UNIVERSITÄT ROSTOCK

New Palladium(0)-Catalyzed Reactions of 2,3-Dibromobenzofuran, 2,3,5-Tribromobenzofuran, and 2,3-Dibromoindenone

Dissertation

zur

Erlangung des Doktorgrades

doctor rerum naturalium (Dr. rer. nat.)

der Mathematisch-Naturwissenschaftlichen Fakultät

der Universität Rostock

vorgelegt von

Nguyen Thai Hung geb. am 05. May 1976 Thai Binh, Viet Nam

Rostock, October 2010

urn:nbn:de:gbv:28-diss2011-0102-7

Die vorliegende Arbeit entstand in der Zeit von Juli 2008 bis Oktober 2010 am Institut für Chemie der Universität Rostock.

Erinreichung der Dissertation:

1. Gutachter: Prof. Dr. Peter Langer, Universität Rostock
2. Gutachter: Prof. Dr. Till Opadtz, Universität Mainz

Tag der Abgabe: 29th Oktober, 2010

Tag der Verteidigung: 24th Mai, 2011

“It is a great pleasure to dedicate all of this work to all my respected **teachers, mentors, my dear parents** and **my wife** !”

Acknowledgements

Vielen Dank

First of all, I wish to express my deep gratitude and infinite thanks to Prof. Dr. Peter Langer, my Ph.D. supervisor, who offered me an unique opportunity, reviving encouragements and tolerance for the successful completion of my Ph.D. During the whole Ph.D work, I always found from him efficient guidance, effective discussions, fulfilled research environment as well as all necessary materials and facilities. Without his help and support, the achievement of this work would not have been possible.

Danke schön

I would like to present special thanks to Dr. Martin Hein and Dr. Dirk Michalik for a number of crucial lectures, to Dr. Holger Feist for the security instructions, to Dr. Alexander Villinger for the professional and accurate of X-ray crytallographic analyses, and also to all the technical and the other members of NMR, IR, UV, MS, and X-ray laboratories of University of Rostock and the Leibniz Institute for Catalysis Rostock as well.

Shukriyah

Thank you

Acknowledgements are made to all my colleagues and friends for their cooperations, especially to Mr. Munawar Hussain, who helped me a lot to overcome many difficulties and due to his exceptionally academic supports .

Lời cảm ơn

Danke schön

A special acknowledgement and expression of appreciation must go to the Ministry of Education and Training of Vietnam (MOET) and DAAD for the financial support to hold up my Ph.D research in Germany.

Trân trọng

It is a great pleasure to acknowledge to all my respected teachers, mentors; sincerely thanks to all of them. I am grateful to all members of my family for their love and adherence to my achievement struggle. Their essential helps and kind supports cannot be expressed by words. I love them so much and I owe all of them in my life !

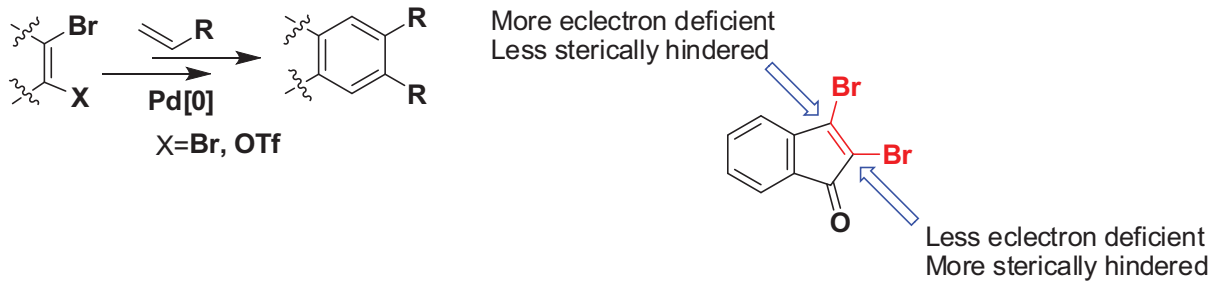
MAIN CONTENTS

SUMMARY Page 1

CHAPTER 1 Page 2 - 12

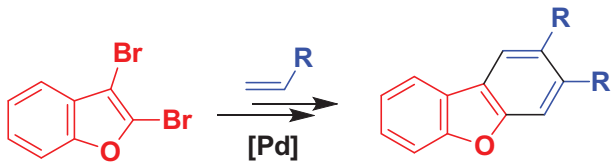
Overview

An overview of Domino Twofold Heck / 6π-Electrocyclization Reactions and Site-Selective Suzuki-Miyaura Reactions is given.



CHAPTER 2 Page 13 - 19

Efficient Synthesis of Functionalized Dibezofurans by Domino Twofold Heck / 6π-Electrocyclization Reactions of 2,3-Dibromobenzofuran



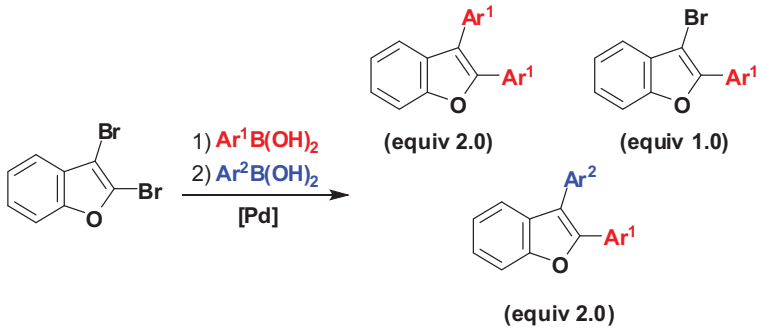
2,3-Dibromobenzofuran and 2,3,5-tribromobenzofuran were prepared from benzofuran. Functionalized dibenzofurans were prepared based on domino twofold Heck / 6π-electrocyclization reactions of 2,3-di- and 2,3,5-tribromobenzofuran.

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

CHAPTER 3 Page 20 - 29

Site-Selective Suzuki-Miyaura Reactions of 2,3-Dibromobenzofuran and 2,3,5-Tribromobenzofuran

The Suzuki-Miyaura reaction of 2,3-dibromobenzofuran with two equivalents of boronic acids gave 2,3-diarylbenzofurans. The reaction with one equivalent of arylboronic acids resulted in site-selective formation of 2-aryl-3-bromobenzofurans. 2,3-Diarylbenzofurans containing two different aryl groups were prepared from 2,3-dibromobenzofuran in a one-pot protocol by sequential addition of two different boronic acids. Site selective Suzuki-Miyaura reactions of 2,3,5-tribromobenzofuran were also investigated.



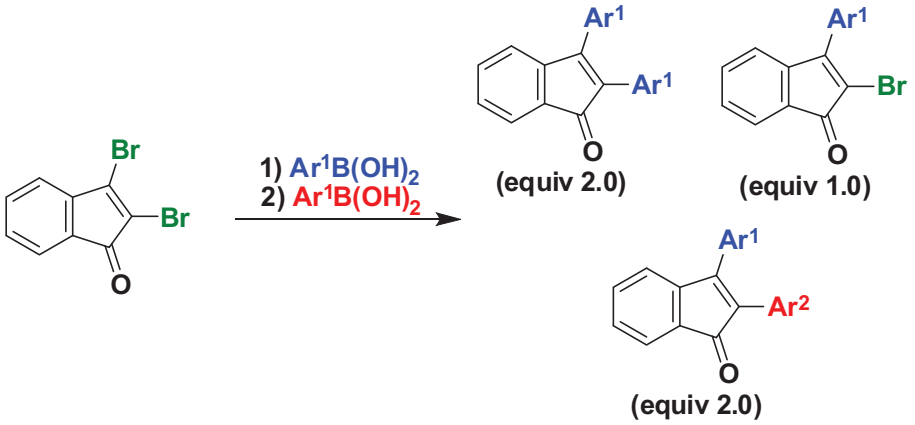
Hung, **N**. **T**.; Hussain M.; Malik, I.; Villinger, A.; Hussain M.; Langer, P., *Tetrahedron Lett.* **2010**, *51*, 2420

CHAPTER 4 Page 30 - 38

One-Pot Synthesis of 2,3-Diarylindenones by Site-Selective Suzuki-Miyaura Reactions of 1,2-Dibromoindenone

The first transition metal-catalyzed cross-coupling reactions of 2,3-dibromo-1*H*-inden-

1-one are reported. The Suzuki-Miyaura reaction of 2,3-dibromo-1*H*-inden-1-one with two equivalents of arylboronic acid gave 2,3-diaryl-1*H*-inden-1-ones. The reaction with one equivalent of arylboronic acids gave 2-bromo-3-aryl-1*H*-inden-1-ones with very good site-selectivity. The one-pot reaction of 2,3-dibromo-1*H*-inden-1-one with two different arylboronic acids afforded 2,3-diaryl-1*H*-inden-1-ones containing two different aryl groups.



Hussain, M.; **Hung, N. T.**; Khera, R. A.; Villinger, A.; Langer, P., *Tetrahedron Lett.* **2010**, *52*, 184.

ABSTRACT Page 39 - 40

EXPERIMENTAL SECTION Page 41 - 83

APPENDIX Page 84 - 89

ABBREVIATIONS Page 90 - 91

ERKLÄRUNG Page 92

REFERENCE Page 93 - 99

DETAILED CONTENTS

1 Overview 2

1.1 Domino Twofold Heck / 6π-Electrocyclization Reaction 2

1.2 Regioselective Arylation by Suzuki-Miyaura Cross-Coupling Reaction 6

2 Efficient Synthesis of Functionalized Dibezofurans by Domino Twofold Heck / 6π-Electrocyclization Reactions of 2,3-Dibromobenzofuran 13

2.1 Introduction 13

2.2 Results and discussion 14

2.3 Conclusion 19

3 Site-Selective Suzuki Cross-Coupling Reactions of 2,3-Dibromobenzofuran and 2,3,5-Tribromobenzofuran 20

3.1 Introduction 20

3.2 Results and discussion 20

3.3 Conclusion 29

4 One-Pot Synthesis of 2,3-Diarylindenones by Site-Selective Suzuki-Miyaura Reactions of 1,2-Dibromoindenone 30

4.1 Introduction 30

4.2 Results and discussion 31

4.3 Conclusion 38

5 Abstract.....39

Experimental Section.....41

6 Material and Methods.....41

6.1 General Remarks 41

6.2 Methods for Compound Characterization and Analysis 41

6.3 Chromatographic Methods 43

7 General Procedures 44

7.1 Efficient Synthesis of Functionalized Dibezofurans by Domino Twofold Heck / 6π-Electrocyclization Reactions of 2,3-Di- and 2,3,5 Tribromo-benzofuran 44

7.1.1 Synthesis of **54** 44

7.1.2 Synthesis of **18** from **55** ……..…..…….…….....47
7.1.3 Synthesis of reduced products **55a,b**……..……..……..51
7.2 Site-Selective Suzuki Cross-Coupling Reactions of 2,3-dibromobenzofuran..... 53
7.2.1 Synthesis of 2,3-diarylbenzofurans 53
7.2.2 Synthesis of 2-aryl-3-bromobenzofuran 60
7.2.3 Synthesis of unsymmetrical 2,3-diarylbenzofurans..... 67
7.3 One-Pot Synthesis of 2,3-Diarylindenones by Site-Selective Suzuki-Miyaura Reaction 1,2-Dibromoindenone 70
7.3.1 Synthesis of 2,3-diarylindenones 70
7.3.2 Synthesis of 3-aryl-2-bromoinden-1-ones..... 75
7.3.3 Synthesis of unsymmetrical 2,3-diarylindenones 79
Appendix.....84
8 Crystallographic Data 84
8.1 Crystal data and structure *refinement* for 2,3-bis(4-tert- butylphenyl)benzofuran..... 84
8.2 Crystal data and structure *refinement* for 2,3-bis(4-chlorophenyl)benzofuran..... 85
8.3 Crystal data and structure *refinement* for 2,3-bis(4-fluorophenyl)benzofuran..... 86
8.4 Crystal data and structure *refinement* for 2-(4-fluorophenyl)-3-p-tolylbenzofuran..... 87
8.5 Crystal data and structure *refinement* for 2,3-diphenyl-1*H*-inden-1-one 88
8.6 Crystal data and structure *refinement* for 2-bromo-3-(2,6-dimethoxyphenyl)-1*H*-inden-1-one) 89
Abbreviations 90
Erklärung 92
Curriculum vitae.....93
References.....97

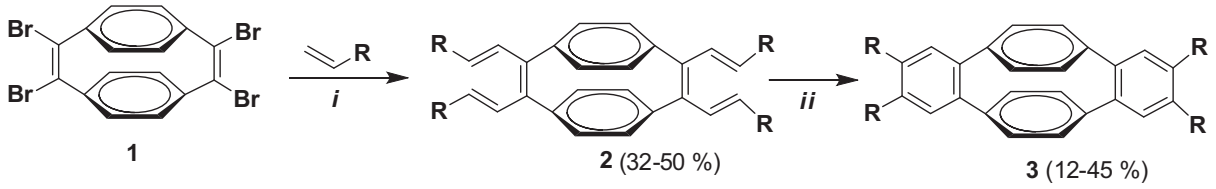
SUMMARY

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 2,3-dibromobenzofuran and 2,3,5-tribromobenzofuran and regioselective Suzuki-Miyaura cross-coupling reactions of brominated benzofurans and 2,3-dibromoindenone.

1 Overview

1.1 Domino Twofold Heck / 6π-Electrocyclization Reaction

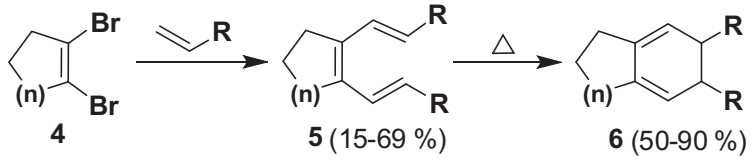
In 1987, Armin de Meijere and co-workers reported the Heck-type vinylation of 1,2,9,10-tetrabromo[2.2]paracyclophanedienes **1** with subsequent thermal electrocyclization and aromatization to give benzo-annulated [2.2]paracyclophanes **3** (Scheme 1).[1]



R = H, $SiMe_3$, CO_2Me, Ph, 4-FPh

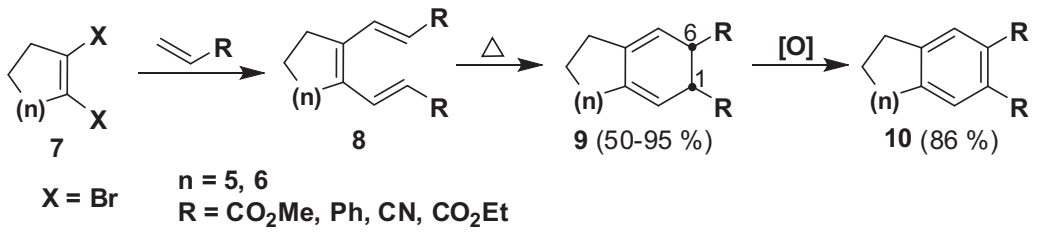
Scheme 1. *Reagents and Conditions*: *(i)* $Pd(OAc)_2$, Bu_4NBr, K_2CO_3 / $NaHCO_3$, DMF, heat (40-100 °C); *(ii)* Pd/C (+O_2) or S_8, xylene, 150 °C

In 1990, the same group again reported twofold Heck reactions of vicinal 1,2-dibromocycloalkenes **4** to synthesize *(E,Z,E)*-l,3,5-hexatrienes **5** in fair to high yields (15-69 %). Thermal electrocyclization in anaerobic conditions provided 1,3-cyclohexadienes **6** (Scheme 2).[2,3]



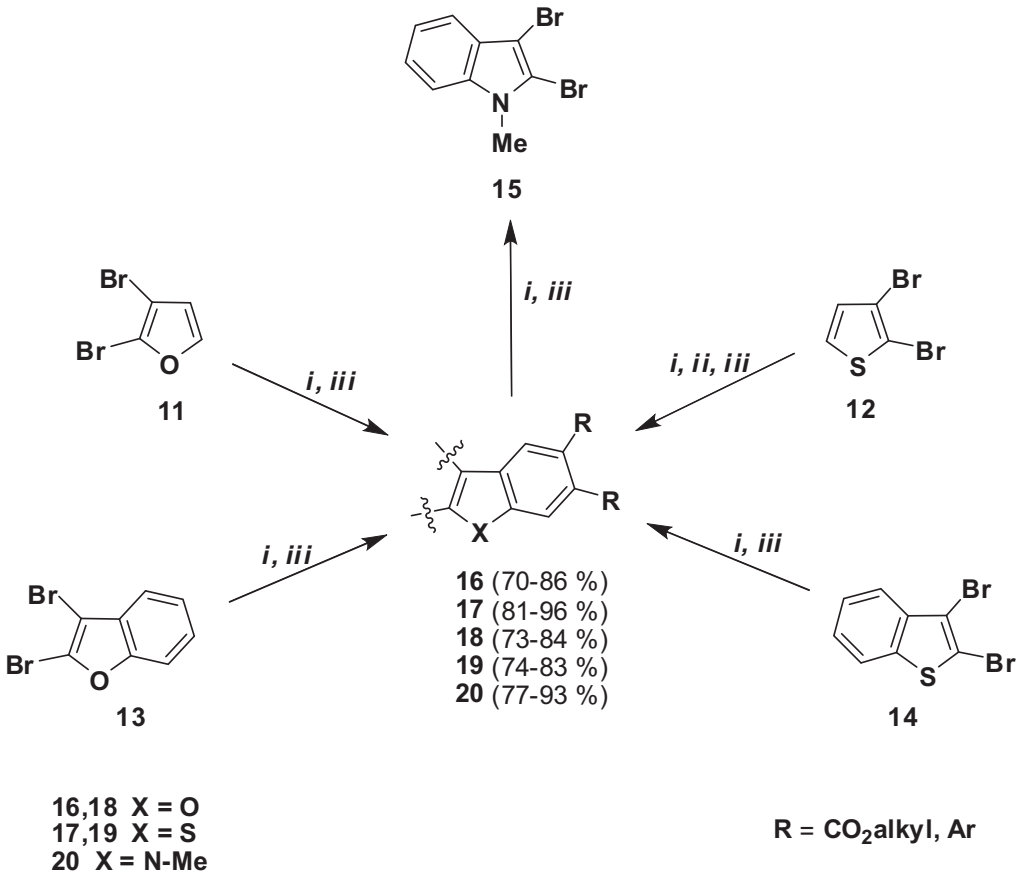
Scheme 2. *Reagents and Conditions*: *(i)* $Pd(OAc)_2$, PPh_3, NEt_3, DMF, heat (90-100 °C); *(ii)* xylene or (n-Bu_2O), 140-150 °C, inert conditions

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).[4] 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 3). [2,3]



Scheme 3. Twofold Heck cross coupling and subsequent electrocyclization. *Reagents and Conditions*: *(i)* $Pd(OAc)_2$, PPh_3, NEt_3 DMF, 90-100 °C; *(ii)* Pd/C (+O_2) or S, xylene, 150 °C

During the last couple of years, Prof. P. Langer's research group has widely studied a number of 1,2-dihalogenated substrates for domino Heck / electrocyclization reactions and has extended the synthetic scope especially for the heteroaromatic 1,2-dihalides. This research group has reported that the corresponding benzo-annulated products can be synthesized by Heck cross-coupling of 2,3-dibromofuran **11**,[5] 2,3-dibromothiophene **12**,[6] 2,3-dibromobenzofuran **13**,[7] 2,3-dibromobenzothiophene **14**,[8] and 2,3-dibromo-*N*-methylindole **15** with subsequent thermal 6π electrocyclization and oxidation in the presence of Pd/C (Scheme 4).[2,3]



Scheme 4. *Reagents and Conditions*: *(i)* Catalyst: $Pd(OAc)_2$ (5 mol-%), XPhos or SPhos (10 mol-%), NEt_3, DMF, 100-130 °C, 36 h; *(ii)* diphenyl ether or xylene, 200 °C, 24 h; *(iii)* Pd/C (10 mol-%), diphenyl ether, 130-200 °C, 24-48 h

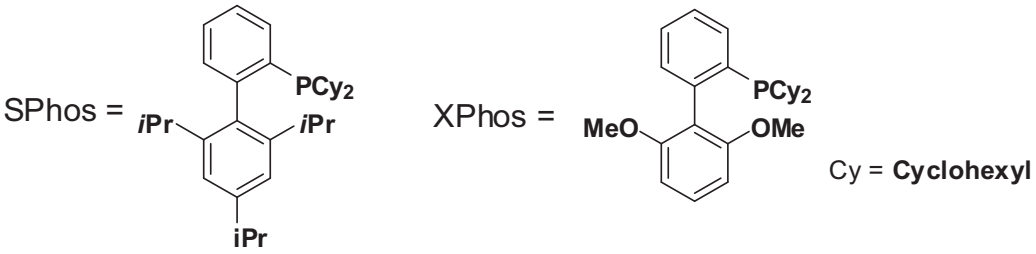
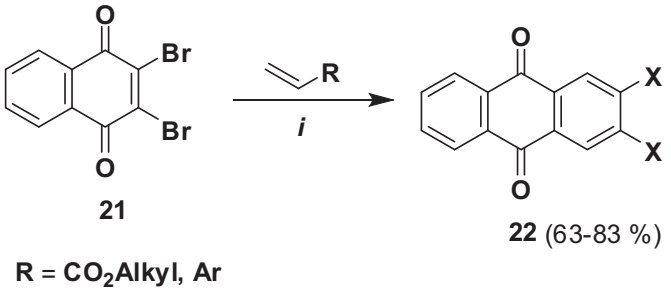


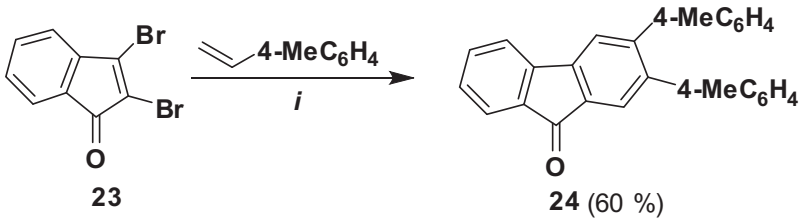
Figure 1. Buchwald ligands[35]

The domino Heck cross-coupling / electrocyclization reaction of various alkenes with 2,3-dibromonaphthoquinone (**21**) provided the anthraquinones **22** in a single step (Scheme 5).[9]



Scheme 5. *Reagents and Conditions*: *(i)* $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), NEt_3 (8.0 equiv.), DMF, >110 °C, 8 h

The domino Heck / electrocyclization reaction of *p*-tolylstyrene with 2,3-dibromoindenone (**23**) directly afforded the substituted fluorenone **24** in 60 % yield (Scheme 6).[10]

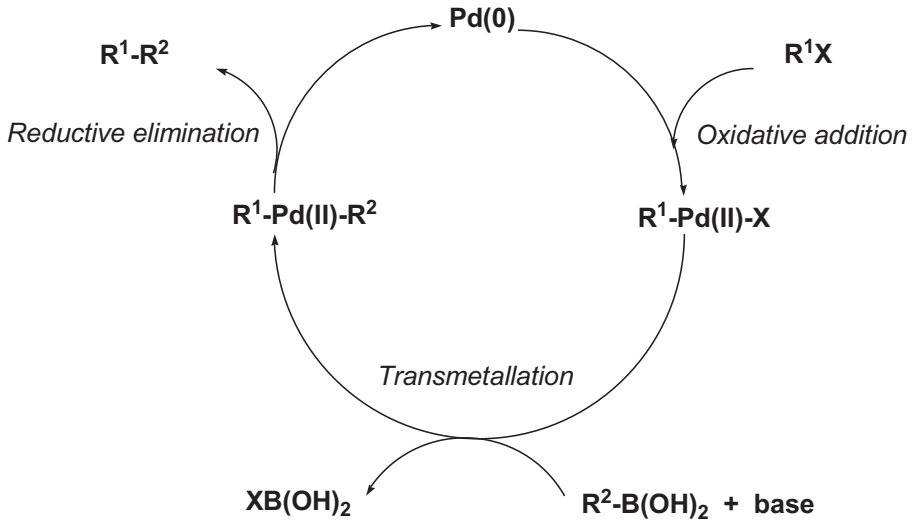


Scheme 6. *Reagents and Conditions*: *(i)* $Pd(OAc)_2$ (5 mol-%), PCy_3 (10 mol-%), NEt_3, DMF, 40 °C, 36 h

My work on twofold Heck / electrocyclization of 2,3-dibromobenzofuran successfully provided substituted dibenzofurans which are discussed in detail in chapter 2 of this dissertation.

1.2 Regioselective Arylation by Suzuki-Miyaura Cross-Coupling Reaction

In 1979 Akira Suzuki together with Miyaura reported the Suzuki-Miyaura reaction and he shared the Nobel Prize of 2010 with Negishi and Heck for palladium catalysis. The Suzuki reaction is a palladium catalyzed cross-coupling of an aryl or vinyl boronic acid with an aryl or vinyl halide or triflate. It is a powerful cross coupling method of arylation and also allows the synthesis of conjugated olefins and styrenes. The Suzuki coupling of a boronic acid with a halide or triflate has been developed into one of the most important cross-coupling reactions, contributing about a quarter of all current palladium-catalyzed cross-coupling reactions.[11]

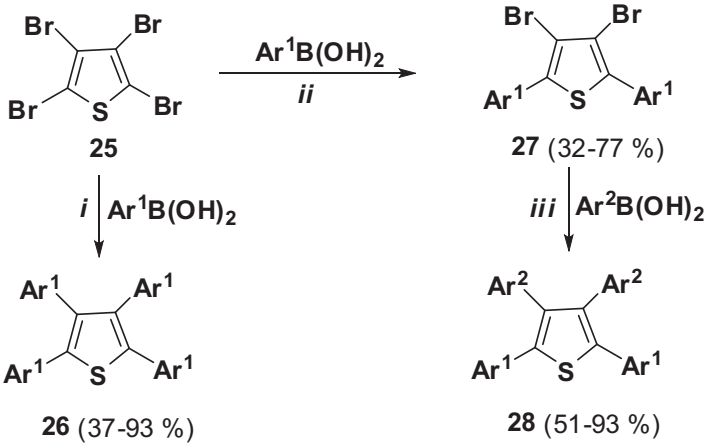


Scheme 7. Catalytic cycle of the Suzuki reaction

The rate of the Suzuki reaction mainly depends on the oxidative addition and transmetallation. The oxidative addition step is dependent on the reactivity of the substrate according to the order Ar-I > Ar-OTf > Ar-Br > Ar-Cl. The transmetallation is accelerated by the presence of base. In fact, the Suzuki-Miyaura cross-coupling reaction refers to the cross-coupling of organoboron compounds and carbon elecrophiles.

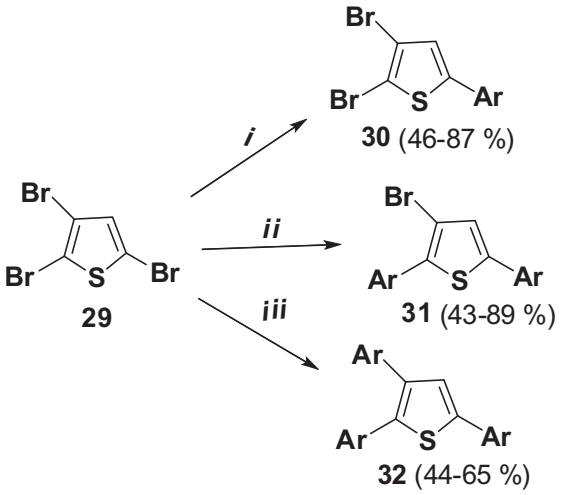
For polyhalogenated substrates, the more electron deficient carbon atom will react first, but steric hinderance may also direct the regioselctivity. Hence, the regioselectivity depends mainly on the electrophilicity of the halide or triflate. During the recent years, Prof. P. Langer's research group has contributed considerable efforts for the regioselective arylation of aromatic halides and triflates. They have synthesized a large number of symmetrical and unsymmetrical arylated aromatic and heteroaromatic organic compounds bearing a broad spectrum of biological activitie and fluorescence activity. As this dissertation presents the continuation of Prof. P. Langer's work in this area, so it will be meaningful to show briefly what has been recently done in this group.[12]

P. Langer *et. al.* have reported the regioselective arylation of tetrabromothiophene **25** where C-2 and C-5 are electronically favoured positions. Tetrabromothiophene with 2.2 equivalents of arylboronic acids provided a regioselective approach to various 2,5-diaryl-3,4-dibromothiophenes (**26**). Unsymmetrical tetraarylthiophenes were prepared by Suzuki reaction of 2,5-diaryl-3,4-dibromothiophenes with different types of aryl groups (Scheme 8). During the optimization of the reaction conditions, the solvent and the catalyst played an important role. In several cases, classical conditions [$Pd(PPh_3)_4$] gave excellent yields.[13]



Scheme 8. Suzuki reactions of **25**. *Reagents and conditions*: *(i)* **25** (1.0 equiv.), $Ar^1B(OH)_2$ (5.0 equiv.), $Pd(PPh_3)_4$ (10 mol-%), K_3PO_4 (8.0 equiv.), solvent; *(ii)* **25** (1.0 equiv.), $Ar^1B(OH)_2$ (2.2 equiv.), $Pd(PPh_3)_4$ (6 mol-%), K_3PO_4 (4.0 equiv.), solvent; *(iii)* **25** (1.0 equiv.), $Ar^2B(OH)_2$ (3.0 equiv.), $Pd(PPh_3)_4$ (10 mol-%), K_3PO_4 (4.0 equiv.), solvent

Interestingly, recent work on Suzuki–Miyaura reactions of 2,3,5-tribromothiophene **29** showed that the reaction with one, two, and three equivalents of arylboronic acids resulted in the formation of 5-aryl-2,3-dibromothiophenes **30**, 2,5-diaryl-3-bromothiophenes **31**, and 2,3,5-triarylthiophenes **32**, respectively. In this case, the first attack was observed at C-5 which is sterically less hindered.[14]



Scheme 9. *Reagents and conditions*: *(i)* **29** (1.0 equiv.), $ArB(OH)_2$ (1.1 equiv.), $Pd(PPh_3)_4$ (5 mol-%), K_2CO_3 (2 M), 1,4-dioxane–toluene (1:1), 100 °C, 8 h; *(ii)* **29** (1.0 equiv.), $ArB(OH)_2$ (2.2 equiv.), $Pd(PPh_3)_4$ (5 mol-%), K_3PO_4 (4.0 equiv.), 1,4-dioxane–toluene (1:1), 100 °C, 12 h; *(iii)* **29** (1.0 equiv.), $ArB(OH)_2$ (4.0 equiv.), $Pd(PPh_3)_4$ (10 mol-%), K_2CO_3 (2 M), 1,4-dioxane, 90 °C, 8 h

The site-selectivity for tetrabromoselenophene,[15] tetrabromofuran[16] and *N*-methyl-tetrabromopyrrole[17] worked in the same way as for tetrabromothiophene **25**. The optimization of the reaction conditions needed lot of efforts to prepare **33**-**35** (Figure 2).

