Universität Rostock Traditio et Innovatio

Synthesis of Functionalized Triarylmethanes and Pyranones Based on Cyclization Reactions of Free and Masked Dianions and Regioselective Palladium(0)-Catalyzed Reactions of Functionalized Sulfones, Benzophenones, Pyrazoles, Indenones, and Furans

Dissertation

zur

Erlangung des Doktorgrades

doctor rerum naturalium (Dr. rer. nat.)

der Mathematisch-Naturwissenschaftlichen Fakultät

der Universität Rostock

vorgelegt von

Rasheed Ahmad Khera geb. am 15 April 1980, Kotla Sadat, Muzaffargarh, (Punjab) Pakistan.

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

urn:nbn:de:gbv:28-diss2010-0163-2

Tag der Abgabe:	08-08-2010
Tag der Verteidigung:	19-10-2010
Prüfer Hauptfach:	**Prof. Dr. Peter Langer** (Universität Rostock)
Prüfungsvorsitzender:	**Prof. Dr. Martin Köckerling** (Universität Rostock)
Prüfer Nebenfach:	**Prof. Dr. Peter Metz** (Universität Dresden)

“I feel a great pleasure to dedicate all of this work to **Pakistan** then my all **teachers** from I learned and will learn even a single word and my dear **parents, brothers** and **sisters.**

Acknowledgements

First of AlI I pay my infinite thanks to Almighty **Allah Azzawajal** who blessed me with the chance and courage to complete this memorable task. And then **Prophet Mohammad** (Sallallah ho alai hi wasallam) whose personality is like a light through which each and everybody can examine his good and bad deeds.

I wish to present my thanks to all who added to the successful completion of my Ph.D.

Danke

I feel it due, to pay my thanks to **Prof. Dr. Peter Langer**, my Ph.D. supervisor, for providing efficient guidance and energetic research environment during whole Ph.D. I always found him ready to facilitate my research, by effective discussions, reviving encouragements, unending trust, providing free hand in research and access to every possible facility.

My special thanks to Prof. Dr. Aamer Saeed due to his exceptional support and company during my stay in Quaid-i-Azam, University (Islamabad) Pakistan, in fact he contributed very much in my research, practical and theoretical understanding during my stay in Pakistan.

Thank you

I wish to express my special gratitude to Dr. Martin Hein and Dr. Dirk Michalik for a number of nice talks about my research, to Dr. Holger Feist for his passion to deliver security instruction and making sure the security, to Dr. Alexander Villinger for their professional and accurate measuring X-ray crytallographic analyses. I would also like to thank the members of NMR, IR, UV, MS, and X-ray laboratories of the University of Rostock and the Leibniz Institute for Catalysis Rostock.

Shukriaa

I would like to pay my deep respectful tributes to my loving ***parents*** for their countless prayers, salutary advices and emboldening attitude that kept my spirit alive. The whole, I achieved is actually their achievements. The words are insufficient to express my feelings for my ever-loving brothers and sisters. They are a symbol of love for me. I will never forget their prayers, support, love, co-operation and

encouragement provided by my brothers Khalil Ahmad Khera, Tufail Ahmad Khera and Saeed Ahmad Madni Khera.

Vielen Dank

Acknowledgements are made to Prof. Dr. Hartmut Laatsch during my stay in Institut für Organische und Biomolekulare Chemie der Universität Göttingen, Germany; in fact he contributed very much during my stay in Pakistan for introducing such a nice Peter Langer research group and taking care of my arrival problems.

I am thankful to all my past and present, foreigner and native colleagues, which I have missed here to mention for their research discussions, nice company and time.

Many thanks to Munawar Hussain, Dr. Muhammad Arfan, Dr. Rasheed Ahmad, Asad Ali, Dr. Muhammad Sher, Ihsan Ullah Marwat, Muhammad Nawaz, Dr. Majid Rahi, Dr. Obaid-ur-Rahman Abid, Aneela Maalik, Jovana Tatar, Muhammad Sharif, Dhafer Saber Zinad, Omer Akravi, Ghazwan Ali Salman, Muhammad Zeeshan, Tariq Mahmood Babar, Sajid Ali, N. T. Hung, Dr. Inam Iqbal, Dr. Imran Iqbal, Naeem Abbas, Hummera Rafique, Ahmed Mahal, Dr. Olumede Fatunsin, Dennis Kleeblatt, Ingo Knepper, Friedrich Erben, Dr. Stefan Büttner, Verena Wolf, Tengho Toguem, Silke Erfle, Alina Bunescu, Franziska Bendrath, Muhammad Farooq Ibad and all of my other colleagues for their contribution and cooperation.

Thanks a lot

I thank to my all countryfellow especially my best friends Abid Hussain Ahash, Naseem Iqbal and all other Pakistanis in all parts of Germany particularly in Gottingen, Frankfurt, Berlin and Rostock as their love, readiness to help and meaningful company gave me not only support but also feeling like own country, and city which made my stay here enjoyable.

Danke schön

It is not possible to forget to pay thanks to Professor Peter Langer to arrange scholarship for me such as DAAD, Friedrich-Irmgard-Harms-Stiftung scholarship from Germany as well as HEC scholarship from

Pakistan for his dedication to support and facilitate me to work out all related problems.

Cam on

Financial support for my Ph.D. from DAAD, Friedrich-Irmgard-Harms-Stiftung and Higher Education Commission (HEC) of Pakistan is gratefully acknowledged.

Many Thanks

Special thanks to all of my teachers for their education and training in both life and chemistry: especially Prof. Dr. Aamer Saeed, Prof. Dr. Humayun Pervez, Prof. Dr. Farzana Latif Ansari, Prof. Dr. Zahid Shafique as i started my research life with them during my my M.Sc, M.Phil. and all others.

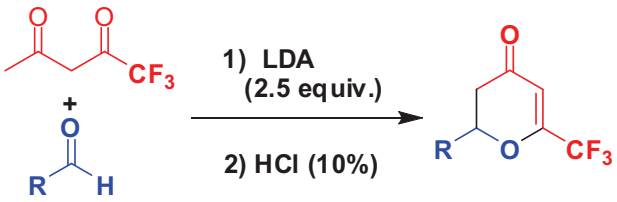
I would like to convey my heartiest thanks to my whole family for their love, support and adherence to my achievement struggle. The significance of their support and help in past and present cannot be expressed by words.

I owe all of them in my life!

MAIN CONTENTS

CHAPTER 3 **Page 32-35**

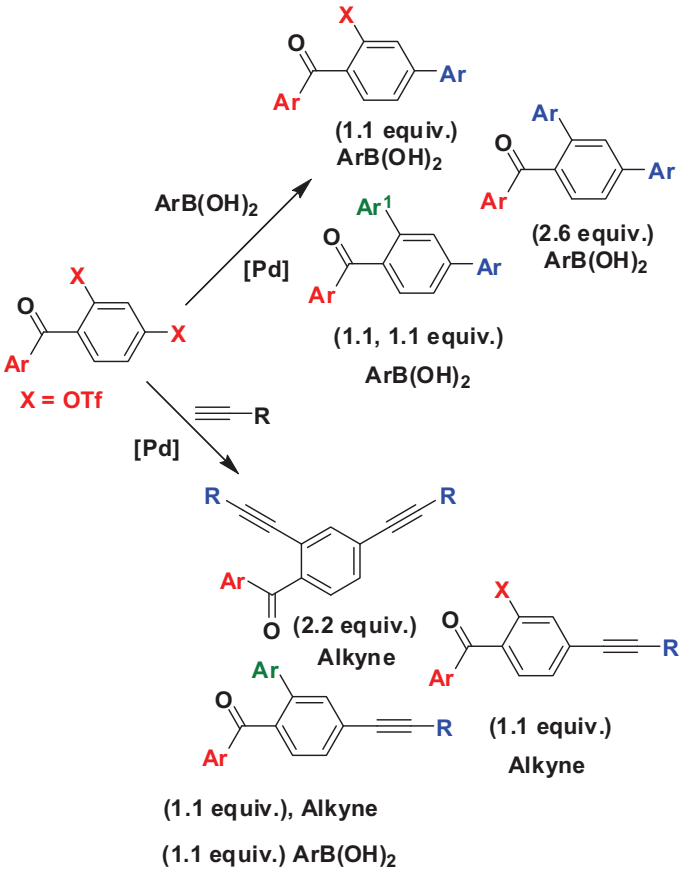
Synthesis of Fluorinated 2,3-Dihydro-4*H*-pyran-4-ones by Cyclocondensation of 1,3-Dicarbonyl Dianions with Aldehydes



The reaction of the dianion of 1,1,1-trifluoro-pentane-2,4-dione with aldehydes and subsequent addition of hydrochloric acid afforded 2,3-dihydro-6-trifluoromethyl-pyran-4-ones.

CHAPTER 4 **Page 36-42**

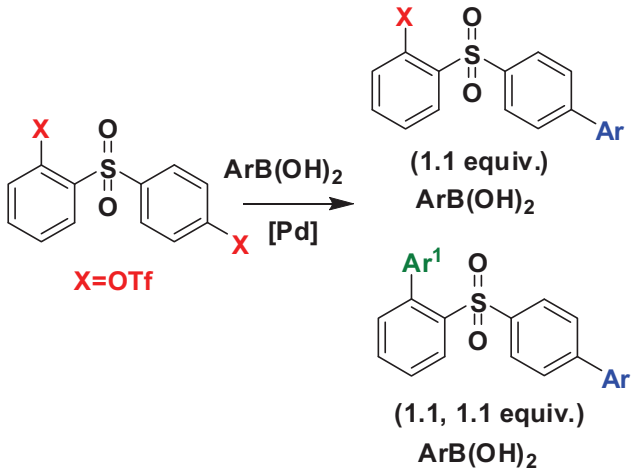
Synthesis of 2,4-Diarylbenzophenones by Site-Selective Suzuki-Miyaura, Sonogashira Cross-Coupling Reactions of 2,4-Bis(trifluoromethylsulfonyloxy)benzophenone



The Suzuki-Miyaura reaction of bis(triflate) of 2,4 dihydroxybenzophenone with aryl boronic acids gave 2,4-diarylbenzophenones. The reaction with one equivalent of arylboronic acids resulted in site-selective attack on less hindered carbon atom at C-4 and two different aryl groups were prepared by sequential addition of two different aryl boronic acids.

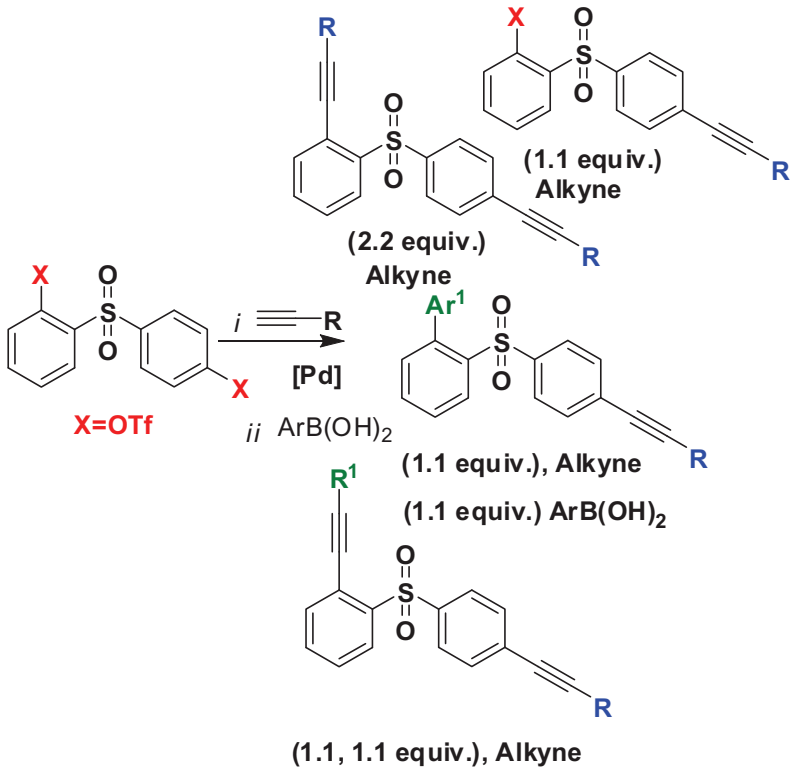
CHAPTER 5 **Page 43-47**

Synthesis of Bis(diaryl)sulfones by Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,4′-Bis(trifluoromethylsulfonyloxy)diphenylsulfone



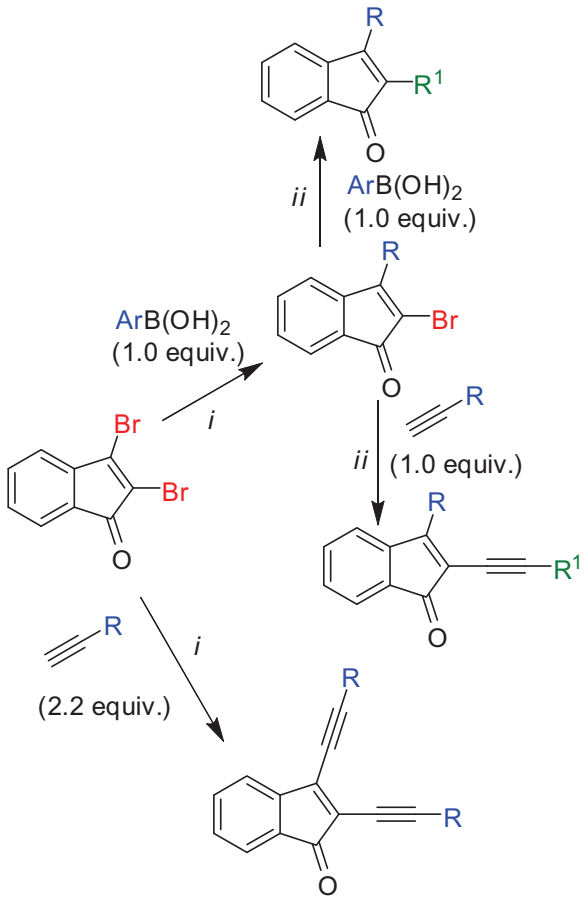
Suzuki-Miyaura reactions of the bis(triflate) of 2,4′-bis(hydroxy)diphenylsulfone with aryl boronic acids gave 2,4′-bis(aryl)diphenylsulfones. The reaction with one equivalent of arylboronic acids resulted in site-selective attack onto carbon atom C-4. 2,4-Diarylsulfones containing two different aryl groups were prepared by sequential addition of two different boronic acids.

Synthesis of Bis(diaryl)sulfones by Site-Selective Sonagashira Cross-Coupling Reactions of 2,4′-Bis(trifluoromethylsulfonyloxy)diphenylsulfone



Sonogashira cross-couplings of bis(triflate) of 2,4′-bis(hydroxy)diphenylsulfone with terminal alkynes. This reaction displays remarkable compatibility with regard to the formation of symmetrical, unsymmetrical alkynyl-alkynyl and alkynyl-aryl substitution. The first attack occurs on the less hindered C-4 carbon atom.

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

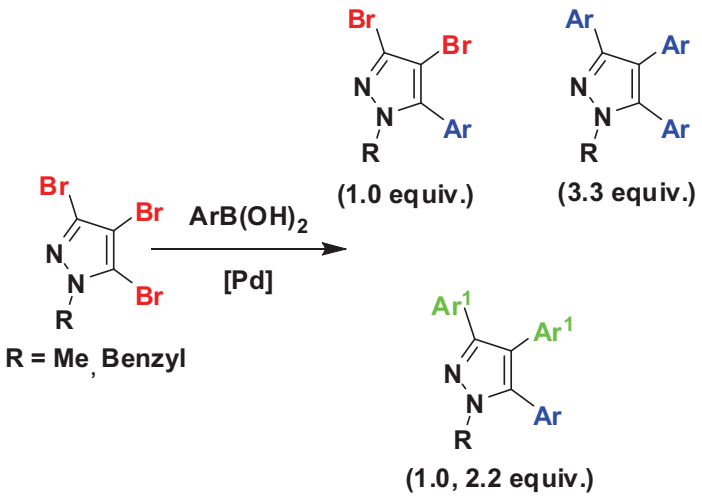


The Suzuki-Miyaura reaction of 2,3-dibromo-1*H*-inden-1-one with one equivalent of arylboronic acid gave 2-bromo-3-aryl-1*H*-inden-1-ones with very good regioselectivity and with two different arylboronic acids afforded 2,3-diaryl-1*H*-inden-1-ones containing two different terminal aryl groups in excellent yields.

The Sonogashira cross-coupling of 2,3-dibromo-1*H*-inden-1-one with terminal alkynes. This reaction gave us the formation of symmetrical, alkynyl-alkynyl, alkynyl-aryl substitution. The first attack occurs on the less hindered C-3 carbon atom.

CHAPTER 8 **Page 61-69**

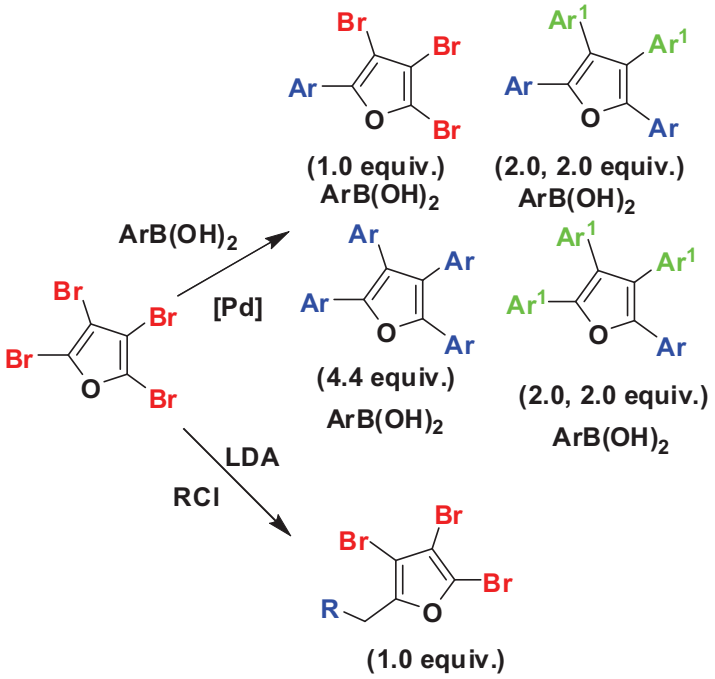
Synthesis of Arylated Pyrazoles by Site-Selective Suzuki-Miyaura Reactions of Tribromopyrazoles



Suzuki-Miyaura reactions of *N*-protected 3,4,5-tribromopyrazoles allowed a convenient synthesis of symmetrical and unsymmetrical monoaryl and triaryl pyrazoles by using the corresponding equivalents of aryl boronic acids. All reactions proceeded with excellent yields and site-selectivity.

CHAPTER 9 **Page 70-76**

Synthesis of Unsymmetrical Arylated Furans by Suzuki-Miyaura Cross Coupling and Metal-Halide Exchange Reactions of 2,3,4,5-Tetrabromofuran



Suzuki-Miyaura reactions of 2,3,4,5-tetrabromofuran allowed a convenient synthesis of aryl-substituted furans, such as symmetrical and unsymmetrical monoaryl, diaryl, and tetraarylfurans by using the corresponding equivalents of aryl boronic acids. Aryl-substituted furans are prepared which are not readily available by other methods. All reactions proceeded with excellent yields and site-selectivity.

Contents

1 Synthesis of Functionalized Triarylmethanes by Combination of $FeCl_3$-Catalyzed Benzylations of Acetylacetone with [3+3] Cyclocondensations

1.1 Introduction

Triarylmethanes[1] and 1,1-diphenylmethyl-salicylates are of considerable biological relevance as antibiotics and cytotoxic agents.[2] Natural products containing a (1,1-diphenylmethyl)phenol moiety include mohsenone, chamaechromone and other molecules.[1a,b] For example, derivatives A and B were isolated as natural products[1] formed by metabolism of the dye phenol red (Figure 23). The triphenylmethanes C and D were isolated from the leaves of the *cajeput* tree *Melaleuca quinqueneruia (Myrtaceae)*.[2a]

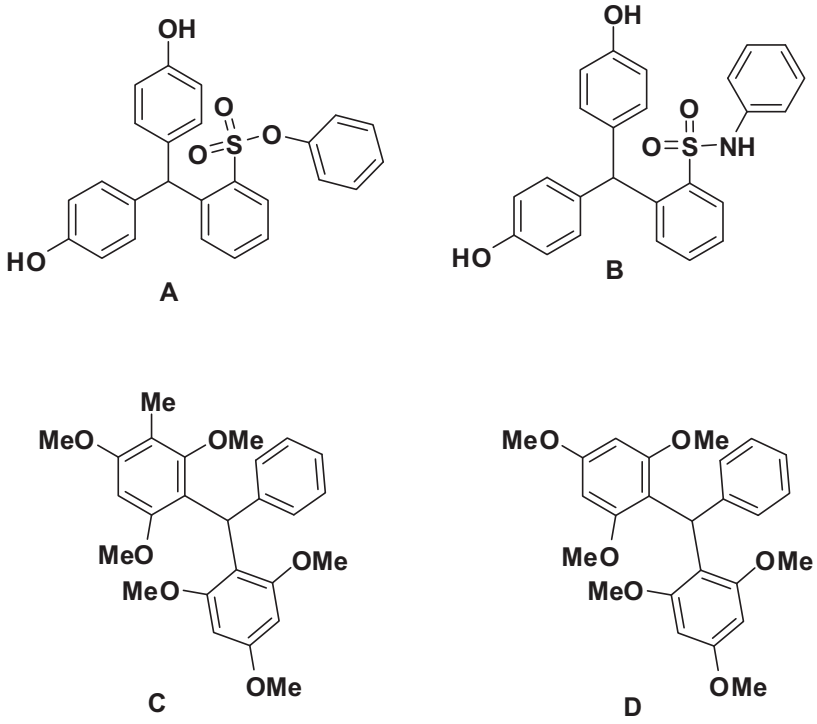


Figure 1. Triarylmethane natural products

Di- and triarylmethanes have been prepared by Friedel–Crafts alkylations. This method is limited by the harsh reaction conditions and by the low regioselectivity. An interesting way to solve this was found by novel $FeCl_3 \cdot 6H_2O$-catalyzed Friedel–Crafts type benzylations of arenes using simple benzylic alcohols under mild conditions and with high regio- and chemoselectivity.[3a,b] Likewise, $FeCl_3$-catalyzed conjugate additions of 1,3-dicarbonyl

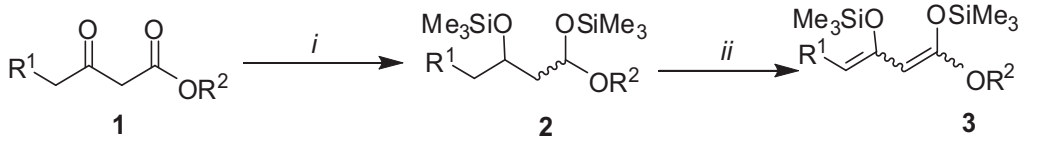
derivatives[4] and reactions of 1,3-dicarbonyl compounds with benzylic alcohols have been reported.[5,6]

In my Ph.D work, I have developed an approach to sterically encumbered, highly substituted triarylmethanes by combination of $FeCl_3$-catalyzed condensations with [3+3] cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-dienes, developed by Chan *et al.,*[7a,b 8a,b, 9] with 3-trimethylsilyloxy-2-en-1-ones. In this chapter, I have discussed my research results related to the scope of this approach. Reaction conditions and methodology discussed in this chapter provided a straightforward way to a variety of $FeCl_3$-catalyzed benzylation/[3+3] cyclocondensation reactions, which other methods did not provide readily. Recently, these results have been published.[9]

1.2 Results and Discussion

1.2.1 Synthesis of 1,3-Bis-Silyl Enol Ethers

The synthesis of 1,3-bis(trimethylsilyloxy)-1,3-dienes, electroneutral 1,3-dicarbonyl dianion equivalents[10a-b, 8b] of type **3**, was carried out according to a two step procedure described by Molander and Chan[10a-b] which was slightly varied.



R^1 = H, Alkyl, Alkoxy, Benzyloxy
R^2 = Alkyl,

Scheme 1. Synthesis of silyl enol ethers of type **2** and **3**. Conditions: *i)* Benzene, NEt_3 (1.4 equiv.) 30 min, then 1.4 eq. Me_3SiCl, 20 °C, 3 d; *ii)* THF, (1.4 equiv.) LDA, –78°C, 2, 1 h, then 1.7 eq. Me_3SiCl, –78 → 20 °C in 12-18 h.

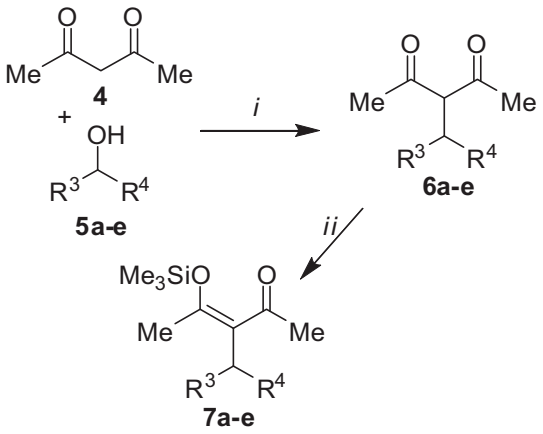
The alkylation of β-dicarbonyl compounds represents one of the most important C–C bond formation methodologies in organic synthesis[11]. Addition of β-dicarbonyl compounds to olefins results in a highly atom efficient protocol. In general, these transformations were performed by the reaction of alcohols[12,5] or alkyl halides[13] with β-dicarbonyl compounds. In

case of alcohols, hydroxy group is a poor leaving group which necessitates its preactivation and which can be achieved using high temperature or by suitable promoter[14].

1.2.2 Synthesis of Mono-Silyl Enol Ethers

Recently, many acid catalysts were employed to perform nucleophilic substitution of benzyl alcohols with active methylene compounds,[12c] whereas, the alkylation of β-dicarbonyl compounds with alcohols was also explored with different types of acid catalysts.[6a-d]

The $FeCl_3 \cdot 6H_2O$-catalyzed benzylation of acetylacetone **4** with benzylalcohols **5a-e**, following conditions reported by Beller *et al.*[5] afforded products **6a-e** in very good yields (Scheme 2, Table 1). The silylation of **6a-e** afforded the 3-silyloxy-2-en-1-ones **7a-e**.



Scheme 2. Synthesis of **7a-e**, *i*: $FeCl_3 \cdot 6H_2O$, NO_2CH_3, 50 °C, 4 h; *ii*: Me_3SiCl, NEt_3, C_6H_6, 20 °C, 72 h

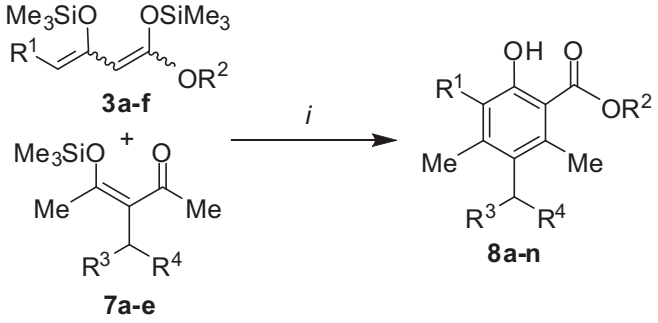
Table 1. Synthesis of **6a-e** and **7a-e**

5	$\mathbf{R^3}$	$\mathbf{R^4}$	% (**6**)[a]	%(**7**)[a]
a	Ph	Ph	91	90
b	4-FC_6H_4	4-FC_6H_4	87	89
c	4-ClC_6H_4	4-ClC_6H_4	85	92
d	Me	4-BrC_6H_4	95	90
e	Me	4-(MeO)C_6H_4	86	90

[a] Isolated yields

1.2.3 Synthesis of di- and triarylmethanes (8a-n)

The $TiCl_4$-mediated formal [3+3] cyclocondensation of **7a-e** with 1,3-bis(silyloxy)-1,3-dienes **3a-f**, available from the corresponding 1,3-dicarbonyl compounds in two steps,[8] afforded the triarylmethanes **8a-n** (Scheme 3, Table 2).



Scheme 3. Synthesis of **8a-n**, Conditions: *i*): **7a-e** (1.0 equiv.), **3a-f** (1.1 equiv.), $TiCl_4$, CH_2Cl_2, -78 -20 ^oC, 12 h.

The formation of **8a-n** can be explained by the mechanism depicted in Figure 2. The yields depended on the type of substrate employed. The best yields were obtained for those products derived from diene **3a** (prepared from benzyl acetoacetate) (Scheme 3, Table 2). The yields of triarylmethanes **8a-n** were similar to the yields of mono-silyl enol ethers **7a-e** (comparing the same type of diene and aryl group R^4). The aryl groups seem to have no major influence on

the yield. During the optimization, it proved to be important to carry out the reactions in a highly concentrated solution.

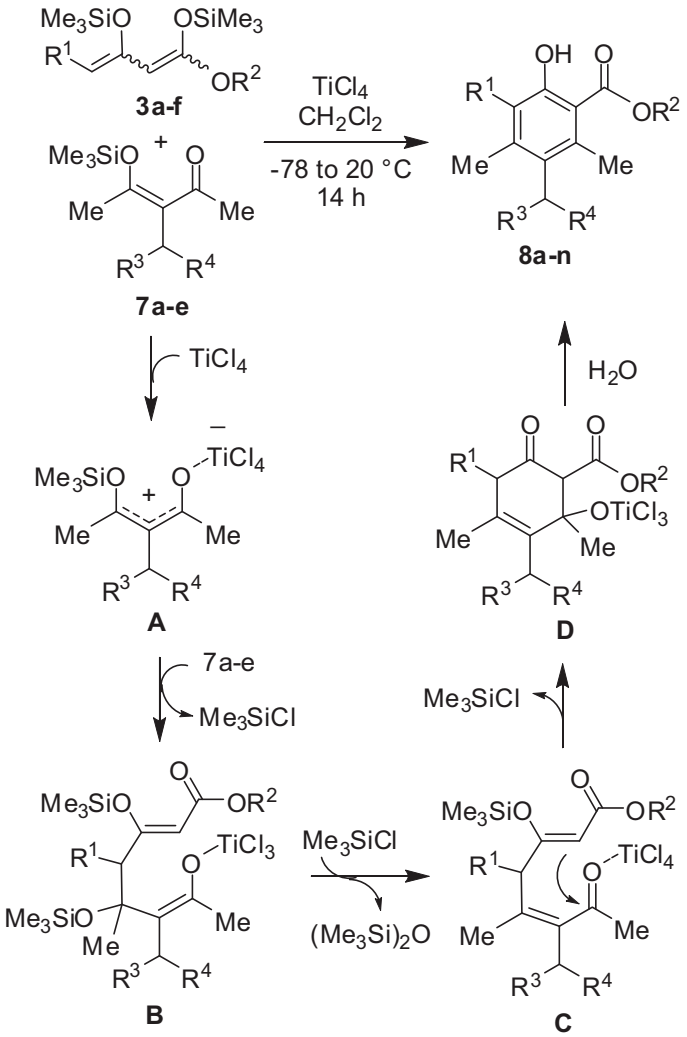


Figure 2. Possible mechanism of the formation of **8a-n**

Table 2. Synthesis of di- and triarylmethanes **8a-n**

7	3	8	R^3	R^4	R^1	R^2	% (**8**)[a]
a	**a**	**a**	Ph	Ph	H	$PhCH_2$	65
a	**b**	**b**	Ph	Ph	*n*Dec	Me	57
b	**a**	**c**	4-FC_6H_4	4-FC_6H_4	H	$PhCH_2$	68
b	**c**	**d**	4-FC_6H_4	4-FC_6H_4	Me	Et	39
b	**d**	**e**	4-FC_6H_4	4-FC_6H_4	Et	Me	41
b	**e**	**f**	4-FC_6H_4	4-FC_6H_4	*n*Bu	Me	53
b	**f**	**g**	4-FC_6H_4	4-FC_6H_4	*n*Non	Me	53
b	**b**	**h**	4-FC_6H_4	4-FC_6H_4	*n*Dec	Me	55
c	**a**	**i**	4-ClC_6H_4	4-ClC_6H_4	H	$PhCH_2$	69
c	**c**	**j**	4-ClC_6H_4	4-ClC_6H_4	Me	Et	43
c	**d**	**k**	4-ClC_6H_4	4-ClC_6H_4	Et	Me	42
c	**b**	**l**	4-ClC_6H_4	4-ClC_6H_4	*n*Dec	Me	57
d	**a**	**m**	Me	4-BrC_6H_4	H	$PhCH_2$	72
e	**e**	**n**	Me	4-(MeO)C_6H_4	Et	Me	47

[a] Isolated yields

The structures of **8a-n** were established by spectroscopic methods. The structures of **8d** and **8m** were independently confirmed by X-ray crystal structure analyses (Figures 3,4). Triarylmethane **8d** adopts a propeller-type structure, due to steric interaction of the aryl with the methyl groups.

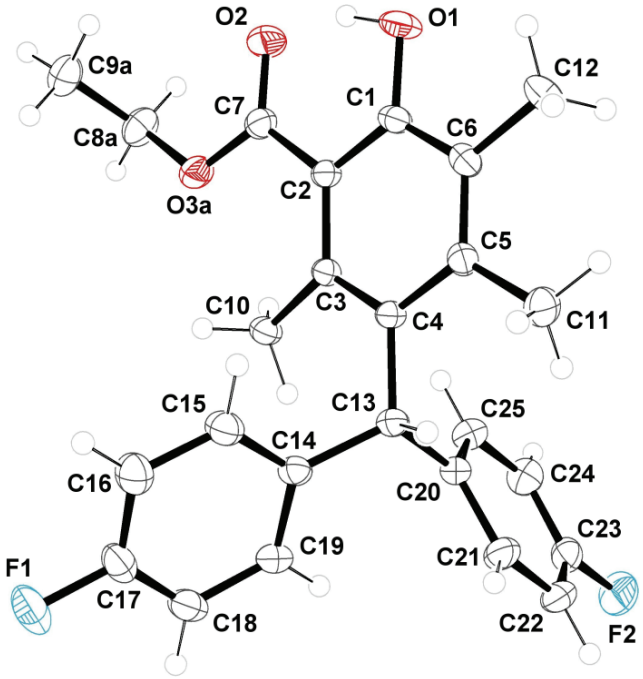


Figure 3. Ortetp plot of **8d** (50 % probability level)

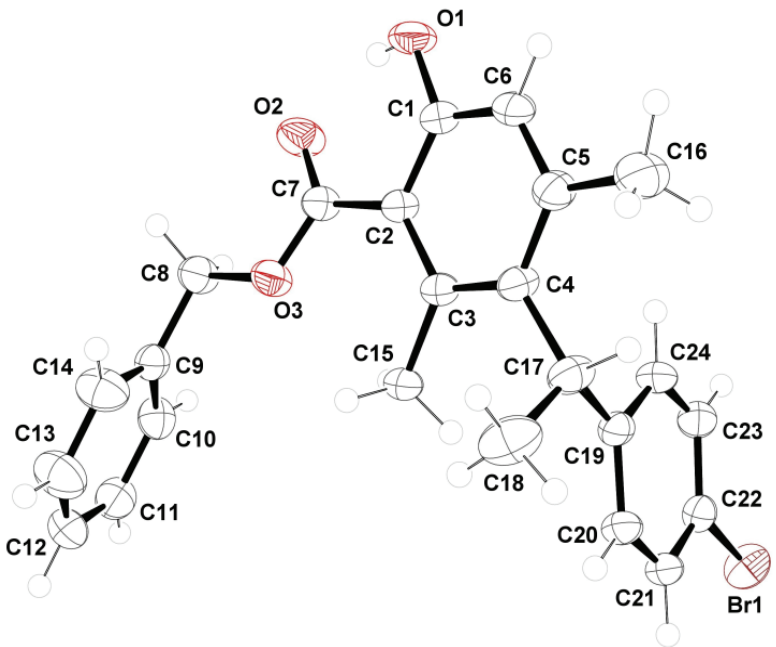


Figure 4. Ortetp plot of **8m** (50 % probability level)

1.3 Conclusions

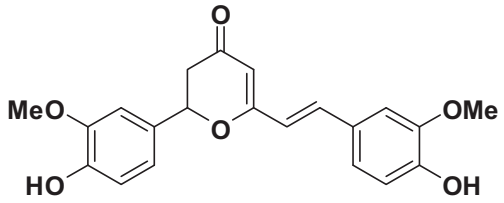
In conclusion, I have synthesized a variety of functionalized and sterically encumbered triarylmethanes by combination of $FeCl_3$-catalyzed benzylations of 1, 3-diketones and formal [3+3] cyclocondensation reactions. The products prepared and discussed in this chapter are not readily accessible by other available methods.

2 Cyclization *versus* Elimination Reactions of 5-Aryl-5-hydroxy-1,3-diones. One-pot Synthesis of 6-Aryl-2,3-dihydro-4*H*-pyran-4-ones

2.1 Introduction

2,3-Dihydro-4*H*-pyran-4-ones are of considerable pharmacological relevance and occur in a variety of natural products (e. g. curcumin, Figure 5).[15] They have been prepared by hetero-Diels–Alder reaction of electron-rich dienes with aldehydes.[16-18] Catalytic variants have also been reported (using chiral Lewis acids or bases).[19] Other syntheses rely on reactions of β-hydroxyenones[20] and β-ethoxy-α,β-unsaturated lactones.[21] In addition, the LDA-mediated reaction of 3-methoxy-2-en-1-ones with aldehydes along with acid-mediated cyclization has been reported.[22] Lithiated dithianes have also been reacted with epoxides to give the desired products.[23]

In Peter Langer group, which have discovered the synthesis of diverse number of compounds by [3+3] cyclocondensation strategy by using Lewis acid $TiCl_4$-mediated as a catalyst to form highly substituted compounds by the treatment of masked dianions[24] (1,3-Bis-Silyl Enol Ethers) with mono-silyl enol Ethers. Due to this detailed study, The reaction of 6-aryl-2,3-dihydro-4*H*-pyran-4-one with 1,3-silyloxy-1,3-butadiene by using $TiCl_4$-mediated resulted in cleavage of pyranones moiety and the formation of highly functionalized benzene derivatives.



Curcumin

Figure 5. Structure of curcumin

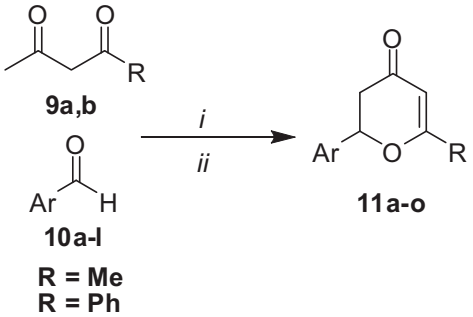
1,3-Dicarbonyl dianions have been reacted with aldehydes to give 5-hydroxy-1,3-dicarbonyl compounds which undergo HCl/MeOH-mediated dehydration or transformation into 2,3-dihydro-4*H*-pyran-4-ones. Importantly, the natural product stegobinone has been prepared using this methodology.[25] 6-Alkyl-2,3-dihydro-4*H*-pyran-4-ones are available from 5-hydroxy-1,3-diketones by action of *para*-toluenesulfonic acid (*p*-TsOH, CH_2Cl_2, 24 h, reflux, Dean-Stark trap, 3Å MS).[26] However, this method is limited to 6-*alkyl*-2,3-dihydro-4*H*-pyran-

4-ones. Dehydration (elimination of water) was observed in case of aromatic substrates. In fact, the reaction of *p*-TsOH with 6-hydroxy-6-phenyl-hexane-2,4-dione, prepared by condensation of the dianion of acetylacetone with benzaldehyde, has been reported to give *(E)*-6-phenylhex-5-ene-2,4-dione and not the desired pyran-4-one (Scheme 2).[27] The facile formation of *(E)*-6-phenylhex-5-ene-2,4-dione might be a result of the conjugation of the double bond with the aryl group. Denmark et al. earlier reported the TFA-mediated transformation of 6-hydroxy-6-phenyl-hexane-2,4-dione into pyran-4-one (0.001 equiv. of TFA in CH_2Cl_2, 0 °C). Recently, the results of my efforts reported in this chapter have been published.[28]

2.2 Results and Discussions

Based on the initial work of my colleague Rasheed Ahmad, who established the methodology in the Langer group (Rasheed Ahmad, Ph.D thesis, 2009, University of Rostock), I extended the scope of this methodology by using different types of masked dianions of β-diketones with LDA mediated and then treated with different types of aldhyde to get an intermediate such as 5-Aryl-5-hydroxy-1,3-dione which is then work-up with hydrochloric acid (10%) to get different substituted pyranones in good yields.

The reaction of the dianions of acetylacetone **9a** and benzoylacetone **9b** with aldehydes **10a-l** afforded the 6-aryl-2,3-dihydro-4*H*-pyran-4-ones **11a-o** in very good yields (Scheme 4, Table 3). The structures of all products were established by spectroscopic methods. The structures of **11i** and **11m** were independently confirmed by X-ray crystal structure analysis (Figures 6 and 7).



Scheme 4. Synthesis of **11a-o**. Conditions: *i)* **1**) LDA (2.5 equiv), THF, 0 °C, 1 h; **2**) –78 °C, **9a,b,** 1h; **3**) **10a-l**, –78 → 20 °C, 12 h; *ii)* addition of HCl (10%), 15 min, 20 °C, then extraction (EtOAc).

Table 3. Synthesis of **11a-o**

9	**10**	**11**	**R**	**Ar**	**%(11)**[a]
a	**a**	**a**	Me	2-ClC_6H_4	65
a	**b**	**b**	Me	3-ClC_6H_4	70
a	**c**	**c**	Me	4-ClC_6H_4	76
a	**d**	**d**	Me	3-MeC_6H_4	76
a	**e**	**e**	Me	2,3-$(MeO)_2C_6H_4$	73
a	**f**	**f**	Me	3-$(HO)C_6H_4$	67
a	**g**	**g**	Me	4-$(NO_2)C_6H_4$	67
a	**h**	**h**	Me	2-Thienyl	82
b	**i**	**i**	Ph	C_6H_5	78
b	**a**	**j**	Ph	2-ClC_6H_4	62
b	**c**	**k**	Ph	4-ClC_6H_4	66
b	**j**	**l**	Ph	2,4-$(OMe)_2C_6H_4$	61
b	**i**	**m**	Ph	3-BrC_6H_4	71
b	**k**	**n**	Ph	3-$(NO_2)C_6H_4$	68
b	**l**	**o**	Ph	4-$(NO_2)C_6H_4$	67

[a] Isolated yields

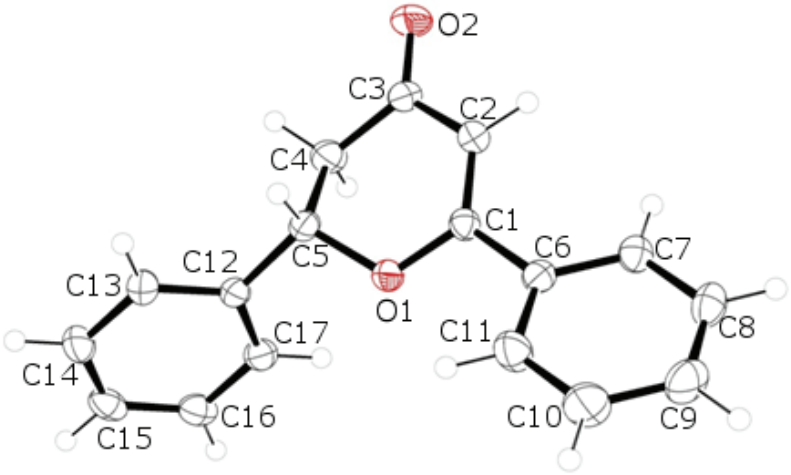


Figure 6. Ortep plot of **11i** (50% probability level)

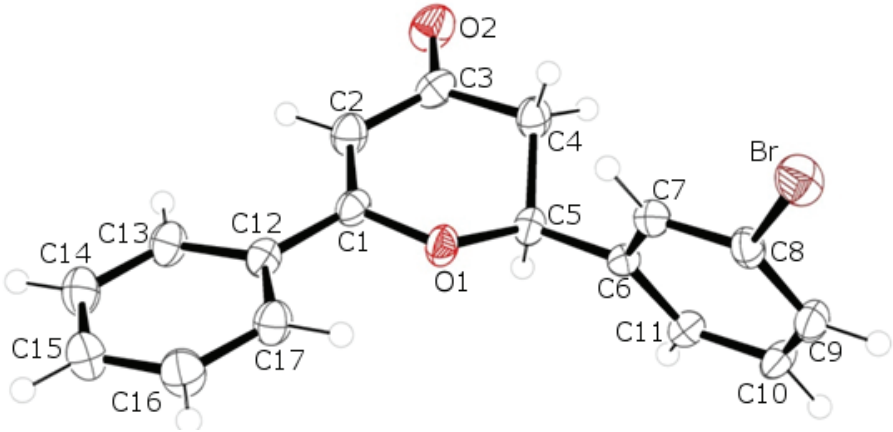
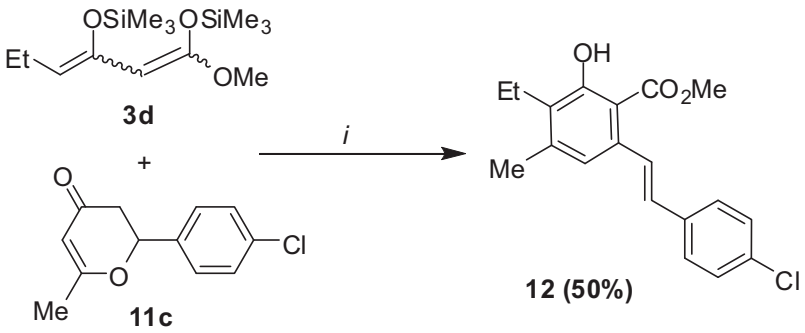


Figure 7. Ortep plot of **11m** (50% probability level)

The reaction of 2-(4-chlorophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one **(11c)** with 1,3-bis(trimethylsilyloxy)-1,3-diene **3d** resulted in the formation of (*E*)-methyl 6-(4-chlorostyryl)-3-ethyl-2-hydroxy-4-methylbenzoate **12** (Scheme 5, Figure 8). The reaction proceeded in good yield and with very good regioselectivity. Its formation can be explained by condensation, pyranone ring opening and following recyclization and aromatization. Unfortunately, the scope could not be extended to other dienes.

The structure **12** was independently confirmed by X-ray crystal structure (Figure 8).



Scheme 5. Synthesis of **12**, Conditions: *i*): **11c** (1.0 equiv.), **3d** (1.1 equiv.), $TiCl_4$ (1.1 equiv.), CH_2Cl_2, -78 -20 ^oC, 12 h.

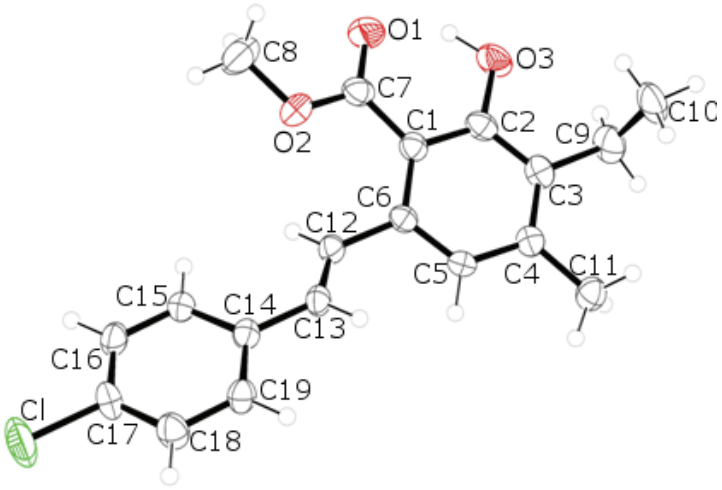


Figure 8. Ortep plot of **12** (50% probability level)

2.3 Conclusion

In conclusion, I have developed a convenient synthesis 6-aryl-2,3-dihydro-4*H*-pyran-4-ones by reaction of the dianion of pentane-2,4-dione and 1-phenylbutane-1,3-dione with aldehydes and subsequent addition of hydrochloric acid. The reaction of the dianion of acetylacetone with benzaldehydes gave the corresponding 2-aryl-2,3-dihydro-6-methyl-4*H*-pyran-4-ones. The $TiCl_4$-mediated cyclization of a 6-aryl-2,3-dihydro-4*H*-pyran-4-one with 1,3-silyloxy-1,3-butadiene resulted in ring opening of the pyranone moiety and formation of a highly functionalized benzene derivative. All reactions proceeded in very good yields and with very good regioselectivity.

3. Synthesis of Fluorinated 2,3-Dihydro-4*H*-pyran-4-ones by Cyclocondensation of 1,3-Dicarbonyl Dianions with Aldehydes

3.1. Introduction

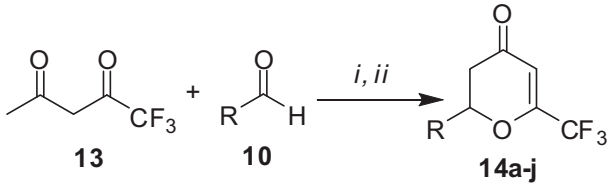
Fluorinated compounds are relevant in medicinal and agricultural chemistry as they show very good bioavailability and metabolic stability[29]. Examples of important fluorinated drugs include 5-fluorouracil (antineoplastic activity), ciprofloxacin and flurithromycin (antimicrobial activity), fluoxetine (prozac, antidepressant activity), and faslodex (antitumor activity), efavirenz (antiviral activity).[30] Organofluorine molecules are also used as ligands[31] and as organocatalysts.[32]. The trifluoromethyl group is of great importance in this context. The high electron-withdrawing effect of the CF_3 group, compared to the methyl group, results in a great difference in the physical properties. This effect plays an important role in drug–receptor interactions. The lipophilicity of CF_3-substituted molecules is often higher than the lipophilicity of their methyl-substituted analogues, which often results in an improvement of their in vivo transport. Unwanted metabolic pathways are often avoided, due to the high chemical and biological stability of the CF_3 group. Therefore, CF_3-substituted arenes and heterocycles play an increasingly important role in drug discovery. Trifluoromethyl- and perfluoroalkyl-substituted molecules show an excellent solubility in fluorophilic solvents. Therefore, CF_3-substituted molecules have been used as ligands[31] in catalytic processes in fluorous biphasic systems and supercritical carbon dioxide. It is worth to be mentioned that CF_3-substituted arenes are present in many organocatalysts [32].

I have synthesized for the first time, fluorinated 2,3-dihydropyran-4-ones by reaction of (either) the dianion of 1,1,1-trifluoro-pentane-2,4-dione with various aldehydes and (or the dianion of) acetylacetone with different fluorinated aldehydes.

3.2 Results and Discussion

The reaction of the dianion of commercially available 1,1,1-trifluoro-pentane-2,4-dione **13** with aldehydes **10** and subsequent addition of hydrochloric acid (stirring for 15 min, then aqueous work-up) afforded the 2,3-dihydro-6-trifluoromethyl-pyran-4-ones **14a-j** in good yields (Scheme 6, Table 4). The formation of the products can be explained as dicussed in Chapter 2. Aromatic, heterocyclic and aliphatic aldehydes could be successfully employed.

The yields of products derived from electron-poor aromatic aldehydes are lower than the yields of products derived from electron-rich aromatic aldehydes and from aliphatic aldehydes.



Scheme 6. Synthesis of **14a-j**. Conditions: *i)* **1**) LDA (2.5 equiv), THF, 0 °C, 1 h; **2**) –78 °C, 1 h; **3**) **2a-l** , –78 → 20 °C, 12 h; *ii)* HCl (10%), 15 min, 20 °C; 2) extraction (EtOAc).

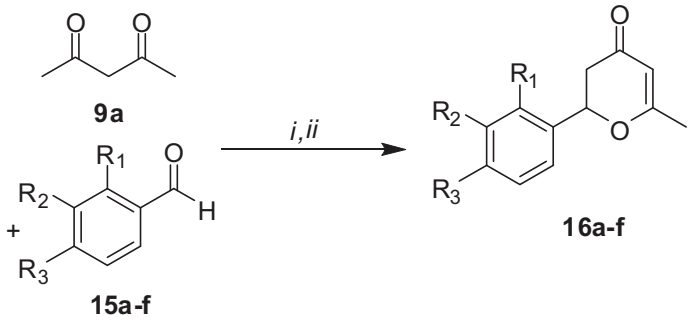
Table 4. Synthesis of **14a-j**

13	**10**	**14**	**R**	% (**14**)[a]
a	**i**	**a**	C_6H_5	80
a	**a**	**b**	2-ClC_6H_4	62
a	**c**	**c**	4-ClC_6H_4	72
a	**k**	**d**	3-$(NO_2)C_6H_4$	63
a	**l**	**e**	4-$(NO_2)C_6H_4$	60
a	**m**	**f**	4-PhC_6H_4	81
a	**h**	**g**	2-Thienyl	71
a	**n**	**h**	*n*-Hep	78
a	**o**	**i**	*n*-Oct	79
a	**p**	**j**	*n*-Non	83

[a] Isolated yields

The reaction of the dianion of acetylacetone **9a** with the fluorinated benzaldehydes **15a-f** gave the 2-aryl-2,3-dihydro-6-methyl-pyran-4-ones **16a-f** (Scheme 7, Table 5). Fluoro substituents

and trifluoromethyl groups at all positions of the phenyl ring were tolerated and the products were isolated in good yields.



Scheme 7. Synthesis of **16a-f**. Conditions: *i)* **1**) LDA (2.5 equiv), THF, 0 °C, 1 h; **2**) –78 °C, 4, 1 h; **3**) **15a-f** , –78 → 20 °C, 12 h; *ii)*: HCl (10%), 15 min, 20 °C, 2) extraction (EtOAc)

Table 5. Synthesis of **18a-f**

15,16	**R^1**	**R^2**	**R^3**	% (**16**)[a]
a	CF_3	H	H	73
b	Cl	CF_3	H	71
c	Cl	H	CF_3	75
d	F	H	H	67
e	H	F	H	72
f	H	H	F	78

[a] Isolated yields

The structures of **16c** was independently confirmed by X-ray crystal structure analysis (Figure 9).

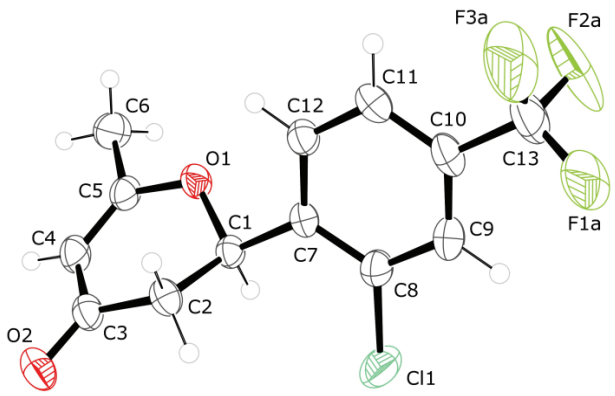


Figure 9. Ortep plot of **16c** (50% probability level)

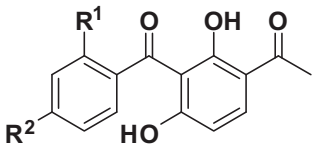
3.3 Conclusion

In conclusion, I have discussed the regioselective synthesis of fluorinated 2,3-dihydro-6-trifluoromethyl-pyran-4-ones by reaction of the dianion of 1,1,1-trifluoro-pentane-2,4-dione with aldehydes and subsequent addition of hydrochloric acid. The reaction of the dianion of acetylacetone with fluorinated benzaldehydes gave the corresponding fluorinated 2-aryl-2,3-dihydro-6-methyl-pyran-4-ones.

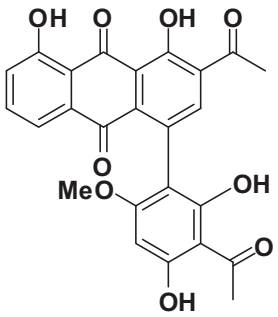
4 Synthesis of 2,4-Diarylbenzophenones by Site-Selective Suzuki-Miyaura Reactions of 2,4-Bis(trifluoromethylsulfonyloxy)benzophenone

4.1 Introduction

Sterically encumbered and functionalized benzophenones are of considerable pharmacological relevance and are present in various natural products.[33] Examples include cynandione A (Figure 10).



Cynandione A



Knipholone

Figure 10. Structure of cynandion A and knipholone

Also, aryl-substituted benzophenones have great pharmacological significance. Biological properties include, for example, cytotoxic and antibacterial activity,[34] inhibition of various enzymes,[35] and activity as selectin antagonists.[36] Structurally associated benzoylfluorenones are also important in this context.[37] knipholone has the center of 4-Arylbenzophenone in the structures of anthraquinones and tetracyclines.[38] 2-Hydroxy- and 2-aminobenzophenones are of importance in anticancer therapy.[39] Functionalized benzophenones are also important as UV-filters (e. g., suncremes) and photosensitizers.[40]

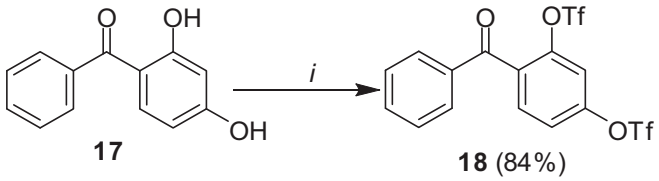
A classic approach to benzophenones relies on the Friedel-Crafts acylation.[39,41] These acylations of highly substituted derivatives not always proceed with excellent regioselectivity. Benzophenones are obtainable also by reaction of organometallic reagents with aldehydes and subsequent oxidation.

