Synthesis of Functionalized Benzofurans, Diaryl-Substituted 1,2,3,4-Tetrahydro-9,10-Anthracen-1-ones, 5,10-Diaryl-11*H*-benzo[*b*]fluoren-11-ones, Benzothieno[3,2-*b*]quinolines, Thieno[3,2-*b*]pyrroles, Benzofuro[3,2-*b*]quinolines, and Furo[3,2-*b*]quinolines by Regioselective Palladium(0)-Catalyzed Cross-Coupling and Domino C-N Coupling/Annulation Reactions

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Affectionately Dedicated to My dearest Father and Mother for their exceptional love. Also, to my loving brothers and sisters for their cares and support.

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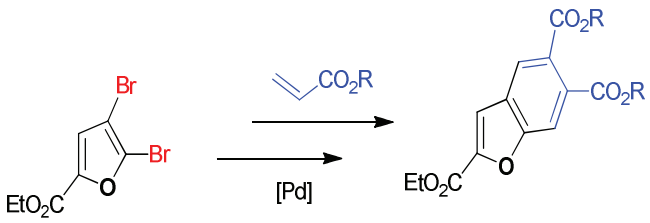
Ghazwan Ali Salman

August 2011, Rostock,

Germany

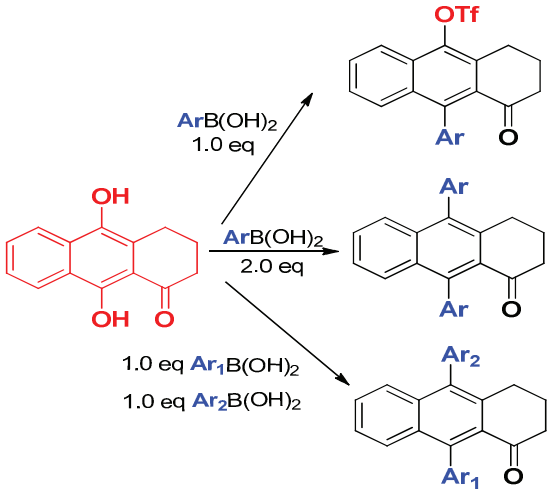
MAIN CONTENTS

Synthesis of Functionalized Benzofurans by Double Heck Reactions of 2,3-dibromo-5-(ethoxycarbonyl)furan and subsequent 6π-Electrocyclization / Dehydrogenation

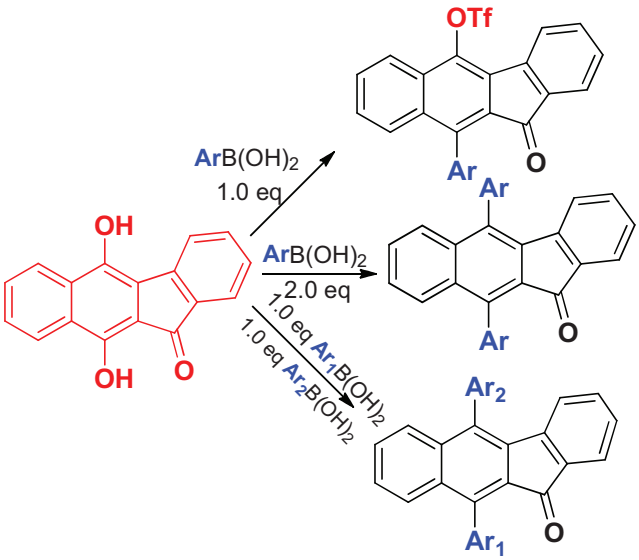


The palladium(0)-catalyzed Heck cross-coupling reactions of 2,3-dibromo-5-(ethoxycarbonyl) furan provided functionalized 2,3-di(alkenyl)-5-(ethoxycarbonyl)furans by domino 'twofold Heck / 6π electrocyclization.The products were transformed to the corresponding functionalized benzofurans.

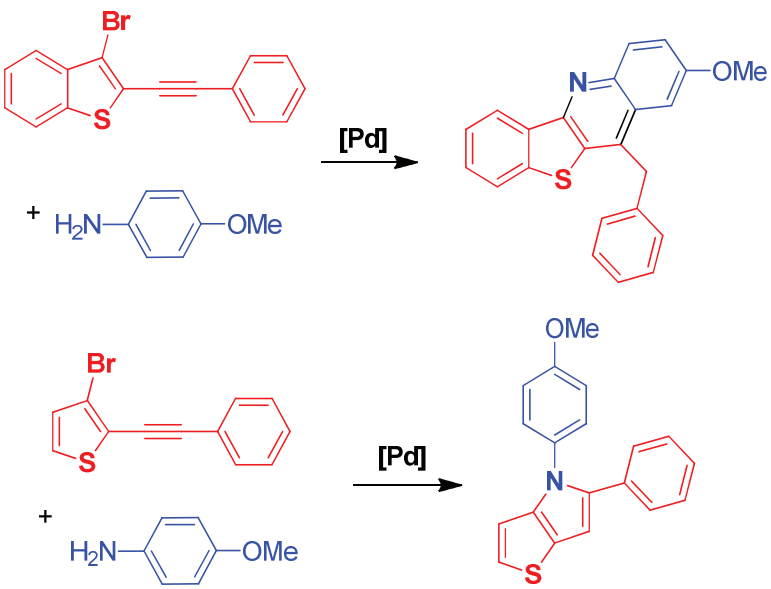
Regioselective Suzuki-Miyaura Reactions of the Bis(triflate) of 1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-one



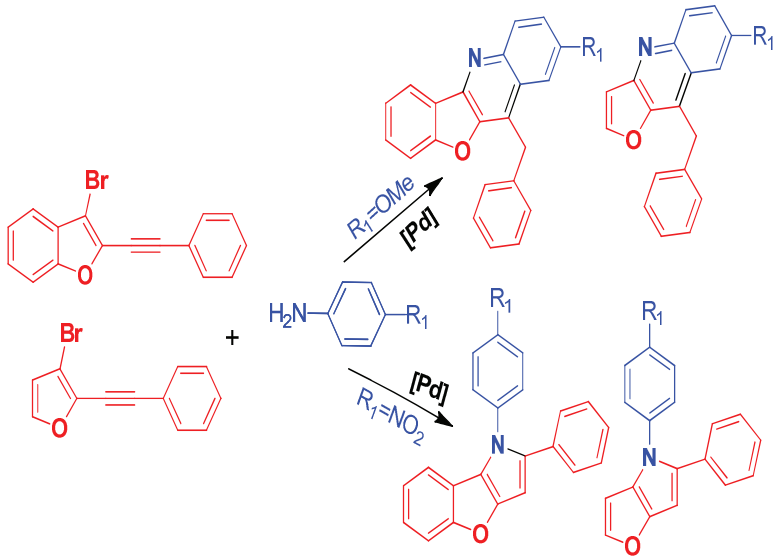
Suzuki-Miyaura cross coupling reactions of the bis(triflate) of 1,2,3,4 tetrahydro-9,10-dihydroxyanthracen-1-one was proceeded with different arylboronic acids to give mono- and diaryl 1,2,3,4-tetrahydro-9,10-dihydroxyanthracen-1-one. The reaction proceeded with very good site-selectivity in favour of position 10, due to electronic reasons.



The Suzuki-Miyaura reaction of the bis(triflate) of 5,10-dihydroxy-11*H*-benzo[*b*]fluoren-11-one with aryl boronic acids gave 5,10-diaryl-11*H*-benzo[*b*]fluoren-11-ones. The reaction with one equivalent of arylboronic acids resulted in site-selective attack at the more hindered and more electronically deficient carbon atom at C-10 and two different aryl groups were prepared by sequential addition of two different aryl boronic acids.



While the palladium catalyzed reaction of 2-alkynyl-3-bromothiophenes with anilines afforded thienopyrroles by a domino C-N coupling / hydroamination process, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines resulted, under identical conditions, in the formation of benzothienoquinolines by a domino C-N coupling / annulation process. The electronic character of the aniline has an influence on the product distribution.



The reaction of 2-alkynyl-3-bromofuran and 2-alkynyl-3-bromobenzofurans with electron rich anilines afforded Furo[3,2-*b*]quinolines and Benzofuro[3,2-*b*]quinolones, respectively by a domino C-N coupling / annulation process, but with anilines containing strong π-acceptor substituents the both substrates afforded Furo[3,2-b]pyrrole and benzofuro[3,2-b]pyrroles, respectively by a domino C-N coupling / hydroamination process.

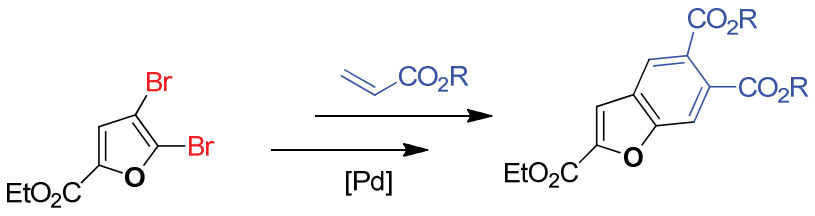
DETAILED CONTENTS

Summary and Task of the Thesis

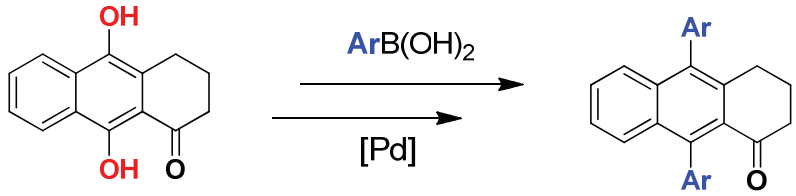
Most of the work mentioned here has already been published in reputed journals (see list of publications). This thesis can be summarized as follows:

The task of this thesis was to synthesize a new diversely substituted heterocycles and aromatic carbacycles by metal catalyzed C-C bond formation, and domino C-N coupling/ annulation or hydroamination reactions. Palladium-catalyzed transformations have especially attracted the attention of chemists and have been used extensively in organic synthesis of a number of natural products, pharmaceutical drugs and advanced materials. The aim of this work is to enhance the scope of palladium catalyzed reactions. In recent years, site-selective palladium(0) catalyzed cross-coupling reactions of dihalogenated molecules or the corresponding triflates have been studied. In this thesis I have studied the site-selectivity of palladium(0)-catalyzed Suzuki cross-coupling of the bis(triflates) of anthracenone and benzofluorenone and, in this context, steric and electronic parameters have been investigated. Also I have synthesized functionalized benzofurans by twofold Heck reactions. In addition, I had the task to study the palladium catalyzed C-N coupling/ annulation and C-N coupling/ hydroamination of various types of heterocycles. Although a diverse set of substrates were studied, the general topic of this thesis was to develope new applications of palladium(0)-catalyzed reactions of dihalogenated substrates or their triflate analogues.

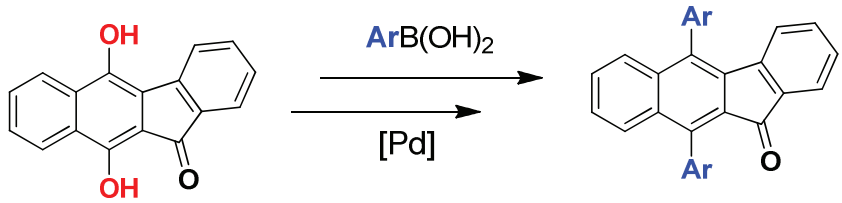
In continuation of related work in our group, I had the task to apply the concept of 'twofold Heck' reaction of 2,3-dibromo-5-(ethoxycarbonyl)furan and subsequent domino 6π-electrocyclization/dehydrogenation reactions, to give functionalized benzofurans.



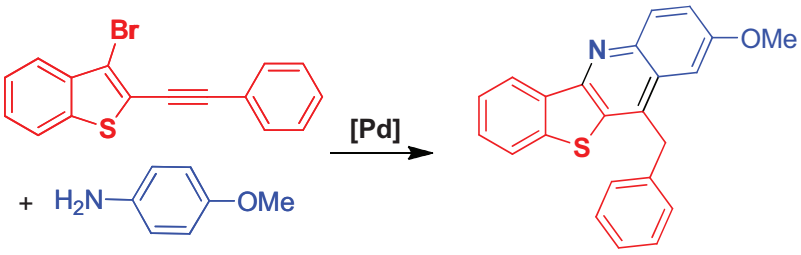
Another task was to study regioselectivity palladium(0) catalyzed Suzuki-Miyaura cross-coupling reactions of the bis-triflate of 1,2,3,4-tetrahydro-9,10-dihydroxyanthracen-1-one. These reactions afforded various aryl-substituted 1,2,3,4-tetrahydroanthracen-1-ones with very good site-selectivity in favour of position 10, due to electronic reasons.

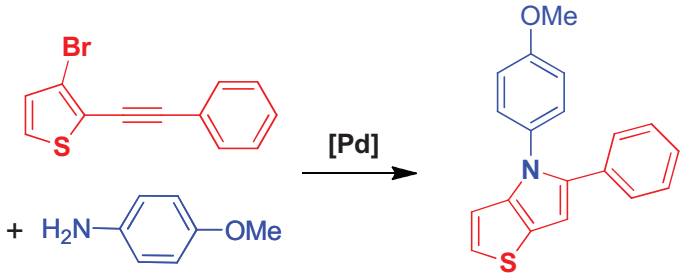


In the same context, I had another task to study also the regioselectivity Suzuki-Miyaura cross-coupling reaction of the bis-triflate of 5,10-dihydroxy-11*H*-benzo[b]fluoren-11-one. These reaction proceed with excellent site-selectivity to afford 5,10-Diaryl-11*H*-benzo[b]fluoren-11-one. The first attack occurs at position 10, due to also electronic reasons.

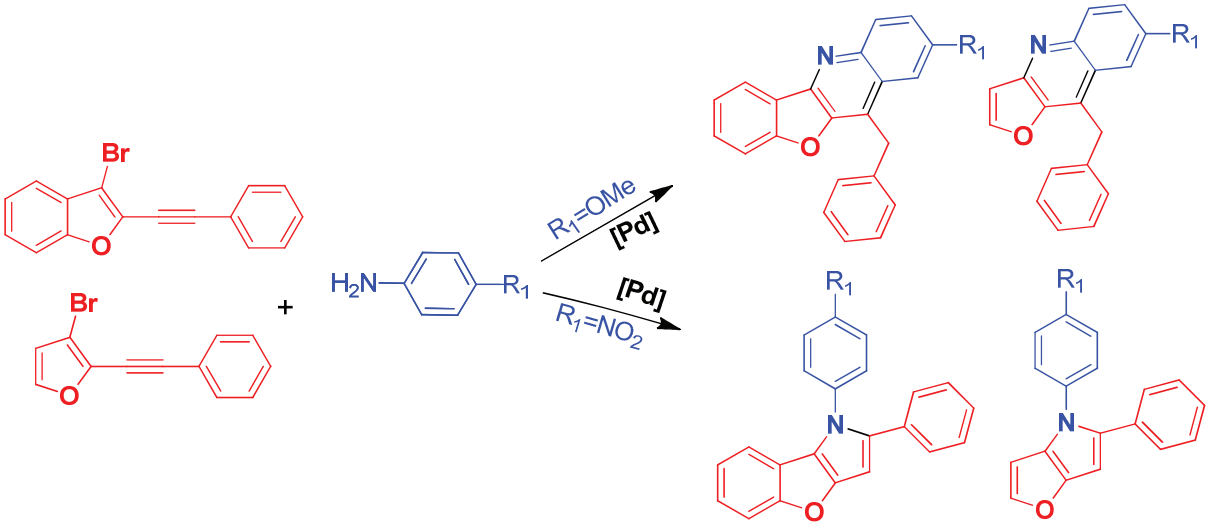


In the course of Prof. Langer's program directed towards the development of new regioselective palladium catalyzed coupling reactions of dihalogenated heterocycles, I have studied the reaction of 2-alkynyl-3-bromothiophenes and 2-alkynyl-3-bromobenzothiophenes with anilines. The reaction of 2-alkynyl-3-bromothiophenes with anilines afforded, as expected, thienopyrroles by a domino C-N coupling / hydroamination process. In contrast, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines surprisingly resulted in the formation of benzothienoquinolines by a domino C-N coupling / annulation process. This type of palladium catalyzed domino reaction has not been previously reported and provides a convenient approach to pharmacologically relevant molecules which are not readily available by other methods.





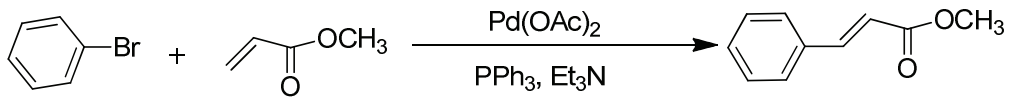
Due to the importance and novelty of this type of palladium catalysed domino reaction, I have studied and applied it to other heterocycles like furan and benzofuran. The reaction of 2-alkynyl-3-bromobenzofurans and 2-alkynyl-3-bromofuran with anilines containing electron donating substituents afforded benzofuro[3,2-*b*]quinolones and furo[3,2-*b*]quinolines, respectively by a domino C-N coupling / annulation process, in contrast, the reaction with anilines containing strong π-acceptor substituents afforded benzofuro[3,2-b]pyrroles and furo[3,2-b]pyrrole, respectively by a domino C-N coupling / hydroamination reaction.These reactions provide a convenient approach to pharmacologically relevant molecules which are not readily available by other methods.

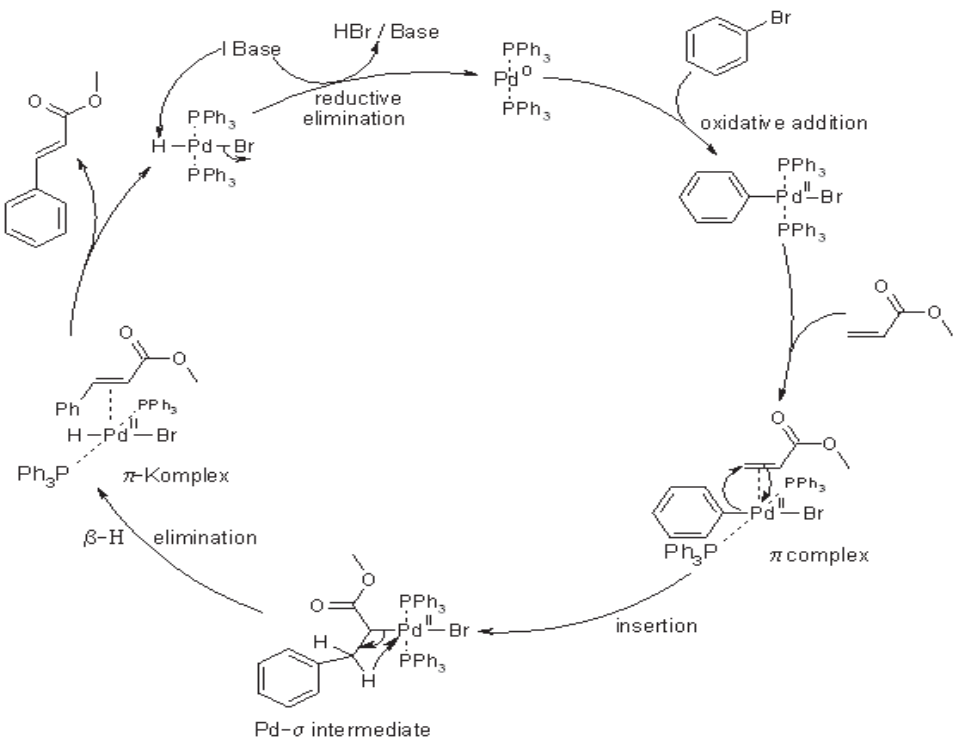


1 Synthesis of Functionalized Benzofurans by Double Heck Reactions of 2,3-dibromo-5-(ethoxycarbonyl)furan and subsequent 6π-Electrocyclization / Dehydrogenation

1.1 General Introduction

Total synthesis has benefited enormously from the Heck reaction, which has been widely applied in both its intermolecular and intramolecular variants. The enabling attributed of this remarkable reaction manifest themselves in many ways, including polyene construction, fragment coupling, and ring-closure reaction.[1] The Heck reaction was widely used as a key step in the total synthesis of natural products, for the preparation of polymers, pharmaceuticals, and hydrocarbons.[2] The Heck reaction is the palladium catalyzed C-C coupling between aryl halides or vinyl halides with activated alkenes in the presence of palladium(0) catalyst and a base.[3] Palladium(II) acetate or Palladium(II) chloride in combination with different ligands, such as triphenyl phosphine (PPh_3), S-Phos, X-Phos, tricyclohexylphosphine (PCy_3), or 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), were used in this reaction. Phosphine ligands stabilize the palladium in its oxidation state zero in the form of stable PdL_4 or PdL_3 species. There are many choices of base used in this reaction, such as triethylamine, diisoproylamine, potassium carbonate, sodium acetate.[4] The reactivity depends on the substituted olefins: more substituted olefins resulted slower reaction. However, electron poor olefins provided higher yields (electron withdrawing groups such as ester, carboxylic acid, nitriles, located at the olefin). The type of leaving group also plays an important role. The reactivity order is I > Br > Cl.[5] The mechanism of the Heck reaction involves the oxidative addition, migratory insertion of the olefins and then β-hydride elimination. The major steps of the general and traditional mechanism for the Heck reaction are depicted in Scheme 1. [6]





Scheme 1: General mechansim for the Heck reaction (picture was taken from *Tetrahedron*, **2005**, *61*, 11771-11835).

In a couple of years, Prof. Langer's research group has extensively studied twofold Heck cross coupling reactions of 2,3-dibromobenzofuran (**a**), [8] 2,3-dibromothiophene (**b**), [9] 2,3-dibromo-N-methylindole (**c**), [10] 2,3-dibromobenzothiophene (**d**), [11] 2,3-dibromoindenone (**e**), [12] 2,3-dibromo naphthaquinone (**f**) [13] (Figure 1). The electrocyclization and dehydrogenation of Heck products provided, upon heating in the presence of Pd/C a variety of aromatized products.

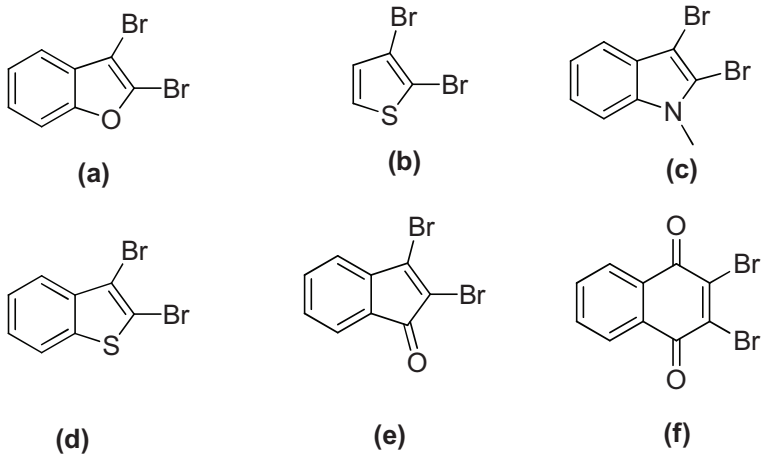


Figure 1. Heck Reaction Studies on vicinal dibromide in Prof Langer's group

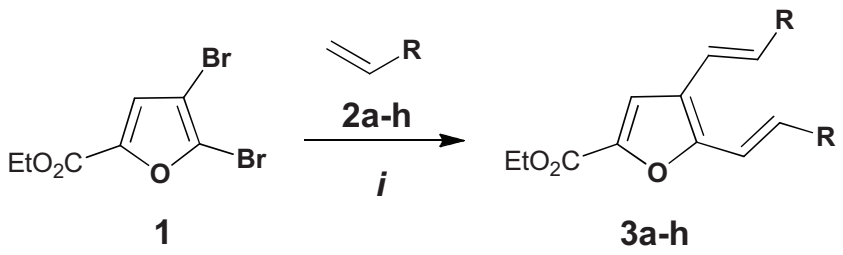
1.2 Introduction

Benzofurans are of considerable pharmacological relevance in medicinal chemistry and occur in many natural products. For example, amiodarone represents a synthetic antiarrythmic and antianginal drug.[14] The core structures of 7-alkanoylbenzofurans and 7-alkanoyl-2,3-dihydrobenzofurans are present in a number of natural products (e. g., longicaudatin,[15] the sessiliflorols A and B, flemistrictin E, tovophenone C, vismiaguianone C or piperaduncin B).[16] Due to the pharmacological relevance a number of syntheses of benzofurans have been reported. Caccihi *et al*. reported the construction of the Benzo[b]furan and furan rings by palladium-catalyzed coupling of terminal alkynes with o-iodophenols.[17] Willis *et al*. demonstrated that the combination of $pd(dba)_3$ and DPEphos generates an effective catalyst for the intramolecular O-arylation of enolates, allowing C_2-haloaryl ketones to be efficiently converted to benzofurans [18]. Polyhalogenated molecules represent interesting substrates in palladium(0)-catalyzed cross-coupling reactions [19,20]. Bach and Krüger reported Sonogashira and Stille reactions of 2,3-dibromofuran [21]. These reactions proceed with very good site-selectivity in favour of position **2**. De Meijere and coworkers reported that the combination of twofold Heck reactions with 6π-electrocyclizations provide a convenient approach to various carbocycles [22]. In recent years, Prof. Langer's group studied the application of this methodology to heterocyclic systems.[23] In this thesis I have studied the double Heck reactions of 2,3-dibromo-5-(ethoxycarbonyl)furan and subsequent 6π-electrocyclization and dehydrogenation. This methodology provides a convenient approach to benzofurans containing substituents located at positions 5 and 6 which are not readily accessible by electrophilic substitution reactions.

1.3 Results and Discussion

The Heck reaction of 2,3-dibromo-5-(ethoxycarbonyl)furan (**1**) with acrylates and styrenes **2a-h** (2.5 equiv.) afforded the 2,3-di(alkenyl)furans **3a-h** in good yields (Scheme 2, Table 2). The reaction was thoroughly optimized for derivatives **3b** and **3f** (Table 1). The best yields were obtained when the reactions were carried out using $Pd(OAc)_2$ (5 mol-%) and the biaryl monophosphine ligands SPhos or XPhos (10 mol-%) which were recently developed by Buchwald and co-workers (Figure 2) [24]. The employment of $Pd(PPh_3)_4$ resulted in considerably lower yields. The reactions were carried out in DMF at (100°C, 24h).

Figure 2. Biaryl monophosphine ligands developed by Buchwald and coworkers [24]



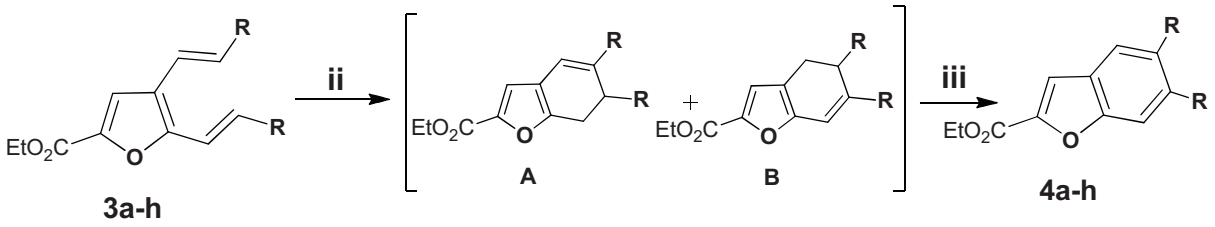
Scheme 2. Synthesis of **3a-h**. Conditions: *i*, **2a-h** (2.5 equiv.), $Pd(OAc)_2$ (5 mol-%), SPhos or XPhos (10 mol-%), NEt_3, DMF, 100 °C, 24 h.

My next target was to find suitable conditions for 6π-electrocyclization. In fact, dialkenylfurans **3** proved to be rather reluctant to undergo the desired transformation. Stirring of a diphenyl ether solution of **3a-h** for 12 h at 170 °C was required to induce the desired electrocyclization. To the reaction mixture was added Pd/C (10 mol-%) and the mixture was stirred for additional 12 h at 170 °C to give benzofurans **4a-h** by dehydrogenation. Heating of **3c** resulted in decomposition of the *tert*-butyl ester moiety. This might be due to the decomposition of tertiary butyl ester at high temperature (170 °C).

Table 1. Optimization of the reaction conditions for the synthesis of **3b,f**

Entry	Catalyst	% (**3b**)[a]	% (**3f**)[a]
1	$Pd(PPh_3)_4$ (5 mol-%)	40	45
2	$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%)	76	78
3	**$Pd(OAc)_2$ (5mol-%), SPhos (10 mol-%)**	**85**	**84**
4	$Pd(OAc)_2$ (3 mol-%), $P(Cy)_3$ (6 mol-%)	60	51
5	$Pd(OAc)_2$ (2 mol-%), triethanolamine[b]	tracs	traces

[a] Yields of isolated products; all reactions were carried out in DMF using NEt_3 as the base (100 °C); [b] triethanolamine was used as solvent, base and ligand.



Scheme 3. Synthesis of **4a-h**. Conditions: *ii*, Diphenyl ether, 170 °C, 12h; *iii*, Pd/C (10 mol-%), diphenyl ether, 170 °C, 12 h.

Table 2. Synthesis of **3a-h** and **4a-h.**

2	**3,4**	R	% (**3**) [a]	% (**4**) [a]
a	**a**	CO_2*i*Bu	81	95
b	**b**	CO_2*n*Hex	85	97
c	**c**	CO_2*t*Bu	83	[b]
d	**d**	CO_2*i*Oct	85	88
e	**e**	CO_2*n*Bu	88	90
f	**f**	CO_2Me	84	93
g	**g**	CO_2Et	90	94
h	**h**	4-ClC_6H_4	83	90

[a] Yields of isolated products; [b] decomposition

It was mentioned above that Sonogashira and Stille reactions of 2,3-dibromofurans are known to proceed with excellent site-selectivity in favour of position 2. The site-selectivity of palladium(0)-catalyzed reactions of polyhalogenated substrates is generally controlled by steric and electronic effects. More electron-deficient carbon atoms are usually more reactive than electron-rich atoms. However, all attempts to carry out site-selective mono-Heck reactions of **1** failed. All reactions resulted in the isolation of double-Heck products **3** and of unreacted starting material. This might be explained by a proximity effect. The first attack occurred at carbon atom C-2 of the furan. The palladium catalyst is coordinated by the alkene and the reactivity of the neighboured carbon atom C-3 might thus be increased. In case of products **3a-f** the increased reactivity of C-3 might alternatively be explained by the electron-withdrawing effect of the acrylate moiety located at carbon C-2.

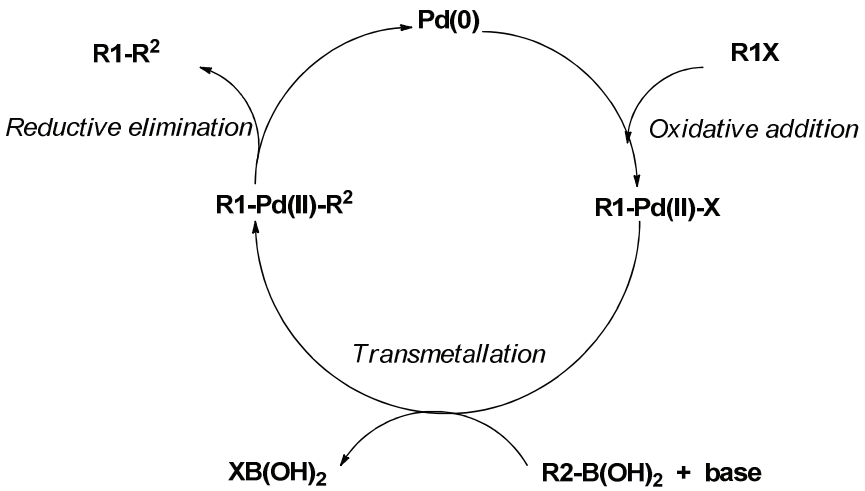
1.4 Conclusion

In conclusion, I have synthesized functionalized benzofurans based on twofold Heck reactions of 2,3-dibromo-5-(ethoxycarbonyl)furan and subsequent domino ′6π-electrocyclization / dehydrogenation′ reactions. The products are not readily available by other methods.

2 Regioselective Suzuki-Miyaura Reactions of the Bis(triflate) of 1,2,3,4-Tetrahydro-9,10 dihydroxyanthracen-1-one

2.1 General Introduction

The Suzuki-Miyaura cross-coupling reaction is one of the most important and highly utilized reactions in organic synthetic process for the construction of C-C bonds, with applications in polymer science as well as in the fine chemicals and pharmaceutical industries. The Suzuki reaction involve the reaction of an aryl- or vinyl-boronic acid with an aryl- or vinyl-halide catalyzed by a palladium(0) complex [25]. It is widely used to synthesize poly-olefins, styrenes, and substituted biphenyls; the reaction also works with pseudohalides, such as triflates (OTf), instead of halides, and also with boronic esters instead of boronic acids. Relative reactivity: I > OTf > Br >> Cl [26]. A general mechanism for the Suzuki-Miyaura cross coupling reaction of organic halides and triflates with organoboron reagents is elaborated in Scheme 4. This mechanism usually involves three steps. In the first step of the reaction, the oxidative addition of organic halides or triflates to the Pd(0) complex to form a organopalladium halide (R^1-Pd(II)-X) takes place. This step is then followed by transmetallation with a boronic acid derivative to give a diorganopalladium complex (R^1-Pd-R^2). In the final step of the reaction, this complex undergoes a reductive elimination resulting in the formation of a carbon-carbon bond and regeneration of the catalyst. Several catalysts are used for this reaction, e.g. $Pd(OAc)_2$ together with phosphine ligands (such as PPh_3, PCy_3, SPhos and XPhos), $Pd(PPh_3)_2Cl_2$, or Pd $(PPh_3)_4$ [27].



Scheme 4. Catalytic cycle of the Suzuki reaction

In a couple of years, Prof. Peter Langer's research group has studied site-selective Suzuki-Miyaura reactions of polyhalogenated heteroaromatic and aromatic compounds or their triflates. In this context, regioselective Suzuki-Miyaura reactions of 2,3-dibromoindenone (**a**) [28], 2,3-dibromobenzofuran (**b**) [29], 2,4,5,6-tetrachloropyrimidine (**c**) [30], tribromopyrazoles (**d**) [31], tetrabromobenzoquinone (**e**)[32], 2,3,5-tribromothiophene (**f**)[33], 1,4-dibromo-2-fluorobenzene (**g**) [34], 2,3,4-tribromothiophene (**h**) [35], were reported (Figure 3).

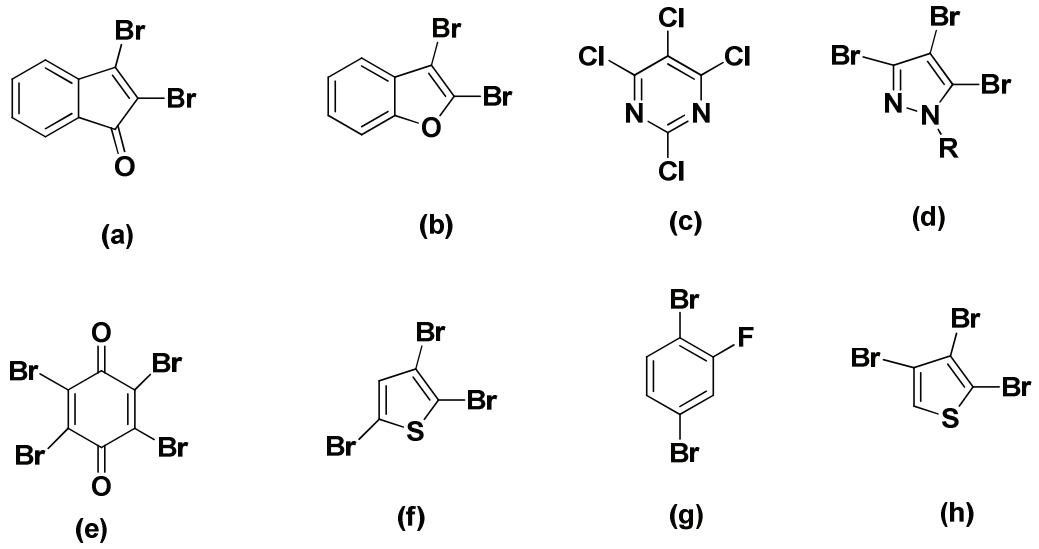


Figure 3. Suzuki reactions of vicinal halides studied in Prof. Langer's group

The Suzuki Miyaura reaction also provided excellent results for dihydroxylated substrates. Their OH groups were converted into OTf groups by using triflic anhydride and subsequently the site-selctivity of Suzuki reactions was studied. The use of aryl triflates instead of aryl halides is particularly important in organic synthesis because it can provide a way of forming a carbon-carbon bond at a phenolic site, which is often useful when appropriate halides are unavailable [36]. The Langer group reported regioselective Suzuki-Miyaura cross coupling reactions of the bis(triflates) of dimethyl 2,4-bis(hydroxyl)di-phenylsulfone (**i**) [37], 1,2-dihydroxyanthraquinone (**j**) [38], 3,4-dihydroxybenzoate (**k**) [39], 1,3-dihydroxythioxanthone (**l**) [40], 4-fluoro-3,5-dihydroxyphthalate (**m**) [41] and methyl-2,5-dihydroxybenzoate (**n**)[42] (Figure 4). All reactions of the mentioned substrates proceeded with excellent site-selectivities.

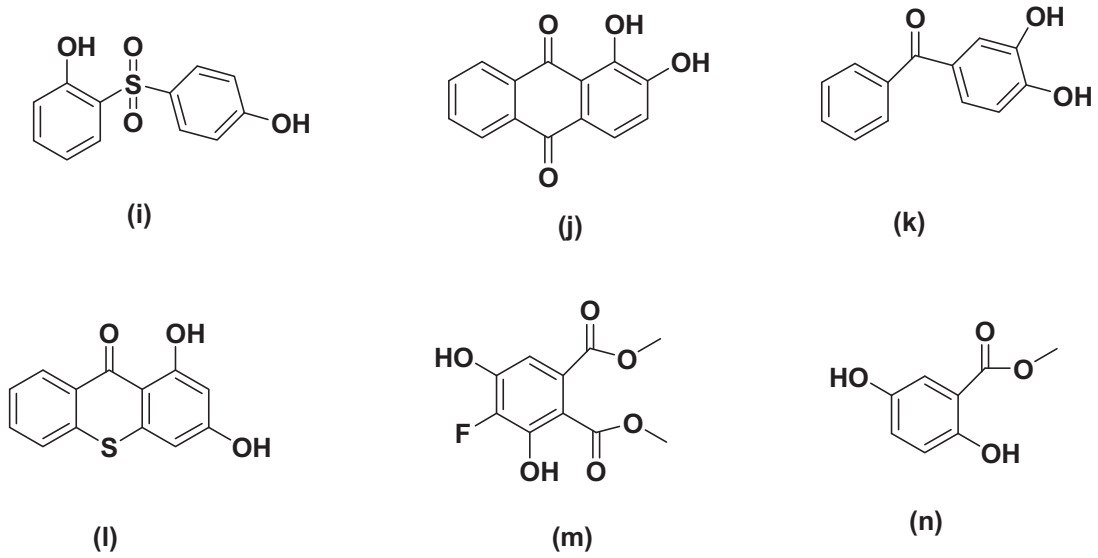


Figure 4. Suzuki Reaction Studies on dihydroxy substrate in Prof. Langer's Group

2.2 Introduction

Functionalized 1,2,3,4-tetrahydroanthracen-1-ones are of considerable pharmacological relevance and occur in various natural products [43]. Examples include the pigments atrochrysone and torosachrysone, isolated from fungi as well as higher plants, which represent key intermediates of the biosynthesis of polyketide-derived pigments (Figure 5) [44]. In fungi (genus *Cortinarius*), they serve as biosynthetic precursors of a large number of anthraquinone pigments [45]. A variety of anthracenones have also been reported to possess potent cytotoxic and anticancer activities [46-49]. For example, olivomycin A is a famous anthracenone and a member of the aureolic acid family of antitumor antibiotics. 4-Hydroxy-α-tetralones act as inhibitors of PTP1B and are considered potential drugs against obesity and type-2 diabetes.

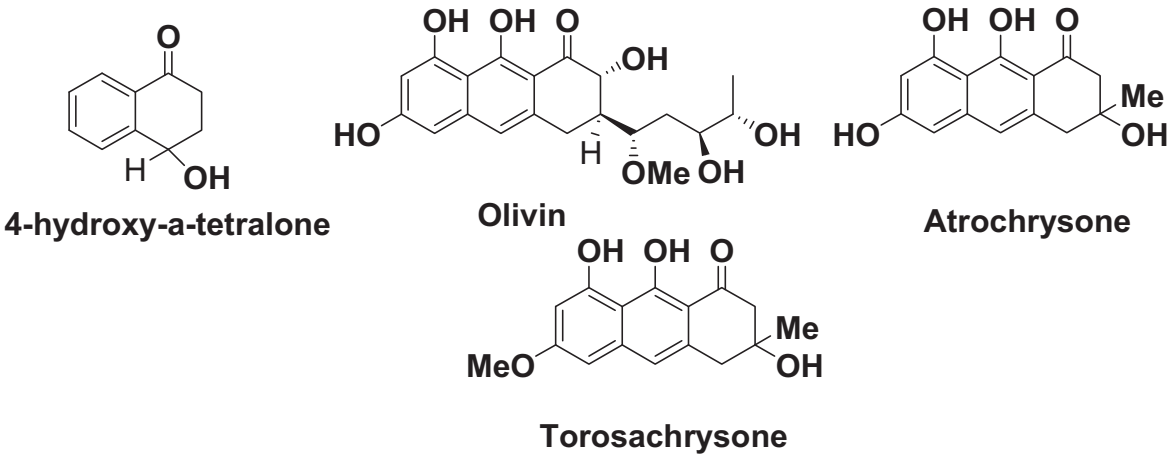
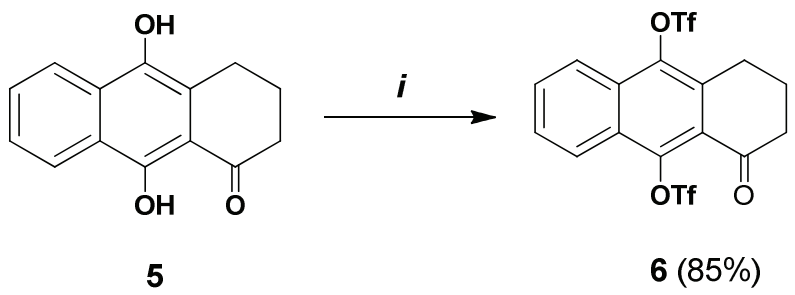


Figure 5. Tetralone and anthracenone natural products

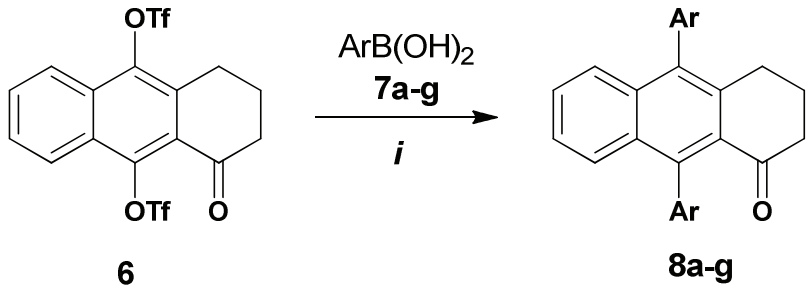
1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-one (**5**) was synthesized by Hauser annulation of 3-(phenylthio) phthalide with cyclohexenone according to ref. (50). Because of the pharmacological relevance of anthracenones, the development of new synthetic approaches is of current interest. In recent years, site-selective palladium(0) catalyzed reactions of polyhalogenated substrates have gained increasing importance [19]. In this context, Suzuki-Miyaura reactions of bis(triflates) have also been developed [51]. In my thesis I have reported a new and convenient approach to aryl-substituted 1,2,3,4-tetrahydroanthracen-1-ones by Suzuki-Miyaura reactions of the bis(triflate) of 1,2,3,4-tetrahydro-9,10-dihydroxyanthracen-1-one. The reactions proceed with very good site-selectivity which is controlled by electronic parameters. The products are not readily available by other methods.

2.3 Results and discussion

1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-one (**5**) was transformed into bis(triflate) **6** in 85% yield (Scheme 5) by using triflic anhydride (2.4 equiv) and pyridine (4 equiv). The addition of triflic anhydride was performed at -78 C^{o}. The Suzuki-Miyaura reaction of **6** with arylboronic acids **7a-g** (2.2 equiv.) afforded the novel 1,2,3,4-tetrahydro-9,10-diarylanthracen-1-ones **8a-g** in 70-90% yield (Scheme 6, Table 3). The reaction conditions were systematically optimized; the best yields were obtained when $Pd(PPh_3)_4$ (6 mol-%) was used as the catalyst and K_3PO_4 (3.0 equiv.) as the base. The reactions were carried out in 1,4-dioxane at 120 °C for 10 h. The yields dropped when $Pd(PPh_3)_2Cl_2$ (5 mol-%) or $Pd(OAc)_2$ (5 mol-%) in the presence of Xphos or $P(OEt)_2Ph$ (10mol-%) were employed. The optimized condition allowed to prepare diarylanthracenone in good yields.



Scheme 5. Synthesis of **6**. *Reagents and conditions:* (*i*) **5** (1.0 equiv), Tf_2O (2.4 equiv), pyridine (4.0 equiv), CH_2Cl_2, -78 ⟶ 20°C, 14h.



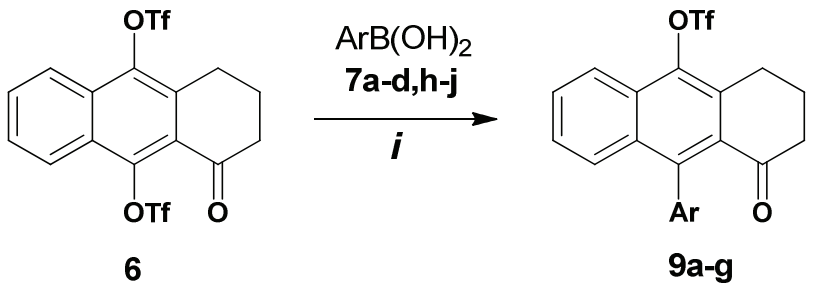
Scheme 6. Synthesis of **8a-g**. *Reagents and conditions:* (*i*), **6** (1.0 equiv), **7a-g** (2.2 equiv), $Pd(PPh_3)_4$ (6 mol-%), K_3PO_4 (3.0 equiv), 1,4-dioxane, 120 °C, 10 h.

Table 3. Synthesis of **8a-g**

7,8	Ar	%(8)[a]
a	4-(MeO)C_6H_4	75
b	4-EtC_6H_4	80
c	4-ClC_6H_4	72
d	4-MeC_6H_4	85
e	4-FC_6H_4	70
f	3-ClC_6H_4	74
g	3,5-$Me_2C_6H_3$	90

[a] Yields of isolated products.

The Suzuki reaction of **6** with arylboronic acids **7a-d,h-j** (1.0 equiv.), in the presence of $Pd(PPh_3)_4$ (3 mol-%), proceeded with very good site-selectivity at position 10 and afforded the 10-aryl-1,2,3,4-tetrahydro-9-trifluoromethyl-sulfonyloxy-anthracen-1-ones **9a-g** in 70-88% yield (Scheme 7, Table 4). During the optimization, it proved to be important to use exactly (1.0 equiv.) of the arylboronic acid and to carry out the reaction at 100 instead of 120 °C to avoid double coupling. Both electron-poor and electron-rich arylboronic acids were successfully used. The reaction conditions were systematically optimized for derivatives **9b,e** (Table 5). The best yields were obtained using $Pd(PPh_3)_4$ (3 mol-%) as the catalyst and K_3PO_4 (2 equiv.) as the base. The yields were lower when $Pd(PPh_3)_2Cl_2$ (5 mol-%) or $Pd(OAc)_2$ (5 mol-%) in the presence of Xphos, and $(EtO)_2PPh$ (10mol-%) were employed (entry 1-3).



Scheme 7. Synthesis of **9a**–**g**. *Reagents and conditions*: (i) **6** (1.0 equiv), **7a**–**d**,**h**–**j** (1.0 equiv), $Pd(PPh_3)_4$ (3 mol%), K_3PO_4 (2 equiv), 1,4-dioxane, 100 °C, 10 h.

Table 4. Synthesis of **9a**–**g**

7	**9**	Ar	% (**9**)[a]
a	**a**	4-(MeO)C_6H_4	75
b	**b**	4-EtC_6H_4	74
c	**c**	4-ClC_6H_4	70
d	**d**	4-MeC_6H_4	87
h	**e**	4-*t*BuC_6H_4	75
i	**f**	3-$CF_3C_6H_4$	73
j	**g**	2,6-$Me_2C_6H_3$	88

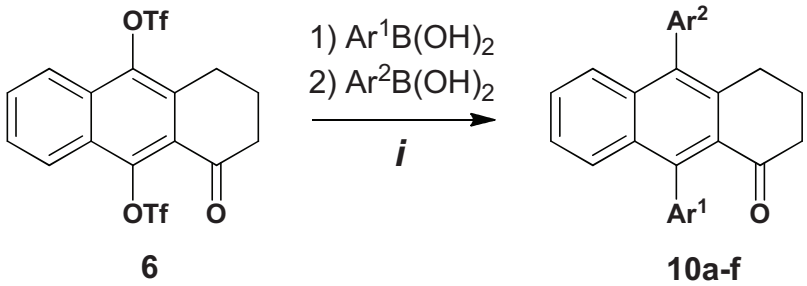
[a] Yields of isolated products.

Table 5. Optimization of the reaction condition for **9b,e**

Entry	**Conditions**	**Temp. (°C)**	**(9b)[a] %**	**(9e)[a] %**
1	$P(OEt)_2Ph$ (10mol-%), $Pd(OAc)_2$ (5mol-%), K_3PO_4	100	24	30
2	$Pd(PPh_3)_2Cl_2$(5mol-%),K_3PO_4	100	40	38
3	X-phos (10 mol-%), $Pd(OAc)_2$ (5 mol-%), K_3PO_4	100	35	32
4	$Pd(PPh_3)_4$ (3mol-%), K_3PO_4	100	74	75

a Yields of isolated products

The one-pot reaction of **6** with two different arylboronic acids, which were sequentially added, afforded the 1,2,3,4-tetrahydro-9,10-diarylanthracen-1-ones **10a-f**, containing two different aryl groups, in 70-80% yields (Scheme 8, Table 6). During the optimization it proved to be important, for the first step of the one-pot protocol, to employ exactly 1.0 equiv. of the arylboronic acid and to carry out the reaction at 100 °C.



Scheme 8. Synthesis of **10a**–**f**. *Reagents and conditions*: (i) **6** (1.0 equiv), **7a,c,d,h,i** (1.0 equiv), $Pd(PPh_3)_4$ (3 mol%), K_3PO_4 (3 equiv.), 1,4-dioxane, 100°C, 10h; (ii) **3a**,**d,f,h** (1.1 equiv), $Pd(PPh_3)_4$ (3 mol%), 120 °C, 10 h.

Table 6. Synthesis of **10a-f**

7	10	Ar^1	Ar^2	% (10)[a]
a,h	**a**	4-(MeO)C_6H_4	4-*t*BuC_6H_4	77
c,h	**b**	4-ClC_6H_4	4-*t*BuC_6H_4	75
c,a	**c**	4-ClC_6H_4	4-(MeO)C_6H_4	70
h,d	**d**	4-*t*BuC_6H_4	4-MeC_6H_4	80
i,d	**e**	3-$CF_3C_6H_4$	4-MeC_6H_4	68
d,f	**f**	4-MeC_6H_4	3-ClC_6H_4	70

[a] Yields of isolated products.

All products were characterized by spectroscopic methods. The constitutions of products **9a-g** and **10a,f** were proved by 2D NMR experiments (HMBC, NOESY). The structure of **9a** was independently confirmed by X-ray crystal structure analysis (Figure 6) [52]. Inspection of the X-ray structure shows that the anthracenone unit located in plane. The attached phenyl group is twisted out of plane, due to steric reasons.

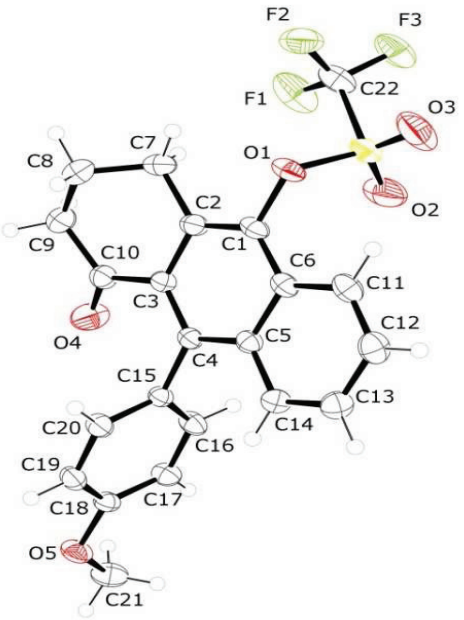


Figure 6. Molecular structure of **9a**

The structure of compound (**9a**) was also confirmed by 2D NMR spectroscopy (Figure 7). Assignments of the signals were done with the help of ^{1}H NMR, HMQC, and COSY experiments. In the NOESY spectrum, aromatic protons H-6′ and H-2′ (δ= 6.90) showed an interaction with proton H-8 (δ= 7.53). The structure was further confirmed by the HMBC correlation of H-6′ to C-10. This clear correlation proved unambiguously the connectivity of the first aryl group at C-10.

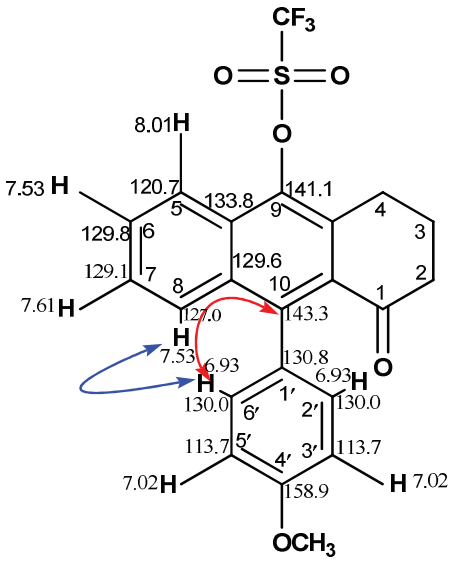
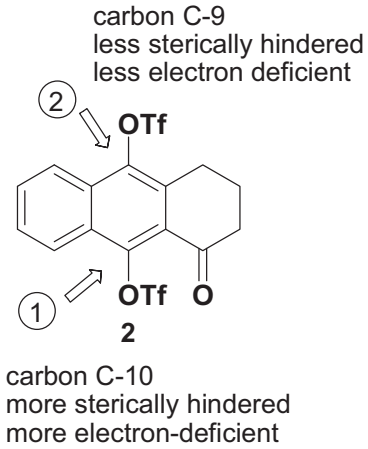


Figure 7. **HMBC** and **NOESY** correlations of **9a**

The first attack of site-selective palladium(0) catalyzed cross-coupling reactions (oxidative addition step) usually takes place at the sterically less encumbered or electronically more deficient position.[53] The regioselective formation of products **9a-g** and **10a-f** can be explained by the fact that position **10** is electronically more deficient than position **9** (Scheme 9). In addition, the regioselectivity might be controlled by chelation of the catalyst to the carbonyl group.



Scheme 9. Possible explanation for the site-selective reactions of **6**

2.4 Conclusion

I have synthesized 1,2,3,4-tetrahydro-9,10-diarylanthracen-1-ones by Suzuki-Miyaura reactions of the bis(triflate) of 1,2,3,4-tetrahydro-9,10-dihydroxyanthracen-1-one. The first attack occurred at the sterically more hindered position C-10, due to electronic reasons.