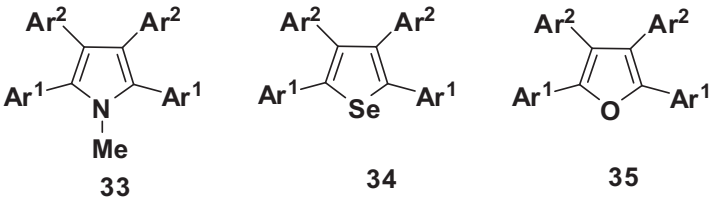
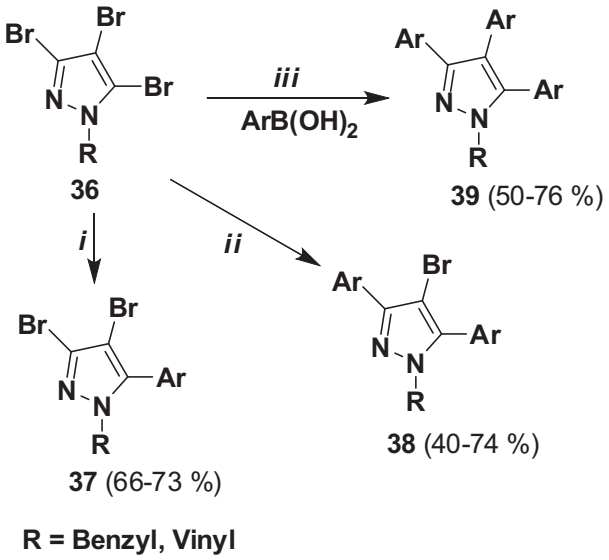


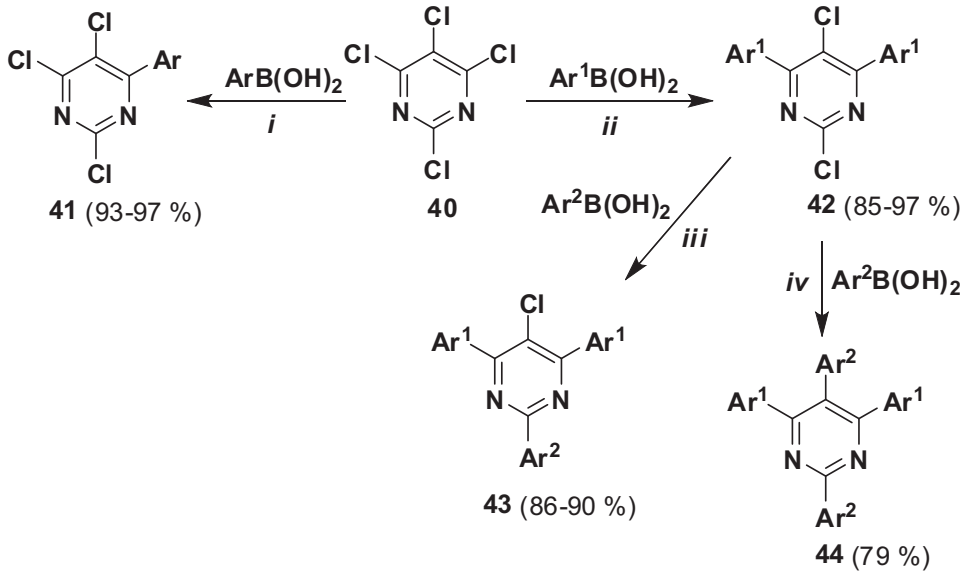
Figure 2. Site-selectivity in Suzuki products

The first Suzuki–Miyaura reactions of *N*-protected tribromopyrazoles **36** provided a series of arylated pyrazoles. Their reaction with three, two, or one equivalents of arylboronic acids afforded triarylpyrazoles **39**, 3,5-diaryl-4-bromopyrazoles **38**, or 5-aryl-3,4-dibromopyrazoles **37**, respectively (Scheme 10). The products are not readily available by other methods. All reactions proceeded with very good site-selectivity.[17]



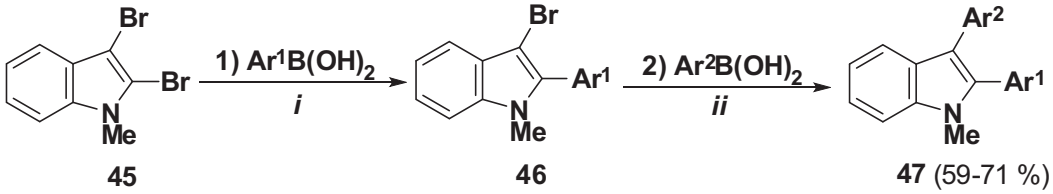
Scheme 10. *Reagents and conditions*: *(i)* **36** (1.0 equiv.), $ArB(OH)_2$ (1.0 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 1,4-dioxane / H_2O (4:1), 100 °C, 12 h; *(ii)* **36** (1.0 equiv.), $ArB(OH)_2$ (2.0 equiv.), K_3PO_4 (3.0 equiv.), $Pd(PPh_3)_4$ (5 mol-%), 1,4-dioxane / H_2O (4:1), 100 °C, 12 h; *(iii)* **36** (1.0 equiv.), $ArB(OH)_2$ (3.5 equiv.), K_3PO_4 (4.5 equiv.), $Pd(PPh_3)_4$ (10 mol-%), 1,4-dioxane / H_2O (4:1), 100 °C, 12 h

Pyrimidines are of considerable pharmacological importance and occur in many synthetic drugs and natural products. Convenient regioeselective syntheses of mono-, di-, tri- and tetraaryl-pyrimidines (**41**-**44**) by Suzuki-Miyaura reactions of 2,4,5,6-tetrachloropyrimidine **40** have been reported. The products reported are not readily available by other methods. All reactions proceeded with excellent site-selectivity under the influence of electronic effects showing the reactivity preference order C-4 > C-6 > C-2 > C-5.[18]



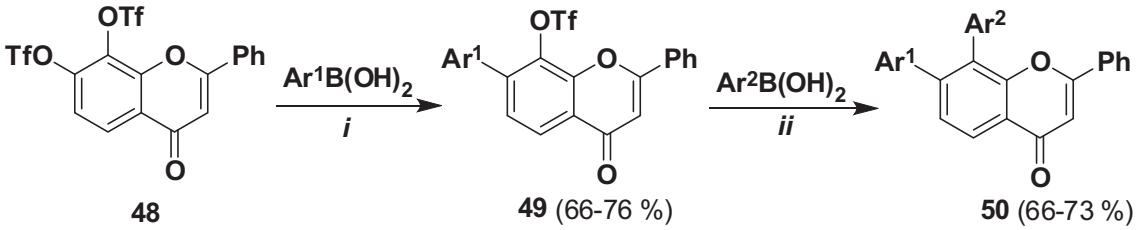
Scheme 11. *Reagents and Conditions*: *(i)* **40** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (3 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 60 °C, 2 h; *(ii)* $Ar^1B(OH)_2$ (2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (3 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 70 °C, 5 h; *(iii)* $Ar^2B(OH)_2$ (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (3 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 80 °C, 5 h; *(iv)* $Ar^2B(OH)_2$ (2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (3 mol-%), K_2CO_3 (H_2O, 2 M), dioxane, 100 °C, 5 h

The synthesis of 2,3-diarylindoles has also been accomplished by Suzuki–Miyaura reactions of *N*-methyl-2,3-dibromoindole **45**. The nitrogen protective groups played an important role for the site-selectivity. The reaction with one equivalent of arylboronic acid resulted in site-selective formation of 2-aryl-3-bromoindoles **46**. To synthesize unsymmetrical diarylindoles **47**, because of the instability of **46,** a one-pot strategy was developed. The one-pot reaction of 2,3-dibromoindole **45** with two different arylboronic acids afforded the unsymmetrical 2,3-diarylindoles **47** containing two different aryl groups (Scheme 12).[19]



Scheme 12. One-pot synthesis of unsymmetrical 2,3-diarylindoles. *Reagents and Conditions*: *(i)* **45** (1.0 equiv.), $Ar^1B(OH)_2$ (1.1 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (4 mol-%), 1,4- dioxane, 70 °C, 6 h; *(ii)* $Ar^2B(OH)_2$ (1.2 equiv.), K_3PO_4 (1.5 equiv.), 110 °C, 8 h

Triflates of many aromatic and heteroaromatic organic compounds have been studied as well for regioselective Suzuki reactions. For example, 7,8-diarylflavones **50** were prepared by Suzuki–Miyaura reactions of the bis(triflate) of 7,8-dihydroxyflavone. The first attack proceeded with very good site selectivity at position 7, due to steric and electronic reasons.[20]



Scheme 13. *Reagents and conditions*: *(i)* **48** (1.0 equiv.), $Ar^1B(OH)_2$ (1.0 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (5 mol-%), 1,4-dioxane, 70 °C, 4 h; *(ii)* **49** (1.0 equiv.), $Ar^2B(OH)_2$ (1.3 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (5 mol-%), 1,4-Dioxane, 100 °C, 4h

In my thesis, I have investigated the site-selective Suzuki-Miyaura cross-coupling reactions of 2,3-dibromobenzofuran and 2,3,5-tribromobenzofuran which are discussed in chapter 3 of this dissertation. My results related to 2,3-dibromoindenone are described in detail in chapter 4.

2 Efficient Synthesis of Functionalized Dibezofurans by Domino Twofold Heck / 6π-Electrocyclization Reactions of 2,3-Dibromobenzofuran

2.1 Introduction

Benzofurans are of significant pharmacological importance and are found in many natural and non-natural products.[21] Substituted furans are among the most significant classes of five-membered heterocycles and contribute a great deal of importance to pharmaceuticals and drugs and are widely found in natural and non-natural products. For example, synthetic amiodarone corresponds to a powerful antiarrythmic and antianginal remedy.[22] 7-Alkanoylbenzofurans and 7-alkanoyl-2,3-dihydrobenzofurans are found in many natural products, for example longicaudatin,[23] the sessiliflorols A and B, flemistrictin E, tovophenone C, vismiaguianone C or piperaduncin B.[24] Dibenzofurans also occur in a variety of pharmacologically active natural products. Examples include simple hydroxylated derivatives (such as α- and γ-cotonefuran and γ-pyrufuran (Figure 3),[25] aryl-substituted hydroxylated derivatives (e. g., candidusin A, vialinin B),[26] brominated derivatives (e. g., corallinafuran),[27] polycyclic derivatives (such as phlorofucofuroeckol A or mallotusinin),[28] and complex glycosylated derivatives (e. g., fulicineroside).[29] Furthermore, polysubstituted furans and benzofurans are significant precursors for the synthesis of natural and non-natural products. Hence, the assembly of polysubstituted benzofurans is an interesting part of organic synthesis.

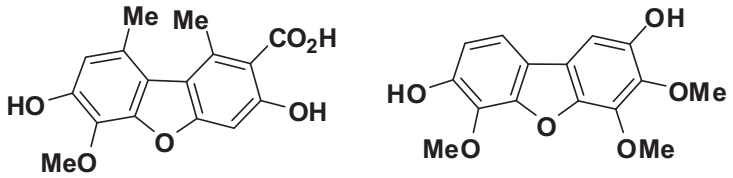
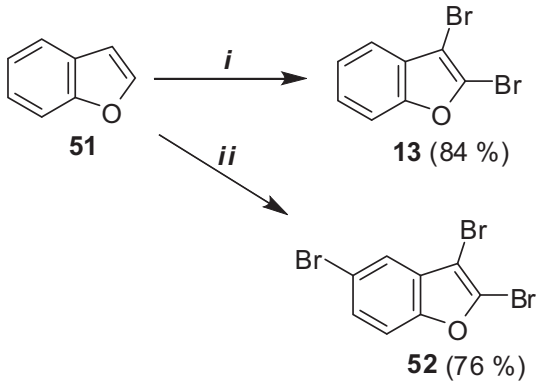


Figure 3. Structures of some naturally occurring dibenzofurans

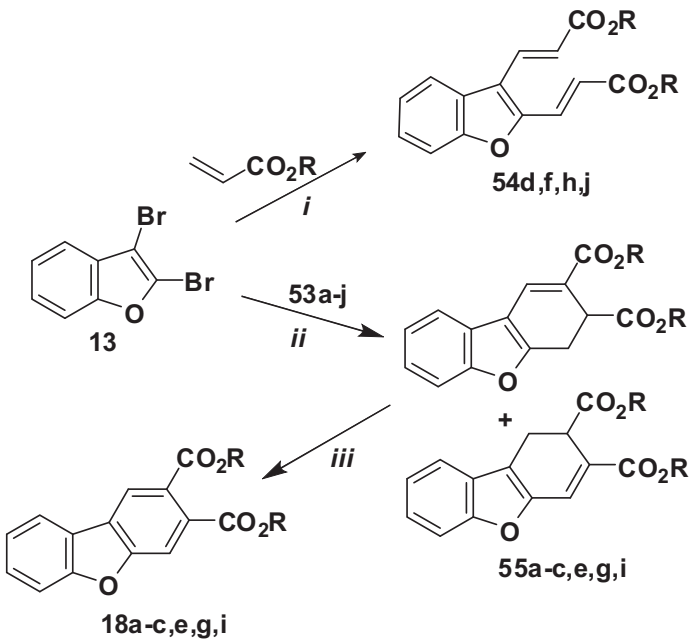
2.2 Results and discussion

In recent years, it has been revealed that polyhalogenated heterocycles can be regioselectively functionalized in palladium(0)-catalyzed cross-coupling reactions by selective activation of a single halogen atom. The regioselectivity is controlled by electronic and steric factors.[12] Sonogashira,[30] Negishi,[31] and Stille [32] coupling reactions of 2,3- and 2,6-dibromobenzofuran have been reported to regioselectively occur at position C-2 and the same results I observed in case of Suzuki-Miyaura cross-coupling reactions of 2,3-dibromobenzofuran. Bach and Bartels reported regioselective Negishi and Kumada cross-coupling reactions of 2,3,5-tribromobenzofuran.[33] Herein, I will discuss the first Heck reactions of 2,3-dibromo- and 2,3,5-tribromobenzofuran which have, to the best of my knowledge, never been reported before. In this context, functionalized dibenzofurans were efficiently prepared based on domino twofold Heck / 6π-electrocyclization reactions.[34]



Scheme 14. Bromination of benzofuran (**51**). *Reagents and Conditions*: *(i)* Br_2 (2.0 equiv.), KOAc (2.0 equiv.) CH_2Cl_2, reflux, 4 h; *(ii)* Br_2 (4.5 equiv.), KOAc (4.5 equiv.), CH_2Cl_2, reflux, 18 h

Bach and Bartels reported that the direct bromination of benzofuran (**51**), following the conditions reported by Antognazza *et al.,*[34] resulted in the formation of a mixture of products. Therefore, a stepwise protocol was suggested for the synthesis of 2,3-dibromobenzofuran (**13**).[30b] I found that the reaction of **51** with bromine (2.0 equiv.) and KOAc (2.0 equiv.) in CH_2Cl_2 (reflux, 4 h) results in regioselective formation of 2,3-dibromobenzofuran (**13**) in 84 % yield (Scheme 1). Bach and Bartels reported a stepwise synthesis of 2,3,5-tribromobenzofuran (**52**) which was prepared from 5-bromobenzofuran in 52 % yield.[30b] I have found that **52** is available in 76 % yield by reaction of **51** with bromine (4.5 equiv.) and KOAc (4.5 equiv.) in CH_2Cl_2 (reflux, 18 h).



Scheme 15. Synthesis of **54d,f,h,j** and **18a-c,e,g,i**. *Reagents and Conditions: (i)* $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3 (8.0 equiv.), DMF, 70 °C, 12 h; *(ii)* $Pd(OAc)_2$ (5 mol-%), **L** (structure see Figure 4, 10 mol-%), NEt_3, DMF, 100 °C, 48 h; *(iii)* Pd/C (10 mol-%), xylene, reflux, 48 h

The Heck reaction of **13** with acrylates and styrenes **53d,f,h,j** (2.5 equiv.) afforded the 2,3-di(alkenyl)benzofurans **54d,f,h,j** in good yields (Scheme 15, Table 1). The reactions were carried successfully by using $Pd(OAc)_2$ (5 mol-%) and the biaryl monophosphine ligand **L** (10 mol-%) which was recently developed by Buchwald and coworkers (Figure 4).[35] The reactions were performed in DMF at 70 °C for 12 h. The employment of $Pd(PPh_3)_4$ was less successful in terms of yield. The $Pd(OAc)_2$/**L**-catalyzed reaction of **13** with alkenes **53a-c,e,g**, carried out at 100 °C rather than 70 °C, afforded the 1,2-dihydrodibenzofurans **55a-c,e,g** as a mixture of two isomers. Their formation can be explained by a domino twofold Heck / thermal 6π-electrocyclization and subsequent double bond migration (isomerization). Heating of a xylene solution of crude **55a-c,e,g** in the presence of Pd/C resulted in the formation of dibenzofurans **18a-c,e,g** in 46-84 % overall yields (based on **13**). It is worth to be noted that, in contrast to Sonogashira and Stille reactions, the Heck monoalkenylated product could not be isolated. The reaction of **13** with only one equivalent of acrylate **53f** mainly resulted in the formation of **54f** and some of the starting material was also recovered. This might be explained by the fact that carbon C-3 becomes more electron-deficient and, thus, more reactive, due to the electron-withdrawing character of the 2-(*tert*-butoxycarbonyl)alkenyl substituent. Alternatively, a neighbourhood effect (chelation of the Pd(0) species by the alkenyl substituent attached to C-2) can be discussed.

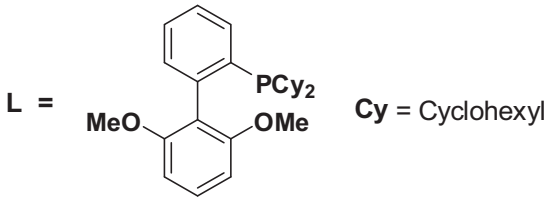


Figure 4. Biaryl monophosphine ligand developed by Buchwald and coworkers.[35]

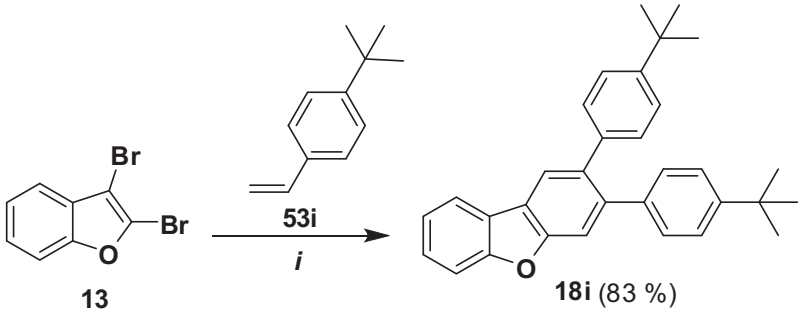
Table 1. Synthesis of **54d,f,h,j** and **18a-c,e,g,i**

54,18	R	% (**54**) [a]	% (**18**) [a]
a	Et	- [b]	73
b	*n*Bu	- [b]	76
c	*i*Bu	- [b]	84
d	*n*Hex	79	- [b]
e	2-Ethylhexyl	- [b]	74
f	*t*Bu	72	- [b]
g	C_6H_5	- [b]	46
h	4-MeC_6H_4	65	- [b]
i	4- *t*BuC_6H_4	- [b]	68
j	2-(OMe)C_6H_4	54	- [b]

[a] Yields of isolated products based on **13**

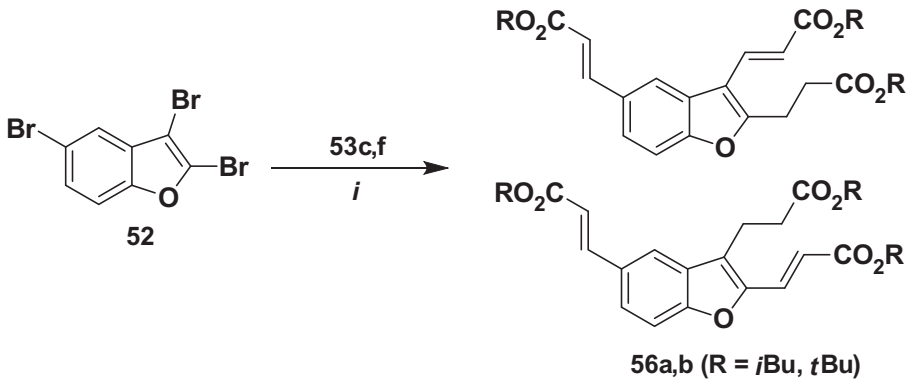
[b] experiment was not carried out

The Heck reaction of **13** with styrene **53i** directly afforded the dibenzofuran **18i** in 83 % yield (Scheme 16). The dehydrogenation spontaneously occurred under the reaction conditions and did not require the use of Pd/C. Other styrenes could be also successfully employed.

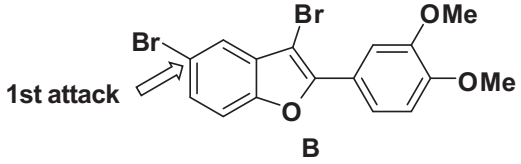


Scheme 16. Synthesis of **18i**. *Reagents and Conditions*: *(i)* $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 100 ˚C, 48 h

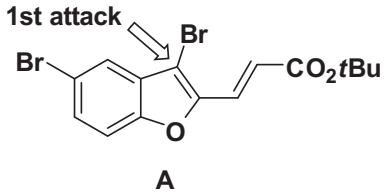
The Heck reaction of 2,3,5-tribromobenzofuran (**52**) with acrylates **53c,f** mainly resulted in the formation of the hydrogenated products **56a** and **56b** which were isolated as single isomers (Scheme 17). However, the exact structure could not be unambiguously assigned. Bach and Bartels reported that the Kumada coupling of 2-aryl-3,5-dibromobenzofuran,[11] derived from **52**, occurs at carbon atom C-5 (Figure 5).[17] I found that the Heck reaction of **52** with 2 equiv of acrylate **53f** resulted in functionalization of carbon atoms C-2 and C-3 and in reduction of C-5 to give **54f**. This result can be explained by the following assumption which has not yet been experimentally proven: the first reaction of **53f** with **52b** occurs at position C-2 to give intermediate **A** (Figure 5). The reactivity of carbon C-3 is increased by the neighbourhood effect of the (*tert*-butoxycarbonyl)-alkenyl substituent located at carbon C-2 (see above). Therefore, the second attack occurs at carbon C-3 rather than at C-5.



Scheme 17. Synthesis of **56a,b**. *Reagents and Conditions*: *(i)* $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 120 °C, 48 h



Bach and Bartels (ref. 35), Kumada coupling



This work

Figure 5. Regioselective reactions of **52**

2.3 Conclusion

In conclusion, 2,3-dialkenylbenzofurans were prepared based on domino twofold Heck / 6π-electrocyclization reactions of 2,3-dibromobenzofuran. The first attack of Pd(0) occurs at carbon C-2 which results in a significant increase of the reactivity of C-3. Therefore, the mono-Heck reaction product of 2,3-dibromobenzofuran could not be isolated. In case of 2,3,5-tribromobenzofuran, carbon atoms C-2 and C-3 are more reactive than C-5.

3 Site-Selective Suzuki Cross-Coupling Reactions of 2,3-Dibromobenzofuran and 2,3,5-Tribromobenzofuran

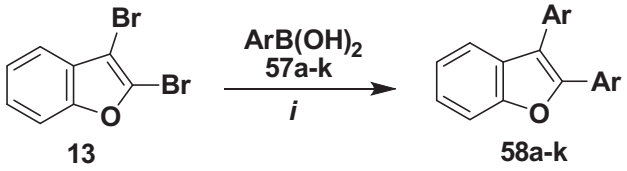
3.1 Introduction

Furans are key structural units as five-membered oxygen heterocycles in organic compounds. Especially, contributions of furans as versatile substrates for synthetic transformations are immense. As it has been described in chapter 2 of this dissertation, benzofurans are pharmacologically important heterocycles.[36] For example, synthetic amiodarone represents a potent antiarrythmic and antianginal drug.[37] 7-Alkanoylbenzofurans and 7-alkanoyl-2,3-dihydrobenzofurans occur in a variety of natural products, such as longicaudatin,[38] flemistrictin E, tovophenone C, vismiaguianone C, piperaduncin B, or the sessiliflorols A and B.[39]

3.2 Results and discussion

2,3-Dibromobenzofuran and 2,6-dibromobenzofuran represent interesting starting materials which have been used in site-selective Sonogashira, Negishi,[30] and Stille[31] coupling reactions. Site-selective Negishi and Kumada cross-coupling reactions of 2,3,5-tribromobenzofuran have also been reported.[32] The Heck reactions of 2,3-dibromobenzofuran have been described in chapter 2 of this dissertation.[40] Herein, I present what are, to the best of my knowledge, the first Suzuki-Miyaura reactions of 2,3-dibromobenzofuran and 2,3,5-tribromobenzofuran. These reactions proceed with excellent site-selectivity. I also have developed a one-pot protocol for the synthesis of unsymmetrical 2,3-diarylbenzofurans.

The Suzuki-Miyaura reaction of 2,3-dibromobenzofuran (**13**) with various arylboronic acids **57a-k** (2.0 equiv.) afforded the 2,3-diarylbenzofurans **58a-k** (Scheme 18, Table 2). High yields were obtained for products derived from both electron-rich and electron-poor boronic acids. As by-products were observed the reduced products **60,** due to the loss of bromine at C-3. Henc, the reduction at C-3 provides the major reason of lower yields during the Suzuki cross-coupling reactions of **13**. This phenomenon was observed more explicitely during the synthesis of 3-bromo-2-arylbenzofurans **59** (Scheme 19, Table 3). Yet, I could isolate the reduced products **60i** and **60j** along with **58a** and **58c** in small yields, respectively.



Scheme 18. Synthesis of **58a-k**. *Reagents and Conditions: (i)* **57a-k** (2.0 equiv.), $Pd(PPh_3)_4$ (5 mol-%), aq. K_2CO_3 (2 M), dioxane, 80 °C, 8 h

Table 2. Synthesis of 2,3-diarylbenzofurans **58a-k**

57,58	Ar	% (**58**) [a]
a	C_6H_5	93[b]
b	4-MeC_6H_4	92
c	2-MeC_6H_4	81[c]
d	4-EtC_6H_4	86
e	4-*t*BuC_6H_4	88
f	2-ClC_6H_4	87
g	4-ClC_6H_4	83
h	4-FC_6H_4	81
i	2-$(MeO)C_6H_4$	82
j	2,5-$(MeO)_2C_6H_3$	85
k	3,5-$Me_2C_6H_3$	79

[a] Yields of isolated products,
[b] reduced product **60i** was isolated as by-product (04 %),
[c] reduced product **60j** was isolated as by-product (09 %)

The structures of **59a-k** were elucidated by NMR spectroscopy, but **58e, 58g** and **58h** were also confirmed by X-ray crystallography (Figures 6-8).

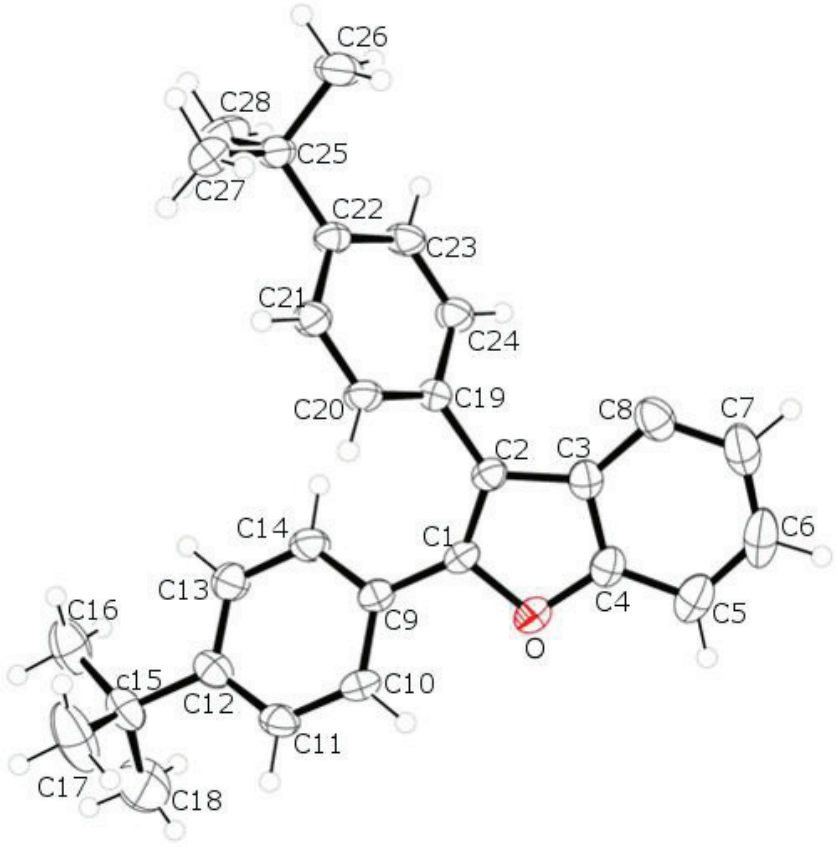


Figure 6. Crystal structure of **58e** (SPGR $P2_1$, wR2 ca. 13 %)

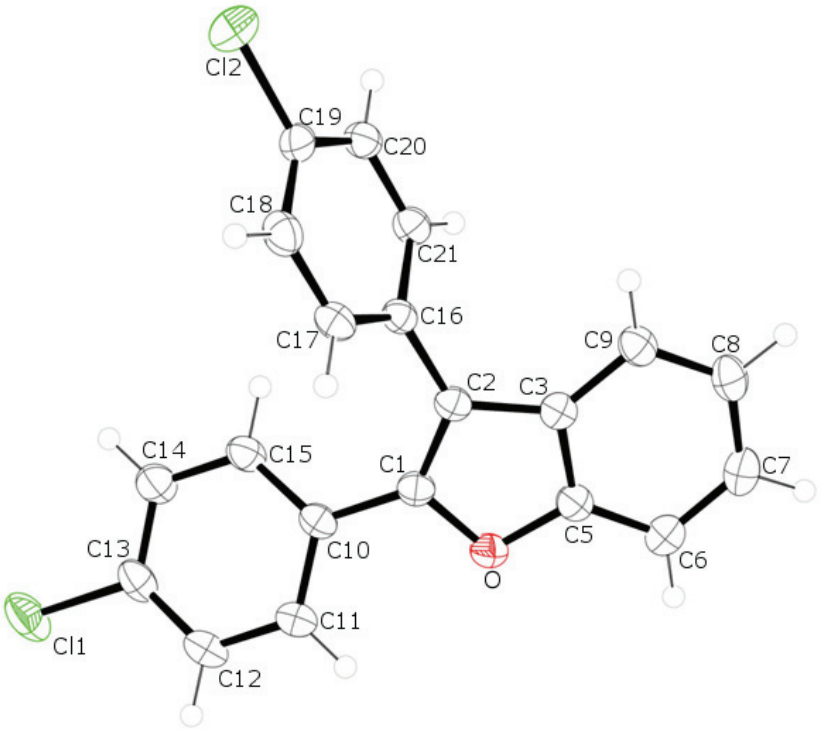


Figure 7. Regioselective reactions of **58g** (SPGR P-1, wR2 ca. 12 %)

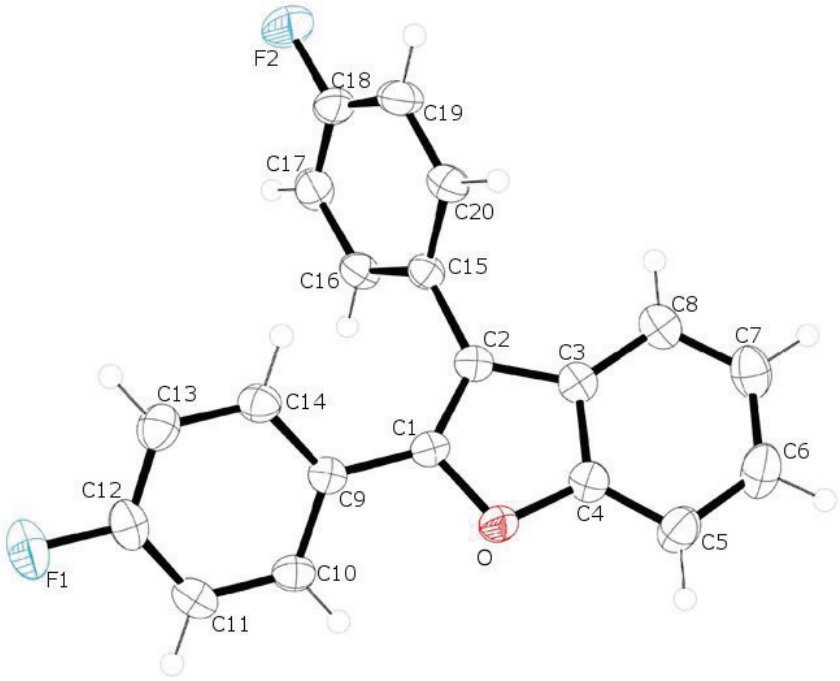
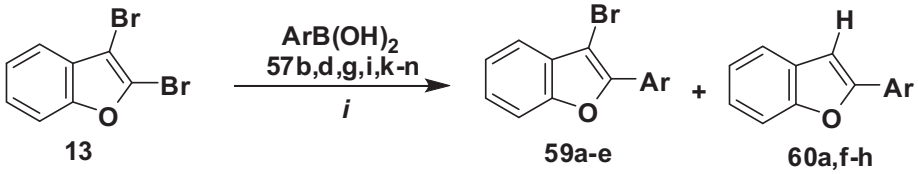


Figure 8. Regioselective reactions of **58h** (SPGR $P2_12_12_1$, wR2 ca. 10 %)

The Suzuki-Miyaura reaction of **13** with 1.0 equiv. of arylboronic acids **57b,d,g,i,k-n** afforded the 2-aryl-3-bromobenzofurans **59a-h** in good yields (Scheme 19, Table 3). The reactions proceeded with very good site-selectivity. Hydrogenated by-products **60a,f-h** were also isolated. Reduction at C-3 during the synthesis of **59g** and **59h** was the major reason for the lower yields (67 % and 63 %, respectively).

