transparent solution. To the stirred solution were added 2,3-dichloropyrazine (**11a**) (149 mg, 1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the acrylate or styrene (1.25 equiv. per Br). The reaction mixture was stirred at the indicated temperature for 48 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with H_2O (3 x 20 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes/EtOAc).

(2E,2'E)-Diethyl 3,3'-(pyrazine-2,3-diyl)diacrylate (12a):



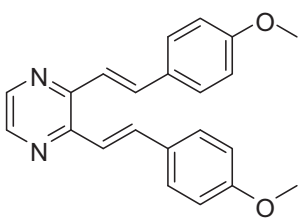
Compound **12a** was prepared from **11a** (149 mg, 1.0 mmol) as a light brown highly viscous oil (229 mg, 83%). Reaction temperature: 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, 6H, J = 7.2 Hz, $2CH_3$), 4.23 (q, 4H, J = 7.1, 14.2 Hz, $2CH_2O$), 7.05 (d, 2H, J = 15.2 Hz, 2CH), 7.94 (d, 2H, J = 15.2 Hz, 2CH), 8.48 (s, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.2 (CH_3), 60.9 (CH_2O), 126.8, 136.3, 145.0 (CH), 146.3 (C), 166.0 (CO). IR (KBr): $\tilde{\nu}$ = 2978 (m), 2934 (w), 1715 (s), 1638 (w), 1400 (m), 1294 (s), 1266 (m), 1177 (s), 1033 (m), 974 (m), 911 (w), 797 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 276 (11) $[M]^+$, 231 (42), 186 (5), 175 (44), 157 (34), 131 (73). HRMS (EI, 70 eV): calcd for $C_{14}H_{16}N_2O_4$ $[M]^+$: 276.11046; found: 276.11092.

2,3-Distyrylpyrazine (12b)*;*



Compound **12b** was prepared from **11a** (149 mg, 1.0 mmol) as a light yellow solid (233 mg, 82%); m.p. 105-107 °C. Reaction temperature: 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28-7.35 (m, 6H, ArH), 7.41 (d, 2H, J = 15.6), 7.54-7.57 (m, 4H, ArH), 7.76 (d, 2H, J = 15.6 Hz), 8.34 (brs, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 121.9, 127.4, 128.8, 128.9 (CH), 136.5 (C), 136.6, 142.5 (CH), 147.8 (C). IR (KBr): $\tilde{\nu}$ = 3369 (w), 3024 (w), 1626 (m), 1599 (w), 1575 (w), 1493 (m), 1447 (m), 1392 (m), 1154 (m), 1072 (m), 962 (m), 744 (s), 687 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 283 (100) $[M-1]^+$, 268 (2), 226 (2), 207 (24), 141 (18). HRMS (EI, 70 eV): calcd for $C_{20}H_{15}N_2$ $[M-1]^+$: 283.12298; found: 283.12297.

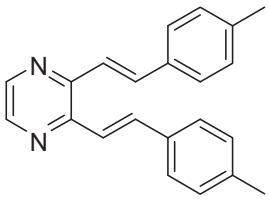
2,3-Bis(4-methoxystyryl)pyrazine (12c)*;*



Compound **12c** was prepared from **11a** (149 mg, 1.0 mmol) as a light brown highly viscous oil (268 mg, 78%). Reaction temperature: 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 6H, $2OCH_3$), 6.95 (d, 4H, J = 8.6 Hz, ArH), 7.36 (d, 2H, J = 15.6 Hz), 7.59 (d, 4H, J = 8.6 Hz, ArH), 7.80 (d, 2H, J = 15.6 Hz), 8.38 (brs, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.3 (CH_3), 114.2, 119.8,

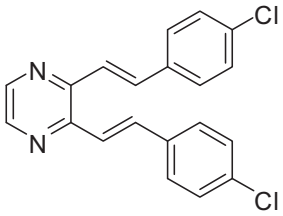
128.8 (CH), 129.4 (C), 135.8, 141.9 (CH), 147.9 I, 160.2 (C). IR (KBr): $\tilde{\nu}$ = 3400 (w), 3033 (w), 2954 (m), 1708 (m), 1601 (s), 1508 (s), 1440 (m), 1399 (w), 1301 (m), 1243 (s), 1028 (s), 970 (m), 823 (s), 708 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 344 (100) $[M]^+$, 329 (12), 313 (4), 299 (4), 237 (30), 172 (05). HRMS (EI, 70 eV): calcd for $C_{22}H_{20}N_2O_2$ $[M]^+$: 344.15193; found: 344.15154.

2,3-Bis(4-methylstyryl)pyrazine (12d);



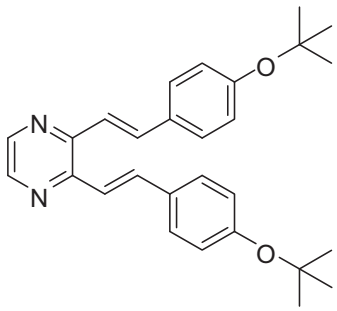
Compound **12d** was prepared from **11a** (149 mg, 1.0 mmol) as a yellow solid (256 mg, 82%); m.p. 111-113 °C. Reaction temperature: 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 6H, $2CH_3$), 7.12 (d, 4H, *J* = 8.1 Hz, ArH), 7.34 (d, 2H, *J* = 15.4), 7.44 (d, 4H, *J* = 8.0 Hz, ArH), 7.72 (d, 2H, *J* = 15.7 Hz), 8.30 (brs, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (CH_3), 121.0, 127.3, 129.5 (CH), 133.8 (C), 136.4 (CH), 139.0 (C), 142.2 (CH), 147.9 (C). IR (KBr): $\tilde{\nu}$ = 3046 (w), 3023 (w), 2920 (w), 2860 (w), 1710 (m), 1444 (m), 1414 (m), 1391 (w), 1360 (w), 1220 (m), 1180 (m), 1153 (m), 971 (s), 905 (w), 866 (w), 845 (w), 803 (s), 750 (w), 656 (w), 596 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 311 (100) $[M-1]^+$, 297 (8), 281 (2), 221 (24), 195 (7), 141 (13). HRMS (EI, 70 eV): calcd for $C_{22}H_{19}N_2$ $[M-1]^+$: 311.15428; found: 311.15432.

2,3-Bis(4-chlorostyryl)pyrazine (12e);



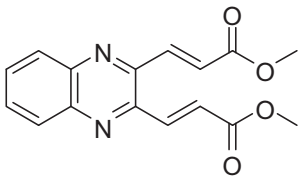
Compound **12e** was prepared from **11a** (149 mg, 1.0 mmol), following the *general procedure*, as a light yellowish highly viscous oil (232 mg, 66 %). Reaction temperature: 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27-7.38 (m, 6H), 7.45-7.56 (m, 4H), 7.69-7.79 (m, 2H), 8.35 (brs, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 122.7, 128.5, 129.0 (CH), 134.9, 134.6 (C), 135.3, 142.6 (CH), 147.4 (C). IR (KBr): $\tilde{\nu}$ = 3026 (w), 2927 (s), 2854 (m), 1706 (s), 1603 (w), 1490 (s), 1090 (s), 1013 (m), 966 (m), 827 (m), 765 (w), 700 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 351 (100) $[M-1]^+$, 317 (10), 280 (02), 241 (48), 227 (07). HRMS (EI, 70 eV): calcd for $C_{20}H_{13}N_2Cl_2$ $[M-1]^+$: 351.04503; found: 351.04518.

2,3-Bis(4-tert-butoxystyryl)pyrazine (12f);



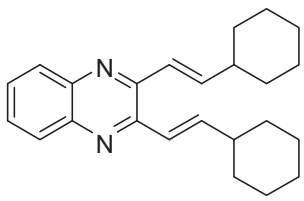
Compound **12f** was prepared from **11a** (149 mg, 1.0 mmol) as a brownish solid (274 mg, 64%); m.p. 125-127 °C. Reaction temperature: 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 18H, $6CH_3$), 6.94 (d, 4H, J = 8.2 Hz, ArH), 7.30 (d, 2H, J = 15.9 Hz), 7.45 (d, 4H, J = 8.6 Hz, ArH), 7.71 (d, 2H, J = 15.5 Hz), 8.30 (brs, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.9 (CH_3), 79.02 (C), 120.6, 124.0, 128.1 (CH), 131.6 (C), 135.9, 142.1 (CH), 147.8, 156.4 (C). IR (KBr): $\tilde{\nu}$ = 3029 (w), 2972 (m), 2928 (w), 1600 (m), 1503 (s), 1445 (m), 1388 (m), 1363 (m), 1234 (s), 1154 (s), 1089 (w), 975 (m), 892 (s), 848 (m), 713 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 428 (09) $[M]^+$, 372 (4), 316 (100), 285 (3), 223 (30), 210 (15). HRMS (EI, 70 eV): calcd for $C_{28}H_{32}N_2O_2$ $[M]^+$: 428.24583; found: 428.24676.

Dimethyl 3,3'-(quinoxaline-2,3-diyl)diacrylate (12g);



Compound **12g** was prepared from **11b** (199 mg, 1.0 mmol) as a light yellow solid (232 mg, 78%); m.p. 134-136 °C. Reaction temperature: 120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.90 (s, 6H, $2CH_3O$), 7.30 (d, 2H, J = 15.2 Hz), 7.80-7.83 (m, 2H, ArH), 8.08-8.11 (m, 2H, ArH , 8.20 (d, 2H, J = 15.2 Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.0 (CH_3O), 127.1, 129.5, 131.2, 137.2 (CH), 142.4, 146.4 (C), 166.4 (CO). IR (KBr): $\tilde{\nu}$ = 3303 (w), 2956 (w), 2920 (w), 1710 (s), 1638 (w), 1433 (m), 1308 (m), 1269 (s), 1170 (s), 1027 (m), 969 (m), 757 (s), 717 (m), 611 (w), 543 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 298 (08) $[M]^+$, 283 (3), 267 (26), 239 (100), 223 (8), 207 (25), 195 (38). HRMS (EI, 70 eV): calcd for $C_{16}H_{14}N_2O_4$ $[M]^+$: 298.0951; found: 298.0954.

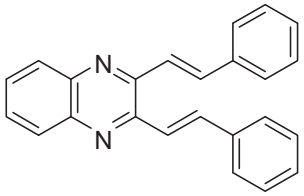
2,3-Bis(E-2-cyclohexylvinyl)quinoxaline (12h);



Compound **12h** was prepared from **11b** (199 mg, 1.0 mmol) as a light yellow highly viscous oil (222 mg, 64%). Reaction temperature: 120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62-1.86 (m, 20H), 2.16-2.28 (m, 2H), 6.77 (d, 2H, J = 15.4

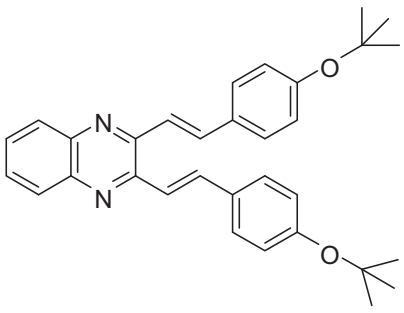
Hz), 6.96 (dd, 2H, J = 6.7, 15.4 Hz), 7.52-7.55 (m, 2H), 7.87-7.91 (m, 2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 25.9, 26.1, 32.5 (CH_2), 41.5, 122.7, 128.7, 128.8 (CH), 141.3 (C), 146.7 (CH), 149.4 (C). IR (KBr): $\tilde{\nu}$ = 3065 (w), 2922 (s), 2850 (m), 1700 (m), 1447 (m), 1259 (s), 1091 (s), 1019 (s), 798 (m), 758 (s), 698 (w), 589 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 346 (35) $[M]^+$, 303 (6), 263 (100), 251 (7), 169 (20). HRMS (EI, 70 eV): calcd for $C_{24}H_{30}N_2$ $[M]^+$: 346.24035; found: 346.23992.

2, 3-Distyrylquinoxaline (12i);



Compound **12i** was prepared from **11b** (199 mg, 1.0 mmol) as a yellow solid (240 mg, 72%); m.p. 143-145 °C. Reaction temperature: 120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24-7.37 (m, 6H), 7.55 (d, 2H, J = 15.5 Hz), 7.58-7.61 (m, 6H), 7.91 (d, 2H, J = 15.5 Hz), 7.94-7.98 (m, 2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 122.6, 127.6, 128.8, 128.9, 129.0, 129.5 (CH), 136.5 (C), 137.9 (CH), 141.6, 149.0 (C). IR (KBr): $\tilde{\nu}$ = 3060 (w), 3029 (w), 2930 (w), 2853 (w), 1706 (m), 1682 (w), 1491 (w), 1320 (m), 1106 (m), 981 (w), 763 (s), 697 (s), 601 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 (93)$[M]^+$, 333 (100), 257 (62), 243 (19), 204 (32), 167 (17). HRMS (EI, 70 eV): calcd for $C_{24}H_{18}N_2$ $[M]^+$: 334.14645; found: 334.14539.

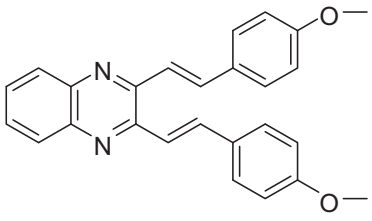
2,3-Bis(4-tert-butoxystyryl)quinoxaline (12j);



Compound **12j** was prepared from **11b** (199 mg, 1.0 mmol) as a yellow highly viscous oil (319 mg, 67%). Reaction temperature: 120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (s, 18H, $6CH_3$), 6.92 (d, 4H, J = 8.5 Hz, ArH), 7.43 (d, 2H, J = 15.5 Hz), 7.49-7.54 (m, 6H), 7.84 (d, 2H, J = 15.6 Hz), 7.86-7.91 (m, 2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.9 (CH_3), 79.1 (C), 121.3, 124.0, 128.3, 128.8, 129.2 (CH), 131.5 (C), 137.7 (CH), 141.5, 149.2, 156.6 (C). IR (KBr): $\tilde{\nu}$ = 3031 (w), 2922 (s), 2851 (m), 1677 (w), 1601 (m), 1504 (s), 1459 (m), 1364 (m), 1237 (m), 1156 (s), 1014 (w), 972 (w), 893 (m), 759 (m), 607 (w), 537 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 478

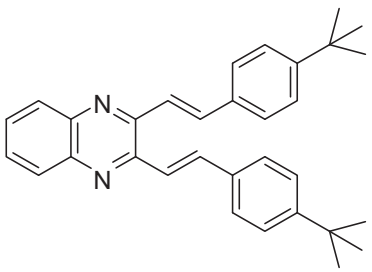
(03)$[M]^+$, 422 (4), 366 (61), 273 (22), 260 (12), 212 (05). HRMS (EI, 70 eV): calcd for $C_{32}H_{34}N_2O_2$ $[M]^+$: 478.26148; found: 478.26059.

2,3-Bis(4-methoxystyryl)quinoxaline (12k);



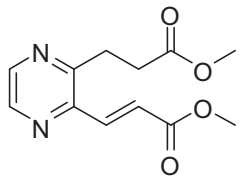
Compound **12k** was prepared from **11b** (199 mg, 1.0 mmol) as a yellow highly viscous oil (327 mg, 83%). Reaction temperature: 120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 6H, $2OCH_3$), 6.85 (d, 4H, J = 8.8 Hz, ArH), 7.42 (d, 2H, J = 15.5 Hz), 7.52-7.57 (m, 6H, ArH), 7.85 (d, 2H, J = 15.6 Hz), 7.90-7.94 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.35 (OCH_3), 114.2, 120.4, 128.7, 129.0, 129.1 (CH), 129.3 (C), 137.3 (CH), 141.5, 149.3 (C), 160.4 (CO). IR (KBr): $\tilde{\nu}$ = 3004 (w), 2963 (w), 2838 (w), 1598 (s), 1541(w), 1508 (s), 1460 (m), 1420 (m), 1299 (w), 1247 (s), 1172 (s), 1109 (m), 1022 (s), 969 (s), 829 (s), 760 (s), 610 (m), 535 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 394 (61)$[M]^+$, 379 (15), 335 (4), 288 (11), 275 (41), 227 (13), 191 (8). HRMS (EI, 70 eV): calcd for $C_{26}H_{22}N_2O_2$ $[M]^+$: 394.16758; found: 394.16667.

2,3-Bis(4-*tert*-butylstyryl)quinoxaline (12l)*;*



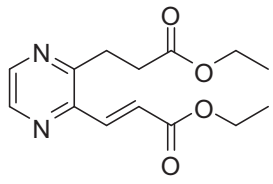
Compound **12l** was prepared from **11b** (199 mg, 1.0 mmol) as a highly viscous brownish oil (321 mg, 72%). Reaction temperature: 120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 18H, $6CH_3$), 7.28 (d, 2H, J = 16.3 Hz), 7.37 (d, 4H, J = 8.5 Hz, ArH), 7.59-7.70 (m, 4H), 7.78 (d, 2H, J = 16.3 Hz), 7.96-8.01 (m, 4H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.3 (CH_3), 33.7 (C), 125.9, 127.3, 129.1, 130.3 (CH), 135.3 (C), 136.3 (CH), 143.4 (C), 144.4 (CH), 149.8, 151.6 (C). IR (KBr): $\tilde{\nu}$ = 3059 (w), 2922 (s), 2852 (m), 1632 (m), 1512 (w), 1457 (m), 1362 (m), 1267 (m), 1202 (m), 1106 (s), 971 (m), 820 (m), 759 (s), 610 (w), 562 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 446 (13)$[M]^+$, 433 (8), 391 (12), 301 (40), 285 (7), 245 (8). HRMS (EI, 70 eV): calcd for $C_{32}H_{34}N_2$ $[M]^+$: 446.28869; found: 446.28780.

(*E*)-Methyl 3-(3-(3-methoxy-3-oxopropyl)pyrazin-2-yl)acrylate (13a)*;*



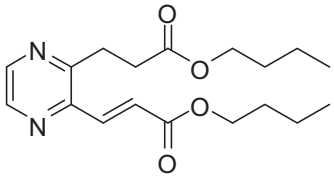
Compound **13a** was prepared from **11a** (149 mg, 1.0 mmol) as a brown highly viscous oil (195 mg, 78%). Reaction temperature: 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.80 (t, 2H, *J* = 7.2 Hz, CH_2), 3.23 (t, 2H, *J* = 7.1 Hz, CH_2), 3.61 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 7.02 (d, 1H, *J* = 15.2 Hz, CH), 7.87 (d,1H, *J* = 15.3 Hz, CH), 8.35-8.38 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.4, 31.3 (CH_2), 51.7, 51.9 (OCH_3), 125.2, 137.6, 142.3, 144.2 (CH), 146.4, 153.8 (C), 166.8, 173.0 (CO). IR (KBr): $\tilde{\nu}$ = 2953 (m), 2932 (w), 1713 (s), 1530 (w), 1436 (m), 1361 (m), 1294 (m), 1171 (m), 1103 (w), 1032 (w), 977 (w), 858 (w), 711 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 250 (02)$[M]^+$, 235 (2), 219 (32), 191 (100), 159 (44), 131 (63). HRMS (EI, 70 eV): calcd for $C_{12}H_{14}N_2O_4$ $[M]^+$: 250.09481; found: 250.09556.

(E)-Ethyl 3-(3-(3-ethoxy-3-oxopropyl)pyrazin-2-yl)acrylate (13b);



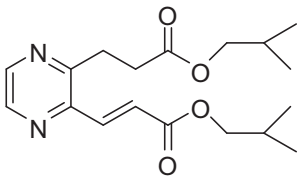
Compound **13b** was prepared from **11a** (149 mg, 1.0 mmol) as a light yellow highly viscous oil (196 mg, 71%). Reaction temperature: 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, 3H, *J* = 7.2 Hz, CH_3), 1.26 (t, 3H, *J* = 7.2 Hz, CH_3), 2.78 (t, 2H, *J* = 7.2 Hz, CH_2), 3.22 (t, 2H, *J* = 7.1 Hz, CH_2), 4.05 (q, 2H, *J* = 7.1, 14.3 Hz, CH_2O), 4.21 (q, 2H, *J* = 7.1, 14.3 Hz, CH_2O), 7.01 (d, 1H, *J* = 15.4 Hz, CH), 7.86 (d, 1H, *J* = 15.4 Hz), 8.34-8.37 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.1, 14.2 (CH_3), 28.4, 31.6 (CH_2), 60.5, 60.8 (CH_2O), 125.6, 137.4, 142.2, 144.1 (CH), 146.4, 154.0 (C), 166.3, 172.5 (CO). IR (KBr): $\tilde{\nu}$ = 2981 (m), 2934 (w), 1712 (s), 1640 (w), 1446 (w), 1404 (m), 1368 (m), 1290 (s), 1174 (s), 1099 (m), 1031 (s), 974 (m), 857 (m), 710 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 278 (03)$[M]^+$, 249 (4), 233 (46), 205 (100), 159 (54), 131 (60). HRMS (EI, 70 eV): calcd for $C_{14}H_{18}N_2O_4$ $[M]^+$: 278.12611; found: 278.126717.

(E)-Butyl 3-(3-(3-butoxy-3-oxopropyl)pyrazin-2-yl)acrylate (13c);



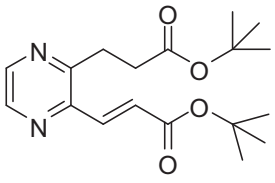
Compound **13c** was prepared from **11a** (149 mg, 1.0 mmol) as a light yellow highly viscous oil (247 mg, 74%). Reaction temperature: 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, 3H, *J* = 7.3 Hz, CH_3), 0.89 (t, 3H, *J* = 7.4 Hz, CH_3), 1.23-1.40 (m, 4H, $2CH_2$), 1.48-1.65 (m, 4H, $2CH_2$), 2.79 (t, 2H, *J* = 7.2 Hz, CH_2), 3.22 (t, 2H, *J* = 7.0 Hz, CH_2), 4.00 (t, 2H, *J* = 6.8 Hz, CH_2O), 4.16 (t, 2H, *J* = 6.8 Hz, CH_2O), 7.02 (d, 1H, *J* = 15.3 Hz, CH), 7.9 (d, 1H, *J* = 15.2 Hz, CH), 8.35-8.37 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7 (CH_3), 19.0, 19.1, 28.4, 30.6, 30.7, 31.6 (CH_2), 64.5, 64.7 (CH_2O), 125.7, 137.4, 142.2, 144.1 (CH), 146.5, 154.0 (C), 166.4, 172.7 (CO). IR (KBr): $\tilde{\nu}$ = 2958 (m), 2933 (w), 1720 (s), 1455 (m), 1405 (m), 1263 (w), 1170 (s), 1063 (m), 1021, 975 (m), 857 (w), 754 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 (05)$[M]^+$, 277 (03), 261 (31), 233 (100), 177 (16), 159 (47). HRMS (EI, 70 eV): calcd for $C_{18}H_{26}N_2O_4$ $[M]^+$: 334.18871; found: 334.18877.

