Synthesis of Functionalized Naphthalenes, Coumarines, Quinolines, and Isoflavones by Chemo- and Site-Selective Palladium-Catalyzed Coupling Reactions

Dissertation
zur
Erlangung des akademischen Grades
doctor rerum naturalium (Dr. rer. nat.)
der Mathematisch-Naturwissenschaftlichen Fakultät
der Universität Rostock

vorgelegt von
M.Sc. Zien Khaddour, geb. am 1. September 1984 in Tartous, Syrien

Rostock

urn:nbn:de:gbv:28-diss2015-0137-3

Gutachter :

Gutchter 1. Prof. Dr. Dr. h.c mult. Peter Langer

Universität Rostock

Institut für Chemie

Gutchter 2. Prof. Dr. Bernd Schmidt

Universität Potsdam
Institut für Chemie

Datum der Einreichung 02. März 2015

Datum der Verteidigung 23. Juni 2015

Dedication

I feel a great pleasure to dedicate all of this work to Rostock University then to all of my colleagues in the department of chemistry of Rostock University and to my dear mother and all of my family.

Acknowledgments

I would like to thank my supervisor Prof. Dr. Dr. h.c. mult. Peter Langer for providing efficient guidance and energetic research environment during my whole Ph. D. I always found him ready to facilitate my research by effective discussion, reviving encouragements, unending trust, providing free hand in research and every possible facility.

I wish to express my special gratitude to Dr. Michalik and Dr. Hein and Dr. Feist for a numbers of nice talk about my work. Also to Dr. Vellinger for his professional and accurate X-ray crystallographic analyses. I would like to thank the members of the NMR, IR, MS, and X-ray laboratories of the University of Rostock.

I would like also to thank my colleagues at the University of Rostock Dr. Nadi Elya, Dr. Omer Akrawi, Mr. Aws Hamdy and finally a special thank from my Hearts for my uncle Dr. Ali Suleiman for all things what he did for me from the beginning of my Studying in Rostock and for my Family in Syria, who are waiting for me that I come back with my Ph.D.

Zien Khaddour…….

ABSTRACT IN ENGLISH

I studied the site-selectivity of Suzuki cross-coupling reactions of the bis(triflate) of naphthoates, coumarines, and isoflavones. In addition, the chemo-selectivity of Suzuki cross-coupling reactions of naphthoates and quinolones containing bromide and triflate leaving groups were studied. In this context, prepared various arylated pharmacologically relevant heterocycles which are not readily available by other synthetic methods.

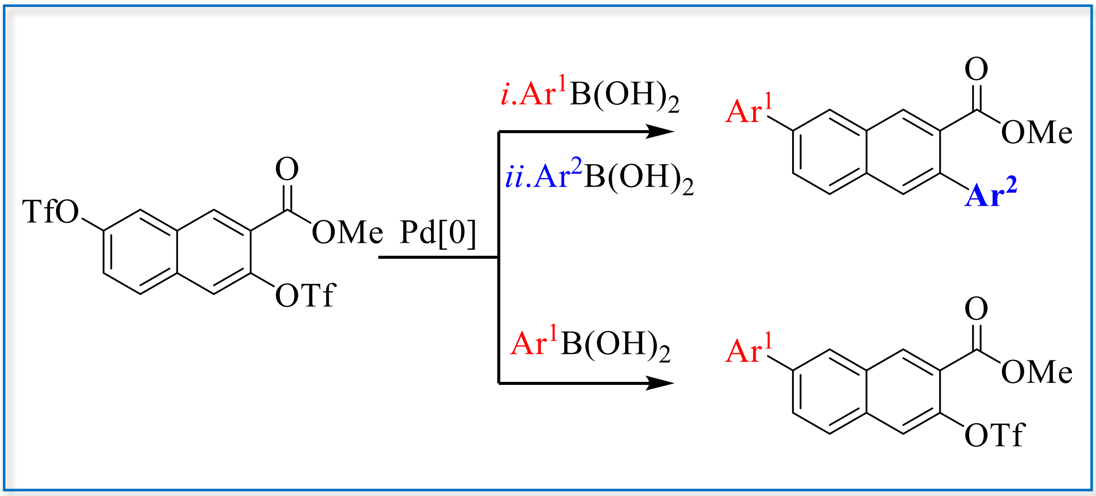
ABSTRACT IN GERMAN

Ich habe die Untersuchung der Regioselektivität von Suzuki-Miyaura Kreuzkupplungsreaktionen von Naphthalinen, Coumarinen, und Isoflavonen untersucht. Weiterhin wurde die Chemoselektivität von Suzuki-Reaktionen von Naphthalinen und Chinoline, die Bromid- und Triflatfluchtgruppen enthalten, untersucht. In diesem Zusammenhang gelang die Synthese arylierter Heterocyclen, die durch andere syntetische Methoden nicht hergestellt werden konnten.

Main Contents

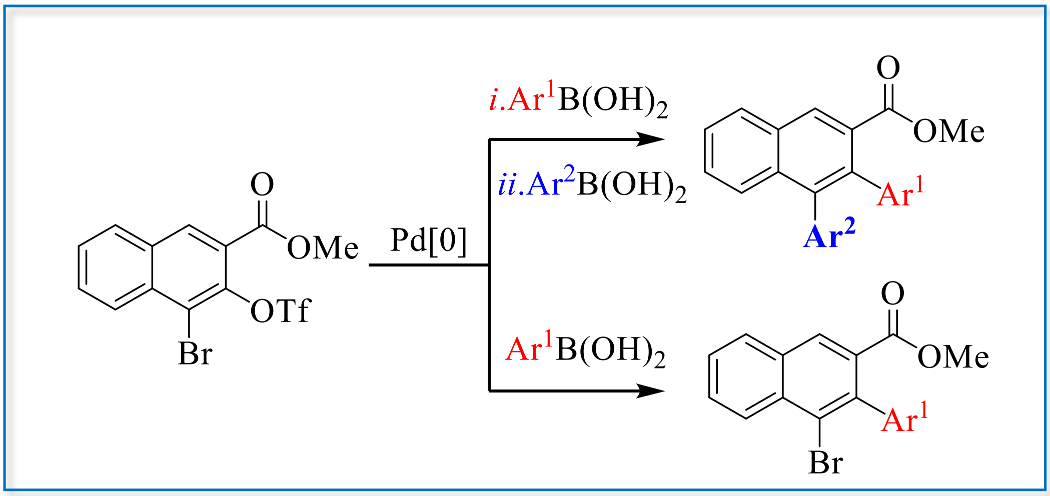
Chapter Two

Site-selective Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of methyl 3,7-dihydroxy-2-naphthoate



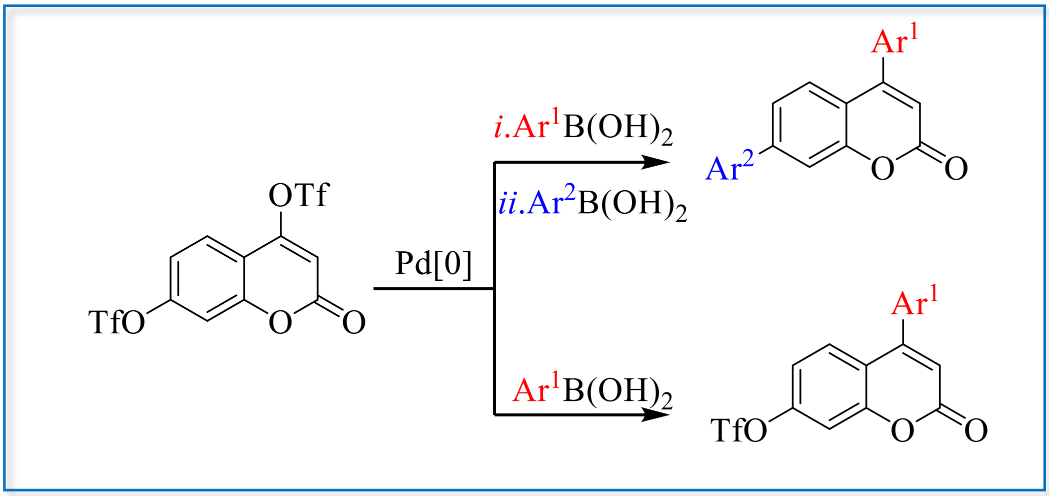
Chapter Three

Chemoselective Suzuki–Miyaura cross-coupling reactions of methyl 4-bromo-3-(trifluoromethanesulfonyloxy)-2-naphthoate



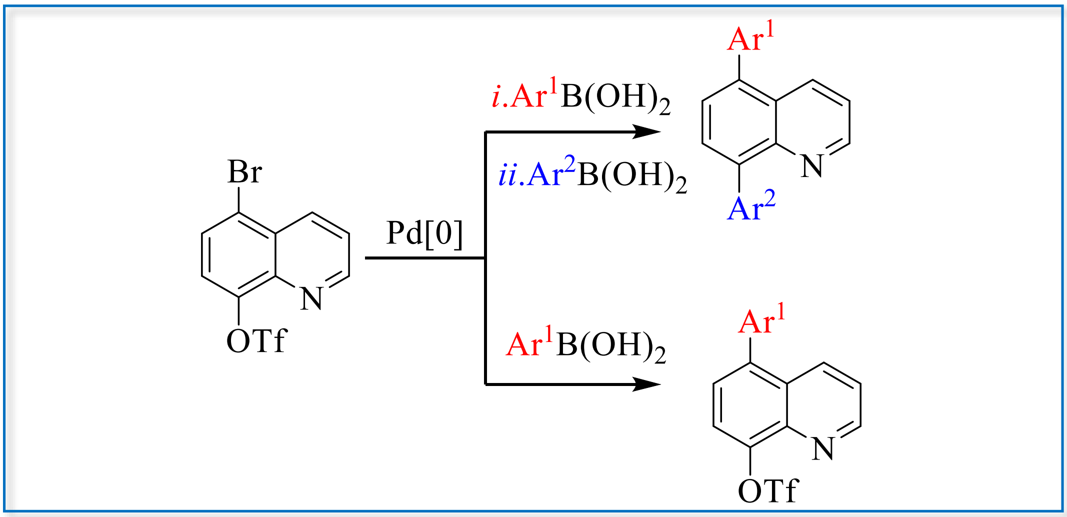
Chapter Four

Site-selective Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of 4,7-dihydroxycoumarin



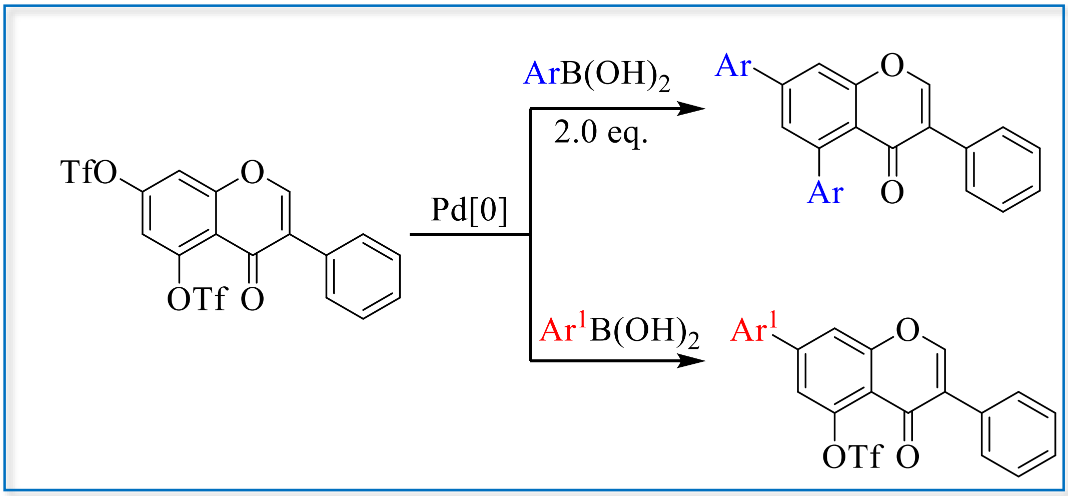
Chapter Five

Chemoselective Suzuki-Miyaura cross-coupling reactions of 5-bromo-quinolin-8-yl trifluoromethanesulfonate



Chapter Six

Site-selective Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of 5,7-dihydroxyisoflavone.



DETAILED CONTENTS

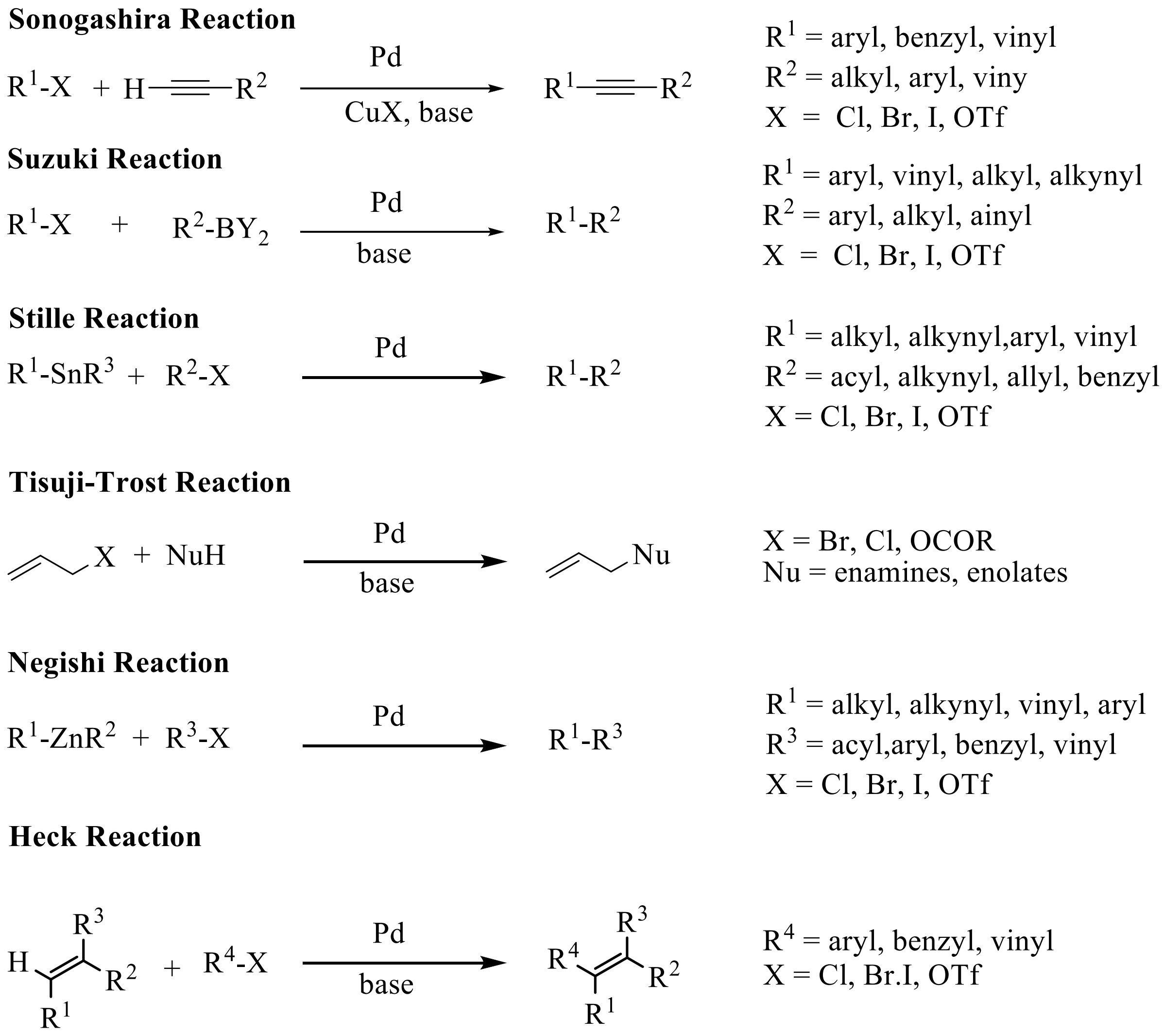
1 Chapter One

1.1 General Introduction

The formation of carbon-carbon bonds is one of the most important themes in synthetic organic chemistry. The diversity and complexity of several natural products and biological active compounds have created the demand to establish and develop efficient synthetic approaches for constructing C-C bond. As a result for this demand, several conventional synthetic methods have been successfully developed for constructing C-C bond such as Aldol, the Diels-Alder, Michael reactions and the Claisen ester condensation.[1a,b,c,d] The first vital synthetic method was discovered by Victor Grignard for constructing carbon-carbon bonds by using organomagnesium reagents. Later, a diverse array of organometallic reagents were developed, which allow to overcome the limitations of the synthetic scope of Grignard reagents. For example, cross-coupling reactions of aryl halides have been realized by a variety of transition metal catalysts.[1e] As a result of these developments, the synthesis of a high number of complex molecules and natural products has become viable in the last decades. This important development in organometallic chemistry has led to award Y. Chauvin, R. H. Grubbs (ruthenium catalysts), and R. R. Schrock (molybdenum catalyst) with the Nobel Prize in 2005 for developing the olefin metathesis reaction, and in (2010) to Ei-ichi Negishi[2], Akira Suzuki[3] and Richard Heck for establishing economic and environmentally-friendly approaches for building carbon-carbon bonds.

1.2 Palladium Chemistry

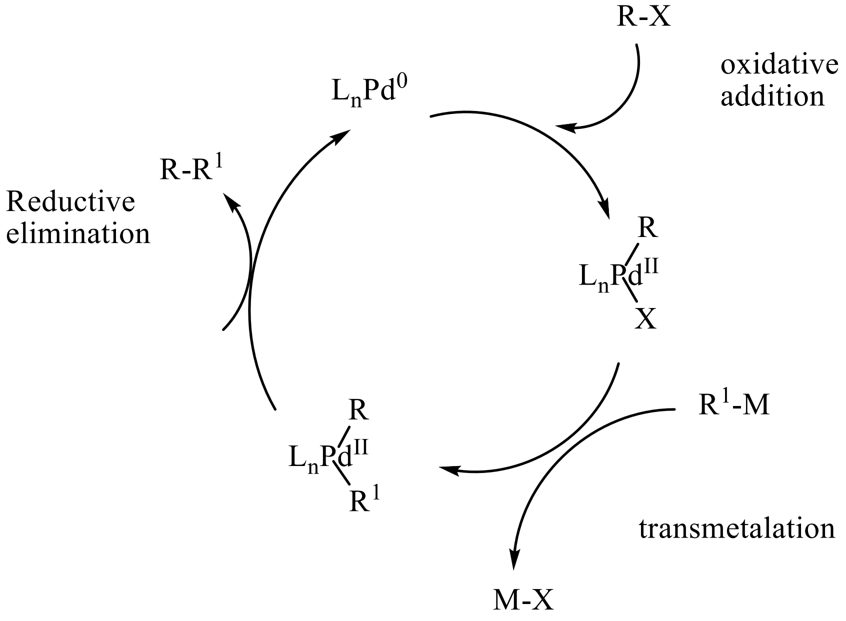
During recent decades, the so-called palladium-(0)-catalyzed reactions have been developed in large areas of organic chemistry[4], for example, in medical and pharmacological chemistry.[5] There are different types of palladium-catalyzed cross-coupling reactions[6,7], which are known in organic synthesis, such as Suzuki, Heck, Stille, Sonogashira, Tsuji-Trost and Negishi reaction. Several groups have been working in the field of organometallic chemistry which developed many reagents based on the chemistry of palladium.



Scheme 1 Palladium-(0)-catalyzed cross-coupling reactions.

The general mechanism of palladium-catalyzed cross-coupling reactions consists of three key steps[7a,b], which involves;

1. Oxidative addition, which includes formation of organometallic intermediate by addition of aryl electrophile to palladium, such as aryl halides or triflates (in this case the oxidation state of palladium-(0)-species will be changed into palladium-(II)-species).[8,9]
2. Transmetallation process, where the organic moiety is transferred from a main group metal, such as Mg (Kumada reaction), Cu (Sonogashira reaction), Zn (Negishi reaction), B (Suzuki reaction) or Sn (Stille reaction), to a metal which is more electronegative, such as palladium to give a diorgano palladium complex.
3. Reductive elimination, where the product is formed and the catalyst is regenerated again.[10,11] (Scheme 2).



Suzuki-Miyaura

Scheme 2 General catalytic cycles for Suzuki-Miyaura reaction.

1.3 Palladium-Catalyzed Suzuki-Miyaura Reaction

The coupling of aryl halides with organoboronic acids is one of the most important palladium-catalyzed cross-coupling reactions for both academic and industrial applications. This reaction may be defined as a reaction between aryl and vinyl-boronic acid with an aryl or vinyl-halide catalyzed by a Palladium-(0)-complex.[12]

$$\text{R-X} \quad + \quad \text{R}^1\text{-BY}_2 \xrightarrow[\text{base}]{\text{Pd(0)}} \text{R-R}^1$$

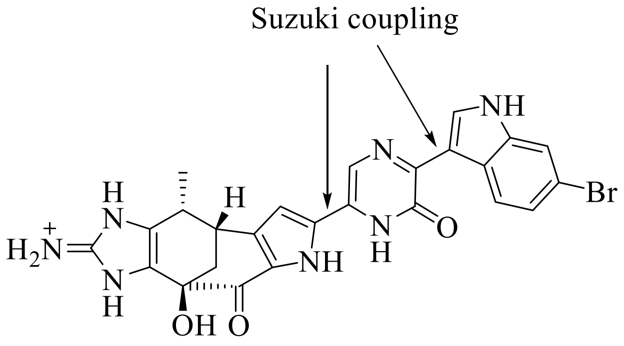
R= alkyl, vinyl, benzyl, aryl, alkenyl
R^1=alkyl, alkinyl, aryl, vinyl
X= Cl, Br, OTf, I

Scheme 3 Palladium-Catalyzed Suzuki coupling.

This reaction is widely used to synthesize poly-olefins, styrenes, and substituted biphenyls and the first work for this reaction was published in 1979 by Akira Suzuki and coworkers.[13] The organboranes and boronic acid in this reaction are very powerful partners. They are commercially available, easy to handle, and relatively tolerant to air and to another functional groups. The main advantages of this reaction are the low temperature, low pressure, high yield, and the nontoxic by-products. Moreover, boron compounds are generally non-toxic. Consequently, all of these mild conditions make this reaction very interesting in the pharmaceutical and chemical industry.[14]

1.4 Applications of Suzuki Coupling Reactions

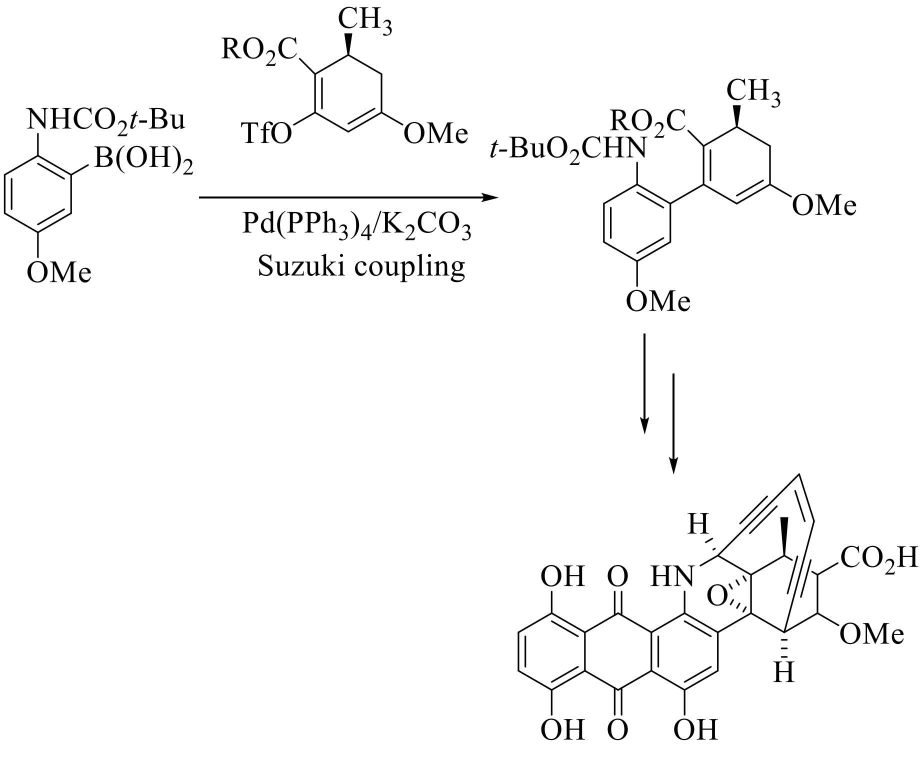
The palladium-catalyzed cross-coupling reactions are important for the pharmacology and the chemical industry, and also in a big area for the synthesis of many important natural products. Thus, the palladium-catalyzed cross-coupling reactions are suitable for wide applications. In the following I present some examples for the use of palladium-catalyzed cross coupling reactions. The Suzuki reaction was used for preparing the antiviral brominated indole alkaloid dragmacidin-F.[15]



Dragamacidin F

Scheme 4 Synthesis of dragamacidin F via palladium-catalyzed Suzuki reaction.

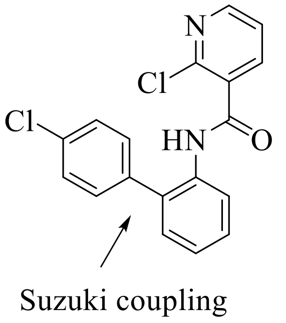
Another application for the Suzuki reaction is the synthesis of the anti-cancer agent (+)-dynemicin A (Scheme 5).[16]



(+)-dynemcin A

Scheme 5 Synthesis of (+)-dynemicin A via palladium-catalyzed Suzuki reaction.

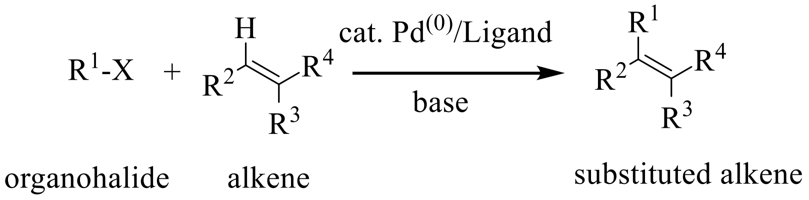
In the chemical industry, the Suzuki reaction could be used for the synthesis of industrial products, such as the drug Boscalid.[17]



Scheme 6 Synthesis of Boscalid via palladium-catalyzed Suzuki reaction.

1.5 Heck reaction

Heck reaction is considered one of the most powerful synthetic tool which includes formation of C-C bond from coupling inactive C-H alkene bonds and (organ halides or triflates) by using palladium as a catalyst and in presence of a base (Scheme 7).[17c]



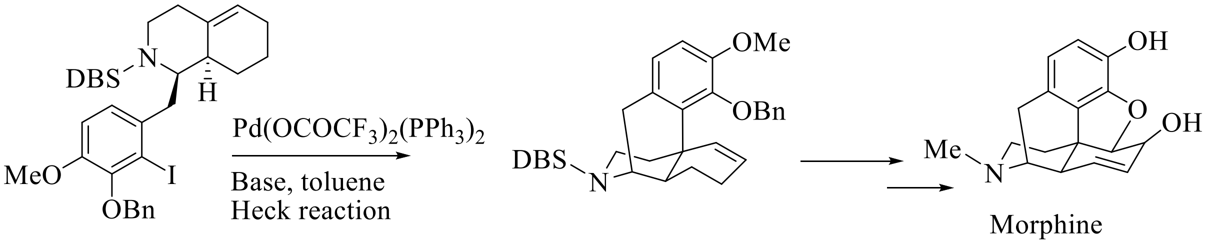
R^1 = alkyl, aryl. vinyl

X = Cl, Br, I, OTf

Scheme 7 Palladium catalyzed Heck coupling reaction.

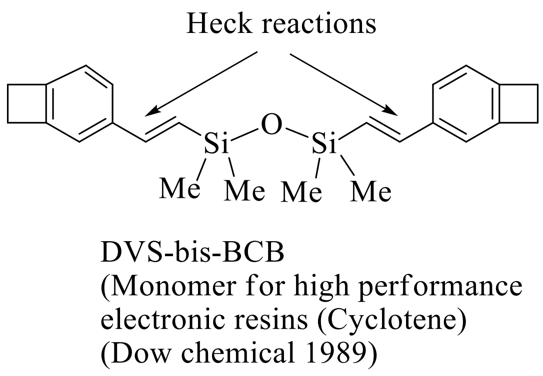
1.6 Applications of Heck Coupling Reaction

The Heck-reaction is one of the most important palladium-catalyzed cross-coupling reactions, which could be used for the synthesis of natural products, such as morphine.[18]



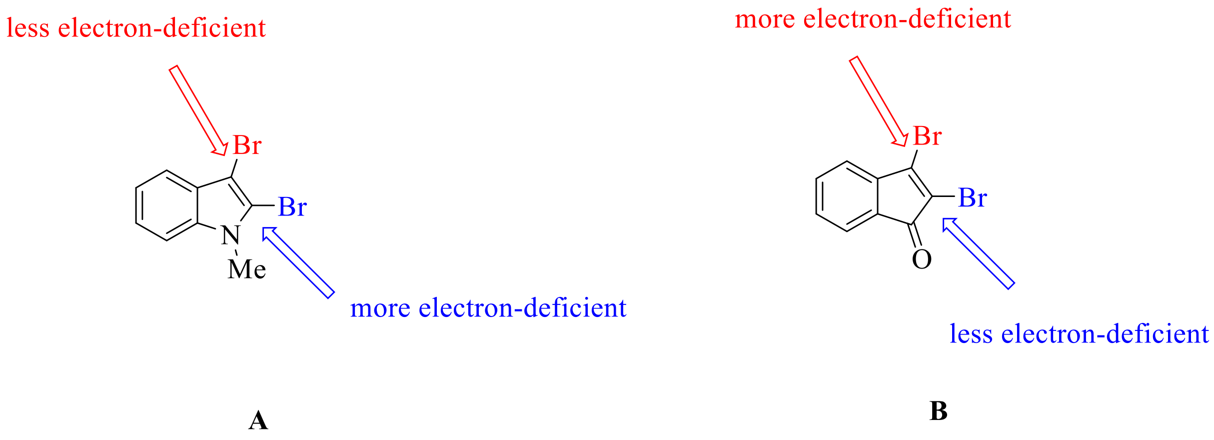
Scheme 8 Synthesis of morphine via palladium-catalyzed Heck reaction.

The Heck reaction has been used also in the chemical industry for the synthesis of several new products, such as fine chemicals[19] as shown in Scheme 9.



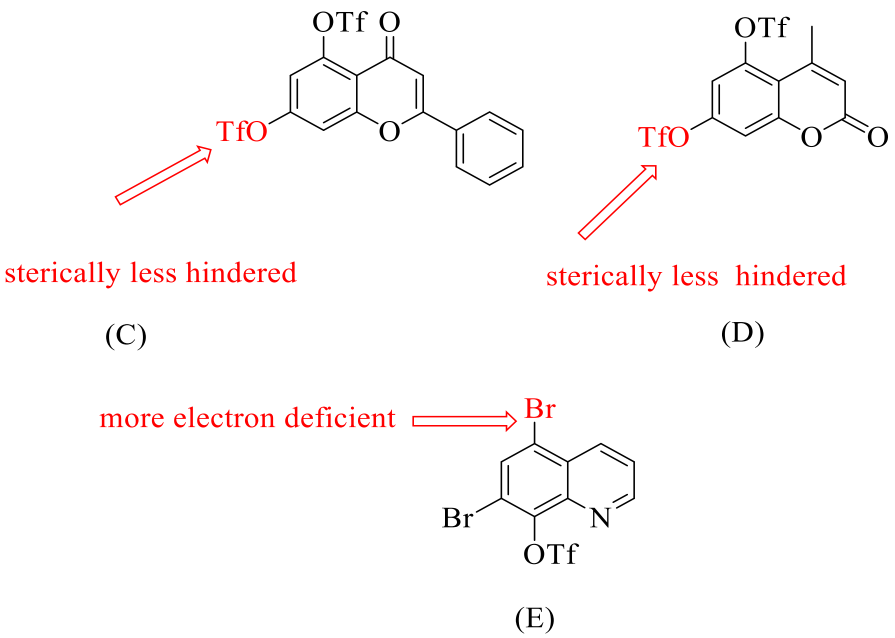
Scheme 9 Synthesis of cyclotene via palladium-catalyzed Heck reaction.

In the last years Prof. Langer's group has extensively studied selective Suzuki-Miyaura cross-coupling reactions preparing some unsymmetrical arylated pharmacologically relevant compounds. For example, the site-selective Suzuki coupling reaction of indole **A** was found to be in favor of the 2-position. This can be explained according to the sufficient difference in the electronic character of C-2 and C-3.[19a] Also, 2,3-dibromoindenone **B** gives an excellent site-selectivity, where the first attack occurred at position 3[19b] (Scheme 10).



Scheme 10 Site-selectivity of **A** and **B.**

Furthermore, the following reactions show examples of site-selective Suzuki coupling reactions. For example, the reactions of the bis(triflate) of 5,7-dihydroxyflavone **C** and of the bis(triflate) of 5,7-dihydroxycoumarine **D** proceed favorably at the 7-position.[19c,19d] In both cases, the reason of the site-selectivity at position 7 in the coumarin and the flavone core structure can be explained by steric effects. The chemo-selective Suzuki coupling reaction of 5,7-dibromo-8-(trifluoromethanesulfonyloxy)quinoline, containing bromide groups in the presence of a triflate, proceeds favorably at the 5-position **E**[19e], because of the more electron deficient and sterically less hindered character of that particular position (Scheme 11).



sterically less hindered

sterically less hindered

(C)

(D)

more electron deficient

(E)

Scheme 11 Site-selectivity of Suzuki reactions of **C** and **D** and of the chemo-selectivity of the reactions of **E**.

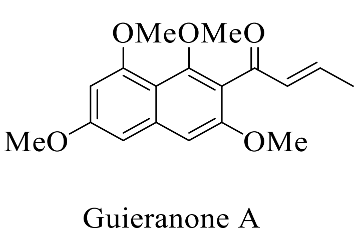
CHAPTER TWO

2 Synthesis of arylated naphthoates by site-selective Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of methyl 3,7-dihydroxy-2-naphthoate

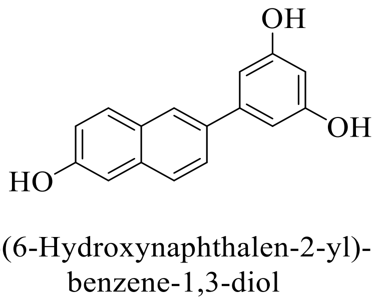
2.1 Introduction

Substituted naphthalenes are important lead structures in medicinal chemistry.[20] They also act as intermediates in the synthesis of organic dyes and surfactants and as supporting agents in polymer industry.[21] Naphthalenes derivatives exhibit a broad range of pharmacological activities, such as antimicrobial activity[22] and activity as antibody inhibitors.[23] Naphthalenes derivatives are found in a number of natural products. Examples include guieranone A which shows potent antifungal activity against *Cladosporium cucumerinum* (Figure 1).[24] Michellamine A, isolated from *Ancistrocladus korupensis*, has attracted the scientific community primarily because of its interesting binaphthyl structure and its antimalaria and anti-HIV activity.[25,26] In contrast, 5-(6-hydroxynaphth-2-yl)benzene-1,3-diol was found to be very active against human breast cancer cell line B. Konzik *et al.* reported that aryl substituents of naphthalenes have a strong influence on their fungistatic activity.[27] Therefore, arylated naphthalenes are of considerable pharmacological relevance.

