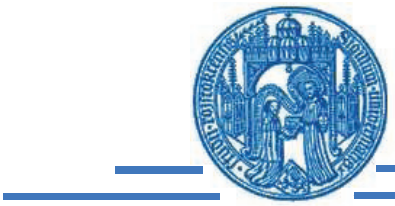

UNIVERSITÄT ROSTOCK

Domino Twofold Heck / 6π-Electrocyclization and Regioselective Palladium(0)-Catalyzed Reactions of Brominated Indoles, Furans, Naphthoquinone and 2,4,5,6-Tetrachloropyrimidine

Dissertation

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Erlangung des Doktorgrades

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“I feel a great pleasure to dedicate all of this work to my respected mentor **Abu Bilal Mohammad Ilyas Attar Qadri** then my all **teachers** from I learned and will learn even a single word and **my dear parents.**

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Alhamdolillahi Rabbil Aalamin Wassalatusalam un Ala Rasool-e-hilkarim

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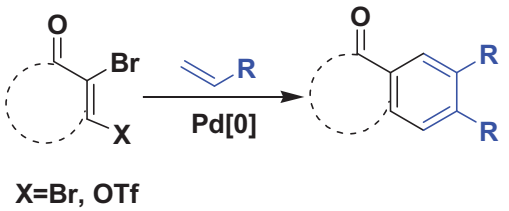
I owe all of them in my life!

MAIN CONTENTS

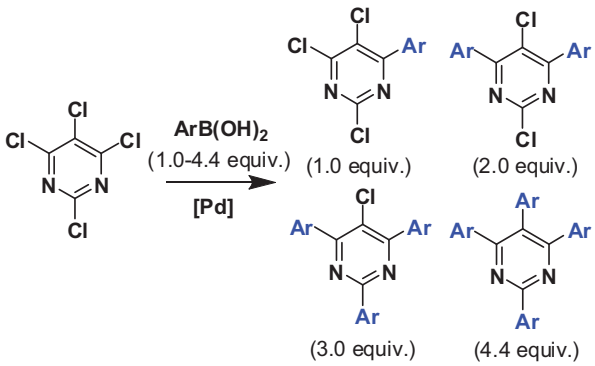
Synthesis of Anthraquinones, Fluorenones and Benzocoumarins by Domino ′Twofold Heck / 6π-Electrocyclization′ Reactions



X=Br, OTf

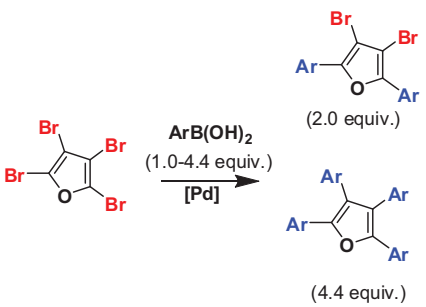
Functionalized anthraquinones, fluorenones and benzocoumarins were prepared by domino ′twofold Heck / 6π-electrocyclization′ reactions.

Synthesis of Aryl-Substituted Pyrimidines by Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,4,5,6-Tetrachloropyrimidine



Suzuki-Miyaura cross coupling reactions of 2,4,5,6-tetrachloropyrimidine provide an expedient synthesis of mono-, di-, tri- and tetraarylpyrimidines which are not readily available by other methods. All reactions proceed with excellent site-selectivity. Optimization of reaction conditions for better yields and loading of lower percentage of catalyst were studied as well.

Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,3,4,5-Tetrabromofuran



Suzuki-Miyaura reactions of 2,3,4,5-tetrabromofuran allowed a convenient synthesis of tetraarylfurans which are not readily available by other methods. Regioselectivity was achieved by using the binary solvent system toluene/dioxane (4:1) at C-2, C-5 and then C-3, C-4. All reactions proceeded with excellent yields and site-selectivity.

DETAILED CONTENTS

SUMMARY

A significant part of this dissertation has been published (see list of publications). Work described in this thesis includes domino ′twofold Heck / 6π-electrocyclization′ reactions of several carba- and heterocyclic 1,2-dibromoalkenes and regioselective Suzuki-Miyaura cross-coupling reactions of 2,3,4,5-tetrabromofuran and 2,4,5,6-tetrachloropyrimidine.

1 An Overview of Domino Twofold Heck / 6π-Electrocyclization Reactions of 1,2-Dihalogenated Compounds

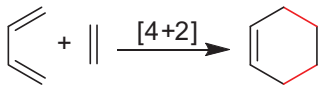
1.1 Pericyclic reactions: These are concerted cyclization reactions wherein the transition state of the molecule has a cyclic geometry in which electrons move round a circle without positive or negative charges. There are three types of pericyclic reactions.

1- Cycloaddition reactions

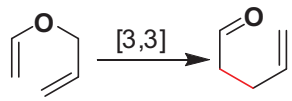
2- Sigmatropic reactions

3- Electrocyclic reactions

1- Cycloaddition reactions: Cycloaddition is a one-step ring-forming reaction between two conjugated π systems in which two new σ bonds are formed joining the two reagents at each end. The mechanism has one step with no intermediates. E.g. Diels-Alder reaction.



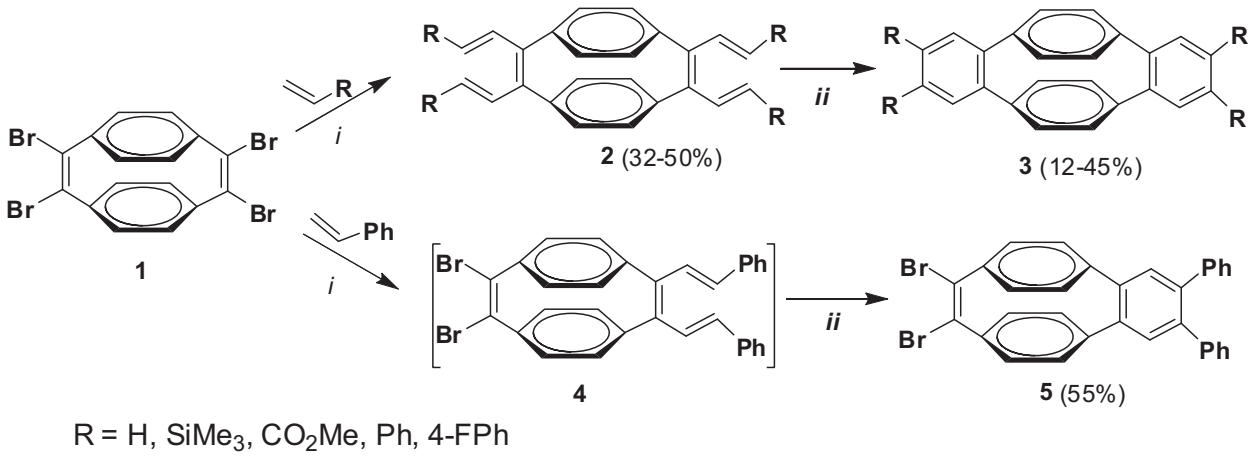
2-Sigmatropic reactions: Sigmatropic reaction is a pericyclic reactions wherein the net result is one σ bond is changed to another σ-bond in an uncatalyzed intramolecular process. E.g. the most famous sigmatropic rearrangement is the [3,3] Claisen rearrangement.



3-Electrocyclic reaction: Electrocyclic reaction is the formation of a new σ bond across the ends of a conjugated polyene or the reverse.[1]

The combination of the Heck cross-coupling reaction with electrocyclization reaction provides a convenient access to a variety of carbacyclic frameworks. Pioneering work in this field was reported by de Meijere and co-workers. In 1987, this research group reported the Heck-type vinylation of 1,2,9,10-tetrabromo[2.2]paracyclophanediene (**1**) to synthesize tetravinyl derivative **2** (Scheme 1). Thermal electrocyclization and subsequent aromatization of **2** provided benzo-anullated [2.2]paracyclophanediene **3**. Interestingly, a prematurely interrupted reaction with styrene provided entirely the vicinal dibromide **4** after cyclization and aromatization. This research group showed the importance of double Heck-coupling of

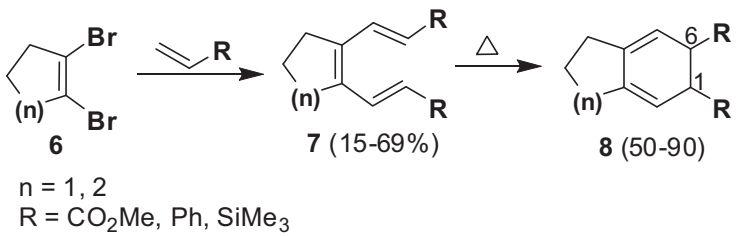
alkenes with vicinal dibromo-alkenes to synthesize **(*E,Z,E*)**-l,3,5-hexatrienes which can undergo the annulation of six-membered rings.[2]



Scheme 1. Conditions: *i*) $Pd(OAc)_2$, Bu_4NBr, K_2CO_3/$NaHCO_3$, DMF, heat (40-100 °C), *ii*) Pd/C (+O_2) or S_8, xylene, 150 °C.

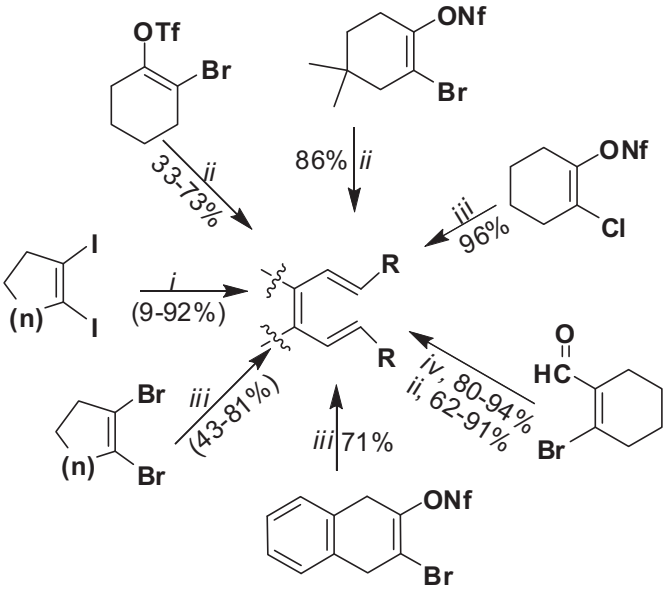
The reactions discussed above include the Heck reaction, electrocyclization, double bond migration (or isomerisation probably by [1,5]-sigmatropic hydrogen shift)[6] and aromatization (oxidation).

In 1990, Armin de Meijere group reported twofold Heck reactions of vicinal 1,2-dibromocycloalkenes **6** to synthesize **(*E,Z,E*)**-l,3,5-hexatrienes **7** in fair to high yields (26-69 %). Thermal electrocyclization in anaerobic conditions provided the annulated 1,3-cyclohexadienes **8** (scheme -2). Two-, three- and fourfold Heck type coupling reactions were also performed with vicinal di-, tri-, and tetra-bromobenzene, but no subsequent electrocyclization was described.[3]



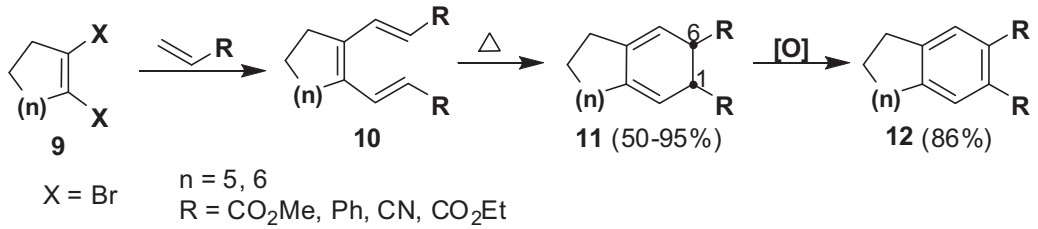
Scheme 2. Conditions: *i*) $Pd(OAc)_2$, PPh_3, NEt_3, DMF, heat (90-100 °C), *ii*) xylene or (n-Bu_2O), 140-150 °C, inert conditions.

In 1998, Armin de Meijere research group reported a domino reaction approach based on twofold Heck cross-coupling reactions of 1,2-dihalocycloalkenes.[4] They prepared (*E,Z,E*)-1,3,5-hexatrienes, these provided appropriate systems for a thermal 6π-electrocyclization to form smoothly functionalized ring-annulated cyclohexa-1,3-dienes. This research group used a variety of starting materials and reaction conditions for the synthesis of (*E,Z,E*)-1,3,5-hexatrienes, such as the Wittig reaction and Heck-type reactions (Scheme 3).



Scheme 3. Conditions: *i*) alkene, $Pd(OAc)_2$, $AgNO_3$, NEt_3, DMSO, heat (20-100 °C), Pressure (1-5 bar), time (5 h-48 h); *ii*), alkene, $Pd(OAc)_2$, PPh_3, LiCl, NEt_3, DMF, heat (60-90 °C), *iii*), alkene, $Pd(OAc)_2$, PPh_3, NEt_3, DMF, heat (60-90 °C), *iv*), $(EtO)_2POCH_2R$, NaH, THF, 0-25 °C, 12 h.

Heating of the reaction mixtures at 130-150 °C in oxygen-free xylene or di-*n*-butyl ether resulted in electrocyclization of the (*E,Z,E*)-1,3,5-hexatrienes. As these electrocyclizations were done under thermal conditions, they proceeded by disrotatory ring closure and the two substituents at position 1 and 6 had a stereochemical *cis* relationship (scheme 4).



Scheme 4. Twofold Heck cross coupling and subsequent electrocyclization, *i*) $Pd(OAc)_2$, PPh_3, NEt_3 DMF, 90-100 °C, *ii*) Pd/C (+O_2) or S, xylene, 150 °C.

The 6π-electrocyclization of bis-alkenylated Heck products results in a product containing two exocyclic double bonds. As stated before probably this isomerization occurred through [1,5]-sigmatropic hydrogen shift.[6] To refurnish the aromaticity of the adjacent ring, migration of the double bonds is necessary. This isomerization must happens in such a way that a more stable product can be formed (thermodynamic control).

Although, Kano and co-workers were the first to report the synthesis of carbazoles by 6π-electrocyclization of 2,3-di(alkenyl)indoles.[5] Later, this approach had also been studied by Pindur and Adam.[6] However, the synthesis of the starting materials was not straightforward and needed many steps which is a severe drawback of this method. Prof. P. Langer and coworkers later studied the application of this concept for various 1,2-dihaloaromatic compounds which includes both carba- and heterocycles. In general, the electrocyclization only works well for substrates in which the central double bond is not involved in a benzene-type aromatic system. The reaction is possible for weakly aromatic systems and for non-aromatic double bonds.

1.2 My Research Objectives:

Although first domino twofold Heck / 6π-electrocyclization reactions was reported in 1987, but never reported for the (*E,Z,E*)-1,3,5-hexatrienes invoving the double bond of aromatic system. My goal was to optimize the reaction conditions to apply this strategy on 1,2-dihalogenated heteroaromatic compounds like 2,3-dibromo-*N*-methylindole, 2,3,6-tribromo-*N*-methylindole and 2,3-dibromofuran. Later on this strategy was also studied for 2,3-dibromonaphthoquinone, 2,3-dibromoindenone and 3-bromo-4-hydroxy coumarin to synthesize their corresponding benzo-annulated analogs.

2 Synthesis of 1,2-Dihydrocarbazoles and Carbazoles by Domino Twofold Heck / 6π-Electrocyclization Reactions of Di- and Tri-*N*-methylindoles

2.1 Introduction

Carbazole is a natural product isolated first time from coal tar in 1872 by Graebe and Glaser. Carbazoles are of significant pharmacological application with antifungal, antibiotic, and antitumor activities. Simple carbazole alkaloids were discovered in 1960s as a natural product from plant. Murrayafoline A and murrayaquinone-B are examples of naturally occurring carbazoles and carbazolequinones isolated from the root bark of *Murraya euchrestifolia* Hayata by Japanese researchers (Figure 1).[16, 17]

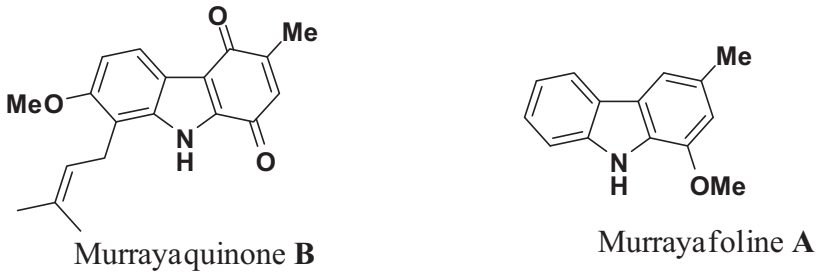


Figure 1. Carbazoles isolated from root bark of Murraya euchrestifolia Hayata

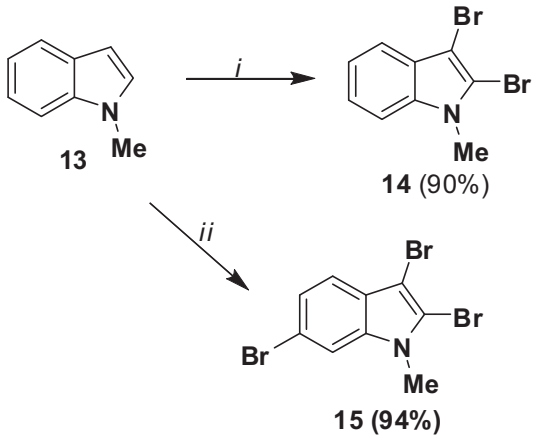
In the literature, iron-mediated (stoichiometric) cyclizations resulted in ingenious synthesis of carbazoles were described by Knölker and coworkers.[16d] Later on the same group reported carbazole syntheses by Buchwald-Hartwig reaction of aryl halides with anilines and following oxidative cyclization.[18] Recently Ackermann *et. al.* have reported a proficient synthesis of carbazoles and other heterocycles by a new palladium-catalyzed domino N-H / C-H activation reaction of anilines with 1,2-dihaloalkenes.[19] Diels-Alder reactions of 2- or 3-vinylindoles have also been used for the preparation of carbazoles.[20] The first report for the synthesis of carbazoles by 6π-electrocyclization using 2,3-di(alkenyl)indoles came from Kano and coworkers.[5] Later, this approach had been also studied further by Pindur and Adam.[6] Nevertheless, the synthesis of the precursors were complicated and essentially needed many steps which is a real disadvantage of this method. The authors prepared acceptor-substituted 2,3-di(alkenyl)indoles by Pd(II)-catalyzed reactions of carbon atom C-3 of 2-formylindoles with alkenes to form 2-formyl-3-vinylindoles and subsequent Wittig reaction provided the

desired product. As this approach did not provide a general method to prepare carbazoles, alternatively, double Wittig reaction approach of (unstable) 2,3-diformyl-*N*-methylindole was reported but it resulted in low yields.

In recent years, it has been revealed that polyhalogenated heterocycles can be functionalized regioselectively by palladium(0)-catalyzed cross-coupling reactions and selective activation of a single halogen atom. The regioselectivity is controlled by electronic and steric parameters.[21] Recently, Langer *et al.* have discovered the synthesis of aryl-substituted thiophenes,[22] pyrroles,[23] and selenophenes,[24] by regioselective Suzuki reactions of tetrabromothiophene, tetrabromo-*N*-methylpyrrole, and tetrabromoselenophene, respectively. Symmetrical and unsymmetrical 2,3-diarylindoles also have been described by twofold Suzuki reactions of 2,3-dihalo-*N*-(phenylsulfonyl)indoles and *N*-methylindole.[25] Other palladium(0)-catalyzed cross-coupling reactions of 2,3-dihaloindoles had never been reported before. A detailed literature study of different approaches described earlier suggested that domino twofold Heck / 6π-electrocyclization might provide a valuable method for the direct, easy and consistent synthesis of substituted dihydrocarbazoles and carbazoles.

2.2 Results and Discussion

Even though 2,3-dibromo-*N*-methylindole (**14**) has been previously synthesized in 64% yield by reaction of *N*-methylindole (**13**) and copper(II) bromide,[26] I studied this reaction again and found that the reaction of *N*-methylindole (**13**) with portion-wise addition of NBS (2.1 equiv.) in THF (−78 °C, 4 h) can result in regioselective formation of 2,3-dibromo-*N*-methylindole (**14**) in 90% yield (Scheme 5). Product **14** and 2,3,6-tribromo-*N*-methylindole (**15**) have been isolated as natural products.[27-30] Gribble and Liu have reported the transformation of **14** into **15** (Br_2, $CHCl_3$) in 70-80% yield.[30] I found that 2,3,6-tribromo-*N*-methylindole (**15**) can be prepared in 94% yield by reaction of **13** with NBS (3.1 equiv.) in THF (−78 °C, 4 h). Addition of NBS to the reaction mixture at room temperature resulted in a very complex mixture of compounds. The same was observed when NBS was added in one portion. In fact, bromination of *N*-methylindole is a highly exothermic reaction. Therefore, to prepare regioselectively brominated *N*-methylindoles, the reaction was performed at -78 °C with portion-wise addition of NBS to the reaction mixture. Applying this strategy, I achieved consistently the regioselective bromination of *N*-methylindole.



Scheme 5. Bromination of *N*-methylindole (**13**); *conditions*: *i*, NBS (2.1 equiv.), THF, −78 °C, 4 h; *ii*, NBS (3.1 equiv.), THF, −78 °C, 4 h, then 20 °C, 14 h.

Table 1. Optimization of the reaction conditions for the synthesis of **17b,d**

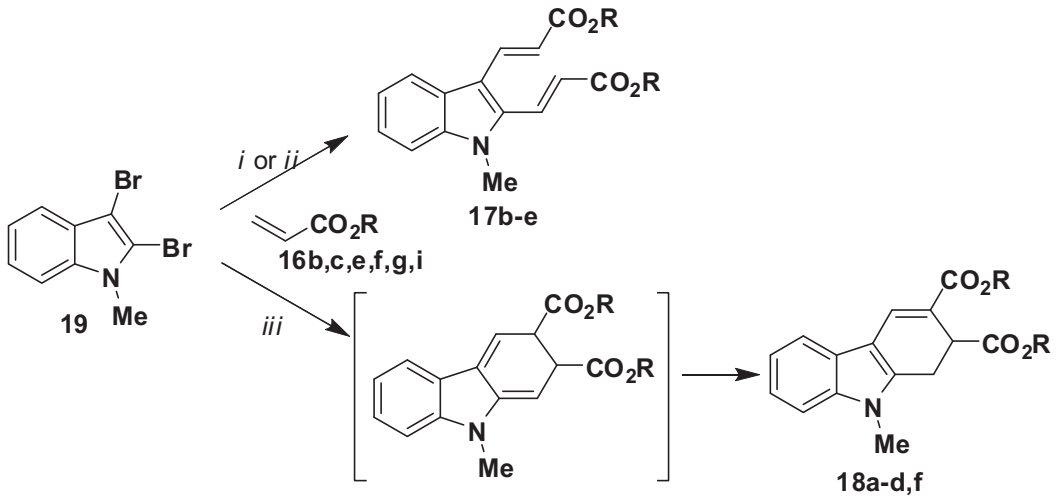
Entry	Catalyst	Temp (°C)	% (**17b**) [a]	% (**17d**) [a]
1	$Pd(PPh_3)_4$ (5 mol-%)	90	Complex mixture	Complex mixture
2	$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%)	90	65	71
3	**$Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%)**	**90**	**72**	**78**
4	**$Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%)**		*b*	*b*
5	$Pd(OAc)_2$ (3 mol-%), SPhos (6 mol-%)	90	Complex mixture	Complex mixture
6	$Pd(OAc)_2$ (2 mol-%), SPhos (4 mol-%)	100	*c*	*c*
7	$Pd(OAc)_2$ (2 mol-%), SPhos (4 mol-%)	120	**18b** (77%)	**18d** (85%)

[a] Yields of isolated products; all reactions were carried out in DMF using NEt_3 as base (36h); [b] mixture of **17b,d** and **18b,d,** respectively (estimated by TLC); [c] Approx. 50% conversion (estimated by tlc)

The Heck cross coupling reaction of **14** with acrylates **16c-g** afforded the 2,3-di(alkenyl)indoles **17b-e** in good yields (Scheme 6, Table 2). The best yields were obtained when the reactions were carried out using $Pd(OAc)_2$ (5 mol-%) and the biaryl monophosphine

ligand **L** (10 mol-%) which has been recently been developed by Buchwald and coworkers.[7] Lower percentage of catalyst resulted in complex mixture (Table 1). The reactions were carried out in DMF at 90 °C for 36 h. Recently, Li and Wang reported[31] that triethanolamine represents an efficient and reusable combined base, ligand, and solvent for palladium(0)-catalyzed Heck reactions. The application of these conditions to the reaction of **14** with acrylate **16g** proved to be successful and resulted in the formation of **17e** in 63% yield.

The $Pd(OAc)_2$/**L**-catalyzed reaction of **14** with acrylates **16b,c,e,f,i** carried out at 120 °C rather than 90 °C, afforded the 1,2-dihydrocarbazoles **18a-d,f** in good yields. The formation of these products can be explained by a domino ′twofold Heck / 6π-electrocyclization′ cyclization and following double bond migration. The initially formed 2,3-dihydrocarbazoles undergo an isomerization into the more stable 1,2-dihydrocarbazoles. The 6π-electrocyclization of bis-alkenylated Heck products results in a product containing two exocyclic double bonds. Possibly this isomerization could occur through 1,5-sigmatropic hydrogen shift. To refurnish the aromaticity of the adjacent ring, migration of the double bonds is necessary. This isomerization must happen in such a way that a more stable product can be formed (thermodynamic control).



Scheme 6. Synthesis of **17b-e** and **18a-d,f**. Conditions: *i*, for **17b-e**: $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 90 ˚C, 36 h; *ii*, for **17e**: $Pd(OAc)_2$ (5 mol-%), $N(CH_2CH_2OH)_3$ (3 mL), 90 ˚C, 36 h; *iii*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3 (8.0 equiv.), DMF, 120 ˚C, 48 h.

Table 2. Synthesis of **17b-e** and **18a-d,f**

17,18	**16**	R	% (**17**) [a]	% (**18**) [a]
a	**b**	Et	- [b]	93
b	**c**	*n*Bu	72	77
c	**e**	*n*Hex	77	81
d	**f**	*t*Bu	78	85
e	**g**	*i*Oct	76	- [b]
f	**i**	$(CH_2)_2NMe_2$	- [b]	79

[a] Yields of isolated products based on **14**; [b] experiment was not carried out

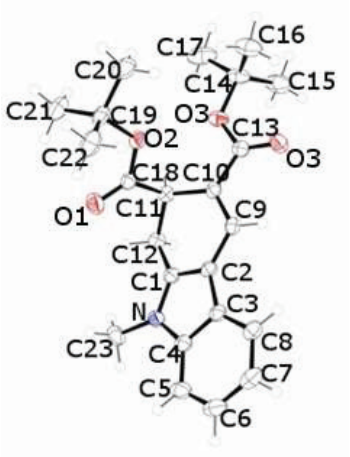
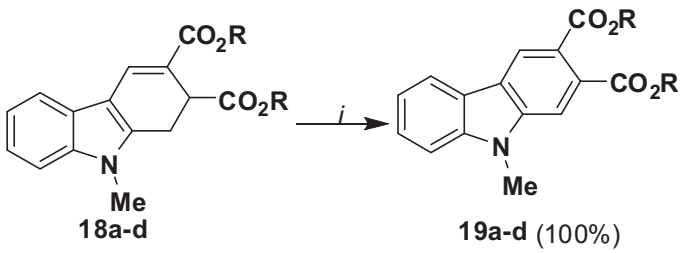


Figure 2. Ortep plot of **18d**

The structures of all products were established by spectroscopic methods. The structure of **18d** was independently confirmed by X-ray crystal structure analysis (Figure 2).

Heating of a dioxane or benzene solution of 1,2-dihydrocarbazole **18b** in the presence of DDQ resulted in the formation of carbazole **19**, albeit, in only 20% yield. Pindur reported the DDQ-mediated formation of 2,3-di(methoxycarbonyl)-*N*-phenylsulfonylcarbazole from the corresponding 1,2-dihydrocarbazole in equally low yield (18%). I found that a dramatic increase of the yield (100%) can be achieved when the reaction is carried out using Pd/C (10 mol-%) in refluxing xylene (Scheme 7).



Scheme 7. Synthesis of carbazole **19a-d**; *conditions*: *i*, Pd/C (10 mol-%), xylene, reflux, 48 h

Table 3. Synthesis of **19a-d**

18	**19**	R	% (**19**) [a]
a	**a**	Et	100
b	**b**	*n*Bu	100
c	**c**	*n*Hex	100
d	**d**	*t*Bu	100

[a] Yields of isolated products based on **18a-d**

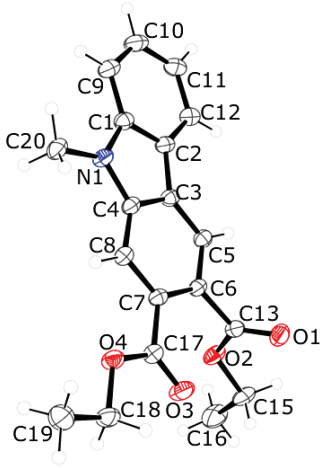
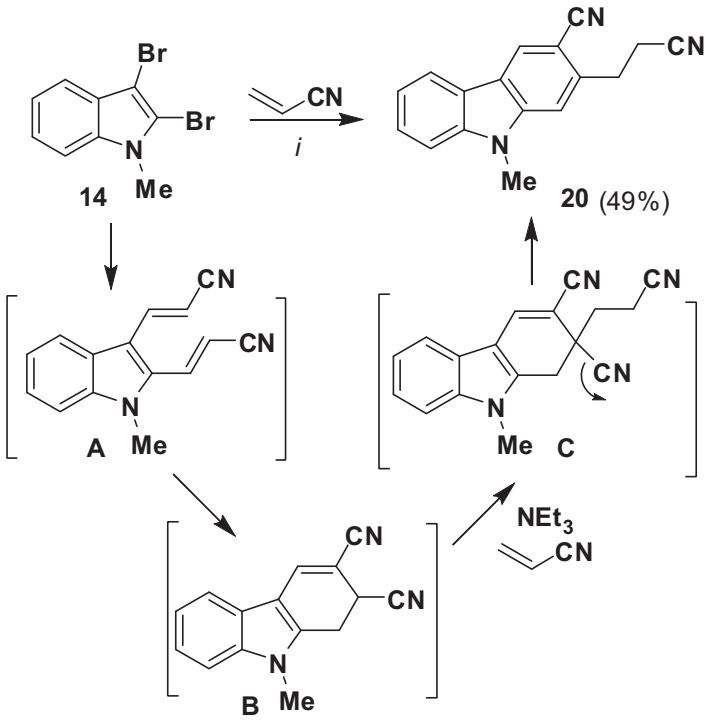


Figure 3. Crystal structure of **19a**

The $Pd(OAc)_2$/**L**-catalyzed reaction of **14** with acrylnitrile (120 °C, 48 h) afforded the unexpected carbazole **20** in 49% yield (Scheme 8). The formation of **20** can be explained by twofold Heck reaction of **14** to give intermediate **A**, electrocyclization (intermediate **B**), base-mediated conjugate addition to give intermediate **C**, and subsequent aromatization by elimination of HCN. The structure of **20** was independently confirmed by X-ray crystal structure analysis (Figure 4).



Scheme 8. Possible mechanism of the formation of **20**. Conditions: *i*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 120 ˚C, 48 h

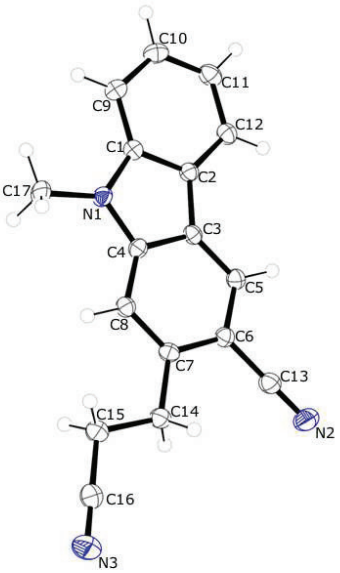
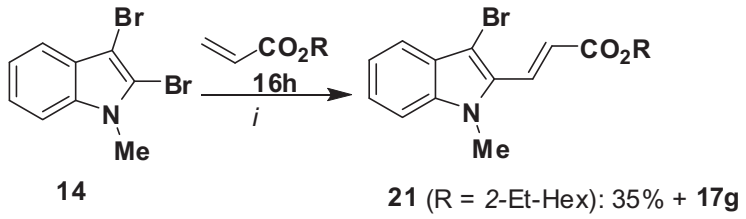


Figure 4. Crystal Structure of **20**

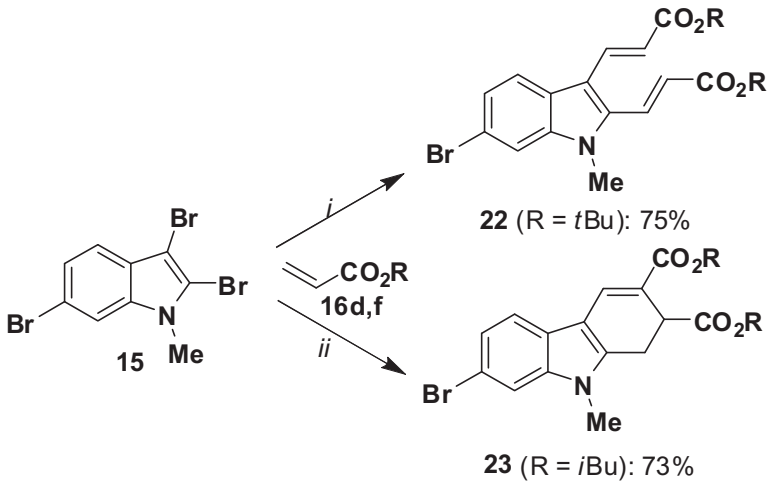
The $Pd(OAc)_2$/**L**-catalyzed reaction of 2,3,6-tribromo-*N*-methylindole **15** with acrylate **16f** (90 °C, 36 h) afforded the di(alkenyl)indole **22** in 75% yield (Scheme 10). The structure was

confirmed by 2D NMR experiments (NOESY, HMBC). The regioselective formation of **22** is worth to be noted because Ohta and coworkers reported[32] that the regioselectivity of the Suzuki reaction of 3,6-dibromo-*N*-TBDS-indole was in favour of carbon atom C-6. My result can be explained by the assumption that the first Heck reaction of **15** occurs at carbon C-2, which is most electron-deficient, to give intermediate **D** (Scheme 20). Due to the electron-withdrawing character of the 2-(*tert*-butoxycarbonyl)alkenyl substituent, carbon C-3 becomes more electron-deficient and, thus, more reactive than C-6. This might also explain the observation that the reaction of 2,3-dibromoindole (**14**) with only one equivalent of acrylate mainly resulted in the formation of 2,3-di[2-(alkoxycarbonyl)ethenyl]indole **17** and starting material, except for the case of acrylate **16h** where I isolated **21** in 35 % yield along with **17g**. Product **21** was an unstable compound and at room temperature it underwent decomposition within 24 h providing a dark brown colored material, probably due to the loss of Br (Scheme 9).

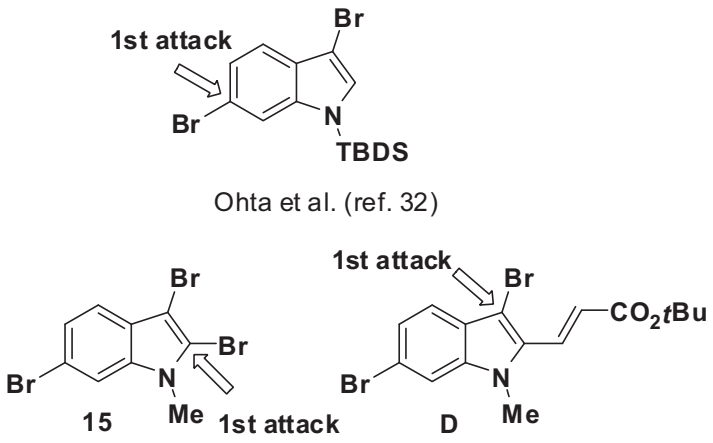


Scheme 9. Synthesis of **21**. Conditions: *i*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 90 °C, 24 h.

The $Pd(OAc)_2$/**L**-catalyzed reaction of **15** with acrylate **16d**, carried out at 120 rather than 90 °C, afforded the 1,2-dihydrocarbazole **23** in 73% yield (Scheme 10).

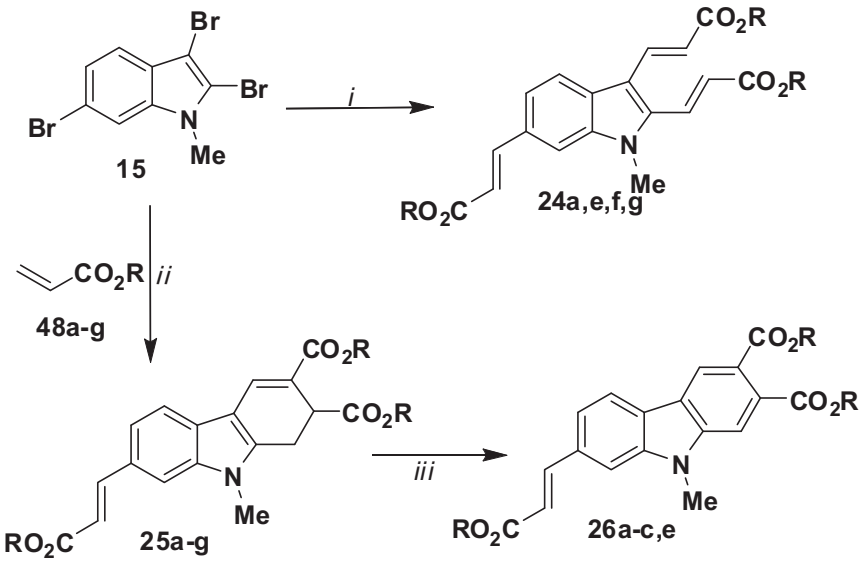


Scheme 10. Synthesis of **22** and **23**. Conditions: *i*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 90 °C, 24 h; *ii*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 120 °C, 48 h



Scheme 11. Possible explanation for the regioselective formation of **22** and **23**

The $Pd(OAc)_2$/**L**-catalyzed reaction of **15** with an excess of acrylates **16a,e,f,g** (90 °C, 36 h) afforded the 2,3,6-tris(alkenyl)indoles **24a,e,f,g** in good yields (Scheme 12, Table 4). The cross-coupling reactions of **15** with **16a-g**, carried out at 120 rather than 90 °C, gave the 7-alkenyl-1,2-dihydrocarbazoles **25a-g**.



Scheme 12. Synthesis of **24a,e,f,g**, **25a-g** and**26a-c,e** . Conditions: *i*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 90 °C, 36 h; *ii*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 120 °C, 48 h; Pd/C (10 mol-%), xylene, reflux, 48 h

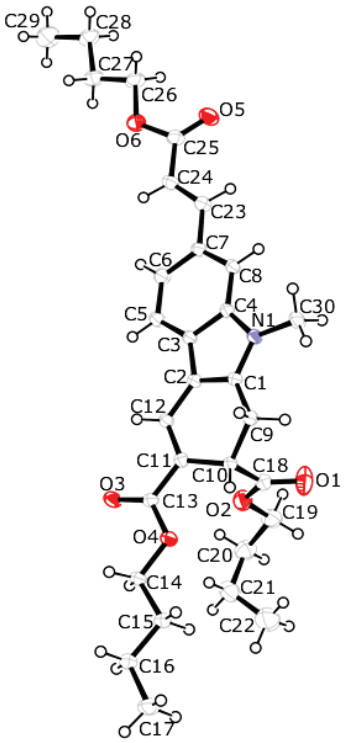


Figure 5. Crystal structure of **25e**

Table 4. Synthesis of **24a,e,f,g** , **25a-g and 26a-c,e**

24,25	R	% (**24**) [a]	% (**25**) [a]	% (**26**) [a]
a	Me	69	79	100
b	Et	- [b]	67+10[c]	100
c	*n*Bu	- [b]	95	100
d	*i*Bu	- [b]	72	- [b]
e	*n*Hex	74	74	100
f	*t*Bu	76	79	- [b]
g	*i*Oct	73	74	- [b]

[a] Yields of isolated products based on **14**; [b] experiment was not carried out; [c] **27** as a by-product in 10 %

Along with **25b**, a side product **27** was also isolated which was formed by reduction of carbon atom C-2 or C-3 (Figure 15). Oxidation of **25a-c,e** was carried out using Pd/C (10 mol-%) in refluxing xylene provided corresponding substituted carbazoles **26a-c,e** (Scheme 12).