Regioselective palladium-catalyzed cross-coupling reactions are of current interest in organic chemistry.[42] Recently, the Langer group reported the synthesis of 3,4-diarylbenzophenones based on site-selective Suzuki-Miyaura cross-coupling reactions of bis(triflates) of 3,4-dihydroxybenzophenones[43]

I have developed the first regioselective palladium(0)-catalyzed cross-coupling reactions of the bis(triflate) of 2,4-dihydroxybenzophenone. The regioselective Suzuki-Miyaura and Sonogashira reactions of 2,4-bis(trifluoromethylsulfonyloxy)benzophenone and optimization of corresponding reaction conditions are described. Reaction conditions and methodology discussed in this chapter provided a straightforward way to a variety of alkynyl- and aryl substituted benzophenones, which other methods did not provide readily.

4.2 Results and Disscussion

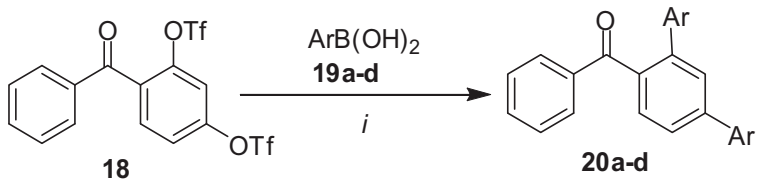
The reaction of 2,4-dihydroxybenzophenone **17** with trifluoromethanesulfonic anhydride by using pyridine as a weak base in CH_2Cl_2 as a solvent at -78 °C, 4h, resulted the formation of 2,4-bis(trifluoromethylsulfonyloxy)benzophenone **18** in 84% yield (Scheme 8).



Scheme 8. Synthesis of **18**. *Reagents and conditions: i*) CH_2Cl_2, **17** (1.0 equiv), -78°C, pyridine (4.0 equiv), Tf_2O (2.4 equiv), -78 →0°C, 4 h.

The Suzuki-Miyaura reaction of **18** with aryl boronic acids **19a-d** (2.2 equiv.) afforded the formation of 2,4-diarylbenzophenones **20a-d** in good yields (Scheme 9, Table 6). Optimization reaction using $Pd(PPh_3)_2Cl_2$ (6 mol-%) with 2.2 equiv. of arylboronic acid did not work satisfactorily in terms of yields.

However, when $Pd(PPh_3)_4$ (6 mol-%) was used as a catalyst with (2.2 equiv.) of arylboronic acid in 1,4-dioxane (reflux, 4 h) using the inorganic base K_3PO_4 as the base, the yield was good to excellent (Scheme 9, Table 6). The structures of all products were established by spectroscopic methods.



Scheme 9. Synthesis of **20a-d**. *Reagents and conditions: i*) **18** (1.0 equiv.), **19a-d** (2.6 equiv.), K_3PO_4 (3.0 equiv.), $Pd(PPh_3)_4$ (6 mol-%), 1,4-dioxane (5 mL per 1 mmol of **2**), 110 °C, 4 h

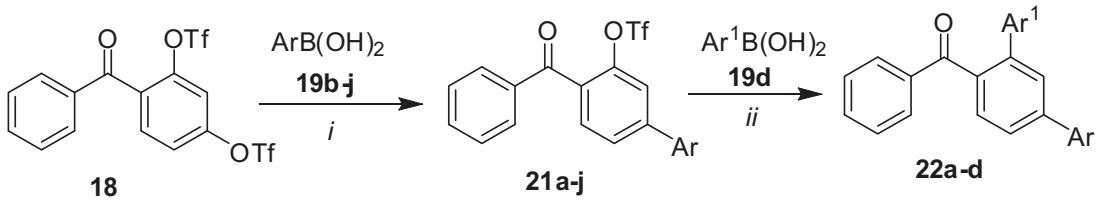
Table 6. Synthesis of **20a-d**

19,20	**Ar**	**% (20)** [a]
a	C_6H_5	82
b	4-MeC_6H_4	84
c	3-ClC_6H_4	75
d	4-$(OMe)C_6H_4$	71

[a] Yields of isolated products

The Suzuki-Miyaura reaction of **18** with (1.1 equiv.) of boronic acids **19b-c,e-j** in the presence of $Pd(PPh_3)_4$ (3 mol-%) as a catalyst, proceeded with very good regioselectivity (first attack at carbon atom C-4) to give the monoaryl benzophenones **21a-i** (Scheme 10, Table 7). In some cases, a small amount of bis-coupled products could be detected in the crude product (by ^1H NMR and GC-MS). The pure mono-coupled products were obtained after chromatographic purification.

The reaction of **21a,e-f** with 4-methoxyphenyl boronic acid (**19d**, 1.1 equiv.) gave the aryl substituted benzophenones **22a-d** which have two different aryl substituents at the positions 2 and 4 (Scheme 10, Table 7).

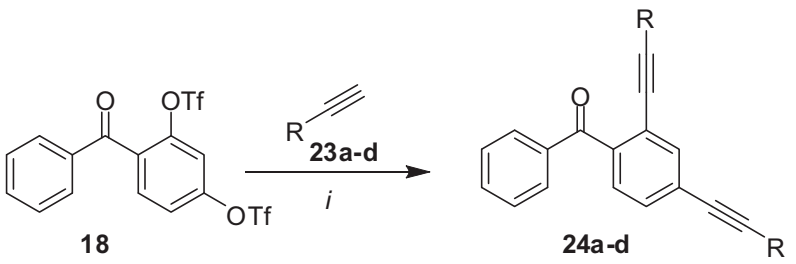


Scheme 10. Synthesis of **21a-i** and **22a-d**. *Reagents and conditions: i)* **18** (1.0 equiv), **19b-c,e-j** (1.1 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol %), 1,4-dioxane, 90 °C, 4 h; *ii)* **21a,e-f** (1.0 equiv), **19d** (1.3 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol%), 1,4-dioxane, 90 °C, 4 h.

Table 7. Synthesis of **21a-i, 22a-d**

19	**Ar**	**21**	%(**21**)[a]	**Ar[1]**	**22**	%(**22**)[a]
b, d	4-MeC_6H_5	**a**	73	4-$(MeO)C_6H_5$	**a**	70
e	4-EtC_6H_5	**b**	75	-	**-**	-
f	3,4-$Me_2C_6H_5$	**c**	68	-	**-**	-
g	3,5-$Me_2C_6H_5$	**d**	67	-	**-**	-
h, d	4-*t*BuC_6H_5	**e**	76	4-$(MeO)C_6H_5$	**e**	71
c, d	3-ClC_6H_5	**f**	65	4-$(MeO)C_6H_5$	**f**	62
j	3-$(MeO)C_6H_5$	**g**	64	-	**-**	-
d	4-$(MeO)C_6H_5$	**h**	63	-	**-**	-
k	3,4,5-$(MeO)_3C_6H_5$	**i**	58	-	**-**	-

[a] Yields of isolated products



Scheme 11. Synthesis of **24a-d.** *Reagents and conditions: i*) **18** (1.0 equiv), **23a-d** (2.2 equiv.), dry CuI (10%), $Pd(PPh_3)_2Cl_2$ (6-mol%), Et_3N (1.25 equiv), DMF, 90 °C, 4 h.

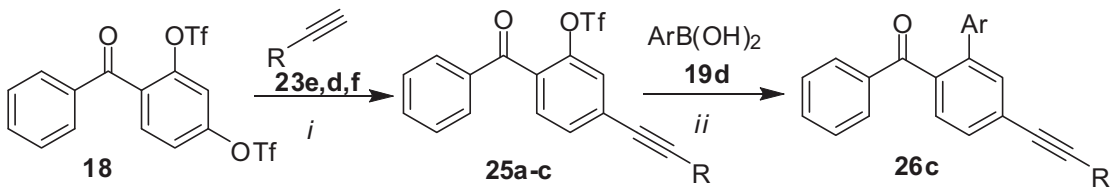
The double Sonogashira reactions of 2,4-bis(trifluoromethylsulfonyloxy)benzophenone (**18**), were accomplished using the catalyst $Pd(PPh_3)_2Cl_2$ (6-mol%), the terminal alkynes (2.2 equiv.), CuI (20 mol%), and Bu_4NI (15 mol%) in DMF. All reactions proceed with good yields (Scheme 11, Table 18).

Table 8. Synthesis of **24a-d**

23	**R**	**24**	%(**24**)[a]
a	C_6H_5	**a**	78
b	3-MeC_6H_4	**b**	71
c	4-MeC_6H_4	**c**	75
d	*n*-Oct	**d**	74

[a] Yields of isolated products

To accomplish the regioselective Sonogashira reactions with 2,4-bis(trifluoromethylsulfonyloxy)benzophenone (**18**), I attempted to optimize the reaction conditions by changing reaction temperature, reaction time, base, solvent, and amount of alkynes. The best yields for the mono-Sonogashira reactions were obtained when $Pd(PPh_3)_2Cl_2$ (3-mol%) was the catalyst, when 1.1 equivalents of the terminal alkyne was used and when CuI (10 mol%), Bu_4NI (15 mol%) in DMF were used.



Scheme 12. Synthesis of **25a-c** and **26c.** *Reagents and conditions: i)* **18** (1.0 equiv), **23a-c** (1.1 equiv), dry CuI (10%), $Pd(PPh_3)_2Cl_2$ (3%), Et_3N (1.25 equiv), DMF, 90 °C, 8 h. *ii)* 25c (1.0 equiv), 4-tert-butylphenylboronic acid (1.3 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol%), 1,4-dioxane, 90 °C, 4 h.

Table 9. Synthesis of **25a-c, 26c**

23	**R**	**(25)**	**%(25)**[a]	**19**	**26**	**Ar**	%(**26**)[a]
e	*n*-propyl	**a**	78	-	-	-	-
d	*n*-octyl	**b**	81	-	-	-	-
f	4-(MeO)C_6H_4	**c**	68	**d**	**c**	4-*t*BuC_6H_4	73

[a] Yields of isolated products

The mono-Sonogashira product **25c** was treated with 4-*tert*-butylphenylboronic acid (1.2 equiv), in the presence of K_3PO_4 (1.5 equiv) and $Pd(PPh_3)_4$ (3 mol%) in 1,4-dioxane at temperature 90 °C, to give **26c** in good yield (73%).

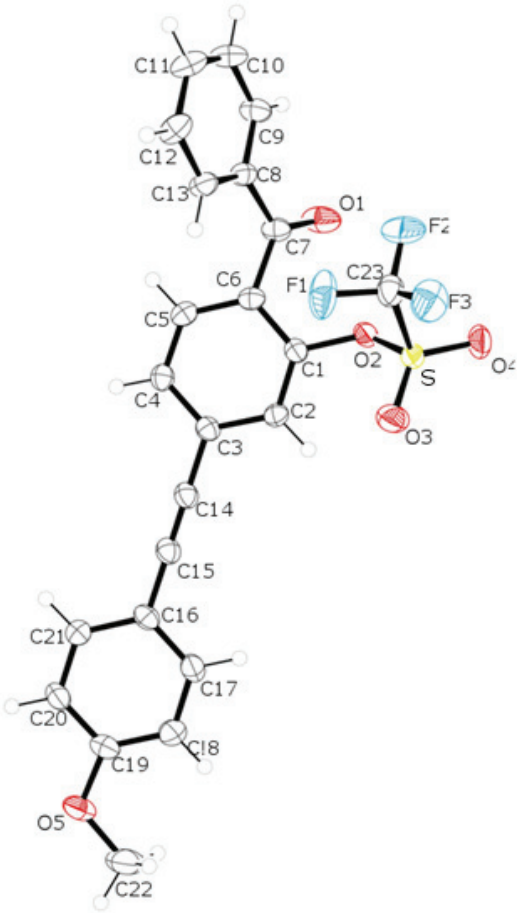


Figure 11. Ortep plot of **25c** (50% probability level)

The structure of **25c** was independently confirmed by X-ray crystal structure

4.3 Conclusion

In conclusion, a versatile and inexpensive optimized reaction conditions for the synthesis of functionalized benzophenones by Suzuki-Miyaura reactions and Sonogashira reactions of the bis(triflate) of 2,4-dihydroxybenzophenone. The reaction with one equivalent of arylboronic acids resulted in a regioselective attack onto carbon atom C-4. Furthermore the same strategy was used successfully for Sonogashira which worked well from good to excellent yields. A Combination of Sonogashira and Suzuki reaction was also investigated in good yield.

5 Synthesis of Bis(diaryl)sulfones by Site-Selective Suzuki-Miyaura and Sonogashira Cross-Coupling Reactions of 2,4′-Bis(trifluoromethylsulfonyloxy)diphenylsulfone

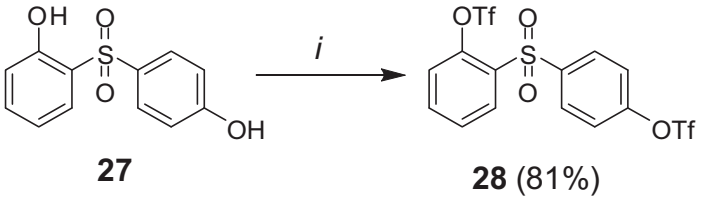
5.1 Introduction

Diarylsulfones are of considerable pharmacological importance and occur in many natural products.[44] They have been prepared by oxidation of diaryl sulfides[45] and by Friedel-Crafts-type acylations.[46] These methods suffer from low yields, harsh reaction conditions and low regioselectivities. Diaryl sulfones have also been prepared by CuI/proline-mediated reaction of aryl iodides with sodium benzenesulfinate and by Suzuki reactions of 4-methoxyphenylboronic acid with benzenesulfonic acid chloride.[47] In addition, $Cu(OAc)_2$-catalyzed reactions[48] of sodium benzenesulfinate with 4-methoxyphenylboronic acid have been reported.[49] The Langer group reported the synthesis of diaryl sulfones by cyclizations of sulfone-containing building blocks.[50]

5.2 Results and Discussions

The project reported in this chapter was started by my colleague Mr. Asad Ali (Ph.D thesis, submitted, University of Rostock, 2010). He studied the synthesis of bis-triflate **28** and its Suzuki reactions with 2 equivalents of boronic acids resulting in a double-coupling. I have studied in my thesis regioselective transformations of **28**. Recently, first results have been published.[51]

The reaction of 2,4'-sulfonyldiphenol **27** with trifluoromethanesulfonic anhydride by using pyridine as a weak base in CH_2Cl_2 as a solvent at -78 °C, 4h, resulted the formation of 2,4-bis(trifluoromethylsulfonyloxy)benzophenone **28** in 81% yield (Scheme 13).



27 **28** (81%)

Scheme 13. Synthesis of **28**. *Reagents and conditions: i)* CH_2Cl_2, **27** (1.0 equiv), -78 °C, pyridine (4.0 equiv), Tf_2O (2.4 equiv), -78 → 0 °C, 4 h.

The Suzuki reaction of bis(trifluoromethylsulfonyloxy)diphenylsulfone **28** with arylboronic acids **19a-d** (1.1 equiv.) and (2.2 equiv.) afforded the mono- and di-substituted products, respectively. For electron rich and also for electron deficient arylboronic acids, the monoarylated products **29a-d** could be isolated in good yields (Scheme 14 and Table 10). The best yields were obtained when the reactions were carried out by using $Pd(PPh_3)_4$ (6 mol %) as a catalyst and the inorganic base K_3PO_4 in dioxane. The employment of other catalysts, such as $Pd(OAc)_2$/XPhos, $Pd(OAc)_2$/SPhos resulted in a decreased yield.

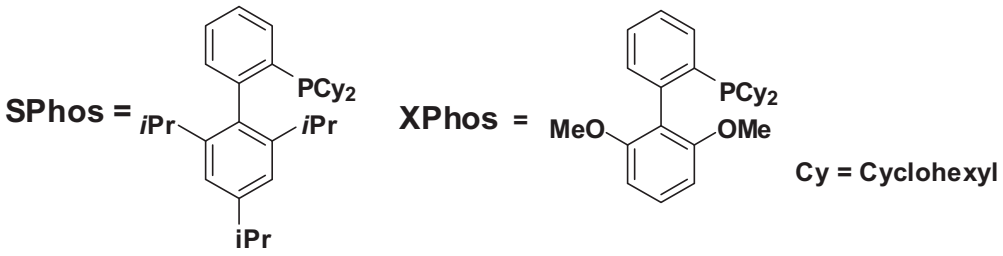
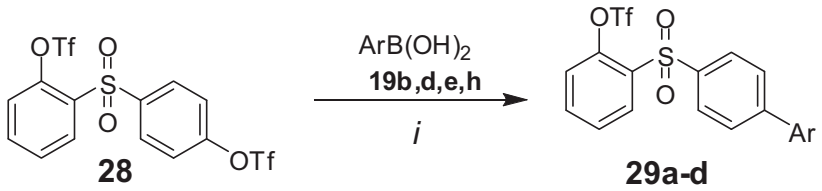


Figure 12: Buchwald ligands

In conclusion, the use of $Pd(PPh_3)_4$ (6 mol-%) as the catalyst for mono- and cross-Suzuki reactions of bis(trifluoromethylsulfonyloxy)diphenylsulfone using the inorganic base K_3PO_4 are given in (Scheme 14 and Table 10).



Scheme 14. Synthesis of **29a-d**. *Reagents and conditions: i*) **28** (1.0 equiv), **19b,d,e,h** (1.1 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol-%), 1,4-dioxane (5 mL per 1 mmol of **28**), 110 °C, 4 h.

Table 10. Synthesis of **29a-d**

19	**29**	**Ar**	% (**29**)[a]
b	**a**	4-MeC_6H_4	77
e	**b**	4-EtC_6H_4	81
h	**c**	4-*t*BuC_6H_4	83
d	**d**	4-(MeO)C_6H_4	74

[a] Yields of isolated products

The structures of the products were proved by 2D NMR experiments (NOESY, HMBC).

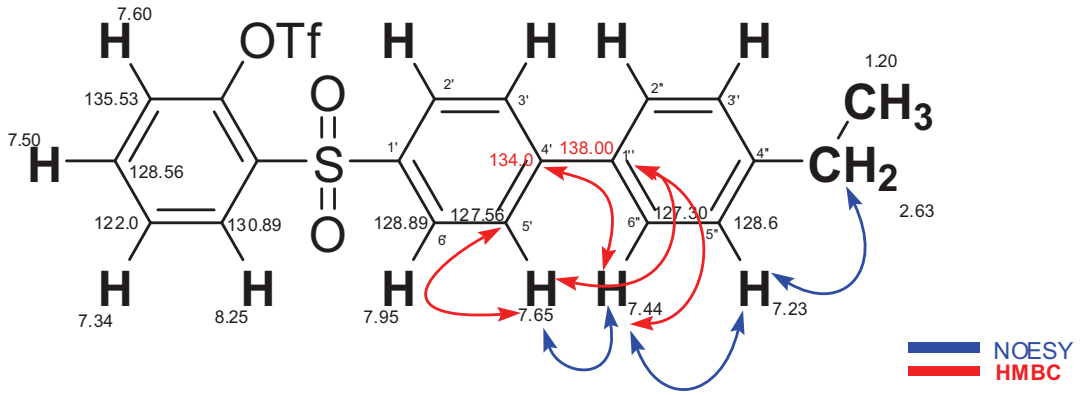
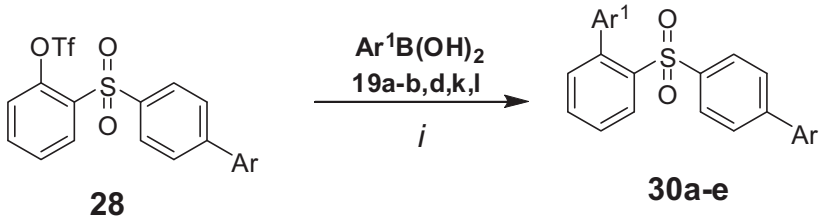


Figure 13: 2D NMR correlations (NOESY and HMBC) of **29b**

The structure of compound **29b** was confirmed by 2D NMR spectroscopy (Figure 13). Assignments of chemical shifts of C and H were done with the help of ^{1}H NMR, HMQC and COSY. The NOESY correlation between CH_2 & H-5″, H-5″ & H-6″ and H-5′ and H-6″ provided the information that the aryl group is connected to carbon C-4′. The structure was further confirmed by the HMBC extensive correlations of H-6″ to C-1″ and H-6″ to C-4′ and from the other ring H-5′ to C-1″. These careful and clear correlations proved unambiguously the connectivity of the first aryl group to C-4′.



Scheme 15. Synthesis of **30a-e**. *Reagents and conditions: i)* **29a,c** (1.0 equiv), **19a-b,d,e,k-l** (1.1 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol-%), 1,4-dioxane, 110 °C, 4 h.

The Suzuki-Miyaura reaction of **29a** and **29c** with aryl boronic acids **19a-b,d-e,k-l** (1.1 equiv.) gave the unsymmetrical 2,4′-bis(aryl)diphenylsulfones **30a-e** containing two different aryl groups (Scheme 15, Table 11).

Table 11. Synthesis of **30a-e**

29	**19**	**Ar^1**	**30**	% (**30**)[a]
a	**a**	C_6H_5	**a**	86
a	**e**	4-EtC_6H_4	**b**	91
a	**d**	4-(MeO)C_6H_4	**c**	73
a	**l**	4-(CF_3)C_6H_4	**d**	81
c	**b**	4-MeC_6H_4	**e**	87

[a] Yields of isolated products

5.3 Conclusions

The Suzuki-Miyaura reaction of the bis(triflate) of 2,4′-bis(hydroxy)diphenylsulfone with two equivalents of aryl boronic acids gave 2,4′-bis(aryl)diphenylsulfones. The reaction with one equivalent of arylboronic acids resulted in site-selective attack onto carbon atom C-4′. The first attack occured on sterically less hindered position due to electronic reasons.

6 Site-Selective Sonogashira Reactions of 2,4′-Bis (trifluoromethylsulfonyloxy)diphenylsulfone

6.1 Introduction

The discovery of strong pharmacological importance such as antifungal agents[52] and novel powerful antitumor antibiotics[53] has motivated intense interest in the chemistry of enynes[54], which is at the source of biological properties of these substances. The conjugated enynes are also important synthetic intermediates since the conjugated enyne moiety can be with good grace converted into the corresponding enynes system in a regioselective manner [55]. Recently, Takahashi *et al*. described the formation of highly substituted enynes by coupling reaction of alkenylzirconium compounds with alkynyl halides[56]. Gimeno *et al*. reported the stereoselective synthesis of chiral terminal (*E*)-1,3-enynes derived from optically active aldehydes[57]. The synthesis of enynes containing functional groups is also of considerable interest in recent years. The stereoselective synthesis of 1,3-enynylsulfides[58], 1,3-enynylselenides[59], 1,3-enynyltellurides[60], 1,3-enynylsilanes[61], 1,3-enynylstannanes[62] and fluoro or CF_3-substituted 1,3-enynes[63] has previously been described in the literature. However, the synthesis of enynylsulfones has received less attention[64] and enynylsulfones have, to the best of my knowledge, not been reported so far. The transition metal-catalyzed cross-coupling reaction is a highly multipurpose method for carbon–carbon bond formation and has been widely used as synthetic tool[65]. The palladium-catalyzed coupling reaction of alkenyl halides with terminal alkynes (Sonogashira reaction) provides a direct approach to 1,3-enynes.[66] I synthesized mono- and dialkynylated as well as aryl substituted diphenylsulfones with very good site-selectivity

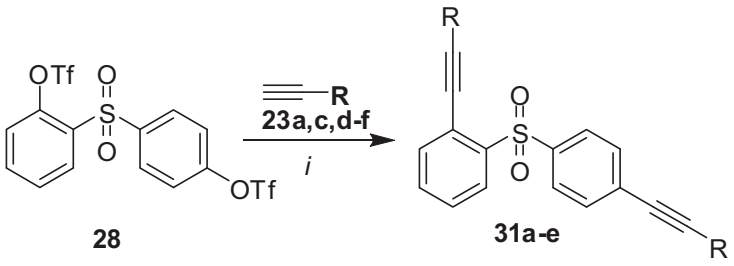
6.2 Results and discussions

Based on the results shown in chapter **5** for Suzuki reactions, I was also interested to see the regioselectivity in Sonogashira reactions.

The Sonogashira reaction of **28** with (2.2 equiv.) of aliphatic and aromatic terminal alkynes **23a,c,d-f** proceeded to the formation of dialkynylated products **31a-e** in good to excellent yields (Scheme 16, Table 12).

The reactions were carried out by using a pressure tube (glass bomb) and a suspension of $Pd(PPh_3)_2Cl_2$ (2.5-5.0 mol%), **30** (258 mg, 0.5 mmol), alkyne (0.50-1.10 mmol), $(Bu)_4NI$ (27

mg, 15 mol%), CuI (10 mol%), and Et_3N (0.62-1.25 mmol) in DMF (5 mL). The reaction mixture was stirred at 60 °C for 2-4 h. The product was purified by flash chromatography and isolated in excellent yield.



Scheme 16. Synthesis of **31a-e**. *Reagents and conditions: i*) 30 (1.0 equiv), **23a,c-f** (2.2 equiv), $(Bu)_4NI$ (15 mol %), CuI (10 mol%), $Pd(PPh_3)_2Cl_2$ (5 mol %), Et_3N (2.5 equiv), DMF, 80 °C, 4 h.

Table 12 Synthesis of **31a-e**

23	**31**	**R**	% (**31**)[a]
a	**a**	C_6H_5	88
c	**b**	4-MeC_6H_4	92
e	**c**	*n*-propyl	85
d	**d**	*n*-pentyl	88
f	**e**	*n*-octyl	90

[a] Yields of isolated products

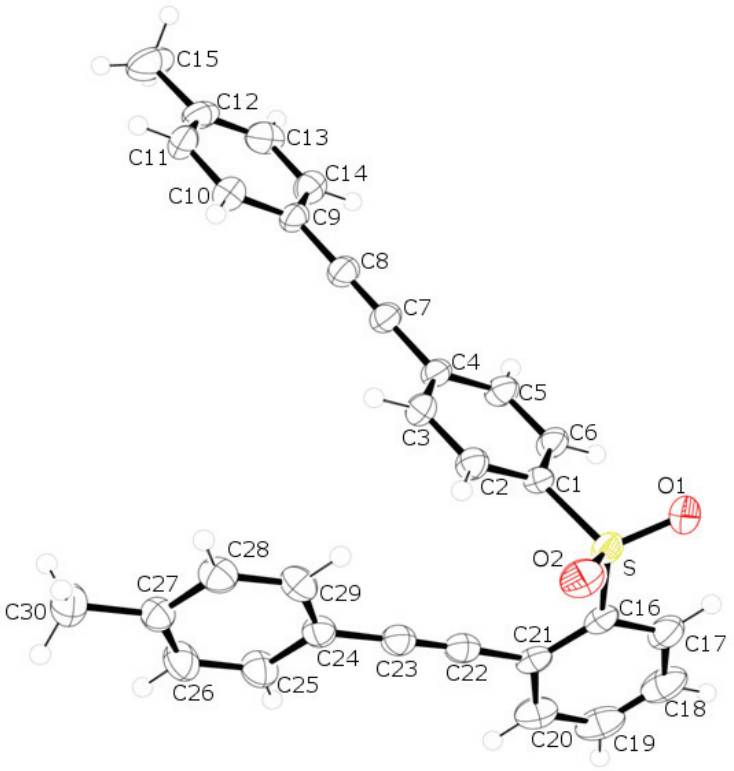


Figure 14. Ortep plot of **31b** (50% probability level)

The structures of **31c** was independently confirmed by X-ray crystal structure (Figure 14).

The Sonogashira-coupling reaction of **28** with alkynes (1.0 equiv.) and $Pd(PPh_3)_2Cl_2$ (2.5 mol-%) resulted in the formation of monoalkynyl substituted diarylsulfones **32a-e** (Scheme 18, Table 13). During the optimization, it proved to be important to use exactly 1.0 equiv. of terminal alkyne and to carry out the reaction at 60 °C (2 h) instead of 80 °C (8 h). Both aliphatic and aromatic terminal acetylenes gave the products which were isolated in good to excellent yields. During optimization, the use of $Pd(PPh_3)_4$ resulted in considerable amount of dimerization of alkynes and regioselectivity was low giving a mixture of products. In case of ligand-free $Pd(OAc)_2$-catalysis, no products were found but all the starting material was recovered. In case of Cu-free reaction conditions, a total decomposition of the starting material was observed. Finally, $Pd(PPh_3)_2Cl_2$ gave fast and selective reactions. A catalyst loading of as low as 3 mol-% for twofold Sonogashira reaction was possible with slight decrease in yield. Both aliphatic and aromatic terminal alkynes were suitable starting materials for this reaction. Mono-alkynyl sulfones were used to prepare alkynyl- and aryl-substituted sulfones as well.

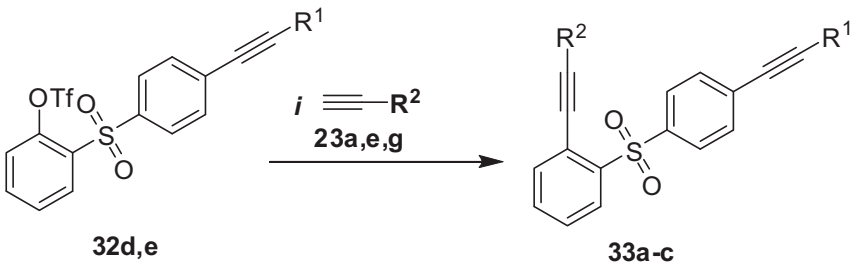
Scheme 17. Synthesis of **32a-e**. *Reagents and conditions: i)* **28** (1.0 equiv), **23a,c-d,f-g** (1.0 equiv), $(Bu)_4NI$ (15 mol %), CuI (10 mol%), $Pd(PPh_3)_2Cl_2$ (2.5 mol %), Et_3N (1.25 equiv), DMF, 60 °C, 1h.

Table 13. Synthesis of **32a-e**

23	**32**	**R**	%(**32**)[a]
a	**a**	3-MeC_6H_4	75
c	**b**	4-MeC_6H_4	83
g	**c**	4-*t*BuC_6H_4	88
d	**d**	$(CH_2)_4C_6H_4$	86
f	**e**	*n*-octyl	91

[a] Yields of isolated products

The cross Sonogashira-coupling reaction of monoalkynyl substituted diaryl sulfones **32d,e** with terminal alkynes (1.0 equiv.), in the presence of $Pd(PPh_3)_2Cl_2$ (2.5 mol-%), CuI (10 mol%), $(Bu)_4NI$ (15 mol %), Et_3N (2.5 equiv) (DMF, 80 °C, 4h), gave products **33a-c** in good yields (83-89%), (Scheme 18, Table 14).



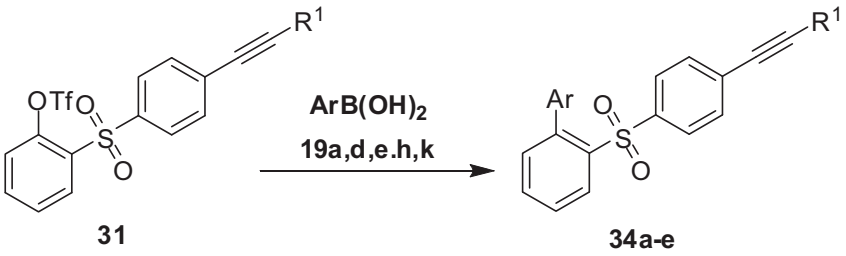
Scheme 18. Synthesis of **33a-c**. *Reagents and conditions: i*) **32** (1.0 equiv), **23a,e,g** (1.0 equiv), $(Bu)_4NI$ (15 mol %), CuI (10 mol%), $Pd(PPh_3)_2Cl_2$ (2.5 mol %), Et_3N (2.50 equiv), DMF, 60 °C, 2 h.

Table 14. Synthesis of **33a-c**

33	**23**	R^2	%(**33**)[a]
a	**e**	$(CH_2)_2CH_3$	87
b	**a**	C_6H_5	83
c	**g**	4-*t*BuC_6H_4	79

[a] Yields of isolated products

The Suzuki-Miyaura reaction of **32b,e** with arylboronic acids **19a,d,e,,h,k**, in the presence of $Pd(PPh_3)_4$ and K_3PO_4, gave us the substituted alkynyl-aryl sulfones **34a-e** (Scheme 19). All these reactions resulted in good yields (80-91%) (Scheme 19, Table 15).



Scheme 19. Synthesis of **34a-e**. *Reagents and conditions: i)* 31 (1.0 equiv), $ArB(OH)_2$ (1.1 equiv), $Pd(PPh_3)_4$ (2.5 mol %), K_3PO_4 (1.5 equiv), Dioxane, 100 °C, 6 h.

Table 15. Synthesis of **34a-e**

19	**31**	**34**	R	Ar	%(**34**)[a]
a	**e**	**a**	$(CH_2)_7CH_3$	C_6H_5	88
e	**e**	**b**	$(CH_2)_7CH_3$	4-EtC_6H_4	91
l	**e**	**c**	$(CH_2)_7CH_3$	4-$(CF_3)C_6H_4$	85
h	**b**	**d**	4-MeC_6H_4	4-*t*BuC_6H_4	91
d	**b**	**e**	4-MeC_6H_4	4-$(MeO)C_6H_4$	80

[a] Yields of isolated products

For 2-(4-(dec-1-ynyl)phenylsulfonyl)-4'-(trifluoromethyl)biphenyl **34c**, the connectivity was established on the basis of 2D NMR. Besides HMQC and COSY, in ^{13}C NMR $J_{C,F}$ coupling constants helped to differentiate the 4-(trifluoromethyl)benzene C and CH atoms. Aliphatic CH_2 (t, δ 2.33) connected to acetylenic quarternary carbon (δ 95.2) showed HMBC correlation with acetylenic C-1 (δ 79.3), phenyl C-4`` (δ 129.2) and CH-3``/5`` (δ 131.4). In aromatic region H-3``/5`` (δ 7.10) showed connectivity to aliphatic $CH_2$ (δ 19.1) and C-4`` (δ 129.1) to show that 1-decyne is connected to C-4``. Furthermore the NOESY correlation of H-6` (δ 7.41) to H-6 verified the connectivity of 4-(trifluoromethyl)benzene to C-1. So by 2D NMR assignments it is recognized explicitly that 1-decyne connectivity is connected to C-4`` and 4-(trifluoromethyl)benzene is linked with C-1 (Figure 15).

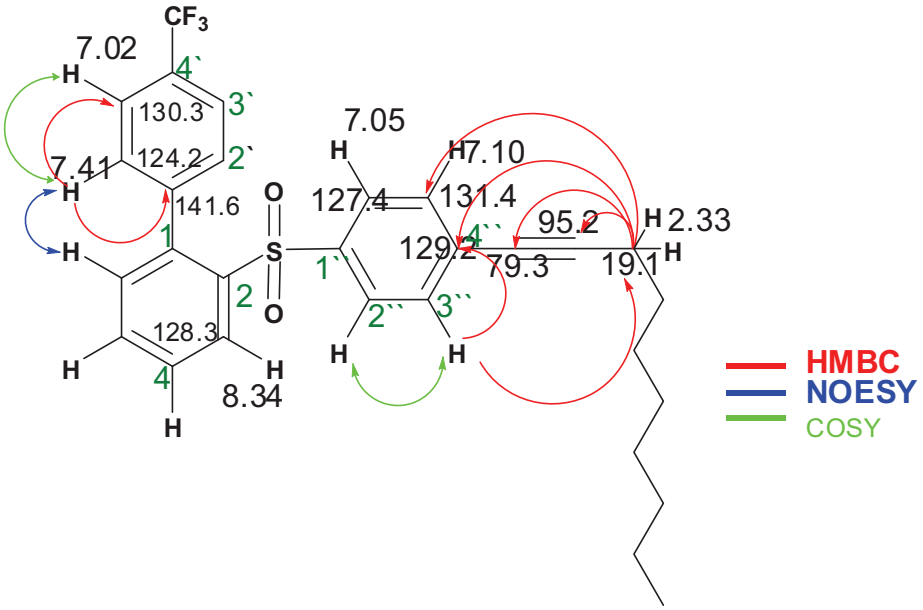


Figure 15: 2D NMR correlations (HMQC and HMBC) of **34c**

6.3 Conclusion

In conclusion, I have developed site-selective Sonogashira reactions of 2-(4-(trifluoromethylsulfonyloxy)diphenylsulfone. As a result, functionalized sulfones were prepared by sequential Sonogashira–Sonogashira and Sonogashira–Suzuki reactions.

7. One-Pot Synthesis of 2,3-Diarylindenones by Site-Selective Suzuki-Miyaura/Sonogashira coupling Reactions Reactions of 2,3-Dibromoindenone

7.1 Introduction

2,3-Diaryl-1*H*-inden-1-ones are of considerable pharmacological relevance.[67] They are available, for example, by intramolecular Friedel-Crafts acylation reactions.[68] 2,3-Diaryl-1*H*-inden-1-ones have also been prepared from dibenzoylmethane[69] and benzophenone derivatives.[70] Recent transition metal-catalyzed syntheses of 2,3-diaryl-1*H*-inden-1-ones include the reaction of 1-methoxy-4-(4'-methoxyphenylethynyl)-benzene with 2-bromobenzaldehyde,[71] and the reaction of diphenyl acetylene with 2-bromophenylboronic acid.[72]

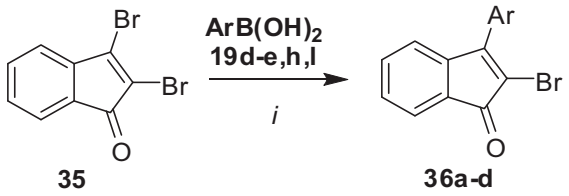
As already mentioned above, a number of site-selective palladium(0)-catalyzed cross-coupling reactions of polyhalogenated heterocycles have been developed. The site-selectivity of these reactions is generally influenced by electronic and steric parameters.[73] We have reported site-selective Suzuki-Miyaura reactions of tetrabrominated thiophene, *N*-methylpyrrole, selenophene, and of other polyhalogenated arenes and hetarenes.[74]

It occurred to us that 2,3-dibromo-1*H*-inden-1-one might be a suitable starting material for such reactions. The reactions of 2,3-dibromo-1*H*-inden-1-one with amines and C-nucleophiles, such as Grignard reagents, ethyl cyanoacetate and ethyl acetoacetate, are already known for a long time.[75] Transition metal-catalyzed cross-coupling reactions of 2,3-dibromo-1*H*-inden-1-one have not been reported so far. In this chapter, I report my results related to Suzuki and Sonogashira reactions of this substrate.

7.2 Results and Discussion

2,3-Dibromo-1*H*-inden-1-one **35** was transformed into 3-aryl-2-bromo-1*H*-inden-1-ones and 2,3-diaryl-1*H*-inden-1-ones in excellent yields, depending of the amount of the introduced boronic acid. The best yields were obtained when the reactions were carried out by using $Pd(PPh_3)_4$ (3 mol%) as catalyst and the inorganic base K_2CO_3 (dioxane, 45 °C, 4 h).

The employment of other catalysts, such as $Pd(PPh_3)_2Cl_2$, $Pd(OAc)_2$/XPhos, $Pd(OAc)_2$/SPhos resulted in a decreased yield and/ or regioselectivity



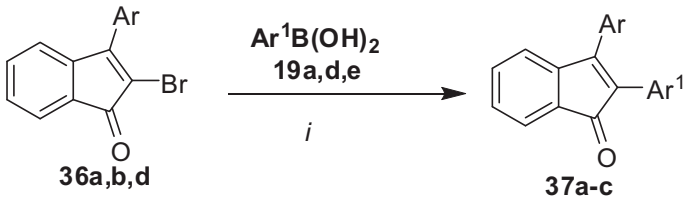
Scheme 20. Synthesis of **36a-c**. *Conditions*: *i)* **35** (1.0 equiv.), **19d-e,h,l** (1.0 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 2M K_2CO_3, dioxane, 45 °C, 4 h.

The S-M reaction of **35** with arylboronic acids **19d,e,h,k** (1.0 equiv.) afforded the 3-aryl-2-bromo-1*H*-inden-1-ones **36a-d** in excellent yields and with very good site-selectivity (Scheme 20, Table 16). The first attack occurred at position **3** of **1** in 2,3-Dibromoindenone. During the optimization it proved to be very important to use exactly 1.0 equiv. of the arylboronic acid and $Pd(PPh_3)_4$ (3 mol-%) as catalyst. The temperature played an important role. A good selectivity was achieved only when the reaction was carried out at 45 °C because the second cross-coupling was slow at this temperature. The formation of a mixture of starting material, mono- and di-substituted products was generally observed when the reaction was carried out at temperatures between 45 and 70 °C. In the case of the highly reactive methoxy-substituted arylboronic acid the temperature had to be further decreased to 40 °C to achieve a good site-selectivity. The reactions were successful for both donor and acceptor substituted arylboronic acids.

Table 16. Synthesis of 3-aryl-2-bromoinden-1-ones **36a-d**

36	**19**	**Ar**	% (**36**)[a]
a	**e**	4-EtC_6H_4	93
b	**h**	4-*t*BuC_6H_4	89
c	**l**	4-$(CF_3)C_6H_4$	88
d	**d**	4-$(MeO)C_6H_4$	85

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



Scheme 21. Synthesis of **37a-c**. *Conditions*: *i)* **36** (1.0 equiv.), **19a,d,e** (1.0 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 2M K_2CO_3, dioxane, at70 °C, 6 h.

The reaction of **36a,b,d** with different arylboronic acids, which were sequentially added, afforded the 2,3-diaryl-1*H*-inden-1-ones **37a-c** containing two different aryl groups (Scheme 21, Table 17). During the optimization, it proved to be important that the first step was carried out at 45 °C (or at 40 °C in case of **36d**) to achieve a good site-selectivity in favour of position 3 of the substrate. The second step had to been carried out at 70 °C to guarantee a complete reaction of position **2**. All reactions proceeded in excellent yields. The structure of **37c** was independently confirmed by X-ray crystal structure analyses (Figure 16).

Table 17. Synthesis of **37a-c**

19	**36**	**37**	**Ar**	**Ar[1]**	**% (37)** [a]
d	**a**	**a**	4-EtC_6H_4	4-$(MeO)C_6H_4$	93
a	**b**	**b**	4-$(CF_3)C_6H_4$	C_6H_5	87
e	**d**	**c**	4-$(MeO)C_6H_4$	$4EtC_6H_4$	86

[a] Yields of isolated products

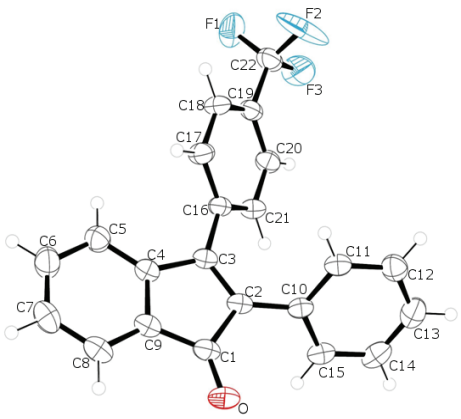


Figure 16. Ortetp plot of **37b** (50 % probability level)

The site-selective formation of **36a-d** and **37a-c** can be explained by electronic reasons. The first attack of palladium(0) catalyzed cross-coupling reactions (oxidative addition step) generally occurs at the more electron deficient and sterically less hindered position.[74,78] Position 3 of 2,3-dibromo-1*H*-inden-1-one **35** is considerably more electron-deficient than position 2 (Figure 17). Handy and Zhang reported a simple guide for the prediction of the site-selectivity of palladium (0) catalyzed cross-coupling reactions of polyhalogenated substrates based on the ^{1}H NMR chemical shift values of the non-halogenated analogues.[78] In fact; the ^{1}H NMR signal of proton H-3 of inden-1-one is shifted downfield compared to proton H-2.

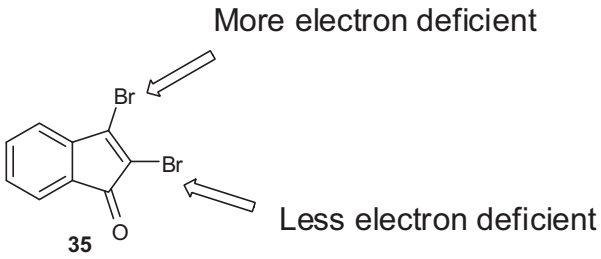
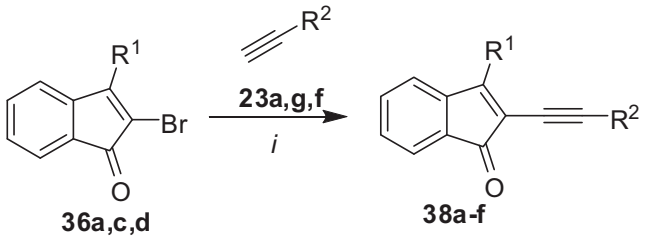


Figure 17. Possible explanation for the site-selectivity of cross-coupling reactions of **35**.



Scheme 22. Synthesis of **38a-f**. *Reagents and conditions: i*, **36 a,c,d** (1.0 equiv), alkynes (1.0 equiv), $(i\text{Pr})_2\text{NH}$ (1.5 equiv), CuI (10 mol%), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (3 mol %), at room temperature, 2h.

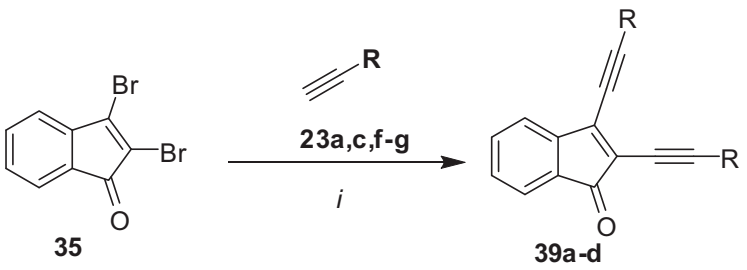
In prolongation of our research work, Sonogashira coupling products **39a-f** were prepared in high yields from **36a**,**c**,**d** and the terminal alkynes **23a,g,f** using $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (5 mol %) as catalyst as well as CuI and $(i\text{Pr})_2\text{NH}$. The structures of compounds **39a-f** were confirmed by spectroscopy. The aliphatic alkynes gave better yields than aromatic alkynes.

Table 18. Synthesis of **39a-f**

38	**36**	**23**	**R^2**	% (**38**)[a]
a	a	**a**	C_6H_5	85
b	c	**a**	C_6H_5	88
c	d	**g**	4-*t*BuC_6H_4	80
d	c	**f**	*n*-Oct.	89
e	d	**h**	$C_{11}H_9O$	78

[a] Yields of isolated products

In addition, I also successfully carried out dialkynylations (products **39**) by Sonogashira couplings (Scheme 23, Table 19). All reactions proceeded in high yields.



Scheme 23. Synthesis of **39a-d** . *Reagents and conditions: i*) **35** (1.0 equiv), alkynes (2.2 equiv), (*i*Pr)$_2$NH (1.5 equiv), CuI (20 mol%), Pd(PPh$_3$)$_2$Cl$_2$ (15 mol %), at room temperature, 2 h.

Table 19. Synthesis of **39a-d**

39	**23**	**R**	% (**39**)[a]
a	**a**	C_6H_5	89
b	**c**	4-MeC_6H_4	93
c	**g**	4-*t*BuC_6H_4	94
d	**f**	$(CH_2)_7CH_3$	92

[a] Yields of isolated products

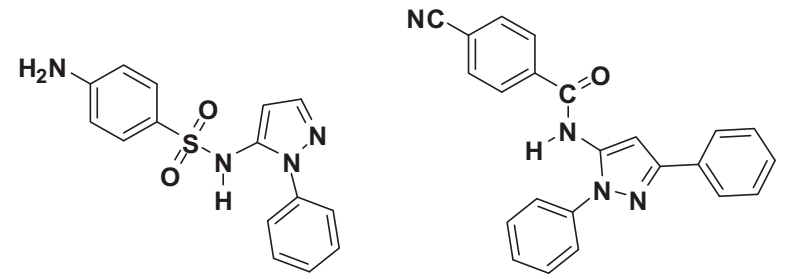
7.3 Conclusion

In conclusion, I developed an efficient method for site-selective Suzuki-Miyaura reactions of 2,3-dibromo-1*H*-inden-1-one which provide a convenient approach to 2,3-diaryl-1*H*-inden-1-ones and 3-aryl-2-bromo-1*H*-inden-1-ones. The scope and applications of the methodology outlined herein are currently studied in our laboratories by my colleague Mr. Hung Nguyen (Ph.D thesis in preparation). Site-selective Suzuki reactions combined with Sonogashira couplings were also developed.

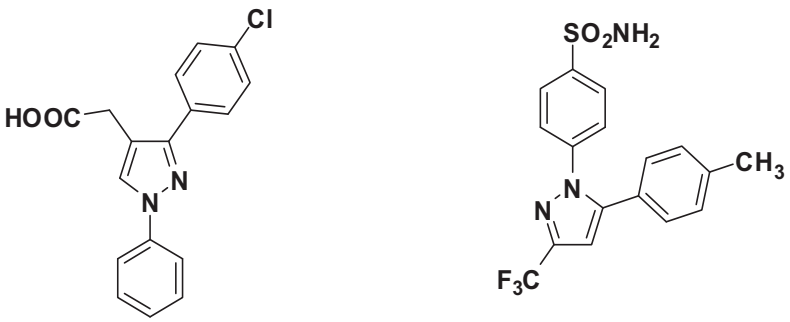
8. Synthesis of Arylated Pyrazoles by Site-Selective Suzuki-Miyaura Reactions of Tribromopyrazoles

8.1 Introduction

Pyrazoles are common building blocks in material[42], agricultural and pharmaceutical[76] sciences. Pyrazole derivatives, specifically 1-phenylpyrazole derivatives, are known to have a broad spectrum of biological activities. For example, 4-amino-N-(1-phenyl-1H-pyrazol-5-yl) benzensulfonamide (sulfaphenazole) derived from 5-amino-1-phenylpyrazole is a potent antibacterial drug[77], while 3-cyano-N-(1,3-diphenyl-1H-pyrazol-5-yl)benzamide (CDPPD) has been identified as a positive allosteric metabotropic modulator of the glutamate receptor (Figure 16)[78]. Nonsteroidal anti-inflammatory drugs such as Lonazolac are (1,3-diphenyl-1H-pyrazol-4-yl)acetic acid derivatives (Figure 18)[79]. The anti-inflammatory activity is also typical for (1,4-diphenylpyrazol-3-yl)acetic acid and related compounds.[80]



Sulfaphenazole CDPPB



Lonazolac Celecoxib

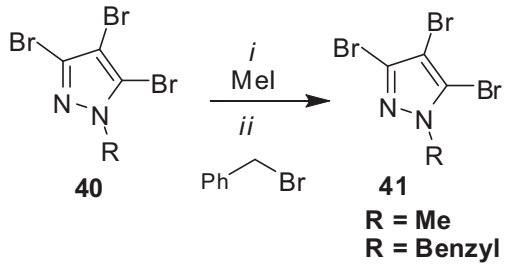
Figure 18. Some pharmaceuticals bearing the N-phenylpyrazole moiety.

Pyrazoles containing heterocyclic moieties such as pyrimidine, 1,3,4-oxadiazole or 1,2,4-triazole[81] have been tested for their antimicrobial, antifungal, and antiviral activities[82]. 4-Alkyl-1,2,5-tris(4-hydroxyphenyl)pyrazoles have been studied as estrogen receptor-selective agonists[83]. Many methods have been described in the literature for the synthesis of symmetrical substituted pyrazoles.[84] However, in the case of unsymmetrical pyrazoles, these routes[85] often face a problem of regioselectivity because pyrazole can act as an ambident nucleophile[85]. In order to develop an efficient synthetic approach, we chose to explore the palladium-catalyzed coupling reactions for incorporating the desired substituents to the fully assembled core. There have been several literature reports on palladium-catalyzed cross-coupling reactions of halo- and pseudohalo-substituted pyrazoles. Most of these studies report the Suzuki cross-couplings with arylboronic acids[86]. Suzuki reactions of tribrominated pyrazoles have, to my knowledge, not yet been reported.

My colleague Mr. Asad Ali started in the Langer group a project related to Suzuki-Miyaura reactions of tribrominated pyrazoles (Asad Ali, Ph.D thesis, University of Rostock, 2010). He studied *N*-benzyl- and *N*-vinyl derivatives in these reactions. In this chapter, I have discussed my results related to Suzuki-Miyaura reactions of tribrominated pyrazole containing a methyl group attached to the nitrogen. The products, monoaryl- and triaryl-pyrazoles, were prepared in good to excellent yields. The methodology discussed in this chapter provided a straightforward way to a variety of aryl-substituted pyrazoles which other methods did not provide readily.

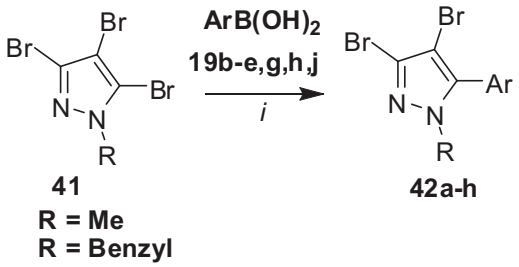
8.2 Results and discussion

N-Benzyl-tribromopyrazole **41** and *N*-methyl-tribromopyrazole **42** were prepared from commercially available tribromopyrazole by a known procedure (Scheme 25). Instead of benzylchloride, which was used in the original procedure for the preparation of **41**, benzylbromide was employed.



Scheme 24. Synthesis of **41a, 41b**. *Reagents and conditions: i*) **40** (1.0 equiv), methyliodide (1.0 equiv), NEt_3 (1.1 equiv), CH_2Cl_2 (5 mL per mmol of **40**), 20 °C, 8 h. *ii)* **40** (1.0 equiv), benzylbromide (1.0 equiv), NEt_3 (1.1 equiv), CH_2Cl_2 (5 mL per mmol of **40**), 20 °C, 4 h.

The Suzuki-Miyaura reaction of **41a-b** with arylboronic acids **19b-e,g,h,j** (1.0 equiv.) afforded the 5-aryl-3,4-dibromopyrazoles **42a-h** in 66-73% yield (Table 20, Scheme 25).



Scheme 25. Synthesis of 5-aryl-3,4-dibromopyrazoles **42a-h**. *Reagents and conditions: i*) **41** (1.0 equiv), $ArB(OH)_2$ (1.0 equiv), K_2CO_3 (2 M), $Pd(PPh_3)_4$ (3 mol-%), 1,4-dioxane / H_2O (4:1), 60 °C, 4 h.

The best yields were obtained when $Pd(PPh_3)_4$ (3 mol-%) was used as catalyst (dioxane, 60 °C, 4 h). The yields dropped when $Pd(PPh_3)_2Cl_2$ was used as a catalyst. The use of K_3PO_4 as the base resulted in lower yields compared to the use of a 2M aqueous solution of K_2CO_3. In conclusion, the application of the reaction conditions allowed the preparation of the 5-monoarylated products in good yields (Scheme 25, Table 20).

The regioselectivity of the monoarylation can be explained by the fact that the oxidative addition of palladium usually occurs first at the most electron deficient carbon atom C-5. The structures of the products were confirmed by 2D NMR experiments.

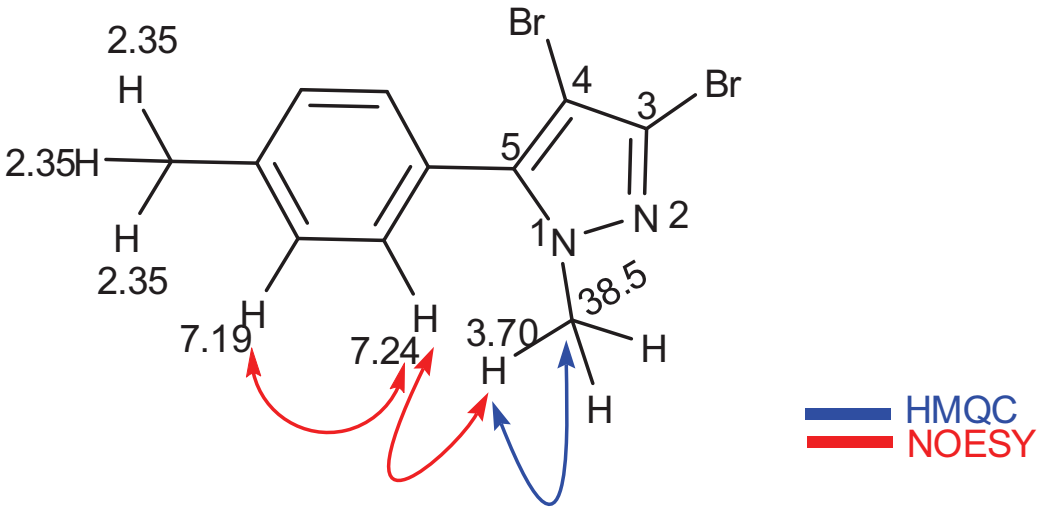


Figure 19: 2D NMR correlations (HMQCand NOSEY) of **42a**

For example, the regioselectivity of compound **42a** was established unambiguously by 2D NMR using H-H (NOESY) and HMQC correlations. Methyl H at δ = 3.70 attached to C at δ = 38.5 showed clear correlation through space with the phenyl H at δ = 7.24 which confirmed that the 4-methylphenyl group is attached to C-5 of pyrazole (Figure 19).