Many methods have been used for the preparation of substituted naphthalenes. For example, 2-substituted naphthalenes were prepared by application of the Baylis–Hillman reaction,[28] or by irradiation of 2-allylacylbenzenes in DMF.[29] Other methods include transition-metal-catalyzed [2+2+2] alkyne cyclizations,[30] Lewis acid catalyzed cyclizations of carbonyl compounds with alkynes and [4+2] cycloadditons.[31] An alternative approach relies on the functionalization of naphthalenes by palladium catalyzed cross-coupling reactions. Recently, Prof. Langer‘s group has reported the synthesis of arylated naphthalene by chemo- and site-selective Suzuki-Miyaura reactions of naphthalene derivatives.[32] Herein, I report what is, to the best of my knowledge, the first site-selective Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of methyl 3,7-dihydroxy-2-naphthoate.



Guieranone A

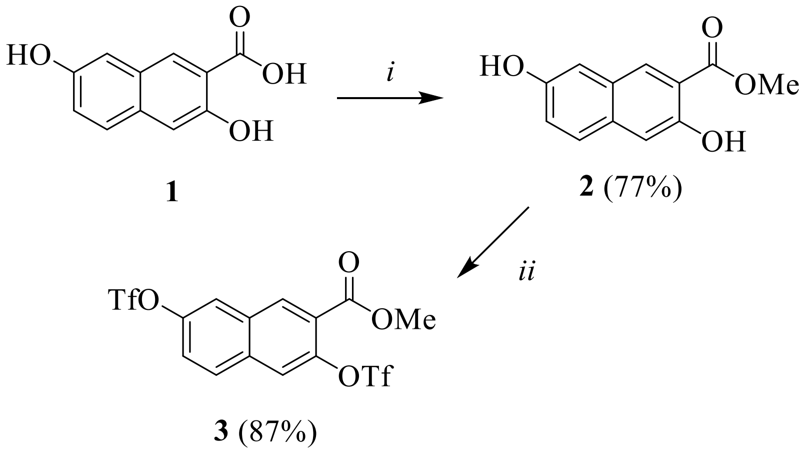


5-(6-Hydroxynaphthalen-2-yl)-benzene-1,3-diol

Figure 1 Pharmacologically important naphthalene derivatives.

2.2 Results and discussion

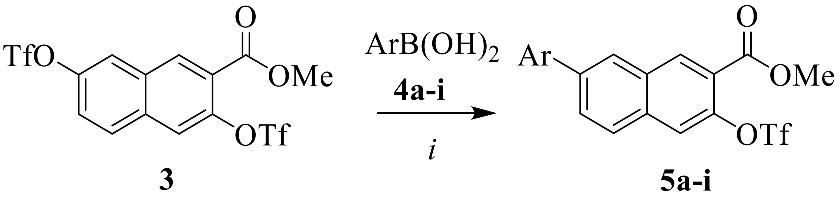
Commercially available 3,7-dihydroxy-2-naphthoic acid (**1**) was transformed into methyl 3,7-dihydroxy-2-naphthoate (**2**) which was converted to bis(triflate) **3** in high yield (Scheme 12).



Scheme 12 Synthesis of **3**. Conditions: *i*, **1** (1.0 equiv.), Me_2SO_4 (2.2 equiv.), DIPEA (1.1 equiv.), DMF, 85 °C, 1 h; *ii*, 1) **2** (1.0 equiv.), pyridine (4.0 equiv.), CH_2Cl_2, -78 °C, 10 min; 2) Tf_2O (2.4 equiv.), -78 → 0 °C, 4 h.

The Suzuki-Miyaura reaction of **3** with arylboronic acids **4a-i** (1.2 equiv.), in the presence of $Pd(PPh_3)_4$ (3 mol-%) and K_3PO_4 (1,5 equiv.) (THF, 20 °C, 9 h), afforded the 7-aryl-3-(trifluoromethanesulfonyloxy)-2-naphthoates **5a-i** in 70-85% yields (Scheme 13, Table 1). The reactions proceeded with very good site-selectivity in favor of position 6.

During the optimization, it proved to be important to carry out the reactions at 20 °C. Higher temperatures resulted in the formation of significant amounts of diarylated products. Very good yields were obtained for products derived from both electron poor and rich arylboronic acids. The structure of **5e** was independently confirmed by X-ray crystal structure analysis (Figure 2).



Scheme 13 Synthesis of **5a-i**. Conditions: *i*, **3** (1.0 equiv.), **4a-i** (1.2 equiv.), $Pd(PPh_3)_4$ (3 mol-%), K_3PO_4 (1,5 equiv.), THF, 20 °C, 9 h.

Table 1 Synthesis of **5a-i**

4	**5**	Ar	%(**5**)[a]
a	**a**	3,5-MeC_6H_3	70
b	**b**	3-MeC_6H_4	77
c	**c**	4-ClC_6H_4	80
d	**d**	4-EtC_6H_4	84
e	**e**	4-(MeO)C_6H_4	83
f	**f**	4-MeC_6H_4	78
g	**g**	4-(EtO)C_6H_4	82
h	**h**	3-(MeO)C_6H_4	85
i	**i**	3-FC_6H_4	82

[a] Yields of isolated products

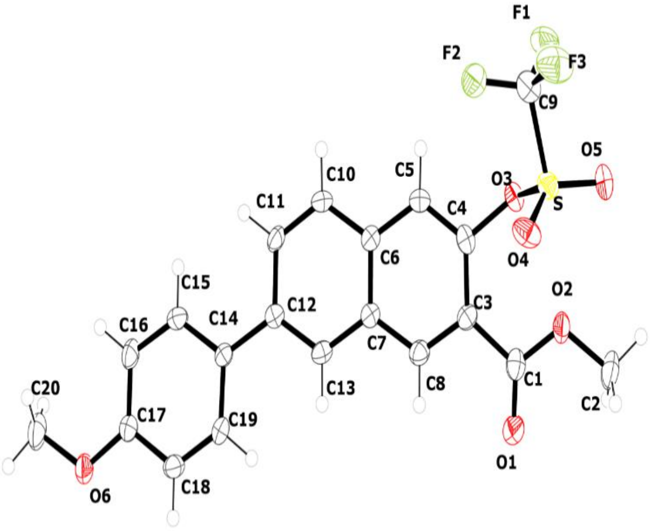
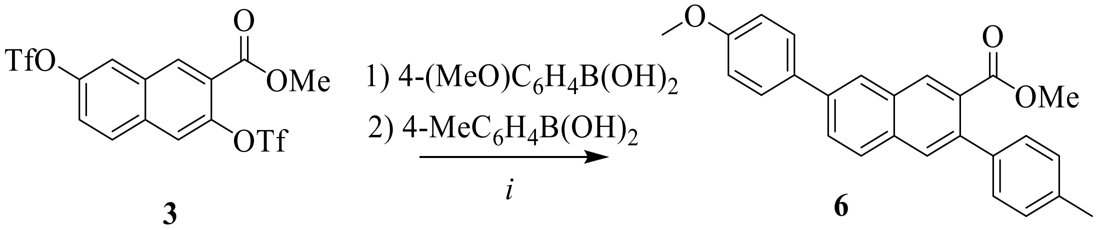


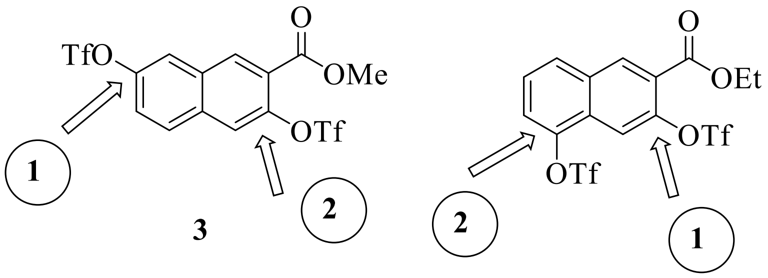
Figure 2 X-ray crystal structure of **5e.**

The one-pot reaction of **3** with two different arylboronic acids (sequential addition of the arylboronic acid) afforded 3,7-diaryl-2-naphthoate **6** in 45% yield . The reaction was carried out at 20 °C for the first step (to avoid double coupling) and at 105 °C in the second step. An additional amount of catalyst and base had to be added together with the second arylboronic acid.



Scheme 14 Synthesis of **7**. Conditions: *i*, 1) **3** (1.0 equiv.), 4-(MeO)$C_6H_4B(OH)_2$ (1.0 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (3 mol-%), THF, 20 °C, 9 h; 2) 4-Me$C_6H_4B(OH)_2$ (1.0 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 1,4-dioxane, 105 °C, 8 h.

Palladium catalyzed cross-coupling reactions usually occur at the electronically more deficient and sterically less hindered position.[33,34] Prof. Langer‘s group has previously reported that Suzuki-Miyaura reactions of the bis(triflate) of phenyl 1,4-dihydroxy-2-naphthoate proceed site-selectively at the more electron deficient, sterically more hindered position 1 located next to the ester group. Also Prof. Langer‘s group has reported that Suzuki-Miyaura reactions of the bis(triflate) of ethyl 3,5-dihydroxy-2-naphthoate (**3.1a**) proceed site-selectively at the more electron deficient, sterically more hindered position 3 located next to the ester group.[35] The selectivity was explained by the electron-withdrawing effect of the ester group and by a catalyst-direting effect of the ester group (chelation control). In case of the bis(triflate) of methyl 3,7-dihydroxy-2-naphthoate (**3**), the reactions proceed with very good site-selectivity in favour of the less electron deficient, sterically less hindered position 7. Therefore, the results are, on the first glance, in contrast to my previous results on substrate **3.1a**. However, the findings might be explained as follows: Position 7 of substrate **3** is less sterically hindered than position 5 of substrate **3.1a**, due to the steric effect of the annulated ring (hydrogen atom at position 1). Therefore, in case of **3**, the easy steric accessibility of position 7 seems to overrule the electron deficient character of position 3. In contrast, this is not possible for substrate **3.1a**, because of the considerable steric demand of position 5.



3

This work

Ref. 3.1a

Scheme 15 Site-selectivity of Suzuki–Miyaura reactions of **3** and **3.1a**.

2.3 Conclusion

In conclusion, I have reported site-selective Suzuki-Miyaura reactions of the bis(triflate) of methyl 3,7-dihydroxy-2-naphthoate. These reactions provide a convenient approach to arylated naphthalene which are not readily available by other methods.

CHAPTER THREE

3 Synthesis of arylated naphthoates by chemo-selective Suzuki-Miyaura cross- coupling reactions of methyl 4-bromo-3-(trifluoromethanesulfonyloxy)-2-naphthoate

3.1 Introduction

Naphthalenes derivatives exhibit a broad range of pharmacological activities, occur in many natural products, for example, Azinomycin A and B (Figure 3) were isolated from Streptomyces exhibit promising activities against leukemia, Ehrlich carcinoma, Lewis lung carcinoma and Meth A fibrosarcoma.[36] Substituted 2-naphthoates represent an important subgroup of naphthalene which show a wide range of pharmacological properties, such as cancerostatic activity.[37] Several synthetic methods such as Baylis–Hillman reaction, transition-metal-catalyzed [2+2+2] alkyne cyclizations, Lewis acid catalyzed cyclizations and [4+2] cycloadditons have been developed for synthesizing substituted naphthalenes.[38] Recently, Prof. Langer’s group has reported the synthesis of arylated 2-naphthoates by site-selective Suzuki–Miyaura reactions of bis(triflates) of dihydroxy-2-naphthoates.[39] Prof. Langer’s group has started a program studying Suzuki–Miyaura reactions of several substrates containing a triflate and a bromide leaving group.[40] These compounds generally reacted first at the bromide position. This was in agreement with earlier reports which showed that, in case of Suzuki–Miyaura reactions, aryl bromides are generally more reactive than aryl triflates, because of the stability of the boron–bromine bond formed during the reaction.[41] As a part from the program, I studied the influence of some parameters, such as the structure of the substrate, on the chemo-selectivity Br/OTf. Herein, I report what is, to the best of my knowledge, the first Suzuki–Miyaura reactions of methyl 4-bromo-3-(trifluoromethylsulfonyloxy)-2-naphthoate. These reactions proceed with very good chemoselectivity in favor of the triflate rather than the bromide group. The change of the chemoselectivity from Br to OTf can be explained by additive electronic *ortho* effects.

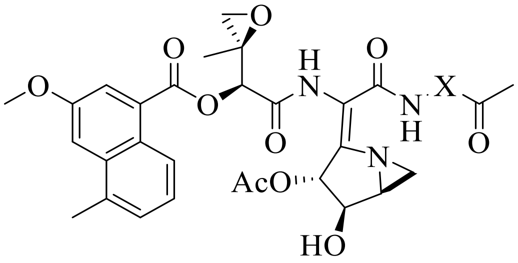
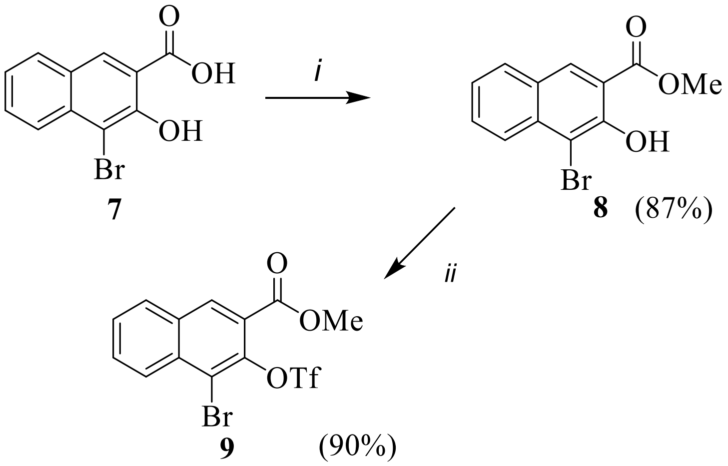


Figure 3 Azinomycin A X=CH_2, Azinomycin B X=CHCHO.

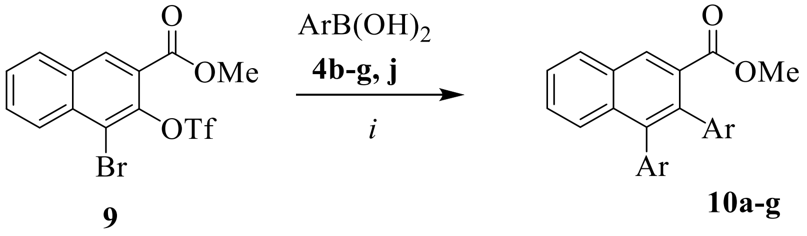
3.2 Results and discussion

The DIPEA mediated reaction of 4-bromo-3-hydroxy-2-naphthoic acid (**7**) with dimethyl sulfate afforded methyl 4-bromo-3-hydroxy-2-naphthoate (**8**) which was transformed into methyl 4-bromo-3-(trifluoromethylsulfonyloxy)-2-naphthoate (**9**) by reaction with triflic anhydride (Scheme 16).



Scheme 16 Synthesis of **9**. Conditions: *i*, **7** (1.0 equiv), Me_2SO_4 (2.2 equiv), DIPEA (1.1 equiv), DMF, 85 °C, 1 h; (*ii*) **8** (1.0 equiv), pyridine (4.0 equiv), CH_2Cl_2, Tf_2O (2.4 equiv), 50 °C, 20 min.

The Suzuki–Miyaura reaction of **9** with arylboronic acids **4b–g, j** (2.4 equiv) afforded methyl 3,4-diaryl-2-naphthoates **10a**–**g** in 69–93% yield (scheme 17) and both electron-poor and electron-rich arylboronic acids were successfully employed, but the yields of the products derived from the (more nucleophilic) electron-rich arylboronic acids were higher (except for **10a**). Very good yields were obtained under standard conditions, using $Pd(PPh_3)_4$ (6 mol %) as the catalyst, K_2CO_3 (2M, 2 mL) as the base, and 1,4-dioxane as the solvent (120 °C, 6 h). The use of 2-methylphenylboronic acid afforded the desired product which, however, could not be isolated in pure form (difficult chromatographic purification due to formation of side-products).



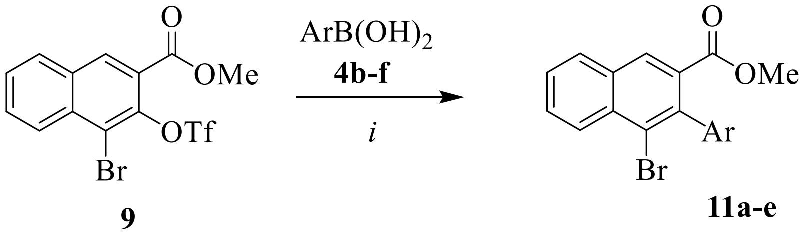
Scheme 17 Synthesis of **10a-g**. Conditions: *i*, **9** (1.0 equiv), **4b–g, j** (2.4 equiv), $Pd(PPh_3)_4$ (6 mol %), K_2CO_3 (2M, 2 mL), 1,4-dioxane, 120 °C, 6 h.

Table 2 Synthesis of **10a-g**

4	10	Ar	%(**10**)[a]
b	**a**	$3\text{-}MeC_6H_4$	72
c	**b**	$4\text{-}ClC_6H_4$	69
d	**c**	$4\text{-}EtC_6H_4$	81
e	**d**	$4\text{-}(MeO)C_6H_4$	86
f	**e**	$4\text{-}MeC_6H_4$	78
g	**f**	$4\text{-}(EtO)C_6H_4$	93
j	**g**	$4\text{-}(CF_3)C_6H_4$	73

[a] Yield of isolated products

The Suzuki–Miyaura reaction of **9** with 1.0 equiv of arylboronic acids **4b–f** afforded 3-aryl-4-bromo-2-naphthoates **11a–e** in 76–92% yield and the reactions proceeded with very good chemoselectivity in favor of the triflate group. 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 60 °C instead of 120 °C to avoid double coupling. Both electron-poor and electron-rich aryl boronic acids were successfully employed. The yields of the products derived from electron-rich arylboronic acids were again higher. The structures of the products were easily confirmed by the fact that, in the ^{13}C NMR spectra, the characteristic quartet of the CF_3 group disappeared. The structure of **11d** was independently confirmed by X-ray crystal structure analysis (Figure 4).



Scheme 18 Synthesis of **11a-e**. Conditions: *i*, **9** (1.0 equiv), **4b–f** (1.0 equiv), $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (2M, 2 mL), 1,4-dioxane, 60 °C, 9 h.

Table 3 Synthesis of **11a-e**

4	**11**	Ar	% (**11**)[a]
b	**a**	3-MeC_6H_4	83
c	**b**	4-ClC_6H_4	76
d	**c**	4-EtC_6H_4	88
e	**d**	4-(MeO)C_6H_4	92
f	**e**	4-MeC_6H_4	79

[a]Yields of isolated

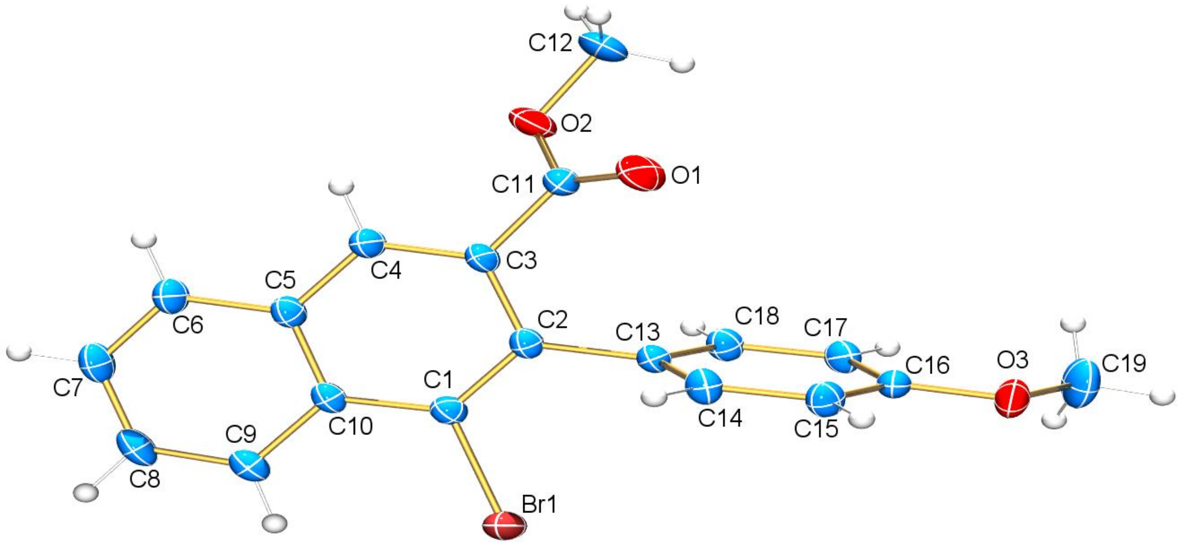
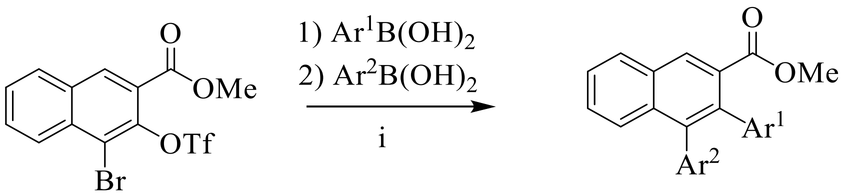


Figure 4 X-ray crystal structure of **11d.**

The one-pot reaction of **9** with two different arylboronic acids (sequential addition) afforded the methyl 3,4-diaryl-2-naphthoates **12a**–**c**, containing two different aryl groups, in 71–86% yield and both electron-poor and electron-rich arylboronic acids were successfully employed. The best yield was obtained for product **12b** derived from two electron-rich arylboronic acids. The lowest yield was obtained for product **12c** where an electron-poor arylboronic acid was employed in the first step.



9

12a-c

Scheme 19 Synthesis of **12a**–**c**. Conditions: *i*,(1) **9** (1.0 equiv), $Ar^1B(OH)$, $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (2M, 2 mL), 1,4-dioxane, 60 °C, 9 h; (2) $Ar^2B(OH)$ (1.2 equiv), $Pd(PPh_3)_4$ (6 mol %), K_2CO_3 (2M, 2 mL), 1,4-dioxane, 120 °C, 6 h.

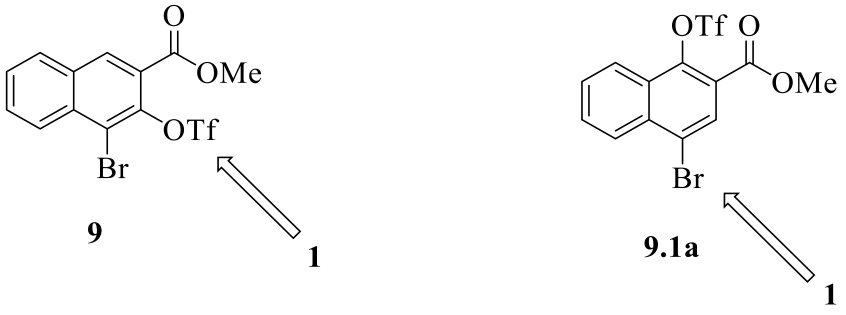
Table 4 Synthesis of **12a-c**

4	**12**	Ar^1	Ar^2	% (**12**)^a
d, j	**a**	4-EtC$_6$H$_4$	4-(CF$_3$)C$_6$H$_4$	79
f, e	**b**	4-MeC$_6$H$_4$	4-(MeO)C$_6$H$_4$	86
c, d	**c**	4-ClC$_6$H$_4$	4-EtC$_6$H$_4$	71

^{a}Yields of isolated Product.

3.3 Conclusion

In conclusion, I have reported that Suzuki–Miyaura reactions of methyl 4-bromo-3-(trifluoromethylsulfonyloxy)-2-naphthoate (**9**) proceeded by chemoselective attack to carbon atom C-3 attached to the triflate group. In contrast, Prof. Langer's group reported earlier that Suzuki–Miyaura reactions of 2-acetyl-4-bromo-1-(trifluorosulfonyloxy)naphthalene (**9.1a**) proceeded by chemoselective attack to carbon atom C-4 attached to the bromine atom.[41a]



Scheme 20 Chemoselectivity of Suzuki–Miyaura reactions of **9** and **9.1a**.

It was mentioned above that, in the case of Suzuki–Miyaura reactions, aryl bromides are usually more reactive than aryl triflates. It is known that palladium catalyzed cross-coupling reactions proceed selectively in favor of the sterically less hindered and electronically more deficient position.[42, 43]

In addition, a carbonyl group can act as a catalyst-directing group (by chelation of the oxygen lone pairs to the metal). Carbon atoms C-3 and C-1 of substrates **9** and **9.1a**, both attached to a triflate group, are more electron deficient than position C-4 of both substrates, because of the neighboring ester group, respectively. On the other hand, the ester carbonyl group can more efficiently chelate to the catalyst, due to the π-donating effect of the methoxy oxygen atom. Therefore, I believe that the chemoselectivity of the Suzuki–Miyaura reactions of **9** might be explained by additive electronic *ortho* effects, while the selectivity in case of **9.1a** is a result of steric effects.

CHAPTR FOUR

4 Synthesis of arylated coumarins by site-selective Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of 4,7-dihydroxycoumarin

4.1 Introduction

Neoflavones (4-arylcoumarins) are of considerable pharmacological relevance and occur in several natural products and synthetic drugs.[44] Natural and synthetic neoflavones have been reported to exhibit various kinds of pharmacological activities, such as anticancer,[45] antimalarial,[46] antibacterial,[47] antiprotozoal,[48] antivirus,[49] antidiabetic,[50] cytotoxic,[51] and anti-inflammatory activity.[52] Merck developed a 7-substituted 4-arylcoumarin as a 5-lipoxygenase inhibitor for the treatment of inflammatory diseases such as asthma, chronic obstructive pulmonary disease and atherosclerosis (Figure 5).[53] As a result of the promising biological and pharmacological activities of neoflavones, several strategies have been developed for the construction of the 4-arylcoumarin framework. Classically, neoflavones have been synthesized using the Pechmann, Perkin, Ponndorf, Houben-Hösch and Knoevenagel reactions.[54] In recent years, transition metal catalyzed reactions have emerged as vital synthetic tools for the preparation of pharmacologically relevant heterocycles. Two synthetic strategies have been developed for the assembly of the neoflavone framework: the first one involves the formation of the pyrone ring by hydroarylation of alkynes,[55] or by reaction of the alkenyl C-H bond with carbon dioxide.[55] The second one relies on cross-coupling reactions of position 4 of activated coumarins with organometallic reagents.[57]

In recent years, site-selective cross coupling reactions of bis(halides) or bis(triflates) have been developed as a promising synthetic tool.[58] In this context, palladium catalyzed cross-coupling reactions of coumarin derivatives have also been reported.[59] Herein, I report what is, to the best of my knowledge, the first Suzuki-Miyaura coupling reaction of the bis(triflate) of 4,7-dihydroxycoumarin. The reactions, which proceed with excellent regioselectivity in favor of position 4, provide a convenient approach to various arylated coumarin derivatives which are not readily available by other methods.

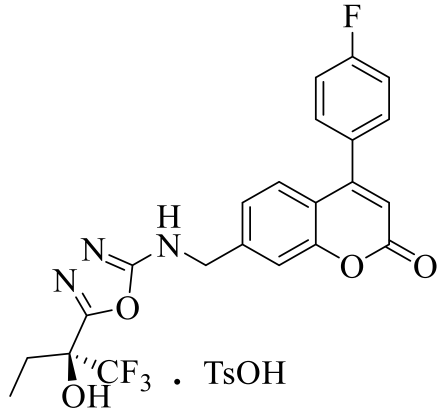
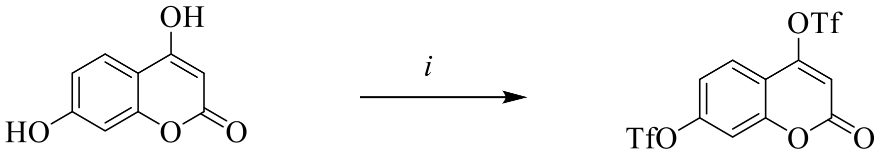


Figure 5 A 5-lipoxygenase inhibitor developed by Merck.

4.2 Results and discussion

The reaction of 4,7-dihydroxycoumarin (**13**) with triflic anhydride gave bis(triflate) (Scheme 21).

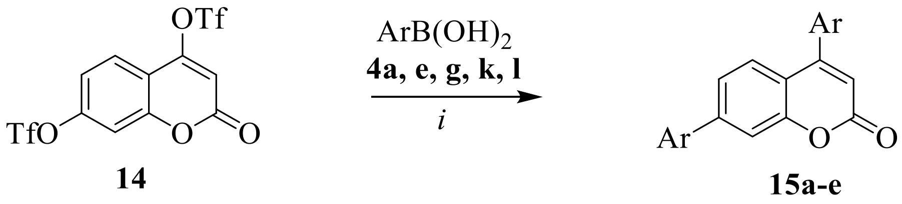


13

14

Scheme 21 Synthesis of **14**. Conditions: *i*, **13** (1.0 equiv.), pyridine (4.0 equiv.), CH_2Cl_2, Tf_2O (2.4 equiv.), 50°C, 4 h.

The Suzuki–Miyaura reaction of **14** with arylboronic acids **4a, e, g, k, l** (2.4 equiv) afforded 4,7-diarylcoumarins **15a-e** in 66-81% yield (Scheme 22, Table 5). Both electron rich and poor arylboronic acids were successfully employed.



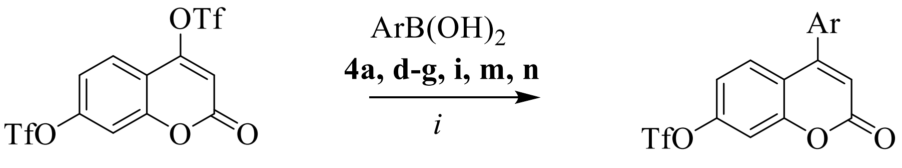
Scheme 22 Synthesis of **15a-e**. Conditions: *i*, **14** (1.0 equiv.), **4a, e, g, k, l** (2.4 equiv.), $Pd(PPh_3)_4$ (6 mol %), K_2CO_3 (2M, 2 mL), 1,4-dioxane, 110 °C, 8 h.

Table 5 Synthesis of **15a-e**

4	**15**	Ar	% (**15**)[a]
a	**a**	3,5-MeC_6H_3	81
e	**b**	4-(MeO)C_6H_4	68
g	**c**	4-(EtO)C_6H_4	66
k	**d**	C_6H_5	79
l	**e**	3,5-(MeO)C_6H_3	69

[a]Yields of isolated product.

The Suzuki–Miyaura reaction of **14** with one equivalent of arylboronic acids afforded the 4-aryl-7-(trifluormethanesulfonyloxy)-coumarins **16a-h** in 64-82 % yield (Scheme 23, Table 6). The reactions proceeded by site-selectivity attack onto 4-position. During the optimization, it proved to be important to carry out the reaction at lower temperature (65 °C) as compared to the synthesis of the diarylated coumarins. In addition, the employment of toluene (instead of 1,4-dioxane) proved to be important to avoid formation of diarylated products. Again, both electron rich and poor arylboronic acids gave good yields. The structure of **16a** was independently confirmed by X-ray crystal structure analyses (Figure 6).



14 **16a-h**

Scheme 23 Synthesis of **16a-h**. Conditions: *i*, **14** (1.0 equiv.), **4a, d-g, i, m, n** (1.0 equiv.), $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (2M, 2 mL), toluene (3 mL), 65 °C, 6 h.

Table 6 Synthesis of **16a-h**

4	**16**	Ar	% (**16**)[a]
a	**a**	3,5-MeC_6H_3	82
d	**b**	4-EtC_6H_4	73
e	**c**	4-$(MeO)C_6H_4$	71
f	**d**	4-MeC_6H_4	70
g	**e**	4-$(EtO)C_6H_4$	78
i	**f**	3-FC_6H_4	64
m	**g**	4-$(OCF_3)C_6H_4$	65
n	**h**	2,3,4-$(MeO)C_6H_2$	67

[a] Yield of isolated products

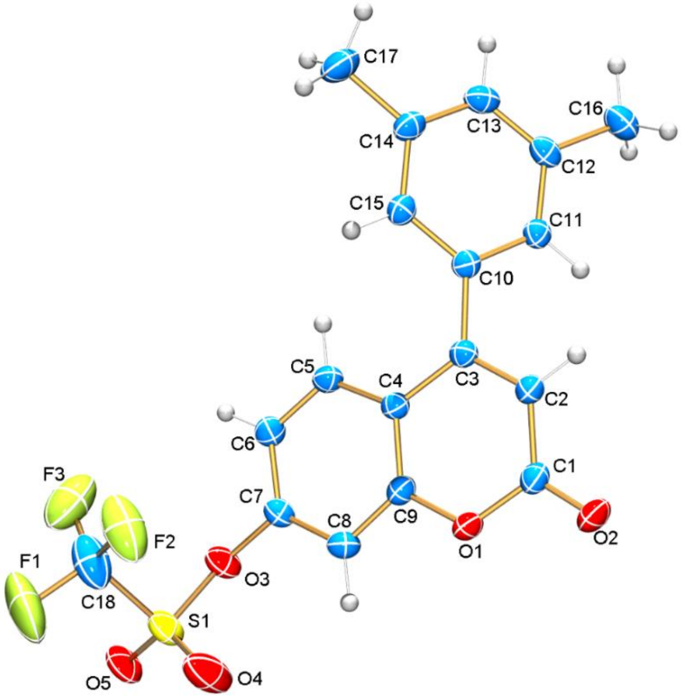
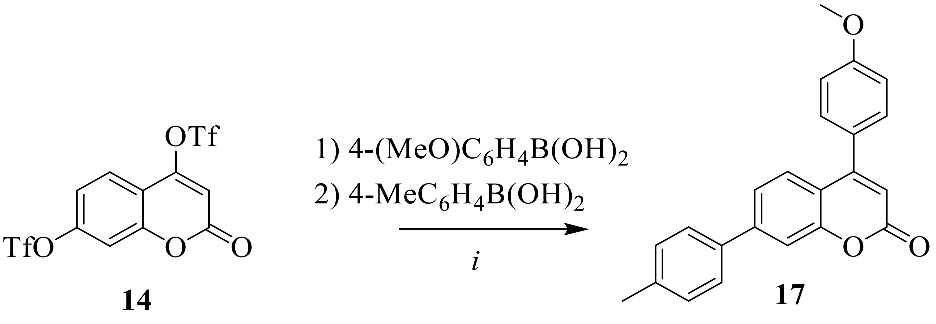


Figure 6 X-ray crystal structure of **16a.**

The one-pot reaction of **14** with two different arylboronic acids (sequential addition) afforded the diarylated coumarin **17** in 84 % yield (Scheme 24). A fresh portion of the catalyst and of solvent (1,4-dioxane) had to be added to the reaction mixture in the second step in order to obtain a good yield of diarylated coumarin **17**.



Scheme 24 Synthesis of **17.** Conditions: *i*, 1) **14** (1.0 equiv.), 4-(MeO)$C_6H_4B(OH)_2$ (1.0 equiv.), $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (2M, 2 mL), toluene, 65 °C, 6 h.; 2) 4-Me$C_6H_4B(OH)_2$ (1.2 equiv.), $Pd(PPh_3)_4$ (6 mol %), K_2CO_3 (2M, 2 mL), 1,4-dioxane, 110 °C, 6 h.