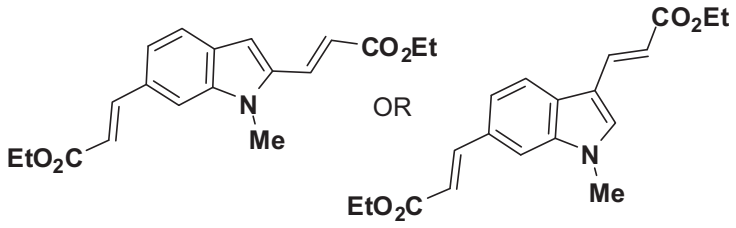
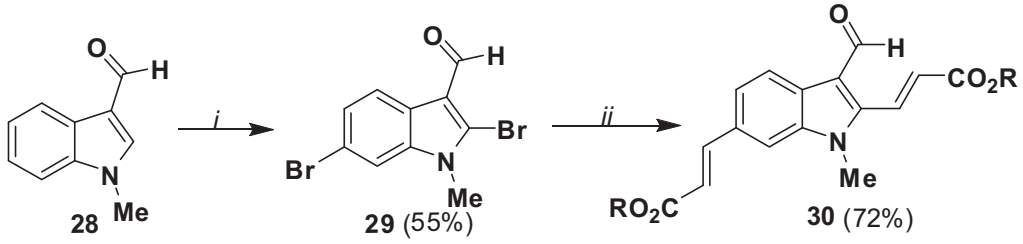


Figure 6. Possible structures of side product **27** derived from **25b**



Scheme 13. Bromination of 1-methyl-1*H*-indole-3-carbaldehyde (**28**) and subsequent twofold Heck cross coupling reaction; *conditions*: *i*, NBS (2.1 equiv.), THF, −78 °C, 8 h; *ii*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), **16c** (2.5 equiv.), NEt_3, DMF, 120 °C, 36 h

1-Methyl-1*H*-indole-3-carbaldehyde (**28**) was brominated as well to afford 2,6-dibromo-1-methyl-1*H*-indole-3-carbaldehyde (**29**). Subsequent twofold Heck cross-coupling reaction with acrylate **16c** provided dialkenylated product (2*E,2'E*)-dibutyl 3,3'-(3-formyl-1-methyl-1*H*-indole-2,6-diyl)diacrylate (**30**) in 72% yield (Scheme 13). Product **30** can be an important precursor for further related studies, e.g. Wittig reactions followed by cyclizations may provide a variety of substituted carbazoles. The corresponding Schiff bases can be prepared from aniline and their subsequent cyclization may provide a route to synthesize dihydrocarbolines.

2.3 Conclusion

In conclusion, I have discussed the synthesis of di- and tri-alkenylindoles by palladium(0)-catalyzed Heck cross-coupling reactions of di- and tri-bromo-*N*-methylindoles. The reactions were carried out at 90 °C using a novel biaryl monophosphine ligand developed by Buchwald and co-workers. 1,2-Dihydrocarbazoles were formed by a domino twofold Heck / 6π-electrocyclization when the reaction was carried out at 120 rather than 90 °C. The regioselectivity of the Heck reaction of 2,3,6-tribromo-*N*-methylindoles was in favour of carbon atoms C-2 and C-3. Some of the 1,2-dihydrocarbazoles prepared were transformed, by Pd/C-catalyzed dehydrogenation, into the corresponding carbazoles in high yield.

3 Efficient Synthesis of Functionalized Benzofurans by Domino ′Twofold Heck / 6π-Electrocyclization′ Reactions

3.1 Introduction

Natural and non-natural benzofurans and dibenzofurans are of significant pharmacological application and found in many natural products.[33] Among these, synthetic amiodarone represents a potent antiarrythmic and antianginal drug.[34] Example of dibenzofurans include simple hydroxylated derivatives (such as α- and γ-cotonefuran and γ-pyrufuran).[35] They possess bioactivities, for example, antimicrobial, antileishmanial, antiprotozoal,[36] antidiabetic,[37] cytotoxic,[38] and genotoxic activity.[39]

Presently and during near past 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.[40] Suzuki and Stille reaction for substituted dibromofurans also have been reported showing first attack at carbon C-2.[41] In my thesis, I have studied Heck reactions of 2,3-dibromofuran, and subsequent 6π-electrocyclizations to give functionalized benzofurans.[4]

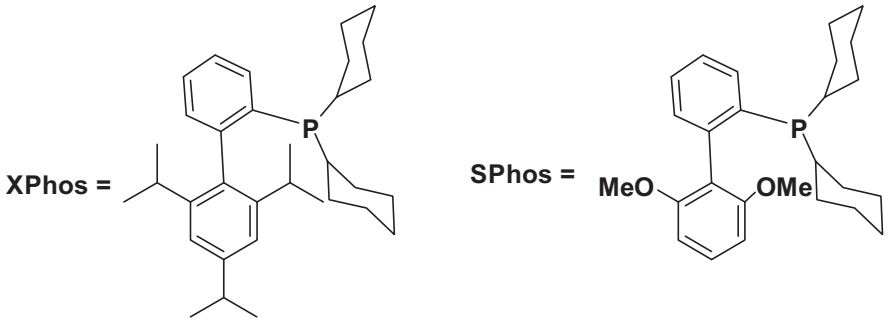


Figure 7. Biaryl monophosphine ligands developed by Buchwald and coworkers.[7]

3.2 Results and Discussion

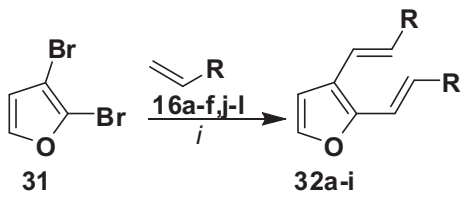
The Heck reaction of **31** with acrylates **16a-f,j-l** (2.5 equiv.) afforded the 2,3-di(alkenyl)furans **32a-i** in good yields (Scheme 14, Table 4). The best yields were obtained when the reactions were carried out using $Pd(OAc)_2$ (5 mol-%) and the biaryl monophosphine ligand XPhos or SPhos (10 mol-%) which were recently developed by Buchwald and coworkers (Figure 1, Table 5).[7] The reactions were carried out in DMF at 120 °C for 36 h. For

Heck cross-coupling with acrylates **16a,d** and styrene **16k**, XPhos was used. For the rest of the acrylates or styrenes, SPhos was used. The employment of $Pd(PPh_3)_4$ was less successful in terms of yield.

Table 5. Optimization of the reaction conditions for the synthesis of **20b,d**

Entry	Catalyst	% (**32b**) [a]	% (**17f**) [a]
1	$Pd(PPh_3)_4$ (5 mol-%)	35	41
2	$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%)	73	72
3	**$Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%)**	**78**	**79**
4	$Pd(OAc)_2$ (3 mol-%), $P(Cy)_3$ (6 mol-%)	65	59
5	$Pd(OAc)_2$ (2 mol-%), Triethanolamine[-b]	traces	traces

[a] Yields of isolated products; all reactions were carried out in DMF using NEt_3 as base (90 °C, 36h); [b] Triethanolamine was used as solvent, base and ligand

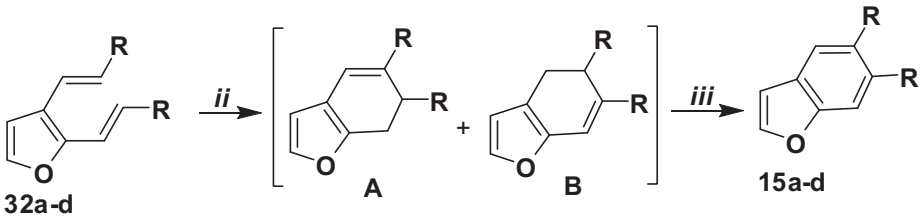


Scheme 14. Synthesis of **32a-i** and **33a-d**. Conditions: *i*, **16a-f,j-l** (2.5 equiv.), $Pd(OAc)_2$ (5 mol-%), SPhos or XPhos (10 mol-%), NEt_3, DMF, 120 °C, 36 h.

2,3-Di(alkenyl)furans **32a-d** were heated in diphenyl ether at 200 °C for 24 h. The addition of Pd/C (10 mol-%) and further heating of the reaction mixture at 200 °C for 24 h provided the benzofurans **33a-d** (Scheme 15, Table 6). Their formation again can be explained by a domino twofold Heck / thermal 6π-electrocyclization cyclization and subsequent double bond migration. In case of bis-alkenylated indoles, one type of isomerized product was observed. Conjugation was further extended with the involvement of the nitrogen lone pair which provides extra stability. In case of furans, mixtures of isomeric products were obtained. This might be explained by the fact that the +M effect of oxygen and sulfur is much less

pronounced than for nitrogen (+M effect order = -NR_2 >O>>S). Therefore, the stabilization by conjugation is less pronounced.

When **32f** was employed for electrocyclization at 200 °C, it showed decomposition and no product was obtained. Below 200 °C, no reaction was observed. This might be due to the decomposition of tertiary butyl ester at high temperature (200 °C).



Scheme 15. Synthesis of **33a-d**. Conditions: *i*, Diphenyl ether, 200 °C, 24h; *ii*, Pd/C (10 mol-%), diphenyl ether, 200 °C, 24 h.

Table 6. Synthesis of **32a-h** and **33a-d.**

32,17	16	R	% (32) [a]	% (33) [a]
a	**a**	CO_2Me	73[b]	90
b	**b**	CO_2Et	78 [c]	93
c	**d**	CO_2iBu	93 [b]	92
d	**c**	CO_2nBu	78 [c]	95
e	**e**	CO_2nHex	88 [c]	[e]
f	**f**	CO_2tBu	79 [c]	[d]
g	**j**	4-$MeOC_6H_4$	90 [c]	[e]
h	**k**	4-MeC_6H_4	89 [b]	[e]
i	**l**	4-tBuOC_6H_4	87 [c]	[e]

[a] Yields of isolated products; [b] XPhos was used; [c] SPhos was used; [d]decomposition; [e] Reaction was not carried out.

3.3 Conclusion

In conclusion, I have synthesized functionalized benzofurans, based on domino twofold Heck / 6π-electrocyclization reactions of 2,3-dibromofuran. For electrocyclization reactions, a high temperature (200 °C) was required. Aromatization proceeded satisfactorily with Pd/C in diphenyl ether.

4 Synthesis of Anthraquinones, Fluorenones and Benzocoumarins by Domino ′Twofold Heck / 6π-Electrocyclization′ Reactions

4.1 Introduction

Anthraquinones, also called anthracenediones or dioxoanthracenes, possess significant pharmacological applications and occur in various natural products.[42] Anthraquinones are essential chemical constituents of fungi, lichens, and higher plants. They represent components of numerous medicines of plant origin as they acquire a broad spectrum of biological activities including antibacterial, purgative, antiinflammatory, astringent, and antiviral properties[42b,c]. The anthracyclines comprise an important class of antitumor agents and antibiotics which include a number of well-known compounds such as daunorubicin, adriamycin, and aclarubicin.[43] Most of the naturally occurring anthracyclines are separated in *O*-glycosylated form, but some of them, such as saintopin, are found as aglycons.[44] Simple hydroxylated anthraquinones (such as chrysophanic acid, vismiaquinone, anthragallol, questin and several others) are also widely dispersed in nature.[45] Anthraquinones provide the basic structure of several natural dyes as well. Anthraquinones are also used as goose repellent.[46]

In literature, fluorenones find significant pharmacological applications and are part of many natural products. Fluorenones had been synthesized in different ways, for example, by Friedel-Crafts acylations of biaryls. Fluorenones had also been prepared based on remote aromatic metalations.[47]

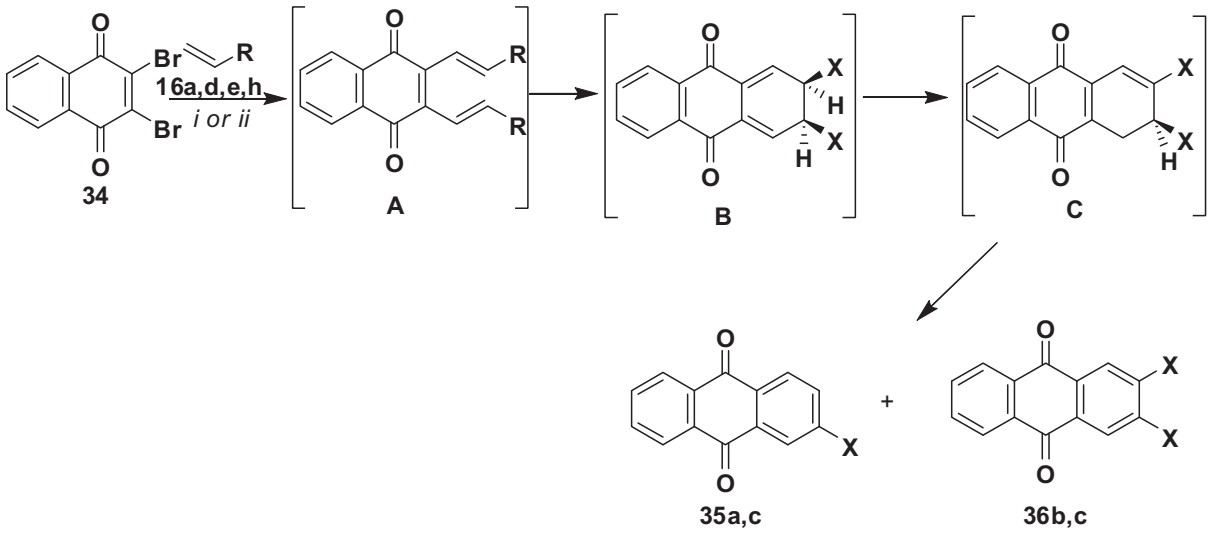
Coumarins are also an important class of organic compounds with substantial pharmacological relevance. Many polycyclic coumarin derivatives are found as potent inhibitors of tumor induction by carcinogenic polycyclic aromatic hydrocarbons. However, primarily anti-carcinogenic activity is established in naturally occurring highly oxygenated coumarins. Coumarins are also used as food and cosmetic additives, optical brightening agents, and dispersed fluorescent and laser dyes. Coumarins had been synthesized by Claisen isomerization, Perkin reaction and knovenagel benzo-annelated coumarins.[48]

In general, in this chapter twofold Heck reaction and subsequent electrocyclization and aromatization for the cross conjugated systems (2,3-dibromonaphthoquinones), α,β unsaturated cyclic ketone (2,3-dibromoindenone) and lactone (3-bromo-4-hydroxy-coumarin) results are discussed. I have studied for the first time the synthesis of functionalized anthraquinones, fluorenones and benzoquinone by domino[50] ′twofold Heck / 6π-

electrocyclization′ reactions of 2,3-di-bromonaphthoquinone, 2,3-dibromoindenone and 3-bromo-2-oxo-2*H*-chromen-4-yl trifluoromethanesulfonate.[4]

4.2 Results and discussion

The Heck reaction of 2,3-dibromonaphthoquinone (**35**) with hexyl acrylate (**16e**) (2.5 equiv.) afforded the dihexyl 9,10-dioxo-9,10-dihydroanthracene-2,3-dicarboxylate (**36b**, 75%) successfully (Scheme 16, Table 8). The formation of **36b** can be explained by twofold Heck reaction, subsequent 6π-electrocyclization and migration of the double bond to give intermediate **B**. Dehydrogenation of the latter afforded **36b**. Use of $Pd(PPh_3)_2Cl_2$ and $Pd(PCy_3)_2$ did not provide satisfactory results in term of yield. The best yields were obtained when the reactions were carried out using $Pd(OAc)_2$ (5 mol-%) and the biaryl monophosphine ligand XPhos (10 mol-%).[7] The use of $Pd(PPh_3)_4$ provided similar results as well (Table 7).



Scheme 16. Synthesis of **35a,c,d** and **36c**. *Conditions*: *i*, method 1: $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), NEt_3 (8.0 equiv.), DMF, 90 °C, 8 h; method 2: *ii*, $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), NEt_3 (8.0 equiv.), DMF, >110 °C, 8 h.

Table 7. Optimization of the reaction conditions for the synthesis of **36b**

Entry	Catalyst	Temp (°C)	% (**36b**) [a]
1	$Pd(PPh_3)_4$ (5 mol-%)	90	73
2	$Pd(PPh_3)_2Cl_2$ (5 mol-%)	90	36
3	$Pd(OAc)_2$ (5 mol-%), $P(Cy)_3$ (10 mol-%)	90	45
4	**$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%)**	**120**	**35+25**[b]
5	**$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%)**	**90**	**75**

[a] Yields of isolated products; all reactions were carried out in DMF using NEt_3 as base, 8 h; [b] Isolated as by-product **35b**

Table 8. Synthesis of **35a-c** and **36b**

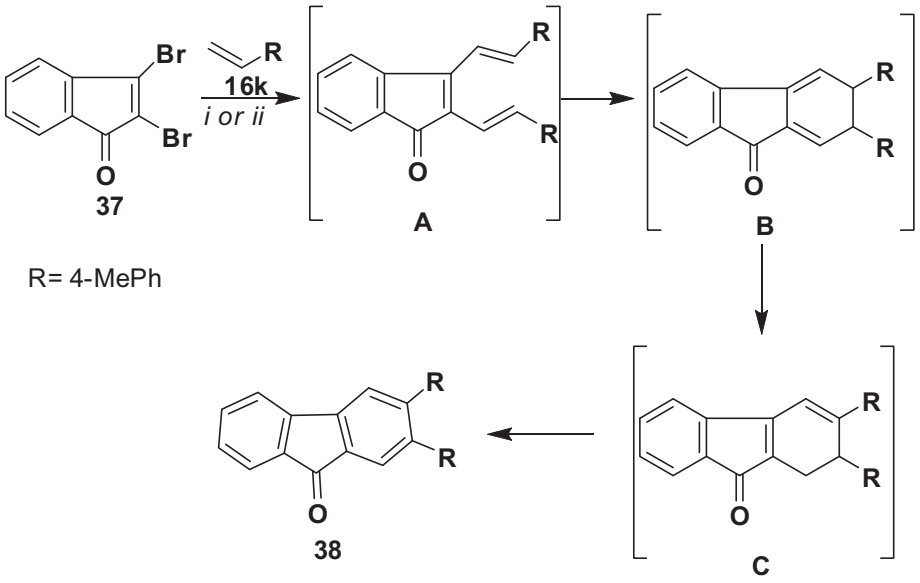
35,36	**16**	R	Method 1 % (**36**) [a]	Method 2 % (**36**)[a] + % (**35**)[a]
a	**a**	CO_2Me	- [b]	Traces + 57
b	**e**	CO_2nHex	75	35 + 25
c	**h**	CO_2(2-Ethylhexyl)	- [b]	Traces + 62

[a] Yields of isolated products; [b] experiment was not carried out

The reaction was carried out in DMF at 90 °C for 8 h (method 1). The yields considerably decreased when the temperature was increased. While a clean reaction was observed when the reaction was carried out at 90 °C, a separable mixture of **36b** (35%) and **35b** (25%) was formed at 110 °C (method 2). Decomposition was observed when the reaction was carried out at temperatures higher than 120 °C. The formation of **35b**, which contains only one ester group, can be explained by the fact that in thermal conditions disrotatory electrocyclization provides intermediate **B** with *cis* sterechemical relationship of two ester groups. At higher temperature, prior to migration of double bond an *anti*-elimination occurs and provides the monsubstituted product **35b**. Acrylates, by means of method II, provided mainly **35a** and **35b** and only traces of **36a** and **36c** were observed.

Disubstituted anthraquinones **36** were generally formed in good yields when the reaction was carried out at 90 °C, while monosubstituted anthraquinones **35** were predominantly formed at 110 °C.

Indanone was brominated by photobromination to give 2,3-dibromoindenone according to a literature protocol.[51] The Heck cross-coupling proceeded at 40 °C. I optimized the reaction conditions for different temperature and reaction conditions. The best result was obtained when PCy_3 (10-mol%) and $Pd(OAC)_2$ (5-mol%) were used as catalyst at 40 °C. 2,3-Dibromoindenone (**37**) with 4-methylstyrene **16k** provided 2,3-di(*p*-tolyl)-9*H*-fluoren-9-one **38** in one step (77 %) (scheme 16). Ligands PCy_3, $(EtO)_2PPh$, $Pd(PPh_3)_4$ and $Pd(Ph_3)_2Cl_2$ provided **38** only in low yield (15-20 %) (Table 9).



Scheme 17. Synthesis of **38**. *Conditions*: *i*: $Pd(OAc)_2$ (5 mol-%), PCy_3 (10 mol-%), NEt_3 (8.0 equiv.), DMF, 40 °C, 36 h.

Table 9. Optimization of the reaction conditions for the synthesis of **38**

Entry	Catalyst	Temp.(°C)	% (**38**) [a]
1	$Pd(PPh_3)_4$ (5 mol-%)	40	20
2	$Pd(PPh_3)_2Cl_2$ (5 mol-%)	40	18
3	$Pd(OAc)_2$ (5 mol-%), $(EtO)_2PPh$ (10 mol-%)	40	15
4	$Pd(OAc)_2$ (5 mol-%), $P(Cy)_3$ (10 mol-%)	90	Complex mixture
5	$Pd(OAc)_2$ (5 mol-%), $P(Cy)_3$ (10 mol-%)	60	35
6	**$Pd(OAc)_2$ (5 mol-%), $P(Cy)_3$ (10 mol-%)**	**40**	**60**
7	$Pd(OAc)_2$ (5 mol-%), $P(Cy)_3$ (10 mol-%)	20	*b*

[a] Yields of isolated products; all reactions were carried out in DMF using NEt_3 as base, 36 h; [b] Reaction did not go to completion after 36 h.

Unlike Heck cross-coupling of 2,3-dibromonaphthoquinone **38**, I never observed the monosubstituted fluorenone. A possible reason might be that the reaction proceeds at much lower temperature which is not sufficient for an anti-elimination. Further synthetic scope of the synthesis of functionalized fluorenones is currently being studied by my colleague Omer Akravi who has successfully prepared until now four more functionalized fluorenones using acrylates and electron donating and withdrawing styrenes.

Triflation and tosylation of 3-bromo-4-hydroxy-2*H*-chromen-2-one **40** afforded **39** and **41**, respectively, according to the literature (Figure 16).[52]

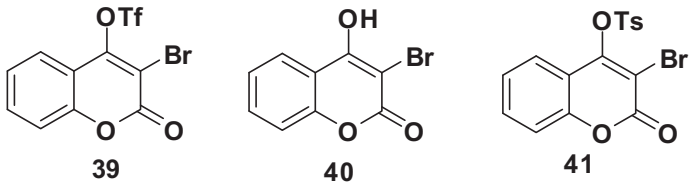
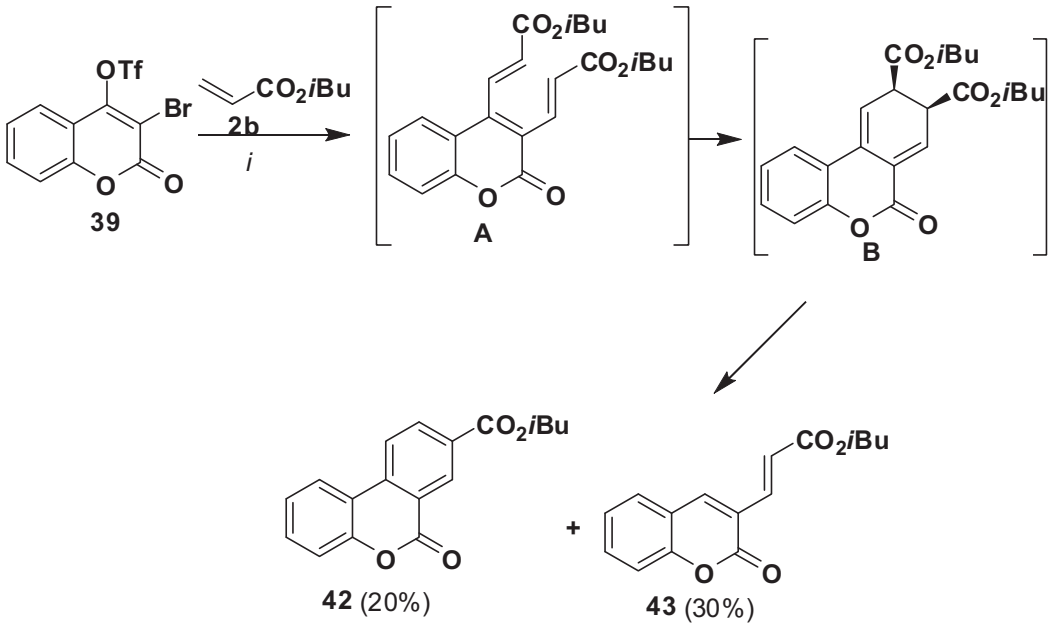


Figure 8. Coumarins **39**, **40**, **41**



Scheme 18. Synthesis of **42**. *Conditions*: *i*: $Pd(PPh_3)_4$ (5-mol%), NEt_3 (8.0 equiv.), DMF, 60 °C, 36 h.

Structure of 6-oxo-6H-benzo[c]chromene-8-carboxylate **42**was also confirmed by X-ray crystallography (Figure 9).

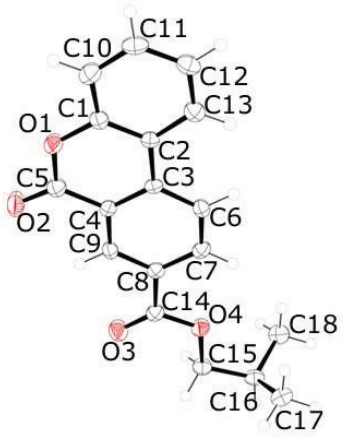
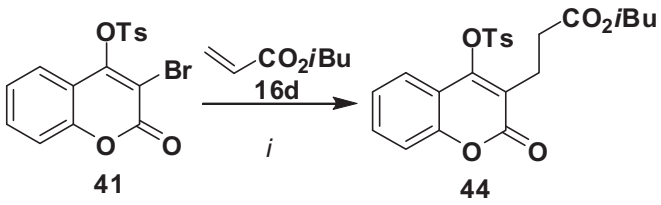


Figure 9. Crystal structure of **42**

The Heck cross-coupling of coumarin **39** provided monosubstituted isobutyl 6-oxo-6H-benzo[c]chromene-8-carboxylate **42** (20%) and by-product **43** (30%) (scheme 18). I also tried to reduce the temperature (50 °C), but always found low yield and only monosubstituted product **42**. Low yields can be explained by decomposition of the starting material, especially the reduction at carbon C-4 of triflate **39**. Then, I synthesized tosylate **41** which has been

successfully employed for Suzuki and Sonogashira cross coupling reactions before.[15] Unfortunately, tosylate **41** did not provide the required product as well, because Heck reaction did not take place at position C-4 even at increased temperature (110 °C). Reduction of the alkene at C-3 provided alkyl-substituted coumarin **44**.



Scheme 19. Synthesis of **44**. *Conditions*: *i*: $Pd(PPh_3)_4$ (5-mol%), NEt_3 (8.0 equiv.), DMF, 110 °C, 36 h.

Further studies to control the decomposition of **39** are in progress by using an additive LiCl[4] by one of my colleagues Dhafer Saber Zinad. Alternatively, 3,4-bromo-2*H*-chromen-2-one might be a more suitable starting material for twofold Heck reactions in the future.

4.3 Conclusion

In conclusion, I have synthesized and optimized the reaction conditions for the synthesis of functionalized anthraquinones by domino 'twofold Heck– 6π-electrocyclization' reactions of 2,3-dibromonaphthoquinone. The synthesis of functionalized anthraquinones works under mild conditions and the products are not readily available by other methods. The temperature performed an important role during the optimization of the reaction conditions. Furthermore, the same strategy was used successfully to synthesize functionalized fluorenones from 2,3-dibromoindenone which also worked at low temperature (40 °C) in one step. 6-Oxo-6*H*-benzo[*c*]chromene-8-carboxylate has also been prepared from 3-bromo-2-oxo-2*H*-chromen-4-yl trifluoromethanesulfonate for which further studies are still in progress by my colleagues.

5 Synthesis of Aryl-Substituted Pyrimidines by Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,4,5,6-Tetrachloropyrimidine

5.1 Introduction

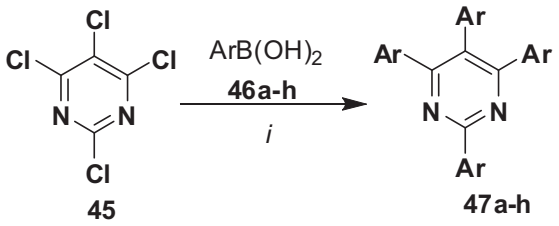
Pyrimidines thymine (T), cytocine (C) and uracil (U) are the nitrogen bases of DNA and RNA They make hydrogen bondings with their complement purines that are adenine (A) and guanine (G). In DNA, two combinations A:T and C:G are found whereas in RNA two combinations A:U and C:G are found. Pyrimidines are prevalent heterocyclic compounds found in several natural products and synthetic pharmacophores with antibacterial, antimicrobial, anticancer and antimycotic activities and occur in many synthetic drugs. Compounds derived from pyrimidine, for example 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine (HEPT) and dihydroalkoxybenzyloxopyrimidines (DABO), show significant anti-HIV-1 activity.[42a,53,54] Pyrimidines are also part of analgesic, antihypertensive, antipyretic, and anti-inflammatory drugs. Pyrimidines and their derivatives are also used as pesticides, herbicides, and plant growth regulators.[54] L-Lathyrine is one of the example to show antitumor and hypoglycemic activity.[55]

Reaction conditions and methodology discussed in this chapter provides a straightforward way to a variety of aryl-substituted pyrimidines. Generally known syntheses of substituted pyrimidines depend on the use of a building block approach or by functionalization of an existing pyrimidine nucleus. Pyrimidines are highly electron-deficient ring systems which allow nucleophilic aromatic substitutions (S_NAr) to be a general strategy for the synthesis of large number of pyrimidine derivatives from the corresponding halopyrimidines.[54i] Nevertheless in literature, Pinner provided the first synthesis of pyrimidines based on the cyclocondensation of amidines with 1,3-diketones[56] and numerous other cyclocondensations have also been discovered.[57,58] Palladium catalyzed 3-component reactions for the synthesis of amidines have been reported by Müller and coworkers.[59] A different approach to synthesize substituted pyrimidines is based on the functionalization of appropriate pyrimidine derivatives. For example, nucleophilic aromatic substitution reactions of Grignard reagents with pyrimidines have been reported.[60,61] Monohalogenated pyrimidines have been effectively used in Negishi[62] and Suzuki[63] coupling reactions. Other nucleophilic aromatic substitution reactions have been reported for 2,4,6-trichloropyrimidine.[61,64] Schomaker and Delia reported site-selective Suzuki-Miyaura reactions of 2,4,6-trichloropyrimidine.[65] 2,4,5,6-

Tetrachloropyrimidine signifies an exciting substrate because all four carbon atoms are halogenated. Nucleophilic substitution reactions of the latter are known and allow the functionalization of carbon atoms C-2, C-4 and C-6 while carbon atom C-5 remains unattacked.[66,67] In this chapter, I have discussed my research results related to Suzuki-Miyaura reactions of 2,4,5,6-tetrachloropyrimidine including optimization of reaction conditions.

5.2 Results and discussion

2,4,5,6-Tetraaryl-pyrimidines had been synthesized by cyclocondensation reactions which required several steps.[68] The Suzuki-Miyaura cross coupling reaction of commercially available 2,4,5,6-tetrachloropyrimidine (**45**) with arylboronic acids **46a-h** (4.4 equiv.) afforded the 2,4,5,6-tetraaryl-pyrimidines **47a-h** (Scheme 20, Table 10). Both for electron rich and poor arylboronic acids the products **47a-g** were isolated in good to excellent yields. The yield of **47h** was rather low and a significant amount of the 2,4,6-triaryl-5-chloropyrimidine was isolated (most probably because of steric effects). The reaction conditions were systematically optimized for derivatives **47a-d** (Table 11). The best yields were obtained when $Pd(PPh_3)_2Cl_2$ (5 mol-%) was used as the catalyst (dioxane, 100 °C, 8 h) (entry 1). Excellent yields were obtained when an aqueous solution of K_2CO_3 (2 M) (entry 1) or when K_3PO_4 were employed as the base (entry 5). The amount of catalyst could be reduced to 2.5 mol-% without decrease in yield (entry 4). However, complex product mixtures were formed when the amount of the catalyst was reduced further (entries 2 and 3). The yields dropped when $Pd(PPh_3)_4$ or $Pd(OAc)_2$ (5 mol-%) in the presence of XPhos or SPhos[7] were employed (entries 8-10). The use of $Pd(OAc)_2$ (5 mol-%) in the presence of $P(t\text{Bu})_3 \cdot HBF_4$ (entry 11) or of $Pd(OAc)_2$ (5 mol-%) in the presence of triethanolamine and 2M K_2CO_3 (entry 12) gave unacceptable results. The employment of $Pd(OAc)_2$ (5 mol-%), $P(n\text{Bu})_3$ gave good yields for **47b** and **47d** (entry 13) but lower than use of $Pd(PPh_3)_2Cl_2$. The amount of $Pd(OAc)_2$ could be reduced to 2.5 mol-% when $P(OEt)_2Ph$ was used as the ligand (entry 14). In conclusion, the conditions given in entries 4 and 14 of Table 11 allowed to prepare the products in excellent yield using only 2.5 mol-% of the palladium catalyst.



Scheme 20. Synthesis of **47a-h**. *Conditions: i*, **46a-h** (4.4 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 100 °C, 8 h; for **47a-g**: 79-98% yields

Table 10. Synthesis of **47a-h**

46,47	Ar	% (**47**) [a]
a	Ph	98
b	4-MeC_6H_4	95
c	4-EtC_6H_4	93[c]
d	4-$(MeO)C_6H_4$	91
e	4-FC_6H_4	89
f	3-$(MeO)C_6H_4$	82
g	3,5-$Me_2C_6H_3$	79
h	3-PhC_6H_4	25+43[b]

[a] Yields of isolated products; [b] besides **47h**, 2,4,6-triaryl-5-chloropyrimidine **48d** was isolated in 43% yield; [c] reduced product 2,4,5-tris(4-ethylphenyl)pyrimidine **69** was isolated as by-product.

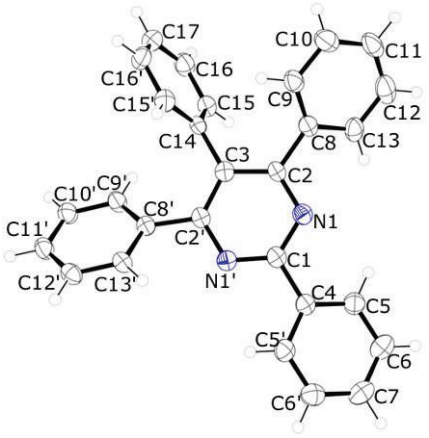


Figure 10. Crystal structure of **47a**

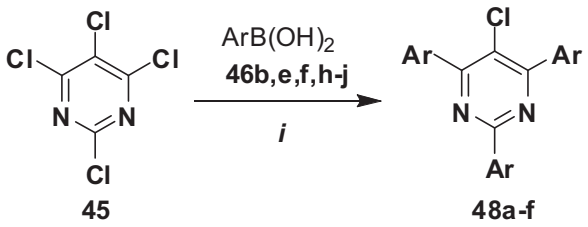
Table 11. Optimization of the reaction conditions for the synthesis of **47a-d**

Entry	Conditions	% (**47a**) [a]	% (**47b**) [a]	% (**47c**) [a]	% (**47d**) [a]
1	$Pd(PPh_3)_2Cl_2$ (5 mol-%), 2M K_2CO_3	98	95	93	91
2	$Pd(PPh_3)_2Cl_2$ (1 mol-%), 2M K_2CO_3	*-b*	*-b*	*-b*	*-b*
3	$Pd(PPh_3)_2Cl_2$ (2 mol-%), 2M K_2CO_3	*-c*	*-c*	*-c*	*-c*
4	**$Pd(PPh_3)_2Cl_2$ (2.5 mol-%), 2M K_2CO_3**	**97**	**94**	**94**	**91**
5	$Pd(PPh_3)_2Cl_2$ (5 mol-%), K_3PO_4	95	94	93	89
6	$Pd(PPh_3)_4$ (5 mol-%), aq. K_2CO_3 (2 M)	81	80	83	77
7	$Pd(PPh_3)_4$ (5 mol-%), K_3PO_4	83	80	82	75
8	$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%), 2M K_2CO_3	71	69	59	58
9	$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%), K_3PO_4	71	65	55	59
10	$Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), 2M K_2CO_3	48	43	33	50
11	$Pd(OAc)_2$ (5 mol-%), P(*t*Bu)$_3$·HBF_4 (10 mol-%), K_3PO_4	*-e*	38	*-e*	32
12	$Pd(OAc)_2$(5 mol-%), triethanolamine, 2M K_2CO_3	*-e*	*-d*	*-e*	*-d*
13	$Pd(OAc)_2$ (5 mol-%), P(*n*Bu)$_3$ (10 mol-%), 2M K_2CO_3	*-e*	70	*-e*	87
14	**$Pd(OAc)_2$ (2.5 mol-%), $P(OEt)_2Ph$ (5 mol-%), 2M K_2CO_3**	**93**	**92**	**90**	**96**

[a] Yields of isolated products; all reactions were carried out in dioxane (100 °C, 8 h); [b] formation of a complex mixture of mono-, di-, tri-, and tetraaryl-pyrimidines and of starting material; [c] approximately 80% conversion after 12 h (estimated by tlc); [d] decomposition; [e] experiment was not carried out

The Suzuki-Miyaura reaction of **45** with arylboronic acids **46b,e,f,h** (3.0 equiv.) gave the 2,4,6-triaryl-5-chloropyrimidines **48a-d** (Scheme 21, Table 12). Good yields were obtained both for electron rich and poor arylboronic acids. During the optimization, it proved to be important to use exactly 3.0 equiv. of the boronic acid and to carry out the reaction at 80 °C (5 h) instead of 100 °C (8 h) to avoid the formation of tetraaryl-pyrimidines. To a small extent, reduction of the unreacted chloride group and formation of tetraaryl-pyrimidines were

observed as side reactions. All products were prepared using $Pd(PPh_3)_2Cl_2$. Initially, 5.0 mol-% of the catalyst was used (**48b-d**). Later, we have found that the use of 2.0 mol-% of catalyst is sufficient to achieve equally good yields (products **48a,e,f**).



Scheme 21. Synthesis of **48a-d**. *Conditions: i*, **46b,e,f,h** (3.0 equiv.), $Pd(PPh_3)_2Cl_2$ (2.0 to 5.0 mol %), K_2CO_3 (H_2O, 2 M), dioxane, 80 °C, 5 h; 80-85% yields

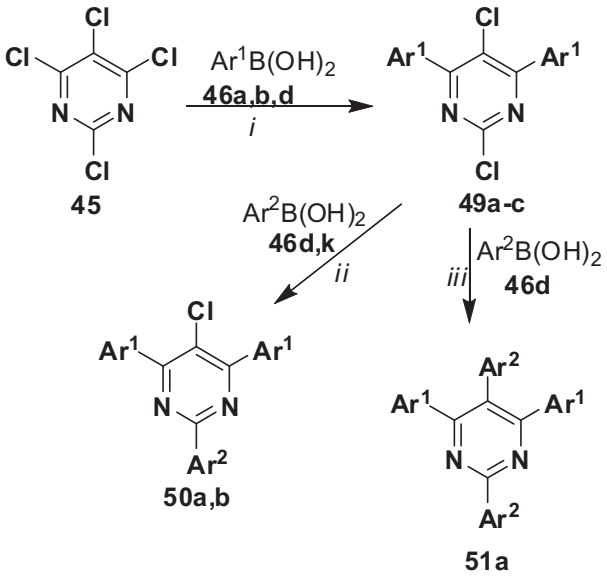
Table 12. Synthesis of 2,4,6-triaryl-5-chloropyrimidine **48a-d**

46	**48**	Ar	% (**48**) [a]
b	**a**	4-MeC_6H_4	83 [b]
e	**b**	4-FC_6H_4	83 [c]
f	**c**	2-$(MeO)C_6H_4$	81 [c]
h	**d**	3-PhC_6H_4	80 [c]
i	**e**	3-$CF_3C_6H_4$	82 [b]
j	**f**	4-$CF_3C_6H_4$	85 [b]

[a] Yields of isolated products; [b] 2.0 mol-% of catalyst was used; [c] 5.0 mol-% of catalyst was used

The Suzuki-Miyaura reaction of **45** with arylboronic acids **46a,b,d** (2.0 equiv.) afforded the 4,6-diaryl-2,5-dichloropyrimidines **49a-c** (Scheme 22, Table 13). The stoichiometry (employment of exactly 2.0 equiv. of the arylboronic acid), the temperature (not more than 70 °C), and the reaction time (5 h) again found an important role to avoid multiple-coupling reactions. Products **49a-c** were prepared using 3 mol-% of $Pd(PPh_3)_2Cl_2$. The reaction of **49a** with arylboronic acids **46d,k** (1.0 equiv.) (80 °C, 5 h) gave the 2,4,6-triaryl-5-chloropyrimidines **50a,b** (Scheme 22, Table 14). The reaction of **49a** with 2.0 instead of 1.0 equiv. of arylboronic acid **46d** (100 °C, 5 h) afforded the 2,4,5,6-tetraarylpyrimidines **51a**.