3 Site-selective Suzuki-Miyaura Reactions of the Bis(triflate) of 5,10-Dihydroxy-11*H*-benzo[*b*]fluoren-11-one

3.1 Introduction

Natural and synthetic fluorenones exhibit a broad spectrum of biological activities and also occur in many natural products. This includes, for example, dengibsin, dengibsinin, or dendroflorin isolated from the orchidee *Dendrobium gibsonii Lindl.*[54] Fluorenones are of great pharmacological importance [55]. They have been used as probes for the redox activity of DNA [56]. Amidofluorenone derivatives have been shown to act as telomerase inhibitors [57]. Kinamycin derivatives of the family of kinamycin natural products have been reported to display antitumor and antimicrobial activity against Gram-positive bacteria [58]. In recent years, new kinamycin analogues, containing a 6,6,5,6 ring system, have also been isolated. For example, kinafluorenone (**A;** Figure **8**) was found to be a major metabolite of a mutant strain of *Streptomyces murayamaensis*. The fluorenone alkaloid cauliphine (**B;** Figure **8**), which possesses anti-myocardial ischemia activity, has also been isolated from *Caulophyllum robustum* [59]. Arylated fluorenones, fluorenes and benzofluorenones along with their oligomers and polymers have been studied extensively for the development of organic light-emitting devices (OLED`s) [60]. Fluorenones are also important compounds in photochemistry [61].

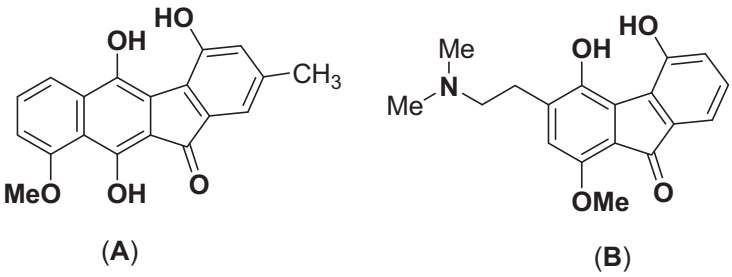


Figure 8. Fluorenone natural products: **A**: a major metabolite isolated from mutant strain of *Streptomyces murayamaensis*; **B**: Cauliphine, a fluorenone alkaloid with anti-myocardial ischemia activity.

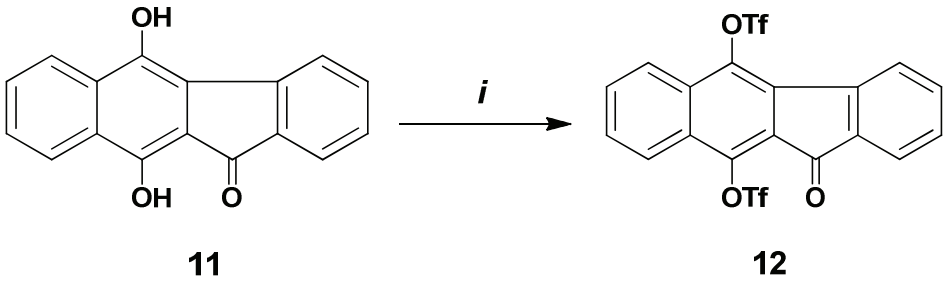
Fluorenones have been prepared by intramolecular Friedel-Crafts acylations of biaryls, [62] by [4+2]-cycloadditions of conjugated enynes, [63] by oxidation of fluorenes,[64] based on remote aromatic metalations,[65] by reaction of malonic acid dinitrile with aromatic aldehydes and methylketones,[66] by Suzuki reaction of boronic acids of benzoic acid amides with aryl triflates

and subsequent cyclization,[67] by acid-mediated intramolecular Friedel-Crafts cyclization of 2-methoxycarbonylbiaryls, and by Suzuki reactions of salicylate-derived enol triflates [68]. The Prof. Langer group have recently reported a synthetic approach to functionalized fluorenones based on formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes [69].

5,10-dihydroxy-11*H*-benzo[*b*]fluoren-11-one (**11**) was synthesized via reaction of 1-indanone dianions with phthalate diesters according to ref. (70). Due to the importance of fluorenones and benzofluorenones, the development of efficient and regioselective methods for the synthesis of aryl-substituted derivatives is of considerable current importance. In my thesis, I have developed a convenient approach to 5,10-diaryl-11*H*-benzo[*b*]fluoren-11-ones by site-selective Suzuki-Miyaura reactions of the bis(triflate) of 5,10-dihydroxy-11*H*-benzo[*b*]fluoren-11-one. These reactions provide a convenient access to products which are difficult to prepare by other methods.

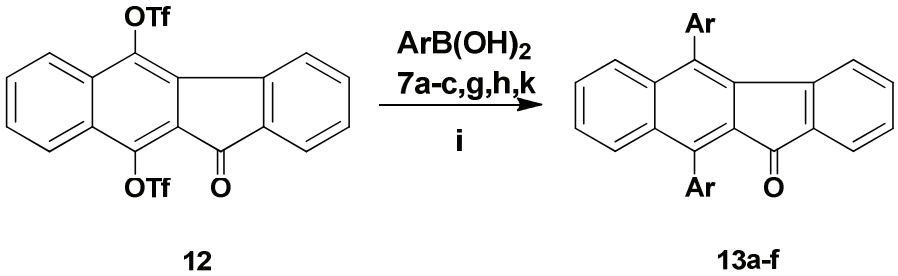
3.2 Results and discussion

The reaction of 5,10-dihydroxy-11*H*-benzo[*b*]fluoren-11-one (**11**) with triflic anhydride (2.4 equiv.) afforded the bis(triflate) **12** in 88% yield (Scheme 10).



Scheme 10. Synthesis of **12**. *Reagents and conditions*: (i) CH_2Cl_2, **1** (1.0 equiv), -78 °C, pyridine (4.0 equiv), Tf_2O (2.4 equiv), -78 °C → 20°C, 14h.

The Suzuki-Miyaura reaction of **12** with arylboronic acids **7a-c,g,h,k** (2.2 equiv.) afforded the 5,10-diaryl-11*H*-benzo[*b*]fluoren-11-ones **13a-f** in 70-85% yield (Scheme 11, Table 7). The yield of product **13c**, derived from the (less reactive) electron poor arylboronic acid **7c**, was lower than the yields of the other products. The best yields were obtained when the reactions were carried out using $Pd(PPh_3)_4$ as the catalyst and K_3PO_4 as the base and when dioxane was used as the solvent.



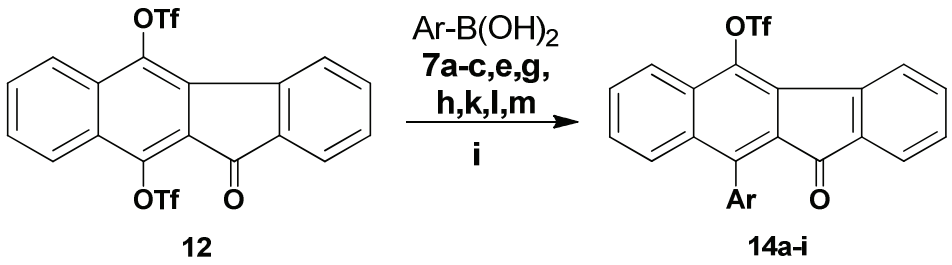
Scheme 11. Synthesis of **13a**–**f**. *Reagents and conditions*: (i) **12** (1.0 equiv), **7a**,**c,f,g,h,k** (2.2 equiv.), $Pd(PPh_3)_4$ (6 mol%), K_3PO_4 (3.0 equiv), 1,4-dioxane, 90°C, 10h.

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

7	13	Ar	Yield of 13(%)[a]
a	**a**	4-(MeO)C_6H_4	80
c	**b**	4-ClC_6H_4	70
f	**c**	3-ClC_6H_4	72
g	**d**	3,5-$Me_2C_6H_3$	85
h	**e**	4-*t*-BuC_6H_4	75
k	**f**	3-MeC_6H_4	78

[a] Yields of isolated products.

The Suzuki-Miyaura reaction of **12** with arylboronic acids **7a-c,e,g,h,k,l,m** (1.0 equiv.) afforded the 10-aryl-5-trifluoromethylsulfonyloxy-11*H*-benzo[*b*]fluoren-11-ones **14a-i** in good yields (Scheme 12, Table 8). The yields of reactions of (more reactive) electron rich arylboronic acids were higher than those of electron poor arylboronic acids. During the optimization, it proved to be important to carry out the reaction at 60 instead of 90 °C, The best yields were obtained when the reactions were carried out by using $Pd(PPh_3)_4$ (3 mol %) as a catalyst and the inorganic base K_3PO_4 in dioxane. The employment of other catalysts, such as $Pd(OAc)_2$/XPhos, $Pd(OAc)_2$/SPhos resulted in a decreased yield.



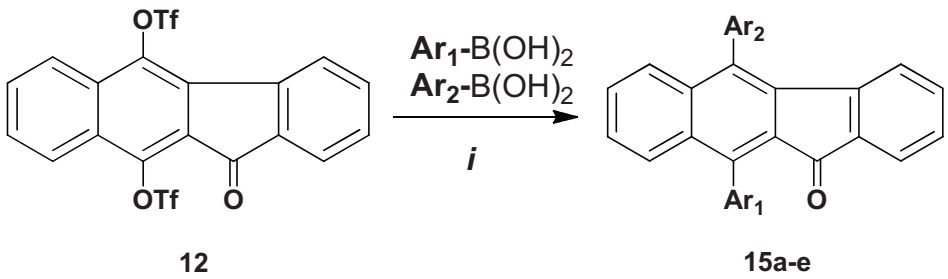
Scheme 12. Synthesis of **14a**–**i**. *Reagents and conditions*: (i) **12** (1.0 equiv), **7a**–**c,e,g,h,k,l,m** (1.1 equiv), $Pd(PPh_3)_4$ (3 mol%), K_3PO_4 (2 equiv), 1,4-dioxane, 60 °C, 10 h.

Table 8. Synthesis of **14a**–**i**

7	14	Ar	Yield of 14(%)[a]
a	**a**	4-(MeO)C_6H_4	90
b	**b**	4-Et-C_6H_4	85
c	**c**	4-ClC_6H_4	78
e	**d**	4-FC_6H_4	75
g	**e**	3,5-$Me_2C_6H_3$	87
h	**f**	4-*t*-BuC_6H_4	76
k	**g**	3-MeC_6H_4	80
l	**h**	3,4-$(MeO)_2C_6H_3$	88
m	**i**	4-$CF_3C_6H_4$	70

[a] Yields of isolated products.

The one-pot reaction of **12** with two different arylboronic acids (sequential addition) afforded the 5,10-diaryl-11*H*-benzo[*b*]fluoren-11-ones **15a-e** containing two different aryl groups (Scheme 13, Table 9). During the optimization, it proved to be important to carry out the first step of the one-pot reaction at 60 °C and the second step at 90 °C.



Scheme 13. Synthesis of **15a**–**e**. *Reagents and conditions*: (i) **12** (1.0 equiv), **7a,h,n** (1.0 equiv), $Pd(PPh_3)_4$ (3 mol%), K_3PO_4 (3 equiv.), 1,4-dioxane, 60 °C, 10h; (ii) **7g,h,k** (1.1 equiv), $Pd(PPh_3)_4$ (3 mol%), 90 °C, 10 h.

Table 9. Synthesis of **15a-e**

7	15	Ar^1	Ar^2	15(%)[a]
a,g	**a**	4-(MeO)C_6H_4	3,5-$Me_2C_6H_3$	72
n,h	**b**	3,4-$(MeO)_2C_6H_4$	4-*t*-BuC_6H_4	75
n,k	**c**	3,4-$(MeO)_2C_6H_4$	3-MeC_6H_4	77
h,g	**d**	4-*t*-BuC_6H_4	3,5-$Me_2C_6H_3$	80
n,b	**e**	3,4-$(MeO)_2C_6H_4$	4-EtC_6H_4	65

[a] Yields of isolated products.

All products were characterized by spectroscopic methods. The constitutions of products **14a-i** and **15a,f** were proved by 2D NMR experiments (HMBC, NOESY). The structure of **14a** was independently confirmed by X-ray crystal structure analysis (Figure 9) [71]. Inspection of the X-ray structure shows that the fluorenone unit is located in plane. The attached phenyl group is twisted out of plane, due to also steric reasons.

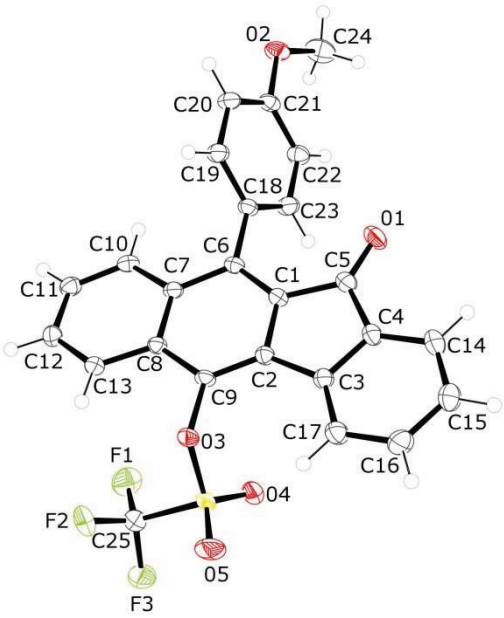


Figure 9. Crystal structure of **14a**

The structure of compound (**14e**) was unambiguously confirmed by 2D-NMR techniques. In the NOESY spectrum, an interaction was observed between the aromatic proton attached to carbon atom C-6 to the aromatic protons attached to the carbon atoms C-2′ and C-6′. This confirmed that the first attack of boronic acid takes place at carbon C-2 of the bis(triflate) (Figure 10).

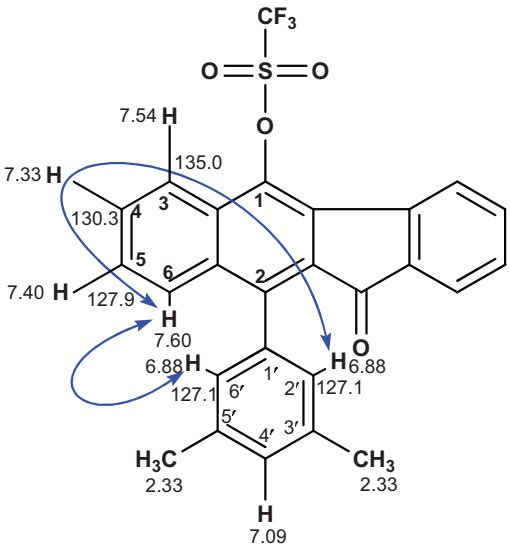
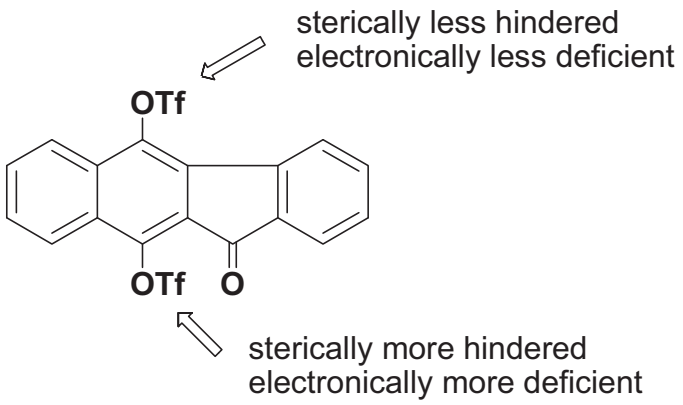


Figure 10. Relevant NOESY-correlation for Compound **14e**

As mentioned, the first attack of palladium(0) catalyzed cross-coupling reactions generally occurs at the electronically more deficient and sterically less hindered position.[53] Position 10 of bis(triflate) **12** is sterically more hindered than position 5 because of the neighbourhood of the carbonyl group (Scheme 14). Therefore, the site-selective formation of **14a-i** and **15a-e** can be explained by electronic reasons. In addition, chelation of the catalyst by the carbonyl group might play a role.



Scheme 14. Possible explanation for the site-selectivity of the reactions of bis(triflate) **12**

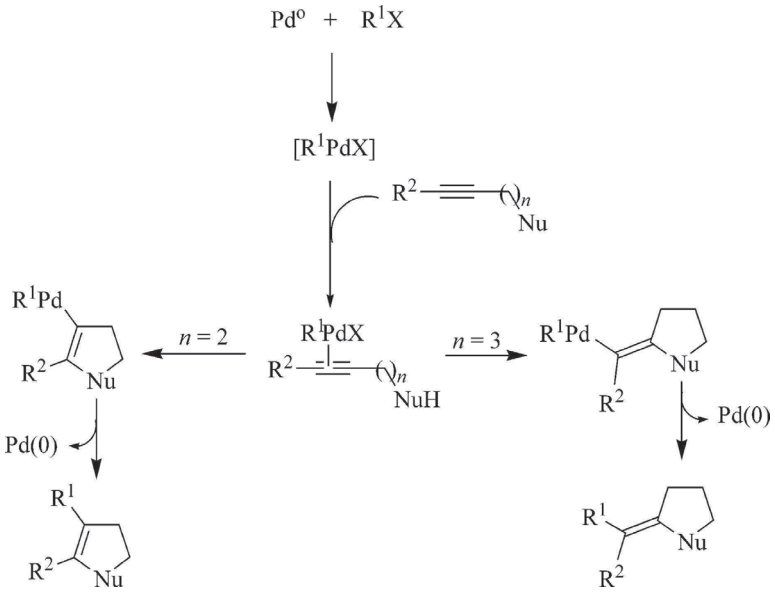
3.3 Conclusion

In conclusion, in this chapter I have reported an efficient synthesis of 5,10-diaryl-11*H*-benzo[*b*]fluoren-11-ones by Suzuki-Miyaura reactions of the bis(triflate) of 5,10-dihydroxy-11*H*-benzo[*b*]fluoren-11-one. The site-selectivity in favour of position 10 can be explained by electronic reasons.

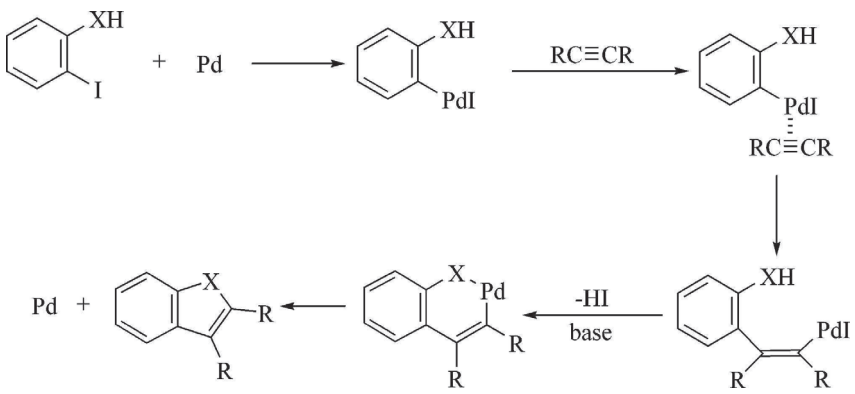
4 Domino C-N coupling / annulation *versus* C-N coupling / hydroamination of 2-alkynyl-3-bromobenzothiophenes and 2-alkynyl-3-bromothiophenes. Highly efficient synthesis of benzothieno[3,2-*b*]quinolines and thieno[3,2-*b*]pyrroles

4.1 General Introduction

Annulation reactions are among the most important processes in organic synthesis, because they rapidly generate organic structures with substantially increased molecular complexity. One of the extraordinarily useful and valuable methods for the synthesis of a wide variety of heterocycle compounds is the palladium-catalyzed cyclization of alkynes [17,72]. This catalytic annulation process can follow two distinctly different reaction pathways. If the alkyne contains an internal nucleophile, the process proceeds by coordination of the organopalladium species to the carbon-carbon triple bond, followed by regioselective addition of the aryl/vinylic palladium intermediate to the carbon-carbon triple bond of the alkyne to produce a cyclic adduct (Scheme 15). Subsequent reductive elimination produces the heterocyclic or carbocyclic product and regenerates the Pd(0) catalysts. Both *endo* and *exo* cyclization products can be obtained depending on the number of carbon atoms between the triple bond and the nucleophilic center. Alternatively, the aryl or vinylic halide may bear a neighboring nucleophile (Scheme 16). After *cis* carbopalladation of the alkyne, the internal nucleophile may effect intramolecular displacement of the palladium, most likely by prior palladacycle formation and reductive elimination. A number of examples of alkyne cyclizations and annulations of these types have been reported in the preparation of *N*- and *O*-heterocycles [72].



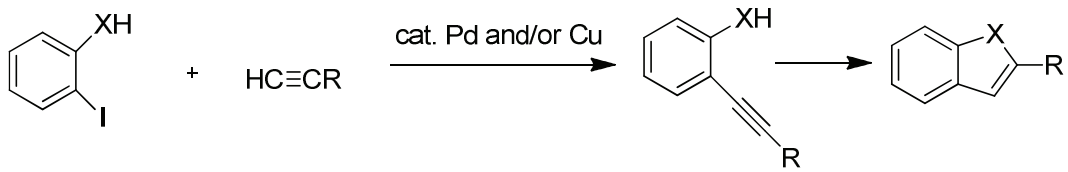
Scheme 15: Catalytic annulation when alkyne contains an internal nucleophile [73].



Scheme 16: Catalytic annulation when the aryl or vinyl halid bear a neighbouring nucleophile.

4.1.1 Annulation of Terminal Alkynes

The Sonogashira reaction has been proven to be a useful method for the synthesis of a variety of aryl alkynes or enynes by cross-coupling of aromatic or vinylic halides or triflate with alkynes using palladium and copper salts catalysts (Scheme 17).

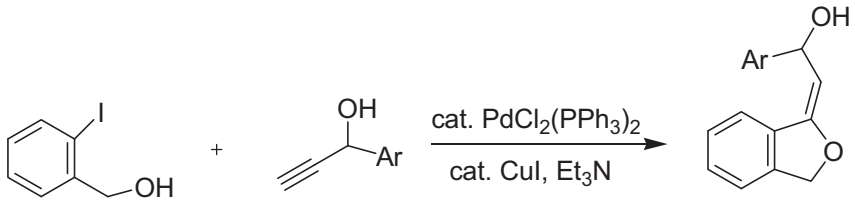


Scheme 17: Annulation reactions of terminal Alkynes

When neighboring functionalities exists in aryl alkynes or enynes, Pd and Cu salts are well known to effect cyclization to the corresponding hetero- or carbocycle. Thus, the reaction of terminal alkynes and aryl or vinylic halides bearing a neighboring functionality often leads directly to heterocycles or carbocycles, providing a particularly useful synthesis of benzofurans and indoles [74].

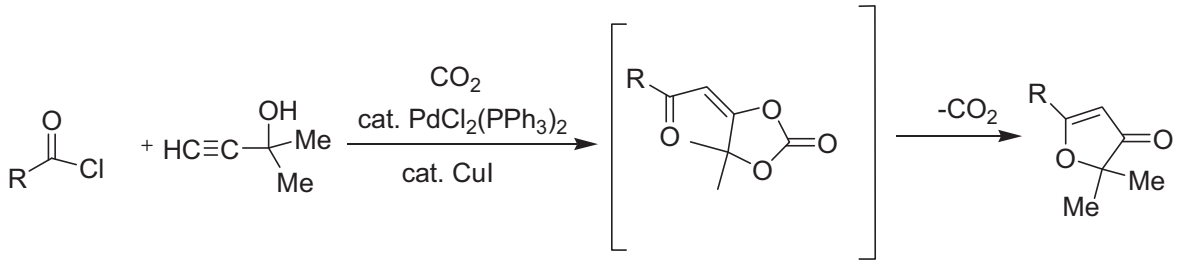
4.1.1.1 Annulation of Acetylenic Alcohols

Two examples of this type of the Pd-catalyzed annulation of terminal acetylenic alcohols are known. *o*-Iodobenzyl alcohol reacts with acetylenic carbinols in the presence of catalytic amounts of $PdCl_2(PPh_3)_2$ and CuI, and Et_3N, to produce 1-alkylidene-1,3 dihydroiso-benzofurans (Scheme 18) [75].



Scheme 18: Annulation of acetylenic alcohols with *o*-Iodobenzyl alcohol

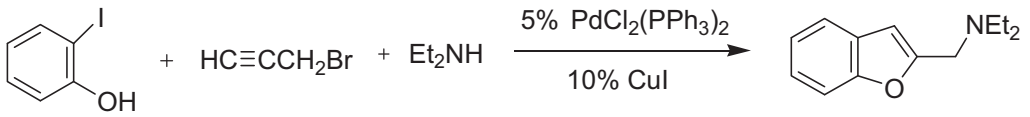
Another example is the reaction of acid halides with 2-methyl- 3-butyn-2-ol, and CO_2, using the same catalysts, to produce 3(2*H*)-furanones (Scheme 19) [76]. This reaction apparently proceeds by initial formation of a cyclic carbonate that subsequently undergoes decarboxylative rearrangement.



Scheme 19: Annulation of acetylenic alcohols with acid halide

4.1.1.2 Annulation by o-Halophenols

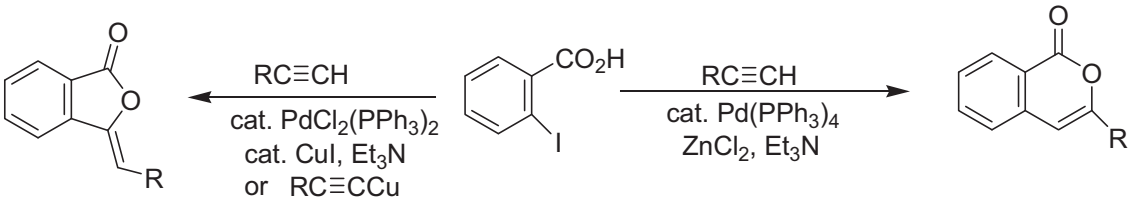
Terminal alkynes reacts with *o*-halophenols in the presence of Pd and/or Cu catalysts to provide a convenient, direct route to benzofurans. The reaction of *o*-iodophenol, propargyl bromide, and Et_2NH in the presence of the $PdCl_2(PPh_3)_2$/CuI, provides the corresponding (diethylaminomethyl)benzofuran in good yield (Scheme 20) [77].



Scheme 20: Annulation of terminal alkynes with *o*-halophenols

4.1.1.3 Annulation of Halogenated Benzoic Acids

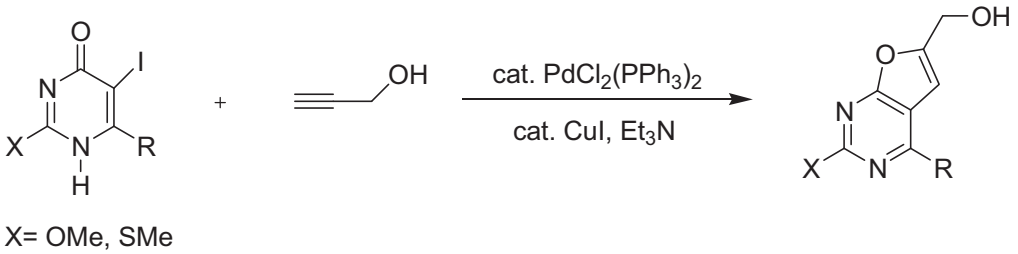
o-Halobenzoic acids react with terminal alkynes and a Pd catalyst to afford either phthalides or isocoumarins depending on the additional metal salt added to the reaction (Scheme 21). Thus, when CuI and Et_3N are added, phthalides are obtained in good yields [78]. Replacing the CuI with $ZnCl_2$ affords primarily isocoumarins [79].



Scheme 21: Annulation of terminal alkynes with *o*-halobenzoic acids

4.1.1.4 Annulation of Halogenated Amides

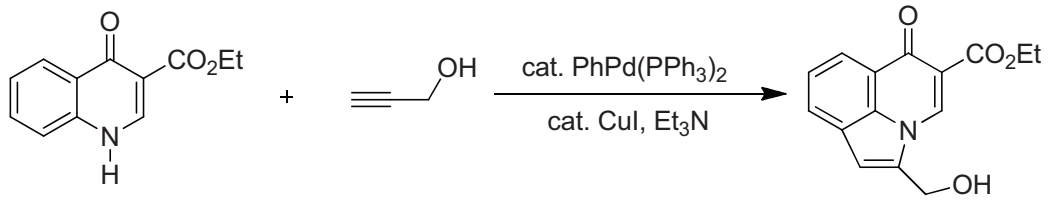
The reaction of iodopyrimidinones and propargyl alcohol in the presence of Pd/Cu has been reported to give products in which cyclization has occurred via the carbonyl oxygen (Scheme 22) [80].



Scheme 22: Annulation of propargyl alcohol with iodopyrimidinones

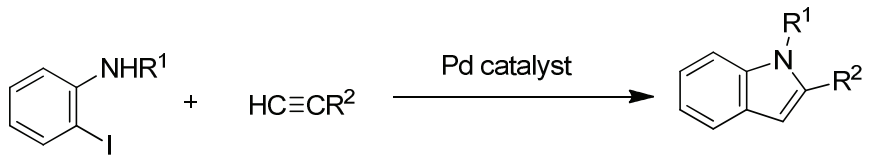
4.1.1.5 Annulation by Halogenated Amines and Derivatives

The synthesis of pyrroloquinolones by Pd-catalyzed reaction of terminal alkynes with iodoquinolones and derivatives has been reported (Scheme 23) [81].



Scheme 23: Annulation of terminal alkynes with iodoquinolones

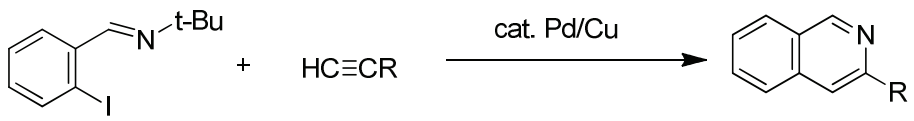
Also, *N*-benzyl-2-iodoaniline has been cross-coupled with terminal alkynes to afford the corresponding benzylindoles using a Pd zeolite catalyst (Scheme 24) [82].



Scheme 24: Annulation of terminal alkynes with *N*-benzyl-2-iodoaniline

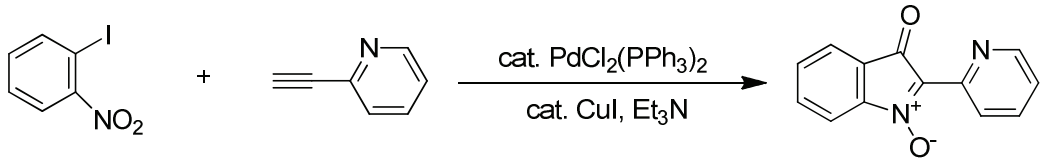
4.1.1.6 Annulation by Halogenated Imines and Nitro Derivatives

In the presence of Pd/Cu catalyst, *t*-butylimines of *o*-iodobenzaldehydes and 3-halo-2-alken-1-ones can be reacted with terminal alkynes to produce isoquinolines and pyridines in a process which apparently involves aryl alkyne formation, followed by cyclization with fragmentation of the *t*-butyl group (Scheme 25) [83].



Scheme 25: Annulation of terminal alkynes with *t*-butylimines of *o*-iodobenzaldehydes

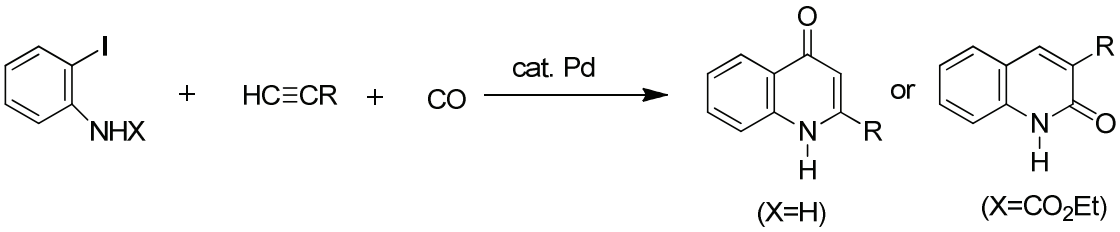
The Sonogashira coupling of 2-ethynylpyridine and *o*-iodonitrobenzene affords a nitrone directly (Scheme 26) [84].



Scheme 26: Annulation of 2-ethynylpyridine with *o*-iodonitrobenzene

4.1.1.7 Annulation by CO and Aryl Halides

4- and 2-quinolines have been obtained from terminal alkynes, CO, *o*-iodoaniline and derivatives (Scheme 27).

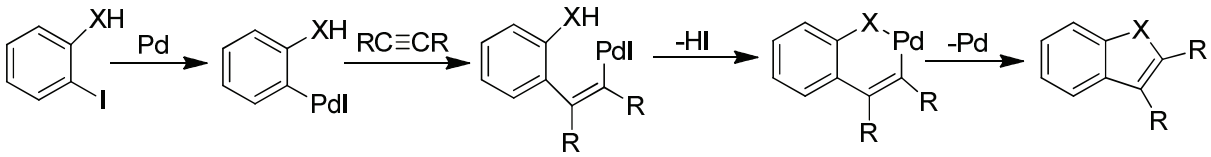


Scheme 27: Annulation of terminal alkynes with CO, and *o*-iodoaniline

Using catalytic amounts of $PdCl_2(PPh_2)3$ or $PdCl_2$(dppf), Et_2NH, and relatively high temperatures and pressures, 4-quinolones have been reported as the sole products from *o*-haloanilines [85].

4.1.2 Annulation of Internal Alkynes

A wide range of heterocycles and carbocycles are also produced by palladium-catalyzed annulation of internal alkynes with substituted aromatic or vinylic halides. The mechanism of this process appears to be quite different from the mechanism for the annulation of terminal alkynes. The reaction usually involves four steps (1) oxidative addition of the organic halide to Pd(0) to produce an organopalladium(II) intermediate, (2) subsequent insertion of the alkyne to produce a vinylic palladium intermediate, (3) cyclization to afford a palladacycle, and (4) reductive elimination to produce the cyclic product and regenerate the Pd(0) catalyst (Scheme 28) [74].



Scheme 28: Annulation of internal alkynes

The generation of the Pd(0) species in this type of organopalladium chemistry usually happens by adding a Pd(II) salt to the reaction and allowing it to suffer from reduction under the reaction conditions. The prediction of regiochemistry of the annulations of unsymmetrical alkynes usually proceeds by looking at the steric bulk of the substituents on the ends of the carbon-carbon triple bond. The addition of the Pd moiety in the organopalladium intermediate normally occurs at the more hindered end of the triple bond. The annulations of internal alkynes is consider as a very valuble route for construction of heterocycles [74].

4.2 Introduction

Nitrogen containing heterocycles are of great importance in the field of medicinal chemistry and material sciences [86]. In recent years, transition metal-catalyzed syntheses of heterocycles have been developed which nicely complement classic synthetic approaches because they proceed under mild conditions and show a high degree of chemoselectivity and functional group tolerance [87]. A variety of palladium catalyzed syntheses of indoles and carbazoles have been reported [88]. Ackermann and coworkers reported the synthesis of carbazoles and related molecules by palladium catalyzed cyclization of 1,2-dihalides with anilines by domino [89] N-H / C-H activation reactions [90]. Stepwise syntheses following this strategy have also been reported [91]. Ackermann *et al.* reported the synthesis of indoles and various other ring systems by domino N-arylation/hydroamination reactions[92]. They also developed an efficient approach to indoles by Pd- or Cu-catalyzed domino C-N coupling / hydroamination reactions of *ortho*-alkynylated aryl halides [93]. Buchwald *et al.* reported the synthesis of pyrroles and pyrazoles by a related strategy [94, 95].

Cryptolepsis sanguinolenta is a shrub found along the west coast of Africa and is still being used significantly in traditional medicine in Ghana. Its strong anti-malarial activity has been proved in clinical trials. Furthermore, it has been shown to possess a considerable antibiotic activity against gram-positive and gram-negative bacteria. Major alkaloids, cryptolepine **(A)** and quindoline **(B)**, have been isolated along with some minor alkaloids from *Cryptolepsis sanguinolenta* (Figure 11) [96].

Benzothienoquinolines are sulfur analogues of these alkaloids and represent interesting target molecules, due to their broad spectrum of antimicrobial, anticancer and cytotoxic activities. For example, benzothienoquinoline **(C)** has been reported to show antitumor activity in vivo, while derivative **(D)** possesses significant cytotoxic activity [97,98].

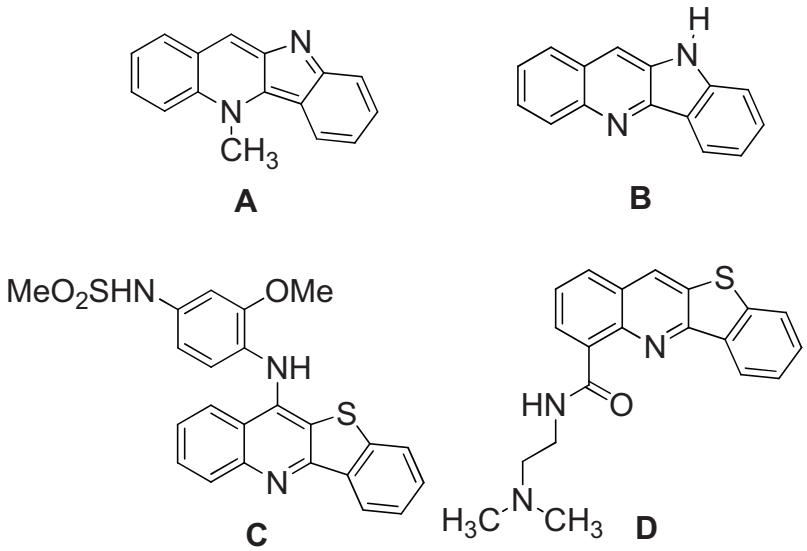


Figure 11. Alkaloids cryptolepine **(A)** and quindoline **(B)** isolated from *Cryptolepsis sanguinolenta* and bioactive benzothienoquinolines **(C)** and **(D)**.

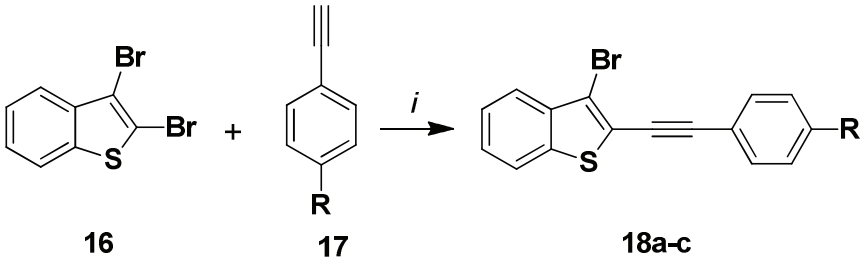
Due to their biological relevance, a number of syntheses of benzothienoquinolines have been reported. Many of them represent modifications of the Pfitzinger synthesis which relies on the base mediated cyclocondensation of isatin with ketones [99]. Recently, Zhu *et. al.* reported a multistep synthesis of benzothienoquinolines from substituted anthranilic acids, acyl chlorides and thiophenols[98]. The above mentioned syntheses of thienopyrroles and benzothienoquinolines proceed under harsh conditions or require several synthetic steps. Therefore, the development of alternative synthetic strategies is of considerable interest.

The development of regioselective palladium catalyzed sonogashira coupling reactions of dihalogenated heterocycles is of considerable current interest [19]. In the course of Prof. Langer's studies in this field,[20] I have studied the reaction of 2-alkynyl-3-bromothiophenes and 2-alkynyl-3-bromobenzothiophenes with anilines. The reaction of 2-alkynyl-3-bromothiophenes with anilines afforded, as expected, thienopyrroles by a domino C-N coupling / hydroamination process. In contrast, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines surprisingly resulted in the formation of benzothienoquinolines by a domino C-N coupling / annulation process. This type of

palladium catalyzed domino reaction has, to the best of my knowledge, not been previously reported and provides a convenient approach to pharmacologically relevant molecules which are not readily available by other methods. I believe that this type of cyclization is mechanistically interesting and has the potential to be extended to other heterocyclic systems in the future.

4.3 Results and discussion

The regioselective synthesis of 2-alkynyl-3-bromothiophenes[100] and 2-alkynyl-3-bromobenzothiophenes[101] by Sonogashira reactions of 2,3-dibromothiophene and 2,3-dibromobenzothiophene with alkynes has been previously reported. The reaction of 2,3-dibromobenzothiophene (**16**) with alkynes **17**, in the presence of $Pd(PPh_3)_2Cl_2$ (5 mol %), afforded the 2-alkynyl-3-bromobenzothiophenes **18a-c** (Scheme 29, Table 10).



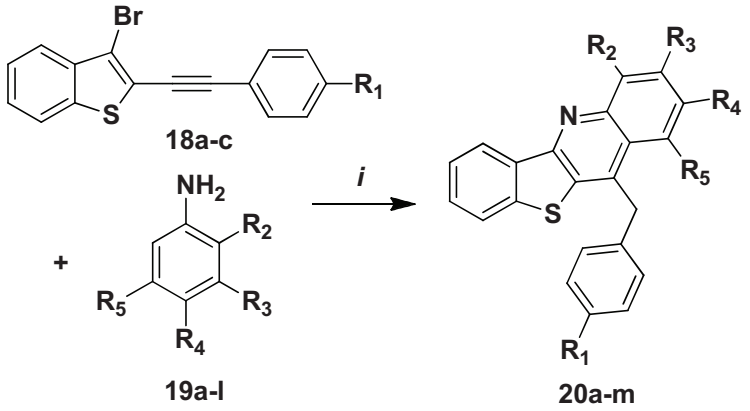
Scheme 29. Synthesis of **18a-c**. *Conditions: i*, **17a-c** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (10-mol%), triethylamine, 20 °C, 24 h.

Table 10. Regioselective alkynylation of 2,3-dibromobenzothiophene

17,18	R	% (**18**) [a]
a	H	80
b	Me	90
c	OCH_3	87

[a] Yields of isolated products

The palladium catalyzed reaction of 2-alkynyl-3-bromobenzothiophenes **18a-c** with anilines **19a-l** afforded the benzothienoquinolines **20a-m** in 55-70% yields (Scheme 30, Table 11). The synthesis of derivative **20j** was optimized by variation of the reaction conditions. The best yield of **20j** was obtained when $Pd(OAc)_2$ (10-mol%) in the presence of $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol %) was used as the catalyst and when KO-*t*-Bu (2 equiv.) and CuI (25 mol%) were employed. The use of stoichiometric amounts of CuI in the absence of a palladium catalyst failed to give the product. No reaction was observed when DMSO and THF were used as solvents. In fact, toluene proved to be the best solvent. The employment of dioxane afforded only trace amounts of product. Likewise, the use of Cs_2CO_3 instead of KO-*t*-Bu provided only traces of **20j**. The use of SPhos, XPhos or $P(Cy)_3$ instead of $P(t\text{-}Bu)_3{\cdot}HBF_4$ again resulted in low yields. The best yield of **20j** (60%) was obtained when 20 mol% of the ligand $P(t\text{-}Bu)_3{\cdot}HBF_4$ was used. The yield decreased to 30% when only 10 mol% of the ligand was employed. The moderate yields of products **20a-m** can be explained by the fact that small amounts of different side-products were formed (TLC of the crude product) which resulted in some practical difficulties during the chromatographic purification.



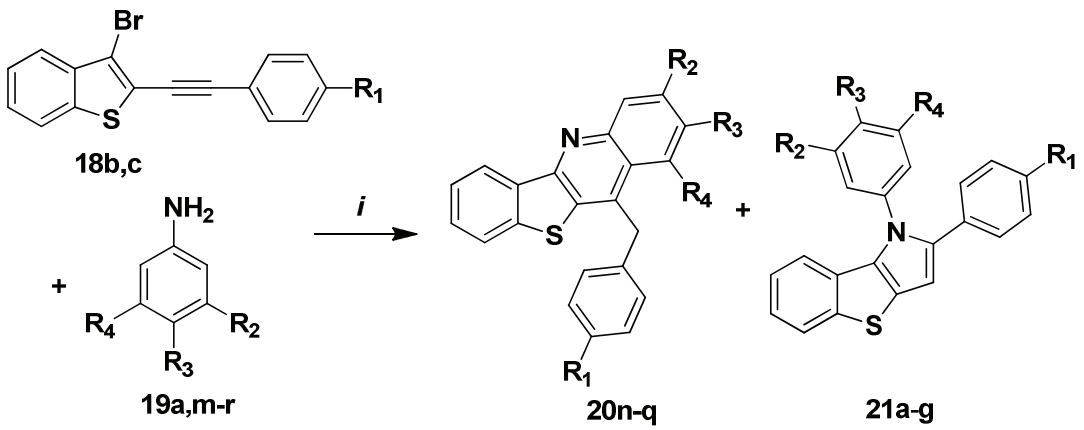
Scheme 30. Synthesis of **20a-m**. *Conditions: i*, **19a-l** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol %), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 105 °C, 12 h.

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

19	20	R_1	R_2	R_3	R_4	R_5	% (20) [a]
a	**a**	H	H	H	OCH_3	H	60
b	**b**	H	H	OCH_3	H	H	65
c	**c**	H	H	H	CH_3	H	61
d	**d**	H	H	H	C_2H_5	H	60
e	**e**	H	H	H	OC_2H_5	H	65
f	**f**	H	CH_3	H	CH_3	H	61
g	**g**	H	H	OCH_3	H	OCH_3	67
h	**h**	CH_3	OCH_3	H	OCH_3	H	70
i	**i**	CH_3	OCH_3	H	H	H	64
e	**j**	CH_3	H	H	OC_2H_5	H	60
j	**k**	OCH_3	H	H	$CH(CH_3)_2$	H	63
k	**l**	CH_3	H	H	F	H	60
l	**m**	OCH_3	H	CF_3	H	H	55

[a] Yields of isolated products

The palladium catalyzed reaction of 2-alkynyl-3-bromobenzothiophenes **18b,c** with anilines **19a,m-r** afforded separable mixtures of benzothienoquinolines **20n-q** and benzothienopyrroles **21a-g** in 50-60 and 30-40% yields, respectively (Scheme 31, Table 12). The reactions were carried out under identical conditions as described for the synthesis of products **20a-m**. The cyclization of anilines **19p-r**, containing strong π-acceptor substituents (nitro, ester, cyano), resulted in exclusive formation of benzothienopyrroles **21e-g**. Thus, the electronic character of the starting materials seems to have an influence on the product distribution. It is a striking observation that the combined yields of products **20n-q** and **21a-g** were higher than the yields of products **20a-m** given in Table 11. This can be explained by the fact that several side products were formed during the synthesis of **20a-m** (resulting in a difficult chromatographic purification), while the reactions leading to those products listed in (Table 12) proceeded more cleanly and the chromatographic purification was relatively easy.



Scheme 31. Synthesis of **20n-q** and **21a-g**. *Conditions: i*, **19a,m-r** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3 \cdot HBF_4$ (20 mol %), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 105°C, 12 h.

Table 12. Synthesis of **20n-q** and **21a-g**

19	20	21	R_1	R_2	R_3	R_4	%(20)[a]	% (21)[a]
a	**n**	**a**	OCH_3	H	OCH_3	H	60	30
m	**o**	**b**	CH_3	OCH_3	OCH_3	OCH_3	53	35
n	**p**	**c**	CH_3	OCH_3	OCH_3	H	50	40
o	**q**	**d**	OCH_3	H	Cl	H	55	32
p	**r**	**e**	OCH_3	NO_2	H	H	0	78
q	**s**	**f**	OCH_3	H	CN	H	0	84
r	**t**	**g**	CH_3	H	CO_2Me	H	0	45

[a] Yields of isolated products

The formation of benzothienoquinolines **20a-m** can be explained by a domino C-N coupling / annulation reaction and isomerization of a double bond (Scheme 32). This type of reaction has, to the best of my knowledge, not been previously reported. The formation of **20a** may proceed by initial palladium catalyzed C-N coupling and subsequent annulation or by the opposite order of events. Buchwald and coworkers showed that (copper catalyzed) domino C-N coupling / hydroamination reactions proceed with the C-N coupling as the first step [92]. Therefore, I believe that this is the case also in our transformation. While the C-N coupling must proceed by palladium catalysis, the subsequent annulation may proceed either by a palladium catalyzed or by a thermal process. A thermal mechanism may involve intermediate **22b** (Scheme 32), its isomerization to a 5-aza-1,2,4,6-tetraene containing an allene unit and subsequent electrocyclization.

The structure of all products were established by spectroscopic methods. The structure of **20a** and **21d** were independently confirmed by an X-ray crystal structure analysis (Figure 12), and (Figure 13) [102].

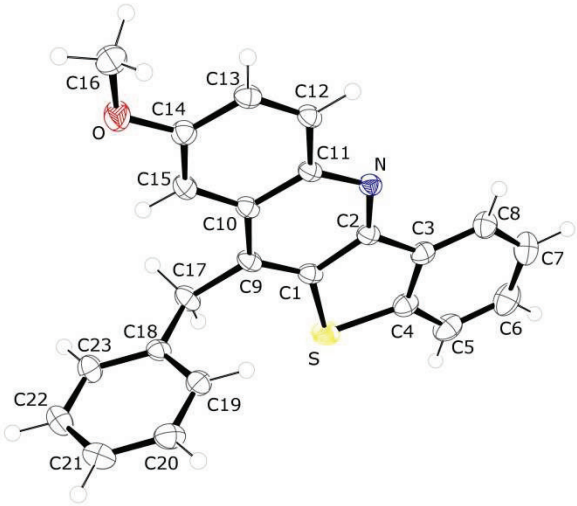


Figure 12: Molecular structure of **20a**

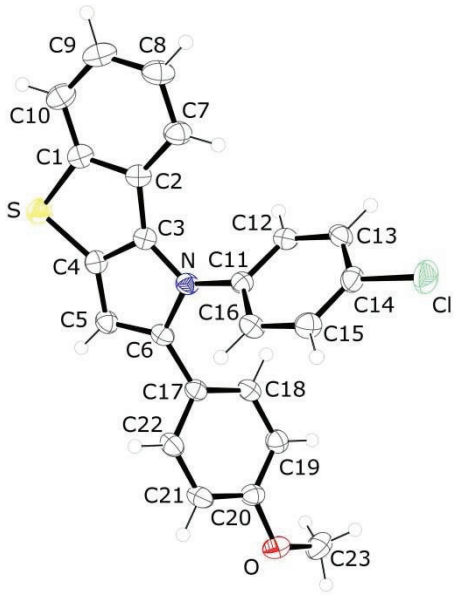
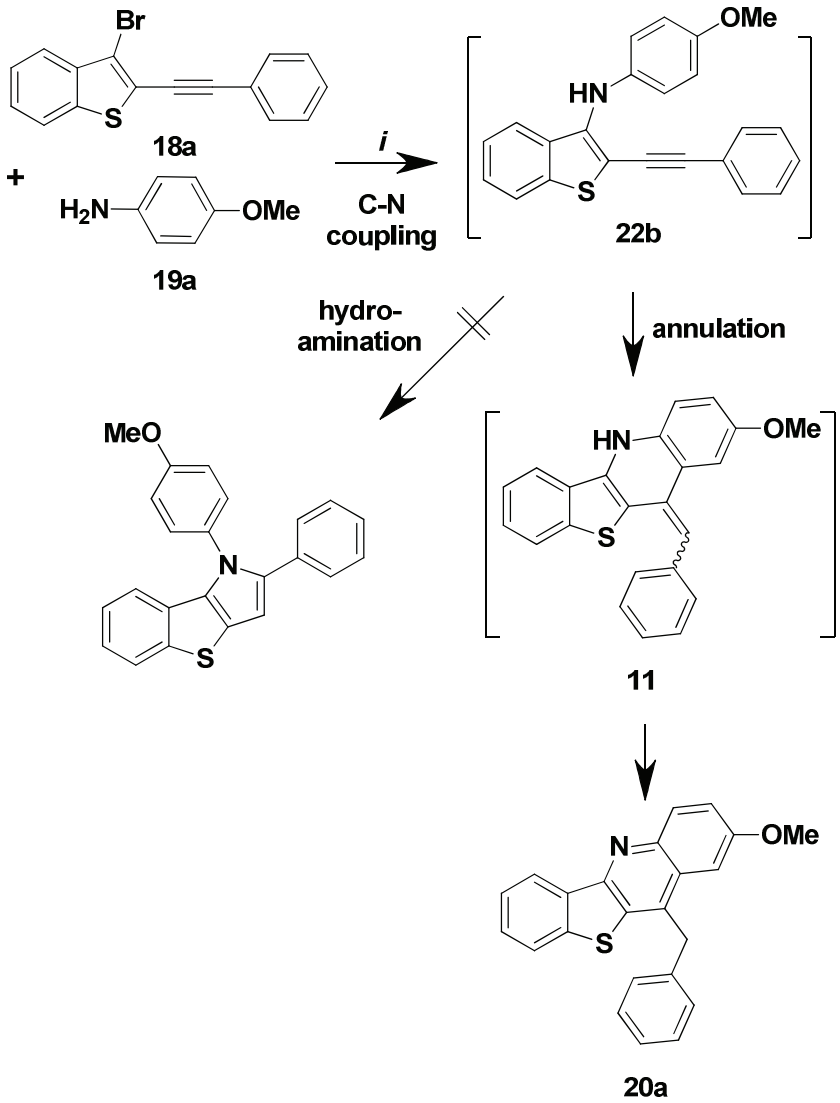
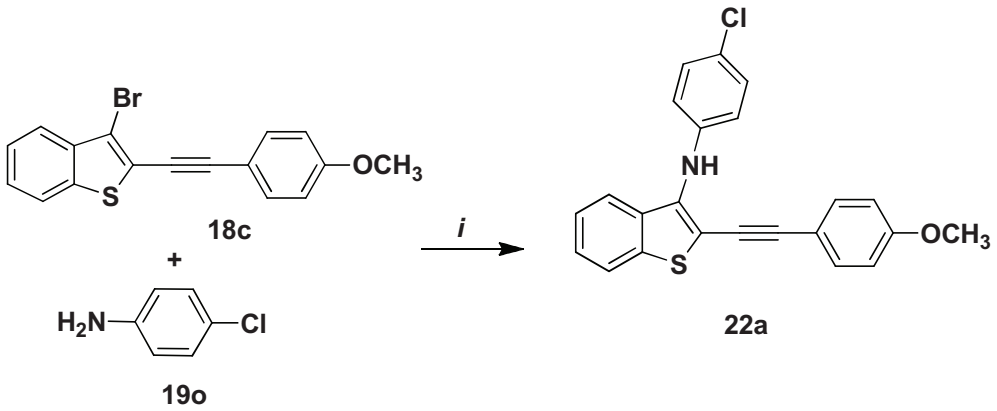


Figure 13: Molecular structure of **21d**



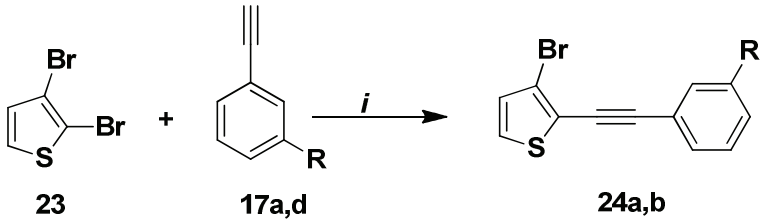
Scheme 32. Formation of **20a**. *Conditions: i*, **19a** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), P(*t*-Bu)$_3$·HBF_4 (20 mol %), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 105 °C, 12 h.

To study the mechanism of the cyclization reaction, I tried to isolate intermediate **22** formed by initial C-N coupling. The reaction of **18c** with **19p**, carried out at at 40 °C (4 h) instead of 105 °C (12 h), afforded the desired product **22a** (Scheme 33). Simple stirring of a toluene solution of **22a** at 105 °C for 12 h, in the absence of a catalyst, failed to give any type of cyclization (decomposition). In contrast, a cyclization could be successfully induced when the reaction was carried out in the presence of $Pd(OAc)_2$ (10 mol%), P(*t*-Bu)$_3$·HBF_4 (20 mol %), KO-*t*-Bu (2 equiv.), and CuI (25 mol%). This result shows that the cyclization step of the one-pot synthesis of products **20** (and **21**) is a palladium catalyzed process and not a thermal electrocyclization.



Scheme 33. Synthesis of intermediate **22a**. *Conditions: i*, **19o** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol %), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 40 °C, 4 h.

2-Alkynyl-3-bromothiophenes **24a,b** were regioselectively prepared in very good yields by Sonogashira reactions of 2,3-dibromothiophene (**23**) with alkynes **17a,d** (Scheme 34, Table 13). The best yields were obtained when $Pd(PPh_3)_2Cl_2$ (5 mol %) was used.