In all reactions, $Pd(PPh_3)_4$ (5 mol-%) was used as the catalyst. The use of $Pd(OAc)_2$ in the presence of XPhos[35] or SPhos[35] proved to be less successful in terms of yield. All reactions were carried out at 70-80 °C. For the mono-coupling it proved to be important to carry out the reaction at 70 °C because higher temperature provides a complex mixture of products. An aqueous solution of K_2CO_3 (2 M) was used as the base. The employment of K_3PO_4 gave equally good results. 1,4-Dioxane was used throughout as the organic solvent.



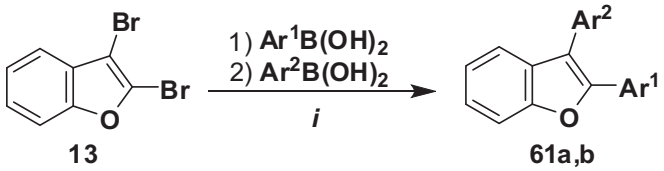
Scheme 19. Synthesis of **59a-e**. *Reagents and Conditions: (i)* **57c,e,g-i** (1.0 equiv.), $Pd(PPh_3)_4$ (5 mol-%), aq. K_2CO_3 (2 M), dioxane, 70 °C, 6 h

Table 3. Synthesis of 2-aryl-3-bromobenzofuran **59a-e**

57	**59, 60**	Ar	% (**59**) [a]	% (**60**) [a]
b	**a**	4-MeC_6H_4	93	04
d	**b**	4-EtC_6H_4	86	[b]
g	**c**	4-ClC_6H_4	90	[b]
i	**d**	2-$(MeO)C_6H_4$	87	[b]
k	**e**	3,5-$Me_2C_6H_3$	79	[b]
l	**f**	2,6-$(MeO)_2C_6H_3$	89	5
m	**g**	3-($C_6H_5)_2C_6H_4$	67	23
n	**h**	2-Thienyl	63	15

[a] Yields of isolated products

The sequential addition of two different arylboronic acids allowed the direct synthesis of 2,3-diarylbenzofurans **61a,b** containing two different aryl groups (Scheme 20, Table 4). The yields of the products were significantly higher when the reactions were carried out following one-pot procedure without isolation of the mono-coupling product.



Scheme 20. Synthesis of **61a,b**. *Reagents and Conditions: (i)* 1) **57b** (1.0 equiv.), $Pd(PPh_3)_4$ (5 mol-%), aq. K_2CO_3 (2 M), dioxane, 70 °C, 6 h; 2) **57h,o** (1.0 equiv.), 80 °C, 6 h

Table 4. Synthesis of unsymmetrical 2,3-diarybenzofuran **61a,b**

61	Ar^1	Ar^2	% (**61**) [a]
a	4-MeC_6H_4	3-(MeO)C_6H_4	76
b	4-MeC_6H_4	4-FC6H4	79

[a] Yields of isolated products

The structures of all products **58, 59, 60** and **61** were established by spectroscopic methods. The structure of **61b** was independently confirmed by X-ray crystal structure analysis as well (Figure 9).

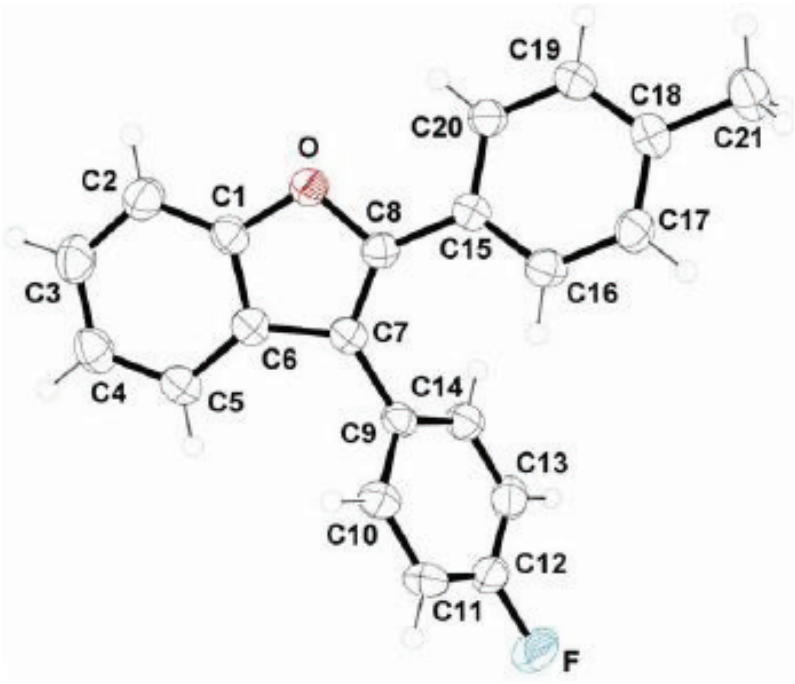


Figure 9. Crystal structure of **61b** (SPGR Pbca, wR2 ca. 15 %)

The site-selectivity of the Suzuki-Miyaura reaction can be explained by the assumption that the oxidative addition of (nucleophilic) Pd(0) occurs more rapidly at the more electron-deficient carbon atom (i.e., C-2) (Figure 10).

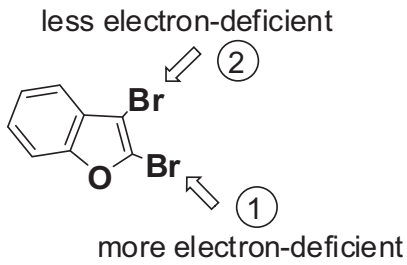


Figure 10. Possible explanation for the site-selectivity of the Suzuki-Miyaura reactions of **13**

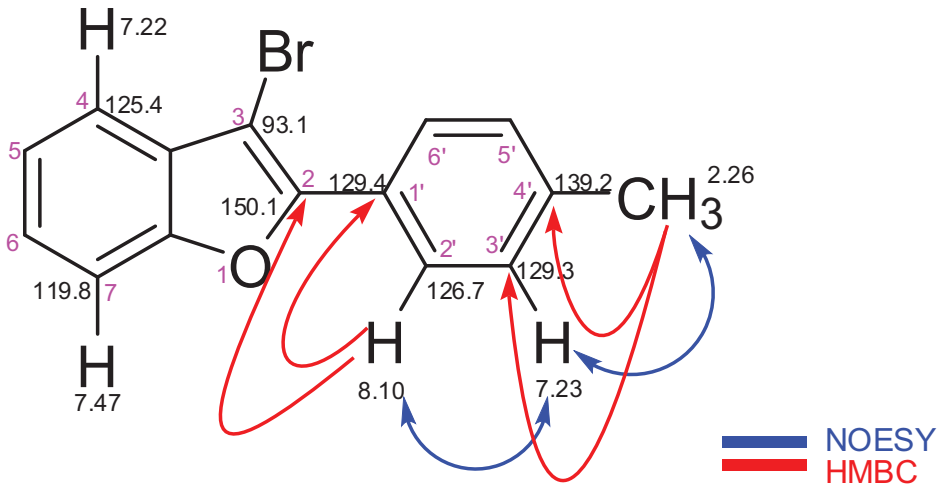
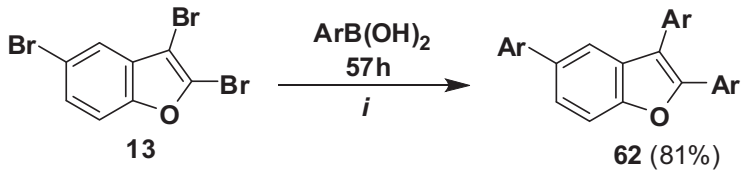


Figure 11. NOESY and HMBC Correlations of Compound **59a**

The regioselectivity of compound **59a** was unambiguously established with the help of 2D NMR as well. The relatively low chemical shift value of C-3 (δ_C 93.1) indicated that C-3 is not attached with any unsaturated moiety or aromatic ring. Tolyl protons H-2'/6' resonating at δ_H 8.10 showed obvious HMBC correlations with carbon C-2 resonating at δ_C 151.8.

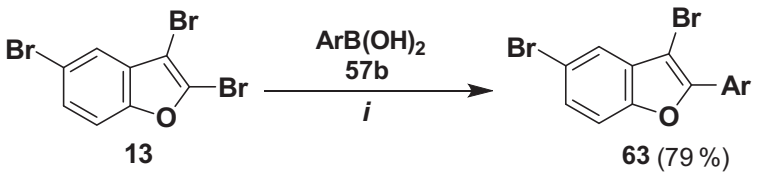
No HMBC correlation of protons H-2'/6' with C-3 was observed. Furthermore, the tolyl aromatic protons did not show a NOESY correlation with benzofuran proton H-4. This HMBC and NOESY correlation pattern including the small chemical shift value for carbon C-3 confirms that the tolyl moiety is attached to carbon C-2 of the benzofuran.

Suzuki reactions of 2,3,5-tribromobenzofuran were also investigated. Its reaction with 3.0 equivalents of 4-fluorophenylboronic acid using 5 mol-% of $Pd(PPh_3)_4$ provided triarylbenzofuran **62** in very good yield (81 %) (Scheme 21).



Scheme 21. Synthesis of **62**. *Reagents and Conditions: (i)* **57h** (3.0 equiv.), $Pd(PPh_3)_4$ (5 mol-%), aq. K_2CO_3 (2 M), dioxane, 90 °C, 8 h

When 2,3,5-tribromobenzofuran was reacted with one equivalent of 4-tolylboronic acid it provided 3,5-dibromo-2-arylbenzofuran **63** in good yield (79 %) (Scheme 22).



Scheme 22. Synthesis of **63**. *Reagents and Conditions: (i)* **57b** (1.0 equiv.), $Pd(PPh_3)_4$ (5 mol-%), aq. K_2CO_3 (2 M), dioxane, 70 °C, 4 h

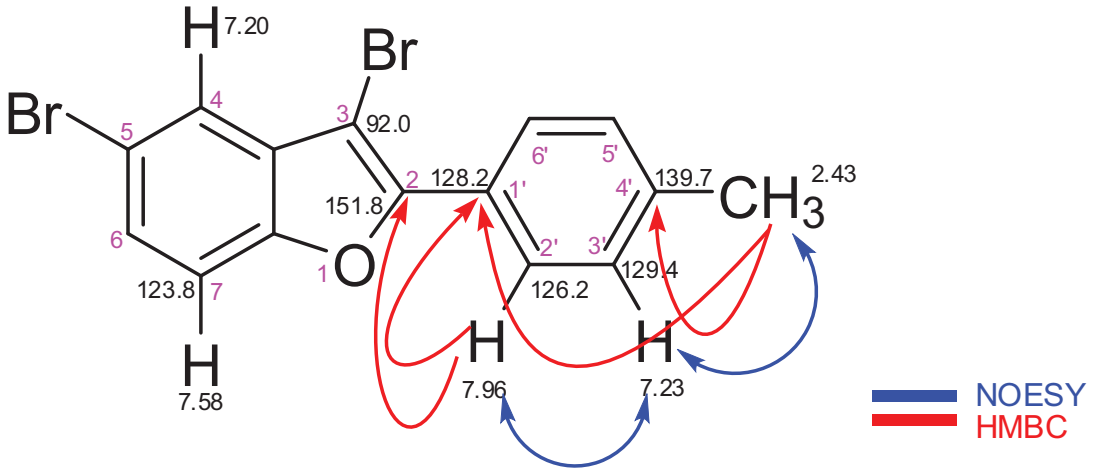


Figure 12. NOESY and HMBC Correlations of Compound **63**

The structure of **63** was confirmed by a detailed study of 1D and 2D NMR. The small chemical shift value of C-3 (δ_C 92.0) is due to the positive mesomeric effect of the furan oxygen atom. The value suggests that C-3 is not attached with any unsaturated moiety. Regioselectivity of compound **63** was explicitly established with the help of 2D NMR. Assignment of chemical shifts for C/CH/CH_3 could be achieved by the splitting pattern of ^{1}H NMR and 2D NMR correlations (NOESY (H-H), HMQC, HMBC (H-C)). Tolyl aromatic protons H-2'/6' resonating at δ_H 7.96 (d, J = 8.6 Hz) showed clear HMBC correlations with C-2 resonating at δ_C 151.8. Furthermore, H-2'/6' did not show HMBC correlation with C-3. No NOESY correlation was observed with H-4 resonating at δ_H 7.20. All these facts established that the tolyl moiety is connected with C-2.

3.3 Conclusion

In conclusion, 2,3-diarylbenzofurans were prepared by Suzuki-Miyaura reactions of 2,3-dibromobenzofuran with two equivalents of boronic acids. The reaction with one equivalent of arylboronic acids resulted in site-selective formation of 2-aryl-3-bromobenzofurans. 2,3-diarylbenzofurans containing two different aryl groups were prepared from 2,3-dibromobenzofuran in a one-pot protocol by sequential addition of two different boronic acids. Hydrogenated products were also isolated which can explain the moderate yields.

4 One-Pot Synthesis of 2,3-Diarylindenones by Site-Selective Suzuki-Miyaura Reactions of 1,2-Dibromoindenone

4.1 Introduction

Type 2 diabetes mellitus, also recognized as non-insulin-dependent diabetes mellitus, accounts for more than 90 % of the diabetes cases. This condition is characterized by high levels of glucose resulting from progressive insulin resistance and, at later stages of the disease, mutilation of insulin secretion. Peroxisome proliferator-activated receptors (PPARs) are one of the attractive diabetes target proteins. The indenone derivatives had been discovered as a unique pattern for the activation of PPARγ. The indenones are a novel and interesting chemical class for the treatment of diabetes type 2. For example, compound **A** (Figure 13) [41] has been reported to have very good agonistic activity with an EC_{50} value of 50 nM and exhibited a new binding mode in the X-ray cocrystal structure. Furthermore, nitrated indenoisoquinolines have been revealed as potent topoisomerase I (Top1) inhibitors as well. Hence, arylated-indenones are of considerable pharmacological relevance and worth for further studies.[41]

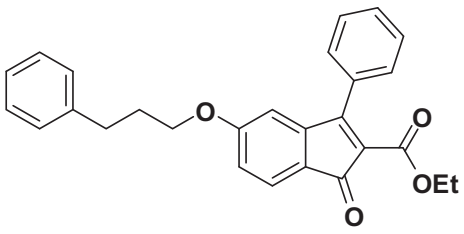


Figure 13. Compound **A**

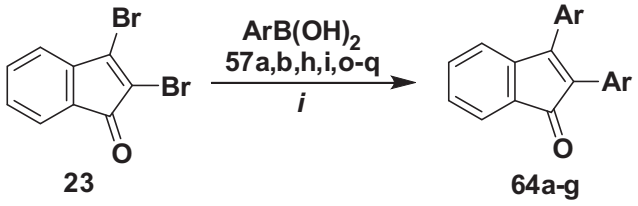
4.2 Results and discussions

Classic syntheses of these molecules rely on intramolecular Friedel-Crafts acylation reactions,[42] on the reaction of 3-(*p*-methoxybenzal)phthalide with phenylmagnesium bromide and subsequent rearrangement,[43] and on the reaction of 2-phenyl-1*H*-inden-1,3(2*H*)-dione with phenylmagnesium bromide and subsequent extrusion of water.[44] 2,3-Diaryl-1*H*-inden-1-ones have also been prepared from dibenzoylmethane [45] and benzophenone derivatives.[46] Recent transition metal-catalyzed syntheses of 2,3-diaryl-1*H*-inden-1-ones include the reaction of 1-methoxy-4-(4'-methoxyphenylethynyl)-benzene with 2-bromobenzaldehyde,[47] and the reaction of diphenyl acetylene with 2-bromobenzeneboronic acid.[48]

In recent years, a number of site-selective palladium(0)-catalyzed cross-coupling reactions of polyhalogenated heterocycles have been developed. The site-selectivity of these reactions is generally influenced by electronic and steric parameters.[12-20]

It occurred to me that 2,3-dibromo-1*H*-inden-1-one might be a suitable starting material for the synthesis of 2,3-diaryl-1*H*-inden-1-ones. The reactions of 2,3-dibromo-1*H*-inden-1-one with amines and C-nucleophiles, such as Grignard reagents, ethyl cyanoacetate and ethyl acetoacetate, are known for a long time.[49] Surprisingly, transition metal-catalyzed cross-coupling reactions of 2,3-dibromo-1*H*-inden-1-one have, to the best of my knowledge, not been studied to date. Herein, I describe my research work for the synthesis of 2,3-diaryl-1*H*-inden-1-ones by site-selective S-M reactions of 2,3-dibromo-1*H*-inden-1-one. The products are not readily available by other methods.

The S-M reaction of 2,3-dibromo-1*H*-inden-1-one (**23**) [50] with two equivalents of arylboronic acids **57a,b,h,i,o-q** gave the 2,3-diaryl-1*H*-inden-1-ones **64a-g** in excellent yields (Scheme 10, Table 5). The best yields were obtained using 2.2 equiv. of the arylboronic acid, $Pd(PPh_3)_4$ (5 mol-%) as the catalyst, and K_2CO_3 (2 M aqueous solution) as the base (1,4-dioxane, 70 °C, 6 h).[51] The employment of $Pd(PPh_3)_2Cl_2$ proved to be less efficient in terms of yield. The reactions could be successfully carried out with both electron-rich and electron-poor arylboronic acids.



Scheme 23. Synthesis of **64a-g**. *Reagents and Conditions*: *(i)* **57a,b,h,i,o-q** (2.2 equiv.), $Pd(PPh_3)_4$ (5 mol-%), 2M K_2CO_3, dioxane, 70 °C, 6 h

Table 5. Synthesis of **64a-g**

57	**64**	Ar	% (**64**)[a]
a	**a**	C_6H_5	97
b	**b**	4-MeC_6H_4	99
h	**c**	4-FC_6H_4	95
i	**d**	2-$(MeO)C_6H_4$	93
o	**e**	3-$(MeO)C_6H_4$	98
p	**f**	4-$(MeO)C_6H_4$	98
q	**g**	3-FC_6H_4	96

[a] Yield of isolated products

The structures of the products were established by NMR. The structure of **65a** was independently confirmed by X-ray crystal structure analysis (Figures 14).

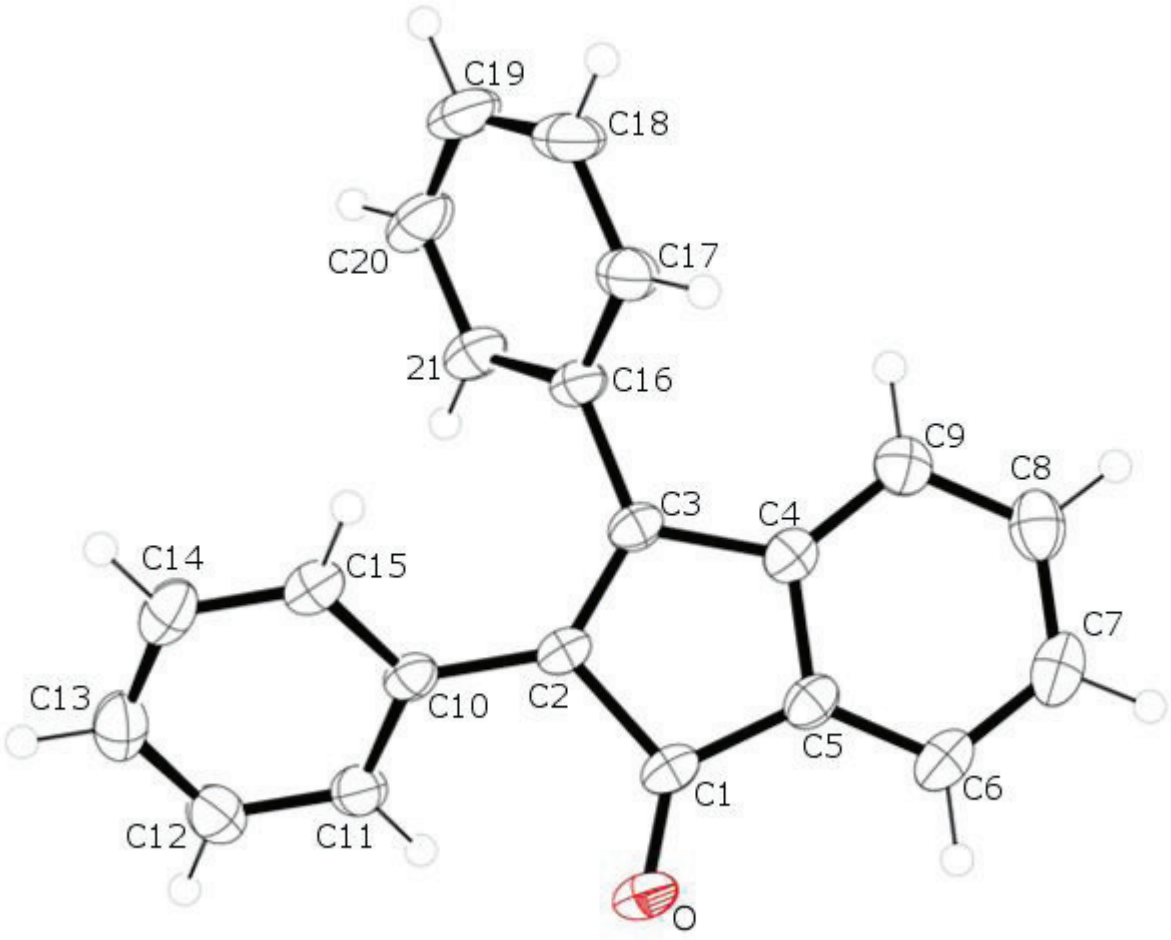
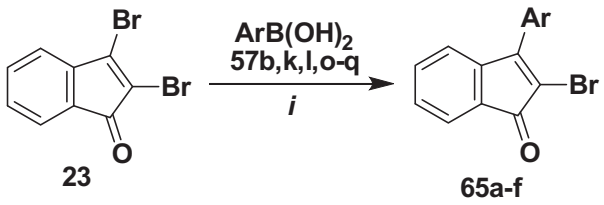


Figure 14. Crystal structure of **64a** (SPGR $P2_1/n$, wR2 ca. 11 %)

The S-M reaction of **23** with arylboronic acids **57b,k,l,o-q** (1.0 equiv.) afforded the 3-aryl-2-bromo-1*H*-inden-1-ones **65a-f** in excellent yields and with very good site-selectivity (Scheme 24, Table 6). The first attack occurred at position C-3 of **23**. During the optimization it proved to be very important to use exactly 1.0 equiv. of the arylboronic acid and $Pd(PPh_3)_4$ (3 mol-%) as the catalyst. The employment of $Pd(PPh_3)_2Cl_2$ resulted in a significant decrease of the yield and of the site-selectivity. The temperature played an important role. A good selectivity was achieved only when the reaction was carried out at 45 °C because the second cross-coupling was slow at this temperature.

The formation of a mixture of starting material, mono- and di-substituted products was generally observed when the reaction was carried out at temperatures between 45 and 70 °C. In case of highly reactive methoxy-substituted arylboronic acids (**57l,o,p**), the temperature had to be further decreased to 40 °C to achieve a good site-selectivity. The reactions were successful for both electron-rich and electron-poor arylboronic acids.



Scheme 24. Synthesis of **65a-f**. *Reagents and Conditions*: *(i)* **57b,k,l,o-q** (1.0 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 2M K_2CO_3, dioxane, 45 °C, 4 h

Table 6. Synthesis of 3-aryl-2-bromoinden-1-ones **65a-f**

57	**65**	Ar	% (**65**)[a]
b	**a**	4-MeC_6H_4	98
k	**b**	3,5-$Me_2C_6H_3$	88
l	**c**	2,6-$(MeO)_2C_6H_3$	83 [b]
o	**d**	3-$(MeO)C_6H_4$	95 [b]
p	**e**	4-$(MeO)C_6H_4$	93[b]
q	**f**	3-FC_6H_4	83

[a] Yields of isolated products; [b] reaction temperature: 40 °C

The structures of the products **65a-f** were established by NMR experiments (NOESY, HMBC). The structure of **65c** was independently confirmed by X-ray crystallography (Figure 15).

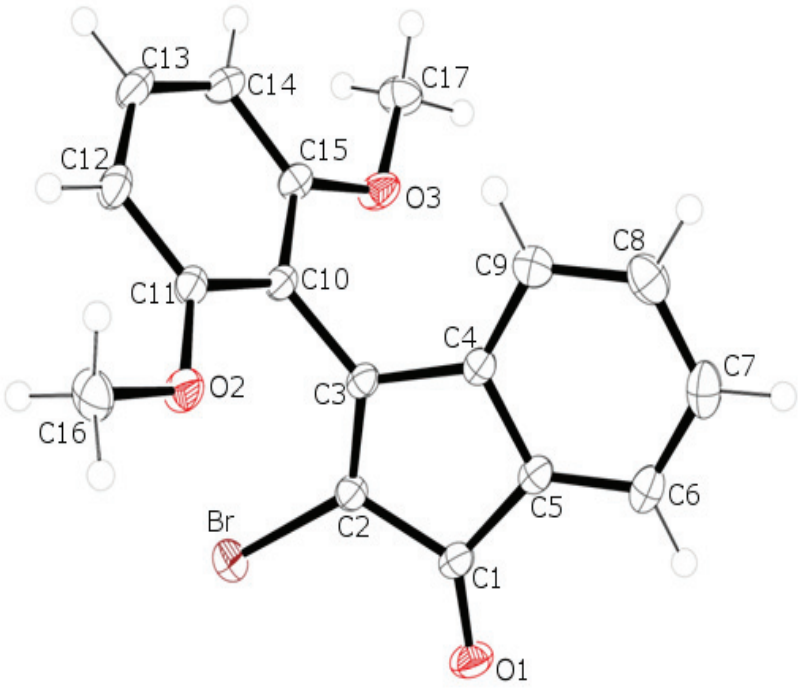


Figure 15. Crystal structure of **65c** (SPGR P-1, wR2 ca. 7 %)

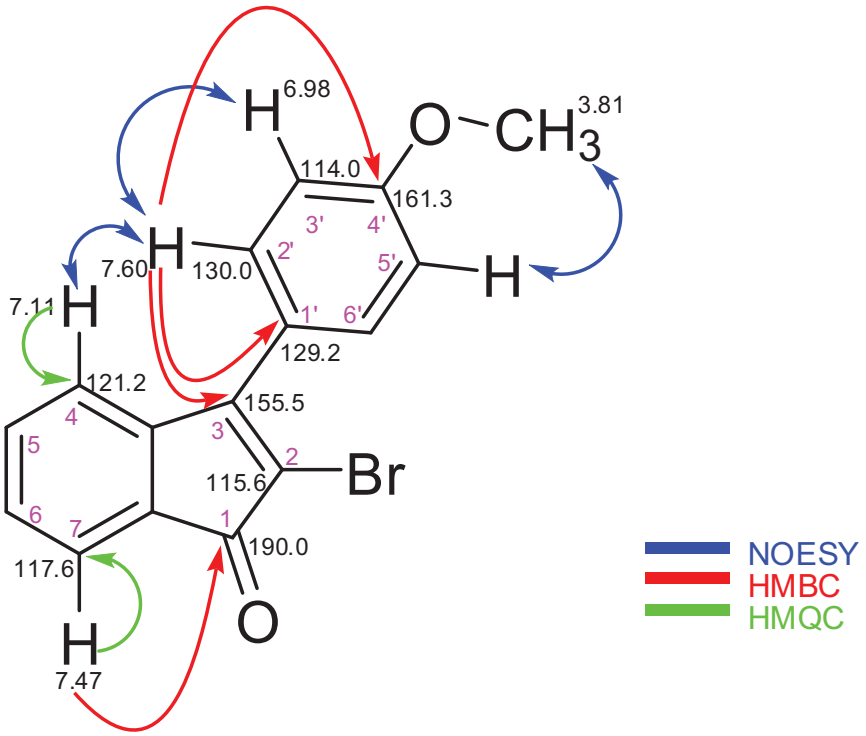
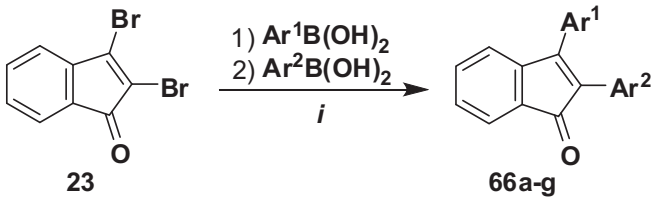


Figure 16. HMQC, NOESY and HMBC Correlations of Compound **65e**

The structure of compound **65e** (Figure 16) was also confirmed by 1D NMR and 2D NMR (HMQC, NOESY and HMBC). The protons of the 4-(MeO)C_6H_4 moiety H-2'/6' (δ_H 7.60) provided a clear HMBC correlation with the indenone carbon C-3 (δ_C 155.5), but no correlation appeared for C-2 (δ_C 115.6) indicating the connectivity of C-3 with carbon C-1'. A key NOESY correlation of H-2'/6' (δ_H 7.60) with proton H-4 (δ_H 7.11) further established the fact that the 4-(MeO)C_6H_4 moiety is connected with C-3.