Reduction of the unreacted chloride group and multiple coupling were again observed as side reactions, albeit, to a small extent.



Scheme 22. Synthesis of **49a-c**, **50a,b** and **51a**. *Conditions: i*, **46a,b,d** (2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (1.25 to 3.0 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 70 °C, 5 h; *ii*, **46d** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (3 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 80 °C, 5 h; *iii*, **46d** (2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (1.25 to 3 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 100 °C, 5 h; for **49a-c**, **50a,b**, and **51a,**: 79-97% yields

Table 13. Synthesis of 2,4,6-diyl-5-chloropyrimidine **49a-c**

46	**49**	Ar^1	% (**49**) [a]
a	**a**	Ph	97 [b]
b	**b**	4-MeC_6H_4	85 [b]
d	**c**	4-(MeO)C_6H_4	93 [b]

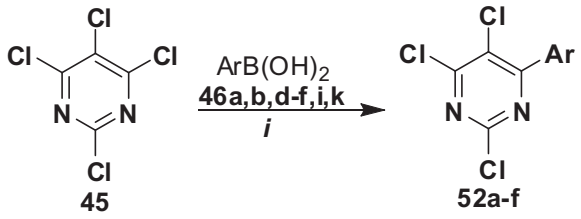
[a] Yields of isolated products; [b] 3.0 mol-% of catalyst was used.

Table 14. Synthesis of **50a,b** and **51a**

46	**49**	**50**	**51**	Ar^1	Ar^2	% (**50,51**)[a]
k	**a**	**a**	-	4-Me-C_6H_4	3-ClC_6H_4	90 [b]
d	**a**	**b**	-	Ph	4-(MeO)C_6H_4	86 [b]
d	**a**	**-**	**a**	Ph	4-(MeO)C_6H_4	79 [b]

[a] Yields of isolated products; [b] 3.0 mol-% of catalyst was used.

The Suzuki-Miyaura reaction of **45** with arylboronic acids **46a,b,d-f,i,k** (1.0 equiv.) gave the 6-aryl-2,4,5-trichloropyrimidines **52a-f** (Scheme 23, Table 15). The stoichiometry (employment of not more than 1.0 equiv. of the arylboronic acid), the temperature, and the reaction time again performed an important role during the optimization. It proved to be important to carry out the reaction at 60 °C for only 2 h to avoid multiple-coupling reactions. All products were again prepared using $Pd(PPh_3)_2Cl_2$ as the catalyst. Although 3.0 mol-% of the catalyst was used in most cases (products **52b-d,f**), the employment of only 1.0 mol-% of catalyst proved to be possible to achieve equally good yields (product **52b-d,f**).



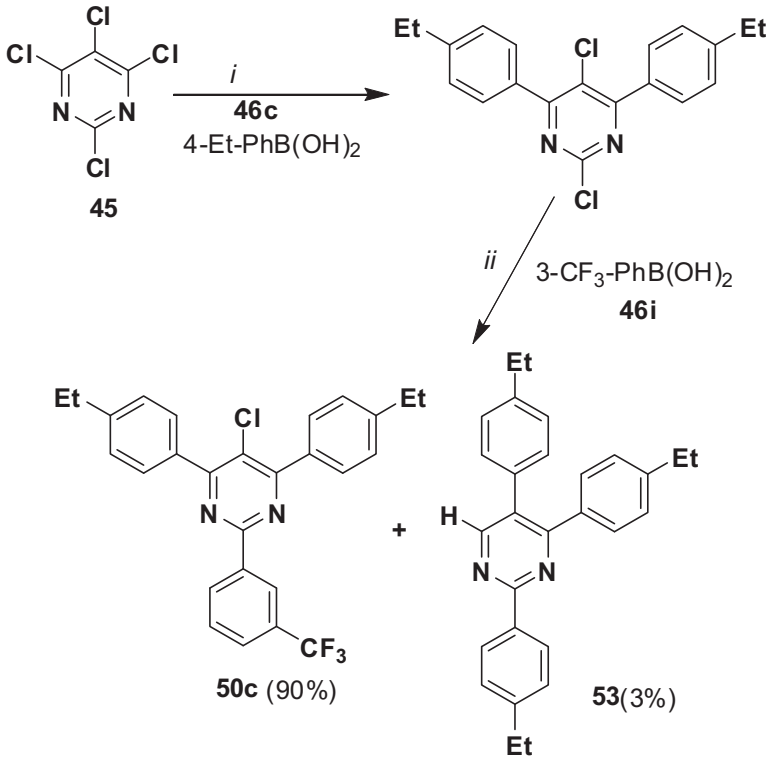
Scheme 23. Synthesis of **52a-f**. *Conditions: i*, **46a,b,d-f,I,k** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (1.0 to 3.0 mol- %), K_2CO_3 (H_2O, 2 M), dioxane, 60 °C, 2 h; 87-97% yields

Table 15. Synthesis of 6-aryl-2,4,5-trichloropyrimidines **52a-f**

46	**52**	Ar	% (**52**) [a]
b	**a**	4-MeC_6H_4	87 [b]
d	**b**	4-$(MeO)C_6H_4$	95 [c]
e	**c**	4-FC_6H_4	93 [c]
f	**d**	2-$(MeO)C_6H_4$	97 [c]
i	**e**	3-$CF_3C_6H_4$	91[b]
k	**f**	4-ClC_6H_4	88 [c]

[a] Yields of isolated products; [b] 1.0 mol-% of catalyst was used; [c] 3.0 mol-% of catalyst was used

One-pot Suzuki-Miyaura reactions to achieve unsymmetrical triarylpyrimidines **50** were also studied. To afford 4,6-diaryl-2,5-dichloropyrimidines (Scheme 24), the Pd-catalyzed reaction of **45** with arylboronic acid **46c** (2.0 equiv.) was performed at 70 °C. After 5 h heating, arylboronic acid **46i** (1.0 equiv.) was added in the same reaction and heated at 80 °C for further 5 h to give the unsymmetrical 5-chloro-4,6-bis(4-ethylphenyl)-2-(3-(trifluoromethyl)phenyl)pyrimidine **50c** (overall yield 92% based on **45**). Reduction of the unreacted chloride group and multiple coupling were again observed as side reactions, albeit, to a small extent. The reduced product **53** was isolated in 3% yield.



Scheme 24. Synthesis of **50c**. *Conditions: i*, **46c** (2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (1.25), K_2CO_3 (H_2O, 2 M), dioxane, 70 °C, 5 h; *ii*, **46i** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (1 mol-%), 80 °C, 5 h.

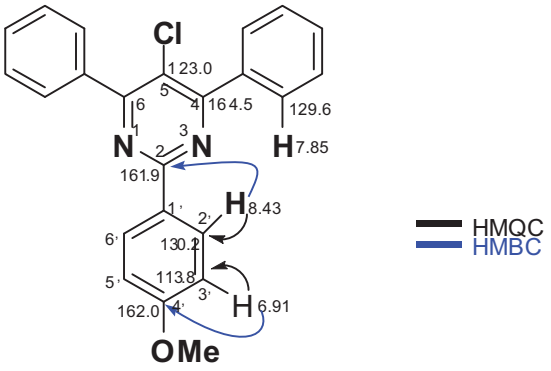


Figure 11. 2D NMR correlations (HMQCand HMBC) of **50b**

The structure of **50b** was confirmed by 2D NMR correlations using HMQC and HMBC. A clear correlation was found between the phenyl protons H-2`/6` at δ 8.43 (d, J = 8.8 Hz) with carbon C-2 resonating at 161.9 ppm. This information established unambiguously that the 4-$(MeO)C_6H_4$ moiety is attached at C-2. (Figure 19).

5.3 Conclusion

In conclusion, I have optimized the reaction conditions to achieve a convenient synthesis of symmetrical and unsymmetrical mono-, di-, tri- and tetraaryl-pyrimidines by Suzuki-Miyaura reactions of 2,4,5,6-tetrachloropyrimidine. $Pd(PPh_3)_2Cl_2$ (2.5 mol-%) and $Pd(OAc)_2$ (2.5 mol-%), using the ligand $P(OEt)_2Ph$ (5 mol-%), were the best catalyst systems observed for these reactions. Products prepared and discussed in this chapter are not readily accessible by other methods. All reactions proceed with excellent site-selectivity. The selectivity mainly depends on the temperature which has been optimized for each type of product. Catalyst loading could be reduced to 3-mol% to synthesize tetraaryl-pyrimidines **47** without affecting yields.

6 Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,3,4,5-Tetrabromofuran

6.1 Introduction

Substituted furans correspond to one of the most important classes of five-membered heterocycles and find great significance in pharmaceuticals and drugs and are widely found in natural and non-natural products.[69] These are prominent substructures in numerous natural products, for example the cembranolides lophotoxin, kallolides, and pukalide.[70,71] Substituted furans form an omnipresent structural entity in different classes of biologically active motifs and are found in commercially important pharmaceuticals, flavor and fragrance compounds (insectlo and fish antifeedants), in addition to anti-leukemic agents.[69c,72] Many furan natural products exhibit exciting biological activities, for instance, cytotoxic, antitumor, antispasmodic, and antifeeding activities. Substituted furans are key synthetic intermediates towards the synthesis of a large number of cyclic and acyclic molecules and serve as versatile building blocks in synthetic organic chemistry.[72] In addition, polysubstituted furans are significant precursors for the synthesis of natural and nonnatural products. The synthetic work to achieve polysubstituted furans thus fits into an extremely active research doma.[73-76]

Classically, direct functionalization of existing furans or cyclization of acyclic substrates provides substituted furans. An attractive approach to furans is based on transition-metal-catalyzed cycloisomerization of unsaturated acyclic precursors. This requires rather advanced starting materials, for example, allenyl ketones, alkynyl ketones, or epoxides. Recently, a synthesis of tetrasubstituted furans from alkynes via palladium catalyzed oxidation and Lewis acid catalyzed cyclization has been reported, but the selective substitution depends on the type of alkyne used.[72,77] Recently, Masaya Nakano and co-workers have reported the synthesis of tetrasubstituted furans from 3-furancarboxylic acids by cleavage of the three C−H bonds and subsequent decarboxylation upon treatment with an excess of aryl bromides in the presence of a palladium catalyst.[77a] But this approach has major draw back of lack of regioselectivity. The tendency of furans to undergo lithiation and reactions at C-2 or C-5 makes the synthesis of 3,4-disubstituted furans a rather demanding task. Although many strategies are existing, they are generally not appropriate for complex furans containing a variety of substituents.[76]

6.2 Results and discussion

The low stability of furans in particular under aerobic and acidic conditions makes cross-coupling reactions more fragile and the product isolation more difficult than in the thiophene series. 2,3-Dibromofuran and substituted dibromofurans have been used in Pd(0) catalyzed (Negishi, Stille, Suzuki and Sonogashira coupling reactions) and other nucleophilic aromatic substitution reactions.[78,79] T. Bach and L. Krüger have reported site-selective Suzuki-Miyaura reactions and showed the selectivity in favour of C-2.[80] 2,3,4,5-Tetrabromofuran signifies an exciting substrate because all four carbon atoms are halogenated. In this chapter, I have discussed my research work related to Suzuki-Miyaura reactions and the optimization of the reaction conditions for arylation of 2,3,4,5-tetrabromofuran. Reaction conditions and methodology discussed in this chapter provided a straightforward way to a variety of aryl-substituted furans which other methods do not provide readily. To my best knowledge, neither Suzuki-Miyaura reactions, nor any other Pd(0)-catalysed reactions of 2,3,4,5-tetrabromofuran have been reported before.

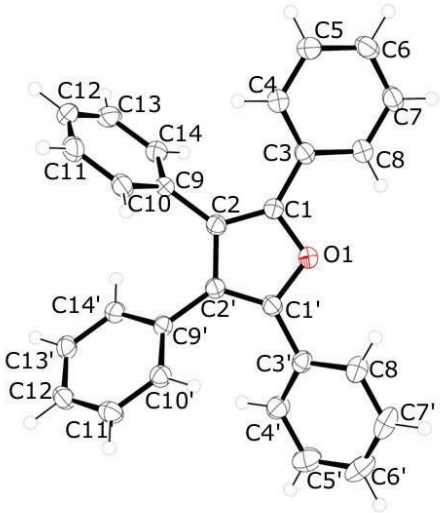
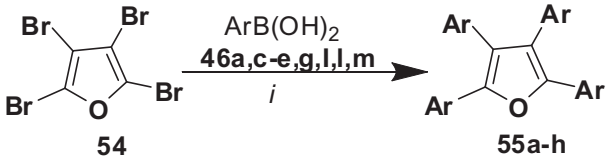


Figure 12. Crystal structure of **55a**



Scheme 25. Synthesis of 55**a-h**. *Conditions: i*, **46a,c-e,g,i,l,m** (4.4 equiv.), $Pd(PPh_3)_4$ (3 mol %), aq. K_2CO_3 (2 M), dioxane, 80 °C, 5 h

Table 16. Optimization of the reaction conditions for the synthesis of tetra-arylfurans.

entry	Conditions	%(**55b**) [a]	% (**55e**) [a]	% (**55g**) [a]
1	$Pd(PPh_3)_2Cl_2$ (3 mol-%), aq. K_2CO_3 (2 M)	90	82	96
2	$Pd(PPh_3)_2Cl_2$ (3 mol-%), K_3PO_4	85	75	88
3	**$Pd(PPh_3)_4$ (3 mol-%), aq. K_2CO_3 (2 M)**	**92**	**85**	**98**
4	$Pd(PPh_3)_4$ (3 mol-%), K_3PO_4	88	78	92
5	$Pd(OAc)_2$ (3 mol-%), XPhos (6 mol-%), aq. K_2CO_3 (2M)	10	05	15
6	$Pd(OAc)_2$ (3 mol-%), $(Cy)_3P$ (6 mol-%), aq. K_2CO_3 (2M)	65	45	69
7	$Pd(OAc)_2$ (3 mol-%), $(Cy)_3P$ (6 mol-%), K_3PO_4	50	43	55

[a] Yields of isolated products; all reactions were carried out in dioxane (80 °C, 5 h)

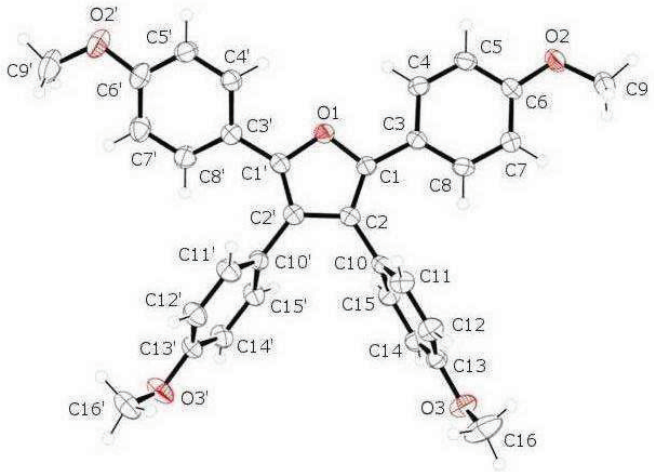


Figure 13. Crystal structure of **55g**

Table 17. Synthesis of tetraarylfurans **55a-h**

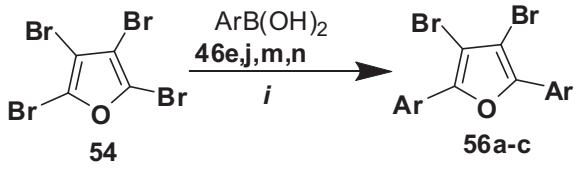
55	**46**	Ar	*%* (**55**) [a]
a	**a**	C_6H_5	92
b	**c**	4-EtC_6H_4	92
c	**l**	4-*t*BuC_6H_4	92
d	**m**	3-ClC_6H_4	80
e	**e**	4-F C_6H_4	85
f	**i**	3-(CF_3)C_6H_4	82
g	**d**	4-(MeO)C_6H_4	98
h	**g**	3,5-$Me_2C_6H_3$	76

[a] Yields of isolated products

2,3,4,5-Tetrabromofuran (TBF) (**54**) is not a commercially available substrate and was prepared according to a literature procedure.[12] The reaction of TBF (**54**) with arylboronic acids **46a,c-e,g,i,l,m** (4.4 equiv.) afforded the stable products of 2,3,4,5-tetraaryl-furans **55a-h** (Scheme 25, Table 17). Both for electron rich and poor arylboronic acids, the products **55a-h** were synthesized in good to excellent yields. The reaction conditions were systematically optimized for the derivatives **55b,e,g** using electron donating and withdrawing boronic acids **2b,e,g** (Table 173). The best yields were obtained when $Pd(PPh_3)_4$ (3 mol-%) was used as the catalyst (dioxane, 80 °C, 5 h) (entry 1, Table 16). Excellent yields were obtained when an aqueous solution of K_2CO_3 (2 M) (entry 3, Table 16) or K_3PO_4 were employed as the base (entry 2, Table 12).

The best yields were obtained when $Pd(PPh_3)_4$ (3 mol-%) was used as the catalyst (dioxane, 80 °C, 5 h) (entry 1, Table 16). Excellent yields were obtained when an aqueous solution of K_2CO_3 (2 M) (entry 3, Table 16) or when K_3PO_4 were employed as the base (entry 2, Table 16). The yields dropped when $Pd(PPh_3)_2Cl_2$ or $Pd(OAc)_2$ (3 mol-%) in the presence of XPhos or $(Cy)_3P$ were employed (entries 1,2 and 5-7, Table 12). The employment of $Pd(PPh_3)_2Cl_2$ (3 mol-%) and $Pd(OAc)_2$ (3 mol-%), $(Cy)_3P$ (6 mol-%) gave fair to very good yields (entries 1,2,6,7, Table 16), albeit lower than for $Pd(PPh_3)_4$. The use of K_3PO_4 as the base resulted in lower yields compared to the use of a 2M aqueous solution of K_2CO_3. In conclusion, the application of the reaction conditions given in entry 3 of Table 16 allowed to prepare the products in excellent yields. It was also noted that electron-poor arylboronic acids provided

slightly lower yields than electron-rich arylboronic acids. This can be explained by the lower nucleophilicity of electron-poor boronic acids.



Scheme 26. Synthesis of **56a-c**. *Conditions: i*, **46e,j,m,n** (2.0 equiv.), $Pd(PPh_3)_4$ (2 mol %), aq. K_2CO_3 (2 M), toluene/dioxane (4:1), 80 °C, 3 h

Table 18. Reaction condition optimization for **s**ynthesis of 2,5-diaryl-3,4-dibromofurans

Entry	solvent	base	ligand	[a]Temp.	Time	**56a**	**56c**
1	dioxane	2M K_2CO_3	$(PPh_3)_4Pd$	60 °C	3h	mixture	mixture
2	dioxane	2M K_2CO_3	Cy_3P, $Pd(OAc)_2$	60 °C	3h	mixture	mixture
3	dioxane	2M K_2CO_3	XPhos, $Pd(OAc)_2$	60 °C	8h	traces	traces
4	dioxane	2M K_2CO_3	$(PPh_3)_2PdCl_2$	60 °C	3h	mixture	mixture
5	dioxane	3 eq. Cs_2CO_3	$(PPh_3)_4Pd$	60 °C	3h	mixture	mixture
6	dioxane	3 eq. K_3PO_4	$(PPh_3)_4Pd$	60 °C	3h	mixture	mixture
7	dioxane	3 eq. K_3PO_4	Cy_3P, $Pd(OAc)_2$	60 °C	3h	mixture	mixture
8	toluene	2M K_2CO_3	$(PPh_3)_4Pd$	80 °C	3h	No reaction	No reaction
9	toluene	2M K_2CO_3	$(PPh_3)_4Pd$	80 °C	6h	No reaction	No reaction
10	toluene	2M K_2CO_3	$(PPh_3)_4Pd$	80 °C	8h	No reaction	No reaction
11	THF	2M K_2CO_3	$(PPh_3)_4Pd$	60 °C	3h	mixture	mixture
12	DME	2M K_2CO_3	$(PPh_3)_4Pd$	80 °C	3h	No reaction	No reaction
13	DME	2M K_2CO_3	$(PPh_3)_4Pd$	80 °C	8h	traces	traces
14	dioxane/toluene (4:1)	2M K_2CO_3	$(PPh_3)_4Pd$	80 °C	3h	mixture	mixture
15	dioxane/toluene (3:2)	2M K_2CO_3	$(PPh_3)_4Pd$	60 °C	8h	mixture	di major
16	dioxane/toluene (1:1)	2M K_2CO_3	$(PPh_3)_4Pd$	80 °C	3h	mixture	di major
17	**dioxane/toluene (1:4)**	**2M K_2CO_3**	**$(PPh_3)_4Pd$**	**[a]80 °C**	**3h**	**87%**	**91%**
18	dioxane/toluene (1:4)	2M K_2CO_3	$(PPh_3)_4Pd$	[a]110 °C	3h	Only di	Only di

[a] Same set of reaction conditions provided the excellent regioselectivity for synthesis of monoaryl tribromofurans ,
[-b] reaction was not carried out.

Table 19. Synthesis of 2,5-biaryl-4,5-dibromofurans **56a-c**

46	**56**	Ar	*%* (**56**) [a]
m	**a**	3-ClC_6H_4	87
e	**b**	4-FC_6H_4	88
j	**c**	3-$(CF_3)C_6H_4$	91
n	**f**	2-Naph	-[b]

[a] Yields of isolated products , [–b] decomposition was observed

The Suzuki-Miyaura reaction of **54** with arylboronic acids **46ej,m** (2.0 equiv.), in the presence of $Pd(PPh_3)_4$, gave the 2,5-diaryl-3,4-dibromofurans **56a-c** (Scheme 26, Table 19). During the synthesis of inhibitors of B-Raf kinase, Andrew and co-workers studied site-selective Suzuki-Miyaura reactions of 2,3-dibromofuran. These reactions, which were carried out in a DME/H_2O/K_2CO_3 system, proceeded in rather low yields.[77a] The application of these conditions to Suzuki reactions of **54** proved to be unsuccessful. Therefore we decided to optimize the reaction conditions methodically for different solvent systems, reaction times and catalyst systems. Arylboronic acids **46j,m,n** were selected for the optimization studies based on their electron-withdrawing nature and steric effects. During the optimization, I found that the temperature did not have an important influence on the yield of **56** and on the regioselectivity provided that exactly 2.0 equiv. of the boronic acids were used.

Using dioxane as the solvent, $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$ and $Pd(OAc)_2$, in the presence of Cy_3P or XPhos, were studied as the catalysts in the reactions of **54** with boronic acids **46j,m,n**. All these reactions resulted in the formation of complex mixtures of mono-, di-, tri- and tetraarylfurans (entries 1-7, Table 18). In case of **46n**, a reduced product by loss of a bromine atom was formed. The use of different bases (2M aqueous solution of K_2CO_3 or the use of K_3PO_4 or Cs_2CO_3 in organic solvents) and a decrease of the reaction temperature did not allow to solve the problems related to the site-selectivity (entries 1-7, Table 18). The reaction suffered from low conversions when the solvents toluene and DME were used. The employment of THF as the solvent, using $Pd(PPh_3)_4$ and 2M K_2CO_3, resulted in the formation of complex mixtures for different reaction times (3-8 h) and temperatures (60-80 °C) (entries 8-13). While the use of a single solvent was unsuccessful for the regioselective synthesis of 2,5-diaryl-3,4-dibromofurans **56a-c**, the use of solvent mixtures allowed to address the problem. I selected dioxane/toluene as a solvent system to control the solubility of the boronic

acids. $Pd(PPh_3)_4$ and 2M K_2CO_3 were again used as the catalyst and base, respectively. While the use of a 4:1 dioxane/toluene mixture again provided mixtures of products, the use of a 3:2 and 1:1 dioxane/toluene mixture showed better results for boronic acids **46j**. In fact, the desired products **56** were formed as the major products among a complex mixture of other products (entries 14-16, Table 18)**.** Gratifyingly, the employment of a 1:4 dioxane/toluene mixture afforded exclusively 2,5-biaryl-3,4-dibromofurans **56a-c** which could be isolated in excellent yields (85-91%) (entry 17, Table 18). It is worth to note that the use of a 1:4 dioxane/toluene mixture of solvents allowed to obtain excellent site-selectivities even when the reactions were carried out at reflux (110 °C) (entry 18, Table 18).

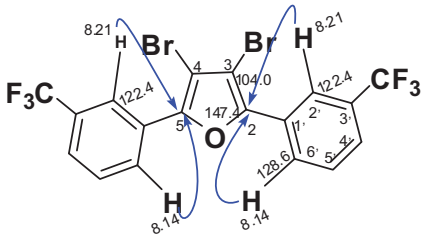


Figure 14: HMBC Correlations of **56c**

The structure of **56c** was established by 2D NMR using HMBC correlations. Phenyl protons H-δ 8.14 and H-δ 8.21 showed strong correlation with furan carbon C- δ 147.4. This confirmed that two phenyls are attached with C-2 and C-5.

The structures of all products were established by 2D NMR techniques (NOESY, HMBC) or by X-ray crystal structure analyses.

6.3 Conclusion

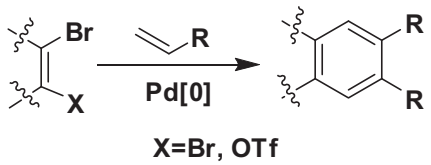
In conclusion, I have optimized the reaction conditions to achieve a convenient synthesis of symmetrical and unsymmetrical di- and tetra-aryl-furans by Suzuki-Miyaura reactions of 2,3,4,5-tetrabromofuran. $Pd(PPh_3)_4$ (3 mol-%) in dioxane solvent was the best catalyst system and solvent to achieve tetra-aryl-furans. Due to extensive studies of reaction conditions to achieve regioselective arylation of TBF it occurred to me that $Pd(PPh_3)_4$, aq. K_2CO_3 (2 M) in 1:4 dioxane/toluene were the best conditions to afford 2,5, diaryl-3,4-dibromofurans (**56**) with neat and clean reactions. Products prepared and discussed in this chapter are not readily accessible by other available methods. All reactions proceed with excellent site-selectivity and selectivity mainly depends on ratio of dioxane in toluene.

7 Abstract

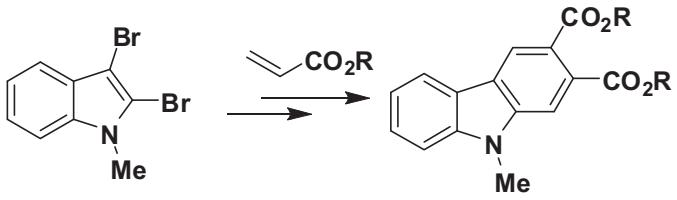
An overview of domino twofold Heck / 6π-electrocyclization reactions of vicinal dihalides is given. The palladium(0)-catalyzed Heck cross-coupling reactions of di- and tribromo-*N*-methylindoles provided 1,2-dihydrocarbazoles are described by a domino ′twofold Heck / 6π-electrocyclization process at 120 °C. The products were transformed by Pd/C-catalyzed oxidation to the corresponding carbazoles. I have synthesized functionalized benzofurans based on domino ′twofold Heck / 6π-electrocyclization′ reactions. Functionalized anthraquinones, fluorenones and benzocoumarines were also prepared by domino ′twofold Heck / 6π-electrocyclization′ reactions

Suzuki-Miyaura cross-coupling reactions of 2,4,5,6-tetrachloropyrimidine provide an expedient synthesis of mono-, di-, tri- and tetraarylpyrimidines which are not readily available by other methods. All reactions proceed with excellent site-selectivity. Optimization of reaction conditions for better yields and loading of lower percentage of catalyst were studied as well. Suzuki-Miyaura reactions of 2,3,4,5-tetrabromofuran allowed a convenient synthesis of tetraarylfurans which are not readily available by other methods. Regioselectivity was achieved by using the solvent system toluene/dioxane (4:1) at C-2, C-5 and then C-3, C-4. All reactions proceeded with excellent yields and site-selectivity.

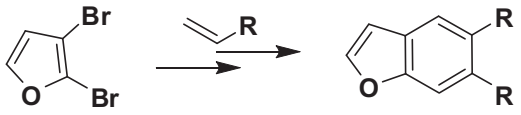
Zunächst wird ein Überblick über zweifache Heck / 6π-Elektrocyclisierungs-Dominoreaktionen von vicinalen Dihalogeniden gegeben.



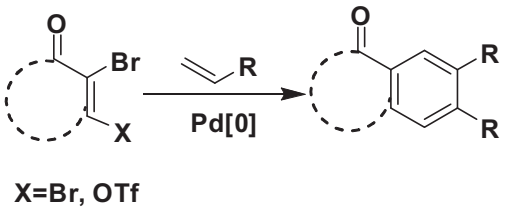
Die Palladium(0)-katalysierte Heck-Kreuzkupplung von Di- und Tribrom-*N*-methylindolen ergab 1,2-Dihydrocarbazole. Der Reaktion liegt eine zweifache Heck / 6π-Elektrocyclisierungs-Dominoreaktion bei einer Temperatur von 120 °C zugrunde. Die Produkte wurden durch eine Palladium/Aktivkohle-katalysierte Oxidation in die entsprechenden Carbazole überführt.



Zusätzlich habe ich funktionalisierte Benzofurane basierend auf der zweifachen Heck / 6π-Elektrocyclisierungs-Dominoreaktionen synthetisiert.

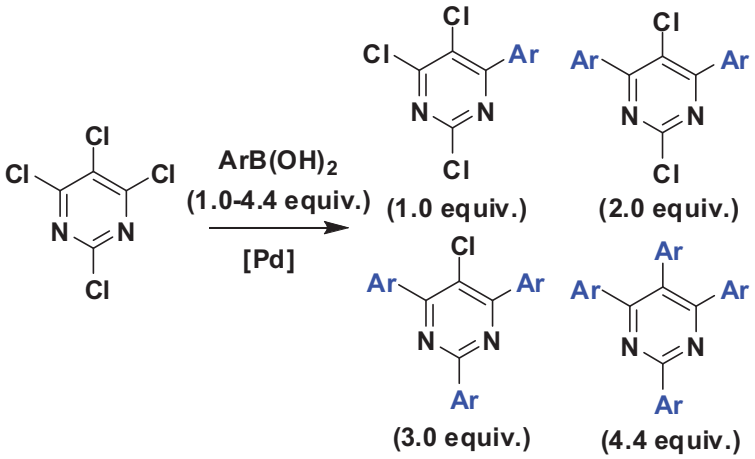


Verschieden funktionalisierte Anthrachinone, Fluorenone und Benzocumarine wurden ebenfalls durch die zweifache Heck / 6π-Elektrocyclisierungs-Dominoreaktionen dargestellt.

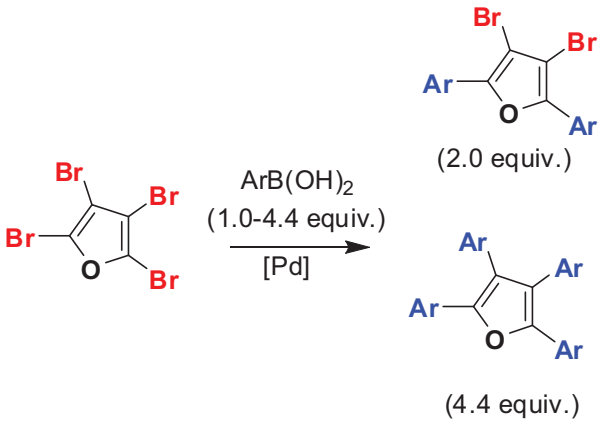


Die Suzuki-Miyaura-Kreuzkupplung von 2,4,5,6-Tetrachlorpyrimidinen ergab Mono-, Di-, Tri- und Tetraarylpyrimidine, die durch andere Synthesemethoden nur schwer zugänglich sind. Alle Reaktionen verlaufen mit exzellenter Regioselektivität. Zusätzlich wurden eine

Veränderung der Reaktionsbedingungen zur Ausbeuteverbesserung und eine Minimierung der Katalysatormenge untersucht.



Die Suzuki-Miyaura-Kreuzkupplung von 2,3,4,5-Tetrabromfuranen ermöglichte die Synthese von Tetraarylfuranen, die durch andere Synthesemethoden nur schwer zugänglich sind. Eine sehr gute Regioselektivität konnte, zunächst an den Atomen C-2 und C-5, dann an den Atomen C-3 und C-4, durch Verwendung des Lösungsmittelgemisches Toluen/Dioxan (4:1) erreicht werden. Alle Reaktionen verlaufen mit sehr guter Ausbeute und Regioselektivität.



Experimental Section

8 Material and Methods

8.1 General Remarks

Reactions were carried out under inert atmosphere (Argon 4.6) in order to simultaneously exclude oxygen and water when appropriate. Pressure tubes were used to avoid condenser. Solvents for reactions were dried and distilled by standard methods or purchased from Merck, Aldrich, Acros Organics, and others whenever exclusion of water was desired. Solvents for liquid chromatography and extraction were always distilled prior to use and partly reused after fractional distillation (*n*-heptane, ethyl acetate).

8.2 Methods for Compound Characterization and Analysis

NMR Spectroscopy

Bruker AC 250, Bruker ARX 300, Bruker ARX 500. For NMR characterization the one-dimensional ^{1}H NMR, proton-decoupled ^{13}C NMR, and DEPT 135 spectra were collected. If necessary, other techniques (NOESY, COSY, HMQC, HMBC) were applied as well. All NMR spectra presented in this work were collected in $CDCl_3$ solution. All chemical shifts are given in ppm.

References (^{1}H NMR): TMS (δ = 0.00) or residual $CHCl_3$ (δ = 7.26) were taken as internal standard.

References (^{13}C NMR): TMS (δ = 0.0) or residual $CHCl_3$ (δ = 77.0) were taken as internal standard.

Multiplicities are given as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal. More complex coupling patterns are represented by combinations of the respective symbols. For example, td indicates a triplet of doublets with the larger coupling constant associated with the first symbol (here: triplet).

Infrared Spectroscopy (IR)

Nicolet 205 FT-IR, Nicolet Protége 460 FT-IR. Peaks are given the following assignments: w = weak, m = medium, s = strong, br = broad.

Mass Spektrometry (MS)

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 Spectrometry (HRMS)

Varian MAT 311, Intecta AMD 402.

Elemental Analysis

LECO CHNS-932, Thermoquest Flash EA 1112.

Melting Points

Micro heating table HMK 67/1825 Kuestner (Büchi Apparatus), Leitz Labolux 12 Pol with heating table Mettler FP 90. Melting points are uncorrected.

Rotation Angles

LμP (IBZ Meßtechnik, Na^D = 589 nm).

X-ray Structures

Bruker X8Apex diffractometer with CCD camera (Mo K_α radiation and graphite monochromator, λ = 0.71073 Å). The space group is determined by the XPREP program and the structures were solved via the SHELX-97 program package. Refinements were carried out according to the minimum square error method.

8.3 Chromatographic Methods

Thin Layer Chromatography (TLC)

Merck Kieselgel 60 F254 on aluminium foil from Macherey-Nagel. Detection was carried out under UV light at 254 nm and 365 nm. As colourizing reagent the following mixtures were used: 1-2/100 p-Anisaldehyde or vanillin, 10/100 glacial acetic acid, 5/100 sulphuric acid, 83-84/100 methanol.

Column Chromatography

Column chromatography was performed with Merck Silica Gel 60 or Macherey-Nagel Silica Gel 60 (0.063-0.200 mm, 70-230 mesh). The finer Merck Silica Gel 60 (0.040-0.063 mm, 230-400 mesh) was chosen when appropriate.

9 General Procedures

9.1 Synthesis of 1,2-Dihydrocarbazoles and Carbazoles by Domino ′Twofold Heck / 6π-Electrocyclization′ Reactions of Di- and Tri-*N*-methylindoles

9.1.1 Synthesis of 2,3-dibromo-*N*-methylindole (14).

To a THF solution (20 mL) of *N*-methylindole (**13**) (1.0 mL, 8.0 mmol) was portionwise added NBS (3.30 g, 18.4 mmol) at – 78 °C and the solution was stirred at this temperature for 4 h. To the solution was added water (25 mL). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$, dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash silica column chromatography (pure heptanes) to yield **14** as a colourless semisolid (1.83 g, 90%).

9.1.2 Synthesis of 2,3,6-tribromo-*N*-methylindole (**15**).

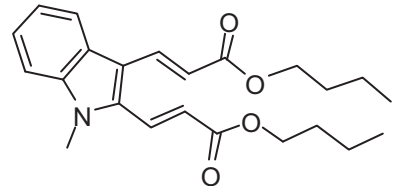
To a THF solution (50 mL) of *N*-methylindole (**13**) (2.0 mL, 16.0 mmol) was portionwise added NBS (9.40 g, 52.8 mmol) at – 78 °C and the solution was stirred at this temperature for 4 h and then at 20 °C for 14 h. To the solution was added water (25 mL). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$, dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash silica column chromatography (pure heptanes) to yield **15** (5.50 g, 94%).

General procedure A for 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 Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl)phosphine (L) (41 mg, 0.10 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C to get a yellowish or brownish transparent solution. To the stirred solution were added the brominated indole **14** or **15**(1.0 mmol), NEt_3 and the acrylate. The reaction mixture was stirred at 90 °C for 36 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

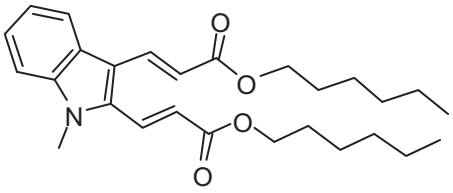
with H_2O (3 x 20 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes/EtOAc).

8.1.3 Synthesis of 2,3-bis(alkenyl)-*N*-methylindoles 17

Dibutyl 3,3'-(1-methyl-1*H*-indole-2,3-diyl)diacrylate (17b). Product **17b** was prepared starting with **14** (289 mg, 1.0 mmol), butyl acrylate **(16c)** (0.36 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 24 h following *general procedure A*, as a brownish oil (276 mg, 72%)**.** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (t, 6H, *J* = 7.1 Hz, $2CH_3$), 1.30-1.40 (m, 4H, $2CH_2$), 1.60-1.70 (m, 4H, $2CH_2$), 3.70 (s, 3H, NCH_3), 4.10 (t, 2H, *J* = 6.3 Hz, CH_2O), 4.20 (t, 2H, *J* = 6.3, $2CH_2O$), 6.30 (d, 1H, *J* = 16.1 Hz, CH), 6.50 (d, 1H, , *J* = 15.8 Hz, CH), 7.20-7.40 (m, 3H, ArH), 7.80 (d, 1H, *J* = 16.1 Hz, CH), 7.80 (bd, 1H, *J* = 8.0 Hz, ArH), 7.90 (d, 1H, *J* = 15.8 Hz, CH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.7, 13.8 (CH_3), 19.2, 19.3 (CH_2), 30.8, 30.9 (CH_2), 31.2 (NCH_3), 64.2, 64.9 (CH_2O), 110.0 (CH), 114.1 (C), 116.6, 121.1, 122.0, 124.7, 124.8 (CH), 125.5 (C), 131.1, 136.5 (CH), 136.8, 139.0 (C), 166.2, 168.0 (CO). IR (KBr): $\tilde{\nu}$ = 2957, 2932, 2872 (m), 1706, 1616, 1466 (s), 1364, 1326 (w), 1274, 1235, 1165 (s), 1132, 1115, 1061, 1046, 1027, 968, 844, 8215 (m), 739 (s), 561 (w) cm. MS (EI, 70 eV): *m/z* (%) = 383 (M^+, 3), 381 (62), 325 (13), 308 (06), 269 (09), 252 (100), 225 (08). HRMS (EI, 70 eV): calcd for $C_{23}H_{29}NO_4$ $[M]^+$: 383.20911; found: 383.208695.

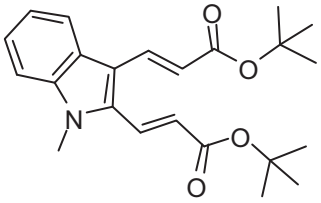


Dihexyl 3,3'-(1-methyl-1*H*-indole-2,3-diyl)diacrylate (17c). Product **17c** was prepared starting with **14** (289 mg, 1.0 mmol), hexyl acrylate **(16e)** (0.44 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 36 h following *general procedure A*, as a deep yellow highly viscous oil (337 mg, 77%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, 6H, *J* = 7.8 Hz, $2CH_3$), 1.20-1.40 (m, 16H, $8CH_2$), 3.70 (s, 3H, NCH_3), 4.20 (t, 4H, *J* = 6.8 Hz, $2CH_2O$), 6.20 (d, 1H, *J* = 16.0 Hz, ArH), 6.50 (d, 1H, *J* = 15.9 Hz, ArH), 7.10-7.30 (m, 3H, ArH), 7.70 (d, 1H, *J* = 15.8 Hz, ArH), 7.80 (d, 2H, *J* = 8.1 Hz, ArH), 7.90 (d, 1H, *J* = 16.0 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.0 ($2CH_3$), 21.4, 21.5, 24.4, 24.8, 27.3, 27.7 (CH_2), 29.9 (NCH_3), 30.3, 30.5 (CH_2), 63.5, 64.2 (CH_2O), 109.7 (CH), 113.0 (C), 120.0, 120.2, 121.0, 123.2, 1236 (CH), 124.5 (C), 130.1, 134.2 (CH), 135.5, 138.0



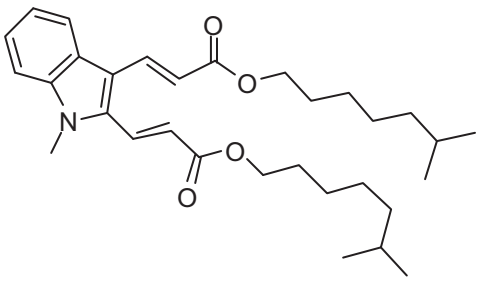
(C), 165.2, 166.9 (CO). IR (KBr): $\tilde{\nu}$ = 2955, 2929, 2857 (m), 1712 (s), 1625, 1529, 1467, 1360, 1283, 1238 (w), 1170 (s), 1133, 1049, 972, 916 (w), 735 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 439 ([M]$^+$, 44), 338 (06), 310 (28), 252 (11), 226 (100), 208 (68), 182 (84). HRMS (EI, 70 eV): calcd for $C_{27}H_{37}NO_4$ [M]$^+$: 439.27171; found: 439.270972.