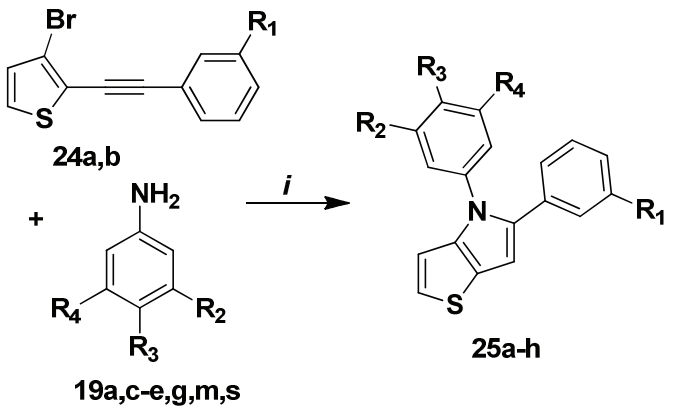
Scheme 34. Synthesis of **24a,b**. *Conditions: i*, **17a,d** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (10-mol%), diisopropylamine (DIPA), 45 °C, 24 h.

Table 13. Regioselective alkynylation of 2,3-dibromothiophene

17	24	R	% (24) [a]
a	**a**	H	75
d	**b**	OCH_3	80

[a] Yields of isolated products

The palladium catalyzed reaction of 2-alkynyl-3-bromothiophenes **24a,b** with anilines **19a,c-e,g,m,s** afforded the thienopyrroles **25a-h** in 55-75% yields (Scheme 35, Table 14).



Scheme 35. Synthesis of **25a-h**. *Conditions: i*, **19a,c-e,g,m,s** (1.2 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3 \cdot HBF_4$ (20 mol%),KO-*t*-Bu (equiv. 2.0), CuI (25 mol%), toluene, 90°C, 12 h.

Table 14. Synthesis of **25a-h**

19	25	R_1	R_2	R_3	R_4	% (25) [a]
a	**a**	H	H	OCH_3	H	65
c	**b**	H	H	CH_3	H	64
d	**c**	H	H	C_2H_5	H	60
e	**d**	H	H	OC_2H_5	H	65
e	**e**	OCH_3	H	OC_2H_5	H	75
g	**f**	H	OCH_3	H	OCH_3	63
m	**g**	H	OCH_3	OCH_3	OCH_3	60
s	**h**	H	H	NO_2	H	55

[a] Yields of isolated products

In conclusion, I have studied the reaction of 2-alkynyl-3-bromothiophenes and 2-alkynyl-3-bromobenzothiophenes with anilines. While the reaction of 2-alkynyl-3-bromothiophenes with anilines afforded thienopyrroles by a domino C-N coupling / hydroamination process, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines resulted, under identical conditions, in the formation of benzothienoquinolines by a domino C-N coupling / annulation process. The type of starting material (both the heterocyclic moiety and the aniline) plays an important role for the product distribution. As mentioned above, Buchwald and coworkers reported the synthesis of thienopyrroles by copper catalyzed domino C-N coupling / hydroamination reaction of 2-alkynyl-3-bromothiophenes with $(BOC)NH_2$ [92]. On the one hand, annulation reactions are, of course, only possible for anilines, but not for alkylamines or $(BOC)NH_2$. On the other hand, the different chemical behaviour of 2-alkynyl-3-bromobenzothiophenes and 2-alkynyl-3-bromothiophenes in their reaction with anilines is

surprising. The most important difference between thiophene and its benzo-analogue lies in the fact that the aromatic character of thiophene is much stronger than the aromaticity of the five membered ring of benzothiophene. The alkene character of the double bond of the bromoenyne system of compounds **18** is, thus, higher than in case of derivatives **24**. It might be that this difference plays a role for the two different reaction paths. The type of aniline employed also has an influence on the product distribution. While 6-membered rings are formed in case of electron rich anilines, 5-membered rings are formed in case of anilines containing strong π-acceptor substituents. This can be explained by the fact that, as shown above, the cyclization proceeds by palladium-catalyzed attack of the *ortho* carbon atom or of the nitrogen atom of the aniline to the alkyne. The nucleophilicity of the aromatic carbon atom is reduced when electron-withdrawing substituents are present and, thus, the cyclization proceeds via the (more nucleophilic) nitrogen atom.

4.4 Conclusion

In this chapter I have reported what are, to the best of my knowledge, the first domino C-N coupling / annulation reactions. These reactions provide a convenient approach to pharmacologically relevant molecules which are not readily available by other methods.

5 Domino C-N Coupling / Annulation *versus* C-N Coupling / Hydroamination of 2-Alkynyl-3-bromobenzofurans and 2-Alkynyl-3-bromofurane. Efficient Synthesis of Benzofuro[3,2-*b*]quinolines and Furo[3,2-b]quinolines

5.1 Introduction

Benzo-carbolines [103] are very rare in nature, and the best representatives of this family are quindoline [104] **(A)** and cryptolepine [105,106] **(B)**, two indoloquinoline alkaloids isolated in 1977 and 1929, respectively, from a West African plant: *Cryptolepis sanguinolenta* (Periplocaceae). Considerable interest in this family has been shown by several teams throughout the world due to their various and important biological properties such as: antimuscarinic, antibacterial, antiviral, antiplasmodial, and antihyperglycemic activities [107,109]. Oxygen analogs of these alkaloids called benzofuro[3,2-*b*]quinolines are interesting target molecules due to their broad spectrum activity against bacteria and protozoa, anticancer and cytotoxic bioactivities. For example substituted oxygen analog **(C)** has been reported as an antituberculosis agent, whereas compound **(D)** found to be void of cytotoxicity [110,111].

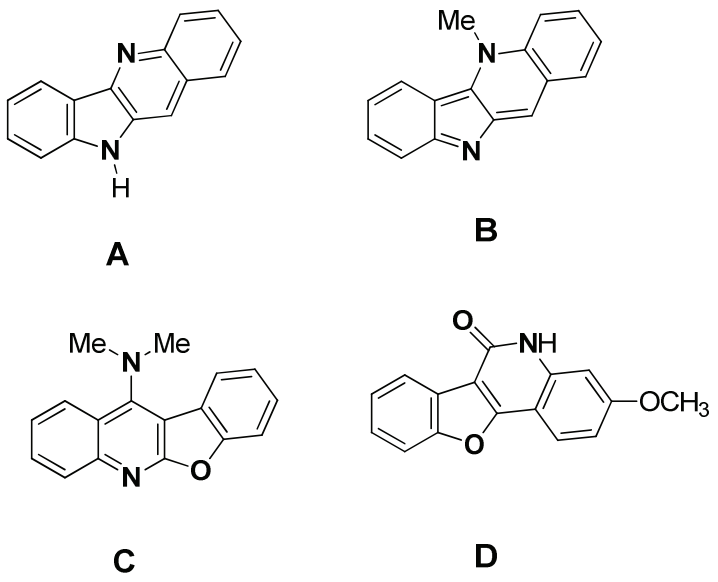


Figure 14: Alkaloids quindoline **(A)** and cryptolepine **(B)** isolated from *Cryptolepis sanguinolenta* and bioactive benzofuroquinolines **(C)** and **(D)**.

Due to their biological relevance, a number of syntheses of benzofuroquinolines have been reported. According to the reported procedures of Kawase, *et. al* [112,113], 4-hydroxy-3-(2-methoxyphenyl)-1,2-dihydroquinolin-2-one, prepared from methyl anthranilate and 2-methoxyphenylacetyl chloride, was treated with pyridine hydrochloride to furnish the linear benzofuro[2,3-b]quinolin-11-one then chlorination of this compound with phosphorus pentachloride afforded 11-Chlorobenzofuro[2,3-b]quinoline. Yang *et. al.*[110] reported a methodology to synthesize a 11-Chlorobenzofuro[2,3-b]quinolone by refluxing anthranilic acid and 2-coumaranone in phosphorus oxychloride. Other methods represent modifications of the Pfitzinger synthesis which relies on the base mediated cyclocondensation of isatin with ketones [99]. Zhu *et. al.* reported a multistep synthesis of benzofuroquinolines from substituted anthranilic acids, acyl chlorides and phenols [98].

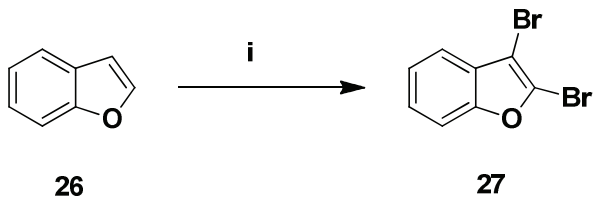
Many natural products containing furoquinoline moiety are known to exhibit a wide range of biological activities such as antiasthmatic [114], anti-inflammatory [115] and antiproliferative activities [116]. Among the methods developed to date for the synthesis of furoquinoline derivatives is the Lewis acids catalysed imino Diels-Alder reaction between *N*-benzylideneanilines and nucleophilic olefins [117].

Avetisyan et al [118] reported another method which involves allylation of 4-Hydroxy-2-methylquinoline with 2,3-dichloropropene in anhydrous ethanol in the presence of sodium metal to afford 2-methyl-4-(2-chloro-2 propenyloxy) quinoline for the synthesis of furo[3,2-*c*] quinolone. Claisen rearrangement of 2-methyl-4-(2-chloro-2 propenyloxy) quinoline in boiling ether in the presence of bromobenzene yielded 3-(2-chloro-2-propenyl)-4-hydroxy-2-methyl quinoline in 6-7 hours. On heating 2-methyl-4-(2-chloro-2 propenyloxy) quinoline to 180-190 ºC, a small amount (20%) of 2-chloro-2,3-dihydro-2,4-dimethylfuro[3,2-*c*]quinoline was obtained. The latter underwent HCl elimination upon heating in the presence of alcoholic NaOH to afford 2,4-dimethylfuro[3,2-*c*]quinoline. Avetisyan et al [119] later developed a more convenient approach which involves treatment 3-(2-chloro-2-propenyl)-4-hydroxy-2-methyl quinoline with a solution of bromine in chloroform at room temperature for 1-2 hours to give 2-bromomethyl-2-chloro-4-methyl-2,3-dihydrofuro[3,2*c*]quinolinehydrobromide.

The bromomethylfuroquinoline reacted with various nucleophiles to afford the corresponding 2-substituted-4-methylfuro[3,2-*c*]quinoline in 83-98% yield. All the above mentioned syntheses of benzofuroquinolines and furoquinoline proceed under harsh conditions or require several synthetic steps. Therefore, the development of alternative synthetic strategies is of considerable interest.

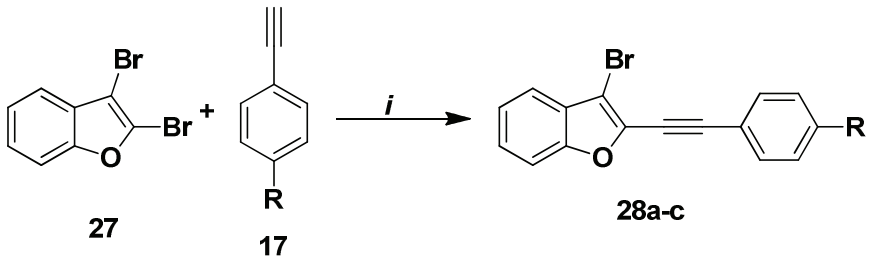
5.2 Results and discussion

The reaction of benzofuran (**26**) with bromine (2.0 equiv.) and KOAc (2.0 equiv.) in CH_2Cl_2 (reflux, 8 h) resulted in the formation of 2,3-dibromobenzofuran (**27**) in 85% yield (Scheme 36) [8]. During optimization and scale-up of the reaction, I have found that more reflexing time was required to avoid the formation of mono-brominated by-products.



Scheme 36. Bromination of benzofuran (**26**). Reagents and conditions: (i) Br_2 (2.0 equiv.), KOAc (2.0 equiv.), CH_2Cl_2, reflex 8h.

The regioselective synthesis of 2-alkynyl-3-bromobenzofuran [120] by Sonogashira reactions of 2,3-dibromobenzofuran with alkynes has been previously reported. The reaction of 2,3-dibromobenzofuran (**27**) with alkynes **17**, in the presence of $Pd(PPh_3)_2Cl_2$ (5 mol %), afforded the 2-alkynyl-3-bromobenzofurans **28a-c** (Scheme 37, Table 15).



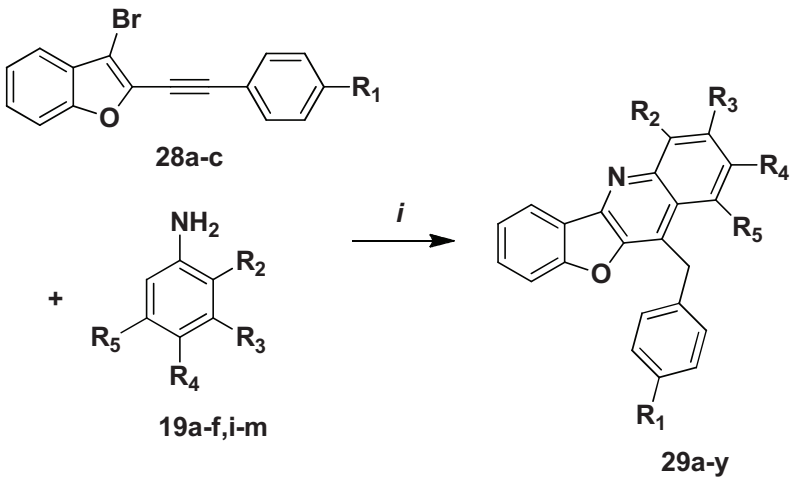
Scheme 37. Synthesis of **28a-c**. *Conditions: i*, **17a-c** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (10-mol%), Diethylamine (1.5 equiv.), THF, 20 °C, 24 h.

Table 15. Regioselective alkynylation of 2,3-dibromobenzofuran

17,28	**R**	% (**28**) [a]
a	H	90
b	Me	82
c	OCH_3	75

[a] Yields of isolated products

The palladium catalyzed reaction of 2-alkynyl-3-bromobenzofurans **28a-c** with anilines **19a-f, i-m** afforded the benzofuroquinolines **29a-y** in 60-75% yields (Scheme 38, Table 16). The synthesis of derivative **29a** was optimized by variation of the reaction conditions. The best yield of **29a** was obtained when $Pd(OAc)_2$ (10-mol%) in the presence of $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol %) was used as the catalyst and when KO-*t*-Bu (2 equiv.) as a base. The use of palladium catalyst in the absence of CuI surprisingly successed to give the product in good yield. No reaction was observed when DMSO and THF were used as solvents. In fact, toluene proved to be the best solvent. The employment of dioxane afforded only trace amounts of product. Likewise, the use of Cs_2CO_3 instead of KO-*t*-Bu provided only traces of **29a**. The use of SPhos, XPhos, $P(Cy)_3$, or $P(OEt)_2Ph$ instead of $P(t\text{-}Bu)_3{\cdot}HBF_4$ again resulted in low yields. The best yield of **29a** (65%) was obtained when 20 mol% of the ligand $P(t\text{-}Bu)_3{\cdot}HBF_4$ was used. The yield decreased to 30% when only 10 mol% of the ligand was employed.



Scheme 38. Synthesis of **29a-y**. *Conditions: i*, **19a-f,i-m** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (20 mol %), KO-*t*-Bu (2 equiv.), 110 °C, 12 h.

Table 16. Synthesis of **29a-y**

19	29	R_1	R_2	R_3	R_4	R_5	%(29)[a]
a	**a**	H	H	H	OCH_3	H	65
c	**b**	H	H	H	CH_3	H	60
d	**c**	H	H	H	C_2H_5	H	60
e	**d**	H	H	H	OC_2H_5	H	68
f	**e**	H	CH_3	H	CH_3	H	65
i	**f**	H	OCH_3	H	H	H	67
j	**g**	H	H	H	$CH(CH_3)_2$	H	61
k	**h**	H	H	H	F	H	60
m	**i**	H	H	OCH_3	OCH_3	OCH_3	70
a	**j**	CH_3	H	H	OCH_3	H	70
b	**k**	CH_3	H	OCH_3	H	H	64
c	**l**	CH_3	H	H	CH_3	H	66
d	**m**	CH_3	H	H	C_2H_5	H	60
e	**n**	CH_3	H	H	OC_2H_5	H	68
f	**o**	CH_3	CH_3	H	CH_3	H	61
i	**p**	CH_3	OCH_3	H	H	H	67
j	**q**	CH_3	H	H	$CH(CH_3)_2$	H	63
a	**r**	OCH_3	H	H	OCH_3	H	67
c	**s**	OCH_3	H	H	CH_3	H	66
d	**t**	OCH_3	H	H	C_2H_5	H	72
e	**u**	OCH_3	H	H	OC_2H_5	H	70
f	**v**	OCH_3	CH_3	H	CH_3	H	75
i	**w**	OCH_3	OCH_3	H	H	H	68
j	**x**	OCH_3	H	H	$CH(CH_3)_2$	H	70
l	**y**	OCH_3	H	CF_3	H	H	55

[a]Yield of isolated products

The structure of all products were established by spectroscopic methods. The structure of **29r** was independently confirmed by an X-ray crystal structure analysis (Figure 15) [125].

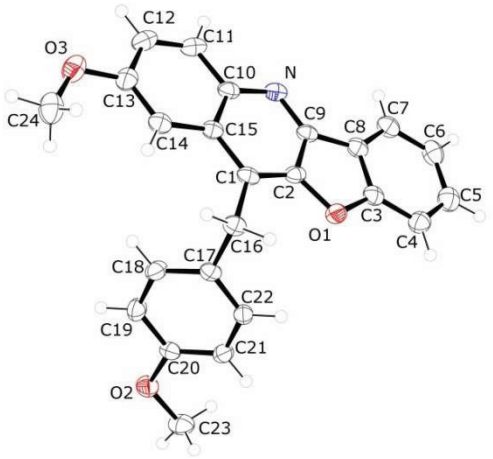
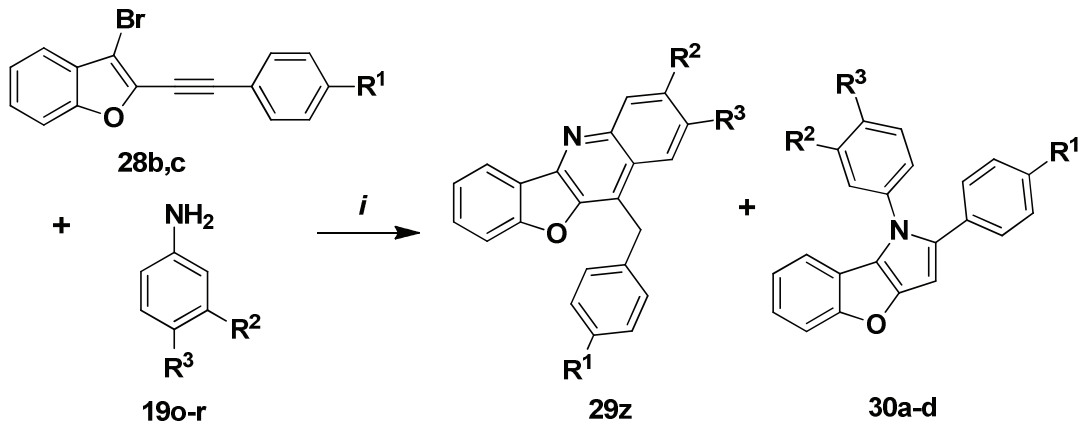


Figure 15: Crystal structure of **29r**

The palladium catalyzed reaction of 2-alkynyl-3-bromobenzofuran **28b,c** with anilines **19o-r** afforded separable mixtures of benzofuroquinolines **29z** and benzofuropyrrole **30a-d** (Scheme 39, Table 17). The reactions were carried out under identical conditions as described for the synthesis of products **29a-y**. The cyclization of anilines **19p-r**, containing strong π-acceptor substituents (nitro, ester, cyano), resulted in exclusive formation of benzofuropyrroles **30b-d**. Thus, the electronic character of the starting materials also seems to have an influence on the product distribution.



Scheme 39. Synthesis of **29z** and **30a-d.** *Reaction conditions: i*, **19lo-r** (1.3 equiv.), $Pd(OAC)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol %), KO-*t*-Bu (2 equiv.), toluene, 110 °C, 12 h.

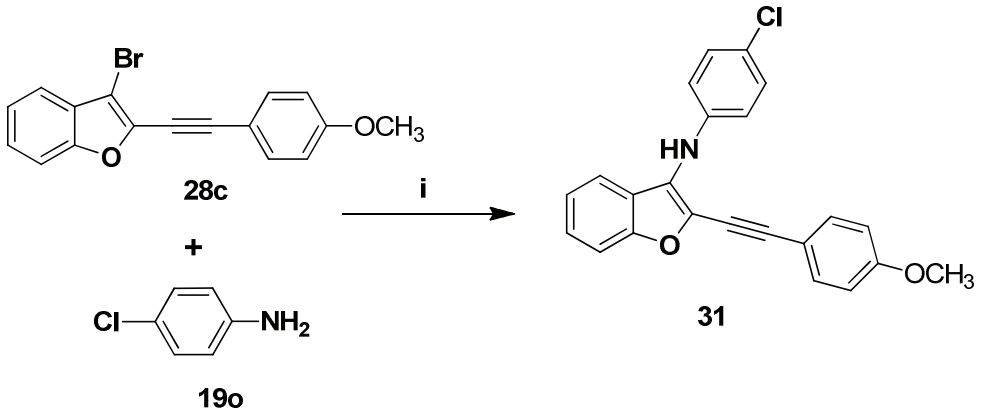
Table 17. Synthesis of **29z** and **30a-d**

19	29	30	R^1	R^2	R^3	% (**29**)[a]	% (**30**)[a]
o	**z**	**a**	OCH_3	H	Cl	40	30
p	**z**	**b**	OCH_3	NO_2	H	0	75
q	**z**	**c**	OCH_3	H	CN	0	88
r	**z**	**d**	CH_3	H	CO_2Me	0	50

[a] Yields of isolated products

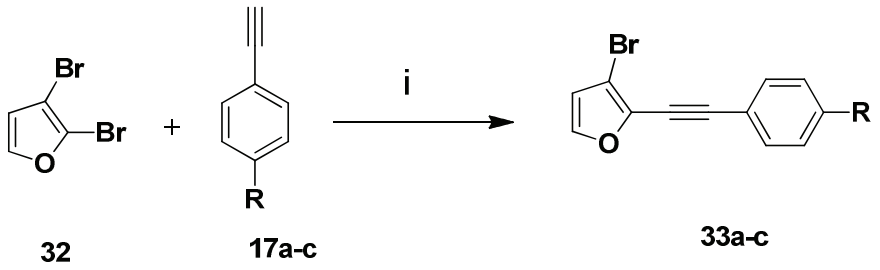
To prove that the mechanism of the cyclization also is a palladium catalyzed reaction and not a thermal electrocyclization, I isolated intermediate **31** formed by initial C-N coupling. The reaction of **28c** with **19o**, carried out at 40 °C (4 h) instead of 105 °C (12 h), afforded the desired product **31** (Scheme 40). Simple stirring of a toluene solution of **31** at 105 °C for 12 h, in the absence of a catalyst, failed to give any type of cyclization (decomposition). In contrast, a cyclization could be successfully induced when the reaction was carried out in the presence of $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol %), and KO*t*Bu (2 equiv.). This result shows

that the cyclization step of the one-pot synthesis of products **29** (and **30**) is a palladium catalyzed process.



Scheme 40. Synthesis of intermediate **31**.*Reaction conditions: i* , **19o** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol %), KO-*t*-Bu (2 equiv.), toluene, 40°C, 4 h.

2-Alkynyl-3-bromofuran **33a-c** were regioselectively prepared in very good yields by Sonogashira reactions of 2,3-dibromofuran (**32**) with alkynes **17a-c** (Scheme 41, Table 18). The best yields were obtained when $Pd(PPh_3)_2Cl_2$ (5 mol %) was used as a catalyst, Triethylamine as a base, and THF as a solvent.



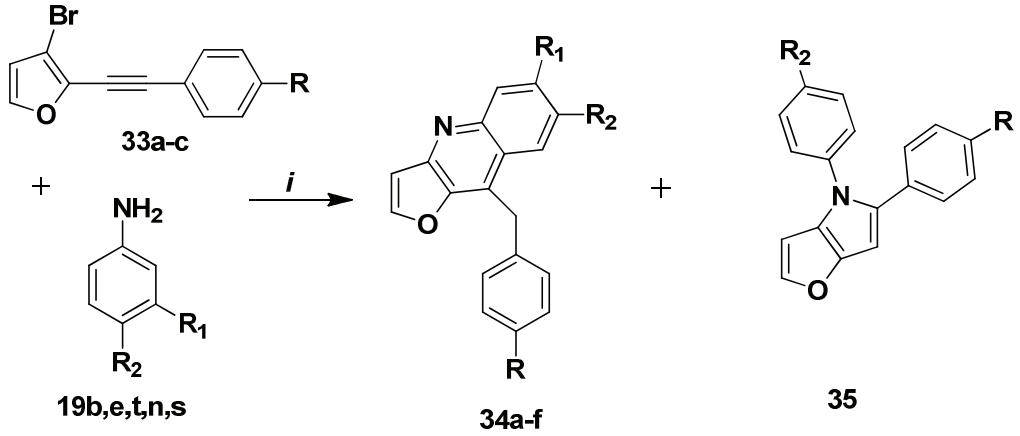
Scheme 41. Synthesis of **33a-c**. *Conditions: i*, **17a-c** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (10-mol%), Triethylamine (1.2 equiv.), THF, 20 °C, 48 h.

Table 18. Regioselective alkynylation of 2,3-dibromofurane

17,33	R	% (33) [a]
a	H	82
b	CH_3	75
c	OCH_3	85

[a] Yields of isolated products

The palladium catalyzed reaction of 2-alkynyl-3-bromofurans **33a-c** with anilines **19b,e,t,n,s** afforded the Furo[3,2-*b*]quinolines **34a-f** and Furo[3,2-b]pyrrole **35** in 55-72% yields (Scheme 42, Table 19).



Scheme 42. Synthesis of **34a-f and 35**. *Conditions: i*, **19a,e,t,n,s** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3 \cdot HBF_4$ (20 mol%), KO-*t*-Bu (equiv. 2.0), toluene, 110 °C, 12 h.

Table 19. Synthesis of **34a-f and 35**

19	34	35	R	R_1	R_2	%(34)[a]	%(35)[a]
a	**a**	**a**	CH_3	H	OCH_3	70	0
a	**b**	**b**	OCH_3	H	OCH_3	65	0
e	**c**	**c**	OCH_3	H	OC_2H_5	64	0
t	**d**	**d**	H	CH_3	CH_3	60	0
t	**e**	**e**	OCH_3	CH_3	CH_3	55	0
n	**f**	**f**	OCH_3	OCH_3	OCH_3	72	0
s	**g**	**g**	H	H	NO_2	0	65

[a] Yields of isolated products

The type of starting material (both the heterocyclic moiety and the aniline) plays an important role for the product distribution. While 6-membered rings are formed (annulation process) in case of electron rich anilines, 5-membered rings are formed (hydroamination process) in case of anilines containing strong π-acceptor substituents. This can be explained by the fact that the cyclization proceeds by palladium-catalyzed attack of the *ortho* carbon atom or of the nitrogen atom of the aniline to the alkyne. The nucleophilicity of the aromatic carbon atom is reduced when electron-withdrawing substituents are present and, thus, the cyclization proceeds via the (more nucleophilic) nitrogen atom.

5.3 Conclusion

I have studied the reaction of 2-alkynyl-3-bromofuran and 2-alkynyl-3-bromobenzofurans with anilines. With electron rich anilines both substrates afforded furo[3,2-*b*]quinolines and benzofuro[3,2-*b*]quinolones, respectively by a domino C-N coupling / annulation process. However, with anilines containing strong π-acceptor substituents, both substrates afforded furo[3,2-b]pyrrole and benzofuro[3,2-b]pyrroles, respectively, by a domino C-N coupling / hydroamination process. These reactions provide a convenient approach to pharmacologically relevant molecules which are not readily available by other methods.

6. Abstract:

In English

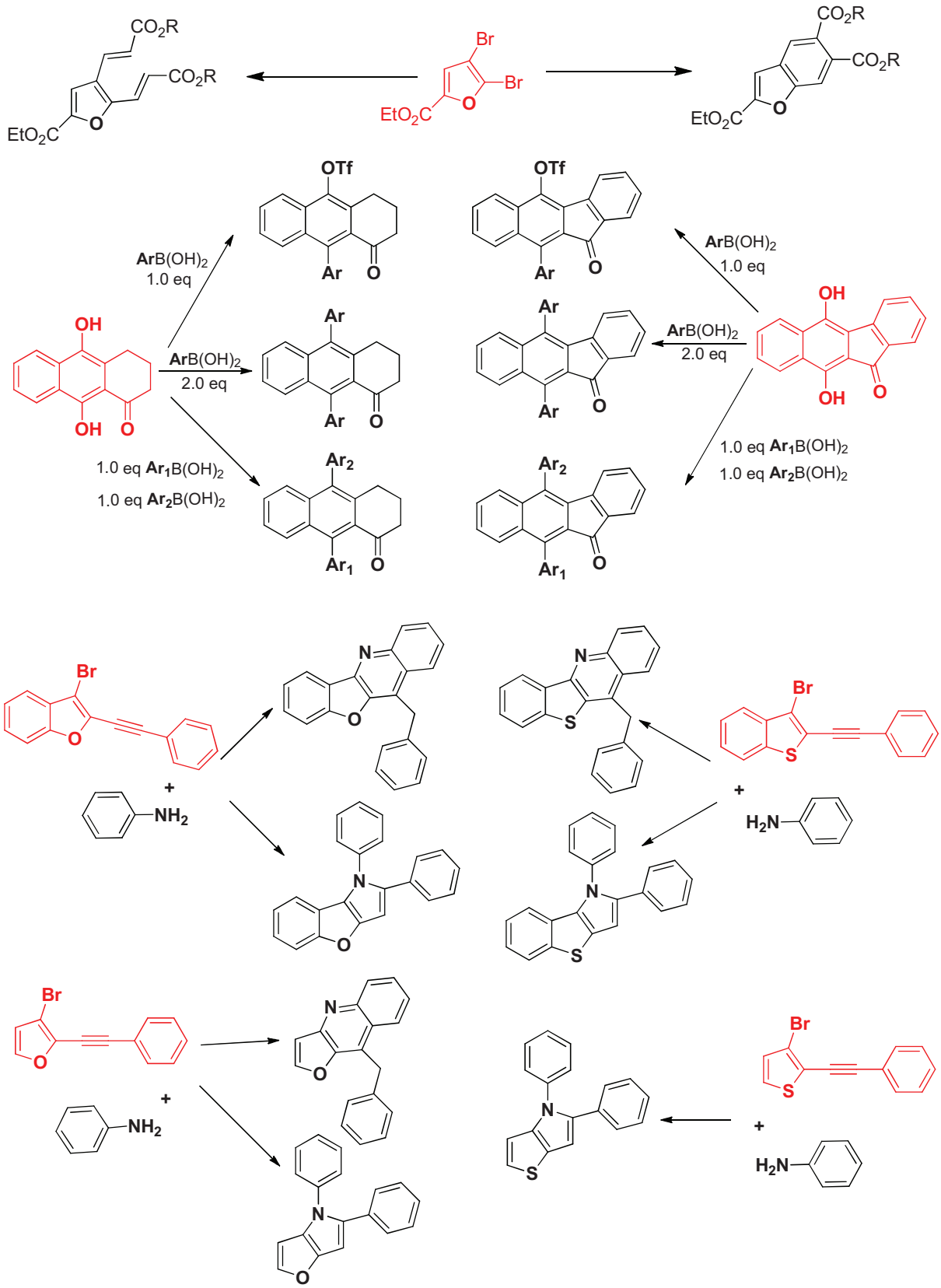
The palladium(0)-catalyzed Heck cross-coupling reaction of 2,3-dibromo-5-(ethoxycarbonyl)-furan provided functionalized benzofurans by domino twofold Heck/ 6π-electrocyclization/dehydrogenation reactions. Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of 1,2,3,4-tetrahydro-9,10-dihydroxyanthracen-1-one, *and* of 5,10-dihydroxy-11*H*-benzo[b]fluoren-11-one with different arylboronic acids produced aryl-substituted anthracenone, *and* benzofluorenone, respectively. The first attack occurred at the more electronically deficient and sterically more hindered position. While the palladium catalyzed reaction of 2-alkynyl-3-bromothiophenes with anilines afforded thienopyrroles by a domino C-N coupling / hydroamination process, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines resulted, under identical conditions, in the formation of benzothienoquinolines by a domino C-N coupling / annulation process, the electronic character of the aniline has influence on the product distribution. The domino C-N coupling / annulation process happened when 2-alkynyl-3-bromobenzofurans *and* 2-alkynyl-3-bromofuran react with electron rich anilines to afford benzofuro[3,2-*b*]quinolones and furo[3,2-*b*]quinolines, respectively. However the reaction was controlled by a domino C-N coupling / hydroamination process when both substrates react with anilines contains a strong π-acceptor substituents to afford benzofuro[3,2-b]pyrroles and furo[3,2-b]pyrrole, respectively.

In German

Die Palladium(0)- katalysierte Heck-Kreuzkupplungsreaktion von 2,3-Dibrom-5-(ethoxycarbonyl)-furan ergibt durch zweifache Heck-6π-Electrocyclisierungs/Dehydrogenierungsreaktion funktionalisierte Benzofurane. Suzuki-Miyaura-Kreuzkupplungen an Bis(triflaten) von 1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-on und 5,10-Dihydroxy-11*H*-benzo[*b*]fluoren-11-on mit verschiedenen Arylboronsäuren ergaben jeweils arylsubstituierte Anthracenone und Benzofluorenone. Der erste Angriff fand an der elektronenärmeren und sterisch mehr gehinderten Position statt.

Während die palladiumkatalysierte Reaktion von 2-Alkinyl-3-bromthiophenen mit Anilinen durch eine Domino-C-N-Knüpfung-Hydroaminierung zu Thienopyrrolen führte, ergab die Umsetzung von 2-Alkinyl-3-brombenzothiophenen mit Anilinen unter identischen Bedingungen eine Domino-C-N-Knüpfung-Annelierung unter Bildung Benzothienochinoline. Der elektronische Charakter des jeweiligen Anilins hat Einfluss auf die Produktverteilung.

Die Domino-C-N-Knüpfung-Annelierung tritt auf, wenn 2-Alkinyl-3-brombenzofurane und 2-Alkinyl-3-bromfuran mit elektronenreichen Anilinen jeweils zu Benzofuro[3,2-b]chinolonen und Furo[3,2-b]chinolinen umgesetzt werden. Eine Domino-C-N-Knüpfung-Hydroaminierung hingegen läuft ab, wenn die beiden o.g. Substrate mit Anilinen mit starken π-Akzeptorsubstituenten umgesetzt werden, so dass sich jeweils Benzofuro[3,2-b]pyrrole und Furo[3,2-b]pyrrole bilden.



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

7. Experimental Section

7.1 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).

7.2 Methods for Compound Characterization and Analysis

NMR Spectroscopy

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

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

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

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

Infrared Spectroscopy (IR)

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

Mass Spectrometry (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.

7.3 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.

8. General Procedures

8.1 Synthesis of Functionalized Benzofurans by Double Heck Reactions of 2,3-dibromo-5-(ethoxycarbonyl)furan and subsequent 6π-Electrocyclization / Dehydrogenation

8.1.1 Synthesis of 2,3-di(alkenyl)furans 3

General procedure A for the synthesis of **3a-h:**. In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (12 mg, 5 mol %) and XPhos or SPhos (10 mol %) in DMF (5 mL) was purged with Ar and stirred at 20 °C to give a yellowish or brownish clear solution. To the stirred solution were added 2,3-dibromo-5-(ethoxycarbonyl)furan (**1**) (300 mg, 1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the acrylate or styrene (2.5 mmol). The reaction mixture was stirred at 100 ˚C (or mentioned) for 24 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes/EtOAc).

***(2E,2'E)-Diisobutyl 3,3'-[5-(ethoxycarbonyl)furan-2,3-diyl]diacrylate* (3a)**. Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ (12 mg, 5 mol%), XPhos (48 mg, 10 mol%), Isobutylacrylate **(2a)** (320 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3a** was isolated as light yellow solid (318 mg, 81%), mp 152–154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (d, 12H, J = 6.7 Hz, $4CH_3$), 1.41 (t, 3H, J = 7.3 Hz, CH_3), 1.96-2.10 (m, 2H, 2CH), 4.01 (d, 2H, J = 3.6 Hz, CH_2O), 4.03 (d, 2H, J = 3.5 Hz, CH_2O), 4.41 (q, 2H, J = 7.1 Hz, CH_2O), 6.34 (d, 1H, J = 15.8 Hz, CH_{vinyl}), 6.71 (d, 1H, J = 15.8 Hz, CH_{vinyl}), 7.37 (s, 1H, ArH), 7.62 (d, 1H, J = 8.6 Hz, CH_{vinyl}), 7.67 (d, 1H, J = 8.4 Hz, CH_{vinyl}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.3 (CH_3), 19.1, 19.2 ($4CH_3$), 27.8 (2CH), 61.7, 71.0, 71.1 ($3CH_2O$), 115.8, 121.5, 121.6 (CH), 125.2 (C), 126.5, 131.5 (CH), 145.5, 152.4 (C), 158.0, 166.2, 166.5 (CO). IR (KBr): ν = 3109, 3069 (w), 2958 (m), 2874 (w), 1709 (s), 1633, 1578, 1515, 1469 (m), 1394 (w), 1368 (m), 1343 (w), 1318 (s), 1300, 1270 (w), 1255 (m), 1239 (w), 1220 (m), 1171 (s), 1114 (m), 1080 (w), 1008, 962 (s), 875, 861, 837 (w), 765, 748, 720, 693, 657 (m), 609, 595, 542 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 392 ($[M]^+$, 80), 347 (22), 336

(18), 320 (10), 319 (49), 280 (53), 263 (16), 235 (72), 219 (100), 206 (44) . HRMS (EI, 70 eV): calcd for $C_{21}H_{28}O_7$ $[M]^+$: 392.18295; found: 392.18259.

(2E,2'E)-Dihexyl 3,3'-[5-(ethoxycarbonyl)furan-2,3-diyl]diacrylate **(3b)**. Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ **(**12 mg, 5 mol%), XPhos (48 mg, 10 mol%), n-Hexylacrylate **(2b)** (390 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3b** was isolated as yellow solid **(**380 mg, 85%), mp 162–164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81-0.86 (m, 6H, $2CH_3$), 1.23-1.35 (m, 12H, $6CH_2$), 1.59-1.68 (m, 4H, $2CH_2$), 4.14 (t, 2H, J = 6.8 Hz, CH_2O), 4.15 (t, 2H, J = 6.7 Hz, CH_2O), 4.32 (q, 2H, J = 7.1 Hz, CH_2O), 6.23 (d, 1H, J = 15.7 Hz, CH_{vinyl}), 6.61 (d, 1H, J = 15.8 Hz, CH_{vinyl}), 7.27 (s, 1H, ArH), 7.53 (d, J = 8.0 Hz, 1H, CH_{vinyl}), 7.58 (d, 1H, J = 8.0 Hz, CH_{vinyl}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 14.3 (CH_3), 22.5, 25.6, 28.6, 31.4 ($2CH_2$), 61.7, 65.0, 65.2 (OCH_2), 115.8, 121.6, 121.7 (CH), 125.2 (C), 126.5, 131.5 (CH), 145.8, 152.4 (C), 158.0, 166.2, 166.5 (CO). IR (KBr): ν = 3107, 2953, 2929, 2857 (w), 1715, 1632 (s), 1579, 1518, 1467 (m), 1453, 1392, 1368, 1346 (w), 1321 (s), 1301, 1265, 1252, 1240 (w), 1223 (m), 1175 (s), 1123, 1107, 1052, 1038 (w), 1024, 977, 961 (m), 910 (w), 875, 860 (m), 822, 799 (w), 764, 724, 661, 596 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 448 ($[M]^+$, 49), 403 (17), 347 (18), 320 (10), 291 (07), 280 (19), 246 (22), 235 (100), 219 (88). HRMS (EI, 70 eV): calcd for $C_{25}H_{36}O_7$ $[M]^+$: 448.24555; found: 448.24519.

(2E,2'E)-Di-tert-butyl 3,3'-[5-(ethoxycarbonyl)furan-2,3-diyl]diacrylate **(3c)**. Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ **(**12 mg, 5 mol%), XPhos (48 mg, 10 mol%), Tert.Butylacrylate **(2c)** (320 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3c** was isolated as orange solid (325 mg, 83%), mp 158–160 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ =1.32 (t, 3H, J = 7.2 Hz, CH_3), 1.46 (s, 18H, $6CH_3$), 4.31 (q, 2H, J = 7.2 Hz, CH_2O), 6.14 (d, 1H, J = 15.4 Hz, CH_{vinyl}), 6.53 (d, 1H, J = 15.7 Hz, CH_{vinyl}), 7.24 (s, 1H, ArH), 7.42 (d, 1H, J = 4.3 Hz, CH_{vinyl}), 7.48 (d, 1H, J = 4.3 Hz, CH_{vinyl}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.3 (CH_3), 28.1 ($6CH_3$), 61.5 (CH_2), 81.1, 81.2 (C), 115.9, 123.4, 123.5 (CH), 124.9 (C), 125.7, 130.5 (CH), 145.6, 152.3 (C), 158.1, 165.3, 165.4 (CO). IR (KBr): ν = 3109, 2979, 2930, (w), 1714, 1699 (s), 1633 (m), 1575, 1509, 1475, 1455, 1391 (w), 1367, 1322,

1280, 1256, 1220 (m), 1141 (s), 1079, 1019 (w), 975, 958 (m), 885, 863, 844 (w), 763, 750, 722, 653 (m), 607, 579 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 392 ($[M]^+$, 11), 336 (09), 280 (100), 235 (23), 219 (17), 206 (34). HRMS (EI, 70 eV): calcd for $C_{21}H_{28}O_7$ $[M]^+$: 392.18295; found: 392.18308.

***(2E,2'E)-Bis(6-methylheptyl)3,3'-[5-(ethoxycarbonyl)furan-2,3-diyl]diacrylate*(3d)**. Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ (12 mg, 5 mol%), XPhos (48 mg, 10 mol%), Isooctylacrylate **(2d)** (460 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3d** was isolated as yellow solid, (428 mg, 85%), 153–155°C. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.72-0.87 (m, 12H, $4CH_3$), 0.89-0.90 (m, 2H, 2CH), 1.10-1.23 (m, 8H, $4CH_2$), 1.32 (t, 3H, *J* = 7.3 Hz, CH_3), 1.36-1.39 (m, 8H, $4CH_2$), 4.10-4.22 (m, 4H, $2CH_2O$), 4.32 (q, 2H, *J* = 7.1 Hz, CH_2O), 6.23 (dd, 1H, *J* = 2.8-15.8 Hz, CH_{vinyl}), 6.61 (dd, 1H, *J* = 2.8-15.8 Hz, CH_{vinyl}), 7.27 (s, 1H, ArH), 7.53 (d, 1H, *J* = 8.2 Hz, CH_{vinyl}), 7.58 (d, 1H, *J* = 8.2 Hz, CH_{vinyl}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.3 (CH_3), 19.5 ($4CH_3$), 27.7 (2CH), 23.4, 25.7, 28.6, 31.4 ($2CH_2$), 61.6, 65.1, 65.4 (OCH_2), 115.7, 121.4, 121.8 (CH), 125.2 (C), 126.7, 131.8 (CH), 145.7, 152.6 (C), 158.4, 166.2, 166.4 (CO). IR (KBr): *v* = 3107, 2956, 2948, 2857 (w), 1717, 1635 (s), 1579, 1517, 1469 (m), 1457, 1392, 1368, 1346 (w), 1323 (s), 1311, 1266, 1253, 1242 (w), 1224 (m), 1178 (s), 1125, 1105, 1053, 1039 (w), 1021, 978, 962 (m), 910 (w), 875, 861 (m), 823, 798 (w), 764, 723, 663, 598 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 504 ($[M]^+$, 40), 459 (30), 457 (60), 392 (35), 376 (100), 348 (53), 317 (33), 280 (26), 246 (50), 219 (72). HRMS (EI, 70 eV): calcd for $C_{29}H_{44}O_7$ $[M]^+$: 504.30816; found: 504.30782.

***(2E,2'E)-Dibutyl 3,3'-[5-(ethoxycarbonyl)furan-2,3-diyl]diacrylate* (3e)**. Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ (12 mg, 5 mol%), XPhos (48 mg, 10 mol%), n-Butylacrylate **(2e)** (320 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3e** was isolated as light yellow solid (345 mg, 88%), 158–160 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, 6H, *J* = 7.4 Hz, $2CH_3$), 1.32 (t, 3H, *J* = 7.1 Hz, CH_3), 1.35-1.42 (m, 4H, $2CH_2$), 1.57-1.67(m, 4H, $2CH_2$), 4.12-4.18 (m, 4H, $2CH_2O$), 4.32 (q, 2H, *J* = 7.1 Hz,

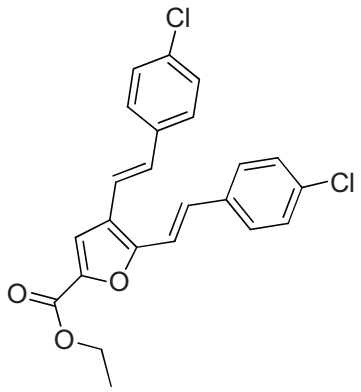
CH_2O), 6.23 (d, 1H, J = 15.8 Hz, CH_{vinyl}), 6.61 (d, 1H, J = 15.5 Hz, CH_{vinyl}), 7.27 (s, 1H, ArH), 7.53 (d, 1H, J =8.1 Hz, CH_{vinyl}), 7.58 (d, 1H, J = 8.1 Hz, CH_{vinyl}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7 ($2CH_3$), 14.3 (CH_3), 19.1 ($2CH_2$), 30.7 ($2CH_2$), 61.6, 64.8, 64.9 (CH_2O), 115.8, 121.6, 121.7 (CH), 125.2 (C), 126.5, 131.4 (CH), 145.9, 152.3 (C), 158.0, 166.1, 166.2 (CO). IR (KBr): ν = 3107, 2953, 2929, 2857 (w), 1715, 1632 (s), 1579, 1518, 1467 (m), 1453, 1392, 1368, 1346 (w), 1321 (s), 1301, 1265, 1252, 1240 (w), 1223 (m), 1175 (s), 1123, 1107, 1052, 1038 (w), 1024, 977, 961 (m), 910 (w), 875, 860 (m), 822, 799 (w), 764, 724, 661, 596 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 392 ($[M]^+$, 43), 347 (09), 336 (11), 319 (23), 291 (16), 263 (15), 235 (60), 219 (49), 191 (100), 179 (21). HRMS (EI, 70 eV): calcd for $C_{21}H_{28}O_7$ $[M]^+$: 392.18295; found: 392.183243.

(2E,2'E)-Dimethyl 3,3'-[5-(ethoxycarbonyl)furan-2,3-diyl]diacrylate **(3f)**. Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ **(**12 mg, 5 mol%), XPhos (48 mg, 10 mol%), Methylacrylate **(2f)** (320 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3f** was isolated as orange solid **(**259 mg, 84%), 150–152 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, 3H, J = 7.1 Hz, CH_3), 3.74 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.32 (q, 2H, J = 7.3 Hz, CH_2O), 6.23 (d, 1H, J = 15.9 Hz, CH_{vinyl}), 6.59 (d, 1H, J = 15.9 Hz, CH_{vinyl}), 7.27 (s, 1H, ArH), 7.54 (d, 1H, J = 8.7 Hz, CH_{vinyl}), 7.59 (d, 1H, J = 8.7 Hz, CH_{vinyl}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.2 (CH_3), 50.9, 51.1 (OCH_3), 60.7 (OCH_2), 114.7, 120.1, 120.2 (CH), 124.2 (C), 125.7, 130.7 (CH), 145.0, 151.3 (C), 157.0, 165.4, 165.5 (CO). IR (KBr): $\tilde{\nu}$ = 3397, 3109, 2985 (w), 1708 (s), 1639 (m), 1580, 1517, 1443, 1395(w), 1367, 1321 (m), 1267, 1256, 1234, 1223 (w), 1182 (s)1117, 1083 (w), 1036, 968, 957 (s), 893, 874, 863, 810 (w), 763, 746, 722, 656 (m), 607, 585 (w), cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 308 ($[M]^+$, 100), 277 (36), 263 (20), 249 (63), 235 (91), 217 (31), 205 (55), 177 (44), 162 (30), 145 (92). HRMS (EI, 70 eV): calcd for $C_{15}H_{16}O_7$ $[M]^+$: 308.08905; found: 308.08870.

(2E,2'E)-Diethyl 3,3'-[5-(ethoxycarbonyl)furan-2,3-diyl]diacrylate **(3g)**. Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ **(**12 mg, 5 mol%), XPhos (48 mg, 10 mol%), n-Ethylacrylate **(2g)** (320 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3g** was isolated as yellow solid **(**302 mg, 90%), 168–170°C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.25-1.35 (m, 9H, $3CH_3$), 4.17-4.25 (m, 4H, $2CH_2O$), 4.32 (q, 2H, J = 7.3 Hz,

CH_2O), 6.23 (d, 1H, J = 15.7 Hz, CH_{vinyl}), 6.60 (d, 1H, J = 15.7 Hz, CH_{vinyl}), 7.27 (s, 1H, ArH), 7.54 (d, 1H, J = 8.1 Hz, CH_{vinyl}), 7.59 (d, 1H, J = 8.1 Hz, CH_{vinyl}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.2 ($2CH_3$), 14.3 (CH_3), 60.8, 61.0, 61.6 (CH_2O), 115.7, 121.6, 121.7 (CH), 125.2 (C), 126.5, 131.4 (CH), 145.9, 152.3 (C), 158.0, 166.0, 166.1 (CO). IR (KBr): $\tilde{\nu}$ =3399, 3108, 2983, 2938, 2906 (w), 1705 (s), 1637 (m), 1579, 1515, 1444, 1392 (w), 1366, 1320 (m), 1268, 1255, 1234, 1221 (w), 1180 (s)1116, 1081 (w), 1037, 969, 958 (s), 893, 874, 863, 810 (w), 763, 746, 722, 656 (m), 607, 585 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 336 ($[M]^+$, 100), 291 (53), 263 (89), 235 (45), 219 (46), 217 (35), 191 (70). HRMS (EI, 70 eV): calcd for $C_{17}H_{20}O_7$ $[M]^+$: 336.12035; found: 336.11988.

Ethyl 4,5-bis(4-chlorostyryl)furan-2-carboxylate **(3h).** Starting with **1** (300 mg, 1.0 mmole), $Pd(OAc)_2$ (12 mg, 5 mol%), XPhos (48 mg, 10 mol%), 4-Chlorostyrene **(2h)** (320 mg, 2.5 mmole), NEt_3 (1.1 ml, 8 mmole), DMF (5 ml), **3h** was isolated as a light brown oil (340 mg, 83%). ^1H NMR (300 MHz, $CDCl_3$): δ= 1.33 (t, 3H, J = 7.2 Hz, CH_3), 4.32 (q, 2 H, J = 7.2 Hz, OCH_2), 6.76 (d, 1H, J = 16.2 Hz, CH_{vinyl}), 6.91 (d, 1H, J = 16.2 Hz, CH_{vinyl}), 6.98 (d, 1H, J = 16.1 Hz, CH_{vinyl}), 7.19 (s, 1 H, ArH), 7.24-7.27 (m, 4H, ArH), 7.32-7.35 (m, 3H, ArH), 7.39 (d, 2H, J = 8.5 Hz, ArH).



^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.4 (CH_3), 61.2 (OCH_2), 113.2, 116.1, 117.2 (CH), 123.2 (C), 127.6, 128.0, 128.9, 129.0, 129.2, 130.0 (CH), 133.6, 134.2, 134.8, 135.3, 143.8, 152.6 (C), 158.7 (CO). IR (KBr): ν= 3052, 2981, 2961, 2921, 2850 (w), 1712 (s), 1633, 1588 (w), 1562, 1508, 1490 (m), 1466, 1443, 1403 (w), 1368 (m), 1315 (s), 1261 (m), 1187, 1116, 1089, 1007, 954 (s), 892, 846, 827 (w), 806 (s), 759, 738 (m), 713, 667, 653, 608 (w), 574 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 414 ($[M, {}^{35}Cl, {}^{37}Cl]^+$, 72), 412 ($[M, {}^{35}Cl, {}^{35}Cl]^+$, 100), 340 (05), 369 (29), 275 (22), 239 (30). HRMS (EI, 70 eV): calcd for $C_{23}H_{18}Cl_2O_3$ $[M, {}^{35}Cl, {}^{35}Cl]^+$: 412.06275; found: 412.06168, calcd for $C_{23}H_{18}Cl_2O_3$ $[M, {}^{35}Cl, {}^{37}Cl]^+$: 414.05980; found: 414.05924.

8.1.2 Synthesis of 5,6-disubstitutedbenzofurans 4

General procedure B for the synthesis of benzofurans **4a-h.** A diphenyl ether solution (3 mL) of **3a-h** (0.5 mmol) was stirred at 170 °C for 12 h in a pressure tube. The solution was allowed to cool to 20 °C and Pd/C- 10% (30 mg, 5.6 mol%) was added. The solution was stirred at 170 °C (or mentioned) for 12 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).

2-Ethyl 5,6-diisobutyl benzofuran-2,5,6-tricarboxylate **(4a)**. Starting with **3a** (196 mg, 0.5 mmole), Pd/C (30 mg, 10 mol%), diphenylether (3 ml), **4a** was isolated as light yellow oil (185 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (s, 6H, $2CH_3$), 0.94 (s, 6H, $2CH_3$), 1.37 (t, 3H, J = 7.1 Hz, CH_3), 1.96-2.01 (m, 2H, 2CH), 4.03 (d, 2H, J = 3.4 Hz, CH_2O), 4.05 (d, 2H, J = 3.3 Hz, CH_2O), 4.40 (q, 2H, J = 7.1 Hz, CH_2O), 7.49 (s, 1H, ArH), 7.87 (s, 1H, ArH), 8.01 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.3 (CH_3), 19.1, 19.2 ($4CH_3$), 27.7 (2CH), 62.0, 72.0, 72.1 (CH_2O), 113.4, 113.5, 124.3 (CH), 128.6, 128.8, 131.9, 148.7, 155.7 (C), 158.8, 167.1, 167.1 (CO). IR (KBr): ν = 3435, 3108 (w), 2960 (m), 2874 (w), 1719 (s), 1621 (w), 1583, 1467 (m), 1442, 1394 (w), 1369, 1345 (m), 1309 (s), 1259 (m), 1194, 1155, 1100 (s), 1038, 982, 943 (m), 901, 846 (w), 765, 740, 690 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 390 ($[M]^+$, 05), 345 (20), 278 (30), 261 (100), 233 (16). HRMS (EI, 70 eV): calcd for $C_{21}H_{26}O_7$ $[M]^+$: 390.16730; found: 390.16659.

2-Ethyl 5,6-dihexyl benzofuran-2,5,6-tricarboxylate **(4b)**. Starting with **3b** (224 mg, 0.5 mmole), Pd/C (30 mg, 10 mol%), diphenylether (3 ml), **4b** was isolated as light yellow oil **(**216 mg, 97%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81-0.85 (m, 6H, $2CH_3$), 1.24-1.28 (m, 12H, $6CH_2$), 1.37 (t, 3H, J = 7.2 Hz, CH_3), 1.63-1.72 (m, 4H, $2CH_2$), 4.22-4.28 (m, 4H, $2CH_2O$), 4.40 (q, 2H, J = 7.4 Hz, CH_2O), 7.50 (s, 1H, ArH), 7.86 (s, 1H, ArH), 8.01 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 14.3 (CH_3), 22.5, 25.6, 28.5, 31.5 ($2CH_2$), 62.0, 66.1, 66.2 (OCH_2), 113.4, 113.5, 124.3 (CH), 128.5, 128.7, 131.9, 148.7, 155.7 (C), 158.8, 167.1, 167.3 (CO). IR (KBr): ν = 2955, 2928, 2857, (w), 1720 (s), 1621, 1582 (w), 1462 (m), 1369, 1344 (w), 1302 (s), 1258 (m), 1193, 1156, 1101 (s), 1017 (m), 944, 900, 836 (w), 765 (m), 740, 690, 574 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 446 ($[M]^+$, 20), 401 (20), 363 (20), 345 (10), 278 (14), 261 (100), 233 (12). HRMS (EI, 70 eV): calcd for $C_{25}H_{34}O_7$ $[M]^+$: 446.22990; found: 446.22914.