The one-pot reaction of **23** with two different arylboronic acids, which were sequentially added, afforded the unsymmetrical 2,3-diaryl-1*H*-inden-1-ones **66a-g** containing two different terminal aryl groups (Scheme 25, Table 7). During the optimization, it proved to be important that the first step was carried out at 45 °C (or at 40 °C in case of **66i,l**) to achieve a good site-selectivity in favour of position C-3 of the substrate. The second step had to be carried out at 70 °C to guarantee a complete reaction of position C-2. All reactions proceeded in excellent yields.



Scheme 25. Synthesis of **66a-g**. *Reagents and Conditions*: *(i)* 1) $Ar^1B(OH)_2$: **57b,d, i,l,r** (1.0 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 2M K_2CO_3, dioxane, 45 °C, 4 h; 2) $Ar^2B(OH)_2$: **57b,g,h,l,p,r** (1.1 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 70 °C, 6 h

Table 7. Synthesis of **66a-g**

57	**66**	Ar^1	Ar^2	% (**66**) [a]
b,p	**a**	4-MeC_6H_4	4-$(MeO)C_6H_4$	93
b,r	**b**	4-MeC_6H_4	3-ClC_6H_4	89
l,h	**c**	2,6-$(MeO)_2C_6H_3$ [b]	4-FC_6H_4	86
b,l	**d**	4-MeC_6H_4	2,6-$(MeO)_2C_6H_3$	90
i,b	**e**	2-$(MeO)C_6H_4$ [b]	4-MeC_6H_4	85
d,g	**f**	4-EtC_6H_4	4-ClC_6H_4	83
r,b	**g**	3-ClC_6H_4	4-MeC_6H_4	79

[a] Yields of isolated products; [b] reaction temperature: 40 °C

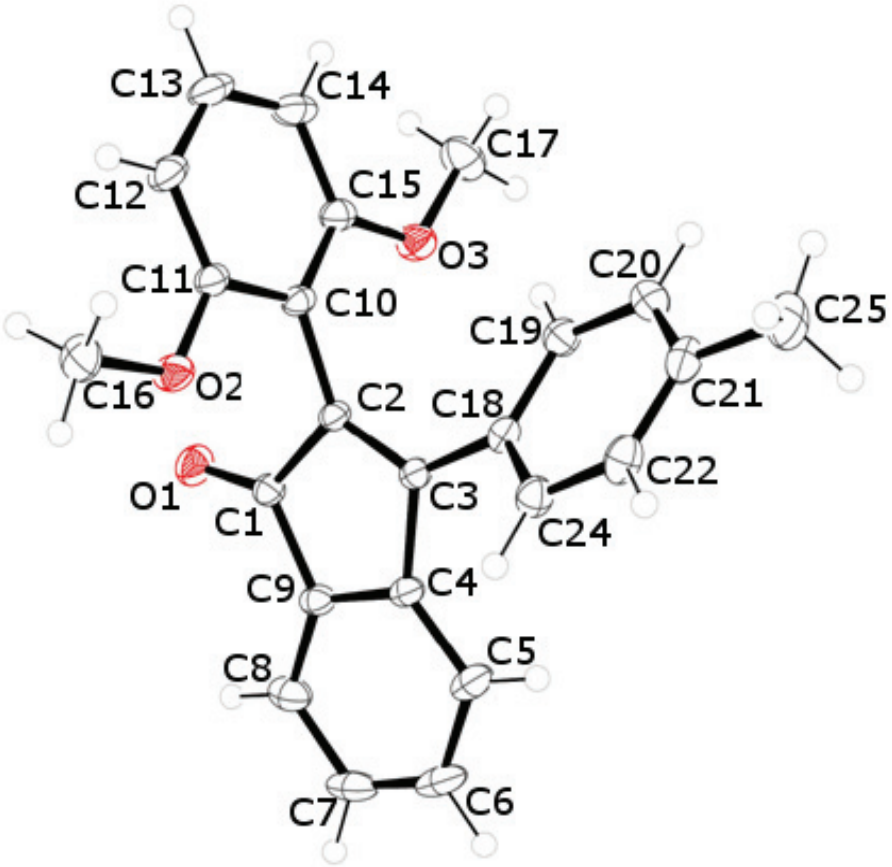


Figure 17. Crystal structure of **66d** (SPGR Pbcn, wR2 ca. 14 %)

The site-selective formation of **65a-f** and **66a-g** can be explained by electronic reasons. The first attack of palladium(0) catalyzed cross-coupling reactions generally occurs at the more electron deficient and sterically less hindered position. Position C-3 of 2,3-dibromo-1*H*-inden-1-one (**23**) is considerably more electron-deficient than position C-2. Handy and Zhang reported a simple guide for the prediction of the site-selectivity of palladium(0) catalyzed cross-coupling reactions of polyhalogenated substrates based on the ^{1}H NMR chemical shift values of the non-halogenated analogues. In fact, the ^{1}H NMR signal of proton H-3 of inden-1-one is shifted downfield compared to proton H-2.

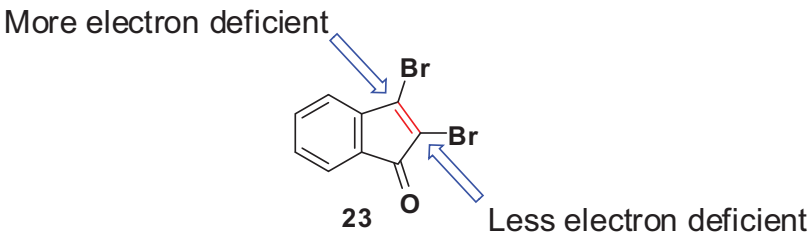


Figure 18. Possible explanation for the site-selectivity of cross-coupling reactions of **23**

4.3 Conclusion

In conclusion, I have performed site-selective Suzuki-Miyaura reactions of 2,3-dibromo-1*H*-inden-1-one which provide a convenient and site-selective approach to achieve arylated indenones. The Suzuki-Miyaura reaction of 2,3-dibromo-1*H*-inden-1-one with two equivalents of arylboronic acid gave 2,3-diaryl-1*H*-inden-1-ones. The reaction with one equivalent of arylboronic acid gave 2-bromo-3-aryl-1*H*-inden-1-ones with very good site-selectivity. The one-pot reaction of 2,3-dibromo-1*H*-inden-1-one with two different arylboronic acids afforded 2,3-diaryl-1*H*-inden-1-ones containing two different terminal aryl groups.

5 Abstract

An overview of domino twofold Heck / 6π-electrocyclization reactions and site-selective Suzuki-Miyaura reactions is given.

2,3-Dibromobenzofuran and 2,3,5-tribromobenzofuran were prepared from benzofuran. Functionalized dibenzofurans were prepared based on domino twofold Heck / 6π-electrocyclization reactions of 2,3-di- and 2,3,5-tribromobenzofuran.

The Suzuki–Miyaura reaction of 2,3-dibromobenzofuran with two equivalents of boronic acids gave 2,3-diarylbenzofurans. The reaction with one equivalent of arylboronic acids resulted in site-selective formation of 2-aryl-3-bromobenzofurans. 2,3-Diarylbenzofurans containing two different aryl groups were prepared from 2,3-dibromobenzofuran in a one-pot protocol by sequential addition of two different boronic acids.

The first transition metal-catalyzed cross-coupling reactions of 2,3-dibromo-1*H*-inden-1-one are investigated. The Suzuki-Miyaura reaction of 2,3-dibromo-1*H*-inden-1-one with two equivalents of arylboronic acid gave 2,3-diaryl-1*H*-inden-1-ones. The reaction with one equivalent of arylboronic acid gave 2-bromo-3-aryl-1*H*-inden-1-ones with very good site-selectivity. The one-pot reaction of 2,3-dibromo-1*H*-inden-1-one with two different arylboronic acids afforded 2,3-diaryl-1*H*-inden-1-ones containing two different terminal aryl groups.

Ein Überblick zu Domino Heck / 6π-Electrocyclisierungs Reaktionen und regioselektiven Suzuki-Miyaura Reaktionen wird gegeben.

2,3-Dibromobenzofuran und 2,3,5-Tribromobenzofuran wurden aus Benzofuran hergestellt. Funktionalisierte Dibenzofurane wurden durch Domino Heck / 6π-Electrocyclisierungs Reaktionen von 2,3-Di- and 2,3,5-Tribromobenzofuran hergestellt.
Die Suzuki–Miyaura Reaktion von 2,3-Dibromobenzofuran mit zwei Äquivalenten Boronsäuren ergab 2,3-Diarylbenzofurane. Die Reaktion mit einem Äquivalent von Arylboronsäure resultierte in regioselektiver Bildung von 2-Aryl-3-bromobenzofuranen. 2,3-Diarylbenzofurane mit zwei unterschiedlichen Arylgruppen wurden ausgehend von 2,3-Dibrombenzofuran in einer One-Pot Reaktion durch sequenzielle Addition von zwei unterschiedlichen Boronsäuren hergestellt.

Die ersten Übergangsmetall-katalysierten Kreuzkupplungsreaktionen von 2,3-Dibrom-1*H*-inden-1-on wurden untersucht. Die Suzuki-Miyaura Reaktion von 2,3-Dibrom-1*H*-inden-1-on mit zwei Äquivalenten von Arylboronsäuren ergab 2,3-Diaryl-1*H*-inden-1-one. Die Reaktion mit einem Äquivalent von Arylboronsäuren lieferte 2-Brom-3-aryl-1*H*-inden-1-one mit sehr guter Regioselektivität. Die One-Pot Reaktion von 2,3-Dibromo-1*H*-inden-1-on mit zwei unterschiedlichen Arylboronsäuren lieferte 2,3-Diaryl-1*H*-inden-1-one mit zwei verschiedenen terminalen Arylgruppen.

Experimental Section

6 Material and Methods

6.1 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).

6.2 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 ($\delta = 0.00$) or residual $CHCl_3$ ($\delta = 7.26$) 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.

6.3 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

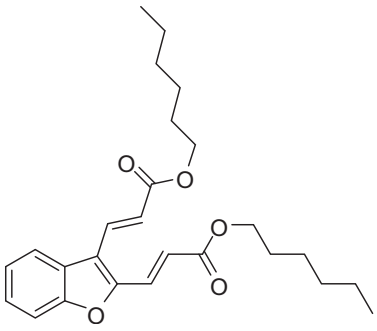
Column chromatography was performed with Merck Silica Gel 60 or Macherey-Nagel Silica Gel 60 (0.063-0.200 mm, 70-230 mesh). The finer Merck Silica Gel 60 (0.040-0.063 mm, 230-400 mesh) was chosen when appropriate.

7 General Procedures

7.1 Efficient Synthesis of Functionalized Dibezofurans by Domino Twofold Heck / 6π-Electrocyclization Reactions of 2,3-Di- and 2,3,5 Tribromobenzofuran

General procedure A for the synthesis of ***54, 55*** *and* **18**. In a pressure tube a DMF suspension (5 mL) of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 2.5 mol-% per Br atom of the substrate) and of dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine (**L**) (41 mg, 0.10 mmol) was purged with Argon and the mixture was stirred at 20 °C to give a yellowish to brownish clear solution. To the stirred solution were added **13** or **52** (1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the acrylate **53** (1.25 equiv. per Br atom of the substrate). The reaction mixture was stirred at 70°C - 100 °C for 12 - 48 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with H_2O (3 x 20 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The residue was chromatographed (flash silica gel, heptanes/EtOAc) to give **54, 55** and **18**.

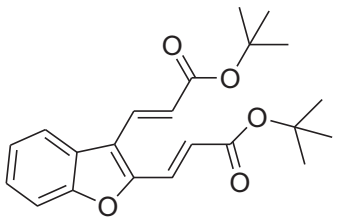
7.1.1 Synthesis of 54



(2E,2'E)-Dihexyl 3,3'-(benzofuran-2,3-diyl)diacrylate (54d): Starting with **13** (276 mg, 1.0 mmol), following the *general procedure A*, **54d** was prepared as a brownish highly viscous oil (337 mg, 79 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.82-0.86 (m, 6H, $2CH_3$), 1.24-1.37 (m, 12H, $6CH_2$), 1.61-1.71 (m, 4H, $2CH_2$), 4.17 (t, 2H, J = 6.8 Hz, CH_2O), 4.18 (t, 2H, J = 6.8 Hz, CH_2O), 6.58 (d, 1H, J = 16.0 Hz, CH), 6.60 (d, 1H, J = 15.5 Hz, CH), 7.24-7.30 (m, 1H,

ArH), 7.36 (td, 1H, *J* = 1.3, 8.3 Hz, ArH), 7.42-7.45 (m, 1H, ArH), 7.73 (d, 1H, *J* = 15.5 Hz, CH), 7.77-7.81 (m, 1H, ArH), 7.85 (d, 1H, *J* = 16.1 Hz, CH). ^{13}C NMR (62.9 MHz,$CDCl_3$): δ = 14.0 ($2CH_3$), 22.5, 25.5, 25.6, 28.6, 28.7, 31.4, 31.5 (CH_2), 65.0, 65.2 (CH_2O), 111.8 (CH), 119.0 (C), 120.8, 121.4, 121.6, 124.1 (CH), 125.8 (C), 127.3, 127.5, 132.8 (CH), 152.9, 155.2 (C), 166.3, 166.8 (CO). IR (KBr): ν = 3070, 3043 (w), 2956, 2931, 2857 (m), 1710, 1628 (s), 1583 (m), 1537 (w), 1469, 1448 (m), 1398, 1378, 1351 (w), 1308 (s), 1292 (m), 1278, 1257 (s), 1201 (m), 1173 (s), 1103, 1062, 1021, 1011 (m), 967, 959 (s), 876, 859, 847, 768 (m), 752 (s), 731, 716, 708, 673, 588 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 426 ([M]$^+$, 5), 297 (29), 296 (20), 239 (15), 214 (15), 213 (100), 212 (30), 195 (56), 169 (30), 168 (11), 139 (10), 43 (20). HRMS Pos (ESI): calcd for $C_{26}H_{35}O_5$ [M+H]$^+$: 427.2479; found: 427.24766.

(2E,2'E)-tert-Butyl 3,3'-(benzofuran-2,3-diyl)diacrylate (54f): Starting with **13** (276 mg, 1.0 mmol), following the *general procedure A*, **54f** was prepared as a brownish highly viscous oil (266 mg, 72 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.47 (s, 9H, $3CH_3$), 1.48 (s, 9H, $3CH_3$), 6.47 (d, *J* = 16.1 Hz, 1H, CH), 6.52 (d, *J* = 15.5 Hz, 1H, CH), 7.18-7.40 (m, 3H, ArH), 7.59 (d, *J* = 15.9 Hz, 1H, CH), 7.71 (d, *J* = 16.1 Hz, 1H, CH), 7.72-7.75 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.1, 28.2 ($3CH_3$), 80.9, 81.1 (C), 111.6 (CH), 118.7 (C), 121.6, 122.6, 123.2, 124.0 (CH), 125.9 (C), 126.7, 127.0, 131.8 (CH), 152.8, 155.1 (C), 165.5, 165.9 (CO). IR (KBr): ν = 3400, 3061 (w), 2976, 2930, 1801 (m), 1704 (s), 1635, 1476, 1450, 1392 (m), 1367 (s), 1304, 1282 (m), 1255, 1143, 969 (s), 949, 880, 844, 809 (m), 746 (s), 670, 632, 611, 581, 539 (m) cm^{-1}.



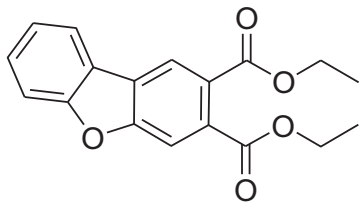
2,3-Bis(4-methylstyryl)benzofuran (54h): Starting with **13** (276 mg, 1.0 mmol), following the *general procedure A*, **54h** was prepared as a brownish highly viscous oil (227 mg, 65 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.22-7.37 (m, 10H, ArH/olefinic CH), 7.50-7.53 (m, 5H, ArH), 7.927.95 (m, 1H, ArH). ^{13}C NMR (62.9 MHz,$CDCl_3$): δ = 21.3, 21.4 (CH_3), 111.0, 113.0 (CH), 116.0 (C), 117.6, 120.9, 123.0, 125.1, 126.2, 126.8 (CH), 127.4 (C), 129.5, 129.6, 130.1, 130.6 (CH), 134.0, 135.0, 137.5, 138.4, 152.6, 154.6 (C). IR (KBr): ν = 3021, 2919, 2857 (m), 1896 (w), 1711 (s), 1605 (m), 1571, 1538 (w), 1510, 1475 (m), 1450 (s), 1442, 1358, 1284, 1266, 1250 (m), 1218, 1193 (s), 1181, 1155, 1122, 1110, 1095, 1038, 1018 (m), 951 (s), 887, 850 (m), 799 (s), 771 (m), 741 (s), 703, 594, 532 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 350 ($[M]^+$, 100), 349 (12), 335 (14), 259 (12), 245 (19). HRMS (EI, 70 eV): calcd for $C_{26}H_{22}O$ $[M]^+$: 350.16652; found: 350.16599.

2,3-Bis(2-methoxystyryl)benzofuran (54j): Starting with **13** (276 mg, 1.0 mmol), following the *general procedure A*, **54j** was prepared as a brownish highly viscous oil (206 mg, 54 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.68-6.98 (m, 4H, Ar/olefinic CH), 7.20-7.33 (m, 6H, ArH), 7.41-7.44 (m, 1H, ArH), 7.53-7.66 (m, 4H, Ar/olefinic CH), 7.87-7.90 (m, 1H, ArH). ^{13}C NMR (62.9 MHz,$CDCl_3$): δ = 55.5, 55.6 (OCH_3), 110.9, 111.0, 111.1, 114.7 (CH), 116.6 (C), 119.0, 120.8, 121.1, 123.0, 124.9, 125.0, 125.5 (CH), 125.8 (C), 126.0, 127.0 (CH), 127.5 (C), 128.6, 129.2 (CH), 153.0, 154.7, 156.8, 157.4 (C). IR (KBr): ν = 3066, 3030, 2999 (w), 2924, 2834, 1595, 1575 (m), 1557, 1538 (w), 1481, 1462 (m), 1450 (s), 1434, 1393, 1349, 1330, 1289 (m), 1239 (s), 1207, 1177, 1160 (m), 1102 (s), 1049 (m), 1024, 949 (s), 887, 849, 784 (m), 741 (s), 670, 645, 615, 574, 535 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 23), 382 ($[M]^+$, 100), 380 (10), 275 (14), 274 (15), 263 (21), 261 (14), 259 (10), 231 (13), 161 (16), 135 (18), 121 (21), 97 (11), 91 (24), 83 (12), 77 (12), 71 (14), 69 (14), 57 (21), 55 (16), 44 (53), 43 (25), 41 (14). HRMS Pos (ESI) calcd for $C_{26}H_{23}O_3$ $[M+H]^+$: 383.16417; found 383.16473.

General procedure B for the synthesis of dibenzofurans **18** from **55.** To the isomeric mixture **55** were added xylene (3 mL) and Pd/C (30 mg, 10 mol-%). The solution was stirred under reflux for 48 h under Argon atmosphere. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **18**.

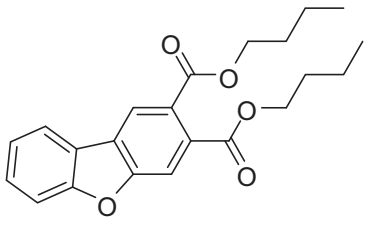
7.1.2 Synthesis of dibenzofurans 18 from 55.

Diethyl dibenzo[b,d]furan-2,3-dicarboxylate *(***18a***):* Starting with **13** (276 mg, 1.0 mmol),



following the *general procedures A and B,* **18a** was prepared as a light yellow highly viscous oil (227 mg, 73 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (t, 3H, *J* = 7.2 Hz, CH_3), 1.35 (t, 3H, *J* = 7.1 Hz, CH_3), 4.35 (q, 4H, *J* = 7.2 Hz, $2CH_2O$), 7.31-7.37 (m, 1H, ArH), 7.47 (td, 1H, *J* = 8.4, 1.5 Hz, ArH), 7.54-7.57 (m, 1H, ArH), 7.82 (s, 1H, ArH), 7.91-7.95 (m, 1H, ArH), 8.29 (d, 1H, *J* = 0.2 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.1, 14.2 (CH_3), 61.7, 61.9 (CH_2O), 112.1, 112.5, 121.4, 122.1 (CH), 123.0 (C), 123.6 (CH), 126.3, 127.0 (C) 128.7 (CH), 131.8, 156.7, 157.5 (C), 167.5, 167.6 (CO). IR (KBr): ν = 3073, 2980, 2928, 2871, 2853 (w), 1717 (s), 1635, 1602, 1578 (w), 1454, 1368, 1304 (m), 1275, 1245, 1220, 1192, 1179, 1100, 1061, 1016 (s), 960, 910, 901, 877, 859, 840, 719, 767 (w), 747 (s), 722, 693, 663, 601, 565 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 312 ($[M]^+$, 37), 267 (15), 240 (18), 239 (100), 166 (8). HRMS (EI, 70 eV): calcd for $C_{18}H_{16}O_5$ $[M]^+$: 312.09923; found: 312.09906.

Dibutyl dibenzo[b,d]furan-2,3-dicarboxylate *(***18b***):* Starting with **13** (276 mg, 1.0 mmol),

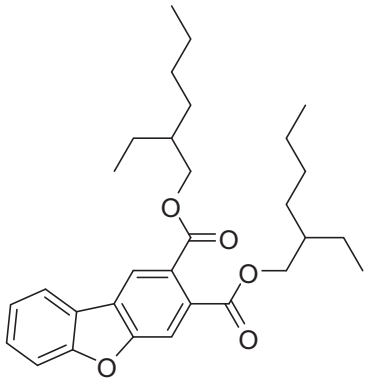


following the *general procedures A and B,* **18b** was prepared as a light yellow highly viscous oil (280 mg, 76 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.2 Hz, CH_3), 0.92 (t, 3H, *J* = 7.5 Hz, CH_3), 1.33-1.45 (m, 4H, $2CH_2$), 1.64-1.76 (m, 4H, $2CH_2$), 4.30 (t, 4H, *J* = 6.7 Hz, $2CH_2O$), 7.31-7.38 (m, 1H, ArH), 7.47 (td, 1H, *J* = 8.3, 1.4 Hz, ArH), 7.54-7.58 (m, 1H, ArH), 7.82 (s, 1H, ArH), 7.92-7.96 (m, 1H, ArH), 8.28 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.8, 13.1 (CH_3), 28.7, 29.6, 29.7, 30.9 (CH_2), 64.7, 64.8 (CH_2O), 111.1, 111.5, 120.4, 121.1, 122.6 (CH), 125.3, 126.2, 126.5 (C), 127.7 (CH), 130.8, 155.7, 156.5 (C), 166.6 (2CO). IR (KBr): ν = 2957 (m), 2922 (s), 2852 (m), 1724 (s), 1638, 1603, 1579 (w), 1454, 1379, 1349, 1305 (m), 1276, 1249, 1220 (s), 1192, 1178 (m), 1101, 1065 (s), 1018, 966, 843, 783, 767 (m), 748 (s), 722, 698 (m), 602, 564 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 368 ([M]$^+$, 13), 256 (32), 240 (14), 239 (100), 212 (10), 57 (14). HRMS (EI, 70 eV): calcd for $C_{22}H_{24}O_5$ [M]$^+$: 368.16183; found: 368.16208.

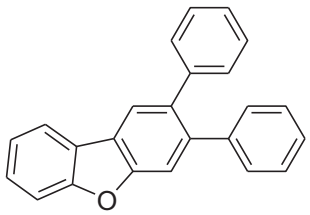
Diisobutyl dibenzo[b,d]furan-2,3-dicarboxylate (**18c**): Starting with **13** (276 mg, 1.0 mmol), following the *general procedures A and B,* **18c** was prepared as a brownish highly viscous oil (309 mg, 84 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.94 (d, 6H, *J* = 6.8 Hz, $2CH_3$), 0.95 (d, 6H, *J* = 6.78 Hz, $2CH_3$), 1.93-2.10 (m, 2H, aliphatic CH), 4.10 (d, 4H, *J* = 6.8 Hz, $2CH_2O$), 7.30-7.37 (m, 1H, ArH), 7.43-7.56 (m, 2H, ArH), 7.82 (s, 1H, ArH), 7.91-7.95 (m, 1H, ArH), 8.27 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.2 ($4CH_3$), 27.7, 27.8 (CH), 71.9, 72.0, (CH_2O), 112.1, 112.5, 121.4, 122.0 (CH), 123.6 (C), 124.1 (CH), 126.3, 127.3 (C), 128.7 (CH), 131.8, 156.6, 157.5 (C), 167.5, 167.6 (CO). IR (KBr): ν = 3072, 2959, 2873 (m), 1719 (s), 1636, 1602, 1577 (w), 1454, 1393, 1376, 1350, 1306 (m), 1274, 1239, 1219, 1778, 1111, 1100, 1060 (s), 1011, 983 (m), 945, 900, 848, 881, 767 (w), 746 (m), 722, 694, 602, 564 cm^{-1}. MS (EI, 70 eV): *m/z* (%) =

368 ([M]$^+$, 9), 256 (62), 240 (15), 239 (100), 213 (11), 212 (13), 195 (10). HRMS (EI, 70 eV): calcd for $C_{22}H_{24}O_5$ [M]$^+$: 368.16183; found: 368.16179.

Bis(2-ethylhexyl) dibenzo[b,d]furan-2,3-dicarboxylate (18e): Starting with **13** (276 mg, 1.0 mmol), following the *general procedures A and B,* **18e** was prepared asa brownish highly viscous oil (355 mg, 74 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82- 0.90 (m, 12H, 4CH_3), 1.25-1.36 (m, 16H, 8CH_2), 1.58-1.70 (m, 2H, aliphatic CH), 4.19 (d, 2H, *J* = 6.0 Hz, CH_2O), 4.20 (d, 2H, *J* = 5.8 Hz, CH_2O), 7.30-7.36 (m, 1H, ArH), 7.46 (td, 1H, *J* = 1.4, 8.2 Hz, ArH), 7.53-7.56 (m, 1H, ArH), 7.80 (d, 1H, *J* = 0.2 Hz, ArH), 7.91-7.93 (m, 1H, ArH), 8.24 (d, 1H, *J* = 0.2 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.0, 14.0 (2CH_3), 23.0, 23.8, 29.0 (4CH_2), 38.8 (CH), 68.3, 68.4 (CH_2O), 112.1, 112.5, 121.3, 122.0 (CH), 123.0 (C), 123.6 (CH), 126.3, 127.4 (C), 128.7 (CH), 131.8, 156.6, 157.5 (C), 167.5, 167.7 (CO). IR (KBr): ν = 2957, 2928, 2872, 2859 (m), 1721 (s), 1637, 1602, 1574 (w), 1454, 1379, 1349, 1305 (m), 1275, 1237, 1219 (s), 1190, 1179 (m), 1101 (s), 1062, 1011, 907, 781, 767 (m), 746, 731 (s), 695, 648 (m), 602, 564 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 480 ([M]$^+$, 1), 257 (25), 256 (69), 240 (17), 239 (100), 57 (9). HRMS (EI, 70 eV): calcd for $C_{30}H_{40}O_5$ [M]$^+$: 480.28703; found: 480.28739.

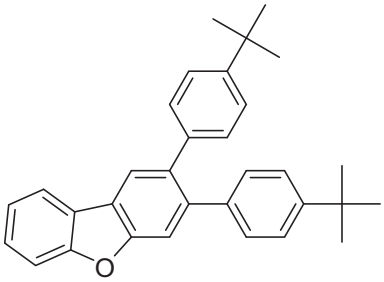


2,3-Diphenyldibenzo[b,d]furan (18g): Starting with **13** (276 mg, 1.0 mmol), following the *general procedures A and B,* **18g** was prepared as a brownish highly viscous oil (147 mg, 46 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17-7.36 (m, 10H, ArH), 7.41- 7.44 (m, 1H, ArH), 7.51-7.54 (m, 4H, ArH), 7.84-7.86 (m, 1H, ArH). ^{13}C NMR (62.9 MHz,$CDCl_3$): δ = 111.1, 113.9 (CH), 116.3 (C), 118.5, 121.0, 123.1, 126.3, 126.9 (CH), 127.3 (C), 128.3, 128.7, 128.8, 130.3, 130.8 (CH), 136.7, 137.7, 152.6, 154.7 (C). IR (KBr): ν = 3079, 3051, 3024, 2924, 2852 (m), 1941, 1888 (w), 1795, 1738, 1660, 1629, 1595, 1577, 1537, 1492, 1475 (m), 1446 (s),



1348, 1316, 1279, 1265, 1248, 1209 (m), 1192 (s), 1155, 1123, 1096, 1072, 1017 (m), 948 (s), 908, 885, 846 (m), 736, 688, 647 (s), 620, 574 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 320 ($[M]^+$, 100), 289 (9). HRMS (EI, 70 eV): calcd for $C_{24}H_{16}O$ $[M]^+$: 320.11957; found: 320.11959.

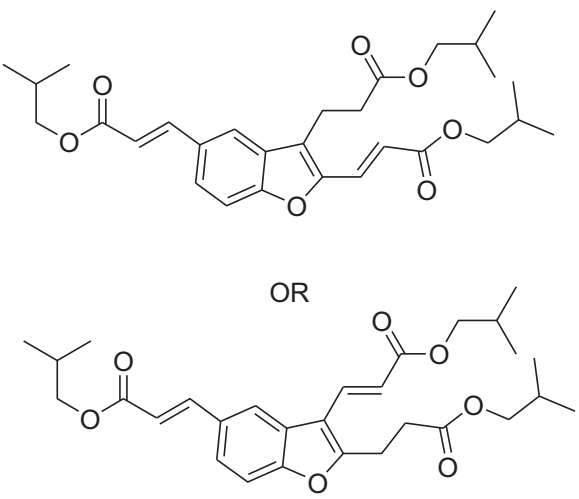
2,3-Bis(4-tert-butylphenyl)dibenzo[b,d]furan (18i): Starting with **13** (276 mg, 1.0 mmol), following the *general procedures A and B,* **18i** was prepared asa brownish highly viscous oil (294 mg, 68 %).