Table 20. Synthesis of **42a-g**

42	R	19	Ar	% (42)[a]
a	Me	**b**	4-MeC_6H_4	76
b	Me	**e**	4-EtC_6H_4	79
c	Me	**h**	4-*t*BuC_6H_4	81
d	Me	**c**	3-ClC_6H_4	73
e	Me	**i**	4-ClC_6H_4	71
f	Me	**l**	4-FC_6H_4	75
g	Me	**d**	4-(MeO)C_6H_4	78
h	Benzyl	**d**	4-(MeO)C_6H_4	84

[a] Yields of isolated compounds

The structure of **42h** was independently confirmed by X-ray crystal structure (Figure 20).

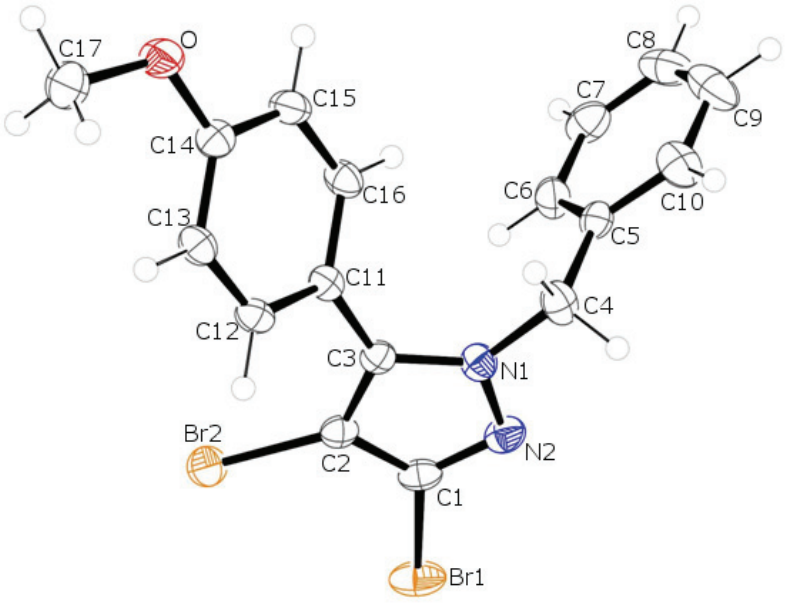


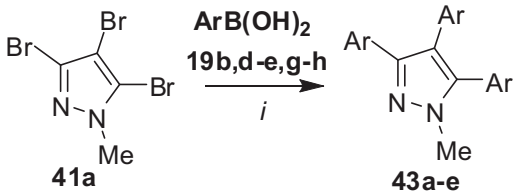
Figure 20. Ortep plot of **42h** (50% probability level)

During the study of the Suzuki reactions of *N*-protected tribromopyrazoles with 3.3 equivalents of boronic acids it was found, that mixtures of products were formed when I used $Pd(PPh_3)_4$ (3 mol-%) and $Pd(PPh_3)_2Cl_2$ as catalysts. Good yields of triarylated products were obtained when $Pd(OAc)_2$ (5 mol-%) in the presence of XPhos (10 mol-%) was used as catalyst (dioxane, 90 °C, 6 h), (entry 4, Table 21). The best yields were obtained when $Pd(OAc)_2$ (5 mol-%) was used in the presence of SPhos (10 mol-%) in an aqueous solution of K_2CO_3 (2 M) (entry 3, Table 21) (for the structures of XPhos and SPhos see (Figure 12, chapter 5). As test reaction for these optimization studies, I investigated the conversion of **42a** with 4-tolylboronic acid. In conclusion, the application of the reaction conditions given in entry 3 of Table 21 allowed the preparation of all triarylated products in good to excellent yields. It was also noted that electron-poor arylboronic acids provided slightly lower yields than electron-rich arylboronic acids. This can be explained by the lower nucleophilicity of electron-poor boronic acids.

Table 21. Reaction condition optimization for the synthesis of 1-methyl-3,4,5-tri(4-methylphenyl)pyrazole (**43a**)

Entry	Conditions	%(**43a**)[a]
1	$Pd(PPh_3)_2Cl_2$ (5 mol-%), aq. K_2CO_3 (2 M)	42
2	$Pd(PPh_3)_4$ (5 mol-%), aq. K_2CO_3 (2 M)	28
3	**$Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), aq. K_2CO_3 (2M)**	**97**
4	$Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%), aq. K_2CO_3 (2M)	80
5	$Pd(OAc)_2$ (5 mol-%), $(EtOH)_3N$, K_2CO_3 (2M)	decomp.
6	$Pd(OAc)_2$ (5 mol-%), $(EtO)_2PPh$, K_2CO_3 (2M)	traces
7	$Pd(OAc)_2$ (5 mol-%), $(n\text{Bu})_3P$, K_2CO_3 (2M)	20

[a] Yields of isolated compounds



Scheme 26. Synthesis of 3,4,5-triaryl-pyrazoles: **43a-e**. *Reagents and conditions: i)* **42** (1.0 equiv), **19b,c,d,e,h** (3.3 equiv), K_2CO_3 (2 M, 1 mL), $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), 1,4-dioxane/H_2O (4:1), 100 °C, 5 h.

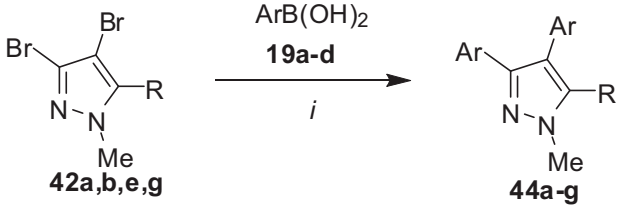
The results of the Suzuki-Miyaura cross coupling reactions of *N*-methyl-2,3,4-tribromopyrazole **41a** with the different arylboronic acids **19b,d-e,g-h** (3.3 equiv.) to the *N*-methyl-3,4,5-triaaryl-pyrazoles **43a-e** are summerized in Table 22 (Scheme 26).

Table 22. Synthesis of **43a-e**

43	**Ar**	**19**	**% (43)[a]**
a	4-MeC_6H_4	**b**	97
b	4-EtC_6H_4	**e**	89
c	4-*t*BuC_6H_4	**h**	86
d	3,5-$Me_2C_6H_4$	**g**	84
e	4-(MeO)C_6H_4	**d**	81

[a] Yields of isolated compounds

The Suzuki reaction of **42a,b,e,g** with 2.2 equiv. of arylboronic acids **19a-d** afforded the diaryl-pyrazoles **44a-g** in good yields (Scheme 27, Table 23).



Scheme 27. Synthesis of **44a-g**.: *Reagents and conditions: i*) **42** (1.0 equiv), $ArB(OH)_2$ (2.2 equiv), K_2CO_3 (2 M, 1 mL), $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%),, 1,4-dioxane / H_2O (4:1), 100 °C, 6 h.

Table 23. Synthesis of **44a-g**

19	**44**	**R**	**Ar**	% (**44**)[a]
a	**a**	4-MeC_6H_4	C_6H_5	92
d	**b**	4-MeC_6H_4	4-$(MeO)C_6H_4$	84
a	**c**	4-EtC_6H_4	C_6H_5	89
d	**d**	4-EtC_6H_4	4-$(MeO)C_6H_4$	82
a	**e**	4-ClC_6H_4	C_6H_5	86
b	**f**	4-$(MeO)C_6H_4$	4-MeC_6H_4	83
c	**g**	4-$(MeO)C_6H_4$	3-ClC_6H_4	71

[a] Yields of isolated products

The structure of **44a** was independently confirmed by X-ray crystal structure (Figure 21).

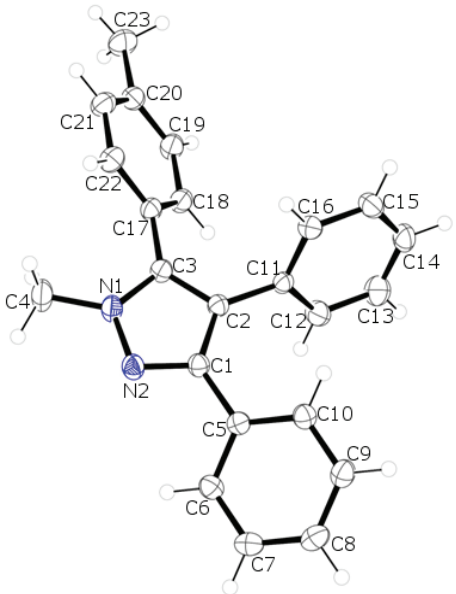


Figure 21. Ortetp plot of **44a** (50 % probability level)

8.3 Conclusions

In conclusion, I have studied a convenient synthesis of arylated *N*-methyl- and *N*-benzyl-pyrazoles by Suzuki-Miyaura reactions of *N*-protected 3,4,5-tribromopyrazole. The products reported herein are not readily available by other methods. All reactions proceed with excellent site-selectivity.

9 Synthesis of Unsymmetrical Arylated Furans by Suzuki-Miyaura Cross-Coupling and Metal-Halide Exchange Reactions of 2,3,4,5-Tetrabromofuran

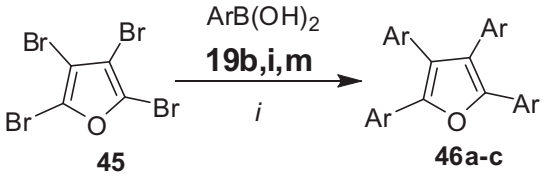
9.1 Introduction:

Furan ring systems are in abundance available in secondary plant metabolites. Furans are not found in animal metabolism.[87] Most of these furan natural products demonstrate exciting biological activities, such as cytotoxic and antitumor properties,[88] antispasmodic,[89] and antifeeding activities.[90] In addition, natural furan containing molecules continue to be uncovered at a rapid speed.[91] Because of their outstanding properties, many synthetic furans are employed as pharmaceuticals.[92] Furthermore, building blocks found in natural molecules polysubstituted furans[93] are important precursors for the synthesis of natural and non-natural products.[94] The synthetic work towards polysubstituted furans belongs therefore to a remarkably dynamic research domain.

Traditionally, substituted furans have been synthesized by direct functionalization of existing furans or cyclization of acyclic substrates.[95] Among these strategies developed for the synthesis of a multi-substituted furan ring, one of the simplest involves starting with either furan itself or a mono-substituted furan followed by introducing functional groups at various positions of the furan ring. This approach, yet, has some disadvantages. First, the introduction of functional groups into the 3- or 4-position is difficult as furan rings lithiate and add electrophiles preferentially at the 2- and 5- position[96]. Second, placement of a group at C-3 results in the 2- and 5-positions becoming regioisomeric. In turn that either regioselective methods or blocking groups strategies must be used to establish new moieties.[94]

9.2 Results and Discussions

2,3,4,5-Tetrabromofuran **48** was prepared following a literature procedure.[97] The reaction of **48** with arylboronic acids **19b,i,m** (4.4 equiv.) afforded the stable 2,3,4,5-tetraarylfurans **49a-c** (Scheme 29, Table 24).



Scheme 28. Synthesis of **46a-c**. *Conditions: i*) **45** (1.0 equiv.), **19** (4.4 equiv.), $Pd(PPh_3)_4$ (3 mol-%), aq. K_2CO_3 (2 M), dioxane, 80 °C, 5 h.

The reaction conditions were systematically optimized. The best yields were obtained when $Pd(PPh_3)_4$(3 mol-%) was used as catalyst. The yields dropped when $Pd(PPh_3)_2Cl_2$ or $Pd(OAc)_2$ (3 mol-%) in the presence of XPhos or $(Cy)_3P$ were employed. Furthermore, best yields were obtained when an aqueous solution of K_2CO_3 (2 M) or when K_3PO_4 were employed as the base. The products were isolated in good to excellent yields for both electron-rich and electron-poor arylboronic acids.

Table 24. Synthesis of symmetrical tetraarylfurans **46a-c**

46	**19**	**Ar**	**% (46)** [a]
a	**b**	4-MeC_5H_4	90
b	**i**	4-ClC_5H_4	82
c	**m**	4-$(CF_3)C_5H_4$	89

[a] Yields of isolated products

The structure of **46c** was independently confirmed by X-ray crystal structure (Figure 22).

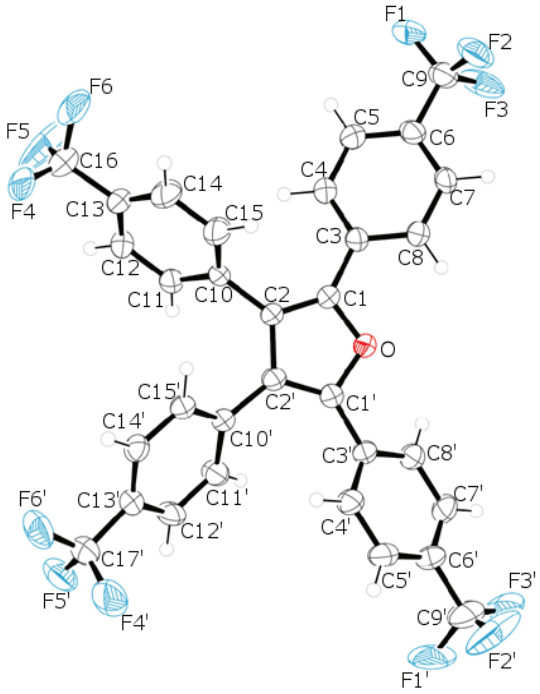
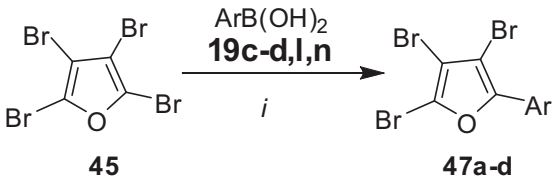


Figure 22. Ortetp plot of **46c** (50 % probability level)



Scheme 29. Synthesis of **47a-d**. *Conditions: i)*, **45** (1.0 equiv.), **19** (1.0 equiv.), $Pd(PPh_3)_4$ (2 mol %), aq. K_2CO_3 (2 M), toluene/dioxane (4:1), 80 °C, 3 h.

The Suzuki-Miyaura reaction of **45** with arylboronic acids **19c,d,l,n** (1.0 equiv.) afforded the 2-aryl-3,4,5-tribromofurans **47a-d** (Scheme 30, Table 25). Andrew and co-workers studied site-selective Suzuki-Miyaura reactions of 2,3-dibromofuran. These reactions, which were carried out in a DME/H_2O/K_2CO_3 system, provided low yields. When I applied these conditions, I could not observe the regioselective formation of 2-substituted 3,4,5-tribromofurans. Solvents like toluene, DME, dioxane and THF provided always a mixture of products. A binary solvent system comprising dioxane and toluene in a 1:4 ratio gave the desired 2-monoarylfurans **47a-d** regioselectively. The stoichiometry (employment of exactly 1.0 equiv. of the arylboronic acid) also played an important role. The best yields (87-89%)

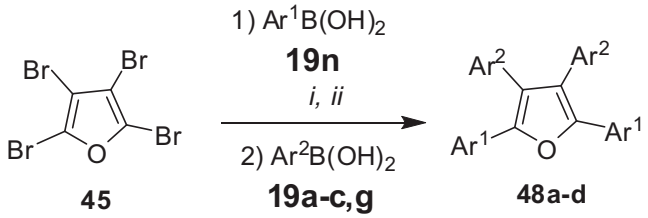
were obtained by using of $Pd(PPh_3)_4$ (2 mol %) as catalyst, the use of an aqueous solution of K_2CO_3 (2 M) as base, and the use of a 4:1 mixture of toluene and dioxane.

Table 25. Synthesis of 2-aryl-3,4,5-tribromofurans **47a-d**

47	**19**	**Ar**	***%* (47)** [a]
a	**c**	3-ClC_5H_4	87
b	**n**	3-$(CF_3)C_5H_4$	85
c	**l**	4-FC_5H_4	88
d	**d**	4-$(MeO)C_5H_4$	89

[a] Yields of isolated compounds

A one-pot strategy to accomplish the synthesis of tetraarylfurans **48a-d** with different aryl substituents at 2-/ 5- and 3-/ 4- positions, respectively, was also studied. The Suzuki-Miyaura reaction of **45** with arylboronic acid **19n** (2.0 equiv.) in toluene/dioxane (4:1), separation of the solution into four equal portions, and subsequent addition of arylboronic acids **19a-c,g** (only one boronic acid to one of the separated portions) afforded products **48a-d** in high yields, respectively (Scheme 30, Table 26).



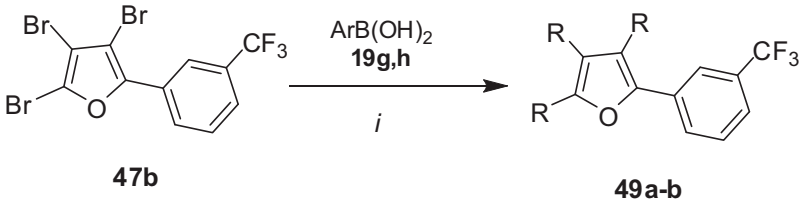
Scheme 30. Synthesis of **48a-d**. *Conditions: i*) **45** (1.0 equiv.), arylboronic acid **19n** (2.0 equiv.) $Pd(PPh_3)_4$ (3 mol %), aq. K_2CO_3 (2 M), toluene/dioxane (4:1), 80 °C, 3 h, *ii)* **19 a-c,g** (2.0 equiv.), 80 °C, 3 h.

Table 26. Synthesis of 2,5-diaryl-3,4-diaryl^{2}furans **48a-d**

48	**19**	**Ar^1**	**Ar^2**	**% (48)** [a]
a	**c**	3-$(CF_3)C_5H_4$	4-*t*BuC_5H_4	93
b	**a**	3-$(CF_3)C_5H_4$	C_5H_5	86
c	**b**	3-$(CF_3)C_5H_4$	4-MeC_5H_4	93
d	**g**	3-$(CF_3)C_5H_4$	3,5-$Me_2C_5H_4$	88

[a] Yields of isolated compounds

In addition, the unsymmetrical 2-monoaryl^1-3,4,5-triaryl^{2}furans **49a-b** were prepared by one-pot Suzuki-Miyaura reaction of 2-aryl-3,4,5-tribromofuran **47b** with the boronic acids **19g** and **19h** in dioxane at 80 °C for 5 h (sequential addition of the boronic acids). The products were isolated in excellent yields (Scheme 31, Table 27).



47b **49a-b**

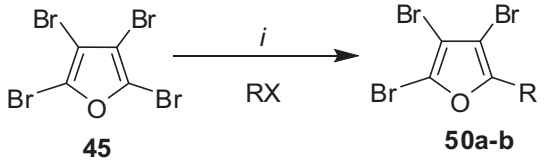
Scheme 31. Synthesis of **49a-b**. *Conditions: i)* **47b** (1.0 equiv.), **19g,h** (3.3 equiv.), $Pd(PPh_3)_4$ (2 mol %), aq. K_2CO_3 (2 M), dioxane 80 °C, 5 h.

Table 27. Synthesis of 2-monoaryl[1]-3,4,5-triaryl[2]furans **49a-b**

49	**19**	**R**	**% (49)** [a]
a	**g**	3,5-$(Me_2)C_5H_3$	87
b	**h**	4-*t*BuC_5H_4	93

[a] Yields of isolated compounds

Beside our investigations of the Suzuki-Miyaura reaction, we have also found that the addition of n-butyllithium (1.1 equiv.) to a THF solution of tetrabromofuran **45** (1.0 equiv.) and subsequent addition of trimethylchlorosilane or benzyl chloride (1.0 equiv., slow addition during 3 h) directly afforded the 2-substituted 3,4,5-tribromofurans in 87–93% yield (Scheme 31, Table 28).



45 **50a-b**

Scheme 32. Synthesis of 2-substituted 3,4,5-triibromofurans **50a-b**. Conditions: *i)* 1) n-BuLi (1.1 equiv.), TMEDA (1.1 equiv.), - 78 to 20°C, 1 h; 2), RX (1.0 equiv., addition during 3 h), 6h.

Table 28. Synthesis of 2-substituted 3,4,5-tribromofurans **50a-b**

50	**R**	**% (50)** [a]
a	Me_3Si	**87**
b	$(CH_2)C_6H_5$	**93**

[a] Yields of isolated compounds

9.3 Conclusions

In conclusion, I have prepared different types of symmetrical and unsymmetrical tetraarylfurans. I have also studied regioselective issues for the synthesis of monoarylfurans by the first Suzuki-Miyaura reactions of 2,3,4,5-tetrabromofuran. The use of a binary solvent system toluene/dioxane was found to play a key role during the optimization of the site-selectivity of these monoarylation reactions. All reactions proceeded with excellent site-selectivity in favour of the more electron-deficient position 2. Metal-halide exchange reaction with tetrabromofuran also provided selectivity at C-2.

Summary

In this work, new diversely substituted heterocycles and aromatic carbacycles could be synthesized by metal catalyzed C-C-bond formation reactions

Functionalized triarylmethanes were prepared in two steps by $FeCl_3$-catalyzed benzylation of acetylacetone to give 3-(diarylmethyl)pentane-2,4-diones and subsequent formal [3+3] cyclization with 1,3-bis(trimethylsilyloxy)-1,3-dienes.

6-Aryl-2,3-dihydro-4*H*-pyran-4-ones were prepared in one step by cyclocondensation of 1,3-diketone dianions with aldehydes. The $TiCl_4$-mediated cyclization of a 6-aryl-2,3-dihydro-4*H*-pyran-4-one with 1,3-bis(silyloxy)-1,3-butadiene resulted in a ring-opening of the pyranone moiety and formation of a highly functionalized benzene derivative.

The reaction of the dianion of 1,1,1-trifluoro-pentane-2,4-dione with aldehydes and subsequent addition of hydrochloric acid afforded 2,3-dihydro-6-trifluoromethylpyran-4-ones.

The Suzuki-Miyaura reaction of the bis(triflate) of 2,4-dihydroxybenzophenone with aryl boronic acids gave 2,4-diarylbenzophenones. The reaction with one equivalent of arylboronic acids resulted in a regioselective selective attack at the less hindered carbon atom C-4. 2,4-Diarylbenzophenones containing two different aryl groups were prepared by sequential addition of two different boronic acids. The Sonogashira cross-coupling reactions with terminal alkynes display remarkable compatibility with regard to the formation of mono- and dialkynyl-substituted benzophenones and could be also carried out in combination with a Suzuki-Miyaura reaction in a one-pot procedure. Analogously to the bis(triflate) of 2,4-dihydroxybenzophenone, 2,4′-bis(trifluoromethylsulfonyloxy)diphenylsulfone could be reacted with aryl boronic acids in Suzuki-Miyaura reactions to give 2,4′-bis(aryl)diphenylsulfones or (with one equivalent of arylboronic acid) monoarylated products at C-4′. Sonogashira cross-coupling reactions of 2,4′-bis(trifluoromethylsulfonyloxy)diphenylsulfone with terminal alkynes were likewise successful. Additionally, 2,4-Diarylsulfones containing two different aryl groups were prepared by sequential addition of two different boronic acids.

The Suzuki-Miyaura reaction of 2,3-dibromo-1*H*-inden-1-one with one equivalent of arylboronic acid gave 2-bromo-3-aryl-1*H*-inden-1-ones with very good regioselectivity and with two different arylboronic acids afforded 2,3-diaryl-1*H*-inden-1-ones containing two different terminal aryl groups in excellent yields.

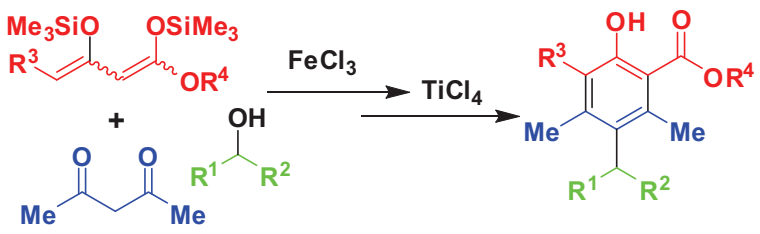
The Sonogashira cross-coupling of 2,3-dibromo-1*H*-inden-1-one with terminal alkynes. This reaction gave us to the formation of symmetrical, alkynyl, alkynyl, alkynyl, aryl substitution. The first attack on less hindered C-3 carbon atom.

Suzuki-Miyaura reactions of *N*- protected 3,4,5-tribromopyrazole allowed a convenient synthesis of mono- and triarylpyrazoles by using corresponding equivalents of aryl boronic acids. All reactions proceeded with excellent yields and in the case of monosubstitution also with high regioselectivity. Suzuki-Miyaura reactions of 2,3,4,5-tetrabromofuran allowed a convenient synthesis of aryl-substituted furans (mono-, tri- and tetraarylfurans) by using the corresponding equivalents of aryl boronic acids. Unsymmetrically aryl-substituted furans were prepared, which are not readily available by other methods. The reactions proceeded with excellent yields and high regioselectivity. Furthermore, regioselective metal-halide exchange reactions at 2-position of the tetrabromofuran afforded an approach to 2-substituted 3,4,5-tribromofurans.

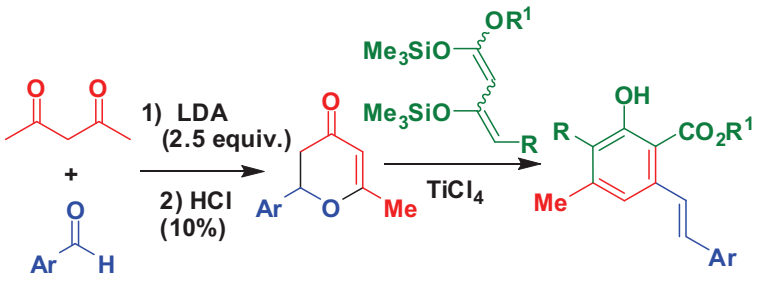
Zusammenfassung (Übersetzung)

In der Arbeit ist es gelungen neue, verschiedenartig substituierte Heterozyklen sowie aromatische Carbazyklen durch Metall-katalysierte C-C-Knüpfungsreaktionen darzustellen.

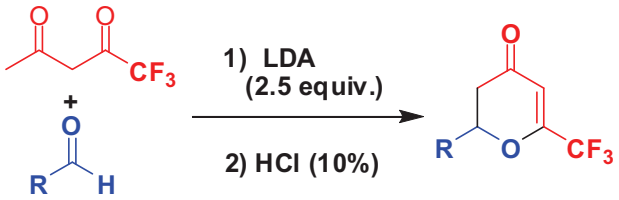
Funktionalisierte Triarylmethane wurden in zwei Schritten dargestellt. Zunächst erfolgte die $FeCl_3$- katalysierte Benzylierung von Acetylaceton zu 3-(Diarylmethyl)pentan-2,4-dionen, die anschließend in einer formalen [3+3]-Zyklisierung mit 1,3-Bis(trimethylsilyloxy)-1,3-dienen umgesetzt wurden.



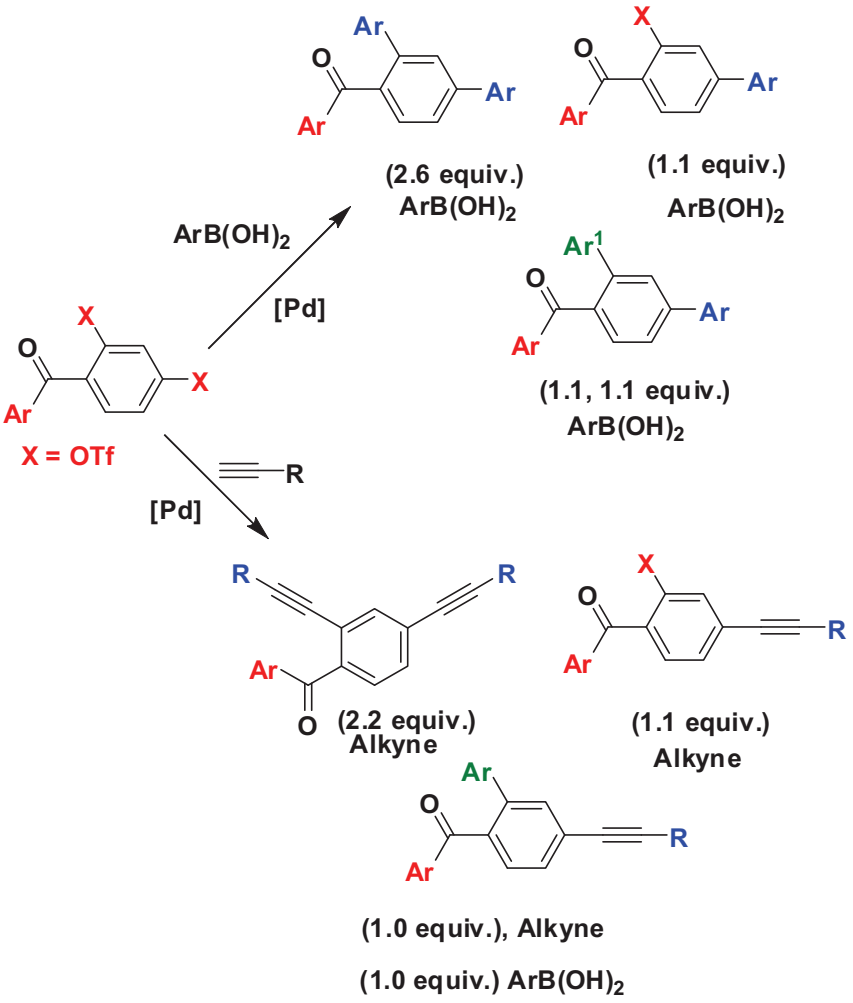
6-Aryl-2,3-dihydro-4*H*-pyran-4-one wurden durch die Zyklokondensation von 1,3-Diketondianionen mit Aldehyden in einem Schritt dargestellt. Die $TiCl_4$-vermittelte Zyklisierung der 6-Aryl-2,3-dihydro-4*H*-pyran-4-one mit 1,3-Bis(silyloxy)-1,3-butadienen führte unter Ringöffnung des Pyranonfragments zu hochfunktionalisierten Benzenderivaten.



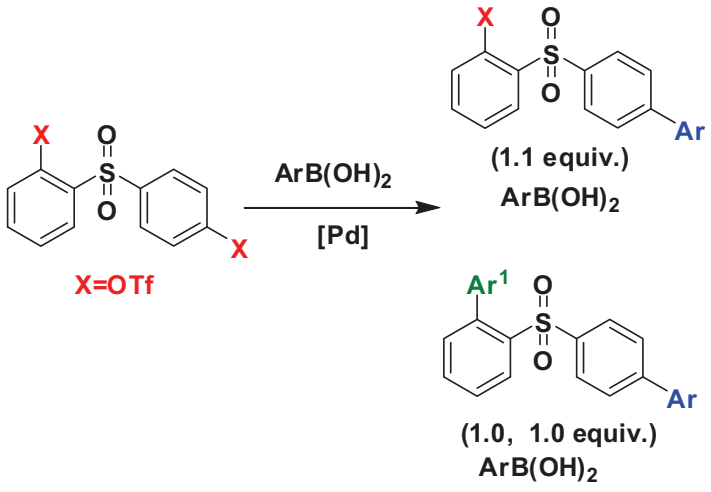
Die Reaktion des Dianions des 1,1,1-Trifluorpentan-2,4-dions mit Aldehyden und anschließende Addition von Chlorwasserstoff führte zu 2,3-Dihydro-6-trifluoromethylpyran-4-onen.



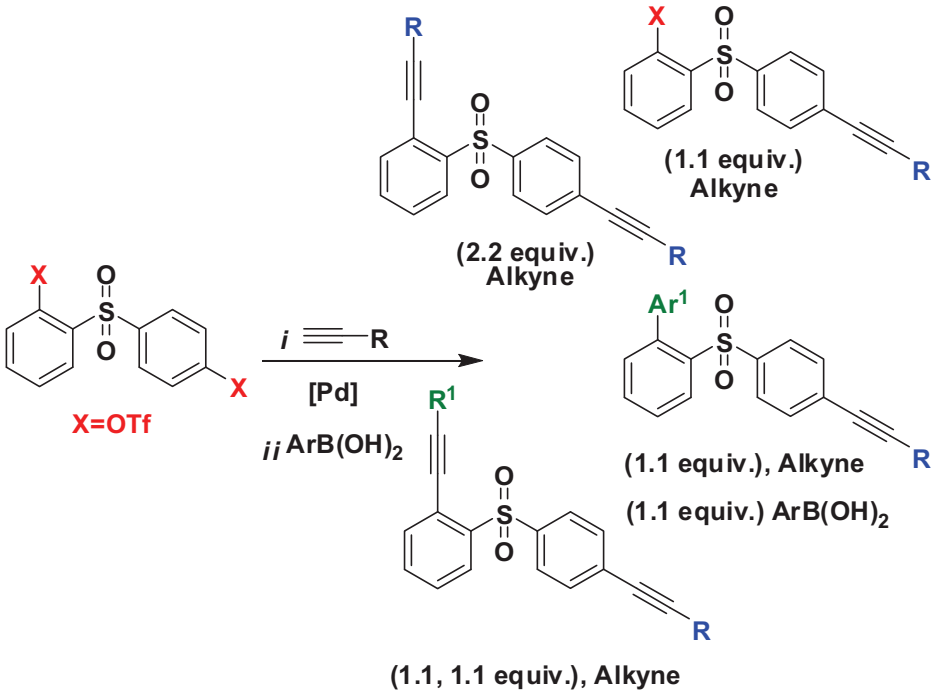
Szuki-Miyaura-Reaktionen des Bistriflates des 2,4-Dihydroxybenzophenons mit Arylboronsäuren ergaben 2,4-Diarylbenzophenone. The Reaktion mit einem Äquivalent der Arylboronsäure führte zu einem regioselektiven Angriff am sterisch weniger gehinderten Kohlenstoffatom C-4-Atom. 2,4-Diarylbenzophenone mit unterschiedlichen Arylsubstituenten wurden durch aufeinanderfolgende Addition von zwei verschiedenen Boronsäuren erhalten. Die Sonogashira-Kreuzkupplungsreaktion mit terminalen Alkinen erwies sich für die Darstellung von mono- und dialkinyl-substituierten Benzophenonen als besonders geeignet, und konnte auch in Kombination mit einer Suzuki-Miyaura-Reaktion in einem Eintopfverfahren durchgeführt werden.



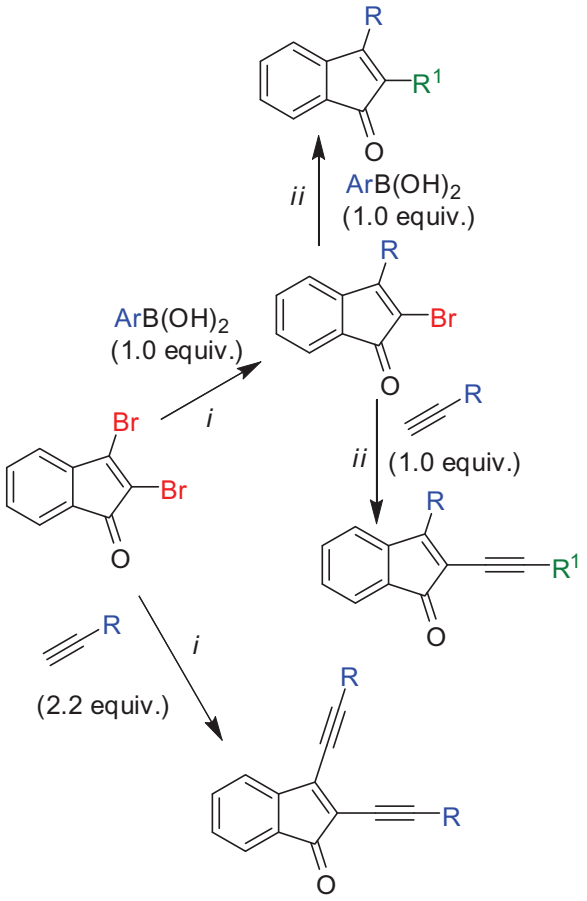
In Analogie zum Bistriflat des 2,4-Dihydroxybenzophenons konnte auch das 2,4′-Bis(trifluormethylsulfonyloxy)diphenylsulfon mit Arylboronsäuren in entsprechenden Suzuki-Miyaura-Reaktionen zu 2,4′-Diaryldiphenylsulfonen bzw. zu am C-4′ monoarylierten Produkten (bei Einsatz von nur einem Äquivalent Arylboronsäure) umgesetzt werden.



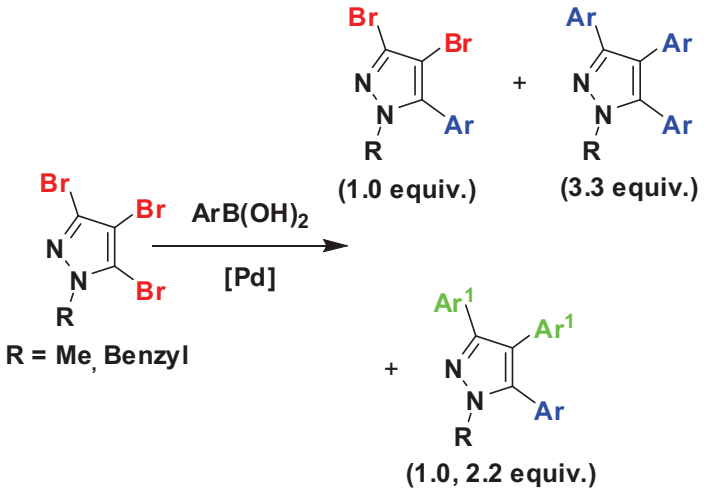
Die Sonogashira- Kreuzkupplungsreaktionen der Bis(triflate) der 2,4-bis(hydroxy)diphenylsulfone mit terminalen Alkynen wurden ebenfalls untersucht. Diese Reaktion erwies sich als besonders geeignet für symmetrische und unsymmetrische Substitutionen.



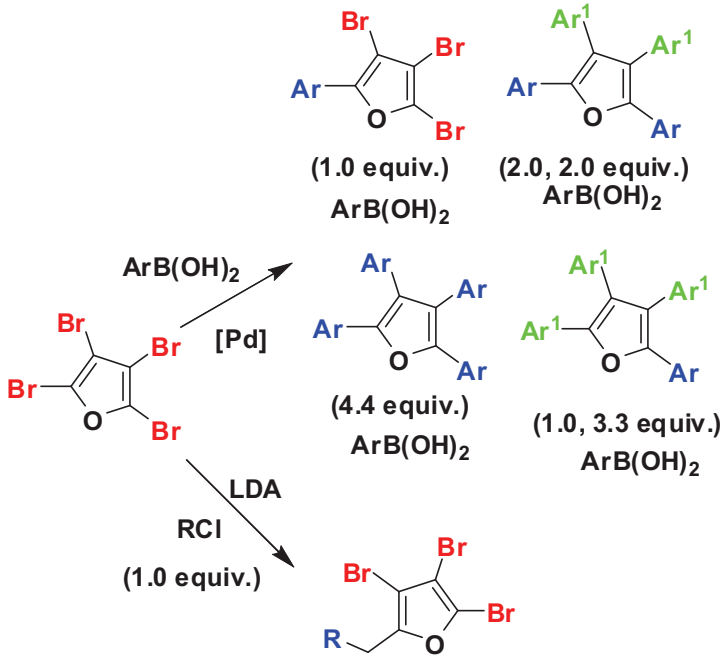
Suzuki- und Sonogashira-Reaktionen von 2,3-Dibromindanon liefert einen regioselektiven Zugang zu verschiedenen Indanonderivaten.



Suzuki-Miyaura-Reaktionen von *N*-geschütztem 3,4,5-Tribrompyrazol erlauben, durch den Einsatz entsprechender Äquivalente an Arylboronsäuren, eine bequeme Synthese von Mono- und Triarylpyrazolen. Alle Reaktionen verliefen in exzellenten Ausbeuten und im Fall der Monosubstitution auch mit hohen Regioselektivitäten.



In Analogie zum *N*-geschützten 3,4,5-Tribrompyrazol lassen sich durch Suzuki-Miyaura-Reaktionen des 2,3,4,5-Tetrabromfurans in bequemer Weise arylsubstituierte Furane (Mono-, Tri- und Tetraarylfurane) bei Einsatz entsprechender Mengen von Arylboronsäuren darstellen. Es konnten auch unsymmetrisch Aryl-substituierte Furane dargestellt werden, die bisher durch andere Synthesestrategien nur schwer zugänglich sind. Die Reaktionen verliefen mit exzellenten Ausbeuten und hoher Regioselektivität. Ferner ermöglichten regioselektive Metall-Halogen-Austauschreaktionen in 2-Position des Tetrabromfurans einen Zugang zu 2-subtituierten 3,4,5-Tribromfuranen.



10 Experimental Section

10.1 General Remarks

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

10.2 Methods for Compound Characterization and Analysis

NMR Spectroscopy

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

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

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

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

Infrared Spectroscopy (IR)

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

Mass Spektrometry (MS)

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

High Resolution Mass Spectrometry (HRMS)

Varian MAT 311, Intecta AMD 402.

Elemental Analysis

LECO CHNS-932, Thermoquest Flash EA 1112.

Melting Points

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

X-ray Structures

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

10.3 Chromatographic Methods

Thin Layer Chromatography (TLC)

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

10.4 Column Chromatography

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

11 General Procedures

11.1 Synthesis of Functionalized Triarylmethanes by Combination of $FeCl_3$-Catalyzed Benzylations of Acetylacetone with [3+3] Cyclocondensations

11.1.1 Synthesis of benzylation of β-dicarbonyl compounds

In a pressure tube, $FeCl_3$-$6H_2O$ (5 mol %), an alcohol (5.0 mmol), and acetylacetone (20 mmol) were dissolved in 10 mL of nitromethane. After stirring for 4 h at 60 °C, the reaction was quenched with water followed by extraction with dichloromethane. The combined organic layers were dried over Na_2SO_4 and the solvents were distilled off. Then, the product was purified by column chromatography (heptanes/ethyl acetate = 1:1).

11.1.2 Synthesis of mono silyl enol ethers of 3-benzhydrylpentane-2,4-dione

To a stirred solution benzene (2.5Ml/1.0 mmol of 6a-e), triethylamine (16.0 mmol) and trimethylchlorosilane (18.0 mmol) was added drop wise. The reaction mixture was stirred at room temperature for 72 hr, the solvent was removed in vacuo and hexane was added to the residue to give a suspension and filterd under argon atmosphere. The filtrate was concentrated in vacuo to give mono silyl enol ethers.

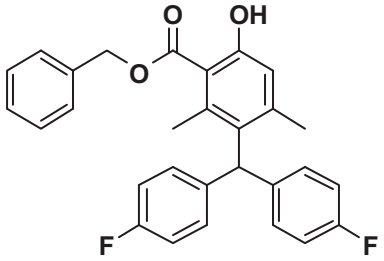
11.1.3 Synthesis of substituted triarylmethanes (8a-n)

To a stirred solution of CH_2Cl_2 5 mL, **7a-e** (1.0 equiv.), **3a-f** (1.1 equiv.) and, subsequently, $TiCl_4$ (1.0 equiv.) at −78°C. The temperature of the solution was allowed to warm to 20 °C during 14 h with stirring. To the solution was added hydrochloric acid (10%, 20 mL) and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purifed by chromatography (silica gel, heptanes / EtOAc) to give **8a-n**.

Benzyl 3-benzhydryl-6-hydroxy-2,4-dimethylbenzoate (8a). Starting with **7a** (0.510 g, 1.5 mmol) and **3a** (0.555 g, 1.65 mmol), **8a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.411 g, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 5.27 (s, 2 H, OCH_2), 6.65 (s, 1 H, CH), 6.98-7.19 (m, 10 H, ArH), 7.24-7.29 (m, 5 H, ArH), 10.51 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ = 21.4, 22.8 (CH_3), 50.7 (CH), 67.3 (CH_2), 112.6 (C), 117.9, 126.0, 128.2, 128.4, 128.5, 128.6, 129.0 (CH), 133.2, 135.1, 140.4, 142.0, 145.6 (C), 160.0 (C_{OH}), 171.3 (CO). IR (KBr): *v* = 3082, 3058, 3023, 2973, 2928, 1729, 1654 (s), 1598, 1566, 1493, 1450, 1379, 1320, 1289, 1260, 1209 (s), 1141 (m), 1140, 1064 (s), 1026 (m), 969 (w), 949, 908 (w), 850, 800, 748, 734, 717, 694 (s), 614, 578 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 422 (M^+, 6), 314 (19), 288 (36), 287 (10), 273 (40), 211 (12), 195 (17), 178 (10), 167 (27), 166 (34), 165 (61), 152 (16), 115 (10), 92 (20), 91 (100), 89 (10), 79 (13), 78 (14), 77 (18), 65 (22), 63 (10), 55 (10), 51 (12), 44 (36), 43 (13), 41 (14). HRMS (EI): calcd. for $C_{29}H_{26}O_3$ $[M]^+$: 422.18765; found: 422.188014.

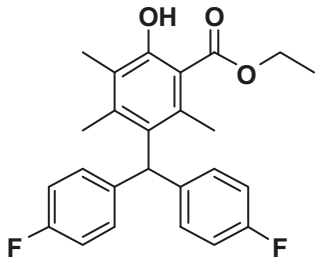
Methyl 3-benzhydryl-5-decyl-6-hydroxy-2,4-dimethyl-benzoate (8b). Starting with **7a** (0.510 g, 1.5 mmol) and **3b** (0.661 g, 1.65 mmol), **8b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.415 g, 57%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (t, ^{3}J = 6.8 Hz, 3 H, $(CH_2)_8CH_2\mathit{CH_3}$), 1.07-1.12 (m, 14 H, 7xCH_2), 1.24-1.29 (m, 2 H, CH_2), 1.84 (s, 3 H, CH_3), 1.95 (s, 3 H, CH_3), 2.48 (t, ^{3}J = 7.2 Hz, 2 H, $\mathit{CH_2}(CH_2)_8CH_3$), 3.70 (s, 3 H, OCH_3), 5.89 (s, 1 H, CH), 6.90-7.09 (m, 10 H, ArH), 10.61 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ = 15.2, 19.5, 22.4 (CH_3), 23.8, 27.9, 30.3, 30.5, 30.6, 30.8, 30.9, 31.2, 33.0 (CH_2), 52.3 (CH), 53.1 (OCH_3), 113.3 (C), 127.0, 129.3 (CH), 129.4 (C), 130.3 (CH), 134.3, 138.0, 143.6, 144.3 (C), 159.0 (C_{OH}), 173.8 (CO). IR (KBr): *v* = 3059, 3023 (w), 2952 (m), 2921 (s), 2852 (m), 1933 (w), 1752, 1703 (m), 1656 (s), 1598, 1493 (m), 1438 (s), 1377 (w), 1322, 1293, 1229 (m), 1201 (s), 1120, 1047, 1030 (m), 959, 903 (w), 841, 806, 746, 724 (m), 698 (s), 623, 615, 583 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{43}O_3$ $[M+H]^+$: 487.32067; found: 487.32048.

Benzyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (8c). Starting with



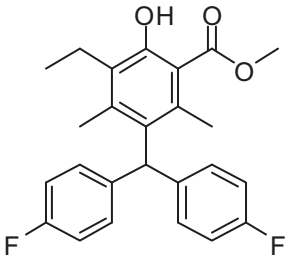
7b (0.564 g, 1.5 mmol) and **3a** (0.555 g, 1.65 mmol), **8c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless solid (0.467 g, 68%), mp. 112-113 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 2.12 (s, 3 H, CH_3), 5.33 (s, 2 H, OCH_2), 5.87 (s, 1 H, CH), 6.70 (s, 1 H, ArH), 6.89-7.01 (m, 8 H, ArH), 7.30-7.37 (m, 5 H, ArH), 10.56 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 21.3, 22.7 (CH_3), 49.3 (CH), 67.4 (OCH_2), 112.8 (C), 114.6 (d, $^{2}J_{C,F}$ = 21.2 Hz, CH), 118.5 (CH), 128.5 (d, $^{3}J_{C,F}$ = 7.7 Hz, CH), 128.6 (C), 137.5 (d, $^{4}J_{C,F}$ = 3.1 Hz, C_{Ar}), 140.2, 145.2 (C_{Ar}), 160.1 (C_{OH}), 161.1 (d, $^{1}J_{C,F}$ = 245.1 Hz, C_{Ar}), 171.1 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -116.8. IR (KBr): *v* = 3070, 3035, 2979, 2931, 2884 (w), 1649 (s), 1598, 1574 (m), 1500 (s), 1426, 1381, 1316, 1292 (m), 1217, 1175 (s), 1145, 1067, 1029, 1012, 953, 860, 829, 817 (m), 794, 748, 698 (s), 647, 598, 528 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 458 (M^+, 18), 350 (34), 91 (100). HRMS (ESI): calcd. for $C_{29}H_{25}O_3F_2$ $[M+H]^+$: 459.17663; found: 459.17593.

Ethyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4,5-trimethylbenzoate (8d). Starting



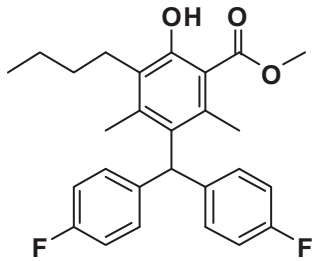
with **7b** (0.564 g, 1.5 mmol) and **3c** (0.476 g, 1.65 mmol), **8d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.239 g, 39%), mp. 63-64 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (t, ^{3}J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 1.88 (s, 3 H, CH_3), 2.10 (s, 6 H, 2xCH_3), 4.32 (q = ^{3}J = 7.1 Hz, 2 H, $\mathit{OCH_2}CH_3$), 5.90 (s, 1 H, CH), 6.86-6.99 (m, 8 H, ArH), 10.83 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 12.2, 14.1, 19.0, 21.0 (CH_3), 49.7 (OCH_3), 61.5 ($O\mathit{CH_2}CH_3$), 112.3 (C), 115.0 (d, $^{2}J_{C,F}$ = 21.0 Hz, CH), 123.5 (C), 130.4 (d, $^{3}J_{C,F}$ = 7.8 Hz, CH), 132.5, 136.5 (C), 137.5 (d, $^{4}J_{C,F}$ = 3.2 Hz, C), 143.2 (C), 159.5 (C_{OH}), 160.4 (d, $^{1}J_{C,F}$ = 244.6 Hz, C), 172.0 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -117.0. IR (KBr): *v* = 3070, 3035, 2979, 2931, 2884 (w), 1649 (s), 1598, 1574 (m), 1500 (s), 1426, 1381, 1316, 1292 (m), 1217, 1175 (s), 1145, 1067, 1029, 1012, 953 , 860, 829, 817 (m), 794, 748, 698 (s), 647, 598, 528 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 410 (M^+, 30), 365 (29), 364 (100), 336 (22), 321 (28), 241 (18), 240 (10), 203 (26), 202 (11), 201 (25), 197 (11), 196 (11), 183 (32), 109 (16), 91 (14), 44 (21), 43 (18). HRMS (ESI): calcd. for $C_{25}H_{24}O_3F_2$ $[M]^+$: 410.16880; found: 410.169602.

Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-ethylbenzoate (8e).



Starting with **7b** (0.564 g, 1.5 mmol) and **3d** (0.476 g, 1.65 mmol), **8e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.252 g, 41%), mp. 82-83 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (t, ^{3}J = 7.4 Hz, 3 H, CH_2CH_3), 1.94 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 2.63 (q, ^{3}J = 7.4 Hz, 2 H, CH_2CH_3), 3.82 (s, 3 H, OCH_3), 5.90 (s, 1 H, CH), 6.86-6.99 (m, 8 H, ArH), 10.73 (s, 1 H, OH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -117.0. ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 12.3, 16.9, 18.9 (CH_3), 20.2 (CH_2CH_3), 48.8 (CH), 51.0 (OCH_3), 111.3 (C), 114.0 (d, $^{2}J_{C,F}$ = 21.2 Hz, CH), 128.5 (C), 129.4 (d, $^{3}J_{C,F}$ = 7.7 Hz, CH), 131.7, 135.7 (C), 136.8 (d, $^{4}J_{C,F}$ = 3.2 Hz, C), 141.6 (C), 156.9 (C_{OH}), 161.1 (d, $^{1}J_{C,F}$ = 244.7 Hz, C), 171.4 (CO). IR (neat, cm^{-1}): 2961, 2929, 2873, 2852, 1732 (w), 1656 (s), 1599 (m), 1563 (w), 1504 (s), 1439, 1398, 1350, 1293 (m), 1258 (s), 1223, 1201 (m), 1157 (s), 1096 (m), 1014 (s), 953, 861, 832 (m), 795, 699 (s), 643 (m), 601 (w), 567, 530 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 410 (M^+, 46), 380 (10), 379 (32), 378 (100), 377 (16), 363 (14), 353 (21), 352 (67), 351 (10), 350 (31), 338 (24), 337 (86), 336 (12), 335 (25), 324 (16), 323 (45), 321 (18), 257 (14), 241 (12), 227 (17), 226 (14), 203 (15), 202 (20), 201 (24), 196 (15), 189 (10), 183 (25), 109 (12). HRMS (EI): calcd. for $C_{25}H_{24}O_3F_2$ $[M]^+$: 410.16880; found: 410.169602.

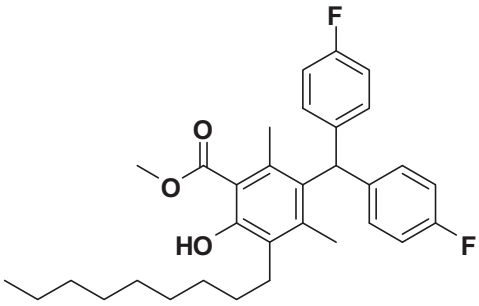
Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-butylbenzoate (8f).



Starting with **7b** (0.564 g, 1.5 mmol) and **3e** (0.521 g, 1.65 mmol), **8f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.348 g, 53%), mp. 116-117 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, ^{3}J = 6.9 Hz, 3 H, $(CH_2)_2CH_2CH_3$), 1.21-1.28 (m, 4 H, 2xCH_2), 1.83 (s, 3 H, CH_3), 1.92 (s, 3 H, CH_3), 2.49 (t, ^{3}J = 7.3 Hz, 2 H, $CH_2(CH_2)_2CH_3$), 3.71 (s, 3 H, OCH_3), 5.79 (s, 1 H, CH), 6.75-6.88 (m, 8 H, ArH), 10.62 (s, 1 H, OH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -117.0. ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 15.2, 18.2, 21.2 (CH_3), 23.1, 26.5, 31.3 (CH_2), 49.8 (CH), 52.08 (OCH_3), 113.5 (C), 116.1 (d, $^{2}J_{C,F}$ = 21.2 Hz, CH), 129.6 (C), 131.5 (d, $^{3}J_{C,F}$ = 7.7 Hz, CH), 133.9, 137.8 (C), 139.1 (d, $^{4}J_{C,F}$ = 3.2 Hz, C), 144.0 (C), 159.2 (C_{OH}), 162.3 (d, $^{1}J_{C,F}$ = 244.7 Hz, C_{Ar}), 173.6 (CO). IR (KBr): *v* = 3034, 2954, 2927, 2871, 2858 (w), 1737, 1655 (m), 1504 (s), 1438, 1397, 1350, 1293 (m), 1223, 1200 (s), 1157 (s), 1115, 1044, 1015, 881, 832, 807 (m), 796, 731 (s), 670, 639, 603 (m), 567 (s), 529 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 438 (M^+ 100), 407 (28),

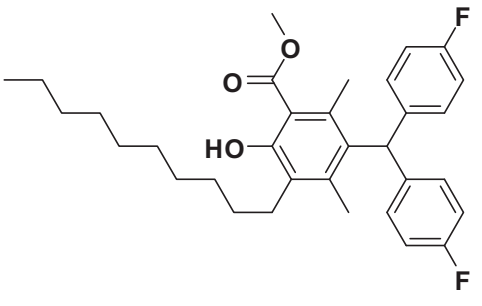
406 (72), 389 (24), 378 (18), 377 (16), 365 (10), 364 (40), 363 (28), 321 (13), 297 (15), 203 (21), 201 (12), 183 (14), 109 (12). HRMS (ESI): calcd. for $C_{27}H_{29}O_3F_2$ $[M+H]^+$: 439.20065; found: 439.20975.

Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-nonylbenzoate (8g).