***2-Ethyl 5,6-bis(6-methylheptyl) benzofuran-2,5,6-tricarboxylate* (4d)**. Starting with **3d** (252 mg, 0.5 mmole), Pd/C (30 mg, 10 mol%), diphenylether (3 ml), **4d** was isolated as light yellow oil (221 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.74-0.89 (m, 12H, $4CH_3$), 0.90-0.91 (m, 2H, 2CH), 1.11-1.23 (m, 8H, $4CH_2$), 1.33 (t, 3H, J = 7.3 Hz, CH_3), 1.37-1.41 (m, 8H, $4CH_2$), 4.12-4.24 (m, 4H, $2CH_2O$), 4.34 (q, 2H, J = 7.1 Hz, CH_2O), 7.49 (s, 1H, ArH), 7.85 (s, 1H, ArH), 8.00 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.4 (CH_3), 19.8 ($4CH_3$), 27.3 (2CH), 23.5, 25.8, 28.7, 31.6 ($2CH_2$), 61.7, 65.2, 65.5 (OCH_2), 113.6, 113.7, 124.5 (CH), 128.7, 128.9, 131.7, 148.4, 155.8 (C), 158.6, 166.3, 166.5 (CO). IR (KBr): ν = 3109, 2958, 2874 (w), 1709 (s), 1633, 1578, 1515, 1469 (m), 1394 (w), 1368 (m), 1343 (w), 1318 (s), 1300, 1270 (w), 1255 (m), 1239 (w), 1220 (m), 1171 (s), 1114 (m), 1080 (w), 1008, 962 (s), 875, 861, 837 (w), 765, 748, 720, 693, 657 (m), 609, 595, 542 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 502 ($[M]^+$, 20), 457 (30), 391 (28), 279 (21), 261 (100), 233 (15). HRMS (EI, 70 eV): calcd for $C_{29}H_{42}O_7$ $[M]^+$: 502.29251; found: 502.29179.

***5,6-Dibutyl 2-ethyl benzofuran-2,5,6-tricarboxylate* (4e)**. Starting with **3e** (196 mg, 0.5 mmole), Pd/C (30 mg, 10 mol%), diphenylether (3 ml), **4e** was isolated as highly viscous yellow oil (175 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, 6H, J = 7.3 Hz, $2CH_3$), 1.32 (t, 3H, J = 7.2 Hz, CH_3), 1.35-1.45 (m, 4H, $2CH_2$), 1.62-1.71(m, 4H, $2CH_2$), 4.12-4.18 (m, 4H, $2CH_2O$), 4.40 (q, 2H, J = 7.2 Hz, CH_2O), 7.49 (s, 1H, ArH), 7.86 (s, 1H, ArH), 8.00 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7 ($2CH_3$), 14.3 (CH_3), 19.2 ($2CH_2$), 30.5, 30.6 (CH_2), 62.0, 65.8, 65.9 (CH_2O), 113.4, 113.5, 124.3 (CH), 128.5, 128.7, 131.9, 148.7, 155.7 (C), 158.8, 167.1, 167.3 (CO). IR (KBr): ν = 2958 (m), 2933, 2873 (w), 1719 (s), 1621 (w), 1583 (m), 1563, 1508, 1488 (w), 1462 (m), 1369, 1344 (w), 1302 (s), 1257, 1242 (w), 1193, 1156, 1100 (s), 1060, 1037, 1015, 961 (w), 941 (m), 901, 840 (w), 765, 740, 691 (m), 643, 603, 579 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 390 ($[M]^+$, 43), 345 (30), 335 (11), 317 (40), 278 (18), 261 (100), 233 (17). HRMS (EI, 70 eV): calcd for $C_{21}H_{26}O_7$ $[M]^+$: 390.16730; found: 390.16658.

***2-Ethyl 5,6-dimethyl benzofuran-2,5,6-tricarboxylate* (4f)**. Starting with **3f** (154 mg, 0.5 mmole), Pd/C (30 mg, 10 mol%), diphenylether (3 ml), **4f** was isolated as light yellow oil (142 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (t, 3H, J = 7.1 Hz, CH_3), 3.86 (s, 3H, CH_3O), 3.88 (s, 3H, CH_3O), 4.40 (q, 2H, J = 7.3 Hz, CH_2O), 7.49 (s, 1H, ArH), 7.86 (s, 1H, ArH), 8.03 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.3 (CH_3), 52.8, 53.0 (OCH_3), 62.1 (CH_2O), 113.4, 113.5, 124.4 (CH), 128.0, 128.9, 131.5, 148.8, 155.8 (C), 158.8, 167.6, 167.7 (CO). IR (KBr): ν = 2951, 2925, 2853 (w), 1721 (s), 1620, 1578 (w), 1564 (m), 1535, 1488, 1475, 1465 (w), 1431, 1372, 1347 (m), 1310 (s), 1265, 1242 (m), 1207, 1156, 1100 (s), 1043, 1019, 966 (m), 934, 919, 876 (w), 854, 825, 785 (m), 765 (s), 742, 690, 667, 641, 568 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 306 ([M]$^+$, 40), 276 (15), 275 (100), 261 (08), 247 (44), 217 (05). HRMS (EI, 70 eV): calcd for $C_{15}H_{14}O_7$ [M]$^+$: 306.07340; found: 306.07314.

***Triethyl benzofuran-2,5,6-tricarboxylate* (4g)**. Starting with **3g** (168 mg, 0.5 mmole), Pd/C (30 mg, 10 mol%), diphenylether (3 ml), **4g** was isolated as highly viscous orange oil (157 mg, 94%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29-1.40 (m, 9H, 3CH_3), 4.18-4.45 (m, 6H, 3CH_2O), 7.49 (s, 1H, ArH), 7.86 (s, 1H, ArH), 8.03 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ= 14.0, 14.1, 14.3 (CH_3), 61.8, 61.9, 62.0 (CH_2O), 113.3, 113.4, 124.3 (CH), 128.4, 128.7, 131.8, 148.7, 155.7 (C), 158.8, 167.1, 167.2 (CO). IR (KBr): ν = 3055, 2981, 2929 (w), 1714 (s), 1622 (w), 1581, 1564 (m), 1536, 1504 (w), 1488, 1474, 1445, 1396 (m), 1368 (s), 1345 (w), 1305, 1238, 1198, 1156, 1102 (s), 1043, 1020, 906, 868, 837, 785 (m), 765 (s), 740, 691, 671, 643, 562 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 ([M]$^+$, 25), 306 (04), 289 (26), 261 (100), 247 (07), 233 (32), 217 (06). HRMS (EI, 70 eV): calcd for $C_{17}H_{18}O_7$ [M]$^+$: 334.10470; found: 334.10407.

***Ethyl 5,6-bis(4-chlorophenyl)-benzofuran-2-carboxylate* (4h).** Starting with **3h** (206 mg, 0.5 mmole), Pd/C (30 mg, 10 mol%), diphenylether (3 ml), **4h** was isolated as a light brown highly viscous oil (184 mg, 90%). ^{1}H NMR (250 MHz, $CDCl_3$): δ= 1.38 (t, 3H, J = 7.2 Hz, CH_3), 4.39 (q, 2 H, J = 7.1 Hz, OCH_2), 6.95 (d, 2H, J = 8.6 Hz, ArH), 7.10 (d, 2H, J = 8.7 Hz, ArH), 7.14 (d, 2H, J =

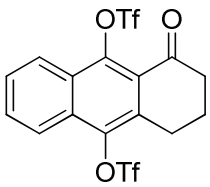
8.6 Hz, ArH), 7.16 (d, 2H, J = 8.6 Hz, ArH), 7.48 (s, 1H, ArH), 7.52 (s, 1H, ArH), 7.59 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.3 (CH_3), 60.7 (OCH_2), 112.5, 112.7, 123.3 (CH), 125.6 (C), 127.3, 127.4, 130.2, 130.3 (CH), 131.9, 132.2, 135.0, 138.2, 138.3, 138.5, 145.8, 154.3 (C), 158.4 (CO). IR (KBr): ν = 2957, 2922, 2852 (w), 1720 (s), 1657, 1622, 1581, 1566, 1555 (w), 1494, 1455 (m), 1434, 1392 (w), 1368, 1328, 1301, 1285, 1261, 1240, 1228 (m), 1183, 1152, 1089, 1012 (s), 953 (m), 934, 889, 871, 854 (w), 827 (s), 765, 756, 743, 728 (m), 697, 682, 646, 636, 625, 590, 537 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 412 ([M, ^{35}Cl, ^{37}Cl]$^+$, 68), 410 ([M, ^{35}Cl, ^{35}Cl]$^+$, 100), 365 (05), 312 (14), 275 (07), 239 (30). HRMS (EI, 70 eV): calcd for $C_{23}H_{16}Cl_2O_3$ [M, ^{35}Cl, ^{35}Cl]$^+$: 410.04710; found: 410.047128, calcd for $C_{23}H_{16}Cl_2O_3$ [M, ^{35}Cl, ^{37}Cl]$^+$: 412.04415; found: 412.04488.

8.2 Regioselective Suzuki-Miyaura Cross-Coupling Reactions of the Bis(triflate) of 1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-one

8.2.1 Procedure for synthesis of 1-oxo-1,2,3,4-tetrahydroanthracene-9,10-diyl bis(trifluoromethanesulfonate) (6):

To a solution of **5** (1.0 equiv.) in CH_2Cl_2 (10 mL per 1 mmol of **5**), was added pyridine (4.0 equiv.) at – 78°C under an argon atmosphere. After stirring for 10 min, Tf_2O (2.4 equiv.) was added at -78 °C. The mixture was allowed to warm up to 0 °C and stirred overnight. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The residue was purified by rapid column chromatography (flash silica gel, heptanes/EtOAc) without prior aqueous work up.

1-Oxo-1,2,3,4-tetrahydroanthracene9,10diylbis(trifluoromethanesulfonate **(6):**



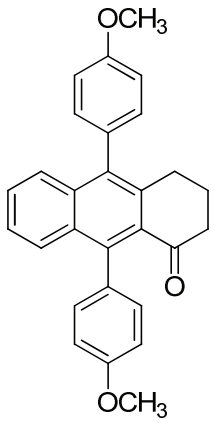
Starting with **5** (2.0 g, 8.8 mmol) in CH_2Cl_2 (88 mL), pyridine (2.8 mL, 35.0 mmol), at r.t. under an argon atmosphere. After 10 min stirring, Tf_2O (3.5 mL, 21 mmol), was added at -78 °C. and **6** was isolated as a yellow solid (3.67 g, 85%), mp 162-164. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10-2.18 (m, 2H, CH_2), 2.76 (t, 2H, J = 6.9 Hz, CH_2), 3.15 (t, 2H, J = 6.4 Hz, CH_2), 7.65-7.79 (m, 2H, ArH), 8.05 (d, 1H, J = 8.5 Hz, ArH), 8.18 (d, 1H, J = 8.5 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.56, -72.55. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.6, 25.2, 39.6 (CH_2), 118.5 (q, $J_{F,C}$ = 320.2 Hz, CF_3), 118.6 (q, $J_{F,C}$ = 319.6 Hz, CF_3), 121.5 (CH), 123.2 (q, $J_{F,C}$ = 1.4 Hz, CH), 123.9, 126.4 (C), 128.8 (CH), 129.8 (C), 131.3 (CH). 133.3, 140.4,

143.8 (C), 195.9 (CO). IR (KBr): ν = 2849, 2880, 2915, 2964 (w), 1697 (m), 1625, 1594, 1564, 1494, 1442 (w), 1422 (s), 1384, 1353, 1326, 1278 (w), 1205, 1185, 1129 (s), 1076, 1027 (m), 962 (s), 909 (m), 862 (s), 823, 809, 785 (w), 771 (m), 749 (s), 709 (m), 670 (s), 654, 644, 631 (w), 595 (s), 564, 532 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 492 (M^+, 92), 359 (82), 295 (97), 253 (54), 209 (73), 198 (100), 170 (94). HRMS (EI, 70 eV): calcd for $C_{16}H_{10}F_6O_7S_2$ $[M]^+$: 491.97666; found: 491.97613.

8.2.2 General Procedure for synthesis of symmetrical 1,2,3,4-tetrahydro-9,10-diarylanthracen-1-ones (*8a-g*) and 10-aryl-1,2,3,4-tetrahydro-9-trifluoromethyl sulfonyloxy-anthracen-1-ones (*9a-g*):

A 1,4-dioxane solution (4-5 mL per 0.3 mmol of **6**) , K_3PO_4 (1.5-2.0 equiv per cross-couplin), $Pd(PPh_3)_4$ (3mol% per cross-coupling) and arylboronic acid **7** (1.0-1.1 equiv per cross-coupling) was stirred at 120 or 100 °C for 10 h under argon atmosphere. After cooling to 20 °C, a saturated aqueous solution of NH_4Cl was added. The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography.

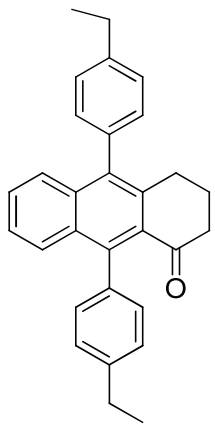
9,10-Bis(4-methoxyphenyl)-3,4-dihydroanthracen-1(2H)-one **(8a):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), $Pd(PPh_3)_4$ (21 mg, 6 mol-%), **7a** (83 mg, 0.66 mmol) and 1,4 dioxane (5 mL), **8a** was isolated as yellow solid (93 mg, 75%), mp. 277-278 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.89-1.98 (m, 2H, CH_2), 2.54 (t, 2H, J = 6.7 Hz, CH_2), 2.71 (t, 2H, J = 6.3 Hz, CH_2), 3.82 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 6.95 (d, 2H, J = 8.7 Hz, ArH), 7.00 (d, 2H, J = 8.7 Hz, ArH), 7.08 (d, 2H, J = 8.7 Hz, ArH), 7.15 (d, 2H, J = 8.7 Hz, ArH), 7.20-7.25 (m, 1H, ArH), 7.30 (td, 1H, J = 1.6, 8.5 Hz, ArH), 7.36-7.39 (m, 1H, ArH), 7.49-7.52 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.7, 29.4, 40.8 (CH_2), 55.2, 55.3 (OCH_3), 113.5, 114.1, 125.4, 126.3, 127.7, 128.6 (CH), 129.7 (C), 130.3 (CH), 131.1 (C), 131.2 (CH), 132.4, 132.5, 134.7, 137.4, 137.6, 141.6, 158.5, 158.9 (C), 200.2 (CO). IR (KBr): ν = 3064, 3033, 3001, 2950, 2904, 2833 (w), 1689, 1607 (m), 1573, 1556 (w), 1509 (s), 1494, 1461, 1455, 1440, 1408, 1373, 1349, 1325, 1303 (w), 1283 (m), 1238 (s), 1172, 1154, 1104

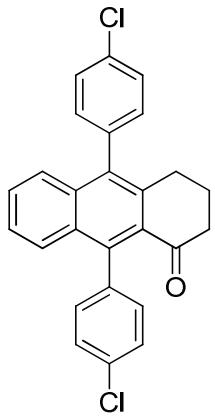
(m), 1031 (s), 1004 (m), 959, 939, 927, 901, 865 (w), 834, 795, 767 (m), 728, 681, 648, 637, 623 (w), 589 (m), 542 (s) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 408 (M^+, 100), 279 (05), 349 (08), 321 (07). HRMS (EI, 70 eV): calcd for $C_{28}H_{24}O_3$ $[M]^+$: 408.17200; found: 408.17115.

***9,10-Bis(4-ethylphenyl)-3,4-dihydroanthracen-1(2H)-one* (8b):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), $Pd(PPh_3)_4$ (21 mg, 6 mol-%), **7b** (99 mg, 0.66 mmol) and 1,4 dioxane (5 mL), **8b** was isolated as a light yellow solid (97 mg, 80%), mp. 253-255 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, 3H, J = 7.6 Hz, CH_3), 1.28 (t, 3H, J = 7.6 Hz, CH_3), 1.89-1.97 (m, 2H, CH_2), 2.53 (t, 2H, J = 6.9 Hz, CH_2), 2.67-2.74 (m, 6H, $3CH_2$), 7.08 (d, 2H, J = 8.0 Hz, ArH), 7.14 (d, 2H, J = 7.8 Hz, ArH), 7.18-7.23 (m, 2H, ArH), 7.25-7.31 (m, 4H, ArH), 7.35 (d, 1H, J = 8.2 Hz, ArH), 7.48 (d, 1H, J = 8.2 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.4, 15.5 ($2CH_3$), 22.7 (CH_2), 28.7 ($2CH_2$), 29.4, 40.9 ($2CH_2$), 125.4, 126.3, 127.5, 127.7, 128.2, 128.6, 129.1 (CH), 129.5 (C), 130.1 (CH), 132.3, 134.6, 136.4, 137.3, 137.7, 137.8, 142.1, 142.4, 143.4 (C), 200.4 (CO). IR (KBr): ν = 3045, 3022, 2961, 2930, 2872 (w), 1687 (s), 1651, 1633, 1608, 1566 (w), 1551, 1511 (m), 1494, 1455, 1439 (w), 1406, 1372 (m), 1349, 1325 (w), 1287, 1218, 1179, 1152 (m), 1113, 1068, 1048, 1034, 1023 (w), 1006 (m), 970 (w), 933 (m), 901, 859 (w), 836, 763 (s), 679 (m), 649, 637, 628, 585 (w), 535 (s) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 404 (M^+, 100), 403 (53), 375 (27), 347 (16), 318 (13), 302 (09), 289 (16). HRMS (EI, 70 eV): calcd for $C_{30}H_{28}O_1$ $[M]^+$: 404.21347; found: 404.21297.

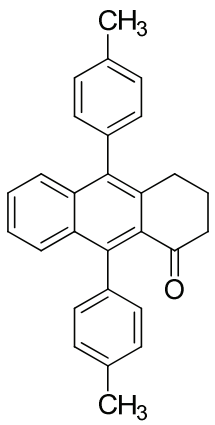
***9,10-Bis(4-chlorophenyl)-3,4-dihydroanthracen-1(2H)-one* (8c):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), $Pd(PPh_3)_4$ (21 mg, 6 mol-%), **7c** (103 mg, 0.66 mmol) and 1,4 dioxane (5 mL), **8c** was isolated as a light yellow solid (90 mg, 72%), mp. 286-288 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.91-1.99 (m, 2H, CH_2), 2.54 (t, 2H, J = 6.7 Hz, CH_2), 2.69 (t, 2H, J = 6.3 Hz, CH_2), 7.09 (d, 2H, J = 8.2 Hz, ArH), 7.18 (d, 2H, J = 8.0 Hz, ArH), 7.22-7.34 (m, 3H, ArH), 7.36-7.39 (m, 3H, ArH), 7.46 (d, 2H, J = 8.2 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.6, 29.4, 40.7 ($3CH_2$), 125.9, 126.0, 128.2, 128.3, 128.4, 129.1 (CH), 129.2 (C), 130.5, 131.5 (CH), 131.9, 132.8, 133.7, 134.3, 136.9, 137.3, 137.4, 138.9, 141.1 (C), 199.5 (CO). IR (KBr): ν = 3078, 3049, 2947, 2870 (w),

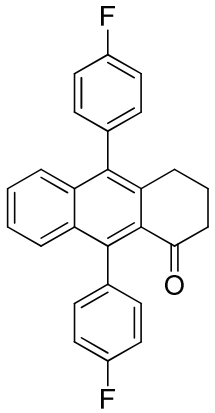
1687 (s), 1650, 1608, 1592, 1548, 1502 (w), 1488 (s), 1455, 1445, 1433 (w), 1393, 1372 (m), 1350, 1329, 1317 (w), 1289 (m), 1248 (w), 1223, 1180, 1157 (m), 1125, 1099 (w), 1085 (s), 1049, 1033 (w), 1016, 1008 (s), 975, 943 (w), 932, 900 (m), 837, 829, 788, 772 (s), 734, 714, 687, 667, 633, 621, 605 (w), 549 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 418 ([M, ^{35}Cl, $^{37}Cl]^+$, 65), 416 ([M, ^{35}Cl, $^{35}Cl]^+$, 100), 416 ($[M]^+$, 100), 387 (05), 352 (15), 318 (17), 389 (51). HRMS (EI, 70 eV): calcd for $C_{26}H_{18}Cl_2O_1$ [M, ^{35}Cl, $^{35}Cl]^+$: 416.07292; found: 416.07282, calcd for $C_{26}H_{18}Cl_2O_1$ [M, ^{35}Cl, $^{37}Cl]^+$: 418.06997; found: 418.07036.

***9,10-Di-p-tolyl-3,4-dihydroanthracen-1(2H)-one* (8d):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), $Pd(PPh_3)_4$ (21 mg, 6 mol-%), **7d** (90 mg, 0.66 mmol) and 1,4 dioxane (5 mL), **8d** was isolated as a yellowish white solid (96 mg, 85%), mp. 245-246 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.87-1.97 (m, 2H, CH_2), 2.38 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.52 (t, 2H, J = 6.8 Hz, CH_2), 2.70 (t, 2H, J = 6.4 Hz, CH_2), 7.05 (d, 2H, J = 7.9 Hz, ArH), 7.11 (d, 2H, J = 8.1 Hz, ArH), 7.19-7.22 (m, 3H, ArH), 7.24-7.31 (m, 3H, ArH), 7.33-7.37 (m, 1H, ArH), 7.47-7.51 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3, 21.4 (2CH_3), 22.7, 29.4, 40.8 (3CH_2), 125.4, 126.3 (CH), 126.8 (C), 127.7, 128.6, 128.8, 129.1, 129.4 (CH), 129.5 (C), 130.0 (CH), 132.2, 134.5, 136.1, 137.1, 137.3, 137.5, 137.7, 142.0 (C), 200.0 (CO). IR (KBr): ν = 3047, 3023, 2962, 2935, 2876 (w), 1688 (s), 1653, 1634, 1607, 1567 (w), 1552, 1513 (m), 1494, 1455, 1439 (w), 1406, 1372 (m), 1349, 1325 (w), 1287, 1218, 1179, 1152 (m), 1113, 1068, 1048, 1034, 1023 (w), 1006 (m), 971 (w), 934 (m), 901, 859 (w), 837, 765 (s), 679 (m), 649, 637, 628, 585 (w), 535 (s) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 376 (M^+, 100), 375 (55), 361 (12), 333 (18), 305 (13), 289 (19). HRMS (EI, 70 eV): calcd for $C_{28}H_{24}O_1$ $[M]^+$: 376.18217; found: 376.18117.

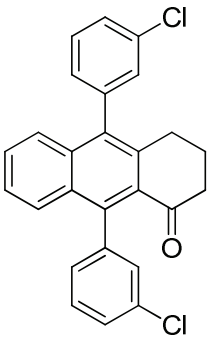
***9,10-Bis(4-fluorophenyl)-3,4-dihydroanthracen-1(2H)-one* (8e):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), $Pd(PPh_3)_4$ (21 mg, 6 mol-%), **7e** (92 mg, 0.66 mmol) and 1,4 dioxane (5 mL), **8e** was isolated as a yellow solid (81 mg, 70%), mp. 260-262 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.91-1.99 (m, 2H, CH_2), 2.54 (t, 2H, J = 6.9 Hz, CH_2), 2.68 (t, 2H, J = 6.5 Hz, CH_2), 7.08-7.11 (m, 3H, ArH), 7.13-7.18 (m, 2H, ArH), 7.19-7.21 (m, 2H, ArH), 7.22-7.29 (m, 2H, ArH), 7.31-7.36 (m, 2H, ArH), 7.41 (dt, 1H, J = 0.8, 8.3 Hz, ArH). ^{19}F NMR (282.4 MHz,

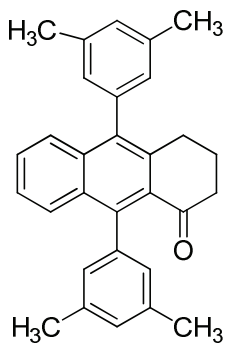
$CDCl_3$): δ = -114.54, -115.9. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.6, 29.4, 40.8 ($3CH_2$), 115.1 (d, $J_{F,C}$ = 21.4 Hz, CH), 115.7 (d, $J_{F,C}$ = 21.3 Hz, CH), 125.8, 126.1, 128.1, 128.4 (CH), 129.5 (C), 130.6 (d, $J_{F,C}$ = 8.0 Hz, CH), 131.7 (d, $J_{F,C}$ = 8.1 Hz, CH), 132.2, 134.5 (C), 134.8 (d, $J_{F,C}$ = 3.5 Hz, C), 136.1 (d, $J_{F,C}$ = 3.7 Hz, C), 137.0, 137.5, 141.2 (C), 162.1 (d, $J_{F,C}$ = 242.4 Hz, CF), 162.8 (d, $J_{F,C}$ = 264.5 Hz, CF), 199.7 (CO). IR (KBr): ν = 3114, 3068, 3044, 2927, 2852, 2248 (w), 1681 (s), 1602, 1550 (m), 1505 (s), 1455, 1439, 1403 (w), 1376, 1328, 1290 (m), 1214, 1156 (s), 1091, 1035 (w), 1009, 903 (m), 841, 806, 767, 726 (s), 696, 681, 646 (w), 581, 535 (s) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 384 (M^+, 100), 356 (12), 355 (30), 327 (27), 325 (21), 307 (10). HRMS (EI, 70 eV): calcd for $C_{26}H_{18}F_2O_1$ $[M]^+$: 384.13202; found: 384.13218.

***9,10-Bis(3-chlorophenyl)-3,4-dihydroanthracen-1(2H)-one* (8f):**



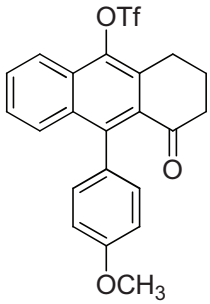
Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), $Pd(PPh_3)_4$ (21 mg, 6 mol-%), **7f** (103 mg, 0.66 mmol) and 1,4 dioxane (5 mL), **8f** was isolated as a yellow solid (92 mg, 74%), mp. 160-162 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.92-2.00 (m, 2H, CH_2), 2.55 (t, 2H, J = 6.4 Hz, CH_2), 2.68-2.72 (m, 2H, CH_2), 7.02-7.07 (m, 1H, ArH), 7.08-7.16 (m, 2H, ArH), 7.23-7.25 (m, 2H, ArH), 7.26-7.27 (m, 1H, ArH), 7.28-7.32 (m, 3H, ArH), 7.33-7.42 (m, 3H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.6, 29.4, 40.7 ($3CH_2$), 125.9, 126.0, 127.0, 127.4, 127.9, 128.3 (CH), 128.9 (C), 129.1, 129.2, 129.3, 130.1, 130.2, 130.3 (CH), 131.8, 133.9, 134.0, 134.1, 134.8, 136.9, 137.2, 140.9, 142.4 (C), 199.2 (CO). IR (KBr): ν = 3063, 2929, 2871 (w), 1687 (s), 1592, 1562 (m), 1501, 1475, 1455, 1443 (w), 1408, 1367 (m), 1351, 1327 (w), 1288, 1221, 1182, 1156, 1076 (m), 1034, 1014, 997 (w), 942, 905, 792 (m), 774, 727, 692 (s), 671, 659, 629, 589, 565 (w), 535 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 418 ([M, ^{35}Cl, $^{37}Cl]^+$, 66), 416 ([M, ^{35}Cl, $^{35}Cl]^+$, 100), 416 ($[M]^+$, 100), 381 (05), 353 (08), 325 (13), 289 (57). HRMS (EI, 70 eV): calcd for $C_{26}H_{18}Cl_2O_1$ [M, ^{35}Cl, $^{35}Cl]^+$: 416.07292; found: 416.07257, calcd for $C_{26}H_{18}Cl_2O_1$ [M, ^{35}Cl, $^{37}Cl]^+$: 418.06997; found: 418.07038.

***9,10-Bis(3,5-dimethylphenyl)-3,4-dihydroanthracen-1(2H)-one* (8g):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), $Pd(PPh_3)_4$ (21 mg, 6 mol-%), **7g** (99 mg, 0.66 mmol) and 1,4 dioxane (5 mL), **8g** was isolated as a yellow solid (109 mg, 90%), mp. 190-192 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.89-1.97 (m, 2H, CH_2), 2.32 (s, 6H, 2CH_3), 2.38 (s, 6H, 2CH_3), 2.55 (t, 2H, J = 6.7 Hz, CH_2), 2.74 (t, 2H, J = 6.2 Hz, CH_2), 6.79 (brs, 2H, ArH), 6.85 (brs, 2H, ArH), 6.99 (brs, 1H, ArH), 7.04 (brs, 1H, ArH), 7.20-7.25 (m, 1H, ArH), 7.27-7.32 (m, 1H, ArH), 7.33-7.37 (m, 1H, ArH), 7.47 (d, 1H, J = 8.4 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (2CH_3), 21.5 (2CH_3), 22.7, 29.4, 40.9 (3CH_2), 125.3, 126.3, 127.0, 127.6, 127.8, 128.4, 128.7, 128.9 (CH), 129.2, 132.1, 134.1, 134.4, 136.9, 137.1, 137.9, 138.2, 139.1, 140.4, 142.2 (C), 200.0 (CO). IR (KBr): ν = 3065, 3012, 2919, 2852, 2730 (w), 1688 (s), 1651 (w), 1598 (s), 1547, 1497 (m), 1454, 1444, 1403, 1370, 1350, 1331, 1317 (w), 1295 (m), 1259, 1230 (w), 1208, 1183, 1151 (m), 1033, 948 (s), 913, 895 (w), 850, 803, 767, 698 (s), 681, 662, 652, 548, 531 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 404 (M^+, 100), 403 (46), 389 (70), 361 (09), 333 (14), 317 (15), 303 (14). HRMS (EI, 70 eV): calcd for $C_{30}H_{28}O_1$ $[M]^+$: 404.21347; found: 404.21291.

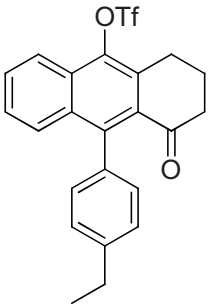
***10-(4-Methoxyphenyl)-4-oxo-1,2,3,4-tetrahydroanthracen-9-yl trifluoromethanesulfonate* (9a):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (127 mg, 0.6 mmol), $Pd(PPh_3)_4$ (11 mg, 3 mol-%), **7a** (45 mg, 0.3 mmol) and 1,4 dioxane (4 mL), **9a** was isolated as a yellow crystals solid (101 mg, 75%), mp. 175-176 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04-2.12 (m, 2H, CH_2), 2.60 (t, 2H, J = 6.7 Hz, CH_2), 3.15 (t, 2H, J = 6.3 Hz, CH_2), 3.81 (s, 3H, OCH_3), 6.92-6.96 (m, 2H, ArH), 6.99-7.02 (m, 2H, ArH), 7.33-7.39 (m, 1H, ArH), 7.53 (d, 1H, J = 8.6 Hz, ArH), 7.58-7.63 (m, 1H, ArH), 8.02 (d, 1H, J = 8.4 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.78. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.9, 25.4, 40.3 (3CH_2), 55.2 (OCH_3), 113 (CH), 118.5 (q, $J_{F,C}$ = 320.8 Hz, CF_3), 120.7, 127.0 (CH), 128.4 (C), 129.1 (CH), 129.6 (C), 129.8, 130.0 (CH), 130.8, 132.7, 133.8, 141.1, 143.3, 158.9 (C), 197.6 (CO). IR (KBr): ν = 3037, 3017, 2961, 2922, 2870, 2841 (w), 1693 (s), 1609, 1591, 1574, 1557 (w), 1514 (s), 1494, 1442 (w), 1414 (s), 1398, 1383, 1362 (w), 1323, 1287 (m), 1204, 1133 (s), 1106, 1075, 1050 (w), 1028, 970 (s), 934, 903, 870 (w), 844, 832 (s), 797, 774, 742, 712, 670 (m), 638 (w), 599 (s), 549, 537 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z

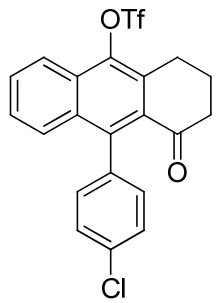
(%) = 450 (M^+, 47), 318 (44), 317 (100), 276 (12), 275 (12). HRMS (EI, 70 eV): calcd for $C_{22}H_{17}F_3O_5S$ $[M]^+$: 450.07433 ; found: 450.0745.

***10-(4-Ethylphenyl)-4-oxo-1,2,3,4-tetrahydroanthracen-9-yl trifluoromethanesulfonate* (9b):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (127 mg, 0.6 mmol), $Pd(PPh_3)_4$ (11 mg, 3 mol%), **7b** (45 mg, 0.3 mmol) and 1,4 dioxane (4 mL), **9b** was isolated as a yellow solid (99 mg, 74%), mp. 125-127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, 3H, J = 7.7 Hz, CH_3), 2.05-2.14 (m, 2H, CH_2), 2.60 (t, 2H, J = 6.7 Hz, CH_2), 2.70 (q, 2H, J = 7.8 Hz, CH_2), 3.17 (t, 2H, J = 6.3 Hz, CH_2), 7.01 (d, 2H, J = 8.1 Hz, ArH), 7.24 (d, 2H, J = 8.1 Hz, ArH), 7.34-7.40 (m, 1H, ArH), 7.51 (d, 1H, J = 8.4 Hz, ArH), 7.59-7.64 (m, 1H, ArH), 8.03 (d, 1H, J = 8.5 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.78. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.3 (CH_3), 21.9, 25.4, 28.7, 40.3 (4CH_2), 118.4 (q, $J_{F,C}$ = 320.7 Hz, CF_3), 120.7, 127.0, 127.6 (CH), 128.4 (C), 128.8, 129.2 (CH), 129.4 (C), 129.8 (CH), 132.7, 133.6, 136.0, 141.2, 143.1, 143.7 (C), 197.5 (CO). IR (KBr): ν = 3079, 3025, 2960, 2931, 2873 (w), 1692 (s), 1615, 1592, 1556, 1512, 1493, 1443 (w), 1417 (s), 1399, 1362 (w), 1321, 1290 (m), 1208, 1134 (s), 1077, 1048 (w), 1028, 964 (s), 930, 900, 876, 860 (w), 844, 832 (s), 806, 772, 760 (m), 705, 671, 644 (w), 599 (s), 566, 533 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 448 (M^+, 23), 315 (100), 286 (10). HRMS (EI, 70 eV):calcd for $C_{23}H_{19}F_3O_4S$ $[M]^+$: 448.09507; found: 448.09429.

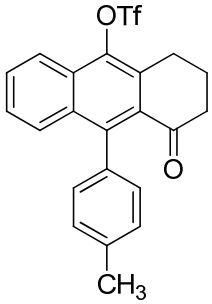
10-(4-Chlorophenyl)-4-oxo-1,2,3,4-tetrahydroanthracen-9-yl trifluoromethanesulfonate(9c)



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (127 mg, 0.6 mmol), $Pd(PPh_3)_4$ (11 mg, 3 mol-%), **7c** (47 mg, 0.3 mmol) and 1,4 dioxane (4 mL), **9c** was isolated as a yellowish white solid (95 mg, 70%), mp. 136-138 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.05-2.14 (m, 2H, CH_2), 2.60 (t, 2H, J = 6.7 Hz, CH_2), 3.18 (t, 2H, J = 6.3 Hz, CH_2), 7.03 (d, 2H, J = 8.4 Hz, ArH), 7.36-7.44 (m, 4H, ArH), 7.60-7.66 (m, 1H, ArH), 8.04 (d, 1H, J = 8.6 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.72. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.9, 25.4, 40.3 (3CH_2), 117.9 (q, $J_{F,C}$ = 320.6 Hz, CF_3), 119.9, 126.3, 127.4, 127.7 (CH), 128.2 (C), 129.0, 129.2 (CH), 131.7, 132.2, 132.3, 136.4, 140.5, 141.1 (C), 196.3 (CO). IR (KBr): ν = 3081, 3032, 2961, 2923, 2870 (w), 1689 (s), 1615, 1589, 1560, 1499, 1488, 1445 (w), 1428 (s), 1410 (m), 1398, 1384, 1363 (w), 1322, 1290 (m), 1201, 1133 (s), 1100 (w), 1089, 1074 (m), 1048 (w), 1030, 1015, 971 (s), 931, 902, 871 (w), 837 (s), 824,

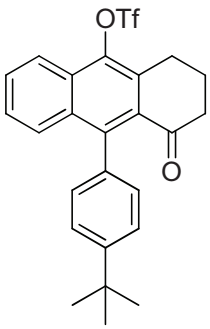
804, 791 (w), 771, 752 (s), 728, 698 (m), 663, 603, 581 (s), 551, 537 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 456 ([M, $^{37}Cl]^+$, 10), 454 ([M, $^{35}Cl]^+$, 28), 323 (32), 321 (100), 279 (17). HRMS (EI, 70 eV): calcd for $C_{21}H_{14}Cl_1F_3O_4S$ [M, $^{35}Cl]^+$: 454.02479; found: 454.02568.

***4-Oxo-10-(p-tolyl)-1,2,3,4-tetrahydroanthracen-9-yl trifluoromethanesulfonate* (9d):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (127 mg, 0.6 mmol), $Pd(PPh_3)_4$ (11 mg, 3 mol-%), **7d** (47 mg, 0.3 mmol) and 1,4 dioxane (4 mL), **9d** was isolated as a yellowish white solid (113 mg, 87%), mp. 129-131 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.04-2.21 (m, 2H, CH_2), 2.38 (s, 3H, CH_3), 2.54 (t, 2H, J = 6.7 Hz, CH_2), 3.17 (t, 2H, J = 6.3 Hz, CH_2), 6.98 (d, 2H, J = 8.0 Hz, ArH), 7.21 (d, 2H, J = 8.0 Hz, ArH), 7.31-7.38 (m, 1H, ArH), 7.51 (d, 1H, J = 8.4 Hz, ArH), 7.56-7.64 (m, 1H, ArH), 8.02 (d, 1H, J = 8.4 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.77. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (CH_3), 21.9, 25.4 , 40.8 (3CH_2), 118.6 (q, $J_{F,C}$ = 320.8 Hz, CF_3), 120.7, 127.0 (CH), 128.4 (C), 128.7, 128.9, 129.3 (CH), 129.5 (C), 129.8 (CH), 132.7, 133.6, 135.9, 136.9, 141.2, 143.7 (C), 197.5 (CO). IR (KBr): ν = 3025, 2964, 2925, 2872 (w), 1696 (s), 1617, 1592, 1561, 1514, 1494, 1444 (w), 1424 (s), 1408, 1385, 1361 (w), 1321, 1290 (m), 1199, 1136 (s), 1072 (m), 1025, 966 (s), 947, 932, 901, 869 (w), 847 (s), 822, 805, 795 (m), 768 (s), 746, 723, 706, 668, 639 (m), 604, 581 (s), 551, 528 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 434 (M^+, 30), 301 (100), 259 (14). HRMS (EI, 70 eV):calcd for $C_{22}H_{17}F_3O_4S$ $[M]^+$: 434.07942; found: 434.07902.

***10-(4-Tert-Butylphenyl)-4-oxo-1,2,3,4-tetrahydroanthracen-9-yl trifluoromethanesulfonate* (9e):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (127 mg, 0.6 mmol), $Pd(PPh_3)_4$ (11 mg, 3 mol-%), **7h** (53 mg, 0.3 mmol) and 1,4 dioxane (4 mL), **9e** was isolated as a yellow solid (105 mg, 75%), mp. 137-138 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 9H, 3CH_3), 2.10-2.14 (m, 2H, CH_2), 2.60 (t, 2H, J = 7.3 Hz, CH_2), 3.17 (t, 2H, J = 6.4 Hz, CH_2), 7.02 (d, 2H, J = 8.2 Hz, ArH), 7.34-7.39 (m, 1H, ArH), 7.41 (d, 2H, J = 8.4 Hz, ArH), 7.51 (d, 1H, J = 8.5 Hz, ArH), 7.59-7.64 (m, 1H, ArH), 8.03 (d, 1H, J = 8.8 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.78. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.9, 25.4 (CH_2), 31.5 (3CH_3), 34.7 (C), 40.3 (CH_2), 118.7 (q, $J_{F,C}$ = 320.6 Hz, CF_3), 120.7, 125.0, 127.0 (CH), 128.3 (C), 128.4, 129.2 (CH), 129.3 (C), 129.8 (CH), 132.6, 133.7, 135.8, 141.1, 143.8, 150.0 (C), 197.5 (CO). IR (KBr): ν = 3077, 3047, 3027, 2961, 2903, 2865 (w), 1693 (m), 1617, 1591, 1563, 1515, 1494, 1476, 1462, 1439 (w), 1404 (m), 1361,

1320, 1292 (w), 1202, 1135 (s), 1076, 1051 (w), 1023, 965 (m), 931, 901 (w), 848, 832 (s), 800, 772 (w), 749 (s), 719, 698, 687 (w), 665 (m), 641, 619 (w), 582, 561 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 476 (M^+, 04), 343 (14), 329 (05), 57 (100). HRMS (EI,70 eV):calcd for $C_{25}H_{23}F_3O_4S$ $[M]^+$: 476.12637; found: 476.12498.

4-Oxo-10-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydroanthracen-9-yl trifluoromethanesulfonate (9f): Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (127 mg, 0.6 mmol), $Pd(PPh_3)_4$ (11 mg, 3 mol-%), **7i** (57 mg, 0.3 mmol) and 1,4 dioxane (4 mL), **9f** was isolated as a yellow solid (107 mg, 73%), mp. 114-116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06-2.14 (m, 2H, CH_2), 2.56-2.61 (m, 2H, CH_2), 3.18 (t, 2H, J = 6.3 Hz, CH_2), 7.28-7.34 (m, 2H, ArH), 7.36-7.42 (m, 2H, ArH), 7.52 (t, 1H, J = 7.8 Hz, ArH), 7.61-7.67 (m, 2H, ArH), 8.06 (d, 1H, J = 8.6 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.72, -62.40. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.9, 25.4 , 40.2 (3CH_2), 118.7 (q, $J_{F,C}$ = 320.4 Hz, CF_3), 121.0 (CH), 124.1 (q, $J_{F,C}$ = 3.7 Hz, CH), 124.2 (q, $J_{F,C}$ = 272.7 Hz, CF_3), 125.6 (q, $J_{F,C}$ = 3.8 Hz, CH), 127.6, 128.4 (CH), 128.5 (C), 128.6 (CH), 129.2 (C), 130.1 (CH), 130.7 (q, $J_{F,C}$ = 32.4 Hz, C-CF_3), 132.2 (CH), 132.8, 133.1, 140.0, 141.6, 141.7 (C), 197.0 (CO). IR (KBr): ν = 3075, 2965, 2930, 2875 (w), 1698 (s), 1617, 1589 (m), 1557, 1499, 1487, 1441 (w), 1398, 1321 (s), 1291 (m), 1275, 1234 (w), 1207 (s), 1180 (m), 1130, 1113 (s), 1093, 1072 (m), 1029, 974 (s), 941, 927, 910 (w), 852 (s), 801 (m), 763 (s), 741, 717, 703, 688 (m), 676, 660 (w), 608 (s), 589, 547 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 488 (M^+, 79), 469 (08), 356 (63), 355 (100), 327 (23), 313 (65). HRMS (EI, 70 eV):calcd for $C_{22}H_{14}F_6O_4S$ $[M]^+$: 488.05115; found: 488.05115.

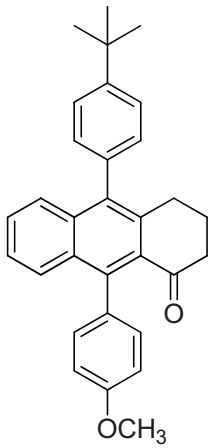
***10-(2,6-Dimethoxyphenyl)-4-oxo-1,2,3,4-tetrahydroanthracen-9-yl trifluoromethanesulfonate* (9g):** Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (127 mg, 0.6 mmol), $Pd(PPh_3)_4$ (11 mg, 3 mol-%), **7j** (55 mg, 0.3 mmol) and 1,4 dioxane (4 mL), **9g** was isolated as a yellowish white solid (127 mg, 88%), mp. 114-116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04-2.13 (m, 2H, CH_2), 2.58 (t, 2H, J = 6.7 Hz, CH_2), 3.16 (t, 2H, J = 6.1 Hz, CH_2), 3.52 (s, 6H, 2OCH_3), 6.63 (d, 2H, J = 8.4 Hz, ArH), 7.30-7.37 (m, 2H, ArH), 7.48 (d, 1H, J = 8.5 Hz, ArH), 7.56-7.62 (m, 1H, ArH), 8.02 (d, 1H, J = 8.6 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.93. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.9, 25.3, 39.6 (3CH_2), 55.8 (2OCH_3), 104 (CH), 116 (C), 118.5 (q,

$J_{F,C}$ = 320.7 Hz, CF_3), 120.9, 126.8, 128.0 (CH), 128.5 (C), 129.2, 129.5 (CH), 130.2, 130.5, 132.6, 133.0, 136.5, 141.1, 157.3 (C), 197.2 (CO). IR (KBr): ν = 3080, 3070, 3004, 2919, 2850 (w), 1693 (s), 1618 (w), 1589 (s), 1557, 1498 (w) 1473 (s), 1433, 1411 (m), 1388 (s), 1359, 1337 (w), 1319 (m), 1300, 1277 (w), 1250, 1224 (m), 1207 (s), 1184, 1158 (w), 1132 (m), 1109, 1024, 962 (s), 933, 899 (m), 835 (s), 801, 772, 750, 730, 684 (m), 670, 651 (w), 641, 599, 575, 547 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 480 (M^+, 84), 348 (27), 347 (100), 319 (13), 305 (15), 301 (25). HRMS (EI, 70 eV): calcd for $C_{23}H_{19}F_3O_6S$ $[M]^+$: 480.08490 ; found: 480.08599.

8.2.3 General Procedure for synthesis of Ansymmetrical 1,2,3,4-tetrahydro-9,10-diarylanthracen-1-ones (10a-f):

The reaction was carried out in a pressure tube as a one-pot reaction with sequential addition of two different boronic acids. To a dioxane suspension (4 mL) of **6** (150 mg, 0.3 mmol), $Pd(PPh_3)_4$ (3 mol%) and K_3PO_4 (127 mg, 0.6 mmol) was added $Ar^1B(OH)_2$ (0.3 mmol) and the solution was degassed by bubbling argon through the solution for 10 min. The reaction mixture was heated at 100 °C under argon atmosphere for 10 h. The reaction mixture was cooled to 20 °C and $Ar^2B(OH)_2$ (0.33 mmol), with fresh amount of catalyst and K_3PO_4 (127 mg, 0.6 mmol) were added. The reaction mixture was heated under Argon atmosphere for 10h at 120 °C. They were 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).

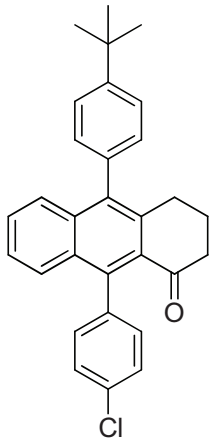
***10-[4-(Tert-butyl)phenyl]-9-(4-methoxyphenyl)-3,4-dihydroanthracen-1(2H)-one* (10a):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (254 mg, 1.2 mmol), **7a** (46 mg, 0.3 mmol), $Pd(PPh_3)_4$ (2 x 11mg, 2 x 3 mol%), 1,4 dioxane (5 mL), and **7h** (59 mg, 0.33 mmol), **10a** was isolated as brownish solid (100 mg, 77%), mp. 272-274 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 9H, $3CH_3$), 1.90-1.98 (m, 2H, CH_2), 2.55 (t, 2H, J = 6.7 Hz, CH_2), 2.71 (t, 2H, J = 6.7 Hz, CH_2), 3.83 (s, 3H, OCH_3), 6.96 (d, 2H, J = 8.6 Hz, ArH), 7.10 (d, 2H, J = 8.7 Hz, ArH), 7.16 (d, 2H, J = 8.6 Hz, ArH), 7.20-7.38 (m, 3H, ArH), 7.45-7.53 (m, 3H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.7, 29.4 ($2CH_2$), 31.5 ($3CH_3$), 34.7 (C), 40.9 (CH_2), 55.3 (OCH_3), 113.5, 125.4, 125.5, 126.4, 127.7, 128.5, 129.8, 130.3 (CH), 132.5, 132.6, 134.6, 136.0, 137.4,

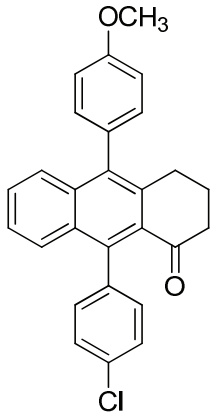
137.8, 141.6, 150.3, 158.5 (C), 200.2 (CO). IR (KBr): ν = 3064, 3042, 3000, 2956, 2899, 2865, 2833, 2252, 2142 (w), 1689 (s), 1608, 1573, 1553 (w), 1510 (m), 1493, 1459, 1440, 1410, 1395, 1373, 1365, 1349, 1327, 1315, 1304, 1284, 1269 (w), 1239 (s), 1224, 1174 (m), 1158, 1131, 1116, 1108, 1073 (w), 1030 (m), 1006, 971, 938, 926 (w), 912, 837 (m), 817, 803, 796 (w), 765, 726 (s), 692, 676, 646, 638, 619, 586 (w), 561, 543 (m) cm−1. GC/MS (EI, 70 eV): m/z (%) = 435 ($[M+H]^+$ 33), 434 (M^+, 100), 419 (11), 349 (14). HRMS (ESI^+): calcd for $C_{31}H_{31}O_2$: $[M+H]^+$: 435.2319;found: 435.2312.

***10-[4-(Tert-butyl)phenyl]-9-(4-chlorophenyl)-3,4-dihydroanthracen-1(2H)-one*(10b):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (254 mg, 1.2 mmol), **7c** (47 mg, 0.3 mmol), $Pd(PPh_3)_4$ (2 x 11mg, 2 x 3 mol%), 1,4 dioxane (5 mL), and **7h** (47 mg, 0.33 mmol), **10b** was isolated as yellow solid (99 mg, 75%), mp. 265-267 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (s, 9H, $3CH_3$), 1.91-2.00 (m, 2H, CH_2), 2.55 (t, 2H, J = 6.7 Hz, CH_2), 2.73 (t, 2H, J = 6.3 Hz, CH_2), 7.11 (d, 2H, J = 8.4 Hz, ArH), 7.16 (d, 2H, J = 8.3 Hz, ArH), 7.22-7.27 (m, 1H, ArH), 7.29-7.35 (m, 1H, ArH), 7.37-7.42 (m, 4H, ArH), 7.48 (d, 2H, J = 8.3 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.7, 29.4 ($2CH_2$), 31.5 ($3CH_3$), 34.7 (C), 40.8 (CH_2), 125.6, 125.7, 126.5, 127.9, 128.1, 128.3 (CH), 129.2 (C), 129.7, 130.5 (CH), 131.9, 132.6, 134.6, 135.8, 137.4, 138.4, 139.2, 140.5, 150.4 (C), 199.9 (CO). IR (KBr): ν = 3066, 3028, 2958, 2928, 2870 (w), 1687 (s), 1651, 1633, 1609 (w), 1546 (m), 1495, 1486, 1455, 1392 (w), 1366, 1329, 1289, 1265, 1222, 1182 (m), 1158, 1128, 1099 (w), 1083, 1007 (s), 941, 930, 900, 873 (w), 828, 789, 774 (s), 732, 705, 687, 670, 631 (w), 559, 535 (s) cm−1. GC-MS (EI, 70 eV): *m/z* (%) = 440 ($[M, ^{37}Cl]^+$, 36), 438 ($[M, ^{35}Cl]^+$, 100), 425 (10), 423 (27), 353 (05), 318 (16), 289 (14). HRMS (EI, 70 eV): calcd for $C_{30}H_{27}Cl_1O_1$ $[M, ^{35}Cl]^+$: 438.17449; found: 438.17481, calcd for $C_{30}H_{27}Cl_1O_1$ $[M, ^{37}Cl]^+$: 440.17154; found: 440.173043.

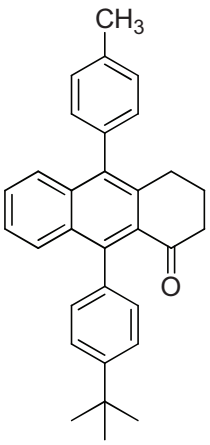
***9-(4-Chlorophenyl)-10-(4-methoxyphenyl)-3,4-dihydroanthracen-1(2H)-one* (10c):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (254 mg, 1.2 mmol), **7c** (47 mg, 0.3 mmol), $Pd(PPh_3)_4$ (2 x 11mg, 2 x 3 mol%), 1,4 dioxane (5 mL), and **7a** (50 mg, 0.33 mmol), **10c** was isolated as yellow solid (87 mg, 70%), mp. 281-283 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90-1.98 (m, 2H, CH_2), 2.53 (t, 2H, J = 6.7 Hz, CH_2), 2.72 (t, 2H, J = 6.5 Hz, CH_2), 3.84 (s, 3H, OCH_3), 7.01 (d, 2H, J = 8.6 Hz, ArH), 7.11 (d, 2H, J = 8.4 Hz,

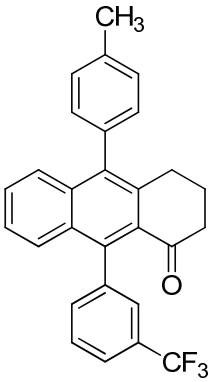
ArH), 7.14 (d, 2H, J = 8.5 Hz, ArH), 7.20-7.26 (m, 1H, ArH), 7.28-7.34 (m, 1H, ArH), 7.35-7.41 (m, 4H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.6, 29.4, 40.8 (3CH_2), 55.4 (OCH_3), 113.2, 124.7, 125.4, 126.9, 127.1, 127.2 (CH), 128.2 (C), 129.5 (CH), 130.0 (C), 130.1 (CH), 130.9, 131.6, 133.8, 136.6, 137.0, 138.1, 139.5, 158.0 (C), 198.8 (CO). IR (KBr): ν = 3066, 3034, 3006, 2953, 2833, 2245 (w), 1679 (s), 1608, 1555 (m), 1512, 1496 (s), 1456 (m), 1439, 1402 (w), 1371 (m), 1350, 1326, 1304 (w), 1286, 1243 (s), 1177 (m), 1154, 1125, 1105 (w), 1088, 1031, 1016, 1005 (m), 962, 944, 932 (w), 903, 834, 788, 767, 723 (s), 689, 675, 646, 622 (w), 582, 541 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 415 (10), 413 (37), 414 ([M, ^{37}Cl]$^+$, 37), 412 ([M, ^{35}Cl]$^+$, 100), 321 (08), 289 (12). HRMS (ESI$^+$): calcd for $C_{27}H_{22}Cl_1O_2$ [M+H, ^{35}Cl]$^+$: 413.1303; found: 413.1299, calcd for $C_{27}H_{22}Cl_1O_2$ [M+H, ^{37}Cl]$^+$: 415.1285; found: 415.1281.

***9-[4-(Tert-butyl)phenyl]-10-(p-tolyl)-3,4-dihydroanthracen-1(2H)-one* (10d):**



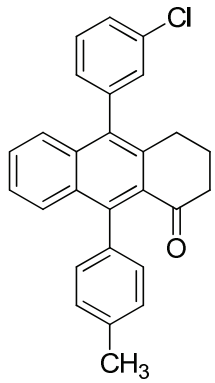
Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (254 mg, 1.2 mmol), **7h** (53 mg, 0.3 mmol), $Pd(PPh_3)_4$ (2 x 11mg, 2 x 3 mol%), 1,4 dioxane (5 mL), and **7d** (45 mg, 0.33 mmol), **10d** was isolated as yellowish white solid (100 mg, 80%), mp. 280-281 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 9H, 3CH_3), 1.89-1.98 (m, 2H, CH_2), 2.41 (s, 3H, CH_3), 2.55 (t, 2H, J = 6.7 Hz, CH_2), 2.71 (t, 2H, J = 6.5 Hz, CH_2), 7.10 (d, 2H, J = 8.2 Hz, ArH), 7.13 (d, 2H, J = 8.1 Hz, ArH), 7.19-7.25 (m, 1H, ArH), 7.27-7.32 (m, 3H, ArH), 7.34-7.37 (m, 1H, ArH), 7.42 (d, 2H, J = 8.3 Hz, ArH), 7.47 (d, 1H, J = 8.3 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 (CH_3), 22.7, 29.4 (2CH_2), 31.6 (3CH_3), 34.6 (C), 40.9 (CH_2), 124.8, 125.4, 126.2, 127.7, 128.7, 128.8 (CH), 129.3 (C), 129.4, 130.0 (CH), 132.3, 134.6, 136.2, 137.1, 137.2, 137.4, 137.7 (C), 199.9 (CO). IR (KBr): ν = 3350, 3070, 3024, 2954, 2921, 2865 (w), 1683 (s), 1642, 1610 (w), 1548, 1513, 1494 (m), 1454, 1444, 1403 (w), 1362, 1327, 1288, 1220, 1178, 1152 (m), 1104, 1034, 1021 (w), 1006, 935 (m), 902, 858 (w), 831, 787, 767 (s), 750, 721, 690, 676, 628 (w), 577, 562 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 418 (M$^+$, 100), 404 (29), 403 (89), 361 (17), 289 (11). HRMS (EI, 70 eV): calcd for $C_{31}H_{30}O_1$ [M]$^+$: 418.22912; found: 418.22887.