(E)-Isobutyl 3-(3-(3-isobutoxy-3-oxopropyl)pyrazin-2-yl)acrylate (13d);



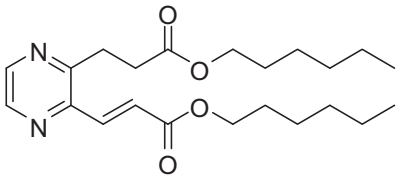
Compound **13d** was prepared from **11a** (149 mg, 1.0 mmol) as a brown highly viscous oil (251 mg, 75%). Reaction temperature: 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (d, 6H, *J* = 6.7 Hz, $2CH_3$), 0.91 (d, 6H, *J* = 6.9 Hz, $2CH_3$), 1.76-1.99 (m, 2H, CH), 2.80 (t, 2H, *J* = 7.1 Hz, CH_2), 3.2 (t, 2H, *J* = 7.1 Hz, CH_2), 3.78 (d, 2H, , *J* = 6.7 Hz, CH_2O), 3.94 (d, 2H, *J* = 6.4 Hz, CH_2O), 7.0 (d, 1H, *J* = 15.3 Hz, CH), 7.9 (d, 1H, *J* = 15.3 Hz, CH), 8.35-8.37 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 19.0 (CH_3), 27.6, 27.7 (CH), 28.4, 31.5 (CH_2), 70.7, 70.9 (CH_2O), 125.7, 137.4, 142.2, 144.2 (CH), 146.5, 153.9 (C), 166.4, 172.6 (CO). IR (KBr): $\tilde{\nu}$ = 2960 (m), 2874 (w), 1716 (s), 1640 (w), 1469 (m), 1405 (m), 1166 (s), 1008 (m), 854 (w), 710 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 (07)$[M]^+$, 277 (4), 261 (51), 233 (100), 205 (12), 177 (44). HRMS (EI, 70 eV): calcd for $C_{18}H_{26}N_2O_4$ $[M]^+$: 334.18871; found: 334.18918.

(E)-Tert-Butyl 3-(3-(3-tert-butoxy-3-oxopropyl)pyrazin-2-yl)acrylate (13e);



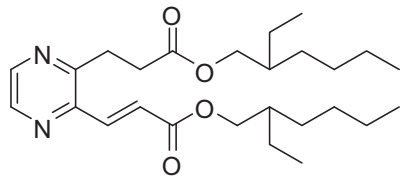
Compound **13e** was prepared from **11a** (149 mg, 1.0 mmol) as a light yellow highly viscous oil (277 mg, 83%). Reaction temperature: 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 9H, $3CH_3$), 1.46 (s, 9H, $3CH_3$), 2.68 (t, 2H, *J* = 7.2 Hz, CH_2), 3.16 (t, 2H, *J* = 7.2 Hz, CH_2), 6.93 (d, 1H, *J* = 15.2 Hz, CH), 7.76 (d, 1H, *J* = 15.3 Hz, CH), 8.33-8.35 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.0 (CH_3), 28.6, 32.8, (CH_2), 80.2, 80.9 (C), 127.6, 136.5, 142.1, 143.9 (CH), 146.6, 154.1 (C), 165.6, 171.7 (CO). IR (KBr): $\tilde{\nu}$ = 2976 (m), 2931 (w), 1708 (s), 1638 (w), 1455 (w), 1366, 1295 (m), 1144 (s), 975 (m), 847 (m), 758 (w), 711 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 (01)$[M]^+$, 261 (31), 222 (23), 205 (64), 177 (100), 159 (22). HRMS (EI, 70 eV): calcd for $C_{18}H_{26}N_2O_4$ $[M]^+$: 334.18871; found: 334.18930.

(E)-Hexyl 3-(3-(3-(hexyloxy)-3-oxopropyl)pyrazin-2-yl)acrylate (13f);



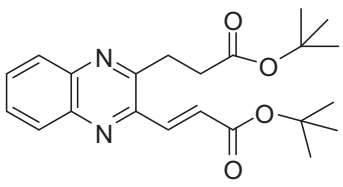
Compound **13f** was prepared from **11a** (149 mg, 1.0 mmol as light yellow highly viscous oil (308 mg, 79%). Reaction temperature: 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78-0.85 (m, 6H, $2CH_3$), 1.20-1.27 (m, 12H, $6CH_2$), 1.47-1.65 (m, 4H, $2CH_2$), 2.79 (t, 2H, *J* = 7.4 Hz, CH_2), 3.22 (t, 2H, *J* = 7.0 Hz, CH_2), 3.99 (t, 2H, *J* = 6.7 Hz, CH_2O), 4.15 (t, 2H, *J* = 6.7 Hz, CH_2O), 7.02 (d, 1H, *J* = 15.3 Hz), 7.86 (d, 1H, *J* = 15.3 Hz), 8.35-8.37 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.4, 22.5, 25.5, 25.6, 28.4, 28.5, 28.6, 31.3, 31.4, 31.6 (CH_2), 64.7, 65.0 (CH_2O), 125.7, 137.3, 142.2, 144.1, (CH), 146.5, 154.0 (C), 166.4, 172.6 (CO). IR (KBr): $\tilde{\nu}$ = 2928 (m), 2857 (w), 1716 (s), 1530 (w), 1404 (m), 1358 (w), 1289 (m), 1168 (s), 976 (m), 854 (w), 725 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 390 (17) $[M]^+$, 289 (22), 261 (100), 205 (9), 177 (18), 159 (35). HRMS (EI, 70 eV): calcd for $C_{22}H_{34}N_2O_4$ $[M]^+$: 390.25131; found: 390.25141.

(E)-2-Ethylhexyl 3-(3-(3-(2-ethylhexyloxy)-3-oxopropyl) pyrazin-2-yl)acrylate (13g);



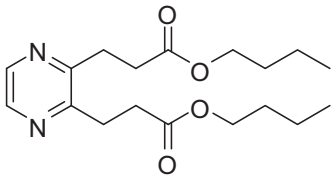
Compound **13g** was prepared from **11a** (149 mg, 1.0 mmol) as a light yellow highly viscous oil (306 mg, 69%). Reaction temperature: 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86-0.93 (m, 12H, $4CH_3$), 1.24-1.35 (m, 16H), 1.50-1.68 (m, 2H), 2.87 (t, 2H, *J* = 7.1 Hz), 3.30 (t, 2H, *J* = 7.1 Hz), 3.99 (d, 2H, *J* = 7.7 Hz), 4.15 (d, 2H, *J* = 7.1 Hz), 7.10 (d, 1H, *J* = 15.2 Hz), 7.94 (d, 1H, *J* = 15.7 Hz), 8.42-8.44 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 10.9, 13.9 (CH_3), 22.9, 22.9, 23.6, 23.8, 28.3, 28.8, 28.9, 30.3, 30.4, 31.5 (CH_2), 38.6, 38.8 (CH), 66.9, 67.2 (CH_2O), 125.7, 137.3, 142.2, 144.1 (CH), 146.5, 153.9, 166.5 (C), 172.7 (CO). IR (KBr): $\tilde{\nu}$ = 2957 (m), 2872 (w), 1717 (s), 1461 (m), 1404 (m), 1264 (m), 1168 (s), 975 (m), 771 (w), 710 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 446 (59)[M]$^{+}$, 417 (8), 389 (5), 335 (45), 317 (73), 289 (100). HRMS (EI, 70 eV): calcd for $C_{26}H_{42}N_2O_4$ [M]$^{+}$: 446.31391; found: 446.314336.

(E)-Tert-Butyl 3-(3-(3-tert-butoxy-3-oxopropyl) quinoxalin-2-yl) acrylate (13h);



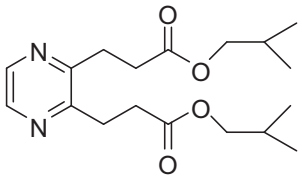
Compound **13h** was prepared from **11b** (199 mg, 1.0 mmol) as a light brown viscous oil (288 mg, 75%). Reaction temperature: 130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 9H, $3CH_3$), 1.49 (s, 9H, $3CH_3$), 2.82 (t, 2H, *J* = 7.1 Hz, CH_2), 3.35 (t, 2H, *J* = 7.1 Hz, CH_2), 7.10 (d, 1H, *J* = 15.4 Hz), 7.61-7.65 (m, 2H), 7.89-7.98 (m, 3H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 27.5, 28.1 (CH_3), 29.6, 32.3 (CH_2), 80.4, 81.1 (C), 128.6, 128.7, 129.4, 129.5, 130.2, 136.7 (CH), 141.1, 142.0, 147.2, 154.0 (C), 165.5, 172.0 (CO). IR (KBr): $\tilde{\nu}$ = 3062 (w), 2976 (m), 2931 (m), 1710 (s), 1482 (m), 1456 (w), 1366 (m), 1247 (m), 1147 (s), 975 (w), 845 (m), 760 (s), 611 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 384 (01)[M]$^{+}$, 328 (9), 311 (25), 272 (15), 255 (25), 227 (100), 209 (13), 181 (32). HRMS (EI, 70 eV): calcd for $C_{22}H_{28}N_2O_4$ [M]$^{+}$: 384.20436; found: 384.20525.

Dibutyl 3,3'-(pyrazine-2,3-diyl)dipropanoate (14a);



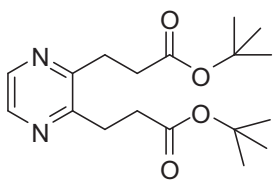
Compound **14a** was prepared from **11a** (149 mg, 1.0 mmol) as a light yellow highly viscous oil (232 mg, 69%). Reaction temperature: 140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, 6H, *J* = 7.4 Hz, $2CH_3$), 1.23-1.31 (m, 4H, $2CH_2$), 1.49-1.54 (m, 4H, $2CH_2$), 2.79 (t, 4H, *J* = 7.2 Hz, $2CH_2$), 3.09 (t, 4H, *J* = 7.1 Hz, $2CH_2$), 4.00 (t, 4H, *J* = 6.7 Hz, $2CH_2O$), 8.21 (s, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.6 (CH_3), 19.0, 28.4, 30.6, 31.2 (CH_2), 64.3(CH_2O), 141.1(CH), 153.5 (C), 173.0 (CO). IR (KBr): $\tilde{\nu}$ = 2958 (m), 2873 (w), 1729 (s), 1536 (w), 1456 (w), 1412 (m), 1165 (s), 1109 (m), 1020 (w), 944 (w), 849 (w), 738 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 336 (66)$[M]^+$, 2263 (65), 235 (100), 207 (6), 188 (12), 161 (71). HRMS (EI, 70 eV): calcd for $C_{18}H_{28}N_2O_4$ $[M]^+$: 336.20436; found: 336.20440.

Isobutyl 3,3'-(pyrazine-2,3-diyl)dipropanoate (14b);



Compound **14b** was prepared from **11a** (149 mg, 1.0 mmol) as a light brown highly viscous oil (255 mg, 76%). Reaction temperature: 140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (d, 12H, *J* = 6.9 Hz, $4CH_3$), 1.77-1.88(m, 2H, 2CH), 2.81 (t, 4H, *J* = 7.3 Hz, $2CH_2$), 3.10 (t, 4H, *J* = 6.9 Hz, $2CH_2$), 3.79 (d, 4H, *J* = 6.9 Hz, $2CH_2O$), 8.20 (s, 2H, Ar-H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.9 (CH_3), 27.6(CH), 28.4, 31.1 (CH_2), 70.6 (CH_2O), 141.2 (CH), 153.4 (C), 173.0 (CO). IR (KBr): $\tilde{\nu}$ = 2959 (m), 2874 (w), 1729 (s), 1535 (w), 1469 (m), 1411 (m), 1379 (m), 1160 (s), 1109 (m), 992 (m), 851 (w), 796 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 336 (49)$[M]^+$, 279 (23), 261 (52), 233 (100), 219 (15), 177 (51), 159 (46). HRMS (EI, 70 eV): calcd for $C_{18}H_{28}N_2O_4$ $[M]^+$: 336.20436; found: 336.20453.

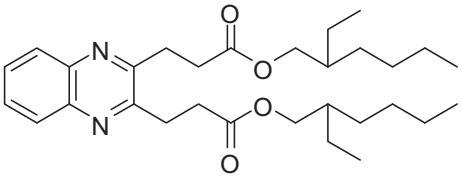
Tert-Butyl 3,3'-(pyrazine-2,3-diyl)dipropanoate (14c);



Compound **14c** was prepared from **11a** (149 mg, 1.0 mmol) as a light yellow highly viscous oil (235 mg, 70%). Reaction temperature: 140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 18H, $6CH_3$), 2.68 (t, 4H, *J* = 7.1 Hz, $2CH_2$), 3.04 (t, 4H, *J* = 7.1

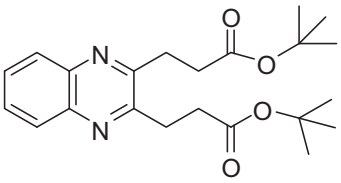
Hz, $2CH_2$), 8.21 (s, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.2 (CH_3), 28.6, 32.5 (CH_2), 80.3 (C), 141.1 (CH), 153.7 (CH), 172.3 (C). IR (KBr): $\tilde{\nu}$ = 2976 (m), 2931 (w), 1723 (s), 1456 (w), 1392 (w), 1366 (m), 1248 (w), 1146 (s), 978 (w), 846 (m), 755 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 336 (02) $[M]^+$, 280 (27), 263 (60), 224 (98), 207 (92), 188 (29), 180 (100), 161 (30). HRMS (EI, 70 eV): calcd for $C_{18}H_{28}N_2O_4$ $[M]^+$: 336.20436; found: 336.20490.

Bis(2-ethylhexyl) 3,3'-(quinoxaline-2,3-diyl) dipropanoate (14d);



Compound **14d** was prepared from **11b** (199 mg, 1.0 mmol) as a light brown highly viscous oil (344 mg, 69%). Reaction temperature: 150 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.77-0.80 (m, 12H), 1.16-1.22 (m, 16H), 1.42-1.52 (m, 2H), 2.95 (t, 4H, *J* = 7.1 Hz), 3.26 (t, 4H, *J* = 6.9 Hz), 3.93 (d, 4H, *J* = 5.8 Hz, $2CH_2O$), 7.54-7.58 (m, 2H, ArH), 7.86-7.89 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.9, 14.0 (CH_3), 22.9, 23.7, 28.9, 29.1, 30.4, 30.9 (CH_2), 38.7 (CH), 66.9 (CH_2O), 128.5, 128.7 (CH), 140.7, 153.8 (C), 173.3 (CO). IR (KBr): $\tilde{\nu}$ = 3063 (w), 2958 (s), 2928 (s), 2860 (m), 1731 (s), 1654 (m), 1545 (s), 1458 (m), 1418 (m), 1378 (m), 1169 (s), 1079 (w), 758 (s), 608 (m), 541 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 498 (52)$[M]^+$, 469 (30), 441 (69), 385 (56), 356 (100), 313 (18), 226 (40), 184 (33). HRMS (EI, 70 eV): calcd for $C_{30}H_{46}N_2O_4$ $[M]^+$: 498.27568; found: 498.27498.

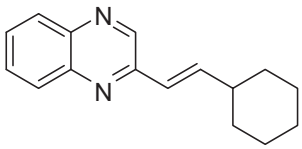
Tert-Butyl 3,3'-(quinoxaline-2,3-diyl)dipropanoate (14e);



Compound **14e** was prepared from **11b** (199 mg, 1.0 mmol) as a light yellow highly viscous oil (297 mg, 77%). Reaction temperature: 150 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 18H, $6CH_3$), 2.83 (t, 4H, *J* = 7.2 Hz, $2CH_2$), 3.21 (t, 4H, *J* = 7.0 Hz, $2CH_2$), 7.54-7.57 (m, 2H), 7.86-7.89 (m, 2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.1 (CH_3), 29.3, 32.0 (CH_2), 80.2 (C), 128.5, 128.6 (CH), 140.6, 154.1 (C), 172.4 (CO). IR (KBr): $\tilde{\nu}$ = 2977 (w), 2930 (w), 1722 (s), 1488 (w), 1365 (m), 1314 (m), 1256 (m), 1143 (s), 953 (w), 846 (m), 760 (s), 662 (w), 609 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z*

(%) = 386 (16)$[M]^+$, 330 (34), 313 (37), 274 (84), 257 (74), 230 (100), 211 (31), 183 (36). HRMS (EI, 70 eV): calcd for $C_{22}H_{30}N_2O_4$ $[M]^+$: 386.22001; found: 386.22006.

(E)-2- (2-Cyclohexylvinyl)quinoxaline (15);

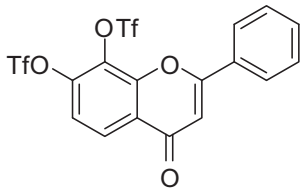


Compound **15** was prepared starting with **11b** (199 mg, 1.0 mmol) as a light yellow solid (167 mg, 70%). ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.46-1.85 (m, 10H), 2.18-2.27 (m, 1H), 6.61 (d, 1H, *J* = 15.91Hz), 6.91 (dd, 1H, *J* = 6.8, 16.1 Hz, CH), 7.57-7.68 (m, 2H), 7.94-7.99 (m, 2H), 8.86 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 25.9, 26.0, 32.3 (CH_2), 41.4, 125.3, 128.9, 129.0, 130.2 (CH), 141.3 (C), 143.9, 146.1 (CH), 151.1, 158.1 (C). IR (KBr): $\tilde{\nu}$ = 3060 (w), 2923 (s), 2850 (m), 1708 (m), 1590 (w), 1544 (w), 1447 (m), 1361 (m), 1247 (m), 1109 (s), 974 (w), 759 (s), 565 (m), 537 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 238 (100)$[M]^+$, 223 (17), 209 (19), 195 (24), 195 (24), 181 (34), 169 (16). HRMS (EI, 70 eV): calcd for $C_{16}H_{18}N_2$ $[M]^+$: 238.14700; found: 238.14701.

7.4 Synthesis of 7, 8-Diarylflavones by Site-Selective Suzuki-Miyaura Cross Coupling Reactions of 7, 8-dihydroxyflavone.

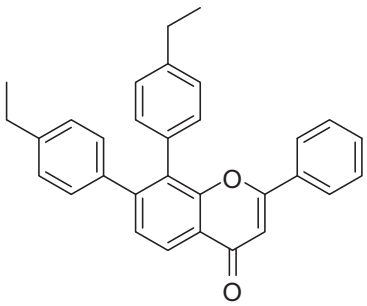
General procedure for Suzuki-Miyaura cross-coupling reactions: A 1,4-dioxane solution (3-4 mL) of **17** (1.0 equiv.), arylboronic acid **18** (1.0-1.3 equiv. per desired cross-coupling reaction), K_3PO_4 (1.5-2.0 equiv. per desired cross-coupling reaction), and $Pd(PPh_3)_4$ (5 mol%) was heated at 70-100 °C for 4 h. After cooling to 20 °C, a saturated aqueous solution of NH_4Cl was added, the organic and aqueous layers were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography.

4-Oxo-2-phenyl-4H-chromene-7,8-diyl-bis(trifluoromethanesulfonate) (17):



To a CH_2Cl_2 solution (10 mL) of **16** (254 mg, 1.0 mmol) was added pyridine (0.32 mL, 4.0 mmol) at – 78 °C under argon atmosphere. After stirring for 10 min, Tf_2O (0.40 mL, 2.4 mmol) was added at –78 °C. The mixture was allowed to warm to 0 °C and stirred for 4 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo. Product **17** was isolated by rapid column chromatography (flash silica gel, heptanes/EtOAc) as a white solid (393 mg, 76%); m.p. 142-143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.82 (s, 1H), 7.43-7.52 (m, 4H, ArH), 7.88-7.91 (m, 2H, ArH), 8.25 (d, J = 9.4 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 108.3 (CH), 118.6 (q, $J_{F,C}$ = 321.6 Hz, CF_3), 118.7 (q, $J_{F,C}$ = 320.4 Hz, CF_3), 118.9 (CH), 124.7 (C), 126.6, 126.7, 129.3 (CH), 129.9, 130.2 (C), 132.6 (CH), 143.9, 149.5, 164.5, 175.3 (C) . ^{19}F NMR (282 MHz, $CDCl_3$): δ = –72.6, –72.8. IR (KBr): $\tilde{\nu}$ = 3080 (w), 1660 (s), 1613 (m), 1427 (s), 1359 (m), 1210 (s), 1126 (s), 1053 (m), 996 (m), 955 (m), 836 (m), 794 (m), 756 (m), 733 (w), 684 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 518 (95) $[M]^+$, 385 (7), 357 (15), 321 (29), 293 (100), 219 (66), 191 (79). HRMS (EI, 70 eV): calcd for $C_{17}H_8F_6O_8S_2$ $[M^+]$: 517.95700; found 517.95651.

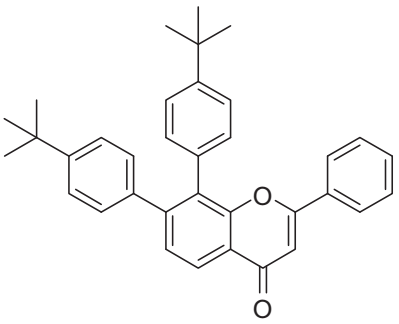
7,8-Bis(4-ethylphenyl)-2-phenyl-4H-chromen-4-one (19a):



Starting with **17** (259 mg, 0.5 mmol), K_3PO_4 (424 mg, 2.0 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-ethylphenylboronic acid (**18a**) (195 mg, 1.3 mmol) and 1,4-dioxane (5 mL), **19a** was isolated as a crystalline white solid (150 mg, 70%); m.p. 148-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, 3H, J = 7.8 Hz, CH_3), 1.18 (t, 3H, J = 7.4 Hz, CH_3), 2.50 (q, 2H, J = 7.4,15.3 Hz), 2.59 (q, 2H, J = 7.4,15.3 Hz), 6.76 (s, 1H), 6.93-7.07 (m, 8H, ArH), 7.22-7.35 (m, 3H, ArH), 7.41 (d, 1H, J = 8.3 Hz, ArH), 7.46-7.50 (m, 2H, ArH), 8.16 (d, 1H, J = 8.3 Hz, ArH). ^{13}C NMR (62MHz, $CDCl_3$): δ = 15.3, 15.8 (CH_3), 28.4, 28.7 (CH_2), 106.6 (CH), 122.7 (C), 124.3, 126.2, 127.3, 127.4, 127.5, 128.8, 129.7 (CH), 130.3 (C), 131.1, 131.4 (CH), 131.6, 132.0, 137.2, 143.3, 143.5, 146.6, 154.0, 163.1, 178.7 (C). IR (KBr): $\tilde{\nu}$ = 3064 (w), 2966 (w), 1643 (s), 1510 (m), 1394 (m), 1370

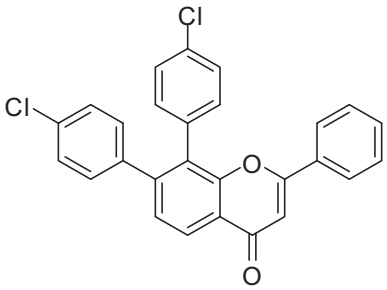
(m), 1147 (m), 1016 (m), 919 (m), 823 (s), 772 (s), 689 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 430 (100) $[M]^+$, 415 (09), 401 (51), 373 (03), 344 (02), 313 (09), 239 (09), 156 (03). HRMS (EI) calcd for $C_{31}H_{26}O_2$ $[M^+]$: 430.19273; found 430.19288.