4.3 Conclusion

In conclusion, I have reported the first Suzuki–Miyaura reactions of 4,7-bis(trifluoromethylsulfonyloxy)coumarin. These reactions provide a convenient access to a variety of arylated coumarins. The reactions proceeded with very good site-selectivity in favor of 4-position. Palladium catalyzed cross-coupling reactions of polyhalogenated substrates or of bis(triflates) usually proceed in favor of the sterically less hindered and electronically more deficient position. Position 4 is sterically more hindered than position 7, due to its location next to the annulated benzene ring. The selectivity can be explained by the highly electron deficient character of the 4-position of the coumarin moiety (electron-withdrawing effect of the carbonyl group).

CHAPTER FIVE

5 Synthesis of arylated quinolines by chemo-selective Suzuki-Miyaura cross-coupling reactions of 5-bromo-quinolin-8-yl-trifluoromethanesulfonate

5.1 Introduction

Arylated quinolines exhibit a wide range of pharmacological and biological activities, such as antivirus[60], antimalarial, antitumor and P-selecting antagonism.[61] They are also promising agents for the treatment of acromegaly[62] and diabetic retinopathy.[63] As a result of their therapeutic value, many synthetic approaches have recently been developed. The classic condensation-type approaches for the synthesis of arylated quinolines include the Skraup, Doebner-Miller, Friedländer, Combes, Pfitzinger and Povarov reactions.[64] Cross-coupling reactions have become an efficient synthetic tool in the synthesis of arylated quinolines and quinolines as well.[65] Also, new transition metal catalytic systems have been developed for construction of arylated quinoline frameworks such as, Rh(III)-catalyzed oxidative annulations of pyridines,[66] Pd-catalyzed hetero-Diels-Alder reactions between imines and olefins,[67] Ru(I)-catalyzed coupling cyclizations of N-aryl imidoyl chloride with alkynes,[68] Ru(II)- catalyzed Friedländer annulations[69] and Pd-catalyzed regioselective hydroarylations of α-(2-aminoaryl)-α,β-alkynones with organoboron derivatives.[70] Recent progress in Pd-catalyzed selective cross-coupling reactions have led to develop various protocols in the synthesis of some drugs and drug candidates in pharmaceutical industry.[71] For example, a diverse range of 4-alkoxy-3,6-diarylquinolines as drug candidates have been synthesized by chemo-selective Suzuki reactions as the key step. The products exhibit potent and selective agonism of the somatostatin receptor subtype 2 (sst_2) (Figure 7).[72]

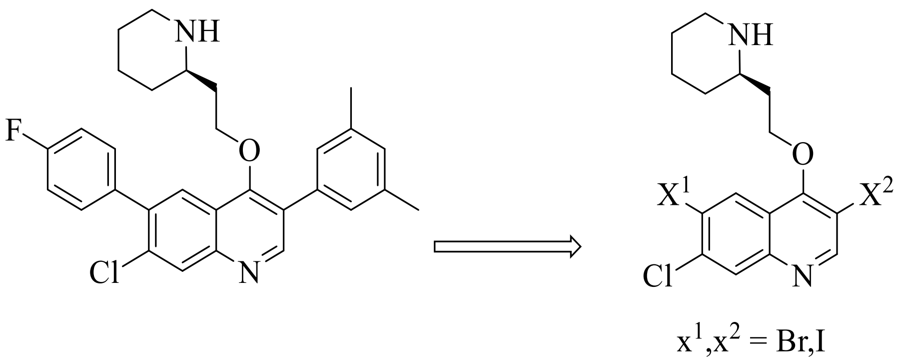
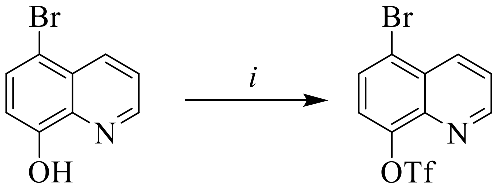


Figure 7 Selective Pd-catalyzed synthesis of 4-alkoxy-3,6-diarylquinolines (sst$_2$), agonists protocol developed by Merck.

Previously, various regioselective Suzuki-Miyaura cross-reactions of dihalogenated pyridines and quinolines have been reported.[73,74] Reactions of mixed triflates and halides are more rare. Some years ago, Prof. Langer's group has reported reactions of quinolones containing a triflate and two bromine atoms. Prof. Langer's group also reported chemoselective transformations of naphthalene derivatives containing triflate and bromide groups.[75] In chapter 3 of this work such reactions are also described. Herein, I report what is, to the best of my knowledge, the first chemo-selective Suzuki-Miyaura reactions of 5-bromoquinolin-8-yl trifluoromethanesulfonate.

5.2 Results and discussion

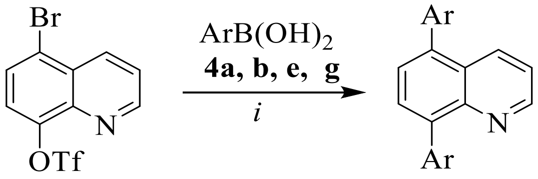
Commercially available 5-bromo-8-hydroxyquinoline was converted to 5-bromoquinolin-8-yl trifluoromethanesulfonate **19** in high yield (Scheme 25).



18 **19**

Scheme 25 Synthesis of **19**. Conditions: *i*, **18** (1.0 equiv.), pyridine (1.2 equiv.), (20 mL) CH_2Cl_2, Tf_2O (1.2 equiv.), 50 °C, 4 h.

The Suzuki-Miyaura reaction of **19** with arylboronic acids **4a, b, e, g** (2.0 equiv.), in the presence of Pd(PPh$_3$)$_4$ (6 mol-%), K$_2$CO$_3$ (2 mL), 1,4-dioxane (3 mL), 110 °C, 10 h, gave 5,8-bis(aryl)quinolines **20a-d** in 68-81% yields (Scheme 26, Table 7). The structure of compound **20c** was independently confirmed by x-ray crystallography (Figure 8).



19

20a-d

Scheme 26 Synthesis of **20a-d**. Conditions: *i*, **19** (1.0 equiv.), **4a, b, e, g** (2.0 equiv.), Pd(PPh$_3$)$_4$ (6 mol-%), K$_2$CO$_3$ (2 mL), 1,4-dioxane (3 mL), 110 °C, 10 h.

Table 7 Synthesis of **20a-d**

4	**20**	Ar	%(**20**)^a
a	**a**	3,5-MeC$_6$H$_3$	81
b	**b**	3-MeC$_6$H$_4$	77
e	**c**	4-(MeO)C$_6$H$_4$	68
g	**d**	4-(EtO)C$_6$H$_4$	72

^{a} Yields of isolated products

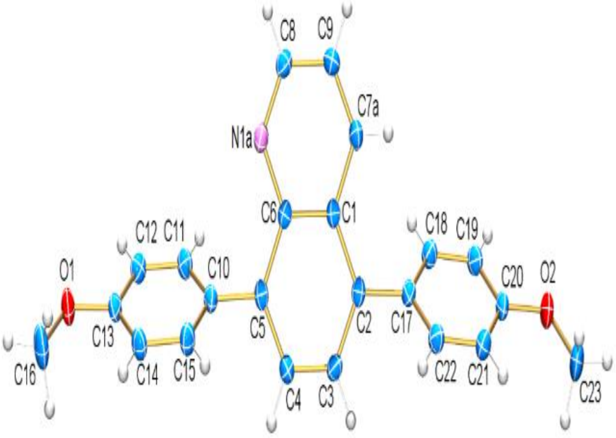
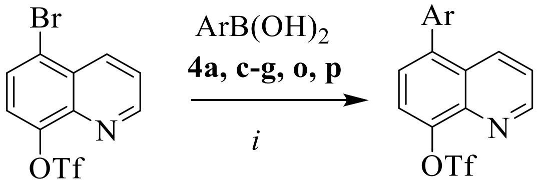


Figure 8 X-ray crystal structure of **20c.**

The Suzuki-Miyaura reaction of **19** with arylboronic acids **4a, c-g, o, p** (1.0 equiv.), in the presence of $Pd(PPh_3)_4$ (3 mol-%), K_3PO_4 (1.0 equiv.), toluene (3 mL), 85 °C, 9 h, afforded 5-arylquinolin-8-yl trifluoromethanesulfonates **21a-h** in 60-84% yields (Scheme 27, Table 8). The reactions proceeded with very good chemoselectivity in favor of position 5. During the optimization, it proved to be important to use exactly one equivalent of the arylboronic acid to carry out the reaction at lower temperature (85 °C) than the double-coupling. Very good yields were obtained for products derived from both electron poor and rich arylboronic acids. The structure of **21a** was confirmed by 2D NMR correlation experiments (NOESY and COSY) (Figure 9).



19 **21a-h**

Scheme 27 Synthesis of **21a-h**. Conditions: *i*, **19** (1.0 equiv.), **4a, c-g, o, p** (1.0 equiv.), $Pd(PPh_3)_4$ (3 mol-%), K_3PO_4 (1.0 equiv.), toluene (3 mL), 85 °C, 9 h.

Table 8 Synthesis of **21a-h**

4	21	Ar	%(**21**)[a]
a	**a**	3,5-MeC_6H_3	76
c	**b**	4-ClC_6H_4	60
d	**c**	4-EtC_6H_4	75
e	**d**	4-(MeO)C_6H_4	84
f	**e**	4-MeC_6H_4	81
g	**f**	4-(EtO)C_6H_4	69
o	**g**	4-FC_6H_4	63
p	**h**	2-(MeO)C_6H_4	79

[a] Yields of isolated product

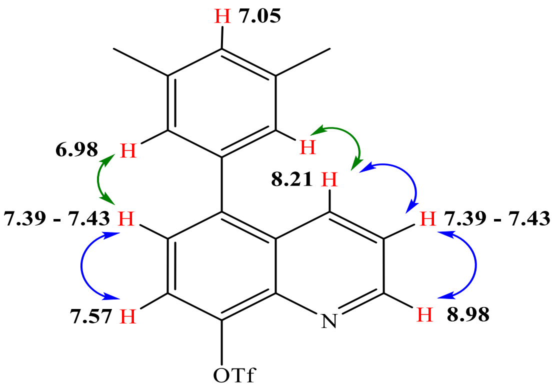
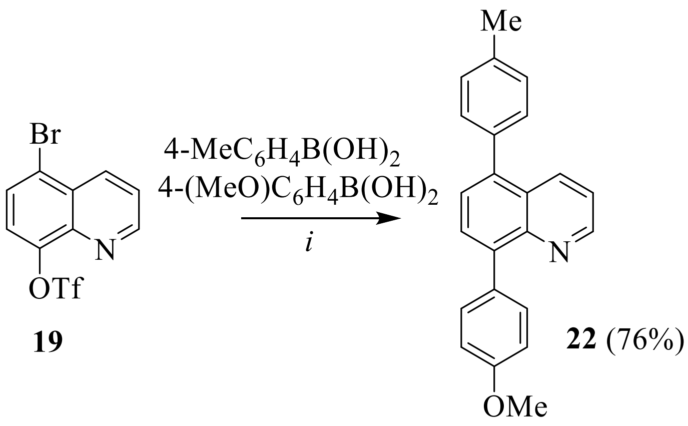


Figure 9 2D NMR correlation experiments of compound **21a** (NOESY: green arrows; COSY: blue arrows).

The one-pot reaction of **19** with two different arylboronic acids (sequential addition of the arylboronic acids) afforded 5,8-diarylquinoline **22** in 76% yield (Scheme 28). The reaction was carried out at 85 °C for the first step (to avoid double coupling) and at 110 °C in the second step (to ensure a complete reaction). An additional amount of catalyst and base had to be added together with the second arylboronic acid. In addition, 1,4-dioxane (3 mL) had to be added to complete the reaction, due to solubility reasons.



Scheme 28 Synthesis of **22**. Conditions: *i*, 1) 4-MeC$_6$H$_4$B(OH)$_2$ (1.0 equiv.), Pd(PPh$_3$)$_4$ (3 mol-%), K$_3$PO$_4$ (1.0 equiv.), toluene, 85 °C, 9 h.; 2) 4-(MeO)C$_6$H$_4$B(OH)$_2$ (2.0 equiv.), Pd(PPh$_3$)$_4$ (6 mol-%), K$_3$PO$_4$ (1.0 equiv.), 1,4-dioxane, 110 °C, 10 h.

In general, aryl bromides undergo Suzuki-Miyaura reactions more rapidly than aryl triflates,[76] because of the stability of the borane-halide bond. However, other parameters influence the selectivity as well.[76e] The reactions of **19** proceed with very good chemoselectivity of the bromide group, despite the proximity of the triflate to the quinoline nitrogen which might exert a catalyst-directing effect based on participation of the nitrogen lone pairs.

5.3 Conclusion

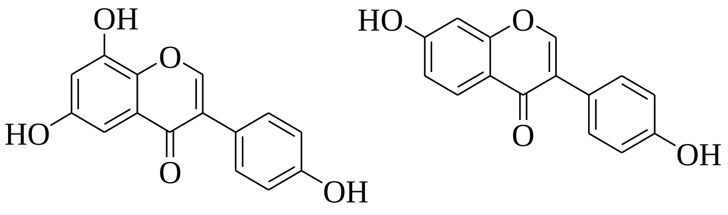
In conclusion, I have reported chemoselective Suzuki-Miyaura reactions of 5-bromoquinolin-8-yl trifluoromethanesulfonate. The reactions proceeded with very good chemoselectivity in favor of the bromide group.

CHAPTER SIX

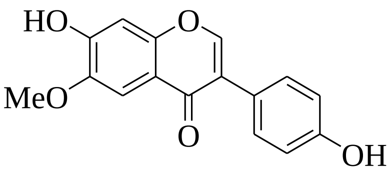
6 Synthesis of arylated isoflavones by site-selective Suzuki-Miyaura cross-coupling reactions of the bis(triflate) of 5,7-dihydroxyisoflavone

6.1 Introduction

Isoflavones are heterocyclic compounds, which belong to flavonoids derivatives. The main body of isoflavone consists of a benzene and a *ortho*-pyrone moiety. Isoflavonoids are a subgroup of flavonoids mainly present in the species of *Leguminosae* (Figure 10). New syntheses of isoflavones have been developed in recent years. Syntheses rely on the cyclization of deoxybenzoin derivatives with suitable building blocks, using various reagents, such as ethoxalyl chloride[77] or triethyl orthoformate.[78] Furthermore, palladium catalyzed cross-coupling reactions have been used for the synthesis of isoflavones.[79] Isoflavone derivatives show anticancer,[80] and antibacterial,[81] antimicrobial,[82] and antiulcer activity.[83] Isoflavones also play a role for the reduction of cholesterol.[84] Isoflavones also possess antioxidant activity,[85] inhibition of cancer cell proliferation,[86] anti-inflammatory activity,[87] and prevention of coronary heart diseases[88] as well as osteoporosis.[89]



Genistein Daidzein

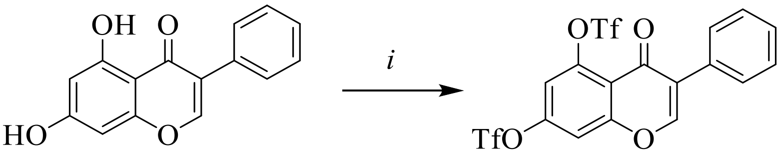


Glycitein

Figure 10 Species of *Leguminosae.*

6.2 Results and discussion

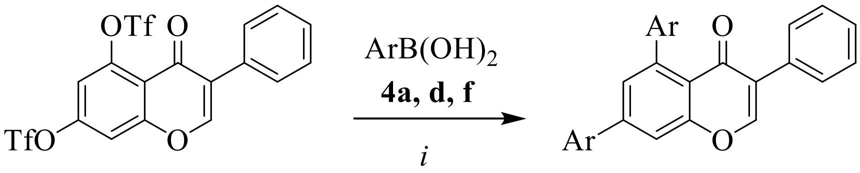
Commercially available 5,7-dihydroxyisoflavone (**23**) was converted to 5,7-bis(trifluoromethanesulfonyloxy)isoflavone (**24**) in high yield 89% (Scheme 29).



23 **24**

Scheme 29 Synthesis of **24**. Conditions: *i*, **23** (1.0 equiv.), pyridine (4.0 equiv.) CH_2Cl_2, Tf_2O (2.4 equiv.), 50 °C, 4 h.

The Suzuki-Miyaura reaction of **24** with arylboronic acids **4a, d, f** (2.0 equiv.), in the presence of $Pd(PPh_3)_4$ (6 mole%), K_2CO_3 (1.5 mL), 1,4-dioxane (3 mL), 110 °C, 10 h., gave the 5,7-diaryl isoflavones **25a-c** in 76-87 % yields **(**Scheme 30, Table 9**)**.



24 **25a-c**

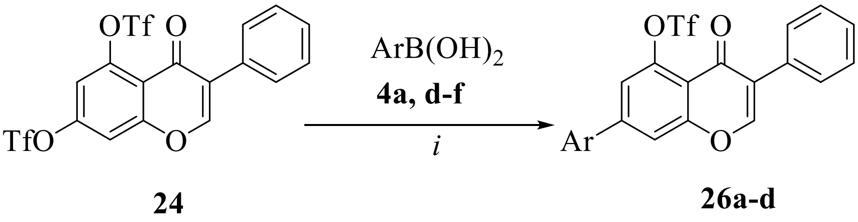
Scheme 30 Synthesis of **25a-c**. Conditions: *i*, **24** (1.0 equiv.), **4a, d, f** (2.0 equiv.), $Pd(PPh_3)_4$ (6 mole%), K_2CO_3 (1.5 mL), 1,4-dioxane (3 mL), 110 °C, 10 h.

Table 9 Synthesis of **25a-c**

4	**25**	Ar	%(**25**)[a]
a	**a**	3,5-MeC_6H_3	87
d	**b**	4-EtC_6H_4	81
f	**c**	4-MeC_6H_4	76

[a] Yields of isolated product

The Suzuki-Miyaura reaction of **24** with arylboronic acids **4a, d-f** (1.0 equiv.), in the presence of Pd(PPh$_3$)$_4$ (3 mole%), K$_3$PO$_4$ (1.0 equiv.), THF (3 mL), 55 °C, 10 h, afforded the 5-arylisoflavone-7-trifluoromethanesulfonates **26a-d** in 73-82% yields (Scheme 31, Table 10). The reactions proceeded with very good chemo-selectivity in favor of position 7. Very good yields were obtained for products derived from both electron poor and rich arylboronic acids. The structure of compound **26c**, confirmed independently by x-ray (Figure 11).



Scheme 31 Synthesis of **26a-d**. Conditions: *i*, 24 (1.0 equiv.), **4a, d-f** (1.0 equiv.), Pd(PPh$_3$)$_4$ (3 mole%), K$_3$PO$_4$ (1.0 equiv.), THF (3 mL), 55 °C, 10 h.

Table 10 Synthesis of **26a-d**

4	26	Ar	%(**26**)[a]
a	**a**	3,5-MeC$_6$H$_3$	73
d	**b**	4-EtC$_6$H$_4$	79
e	**c**	4-(MeO)C$_6$H$_4$	80
f	**d**	4-MeC$_6$H$_4$	82

[a] Yields of isolated product

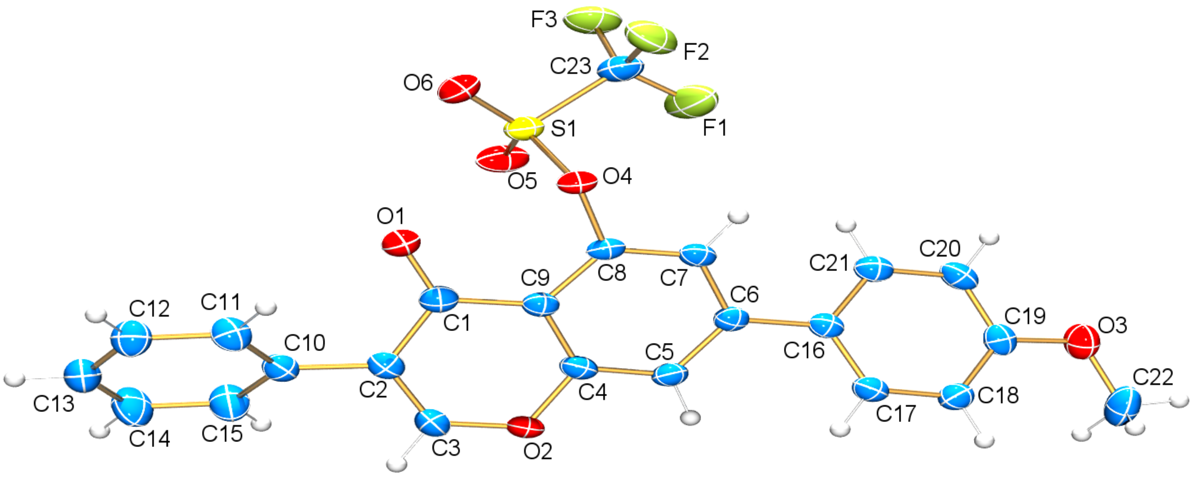


Figure 11 X-ray crystal structure of **26c**.

6.3 Conclusion

In conclusion, I have reported site-selectivity Suzuki-Miyaura reactions of bis (triflate) of 5,7-dihydroxyisoflavone. The reactions proceeded with very good site-selectivity in favor of 5-position.

7 EXPERMENTAL SECTION

7.1 NMR Spectroscopy

Burker AC 250, Burker ARX 300, Burker 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 techniqes (NOESY, COSY, HMQC, and HMBC) were applied as well. All NMR spectra presented in this work were collechted in $CDCl_3$ Solution. All chemical schift are given in ppm.References (^{1}H NMR): TMS (γ= 0.00) or residual $CHCl_3$ (γ= 7.26) were taken as internal standard.References (^{13}C NMR): TMS (γ= 0.00) or residual $CHCl_3$ (γ= 77.0) were taken as internal standard.Multiplicities are given as follows: s = singlet, d = doublet, t = triplet, q= quartet, m = multiplet, br = broad singlet. More complex patterns are represented by combinations of the respective symbols.Td indicates a triplet of doublets with the larger coupling constant associated with the first symbol (here, triplet).

7.2 Infraed Spectroscopy (IR)

Nicolet 205 FT-IR, Nicolet Protégé 460 FT-IR. Peaks are given the following assignments: W = Weak, m = medium, s = strong, br = broad.

7.3 Mass Spectroscopy (MS)

AMD MS40, Varian MAT CH 7, MAT 731 (ET, 70 eV), Intecta AMD 402 (ET, 70 eV and Cl), Finnigan MAT 95 (Cl, 200 eV)

7.4 High Resolution Mass Spectrometry (HRMS)

Varian MAT 311, Intecta AMD 402.

7.5 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.

7.6 X-ray Structures

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

7.7 Chromatographic Methods

7.7.1 Thin Layer Chromatography (TLC)

Merck Kiesslgel 60 F254 on aluminium foil from Macherey-Nagel. Detection was carried oht 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, 5/100 sulphuric acid, 83-84/100 methanol.

7.7.2 Column Chromatography

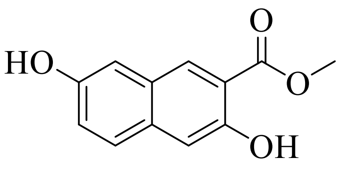
Column chromatography was performed with Merck Silica Gel 60 or Macherey-Nagel Silica Gel 60 (0,063-0.0200 mm, 70-320 mesh). The finer Merck Silica Gel 60 (0.040-0.063 mm, 230-400 mesh) was chosen when appropriate.

7.8 Equipment, Chemicals and work Technique

All solvents for using were distilled by standard methods. The coupling reactions were carried out in pressure tubes or Schlenck flask under inert atmosphere (Argon 4.6), oxygen and humidity exclusion. All of the chemicals are standard, commercially available from Merck, Aldrich, Arcos, and others. The order of the characterized connections effected numerically, but does not correspond to the order in the main part of dissertation.

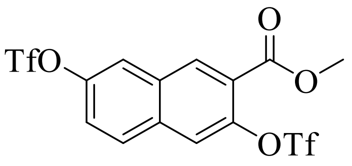
7.9 Procedures and Spectroscopic Data

Methyl 3,7-dihydroxy-2-naphthoate (2)



To a solution of 3,7-dihydroxy-2-naphthoic acid **1** (2.0 g, 9.8 mmol) in DMF (30 mL), dimethyl sulfate (2.72 g, 21.56 mmol) and N,N-diisopropylethylamine (1.4 g, 10.78 mmol) were added. The reaction mixture was heated for 1 h at 85 °C. After cooling to room temperature, the mixture was poured into ice water. A white precipitate formed which was filtered off and the filtrate was concentrated in vacuo. The product **2** was isolated by column chromatography (flash silica gel, heptane/EtOAc) as a yellow solid (1.6 g, 77%); mp 101-102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.95 (s, 3H, OCH_3), 4.79 (s, 1H, OH), 7.04-7.05 (m, 1H, ArH), 7.08 (dd, J = 2.4, 8.8 Hz, 1H, ArH), 7.20 (s, 1H, ArH), 7.55 (d, J = 8.9 Hz, 1H, ArH), 8.25 (s, 1H, ArH), 10.19 (s, 1H, OH). ^{13}C NMR (62.90 MHz, $CDCl_3$): = 52.5 (OCH_3), 110.1, 111.8 (CH), 114.6 (C), 121.6 (CH), 127.7 (C), 128.1, 130.3 (CH), 133.4, 151.7, 154.7 (C), 170.2 (CO). IR (KBr, cm^{-1}): ν = 3328 (m), 3038, 3003, 2953 (w), 1681 (m), 1651, 1633, 1609, 1576, 1556 (w), 1531 (m), 1505, 1479, 1462 (w), 1441, 1392, 1345, 1263, 1214 (s), 1180, 1147, 1130, 1072 (m), 1012, 969 (w), 944, 903, (w), 860 (s), 836, 812 (m), 783 (s), 746 (w), 716 (s), 665, 620, 610 (w), 587, 550 (w). GC-MS (EI, 70 eV): m/z (%) = 218 ([M]$^+$, 52), 187 (17), 186 (100), 185 (10), 159 (10), 158 (80), 130 (45), 102 (20). HRMS (EI, 70 eV) calcd for $C_{12}H_{10}O_4$ [M]$^+$: 218.0579; found: 218.0599.

Methyl 3,7-bis(trifluoromethylsulfonyloxy)-2-naphthoate (3)

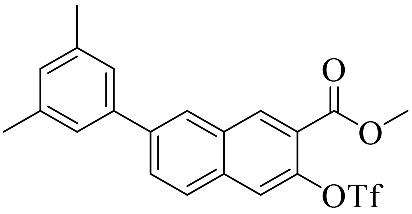


To a CH_2Cl_2 solution (46 mL) of **2** (1.0 g, 4.6 mmol) was added pyridine (1.5 mL, 18.4 mmol) and the solution was stirred at 20 °C for 10 min under argon atmosphere. Then Tf_2O (1.8 mL, 11.0 mmol) was added at –78 °C and the reaction mixture was allowed to warm to room temperature and was stirred for 14 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The product **3** was isolated by column chromatography (flash silica gel, heptane/EtOAc) as a colourless solid (1.9 g, 87%); mp 75-77 ºC. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.06 (s, 3H, OCH_3), 7.47-7.70 (m, 1H, ArH), 7.85 (s, 1H, ArH), 7.94 (d, J = 2.3 Hz, 1H, ArH), 8.03 (d, J = 9.0 Hz, 1H, ArH), 8.72 (s, 1H, ArH). ^{13}C NMR (62.90 MHz, $CDCl_3$ = 52.99 (OCH_3), 117.7 (q, $J_{F,C =}$ 320.2 Hz, CF_3), 117.9 (q, $J_{F,C =}$ 320.8 Hz, CF_3), 120.4, 121.2, 123.6 (CH), 130.5 (C), 130.8 (CH), 131.8, 133.8 (C), 134.6 (CH), 145.5, 148.3 (C), 163.7 (CO). IR (KBr, cm^{-1}): ν = 3070, 2963 (w), 1713 (s), 1678, 1633 (w), 1599 (m), 1502, 1461, 1443 (w), 1426, 1398 (s), 1365, 1309 (m), 1276 (s), 1249 (m),1203, 1131, 1116, 1048 (s), 965 (w), 937, 909, 937, 909, 845, 813, 795 (s), 779, 766, 754, 739 (m), 697 (w), 676 (m), 650, 609, (s), 597, 582 (m), 565 (w). GC-MS (EI, 70 eV): *m/z* (%) = 482 ([M]$^+$, 61), 451 (16), 350 (14), 349 (100), 257 (24), 129 (17). HRMS (ESI-TOF/MS) calcd for $C_{14}H_9F_6O_8S_2$ [M+H]$^+$: 482.96375; found: 482.96348.

General procedure for the synthesis of 5a-i

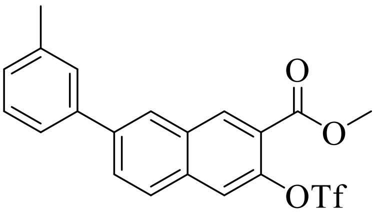
A THF solution of **3** (0.145 mmol), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol-%) and of arylboronic acid **4** (1.2 equiv.) was stirred at 20 °C for 9 h under argon atmosphere. To the reaction mixture were added H_2O (20 mL) and CH_2Cl_2 (25 mL). The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, heptane / EtOAc = 100:5).

Methyl 7-(3,5-dimethylphenyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5a)



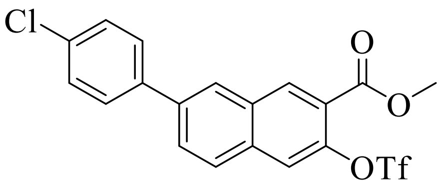
Starting with **3** (70 mg, 0.145 mmol), **4a** (26 mg, 0.174 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%), K_3PO_4 (46 mg, 0.22 mmol), and THF (4 mL), **5a** was isolated as a white solid (45 mg, 70%); mp 102-104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 6H, $2CH_3$), 3.96 (s, 3H, OCH_3), 7.01 (s, 1H, ArH), 7.24 (br. s, 2H, ArH), 7.68-8.08 (m, 4H, ArH), 8.63 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.1. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.4 ($2CH_3$), 51.7 (OCH_3), 117.8 (q, $J_{C,F}$ = 321.3 Hz, CF_3), 119.8 (CH), 121.2 (C), 124.3, 125.2, 125.6, 128.1, 128.8 (CH), 130.7, 132.9 (C), 134.0 (CH), 137.7, 138.7, 140.2, 143.6 (C), 164.4 (C=O). IR (KBr, cm^{-1}): *v* = 3028, 3012, 2958, 2920, 2851 (w), 1721 (s), 1632 (w), 1596 (m), 1462 (w), 1420 (s), 1364, 1319, 1303, 1285, 1261, 1247 (w), 1198 (s), 1134, 1112, 1051, 1018, 946 (m). GC-MS (EI, 70eV): *m/z* (%) = 438 ([M]$^+$, 44), 305 (100), 275 (15), 247 (39), 219 (20), 202 (24). HRMS (EI, 70 eV): *m/z* calcd. for $C_{21}H_{17}O_5F_3S$ [M]$^+$: 438.07433; found: 438.07419.

Methyl 7-(*m*-tolyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5b)



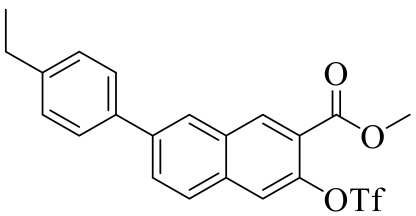
Starting with **3** (70 mg, 0.145 mmol), **4b** (24 mg, 0.174 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%), K_3PO_4 (46 mg, 0.22 mmol), and THF (4 mL), **5b** was isolated as a white solid (48 mg, 77%); mp 152-154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3H, CH_3), 3.96 (s, 3H, OCH_3), 7.00 (s, 1H, ArH), 7.18-7.24 (m, 3H, ArH), 7.68 (s, 1H, ArH), 7.87 (br. s, 2H, ArH), 8.10 (s, 1H, ArH), 8.63 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, CDCl$_3$): δ = -73.07. ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 21.4 (CH$_3$), 52.7 (OCH$_3$), 118.9 (q, $J_{C,F}$ = 320.9 Hz, CF$_3$), 119.8 (CH), 121.3 (C), 123.5, 125.6 (CH), 127.1 (C), 127.7 (CH), 127.9 (2CH), 128.1, 128.6 (CH), 130.7, 133.0 (C), 134.0 (CH), 137.8, 138.7, 144.6 (C), 163.9 (C=O). IR (KBr, cm^{-1}): v = 3042, 3018, 2960, 2916 (w), 1721 (s), 1602, 1505, 1422, 1319, 1287, 1258, 1201 (m), 1134, 1085 (w), 1013 (s), 955, 944 (w). GC-MS (EI, 70eV): m/z (%) = 424 ([M]$^+$, 57), 292 (19), 291 (100), 263 (10), 261 (15), 233 (48), 205 (23). HRMS (ESI-TOF/MS): *m/z* calcd for $C_{20}H_{16}O_5F_3S$ [M+H]$^+$: 425.05923; found: 425.05934.

Methyl 7-(4-chlorophenyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5c)



Starting with **3** (70 mg, 0.145 mmol), **4c** (27 mg, 0.174 mmol), Pd(PPh$_3$)$_4$ (5 mg, 3 mol-%), K$_3$PO$_4$ (46 mg, 0.22 mmol), and THF (4 mL), **5c** was isolated as a white solid (52 mg, 80%); mp 98-100 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.95 (s, 3H, OCH$_3$), 7.18-7.33 (m, 1H, ArH), 7.38 (d, *J* = 8.1 Hz, 2H, ArH), 7.55 (d, *J* = 8.1 Hz, 2H, ArH), 7.69 (s, 1H, ArH), 7.76-7.90 (m, 1H, ArH), 8.04 (s, 1H, ArH), 8.62 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, CDCl$_3$): δ = -73.1. ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 52.8 (OCH$_3$), 118.3 (q, $J_{C,F}$ = 320.9 Hz, CF$_3$), 119.9 (CH), 121.8 (C), 125.6, 127.4, 127.6, 128.2, 128.3 (CH), 130.6, 133.0, 133.4 (C), 133.9 (CH), 137.2, 138.7, 143.8 (C), 163.3 (C=O). IR (KBr, cm^{-1}): v = 3033, 3000, 2956, 1723 (s), 1632, 1604, 1490 (m), 1420 (s), 1318, 1260, 1248 (w), 1201 (s), 1131, 1091, 1050, 1011 (w), 963, 928 (m). GC-MS (EI, 70 eV): *m/z* (%) = 446 ([M], ^{37}Cl]$^+$, 24), 444 ([M], ^{35}Cl]$^+$, 61), 410 (40), 329 (15), 311 (100), 270 (10). HRMS (ESI-TOF): *m/z* calcd. for $C_{19}H_{13}ClF_3O_5S$ ([M+H], ^{35}Cl)$^+$: 445.01188; found: 445.01173; calcd for $C_{19}H_{13}ClF_3O_5S$ ([M+H], ^{37}Cl)$^+$: 447.00951; found 447.00954.