***10-(P-tolyl)-9-[3-(trifluoromethyl)phenyl]-3,4-dihydroanthracen-1(2H)-one* (10e):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (254 mg, 1.2 mmol), **7i** (57 mg, 0.3 mmol), $Pd(PPh_3)_4$ (2 x 11mg, 2 x 3 mol%), 1,4 dioxane (5 mL), and **7d** (45 mg, 0.33 mmol), **10e** was isolated as yellowish white solid (88 mg, 68%), mp. 192-194 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.91-2.00 (m, 2H, CH_2), 2.41 (s, 3H, CH_3), 2.53 (t, 2H, J = 6.7 Hz, CH_2), 2.73 (t, 2H, J = 6.3 Hz, CH_2), 7.12 (d, 2H, J = 8.2 Hz, ArH), 7.20-7.25 (m, 1H, ArH), 7.26-7.28 (m, 2H, ArH), 7.29-7.33 (m, 2H, ArH), 7.35-7.39 (m, 2H, ArH), 7.43 (brs, 1H, ArH), 7.52 (t, 1H, J = 7.7 Hz, ArH), 7.62 (d, 1H, J = 8.2 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -62.26. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3 (CH_3), 21.6, 28.4 , 39.7 (3CH_2), 122.4 (q, $J_{F,C}$ = 3.6 Hz, CH), 124.3 (q, $J_{F,C}$ = 272.4 Hz, CF_3), 124.8 (CH), 124.9 (q, $J_{F,C}$ = 3.6 Hz, CH), 125.4, 126.9, 127.3 (CH), 128.1 (C), 128.5 (q, $J_{F,C}$ = 2.2 Hz, CH), 128.8, 128.9 (CH), 129.4 (q, $J_{F,C}$ = 32.0 Hz, C-CF_3), 130.7 (C), 131.5 (CH), 133.6, 134.8, 136.2, 136.3, 137.7, 139.1, 140.6 (C), 198.5 (CO). IR (KBr): ν = 3048, 3023, 2948, 2922, 2851 (w), 1689 (s), 1608, 1548, 1514, 1496, 1403 (w), 1436, 1375 (m), 1323 (s), 1307, 1288, 1270, 1245, 1220 (w), 1159, 1118, 1070 (s), 1011, 941, 917 (m), 892, 846 (w), 829, 790 (m), 767, 702 (s), 663, 573, 534 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 430 (M^+, 100), 387 (11), 373 (09), 359 (18), 289 (14). HRMS (EI, 70 eV): calcd for $C_{28}H_{21}F_3O_1$ $[M]^+$: 430.15390; found: 430.1541.

***10-(3-Chlorophenyl)-9-(p-tolyl)-3,4-dihydroanthracen-1(2H)-one* (10f):**



Starting with **6** (150 mg, 0.3 mmol), K_3PO_4 (254 mg, 1.2 mmol), **7d** (41 mg, 0.3 mmol), $Pd(PPh_3)_4$ (2 x 11mg, 2 x 3 mol%), 1,4 dioxane (5 mL), and **7f** (51 mg, 0.33 mmol), **10f** was isolated as yellow solid (83 mg, 70%), mp. 199-201°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.91-2.01 (m, 2H, CH_2), 2.39 (s, 3H, CH_3), 2.55 (t, 2H, J = 6.8 Hz, CH_2), 2.66-2.71 (m, 2H, CH_2), 7.05 (d, 2H, J = 8.3 Hz, ArH), 7.12-7.16 (m, 1H, ArH), 7.21-7.27 (m, 4H, ArH), 7.29-7.34 (m, 2H, ArH), 7.36-7.42 (m, 2H, ArH), 7.51 (dt, 1H, J = 0.8, 8.3 Hz, ArH. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.4 (CH_3), 22.6, 29.3, 40.7 (3CH_2), 125.6, 125.8, 127.7, 128.1, 128.4, 128.7, 128.8, 128.9 (CH), 129.4 (C), 130.1, 130.2 (CH), 132.2, 134.0, 134.7, 136.1, 136.3, 137.2, 137.3, 141.1, 142.7 (C), 199.7 (CO). IR (KBr): ν = 3359, 3065, 3044, 3018, 2958, 2922 (w), 1682 (s), 1609, 1591 (w), 1562, 1552 (m), 1514, 1497, 1444, 1404, 1397 (w), 1368 (m), 1352, 1338, 1324 (w), 1288, 1218, 1179, 1153 (m), 1128, 1107, 1077, 1034, 1009 (w), 937, 915, 888, 827, 796 (m), 778, 767, 728, 701 (s), 668,

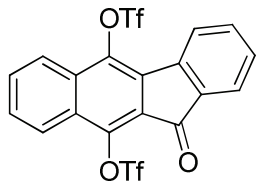
649, 626 (w), 529 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 398 ([M, $^{37}Cl]^+$, 33), 396 ([M, $^{35}Cl]^+$, 100), 381 (18), 367 (07), 353 (08), 333 (09), 303 (10), 289 (30). HRMS (EI, 70 eV): calcd for $C_{27}H_{21}Cl_1O_1$ [M, $^{35}Cl]^+$: 396.12754; found: 396.127005, calcd for $C_{27}H_{21}Cl_1O_1$ [M, $^{37}Cl]^+$: 398.12459; found: 398.12483.

8.3 Site-selective Suzuki-Miyaura Reactions of the Bis(triflate) of 5,10-dihydroxy-11*H*-benzo[*b*]fluoren-11-one

8.3.1 Procedure for the synthesis of 11-oxo-11*H*-benzo*[b]*fluorene-5,10-diaryl bis(trifluoromethanesulfonate) (12):

To a solution of **11** (1.0 equiv.) in CH_2Cl_2 (10 mL per 1 mmol of **11**), was added pyridine (4.0 equiv.) at – 78°C under an argon atmosphere. After stirring for 10 min, Tf_2O (2.4 equiv.) was added at -78 °C. The mixture was allowed to warm up to 0 °C and stirred overnight. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The residue was purified by rapid column chromatography (flash silica gel, heptanes/EtOAc) without prior aqueous work up.

***11-Oxo-11H-benzo[b]fluorene-5,10-diyl bis(trifluoromethanesulfonate)* (12):**

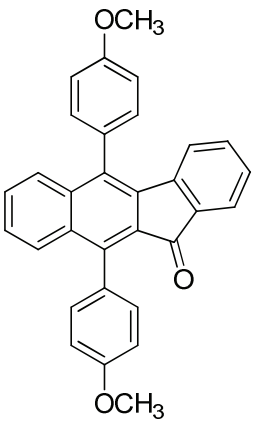


Starting with **11** (2.0 g, 7.6 mmol) in CH_2Cl_2 (88 mL), pyridine (2.5 mL, 31.0 mmol), at 20 C° under an argon atmosphere. After 10 min stirring, Tf_2O (3.1 mL, 18 mmol), was added at -78 °C. and **12** was isolated as a yellow solid (3.5 g, 88%), mp 186-188. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.43 (t, 1H, J = 7.7 Hz, ArH), 7.59-7.79 (m, 4H, ArH), 8.01 (t, 2H, J = 8.0 Hz, ArH), 8.10 (d, 1H, J = 8.3 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.29, -72.3. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 118.6 (q, $J_{F,C}$ = 320.5 Hz, CF_3), 118.7 (q, $J_{F,C}$ = 321.4 Hz, CF_3), 122.8, 124.0, 125.3, 125.4 (CH), 128.2 (C), 129.4, 131.2, 131.3 (CH), 132.0, 135.7 (C), 135.9 (CH), 136.8, 140.2, 141.2 (C), 187.2 (CO). IR (KBr): ν = 3085, 2926, 2854 (w), 1721 (m), 1635, 1600, 1591, 1581, 1516, 1466 (w), 1435, 1405 (m), 1391, 1337, 1289, 1274, 1241 (w), 1203 (s), 1173 (m), 1128 (s), 1082 (m), 1043 (w), 1011, 975 (m), 891 (s), 865, 814, 782 (m), 760, 747, 722 (s), 688 (m), 662, 651, 638 (w), 621, 595, 590 (s), 570, 528 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 526 (M^+, 53), 393 (77), 329 (99), 301 (100). HRMS (EI, 70 eV): calcd for $C_{19}H_8F_6O_7S_2$ $[M]^+$: 525.96101; found: 525.96157.

8.3.2 General Procedure for synthesis of symmetrical 5,10-diaryl-11*H*-benzo[*b*]fluoren-11-ones (13a-f) and 10-aryl-trifluoromethylsulfonyloxy-11*H*- benzo[*b*]fluoren-11-ones (14a-i) :

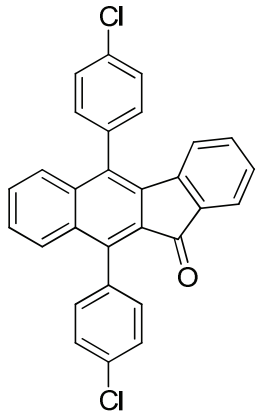
A 1,4-dioxane solution (4-5 mL per 0.3 mmol of **12**) , K_3PO_4 (1.5-2.0 equiv per cross-couplin), $Pd(PPh_3)_4$ (3 mol% per cross-coupling) and arylboronic acid **7** (1.0-1.1 equiv per cross-coupling) was stirred at 60 or 90 °C for 10 h under argon atmosphere. After cooling to 20 °C, a saturated aqueous solution of NH_4Cl was added. The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography.

5,10-Bis(4-methoxyphenyl)-11H-benzo[b]fluoren-11-one **(13a):**



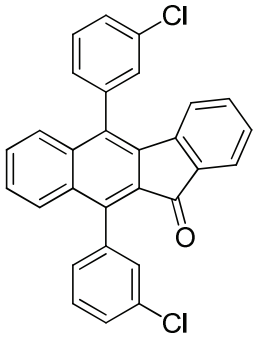
Starting with **12** (150 mg, 0.28 mmol), **7a** (96 mg, 0.63 mmol), $Pd(PPh_3)_4$ (19 mg, 6 mol%), K_3PO_4 (178 mg, 0.84 mmol) and 1,4-dioxane (5mL), **13a** was isolated as yellow solid (100 mg, 80%); mp 243–245 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.31-6.36 (m, 1H, ArH), 7.02 (d, 2H, J = 8.4 Hz, ArH), 7.07-7.12 (m, 4H, ArH), 7.25-7.31 (m, 5H, ArH), 7.35 (td, 1H, J = 1.4, 8.1 Hz, ArH), 7.43-7.46 (m, 1H, ArH), 7.50-7.5 (m, 1H, ArH), 7.63-7.66 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.3, 55.4 (OCH_3), 113.6, 114.8, 123.8, 123.9, 126.5, 127.1 (CH), 127.8, 128.4 (C), 128.5, 129.0 (CH), 129.8 (C), 130.9, 131.0 (CH), 133.9, 134.0 (C), 134.3 (CH), 135.8, 136.8, 137.2, 140.5, 144.5, 159.4, 159.6 (C), 192.6 (CO). IR (KBr): ν = 3064, 2997, 2952, 2929, 2849, 2831 (w), 1704 (s), 1606, 1589 (m), 1579 (w), 1510 (s), 1462, 1441, 1410, 1361, 1335, 1311 (w), 1286 (m), 1243 (s), 1215, 1191 (m), 1173 (s), 1107, 1086, 1048 (w), 1034, 1026 (m), 1005 (w), 963 (m), 932, 899 (w), 870, 830, 805, 791 (m), 759, 727 (s), 693, 681, 655, 633 (w), 623, 596 (m), 573 (w), 559, 531 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 442 (M^+, 100), 441 (28), 411 (06), 326 (05). HRMS (EI, 70 eV): calcd for $C_{31}H_{22}O_3$ $[M]^+$: 442.15635; found: 442.15549.

5,10-Bis(4-chlorophenyl)-11H-benzo[b]fluoren-11-one **(13b):**



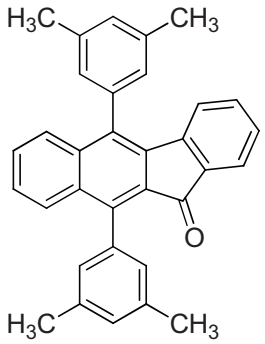
Starting with **12** (150 mg, 0.28 mmol), **7c** (98 mg, 0.63 mmol), $Pd(PPh_3)_4$ (19 mg, 6 mol%), K_3PO_4 (178 mg, 0.84 mmol) and 1,4-dioxane (5mL), **13b** was isolated as yellow solid (88 mg, 70%); mp 214–216 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.30-6.35 (m, 1H, ArH), 7.14-7.17 (m, 2H, ArH), 7.26 (d, 2H, J = 8.2 Hz, ArH), 7.30-7.35 (m, 3H, ArH), 7.37-7.39 (m, 2H, ArH), 7.46 (d, 2H, J = 8.3 Hz, ArH), 7.52-7.57 (m, 4H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 123.7, 124.1, 126.8, 126.9 (CH), 128.4 (C), 128.5, 128.7, 128.9, 129.1, 129.8, 131.0, 131.3 (CH), 133.1, 133.4, 134.1, 134.2, 134.5 (C), 134.6 (CH), 135.5, 136.0, 136.5, 136.6, 139.5, 144.0 (C), 192.1 (CO). IR (KBr): ν = 3065, 2922, 2851 (w), 1704 (s), 1608, 1586 (m), 1516 (w), 1490, 1469 (m), 1394, 1363, 1337, 1310, 1294, 1260, 1215, 1191, 1117 (w), 1086 (s), 1046, 1015, 963 (m), 943, 901 (w), 871, 829 (m), 763, 726 (s), 675, 647, 619 (w), 602, 588 (m), 572, 544 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 452 ([M, ^{35}Cl, ^{37}Cl]$^+$, 65), 450 ([M, ^{35}Cl, ^{35}Cl]$^+$, 100), 415 (18), 386 (06), 350 (27). HRMS (EI, 70 eV): calcd for $C_{29}H_{16}Cl_2O$ [M, ^{35}Cl, ^{35}Cl]$^+$: 450.05727; found: 450.05649.

5,10-Bis(3-chlorophenyl)-11H-benzo[b]fluoren-11-one **(13c):**



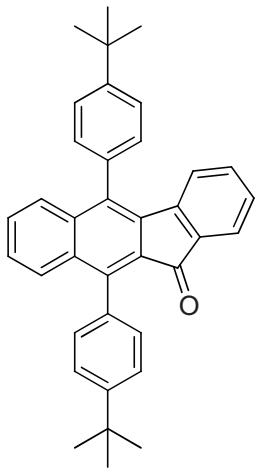
Starting with **12** (150 mg, 0.28 mmol), **7f** (98 mg, 0.63 mmol), $Pd(PPh_3)_4$ (19 mg, 6 mol%), K_3PO_4 (178 mg, 0.84 mmol) and 1,4-dioxane (5mL), **13c** was isolated as a dark yellow solid (90 mg, 72%); mp 180–182 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.24-6.32 (m, 1H, ArH), 7.11-7.16 (m, 2H, ArH), 7.19-7.23 (m, 1H, ArH), 7.26-7.34 (m, 3H, ArH), 7.35-7.47 (m, 5H, ArH), 7.50-7.55 (m, 4H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 122.6, 123.1, 125.8, 126.0, 126.8, 127.1, 127.2 (CH), 127.4 (C), 127.7, 128.0, 128.4, 128.6, 128.9, 129.0, 129.7, 129.8 (CH), 131.8, 132.3, 133.1 (C), 133.6 (CH), 134.3, 134.4, 135.2, 135.5, 136.5, 138.1, 138.4, 142.8 (C), 190.8 (CO). IR (KBr): ν = 3065, 2922, 2851 (w), 1706 (s), 1607, 1583 (m), 1516 (w), 1490, 1469 (m), 1394, 1363, 1337, 1310, 1294, 1260, 1215, 1191, 1117 (w), 1084 (s), 1046, 1015, 963 (m), 943, 901 (w), 871, 829 (m), 761, 725 (s), 675, 647, 619 (w), 604, 587 (m), 572, 544 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 452 ([M, ^{35}Cl, ^{37}Cl]$^+$, 69), 450 ([M, ^{35}Cl, ^{35}Cl]$^+$, 100), 415 (23), 386 (06), 350 (28). HRMS (EI, 70 eV): calcd for $C_{29}H_{16}Cl_2O$ [M, ^{35}Cl, ^{35}Cl]$^+$: 450.05727; found: 450.05652.

5,10-Bis(3,5-dimethylphenyl)-11H-benzo[b]fluoren-11-one **(13g):**



Starting with **12** (150 mg, 0.28 mmol), **7g** (95 mg, 0.63 mmol), $Pd(PPh_3)_4$ (19 mg, 6 mol%), K_3PO_4 (178 mg, 0.84 mmol) and 1,4-dioxane (5mL), **13g** was isolated as a dark yellow solid (104 mg, 85%); mp 251–252 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 6H, $2CH_3$), 2.41 (s, 6H, $2CH_3$), 6.26-6.33 (m, 1H, ArH), 6.93 (brs., 2H, ArH), 6.98 (brs., 2H, ArH), 7.06-7.14 (m, 4H, ArH), 7.21-7.28 (m, 1H, ArH), 7.29-7.35 (m, 1H, ArH), 7.43 (dd, 1H, J = 1.1, 8.2 Hz, ArH), 7.49-7.52 (m, 1H, ArH), 7.57 (dd, 1H, J = 1.1, 8.0 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 ($2CH_3$), 21.5 ($2CH_3$), 123.8, 123.9, 126.5, 127.2, 127.3, 127.4 (CH), 128.2 (C), 128.4, 129.1, 129.6, 129.8 (CH), 133.9 (C), 134.3 (CH), 134.5, 135.1, 135.8, 136.7, 136.8, 137.4, 137.6, 138.9, 140.9, 144.5 (C), 192.5 (CO). IR (KBr): ν = 3409, 3065, 3025, 2913, 2856, 2730 (w), 1712, 1596 (s), 1512, 1469 (m), 1445, 1417 (w), 1367, 1299 (m), 1280, 1267, 1255 (w), 1209, 1201, 1182 (m), 1144, 1130, 1118 (w), 1088, 1062, 1034, 994, 969 (m), 872, 851 (s), 792 (m), 762, 725, 699 (s), 678, 612, 580, 550 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 438 (M^+, 100), 423 (59), 363 (06). HRMS (EI, 70 eV): calcd for $C_{33}H_{26}O$ $[M]^+$: 438.19782; found: 438.19747.

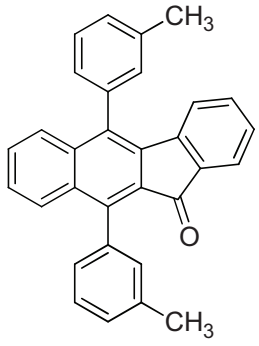
5,10-Bis[4-(tert-butyl)phenyl]-11H-benzo[b]fluoren-11-one **(13e):**



Starting with **12** (150 mg, 0.28 mmol), **7h** (112 mg, 0.63 mmol), $Pd(PPh_3)_4$ (19 mg, 6 mol%), K_3PO_4 (178 mg, 0.84 mmol) and 1,4-dioxane (5mL), **13e** was isolated as a yellow solid (104 mg, 75%); mp 380–382 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (s, 9H, $3CH_3$), 1.40 (s, 9H, $3CH_3$), 6.17-6.23 (m, 1H, ArH), 7.03-7.12 (m, 2H, ArH), 7.24-7.30 (m, 5H, ArH), 7.33-7.36 (m, 1H, ArH), 7.44 (dd, 1H, J = 1.1, 8.2 Hz,ArH), 7.47-7.52 (m, 3H, ArH), 7.55 (d, 2H, J = 8.2 Hz, ArH), 7.62 (dd, 1H, J = 1.1, 8.0 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 31.5 ($3CH_3$), 31.6 ($3CH_3$), 34.7, 34.8 (C), 123.8, 125.0, 126.2, 126.5, 126.8, 127.2 (CH), 128.3 (C), 128.4, 128.5, 129.1, 129.3, 129.4 (CH), 132.7, 133.9 (C), 134.3 (CH), 134.6, 135.5, 136.7, 136.9, 140.8, 144.5, 150.6, 151.4 (C), 192.6 (CO). IR (KBr): ν = 3065, 3031, 2956, 2899, 2863 (w), 1710, 1613, 1591 (s), 1504, 1470, 1456 (m), 1393 (w), 1361 (s), 1311, 1292, 1263 (w), 1216, 1190 (m), 1130, 1116, 1101, 1086 (w), 1045, 1008 (m), 964, 873, 832 (s), 790, 778 (w), 763, 727 (s), 700, 684, 614 (w), 596, 558 (m) cm^{-1}.

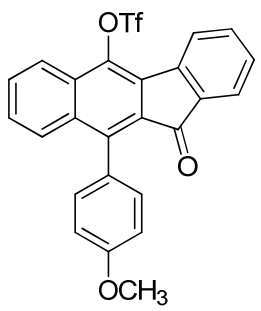
GC/MS (EI, 70 eV): m/z (%) = 494 (M^+, 100), 480 (23), 479 (99), 452 (05), 405 (09), 365 (10). HRMS (EI, 70 eV): calcd for $C_{37}H_{34}O$ $[M]^+$: 494.26042 ; found: 494.25996.

***5,10-Di-m-tolyl-11H-benzo[b]fluoren-11-one* (13f):**



Starting with **12** (150 mg, 0.28 mmol), **7k** (86 mg, 0.63 mmol), $Pd(PPh_3)_4$ (19 mg, 6 mol%), K_3PO_4 (178 mg, 0.84 mmol) and 1,4-dioxane (5 mL), **13f** was isolated as a yellow solid (90 mg, 78%); mp 182–184 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 6.23-6.28 (m, 1H, ArH), 7.06-7.11 (m, 2H, ArH), 7.12-7.15 (m, 2H, ArH), 7.18 (brs., 2H, ArH), 7.24-7.29 (m, 2H, ArH), 7.30-7.37 (m, 3H, ArH), 7.42 (d, 2H, J = 8.2 Hz, ArH), 7.47-7.53 (m, 1H, ArH), 7.58 (dd, 1H, J = 1.3, 8.2 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.6, 21.7 ($2CH_3$), 123.9, 126.5, 126.6, 126.7, 126.8, 127.2, 128.0 (CH), 128.3 (C), 128.6, 128.7, 129.0, 129.1, 129.2, 130.1, 130.2, 130.4, (CH), 133.8 (C), 134.3 (CH), 134.4, 135.3, 135.8, 136.7, 136.8, 137.6, 137.7, 139.1, 140.8, 144.4 (C), 192.5 (CO). IR (KBr): ν = 3016, 2951, 2919, 2856 (w), 1705, 1599 (s), 1514 (m), 1484 (w), 1468 (m), 1446, 1420 (w), 1363 (m), 1338 (w), 1310, 1294 (m), 1265, 1228 (w), 1204 (m), 1182, 1165 , 1144 (w), 1116, 1086, 1050 (m), 1014, 998 (w), 970 (m), 906 (s), 867, 785 (m), 762, 724, 700 (s), 674, 661, 647 (w), 605 (m), 576, 541 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 410 (M^+, 100), 409 (47), 395 (30), 350 (07), 319 (05). HRMS (EI,70 eV): calcd for $C_{31}H_{22}O_1[M]^+$: 410.16652; found: 410.166103.

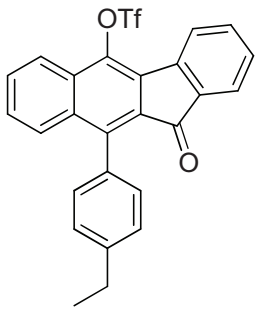
***10-(4-Methoxyphenyl)-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate* (14a):**



Starting with **12** (150 mg, 0.28 mmol), **7a** (46 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14a** was isolated as a yellow crystals solid (122 mg, 90%); mp 218–220 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3H, OCH_3), 7.01 (d, 2H, J = 8.6 Hz, ArH), 7.22 (d, 2H, J = 8.6 Hz, ArH), 7.35 (td, 1H, J = 0.8, 7.8 Hz, ArH), 7.38-7.44 (m, 1H, ArH), 7.54-7.64 (m, 3H, ArH), 7.67 (d, 1H, J = 8.6 Hz, ArH), 8.06 (d, 2H, J = 8.1 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.48. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 113.8 (CH), 118.4 (q, $J_{F,C}$ = 320.5 Hz, CF_3), 122.1, 124.4, 125.0 (CH), 126.3 (C), 127.9 (CH), 129.4 (C), 129.5, 129.8, 130.3 (CH), 130.4 (C), 130.9, 135.1 (CH), 135.8, 136.6, 137.6, 140.4, 141.6, 159.8 (C), 190.4 (CO). IR (KBr): ν = 3077, 3024, 2962, 2921, 2840 (w), 1711 (s), 1650, 1625 (w), 1596, 1573, 1504 (m), 1469, 1442 (w), 1420 (s), 1371 (w), 1346 (m), 1313,

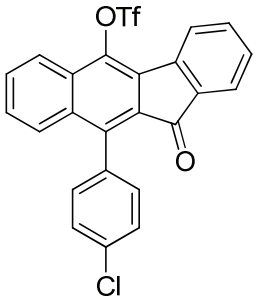
1297, 1286 (w), 1248 (m), 1225, 1200 (s), 1170, 1160 (w), 1129 (m), 1091, 1049, 1029 (w), 994, 949 (m), 929, 884, 869 (w), 835, 792, 763, 723 (s), 698, 684 (w), 656, 630 (m), 605, 588 (s), 556, 534 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 484 (M^+, 12), 351 (100), 323 (11). HRMS (EI,70 eV):calcd for $C_{25}H_{15}F_3O_5S$ $[M]^+$: 484.05868; found: 484.05879.

***10-(4-Ethylphenyl)-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate* (14b):**



Starting with **12** (150 mg, 0.28 mmol), **7b** (45 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14b** was isolated as a yellowish white solid (115 mg, 85%); mp 186–188 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.29 (t, 3H, J = 7.6 Hz, CH_3), 2.74 (q, 2H, J = 7.7 Hz, CH_2), 7.20 (d, 2H, J = 8.3 Hz, ArH), 7.31 (d, 2H, J = 8.2 Hz, ArH), 7.36 (td, 1H, J = 0.8, 7.6 Hz, ArH), 7.40-7.43 (m, 1H, ArH), 7.55 (dd, 1H, J = 1.2, 7.7 Hz, ArH), 7.58-7.66 (m, 3H, ArH), 8.06 (d, 2H, J = 8.1 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.48. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.3 (CH_3), 28.8 (CH_2), 118.6 (q, $J_{F,C}$ = 320.4 Hz, CF_3), 122.0, 124.4, 125.0, 127.8, 127.9 (CH), 129.3 (C), 129.4, 129.6, 129.8, 130.4 (CH), 130.9, 131.5 (C), 135.1 (CH), 135.6, 136.6, 137.7, 140.4, 141.9, 144.5 (C), 190.4 (CO). IR (KBr): ν = 3052, 2963, 2927, 2845 (w), 1711 (s), 1627, 1581 (m), 1519, 1505, 1470, 1449, 1429 (w), 1404 (s), 1388, 1371 (w), 1345, 1335 (m), 1311, 1295 (w), 1220 (s), 1172, 1161 (w), 1132 (s), 1089, 1049, 1008 (m), 993 (s), 951, 938 (m), 868 (w), 837 (s), 788 (m), 760, 721, 688, 655, 618 (s), 594, 567 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 482 (M^+, 15), 351 (15), 349 (100), 321 (35), 306 (12), 276 (14). HRMS (EI, 70 eV): calcd for $C_{26}H_{17}F_3O_4S$ $[M]^+$: 482.07942; found: 482.07949.

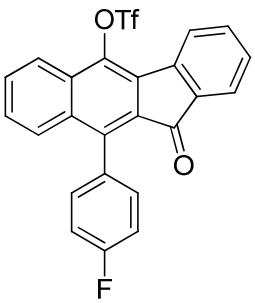
***10-(4-Chlorophenyl)-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate* (14c):**



Starting with **12** (150 mg, 0.28 mmol), **7c** (47 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14c** was isolated as a yellowish white solid (107 mg, 78%); mp 207–209 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.22 (d, 2H, J = 8.4 Hz, ArH), 7.36 (td, 1H, J = 0.8, 7.6 Hz, ArH), 7.41-7.44 (m, 1H, ArH), 7.46 (d, 2H, J = 8.4 Hz, ArH), 7.55-7.59 (m, 2H, ArH), 7.61-7.67 (m, 2H, ArH), 8.03 (d, 1H, J = 7.8 Hz, ArH), 8.04 (d, 1H, J = 8.4 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.44. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 117.8 (q, $J_{F,C}$ = 321.5 Hz, CF_3), 121.2, 123.5, 124.1, 127.2, 127.6, 128.0 (CH), 128.5 (C), 129.0 (CH),

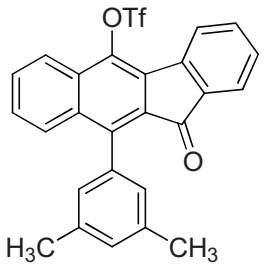
129.4 (C), 129.5 (CH), 129.8 (C), 129.9 (CH), 131.8, 133.7, 134.2 (C), 134.3 (CH), 135.3, 136.9, 139.1, 139.4 (C), 189.2 (CO). IR (KBr): ν = 3065, 2959, 2922, 2851 (w), 1709 (s), 1624, 1595 (m), 1516, 1488, 1469 (w), 1422 (s), 1371, 1338, 1292, 1259 (w), 1234, 1207 (s), 1171, 1162 (w), 1128, 1087, 1047, 997 (m), 953, 938, 870 (w), 836 (s), 786, 755, 725 (m), 696, 683, 654 (w), 607, 594 (s), 578 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 490 ([M, $^{37}Cl]^+$, 06), 488 ([M, $^{35}Cl]^+$, 14), 371 (06), 355 (100), 327 (22), 263 (17). HRMS (EI, 70 eV): calcd for $C_{24}H_{12}Cl_1O_4F_3S_1$ [M, $^{35}Cl]^+$: 488.00914; found: 488.00937, calcd for $C_{24}H_{12}Cl_1F_3O_4S$ [M, $^{37}Cl]^+$: 490.00619; found: 490.00634.

***10-(4-Fluorophenyl)-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate* (14d):**



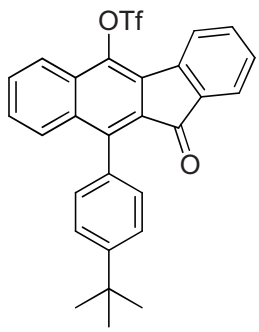
Starting with **12** (150 mg, 0.28 mmol), **7e** (42 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14d** was isolated as a yellow solid (99 mg, 75%); mp 210–212 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.40-6.45 (m, 2H, ArH), 6.48-6.53 (m, 2H, ArH), 6.61 (t, 1H, J = 7.5 Hz, ArH), 6.66-6.71 (m, 1H, ArH), 6.81-6.86 (m, 3H, ArH), 6.88-6.91 (m, 1H, ArH), 7.27-7.30 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.07, -113.79. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 115.4 (d, $J_{F,C}$ = 22.4 Hz, CH), 118.5 (q, $J_{F,C}$ = 320.3 Hz, CF_3), 122.2, 124.5, 125.1 128.2, 129.1 (CH), 129.6 (C), 129.9 (CH), 130.1, 130.2, 130.4 (C), 130.5 (CH), 130.8 (C), 131.3 (d, $J_{F,C}$ = 8.4 Hz, CH), 135.3 (CH), 135.4, 136.4, 137.9, 140.4 (C), 162.6 (d, $J_{F,C}$ = 247.2 Hz, CF), 190.3 (CO). IR (KBr): ν = 3064, 2922, 2852 (w), 1711 (s), 1597, 1504 (m), 1467 (w), 1423 (s), 1371 (w), 1345 (m), 1314, 1293 (w), 1211 (s), 1157, 1129 (m), 1092, 1050, 1012 (w), 999 (s), 951, 934 (m), 897, 881, 869 (w), 839 (s), 821, 808, 782 (w), 765, 752, 726 (m), 691, 656 (w), 628, 607 (m), 594, 584, 540 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 472 (M^+, 08), 408 (04), 339 (100), 311 (39), 281 (19). HRMS (EI, 70 eV): calcd for $C_{24}H_{12}F_4O_4S$ $[M]^+$: 472.03869; found: 472.03868.

***10-(3,5-Dimethylphenyl)-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate* (14e)**



Starting with **12** (150 mg, 0.28 mmol), **7g** (45 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14e** was isolated as a yellow solid (117 mg, 87%); mp 184–186 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.33$ (s, 6H, $2CH_3$), 6.88 (brs., 2H, ArH), 7.09 (brs., 1H, ArH), 7.34 (td, 1H, $J = 0.9$, 7.5 Hz, ArH), 7.37-7.43 (m, 1H, ArH), 7.55 (dd, 1H, $J = 1.3$, 7.7 Hz, ArH), 7.58-7.63 (m, 3H, ArH), 8.01-8.03 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): $\delta = -72.49$.^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 21.4$ ($2CH_3$), 118.6 (q, $J_{F,C} = 321.4$ Hz, CF_3), 121.9, 124.4, 125.0, 127.1, 127.9 (CH), 129.3 (C), 129.6, 129.8, 130.1 (CH), 130.2 (C), 130.3 (CH), 130.8, 134.3 (C), 135.1 (CH), 135.6, 136.6, 137.6, 137.7, 140.4, 142.1 (C), 190.3 (CO). IR (KBr): ν = 3002, 2953, 2921, 2853, 2738 (w), 1714 (s), 1626, 1599, 1580, 1515, 1471, 1434 (m), 1402 (s), 1386, 1351, 1332, 1310 (w), 1243, 1221, 1204 (s), 1174, 1160, 1151 (w), 1137 (s), 1092, 1064, 1040 (w), 1003, 989, 879 (s), 866, 849 (m), 803, 760, 722, 684 (s), 652 (m), 630, 614, 595 (s), 562 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 482 (M^+, 13), 350 (26), 349 (100), 321 (10), 276 (06). HRMS (EI, 70 eV): calcd for $C_{26}H_{17}F_3O_4S$ $[M]^+$: 482.07942; found: 482.07947.

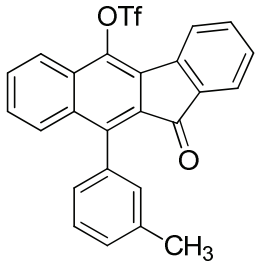
***10-[4-(Tert-butyl)phenyl]-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate*(14f)**



Starting with **12** (150 mg, 0.28 mmol), **7h** (53 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14f** was isolated as a yellow solid (109 mg, 76%); mp 215–217 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.37$ (s, 9H, $3CH_3$), 7.22 (d, 2H, $J = 8.5$ Hz, ArH), 7.35 (td, 1H, $J = 0.8$, 7.6 Hz, ArH), 7.39-7.45 (m, 1H, ArH), 7.50 (d, 2H, $J = 8.4$ Hz, ArH), 7.56 (dd, 1H, $J = 1.3$, 7.8 Hz, ArH), 7.59-7.61 (m, 1H, ArH), 7.62-7.66 (m, 2H, ArH), 8.01 (d, 2H, $J = 8.1$ Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): $\delta = -72.48$. ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 31.5$ ($3CH_3$), 33.8 (C), 118.6 (q, $J_{F,C} = 320.8$ Hz, CF_3), 121.0, 123.4, 124.0, 124.1,126.9, 128.2 (CH), 128.3 (C), 128.6, 128.8, 129.3 (CH), 129.8, 130.2 (C), 134.1 (CH), 134.6, 135.5, 136.6, 139.4, 140.9, 150.3 (C), 189.4 (CO). IR (KBr): ν = 3076, 2958, 2905, 2870 (w), 1712 (s), 1625, 1579 (m), 1513, 1503, 1462, 1450, 1427 (w), 1398 (s), 1364, 1334, 1295, 1261, 1245 (w), 1227, 1212 (s), 1175, 1163 (w), 1132 (s), 1090 (w), 1050 (m), 1000 (s), 953, 942 (m), 853 (s), 837, 790, 778 (w), 766, 725, 685 (s), 654, 634 (m), 615, 595 (s), 566, 559 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 510 (M^+, 08), 377 (100), 342 (31), 327

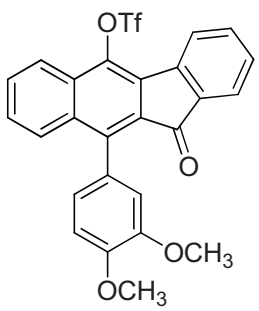
(10), 299 (23), 285 (52). HRMS (EI,70 eV):calcd for $C_{28}H_{21}F_3O_4S$ $[M]^+$: 510.11072; found: 510.10965.

***11-Oxo-10-(m-tolyl)-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate* (14g):**



Starting with **12** (150 mg, 0.28 mmol), **7k** (41 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14g** was isolated as a yellow solid (105 mg, 80%); mp 215–217 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 3H, CH_3), 7.08-7.06 (m, 2H, ArH), 7.26-7.32 (m, 1H, ArH), 7.34-7.40 (m, 2H, ArH), 7.42 (dd, 1H, J = 1.8, 7.7 Hz, ArH), 7.55 (dd, 1H, J = 1.3, 7.7 Hz, ArH), 7.59-7.64 (m, 3H, ArH), 8.02 (d, 2H, J = 8.1 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.48. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.6 (CH_3), 118.3 (q, $J_{F,C}$ = 320.8 Hz, CF_3), 122.0, 124.4, 125.0, 126.5, 127.9, 128.2, 129.2 (CH), 129.3 (C), 129.5, 129.8, 129.9 (CH), 130.3 (C), 130.4 (CH), 130.8, 134.4 (C), 135.1 (CH), 135.5, 136.6, 137.7, 137.9, 140.4, 141.8 (C), 190.3 (CO). IR (KBr): ν = 3045, 3016, 2952, 2920, 2853 (w), 1713 (s), 1625, 1604, 1579 (m), 1515, 1486, 1470, 1421 (w), 1407 (s), 1389, 1375 (w), 1346, 1336 (m), 1312, 1296 (w), 1225, 1205 (s), 1172 (m), 1137 (s), 1091, 1055 (m), 992, 957 (s), 912 (w), 882, 866, 815, 794, 760 (s), 739, 721 (m), 686, 649, 627 (s), 606, 589, 561 (m) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 468 (M^+, 10), 410 (05), 335 (100), 307 (16), 276 (09). HRMS (EI,70 eV):calcd for $C_{25}H_{15}F_3O_4S$ $[M]^+$: 468.06377; found: 468.0641.

***10-(3,4-dimethoxyphenyl)-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate*14h**



Starting with **12** (150 mg, 0.28 mmol), **7l** (56 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14h** was isolated as yellow solid (129mg, 88%); mp 221–222 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.79-6.85 (m, 2H, ArH), 6.97 (d, 1H, J = 8.2 Hz, ArH), 7.33 (td, 1H, J = 0.8, 7.4 Hz, ArH), 7.39-7.44 (m, 1H, ArH), 7.53-7.68 (m, 4H, ArH), 8.02 (d, 2H, J = 7.8 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -72.47. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.9, 56.0 (OCH_3), 110.9, 112.9 (CH), 118.7 (q, $J_{F,C}$ = 321.6 Hz, CF_3), 122.1, 124.5, 125.0 (CH), 126.6 (C), 128.0 (CH), 129.4 (C), 129.5, 129.9 (CH), 130.3 (C), 130.4 (CH), 130.9 (C), 135.1 (CH), 135.7, 136.5, 137.7, 140.3, 141.5, 148.8, 149.2 (C), 190.3 (CO). IR (KBr): ν = 3076, 3012, 2966, 2939, 2919, 2838, 2249 (w), 1718 (s), 1623, 1600, 1579 (w), 1517, 1511 (m), 1468, 1448 (w), 1404 (s), 1374, 1345, 1334,

1319, 1297, 1255 (w), 1215 (s), 1172 (m), 1134 (s), 1090, 1054 (w), 1020 (m), 998 (s), 963 (m), 913 (w), 892 (m), 866 (w), 817, 804 (s), 788, 777 (w), 758 (s), 745 (w), 722 (s), 687 (m), 665 (w), 653, 647 (m), 629, 611 (s), 589, 559 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 514(M^+, 28), 381 (100), 353 (04). HRMS (EI,70 eV):calcd for $C_{26}H_{17}F_3O_6S$ $[M]^+$: 514.06925; found: 514.07013.

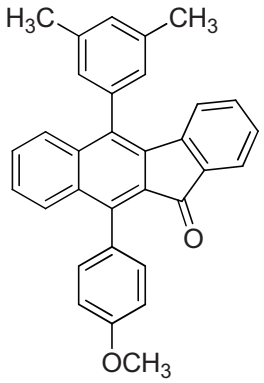
***11-Oxo-10-[4-(trifluoromethyl)phenyl]-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate* (14i):** Starting with **12** (150 mg, 0.28 mmol), **7m** (57 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol) and 1,4-dioxane (5 mL), **14i** was isolated as yellow solid (102mg, 70%); mp 200–202 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.34-7.51 (m, 5H, ArH), 7.57-7.68 (m, 3H, ArH), 7.75 (d, 2H, J = 8.1 Hz, ArH), 8.03-8.08 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -62.52, -72.48. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 118.7 (q, $J_{F,C}$ = 321.2 Hz, CF_3), 122.3 (CH), 123.6 (q, $J_{F,C}$ = 272.3 Hz, CF_3), 124.6, 125.2 (CH), 125.3 (q, $J_{F,C}$ = 3.7 Hz, CH), 126.1 (C), 128.4, 128.9 (CH), 129.6 (C), 129.9, 130.1 (CH), 130.3 (q, $J_{F,C}$ = 31.4 Hz, C-CF_3), 130.6 (CH), 134.9 (C), 135.4 (CH), 136.3, 138.1, 138.4, 139.6, 140.4 (C), 190.2 (CO). IR (KBr): ν = 3074, 2921, 2851 (w), 1715 (s), 1628, 1591 (m), 1510, 1466 (w), 1402, 1320 (s), 1230, 1209 (m), 1162, 1124, 1066 (s), 1050, 1018, 1009 (w), 995, 942 (w), 835 (s), 788 (m), 763, 725, 688 (s), 653, 631, 612, 597 (m), 566, 543 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 522 (M^+, 18), 518 (12), 458 (26), 389 (100), 361 (43). HRMS (EI,70 eV):calcd for $C_{25}H_{12}F_6O_4S$ $[M]^+$: 522.03550; found: 522.03586.

8.3.3 General Procedure for synthesis of Ansymmetrical 5,10-diaryl-11*H*-benzo[*b*]fluoren-11-ones (15a-e) :

The reaction was carried out in a pressure tube as a one-pot reaction with sequential addition of two different boronic acids. To a dioxane suspension (4 mL) of **12** (150 mg, 0.3 mmol), $Pd(PPh_3)_4$ (3 mol%) and K_3PO_4 (119 mg, 0.56 mmol) was added $Ar^1B(OH)_2$ (0.28 mmol) and the solution was degassed by bubbling argon through the solution for 10 min. The reaction mixture was heated at 60 °C under argon atmosphere for 10 h. The reaction mixture was cooled to 20 °C and $Ar^2B(OH)_2$ (0.31 mmol), was added. The reaction mixture was heated under Argon atmosphere for 10 h at 90 °C. They were 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

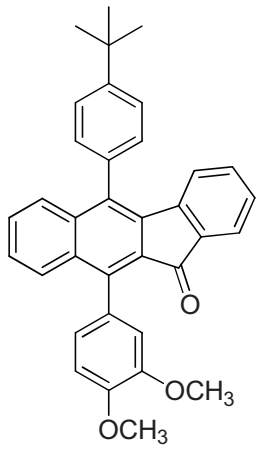
filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, EtOAc / heptanes).

5-(3,5-Dimethylphenyl)-10-(4-methoxyphenyl)-11H-benzo[b]fluoren-11-one **(15a):**



Starting with **12** (150 mg, 0.28 mmol), **7a** (43 mg, 0.28 mmol), $Pd(PPh_3)_4$ (10mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol), 1,4-dioxane (5 mL), and **7g** (46 mg, 0.31 mmol), **15a** was isolated as yellow solid (90 mg, 72%); mp 220–222 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 6H, $2CH_3$), 3.85 (s, 3H, OCH_3), 6.27-6.33 (m, 1H, ArH), 6.98 (brs, 2H, ArH), 7.02 (d, 2H, J = 8.8 Hz, ArH), 7.08-7.14 (m, 3H, ArH), 7.26 (d, 2H, J = 8.8 Hz, ArH), 7.27-7.30 (m, 1H, ArH), 7.34 (td, 1H, J = 1.3, 8.2 Hz, ArH), 7.43-7.46 (m, 1H, ArH), 7.50-7.53 (m, 1H, ArH), 7.63-7.66 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.5 ($2CH_3$), 55.3 (OCH_3), 113.6, 123.8, 123.9, 126.5, 127.3, 127.4 (CH), 127.8, 128.4 (C), 128.5, 128.9, 129.8, 131.0 (CH), 134.0 (C), 134.4 (CH), 134.5, 135.2, 136.7, 136.8, 137.6, 139.9, 140.4, 144.5, 159.4 (C), 192.6 (CO). IR (KBr): ν = 3068, 3000, 2955, 2923, 2852 (w), 1703, 1695, 1598, 1505 (s), 1466, 1435, 1423, 1363, 1336, 1311, 1302, 12871259 (w), 1244 (s), 1202 (m), 1172 (s), 1130, 1105, 1087, 1049 (w), 1029, 998 (m), 969, 950, 939, 926, 906 (w), 873 (m), 848, 834 (w), 826, 790, 778 (m), 761 (s), 742 (w), 724 (s), 710, 703, 680, 661, 631 (w), 613, 595 (m), 579 (w), 562, 538 (m) cm−1. GC/MS (EI, 70 eV): m/z (%) = 440 (M^+, 100), 409 (06), 396 (04). HRMS (EI, 70 eV): calcd for $C_{32}H_{24}O_2$ $[M]^+$: 440.17708 ;found: 440.17687.

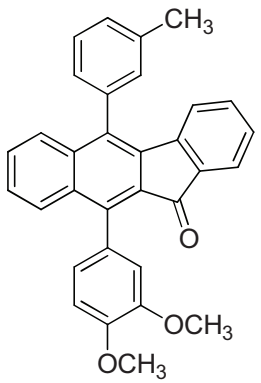
5-[4-(Tert-butyl)phenyl]-10-(3,4-dimethoxyphenyl)-11H-benzo[b]fluoren-11-one **(15b):**



Starting with **12** (150 mg, 0.28 mmol), **7n** (51 mg, 0.28 mmol), $Pd(PPh_3)_4$ (10mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol), 1,4-dioxane (5 mL), and **7h** (55 mg, 0.31 mmol), **15b** was isolated as a dark yellow solid (105 mg, 75%); mp 259–260 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 9H, $3CH_3$), 3.82 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.27-6.33 (m, 1H, ArH), 6.85-6.86 (m, 1H, ArH), 6.90 (dd, 1H, J = 1.8, 8.2 Hz, ArH), 7.00 (d, 1H, J = 8.2 Hz, ArH), 7.04-7.13 (m, 2H, ArH), 7.26-7.32 (m, 3H, ArH), 7.33-7.38 (m, 1H, ArH), 7.43-7.46 (m, 1H, ArH), 7.50-7.53 (m, 1H, ArH), 7.55 (d, 2H, J = 8.4 Hz, ArH), 7.65 (dd, 1H, J = 1.2, 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 31.5 ($3CH_3$), 31.5 (C), 55.8, 55.9 ($2OCH_3$), 110.9, 113.1, 122.1, 123.8, 126.2, 126.6, 127.2 (CH), 128.2, 128.4 (C),

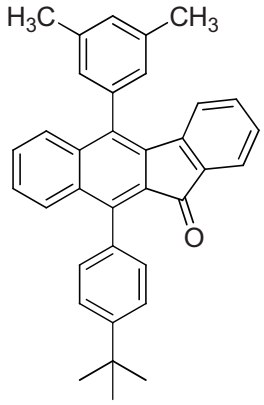
128.5, 128.6, 128.9, 129.3, 129.4 (CH), 134.0 (C), 134.2 (CH), 134.3, 134.6, 135.5, 136.7, 136.9, 140.3, 144.4, 148.7, 148.8, 151.4 (C), 192.4 (CO). IR (KBr): ν = 3399, 3064, 3004, 2948, 2902, 2866, 2829 (w), 1706, 1605, 1583, 1509 (s), 1464, 1405, 1361 (m), 1310, 1294 (w), 1256, 1237, 1211, 1189, 1165, 1137 (m), 1116, 1104, 1085, 1050 (w), 1027, 966 (s), 938, 873, 836, 808, 787 (m), 764, 728 (s), 703, 683, 644 (w), 613 (m), 576, 560, 547 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 498 (M^+, 22), 421 (100), 406 (10), 390 (38), 349 (12), 281 (14). HRMS (EI, 70 eV): calcd for $C_{35}H_{30}O_3$ $[M]^+$: 498.21895 ; found: 498.21866.

10-(3,4-Dimethoxyphenyl)-5-(m-tolyl)-11H-benzo[b]fluoren-11-one **(15c):**



Starting with **12** (150 mg, 0.28 mmol), **7n** (51 mg, 0.28 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol), 1,4-dioxane (5 mL), and **7k** (42 mg, 0.31 mmol), **15c** was isolated as a dark yellow solid (98 mg, 77%); mp 181–182 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.24-6.27 (m, 1H, ArH), 6.85-6.86 (m, 1H, ArH), 6.90 (dd, 1H, J = 1.8, 8.2 Hz, ArH), 7.00 (d, 1H, J = 8.1 Hz, ArH), 7.07-7.12 (m, 2H, ArH), 7.16-7.18 (m, 2H, ArH), 7.27-7.36 (m, 3H, ArH), 7.42 (brs., 1H, ArH), 7.44-7.47 (m, 1H, ArH), 7.51-7.54 (m, 1H, ArH), 7.64-7.67 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 31.6 (CH_3), 55.8, 55.9 ($2OCH_3$), 110.9, 113.1, 122.0, 122.1, 123.8, 126.6, 126.7, 126.8, 127.2 (CH), 128.2, 128.4 (C), 128.5, 128.9, 129.2, 130.3, 130.4 (CH), 134.0 (C), 134.3 (CH), 134.4, 135.3, 136.7, 137.6, 139.1, 140.4, 144.3, 148.7, 148.8 (C), 192.4 (CO). IR (KBr): ν = 3067, 2929, 2838 (w), 1707, 1602, 1588, 1509 (s), 1463, 1445, 1405, 1362, 1309 (m), 1244 (s), 1227, 1214, 1197 (w), 1164, 1137 (s), 1123, 1085, 1054 (w), 1025, 970 (s), 917 (w), 882, 869 (m), 806, 796 (w), 763, 726 (s), 712, 695, 669, 650, 627, 573 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 456 (M^+, 100), 425 (05), 369 (08). HRMS (EI, 70 eV): calcd for $C_{32}H_{24}O_3$ $[M]^+$: 456.17200 ; found: 456.17228.

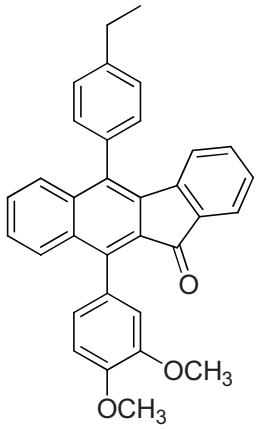
10-[4-(Tert-butyl)phenyl]-5-(3,5-dimethylphenyl)-11H-benzo[b]fluoren-11-one **(15d):**



Starting with **12** (150 mg, 0.28 mmol), **7h** (50 mg, 0.28 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol), 1,4-dioxane (5 mL), and **7g** (47 mg, 0.31 mmol), **15d** was isolated as a yellow solid (104 mg, 80%); mp 270–272 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.37 (s, 9H, $3CH_3$), 2.35 (s, 6H, $2CH_3$), 6.27-6.33 (m, 1H, ArH), 6.98 (brs., 2H, ArH), 7.08-7.11 (m, 2H, ArH), 7.14 (brs., 1H, ArH), 7.24-7.30

(m, 3H, ArH), 7.33-7.36 (m, 1H, ArH), 7.43-7.48 (m, 2H, ArH), 7.50-7.53 (m, 2H, ArH), 7.62 (dd, 1H, J = 1.2, 8.0 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.5 (2CH_3), 31.5 (3CH_3), 33.7 (C), 122.7, 122.9, 123.9, 124.4, 125.4, 126.2, 126.4 (CH), 127.3 (C), 127.4, 128.0, 128.3, 128.7 (CH), 131.7, 132.8 (C), 133.3 (CH), 133.5, 134.1, 135.6, 135.7, 136.5, 137.8, 139.7, 143.5, 149.6 (C), 191.6 (CO). IR (KBr): ν = 3390, 3066, 3029, 2958, 2922, 2856 (w), 1702, 1597 (s), 1510, 1467 (m), 1404, 1385 (w), 1362, 1311 (m), 1280, 1262 (w), 1202 (m), 1180, 1130, 1105, 1088 (w), 1048, 1020, 1006, 969, 933, 906 (m), 874, 833, 764, 726 (s), 679, 607 (m), 596, 555 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 466 (M^+, 98), 452 (36), 451 (100), 409 (17), 363 (05). HRMS (EI, 70 eV): calcd for $C_{35}H_{30}O_1$ $[M]^+$: 466.22912 ; found: 466.22893.

10-(3,4-Dimethoxyphenyl)-5-(4-ethylphenyl)-11H-benzo[b]fluoren-11-one **(15e):**



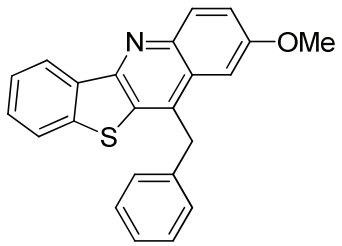
Starting with **12** (150 mg, 0.28 mmol), **7n** (51 mg, 0.28 mmol), $Pd(PPh_3)_4$ (10 mg, 3 mol%), K_3PO_4 (119 mg, 0.56 mmol), 1,4-dioxane (5 mL), and **7b** (47 mg, 0.31 mmol), **15e** was isolated as a yellow solid (86 mg, 65%); mp 252–254 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, 3H, J = 7.6 Hz, CH_3), 2.78 (q, 2H, J = 7.8 Hz, CH_2), 3.80 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.24-6.29 (m, 1H, ArH), 6.85-6.86 (m, 1H, ArH), 6.90 (dd, 1H, J = 1.8, 8.1 Hz, ArH), 7.00 (d, 1H, J = 8.2 Hz, ArH), 7.06-7.13 (m, 2H, ArH), 7.25-7.31 (m, 3H, ArH), 7.32-7.35 (m, 1H, ArH), 7.37-7.40 (m, 2H, ArH), 7.43-7.46 (m, 1H, ArH), 7.51-7.54 (m, 1H, ArH), 7.64-7.67 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.6 (CH_3), 28.8 (CH_2), 55.8, 55.9 (2OCH_3), 110.9, 113.1, 122.1, 123.8, 126.6, 127.2 (CH), 128.2, 128.4 (C), 128.5, 128.8, 129.0, 129.6, 129.7 (CH), 134.0 (C), 134.2 (CH), 134.3, 134.8, 135.5, 136.7, 136.9, 140.4, 144.4, 144.5, 148.7, 148.8 (C), 192.5 (CO). IR (KBr): ν = 3072, 3015, 2994, 2960, 2925, 2835 (w), 1706, 1606, 1587, 1512 (s), 1465, 1446, 1404, 1364, 1310 (m), 1242, 1215, 1167, 1140 (s), 1126, 1086, 1055 (w), 1026, 967 (s), 937, 916 (w), 873, 834, 806, 794 (m), 764, 729 (s), 681, 646, 611 (m), 582, 568, 541 (w) cm^{-1}. GC/MS (EI, 70 eV): m/z (%) = 471 ($[M+H]^+$ 35), 470 (M^+, 100), 455 (05), 439 (05). HRMS (ESI^+): calcd for $C_{33}H_{27}O_3$ $[M+H]^+$: 471.1955; found: 471.1959.