Di(*tert*-Butyl) 3,3'-(1-methyl-1*H*-indole-2,3-diyl)diacrylate (17d). Product **17d** was



synthesized starting with **14** (289 mg, 1.0 mmol), *tert*-butyl acrylate **(16f)** (0.37 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 36 h following *general procedure A*, as a yellowish highly viscous oil (299 mg, 78%, *E/Z* = 7:3). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.50 (s, 18H, $6CH_3$), 3.70 (s, 3H, NCH_3), 6.20 (d, 1H, *J* = 16.0 Hz, ArH), 6.40 (d, 1 H, *J* = 16.0 Hz, ArH), 7.20–7.30 (m, 3H, ArH), 7.60 (d, 1H, *J* = 15.8 Hz, ArH), 7.70 (d, 1H, *J* = 16.0 Hz, ArH), 8.00 (d, 1H, *J* = 7.9 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2 , 27.3 ($3CH_3$), 30.1 (NCH_3), 79.0, 80.2 (C-O), 108.6 (CH), 112.8 (C), 117.2, 120.2, 120.6 , 123.8 (CH), 124.5 (C), 125.4, 129.2, 134.7 (CH), 135.9, 137.2 (C), 164.4, 166.3 (C=O). IR (KBr): $\tilde{\nu}$ = 2964, 2930 (w), 1722, 1710, 1693, 1680, 1613 , 1469, 1453, 1391, 1366 (m), 1281, 1258, 1144, 1090, 1017 (s), 845 (m), 797, 741 (s), 663, 563 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 383 (M$^+$, 39), 271 (13), 227 (84), 226 (100), 225 (52), 208 (31), 182 (69), 167 (54), 152 (21), 57 (79), 41 (42). HRMS (EI, 70 eV): calcd for $C_{23}H_{29}NO_4$ [M]$^+$: 383.20911; found: 383.20905.

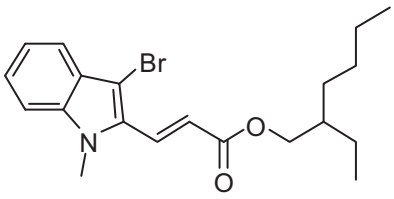
Bis(6-methylheptyl) 3,3'-(1-methyl-1*H*-indole-2,3-diyl)diacrylate (17e). Product **17e** was



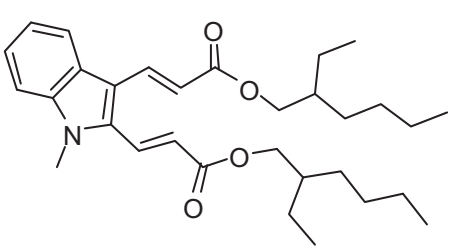
prepared starting with **14** (289 mg, 1.0 mmol), isooctyl acrylate (**17e**) (0.52 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 36 h following *general procedure A*, as a yellow oil (377 mg, 76%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.60-0.90 (m, 12H, $4CH_3$), 1.00-1.40 (m, 12H, $6CH_2$), 1.50-1.60 (m, 6H, aliphatic), 3.80 (s, 3H, NCH_3), 4.10 (t, 2H, *J* = 6.7 Hz, CH_2O), 4.20 (t, 2H, *J* = 6.8 Hz, CH_2O), 6.40 (d, 1H, *J* = 16.1 Hz, ArH), 6.50 (d, 1H, *J* = 16.0 Hz, ArH), 7.10-7.20 (m, 3H, ArH), 7.80 (d, 1H, *J* = 15.7 Hz, ArH), 7.80 (bd, 1H, *J* = 7.6 Hz, ArH), 7.90 (d, 1H, *J* = 15.7 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.0, 14.6 (CH_3), 21.5, 24.5, 27.5 (CH_2) 29.5 (NCH_3), 45.5 (CH_2), 63.7, 63.8 (CH_2O), 108.1 (C), 108.7 (CH), 115.7, 120.0, 120.4, 123.2 (CH), 124.5, 125.0 (C), 127.6, 130.1, 134.3 (CH),

137.3 (C), 165.3, 167.0 (CO). IR (KBr): $\tilde{\nu}$ = 2955, 2927, 2871 (m), 1709, 1620, 1465 (s), 1367, 1280, 1235 (m), 1164 (s), 1132, 1048, 969, 849, 818 (w), 740 (s), 662, 561 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 495 ([M]$^+$, 32), 337 (16), 281 (14), 253 (10), 252 (22), 226 (100), 208 (75), 182 (45). HRMS (EI, 70 eV): calcd for $C_{31}H_{45}NO_4$ [M]$^+$: 495.33431; found: 495.33390.

(E)-2-ethylhexyl 3-(3-bromo-1-methyl-1*H*-indol-2-yl)acrylate (21). Product **21** (138 mg, 35%) was found alongwith **17g** (50 mg, 10%) as a light brown oil (138 mg, 35%+10% **17g).**. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.3, 6H, $2CH_3$), 1.18-1.45 (m, 8H), 1.53-1.66 (m, 1H), 3.75 (s, 3H, CH_3N), 4.08 (dd, *J* = 0.8, 6.0 Hz, 2H, CH_2O), 6.80 (d, 1H, *J* = 16.2 Hz, CH), 7.08-7.15 (m, 1H, ArH), 7.22-7.25 (m, 2H, ArH), 7.48-7.52 (m, 1H, ArH), 7.774 (d, 1H, , *J* = 16.3 Hz, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 9.8, 13.1 (CH_3), 22.0, 22.9, 27.8, 29.5 (CH_2), 30.2 (CH), 37.9 (NCH_3), 66.2 (CH_2O), 95.0 (C), 108.8, 119.1, 119.4, 120.0, 124.0 (CH), 126.2, 129.8 (C), 130.0 (CH), 137.0 (C), 166.2 (CO). IR (KBr): $\tilde{\nu}$ = 2956, 2926, 2871, 2858 (m), 1706 (s), 1625, 1462, 1372, 1325, 1260, 1233, 1207 (m), 1167 (s), 1014, 930, 767 (w), 738 (m) cm. HRMS (ESI$^+$): calcd for $C_{20}H_{26}BrNO_2$ (M$^+$, [^{79}Br]): 391.11469; found: 391.11433, calcd for $C_{20}H_{26}BrNO_2$ (M$^+$, [^{81}Br]): 393.11263; found: 393.11453.



Synthesis of bis(2-ethylhexyl) 3,3'-(1-methyl-1*H*-indole-2,3-diyl)diacrylate (17g). Product **17g** was prepared starting with **14** (289 mg, 1.0 mmol), 2-Ethylhexyl acrylate (0.27 mL, 1.25 mmol) (0.52 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 24 h following *general procedure A*, as a yellow oil (50 mg, 10% + 35 % **22**). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (t, 12H, *J* = 7.5 Hz, $4CH_3$), 1.20-1.40 (m, 16, $8CH_2$), 1.20-1.60 (m, 2H, CH), 3.80 (s, 3H, NCH_3), 4.00-4.10 (m, 4H, CH_2O), 6.30 (d, 1H, *J* = 16.0 Hz, ArH), 6.50 (d, 1H, *J* = 16.0 Hz, ArH), 7.20-7.30 (m, 3H, ArH), 7.80 (d, 1H, *J* = 16.0 Hz, ArH), 7.90 (d, 1H, *J* = 8.1 Hz, ArH), 8.00 (d, 1H, *J* = 15.9 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.0, 11.1, 14.0 (CH_3), 22.9, 23.0, 23.8, 24.0, 28.9, 29.0, 30.4, 30.5 (CH_2), 31.2 (CH_3CN), 38.8, 38.9 (CH aliphatic), 66.8, 67.6 (CH_2O), 109.0 (CH), 113 (C), 115.7, 121.2, 122.0, 123.5, 123.6 (CH), 124.5 (C), 131.1, 135.5 (CH), 135.8, 138.0 (C), 165.3, 167.0 (CO). IR (KBr): $\tilde{\nu}$ = 3052 (w), 2957, 2927, 2872, 2858 (m), 1706,

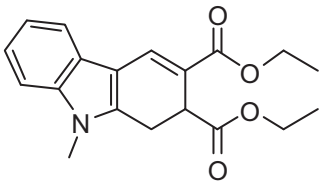


1620 (s), 1464 (m), 1411, 1378, 1352, 1339 (w), 1280, 1250, 1235 (m), 1165 (s), 1132, 1031, 1016, 1016, 968 (m), 850, 818, 766 (w), 740 (s), 655, 561 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 595 ($[M]^+$, 60), 367 (9), 337 (15), 269 (10), 253 (15), 226 (72), 208 (100), 151 (13). HRMS (EI, 70 eV): calcd for $C_{31}H_{45}NO_4$ $[M]^+$: 495.33431; found: 495.33712.

9.1.4 Synthesis of 2,3-dihydrocarbazoles 18

General procedure B for Heck cross-coupling reactions. In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 1.25 mol% per Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl) phosphine (L) (41 mg, 0.10 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C to get a yellowish or brownish transparent solution. To the stirred solution were added the brominated indole **14** or **15** (1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the acrylate (1.25 equiv. per Br). The reaction mixture was stirred at 120 ˚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 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).

Diethyl 9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (18a). Product **18a** was



prepared starting with **14** (289 mg, 1.0 mmol), ethyl acrylate **(16b)** (0.27 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (mL) at 120 °C for 48 h according to *general procedure B*, as a yellow solid (303 mg, 93%). The synthesis of **18a** has been previously reported.[81] Mp = 125 °C (lit.[81], 125-126 °C). Mp 100-103 ˚C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.10 (s, 3H, CH_3), 1.30 (s, 3H,CH_3), 2.90 (dd, 1H$_\alpha$, *J* = 8.8, 17.1 Hz, H-1), 3.50 (dd, 1 H$_\beta$, *J* = 2.6, 17.2 Hz, H-1), 3.60 (s, 3H, NCH_3), 3.90-4.10 (m, 3H, H$_\alpha$ and CH_2O), 4.20 (q, *J* = 7.1, 13.5 Hz, 2H, CH_2O), 7.10-7.20 (m, 3H, ArH), 7.50-7.60 (m, 1H, ArH), 7.90 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0 (CH_3), 13.5 (CH_3), 22.8 (CH_2), 28.7 (CH, C-4), 37.7 (NCH_3), 59.3 (CH_2O), 60.1 (CH_2O), 108.3 (C), 108.6 (CH), 115.4 (C), 116.9, 120.0, 120.8 (CH), 124.1(C), 131.2 (CH), 137.0, 138.6 (C), 166.3, 172.3 (CO). IR (KBr): $\tilde{\nu}$ = 2981, 2928, 2854 (w), 1725(s), 1629, 1599 (w), 1470 1454 (m), 1372, 1261, 1238 (s), 1109, 1079, 147 (m), 787, 747, 723, 608, 561 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 325 ($[M-2]^+$ (carbazole), 89), 280 (13), 252 (100), 208 (07),

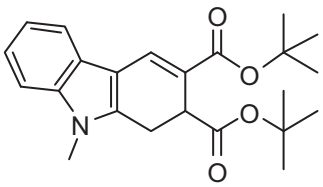
179 (13); HRMS (ESI$^+$): calcd for $C_{19}H_{19}NO_4$ $[M-2]^+$ (carbazole): 325.13141; found: 325.13161.

Dibutyl 9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (18b). Product **18b** was prepared starting with **14** (289 mg, 1.0 mmol), butyl acrylate **(16c)** (0.36 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (mL) at 120 °C for 48 h according to *general procedure B*, as a yellow highly viscous oil (294 mg, 77%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, 3H, J = 7.3 Hz, CH_3), 0.90 (t, 3H, J = 7.4 Hz, CH_3), 1.10-1.30 (m, 2H, CH_2), 1.30-1.50 (m, 4H, $2CH_2$), 1.60-1.70 (m, 2H, CH_2), 3.00 (dd, $1H_\alpha$, J = 8.6, 17.0 Hz, H-1), 3.60 (dd, $1H_\beta$, J = 2.3, 17.0 Hz, H-1), 3.70 (s, 3H, NCH_3), 3.80-4.00 (m, 2H, CH_2O), 4.00 (dd, $1H_\alpha$, J = 2.3, 8.3 Hz, H-2), 4.20 (t, 2H, J = 6.6 Hz, CH_2O), 7.00-7.20 (m, 3H, ArH), 7.50- 7.60 (m, 1H, ArH), 7.90 (s, 1H, H-4). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.6 (CH_3), 13.8 (CH_3), 19.0, 19.3, 23.8 (CH_2), 29.8 (CH_3N), 30.5, 31.0 (CH_2), 39.0 (CH, C-2), 64.2, 65.0 (CH_2O), 109.4 (C), 109.6 (CH), 116.5 (C), 118.0, 121.0, 121.8 (CH), 125.2 (C), 132.1 (CH), 138.0, 139.7 (C), 167.4, 173.4 (CO). IR (KBr): $\tilde{\nu}$ = 2956, 2932, 2872 (m), 1709 (s), 1629, 1599, 1559, 1562 (w), 1500, 1464, 1387, 1362, 1340, 1325 (m), 1257, 1222 (s), 1131, 1106, 1077, 1045, 1015 (m), 950, 902, 843, 830, 783, 765 (w), 742, 720 (m), 632, 608, 561 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 383 ($[M]^+$, 46), 310 (06), 282 (34), 226 (87), 208 (67), 182 (100), 152 (13); HRMS (EI, 70 eV): *m/z* calcd for $C_{23}H_{29}NO_4$ $[M]^+$: 383.20911; found: 383.20824.

Dihexyl 9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (18c). Compound **18c** was synthesized starting with **14** (289 mg, 1.0 mmol), hexyl acrylate **(16e)** (0.44 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (mL) at 120 °C for 48 h following *general procedure B*, as a yellowish solid (357 mg, 81%). Mp 107-109 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.70 (t, 3H, J = 7.0 Hz, CH_3), 0.80 (t, 3H, J = 7.0 Hz, CH_3), 1.10-1.20 (m, 6H, $3CH_2$), 1.20-1.50 (m, 8H, $4CH_2$), 1.60-1.70 (m, 2H, CH_2), 3.00 (dd, $1H_\alpha$, J = 8.8, 17.1 Hz, H-1), 3.50 (dd, $1H_\beta$, J = 2.3, 17.1 Hz, H-1), 3.60 (s, 3H, NCH_3), 3.80-4.00 (m, 2H, CH_2O), 4.00 (dd, $1H_\alpha$, J = 2.4, 8.8 Hz, H-2), 4.10 (t, 2H, J = 6.8 Hz, CH_2O), 7.00-7.20 (m, 3H, ArH), 7.50-7.60 (m, 1H, ArH), 7.90 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.9, 13.0 (CH_3), 21.5, 21.6, 22.8, 24.4, 24.8, 27.4, 27.9 (CH_2), 28.7 (NCH_3), 30.3, 30.5 (CH_2), 38.0 (CH, C-4), 63.5,

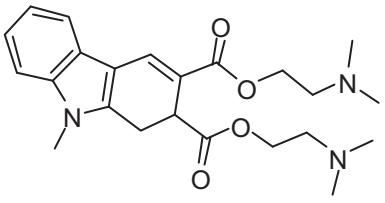
64.2 (CH_2O), 108.3(C), 108.5 (CH), 115.5 (C), 116.9, 120.0, 121,0 (CH), 124.1 (C), 131.0 (CH), 137.0, 138.7 (C), 166.4, 172.3 (CO). IR (KBr): $\tilde{\nu}$ = 2953, 2928, 2857 (m), 1724, 1691 (s), 1615, 1605, 1526, 1465, 1392, 1311, 1307, 1268 (m), 1223, 1180 (s), 1086, 1046 (m), 915, 835, 767 (w), 738 (s), 653, 626, 546 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 439 ($[M]^+$, 41), 310 (30), 226 (100), 208 (68), 182 (84), 152(08). HRMS (EI, 70 eV): calcd for $C_{27}H_{37}NO_4$ $[M]^+$: 439.27171; found: 439.27110.

Di-tert-butyl 9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (18d). Compound



18d was prepared starting with **14** (367 mg, 1.0 mmol), *tert*-butyl acrylate **(16f)** (0.37 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (mL) at 120 °C for 48 h according to *general procedure B*, as a light brown solid (325 mg, 85%). Mp 105-107 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (s, 9H, $3CH_3$), 1.50 (s, 9H, $3CH_3$), 2.90 (dd, $1H_\alpha$, *J* = 8.9, 17.1 Hz, H-1), 3.50 (dd, $1H_\beta$, *J* = 2.5, 17.1 Hz, H-1), 3.60 (s, 3H, NCH_3), 3.90 (dd, $1H_\alpha$, *J* = 2.1, 8.9 Hz, H-2), 7.00-7.10 (m, 2H, ArH), 7.10-7.20 (m, 1H, ArH), 7.50-7.60 (m, 1H, ArH), 7.80 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6 (CH_2), 27.9 ($3CH_3$), 28.4 ($3CH_3$), 29.7 (CH, C-4), 39.7 (CH_3N), 79.7 (C-O), 81.0 (C-O), 109.2 (C), 109.5 (CH), 118.0 (CH), 118.7 (C), 120.7, 121.5 (CH), 125.2 (C), 130.6 (CH), 137.9, 139.6 (C), 166.8, 172.5 (CO). IR (KBr): $\tilde{\nu}$ = 3049, 2973, 2930 (w), 1712 (s), 1614, 1598, 1470, 1455, 1390 (m), 1365, 1272, 1242, 1152, 1128, 1110 (s), 1046, 1014 (w), 872, 846, 836 (m), 747, 739 (s), 666, 597, 550 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 383 ($[M]^+$, 7), 325 (54), 269 (100), 252 (86), 225 (80), 207 (44), 179 (82). HRMS (EI, 70 eV): calcd for $C_{23}H_{29}NO_4$ $[M]^+$: 383.20966; found: 383.20855.

Bis[2-(dimethylamino)ethyl] 9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (18f).



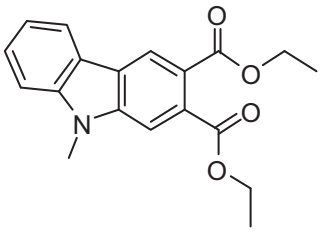
Compound **18f** was synthesized starting with **14** (289 mg, 1.0 mmol), 2-(Diethylamino)ethyl acrylate (**16i**) (0.38 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (mL) at 120 °C for 48 h following *general procedure B*, as a yellow highly viscous oil (326 mg, 79%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.10 (s, 6H, $2CH_3$), 2.30 (s, 6H, $2CH_3$), 3.00 (dd, 1Hα, *J* = 8.8, 17.1 Hz), 3.50-3.60 (m, 4H, NCH_3 and H_β-1), 4.00-4.10 (m, 5H, $2NCH_2$ and H_α-2), 3.30 (t, 4H, *J* = 6.3 Hz, $2CH_2O$), 7.10-7.20 (m, 3H, ArH), 7.50 (dd, 1H, *J* = 2.3, 8.5 Hz, ArH), 7.90 (s, 1H, H-4). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 23.8 (CH_2, C-1), 29.8 (NCH_3), 38.9 (CH, C-2), 45.5, 45.8

($2CH_3$), 57.3, 57.9 (NCH_2), 62.3, 63.2 (CH_2O), 109.3 (C), 109.6 (CH), 115.7 (C), 117.9, 121.1, 122.0 (CH), 125.1 (C), 132.8 (CH), 138.0, 139.8 (C), 167.2, 173.1 (CO). IR (KBr): $\tilde{\nu}$ = 2943, 2857, 2820, 2769 (w), 1691, 1614, 1525, 1455 (s), 1394, 1370, 1332, 1286 (m), 1225, 1166 (s), 1130, 1097 (m), 1031 (s), 954, 919, 835 (w), 739 (s), 627 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 413 ($[M]^+$, 13), 297 (98), 252 (06), 227 (04), 225 (13), 208 (56), 180 (17), 58 (100). HRMS (EI, 70 eV): calcd for $C_{23}H_{31}N_3O_4$ $[M]^+$: 413.23091; found: 413.230881.

9.1.5 Synthesis of 3,4-di-substitutedcarbazoles 19

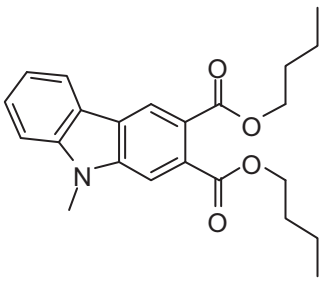
General procedure C for the transformation of 1,2-dihydrocarbazoles to carbazoles. To of xylene (5 mL) were added the 1,2 dihydrocarbazole (100 mg) and Pd/C (10 mg, 10 mol-%). The solution was stirred under reflux for 48 h under argon atmosphere. The reaction mixture was filtered and the filtrate was concentrated in vacuo.

Diethyl 9-methyl-9*H*-carbazole-2,3-dicarboxylate (19a). Starting with **18a** (100 mg)

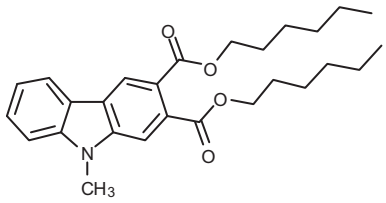


following *general procedure C* **19a** was prepared as a light yellow oïl (99 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (t, 3H, *J* = 7.1 Hz , CH_3), 1.33 (t, 3H, *J* = 7.1 Hz , CH_3), 3.81 (s, 3H, CH_3N), 4.32 (q, 2H, *J* = 7.2 Hz, CH_2O), 4.43 (q, 2H, *J* = 7.2 Hz, CH_2O), 7.21-7.31 (m, 1H, ArH), 7.32-7.41 (m, 1H, ArH), 7.40-7.51 (m, 1H, ArH), 7.60 (s,1H, ArH), 8.00-8.11 (m, 1H, ArH), 8.51 (s, 1H, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.2, 13.3 (CH_3), 28.4 (CH_3N), 60.3 (CH_2O), 60.7 (CH_2O) , 108.0, 108.1, 114.2, 120.0 (CH) 120.6, 121.2 (C), 121.4 (CH), 122.7, (C), 126.1 (CH), 130.1, 140.5, 141.2 (C), 166.8, 168.2 (CO). IR (KBr): $\tilde{\nu}$ = 2916 (w), 1713, 1702, 1628, 1599, 1559, 1499, 1475, 1447, 1427 (m), 1392, 1372, 1339, 1328 (s), 1254, 1240, 1227 (w), 1124, 1106, 1080, 1047, 1030, 953, 913, 868, 835, 794, 781, 765, 748, 725, 664, 656, 626, 590, 556 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 325 (M^+, 95), 280 (12), 253 (21), 252 (100), 251 (5), 208 (7), 179 (12), 152 (9); HRMS: *m*/*z* calcd for $C_{19}H_{19}NO_4$ $[M]^+$: 325.13141; found: 325.131001.

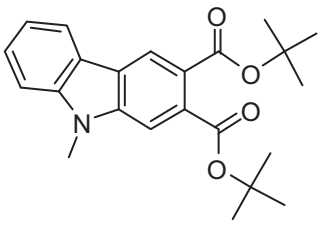
Dibutyl 9-methyl-9*H*-carbazole-2,3-dicarboxylate (19b). Product **19b** was prepared starting with **18b** (100 mg, 0.26 mmol), following *general procedure B*, as a light yellows semisolid (99 mg, 100%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (t, 3H, J = 7.4 Hz, CH_3), 0.90 (t, 3H, J = 7.3 Hz, CH_3), 1.30-1.50 (m, 4H, $2CH_2$), 1.60-1.80 (m, 4H, $2CH_2$), 3.80 (s, 3H, NCH_3), 4.30 (t, 2H, J = 6.8 Hz, CH_2O), 4.30 (t, 2H, J = 6.7 Hz, CH_2O), 7.20-7.30 (m, 1H, ArH), 7.30-7.40 (m, 1H, ArH), 7.40- 7.50 (m, 1H, ArH), 7.60 (s, 1H, H-1), 8.00 -8.10 (m, 1H, ArH), 8.40 (s, 1H, H-4). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.7, 13.8 (CH_3), 19.2, 19.3 (CH_2), 29.4 (NCH_3), 30.6, 30.8 (CH_2), 65.3, 65.7 (CH_2O), 109.0, 109.1, 120.2, 121.0 (CH), 121.7, 122.2 (C), 122.4 (CH), 123.6 (C), 127.1 (CH), 131.1, 141.5, 142,1 (C), 167.9, 169.4 (CO). IR (KBr): $\tilde{\nu}$ = 2956, 2931, 2871 (w), 1709 (s), 1464, 1387, 1362, 1340, 1325 (m) 1255, 1221 (s), 1131, 1106, 1077, 1045 (m), 950, 902, 843, 829 (w), 784, 743, 721 (m), 632, 608, 561 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 381(M^+, 56), 308 (15), 280 (100), 224 (87), 212 (27), 206 (77), 180 (10), 152 (11). HRMS (EI, 70 eV): calcd for $C_{23}H_{27}NO_4$ $[M]^+$: 381.19401; found: 381.19422.



Dihexyl 9-methyl-9*H*-carbazole-2,3-dicarboxylate (19c). Starting with **18c** (100 mg) following *general procedure C*, as a yellow oil (99 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, 3H, J = 7.1 Hz, CH_3), 0.83 (t, 3H, J = 7.0 Hz, CH_3), 1.24-1.30 (m, 8H, $4CH_2$), 1.33-1.40 (m, 4H, $2CH_2$), 1.66-1.73 (m, 4H, $2CH_2$), 3.75 (s, 3H, CH_3N), 4.26 (t, 2H, J = 6.7 Hz, CH_2O), 4.28 (t, 2H, J = 6.7 Hz, CH_2O), 7.17-7.23 (m, 1H, ArH), 7.32 (d, 1H, J = 8.2 Hz, ArH), 7.42-7.47 (m, 1H, ArH), 7.53 (s, 1H, ArH), 8.01 (d, 1H, J = 7.8 Hz, ArH), 8.42 (s, 1H, ArH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 22.6 ($2CH_2$), 25.7, 25.7, 28.6, 28.7 (CH_2), 28.7 (CH_3N), 31.5, 30.6 (CH_2) 65.6, 66.0 (CH_2O), 109.0, 109.1, 120.1, 120.9 (CH), 118.7, 122.2 (C), 122.3 (CH), 123.6 (C), 127.1 (CH), 131.1, 141.4, 142.1 (C), 167.8, 169.3 (CO). IR (KBr): $\tilde{\nu}$ = 3054, 2953, 2928, 2856 (w), 1712 (s), 1629, 1599, 1561, 1501 (w), 1466 (m), 1387 (w), 1363, 1340, 1325 (m), 1257, 1222 (s), 1132 (m), 1108 (s) 1079, 1046, 1015, 981, 907 (m), 867, 883 (w), 785, 766 (m), 729, 722 (s), 646 (m), 633, 609, 561 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 437 (M^+, 41), 353 (10), 252 (100), 225 (10), 182 (84), 152(08); HRMS: *m/z* calcd for $C_{27}H_{35}NO_4$ $[M]^+$: 437.25661; found: 437.25410.

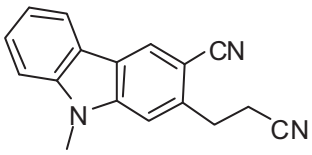


Di-tert-butyl 9-methyl-9*H*-carbazole-2,3-dicarboxylate (19d). Starting with **18d** (100 mg) following *general procedure C*, as a light yellow oil (99 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.57 (s, 9 H, $3CH_3$), 1.58 (s, 9 H,$3CH_3$), 3.78 (s, 3H, CH_3N); 7.17-7.23 (m, 1H, ArH), 7.33 (d, 1H, J = 8.2 Hz, ArH), 7.42-7.47 (m, 1H, ArH), 7.50 (s,1H, ArH), 8.03 (d, 1H, J = 7.8 Hz, ArH), 8.33 (s,1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1 ($3CH_3$), 28.3 ($3CH_3$), 29.4 (CH_3N); 81.2 (C-O), 81.8 (C-O) , 109.0, 109.1, 119.0, 120.9, 122.0 (CH), 122.4, 123.2, 123.8 (C), 126.8 (CH),132.8, 141.3, 142.2 (C), 167.0, 168.4 (CO). IR (KBr): $\tilde{\nu}$ = 2975, 2929, 2849 (w), 1713 (s), 1702, 1628, 1596, 1562, 1530, 1503, 1475, 1455, 1390 (w), 1365, 1337, 1324, 1269, 1251, 1228, 1165, 1129, 1108 (s), 1079, 1046, 1014, 955, 895, 876, 863, 834, 800, 787, 777, 763, 756, 738, 718 (m), 666, 634, 598, 565, 555 (w) cm. EI$^+$ (70 eV): *m/z* (%) = 381 ([M]$^+$, 27), 325 (5), 270 (13), 269 (100), 251 (48), 252 (33), 225 (8), 207 (10), 179 (35); HRMS: *m*/*z* calcd for $C_{23}H_{28}NO_4$ [M+H]$^+$: 382.20128; found: 382.20055.



9.1.6 Synthesis of 2-(2-cyanoethyl)-9-methyl-9*H*-carbazole-3-carbonitrile 20

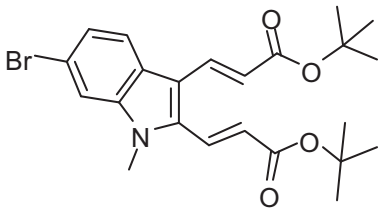
Product **7** was prepared, starting with **14** (289 mg, 1.0 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), acrylonitrile (0.17 mL, 2.5 mmol), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h according to *general procedure A*, as a light yellow crystals (127 mg, 49%), mp 185-187 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.80 (t, 2H, J = 7.1 Hz, CH_2), 3.30 (t, 2H, J = 7.1 Hz, CH_2), 3.80 (s, 3H, NCH_3), o7.20-7.30 (m, 1H, ArH), 7.30 (s, 1H, H-1), 7.40 (d, 1H, J = 8.2 Hz, ArH), 7.40- 7.50 (m, 1H, ArH), 8.00 (d, 1H, J = 7.9 Hz, ArH), 8.30 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0 (CH_2), 28.4 (NCH_3), 30.0 (CH_2), 100.4 (C), 108.2, 108.9 (CH), 117.6, 118.1 (CN), 119,6, 119.7 (CH), 120.6, 121.2 (C), 125.1, 126.3 (CH), 137.1, 140.8, 141.9 (C). IR (KBr): $\tilde{\nu}$ = 2914, 2852 (w), 2206 (s), 1631, 1597, 1557, 1504, 1464, 1432, 1366, 1330,1320, 1264, 1253 (m), 1112, 1153, 1014, 966, 898 (w), 844, 800, 767, 754 (s), 725, 666, 652, 550, 530 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 259 ([M]$^+$, 53), 243 (23), 198 (100), 152 (68), 112 (38). HRMS (EI, 70 eV): calcd for $C_{17}H_{13}N_3$ [M]$^+$: 259.11095; found: 259.11041.



9.1.7 Synthesis of 6-Bromo-2,3-bis(alkenyl)-*N*-methylindole 22

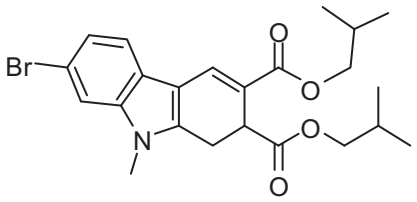
General procedure D for Heck cross-coupling reactions. In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 2.5 mol% per Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl)phosphine (L) (41 mg, 0.10 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C to get a yellowish or brownish transparent solution. To the stirred solution were added the 2,3,6-tribromo-*N*-methylindole (**15**) (368 mg, 1.0 mmol), NEt_3 (0.55 mL, 4.0 mmol) and the acrylate (2.5 mmol). The reaction mixture was stirred at 90 °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 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).

Di(*tert*-butyl) 3,3′-(6-bromo-1-methyl-1*H*-indole-2,3-diyl)diacrylate (**22**). Product **22** was



prepared starting with **15** (368 mg, 1.0 mmol) and *tert*-butyl acrylate (**16f**) (0.37 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 24 h *following general procedure D*, as a yellow solid (276 mg, 75%). Mp 148-152 °C. The structure was confirmed by 2D NMR analysis (NOESY, HMBC). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.50 (s, 18 H, $6CH_3$), 3.70 (s, 3H, NCH_3), 6.20 (d, 1 H, J = 16.1 Hz, ArH), 6.30 (d, 1 H, J = 16.1 Hz, ArH), 7.20 (d, 1H, J = 8.4 Hz, ArH), 7.20 (dd, 1H, J = 1.7, 8.6 Hz, ArH), 7.20 (d, J = 1.5 Hz, 1H, ArH), 7.80 (d, 1 H, J = 16.1 Hz), 7.70 (d, 1 H, J = 15.9 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.0 ($2CH_3$), 28.2 ($2CH_3$), 28.3 ($2CH_3$), 31.3 (NCH_3), 81.0, 81.3 (C-O), 113.0 (CH), 113.8, 118.0 (C), 118.9, 122.3 (CH), 124.3 (C), 124.9, 127.0, 129.8, 135.2 (CH), 137.0, 139.0 (C), 165.2, 167.0 (C=O). IR (KBr): $\tilde{\nu}$ = 3090, 2978, 2929 (w), 1709, 1674, 1633, 1615 (s), 1470 1454 (m), 1365, 1278, 1252, 1147 (s), 1064, 1038 (w), 970, 948 (m), 843, 829, 805 (s), 772, 757, 737, 640, 589 (w) cm. MS (EI, 70 eV): *m/z* (%) = 463 ([M^+, ^{81}Br], 12), 461 ([M^+, ^{79}Br] 13), 349 (16), 331 (17), 305 (46), 259 (35), 225 (100), 181 (97), 57 (38). HRMS (EI, 70 eV): calcd for $C_{23}H_{28}BrNO_4$ [M, ^{79}Br]$^+$: 461.11962; found: 461.11828.

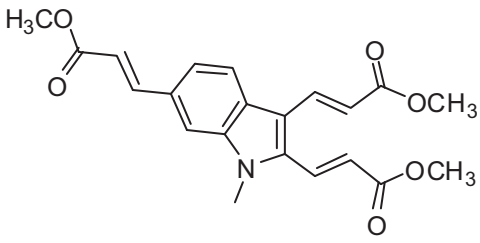
Di(isobutyl) 7-bromo-9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (23). Product



9 was synthesized starting with **47** (367 mg, 1.0 mmol), *iso*-butyl acrylate (**16d**) (0.36 mL, 2.5 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h according to *general procedure D*, as a yellowish highly viscous oil (335 mg, 73%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.70 (d, 6H, *J* = 6.7 Hz, $2CH_3$), 0.80 (d, 6H, *J* = 6.7 Hz, $2CH_3$), 1.60-1.80 (m, 1H, CH), 1.90-2.00 (m, 1H, CH), 3.50 (dd, $1H_\alpha$, *J* = 2.1, 17.2 Hz, H-1), 3.60 (s, 3H, NCH_3), 3.70 (dd, 2H, *J* = 3.6, 6.6 Hz, CH_2O), 3.90 (dd, 2H, *J* = 0.7, 6.5 Hz, CH_2O), 3.90 (dd, $1H_\beta$, *J* = 0.7, 6.5 Hz, H-1), 4.00 (dd, $1H_\alpha$, *J* = 2.0, 8.6 Hz, H-2), 7.20 (dd, 1H, *J* = 1.6, 8.4 Hz, ArH), 7.30 (d, 1H, *J* = 1.4 Hz, ArH), 7.40 (d, 1H, *J* = 8.4 Hz, ArH), 7.80 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 18.9 (CH_3), 19.3 ($2CH_3$), 23.7 (CH_2), 27.6, 28.0 (CH), 29.9 (NCH_3), 38.8 (CH, C-2), 70.6, 71.2 (CH_2O), 109.4 (C), 112.7 (CH), 115.2, 117.5 (C), 119.1 (CH), 123.9 (C), 124.1, 131.3 (CH), 138.8, 140.2 (C), 167.2, 173.1 (CO). IR (KBr): $\tilde{\nu}$ = 3052, 2948, 2867 (w), 1728, 1703, 1664, 1588, 1573, 1473, 1435 (s), 1392, 1379, 1325 (m), 1269, 1244, 1189, 1140, 1079, 1040 (s), 998, 975, 934, 904, 872, 853, 813 (w), 776, 736, 691 (s), 660, 646, 608, 576, 562 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 463 ([M^+, ^{81}Br], 4), 461 ([M, ^{79}Br]$^+$, 5), 436 (54), 389(10), 299 (100), 267 (70), 225 (12), 178 (17). HRMS (EI, 70 eV): calcd for $C_{23}H_{28}BrNO_4$ [M, ^{79}Br]$^+$: 461.12017; found: 461.12020.

9.1.8 Synthesis of 2,3,6-tris(alkenyl)-*N*-methylindoles 24

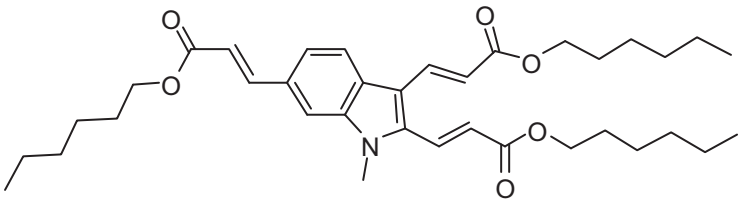
Trimethyl 3,3',3''-(1-methyl-1*H*-indole-2,3,6-triyl)triacrylate (24a). Product **24a** was



prepared starting with **15** (368 mg, 1.0 mmol), methyl acrylate (**16a**) (0.34 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), DMF (5 mL), NEt_3 (1.10 mL, 8.0 mmol) and *tert*-butyl acrylate (0.3 mL, 3.3 mmol), at 90 °C for 36 h following *general procedure D*, as a yellowish highly viscous oil (264 mg, 69%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.60 (s, 3H, CH_3O), 3.70 (s, 3H, OCH_3), 3.70 (s, 3H, NCH_3), 3.80 (s, 3H, OCH_3), 6.20 (d, 1 H, *J* = 16.1 Hz, ArH), 6.40 (d, 1 H, *J* = 15.9 Hz, ArH), 6.40 (d, 1 H, *J* = 15.9 Hz, ArH), 7.20-7.40 (m, 2H, ArH), 7.70 (d, 1H, *J* = 15.9 Hz, ArH), 7.80 (d, 1H, *J* = 16.2 Hz, ArH), 7.80 (dd, 1H, *J* = 1.3, 7.5 Hz, ArH), 7.90 (d, 1H, *J* = 15.9 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.4 (CH_3CN), 51.0, 52.1, 52.2 (OCH_3), 108.7 (C), 110.6, 115.0, 115.3, 119.3, 119.4, 123.0

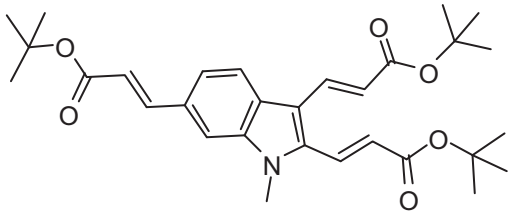
(CH), 125 (C), 128.9 (CH), 129.0 (C), 134.2 (CH), 136.3, 137.1 (C), 143.2 (CH), 164.4, 165.6, 166.1 (CO). IR (KBr): $\tilde{\nu}$ = 3028, 2950, 2848 (w), 1710, 1615, 1606 (s), 1298, 1283 (m), 1163, 1138 (s), 1037, 973 (m), 842, 781, 767, 746, 628, 606, 585 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 383 (M^+, 60), 352 (07), 324 (64), 292 (100), 265 (32), 234 (19), 204 (19). HRMS (EI, 70 eV): calcd for $C_{21}H_{21}NO_6$ $[M]^+$: 383.13634; found: 383.136074.