Starting with **7b** (0.564 g, 1.5 mmol) and **3f** (0.614 g, 1.65 mmol), **8g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.402 g, 53%), mp. 147-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (t, ^3J = 7.0 Hz, 3 H, $(CH_2)_7CH_2CH_3$), 1.09-1.16 (m, 12 H, 6xCH_2), 1.27-1.31 (m, 2 H, CH_2), 1.82 (s, 3 H, CH_3), 1.92 (s, 3 H, CH_3), 2.48 (t, ^3J = 7.1 Hz, 2 H, $CH_2(CH_2)_7CH_3$), 3.71 (s, 3 H, OCH_3), 5.79 (s, 1 H, CH), 6.75-6.88 (m, 8 H, ArH), 10.67 (s, 1 H, OH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -117.1. ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 15.2, 23.8, 27.9 (CH_3) 28.3, 30.3, 30.5, 30.7, 30.8, 30.9, 31.2, 33.0 (CH_2), 51.0 (CH), 53.2 (OCH_3), 113.5 (C), 116.1 (d, $^2J_{C,F}$ = 21.2 Hz, CH), 129.6 (C), 131.5 (d, $^3J_{C,F}$ = 7.7 Hz, CH), 133.9, 137.8 (C), 139.1 (d, $^4J_{C,F}$ = 3.4 Hz, C), 143.9 (C_{Ar}), 159.2 (C_{OH}), 162.3 (d, $^1J_{C,F}$ = 244.7 Hz, C), 173.6 (CO). IR (KBr): ν = 2952, 2922, 2853, 1751, 1654 (m), 1558 (s), 1506, 1446, 1351 (m), 1227, 1157 (s), 1148, 1030, 1016, 841, 798, 778, 721, 667 (m), 628 (w), 568, 530 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 508 (M^+ 100), 473 (18), 405 (16), 381 (20), 377 (18), 365 (19), 364 (51), 336 (14), 276 (13), 275 (76), 183 (10), 109 (16), 57 (13), 43 (14). HRMS (ESI): calcd. for $C_{32}H_{38}F_2O_3$ $[M+H]^+$: 509.2789; found: 509.2787.

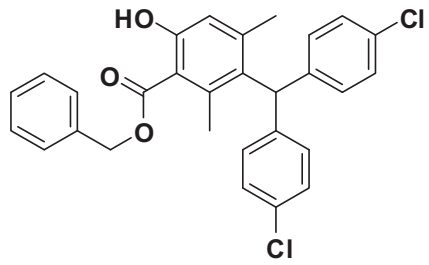
Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-decylbenzoate (8h).



Starting with **7b** (0.564 g, 1.5 mmol) and **3b**(0.661 g, 1.65 mmol), **8h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.429 g, 55%), mp. 161-162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, ^3J = 6.8 Hz, 3 H, $(CH_2)_8CH_2CH_3$), 1.08-1.12 (m, 14 H, 7xCH_2), 1.17-1.25 (m, 2 H, CH_2), 1.82 (s, 3 H, CH_3), 1.92 (s, 3 H, CH_3), 2.48 (t, ^3J = 7.2 Hz, 2 H, $CH_2(CH_2)_8CH_3$), 3.71 (s, 3 H, OCH_3), 5.78 (s, 1 H, ArH), 6.76-6.89 (m, 8 H, ArH), 10.61 (s, 1 H, OH). ^{19}F NMR (282 MHz,

$CDCl_3$): δ = -117.0. ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 15.2, 19.4, 22.4 (CH_3), 23.8, 27.9, 28.3, 30.3, 30.5, 30.7, 30.8, 31.2, 33.0 (CH_2), 51.0 (CH), 53.2 (OCH_3), 113.5 (C), 116.1 (d, $^2J_{C,F}$ = 21.1 Hz, CH), 129.6 (C), 131.5 (d, $^3J_{C,F}$ = 8.2 Hz, CH), 133.9, 137.8 (C), 139.1 (d, $^4J_{C,F}$ = 3.0 Hz, C), 144.0 (C), 159.2 (C_{OH}), 162.3 (d, $^1J_{C,F}$ = 245.0 Hz, C), 173.6 (CO). IR (KBr): *v* = 2952, 2922, 2853 (w), 1751, 1658, 1600 (m), 1505 (s), 1437, 1399, 1351, 1294 (m), 1225 (s), 1201 (m), 1157 (s), 1120, 1048, 1015, 907, 840 (m), 797 (s), 733, 671, 628 (m), 568 (s), 530 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 522 (100) (M^+ 100), 490 (83), 473 (17), 405 (15), 381 (23), 377 (14), 365 (11), 364 (51), 363 (34), 336 (13), 321 (11), 276 (12), 275 (80), 203 (59), 201 (10), 183 (11), 109 (14), 57 (10), 43 (13). HRMS (ESI): calcd. for $C_{33}H_{41}O_3F_2$ $[M+H]^+$: 523.29465; found: 522.29452.

Benzyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (8i). Starting with



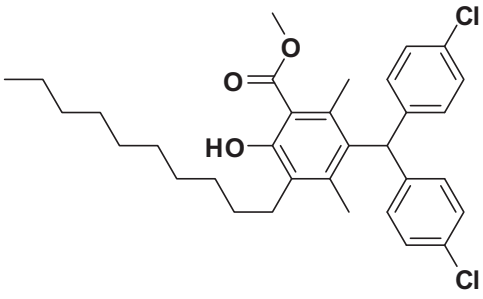
7c (0.614 g, 1.5 mmol) and **3a** (0.429 g, 1.65 mmol), **8i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.507 g, 69%), mp. 137-138 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 5.28 (s, 2 H, CH_2), 5.80 (s, 1 H, CH), 6.66 (ArH), 6.89-6.93 (m, 4 H, ArH), 7.14-7.18 (m, 4 H, ArH), 7.26-7.31 (m, 5 H, ArH), 10.54 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 21.4, 22.8 (CH_3), 49.6 (CH), 67.4 (OCH_2), 112.8 (C), 118.1, 128.2, 128.4, 128.6, 128.7, 130.3 (CH), 132.0, 133.2, 135.0, 140.1, 140.2, 145.2 (C), 160.2 (C_{OH}), 171.1 (CO). IR (neat, cm^{-1}): 3031, 2979, 2928, 1660 (s), 1598, 1567, 1487, 1462, 1387, 1341, 1270, 1257, 1231, 1208, 1144, 1089 (m), 1068 (s), 1012 (m), 949 (w), 838, 801, 749, 737 (m), 693 (s), 636, 583, 539 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 492 ([M, $^{37}Cl_2$, 39)]$^+$, 490 ([M, $^{35}Cl^{37}Cl$, 60)]$^+$, 488 ([M, $^{35}Cl_2$, 83)]$^+$, 401 (10), 399 (16), 385 (15), 384 (75), 383 (28), 382 (100), 165 (15), 92 (22), 91 (40), 57 (13), 54 (16), 43 (11). HRMS (EI): calcd. for $C_{29}H_{25}Cl_2O_3$ [(M^+, Cl^{35},Cl^{37}])$^+$: 490.10970; found: 490.110097.

Ethyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4,5-trimethylbenzoate (8j). Starting with **7c** (0.614 g, 1.5 mmol) and **3c** (0.476 g, 1.65 mmol), **8j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.275 g, 43%), mp. 111-112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, ^{3}J = 7.1 Hz, 3 H, OCH_2CH_3), 1.78 (s, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 2.00 (s, 3 H, CH_3), 4.22 (q, ^{3}J = 7.1 Hz, 2 H, OCH_2CH_3), 5.78 (s, 1 H, CH), 6.82-6.85 (m, 4 H, ArH), 7.06-7.09 (m, 4 H, ArH), 10.77 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 12.2, 14.1, 19.0, 21.0 (CH_3), 50.0 (CH), 61.6 (OCH_2CH_3), 112.3, 123.6 (C), 128.4, 130.3 (CH), 131.8, 136.5, 139.5, 140.5, 143.2 (C), 158.1 (C_{OH}), 171.9 (CO). IR (KBr): *v* = 3070, 3035, 2979, 2931, 2884 (w), 1649 (s), 1598, 1574 (m), 1500 (s), 1426, 1381, 1316, 1292 (m), 1217, 1175 (s), 1145, 1067, 1029, 1012, 953, 860, 829, 817 (m), 794, 748, 698 (s), 647, 598, 528 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 442 ([M, $^{37}Cl_2$, 10])$^{+}$, 440 ([M, $^{37}Cl^{35}Cl$, 13)]$^{+}$, 438 ([M, $^{35}Cl_2$, 56)]$^{+}$, 413 (21), 412 (63), 411 (30), 410 (100), 384 (16), 382 (28), 367 (13), 285 (12), 285 (12), 165 (15), 71 (11), 69 (12), 57 (14), 57 (11), 43 (16). HRMS (ESI^{-}): calcd. for $C_{25}H_{23}Cl_2O_3$ [(M^{+}, Cl^{35},Cl^{37}])$^{+}$: [M-1]$^{+}$: 441.10297; found: 441.10289.

Methyl 3-(bis(4-chlorophenyl)methyl)-5-ethyl-6-hydroxy-2,4-dimethylbenzoate (8k). Starting with **7c** (0.614 g, 1.5 mmol) and **3d** (0.476 g, 1.65 mmol), **8k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.278 g, 42%), mp. 127-128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, ^{3}J = 7.4 Hz, 3 H, OCH_2CH_3), 1.94 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 2.63 (q, ^{3}J = 7.4 Hz, 2 H, OCH_2CH_3), 3.82 (s, 3 H, OCH_3), 5.88 (s, 1 H, CH), 6.92-6.95 (m, 4 H, ArH), 7.16-7.19, (m, 4 H, ArH), 10.77 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 12.3, 17.0, 19.0, 20.3 (CH_3), 28.6 (CH_2), 49.1 (CH), 51.1 (OCH_3), 111.3 (C), 127.4 (CH), 128.6 (C), 129.3 (CH), 130.8, 131.1, 135.7, 139.5, 141.5 (C), 157.0 (C_{OH}), 171.4 (CO). IR (KBr): *v* = 2953, 2927, 2871, 2854, 1731 (w), 1656 (s), 1593, 1561 (m), 1489 (s), 1439, 1350, 1324, 1290, 1223, 1178, 1106, 1091 (m), 1013 (s), 877 (w), 807, 781, 705, 653 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 446 ([M, $^{37}Cl_2$, 18]$^{+}$), 444 ([M, $^{35}Cl^{37}Cl$, 27]$^{+}$), 442 ([M, $^{35}Cl_2$, 42])$^{+}$, 414 (10), 413 (17), 412 (63), 411 (31), 410 (100), 384 (17), 382 (27), 367 (12), 285 (13), 285 (13), 165 (14), 71 (10), 69 (10), 57 (16), 57 (10), 43 (17). HRMS (EI): calcd. for $C_{24}H_{25}Cl_2O_3$ [(M^{+}, Cl^{35},Cl^{35}]):

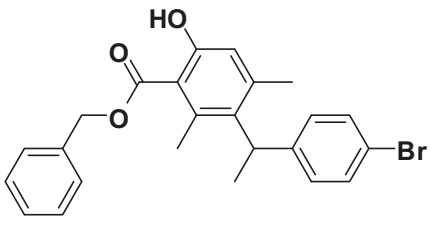
442.10970; found: 442.110226, calcd. for $C_{24}H_{25}Cl_2O_3$ [(M^+, Cl^{35},Cl^{37}]): 444.10675; found: 444.107921.

Methyl 3-(bis(4-chlorophenyl)methyl)-5-decyl-6-hydroxy-2,4-dimethylbenzoate (8l).



Starting with **7c** (0.614 g, 1.5 mmol) and **3b** (0.661 g, 1.65 mmol), **8l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.478 g, 57%), mp. 141-142 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (t, ^3J = 6.9 Hz, 3 H, $CH_2(CH_2)_8CH_3$), 1.03-1.08 (m, 14 H, 7xCH_2), 1.23-1.30 (m, 2 H, CH_2), 1.82 (s, 3 H, CH_3), 1.91 (s, 3 H, CH_3), 2.48 (t, ^3J = 7.0 Hz, 2 H, $CH_2(CH_2)_8CH_3$), 3.71 (s, 3 H, OCH_3), 5.77 (s, 1 H, CH), 6.81-6.84 (m, 4 H, ArH), 7.05-7.08 (m, 4 H, ArH), 10.65 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 15.2, 19.4, 22.5 (CH_3), 23.8, 28.0, 28.3, 30.3, 30.5, 31.2 (CH_2), 51.3 (CH), 53.2 (OCH_3), 113.5 (C), 129.6, 131.5 (CH), 133.0, 133.3, 137.8, 141.7, 144.0 (C), 159.3 (C_{OH}), 173.6 (CO). IR (KBr): *v* = 2952, 2922, 2852, 1933 (w), 1745, 1702 (m), 1658 (s), 1594, 1562, 1489, 1455, 1437 (m), 1377 (w), 1323, 1278, 1244 (m), 1235 (s), 1201, 1178 (m), 1120 (w), 1091 (m), 1013 (m), 906 (w), 840 (s), 807, 766, 732, 627, 578 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 558 ([M, $^{37}Cl_2$, 13]$^+$), 556 ([M, $^{37}Cl^{35}Cl$, 47]$^+$), 554 ([M, $^{35}Cl^{35}Cl$, 59]$^+$), 552 ([M, $^{35}Cl_2$, 74]$^+$), 526 (12), 525 (22), 524 (62), 523 (40), 522 (89), 521 (10), 509 (11), 507 (27), 505 (19), 457 (10), 439 (16), 437 (22), 423 (10), 411 (12), 409 (17), 40 (10) 399 (31) 398 (45) 397 (100), 396 (45), 395 (30), 370 (13), 369 (15) 368 (19), 355 (12), 353 (10), 333 (10), 285 (13), 257 (14), 256 (15), 243 (17), 237 (21), 235 (32), 201 (14), 199 (12), 180 (10), 178 (10), 166 (10), 165 (30), 139 (12), 127 (10), 125 (24), 97 (14), 95 (1), 85 (12), 83 (16), 81 (13), 71 (17), 69 (20), 67 (12), 57 (31), 56 (11), 55 (29), 45 (12), 44 (57) 43 (52) 41 (29). HRMS (EI): calcd. for $C_{33}H_{40}Cl_2O_3$ [(M^+, Cl^{35},Cl^{35}]): 554.23490; found: 554.23490, calcd. for $C_{33}H_{40}Cl_2O_3$ [(M^+, Cl^{35},Cl^{37}]): 556.23195; found: 556.233268.

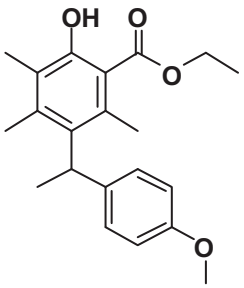
Benzyl 3-(1-(4-bromophenyl)ethyl)-6-hydroxy-2,4-dimethylbenzoate (8m).



Starting with **7d** (0.535 g, 1.5 mmol) and **3a** (0.429 g, 1.65 mmol), **8m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.473 g, 72%), mp. 147-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.53 (d, ^3J = 7.2 Hz,

3 H, CH_3), 2.10 (s, 3 H, CH_3), 2.12 (s, 3 H, CH_3), 4.45 (q, ^3J, 7.2 Hz, 1 H, CH), 5.28 (s, 2 H, OCH_2), 6.63 (s, 1 H, ArH), 6.89-6.92 (m, 2 H, ArH), 7.26-7.30 (m, 7 H, ArH), 10.45 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 16.3, 19.3, 21.1 (CH_3), 36.2 (CH), 66.3 (CH_2), 111.7, 116.7 (CH), 118.1 (C), 128.1, 128.5, 128.6, 128.7, 131.2 (CH), 134.1, 138.2, 143.3, 143.4 (C), 158.7 (C_{OH}), 170.0 (CO). IR (KBr): ν = 3063, 3034, 2941, 2880 (w), 1650 (s), 1596, 1567, 1482, 1463, 1453, 1383, 1343, 1328, 1291 (m), 1222 (s), 1162, 1069, 1017 (m), 1005 (s), 909, 866, 843 (w) 817, 749, 733 (m), 698 (s), 644, 582, 546 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 440 ([M^+, ^{81}Br, 3]), 438 ([M^+, ^{79}Br, 3]), 291 (10), 289 (11), 195 (10), 92 (13), 91 (100), 77 (10), 65 (12), 44 (12). HRMS (EI): calcd. for $C_{24}H_{23}O_3Br$ [(M^+, Br^{79}])$^+$: 438.08251; found: 438.082911, calcd. for $C_{24}H_{23}O_3Br$ [(M^+, Br^{79},Br^{81}])$^+$: 440.08046; found: 440.081149.

Ethyl 6-hydroxy-3-(1-(4-methoxyphenyl)ethyl)-2,4-dimethylbenzoate (8n). Starting with



7e (0.462 g, 1.5 mmol) and **3e** (0.452 g, 1.65 mmol), **8n** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.225 g, 46%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.53 (d, ^3J = 7.2 Hz, 3 H, CH_3), 2.09 (s, 3 H, CH_3), 2.14 (s, 3 H, CH_3), 3.67 (s, 3 H, OCH_3), 4.28 (q, ^3J, 7.1 Hz, 2 H, OCH_2CH_3), 4.48 (q, ^3J, 7.2 Hz, 1 H, CH), 6.59 (s, 1 H, CH), 6.69-6.72 (m, 2H, ArH), 6.92-6.95 (m, 2H, ArH), 10.44 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 14.1, 17.5, 20.0, 22.1 (CH_3), 36.8 (CH), 55.2 (OCH_3), 112.9 (C), 113.6 (CH), 117.5 (C), 127.31 (CH), 135.8, 137.4, 139.2, 144.1, 157.3 (C), 159.3 (C_{OH}), 171.5 (CO). IR (KBr): ν = 2975, 2935, 2834, 1736 (w), 1655 (s), 1607, 1568 (m), 1509 (s), 1462, 1393, 1370, 1299 (m), 1242, 1224 (s), 1117, 1153, 1074, 1030 (m), 953, 859 (w), 830, 755, 743, 607, 562 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 328 (M^+, 40), 313 (21), 283 (16), 282 (45), 268 (18), 267 (100). HRMS (EI): calcd. for $C_{20}H_{24}O_4$ [M]$^+$: 328.16691; found: 328.167020.

11.2 Cyclization *versus* Elimination Reactions of 5-Aryl-5-hydroxy-1,3-diones. One-pot Synthesis of 6-Aryl-2,3-dihydro-4*H*-pyran-4-ones

11.2.1 Synthesis of 2,3-dihydro-4*H*-pyran-4-ones (11a-o)*:* A THF Solution of LDA (12.5 mmol) was prepared by addition of *n*BuLi (5 ml, 12.5 mmol, 2.5 M solution in hexanes) to a

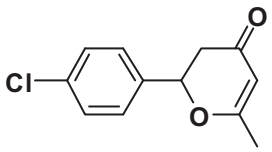
THF solution (15 ml) of diisopropylamine (1.26 g, 12.5 mmol) at 0°C. After stiring for 1 h, the solution was cooled to -78 °C and 2,4-pentadion (0.50 g, 5.0 mmol) was added. After stirring for 1 h at -78 °C, aldehyde (5.0 mmol) was added and the solution was allowed to warm to 20 °C within 24 h. Hydrochloric acid (10%, 15 mL) was added and the mixture was allowed to stand for 15 min. The reaction mixture was extracted with ethyl acetate (3 x 30mL) and washed with a an aqueous solution of NaCl, dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate = 2:1) to give **13a-o**.

2-(2-Chlorophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (11a). Starting with a THF solution of LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **10a** (0.70 g, 5.0 mmol) in THF (15 mL), **13a** was isolated as a colourless viscous oil (0.72 g, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 2.58 (dd, *J* = 13.7 Hz, 1 H, H_A), 2.71 (dd, *J* = 4.0, 16.8 Hz, 1H, H_B), 5.44 (s, 1 H, CH_{Olf}), 5.76 (dd, *J* = 4.0, 13.7 Hz, 1 H, CH), 7.28 (t, *J* = 7.4 Hz, 1 H, ArH), 7.32 (d, *J* = 8.6 Hz, 1 H, ArH), 7.36 (t, *J* = 7.5 Hz, 1 H, ArH), 7.59 (d, *J* = 7.5 Hz, 1 H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.0 (CH_3), 41.1 (CH_2), 77.7 (CH), 105.3 (CH_{Olf}), 127.2, 127.3, 127.6, 127.8 (CH), 131.7, 136.1 (C), 174.2 (C_{Olf}), 191.7 (CO). IR (KBr): *v* = 3411, 3066, 2918, 1706 (w), 1604, 1575 (s), 1471, 1437, 1398, 1358, 1287, 1232 (m), 1032, 752 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 224 ([M, ^{37}Cl, 1)]$^+$, 222 ([M, ^{35}Cl, 3)]$^+$, 187 (20), 181 (10), 179 (26), 140 (33), 139 (11), 138 (100), 103 (38), 102 (10), 77 (13). HRMS (EI): calcd. for $C_{12}H_{11}O_2Cl$ [(M^+, Cl^{35}])$^+$: 222.04421; found: 222.044214.

2-(3-Chlorophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (11b). Starting with a THF solution of LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **10b** (0.70 g, 5.0 mmol) in THF (15 mL), **11b** was isolated as a solid (0.78 g, 70%), mp 54-55 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.02 (s, 3 H, CH_3), 2.52 (dd, *J* = 3.5, 16.8 Hz, 1 H, H_A), 2.74 (dd, *J* = 13.9 Hz, 1 H, H_B), 5.28 (dd, *J* = 3.6, 13.9 Hz, 1 H, CH), 5.37 (s, 1 H, CH_{Olf}), 7.27 (t, *J* = 6.7 Hz, 1 H, ArH), 7.29 (d, *J* = 8.7 Hz, 1H, ArH), 7.32 (d, *J* = 8.4 Hz, 1 H, ArH), 7. 35 (s, 1 H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.0 (CH_3), 42.3 (CH_2), 79.9 (CH), 105.4 (CH_{Olf}), 124.1, 126.3, 128.9, 130.1 (CH), 134.7, 140.2 (C), 174.0 (C_{Olf}), 191.7 (CO). IR (KBr): *v* = 3399, 3066, 2958, 2921,

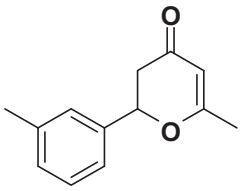
2853, 1714 (w), 1663, 1607 (s), 1573, 1431 (m), 1391, 1325 (s), 1237, 1159, 1064, 1002, 879, 783, 690, 582 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 224 ([M, ^{37}Cl, 2)]$^+$, 222 ([M, ^{35}Cl, 1)]$^+$, 204 (10), 179 (24), 140 (32), 139 (10), 138 (100), 103 (33), 77 (13). HRMS (EI): calcd. for $C_{12}H_{11}O_2Cl$ [(M^+, Cl^{35}])$^+$: 222.04421; found: 222.043856.

2-(4-Chlorophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (11c). Starting with a THF solution of



LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **10c** (0.70 g, 5.0 mmol) in THF (15 mL), **11c** was isolated as a colourless crystalline solid (0.84 g, 76%), mp 81-82 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.09 (s, 3 H, CH_3), 2.59 (dd, *J* = 3.7, 16.7 Hz, 1 H, H_A), 2.77 (dd, *J* = 14.0 Hz, 1 H, H_B), 5.37 (dd, *J* = 3.8, 14.0 Hz, 1 H, CH), 5.45 (s, 1 H, CH_{Olf}), 7.33-7.37 (m, 2 H, CH), 7.39-7.42 (m, 2 H, CH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.0 (CH_3), 42.3 (CH_2), 80.0 (CH), 105.3 (CH_{Olf}), 127.5, 129.0 (CH), 134.6, 137.7 (C), 174.0 (C_{Olf}), 191.8 (CO). IR (KBr): *v* = 3037, 2965, 2808, 2889, 1714 (w), 1600 (s), 1489, 1392, 1245, 1087, 1001 (m), 822 (s), 652, 547 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 224 ([M, ^{37}Cl, 2)]$^+$, 222 ([M, ^{35}Cl, 3)]$^+$, 204 (11), 179 (24), 140 (33), 139 (10), 138 (100), 103 (23), 77 (10). HRMS (EI): calcd. for $C_{12}H_{11}O_2Cl$ ([M^+, ^{35}Cl]): 222.04421; found: 222.044338.

6-Methyl-2-m-tolyl-2*H*-pyran-4(3*H*)-one (**11d**). Starting with a THF solution of LDA (12.5



mmol), **9a** (0.50 g, 5.0 mmol) and **10d** (0.60 g, 5 mmol) in THF (15 mL), **11d** was isolated as a colourless oil (0.77 g, 76%). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.08 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_{3Ar}), 2.53 (dd, *J* = 3.5, 16.8 Hz, 1 H, H_A), 2.78 (dd, *J* = 14.1 Hz, 1 H, H_B), 5.33 (dd, *J* = 3.5, 14.1 Hz, 1 H, CH), 5.42 (s, 1 H, CH_{Olf}), 7.17 (d, *J* = 7.8 Hz, 1 H, ArH), 7.20 (d, *J* = 7.2 Hz, 1 H, ArH), 7.22 (s, 1 H, ArH), 7.29 (t, *J* = 7.5 Hz, 1 H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.1 (CH_3), 21.4 (CH_{3Ar}), 42.3 (CH_2), 80.9 (CH), 105.1 (CH_{Olf}), 123.2, 126.9, 128.7, 129.5 (CH), 138.1, 138.5 (C), 174.2 (C_{Olf}), 192.2 (CO). IR (KBr): *v* = 3317, 3028, 2918, 2734, 2610 (w), 1664, 1604 (s), 1490, 1435 (w), 1359, 1256, 1183 (m), 1095 (w), 1025, 951, 886, 808, 759, 699 (m), 660, 618, 551 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 202 (M^+, 3), 184 (14), 160 (15), 159 (41), 119 (10), 118 (100), 117 (60), 115 (17), 91 (17). HRMS (EI): calcd. for $C_{13}H_{14}O_2$ $[M]^+$: 202.09883; found: 202.098878. Anal. Calcd. $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.01; H, 6.794.

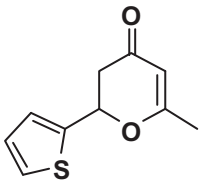
2-(2,3-Dimethoxyphenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (**11e**). Starting with a THF solution of LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **10e** (0.83 g, 5.0 mmol) in THF (15 mL), **11e** was isolated as a solid (0.91 g, 73%), mp 86-87 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 2.49 (dd, *J* = 3.5, 16.8 Hz, 1 H, H_A), 2.66 (dd, *J* = 14.3, 1 H, H_B), 3.79 (s, 3 H, OCH_{3Ar}), 3.81 (s, 3 H, OCH_{3Ar}), 5.45 (s, 1 H, CH_{Olf}), 5.65 (dd, *J* = 3.5, 14.3 Hz, 1 H, CH), 6.77 (d, *J* = 7.7 Hz, 1 H, ArH), 7.01 (t, *J* = 7.4 Hz, 1 H, ArH), 7.8 (d, *J* = 7.8, 1 H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.1 (CH_3), 41.7 (CH_2), 55.8, 60.0 (OCH_{3Ar}), 76.1 (CH), 105.0 (CH_{Olf}), 111.6, 118.3, 124.3 (CH), 132.0, 146.2, 152.3 (C_{Ar}), 174.5 (C_{Olf}), 192.7 (CO). IR (KBr): *v* = 2962, 2937, 2835, 1721, 1664 (w), 1602, 1586, 1478, 1429, 1395, 1302, 1273, 1219, 1082 (m), 999 (s), 927, 856, 785, 747, 629, 558 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 248 (M^+, 37), 230 (19), 217 (30), 206 (47), 205 (51), 175 (21), 174 (20), 164 (78), 150 (10), 149 (100), 121 (75), 91 (29), 78 (20), 77 (21). HRMS (ESI-TOF): calcd. for $C_{14}H_{16}O_4$ $[M+H]^+$: 249.11214; found: 249.1118. C, 50.19; Anal. Calcd. $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.70; H, 7.19.

2-(3-Hydroxyhenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (**11f**). Starting with a THF solution of LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **10f** (0.61 g, 5.0 mmol) in THF (15 mL), **11f** was isolated as a solid (0.68 g, 67%), mp 140-142 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.10 (s, 3 H, CH3), 2.55 (dd, *J* = 3.7, 16.9 Hz, 1 H, H_A), 2.81 (dd, *J* = 13.8 Hz, 1 H, H_B), 5.40 (dd, *J* = 3.6, 13.8 Hz, CH, 1 H), 5.46 (s, 1 H, CH_{Olf}), 6.78 (t, *J* = 7.4 Hz, 1 H, ArH), 6.89 (d, *J* = 7.8 Hz, 1 H, ArH), 6.91 (d, *J* = 7.3 Hz, 1 H, ArH), 7.24 (s, 1 H, ArH), 9.46 (b.s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 21.1 (CH_3), 42.9 (CH_2), 82.1 (CH), 105.3 (CH_{Olf}), 114.1, 116.6, 118.3, 130.8 (CH), 141.2, 158.9 (C_{Ar}), 177.5 (C_{Olf}), 195.4 (CO). IR (KBr): *v* = 3052, 2957 (m), 2829, 2600 (w), 1633, 1596 (m), 1580, 1574 (s), 1484, 1397 (m), 1360, 1220 (s), 1175, 1025, 1004, 939, 786, 697, 529 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 204 (M^+, 12), 186 (13), 161 (24), 120 (100), 91 (21). HRMS (EI): calcd. for $C_{12}H_{12}O_3$ $[M]^+$: 204.07810; found: 204.078399.

2-(4-Nitrophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (**11g**). Starting with a THF solution of LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **10g** (0.75 g, 5.0 mmol) in THF (15 mL), **11g** was isolated as a colourless crystalline solid

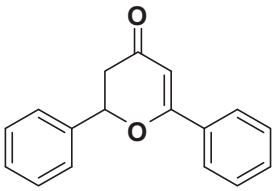
(0.70 g, 60%), mp 128-130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.05 (s, 3 H, CH_3), 2.58 (dd, *J* = 4.4, 16.7 Hz, 1 H_A), 2.67 (dd, *J* = 13.1 Hz, 1 H_B), 5.62 (s, 1 H, CH_{Olf}), 5.45 (dd, *J* = 4.5, 13.1 Hz, 1 H, CH), 7.51-7.54 (m, 2 H, ArH), 8.20-8.23 (m, 2 H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.0, (CH_3), 42.3 (CH_2), 79.4 (CH), 105.7 (CH_{Olf}), 124.1, 126.7 (CH), 145.2, 148.0 (C), 173.7 (C_{Olf}), 190.9 (CO). IR (KBr): *v* = 3074, 2905, 2847 (w), 1721 (m), 1651, 1598, 1512 (s), 1494, 1436, 1396 (m), 1342, 1330 (s), 1296, 1234, 1184, 1161, 1104, 1071, 1030, 1009, 950, 899 (m), 850, 833 (s), 747, 697, 682, 648 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 233 (M^+, 10), 200 (11), 191 (23), 174 (15), 149 (100), 119 (41), 103 (32), 102 (14), 91 (28), 77 (42), 69 (10), 51 (11), 43 (19). HRMS HRMS (EI): calcd. for $C_{12}H_{11}O_4N$ $[M]^+$: 233.06826; found: 233.067763.

6-Phenyl-2-(thiophen-2-yl)-2*H*-pyran-4(3*H*)-one (**11h**). Starting with a THF solution of



LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **10h** (0.56 g, 5.0 mmol) in THF (15 mL), **11h** was isolated as a redish viscous oil (0.80 g, 82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 2.77 (dd, *J* = 4.0, 16.7 Hz, 1 H, H_A), 2.93 (dd, *J* = 12.6 Hz, 1 H, H_B), 5.44 (s, 1 H, CH), 5.64 (dd, *J* = 4.0, 12.6 Hz, 1 H, CH), 7.04 (d, *J* = 3.5 Hz, 1 H, $CH_{thienyl}$), 7.12 (t, *J* = 3.5 Hz, 1 H, $CH_{thienyl}$), 7.39 (d, *J* = 5.0 Hz, 1 H, $CH_{thienyl}$). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.1 (CH_3), 42.1 (CH_2), 76.2 (CH), 105.4 (CH), 126.1, 126.6, 126.9 ($CH_{thienyl}$), 140.8 ($C_{thienyl}$), 173.7 (C_{Olf}), 191.5 (CO). IR (KBr): *v* = 3139, 3127, 3078, 2914 (w), 1657 (m), 1604 (s), 1503, 1439 (m), 1387, 1322, 1183, 1147, 1000 (s), 900, 864, 841, 820 (m), 741 (s), 683, 597 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 194 (M^+, 7), 176 (16), 161 (10), 151 (12), 110 (100), 109 (13). HRMS (EI): calcd. for $C_{10}H_{10}O_2S$ $[M]^+$: 194.03960; found: 194.039943.

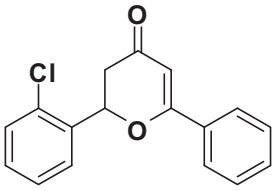
2-(Phenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (**11i**). Starting with a THF solution of LDA (12.5



mmol), **9b** (0.81 g, 5.0 mmol) and **10i** (0.53 g, 5.0 mmol) in THF (15 mL), **11i** was isolated as a colourless crystalline solid (0.97 g, 78%), mp 93-94 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.69 (dd, *J* = 3.4, 16.6 Hz, 1 H, H_A), 3.02 (dd, *J* = 13.6 Hz, 1 H, H_B), 5.75 (dd, *J* = 3.4, 13.6 Hz, 1 H, CH), 6.21 (s, 1 H, CH_{Olf}), 7.40-7.88 (m, 10 H, Ph). ^{13}C NMR (75 MHz, DMSO-d_6): = 41.8 (CH_2), 80.1 (CH), 101.9 (CH_{Olf}), 126.4, 126.5, 128.54, 128.59, 128.8, 131.7 (CH), 132.2, 138.5 (C), 168.7 (C_{Olf}), 192.0 (CO). IR (KBr): *v* = 3292, 3064, 3029, 2896

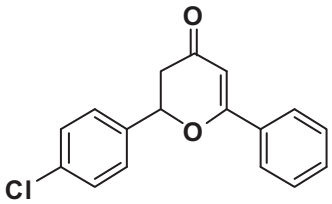
(w), 1710, 1650 (s), 1592, 1570, 1490, 1382, 1315, 1245, 1178, 1046, 937, 854 (m), 762, 692 (s), 664, 614, 569 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 250 (M^+, 6), 232 (11), 145 (25), 144 (17), 105 (40), 104 (100), 103 (18), 78 (16), 77 (23). HRMS (EI): calcd. for $C_{17}H_{14}O_2$ $[M]^+$: 250.09883; found: 250.099148. Anal. Calcd. $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.56; H, 5.72.

2-(2-Chlorophenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (**11j**). Starting with a THF solution of



LDA (12.5 mmol), **9b** (0.81 g, 5.0 mmol) and **10a** (0.70 g, 5.0 mmol) in THF (15 mL), **11j** was isolated as a colourless crystalline solid (0.88 g, 62%), mp 96-98 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.68 (dd, *J* = 3.3, 16.7 Hz, 1 H, H_A), 3.07 (dd, *J* = 14.0 Hz, 1 H, H_B), 5.95 (dd, 1 H, *J* = 3.2, 14.0 Hz, CH), 6.25 (s, 1 H, CH_{Olf}), 7.47-7.89 (m, 9 H, ArH). ^{13}C NMR (62.8 MHz, DMSO-d_6): δ = 40.2 (CH_2), 77.2 (CH), 101.9 (CH_{Olf}), 126.4, 127.7, 128.1, 128.8, 129.7, 130.4, 131.8 (CH), 131.9, 132.0, 135.3 (C), 168.8 (C_{Olf}), 191.6 (CO). IR (KBr): *v* = 3282, 3063, 3035, 2968, 2916 (w), 1651, 1595 (s), 1570, 1450 (m), 1378, 1327 (s), 1293, 1233, 1131, 1071, 993, 941, 856, 805, 772 (m), 754, 685, 669 (s), 616, 567, 540 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 286 ([M, ^{37}Cl, 3]$^+$), 284 ([M, ^{35}Cl, 9]$^+$), 249 (22), 179 (10), 178 (10), 140 (34), 139 (10), 138 (100), 105 (48), 103 (35), 102 (11), 77 (29). HRMS (EI): calcd. for $C_{17}H_{13}ClO_2$ [M^+, ^{35}Cl]: 284.05986; found: 284.059945. Anal. Calcd. $C_{17}H_{13}O_2Cl$: C, 71.71; H, 4.60. Found: C, 71.74; H, 4.62.

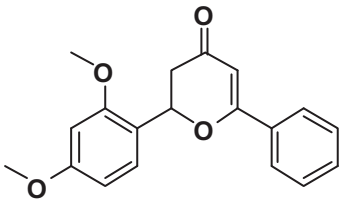
2-(4-Chlorophenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (11k). Starting with a THF solution of



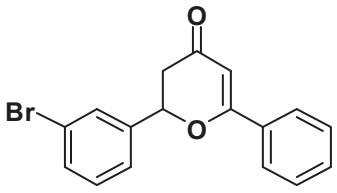
LDA (12.5 mmol), **9b** (0.81 g, 5.0 mmol) and **10c** (0.70 g, 5.0 mmol) in THF (15 mL), **11k** was isolated as a colourless crystalline solid (0.94 g, 82%), mp 90-92 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.72 (dd, *J* = 3.4, 16.6 Hz, 1 H, H_A), 3.05 (dd, *J* = 13.6 Hz, 1 H, H_B), 5.78 (dd, 1 H, *J* = 3.4, 13.6, CH), 6.21 (s, 1 H, CH_{Olf}), 7.35-7.56 (m, 5 H, ArH), 7.62-7.65 (m, 2 H, ArH), 7.84-7.88 (m, 2 H, ArH). ^{13}C NMR (62 MHz, DMSO-d_6): δ = 41.6 (CH_2), 79.3 (CH), 101.9 (CH_{Olf}), 126.4, 128.4, 128.5, 128.8, 131.7 (CH), 132.1, 133.1, 137.5 (C), 168.6 (C_{Olf}), 191.8 (CO). IR (KBr): *v* = 3281, 3089, 3058, 2965, 2895 (w), 1651, 1595, 1568, 1492 (s), 1449, 1376, 1328, 1293, 1215, 1160, 1089, 993, 855, 835, 804 (m), 768, 681, 664 (s), 615, 566, 540 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 286 ([M, ^{37}Cl,

6]$^+$), 284 ([M, ^{35}Cl, 7]$^+$), 179 (13), 178 (10), 140 (32), 139 (10), 138 (100), 105 (44), 103 (25), 102 (10), 77 (24). HRMS (ESI-TOF): calcd. for $C_{17}H_{13}ClO_2$ [M$^+$, ^{37}Cl]: 284.05986; found: 284.060349. Anal. Calcd. $C_{17}H_{13}ClO_2$: C, 71.71; H, 4.60. Found: C, 71.65; H, 4.95.

2-(2,4-Dimethoxyphenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (**11l**). Starting with a THF solution of LDA (12.5 mmol), **9b** (0.81 g, 5.0 mmol) and **10j** (0.83 g, 5.0 mmol) in THF (15 mL), **11l** was isolated as a colourless crystalline solid (0.96 g, 73%), mp 101-102 °C. ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.67 (dd, *J* = 4.0, 16.8 Hz, 1 H, H_A), 2.78 (dd, *J* = 13.5 Hz, 1 H, H_B,), 3.77 (s, 6 H, 2CH_{3Ar}), 5.80 (dd, *J* = 4.0, 13.5 Hz, 1 H, CH), 6.03 (s, 1 H, CH_{Olf}), 6.45 (s, 1 H, ArH), 6.50 (d, *J* = 8.4 Hz, 1 H, ArH), 7.34-7.42 (m, 4 H, ArH), 7.71 (d, *J* = 8.1 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 41.9 (CH_2), 55.4 (2 x OCH_3), 76.2, 98.5, 102.1, 104.4 (CH), 117.4, 124.7 (C), 126.6, 127.4, 128.6, 131.5 (CH), 155.5, 159.1 (C), 168.9 (C_{Olf}), 192.0 (CO). IR (KBr): *ν* = 3271, 3082, 2966, 2933, 2837 (w), 1650, 1613, 1566, 1453, 1375, 1288, 1209, 1158, 1029, 954, 835 (m), 773, 695 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 310 (M$^+$, 20), 205 (67), 165 (13.4), 164 (100), 149 (73), 121 (39.1), 105 (24.8), 91 (11), 77 (20). HRMS (M+H): calcd. for $C_{19}H_{19}O_4$ [M+H]$^+$: 311.12779; found: 311.12746.

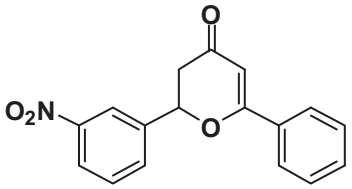


2-(3-Bromophenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (**11m**). Starting with a THF solution of LDA (12.5 mmol), **9b** (0.81 g, 5.0 mmol) and **10i** (0.92 g, 5.0 mmol) in THF (15 mL), **11m** was isolated as a colourless crystalline solid (1.16 g, 72%), mp 103-104 °C. ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.70 (dd, *J* = 3.4, 16.7 Hz, 1 H, H_A), 3.04 (dd, *J* = 13.7 Hz, 1 H, H_B), 5.80 (dd, 1 H, *J* = 3.3, 13.7 Hz, 1 H, CH), 6.21 (s, 1 H, CH_{Olf}), 7.41-7.64 (m, 6 H, ArH), 7.81-7.88 (m, 3 H, ArH). ^{13}C NMR (62.8 MHz, DMSO-d$_6$): δ = 41.2 (CH_2), 79.3 (CH**),** 102.0 (CH_{Olf}), 121.8 (C), 125.6, 126.4, 128.8, 129.3, 130.8, 131.4, 131.7 (CH), 132.1, 141.2 (C), 168.6 (C_{Olf}), 191.8 (CO). IR (KBr): *ν* = 3291, 3057, 2976, 2910, 1722 (w), 1651, 1593 (s), 1567, 1492, 1448, 1366, 1292, 1241, 1174, 1073, 991, 946, 880, 830, 783 (m), 767, 684 (s), 661, 612, 586 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 330 ([M, ^{81}Br, 4]$^+$), 328 ([M, ^{79}Br, 5]$^+$), 312 (13), 310 (12), 224 (12), 222 (11), 184 (85), 183 (10), 182 (88), 144 (14), 106 (10), 105 (100), 103 (46), 102 (21), 77 (55), 51 (13). HRMS: calcd. for $C_{17}H_{13}O_2Br$



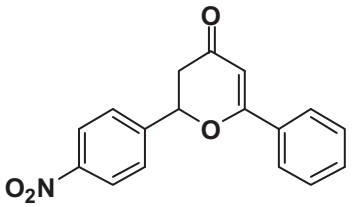
[M^+, ^{79}Br]: 328.00934; found: 328.008852.; calcd. for $C_{17}H_{13}O_2Br$ [M^+, ^{81}Br]: 330.00730; found: 330.00730. Anal. Calcd.: C, 62.03; H, 3.98. Found: C, 62.01; H, 3.97.

2-(3-Nitrophenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (11n) Starting with a THF solution of



LDA (12.5 mmol), **9b** (0.81 g, 5.0 mmol) and **10k** (0.75 g, 5.0 mmol) in THF (15 mL), **11n** was isolated as a colourless crystalline solid (1.0 g, 68 %), mp 104-105 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.77 (dd, J = 3.4, 16.5 Hz, 1 H, H_A), 3.07 (dd, J = 13.8 Hz, 1 H, H_B), 5.93 (dd, J = 3.4, 13.7 Hz, 1 H, CH), 6.24 (s, 1 H, CH_{Olf}), 7.46-8.28 (m, 8 H, ArH), 8.46 (s, 1 H, ArH). ^{13}C NMR (62.8 MHz, DMSO-d_6): δ = 41.7 (CH_2), 79.0, 102.1, 121.2, 123.3, 126.4, 128.8, 130.2, 131.7, 133.0 (CH), 140.7, 147.8 (C), 168.5 (C_{Olf}), 191.5 (CO). IR (KBr): ν = 3107, 3088, 3068, 2930, 2894 (w), 1613, 1573 (s), 1519, 1494, 1458, 1393 (m), 1345 (s), 1285, 1237, 1185, 1147, 1060, 1019, 898, 874 818 (m), 764, 684 (s), 616, 541 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 295 (M^+, 2), 162 (34), 161 (27), 151 (37), 150 (34), 147 (28), 120 (11), 105 (100), 104 (7), 78 (12), 77 (85), 76 (10), 69 (47), 51 (37), 50 (13), 43 (18). HRMS (EI): calcd. for $C_{17}H_{13}NO_4$ $[M]^+$: 295.08391; found: 295.084032.

2-(4-Nitrophenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (**11o**) Starting with a THF solution of

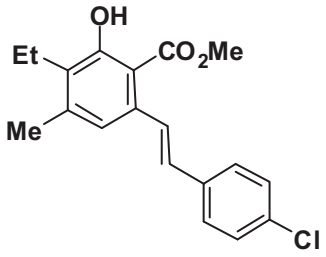


LDA (12.5 mmol), **9b** (0.81 g, 5.0 mmol) and **10l** (0.75 g, 5.0 mmol) in THF (15 mL), **11o** was isolated as a solid (0.98 g, 67%), mp 118-119 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.73 (dd, J = 4.2, 16.8 Hz, 1 H, H_A), 2.82 (dd, J = 13.2 Hz, 1 H, H_B), 5.64 (dd, J = 4.1, 13.2 Hz, 1 H, CH), 6.09 (s, 1 H, CH_{Olf}), 7.37-8.27 (m, 9 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 42.9 (CH_2), 79.7 (CH), 102.6 (CH_{Olf}), 124.2, 126.6, 126.8, 128.8, 132.1 (CH), 135.4, 145.2 (C), 169.8 (C_{Olf}), 191.4 (CO). IR (KBr): ν = 3108, 3089, 3068, 2931, 2895 (w), 1611, 1573 (s), 1519, 1495, 1457, 1394 (m), 1346 (s), 1286, 1238, 1185, 1147, 1060, 1019, 898, 874, 818 (m), 764, 684 (s), 616, 541 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 295 (M^+, 48), 294 (14), 176 (19), 173 (26), 144 (14), 115 (14), 106 (12), 105 (100), 102 (15), 77 (36), 69 (22), 51 (11). HRMS (EI): calcd. for $C_{17}H_{13}NO_4$ $[M]^+$: 295.08391; found: 295.084160.

11.2.2 [3+3] Reaction of 2,3-dihydro-4H-pyran-4-ones

To a stirred dichloromethane solution (2 mL per 1.0 mmol of **11c**) of **11c** (1.0 equiv.) and of 1,3-bis(silyl enol ether) **3d** (1.1 equiv.) was added $TiCl_4$ (1.1 equiv.) at −78 °C under an argon atmosphere. The temperature of the reaction mixture was allowed to rise to 20 °C during 16 h. To the solution was added hydrochloric acid (10%, 3 mL per 1.0 mmol of **11c**) and the mixture was extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, heptanes → EtOAc/heptanes = 1:10).

(E)-Methyl 6-(4-chlorostyryl)-3-ethyl-2-hydroxy-4-methylbenzoate (12). Starting with **11c**



(0.334 g, 1.5 mmol) and **3d** (0.476 g, 1.65 mmol), **12** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as white solid crystal (0.23 g, 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.28 (s, 3 H, CH_3), 2.64 (q, *J* = 7.5 Hz, 2 H, CH_2), 3.88 (s, 3 H, OCH_3), 6.66 (d, *J* = 16.0 Hz, 1 H, CH), 6.81 (s, 1 H, ArH), 7.24-7.35 (m, 4 H, ArH), 7.56 (d, *J* = 16.0 Hz, 1 H, ArH), 11.44 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1, 19.6 (CH_3), 19.7 (CH_2), 52.4 (OCH_3), 108.2 (*C*$COOCH_3$), 121.4 (CH), 127.7 (2×CH), 128.6 (CH), 128.9 (2×CH), 130.7 (CH), 130.8, 133.1, 136.3, 137.4, 143.0 (C_{Ar}), 160.5 (*C*OH), 172.1 (CO).). IR (KBr): *ν* = 3030, 2953, 2931, 2872, 1786, 1724 (w), 1655 (s), 1603, 1557, 1490, 1436, 1394, 1357, 1318 (m), 1273, 1233 (s), 1194 (m), 1152, 1090 (s), 1051, 962, 849 (m), 814 (s), 786, 731, 629, 596 (m). GC-MS (EI, 70 eV): *m/z* (%) = 332 ([M, ^{37}Cl, 29]$^+$), 330 ([M, ^{35}Cl, 100]$^+$), 283 (42), 207 (22), 165 (9), 131 (8), 91 (11), 69 (32), 44 (12). HRMS (EI): Calcd. for $C_{19}H_{19}O_3Cl$ [M^+, ^{35}Cl]: 330.10172; found: 330.101981.

11.3 Synthesis of Fluorinated 2,3-Dihydro-4*H*-pyran-4-ones by Cyclocondensation of 1,3-Dicarbonyl Dianions with Aldehydes

11.3.1 Synthesis of Fluorinated 2,3-dihydro-4*H*-pyran-4-ones (14a-j) and (16a-f)*:* A THF solution of LDA (12.5 mmol) was prepared by addition of *n*BuLi (5 ml, 12.5 mmol, 2.5 M solution in hexanes) to a THF solution (15 ml) of diisopropylamine (1.26 g, 12.5 mmol) at 0°C. After stiring for 1 h, the solution was cooled to -78 °C and 1,1,1-trifluoro-pentane-2,4-dione (0.77 g, 5.0 mmol) was added. After stirring for 1 h at -78 °C, aldehydes (5.0 mmol) was added and the solution was allowed to warm to 20 °C within 24 h. Hydrochloric acid (10%, 15 mL) was added and the mixture was allowed to stand for 15 min. Ethyl acetate (25 mL) was added. The organic and aqueous layers were separated and the latter was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate = 2:1) to give the products (**14a-j**) and (**16a-f**).

6-(Trifluoromethyl)-2-phenyl-2*H*-pyran-4(3*H*)-one (14a). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10i** (0.53 g, 5.0 mmol) in THF (15 mL), **14a** was isolated as a slightly yellow oil (0.97 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.81 (ddd, J = 1.1, 3.6, 17.1 Hz, 1 H, H_A), 3.01 (dd, J = 13.6, 17.1 Hz, 1 H, H_B), 5.61 (dd, J = 3.6, 13.7 Hz, 1 H, CH), 5.98 (q, J = 1.0 Hz, 1 H, CH_{Olf}), 7.41-7.47 (m, 5 H, ArH). ^{19}F NMR 282.4 MHz, $CDCl_3$): δ = -73.3. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 42.7 (CH_2), 82.6 (CH), 105.2 (q, $J_{C,F}$ = 2.8 Hz, CH_{Olf}), 118 (q, $J_{C,F}$ = 274.8 Hz, CF_3), 126.1, 129.0, 129.4 (CH), 136.3 (C_{Ar}), 159.4 (q, $J_{C,F}$ = 37.3 Hz, C_{Olf}), 191.2 (CO). IR (KBr): ν = 3368, 3093, 3067, 2976, 2901, 2707 (w), 1687, 1638 (s), 1585 (m), 1498, 1455 (w), 1413 (m), 1367 (w), 1270 (s), 1243 (m), 1194, 1142, 1067 (s), 986, 941, 877, 828, 756 (m), 695 (s), 620, 593, 533 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 242 (M^+, 5), 173 (7), 145 (9), 117 (9), 105 (12), 104 (100), 103 (20), 78 (15), 77 (11), 69 (12), 51 (8). HRMS (ESI-TOF): calcd. for $C_{12}H_8O_2F_3$ $[M-H]^+$: 241.04819 found: 241.04775. Anal. Calcd. $C_{12}H_9O_2F_3$: C, 59.51; H, 3.75. Found: C, 59.75; H, 3.92.

2-(2-Chlorophenyl)-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14b). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10a** (0.70 g, 5.0 mmol) in THF (15 mL), **14b** was isolated as a colourless oil (0.86 g, 62%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.81 (dd, J = 13.9, 17.1 Hz, 1 H, H_A), 2.95 (ddd, J = 1.2, 3.6, 17.1 Hz, 1 H, H_B), 5.97 (dd, J = 3.7, 14.0 Hz, 1 H, CH), 6.02 (q, = 1.0 Hz, CH_{Olf}), 7.37-7.47 (m, 3 H, ArH), 7.61-7.64 (m, 1 H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.2. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.7 (CH_2), 79.7 (CH), 105.4 (q, $J_{C,F}$ = 3.0 Hz, CH_{Olf}), 115.1 (q, $J_{C,F}$ = 275.2 Hz, CF_3), 127.0, 127.6, 129.9, 130.3 (CH), 131.7, 134.5 (C), 159.3 (q, $J_{C,F}$ = 36.9 Hz, C_{Olf}), 190.7 (CO). IR (KBr): v = 3034, 2922 (w), 1678, 1631, 1410 (s), 1344 (m), 1261, 1167, 1152, 1069 (s), 994, 960, 938 (m), 811 (s), 720, 710, 605 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 278 ([M, ^{37}Cl, 1]$^{+}$), 276 ([M, ^{35}Cl, 4]$^{+}$), 241 (13), 118 (100), 117 (51), 91 (15), 69 (12). HRMS (ESI-TOF): calcd. for $C_{12}H_9O_2ClF_3$ [M+H]$^{+}$, (M^{+}, [^{35}Cl]): 277.02377; found: 277.02388.

2-(4-Chlorophenyl)-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14c). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10c** (0.70 g, 5.0 mmol) in THF (15 mL), **14c** was isolated as a colourless crystalline solid (1.04 g, 72%), mp 76-77 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.69 (ddd, J = 0.9, 3.8, 17.0 Hz, 1 H, H_A), 2.87 (dd, J = 13.3, 17.0 Hz, 1 H, H_B), 5.48 (dd, J = 3.8, 13.6 Hz, 1 H, CH), 5.88 (brs, 1 H, CH_{Olf}), 7.25-7.36 (m, 4 H, ArH).^{19}F NMR 282 MHz, $CDCl_3$): δ = -73.3. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 42.6 (CH_2), 81.8 (CH), 105.3 (q, $J_{C,F}$ = 3.1 Hz, CH_{Olf}), 118.7 (q, $J_{C,F}$ = 275.0 Hz, CF_3), 127.5, 129.2 (CH), 135.4, 134.8 (C), 158.9 (q, $J_{C,F}$ = 37.0 Hz, C_{Olf}), 190.6 (CO). IR (KBr): v = 3104, 2884 (w), 1680, 1634, 1494 (s), 1410, 1324 (m), 1274, 1175, 1141, 1068 (s), 993, 959, 939, 877 (m), 835 (s), 719, 638, 548 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 278 ([M, ^{37}Cl, 2]$^{+}$), 276 ([M, ^{35}Cl, 6]$^{+}$), 140 (33), 139 (12), 138 (100), 103 (23), 69 (13). HRMS (EI): calcd. for $C_{12}H_8O_2F_3Cl$ [M^{+}, ^{35}Cl]: 276.01594; found: 276.015382.

2-(3-Nitrophenyl)-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14d). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10k** (0.75 g, 5.0 mmol) in THF (15 mL), **14d** was isolated as a solid (0.90 g, 63%), mp 102-103 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.79 (ddd, J = 1.2, 3.9, 16.9 Hz, 1 H, H_A), 2.92 (dd, J = 13.4, 16.8 Hz, 1 H, H_B), 5.63 (dd, J = 4.4, 13.9 Hz, 1 H, CH), 5.95 (brs, 1 H, CH_{Olf}), 7.57-7.62 (m, 1 H, ArH),

7.67-7.73 (m, 1 H, ArH), 8.21-8.26 (m, 2 H, ArH). ^{19}F NMR 282 MHz, $CDCl_3$): δ = -73.1. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 42.6 (CH_2), 81.2, 105.7 (q, $J_{C,F}$ = 3.0 Hz, 1 H, CH_{Olf}), 115 (q, $J_{C,F}$ = 275.2 Hz, CF_3), 121.2, 124.3, 130.3, 131.9 (CH), 138.4, 148.6 (C), 159.0 (q, $J_{C,F}$ = 37.7 Hz, C_{Olf}), 189.8 (CO). IR (KBr): ν = 3093, 3067, 2912, 2878 (w), 1688, 1640, 1531 (s), 1417, 1353 (m), 1271, 1192, 1143, 1075 (s), 1005, 943, 912, 868 (m), 808 (s), 736 (m), 683 (s), 626, 538 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 287 (M^+, 43), 286 (6), 270 (8), 219 (13), 218 (100), 200 (14), 190 (12), 176 (84), 173 (28), 172 (13), 171 (12), 165 (17), 144 (25), 143 (20), 131 (12), 130 (10), 129 (17), 118 (11), 116 (19), 115 (64), 103 (17), 102 (33), 89 (12), 77 (13), 76 (14), 75 (11), 69 (49), 63 (12), 51 (12). HRMS (ESI-TOF): calcd. for $C_{12}H_7F_3NO_4$ $[M-H]^+$: 286.03327 found: 286.03353. Anal. Calcd $C_{12}H_8F_3NO_4$: C, 50.19; H, 2.81; N, 4.88. Found: C, 50.18; H, 2.82; N, 4.87.