8.4 Domino C-N coupling / annulation *versus* C-N coupling / hydroamination of 2-alkynyl-3-bromobenzothiophenes and 2-alkynyl-3-bromothiophenes. Highly efficient synthesis of benzothieno[3,2-*b*]quinolines and thieno[3,2-*b*]pyrroles

8.4.1 General Procedure for the Synthesis of benzothienoquinolines (20a-m), benzothienopyrroles (21a-g), and thienopyrroles (25a-h).

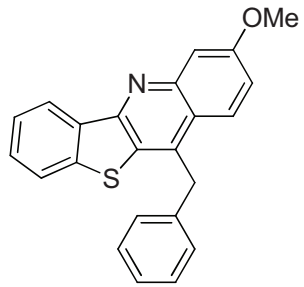
In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (10 mol%), $Pd(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol%), KO-*t*-Bu (2 equiv.) in toluene (5 mL) was purged with argon and stirred at 20 °C to give a brownish clear solution. To the stirred solution was added **18a-c** or **24a,b** (1.0 equiv.), aniline **19a-s** (1.3 equiv.) and CuI (25 mol%). The reaction mixture was heated at 105 °C for 12 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried (Na_2SO_4), concentrated in vacuo, and the residue was purified by chromatography (flash silica gel, heptanes–EtOAc) to give **20** and/or **21** and **25**.

2-Methoxy-11(benzyl)benzothieno[3,2-b]quinoline (20a).



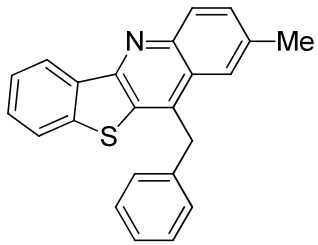
Starting with **18a** (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 4-methoxyaniline (**19a**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20a** was isolated as a brown crystals solid (106 mg, 60%); mp 154-156 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 3H, OCH_3), 4.46 (s, 2H, CH_2), 7.06-7.13 (m, 6H, ArH), 7.26 (dd, 1H, J = 2.8, 9.3 Hz, ArH), 7.38-7.47 (m, 2H, ArH), 7.65-7.68 (m, 1H, ArH), 8.08 (d, 1H, J = 9.2 Hz, ArH),), 8.47-8.50 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 37.9 (CH_2), 55.4 (OCH_3), 101.2, 121.4, 123.0, 123.6, 125.1 (CH), 126.7 (C), 126.8, 128.5, 128.8, 129.3, 131.6 (CH), 133.3, 135.1, 137.5, 137.9, 140.2, 143.4, 151.6, 157.6 (C). IR (KBr): ν = 3080, 3060, 3023, 3000, 2956, 2928, 2912, 2830 (w), 1616, (m), 1601, 1564, 1549 (w), 1502 (s), 1492, 1469 (w), 1446 (s), 1390, 1368 (w), 1333, 1266 1251 (m), 1237, 1214, 1171 (s), 1158, 1145, 1120, 1106 (w), 1075, 1053, 1029 (m), 1018, 981 (w), 967 (s), 937, 928, 910 (w), 854, 827 (s), 814, 780 (w), 757, 743, 730 (s), 708 (w), 696 (s), 672, 648 (m), 620 (w), 601, 585, 558, 549 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 355 ([M]$^+$, 100), 339 (11), 322 (19), 310 (11), 278 (06), 161 (20). HRMS (EI, 70 eV): calcd for $C_{23}H_{17}NOS$ [M]$^+$: 355.10254; found: 355.10184.

3-Methoxy-11(benzyl)benzothieno[3,2-b]quinoline (20b).



Starting with (**18a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 3-methoxyaniline (**19b**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20b** was isolated as a yellow solid (115 mg, 65%); mp 207-209 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3H, OCH_3), 4.90 (s, 2H, CH_2), 6.77 (d, 1H, J = 7.4 Hz, ArH), 7.05-7.12 (m, 5H, ArH), 7.42-7.55 (m, 3H, ArH), 7.70-7.72 (m, 1H, ArH), 7.84 (dd, 1H, J = 0.98, 8.6 Hz, ArH), 8.53-8.56 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 41.6 (CH_2), 55.5 (OCH_3), 105.2, (CH), 118.9 (C), 122.9, 123.0, 124.1, 125.0, 125.9, 128.1, 128.3, 129.8 (CH), 134.5, 135.0, 139.6, 140.0, 141.0, 149.5, 153.4, 156.6 (C). IR (KBr): ν = 3065, 3023, 2996, 2956, 2919, 2849, 1614 (w), 1593 (m), 1564, 1558 (s), 1505 (w), 1493 (m), 1475, 1449, 1440, 1435, 1428 (w), 1353, 1331 (m), 1256 (s), 1232 (m), 1197, 1176, 1164 (w), 1142 (m), 1117, 1102 (w), 1077, 1046 (m), 1030, 1018 (w), 965 (m), 948, 906, 867 (w), 824, 796, 774 (m), 725, 692 (s), 644, 621, 583, 562, 538 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 356 ([M+H]$^+$ 26), 355 ([M]$^+$, 100), 340 (11), 322 (14), 310 (08), 278 (08), 262 (14). HRMS (ESI$^+$): calcd for $C_{23}H_{18}NOS$ [M+H]$^+$: 356.1104; found: 356.1108.

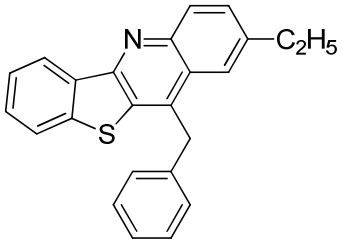
2-Methyl-11(benzyl)benzothieno[3,2-b]quinoline (20c).



Starting with (**18a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{Bu})_3.HBF_4$ (29 mg, 20 mol%), 4-methylaniline (**19c**) (70 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20c** was isolated as a brown solid (103 mg, 61%); mp 194-196 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.01 (s, 3H, OCH_3), 4.56 (s, 2H, CH_2), 7.09-7.16 (m, 5H, ArH), 7.41-7.52 (m, 3H, ArH), 7.67-7.74 (m, 1H, ArH), 7.78 (brs, 1H, ArH), 8.12 (d, 1H, J = 8.5 Hz, ArH), 8.50-8.57 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.1 (CH_3), 37.3 (CH_2), 122.0, 123.0, 123.8, 125.1, (CH), 125.8 (C), 126.7, 128.4, 128.7, 129.36, 130.0, 131.0 (CH), 132.8, 135.0, 136.2, 137.8, 138.3, 140.6, 145.9, 153.0 (C). IR (KBr): ν = 3056, 3023, 2946, 2914, 2857, 2731, 1621 (w), 1594 (m), 1575, 1565, 1551 (w), 1502, 1491 (m), 1469 (w), 1443 (m), 1426, 1402, 1376, 1364, (w), 1337 (m), 1286, 1262, 1231, 1194, 1179, 1169, 1146, 1123, (w), 1109, 1068, 1043 (m), 1024, 1015, 1001, 958, 927, 903, 872, 858, (w), 820 (s), 783, 763, (m), 748, 732, 702, (s), 691, 672, (w), 644 (m), 620 (w), 589, 571, 554, cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 340 ([M+H]$^+$ 27),

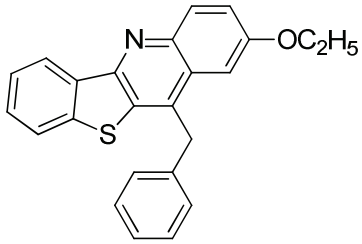
339 ([M]$^+$, 100), 338 (23), 323 (16), 262 (15). HRMS (ESI$^+$): calcd for $C_{23}H_{18}NS$ [M+H]$^+$: 340.1154; found: 340.1158.

2-Ethyl-11(benzyl)benzothieno[3,2-b]quinoline (20d):



Starting with (**18a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-ethylaniline (**19d**) (78 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20d** was isolated as a brown solid (106 mg, 60%); mp 188-190 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (t, 3H, J = 7.4 Hz, CH_3), 2.75 (q, 2H, J = 7.4 Hz, CH_2), 4.58 (s, 2H, CH_2), 7.08-7.16 (m, 5H, ArH), 7.41-7.53 (m, 3H, ArH), 7.69-7.71 (m, 1H, ArH), 7.80 (brs, 1H, ArH), 2.75 (d, 1H, J = 8.8 Hz, ArH), 8.53-8.55 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.3 (CH_3), 29.3, 37.4 (2CH_2), 120.7, 123.0, 123.9, 125.1 (CH), 125.9 (C), 126.7, 128.5, 128.7, 129.6, 129.9, 130.1(CH), 132.8, 135.1, 138.0, 138.6, 140.7, 142.3, 146.1, 153.0 (C). IR (KBr): ν = 3055, 3024, 2956, 2923, 2866, 1621 (w), 1594 (m), 1575, 1564, 1555 (w), 1503, 1490 (m), 1470 (w), 1445 (s), 1403, 1366 (w), 1340, 1331 (m), 1285, 1264, 1245, 1230, 1179, 1170, 1148, 1128 (w), 1110 (m), 1068, 1056 (w), 1042 (m), 1025, 1015, 1001, 993, 981, 953, 937, 927, 908, 899 (w), 878 (m), 856 (w), 830 (s), 784, 760, 748 (m), 733, 725, 700 (s), 672, 646, 620, 605, 587, 556 (m), cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 354 ([M+H]$^+$ 28), 353 ([M]$^+$, 100), 338 (20), 324 (15), 323 (27), 322 (17). HRMS (ESI$^+$): calcd for $C_{24}H_{20}NS$ [M+H]$^+$: 354.1311; found: 354.1316.

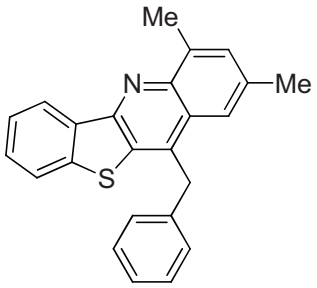
2-Ethoxy-11(benzyl)benzothieno[3,2-b]quinoline (20e):



Starting with (**18a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-ethoxyaniline (**19e**) (90 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20e** was isolated as a brown solid (120 mg, 65%); mp 185-187 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.34 (t, 3H, J = 6.6 Hz, CH_3), 3.96 (q, 2H, J = 6.6 Hz, CH_2), 4.51 (s, 2H, CH_2), 7.07-7.17 (m, 6H, ArH), 7.29 (dd, 1H, J = 2.6, 9.3 Hz, ArH), 7.41-7.51 (m, 2H, ArH), 7.66-7.76 (m, 1H, ArH), 8.11 (d, 1H, J = 9.3 Hz, ArH), 8.48-8.54 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.7 (CH_3), 37.8, 63.6 (2CH_2), 101.8, 121.7, 122.7, 123.6, 125.1, 126.7 (CH), 126.8 (C), 128.4, 128.7, 129.3, 131.5 (CH), 133.2, 135.2, 137.3, 137.9, 140.1, 143.3, 151.5, 157.0 (C). IR (KBr): ν = 3085, 3063, 3026, 2986,

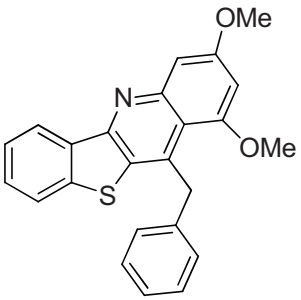
2974, 2922, 2870 (w), 1618 (m), 1602, 1593, 1580, 1567, 1556, 1516 (w), 1492 (s), 1473, 1449, 1437, 1416, 1385, 1341 (m), 1275, 1261, 1228 (w), 1216 (s), 1165, 1156, 1141 (w), 1107 (s), 1065, 1050, 1036, 1029 (m), 1016, 1002, 980, 963 (w), 944 (m), 925, 901, 862, 830 (w), 818 (s), 798, 780 (w), 757, 733, 721 (s), 694, 683, 667, 653, 645, 623 (w), 605, 584, 569, 539 (m), cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 370 ($[M+H]^+$ 28), 369 ($[M]^+$, 100), 341 (22), 340 (25), 322 (25), 310 (15), 264 (08). HRMS (ESI^+): calcd for $C_{24}H_{20}NOS$ $[M+H]^+$: 370.1260; found: 370.1264.

11-Benzyl-2,4-dimethylbenzo[4,5]thieno[3,2-b]quinolone (20f):



Starting with (**18a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 3,5-dimethylaniline (**19f**) (78 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20f** was isolated as a brown solid (107 mg, 61%); mp 150-152 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.44 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 4.82 (s, 2H, CH_2), 6.93 6.96 (m, 2H, ArH), 7.08-7.17 (m, 4H, ArH), 7.43-7.47 (m, 2H, ArH), 7.63-7.67 (m, 1H, ArH), 7.92 (s, 1H, ArH), 8.51-8.54 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.2, 23.8 ($2CH_3$), 39.7 (CH_2), 121.8, 122.8 (CH), 123.7 (C), 124.0, 125.4, 126.9, 127.3, 127.7, 128.6, 131.5 (CH), 132.6, 133.6, 134.0, 137.0, 137.2, 137.9, 139.7, 148.4, 151.6 (C). IR (KBr): ν = 3044, 3023, 2997, 2958, 2916, 2851, 1721, 1704, 1682, 1672, 1657, 1622 (w), 1594, 1564 (m), 1527, 1516 (w), 1493, 1469 (m), 1449 (s), 1392, 1378, 1348, 1327 (w), 1259 (s), 1235, 1179, 1153, 1137 (w), 1075, 1063 (m), 1017 (s), 983, 950, 941, 914, 897, 884 (w), 854, 799 (s), 775, 762 (w), 732, 723 (s), 695, 685, 669 (m), 645, 622, 597, 588, 572, 546 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 354 ($[M+H]^+$ 28), 353 ($[M]^+$, 100), 352 (20), 338 (14), 323 (08), 276 (16), 260 (07). HRMS (ESI^+): calcd for $C_{24}H_{20}NS$ $[M+H]^+$: 354.1311; found: 354.1312.

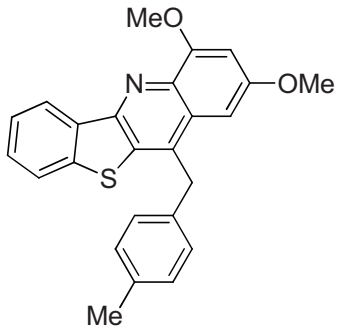
1,3-Dimethoxy-11(benzyl)benzothieno[3,2-b]quinoline (20g):



Starting with (**18a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20-mol%), 3,5-dimethoxyaniline (**19g**) (100 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20g** was isolated as a yellow solid (129 mg, 67%); mp 191-193 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.68 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.86 (s, 2H, CH_2), 6,45 (d, 1H, *J* = 2.5 Hz, ArH), 7.04-7.18 (m, 6H, ArH), 7.42-7.52 (m, 2H, ArH), 7.71-7.74 (m, 1H, ArH),

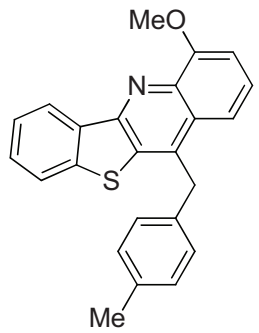
8.50-8.53 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 41.3 (CH_2), 55.5, 55.6 (2OCH_3), 99.1, 100.5 (CH), 115.0 (C), 123.0, 123.9, 125.0, 125.9, 128.1, 128.3, 129.6 (CH), 132.5, 135.0, 139.5, 140.3, 141.1, 150.9, 153.4, 157.4, 160.1(C). IR (KBr): ν = 3054, 3012, 2956, 2920, 2849, 1737, 1731, 1642 (w), 1614, 1595, 1571 (s), 1494 (m), 1446, 1399 (s), 1350, 1334 (m), 1306 (w), 1276 (m), 1235, 1204 (s), 1185, 1168, 1154 (w), 1140 (s), 1126, 1072, 1054, 1040, 1016 (w), 960 (m), 898, 972, 851 (w), 829, 820 (s), 792, 779, 762 (w), 728 (s), 701, 683 (m), 653, 633 (w), 616, 581, 540 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 386 ([M+H]$^+$ 30), 385 ([M]$^+$, 100), 370 (08), 309 (08), 292 (07), 264 (06). HRMS (ESI$^+$): calcd for $C_{24}H_{20}NO_2S$ [M+H]$^+$: 386.1209; found: 386.1213.

2,4-Dimethoxy-11(4-methylbenzyl)benzothieno[3,2-b]quinoline (20h):



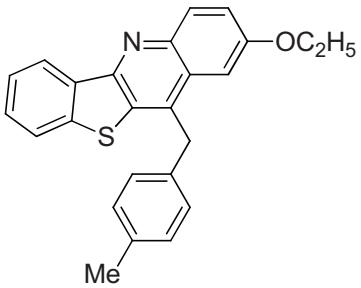
Starting with (**18b**) (160 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 2,4-dimethoxyaniline (**19h**) (99 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20h** was isolated as a white solid (139 mg, 70%); mp 163-165 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 4.49 (s, 2H, CH_2), 6.66 (d, 1H, *J* = 2.5 Hz, ArH), 6.82 (d, 1H, *J* = 2.3 Hz, ArH), 6.96 (d, 2H, *J* = 7.9 Hz, ArH), 7.06 (d, 2H, *J* = 8.1 Hz, ArH), 7.41-7.50 (m, 2H, ArH), 7.69-7.72 (m, 1H, ArH), 8.59-8.62 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.0 (CH_3), 37.9 (CH_2), 55.4, 56.4 (2OCH_3), 93.2, 100.4, 122.8, 124.1, 124.9 (CH), 127.5 (C), 128.3, 129.2, 129.4 (CH), 134.2, 134.7, 135.3, 136.2, 136.3, 137.9, 140.0, 150.4, 156.8, 158.1 (C). IR (KBr): ν = 3119, 3039, 3008, 2922, 2852, 2825, 1899, 1728 (w), 1614 (s), 1567 (w), 1555 (m), 1512 (w), 1494 (s), 1461 (w), 1444, 1409 (s), 1337 (m), 1316, 1293 (w), 1257, 1207 (s), 1188 (w), 1151 (s), 1129, 1108, 1050, 1038, 1015, 975 (w), 931 (m), 912, 859 (w), 825, 803 (s), 779 (m), 765, 731 (s), 696, 641, 624, 599, 566, 531 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 399 ([M]$^+$, 100), 398 (87), 370 (47), 369 (13), 368 (18), 310 (08). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO_2S$ [M]$^+$: 399.12875; found: 399.12779.

4-Methoxy-11(4-methylbenzyl)benzothieno[3,2-b]quinoline (20i):



Starting with (**18b**) (160 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 2- methoxyaniline (**19i**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20i** was isolated as a yellow solid (118 mg, 64%); mp 179-181 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 4.08 (s, 3H, OCH_3), 4.57 (s, 2H, CH_2), 6.95-7.06 (m, 5H, ArH), 7.40 (t, 1H, J = 7.7 Hz, ArH), 7.45-7.54 (m, 2H, ArH), 7.64 (dd, 1H, J = 1.0, 8.7 Hz, ArH), 7.71-7.74 (m, 1H, ArH), 8.65-8.69 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.0 (CH_3), 37.5 (CH_2), 56.3 (OCH_3), 106.6, 115.3, 122.9, 124.6, 124.9, 126.3 (CH), 126.9 (C), 128.3, 129.4, 129.7 (CH), 133.5, 134.7, 135.0, 136.3, 139.4, 139.6, 140.6, 152.6, 155.9 (C). IR (KBr): ν = 3071, 3042, 3015, 2917, 2852, 2825 (w), 1611 (m), 1594 (w), 1552, 1494, 1480, 1459, 1440 (m), 1396 (s), 1355 (w), 1337 (m), 1302, 1280 (w), 1255 (s), 1211, 1185, 1181, 1173 (w), 1153 (s), 1135, 1108, 1077 (w), 1038 (s), 1019 (m), 957, 950, 937, 921, 903, 856, 849, 842, 820 (w), 804 (s), 769, 757 (w), 741, 731 (s), 706 (w), 666 (m), 653, 640, 623 (w), 596 (m), 581, 559 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 370 ($[M+H]^+$ 30), 369 ($[M]^+$, 99), 368 (100), 340 (56), 339 (14), 323 (15), 310 (08), 248 (07). HRMS (ESI^+): calcd for $C_{24}H_{20}NOS$ $[M+H]^+$: 370.126; found: 370.1264.

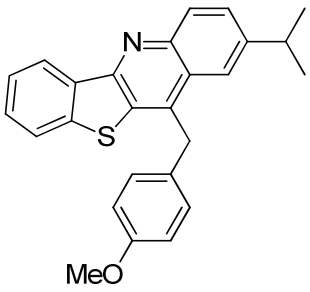
2-Ethoxy-11(4-methylbenzyl)benzothieno[3,2-b]quinoline (20j):



Starting with (**18b**) (160 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 4-ethoxyaniline (**19e**) (95 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20j** was isolated as a white solid (115 mg, 60%); mp 170-171 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, 3H, J = 7.00 Hz, CH_3), 2.16 (s, 3H, CH_3), 3.94 (q, 2H, J = 6.9 Hz, OCH_2), 4.42 (s, 2H, CH_2), 6.93 (d, 2H, J = 8.0 Hz, ArH), 7.02 (d, 2H, J = 8.1 Hz, ArH), 7.14-7.16 (m, 1H, ArH), 7.27 (dd, 1H, J = 2.7, 9.2 Hz, ArH), 7.39-7.46 (m, 2H, ArH), 7.66-7.69 (m, 1H, ArH), 8.08 (d, 1H, J = 9.3 Hz, ArH), 8.47-8.51 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.7, 21.0 (CH_3), 37.4 (CH_2), 63.7 (OCH_2), 101.9, 121.7, 123.0, 123.6, 125.1 (CH), 126.8 (C), 128.3, 129.3, 129.4, 131.5 (CH), 133.2, 134.8, 135.2, 136.3, 137.7, 140.2, 143.4, 151.5, 157.0 (C). IR (KBr): ν = 3047, 3015, 2974, 2920, 2894, 2874 (w), 1619 (m), 1592, 1567, 1552, (w), 1502 (m), 1471, 1448 (w), 1440 (m), 1419, 1403, 1390, 1383, 1335, 1316, 1264, 1254 (w), 1228, 1220, 1214 (m), 1181, 1156, 1148 (w), 1114,

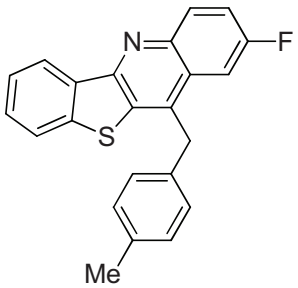
1107 (m), 1069, 1056, 1039, 1016, 988, 950, 929, 893, 861, 850, 825 (w), 812, 796, 780, 762 (m), 734 (s), 713, 696, 682, 643, 596, 585, 579, 561, 532 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 384 ($[M+H]^+$ 28), 383 ($[M]^+$, 100), 355 (14), 339 (18), 310 (11), 264 (06). HRMS (ESI^+): calcd for $C_{25}H_{22}NOS$ $[M+H]^+$: 384.1417; found: 384.1418.

2-Isopropyl-11(4-methoxylbenzyl)benzothieno[3,2-b]quinoline (20k):



Starting with (**18c**) (150 mg, 0.44 mmol), $Pd(OAC)_2$ (10 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (25 mg, 20 mol%), 4-isopropylaniline (**19j**) (77 mg, 0.6 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (21 mg, 25%), **20k** was isolated as a yellow solid (110mg, 63%); mp 127-129 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, 6H, *J* = 6.9 Hz, ArH), 2.96- 3.08 (m, 1H, CH), 3.66 (s, 3H, OCH_3), 4.56 (s, 2H, CH_2), 6.71 (d, 2H, *J* = 8.9 Hz, ArH), 7.11 (d, 2H, *J* = 8.9 Hz, ArH), 7.43-7.53 (m, 2H, ArH), 7.58 (dd, 1H, *J* = 1.9, 8.8 Hz, ArH), 7.72-7.75 (m, 1H, ArH), 7.87 (d, 1H, *J* = 1.9 Hz, ArH), 8.17 (d, 1H, *J* = 8.9 Hz, ArH), 8.55-8.58 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.9 (2CH_3), 34.4 (CH), 36.7 (CH_2), 55.2 (OCH_3), 114.1, 119.4, 123.0, 123.9, 125.1 (CH), 125.7 (C), 128.5, 129.5, 129.6, 129.9 (CH), 130.0, 132.5, 135.0, 139.3, 140.7, 146.1, 146.8, 153.0, 158.4 (C). IR (KBr): ν = 3063, 2994, 2951, 2921, 2861, 2838 (w), 1608 (m), 1593, 1583, 1563, 1548 (w), 1509 (s), 1461 (w), 1442 (s), 1418, 1392, 1384, 1362, 1328 (w), 1303, 1265 (m), 1243 (s), 1179, 1105 (m), 1070, 1057 (w), 1041 (s), 1015 (m), 966, 935, 911, 884, 844 (w), 827, 816 (s), 791 (w), 763, 730 (s), 718, 711, 706, 670 (w), 646, 635, 607, 588, 544, 530 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 397 ($[M]^+$, 100), 382 (25), 354 (10), 323 (07), 274 (31). HRMS (EI, 70 eV): calcd for $C_{26}H_{23}NOS$ $[M]^+$: 397.14949; found: 397.14955.

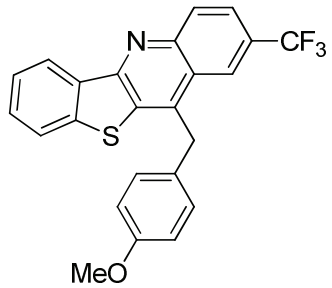
2-Fluoro-11(4-methoxylbenzyl)benzothieno[3,2-b]quinoline (20l):



Starting with (**18b**) (160 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-fluoro aniline (**19k**) (61 mg, 0.55 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20l** was isolated as a white solid (107 mg, 60%); mp 229-231 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s, 3H, CH_3), 4.50 (s, 2H, CH_2), 7.01 (dd, 4H, *J* = 8.1, 18.5 Hz, ArH), 7.39-7.55 (m, 3H, ArH), 7.63 (dd, 1H, *J* = 2.7, 10.1 Hz ArH), 7.74 (d, 1H, *J* = 7.8 Hz, ArH), 8.19-8.24 (m, 1H, ArH), 8.51 (d, 1H, *J* = 7.8 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -112.39. ^{13}C

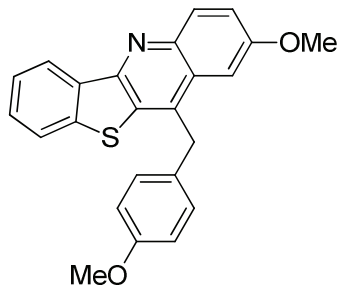
NMR (62.9 MHz, $CDCl_3$): δ = 20.0 (CH_3), 37.3 (CH_2), 106.7 (d, $J_{F,C}$ = 24.1 Hz, CH), 118.9 (d, $J_{F,C}$ = 24.2 Hz, CH), 123.1, 123.9, 125.3, 128.5, 128.8, 128.9, 130.0 (CH), 131.5 (d, $J_{F,C}$ = 9.3 Hz, C), 132.6, 133.2, 133.7, 135.5 (C), 137.8 (d, $J_{F,C}$ = 5.9 Hz, C), 139.6, 143.3 (C), 152.2 (d, $J_{F,C}$ = 2.4 Hz, C), 158.7 (d, $J_{F,C}$ = 247.8 Hz, CF). IR (KBr): ν = 3064, 2920, 2857 (w), 1622 (s), 1595, 1597, 1557 (w), 1502 (s), 1473 (w), 1440 (s), 1399, 1363, 1336 (m), 1283, 1261, 1243 (w), 1226, 1184 (s), 1151, 1124 (w), 1107, 1065, 1039, 1018 (m), 979, 945 (w), 914, 859, 840 (m), 822 (s), 806, 782, 762 (w), 730 (s), 709, 687, 671 (w), 638, 590, 539 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) =358 ($[M+H]^+$ 26), 357 ($[M]^+$, 100), 356 (20), 342 (18), 341 (14), 340 (10), 322 (06), 266 (18). HRMS (ESI^+): calcd for $C_{23}H_{17}FNS$ $[M+H]^+$: 358.10602; found: 358.10579.

3-Trifluoromethyl-11(4-methoxylbenzyl)benzothieno[3,2-b]quinoline (20m):



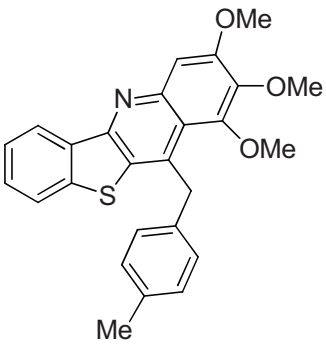
Starting with (**18c**) (150 mg, 0.44 mmol), $Pd(OAC)_2$ (10 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (25mg, 20mol%), 3-(trifluoromethyl)aniline (**19l**) (84 mg, 0.5 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (21 mg, 25%), **20m** was isolated as a brown solid (102 mg, 55%); mp 226-228 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.65 (s, 3H, OCH_3), 4.57 (s, 2H, CH_2), 6.71 (d, 2H, J = 8.1 Hz, ArH), 7.06 (d, 2H, J = 8.1 Hz, ArH), 7.48-7.59 (m, 2H, ArH), 7.60 (dd, 1H, J = 1.8, 8.8 Hz, ArH), 7.76 (d, 1H, J = 7.7 Hz, ArH), 8.16 (d, 1H, J = 8.6 Hz, ArH), 8.57 (d, 2H, J = 9.1 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -62.49. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 36.7 (CH_2), 55.2 (OCH_3), 114.3, 121.7 (q, $J_{F,C}$ = 2.8 Hz, CH), 123.1, 124.3, 124.6, 125.5 (CH), 125.9 (C), 127.7 (q, $J_{F,C}$ = 272.2 Hz, CF_3), 128.1 (q, $J_{F,C}$ = 4.7 Hz, CH), 129.3 (C), 129.4 (CH), 129.7, 129.9 (q, $J_{F,C}$ = 32.6 Hz, C-CF_3), 130.5 (CH), 134.4, 134.7, 139.7, 141.0, 146.1, 155.0, 158.6 (C). IR (KBr): ν = 3062, 3036, 3003, 2923, 2838, 1651, 1630, 1608, 1592, 1581, 1556, 1538 (w), 1510 (s), 1468 (m), 1452 (s), 1409, 1367, 1345, 1333 (m), 1304, 1281, 1243 (s), 1174, 1162, 1145 (m), 1106 (s), 1073 (w), 1061, 1032 (m), 962 (w), 950, 921, 907 (m), 864, 845 (w), 813, 765, 738,709, 695, 660 (m), 631, 611, 580, 529 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 424 ($[M+H]^+$ 27), 423 ($[M]^+$, 100), 422 (17), 408 (23), 391 (08), 378 (07), 316 (12). HRMS (ESI^+): calcd for $C_{24}H_{17}F_3NOS$ $[M+H]^+$: 424.09775; found: 424.09789.

2-Methoxy-11(4-methoxylbenzyl)benzothieno[3,2-b]quinoline (20n):



Starting with (**18c**) (172 mg, 0.50 mmol), $Pd(OAC)_2$ (11mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 4-methoxyaniline (**19a**) (80 mg, 0.65 mmole), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmole), and CuI (25 mg, 25 mol%), **20n** was isolated as a red solid (115 mg, 60%); mp 172-173 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.64 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 4.46 (s, 2H, CH_2), 6.69 (d, 2H, *J* = 8.7 Hz, ArH), 7.08 (d, 2H, *J* = 8.7 Hz, ArH), 7.20 (d, 1H, *J* = 2.8 Hz, ArH), 7.30 (d, 1H, *J* = 2.8, 9.2 Hz, ArH), 7.41-7.51 (m, 2H, ArH), 7.69-7.73 (m, 1H, ArH), 8.11 (d, 1H, *J* = 9.2 Hz, ArH), 8.49-8.52 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 37.0 (CH_2), 55.2, 55.4 (OCH_3), 101.1, 114.1, 121.4, 123.0, 123.6, 125.1 (CH), 126.7 (C), 129.3, 129.4 (CH), 129.8 (C), 131.6 (CH), 133.1, 135.1, 137.8, 140.2, 143.4, 151.6, 157.6, 158.4 (C). IR (KBr): ν = 3048, 3029, 3002, 2955, 2920, 2837, 1619, 1608, 1581, 1565 (w), 1509, 1497, 1446, 1438 (m), 1408, 1361, 1333, 1305, 1286, 1264 (w), 1244, 1234, 1219 (s), 1171 (m), 1153, 1140, 1118, 1108, 1066, 1046 (w), 1026 (s), 984, 963, 948, 922, 906, 841 (w), 822, 810 (s), 784 (w), 764 (s), 749 (w), 740, 732, 709 (m), 691, 680 (w), 642, 638 (m), 600, 584 (w), 555 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 386 ($[M+H]^+$ 27), 385 ($[M]^+$, 100), 370 (16), 339 (07), 278 (05). HRMS (ESI^+): calcd for $C_{24}H_{20}NO_2S$ $[M+H]^+$: 386.1209; found: 386.1211.

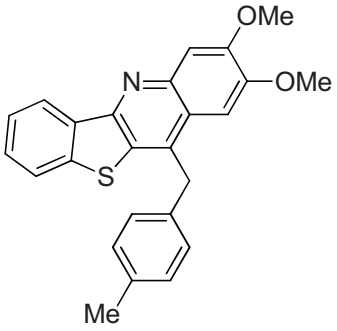
1,2,3-Trimethoxy-11(4-methylbenzyl)benzothieno[3,2-b]quinoline (20o):



Starting with (**18b**) (160 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29mg, 20 mol%), 3,4,5- trimethoxyaniline (**19m**) (110 mg, 0.6 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **20o** was isolated as a red solid (109 mg, 53%); mp 112-114 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 3.61 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.87 (s, 2H, CH_2), 6.88-7.02 (m, 4H, ArH), 7.41 (s, 1H, ArH), 7.43-7.51 (m, 2H, ArH), 7.68-7.71 (m, 1H, ArH), 8.48-8.51 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.0 (CH_3), 39.7 (CH_2), 56.1, 61.0, 61.5 (3OCH_3), 104.8 (CH), 117.4 (C), 123.0, 123.6, 124.9, 128.0, 129.1, 129.4 (CH), 133.3, 134.9, 135.5, 136.0, 138.8, 140.8, 142.0, 146.2, 149.0, 152.6, 154.8 (C). IR (KBr): ν = 3051, 2997, 2922, 2850, 2833, 2731 (w), 1614, 1594 (m), 1556 (s), 1512, 1483, 1463, 1449 (m), 1406 (s), 1326, 1321 (m), 1273 (w), 1231 (s), 1214, 1192 (w), 1108 (s), 1070 (w), 1051, 1034 (m), 1020 (w), 992, 969 (m), 947, 915, 877, 833, 793 (m), 771, 759 (w), 731 (s), 713, 676, 650, 628, 606, 568 (w),

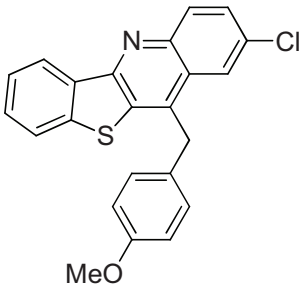
549 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 429 ($[M]^+$, 100), 399 (12), 382 (34), 367 (07), 339 (15). HRMS (EI, 70 eV): calcd for $C_{26}H_{23}NO_3S$ $[M]^+$: 429.13932; found: 429.13915.

2,3-Dimethoxy-11(4-methylbenzyl)benzothieno[3,2-b]quinoline (20p):



Starting with (**18b**) (160 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 3,4- dimethoxyaniline (**19n**) (99 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25 %), **20p** was isolated as a yellow solid (98 mg, 50%); mp 171-173 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.47 (s, 2H, CH_2), 6.96 (d, 2H, *J* = 7.8 Hz, ArH), 7.05 (d, 2H, *J* = 8.3 Hz, ArH), 7.16 (s, 1H, ArH), 7.41-7.50 (m, 2H, ArH), 7.51 (s, 1H, ArH), 7.71-7.74 (m, 1H, ArH), 8.48-8.51 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.0 (CH_3), 37.6 (CH_2), 55.9, 56.2 (2OCH_3), 101.2, 108.3 (CH), 121.6 (C), 123.0, 123.4, 125.0, 128.3, 129.0, 129.4 (CH), 131.2, 134.8, 135.2, 136.4, 137.8, 140.2, 144.6, 149.7, 151.6, 151.9 (C). IR (KBr): ν = 3045, 3001, 2919, 2852, 2828 (w), 1625 (m), 1594 (w), 1567 (m), 1503 (s), 1470, 1462, 1454 (w), 1427, 1418, 1339 (m), 1299, 1266 (w), 1235, 1205, 1167 (s), 1131, 1106 (w), 1073 (m), 1046, 1027 (w), 1002 (s), 955, 937, 920, 846, 837, 825, 815, 804, 784 (w), 761, 746 (m), 729 (s), 707, 671, 633, 587 (m), 553, 536 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 399 ($[M]^+$, 100), 369 (05), 324 (05). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO_2S$ $[M]^+$: 399.12875; found: 399.12898.

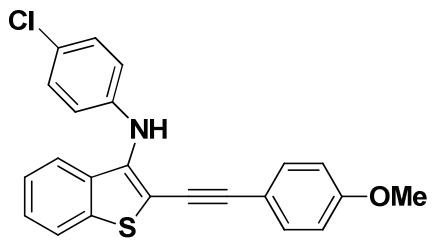
2-Chloro-11(4-methoxybenzyl)benzothieno[3,2-b]quinoline (20q):



Starting with (**18c**) (150 mg, 0.44 mmol), $Pd(OAC)_2$ (10 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (25 mg, 20 mol%), 4-chloroaniline (**19o**) (82 mg, 0.5 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (21 mg, 25 %), **20q** was isolated as a white solid (94 mg, 55%); mp 188-190 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 3H, OCH_3), 4.46 (s, 2H, CH_2), 7.06-7.13 (m, 5H, ArH), 7.26 (dd, 1H, *J* = 2.8, 9.3 Hz, ArH), 7.38-7.47 (m, 2H, ArH), 7.65-7.68 (m, 1H, ArH), 8.08 (d, 1H, *J* = 9.2 Hz, ArH),), 8.47-8.50 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 37.9 (CH_2), 55.4 (OCH_3), 101.2, 121.4, 123.0, 123.6, 125.1 (CH), 126.7 (C), 126.8, 128.5, 128.8, 129.3 (CH), 131.6, 133.3, 135.1, 137.5, 137.9, 140.2, 143.4, 151.6, 157.6 (C). IR (KBr): ν = 3068, 2922, 2853, 1606, 1581, 1552 (w), 1508, 1486 (s), 1461, 1448, 1388 (w), 1335, 1301 (m), 1263, 1237 (s),

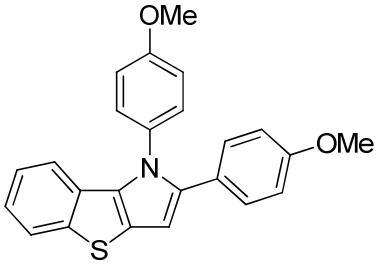
1175 (m), 1142, 1120, 1103 (w), 1091 (m), 1065 (w), 1038 (s), 1017, 956 (w), 888, 867 (m), 834, 800 (m), 765, 734 (s), 707, 680 (w), 661 (s), 630, 586, 573, 538 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 391 ([M^+, ^{37}Cl], 40), 389 ([M^+, ^{35}Cl], 100), 388 (08), 374 (16), 310 (21), 354 (12), 323 (15), 310 (17), 282 (10). HRMS (ESI^+): calcd for $C_{23}H_{17}ClNOS$ [M+H, $^{35}Cl]^+$: 390.07139; found: 390.07118, calcd for $C_{23}H_{17}ClNOS$ [M+H, $^{37}Cl]^+$: 392.0691; found: 392.06887.

N-(4-chlorophenyl)-2-[(4-methoxyphenyl)ethynyl]benzo[b]thiophen-3-amine(22a):



Following *general procedure* but with reduced temperature (40°C), and reduced reaction time 4 h, **22a** was isolated from reaction of 3-Bromo-2-(4-methoxy-phenylethynyl)-benzo[b]thiophene (**18c**) (150 mg, 0.44 mmol), $Pd(OAC)_2$ (10 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (25 mg, 20 mol%), with 4-chloroaniline (**19o**) (82 mg, 0.5 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (21 mg, 25 %) as a dark brown solid mp 50-52 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.74 (s, 3H, OCH_3), 5.95 (brs, 1H, NH), 6.71-6.79 (m, 4H, ArH), 7.10 (d, 2H, *J* = 8.7 Hz, ArH), 7.18-7.25 (m, 3H, ArH), 7.28-7.33 (m, 1H, ArH), 7.40 (d, 1H, *J* = 7.8 Hz, ArH), 7.66 (d, 1H, *J* = 7.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 80, 100.7, 110.0 (C), 114.1 (CH), 114.6 (C), 118.1, 122.3, 122.7, 124.3 (CH), 125.2 (C), 125.9, 128.9, 132.9 (CH), 133.8, 137.6, 138.1, 142.7, 160.0 (C). IR (KBr): *v* = 3374, 2925, 2835, 2538, 2192, 1873, 1656 (w), 1594 (s), 1566, 1533 (m), 1502, 1488 (s), 1461, 1439, 1400 (w), 1377, 1285 (m), 1244, 1170 (s), 1104, 1089, 1065 (w), 1025 (s), 951, 929, 851 (w), 817 (s), 759, 751 (m), 728 (s), 659, 631, 590, 531 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 391 ([M^+, ^{37}Cl], 39), 389 ([M^+, ^{35}Cl], 100), 376 (15), 374 (36), 310 (21), 309 (06). HRMS (ESI^+): calcd for $C_{23}H_{17}ClNOS$ [M+H, $^{35}Cl]^+$: 390.07139; found: 390.07138, calcd for $C_{23}H_{17}ClNOS$ [M+H, $^{37}Cl]^+$: 392.0691; found: 392.06913.

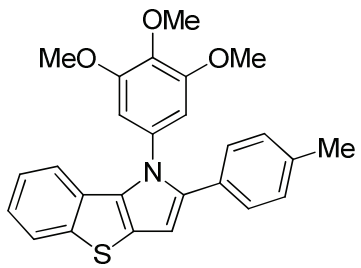
1,2-Bis(4-methoxyphenyl)-1H-[1]benzothieno[3,2-b]pyrrole (21a):



Compound **21a** was isolated together with **20n** as a by-product as a dark brown solid (57 mg, 30%); mp 171-172 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.68 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 6.56 (s, 1H, ArH), 6.68 (d, 2H, *J* = 8.7 Hz, ArH), 6.86-6.95 (m, 3H, ArH), 6.98-7.10 (m, 4H, ArH), 7.22 (d, 2H, *J* = 8.7 Hz, ArH), 7.66-7.70 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.2, 55.5 (OCH_3), 101.6, 113.7, 114.4, 118.5, 122.5 (CH), 122.7 (C),

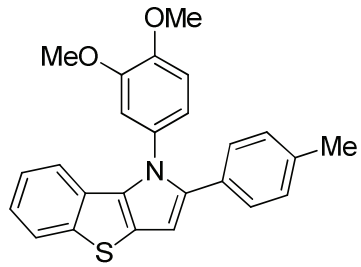
123.7, 124.0 (CH), 125.3, 127.5 (C), 129.6, 129.8 (CH), 131.7, 134.4, 140.3, 141.9, 158.6, 159.3 (C). IR (KBr): ν = 3013, 2997, 2957, 2922, 2852, 2828, 1608, 1588, 1574, 1556, 1536 (w), 1511, 1488, 1463, 1456 (m), 1441, 1409, 1392, 1350 (w), 1292 (m), 1237 (s), 1173 (m), 1114 (w), 1102 (m), 1073, 1056 (w), 1022 (m), 966, 953, 931, 907 (w), 839 (m), 829 (s), 815, 806, 795, 782 (m), 754, 748 (s), 726, 696, 663, 641, 613, 599, 542, 531 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) =386 ($[M+H]^+$ 27), 385 ($[M]^+$, 100), 370 (33), 298 (07), 193 (08). HRMS (ESI^+): calcd for $C_{24}H_{20}NO_2S$ $[M+H]^+$: 386.1209; found: 386.1206.

(3,4,5-Trimethoxyphenyl)-2(4-methylphenyl)-1H-[1]benzothieno[3,2-b]pyrrole (21b):



Compound **21b** was isolated together with **20o** as a by-product as a dark brownish solid (68 mg, 35%); mp 97-99 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3H, CH_3), 3.66 (s, 6H, $2OCH_3$), 3.74 (s, 3H, OCH_3), 6.02 (s, 1H, ArH), 6.12 (s, 2H, ArH), 7.05 (d, 2H, *J* = 8.1 Hz, ArH), 7.19-7.25 (m, 3H, ArH), 7.05 (td, 1H, *J* = 1.4, 8.1 Hz, ArH), 7.47 (brd, 1H, *J* = 7.5 Hz, ArH), 7.90 (brd, 1H, *J* = 7.5 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.6 (CH_3), 56.0, 61.1 ($3OCH_3$), 81.1, (C), 95.4 (CH), 100.8, 107.4, 119.6 (C), 122.5, 122.7, 124.1, 126.0, 129.2, 129.4, 131.2 (CH), 132.6, 133.6, 138.3, 138.6, 138.9, 139.9, 153.6 (C). IR (KBr): ν = 3331, 2952, 2922, 2851, 1666, 1660 (w), 1597 (s), 1567, 1536 (w), 1503 (s), 1484, 1461, 1449 (w), 1409 (m), 1380, 1346, 1319, 1283 (w), 1229 (s), 1199, 1179 (w), 1119 (s), 1037 (w), 1005 (m), 864, 914 (w), 813 (s), 763 (m), 730 (s), 661, 641, 627, 610, 528 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 429 ($[M]^+$, 100), 399 (07), 382 (31), 367 (07), 339 (15). HRMS (EI, 70 eV): calcd for $C_{26}H_{23}NO_3S$ $[M]^+$: 429.13932; found: 429.13902.

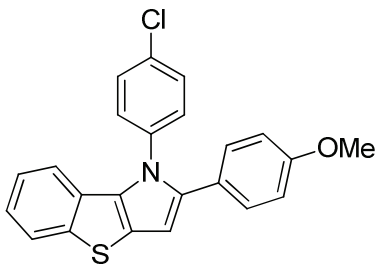
1(3,4-Dimethoxyphenyl)-2(4-methylphenyl)-1H-[1]benzothieno[3,2-b]pyrrole(*21c*):



Compound **21c** was isolated together with **20p** as a by-product as a dark brownish solid (72 mg, 40%); mp 100-102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 6.00 (s, 1H, ArH), 6.42 (dd, 1H, *J* = 1.5, 8.5 Hz, ArH), 6.54 (d, 1H, *J* = 2.5 Hz, ArH), 6.69 (d, 1H, *J* = 8.6 Hz, ArH), 7.04 (d, 2H, *J* = 8.0 Hz, ArH), 7.15-7.22 (m, 3H, ArH), 7.28 (td, 1H, *J* = 1.3, 8.2 Hz, ArH), 7.37 (brd, 1H, *J* = 7.9 Hz, ArH), 7.64 (brd, 1H, *J* = 7.9 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.5 (CH_3), 55.9, 56.4 ($2OCH_3$), 81.2, 100.2 (C), 104.1 (CH), 105.6 (C), 110.5, 112.4, 119.7, 122.6, 122.7, 124.0, 125.8, 129.1, 131.2 (CH), 133.3, 137.5, 138.4, 138.7, 139.7, 144.3, 149.5 (C). IR (KBr): ν = 3367, 3056,

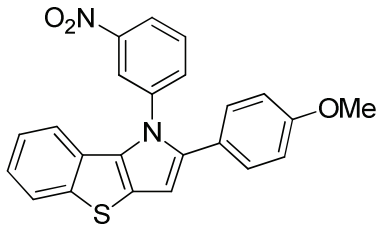
3025, 2999, 2917, 2843 (w), 1592 (m) , 1566, 1537 (w), 1504 (s), 1461 (m), 1435, 1393 (w), 1373 (m), 1335, 1319, 1287, 1256 (w), 1228 (s), 1201, 1166, 1135 (m), 1118, 1049 (w), 1023 (s), 951, 904, 880 (w), 842, 810 (m), 792, 762, 747 (w), 725 (m), 707, 665, 644, 609, 566, 556 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 399 ($[M]^+$, 100), 369 (05), 340 (05), 184 (12). HRMS (EI, 70 eV): calcd for $C_{26}H_{21}NO_2S$ $[M]^+$: 399.12875; found: 399.12879.

1-(4-Chlorophenyl)-2(4-methoxylphenyl)-1H-[1]benzothieno[3,2-b]pyrrole (21d):



Starting with (**18c**) (150 mg, 0.44 mmol), $Pd(OAC)_2$ (10 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (25 mg, 20 mol%), 4-chloroaniline (**19o**) (82 mg, 0.5 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (21 mg, 25 %), **21d** was isolated as a yellow solid (54 mg, 32%); mp 173-175 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 3H, OCH_3), 6.55 (s, 1H, ArH), 6.67 (d, 2H, *J* = 8.5 Hz, ArH), 6.95-7.10 (m, 5H, ArH), 7.15 (d, 2H, *J* = 8.5 Hz, ArH), 7.34 (d, 2H, *J* = 8.5 Hz, ArH), 7.66-7.69 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =54.1 (OCH_3), 101.4, 112.8, 117.4, 121.7, 122.4 (CH), 122.7 (C), 123.1 (CH), 123.7, 126.1 (C), 128.5, 128.7, 128.9 (CH), 132.7, 132.9, 136.4, 139.1, 140.9, 157.8 (C). IR (KBr): ν = 3088, 2958, 2834 (w), 1484 (s), 1459 (m), 1435, 1402 (w), 1347 (m), 1287, 1273 (w), 1242, 1171 (s), 1155, 1113 (w), 1087 (s), 1068, 1057 (w), 1024 (s), 964, 951, 937 (w), 848, 832 (m), 822, 801 (w), 784, 747, 723 (s), 711, 694, 676 (w), 666, 651 (m), 632, 620 (w), 605, 567 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 391 ($[M^+, {}^{37}Cl]$, 41), 389 ($[M^+, {}^{35}Cl]$, 100),, 376 (15), 374 (38), 310 (22), 309 (06). HRMS (ESI^+): calcd for $C_{23}H_{17}ClNOS$ $[M+H, {}^{35}Cl]^+$: 390.07139; found: 390.07075.

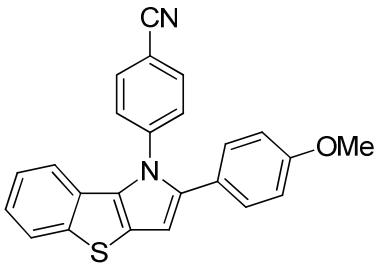
(3-Nitrophenyl)-2(4-methoxylphenyl)-1H-[1]benzothieno[3,2-b]pyrrole (21e):



Starting with (**18c**) (150 mg, 0.44 mmol), $Pd(OAC)_2$ (10 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (25 mg, 20 mol%), 3-nitroaniline (**19p**) (73 mg, 0.5 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (21 mg, 25%), **21e** was isolated as a red solid (135 mg, 78%); mp 186-188 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.70 (s, 3H, OCH_3), 6.61 (s, 1H, ArH), 6.70 (d, 2H, *J* = 8.7 Hz, ArH), 6.92 (d, 1H, *J* = 7.9 Hz, ArH), 7.01 (d, 2H, *J* = 8.6 Hz, ArH), 7.05-7.16 (m, 2H, ArH), 7.53-7.64 (m, 2H, ArH), 7.73 (d, 1H, *J* = 7.6 Hz, ArH), 8.18-8.25 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ =55.2 (OCH_3), 103.3, 114.0, 118.1, 122.9, 123.0, 123.4, 124.0 (CH),

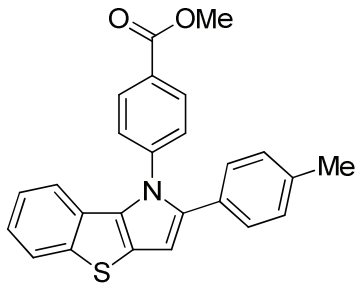
124.1, 124.2 (C), 124.3, 126.9 (CH), 130.1 (C), 130.3 (CH), 133.5 (C), 134.5 (CH), 140.1, 140.3, 142.1, 148.6, 159.1 (C). IR (KBr): ν = 3073, 2921, 2852 (w), 1731, 1606 (m), 1585, 1575 (w), 1525 (s), 1481, 1461 (m), 1405, 1375 (w), 1344 (s), 1290 (m), 1245, 1176 (s), 1116, 1107, 1058 (m), 1033 (s), 1001, 956, 929, 907 (w), 895, 870 (m), 833 (s), 816, 801, 771, 745, 722 (m), 698, 682, 664, 605, 548 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 400 ($[M]^+$, 100), 385 (15), 370 (07), 339 (07), 310 (15), 207 (16). HRMS (EI, 70 eV): calcd for $C_{23}H_{16}N_2O_3S$ $[M]^+$: 400.08761; found: 400.08837.

(4-Cyanophenyl)-2(4-methoxyphenyl)-1H-[1]benzothieno[3,2-b]pyrrole (21f):



Starting with (**18c**) (150 mg, 0.44 mmol), $Pd(OAC)_2$ (10 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (25 mg, 20 mol%), 4-aminobenzonitrile (**19q**) (62 mg, 0.5 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (21 mg, 25%), **21f** was isolated as a yellow solid (140 mg, 84%); mp 199-201 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3H, OCH_3), 6.59 (s, 1H, ArH), 6.71 (d, 2H, *J* = 8.2 Hz, ArH), 6.97 (d, 2H, *J* = 8.7 Hz, ArH), 6.99-7.02 (m, 1H, ArH), 7.05-7.13 (m, 2H, ArH), 7.41 (d, 2H, *J* = 8.4 Hz, ArH), 7.67 (d, 2H, *J* = 8.4 Hz, ArH), 7.70-7.73 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 103.4 (CH), 111.8 (C), 113.9 (CH), 118.1 (C), 118.1, 118.4, 123.0, 124.0, 124.3 (CH), 124.4, 126.9 (C), 129.1, 130.2 (CH), 133.1 (C), 133.2 (CH), 140.1, 142.1, 142.8, 159.1 (C). IR (KBr): ν = 3121, 3008, 2937, 2838 (w), 2226 (m), 1603 (s), 1573, 1532 (w), 1506 (m), 1488, 1463 (s), 1438, 1406 (m), 1350 (s), 1297, 1290 (m), 1247, 1176 (s), 1118, 1069, 1057 (w), 1028 (s), 964, 951, 929 (w), 853 (m), 831, 803, 743, 723 (s), 695 (w), 667, 659, 626 (m), 607 (s), 585 (w), 551 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 380 ($[M]^+$, 100), 365 (41), 335 (12). HRMS (EI, 70 eV): calcd for $C_{24}H_{16}N_2OS$ $[M]^+$: 380.09779; found: 380.09799.

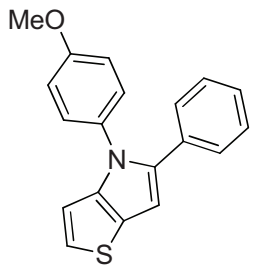
(4-Methylbenzoate)-2(4-methylphenyl)-1H-[1]benzothieno[3,2-b]pyrrole (21g):



Starting with (**18b**) (160 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), methyl 4-aminobenzoate (**19r**) (98 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), CuI (25 mg, 25%), **21g** was isolated as a yellow solid (89 mg, 45%); mp 190-192 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.23 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 6.63 (s, 1H, ArH), 6.93-7.11 (m, 7H, ArH), 7.39 (d, 2H, *J* = 7.4 Hz, ArH), 7.71 (d,

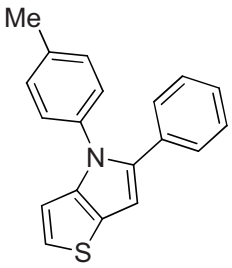
1H, J = 7.5 Hz, ArH), 8.07 (d, 2H, J = 7.5 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 29.7 (CH_3), 52.4 (OCH_3), 103.2, 118.6, 122.8, 123.8 (CH), 123.9 (C), 124.1 (CH), 127.1 (C), 128.4, 128.6, 129.1 (CH), 129.3, 129.7 (C), 130.7 (CH), 133.7, 137.1, 140.3, 142.1, 142.9 (C), 166.3 (CO). IR (KBr): ν =3118, 3027, 2921, 2852 (w), 1714 (s), 1602, 1586 (m), 1532 (w), 1512, 1486, 1460, 1434 (m), 1413, 1404, 1377 (w), 1355, 1275 (s), 1170, 1116, 1097, 1055 (w), 1016, 964, 869 (m), 848 (w), 812 (s), 781, 748 722, 703, 669 (m), 651, 627 (w), 603, 562 (m) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) =398 ([M+H]$^+$ 08), 397 ([M]$^+$, 100), 382 (05), 338 (09), 337 (08), 281 (14). HRMS (ESI$^+$): calcd for $C_{25}H_{20}NO_2S$ [M+H]$^+$: 398.12093; found: 398.12060.