Trihexyl 3,3',3''-(1-methyl-1*H*-indole-2,3,6-triyl)triacrylate (24e). Product **24e** was



prepared starting with **15** (367 mg, 1.0 mmol), *n*-hexyl acrylate (**16e**) (0.66 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 36 h following *general procedure D*, as a yellow highly viscous oil (437 mg, 74%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, 9 H, *J* = 6.6 Hz, $3CH_3$), 1.10-1.30 (m, 16H, $8CH_2$), 1.60-1.70 (m, 8H, $4CH_2$), 3.80 (s, 3H, NCH_3), 3.90 (t, *J* = 6.7 Hz, 2H, CH_2), 4.10-4.30 (m, 4H, $2CH_2$), 6.20 (d, 1H, *J* = 16.0 Hz, ArH), 6.40 (d, 1H, *J* = 15.9 Hz, ArH), 6.50 (d, 1H, *J* = 16.0 Hz, ArH), 7.20-7.40 (m, 2H, ArH), 7.70 (d, 1H, *J* = 15.9 Hz, ArH), 7.70 (d, 1H, *J* = 16.1 Hz, ArH), 7.80 (d, 1H, *J* = 8.9 Hz, ArH), 7.90 (d, 1H, *J* = 16.0 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 ($3CH_3$), 22.6, 25.7, 28.7 ($3CH_2$), 31.3 (CH_3N), 31.5 ($3CH_2$), 64.0, 64.7, 65.3 (CH_2O), 109.5 (C), 110.5, 117.3, 117.6 (CH), 117.6(C), 120.3, 120.4, 125.3 (CH), 126.9, 129.6 (C), 130.6, 136.0 (CH), 137.3, 138.0 (C) 143.9 (CH), 165.0, 166.1, 167.7 (CO). IR (KBr): $\tilde{\nu}$ = 2953, 2927, 2857 (m), 1703, 1610 (s), 1560, 1530 (w), 1465, 1269, 1241, 1204 (m), 1160 (s), 1037, 979, 906, 845, 808, 764, 724, 609, 583 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 593 (M^+, 90), 492 (12), 463 (69), 406 (29), 380 (100), 362 (74), 336 (14), 278 (25), 234 (69). HRMS (EI, 70 eV): calcd for $C_{36}H_{51}NO_6$ $[M]^+$: 593.37109; found: 593.36965.

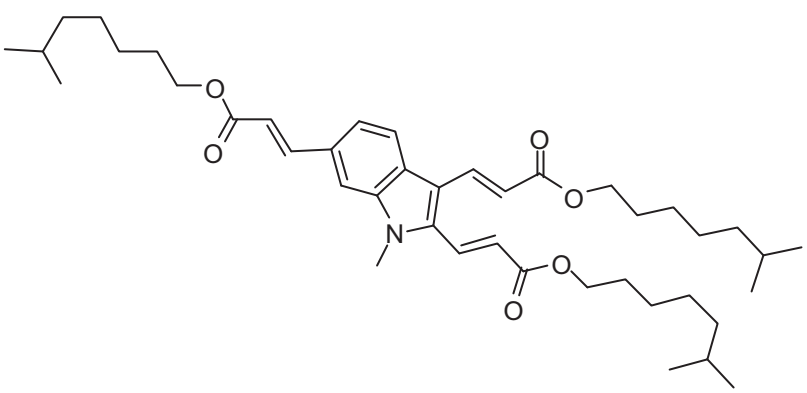
Tris(*tert*-butyl) 3,3',3''-(1-methyl-1*H*-indole-2,3,6-triyl)triacrylate (24f). Product **24f** was



synthesized starting with **15** (367 mg, 1.0 mmol), *tert*-butyl acrylate (**16f**) (0.55 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 36 h following *general procedure D*, as a yellow oil (387 mg, 76 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.50 (s, 9H, $3CH_3$), 1.50 (s, 18H, $6CH_3$), 3.80 (s, 3H, NCH_3), 6.20 (d, 1 H, *J* = 16.1 Hz, ArH), 6.40 (d, 1 H, *J* = 15.8 Hz, ArH), 6.40 (d, 1 H, *J* = 16.1 Hz, ArH), 7.30 (dd, 1H,

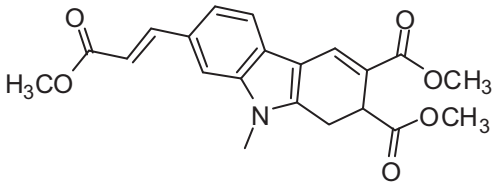
J = 1.0, 8.4 Hz, ArH), 7.40 (s, 1H, ArH), 7.70 (d, 1H, *J* = 16.1 Hz, ArH), 7.80 (d, 1H, *J* = 16.1 Hz, ArH), 7.80 (d, 1H, *J* = 16.1 Hz, ArH), 7.90 (d, 1H, *J* = 8.5 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1 ($3CH_3$), 28.2 ($3CH_3$), 28.3 ($3CH_3$), 31.2 (NCH_3), 80.1, 80.4, 81.4 (C-O), 110.6 (CH), 114.0 (C), 118.9, 119.5, 121.2, 121.4 (CH), 127.0 (C), 127.2, 129.9 (CH), 130.9 (C), 135.3 (CH), 138.3, 139.0 (C), 144.0 (CH), 165.2, 166.4, 167.0 (CO). IR (KBr): $\tilde{\nu}$ = 2976, 2931 (w), 1699, 1621, 1614 (s), 1455, 1391, 1366 (m), 1306, 1280, 1252, 1140 (s), 1038, 975, 844, 809, 763, 729, 609 (m), 584 (w) cm. MS (EI, 70 eV): *m/z* (%) = 509 (M^+, 10), 453 (04), 395 (06), 352 (13), 339 (100), 321 (53), 311 (06), 295 (38), 265 (32), 234 (29), 204 (12). HRMS (EI, 70 eV): calcd for $C_{30}H_{39}NO_6$ $[M]^+$: 509.27719; found: 509.27692.

Tris(6-methylheptyl) 3,3',3''-(1-methyl-1*H*-indole-2,3,6-triyl)triacrylate (24g). Product

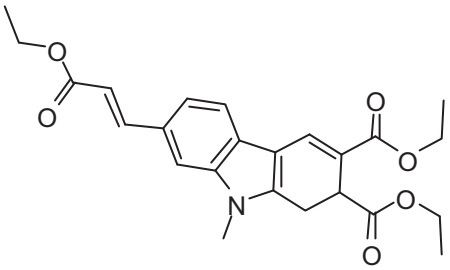


24g was synthesized starting with **15** (367 mg, 1.0 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), isooctyl acrylate (**16g**) (0.79 mL, 3.75 mmol), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 90 °C for 36 h following *general procedure D*, as a yellow oil (493 mg, 73%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.60-1.80 (m, 45H, aliphatic protons), 3.80 (s, 3H, NCH_3), 4.00-4.30 (m, 6H, $3CH_2O$), 6.30 (d, 1H, *J* = 15.7 Hz, ArH), 6.40 (d, 1H, *J* = 16.4 Hz, ArH), 6.50 (d, 1H, *J* = 16.1 Hz, ArH), 7.30-7.40 (m, 2H, ArH), 7.70 (d, 1H, *J* = 16.1 Hz, ArH), 7.80 (bd, 1H, *J* = 8.7 Hz, ArH), 7.80 (d, 1H, *J* = 16.8 Hz, ArH), 7.80 (d, 1H, *J* = 15.9 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.0, 14.6, 15.2 (CH_3), 20.1, 22.9, 24.5, 25.9, 26.7, 27.5 (CH_2), 31.2 (NCH_3), 45.6 (CH_2), 63.0, 63.8, 65.6 (CH_2O), 110.6 (CH), 114 (C), 117.0, 117.9, 121.3, 121.4, 125.3 (CH), 126.9, 130.7 (C), 130.9, 136.0 (CH), 138.3, 139.0 (C), 145 (CH), 165.9, 167.3, 167.7 (CO). IR (KBr): $\tilde{\nu}$ = 2955, 2927, 2870 (m), 1705, 1623 (s), 1561, 1533 (w), 1463 (s) 1380 (w), 1267, 1234, 1161 (s), 1036, 977, 845, 808, 768, 740, 609 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 677 (M^+, 90), 563 (16), 519 (60), 436 (38), 408 (69), 390 (59), 295 (30), 278 (34), 252 (22), 226 (06), 208 (10), 194 (11). HRMS (EI, 70 eV): calcd for $C_{42}H_{63}NO_6$ $[M]^+$: 677.46499; found: 677.463279.

9.1.9 Synthesis of 6-alkenyl-2,3-dihydrocarbazoles 25

Dimethyl 7-(3-methoxy-3-oxoprop-1-enyl)-9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (25a). 

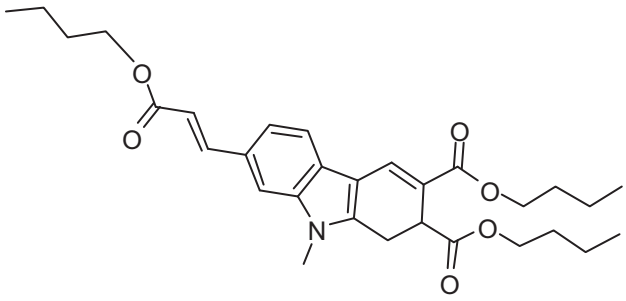
Compound **25a** was prepared starting with **15** (367 mg, 1.0 mmol), methyl acrylate (**16a**) (0.34 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h according to *general procedure B*, as a brownish highly viscous oil (302 mg, 79%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.00 (dd, 1H$_\alpha$, J = 8.5, 17.3 Hz, H-1), 3.50 (s, 3H, NCH_3), 3.60 (dd, 1H$_\beta$, J = 2.4, 17.3 Hz, H-1), 3.60 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.00 (dd, 1H$_\alpha$, J = 2.4, 8.8 Hz, H-2), 6.40 (d, 1H, J = 15.9 Hz, ArH), 7.30-7.40 (m, 2H, ArH), 7.50 (d, 1H, J = 8.6 Hz, ArH), 7.70 (d, 1H, J = 15.9 Hz, ArH), 7.90 (s, 1 H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.0 (CH_2), 29.7 (CH, C-4), 38.7 (NCH_3), 51.6 (OCH_3), 51.8 (OCH_3), 52.6 (OCH_3), 108.7, 110.4 (CH), 114.6, 115.9 (CH), 117.3, 120.0 (CH), 125.8, 127.4, 131.0 (CH), 137.2, 141.0, 145.0 (CH), 166.5, 166.8, 172.5 (C). IR (KBr): $\tilde{\nu}$ = 2999, 2950, 2846 (w), 1709 (s), 1628, 1605, 1270, 1231, 1188, 1166, 1110, 1040, 1060 (m), 973, 803 (s), 778 (s), 727 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 383 $[M]^+$, 353 (69), 323 (61), 293 (40), 284 (51), 189 (31), 102 (100), 77 (22). HRMS (EI, 70 eV): calcd for $C_{21}H_{21}NO_6$ $[M]^+$: 383.13689; found: 383.13632.

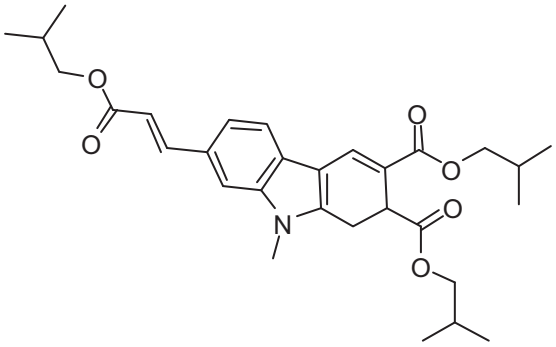
Diethyl 7-(3-ethoxy-3-oxoprop-1-enyl)-9-methyl-2,9-dihydro-1*H*-carbazole-2,3 dicarboxylate (25b). 

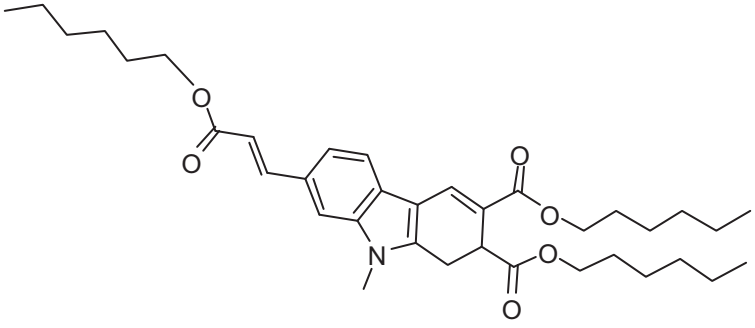
Product **25b** was synthesized starting with **15** (367 mg, 1.0 mmol), ethyl acrylate (**16b**) (0.41 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.1o mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h following *general procedure B*, as yellowish highly viscous oil (410 mg, 78%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.10 (t, 3H, J = 7.3 Hz, CH_3), 1.20 (t, 3H, J = 7.1 Hz, CH_3), 1.30 (t, 3H, J = 7.0 Hz, CH_3), 3.00 (dd, 1H$_\alpha$, J = 8.8, 17.2 Hz, H-1), 3.50 (dd, 1H$_\beta$, J = 2.4, 17.2 Hz, H-1), 3.60 (s, 3H, NCH_3), 3.80-4.10 (m, 3H and 1H$_\alpha$, H-2 and CH_2O), 4.10-4.30 (m, 4H, 2CH_2O), 6.40 (d, 1H, J = 15.9 Hz), 7.30 (m, 2H, ArH), 7.50 (d, 1H, J = 8.5 Hz, ArH), 7.70 (d, 1H, J = 15.8 Hz), 7.80 (s, 1H, H-4). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 (CH_3), 14.4 (CH_3), 14.5 (CH_3), 23.8 (CH_2), 29.8 (NCH_3), 38.8 (CH, C-2), 60.3 (CH_2O), 60.4 (CH_2O), 61.2 (CH_2O), 109.6 (C), 110.2, 115.9 (CH), 117.4 (C), 118.2, 120.8 (CH), 126.7, 128.3 (C), 131.5 (CH), 138.1, 141.8 (C), 145.7 (CH), 167.1,

167.3, 173.0 (CO). IR (KBr): $\tilde{\nu}$ = 2979, 2931 (m), 1731, 1697, 1606 (s), 1475, 1274 (m), 1227, 1168 (s), 1034, 982, 962, 852, 811, 771, 710 (s), 605, 582 (w) cm. MS (EI, 70 eV): *m/z* (%) = 425 (M^+, 76), 380 (12), 352 (100), 324 (23), 306 (98), 279 (77), 262 (30), 251 (16), 234 (92), 206 (22). HRMS (EI, 70 eV): calcd for $C_{24}H_{27}NO_6$ $[M]^+$: 425.18329; found: 425.18236.

Dibutyl 7-(3-butoxy-3-oxoprop-1-enyl)-9-methyl-2,9-dihydro-*1H*-carbazole-2,3-dicarboxylate (25c). Product **25c** was prepared, following *general procedure B*, starting with **15** (367 mg, 1.0 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), *n*-butyl acrylate (**16c**) (0.53 mL, 3.75 mmol), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h as a yellow solid (483 mg, 95%). Mp 112-114 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, 3H, *J* = 7.3 Hz, CH_3), 0.90 (t, 3H, *J* = 7.3 Hz, CH_3), 0.90 (t, 3H, *J* = 7.3 Hz, CH_3), 1.10-1.30 (m, 2H, CH_2), 1.30-1.50 (m, 6H, $3CH_2$), 1.60-1.70 (m, 4H, $2CH_2$), 3.00 (dd, $1H_\alpha$, *J* = 8.6, 17.2 Hz, H-1), 3.60 (dd, $1H_\beta$, *J* = 2.2, 17.2 Hz, H-1), 3.70 (s, 3H, NCH_3), 3.80-4.00 (m, 2H, CH_2O), 4.00 (dd, $1H_\alpha$, *J* = 1.9, 8.6 Hz, H-2), 4.10-4.20 (m, 4H, $2CH_2O$), 6.40 (d, 1H, *J* = 15.8 Hz, CH), 7.20-7.30 (m, 2H, ArH), 7.50 (d, 1H, *J* = 8.3 Hz, ArH), 7.70 (d, 1H, *J* = 16.1 Hz, ArH), 7.80 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6 (CH_3), 13.7 (CH_3), 13.8 (CH_3), 19.0 (CH_2), 19.2 (CH_2), 19.3 (CH_2), 24.0 (CH_2), 29.9 (CH_3), 30.4 (CH_2), 30.8 (CH_2), 31.0 (CH_2), 38.8 (NCH_3), 64.3 (CH_2O), 64.4 (CH_2O), 65.1 (CH_2O), 109.7 (C), 110.2, 116.0 (CH), 117.6 (C), 118.2, 120.8 (CH), 126.7, 128.4 (C), 131.4 (CH), 138.2, 141.8 (C), 145 (CH), 167.2, 167.5, 173.1 (CO). IR (KBr): $\tilde{\nu}$ = 2954, 2931 (m), 1721, 1703, 1676 (s), 1469, 1277 (m), 1219, 1167 (s), 1042, 998, 960, 854 (w), 821, 770, 735 (m), 605, 582, 553 (w) cm. MS (EI, 70 eV): *m/z* (%) = 509 ($[M]^+$, 78), 436 (14), 408 (72), 378 (20), 352 (100), 334 (94), 308 (18), 278 (31), 234 (94). HRMS (EI, 70 eV): calcd for $C_{30}H_{39}NO_6$ $[M]^+$: 509.27719; found: 509.276955.

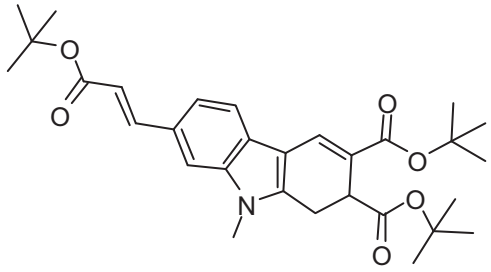


Di(isobutyl) 7-(3-isobutoxy-3-oxoprop-1-enyl)-9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (25d).  Product **25d** was prepared starting with **15** (367 mg, 1.0 mmol), *iso*-butyl acrylate (**16d**) (0.54 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h following *general procedure B*, as a yellow semisolid (363 mg, 72%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.70 (d, 6H, J = 6.7 Hz, $2CH_3$), 0.90 (dd, 12H, J = 3.4, 6.7 Hz, $4CH_3$), 1.70-1.80 (m, 1H, CH), 1.90-2.00 (m, 2H, CH), 3.00 (dd, $1H_\alpha$, J = 8.7, 17.2 Hz, H-1), 3.60 (dd, $1H_\beta$, J = 2.0, 17.2 Hz, H-1), 3.60-3.70 (m, 5H, NCH_3 and CH_2O), 3.90-4.00 (m, 4H, $2CH_2O$), 4.10 (dd, $1H_\alpha$, J = 2.0, 8.5 Hz, H-2), 6.20 (d, 1H, J = 15.8 Hz, ArH), 7.30 (d, 1H, J = 8.4 Hz, ArH), 7.40 (s, 1H, ArH), 7.60 (d, 1H, J = 8.2 Hz, ArH), 7.80 (d, 1H, J = 15.9 Hz, ArH), 7.90 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8 (CH_3), 18.9 (CH_3), 19.2 ($2CH_3$), 19.3 ($2CH_3$), 23.9 (CH_2), 27.6, 27.9, 28.0 (CH), 29.9 (NCH_3), 38.8 (CH, C-2), 70.5, 70.6, 71.2 (CH_2O), 109.7 (C), 110.3, 116.3 (CH), 117.6 (C), 118.2, 120.9 (CH), 126.7, 128.4 (C), 131.3 (CH), 138.2, 141.9 (C), 145.7(CH), 167.1, 167.5, 173.0 (CO). IR (KBr): $\tilde{\nu}$ = 2956, 2872 (w), 1715, 1693 (s), 1633, 1608, 1529, 1494, 1468, 1454, 1392, 1375, 1355, 1309, 1278 (m), 1228, 1205, 1166 (s), 1110, 1086, 1038, 1017, 989 (m), 942, 930, 852, 832, 799, 779, 756, 731, 705, 650, 615, 600, 550 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 507 ($[M-2]^+$ (carbazole), 100), 451 (36), 407 (22), 378 (78), 352 (29), 278 (18), 251 (11), 234 (25), 204 (12). HRMS (EI, 70 eV): calcd for $C_{30}H_{37}NO_6$ $[M-2]^+$ (carbazole): 507.26154; found: 507.26138.

Dihexyl 7-(3-(hexyloxy)-3-oxoprop-1-enyl)-9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (25e).  Product **25e** was prepared, starting with **15** (367 mg, 1.0 mmol), *n*-hexyl acrylate (**16e**) (0.66 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h following *general procedure B*, as a yellowish highly viscous oil (435 mg, 74%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (t, 3H, J = 6.9 Hz, CH_3), 0.80 (t, 3H, J =

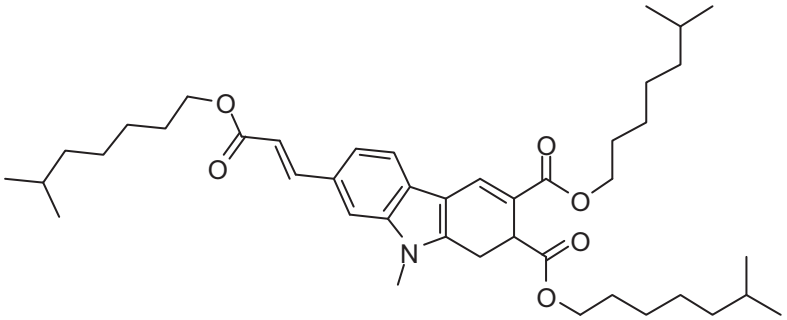
6.3 Hz, CH_3), 0.80 (t, 3H, *J* = 6.9 Hz, CH_3), 1.00-1.20 (m, 6H, $3CH_2$), 1.20-1.40 (m, 14H, $7CH_2$), 1.60-1.70 (m, 4H, $2CH_2$), 3.00 (dd, $1H_\alpha$, *J* = 8.6, 17.1 Hz, H-1), 3.60 (dd, $1H_\beta$, *J* = 2.1, 17.1 Hz, H-1), 3.70 (s, 3H, NCH_3), 3.80-4.00 (m, 2H, CH_2O), 4.00 (dd, $1H_\alpha$, *J* = 2.1, 8.7 Hz, H-2), 4.10 (t, 2H, *J* = 6.8 Hz, CH_2O), 4.20 (t, 2H, *J* = 6.8 Hz, CH_2O), 6.40 (d, 1H, *J* = 15.8 Hz, ArH), 7.30 (d, 1H, *J* = 8.4 Hz, ArH), 7.30 (s, 1H, ArH), 7.50 (d, 1H, *J* = 8.1 Hz, ArH), 7.70 (d, 1H, *J* = 16.0 Hz, CH), 7.80 (s, 1H, H-4). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.9 (CH_3), 14.0 ($2CH_3$), 22.4 (CH_2), 22.5 ($2CH_2$), 23.9, 25.4, 25.6, 25.7, 28.4, 28.7, 28.8 (CH_2), 29.9 (NCH_3), 31.3, 31.4, 31.5 (CH_2), 38.8, C(2)H), 64.5, 64.7, 65.3 (CH_2O), 109.7 (C), 110.2, 116.0 (CH), 117.6 (C), 118.2, 120.8 (CH), 126.7, 128.4 (C), 131.4 (CH), 138.1, 141.8 (C), 145,7 (CH), 167.1, 167.4, 173.1 (CO). IR (KBr): $\tilde{\nu}$ = 2954, 2928, 2857 (m), 1715, 1695, 1629, 1605 (s), 1558, 1527, 1488 (w), 1471(w), 1395, 1303, 1278 (m), 1245, 1228 (w), 1162 (s), 974, 908, 848, 821, 754, 730, 700, 607, 592 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 593 ($[M]^+$, 62), 492 (09), 464 (41), 406 (07), 380 (100), 362 (72), 336 (08), 278 (20), 251 (9), 234 (53). HRMS (EI, 70 eV): calcd for $C_{36}H_{51}NO_6$ $[M]^+$: 593.37109; found: 593.37046.

Di(*tert*-butyl) 7-(3-tert-butoxy-3-oxoprop-1-enyl)-9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (25f). Product **25f** was synthesized starting with **15** (367 mg, 1.0 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), *tert*-butyl acrylate (**16f**) (0.55 mL, 3.75 mmol), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h following *general procedure B*, as a yellow oil (401 mg, 79%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (s, 9H, $3CH_3$), 1.40 (s, 9H, $3CH_3$), 1.50 (s, 9H, $3CH_3$), 3.00 (dd, $1H_\alpha$, *J* = 8.7, 17.1 Hz, H-1), 3.60 (dd, $1H_\beta$, *J* = 2.2, 17.1 Hz, H-1), 3.70 (s, 3H, NCH_3), 3.90 (dd, $1H_\alpha$, *J* = 2.2, 8.7 Hz, H-2), 6.30 (d, 1H, *J* = 16.0 Hz, ArH), 7.30 (dd, 1H, *J* = 1.2, 8.2 Hz, ArH), 7.30 (s, 1H, ArH), 7.50 (d, 1H, *J* = 8.2 Hz, ArH), 7.60 (d, 1H, *J* = 15.9 Hz, ArH), 7.70 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6 (CH_2), 27.9, 28.2, 28.3 ($3CH_3$), 29.8 (NCH_3), 39.6 (CH, C-2), 78.9, 79.2, 80.1 (C-O), 108.5 (C), 109.9, 116.7, 117.2 (CH), 118.6, (C), 119.6 (CH), 125.6, 127.3 (C), 130 (CH), 137.1, 140.7 (C), 143.8 (CH), 165.5, 165.7, 171.2 (C=O). IR (KBr): $\tilde{\nu}$ = 2976, 2931 (w), 1705 (s), 1631, 1612, 1469, 1461, 1454, 1391 (w), 1366, 1277, 1255 (m), 1147 (s), 1113, 1080, 1041, 980, 846, 812, 791, 765, 608 (w) cm. MS (EI, 70 eV): *m/z* (%) = 509 ($[M]^+$, 02), 507 (33), 451 (51), 395 (39), 378 (15), 339 (95), 321 (100), 295 (17), 277 (34), 249 (80), 204 (12), 176 (5). HRMS (EI, 70 eV): calcd for $C_{30}H_{37}NO_6$ ($[M-2H]^+$ (carbazole): 507.26154; found: 507.26178.

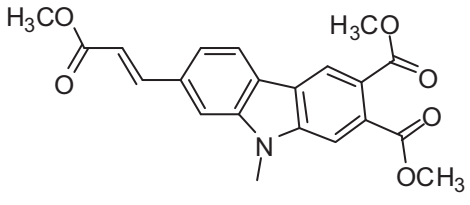
Bis(6-methylheptyl) 9-methyl-7-(3-(6-methylheptyloxy)-3-oxoprop-1-enyl)-2,9-dihydro-1H-carbazole-2,3-dicarboxylate (25g).



Compound **25g** was synthesized starting with **15** (367 mg, 1.0 mmol), isooctyl acrylate (**16g**) (0.79 mL, 3.75 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (1.10 mL, 8.0 mmol), DMF (5 mL) at 120 °C for 48 h following *general procedure B*, as a yellow oil (501 mg, 74%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.60-1.80 (m, 45H, aliphatic), 3.00 (dd, 1H$_\alpha$, J = 8.9, 17.2 Hz, H-1), 3.60-3.70 (m, 4H, 1 x H$_\beta$-1 and NCH_3), 3.90-4.30 (m, 7H, $3CH_2O$ and H$_\alpha$-2), 6.40 (d, 1H, J = 15.9 Hz, ArH), 7.30-7.40 (m, 2H, ArH), 7.50 (d, 1H, J = 8.8 Hz, ArH), 7.80 (d, 1H, J = 16.4 Hz), 7.90 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.2 ($2CH_3$), 14.1 ($2CH_3$), 14.4 ($2CH_3$), 19.6, 23.4, 29.1 (CH_2), 25.0, 27.0 (CH), 29.9 (CH_3N), 31.9 (CH), 38.8 (CH, C-2), 46.5, 46.6, 46.7 (CH_2), 64.9, 65.0, 65.3 (CH_2O), 108.7 (C), 109.2, 115.0 (CH), 116.6 (C), 117.2, 119.9 (CH), 125.7, 127.6 (C), 130.4 (CH), 137.2, 140.9 (C), 145.7 (CH), 166.1, 166.5, 172.1 (CO). IR (KBr): $\tilde{\nu}$ = 2955, 2927 (w), 1704, 1631, 1608 (s), 1562, 1527 (w), 1462, 1382, 1366, 1305 (m), 1267, 1228, 1206, 1161 (s), 1112, 1084, 1039, 847, 809, 780 (m), 609, 581 (w) cm. MS (EI, 70 eV): *m/z* (%) = 677 ([M]$^{+\cdot}$, 100), 563 (21), 548 (14), 519 (44), 434 (60), 408 (99), 390 (81), 234 (44). HRMS (EI, 70 eV): calcd for $C_{42}H_{63}NO_6$ [M]$^+$: 677.46499; found: 677.46337.

9.1.10 Synthesis of 6-alkenylcarbazoles 26

(E)-Dimethyl 7-(3-methoxy-3-oxoprop-1-enyl)-9-methyl-9*H*-carbazole-2,3-dicarboxylate (26a).



Starting with **25a** (100 mg) following *general procedure C*, **26a** was isolated as a yellow oil (98 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.77 (s, 3H, CH_3N), 3.83 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 3.91 (s, 3H, CH_3O), 6.51 (d, 1H J = 16.0 Hz), 7.44 (d, 1H, J = 8.2 Hz, ArH), 7.49 (s, 1H, ArH), 7.59 (s, 1H, ArH), 7.82 (d, 1 H, J = 16.0 Hz, ArH), 8.03 (d, 1H, J = 8.1 Hz, ArH), 8.48 (s, 1 H, ArH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 29.5 (CH_3N), 51.8, 52.5, 52.8 (CH_3O), 109.2, 109.3, 118.0, 120.1, 121.3 (CH) 121.7 (C), 122.9

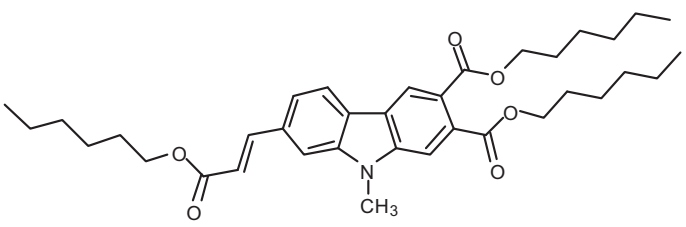
(CH), 123.3, 123.9, 131.4, 133.5, 142.3, 142.4 (C), 145.3 (CH), 167.4, 168.0, 169.4 (CO); IR (KBr): $\tilde{\nu}$ = 3047, 3004, 2917, 2848 (w), 1708 (s), 1627 (m), 1563, 1498 (w), 1431 (m), 1376 (w), 1351, 1314 (m), 1272, 1259, 1245, 1232, 1173, 1110 (s), 1080, 1039, 974, 964 (m), 930, 900, 881 (w), 839, 826,803, 777, 760 (m), 747, 729 (w), 711, 653, 603, 584 (m), 551(w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 381 ($[M]^+$, 100), 351 (16), 350 (80), 204 (11), 159 (42), 145 (22); HRMS: *m*/*z* calcd for $C_{21}H_{19}NO_6$ $[M]^+$: 381.12069; found: 381.120947.

(E)-Diethyl 7-(3-ethoxy-3-oxoprop-1-enyl)-9-methyl-9*H*-carbazole-2,3-dicarboxylate (26b). Starting with **25b** (100 mg) following *general procedure C*, **26b** was prepared as a yellow oil (98 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, 3H, *J* = 7.1 Hz, CH_3), 1.31 (t, 3H, *J* = 7.1 Hz, CH_3), 1.32 (t, 3H, *J* = 7.1 Hz, CH_3), 3.81 (s, 3H, CH_3N), 4.20 (q, 2H, *J* = 7.0 Hz, CH_2O), 4.31 (q, 2H, *J* = 7.0 Hz, CH_2O), 4.31 (q, 2H, *J* = 7.0 Hz, CH_2O), 6.51 (d, 1H, *J* = 15.7 Hz), 7.40 (d, 1H, *J* = 7.9 Hz, ArH), 7.41 (s, 1H, ArH), 7.51 (s, 1H, ArH), 7.80 (d, 1H, *J* = 15.7 Hz), 8.02 (d, 1H, *J* = 7.9 Hz, ArH), 8.41 (s,1H, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.1 (CH_3), 14.3 (CH_3), 14.4 (CH_3), 29.4 (CH_3N), 60.5, 61.4, 61.8 (CH_2O), 109.0, 109.2, 118.4, 120.0, 121.3 (CH) 122.1 (C) 122.7 (CH), 123.1, 123.8, 131.7, 133.4, 142.2, 142.3 (C), 145.0 (CH), 167.0, 167.5, 169.0 (CO). IR (KBr): $\tilde{\nu}$ = 2979, 2849 (m), 1703 (s), 1628, 1604, 1560, 1498, 1473, 1391, 1373, 1343, 130 (m), 1258, 1240, 1227 (s), 1173, 1108, 1078, 1039, 975 (m), 908, 874, 842, 804 (w), 779, 730, 664, 606, 585 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 423 ($[M]^+$, 99), 378 (6), 349 (41), 322 (6), 162 (7), 153 (100), 139 (58) ; HRMS: *m*/*z* calcd for $C_{24}H_{25}NO_6$ $[M]^+$: 423.16764; found: 423.16659.

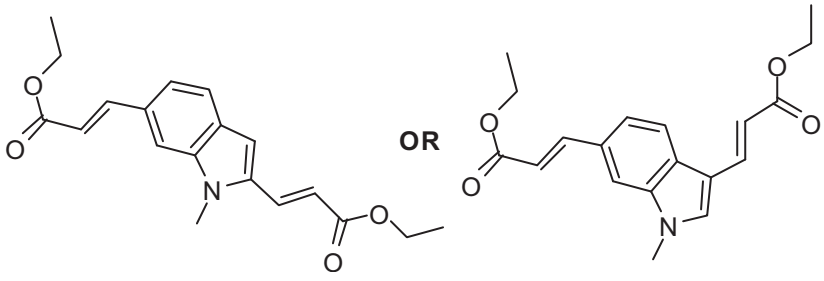
(E)-Dibutyl 7-(3-butoxy-3-oxoprop-1-enyl)-9-methyl-9*H*-carbazole-2,3-dicarboxylate (26c). Starting with **25c** (100 mg) following *general procedure C*, **26c** was prepared as a yellow oil (99 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, 3H, *J* = 7.4 Hz, CH_3), 0.91 (t, 3H, *J* = 7.4 Hz, CH_3), 0.93 (t, 3H, *J* = 7.4 Hz, CH_3), 1.10-1.31 (m, 2H, CH_2), 1.31-1.52 (m, 6H, $3CH_2$), 1.57-1.71 (m, 4H, $2CH_2$), 3.71 (s, 3H, CH_3N), 4.22 (t, 2H, *J* = 6.9 Hz, CH_2O), 4.31 (t, 2H, *J* = 6.6 Hz, CH_2O), 4.34 (t, 2H, *J* = 6.6 Hz, CH_2O), 6.52 (d, 1H, *J* = 16.1 Hz, CH), 7.42 (d, 1H, *J* = 8.5 Hz, ArH), 7.51 (s, 1H, ArH), 7.62 (s, 1H, ArH), 7.80 (d, 1H, *J* = 15.3 Hz, CH), 8.01 (d, 1H, *J* =

7.6 Hz, ArH), 8.51 (s, 1H, ArH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.8 ($3CH_3$), 19.3 ($3CH_2$), 29.5 (CH_3N), 30.6, 30.7, 30.8 (CH_2), 64.5, 65.4, 65.8 (CH_2O), 109.1, 109.2, 118.4, 120.1, 121.3 (CH), 122.3 (C), 122.7 (CH), 123.2, 123.9, 131.8, 133.5, 142.3, 142.4 (C), 145.0 (CH), 167.1, 167.6, 169.1 (CO). IR (KBr): $\tilde{\nu}$ = 2931 (w), 1706, 1627, 1602, 1563, 1500, 1455, 1387, 1343 (w), 1258 (m), 1223, 1163, 1106, 1077, 1038, 977, 901, 843, 810, 779, 738, 715, 663, 609, 583 (s) cm. (EI, 70 eV): *m/z* (%) = 507 ([M]$^+$, 100), 434 (6), 378 (33), 332 (7), 278 (4); HRMS: *m*/*z* calcd for $C_{30}H_{37}NO_6$ [M]$^+$: 507.26154; found: 507.26156.

(E)-Dihexyl 7-(3-(hexyloxy)-3-oxoprop-1-enyl)-9-methyl-9*H*-carbazole-2,3-dicarboxylate (26e). Starting with **25e** (100 mg) following *general procedure C*, **26e** was isolated as yellow oil (98 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, 3H, *J* = 6.9 Hz, CH_3), 0.82 (t, 6H, *J* = 7.0 Hz, $2CH_3$), 1.21-1.33 (m, 12H, $6CH_2$), 1.30-1.41 (m, 6H, $3CH_2$), 1.61-1.70 (m, 6H, $3CH_2$), 3.81 (s, 3H, CH_3N), 4.10 (t, 2H, *J* = 6.7 Hz, CH_2O), 4.21 (t, 2H, *J* = 7.0 Hz, CH_2O), 4.32 (t, 2H, *J* = 7.0 Hz, CH_2O), 6.52 (d, 1H, *J* = 16.2 Hz), 7.41 (d, 1H, *J* = 8.1 Hz, ArH), 7.51 (s, 1H, ArH), 7.63 (s, 1H, ArH), 7.81 (d, 1H, *J* = 16.2 Hz), 8.01 (d, 1H, *J* = 8.1 Hz, ArH), 8.41 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0 ($3CH_3$), 22.6 ($4CH_2$), 24.5 ($3CH_2$), 27.5, 27.6, 27.7 (CH_2), 28.4 (CH_3N), 30.5 ($2CH_2$), 63.8, 64.7, 65.1 (CH_2O), 108,0, 108.2, 117.4, 119.0 , 120.3 (CH), 121.2 (C), 121.7 (CH), 122.1, 122.9, 130.8, 132.4, 141.2 ,141.3 (C), 144.0 (CH), 166.1, 166.6, 168.1 (CO). IR (KBr): $\tilde{\nu}$ = 2927 (w), 1708 (s), 1627, 1602, 1563, 1500, 1455, 1388, 1369, 1343, 1305 (m), 1259, 1224, 1163, 1108 (s), 1078, 1038, 979, 905, 845, 810, 781, 725, 663, 642, 609, 583,543 (w) cm. (EI$^+$, 70 eV): *m/z* (%) = 591 ([M]$^+$, 100), 406 (26), 322 (05), 43 (08); HRMS: *m*/*z* calcd for $C_{36}H_{49}NO_6$ [M]$^+$: 591.35544; found: 591.35593.



(2E,2'E)-Diethyl 3,3'-(1-methyl-1*H*-indole-2,6-diyl)diacrylate OR (2E,2'E)-diethyl 3,3'-(1-methyl-1*H*-indole-3,6-diyl)diacrylate (27). Product **27** was found as byproduct of **25b** as a light brown oil**.** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19-1.31 (m, 6H, $2CH_3$), 3.78 (s, 3H, NCH_3), 4.16-4.26 (m, 4H, $2CH_2O$), 6.41



(d, 1H, *J* = 15.9 Hz, CH), 6.44 (d, 1H, , *J* = 15.7 Hz, CH), 6.87 (s, 1H, ArH), 7.27 (dd, *J* = 1.2, 8.5, ArH), 7.3 (s, 1H, ArH), 7.50 (d, 1H, *J* = 8.5 Hz, ArH), 7.70 (d, 1H, *J* = 15.4 Hz, ArH), 7.73 (d, 1H, *J* = 15.4 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.4, 30.1 (NCH_3), 60.4, 60.7 (CH_2O), 102.7, 110.5, 116.6, 119.4, 119.9, 121.6 (CH), 128.1, 128.9 (C), 131.0 (CH), 136.0, 138.0 (C), 144.7 (CH), 165.8, 166.3 (CO). IR (KBr): $\tilde{\nu}$ = 2978, 2929, 2852 (w), 1705, 1699, 1628, 1604 (s), 1464, 1362, 1302, 1284, 1261, 1242 (m), 1157, 1137, 1090, 1032, 975, 964 (s), 867 (m), 805 (s), 744, 700, 646, 600, 582 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 327 (M^+, 100), 282 (15), 255 (04), 180 (05). HRMS (EI, 70 eV): calcd for $C_{23}H_{29}NO_4$ $[M]^+$: 327.14706; found: 327.14715.