7,8-Bis(4-tert-butylphenyl)-2-phenyl-4H-chromen-4-one (*19b*):



Starting with **17** (259 mg, 0.5 mmol), K_3PO_4 (424 mg, 2.0 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-tert-butylphenyl boronic acid (**18b**) (231 mg, 1.3 mmol) and 1,4-dioxane (5 mL), **19b** was isolated as a white solid (143 mg, 59%); m.p. 162-164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (s, 9H, $3CH_3$), 1.28 (s, 9H, $3CH_3$), 6.80 (s, 1H), 7.03-7.17 (m, 7H, ArH), 7.23-7.30 (m, 4H, ArH), 7.44-7.51 (m, 3H, ArH), 8.18 (d, 1H, J = 8.1 Hz, ArH). ^{13}C NMR (75MHz, $CDCl_3$): δ = 31.2, 31.4 (CH_3), 34.4, 34.6 (C), 106.6 (CH), 122.7 (C), 124.3, 124.7, 124.8, 126.2, 127.2, 128.8, 129.5 (CH), 130.4 (C), 130.8, 131.4 (CH), 131.6, 131.8, 136.8, 146.5, 150.3, 150.4, 154.0, 163.0, 178.7 (C). IR (KBr): $\tilde{\nu}$ = 3059 (w), 2958 (m), 1635 (s), 1372 (m), 1258 (m), 1142 (w), 1090 (m), 1014 (m), 919 (w), 794 (s), 684 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 486 (95) $[M]^+$, 471 (100), 455 (02), 429 (06), 415 (86), 387 (05), 373 (19), 339 (04), 313 (07), 228 (14), 200 (08), 177 (15). HRMS (EI) calcd for $C_{35}H_{34}O_2$ $[M^+]$: 486.25533; found 486.25569.

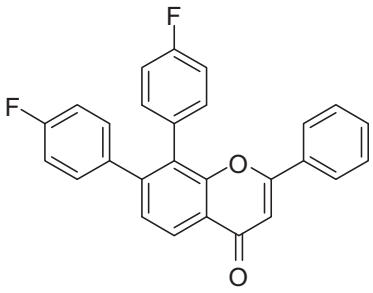
7,8-Bis(4-chlorophenyl)-2-phenyl-4H-chromen-4-one (*19c*):



Starting with **17** (259 mg, 0.5 mmol), K_3PO_4 (424 mg, 2.0 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-chlorophenylboronic acid (**18c**) (203 mg, 1.3 mmol) and 1,4-dioxane (5 mL), **19c** was isolated as a light yellow solid (160 mg, 72%); m.p. 192-194 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.82 (s, 1H), 7.01 (d, 2H, J = 8.8 Hz, ArH) 7.10-7.18 (m, 5H, ArH), 7.29 (d, 2H, J = 8.6 Hz, ArH) 7.37-7.43 (m, 3H, ArH), 7.48-7.53 (m, 2H, ArH), 8.23 (d, 1H, J = 8.2 Hz, ArH). ^{13}C NMR (62MHz, $CDCl_3$): δ = 107.0 (CH), 123.2 (C), 125.2, 126.1, 127.1, 128.4, 128.5, 129.1, 131.0 (CH), 131.3 (C), 131.6, 132.4 (CH),

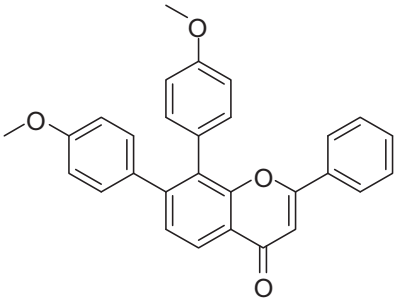
132.8, 133.8, 133.9, 137.9, 143.0, 145.4, 154.0, 163.4, 178.2 (C). IR (KBr): $\tilde{\nu}$ = 3055 (w), 1682 (w), 1587 (w), 1486 (m), 1248 (w), 1088 (m), 1009 (m), 940 (m), 820 (m), 742 (s), 723 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 442 (100) $[M]^+$, 407 (23), 378 (01), 339 (09), 305 (12), 249 (27), 213 (27), 172 (14). HRMS (EI) calcd for $C_{27}H_{16}O_2Cl_2$ $[M^+]$: 442.05219; found 442.05234.

7,8-Bis(4-fluorophenyl)-2-phenyl-4H-chromen-4-one (*19d*):



Starting with **17** (259 mg, 0.5 mmol), K_3PO_4 (424 mg, 2.0 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-fluorophenylboronic acid (**18d**) (182 mg, 1.3 mmol) and 1,4-dioxane (5 mL), **19d** was isolated as a white solid (127 mg, 62%); m.p. 233-235 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.84 (s, 1H), 6.89 (d, 2H, *J* = 8.7 Hz, ArH), 7.01-7.07 (m, 4H, ArH), 7.12-7.18 (m, 2H, ArH), 7.34 (d, 2H, *J* = 8.1 Hz, ArH), 7.42 (d, 2H, *J* = 8.2 Hz, ArH) 7.50-7.53 (m, 2H, ArH), 8.22 (d, 1H, *J* = 8.2 Hz, ArH). ^{13}C NMR (62MHz, $CDCl_3$): δ = 107.0 (CH), 115.2 (d, J_{CF} = 21.3 Hz, CH), 123.1 (C), 125.0, 126.1, 127.2, 129.0, (CH), 129.3 (C), 130.4 (d, J_{CF} = 3.5 Hz, C), 131.3 (CH), 131.4 (C), 131.5 (d, J_{CF} = 20 Hz, CH), 132.7, 132.8 (CH), 135.6 (d, J_{CF} = 3.2 Hz, C), 145.8, 153.7, 163.4 (C), 162.8 (d, J_{CF} = 247 Hz, CF), 162.9 (d, J_{CF} = 247 Hz, CF), 178.3 (C). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -113.3 (ArF), -112.4 (ArF). IR (KBr): $\tilde{\nu}$ = 3062 (w), 1630 (s), 1602 (m), 1509 (s), 1449 (m), 1415 (m), 1373 (s), 1219 (s), 1159 (s), 1093 (m), 1014 (m), 834 (s), 771 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 410 (100) $[M]^+$, 382 (16), 351 (02), 307 (17), 280 (06), 262 (09), 251 (40), 225 (03). HRMS (EI) calcd for $C_{27}H_{16}O_2F_2$ $[M^+]$: 410.11129; found 410.11046.

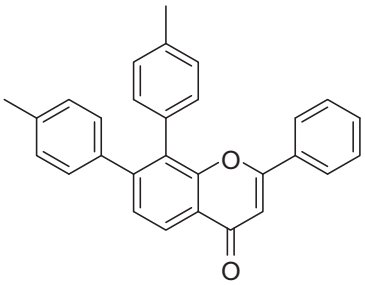
7,8-Bis(4-methoxyphenyl)-2-phenyl-4H-chromen-4-one (*19e*):



Starting with **17** (259 mg, 0.5 mmol), K_3PO_4 (424 mg, 2.0mmol), $Pd(PPh_3)_4$ (5 mol%), 4-methoxphenyl boronic acid (**18e**) (197 mg, 1.3 mmol) and 1,4-dioxane (5 mL), **19e** was isolated as a white crystalline (147 mg, 68%); m.p.172-174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 6.70 (d, 2H,

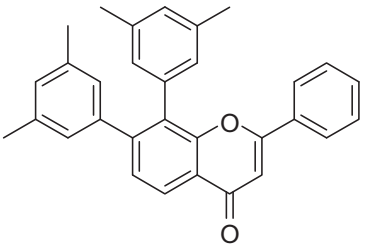
J = 8.8 Hz, ArH), 6.80 (s, 1H), 6.82 (d, 2H, *J* = 8.8 Hz, ArH), 7.02 (d, 2H, *J* = 8.8 Hz, ArH), 7.10 (d, 2H, *J* = 8.8 Hz, ArH), 7.32-7.36 (m, 3H, ArH), 7.42 (d, 1H, *J* = 8.2 Hz, ArH), 7.54-7.58 (m, 2H, ArH) 8.17 (d, 1H, *J* = 8.2 Hz, ArH). ^{13}C NMR (75MHz, $CDCl_3$): δ = 55.2, 55.3 (OCH_3), 106.7, 113.4, 113.5 (CH), 121.7, 123.3 (C), 124.3 (CH), 126.0 (C), 126.2, 127.3, 128.9 (CH), 130.4, 130.7 (C), 131.0, 131.4, 132.4 (CH), 145.5, 153.0, 157.8, 157.9, 162.2, 177.7 (C). IR (KBr): $\tilde{\nu}$ = 2922 (w), 1635 (s), 1512 (m), 1423 (m), 1372 (m), 1285 (m), 1243 (s), 1177 (m), 1112 (w), 1017 (m), 916 (w), 822 (s), 769 (s), 687 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 434 (100) $[M]^+$, 403 (07), 331 (04), 281 (09), 253 (05), 207 (17), 189(11). HRMS (EI) calcd for $C_{27}H_{14}O_6$ $[M^+]$: 434.07849; found 434.07952.

2-Phenyl-7,8-di(p-tolyl)-4H-chromen-4-one (*19f*):



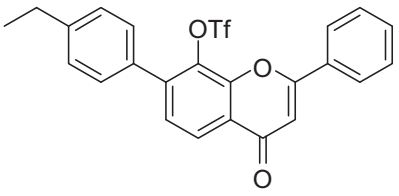
Starting with **17** (259 mg, 0.5 mmol), K_3PO_4 (424 mg, 2.0 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-methylphenylboronic acid (**18f**) (177 mg, 1.3 mmol) and 1,4-dioxane (5 mL), **19f** was isolated as a crystalline light yellow solid (148 mg, 74%); m.p. = 248-249 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 6.75 (s, 1H), 6.90-7.04 (m, 8H, ArH), 7.24-7.33 (m, 3H, ArH), 7.39 (d, 1H, *J* = 8.2 Hz, ArH), 7.48-7.51 (m, 2H, ArH), 8.16 (d, 1H, *J* = 8.2 Hz, ArH). ^{13}C NMR (75MHz, $CDCl_3$): δ = 21.2, 21.4 (CH_3), 106.7 (CH), 122.8 (C), 124.4, 126.2, 127.4, 128.6, 128.7, 128.9, 129.7 (CH), 130.2 (C), 131.0, 131.4 (CH), 131.6, 131.7, 137.0, 137.1, 146.7, 153.9, 163.2, 178.6 (C). IR (KBr): $\tilde{\nu}$ = 2917 (w), 1631 (m), 1592 (w), 1446 (m), 1371 (m), 1238 (w), 1145 (m), 1016 (m), 917 (w), 816 (s), 773 (s), 690 (s), 665 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 402 (100) $[M]^+$, 387 (34), 359 (03), 331 (4), 299 (4), 285 (07), 243 (09), 229 (12). HRMS (EI) calcd for $C_{29}H_{22}O_2$ $[M^+]$: 402.16143; found 402.161442.

7,8-Bis(3,5-dimethylphenyl)-2-phenyl-4H-chromen-4-one (19g):



Starting with **17** (259 mg, 0.5 mmol), K_3PO_4 (424 mg, 2.0 mmol), $Pd(PPh_3)_4$ (5 mol%), 3,5-dimethylphenylboronic acid (**18g**) (195 mg, 1.3 mmol) and 1,4-dioxane (5 mL), **19g** was isolated as a colorless crystalline (152 mg, 71%); m.p. 233-235 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 6H, $2CH_3$), 2.19 (s, 6H, $2CH_3$), 6.73 (Brs, 2H), 6.77 (Brs, 1H), 6.80 (Brs, 2H), 6.82 (s, 1H), 6.87 (Brs, 1H), 7.28-7.37 (m, 3H, ArH), 7.43 (d, 1H, J = 8.2 Hz, ArH), 7.56-7.59 (m, 2H, ArH), 8.24 (d, 1H, J = 8.2 Hz, ArH). ^{13}C NMR (75MHz, $CDCl_3$): δ = 21.2 (CH_3), 106.5 (CH), 122.7 (C), 124.2, 126.2, 127.3, 127.7, 128.8, 128.9, 129.0 (CH), 130.4 (C), 131.4 (CH), 131.7, 134.4, 137.0, 137.2, 139.8, 147.0, 153.8, 163.2, 178.8 (C). IR (KBr): $\tilde{\nu}$ = 2951 (w), 1709 (m), 1663 (m), 1629 (s), 1593 (m), 1435 (m), 1366 (m), 1332 (m), 1272 (m), 1190 (s), 1024 (m), 849 (w), 819 (m), 764 (m), 680 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 430 (100) $[M]^+$, 415 (73), 402 (07), 355 (05), 313 (09), 285 (06), 239 (07), 164 (17). HRMS (EI) calcd for $C_{31}H_{26}O_2$ $[M^+]$: 430.19273; found 430.19366.

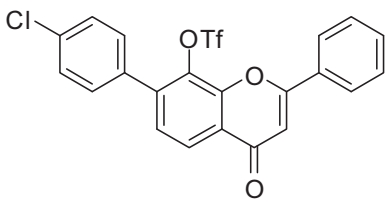
7-(4-Ethylphenyl)-4-oxo-2-phenyl-4H-chromen-8-yl Trifluoromethanesulfonate (20a):



Starting with **17** (156 mg, 0.30 mmol), K_3PO_4 (96 mg, 0.45 mmol), $Pd(PPh_3)_4$ (5 mol%), (4-ethylphenyl) boronic acid (**18a**) (45 mg, 0.30 mmol) and 1,4-dioxane (3mL), **20a** was isolated as a white solid (102 mg, 72%), m.p. 167-168 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.22 (t, 3H, J = 7.7 Hz, CH_3), 2.66 (q, 2H, J = 7.5 Hz, CH_2), 6.83 (s, 1H), 7.27 (d, 2H, J = 8.0 Hz, ArH), 7.38 (d, 2H, J = 8.3 Hz, ArH), 7.44 (d, 1H, J = 8.3 Hz, ArH), 7.46-7.50 (m, 3H, ArH), 7.95-7.97 (m, 2H, ArH), 8.18 (d, 1H, J = 8.3 Hz, ArH). ^{13}C NMR (125.76 MHz, $CDCl_3$): δ = 15.5 (CH_3), 28.7 (CH_2), 108.2 (CH), 118.0 (q, $J_{F,C}$ = 320 Hz, CF_3), 124.2 (C), 125.1, 126.7, 127.4, 128.3, 129.1, 129.2 (CH), 130.8, 131.6 (C), 132.1 (CH), 135.1, 140.7, 145.9, 149.0, 163.8, 176.7 (C). ^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.3. IR (KBr): $\tilde{\nu}$ = 2916 (w), 2850 (w), 1622 (m), 1568 (m), 1447 (m), 1386 (s), 1271 (m), 1164 (s), 1041 (m), 906 (w), 811 (s), 767 (s), 681 (s), 634 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 474 (40)

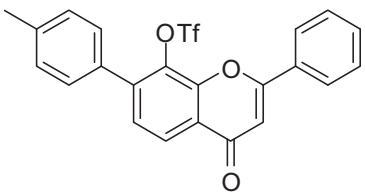
$[M]^+$, 410 (28), 395 (18), 366 (03), 341 (100), 326 (08), 313 (20), 281 (04). HRMS (EI) calcd for $C_{24}H_{17}F_3O_5S$ $[M^+]$: 474.07471 found 474.07492.

7-(4-Chlorophenyl)-4-oxo-2-phenyl-4H-chromen-8-yl trifluoromethanesulfonate (*20b*)



Starting with **17** (156 mg, 0.30 mmol), K_3PO_4 (96 mg, 0.45 mmol), $Pd(PPh_3)_4$ (5 mol%), (4-chlorophenyl boronic acid (**18c**) (47 mg, 0.30 mmol) and 1,4-dioxane (3mL), **20b** was isolated as a light yellow amorphous solid (95 mg, 66%); m.p. 143-145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.84 (s, 1H), 7.39-7.43 (m, 5H, ArH), 7.48-7.52 (m, 3H, ArH), 7.93-7.96 (m, 2H, ArH), 8.20 (d, 1H, *J* = 8.3 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 108.2 (CH), 118.2 (q, J_{CF} = 321 Hz, CF_3), 124.7 (C), 125.4, 126.7, 127.0, 129.1, 129.2, 130.6 (CH), 130.7 (C), 132.2 (CH), 132.8, 135.8, 139.2, 145.5, 149.0, 164.0, 176.5 (C). ^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.1. IR (KBr): $\tilde{\nu}$ = 2928 (w), 1656 (s), 1426 (m), 1359 (m), 1212 (s), 1134 (s), 1090 (m), 1015 (m), 966 (m), 880 (w), 803 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 480 (16) $[M]^+$, 347 (100), 332 (02), 284 (05), 345 (08), 210 (08), 189 (10). HRMS (EI) calcd for $C_{22}H_{12}F_3O_5S$ $[M^+]$: 480.00406 found 480.00345.

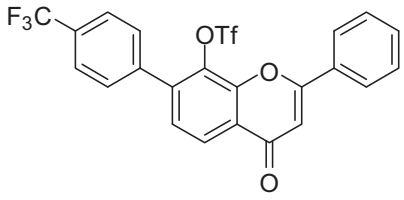
4-Oxo-2-phenyl-7-p-tolyl-4H-chromen-8-yl trifluoromethanesulfonate (*20c*):



Starting with **17** (156 mg, 0.30 mmol), K_3PO_4 (96 mg, 0.45 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-methylphenylboronic acid (**18f**) (41 mg, 0.30 mmol) and 1,4-dioxane (3mL), **20c** was isolated as a amorphous white solid (105 mg, 76%); m.p. 156-158 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3H, CH_3), 6.78 (s, 1H), 7.26-7.30 (m, 3H, ArH), 7.42-7.49 (m, 4H, ArH), 7.74 (d, 1H, *J* = 8.3 Hz, ArH), 7.84-7.88 (m, 2H, ArH) 8.24 (d, 1H, *J* = 8.3 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 107.8, 116.4 (CH), 118.2 (q, J_{CF} = 320 Hz, CF_3), 124.7 (C), 126.4, 126.5, 128.9, 129.2, 129.8 (CH), 130.6 (C), 131.7 (CH), 131.8, 132.7, 135.0, 145.1, 149.6, 164.0, 176.8 (C). ^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.3. IR (KBr): $\tilde{\nu}$ = 2917 (m), 1623 (s), 1389 (m), 1248 (m), 1167 (s), 1019 (m), 811 (m), 767 (m), 682 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 460 (40) $[M]^+$, 418 (03), 380 (02), 355 (14), 328 (100), 300 (04), 262

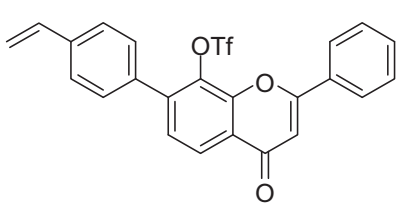
(02), 226 (73), 211 (22), 198 (10). HRMS (EI) calcd for $C_{23}H_{15}F_3O_5S$ [M^+]: 460.06230 found 460.06350.

4-Oxo-2-phenyl-7-(4-(trifluoromethyl)phenyl)-4H-chromen-8-yl trifluoromethanesulfonate (*20d*):



Starting with **17** (156 mg, 0.30 mmol), K_3PO_4 (96 mg, 0.45 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-(trifluoromethyl) phenylboronic acid (**18h**) (57 mg, 0.30 mmol) and 1,4-dioxane (3mL), **20d** was isolated as a white solid (107 mg, 69%); m.p. 176-178 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 6.85 (s, 1H), 7.42 (d, 2H, J = 8.3 Hz, ArH), 7.49-7.51 (m, 2H, ArH), 7.60(d, 2H, J = 8.0 Hz, ArH), 7.72 (d, 2H, J = 8.2 Hz, ArH), 7.94-7.97 (m, 2H, ArH) 8.24 (d, 1H, J = 8.3 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ= 108.3, (CH), 118.3 (q, J_{CF} = 319 Hz, CF_3), 124.2 (q, J_{CF} = 280 Hz, CF_3), 125.1 (C), 125.5 (q, J_{CF} = 3.6 Hz, 2CH), 125.8, 126.7, 127.0, 129.2, 129.7 (CH), 130.1 (q, J_{CF} = 34.2 Hz, C), 130.6, 132.0 (C), 132.3 (CH), 139.0, 145.3, 149.2, 164.1, 176.4 (C). ^{19}F NMR (282 MHz, $CDCl_3$): δ= –74.2, –62.8 . IR (KBr): $\tilde{\nu}$ = 2923 (w), 1649 (m), 1421 (m), 1326 (m), 1205 (m), 1115 (s), 1070 (m), 1017 (m), 963 (m), 829 (m), 802 (s), 763 (m), 682 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 514 (19) [M]$^+$, 381 (100), 325 (02), 279 (08), 251 (08), 223 (13), 183 (06). HRMS (EI) calcd for $C_{23}H_{12}F_6O_5S$ [M^+]: 514.03041 found 514.03132.