2-(4-Nitrophenyl)-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14e). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10l** (0.75 g, 5.0 mmol) in THF (15 mL), **14e** was isolated as a colourless crystalline solid (0.86 g, 60%), mp 112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.79 (ddd, J = 0.8, 4.5, 17.0 Hz, 1 H, H_A), 2.88 (dd, J = 12.7, 17.1 Hz, 1 H, H_B), 5.64 (dd, J = 4.6, 12.7 Hz, 1 H, CH), 5.95 (brs, 1 H, CH_{Olf}), 7.54-7.57 (m, 2 H, ArH), 8.24-8.26 (m, 2 H, ArH). ^{19}F NMR 282 MHz, $CDCl_3$): δ = -73.3. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 42.7 (CH_2), 81.1 (CH), 105.7 (q, $J_{C,F}$ = 3.0 Hz, 1 H, CH_{Olf}), 118.8 (q, $J_{C,F}$ = 274.4 Hz, CF_3), 124.1, 126.8 (CH), 143.8, 148.3 (C), 158.4 (q, $J_{C,F}$ = 37.6 Hz, C_{Olf}), 189.8 (CO). IR (KBr): ν = 3094, 3068, 2912, 2879 (w), 1689, 1640, 1530 (s), 1418, 1354 (m), 1270, 1193, 1144, 1075 (s), 1005, 944, 912, 868 (m), 807 (s), 737 (m), 684 (s), 626, 539 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 287 (M^+, 4), 218 (9), 162 (11), 150 (10), 149 (100), 119 (31), 103 (31), 102 (11), 91 (24), 77 (38), 69 (19), 51 (10). HRMS (EI): calcd. for $C_{12}H_8O_2F_3$ $[M]^+$: 287.04054 found: 287.040243.

2-(Biphenyl-4-yl)-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14f). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10m** (0.91 g, 5.0 mmol) in THF (15 mL), **17f** was isolated as a colourless crystalline solid (1.29 g, 81 %), mp 124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.75 (ddd, J = 1.0, 3.6, 17.1 Hz, 1 H, H_A), 2.96 (dd, J = 13.6, 17.1 Hz, 1 H, H_B), 5.56 (dd, J = 3.5, 13.6 Hz, 1 H, CH), 5.90 (q, J = 1.0 Hz, 1 H, CH_{Olf}), 7.36-7.43 (m, 4 H, ArH), 7.51-7.61 (m, 5 H,

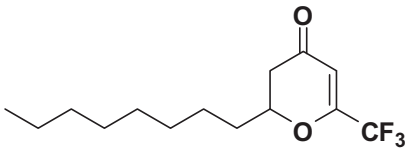
ArH). ^{19}F NMR 282 MHz, $CDCl_3$): δ = -73.2. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 42.6 (CH_2), 82.4 (CH), 105.2 (q, $J_{C,F}$ = 3.0 Hz, CH_{Olf}), 118.5 (q, $J_{C,F}$ = 275.0 Hz, CF_3), 126.6, 127.1, 127.71, 127.7, 128.8 (CH), 135.1, 140.1, 142.5 (C), 159.7 (q, $J_{C,F}$ = 37.2 Hz, C_{Olf}), 191.1 (CO). IR (KBr): ν = 3057, 3028, 2991, 2837, 1712 (w), 1660, 1601 (s), 1485, 1432 (m), 1394, 1332, 1235, 1000 (s), 950, 898, 873 (m), 762, 731, 701 (s) 657 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 318 (M^+, 32), 181 (16), 180 (100), 179 (13), 178 (18), 165 (10), 69 (10). HRMS (ESI-TOF): calcd. for $C_{18}H_{14}O_2F_3$ $[M+H]^+$: 319.09404; found: 319.09435.

2-(Thien-2-yl)-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14g). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10h** (0.56 g, 5.0 mmol) in THF (15 mL), **14g** was isolated as a slight yellow oil (0.88 g, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.88 (ddd, J = 0.9, 4.3, 17 Hz, 1 H, H_A), 3.03 (dd, J = 13.5, 17.0 Hz, 1 H, H_B), 5.46 (brs, 1 H, CH_{Olf}), 5.77 (dd, J = 4.2, 11.4 Hz, 1 H, CH), 7.04 (d, J = 3.3 Hz, 1 H, $CH_{thienyl}$), 7.12 (t, J = 3.5 Hz, 1 H, $CH_{thienyl}$), 7.39 (d, J = 5.0 Hz, 1 H, $CH_{thienyl}$).^{19}F NMR 282 MHz, $CDCl_3$): δ = -73.2. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 42.3 (CH_2), 76.2 (CH), 105.3 (q, $J_{C,F}$ = 3.0 Hz, CH_{Olf}), 118.3 (q, $J_{C,F}$ = 273.0 Hz, CF_3), 126.3, 126.6, 127.3 ($CH_{thienyl}$), 140.8 ($C_{thienyl}$), 159.3 (q, $J_{C,F}$ = 37.2 Hz, C_{Olf}), 191.6 (CO). IR (KBr): ν = 3086, 3070 (m), 1686 (s), 1637, 1410, 1358, 1317 (m), 1262, 1193, 1145 (s), 1065, 965, 823 (m), 701 (s) 640 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 248 (M^+, 19), 111 (10), 110 (100), 109 (10), 69 (15). HRMS (ESI-TOF): calcd. for $C_{10}H_7O_2F_3S$ $[M]^+$: 248.01134; found: 248.010271.

2-Heptyl-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14h). Starting with a THF solution of LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10n** (0.64 g, 5.0 mmol) in THF (15 mL), **14h** was isolated as a slight yellow oil (1.02 g, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, J = 7.0 Hz, 3 H, $CH_3(CH_2)(CH2)_5$), 1.19-1.26 (m, 8 H, $CH_3(CH_2)_4(CH_2)_2$), 1.34-1.42 (m, 2 H, $CH_3(CH_2)_4(CH_2)(CH_2)$), 1.59-1.84 (m, 2 H), 2.50 (t, J = 7.1 Hz, 2 H, $CH_3(CH_2)_4(CH_2)(CH_2)$), 4.44-4.51 (m, 1 H, CH), 5.75 (brs, 1 H, CH_{Olf}). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.6. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.5, 23.6, 28.0, 28.1, 30.7, 32.9, 40.3 (CH_2), 80.7 (CH), 103.6 (q, J = 3 Hz, CH_{Olf}), 121.5 (q, $J_{C,F}$ = 276.5 Hz, CF_3), 158.3 (q, $J_{C,F}$ = 36.9 Hz, C), 190.8 (CO). IR (KBr): ν = 2921, 2852 (m), 1688 (s), 1465, 1417 (m), 1340 (w), 1270, 1197, 1156 (s), 1073, 909, 820 (m), 720 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 264 (M^+, 16), 195 (29), 193 (10), 167 (16), 165 (100), 139 (68), 110 (17), 109 (10), 98 (11), 97 (23), 95 (10), 85

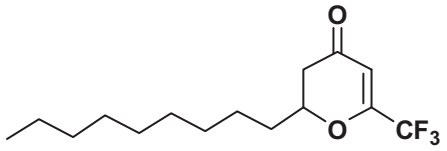
(12), 84 (22), 83 (18), 82 (12), 81 (14), 70 (22), 69 (86), 68 (13), 67 (16), 56 (30), 55 (41), 54 (15), 43 (30), 42 (13), 41 (48), 39 (17), 29 (17). HRMS: calcd. for $C_{13}H_{19}O_2F_3$ $[M]^+$: 264.3371; found: 264.33711.

2-Octyl-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14i). Starting with a THF solution of



LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10o** (0.71 g, 5.0 mmol) in THF (15 mL), **14i** was isolated as a slight yellow oil (1.10 g, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7.0 Hz, 3 H, *CH*$_3$(CH_2)(CH_2)$_6$), 1.19-1.46 (m, 12 H, CH_3(*CH_2*)$_6$(CH_2)), 1.58-1.88 (m, 2 H), 2.47-2.51 (m, 2 H, CH_2), 4.43-4.52 (m, 1 H, CH), 5.74 (s, 1 H, CH_{Olf}). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.6. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.5, 23.6, 28.0, 28.1, 28.2, 30.7, 32.9, 40.2 (CH_2), 80.6 (CH), 103.4 (q, *J* = 3 Hz, CH_{Olf}), 121.9 (q, $J_{C,F}$ = 276.4 Hz, CF_3), 158.2 (q, $J_{C,F}$ = 36.7 Hz, C), 190.7 (CO). IR (KBr): *v* = 2925, 2855 (m), 1691 (s), 1466, 1417 (m), 1339 (w), 1269, 1194, 1149 (s), 1073, 909, 819 (m), 720 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 278 (M^+, 2), 209 (18), 167 (13), 165 (100), 139 (45), 97 (14), 83 (15), 82 (12), 81 (10), 70 (18), 69 (52), 67 (10), 57 (12), 56 (17), 55 (30), 54 (10), 43 (19), 41 (33), 39 (10), 29 (11). HRMS: calcd. for $C_{14}H_{21}F_3O_2$ $[M]^+$: 278.14882; found: 278.149378.

2-Nonyl-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14j). Starting with a THF solution of



LDA (12.5 mmol), **13** (0.77 g, 5.0 mmol) and **10p** (0.78 g, 5.0 mmol) in THF (15 mL), **14j** was isolated as a colourless crystalline solid (1.21 g, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.0 Hz, 3 H, *CH*$_3$(CH_2)$_8$), 1.17-1.26 (m, 12 H, CH_2(*CH_2*)$_6$(CH_2)$_2$), 1.35-1.43 (m, 2 H, CH_3(CH_2)$_6$(*CH_2*)(CH_2)), 1.60-1.87 (m, 2 H, CH_2), 2.47-2.51 (m, 2 H, CH_2), 4.46-4.52 (m, 1 H, CH), 5.75 (brs, 1 H, CH_{Olf}). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.6. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6, 24.5, 29.1, 29.3, 29.4, 31.8, 32.3, 33.8, 41.3 (CH_2), 81.6 (CH), 106.6 (q, J = 3 Hz, CH_{Olf}), 118.5 (q, $J_{C,F}$ = 277.9 Hz, CF_3), 159.2 (q, $J_{C,F}$ = 36.5 Hz, C_{Olf}), 191.8 (CO). IR (KBr): *v* = 2924, 2854 (m), 1691 (s), 1466, 1418 (m), 1340 (w), 1269, 1195, 1150 (s), 1073, 912, 820 (m), 720 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 292 (M^+, 1), 223 (14), 165 (100), 139 (30), 97 (11), 83 (12), 70 (12), 69 (35), 56 (10), 55 (22), 43 (15), 41 (25), 29 (10). HRMS: calcd. for $C_{15}H_{23}O_2F_3$ $[M]^+$: 319.09404; found: 319.09435.

6-Methyl-2-(2-(trifluoromethyl)phenyl)-2*H*-pyran-4(3*H*)-one (16a). Starting with a THF solution of LDA (12.5 mmol), **9** (0.50 g, 5.0 mmol) and **15a** (0.87 g, 5.0 mmol) in THF (15 mL), **16a** was isolated as a colourless crystalline solid (0.94 g, 73%), mp 127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, CH_3), 2.2.49 (ddd, *J* = 0.7, 3.7, 16.8 Hz, 1 H, H_A), 2.64 (dd, *J* = 14.1, 16.9 Hz, 1 H, H_B), 5.38 (s, 1 H, CH_{Olf}), 5.69 (dd, *J* = 3.7, 14.0 Hz, 1 H, CH), 7.38-7.43 (m, 1 H, ArH), 7.55-7.62 (m, 2 H, ArH), 7.71-7.74 (m, 1 H, ArH). ^{19}F NMR 282 MHz, $CDCl_3$): δ = -58.4. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.0 (CH_3), 43.1 (CH_2), 77.1 (q, $J_{C,F}$ = 2.3 Hz, CH), 105.3 (CH_{Olf}), 125.9 (q, J = 5.6 Hz, ArH), 128.0, 128.7, 132.5 (ArH), 123.9 (q, $J_{C,F}$ = 274.3 Hz, CF_3), 127.0 (q, $J_{C,F}$ = 32.1 Hz, C_{Ar}), 137.2 (q, $J_{C,F}$ = 1.0 Hz, ArH), 174.2 (C_{Olf}), 191.3 (CO). IR (KBr): *v* = 3078, 3017, 2970 (w), 1660, 1613 (s), 1486, 1396, 1359 (m), 1310 (s), 1288, 1240 (m), 1152, 1100 (s), 1060, 1035, 1000, 948, 879, 810 (m), 770 (s), 751, 652, 548 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 256 (M^+, 5), 213 (23), 173 (11), 172 (100), 171 (40), 151 (24). HRMS (ESI-TOF): calcd. for $C_{13}H_{12}O_2F_3$ $[M+H]^+$: 257.0784; found: 257.0787.

2-(2-Chloro-3-(trifluoromethyl)phenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (16b). Starting with a THF solution of LDA (12.5 mmol), **9a** (0.50 g, 5.0 mmol) and **15b** (1.04 g, 5.0 mmol) in THF (15 mL), **16b** was isolated as a colourless crystalline solid (1.03 g, 71%), mp 137 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00 (s, 3H, CH_3), 2.45-2.64 (m, 2 H, $H_{A,B}$), 5.38 (s, 1 H, CH_{Olf}), 5.63 (dd, *J* = 4.2, 13.6 Hz, 1 H, CH), 7.35-7.39 (m, 1 H, ArH), 7.54 (d, 1 H, *J* = 8.3 Hz, 1 H, ArH), 7.71-7.73 (m, 1 H, ArH). ^{19}F NMR 282 MHz, $CDCl_3$): δ = -58.4. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 20.9 (CH_3), 43.0 (CH_2), 76.6 (q, $J_{C,F}$ = 5.7 Hz, CH), 105.4 (CH_{Olf}), 121.7 (q, $J_{C,F}$ = 273 Hz, CF_3), 125.6 (q, $J_{C,F}$ = 31.3 Hz, CH), 127.4 (q, $J_{C,F}$ = 5.7 Hz, CH), 128.6 (q, $J_{C,F}$ = 42.0 Hz, CH), 139.1 (q, $J_{C,F}$ = 28.1 Hz, C_{Ar}), 173.8 (C_{Olf}), 190.6 (CO). IR (KBr): *v* = 3117, 2976, 2926, 1660 (w), 1601 (s), 1575, 1440, 1392, 1330, 1234 (m), 1557 (s), 1126 (m), 1105 (s), 1042, 1000, 958, 880, 848, 770, 706, 596 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 292 ([M, ^{37}Cl, 1]$^+$), 290 ([M, ^{35}Cl, 6]$^+$), 255 (16), 247 (16), 208 (49), 207 (15), 206 (100), 171 (39), 151 (14), 43 (13). HRMS (ESI-TOF): calcd. for $C_{13}H_{11}ClO_2F_3$ $[M+H]^+$, (M^+, [^{35}Cl]): 291.09305; found: 291.093056.

2-(2-Chloro-4-(trifluoromethyl)phenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (16c). Starting with a THF solution of LDA (12.5 mmol), **9** (0.50 g, 5.0 mmol) and **15c** (1.04g, 5.0 mmol) in THF (15 mL), **16c** was isolated as a colourless crystalline solid (1.09 g, 75%), mp 143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.03 (s, 3 H, CH_3), 2.47 (dd, J = 14.1, 14.1 Hz, 1 H, H_A), 2.68 (ddd, J = 1.1, 3.5, 14.1 Hz, 1 H, H_B), 5.40 (s, 1 H, CH_{Olf}), 5.71 (dd, J = 3.5, 14.1 Hz, CH), 7.54 (d, J = 8.1 Hz, 1 H, ArH), 7.58 (s, 1 H, ArH), 7.69 (d, J = 8.3 Hz, 1 H, ArH). ^{19}F NMR 282 MHz, $CDCl_3$): δ = -62.8. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 20.5 (CH_3), 40.8 (CH_2), 77.3 (CH), 105.6 (CH_{Olf}), 127.1 (q, $J_{C,F}$ = 272 Hz, CF_3), 131.8 (q, $J_{C,F}$ = 33.8 Hz, C_{Ar}), 124.2 (q, $J_{C,F}$ = 3.8 Hz, CH), 126.7 (q, $J_{C,F}$ = 3.8 Hz, CH), 127.7 (q, $J_{C,F}$ = 3.8 Hz, CH), 131.8 (q, $J_{C,F}$ = 33.8 Hz, C), 140.2 (C), 173.8 (C_{Olf}), 190.9 (CO). IR (KBr): ν = 3092, 2966, 2848 (w), 1666, 1613 (s), 1388 (m), 1319 (s), 1240 (m), 1118 (s), 1064, 1006, 945, 846, 815, 713, 649, 538 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 292 ([M, ^{37}Cl, 5]$^{+}$), 290 ([M, ^{35}Cl, 4]$^{+}$), 255 (13), 247 (15), 208 (32), 207 (11), 206 (100), 171 (27), 151 (17), 43 (10). HRMS: calcd. for $C_{13}H_{10}ClO_2F_3$ [M^{+}, ^{35}Cl]: 290.09404; found: 319.09435.

2-(2-Fluorophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (16d). Starting with a THF solution of LDA (12.5 mmol), **9** (0.50 g, 5.0 mmol) and **15d** (0.62 g, 5.0 mmol) in THF (15 mL), **16d** was isolated as a slight yellow oil (0.69 g, 67%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.51 (dd, J = 3.2, 16.8 Hz, 1 H, H_B), 2.69 (dd, J = 14.1, 16.8 Hz, 1 H, H_B), 5.35 (s, 1 H, CH_{Olf}), 5.58 (dd, J = 3.6, 14.1 Hz, 1 H, CH), 6.96-7.03 (m, 1 H, CH), 7.09-7.14 (m, 1 H, CH), 7.22-7.29 (m, 1 H, ArH), 7.39-7.45 (m, 1 H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -118.2. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.0 (CH_3), 41.3 (CH_2), 75.1 (d, $J_{F,C}$ = 3.1 Hz, CH), 105.2 (CH_{Olf}), 115.8 (d, $J_{F,C}$ = 21.7 Hz, CH), 124.5 (d, $J_{F,C}$ = 3.6 Hz, CH), 125.5 (d, $J_{F,C}$ = 12.7 Hz, CH), 127.5 (d, $J_{F,C}$ = 3.4 Hz, C_r), 130.4 (d, $J_{F,C}$ = 8.3 Hz, C_{Ar}), 159.7 (d, $J_{F,C}$ = 247.8 Hz, C), 174.2 (C_{Olf}), 191.8 (CO). IR (KBr): ν = 3067, 296, 1722 (w), 1660 (m), 1605 (s), 1491, 1436, 1360, 1330, 1230, 1151, 1065, 1001, 950, 871, 810 (m), 755 (s), 657, 553 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 206 (M^{+}, 2), 163 (20), 123 (10), 122 (100), 121 (14), 96 (11). HRMS: calcd. for $C_{12}H_{11}O_2F$ [M] $^{+}$: 206.07376; found: 206.07373. Anal. Calcd. $C_{12}H_{11}O_2F$: C, 69.89; H, 5.38. Found: C, 69.86; H, 5.51.

2-(3-Fluorophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (16e). Starting with a THF solution of LDA (12.5 mmol), **9** (0.50 g, 5.0 mmol) and **15e** (0.62 g, 5.0 mmol) in THF (15 mL), **16e** was isolated as a slight yellow oil (0.75 g, 72%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.02 (d, 3 H, CH_3), 2.53 (ddd, J = 1.0, 3.8, 16.7 Hz, 1 H, H_A), 2.68 (dd, J = 13.8, 16.8 Hz, 1 H, H_B), 5.31 (dd, J = 3.8, 13.8 Hz, 1 H, CH), 5.36 (s, 1 H, CH_{Olf}), 6.96-7.03 (m, 1 H, ArH), 7.05-7.11 (m, 2 H, ArH), 7.28-7.36 (m, 1 H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -115.4. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.0 (CH_3), 42.3 (CH_2), 79.9 (CH), 105.3 (CH_{Olf}), 113.0 (d, $J_{F,C}$ = 23.0 Hz, CH), 115.6 (d, $J_{F,C}$ = 21 Hz, CH), 121.6 (d, $J_{F,C}$ = 3.7 Hz, CH), 130.8 (d, $J_{F,C}$ = 8.7 Hz, CH), 140.6 (d, $J_{F,C}$ = 7.5 Hz, C), 162.1 (d, $J_{F,C}$ = 246.5, C), 174.1 (C_{Olf}), 191.8 (CO). IR (KBr): v = 3067, 2921, 1722 (w), 1666 (m), 1607, 1590 (s), 1488, 1448 (m), 1392, 1392 (s), 1359 (m), 1326, 1237 (s), 1041 (m), 1003 (s), 890 (m), 785, 691 (s), 627), 592 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 206 (M^+, 6), 188 (7), 173 (6), 163 (22), 122 (100), 121 (14), 96 (13). HRMS: calcd. for $C_{12}H_{11}O_2F$ [M^+]: 206.07376; found: 206.07469. Anal. Calcd. $C_{12}H_{11}O_2F$: C, 69.89; H, 5.38. Found: C, 69.74; H, 5.66.

2-(4-Fluorophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (16f). Starting with a THF solution of LDA (12.5 mmol), **9** (0.50 g, 5.0 mmol) and **15f** (0.62 g, 5.0 mmol) in THF (15 mL), **16f** was isolated as a colourless crystalline solid (0.80 g, 78%), mp 61-62 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 2.50 (dd, J = 3.4, 16.8 Hz 1 H, H_A), 2.70 (dd, J = 14.0, 16.6 Hz, 1 H, H_B), 5.29 (dd, J = 3.8, 13.9 Hz, 1 H, CH), 5.36 (s, 1 H, CH_{Olf}), 6.95-7.06 (m, 2 H, ArH), 7.28-7.34 (m, 2 H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -112.7. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.1 (CH_3), 42.3 (CH_2), 80.1 (CH), 105.3 (CH_{Olf}), 115.7 (d, $J_{F,C}$ = 21.8 Hz, CH), 128.1 (d, $J_{F,C}$ = 7.2 Hz, CH), 134.0 (d, $J_{F,C}$ = 3 Hz, C), 162.8 (d, $J_{F,C}$ = 247.0, C), 174.2 (C_{Olf}), 192.0 (CO). IR (KBr): v = 3295, 3119, 2966, 2849, 1898 (w), 1651 (m), 1600 (s), 1511, 1426, 1396, 1335, 1248 (m), 1219 (s), 1159, 1024, 997, 903 (m), 818 (s), 659, 554 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 206 (M^+, 4), 188 (10), 163 (17), 122 (100), 121 (15), 96 (10), HRMS: calcd. for $C_{12}H_{11}O_2F$ [M^+]: 206.07376; found: 206.073710. Anal. Calcd. $C_{12}H_{11}O_2F$: C, 69.89; H, 5.38. Found: C, 69.88; H, 5.56.

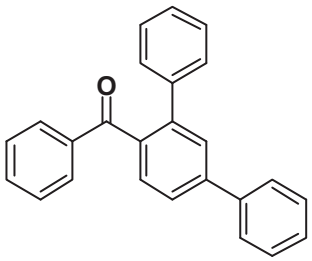
11.4 Synthesis of 2,4-Diarylbenzophenones by Site-Selective Suzuki-Miyaura Reactions of 2,4-Bis(trifluoromethylsulfonyloxy)benzophenone

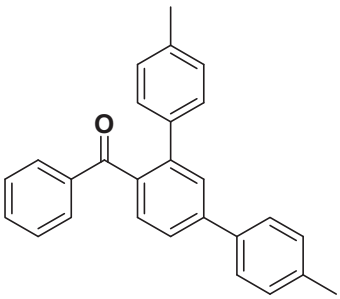
11.4.1 Synthesis of 2,4-Bis(trifluoromethylsulfonyloxy)benzophenone (**18**): To a CH_2Cl_2 solution (10 mL/mmol) of **17** (1.0 equiv.) was added pyridine (4.0 equiv) at – 78 °C under argon atmosphere. After 10 min, Tf_2O (2.4 equiv.) was added at -78 °C. The mixture was allowed to warm to 0 °C during 4 h with stirring. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The product was isolated by rapid column chromatography (flash silica gel, heptanes/EtOAc). Starting with **20** (214 mg, 1.0 mmol), pyridine (0.32 ml, 4.0 mmol) and Tf_2O (0.40 ml, 2.4 mmol), **21** was isolated as a highly viscous oil (420 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.54-6.55 (m, 1 H, ArH), 6.59-6.69 (m, 3H, ArH), 7.79-6.87 (m, 2 H, ArH), 6.93-6.96 (m, 2 H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 114.0 (q, $J_{F,C}$ = 320 Hz, CF_3), 122.9 (q, $J_{F,C}$ = 320 Hz, CF_3), 116.5, 121.2, 128.8, 130.1, 132.5 (CH), 132.7 (C_{Ar}), 134.3 (CH), 135.7, 147.0, 150.5 (C_{Ar}), 190.9 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.7, -73.0 (CF). IR (KBr): = 3303, 3092 (w), 1657 (s), 1600, 1597, 1493, 1433, 1427(m), 1319 (w), 1295, 1274, 1242, 1216 (m), 1189, 1133 (s), 1087, 966, 936, 923, 892, 859, 854, 795, 752, 693, 664, 603, 584, 570 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 478 (M^+, 50), 401 (22), 184 (19), 156 (10), 128 (8), 105 (100), 77 (34), 69 (27), 51 (10). HRMS (EI, 70 eV): calcd for $C_{15}H_8F_6O_7S_2$ [M^+]: 477.96101; found 477.961098.

11.4.2 Synthesis of diaryl-substituted benzophenones (20a-d), (21a-j) and (22a-d)

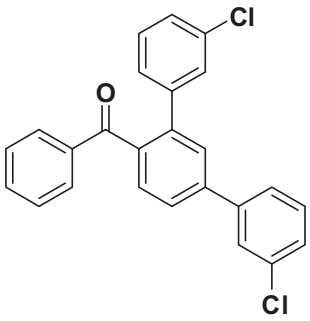
The reaction was carried out in a pressure tube. To a dioxane suspension (5 mL) of **18** or **5** (1.0 mmol), $Pd(PPh_3)_4$ (5-10 mol-%) and of the arylboronic acid (1.3 mmol per Br), K_3PO_4 was added. The mixture was stirred at 110 °C under argon atmosphere for the indicated period of time (6-8 h). The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, EtOAc / heptanes).

11.4.3 Synthesis of symmetrical diaryl benzophenones

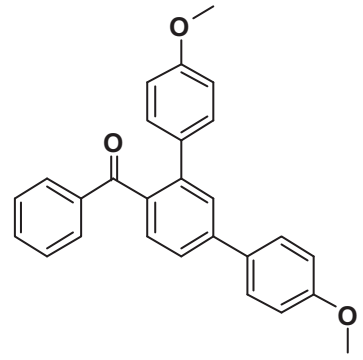
(2,4-Bis(phenyl)phenyl)(phenyl)methanone (20a) Starting with **18** (220 mg, 0.46 mmol), 
K_3PO_4 (292 mg, 1.38 mmol), $Pd(PPh_3)_4$ (32 mg, 6 mol%), phenylboronic acid (146 mg, 1.2 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **20a** was isolated as a white solid (125 mg, 82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06-7.09 (m, 2 H, ArH), 7.11-7.15 (m, 2 H, ArH), 7.17-7.23 (m, 3 H, ArH), 7.27-7.33 (m, 3 H, ArH), 7.35-7.40 (m, 2 H, ArH), 7.49-7.51 (m, 1 H, ArH), 7.56-7.61 (m, 5 H, ArH). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 125.7, 127.3, 127.4, 128.0, 128.1, 128.3, 128.9, 129.0, 129.1, 129.6, 129.9, 132.8 (CH), 137.5, 137.7, 140.1, 140.2, 141.9, 143.3 (C), 198.5 (CO). IR (KBr): *v* = 3050, 3026, 2923, 2853 (w), 1657 (s), 1595 (m), 1552, 1496 (w), 1441, 1393, 1315 (m), 1279 (s), 1234, 1158, 1132, 1073, 1025, 960, 936, 922, 902, 843, 800, 773 (m), 760, 742, 690 (s), 638, 584 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 334 (M^+, 100), 333 (73), 258 (18), 257 (85), 229 (14), 228 (35), 227 (15), 226 (21), 105 (12), 77 (18). HRMS (EI): calcd. for $C_{25}H_{18}O$ $[M]^+$: 334.13522; found: 334.134518.

(2,4-Bis(p-tolyl)phenyl)(phenyl)methanone (20b). Starting with **18** (220 mg, 0.46 mmol), 
K_3PO_4 (292 mg, 1.38 mmol), $Pd(PPh_3)_4$ (32 mg, 6 mol%), *P*-tolylboronic acid (163 mg, 1.2 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **20b** was isolated as a white solid (139 mg, 84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.16 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 6.93-6.96 (m, 2 H, ArH), 7.04-7.13 (m, 2 H, ArH), 7.19-7.25 (m, 4 H, ArH), 7.27-7.37 (m, 2 H, ArH), 7.45-7.51 (m, 3 H, ArH), 7.53-7.65 (m, 3 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 127.1, 128.1, 128.6, 128.7, 128.8, 129.0, 129.5, 129.6, 129.9, 130.0 (CH), 137.5, 137.7, 140.1, 140.2, 141.9, 143.3 (C), 198.5 (CO).). IR (KBr): *v* = 3079, 3032, 1661, 1596, 1490, 1445, 1426, 1314, 1283, 1242, 1178, 1138, 1069, 999, 914, 835, 751 (s), 698 (m), 785 (s) 621 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 362 (M^+, 100), 333 (73), 258 (18), 257 (85), 229 (14), 228 (35), 227 (15), 226 (21), 105 (12), 77 (18). HRMS (EI): calcd. for $C_{27}H_{22}O$ $[M]^+$: 362.13522; found: 362.134518.

(2,4-Bis(m-chlorophenyl)phenyl)(phenyl)methanone (20c) Starting with **18** (220 mg, 0.46mmol), K_3PO_4 (292 mg, 1.38 mmol), $Pd(PPh_3)_4$ (32 mg, 6 mol%), m-chlorophenylboronic acid (187 mg, 1.2 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **20c** was isolated as a white solid (138 mg, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06-7.08 (m, 2 H, ArH), 7.23-7.40 (m, 6 H, ArH), 7.45-7.53 (m, 2 H, ArH), 7.54-7.61 (m, 6 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 125.4, 126.1, 127.2, 127.4, 127.6, 128.1, 128.2, 128.4, 128.7, 128.9, 129.5, 129.7, 130.2, 133.0 (CH), 133.0, 134.2, 134.9, 137.2, 137.7, 138.1, 140.5, 141.6, 142.0 (C), 197.9 (CO).). IR (KBr): *v* = 3080, 3034 (w), 1665 (s), 1595, 1545, 1494, 1443, 1430, 1316, 1285, 1244, 1180, 1135, 1071, 1002, 915, 837 (m), 753 (s), 700 (m), 787 (s), 671, 667, 624, 530 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 404 ([M, $^{37}Cl_2$, 63]$^+$), 402 ([M, $^{35}Cl_2$, 100]$^+$), 401 (49), 369 (12), 368 (10), 367 (36), 329 (10), 328 (11), 327 (55), 326 (20), 325 (85), 290 (12), 264 (14), 263 (10), 262 (44), 227 (13), 226 (54), 225 (10), 224 (14), 184 (20), 105 (39), 77 (33). HRMS (EI): calcd. for $C_{25}H_{16}Cl_2O$ [(M^+, Cl^{35},Cl^{37}])$^+$: 402.05727; found: 402.056201.



(2,4-Bis(p-methoxyphenyl)phenyl)(phenyl)methanone (20d): Starting with **18** (220 mg, 0.46 mmol), K_3PO_4 (292 mg, 1.38 mmol), $Pd(PPh_3)_4$ (32 mg, 6 mol%), *p*-methoxyphenylboronic acid (182 mg, 1.2 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **20d** was isolated as a white solid (128 mg, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.65 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 6.66-6.69 (m, 1 H, ArH), 6.92-6.97 (m, 2 H, ArH), 7.13-7.18 (m, 2 H, ArH), 7.41-7.53 (m, 9 H, ArH), 7.75-7.78 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 55.3, 55.4 (OCH_3), 114.3, 114.6, 12.7, 128.0, 128.3, 129.4, 128.5, 130.1, 130.9, 133.6 (CH), 136.7, 137.5, 141.4, 142.7, 145.9, 147.4, 158.9, 159.6 (C), 197.8 (CO).). IR (KBr): *v* = 3061, 2937 (w), 2842 (m), 1657, 1601 (s), 1526, 1490, 1443, 1425 (m), 1396 (s), 1296, 1246, 1211, 1139, 1062, 971, 910 (m), 832, 694 (s), 611, 539 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 394 (M^+, 100), 333 (73), 258 (18), 257 (85), 229 (14), 228 (35), 227 (15), 226 (21), 105 (12), 77 (18). HRMS (EI): calcd. for $C_{25}H_{18}O$ [M]$^+$: 394.04522; found: 394.044518.

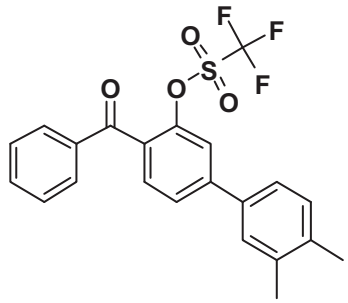


11.4.4 Synthesis of monoaryl-benzophenones

4-Benzoyl-4'-methylbiphenyl-3-yl trifluoromethanesulfonate (21a). Starting with **18** (220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol%), *p*-tolylboronic acid (81 mg, 0.6 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21a** was isolated as a white solid (141 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3 H, CH_3), 7.20-7.23 (m, 2 H, ArH), 7.39-7.43 (m, 4 H, ArH), 7.49-7.56 (m, 4 H, ArH), 7.74-7.77 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.2 (CH_3), 120.5 (q, *J* = 321 Hz), 120.7, 126.1, 127.0, 128.5, 130.0, 130.1 (CH), 130.3 (C), 131.9, 133.6 (CH), 135.2, 136.7, 139.2, 146.3, 147.4 (C), 192.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3026, 2950, 2857 (w), 1657, 1615, 1598 (m), 1548, 1448 (w), 1422 (s), 1286, 1242 (m), 1206, 1136 (s), 1085 (m), 1018 (w), 945, 899 (m), 814 (s), 746, 703, 622, 604, 540 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 420 (M^+, 100), 343 (36), 287 (23), 210 (10), 105 (32), 77 (17). HRMS (EI): calcd. for $C_{21}H_{15}O_4F_3S$ $[M]^+$: 420.06377; found: 420.063866.

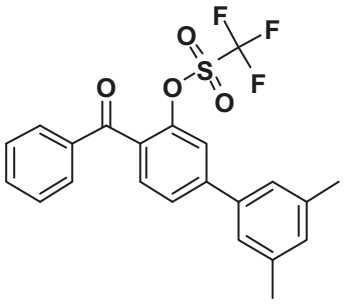
4-Benzoyl-4'-ethylbiphenyl-3-yl trifluoromethanesulfonate (21b). Starting with **18** (220 mg, 0.46 mmol), K_3PO_4 (32 mg, 146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (3 mol%), 4-ethylphenylboronic acid (90 mg, 0.6 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21b** was isolated as a white solid (150 mg, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.6Hz, 3 H, $CH_2\mathit{CH_3}$), 2.64 (q, *J* = 7.6Hz, 3 H, $\mathit{CH_2}CH_3$), 7.16-7.27 (m, 2 H, ArH), 7.38-7.47 (m, 4 H, ArH), 7.50-7.60 (m, 4 H, ArH), 7.75-7.78 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.4 (CH_3), 28.6 (CH_2), 118.5 (q, *J* = 319.1Hz), 120.7, 126.1, 127.1, 128.5, 128.8, 130.1 (CH), 131.6 (C_{Ar}), 131.8, 133.6 (CH), 135.4, 136.7, 145.5, 146.3, 147.3 (C), 192.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3025, 2961, 2918, 2854 (w), 1655, 1615 (m), 1523, 1448 (w), 1422 (s), 1322, 1285, 1240 (m), 1205, 1137 (s), 1086 (m), 1018, 979 (w), 930, 898 (m), 828 (s), 798, 703, 603, 534 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 434 (M^+, 100), 419 (10), 357 (31), 301 (16), 105 (33), 77 (16). HRMS (EI): calcd. for $C_{22}H_{17}F_3O_4S$ $[M]^+$: 434.07942; found: 434.078943.

4-Benzoyl-3',4'-dimethylbiphenyl-3-yl trifluoromethanesulfonate (21c). Starting with **18**



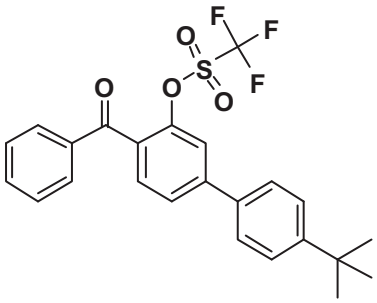
(220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol%), 3,4-dimethylphenylboronic acid (90 mg, 0.60 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21c** was isolated as a white solid (135 mg, 68%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 7.14-7.27 (m, 3 H, ArH), 7.36-7.41 (m, 2 H, ArH), 7.48-7.58 (m, 3 H, ArH), 7.73-7.76 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.5 (CH_3), 19.9 (CH_3), 118.5 (q, *J* = 320.5Hz), 120.7, 124.5, 126.1, 128.3, 128.5, 130.1, 130.5, 131.8, 133.6 (CH), 135.6, 136.7, 137.6, 139.0, 146.5, 147.3, 153.8 (C), 192.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3022, 2946, 2858, 2659 (w), 1655, 1614, 1598, 1513, 1447 (m), 1421 (s), 1319, 1280, 1242 (m), 1208, 1138 (s), 1084, 953, 862, 822, 742, 701, 651, 607, 572 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 434 (M^+, 100), 357 (29), 301 (22), 258 (10), 105 (29), 77 (15). HRMS (EI): calcd. for $C_{22}H_{17}O_4F_3S$ $[M]^+$: 434.07942; found: 434.079871.

4-Benzoyl-3', 5'-dimethylbiphenyl-3-yl trifluoromethanesulfonate (21d). Starting with **18**

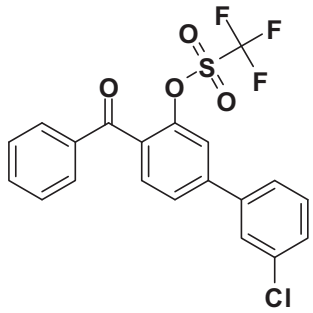


(220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol-%), 3,5-dimethylphenylboronic acid (81 mg, 0.6 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21d** was isolated as a white solid (133 mg, 67%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 6.98 (s, 1 H, ArH), 7.11 (s, 2 H, ArH), 7.34-7.39 (m, 2 H, ArH), 7.48-7.56 (m, 4 H, ArH), 7.72-7.75 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.3 ($2CH_3$), 120.6 (q, *J* = 319Hz), 121.0, 125.1, 126.4, 128.5, 130.1 (CH), 130.4 (C_{Ar}), 130.7, 131.8, 133.7 (CH), 136.7, 138.1, 138.9, 146.7, 147.3 (C), 192.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3028, 2952, 2859 (w), 1667, 1612, 1597 (m), 1553 (w), 1423 (s), 1389, 1315, 1285, 1246 (m), 1204, 1135 (s), 1069 (m), 1000 (w), 955, 899 (m), 836 (s), 755, 696, 602, 544 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 434 (M^+, 100), 357 (37), 301 (23), 258 (10), 152 (10), 105 (33), 77 (17). HRMS (EI): calcd. for $C_{22}H_{17}O_4F_3S$ $[M]^+$: 434.07942; found: 434.079065.

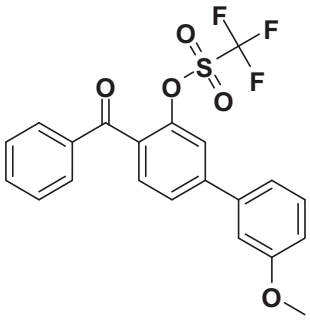
4-Benzoyl-4'-tert-butylbiphenyl-3-yl trifluoromethanesulfonate (21e). Starting with **18** (220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol%), 4-*tert*-butylphenylboronic acid (106 mg, 0.60 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21e** was isolated as a white solid (161 mg, 76%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 9 H, CH_3), 7.37-7.42 (m, 2 H, ArH), 7.45-7.51 (m, 5 H, ArH), 7.52-7.60 (m, 3 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 31.2 ($3CH_3$), 34.7 (C), 120.7, 120.6 (q, *J* = 319Hz), 121.7, 126.2, 126.3, 126.9, 128.5, 130.1 (CH), 130.3 (C), 131.9, 133.6 (CH), 136.7, 146.2, 147.4, 152.4 (C), 192.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3060, 2959, 2866 (w), 1660, 1614, 1596 (m), 1554 (w), 1462, 1415, 1318, 1241 (m), 1207, 1137 (s), 1089, 948, 895 (m), 810 (s), 696, 603, 569 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 462 (M^+, 33), 447 (100), 313 (15). HRMS (EI): calcd. for $C_{24}H_{21}O_4F_3S$ $[M]^+$: 462.11072; found: 462.110339.



4-Benzoyl-3'-chlorobiphenyl-3-yl trifluoromethanesulfonate (21f). Starting with **18** (220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol%), 3-chlorophenylboronic acid (93 mg, 0.60 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21f** was isolated as a white solid (131 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.83-6.93 (m, 5 H, ArH), 6.98-7.07 (m, 5 H, ArH), 7.24-7.27 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 118.5 (q, *J* = 319.1Hz), 121.0, 125.4, 126.5, 127.3, 128.6, 129.0, 130.1, 130.5, 131.9, 133.8 (CH), 135.2, 136.5, 139.9, 144.7, 147.2, 160.2 (C), 192.3 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.9. IR (KBr): *v* = 3085, 3034 (w), 1665 (s), 1593, 1545, 1493, 1447, 1429, 1317, 1286, 1245, 1182, 1141, 1071, 997, 915, 833 (m), 746 (s), 696 (m), 783 (s), 671, 666, 621, 527 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 442 ([M, ^{37}Cl, 40]$^+$), 440 (M^+, 100), 365 (20), 363 (52), 309 (10), 307 (27), 244 (21), 230 (13), 215 (19), 139 (27), 105 (76), 77 (31). HRMS (EI): calcd. for $C_{20}H_{12}ClF_3O_4S$ [M^+, ^{35}Cl]: 440.06021; found: 440.060214.

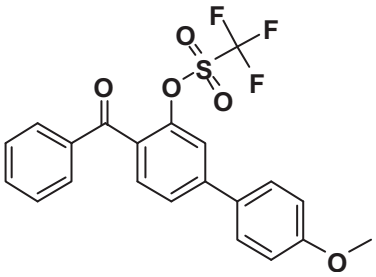


4-Benzoyl-3'-methoxybiphenyl-3-yl trifluoromethanesulfonate (21g). Starting with **18**



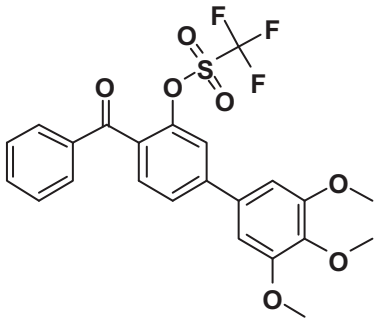
(220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol%), 3-methoxyphenylboronic acid (91 mg, 0.60 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21g** was isolated as a white solid (128 mg, 64%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 6.88-7.11 (m, 3 H, ArH), 7.30-7.42 (m, 3 H, ArH), 7.49-7.60 (m, 4 H, ArH), 7.74-7.77 (m, 1 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 55.4 (OCH_3), 113.2, 114.1, 119.6 (CH), 120.7 (q, *J* = 319.7 Hz, C), 121.0, 126.5, 128.5, 130.1, 130.3 (CH), 130.8 (C), 131.8, 133.7 (CH), 136.6, 139.5, 146.2, 147.2, 160.2 (C), 192.4 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3078, 3030 (w), 1663 (s), 1596, 1540, 1492, 1443, 1428, 1316, 1285, 1244, 1180, 1140, 1071, 998, 913, 833 (m), 753 (s), 697 (m), 783 (s), 667, 529 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 436 (M^+, 100), 359 (24), 303 (14), 260 (14), 226 (11), 105 (28), 77 (16). HRMS (EI): calcd. for $C_{21}H_{15}O_5S$ $[M]^+$: 436.05868; found: 436.058189.

4-Benzoyl-4'-methoxybiphenyl-3-yl trifluoromethanesulfonate (21h). Starting with **18**



(220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol%), 4-methoxyphenylboronic acid (91 mg, 0.60 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21h** was isolated as a white solid (126 mg, 63%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 6.92-6.96 (m, 2 H, ArH), 7.37-7.43 (m, 2 H, ArH), 7.46-7.52 (m, 4 H, ArH), 7.54-7.55 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 55.4 (OCH_3), 114.6, 118.4 (q, *J* = 319Hz), 120.3, 125.7, 128.4, 128.5 (CH), 129.8 (C_{Ar}), 130.1, 131.9, 133.6 (CH), 136.7, 145.9, 147.4, 160.5 (C), 192.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3082, 2962, 2867 (w), 1662, 1613, 1599 (m), 1556 (w), 1463, 1414, 1317, 1243 (m), 1209, 1136 (s), 1092, 947, 893 (m), 809 (s), 697, 605, 570 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 436 (M^+, 100), 359 (14), 303 (15), 226 (15), 105 (35), 77 (16). HRMS (EI): calcd. for $C_{21}H_{15}O_5F_3S$ $[M]^+$: 436.05868; found: 436.058078.

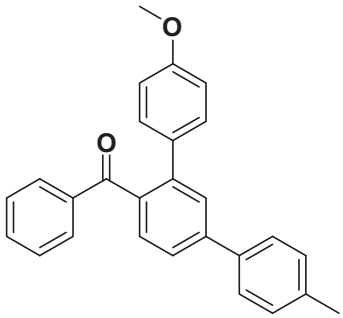
4-Benzoyl-3',4',5'-trimethoxybiphenyl-3-yl trifluoromethanesulfonate (21i). Starting with



18 (220 mg, 0.46 mmol), K_3PO_4 (146 mg, 0.69 mmol), $Pd(PPh_3)_4$ (32 mg, 3 mol%), 3,4,5-trimethoxyphenylboronic acid (127 mg, 0.60 mmol) and 1,4-dioxane (5 mL per 1 mmol of **18**), **21i** was isolated as a white solid (132 mg, 58%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 3.85 (s, 6 H, OCH_3), 6.70 (s, 2 H, OCH_3), 7.36-7.46 (m, 3 H, CH), 7.50-7.55 (m, 3 H, CH), 7.73-7.75 (m, 2 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 56.3 (2xOCH_3), 60.9 (OCH_3), 104.6 120.9 (CH), 122.5 (q, *J* = 319.5Hz, C), 126.4, 128.5, 130.1, 131.8, 133.7 (CH), 133.9, 136.6, 139.0, 146.4, 147.2, 153.8 (C), 192.3 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. IR (KBr): *v* = 3062 (w), 2923 (m), 2851 (w), 1665, 1611, 1585, 1515, 1487, 1412, 1316, 1272 (m), 1204, 1138, 1095, 965, 913, 854, 824, 756, 700, 646, 597 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 496 (M^+, 100), 481 (28), 105 (17), 77 (10). HRMS (EI): calcd. for $C_{23}H_{19}F_3O_7S$ $[M]^+$: 496.07981; found: 496.079565.

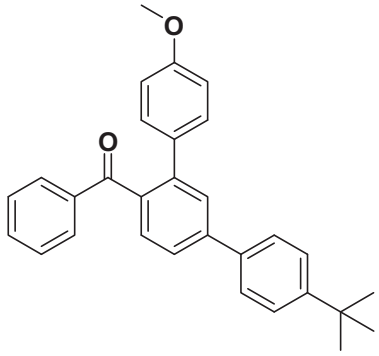
11.4.5 Synthesis of unsymmetrical diaryl benzophenones

Phenyl(4-(p-tolyl)-2-(p-methoxyphenyl)phenyl)methanone (22a). Starting with **21a** (147



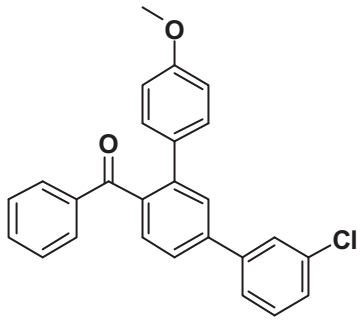
mg, 0.35 mmol), K_3PO_4 (111 mg, 0.52 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol%), 4-methoxyphenylboronic acid (68 mg, 0.45 mmol) and 1,4-dioxane (5 mL per 1 mmol of **21**), **22a** was isolated as a white solid (92 mg, 70%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.16 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 6.93-6.96 (m, 2 H, ArH), 7.04-7.13 (m, 2 H, ArH), 7.19-7.25 (m, 4 H, ArH), 7.27-7.37 (m, 2 H, ArH), 7.45-7.51 (m, 3 H, ArH), 7.53-7.65 (m, 3 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 127.1, 128.1, 128.6, 128.7, 128.8, 129.0, 129.5, 129.6, 129.9, 130.0 (CH), 137.5, 137.7, 140.1, 140.2, 141.9, 143.3 (C), 198.5 (CO). IR (KBr): *v* = 3086, 3035 (w), 1663 (s), 1598, 1544, 1495, 1443, 1425, 1311, 1280, 1239, 1176, 1138, 1069, 999, 924, 836 (m), 753 (s), 698 (m), 783 (s), 671, 667, 623, 530 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 379 (29), 378 (100), 347 (16), 301 (11), 287 (26), 273 (10), 105 (39), 91 (26). HRMS (EI): calcd. for $C_{25}H_{18}O$ $[M]^+$: 379.06870; found: 379.068576.

Phenyl(4-(*p-tert*-butylphenyl)-2-(p-methoxyphenyl)phenyl)methanone (22e) Starting with



21e (161 mg, 0.35 mmol), K_3PO_4 (111 mg, 0.52 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol%), 4-methoxyphenylboronic acid (68 mg, 0.45 mmol) and 1,4-dioxane (5 mL per 1 mmol of **21e**), **22e** was isolated as a white solid (104 mg, 71%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (s, 9 H, $3CH_3$), 3.65 (s, 3 H, OCH_3), 6.65-6.69 (m, 2 H, ArH), 7.13-7.24 (m, 5 H, ArH), 7.41-7.49 (m, 4 H, ArH), 7.53-7.61 (m, 5 H, ArH), 7.64-7.65 (m, 1 H, ArH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 31.3 (CH_3), 55.1 (OCH_3), 113.7, 125.1, 125.8, 126.9, 128.0, 128.6, 129.4, 129.9, 130.1, 132.7 (CH), 137.2, 137.3, 137.5, 139.1, 141.3, 143.0, 151.0, 158.9 (C), 198.3 (CO). IR (KBr): *v* = 3081, 3033 (w), 1663 (s), 1596, 1541, 1492, 1447, 1428, 1316, 1285, 1243, 1179, 1140, 1072, 1006, 913, 832, 698 (m), 785 (s), 670, 621, 529 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 421 (30), 420 (100), 419 (19), 406 (24), 405 (79), 443 (10), 105 (17). HRMS (EI): calcd. for $C_{30}H_{28}O_2$ $[M]^+$: 421.07981; found: 421.079910.

Phenyl(4-(*m*-chlorophenyl)-2-(*p*-methoxyphenyl)phenyl)methanone (22f). Starting with



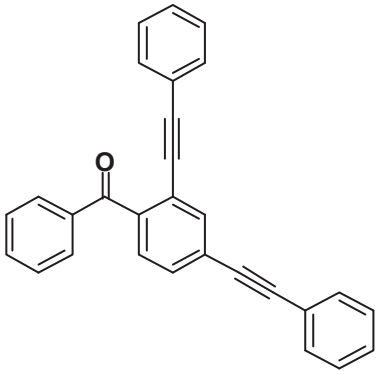
21f (154 mg, 0.35 mmol), K_3PO_4 (111 mg, 0.52 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol%), 4-methoxyphenylboronic acid (68 mg, 0.45 mmol) and 1,4-dioxane (5 mL per 1 mmol of **21f**), **22f** was isolated as a white solid (86 mg, 62%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.65 (s, 3 H, OCH_3), 6.66-6.69 (m, 2 H, ArH), 7.08-7.38 (m, 9 H, ArH), 7.47-7.62 (m, 5 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 55.2 (OCH_3), 113.8, 114.0, 119.3, 125.3, 127.5, 128.1, 128.3, 129.8, 130.0, 130.1 (C), 130.6 (CH), 132.3 (C), 132.9, 133.3 (CH), 136.5, 137.7, 138.8, 143.4, 150.2 (CH), 159.6 (C), 197.1 (CO). IR (KBr): *v* = 3062, 3025 (w), 2871 (m), 1667 (s), 1605, 1550, 1518, 1453, 1408, 1360, 1316, 1279, 1246, 1211, 1139, 1061, 976, 907, 850 (m), 833, 726, 696 (s), 660, 610, 536 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 398 ([M, ^{37}Cl, 45]$^+$), 396 ([M, ^{35}Cl, 100]$^+$), 363 (26), 287 (11). 105 (36), 91 (10) HRMS (EI): calcd. for $C_{26}H_{19}Cl_2O$ [M^+, ^{35}Cl]: 398.06872; found: 398.0687210.

11.4.6 Synthesis of symmetrical and unsymmetrical dialkynyl-benzophenones (24a-d), (25a-c).

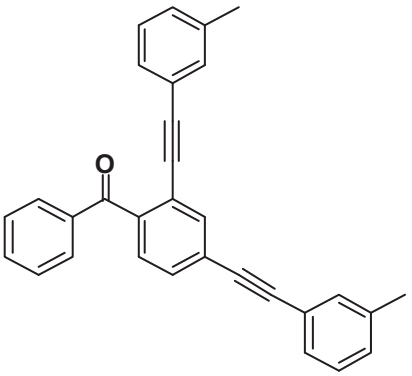
In a pressure tube (glass bomb) a suspension of $Pd(PPh_3)_4$ (3-5.0 mol%), **18** (0.50 mmol), alkyne (0.50-1.10 mmol), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10-20mol%), Et_3N (0.62-1.25 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C for 10 min. The reaction mixture was stirred at 60 -80 °C for 2-4 h. The reaction mixture was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with H_2O (3 x 20 mL), dried (Na_2SO_4), concentrated in vacuo and the residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **24a-d** and **25a-c**.

11.4.7 Synthesis of symmetrical dialkynyl-benzophenones (24a-d)

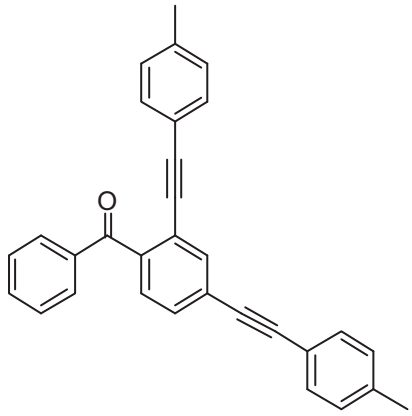
(2,4-Bis(phenylethynyl)phenyl)(phenyl)methanone (24a). Starting with **18** (238 mg, 0.50 mmol), Pd $(PPh_3)_2Cl_2$ (20mg, 6 mol%), dry CuI (19 mg, 20 mol%), $(Bu)_4NI$ (27 mg, 15 mol-%), triethylamine (252 mg, 2.5 mmol), 1-ethynylbenzene (112 mg, 1.1 mmol) was added in DMF (5mL per 1 mmol of **18**), **24a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (149 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.94-6.97 (m, 2 H, ArH), 7.08-7.15 (m, 3 H, ArH), 7.26-7.29 (m, 3 H, ArH), 7.34-7.48 (m, 7 H, ArH), 7.69-7.80 (m, 3 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 86.8, 87.9, 91.9, 95.7, 122.4, 125.9 (C), 126.1, 128.4, 128.6, 128.8 (CH), 129.3 (C), 129.0, 130.2, 131.0 (CH), 131.3 (C), 131.5, 131.8, 131.9, 133.2, 135.5 (CH), 137.2, 140.6 (C), 196.4 (CO). IR (KBr): *v* = 3079, 3032 (w), 1661, 1596, 1541, 1490, 1445, 1426, 1314, 1283, 1242, 1178, 1138, 1069, 999, 914, 835 (m), 751 (s), 698 (m), 785 (s), 669, 666, 621, 528 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 382 (M^+, 100), 381 (57), 365 (19), 353 (13), 352 (20), 351 (11), 350 (14), 276 (28), 274 (19), 77 (10). HRMS (EI): calcd. for $C_{29}H_{18}O$ $[M]^+$: 382.02323; found: 382.023235.