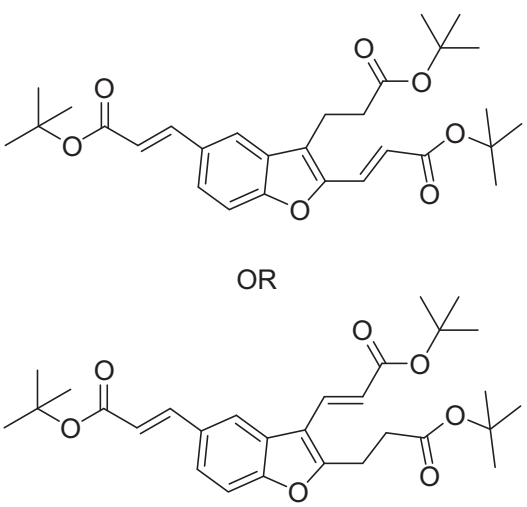
^1H NMR (250 MHz, $CDCl_3$): δ = 1.21 (s, 9H, $3CH_3$), 1.22 (s, 9H, $3CH_3$), 7.03 (d, 4H, *J* = 8.2 Hz, ArH), 7.14 (d, 2H, *J* = 8.4 Hz, ArH), 7.16 (d, 2H, *J* = 8.6 Hz, ArH), 7.22-2.30 (m, 1H, ArH), 7.36 (td, 1H, *J* = 1.5, 8,4 Hz, ArH), 7.47-7.51 (m, 1H, ArH), 7.53 (s, 1H, ArH), 7.7.83-7.86 (m, 1H, ArH), 7.88 (s, 1H, ArH). ^{13}C NMR (75.5 MHz,$CDCl_3$): δ = 31.3, 31.4 ($3CH_3$), 34.4, 34.5 (C), 111.7, 113.1, 120.7, 122.4, 122.8 (CH), 123.2, 124.3 (C), 124.6, 124.7, 127.1, 129.7, 129.9 (CH), 136.1, 138.7, 138.8, 140.4, 149.2, 149.5, 155.7, 156.8 (C). IR (KBr): ν = 3026 (w), 2959, 2902, 2865, 1600, 1512 (m), 1452 (s), 1423, 1391, 1362, 1348, 1267, 1220, 1184, 1166, 1109, 1011 (m), 909 (s), 892, 874 (m), 833, 748, 729 (s), 691, 648, 615, 605, 559 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 432 ($[M]^+$, 100), 418 (18), 417 (54), 201 (13), 173 (10), 57 (15). HRMS (EI, 70 eV): calcd for $C_{32}H_{32}O$ $[M]^+$: 432.24477; found: 432.24480.

7.1.3 Synthesis of reduced products 55a,b

Diisobutyl dibenzo[b,d]furan-2,3-dicarboxylate (**55a**)*:* Starting with **52** (350 mg, 1.0 mmol), following the *general procedures A,* **55a** was prepared as a brownish highly viscous oil (378 mg, 76 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (d, 6H, *J* = 6.7 Hz, $2CH_3$), 0.93 (d, 6H, *J* = 6.7 Hz, $2CH_3$), 0.94 (d, 6H, *J* = 6.7 Hz, $2CH_3$), 1.76- 2.03 (m, 2H, 3CH), 2.75 (t, 2H, *J* = 7.4 Hz, CH_2), 3.20 (t, 2H, *J* = 7.7 Hz, CH_2), 3.81 (d, 2H, *J* = 6.8 Hz, CH_2O), 3.94 (d, 2H, *J* = 6.7 Hz, CH_2O), 3.95 (d, 2H, *J* = 6.7 Hz, CH_2O), 6.42 (d, 1H, *J* = 15.9 Hz, CH), 6.46 (d, 1H, *J* = 16.1 Hz, CH), 7.38-7.52 (m, 3H, ArH), 7.69 (d, 1H, *J* = 16.3 Hz, CH), 7.73 (d, 1H, *J* = 16.3 Hz, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 19.0, 19.1, 19.2 ($2CH_3$), 22.4 (CH_2), 27.7 (CH), 27.9 (2CH), 32.0 (CH_2), 70.7, 70.8, 71.0 (CH_2O), 110.7 (CH), 113.1 (C), 118.2, 118.3, 120.8, 123.8 (CH), 127.9, 131.4 (C), 134.0, 144.3 (CH), 154.7, 161.4 (C), 167.0, 167.2, 171.7 (CO). IR (KBr): ν = 3072, 2959, 2873 (m), 1719 (s), 1636, 1602, 1577 (w), 1454, 1393, 1376, 1350, 1306 (m), 1274, 1239, 1219, 1778, 1111, 1100, 1060 (s), 1011, 983 (m), 945, 900, 848, 881, 767 (w), 746 (m), 722, 694, 602, 564 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 498 ([M]$^{+}$, 100), 426 (16), 425 (63), 422 (10), 396 (19), 368 (11), 367 (15), 365 (11), 350 (35), 340 (11), 339 (11), 323 (14), 322 (24), 294 (12), 267 (12), 221 (17), 57 (80), 41 (38).

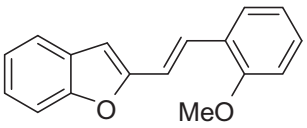


(2E,2'E)-dihexyl 3,3'-(benzofuran-2,3-diyl)diacrylate (55b): Starting with **52** (350 mg, 1.0 mmol), following the *general procedures A,* **55b** was prepared asa brownish highly viscous oil (393 mg, 79 %). ^{1}H NMR (300 MHz, $CDCl_3$):



δ = 1.36 (s, 9H, $3CH_3$), 1.48 (s, 9H, $3CH_3$), 1.49 (s, 9H, $3CH_3$), 2.63 (t, *J* = 7.5 Hz, 2H, CH_2), 3.13 (t, 2H, *J* = 7.9 Hz, CH_2), 6.33 (d, *J* = 15.8 Hz, 1H, CH), 6.37 (d, *J* = 16.5 Hz, 1H, CH), 7.39 (dd, *J* = 1.3, 8.2 Hz, 1H, ArH), 7.49 (d, *J* = 0.9 Hz, 1H, ArH), 7.67-7.70 (m, 3H, ArH/olefinic CH). IR (KBr): ν = 3400, 3061 (w), 2976, 2930, 1801 (m), 1704 (s), 1635, 1476, 1450, 1392 (m), 1367 (s), 1304, 1282 (m), 1255, 1143, 969 (s), 949, 880, 844, 809 (m), 746 (s), 670, 632, 611, 581, 539 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 498 ($[M]^+$, 6), 494 (10), 442 (31), 436 (13), 425 (12), 387 (19), 386 (95), 380 (28), 369 (16), 331 (16), 330 (100), 328 (13), 326 (37), 325 (10), 313 (11), 310 (15), 308 (16), 284 (28), 266 (32), 221 (12), 188 (13), 57 (97), 41 (83).

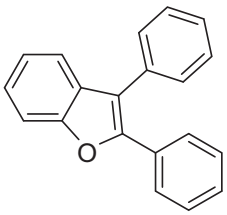
(E)-2-(2-methoxystyryl)benzofuran (54jA): 54jA was isolated as a by-product of **54j** as a brownish highly viscous oil (37 mg, 15 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.96 (s, 3H, OCH_3), 6.69 (s, 1H, ArH), 6.94-7.03 (m, 2H, ArH), 7.12 (d, 1H, *J* = 16.3 Hz, CH), 7.19-7.33 (m, 3H, ArH), 7.49-7.61 (m, 3H, ArH), 7.66 (d, 1H, *J* = 16.4 Hz, CH). ^{13}C NMR (75.5 MHz,$CDCl_3$): δ = 55.5 (OCH_3), 104.7, 110.9, 111.1, 117.1, 120.7, 120.8, 122.8, 124.4, 125.5 (CH), 125.6 (C), 127.1, 129.2 (CH), 129.3, 154.9, 155.8, 157.3 (C). IR (KBr): ν = 3121, 3060 (w), 2999, 2931, 2835 (m), 1932, 1896, 1863, 1810 (w), 1592, 1578, 1551, 1481 (m), 1462, 1449, 1433 (s), 1312, 1291 (m), 1252 , 1237 (s), 1190, 1177, 1160 (m), 1102 (s), 1047 (m), 1027, 962, 942 (s), 932, 909, 885, 860, 845, 832 (m), 796 (s), 781 (m), 748, 740 (s), 652, 613, 598, 572, 535 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 250 ($[M]^+$, 100), 219 (20), 217 (20), 178 (31), 144 (35). HRMS Pos (ESI) calcd for $C_{17}H_{14}O_2$ $[M+H]^+$: 250.0994; found: 250.09884.



7.2 Site-Selective Suzuki Cross-Coupling Reactions of 2,3 dibromobenzofuran

General procedure for the synthesis of **58a-k**, **59a-e** and **61a-e**: The reaction was carried out in a pressure tube. To a dioxane suspension (5 mL) of **1** (276 mg, 1.0 mmol), $Pd(PPh_3)_4$ (58 mg, 5 mol-%, 0.05 mmol) and the arylboronic acid (**9**) (1.0 mmol per coupling) was added an aqueous solution of K_2CO_3 (2 M, 1 mL). The mixture was heated at the indicated temperature (70-80 °C) under an argon atmosphere for the indicated period of time (6-8 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).

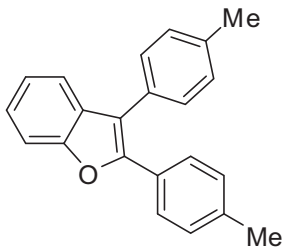
7.2.1 Synthesis of 2,3-diarylbenzofurans 58a-k



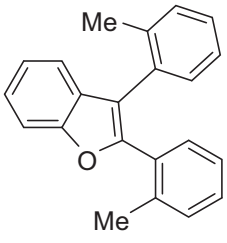
2,3-Diphenylbenzofuran (58a). Compound **58a** was prepared from **13** (276 mg 1.0 mmol), phenylboronic acid (244 mg, 2.0 mmol), according to the *General procedure*, as a white solid (251 mg, 93 %). Reaction temperature: 80 °C. M. p. 84-85 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.13-7.49 (m, 12H, ArH), 7.57-7.60 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 111.1 (CH), 117.5 (C), 120.0, 122.9, 134.7, 127.0, 127.6, 128.3, 128.4, 129.0, 129.8 (CH), 130.2, 130.7, 132.9, 150.5, 154.0 (C). IR (KBr): ν = 3062, 3027, 2921, 2852, 1602, 1568, 1558, 1498, 1487, 1472 (w), 1455, 1441 (m), 1369, 1340, 1315, 1291 (w), 1255, 1203, 1188, 1110, 1079, 1062, 1022, 1008, 960, 917, 891, 836, 828 (m), 764, 746, 700, 692, 676 (s), 621 (m), 608 (s), 582, 561 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) =

270 ([M]$^+$, 100), 269 (19), 255 (10), 241 (21), 239 (22), 134 (9), 120 (9). HRMS (EI, 70 eV): calcd for $C_{20}H_{14}O$ [M]$^+$: 270.10392; found: 270.10393.

2,3-Di-*p*-tolylbenzofuran (58b). Compound **58b** was prepared from **13** (276 mg, 1.0 mmol) and *p*-tolylboronic acid (272 mg, 2.0 mmol), according to the *General procedure*, as a colourless highly viscous oil (274 mg, 92 %). Reaction temperature: 80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 7.05 (dd, 2H, *J* = 0.5, 8.5 Hz, ArH), 7.12-7.26 (m, 4H, ArH), 7.32 (d, 2H, *J* = 8.1 Hz, ArH), 7.40-7.51 (m, 4H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 ($2CH_3$), 111.0 (CH), 116.8 (C), 120.0, 122.8, 124.4, 127.0 (CH), 128.0 (C), 129.1, 129.6, 129.7 (CH), 129.9, 130.5, 137.2, 138.3, 150.7, 153.9 (C). IR (KBr): ν = 3025 (w), 2919, 2853 (m), 2731 (w), 1906, 1770, 1611 (w), 1519, 1500 (m), 1451 (s), 1371, 1289 (m), 1255 (s), 1205, 1178, 1109 (m), 1065 (s), 1019, 986 (m), 964 (s), 898, 838 (m), 816 (s), 785, 760 (m), 743, 719 (s), 649, 636 (m), 600 (s), 566 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 298 ([M]$^+$, 100), 268 (9), 255 (9). HRMS (EI, 70 eV): calcd for $C_{22}H_{18}O$ [M]$^+$: 298.13522; found: 298.13449.

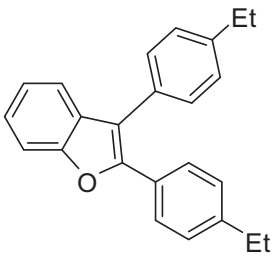


2,3-Di-*o*-tolylbenzofuran (58c). Compound **58c** was prepared from **13** (276 mg, 1.0 mmol) and 2-methylphenylboronic acid (272 mg, 2.0 mmol), according to the *General procedure*, as a colourless highly viscous oil (241 mg, 81 %). Reaction temperature: 80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 7.12-7.20 (m, 1H, ArH), 7.28-7.49 (m, 10H, ArH), 7.64 (brd, 1H, *J* = 8.7 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.1, 20.6 (CH_3), 111.3 (CH), 118.4 (C), 120.5, 122.8, 124.3, 125.6, 126.0, 127.8, 129.0 (CH), 129.7 (C), 130.5, 130.6, 130.8, 131.0 (CH), 131.9, 137.2, 137.5, 152.6, 154.4 (C). IR (KBr): ν = 3058, 3017, 2953, 2923, 2859 (w), 1479 (m), 1450 (s), 1379, 1364,



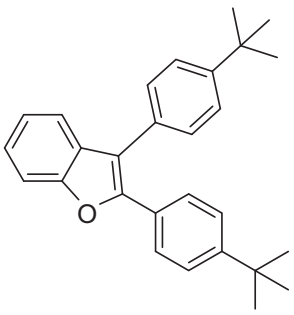
1294, 1280 (m), 1252 (s), 1207, 1196, 1114, 1066, 1055, 1036, 1008 (m), 961 (s), 945, 928, 899, 835 (m), 761, 743, 723 (s), 683, 666 (m), 616 (s), 590, 576, 549 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 298 ($[M]^+$, 100), 268 (9), 255 (9). HRMS (EI, 70 eV): calcd for $C_{22}H_{18}O$ $[M]^+$: 298.13522; found: 298.13449.

2,3-Bis(4-ethylphenyl)benzofuran (58d). Compound **58d** was prepared from **13**



(276 mg, 1.0 mmol) and 4-ethylphenylboronic acid (300 mg, 2.0 mmol), according to the *General procedure*, as a colourless highly viscous oil (280 mg, 86 %). Reaction temperature: 80 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.30 (t, 3H, *J* = 7.4 Hz, CH_3), 1.38 (t, 3H, *J* = 7.4 Hz, CH_3), 2.69 (q, 2H, *J* = 7.8 Hz, CH_2), 2.81 (q, 2H, *J* = 7.8 Hz, CH_2), 7.19-7.40 (m, 6H, ArH), 7.48-7.69 (m, 6H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.3, 15.4 (CH_3), 28.7 ($2CH_2$), 111.0 (CH), 116.9 (C), 120.0 (CH), 120.8 (C), 122.8, 124.4, 127.0, 128.0, 128.3, 129.7 (CH), 130.2, 130.6, 143.5, 144.6, 150.7, 154.0 (C). IR (KBr): ν = 3025 (w), 2962 (m), 2929, 2871, 1909, 1667, 1592 (w), 1519, 1499 (m), 1451 (s), 1413, 1372, 1337, 1289, 1256, 1207, 1177, 1109 (m), 1067 (s), 1048, 1018, 1008 (m), 963 (s), 928, 899 (m), 834 (s), 761 (m), 743(s), 691, 660, 647, 633 (m), 603 (s), 582, 557 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 326 ($[M]^+$, 100), 311 (34), 148 (9). HRMS (EI, 70 eV): calcd for $C_{24}H_{22}O$ $[M]^+$: 326.16652; found: 326.16642.

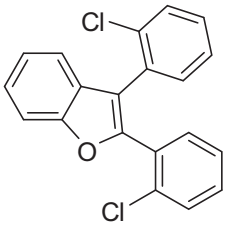
2,3-Bis(4-tert-butylphenyl)benzofuran (58e). Compound **58e** was prepared from **13**



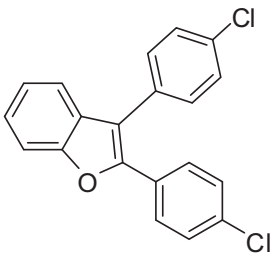
(276 mg, 1.0 mmol) and 4-*tert*-butylphenylboronic acid (356 mg, 2.0 mmol), according to the *General procedure*, as a white crystalline solid (336 mg, 88 %). Reaction temperature: 80 °C. M. p. 121-122 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.37 (s, 9H, $3CH_3$), 1.46 (s, 9H, $3CH_3$), 7.23-7.35(m, 2H, 13rH), 7.39 (d, 2H, *J* = 8.7 Hz, ArH), 7.51-7.60 (m, 6H, ArH), 7.71 (d, 2H, *J* = 8.7 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$):

δ = 31.3, 31.5 ($3CH_3$), 34.7, 34.8 (C), 111.0 (CH), 116.9 (C), 120.1, 122.7, 124.4, 125.4, 125.8, 126.6 (CH), 128.1 (C), 129.4, (CH), 129.9, 130.7, 150.4, 150.5, 151.4, 153.9 (C). IR (KBr): ν = 3035 (w), 2960 (m), 2902, 2866, 1589 (w), 1520, 1497, 1472 (m), 1452 (s), 1408, 1393, 1362, 1267 (m), 1257 (s), 1209 (m), 1106 (s), 1064, 1015 (m), 965 (s), 907, 901 (m), 836 (s), 821 (m), 746, 739 (s), 625, 596, 582 (m), 547 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 382 ($[M]^+$, 100), 368 (26), 367 (89), 176 (14), 148 (23), 57 (12). HRMS (EI, 70 eV): calcd for $C_{28}H_{30}O$ $[M]^+$: 382.22912; found: 382.22904.

2,3-Bis(2-chlorophenyl)benzofuran (58f). Compound **58f** was prepared from **13** (276 mg 1.0 mmol), 2-chlorophenylboronic acid (312 mg, 2.0 mmol), according to the *General procedure*, as a white solid (294 mg, 87 %). Reaction temperature: 80 °C. M. p. 104-105 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.06-7.19 (m, 6H, ArH), 7.23-7.38 (m, 5H, ArH), 7.48 (dt, *J* = 0.7, 8.1 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 111.5 (CH), 118.1 (C), 121.0, 123.0, 124.9, 126.6, 126.9 (CH), 128.7 (C), 129.2 (CH), 129.9 (C), 130.1, 130.3, 130.4 (CH), 131.4 (C), 132.2, 132.3 (CH), 134.1, 134.3, 150.4, 154.5 (C). IR (KBr): ν = 3056, 1631, 1581, 1564, 1537, 1513 (w), 1486, 1448, 1438, 1369, 1295, 1271, 1245, 1204, 1161, 1111, 1088, 1061, 1041, 1030, 1008, 966, 949, 905, 829 (m), 760, 748, 736, 724, 713 (s), 697, 664, 658, 613, 570 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 338 ($[M]^+$, 94), 302 (11), 275 (11), 269 (22), 268 (100), 240 (11), 239 (47), 237 (16), 134 (32), 120 (27), 119 (20). HRMS (EI, 70 eV): calcd for $C_{20}H_{12}Cl_2O$ $[M]^+$: 338.02597; found: 338.02554.

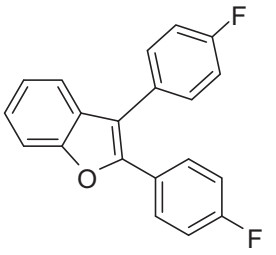


2,3-Bis(4-chlorophenyl)benzofuran (58g). Compound **58g** was prepared from **13**



(276 mg, 1.0 mmol) and 4-chlorophenylboronic acid (312 mg, 2.0 mmol), according to the *General procedure*, as a white crystalline solid (281 mg, 83 %). Reaction temperature: 80 °C. M. p. 102-103 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.15-7.39 (m, 9H, ArH), 7.45-7.51 (m, 3H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 111.3 (CH), 101.8, 116.8 (C), 119.9, 123.3, 125.2, 128.2, 128.5, 129.2 (CH), 129.8, 133.8, 134.5, 149.7, 154.0 (C), 131.0 (CH). IR (KBr): ν = 3078, 3054, 3037, 2923, 2852 (w), 1581 (m), 1558 (w), 1497, 1484 (m), 1449 (s), 1401, 1373, 1289 (w), 1253, 1201, 1174 (m), 1089, 1066, 1011, 963 (s), 945, 930, 919, 899 (m), 832, 821, 811 (s), 760 (m), 749, 742, 720 (s), 682, 646, 631, 624, 616, 582 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 338 ([M]$^+$, 100), 302 (11), 268 (27), 239 (29), 134 (20), 120 (20), 119 (12). HRMS (EI, 70 eV): calcd for $C_{20}H_{12}Cl_2O$ [M]$^+$: 338.02597; found: 338.02559.

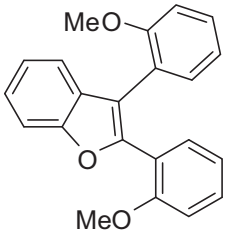
2,3-Bis(4-fluorophenyl)benzofuran (58h). Compound **58h** was prepared from **13**



(276 mg, 1.0 mmol) and 4-fluorophenylboronic acid (280 mg, 2.0 mmol), according to the *General procedure*, as a white crystalline solid (248 mg, 81 %). Reaction temperature: 80 °C. M. p. 80-81 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.88-6.95 (m, 2H, ArH), 7.03-7.27 (m, 4H, ArH), 7.31-7.64 (m, 6H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 111.2 (CH), 115.6 (d, $J_{F,C}$ = 21.2 Hz, CH), 116.2 (d, $J_{F,C}$ = 21.6 Hz, CH), 119.8, 123.1, 124.9 (CH), 127.7 (d, $J_{F,C}$ = 3.3 Hz, C), 128.6 (d, $J_{F,C}$ = 3.5 Hz, C), 128.8 (d, $J_{F,C}$ = 8.2 Hz, CH), 130.1 (C), 131.4 (d, $J_{F,C}$ = 8.0 Hz, CH), 149.8, 153.9 (C), 162.4 (d, $J_{F,C}$ = 247.2 Hz, CF), 162.5 (d, $J_{F,C}$ = 249.5 Hz, CF). IR (KBr): ν = 3067, 3045, 3016, 2925, 2852 (w), 1594, 1582, 1515 (m), 1498, 1450 (s), 1409, 1374, 1338, 1302, 1254 (m), 1223 (s), 1205, 1161, 1155, 1109, 1099, 1088, 1068, 1014, 1009, 965, 934 (m), 836, 821, 814 (s), 802, 794 (m), 749 (s),

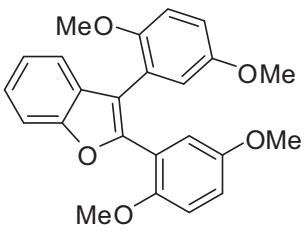
720, 686, 665, 627 (m), 598 (s), 580 (m), 564, 536 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 306 ($[M]^+$, 100), 305 (9), 277 (18), 275 (13). HRMS (EI, 70 eV): calcd for $C_{20}H_{12}F_2O$ $[M]^+$: 306.08507; found: 306.08454.

2,3-Bis(2-methoxyphenyl)benzofuran (58i). Compound **58i** was prepared from **13**



(276 mg 1.0 mmol), 2-methoxyphenylboronic acid (304 mg, 2.0 mmol), according to the *General procedure*, as a white solid (270 mg, 82 %). Reaction temperature: 80 °C. M. p. 78-79 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.48 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 6.90 (d, 1H, *J* = 8.3 Hz, ArH), 6.97-7.06 (m, 3H, ArH), 7.26-7.40 (m, 5H, ArH), 7.56-7.64 (m, 3H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.0, 55.2 (OCH_3), 111.0, 111.1, 111.2 (CH), 115.9 (C), 120.4, 120.5 (CH), 120.9 (C), 121.0, 122.4 (CH), 123.0 (C), 124.0, 128.5 (CH), 129.7 (C), 130.1, 130.7, 130.9 (CH), 149.9, 154.5, 157.0, 157.1 (C). IR (KBr): ν = 3062, 2998, 2934 (w), 2833 (m), 1600, 1586, 1499, 1486 (m), 1459, 1447, 1433 (s), 1368 (w), 1289 (m), 1242 (s), 1203, 1194, 1178, 1161, 1115, 1054, 1041 (m), 1024, 962 (s), 907, 899, 793, 785 (m), 743 (s), 696, 666, 647, 602, 615, 591, 570, 559, 536 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 330 ($[M]^+$, 100), 271 (9), 255 (14), 121 (12). HRMS (EI, 70 eV): calcd for $C_{22}H_{18}O_3$ $[M]^+$: 330.12505; found: 330.12479.

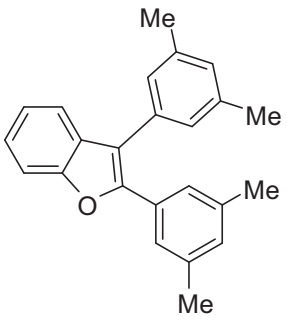
2,3-Bis(2,5-dimethoxyphenyl)benzofuran (58j). Compound **58j** was prepared from **13**



(274 mg 1.0 mmol), 2,5-dimethoxyphenylboronic acid (364 mg, 2.0 mmol), according to the *General procedure*, as a lightly brown solid (331 mg, 85 %). Reaction temperature: 80 °C. M. p. 79-80 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.46 (s, 3H, OCH_3), 3.62 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.82-6.96 (m, 5H, ArH), 7.18-7.38 (m, 3H, ArH), 7.56-7.63 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.7, 55.8, 55.9 (OCH_3), 111.2, 112.3, 112.7, 113.5, 115.6, 115.8 (CH), 115.9 (C), 116.6, 121.0 (CH), 121.3 (C),

122.5 (CH), 123.8 (C), 124.1 (CH), 129.5, 149.8, 151.4, 151.5, 153.4, 153.6, 154.4 (C). IR (KBr): ν = 3057, 2995, 2934, 2903 (w), 2831 (m), 1606, 1581 (w), 1492, 1453 (s), 1421 (m), 1359 (w), 1306, 1293, 1270, 1245 (m), 1216, 1175 (s), 1160 (m), 1042, 1022 (s), 991, 927, 909, 873, 861, 849, 799, 768 (m), 730 (s), 691, 647, 626, 611, 573, 556 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 390 ($[M]^+$, 100), 345 (15), 344 (47), 301 (14), 172 (9). HRMS (EI, 70 eV): calcd for $C_{24}H_{22}O_5$ $[M]^+$: 390.14618; found: 390.14603.

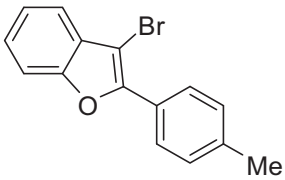
2,3-Bis(3,5-dimethylphenyl)benzofuran (58k). Compound **58k** was prepared from **13**



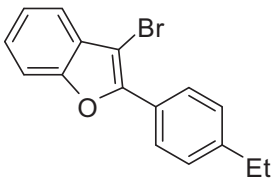
(276 mg 1.0 mmol), 3,5-dimethylphenylboronic acid (300 mg, 2.0 mmol), according to the *General procedure*, as a white solid (258 mg, 79 %). Reaction temperature: 80 °C. M. p. 106-107 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.18 (s, 6H, $2CH_3$), 2,27 (s, 6H, $2CH_3$), 6.85 (s, 1H, ArH), 6.85 (s, 1H, ArH), 6.02 (s, 2H, ArH), 7.11-7.20 (m, 4H, ArH), 7.41-7.47 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3, 21.4 ($2CH_3$), 111.0 (CH), 117.5 (C), 120.1, 120.7, 124.4, 124.7, 127.4, 129.2, 130.0 (CH), 130.4, 130.6, 132.7, 167.8, 168.3, 150.6, 153.9 (C). IR (KBr): ν = 3011, 2913, 2855, 2730, 2142 (w), 1600, 1582 (m), 1566, 1503 (w), 1454, 1377, 1338, 1259, 1234, 1192, 1182, 1169, 1159, 1097, 1054, 1037, 1009 (m), 976, 947 (w), 924, 896 885, 873 (m), 856, 845 (s), 811, 757 (m), 738, 703, 680 (s), 628 (m), 591, 541, 534 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 326 ($[M]^+$, 100), 296 (5), 252 (4). HRMS (EI, 70 eV): calcd for $C_{24}H_{22}O$ $[M]^+$: 326.16652; found: 326.16664.

7.2.2 Synthesis of 2-aryl-3-bromobenzofuran 59a-e

3-Bromo-2-*p*-tolylbenzofuran (59a). Compound **59a** was prepared from **13** (276 mg 1.0 mmol), *p*-tolylboronic acid (136 mg, 1.0 mmol), according to the *General procedure*, as a white solid (265 mg, 93 %). Reaction temperature: 70 °C. M. p. 81-82 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3H, CH_3), 7.03-7.26 (m, 4H, ArH), 7.51-7.60 (m, 2H, ArH), 8.10 (d, 2H, J = 8.3 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.5 (CH_3), 93.1 (C), 111.2, 119.8, 123.4, 125.4, 126.7, 129.3 (CH), 129.4, 139.2, 150.6, 153.1 (C). IR (KBr): ν = 3030, 2967, 2917, 2858 (w), 1502 (m), 1450 (s), 1412, 1342, 1325, 1303, 1271, 1252, 1203, 1189, 1175, 1107 (m), 1073 (s), 1018, 1007 (m), 985 (s), 932, 889, 830 (m), 816 (s), 785 (m), 739 (s), 712, 653, 632, 574, 537 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 288 ([M, ^{81}Br]$^{+}$, 100), 286 ([M, ^{79}Br]$^{+}$, 100), 207 (10), 179 (30), 178 (33), 152 (10), 89 (11), 76 (9), 237 (16), 134 (32), 120 (27), 119 (20). HRMS (EI, 70 eV): calcd for $C_{15}H_{11}$Br O [M, ^{79}Br]$^{+}$: 285.99878; found: 285.99869.

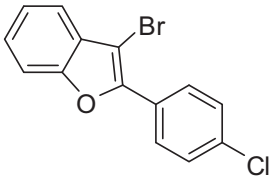


3-Bromo-2-(4-ethylphenyl)benzofuran (59b). Compound **59b** was prepared from **13** (276 mg 1.0 mmol), 4-ethylphenylboronic acid (150 mg, 1.0 mmol), according to the *General procedure*, as a white solid (258 mg, 86 %). Reaction temperature: 70 °C. M. p. 89-90 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (t, 1H, J = 7.6 Hz, CH_3), 2.62 (q, 2H, J = 7.6 Hz, CH_2), 7.18-7.28 (m, 4H, ArH), 7.38-7.48 (m, 2H, ArH), 8.00 (d, 2H, J = 8.4 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.4 (CH_3), 28.8 (CH_2), 93.1 (C), 111.2, 119.7, 123.4, 125.3, 126.8 (CH), 127.0 (C), 128.1 (CH), 129.7, 145.5, 150.6, 153.1 (C). IR (KBr): ν = 3028 (w), 2962, 2927 (m), 2871, 2422, 1907, 1771, 1714, 1666, 1612, 1590 (w), 1502 (m), 1449 (s), 1416, 1345, 1319, 1297, 1272, 1254, 1205, 1185, 1108 (m), 1073 (s), 1049, 1018, 1006 (m), 985 (s), 926,



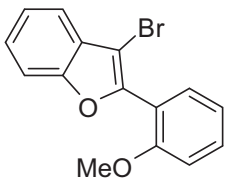
890 (m), 831, 738 (s), 659, 642, 631, 579, 552 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 302 ($[M]^+$, ^{81}Br, 3), 300 ($[M, ^{79}Br]^+$, 2), 298 (100), 255 (11), 178 (9). HRMS (EI, 70 eV): calcd for $C_{16}H_{13}BrO$ [M, $^{79}B]^+$: 300.015065; found: 300.015364.