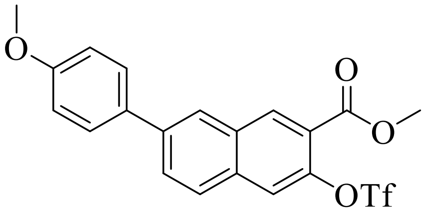
Methyl 7-(4-ethylphenyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5d)



Starting with **3** (70 mg, 0.145 mmol), **4d** (26 mg, 0.174 mmol), Pd(PPh$_3$)$_4$ (5 mg, 3 mol-%), K$_3$PO$_4$ (46 mg, 0.22 mmol), and THF (4 mL), **5d** was isolated as a white solid (54 mg, 84%); mp 66-68 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.21 (t, *J* = 7.5 Hz, 3H, CH$_3$), 2.66 (q, *J* = 7.5 Hz, 2H, CH$_2$), 3.95 (s, 3H, OCH$_3$), 7.27 (d, *J* = 8.1 Hz, 2H, ArH), 7.55 (d, *J* = 8.1 Hz, 2H, ArH), 7.68 (s, 1H, ArH), 7.87 (br. s, 2H, ArH), 8.07 (s, 1H, ArH), 8.62 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, CDCl$_3$): δ = -73.05. ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 15.5 (CH$_3$), 28.5 (CH$_2$), 52.7

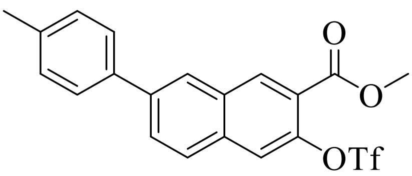
(OCH_3), 119.7 (q, $J_{C,F}$ = 322.1 Hz, CF_3), 119.8 (C), 125.3, 126.3, 126.7, 127.1, 127.6 (CH), 128.5 (C), 129.5 (CH), 132.8, 133.9 (C), 136.0 (CH), 139.9, 143.5, 143.6 (C), 163.4 (C=O). IR (KBr, cm^{-1}): v = 3023, 2960, 2924, 2851 (w), 1716 (s), 1632, 1602, 1516, 1500 (w), 1423 (s), 1393, 1317, 1265, 1248 (w), 1204, 1136 (s), 1114, 1047, 963, 940 (w), 925, 896, 868, 840, 812, 796 (m), 719, 677, 632, 608, 591, 574 (w). GC-MS (EI, 70 eV): m/z (%) = 438 ($[M]^+$, 100), 407 (4), 305 (44), 275 (14), 247 (35), 219 (13), 202 (19). HRMS (EI,70eV): m/z calcd for $C_{21}H_{17}O_5F_3S$ ($[M]^+$: 438.07433; found: 438.07418.

Methyl 7-(4-methoxyphenyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate(5e)



Starting with **3** (70 mg, 0.145 mmol), **4e** (26 mg, 0.174 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%), K_3PO_4 (46 mg, 0.22 mmol), and THF (4 mL), **5e** was isolated as a white solid (53 mg, 83%); mp 142-144 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.97 (d, J = 8.7 Hz, 2H, ArH), 7.57 (d, J = 8.7 Hz, 2H, ArH), 7.67 (s, 1H, ArH), 7.86 (br. s, 2H, ArH), 8.04 (s, 1H, ArH), 8.61 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.09. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 52.7, 55.4 (OCH_3), 114.6 (CH), 117.6 (q, $J_{C,F}$ = 320.8 Hz, CF_3), 120.8, 122.3 (C), 125.8, 128.1, 128.5, 129.4 (CH), 132.1, 133.6 (C), 134.1, 134.9 (CH), 140.6, 144.5, 159.8 (C), 164.4 (C=O). IR (KBr, cm^{-1}): v = 3046, 3028 (w), 2958, 2919, 2849 (m), 2663, 1728 (w), 1722 (s), 1681, 1650, 1644 (m), 1603 (s), 1578, 1557, 1502 (m), 1460 (w), 1425, 1401, 1321 (s), 1282, 1268 (m), 1246, 1216, 1200 (s), 1115 (m). GC-MS (EI,70 eV): m/z (%) = 440 ($[M]^+$, 50), 409 (4), 307 (100), 277 (13), 249 (23), 221 (15), 176 (14). HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}O_6F_3S$ $[M+H]^+$: 441.06142; found: 441.06173.

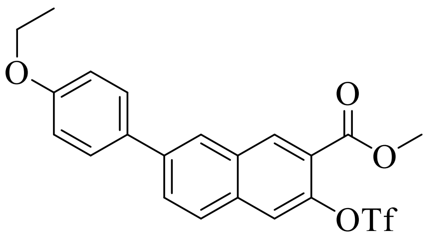
Methyl 7-(*p*-tolyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5f)



Starting with **3** (70 mg, 0.145 mmol), **4f** (24 mg, 0.174 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%), K_3PO_4 (46 mg, 0.22 mmol) and THF (4 mL), **5f** was isolated as a white solid (48 mg, 78%); mp: 133-135 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 3.95 (s, 3H, OCH_3), 7.24 (d, J = 7.9 Hz, 2H, ArH), 7.52 (d, J = 8.0 Hz, 2H, ArH), 7.67 (s, 1H, ArH), 7.86 (br. s, 2H, ArH), 8.06 (s, 1H, ArH), 8.62 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.08. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.1 (CH_3), 51.7 (OCH_3), 118.8 (q, $J_{C,F}$ = 320.7 Hz, CF_3), 119.8 (CH), 121.3 (C), 125.3, 126.2, 127.1, 128.5, 128.8 (CH), 130.7, 132.8 (C), 133.9 (CH), 135.8, 137.2, 139.9, 143.6 (C), 163.4 (C=O). IR (KBr, cm^{-1}): v =

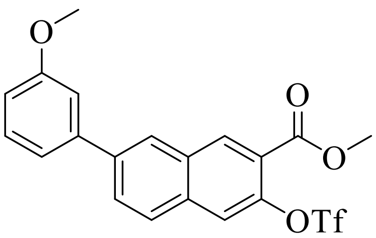
3033, 3024, 3001 (w), 2985, 2978 (s), 2932, 2896 (m), 2862 (w), 2820 (s), 2764, 2719, 2680, 2655 (w), 2600, 2558 (s), 2552, 2520, 2487, 2430, 2390 (w), 2327, 1984, 1920 (s), 1690, 1620, 1570 (w), 1480, 1470, 1390, 1320 (s), 1290, 1245 (m). GC-MS (EI, 70 eV): m/z (%) = 424 ($[M]^+$, 50), 392 (18), 291 (100), 261 (15), 233 (39), 205 (21). HRMS (EI, 70 eV): *m/z* calcd for $C_{20}H_{15}O_5F_3S$ $[M]^+$: 424.05868; found: 424.05848.

Methyl 7-(4-ethoxyphenyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5g)



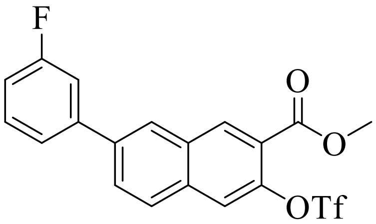
Starting with **3** (70 mg, 0.145 mmol), **4g** (29 mg, 0.174 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%), K_3PO_4 (46 mg, 0.22 mmol), and THF (4 mL), **5g** was isolated as a white solid (54 mg, 82%); mp 105-108 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.2 Hz, 3H, CH_3), 2.85 (s, 3H, OCH_3), 3.96 (q, *J* = 7.2 Hz, 2H, OCH_2), 6.88 (d, *J* = 8.9 Hz, 2H, ArH), 7.23 (d, *J* = 8.7 Hz, 2H, ArH), 7.40 (dd, *J* = 8.9, 2.5 Hz, 1H, ArH), 7.76 (d, *J* = 2.3 Hz, 1H, ArH), 7.79 (s, 1H, ArH), 7.86 (s, 1H, ArH), 8.28 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.1 (CH_3), 55.4 (OCH_3), 62.5 (OCH_2), 113.2 (CH), 118.2 (q, $J_{C,F}$ = 321.3 Hz, CF_3), 118.7, 120.1 (C), 120.8, 128.3 (CH), 128.5 (C), 129.4, 129.6 (CH), 129.9 (C), 130.2, 135.6 (CH), 141.5, 143.7, 158.1 (C), 167.8 (C=O). IR (KBr, cm^{-1}): *v* = 3022, 3012, 2987 (w), 2925, 2912 (m), 1756, 1734 (s), 1722, 1686 (w), 1623 (m), 1605, 1592 (s), 1578, 1557, 1532 (m), 1517 (w), 1463, 1445, 1422, 1406 (m), 1361, 1333, 1328, 1312 (w), 1282 (m), 1278, 1245, 1232 (w), 1216 (s), 1175, 1132, 1128, 1116 (m). GC-MS (EI,70eV): m/z (%) = 454 ($[M]^+$, 46), 322 (23), 321 (100), 293 (15), 265 (15), 234 (17), 205 (12). HRMS (ESI-TOF): *m/z* calcd for $C_{21}H_{18}F_3O_6S$ $[M+H]^+$: 455.07707; found: 455.07661.

Methyl 7-(3-methoxyphenyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5h)



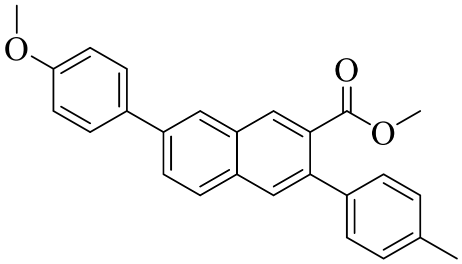
Starting with **3** (70 mg, 0.145 mmol), **4h** (26 mg, 0.174 mmol), K_3PO_4 (46 mg, 0.22 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%), and THF (4 mL), **5h** was isolated as a white solid (54 mg, 85%); mp: 82-83 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.89- 6.93 (m, 1H, ArH), 7.14-7.22 (m, 3H, ArH), 7.36 (t, *J* = 7.9 Hz, 1H, ArH), 7.69 (br. s, 1H, ArH), 7.87-7.88 (m, 2H, ArH), 8.09 (br. s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.09. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 52.7, 55.4 (OCH_3), 113.3, 113.4 (CH), 117.9 (q, $J_{C,F}$ = 319.3 Hz, CF_3), 119.8, 120.8 (CH), 122.4 (C), 126.7, 128.2, 129.6, 130.1 (CH), 131.7, 134.1 (C), 135.0 (CH), 140.9, 141.2, 144.7, 160.2 (C), 164.4 (C=O). IR (KBr, cm^{-1}): v = 3002, 2954, 2927, 2847 (w), 1726 (s), 1632, 1599, 1509, 1488, 1459 (w), 1422 (s), 1402, 1370, 1314, 1286, 1263, 1249 (w), 1202, 1136 (s), 1052, 1031 (m), 969, 939 (w), 897, 853, 810, 792, 776, 722 (m), 696, 667, 643 (w), 609, 600 (m). GC-MS (EI, 70 eV): m/z (%) = 440 ($[M]^+$, 59), 308 (20), 307 (100), 277 (15), 249 (50), 221 (18). HRMS (EI, 70 eV): m/z calcd for $C_{20}H_{15}O_6F_3S$ $[M]^+$: 440.05359; found: 440.05333.

Methyl 7-(3-fluorophenyl)-3-(trifluoromethylsulfonyloxy)-2-naphthoate (5i)



Starting with **3** (70 mg, 0.145 mmol), **4i** (24 mg, 0.174 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%), K_3PO_4 (46 mg, 0.22 mmol), and THF (4 mL), **5i** was isolated as a white solid (51 mg, 82%); mp 54-56 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.96 (s, 3H, OCH_3), 7.25-7.41 (m, 3H, ArH), 7.70 (s, 1H, ArH), 7.79-7.92 (m, 3H, ArH), 8.07 (s, 1H, ArH), 8.64 (s, 1H, ArH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -112.3, -73.1. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 52.8 (OCH_3), 114.2 (d, $J_{C,F}$ = 21.7 Hz, CH), 114.9 (d, $J_{C,F}$ = 22.4 Hz, CH), 115.2 (C), 119.4 (q, $J_{C,F}$ = 321.8 Hz, CF_3), 120.9 (CH), 122.6 (C), 123.1, 126.9, 128.5, 129.3, 129.7 (CH), 130.7 (d, $J_{C,F}$ = 8.3 Hz, CH), 131.7 (d, $J_{C,F}$ = 3.2 Hz, CH), 134.7 (d, $J_{C,F}$ = 8.9 Hz, C), 135.1 (CH), 142.0, 145.0 (C), 164.9 (d, $J_{C,F}$ = 245.2 Hz, CF), 168.8 (C=O). IR (KBr, cm^{-1}): v = 3079, 3038, 2956, 2918, 2849 (w), 1720 (s), 1633, 1602, 1586, 1511, 1488 (w), 1420 (s), 1371, 1321, 1284, 1248 (w), 1201, 1135 (s). GC-MS (EI,70eV): m/z (%) = 428 ($[M]^+$, 38), 295 (62), 269 (20), 267 (75), 265 (14), 264 (13), 237 (100), 236 (29), 209 (39), 207 (64). HR-MS (ESI-TOF/MS, 70 eV): m/z calcd. for $C_{19}H_{12}O_5F_4S$ $[M+H]^+$: 429.04234; found: 429.04275.

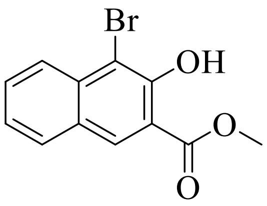
Methyl 7-(*p*-methoxyphenyl)-3-(*p*-tolyl)-2-naphthoate (6)



The reaction was carried out in a pressure tube. To the THF suspension (4 mL) of **3** (70 mg, 0.145 mmol), arylboronic acid $Ar^1B(OH)_2$ **4e** (22 mg, 0.145 mmol), and $Pd(PPh_3)_4$ (5 mg, 3 mol%) was added K_3PO_4 (46 mg, 0.22 mmol), and the resulting solution was degassed by bubbling argon through the solution for 10 min. The mixture was stirred at 20°C under an argon atmosphere for 9 h. Arylboronic acid $Ar^2B(OH)_2$ **4f** (20 mg, 0.145 mmol), $Pd(PPh_3)_4$ (3 mol-%), K_3PO_4 (46 mg, 0.22 mmol) were added. The reaction mixtures were heated under an argon atmosphere at 105 °C for 8 h. They were diluted with H_2O and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried

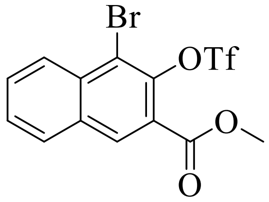
(Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel, heptane/EtAOc). **6** was isolated as a white solid (25 mg, 45 %); mp 82-83°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2,36 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.91 (d, *J* = 8.8 Hz, 2H, ArH), 7.23-7.31 (m, 4H, ArH), 7.56 (d, *J* = 8.8 Hz, 2H, ArH), 7.74 (s, 1H, ArH), 7.75-7.77 (m, 2H, ArH), 7.82 (s, 1H, ArH), 8.06 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.1 (CH_3), 52.7, 55.4 (OCH_3), 113.1, 119.8 (CH), 121.3 (C), 125.3, 126.2, 126.7, 127.1, 128.5, 128.8 (CH), 130.8, 132,9 (C), 133.9 (CH), 134.2, 134.6, 135.8, 137.2, 139.9, 143.6 (C), 164.3 (C=O). IR (KBr, cm^{-1}): ν = 3002, 2954, 2927, 2847 (w), 1726 (s), 1632, 1599, 1509, 1488, 1459 (w), 1422 (s), 1402, 1370, 1314, 1286, 1263, 1249 (w), 1202, 1136 (s), 1052, 1031 (m), 969, 939 (w), 897, 853, 810, 792, 776, 722 (m), 696, 667, 643 (w), 609, 600 (m). GC-MS (EI, 70eV): *m/z* (%) = 382 ([M]$^+$, 87), 367 (09), 311 (100), 281 (23), 207 (50), 198 (18). HR-MS (ESI-TOF): *m/z* calcd. for $C_{26}H_{22}O_3$ [M+H]$^+$: 383.15678; found: 383.15623.

Methyl 4-bromo-3-hydroxy-2-naphthoate (8)



To a solution of 4-bromo-3-hydroxy-2-naphthoic acid **7** (1.0 g, 3.7 mmol) in DMF (15 mL), dimethyl sulfate (1.04 g, 8.3 mmol) and N,N-diisopropylethylamine (0.5 g, 4.1 mmol) were added. The reaction mixture was heated for 1 h at 85 °C. After cooling to room temperature, the mixture was poured into ice water. A white precipitate formed which was filtered off and the filtrate was concentrated in vacuo. The product **8** was isolated by column chromatography (flash silica gel, heptane/EtOAc) as a yellow solid (0.9 g, 87 %); mp 88 - 95 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.96 (s, 3H, OCH_3), 7.27-7.33 (m, 1H, ArH), 7.52-7.58 (m, 1H, ArH), 7.70 (d, *J* = 8.2 Hz, 1H, ArH), 8.07 (d, *J* = 8.5 Hz, 1H, ArH), 8.36 (s, 1H, ArH), 11.16 (s, 1H, OH). ^{13}C NMR (62.90 MHz, $CDCl_3$): = 52.0 (OCH_3), 106.0, 113.6 (C), 123.6, 124.8 (CH), 126.4 (C), 128.7, 129.5, 130.8 (CH), 135.1, 152.1 (C), 169.0 (CO). IR (KBr, cm^{-1}): ν = 3329 (m), 3039, 3004, 2955 (w), 1684 (m), 1652, 1634, 1609, 1574, 1557 (w), 1532 (m), 1504, 1479, 1464 (w), 1399, 1360, 1280, 1213, 1100 (s), 967, 901 (w), 830, 760, 680 (s). GC-MS (EI, 70 eV): m/z (%) = 282 ([M, ^{81}Br]$^+$, 37), 280 ([M, ^{79}Br]$^+$, 40), 250 (94), 248 (92), 251 (43), 194 (100), 192 (18). HRMS (EI, 70 eV) calcd. for $C_{12}H_9BrO_3$ [M, ^{81}Br]$^+$:281.98970; found: 281.98921; calcd for $C_{12}H_9BrO_3$ [M, ^{79}Br]$^+$: 279.99351; found: 279.99354.

Methyl 4-bromo-3-(trifluoromethylsulfonyloxy)-2-naphthoate (9)

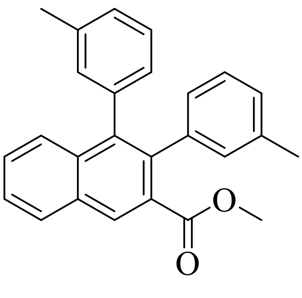


To a CH_2Cl_2 solution (50 mL) of **8** (1.0 g, 3.6 mmol) was added pyridine (1.1 mL, 14.2 mmol) and the solution was stirred at 20 °C for 10 min under argon atmosphere. Then Tf_2O (1.5 mL, 8.6 mmol) was added at 20 °C and the reaction mixture was heated at 50 °C for 20 min. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The product **9** was isolated by column chromatography (flash silica gel, heptane/EtOAc) as a colourless solid (1.33 g, 90 %); mp 90 - 92 ºC. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.96 (s, 3H, OCH_3), 7.59-7.64 (m, 1H, ArH), 7.70-7.75 (m, 1H, ArH), 7.91 (d, J = 8.1 Hz, 1H, ArH), 8.29 (d, J = 8.5 Hz, 1H, ArH), 8.47 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) = 53.0 (OCH_3), 117.7 (C), 118.5 (q, $J_{C,F}$ = 317.4 Hz, CF_3), 123.8, 128.1 (CH), 128.6 (C), 129.5, 130.8, 131.6 (CH), 133.4, 134.2, 142.4 (C), 164.6 (CO). IR (KBr, cm^{-1}): v = 3071, 2962 (w), 1714 (s), 1676, 1630 (w), 1598 (m), 1503, 1462, 1441 (w), 1427 (w), 1345, 1233 (s), 1143, 1102, 985, (m), 865, 750, 701, 633 (w). GC-MS (EI, 70 eV): *m/z* (%) = 414 ([M, ^{81}Br]$^+$, 25), 412 ([M, ^{79}Br]$^+$, 26), 281 (40), 279 (43), 251 (100), 248 (24), 223 (36), 221 (32). HRMS (EI, 70 eV) calcd for $C_{13}H_8BrF_3O_5S$ [M, ^{81}Br]$^+$:413.99740; found: 413.99696; calcd for $C_{13}H_8BrF_3O_5S$ [M, ^{79}Br]$^+$: 411.98531; found: 411.98491.

General procedure for the synthesis of 10a-g

A solution of **9** (50 mg, 0.122 mmol), K_2CO_3 (2M, 2 mL), $Pd(PPh_3)_4$ (6 mmol-%) and arylboronic acid **4** (2.4 equiv.) in 1,4-dioxane (3 mL) was stirred at 120 °C for 6 h under argon atmosphere. To the reaction mixture H_2O (20 mL) and CH_2Cl_2 (25 mL) were added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, heptane/EtOAc).

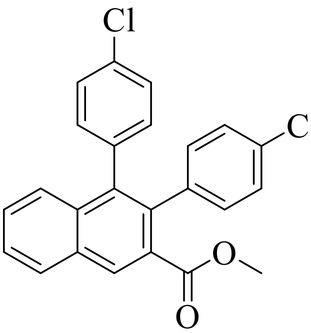
Methyl 3,4-bis(3-methylphenyl)-2-naphthoate (10a)



Starting with **9** (50 mg, 0.122 mmol), **4b** (39 mg, 0.29 mmol), $Pd(PPh_3)_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **10a** was isolated as a white solid (32 mg, 72 %); mp 95-97 °C. ^{1}H NMR (300 MHz. $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 6.74-6.84 (m, 5H, ArH), 6.92-6.98 (m, 2H, ArH), 7.02-7.08 (m, 1H, ArH), 7.35-7.50 (m, 3H, ArH), 7.89 (d, J = 8.51 Hz, 1H, ArH), 8.28 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.2 (CH_3), 21.3

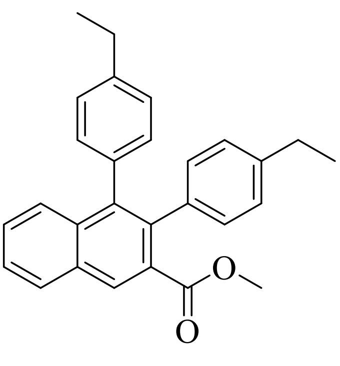
(CH_3), 53.4 (OCH_3), 126.3, 126.84, 126.88, 126.9, 127.1, 127.3, 127.6, 127.8, 128.0, 128.6 (CH), 129.2 (C), 129.4 (CH), 130.3 (C), 130.6 (CH), 131.6 (C), 131.7 (CH), 133.8, 136.3, 136.9, 137.0, 138.2, 139.9 (C), 169.2 (C=O). IR (KBr, cm^{-1}): ν = 3028, 2946, 2918, 2857, 2732 (w), 1727 (s), 1621, 1604, 1584, 1484 (w), 1436 (m), 1372, 1332 (w), 1301 (s), 1267 (m), 1226, 1202, 1190, 1163 (s), 1126 (m), 1101, 1087 (s), 1033, 1022 (m), 999, 970 (w). GC-MS (EI, 70 eV): m/z (%) = 366 ([M]$^+$, 100), 335 (32), 319 (10), 292 (13), 291 (12), 289 (14), 276 (14). HRMS (EI, 70 eV) calcd. for $C_{26}H_{22}O_2$ [M]$^+$: 366.16143; found: 366.16095.

Methyl 3,4-bis(4-chlorophenyl)-2-naphthoate (10b)



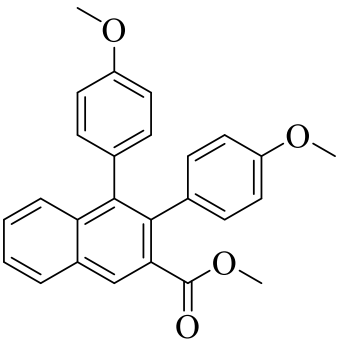
Starting with **9** (50 mg, 0.122 mmol), **4c** (45 mg, 0.29 mmol), $Pd(PPh_3)_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **10b** was isolated as a white solid (34 mg, 69 %); mp 81-84 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.57 (s, 3H, OCH_3), 6.85-6.96 (m, 4H, ArH), 7.05-7.09 (m, 2H, ArH), 7.17-7.19 (m, 2H, ArH), 7.40-7.53 (m, 3H, ArH), 7.92 (d, J = 7.5 Hz, 1H, ArH), 8.37 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.15 (OCH_3), 126.6, 126.8, 127.5, 128.2, 128.5, 128.9 (CH), 129.6 (C), 130.6, 131.1 (CH), 131.8 (C), 132.2 (CH), 132.4, 133.0, 133.6, 135.9, 136.5, 138.3, 138.7 (C), 168.4 (C=O). IR (KBr, cm^{-1}): ν = 3057, 2961, 2925, 2855, 1716 (w), 1608, 1589 (m), 1536, 1482 (w), 1235, 1209 (m), 1137, 1117, 1095, 1070 (s). GC-MS (EI, 70 eV): m/z (%) = 408 ([M, ^{37}Cl]$^+$, 68), 406 ([M, ^{35}Cl]$^+$, 100) 410 (12), 409 (18), 377 (24), 375 (37), 340 (17), 312 (24), 277 (18), 274 (18). HRMS (EI, 70 eV) calcd. for $C_{24}H_{16}O_2C_{l2}$ [M, ^{35}Cl]$^+$: 406.05219; found:406.05154; calcd. for $C_{24}H_{16}O_2C_{l2}$ [M, ^{73}Cl]$^+$: 408.04924; found: 408.04910.

Methyl 3,4-bis(4-ethylphenyl)-2-naphthoate (10c)



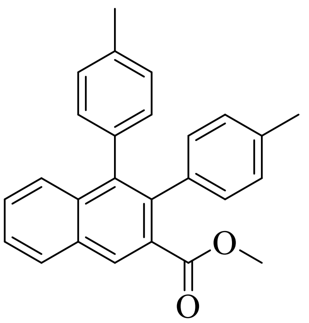
Starting with **9** (50 mg, 0.122 mmol), **4d** (43 mg, 0.29 mmol), $Pd(PPh_3)_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **10c** was isolated as a white solid (39 mg, 81 %); mp 92-95 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 (m, 6H, $2CH_3$), 2.52 (dq, J = 18.4, 7.6 Hz, 4H, $2CH_2$), 3,51 (s, 3H, OCH_3), 6.84-6.92 (m, 6H, ArH), 6.99 (d, J = 8.12 Hz, 2H, ArH), 7.35-7.52 (m, 3H, ArH), 7.88 (d, J = 7.8 Hz, 1H, ArH), 8.26 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ =14.4 (CH_3), 14.5 (CH_3), 27.4 (CH_2), 27.5 (CH_2), 51.9 (OCH_3), 125.3, 125.5 (C), 126.3, 126.6, 127.0, 127.1, 127.8, 128.7, 129.3, 129.8, 130.9 (CH), 133.0, 134.6, 136.0, 136.3, 138.9, 140.8, 141.4 (C), 168.3 (C=O). IR (KBr, cm^{-1}): *ν* = 3059, 3022 (w), 2965, 2945 (m), 2930, 2871 (w), 1720 (s), 1618, 1591 (w), 1513 (m), 1490 (w), 1453, 1443, 1424, 1405 (m), 1370, 1334 (w), 1300, 1261, 1232, 1208 (s), 1179, 1149, 1127 (w), 1115 (m). GC-MS (EI, 70 eV): m/z (%) = 394 ([M]$^+$, 100), 347 (10), 305 (11), 289 (17), 276 (10). HRMS (EI, 70 eV) calcd. for $C_{28}H_{26}O_2$ [M]$^+$: 394.19273; found: 394.19229.

Methyl 3,4-bis(4-methoxyphenyl)-2-naphthoate (10d)



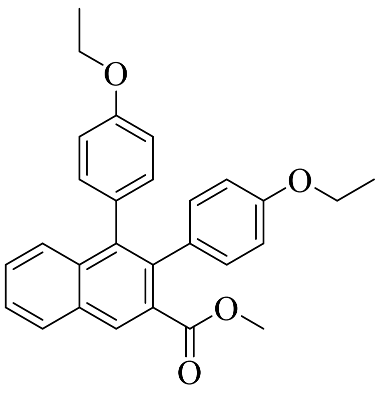
Starting with **9** (50 mg, 0.122 mmol), **4e** (44 mg, 0.29 mmol), $Pd(PPh_3)_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **10d** was isolated as a white solid (42 mg, 86 %); mp 113 - 115 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.56 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 6.63 (d, *J* = 8.8 Hz, 2H, ArH), 6.73 (d, *J* = 8.8 Hz, 2H, ArH), 6.87 (d, *J* = 8.7 Hz, 2H, ArH), 6.92 (d, *J* = 8.8 Hz, 2H, ArH), 7.35-7.51 (m, 3H, ArH), 7.89 (d, *J* =8.4 Hz, 1H, ArH), 8.25 (br. s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.1, 55.0, 55.1 (OCH_3), 112.7, 113.2, 126.3, 126.9, 127.8, 128.7, 129.3 (CH), 130.7, 130.8 (C), 130.9 (CH), 131.6 (C), 132.1 (CH), 132.5, 134.2, 136.8, 139.7, 157.8, 158.2 (C), 169.5 (C=O). IR (KBr, cm^{-1}): *ν* = 3243, 3152, 2862, 2800, 2739 (w), 1700 (m), 1655 (s), 1614, 1428, 1405 (m), 1377, 1315 (w), 1298 (m), 1233 (w), 1201, 1184, 1144, 1115 (s). GC-MS (EI, 70 eV): m/z (%) = 398 ([M]$^+$, 100), 367 (13), 256 (16). HRMS (EI, 70 eV) calcd. for $C_{26}H_{22}O_4$ [M]$^+$: 398.15126; found: 398.15102.

Methyl 3,4-bis(4-methylphenyl)-2-naphthoate (10e)



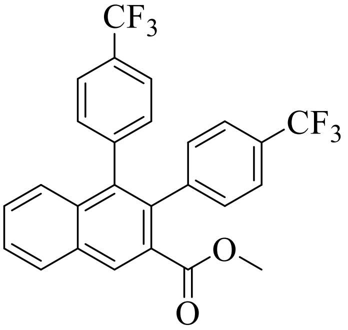
Starting with **9** (50 mg, 0.122 mmol), **4f** (39 mg, 0.29 mmol), $Pd(PPh_3)_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **10e** was isolated as a white solid (35 mg, 78 %); mp 97 - 100 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.19 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 6.82-6.86 (m, 4H, ArH), 6.89 (d, *J* = 8.04 Hz, 2H, ArH), 6.98 (d, *J* = 7.8 Hz, 2H, ArH), 7.33-7.47 (m, 2H, ArH), 7.86-7.90 (m, 2H, ArH), 8.26 (br. s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.2 (CH_3), 29.7 (CH_3), 55.2 (OCH_3), 126.3, 127.0, 127.8, 127.9, 128.3, 128.6, 129.4, 129.7 (CH), 130.6 (C), 130.9 (CH), 131.6, 134.0, 135.4, 135.5, 136.1, 136.9, 137.1, 139.9 (C), 169.3 (C=O). IR (KBr, cm^{-1}): *ν* = 3043, 3022, 2952, 2918, 2849, 1900 (w), 1716 (s), 1514, 1488, 1435 (m), 1417, 1408 (w), 1379 (m), 1333 (w), 1301, 1262, 1232, 1207, 1180 (s), 1153, 1128 (m). GC-MS (EI, 70 eV): m/z (%) = 366 ([M]$^+$, 100), 335 (29), 319 (12), 306 (12), 292 (16), 291 (13), 289 (18). HRMS (EI, 70 eV) calcd. for $C_{26}H_{22}O_2$ [M]$^+$: 366.16134; found: 366.16134.

Methyl 3,4-bis(4-ethoxyphenyl)-2-naphthoate (10f)



Starting with **9** (50 mg, 0.122 mmol), **4g** (48 mg, 0.29 mmol), Pd(PPh_3)$_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **10f** was isolated as a white solid (48 mg, 93%); mp 102 - 105 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28-1.35 (m, 6H, 2CH_3), 3.54 (s, 3H, OCH_3), 3.84-3.97 (m, 4H, 2OCH_2), 6.60 (d, *J* = 8.6 Hz, 2H, ArH), 6.71 (d, *J* = 8.6 Hz, 2H, ArH), 6.85 (d, *J* = 8.6 Hz, 2H, ArH), 6.9 (d, *J* = 8.8 Hz, 2H, ArH), 7.34-7.51 (m, 3H, ArH), 7.87 (d, *J* = 7.4 Hz, 1H, ArH), 8.23 (br. s,1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.9, 29.7 (2CH_3), 52.1 (OCH_3), 63.2, 63.3 (2OCH_2), 113.3, 113.7, 126.3, 127.0, 127.8, 128.7, 129.2 (CH), 130.6, 130.8 (C), 130.9 (CH), 131.7 (C), 132.1 (CH), 132.4, 134.2, 136.8, 139.8, 157.2, 157.6 (C), 169.5 (C=O). IR (KBr, cm^{-1}): *ν* = 3044, 2979, 2950, 2921, 2894, 2873, 2849 (w), 1721, 1715, 1608 (s), 1573 (w), 1512 (s), 1489, 1473, 1441, 1390, 1376 (m), 1331 (w), 1300 (s), 1284, 1258 (m), 1240, 1205, 1174 (s), 1129 (w), 1112 (s), 1097 (m), 1045 (s). GC-MS (EI, 70 eV): m/z (%) = 426 ([M]$^+$, 100), 281 (10), 252 (10). HRMS (EI, 70 eV) calcd. for $C_{28}H_{26}O_4$ [M]$^+$: 426.18256; found: 426.18189.

Methyl 3,4-bis(4-trifluoromethylphenyl)-2-naphthoate (10g)

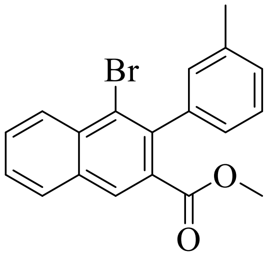


Starting with **9** (50 mg, 0.122 mmol), **4j** (55 mg, 0.29 mmol), Pd(PPh_3)$_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **10g** was isolated as a white solid (42 mg, 73 %); mp 94 - 97 °C. ^{1}H NMR (300 MHz. $CDCl_3$): δ = 3.56 (s, 3H, OCH_3), 7.08 (d, *J* = 7.9 Hz, 2H, ArH), 7.13 (d, *J* = 7.9 Hz, 2H, ArH), 7.34 (d, *J* = 8.5 Hz, 3H, ArH), 7.43-7.48 (m, 3H, ArH), 7.53 (dd, *J* = 8, 1.4 Hz, 1H, ArH), 7.95 (d, *J* = 7.9 Hz, 1H, ArH), 8.46 (s, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -62.52, -62.60. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 51.2 (OCH_3), 123.2 (q, $J_{C,F}$ = 3.9 Hz, CH), 123.7 (CH), 123.8 (q, $J_{C,F}$ = 3.3 Hz, CH), 124.0 (q, $J_{C,F}$ = 271 Hz, CF_3), 124.1 (q, $J_{C,F}$ = 271 Hz, CF_3), 125.4, 126.1 (C), 127.8, 128.0, 128.1, 129.1, 130.2 (CH), 130.9 (q, $J_{C,F}$ = 31 Hz, C), 131.1 (q, $J_{C,F}$ = 35 Hz, C), 132.4, 134.8, 137.5, 140.8, 142.5 (C), 167.2 (C=O). IR (KBr, cm^{-1}): *ν* = 3313, 3252 (w), 2962, 2870 (m), 2659, 1900 (w), 1785, 1754, 1608 (s), 1585, 1490, 1415 (w), 1328 (m), 1283, 1251 (s), 1154 (m). GC-MS (EI, 70 eV): m/z (%) = 474 ([M]$^+$, 100), 444 (14), 443 (57), 423 (13), 346 (23), 345 (10), 344 (13), 276 (22). HRMS (EI, 70 eV) calcd. for $C_{26}H_{16}O_2F_6$ [M]$^+$: 474.10490; found: 474.10420.