(2,4-Bis(m-tolylethynyl)phenyl)(phenyl)methanone (24b). Starting with **18** (238mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (20 mg, 6 mol%), dry CuI (19 mg, 20 mol%), $(Bu)_4NI$ (27 mg, 15 mol-%), triethylamine (252 mg, 2.5 mmol), 1-ethynyl-3-methylbenzene (128mg, 1.1mmol) was added in DMF (5mL per 1 mmol of **18**), **24b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (151mg, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.14 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 6.71-6.78 (m, 2 H, ArH), 6.93-7.18 (m, 4 H, ArH), 7.26-7.50 (m, 7 H, ArH), 7.66-7.80 (m, 3 H, ArH). ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ = 21.1, 21.2 (2xCH_3), 86.5, 87.6, 92.1, 96.0 (C), 122.2, 122.4, 126.0 (C), 128.0 (CH), 128.1 (C), 128.4, 128.8, 129.0, 129.5, 129.7, 130.2, 130.9, 132.1, 132.3, 133.2, 135.4 (CH), 137.2, 137.8, 138.1, 140.5 (C), 196.4 (CO). IR (KBr): *v* = 3055, 2918, 2858, 1660, 1594, 1579, 1539, 1485, 1447, 1314, 1283, 1243, 1192, 1154, 1093, 1039, 999, 962, 922, 834 (m), 780 (s), 748, 700, 686 (s), 669, 624, 584 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 410 (M^+, 100), 409 (33), 408 (15), 395 (29), 393 (12), 289 (16), 181 (10), 77 (10). HRMS (EI): calcd. for $C_{33}H_{42}O$ $[M]^+$:.

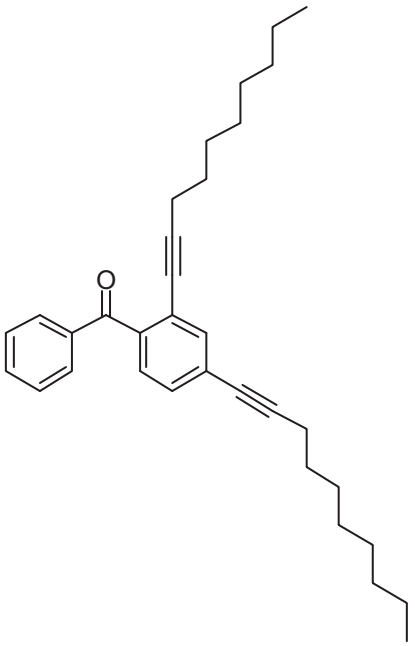


(2,4-Bis(p-tolylethynyl)phenyl)(phenyl)methanone (24c): Starting with **18** (238mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (20 mg, 6 mol%), dry CuI (19 mg, 20 mol%), $(Bu)_4NI$ (27 mg, 15 mol-%), triethylamine (252 mg, 2.5 mmol), 1-ethynyl-4-methylbenzene (128 mg, 1.1 mmol) was added in DMF (5mL per 1 mmol of **18**), **24c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (159mg, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 6.84-6.95 (m, 4 H, ArH), 7.10-7.18 (m, 3 H, ArH), 7.37-7.51 (m, 6 H, ArH), 7.68-7.82 (m, 3 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.4, 21.5 (2xCH_3), 86.2, 86.8, 87.3, 92.1, 119.3, 119.5, 122.5, 126.0 (C), 128.4, 128.8, 129.0, 129.2, 130.1, 130.7, 131.3, 131.6, 133.1, 135.3 (CH), 137.3, 138.7, 139.0, 140.3 (C), 196.5 (CO). IR (KBr): *v* = 3055, 3025, 2916, 2860 (w), 1659, 1591, 1555, 1477, 1445, 1406, 1316, 1286, 1241, 1178, 1116, 1088, 1037, 999, 917, 836 (m), 812 (s), 699 (m), 686 (s), 651, 621, 596 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 410 (M^+, 100), 409 (17), 408 (15), 396 (12), 395 (28), 366 (14), 204 (14), 197 (10), 196 (23), 191 (10), 190 (18), 182 (59), 181 (16), 176 (33), 170 (17),



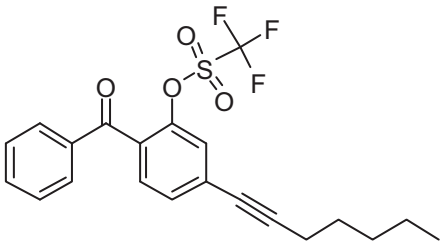
144 (13), 143 (14), 131 (12), 77 (13). HRMS (EI): calcd. for $C_{31}H_{22}O$ $[M]^+$: 410.32359; found: 410.324468.

(2,4-Di(dec-1-ynyl)phenyl)(phenyl)methanone (24d): Starting with **18** (238mg, 0.30 mmol), $Pd(PPh_3)_2Cl_2$ (20 mg, 6 mol%), dry CuI (19 mg, 10 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), triethylamine (126 mg, 1.25 mmol), 1-decyne (45mg, 0.33 mmol) was added in DMF (5mL per 1 mmol of **18**), **24d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (100mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.78-0.82 (m, 6 H, 2xCH_3), 1.16-1.28 (m, 20 H, 10×CH_2), 1.36-1.44 (m, 4 H, 2×CH_2), 1.51-1.60 (m, 4 H, 2xCH_2), 7.37-7.41 (m, 3 H, ArH), 7.48-7.54 (m, 3 H, ArH), 7.67-7.71 (m, 2 H, ArH). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.0 (CH_3), 19.6, 19.8, 22.6, 28.6, 28.7, 28.9, 29.1, 29.2, 31.8 (CH_2), 78.8, 79.3, 95.3, 97.7, 126. 5 (C), 128.3, 128.4, 129.9 (CH), 130.4 (C), 131.7, 132.4 133.3 (CH), 135.9, 137.3 (C), 195.4 (CO). IR (KBr): *v* = 3059 (w), 2952 (m), 2922 (s), 2852 (m), 2224 (w), 1659, 1593, 1543, 1481, 1446, 1404, 1317, 1292, 1264, 1239, 1177, 1159, 1123, 1027, 939, 841, 793, 744 (m), 713 (s), 694, 666 (m), 615 (w), 594 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 454 (M^+, 6), 285 (10), 105 (100), 77 (15). HRMS (EI): calcd. for $C_{33}H_{42}O[M]^+$: 454.31347; found: 454.313394.



11.4.8 Synthesis of mono-alkynyl-benzophenones (25a-c)

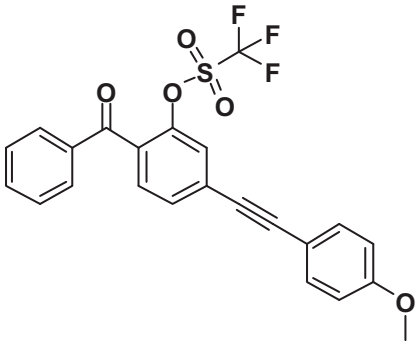
2-Benzoyl-5-(hept-1-ynyl)phenyl (25a-ctrifluoromethanesulfonate (25a). Starting with **18** (238mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 3 mol%), dry CuI (10 mg, 10 mol-%), $(Bu)_4NI$ (27 mg, 15mol%), triethylamine (126 mg, 1.25 mmol), 1-pentyne (51mg, 0.55 mmol) was added in DMF (5mL per 1 mmol of **18**), **25a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (165mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t,



J = 7.2 Hz, 3 H, $CH_2(CH_2)_3\mathit{CH_3}$), 1.25-1.36 (m, 4 H, CH_2 $CH_2(\mathit{CH_2})_2CH_3$), 1.51-1.58 (m, 2 H, $CH_2\mathit{(CH_2)}(CH_2)_2CH_3$), 2.36 (t, *J* = 7.2 Hz, 2 H, $\mathit{CH_2}(CH_2)_3CH_3$), 7.31 (s,1 H, ArH), 7.38-7.41 (m, 4 H, ArH), 7.50-7.53 (m, 1 H, ArH), 7.68-7.72 (m, 2 H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.4. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9 (CH_3), 19.4, 22.1, 28.0, 31.1 (CH_2), 78.4, 95.9 (C), 118.4 (q, *J* = 320 Hz, CF_3), 125.2, 128.5 (CH), 129.3 (C), 130.1, 130.9 (CH), 131.0 (C), 131.1, 133.7 (CH), 136.4, 146.6 (C), 192.2 (CO). IR (KBr): *v* = 3065 (w), 2931 (m), 2860 (w), 1668 (s), 1608, 1598 (m), 1493 (w), 1448 (s), 1317, 1283, 1236 (m), 1205, 1136 (s), 1086 (m), 1000 (w), 941, 970, 839, 803, 762, 697, 602 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 424 (M^+, 6), 295 (10), 105 (100), 77 (15), 29 (10). HRMS (EI): calcd. for $C_{21}H_{19}F_3O_4S$ $[M]^+$: 424.44556; found: 424.445487.

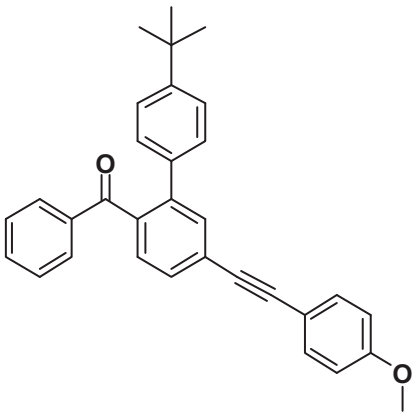
2-Benzoyl-5-(dec-1-ynyl)phenyl trifluoromethanesulfonate (25b):Starting with **18** (238mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 3 mol%),, dry CuI (10 mg, 10 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), triethylamine (126 mg, 1.25 mmol), 1-decyne (72mg, 0.55 mmol) was added in DMF (5mL per 1 mmol of **18**), **25b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (188mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.3 Hz, 3 H, $CH_2(CH_2)_6\mathit{CH_3}$), 1.17-1.26 (m, 8 H, $CH_2(CH_2)_2(\mathit{CH_2})_4CH_3$), 1.33-1.38 (m, 2 H, $CH_2\mathit{(CH_2)}(CH_2)_5CH_3$), 1.50-1.55 (m, 2 H, $CH_2\mathit{(CH_2)}$ $(CH_2)_5CH_3$), 2.36 (t, *J* = 6.9 Hz, 2 H, $\mathit{CH_2}(CH_2)_6CH_3$), 7.32 (s,1 H, ArH), 7.37-7.42 (m, 4 H, ArH), 7.51-7.55 (m, 1 H, ArH), 7.69-7.72 (m, 2 H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.4. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0 (CH_3), 19.5, 22.6, 28.3, 28.9, 29.0, 29.1, 31.8 (CH_2), 78.4, 95.9 (C), 114.2 (q, *J* = 320 Hz, CF_3), 125.2, 128.5 (CH), 129.3 (C), 130.1, 130.9 (CH), 131.0 (C), 131.1, 133.7 (CH), 136.5, 146.6 (C), 192.2 (CO). IR (KBr): *v* = 2924 (m), 2854 (w), 1669 (s), 1608, 1542, 1465 (m), 1426 (s), 1316, 1283, 1235 (m), 1206, 1138 (s), 1087, 1013, 970, 939, 884, 798, 698, 661, 603 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 466 (M^+, 9), 410 (14), 396 (10), 395 (10), 105 (100), 77 (16). HRMS (EI): calcd. for $C_{24}H_{25}F_3O_4S$ $[M]^+$: 466.63943; found: 466.639334.

2-Benzoyl-5-((4-methoxyphenyl)ethynyl)phenyl trifluoromethanesulfonate (25c). Starting with **18** (238mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 3 mol%), dry CuI (10 mg, 10 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), triethylamine (126 mg, 1.25 mmol), 4-methoxyphenylacetylene (72mg, 0.55 mmol) was added in DMF (5mL per 1 mmol of **18**), **25c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (156mg, 68%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3 H, OCH_3), 6.78-6.81 (m, 2 H, ArH), 7.34-7.50 (m, 8 H, ArH), 7.68-7.71 (m, 2 H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.3. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 55.3 (OCH_3), 85.7, 94.3 (C), 114.2 (CH), 117.5 (q, J = 320 Hz, CF_3), 124.8, 128.6 (CH), 128.8 (C), 130.1, 130.7 (CH), 131.0 131.2 (C), 131.3, 133.4, 133.8 (CH), 136.4, 146.7, 160.4 (C), 192.2 (CO). IR (KBr): ν = 3085 (w), 2958 (m), 2837 (w), 1665 (s), 1596, 1539, 1513 (m), 1428 (s), 1394, 1282, 1246 (m), 1207, 1139 (s), 1076, 1025, 968, 912, 849 (m), 829 (s), 801, 745, 695, 653 (m), 600 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 460 (M^+, 100), 327 (21), 312 (12), 105 (16), 77 (11). HRMS (EI): calcd. for $C_{23}H_{15}F_3O_5S$ $[M]^+$: 460.32357; found: 460,323471.



11.4.9 Synthesis of alkynyl-aryl-benzophenones

(4'-tert-Butyl-5-((4-methoxyphenyl)ethynyl)biphenyl-2-yl)(phenyl)methanone (26c). Starting with **27c** (92 mg, 0.20 mmol), K_3PO_4 (63 mg, 0.30 mmol), $Pd(PPh_3)_4$ (7mg, 3 mol-%), *4-tert*-butylphenylboronic acid (46 mg, 0.26 mmol) and 1,4-dioxane (5 mL per 1 mmol of **25c**), **26c** was isolated as a white solid (65 mg, 73%), mp. 131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 9 H, $3CH_3$), 3.77 (s, 3 H, OCH_3), 6.81-6.84 (m, 2 H, ArH), 7.11-7.31 (m, 6 H, ArH), 7.40-7.56 (m, 8 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 31.1 ($3CH_3$), 34.3 (C), 55.3 (OCH_3), 87.5, 91.2 (C), 114.0 (CH), 114.9 (C), 125.1 (CH), 125.8 (C), 127.9, 128.6, 129.0, 129.7, 132.6, 132.9, 133.2 (CH), 136.4, 137.4, 138.0, 141.5, 150.4, 159.9 (C), 198.3 (CO). IR (KBr): ν = 3057, 3031 (w), 2957 (m), 2903, 2866, 2837 (w), 2220, 2201, 1713 (m), 1663 (s), 1593, 1543 (m), 1509 (s), 1462 (m), 1446 (w), 1412, 1362, 1280



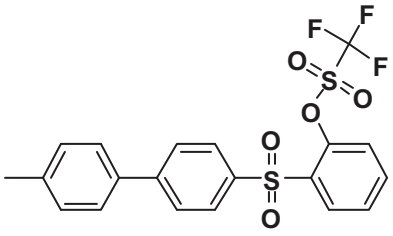
(m), 1245 (s), 1217, 1173, 1105, 1027, 927, 887 (m), 829 (s), 802, 762 (m), 701 (s), 655, 621, 536 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 444 (M^+, 100), 430 (17), 429 (42), 387 (10), 105 (24), 77 (13). HRMS (EI): calcd. for $C_{32}H_{28}O_2$ $[M]^+$: 444.20838; found: 444.208616.

11.5 Synthesis of Bis(diaryl)sulfones by Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,4′-Bis(trifluoromethylsulfonyloxy)-diphenylsulfone

11.5.1 Regioselective Suzuki reactions. Synthesis of (29a-d).

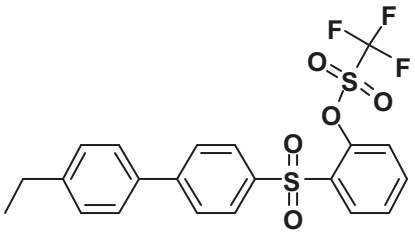
A 1,4-dioxane solution of the arylboronic acid **19** (1.1-2.2 equiv.), K_3PO_4 (3.0 equiv.), $Pd(PPh_3)_4$ and **28** or **30** was stirred at 60-90 °C for 4 h under argon atmosphere. After cooling to 20 °C, a saturated aqueous solution of NH_4Cl was added. The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography.

2-(4'-Methylbiphenyl-4-ylsulfonyl)phenyl trifluoromethanesulfonate (29a) Starting with



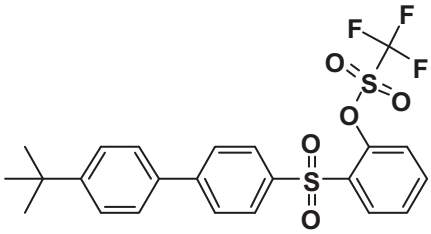
with **28** (257 mg, 0.5 mmol), K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (26 mg, 3 mol%), 4-methylphenylboronic acid (75 mg, 0.55 mmol) and 1,4-dioxane (5 mL per 1 mmol of **28**), **29a** was isolated as a white solid (164 mg, 77%). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 7.19-7.22 (d, *J* = 8.0 Hz, 2H, ArH), 7.32-7.35 (m, 1H, $2CH_2$), 7.41 (d, *J* = 8.2 Hz, 2H, ArH), 7.47-7.53 (m, 1H, ArH), 7.58-7.61 (m, 1H, ArH), 7.63-7.66 (m, 2H, ArH), 7.95 (d, *J* = 8.6 Hz, 2H, ArH), 8.23-8.27 (m, 1H, ArH). ^{19}F NMR (282MHz, $CDCl_3$): δ = -73.1. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.1 (CH_3), 122.2 (CH), 124.0 (q, *J* = 321.7 Hz, CF_3), 127.2, 127.5, 128.5, 128.9, 129.7, 130.9 (CH), 134.4 (C), 135.5 (CH), 136.0, 138.3, 138.8, 146.5, 146.8 (C). IR (KBr): *v* = 2959, 2928, 2869 (w), 1590, 1514, 1467, 1392, (m), 1313, 1151 (s), 1093, 1003 (m), 820 (s), 752, 623, 565 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 426 ($[M]^+$, 100), 333 (19), 332 (21), 305 (10), 304 (14), 198 (28), 197 (23), 180 (18), 178 (14), 166 (26), 165 (83), 152 (25). HRMS (EI, 70 eV): calcd for $C_{17}H_{13}O$: 312.01443; found 312.013869: calcd for $C_{28}H_{26}O_2$: 426.16480; found 426.164948.

2-(4'-Ethylbiphenyl-4-ylsulfonyl)phenyl trifluoromethanesulfonate (29b) Starting with



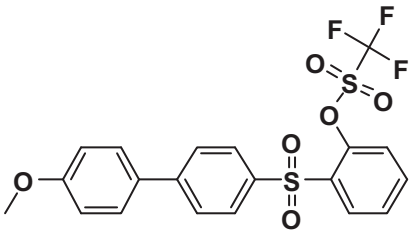
with **28** (257 mg, 0.5 mmol), K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (26 mg, 3 mol%), 4-ethylphenylboronic acid (82 mg, 0.55 mmol) and 1,4-dioxane (5 mL per 1 mmol of **28**), **29b** was isolated as a white solid (190 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (d, J = 7.6 Hz, 3H, CH_3), 7.22 (d, J = 8.4 Hz, 2H, ArH), 7.32-7.35 (m, 1H, ArH), 7.44 (d, J = 8.2 Hz, 2H, ArH), 7.47-7.53 (m, 1H, ArH), 7.58-7.62 (m, 1H, ArH), 7.65 (d, J = 8.7 Hz, 2H, ArH), 7.94 (d, J = 8.7 Hz, 2H, ArH), 8.23-8.24 (m, 1H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -73.1. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 15.4 (CH_3), 28.5 (CH_2), 122.2 (CH), 123.5 (q, J = 322.0 Hz, CF_3), 127.3, 127.5, 128.5, 128.6, 128.8, 130.9 (CH), 134.4 (C), 135.5 (CH), 136.3, 138.3, 145.1, 146.5, 146.9 (C). IR (KBr): ν = 3108, 3023, 2965, 2852 (w), 1591, 1468 (m), 1433, 1332, 1200, 1157, 1128, 870 (s), 786, 728, 619, 561 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 470 ([M]$^+$, 100), 455 (12), 258 (15), 257 (33), 245 (38), 244 (42), 229 (16), 227 (12), 197 (24), 165 (28), 152 (15). HRMS (ESI M+H, 70 eV): calcd for $C_{21}H_{18}F_3O_5S_2$: 471.05423; found 471.05405.

2-(4'-tert-Butylbiphenyl-4-ylsulfonyl)phenyl trifluoromethanesulfonate (31c) Starting



with with **28** (257 mg, 0.5 mmol), K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (26 mg, 3 mol%), *4-tert*-butylphenylboronic acid (98 mg, 0.55 mmol) and 1,4-dioxane (5 mL per 1 mmol of **28**), **29c** was isolated as a white solid (206 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 9H, $3CH_3$), 7.34 (d, J = 8.2 Hz, 1H, ArH), 7.44 (d, J = 7.0 Hz, 2H, ArH), 7.47-7.48 (m, 1H, ArH), 7.52 (d, J = 7.7 Hz, 2H, ArH), 7.60 (d, J = 8.1 Hz, 1H, ArH), 7.64 (d, J = 8.7 Hz, 2H, ArH), 7.95 (d, J = 8.6 Hz, 2H, ArH), 8.25 (d, J = 7.8 Hz, 1H, ArH). ^{19}F NMR (282MHz, $CDCl_3$): δ = -73.1. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 31.2 ($3CH_3$), 34.6 (C), 122.2 (CH), 123.5 (q, J = 322.3 Hz, CF_3), 126.0, 127.0, 127.5, 128.5, 128.8, 130.9 (CH), 134.4 (C), 135.5 (CH), 136.0, 138.3, 146.5, 146.7, 152.0 (C). IR (KBr): ν = 3023, 2959, 2862 (w), 1592, 1467 (m), 1433, 1331 (s), 1247, 1215, 1200 (m), 1156, 1128, 870 (s), 821, 786, 723, 709, 613, 580, 566, 554 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 498 ([M]$^+$, 35), 485 (13), 484 (25), 483 (100), 285 (18), 271 (25). HRMS (ESI M+H, 70 eV): calcd for $C_{21}H_{18}F_3O_5S_2$: 471.05423; found 471.05405.

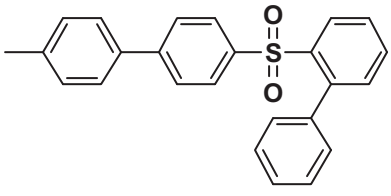
2-(4'-Methoxybiphenyl-4-ylsulfonyl)phenyl trifluoromethanesulfonate (29d) Starting with



28 (257 mg, 0.4 mmol), K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (26 mg, 3 mol%), 4-methoxyphenylboronic acid (83 mg, 0.55 mmol) and 1,4-dioxane (5 mL per 1 mmol of **28**), **29d** was isolated as a white solid (115 mg, 74%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3H, OCH_3), 6.90 (d, J = 7.0 Hz, 2H, ArH), 7.30-7.33 (m, 1H, ArH), 7.45 (d, J = 7.0 Hz, 2H, ArH), 7.48-7.51 (m, 1H, ArH), 7.57-7.63 (m, 3H, ArH), 7.92 (d, J = 8.7 Hz, 2H, ArH), 8.21-8.24 (m, 1H, ArH). ^{19}F NMR (282MHz, $CDCl_3$): δ = -73.2. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 114.5, 122.2, 122.3 (CH), 123.5 (q, J = 322.0 Hz, CF_3), 128.5, 128.6, 128.9, 130.9 (CH), 131.2, 134.5 (C), 135.5 (CH), 137.9, 146.4, 146.5, 160.3 (C). IR (KBr): ν = 3070, 2964, 2838 (w), 1589 (m), 1426, 1331 (s), 1229 (m), 1200, 1157, 1128 (s), 1093, 1034 (m), 881 (m), 827, 774, 738, 684, 618, 564 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 426 ([M]$^+$, 100), 333 (19), 332 (21), 305 (10), 304 (14), 198 (28), 197 (23), 180 (18), 178 (14), 166 (26), 165 (83), 152 (25). HRMS (EI, 70 eV): calcd for $C_{17}H_{13}O$: 312.01443; found 312.013869: calcd for $C_{28}H_{26}O_2$: 426.16480; found 426.164948.

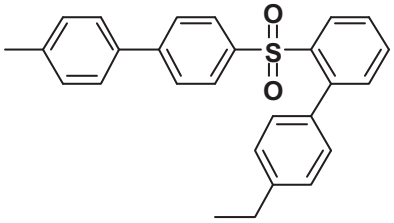
11.5.2 Synthesis of unsymmetrical Bis(diaryl)sulfones (30a-e)

2-(4'-Methylbiphenyl-4-ylsulfonyl)biphenyl (30a) Starting with **29a** (228 mg, 0.50 mmol),

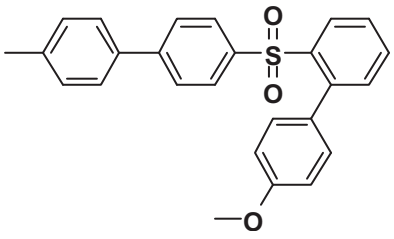


K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%), phenylboronic acid (67 mg, 0.55 mmol) and 1,4-dioxane (5 mL per 1 mmol of **29a**), **30a** was isolated as a solid (165 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 6.91 (d, J = 7.0 Hz, 2H, ArH), 7.08-7.14 (m, 3H, ArH), 7.16-7.20 (m, 5H, ArH), 7.29-7.33 (m, 1H, ArH), 7.28 (d, J = 8.0 Hz, 2H, ArH), 7.34 (d, J = 8.2 Hz, 2H, ArH), 7.49-7.53 (m, 2H, ArH), 8.36-8.39 (m, 1H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.1 (CH_3), 126.6, 127.0, 127.2, 127.5, 127.6, 128.1, 128.4, 129.7, 130.0, 132.6, 132.8 (CH), 136.4, 138.1, 138.5, 139.0, 139.9, 142.1, 145.2 (C). IR (KBr): ν = 3052, 2918, 2852 (w), 1591, 1464 (m), 1297, 1147 (s), 1090, 1005, 813, 757, 702, 690 (m), 625, 582 (s), 541 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 384 ([M]$^+$, 100), 320 (28), 304 (19), 289 (19), 215 (13), 183 (43), 165 (26), 152 (75). HRMS (EI, 70 eV): calcd for $C_{25}H_{20}O_2S$: 384.11785; found 384.117575.

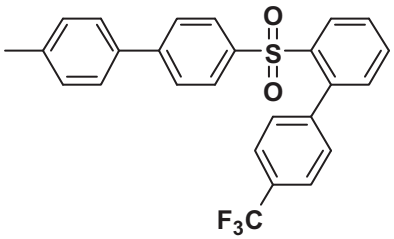
4'-Ethyl-2-(4'-methylbiphenyl-4-ylsulfonyl)biphenyl (30b) Starting with **29a** (228 mg, 0.50 mmol), K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%), 4 -ethylphenylboronic acid (82 mg, 0.55 mmol) and 1,4-dioxane (5 mL per 1 mmol of **29a**), **30b** was isolated as a solid (187 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, J = 7.7 Hz, 3 H, CH_2CH_3), 2.31 (s, 3 H, CH_3), 2.61 (q, J = 7.6Hz, 2 H, CH_2CH_3), 6.80-6.82 (m, 2 H, ArH), 6.89-6.93 (m, 2 H, ArH), 7.07-7.20 (m, 5 H, ArH), 7.23-7.36 (m, 4 H, ArH), 7.44-7.48 (m, 2 H, ArH), 8.32-8.36 (m, 1 H, ArH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.4, 21.1 (CH_3), 28.5 (CH_2), 127.1 (C), 127.2, 127.3, 127.5, 127.6, 128.6, 128.9, 129.8, 130.9, 135.5, 136.1 (CH), 138.3, 138.8, 139.7, 145.1, 146.5, 146.7, 146.9 (C). IR (KBr): ν = 3104 (w) 3058 (w), 2967 (w), 2920 (w), 2873 (w), 1592 (m), 1555 (w), 1484 (w), 1450 (w), 1423 (s), 1406 (w), 1333 (s), 1297 (m), 1228 (m), 1209 (s), 1157 (s), 1128 (s), 1089 (m), 1054 (m), 1003 (m), 958 (w), 884 (s), 781 (m), 717 (m), 685 (m), 622 (m), 595 (s), 560 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 412 ([M]$^+$, 100), 348 (12), 333 (22), 318 (26), 197 (26), 165 (50), 152 (32). HRMS (EI, 70 eV): calcd for $C_{27}H_{24}O_2S$: 412.14973; found: 412.14882.



4'-Methoxy-2-(4'-methylbiphenyl-4-ylsulfonyl)biphenyl (30c) Starting with **29a** (228 mg, 0.5 mmol), K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%), 4-methoxyphenylboronic acid (83 mg, 0.5 mmol) and 1,4-dioxane (5 mL per 1 mmol of **29a**), **30c** was isolated as a solid (151 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 6.91 (d, J = 7.0 Hz, 2H, ArH), 7.08-7.14 (m, 3H, ArH), 7.16-7.20 (m, 4H, ArH), 7.29-7.33 (m, 1H, ArH), 7.28 (d, J = 8.0 Hz, 2H, ArH), 7.34 (d, J = 8.2 Hz, 2H, ArH), 7.49-7.53 (m, 1H, ArH), 8.36-8.39 (m, 1H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.1 (CH_3), 55.3 (OCH_3), 112.7, 126.5, 127.0, 127.2, 127.4, 128.1, 128.5, 129.7 (CH), 130.5 (C), 131.2, 132.9 (CH), 135.3, 136.4, 137.3, 139.1, 140.0, 142.3, 145.1, 151.7 (C). IR (KBr): ν = 3056, 2952, 2921, 2851 (w), 1612, 1574, 1514, 1462, 1391, 1309, 1245, 1032, 832 (m), 758 (s), 672 (m), 625 (s), 538 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 414 ([M]$^+$, 100), 335 (14), 305 (10), 168 (14), 167 (10), 152 (26), 140 (14), 139 (24). HRMS (EI, 70 eV): calcd for $C_{26}H_{22}O_2S$: 414.12842; found 414.128525.

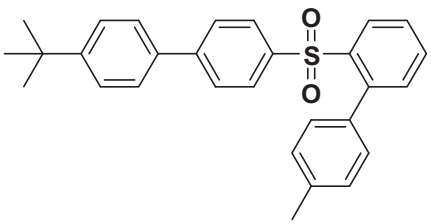


2-(4'-Methylbiphenyl-4-ylsulfonyl)-4'-(trifluoromethyl)biphenyl (30d) Starting with **29a**



(228 mg, 0.50 mmol), K_3PO_4 (159 mg, 0.75 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%), 4 (trifluoromethyl) phenylboronic acid (104 mg, 0.55 mmol) and 1,4-dioxane (5 mL per 1 mmol of **29a**), **30c** was isolated as a solid (183 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 7.04 (d, J = 7.9 Hz, 2H, ArH), 7.10-7.13 (m, 1H, ArH), 7.16-7.21 (m, 4H, ArH), 7.28-7.33 (m, 3H, ArH), 7.36 (d, J = 7.2 Hz, 2H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.8. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.1 (CH_3), 122.6 (q, J = 274 Hz, C), 124.1 (d, J = 3.8 Hz, CH), 126.7, 127.0, 128.0, 128.3, 128.5 (CH), 129.6 (C), 129.8 (CH), 130.1 (C), 130.4, 132.0, 133.0 (CH), 136.1, 138.7, 140.1 (q, J = 36.5 Hz, CH), 140.5, 141.7, 145.5 (C). IR (KBr): v = 3062, 2849 (w), 1591, 1470, 1392 (m), 1313, 1152 (s), 1107, 1062 (m), 811 (s), 756, 626 (m), 582 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 452 ([M]$^+$, 100), 215 (10), 201 (15), 183 (55), 167 (12), 155 (15), 152 (46). HRMS (EI, 70 eV): calcd for $C_{26}H_{19}O_2F_3S$: 452.10524; found 452.104506.

2-(4'-tert-Butylbiphenyl-4-ylsulfonyl)-4'-methylbiphenyl (29e) Starting with **29c** (249 mg,



0.40 mmol), K_3PO_4 (127 mg, 0.60 mmol), $Pd(PPh_3)_4$ (14 mg, 3 mol%), 4 -methylphenylboronic acid (72 mg, 0.44 mmol) and 1,4-dioxane (5 mL per 1 mmol of **29c**), **30e** was isolated as a solid (153 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 9H, $3CH_3$), 2.32 (s, 3H, CH_3), 6.91 (d, J = 7.0 Hz, 2H, ArH), 7.08-7.14 (m, 3H, ArH), 7.16-7.20 (m, 5H, ArH), 7.29-7.33 (m, 1H, ArH), 7.28 (d, J = 8.0 Hz, 2H, ArH), 7.34 (d, J = 8.2 Hz, 2H, ArH), 7.49-7.53 (m, 2H, ArH), 8.34-8.37 (m, 1H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.2, 31.2 (CH_3), 34.6 (C), 125.9, 126.5, 126.9, 127.5, 127.9, 128.2, 128.4, 129.8, 132.7, 132.8 (CH), 135.3, 136.4, 137.3, 139.1, 140.0, 142.3, 145.1, 151.7 (C). IR (KBr): v = 3051, 2954, 2864 (w), 1591, 1463, 1312 (m), 1153 (s), 1109, 1002 (m), 813 (s), 761, 739, 708 (m), 603, 559, 535 (s)cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 440 ([M]$^+$, 48), 426 (31), 425 (100), 166 (11), 165 (23), 152 (17). HRMS (EI, 70 eV): calcd for $C_{29}H_{28}O_2S$: 440.18045; found 440.180674.

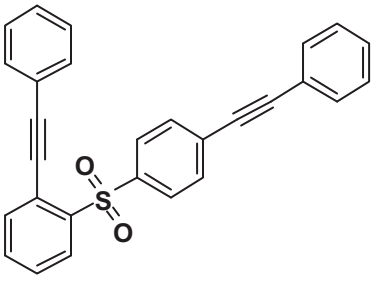
11.6 Site-Selective Sonogashira Reactions of 2,4′-Bis(trifluoromethylsulfonyloxy)diphenylsulfone

11.6.1 Synthesis of dialkynyl-diphenylsulfones

In a pressure tube (glass bomb) a suspension of $Pd(PPh_3)_2Cl_2$ (2.5-5.0 mol%), **28** (257 mg, 0.5 mmol), alkyne (0.50-1.10 mmol), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10mol%), Et_3N (0.62-1.25 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C for 10 min. The reaction mixture was stirred at 60 -80 °C for 2-4 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with H_2O (3 x 20 mL), dried (Na_2SO_4), concentrated in vacuo and the residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **(31a-e)** and **(32a-e)**.

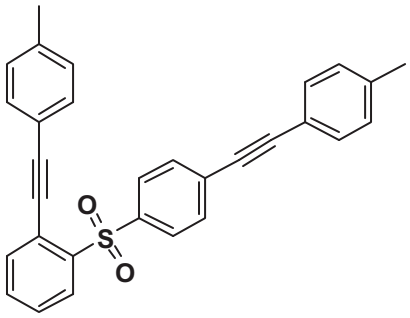
11.6.1 Synthesis of symmetrical dialkynyl-diphenylsulfones (31a-31e)

2,4'-Sulfonylbis((phenylethynyl)benzene) (31a). Starting with **28** (257mg, 0.50 mmol), Pd

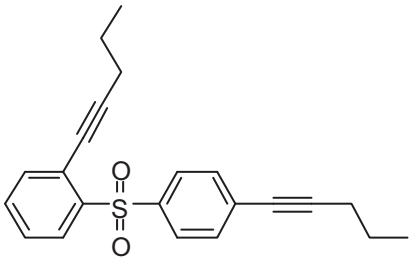


$(PPh_3)_2Cl_2$ (18 mg, 5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.18 mL, 1.25 mmol), ethynylbenzene (0.12 mL, 1.1 mmol) and DMF (4 mL), following the *general procedure* **31a** was prepared as a colourless soild (184 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.02-7.17 (m, 4H, ArH), 7.15-7.26 (m, 3H, ArH), 7.29-7.31 (m, 2H, ArH), 7.33-7.39 (m, 1H, ArH), 7.45-7.48 (d, 1 H, J = 1.8, 7.8 Hz, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 85.8, 87.8, 93.0, 98.2, 122.3, 122.4, 122.7 (C), 128.3, 128.4, 128.5, 129.0, 129.1, 129.2, 131.6, 131.7, 131.8, 132.3, 133.1, 134.8 (CH), 135.2, 139.7, 141.0 (C). IR (KBr): ν = 3060, 2924, 2853 (w), 1780, 1597, 1587, 1491, 1465, 1441, 1395, 1359 (m), 1319 (s), 1279, 1249, 1220, 1155 (s), 1123, 1086, 916, 834 (m), 746, 688, 673, 622, 583 (s), 548 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 418 ([M]$^+$, 21), 352 (33), 313 (100), 284 (21), 213 (10). HRMS (EI, 70 eV): calcd for $C_{28}H_{18}O_2S$: 418.10220; found: 418.102241.

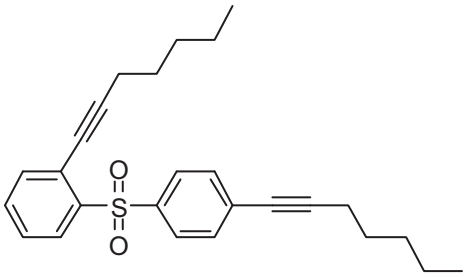
2,4'-Sulfonylbis((p-tolylethynyl)benzene) (31b) Starting with **28** (257mg, 0.50 mmol), Pd $(PPh_3)_2Cl_2$ (18 mg, 5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.18 mL, 1.25 mmol), 1-ethynyl-4-methylbenzene (0.14 mL, 1.1 mmol) and DMF (4 mL), following the *general procedure* **31b** was prepared as a colourless oil (205 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25-7.27 (m, 4H, ArH), 7.31-7.34 (m, 3H, ArH), 7.40-7.56 (m, 8H, ArH), 7.77-7.80 (m, 2H, ArH), 8.18 (dd, 1H, *J* = 1.8, 7.8 Hz, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 19.2, 19.3 (CH_3), 82.9, 85.0, 91.0, 96.2, 116.9, 117.0, 120.6 (C), 125.9, 126.0, 126.4, 126.9, 127.0, 129.2, 129.3, 129.4, 130.7 (CH), 132.5, 136.9, 137.1, 137.2, 138.6 (C). IR (KBr): *v* = 3060, 2924, 2853 (w), 2216, 1780, 1597, 1587, 1491, 1465, 1441, 1395, 1359 (m), 1319 (s), 1279, 1249, 1220, 1155 (s), 1123, 1086, 916, 834 (m), 746, 688, 673, 622, 583 (s), 548 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 446 ([M]$^+$, 19), 382 (18), 366 (10), 350 (10), 328 (24), 327 (100), 189 (18), 176 (10), 119 (33). HRMS (EI, 70 eV): calcd for $C_{30}H_{22}O_2S$: 446.13350; found: 446.133844.



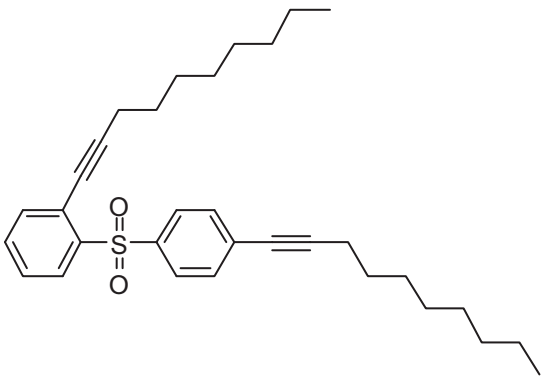
2,4'-Sulfonylbis(pent-1-ynylbenzene) (31c). Starting with **28** (257mg, 0.50 mmol), Pd $(PPh_3)_2Cl_2$ (18 mg, 5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.18 mL, 1.1 mmol), 1-pentyne (0.10 mL, 1.1 mmol) and DMF (4 mL), following the *general procedure* **31c** was prepared as a colourless oil (149 mg, 85%).^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.92-0.99 (m, 6H, $2CH_3$), 1.48-1.60 (m, 4H, CH_2), 2.28-2.35 (m, 4H, $2CH_2$), 7.37-7.42 (m, 4H, ArH), 7.74-7.79 (m, 2H, ArH), 8.16-8.20 (m, 1H, ArH). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 13.5, 13.6 (CH_3), 21.4, 21.6, 21.8, 21.9 (CH_2), 79.6, 79.7, 94.6, 100.3, 123.5 (C), 127.6, 128.1, 128.9 (CH), 129.3 (C_{Ar}), 131.4, 132.9, 135.1 (CH), 139.1, 141.7 (C_{Ar}). IR (KBr): *v* = 3063 (w) 2961 (m), 2870 (w), 1590, 1467, 1317 (m), 1153 (s), 1128, 1089, 835 (m), 748, 611 (s), 580 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 350 ([M]$^+$, 4), 323 (22), 322 (100), 280 (17), 279 (83), 263 (12), 257 (31), 241 (10), 229 (11), 228 (16), 226 (16), 215 (14), 171 (12), 136 (11), 128 (12), 115 (14). HRMS (EI, 70 eV): calcd for $C_{22}H_{22}O_2S$: 350.10900; found: 350.109274.



2,4'-Sulfonylbis(hept-1-ynylbenzene) (31d) Starting with **28** (257mg, 0.50 mmol), Pd $(PPh_3)_2Cl_2$ (18 mg, 5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.18 mL, 1.25 mmol), 1-heptyne (0.14 mL, 1.1 mmol) and DMF (4 mL), following the *general procedure* **31d** was prepared as a colourless oil (179 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0. 82-0.87 (m, 6H, $2CH_3$), 1.23-1.36 (m, 8H, $4CH_2$), 1.48-1.55 (m, 4H, $2CH_2$), 2.29-2-35 (m, 4H, $2CH_2$), 7.36-7.42 (m, 5H, ArH), 7.74-7.77 (m, 2H, ArH), 8.16-8.19 (m, 1H, ArH). ^{13}CNMR (75 MHz, $CDCl_3$): δ = 13.9, 14.0 (CH_3), 19.4, 19.8, 22.1, 22.2, 27.8, 28.1, 31.0, 31.1 (CH_2), 79.4, 79.5, 94.8, 100.5 (C), 123.5 (C_{Ar}), 127.6, 128.1, 128.9 (CH), 129.3 (C), 131.4, 132.9, 135.1 (CH), 139.1, 140.7 (C). IR (KBr): v = 3063 (w) 2927 (m), 2857 (w), 1590, 1467, 1319 (m), 1154 (s), 1128, 1090, 835 (m), 755 (s), 667 (m), 612 (s), 581 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 406 ([M]$^+$, 1), 351 (10), 350 (42), 323 (39), 308 (10), 307 (40), 228 (10), 226 (11), 221 (14), 220 (14), 219 (100), 215 (11), 207 (10), 163 (15), 137 (10), 129 (10), 128 (11), 115 (16), 81 (10). HRMS (ESI$^+$): calcd for $C_{26}H_{31}O_2S$: 407.2039; found: 407.2048.



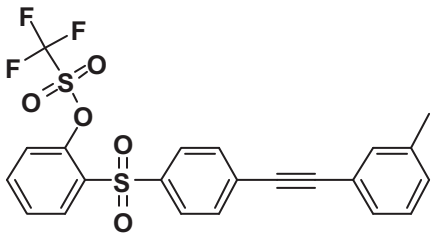
2,4'-Sulfonylbis(dec-1-ynylbenzene) (31e) Starting with **28** (257mg, 0.50 mmol), Pd $(PPh_3)_2Cl_2$ (18 mg, 5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.2 mL, 1.25 mmol), 1-decyne (0.20 mL, 1.1 mmol) and DMF (4 mL), following the *general procedure* **31e** was prepared as a colourless oil (220 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.78-0.83 (m, 6H, $2CH_3$), 1.19-1.24 (m, 16H, $8CH_2$), 1.30-1.39 (m, 4H, $2CH_2$), 1.45-1.54 (m, 4 H, $2CH_2$), 2.29-2.35 (m, 4 H, $2CH_2$), 7.35-7.42 (m, 5 H, ArH), 7.73-7.77 (m, 2 H, ArH), 8.16-8.19 (m, 1 H, ArH). ^{13}CNMR (75 MHz, $CDCl_3$): δ = 14.0, 14.1 (CH_3), 19.4, 19.9, 22.6, 23.1, 23.3, 22.7, 28.1, 28.4, 28.9, 29.0, 29.1, 29.2, 31.8, 31.9 (CH_2), 79.4, 79.5, 94.8, 100.5, 123.5 (C), 127.6, 128.1, 128.9 (CH), 129.3 (C), 131.4, 132.9, 135.0 (CH), 139.1, 140.7 (C). IR (KBr): v = 3060, 2924, 2853 (w), 2216, 1780, 1597, 1587, 1491, 146, 1441, 1395, 1359 (m), 1319 (s), 1279, 1249, 1220 (m), 1155 (s), 1123, 1086, 916, 834, 746, 688, 673 (m), 622, 583 (s), 548 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z*



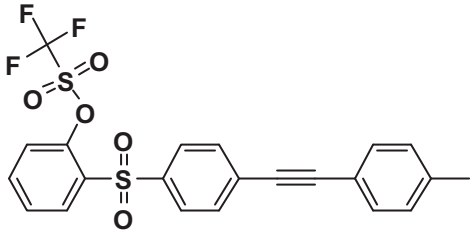
(%) = 490 ([M]$^+$, 1), 392 (28), 366 (10), 365 (37), 350 (13), 349 (38), 262 (16), 261 (100), 207 (25), 123 (15), 115 (10). HRMS (EI, 70 eV): calcd for $C_{32}H_{42}O_2S$: 490.29000; found: 490.288484.

11.6.2 Synthesis of alkynyl-diphenylsulfones

2-(4-(m-Tolylethynyl)phenylsulfonyl)phenyl trifluoromethanesulfonate (32a) Starting with **28** (257 mg, 0.50 mmol), Pd $(PPh3)_2Cl_2$ (09 mg, 2.5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), 1-ethynyl-3-methylbenzene **32a** (0.06 mL, 0.5 mmol) and DMF (4 mL), following the *general procedure* **32a** was prepared as a colourless oil (180 mg, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 (t, 3H, J = 7.2 Hz, CH_3), 1.16-1.26 (m, 8H, $4CH_2$), 1.30-1.38 (m, 2H, CH_2), 1.46-1.55 (m, 2H, CH_2), 2.32 (t, 2H, J = 7.0 Hz, CH_2), 7.28-7.31 (m, 2H, ArH), 7.40-7.62 (m, 3H, ArH), 7.78-7.81 (m, 2H, ArH), 8.17-8.20 (m, 1H, ArH) . ^{19}FNMR (282 MHz, $CDCl_3$): δ = -73.1. ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 13.0 (CH_3), 18.4, 21.6, 27.3, 27.8, 28.0, 28.1, 30.7 (CH_2), 78.3, 94.8 (C), 119.8 (q, $J_{C,F}$ = 321.0 Hz, CF_3), 121.4 (C), 121.4, 127.2, 127.6 (CH), 129.5 (C), 129.8, 131.2, 134.7 (CH), 137.4, 145.4 (C). IR (KBr): v = 3080, 2956 (w), 2875, 2855, 1596, 1469 (m), 1433 (s), 1335, 1223, 1189, 1156 (m), 1129 (s), 1090, 884 (s), 783, 765, 688 (m), 619, 576 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 480 (100), 348 (12), 282 (49), 268 (77), 255 (22), 252 (13), 239 (62), 207 (47), 192 (25), 189 (46), 176 (15), 152 (12), 115 (24), 64 (15). HRMS (EI, 70 eV): calcd for $C_{22}H_{15}O_5F_3S_2$: 480.03075; found: 480.029308.

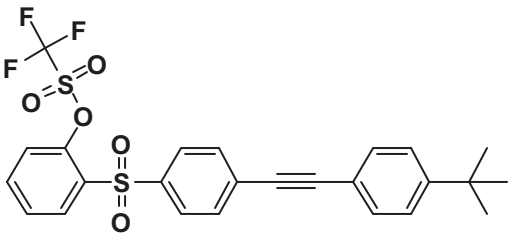


2-(4-(p-tolylethynyl)phenylsulfonyl)phenyl trifluoromethanesulfonate (32b) Starting with **28** (257 mg, 0.50 mmol), Pd $(PPh3)_2Cl_2$ (09 mg, 2.5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), 1-ethynyl-4-methylbenzene (0.06 mL, 0.5 mmol) and DMF (4 mL), following the *general procedure* (**32b)** was prepared as a colourless oil (199 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 3H,



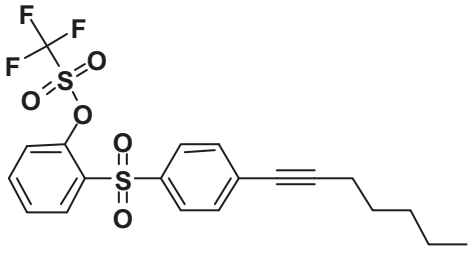
CH_3), 7.10 (d, J = 7.9 Hz, 2H, ArH), 7.31-7.36 (m, 3H, ArH), 7.48-7.55 (m, 2H, ArH), 7.57-7.65 (m, 2H, ArH), 7.87 (d, J = 8.7 Hz, 2H, ArH), 8.21-8.25 (m, 1H, ArH). ^{19}FNMR (282 MHz, $CDCl_3$): δ = -73.1. ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 21.5 (CH_3), 87.1, 94.1 (C), 116.3, 120.5 (C), 119.8 (q, $J_{C,F}$ = 321.0 Hz, CF_3), 122.3, 128.3, 128.6, 129.2,130.9, 131.7, 132.0, 135.7 (CH), 129.8, 131.2, 134.7 (CH), 135.7, 138.9, 139.5, 146.5 (C). IR (KBr): v = 3068, 2919 (w), 1586 (m), 1426, 1332 (s), 1231, 1198, 1157 (m), 1127 (s), 1087 (m), 882 (s), 771, 719, 608 (m), 572 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 480 (100), 282 (18), 268 (33), 239 (27), 189 (16). HRMS (EI, 70 eV): calcd for $C_{22}H_{15}O_5F_3S_2$: 480.03075; found: 480.030830.

2-(4-((4-tert-Butylphenyl)ethynyl)phenylsulfonyl)phenyl trifluoromethanesulfonate (32c)



Starting with **28** (258 mg, 0.50 mmol), Pd $(PPh3)_2Cl_2$ (9 mg, 2.5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), 4-*tert*-butylphenylacetylene (0.09 mL, 0.5 mmol) and DMF (4 mL), following the *general procedure* **32c** was prepared as a colourless oil (211 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 9H, 3CH_3), 7.29-7.34 (m, 3H, ArH), 7.39 (d, J = 8.4 Hz, 2H, ArH), 7.47-7.55 (m, 2H, ArH), 7.58-7.65 (m, 2H, ArH), 7.87 (d, J = 8.6 Hz, 2H, ArH), 8.21-8.24. ^{19}FNMR (282 MHz, $CDCl_3$): δ = -73.1. ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 31.1 (3CH_3), 34.9, 87.1, 94.1 (C), 119.1 (C), 114.2 (q, $J_{C,F}$ = 320.0 Hz, CF_3), 122.3, 125.5, 128.3, 128.6 (CH), 129.7 (C), 130.9, 131.6, 132.0 (CH), 134.1 (C), 135.8 (CH), 138.9, 146.4, 152.6 (C). IR (KBr): v = 3068, 2919 (w), 1586 (m), 1426, 1332 (s), 1231, 1198, 1157 (m), 1127 (s), 1087 (m), 882 (s), 771, 719, 608 (m), 572 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 522 ([M]$^+$, 2), (2), 507 (4), 309 (4), 57 (10), 43 (100), 42 (43), 41 (53). HRMS (EI, 70 eV): calcd for $C_{22}H_{15}O_5F_3S_2$: 480.03075; found: 480.030830.

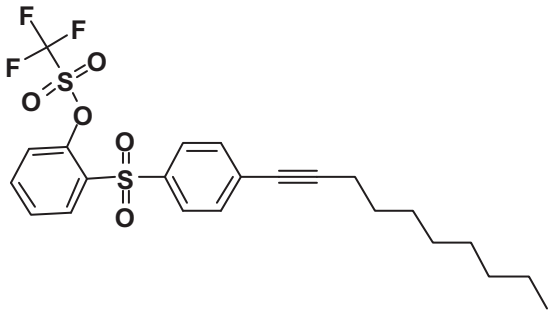
2-(4-(Hept-1-ynyl)phenylsulfonyl)phenyl trifluoromethanesulfonate (32d) Starting with



28 (257 mg, 0.50 mmol), Pd $(PPh3)_2Cl_2$ (9 mg, 2.5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), hept-1-yne **32d** (0.06 mL, 0.5 mmol) and DMF (4 mL), following the *general procedure* **32d** was prepared as a

colourless oil (197 mg, 86 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, 3H, J = 7.0 Hz, CH_3), 1.22-1.36 (m, 8H, $4CH_2$), 1.47-1.53 (m, 2H, CH_2), 2.33 (t, 2H, J = 7.0 Hz, CH_2), 7.28-7.32 (m, 2H, ArH), 7.40-7.44 (m, 2H, ArH), 7.46-7.51 (m, 1H, ArH), 7.80 (d, J = 7.0 Hz, 2H, ArH), 8.18-8.22 (m, 1H, ArH) . ^{19}FNMR (282 MHz, $CDCl_3$): δ = -73.2. ^{13}CNMR (62.8 MHz, $CDCl_3$): δ = 13.9 (CH_3), 19.4, 22.1, 28.0, 31.0 (CH_2), 79.3, 95.8 (C), 121.0 (q, $J_{C,F}$ = 322.0 Hz, CF_3), 121.4 (C), 122.2, 128.2, 128.6 (CH), 130.4 (C), 130.9, 132.1 (CH), 134.1 (C), 135.7 (CH), 138.4, 146.4 (C). IR (KBr): ν = 3079, 2954 (w), 2873, 2858, 1591, 1465 (m), 1430 (s), 1332, 1219, 1199, 1154 (m), 1127 (s), 1088 (m), 880 (s), 782, 763, 686 (m), 617, 574 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 460 (51), 446 (44), 445 (10), 433 (11), 432 (25), 431 (100), 406 (15), 273 (23), 234 (13), 233 (45), 219 (23), 206 (17), 205 (68), 181 (23), 178 (17), 143 (20), 142 (46), 141 (30), 129 (65), 128 (41), 116 (46), 115 (48), 81 (15), 69 (16). HRMS (EI, 70 eV): calcd for $C_{20}H_{19}O_5F_3S_2$: 460.06205; found: 460.062589.

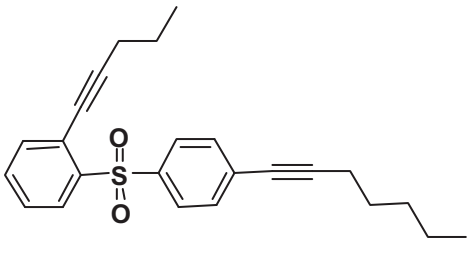
2-(4-(Dec-1-ynyl)phenylsulfonyl)phenyl trifluoromethanesulfonate (32e) Starting with **28**



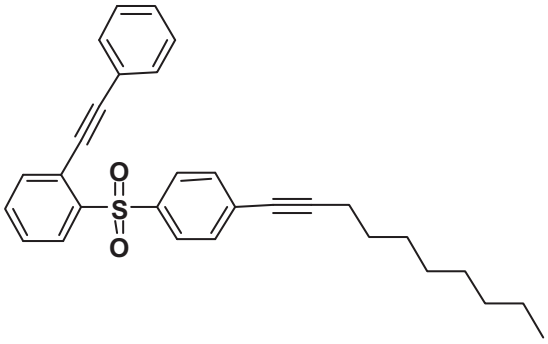
(257 mg, 0.50 mmol), Pd $(PPh3)_2Cl_2$ (9 mg, 2.5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), dec-1-yne (0.09 mL, 0.5 mmol) and DMF (4 mL), following the *general procedure A* **32e** was prepared as a colourless oil (228 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 (t, 3H, J = 7.2 Hz, CH_3), 1.16-1.26 (m, 8H, $4CH_2$), 1.30-1.38 (m, 2H, CH_2), 1.46-1.55 (m, 2H, CH_2), 2.32 (t, 2H, J = 7.0 Hz, CH_2), 7.28-7.31 (m, 2H, ArH), 7.40-7.62 (m, 3H, ArH), 7.78-7.81 (m, 2H, ArH), 8.17-8.20 (m, 1H, ArH) . ^{19}FNMR (282 MHz, $CDCl_3$): δ = -73.2. ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 13.0 (CH_3), 18.4, 21.6, 27.3, 27.8, 28.0, 28.1, 30.7 (CH_2), 78.3, 94.8 (C), 119.8 (q, $J_{C,F}$ = 274.0 Hz, CF_3), 121.4 (C), 121.4, 127.2, 127.6 (CH), 129.5 (C), 129.8, 131.2, 134.7 (CH), 137.4, 145.4 (C). IR (KBr): ν = 3083, 2957 (w), 2922, 2852, 1591, 1465 (m), 1431, 1332 (s), 1246, 1218, 1200 (m), 1128 (s), 1088, 879 (s), 784, 724, 686 (m), 618, 576 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 502 (21), 446 (44), 445 (29), 433 (12), 432 (41), 431 (28), 406 (20), 277 (19), 273 (18), 262 (37), 233 (19), 207 (12), 205 (27), 183 (23), 181 (14), 170 (17), 157 (24), 156 (39), 155 (19), 143 (29), 142 (32), 141 (20), 131 (12), 129 (45), 128 (28), 123 (14), 117 (20), 116 (29), 115 (28), 81 (14), 69 (12), 67 (10), 57 (13), 55 (19), 43 (100). HRMS (EI, 70 eV): calcd for $C_{23}H_{25}O_5F_3S_2$: 502.10900; found: 502.109274.