9.1.10 (2E,2'E)-Dibutyl 3,3'-(3-formyl-1-methyl-1*H*-indole-2,6-diyl)diacrylate 30

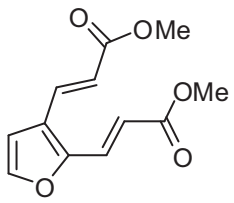
Product **30** was prepared starting with **29** (158 mg, 0.5 mmol), butyl acrylate **(16c)** (0.18 mL, 1.25 mmol), $Pd(OAc)_2$ (11 mg, 5 mol-%), SPhos (10 mol-%), NEt_3 (0.50 mL, 4.0 mmol), DMF (5 mL) at 120 °C for 36 h following *general procedure D*, as a brownish oil (147 mg, 72%)**.** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, 3H, *J* = 7.4 Hz, CH_3), 0.90 (t, 3H, *J* = 7.3 Hz, CH_3), 1.42-1.61 (m, 4H, $2CH_2$), 1.63-1.71 (m, 4H, $2CH_2$), 3.71 (s, 3H, NCH_3), 4.18 (t, 2H, *J* = 6.9 Hz, CH_2O), 4.19 (t, 2H, *J* = 6.6, CH_2O), 6.46 (d, 1H, *J* = 15.9 Hz, CH), 6.51 (d, 1H, , *J* = 16.1 Hz, CH), 7.42-7.50 (m, 2H, ArH), 7.73 (d, 1H, *J* = 16.2 Hz, CH), 8.30 (d, 1H, *J* = 7.4 Hz, ArH), 10.13 (s, 1H, CHO). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7, 13.8 (CH_3), 19.1, 19.2, 30.6, 30.8 (CH_2), 31.3 (NCH_3), 64.5, 65.3 (CH_2O), 110.2 (CH), 117.1 (C), 118.1, 122.6, 123.1 (CH), 127.2 (C), 128.6, 129.6 (CH), 131.6, 138.1, 143.1 (C), 144.7 (CH), 165.4, 167.1 (CO), 184.7 (CH). IR (KBr): $\tilde{\nu}$ = 2958, 2932, 2873 (m), 1706, 1617, 1476 (s), 1364, 1327 (w), 1274, 1235, 1166 (s), 1132, 1115, 1061, 1046, 1027, 968, 844, 8215 (m), 740 (s), 561 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 411 (M^+, 02), 384 (02), 379 (12), 310 (100), 254 (09). HRMS (ESI^+): calcd for $C_{24}H_{30}NO_5$ [M+H]: 412.21185; found: 412.21191.

9.2 Efficient Synthesis of Functionalized Benzofurans by Domino ′Twofold Heck / 6π-Electrocyclization′ Reactions

9.2.1 Synthesis of 2,3-bis(alkenyl)furans 32

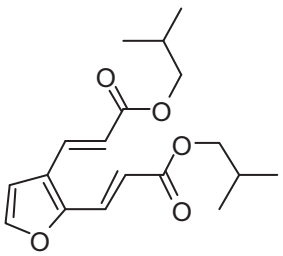
General procedure A for the synthesis of **32a-h:**. In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 5 mol %) and XPhos or SPhos (10 mol %) in DMF (5 mL) was purged with Ar and stirred at 20 °C to give a yellowish or brownish clear solution. To the stirred solution were added 2, 3-dibromofuran (**31**) (0.12 ml, 1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the acrylate (2.5 mmol). The reaction mixture was stirred at 120 ˚C (or mentioned) for 36h. 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 dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes/EtOAc).

(2E,2'E)-Dimethyl 3,3'-(furan-2,3-diyl)diacrylate (32a). Following the *general procedure A*



32a was isolated as light yellow oil **(**172 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3H, CH_3O), 3.74 (s, 3H, CH_3O), 6.16 (d, 1H, *J* = 15.8 Hz, CH), 6.34 (d, 1H, *J* = 15.8 Hz, CH), 6.57 (d, 1H, *J* = 2.2 Hz, ArH), 7.38 (d, 1H, *J* = 1.7 Hz, ArH), 7.55 (d, 1H, *J* = 15.8 Hz, CH), 7.62 (d, 1H, *J* = 15.8 Hz, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 51.79, 51.85 (CH_3O), 109.4, 117.8, 119.8 (CH), 124.8 (C), 127.4, 132.7, 145.2 (CH), 150.5 (C), 166.9, 167.0 (CO). IR (KBr): $\tilde{\nu}$ = 3100, 3108 (w), 2850 (m), 1711 (s), 1676 (w), 1631 (m), 1510 (w), 1445, 1292 (m), 1275, 1245, 1178 (s), 1035, 1970, 872, 749 (m), 861, 756 (w), 721 (m), 530 (m), cm. GC-MS (EI, 70 eV): *m/z* (%) = 236 ($[M]^+$, 11), 230 (14), 213 (29), 187 (100), 173 (05), 151 (06), 111 (04). HRMS (EI, 70 eV): calcd for $C_{12}H_{12}O_5$ $[M]^+$: 236.06847; found: 236.06801.

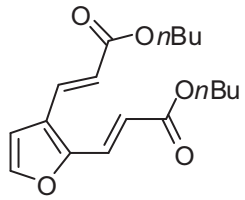
(2E,2'E)-Isobutyl 3,3'-(furan-2,3-diyl)diacrylate (32c). Following the *general procedure A*



32c was isolated as light yellow oil **(**297 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, 12H, *J* = 6.8 Hz, $4CH_3$), 1.86-1.97 (m, 2H, 2CH), 3.90 (d, 2H, *J* = 6.7 Hz, CH_2O), 3.91 (d, 2H, *J* = 6.7 Hz, CH_2O), 6.17 (d, 1H, *J* = 15.6 Hz, CH), 6.35 (d, 1H, *J* = 15.6 Hz, CH), 6.58 (d, 1H, *J* =1.8 Hz, ArH), 7.37 (d, 1H, *J* = 2.0 Hz, ArH), 7.55 (d, 1H, *J* = 15.6 Hz, CH), 7.59 (d, 1H, *J* = 15.6 Hz, CH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.1 ($4CH_3$), 27.8 (2CH), 70.7, 70.8 (CH_2O), 109.3, 118.2, 120.3 (CH), 124.7 (C), 127.2, 132.4,

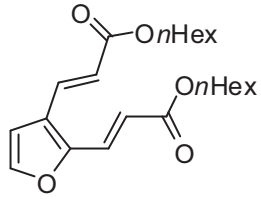
145.1 (CH), 150.5 (C), 166.4, 166.5 (CO). IR (KBr): $\tilde{\nu}$ = 3000, 3119 (w), 2935 (s), 2852 (m), 1711 (s), 1631 (m), 1579, 1509 (w), 1290 (m), 1272, 1257 (s), 1045, 1968, 832, 740 (m), 8761, 746 (w), 658, 606 (w), 530 (m), cm. GC-MS (EI, 70 eV): *m/z* (%) = 320 ([M]$^+$, 71), 305 (18), 290 (11), 262 (11), 249 (20), 189 (17), 153 (19). HRMS (EI, 70 eV): calcd for $C_{18}H_{24}O_5$ [M]$^+$: 320.16237; found: 320.16360.

(2E, 2'E)-Dibutyl 3,3'-(furan-2, 3-diyl) Diacrylate (32d). Following the general procedure



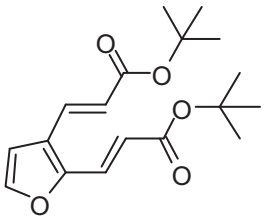
32d was isolated as light yellow oil (249 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 6H, *J* = 7.3 Hz, $2CH_3$), 1.28-1.40 (m, 4H, $2CH_2$), 1.56-1.65(m, 4H, $2CH_2$), 4.10-4.15 (m, 4H, $2CH_2O$), 6.14 (d, 1H, *J* = 15.6 Hz, CH), 6.32 (d, 1H, *J* = 15.6 Hz, CH), 6.56 (d, 1H, *J* =1.9 Hz, ArH), 7.36 (d, 1H, *J* = 2.0 Hz, ArH), 7.52 (d, 1H, *J* = 15.6 Hz, CH), 7.57 (d, 1H, *J* = 15.5 Hz, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.6 ($2CH_3$), 19.1 ($2CH_2$), 30.7 ($2CH_2$), 64.4, 64.5 (CH_2O), 109.3, 118.2, 120.3 (CH), 124.7 (C), 127.2, 132.3, 145.1 (CH), 150.5 (C), 166.5, 166.6 (CO). IR (KBr): $\tilde{\nu}$ = 3133, 3118 (w), 2925 (s), 2850 (m), 1711 (s), 1676 (w), 1631 (m), 1549, 1500 (w), 1445 (m), 1290 (m), 1275, 1255, 1168 (s), 1035, 1969, 862, 749 (m), 8761, 746 (w), 720 (m), 648, 606 (w), 539 (m), cm. GC-MS (EI, 70 eV): *m/z* (%) = 320 ([M]$^+$, 71), 264 (08), 247 (23), 190 (17), 163 (86), 147 (100), 134 (11), 119 (53). HRMS (EI, 70 eV): calcd for $C_{18}H_{24}O_5$ [M]$^+$: 320.16238; found: 320.16236.

(2E,2'E)-Dihexyl 3,3'-(furan-2,3-diyl)diacrylate (32e). Following the *general procedure A*



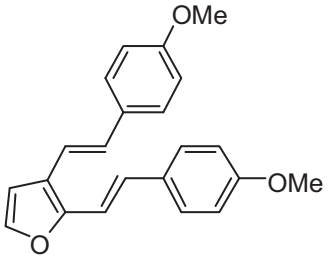
32e was isolated as light yellow oil (331 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83-0.86 (m, 6H, $2CH_3$), 1.16-1.34 (m, 12H, $6CH_2$), 1.58-1.68 (m, 4H, $2CH_2$), 4.13 (t, 2H, *J* = 6.8 Hz, CH_2O), 4.14 (t, 2H, *J* = 6.7 Hz, CH_2O), 6.16 (d, 1H, *J* = 15.5 Hz, CH), 6.35 (d, 1H, *J* = 15.5 Hz, CH), 6.57 (d, *J* = 2.4 Hz, 1H, ArH), 7.37 (d, 1H, *J* = 1.9 Hz, ArH), 7.55 (d, 1 H, *J* = 15.5 Hz, CH), 7.60 (d, 1H, *J* = 15.6 Hz, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 22.5, 22.6, 28.7, 31.4 ($2CH_2$), 64.9, 65.0 (OCH_2), 109.4, 118.3, 120.3 (CH), 124.7 (C), 127.2, 1324, 145.1 (CH), 150.5 (C), 166.5, 166.6 (CO). IR (KBr): $\tilde{\nu}$ = 3122, 3108 (w), 2921, 1711 (s), 1631 (m), 1549, 1500 (w), 1445 (m), 1377 (w), 1292 (m), 1275, 1255, 1167 (s), 1069 (w), 1035 (m), 1018 (w), 1959 (m), 933 (w), 862 (m), 825 (w), 749 (m), 8761, 746 (w), 721 (m), 648, 607 (w), 538 (m), cm. GC-MS (EI, 70 eV): *m/z* (%) = 376 ([M]$^+$, 01), 345 (08), 291 (03), 206 (10), 189 (100), 162 (08). HRMS (EI, 70 eV): calcd for $C_{22}H_{32}O_5$ [M]$^+$: 376.22497; found: 376.22397.

(2E,2'E)-*Tert*-butyl 3,3'-(furan-2,3-diyl)diacrylate (32f). Following the general procedure



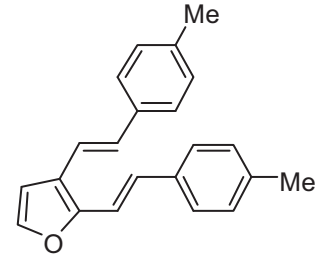
32f was isolated as light yellow oil **(**252 mg, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46 (s, 18H, $6CH_3$), 6.03 (d, 1H, *J* = 16.1 Hz, CH), 6.27 (d, 1H, *J* = 15.5 Hz, CH), 6.54 (d, 1H, *J* = 2.3 Hz, ArH), 7.34 (d, 1H, *J* = 2.3 Hz, ArH), 7.44 (d, 1H, *J* = 15.5 Hz, CH), 7.45 (d, 1H, *J* = 15.7 Hz, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.2 ($6CH_3$), 80.7, 80.8 (C), 109.4, 120.1, 122.1 (CH), 124.4 (C), 126.5, 131.6, 144.8 (CH), 150.5 (C), 165.8, 165.9 (CO). IR (KBr): $\tilde{\nu}$ = 2976, 2931 (m), 1705 (s), 1636, 1454, 1392, 1367, 1313, 1283, 1253 (m), 1146 (s), 1018, 977, 844, 767, (m), 711, 685, 594, 574 (w), cm. GC-MS (EI, 70 eV): *m/z* (%) = 320 ($[M]^+$, 15), 247 (11), 208 (100), 163 (31), 147 (21), 119 (26). HRMS (EI, 70 eV): calcd for $C_{18}H_{24}O_5$ $[M]^+$: 320.16183; found: 320.16232.

2,3-Bis(4-methoxystyryl)furan (32g). Following the general procedure **32g** was isolated as



light yellow oil **(**299 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.74 (s, 6H, $2OCH_3$), 6.56 (d, *J* = 2.1 Hz, 1H, ArH), 6.71 (d, 1H, *J* = 16.2 Hz, CH), 6.82 (d, *J* = 8.8 Hz, 4H, ArH), 6.87-6.92 (m, 3H), 7.25 (d, *J* = 2.0 Hz, 1H, ArH), 7.34 (d, 2H, *J* = 8.6 Hz, ArH), 7.38 (d, 2H, *J* = 8.7 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 108.7, 112.1, 114.1, 114.2, 116.0 (CH), 121.6 (C), 126.8, 127.4, 127.7, 128.1 (CH), 130.0, 130.3 (C), 142.1(CH), 150.0, 159.2, 159.4 (C). IR (KBr): $\tilde{\nu}$ = 3030, 2996, 2992, 2930, 2963, 2833 (w), 1599, 1571, 1508, 1497, 1456, 1436, 1417, 1298, 1290, 1267 (m), 1246 (s), 1174, 1145, 1109, 1061, 958, 934, 895, 852, 845 (m), 815 (s), 740, 720 (m), 696, 659, 679, 637, 610, 561, 547 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 332 ($[M]^+$, 100), 207 (20), 166 (10), 121 (17). HRMS (EI, 70 eV): calcd for $C_{22}H_{20}O_3$ $[M]^+$: 332.14070; found: 332.140727.

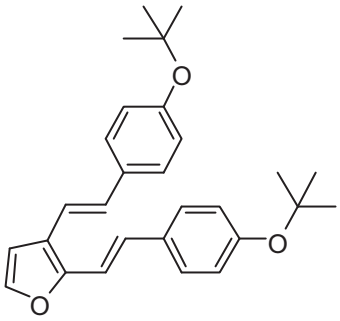
2,3-Bis(4-methylstyryl)furan (32h). Following the *general procedure A* **32h** was isolated as



light yellow oil **(**270 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 6H, $2CH_3$), 6.54 (d, *J* = 2.0 Hz, 1H, ArH), 6.68 (d, 1H, *J* = 16.2 Hz, CH), 6.97 (m, 3H), 7.05 (d, *J* = 7.9 Hz, 4H, ArH), 7.22 (d, 1H, *J* = 2.0 Hz, ArH), 7.28 (d, 2H, *J* = 7.9 Hz, ArH), 7.29 (d, *J* = 8.2 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3, 21.4 (CH_3), 108.8, 113.1, 117.1 (CH), 122.0 (C), 126.2, 126.5, 127.4, 128.7, 129.4, 129.5 (CH),

134.4, 134.8, 137.3, 137.7 (C), 142.3 (CH), 150.1 (C). IR (KBr): $\tilde{\nu}$ = 3020, 2992, 2963, 2833 (w), 1599, 1571, 1508, 1498, 1456, 1436, 1418, 1298, 1290 (m), 1246, 1174 (s), 1029, 959, 815, 740, 720 (m), 659, 679, 638, 610, 562, 548 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 300 ($[M]^+$, 100), 245 (08), 281 (33), 216 (10), 198 (10), 204 (08). HRMS (EI, 70 eV): calcd for $C_{22}H_{20}O$ $[M]^+$: 300.15142; found: 300.15133.

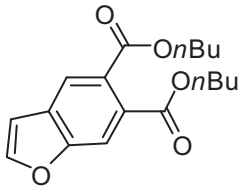
2,3-Bis(4-*tert*-butoxystyryl)furan (32i). Following the *general procedure A* **32i** was isolated as light yellow oil (361 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (s, 18H, $6CH_3$), 6.54 (d, *J* = 2.0 Hz, 1H, ArH), 6.67 (d, 1H, *J* = 16.1 Hz, CH), 6.8-6.94 (m, 7H), 7.23 (d, *J* = 2.0 Hz, 1H, ArH), 7.30 (d, 2H, *J* = 8.5 Hz, ArH), 7.31 (d, 2H, *J* = 8.6 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.9 ($6CH_3$), 78.7, 78.8 (O-C), 108.8, 112.9, 116.9 (CH), 121.8 (C), 124.2, 124.3, 126.7, 126.9, 127.0, 128.3 (CH), 132.4, 132.7 (C), 142.3 (CH), 150.1, 155.0, 155.3 (C). IR (KBr): $\tilde{\nu}$ = 3033, 2972, 2929, 2872, 1623 (w), 1503, 1362, 1271 (m), 1159 (s), 1102, 1060, 1029, 968, 959, 947 (w), 891, 864, 832, 743, 690, 677, 591 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 416 ($[M]^+$, 14), 360 (07), 304 (100), 210 (07). HRMS (EI, 70 eV): calcd for $C_{28}H_{32}O_3$ $[M]^+$: 416.23460; found: 416.235161.



9.2.2 Synthesis of 5,6-disubstitutedbenzofuranfurans 33

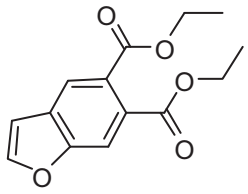
General procedure B for the synthesis of benzofurans **33a-d.** A diphenyl ether solution (3 mL) of **32a-d** (0.5 mmol) was stirred at 200 °C for 24 h (or 12h) in a pressure tube. The solution was allowed to cool to 20 °C and Pd/C (30 mg, 10 mol %) was added. The solution was stirred at 200 °C (or mentioned) for 24 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).

Dibutyl benzofuran-5,6-dicarboxylate (33d). 33d was prepared starting with **32d** (160 mg, 0.5 mmol), following *the general procedures A and B*, as a light yellow highly viscous oil (151 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 6H, *J* = 7.3 Hz, $2CH_3$), 1.30-1.43 (m, 4H, $2CH_2$), 1.60-1.69 (m, 4H, $2CH_2$), 4.24 (t, 2H, *J* = 6.7 Hz, CH_2O), 4.25 (t, 2H, *J* = 6.7 Hz, CH_2O), 6.74 (d, 1H, *J* = 2.2 Hz, ArH), 6.67 (d, 1H, *J* = 2.2 Hz, ArH), 7.78 (s, 1H, ArH), 7.88 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7 ($2CH_3$), 19.2 ($2CH_2$), 30.6 ($2CH_2$), 65.5, 65.6



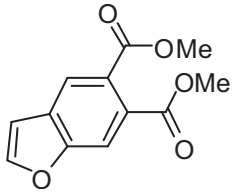
(CH_2O), 107.0, 112.5, 122.5 (CH), 127.8, 128.7, 129.4 (C), 148.1 (CH), 155.1 (C), 167.5, 168.0 (CO). IR (KBr): $\tilde{\nu}$ = 3144, 3117 (w), 2959, 2921, 2852 (m), 1711 (s), 1631, 1462, 1446, 1377, 1292 (w), 1275, 1255, 1223, 1169 (m), 1036, 969, 862, 794, 721, 539 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 318 ($[M]^+$, 05), 245 (05), 189 (100), 16 (10). HRMS (ESI^+): calcd for $C_{18}H_{22}O_5$ $[M]^+$: 318.14623; found: 318.14626.

Diethyl benzofurane-5,6-dicarboxylate (33b). Following the general procedure **33b** was



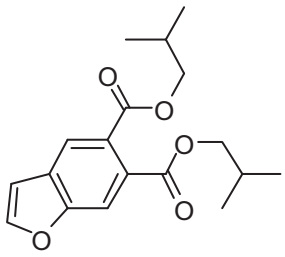
isolated as light yellow oil **(**122 mg, 93%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 6H, *J* = 7.5 Hz, $2CH_3$), 4.30-4.35 (m, 4H, $2CH_2O$), 6.77 (d, 1H, *J* = 2.2 Hz, ArH), 7.69 (d, 1H, *J* =2.2 Hz, ArH), 7.81 (s, 1H, ArH), 7.91 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.1 ($2CH_3$), 61.6, 61.7 (CH_2O), 107.3, 112.4, 122.5 (CH), 127.8, 128.8, 129.5 (C), 148.2 (CH), 155.2 (C), 167.6, 168.0 (CO). IR (KBr): $\tilde{\nu}$ = 3411, 3120, 2931, 2872 (w), 1715 (s), 1619, 1586, 1529 (w), 1488, 1465 (m), 1391 (w), 1367 (m), 1300, 1219, 1149, 1125, 1102, 1039 (s), 896, 859, 772, 691, 588 (m), cm. GC-MS (EI, 70 eV): *m/z* (%) = 262 ($[M]^+$, 18), 234 (04), 217 (19), 189 (100), 175 (05), 145 (06), 133 (04), 116 (07). HRMS (EI, 70 eV): calcd for $C_{14}H_{14}O_5$ $[M]^+$: 262.08458; found: 262.084126.

Dimethyl benzofurane-5,6-dicarboxylate (**33a**). Following the general procedure **33a** was



isolated as light yellow oil **(**105 mg, 90%). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3H, CH_3O), 3.82 (s, 3H, CH_3O), 6.75 (d, 1H, *J* = 2.1 Hz, ArH), 7.63 (d, 1H, *J* =2.2 Hz, ArH), 7.80 (s, 1H, ArH), 7.90 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 52.6, 52.7 ($2CH_3O$), 107.0, 112.6, 122.6 (CH), 127.4, 128.2, 129.6 (C), 148.3 (CH), 155.2 (C), 167.9, 168.4 (CO). IR (KBr): $\tilde{\nu}$ = 3010, 3121, 2850 (w), 1723, 1716 (s), 1583, 1486, 1435, 1529 (w), 1229, 1202, 1165, 1071, 1021, 981, 865, 797, 750, 692, 666 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 234 ($[M]^+$, 10), 204 (04), 215 (19), 187 (100), 171 (05), 149 (06), 111 (04). HRMS (EI, 70 eV): calcd for $C_{12}H_{10}O_5$ $[M]^+$: 234.05282; found: 234.05277.

Diisobutyl benzofuran-5,6-dicarboxylate (33c). Following the general procedure **33c** was isolated as light yellow oil **(**146 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, 6H, *J* = 6.7 Hz, $2CH_3$), 0.93 (d, 1 H, *J* = 6.8 Hz, $2CH_3$), 1.96-2.01 (m, 2H, 2CH), 4.02 (d, *J* = 6.7 Hz, 4H, CH_2O), 4.03 (d, 2H, *J* = 6.7 Hz, CH_2O), 6.76 (d, 1H, *J* = 2.2 Hz, ArH), 7.71(d, 1H, *J* =2.1 Hz, ArH), 7.81 (s, 1H, ArH), 7.91 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ= 19.1 ($4CH_3$), 27.5 (2CH), 71.8, 71.9 (CH_2O), 107.0, 112.6, 122.6 (CH), 127.9, 128.8, 129.5 (C), 148.2 (CH), 155.2 (C), 167.6, 168.0 (CO). IR (KBr): $\tilde{\nu}$ = 3434 (w), 2959, 2874 (m), 1769 (w), 1716 (s), 1614, 1585, 1529 (w), 1468, 1377 (m), 1305, 1218 (s), 1125 (m), 1103, 1035, 938 (s), 893, 773 (m), 691, 632 (w), cm. GC-MS (EI, 70 eV): *m/z* (%) = 318 ([M]$^+$, 01), 263 (03), 189 (100), 162 (09), 144 (04), 133 (02), 116 (06). HRMS (ESI$^+$): calcd for $C_{18}H_{22}O_5$ [M]$^+$: 318.14674;found: 318.14664.



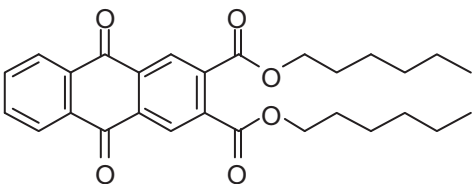
9.3 Synthesis of Anthraquinones, Fluorenone and Benzocoumarine by Domino ′Twofold Heck / 6π-Electrocyclization′ Reactions

9.3.1 Synthesis of mono- and disubstituted anthraquinones

General procedure for the synthesis of 35a-c and **36bc**.

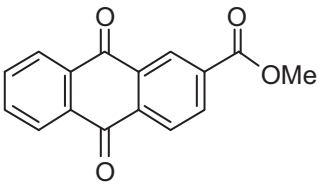
In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 5 mol%) and XPhos (48 mg, 0.10 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C to give a yellowish or brownish clear solution. To the stirred solution were added **34** (316 mg, 1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the alkene **16a,e,h** (2.5 equiv.). The reaction mixture was stirred at 90 °C (for **36b**) or 110 °C (for **35a-c**) for 8 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), concentrated in vacuo and the residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **36b** or **35a-c**.

Dihexyl 9,10-dioxo-9,10-dihydroanthracene-2,3-dicarboxylate (**36e**). Starting with **34** (316 mg, 1.0 mmol), **36b** was isolated as a violet highly viscous oil (348 mg, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, 6H, *J* = 7.2 Hz, $2CH_3$), 1.25-1.38 (m, 12H, $6CH_2$), 1.66-1.76 (m, 4H, $2CH_2$), 4.31 (t, 4H,

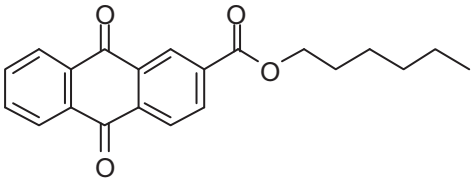


J = 6.9 Hz, $2CH_2O$), 7.77-7.81 (m, 2H, ArH), 8.26-8.30 (m, 2H, ArH), 8.55 (s, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 27.5, 25.6, 28.5, 31.4 ($2CH_2$), 66.6 ($2CH_2O$), 127.6, 128.1 (2CH), 133.3, 134.6 (2C), 134.7 (2CH), 137.0 (2C), 166.2 (2CO), 181.7 (2CO). IR (KBr): $\tilde{\nu}$ = 3061, 2957, 2930, 2875 (m), 1728, 1680 (s), 1647, 1615 (w) 1590, 1520 (m), 1411, 1393, 1370, 1343 (w), 1250 (s), 1170, 1120, 1040, 957, 800, 783 (m), 711 (s), 575 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 464 ($[M]^+$, 02), 381 (17), 279 (100), 207 (04%). HRMS (ESI^+): calcd for $C_{28}H_{32}O_6$ $(M)^+$: 464.21934; found: 464.220607.

Methyl 9,10-dioxo-9,10-dihydroanthracene-2-carboxylate (**35a**). Starting with **34** (316 mg, 1.0 mmol), **35a** was isolated as a violet highly viscous oil (152 mg, 57%). The synthesis of **36a** has been previously reported.[82] ^1H NMR (300 MHz, $CDCl_3$): δ = 3.93 (s, 3H, CH_3O), 7.71-7.77 (m, 2H, ArH), 8.20-8.35 (m, 4H, ArH), 8.83 (dd, 1H, J = 0.5, 1.2 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.7 (CH_3O), 127.3, 127.4, 127.5, 128.6 (CH), 133.3, 133.4, 133.5(C), 134.3, 134.4, 135.5 (CH), 135.1, 136.0 (C), 165.5 (CO), 182.2, 182.5 (CO). IR (KBr): $\tilde{\nu}$ = 2957, 2828, 2870 (m), 1720, 1680 (s), 1640, 1615 (w) 1580, 1519, 1470 (m), 1411, 1389, 1386, 1370 (w), 1253 (s), 1171, 1144, 1100, 1034, 956, 947, 792, 782 (m), 711 (s), 655, 576 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 266 ($[M]^+$, 57), 235 (100), 207 (21), 151 (34%). HRMS (ESI^+): calcd for $C_6H_{10}O_4$ $(M)^+$: 266.05791; found: 266.05666.



Hexyl 9,10-dioxo-9,10-dihydroanthracene-2-carboxylate (35b). Starting with **34** (316 mg, 1.0 mmol), **35b** was isolated as a violet highly viscous oil (84 mg, 25% + **36b**). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, 3H, J = 7.1 Hz, CH_3), 1.28-1.31 (m, 6H, $3CH_2$), 1.69-1.79 (m, 2H, CH_2), 4.32 (t, 2H, J = 6.7 Hz, CH_2O), 7.71-7.77 (m, 2H, ArH), 8.21-8.35 (m, 4H, ArH), 8.83 (dd, 1H, J = 0.4, 1.6 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.5, 24.6, 27.6, 30.4 (CH_2), 65.1 (CH_2O), 127.3, 127.4, 127.5, 128.5 (CH), 132.3, 132.4, 132.5(C), 134.3, 134.4, 135.5 (CH), 136.5, 136.0 (C), 164.0 (CO), 181.2, 181.5 (CO). IR (KBr): $\tilde{\nu}$ = 2999, 2957, 2930 (m), 1730 (s), 1650 (w) 1590, 1520 (m), 1400, 1390, 1369, 1333 (w), 1249 (s), 1171, 1122, 1044, 967, 811, 785 (m), 710 (s), 565 (w) cm. cm. GC-MS (EI, 70 eV): *m/z* (%) = 336 ($[M]^+$, 05), 253 (100), 235 (38), 151 (32%). HRMS (ESI^+): calcd for $C_{21}H_{20}O_4$ $(M)^+$: 336.13616; found: 336.13611.



2-Ethylhexyl 9,10-dioxo-9,10-dihydroanthracene-2-carboxylate (35c). Starting with **34** (316 mg, 1.0 mmol), **35c** was isolated as a violet highly viscous oil (225 mg, 62%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85-0.98 (m, 6H, $2CH_3$), 1.29-1.33 (m, 8H, $4CH_2$), 1.70-1.78 (m, 1H, CH), 4.21 (d, 2H, J = 6.8 Hz, CH_2O), 7.70-7.76 (m, 2H, ArH), 8.19-8.33 (m, 4H, ArH), 8.83 (brs, 1H, Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.0, 14.0 (CH_3), 22.1, 23.9, 29.0, 30.5 (CH_2), 38.9 (CH), 68.3 (CH_2O), 127.3, 127.4, 127.5, 128.5 (CH), 132.3, 132.4, 132.5(C), 134.3, 134.4, 135.5 (CH), 135.6, 136.0 (C), 165.0 (CO), 182.2, 182.5 (CO). IR (KBr): $\tilde{\nu}$ = 3000, 2928, 2935 (m), 1733 (s), 1655 (w) 1588, 1519 (m), 1399, 1391, 1358, 1344 (w), 1250 (s), 1169, 1111, 1035, 966, 809, 783 (m), 709 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 364 ($[M]^+$, 01), 253 (86), 235 (100), 207 (31), 151 (67). HRMS (ESI^+): calcd for $C_{21}H_{20}O_4$ $(M)^+$: 364.16746; found: 364.16681.

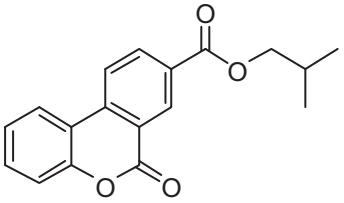
9.3.2 Synthesis of disubstituted Fluorenone 38

Synthesis of 2,3-di*p*-tolyl-9*H*-fluoren-9-one (**38**). In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 5 mol%) and Cy_3P (28 mg, 0.10 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C to give a yellowish solution. To the stirred solution were added 2,3-dibromo-1H-inden-1-one (**37**) (288 mg, 1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the 4-Methylstyrene (0.33 mL, 2.5 mmol). The reaction mixture was stirred at 60 °C 36 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), concentrated in vacuo and the residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **38** as a light brown highly viscous oil (276 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 6.96 (brs, 4H, ArH), 7.01 (brs, 4H, ArH), 7.21-7.26 (m, 1H, ArH), 7.39-7.48 (m, 3H, ArH), 7.60-7.63 (m, 1H, ArH), 7.64 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.1, 21.2 (CH_3), 120.3, 122.7, 124.3, 126.7, 128.7, 128.9, 129.0, 129.4, 129.5 (CH), 133.1 (C), 134.7 (CH), 136.6, 137.1, 137.6, 138.1, 141.5, 144.2, 146.9 (C), 193.7 (CO). IR (KBr): $\tilde{\nu}$ = 3072, 2960, 2931, 2863 (m), 1727, 1680 (s), 1640, 1617 (w) 1590, 1522, 1470 (m), 1411, 1390, 1378, 1370, 1344 (w), 1248 (s), 1172, 1134, 1119, 1035, 955, 946, 795, 780 (m), 710 (s), 654, 575 (w) cm. GC-MS (EI, 70 eV): *m/z*

(%) = 360 ([M]$^+$, 100), 345 (29), 332 (10), 302 (18), 207 (09), 151 (17). HRMS (ESI$^+$): calcd for $C_{27}H_{20}O$ (M)$^+$: 360.15087; found: 360.149855.

9.3.3 Synthesis of Benzocoumarin 42

Synthesis of isobutyl 6-oxo-6*H*-benzo[c]chromene-8-carboxylate (**42**). In a pressure tube



(glass bomb) a suspension of $Pd(PPh_3)_4$ (58 mg, 0.05 mmol, 5 mol%), 3-bromo-2-oxo-2H-chromen-4-yl trifluoromethanesulfonate (**39**) (373 mg, 1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the isobutyl acrylate (0.36 mL, 2.5 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C. The reaction mixture was stirred at 60 °C 36 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), concentrated in vacuo and the residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **42** as a highly viscous light brown oil (60 mg, 20%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (d, 6H, J = 6.7 Hz, $2CH_3$), 1.94-2.16 (m, 1H, CH), 4.10 (d, 2H, J = 6.7 Hz, CH_2O), 7.28-7.35 (m, 2H, ArH), 7.45-7.52 (m, 1H, ArH), 8.05 (dd, 1H, J = 1.4, 7.9 Hz, ArH), 8.13 (d, 1H, J = 8.2 Hz, ArH), 8.40 (dd, 1H, J = 1.9, 8.5 Hz, ArH), 8.99 (d, 1H, J = 1.6 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 19.1 (CH_3), 27.9 (CH), 71.7 (CH_2O), 117.3 (C), 118.0 (CH), 121.3 (C), 123.4, 124.9 (CH), 130.98 (C), 131.7, 132.2, 135.3 (CH), 138.3, 151.9 (C), 160.5, 165.1 (CO). IR (KBr): $\tilde{\nu}$ = 3071, 2959, 2929 (m), 1726, 1679 (s), 1637, 1616 (w) 1592, 1522, 1470 (m), 1407, 1390, 1378, 1369, 1334 (w), 1249 (s), 1173, 1135, 1119, 1035, 956, 946, 796, 781 (m), 710 (s), 654, 574 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 296 ([M]$^+$, 18), 240 (100), 195 (13), 139 (27). HRMS (ESI$^+$): calcd for $C_{18}H_{16}NaO_4$ (M+Na)$^+$: 319.0941; found: 319.094.

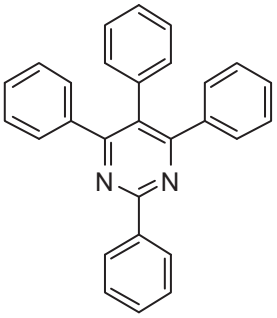
9.4 Synthesis of Aryl-Substituted Pyrimidines by Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,4,5,6-Tetrachloropyrimidine

General procedure for Suzuki Cross Coupling: The reaction was carried out in a pressure tube. To a dioxane suspension (3-5 mL) of the chlorinated pyrimidine, $Pd(PPh_3)_2Cl_2$ (3-5 mol%) and of the arylboronic acid was added an aqueous solution of K_2CO_3 (2 M, 1-2 mL). The mixture was heated at the indicated temperature (60-100 °C) under Argon atmosphere for the indicated period of time (2-8 h). The reaction mixture was diluted with water and

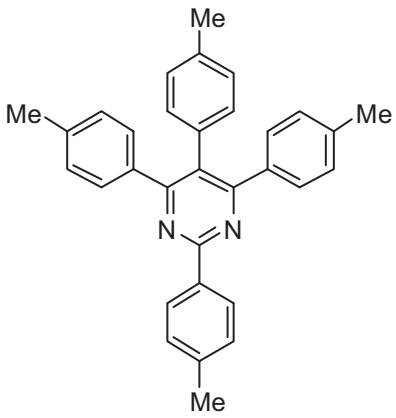
extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, EtOAc / heptanes).

9.4.1 Synthesis of tetra-aryl-pyrimidines 47

2,4,5,6-Tetraphenylpyrimidine (47a). Starting with **45** (87 mg, 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and phenylboronic acid (215 mg, 1.76 mmol), **47a** was isolated as a white solid (150 mg, 98%). Reaction temperature: 100 °C for 8 h. The synthesis of **47a** has been previously reported.[83] Mp = 129 °C (lit.[83], 129 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.88-6.92 (m, 2H, ArH), 7.06-7.20 (m, 8H, ArH), 7.31-7.44 (m, 8H, ArH), 8.55-8.59 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 127.2 (C), 127.3, 127.8, 128.3, 128.4, 128.5, 128.6, 130.0, 130.6, 131.1 (CH), 136.6, 137.8, 138.8, 162.9, 165.4 (C). IR (KBr): $\tilde{\nu}$ = 3059, 2916, 2852 (w), 1536, 1488 (s), 1442, 1370, 1298 (m), 1246 (s), 1194, 1179, 1090, 1079, 1024, 1000 (m), 965, 929, 912 (w), 866, 800, 750, 729, (m), 688 (s), 620, 614, 605, 592 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 383 ($[M-1]^+$, 30), 383 ($[M-1]^+$, 100), 331 (01), 305 (04), 280 (05), 178 (09). HRMS (EI, 70 eV): calcd for $C_{22}H_{20}N_2$ $[M]^+$: 384.16265; found: 384.162991.

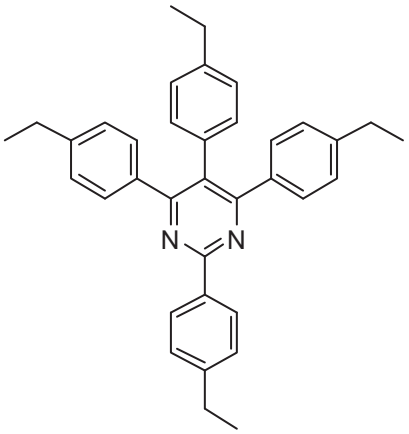


2,4,5,6-Tetra*p*-tolylpyrimidine (47b). Starting with **45** (87 mg, 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and *p*-tolylboronic acid (240 mg, 1.76 mmol), **47b** was isolated as a white solid (167 mg, 95%). Reaction temperature: 100 °C for 8 h. Mp = 105-107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3H, CH_3), 2.23 (s, 6H, $2CH_3$), 2.34 (s, 3H, CH_3), 6.79 (d, J = 8.3, 2H, ArH), 6.89 (d, J = 7.7, 2H, ArH), 6.96 (d, J = 7.7, 4H, ArH), 7.16-7.25 (m, 6H, ArH), 8.44 (d, J = 8.3, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3, 21.5 (CH_3), 128.3, 128.4, 129.0, 129.1, 129.9, 130.9 (CH), 133.9, 135.3, 136.3, 136.7, 138.4, 140.5, 162.6, 165.1 (C). IR (KBr): $\tilde{\nu}$ = 3060, 3029, 2947, 2863, 2258 (w), 1606 (m), 1521, 1504 (s), 1409, 1391, 1354, 1186, 1175, 1020, 901, 825, 813 (m), 798, 728 (s), 650, 627, 570 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 440 ($[M]^+$, 66), 439 ([M-

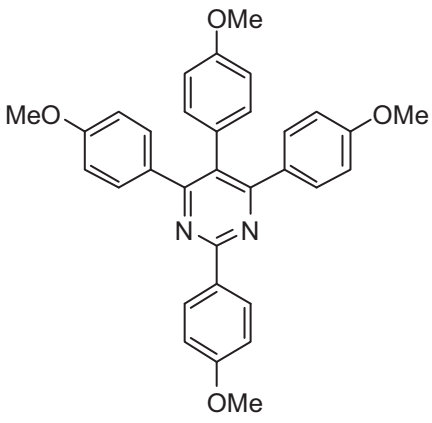


1]$^+$, 100), 347 (02), 205 (09). HRMS (EI, 70 eV): calcd for $C_{32}H_{28}N_2$ [M-1]$^+$: 439.21688; found: 439.217130.