General procedure for the synthesis of 11a-e

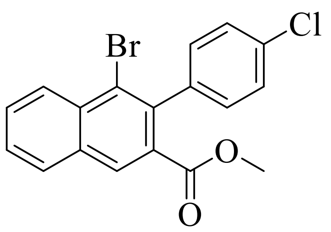
A 1,4-dioxan solution of **9** (50 mg, 0.122 mmol), K_2CO_3 (2M, 2 mL), $Pd(PPh_3)_4$ (3 mol-%) and of arylboronic acid **4** (1.0 equiv.) was stirred at 60 °C for 9 h under argon atmosphere. To the reaction mixture were added H_2O (20 mL) and CH_2Cl_2 (25 mL). The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, heptane / EtOAc = 100:5).

Methyl 4-bromo-3-(3-methylphenyl)-2-naphthoate (11a)



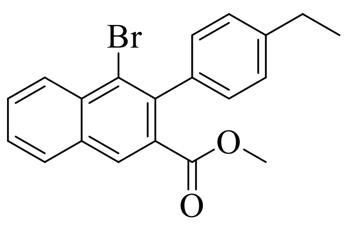
Starting with **9** (50 mg, 0.122 mmol), **4b** (17 mg, 0.122 mmol), $Pd(PPh_3)_4$ (4 mg, 3 mole %), K_2CO_3 (2M, 2 mL), and 1,4-dioxane (3 mL), **11a** was isolated as a white solid (36 mg, 83 %); mp 105 - 108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 6.77 (s, 1H, ArH), 7.01 (d, *J* = 7.1 Hz, 2H, ArH), 7.14-7.16 (m, 1H, ArH), 7.24-7.29 (m, 1H, ArH), 7.51-7.56 (m, 1H, ArH), 7.64 (ddd, *J* = 8.5, 7, 1.3 Hz, 1H, ArH), 7.87 (d, *J* = 7.9 Hz, 1H, ArH), 8.33 (d, *J* = 8.7 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5 (CH_3), 51.17 (OCH_3), 125.3, 126.3, 126.6, 127.1, 127.2 (CH), 127.6 (C), 128.1, 128.6, 128.8, 128.9 (CH), 129.6, 131.5, 132.6, 136.2, 138.4, 140.1 (C), 166.7 (C=O). IR (KBr, cm^{-1}): v = 3050, 3023 (w), 2984, 2921 (m), 2845 (w), 1728 (s), 1621, 1545, 1512 (w), 1484, 1439 (m), 1375, 1322, 1303 (w), 1256, 1232, 1190 (s). GC-MS (EI, 70 eV): m/z (%) = 356 ([M, ^{81}Br]$^+$, 83), 354 ([M, ^{79}Br]$^+$, 83), 357 (17), 325 (19), 323 (19), 260 (10), 244 (100), 243 (18), 216 (21). HRMS (EI, 70 eV) calcd. for $C_{19}H_{15}BrO_2$ [M, ^{79}Br]$^+$: 354.02499; found: 354.02481; calcd. for $C_{19}H_{15}BrO_2$ [M, ^{81}Br]$^+$: 356.02295; found: 354.02303.

Methyl 4-bromo-3-(4-chlorophenyl)-2-naphthoate (11b)



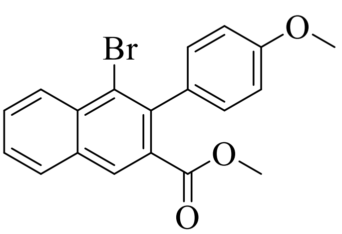
Starting with **9** (50 mg, 0.122 mmol), **4c** (19 mg, 0.122 mmol), $Pd(PPh_3)_4$ (4 mg, 3 mole %), K_2CO_3 (2M, 2 mL), and 1,4-dioxane (3 mL), **11b** was isolated as a white solid (34 mg, 76 %); mp 88-91°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.58 (s, 3H, OCH_3), 7.12-7.16 (m, 2H, ArH), 7.35 (d, *J* = 8.5 Hz, 2H, ArH), 7.53-7.70 (m, 2H, ArH), 7.88 (dd, *J* = 8.1, 1.2 Hz, 1H, ArH), 8.33 (d, *J* = 8.9 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.3 (OCH_3), 124.6, 126.4 (C), 127.6, 128.0, 128.1, 129.2, 129.8, 130.4, 130.5 (CH), 131.5, 132.4, 132.5, 137.2, 138.7 (C), 166.2 (C=O). IR (KBr, cm^{-1}): *ν* = 3100, 3083, 3051, 2997, 2947, 2918, 2849 (w), 1730, 1720 (s), 1621, 1596, 1555 (w), 1494, 1439, 1395, 1346, 1314 (m), 1263, 1227, 1208, 1140, 1099, 1083 (s), 1029 (w). GC-MS (EI, 70 eV): m/z (%) = 376 ([M, ^{81}Br, ^{35}Cl]$^{+,}$ 100), 374 ([M, ^{79}Br, ^{35}Cl]$^{+,}$ 75), 345 (28), 343 (22), 280 (14), 266 (26), 265 (19), 264 (77), 238 (10), 199 (13). HRMS (EI, 70 eV) calcd. for $C_{18}H_{12}BrO_2Cl$ [M,^{79}Br,^{35}Cl]$^+$: 373.97032; found: 373.97039; calcd. for $C_{18}H_{12}BrO_2Cl$ [M,^{81}Br,^{35}Cl]$^+$: 375.96832; found: 375.96804.

Methyl 4-bromo-3-(4-ethylphenyl)-2-naphthoate (11c)



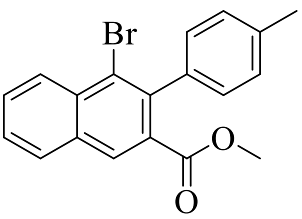
Starting with **9** (50 mg, 0.122 mmol), **4d** (18 mg, 0.122 mmol), $Pd(PPh_3)_4$ (4 mg, 3 mole %), K_2CO_3 (2M, 2 mL), and 1,4-dioxane (3 mL), **11c** was isolated as a white solid (39 mg, 88 %); mp 101-104 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ =1.23 (m, 3H, CH_3), 2.67 (m, 2H, CH_2), 3.52 (s, 3H, OCH_3), 7.12 (d, *J* = 8.31 Hz, 2H, ArH), 7.18-7.22 (m, 3H, ArH), 7.50-7.55 (m, 1H, ArH), 7.63 (ddd, *J* = 8.5, 7, 1.3 Hz, 1H, ArH), 7.86 (d, *J* = 7.1 Hz, 1H, ArH), 8.32 (d, *J* = 8.50 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.3 (CH_3), 28.7 (CH_2), 52.2 (OCH_3), 125.5 (C), 127.2, 127.3, 128.1, 129.0, 129.1, 129.5, 129.8 (CH), 130.8, 132.4, 133.6, 138.4, 139.3, 143.4 (C), 167.8 (C=O). IR (KBr, cm^{-1}): *ν* = 3050, 3020 (w), 2961, 2927, 2871, 2855 (m), 1729 (s), 1621, 1553 (w), 1515, 1484 (m), 1437 (s), 1409, 1373, 1346 (m), 1282, 1262, 1233, 1202 (s), 1145 (w), 1138, 1116 (s). GC-MS (EI, 70 eV): m/z (%) = 370 ([M, ^{81}Br]$^+$, 56), 368 ([M, ^{79}Br]$^+$, 100), 314 (15), 251 (17), 149 (10). HRMS (EI, 70 eV) calcd. for $C_{20}H_{17}BrO_2$ [M, ^{79}Br]$^+$: 368.04221; found: 368.04102; calcd. for $C_{20}H_{17}BrO_2$ [M, ^{81}Br]$^+$: 370.03921; found: 370.03100.

Methyl 4-bromo-3-(4-methoxyphenyl)-2-naphthoate (11d)



Starting with **9** (50 mg, 0.122 mmol), **4e** (19 mg, 0.122 mmol), $Pd(PPh_3)_4$ (4 mg, 3 mole %), K_2CO_3 (2M, 2 mL), and 1,4-dioxane (3 mL), **11d** was isolated as a white solid (41 mg, 92 %); mp 107 - 110 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.56 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 6.91 (d, J = 8.69 Hz, 1H, ArH), 7.11-7.19 (m, 3H, ArH), 7.50-7.56 (m, 1H, ArH), 7.64 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H, ArH), 7.86 (d, J = 7.93 Hz, 1H, ArH), 8.25 (s, 1H, ArH), 8.32 (d, J = 8.69 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.3, 55.2 (OCH_3), 113.2 (CH), 125.9 (C), 127.3, 128.1, 129.0, 129.5, 129.8, 130.5 (CH), 132.4, 133.5, 133.6, 137.8, 138.9, 142.2 (C), 167.9 (C=O). IR (KBr, cm^{-1}): ν = 3041, 3000, 2951, 2931, 2849, 2832, 1881 (w), 1729 (s), 1607 (m), 1575, 1552 (w), 1513 (s), 1483 (w), 1455 (m), 1436 (s), 1346, 1314, 1304, 1285 (m), 1257, 1238, 1229, 1200, 1177, 1135, 1099, 1029 (s). GC-MS (EI, 70 eV): m/z (%) = 372 ([M, $^{81}Br]^+$, 100), 370 ([M, $^{79}Br]^+$, 100), 339 (11), 261 (16), 260 (68), 245 (22), 217(10). HRMS (EI, 70 eV) calcd. for $C_{19}H_{15}BrO_3$ [M, $^{79}Br]^+$: 370.01991; found: 370.01940; calcd. for $C_{19}H_{15}BrO_3$ [M, $^{81}Br]^+$: 372.01786; found: 372.01693.

Methyl 4-bromo-3-(4-methylphenyl)-2-naphthoate (11e)

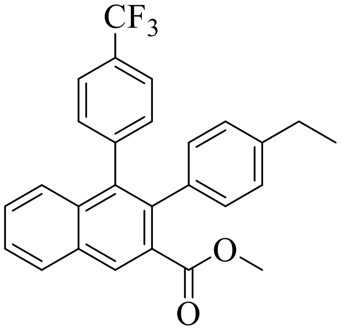


Starting with **9** (50 mg, 0.122 mmol), **4f** (17 mg, 0.122 mmol), $Pd(PPh_3)_4$ (4 mg, 3 mole %), K_2CO_3 (2M, 2 mL), and 1,4-dioxane (3 mL), **11e** was isolated as a white solid (34 mg, 79 %); mp 104- 107 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3H, CH_3), 3.55 (s, 3H, OCH_3), 6.85-6.91 (m, 1H, ArH), 7.10 (d, J = 8.12 Hz, 2H, ArH), 7.17-7.20 (m, 2H, ArH), 7.51-7.56 (m, 1H, ArH), 7.65 (ddd, J = 8.5, 7, 1.3 Hz, 1H, ArH), 7.87 (d, J = 7.93 Hz, 1H, ArH), 8.33 (d, J = 8.69 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5 (CH_3), 52.23 (OCH_3), 127.4, 127.9, 128.1 (CH), 128.4 (C), 128.5, 129.1, 129.6, 129.9 (CH), 130.7, 132.5, 137.1, 138.3, 139.4, 139.9 (C), 167.9 (C=O). IR (KBr, cm^{-1}): ν = 3049, 3020, 2993, 2947 (w), 2920, 2853 (m), 1728 (s), 1621, 1591, 1554 (w), 1515, 1484 (m), 1438 (s), 1376, 1345 (w), 1322, 1300 (m), 1261, 1228, 1203, 1183 (s), 1150, 1138 (m), 1097 (s). GC-MS (EI, 70 eV): m/z (%) = 356 ([M, $^{81}Br]^+$, 81), 354 ([M, $^{79}Br]^+$, 81), 357 (17), 325 (16), 260 (11), 243 (17), 242 (100), 214 (11). HRMS (EI, 70 eV) calcd. for $C_{19}H_{15}BrO_2$ [M, $^{79}Br]^+$: 354.02499; found: 354.02459; calcd. for $C_{19}H_{15}BrO_2$ [M, $^{81}Br]^+$: 356.02295; found: 356.02276.

General procedure for the synthesis of 12a-c

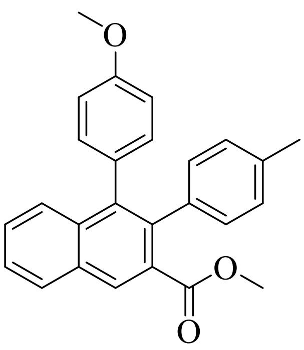
A dioxan solution of **9** (50 mg, 0.122 mmol), Ar^{1}B(OH)$_2$ (1.0 equiv.), K_2CO_3 2M (2mL) and Pd(PPh$_3$)$_4$ (3 mol-%) was heated at 60 °C for 9 h under argon atmosphere. After cooling to 20 °C, Ar^{2}B(OH)$_2$ (1.2 equiv), Pd(PPh$_3$)$_4$ (6 mol-%) were added and the reaction mixture was heated at 120 °C for further 6 h. The reaction mixture was cooled again to 20 °C, H_2O was added and the reaction mixture was 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 column chromatography (EtOAc / heptanes).

Methyl 3-(4-ethylphenyl)-4-(4-trifluoromethylphenyl)-2-naphthoate (12a)



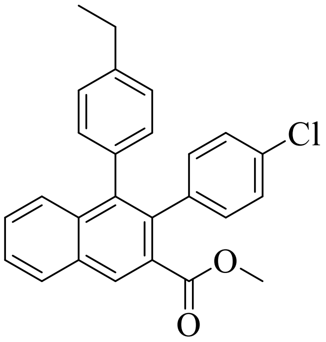
Starting with **9** (50 mg, 0.122 mmol), **4d** (18 mg, 0.122 mmol), Pd(PPh$_3$)$_4$ (4 mg, 3 mole %), K_2CO_3 (2M, 2 mL), and 1,4-dioxane (3 ml), and **4j** (28 mg, 0.146 mmol), Pd(PPh$_3$)$_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **12**a was isolated as a white solid (41 mg, 79%); mp 98-101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.6, 2 Hz, 3H, CH_3), 2.49 (q, *J* = 7.6, 3 Hz, 2H, CH_2), 3.53 (s, 3H, OCH_3), 6.81-6.88 (m, 4H, ArH), 7.13-7.18 (m, 3H, ArH), 7.37-7.49 (m, 4H, ArH), 7.92 (d, *J* = 7.9 Hz, 1H, ArH), 8.33 (s, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -62.48. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.3 (CH_3), 27.4 (CH_2), 51.0 (OCH_3), 121.4 (C), 123.5 (q, $J_{C,F}$ = 3.6 Hz, CH), 124.6 (q, $J_{C,F}$ = 245 Hz, CF_3), 126.8, 128.3, 128.9, 129.7, 130.2 (CH), 131.4 (q, $J_{C,F}$ = 31 Hz, CF), 132.3, 135.6, 137.3, 141.4 (C), 167.8 (C=O). IR (KBr, cm^{-1}): *v* = 3451 (w), 3036, 2985, 2948, 2921 (w), 2856, 2744, 1962, 1935 (w), 1846, 1793 (m), 1732 (s), 1692 (w), 1576, 1534, 1478 (m), 1443, 1412 (w), 1376, 1344, 1317 (m), 1265, 1255 (s), 1232, 1201 (w), 1192 (s). GC-MS (EI, 70 eV): m/z (%) = 434 ([M]$^+$, 100), 419 (21), 405 (11), 403 (16), 387 (12), 375 (12), 373 (10), 359 (10), 289 (15), 276 (17). HRMS (EI, 70 eV) calcd. for $C_{27}H_{21}O_2F_3$ [M]$^+$: 434.14882; found: 434.14868.

Methyl 4-(*p*-methoxyphenyl)-3-(*p*-tolyl)-2-naphthoate (12b)



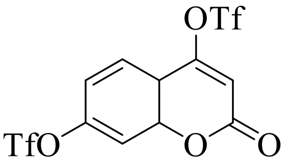
Starting with **9** (50 mg, 0.122 mmol), **4f** (17mg, 0122 mmol), K_2CO_3 (2M, 2 mL) , $Pd(PPh_3)_4$ (4 mg, 3 mol-%) and **4e** (22 mg, 0.146 mmol), $Pd(PPh_3)_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **12b** was isolated as a white solid (39 mg, 86 %); mp 87-88 °C .^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 6.73 (d, *J* = 8.9 Hz, 2H, ArH), 6.82-6.90 (m, 4H, ArH), 6.93 (d, *J* = 8.7 Hz, 2H, ArH), 7.35-7.45 (m, 2H, ArH), 7.47-7.50 (m, 1H, ArH), 7.88 (br. d, *J* = 7.7 Hz, 1H, ArH), 8.3 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 29.9 (CH_3), 51.0, 54.2 (OCH_3), 112.1 (C), 113.1, 119.8 (CH), 125.3, 125.8 (C), 126.3 (CH), 126.9, 127.7 (C), 127.8, 127.9 (CH), 128.4, 128.7 (C), 128.9 (CH), 131.1 (C), 131.7, 132.1 (CH), 134.2 (C), 135.7 (CH), 169.4 (C=O). IR (KBr, cm^{-1}): *v* = 3003, 2956, 2928, 2849 (w), 1727 (s), 1634, 1598, 1507, 1489 (m), 1346, 1277, 1209, 1144 (s), 976, 944, 855, 820, 744 (m), 699, 640 (s). GC-MS (EI,70eV) : m/z (%) = 382 ([M]$^+$, 88), 370 (78), 311 (100), 298 (21), 245 (33), 198 (18). HRMS (EI, 70 eV) calcd for $C_{26}H_{22}O_3$ [M]$^+$:382.01653; found: 382.01693.

Methyl 3-(4-chlorophenyl)-4-(4-ethylphenyl)-2-naphthoate (12c)



Starting with **9** (50 mg, 0.122 mmol), **4c** (19 mg, 0.122 mmol), $Pd(PPh_3)_4$ (4 mg, 3 mole %), K_2CO_3 (2M, 2 mL), and 1,4-dioxane (3 mL), and **4d** (22 mg, 0.146 mmol), $Pd(PPh_3)_4$ (8 mg, 6 mole %), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **12c** was isolated as a white solid (35 mg, 71%); mp 112-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (m, 3H, CH_3), 2.57 (q, *J* = 7.3, 3 Hz, 2H, CH_2), 3.57 (s, 3H, OCH_3), 6.88-6.91 (m, 4H, ArH), 7.00-7.06 (m, 4H, ArH), 7.37-7.50 (m, 3H, ArH), 7.88-7.90 (m, 1H, ArH), 8.33 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.3 (CH_3), 27.4 (CH_2), 51.0 (OCH_3), 125.6, 126.1, 126.2, 126.3, 127.1, 127.7 (CH), 128.7 (C), 128.9, 129.7, 130.2 (CH), 130.8, 131.1, 133.1, 134.1, 134.7, 137.8, 139.2, 141.8 (C), 167.7 (C=O). IR (KBr, cm^{-1}): *v* = 3422, 3365 (w), 2964, 2902 (m), 2835, 2831, 2780 (w), 1983, 1934, 1868 (m), 1721 (s), 1650, 1577, 1562, 1492, 1445 (m), 1432 (s), 1388, 1376, 1322 (w), 1281, 1264, 1218 (s), 1194, 1163, 1114 (m). GC-MS (EI, 70 eV): m/z (%) = 402([M, ^{37}Cl]$^+$, 35), 400([M, ^{35}Cl]$^+$, 100), 369 (12), 304 (11), 291 (10), 290 (13), 289 (28), 277 (12), 276 (31). HRMS (EI, 70 eV) calcd. for $C_{26}H_{21}O_2Cl$ [M, ^{35}Cl]$^+$: 400.12246; found: 400.12207; calcd. for $C_{26}H_{21}O_2Cl$ [M, ^{37}Cl]$^+$: 402.11951; found: 402.12002.

Synthesis of 4,7-Bis-(trifluoromethylsulfonyloxy)-chromen-2-on (14)

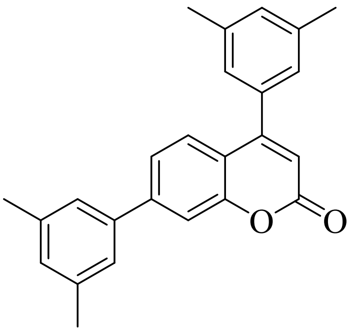


To a CH_2Cl_2 solution (50 mL) of **13** (1.0 g, 5.6 mmol) was added pyridine (1.8 mL, 22.4 mmol) and the solution was stirred at 20 °C for 10 min under argon atmosphere. Then Tf_2O (2.3 mL, 13.5 mmol) was added at 20 °C and the reaction mixture was heated at 50 °C for 20 min. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The product **14** was isolated by column chromatography (flash silica gel, heptane/EtOAc) as a colourless solid (2.1 g, 85 %); mp 79-77 °C. ^{1}H NMR (300 MHz. $CDCl_3$): δ = 6.51 (s, 1H, CH=CH), 7.27-7.32 (m, 2H, ArH), 7.74 (d, J = 8.7 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 105.6, 110.1, 111.6 (CH), 112.9 (C), 118.3 (q, $J_{C,F}$ = 320.0 Hz, CF_3), 118.6 (q, $J_{F,C}$ = 320.0 Hz, CF_3), 123.6 (CH), 151.4, 152.0, 154.9 (C), 157.3 (C=O). ^{19}F NMR (282.4, MHz): δ = -72.5, -72.4. IR (KBr, cm^{-1}): ν = 3171, 2988 (w), 1755 (s), 1698, 1643 (w), 1577 (m), 1550, 1499, 1475, 1433 (w). GC-MS (EI, 70 eV): m/z (%) = 441 ([M]$^+$, 100), 356 (15), 276 (33), 234(23), 195 (16), 168 (17). HRMS (EI, 70 eV) calcd. for $C_{11}H_4O_8F_6S_2$ [M]$^+$: 441.93145; found: 441.93087.

General procedure for the synthesis of (15a-e)

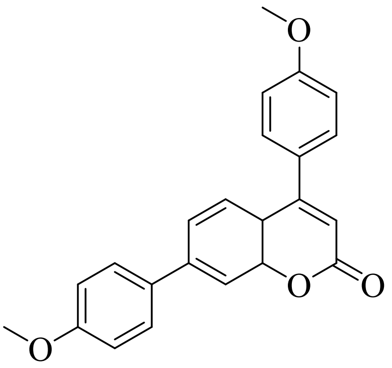
A solution of **14** (0.045 mmol), K_2CO_3 (2M, 2 mL), $Pd(PPh_3)_4$ (6 mol %) and arylboronic acid (2.4 equiv.) in 1,4-dioxane (3 mL) was stirred at 110 °C for 8 h under argon atmosphere. To the reaction mixture H_2O (20 mL) and CH_2Cl_2 (25 mL) were added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried over (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, heptane/EtOAc).

4,7-Bis(3,5-dimethylphenyl)-chromen-2on (15a)



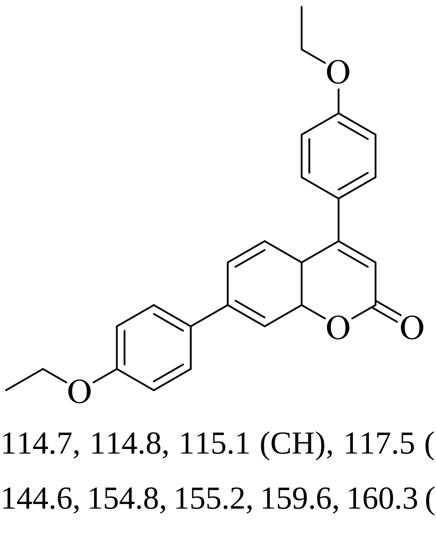
Starting with **14** (20 mg, 0.045 mmol), **4a** (16 mg, 0.11 mmol), $Pd(PPh_3)_4$ (3 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **15a** was isolated as a white solid (13 mg, 81 %); mp: 127-130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ =2.33 (s, 6H, 2CH_3), 2.34 (s, 6H, 2CH_3), 6.27 (s, 1H, ArH), 6.99-7.02 (m, 4H, ArH), 7.09 (s, 1H, ArH), 7.37-7.40 (m, 1H, ArH), 7.46-7.50 (m, 2H, ArH), 7.52-7.53 (m, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3 (2CH_3), 21.4 (2CH_3), 114.3, 115.3 (CH), 117.9 (C), 122.9, 125.1, 126.2, 127.3, 130.2, 131.2 (CH), 135.3, 138.5, 138.6, 139.1, 145.2, 154.5, 155.8 (C), 161.0 (C=O). IR (KBr, cm^{-1}): ν = 3356, 3312, 2961, 1943 (m), 1902, 1831, 1805 (s), 1778, 1709 (w), 1688 (m), 1583, 1550, 1470 (s), 1419, 1352, 1315 (w), 1255, 1221, 1218 (s), 1157, 1144, 1103 (m). GC-MS (EI, 70 eV): m/z (%) = 354 ([M]$^+$, 100), 340 (10), 339 (40), 327 (15), 326 (60), 162 (12). HRMS (EI, 70 eV) calcd. for $C_{25}H_{22}O_2$ [M]$^+$: 354.16143; found: 354.16190.

4,7-Bis(4-methoxyphenyl)-chromen-2-on (15b)



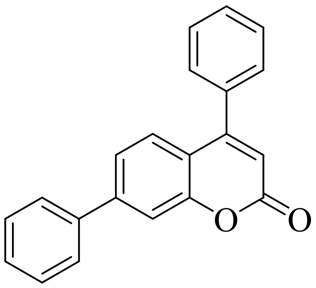
Starting with **14** (20 mg, 0.045 mmol), **4e** (17 mg, 0.11 mmol), Pd(PPh_3)$_4$ (3 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **15b** was isolated as a white solid (11 mg, 68 %); mp: 112-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.26 (s, 1H, CH), 6.95 (d, *J* = 8.9 Hz, 2H, ArH), 6.99 (d, *J* = 8.9 Hz, 2H, ArH), 7.35-7.39 (m, 3H, ArH), 7.50-7.54 (m, 4H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.4, 55.7 (2OCH_3), 110.3, 112.4, 113.0, 114.6 (CH), 117.8 (C), 122.4, 124.4, 127.6, 128.2 (CH), 131.7, 138.2, 143.2, 155.5, 156.9, 157.8, 159.7 (C), 161.0 (C=O). IR (KBr, cm^{-1}): ν = 3377 (m), 3012, 2961, 1921, 1850 (w), 1721, 1605 (s), 1578, 1529, 1510 (m), 1463, 1450, 1440, 1419, 1372, 1309 (w), 1295, 1278 (m), 1257, 1244 (s), 1197, 1179, 1164, 1131, 1110 (m), 1094 (w). GC-MS (EI, 70 eV): m/z (%) = 358 ([M]$^+$, 100), 331 (10), 330 (43), 315 (30). HRMS (EI, 70 eV) calcd. for $C_{23}H_{18}O_4$ [M]$^+$: 358.11996; found: 358.11953.

4,7-Bis(4-ethoxyphenyl)-chromen-2-on (15c)



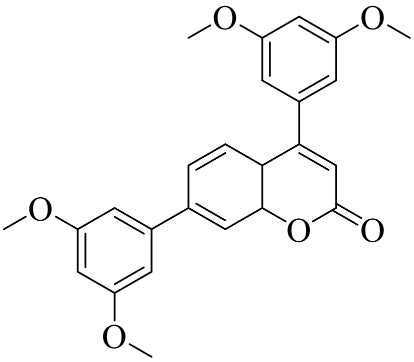
Starting with **14** (20 mg, 0.045 mmol), **4g** (18 mg, 0.11 mmol), Pd(PPh_3)$_4$ (3 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **15c** was isolated as a white solid (12 mg, 66 %); mp 114-117 °C. ^{1}H NMR (300 MHz. $CDCl_3$): δ = 1.36-1.43 (m, 6H, 2CH_3), 3.99-4.09 (m, 4H, 2OCH_2), 6.25 (s, 1H, CH), 6.91-6.99 (m, 4H, ArH), 7.37 (d, *J* = 8.7 Hz, 3H, ArH), 7.49-7.59 (m, 4H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.8 (2CH_3), 63.6, 63.7 (2OCH_2), 113.7, 114.7, 114.8, 115.1 (CH), 117.5 (C), 122.4, 127.3 (CH), 127.4 (C), 128.3, 129.9 (CH), 131.2, 144.6, 154.8, 155.2, 159.6, 160.3 (C), 162.2 (C=O). IR (KBr, cm^{-1}): ν = 3051, 3037, 2990, 2972, 2928, 2894, 2850 (w), 1722, 1605 (s), 1576, 1569 (w), 1510 (m), 1476, 1455 (w), 1436 (m), 1397, 1386 (w), 1370 (m), 1308 (w), 1295 (m), 1257, 1242 (s). GC-MS (EI, 70 eV): m/z (%) = 386 ([M]$^+$, 100), 358 (16), 330 (16), 329 (10), 302 (19), 273 (10). HRMS (EI, 70 eV) calcd. for $C_{25}H_{22}O_4$ [M]$^+$: 386.15126; found: 386.15104.

4,7-Bis(phenyl)-chromen-2-on (15d)



Starting with **14** (20 mg, 0.045 mmol), **4k** (13 mg, 0.11 mmol), $Pd(PPh_3)_4$ (3 mg, 6 mole%), K_2CO_3 (2M, 2mL) and 1,4-dioxane (3 mL), **15d** was isolated as a white solid (11 mg, 79 %); mp 131-133 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.31 (s, 1H, CH), 7.34-7.37 (m, 1H, ArH), 7.39-7.44 (m, 5H, ArH), 7.47-7.49 (m, 4H, ArH), 7.56-7.58 (m, 3H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 113.8, 114.4 (CH), 116.8 (C), 121.9, 126.2, 126.3 (CH), 126.5 (C), 127.4, 127.6, 127.9, 128.1, 128,7 (CH), 134.3, 138.0, 144.1, 153.6 (C), 162.1 (C=O). IR (KBr, cm^{-1}): ν = 3399, 3070, 3051, 2959, 2918, 2849, 1722, 1707, 1650, 1631, 1593 (w), 1573, 1535 (m), 1512, 1495 (w), 1446, 1428, 1402 (m), 1315, 1290 (w), 1285 (s), 1227 (w), 1163, 1156 (m), 1123, 1076, 1012 (s). GC-MS (EI, 70 eV): m/z (%) = 298 ($[M]^+$, 100), 297 (17), 271 (20), 241(28), 240 (11), 239 (32). HRMS (EI, 70 eV) calcd. for $C_{21}H_{14}O_2$ $[M]^+$: 298.09883; found: 298.09803.

4,7-Bis(3,5-dimethoxyphenyl)-chromen-2-on (15e)

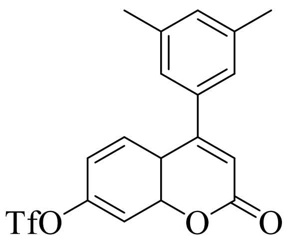


Starting with **14** (20 mg, 0.045 mmol), **4l** (18 mg, 0.11 mmol), $Pd(PPh_3)_4$ (3 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **15e** was isolated as a white solid (13 mg, 69 %); mp 111-114 °C. ^1H NMR (300 MHz. $CDCl_3$): δ = 3.02 (s, 6H, $2OCH_3$), 3.04 (s, 6H, $2OCH_3$), 5.56 (s, 1H, CH), 5.70 (s, 1H, ArH), 5.75-5.79 (m, 3H, ArH), 5.92-5.93 (m, 2H, ArH), 6.60-6.63 (m, 1H, ArH), 7.76-7.78 (m, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 53.4 ($2OCH_3$), 55.5 ($2OCH_3$), 99.9, 100.5, 101.4, 105.4, 110.7, 116.6, 122.6 (CH), 123.8 (C), 130.0 (CH), 132.5, 135.7, 150.2, 156.4, 157.5, 160.5, 160.9 (C), 161.2 (C=O). IR (KBr, cm^{-1}): ν = 3377 (m), 3012, 2961, 1921, 1850 (w), 1721, 1605 (s), 1578, 1529, 1510 (m), 1463, 1450, 1440, 1419, 1372, 1309 (w), 1295, 1278 (m), 1257, 1244 (s), 1197, 1179, 1164, 1131, 1110 (m), 1094 (w). GC-MS (EI, 70 eV): m/z (%) = 418 ($[M]^+$, 100), 390 (28), 369 (13). HRMS (EI, 70 eV) calcd. for $C_{25}H_{22}O_6$ $[M]^+$: 418.14313; found: 418.14202.

General procedure for the synthesis of 16a-h

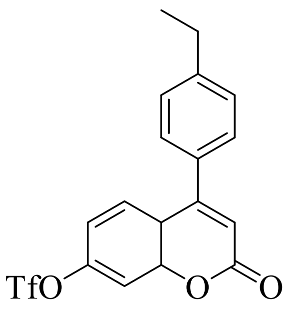
A solution of **14** (0.045 mmol), K_2CO_3 (2M, 2 mL), $Pd(PPh_3)_4$ (3 mole%) and arylboronic acid (1.0 equiv.) in toluene (3 mL) was stirred at 65 °C. for 6 h. under argon atmosphere. To the reaction mixture H_2O (20 mL) and CH_2Cl_2 (25 mL) were added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried over (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, heptane/EtOAc).

4-(3,5-Methylphenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16a)



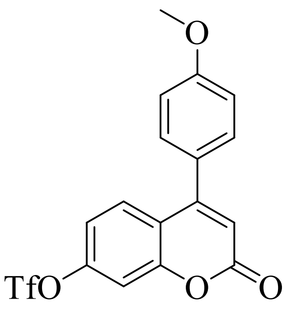
Starting with **14** (20 mg, 0.045 mmol), **4a** (7 mg, 0.045 mmol), $Pd(PPh_3)_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16a** was isolated as a white solid (15 mg, 82 %); mp 93-96 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 6H, $2CH_3$), 6.33 (s, 1H, CH), 6.96 (s, 2H, ArH), 7.07-7.11 (m, 2H, ArH), 7.26-6.27 (m, 1H, ArH), 7.55 (d, J = 8.9 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -72.51. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3 ($2CH_3$), 110.6, 115.6, 117.3 (CH), 118.1 (q, $J_{C,F}$ = 320.6 Hz, CF_3), 119.3 (C), 125.9, 128.9, 131.7 (CH), 134.3, 150.7, 154.6, 154.9, 159.9 (C), 161.8 (C=O). IR (KBr, cm^{-1}): v = 3085, 3059, 3028, 2956 (w), 2921 (m), 2852 (w), 1650, 1624, 1600 (s), 1545 (m), 1488 (w), 1444 (m), 1428, 1412, 1400, 1376 (s), 1317 (m), 1269 (w), 1247, 1226 (m), 1204, 1190 (s), 1160 (m), 1141 (s), 1087, 1075, 1052 (w). GC-MS (EI, 70 eV): m/z (%) = 398 ([M]$^+$, 100), 397 (16), 384 (19), 265 (14), 250 (11), 238 (11), 237 (65), 209 (48), 181 (12), 166 (32), 165 (45), 152 (10). HRMS (EI, 70 eV) calcd. for $C_{18}H_{13}O_5F_3S$ [M]$^+$: 398.04303; found: 398.04260.