3-Bromo-2-(4-chlorophenyl)benzofuran (59c). Compound **59c** was prepared from **13**



(138 mg 0.5 mmol), 4-chlorophenylboronic acid (156 mg, 1.0 mmol), according to the *General procedure*, as a white solid (138 mg, 90 %). Reaction temperature: 70 °C. M. p. 114- 115 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.33-7.60 (m, 6H, ArH), 8.14 (d, 2H, *J* = 8.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 94.3 (C), 111.3, 120.0, 123.6, 125.9, 127.9 (CH), 128.0 (C), 128.9 (CH), 134.9, 149.2, 153.1 129.4 (C). IR (KBr): ν = 3066 (w), 1889, 1769, 1714, 1594, 1556 (w), 1485, 1474 (m), 1449 (s), 1416, 1403, 1342, 1320, 1300, 1268, 1249, 1201 (m), 1177, 1111 (w), 1093, 1068 (s), 1011 (m), 986 (s), 928, 903, 889 (m), 822 (s), 814 (m), 737, 721 (s), 758, 648, 625, 600, 573 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 308 ([M, ^{81}Br or $^{37}Cl]^+$, 100), 306 ([M, $^{79}Br]^+$, ^{35}Cl 77), 201 (12), 199 (36), 164 (15), 163 (27), 99 (10), 82 (9). HRMS (EI, 70 eV): calcd for $C_{14}H_8BrClO$ [M, ^{79}Br, $^{35}Cl]^+$: 305.94416; found: 305.94395.

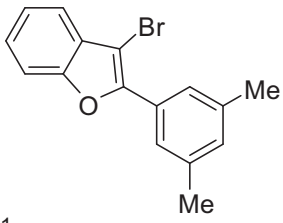
3-Bromo-2-(2-methoxyphenyl)benzofuran (59d). Compound **59d** was prepared from **13**



(138 mg, 0.5 mmol) and 2-methoxyphenylboronic acid (152 mg, 1.0 mmol), according to the *General procedure,* as white solid (181 mg, 87 %). Reaction temperature: 70 °C. M. p. 86-87 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.77 (s, 3H, OCH_3), 6.91-7.00 (m, 2H, ArH), 7.19-7.24 (m, 2H, ArH), 7.24-7.28 (m, 2H, ArH), 7.31-7.33 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.7 (OCH_3), 96.7 (C), 111.5, 111.6 (CH), 118.3 (C), 119.8, 120.5, 123.3, 125.2 (CH), 129.0 (C), 131.4, 131.7 (CH), 150.5, 153.9, 157.7 (C). IR (KBr): ν = 3062, 3037, 3003, 2959, 2934, 2835 (w), 1610, 1586 (m), 1485 (s), 1461 (m), 1446, 1433 (s), 1313, 1296 (m), 1255, 1243 (s), 1200,

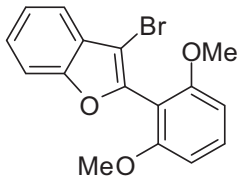
1180, 1162, 1120, 1107, 1073 (m), 1057, 1043, 1023, 984 (s), 932, 891, 827, 781 (m), 739 (s), 667, 636, 588, 554 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 304 ([M, $^{81}Br]^+$, 84), 302 ([M, $^{79}Br]^+$, 86), 223 (22), 209 (28), 208 (100), 167 (12), 165 (24), 152 (30), 151 (17). HRMS (EI, 70 eV): calcd for $C_{15}H_{11}BrO_2$ [M, $^{79}Br]^+$: 301.99369; found: 301.99370.

3-Bromo-2-(3,5-dimethylphenyl)benzofuran (59e). Compound **59e** was prepared from



13 (276 mg, 1.0 mmol), 3,5-dimethylphenylboronic acid (150 mg, 1.0 mmol), according to the *General procedure*, as a white solid (237 mg, 79 %). Reaction temperature: 70 °C. M. p. 95-96 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.45 (s, 6H, $2CH_3$), 7.08 (s, 1H, ArH), 7.31-7.41 (m, 2H, ArH), 7.51-7.60 (m, 2H, ArH), 7.82 (s, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5 ($2CH_3$), 93.6 (C), 111.2, 119.8, 123.4, 124.6, 125.4 (CH), 129.4, 129.7 (C), 130.9 (CH), 138.2, 150.7, 153.1 (C). IR (KBr): ν = 3063, 3037, 2947 (w), 2916 (m), 2855, 2724, 1925, 1888, 1767, 1740 (w), 1602, 1558 (m), 1451 (s), 1419, 1371, 1343, 1319, 1302, 1263, 1229, 1190, 1176, 1148, 1115, 1099 (m), 1019 (s), 1006, 980, 949, 926, 894, 872, 862 (m), 848 (s), 755 (m), 740, 692 (s), 662, 639, 592, 539, 531 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 302 ([M, $^{81}Br]^+$, 99), 300 ([M, $^{79}Br]^+$, 100), 193 (17), 178 (19). HRMS (EI, 70 eV): calcd for $C_{16}H_{13}BrO$ [M, $^{79}Br]^+$: 300.01443; found: 300.01422.

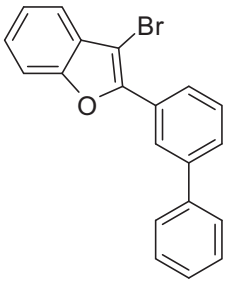
3-Bromo-2-(2,6-dimethoxyphenyl)benzofuran (59f). Compound **59f** was prepared from



13 (276 mg 1.0 mmol), 2,6-dimethoxyphenylboronic acid (182 mg, 1.0 mmol), according to the *General procedure*, as a white solid (295 mg, 89 %). Reaction temperature: 70 °C. M. p. 79- 80 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3H, OCH_3), 6.57 (d, *J* = 8.47, 2H, ArH), 7.11- 7.53 (m, 5H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 56.2 ($2OCH_3$), 98.8 (C), 104.0, 111.6, 119.5 (CH), 120.7 (C), 122.9, 124.7 (CH), 128.7 (C), 132.2 (CH), 154.3, 159.2, 159.7 (C). IR (KBr): ν = 3056, 3003, 2961, 2936, 2837 (w), 1619, 1587 (m), 1473 (s), 1448 (m),

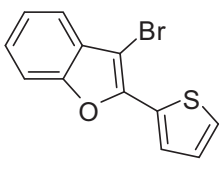
1431 (s), 1297 (m), 1247 (s), 1202, 1134 (m), 1106 (s), 1050, 1031, 1012, 986, 919, 906 890, 820, 781, 748 (m), 728 (s), 693, 637, 591, 556 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 ([M, $^{81}Br]^+$, 100), 332 ([M, $^{79}Br]^+$, 100), 238 (29), 237 (16), 223 (78), 165 (9), 152 (11), 147 (42), 139 (16), 131 (20). HRMS (EI, 70 eV): calcd for $C_{16}H_{13}BrO_3$ [M, $^{79}Br]^+$: 332.00426; found: 332.00332.

2-(Biphenyl-3-yl)-3-bromobenzofuran (59g). Compound **59g** was prepared from **13** (276



mg 1.0 mmol), biphenyl-3-ylboronic acid (198 mg, 1.0 mmol), according to the *General procedure*, as a white solid (233 mg, 67 %). Reaction temperature: 70 °C. M. p. 78-79 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.22-7.62 (m, 11H, ArH), 8.08 (dt, 1H, *J* = 1.5, 7.7 Hz, ArH), 8.33 (t, 1H, *J* = 1.4 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 94.16 (C), 111.3, 120.0, 123.6, 125.5, 125.6, 125.7, 127.3, 127.7, 127.8, 128.9, 129.1 (CH), 129.6, 130.0, 140.7, 141.7, 150.3, 153.2 (C). IR (KBr): ν = 3053, 3031 (m), 2918, 2849, 2790, 2682, 2351, 1953, 1894, 1811, 1705, 1674 (w), 1593, 1573, 1472 (m), 1453 (s), 1401, 1341, 1299, 1265, 1198, 1173, 1113 (m), 1071 (s), 1051, 1024, 1007 (m), 988 (s), 893, 843, 810 (m), 757, 741, 690, 671 (s), 640, 613, 577, 569 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 350 ([M, $^{81}Br]^+$, 99), 348 ([M, $^{79}Br]^+$, 100), 241 (21), 239 (36), 119 (10). HRMS (EI, 70 eV): calcd for $C_{20}H_{13}BrO$ [M, $^{79}Br]^+$: 348.01443; found: 348.01390.

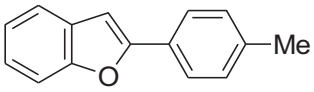
3-Bromo-2-(thiophen-2-yl)benzofuran (59h). Compound **59h** was prepared from **13**



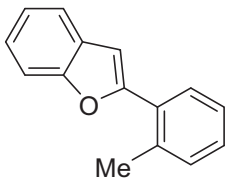
(276 mg 1.0 mmol), thiophen-2-ylboronic acid (128 mg, 1.0 mmol), according to the *General procedure,* as a white solid (154 mg, 10 %). Reaction temperature: 70 °C. M. p. 194-195 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 6.98-7.02 (m, 1H, ArH), 7.08-7.21 (m, 2H, ArH), 7.27-7.37 (m, 3H, ArH), 7.69 (dd, 1H, *J* = 0.8, 3.7 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 93.0 (C), 111.2,

119.6, 123.7, 125.6, 126.6, 127.0, 127.7 (CH), 129.3, 131.3, 147.5, 153.1 (C). IR (KBr): ν = 3097, 3071, 3034, 3016, 1932, 1895, 1779, 1667, 1551 (w), 1586 (m), 1494, 1471 (w), 1448 (s), 1420, 1362, 1341, 1303, 1270, 1254, 1223, 1206, 1194, 1171, 1148, 1082 (m), 1064, 1031 (s), 1004, 970, 887, 877, 848, 824, 791 (m), 741, 694 (s), 657, 634, 574, 547 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 280 ([M, $^{81}Br]^+$, 100), 278 ([M, $^{79}Br]^+$, 98), 171 (59), 139 (9), 127 (14), 85 (18). HRMS (EI, 70 eV): calcd for $C_{12}H_7BrOS$ [M, $^{79}Br]^+$: 277.93955; found: 277.93989.

2-*p*-Tolylbenzofuran (60a). Compound **60a** was obtained as a by-product of **58a** (9.0 mg, 4.1 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 7.11-7.21 (m, 5H, ArH), 7.41-7.50 (m, 2H, ArH), 7.66-7.70 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.8 (CH_3), 100.0, 110.5, 120.1, 122.2, 123.4, 124.3 (CH), 127.2, 128.7 (C), 128.9 (CH), 138.0, 154.2, 155.6 (C). IR (KBr): ν = 3060, 2953, 2928, 2865, 1923, 1847, 1809, 1771, 1667, 1604, 1575 (w), 1488, 1473 (m), 1449 (s), 1379, 1356, 1311, 1285 (w), 1254 (s), 11207, 1170, 1119, 1107 (m), 1054, 1034 (w), 1017 (s), 920, 885, 803 (m), 760, 744, 737, 718 (s), 662, 614, 572, 555, 530 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 208 ($[M]^+$, 100), 207 (74), 189 (16), 179 (18), 178 (27), 165 (12), 115 (10), 89 (14). HRMS (EI, 70 eV): calcd for $C_{15}H_{12}O$ $[M]^+$: 208.08827; found: 208.087597.

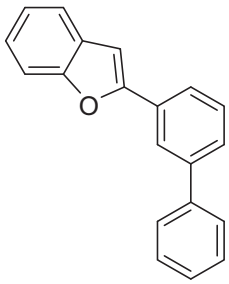


2-*o*-Tolylbenzofuran (60c). Compound **60c** was obtained as a by-product of **58c** (19 mg, 9.1 %). ^1H NMR (250 MHz, $CDCl_3$): δ = 2.61 (s, 3H, CH_3), 6.92 (s, 1H, ArH), 7.23-7.37 (m, 5H, ArH), 7.53-7.65 (m, 2H, ArH), 7.85-7.89 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.9 (CH_3), 105.1, 111.1, 120.9, 122.8, 124.2, 126.1, 128.2, 128.5 (CH), 129.2, 129.9 (C), 131.3 (CH), 135.8, 154.4, 155.7 (C). IR (KBr): ν = 3060, 2953, 2928, 2865, 1923, 1847, 1809, 1771, 1667, 1604,



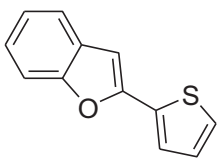
1575 (w), 1488, 1473 (m), 1449 (s), 1379, 1356, 1311, 1285 (w), 1254 (s), 11207, 1170, 1119, 1107 (m), 1054, 1034 (w), 1017 (s), 920, 885, 803 (m), 760, 744, 737, 718 (s), 662, 614, 572, 555, 530 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 208 ($[M]^+$, 100), 207 (74), 189 (16), 179 (18), 178 (27), 165 (12), 115 (10), 89 (14). HRMS (EI, 70 eV): calcd for $C_{15}H_{12}O$ $[M]^+$: 208.08827; found: 208.08759.

2-(Biphenyl-3-yl)benzofuran (60g). Compound **60g** was obtained as a by-product of **58g**



(62 mg, 23 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.01 (s, 1H, ArH), 7.13-7.61 (m, 11H, ArH), 7.77 (dt, *J* = 1.6, 7.5 Hz, 1H, ArH), 8.02 (t, *J* = 1.7 Hz, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 101.6, 111.2, 121.0, 123.0, 123.7, 123.8, 124.4, 127.2, 127.4, 127.6, 128.9 (CH), 129.2 (C), 129.3 (CH) 131.0, 140.9, 141.9, 155.0, 155.9 (C). IR (KBr): ν = 3119, 3053, 3026 (w), 1598, 1556, 1471, 1453, 1421 (m), 1391 (w), 1347, 1305, 1253, 1200, 1167 (m), 1144, 1107, 1095, 1074, 1056 (w), 1036 (m), 1018, 1004, 967 (w), 925, 892, 882, 820, 809 (m), 795, 760, 748, 740, 693, 675 (s), 617, 609, 578, 560, 537 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 270 ($[M]^+$, 100), 241 (9), 239 (14), 135 (10). HRMS (EI, 70 eV): calcd for $C_{20}H_{14}O$ $[M]^+$: 270.10392; found: 270.10402.

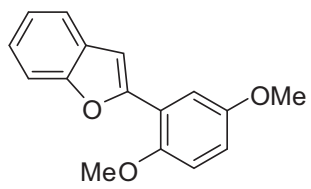
2-(Thiophen-2-yl)benzofuran (60h). Compound **60h** was obtained as a by-product of **58h**



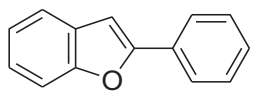
(30 mg, 15 %). ^1H NMR (250 MHz, $CDCl_3$): δ = 6.88 (d,*J* = 0.8 Hz, 1H, ArH), 7.12 (dd, *J* = 3.7, 5.1 Hz, 1H, ArH), 7.20-7.36 (m, 3H, ArH), 7.49-7.58 (m, 3H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 101.1, 111.1, 120.8, 123.1, 124.3, 124.6, 125.8, 127.9 (CH), 129.1, 133.3, 151.3, 154.6 (C). IR (KBr): ν = 3097, 3071, 3034, 3016, 1932, 1895, 1779, 1667, 1551 (w), 1586 (m), 1494, 1471 (w), 1448 (s), 1420, 1362, 1341, 1303, 1270, 1254, 1223, 1206, 1194, 1171, 1148, 1082 (m), 1064, 1031 (s), 1004, 970, 887, 877, 848, 824, 791 (m), 741, 694 (s), 657, 634, 574, 547 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 280 ([M, $^{81}Br]^+$, 100), 278 ([M, $^{79}Br]^+$, 100),

171 (59), 139 (9), 127 (14), 85 (18). HRMS (EI, 70 eV): calcd for $C_{12}H_7OBrS$ [M, $^{79}Br]^+$: 277.93955; found: 277.939899.

2-(2,5-Dimethoxyphenyl)benzofuran (60j). Compound **60j** was obtained as a by-product of **58j** (20 mg, 8.1 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.80 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.77-6.88 (m, 2H, ArH), 7.10-7.25 (m, 2H, ArH), 7.30 (d, J = 0.8 Hz, 1H, ArH), 7.42-7.56 (m, 3H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 54.9 (OCH_3), 55.0 (OCH_3), 105.6, 109.8, 110.9, 111.4, 113.8 (CH), 118.9 (C), 120.1, 121.7, 123.2 (CH), 127.5, 150.0, 150.1 152.7, 152.8 (C). IR (KBr): ν = 3060, 2996, 2946, 2931, 2904, 2831, 2495, 2349, 2068, 1613, 1584 (w), 1567 (m), 1500, 1453 (s), 1438 (m), 1347, 1322 (w), 1301 (m), 1273, 1259, 1242 (m), 1219, 1197 (s), 1180, 1160, 1132, 1122, 1108 (m), 1045, 1024 (s), 940, 868 (m), 809, 733 (s), 695, 666, 614, 540 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 254 ($[M]^+$, 100), 240 (16), 239 (96), 211 (16), 196 (13), 168 (18), 142 (14), 127 (9).

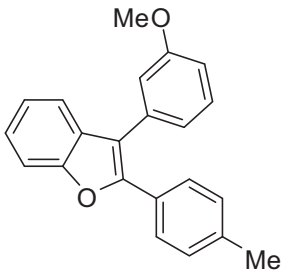


2-Phenylbenzofuran (60l). Compound **60l** was obtained as a by-product of **58l** (08 mg, 04 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.95 (d, J = 0.8 Hz, 1H, ArH), 7.12-7.31 (m, 3H, ArH), 7.35-7.53 (m, 4H, ArH), 7.78-7.81 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 101.3, 111.2, 120.9, 122.9, 124.3, 125.0 (CH), 127.5 (C), 128.6, 128.8 (CH), 130.5, 154.9, 154.9 (C).



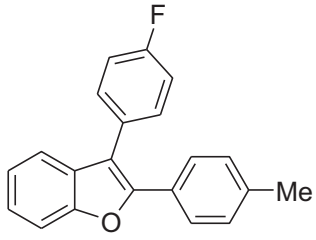
7.2.3 Synthesis of unsymmetrical 2,3-diarylbenzofurans 61a-e

3-(3-Methoxyphenyl)-2-*p*-tolylbenzofuran (61a). Compound **61a** was prepared from **13**



(276 mg, 1.0 mmol), *p*-tolylboronic acid (136 mg, 1.0 mmol), 3-methoxyphenylboronic acid (152 mg, 1.0 mmol), according to the *General procedure (with one-pot stratergy and p-tolylboronic acid was added first; the yield was calculated over 2 steps)*, as a white solid (238 mg, 76 %). Reaction temperature: 70-80 °C. M. p. 73-74 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 6.82-6.86 (m, 1H, ArH), 6.95-7.12 (m, 4H), ArH), 7.14-7.25 (m, 3H, ArH), 7.39-7.50 (m, 4H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (CH_3), 55.3 (OCH_3), 111.1, 113.4, 115.1 (CH), 116.7 (C), 120.0, 122.3, 122.9, 124.5, 127.0 (CH), 127.8 (C), 129.2, 130.0 (CH), 130.3, 134.4, 138.5, 150.9, 153.9, 160.1 (C). IR (KBr): ν = 3031, 2997, 2917, 2832 (w), 1607, 1592, 1574, 1512, 1484 (m), 1451 (s), 1427, 1369, 1314, 1282 (m), 1246, 1234 (s), 1205, 1184, 1156, 1064 (m), 1042 (s), 1019, 1009, 987, 876, 838 (m), 819 (s), 779 (m), 742, 701 (s), 618, 610, 587, 563, 537 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 314 ([M]$^+$, 100), 271 (9), 255 (14), 121 (12). HRMS (EI, 70 eV): calcd for $C_{22}H_{14}O_2$ [M]$^+$: 314.1307; found: 314.12999.

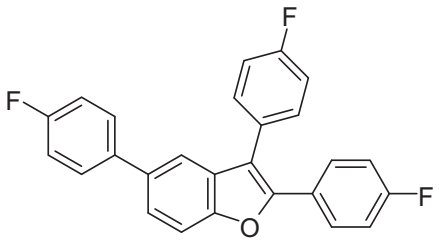
3-(4-Fluorophenyl)-2-*p*-tolylbenzofuran (61b*)*: Compound **61b** was prepared from **13**



(276 mg 1.0 mmol), *p*-tolylboronic acid (136 mg, 1.0 mmol), 4-fluorophenylboronic acid (154 mg, 1.1 mmol), according to the *General procedure (with one-pot stratergy and p-tolylboronic acid was added first; the yield was calculated over 2 steps)*, as a white crystalline solid (244 mg, 79 %). Reaction temperature: 70 °C. M. p. 103-104 °C.

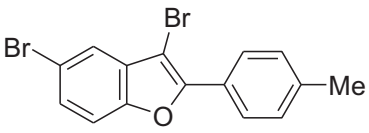
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 7.17- 7.31 (m, 5H, ArH), 7.35-7.40 (m, 1H, ArH), 7.50-7.54 (m, 3H, ArH), 7.57-7.61 (m, 3H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -114.35. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.4 (CH_3), 111.1 (CH), 115.8 (C), 116.1 (d, $J_{F,C}$ = 21.0 Hz), 119.6, 123.0, 124.6, 127.0 (CH), 127.7, 128.9 (d, $J_{F,C}$ = 3.3 Hz) (C), 129.2 (CH), 130.2 (C), 131.4 (d, $J_{F,C}$ = 8.1 Hz) (CH), 136.6, 151.1, 153.9, 162.3 (d, $J_{F,C}$ = 246.7 Hz) (C). IR (KBr): ν = 3066, 3036, 2918, 2853, 2790, 1613, 1601, 1557 (w), 1515, 1495 (m), 1452 (s), 1432, 1371, 1337, 1292 (3), 1254, 1230, 1216, 1205, 1196, 1182, 1156, 1091, 1066 (s), 1037, 1020, 1008, 964, 930, 897 (m), 842, 817, 811, 744 (s), 718, 716, 663, 598, 564 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 302 ([M]$^+$, 100), 286 (10), 259 (9), 257 (10). HRMS (EI, 70 eV): calcd for $C_{21}H_{15}FO$ [M]$^+$: 302.11014; found: 302.11031.

2,3,5-Tris(4-fluorophenyl)benzofuran (**62**). Compound **62** was prepared from **13** (174 mg, 0.6 mmol) and 4-fluorophenylboronic acid (280 mg, 2.0 mmol), according to the *General procedure*, as a colourless highly viscous oil (162 mg, 81 %). Reaction temperature: 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.42-6.67 (m, 6H, ArH), 6.86-7.06 (m, 9H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -116.8, -114.3, -112.3. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 111.2 (CH), 115.6 (d, $J_{F,C}$ = 21.2 Hz, CH), 116.2 (d, $J_{F,C}$ = 21.6 Hz, CH), 119.8, 123.1, 124.9 (CH), 127.7 (d, $J_{F,C}$ = 3.3 Hz, C), 128.6 (d, $J_{F,C}$ = 3.5 Hz, C), 128.8 (d, $J_{F,C}$ = 8.2 Hz, CH), 130.1 (C), 131.4 (d, $J_{F,C}$ = 8.0 Hz, CH), 149.8, 153.9 (C), 1162.3 (d, $J_{F,C}$ = 247.0 Hz, CF), 1162.4 (d, $J_{F,C}$ = 247.2 Hz, CF), 1162.5 (d, $J_{F,C}$ = 249.5 Hz, CF). IR (KBr): ν = 3067, 3045, 3016, 2925, 2852 (w), 1594, 1582, 1515 (m), 1498, 1450 (s), 1409, 1374, 1338, 1302, 1254 (m),



1223 (s), 1205, 1161, 1155, 1589, 1099, 1088, 1068, 1014, 1009, 965, 934 (m), 836, 821, 814 (s), 802, 794 (m), 749 (s), 720, 686, 665, 627 (m), 598 (s), 580 (m), 564, 536 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 400 ($[M]^+$, 100), 371 (7), 275 (8). HRMS (EI, 70 eV): calcd for $C_{26}H_{15}F_3O$ $[M]^+$: 400.10695; found: 400.10681.

3,5-Dibromo-2-p-tolylbenzofuran (63). Compound **63** was prepared from **13** (138 mg, 0.5 mmol), *p*-tolylboronic acid (68 mg, 0.5 mmol), according to the *General procedure,* as a white solid (143 mg, 79 %).



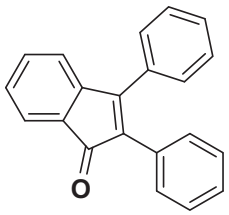
Reaction temperature: 70 °C. M. p. 114-115 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.43 (s, 3H, CH_3), 7.16-7.37 (m, 4H, ArH), 7.58-7.70 (m, 1H, ArH), 7.91-7.98 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5 (CH_3), 92.0 (C), 112.7 (CH), 116.3 (C) 122.5 (CH), 123.8, 126.2 (C), 126.8, 128.2, 129.4 (CH), 131.6, 139.7, 151.8 (C). IR (KBr): ν = 3086, 3027, 2917, 2853, 2723, 1907, 1855, 1714, 1608, 1575 (w), 1500, 1461 (m), 1450, 1435 (s), 1409, 1390, 1325, 1298, 1257, 1203, 1191, 1186, 1133, 1112 (m), 1071 (s), 1050, 1017 (m), 986 (s), 902 (m), 858 (s), 833 (m), 813, 794 (s), 735, 710, 683 (m), 655 (s), 640, 593, 580, 551, 532 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 368 ([M, ^{81}Br, ^{81}Br $]^+$, 49), 366 ([M, ^{81}Br, $^{79}Br]^+$, 100), 364 ([M, ^{79}Br, $^{79}Br]^+$, 52), 259 (13), 257 (14), 177 (10), 176 (12). HRMS (EI, 70 eV): calcd for $C_{15}H_{10}OBr$ [M, ^{79}Br, $^{79}Br]^+$: 363.90929; found: 363.90898.

7.3 One-Pot Synthesis of 2,3-Diarylindenones by Site-Selective Suzuki-Miyaura Reactions of 1,2-Dibromoindenone

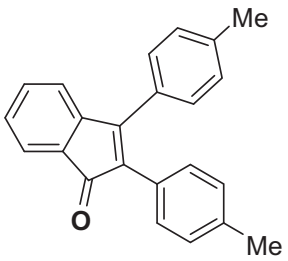
General procedure A: In a pressure tube to a suspension of 2,3-dibromoindenone **23** (144 mg, 0.5 mmol), tetrakis (triphenylphosphine) palladium (0) (2.5-3.0 mol-% per cross-coupling) and boronic acid (0.5 to 0.55 mmol per cross-coupling) in dioxane (5 mL) was added a 2M solution of K_2CO_3 (1 mL). The mixture was heated at indicated temperature (40-70 °C) under Ar for indicated duration of time (4-6 h). The reaction was diluted with water and extracted with DCM (25ml x 3). The combined organics were dried (Na_2SO_4) and concentrated and the resulting residue was subjected to flash silica chromatography (EtOAc/*n*-heptane).

7.3.1 Synthesis of 2,3-diarylindenones 64a-g

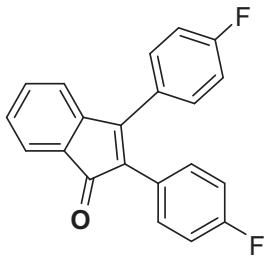
2,3-Diphenyl-1*H*-inden-1-one (64a). Compound **64a** was prepared from **23** (144 mg, 0.5 mmol) and phenylboronic acid (135 mg, 1.1 mmol), according to the *General procedure A*, as a yellow crystalline solid (137 mg, 97 %). Reaction temperature: 70 °C. M. p. 154-155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04-7.07 (m, 1H, ArH), 7.16-7.22 (m, 6H, ArH), 7.30-7.34 (m, 6H, ArH), 7.45--7.51 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 121.3, 123.0, 127.7, 128.1, 128.5, 128.8, 129.0, 129.3, 130.0 (CH), 130.8, 132.4, 132.7 (C), 133.4 (CH), 145.2, 155.3 (C), 196.0 (CO). IR (KBr): ν = 3381, 3070 (w), 1700, 1604, 1455, 1444, 1348, 1178, 1157, 1149, 1081, 1065 (m), 1027, 1010, 999, 929, 918, 858, 840, 807 (w), 780, 760, 751, 723, 699, 675 (s), 637, 612, 587, 549 (s), 1205, 1183, 1156, 1065, 1042 (m), 818, 742, 701 (s), 617, 610, 587, 562, 537 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 282 ([M]$^+$, 100), 281 (82), 265 (16), 253 (39), 252 (47), 250 (18), 126 (12). HRMS (EI, 70 eV): calcd for $C_{21}H_{14}O$ [M]$^+$: 282.10392; found: 282.10341.



2,3-Di-*p*-tolyl-1*H*-inden-1-one (64b). Compound **64b** was prepared from **23** (144 mg 0.5 mmol), *p*-tolylboronic acid (150 mg, 1.1 mmol), according to the *General procedure A*, as a yellow solid (154 mg, 99 %). Reaction temperature: 70 °C. M. p. 147-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 6.98-7.29 (m, 11H, ArH), 7.46-7.49 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.3, 21.5 (CH_3), 121.1, 122.8 (CH), 128.0 (C), 128.5, 128.7, 128.9, 129.5, 129.9 (CH), 130.0, 131.0, 132.1 (C), 133.3 (CH), 137.5, 139.4, 145.5, 154.8 (C), 196.8 (CO). IR (KBr): ν = 3392, 3032, 2956, 2921, 2865, 2770, 2734, 2677, 2143, 1915 (w), 1706, 1699 (s), 1605, 1595, 1583, 1502, 1454, 1386, 1362, 1342, 1313, 1283, 1175, 1150, 1066, 1038, 1020, 1009, 973, 963, 949, 922, 851, 824 (m), 806, 794 (s), 783 (m), 763, 727, 708 (s), 689, 644, 638, 623, 573, 540 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 310 ([M]$^+$, 100), 309 (21), 296 (15), 295 (62), 293 (10), 266 (11), 265 (20), 263 (10), 252 (18). HRMS (EI, 70 eV): calcd for $C_{23}H_{18}O$ [M]$^+$: 310.13522; found: 310.13515.