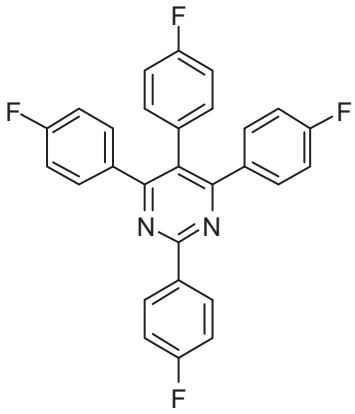
2,4,5,6-Tetrakis(4-ethylphenyl)pyrimidine (47c). Starting with **45** (87 mg, 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-ethylphenylboronic acid (264 mg, 1.76 mmol), **47c** was isolated as a white solid (184 mg, 93%). Reaction temperature: 100 °C for 8 h. Mp = 129-131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08-1.14 (m, 9H, $3CH_3$), 1.90 (t, J = 7.6 Hz, 3H, CH_3), 2.47-2.53 (m, 6H, $3CH_2$), 2.67 (q, J = 7.7 Hz, 2H, CH_2), 6.82 (d, J = 8.3 Hz, 2H, ArH), 6.90 (d, J = 8.3 Hz, 2H, ArH), 6.96 (d, J = 8.6 Hz, 4H, ArH), 7.20-7.26 (m, 6H, ArH), 8.47 (d, J = 8.3 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.2, 15.4, 15.5 (CH_3), 28.6, 28.7, 28.9 (CH_2), 127.8, 127.8, 127.9, (CH), 128.4 (C), 128.5, 130.0, 131.0 (CH), 134.2, 135.6, 136.6, 143.2, 144.7, 146.8, 162.7, 165.1 (C). IR (KBr): $\tilde{\nu}$ = 3059, 3030, 2964, 2929, 2868, 1609, 1574, 1567, 1556 (w), 1522, 1413, 1392, 1185, 1177, 1062, 1047, 1020, 946, 855, 844, 826 (m), 810 (s), 741, 692, 652, 628, 572, 548 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 496 ([M]$^+$, 69), 495 ([M-1]$^+$, 100), 467 (06), 204 (05). HRMS (ESI$^+$): calcd for $C_{36}H_{36}N_2$ [M]$^+$: 496.28785; found: 496.28780.



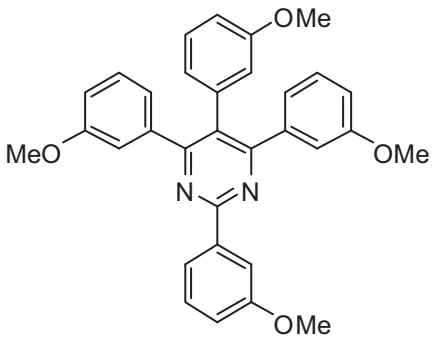
2,4,5,6-Tetrakis(4-methoxyphenyl)pyrimidine (47d). Starting with **45** (87 mg, 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-methoxyphenylboronic acid (268 mg, 1.76 mmol), **47d** was isolated as a white solid (183 mg, 91%). Reaction temperature: 100 °C for 8 h. Mp = 134-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 3H, OCH_3), 3.68 (s, 6H, $2OCH_3$), 3.77 (s, 3H, OCH_3), 6.67 (d, J = 8.9, 6H, ArH), 6.80 (d, J = 8.7, 2H, ArH), 6.90 (d, J = 8.9, 2H, ArH), 7.28 (d, J = 8.9 4H, ArH), 8.49 (d, J = 8.6, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.1, 55.2, 55.4 (OCH_3), 113.2, 113.7, 114.0 (CH), 127.2, 129.5 (C), 130.0 (CH), 130.8 (C), 131.5 (CH), 131.6 (C), 132.2 (CH), 158.7, 159.8, 161.7, 162.2, 164.7 (C). IR (KBr): $\tilde{\nu}$ = 3075, 3002, 2955, 2934, 2912, 2837 (w), 1601, 1574, 1526, 1515, 1501, 1463, 1453, 1415, 1391, 1361, 1299, 1283 (m), 1247, 1167 (s) 1025,



907, 850, 834, 818, 805, 728, 667, 648, 636, 621, 578 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 504 ($[M]^+$, 90), 503 ($[M-1]^+$, 100), 489 (04), 459 (05), 223 (09). HRMS (ESI^+): calcd for $C_{32}H_{28}N_2O_4$ $[M]^+$: 504.20491; found: 504.20491.

2,4,5,6-Tetrakis(4-fluorophenyl)pyrimidine (47e). Starting with **45** (87 mg, 0.40 mmol), 

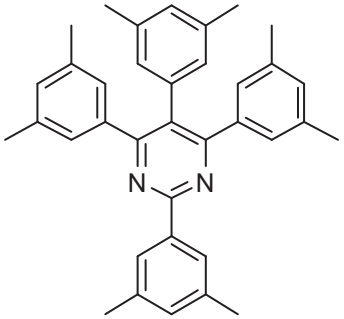
$Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-fluorophenylboronic acid (247 mg, 1.76 mmol), **47e** was isolated as a white solid (162 mg, 89%). Reaction temperature: 100 °C for 8 h. Mp = 228-229 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.81-6.90 (m, 8H, ArH), 7.03-7.11 (m, 2H, ArH), 7.25-7.31 (m, 4H, ArH), 8.49-8.56 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ = -113.3, -111.7, -110.0 .^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 114.9 (d, $J_{F,C}$ = 21.7, CH), 115.5 (d, $J_{F,C}$ = 21.6, CH), 115.9 (d, $J_{F,C}$ = 21.6, CH), 127.6 (C), 130.5 (d, $J_{F,C}$ = 8.7, CH), 131.8 (d, $J_{F,C}$ = 8.4, CH), 132.2 (d, $J_{F,C}$ = 3.7, C), 132.6 (d, $J_{F,C}$ = 8.1, CH), 133.5 (d, $J_{F,C}$ = 2.8, C), 1134.4 (d, $J_{F,C}$ = 3.3, C), 162.1, (C), 162.2 (d, $J_{F,C}$ = 250.0, CF), 163.2 (d, $J_{F,C}$ = 273.3, CF), 164.6 (C), 164.9 (d, $J_{F,C}$ = 250.7, CF). IR (KBr): $\tilde{\nu}$ = 3071, 3063, 1912 (w), 1598, 1529, 1512 (m), 1500 (s), 1413, 1390, 1364, 1355 (m), 1297, 1289, 1267 (w), 1225 (s), 1193, 1158, 1148, 1100, 1088, 1013 (m), 1002, 962, 954, 940, 872 (w), 856, 894, 827, 809, 736, 669, 646, 634, 620, 570, 527 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 456 ($[M]^+$, 67), 455 ($[M-1]^+$, 100), 359 (05), 214 (15). HRMS (ESI^+): calcd for $C_{28}H_{16}F_4N_2$ $[M]^+$: 456.12496; found: 456.12500.

2,4,5,6-Tetrakis(3-methoxyphenyl)pyrimidine (47f). Starting with **45** (87 mg, 0.40 mmol), 

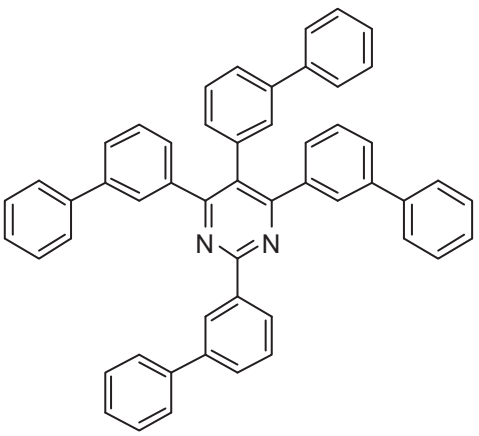
$Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and 3-methoxyphenylboronic acid (268 mg, 1.76 mmol), **47f** was isolated as a white solid (165 mg, 82%). Reaction temperature: 100 °C for 8 h. Mp = 100-102 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.45 (s, 3H, OCH_3), 3.51 (s, 6H, $2OCH_3$), 3.79 (s, 3H, OCH_3), 6.45-6.47 (m, 1H, ArH),6.50- 6.55 (m, 1H, ArH), 6.62-6.67 (m, 1H, ArH), 6.72-6.77 (m, 2H, ArH), 6.87 (t, J = 1.5, 2H, ArH), 6.95-6.99 (m, 4H, ArH), 7.04 (s, 1H, ArH), 7.07 (s, 1H, ArH), 7.31 (t, J = 8.0, 1H, ArH), 8.11-8.18 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.1, 55.3, 55.4 (OCH_3), 113.4, 113.5, 114.8, 115.2, 116.3, 116.8, 121.1, 122.4, 123.6128.8 (CH), 128.9 (C), 129.4, 129.5 (CH), 138.1, 139.2, 140.0, 159.0,

159.6, 159.9, 162.6, 165.1 (C). IR (KBr): $\tilde{\nu}$ = 3078, 2997, 2931, 2832 (w), 1595, 1584, 1522 (s), 1487, 1462, 1449, 1420, 1384, 1350, 1316, 1275 (m), 1233 (s), 1210, 1176, 1157, 1149, 1124, 1080 (m), 1034 (s), 994, 918, 907, 878 (w), 865, 860, 802, 786, 775, 751, 731, 711, 692, 670, 634 (m), 605, 581, 549, 533 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 504 ($[M]^+$, 65), 503 ($[M-1]^+$, 100), 489 (21), 397 (13), 236 (13). HRMS (ESI^+): calcd for $C_{32}H_{28}N_2O_4$ $[M]^+$: 504.20491; found: 504.20480.

2,4,5,6-Tetrakis(3,5-dimethylphenyl)pyrimidine (47g). Starting with **45** (87 mg, 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and 3,5-dimethylphenylboronic acid (264 mg, 1.76 mmol), **47g** was isolated as a white solid (157 mg, 79%). Reaction temperature: 100 °C for 8 h. Mp = 190-192 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.04 (s, 6H, $2CH_3$), 2.13 (s, 12H, $4CH_3$), 2.34 (s, 6H, $2CH_3$), 6.50 (s, 2H, ArH), 6.72 (s, 1H, ArH), 6.83 (s, 2H, ArH), 6.96 (s, 4H, ArH), 7.04 (s, 1H, ArH), 8.17 (s, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.1, 21.3, 21.4 (CH_3), 126.3, 127.8, 128.4, 128.8, 130.1, 132.2 (CH), 136.5, 136.9, 137.2, 137.8, 137.9, 138.4, 138.7, 162.7, 165.3 (C). IR (KBr): $\tilde{\nu}$ = 3009, 2912, 2858, 2727, 1598, 1573, 1567 (w), 1515 (s), 1433, 1386, 1371 (m), 1252, 1191, 1177, 1036, 914, 908 (w), 861, 845, 724, 717, 696, 684, 669, 654, 541 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 496 ($[M]^+$, 65), 481 (100), 331 (08), 233 (08). HRMS (EI, 70 eV): calcd for $C_{36}H_{36}N_2$ $[M-1]^+$: 496.28730; found: 496.285615.



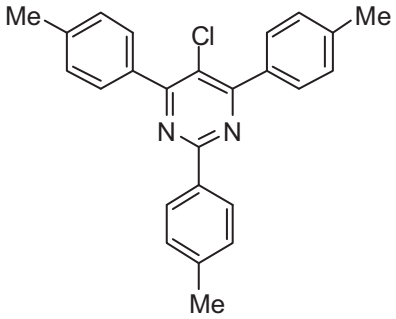
2,4,5,6-Tetra(biphenyl-3-yl)pyrimidine (47h). Starting with **45** (87 mg, 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (15 mg, 5 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and biphenyl-3-ylboronic acid (349 mg, 1.76 mmol), **47h** was isolated as a white solid (69 mg, 25%). Mp = 185-186 °C. Reaction temperature: 100 °C for 8 h. ^1H NMR (250 MHz, $CDCl_3$): δ = 6.99-7.3 (m, 1H, ArH), 7.21-7.60 (m, 30H, ArH), 7.65-7.69 (m, 3H, ArH), 8.51-8.64 (m, 1H, ArH), 8.86 (t, J = 1.7, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 126.3, 127.1, 127.2, 127.2, 127.3, 127.4, 127.5, 127.6, 128.6, 128.7, 128.8, 128.9, 129.0, 129.1 (CH), 129.2 (C),129.3, 129.5, 130.1, 130.5 (CH), 137.5, 138.2, 139.0, 140.6, 140.7, 141.2, 141.5, 141.9, 163.0, 163.4 (C).



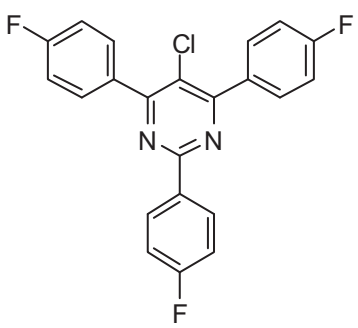
IR (KBr): $\tilde{\nu}$ = 3058, 3030, 2928, 1712, 1598 (w), 1525 (s), 1498, 1478, 1451, 1418, 1383, 1356 (m), 1260, 1220, 1183, 1169, 1090, 1076, 901, 804 (w), 756, 698 (s), 637, 615 (m) $\tilde{cm}^{-1}$. GC-MS (EI, 70 eV): *m/z* (%) = 688 ($[M]^+$, 85), 687 ($[M-1]^+$, 100), 611 (07), 508 (08), 326 (08), 252 (06). HRMS (EI, 70 eV): calcd for $C_{52}H_{36}N_2$ $[M]^+$: 688.28785; found: 688.28777.

9.4.2 Synthesis of 2,4,6-triaryl-5-chloropyrimidines 48

5-Chloro-2,4,6-tri*p*-tolylpyrimidine (48a). Starting with **45** (217 mg, 1.00 mmol), $Pd(PPh_3)_2Cl_2$ (14 mg, 2 mol%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and *p*-tolylboronic acid (408 mg, 3.00 mmol), **48a** was isolated as a white solid (318 mg, 83%). Reaction temperature: 80 °C for 5 h. Mp = 113-114 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 2.38 (s, 6H, CH_3), 7.18 (d, *J* = 8.0 Hz, 2H, ArH), 7.25 (d, *J* = 7.9 Hz, 4H, ArH), 7.77 (d, *J* = 8.1 Hz, 4H, ArH), 7.36 (d, *J* = 8.2 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.4, 21.5 (CH_3), 124.1 (C), 128.4, 128.8, 129.2, 129.7 (CH), 134.3, 134.5, 140.4, 141.0, 161.5, 164.4 (C). IR (KBr): $\tilde{\nu}$ = 3061, 3033, 2916, 2855, 2720, 1614, 1584 (w), 1539, 1530, 1520 (m), 1503 (s), 1456, 1406 (w), 1358 (s), 1308, 1298, 1263, 1210 (w), 1181 (s), 1110, 1070, 1053 (w), 1033, 1021 (m), 967, 955, 939, 907, 867 (w), 833, 817 (m), 785 (s), 768, 754, 728, 721, 709, 677, 643, 630, 619, 567 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) =386 ($[M, ^{37}Cl]^+$, 32), 384 ($[M, ^{35}Cl]^+$, 100), 357 (03), 337 (04), 204 (12), 136 (22). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}ClN_2$ [M, ^{35}Cl]$^+$: 384.13933; found: 384.13991.

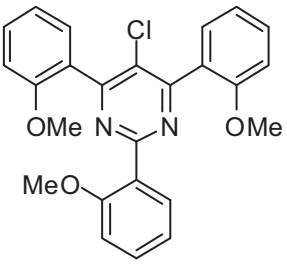


5-Chloro-2,4,6-tris(4-fluorophenyl)pyrimidine (**48b**). Starting with **45** (217 mg, 1.00 mmol), $Pd(PPh_3)_2Cl_2$ (35 mg, 5 mol%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 4-fluorophenylboronic acid (420 mg, 3.00 mmol), **48b** was isolated as a white solid (329 mg, 83%). Reaction temperature: 80 °C for 5 h. Mp = 236-238 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.05- 7.18 (m, 6H, ArH), 7.85-7.90 (m, 4H, ArH), 8.44-8.49 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 115.3 (d, $J_{F,C}$ = 22.6 Hz, ArH), 115.5 (d, $J_{F,C}$ = 22.5 Hz, ArH), 124.3 (C), 130.5 (d, $J_{F,C}$ = 8.6 Hz, ArH), 131.9 (d, $J_{F,C}$ = 8.6 Hz, ArH), 132.7 (d, $J_{F,C}$ = 3.4 Hz, C), 132.9 (d, $J_{F,C}$ = 3.3 Hz, C), 162.7 (C), 163.6 (d, $J_{F,C}$ = 251.7 Hz, CF), 163.6 (d, $J_{F,C}$ = 251.7 Hz, CF), 163.7 (C). IR (KBr): $\tilde{\nu}$ = 3067, 2959, 2914, 2855 (w),

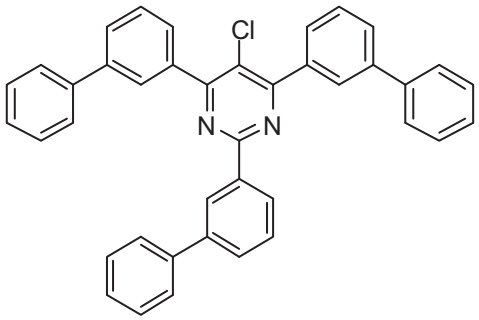


1600, 1537 (m), 1501 (s), 1411, 1380, 1359, 1231, 1149, 1099, 1029, 1013, 990, 956, 871 (m), 834, 795 (s), 741, 731, 675, 637, 625, 613 (w), 565, 530 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 398 ([M, $^{37}Cl]^+$, 35), 396 ([M, $^{35}Cl]^+$, 100), 361 (17), 275 (07), 240 (51), 154 (72). HRMS (ESI^+): calcd for $C_{22}H_{13}ClF_3N_2$ [M+1, $^{35}Cl]^+$: 397.0714; found: 397.0711, calcd for $C_{22}H_{13}ClF_3N_2$ [M+1, $^{37}Cl]^+$: 399.0692; found: 399.0689.

5-Chloro-2,4,6-tris(2-methoxyphenyl)pyrimidine (**48c**). Starting with **45** (217 mg, 1.00 mmol), $Pd(PPh_3)_2Cl_2$ (35 mg, 5 mol%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 2-methoxyphenylboronic acid (456 mg, 3.00 mmol), **48c** was isolated as a brownish semisolid (350 mg, 81%). Reaction temperature: 80 °C for 5 h. Mp = 149-150 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 3.76 (s, 6H, $2OCH_3$), 3.78 (s, 3H, OCH_3), 6.87-7.03 (m, 6H, ArH), 7.24-7.42 (m, 5H, ArH), 7.69 (dd, *J* = 1.8, 7.6 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.6, 56.1 (OCH_3), 111.1, 112.1, 120.6, 120.8 (CH), 126.9, 128.2, 129.0 (C), 130.6, 130.8, 130.9, 131.9 (CH), 156.9, 157.7, 162.8, 163.0 (C). IR (KBr): $\tilde{\nu}$ = 3061, 2970, 2927 (w), 1602, 1531, 1510 (m), 1483 (s), 1458, 1446, 1372, 1317, 1309, 1284 (m), 1253 (s), 1177, 1097, 1038, 1025 (m), 867, 832, 820, 807, 773, 766 (s), 729, 691, 668, 660 (w), 634, 615, 578, 586 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 434 ([M, $^{37}Cl]^+$, 34), 432 ([M, $^{35}Cl]^+$, 100), 417 (51), 397 (59), 367 (17), 266 (29). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}ClN_2$ [M, $^{35}Cl]^+$: 432.12407; found: 432.12401.



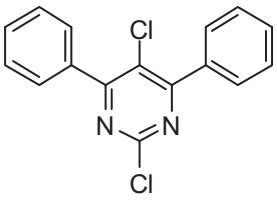
2,4,6-Tri(biphenyl-3-yl)-5-chloropyrimidine (**48d**). Starting with **45** (217 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 2.5 mol%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and biphenyl-3-ylboronic acid (298 mg, 1.50 mmol), **48d** was isolated as a white solid (228 mg, 80%). Reaction temperature: 80 °C for 5 h. Mp = 189-191 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.27-7.48 (m, 10H, ArH), 7.51-7.71 (m, 11H, ArH), 7.85 (dt, *J* = 1.4, 7.7 Hz, 2H, ArH), 8.10 (t, *J* = 1.5 Hz, 2H, ArH), 8.50 (dt, *J* = 1.4, 7.9 Hz, 1H, ArH), 8.74 (t, *J* = 1.7 Hz, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 123.9 (C), 126.2, 126.3, 126.4, 126.5, 126.6, 127.5, 127.6, 127.7, 127.8, 128.0, 128.7 (CH), 136.3, 136.6, 139.6, 139.9, 140.2, 140.6, 160.6, 163.7 (C). IR (KBr): $\tilde{\nu}$ = 3059, 3028, 2962, 2918, 2849 (w), 1531, 1510, 1496, 1478, 1362, 1347 (m), 1262, 1254, 1186, 1166, 1088, 1071, 1050, 1035, 1019, 918, 909, 888, 798, 788 (w), 744, 689



(s), 632, 601 (m) cm. MS (EI, 70 eV): *m/z* (%) = 572 ([M, ^{37}Cl]$^+$, 34), 570 ([M, ^{35}Cl]$^+$, 100), 536 (17), 391 (05), 356 (34), 285 (14). HRMS (ESI$^+$) calcd for $C_{40}H_{28}ClN_2$ [M+1, ^{35}Cl]$^+$: 571.19360; found: 571.19333.

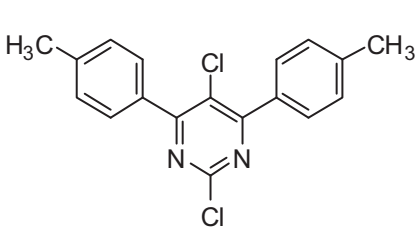
9.4.3 Synthesis of 4,6-diaryl-2,5-dichloropyrimidines 49

2,5-Dichloro-4,6-diphenylpyrimidine (**49a**). Starting with **45** (217 mg, 1.0 mmol),



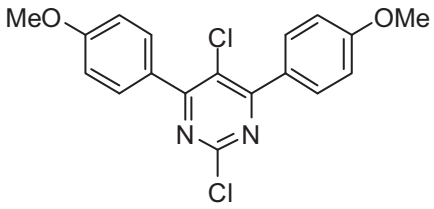
$Pd(PPh_3)_2Cl_2$ (21 mg, 3 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and phenylboronic acid (244 mg, 2.0 mmol), **49a** was isolated as a white solid (291 mg, 97%). Reaction temperature: 70 °C for 5 h. Mp = 135-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.21-7.42 (m, 6H, ArH), 7.62-7.81 (m, 4H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 125.7 (C), 128.4, 129.6, 130.7 (CH), 135.5, 158.3, 167.4 (C). IR (KBr): $\tilde{\nu}$ = 3059, 2916, 2852 (w), 1535, 1487 (s), 1442, 1370, 1297 (m), 1245 (s), 1179, 1090, 1024, 865, 750 (m), 750, 688, 606, 592 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 302 ([M, ^{35}Cl, ^{37}Cl]$^+$, 65), 300 ([M, ^{35}Cl, ^{35}Cl]$^+$, 100), 255 (33), 225 (18). HRMS (EI, 70 eV): calcd for $C_{16}H_{10}Cl_2N_2$[M, ^{35}Cl, ^{35}Cl]$^+$: 300.0221; found: 300.02211.

2,5-Dichloro-4,6-di*p*-tolylpyrimidine (**49b**). Starting with **45** (217 mg, 1.0 mmol),



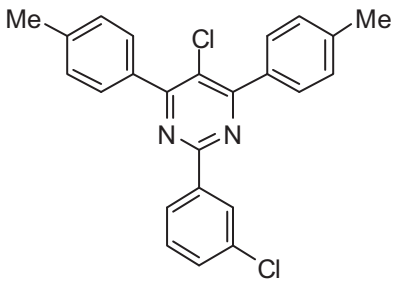
$Pd(PPh_3)_2Cl_2$ (21 mg, 3 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and *p*-tolylboronic acid (270 mg, 2.0 mmol), **49b** was isolated as a white solid (279 mg, 85%). Reaction temperature: 70 °C for 5 h. Mp = 109-110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 6H, 2CH_3), 7.20 (d, *J* = 7.9 Hz, 4H, ArH), 7.79 (d, *J* = 8.2 Hz, 4H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 129.0 (C, CH), 129.6 (C, CH), 132.7, 141.0, 167.2 (C). IR (KBr): $\tilde{\nu}$ = 3062, 3028, 2919, 2859 (w), 1609 (m), 1532, 1484 (s), 1456, 1406 (w), 1244 (s), 1175, 1084, (w), 1033, 1021 (m), 869, 819, 782, 750, 712, 612, 561 (m) cm.. GC-MS (EI, 70 eV): *m/z* (%) = 330 ([M, ^{35}Cl, ^{37}Cl]$^+$, 63), 328 ([M, ^{35}Cl, ^{35}Cl]$^+$, 100), 281 (24), 155 (18. HRMS (EI, 70 eV): calcd for $C_{18}H_{14}Cl_2N_2$ [M, ^{35}Cl, ^{35}Cl]$^+$: 328.5341; found: 328.5341.

2,5-Dichloro-4,6-bis(4-methoxyphenyl)pyrimidine *(***45d***)*. Starting with **45** (217 mg, 1.0 mmol), $Pd(PPh_3)_2Cl_2$ (21 mg, 3 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and 4-methoxyphenylboronic acid (304 mg, 2.0 mmol), **48c** was isolated as a white solid (334 mg, 93%). Reaction temperature: 70 °C for 5 h. mp = 105-107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 6H, OCH_3), 6.95 (d, 4H, J = 9.1 Hz, ArH), 7.85 (d, 4H, J = 9.1 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 113.6 (CH), 124.6, 127.9 (C), 131.5 (CH), 158.0, 161.6, 166.5 (C). IR (KBr): $\tilde{\nu}$ = 2878, 2966, 2935, 2826 (w), 1611, 1523, 1513, 1511, 1483, 1468, 1433, 1333, 1325, 1321, 1274 (m), 1255 (s), 1178, 1117, 1097, 1038, 1018 (m), 961 (w), 866 (m), 822, 820, 806, 773, 766 (s), 728 (m), 692, 667, 632 (w), 614, 578, 562 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 362 ([M, ^{35}Cl, ^{37}Cl]$^+$, 65), 360 ([M, ^{35}Cl, ^{35}Cl]$^+$, 100), 325 (33), 253 (11), 252 (04), 236 (09), 132 (10). HRMS (EI, 70 eV): calcd for $C_{18}H_{14}Cl_2N_2O_2$ [M, ^{35}Cl, ^{35}Cl]$^+$: 360.04323; found: 360.04311.

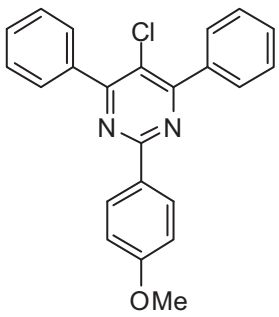


9.4.4 Synthesis of unsymmetrical 2,4,6-triaryl-5-chloropyrimidines 50

5-Chloro-2-(3-chlorophenyl)-4,6-di*p*-tolylpyrimidine *(***50a***)*. Starting with **49b** (82 mg, 0.25 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 3 mol%), dioxane (3 mL), 2M K_2CO_3 (1 mL) and 3-chlorophenylboronic acid (39 mg, 0.25 mmol), **50a** was isolated as a white solid (91 mg, 90%). Reaction temperature: 80 °C for 5 h. Mp = 195-197 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.37 (s, 6H, $2CH_3$), 7.24-7.35 (m, 6H, ArH), 7.75 (d, J = 8.1 Hz, 4H, ArH), 8.40 (dt, J = 1.7, 7.5 Hz, 1H, ArH), 8.40 (t, J = 1.8 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.1 ($2CH_3$), 124.0 (C), 125.5, 127.4, 127.8, 128.7, 129.7, 129.7 (CH), 133.2, 133.6, 137.6, 139.3, 159.0, 163.6 (C). IR (KBr): $\tilde{\nu}$ = 3058, 3034, 2918, 2851, 1613 (w), 1537, 1500, 1364 (s), 1307, 1261, 1184, 1091, 1074, 1034, 883, 822, 807 (m), 780.1 (s), 741, 735, 722, 703 (m), 673, 661, 622, 598, 567 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 406 ([M, ^{35}Cl, ^{37}Cl]$^+$, 66), 404 ([M, ^{35}Cl, ^{35}Cl]$^+$, 100), 389 (04), 369 (29), 252 (12), 232 (42). HRMS (ESI$^+$): calcd for $C_{24}H_{19}Cl_2N_2$ [M+H, ^{35}Cl, ^{35}Cl]$^+$: 405.0920; found: 405.0923, calcd for $C_{24}H_{19}Cl_2N_2$ [M+H, ^{35}Cl, ^{37}Cl]$^+$: 407.0895; found: 407.0897.

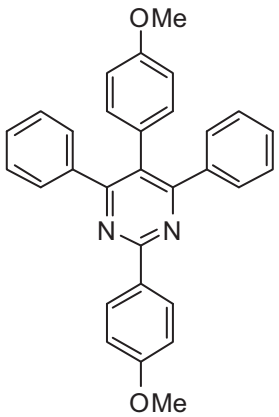


5-Chloro-2-(4-methoxyphenyl)-4,6-diphenylpyrimidine (**50b**). Starting with **49a** (75 mg, 0.25 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 3 mol%), dioxane (3 mL), 2M K_2CO_3 (1 mL) and 4-methoxyphenylboronic acid (38 mg, 0.25 mmol), **50b** was isolated as a white solid (80 mg, 86%). Reaction temperature: 80 °C for 5 h. Mp = 189-191 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 6.90 (d, 2H, J = 9.0 Hz, ArH), 7.43-7.50 (m, 6H, ArH), 7.82-7.87 (m, 4H, ArH), 8.44 (d, 2H, J = 9.0 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 113.8 (CH), 123 (C), 128.1 (CH), 129.5 (C), 129.7, 129.8, 130.2 (CH), 137.3, 162.0, 164.5 (2C). IR (KBr): $\tilde{\nu}$ = 3059, 3028, 3006, 2954, 2931, 2835 (w), 1608, 1560, 1534 (m), 1504, 1490 (s), 1468, 1444, 1423, 1385 (m), 1361 (s), 1302 (m), 1250 (s), 1174, 1106, 1075, 1058, 1037, 1030, 1002 (m), 980, 969, 958, 912, 864 (w), 838, 797, 787, 771 (m), 757 (s), 729 (m), 687 (s), 632, 615, 540 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 372 ([M]$^+$, 100), 357 (03), 337 (04), 204 (12), 136 (22). HRMS (EI, 70 eV): calcd for $C_{23}H_{17}ClN_2O$ [M]$^+$: 372.10294; found: 372.10278.

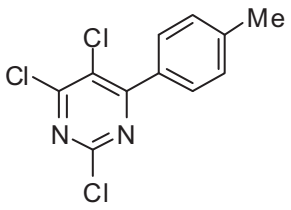


9.4.5 Synthesis of unsymmetrical 2,4,5,6-tetra-aryl-pyrimidine 51a

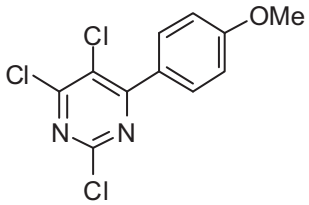
2,5-Bis(4-methoxyphenyl)-4,6-diphenylpyrimidine (51a). Starting with **49a** (75 mg, 0.25 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 3 mol%), dioxane (3 mL), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-methoxyphenylboronic acid (76 mg, 0.5 mmol), **51a** was isolated as a white solid (87 mg, 79%). Reaction temperature: 100 °C for 5 h. Mp = 175-177 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.77 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 6.87-6.93 (m, 4H, ArH), 7.42 (d, J = 8.8, 2H, ArH), 7.45-7.47 (m, 6H, ArH), 7.83-7.87 (m, 4H, ArH), 8.44 (d, J = 8.7, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.3, 55.4 (OCH_3), 113.8, 114.2 (CH), 123.8 (C), 127.7, 128.1 (CH), 129.5 (C), 129.7, 129.8, 130.2 (CH), 133.5, 137.3, 158.5, 161.3, 162.0, 164.5 (C). IR (KBr): $\tilde{\nu}$ = 3058, 3005, 2955, 2934, 2930, 2835 (w), 1607, 1585, 1534 (m), 1503, 1491 (s), 1467, 1444, 1385 (w), 1362, 1250, 1174, 1039 (s), 1012, 969, 958, 912 (w), 837, 821, 804, 797, 772 (m), 687, 615, 541 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 444 ([M]$^+$, 100), 411 ([10), 369 (14), 223 (19). HRMS (ESI$^+$): calcd for $C_{30}H_{24}N_2O_2$ [M]$^+$: 444.1837; found: 444.1830.



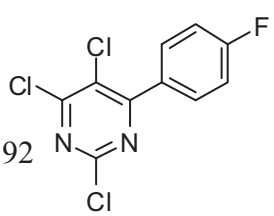
9.4.6 Synthesis of 4-aryl-2,5,6-trichloropyrimidines 52

2,4,5-Trichloro-6-*p*-tolylpyrimidine (**52a**). Starting with **45** (217 mg, 1.0 mmol), 

$Pd(PPh_3)_2Cl_2$ (07 mg, 1 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and p-tolylboronic acid (136 mg, 1.0 mmol), **52a** was isolated as a white solid (238 mg, 87%). Reaction temperature: 60 °C for 2 h. Mp = 130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3H, CH_3), 7.21 (d, 2H, J = 8.2 Hz, ArH), 8.20 (d, 2H, J = 8.5 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6 (CH_3), 125.2 (C), 128.8, 129.6 (CH), 131.5, 143.0, 159.6, 161.9 (C). IR (KBr): $\tilde{\nu}$ = 2916, 2854, 2720 (w), 1612, 1530 (m), 1503 (s), 1406 (w), 1358 (s), 1307, 1297, 1266 (w), 1180 (s), 1032, 1020 (m), 966, 955, 938 (w), 832, 817 (m), 784 (s), 766, 753, 728, 720, 709, 676, 642, 629, 618, 597 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 278 ([M, $^{37}Cl_3]^+$, 02), 276 ([M, ^{35}Cl, $^{37}Cl_2]^+$, 25), 274 ([M, $^{35}Cl_2$, ^{37}Cl]$^+$, 100), 272 ([M, $^{35}Cl_3]^+$, 88), 237 (42), 116 (24). HRMS (EI, 70 eV): calcd for $C_{11}H_7Cl_3N_2$ [M, $^{35}Cl_3]^+$: 271.96748; found: 271.96649.

2,4,5-Trichloro-6-(4-methoxyphenyl)pyrimidine (**52b**). Starting with **45** (217 mg, 1.0 

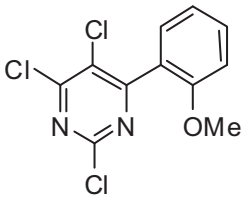
mmol), $Pd(PPh_3)_2Cl_2$ (21 mg, 3 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and 4-methoxyphenylboronic acid (152 mg, 1.0 mmol), **52b** was isolated as a brownish semisolid (275 mg, 95%). Reaction temperature: 60 °C for 2 h. Mp = 120-121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3H, OCH_3), 6.94 (d, 2H, J = 9.0 Hz, ArH), 7.83 (d, 2H, J = 9.0 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.5 (OCH_3), 113.8 (CH), 126.8 (C), 131.7 (CH), 156.9, 161.4, 162.2, 166.0 (C). IR (KBr): $\tilde{\nu}$ = 2971, 2928, 2836 (w), 1604, 1574, 1530, 1511, 1483, 1458, 1446, 1372, 1325, 1317, 1309, 1284 (m), 1253 (s), 1177, 1116, 1097, 1038, 1025 (m), 962 (w), 867 (m), 832, 820, 807, 774, 766 (s), 729 (m), 691, 668, 634 (w), 615, 579, 569, 537 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 294 ([M, $^{37}Cl_3]^+$, 03), 292 ([M, ^{35}Cl, $^{37}Cl_2]^+$, 26), 290 ([M, $^{35}Cl_2$, ^{37}Cl]$^+$, 92), 288 ([M, $^{35}Cl_3]^+$, 100), 275 (04), 253 (17), 210 (14), 157 (07). HRMS (EI, 70 eV): calcd for $C_{11}H_7Cl_3N_2O$ [M]$^+$: 287.96240; found: 287.96228.

2,4,5-Trichloro-6-(4-fluorophenyl)pyrimidine (**52c**). Starting with **45** (217 mg, 1.0 mmol), 

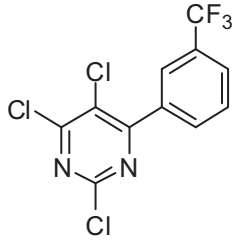
$Pd(PPh_3)_2Cl_2$ (21 mg, 3 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and 4-fluorophenylboronic acid (140 mg, 1.0 mmol), **52c** was isolated

as a white solid (258 mg, 93%). Reaction temperature: 60 °C for 2 h. Mp = 148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10-7.16 (m, 2H, ArH), 7.78-7.82 (m, 2H, ArH). NMR (62.9 MHz, $CDCl_3$): δ = 115.5 (d, $J_{F,C}$ = 21.8 Hz, CH), 125.2 (C), 131.3 (d, $J_{F,C}$ = 3.4 Hz, C), 131.5 (d, $J_{F,C}$ = 8.8 Hz, CH), 158.2 (C), 164.2 (d, $J_{F,C}$ = 252.1 Hz, CF), 166.3 (C). IR (KBr): $\tilde{\nu}$ = 3068, 2960, 2924, 2853 (w), 1601, 1538 (m), 1502 (s), 1410, 1381, 1359, 1231, 1149, 1099, 1029, 1014, 989, 955, 871, 845 (m), 834, 794 (s), 740, 731, 673, 636, 625, 613 (w), 564, 528 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 292 ([M, $^{37}Cl_3]^+$, 280 ([M, ^{35}Cl, $^{37}Cl_2]^+$, 25), 278 ([M, $^{35}Cl_2$, ^{37}Cl]$^+$, 100), 276 ([M, $^{35}Cl_3]^+$, 95), 253 (17), 240 (14), 182 (07). HRMS (EI, 70 eV): calcd for $C_{10}H_4Cl_3FN_2$ $[M]^+$: 275.94241; found: 275.94228.

2,4,5-Trichloro-6-(2-methoxyphenyl)pyrimidine (**52d**). Starting with **45** (217 mg, 1.0 mmol), $Pd(PPh_3)_2Cl_2$ (21 mg, 3 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and 2-methoxyphenylboronic acid (152 mg, 1.0 mmol), **52d** was isolated as a white solid (281 mg, 97%). Reaction temperature: 60 °C for 2 h. Mp = 108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 3H, OMe), 6.89-6.96 (m, 2H, ArH), 7.15-7.27 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.7 (OMe), 111.1, 120.3 (CH), 127.8 (C), 128.6 (CH), 131.5 (CH), 132.5, 157.0, 167.8 (C). IR (KBr): $\tilde{\nu}$ = 3060, 2971, 2928 (w), 1604, 1530, 1512 (m), 1483 (s), 1458, 1446, 1372, 1317, 1309, 1284 (m), 1253 (s), 1177, 1116, 1097, 1038, 1025 (m), 867, 832, 820, 807, 773, 766 (s), 729, 691, 668, 660 (w), 634, 615, 579, 587 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 294 ([M, $^{37}Cl_3]^+$, 03), 292 ([M, ^{35}Cl, $^{37}Cl_2]^+$, 25), 290 ([M, $^{35}Cl_2$, ^{37}Cl]$^+$, 90), 288 ([M, $^{35}Cl_3]^+$, 100), 275 (04), 253 (17), 210 (14), 157 (07). HRMS (ESI$^+$): calcd for $C_{11}H_8Cl_3N_2O$ $[M+1]^+$: 287.9697; found: 288.969696, calcd for $C_{11}H_8Cl_2{}^{37}ClN_2O$ $[M+1]^+$: 290.9668; found: 290.9669.

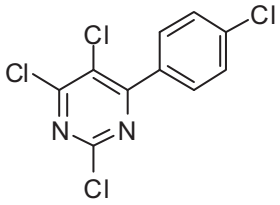


2,4,5-Trichloro-6-(3-(trifluoromethyl)phenyl)pyrimidine (52e). Starting with **45** (217 mg, 1.0 mmol), $Pd(PPh_3)_2Cl_2$ (09 mg, 1.25 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and 3-(trifluoromethyl)phenylboronic acid (189 mg, 1.0 mmol), **16e** was isolated as a white solid (297 mg, 91%). Reaction temperature: 70 °C for 5 h. Mp = 168-169 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53-7.58 (m, 1H, ArH), 7.71-7.74 (m, 1H, ArH), 8.51-8.54 (m, 1H, ArH), 8.60 (brs, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ = -62.7. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 125.6 (q, $J_{F,C}$ = 4.2 Hz, CH), 126.8 (C), 128.6 (q, $J_{F,C}$ = 3.2 Hz, CH), 128.9 (q, $J_{F,C}$ = 274.7 Hz, CF_3), 129.4, 131.8 (CH), 131.2 (C), 132.0 (q, $J_{F,C}$ = 32.9 Hz, C-CF_3), 135.0, 160.0, 160.3 (C). IR (KBr): $\tilde{\nu}$ = 3075, 2919, 2851 (w), 1529, 1504, 1485, 1445, 1380 (m), 1318, 1305,



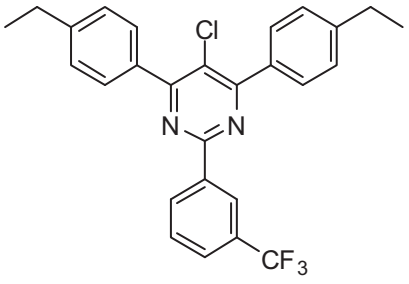
1265 (s),1161 (m), 1124, 1101, 1073 (s), 1049 (m), 999, 991, 934 (w), 921 (m), 881, 844 (w), 816, 773, 696 (s), 652, 554 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 332 ([M, $^{37}Cl_3]^+$, 03), 330 ([M, ^{35}Cl, $^{37}Cl_2]^+$, 28), 328 ([M, $^{35}Cl_2$, $^{37}Cl]^+$, 100), 326 ([M, $^{35}Cl_3]^+$, 97), 326 (97), 291 (87), 230 (10), 170 (11), 152 (14). HRMS (EI, 70 eV): calcd for $C_{11}H_4Cl_3F_3N_2$ [M, $^{35}Cl_3]^+$: 325.93921; found: 325.9380.