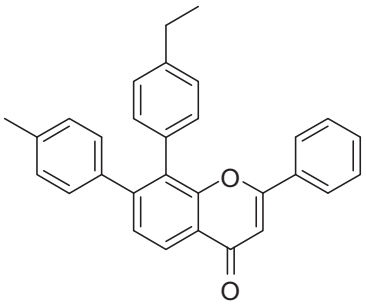
4-Oxo-2-phenyl-7-(4-vinylphenyl)-4H-chromen-8-yl trifluoromethanesulfonate (*20e*):



Starting with **17** (156 mg, 0.30 mmol), K_3PO_4 (96 mg, 0.45 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-vinylphenylboronic acid (**18i**) (44 mg, 0.30 mmol) and 1,4-dioxane (3mL), **20e** was isolated as a amorphous white solid (105 mg, 74%); m.p. 113-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.30 (d, 1H, J = 11.6 Hz), 5.80 (d, 1H, J = 16.9 Hz), 6.71 (dd, 1H, J = 10.8, 17.6 Hz), 6.84 (s, 1H), 7.42-7.50 (m, 8H, ArH), 7.94-7.97 (m, 2H, ArH), 8.19 (d, 1H, J = 8.4 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 115.4 (CH_2), 108.2 (CH), 117.8 (q, J_{CF} = 319 Hz, CF_3), 124.4 (C), 125.2, 126.6, 126.7, 127.2, 129.1, 129.5 (CH), 130.8 (C), 132.1 (CH), 133.6, 135.0 (C), 136.0

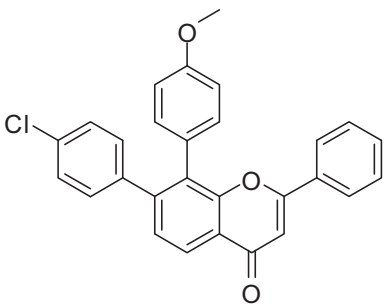
(CH), 138.6, 140.2, 149.5, 163.9, 176.7 (C). ^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.2. IR (KBr): $\tilde{\nu}$ = 2923 (w), 1645 (s), 1484 (w), 1423 (s), 1354 (s), 1216 (s), 1128 (s), 1017 (m), 963 (m), 803 (m), 763 (m), 681 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 472 (16) $[M]^+$, 339 (100), 311 (01), 383 (11), 237 (07), 210 (03), 181 (07). HRMS (EI) calcd for $C_{24}H_{15}F_3O_5S$ $[M^+]$: 472.05868 found 472.05988.

***8-(4-Ethylphenyl)-2-phenyl-7-(p-tolyl)-4H-chromen-4-one* (21a):**



Following the *general procedure* starting with **20c** (101 mg, 0.22 mmol), K_3PO_4 (93 mg, 0.44 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-ethylphenylboronic acid (44 mg, 0.29 mmol) and 1,4-dioxane (3 mL), **21a** was isolated as a yellow solid (60 mg, 66%); m.p. 198-199 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, 3H, *J* = 7.9 Hz, CH_3), 2.23 (s, 3H, CH_3), 2.62 (q, 2H, *J* = 7.5 Hz), 6.79 (s, 1H), 6.95-7.01 (m, 4H, ArH), 7.07-7.12 (m, 4H, ArH), 7.26-7.38 (m, 3H, ArH), 7.43 (dd, 1H, *J* = 3.4, 8.3 Hz, ArH), 7.50-7.54 (m, 2H, ArH), 8.18 (d, 1H, *J* = 8.3 Hz, ArH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 15.8, 21.1 (CH_3), 28.7 (CH_2), 122.8 (C), 124.3, 126.2, 127.4, 128.6, 128.7, 128.8, 128.9, 129.6, 131.0, 131.3 (CH), 131.6, 131.7, 132.0, 137.0, 143.5, 146.5, 146.7, 153.9, 136.1, 178.7 (C). IR (KBr): $\tilde{\nu}$ = 2962 (s), 2923 (s), 1644 (s), 1597 (w), 1371 (m), 1202 (w), 1096 (w), 1016 (w), 815 (m), 771 (m), 688 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 416 (100) $[M]^+$, 402 (16), 387 (49), 313 (06), 285 (14), 271 (05), 253 (06), 239 (09). HRMS (EI) calcd for $C_{30}H_{24}O_2$ $[M^+]$: 416.17783; found 416.17762.

***7-(4-Chlorophenyl)-8-(4-methoxyphenyl)-2-phenyl-4H-chromen-4-one* (21b):**



Following the *general procedure* starting with **20b** (101 mg, 0.22 mmol), K_3PO_4 (93 mg, 0.44 mmol), $Pd(PPh_3)_4$ (5 mol%), 4-methoxyphenylboronic acid (44 mg, 0.29 mmol) and 1,4-dioxane (3 mL), **21b** was isolated as a yellow solid (60 mg, 73%), m.p. 152-154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 6.82 (s, 1H), 6.96 (d, 2H, *J* = 8.8 Hz), 7.01-7.10 (m, 3H), 7.40 (d, 5H, *J*

= 8.5 Hz, ArH), 7.47-7.49 (m, 2H), 7.93-7.97 (m, 2H), 8.16 (d, 1H, *J* = 8.3 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 108.1, 114.3 (CH), 124.0 (C), 125.0, 126.2, 126.7, 127.2, 128.3, 129.1 (CH), 129.5 (C), 130.6 (CH), 130.8, 131.3 (C), 132.1 (CH), 135.0, 140.3, 145.5, 149.1, 160.6, 163.8, 176.7. IR (KBr): $\tilde{\nu}$ = 3066 (w), 1649 (s), 1519 (m), 1438 (s), 1357 (m), 1246 (m), 1216 (s), 1134 (m), 963 (m), 802 (s), 684 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 438 (100) $[M]^+$, 407 (05), 360 (02), 335 (05), 301 (03), 249 (03), 202 (16). HRMS (EI) calcd for $C_{28}H_{19}ClO_3$ $[M^+]$: 438.10230; found 438.10250.

7.5 Regioselective Sonogashira coupling reactions of 2,4,5,6-tetra chloropyrimidine.

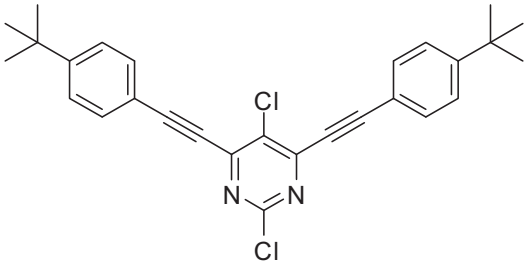
General Procedure for Sonogashira coupling Reaction

A suspension of 2,4,5,6–tetrachloropyrimidine (**22**), $Pd(PPh_3)_2Cl_2$ (10 mol %), CuI (5 mol %) in Diisopropylamine was degassed three time in ace pressure tube. Acetylene (1.2 eq per chlorine atom) were added using a syringe. The mixture was heated at the indicated temperature (60–80 °C) for 4-10 h. The reaction mixture was filtered and residue washed with CH_2Cl_2. The filtrate was washed with saturated solution of ammonium chloride (2 x 25mL), water (2 x 25mL) and dried over anhydrous Na_2SO_4. Solvent was removed in vacuo. The product was purified by column chromatography on silica gel.

General Procedure for Suzuki cross coupling Reaction

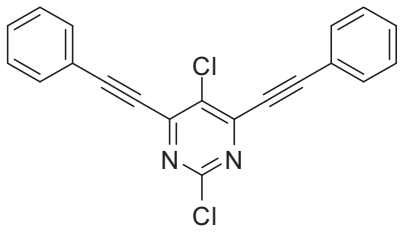
The reaction was carried out in a pressure tube. To a dioxane suspension (3-5 mL) of 2,4,5,6–tetrachloropyrimidine (**22**), $Pd(PPh_3)_2Cl_2$ (3-5 mol %) and arylboronic acid was added an aqueous solution of K_2CO_3 (2M, 1-2 mL). The mixture was heated at the indicated temperature (60-100 °C) for the indicated period of time (2-8 h). The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 x 25mL). The combined organic layers were dried over Na_2SO_4, filtrated and the filtrate was concentrated in vacuo the residue was purified by flash chromatography (silica gel, ethyl acetate / heptanes)

***4,6-Bis((4-tert-butylphenyl)ethynyl)-2,5-dichloropyrimidine* (24a):**



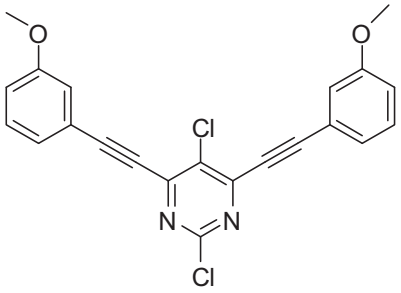
starting with **22** (217 mg; 1mmol), 4-(tert-butyl)phenylacetylene (**23a**) (0.4mL; 2.4mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **24a** was isolated as yellowish highly viscous oil (350 mg; 76 %). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 1.24 (s, 18H, $6CH_3$), 7.34 (d, 4H, *J* = 8.5 Hz), 7.52 (d, 2H, *J* = 8.5 Hz), 7.54 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.0 (CH_3), 35.1, 84.0, 102.6, 117.4 (C), 125.7, 125.8, 132.5, 132.7 (CH), 133.1, 151.3, 154.6, 158.0 (C). IR (KBr): $\tilde{\nu}$ = 2960 (w), 2208 (s), 1516 (s), 1362 (m), 1259 (s), 1106 (m), 1016 (m), 922 (m), 832 (s), 774 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 460 (33) $[M]^+$, 445 (100), 417 (07), 364 (03), 305 (07), 273 (05), 245 (06), 215 (45), 202 (33). HRMS (EI, 70 eV): calcd for $C_{28}H_{26}Cl_2N_2$ $[M^+]$; 460.14685; found 460.14730.

***2,5-Dichloro-4,6-bis(phenylethynyl)pyrimidine* (24b):**



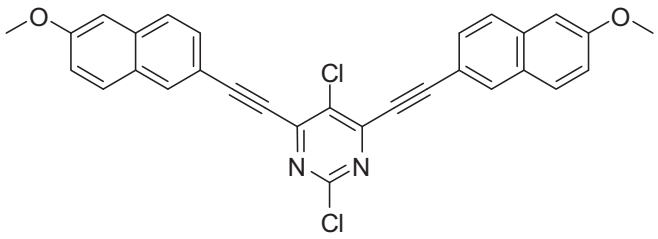
starting with **22** (217 mg; 1mmol), phenylacetylene (**23b**) (0.2mL; 2.4mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **24b** was isolated as light brown solid (254 mg; 73 %); m.p. 197–199 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.32–7.41 (m, 6H), 7.59–7.62 (m, 4H). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 84.1, 102.0, 120.4 (C), 128.6, 130.8, 132.8 (CH), 137.1, 151.2, 158.0 (C). IR (KBr): $\tilde{\nu}$ = 2961 (w), 2209 (s), 1517 (s), 1471 (m), 1261 (s), 1025 (m), 927 (m), 770 (m), 751 (s), 679 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 348 (100) $[M]^+$, 331 (01), 315 (02), 276 (04), 251 (08), 226 (03), 186 (02), 160 (20). HRMS (EI, 70 eV): calcd for $C_{20}H_{10}Cl_2N_2$ $[M^+]$; 348.02156; found 348.02110.

***2, 5- Dichloro-4,6-bis (3-methoxyphenyl)ethynyl pyrimidine* (24c):**



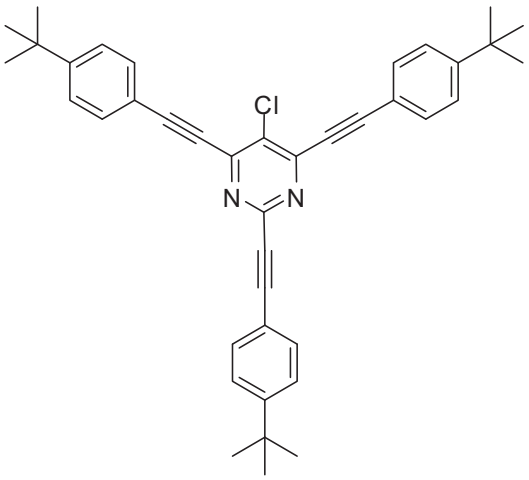
starting with **1** (217 mg; 1mmol), 3-ethynylanisole(**23c**) (0.3mL; 2.4mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **24c** was isolated as brown solid (331 mg; 81 %); m.p. 177–179 °C. ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 3.76 (s, 6H, $2OCH_3$), 6.93–6.97 (m, 2H), 7.09–7.10 (m, 2H), 7.17-7.25 (m, 4H). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 83.8, 101.9 (C), 117.2, 117.6 (CH), 121.3 (C), 125.4, 129.8 (CH), 132.1, 151.2, 158.0, 159.4 (C). IR (KBr): $\tilde{\nu}$ = 2974 (w), 2207 (m), 1596 (m), 1518 (m), 1268 (s), 1151 (m), 1035 (m), 955 (w), 850 (m), 772 (s), 673 (s), 541 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 408 (M^+, 87), 379 (04), 356 (02), 331 (05), 281 (23), 253 (17), 207 (100), 170 (05), 147 (08). HRMS (EI, 70 eV): calcd for $C_{22}H_{14}Cl_2N_2O_2$ [M^+] ; 408.04370; found 408.04320.

***2,5-Dichloro-4,6-bis((6-methoxynaphthalen-2-yl)ethynyl)pyrimidine* (24d):**



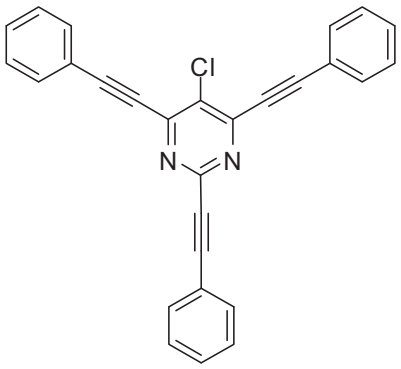
Starting with **22** (217 mg; 1mmol), 2-ethynyl-6-methoxynaphthalene (**23d**) (436 mg; 2.4mmol) CuI (5 mole %), $Pd(PPh_3)_2Cl_2$ (10mol%) and diisopropylamine (5mL), **24d** was isolated as light yellow solid (463 mg; 91 %); m.p. 206–208 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.87 (s, 6H, $2OCH_3$), 7.07 (s, 2H), 7.13 (d, 2H, *J* = 8.9 Hz), 7.54 (d, 2H, *J* = 8.5 Hz), 7.67 (d, 2H, *J* = 8.5 Hz), 7.69 (d, 2H, *J* = 8.9 Hz), 8.07 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 84.2, 104.2 (C), 106.0 (CH), 114.7 (C), 120.1, 127.3 (CH), 128.1 (C), 128.8 (CH), 129.5 (C), 130.0, 134.1 (CH), 135.7, 152.0, 157.0, 159.6 (C). IR (KBr): $\tilde{\nu}$ = 2934 (w), 2199 (s), 1626 (m), 1515 (m), 1476 (s), 1394 (w), 1266 (s), 1225 (m), 1192 (m), 1176 (m), 1032 (m), 969 (m), 849 (m), 798 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 508 (100) $[M]^+$, 493 (03), 465 (22), 422 (12), 362 (03), 325 (06), 281 (04), 254 (10), 211 (21). HRMS (EI, 70 eV): calcd for $C_{30}H_{18}Cl_2N_2O_2$ [M^+] ; 508.07428; found 508.07450.

***2,4,6-Tris((4-tert-butylphenyl)ethynyl)-5-chloropyrimidine* (25a)**



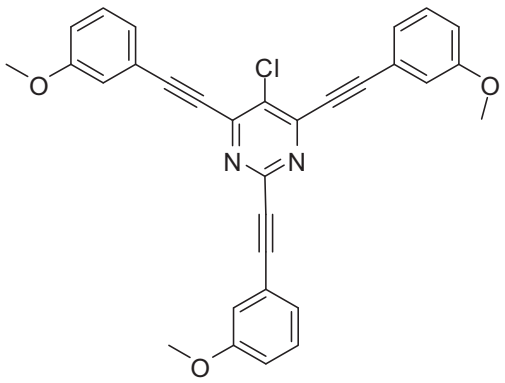
starting with **22** (217 mg; 1mmol), 4-(tert-butyl)phenylacetylene (**23a**) (0.6mL; 3.6mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **25a** was isolated as dark yellow solid (468 mg; 80 %); m.p. 227–229 °C. ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 1.24 (s, 9H, $3CH_3$), 1.29 (s, 18H, $6CH_3$), 6.99 (d, 3H, *J* = 8.3 Hz), 7.29 (d, 3H, *J* = 8.5 Hz), 7.33 (d, 3H, *J* = 8.4 Hz) 7.45 (d, 3H, *J* = 8.5 Hz). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 31.1, 31.4 (CH_3), 34.7, 34.9, 84.9, 93.2, 97.4, 118.6, 124.8 (C), 125.4, 125.5, 127.4, 132.1 (CH), 134.0, 146.9, 151.6, 153.1, 156.0 (C). IR (KBr): $\tilde{\nu}$ = 2959 (m), 1504 (s), 1432 (s), 1356 (m), 1292 (m), 1263 (s), 1133 (s), 1036 (s), 931 (m), 816 (s), 767 (m), 735 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 582 (70) $[M]^+$, 567 (16), 552 (38), 537 (46), 518 (100), 482 (03), 462 (02), 447 (02), 410 (12), 382 (02), 344 (31). HRMS (EI, 70 eV): calcd. for $C_{40}H_{39}ClN_2$ $[M^+]$; 582.28004 found 582.28020.

***5-Chloro-2,4,6-tris(phenylethynyl)pyrimidine* (25b):**



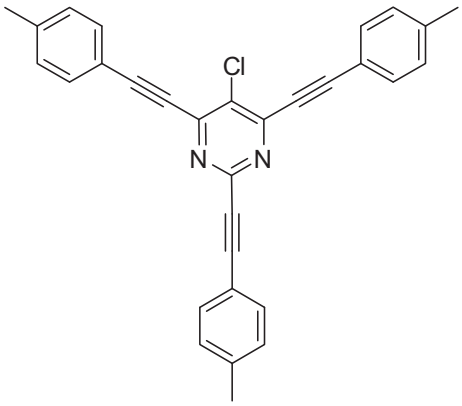
starting with **22** (217 mg; 1mmol), phenylacetylene (**23b**) (0.4mL; 3.6mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **25b** was isolated as light brown solid (294 mg; 71 %); m.p. 220–222 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.30–7.40 (m, 10H), 7.58–7.63 (m, 5H). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 84.4, 87.1, 89.2, 100.5, 120.8, 121.1 (C), 128.4, 128.6, 129.9, 130.5 (CH), 132.0 (C), 132.7 (CH), 149.8, 150.4 (C). IR (KBr): $\tilde{\nu}$ = 3054 (w), 2215 (s), 1512 (s), 1490 (m), 1363 (s), 1229 (m), 1177 (m), 1025 (m), 970 (m), 918 (w), 842 (w), 751 (s), 686 (s) cm^{-1}.GC-MS (EI, 70 eV): *m/z* (%) = 414 (89) $[M]^+$, 377 (60), 346 (20), 315 (12), 250 (27), 238 (23), 189 (33). HRMS (EI, 70 eV): calcd. for $C_{28}H_{15}ClN_2$ $[M^+]$; 414.09215 found 414.09240.

***5-Chloro-2,4,6-tris((3-methoxyphenyl)ethynyl)pyrimidine* (25c)**



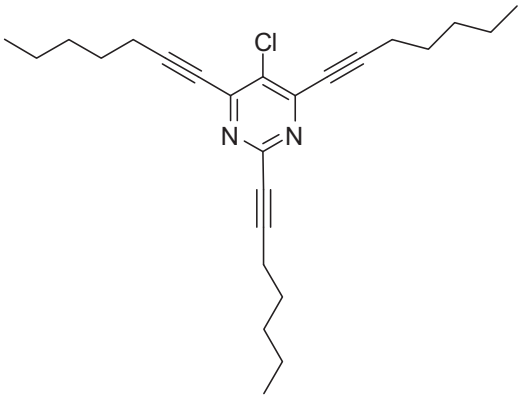
starting with **22** (217 mg; 1mmol), 3-ethynyl anisole (**23c**) (0.45mL; 3.6mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropyl amine (5mL), **25c** was isolated as dark brown solid (388 mg; 77 %); m.p. 163–165 °C. ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 3.74 (s, 3H, OCH_3), 3.76 (s, 6H, $2OCH_3$), 6.87–6.96 (m, 3H), 7.11–7.13 (m, 3H), 7.18–7.25 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3, 55.4 (OCH_3), 84.2, 86.8, 89.2, 100.4 (C), 117.0, 117.1, 117.2, 117.4 (CH), 121.7, 122.0 (C), 125.3, 129.5, 129.7 (CH), 132.0, 149.8, 150.4, 159.3, 159.4 (C). IR (KBr): $\tilde{\nu}$ = 2940 (w), 2214 (s), 1573 (m), 1513 (s), 1483 (m), 1368 (m), 1261 (s), 1162 (m), 1039 (s), 848 (m), 769 (s), 677 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 504 (100) $[M]^+$, 473 (03), 431 (02), 389 (04), 355 (12), 312 (22), 252 (31), 190 (31). HRMS (EI, 70 eV): calcd. for $C_{31}H_{21}ClN_2O_3$ $[M^+]$; 504.12392 found 504.12410.

***5- Chloro -2,4,6-tris(P-tolylethynyl) pyrimidine* (25d)**



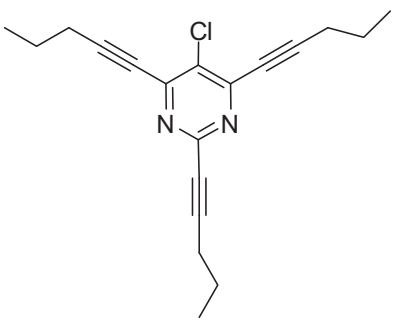
starting with **22** (217 mg; 1mmol), *P*-tolylacetylene (**23e**) (0.4mL; 3.6mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **25d** was isolated as yellow solid (383 mg; 84 %); m.p.102–104°C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 3H, CH_3), 2.32 (s, 6H, $2CH_3$), 7.09–7.15 (m, 8H), 7.50 (d, 4H, *J* = 8.1 Hz). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.6, 21.7 (CH_3), 84.2, 86.8, 89.5, 100.9, 117.5, 118.1 (C), 129.2, 129.3, 132.6 (CH), 140.3, 141.1,149.8, 150.5 (C). IR (KBr): $\tilde{\nu}$ = 2918 (w), 2208 (s), 1682 (w), 1510 (s), 1479 (s), 1361 (m), 1226 (w), 1176 (m),1019 (m), 969 (m), 907 (m), 810 (s), 727 (m) cm^{-1}.GC-MS (EI, 70 eV): *m/z* (%) = 456 (100) $[M]^+$, 422 (04), 280 (07), 264 (05), 230 (11), 174 (36), 139 (54). HRMS (EI, 70 eV): calcd. for $C_{31}H_{21}ClN_2$ $[M^+]$; 456.13971 found 456.13930.