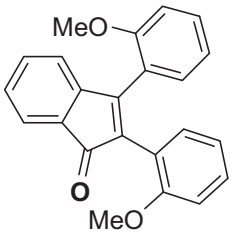


2,3-Bis(4-fluorophenyl)-1*H*-inden-1-one (**64c**). Starting with **23** (144 mg, 0.50 mmol), $Pd(PPh_3)_4$ (29 mg, 5 mol-%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 4-fluorophenylboronic acid (154 mg, 1.10 mmol), according to the *General procedure A*, **64c** was isolated as a brownish yellow solid (151 mg, 95 %). Reaction temperature: 70 °C for 6h. M. p. 134- 135 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.85-6.94 (m, 2H, ArH), 7.01-7.08 (m, 3H, ArH), 7.13-7.34 (m, 6H, ArH), 7.49-7.52 (m, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -113.0, -110.4 (ArF). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 115.3 (d, $J_{C,F}$ = 21.5 Hz, CH), 116.2 (d, $J_{C,F}$ = 21.5 Hz, CH), 121.1, 123.2 (CH), 126.6 (d, $J_{C,F}$ = 3.4 Hz, C), 128.5 (d, $J_{C,F}$ = 3.6 Hz, C), 129.2 (CH), 130.5 (d, $J_{C,F}$ = 8.3 Hz, CH), 131.5 (C), 131.8 (d, $J_{C,F}$ = 8.3 Hz, CH), 133.6 (CH), 144.9, 154.1 (C), 162.4 (d, $J_{C,F}$ = 248.4 Hz, CF),



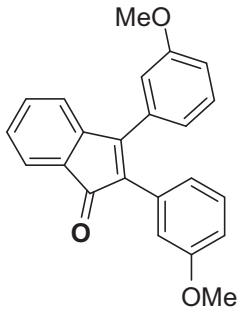
163.2 (d, $J_{C,F}$ = 250.3 Hz, CF), 196.2 (CO). IR (KBr): ν = 3070(w), 1705, 1592, 1575, 1512 (m), 1498 (s), 1464, 1455, 1410, 1358, 1344, 1303 (m), 1221 (s), 1184 (s), 1159, 1149, 1098, 1082, 1071, 1011, 924 (m), 861 (s), 838 (m), 824, 816, 794, 768, 733, 708 (s), 680, 658, 641, 630, 572 (m), 541 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 318 ($[M]^+$, 100), 317 (53), 301 (14), 289 (19), 288 (36), 270 (11), 268 (12). HRMS (EI, 70 eV): calcd for $C_{21}H_{12}F_2O$ $[M]^+$: 318.08507; found: 318.08533.

2,3-Bis(2-methoxyphenyl)-1*H*-inden-1-one (**64d**). Starting with **23** (144 mg, 0.50 mmol),



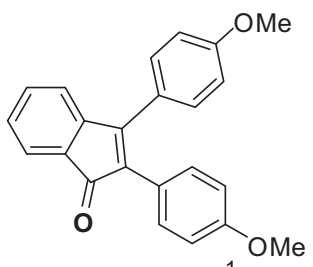
$Pd(PPh_3)_4$ (5 mol-%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 2-methoxyphenylboronic acid (167 mg, 1.10 mmol), according to the *General procedure A*, **64d** was isolated as a brownish yellow solid (147 mg, 86 %). Reaction temperature: 70 °C for 6h. M. p. 121-122 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.42 (s, 3H, OCH_3), 3.54 (s, 3H, OCH_3), 6.72-6.91 (m, 5H, ArH), 7.01-7.28 (m, 6H, ArH), 7.44-7.48 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.1, 55.2 (OCH_3), 111.0, 111.1, 120.3, 120.5 (CH), 120.2 (C), 121.5, 122.5 (CH), 123.0 (C), 128.3, 129.1, 129.2, 130.3 (CH), 131.0 (C), 131.1 (CH), 132.5 (C), 133.1 (CH), 145.6, 154.8, 156.8, 157.4 (C), 196.2 (CO). IR (KBr): ν = 3391, 3064, 2999, 2930, 2833 (w), 1699, 1600, 1594, 1579, 1494, 1484, 1456, 1433, 1341, 1293, 1277 (m), 1243 (s), 1177, 1161, 1126, 1109, 1072, 1045 (m), 1022 (s), 937, 924, 908, 855, 846, 769 (m), 745, 733, 717 (s), 686, 671, 647, 633, 598, 566, 543, 535 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 342 ($[M]^+$, 100), 312 (18), 311 (12), 281 (9), 255 (16), 252 (9), 239 (15), 234 (16), 226 (10), 207 (10). HRMS (EI, 70 eV): calcd for $C_{23}H_{18}O_3$ $[M]^+$: 342.12559; found: 342.12558.

2,3-Bis(3-methoxyphenyl)-1*H*-inden-1-one (**64e**). Starting with **23** (144 mg, 0.50 mmol),



$Pd(PPh_3)_4$ (5 mol-%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 3-methoxyphenylboronic acid (167 mg, 1.10 mmol), according to the *General procedure A*, **64e** was isolated as a brownish yellow solid (168 mg, 98 %). Reaction temperature: 70 °C for 6h. M. p. 83-84 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.57 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 6.69-6.90 (m, 7H, ArH), 7.05-7.30 (m, 4H, ArH), 7.46- 7.50 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.1, 55.3 (OCH_3), 113.7, 114.1, 115.0, 115.1, 120.8, 121.4, 122.5, 123.0, 129.0, 1291, 130.0 (CH), 130.7, 132.0, 132.3 (C), 133.5 (CH), 134.0, 145.2, 155.4, 159.2, 159.8 (C), 196.3 (CO). IR (KBr): ν = 3403, 3079, 3012, 2960, 2939, 2916, 2843, 2831 (w), 1708 (s), 1606, 1595 (m), 1572 (s), 1476, 1454, 1446 (m), 1429 (s), 1333, 1290 (m), 1280, 1231 (s), 1194, 1178, 1162 (m), 1128 (s), 1100, 1092, 1074 (m), 1045 (s), 995, 969, 954, 903, 887, 878, 872, 846, 791 (m), 769 (s), 726, 708, 695, 683, 675 (s), 626, 639, 599, 560, 542 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 342 ([M]$^+$, 100), 327 (11), 311 (21), 284 (10), 268 (12), 239 (17). HRMS (EI, 70 eV): calcd for $C_{23}H_{18}O_3$ [M]$^+$: 342.12505; found: 342.12429.

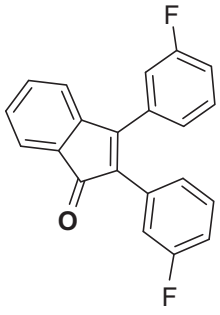
2,3-Bis(4-methoxyphenyl)-1*H*-inden-1-one (**64f**). Starting with **23** (144 mg, 0.50 mmol),



$Pd(PPh_3)_4$ (5 mol-%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 4-methoxyphenylboronic acid (167 mg, 1.10 mmol), according to the *General procedure A*, **64f** was isolated as a brownish yellow solid (166 mg, 97 %). Reaction temperature: 70 °C for 6h. M. p. 94-95 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 6.72 (d, 2H, *J* = 8.9 Hz, ArH), 6.84 (d, 2H, *J* = 8.9 Hz, ArH), 7.06 (d, 1H, *J* = 7.2 Hz, ArH), 7.12-7.18 (m, 3H, ArH), 7.22-7.28 (m, 3H, ArH), 7.42- 7.46 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.2, 55.3 (OCH_3), 113.7, 114.2, 121.0, 122.7 (CH), 123.4, 125.1 (C), 128.6, 130.2 (CH), 131.0, 131.2 (C), 131.3, 133.3 (CH), 145.5, 153.8,

159.1, 160.3 (C), 196.9 (CO). IR (KBr): ν = 3390, 3040, 3001, 2955, 2932, 2905, 2835, 2542, 2251, 2023, 1892 (w), 1698, 1603 (s), 1514 (m), 1500 (s), 1454, 1441, 1343, 1291 (m), 1244, 1173 (s), 1111, 1072 (m), 1026 (s), 922, 908, 855, 833, 819, 798, 785, 766 (m), 733, 713 (s), 682, 656, 647, 631, 582, 560, 532 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 342 ($[M]^+$, 100), 327 (15), 226 (11). HRMS (EI, 70 eV): calcd for $C_{23}H_{18}O_3$ $[M]^+$: 342.12505; found: 342.12509.

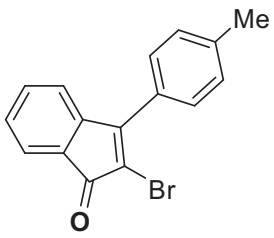
2,3-Bis(3-fluorophenyl)-1*H*-inden-1-one (**64g**). Starting with **23** (144 mg, 0.50 mmol),



$Pd(PPh_3)_4$ (5 mol-%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 4-fluorophenylboronic acid (154 mg, 1.10 mmol), according to the *General procedure A*, **64g** was isolated as a brownish yellow solid (152 mg, 96 %). Reaction temperature: 70 °C for 6h. M. p. 124-125 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.83-7.08 (m, 7H, ArH), 7.10-7.36 (m, 4H, ArH), 7.49-7.52 (m, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -112.8, -111.3. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 114.1 (d, $J_{C,F}$ = 21.3 Hz, CH), 114.4 (d, $J_{C,F}$ = 22.3 Hz, CH), 115.5 (d, $J_{C,F}$ = 21.1 Hz, CH), 115.8 (d, $J_{C,F}$ = 22.2 Hz, CH), 120.4, 122.4 (CH), 123.2 (d, $J_{C,F}$ = 3.3 Hz, CH), 124.7 (d, $J_{C,F}$ = 3.0 Hz, CH), 128.5 (CH), 129.3 (C), 128.7 (d, $J_{C,F}$ = 8.4 Hz, CH), 130.6 (d, $J_{C,F}$ = 2.2 Hz, C), 129.8 (d, $J_{C,F}$ = 8.4 Hz, CH), 131.4 (d, $J_{C,F}$ = 8.3 Hz, C), 132.8 (CH), 133.4 (d, $J_{C,F}$ = 8.0 Hz, C), 143.5 (C), 153.6 (d, $J_{C,F}$ = 1.9 Hz, C), 161.6 (d, $J_{C,F}$ = 245.2 Hz, C-F), 161.9 (d, $J_{C,F}$ = 247.5 Hz, C-F), 194.5 (CO). IR (KBr): ν = 3391, 3065, 2961, 2921, 2852 (w), 1702, 1610, 1598, 1580, 1475, 1455, 1437, 1339, 1266, 1243, 1220, 1184, 1170, 1157, 1125, 1080, 1059, 973, 930, 890, 859, 797 (m), 776, 763, 725, 706, 690 (s), 682, 670, 639, 596, 583, 559 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 318 ($[M]^+$, 100), 317 (49), 301 (14), 289 (30), 288 (36), 270 (11), 268 (12). HRMS (EI, 70 eV): calcd for $C_{21}H_{12}F_2O$ $[M]^+$: 318.08507; found: 318.08557.

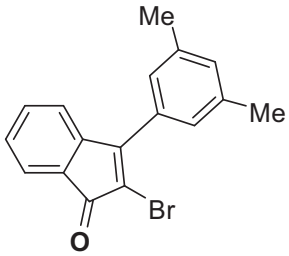
7.3.2 Synthesis of 3-aryl-2-bromoinden-1-ones 65a-g

2-Bromo-3-*p*-tolyl-1*H*-inden-1-one (65a). Compound **65a** was prepared from **23**



(144 mg, 0.5 mmol), $(PPh_3)_4Pd$ (0) (18 mg, 3 mol-%) and *p*-tolylboronic acid (68 mg, 0.5 mmol), according to the *General procedure A*, as a yellow solid (147 mg, 98 %). Reaction temperature: 45 °C. M. p. 100-101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3H, CH_3), 7.08 (dt, 1H, *J* = 7.2, 1.0 Hz, ArH), 7.18 (td, 1H, *J* = 7.9, 1.1 Hz, ArH), 7.24-7.29 (m, 3H, ArH), 7.45-7.51 (m, 3H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.6 (CH_3), 117.4 (C), 121.3, 123.6 (CH), 128.2 (C), 128.3, 128.9, 129.5 (CH), 130.1 (C), 133.7 (CH), 140.8, 144.6, 157.0 (C) 189.9 (CO). IR (KBr): ν = 3414, 3049, 3022, 2919, 2856, 2141, 1911, 1748 (w), 1712 (s), 1607, 1599, 1569, 1557, 1504, 1451, 1362, 1285, 1182, 1160, 1099, 1080, 1020, 1013, 918, 833, 826, 800, 776 (m), 755 (s), 719 (m), 702 (s), 669, 629, 622, 596 cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 300 ([M, ^{81}Br]$^+$, 98), 298 ([M, ^{79}Br]$^+$, 100), 219 (37), 191 (21), 190 (18), 189 (50), 176 (13), 165 (9), 110 (9). HRMS (EI, 70 eV): calcd for $C_{16}H_{11}BrO$ [M, ^{79}Br]$^+$: 297.99878; found: 297.99832.

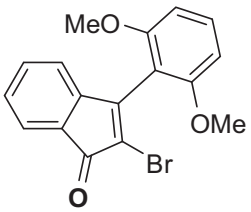
2-Bromo-3-(3,5-dimethylphenyl)-1*H*-inden-1-one (65b). Compound **65b** was prepared



from **23** (144 mg, 0.5 mmol), $(PPh_3)_4Pd$ (0) (18 mg, 3 mol-%) and 3,5-dimethylphenylboronic acid (75 mg, 0.5 mmol), according to the *General procedure A*, as a yellow solid (138 mg, 88 %). Reaction temperature: 45 °C. M. p. 136-137 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 6H, $2CH_3$), 7.03-7.29 (m, 6H, ArH), 7.43-7.46 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (CH_3), 117.6 (C), 121.4, 123.5, 125.8, 128.9 (CH), 130.0, 131.0 (C), 132.1, 133.7 (CH), 138.4, 144.7, 157.3 (C) 190.0 (CO). IR (KBr): ν = 3412, 3072, 3009, 2959, 2913, 2856, 2731, 2677 (w), 1713 (s), 1600, 1553, 1455,

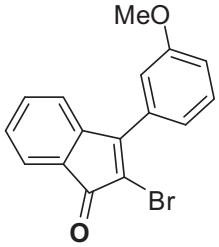
1374, 1361, 1309, 1285, 1227, 1185, 1104, 1080, 1015, 995, 959, 949, 905, 890, 859, 844, 819, 801, 785 (m), 757 (s), 731 (m), 705, 668 (s), 640, 621, 547 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 314 ([M, $^{81}Br]^+$, 99), 312 ([M, $^{79}Br]^+$, 100), 233 (37), 205 (10), 203 (14), 202 (19), 190 (15), 189 (43), 109 (10). HRMS (EI, 70 eV): calcd for $C_{17}H_{13}BrO$ [M, $^{79}Br]^+$: 312.01443; found: 312.01477.

2-Bromo-3-(2,6-dimethoxyphenyl)-1*H*-inden-1-one (65c). Compound **65c** was prepared



from **23** (144 mg, 0.5 mmol), $(PPh_3)_4Pd$ (0) (18 mg, 3 mol-%) and 2,6-dimethoxyphenylboronic acid (91 mg, 0.5 mmol), according to the *General procedure A*, as a yellow crystalline solid (143 mg, 83 %). Reaction temperature: 40 °C. M. p. 189-190 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 3.71 (s, 6H, $2OCH_3$), 6.58-6.68 (m, 3H, ArH), 7.05-7.18 (m, 2H, ArH), 7.22-7.34 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 54.8 ($2OCH_3$), 103.0 (CH), 107.8 (C), 120.1 (CH), 120.6 (C), 121.8, 127.1 (CH), 128.3 (C), 129.8, 132.7 (CH), 144.3, 153.3, 156.7 (C), 189.1 (CO). IR (KBr): ν = 3009, 2965, 2934, 2836 (w), 1729, 1594, 1583, 1470, 1457, 1441, 1423 (s), 1358, 1300 (w), 1290 (m), 1249 (s), 1189, 1169, 1151 (w), 1101, 1078, 1028 (s), 952, 942, 918, 903, 873, 845 (w), 817, 800, 771, 756, 729, 721 (m), 703 (s), 667, 650, 633, 614, 595, 577, 544 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 346 ([M, $^{81}Br]^+$, 43), 344 ([M, $^{79}Br]^+$, 44), 265 (13), 251 (18), 250 (100), 237 (16), 235 (17), 234 (16), 221 (9), 207 (14), 165 (14), 163 (12), 151 (10). HRMS (EI, 70 eV): calcd for $C_{17}H_{13}O_3Br$ $[M]^+$: 344.00481; found: 344.00480.

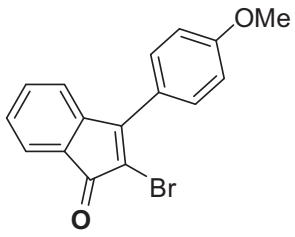
2-Bromo-3-(3-methoxyphenyl)-1*H*-inden-1-one (65e). Compound **65e** was prepared



from **23** (144 mg, 0.5 mmol), $(PPh_3)_4Pd$ (0) (18 mg, 3 mol-%) and 3-methoxyphenylboronic acid (76 mg, 0.5 mmol), according to the *General procedure A*, as a yellow solid (138 mg, 88 %). Reaction

temperature: 45 °C. M. p. 108-109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3H, OCH_3), 6.96- 7.00 (m, 1H, ArH), 7.07-7.21 (m, 4H, ArH), 7.25-7.30 (m, 1H, ArH), 7.38 (t, *J* = 7.9 Hz, 1H, ArH), 7.46-7.49 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 113.7, 116.0 (CH), 118.1 (C), 120.5, 121.3, 123.7, 128.9, 129.9 (CH), 132.4 (C), 133.8 (CH), 144.5, 156.8, 159.7 (C) 189.8 (CO). IR (KBr): ν = 3411, 3069, 3005, 2966, 2942, 2217, 2839 (w), 1714 (s), 1603, 1593, 1584, 1374, 1563, 1483, 1462, 1453, 1427, 1365, 1305, 1287, 1269 (m), 1234 (s), 1182, 1173, 1162, 1145, 1101, 1080 (m), 1030 (s), 993, 964, 957, 888, 874, 866, 819, 822 (m), 793 (s), 780 (m), 758, 707, 699, 673 (s), 659, 644, 614, 571, 549 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 316 ([M, ^{81}Br]$^{+}$, 100), 314 ([M, ^{79}Br]$^{+}$, 100), 235 (31), 192 (10), 176 (12), 164 (27), 163 (38), 117 (10). HRMS (EI, 70 eV): calcd for $C_{16}H_{11}BrO_2$ [M, ^{79}Br]$^{+}$: 313.99369; found: 313.99384.

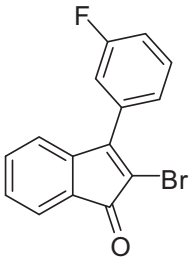
2-Bromo-3-(4-methoxyphenyl)-1*H*-inden-1-one (65f). Compound **65f** was prepared from



23 (144 mg, 0.5 mmol), $(PPh_3)_4Pd$ (0) (18 mg, 3 mol-%) and 4-methoxyphenylboronic acid (76 mg, 0.5 mmol), according to the *General procedure A*, as a white yellow solid (139 mg, 88 %). Reaction temperature: 40 °C. M. p. 100-101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 6.97 (d, 2H, *J* = 8.8 Hz, ArH), 7.09-7.19 (m, 2H, ArH), 6.26 ((td, 1H, *J* = 7.7, 1.3 Hz, ArH), 7.44-7.47 (m, 1H, ArH), 7.59 (d, 2H, *J* = 8.9 Hz, ArH),. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 54.4 (OCH_3), 113.1 (CH), 115.6 (C), 120.3 (CH), 122.3 (C), 122.4, 127.8, 129.1 (CH), 129.2 (C), 132.5 (CH), 143.4, 155.5, 160.2 (C), 188.9 (CO). IR (KBr): ν = 3412, 3080, 3064, 3043, 3016, 2968, 2953, 2917, 2841,1747 (w), 1715, 1607, 1597 (s), 1577 (m), 1505 (s), 1468, 1455, 1445, 1417, 1367, 1352, 1301 (m), 1258,1178 (s), 1113, 1098, 1078, 1028, 1011, 918, 830, 810, 791 (m), 769 (s), 759, 724 (m), 704 (s), 667, 652, 624, 617, 576, 546 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 316 ([M, ^{81}Br]$^{+}$, 97), 314 ([M, ^{79}Br]$^{+}$, 100), 235 (15), 164 (24), 163 (38),

118 (10). HRMS (EI, 70 eV): calcd for $C_{16}H_{11}BrO_2$ [M, $^{79}Br]^+$: 313.99369; found: 313.99354.

2-Bromo-3-(3-fluorophenyl)-1*H*-inden-1-one (65f). Compound **65f** was prepared from

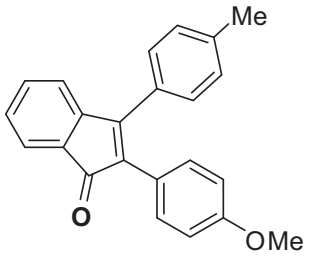


16 (144 mg, 0.5 mmol), $(PPh_3)_4Pd$ (0) (18 mg, 3 mol-%) and 3-fluorophenylboronic acid **23c** (70 mg, 0.5 mmol), according to the *General procedure A*, as a yellow solid (125 mg, 83 %). Reaction temperature: 45 °C. M. p. 116-117 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04-7.07 (m, 1H, ArH), 7.11-7.23 (m, 2H, ArH), 7.27-7.38 (m, 3H, ArH), 7.42-7.51 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -111.3. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 115.3 (d, $J_{C,F}$ = 22.8 Hz, CH), 117.3 (d, $J_{C,F}$ = 21.8 Hz, CH), 118.8 (C), 121.1, 123.9 (CH), 124.1 (d, $J_{C,F}$ = 3.1 Hz, CH), 129.1 (CH), 129.7 (C), 130.6 (d, $J_{C,F}$ = 8.3 Hz, CH), 133.1 (d, $J_{C,F}$ = 8.2 Hz, C), 134.0 (CH), 144.2 (C), 155.5 (d, $J_{C,F}$ = 2.5 Hz, C), 133.1 (d, $J_{C,F}$ = 247.5 Hz, C), 189.5 (CO). IR (KBr): ν = 3425, 3080, 3054 (w), 1715 (s), 1596, 1580, 1565, 1484, 1451, 1427, 1418, 1365, 1354, 1298, 1284, 1263, 1209, 1178, 1158, 1134, 1099, 1081, 1071, 965, 893, 870, 824, 787, 765 (m), 710, 705, 700, 670 (s), 657, 640, 614, 599, 555, 536 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 304 ([M, $^{81}Br]^+$, 99), 302 ([M, $^{79}Br]^+$, 100), 224 (11), 223 (64), 195 (28), 194 (63), 175 (24), 169 (13), 168 (16), 112 (11), 97 (14). HRMS (EI, 70 eV): calcd for $C_{15}H_9BrFO$ [M, 79Br]+: 302.98153; found: 302.98157.

7.3.3 Synthesis of unsymmetrical 2,3-diarylindenones 66a-g

General procedure B for One-pot sequential arylation 2,3-dibromo-1*H*-inden-1-one (**66**): In a pressure tube to a suspension of 2,3-dibromo-1*H*-inden-1-one **23** (288 mg, 1.0 mmol), tetrakis(triphenylphosphine)palladium (0) (35 mg, 3 mol-%) and $Ar^1B(OH)_2$ (1.0 mmol) in dioxane (5 mL) was added a 2M solution of K_2CO_3 (1 mL). The mixture was heated at 40-45 °C under Ar for 6 h. Reaction was cooled to rt and added with 1.1 mmol of $Ar^2B(OH)_2$ and tetrakis (triphenylphosphine) palladium (0) (35 mg, 3 mol-%). Reactions was heated under Ar for another 6h at 70 °C. After cooling the eactions to rt, reaction mixture was diluted with water and extracted with DCM (25ml x 3). The organics were dried (Na_2SO_4) and concentrated and the resulting residue was subjected to flash chromatography (EtOAc/*n*-heptane) which gave pure **66a-g**.

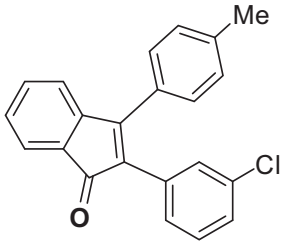
2-(4-Methoxyphenyl)-3-*p*-tolyl-1*H*-inden-1-one (66a). Compound **66a** was prepared from **23** (288 mg, 1.0 mmol), *p*-tolylboronic acid (136 mg, 1.0 mmol) and 4-methoxyphenylboronic acid (167 mg, 1.1 mmol), according to the *General procedure B*, as a brown crystalline solid (303 mg, 93 %). Reaction temperature: 45 and 70 °C respectively.



M. p. 115-116 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.81 (d, J = 8.52 Hz, 2H, ArH), 7.12-7.21 (m, 1H), ArH), 7.14-7.28 (m, 8H, ArH), 7.52-57 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5 (CH_3), 55.2 (OCH_3), 113.6, 121.0, 127.7 (CH), 123.3 (C), 128.5, 128.6, 129.5 (CH), 130.0, 130.9 (C), 131.3 (CH), 131.6 (C) 133.3 (CH), 139.3, 145.6, 154.0, 159.1 (C), 197.0 (CO). IR (KBr): ν = 3387, 3042, 2999, 2937, 2843, 2548, 2368, 2335 (w), 1704, 1699 (s), 1596, 1582, 1515, 1501, 1453, 1417, 1380, 1366, 1340, 1295 (m), 1251, 1176 (s), 1151, 1114, 1068 (m), 1029 (s), 1006, 922, 850 (m), 831, 806, 798 (s), 775 (m), 764, 733 (s), 722, 713, 680, 631, 575 (m), 555, 533 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 326 ($[M]^+$, 100),

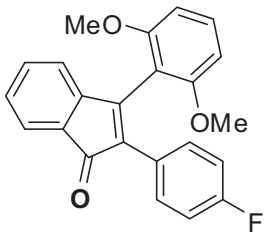
311 (20), 268 (11), 239 (19). HRMS (EI, 70 eV): calcd for $C_{23}H_{18}O_2$ $[M]^+$: 326.130186; found: 326.13019.

2-(3-Chlorophenyl)-3-p-tolyl-1*H*-inden-1-one (**66b**). Compound **66b** was prepared from



23 (288 mg, 1.0 mmol), *p*-tolylboronic acid (136 mg, 1.0 mmol) and 3-chlorophenylboronic acid (172 mg, 1.1 mmol), according to the *General procedure B*, as a white yellow solid (294 mg, 89 %). Reaction temperature: 45 and 70 °C respectively. M. p. 147-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 7.00-7.32 (m, 11H, ArH), 7.50 (dd, 1H, *J* = 7.1, 0.6 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.6 (CH_3), 121.6, 123.0, 127.7, 128.1, 128.4, 129.2 (CH), 129.2 (C), 129.3, 129.6, 129.9 (CH), 130.6, 130.8, 132.9 (C), 133.5 (CH), 133.9, 139.9, 144.9, 156.6 (C), 195.9 (CO). IR (KBr): ν = 3382, 3057, 3043, 3028, 2917, 2854, 2354, 2138, 2001, 1938 (w), 1702 (s), 1606, 1595, 1575, 1563, 1509, 1505, 1454, 1403, 1340, 1311, 1300, 1284, 1264, 1184, 1148, 1115, 1101, 1081, 1062, 1017, 998, 959, 921, 885, 854, 824, 788 (m), 776, 767, 731, 726 (s), 716 (m), 693, 678 (s), 662, 601, 567, 558 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 332 ([M, ^{37}Cl]$^+$, 35), 330 ([M, ^{35}Cl]$^+$, 100), 317 (11), 315 (32), 295 (42), 280 (14), 265 (19), 263 (14), 252 (27), 250 (13), 131 (9). HRMS (EI, 70 eV): calcd for $C_{22}H_{15}ClO$ $[M]^+$: 330.08059; found: 330.08018.

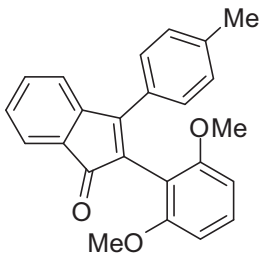
3-(2,6-Dimethoxyphenyl)-2-(4-fluorophenyl)-1*H*-inden-1-one (**66c**). Starting with



23 (288 mg, 1.00 mmol), $Pd(PPh_3)_4$ (35 mg, 3 mol-%), dioxane (5 mL), 2M K_2CO_3 (1 mL) and 2,6-dimethoxyphenylboronic acid ($Ar^1B(OH)_2$) (182 mg, 1.00 mmol), 4-fluorophenylboronic acid ($Ar^2B(OH)_2$) (154 mg, 1.10 mmol) and additional $Pd(PPh_3)_4$ (35 mg, 3 mol-%), according to the *General procedure B*, **66c** was isolated as a brownish yellow solid (309 mg, 86 %). Reaction temperature: 40 °C for 6h (1st step), 70 °C for 6h (2nd step). M. p. 206-207 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.51 (s, 6H, $2OCH_3$), 6.53 (d, 2H,

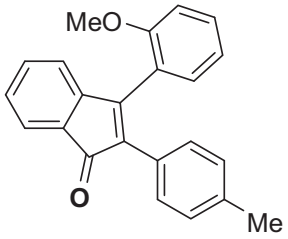
J = 8.4 Hz, ArH), 6.68 (dt, 1H, *J* = 7.1, 0.8 Hz, ArH), 6.70-6.87 (m, 2H, ArH), 7.10-7.31 (m, 5H, ArH), 7.43-7.46 (m, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -114.2. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.7 ($2OCH_3$), 104.3 (CH), 110.5 (C), 114.7 (d, $J_{C,F}$ = 21.4 Hz, CH), 121.2, 121.3, 128.3 (CH), 128.5 (d, $J_{C,F}$ = 3.3 Hz, C), 1130.3 (d, $J_{C,F}$ = 8.0 Hz, CH), 130.4 (C), 130.9, 133.5 (CH), 145.8, 150.6, 157.8 (C), 162.1 (d, $J_{C,F}$ = 247.4 Hz, CF), 196.8 (CO). IR (KBr): ν = 3046, 2963, 2931, 2838 (w), 1696, 1591, 1581, 1574, 1504, 1471, 1462, 1455, 1442, 1432 (m), 1359, 1341, 1296 (w), 1255, 1222, 1156 (m), 1109 (s), 1094, 1068, 1027, 1014 (m), 974, 960, 941, 925, 903 (w), 853, 825, 794, 781 (m), 761, 731, 721, 709 (s), 684, 662, 643, 626 (w), 585, 550, 542 (m), 528 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 360 ([M]$^+$, 100), 273 (10), 257 (9), 172 (8). HRMS (EI, 70 eV): calcd for $C_{23}H_{17}FO_3$ [M]$^+$: 360.11562; found: 360.11556.