2,5-Dichloro-4,6-bis(4-chlorophenyl)pyrimidine (**52f**). Starting with **45** (217 mg, 1.0 mmol), $Pd(PPh_3)_2Cl_2$ (09 mg, 1.25 mol%), dioxane (5 mL), 2M K_2CO_3 (2 mL) and 4-chlorophenylboronic acid (156 mg, 1.0 mmol), **52f** was isolated as a white solid (258 mg, 88%). Reaction temperature: 70 °C for 5 h. Mp = 155-156 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39 (d, 2H, J = 8.8 Hz, ArH), 8.25 (d, 2H, J = 8.86 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 126.1 (C), 129.1, 130.1 (CH), 132.7, 138.7, 159.8, 160.8 (C). IR (KBr): $\tilde{\nu}$ = 1592, 1575, 1544, 1526 (w), 1486 (s), 1382, 1329, 1286, 1265, 1246, 1188, 1174, 1091, 1047, 1011 (m), 840, 814, 769 (s), 727, 716, 657, 630, 577 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 300 ([M, $^{37}Cl_4$,]$^+$, 01), 298 ([M, ^{35}Cl, $^{37}Cl_3]^+$, 07), 296 ([M, $^{35}Cl_2$, $^{37}Cl_2]^+$, 42), 94 ([M, $^{35}Cl_3$, $^{37}Cl]^+$, 100), 292 ([M, $^{35}Cl_4]^+$, 75), 257 (54), 222 (03), 137 (21). HRMS (EI, 70 eV): calcd for $C_{10}H_4Cl_4N_2$ [M, $^{35}Cl_4]^+$: 291.9129; found: 291.91288.



9.4.7 One-pot Synthesis of unsymmetrical 2,4,6-triaryl-5-chloropyrimidine 50c

5-Chloro-4,6-bis(4-ethylphenyl)-2-(3-(trifluoromethyl)phenyl)pyrimidine (**50c**). The reaction was carried out in a pressure tube. To a dioxane suspension (5 mL) of the chlorinated pyrimidine **45**, $Pd(PPh_3)_2Cl_2$ (09 mg, 1.25 mol%) and of the 4-ethylphenylboronic acid (300 mg, 2.0 mmol), was added an aqueous solution of K_2CO_3 (2 M, 2 mL). The mixture was heated at the indicated temperature 70 °C under Argon atmosphere for 5 h. Reaction was cooled down to room temperature (20 °C) and 3-(trifluoromethyl)phenylboronic acid (190 mg, 1.0 mmol) The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, EtOAc / heptanes) to yield **50c** as white solid (428 mg, 92%) a reduced by product **9** (13 mg, 03%). Mp = 183 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50 (t,



J = 7.6 Hz, 6H, $2CH_3$), 2.44 (q, J = 7.6 Hz, 4H, $2CH_2$), 7.56 (d, J = 8.5 Hz, 4H, ArH), 7.76 (t, J = 8.1 Hz, 1H, ArH), 7.90 (brd, J = 8.1 Hz, 1H, ArH), 8.03-7.07 (m, 4H, ArH), 8.62 (brd, J = 7.93 Hz, 1H, ArH), 8.49 (brs, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ = -63.1. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.3 ($2CH_3$), 28.86 ($2CH_2$), 124.1 (C), 125.3 (q, $J_{F,C}$ = 3.6 Hz, CH), 127.3 (q, $J_{F,C}$ = 3.8 Hz, CH), 127.7 (CH), 127.8 (q, $J_{F,C}$ = 274.2 Hz, CF_3), 128.5 (C), 129.0, 129.8 (CH), 130.6 (q, $J_{F,C}$ = 32.7 Hz, C-CF_3), 131.6 (CH), 134.4, 137.8, 160.0, 164.8 (C). IR (KBr): $\tilde{\nu}$ = 3034, 2968, 2934, 2876 (w), 1610, 1537, 1503, 1488, 1450, 1355 (m), 1319 (s), 1272, 1162, (m), 1119 (s), 1089, 1074, 1054, 1031 (m), 1017, 1001, 921, 887 (w), 840, 794, 693 (m), 652, 636, 601, 576, 538 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 466 ($[M]^+$, 100), 451 (34), 260 (05). HRMS (ESI^+): calcd for $C_{27}H_{23}ClF_3N_2$ $[M+1]^+$: 467.1496; found: 467.1502.

2,4,5-Tris(4-ethylphenyl)pyrimidine (53). Compound **53** was isolated as a white solid by-product of **50c** (12 mg, 3%). Melting point could not be measured due to very small yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09-1.25 (m, 9H, $3CH_3$), 2.54-2.70 (m, 6H, $3CH_2$), 7.06 (d, J = 8.3 Hz, 2H, ArH), 7.11 (brs, 4H, ArH), 7.26 (d, J = 8.4 Hz, 2H, ArH), 7.43 (d, J = 8.3 Hz, 2H, ArH), 8.41 (d, J = 8.4, 2H, ArH), 8.66 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.2, 15.3, 15.4 (CH_3), 28.5, 28.7, 28.8 (CH_2), 127.6, 128.1, 128.2, 128.3, 129.2, 130.0 (CH), 130.3, 134.1, 135.1, 135.4, 143.9, 145.7, 147.1 (C), 158.5 (CH) 162.9, 163.2 (C). IR (KBr): $\tilde{\nu}$ = 3020, 2962, 2929, 2870, 1609, 1575, 1523, 1501 (m), 1417 (s), 1375 (m), 1334, 1320, 1278, 1245, 1223 (w), 1175, 1048, 1017, 999, 964 (m), 830 , 806 (s), 783, 692, 685, 592, 571, 531 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 392 ($[M]^+$, 67), 391 ($[M-1]^+$, 100), 373 (08), 204 (01). HRMS (EI, 70 eV): calcd for $C_{28}H_{27}N_2$ $[M-1]^+$: 391.21688; found: 391.217041.

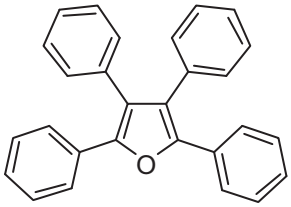
9.5 Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,3,4,5-Tetrabromofuran

9.5.1 Synthesis of tetraarylfurans 55

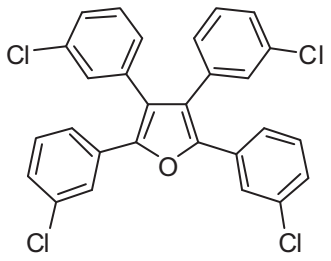
General procedure A for Suzuki Cross Ccoupling Reactions:

The reaction was carried out in a pressure tube. To a dioxane or toluene/dioxane (4:1) suspension (2.5 mL) of the brominated furan, $Pd(PPh_3)_4$ (2-3 mol%) and of the arylboronic acid (1.0 to 1.1 equiv.) was added an aqueous solution of K_2CO_3 (2 M, 0.5 mL). The mixture was heated at the indicated temperature (80 °C) under Argon atmosphere for the indicated period of time (3-5 h). The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, EtOAc / heptanes).

2,3,4,5-Tetraphenylfuran (55a). Following the *General procedure A* compound **55a** was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and phenylboronic acid (132 mg, 1.10 mmol) as a white crystalline solid (86 mg, 92%). The synthesis of **55a** has been previously reported.[85] Mp = 171 °C (lit.[84], 171 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.05-7.10 (m, 4H, ArH), 7.13-7.22 (m, 8H, ArH), 7.41-7.46 (m, 4H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ = 125.1 (C), 125.9, 127.2, 127.3, 128.3, 128.4, 130.4 (CH), 130.9, 133.2, 147.7 (C). IR (KBr): $\tilde{\nu}$ = 3082, 3047, 2918, 2852 (w), 1482, 1443 (m), 1387, 1315, 1249, 1152 (w), 1071, 1024, 946, 917, 908, 793, 765, 756, 739, 704 (m), 689, 679 (s), 657, 648, 618 (m), 580, 536 (w) cm; GC-MS (EI, 70 eV): *m/z* (%) = 72 ($[M]^+$, 100), 267 (23), 165 (05). HRMS (EI, 70 eV): calcd for $C_{28}H_{20}O$ $[M]^+$: 372.15087 found 472.150596.



2,3,4,5-Tetrakis(3-chlorophenyl)furan (55d). Following the *General procedure A* compound **55d** was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and 3-chlorophenylboronic acid (171 mg, 1.10 mmol) as a white crystalline solid (101 mg, 80%). Mp = 118-119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.93-7.00 (m, 2H, ArH), 7.06-7.23 (m, 12H, ArH), 7.47-7.48 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) : δ = 124.0 (CH), 124.5 (C), 125.8, 128.0, 128.1, 128.4, 129.8, 130.0, 130.1 (CH), 131.6, 133.9, 134.5, 134.7, 147.2(C). IR (KBr): $\tilde{\nu}$ = 1598, 1569, 1470 (m), 1426, 1321, 1300, 1257, 1136 (w), 1111, 1100, 1090, 878, 789 (m), 780, 755, 681 (s), 665, 616, 550 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 516 ($[M, {}^{37}Cl_4]^+$, 02), 514 ($[M, {}^{35}Cl, {}^{37}Cl_3]^+$, 19), 512 ($[M, {}^{35}Cl_2, {}^{37}Cl_2]^+$, 52), 510 ([M,



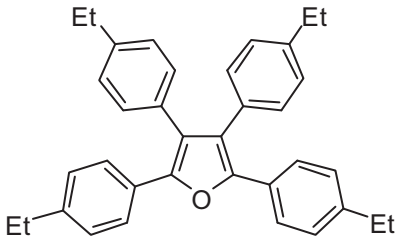
$^{35}Cl_3$, $^{37}Cl]^+$, 100), 508 ([M, $^{35}Cl_4]^+$, 19), 369 (14), 263 (15). HRMS (EI, 70 eV): calcd for $C_{28}H_{16}Cl_4O$ [M, $^{35}Cl_4]^+$:507.9955 found 507.99534.

2,3,4,5-Tetrakis(3-(trifluoromethyl)phenyl)furan (55f). Following the *General procedure A* compound **55f** was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and 3-(trifluoromethyl)phenylboronic acid (208 mg, 1.10 mmol) as a white crystalline solid (132 mg, 82%). Mp = 125-126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23-7.27 (m, 2H, ArH), 7.32-7.39 (m, 6H, ArH), 7.45-7.58 (m, 6H, ArH), 7.67 (brs, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -63.11, -63.20. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ= 122.7 (q, $J_{F,C}$ = 4.1 Hz, CH), 123.8 (q, $J_{F,C}$ = 272.2 Hz, CF_3), 123.9 (q, $J_{F,C}$ = 273.3 Hz, CF_3), 124.5 (C), 124.7 (q, $J_{F,C}$ = 3.9 Hz, CH), 124.8 (q, $J_{F,C}$ = 3.9 Hz, CH), 122.7 (q, $J_{F,C}$ = 3.6 Hz, CH), 128.9, 129.2, 129.4 (CH), 130.4 (C), 131.3 (q, $J_{F,C}$ = 36.7 Hz, C-CF_3), 131.4 (q, $J_{F,C}$ = 36.7 Hz, C-CF_3), 132.5 (C), 133.4 (CH), 147.7 (C). IR (KBr): $\tilde{\nu}$ = 1617, 1611, 1492, 1476, 1462, 1439, 1354 (w), 1324 (s), 1294, 1284, 1205 (m), 1160, 1113, 1097, 1068 (s), 1000, 967, 897, 850 (m), 800 (s), 739 (w), 707, 700, (s), 652 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 644 ([M]$^+$, 100), 555 (11), 411 (12), 325 (10). HR-MS (EI, 70 eV): m/z= 644.10095;, calcd. for $C_{32}H_{16}F_{12}O$ (M^+) found: 644.099515.

2,3,4,5-Tetrakis(4-methoxyphenyl)furan (55g). Following the *General procedure A* compound **55g** was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-methoxyphenylboronic acid (167 mg, 1.10 mmol) as a white crystalline solid (120 mg, 98%). The synthesis of **55g** has been previously reported.[85] Mp = 206-207 °C (lit.[85], 206-208 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 12H, 4OCH_3), 6.67-6.98 (m, 8H, ArH), 6.96 (d, 4H, *J* = 8.3 Hz, ArH), 7.34 (d, 4H, *J* = 8.9 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) : δ= 55.1, 55.2 (OCH_3), 113.8, 113.9 (CH), 123.3, 124.1, 125.8 (C), 127.2, 131.6 (CH), 147.2, 158.5, 158.7 (C). IR (KBr): $\tilde{\nu}$ = 3433 (w), 3020, 3001, 2953, 2922, 2839, 1603 (m), 1501, 1492, 1283, 1172, 1029, 831 (s), 788 (m) cm;

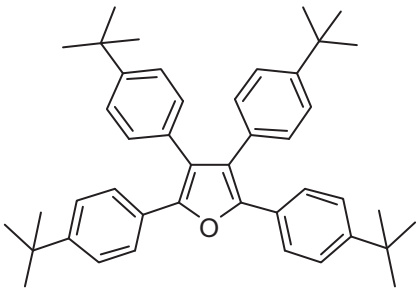
GC-MS (EI, 70 eV): *m/z* (%) = 492 ($[M]^+$, 100), 377 (15), 357 (09), 246 (05), 246 (22). HRMS (EI, 70 eV): calcd for $C_{32}H_{28}O_5$ $[M]^+$: 492.19313 found 492.193346.

2,3,4,5-Tetrakis(4-ethylphenyl)furan (55b). Following the *General procedure A* compound



55b was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-ethylphenylboronic acid (165 mg, 1.10 mmol) as a white solid (111 mg, 92%). Mp = 167-168 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, 6H, *J* = 7.6 Hz, $2CH_3$), 1.16 (t, 6H, *J* = 7.6 Hz, $2CH_3$), 2.51-2.58 (m, 8H, $4CH_2$), 6.89-7.03 (m, 12H, ArCH), 7.35 (d, 4H, *J* = 8.2 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) : δ = 15.1, 15.3 ($2CH_3$), 28.5, 28.6 ($2CH_2$), 124.4 (C), 125.8, 127.7, 127.8 (CH), 128.7 (C), 130.3 (CH), 130.6, 142.7, 143.2, 147.5 (C). IR (KBr): $\tilde{\nu}$ = 3023 (w), 2964, 2929, 2869, 2859, 1518, 1454, 1372 (m), 1317, 1298, 1261, 1242, 1185 (w), 1184, 1114, 1104, 1062, 1045, 1018, 966, 944 (m), 832 (s), 795, 782, 747 (w), 686, 647, 637, 628 (m), 595, 587, 551 (w) cm; GC-MS (EI, 70 eV): *m/z* (%) = 484 ($[M]^+$, 100), 469 (15), 351 (09). HRMS (EI, 70 eV): calcd for $C_{36}H_{36}O$ $[M]^+$: 484.27607 found 484.275860.

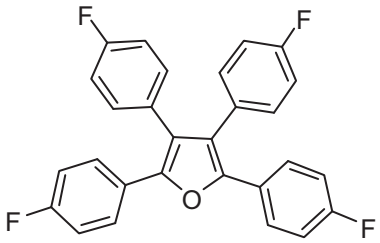
2,3,4,5-Tetrakis(4-tert-butylphenyl)furan (55c). Following the *General procedure A* compound



55c was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-tert-butylphenylboronic acid (195 mg, 1.10 mmol) as a white solid (137 mg, 92%). Mp = 163 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 18H, $6CH_3$), 1.23 (t, 18H, $6CH_3$), 7.00 (d, 4H, *J* = 8.7 Hz, ArH), 7.16 (d, 4H, *J* = 8.9 Hz, ArH), 7.20 (d, 4H, *J* = 8.7 Hz, ArH), 7.4 0 (d, 4H, *J* = 8.7 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) : δ = 131.3, 31.4 ($6CH_3$), 34.5, 34.6, 124.7 (C), 125.0, 125.2, 125.3 (CH), 128.5 (C), 130.0 (CH), 130.4, 147.3, 149.7, 149.9 (C). IR (KBr): $\tilde{\nu}$ = 2960 (s), 2904, 2867 (m), 1789, 1766 (w) 1681, 1674, 1604, 1475, 1462, 1407, 1362, 1298 (m), 1267 (s), 1182, 1108, 1012 (m), 974, 942, 926, 887, 856 (w), 828 (s), 784, 770, 702, 687, 649, 626,

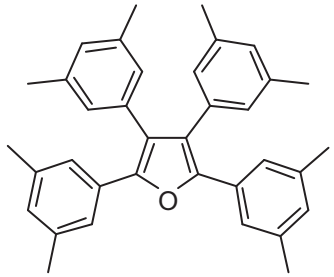
575, 545 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 484 ($[M]^+$, 100), 469 (15), 351 (09). HRMS (EI, 70 eV): calcd for $C_{44}H_{52}O$ $[M]^+$: 596.40182 found 596.40177.

2,3,4,5-Tetrakis(4-fluorophenyl)furan (55e). Following the *General procedure A* compound



55e was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-fluorophenylboronic acid (154 mg, 1.10 mmol) as a white solid (94 mg, 80%). The synthesis of **55e** has been previously reported. [85] Mp = 122-123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.86-6.85 (m, 8H, ArH), 6.98-7.04 (m, 4H, ArH), 7.31-7.41 (m, 4H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -113.35, -111.25 . ^{13}C NMR (75.5 MHz, $CDCl_3$) : δ = 115.6 (d, $J_{F,C}$ = 21.9 Hz, CH), 115.7 (d, $J_{F,C}$ = 21.3 Hz, CH), 123.5 (C), 126.6 (d, $J_{F,C}$ = 3.3 Hz, C), 127.6 (d, $J_{F,C}$ = 8.2 Hz, CH), 128.6 (d, $J_{F,C}$ = 3.5 Hz, C), 131.9 (d, $J_{F,C}$ = 8.0 Hz, CH), 147.1, (C), 127.6 (d, $J_{F,C}$ = 248.5 Hz, 2CF). IR (KBr): $\tilde{\nu}$ = 3054, 2920, 2851 (w), 1738, 1732, 1589, 1475 (w), 1434 (m), 1393, 1378, 1307, 1260 (w), 1192, 1117 (s), 1089, 1068, 1025, 996 (m), 747, 743, 718, 691, 537 (s) cm. GC-MS (EI, 70 eV): *m/z* (%) = 444 ($[M]^+$, 100), 321 (30), 201 (05). HRMS (EI, 70 eV): calcd for $C_{28}H_{16}O_4$ $[M]^+$: 444.11318 found 444.11267.

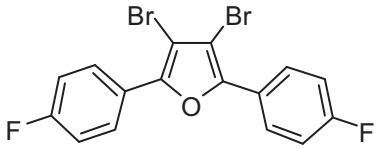
2,3,4,5-Tetrakis(3,5-dimethylphenyl)furan (55h). Following the *General procedure A*



compound **55h** was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), 1,4-dioxane (2.5 mL), 2M K_2CO_3 (0.5 mL) and 3,5-dimethylphenylboronic acid (165 mg, 1.10 mmol) as a white crystalline solid (91 mg, 76%). Mp = 156 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s, 12H, $4CH_3$), 2.15 (s, 12H, $4CH_3$), 6.71 (s, 2H, ArH), 6.72 (s, 2H, ArH), 6.76 (s, 4H, ArH), 7.08 (s, 4H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) : δ = 21.1, 21.4, 123.6 (CH), 125.2 (C), 128.3, 128.5, 128.8 (CH), 131.1, 133.2, 137.3, 137.6, 147.5 (C). IR (KBr): $\tilde{\nu}$ = 3003, 2915, 2860 (w), 1618, 1599, 1462, 1444, 1377, 1299, 1213, 1198, 1176, 1148, 1036, 913, 894 (m), 848 (s), 801, 729, 702, 692, 675 (m) cm. GC-MS (EI, 70 eV): *m/z* (%) = 484 ($[M]^+$, 100), 351 (33), 321 (05), 242 (06). HRMS (EI, 70 eV): calcd for $C_{36}H_{36}O$ $[M]^+$: 484.27607 found 484.27587.

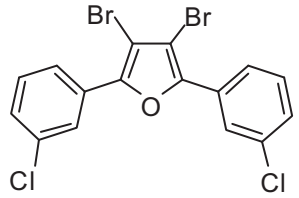
9.5.2 Synthesis of 2,5-diaryl-3,4-dibromofurans 56

3,4-Dibromo-2,5-bis(4-fluorophenyl)furan (56b). Following the *General procedure A*



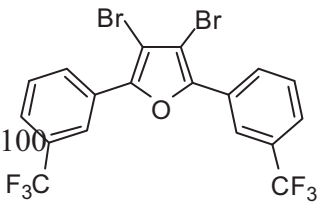
compound **56b** was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-fluorophenylboronic acid (70 mg, 0.50 mmol) as a white solid (90 mg, 87%). Mp = 83-84 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.05-7.17 (m, 4H, ArH), 7.91-7.96 (m, 4H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -111.4. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 102.1 (C), 115.6, 116.0 (CH), 125.2 (d, $J_{C,F}$ = 3.6 Hz, C), 127.6, 127.8 (CH), 147.4, 162.3 (d, $J_{C,F}$ = 251.9 Hz, CF). IR (KBr): $\tilde{\nu}$ = 1786, 1760, 1605, 1497, 1523, 1492 (m), 1410, 1298, 1275 (w), 1233, 1159 (s), 1072, 996, 943, 829 (m), 729, 641, 632, 597, 587 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 416 ([M, ^{81}Br,^{81}Br]$^+$, 50), 414 ([M, ^{79}Br,^{81}Br]$^+$, 100), 412 ([M, ^{79}Br,^{79}Br]$^+$, 50), 305 (18), 225 (18), 207 (10). HR-MS (EI, 70 eV): m/z= 411.89100, calcd. for $C_{16}H_8OBr_2F_2$ (M^+, [^{79}Br,^{79}Br]) found: 411.890019; 413.88840, calcd. for (M^+, [^{79}Br,^{81}Br]) found 413.888075; 415.88635, calcd. for (M^+, [^{81}Br,^{81}Br]) found 415.886165.

3,4-Dibromo-2,5-bis(3-chlorophenyl)furan (56a). Following the *General procedure A*



compound **56a** was prepared from **54** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 3-chlorophenylboronic acid (78 mg, 0.50 mmol) as a white solid (87 mg, 85%). Mp = 91-92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26-7.33 (m, 4H, ArH), 7.83 (dt, J = 1.6, 7.4 Hz, 2H, ArH), 7.89-7.91 (m, 2H, ArH). ^{13}C NMR (75.7 MHz, $CDCl_3$): δ = 103.7 (C), 123.7, 125.5, 128.2, 130.0 (CH), 130.4, 134.8, 147.1 (C). IR (KBr): $\tilde{\nu}$ = 1596, 1567, 1471, 1461 (m), 1426, 1401, 1321, 1302, 1258, 1241, 1136 (w), 1112, 1102, 1092, 1074, 991, 958, 878, 789 (m), 779, 754, 681 (s), 664, 615, 549, 529 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 446 ([M, ^{79}Br, ^{81}Br, ^{35}Cl, ^{35}Cl]$^+$ or [M, ^{79}Br, ^{79}Br, ^{35}Cl, ^{37}Cl]$^+$, 100), 444 ([M, ^{79}Br, ^{79}Br, ^{35}Cl, ^{35}Cl]$^+$, 36), 450 ([^{81}Br, ^{81}Br, ^{37}Cl, ^{37}Cl]$^+$, 31), 339 (10), 223 (14). HR-MS (EI, 70 eV): m/z= 443.83135, calcd. for $C_{16}H_8OBr_2Cl_2$ (M^+, [^{79}Br, ^{79}Br, ^{35}Cl, ^{35}Cl]) found: 443.832061.

3,4-Dibromo-2,5-bis(3-(trifluoromethyl)phenyl)furan (56c). Following the *General procedure A* compound **56c** was prepared from **54** (96 mg, 0.25



mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 3-(trifluoromethyl)phenylboronic acid (95 mg, 0.50 mmol) as a white solid (109 mg, 85%). Mp = 103-104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50-7.59 (m, 4H, ArH), 8.12-8.15 (m, 2H, ArH), 8.21 (brs, 2H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = 62.87. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 104.0 (C), 122.4 (q, $J_{F,C}$ = 4.0 Hz, CH), 124.23 (q, $J_{F,C}$ = 272.6 Hz, CF_3), 125.4 (q, $J_{F,C}$ = 3.7 Hz, CH), 128.7, 129.3 (CH), 129.4 (C), 131.3 (q, $J_{F,C}$ = 32.7 Hz, C-CF_3), 147.4 (C). IR (KBr): $\tilde{\nu}$ = 3028 , 2922, 2867, 1746, 1692, 1610, 1511, 1445, 1428 (w), 1327, 1307, 1147 (m), 1122, 1071 (s), 1052, 961, 946, 902, 845 (w), 801 (m), 750, 740, 715 (w), 693 (s), 664, 655, 573 (w) cm. GC-MS (EI, 70 eV): *m/z* (%) = 514 ([M, ^{79}Br,^{79}Br]$^+$, 52), 514 ([M, ^{81}Br,^{81}Br]$^+$, 100), 516 ([M, ^{81}Br,^{81}Br]$^+$, 49), 495 (07), 407 (12), 326 (07), 257 (15), 173 (37). HR-MS (EI, 70 eV): m/z= 511.88406, calcd. for $C_{18}H_8Br_2OF_6$ (M^+, [^{79}Br, ^{79}Br]) found: 511.884645; 513.88201, calcd. for (M^+, [^{81}Br,^{79}Br]) found 513.882475; 515.87997, calcd. for (M^+, [^{81}Br, ^{81}Br]) found 515.880736

Appendix

10 Crystallographic Data

10.1 Crystal data and structure refinement for **Diethyl 9-methyl-9H-carbazole-2,3-dicarboxylate (19a)**

Identification code	mh96-3	
Empirical formula	$C_{19}H_{19}NO_4$	
Formula weight	325.35	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.135 (4) Å	α = 71.282°.
	b = 9.673 (5) Å	β = 79.208°.
	c = 12.548 (7) Å	γ = 78.97°.
Volume	794.7 (8) $Å^3$	
Z	2	
Density (calculated)	1.360 Mg/m^3	
Absorption coefficient	0.096 mm^{-1}	
F(000)	344	
Crystal size	0.32 x 0.15 x 0.08 mm^3	
Θ range for data collection	7.891 to 59.925°.	
Index ranges	$-10\leq h\leq 10$, $-13\leq k\leq 13$, $-17\leq l\leq 15$	
Reflections collected	4557	
Independent reflections	2986 [R(int) = 0.032]	
Absorption correction	multi-scan	
Max. and min. transmission	0.9924 and 0.9700	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.080	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0477, wR2 = 0.1157	
R indices (all data)	R1 = 0.0879, wR2 = 0.1271	

10.2 Crystal data and structure refinement for **2-(2-cyanoethyl)-9-methyl-9H-carbazole-3-carbonitrile(20)**

Identification code	mh95a	
Empirical formula	$C_{17}H_{13}N_3$	
Formula weight	259.3	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.512 (11) Å	α = 67.65°.
	b = 9.495 (13) Å	β = 88.51°.
	c = 10.261 (13) Å	γ = 71.31°.
Volume	637.4 (15) $Å^3$	
Z	2	
Density (calculated)	1.351 Mg/m^3	
Absorption coefficient	0.082 mm^{-1}	
F(000)	272	
Θ range for data collection	4.910 to 40.817°.	
Index ranges	$-7\leq h\leq 9$, $-12\leq k\leq 12$, $-13\leq l\leq 13$	
Reflections collected	2424	
Independent reflections	2524 [R(int) = 0.026]	
Absorption correction	multi-scan	
Max. and min. transmission	0.9975 and 0.9127	

10.3 Crystal data and structure refinement for **Isobutyl 6-oxo-6H-benzo[c]chromene-8-carboxylate (42)**

Identification code	mh15	
Empirical formula	$C_{18}H_{16}O_4$	
Formula weight	296.31	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	P n m a	
Space group (Hall)	-P 2ac 2n	
Unit cell dimensions	a = 11.943 (5) Å	α = 90°.
	b = 6.772 (5) Å	β = 90°.
	c = 17.526 (5) Å	γ = 90°.
Volume	417.5 (13) $Å^3$	
Z	4	
Density (calculated)	1.388 Mg/m^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)	624	
Crystal size	0.63 x 0.04 x 0.04 mm^3	
Θ range for data collection	6.450 to 50.167°.	
Index ranges	$-15\leq h\leq 15$, $-8\leq k\leq -8$, $-22\leq l\leq 22$	
Reflections collected	1747	
Independent reflections	864 [R(int) = 0.109]	
Absorption correction	multi-scan	
Max. and min. transmission	0.9961 and 0.9409	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	0.894	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0525, wR2 = 0.0946	
R indices (all data)	R1 = 0.1463, wR2 = 0.1138	

10.4 Table 6. Crystal data and structure refinement for **2,4,5,6-Tetraphenylpyrimidine 47a**

Identification code	mh201	
Empirical formula	$C_{28}H_{20}N_2$	
Formula weight	384.47	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	F d d 2	
Space group (Hall)	F 2 -2d	
Unit cell dimensions	a = 23.815 (5) Å	α = 90°.
	b = 57.776 (9) Å	β = 90°.
	c = 5.814 (5) Å	γ = 90°.
Volume	8000 (7) $Å^3$	
Z	16	
Density (calculated)	1.277 Mg/m^3	
Absorption coefficient	0.075 mm^{-1}	
F(000)	3232	
Crystal size	0.51 x 0.06 x 0.06 mm^3	
Θ range for data collection	4.81 to 25.55°.	
Index ranges	$-28\leq h\leq 26$, $-67\leq k\leq 70$, $-7\leq l\leq 6$	
Reflections collected	13820	
Independent reflections	2590 [R(int) = 0.066]	
Absorption correction	multi-scan	
Max. and min. transmission	0.9955 and 0.9626	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.005	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0452, wR2 = 0.0747	
R indices (all data)	R1 = 0.0834, wR2 = 0.0833	

10.5 Table 12. Crystal data and structure refinement for **2,3,4,5-tetraphenylfuran (55a)**

Identification code	mh350	
Empirical formula	$C_{28}H_{20}O$	
Formula weight	372.44	
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 = 25.6061 (11) Å	α = 90.00°.
	b = 8.0159 (3) Å	β = 117.206°.
	c = 21.5847 (8) Å	γ = 90.00°.
Volume	3940.2 (3) $Å^3$	
Z	8	
Density (calculated)	1.256 Mg/m^3	
Absorption coefficient	0.075 mm^{-1}	
F(000)	1568	
Crystal size	0.37 x 0.29 x 0.10 mm^3	
Θ range for data collection	4.114 to 59.926°.	
Index ranges	$-36\leq h\leq 36$, $-10\leq k\leq 11$, $-30\leq l\leq 30$	
Reflections collected	5745	
Independent reflections	3872 [R(int) = 0.040]	
Absorption correction	multi-scan	
Max. and min. transmission	0.9926 and 0.9730	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.037	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0476, wR2 = 0.1192	
R indices (all data)	R1 = 0.0819, wR2 = 0.1294	

10.6 Table 12. Crystal data and structure refinement for **2,3,4,5-tetrakis(4-methoxyphenyl)furan (55g)**

Identification code	mh236	
Empirical formula	$C_{32}H_{28}O_5$	
Formula weight	492.54	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 9.9197 (2) Å	α = 87.7670°.
	b = 11.0554 (3) Å	β = 81.3120°.
	c = 24.3304 (6) Å	γ = 78.6210°.
Volume	2585.65 (11) $Å^3$	
Z	4	
Density (calculated)	1.265 Mg/m^3	
Absorption coefficient	0.085 mm^{-1}	
F(000)	1040	
Crystal size	0.48 x 0.26 x 0.20 mm^3	
Θ range for data collection	4.785 to 59.182°.	
Index ranges	$-13\leq h\leq 13$, $-15\leq k\leq 15$, $-34\leq l\leq 34$	
Reflections collected	15043	
Independent reflections	10035 [R(int) = 0.035]	
Absorption correction	multi-scan	
Max. and min. transmission	0.9832 and 0.9604	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.060	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0469, wR2 = 0.1084	
R indices (all data)	R1 = 0.817, wR2 = 0.1189	

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*-$MeC_6H_4SO_2$

Erklärung

Ich versichere hiermit an Eides statt, daß ich die vorliegende Arbeit selbständig angefertigt und ohne fremde Hilfe verfasst habe, keine außer den von mir angegebenen Hilfsmitteln und Quellen dazu verwendet habe und die den benutzten Werken inhaltlich und wörtlich entnommenen Stellen als solche kenntlich gemacht habe.

Rostock, Juli 2010.

CURRICULUM VITAE

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Nationality	Pakistan
Marital status	Single

Education

2008 - 2010	**Ph.D Student,** University of Rostock, Institute of Chemistry, Department of Organic Chemistry, Rostock, **Germany** Dissertation Title: "Domino Twofold Heck / 6-pi-Electrocyclization and Regioselective Palladium(0)-Catalyzed Reactions of Brominated Indoles, Furans, Naphthoquinone and 2,4,5,6-Tetrachloro-pyrimidine"
2006 - 2007	**Visiting Scientist**, Bioorganic Synthesis, Synthesis of PTP1B inhibitors to cure Diabetes Type 2 and Obesity, University of Waterloo, ON, **Canada**
2002 - 2005	**Research Fellow** Phytochemical Investigation of Chemical constituents of *Abutilon pakistanicum* and *Abutilon indicum*, , HEJ Research Institute of Chemistry,University of Karachi, Karachi, **Pakistan**
2002	**M.Sc** Organic Chemistry, University of Karachi, Karachi, **Pakistan** **1st Class**

2000	**B.Sc** Chemistry, Botany, Zoology, Islamia University Bahawalpur, **Pakistan** **1st Class**
1995	**H. S. C.** Chemistry, Biology, Physics, Board of Intermediate and Secondar Schools Bahawalpur, Bahawalpur, Pakistan **1st Class**
1993	**S. S. C.** Chemistry, Biology, Physics, Mathematics, Board of Intermediate and Secondar Schools Bahawalpur, Bahawalpur, Pakistan **1st Class**

Experience

Synthesis	Five (5) years Synthetic Organic Chemistry research experience which includes Pd(0) Catalysis, $TiCl_4$ mediated 3+3 cyclization, electrocyclization, Lithium Metal-Halide exchange reaction, Regioeselective Halogenation, Cu, Mg, Pd Catalyzed reactions and Microwave assisted Reaction operations and multi-step synthesis etc.
Natural Products	Three (3) year experience Natural Product Isolation and structure elucidation of natural products from plants
Chromatography	Thin Layer Chromatography, Column Chromatography, HPLC Analytic and Preparative, Chromatotron
Spectroscopy	1D and 2D NMR (^{1}H-NMR, ^{13}C-NMR, DEPT, COSY, HSQC, HMQC, HMBC, NOESY), IR and MS
Computer & Software	System: Windows (Operating System), Internet resources Software: Word, Excel, PowerPoint, ChemDraw, Top-spin Databases: Beilstein, SciFinder Scholar, Cross-fire
Teaching & Training Experience	Teaching Assistance at University of Waterloo, ON, **Canada** Over 15 Ph. Student trained for practical organic synthesis at University of Rostock, Rostock, **Germany**

Seminar Presentation

2005	Conversion Seminar at HEJ Research Institute of Chemistry, University of Karachi, **Karachi**

Awards / Scholarships

2000	Top-Ten Scholarship in Master of Science, from Federal Urdu Science College Karachi, Karachi, **Pakistan**
2002-2003	Research Fellow Scholarship from HEJ Research Institute of Chemistry, University of Karachi, **Pakistan**
2004-2008	Split Ph.D. Scholarship, Development of High Level S&T Manpowr through Higher Education Commission of **Pakistan**
2009-2010	Mecklenburg-State Scholarship, University of Rostock, Rostock, **Germany**

Certificate Courses

05/2002-12/2002	Advance Organic Chemistry Ph.D. course at HEJ Research Institute of Cemistry, University of Karachi, **Pakistan**
06/2003	Advanced Courses entitled, "Bio-inorganic Chemistry and Medicinal Chemistry of Transition Metals" at HEJ Research Institute of Chemistry, University of Karachi, Karachi, **Pakistan** in collaboration with St. Cloud State University USA
04/2003	Advanced Course entitled, "Biochemical Basis of Diabetics and Aging"held at HEJ Research Institute of Chemistry, Karachi, Pakistan, Institute of Chemistry, **Pakistan**
Winter 2006	"Synthetic Organic Reactions" by Dr. William Tam at University of Waterloo held jointly with Guelph University in Ontarion **Canada**
Spring 2007	"Topics in Natural Product Chemistry" based on designing a Total Synthesis of Natural Products at University of Waterloo, ON, **Canada**

Conference/Workshops

12/2002	13th National Chemistry Conference jointly organized by the Department of Chemistry, University of Karachi and HEJ Research Institute of Chemistry, University of Karachi, Karachi, **Pakistan**
01/2004	"9th International Symposium on Natural Product Chemistry" Organized by HEJ Research Institute of Chemistry, University of Karachi, Karachi, **Pakistan**

Poster Presentation	**QOMBSBOC** conference Poster entitled "Synthesis of an α,α-Difluorosulfonate Analog of a High Affinity Small Molecule Phosphonate Inhibitor of PTP 1B" at Western Ontario University, ON, Canada, **Canada**

Languages

Urdu	Native speaker
German	Learning
English	Fluently in writing, listening and speaking

PUBLICATIONS

[1] Site-Selective Suzuki-Miyaura Reactions of the Bis(triflate) of 1,3-Dihydroxyanthraquinone. Omer A. Akrawi, Munawar Hussain, Peter Langer *Tetrahedron Lett,* **2011,** *(In Press).*

[2] Regioselective Suzuki-Miyaura Reactions of the Bis(triflate) of 1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-one. Ghazwan Ali Salman, Ahmad Mahal, Mohanad Shkoor, **Munawar Hussain**, Alexander Villinger, Peter Langer. *Tetrahedron Lett,* **2011,** *52*, 392.

[3] Site-Selective Suzuki-Miyaura Reactions of Ethyl 3,5-(bistrifluoromethylsulfonyloxy)-2-naphthoate. Nadi Eleya, Ahmed Mahal, **Munawar Hussain**, Peter Langer. *Synthesis.* **2011**, (*Submitted*)

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[5] Site-selective Suzuki-Miyaura Reactions of the Bis(triflate) of 5,10-dihydroxy-11*H*-benzo[*b*]fluoren-11-one. Ghazwan Ali Salman, **Munawar Hussain**, Alexander Villinger, Peter Langer, *Synlett.* **2011**, 3031.

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[8] "Synthesis of 7,8-Diarylflavones by Site-Selective Suzuki-Miyaura Reactions", Malik, I.; **Hussain, M.;** Hung, N. T.; Villinger, A.; Langer, P. *Synlett.* **2010**, *15*, 2244.

[9] Synthesis of Fluorinated 2,3-Dihydro-4*H*-pyran-4-ones by Cyclocondensation of 1,3-"Dicarbonyl Dianions with Aldehydes", Khera, R. A.; **Hussain, M.;** Ahmad, R.; Villinger, A.; Saeed, A.; Fischer, C.; Langer, P. *J. Fluorine Chem.* **2010** *131*, 892.

[10] "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. *Advanced Synthesis & Catalaysis,* **2010,** *352*, 1429.

[11] "Synthesis of Arylated Pyrazoles by Site-Selective Suzuki-Miyaura Reactions of Tribromopyrazoles", Ali, A.; Khera, R. A.; **Hussain, M.;** Tatar, J.; Villinger, A.; Langer, P. *Synlett,* **2010,** *13*, 1923.

[12] "Twofold Heck cross-coupling reactions of dibrominated pyridines", Ali, A.; **Hussain, M.;** Malik, I.; Fischer, C.; Langer, P. *Helv. Chim. Acta.* **2010**, *93*, 1764

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