***5-Chloro-2,4,6-tri(hept-1-ynyl)pyrimidine* (25e)**



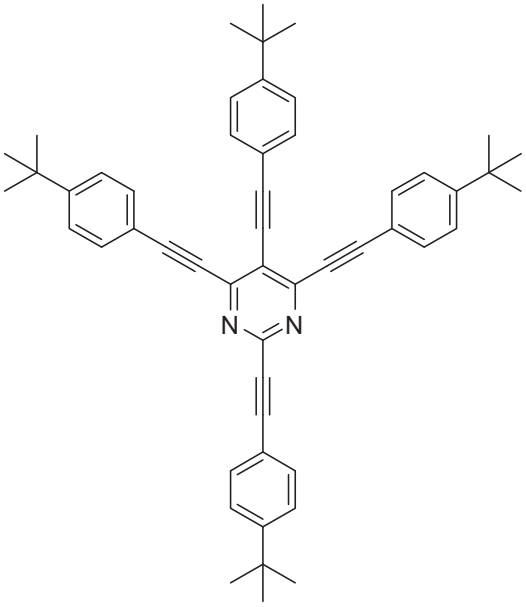
starting with **22** (217 mg; 1mmol), 1-Heptyne (**23e**) (0.5mL; 3.6mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropyl amine (5mL), **25e** was isolated as yellowish highly viscous oil (270 mg; 68 %). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 0.84 (t, 6H, *J* = 7.1 Hz, CH_3), 1.07 (t, 3H, *J* = 7.0 Hz, CH_3), 1.21–1.43 (m, 12H), 1.53–1.64 (m, 6H), 2.33 (t, 2H, *J* = 7.1 Hz), 2.41 (t, 4H, *J* = 7.2 Hz). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.9, 13.9 (CH_3), 19.7, 22.1, 27.7, 28.2, 29.5, 30.9, 40.8, 41.7 (CH_2), 80.2, 91.2, 99.0, 131.5, 149.6, 150.2 (C). IR (KBr): $\tilde{\nu}$ = 2930 (m), 2232 (w), 1604 (s), 1455 (m), 1165 (m), 1079 (m), 783 (m), 760 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 396 (90) $[M]^+$, 382 (60), 368 (41), 344 (100), 330 (40), 316 (07), 301 (04), 287 (06), 231 (04), 209 (04). HRMS (EI, 70 eV): calcd. for $C_{25}H_{33}ClN_2$ $[M^+]$; 396.23160 found 396.23176.

***5-Chloro-2,4,6-tri(pent-1-ynyl)pyrimidine* (25f)**



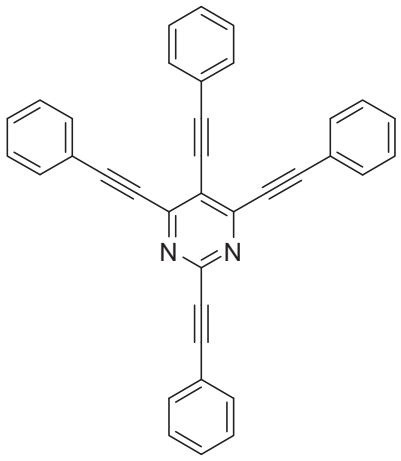
starting with **22** (217 mg; 1mmol), 1-Pentyne (**23f**) (0.3mL; 3.6mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **25f** was isolated as brownish highly viscous oil (216 mg; 69 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, 6H, *J* = 7.3 Hz, CH_3), 0.99 (t, 3H, *J* = 7.4 Hz, CH_3), 1.53–1.64 (m, 6H), 2.32 (t, 2H, *J* = 7.1 Hz), 2.42 (t, 4H, *J* = 7.0 Hz). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.5, 13.6 (CH_3), 21.4, 21.7, 29.6, 30.1 (CH_2), 79.1, 91.4, 103.1, 131.5, 149.7, 150.1 (C). IR (KBr): $\tilde{\nu}$ = 2926 (m), 2228 (m), 1727 (w), 1515 (s), 1489 (s), 1359 (s), 1172 (m), 1080 (w), 962 (m), 790 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 312 (100) $[M]^+$, 297 (21), 282 (40), 267 (13), 254 (15), 225 (23), 211 (33), 183 (43). HRMS (EI, 70 eV): calcd. for $C_{19}H_{21}ClN_2$ $[M^+]$; 312.14321 found 312.14336.

2,4,5,6-Tetrakis((4-tert-butylphenyl)ethynyl)pyrimidine (26a)



starting with **22** (217 mg; 1mmol), 4-(tert-butyl) phenylacetylene (**23a**) (1.0mL; 6.0 mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), Dioxane (7mL) and diisopropylamine (3mL), **26a** was isolated as dark brown solid (535 mg; 76 %); m.p. 110–112 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 9H, CH_3), 1.26 (s, 18H, CH_3), 1.28 (s, 9H, CH_3), 7.31–7.37 (m, 8H), 7.49–7.56 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.0, 30.1 (CH_3), 33.9, 34.0, 82.2, 85.0, 86.7, 89.2, 98.2, 102.4, 117.3 (C), 124.4, 124.6, 130.5, 131.4, 131.6 (CH), 149.2, 151.2, 151.9, 152.3, 152.8 (C). IR (KBr): $\tilde{\nu}$ = 2959 (w), 2209 (w), 1483 (m), 1398 (m), 1264 (m), 1106 (m), 1016 (m), 831 (s), 634 (w), 560 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 704 (100) $[M]^+$, 644 (09), 471 (02), 337 (12), 281 (02), 207 (04), 173 (39). HRMS (EI, 70 eV): calcd. for $C_{52}H_{52}N_2$ $[M^+]$; 704.41250 found 704.41482.

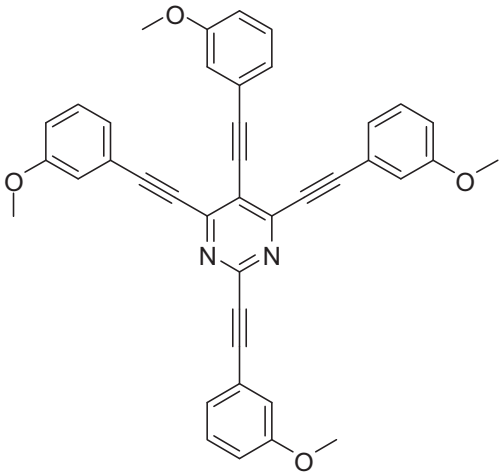
2,4,5,6-Tetrakis(phenylethynyl)pyrimidine (26b)



starting with **22** (217 mg; 1mmol), phenylacetylene (**23b**) (0.62mL; 6.0 mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), Dioxane (7mL) and diisopropylamine (3mL), **26b** was isolated as light brown solid (349 mg; 73 %); m.p. 188–190 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.77–6.86 (m, 12H), 7.02 – 7.11 (m, 8H). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 83.5, 86.2, 87.9, 90.0, 98.9, 103.4, 121.2, 121.3, 122.3 (C), 128.4, 128.6, 128.7, 129.5, 129.8, 130.3, 131.7, 132.6, 132.7 (CH), 150.3, 152.3 (C). IR (KBr): $\tilde{\nu}$ = 2918 (w), 2213 (m), 1479 (s), 1398 (s), 1211 (w), 1067 (w), 970 (w), 797 (m), 767 (m), 748 (s), 680 (s) cm^{-1}. GC-MS

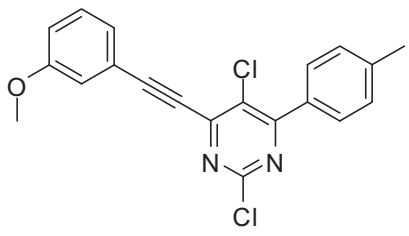
(EI, 70 eV): *m/z* (%) = 480 (92) $[M]^+$, 375 (40), 330 (20), 305 (10), 260 (18), 218 (23). HRMS (EI, 70 eV): calcd. for $C_{36}H_{20}N_2$ $[M^+]$; 480.16292 found 480.16260.

2,4,5,6-Tetrakis((3-methoxyphenyl)ethynyl)pyrimidine (26c)



starting with **22** (217 mg; 1mmol), 3-ethynyl anisole (**23c**) (0.76mL; 6.0 mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), Dioxane (7mL) and diisopropylamine (3mL), **26c** was isolated as dark brown solid (474 mg; 79 %); m.p. 152–154 °C.^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 6H, $2OCH_3$), 3.74 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 6.81–6.85 (m, 2H), 6.93–6.97 (m, 4H) 7.00–7.03 (m, 2H), 7.12–7.23 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2, 55.3, 55.4 (OCH_3), 83.5, 84.2, 86.8, 89.2, 100.4, 102.7 (C), 115.4, 116.9, 117.0, 117.1, 117.2, 117.3 (CH), 121.7, 122.0, 123.1 (C), 124.6, 125.3, 129.4, 129.5, 129.7 (CH), 149.8, 150.4, 159.2, 159.3, 159.4 (C). IR (KBr): $\tilde{\nu}$ = 2939 (w), 2213 (s), 1574 (m), 1513 (s), 1483 (m), 1367 (m), 1315 (m), 1261 (s), 1161 (m), 1039 (s), 848 (m), 769 (s), 677 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 600 (80) $[M]^+$, 569 (60), 538 (34), 507 (100), 470 (51), 440 (12), 410 (17), 380 (32), 304 (56), 280 (40), 204 (12). HRMS (EI, 70 eV): calcd. for $C_{40}H_{28}N_2O_4$ $[M^+]$; 600.20221 found 600.20246.

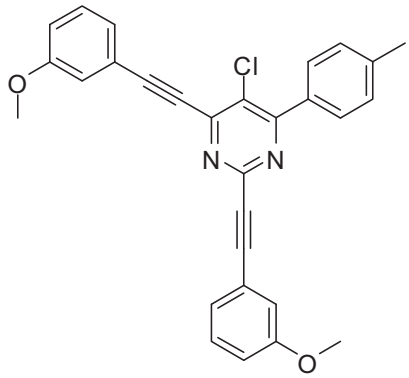
2,5-Dichloro-4-[(3-methoxyphenyl)ethynyl]-6-P-tolylpyrimidine* (28*)



Starting with **27** (100 mg; 0.36mmol), 3-ethynylanisole (**23c**) (0.05 mL, 0.36 mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **28** was isolated as crystalline light brown solid (79 mg; 59 %); m.p. 110–112 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 6.91–6.95 (m, 1H), 7.09–7.10 (m, 1H), 7.17–7.25 (m, 4H), 7.72 (d, 2H, *J* = 8.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (CH_3), 55.4 (OCH_3), 84.4, 100.7 (C), 117.2, 117.4 (CH), 121.6 (C), 125.3 (CH), 128.5 (C), 129.1,

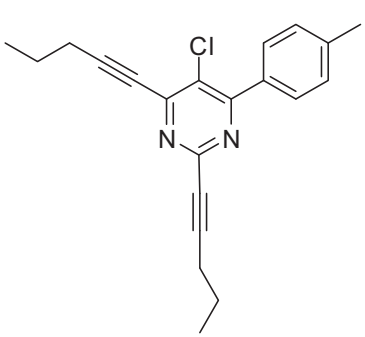
129.6, 129.7 (CH), 131.9, 141.6, 152.2, 158.1, 159.4, 165.8 (C). IR (KBr): $\tilde{\nu}$ = 3013 (w), 2935 (w), 2213 (w), 1578 (m), 1481 (m), 1255 (s), 1151 (s), 1035 (s), 914 (m), 838 (m), 775 (s), 676 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 368 (100) $[M]^+$, 333 (10), 325 (02), 303 (02), 290 (12), 227 (20), 184 (26), 140 (40). HRMS (EI, 70 eV): calcd. for $C_{20}H_{14}ON_2Cl_2$ $[M^+]$; 368.04777 found 368.04752.

5-Chloro-2,4-bis((3-methoxyphenyl)ethynyl)-6-p-tolylpyrimidine(29)



Starting with **27** (100 mg; 0.36mmol), 3-ethynylanisole (**23c**) (0.1 mL, 0.72 mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **29** was isolated as crystalline brown solid (114 mg; 67 %); m.p. 167–169 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.34 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 6.85–6.93 (m, 2H), 7.10–7.12 (m, 2H), 7.19–7.25 (m, 6H), 7.69 (d, 2H, *J* = 8.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (CH_3), 55.3 (OCH_3), 55.4 (OCH_3), 84.7, 87.3, 88.6, 99.3 (C), 116.8, 117.0, 117.1, 117.2 (CH), 121.9, 122.2 (C), 125.2 (CH), 128.5 (C), 129.0, 129.3, 129.5, 129.6, 129.7 (CH), 132.7, 141.0, 150.2, 150.6, 159.3, 159.4, 164.1 (C). IR (KBr): $\tilde{\nu}$ = 3008 (w), 2214 (m), 1573 (w), 1525 (m), 1486 (s), 1357 (s), 1287 (m), 1255 (s), 1180 (m), 1043 (m), 859 (m), 774 (s), 683 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 464 (100) $[M]^+$, 424 (61), 389 (09), 272 (02), 232 (27), 190 (10), 150 (06). HRMS (EI, 70 eV): calcd. for $C_{29}H_{21}O_2N_2Cl$ $[M^+]$; 464.12926 found 464.12920.

***5-Chloro-2,4-di(pent-1-ynyl)-6-p-tolylpyrimidine* (30)**



starting with **27** (100 mg; 0.36mmol), 1-Pentyne (**23f**) (0.07mL; 0.72mmol) CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **30** was isolated as light yellow semisolid (66 mg; 54 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, 3H, *J* = 7.4 Hz, CH_3), 0.98 (t, 3H, *J* = 7.3 Hz, CH_3), 1.53–1.64 (m, 4H), 2.31 (s, 3H, CH_3) 2.34 (t, 2H, *J* = 7.1 Hz), 2.42 (t, 2H, *J* = 7.0 Hz), 7.19 (d, 2H, *J* = 8.1 Hz) 7.62 (d, 2H, *J* = 8.3 Hz). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.5, 13.7 (CH_3),

21.3 (CH_2), 21.4 (CH_3), 21.5, 21.7 (CH_2), 80.0, 90.7, 102.3 (C), 128.8, 129.5 (CH), 129.9, 132.8, 133.5, 150.2, 150.8, 163.7 (C). IR (KBr): $\tilde{\nu}$ = 2961 (w), 2232 (m), 1611 (w), 1529 (m), 1492 (s), 1355 (s), 1179 (m), 1149 (m), 1035 (m), 821 (m), 795 (m), 756 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 336 (20) $[M]^+$, 321 (04), 308 (100), 292 (03), 279 (03), 256 (01), 229 (20), 243 (10), 208 (15), 178 (21). HRMS (EI, 70 eV): calcd. for $C_{21}H_{21}ClN_2$ $[M^+]$; 336.13915 found 336.13930.

7.6 Regioselective Sonogashira coupling reactions of 2, 3, 4, 5- tetra bromofuran.

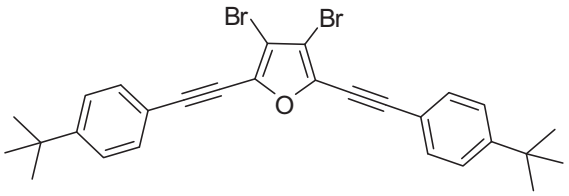
General Procedure for Sonogashira coupling Reaction

A suspension of tetrabromofuran (**31**), $Pd(PPh_3)_2Cl_2$ (10 mol %), CuI (5 mol %) in Diisopropylamine was degassed three time in ace pressure tube. Acetylene (1.2 eq per bromine atom) were added using a syringe. The mixture was heated at the indicated temperature (60–80 °C) for 2-4 h. The reaction mixture was filtered and residue washed with CH_2Cl_2. The filtrate was washed with saturated solution of ammonium chloride (2 x 25ml), water (2 x 25ml) and dried over anhydrous Na_2SO_4. Solvent was removed in vacuo. The product was purified by column chromatography on silica gel.

General Procedure for Suzuki cross coupling Reaction

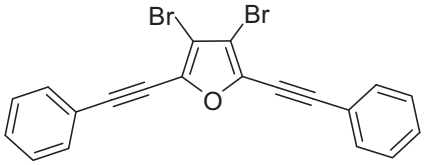
The reaction was carried out in a pressure tube. To a dioxane suspension (3-5 ml) of di sonogashira product of tetrabromofuran, $Pd(PPh_3)_2Cl_2$ (3-5 mol %), arylboronic acid (1.0 eq per bromine atom) and K_2CO_3 (3eq) was added. The mixture was heated at the indicated temperature (60-100 °C) for the indicated period of time (2-4 h). The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 x 25ml). The combined organic layers were dried over Na_2SO_4, filtrated and the filtrate was concentrated in vacuo the residue was purified by flash chromatography (silica gel, ethyl acetate / heptanes)

***3,4-Dibromo-2,5-bis((4-tert-butylphenyl)ethynyl)furan*(32a)**



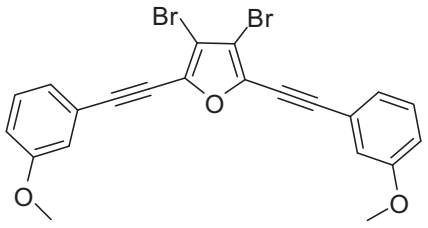
starting with **31** (150 mg; 0.40mmol), 4-ter-butylphenylacetylene(**23a**) (0.16mL; 0.94mmol), CuI (5 mol %),$Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **32a** was isolated as white solid (163 mg; 78 %); m.p. 197–199 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 18H, CH_3), 7.40 (d, 4H, *J* = 8.6Hz), 7.51 (d, 4H, *J* = 8.6Hz). ^{13}C NMR (75.4MHz, $CDCl_3$): δ = 31.1 (CH_3), 34.9, 81.5, 98.8, 109.3, 118.8 (C), 125.5, 132.3 (CH), 136.7, 152.6 (C). IR (KBr): $\tilde{\nu}$ = 2952 (w), 1497 (m), 1461 (m), 1362 (m), 1266 (m), 1102 (m), 1013 (m), 923 (w), 833 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 536 (M^+, [^{79}Br, ^{79}Br], 30), 538 (M^+, [^{79}Br, ^{81}Br], 100), 540 (M^+, [^{81}Br, ^{81}Br], 62), 523 (52), 508 (02), 493 (04), 467 (03), 350 (03), 314 (18), 299 (26), 254 (15), 226 (09). HRMS (EI, 70 eV): calcd for $C_{28}H_{26}Br_2O$ (M^+, [^{79}Br, ^{79}Br]: 536.03449; found 536.03353; calcd for $C_{28}H_{26}Br_2O$ (M^+, [^{79}Br, ^{81}Br]: 538.03245; found 538.03238; calcd for $C_{28}H_{26}Br_2O$ (M^+, [^{81}Br, ^{81}Br]: 540.03040; found 540.03176.

***3,4-Dibromo-2,5-bis(phenylethynyl)furan* (32b)**



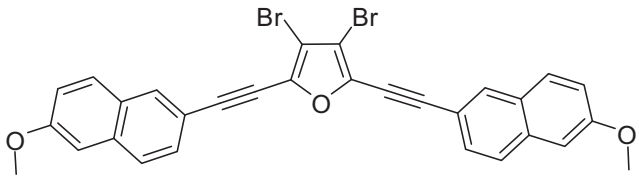
starting with **31** (150 mg; 0.40mmol), phenylacetylene (**23b**) (0.10mL; 0.94mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **32b** was isolated as brown semisolid (118 mg; 71 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.23–7.33 (m, 6H), 7.43–7.50 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 81.6, 98.5, 109.6, 121.3 (C), 128.4, 128.5, 132.5 (CH), 136.7 (C). IR (KBr): $\tilde{\nu}$ = 3045 (w), 2214 (w), 1557 (m), 1494 (m), 1440 (m), 1342 (w), 1177 (w), 1043 (w), 1010 (m), 914 (w), 746 (s), 681 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 424 (M^+, [^{79}Br, ^{79}Br], 53), 426 (M^+, [^{79}Br, ^{81}Br], 100), 428 (M^+, [^{81}Br, ^{81}Br], 49), 397 (10), 345 (20), 319 (29), 299 (21), 266 (23), 238 (36), 213 (06), 185 (02), 158 (01), 137 (12), 129 (25). HRMS (EI, 70 eV): calcd for $C_{20}H_{10}Br_2O$ (M^+, [^{79}Br, ^{79}Br]: 424.01121; found 424.01081; calcd for $C_{20}H_{10}Br_2O$ (M^+, [^{79}Br, ^{81}Br]: 426.02136; found 426.02087; calcd for $C_{20}H_{10}Br_2O$ (M^+, [^{81}Br, ^{81}Br]: 428.31251; found 428.31202.

***3,4-Dibromo-2,5-bis((3-methoxyphenyl)ethynyl)furan* (32c):**



starting with **31** (150 mg; 0.40mmol), 3-ethynyl anisole (**23c**) (0.12mL; 0.94mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %) and diisopropylamine (5mL), **32c** was isolated as white solid (154 mg; 81 %); m.p. 181–183 °C. ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 3.76 (s, 6H, $2OCH_3$), 6.79–6.86 (m, 3H), 6.93–6.97 (m, 3H), 7.03 (Brs, 2H). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 81.5, 98.5, 109.7, 122.7 (C), 116.0, 117.1, 125.1, 129.6 (CH), 136.6, 159.4 (C). IR (KBr): $\tilde{\nu}$ = 2958 (w), 2206 (w), 1579 (m), 1482 (m), 1415 (m), 1312 (m), 1258 (m), 1224 (m), 1152 (m), 1034 (s), 1012 (m), 838 (m), 776 (s), 676 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 484 (M^+, [^{79}Br, ^{79}Br], 55), 486 (M^+, [^{79}Br, ^{81}Br], 11), 488 (M^+, [^{81}Br, ^{81}Br], 443 (01), 379 (20), 326 (02), 298 (24), 262 (13), 243 (08), 224 (03), 159 (11). HRMS (EI, 70 eV): calcd for $C_{22}H_{14}Br_2O_3$ (M^+, [^{79}Br, ^{79}Br]: 483.93042; found 483.93122; calcd for $C_{22}H_{14}Br_2O_3$ (M^+, [^{79}Br, ^{81}Br]: 485.92837; found 485.92982; calcd for $C_{22}H_{14}Br_2O_3$ (M^+, [^{81}Br, ^{81}Br]: 487.92633; found 487.92704.