4-(Ethylphenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16b)



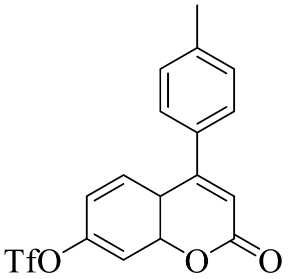
Starting with **14** (20 mg, 0.045 mmol), **4d** (7 mg, 0.045 mmol), $Pd(PPh_3)_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16b** was isolated as a white solid (13 mg, 73 %); mp 81-84 °C. ^{1}H NMR (300 MHz. $CDCl_3$): δ = 1.24 (t, J = 7.5 Hz, 3H, CH_3), 2.69 (q, J = 7.4 Hz, 2H, CH_2), 6.35 (s, 1H, CH), 7.09 (d, J = 8.5 Hz, 1H, ArH), 7.19 (s, 1H, ArH), 7.30 (s, 4H, ArH), 7.58 (d, J = 9.0 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -72.52. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.7 (CH_3), 28.7 (CH_2), 110.7, 115.1, 115.3, 117.2 (CH), 118.6 (q, $J_{C,F}$ = 321.2 Hz, CF_3), 119.3, 126.4 (C), 128.9, 129.9 (CH), 150.8, 154.3, 154.8, 159.7 (C), 160.6 (C=O). IR (KBr, cm^{-1}): v = 3371 (m), 3124, 3081, 3025, 3006, 2968, 2919, 2880, 2850 (w), 1715, 1606 (s), 1555, 1509, 1507, 1489, 1416 (w), 1424, 1412 (s), 1361 (m), 1331, 1318 (w), 1238, 1206, 1186 (s), 1155 (w), 1135, 1101, 1017 (s). GC-MS (EI, 70 eV): m/z (%) = 398 ($[M]^+$, 97), 370 (15), 369 (52), 265 (13), 238 (16), 237 (100), 209 (31), 181 (18), 166 (10), 153 (35). HRMS (EI, 70 eV) calcd. for $C_{18}H_{13}F_3O_5S$ $[M]^+$: 398.04303; found: 398.04292.

4-(Methoxyphenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16c)



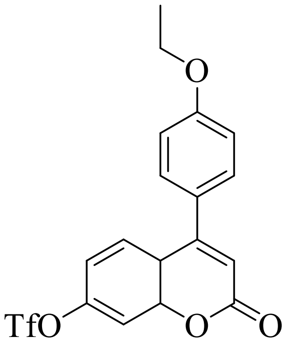
Starting with **14** (20 mg, 0.045 mmol), **4e** (7 mg, 0.045 mmol), $Pd(PPh_3)_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16c** was isolated as a white solid (13 mg, 71 %); mp 86-88 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3H, OCH_3), 6.33 (s, 1H, CH), 6.95 (d, J = 8.7 Hz, 2H, ArH), 7.10 (dd, J = 8.9, 2,3 Hz, 1H, ArH), 7.24 (d, J = 2.3 Hz, 1H, ArH), 7.33 (d, J = 8.7 Hz, 2H, ArH), 7.59 (d, J = 8.9 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -72.5. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.51 (OCH_3), 110.8, 114.3, 114.6, 117.3 (CH), 118.3 (q, $J_{C,F}$ = 320.0 Hz, CF_3), 119.3, 126.6 (C), 128.9, 129.9 (CH), 150.6, 153.0, 154.8, 159.7 (C), 161.2 (C=O). IR (KBr, cm^{-1}): ν = 3039, 2967, 2929 (w), 1756, 1699 (s), 1651, 1645, 1596 (s), 1577, 1538, 1519, 1503, 1474, 1453 (w), 1435 (m), 1396, 1378, 1353 (m), 1295, 1259, 1243, 1209, 1196 (w), 1136 (m), 1084, 1072, 1029, 999 (w), 960 (m), 907 (w), 868, 848, 816, 777 (m), 760 (s), 731 (w), 705, 692 (s), 676, 630, 618, 565, 553, 546 (w). GC-MS (EI, 70 eV): m/z (%) = 400 ($[M]^+$, 100), 240 (15), 211 (33), 183 (23), 168 (19). HRMS (EI, 70 eV) calcd. for $C_{17}H_{11}O_6F_3S$ $[M]^+$: 400.02197; found: 400.02229.

4-(Methylphenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16d)



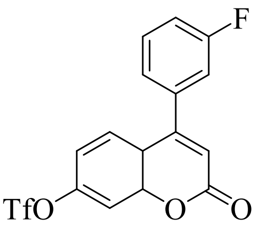
Starting with **14** (20 mg, 0.045 mmol), **4f** (6 mg, 0.045 mmol), $Pd(PPh_3)_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16d** was isolated as a white solid (12 mg, 70 %); mp 79-82 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 3H, CH_3), 6.31 (s, 1H, CH), 6.99 (d, J = 8.7 Hz, 2H, ArH), 7.08 (dd, J = 8.9, 2,3 Hz, 1H, ArH), 7.27 (d, J = 2.5 Hz, 1H, ArH), 7.33 (d, J = 8.7 Hz, 2H, ArH), 7.59 (d, J = 8.9 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -72.5. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.2 (CH_3), 110.8, 114.3, 115.8, 117.6 (CH), 118.3 (q, $J_{C,F}$ = 320.3 Hz, CF_3), 119.5, 125.6 (C), 128.3, 129.0 (CH), 150.8, 152.8, 155.8, 159.7 (C), 163.4 (C=O). IR (KBr, cm^{-1}): ν = 3139, 2867, 2729 (w), 1756, 1699, 1675, 1596 (s), 1557, 1528, 1512, 1503, 1484, 1453 (w), 1405, 1396, 1378, 1353 (m), 1265, 1239, 1213, 1209, 1156 (w), 1112 (m), 1084, 1072 (s), 1009, 980, 960 (m), 907 (w), 888, 854, 832 (m), 777, 760 (s), 731 (w), 705, 692 (s), 696, 640, 607, 553, 546 (w). GC-MS (EI, 70 eV): m/z (%) = 384 ([M]$^+$, 100), 335 (17), 295 (22), 265 (17), 237 (17), 152 (15). HRMS (EI, 70 eV) calcd. for $C_{17}H_{11}O_5F_3S$ [M]$^{+:}$ 384.03225; found: 384.0342.

4-(Ethoxyphenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16e)



Starting with **14** (20 mg, 0.045 mmol), **4g** (8 mg, 0.045 mmol), Pd(PPh_3)$_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16e** was isolated as a white solid (15 mg, 78 %); mp 88-91 °C. ^{1}H NMR (300 MHz. $CDCl_3$): δ = 1.40 (t, *J* = 7.0 Hz, 3H, CH_3), 4.05 (q, *J* = 7.1 Hz, 2H, OCH_2), 6.33 (s, 1H, CH), 6.95-7.00 (m, 2H, ArH), 7.10 (dd, *J* = 8.9 , 2.5 Hz, 1H, ArH), 7.27 (s, 1H, ArH), 7.30-7.33 (m, 2H, ArH), 7.61 (d, *J* = 8.9 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -72.54. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.8 (CH_3), 63.8 (OCH_2), 110.7, 115.1, 115.3, 117.2 (CH), 117.9 (q, $J_{C,F}$ = 321.1 Hz, CF_3), 119.3, 126.4 (C), 128.9, 129.8 (CH), 150.8, 154.3, 154.8, 159.7 (C), 160.6 (C=O). IR (KBr, cm^{-1}): *v* = 3069, 3052, 2977, 2958, 2924, 2872 (s), 1692, 1679, 1666, 1649, 1642 (w), 1606 (m), 1573, 1565 (m), 1553 (w), 1512 (m), 1475 (w), 1428 (s), 1394 (w), 1366 (m), 1293 (w), 1261 (m), 1243, 1214, 1199, 1179, 1140, 1107 (s). GC-MS (EI, 70 eV): m/z (%) = 414 ([M]$^+$, 100), 386 (13), 225 (52), 197 (22), 169 (19). HRMS (EI, 70 eV) calcd. for $C_{18}H_{13}F_3O_6S$ [M]$^+$: 414.03794; found: 414.03693.

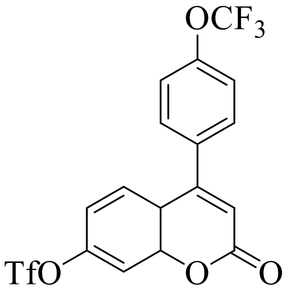
4-(3-Fluorophenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16f)



Starting with **14** (20 mg, 0.045 mmol), **4i** (6 mg, 0.045 mmol), Pd(PPh_3)$_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16f** was isolated as a white solid (11 mg, 64 %); mp 65-68 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.61 (s, 1H, CH), 6.31-6.39 (m, 3H, ArH), 6.43 (s, 1H, ArH), 6.53-6.55 (m, 1H, ArH), 6.72-6.75 (m, 2H, ArH). ^{19}F NMR (282.4, MHz): δ = -111.34, -73.14. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 110.9 (CH), 115.7 (d, $J_{C,F}$ = 23 Hz, CH), 116.3 (CH), 117.3 (d, $J_{C,F}$ = 21 Hz, CH), 117.6 (CH), 118.3 (q, $J_{C,F}$ = 321.1 Hz, CF_3), 124.1 (d, $J_{C,F}$ = 3.3 Hz, CH), 128.5 (CH), 131.1 (d, $J_{C,F}$ = 8 Hz, CH), 136.4 (d, $J_{C,F}$ = 7.7 Hz, CF), 151.0, 153.1 (C), 153.2 (d, $J_{C,F}$ = 1.0 Hz, CF), 154.7 (C), 159.1 (C=O), 164.4 (d, $J_{C,F}$ = 249 Hz, CF). IR (KBr, cm^{-1}): *v* = 3086, 3062, 2957, 2918, 2849 (w), 1711, 1605 (s), 1584, 1563, 1483 (m), 1411 (s), 1371 (m), 1326, 1307, 1278, 1255 (w), 1239, 1200 (s), 1161 (m), 1136, 1125, 1110 (s), 1079 (m), 990, 978, 859 (s). GC-MS (EI, 70 eV): m/z (%) = GC-MS

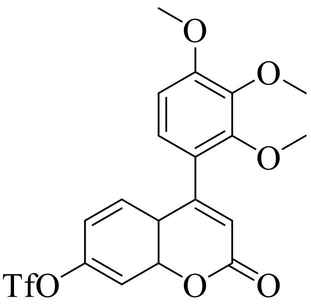
(EI, 70 eV): m/z (%) = 388 ([M]$^+$, 100), 296 (24), 228 (14), 225 (25), 199 (43). HRMS (EI, 70 eV) calcd. for $C_{16}H_8O_5F_4S$ [M]$^+$: 388.00231; found: 388.00187.

4-(Trifluoromethoxyphenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16g)



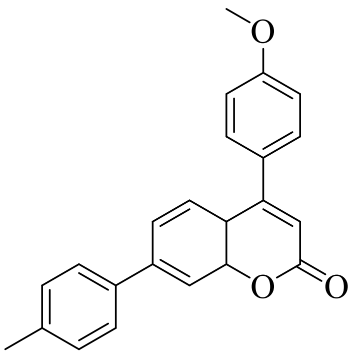
Starting with **14** (20 mg, 0.045 mmol), **4m** (9 mg, 0.045 mmol), Pd(PPh$_3$)$_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16g** was isolated as a white solid (13 mg, 65 %); mp 61-64 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.37 (s, 1H, ArH), 7.10-7.14 (m, 1H, ArH), 7.29-7.30 (m, 1H, ArH), 7.34 (d, J = 8.12 Hz, 2H, ArH), 7.41-7.49 (m, 3H, ArH). ^{19}F NMR (282.4, MHz): δ = -72.52, -57.74. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 109.9, 115.4, 116.5 (CH), 117.8 (C), 118.8 (q, $J_{C,F}$ = 320.4 Hz, CF$_3$), 120.5 (CH), 123.4 (q, $J_{C,F}$ = 259 Hz, CF), 127.5, 129.0 (CH), 149.4 (q, $J_{C,F}$ = 2 Hz, CF), 150.0, 152.1, 153.7 (C), 158.1 (C=O). IR (KBr, cm^{-1}): ν = 3102, 2961, 2923, 2851 (w), 1739 (s), 1620 (m), 1608 (s), 1565, 1507 (m), 1493 (w), 1425 (s), 1411, 1367 (m), 1323 (w), 1256, 1235, 1198, 1162, 1137, 1099, 1028, 987 (s). GC-MS (EI, 70 eV): m/z (%) = 454 ([M]$^+$, 86), 362 (21), 321 (18), 294 (17), 293 (100), 237 (25), 152 (23). (ESI-TOF/MS) calcd. for $C_{17}H_9F_6O_6S$ [M+H]$^+$: 455.00185; found: 455.00181.

4-(2, 3, 4-Trimethoxyphenyl)-7-(trifluoromethylsulfonyloxy)-chromen-2-on (16h)



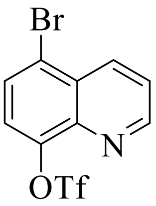
Starting with **14** (20 mg, 0.045 mmol), **4n** (10 mg, 0.045 mmol), Pd(PPh$_3$)$_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL), and toluene (3 mL), **16h** was isolated as a white solid (14 mg, 67 %), mp: 97-100 °C. ^{1}H NMR (300 MHz. CDCl$_3$): δ = 3.68 (s, 3H, OCH$_3$), 3.87 (s, 6H, 2OCH$_3$), 6.34 (s, 1H, CH), 6.72 (d, J = 8.5 Hz, 1H, ArH), 6.85-6.87 (m, 1H, ArH), 7.05 (dd, J = 8.9, 2.5 Hz, 1H, ArH), 7.53-7.66 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, CDCl$_3$): δ = -72.06. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 56.9 (OCH$_3$), 61.0, 61.5 (2OCH$_3$), 107.6, 116.7 (CH), 117.1 (C), 118.3 (q, $J_{C,F}$ = 321.1 Hz, CF$_3$), 121.0, 122.9 (C), 124.2, 128.5, 129.2, 132.1 (CH), 142.4, 150.6, 152.4, 154.2, 155.4 (C), 159.7 (C=O). IR (KBr, cm^{-1}): ν = 3075, 2917, 2848 (w), 1733 (s), 1607 (w), 1573, 1539, 1494, 1463 (w), 1414 (m), 1369, 1325, 1296, 1259 (w), 1237, 1209, 1137 (m), 1095 (s). GC-MS (EI, 70 eV): m/z (%) = 460 ([M]$^+$, 100), 355 (10), 281 (10), 207 (11), 165 (13), 139 (71), 137 (21), 135 (13). HRMS (EI, 70 eV) calcd. for $C_{19}H_{15}O_8F_3S$ [M]$^+$: 460.04342; found 460.04260.

4-(Methoxyphenyl)-7-(methylphenyl)-chromen-2-on (17)



Starting with **14** (20 mg, 0.045 mmol), **4e** (7 mg, 0.045 mmol), Pd(PPh$_3$)$_4$ (1.5 mg, 3 mole%), K_2CO_3 (2M, 2 mL) and toluene (3 mL), and **4f** (7 mg, 0.054 mmol), Pd(PPh$_3$)$_4$ (3 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (2 mL), **17** was isolated as a white solid (13 mg, 84%); mp 104-107 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.38 (s, 3H, CH$_3$), 3.84 (s, 3H, OCH$_3$), 6.28 (s, 1H, C=CH), 7.01 (d, *J* = 8.7 Hz, 2H, ArH), 7.28 -7.33 (m, 1H, ArH), 7.37-7.41 (m, 6H, ArH), 7.53 (d, *J* = 8.00 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 21.3 (CH$_3$), 55.5 (OCH$_3$), 114.2 (C), 114.4, 115.5 (CH), 118.0 (C), 122.9, 124.4 (CH), 127.6 (C), 127.9, 129.0, 129.3, 129.9 (CH), 138.8, 145.2, 152.5, 154.7, 155.2 (C), 161.2 (C=O). IR (KBr, cm^{-1}): v = 3012, 2878, 2822 (w), 1966, 1844 (s), 1744, 1696 (m), 1601, 1578, 1522, 1504 (w), 1487, 1454, 1412 (m). GC-MS (EI, 70 eV): m/z (%) = 342 ([M]$^+$, 100), 318 (23), 280 (16), 234 (10), 187 (19). HRMS (EI, 70 eV) calcd. for $C_{23}H_{18}O_3$ [M]$^+$: 342.12505; found: 342.12459.

5-Bromo-quinolin-8-yl trifluoromethanesulfonate (19)

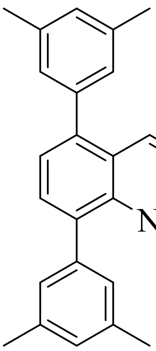


To a CH$_2$Cl$_2$ solution (20 mL) of **18** (1.0 g, 4.5 mmol) was added pyridine (0.45 mL, 5.4 mmol) and the solution was stirred at 20 °C for 10 min under argon atmosphere. Then Tf$_2$O (0.9 mL, 5.4 mmol) 2 was added at 20 °C and the reaction mixture was heated at 50 °C for 20 min. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The product **19** was isolated by column chromatography (flash silica gel, heptanes/EtOAc) as a colourless solid (1.35 g, 85%); mp 89-91 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.45 (d, *J* = 8.31 Hz, 1H, ArH), 7.59 (dd, *J* = 8.59, 4.25 Hz, 1H, ArH), 7.80 (d, *J* = 8.31 Hz, 1H, ArH), 8.51 (dd, *J* = 8.69, 1.51 Hz, 1H, ArH), 9.01 (dd, *J* = 4.15, 1.51 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -73.6. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 118.9 (q, $J_{C,F}$ = 321.3 Hz, CF$_3$), 121.4 (CH), 121.8 (C), 123.7 (CH), 129.0 (C), 129.4, 135.7 (CH), 141.6, 145.6 (C), 152.2 (CH). IR (KBr, cm^{-1}): v = 3171, 2959, 2845 (w), 1753, 1733 (s), 1666, 1632, 1588 (m), 1541 (s), 1480, 1476, 1422 (w), 1366 (s), 1244, 1198, 1170 (m), 1085 (s). GC-MS (EI, 70 eV): m/z (%) = 357 ([M, ^{81}Br]$^+$, 31) 355 ([M, ^{79}Br]$^+$, 34), 304 (28), 283 (51), 239 (100), 198 (11), 173 (14). HRMS (EI, 70 eV): calcd. for $C_{10}H_5BrF_3NO_3S$ [M, ^{81}Br]$^+$: 356.91051; found: 356.90991; calcd. for $C_{10}H_5BrF_3NO_3S$ [M, ^{79}Br]$^+$: 354.91256; found: 354.91241.

General procedure for the synthesis of 20a-d

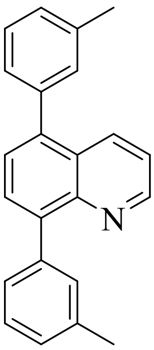
A solution of **19** (0.056 mmol), K_2CO_3 (2M, 2 mL), $Pd(PPh_3)_4$ (6 mmol%) and arylboronic acid (2.0 equiv.) in 1,4-dioxane (3 mL) was stirred at 110 °C for 10 h. under argon atmosphere. To the reaction mixture H_2O (20 mL) and CH_2Cl_2 (25 mL) were added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuum .The residue was purified by column chromatography (silica gel, heptane/EtOAc).

5,8-Bis(3,5-dimethylphenyl)quinoline (20a)



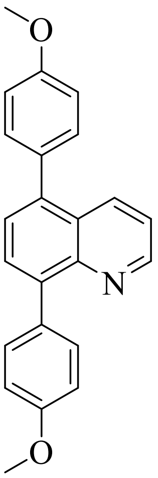
Starting with **19** (20 mg, 0.056 mmol), **a4** (17 mg, 0.112 mmol), $Pd(PPh_3)_4$ (4 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **20a** was isolated as a white solid (15 mg, 81 %); mp 105-107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (br. s, 12H, $4CH_3$), 6.98 (br. s, 1H, ArH), 7.04 (br. s, 3H, ArH), 7.21-7.30 (m, 3H, ArH), 7.44 (d, *J* = 7.37 Hz, 1H, ArH), 7.64 (d, *J* = 7.37 Hz, 1H, ArH), 8.23 (dd, *J* = 8.59, 1.79 Hz, 1H, ArH), 8.86 (dd, *J* = 4.15, 1.70 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.4 ($4CH_3$), 120.7 (CH), 125.7 (C), 126.7 (CH), 126.9 (C), 127.9, 128.4, 129.1, 129.2, 129.7, 134.7 (CH), 136.3, 136.9, 138.4, 138.5, 139.1, 145.4 (C), 149.9 (CH). IR (KBr, cm^{-1}): *v* = 3011, 2955, 2917, 2850, 2730 (w), 1727, 1683, 1596, 1576, 1500, 1455, 1392 (m), 1373, 1355, 1325, 1290, 1259 (w), 1227, 1200, 1184, 1167, 1155 (m), 1093, 1035 (s). GC-MS (EI, 70 eV): m/z (%) = 337 ([M]$^+$, 67), 336 (100), 322 (78), 232 (12). HRMS (ESI-TOF/MS): calcd for $C_{25}H_{24}N$ [M+H]$^+$: 338.19033 ;found: 338.19043.

5,8-Bis(3-methylphenyl)quinoline (20b)



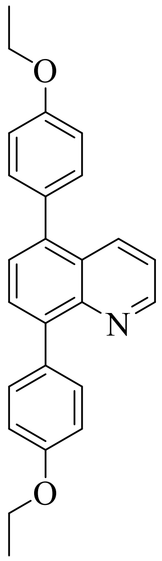
Starting with **19** (20 mg, 0. 056 mmol), **4b** (15 mg, 0.112 mmol), $Pd(PPh_3)_4$ (4 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **20b** was isolated as a white solid (14 mg, 77 %); mp 79-80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 6H, $2CH_3$), 7.15-7.24 (m, 3H, ArH), 7.32-7.34 (m, 1H, ArH), 7.39-7.46 (m, 3H, ArH), 7.56-7.60 (m, 2H, ArH), 7.80 (d, *J* = 8.3 Hz, 1H, ArH), 8.19 (dd, *J* = 8.7, 1.7 Hz, 1H, ArH), 8.51 (dd, *J* = 8.7, 1.7 Hz, 1H, ArH), 8.99 (dd, *J* = 4.72, 1.7 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3 ($2CH_3$), 120.3, 121.4 (CH), 121.8 (C), 123.7, 126.2, 127.0 (CH), 128.2 (C), 128.5, 129.0, 129.4, 130.6, 134.6, 135.7 (CH), 137.9, 138.5, 141.1, 141.4, 145.2, 145.6 (C), 151.3, 152.2 (CH). IR (KBr, cm-^{1}): ν = 3042, 2956, 2924, 2854 (w), 1727, 1593 (m), 1573, 1562 (w), 1499, 1491, 1463 (m), 1422 (s), 1382, 1352, 1308, 1293 (w), 1246 (m), 1205, 1138 (s). GC-MS (EI, 70 eV): m/z (%) = 309 ($[M]^+$,54), 289 (81), 247 (100), 211 (21), 177 (18), 163 (09). HRMS (ESI-TOF/MS): calcd for $C_{23}H_{20}N$ $[M+H]^+$: 310. 15175; found: 310.15139.

5,8-Bis(*p*-methoxyphenyl)quinoline (20c)



Starting with **19** (20 mg, 0.056 mmol), **4e** (17 mg, 0.112 mmol), $Pd(PPh_3)_4$ (4 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **20c** was isolated as a white solid (13 mg, 68 %); mp 119-120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.99 (br. d, *J* = 8.5 Hz, 4H, ArH), 7.28 (dd, *J* = 8.7, 4.2 Hz, 1H, ArH), 7.36 (d, *J* = 8.9 Hz, 2H, ArH), 7.45 (d, *J* = 7.6 Hz, 1H, ArH), 7.62 (d, *J* = 8.9 Hz, 2H, ArH), 7.67 (d, *J* = 7.4 Hz, 1H, ArH), 8.23 (dd, *J* = 8.6, 1.8 Hz, 1H, ArH), 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.3, 55.4 (OCH_3), 113.6, 113.9, 120.7, 126.9 (CH), 127.3 (C), 129.5, 131.1, 131.7 (CH), 131.9, 132.0 (C), 134.6 (CH), 139.3, 139.4, 146.3 (C), 149.8 (CH), 159.1, 159.3 (C). IR (KBr, cm^{-1}): ν = 2989 (w), 2967, 2855, 2821 (m), 1788, 1756 (s), 1689, 1644, 1632, 1619, 1589, 1576 (w), 1512 (s), 1477, 1435, 1412, 1344, 1312 (m), 1298, 1276, 1254 (s), 1176, 1144, 1132, 1117, 1098 (m). GC-MS (EI, 70 eV): m/z (%) = 341 ($[M]^+$, 86), 340 (100), 326 (16), 297 (7), 254 (10), 234 (11). HRMS (ESI-TOF/MS): calcd for $C_{23}H_{20}NO_2$ $[M+H]^+$: 342.14886; found: 342.14897.

5,8-Bis(*p*-ethoxyphenyl)quinoline (20d)

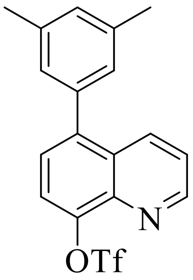


Starting with **19** (20 mg, 0.056 mmol), **4g** (19 mg, 0.112 mmol), $Pd(PPh_3)_4$ (4 mg, 6 mole%), K_2CO_3 (2M, 2 mL) and 1,4-dioxane (3 mL), **20d** was isolated as a white solid (15 mg, 72 %); mp 127-129 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37-1.44 (m, 6H, $2CH_3$), 4.02-4.10 (m, 4H, $2OCH_2$), 6.96-6.99 (m, 4H, ArH), 7.27 (dd, *J* = 8.6, 4.1 Hz, 1H, ArH), 7.34 (d, *J* = 7.8 Hz, 2H, ArH), 7.45 (d, *J* = 7.3 Hz, 1H, ArH), 7.6 (d, *J* = 8.7 Hz, 2H, ArH), 7.67 (d, *J* = 7.3 Hz, 1H, ArH), 8.24 (dd, *J* = 8.7, 1.7 Hz, 1H, ArH), 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 28.6, 29.9 ($2CH_3$), 62.4, 62.5 ($2OCH_2$), 113.1, 113.4, 119.6, 125.9 (CH), 126.2 (C), 128.4, 130.1, 130.7 (CH), 130.8 (C), 133.6 (CH), 138.2, 128.4, 142.3, 145.2 (C), 148.7 (CH), 157.4, 157.5 (C). IR (KBr, cm^{-1}): ν = 3041, 2957 (w), 2885, 2842 (m), 1713 (s), 1574 (m), 1512 (s), 1490 (w), 1472 (m), 1431, 1410 (w), 1299, 1282 (m), 1258 (w), 1239 (s), 1175 (m), 1151, 1131 (w), 1110. 1098 (m). GC-MS (EI, 70 eV): m/z (%) = 369 ([M]$^+$, 100), 368 (98), 341 (10), 340 (45), 312 (11), 283 (11), 282 (14). HRMS (ESI-TOF/MS): calcd for $C_{25}H_{24}NO_2$ [M+H]$^+$: 370.18016; found: 370.18022

General procedure for the synthesis of 21a-h

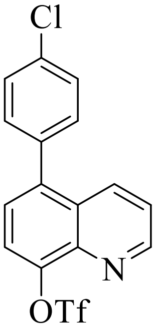
A solution of **19** (0.056 mmol), K_3PO_3 (1.0 equiv.), $Pd(PPh_3)_4$ (3 mmol%) and arylboronic acid (1.0 equiv.) in toluene (3 mL) was stirred at 85 °C for 9 h under argon atmosphere. To the reaction mixture H_2O (20 mL) and CH_2Cl_2 (25 mL) were added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, heptane/EtOAc).

5-(3,5-Methylphenyl)-quinolin-8-yl trifluoromethanesulfonate (21a)



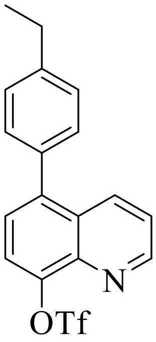
Starting with **19** (20 mg, 0.056 mmol), **4a** (8 mg, 0.056 mmol), $Pd(PPh_3)_4$ (2 mg, 3 mole%), K_3PO_4 (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL), **21a** was isolated as a white solid (16 mg, 76 %); mp 97-99 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 6H, $2CH_3$), 6.98 (br. s, 2H, ArH), 7.05 (br. s, 1H, ArH), 7.39-7.43 (m, 2H, ArH), 7.57 (d, J = 7.9 Hz, 1H, ArH), 8.21 (dd, J = 8.69, 1.70 Hz, 1H, ArH), 8.98 (dd, J = 4.15, 1.51 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -73.7. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3 ($2CH_3$), 118.3 (q, $J_{C,F}$ = 320.8 Hz, CF_3), 119.3, 121.4, 125.2 (CH), 126.5 (C), 126.7, 128.8 (CH), 132.3 (C), 133.7 (CH), 136.9, 137.3, 140.1, 140.6 (C), 150.2 (CH). IR (KBr, cm^{-1}): v = 2961 (m), 2922, 2853, 1594, 1499 (w), 1423 (m), 1257 (s), 1222, 1209 (w), 1078 (m), 1008 (s). GC-MS (EI, 70 eV): m/z (%) = 381 ([M]$^+$, 37), 249 (19), 248 (100), 221 (13), 220 (78), 204 (32). HRMS (EI, 70 eV) calcul for $C_{18}H_{14}F_3NO_3S$ [M]$^+$: 381.06381; found: 381.06410.

5-(4-Chloro)-quinolin-8-yl trifluoromethanesulfonate (21b)



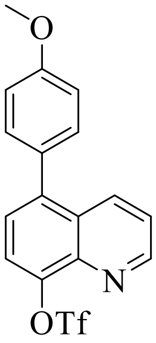
Starting with **19** (20 mg, 0.056 mmol), **4c** (9 mg, 0.056 mmol), $Pd(PPh_3)_4$ (2 mg, 3 mole%), K_3PO_4 (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL), **21b** was isolated as a white solid (13 mg, 60 %); mp 143-145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, J = 8.5 Hz, 2H, ArH), 7.42-7.46 (m, 4H, ArH), 7.59 (d, J = 7.9 Hz, 1H, ArH), 8.13 (dd, J = 8.7, 1.5 Hz, 1H, ArH), 9.01 (dd, J = 4.5, 1.5 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -73.7. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 119.1 (q, $J_{C,F}$ = 320.4 Hz, CF_3), 119.4, 121.6, 126.5 (CH), 127.0 (C), 127.9, 130.2, 133.2 (CH), 133.6, 135.3, 138.8, 140.2, 146.5 (C), 150.5 (CH). IR (KBr, cm^{-1}): v = 3070, 3050, 2959, 2929, 2873, 2850 (w), 1731 (m), 1597 (w), 1501, 1467 (m), 1424 (s), 1400, 1309 (w), 1258, 1243, 1208, 1172 (m), 1139, 1123, 1082, 1043, 1024, 1013 (s). GC-MS (EI, 70 eV): m/z (%) = 389 ([M, ^{37}Cl]$^+$, 14), 387([M, ^{35}Cl]$^+$, 36), 256 (34), 255 (17), 254 (99), 228 (34), 227 (17), 226 (100). HRMS (EI, 70 eV) calculd for $C_{16}H_9O_3NClF_3S$ ([M, ^{35}Cl]$^+$): 386.99341; found: 386.99383; calculd for ([M, ^{37}Cl]$^+$): 388.99088; found: 388.990297.

5-(4-Ethylphenyl)-quinolin-8-yl trifluoromethanesulfonate (21c)



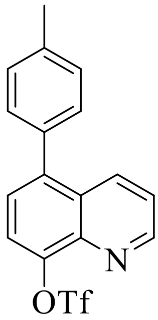
Starting with **19** (20 mg, 0. 056 mmol), **4d** (8 mg, 0.056 mmol), Pd(PPh$_3$)$_4$ (2 mg, 3 mole%), K$_3$PO$_4$ (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL), **21c** was isolated as a white solid (16 mg, 75 %); mp 106-108 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.26 (t, J = 7.5 Hz, 3H, CH$_3$), 2.71 (q, J = 7.6 Hz, 2H, CH$_2$), 7.29 (br. s, 4H, ArH), 7.39-7.44 (m, 2H, ArH), 7.58 (d, J = 8.2 Hz, 1H, ArH), 8.22 (dd, J = 8.7, 1.7 Hz, 1H, ArH), 8.99 (dd, J = 4.2, 1.5 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -73.6. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 15.5 (CH$_3$), 30.9 (CH$_2$), 119.1 (q, $J_{C,F}$ = 320.8 Hz, CF$_3$), 120.4, 122.4, 126.3 (CH), 127.3 (C), 128.2, 129.8, 134.7 (CH), 135.3, 141.2, 141.4, 144.5, 145.2 (C), 151.3 (CH). IR (KBr, cm^{-1}): ν = 2959 (w), 2917, 2849 (s), 1736, 1711, 1611, 1592, 1569, 1513, 1495 (w), 1467, 1464 (m), 1421 (s), 1401, 1382, 1357, 1306, 1260 (w), 1244, 1202 (s), 1170 (m), 1140 (s). GC-MS (EI, 70 eV): m/z (%) = 381 ([M]$^+$, 35), 250 (23), 249 (22), 248 (100), 222 (11), 221 (10), 220 (44), 205 (22), 204 (12), 193 (29). HRMS (EI, 70 eV): calcd. for C$_{18}$H$_{14}$F$_3$NO$_3$S [M]$^+$: 381.06465; found: 381.06449.

5-(4-Methoxyphenyl)-quinolin-8-yl trifluoromethanesulfonate (21d)



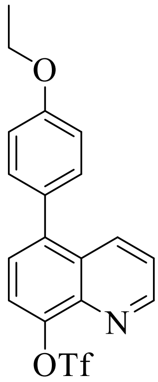
Starting with **19** (20 mg, 0.056 mmol), **4e** (9 mg, 0.056 mmol), Pd(PPh$_3$)$_4$ (2 mg, 3 mole%), K$_3$PO$_4$ (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL), **21d** was isolated as a white solid (18 mg, 84 %); mp 108-110 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.82 (s, 3H, OCH$_3$), 6.99 (d, J = 8.9 Hz, 2H, ArH), 7.39-7.43 (m, 2H, ArH), 7.45 (d, J = 8.9 Hz, 2H, ArH), 7.57 (d, J = 7.9 Hz, 1H, ArH), 8.21 (dd, J = 8.7, 1.7 Hz, 1H, ArH), 8.98 (dd, J = 4.2, 1.5 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -73.7. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 55.4 (OCH$_3$), 114.2 (CH), 118.5 (q, $J_{C,F}$ = 322.5 Hz, CF$_3$), 120.4, 122.4, 126.2 (CH), 131.0 (C), 131.1 (CH), 133.1 (C), 134.6 (CH), 135.9, 139.2, 143.7 (C), 151.2 (CH), 159.7 (C). IR (KBr, cm^{-1}): ν = 3189, 2974, 2966 (w), 2898, 2876, 2833 (m), 1798 (s), 1783, 1766 (m), 1723, 1693, 1665, 1622 (w), 1584, 1566 (s), 1532, 1487, 1466 (w), 1411, 1382, 1354, 1334, 1312 (m), 1276 (s), 1273, 1244 (w), 1212, 1167, 1154, 1134, 1089 (m). GC-MS (EI, 70 eV): m/z (%) = 383 ([M]$^+$, 23), 251 (14), 250 (100), 222 (63), 179 (20), 178 (22). HRMS (EI, 70 eV): calcd for C$_{17}$H$_{12}$F$_3$NO$_4$S [M]$^+$: 383.04336; found: 383.04323.