4-(4-Methoxyphenyl)-5-phenyl-4H-thieno[3,2-b]pyrrole (25a):



Starting with (**24a**) (100 mg, 0.38 mmol), $Pd(OAc)_2$ (8.5 mg, 10 mol%), P(t-Bu)$_3$.HBF_4 (22 mg, 20 mol%), 4-methoxyaniline **(19a)** (56 mg, 0.46 mmol), KO-t-Bu (85 mg, 0.76 mmol), toluene (5 mL), CuI (18 mg, 25 mol%), **25a** was isolated as a dark brown solid (75 mg, 65%); mp 137-139 C^o. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.75 (s, 3H, OCH_3), 6.60 (s, 1H, ArH), 6.78-6.82 (m, 3H, ArH), 7.00 (d, 1H, J = 5.3 Hz, ArH), 7.09 (d, 2H, J = 8.9 Hz, ArH), 7.13-7.17 (m, 5H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 102.2, 111.3, 114.4, 123.5, 126.6, 127.5, 128.2, 128.4 (CH), 132.6|, 133.0, 139.0, 142.7, 157.7 (C). IR (KBr): ν = 3078, 3012, 3101, 2961, 2927, 2833, 1609 (w), 1596 (m), 1511 (s), 1462, 1439, 1417, 1398 (w), 1353, 1293 (m), 1245 (s), 1166 (m), 1101, 1087, 1075, 1049 (w), 1021 (s), 957, 931 (w), 915 (m), 832 (s), 800, 780 (w), 755, 737 (s), 706, 693 (m), 667, 657, 645 (w), 626, 582, 541 (m), cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 305 (M$^+$, 100), 290 (19), 260 (09). HRMS (EI, 70 eV): calcd for $C_{19}H_{15}NOS$ [M]$^+$: 305.08689; found: 305.08755.

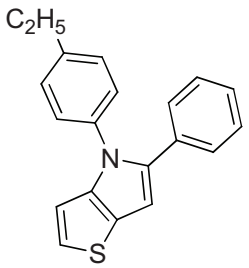
5-Phenyl-4-p-tolyl-4H-thieno[3,2-b]pyrrole (25b):



Starting with (**24a**) (100mg, 0.38mmol), $Pd(OAc)_2$ (8.5 mg, 10 mol%), P(t-Bu)$_3$.HBF_4 (22 mg, 20 mol%), 4-methylaniline **(19c)** (48 mg, 0.46 mmol), KO-t-Bu (85 mg, 0.76 mmol), toluene (5 mL), CuI (18 mg, 25mol%), **25b** was isolated as a dark brown solid (70 mg, 60%); mp 136-138 C^o. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 3H, CH_3), 6.61 (brs, 1H, ArH), 6.82 (dd, 1H, J = 0.5-5.3 Hz, ArH), 7.01 (d, 1H, J = 5.2 Hz, ArH), 7.03-7.08 (m, 4H, ArH), 7.11-7.17(m, 5H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$):

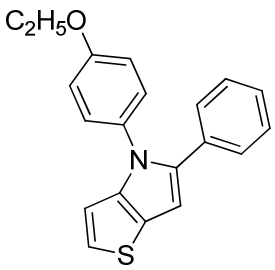
δ = 21.1 (CH_3), 102.5, 111.5, 123.5, 126.1, 126.6, 128.1, 128.4, 129.8 (CH), 133.0, 136.5, 137.0, 138.9, 142.5 (C). IR (KBr): ν = 3078, 3029, 3101, 2918, 2850 (w), 1598 (m), 1514 (s), 1499, 1467, 1442, 1417, 1395, 1380, 1370 (w), 1346 (m), 1277, 1262, 1210 (w), 1170 (m), 1104, (w), 1086, 1073 (m), 1027, 1020, 999, 956 (w), 915 (m), 855, 839 (w), 826 (s), 798, 786, 775 (w), 759, 736, 696 (s), 661, 646, 625, 580 (m), 552 (w), 532 (m) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 290 ($[M+H]^+$ 30), 289 (M^+, 100), 288 (10), 273 (07). HRMS (ESI^+): calcd for $C_{19}H_{16}NS$ $[M+H]^+$: 290.0998; found: 290.0997.

4-(4-Ethylphenyl)-5-phenyl-4H-thieno[3,2-b]pyrrole (25c):



Starting with (**24a**) (100 mg, 0.38 mmol), $Pd(OAc)_2$ (8.5 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (22 mg, 20 mol%), 4-ethylaniline **(19d)** (55 mg, 0.46 mmol), KO-*t*-Bu (85 mg, 0.76 mmol), toluene (5 mL), CuI (18 mg, 25 mol%), **25c** was isolated as a white solid (70 mg, 60%); mp 101-103 C^o. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, 3H, J = 7.5 Hz, CH_3), 2.65 (q, 2H, J = 7.4 Hz, CH_2), 6.61 (s, 1H, ArH), 6.84 (dd, 1H, J = 0.6-5.3 Hz, ArH), 7.01 (d, 1H, J = 5.2 Hz, ArH), 7.06-7.11 (m, 4H, ArH), 7.12-7.16 (m, 5H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.3 (CH_3), 28.4 (CH_2), 102.5, 111.5, 123.5 (CH), 123.7 (C), 126.1, 126.6, 128.1, 128.4, 128.5 (CH), 133.0, 137.1, 138.9, 142.5, 142.8 (C). IR (KBr): ν = 3096, 3078, 2962, 2919, 2851 (w), 1595 (m), 1579, 1568 (w), 1514 (s), 1481 (w), 1466 (m), 1455, 1417 (w), 1397 (m), 1371 (w), 1348 (s), 1170 (m), 1108 (w), 1087, 1076 (m), 1044, 1028, 1019, 999, 970, 956, 942 (w), 913 (m), 934 (s), 780 (m), 755 (s), 742, 705 (m), 695 (s), 667, 644, 626, 582, 540 (m) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 303 (M^+, 100), 288 (14), 274 (08). HRMS (EI, 70 eV): calcd for $C_{20}H_{17}NS$ $[M]^+$: 303.10762; found: 303.10847.

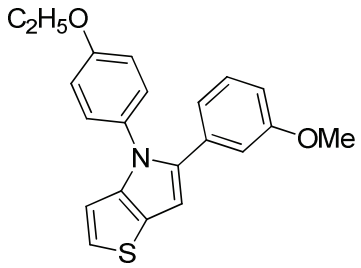
4-(4-Ethoxyphenyl)-5-phenyl-4H-thieno[3,2-b]pyrrole (25d):



Starting with (**24a**) (100 mg, 0.38 mmol), $Pd(OAc)_2$ (8.5 mg, 10 mol%), P(*t*-Bu)$_3$·HBF_4 (22 mg, 20 mol%), 4-ethoxyaniline (**19e**) (60 mg, 0.46 mmol), KO-*t*-Bu (85 mg, 0.76 mmol), toluene (5 mL), and CuI (18 mg, 25 mol%), **25d** was isolated as a dark brownish solid (79 mg, 65%); mp 104-105 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (t, 3H, J = 7.0 Hz, CH_3), 3.96 (q, 2H, J = 6.9 Hz, OCH_2), 6.60 (s, 1H, ArH), 6.77-6.81 (m, 3H, ArCH), 6.79 (d, J = 5.3 Hz, 1H, ArH), 7.08 (d, J = 8.8 Hz, 2H, ArH), 7.11-7.17 (m, 5H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.8 (CH_3), 63.7 (OCH_2), 102.2, 111.4, 114.9, 123.4, 126.6, 127.5, 128.2, 128.4 (CH), 132.4, 133.0, 139.0, 142.7, 157.7 (C). IR (KBr): ν = 3113,

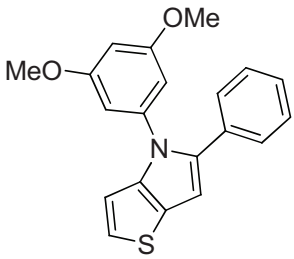
2981, 2921, 1597 (w), 1510 (s), 1475, 1436, 1388, 1357, 1258 (m), 1239 (s), 1170, 1110, 1090, 1047, 917, 829 (s), 808, 781 (m), 759, 742, 705, 696, 660, 643 (s), 622, 583, 552 (m) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 319 (M^+, 100), 290 (20), 262 (13), 260 (09). HRMS (EI, 70 eV): calcd for $C_{20}H_{17}NOS$ $[M]^+$: 319.10254; found: 319.10283.

4-(4-Ethoxyphenyl)-5-(3-methoxyphenyl)-4H-thieno[3,2-b]pyrrole (25e):



Starting with (**24b**) (100 mg, 0.34 mmol), $Pd(OAc)_2$ (7.5 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (20 mg, 20 mol%), 4-ethoxyaniline **(19e)** (56 mg, 0.4 mmol), KO-*t*-Bu (85 mg, 0.76 mmol), toluene (5 mL), CuI (16 mg, 25 mol%), **25e** was isolated as a dark brown solid (89 mg, 75%); mp 56-58 C^o. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (t, 3H, *J* = 6.9 Hz, CH_3), 3.58 (s, 3H, OCH3), 3.69 (q, 2H, *J* = 7.0 Hz, OCH_2), 6.60 (s, 1H, ArH), 6.64-6.69 (m, 2H, ArH), 6.73 (td, 1H, *J* = 1.1, 7.7 Hz, ArH), 6.77-6.82 (m, 3H, ArH), 7.00 (d, 1H, *J* = 5.3 Hz, ArH), 7.08-7.1 (m, 3H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 32.5 (CH_3), 55.1 (OCH_3), 63.7 (CH_2), 102.3, 111.3, 112.6, 113.6, 114.9, 120.9 (CH), 123.4 (C), 123.6, 127.5, 129.1 (CH), 132.4, 134.2, 138.8, 142.8, 157.7, 159.2 (C). IR (KBr): ν = 3106, 3082, 3046, 2991, 2867, 2852, 2833 (w), 1598 (s), 1579 (w), 1510 (s), 1476, 1441 (w), 1391 (m), 1368 (w), 1349, 1283 (m), 1243, 1227 (s), 1166, 1158 (m), 1114, 1091 (w), 1044 (s), 993, 973, 922, 871, 857 (w), 834 (m), 807, 774, 760 (w), 738, 710 (m), 694, 666, 653, 629, 596, 567, 537 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 350 ($[M+H]^+$ 25), 349 ($[M]^+$, 100), 320 (14), 276 (05), 248 (05). HRMS (ESI^+): calcd for $C_{21}H_{20}NO_2S$ $[M+H]^+$: 350.1209; found: 350.1212.

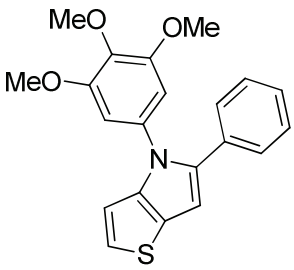
4-(3,5-Dimethoxyphenyl)-5-phenyl-4H-thieno[3,2-b]pyrrole (25f):



Starting with (**24a**) (100 mg, 0.38 mmol), $Pd(OAc)_2$ (8.5 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (22 mg, 20 mol%), 3,5-dimethoxyaniline **(19g)** (70 mg, 0.46 mmol), KO-*t*-Bu (85 mg, 0.76 mmol), toluene (5 mL), CuI (18 mg, 25 mol%), **25f** was isolated as a dark brown solid (80 mg, 63%); mp 58-60 C^o. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 6H, $2OCH_3$), 6.02 (t, 1H, *J* = 2.2 Hz, ArH), 6.11 (s, 1H, ArH), 6.13 (d, 2H, *J* = 2.1 Hz ArH), 7.02 (d, 1H, *J* = 5.6 Hz, ArH), 7.10 (d, 1H, *J* = 5.5 Hz, ArH), 7.24-7.28(m, 3H, ArH), 7.39-7.42(m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.4 ($2OCH_3$), 81.0 (C), 93.4, 95.8 (CH), 97.8, 102.7 (C), 104.6, 120.0, (CH), 123.1(C), 126.3, 128.3, 128.4, 131.3 (CH), 144.9, 145.4, 161.7 (C). IR (KBr): ν = 3354, 3079, 3055, 2999,

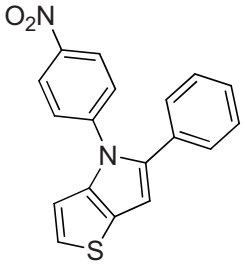
2929, 2837 (w), 1595, 1555 (s), 1496, 1488, 1477, 1453, 1441 (w), 1406 (s), 1360, 1341, 1301, 1284 (w), 1260, 1232 (m), 1202, 1194, 1149 (s), 1114 (w), 1059 (s), 1026, 989, 968, 925, 910 (w), 817, 753, 723, 687 (s), 640 (m), 605, 587, 568, 533 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 335 (M^+, 100), 334 (42), 320 (08), 304 (13), 276 (07), 260 (14). HRMS (EI, 70 eV): calcd for $C_{20}H_{17}NO_2S$ $[M]^+$: 335.09745; found: 335.09658.

5-Phenyl-4-(3,4,5-trimethoxyphenyl)-4H-thieno[3,2-b]pyrrole (25g):



Starting with (**24a**) (100 mg, 0.38 mmol), $Pd(OAc)_2$ (8.5 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (22 mg, 20 mol%), 3,4,5-trimethoxyaniline **(19m)** (83 mg, 0.46 mmol), KO-*t*-Bu (85 mg, 0.76 mmol), toluene (5 mL), CuI (18 mg, 25 mol%), **25g** was isolated as a white solid (83 mg, 60%); mp 60-62 C°. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.74 (s, 3H, OCH_3), 3.76 (s, 6H, $2OCH_3$), 6.03 (s, 1H, ArH), 6.24 (s, 2H, ArH), 6.94 (d, 1H, *J* = 5.2 Hz, ArH), 7.11 (d, 1H, *J* = 5.7 Hz, ArH), 7.25-7.28 (m, 3H, ArH), 7.39-7.42(m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 56.1, 61.1 ($3OCH_3$), 81.1 (C), 95.9 (CH), 97.8, 101.4 (C), 119.4, (CH), 123.1(C), 126.5, 128.3, 128.4, 131.3 (CH), 133.1, 139.2, 146.2, 153.9 (C). IR (KBr): ν = 3342, 3080, 2993, 2926, 2838 (w), 1593, 1552, 1503 (s), 1446, 1429, 1408, 1394, 1349, 1326, 1252 (w), 1228 (s), 1195, 1182 (w), 1122 (s), 1048 (w), 1020, 1002 (m), 914, 838, 807, 778 (w), 753, 722, 688 (m), 664, 636, 606, 550 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 366 ($[M+H]^+$ 24), 365 (M^+, 100), 350 (15), 275 (06), 207 (05). HRMS (ESI^+): calcd for $C_{21}H_{20}NO_3S$ $[M+H]^+$: 366.1158; found: 366.1153.

4-(4-Nitrophenyl)-5-phenyl-4H-thieno[3,2-b]pyrrole (25h):



Starting with (**24a**) (100 mg, 0.38 mmol), $Pd(OAc)_2$ (8.5 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (22 mg, 20 mol%), 4-nitro-aniline **(19s)** (63 mg, 0.46 mmol), KO-*t*-Bu (85 mg, 0.76 mmol), toluene (5 mL), CuI (18 mg, 25 mol%), **25h** was isolated as a brownish oil (67 mg, 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.65 (brs, 1H, ArH), 6.90 (dd, 1H, *J* = 0.6-5.4 Hz, ArH), 7.07-7.13 (m, 3H, ArH), 7.16-7.22(m, 3H, ArH), 7.27 (d, 2H, *J* = 9.1 Hz, ArH), 8.14 (d, 2H, *J* = 9.1 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 105.1, 111.1, 124.8, 124.9 (CH), 125.4 (C), 126.0, 127.5, 128.7 (CH), 132.2, 138.8, 141.6, 145.0, 145.5 (C). IR (KBr): ν = 3108, 3079, 3026, 2927, 2851, 2448, 2360, 2331, 2251 (w), 1592, 1514, 1497 (s), 1468, 1442, 1417 (w), 1391 (m), 1330 (s), 1244 (w), 1168, 1108, 1093 (m), 1073, 1045, 1027, 1011 (w), 954 (m), 906, 853, 835 (s), 797, 786 (w), 756 (s), 744, 729 (w),

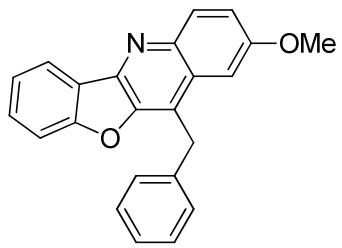
705, 660 (s), 619, 585 (m), 574, 530 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 320 (M^+, 100), 290 (23), 274 (27), 273 (18), 207 (29). HRMS (EI, 70 eV): calcd for $C_{18}H_{12}N_2O_2S$ $[M]^+$: 320.06140; found: 320.06158.

8.5 Domino C-N Coupling / Annulation *versus* C-N Coupling / Hydroamination of 2-Alkynyl-3-bromobenzofurans and 2-Alkynyl-3-bromofurane. Highly Efficient Synthesis of Benzofuro[3,2-*b*]quinolines and Furo[3,2-b]quinolines

8.5.1 General Procedure A for the Synthesis of benzofuroquinolines (29a-z), benzofuropyrroles (30a-d), furo[3,2-*b*]quinolines (34a-f), and furo[3,2-*b*]pyrroles (35).

In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (10 mol%), $Pd(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol%), KO-*t*-Bu (2 equiv.) in toluene (5 mL) was purged with argon and stirred at 20 °C to give a brownish clear solution. To the stirred solution was added **28a-c** (1.0 equiv.), or **33a-c** and aniline **5a-s** (1.3 equiv.). The reaction mixture was heated at 110 °C for 12 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried (Na_2SO_4), concentrated in vacuo, and the residue was purified by chromatography (flash silica gel, heptane–EtOAc) to give **29** and/or **30, 34** and/or **35**.

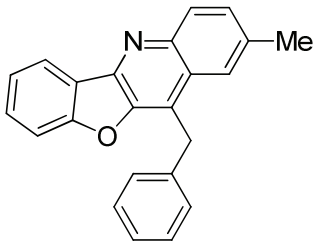
11-Benzyl-2-methoxybenzofuro[3,2-b]quinoline (29a):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 4-Methoxyaniline (**19a**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29a** was isolated as a yellow solid (100 mg, 65%); mp 184-186 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3H, OCH_3), 4.58 (s, 2H, CH_2), 7.04-7.19 (m, 6H, ArH), 7.26 (dd, 1H, J = 2.8, 9.3 Hz, ArH), 7.31-7.36 (m, 1H, ArH), 7.48-7.49 (m, 2H, ArH), 8.11 (d, 1H, J = 9.2 Hz, ArH), 8.25 (d, 1H, J = 7.5 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 31.5 (CH_2), 55.4 (OCH_3), 102.4, 112.1, 120.2, 121.9, 123.5 (CH), 123.6, 124.4 (C), 126.5 (CH), 127.7 (C), 128.5, 128.7, 130.2, 131.2 (CH), 138.5, 142.5, 144.3, 147.3, 157.5, 158.9 (C). IR (KBr): ν =3079, 3044, 3016, 2962,

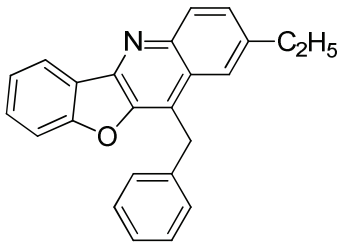
2938, 2836, 1650 (w), 1622 (s), 1600, 1574, 1556 (w), 1515 (s), 1491 (w), 1459 (s), 1431, 1409 (w), 1385, 1346 (m), 1316, 1289 (w), 1260, 1226, 1197, 1174 (s), 1152 (m), 1111, 1083, 1068 (w), 1034, 1017, 1004 (m), 977, 964, 952, 938, 891 (w), 850, 823, 781, 751 (s), 723, 711 (m), 695 (s), 649, 633, 608 (w), 597, 549 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 339 ($[M]^+$, 100), 323 (11), 307 (15), 306 (19), 294 (07). HRMS (EI, 70 eV): calcd for $C_{23}H_{17}NO_2$ $[M]^+$: 339.12538; found: 339.12487.

11-Benzyl-2-methylbenzofuro[3,2-b]quinoline (29b):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Methylaniline (**19c**) (70 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29b** was isolated as a yellow solid (97 mg, 60%); mp 195-197 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.45 (s, 3H, CH_3), 4.66 (s, 2H, CH_2), 7.06-7.22 (m, 5H, ArH), 7.34-7.39 (m, 1H, ArH), 7.44 (dd, 1H, *J* = 1.8, 8.8 Hz, ArH), 7.51-7.54 (m, 2H, ArH), 7.78 (brs, 1H, ArH), 8.12 (d, 1H, *J* = 8.8 Hz, ArH),), 8.30 (d, 1H, *J* = 7.7 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.1 (CH_3), 31.1 (CH_2), 112.2, 122.2, 122.9, 123.5 (CH), 125.1 (C), 126.4 (CH), 126.6 (C), 128.4, 128.6, 129.5, 130.0, 130.5 (CH), 136.0, 138.6, 145.0, 145.7, 147.0, 159.2 (C). IR (KBr): ν = 3078, 3048, 3021, 2918, 2851, 1647, 1624 (w), 1602 (m), 1573 (w), 1510, 1492, 1460, 1452 (m), 1432, 1414 (w), 1377, 1343 (s), 1315, 1288, 1260, 1238 (w), 1191, 1184 (s), 1150, 1140, 1106, 1079 (m), 1066, 1028, 1013, 985, 963, 946, 907, 892 (w), 857 (m), 819 (s), 784, 762 (m), 751, 697 (s), 645, 630, 597, 579 (m), 563, 553, 530 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 323 ($[M]^+$, 100), 322 (22), 308 (13), 307 (13), 246 (13). HRMS (EI, 70 eV): calcd for $C_{23}H_{17}NO$ $[M]^+$: 323.13047; found: 323.13001.

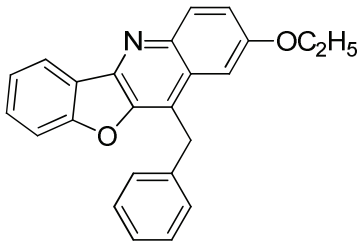
11-Benzyl-2-ethylbenzofuro[3,2-b]quinoline (29c):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Ethylaniline (**19d**) (78 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29c** was isolated as a orange solid (100 mg, 60%); mp 148-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, 3H, *J* = 7.7 Hz, CH_3), 2.75 (q, 2H, *J* = 7.7 Hz, CH_2), 4.69 (s, 2H, CH_2), 7.08-7.12 (m, 1H, ArH), 7.14-7.19 (m, 3H, ArH), 7.21-7.24 (m, 2H, ArH), 7.35-7.41 (m, 1H, ArH), 7.49 (dd, 1H, *J* = 1.8, 8.6 Hz, ArH), 7.54-7.56 (m, 2H, ArH), 7.82 (brs, 1H, ArH), 8.16 (d, 1H, *J* = 8.8 Hz, ArH),

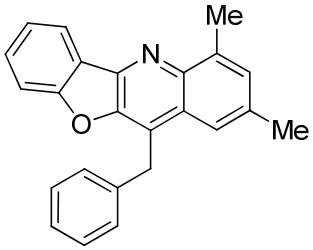
8.30 (d, 1H, J = 7.7 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.3 (CH_3), 28.2, 30.2 ($2CH_2$), 111.2, 120.6, 121.2, 122.5, 125.4 (CH), 125.6, 126.3 (C), 127.4, 127.6, 127.9, 128.5, 129.5 (CH), 137.6, 141.1, 144.2, 144.8, 145.9, 158.2 (C). IR (KBr): ν = 3057, 3024, 2958, 2924, 2867 (w), 1643, 1598, 1572, 1509, 1492 (m), 1449 (s), 1414 (w), 1374, 1341 (m), 1313, 1259, 1200 (w), 1183 (s), 1134 (m), 1103 (w), 1074 (m), 1025, 1010, 964, 941, 898 (w), 879, 856, 832 (m), 804, 790, 769 (w), 745, 698 (s), 672, 650, 632, 613, 593 (w), 554 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 337 ([M]$^+$, 100), 322 (39), 308 (14), 307 (22), 306 (15), 278 (05). HRMS (EI, 70 eV): calcd for $C_{24}H_{19}NO$ [M]$^+$: 337.14612; found: 337.14584.

11-Benzyl-2-ethoxybenzofuro[3,2-b]quinoline (29d):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(t-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Ethoxyaniline (**19e**) (89 mg, 0.65 mmol), toluene (5 mL), KO-t-Bu (112 mg, 1.0 mmol), **29d** was isolated as a orange solid (120 mg, 68%); mp 142-144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, 3H, J = 7.1 Hz, CH_3), 3.93 (q, 2H, J = 7.0 Hz, OCH_2), 4.59 (s, 2H, CH_2), 7.07-7.20 (m, 6H, ArH), 7.23 (dd, 1H, J = 2.6, 9.2 Hz, ArH), 7.32-7.39 (m, 1H, ArH), 7.49-7.50 (m, 2H, ArH), 8.11 (d, 1H, J = 9.2 Hz, ArH), 8.26 (d, 1H, J = 7.8 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.7 (CH_3), 31.5 (CH_2), 63.6 (OCH_2), 103.1, 112.1, 120.5, 121.9, 123.5 (CH), 123.6, 124.3 (C), 126.5 (CH) 127.8 (C), 128.5, 128.7, 130.1, 131.2 (CH), 138.6, 142.4, 144.2, 147.3, 156.9, 158.9 (C). IR (KBr): ν = 3058, 3024, 2978, 2925, 2878, 1650 (w), 1620 (m), 1601, 1573 (w), 1509 (s), 1494 (w), 1452, 1389, 1344 (s), 1315, 1287, 1272, 1258 (w), 1224, 1195 (s), 1181, 1142, 1129, 1114, 1101, 1069 (w), 1045 (m), 1028, 1019 (w), 944 (m), 910, 889, 852 (w), 810 (s), 778 (m), 746, 696 (s), 650, 632, 621, 596, 572 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 353 ([M]$^+$, 100), 325 (28), 324 (28), 307 (17), 306 (22), 294 (10). HRMS (EI, 70 eV): calcd for $C_{24}H_{19}NO_2$ [M]$^+$: 353.14103; found: 353.14043.

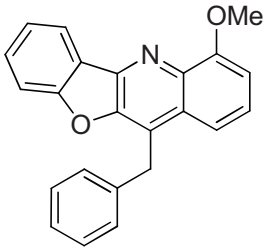
11-Benzyl-2,4-dimethylbenzofuro[3,2-b]quinoline (29e):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(t-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 2,4-Dimethylaniline (**19f**) (78 mg, 0.65 mmol), toluene (5 mL), KO-t-Bu (112 mg, 1.0 mmol), **29e** was isolated as a yellow solid (110 mg, 65%); mp 132-134 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40, 2.85 (s, 3H, $2CH_3$), 4.63 (s, 2H, CH_2), 7.07-7.12 (m, 1H, ArH), 7.13-7.15 (m, 1H, ArH), 7.16-7.19 (m, 3H, ArH),

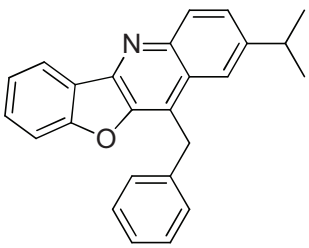
7.29 (brs., 1H, ArH), 7.31-7.38 (m, 1H, ArH), 7.49-7.51 (m, 2H, ArH), 7.62 (brs., 1H, ArH), 8.28 (d, 1H, J = 7.6 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.7, 22.1 (2CH_3), 31.2 (CH_2), 112.1, 120.9, 122.2, 123.3 (CH), 124.1, 124.7 (C), 126.3 (CH), 126.7 (C), 128.4, 128.6, 130.1, 130.2 (CH), 135.5, 137.5, 138.9, 144.2, 144.5, 146.9, 159.1 (C). IR (KBr): ν = 3056, 3031, 2962, 2921, 2853, 2730 (w), 1650, 1621, 1602 (m), 1591, 1573 (w), 1505, 1494 (m), 1481, 1463 (w), 1448 (m), 1434, 1425, 1399, 1376 (w), 1366 (s), 1339, 1316, 1279 (m), 1265, 1229, 1221 (w), 1188 (s), 1119, 1094, 1065, 1028 (m), 1008, 987, 939, 928 (w), 886 (m), 841 (s), 804, 781, 766 (m), 753, 730, 698 (s), 638, 621, 578, 568 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 337 ([M]$^+$, 100), 336 (10), 322 (09), 321 (07), 307 (08), 306 (06), 260 (05). HRMS (EI, 70 eV): calcd for $C_{24}H_{19}NO$ [M]$^+$: 337.14612; found: 337.14558.

11-Benzyl-4-methoxybenzofuro[3,2-b]quinoline (29f):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(t-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 2-Methoxyaniline (**19i**) (80 mg, 0.65 mmol), toluene (5 mL), KO-t-Bu (112 mg, 1.0 mmol), **29f** was isolated as a brown solid (113 mg, 67%); mp 160-162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.09 (s, 3H, OCH_3), 4.70 (s, 2H, CH_2), 6.98 (d, 1H, J = 7.8 Hz, ArH), 7.09-7.22 (m, 5H, ArH), 7.35-7.42 (m, 2H, ArH), 7.52-7.56 (m, 2H, ArH), 7.63 (dd, 1H, J = 1.0, 8.6 Hz, ArH), 8.45 (d, 1H, J = 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 31.6 (CH_2), 56.2 (OCH_3), 105.9, 112.1, 116.1, 123.1, 123.4 (CH), 125.9 (C), 126.3, 126.5 (CH), 127.9 (C), 128.4, 128.7, 130.7 (CH), 138.5, 142.5, 145.4, 147.3, 155.8, 159.4 (C). IR (KBr): ν = 3052, 3020, 2922, 2850, 1711 (w), 1650, (m), 1604, 1514 (s), 1487 (w), 1471, 1452, 1400, 1372, 1347 (m), 1317, 1282 (w), 1262, 1220, 1194, 1182 (s), 1137, 1099, 1083, 1060, 1027 (w), 1013, 1006 (m), 937, 858, 840, 824, 797 (w), 737, 695 (s), 677, 629, 605, 594, 561 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 339 ([M]$^+$, 100), 338 (94), 311 (15), 310 (59), 309 (18), 307 (13), 232 (06). HRMS (EI, 70 eV): calcd for $C_{23}H_{17}NO_2$ [M]$^+$: 339.12538; found: 339.12462.

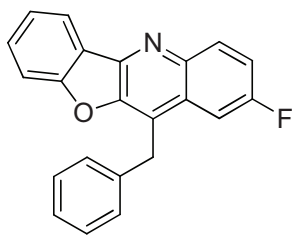
11-Benzyl-2-isopropylbenzofuro[3,2-b]quinoline (29g):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(t-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Isopropylaniline (**19j**) (87 mg, 0.65 mmol), toluene (5 mL), KO-t-Bu (112 mg, 1.0 mmol), **29g** was isolated as a yellow solid (107 mg, 61%); mp 121-123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (d, 6H, J = 6.9 Hz, 2CH_3),

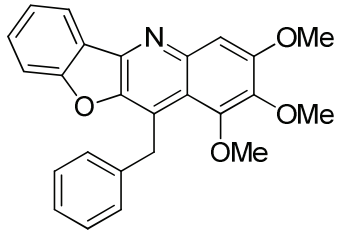
2.96- 3.05 (m, 1H, CH), 4.68 (s, 2H, CH_2), 7.10 (d, 1H, J = 7.1 Hz, ArH), 7.13-7.18 (m, 2H, ArH), 7.22-7.24 (m, 2H, ArH), 7.34-7.39(m, 1H, ArH), 7.50-7.54 (m, 3H, ArH), 7.84 (d, 1H, J = 1.9 Hz, ArH), 8.16 (d, 1H, J = 8.6 Hz, ArH), 8.31 (d, 1H, J = 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.9 ($2CH_3$), 31.3 (CH_2), 34.3 (CH), 112.2, 120.4, 122.1, 123.5 (CH), 123.6, 125.4 (C), 126.4 (CH), 126.5 (C), 127.5, 128.5, 128.6, 129.8, 130.5 (CH), 138.8, 145.4, 145.9, 146.5, 159.2 (C). IR (KBr): ν = 3083, 3058, 3022, 2954, 2922, 2864 (w), 1644, 1602 (m), 1572, 1507, 1493 (w), 1451 (s), 1414 (w), 1377 (s), 1332, 1302, 1285, 1258 (w), 1193 (s), 1168 (w), 1139 (s), 1101 (w), 1078 (m), 1067, 1044, 1029 (w), 1019 (m), 939, 928, 896 (w), 875, 858 (m), 839 (s), 803, 762 (w), 749, 737 (s), 720, 712 (w), 697 (s), 650, 621, 595, 554 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 351 ([M]$^+$, 88), 337 (25), 336 (100), 307 (08), 258 (20). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO$ [M]$^+$: 351.16177; found: 351.16168.

11-Benzyl-2-fluorobenzofuro[3,2-b]quinoline (29h):



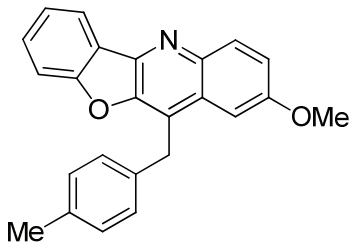
Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(t-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Fluoroaniline (**19k**) (72 mg, 0.65 mmol), toluene (5 mL), KO-t-Bu (112 mg, 1.0 mmol), **29h** was isolated as a yellow solid (98 mg, 60%); mp 122-124 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.60 (s, 2H, CH_2), 7.11-7.18 (m, 5H, ArH), 7.33-7.41 (m, 2H, ArH), 7.51-7.56 (m, 2H, ArH), 7.60 (dd, 1H, J = 2.9-9.8 Hz ArH), 8.17-8.23 (m, 1H, ArH), 8.31 (d, 1H, J = 7.8 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -112.39. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ =31.4 (CH_2), 107.6 (d, $J_{F,C}$ = 25.1 Hz, CH), 112.3 (CH), 117.9 (d, $J_{F,C}$ = 25.8 Hz, CH), 122.2 (CH), 123.2 (C), 123.7 (CH), 125.2 (d, $J_{F,C}$ = 6.1 Hz, C), 126.7 (CH), 127.5 (d, $J_{F,C}$ = 9.7 Hz, C), 128.4, 128.8, 130.9 (CH), 132.2 (d, $J_{F,C}$ = 12.5 Hz, CH), 138.0, 143.5, 146.3, 147.2, 159.3 (C), 160.7 (d, $J_{F,C}$ = 245.3 Hz, CF). IR (KBr): ν = 3053, 3027, 2921, 2852 (w), 1650, 1620, 1602 (m), 1511, 1455, 1410, 1376, 1341 (s), 1297, 1278, 1248, 1235 (w), 1185 (s), 1161, 1140 (w), 1129, 1097 (m), 1076, 1030, 1018, 1006, 975 (w), 928 (s), 898 (m), 860, 852, 832, 794 (m), 742 (s), 710 (m), 695 (s), 646, 628 (w), 595 (m), 564, 556, 528 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 327 ([M]$^+$, 100), 326 (36), 325 (11), 324 (05), 312 (05), 306 (07), 250 (16). HRMS (EI, 70 eV): calcd for $C_{22}H_{14}FNO$ [M]$^+$: 327.10539; found: 327.10497.

11-Benzyl-1,2,3-trimethoxybenzofuro[3,2-b]quinoline (29i):



Starting with (**28a**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 3,4,5-Trimethoxyaniline (**19m**) (120 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29i** was isolated as a yellow solid (140 mg, 70%); mp 145-147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.56, 3.86, 3.97 (s, 3H, 3OCH_3), 4.96 (s, 2H, CH_2), 7.03-7.14 (m, 5H, ArH), 7.32-7.37 (m, 1H, ArH), 7.41 (brs., 1H, ArH), 7.47-7.54 (m, 2H, ArH), 8.30 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 32.1 (CH_2), 55.0, 60.0, 60.3 (3OCH_3), 103.7, 111.2 (CH), 116.4 (C), 120.9 (CH), 122.2 (C), 122.3, 124.8 (CH), 124.9 (C), 127.0, 127.3 (CH), 128.0 (C), 129.3 (CH), 139.2, 140.8, 144.1, 146.4, 148.8, 153.1, 157.9 (C). IR (KBr): ν = 3083, 3057, 3021, 2969, 2933, 2853, 2827 (w), 1638, 1616 (m), 1571, 1493, 1460 (s), 1432, 1421 (w), 1401, 1367, 1326 (s), 1278 (m), 1250 (s), 1234 (w), 1219, 1193, 1148 (m), 1119 (s), 1099 (w), 1065, 1056 (m), 1027, 1007 (w), 986 (s), 938, 922, 907, 859 (w), 829, 819 (s), 784, 767 (w), 752, 733 (s), 714, 696 (m), 680, 651, 620 (w), 594, 573 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 399 ($[M]^+$, 100), 384 (08), 352 (43), 337 (08), 324 (07), 309 (15). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO_4$ $[M]^+$: 399.14651; found: 399.14609.

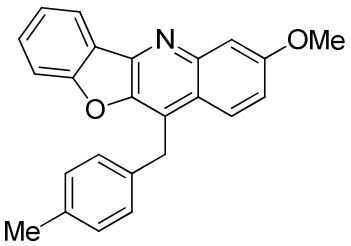
2-Methoxy-11-(4-methylbenzyl)benzofuro[3,2-b]quinoline (29j):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Methoxyaniline (**19a**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29j** was isolated as a brown solid (123 mg, 70%); mp 170-172 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 4.61 (s, 2H, CH_2), 6.97 (d, 2H, *J* = 8.0 Hz, ArH), 7.10 (d, 2H, *J* = 8.0 Hz, ArH), 7.25-7.29 (m, 2H, ArH), 7.35-7.40 (m, 1H, ArH), 7.53 (d, 2H, *J* = 3.8 Hz, ArH), 8.12 (d, 1H, *J* = 8.7 Hz, ArH), 8.30 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.0 (CH_3), 31.1 (CH_2), 55.5 (OCH_3), 102.5, 112.2, 120.3, 122.0, 123.5 (CH), 125.0, 125.8, 127.8 (C), 128.4, 129.4, 130.2, 131.1 (CH), 135.4, 136.1, 142.4, 144.3, 147.3, 157.5, 159.0 (C). IR (KBr): ν = 3080, 3060, 3023, 3000, 2956, 2928, 2912, 2833, (w), 1621, (m), 1601, 1564, 1549 (w), 1512 (s), 1492, 1469 (w), 1446 (s), 1390, 1368 (w), 1333, 1266 1251 (m), 1237, 1214, 1174 (s), 1158, 1145, 1120, 1106 (w), 1075, 1053, 1029 (m), 1018, 981 (w), 967 (s), 937, 928, 910 (w), 854, 827 (s), 814, 780 (w), 757, 749, 730 (s), 708 (w), 696 (s), 672, 648 (m), 620 (w), 601, 585, 556, 549 (m) cm^{-1}. GC-

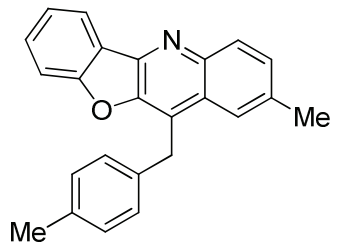
MS (EI, 70 eV): *m/z* (%) = 354 ([M+H]$^+$ 26), 353 ([M]$^+$, 100), 323 (13), 322 (09), 320 (09). HRMS (ESI$^+$): calcd for $C_{24}H_{20}NO_2$ [M+H]$^+$: 354.1489; found: 354.1491.

3-Methoxy-11-(4-methylbenzyl)benzofuro[3,2-b]quinoline (29k):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 3-Methoxyaniline (**19b**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29k** was isolated as a yellow solid (113 mg, 64%); mp 169-171 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.17 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.94 (s, 2H, CH_2), 6.80 (d, 1H, *J* = 7.9 Hz, ArH), 6.92 (d, 2H, *J* = 8.1 Hz, ArH), 7.00 (d, 2H, *J* = 8.1 Hz, ArH), 7.33-7.39 (m, 1H, ArH), 7.46 (d, 1H, *J* = 8.3 Hz, ArH), 7.51-7.55 (m, 2H, ArH), 7.82 (dd, 1H, *J* = 0.9, 8.3 Hz, ArH), 8.30 (d, 1H, *J* = 7.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.9 (CH_3), 33.6 (CH_2), 55.4 (OCH_3), 105.1, 112.3 (CH), 119.2 (C), 122.3, 122.6, 123.4, 127.3 (CH), 127.4 (C), 128.0, 128.9, 130.6 (CH), 135.1, 137.5, 146.1, 147.9, 148.6, 157.6, 159.3 (C). IR (KBr): ν = 3044, 3026, 2997, 2949, 2921, 2851, 2831 (w), 1641 (m), 1615, 1604, 1595 (w), 1577, 1512 (s), 1487 (w), 1461, 1373, 1333 (s), 1301, 1283 (w), 1258, 1200 (s), 1159, 1143, 1125 (m), 1104, 1084 (w), 1067 (s), 1013 (w), 992 (m), 976, 961, 930, 907, 868, 843 (w), 824, 810, 790, 774 (m), 734, 708 (s), 647, 602, 564, 541 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 354 ([M+H]$^+$ 27), 353 ([M]$^+$, 100), 338 (08), 306 (12), 246 (15). HRMS (ESI$^+$): calcd for $C_{24}H_{20}NO_2$ [M+H]$^+$: 354.14886; found: 354.14942.

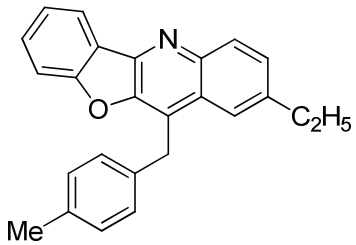
2-Methyl-11-(4-methylbenzyl)benzofuro[3,2-b]quinoline (29l):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Methylaniline (**19c**) (70 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29l** was isolated as a yellow solid (112 mg, 66%); mp 195-197 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 4.63 (s, 2H, CH_2), 6.97 (d, 2H, *J* = 8.0 Hz, ArH), 7.10 (d, 2H, *J* = 8.0 Hz, ArH), 7.34-7.40 (m, 1H, ArH), 7.45 (dd, 1H, *J* = 1.7-8.6 Hz), 7.51-7.54 (m, 2H, ArH), 7.81 (brs, 1H, ArH), 8.12 (d, 1H, *J* = 8.6 Hz, ArH), 8.30 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.0, 22.1 (2CH_3), 30.7 (CH_2), 112.2, 122.1, 122.9, 123.5 (CH), 125.4, 126.6 (C), 128.3, 129.3, 129.5, 130.0, 130.5 (CH), 135.5, 135.9, 136.0 145.0, 145.7, 147.0, 159.2 (C). IR (KBr): ν = 3056, 3023, 2946, 2914, 2857, 2731, 1621 (w), 1594 (m), 1575,

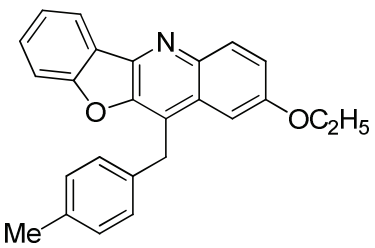
1565, 1551 (w), 1502, 1491 (m), 1469 (w), 1443 (m), 1426, 1402, 1376, 1364, (w), 1337 (m), 1286, 1262, 1231, 1194 (w), 1182 (s), 1179, 1169, 1146, 1123, (w), 1109, 1068, 1043 (m), 1024, 1015, 1001, 958, 927, 903, 872, 858, (w), 820 (s), 783, 763, (m), 748, 732, 702, (s), 691, 672, (w), 644 (m), 620 (w), 589, 571, 554, cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 338 ($[M+H]^+$ 27), 337 ($[M]^+$, 100), 336 (20), 322 (17), 307 (11), 246 (10). HRMS (ESI^+): calcd for $C_{24}H_{20}NO$ $[M+H]^+$: 338.1539; found: 338.1544.

2-Ethyl-11-(4-methylbenzyl)benzofuro[3,2-b]quinoline (29m):



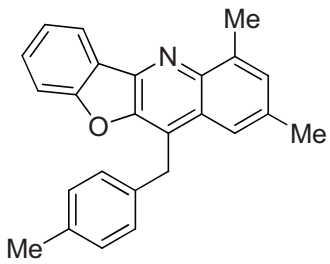
Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Ethylaniline (**19d**) (78 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29m** was isolated as a brown solid (105 mg, 60%); mp 153-155 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, 3H, *J* = 7.6 Hz, CH_3), 2.17 (s, 3H, CH_3), 2.76 (q, 2H, *J* = 7.6 Hz, CH_2), 4.63 (s, 2H, CH_2), 6.96 (d, 2H, *J* = 7.8 Hz, ArH), 7.10 (d, 2H, *J* = 8.1 Hz, ArH), 7.33-7.39 (m, 1H, ArH), 7.48 (dd, 1H, *J* = 1.9, 8.8 Hz, ArH), 7.52-7.54 (m, 2H, ArH), 7.82 (brs, 1H, ArH), 8.14 (d, 1H, *J* = 8.8 Hz, ArH), 8.31 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.4, 21.0 (2CH_3), 29.2, 30.8 (2CH_2), 112.2, 121.7, 122.2, 123.5 (CH), 123.5, 125.7, 126.7 (C), 128.4, 128.9, 129.3, 129.7, 130.5 (CH), 135.6, 136.0, 142.0, 145.2, 145.8, 146.9, 159.2 (C). IR (KBr): ν = 3055, 3024, 2956, 2923, 2866, 1621 (w), 1594 (m), 1575, 1564, 1555 (w), 1503, 1490 (m), 1470 (w), 1445 (s), 1403, 1366 (w), 1340, 1331 (m), 1285, 1264, 1245, 1230 (w), 1182 (s), 1170, 1148, 1128 (w), 1110 (m), 1068, 1056 (w), 1042 (m), 1025, 1015, 1001, 993, 981, 953, 937, 927, 908, 899 (w), 878 (m), 856 (w), 830 (s), 784, 760, 748 (m), 733, 725, 700 (s), 672, 646, 620, 605, 587, 556 (m), cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 351 ($[M]^+$, 100), 336 (23), 322 (13), 321 (16), 307 (13), 259 (06). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO$ $[M]^+$: 351.16177; found: 351.16165.

2-Ethoxy-11-(4-methylbenzyl)benzofuro[3,2-b]quinoline (29n):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 4-Ethoxyaniline (**19e**) (95 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29n** was isolated as a yellow solid (125 mg, 68%); mp 141-143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (t, 3H, J = 7.0 Hz, CH_3), 2.18 (s, 3H, CH_3), 3.98 (q, 2H, J = 7.1 Hz, OCH_2), 4.56 (s, 2H, CH_2), 6.96 (d, 2H, J = 8.1 Hz, ArH), 7.10 (d, 2H, J = 8.1 Hz, ArH), 7.21 (d, 1H, J = 2.5 Hz, ArH), 7.24 (dd, 1H, J = 2.7, 9.1 Hz, ArH), 7.33-7.38 (m, 1H, ArH), 7.50-7.53 (m, 2H, ArH), 8.11 (d, 1H, J = 9.1 Hz, ArH), 8.26 (dt, 1H, J = 0.9, 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.7, 21.0 ($2CH_3$), 31.0 (CH_2), 63.6 (OCH_2), 103.0, 112.1, 120.5, 121.9, 123.4 (CH), 123.6, 124.6, 127.8 (C), 128.3, 129.3, 130.1, 131.2 (CH), 135.5, 136.0, 142.4, 144.2, 147.3, 156.8, 158.9 (C). IR (KBr): ν = 3233, 3043, 3018, 2980, 2924, 2885 (w), 1620 (s), 1574, 1549 (w), 1512, 1459, 1391, 1343 (s), 1315, 1299, 1288 (w), 1263, 1245 (m), 1215, 1183, 1148, 1105, 1041 (s), 1019, 948, 931 (m), 892 (w), 855, 837 (m), 815 (s), 784 (m), 746, 730 (s), 699, 680, 666, 631 (w), 605, 577 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 368 ($[M+H]^+$ 29), 367 ($[M]^+$, 100), 339 (16), 338 (16), 323 (18), 322 (12), 294 (09). HRMS (ESI^+): calcd for $C_{25}H_{22}NO_2$ $[M+H]^+$: 368.16451; found: 368.16447.

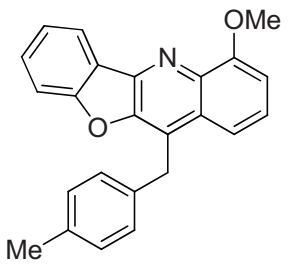
11-Benzyl-1,3-dimethylbenzofuro[3,2-b]quinoline (29o):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 2,4-Dimethylaniline (**19f**) (78 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29o** was isolated as a brown solid (107 mg, 61%); mp 198-200 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18, 2.41, 2.85 (s, 3H, $3CH_3$), 4.61 (s, 2H, CH_2), 6.95 (d, 2H, J = 8.0 Hz, ArH), 7.07 (d, 2H, J = 8.0 Hz, ArH), 7.30 (brs, 1H, ArH), 7.32-7.38 (m, 1H, ArH), 7.50-7.52 (m, 2H, ArH), 7.65 (brs, 1H, ArH), 8.30 (d, 1H, J = 7.8 Hz, ArH). ^{13}C NMR (75.5MHz, $CDCl_3$): δ = 18.7, 21.0, 22.1 ($3CH_3$), 30.8 (CH_2), 112.1, 120.9, 122.1, 123.2 (CH), 124.2, 125.0, 126.7 (C), 128.3, 129.3, 130.0, 130.1 (CH), 135.5, 135.8, 135.9, 137.5, 144.3, 144.6, 146.9, 159.2 (C). IR (KBr): ν = 2998, 2916, 2852, 2726, (w), 1644, 1604 (m), 1573 (w), 1507, 1452 (m), 1427, 1413 (w), 1365, 1340 (m), 1318, 1277, 1256, 1228, 1219 (w), 1185 (s), 1150, 1119, 1112, 1095 (w), 1059 (m), 1014, 931, 882 (w), 851, 806, 779 (m), 743 (s), 711, 662 (w), 632, 579, 561 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 352 ($[M+H]^+$ 27), 351 ($[M]^+$, 100), 336

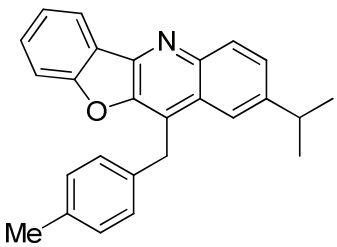
(09), 321 (09), 320 (07), 260 (05). HRMS (ESI$^+$): calcd for $C_{25}H_{22}NO$ $[M+H]^+$: 352.1696; found: 352.1696.

1-(4-Methylbenzyl)benzofuro[3,2-b]quinoline (29p):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 2-Methoxyaniline (**19i**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29p** was isolated as a brown solid (118 mg, 67%); mp 196-198 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.18 (s, 3H, CH_3), 4.08 (s, 3H, OCH_3), 4.65 (s, 2H, CH_2), 6.95-6.98 (m, 3H, ArH), 7.10 (d, 2H, *J* = 7.9 Hz, ArH), 7.34-7.42 (m, 2H, ArH), 7.51-7.55 (m, 2H, ArH), 7.64 (d, 1H, *J* = 8.7 Hz, ArH), 8.44 (d, 1H, *J* = 7.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.0 (CH_3), 31.1 (CH_2), 56.2 (OCH_3), 105.8, 112.1, 116.2, 123.0, 123.4 (CH), 123.6, 126.1 (C), 126.2 (CH), 127.9 (C), 128.3, 129.3, 130.6 (CH), 135.5, 136.0, 138.5, 145.5, 147.3, 155.8, 159.4 (C). IR (KBr): ν = 3071, 3042, 3015, 2917, 2852, 2825 (w), 1611 (m), 1594 (w), 1552, 1494, 1480, 1459, 1440 (m), 1396 (s), 1355 (w), 1337 (m), 1302, 1280 (w), 1255 (s), 1211, 1185, 1181, 1173 (w), 1153 (s), 1135, 1108, 1077 (w), 1038 (s), 1019 (m), 957, 950, 937, 921, 903, 856, 849, 842, 820 (w), 804 (s), 769, 757 (w), 741, 731 (s), 706 (w), 666 (m), 653, 640, 623 (w), 596 (m), 581, 559 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 354 ($[M+H]^+$ 23), 353 ($[M]^+$, 100), 352 (99), 325 (15), 324 (62), 323 (17), 307 (12). HRMS (ESI$^+$): calcd for $C_{24}H_{20}NO_2$ $[M+H]^+$: 354.1489; found: 354.1493.

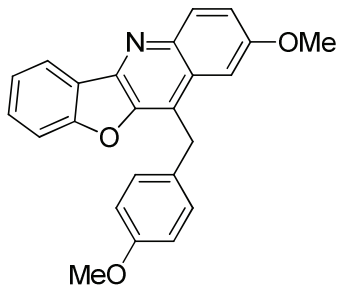
2-Isopropyl-11-(4-methylbenzyl)benzofuro[3,2-b]quinoline (29q):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-isopropylaniline (**19j**) (87 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29q** was isolated as a dark brown solid (115 mg, 63%); mp 94-96 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, 6H, *J* = 6.9 Hz, 2CH_3), 2.19 (s, 3H, CH_3), 2.98-3.08 (m, 1H, CH), 4.66 (s, 2H, CH_2), 6.98 (d, 2H, *J* = 7.8 Hz, ArH), 7.14 (d, 2H, *J* = 7.8 Hz, ArH), 7.35-7.42 (m, 1H, ArH), 7.52-7.56 (m, 3H, ArH), 7.87 (d, 1H, *J* = 1.8 Hz, ArH), 8.17 (d, 1H, *J* = 9.1 Hz, ArH), 8.33 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.0 (CH_3), 23.9 (2CH_3), 30.9 (CH_2), 34.3 (CH), 112.2, 120.4, 122.3, 123.5 (CH), 125.9, 126.6 (C), 127.6, 128.4, 129.3, 129.6, 130.5 (CH), 135.7, 136.0, 145.3, 145.8, 146.5, 146.9, 159.2 (C). IR (KBr): ν = 3047, 3018, 2953, 2921, 2853, 1645, 1603, 1593, 1571 (m), 1539 (w), 1510 (s), 1482 (w), 1456 (s), 1412 (w), 1377,

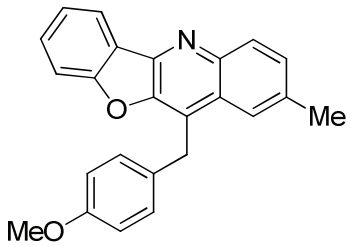
1344 (m), 1287, 1260, 1234 (w), 1182, 1141 (s), 1103, 1083, 1072, 1020 (m), 958, 936, 912, 874 (w), 859, 825 (m), 805, 790, 764 (w), 744 (s), 711, 681, 668, 644 (w), 633, 613 (m), 595, 562 (w), 539 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 366 ($[M+H]^+$ 29), 365 ($[M]^+$, 100), 351 (24), 350 (89), 322 (08), 307 (08), 258 (35). HRMS (ESI^+): calcd for $C_{26}H_{24}NO$ $[M+H]^+$: 366.1852; found: 366.1855.