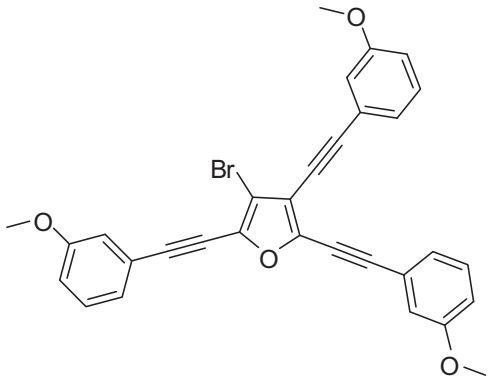
***3,4-Dibromo-2,5-bis((6-methoxynaphthalen-2-yl)ethynyl)furan* (32d):**



starting with **31** (150 mg; 0.40mmol), 2-ethynyl-6-methoxynaphthalene (**23d**) (171 mg; 0.94mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **32d** was isolated as light yellow solid (174 mg; 76 %); m.p. 198–200 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 6H, $2OCH_3$), 7.03–7.15 (m, 5H), 7.60–7.68 (m, 5H), 7.90 (Brs, 2H). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 82.2, 99.3 (C), 105.7 (CH), 109.3, 116.7 (C), 119.4, 126.8, 129.1, 129.3, 132.0 (CH), 132.7, 134.6, 136.8, 158.7 (C). IR (KBr): $\tilde{\nu}$ = 2935 (w), 1619 (m), 1593 (m), 1478 (m), 1381 (m), 1266 (m), 1227 (s), 1164 (s), 1025 (s), 898 (m), 853 (s), 823 (s), 808 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 584(M^+, [^{79}Br, ^{79}Br], 49), 586 (M^+, [^{79}Br, ^{81}Br], 100), 588 (M^+, [^{81}Br, ^{81}Br], 51), 562(20), 493 (29), 429 (37), 362 (100), 347 (22), 319 (20), 304 (06), 276 (19), 207 (01), 181 (12). HRMS (EI, 70 eV): calcd for $C_{30}H_{18}Br_2O_3$ (M^+, [^{79}Br,

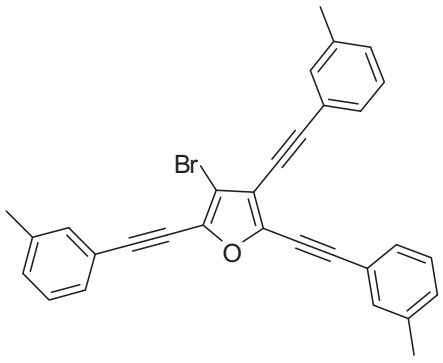
^{79}Br]: 583.96172; found 583.96297; calcd for $C_{30}H_{18}Br_2O_3$ (M^+, [^{79}Br, ^{81}Br]: 585.95967; found 585.96120; calcd for $C_{30}H_{18}Br_2O_3$ (M^+, [^{81}Br, ^{81}Br]: 587.96014; found 587.95966.

***3-Bromo-2,4,5-tris((3-methoxyphenyl)ethynyl)furan* (33a)**



starting with **31** (150 mg; 0.40mmol), 3-ethynyl anisole (**23c**) (0.18mL; 1.44mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diiso propylamine (5mL), **33a** was isolated as brown highly viscous oil (161 mg; 77 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.73 (s, 3H, OCH_3), 3.74 (s, 6H, $2OCH_3$), 6.82–6.88 (m, 3H), 6.99–7.03 (m, 3H), 7.07–7.12 (m, 3H), 7.17–7.22 (m, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 55.3, 55.4 (CH_3), 77.8, 77.9, 97.7, 98.0, 99.0, 108.6, 113.6 (C), 115.3, 115.5, 115.9, 116.2, 116.3, 116.4, 116.6 (CH), 122.3, 123.4 (C), 124.2, 124.3, 124.4, 129.5, 129.6 (CH), 136.5, 139.6, 159.3, 159.4 (C). IR (KBr): $\tilde{\nu}$ = 2935 (w), 1594 (m), 1571 (s), 1422 (m), 1282 (m), 1228 (s), 1036 (s), 849 (m), 774 (s), 680 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 536 (M^+, [^{79}Br], 90), 538 (M^+, [^{81}Br], 100), 458 (38), 429 (97), 386 (19), 343 (07), 300 (18), 269 (11). HRMS (EI, 70 eV): calcd for $C_{31}H_{21}BrO_4$ (M^+, [^{79}Br]: 536.06177; found 536.06195; calcd for $C_{31}H_{21}BrO_4$ (M^+, [^{81}Br]: 538.05973; found 538.06091.

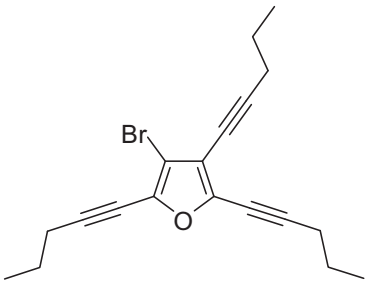
***3-Bromo-2,4,5-tris(m-tolylethynyl)furan* (33b)**



starting with **31** (150 mg; 0.40mmol), 3-ethynyl toluene (**23h**) (0.18mL; 1.44mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **33b** was isolated as brown highly viscous oil (139 mg; 73 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.40 (Brs, 9H, $3CH_3$), 7.20–7.32 (m, 6H), 7.41–7.45 (m, 6H). ^{13}C-NMR (62 MHz, $CDCl_3$): δ = 21.2 ($3CH_3$), 76.9, 77.8, 77.9, 97.9, 98.2, 99.2, 108.5, 115.8, 121.2, 121.3, 122.3 (C), 128.3, 128.4, 128.8, 128.9, 129.8, 130.3, 130.4, 132.2, 132.3 (CH), 138.1, 138.2 (C). ; IR (KBr): $\tilde{\nu}$ = 2919 (w), 2200 (m), 1710 (m), 1600 (m), 1481 (m), 1359 (w), 1274 (w), 1218 (w),

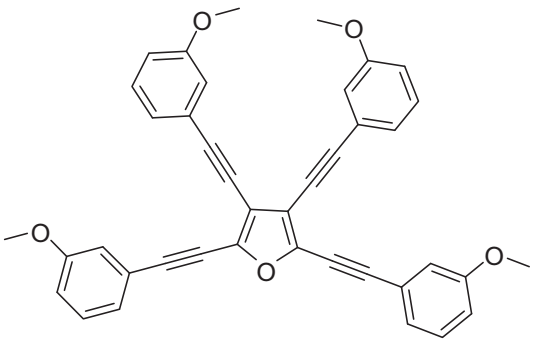
1086 (m), 1026 (m), 906 (w), 780 (s), 686 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 488 (M^+, [^{79}Br], 62), 490 (M^+, [^{81}Br], 66), 447 (02), 410 (02), 381 (100), 363 (06), 350 (04), 287 (02), 263 (09), 245 (07), 224 (02), 182 (10), 175 (15). HRMS (EI, 70 eV): calcd for $C_{31}H_{21}BrO$ (M^+, [^{79}Br]: 488.07703; found 488.07687; calcd for $C_{31}H_{21}BrO$ (M^+, [^{81}Br]: 490.07498; found 490.07535.

***3-Bromo-2,4,5-tri(pent-1-ynyl)furan* (33c)**



starting with **31** (150 mg; 0.40mmol), 1-pentyne (**23g**) (0.14mL; 1.44mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), and diisopropylamine (5mL), **33c** was isolated as brown highly viscous oil (86 mg; 64 %). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 0.92–1.02 (m, 9H), 1.46–1.63 (m, 6H), 2.35–2.41 (m, 6H). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.3(CH_3), 13.4 (2CH_3), 21.5, 21.6, 21.9, 29.6, 30.1, 31.4 (CH_2), 69.1, 69.7, 70.0, 98.0, 99.1, 99.5, 107.0, 114.7, 135.7, 139.0 (C). IR (KBr): $\tilde{\nu}$ = 2961 (m), 2224 (w), 1714 (s), 1455 (m), 1378 (w), 1181 (w), 1077 (w), 967 (w), 799 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 344 (M^+, [^{79}Br], 100), 346 (M^+, [^{81}Br], 95), 317 (57), 304 (03), 281 (07), 237 (05), 193 (14), 178 (26), 165 (21). HRMS (EI, 70 eV): calcd for $C_{19}H_{21}BrO$ (M^+, [^{79}Br]: 344.08012; found 344.08031; calcd for $C_{19}H_{21}BrO$ (M^+, [^{81}Br]: 346.01215; found 346.01166.

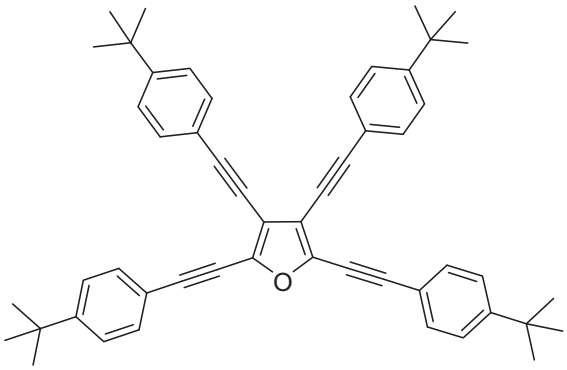
***2,3,4,5-Tetrakis((3-methoxyphenyl)ethynyl)furan*(34a)**



starting with **31** (150 mg; 0.40mmol), 3-ethynylanisole (**23c**) (0.24mL; 1.92 mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), diisopropylamine (5mL), **34a** was isolated as brown viscous oil (191 mg; 83 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ =3.73 (s, 6H, OCH_3), 3.75 (s, 6H, OCH_3), 6.82-6.89 (m, 4H), 7.02-7.04 (m, 4H), 7.09-7.13 (m, 4H), 7.17-7.21 (m, 4H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 55.3, 55.4 (CH_3), 77.9, 78.5, 97.3, 98.5, 115.3 (C), 115.4, 116.1, 116.3, 116.5 (CH),

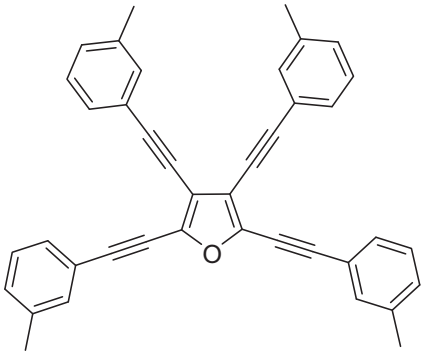
122.5, 123.8 (C), 124.3, 129.5, 129.6 (CH),139.3, 159.3, 159.4 (C). IR (KBr): $\tilde{\nu}$ = 2935 (w), 1571 (s), 1426 (m), 1283 (s), 1159 (s), 1036 (s), 850 (m), 776 (s), 681 (s) cm^{-1}.GC-MS (EI, 70 eV): *m/z* (%) = 588 (100) $[M]^+$, 529 (02), 486 (11), 429 (23), 400 (14), 294 (06), 262 (26), 243(03), 207 (04). HRMS (EI, 70 eV): calcd. for $C_{40}H_{28}O_5$ $[M^+]$; 588.19313 found 588.19343.

2,3,4,5-Tetrakis((4-tert-butylphenyl)ethynyl)furan **(34b)**



starting with **31** (150 mg; 0.40mmol), 4-(tert-butyl)phenylacetylene (**23a**) (0.31mL; 1.92 mmol), CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), diisopropylamine (5mL), **34b** was isolated as brown semisolid (219 mg; 81 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ =1.24 (s, 18H, $6CH_3$), 1.25 (s, 18H, $6CH_3$), 7.30 (d, 4H, *J* = 8.5 Hz) 7.32 (d, 4H, *J* = 8.3 Hz) 7.42 (d, 4H, *J* = 8.2Hz) 7.44 (d, 4H, *J* = 8.6 Hz). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 31.1, 31.2 (CH_3), 34.8, 34.9, 76.7, 77.6, 97.7, 98.2, 115.7, 118.5, 119.5 (C), 125.4, 125.5, 131.4, 131.5 (CH), 139.5, 152.2, 152.8 (C). IR (KBr): $\tilde{\nu}$ = 2954 (m), 2199 (w), 1659 (w), 1603 (w), 1566 (w), 1499 (m), 1460 (m), 1362 (m), 1266 (m), 1105 (m), 1015 (m), 831 (s), 735 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 692 (100) $[M]^+$, 677 (10), 647 (01), 632 (10), 616 (15), 599 (03), 536 (02), 477(20), 331 (13), 293 (02). HRMS (EI, 70 eV): calcd. for $C_{52}H_{52}O$ $[M^+]$; 692.40127 found 692.40322.

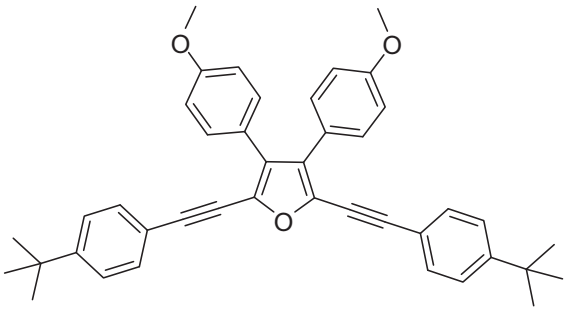
2,3,4,5-Tetrakis(m-tolylethynyl)furan **(34c)**



starting with **31** (150 mg; 0.40mmol), 3-ethynyltoluene (**23h**) (0.24mL; 1.92 mmol),CuI (5 mol %), $Pd(PPh_3)_2Cl_2$ (10 mol %), diisopropylamine (5mL), **34c** was isolated as brown semisolid (153 mg; 75 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 6H, $2CH_3$), 2.29 (s, 6H, $2CH_3$), 7.08–7.22 (m, 9H), 7.31–7.35 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CH_3), 77.9, 78.6, 97.5, 98.6, 115.3, 121.5, 122.7 (C), 128.3, 128.4, 128.8, 129.6, 130.2, 132.2, 132.4

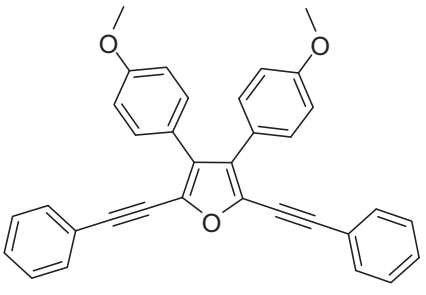
(CH), 138.0, 138.2, 139.3 (C). IR (KBr): $\tilde{\nu}$ = 2917 (w), 2197 (w), 1709 (m), 1600 (w), 1360 (m), 1219 (m), 1058 (w), 899 (m), 874 (m), 775 (s), 683 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 524 (100) $[M]^+$, 481 (05), 464 (02), 381 (04), 329 (03), 281 (02), 262 (08), 242 (06), 226 (05), 207 (04), 169 (02). HRMS (EI, 70 eV): calcd. for $C_{40}H_{28}O$ $[M^+]$; 524.21347 found 524.21434.

***2,5-Bis((4-tert-butylphenyl)ethynyl)-3,4-bis(3-methoxyphenyl)furan* (35a)**



starting with **32b** (108 mg; 0.2mmol), 4-methoxyphenylboronic acid (**18e**) (61 mg; 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), K_2CO_3(83 mg; 0.60 mmol) Dioxane (5mL), **35a** was isolated as light brown crystalline solid (90 mg; 76 %); m.p. 162–164 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ =1.24 (s, 18H, CH_3), 3.75 (s, 6H, OCH_3), 6.80(d, 4H, *J* = 8.8Hz), 7.23-7.41 (m, 12H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ = 31.1 (CH_3), 34.9 (C), 55.2 (CH_3), 79.5, 95.8 (C), 113.6 (CH), 114.2, 119.3, 123.5 (C),125.4, 130.6, 131.1 (CH), 134.5, 152.1, 159.0 (C). IR (KBr): $\tilde{\nu}$ = 2959 (m), 2188 (m), 1729 (w), 1608 (m), 1512 (m), 1247 (s), 1175 (m), 1034 (m), 981 (m), 832 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 592 (100) $[M]^+$, 577 (12), 562 (03), 547 (02), 532 (02), 407 (30), 391 (19), 377 (26), 296 (05), 281 (16). HRMS (EI, 70 eV): calcd. for $C_{42}H_{40}O_3$ $[M^+]$; 592.29720 found 592.29492.

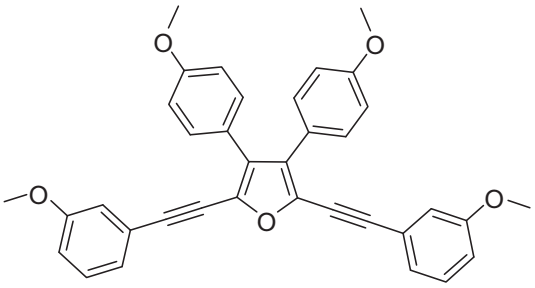
***3,4-Bis(4-methoxyphenyl)-2,5-bis(phenylethynyl)furan* (35b)**



starting with **32c** (90 mg; 0.2mmol), 4-methoxy phenylboronic acid (**18e**) (61 mg; 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), K_2CO_3 (83mg; 0.60 mmol) Dioxane (5mL), **35b** was isolated as light brown crystalline solid (70 mg; 69 %); m.p. 146–148 °C. ^{1}H-NMR (250 MHz, $CDCl_3$): δ =3.75 (s, 6H, 3OCH_3), 6.81 (d, 4H, *J* = 8.8Hz). 7.24-7.28 (m, 10H), 7.37-7.41 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2 (OCH_3), 80.1, 95.6 (C), 113.7 (CH), 122.3, 123.4 (C), 128.4, 128.7

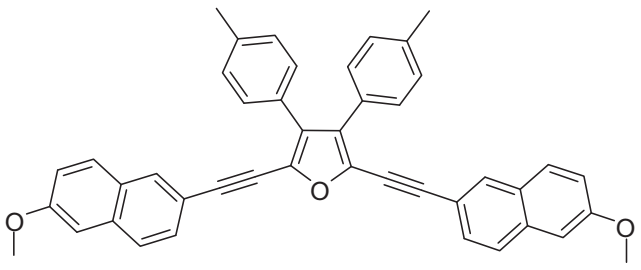
(CH), 129.8 (C), 130.6, 131.4 (CH), 134.5, 159.1 (C). IR (KBr): $\tilde{\nu}$ = 2916 (w), 1611 (m), 1509 (m), 1441 (m), 1395 (w), 1291 (m), 1248 (s), 1172 (m), 1108 (w), 1029 (m), 979 (m), 825 (s), 751 (s), 689 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 480 (100) $[M]^+$, 465 (02), 421 (20), 351 (08), 336 (13), 308 (02), 263 (21), 240 (33), 213 (09). HRMS (EI, 70 eV): calcd. for $C_{34}H_{24}O_3$ $[M^+]$; 480.17200 found 480.17223.

***3,4-Bis(4-methoxyphenyl)-2,5-bis((3-methoxyphenyl)ethynyl)furan* (35c)**



starting with **32a** (100 mg; 0.2mmol), 4-methoxyphenylboronic acid (**18e**) (61 mg; 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), K_2CO_3 (83mg; 0.60 mmol) Dioxane (5mL), **35c** was isolated as light brown crystalline solid (87 mg; 79 %); m.p. 144–146 °C. ^{1}H-NMR (250MHz, $CDCl_3$): δ =3.73 (s, 6H, $2OCH_3$), 3.75 (s, 6H, $2OCH_3$), 6.79–6.84 (m, 5H), 6.90–6.92 (m, 2H), 6.99 (d, 2H, *J* = 8.1 Hz), 7.13–7.19 (m, 3H), 7.26 (d, 4H, *J* = 8.7 Hz). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 55.2, 55.3 (CH_3), 79.8, 95.6 (C), 113.7 (CH), 114.8 (C), 115.3, 116.1 (CH), 123.2, 123.3 (C), 124.0, 129.5 (CH), 130.0 (C), 130.6 (CH), 134.4, 159.1, 159.3 (C). IR (KBr): $\tilde{\nu}$ = 2932 (w), 1583 (m), 1507 (m), 1461 (m), 1424 (m), 1289 (m), 1246 (s), 1177 (m), 1145 (m), 1032 (s), 984 (m), 829 (s), 772 (s), 682 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 540 (100) $[M]^+$, 481 (04), 423 (04), 381 (13), 338 (06), 270 (06), 211 (06). HRMS (EI, 70 eV): calcd. for $C_{36}H_{28}O_5$ $[M^+]$; 540.19313 found 540.19213.

***2,5-Bis((6-methoxynaphthalen-2-yl)ethynyl)-3,4-dip-tolylfuran* (35d)**



starting with **32d** (120 mg; 0.2 mmol), 4-methylphenylboronic acid (**18f**) (54 mg; 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), K_2CO_3 (83 mg; 0.60 mmol) Dioxane (5mL), **35d** was isolated as dark brown semisolid (92 mg; 74 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ =2.31 (s, 6H, $2CH_3$), 3.86 (s, 6H, $2OCH_3$), 7.07–7.11 (m,

7H), 7.27 (d, 4H, *J* = 8.1Hz), 7.40 (d, 2H, *J* = 8.5Hz), 7.56–7.67 (m, 5H), 7.84 (Brs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 55.4 (OCH_3), 79.8, 96.3 (C), 106.0 (CH), 117.1 (C), 119.5, 126.9 (CH), 128.4 (C), 128.5, 128.9, 129.3, 129.4 (CH), 129.8, 130.0, 134.3, 134.9, 137.4, 158.5 (C). IR (KBr): $\tilde{\nu}$ = 2923 (m), 2180 (m), 1713 (m), 1621 (s), 1602 (s), 1497 (m), 1480 (m), 1390 (m), 1264 (s), 1212 (s), 1163 (s), 1027 (s), 885 (m), 851 (s), 811 (m), 736 (w) cm^{-1}.GC-MS (EI, 70 eV): *m/z* (%) = 608 (12) $[M]^+$, 549 (23), 503 (42), 476 (29), 419 (15), 343 (100), 328 (05), 287 (28), 259 (13), 231 (03), 202 (06). HRMS (EI, 70 eV): calcd. for $C_{44}H_{32}O_3$ $[M^+]$; 608.23460 found 608.23805.