5-(*p*-Tolyl)-quinolin-8-yl trifluoromethanesulfonate (21e)



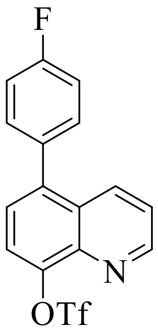
Starting with **19** (20 mg, 0.056 mmol), **4f** (8 mg, 0.056 mmol), Pd(PPh$_3$)$_4$ (2 mg, 3 mole %), K$_3$PO$_4$ (1.0 equiv) (12 mg, 0.056 mmol), and toluene (3 mL), **21e** was isolated as a white solid (17 mg, 81 %); mp 102-104 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.40 (s, 3H, CH$_3$), 7.27 (br. s, 4H, ArH), 7.38-7.44 (m, 2H, ArH), 7.58 (d, J = 7.9 Hz, 1H, ArH), 8.21 (dd, J = 8.6, 1.6 Hz, 1H, ArH), 8.99 (dd, J = 4.2, 1.5 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -73.7. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 21.2 (CH$_3$), 117.7 (q, $J_{C,F}$ = 321.5 Hz, CF$_3$), 120.5, 122.3 (CH), 126.2 (C), 128.2, 129.4, 129.8, 134.5 (CH), 135.1, 138.2, 141.2, 141.3, 145.2 (C), 151.2 (CH). IR (KBr, cm^{-1}): v = 3058, 3018, 2952, 2920, 2850 (w), 1722, 1671, 1587 (m), 1500 (w), 1454, 1423 (s), 1395, 1379, 1354 (m), 1242, 1208 (s), 1171 (w), 1157, 1139 (m). GC-MS (EI, 70 eV): m/z (%) = 367 ([M]$^+$, 37), 235 (16), 234 (100), 207 (15), 206 (88), 205 (10), 204 (28), 191 (11). HRMS (EI, 70 eV) calcd for C$_{17}$H$_{12}$F$_3$NO$_3$S [M]$^+$: 367.04845; found: 367.04755.

5-(4-Ethoxyphenyl)-quinolin-8-yl trifluoromethanesulfonate (21f)



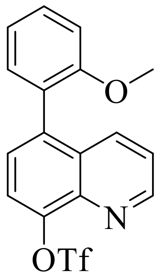
Starting with **19** (20 mg, 0.056 mmol) **4g** (9 mg, 0.056 mmol), Pd(PPh$_3$)$_4$ (4 mg, 3 mole %), K$_3$PO$_4$ (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL), **21f** was isolated as a white solid (15 mg, 69 %); mp 113-114 °C.^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.41 (t, J = 7.0 Hz, 3H, CH$_3$), 4.06 (q, J = 7.1 Hz, 2H, OCH$_2$), 6.97 (d, J = 8.7 Hz, 2H, ArH), 7.28 (d, J = 8.9 Hz, 2H, ArH), 7.38-7.42 (m, 2H, ArH), 7.57 (d, J = 7.9 Hz, 1H, ArH), 8.21 (dd, J = 8.7, 1.70 Hz, 1H, ArH), 8.98 (dd, J = 4.2, 1.5 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -73.6. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 14.8 (CH$_3$), 63.6 (OCH$_2$), 114.7 (CH), 119.2 (q, $J_{C,F}$ = 320.9 Hz, CF$_3$), 120.4, 122.3, 126.2 (CH), 128.3, 130.1 (C), 131.0, 134.6 (CH), 137.2, 141.0, 144.3 (C), 151.2 (CH), 159.1 (C). IR (KBr, cm^{-1}): v = 3042, 2994, 2917, 2849 (w), 1606 (s), 1591, 1572 (w), 1514 (s), 1493, 1475, 1461 (m), 1443 (w), 1420 (s), 1405, 1395, 1381 (m), 1354, 1342 (w), 1303 (m), 1290, 1255, 1227, 1206, 1179, 1130, 1117, 1083, 1044 (s). GC-MS (EI, 70 eV): m/z (%) = 397 ([M]$^+$, 28), 265 (19), 264 (100), 236 (14), 209 (10), 152 (11). HRMS (EI, 70 eV) calculd for C$_{18}$H$_{14}$F$_3$NO$_4$S [M]$^+$: 397.05901; found: 397.5842.

5-(4-Fluorophenyl)-quinolin-8-yl trifluoromethanesulfonate (21g)



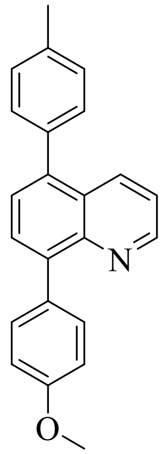
Starting with **19** (20 mg, 0.056 mmol), **4o** (8 mg, 0.056 mmol), Pd(PPh$_3$)$_4$ (2 mg, 3 mole%), K$_3$PO$_4$ (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL), **21g** was isolated as a white solid (13 mg, 63 %); mp 134-136 °C. ^{1}H NMR (300 MHz. CDCl$_3$): δ = 7.15 (d, *J* = 8.7 Hz, 2H, ArH), 7.32-7.38 (m, 2H, ArH), 7.41-7.46 (m, 2H, ArH), 7.59 (d, *J* = 7.9 Hz, 1H, ArH), 8.14 (dd, *J* = 8.7, 1.5 Hz, 1H, ArH), 9.00 (dd, *J* = 4.2, 1.5 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -113.4, -73.8. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 115.8 (d, $J_{C,F}$ =21.5 Hz, CH), 118.6 (q, $J_{C,F}$ = 321.2 Hz, CF$_3$), 120.4, 122.7, 126.5 (CH), 128.0, 128.2, 130.7 (C), 131.6 (d, $J_{C,F}$ = 8.7 Hz, CH), 133.9 (C), 134.2 (CH), 145.4 (C), 151.4 (CH), 163.4 (d, $J_{C,F}$ = 245.7 Hz, CF). IR (KBr, cm^{-1}): *v* = 2955, 2918, 2849, 1738 (w), 1605 (m), 1573 (w), 1511 (s), 1495 (w), 1468 (m), 1420, 1403 (s), 1381, 1356, 1335, 1309, 1274 (w), 1243, 1225, 1210 (s), 1172, 1165 (m), 1134 (s), 1085 (m). GC-MS (EI, 70 eV): m/z (%) = 371 ([M]$^+$, 28), 239 (12), 211 (15), 210 (100), 128 (75). HRMS (EI, 70 eV) calculd for C$_{16}$H$_9$O$_3$NF$_4$S [M]$^+$: 371.02338; found: 371.02351.

5-(2-Methoxyphenyl)-quinolin-8-yl trifluoromethanesulfonate (21h)



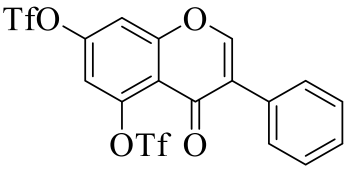
Starting with **19** (20 mg, 0.056 mmol), **4p** (9 mg, 0.056 mmol), Pd(PPh$_3$)$_4$ (2 mg, 3 mole%), K$_3$PO$_4$ (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL), **21h** was isolated as a white solid (17 mg, 79 %); mp 85-87 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.36 (s, 3H, OCH$_3$), 6.98-7.06 (m, 2H, ArH), 7.17-7.21 (m, 1H, ArH), 7.34-7.44 (m, 3H, ArH), 7.58 (d, *J* = 7.9 Hz, 1H, ArH), 7.87 (dd, *J* = 8.6, 1.6 Hz, 1H, ArH), 8.96 (dd, *J* = 4.1, 1.4 Hz, 1H, ArH). ^{19}F NMR (282.4, MHz): δ = -72.8. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 55.4 (OCH$_3$), 111.0 (CH), 119.3 (q, $J_{C,F}$ = 318.9 Hz, CF$_3$), 120.4, 120.9, 122.6, 126.5 (CH), 128.0, 128.2, 129.1 (C), 131.5, 131.6 (CH), 133.9 (C), 135.1 (CH), 145.4 (C), 151.2 (CH), 156.9 (C). IR (KBr, cm^{-1}): *v* = 3062, 2958, 2918, 2849, 1931, 1901, 1737, 1618 (w), 1600 (m), 1579 (w), 1502, 1493, 1471, 1435 (m), 1416, 1402 (s), 1388, 1362, 1312 (w), 1290, 1263 (m), 1236, 1208, 1201 (s), 1173, 1164 (m), 1140, 1121 (s). GC-MS (EI, 70 eV): m/z (%) = 383 ([M]$^+$, 53), 251 (18), 250 (100), 222 (20), 220 (10), 206 (15), 204 (12), 194 (26), 193 (10), 191 (17), 178 (12), 151 (10). HRMS (ESI-TOF/MS): calcd for C$_{17}$H$_{13}$F$_3$NO$_4$S [M+H]$^+$: 384.05119; found: 384.05153.

5-(*p*-Methylphenyl)-8-(*p*-methoxyphenyl)quinoline (22)



Starting with **19** (20 mg, 0.056 mmol), **4f** (8 mg, 0.056 mmol), $Pd(PPh_3)_4$ (2 mg, 3 mol-%), K_3PO_4 (1.0 equiv.) (12 mg, 0.056 mmol), and toluene (3 mL) and **4e** (17 mg, 0.112 mmol), $Pd(PPh_3)_4$ (4 mg, 6 mole %), K_3PO_4 (1.0 equiv.) (12 mg, 0.056 mmol) and 1,4-dioxane (3 mL), **22** was isolated as a white solid (14 mg, 76%), mp: 118-119 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 6.99 (d, *J* = 8.5 Hz, 2H, ArH), 7.23-7.29 (m, 3H, ArH), 7.36 (d, *J* = 8.8 Hz, 2H, ArH), 7.46 (d, *J* = 7.3 Hz, 1H, ArH), 7.56 (d, *J* = 7.9 Hz, 2H, ArH), 7.68 (d, *J* = 7.3 Hz, 1H, ArH), 8.23 (dd, *J* = 8.5, 1.9 Hz, 1H, ArH), 8.87 (dd, *J* = 4.1, 1.9 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3 (CH_3), 54.4 (OCH_3), 112.9, 119.7 (CH), 124.6 (C), 125.9 (CH), 126.2 (C), 127.8, 128.5, 129.5, 130.2 (CH), 130.5, 130.9 (C), 133.5 (CH), 135.9, 139.5, 139.9 (C), 148.8 (CH), 158.2 (C). IR (KBr, cm^{-1}): *v* = 3034, 2973 (w), 2878 (m), 1986, 1964 (s), 1875, 1844, 1776 (m), 1722, 1702 (w), 1656, 1634, 1612 (m), 1587, 1564, 1532 (w), 1455, 1412 (m), 1376, 1347 (s), 1289, 1244 (m), 1167, 1133 (w), 1057, 988 (m). GC-MS (EI, 70 eV): m/z (%) = 325 ([M]$^+$, 66), 324 (100), 310 (20), 281 (11), 266 (10), 218 (11), 140 (10), 133 (24). HRMS (ESI-TOF/MS): calculd for $C_{23}H_{19}NO$ [M+H]$^+$: 326.15394; found: 326.15404.

5,7-Bis(trifluoromethanesulfonyloxy)isoflavone (24)

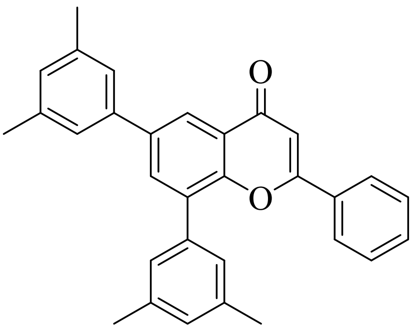


To a CH_2Cl_2 solution (30 mL) of **23** (1.0 g, 3.9 mmol) was added pyridine (1.3 mL, 15.7 mmol) and the solution was stirred at 20 °C for 10 min under argon atmosphere. Then Tf_2O (1.6 mL, 9.4 mmol) was added at 50 °C and the reaction mixture was allowed to warm to room temperature and was stirred for 4 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The product **24** was isolated by column chromatography (flash silica gel, heptane/EtOAc) as a colourless solid (1.8 g, 89%); mp 75-77 ºC. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.09 (s, 1H, ArH), 7.35-7.39 (m, 3H, ArH), 7.42-7.47 (m, 3H, ArH), 7.92 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.10, -72.19. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 111.3, 112.3 (CH), 117.3 (C), 117.6 (q, $J_{C,F}$ = 321.9 Hz, CF_3), 117.7 (q, $J_{C,F}$ = 321.9 Hz, CF_3), 126.4 (C), 127.7 (CH), 128.0 (2CH), 128.9, 147.3, 149.7 (C), 151.3 (CH), 156.3 (C), 172.0 (CO). IR (KBr, cm^{-1}): *v* = 3095, 2961, 2918, 2849 (w), 1645, 1619 (s), 1578, 1569, 1497, 1469 (w), 1424 (s), 1377, 1364, 1316 (w), 1243 (m), 1203, 1173, 1137, 1099 (s). GC-MS (EI, 70 eV): m/z (%) = 518 ([M+H]$^+$, 100), 384 (12), 293 (36), 224 (34). HRMS (EI, 70 eV) calcd. for $C_{17}H_9O_8F_6S_2$ [M+H]$^+$: 518.96375; found: 518.96486.

General procedure for the synthesis of 25a-c

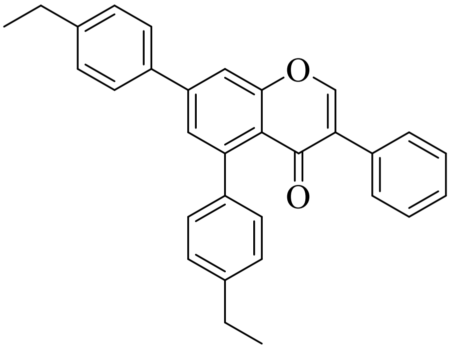
A solution of **24** (0.039 mmol), K_2CO_3 (2M, 1.5 mL), $Pd(PPh_3)_4$ (6 mmol%) and arylboronic acid (2.0 equiv.) in 1,4-dioxane (3 mL) was stirred at 110 °C for 10 h. under argon atmosphere. To the reaction mixture H_2O (20 mL) and CH_2Cl_2 (25 mL) were added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuum .The residue was purified by column chromatography (silica gel, heptane/EtOAc).

5,7-Bis(3,5-dimethylphenyl)-3-phenyl-4*H*-chromen-4-one (25a)



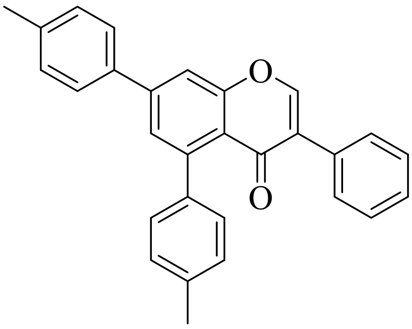
Starting with **24** (20 mg, 0.039 mmol), **4a** (12 mg, 0.078 mmol), $Pd(PPh_3)_4$ (2.7 mg, 6 mole%), K_2CO_3 (1.5 mL), and 1,4-dioxane (3 mL), **25a** was isolated as a white solid (14 mg, 87%); mp 111-113 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 6H, $2CH_3$), 2.32 (s, 6H, $2CH_3$), 6.89 (s, 2H, ArH), 6.92 (s, 1H, ArH), 7.00 (s, 1H, ArH), 7.21-7.31 (m, 5H, ArH), 7.34 (d, *J* = 1.7 Hz, 1H, ArH), 7.42-7.46 (m, 2H, ArH), 7.59 (d, *J* =1.9 Hz, 1H, ArH), 7.90 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 ($2CH_3$), 21.5 ($2CH_3$), 115.2 (CH), 118.4 (C), 125.2, 126.3, 127.6, 127.9, 128.3, 128.8, 129.2, 130.3 (CH), 136.2, 138.7, 141.9, 144.4, 145.3, 150.85 (C), 151.8 (CH), 152.9, 154.4, 157.2 (C), 172.2 (CO). IR (KBr, cm^{-1}): *v* = 3092, 3053, 3026 (w), 2919, 2850 (m), 2725, 1737, 1710 (w), 1637 (s), 1619 (m), 1608, 1599 (s), 1553 (m), 1487, 1455, 1445 (w), 1375 (m), 1329, 1312, 1293 (w), 1259, 1217 (m), 1118, 1083 (w). GC-MS (EI, 70 eV): m/z (%) =429 ($[M-H]^+$, 100), 412 (12). HRMS (EI, 70 eV) calcd. for $C_{31}H_{25}O_2$ $[M-H]^+$: 429.18491; found: 429.18478.

5,7-Bis(4-ethylphenyl)-3-phenyl-4*H*-chromen-4-one *(*25b)



Starting with **24** (20 mg, 0.039 mmol), **4d** (12 mg, 0.078 mmol), $Pd(PPh_3)_4$ (2.7 mg, 6 mole%), K_2CO_3 (1.5 mL), and 1,4-dioxane (3 mL), **25b** was isolated as a white solid (13.5 mg, 81%); mp 101-103 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19-1.24 (m, 6H, $2CH_3$), 2.60-2.68 (m, 4H, $2CH_2$), 7.14-7.18 (m, 2H, ArH), 7.20-7.29 (m, 7H, ArH), 7.38 (d, *J* = 1.9 Hz, 1H, ArH), 7.41-7.44 (m, 2H, ArH), 7.55 (d, *J* = 8.2 Hz, 2H, ArH), 7.60 (d, *J* = 1.9 Hz, 1H, ArH), 7.88 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.2 (CH_3), 15.5 (CH_3), 28.6 (CH_2), 29.7 (CH_2), 115.0 (CH), 120.5, 126.4 (C), 127.1, 127.3, 127.6, 127.9, 128.3, 128.6, 128.7, 129.3 (CH), 132.0, 136.0, 139.1, 142.8, 144.3, 145.1, 145.2 (C), 151.8 (CH), 157.9 (C), 175.9 (CO). IR (KBr, cm^{-1}): *v* = 3052, 3024 (w), 2961, 2923, 2869, 2850 (m), 1902, 1789, 1713 (w), 1647, 1605 (s), 1548, 1514, 1493, 1445 (m), 1423 (w), 1384, 1372, 1360 (s), 1304 (m), 1244 (s), 1187 (m), 1157 (w). GC-MS (EI, 70 eV): m/z (%) = 429 ([M-H]$^+$,100), 431 (11), 414 (8). HRMS (EI, 70 eV) calcd. for $C_{31}H_{25}O_2$ [M-H]$^+$: 429.18491; found: 429.18465.

5,7-Bis(*p*-tolyl)-3-phenyl-4*H*-chromen-4-one (25c)

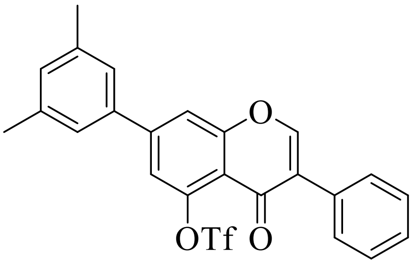


Starting with **24** (20 mg, 0.039 mmol), **4f** (11 mg, 0.078 mmol), Pd(PPh$_3$)$_4$ (2.7 mg, 6 mole%), K_2CO_3 (1.5 mL), and 1,4-dioxane (3 mL), **25c** was isolated as a white solid (12 mg, 76%); mp 107-110 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.19 (m, 6H, 2CH$_3$), 7.11-7.14 (m, 2H, ArH), 7.18-7.21 (m, 3H, ArH), 7.24-7.29 (m, 4H, ArH), 7.37 (d, *J* = 1.9 Hz, 1H, ArH), 7.41-7.44 (m, 2H, ArH), 7.52 (d, *J* = 8.1 Hz, 2H, ArH), 7.60 (d, *J* = 1.9 Hz, 1H, ArH), 7.89 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 29.7 (2CH$_3$), 115.0 (CH), 115.7 (C), 116.9 (CH), 126.8 (C), 127.2 (CH), 127.5, 128.0 (C), 128.2 (2CH), 128.3, 128.4, 129.3, 129.9 (CH) 130.1, 130.3, 131.5, 134.8, 141.2, 145.2 (C), 153.1 (CH), 173.0 (CO). IR (KBr, cm^{-1}): *v* = 3047, 3025, 2953 (w), 2918 (s), 2850 (m), 1902, 1799, 1736 (w), 1657 (s), 1621 (m), 1606 (s), 1577, 1549, 1516, 1494, 1461, 1446, 1431, 1418, 1400 (w), 1375, 1371 (m), 1314, 1306, 1295 (w) 1247, 1239 (w), 1212, 1195, 1185, 1160, 1109, 1096 (w), 1073 (m), 1045, 1038 (w), 1017 (m). GC-MS (EI, 70 eV): m/z (%) = 401 ([M-H]$^+$, 100), 402 (48), 403 (10). HRMS (EI, 70 eV) calcd. for $C_{29}H_{21}O_2$ [M-H]$^+$: 401.15361; found: 401.15322.

General procedure for the synthesis of 26a-d

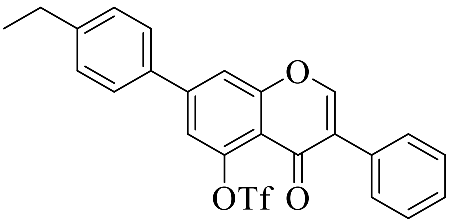
A solution of **24** (0.039 mmol), K_3PO_4 (0.039 mmol), Pd(PPh$_3$)$_4$ (3 mmol%) and arylboronic acid (1.0 equiv.) in THF (3 mL) was stirred at 55 °C for 10 h. under argon atmosphere. To the reaction mixture H_2O (20 mL) and CH_2Cl_2 (25 mL) were added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuum .The residue was purified by column chromatography (silica gel, heptane/EtOAc).

7-(3,5-Methylphenyl)-4-oxo-3-phenyl-4*H*-chromen-5-yl trifluoromethanesulfonate (26a)



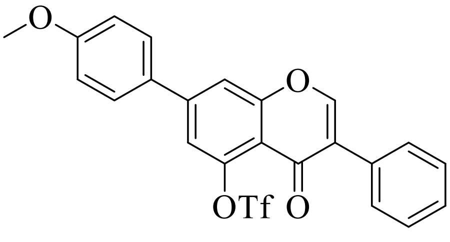
Starting with **24** (20 mg, 0.039 mmol), **4a** (6 mg, 0.039 mmol), $Pd(PPh_3)_4$ (1.4 mg, 3 mole%), K_3PO_4 (8.2 mg, 0.039 mmol), and THF (3 mL), **26a** was isolated as a white solid (13 mg, 73%); mp 96-100 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 6H, $2CH_3$), 7.07 (s, 1H, ArH), 7.15 (s, 2H, ArH), 7.32-7.40 (m, 4H, ArH), 7.47-7.51 (m, 2H, ArH), 7.64 (d, J = 1.7 Hz, 1H, ArH), 7.91 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.10. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.4 ($2CH_3$), 116.6 (CH), 117.9 (C), 118.3 (q, $J_{C,F}$ = 320.8 Hz, CF_3), 125.1 (CH), 126.4 (C), 126.6, 126.7 (CH), 129.2 (2CH), 130.8 (C), 131.4 (CH), 137.2, 139.2, 147.2, 147.5 (C), 152.2 (CH), 157.4 (C), 174.0 (CO). IR (KBr, cm^{-1}): ν = 3058, 3028, 2955 (w), 2922 (m), 2852, 2733 (w), 1727 (m), 1650, 1623 (s), 1600 (m), 1545, 1487, 1444 (w), 1429 (s), 1411 (w), 1400, 1375, 1365 (m), 1316, 1287, 1269 (w), 1247, 1225 (m), 1204, 1190 (s), 1159 (m), 1141 (s), 1074, 1051 (w). GC-MS (EI, 70 eV): m/z (%) = 474 ($[M]^+$,100), 409 (11), 382 (10), 313 (34). HRMS (ESI/TOF) calcd. for $C_{24}H_{18}O_5F_3S$ $[M+H]^+$: 475.08216; found: 475.08218.

7-(4-Ethylphenyl)-4-oxo-3-phenyl-4*H*-chromen-5-yl trifluoromethanesulfonate (26b)



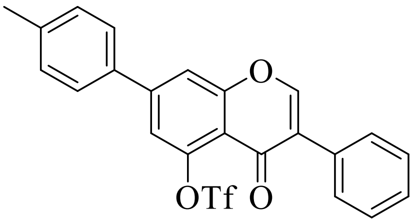
Starting with **24** (20 mg, 0.039 mmol), **4d** (6 mg, 0.039 mmol), $Pd(PPh_3)_4$ (1.4 mg, 3 mole%), K_3PO_4 (8.2 mg, 0.039 mmol), and THF (3 mL), **26b** was isolated as a white solid (15 mg, 79%); mp 99-101 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.6 Hz, 3H, CH_3), 2.67 (q, J = 7.6 Hz, 2H, CH_2), 7.30 (d, J = 8.2 Hz, 2H, ArH), 7.33-7.38 (m, 4H, ArH), 7.47-7.50 (m, 4H, ArH), 7.65 (d, J = 1.7 Hz, 1H, ArH), 7.91 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.27. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.4 (CH_3), 29.7 (CH_2), 115.2 (C), 116.3, 117.7 (CH), 118.1 (q, $J_{C,F}$ = 321.3 Hz, CF_3), 125.8 (C), 127.2 (CH), 128.6 (2CH), 129.0, 129.1 (CH), 129.8, 133.5, 145.3, 145.8, 146.5, (C), 152.2 (CH), 156.5 (C), 172.3 (CO). IR (KBr, cm^{-1}): ν = 3056, 3026 (w), 2959, 2922, 2851, 2817 (m), 1911, 1816, 1728, 1691 (w), 1646, 1626 (s), 1543, 1521, 1494, 1461, 1446 (w), 1426 (s), 1401, 1376, 1367 (m), 1313, 1281 (w), 1256 (m), 1243, 1208 (s). GC-MS (EI, 70 eV): m/z (%) = 474 ($[M]^+$, 100), 342 (51), 326 (21), 313 (22). HRMS (EI, 70 eV) calcd. for $C_{24}H_{17}O_5F_3S$ $[M]^+$: 474.07433; found: 474.07343.

7-(4-Methoxyphenyl)-4-oxo-3-phenyl-4*H*-chromen-5-yl trifluoromethanesulfonate (26c)



Starting with **24** (20 mg, 0.039 mmol), **4e** (6 mg, 0.039 mmol), Pd(PPh_3)$_4$ (1.4 mg, 3 mole%), K_3PO_4 (8.2 mg, 0.039 mmol), and THF (3 mL), **26c** was isolated as a white solid (15 mg, 80%); mp 85-87 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3H, OCH_3), 6.98 (d, *J* =8.6 Hz, 2H, ArH), 7.33-7.37 (m, 4H, ArH), 7.48-7.53 (m, 4H, ArH), 7.61 (d, *J* = 1.7 Hz, 1H, ArH), 7.90 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.28. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 55.5 (OCH_3), 113.9, 114.7 (CH), 115.3 (C), 116.3 (CH), 117.9 (q, $J_{C,F}$ = 321.3 Hz, CF_3), 125.7 (C), 127.1, 128.5, 128.6 (CH), 129.8 (C), 131.0 (CH), 131.2, 145.4, 146.6 (C), 151.2 (CH), 156.5, 160.0 (C), 172.9 (CO). IR (KBr, cm^{-1}): *v* = 3072, 3057, 3020 (w), 2955, 2917, 2849 (m), 1728 (m), 1650, 1627, 1601 (s), 1580, 1545 (w), 1519 (m), 1493, 1462 (w), 1427 (s), 1403, 1373, 1364, 1292 (w), 1257, 1243, 1202, 1179, 1141, 1117 (s), 1071, 1043 (m). GC-MS (EI, 70 eV): m/z (%) = 476 ([M]$^+$, 100), 475 (18), 344 (44), 328 (20), 315 (18). HRMS (EI, 70 eV) calcd. for $C_{23}H_{15}O_6F_3S$ [M]$^+$: 476.07433; found: 476.07343.

7-(4-Methylphenyl)-4-oxo-3-phenyl-4*H*-chromen-5-yl trifluoromethanesulfonate (26d)



Starting with **24** (20 mg, 0.039 mmol), **4f** (5 mg, 0.039 mmol), Pd(PPh_3)$_4$ (1.4 mg, 3 mole %), K_3PO_4 (8.2 mg, 0.039 mmol), and THF (3 mL), **26d** was isolated as a white solid (15 mg, 82%); mp101-102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3H, CH_3), 7.26 (d, *J* = 7.9 Hz, 2H, ArH), 7.33-7.38 (m, 4H, ArH), 7.44-7.47 (m, 4H, ArH), 7.64 (d, *J* = 1.7 Hz, 1H, ArH), 7.90 (s, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -73.23. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.2 (CH_3), 116.2 (CH), 116.6 (C), 117.7 (CH), 118.4 (q, $J_{C,F}$ = 320.8 Hz, CF_3), 126.8 (C), 127.1 (CH), 128.6 (2CH), 129.1, 130.2 (CH), 130.8, 134.3, 140.1, 146.8, 147.6 (C), 152.2 (CH), 157.5 (C), 174.0 (CO). IR (KBr, cm^{-1}): *v* = 3074, 2955, 2923, 2815, 1732 (w), 1640 (m), 1624 (s), 1575, 1568, 1557, 1542, 1524, 1506, 1496, 1472, 1455, 1447 (w), 1424 (s), 1398, 1380, 1372 (m), 1320, 1286, 1274 (w), 1256, 1244 (m), 1200, 1138 (s). GC-MS (EI, 70 eV): m/z (%) = 460 ([M)$^+$, 100), 459 (54), 395 (13), 327 (16), 228 (12). HRMS (ESI/TOF) calcd. for $C_{23}H_{16}O_5F_3S$ [M+H]$^+$: 461.06651; found: 461.06672.

X-Ray Crystal Data

Crystal data and structure refinement for 5e

Identification code	N1-Mono-4OMe	
Empirical formula	$C_{20}H_{15}F_3O_6S$	
Formula weight	440.38	
Temperature	173 (2) K	
Wavelength	0.71073Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21/n	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 8.1302(19) Å	α = 90.00
	b = 5.3259(13) Å	β = 94.470(15)
	c = 42.899(10) Å	γ = 90.00
Volume	1851.9(8) Å^3	
Z	4	
Density (calculated)	1.580 Mg m^{-3}	
Absorption coefficient	0.222 mm^{-1}	
F(000)	904	
Crystal size	0.34 × 0.10 × 0.02 mm	
Θ range for data collection	θ = 1.90- 24.30°	
Index ranges	$-9 \leq h \leq 9, -6 \leq k \leq 6, -48 \leq l \leq 49$	
Reflections collected	15118	
Independent reflections	2952 [R(int) = 0.0672]	

Completeness to Θ = 24.30°	97.8%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9222 and 0.9952
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	2952/0/ 273
Goodness-of-fit on F2	1.016
Final R indices [I>2σ(I)]	R1 = 0.0450, wR2 = 0.0913
R indices (all data)	R1 = 0.0888, wR2 = 0.1075
Largest diff. peak and hole	0.243 and - 0.406 e $Å^{-3}$

Crystal data and structure refinement for 11d

Identification code	N2-Mono-4OMe	
Empirical formula	$C_{19} H_{15} Br O_3$	
Formula weight	371.22	
Temperature	173 (2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	C 2/c	
Space group (Hall)	-C 2yc	
Unit cell dimensions	*a* = 19.8135(6) Å	α = 90.00
	b = 8.6733(2) Å	β=112.5630(10)
	c = 20.2861(5) Å	γ = 90.00
Volume	3219.30 (15) Å	

Z	8
Density (calculated)	1.532 Mg m^{-3}
Absorption coefficient	2.566 mm^{-1}
F(000)	1504
Crystal size	0.38 × 0.22 × 0.15 mm
Θ range for data collection	2.98-32.50
Index ranges	$-29\le h\le 29, -12\le k\le 13, -29\le l\le 30$
Reflections collected	22818
Independent reflections	5824[R(int) = 0.0256]
Completeness to Θ = 32.50°	99.8%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.4422and 0.6995
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	5824/0/210
Goodness-of-fit on F2	1.011
Final R indices [I>2σ(I)]	R1 = 0.0313, wR2 = 0.0714
R indices (all data)	R1 = 0.0495, wR2 = 0.0775
Largest diff. peak and hole	0.47 and −0.23 e Å^{-3}

Crystal data and structure refinement for 16a

Identification code	K-Mono-3,5.Me	
Empirical formula	$C_{18}H_{13}F_3O_5S$	
Formula weight	398.34	
Temperature	173 (2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21/c	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	*a* = 15.7620(7) Å	α = 90.00
	b = 7.7357(4) Å	β = 115.035(2)
	c =15.5226(6 Å	γ = 90.00
Volume	1714.85(13)Å^3	
Z	4	
Density (calculated)	1.543 Mg m^{-3}	
Absorption coefficient	0.248 mm^{-1}	
F(000)	816	
Crystal size	0.85× 0.37 × 0.02 mm	
Θ range for data collection	θ = 2.63-29.06	
Index ranges	-20≤h≤21,-10≤k≤10, -21≤l≤91	
Reflections collected	20048	

Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	4477/15/ 268
Goodness-of-fit on F2	1.031
Final R indices [I>2σ(I)]	R1 = 0.0532, wR2 = 0.1182
R indices (all data)	R1 = 0.0983, wR2 = 0.1382
Largest diff. peak and hole	0.268 and -0.384e Å^{-3}

Crystal data and structure refinement for 20c

Identification code	Chin-D-OMe	
Empirical formula	$C_{23}H_{19}NO_2$	
Formula weight	341.39	
Temperature	173 (2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	P 21/n	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 21.2098(11) Å	α = 90.00
	b = 5.9382(3) Å	β = 93.634(3)°
	c = 26.9576(12) Å	γ = 90.00
Volume	3388.4(3) Å^3	

Z	8
Density (calculated)	1.338 Mg m^{-3}
Absorption coefficient	0.085 mm^{-1}
F(000)	1440
Crystal size	0.99 × 0.43 × 0.05 mm
Θ range for data collection	θ = 1.19- 19.00°
Index ranges	-28≤h≤27,-8≤k≤7, -36≤l≤36
Reflections collected	45074
Independent reflections	8958[R(int) = 0.0424]
Completeness to Θ = 30.00°	99.7%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9204 and 0.9958
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	8958/0/475
Goodness-of-fit on F2	1.003
Final R indices [I>2σ(I)]	R1 = 0.0489, wR2 = 0.1084
R indices (all data)	R1 = 0.1110, wR2 = 0.1410
Largest diff. peak and hole	0.287 and -0.242 e Å^{-3}

Crystal data and structure refinement for 26c

Identification code	Isoflavone-Mono-4OMe	
Empirical formula	$C_{23} H_{15} F_3 O_6 S$	
Formula weight	476.41	
Temperature	173 (2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	C 2/c	
Space group (Hall)	C 2yc	
Unit cell dimensions	*a* = 24.0109(9) Å	α = 90°
	b = 9.9045(4) Å	β =113.994(2)°
	c = 18.7132(8) Å	γ = 90°
Volume	4065.7(3) Å	
Z	8	
Density (calculated)	1.557 Mg m^{-3}	
Absorption coefficient	0.227 mm^{-1}	
F(000)	1952	
Crystal size	0.270 × 0.150 × 0.060 mm	
Θ range for data collection	θ = 2.26- 22.86°	
Index ranges	-33≤h≤33,-13≤k≤13, -25≤l≤25	
Reflections collected	25514	
Independent reflections	5704[R(int) = 0.0613]	
Completeness to Θ = 31.00°	99.8%	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9839 and 0.9125
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	5704/0/299
Goodness-of-fit on F2	1.092
Final R indices [$I>2\sigma(I)$]	R1 = 0.0460, wR2 = 0.1158
R indices (all data)	R1 = 0.0696, wR2 = 0.1251
Largest diff. peak and hole	0.337and - 0.479e Å^{-3}

Abbreviations

EtOAc	Ethylacetate
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
NEt_3	Triethylamine
Tf_2O	Trifluoromethanesulfonic Anhydride
THF	Tetrahydrofurane
DIPEA	Ethyldiisopropylamine
NMR	Nuclear Magnetic Resonance
HMQC	Heteronuclear Multiple Quantum Coherence
HMBC	Heteronuclear Multiple Bond Correlation
DEPT	Distortionless Enhancement by Polarisation Transfer
MS	Mass spectrometry
EI	Electronic Impact
ESI	Electrospray Ionization
HRMS	High Resolution Mass Spectroscopy
IR	Infrared Spectroscopy
Ar	Aromatic
Ph	Phenyl
TLC	Thin Layer Chromatography
HZ	Hertz