11.6.3 Synthesis of unsymmetrical dialkynyl diphenylsulfone

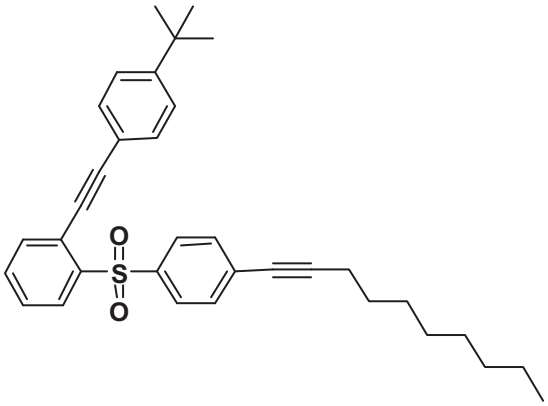
1-(4-(Hept-1-ynyl)phenylsulfonyl)-2-(pent-1-ynyl)benzene (33a). Starting with **32d** (230 mg, 0.5 mmol), $Pd(PPh_3)_2Cl_2$ (9 mg, 2.5 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), 1-pentyne (38 mg, 0.55 mmol) and DMF (5 mL) following *the general procedure,* **33a** was prepared as a colourless oil (170 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77-0.93 (m, 6H, $2CH_3$), 1.18-1.24 (m, 8H, $4CH_2$), 1.29-1.61 (m, 8H, $4CH_2$), 2.30-2.36 (m, 4H, $2CH_2$), 7.36-7.42 (m, 5H, ArH), 7.74-7.78 (m, 2H, ArH), 8.16-8.19 (m, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 13.6, 14.0 (CH_3), 19.4, 19.5, 22.1, 22.6, 28.4, 28.9, 29.1, 30.2, 31.8 (CH_2), 78.1, 79.5, 94.8, 100.4, 123.5 (C), 127.6, 128.1, 128.9 (CH), 129.3 (C), 131.4, 132.9, 135.1 (CH), 139.1, 140.7 (C). IR (KBr): ν = 3063, 2924 (w), 2929, 2859, 1590, 1467 (m), 1318, 1153 (s), 1089, 835, 754, 730 (m), 612, 581 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 392 ([M]$^+$, 100), 365 (17), 350 (16), 349 (56), 228 (10), 205 (38), 163 (12), 115 (12). HRMS (EI, 70 eV): calcd for $C_{25}H_{28}O_2S$: 392.18045; found: 392.180237.



1-(4-(Dec-1-ynyl)phenylsulfonyl)-2-(phenylethynyl)benzene (33b) Starting with **32e** (252 mg, 0.5 mmol), $Pd(PPh_3)_2Cl_2$ (9 mg, 2.5 mol-%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), ethynylbenzene (56 mg, 0.55 mmol) and DMF (5 mL) following *the general procedure*, **33b** was prepared as a colourless oil (188 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79 (t, J = 7.3 Hz, CH_3), 1.16-1.24 (m, 8H, $4CH_2$), 1.24-1.36 (m, 4H, $2CH_2$), 1.43-1.52 (m, 2H, CH_2), 2.30 (t, J = 6.9 Hz, CH_2), 7.29-7.33 (m, 4H, ArH), 7.42-7.54 (m, 6H, ArH), 7.79 (d, J = 7.4 Hz, 2H, ArH), 8.21-8.24 (m, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.4, 22.6, 28.4, 28.8, 29.0, 29.1, 31.7 (CH_2), 79.4, 85.8, 94.9, 98.0, 122.4, 122.6 (C), 128.2, 128.4, 128.5, 129.1, 129.2 (CH), 129.4 (C), 131.6, 131.7, 133.0, 134.8 (CH), 139.0, 141.1 (C). IR (KBr): ν = 3059 (w), 2922, 2852 (m), 1590, 1490 (m), 1321, 1154 (s), 1124, 1088, 835 (m) 753 (s), 689, 673 (m), 612, 582 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 454 ([M]$^+$, 3), 350 (24), 350 (25), 349 (100), 289 (13), 207 (10), 105 (12). HRMS (EI, 70 eV): calcd for $C_{30}H_{30}O_2S$: 454.19610; found: 454.197202.

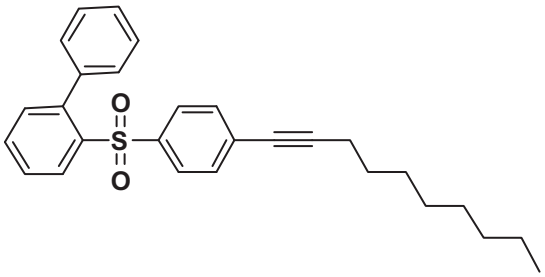


1-((4-tert-Butylphenyl)ethynyl)-2-(4-(dec-1-ynyl)phenylsulfonyl)benzene (33c) Starting with **32e** (252 mg, 0.5 mmol), $Pd(PPh_3)_2Cl_2$ (9mg, 2.5 mol-%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), 4-*tert*-butylphenylacetylene (87 mg, 0.55 mmol) and DMF (5 mL) following *the general procedure*, **33c** was prepared as a colourless oil (201 mg, 79%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78 (t, J = 7.1 Hz, CH_3), 1.16-1.29 (m, 18H, $4CH_2$), 1.16 (s, 9H, $3CH_3$), 1.22-1.30 (m, 4H, $2CH_2$), 1.43-1.54 (m, 2H, CH_2), 2.29 (t, J = 7.3 Hz, CH_2), 7.29-7.35 (m, 4H, ArH), 7.39-7.53 (m, 5H, ArH), 7.81 (d, J = 8.5 Hz, 2H, ArH), 8.19-8.23 (m, 1H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.4, 22.6, 28.4, 28.8, 29.0, 29.1 (CH_2), 31.1 (CH_3), 31.7 (CH_2), 79.5, 85.2, 94.9, 98.4, 119.4, 122.9 (C), 125.5, 128.2, 128.3, 129.1 (CH), 129.4 (C), 131.3, 131.6, 132.9, 134.8 (CH), 139.0, 141.0, 152.5 (C). IR (KBr): ν = 3055 (w), 2920, 2845 (m), 1585, 1485 (m), 1316, 1150 (s), 1115, 1077, 830 (m) 751 (s), 685, 670 (m), 607, 584 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 510 ([M]$^+$, 16), 495 (15), 350 (25), 349 (100), 161 (36). HRMS (EI, 70 eV): calcd for $C_{34}H_{38}O_2S$: 510.19610; found: 510.197202.



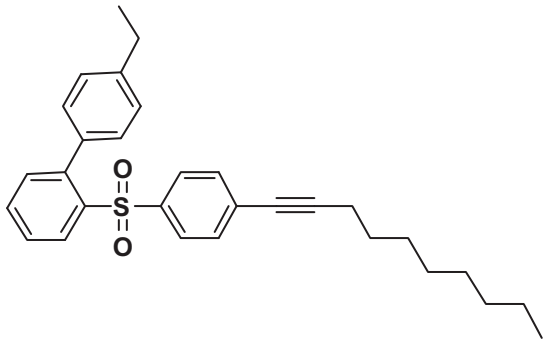
11.6.4 Synthesis of alkynyl-aryl-diphenylsulfone (34a-34e)

2-(4-(Dec-1-ynyl)phenylsulfonyl)biphenyl (34a) Starting with **32e** (252 mg, 0.50 mmol), $Pd(PPh_3)_4$ (15 mg, 2.5 mol%), phenylboronic acid (67 mg, 0.55 mmol) was added in dioxane (5mL) and K_3PO_4 (159 mg, 0.75 mmol) following the *general procedure,* **34a** was prepared as colourless oil (189 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, J = 7.1 Hz, 3H, CH_3), 1.19-1.27 (m, 8 H, $4(CH_2)$, 1.32-1.39 (m, 2 H, CH_2), 1.47-1.54 (m, 2 H, CH_2), 2.33 (t, J = 7.4 Hz, 2 H, CH_2), 6.87-6.90 (m, 2 H, ArH), 7.01-7.16 (m, 5 H, ArH), 7.21-7.26 (m, 1 H, ArH), 7.36-7.52 (m, 3 H, ArH), 7.74-7.77 (m, 1 H, ArH), 8.32-8.35 (m, 1 H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.4, 22.6, 28.4, 28.9, 29.0, 29.1, 31.8 (CH_2), 79.5,

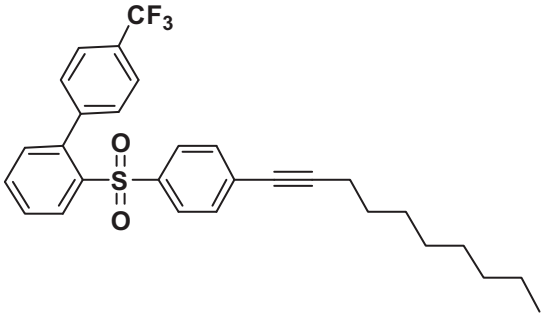


94.8 (C), 127.3, 127.5 (CH), 127.6 (C), 127.9, 128.5, 130.0, 131.2, 131.4, 132.5, 132.9 (CH), 135.0, 137.9, 139.3, 142.3 (C). IR (KBr): ν = 2951, 2922, 2853 (m), 2852 (w), 1591, 1464, 1316 (m), 1152 (s), 1128, 1090, 1007, 835 (m), 758 (s), 698 (m), 610 (s), 576 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 430 ($[M]^+$, 84), 374 (16), 373 (15), 360 (20), 359 (19), 334 (19), 295 (13), 281 (13), 267 (13), 266 (13), 265 (27), 253 (30), 252 (36), 241 (14), 239 (11), 228 (10), 217 (79), 207 (38), 201 (16), 185 (15), 184 (50), 183 (30), 169 (15), 168 (38), 157 (14), 156 (19), 155 (17), 153 (96), 152 (100), 151 (22), 143 (19), 142 (18), 141 (26), 129 (40),128 (31), 127 (15), 117 (27), 115 (31), 114 (16), 91 (12), 43 (11), 41 (14). HRMS (EI, 70 eV): calcd for $C_{28}H_{30}O_2S$: 430.19610; found: 430.196883.

2-(4-(Dec-1-ynyl)phenylsulfonyl)-4'-ethylbiphenyl (34b) Starting with **32e** (252 mg, 0.50 mmol), $Pd(PPh_3)_4$ (15 mg, 2.5 mol%), 4-ethylphenylboronic acid (82 mg, 0.55 mmol) was added in dioxane (5mL) and K_3PO_4 (159 mg, 0.75 mmol) following the *general procedure,* **34b** was prepared as colourless oil (208 mg, 91%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.79-0.83 (m, 6H, $2CH_3$), 1.18-1.26 (m, 8 H, $4CH_2$), 1.26-1.39 (m, 2 H, CH_2), 1.47-1.55 (m, 2 H, CH_2), 2.32 (t, J = 7.0 Hz, 2 H,CH_2), 2.60 (t, J = 7.5 Hz, 2 H, CH_2), 6.79-6.82 (m, 1 H, ArH), 6.95-7.14 (m, 7 H, ArH), 7.36-7.45 (m, 2 H, ArH), 7.47-7.53 (m, 3 H, ArH), 7.74-7.77 (m, 1 H, ArH), 8.31-8.34 (m, 1 H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 15.9 (CH_3), 19.4, 22.6, 28.4, 28.6, 28.9, 29.0, 29.1, 31.8 (CH_2), 79.5, 94.5 (C), 126.8, 127.5 (CH), 127.6 (C), 128.1, 128.4, 129.9, 131.1, 132.7, 132.9 (CH), 139.3, 139.7, 142.3, 143.9 (C). IR (KBr): ν = 3056 (w) 2923 (m), 2853 (w), 1591, 1464, 1315 (m), 1153 (s), 1090, 831 (m), 756, 614 (s), 572 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 458 ($[M]^+$, 100), 387 (11), 277 (32), 269 (13), 268 (77), 265 (10), 255 (22), 252 (13), 240 (34), 239 (62), 208 (10), 207 (47), 192 (25), 190 (11), 189 (46), 178 (10), 176 (15), 165 (11), 152 (12), 115 (24), 69 (14), 64 (15). HRMS (ESI^+): calcd for $C_{30}H_{35}O_2S$: 459.2352; found: 459.2358.

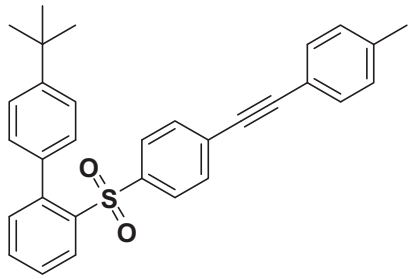


2-(4-(Dec-1-ynyl)phenylsulfonyl)-4'-(trifluoromethyl)biphenyl (34c) Starting with **32e**



(252 mg, 0.50 mmol), Pd $(PPh_3)_4$ (15 mg, 2.5 mol%), 4-(trifluoromethyl)phenylboronic acid (104 mg, 0.50 mmol) was added in dioxane (5mL) and K_3PO_4 (159 mg, 0.75 mmol) following the *general procedure,* **34c** was prepared as colourless oil (211 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, 3H, J = 7.2 Hz, CH_3), 1.19-1.27 (m, 8H, $4CH_2$), 1.27-1.41 (m, 2H, CH_2), 1.48-1.58 (m, 2H, CH_2), 2.33 (t, 2H, J = 7.0 Hz, CH_2), 7.01-7.06 (m, 4H, ArH), 7.09-7.14 (m, 3H, ArH), 7.39-7.42 (m, 2H, ArH), 7.54-7.57 (m, 2H, ArH), 8.33-8.36 (m, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.4, 22.6, 28.4, 28.8, 29.0, 29.1, 31.7 (CH_2), 79.2, 95.1 (C), 116.8, 127.5, 127.6, 128.4, 128.6, 129.2, 131.1, 131.6, 132.9, 133.0 (CH), 139.3, 139.8, 142.1, 159.3 (C_{Ar}). IR (KBr): v = 3059 (w), 2924 (m), 2854 (w), 1591, 1466 (m), 1317, 1153, 1124, 1106 (s), 1061, 836 (m), 757, 613, 574 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 498 ($[M]^+$, 36), 443 (18), 429 (18), 428 (58), 403 (13), 376 (12), 285 (43), 269 (20), 265 (10), 252 (45), 249 (26), 236 (32), 222 (12), 207 (36), 201 (100), 170 (22), 169 (14), 157 (18), 142 (41). HRMS (EI, 70 eV): calcd for $C_{29}H_{29}F_3O_2S$: 498.18404; found: 498.18324.

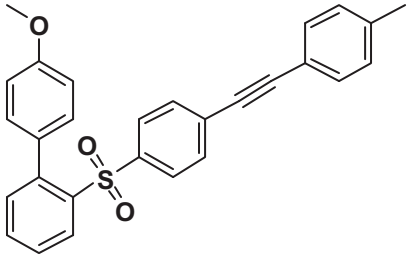
4'-tert-Butyl-2-(4-(p-tolylethynyl)phenylsulfonyl)biphenyl (34d)



Starting with **32b** (240 mg, 0.50 mmol), Pd $(PPh_3)_4$ (15 mg, 2.5 mol%), 4-tert-butylphenylboronic acid (98 mg, 0.55 mmol) was added in dioxane (5mL) and K_3PO_4 (137 mg, 0.65 mmol) following the *general procedure,* **34d** was prepared as colourless oil (219 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 3H, CH_3), 1.25 (s, 9H, $3CH_3$), 6.83 (d, J, 8.1 Hz, 2H, ArH), 6.97 (d, J, 8.2 Hz, 2H, ArH), 7.07-7.21 (m, 5H, ArH), 7.31 (d, J, 8.6 Hz, 2H, ArH), 7.38 (d, J, 8.6 Hz, 2H, ArH), 7.48-7.52 (m, 2H, ArH), 8.33-8.36 (m, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 15.9 (CH_3), 28.6 (CH_2), 31.1 ($3CH_3$), 34.8, 87.4, 93.0, 119.3 (C), 125.4, 126.8, 127.5, 127.6, 128.4 (CH), 128.8 (C), 130.0, 131.0, 131.5, 132.7, 133.0 (ArH), 135.2, 139.6, 139.8, 142.3, 144.0, 152.4 (C_{Ar}). IR (KBr): v = 3059 (w), 2924 (m), 2854 (w), 1591, 1466 (m), 1317, 1153, 1124, 1106 (s), 1061, 836 (m), 757, 613, 574 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 498 ($[M]^+$, 36), 443 (18), 429 (18), 428 (58), 403 (13), 376 (12), 285 (43), 269 (20), 265 (10), 252 (45), 249 (26), 236 (32), 222 (12), 207 (36), 201

(100), 170 (22), 169 (14), 157 (18), 142 (41). HRMS (EI, 70 eV): calcd for $C_{29}H_{29}F_3O_2S$: 498.18404; found: 498.18324.

4'-Methoxy-2-(4-(p-tolylethynyl)phenylsulfonyl)biphenyl (34e)



Starting with **32b** (240 mg, 0.50 mmol), Pd $(PPh_3)_4$ (15 mg, 2.5 mol%), 4-methoxyphenylboronic acid (74 mg, 0.55 mmol) was added in dioxane (5mL) and K_3PO_4 (137 mg, 0.65 mmol) following the *general procedure,* **34e** prepared as colourless oil (175 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3H, CH_3), 3.77 3.77 (s, 3H, OCH_3), 6.68 (d, *J* = 7.1 Hz, 2H, ArH), 6.83 (d, *J* = 7.6 Hz, 2H, ArH), 7.08-7.13 (m, 6H, ArH), 7.23 (d, *J* = 7.4 Hz, 2H, ArH), 7.34 (d = *J*, 7.6 Hz, 2H, ArH), 7.47-7.51 (m, 2H, ArH), 8.32-8.35 (m, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.5 (CH_3), 29.7 (CH_2), 55.3 (OCH_3), 87.4, 93.1 (C), 112.8 (CH), 119.2 (C), 127.5, 127.6, 128.6, 129.2 (CH), 130.3 (C), 131.1, 131.3, 131.6, 132.9, 133.0 (ArH), 135.2, 139.6, 139.8, 142.3, 144.0, 152.4 (C_{Ar}). IR (KBr): *v* = 3030, 2953, 2848 (w), 1609, 1511, 1463 (m), 1316 (s), 1235 (m), 1154, 1111, 1033, 1016 (m), 832 (s), 753, 736, 704 (m), 610, 559 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 438 ([M]$^+$, 100), 189 (10), 168 (8), 140 (10), 139 (15). HRMS (EI, 70 eV): calcd for $C_{28}H_{22}O_3S$: 438.12842; found: 438.127933.

11.7 One-Pot Synthesis of 2,3-Diarylindenones by Site-Selective Suzuki-Miyaura Sonogashira cross coupling Reactions Reactions of 2,3-Dibromoindenone

11.7.1 Synthesis of Arylindenones (36a-e) and (37a-e)

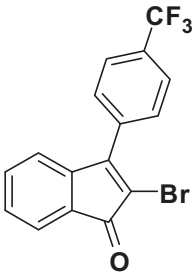
The reaction was carried out in a pressure tube. To a suspension of **35** (144 mg, 0.5 mmol), $Pd(PPh_3)_4$ (2.5-3.0 mol% per cross-coupling) and boronic acid **19** (0.5 to 0.55 mmol per cross-coupling) in dioxane (5 mL) was added a 2M solution of K_2CO_3 (1 mL). The mixture was heated at the indicated temperature (40-70 °C) under Argon atmosphere for 4-6 h. The reaction was diluted with water and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography (silica gel, EtOAc / heptanes).

11.7.2 Synthesis of 3-Arylindenones (36a-d)

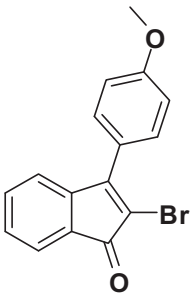
2-Bromo-3-(4-ethylphenyl)-1H-inden-1-one (36a) Starting with **35** (144 mg, 0.5 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%) and 4-ethylphenylboronic acid (75 mg, 0.5 mmol), **36a** was isolated as a colourless crystalline solid (145 mg, 93%). Reaction temperature: 40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (t, J = 7.8 Hz, CH_3), 2.16 (q, J = 7.5 Hz, CH_2), 6.57-6.55 (m, 1H, ArH), 6.63-6.68 (m, 2H, ArH), 6.78 (d, J = 6.9 Hz, 2H, ArH), 6.95-6.97 (m, 1H, ArH), 7.01 (d, J = 6.9 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 15.2 (CH_3), 28.9 (CH_2), 117.4 (C), 121.3, 123.5, 128.2, 128.3, 128.4 (C), 128.8, 130.1 (C), 133.6 (CH), 144.6, 147.0, 156.9, 189.9 (C). IR (KBr): ν = 3066 (w), 2962 (m), 2928, 2871 (w), 1712 (s), 1606, 1596, 1503, 1455, 1284, 1183, 1101, 1018, 918, 843, 759 (m), 704 (s), 627, 545 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 314 ([M, ^{81}Br]$^+$, 100), 312([M, ^{79}Br]$^+$, 99), 299 (58), 297 (56), 202 (14), 190 (16), 189 (43), 176 (10), 109 (12), 95 (10). HRMS (EI, 70 eV): calcd for $C_{17}H_{13}OBr$ (M^+, [^{79}Br]): 312.01443; found 312.013869, calcd for (M^+, [^{81}Br]): 314.01238; found 314.012420.

2-Bromo-3-(4-tert-butylphenyl)-1H-inden-1-one (36b) Starting with **35** 144 mg, 0.5 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%) and 4-tert-butylphenylboronic acid (89 mg, 0.5 mmol), **36b** was isolated as a colourless crystalline solid (151 mg, 89%). Reaction temperature: 40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 9H, $3CH_3$), 7.10-7.13 (m, 1H, ArH), 7.15-7.20 (m, 1H, ArH), 7.24-7.30 (m, 2H, ArH), 7.47 (d, J = 8.5 Hz, 2H, ArH), 7.55 (d, J = 8.5 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 31.2 (CH_3), 35.0, 117.4 (C), 121.4, 123.5, 125.6, 128.1 (CH), 128.2 (C), 128.8 (CH), 130.1 (C), 133.6 (CH), 144.5, 153.8, 156.8, 189.9 (C). IR (KBr): ν = 3066 (w), 2959 (m), 2902, 2865 (w), 1713 (s), 1606, 1556, 1407, 1362, 1267, 1099, 1015, 919, 800, 764 (m), 704 (s), 626, 533 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 342 ([M]$^+$, ^{81}Br, 52), 340 ([M]$^+$, ^{79}Br, 51), 327 (96), 325 (100), 299 (16), 297 (15), 231 (12), 202 (23), 189 (12), 176 (14), 109 (29), 95 (16). HRMS (EI, 70 eV): calcd for $C_{19}H_{17}OBr$ (M^+, [^{79}Br]): 340.04573; found 340.045511, calcd for (M^+, [^{81}Br]): 342.04368; found 342.043848.

2-Bromo-3-(4-(trifluoromethyl)phenyl)-1H-inden-1-one (36c) Starting with **35** (144 mg, 0.5 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%) and 4-(trifluoromethyl)phenylboronic acid (95 mg, 0.5 mmol), **36c** was isolated as a colourless crystalline solid (155 mg, 88%). Reaction temperature: 40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.24 (d, J = 7.2 Hz, 1H, ArH), 6.41-6.47 (m, 1H, ArH), 6.51-6.56 (m, 1H, ArH), 6.74 (d, J = 7.0 Hz, 1H, ArH), 6.91-6.93 (m, 2H, ArH), 6.96-6.99 (m, 2H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -63.4. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 120.2 (CH), 118.8, 119.5 (CH), 120.2 (q, J = 275 Hz, C), 122.4 (C), 126.7 (q, J = 1 Hz, C), 132.6 (q, J = 8 Hz, CH), 128.9 (q, J = 3 Hz, CH), 132.6 (q, J = 8 Hz, CH), 135.2 (C), 138.1 (CH), 152.5 (q, J = 36.1 Hz, C), 157.8 (CH), 163.2, 165.7, 196.7 (C). IR (KBr): ν = 3080, 2929 (w), 1718 (s), 1598, 1407 (m), 1318 (s), 1156 (m), 1109, 1099, 1064 (s), 1014, 850, 761 (m), 704 (s), 622 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 354 ([M]$^+$, ^{81}Br, 100), 352 ([M]$^+$, ^{79}Br, 99), 274 (11), 274 (61), 245 (28), 225 (27), 176 (34), 112 (10). HRMS (EI, 70 eV): calcd for $C_{16}H_8OBr$: (M$^+$, [^{81}Br]): 351.97051; found 351.970583, calcd for (M$^+$, [^{79}Br]): 353.96847; found 353.968672. (M$^+$, [^{79}Br]):

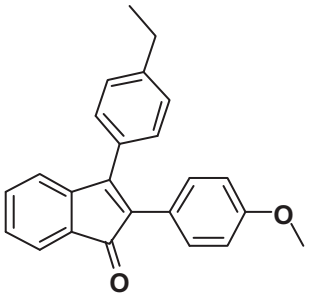


2-Bromo-3-(4-methoxyphenyl)-1H-inden-1-one (36d) Starting with **35** (144 mg, 0.5 mmol), $Pd(PPh_3)_4$ (18 mg, 3 mol%) and 4-methoxyphenylboronic acid (76 mg, 0.5 mmol), **36d** was isolated as a colourless crystalline solid (133 mg, 85%). Reaction temperature: 40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10-7.13 (m, 1H, ArH), 7.15-7.20 (m, 1H, ArH), 7.24-7.30 (m, 2H, ArH), 7.47 (d, J = 8.5 Hz, 2H, ArH), 7.55 (d, J = 8.5 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 15.2 (CH_3), 28.6 (CH_2), 55.3 (OCH3), 121.4, 123.5, 125.6, 128.1 (CH), 128.2 (C), 128.8 (CH), 130.1 (C), 133.6 (CH), 144.5, 153.8, 156.8, 189.9 (C). IR (KBr): ν = 3063, 2916, 2840 (w), 1715 (s), 1607, 1505, 1258, 1178, 1099, 1028, 830, 769 (m), 704 (s), 624, 576 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 316 ([M]$^+$, ^{81}Br, 98), 314 ([M]$^+$, ^{81}Br, 100), 235 (18), 207 (10), 164 (27), 163 (42), 117 (15). HRMS (EI, 70 eV): calcd for $C_{16}H_{11}O_2{}^{79}Br$: 313.99369; found 313.993877, calcd for $C_{19}H_{17}O_2{}^{81}Br$: 315.99165; found 315.991975.



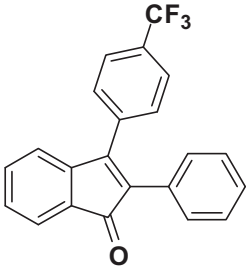
11.7.3 Synthesis of unsymmetrical 2,3-diarylindenones (37a-c)

3-(4-Ethylphenyl)-2-(4-methoxyphenyl)-1H-inden-1-one (37a)

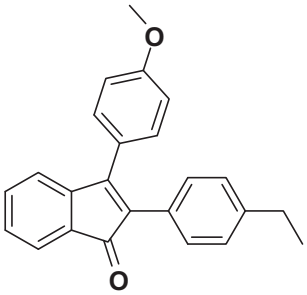


Starting with **36a** (156 mg, 0.5 mmol), $Pd(PPh_3)_4$ (17 mg, 3 mol%), 4-methoxyphenylboronic acid (76 mg, 0.5 mmol), **37a** was isolated as a colourless crystalline solid (158 mg, 93%). Reaction temperature: 70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (t, J = 7.8 Hz, 3H, CH_3), 2.54 (q, J = 7.8 Hz, 3H, CH_2), 3.77 (s, 3H, OCH_3), 6.86 (d, J = 6.9 Hz, 2H, ArH), 7.03 (d, J = 8.2 Hz, 2H, ArH), 7.10 (d, J = 8.3 Hz, 2H, ArH), 7.13-7.23 (m, 3H, ArH), 7.28 (d, J = 8.4 Hz, 2H, ArH), 7.47-7.50 (m, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 15.2 (CH_3), 28.6 (CH_2), 55.3 (OCH_3), 114.1, 121.0, 122.7 (CH), 125.0 (C), 127.6 (CH), 128.3 (C), 128.7, 129.9, 130.2 (CH), 131.0, 131.7 (C), 133.2 (CH), 143.7, 145.4, 154.5, 160.3, 196.7 (C). IR (KBr): v = 3000, 2956, 2927, 2840 (w), 1695 (s), 1605, 1497, 1456, 1339, 1289, 1240, 1171 (s), 1032, 952, 922, 854, 802, 734, 680, 581 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 340 ([M]$^+$, 100), 325 (26), 311 (23), 252 (12), 239 (12). HRMS (EI, 70 eV): calcd for $C_{24}H_{20}O_2$: 340.14578; found 340.145705.

2-Phenyl-3-(4-(trifluoromethyl)phenyl)-1H-inden-1-one (37b) Starting with **36c** (176 mg, 0.5 mmol), $Pd(PPh_3)_4$ (17 mg, 3 mol%), phenylboronic acid (61 mg, 0.5 mmol), **37b** was isolated as a colourless crystalline solid (152 mg, 87%). Reaction temperature: 70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.01 (d, J = 7.0 Hz, 1H, ArH), 7.13-7.21 (m, 5H, ArH), 7.28-7.33 (m, 2H, ArH), 7.42 (d, J = 8.0 Hz, 2H, ArH), 7.51-7.54 (m, 1H, ArH), 7.59 (d, J = 7.0 Hz, 2H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.7. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 120.9, 122.7 (q, J = 274.5 Hz, C), 123.3, 125.8 (q, J = 3.8 Hz, CH), 128.1, 128.2, 128.9, 129.2 (CH), 129.9 (q, J = 8 Hz, CH), 130.1 (q, J = 33.5 Hz, C), 132.4, 132.6, 135.5 (C), 133.6 (CH), 143.7, 152.3, 194.9 (C). IR (KBr): v = 3070, 2961, 2855 (w), 1707 (s), 1596, 1455, 1408 (m), 1318 (s), 1165 (m), 1108, 1063, 1013 (s), 858, 801 (m), 752, 699 (s), 656, 599 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 350 ([M]$^+$, ^{81}Br, 100), 349 (40), 333 (10), 281 (38), 253 (14), 252 (39), 250 (12), 126 (13). HRMS (EI, 70 eV): calcd for $C_{22}H_{13}OF_3$: 350.09130; found 350.091245.



2-(4-Ethylphenyl)-3-(4-methoxyphenyl)-1H-inden-1-one (37c) Starting with **36d** (158 mg, 0.5 mmol), $Pd(PPh_3)_4$ (17 mg, 3 mol%), 4-ethylphenylboronic acid (75 mg, 0.5 mmol), **37b** was isolated as a colourless crystalline solid (146 mg, 86%). Reaction temperature: 70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.7 Hz, CH_3), 2.62 (q, J = 7.2 Hz, CH_2), 3.70 (s, 3H, OCH_3), 6.72 (d, J = 8.4 Hz, 2H, ArH), 7.05 (d, J = 7.2 Hz, 1H, ArH), 7.14-7.19 (m, 5H, ArH), 7.22-7.28 (m, 3H, ArH), 7.45-7.48 (m, 1H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 15.2 (CH_3), 28.7 (CH_2), 55.1 (OCH_3), 113.6, 121.0, 122.7 (CH), 123.3, (C), 128.2, 128.5, 128.6 (CH), 130.1, 130.8 (C), 131.2 (CH), 131.5 (C), 133.3 (CH), 145.5, 154.0, 159.1, 197.0 (C). IR (KBr): ν = 2968, 2933, 2841 (w), 1706 (s), 1603, 1583, 1513, 1453, 1338, 1296 (m), 1250, 1175 (s), 1149, 1066 (m), 1028 (s), 919, 832, 808, 764, 733, 713, 630, 562, 532 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 340 ([M]$^+$, 100), 325 (11), 311 (11), 268 (12), 239 (14). HRMS (EI, 70 eV): calcd for $C_{24}H_{20}O_2$: 340.14577; found 340.145895.

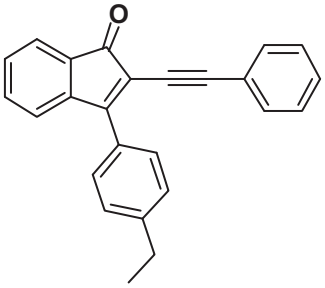


11.7.4 Synthesis of alkynylindenones (38a-f), (39a-d).

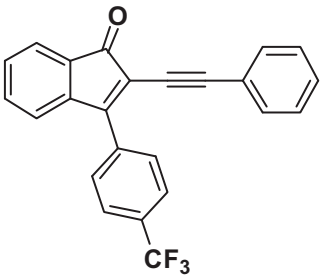
In a pressure tube (glass bomb) a suspension of $Pd(PPh_3)_2Cl_2$ (5-15 mol%), **35** and **38** (0.5 mmol), alkyne (0.50-1.10 mmol), CuI (10-20 mol%), (iPr)$_2$NH (1.5 equiv) in DMF (5 mL) was purged with argon and stirred at 20 °C for 10 min. The reaction mixture was stirred at room temperature for 6-8 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with H_2O (3 x 20 mL), dried (Na_2SO_4), concentrated in vacuo and the residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **38a-f** and **39a-d.**

11.7.5 Synthesis of 3-aryl-2-alkynylindenones

3-(4-Ethylphenyl)-2-(phenylethynyl)-1H-inden-1-one (38a) Starting with **36a** (156 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 5 mol%), dry CuI (10 mol%), di-isopropylamine (1ml/0.1 mmol of **36a**), ethynylbenzene (56 mg, 0.55 mmol) was added at room temperature, **38a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (142 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.94-7.10 (m, 2H, ArH), 7.22-7.25 (m, 3H, ArH), 7.30-7.32 (m, 3H, ArH), 7.40-7.43 (m, 2H, ArH), 7.47-7.50 (m, 1H, ArH), 7.61-7.65 (m, 1H, ArH), 7.75-7.78 (m, 1H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 15.2 (CH_3), 28.9 (CH_2), 82.3, 99.6 (C), 117.1, 122.2, 123.3, 126.9 (C), 128.1, 128.2, 128.5, 128.6, 131.8, 133.5 (CH), 144.2, 151.9, 159.5, 161.4, 193.5 (C). IR (KBr): ν = 3053, 2961, 2870 (w), 1712 (s), 1596, 1487, 1356, 1232, 1184, 1067, 911, 825 (m), 753, 687 (s), 617 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 ($[M]^+$, 100), 333 (17), 319 (17), 305 (23), 289 (22), 276 (18), 144 (14). HRMS (EI, 70 eV): calcd for $C_{25}H_{18}O$: 334.13522; found 334.135337.

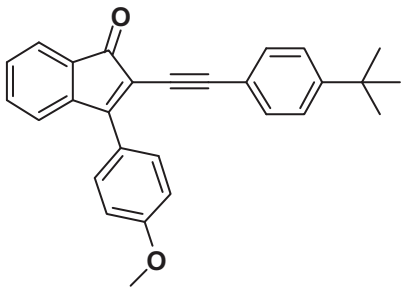


2-(Phenylethynyl)-3-(4-(trifluoromethyl)phenyl)-1H-inden-1-one (38b) Starting with **36c** (176 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 5 mol%), dry CuI (10 mol%), di-isopropylamine (1ml/0.1 mmol of 38b), ethynylbenzene (56 mg, 0.55 mmol) was added at room temperature, **38b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (164 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17-7.22 (m, 2H, ArH), 7.24-7.29 (m, 4H, ArH), 7.32-7.35 (m, 1H, ArH), 7.37-7.41 (m, 1H, ArH), 7.50-7.53 (m, 1H, ArH), 7.73 (d, J = 8.3 Hz, 2H, ArH), 7.90 (d, J = 8.3 Hz, 2H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.7. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 80.4, 99.8 (C), 120.7 (CH), 121.4 (C), 122.6 (q, J = 273 Hz, C), 122.8, 124.5 (q, J = 3.9 Hz, CH), 127.3, 127.6, 128.0, 128.8 (CH), 129.3 (C), 129.9 (d, J = 32.9 Hz, C), 130.9, 132.8 (CH), 134.6, 142.7, 156.9, 191.7 (C). IR (KBr): ν = 3062, 2961 (w), 1715 (s), 1595, 1488, 1455, 1409 (m), 1320 (s), 1165 (m), 1122, 1064, 1014 (s), 925, 855, 795 (m), 750, 716



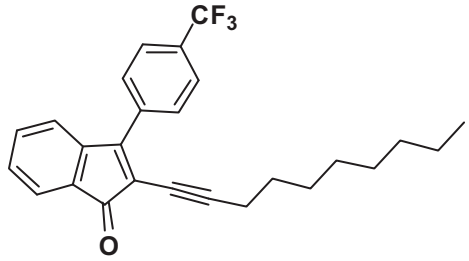
(m), 686 (s), 591(m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 374 ($[M]^+$, 100), 373 (34), 305 (10), 276 (29). HRMS (EI, 70 eV): calcd for $C_{24}H_{13}OF_3$: 374.09130; found 374.090996.

2-((4-Tert-butylphenyl)ethynyl)-3-(4-methoxyphenyl)-1H-inden-1-one (38c) Starting with



36d (157 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 5 mol%), dry CuI (10 mol%), di-isopropylamine (1ml/0.1 mmol of **36c**), 1-*tert*-butyl-4-ethynylbenzene (87 mg, 0.55 mmol) was added at room temperature, **38c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (157 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.98 (d, *J* = 9.0 Hz, 2H, ArH), 7.20-7.32 (m, 4H, ArH), 7.36 (d, *J* = 6.9 Hz, 2H, ArH), 7.47 (d, *J* = 9.0 Hz, 2H, ArH), 7.85 (d, *J* = 8.6 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 31.4 (CH_3), 34.8 (C), 55.4 (OCH_3), 81.9, 99.7 (C), 114.0, 116.5, 120.0 (C), 122.0, 123.2 (CH), 124.8 (C), 125.3, 129.4, 130.3 (CH), 131.1 (C), 131.5, 133.4 (CH), 144.2, 151.9, 159.5, 161.4, 193.5 (C). IR (KBr): *v* = 3080, 2929 (w), 1718 (s), 1598, 1407 (m), 1318 (s), 1156 (m), 1109, 1099, 1064 (s), 1014, 850, 761 (m), 704 (s), 622 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 392 ($[M]^+$, 100), 378 (23), 377 (77), 207 (26), 144 (13), 32 (18). HRMS (EI, 70 eV): calcd for $C_{28}H_{24}O_2$: 392.17708; found 392.177463.

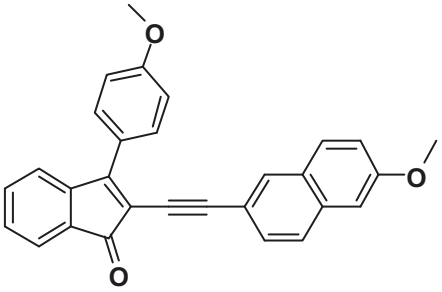
2-(Dec-1-ynyl)-3-(4-(trifluoromethyl)phenyl)-1H-inden-1-one (38d) Starting with **36c** (176



mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 5 mol%), dry CuI (10 mol%), di-isopropylamine (1ml/0.1 mmol of **36c**), dec-1-yne (76 mg, 0.55 mmol) was added at room temperature, **38d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (182 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *j* = 6.9 Hz, CH_3), 1.12-1.16 (m, 6H, CH_2), 1.44-1.51 (m, 2H, CH_2), 2.38 (t, *J* = 7.4 Hz, CH_2), 7.14-7.34 (m, 3H, ArH), 7.46-7.50 (m, 1H, ArH), 7.69 (d, *J* = 7.9 Hz, 2H, ArH), 7.82 (d, *J* = 7.6 Hz, 2H, ArH). ^{13}C NMR (282 MHz, $CDCl_3$): δ = -62.8. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 20.1, 22.5, 28.3, 28.8, 29.0, 29.1, 31.8 (CH_2), 72.3, 103.3 (C), 121.4 (CH), 122.2 (q, *J* = 273.1 Hz, C), 123.7 (CH), 125.4 (q, *J* = 3.8 Hz, CH), 128.5, 129.5 (CH), 133.7 (q, *J* = 8.1 Hz, CH), 135.7 (q, *J* = 36.3 Hz, C), 136.5, 143.8, 157.2, 193.3 (C). IR (KBr): *v* = 2954, 2925, 2855 (w),

1710 (s), 1596, 1461, 1410 (m), 1319 (s), 1161 (m), 1125, 1066 (s), 1016, 926, 827, 761, 717, 681, 601 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 410 ($[M]^+$, 58), 381 (18), 367 (41), 354 (34), 353 (100), 339 (54), 325 (47), 313 (66), 311 (69), 287 (83), 262 (34), 243 (39), 231 (26), 226 (32), 213 (63), 183 (11), 123 (39), 81 (42), 67 (28), 43 (23), 29 (10). HRMS (EI, 70 eV): calcd for $C_{26}H_{25}OF_3$: 410.18520; found 410.185602.

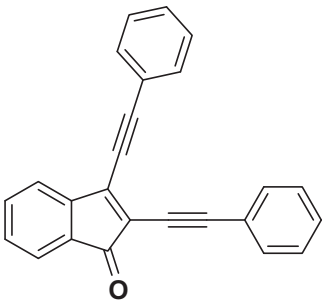
2-((6-Methoxynaphthalen-2-yl)ethynyl)-3-(4-methoxyphenyl)-1H-inden-1-one (39e)



Starting with **36d** (157 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 5 mol%), dry CuI (10 mol%), di-isopropylamine (1ml/0.1 mmol of **36d**), dec-1-yne (76 mg, 0.55 mmol) was added at room temperature, **39e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (162 mg, 78%). ^1H NMR (300 MHz, $CDCl_3$): δ = ^1H NMR (300 MHz, $CDCl_3$): δ = 0.79 (t, *J* = 7.0 Hz, CH_3), 1.17-1.24 (m, 8H, $4CH_2$), 1.31-1.36 (m, 2H, CH_2), 2.39 (t, *J* = 7.0 Hz, CH_3), 6.96 (d, *J* = 8.6 Hz, ArH), 7.17-7.29 (m, 3H, ArH), -7.01 (m, 2H, ArH), 7.13-7.21 (m, 5H, ArH), 7.22-7.33 (m, 2H, ArH), 7.40-7.43 (m, ArH), 7.43-7.51 (m, 2H, ArH), 7.77 (d, J = 8.7 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 55.3, 55.4 (OCH_3), 82.3, 100.2 (C), 105.8, 114.0 (CH), 116.5, 117.9 (C), 119.4, 119.6, 122.0, 123.2 (CH), 124.8 (C), 126.7 (CH), 126.9, 128.4 (C), 129.0, 129.4, 130.3 (CH), 131.2 (C), 131.7, 133.4 (CH), 144.2, 158.4, 159.4, 161.4, 193.5 (C). IR (KBr): ν = 3014, 2932, 2849 (w), 1704, 1599 (s), 1512, 1453, 1388, 1303, 1255 (s), 1162 (m), 1025 (s), 947, 894 (m), 850 (s), 811, 728, 710, 661, 585 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 416 ($[M]^+$, 100), 330 (6), 97 (5), 69 (12), 43 (10). HRMS (ESI^+): calcd for $C_{29}H_{21}O_3$: 417.1485; found 417.1484.

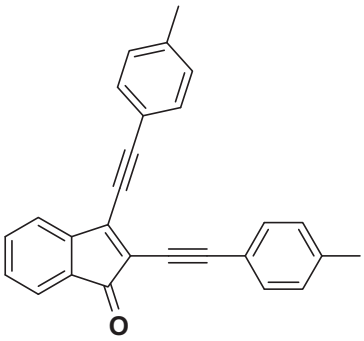
11.7.6 Synthesis of 2,3-dialkynylindenones (39a-d)

2,3-Bis(phenylethynyl)-1H-inden-1-one (39a) Starting with **35** (144 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (52 mg, 15 mol%), dry CuI (19 mg, 20 mol%), diisopropylamine (1ml/0.1 mmol of **35**), ethynylbenzene (112 mg, 1.1 mmol) was added at room temperature, **39a** was isolated after

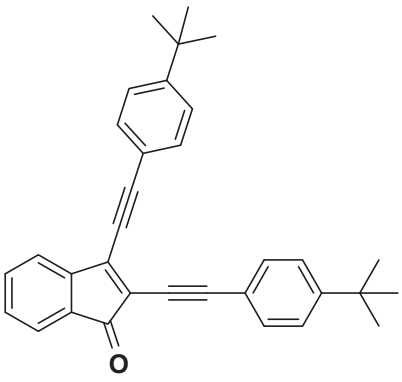


chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (147 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26-7.32 (m, 5H, ArH), 7.35-7.39 (m, 3H, ArH), 7.41-7.45 (m, 2H, ArH), 7.53-7.60 (m, 4H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 81.9, 83.1, 103.5, 111.3 (C), 121.1 (CH), 121.9, 122.7 (C), 123.0, 128.3, 128.6, 129.0 (CH), 129.3 (C), 129.9, 130.1, 132.0, 132.3, 134.3 (CH), 142.9, 143.1, 192.8 (C). IR (KBr): ν = 3050, 2921, 2853 (w), 1708 (s), 1596, 1489, 1442, 1358, 1219, 1157, 1069, 915, 868 (m), 754, 688 (s), 528 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 330 ([M]$^{+}$, 100), 329 (17), 301 (16), 300 (45), 298 (12), 165 (15), 150 (21), 140 (12). HRMS (EI, 70 eV): calcd for $C_{26}H_{28}O_2$: 372.20838; found 372.208533.

2,3-Bis(p-tolylethynyl)-1H-inden-1-one (39b) Starting with **35** (144 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (52 mg, 15 mol%), dry CuI (19 mg, 20 mol%), diisopropylamine (1ml/0.1 mmol of **35**), 1-ethynyl-4-methylbenzene (127 mg, 1.1 mmol) was added at room temperature, **39b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (166 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 7.06 (d, J = 8.4 Hz, 2H, ArH), 7.10 (d, J = 8.2 Hz, 2H, ArH), 7.22 (d, J = 8.0 Hz, 2H, ArH), 7.30-7.39 (m, 4H, ArH), 7.42 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 20.5, 20.7 (CH_3), 80.6, 82.0, 102.7, 110.9, 117.9, 118.8 (C), 120.0, 121.7 (CH), 122.5 (C), 128.1 (CH), 128.3 (C), 128.4, 128.7, 130.8, 131.3, 133.2 (CH), 138.2, 139.7, 141.7, 142.1, 191.1 (C). IR (KBr): ν = 3083, 2930 (w), 1714 (s), 1597, 1406 (m), 1314 (s), 1152 (m), 1106, 1093, 1060 (s), 1014, 850, 761 (m), 702 (s), 599 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 358 ([M]$^{+}$, 100), 313 (12), 97 (10), 83 (11), 71 (13), 69 (26), 57 (19), 43 (15), 41 (11). HRMS (EI, 70 eV): calcd for $C_{27}H_{18}O$: 358.13522; found 358.134682.

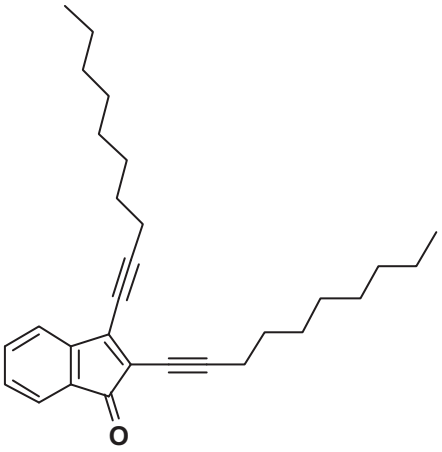


2,3-Bis((4-tert-butylphenyl)ethynyl)-1H-inden-1-one (39c) Starting with **35** (144 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (52 mg, 15 mol%), dry CuI (19 mg, 20 mol%), diisopropylamine (1ml/0.1 mmol of **35**), 1-tert-butyl-4-ethynylbenzene (174 mg, 1.1 mmol) was added at room temperature, **39c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (207 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (s, 3H, $3CH_3$),



1.27 (s, 3H, $3CH_3$), 7.24-7.27 (m, 2H, ArH), 7.31 (d, J = 8.6 Hz, ArH), 7.37 (d, J = 8.6 Hz, ArH), 7.37-7.42 (m, 2H, ArH), 7.47 (d, J = 8.6 Hz, 2H, ArH), 7.52 (d, J = 8.6 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 31.1, 31.2 ($6CH_3$), 34.9, 35.0, 81.5, 83.0, 103.8, 111.9 (C), 120.0, 121.7 (CH), 121.9, 122.7 (C), 123.0, 128.3, 128.6, 129.0 (CH), 129.3 (C), 129.9, 130.1, 132.0, 132.3, 133.2 (CH), 142.9, 143.2, 152.4, 153.8, 193.0 (C). IR (KBr): v = 3082, 2931 (w), 1720 (s), 1590, 1405 (m), 1312 (s), 1156 (m), 1109, 1096, 1063 (s), 1010, 850, 761 (m), 703 (s), 621 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 442 ([M]$^+$, 32), 428 (10), 427 (28), 426 (13), 355 (10), 281 (10), 253 (10), 207 (13), 178 (12), 165 (13), 163 (20), 161 (23), 149 (15), 135 (10), 111 (12), 97 (20), 91 (17), 85 (18), 83 (24), 81 (12), 78 (65), 73 (23), 71 (32), 60 (16), 57 (74), 44 (90), 43 (49), 41 (21). HRMS (EI, 70 eV): calcd for $C_{33}H_{30}O$: 442.22912; found 442.227998.

2,3-Di(dec-1-ynyl)-1H-inden-1-one (39d) Starting with **35** (142 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (52 mg, 15 mol%), dry CuI (19 mg, 20 mol%), diisopropylamine (1ml/0.1 mmol of **35**), dec-1-yne (152 mg, 1.1 mmol) was added at room temperature, **39d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (185 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79-0.83 (m, 6H, $2CH_3$), 1.19-1.27(m, 20H, $10CH_2$), 1.36-1.46 (m, 4H, $2CH_2$), 1.53-1.64(m, 4H, $2CH_2$), 7.11-7.16 (m, 1H, ArH), 7.18-7.21 (m, 1H, ArH), 7.30-7.35 (m, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 14.0 ($2CH_3$), 20.3, 20.6, 22.6, 28.4, 28.5, 28.8, 29.0, 29.1, 29.2, 31.8, 31.9, 72.6, 74.7, 104.7, 113.4 (C), 120.7, 122.5 (CH), 124.1, 129.1 (C), 129.4, 134.0 (CH), 143.4, 143.6, 192.8 (C). IR (KBr): v = 2961, 2932, 2872 (w), 1708 (s), 1600, 1462, 1359, 1219, 1089, 763, 528 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 358 ([M]$^+$, 100), 313 (12), 97 (10), 83 (11), 71 (13), 69 (26), 57 (19), 43 (15), 41 (11). HRMS (EI, 70 eV): calcd for $C_{27}H_{18}O$: 372.20838; found 372.208533.



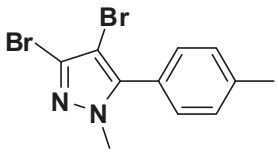
11.8 Synthesis of Arylated Pyrazoles by Site-Selective Suzuki-Miyaura Reactions of Tribromopyrazoles.

11.8.1 Synthesis of Arylated Pyrazoles

To a 1,4-dioxane solution (4 mL) of **41a-b** (0.5 mmol) was added $Pd(PPh_3)_4$ (3-5 mol %) or $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), at 20 °C under argon atmosphere. After stirring for 30 min, the arylboronic acid **19** (1.0) equiv. per bromine atom of the substrate), K_3PO_4 (1.5 equiv. per bromine atom of the substrate) and water (1.0 mL) were added. The mixture was heated for 12 h at 100 ˚C. After cooling to 20 °C, the mixture was diluted with H_2O, extracted with CH_2Cl_2 (3 x 25 mL), dried (Na_2SO_4), and filtered. The solvent of the filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (heptanes/EtOAc).

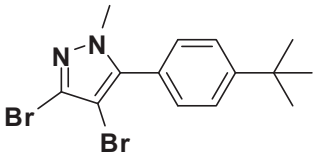
11.8.2 Synthesis of mono-arylated Pyrazoles (42a-e)

3,4-Dibromo-1-methyl-5-p-tolyl-1H-pyrazole (42a) Starting with **41a** (200 mg, 0.62 mmol),



$Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and *p*-tolylboronic acid (84 mg, 0.62 mmol), 4**2a** was isolated as a white solid (155 mg, 76%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 3.70 (s, 3H, NCH_3), 7.19 (d, 2H, J = 8.5 Hz, ArH), 7.24 (d, 2H, J = 8.5 Hz, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.4 (CH_3), 38.5 (NCH_3), 96.2, 125.0, 127.1 (C), 129.5, 129.6 (CH), 139.9, 143.3 (C). IR (KBr): v = 2948, 2918, 2852 (w), 1484, 1361, 1273, 995 (m), 823 (s), 720 (w), 575 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 330 ([M, $^{81}Br_2]^+$, 100), 329 ([M, $^{79}Br^{81}Br]^+$, 100), 328 ([M, $^{79}Br_2]^+$, 51), 170 (10), 169 (10). HRMS (EI, 70 eV): calcd for $C_{12}H_{10}N_2Br_2$ (M^+, [^{79}Br, ^{81}Br]): 329.91848; found 329.919092.

3,4-Dibromo-5-(4-ethylphenyl)-1-methyl-1H-pyrazole (42b) Starting with **41a** (200 mg, 0.62 mmol), $Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-ethylphenylboronic acid (93 mg, 0.62 mmol), 4**2b** was isolated as a white solid (168 mg, 79%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.4 Hz, CH_2CH_3), 2.63 (q, J = 7.6 Hz, CH_2), 3.69 (s, 3H, NCH_3), 7.20 (d, J = 8.4 Hz, 2H, ArH), 7.25 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.2 (CH_3), 28.7 (CH_2), 38.5 (NCH_3), 96.2, 125.1, 127.1 (C), 128.3, 129.5 (CH), 143.3, 146.0 (C). IR (KBr): ν = 2963, (m), 2929, 2848 (w), 1613 (m), 1485 (m), 1363 (s), 1274, 1117, 1004 (m) 994, 837 (s), 791, 613 (w), 577 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 344 ([M, $^{81}Br_2]^+$, 100), 343 ([M, $^{79}Br^{81}Br]^+$, 100), 342 ([M, $^{79}Br_2]^+$, 51), 331 (37), 329 (75), 327 (38). HRMS (ESI^+): calcd for $C_{12}H_{13}Br_2N_2$ ([M+1]$^+$, $^{79}Br_2$): 342.944; found 342.9442, calcd for ([M+1]$^+$, $^{79}Br^{81}Br$): 344.942; found 344.9424, calcd for ([M+1]$^+$, $^{81}Br_2$): 346.9401; found 346.9402.



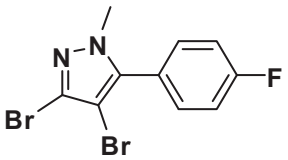
3,4-Dibromo-5-(4-tert-butylphenyl)-1-methyl-1H-pyrazole (42c) Starting with **41a** (200 mg, 0.62 mmol), $Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and *4-tert*-butylphenylboronic acid (110 mg, 0.62 mmol), 4**2c** was isolated as a white solid (186 mg, 81%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 9H, $3CH_3$), 3.72 (s, 3H, NCH_3), 7.25 (d, J = 7.1 Hz, 2H, ArH), 7.44 (d, J = 6.9 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 31.2 (CH_3), 34.8 (C), 38.6 (NCH_3), 96.2, 124.9 (C), 125.7 (CH), 127.2 (C), 129.2 (CH), 143.3, 152.8 (C). IR (KBr): ν = 3031, 2954, 2865 (w), 1680 (m), 1363 (m), 1266 (s), 1109 (m), 994, 839 (s), 694 (m), 587 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 374 ([M, $^{81}Br_2]^+$, 23), 373 ([M, $^{79}Br_2{}^{81}Br_2]^+$, 7), 372 ([M, $^{79}Br_2]^+$, 48), 370 (27), 359 (45), 358 (11), 357 (100), 356 (13), 355 (54), 329 (18), 164 (17). HRMS (ESI^+): calcd for $C_{14}H_{17}Br_2N_2$ ([M+1]$^+$, $^{79}Br_2$): 370.9753; found 370.9751, calcd for ([M+1]$^+$, $^{79}Br^{81}Br$): 372.9733; found 372.973, calcd for ([M+1]$^+$, $^{81}Br_2$): 374.9714; found 374.9709.