Table 25. Crystal data and structure refinement for **7d**

Identification code	7d	
Empirical formula	$C_{16}H_{12}S$	
Formula weight	236.32	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group (H.-M.)	F d d 2	
Space group (Hall)	F2 2$\bar{d}$	
Unit cell dimensions	a = 26.425(15) Å	α= 90.00.
	b = 31.214(15) Å	β= 90.00
	c = 5.775(3) Å	γ = 90.00.
Volume	4764(4) $Å^3$	
Z	8	
Density (calculated)	1.388 Mg/m^3	
Absorption coefficient	0.243mm^{-1}	
F(000)	1984	
Crystal size	0.31x 0.12x 0.11mm^3	
Θ range for data collection	2.02 to 30.00°.	
Index ranges	-36≤h≤25, -43≤k≤39, -4≤l≤8	
Reflections collected	7610	
Independent reflections	2711 [R(int) = 0.0368]	
Completeness to Θ = 29.00°	99.2%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9285 and 0.9738	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2173 / 1 / 154	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2σ(I)]	R1 = 0.0409, wR2 = 0.0901	
R indices (all data)	R1 = 0.0593, wR2 = 0.0970	
Largest diff. peak and hole	0.262and -0.224e.$Å^{-3}$	

Table 26. Crystal data and structure refinement for **19f**

Identification code	19f	
Empirical formula	$C_{29}\ H_{22}\ O_2$	
Formula weight	402.47	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21/c	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 9.709(8) Å	α= 90.00.
	b = 9.924(7) Å	β= 99.40(3).
	c = 22.922(18) Å	γ = 90.00.
Volume	2179(3) $Å^3$	
Z	4	
Density (calculated)	1.227Mg/m^3	
Absorption coefficient	0.076 mm^{-1}	
F(000)	848	
Crystal size	0.64x 0.50x 0.21mm^3	
Θ range for data collection	3.00 to 28.50°.	
Index ranges	-12≤h≤13, -12≤k≤13, -30≤l≤20	
Reflections collected	21616	
Independent reflections	5505 [R (int) = 0.0364]	
Completeness to Θ = 29.00°	99.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9532 and 0.9843	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4207 / 0 / 282	
Goodness-of-fit on F^2	1.078	
Final R indices [I>2σ(I)]	R1 = 0.0514, wR2 = 0.1360	
R indices (all data)	R1 = 0.0688, wR2 = 0.1453	
Largest diff. peak and hole	0.369 and -0.303e.$Å^{-3}$	

Table 27. Crystal data and structure refinement for **24c**

Identification code	24c	
Empirical formula	$C_{22}H_{14}Cl_2N_2O_2$	
Formula weight	409.25	
Temperature	173(2) K	
Wavelength	0.71073Å	
Crystal system	orthorhombic	
Space group (H.-M.)	P b c n	
Space group (Hall)	P 2n 2ab	
Unit cell dimensions	a = 3.8669(17) Å	α= 90.00.
	b = 17.742(6) Å	β= 90.00.
	c = 27.590(9) Å	γ = 90.00.
Volume	1892.8(12) $Å^3$	
Z	4	
Density (calculated)	1.436Mg/m^3	
Absorption coefficient	0.364mm^{-1}	
F(000)	840	
Crystal size	0.42x 0.08x 0.07mm^3	
Θ range for data collection	2.30to 22.82°.	
Index ranges	-4≤h≤4, -19≤k≤19, -23≤l≤30	
Reflections collected	13846	
Independent reflections	1294 [R (int) = 0.0405]	
Completeness to Θ = 29.00°	99.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8622 and 0.9750	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1041/ 0 / 130	
Goodness-of-fit on F^2	1.042	
Final R indices [I>2σ(I)]	R1 = 0.0290, wR2 = 0.0672	
R indices (all data)	R1 = 0.0414, wR2 = 0.0708	
Largest diff. peak and hole	0.144and -0.193e.$Å^{-3}$	

Table 28. Crystal data and structure refinement for **28**

Identification code	28	
Empirical formula	C_{20} H_{14} C_{l2} N_2 O	
Formula weight	369.23	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	C 2/c	
Space group (Hall)	-C 2yc	
Unit cell dimensions	a = 18.9682(7) Å	α= 90.00.
	b = 10.5747(3) Å	β= 103.206(2) °.
	c = 17.6689(5) Å	γ= 90.00°.
Volume	3450.36(19) $Å^3$	
Z	8	
Density (calculated)	1.422Mg/m^3	
Absorption coefficient	0.386 mm^{-1}	
F (000)	1520	
Crystal size	0.69 x 0.64 x 0.10 mm^3	
Θ range for data collection	2.22 to 29.99°.	
Index ranges	-26≤h≤26, -14≤k≤14, -24≤l≤24	
Reflections collected	34320	
Independent reflections	5012 [R(int) = 0.0239]	
Completeness to Θ = 29.00°	99.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7764 and 0.9624	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3954 / 0 / 228	
Goodness-of-fit on F^2	1.087	
Final R indices [I>2σ(I)]	R1 = 0.0449, wR2 = 0.1261	
R indices (all data)	R1 = 0.0614, wR2 = 0.1364	
Largest diff. peak and hole	0.523 and -0.317 e.$Å^{-3}$	

Table 29. Crystal data and structure refinement for **29**

Identification code	29	
Empirical formula	$C_{29}\ H_{21}\ Cl_1\ N_2\ O_2$	
Formula weight	464.93	
Temperature	173(2) K	
Wavelength	0.71073Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 10.4979(9) Å	α= 113.847(2) °.
	b = 11.1694(5) Å	β= 102.708(2) °.
	c = 11.4714(5) Å	γ = 97.191(3) °.
Volume	1165.04(12) $Å^3$	
Z	2	
Density (calculated)	1.325Mg/m^3	
Absorption coefficient	0.194mm^{-1}	
F(000)	484	
Crystal size	0.66x 0.23x 0.10mm^3	
Θ range for data collection	2.89 to 27.99°.	
Index ranges	-13≤h≤13, -14≤k≤14, -15≤l≤14	
Reflections collected	18933	
Independent reflections	5511 [R(int) = 0.0271]	
Completeness to Θ = 29.00°	98.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8828 and 0.9809	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3816 / 0 / 321	
Goodness-of-fit on F^2	1.098	
Final R indices [I>2σ(I)]	R1 = 0.0482, wR2 = 0.1290	
R indices (all data)	R1 = 0.0807, wR2 = 0.1397	
Largest diff. peak and hole	0.279and -0.302e.$Å^{-3}$	

Table 30. Crystal data and structure refinement for **35a**

Identification code	35b	
Empirical formula	$C_{42}\ H_{40}\ O_3$	
Formula weight	592.74	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P c	
Space group (Hall)	P $2\bar{y}$ c	
Unit cell dimensions	a = 9.8252(2) Å	α= 90.00.
	b = 19.0652(4) Å	β= 97.1530(10) °
	c = 18.3191(4) Å	γ = 90.00.
Volume	3404.82(12) $Å^3$	
Z	4	
Density (calculated)	1.156Mg/m^3	
Absorption coefficient	0.071mm^{-1}	
F(000)	1264	
Crystal size	0.69x 0.55x 0.38mm^3	
Θ range for data collection	2.14 to 29.00°.	
Index ranges	-13≤h≤13, -23≤k≤26, -24≤l≤24	
Reflections collected	34636	
Independent reflections	16746 [R(int) = 0.0282]	
Completeness to Θ = 29.00°	99.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9526 and 0.9735	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	11566 / 2 / 843	
Goodness-of-fit on F^2	1.022	
Final R indices [I>2σ(I)]	R1 = 0.0523, wR2 = 0.1152	
R indices (all data)	R1 = 0.0880, wR2 = 0.1262	
Largest diff. peak and hole	0.226 and -0.160e.$Å^{-3}$	

Abbreviations

Ac	Acetyl
Anal	Elemental Analysis
bp	Boiling point
calcd	Calculated
CI	Chemical Ionization
COSY	Correlated Spectroscopy
DEPT	Distortionless Enhancement by Polarization Transfer
dr	Diastereomeric ratio
ee	Enantiomeric excess
EI	Electron Impact
Et_2O	Diethyl ether
EtOH	Ethanol
GC	Gas Chromatography
GP	General Procedure
HMBC	Heteronuclear Multiple Bond Correlation
HPLC	High Performance Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
IR	Infrared Spectroscopy
MS	Mass Spectrometry
mp	Melting point
NaOEt	Sodium ethanolate
*n*BuLi	*n*-Butyllithium
NEt_3	Triethylamine
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser and Exchange Spectroscopy
ORTEP	Oak Ridge Thermal Ellipsoid Plot
OTf	Triflate
Ph	Phenyl
ppm	Parts per million
R_f	Retention factor
Tf_2O	Trifluoromethanesulfonic anhydride (triflic anhydride)
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Tetramethylsilane
Tol	Tolyl (*p*-MeC_6H_4)
Tos	Tosyl (*p*-$MeC_6H_4SO_2$

References

[1] Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5518.

[2] (a) Heck, R. F.; Nolley, J. P. *J. Org. Chem*. **1972**, *37*, 2320; (b) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jap*. **1971**, *44*, 581.

[3] (a) Loiseleur, O.; Hayashi, M.; Keenan, M.; Schmees, N.; Pfaltz, A. *J. Organomet. Chem*. **1999**, *576*, 16; (b) Ebran, J. P.; Hansen, A. L.; Gogsig, T. M.; Skrydstrup, T. *J. Am. Chem. Soc*. **2007**, *129*, 6931; (c) Xu, C.; Gong, J. F, Yue, S. F.; Zhu, Y.; Wu, Y. J. *Dalton Trans* **2006**, 4730; (d) Meijere, A. D.; Meyer, F. E. *Angew. Chem. Int. Ed*. **1994**, *33*, 2379; (e) Crisp, G.T. *Chem. Soc. Rev*. **1998**, *27*, 427.

[4] Jutand, A.; Mosleh, A. *Organometallics* **1995**, *14*, 1810.

[5] Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev*. **2000**, *100*, 3009.

[6] (a) Masters, J. J.; Jung, D. K.; Bornmann, W. G.; Danishefsky, S. J.; de Gala, S *Tetrahedron Lett*. **1993**, *34*, 7253; (b) Tsuji, J. *Palladium Reagents and Catalysts, Innovations in Organic Synthesis*, Wiley, New York, **1995**; (c) Cheng, J. Y. G.; Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1986**, *51*, 3093.

[7] Hussain, M.; Hung, N. T.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 3929.

[8] Toguem, S. M. T.; Hussain, M.; Malik, I.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 4962.

[9] Hussain, M.; Dang, T. T.; Langer, P. *Synlett*. **2009**, 1822.

[10] Hussain, M. Dissertation. University of Rostock.

[11] Hussain, M.; Zinad, D. S.; Salman, G. A.; Sharif, M.; Villinger, A.; Langer, P. *Synlett*. **2010**, 276.

[12] (a) Iddon, B.; Scrowston, R. M. *Adv. Heterocycl. Chem*. **1970**, *11*, 177; (b) Scrowston, R. M. *Adv. Heterocycl. Chem*. **1981**, *29*, 171; (c) *New Trends in Heterocyclic Chemistry*; Mitra, R. B., Ed.; Elsevier: Amsterdam, **1979**, 250; (d) Williams, C. H.; Casterline, J. L., Jr.; Jacobson, K. H. *Toxicol. Appl. Pharm*. **1967**, *11*, 302; (e) Kurtz, P. J. *Pharmacol. Biochem. Behav*. **1977**, *6*, 303; (f) Kropp; K. G., Fedorak; P. M. *Can. J. Microbiol.* **1998**, *44*, 605.

[13] El-Naggar, A. M.; Ahmed, F. S. M.; Donia, S. G. *J. Ind. Chem. Soc.* **1983**, *60*, 479.

[14] Brendle, J. J.; Outlaw, A.; Kumar, A.; Boykin, D. W.; Patrick, D. A.; Tidwell, R. R.; Werbovetz, K. A. *Antimicrob. Agents. Chemother.* **2002**, *46*, 797.

[15] Patrick, D. A.; Hall, J. E.; Bender, B. C.; McCurdy, D. R.; Wilson, W. D.; Tanious, F. A.; Saha, S.; Tidwell, R. R. *Eur. J. Med. Chem. Chim. Ther.* **1999**, *34*, 575.

[16] Wrobel, J.; Sredy, J.; Moxham, C.; Dietrich, A.; Li, Z.; Sawicki, D. R.; Seestaller, L.; Wu, L.; Katz, A.; Sullivan, D.; Tio, C.; Zhang, Z.-Y. *J. Med. Chem.* **1999**, *42*, 3199.

[17] (a) Saulnier, M. G.; Balasubramanian, B. N.; Long, B. H.; Frennesson, D. B.; Ruediger, E.; Zimmermann, K.; Eummer, J. T.; Laurent, D. R. S; Stoffan, K. M.; Naidu, B. N.; Mahler, M. *J. Med. Chem*. **2005**, *48*, 2258; (b) Li, Z.; Yang, Q.; Qian, X. *Tetrahedron* **2005**, *61*, 8711; (c) Durant, J. L.; Busby, W. F.; Lafleur, A. L.; Penman, B. W.; Crespi, C. L. *Mutat. Res.* **1996**, *371*, 123; (d) King, L. C.; Kohan, M. J.; Brooks, L.; Nelson, G. B.; Ross, J. A.; Allison, J.; Adams, L.; Desai, D.; Amin, S.; Padgett, W.; Lambert, G. R. *Chem. Res. Toxicol.* **2001**, *14*, 661.

[18] Xu, Y.; Qian, X.; Yao, W.; Mao, P.; Cui, J. *Bioorg. Med. Chem.* **2003**, *11*, 5427.

[19] (a) Ellefson, C. R.; Prodan, K. A. *J. Med. Chem.* **1981**, *24*, 1107; (b) Arlt, M.; Boettcher, H.; Riethmueller, A.; Schneider, G.; Bartoszyk, G. D. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2033.

[20] (a) Mori, Y.; Taneda, S.; Hayashi, H.; Sakushima, A.; Kamata, K.; Suzuki, A. K.; Yoshino, S.; Sakata, M.; Sagai, M.; Seki, K. I. *Biol. Pharm. Bull.* **2002**, *25*, 145; (b) Wallace, O. B.; Bryant, H. U.; Shetler, P. K.; Adrian, M. D.; Geiser, A. G. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5103.

[21] Clark, R. D.; Jahangir, A.; Severance, D.; Salazar, R.; Chang, T.; Chang, D.; Jett, M. F.; Smith, S.; Bley, K. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1053.

[22] Shim, Y. S.; Kim, K. C.; Lee, K. A.; Shrestha, S.; Lee, K. H.; Kim, C. K.; Cho, H. *Bioorg. Med. Chem.* **2005**, *13*, 1325.

[23] Harfenist, M.; Joyner, C. T.; Mize, P. D.; White, H. L. *J. Med. Chem.* **1994**, *37*, 2085.

[24] Larose, C. D.; Labbe, D.; Bergerone, H.; Jones, A. M.; Greer, C. W.; AL-Hawari, J.; Grossman, M. J.; Sankey, B. M. and Lau; P. C. K. *App. & Environ. Microbiol.* **1997**, 63, 2915.

[25] Review: Schröter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245.

[26] (a) Dang, T. T.; Dang, T. T.; Ahmad, R.; Reinke, H.; Langer, P. *Tetrahedron Lett.* **2008**, *49*, 1698; (b) Dang, T. T.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2008**, *350*, 2109; (c) Hussain, M.; Nguyen, T. H.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 3929; (d) Toguem, S. M. T.; Hussain, M.; Malik, I.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 4962; (e) Dang, T. T.; Dang, T. T.; Rasool, N.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2009**, *351*, 1595.

[27] (a) Bussenius, J.; Laber, N.; Müller, T.; Eberbach, W. *Chem. Ber.* **1994**, *127*, 247; (b) Heynderickx, A; Samat, A.; Gugliemetti, R. *Synthesis* **2002**, 213; (c) Yamamura, K.; Houda, Y.; Hashimoto, M.; Kimura, T.; Kamezawa, M.; Otani, T. *Org. Biomol. Chem.* **2004**, *2*, 1413.

[28] Voigt, K.; von Zezschwitz, P.; Rosauer, K.; Lansky, A.; Adams, A.; Reiser, O.; de Meijere, A. *Eur. J. Org. Chem.* **1998**, 1521.

[29] Billingsley, K.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3358.

[30] CCDC-xxx contains all crystallographic details of this publication and is available free of charge at **www.ccdc.cam.ac.uk/conts/retrieving.html** or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: (+44)1223-336-033; or **deposit@ccdc.cam.ac.uk**.

[31] (a) Au, A. L. S.; Kwan, Y. W.; Kwok, C. C.; Zhang, R.-Z.; He, G.-W. *Eur. J. Pharmacol.* **2003**, *468*, 199; (b) Jeng, S. N.; Tsai, S. J.; Lee, H. *Mutagenesis.* **1994**, *9*, 483; (c) Chen, H. P.; He, M.; Huang, Q. R.; Zeng, G. H.; Liu, D. *Basic Clin. Pharmacol. Toxicol.* **2007**, *100*, 366.

[32] Duran, R.; Zubia, E.; Ortega, M. J.; Naranjo, S.; Salva, J. *Tetrahedron* **1999**, *55*, 13225.

[33] Shaaban, M.; Maskey, R. P.; Wagner-Doebler, I.; Laatsch, H. *J. Nat. Prod.* **2002**, *65*, 1660.

[34] (a) Otsuka, H.; Shoji, J.; Kawano, K.; Kyogoku, Y. J. *Antibiotics* **1976**, *29*, 107; (b) Martin, D. A.; Mizsak, S. A.; Biles, C.; Meulman, P. A. J. *Antibiotics* **1975**, *28*, 332; (c) Shoji, J.; Katakiri, K. J. *Antibiotics Ser. A*. **1961**, *14*, 335; (d) Mutssuura, S. J. *Antibiotics Ser. A*. **1965**, *18*, 335. (e) Waring, M. J.; Makoff, A. *Mol. Pharmacol*. **1974**, *10*, 214; (f) Kim, Y. B.; Kim, Y. H.; Park, Y. J.; Kim, S. K. *Bioorg. Med. Chem. Lett*. **2004**, *14,* 541.

[35] Pathirana, C.; Jensen, P. R.; Dwight, R.; Fenical, W. *J. Org. Chem.* **1992**, *57*, 740.

[36] Forrest, Mitchell. *J. Am. Chem. Soc*. **1955**, *77*, 4865.

[37] Meyer, E. A.; Donati, N.; Guillot, M.; Schweizer, W. B.; Diederich, F.; Stengl, B.; Brenk, R.; Reuter, K.; Klebe, G. *Helv. Chim. Acta.* **2006**, *89*, 573.

[38] Kawagishi, H.; Tanaka, A.; Sugiyama, K.; Mori, H.; Sakamoto, H. *Phytochemistry* **1996**, *42*, 547.

[39] (a) Pettit, G. R.; Kamano, Y.; Dufresne, C.; Inoue, M.; Christie, N. *Can. J. Chem.* **1989**, *67*, 1509; (b) Pettit, G. R.; Kamano, Y.; Inoue, M.; Dufresne, C.; Boyd, M. R. *J. Org. Chem.* **1992**, *57*, 429; (c) Fukuzawa, S.; Matsunaga, S.; Fusetani, N. *Tetrahedron* **1995**, *51*, 6707; (d) LaCour, T. G.; Guo, C.; Boyd, M. R.; Fuchs, P. L. *Org. Lett.* **2000**, *2*, 33; (e) Fukuzawa, S.; Matsunaga, S.; Fusetani, N. *J. Org. Chem.* **1997**, *62*, 4484.

[40] Gryko, D.; Piechowska, J.; vetokhina, V.; Wojcik, D. *Bull. Chem. Soc. Jap.* **2009,** *82*, 1514.

[41] Carter, S. D.; Cheeseman, G. W. H. *Tetrahedron* **1977**, *33*, 827.

[42] Okafor, C. O. *J. Heterocycl. Chem.* **1981**, *18*, 1445.

[43] Martin, G. E.; Gampe, R. T.; Ford, J. J.; Willcott, M. R.; Morgan, M. *J. Heterocycl. Chem.* **1983**, *20*, 1063.

[44] Okafor, C. O. *J. Org. Chem.* **1982**, *47*, 592.

[45] Cheeseman, G. W. H.; Rishman, G. *Tetrahedron* **1980**, *36*, 2681.

[46] Litvinenko, S. V.; Volovenko, Y. M.; Savich, V. I.; Babichev, F. S. *Chem. Heterocycl. Compd. (Engl.Transl.)* **1992**, *28*, 93; *Khim. Geterotsikl. Soedin.* **1992**, *1*, 107.

[47] (a) Carver, D. R.; Greenwood, T. D.; Hubbard, J. S.; Komin, A. P.; Sachdeva, Y. P.; Wolfe, J. F. *J. Org. Chem.* **1983**, *48*, 1180; (b) Chekmarev, D. S.; Shorshnev, S. V.; Stepanov, A. E.; Kasatkin, A. N. *Tetrahedron* **2006**, *62*, 9919.

[48] Barlin, G. B.; Brown, D. J.; Cronin, B. J.; Ngu, M. *Aust. J. Chem.* **1986**, *39*, 69.

[49] Schmidt, A.; Mordhorst, T. *Heterocycles* **2006**, *68*, 1393.

[50] (a) Schultheiss, N.; Bosch, E. *Heterocycles* **1981**, *60*, 1891; (b) Ding, S.; Gray, N. S.; Wu, X.; Ding, Q.; Schultz, P. G. *J. Am. Chem. Soc.* **2002**, *124*, 1594.

[51] Zeidan, T. A.; Kovalenko, S. V.; Manoharan, M.; Clark, R. J.; Ghiviriga, I.; Alabugin, I. V. *J. Am. Chem. Soc.* **2005**, *127*, 4270.

[52] Schröter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245.

[53] (a) Dang, T. T.; Dang, T. T.; Ahmad, R.; Reinke, H.; Langer, P. *Tetrahedron Lett.* **2008**, *49*, 1698; (b) Dang, T. T.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2008**, *350*, 2109; (c) Hussain, M.; Nguyen, T. H.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 3929; (d) Dang, T. T.; Dang, T. T.; Rasool, N.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2009**, *351*, 1595.

[54] Suzuki, A. *Pure. Appl. Chem*. **1991**, *63*, 419; (b) Miyaura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457; (c) Suzuki, A. *Organomet. Chem*. **1999**, *576*, 147; (d) Little, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4177; (e) Molander, G.A.; Canturk, B.; Kennedy, L.E. *J. Org. Chem*. **2009**, *74*, 973.

[55] Meijere, A.; Diederich, F. *Metal- Catalyzed Cross-Coupling Reactions*. 2nd Ed. **2004**, Willey-VCH; (b) "*Coupling Reactions Between sp^3 and sp^2 Carbon Centers":* K. Tamao in *comprehensive Organic Synthesis*. *Vol. 3* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**; (c) *New Trends in Heterocyclic Chemistry*; Mitra, R. B., Ed.; Elsevier: Amsterdam, **1979**; (d) *Palladium in heterocyclic chemistry*. *Vol 26*; Elsevier, **2007**; (e) Hou, X. L.; Yang, Z.; Wong, H. N. C. In *Progress in Heterocyclic Chemistry*. *Vol. 15*; Gribble, G. W.; Gilchrist, T. L., Eds.; Pergamon: Oxford, **2003**. (f) Beller, M.; Bohm, C. *Transition Metals in Organic Synthesis*. 2nd Ed. **2005**.

[56] Matose, K.; Soderquist, J. A. *J. Org. Chem*. **1998**, *63*, 461.

[57] (a) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc*. **2005**, *127*, 4685; (b) Baxter, J.; Steinhuebel, D.; Palucki, M.; Davies, I. W.

Org. Lett. **2005**, *7*, 215; (c) Kingston, J. V.; Verkade, J. G. *J. Org. Chem*. **2007**, 72, 2816.

[58] Bahl, A.; Grahn, W.; Stadler, S.; Feiner, F.; Bourhill, G.; Brauchle, C.; Reisner, A.; Jones, P. G. *Angew. Chem. Int. Ed. Engl*. **1995**, *34*, 1485.