References

1. (a) Mahrwald, R. Aldol Reactions, Springer Science & Business Media B. V.: New York, **2009.** (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew.Chem.Int. Ed.* **2002**, *41*, 1668. (c) Tokoroyama, T. *Eur. J. Org. Chem*. **2010, 2009**. (d) Hund, R. N.; Shah, D. H. *J. Org. Chem*. **1973**, *38,* 390. (e) Ghelis, C.; Labouesse, J.; Labouesse, B. *Biochem, Biophys, Res, Commun*. **1969**, *221*, 337.
2. Negishi, E. *Angew, Chem*. **2011**, *123,* 6870; *Angew. Chem. Int*. Ed. **2011**, *50*, 6738.
3. Suzuki, A. *Angew, Chem*. **2011**, *123,* 6854; *Angew. Chem. Int*. Ed. **2011**, *50*, 6722.
4. Tsuji, J. *Palladium Reagents and Catalysts-new perspectives of the 21st century*, 2 ed.; John Wiley & Sons Ltd: Chi Chester, **2004**.
5. Garrett, C.E.; Prasad, K. *Adv. Synth. Catal*. **2004,** *346*, 889.
6. For the first examples of alkyl-alkyl Suzuki cross-coupling reactions, see: Ishiyama, T.; Abs, S.; Suzuki, A. *Chem. Lett*. **1992**, 691.
7. Nicolauo, K.C.; Bulger, P.G.; Sarlah, D. *Angew. Chem. Ind. Ed.* **2005**, *44*, 4442.(a) Metal-Catalyzed Cross-Coupling Reactions, Eds.: de Meijere, A.; Diederich, F. Wiley-VCH, Weinheim, **2004**. b) Handbook of Organopalladium Chemistry for Organic Synthesis Eds.: Negishi, E.; de Meijere, A. Wiley, New York, 2002.
8. Goossen, L. J.; Koley, D.; Hermann, H.; Thiel, W. *Chem. Commen*. **2004**, 214.
9. Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev*. **2000**, *100*, 3009.
10. Casado, A. L.; Espinet, P. *J. Am. Chem. Soc*. **1998**, *120*, 8978.
11. Espinet, P.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2004**, *43*, 4704.
12. Geissler, H. *In Tranasition Metal for Organic Synthesis*; Beller, M.; Bolm, C., Eds.; Wiley-VCH: Weinheim, **1998**, *1*, 158.
13. Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun*. **1979**, *19*, 866.
14. Lipton, M. F.; Mauragis, M. A.; Maloney, M. T. *Org Process Res Dev*, **2003**, *7*, 385.
15. Garg, N. K.; Caspi, D. D.; Stoltz, B. M. *J. Am. Chem.* Soc. **2004**, *126*, 9552.
16. Myers, A. G.; Tom, N. J.; Fraley, M. E.; Cohen, S. B.; Madar, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 6072.
17. Eicken, K.; Rang, H.; Harreus, A.; Götz, N.; Ammermann, E.; Lorentz, G.; Strathmann, S.; German Patent DE19531813, **1997**. (b) Eicken, K.; Rack, M.; Wetterich, F.; Ammermann, E.; Lorentz, G.; Strathmann, S.; German Patent DE19735224, **1999**. (c) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5518-5526
18. Hong, C. Y.; Kado, N.; Overman, L. E. *J. Am. Chem. Soc.* **1993**, *115*, 11028

19. Schrock, A. K.; U.S. Patent US4812588, **1989**. (a) Ibad, M. F.; Hussain, M.; Abid, O. U. Rahman.; Ali, Ullah, A.; Zinad, I.; Langer, P. *Synlett* **2010**, 411. (b) Hussain, M.; Nguyen, T. H.; Khera, R. A.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2011**, *52*, 184. (c) Eleya, N.; Malik, I.; Reimann, S.; Wittler, K.; Hein, M.; Patonay, T.; Villinger, A.; Ludwig, R.; Langer, P. *Eur. J. Org. Chem.* **2012**, 1639. (d) Eleya, N.; Khaddour, Z.; Patonay, T.; Langer, P. *Synlett* **2012**, *223*. (e) Eleya, N.; Mahal, A.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2011**, *353*, 2761.
20. Cancerostatic activity has been reported for 1,4-dihydroxy-2-naphthoates, such as the antitumor agent rhinacanthin N: (a) Kongkathip, N.; Luangkamin, S.; Kongkathip, B.; Sangma, C.; Grigg, R.; Kongsaeree, P.; Prabpai, S.; Pradidphol , N.; Piyaviriyagul, S.; Siripong, P. *J. Med. Chem*. **2004**, *47*, 4427. (b) Jiang, Z. H.; Tanaka, T.; Inutsuka, C.; Kouno, I. *Chem. Pharm. Bull*. **2001**, *49*, 737. Anti-cancer activity has also been reported for 4-aryl-2-naphthoates. Examples include eritrichin and globoidnan A: (c) Cullmann, F.; Schmidt, A.; Schuld, F.; Trennheuser, M. L.; Becker, H. *Phytochemistry* **1999**, *52*, 1647. (d) Fedoreyev, S. Veselova, A.; Krivoschekova, M. V.; Mischenko, O. E.; Denisenko, N. P.; Dmitrenok, V. A.; Glazunov, P. S.; Bulgakov, V. P.; Tchernoded, V. P.; Zhuravlev, G. K. *Planta Med*. **2005**, *71*, 446. (e) Ovenden, S. P. B.; Wan, S. S.; Sberna, G.; Tait, R. M.; Rhodes, D.; Cox, S.; Coates, J.; Walsh, N. G.; Meurer-Grimes, B. M. *Phytochemistry* **2004**, *65*, 3255. Anti-malaria activity has been reported for a number of naphthyl tetrahydroisoquinoline alkaloids. Prominent examples include dioncophylline Can the michellamines: (f) Bringmann, G. *The Naphthyl Isoquinoline Alkaloids* in *The Alkaloids***, 1986,** vol. 29, Brossi, ed., Academic Press, New York, p.141.
21. Donaldson, N. *The Chemistry and Technology of Naphthalene Compounds*, London: Edward Arnold, **1958.**
22. Rokade, Y. B.; Sayyed, R. Z.; Rasyan, *J. Chem* **2009**, *2*, 972.
23. Hasegawa, M.; Takenouchi, K.; Takahashi, K.; Takeuchi, T.; Komoriya, K.; Uejima, *Microbiology*, **2007**, *153*, 2613.
24. Silva, O.; Elsa, T. *J. Nat. Prod.* **2003,** *66*, 447.
25. De Koning, C. B.; Michael, J. P.; van Otterlo, W. A. L. *Tetrahedron Lett.* **1999**, *40*, 3037. (b) Manfredi, K. P.; Blunt, J. W.; Cardellina, J. H. II.; Macmahon, J. B.; Pannell, L. K.; Cragg, G. M.; Boyd, M. R. *J. Med. Chem.* **1991**, *34*, 3402.

26. Bringmann, G.; Gotz, R.; Keller, P. A.; Walter, R.; Boyd, M. R.; Lang, F.; Garcia, A.; Walsh, J. J.; Tellitu, I.; Bhaskar, K. V.; Kelly, T. R. *J. Org. Chem.* **1998**, *63*, 1090
27. (a) Signorelli, P.; Ghidoni, R. *J. Nutr. Biochem.* **2005**, *16*, 449. (b) Minutolo, F.; Sala, G.; Bagnacani, A.; Bertini, S.; Carboni, I.; Placanica, G.; Prota, G.; Rapposelli, S.; Sacchi, N.; Macchia, M.; Ghadoni, R. *J. Med. Chem.* **2005**, *48*, 6783. (c) Viswanathan, G. S.; Wang, M.; Li, C. J. *Angew. Chem. Int. Ed.* **2002**, *41*, 2138. (d) Kozik, B.; Burgie, Z. J.; Sepiot, J. J.; Wilamowski, J.; Kuczynski, M.; Góra, M. *Environ. Biotechnol.* **2006**, 20.
28. Jae Nyoung, K.; Yang Jin, I.; Ji Hyeon, G.; Ka Young, L. *Tetrahedron Lett.* **2001**, *42*, 4195.
29. De Koning, C. B.; Michael, J. P.; Rousseau, A. L. *Tetrahedron Lett.* **1997**, *38*, 893.
30. For reviews, see: (a) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901. (b) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (c) Lautens, M.; Klute,W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (d) Trost, B. M. *Angew. Chem.* **1995**, *107*, 285. (e) Grotjahn, D. B. in *Comprehensive Organometallic Chemistry II*; Hegedus, L. S.; Abel, E. W.; Stone, ***F***. G. A.; Wilkinson, G.; Eds.; Pergamon: Oxford, **1995**; Vol. 12, p 741. (f) Schore, N. E. *in Comprehensive Organic Synthesis;* Trost, B. M.; Fleming, I.; eds., Pergamon: Oxford, **1991**; Vol. 5, p 1129.
31. (a) Viswanathan, G. S.; Wang, M.; Li, C. J. *Angew. Chem.* **2002**, *114*, 2242; *Angew. Chem., Int. Ed.* **2002**, *41*, 2138. (b) Kabalka, G. W.; Ju, Y.; Wu, Z. *J. Org. Chem.* **2003**, *68*, 7915. (c) Asao, A.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am.Chem. Soc.* **2002**, *124*, 12650. (d) Asao, A.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921.
32. Ibad, M.F.; Eleya, N.; Abid, O. u. R.; Mahal, A.; Hussain, M.; Villinger, A.; Langer, P. *Synthesis* **2011**, 2101.
33. For reviews of cross-coupling reactions of polyhalogenated heterocycles and triflates, see: (a) Schröter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245. (b) Schnürch, M.; Flasik, R.; Khan, A. F.; Spina, M.; Mihovilovic, M. D.; Stanetty, P. *Eur. J. Org. Chem.* **2006**, 3283. (c) Rossi, R.; Bellina, F.; Lessi, M. *Adv. Synth. Catal.* **2012**, *354*, 1181.
34. For a simple guide to predict the regioselectivity of Pd catalyzed cross-coupling reactions, see: Handy, S. T.; Zhang, Y. *Chem. Commun.* **2006**, 299.

35. Ibad, M.F.; Eleya, N.; Abid, O. u. R.; Mahal, A.; Hussain, M.; Villinger, A.; Langer, P. *Synthesis* **2011**, 2101.
36. Ishizeki, S.; Ohtsuka, M.; Irinoda, K.; Kukita, K.; Nagaoka, K.; Nakashima, T. *J Antibiot.* (Tokyo), **1987**, *40*, 60.
37. Manfredi, K. P.; Blunt, W.; Cardellina II, J. H.; Macmahon, J. B.; Pannell, L. K.; Cragg, G. M.; Boyd, M. R. *J. Med. Chem*. **1991**, *34*, 3402.
38. Asao, A.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc*. **2002**, *124*, 12650.
39. Ibad, M.F.; Eleya, N.; Abid, O. u. R.; Mahal, A.; Hussain, M.; Villinger, A.; Langer, P. *Synthesis* **2011**, 2101.
40. Hassan, Z.; Hussain, M.; Villinger, A.; Langer. P. *Tetrahedron* **2012**, *68*, 6305.
41. Kamikawa, T.; Hayashi. T. *Tetrahedron Lett.* **1997**, *38*, 7087.(a) Hassan, Z.; Hussain, M.; Villinger, A.; Langer. P. *Tetrahedron* **2012**, *68*, 6305
42. Schröter, S.; Stock, C.; Bach, T.; for reviews of cross-coupling reactions of polyhalogenated heterocycles and triflates, see: *Tetrahedron* **2005**, *61*, 2245.
43. Handy, S.T.; Zhang, Y.; for a simple guide to predict the regioselectivity of Pd catalyzed cross-coupling reactions, see: *Chem. Commun*. **2006**, 299.
44. (a) Murray, R. D. H. *Nat. Prod. Rep*. **1995**, *12*, 477; (b) Estevez-Braun, A.; Gonzalez, A. G. *Nat. Prod. Rep*. **1997**, *14*, 465; (c) Malikov, V. M.; Saidkhodzhaev, A. I. *Khim. Prir. Soedin*. **1998**, *34*, 250.
45. (a) Bailly, C.; Bal, C.; Barbier, P.; Combes, S.; Finet, J. P.; Hildebrand, M. P.; Peyrot, V.; Wattez, N. *J. Med. Chem.* **2003**, *46*, 5437; (b) Rappl, C.; Barbier, P.; Bourgarel-Rey, V.; Gregoire, C.; Gilli, R.; Carre, M.; Combes, S.; Finet, J. P.; Peyrot, V. *Biochemistry* **2006**, *45*, 9210.
46. Argotte-Ramos, R.; Ramírez-Avila, G.; Rodriguez-Gutierrez, M. C.; Ovilla-Munoz, M.; Lanz-Mendoza, H. M.; Rodriguez, Gonzalez-Cortazar, M.; Alvarez, L. *J. Nat. Prod.* **2006**, *69*, 1442.
47. Verotta, L.; Lovaglio, E.; Vidari, G.; Finzi, P. V.; Neri, M. G.; Raimondi, A.; Parapini, S.; Taramelli, D.; Riva, A.; Bombardelli, E. *Phytochemistry* **2004**, *65*, 2867.
48. Pierson, J. T.; Dumetre, A.; Hutter, S.; Delmas, F.; Laget, M.; Finet, J. P.; Azas, N.; Combes, S. *Eur. J. Med. Chem*. **2010**, *45*, 864.
49. Marçal de Queiroz, P. *Patent WO 98/25608*, **1997**.
50. Korec, R.; Sensch, K. H.; Zoukas, T. *Arzneim. Forsch.* **2000**, *50*, 122.

51. Combes, S. B.; Barbier, P.; Douillard, S.; McLeer-Florin, A.; Bourgarel-Rey, V. R.; Pierson, J.T.; Fedorov, A.Y.; Finet, J.P.; Boutonnat, J.; Peyrot, V. *J. Med. Chem*. **2011**, *54*, 3153.
52. Taechowisan, T.; Lu, C.; Shen, Y.; Lumyong, S. *Food Agric. Immunol*. **2007**, *18*, 203.
53. Gosselin, F.; Britton, R. A.; Davies, I. W.; Dolman, S. J.; Gauvreau, D.; Hoerrner, R.S.; Hughes, G.; Janey, J.; Lau, S.; Molinaro, C.; Nadeau, C.; O'Shea, P. D.; Palucki, M.; Sidler, R. *J. Org. Chem*. **2010**, *75*, 4154.
54. (a) Garazd, M. M.; Garazd, Y. L.; Khilya, V. P. *Chem. Nat. Compd*. **2005**, *41*, 245; (b) Crecente-Campo, J.; Vanzquez-Tato, M.P.; Seijas, J. A. *Eur. J. Org. Chem.* **2010**, 4130.
55. (a) Kutubi, S.; Hashimoto, T.; Kitamura, T. *Synthesis* **2011**, 1283; (b) Yamamoto, Y.; Kirai, N. *Org. Lett*. **2008**, *10*, 5513.
56. Sasono, K.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc*. **2013**, *135*, 10954.
57. (a) Zhang, L.; Meng, T.; Fan, R.; Wu, J. *J. Org. Chem*. **2007**, *72*, 7279; (b) Rao, M. L. N.; Venkatesh, V.; Jadhav, D. N. *Eur. J. Org. Chem*. **2010**, 3945; (c) Oh, S.; Jang, H. J.; Ko, S. K.; Ko, Y.; Park, S. B. *J. Comb. Chem.* **2010**, *12*, 548; (d) Combes, S.; Pierson, J. T.; Finet, J. P.; Barbier, P.; Douillard, S.; Bourgarel-Rey, V.; Peyrot, V.; McLeer-Florin, A.; Boutonnat, J.; Fedorov, A. Y. *J. Med. Chem*. **2011**, *54*, 3153; (e) Kuroda, J.I.; Inamoto, K.; Hiroya, K.; Doi, T.; *Eur. J. Org. Chem*. **2009**, 2251; (f) Luo, Y.; Wu, J. *Tetrahedron Lett*. **2009**, *50*, 2103; (g) Gao, W.; Luo, Y.; Ding, Q.; Peng, Y.; Wu, J. *Tetrahedron Lett*. **2010**, *51*, 136; (h) Wong, P. Y.; Chow, W. K.; Chung, K. H.; So, C. M.; Lau, C. P.; Kwong, F. Y. *Chem. Commun*. **2011**, *47*, 8328; (i) Xing, C.H.; Lee, J. R.; Tang, Z.Y.; Zheng, J. R.; Hu, Q.S. *Adv. Synth. Catal*. **2011**, *353*, 2051; (j) Wu, J.; Yang, Z. *J. Org. Chem.* **2001**, *66*, 7875; (k) Xu, L.; Li, B.J.; Wu, Z.H.; Lu, X.Y.; Guan, B.T.; Wang, B.Q.; Zhao, K.Q. *Org. Lett*. **2010**, *12*, 884.
58. For reviews of cross-coupling reactions of polyhalogenated heterocycles and triflates, see: (a) Schröter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245; (b) Schnürch, M.; Flasik, R.; Khan, A. F.; Spina, M.; Mihovilovic, M. D.; Stanetty, P. *Eur. J. Org. Chem.* **2006**, 3283; (c) Rossi, R.; Bellina, F.; Lessi, M. *Adv. Synth. Catal.* **2012**, *354*, 1181; (d) Magano, J.; Dunetz, J. R. *Chem. Rev*. **2011**, *111*, 2177; (e) Hassan, Z.; Patonay, T.; Langer, P. *Synlett* **2013**, *24*, 412.

59. (a) Zhang, L.; Meng, T.; Fan, R.; Wu, J. *J. Org. Chem.* **2007**, *72*, 7279; (b) Wang, L.; Xia, J.; Tian, H.; Qian, C.; Ma, Y. *Indian J. Chem., Sect. B* **2003**, *42*, 2097; (c) Akrawi, O. A.; Nagy, G.; Patonay, T.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2012**, *53*, 3206; (d) Eleya, N.; Khaddour, Z.; Patonay, T.; Langer, P. *Synlett* **2012**, 223; (e) Hamdy, A.; Eleya, N.; Mohammed, M.; Khaddour, Z.; Patonay, T.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2013**, *54*, 3568.

60. Godell, J. R.; Puig-Basagoiti, F.; Forshey, B. M.; Shi, P. Y.; Ferguson, D. M. *J. Med.Chem.* **2006**, *49*, 2127.

61. (a) Kaila, N.; Janz, K.; De Bernardo, S.; Bedard, P. W.; Camphausen, R. T.; Tam, S.; Tsao, D. H. H.; Keith, J. C.; Nickerson-Nutter, Jr. C.; Shilling, A.; Young-Sciame, R.; Wang, Q. *J. Med. Chem*. **2007**, *50*, 21. (b) Krishnamurthy, M.; Simon, K.; Orendt, A. M.; Beal, P. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 7044. (c) Krishnamurthy, M.; D.Gooch, B.; Beal, P. A. *Org. Lett.* **2004**, *6*, 63. (d) Chaires, J. B.; Ren, J.; Henary, M.; Zegrocka, O.; Bishop, G. R.; Strekowski, L. *J. Am. Chem. Soc.* **2003**, *125*, 7272. (e) Strekowski, L.; Say, M.; Henary, M.; Ruiz, P.; Manzel, L.; Macfarlane, D. E.; Bojarski, A. J. *J. Med. Chem.* **2003**, *46*, 1242. (f) Strekowski, L.; Gulevich, Y.; C.Baranowski, T.; Parker, A. N.; Kiselyov, A. S.; Lin, S. Y.; Tanious, F. A.; Wilson, W. D. *J. Med. Chem*. **1996**, *39*, 3980. (g) Atwell, G. J.; Baguley, B. C.; Denny, W. A. *J. Med. Chem.***1989**, *32*, 396. (h) Craig, P. N. *J. Med. Chem.***1972**, *15*, 144.

62. (a) Gola, M.; Bonadonna, S.; Mazziotti, G.; Amato, G.; Giustina, A. *J. Endocrinol. Invest.* **2006**, *29*, 86. (b) Ma, P.; Wang, Y.; van der Hoek, J.; Nedelman, J.; Schran, H.; Tran, L. L.; Lamberts, S. W. *J. Clin. Pharmacol. Ther.* **2005**, *78*, 69.

63. (a) Mastrodimou, N.; Kiagiadaki, F.; Hodjarova, M.; Karagianni, E.; Thermos, K. Regul. *Peptides* **2006**, *133*, 41. (b) Grant, M. B.; Caballero, S. *Drugs Today* **2002**, *38*, 783. (c) Higgins, R. D.; Yan, Y.; Schrier, B. K.Exp. *Eye Res.* **2002**, *74*, 553. (d) Boehm, B. O.; Lang, G. K.; Jehle, P. M.; Feldmann, B.; Lang, G. E. *Horm. Metab. Res.* **2001**, *33*, 300. (e) Smith, L. E. H.; Kopchick, J. J.; Chen, W.; Knapp, J.; Kinose, F.; Daley, D.; Foley, E.; Smith, R. G.; Schaeffer, J. M. *Science* **1997**, *276*, 1706.

64. (a) Name Reactions in Organic Chemistry; Li, J.J., Ed.; Wiley-Interscience: New York, NY, **2005**, *375*-494. (b) *J. Org. Chem.* **2008**, *73*, 7451. (c) Jones, G. in *Comprehensive Heterocyclic Chemistry*, katritzky, A. R.; res, C.W., Eds., Pergamon: New York, **1984**; vol.2, p 395.

65. (a) Ahmad, N. M. Quinolines In Palladium in Heterocyclic Chemistry, 2nd ed.; Li, J.J.; Gribble, G. W.; Eds.; Elsevier: New York, NY, **2007**; pp 512-540. (b) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.***1987**, *109*, 5478; (c) Badone, D.; Cecchi, R.; Guzzi, U. *J. Org. Chem.* **1992**, *57*, 6323. (d) Gavryushin, A.; Kofink, C.; Manolikakes, G.; Knochel, P. *Org. Lett.* **2005**, *7*, 4871. (e) Gavryushin, A.; Kofink, C.; Manolikakes, G.; Knochel, P. *Tetrahedron* **2006**, *60*, 7521. (f) Organ, M.G.; Abdel-Hadi, M.; Avola, S.; Hadei, N.; Nasielski, J.; O` Brien, C.J.; Valente, C. *Chem. Eur. J.* **2007**, *13*, 150. (g) Hirner, J. J.; Zacutto, M. J. *Tetrahedron Lett.* **2009**, *50*, 4989. (h) babudri, F.; cardone, A.; Cioffi, C. T.; Farinola, G. M.; Naso, F.; Ragnib, R. *Synthesis* **2006**, 1325.
66. Song, G.; Xue, G.; Li, X. *J. Org. Chem.* **2011**, *76*, 2583.
67. Ji, X.; Huang, H.; Li, Y.; Chen, H.; Jiang, H. *Angew. Chem. Int. Ed.* **2012**, *51*, 7292.
68. Amii, H.; Kishikawa, Y.; Uneyama, K. *Org. Lett.* **2001**, *3*, 1109.
69. Martínez, R.; Ramón, D. J.; Yus, Miguel. *Eur. J. Org. Chem.* **2007**, 1599.
70. Arcadi, A.; Aschi, M.; Marinelli, F.; Verdecchia, M. *Tetrahedron* **2008**, 5354.
71. Magano, J.; Dunetz, J. R. *Chem. Re*v. **2011**, *111*, 2177.
72. Nolt, M. B.; Zhao, Z.; Wolkenberg, S. E. *Tetrahedron Lett.* **2008,** *49*, 3137.
73. (a) Février, F. C.; Smith, E. D.; Comins, D. L. *Org. Lett.*, **2005**, *7*, 5457. (b) Tilley, J. W.; Zawoiski, S. *J. Org. Chem.* **1988**, *53*, 386. (c) Madar, D. J.; Kopecka, H.; Pireh, D.; Pease, J.; Pliushchev, M.; Sciotti, R. J.; Wiedeman, P. E.; Djuric, S. W. *Tetrahedron Lett.* **2001**, *42*, 3681. (d) Lang, F.; Zewge, D.; Houpis, I. N.; Volante, R. P. *TetrahedronLett.* **2001**, *42*, 3251. (e) Arterburn, J. B.; Rao, K. V.; Ramdas, R.; Dible, B. R. *Org. Lett.* **2001**, *3*, 1351. (f) Ji, J.; Li, T.; Bunnelle, W. H. *Org. Lett.* **2003**, *5*, 4611. (g) Jiang, W.; Guan, J.; Macielag, M. J.; Zhang, S.; Qui,Y.; Kraft, P.; Bhattacharjee, S.; John, T. M.; Haynes-Johnson, D.; Lundeen, S.; Sui, Z. *J. Med. Chem.* **2005**, *48*, 2126. (h) Zhang, H.; Cai, Q.; Ma, D. *J. Org. Chem.* **2005**, *70*, 5164. (i) Schwab, P. F. H.; Fleischer, F.; Michl, J. *J. Org. Chem.* **2002**, *67*, 443. (j) Haino, T.; Araki, H.; Yamanaka, Y.; Fukazawa, Y. *Tetrahedron Lett.* **2001**, *42*, 3203. (k) Sandee, A. J.; Williams, C. K.; Evans, N. R.; Davies, J. E.; Boothby, C. E.; Koehler, A.; Friend, R. H.; Holmes, A. B. *J. Am. Chem. Soc.* **2004**, *126*, 7041. (l) Vice, S.; Bara, T.; Bauer, A.; Evans, C. A.; Ford, J.; Josien, H.; McCombie, S.; Miller, M.; Nazareno, D.; Palani, A.; Tagat, J. *J. Org. Chem.* **2001**, *66*, 248. (m) Couve-Bonnaire, S.; Carpentier, J. F.; Mortreux, A.; Castanet, Y. *Tetrahedron Lett.*

2001, *42*, 3689. (n) Fang, Y. Q.; Hanan, G. S. *Synlett* **2003**, 852. (o) Nakano, Y.; Ishizuka, K.; Muraoka, K.; Ohtani, H.; Takayama, Y.; F. Sato, *Org. Lett.* **2004**, *6*, 2373. (p) Gelman, D.; Tsvelikhovsky, D.; Molander, G. A.; Blum. J. *J. Org. Chem.* **2002**, *67*, 6287. (q) Hartner, F. W.; Hsiao, Y.; Eng, K. K.; Rivera, N. R.; Palucki, M.; Tan, L.; Yasuda, N.; Hughes, D. L.; Weissman, S.; Zewge, D.; King, T.; Tschaen, D.; Volante, R. P. *J. Org. Chem.* **2004**, *69*, 8723. (r) Bonnet, V.; Mongin, F.; Trecourt, F.; Queguiner, G.; Knochel, P. *Tetrahedron* **2002**, *58*, 4429. (s) Handy, S. T.; Wilson, T.; Muth, A. *J. Org. Chem.* **2007**, *72*, 8496, and references cited therein. (t) Sicre, C.; Alonso-Gómez, J. L.; Cid, M. M. *Tetrahedron* **2006**, *62*, 11063. (u) García-Lago, R.; Alonso-Gómez, J. L.; Sicre, C.; Cid, M. M. *Heterocycles* **2008**, *75*, 57. (v) Reisch, J.; Gunaherath, G. M. K. B. *J. Heterocycl. Chem.* **1993**, *30*, 1057; the original assignment of the regioselectivity was corrected later on: (w) Comins, D. L.; Nolan, J. M. *Org. Lett.* **2001**, *3*, 4255.

74. (a) Shiota, T.; Yamamori, T. *J. Org. Chem.* **1999**, *64*, 453. (b) Nolan, J. M.; Comins, D. L. *J. Org. Chem.* **2003**, *68*, 3736. (c) Comins, D. L.; Nolan, J. M.; Bori, I. D. *Tetrahedron Lett.* **2005**, *46*, 6697. (d) Tsvetkov, A. V.; Latyshev, G. V.; Lukashev, N. V.; Beletskaya, I. P. *Tetrahedron Lett.* **2002**, *43*, 7267. (e) Beletskaya, I. P.; Tsvetkov, A. V.; Latyshev, G. V.; Lukashev, N. V. *Russ. J. Org. Chem.* **2003**, *39*, 1660. (f) Beletskaya, I. P.; Latyshev, G. V.; Tsvetkov, A. V.; Lukashev, N. V. *Russ. Chem. Bull.* **2004**, *53*, 189. (g) Beletskaya, I. P.; Tsvetkov, A. V.; Tsvetkov, P. V.; Latyshev, G.; Lukashev, N. V. *Russ. Chem. Bull.* **2005**, *54*, 215. (h) Simkovsky, N. M.; Ermann, M.; Roberts, S. M.; Parry, D. M.; Baxter, A. D. *J. Chem. Soc., Perkin Trans. 1.* **2002**, 1847. (i) Dubé, D.; Blouin, M.; Brideau, C.; Chan, C. C.; Desmarais, S.; Ethier, D.; Falgueyret, J. P.; Friesen, R. W.; Girard, M.; Guay, J.; Riendeau, D.; Tagari, P.; Young, R. N. *Bioorg.Med. Chem. Lett.* **1998**, *8*, 1255. (j) Legros, J. Y.; Primault, G.; Fiaud, J. C. *Tetrahedron* **2001**, *57*, 2507. (k) Trécourt, F.; Mongin, F.; Mallet, M.; Quéguiner, G. *J. Heterocycl. Chem.* **1995**, *32*, 1261. (l) Csányi, D.; Timári, G.; Hajós, G. *Synth. Commun.* **1999**, *29*, 3959. (m) Swahn, B. M.; Andersson, F.; Pelcman, B.; Söderberg, J.; Claesson, A. *J. Labelled Comp. Radiopharm.* **1997**, *39*, 259. (n) Piala, A.; Mayi, D.; Handy, S. T. *Tetrahedron* **2011**, *67*, 4147. (o) Eleya, N.; Mahal, A.; Hein, M.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2011**, *353*, 2761, and references cited therein.

75. Hassan, Z.; Hussain, M.; Villinger, A.; Langer, P. *Tetrahedron* **2012**, *68*, 6305.

76. (a) Kamikawa, T.; Hayashi, T. *Tetrahedron Lett.* **1997**, 38, 7087. (b) Littke, A. F.; Dai, C. Y.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020. (c) Roy, A. H.; Hartwig, J. F. *Organometallics* **2004**, *23*, 194. (d) Espinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704. (e) Espino, G.; Kurbangalieva, A. and Brown, J. M. *Chem. Comm.* **2007**, 1742, and references cited therein.
77. Baker; W; Chadderton, J.; Harborne, J. B.; Ollis, W. D. *J Chem Soc*, **1953**, 1852
78. Kagal S. A.; Karmakov, S. S.; Venkatarman, K. *Proc Indian Acad Sci*, **1956**, *44a*, 36.
79. Yokoe, I.; Sugita, Y.; Shirataki, Y. *Chem. Pharm. Bull.* **1989,** *37*, 529.
80. Peterson, G.; Branes, S. *Biochem. Biophys. Res. Commun*. **1991**, *179*, 661.
81. Bandyukova, V. A.; Cherevatye, V. S.; Ozimina, I. I.; Andreera, O. A.; Lebedava, A. L.; Davydov, V. S.; Vashchenko, T. N.; Postnikova, N. V. *Rastit. Resur*. **1987**, *23*, 607; *Chem Abstr*, **1990**, *108*, 71937v.
82. EI-Gammal A. A.; Mansour R. M. *Zentralbl. Mikrobiol.* **1986**, *141*, 561; *Chem Abstr*, **1987**, *106*, 135070a.
83. Takai, M.; Yamaguchi, H.; Saitoh, T.; Shibata, S. *Chem. Pharm. Bull.* **1972**, *20*, 488
84. Nestel, P.; Cehun, M.; Chronopoulos, A.; DaSilva, L.; Teede, H.; McGrath, B.; A *Eur. J. Clin. Nutr.* **2004**, *48*, 403.
85. Kao, T. H.; Chen, B. H. *J. Agric. Food Chem.* **2006**, *54*, 7544.
86. Kao, T. H.; Huang, R. F; Chen, B.H. *Int. J. Mol. Sci.* **2007**, *8*, 1095.
87. Kao, T. H.; Wu, W. M.; Hung, C. F.; Wu, W. B.; Chen, B. H. *J. Agric. Food Chem*. **2007**, *55*, 11068.
88. Dalais, F. S.; Ebeling, P. R.; Kotsopoulos, D.; McGrath, B. P.; Teede, H. J. *Clin. Endocrinol. (Oxf.)* **2003**, *58*, 704.
89. Migliaccio, S.; Anderson, J. J. *Osteoporos. Int*. **2003**, *14*, 361.

Declaration

Here by I declare that this work has so for neither submitted to the Faculty of Mathematics and Natural Sciences at the University of Rostock nor to any other scientific Institution for the purpose of doctorate. Furthermore, 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.

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

Erklärung

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.

Zien Khaddour

List of Publications

1. Eleya, N.; **Khaddour, Z**.; Patonay, T.; Langer, P. *Synlett* **2012**, 223.
   Efficient Synthesis of Arylated Coumarins by Site-Selective Suzuki–Miyaura Cross-Coupling Reactions of the Bis(triflate) of 4-Methyl-5,7-dihydroxycoumarin.

2. **Khaddour, Z**.; Eleya, N.; Akrawi, O.; Hamdy, A.; Patonay, T.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2013**, 5201-5203.

   Chemoselective Suzuki–Miyaura cross-coupling reactions of methyl 4-bromo-3-(trifluoromethylsulfonyloxy)-2-naphthoate.

3. **Khaddour, Z**.; Eleya, N.; Akrawi, O.; Hamdy, A.; Patonay, T.; Villinger, A.; Langer, P. *Synlett* **2013**, *24*, 2114-2118.
   Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of the Bis(triflate) of Methyl 3,7-Dihydroxy-2-naphthoate.

4. Hamdy, A.; Eleya, N.; Mohammed, H.; **Khaddour, Z.**; Patonay, T.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2013**, *54*, 3568-3571.
   Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 4-Methyl-5,7-bis(trifluoromethylsulfonyloxy)-coumarine.

5. **Khaddour, Z**.; Akrawi, O.; Suleiman, A.; Patonay, T.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2014**, 4421–4423.

   Regioselective Suzuki–Miyaura cross-coupling reactions of the bis(triflate) of 4,7-dihydroxycoumarin.

6. **Khaddour, Z**.; Akrawi, O.; Hamdy, A.; Suleiman, A.; Jamous, K.; Villinger, A.; Langer, P.

   Tetrahedron Lett. **2014**. Chemoselective Suzuki-cross coupling reactions of 5-bromoquinolin-8-yl trifluoromethanesulfonate.

CURRICULUM VITAE

Personal Particular

Name	Zien Suleiman Khaddour
Date of Birth	01.09.1984
Nationality	Syrian
Gender	Male
Marital Status	Single
Languages	Arabic (Mother Tongue) English, German
E-mail address	Zien.khaddour@yahoo.de

Educational Background

1. The baccalaureate Abo-zir-algefari Alhasaka Syria 2002.
2. B.Sc. Degree in Chemistry, from Department of Chemistry, College of Science, University of Damascus, Damascus-Syria 2006.
3. M.Sc. Degree in Organic Chemistry, Department of Chemistry, College of Science, University of Rostock, Rostock-Germany 2012
4. Since March 2012 till now promotion study program at the University of Rostock.