2-(2,6-Dimethoxyphenyl)-3-p-tolyl-1*H*-inden-1-one (**66d**). Compound **66d** was prepared



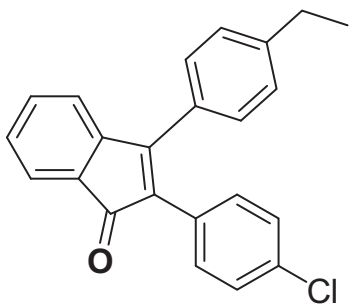
from **23** (288 mg, 1.0 mmol), *p*-tolylboronic acid (136 mg, 1.0 mmol) and 2,6-dimethoxyphenylboronic acid (200 mg, 1.1 mmol), according to the *General procedure B*, as a yellow crystalline solid (320 mg, 90 %). Reaction temperature: 45 and 70 °C respectively. M. p. 207-208 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3H, CH_3), 3.49 (s, 6H, $2OCH_3$), 6.44 (d, 2H, *J* = 8.3 Hz, ArH), 7.05 (d, 2H, *J* = 7.9 Hz, ArH), 7.12-7.29 (m, 6H, ArH), 7.45-7.48 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.1 (CH_3), 55.8 (OCH_3), 104.3 (CH), 109.8 (C), 120.9, 122.6, 127.4, 128.4 (CH), 128.6 (C), 128.9, 129.7 (CH), 130.9, 132.0 (C), 132.8 (CH), 139.0, 145.5, 157.4, 158.8 (C), 196.0 (CO). IR (KBr): ν = 3390, 3077, 3025, 2996, 2971, 2941, 2918, 2837, 2141 (w), 1704, 1673, 1604, 1580, 1530, 1470, 1455, 1445, 1430,1360, 1332 (m), 1250 (s), 1180 (m), 1106 (s), 1062, 1030, 1017, 924, 855, 817 (m), 765, 724 (s), 677, 657, 645, 604, 586, 561, 545 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 356 ([M]$^+$, 100), 326 (27), 311 (17), 252 (10), 239 (12), 233 (34), 226 (9), 119 (9). HRMS (EI, 70 eV): calcd for $C_{24}H_{20}O_3$ [M]$^+$: 356.14070; found: 356.13996.

3-(2-Methoxyphenyl)-2-*p*-tolyl-1*H*-inden-1-one (**66e**). Compound **66e** was prepared



from **23** (288 mg, 1.0 mmol), 2-methoxyphenylboronic acid (152 mg, 1.0 mmol) and *p*-tolylboronic acid (150 mg, 1.1 mmol), according the *General procedure B*, as a yellow solid (277 mg, 85 %). Reaction temperature: 40 and 70 °C respectively. M. p. 157-158 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3H, CH_3), 3.52 (s, 3H, OCH_3), 6.80 (dt, 1H, *J* = 7.2, 0.8, Hz, ArH), 6.87-6.97 (m, 4H, ArH), 7.09-7.34 (m, 6H, ArH), 7.44-7.47 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.3 (CH_3), 55.3 (OCH_3), 111.6, 120.9, 121.3 (CH), 122.4 (C), 122.5, 128.4, 128.7, 129.1, 129.8, 130.5 (CH), 130.6, 133.2 (C), 133.4 (CH), 137.4, 145.8, 152.8, 157.0 (C), 196.9 (CO). IR (KBr): ν = 3071, 3030, 3006, 2973, 2943, 2917, 2841 (w), 1705, 1699, 1603, 1594, 1585, 1575, 1511, 1483, 1461, 1456, 1435, 1344, 1293,1270 (m), 1245 (s), 1176, 1162, 1114, 1068, 1042, 1022, 982, 939, 922, 849, 825, 791 (m), 761 (s), 745 (m), 725, 708 (s), 683, 665, 621, 549 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 326 ([M]$^+$, 100), 295 (16), 252 (12), 239 (15). HRMS (EI, 70 eV): calcd for $C_{23}H_{18}O_2$ [M]$^+$: 326.13013; found: 326.13016.

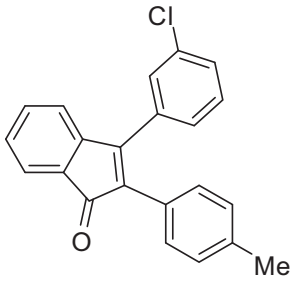
2-(4-Chlorophenyl)-3-(4-ethylphenyl)-1*H*-inden-1-one (**66f**). Compound **16f** was



prepared from **23** (288 mg, 1.0 mmol), 4-ethylphenylboronic acid (150 mg, 1.0 mmol) and 4-chlorophenylboronic acid (172 mg, 1.1 mmol), according to the *General procedure B*, as a yellow solid (272 mg, 79 %). Reaction temperature: 45 and 70 °C respectively. M. p. 94-95 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (t, 3H, *J* = 7.61 Hz, CH_3), 2.64 (q, 2H, *J* = 7.61 Hz, CH_2), 7.12-7.33 (m, 11H, ArH), 7.48-7.51 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.2 (CH_3), 28.8 (CH_2), 121.5, 123.0, 128.3, 128.4, 128.5, 129.1 (CH), 129.5, 129.6, 130.8 (C), 131.3, 133.5 (CH), 133.6, 145.1, 146.0, 156.0 (C) 196.3 (CO). IR (KBr): ν = 3393, 3026, 2963, 2930, 2872, 2676, 2251, 2141, 1915, 1771 (w), 1704 (s), 1607, 1597, 1579, 1510, 1501 (m), 1487, 1455, 1340, 1181 (s), 1089 (m), 1069, 1013 (s), 923, 908 (m), 858, 832, 814, 794, 764, 727, 715,

708 (s), 679, 648, 628, 574, 553, 542 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 346 ([M^+, ^{37}Cl], 35), 344 ([M^+, ^{35}Cl], 100), 317 (12), 315 (33), 309 (11), 280 (15), 265 (19), 263 (13), 252 (16), 250 (9). HRMS (EI, 70 eV): calcd for $C_{23}H_{17}ClO$ $[M]^+$: 344.09624; found: 344.09513.

3-(3-Chlorophenyl)-2-*p*-tolyl-1*H*-inden-1-one (**66g**). Compound **66g** was prepared from



16 (288 mg, 1.0 mmol), 3-chlorophenylboronic acid (172 mg, 1.1 mmol) and *p*-tolylboronic acid (136 mg, 1.0 mmol), according to the *General procedure B*, as a yellow solid (262 mg, 79 %). Reaction temperature: 45 and 70 °C respectively. M. p. 147-148 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3H, CH_3), 6.96-7.00 (m, 3H, ArH), 7.05-7.32 (m, 8H, ArH), 7.46-7.49 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (CH_3), 120.9, 123.2, 126.9 (CH), 127.3 (C), 128.3, 129.0, 129.3, 129.8, 130.3 (CH), 130.5, 133.0 (C), 133.6 (CH), 134.7, 134.8, 137.7, 145.1, 152.8 (C), 196.4 (CO). IR (KBr): ν = 3058, 3024, 2918, 2860 (w), 1703 (s), 1601, 1590, 1558, 1337, 1311, 1181, 1148, 1115, 1101, 1081, 1062, 1017, 998, 959, 921, 885, 854, 824, 788 (m), 788, 723, 710, 700, (s), 716 (m), 693, 678 (s), 677, 640, 567, 553 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 332 ([M, $^{37}Cl]^+$, 35), 330 ([M, $^{35}Cl]^+$, 100), 315 (20), 295 (33), 280 (12), 265 (19), 265 (18), 252 (27), 252 (31). HRMS (ESI^+): calcd for $C_{22}H_{15}ClO$ $[M+H]^+$: 331.0884; found: 331.0883.

Appendix

8 Crystallographic Data

8.1 Crystal data and structure *refinement* for 2,3-bis(4-tert butylphenyl)benzofuran (58e)

Identification code	tn6801	
Empirical formula	$C_{28}H_{30}O$	
Formula weight	382.52	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	P 21	
Space group (Hall)	P 2yb	
Unit cell dimensions	a = 11.538 (11) Å	α = 90°.
	b = 17.067 (14) Å	β = 114.199(18)°.
	c = 12.504 (12) Å	γ = 90°.
Volume	2246 (4) $Å^3$	
Z	4	
Density (calculated)	1.131 Mg/m^3	
Absorption coefficient	0.066 mm^{-1}	
F(000)	824	
Crystal size	0.90 x 0.30 x 0.18 mm^3	
Θ range for data collection	6.2 to 58.2°	
Index ranges	-16≤h≤16, -12≤k≤23, -17≤l≤17	
Reflections collected	23653	
Independent reflections	9998 [R(int) = 0.040]	
Absorption correction	multi-scan	
Max. and min. transmission	0.988 and 0.943	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.030	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0510, wR2 = 0.1218	
R indices (all data)	R1 = 0.0804, wR2 = 0.1338	

8.2 Crystal data and structure *refinement* for 2,3-bis(4-chlorophenyl)benzofuran (58g)

Identification code	tn6301	
Empirical formula	$C_{20}H_{12}Cl_2O$	
Formula weight	339.20	
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 = 6.0071 (3) Å	α = 64.577°.
	b = 11.043 (6) Å	β = 88.917°.
	c = 12.5267 (7) Å	γ = 88.062°.
Volume	794.99 (7) $Å^3$	
Z	2	
Density (calculated)	1.421 Mg/m^{-3}	
Absorption coefficient	0.410 mm^{-1}	
F(000)	348	
Θ range for data collection	3.9 to 30.0°.	
Index ranges	-8≤h≤7, -16≤k≤16, -17≤l≤17	
Reflections collected	3518	
Independent reflections	4478 [R(int) = 0.034]	
Absorption correction	multi-scan	
Max. and min. transmission	0.968 and 0.697	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.091	
Final R indices [I>2σ(I)]	R1 = 0.0436, wR2 = 0.1123	
R indices (all data)	R1 = 0.0594, wR2 = 0.1209	

8.3 Crystal data and structure *refinement* for 2,3-bis(4-fluorophenyl)benzofuran (58h)

Identification code	tn6601	
Empirical formula	$C_{20}H_{12}F_2O$	
Formula weight	306.30	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	P 21 21 21	
Space group (Hall)	P 13c 13b	
Unit cell dimensions	a = 6.0318 (12) Å	α = 90°.
	b = 11.417 (2) Å	β = 90°.
	c = 21.460 (4) Å	γ = 90°.
Volume	1477.9 (5) $Å^3$	
Z	4	
Density (calculated)	1.377 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	
F(000)	632	
Crystal size	0.60 x 0.21 x 0.15 mm^3	
Θ range for data collection	5.2 to59.1°	
Index ranges	-4≤h≤8, -15≤k≤16, -27≤l≤30	
Reflections collected	9883	
Independent reflections	4274 [R(int) = 0.033]	
Absorption correction	multi-scan	
Max. and min. transmission	0.985 and 0.942	
Refinement method	Full-matrix least-squares on F^2	
Goodness-of-fit on F^2	1.056	
Final R indices [I>2σ(I)]	R1 = 0.0411, wR2 = 0.0936	
R indices (all data)	R1 = 0.0538, wR2 = 0.0985	

8.4 Crystal data and structure *refinement* for 2-(4-fluorophenyl)-3-p-tolylbenzofuran (13b)

Identification code	tn9001	
Empirical formula	$C_{21}H_{15}FO$	
Formula weight	302.33	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	P b c a	
Space group (Hall)	P 13c 13b	
Unit cell dimensions	a = 14.887 (14) Å	α = 90°.
	b = 10.191 (58) Å	β = 90°.
	c = 20.539 (18) Å	γ = 90°.
Volume	3116 (5) $Å^3$	
Z	8	
Density (calculated)	1.289 Mg/m^3	
Absorption coefficient	0.075 mm^{-1}	
F(000)	1264	
Crystal size	0.60 x 0.21 x 0.15 mm^3	
Θ range for data collection	5.2 to 59.1°.	
Index ranges	-4≤h≤8, -15≤k≤16, -27≤l≤30	
Reflections collected	9883	
Independent reflections	3574 [R(int) = 0.033]	
Absorption correction	multi-scan	
Max. and min. transmission	0.985 and 0.942	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.017	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0549, wR2 = 0.1357	
R indices (all data)	R1 = 0.0995, wR2 = 0.1525	

8.5 Crystal data and structure *refinement* for 2,3-diphenyl-1*H*-inden-1-one (17a)

Identification code	tn12301	
Empirical formula	$C_{21}H_{14}O$	
Formula weight	282.32	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinbic	
Space group (H.-M.)	P 21/ n	
Space group (Hall)	P 2yn	
Unit cell dimensions	a = 14.887 (14) Å	α = 90°.
	b = 10.191 (10) Å	β = 110.201 (10)°.
	c = 20.539 (18) Å	γ = 90°.
Volume	1492.8 (14) $Å^3$	
Z	4	
Density (calculated)	1.256 Mg/m^3	
Absorption coefficient	0.075 mm^{-1}	
F(000)	592	
Crystal size	0.52 x 0.38 x 0.18 mm^3	
Θ range for data collection	5.0 to 59.8°	
Index ranges	-13≤h≤13, -23≤k≤23, -13≤l≤13	
Reflections collected	16734	
Independent reflections	4348 [R(int) = 0.022]	
Absorption correction	multi-scan	
Max. and min. transmission	0.987 and 0.962	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2σ(I)]	R1 = 0.0424, wR2 = 0.1087	
R indices (all data)	R1 = 0.0547, wR2 = 0.1149	

8.6 Crystal data and structure *refinement* for 2-bromo-3-(2,6-dimethoxyphenyl)-1*H*-inden-1-one (18c)

Identification code	tn12703	
Empirical formula	$C_{17}H_{13}BrO_3$	
Formula weight	345.18	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinbic	
Space group (H.-M.)	P 21/ n	
Space group (Hall)	P 1	
Unit cell dimensions	a = 6.787 (5) Å	α = 96.563 (12)°.
	b = 9.279 (7) Å	β = 98.53 (2)°.
	c = 11.420 (8) Å	γ = 98.921 (8)°.
Volume	695.7 (8) $Å^3$	
Z	2	
Density (calculated)	1.648 Mg/m^3	
Absorption coefficient	0.075 mm^{-1}	
F(000)	348	
Crystal size	0.45 x 0.30 x 0.08 mm^3	
Θ range for data collection	5.4 to 60.0°	
Index ranges	-9≤h≤9, -12≤k≤13, -16≤l≤14	
Reflections collected	14592	
Independent reflections	4035 [R(int) = 0.025]	
Absorption correction	multi-scan	
Max. and min. transmission	0.798 and 0.349	
Refinement method	Full-matrix	
Goodness-of-fit on F^2	1.052	
Final R indices [I>2σ(I)]	R1 = 0.0247, wR2 = 0.0616	
R indices (all data)	R1 = 0.0281, wR2 = 0.0625	

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, 29th Oktober, 2010.

References

[1] (a) Reiser, O.; S. Reichow, S.; de Meijere, A. *Angew. Chem.* **1987** *99*, 1285. (b) *Angew. Chem. Int. Ed. Engl.* **1987**, *26,* 1277.

[2] Lansky, A.; Reiser, O.; de Meijere, A. *Synlett* **1990**, 405.

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

[4] Hussain, M. dissertation, University of Rostock, in preparation.

[5] Toguem, S. M. T. dissertation, University of Rostock, in preparation.

[6] Hussain, M.; Hung, N. T. *Tetrahedron Lett.* **2009**, *11*, 1822.

[7] Malik, I. dissertation , University of Rostock, in preparation.

[8] Hussain, M.; Zinad, D. S.; Salman, G. A.; Sharif, M.; Villinger, A.; Langer, P. *Synlett,* **2010**, *02*, 276.

[9] Akravi, O. A. M. dissertation, University of Rostock, in preparation

[10] Ali, A., dissertation , University of Rostock, in preparation.

[11] (a) *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann.W. A., Ed.; Wiley-VCH: Weiheim, **1996**. (b) *Handbook of Organopalladium Chemistry for Organic Synthesi*s; Negishi. E., de Meijere, A., Eds.; Wiley: New York, **2002**. (c) *Cross-Coupling Reactions*; Miyaura, N., Ed.; Springer: Berlin, **2000**. (d) *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; Diederich, F., de Meijere, A., Eds.; Wiley-VCH: Weiheim, **2004**. (e) *Transition Metals for Organic Synthesis; Building Block and Fine Chemicals*, 2nd ed.; Beller, N., Bolm, C., Eds.; Wiley-VCH: Weinheim, **2004**. (f) Tsuji, J. *Palladium Reagents and Catalysts, Innovations in Organic Synthesis*; Wiley: New York, **1995**.

[12] Schroter, S.; Stock, C.; Bach, T.*Tetrahedron*, **2005**, *61*, 2245.

[13] Dang, T. T.; Rasool, N.; **Dang**, T. T.; Reinke, H.; Langer, P. *Tetrahedron Lett.* **2007**, *48*, 845.

[14] Tengho. T. S-M; Villinger, A.; Langer, P: Synlett, **2009**, *20*, 3311.

[15] Dang, T. T.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2008**, *350*, 2109.

[16] Hussain, M.; Khera, R. A.; Hung, N. T. Langer, P. *Organic and Biomolecular Chemistry*, **2010**, (In press).

[17] Dang, Tung T.; Dang, Tuan T.; Ahmad, R.; Reinke, H.; Langer, P. *Tetrahedron Lett.* **2008**, *49*, 1698.

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

[19] Ibad, M. F.; Hussain, M.; Abid, O.-U.-R.; Ali, A.; Ullah, I.; Zinad, D. S. Langer, P. *Synlett,* **2010**, 411.

[20] Malik, I.; Hussain, M.; Hung, N. T.; Villinger, A.; Langer, P. *Synlett,* **2010**, 2244.

[21] (a) Miyata, O.; Takeda, N.; Morikami, Y.; Naito, T. *Org. Biomol. Chem.* **2003**, *1*, 254; (b) Xie, X.; Chen, B.; Lu, J.; Han, J.; She, X.; Pan, X. *Tetrahedron Lett.* **2004**, *45*, 6235; (c) Zhang, H.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 6144; (d) Hagiwara, H.; Sato, K.; Nishino, D.; Hoshi, T.; Suzuki, T.; Ando, M. *J. Chem. Soc., Perkin Trans. 1*, **2001**, 2946; review: (e) Butin, A. V.; Gutnow, A. V.; Abaev, V. T.; Krapivin, G. D. *Molecules* **1999**, *4*, 52; (f) Fuerst, D. E.; Stoltz, B. M.; Wood, J. L. *Org. Lett.* **2000**, *22*, 3521; (g) Schneider, B. *Phytochemistry* **2003**, *64*, 459; (h) Katritzky, A. R.; Kirichenkok, K.; Ji, Y.; Steel, P. J.; Karelson, M. *ARKIVOC* **2003**, *vi*, 49.

[22] (a) Wendt, B.; Ha, H. R.; Hesse, M. *Helv. Chim. Acta* **2002**, *85*, 2990; (b) Carlsson, B.; Singh, B. N.; Temciuc, M.; Nilsson, S.; Li, Y. L.; Mellin, C.; Malm, J. *J. Med. Chem.* **2002**, *45*, 623, and references cited therein; (c) Kwiecien, H.; Baumann, E. *J. Heterocycl. Chem.* **1997**, 1587; (d) Larock, R. C.; Harrison, L. W. *J. Am. Chem. Soc.* **1984**, *106*, 4218; (e) Matyus, P.; Varga I.; Rettegi, T.; Simay, A.; Kallay, N.; Karolyhazy, L.; Kocsis, A.; Varro, A.; Penzes, I.; Papp, J. G. *Current Medicinal*

Chemistry **2004**, *1*, 61; (f) Wong, H.N.C.; Pei Yu; Yick, C.Y. *Pure Appl. Chem.*, **1999**, *71*, 1041.

[23] Longicaudatin: (a) Joshi, A. S.; Li, X.-C.; Nimrod, A. C.; ElSohly, H. N.; Walker, L. A.; Clark, A. M. *Planta Med.* **2001**, *67*, 186; for related natural products, see: (b) Sigstad, E.; Catalan, C. A. N.; Diaz, J. G.; Herz, W. *Phytochemistry* **1993**, *33*, 165; (c) Drewes, S. E.; Hudson, N. A.; Bates, R. B. *J. Chem. Soc., Perkin Trans.1* **1987**, 2809.

[24] Sessiliflorol A: (a) Chan, J. A.; Shultis, E. A.; Carr, S. A.; DeBrosse, C. W.; Eggleston, D. S. *J. Org. Chem.* **1989**, *54*, 2098; sessiliflorol B: (b) Marston, A.; Zagorski, M. G.; Hostettmann, K. *Helv. Chim. Acta* **1988**, *71*, 1210; (c) Drewes, S. E.; Hudson, N. A.; Bates, R. B.; Linz, G. S. *Tetrahedron Lett.* **1984**, *25*, 105; flemistrictin E: (d) Subrahmanyam, K.; Rao, J. M.; Vemuri, V. S. S.; Babu, S. S.; Roy, C. P.; Rao, K. V. J. *Ind. J. Chem. Sect. B* **1982**, *21*, 895; tovophenone C: (e) Seo, E.-K.; Wall, M. E.; Wani, M. C.; Navarro, H.; Mukherjee, R.; Farnsworth, N. R.; Kinghorn, A. D. *Phytochemistry* **1999**, *52*, 669; vismiaguianone C: (f) Seo, E.-K.; Wani, M. C.; Wall, M. E.; Navarro, H.; Mukherjee, R.; Farnsworth, N. R.; Kinghorn, A. D. *Phytochemistry* **2000**, *55*, 35; piperaduncin B: (g) Joshi, A. S.; Li, X.-C.; Nimrod, A. C.; ElSohly, H. N.; Walker, L. A.; Clark, A. M. *Planta Med.* **2001**, *67*, 186; see also: (h) Bohlmann, F.; Zdero, C. *Chem. Ber.* **1976**, *109*, 1436.

[25] (a) Kokubun, T.; Harborne, J. B. *Phytochemistry* **1995**, *40*, 1649. (b) Burden, R. S.; Kemp, M. S.; Wiltshire, C. W.; Owen, J. D. *J. Chem. Soc. Perkin Trans. 1* **1984**, 1445.

[26] (a) Kobayashi, A.; Takemura, A.; Koshimizu, K.; Nagano, H.; Kawazu, K. *Agric. Biol. Chem.* **1982**, *46*, 585. (b) Ma, B.-J.; Liu, J.-K. *Z. Naturforsch. B* **2005**, *60*, 565. (c) Takahashi, A.; Kudo, R.; Kusano, G.; Nozoe, S. *Chem. Pharm. Bull.* **1992**, *40*,

3194. (d) Xie, C.; Koshino, H.; Esumi, Y.; Onose, J.-i.; Yoshikawa, K.; Abe, N. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5424.

[27] Kitamura, M.; Koyama, T.; Nakano, Y.; Uemura, D. *Chem. Lett.* **2005**, *34*, 1272.

[28] (a) Jaegers, E.; Hillen-Maske, E.; Steglich, W. *Z. Naturforsch. B* **1987**, *42*, 1349. (b) Anh, M.-J.; Yoon, K.-D.; Min, S.-Y.; Lee, J. S.; Kim, J. H.; Kim, T. G.; Kim, S. H.; Kim, N.-G.; Huh, H.; Kim, J. *Biol. Pharm. Bull.* **2004**, *27*, 544. (c) Liu, K. C. S. C.; Lin, M.-T.; Lee, S.-S.; Chiou, J.-F.; Ren, S.; Lien, E. J. *Planta Med.* **1999**, *65*, 43. (d) Yoshikawa, M.; Xu, F.; Morikawa, T.; Ninomiya, K.; Matsuda, H. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1045.

[29] Rezanka, T.; Hanus, L. O.; Kujan, P.; Dembitsky, V. M. *Eur. J. Org. Chem.* **2005**, 2708.

[30] (a) Bach, T.; Bartels, M. *Synlett* **2001**, 1284. (b) Bach, T.; Bartels, M. *Synthesis* **2003**, 925.

[31] Lin, S.-Y.; Chen, C.-L.; Lee, Y.-J. *J. Org. Chem.* **2003**, *68*, 2968.

[32] Bach, T.; Bartels, M. *Tetrahedron Lett.* **2002**, *43*, 9125.

[33] De Meijere and coworkers reported twofold Heck reactions of 1,2-dibromocycloalk-1-enes and related substrates and subsequent 6π-electrocyclization: Voigt, K.; von Zezschwitz, P.; Rosauer, K.; Lansky, A.; Adams, A.; Reiser, O.; de Meijere, A. *Eur. J. Org. Chem.* **1998**, 1521, and references cited therein.

[34] Benincori, T.; Brenna, E.; Sannicolo, F.; Trimarco, L.; Antognazza, P. *J. Org. Chem.* **1996**, *61*, 6244.

[35] K. Billingsley, S. L. Buchwald, *J. Am. Chem. Soc.* **2007**, *129*, 3310, and references cited therein.

[36] For a review, see: (a) Butin, A. V.; Gutnow, A. V.; Abaev, V. T.; Krapivin, G. D. *Molecules* **1999**, *4*, 52; see also: (b) Fuerst, D. E.; Stoltz, B. M.; Wood, J. L. *Org. Lett.* **2000**, *22*, 3521; (c) Schneider, B. *Phytochemistry* **2003**, *64*, 459; (d) Katritzky,

A. R.; Kirichenkok, K.; Ji Y.; Steel, P. J.; Karelson, M. *ARKIVOC* **2003**, *vi*, 49; (e) Miyata, O.; Takeda, N.; Morikami, Y.; Naito, T. *Org. Biomol. Chem.* **2003**, *1*, 254; (f) Xie, X.; Chen, B.; Lu, J.; Han, J.; She, X.; Pan, X. *Tetrahedron Lett.* **2004**, *45*, 6235; (g) Zhang, H.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 6144; (h) Hagiwara, H.; Sato, K.; Nishino, D.; Hoshi, T.; Suzuki, T.; Ando, M. *J. Chem. Soc., Perkin Trans. 1*, **2001**, 2946.

[37] For reviews, see: (a) Matyus P.; Varga I.; Rettegi T.; Simay A.; Kallay N.; Karolyhazy L.; Kocsis A.; Varro A.; Penzes I.; Papp J. G. *Current Medicinal Chemistry* **2004**, *1*, 61; (b) Wong, H. N. C.; Pei Yu; Yick, C. Y. *Pure Appl. Chem.*, **1999**, *71*, 1041; see also: (c) Larock, R. C.; Harrison, L. W. *J. Am. Chem. Soc.* **1984**, *106*, 4218; (d) Wendt, B.; Ha, H. R.; Hesse, M. *Helv. Chim. Acta* **2002**, *85*, 2990; (e) Carlsson, B.; Singh, B. N.; Temciuc, M.; Nilsson, S.; Li, Y. L.; Mellin, C.; Malm, J. *J. Med. Chem.* **2002**, *45*, 623, and references cited therein; (f) Kwiecien, H.; Baumann, E. *J. Heterocycl. Chem.* **1997**, 1587.

[38] Longicaudatin: (a) Joshi, A. S.; Li, X.-C.; Nimrod, A. C.; ElSohly, H. N.; Walker, L. A.; Clark, A. M. *Planta Med.* **2001**, *67*, 186; for related natural products, see: (b) Sigstad, E.; Catalan, C. A. N.; Diaz, J. G.; Herz, W. *Phytochemistry* **1993**, *33*, 165; (c) Drewes, S. E.; Hudson, N. A.; Bates, R. B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2809.

[39] Tovophenone C: (a) Seo, E.-K.; Wall, M. E.; Wani, M. C.; Navarro, H.; Mukherjee, R.; Farnsworth, N. R.; Kinghorn, A. D. *Phytochemistry* **1999**, *52*, 669; vismiaguianone C: (b) Seo, E.-K.; Wani, M. C.; Wall, M. E.; Navarro, H.; Mukherjee, R.; Farnsworth, N. R.; Kinghorn, A. D. *Phytochemistry* **2000**, *55*, 35; piperaduncin B: (c) Joshi, A. S.; Li, X.-C.; Nimrod, A. C.; ElSohly, H. N.; Walker, L. A.; Clark, A. M. *Planta Med.* **2001**, *67*, 186; see also: (d) Bohlmann, F.; Zdero, C. *Chem. Ber.* **1976**, *109*, 1436; sessiliflorol A: (e) Chan, J. A.; Shultis, E. A.; Carr, S. A.;

DeBrosse, C. W.; Eggleston, D. S. *J. Org. Chem.* **1989**, *54*, 2098; sessiliflorol B: (f) Marston, A.; Zagorski, M. G.; Hostettmann, K. *Helv. Chim. Acta* **1988**, *71*, 1210; (g) Drewes, S. E.; Hudson, N. A.; Bates, R. B.; Linz, G. S. *Tetrahedron Lett.* **1984**, *25*, 105; flemistrictin E: (h) Subrahmanyam, K.; Rao, J. M.; Vemuri, V. S. S.; Babu, S. S.; Roy, C. P.; Rao, K. V. J. *Ind. J. Chem. Sect. B* **1982**, *21*, 895.

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

[41] (a) Anstead, G. M.; Wilson, S. R.; Katzenellenbogen, J. A. *J. Med. Chem.* **1989**, *32*, 2163. (b) Hajela, K.; Kapil, R. S. *Ind. J. Chem., Sect. B* **1995**, *34*, 361. (c) McDevitt, R. E.; Malamas, M. S.; Manas, E. S.; Unwalla, R. J.; Xu, Z. B.; Miller, C. P.; Harris, H. A. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3137. (d) Jin, H. A; Mi, S.S; Sun, H. J. ; Seung, K. K.; Kwang, R. K.; Sang, D. R.; Won, H. J.; Sung, D. Y.; Seung, J. K.; Joo, R. W.; Jeong, H. L.; Hyae, G. C. ; Sung, S.K. *J. Med. Chem.* **2006,** *49,* 4781.

[42] Weitz, E.; Scheffer, A. *Chem. Ber.* **1921**, *54*, 2343.

[43] Bergmann, J. *J. Org. Chem.* **1956**, *21*, 461.

[44] Frank, R. L.; Eklund, H.; Richter, J. W.; Vanneman, C. R.; Wennerberg, A. N. *J. Am. Chem. Soc.* **1944**, *66*, 1.

[45] Beringer, F. M.; Forgione, P. S.; Yudis, M. D. *Tetrahedron* **1960**, *8*, 49.

[46] Koelsch, F. *J. Am. Chem. Soc.* **1932**, *54*, 2487.

[47] Jeffrey, J. L.; Sarpong, R. *Org. Lett.* **2009**, *11*, 5450.

[48] (a) Morimoto, T.; Yamasaki, K.; Hirano, A.; Tsutsumi, K.; Kagawa, N.; Kakiuchi, K.; Harada, Y.; Fukumoto, Y.; Chatani, N.; Nishioka, T. *Org. Lett.* **2009**, *11*, 1777. For a classic synthesis of 2,3-diphenyl-1*H*-inden-1-one starting with diphenyl acetylene, see: (b) Eisch, J. J.; Kaska, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 2976.

[49] (a) Liebermann, C. *Chem. Ber.* **1898**, *31*, 2083. (b) Liebermann, C. **1899**, *32*, 261. (c) Liebermann, C. *Chem. Ber.* **1899**, *32*, 920. (d) Liebermann, C. *Chem. Ber.* **1900**, *33*, 569. (e) Simonis, H.; Kirschten, C. Chem. Ber. **1912**, *45*, 567.

[50] Basurto, S.; Garcia, S.; Neo, A. G.; Torroba, T.; Marcos, C. F.; Miguel, D.; Barbera, J.; Blanca Ros, M.; de la Fuente, M. R. *Chem. Eur. J.* **2005**, *11*, 5362.

[51] Handy, S. T.; Zhang, Y. *Chem. Commun.* **2006**, 299.