[59] (a) Ichimura, K. *Chem. Rev*. **2000**, *100*, 1847; (b) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 402; (c) Taylor**,** R. H.; Felpin, F-X. *Org. Lett*. **2007**, *9*, 2911.

[60] Blouin, N.; Michaud, A.; Gendron, D.; Wakim, S.; Blair, E.; Neagu-Plesu, R.; Belletete, M.; Durocher, G.; Tao, Y.; Leclerc, M. *J. Am. Chem. Soc.* **2008**, *130*, 732.

[61] Hung, N. T.; Hussain, M.; Malik, I.; Villinger, a.; Langer, P. *Tetrahedron. Lett*. **2010**, *51*, 2420.

[62] Khera, R. A.; Ali, A.; Hussain, M.; Tater, J.; Villinger, A.; Langer, P. *Synlett*. **2010**, 1923.

[63] Hussain, M.; Hung, N. T.; Khera, R. A.; Malik, I.; Zinad, D. S.; Langer, P. *Adv. Syn. Catal*. **2010**, *352*, 1429.

[64] Ullah, I.; Khera, R. A.; Hussain, M.; Villinger, A.; Langer, P. *Tetrahedron. Lett*. **2009**, **50**, 4651.

[65] Sharif, M.; Reimann, S.; Villinger, A.; Langer, P. *Synlett*. **2010**, *6*, 913.

[66] Sharif, M.; Zeeshan, M.; Reimann, S.; Villinger, A.; Langer, P. *Tetrahedron. Lett*. **2010**, *51*, 2810.

[67] Toguem, S. M. T.; Villinger, A.; Langer, P. *Synlett*. **2010**, *6*, 909.

[68] Toguem, S. M. T.; Villinger, A.; Langer, P. *Synlett*. **2009**, 3311.

[69] Ibad, M. F.; Abid, O. R.; Nawaz, M.; Adeel, M.; Villinger, A.; Langer, P. *Synlett*. **2010**, *2*, 195.

[70] Abid, O. R.; Ibad, M. F.; Nawaz, M.; Ali, A.; Sher, M.; Rama, N. H.; Villinger, A.; Langer, P. *Tetrahedron. Lett*. **2010**, *51*, 1541.

[71] Nawaz, M.; Ibad, M. F.; Abid, O. R.; Khera, R. A.; Villinger, A.; Langer, P. *Synlett*. **2010**, *1*, 150.

[72] Nawaz, M.; Khera, R. A.; Malik, I.; Ibad, M. F.; Abid, O. R.; Villinger, A.; Langer, P. *Synlett*. **2010**, *6*, 979.

[73] Ali, A.; Khera, R. A.; Ibad, M. F.; Hussain, M.; Langer, P. *Synlett*. **2010**, 731.

[74] Mahal, A.; Villinger, A.; Langer, P. *Synlett*. **2010**, *7*, 1085.

[75] (a) Williams, C. A.; Harborne, J. B.; Newman, M.; Greenham, J. and Eagles, J. *Phytochemistry* **1997**, *46*, 1349; (b) Woo, K. J.; Jeong, Y. J.; Inoue, H.; Park, J. W.; Kwon, J. K. *FEBS. Lett*. **2005**, *579*, 705; (c) Beecker, G. R. *J. Nutr*. **2003**, *133*, 3248S; (d) Havsteen, B. H. *Pharmacol*. *Ther*. **2002**, *96*, 67; (e) Middleton, E. Jr.; Kandaswami, C.; Theoharides, T. C. *Pharmacol*. *Rev*. **2000**, *52*, 672; (f) *Römpp Lexikon Naturstoffe* (W. Steglich, B. Fugmann, S. Lang-Fugmann, eds.), Thieme, Stuttgart: **1997**.

[76] Cermak, R.; Wolffram, S. *Current drug metabolism* **2006**, *7*, 729.

[77] Harborne, J. B.; Baxter, H. *The Handbook of Natural Flavonoids*, *Vol. 1*, John Wiley & Sons, Chichester, **1999**.

[78] Si, D.; Wang, Y.; Zhou, Y.H.; Guo, Y.; Wang, J.; Zhou, H.; Li, Z. S.; Fawcett, J. P. *Drug metabolism and disposition* **2009**, *37*, 629.

[79] Jang, S.W.; Liu, X.; Yepes, M.; Sheperd, K.R.; Miller, G.W.; Liu, Y.; Wilson, W.D.; Xiao, G.; Blanchi, B.; Sun, Y.E.; Ye, K. *PNAS*. **2010**, *107*, 2687.

[80] (a) Habtemariam, S. *J. Nat. Prod.* **1997**, *60*, 775; (b) Koganov, M. M.; Dueva, O.V. and Tsorin, B. L. *J. Nat. Prod*. **1999**, *62*, 481; (c) Lapidot, T.; Walker, M. D. and Kanner, J. *J. Agric. Food Chem*. **2002**, *50*, 7220; (d) Cho, H.; Yun, C.W.; Park, W. K.; Kong, J. Y.; Kim, K. S.; Park, Y.; Lee, S. and Kim, B. K. *Pharmacol. Res*. **2004**, *49*, 37; (e) Critchfield, J. W.; Butera, S.T. and Folks, T. M. *AIDS. Res. Hum. Retroviruses*. **1996**, *12*, 39.

[81] Datla, K. p.; Christidou, M.; Widmer, W. W.; Rooprai, H. K.; Dexter, D. T. *Neuroreport*. **2001**, *12*, 3871.

[82] Wang, Q. A.; Tougen.; Tang, J. G.; Fan, H. F. *Hunan Daxue Xuebao*. **2004**, *31*, 1.

[83] Kuemmerle, J.; Jiang, S.; Tseng, B.; Kasibhatla, S.; Drewe, J.; Cai, S.X. *Bioorg. Med. chem*. **2008**, *16*, 4233.

[84] Ertan, R.; Goker, H.; Ertan, M.; Pindur, U. *Arch. Pharm*. **1989**, *322*, 237.

[85] (a) Zembower, D.; Zhang, H. *J. Org*. *Chem*. **1998**, *63*, 9300; (b) Zheng, X.; Meng, W.; Qing, F. *Tetrahedron. Lett*. **2004**, *45*, 8083; (c) Huang, X.; Tang, E.; Xu, W.

M.; Cao, J. *J. Comb. Chem*. **2005**, *7*, 802; (d) Peng, W.-J.; Han, X.-W.; Yu, B. *Chin. J. Chem.* **2006**, *24*, 1154.

[86] Park, H.; Dao, T. T.; kim, H. P. *Eur. J. Med. Chem*. **2005**, *40*, 943.

[87] CCDC-xxx contains all crystallographic details of this publication and is available free of charge at **www.ccdc.cam.ac.uk/conts/retrieving.html** or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: (+44)1223-336-033; or **deposit@ccdc.cam.ac.uk**.

[88] (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. Tetrahedron. Lett. 1975, 16 (50), 4467; (b) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979; (c) *Transition Metals for Organic Synthesis; Building Block and Fine Chemicals*, 2nd ed.; Beller, N., Bolm, C., Eds.; Wiley-VCH: Weinheim, **2004**.

[89] (a) Chinchilla, R.; Najera, C. *Chem. Rev*. **2007**, *107*, 874; (b) Tsuji, J. *Palladium Reagents and Catalysts, Innovations in Organic Synthesis*; Wiley: New York, **1995**.

[90] (a) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem. Int. Ed*. **2000**, *39*, 2632; (b) Cacchi, S. *Synthesis* **1986**, 320; (c) Alami, M.; Ferri, F.; Linstrumelle, G. *Tetrahedron. Lett*. **1993**, *34 (40)*, 6403. (d) Bohm, V. P. W.; Herrmann, W. A. *Eur. J. Org. Chem*. **2000**, 3679.

[91] (a) Ricks, H. L.; Shimizu, L. S.; Smith, M. D.; Bunz, U. H. F.; Shimizu, K. D. *Tetrahedron Lett.* **2004**, *45*, 3229; (b) Tykwinski, R. R. *Angew. Chem., Int. Ed.* **2003**, *42*, 1566; (c) Wilson, J. N.; Josowicz, M.; Wang, Y.; Bunz, U. H. F. *Chem. Commun.* **2003**, 2982; (d) Bunz, U. H. F. *Chem. Rev.* **2000**, *100*, 1605; (e) Martin, R. E.; Diederich, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1350.

[92] Ullah, F.; Dang, T.T.; Heinicke, J.; Villinger, A.; Langer, P. *Synlett*. **2009**, 5, 838.

[93] Tung, D. T.; Villinger, A.; Langer, P. *Adv. Synth. Catal*. **2008**, *350*, 2109.

[94] Abid, O. R. dissertation, May 2010, University of Rostock.

[95] (a) Palucki, M. *Palladium in heterocyclic chemistry*, *Vol 26*; Elsevier, **2007**, p. 475; (b) Sirichaiwat, C.; Intaraudom, C.; Kamchonwongpaisan, S.; Vanichtanankul, J.; Thebtarananth,Y.; Yuthavong, Y. *J. Med. Chem*. **2004**, *47*, 345; (c) White, N. J. *Br. Med. Bull*. **1998**, *54*, 703; (d) McKie, J. H.; Douglas, K.

T.; Chan, C.; Roser, S. A.; Yates, R.; Read, M.; Hyde, J. E.; Dascombe, M. J.; Yuthavong, Y.; Sitrawarapoln,W. *J . Med . Chem*. **1998**, *41*, 1367.

[96] (a) Jian, K. S.; Chitre, T. S.; Miniyar, P. B.; Kathiravan, M. K.; Bendre, V. S.; Veer, V. S.; Shahane, S. R.; Shishoo, S. J. *Current Science* March **2006,** *90(6)*, 793; (b) N. A. Hassan, *Molecules* **2000**, *5*, 827; (c) Pemmsin, M.; Lnu-Due, C.; Hoguet, F.; Gaultier, C.; Narcisse, J. *Eur. J. Med. Chem.* **1988**, *23*, 543; (d) Cannito, A.; Pemmsin, M.; Lnu-Due, C.; Hoguet, F.; Gaultier, C.; Narcisse, J. *Eur. J. Med. Chem.* **1990**, *25*, 635; (e) Smith, P.A.S.; Kan, R.O. *J. Org. Chem.* **1964**, *29*, 2261; (f) Nega, S.; Aionso, J.; Diazj, A.; Junquere, F. *J. Heterocycl. Chem.* **1990**, *27*, 269; (g) Shishoo, C.J.; Jain, K.S. *J. Heterocycl. Chem.* **1992**, *29*, 883.

[97] (a) Balzarini, J.; McGuigan, C. *J. Antimicrob. Chemother*. **2002**, *50*, 5; (b) McGuigan, C.; Yarnold, C. J.; Jones, G.; Velazquez, S.; Barucki, H.; Brancale, A. et al. *J. Med. Chem*. **1999**, *42*, 4479; (C) McGuigan, C.; Barucki, H.; Blewett, S.; Carangio, A.; Erichsen, J. T.; Andrei, G. et al. *J. Med. Chem*. **2000**, *43*, 4993.

[98] Wang, T, et.al. *J . Med. Chem*. **2008**, *51*, 4672.

[99] Movassaghi, M.; Hill, M.D. *J. Am. Chem. Soc*, **2006**, *128(44)*, 14254.

[100] Muller, T. J. J.; Braun, R.; Ansorge, M. *Org. Lett*. **2000**, *2(13)*, 1967.

[101] (a) Yang, Y.; Martin, A. R. *Heterocycles.* **1992**, *34*, 1395; (b) Gronowitz, S.; Hoenfeldt, A.-B.; Kristjannson, V.; Musil, T. *Chem. Scripta.* **1986**, *26*, 305; (c) Peters, D.; Hoenfelt, A-B.; Gronowitz, S. *J. Heterocycl. Chem*. **1990**, *27*, 2165.

[102] Acelle, S.; Ramondenc, Y.; Dupas, G.; Ple, N. *Tetrahedron* **2008**, *64*, 2783.

[103] Hussain, M**.;** Hung, N. T.; Khera, R. A.; Malik, I.; Zinad, D. S.; Langer, P. *Adv. Synth. Catal.,* **2010,** *352*, 1429.

[104] (a) Gray, G.W.; Hird, M.; Toyne, K.J. *Mol. Cryst. Liq. Cryst.* **1991**, *195*, 221 ; (b) Lincker, F. ; Bourgun, P. ; Masson, P. ; Dider, P. ; Guidoni, L.; Bigot, J.Y. ; Nicoud, J.F. ; Donnio, B. ; Guillon, D. *Org. Lett.* **2005**, *7*, 1505; (c) Kraft, A.; Grimsdale, A.C.; Holmes, A. B. *Angew. Chem. Int. Ed.* **1998**, *37*, 402; (d) Lo, S. C.; Burn, P. L. *Chem. Rev.* **2007**, *107*, 1097. (e) Fichou, D. *J. Mater. Chem.* **2000**, *10*, 571. (f) Funahashi, M.; Zhang, F.; Tamaoki, N. *Adv. Mater.* **2007**, *19*, 353; (g)

Yu, G.; Gao, J.; Hummelen, J. C.; Wudl, F.; Heeger, A. J. *Science* **1995**, *270*, 1789; (h) Denk, W.; Strickler, J. H.; Webb, W. W. *Science* **1990**, *248*, 73.

[105] (a) Itami, K.; Yamazaki, D.; Yoshida, J-I. *J. Am. Chem. Soc*. **2004**, *126*, 15396; (b) Lin, Y-C.; Lai, C. K.; Chang, Y. C.; Liu.K. T. *Liq.Cryst*. **2002**, *29*, 237.

[106] (a) Hou, X. L.; Yang, Z.; Wong, H. N. C. In *Progress in Heterocyclic Chemistry*, *Vol. 15*; Gribble, G. W.; Gilchrist, T. L., Eds.; Pergamon: Oxford, **2003**, 167; (b) Friedrichsen, W. in *Comprehensive Heterocyclic Chemistry* (Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., eds.), *vol. 2*, Elsevier: **1996**, p. 359; (c) Shea, K. M. *Palladium in heterocyclic chemistry, Vol 26*; Elsevier, **2007**, p. 303.

[107] (a) Culver, P.; Jacobs, R.S. *Toxicon* **1981**, *19*, 825; (b) Missakian, M. G.; Burreson, B. J.; Schever, P. J. *Tetrahedron* **1975**, *31*, 2513. (c) Shen, Y.C.; Chatervedula, V. S. P.; Kuo, Y. H. *J. Nat. Prod*. **2001**, *64*, 324; (d) Karasawa, D.; Shatar, S.; Erdenechimeg, A.; Okamoto, Y.; Tateba, H.; Shimizu, S. *J. Essent. Oil. Res*. **1995**, *7*, 255. (e) Look, S.A.; Burch, N. T.; Fenical, W. *J. Org. Chem*. **1985**, *50*, 5741; (f) Kobayashi, M.; Mahmud, T.; Tajima, H.; Wang, W-Q.; Aoki, S.; Nakagawa, S.; Mayumi, T.; Kitagawa, I. *Chem. Pharm. Bull*. **1996**, *44*, 720; (g) Chang, H. M.; Cheng, K. P.; Choang, T. F.; Chow, H. F.; Chui, K. Y.; Hon, P. M.; Tan, F. W. L.; Yang, Y.; Zhong, Z. P.; Lee, C. M.; Sham, H. L.; Chan, C. F.; Cui, Y. X.; Wong, H. N. C. *J. Org. Chem*. **1990**, *55*, 3537; (h) Bernard, R.; Cardani, C.; Selva, D.; Baggini, A.; Pavan, M. *Tetrahedron Lett*. **1967**, *8*, 3893; Barma, D.K.; Kundu, A.; Baati, R.; Mioskowski, C.; Falck, J.R. *Org. Lett*. **2002**, *4*, 1387.

[108] (a) Brunton, L.; Lazo, J.; Keith, P. *The pharmacological basis of therapeutics*. McGraw Hill, **2005**; (b) Cadwallader, D. E. *J. Am. Pharm. Assoc.* **1975**, *NS15*, 409.

[109] (a) Tangallapally, R. P.; Lee, R. E. B.; Lenaerts, A. J. M.; Lee, R. E. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 2584; (b) Srivastava, V.; Negi, A. S.; Kumar, J. K.; Faridu, U.; Sisodia, B. S.; Darokar, M. P.; Luqman, S.; Khanuja, S. P. S. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 911; (c) Nagaraja, G. K.; Kumaraswamy, M. N, Vaidya, V. P.; Mahadeven, K. M. *ARKIVOC*. **2006**, *10*, 1; (d) Sondhi, S. M.; Jain, S.; Rani, R.; Kumar, A. *Ind. J. chem*. **2007**, *46B*, 1848.

[110] (a) Dulop, A. P. and Peters, F. N. *The Furans*. Reinhold Publishing: Baltimore. **1953**. p. 35; (b) Grieco, P.; Pogonowski, C.; Burke, S. *J. Org. Chem*. **1975**, *40*, 542; (c) Scott, L. T.; Naples, J. O. *Synthesis* **1973**, 209.

[111] Bisagni, E.; Marquet, J. P.; Bourzat, J. D.; Depin, J. J.; Andre-Louisfert, *J. Bull. Chem. Soc. Fr*. **1971**, 4041.

[112] Courmier, R. A.; Grosshans, C. A.; Skibbe, S. L. *Synth. Commun*, **1988**, *7*, 677.

[113] Sammond, D. M.; Sammakia, T. *Tetrahedron letter*. **1996**, *37*, 6065.

[114] (a) Zeni, G. and Larock, R. C. *Chem. Rev*. **2004**, *104*, 2285; (b) Kirsch, G.; Hesse, S. and Comel, A. *Curr. Org. Synth*. **2004**, *1*, 47. (c) Marson, C.; Harper, S. and Wrigglesworth, R. *J. Chem. Soc., Chem. Commun*. **1994**, 1879.

[115] Mross, G.; Holtz, E.; Langer, P. *J. Org. Chem*. **2006**, *71*, 8045.

[116] Marshall, J. A. and Bennett, C. *J. Org. Chem*. **1994**, *59*, 6110.

[117] Tso, H. H.; Tsay, H. *Tetrahedron. Lett*. **1997**, *38*, 6869.

[118] Mortensn, D. S.; Rodriguez, A. L.; Carlson, K. E.; Sun, J.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A. *J. Med. Chem*. **2001**, *44*, 3838.

[119] Lind, P.; Carlsson, M.; Eliasson, B.; Glimsdal, E.; Lindgren, M.; Lopes, C.; Boman, L.; Norman, P. *Mol. Phys.* **2009**, *107*, 629.

[120] Greco, N. J.; Tor, Y. *Tetrahedron* **2007**, *63*, 3515.

[121] Yamaguchi, T.; Irie, M. *J. Mat. Chem.* **2006**, *16*, 4690.

[122] Lechel, T.; Dash, J.; Brudgam, I.; Reissig, H. U. *Eur. J. Org. Chem*. **2008**, 3647.

[123] Bach, T.; Krüger, L. *Tetrahedron Lett*. **1998**, *39*, 1729.; Bach, T.; Krüger, L. *Eur. J. Org. Chem*. **1999**, 2045.

Erklärung/ Daclaration

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

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

IMRAN MALIK
September 2010, Rostock, Germany

List of Publications

[1] "Efficient Synthesis of Functionalized 2,3-Di(alkenyl)benzothiophenes and Dibenzothiophenes based on the First Heck Reactions of 2,3-Di- and 2,3,5-Tribromobenzothiophene". Hussain, M.; **Malik, I**.; Langer, P. *Synlett.* **2009**, *16*, 2691.

[2] "Synthesis of 2,3-Disubstituted Pyrazines and Quinoxalines by Heck Cross-Coupling Reactions of 2,3-Dichloropyrazine and 2,3-Dichloroquinoxaline. Influence of the Temperature on the Product Distribution". **Malik, I.;** Hussain, M.; Ali, A.; Toguem, S. M. T.; Basha, F. Z.; Fischer, C.; Langer, P. *Tetrahedron* **2010**, *66*, 1637.

[3] "Synthesis of Functionalized Benzothiophenes by Twofold Heck and subsequent 6π-Electrocyclization Reactions of 2,3-Dibromothiophene". Toguem, S. M. T.; Hussain, M.; **Malik, I.;** Villinger, A.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 4962.

[4] "Site-Selective Suzuki Cross-Coupling Reactions of 2,3" Dibromobenzofuran". Hung, N. T.; Hussain, M.; **Malik, I.;** Villinger, A.; Langer, P. *Tetrahedron Lett.* **2010**, *51*, 2420.

[5] "Twofold Heck Cross-Coupling Reactions of Dibrominated Pyridines", Ali, A.; Hussain, M.; **Malik, I.;** Fischer, C.; Langer, P. *Helv. Chim. Acta.* **2010**, in print.

[6] "Synthesis of 7,8-Diarylflavones by Site-Selective Suzuki-Miyaura Reactions", **Malik, I.;** Hussain, M.; Hung, N. T.; Villinger, A.; Langer, P. *Synlett.* **2010**, 2244.

[7] "Synthesis of 3,4-Diarylbenzophenones by Site-Selective Suzuki-Miyaura Reactions of 3,4-Bis(trifluoromethylsulfonyloxy)benzophenone", Nawaz, M.; Khera, R. A.; **Malik, I.;** Ibad, M. F.; Abid, O. R.; Villinger, A.; Langer, P. *Synlett.* **2010**, 979.

[8] "Synthesis of Aryl-Substituted Pyrimidines by Site-Selective Suzuki-Miyura Cross-Coupling Reactions of 2,4,5,6-Tetrachloropyrimidines", Hussain, M.; Hung, N. T.; Khera, R. A.; **Malik, I.;** Zinad, D. S.; Langer, P. *Adv. Synth. Catal.* **2010,** *352*, 1429.

[9] "A Pentacyclic Triterpene from *Litchi Chinensis*", **Malik, I.**; Ahmad, V. U.; Anjum, S.; Basha, F. Z. *Nat. Prod. Comm.* **2010,** *5 (4),* 529.

[10] "Case Study of Trash Fish under Environmental Stress for their Survival and Utilization", Azmat, R.; Ahmad, K.; Jehanzeb, Q.; **Malik, I.**; Ahmed, T. *Int.J. Zool. Res.* **2008**, *4(4)*, 225.

[11] "Synthesis and Photophysical Properties of Alkynylated Pyrimidines by Site Selective Sonogashira Reaction of 2,4,5,6-Tetrachloropyrimidine. First Synthesis of Tetraalkynylpyrimidines", **Malik, I.**; Ahmad, Z.; Reimann, S.; Ali, I.; Langer, P. *Manuscript in preparation*.

[12] "Sonogashira Cross Coupling Reactions of 2,3,4,5-Tetrabromofuran. Synthesis and Fluorescence of Alkyne-Substituted Furans", **Malik, I.**; Ahmad, Z.; Reimann, S.; Langer, P. *Manuscript in preparation*.