2-Methoxy-11-(4-methoxybenzyl)benzofuro[3,2-b]quinoline (29r):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Methoxyaniline (**19a**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29r** was isolated as a light yellow crystals (123 mg, 67%); mp 145-147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.63 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.54 (s, 2H, CH_2), 7.11 (d, 2H, *J* = 8.6 Hz, ArH), 7.11 (d, 2H, *J* = 8.6 Hz, ArH), 7.20 (d, 1H, *J* = 2.7 Hz, ArH), 7.25 (dd, 1H, *J* = 2.7, 9.3 Hz, ArH), 7.32-7.38 (m, 1H, ArH), 7.51 (d, 2H, *J* = 3.7 Hz, ArH), 8.01 (d, 1H, *J* = 9.1 Hz, ArH), 8.27 (d, 1H, *J* = 7.4 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 30.6 (CH_2), 55.2, 55.4 (2OCH_3), 102.4, 112.1, 114.1, 120.2, 121.9, 123.5 (CH), 123.6, 124.8, 127.7 (C), 129.4, 130.1 (CH), 130.5 (C), 131.2 (CH), 142.5, 144.3, 147.2, 157.5, 158.2, 158.9 (C). IR (KBr): ν = 3068, 3020, 2998, 2959, 2920, 2925, 2834, 1641 (w), 1621, 1608 (m), 1583, 1574 (w), 1508, 1464, 1443 (s), 1419, 1375 (m), 1345 (s), 1314 (w), 1301 (m), 1246, 1223 (s), 1197 (w), 1182 (s), 1130 (m), 1113, 1099 (w), 1031 (s), 1011, 956, 943, 911 (w), 851 (m), 827 (s), 814, 798, 788, 762 (w), 748 (s), 715, 669, 634, 605, 566, 550, 528 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 369 ($[M]^+$, 100), 354 (10), 323 (08), 294 (06). HRMS (EI, 70 eV): calcd for $C_{24}H_{19}NO_3$ $[M]^+$: 369.13594; found: 369.13636.

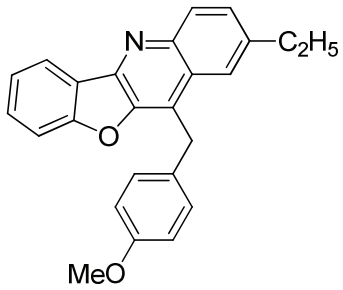
11-(4-Methoxybenzyl)-2-methylbenzofuro[3,2-b]quinoline (29s):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Methylanilin (**19c**) (70 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29s** was isolated as a brownish solid (116 mg, 66%); mp 162-164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.47 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 4.60 (s, 2H, CH_2), 6.70 (d, 2H, *J* = 8.7 Hz, ArH), 7.12 (d, 2H, *J* = 8.6 Hz, ArH), 7.35-7.39 (m, 1H, ArH), 7.45 (dd, 1H, *J* = 1.7, 8.7 Hz, ArH), 7.51-7.55 (m, 2H, ArH), 7.81 (brs, 1H, ArH), 8.13 (d, 1H, *J* = 8.4 Hz, ArH), 8.32 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C

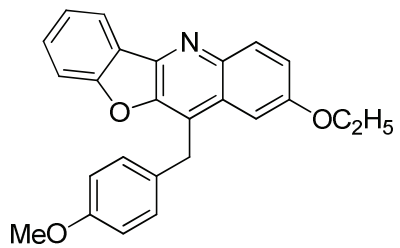
NMR (62.9 MHz, $CDCl_3$): δ = 22.1 (CH_3), 30.2 (CH_2), 55.2 (OCH_3), 112.2, 114.1, 122.2, 122.9, 123.5 (CH), 125.7, 126.6 (C), 129.4, 130.1, 130.5 (CH), 130.6 (C), 131.2 (CH), 136.0, 142.1, 145.3, 145.8, 146.9, 158.2, 159.2 (C). IR (KBr): ν = 3033, 3002, 2919, 2852, 2837 (w), 1643 (m), 1607 (s), 1581, 1548 (w), 1507 (s), 1455, 1441 (m), 1417 (w), 1374, 1342, 1301, 1279 (m), 1243 (s), 1205 (w), 1176 (s), 1137, 1110, 1070 (m), 1033 (s), 1010, 984, 968, 939, 905, 857 (w), 817 (s), 793, 762 (w), 746 (s), 712, 672, 642 (w), 630 (s), 594, 577 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 353 ($[M]^+$, 100), 338 (26), 322 (06), 307 (08), 294 (08), 246 (10). HRMS (EI, 70 eV): calcd for $C_{24}H_{19}NO_2$ $[M]^+$: 353.14103; found: 353.14085.

2-Ethyl-11-(4-methoxybenzyl)benzofuro[3,2-b]quinoline (29t):



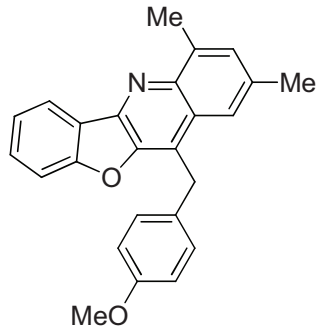
Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(tBu)_3.HBF_4$ (29 mg, 20 mol%), 4-Ethylaniline (**19d**) (78 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29t** was isolated as a yellowish white solid (132 mg, 72%); mp 135-137 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.23 (t, 3H, J = 7.6 Hz, CH_3), 2.76 (q, 2H, J = 7.6 Hz, CH_2), 3.63 (s, 3H, OCH_3), 4.60 (s, 2H, CH_2), 6.70 (d, 2H, J = 8.7 Hz, ArH), 7.13 (d, 2H, J = 8.7 Hz, ArH), 7.33-7.39 (m, 1H, ArH), 7.47 (dd, 1H, J = 1.8, 8.7 Hz, ArH), 7.51-7.54 (m, 2H, ArH), 7.82 (brs, 1H, ArH), 8.14 (d, 1H, J = 8.7 Hz, ArH), 8.30 (dt, 1H, J = 0.9, 7.6 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.4 (CH_3), 29.2, 30.3 ($2CH_2$), 55.2 (OCH_3), 112.2, 114.1, 121.7, 122.2, 123.4 (CH), 123.5, 125.7, 126.6 (C), 128.9, 129.4, 129.7, 130.5 (CH), 130.7, 142.0, 145.3, 145.8, 146.9, 158.2, 159.2 (C). IR (KBr): ν = 3065, 3030, 2998, 2958, 2926, 2868, 2831 (w), 1645, 1607 (m), 1582, 1572, 1549 (w), 1507 (s), 1461, 1439 (m), 1417 (w), 1376 (m), 1345, 1301, 1280 (w), 1245, 1175 (s), 1148, 1135, 1102, 1073 (w), 1040 (m), 1011, 956, 944, 929, 899, 879, 857, 844 (w), 829 (m), 811, 793, 763 (w), 746 (s), 670, 644, 631, 608, 562 (w), 542 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 367 ($[M]^+$, 100), 352 (15), 338 (17), 322 (06), 307 (10), 294 (08), 259 (06). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO_2$ $[M]^+$: 367.15668; found: 367.15654.

2-Ethoxy-11-(4-methoxybenzyl)benzofuro[3,2-b]quinoline (29u):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 4-ethoxyanilin (**19e**) (95 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29u** was isolated as a yellow solid (134 mg, 70%); mp 158-160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (t, 3H, J = 7.00 Hz, CH_3), 3.62 (s, 3H, CH_3), 3.94 (q, 2H, J = 6.9 Hz, OCH_2), 4.52 (s, 2H, CH_2), 6.68 (d, 2H, J = 8.8 Hz, ArH), 7.10 (d, 2H, J = 8.6 Hz, ArH), 7.20 (d, 1H, J = 2.7 Hz, ArH), 7.24 (dd, 1H, J = 2.7, 9.3 Hz, ArH), 7.31-7.38 (m, 1H, ArH), 7.50 (d, 2H, J = 4.1 Hz, ArH), 8.10 (d, 1H, J = 9.1 Hz, ArH), 8.26 (d, 1H, J = 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.7 (CH_3), 30.5 (CH_2), 55.2 (OCH_3), 63.7 (OCH_2), 103.0, 112.1, 114.1, 120.5, 121.8, 123.4 (CH), 123.6, 124.7, 127.7 (C), 129.4, 130.1 (CH), 130.6 (C), 131.2 (CH), 142.4, 144.2, 147.2, 156.8, 158.2, 158.9 (C). IR (KBr): ν = 3047, 3015, 2974, 2920, 2894, 2874 (w), 1619 (m), 1592, 1567, 1552, (w), 1502 (s), 1471, 1448 (w), 1440 (m), 1419, 1403, 1390, 1383, 1335, 1316, 1264, 1254 (w), 1228, 1220, 1218 (m), 1181, 1156, 1148 (w), 1114, 1107 (m), 1069, 1056, 1039, 1016, 988, 950, 929, 893, 861, 850, 825 (w), 812, 796, 780, 762 (m), 734 (s), 713, 696, 682, 643, 596, 585, 579, 561, 532 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 383 ($[M]^+$, 100), 354 (09), 323 (14), 206 (06). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO_3$ $[M]^+$: 383.15160; found: 383.15173.

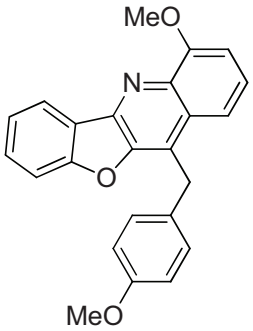
11-(4-Methoxybenzyl)-2,4-dimethylbenzofuro[3,2-b]quinoline (29v):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 2,4-Dimethylaniline (**19f**) (78 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29v** was isolated as a brown solid (138 mg, 75%); mp 198-200 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 2.85 (s, 3H, CH_3), 3.63 (s, 3H, OCH_3), 4.58 (s, 2H, CH_2), 6.68 (d, 2H, J = 8.7 Hz, ArH), 7.10 (d, 2H, J = 8.6 Hz, ArH), 7.30 (s, 1H, ArH), 7.32-7.37 (m, 1H, ArH), 7.50-7.52 (m, 2H, ArH), 7.64 (s, 1H, ArH), 8.29 (d, 1H, J = 7.6 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.7, 22.1 ($2CH_3$), 30.3 (CH_2), 55.2 (OCH_3), 112.1, 114.0, 120.9, 122.1, 123.2 (CH), 124.1. 125.2, 126.6 (C), 129.4, 130.0, 130.2 (CH), 130.9, 135.5, 137.5, 144.3, 144.6, 146.8, 158.1, 159.1 (C). IR (KBr): ν = 3044, 3023, 2997, 2958, 2916, 2851, 1721, 1704, 1682, 1672, 1657, 1622 (w), 1594, 1564 (m), 1527, 1516 (w), 1508 (s), 1493, 1469 (m), 1439 (s), 1392, 1378, 1348, 1327 (w), 1246 (s), 1235,

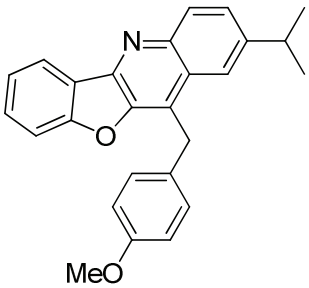
1179, 1153, 1137 (w), 1075, 1063 (m), 1017 (s), 983, 950, 941, 914, 897, 884 (w), 854, 799 (s), 775, 762 (w), 732, 723 (s), 695, 685, 669 (m), 645, 622, 597, 588, 572, 546 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 367 ($[M]^+$, 100), 352 (14), 337 (05), 308 (05). HRMS (EI, 70 eV): calcd for $C_{25}H_{21}NO_2$ $[M]^+$: 367.15668; found: 367.15613.

4-Methoxy-11-(4-methoxybenzyl)benzofuro[3,2-b]quinoline (29w):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 2-Methoxyaniline (**19i**) (80 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29w** was isolated as a brown solid (125 mg, 68%); mp 173-175 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.63 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3), 4.61 (s, 2H, CH_2), 6.69 (d, 2H, *J* = 8.3 Hz, ArH), 6.97 (d, 1H, *J* = 7.9 Hz, ArH), 7.11 (d, 2H, *J* = 8.3 Hz, ArH), 7.33-7.41 (m, 2H, ArH), 7.53 (d, 2H, *J* = 4.1 Hz, ArH), 7.63 (d, 1H, *J* = 8.7 Hz, ArH), 8.43 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 29.6 (CH_2), 54.2, 55.2 (2OCH_3), 104.8, 111.1, 113.1, 115.1, 121.9, 122.3 (CH), 122.5 (C), 125.1 (CH), 125.3, 126.8 (C), 128.4, 129.6 (CH), 137.5, 144.5, 146.2, 154.8, 157.2, 158.3 (C). IR (KBr): *v* = 3068, 3046, 2998, 2959, 2926, 2851, 2833, 1645 (w), 1607 (s), 1581 (w), 1509, 1452, 1441 (s), 1400, 1367, 1346 (m), 1331, 1317, 1303, 1278 (w), 1264, 1246 (s), 1216, 1195 (w), 1178 (s), 1152, 1138, 1111, 1098, 1080 (w), 1060, 1031, 1011, 995 (m), 966, 947, 929, 908, 857, 833 (w), 810 (m), 739 (s), 671, 631, 605, 589, 561, 539 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 369 ($[M]^+$, 100), 368 (88), 341 (13), 340 (52), 339 (15), 294 (08). HRMS (EI, 70 eV): calcd for $C_{24}H_{19}NO_3$ $[M]^+$: 369.13594; found: 369.13490.

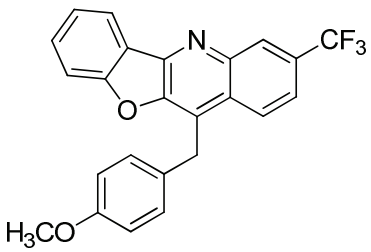
2-Isopropyl-11-(4-methoxybenzyl)benzofuro[3,2-b]quinoline (29x):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-isopropylaniline (**19j**) (88 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29x** was isolated as a dark brown solid (133 mg, 70%); mp 116-118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (d, 6H, *J* = 6.9 Hz, ArH), 2.96- 3.09 (m, 1H, CH), 3.64 (s, 3H, OCH_3), 4.62 (s, 2H, CH_2), 6.71 (d, 2H, *J* = 8.8 Hz, ArH), 7.15 (d, 2H, *J* = 8.6 Hz, ArH), 7.35-7.40 (m, 1H, ArH), 7.52-7.55 (m, 3H, ArH), 7.86 (d, 1H, *J* = 1.8 Hz, ArH), 8.16 (d, 1H, *J* = 8.8 Hz, ArH), 8.33 (d, 1H, *J* = 7.8 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.9 (2CH_3), 30 (CH_2), 34.3 (CH), 55.2 (OCH_3), 112.2, 114.0, 120.3, 122.3 (CH), 123.4 (C), 123.5 (CH), 126.2, 126.5 (C), 127.6,

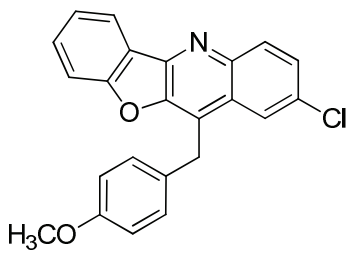
129.4, 129.5 130.5 (CH), 130.8, 145.2, 145.7, 146.5, 146.8, 158.2, 159.2 (C). IR (KBr): ν = 3067, 3034, 2985, 2954, 2928, 2868, 2832 (w), 1641, 1607 (m), 1584, 1573 (w), 1509 (s), 1483 (w), 1457, 1441 (m), 1418 (w), 1377, 1344, 1301 (m), 1245, 1182 (s), 1140 (m), 1111, 1102, 1078, 1061 (w), 1035 (s), 1010, 997, 955, 941, 919, 909, 878849 (w), 829, 822 (m), 810, 792, 771 (w), 747 (s), 718, 668 (w), 647 (m), 629, 613, 594, 563 (w), 544 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 382 ($[M+H]^+$ 28), 381 ($[M]^+$, 100), 367 (14), 366 (54), 338 (12), 307 (06), 273 (12), 258 (44). HRMS (ESI^+): calcd for $C_{26}H_{24}NO_2$ $[M+H]^+$: 382.18016; found: 382.1804.

11-(4-Methoxybenzyl)-3-(trifluoromethyl)benzofuro[3,2-b]quinoline (29y):



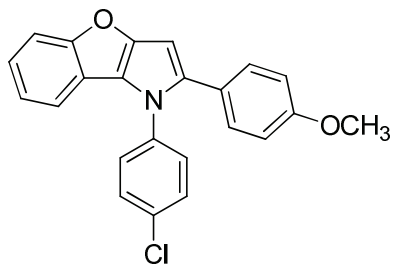
Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 3-(trifluoromethyl)aniline (**19l**) (105 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29y** was isolated as a white solid (112 mg, 55%); mp 116-118 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.66 (s, 3H, OCH_3), 4.56 (s, 2H, CH_2), 6.73 (d, 2H, J = 8.2 Hz, ArH), 7.08 (d, 2H, J = 8.3 Hz, ArH), 7.48-7.59 (m, 2H, ArH), 7.61 (dd, 1H, J = 1.8, 8.7 Hz, ArH), 7.77 (d, 1H, J = 7.9 Hz, ArH), 8.17 (d, 1H, J = 8.4 Hz, ArH), 8.54 (d, 2H, J = 8.4 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -62.48. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =36.5 (CH_2), 55.4 (OCH_3), 114.7 (CH), 121.5 (q, $J_{F,C}$ = 2.8 Hz, CH), 123.2, 124.3, 124.7, 125.5 (CH), 125.9 (C), 127.8 (q, $J_{F,C}$ = 272.2 Hz, CF_3), 128.1 (q, $J_{F,C}$ = 4.7 Hz, CH), 129.3 (C), 129.4 (CH), 129.9 (q, $J_{F,C}$ = 32.6 Hz, C-CF_3), 130.5 (CH), 134.4, 134.7, 139.7, 141.0, 146.1, 155.0, 158.6 (C). IR (KBr): ν = 3063, 3037, 3003, 2923, 2838, 1651, 1630, 1608, 1592, 1581, 1556, 1538 (w), 1510 (s), 1468 (m), 1452 (s), 1409, 1367, 1345, 1333 (m), 1304, 1281, 1243 (s), 1174, 1162, 1145 (m), 1106 (s), 1073 (w), 1061, 1032 (m), 962 (w), 950, 921, 907 (m), 864, 845 (w), 813, 765, 738, 709, 695, 660 (m), 631, 611, 580, 529 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 408 ($[M+H]^+$ 30), 407 ($[M]^+$, 100), 393 (13), 363 (07), 294 (12). HRMS (ESI^+): calcd for $C_{24}H_{17}F_3NO_2$ $[M+H]^+$: 408.09766; found: 408.0987.

2-Chloro-11-(4-methoxybenzyl)benzofuro[3,2-b]quinoline (29z):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Chloroaniline (**19o**) (82 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **29z** was isolated as a yellowish white solid (67 mg, 40%); mp 126-128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.55 (s, 3H, OCH_3), 4.51 (s, 2H, CH_2), 6.69 (d, 2H, *J* = 8.4 Hz, ArH), 7.10 (d, 2H, *J* = 8.1 Hz, ArH), 7.45-7.61 (m, 2H, ArH), 7.66 (dd, 1H, *J* = 1.8, 8.5 Hz, ArH), 7.78 (d, 1H, *J* = 8.0 Hz, ArH), 8.18 (d, 1H, *J* = 8.3 Hz, ArH), 8.56 (d, 2H, *J* = 8.2 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =55.4 (OCH_3), 103.4 (CH), 111.8 (C), 113.9 (CH), 118.1 (C), 118.1, 118.4, 123.0, 124.0, 124.3 (CH), 124.4, 126.9, 127.3 (C), 129.1, 130.2 (CH), 133.1, 140.1, 142.1, 142.8, 159.1 (C). IR (KBr): *v* = 3055, 3030, 2927, 2857 (w), 1654, 1630, 1600 (m), 1515, 1460 (s), 1412, 1380, 1345 (m), 1301, 1280, 1250 (w), 1187 (s), 1153, 1124 (w), 1110, 1066, 1040, 1020 (m), 980, 948 (w), 915, 860, 844 (m), 823 (s), 782, 764 (w), 742, 701 (s), 687, 673 (w), 640, 592, 540 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 375 ([M$^+$, ^{37}Cl], 45), 374 (27), 373 ([M$^+$, ^{35}Cl], 100), 360 (15), 358 (35), 294 (22), 290 (06). HRMS (ESI$^+$): calcd for $C_{23}H_{17}ClNO_2$ [M+H, ^{35}Cl]$^+$: 374.0714; found: 374.07135.

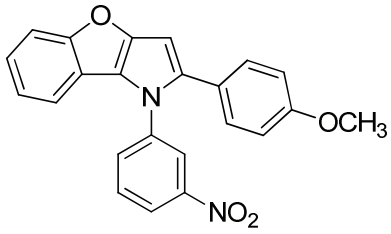
1-(4-Chlorophenyl)-2-(4-methoxyphenyl)-1H-benzofuro[3,2-b]pyrrole (30a):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Chloroaniline (**19o**) (82 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **30a** was isolated as a yellow solid (56 mg, 30%); mp 98-100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3H, OCH_3), 6.42 (s, 1H, ArH), 6.63 (d, 2H, *J* = 8.3 Hz, ArH), 6.94-7.11 (m, 5H, ArH), 7.18 (d, 2H, *J* = 8.4 Hz, ArH), 7.36 (d, 2H, *J* = 8.2 Hz, ArH), 7.67-7.71 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =54.3 (OCH_3), 101.6, 112.7, 118.4, 121.4, 122.2 (CH), 122.7 (C), 123.2 (CH), 123.5, 126.3 (C), 128.4, 128.6, 128.9 (CH), 132.5, 133.0, 136.7, 139.2, 141.0, 158.0 (C). IR (KBr): *v* = 3088, 2958, 2834 (w), 1479 (s), 1460 (m), 1437, 1404 (w), 1350 (m), 1287, 1273 (w), 1245, 1173 (s), 1155, 1113 (w), 1090 (s), 1070, 1057 (w), 1028 (s), 964, 951, 937 (w), 848, 832 (m), 822, 801 (w), 784, 747, 730 (s), 711, 694, 676 (w), 666, 651 (m), 632, 620 (w), 605, 567 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 375 ([M$^+$, ^{37}Cl], 45), 374 (28), 373 ([M$^+$, ^{35}Cl], 100), 360 (15), 385 (40),

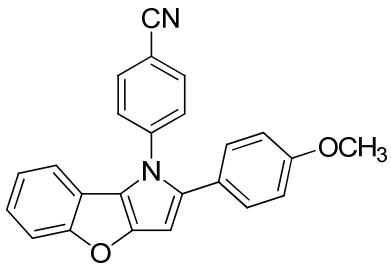
294 (20), 393 (08). HRMS (ESI$^+$): calcd for $C_{23}H_{17}ClNO_2$ [M+H, $^{35}Cl]^+$: 374.0714; found: 374.0716.

2-(4-Methoxyphenyl)-1-(3-nitrophenyl)-1H-benzofuro[3,2-b]pyrrole (30b):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 3-Nitroaniline (**19p**) (90 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **30b** was isolated as an orange solid (144 mg, 75%); mp 110-112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3H, OCH_3), 6.63 (s, 1H, ArH), 6.72 (d, 2H, *J* = 8.5 Hz, ArH), 6.94 (d, 1H, *J* = 8.1 Hz, ArH), 7.02 (d, 2H, *J* = 8.3 Hz, ArH), 7.05-7.16 (m, 2H, ArH), 7.53-7.66 (m, 2H, ArH), 7.75 (d, 1H, *J* = 7.8 Hz, ArH), 8.18-8.25 (m, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =55.3 (OCH_3), 103.4, 114.3, 118.2, 122.7, 123.1, 123.6, 124.0 (CH), 124.1, 124.2 (C), 124.3, 126.9 (CH), 130.1 (C), 130.3 (CH), 133.5 (C), 134.5 (CH), 140.1, 140.6, 142.3, 148.7, 159.3 (C). IR (KBr): ν = 3073, 2962, 2821 (w), 1731, 1606 (m), 1585, 1575 (w), 1525 (s), 1481, 1461 (m), 1405, 1375 (w), 1344 (s), 1290 (m), 1245, 1176 (s), 1116, 1107, 1058 (m), 1033 (s), 1001, 956, 929, 907 (w), 895, 870 (m), 833 (s), 816, 801, 771, 745, 722 (m), 698, 682, 664, 605, 548 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 384 ([M]$^+$, 100), 369 (17), 363 (28), 325 (07), 297 (16). HRMS (EI, 70 eV): calcd for $C_{23}H_{16}N_2O_4$ [M]$^+$: 384.08775; found: 384.08837.

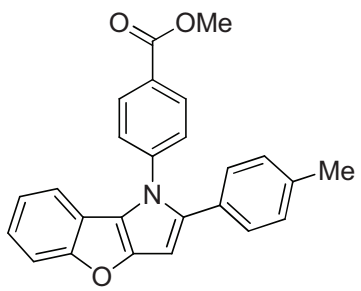
4-{2-(4-Methoxyphenyl)-1H-benzofuro[3,2-b]pyrrol-1-yl}benzonitrile (30c):



Starting with (**28c**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10 mol%), P(*t*-Bu)$_3$.HBF_4 (29 mg, 20 mol%), 4-Aminobenzonitrile (**19q**) (76 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **30c** was isolated as an orange solid (160 mg, 88%); mp 98-100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.75 (s, 3H, OCH_3), 6.60 (s, 1H, ArH), 6.72 (d, 2H, *J* = 8.1 Hz, ArH), 6.95 (d, 2H, *J* = 8.5 Hz, ArH), 6.70-7.04 (m, 1H, ArH), 7.10 (qd, 2H, *J* = 1.3, 7.1 Hz, ArH), 7.41 (d, 2H, *J* = 8.4 Hz, ArH), 7.67 (d, 2H, *J* = 8.4 Hz, ArH), 7.70-7.73 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =55.3 (OCH_3), 103.4 (CH), 111.8 (C), 113.9 (CH), 118.1 (C), 118.1, 118.4, 123.0, 124.0, 124.3 (CH), 124.4, 126.9 (C), 129.1, 130.2 (CH), 133.1, 133.2, 140.1, 142.1, 142.8, 159.1 (C). IR (KBr): ν = 3121, 3008, 2937, 2838 (w), 2226 (m), 1603 (s), 1573, 1532 (w), 1506 (m), 1488, 1463 (s), 1438, 1406

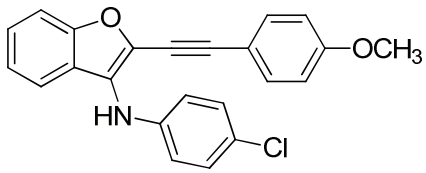
(m), 1350 (s), 1297, 1290 (m), 1247, 1176 (s), 1118, 1069, 1057 (w), 1028 (s), 964, 951, 929 (w), 853 (m), 831, 803, 743, 723 (s), 695 (w), 667, 659, 626 (m), 607 (s), 585 (w), 551 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 364 ($[M]^+$, 100), 349 (41), 319 (12). HRMS (EI, 70 eV): calcd for $C_{24}H_{16}N_2O_2$ $[M]^+$: 364.12063; found: 364.12023.

(4-Methylbenzoate)-2(4-methylphenyl)-1H-[1]benzothieno[3,2-b]pyrrole (30d):



Starting with (**28b**) (150 mg, 0.5 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), methyl 4-aminobenzoate (**19r**) (98 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), **30d** was isolated as an orange solid (160 mg, 50%); mp 98-100 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.25 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 6.61 (s, 1H, ArH), 6.91-7.10 (m, 7H, ArH), 7.39 (d, 2H, *J* = 7.4 Hz, ArH), 7.71 (d, 1H, *J* = 7.5 Hz, ArH), 7.98 (d, 2H, *J* = 7.5 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 29.5 (CH_3), 53.4 (OCH_3), 104.2, 119.6, 122.5, 123.8 (CH), 123.9 (C), 125.1 (CH), 127.4 (C), 128.3, 128.7, 129.1 (CH), 129.3, 129.6 (C), 130.7 (CH), 133.7, 137.1, 140.3, 142.1, 142.9 (C), 166.3 (CO). IR (KBr): ν = 2852, 2921, 3027, 3118 (w), 1714 (s), 1602, 1586 (m), 1532 (w), 1512, 1486, 1460, 1434 (m), 1413, 1404, 1377 (w), 1355, 1275 (s), 1170, 1116, 1097, 1055 (w), 1016, 964, 869 (m), 848 (w), 812 (s), 781, 748 722, 703, 669 (m), 651, 627 (w), 603, 562 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 382 ($[M+H]^+$ 22), 381 ($[M]^+$, 100), 323 (23), 309 (11), 255 (08), 142 (14). HRMS (ESI^+): calcd for $C_{25}H_{20}NO_3$ $[M+H]^+$: 382.13094; found: 382.1306.

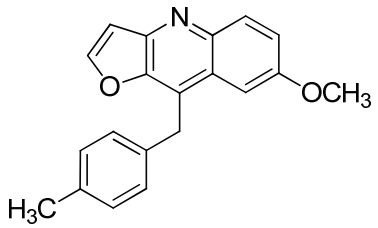
N-(4-Chlorophenyl)-2-[(4-methoxyphenyl)ethynyl]benzofuran-3-amine (31):



Following the *general procedure* but with reduced temperature (40 °C) and reduced reaction time (4 h), **31** was prepared by reaction of 3-bromo-2-((4-methoxyphenyl)ethynyl)benzofuran (**28c**) (150 mg, 0.5 mmol), $Pd(OAc)_2$ (11 mg, 10 mol %), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (29 mg, 20 mol %), with 4-chloroaniline (**19o**) (82 mg, 0.65 mmol), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmol), as a dark brown solid, mp 133-135 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 3H, OCH_3), 6.23 (brs, 1H, NH), 6.71-6.80 (m, 4H, ArH), 7.13 (d, 2H, *J* = 8.4 Hz, ArH), 7.17-7.24 (m, 3H, ArH), 7.27-7.34 (m, 1H, ArH), 7.43 (d, 1H, *J* = 8.0 Hz, ArH), 7.67 (d, 1H, *J* = 7.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 83.1, 100.5, 110.3 (C), 114.1 (CH), 114.6 (C), 118.3, 122.2, 122.9, 124.5 (CH), 125.3 (C), 126.0, 128.7, 132.8 (CH), 133.4, 137.4, 138.3, 142.7, 161.3 (C). IR (KBr): ν = 3374, 2925, 2835, 2538, 2192, 1873, 1656 (w), 1594 (s), 1566, 1533

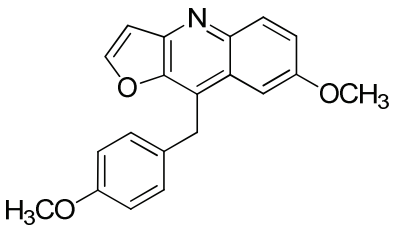
(m), 1510, 1473 (s), 1461, 1439, 1400 (w), 1377, 1285 (m), 1244, 1167 (s), 1108, 1090, 1065 (w), 1034 (s), 951, 929, 851 (w), 817 (s), 759, 751 (m), 730 (s), 659, 631, 591, 533 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 375 ([M^+, ^{37}Cl], 40), 373 ([M^+, ^{35}Cl], 100), 360 (15), 358 (35), 294 (22), 290 (06). HRMS (ESI^+): calcd for $C_{23}H_{17}ClNO_2$ [M+H, $^{35}Cl]^+$: 374.0714; found: 374.07137.

7-Methoxy-9-(4-methylbenzyl)furo[3,2-b]quinoline (34a):



Starting with (**33b**) (150 mg, 0.60 mmol), $Pd(OAC)_2$ (13 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (39 mg, 20 mol%), 4-Methoxyaniline **(19a)** (95 mg, 0.78 mmole), toluene (5 mL), KO*t*-Bu (134 mg, 1.2 mmole), **34a** was isolated as a dark oil (127 mg, 70%). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 4.55 (s, 2H, CH_2), 6.95-6.97 (m, 2H, ArH), 6.98 (brs., 1H, ArH), 7.07 (d, 2H, *J* = 8.1 Hz, ArH), 7.22-7.27 (m, 2H, ArH), 7.89 (d, 1H, *J* = 2.4 Hz, ArH), 8.01 (dd, 1H, *J* = 0.8, 8.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.9 (CH_3), 31.0 (CH_2), 55.4 (OCH_3), 102.1, 108.1, 120.6 (CH), 125.0, 126.1 (C), 128.3, 129.3, 131.0 (CH), 135.4, 136.1, 143.4, 145.6, 147.7 (C), 151.4 (CH), 156.9 (C). IR (KBr): ν = 3367, 3138, 3093, 2995 (w), 2922 (m), 2852, 2827 (w), 1632, 1622 (m), 1568 (w), 1541 (m), 1507 (s), 1472 (m), 1450, 1422, 1373 (w), 1344 (m), 1328, 1298, 1261 (w), 1225 (s), 1183, 1173, 1138 (w), 1127 (s), 1114, 1042 (w), 1027 (s), 960, 913, 891, 865, 843 (w), 823 (s), 783, 766, 721, 680, 631, 600, 579, 543 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 304 ($[M+H]^+$ 22), 303 ($[M]^+$, 100), 288 (05), 273 (14), 273 (09), 272 (10), 270 (09), 256 (07). HRMS (ESI^+): calcd for $C_{20}H_{18}NO_2$ $[M+H]^+$: 304.13321; found: 304.13283.

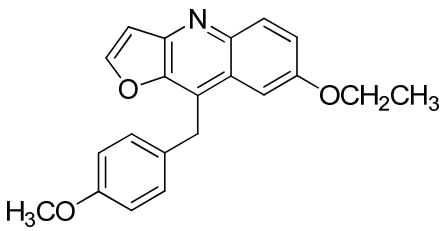
7-Methoxy-9-(4-methoxybenzyl)furo[3,2-b]quinoline (34b):



Starting with (**33c**) (140 mg, 0.50 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{Bu})_3.HBF_4$ (29 mg, 20 mol%), 4-Methoxyanilin **(19a)** (80 mg, 0.65 mmole), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmole), **34b** was isolated as a dark oil (103 mg, 65%). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.66, 3.78 (s, 3H, $2OCH_3$), 4.53 (s, 2H, CH_2), 6.71 (d, 2H, *J* = 8.6 Hz, ArH), 7.00 (brs., 1H, ArH), 7.08 (d, 2H, *J* = 8.6 Hz, ArH), 7.23-7.27 (m, 2H, ArH), 7.91 (d, 1H, *J* = 2.0 Hz, ArH), 8.03 (d, 1H, *J* = 8.6 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 30.6 (CH_2), 55.2, 55.4 ($2OCH_3$), 102.1, 108.0, 114.1, 120.8 (CH), 125.6, 126.1 (C), 129.4 (CH), 130.4 (C), 130.8 (CH), 143.0, 145.6, 147.4 (C), 151.6 (CH), 156.9, 158.2 (C). IR (KBr): ν = 3435, 3369, 3141, 3092, 2997 (w), 2923 (m),

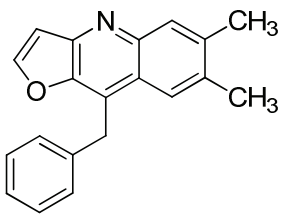
2852, 2831 (w), 1623, 1539 (m), 1507 (s), 1472 (m), 1440, 1426, 1394, 1373 (w), 1346 (m), 1328, 1302, 1279 (w), 1226, 1176 (s), 1139, 1127 (m), 1024 (s), 912, 867, 843 (w), 785, 772, 721 (m), 678, 629, 601 (w), 580 (m), 566, 550 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 320 ($[M+H]^+$ 23), 319 ($[M]^+$, 100), 304 (14), 288 (08), 273 (09), 244 (06). HRMS (ESI^+): calcd for $C_{21}H_{20}NO_4$ $[M+H]^+$: 320.12812; found: 320.12813.

7-Ethoxy-9-(4-methoxybenzyl)furo[3,2-b]quinoline (34c):



Starting with (**33c**) (140 mg, 0.50 mmol), $Pd(OAC)_2$ (11mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 4-Ethoxyaniline **(19e)** (89 mg, 0.65 mmole), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmole), **34c** was isolated as a dark oil (106 mg, 64%). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.37 (t, 3H, *J* = 7.1 Hz, CH_3), 3.66 (s, 3H, OCH_3), 4.01 (q, 2H, *J* = 6.9 Hz, OCH_2), 4.52 (s, 2H, CH_2), 6.71 (d, 2H, *J* = 8.6 Hz, ArH), 6.98 (d, 1H, *J* = 2.5 Hz, ArH), 7.08 (d, 2H, *J* = 8.7 Hz, ArH), 7.21 (d, 1H, *J* = 2.7 Hz, ArH), 7.25 (dd, 1H, *J* = 2.6, 9.1 Hz, ArH), 7.89 (d, 1H, *J* = 2.4 Hz, ArH), 8.01 (d, 1H, *J* = 9.1 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.1 (CH_3), 29.9 (CH_2), 54.6 (OCH_3), 63.0 (OCH_2), 102.2, 107.4, 113.5, 120.4 (CH), 124.6, 125.5 (C), 128.8 (CH), 129.9 (C), 130.2 (CH), 142.5, 145.0, 146.9 (C), 150.8 (CH), 155.6, 157.6 (C). IR (KBr): ν = 3140, 3116, 3067, 2985, 2927, 2829 (w), 1624 (m), 1608, 1581, 1567 (w), 1537 (m), 1506 (s), 1463 (m), 1435, 1392, 1369 (w), 1346, 1326 (m), 1304, 1277 (w), 1239, 1225 (s), 1175, 1140, 1113 (m), 1033, 1008 (s), 944, 922, 864 (w), 822, 791, 764 (s), 745, 722, 685, 632 (w), 582, 551 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 ($[M+H]^+$ 23), 333 ($[M]^+$, 100), 305 (11), 304 (08), 290 (08), 273 (13), 272 (11), 244 (06). HRMS (ESI^+): calcd for $C_{21}H_{20}NO_3$ $[M+H]^+$: 334.14377; found: 334.14409.

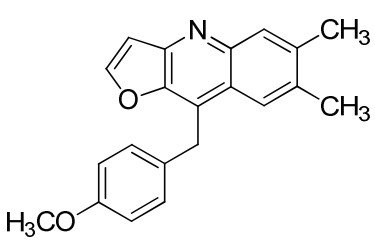
9-Benzyl-6,7-dimethylfuro[3,2-b]quinoline (34d):



Starting with (**33a**) (150 mg, 0.60 mmol), $Pd(OAC)_2$ (13 mg, 10 mol%), $P(t\text{Bu})_3.HBF_4$ (39 mg, 20 mol%), 3,4-Dimethylaniline **(19t)** (94 mg, 0.78 mmole), toluene (5 mL), KO-*t*-Bu (134 mg, 1.2 mmole), **34d** was isolated as a dark oil (103 mg, 60%). ^1H NMR (250 MHz, $CDCl_3$): δ = 2.38, 2.58 (s, 3H, $2CH_3$), 4.92 (s, 2H, CH_2), 6.95-6.98 (m, 3H, ArH), 7.11-7.22 (m, 3H, ArH), 7.42 (d, 1H, *J* = 8.6 Hz, ArH), 7.85 (d, 1H, *J* = 2.3 Hz, ArH), 7.95 (d, 1H, *J* = 8.6 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.8, 21.7 ($2CH_3$), 34.2 (CH_2), 107.7 (CH), 111.3, 116.1 (C), 126.2, 127.7, 127.8, 128.7, 131.3 (CH), 132.3, 134.4, 139.3, 145.8,

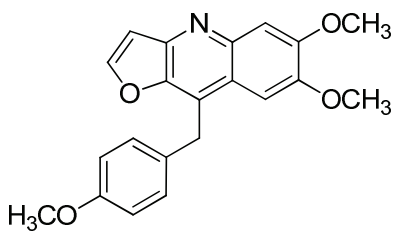
146.8, 147.4 (C), 152.2 (CH). IR (KBr): ν = 3131, 3095, 3042, 2920, 2852, 1622 (w), 1601, 1566, 1541 (m), 1494, 1450 (s), 1380 (w), 1363 (s), 1340, 1327, 1315, 1220, 1175 (w), 1129 (s), 1098, 1074, 1052 (w), 1022 (s), 978, 908, 875, 857 (m), 828, 792, 773, 730, 691 (s), 672, 622, 598, 574, 535 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 288 ($[M+H]^+$ 23), 287 ($[M]^+$, 100), 272 (30), 258 (18), 244 (07), 194 (09). HRMS (ESI^+): calcd for $C_{20}H_{18}NO$ $[M+H]^+$: 288.13829; found: 288.13882.

9-(4-Methoxybenzyl)-6,7-dimethylfuro[3,2-b]quinoline (**34e**):



Starting with (**33c**) (140 mg, 0.50 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(tBu)_3.HBF_4$ (29 mg, 20 mol%), 3,4-Dimethylaniline **(19t)** (78 mg, 0.65 mmole), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmole), **34e** was isolated as a dark oil (87 mg, 55%). ^1H NMR (250 MHz, $CDCl_3$): δ = 2.39, 2.60 (s, 3H, $2CH_3$), 3.68 (s, 3H, OCH_3), 4.86 (s, 2H, CH_2), 6.72 (d, 2H, J = 8.7 Hz, ArH), 6.88 (d, 2H, J = 8.7 Hz, ArH), 7.01 (d, 1H, J = 2.3 Hz, ArH), 7.44 (d, 1H, J = 8.6 Hz, ArH), 7.87 (d, 1H, J = 2.3 Hz, ArH), 7.98 (d, 1H, J = 8.5 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.8, 21.8 ($2CH_3$), 33.4 (CH_2), 55.2 (OCH_3), 107.5 (CH), 111.3 (C), 114.1 (CH), 116.1 (C), 126.2, 127.8, 128.7, 131.3 (CH), 132.3, 134.4, 139.3, 145.8, 146.8, 152.4, 158.1 (C). IR (KBr): ν = 3118, 2922 (m), 2854, 2835 (w), 1737, 1619 (m), 1581, 1568, 1541 (w), 1509 (s), 1441, 1360 (m), 1331, 1302, 1273 (w), 1243, 1175, 1125, 1025 (s), 978, 882, 858 (w), 811, 767 (m), 725, 665, 636, 596, 580, 544 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 318 ($[M+H]^+$ 20), 317 ($[M]^+$, 100), 302 (31), 287 (18), 269 (09). HRMS (ESI^+): calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$: 318.13730; found: 318.13781.

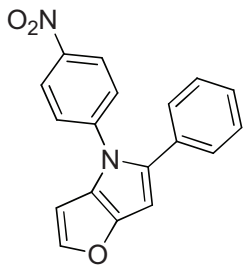
6,7-Dimethoxy-9-(4-methoxybenzyl)furo[3,2-b]quinoline (34f):



Starting with (**33c**) (140 mg, 0.50 mmol), $Pd(OAC)_2$ (11 mg, 10-mol%), $P(t\text{-}Bu)_3.HBF_4$ (29 mg, 20 mol%), 3,4-Dimethoxyanilin **(19n)** (99 mg, 0.65 mmole), toluene (5 mL), KO-*t*-Bu (112 mg, 1.0 mmole), **34f** was isolated as a dark oil (125 mg, 72%). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.66, 3.84, 3.95 (s, 3H, $3OCH_3$), 4.53 (s, 2H, CH_2), 6.71 (d, 2H, J = 8.7 Hz, ArH), 6.94 (d, 1H, J = 2.4 Hz, ArH), 7.08 (d, 2H, J = 8.6 Hz, ArH), 7.17 (d, 1H, J = 7.6 Hz, ArH), 7.42 (s, 1H, ArH), 7.87 (d, 1H, J = 2.4 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 30.7 (CH_2), 55.2, 55.9, 56.0 ($3OCH_3$), 101.9, 107.8, 107.9, 114.1 (CH), 120.5, 125.6 (C), 129.4 (CH),

130.6, 144.2, 144.8, 147.3, 149.1 (C), 150.9 (CH), 151.3, 158.2 (C). IR (KBr): ν = 3142, 3120, 3055, 2999, 2929, 2832 (w), 1633, 1612, 1539 (m), 1503, 1487 (s), 1469, 1454, 1428 (w), 1369 (m), 1351 (s), 1302 (w), 1246 (s), 1203, 1157, 1125 (m), 1021 (s), 978, 927 (w), 879, 839, 791, 758, 745 (m), 714, 701, 684 (w), 622, 581, 543 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 350 ($[M+H]^+$ 23), 349 ($[M]^+$, 100), 334 (05), 318 (08), 303 (06). HRMS (ESI^+): calcd for $C_{21}H_{20}NO_4$ $[M+H]^+$: 350.13868; found: 350.13897.

4-(4-Nitrophenyl)-5-phenyl-4H-furo[3,2-b]pyrrole (35):



Starting with (**33a**) (150 mg, 0.60 mmol), $Pd(OAC)_2$ (13 mg, 10 mol%), $P(tBu)_3.HBF_4$ (39 mg, 20 mol%), 4-Nitroaniline **(19s)** (107 mg, 0.78 mmole), toluene (5 mL), KO-*t*-Bu (134 mg, 1.2 mmole), **35** was isolated as a brown oil (118 mg, 65%). ^1H NMR (300 MHz, Acetone): δ = 6.68 (brs, 1H, ArH), 6.94 (dd, 1H, J = 0.6-5.3 Hz, ArH), 7.09-7.14 (m, 4H, ArH), 7.15-7.18 (m, 2H, ArH), 7.36 (d, 2H, J = 9.1 Hz, ArH), 8.13 (d, 2H, J = 9.1 Hz, ArH). ^{13}C NMR (75.5 MHz, Acetone): δ = 105.6, 112.3, 125.7, 125.8 (CH), 126.0 (C), 127.4, 128.2, 129.4, 129.5 (CH), 133.3, 139.7, 142.9, 145.9, 146.6 (C). IR (KBr): ν = 3110, 3079, 3027, 2927, 2851, 2448, 2360, 2331, 2251 (w), 1592, 1514, 1497 (s), 1468, 1442, 1417 (w), 1393 (m), 1331 (s), 1244 (w), 1168, 1108, 1093 (m), 1073, 1045, 1027, 1011 (w), 954 (m), 906, 853, 835 (s), 797, 786 (w), 758 (s), 744, 729 (w), 706, 661 (s), 619, 585 (m), 574, 530 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 304 (M^+, 100), 275 (22), 260 (25), 259 (14), 196 (26). HRMS (EI, 70 eV): calcd for $C_{18}H_{12}N_2O_3$ $[M]^+$: 304.06147; found: 304.06158.

Appendix

9. Crystallographic Data

9.1 Crystal data and structure refinement for 10-(4-methoxyphenyl)-4-oxo-1,2,3,4 tetrahydroanthracen-9-yl trifluoromethanesulfonate (9a)

Table 20. Crystal data and structure refinement for **(9a)**

Identification code	GS-75	
Empirical formula	$C_{22}H_{17}F_3O_5S$	
Formula weight	450.42	
Temperature	173 (2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H-M)	P b c a	
Space group (Hall)	- P 2ac 2ab	
Unit cell dimensions	a = 14.3748 (4) Å	α = 90.00°
	b = 9.4291 (2) Å	β = 90.00°
	c = 29.4268 (7) Å	γ = 90.00°
Volume	3988.55 (17) $Å^3$	
Z	8	
Density (calculated)	1.500 Mg/ m^3	
Absorption coefficient	0.223 mm^{-1}	
F(000)	1856	
Crystal size	0.60 × 0.41 × 0.08 mm^3	
Θ range for data collection	5.4 – 60.1 °	
Reflections collected	42998	
Independent reflections	5815	
Absorption correction	multi-scan	
Max. and Min. transmission	0.982 and 0.878	
Refinement method	full-matrix	
Goodness-of-fit F2	1.062	
Final R indices [I>2σ (I)]	R1 = 0.0440, wR2 = 0.1123	
R indices (all data)	R1 = 0.0690, wR2 = 0.1239	

9.2 Crystal data and structure refinement for 10-(4-methoxyphenyl)-11-oxo-11H-benzo[b]fluoren-5-yl trifluoromethanesulfonate (14a)

Table 21. Crystal data and structure refinement for **(14a)**

Identification code	GS-106	
Empirical formula	$C_{25}H_{15}F_3O_5S$	
Formula weight	484.43	
Temperature	173 (2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H-M)	P 21/ C	
Space group (Hall)	-P 2 ybc	
Unit cell dimensions	a = 6.4919 (2) Å	α = 90.00 (0)°
	b = 31.6277 (9) Å	β = 99.497 (2)°
	c = 10.1882 (3) Å	γ = 97.545 (16)°
Volume	2063 (11) $Å^3$	
Z	4	
Density (calculated)	1.560 Mg/m^3	
Absorption coefficient	0.222 mm^{-1}	
F(000)	992	
Crystal size	0.48 × 0.14 × 0.05 mm^3	
Θ range for data collection	5.6 – 59.9 °	
Reflections collected	23635	
Independent reflections	6018	
Absorption correction	multi-scan	
Max. and Min. transmission	0.989 and 0.901	
Refinement method	full-matrix	
Goodness-of-fit F2	1.031	
Final R indices [I>2σ (I)]	R1 = 0.0472, wR2 = 0.1051	
R indices (all data)	R1 = 0.0845, wR2 = 0.1183	

9.3 Crystal data and structure refinement for 2-Methoxy-11(benzyl)benzothieno[3,2-b]quinoline (20a)

Table 22. Crystal data and structure refinement for **(20a)**

Identification code	GS-N-82	
Empirical formula	$C_{23}H_{17}NOS$	
Formula weight	355.44	
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 = 8.5241 (4) Å	α = 70.630 (2)°
	b = 8.9223 (4) Å	β = 86.008 (3)°
	c = 12.8073 (6) Å	γ = 68.671 (2)°
Volume	854.54 (7) $Å^3$	
Z	2	
Density (calculated)	1.381 Mg/m^3	
Absorption coefficient	0.201 mm^{-1}	
F(000)	372	
Crystal size	0.95 × 0.41 × 0.09 mm^3	
Θ range for data collection	2.6 – 30.0 °	
Reflections collected	17641	
Independent reflections	4918	
Absorption correction	multi-scan	
Max. and Min. transmission	0.982 and 0.832	
Refinement method	full-matrix	
Goodness-of-fit F2	1.060	
Final R indices [I>2σ (I)]	R1 = 0.0453, wR2 = 0.124	
R indices (all data)	R1 = 0.0651, wR2 = 0.133	

9.3 Crystal data and structure refinement for 1-(4-Chlorophenyl)-2(4 methoxylphenyl) -1H-[1]benzothieno[3,2-b]pyrrole (21d)

Table 23. Crystal data and structure refinement for **(21d)**

Identification code	GS-N-129	
Empirical formula	$C_{23}H_{16}ClNOS$	
Formula weight	389.88	
Temperature	173 (2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H-M)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 10.0944(6) Å	α = 90.00°
	b = 23.0699 (13) Å	β = 110.958(2)°
	c = 8.4740 (4) Å	γ = 90.00°
Volume	1842.84 (17) $Å^3$	
Z	4	
Density (calculated)	1.405 Mg/ m^3	
Absorption coefficient	0.334 mm^{-1}	
F(000)	808	
Crystal size	0.90 × 0.43 × 0.07 mm	
Θ range for data collection	2.8 – 30.0 °	
Reflections collected	21004	
Independent reflections	5362	
Absorption correction	multi-scan	
Max. and Min. transmission	0.977 and 0.753	
Refinement method	full-matrix	
Goodness-of-fit F2	1.03	
Final R indices [I>2σ (I)]	R1 = 0.041, wR2 = 0.0916	
R indices (all data)	R1 = 0.0543, wR2 = 0.098	

9.3 Crystal data and structure refinement for 2-methoxy-11-(4-methoxybenzyl) benzofuro[3,2-b]quinoline (29r)

Table 24. Crystal data and structure refinement for **(29r)**

Identification code	ch_n139a	
Empirical formula	$C_{24}H_{19}NO_3$	
Formula weight	369.40	
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 = 4.9087 (3) Å	α = 90.00°
	b = 16.9957 (10) Å	β = 94.094(3)°
	c = 10.9317 (7) Å	γ = 90.00°
Volume	909.67 (10) $Å^3$	
Z	2	
Density (calculated)	1.349 Mg/m^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	388	
Crystal size	0.46 × 0.16 × 0.10 mm^3	
Θ range for data collection	6.1 – 57.4 °	
Reflections collected	8594	
Independent reflections	3901	
Absorption correction	multi-scan	
Max. and Min. transmission	0.991 and 0.960	
Refinement method	full-matrix	
Goodness-of-fit F2	1.007	
Final R indices [I>2σ (I)]	R1 = 0.0402, wR2 = 0.0814	
R indices (all data)	R1 = 0.0626, wR2 = 0.0899	

Abbreviations

Ar	Aromatic
A^o	Angstrom
DIPA	Diisopropylamine
DMF	N,N-Dimethylformamide
EI	Electron Impact
ESI	Electrospray Ionization
EtOAc	Ethylacetate
HRMS	High Resolution Mass Specrometry
IR	Infrared Spectroscopy
GC	Gas Ghromatography
MS	Mass Spectrometry
Ph	Phenyl
NEt_3	Triethylamine
$NHEt_3$	Diethylamine
NMR	Nuclear Magnetic Resonance
DEPT	Distortionless Enhancement by Polarization Transfer
HMQC	Heteronuclear Multiple Quantum Coherence
HMBC	Heteronuclear Multiple Bond Correlation
COSY	Correlated Spectroscopy
NOESY	Nuclear Overhauser and Exchange Spectroscopy
Tf_2O	Trifluorometanesulfonic Anhydride
THF	Tetrahydrofurane
TLC	Thin Layer Chromatography
TMS	Trimethylsilane
UV	Ultraviolet Spectroscopy
OAc	Acetate
^oC	Degrees Celsius
PCy_3	Tricyclohexylphosphine
ppm	parts per million
bp	Boiling point
mp	melting point
calcd	Calculated
CI	Chemical Ionization
R_f	Retention factor
DMSO	Dimethylsulfoxide
Hz	Hertz
g	Gram(s)
Cy	Cyclohexyl
OTf	Triflate
dt	Doublet of triplet

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Declaration/Erklärung

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

Hiermit erkläre ich, daß diese Arbeit bisher von mir weder an der Mathematisch-Naturwissenschaftlichen Fakultät der Universität Rostock noch einer anderen wissenschaftlichen Einrichtung zum Zwecke der Promotion eingereicht wurde.

Ferner erkläre ich, dass ich diese Arbeit selbständig verfasst und keine anderen als die darin angegebenen Hilfsmittel benutzt habe.

I hereby apply irrevocably to take oral examination in the form of a private viva voce and a public presentation.

Ghazwan Ali Salman

August 2011, Rostock,

Germany

List of Publications

[1] "Domino C-N coupling / annulation versus C-N coupling / hydroamination of 2-alkynyl-3-bromobenzothiophenes and 2-alkynyl-3-bromothiophenes. Highly efficient synthesis of benzothieno[3,2-b]quinolines and thieno[3,2-b]pyrroles. **Salman, G. A.**; Hussain, M.; Iaroshenko, V. O.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2011**, *353*, 331.

[2] "Regioselective Suzuki-Miyaura Reactions of the Bis(triflate) of 1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-one". **Salman, G. A.**;Mahal, A.; Shkoor, M.; Hussain, M.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2011**, *52*, 392.

[3] "Site-selective Suzuki-Miyaura Reactions of the Bis(triflate) of 5,10-Dihydroxy-11*H*-benzo[*b*]fluoren-11-one". **Salman, G. A.**; Hussain, M.; Villinger, A.; Langer, P. *Synlett* **2010**, 3031.

[4] "Synthesis of Functionalized Benzofurans by a Double Heck Reaction of 2,3-Dibromofurans and Subsequent 6π-Electrocyclization/Dehydrogenation".**Salman, G. A.** ; Ali, A.; Hussain, M.; Khera, R. A.; Langer, P. *Synthesis*, **2011**, No. *14*, 2208.

[5] "Efficient Synthesis of Functionalized Anthraquinones by Domino Twofold Heck / 6π-Electrocyclization Reactions of 2,3-Dibromonaphthoquinone". Hussain, M.; Zinad, D. S.; **Salman, G. A.;** Sharif, M.; Villinger, A.; Langer, P. *Synlett* **2010**, 276-280.

[6] "Domino C-N Coupling / Annulation *versus* C-N Coupling / Hydroamination of 2-Alkynyl-3-bromobenzofurans and 2-Alkynyl-3-bromofurane. Highly Efficient Synthesis of Benzofuro[3,2-*b*]quinolines and Furo[3,2-b]quinolines". **Salman, G. A.**; Langer, P. *Manuscript in preparation*.