3,4-Dibromo-5-(3-chlorophenyl)-1-methyl-1H-pyrazole (42d). Starting with **41a** (200 mg, 0.62 mmol), $Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and 3-chlorophenylboronic acid (97 mg, 0.62 mmol), 4**2d** was isolated as a white solid (158 mg, 73%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.73 (s, 3H, NCH_3), 7.20-7.23 (m, 1H, ArH), 7.31-7.33 (m, 1H, ArH), 7.38 (s, 1 H, ArH), 7.39-7.40 (m, 1 H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 38.7 (NCH_3), 96.8, 125.7, 127.4 (C), 127.8, 129.6, 129.9, 130.2 (CH), 134.8, 141.8 (C). IR (KBr): ν = 3059, 2945, 2926, 2850 (w), 1600, 1565, 1461, 1366, 1272, 1080, 996, 897 (m), 784 (s), 686 (s), 593 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 354 ([M, $^{81}Br_2{}^{37}Cl_2]^+$, 14), 353 ([M, $^{81}Br_2{}^{37}Cl^{35}Cl]^+$, 8), 352 ([M, $^{81}Br_2{}^{35}Cl]^+$, 70), 351 ([M, $^{81}Br^{37}Cl]^+$, 100), 350 ([M, $^{81}Br_2]^+$, 100), 349 ([M, $^{79}Br^{81}Br]^+$, 9), 348 ([M, $^{79}Br_2]^+$, 45), 147 (10). HRMS (ESI^+): calcd for $C_{10}H_8Br_2Cl_2N_2$ ([M+1]$^+$, $^{79}Br_2$): 348.8737; found 348.874, calcd for ([M+1]$^+$, $^{81}Br_2$): 350.8716; found 350.8726, calcd for ([M+1]$^+$, $^{81}Br_2{}^{35}Cl_2$): 352.8693; found 352.8700.

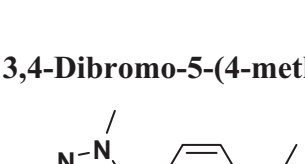
.

3,4-Dibromo-5-(4-chlorophenyl)-1-methyl-1H-pyrazole (42e). Starting with **41a** (200 mg, 0.62 mmol), $Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-chlorophenylboronic acid (97 mg, 0.62 mmol), 4**2e** was isolated as a white solid (156 mg, 71%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3H, NCH_3), 7.26 (d, J = 8.5 Hz, 2H, ArH), 7.42 (d, J = 8.5 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 38.6 (NCH_3), 96.6, 126.3, 127.3 (C), 129.2, 130.9 (CH), 136.0, 142.1 (C). IR (KBr): ν = 3028, 2952, 2851 (w), 1473, 1359, 1264, 1089 (m), 996, 836 (s), 775, 715, 644, 574 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 354 ([M, $^{81}Br_2{}^{37}Cl_2]^+$, 13), 353 ([M, $^{81}Br_2{}^{37}Cl^{35}Cl]^+$, 8), 352 ([M, $^{81}Br_2{}^{35}Cl]^+$, 70), 351 ([M, $^{81}Br^{37}Cl]^+$, 12), 350 ([M, $^{81}Br_2]^+$, 100), 349 ([M, $^{79}Br^{81}Br]^+$, 8), 348 ([M, $^{79}Br_2]^+$, 45), 147 (11). HRMS (ESI^+): calcd for $C_{10}H_8Br_2Cl_2N_2$ ([M+1]$^+$, $^{79}Br_2$): 348.8736; found 348.873, calcd for ([M+1]$^+$, $^{81}Br_2$): 350.8715; found 350.8725, calcd for ([M+1]$^+$, $^{81}Br_2{}^{35}Cl_2$): 352.8692; found 352.8709.

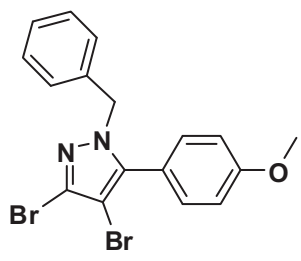
3,4-Dibromo-5-(4-fluorophenyl)-1-methyl-1H-pyrazole (42f). Starting with **41a** (200 mg, 0.62 mmol), $Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-fluorophenylboronic acid (87 mg, 0.62 mmol), 4**2f** was isolated as a white solid (155 mg, 75%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3H, NCH_3), 7.13-7.19 (m, 2H, 2H, ArH), 7.28-7.34 (m, 2H, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -110.1. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 38.5 (NCH_3), 96.6 (C), 116.1 (d, J = 21.8 Hz, CH), 123.9 (d, J = 3.2 Hz, C), 127.2 (C), 131.6 (d, J = 10.8 Hz, CH), 142.3 (C), 163.4 (d, J = 244.7 Hz, C). IR (KBr): ν = 3038, 2951, 2855 (w), 1730 (w), 1606, 1541 (m), 1484, 1361, 1219 (s), 1159, 997 (m), 839 (s), 816, 721, 611, 575 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 334 ([M, $^{81}Br_2]^+$, 100), 334 ([M, $^{79}Br^{81}Br]^+$, 8), 332 ([M, $^{79}Br_2]^+$, 79), 174, 136 (11), 131 (12). HRMS (ESI$^+$): calcd for $C_{10}H_8Br_2N_2$ ([M+1]$^+$, $^{79}Br^{81}Br$): 334.9013; found 334.9016.



3,4-Dibromo-5-(4-methoxyphenyl)-1-methyl-1H-pyrazole (42g). Starting with **41a** (200 mg, 0.62 mmol), $Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-methoxyphenylboronic acid (94 mg, 0.62 mmol), 4**2g** was isolated as a white solid (167 mg, 78%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 6.93 (d, J = 8.8 Hz, 2H, ArH), 7.23 (d, J = 8.8 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 37.5 (NCH_3), 54.3 (OCH_3), 95.2 (C), 113.2 (CH), 118.9, 126.0 (C), 129.9 (CH), 142.1, 159.5 (C). IR (KBr): ν = 3012, 2922, 2839 (w), 1607, 1539, 1481, 1366, 1257, 1176, 1025, 991 (m), 831 (s), 803 (m), 765, 687, 613, 573 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 346 ([M, $^{81}Br_2]^+$, 100), 345 ([M, ^{79}Br $^{81}Br]^+$, 8), 344 ([M, $^{79}Br]^+$, 51), 333 (11), 331 (23), 329 (11). HRMS (ESI$^+$): calcd for $C_{11}H_{11}Br_2N_2$ ([M+1]$^+$, $^{79}Br_2$): 344.9233; found 344.9234, calcd for ([M+1]$^+$, $^{79}Br^{81}Br$): 346.9213; found 346.9214, calcd for ([M+1]$^+$, $^{81}Br_2$): 348.9193; found 348.9194.



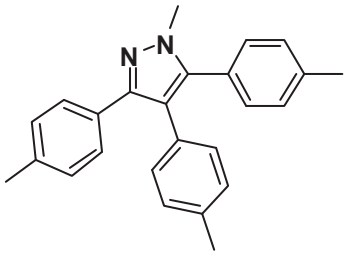
1-Benzyl-3,4-dibromo-5-(4-methoxyphenyl)-1H-pyrazole (42h). Starting with **41b** (200 mg, 0.50 mmol), $Pd(PPh_3)_2Cl_2$ (13 mg, 3 mol%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-methoxyphenylboronic acid (79 mg, 0.50 mmol), 4**2h** was isolated as a white solid (165 mg, 78%). Reaction temperature: 60 °C for 4h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.75 (s, 3H, OCH_3), 5.12 (s, 2H, CH_2), 6.86 (d, J = 7.1 Hz, 2H, ArH), 6.94 (d, J = 7.0 Hz,



ArH), 7.09-7.20 (m, 5 H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 54.5 (CH_2), 55.3 (OCH_3), 97.0 (C), 114.3 (CH), 120.0 (C), 127.1 (CH), 127.8 (C), 127.9, 128.7, 131.1 (CH), 136.3, 143.5, 160.6 (C). IR (KBr): ν = 3031, 3002, 2957, 2917, 2833 (w), 1608, 1540, 1482, 1447, 1367, 1357 (m), 1248, 1174 (s), 1029, 998 (s), 833 (m), 726 (s), 562 (m). GC-MS (EI, 70 eV): *m/z* (%) = 424 ([M, $^{81}Br_2$]$^+$, 41), 322 ([M, ^{79}Br ^{81}Br]$^+$, 85), 420 ([M, $^{79}Br_2$]$^+$, 45), 234 (10), 143 (11), 91 (100), 65 (11). HRMS (ESI$^+$): calcd for $C_{17}H_{15}Br_2N_2O$ ([M+1]$^+$, $^{79}Br_2$): 420.9546; found 420.9543, calcd for ([M+1]$^+$, ^{79}Br^{81}Br): 422.9526; found 422.9526, calcd for ([M+1]$^+$, $^{81}Br_2$): 424.9508; found 424.9506.

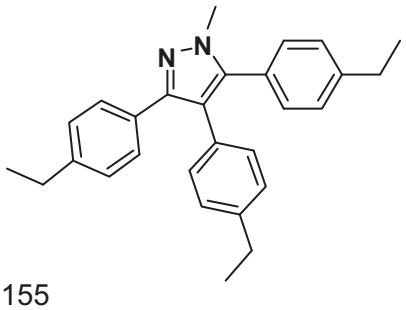
11.8.3 Synthesis of symmetrical triarylPyrazoles (43a-e)

1-Methyl-3,4,5-tri-(p-tolyl)-1H-pyrazole (43a). Starting with **41a** (200 mg, 0.62 mmol),



$Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and *p*-tolylboronic acid (272 mg, 2.0 mmol), 4**6a** was isolated as a white solid (198 mg, 91%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 3.76 (s, 3H, NCH_3), 6.84 (d, *J* = 8.3 Hz, 2H, ArH), 6.89 (d, *J* = 8.3 Hz, 2H, ArH), 6.99 (d, *J* = 8.3 Hz, 2H, ArH), 7.03 (d, *J* = 8.3 Hz, 2H, ArH), 7.09 (d, *J* = 7.8 Hz, 2H, ArH), 7.27 (d, *J* = 8.1 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.1, 21.2, 21.3 (CH_3), 37.2 (NCH_3), 118.7, 127.3 (C), 127.9, 128.7, 128.9, 129.1 (CH), 129.3 (C), 130.0, 130.2 (CH), 130.7, 135.6, 136.8, 138.2, 142.1, 148.4 (C). IR (KBr): ν = 3018, 2919, 2872 (w), 1579, 1523, 1440, 1315, 1277, 1182, 1112, 1005, 975 (m), 818 (s), 750, 723, 657, 613 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 352 ([M]$^+$, 100), 351 (36). HRMS (ESI$^+$): calcd for $C_{25}H_{25}N_2$ [M+1]$^+$: 353.2012; found 353.2012.

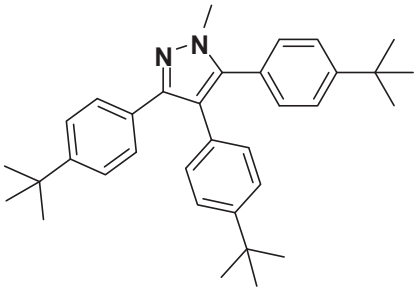
3,4,5-Tris(4-ethylphenyl)-1-methyl-1H-pyrazole (43b). Starting with **41** (200 mg, 0.62



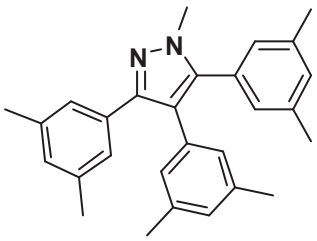
mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-ethylphenylboronic acid (300 mg, 2.0 mmol), **46b** was isolated as a white solid (217 mg, 89%). Reaction temperature: 90 °C for 6h. ^{1}H

NMR (300 MHz, $CDCl_3$): δ = 1.09-1.20 (m, 9H, $3CH_3$), 2,46-2.63 (m, 6H, $3CH_2$), 3.76 (s, 3H, NCH_3), 6.89 (d, J = 8.2 Hz, 2H, ArH), 6.92 (d, J = 8.4 Hz, 2H, ArH), 7.02 (d, J = 8.0 Hz, 2H, ArH), 7.06 (d, J = 8.3 Hz, 2H, ArH), 7.10 (d, J = 8.7 Hz, 2H, ArH), 7.30 (d, J = 8.2 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 14.1, 14.2, 14.3 (CH_3), 27.3, 27.5, 27.6 (CH_2), 36.2 (NCH_3), 117.6 (C), 126.4, 126.5 (CH), 126.6 (C), 126.8, 126.9, 129.0, 129.2 (CH), 129.7, 130.0, 140.8 141.1, 142.0, 143.3, 147.4 (C). IR (KBr): ν = 3019, 2961, 2871 (w), 1573, 1521, 1440, 1358, 1260, 1114, 1047, 1006, 976 (m), 833 (s), 753, 657, 615 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 394([M]$^+$, 100), 379 (29). HRMS (ESI$^+$): calcd for $C_{28}H_{31}N_2$ (M+ 1): 395.2482; found 395.24.86.

3,4,5-Tris(4-tert-butylphenyl)-1-methyl-1H-pyrazole (43c). Starting with **41** (200 mg, 0.62 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-tert-butylphenylboronic acid (356 mg, 2.0 mmol), **46c** was isolated as a white solid (254 mg, 86%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20 (s, 9H, $3CH_3$), 1.22 (s, 9H, $3CH_3$), 1.25 (s, 9H, $3CH_3$), 3.75 (s, 3H, NCH_3), 6.93 (d, J = 8.4 Hz, 2H, ArH), 7.08 (d, J = 8.5 Hz, 2H, ArH), 7.10 (d, J = 7.3 Hz, 2H, ArH), 7.18 (d, J = 8.2 Hz, 2H, ArH), 7.28 (d, J = 8.2 Hz, 2H, ArH), 7.33 (d, J = 8.5 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 31.2, 31.3, 31.4 (CH_3), 37.3 (NCH_3), 118.6 (C), 124.8, 125.0, 125.2, (CH), 126.2 (C), 127.5, 129.8, 130.0 (CH), 130.4, 130.8, 142.1, 148.3, 148.8, 149.9, 151.2 (C). IR (KBr): ν = 3029, 2959, 2867 (w), 1525, 1436, 1362, 1264, 1201, 1128, 1016, 975 (m), 838 (s), 799, 727, 656, 550 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 478 ([M]$^+$, 96), 464 (37), 463 (100), 224 (14). HRMS (ESI, 70 eV): calcd for $C_{34}H_{42}N_2$ (M+ 1): 478.33425; found 478.334253.



3,4,5-Tris(3,5-dimethylphenyl)-1-methyl-1H-pyrazole (43d). Starting with **41** (200 mg, 0.62 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and 3,5-dimethylphenylboronic acid (300 mg, 2.0 mmol), **46d** was isolated as a white solid (204 mg, 84%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.06 (s, 6H, $2CH_3$), 2.14 (s, 6H, $2CH_3$), 2.20 (s, 6H, $2CH_3$),



3.74 (s, 3H, NCH_3), 6.61 (s, 2H, ArH), 6.69 (s, 1H, ArH), 6.74 (s, 1H, ArH), 6.79 (s, 2H, ArH), 6.89 (s, 1H, ArH), 7.04 (s, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.1, 21.2, 21.3 ($6CH_3$), 37.3 (NCH_3), 123.3 (C), 125.8, 127.8, 127.9, 128.2, 128.8, 130.0 (CH), 130.2, 133.2, 133.4, 136.9, 137.3, 138.0, 142.3, 148.3 (C). IR (KBr): ν = 3003, 2915, 2857, 1738 (w), 1600 (s), 1444, 1358, 1261, 1152, 1036, 912 (m), 848 (s), 789, 733, 694, 651 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 394([M]$^+$, 100), 393 (26). HRMS (ESI$^+$): calcd for $C_{28}H_{31}N_2$ (M+1): 395.2482; found 395.2483.

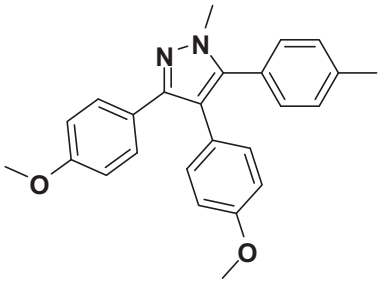
3,4,5-Tris(4-methoxyphenyl)-1-methyl-1H-pyrazole (43e). Starting with **41** (200 mg, 0.62 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-methoxyphenylboronic acid (304 mg, 2.0 mmol), 4**6e** was isolated as a white solid (200 mg, 81%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.66 (s, 3H, CH_3), 3.69 (s, 3H, CH_3), 3.71 (s, 3H, CH_3), 3.74 (s, 3H, CH_3), 6.63 (d, *J* = 8.8 Hz, 2H, ArH), 6.72 (d, *J* = 8.8 Hz, 2H, ArH), 6.79 (d, *J* = 8.8 Hz, 2H, ArH), 6.88 (d, *J* = 8.8 Hz, 2H, ArH), 7.06 (d, *J* = 8.5 Hz, 2H, ArH), 7.31 (d, *J* = 8.5 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 37.2 (NCH_3), 55.0 (OCH_3), 55.1 (OCH_3), 55.2 (OCH_3), 113.6, 113.7, 113.9 (CH), 118.1, 122.5, 126.0, 126.3, 126.7 (C), 129.2, 131.4, 131.5 (CH), 141.8, 148.1, 158.0, 158.8, 159.9 (C). IR (KBr): ν = 3019, 2961, 2871 (w), 1573, 1521, 1440, 1358, 1260, 1114, 1047, 1006, 976 (m), 833 (s), 753, 657, 615 cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 400 ([M]$^+$, 100), 399 (13), 385 (20). HRMS (ESI, 70 eV): calcd for $C_{25}H_{25}N_2O_3$ (M+ H): 401.186; found 401.1868.

11.8.4 Synthesis of unsymmetrical triarylated Pyrazoles (44a-g)

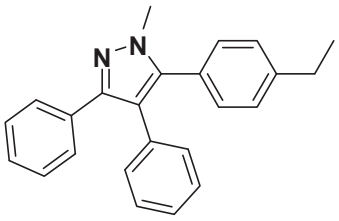
1-Methyl-3,4-diphenyl-5-p-tolyl-1H-pyrazole (44a). Starting with **42a** (200 mg, 0.60 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and *p*-tolylboronic acid (158 mg, 1.3 mmol), 4**7a** was isolated as a white solid (188 mg, 97%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s,

3 H, CH_3), 3.78 (s, 3 H, NCH_3), 6.95-6.98 (m, 2H, ArH), 7.03-7.05 (m, 1H, ArH), 7.07-7.10 (m, 4H, ArH), 7.06-7.09 (m, 2H, ArH), 7.15-7.22 (m, 4H, ArH), 7.37-7.40 (m, 1H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.3, 37.3 (NCH_3), 118.9 (C), 126.2, 128.0, 129.2, 130.0, 130.4 (CH), 122.5 (C), 127.9, 128.8, 128.9, 130.2 (CH), 130.4, 133.4, 138.3, 142.3, 148.4 (C). IR (KBr): ν = 3051, 2921, 2850 (w), 1600, 1519 (w), 1483, 1356, 1232, 1006, 831 (m), 760, 694 (s), 626, 566 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 324 ([M]$^+$, 100), 323 (53). HRMS (ESI$^+$): calcd for $C_{23}H_{21}N_2$ ([M+1]$^+$): 325.1699; found 325.1703.

3,4-Bis(4-methoxyphenyl)-1-methyl-5-p-tolyl-1H-pyrazole (44b). Starting with **42a** (200 mg, 0.60 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and *4*-methoxyphenylboronic acid (197 mg, 1.3 mmol), 4**7b** was isolated as a white solid (193 mg, 84%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 3.68 (s, 3 H, CH_3), 3.71 (s, 3 H, CH_3), 3.76 (s, 3H, CH_3), 6.63-6.66 (m, 3H, ArH), 6.72-6.75 (m, 3H, ArH), 6.87-6.90 (m, 3H, ArH), 7.02-7.10 (m, 5H, ArH), 7.30-7.33 (m, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 21.3 (CH_3), 37.2 (NCH_3), 37.2 (NCH_3), 55.0, 55.1 (OCH_3), 113.5, 113.6 (CH), 118.1, 125.9, 126.2, 127.3 (C), 129.1, 129.2, 130.0, 131.4 (CH), 138.1, 142.0, 148.1, 157.9, 158.8 (C). IR (KBr): ν = 3011, 2923, 2832, 1611 (w), 1520, 1432, 1283 (m), 1241 (s), 1172 (s), 1033, 837, 807 (m), 755, 612, 530 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 384 ([M]$^+$, 100), 341 (13), 327 (22), 277 (39), 246 (22), 198 (23). HRMS (ESI$^+$): calcd for $C_{25}H_{25}N_2O_2$ [M+1]: 385.1911; found 385.1914.

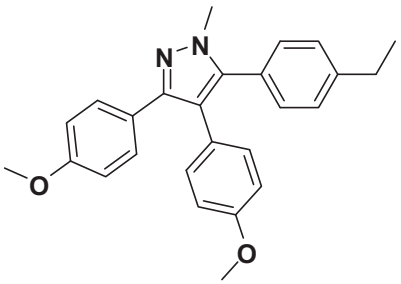


5-(4-Ethylphenyl)-1-methyl-3,4-diphenyl-1H-pyrazole (44c). Starting with **42b** (200 mg, 0.58 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and phenylboronic acid (155 mg, 1.27 mmol), 4**7c** was isolated as a white solid (174 mg, 89%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, *J* = 7.5 Hz, 3H, CH_3), 2.59 (q, *J* = 7.6 Hz, 2H, CH_2), 3.79 (s, 3H, NCH_3), 6.96-6.99 (m, 2H, ArH), 7.05-7.10 (m, 5H, ArH), 7.17-7.21 (m, 5H, ArH), 7.37-7.40 (m, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 15.1 (CH_3), 28.5 (CH_2), 37.3 (NCH_3), 125.5 (C), 126.2, 127.2, 127.9, 128.0, 128.1 (CH), 128.5, 128.7 (C), 130.0, 130.4 (CH), 133.5, 142.3, 144.5,



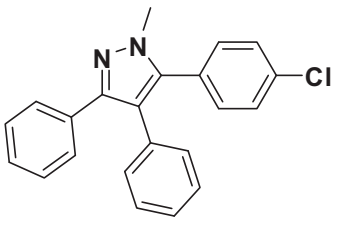
148.4 (C). IR (KBr): ν = 3051, 2959, 2924, 2848, 1603, 1519, 1454, 1361, 1277, 1117, 1058, 1007, 973, 916 (w), 841 (m), 761, 696 (s), 627, 536 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 338 ($[M]^+$, 100), 337 (45). HRMS (EI, 70 eV): calcd for $C_{24}H_{23}N_2$ [M+H]: 339.1856; found 339.1861.

5-(4-Ethylphenyl)-3,4-bis(4-methoxyphenyl)-1-methyl-1H-pyrazole (44d). Starting with



42b (200 mg, 0.58 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and 4-methoxyphenylboronic acid (193 mg, 1.27 mmol), 4**7d** was isolated as a white solid (189 mg, 82%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (t, J = 7.5 Hz, 3H, CH_3), 2.58 (q, J = 7.6 Hz, 2H, CH_2), 3.68 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.76 (s, 3H, NCH_3), 6.64 (d, J = 8.8 Hz, 2H, ArH), 6.73 (d, J = 9.0 Hz, 2H, ArH), 6.89 (d, J = 8.8 Hz, 2H, ArH), 7.07 (d, J = 8.2 Hz, 2H, ArH), 7.11 (d, J = 8.2 Hz, 2H, ArH), 7.32 (d, J = 9.1 Hz, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 15.1 (CH_3), 28.5 (CH_2), 37.2 (NCH_3), 55.0, 55.1 (OCH_3), 113.5, 113.6 (CH), 118.1, 125.9, 126.2, 127.4 (C), 127.9, 129.2, 130.0, 131.4 (CH), 142.1, 144.3, 148.1, 157.9, 158.8 (C). IR (KBr): ν = 3010, 2961, 2925, 2832 (w), 1612, 1578, 1547, 1520, 1463, 1433, 1354, 1283 (m), 1242, 1171 (s), 1110, 1034, 973 (m), 833 (s), 809, 756, 608, 544 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 398 ($[M]^+$, 100), 397 (12), 383 (18). HRMS (ESI^+): calcd for $C_{26}H_{27}N_2O_2$ [M+1]: 399.2067; found 399.2071.

5-(4-Chlorophenyl)-1-methyl-3,4-diphenyl-1H-pyrazole (44e). Starting with **42e** (200 mg,

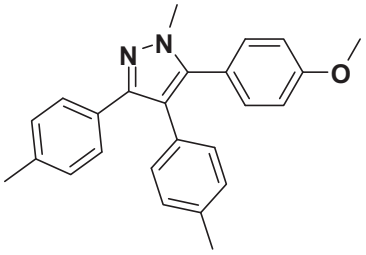


0.57 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1mL) and phenylboronic acid (152 mg, 1.25 mmol), 4**7e** was isolated as a white solid (169 mg, 86%). Reaction temperature: 90 °C for 6h. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3H, NCH_3), 6.99-7.02 (m, 2H, ArH), 7.09-7.12 (m, 2H, ArH), 7.22-7.25 (m, 3H, ArH), 7.28-7.34 (m, 2H, ArH), 7.38-7.42 (m, 3H, ArH), 7.50-7.54 (m, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 37.5 (NCH_3), 119.2 (C), 127.0 (CH), 127.1 (C), 127.2, 128.1, 128.2, 128.3, 128.8, 130.4, 130.5 (CH), 133.4, 133.5, 140.2, 141.1, 141.9, 148.5 (C). IR (KBr): ν = 3011, 2923, 2832, 1611 (w), 1520, 1432, 1283 (m), 1241 (s), 1172 (s), 1033, 837,

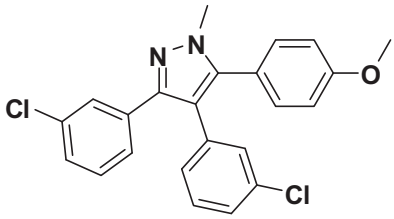
807 (m), 755, 612, 530 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 346 ([M, $^{37}Cl_2]^+$, 100), 345 ([M, $^{35}Cl\ ^{37}Cl]^+$, 34), 344 ([M, $^{35}Cl_2]^+$, 99). HRMS (EI, 70 eV): calcd for $C_{22}H_{17}N_2ClO$ (M^+, [^{37}Cl]): 346.91433; found 346.914332, calcd for (M^+, [^{35}Cl]): 344.91324; found 344.9133.

.

5-(4-Methoxyphenyl)-1-methyl-3,4-dip-tolyl-1H-pyrazole (44f). Starting with **42g** (200 mg, 0.58 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and *p*-tolylboronic acid (172 mg, 1.27 mmol), 4**7g** was isolated as a white solid (177 mg, 83%). Reaction temperature: 90 °C for 6h. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, CH_3), 2.24 (s, 3 H, CH_3), 3.73 (s, 3 H, CH_3), 3.75 (s, 3H, CH_3), 6.80 (d, *J* = 7.1 Hz, 2H, ArH),), 6.84 (d, *J* = 8.3 Hz, 2H, ArH), 6.90 (d, *J* = 8.0 Hz, 2H, ArH), 7.00 (d, *J* = 7.9 Hz, 2H, ArH), 7.08 (d, *J* = 7.0 Hz, 2H, ArH), 7.28 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.1, 21.2 (CH_3), 37.2 (NCH_3), 55.2 (OCH_3), 113.9 (CH), 118.6, 122.5 (C), 127.9, 128.8, 128.9, 130.2 (CH), 130.6, 130.8 (C), 131.4 (CH), 135.6, 136.8, 141.9, 148.4, 159.5 (C). IR (KBr): *v* = 2951, 2920, 2851 (w), 1612, 1529, 1492, 1353, 1286 (m), 1243, 1178 (s), 1107 (m), 1034 (s), 1020, 845 (m), 824 (s), 800, 755, 721, 614, 530 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 368 ($[M]^+$, 100), 367 (31). HRMS (ESI^+): calcd for $C_{25}H_{25}N_2O$ $[M+1]^+$: 369.1961; found 369.1962.



3,4-Bis(3-chlorophenyl)-5-(4-methoxyphenyl)-1-methyl-1H-pyrazole (44g). Starting with **42g** (200 mg, 0.58 mmol), $Pd(OAc)_2$ (7 mg, 5 mol-%), SPhos (25 mg, 10 mol-%), K_2CO_3 (H_2O, 2 M, 1 mL) and 3-chlorophenylboronic acid (198 mg, 1.27 mmol), 4**7h** was isolated as a white solid (175 mg, 74%). Reaction temperature: 90 °C for 6h. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.75 (s, 3 H, CH_3), 3.76 (s, 3H, CH_3), 6.81-6.82 (m, 4H, ArH), 6.85 (s, 1H, ArH), 6.94 (s, 1H, ArH), 7.03-7.08 (m, 4H, ArH), 711-7.15 (m, 2H, ArH). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 37.3 (NCH_3), 55.2 (OCH_3), 114.1 (CH), 117.7, 121.4, (C), 126.2, 126.7, 127.5, 127.9, 128.5, 129.4, 130.0, 130.1, 131.3 (CH), 133.9, 134.2, 135.0, 135.1, 142.4, 146.9, 159.8 (C). IR (KBr): *v* = 3057, 2926, 2835 (w), 1611, 1597, 1469, 1358, 1290 (m), 1247 (s), 1174, 1077, 1032, 998, 846 (m), 784, 730, 698 (s), 604 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 410 ([M, $^{37}Cl_2]^+$, 100), 409 ([M, $^{35}Cl^{37}Cl]^+$, 40), 408 ([M, $^{35}Cl_2]^+$, 100), 407 ([M^+, 25). HRMS (ESI^+): calcd for $C_{23}H_{19}Cl_2N_2O$ $[M+1]^+$:



(M^+, $^{35}Cl^{37}Cl$]): 409.0869; found 409.0867, calcd for $[M+1]^+$: (M^+, [$^{37}Cl_2$]): 411.0844; found 411.0855.

11.9 Synthesis of Unsymmetrical Arylated Furans by Suzuki-Miyaura Cross-Coupling and Metal-Halide exchange Reactions of 2,3,4,5-Tetrabromofuran

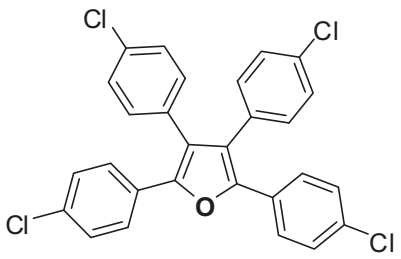
11.9.1 Synthesis of arylfurans

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

11.9.2 Synthesis of symmetrical tetraarylfurans (46a-c)

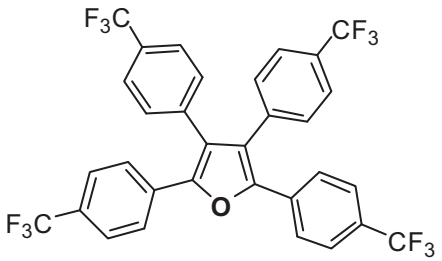
2,3,4,5-*Tetra-p*-tolylfuran (46a). Following the *General procedure* compound **46a** was prepared from **45** (96 mg, 1.0 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and *p*-tolylboronic acid **19b** (136 mg, 1.0 mmol) as a white solid (108 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s, 12H, $4CH_3$), 6.94-6.99 (m, 10H, ArH), 7.30-7.33 (m, 4H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.2, 21.3 (CH_3), 124.3 (C), 125.7 (CH), 128.4 (C), 128.9, 129.0, 130.2 (CH), 130.3, 136.4, 136.8, 147.5 (C). IR (KBr): ν = 2958, 2931, 2835 (w), 1782, 1604 (m), 1520, 1493, 1234 (m), 1161 (s), 1073, 944 (m), 820 (s), 640, 567 (m). cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 484 (M^+, 100), 351 (13). HRMS (EI, 70 eV): calcd. for $C_{36}H_{36}O$ (M^+): 484.27607; found: 484.27607.

2,3,4,5-Tetrakis(4-chlorophenyl)furan (46b). Following the *General procedure* compound



46b was prepared from **45** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-chlorophenylboronic acid (156 mg, 1.0 mmol) as a highly viscous colourless oil (104 mg, 82%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.94-6.98 (m, 4H, ArH), 7.16-7.19 (m, 8H, ArH), 7.30-7.33 (m, 4H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 123.9 (C), 127.1, 128.6, 128.7, 129.0 (CH), 130.8, 131.4, 133.6, 133.7, 147.3 (C). IR (KBr): ν = 2948, 2923, 2805 (w), 1784, 1602 (m), 1510, 1483, 1224 (m), 1151 (s), 1063, 934 (m), 810 (s), 645, 566 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 515 (M^+, [$^{37}Cl_4$], 3), 513 (M^+, [$^{35}Cl^{37}Cl_3$], 18), 511 (M^+, [$^{35}Cl_2{}^{37}Cl_2$], 28), 509 (M^+, [$^{35}Cl_3{}^{37}Cl_1$], 74), 507 (M^+, [$^{35}Cl_4$], 100), 371 (22), 369 (26), 299 (10), 184 (12), 183 (23), 170 (51), 168 (15), 155 (13), 139 (16), 131 (15). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{28}H_{16}OCl_4$ (M^+, [$^{35}Cl_4$]): 507.99498, found: 507.99498; calcd. for (M^+, [$^{35}Cl_3{}^{37}Cl$]): 509.99203, found 509.99605; calcd. for (M^+, [$^{35}Cl_2{}^{37}Cl_2$]): 511.98908, found 511.989530; calcd. for (M^+, [$^{35}Cl^{37}Cl_3$]): 513.98613, found 513.987468.

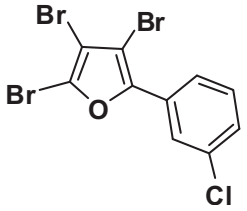
2,3,4,5-Tetrakis(4-(trifluoromethyl)phenyl)furan (46c). Following the *General procedure*



compound **46c** was prepared from **45** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-(trifluoromethyl) phenylboronic acid (190 mg, 0.25 mmol) as a white solid (143 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.19 (d, 4H, J = 7.9 Hz, ArH), 7.48-7.51 (m, 12H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -62.6, -62.8. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 123.8 (q, $J_{F,C}$ = 272.2 Hz, CF_3), 125.1 (C), 125.7 (q, $J_{F,C}$ = 3.9 Hz, CH), 125.9 (q, $J_{F,C}$ = 3.4 Hz, CH), 126.2 (CH), 129.6 (q, $J_{F,C}$ = 32.8 Hz, C-CF_3), 129.7 (q, $J_{F,C}$ = 32.0 Hz, C-CF_3), 130.5 (CH), 132.9, 135.6, 148.0. IR (KBr): ν = 3052, 2923(w), 1695, 1612, 1446 (m), 1333 (s), 1168 (m), 1132 (m), 1080, 810, 740 (m), 682 (s), 642, 589 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 644 (M^+, 100), 625 (11), 471 (31), 173 (27), 145 (22). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{32}H_{16}OF_{12}$ [M^+]: 644.10041, found: 644.100370.

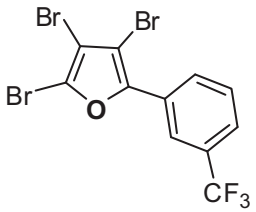
11.9.3 Synthesis of 2-aryl-3,4,5-tribromofurans (47a-d)

2,3,4-Tribromo-5-(3-chlorophenyl)furan (**47a**). Following the *General procedure A*



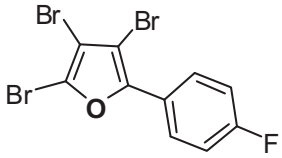
compound **47a** was prepared from **45** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 5 mL), 2M K2CO3 (0.5 mL) and 3-chlorophenylboronic acid **19c** (39 mg, 0.25 mmol) as a highly viscous colourless oil (90 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25-7.33 (m, 2H, ArH), 7.73-7.76 (m, 2H, ArH), 7.82 (brs, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 100.9, 107.3, 122.1, 122.2 (C), 122.4, 124.3, 127.9, 128.9 (CH), 133.8, 149.2 (C). IR (KBr): v = 3093, 3066, 2961, 2921 (w), 1789, 1769, 1596 (s), 1514, 1471 (m), 1418, 1401, 1315, 1260, 1204 (w), 1164, 1111, 1089, 1065, 1003, 958, 884 (m), 681 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 416 (M^+, [$^{81}Br_2{}^{79}Br$], 100), 379 (9), 351 (16), 307 (94), 256 (19), 228 (17). HRMS (EI, 70 eV): calcd. for $C_{10}H_4OClBr_3$ (M^+, [$^{79}Br_3$]): 411.74953, found: 411.749450; calcd. For (M^+, [$^{81}Br^{79}Br_2$]): 413.74749, found 413.747368; calcd. for (M^+, [$^{81}Br_2{}^{79}Br$]): 415.74544, found 415.745451; (M^+, [$^{81}Br_3$]): 417.74339, found 417.743243.

2,3,4-Tribromo-5-(4-(trifluoromethyl)phenyl)furan (47b). Following the *General procedure A* compound **47b** was prepared from **45** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 3-(trifluoromethyl)phenylboronic acid (51 mg, 0.27 mmol) as a highly viscous colourless oil (95 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46-7.57 (m, 2H, ArH), 8.03-8.10 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -62.9. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 102.2, 108.4 (C), 122.1 (q, $J_{F,C}$ = 3.9 Hz, CH), 123.4 (C), 123.8 (q, $J_{F,C}$ = 272.3 Hz, CF_3), 125.4 (q, $J_{F,C}$ = 3.6 Hz, CH), 128.3 (CH), 129.1 (C), 129.2 (CH), 132.8 (q, $J_{F,C}$ = 32.9 Hz, C-CF_3), 150.1 (C). IR (KBr): v = 3083, 3060, 2951, 2931 (w), 1776, 1757, 1583 (s), 1504, 1461 (m), 1418, 1403, 1317, 1261, 1203 (w), 1167, 1088, 1064, 998, 884 (m), 676 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 451 ([M^+, $^{81}Br_3$], 12), 449 ([M^+, $^{79}Br^{81}Br_2$]$^+$, 12), 447 ([M^+, $^{81}Br^{79}Br_2$]$^+$, 100), 445 ([M^+, $^{79}Br_3$]$^+$, 33), 343 (49), 342 (11), 341 (97), 339 (49), 290 (11), 288 (12), 262 (22), 260 (22), 181 (31), 161 (11). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{11}H_4OBr_3F_3$ (M^+, [^{79}Br,^{79}Br,^{79}Br]): 445.77589, found: 445.775839; calcd. for (M^+, [^{81}Br,^{79}Br,^{79}Br]): 447.77384,



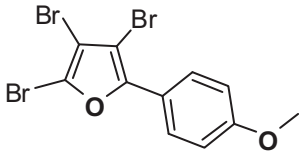
found 447.773857; calcd. for (M^+, [^{81}Br,^{81}Br,^{79}Br]): 449.77180, found 449.771888; calcd. for (M^+, [^{81}Br,^{81}Br,^{81}Br]): 451.76975, found 451.76975.

2,3,4-Tribromo-5-(4-fluorophenyl)furan (47c). Following the *General procedure A*



compound **47c** was prepared from **45** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-fluorophenylboronic acid (38 mg, 0.27 mmol) as a highly viscous colourless oil (87 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.01-7.09 (m, 2H, ArH), 7.77-7.85 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -110.9. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 100.5, 108.0 (C), 115.8 (d, $J_{F,C}$ = 22.3 Hz, CH), 122.3 (C), 124.8 (d, $J_{F,C}$ = 1.0 Hz, C), 127.5 (d, $J_{F,C}$ = 8.1 Hz, CH), 150.9 (C), 162.6 (d, $J_{F,C}$ = 249.2 Hz, CF). IR (KBr): v = 3072, 1887 (w), 1782, 1604 (m), 1523, 1491, 1233, 1159 (s), 1071, 943 (m), 828 (s), 641, 597 (m). cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 402 (M^+, [$^{81}Br_3$], 5), 400 (M^+, [$^{81}Br_2{}^{79}Br$], 10), 398 (M^+, [$^{81}Br_2{}^{79}Br_2$], 34), 396 (M^+, [$^{79}Br_3$], 100), 376 (10). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{10}H_4Br_3FO$ (M^+, [$^{81}Br_3$]): 402.79186, found: 402.791732; calcd. for (M^+, [$^{79}Br^{81}Br_2$]): 400.87112, found 400.871257; calcd. for (M^+, [$^{79}Br_2{}^{81}Br$]): 398.77613, found 398. 776221; calcd. for (M^+, [$^{81}Br_3$]): 396.67324, found 396.6731562.

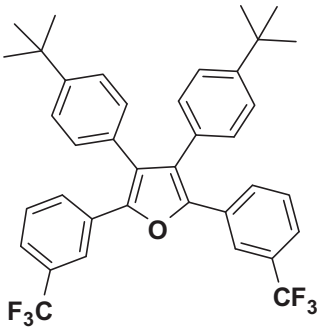
2,3,4-Tribromo-5-(4-methoxyphenyl)furan (47d). Following the *General procedure A*



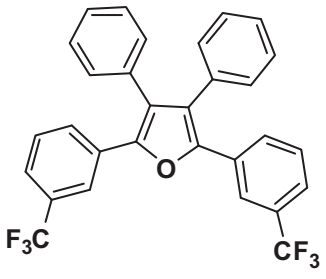
compound **47d** was prepared from **45** (96 mg, 0.25 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 4-methoxyphenylboronic acid (41 mg, 0.27 mmol) as a highly viscous colourless oil (90 mg, 91%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.77 (s, 3H, OCH_3), 6.87 (d, J = 8.7 Hz, 2H, ArH), 7.75 (d, J = 8.9 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 99.1, 107.7 (C), 114.0 (CH), 121.2, 121.3 (C), 127.1 (CH), 151.8, 160.0 (C). IR (KBr): v = 3070, 1886 (w), 1781, 1601 (m), 1520, 1481, 1222, 1145 (s), 1064, 932 (m), 815 (s), 634, 577 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 414 (M^+, [$^{81}Br_3$], 4), 412 (M^+, [$^{81}Br_2{}^{79}Br$], 12) 410 (M^+, [$^{81}Br_2{}^{79}Br_2$], 43), 408 (M^+, [$^{79}Br_3$], 100), 376 (10), 300 (13). HRMS (EI, 70 eV): calcd. for $C_{11}H_7Br_3O_2$ (M^+, [$^{81}Br_3$]): 414.89397, found: 414.893850; calcd. for (M^+, [$^{79}Br^{81}Br_2$]): 412.99102, found 412.991369; calcd. for (M^+, [$^{79}Br_2{}^{81}Br$]): 410.88710, found 410.887321; calcd. for (M^+, [$^{81}Br_3$]): 408.76424, found 408.764562.

11.9.4 Synthesis of unsymmetrical tetraarylfurans (48a-d)

3,4-Bis(4-tert-butylphenyl)-2,5-bis(3-(trifluoromethyl)phenyl)furan (48a). Following the *General procedure A* compound **48a** was prepared from **45** (102 mg, 0.20 mmol), $Pd(PPh_3)_4$ (05 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and *4-tert*-butylphenylboronic acid (78 mg, 0.44 mmol) as a highly viscous colourless oil (115 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 18H, $6CH_3$), 8.03 (d, 4H, J = 8.4 Hz, ArH), 7.23 (d, 4H, J = 8.4 Hz, ArH), 7.32-7.39 (m, 4H, ArH), 7.54 (brs, 2H, ArH), 7.62-7.66 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -63.1. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 31.2 ($6CH_3$), 34.6 (C), 122.5 (q, $J_{F,C}$ = 3.9 Hz, CH), 123.7 (q, $J_{F,C}$ = 3.9 Hz, CH), 124.2 (q, $J_{F,C}$ = 278 Hz, CF_3), 125.5 (CH), 126.6 (C), 128.7, 128.8, 129.7 (CH), 129.9 (C), 130.7 (d, $J_{F,C}$ = 32.7 Hz, C-CF_3), 131.4, 146.9, 150.7. IR (KBr): ν = 3023, 3060, 2953, 2911 (w), 1782, 1760, 1556 (s), 1510, 1462 (m), 1405, 1314, 1260, 1203 (w), 1162, 1114, 1080, 1060, 999, 948, 871 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 620 (M^+, 71), 605 (26), 565 (11), 564 (33), 492 (11), 491 (37), 479 (14), 173 (100), 161 (84), 145 (20), 57 (24), 43 (12). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{38}H_{34}OF_6$ [M^+]: 620.25084, found: 620.250900.

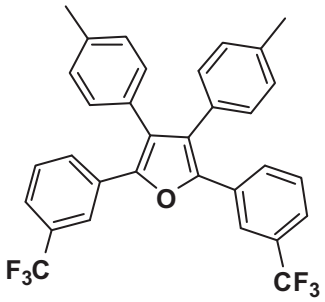


3,4-Diphenyl-2,5-bis(3-(trifluoromethyl)phenyl)furan (48b). Following the *General procedure A* compound **48b** was prepared from **45** (102 mg, 0.20 mmol), $Pd(PPh_3)_4$ (05 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and phenylboronic acid (54 mg, 0.44 mmol) as a highly viscous colourless oil (87 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06-7.09 (m, 4H, ArH), 7.18-7.22 (m, 6H, ArH), 7.29-7.46 (m, 4H, ArH), 7.57 (d, 2H, J = 7.7 Hz, ArH), 7.69 (brs, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -63.0. ^{13}C NMR (65.5 MHz, $CDCl_3$): δ = 122.4 (q, $J_{F,C}$ = 3.9 Hz, CH), 123.9(q, $J_{F,C}$ = 272.7 Hz, CF_3), 124.0 (q, $J_{F,C}$ = 3.9 Hz, CH), 125.2 (C), 126.0, 127.7, 128.7, 128.9, 130.1 (CH), 130.9 (d, $J_{F,C}$ = 32.3 Hz, C-CF_3), 131.3, 132.1, 146.9 (C). IR (KBr): ν = 3062, 2926 (w), 1693, 1610, 1448 (m), 1330 (s), 1166 (m), 1122 (m), 1070, 801, 750 (m), 692 (s), 652, 579 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) =

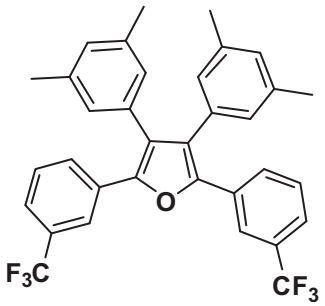


508 (M^+8), 368 (10), 367 (39), 257 (13), 236 (12), 173 (87), 165 (10), 145 (27), 137 (14), 135 (13), 125 (14), 123 (15), 121 (10), 112 (12), 111 (25), 110 (13), 109 (16), 105 (100), 99 (11), 98 (17), 97 (42), 96 (23), 95 (27), 93 (10), 91 (10), 85 (28), 84 (20), 83 (46), 82 (25), 81 (44), 78 (13), 77 (30), 73 (13), 71 (44), 70 (24), 69 (96), 68 (17), 67 (22), 63 (11), 57 (71), 56 (21), 55 (51), 43 (50), 41 (38). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{30}H_{18}OF_6$ [M^+]: 508.12564, found: 508.125078.

3,4-Bis(4-tolyl)-2,5-bis(3-(trifluoromethyl)phenyl)furan (48c). Following the *General procedure A* compound **48c** was prepared from **45** (102 mg, 0.20 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and *p*-tolylboronic acid (60 mg, 0.44 mmol) as a highly viscous colourless oil (100 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 6H, CH_3), 6.94-7.02 (m, 8H, ArH), 7.25-7.30 (m, 2H, ArH), 7.38 (d, *J* = 7.95, 2H, ArH), 7.55 (d, *J* = 7.95, 2H, ArH), 7.71 (brs, 2H, ArH). ^{19}F NMR (300 MHz, $CDCl_3$): δ = -63.01. ^{13}C NMR (62.9 MHz, $CDCl_3$): □ = 21.3 (CH_3), 122.4 (q, $J_{F,C}$ = 4.1 Hz, CH), 123.8 (q, $J_{F,C}$ = 3.8 Hz, CH), 123.9 (q, $J_{F,C}$ = 272.6 Hz, CF_3), 126.6 (C), 128.8 (CH), 129.1 (C), 129.4, 129.9 (CH), 130.9 (q, $J_{F,C}$ = 32.4 Hz, C-CF_3), 131.4, 137.4, 146.8 (C). IR (KBr): ν = 3028, 2922, 2867 (w), 1746, 1691, 1609, 1511, 1327, 1222, 1164 (w), 1123 (s), 1071, 961, 801 (m), 693 (s), 655, 572 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 536 [M^+], 100), 363 (18). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{32}H_{22}OF_6$ [M^+]: 536.15694, found: 536.157343.

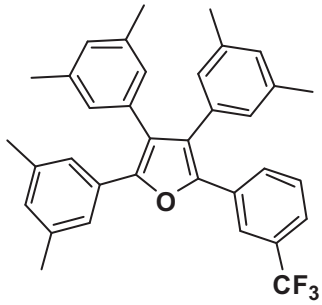


3,4-Bis(3,5-dimethylphenyl)-2,5-bis(3-(trifluoromethyl)phenyl)furan (48d). Following the *General procedure A* compound **48d** was prepared from **45** (102 mg, 0.20 mmol), $Pd(PPh_3)_4$ (06 mg, 2 mol%), toluene/dioxane (4:1, 2.5 mL), 2M K_2CO_3 (0.5 mL) and 3,5-dimethylphenylboronic acid (66 mg, 0.44 mmol) as a highly viscous colourless oil (99 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 12H, 4CH_3), 6.71 (s, 4H, ArH), 6.82 (s, 2H, ArH), 7.27-7.39 (m, 4H, A rH), 7.56-7.61 (m, 2H, ArH), 7.72 (brs, 2H, ArH). ^{19}F NMR (300 MHz, $CDCl_3$): δ = -63.05. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3 (CH_3), 122.4 (q, $J_{F,C}$ = 4.1 Hz, CH), 123.7 (q, $J_{F,C}$ = 4.1 Hz, CH), 124.0 (q, $J_{F,C}$ = 270.3 Hz, CF_3), 126.9 (C), 127.8, 128.6, 128.8, 129.3 (CH), 130.7 (q,



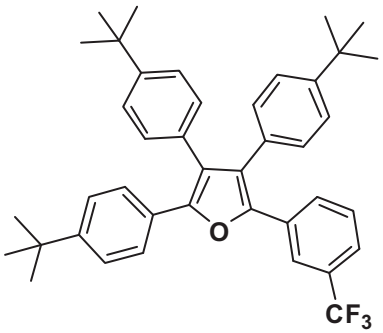
$J_{F,C}$ = 31.2 Hz, C-CF_3), 131.5, 131.9, 137.9, 146.6 (C). IR (KBr): ν = 3076, 3066, 2919, 2862 (w), 1789, 1769, 1596 (s), 1514, 1471 (m), 1418, 1401, 1315, 1260, 1204 (w), 1164, 1111, 1089, 1065, 1601, 1485, 1446, 1353, 1322, 1164 (m), 1113, 1072 (s), 899, 864, 797 (m), 688 (s), 694 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 564 (M^+, 100), 391 (19). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{34}H_{26}OF_6$ [M^+]: 564.18824, found: 564.188743.

2,3,4-Tris(3,5-dimethylphenyl)-5-(3-(trifluoromethyl)phenyl)furan (49a). Following the



General procedure compound **49a** was prepared from **47b** (112 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 3 mol%), dioxane 5 mL, 2M K_2CO_3 (0.5 mL) and 3,5-dimethylphenylboronic acid (123 mg, 0.82 mmol) as a highly viscous colourless oil (113 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 6H, $2CH_3$), 2.13 (s, 6H, $2CH_3$), 2.17 (s, 6H, $2CH_3$), 6.72 (brs, 4H, ArH), 6.72 (s, 1H, ArH), 6.72 (brs, 2H, ArH), 7.08 (s, 2H, ArH), 7.24-7.36 (m, 2H, ArH), 7.57 (d, 1H, *J* = 8.0 Hz, ArH), 7.72 (brs, 1H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -63.0. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.1, 21.2, 21.3 ($2CH_3$), 122.2 (q, $J_{F,C}$ = 3.8 Hz, CH), 123.2 (q, $J_{F,C}$ = 4.0 Hz, CH), 123.7 (CH), 124.3 (q, $J_{F,C}$ = 276 Hz, CF_3), 125.3, 126.8 (C), 127.9, 128.1, 128.5, 128.6, 128.7, 129.0, 129.2 (CH), 130.6 (C), 130.7 (d, $J_{F,C}$ = 32.9 Hz, C-CF_3), 131.9, 132.4, 132.6, 137.4, 137.7, 137.8, 145.7, 148.4 (C). IR (KBr): ν = 3055, 2917 (w), 1678, 1600, 1428 (m), 1320 (s), 1101 (m), 1111 (m), 1060, 794, 740 (m), 682 (s), 651, 576 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 524 (M^+), 10), 423 (18), 383 (15), 173 (13), 133 (100), 105 (20). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{35}H_{31}F_3$ [M^+]: 524.23215, found: 524.231988.

2,3,4-Tris(4-*tert*-butylphenyl)-5-(3-(trifluoromethyl)phenyl)furan (49b). Following the



General procedure A compound **49b** was prepared from **47b** (112 mg, 0.25 mmol), $Pd(PPh_3)_4$ (09 mg, 2 mol%), dioxane .5 mL), 2M K_2CO_3 (0.5 mL) and 4-*tert*-butylphenylboronic acid (146 mg, 0.82 mmol) as a highly viscous colourless oil (141 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 9H, $3CH_3$), 1.24 (s, 9H, $3CH_3$), 1.24 (s, 9H, $3CH_3$), 6.98-7.05 (m, 4H, ArH), 7.17-7.25 (m, 8H, ArH), 7.39-7.43 (m, 2H, ArH), 7.56-7.61 (m, 2H, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -63.1. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 31.2, 31.3, 31.3

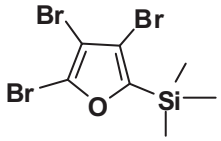
(CH_3), 34.5, 34.6 (C), 122.3 (q, $J_{F,C}$ = 4.2 Hz, CH), 123.2 (q, $J_{F,C}$ = 3.9 Hz, CH), 124.2 (q, $J_{F,C}$ = 277.8 Hz, CF_3), 124.6 (C), 125.1, 125.3, 125.4, 125.5 (CH), 126.6, 128.0 (C),128.4 (CH), 128.9, 129.6 (C), 129.8, 129.9 (CH), 130.3 (q, $J_{F,C}$ = 31.3 Hz, C-CF_3), 131.8, 145.8, 148.4, 149.9, 150.4, 150.5 (C). IR (KBr): ν = 3064, 2922 (w), 1692, 1603, 1437 (m), 1320 (s), 1155 (m), 1103 (m), 1055, 740 (m), 682 (s), 642, 569 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 608 (M^+, 50), 593 (14), 251 (18), 173 (11), 163 (16), 162 (15), 161 (100), 57 (14). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{41}H_{43}OF_3$ [M^+]: 608.32605, found: 608.326028.

11.9.5 Synthesis of 3,4,5-Tribromofurans (50a-b)

To a THF solution of tetrabromofuran (96 mg, 0.25 mmol) was added of n-butyllithium (0.28 mmol in heptane) at -78°C. After stirring for 10 min at -78 °C, the electrophile (0.28 mmol) was added. After warming of the mixture to 20 °C within 6 h, a saturated aqueous solution of NH_4Cl (30 mL) was added. The organic and the aqueous layer were separated and the latter was extracted with ethyl acetate (2x10 mL). The combined organic layers were dried (Na_2SO_4), filtered and the solvent of the filtrate was removed under vacuum. The residue was purified by chromatography (fine silica gel, n-heptane).

11.9.6 Metal-halide exchange reactions. Synthesis of (50a-b)

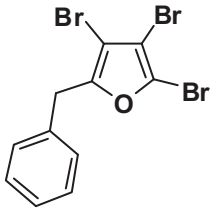
Trimethyl(3,4,5-tribromofuran-2-yl)silane (50a) Following the *General procedure A*



compound **50a** was prepared from **45** (96 mg, 0.25 mmol), n-BuLi (0.14 mL, 0.28 mmol), Me_3SiCl (0.03 mL, 0.25 mmol), TMEDA (0.04 mL, 0.28 mmol) in 5 mL THF. as a highly viscous colourless oil (81 mg, 87%). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.00 (s, 9H, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 0.00 (CH_3), 107.6, 116.5, 128.5, 162.2 (C). IR (KBr): ν = 2813, 2643, 2511 (m), 1694, 1582 (s), 1414 (m), 1263 (s), 1049, 895, 853, 760, 712, 689, 640 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 381 (M^+, [$^{81}Br_3$], 2), 379 (M^+, [$^{81}Br_2{}^{79}Br$], 12), 377 (M^+, [$^{81}Br_2{}^{79}Br_2$], 100), 375 (M^+, [$^{79}Br_3$], 99), 300 (15), 73 (13). HRMS (EI, 70 eV): *m/z* = calcd. for $C_7H_9Br_3OSi$ (M^+, [$^{81}Br_3$]): 381.78286, found: 414.782753; calcd. for (M^+, [$^{79}Br^{81}Br_2$]): 379.88210, found 379.882457;

calcd. for (M^+, [$^{79}Br_2{}^{81}Br$]): 377.77609, found 377.776132; calcd. for (M^+, [$^{81}Br_3$]): 375.87519, found 375.875023.

2-Benzyl-3,4,5-tribromofuran (50b)



Following the *General procedure A* compound **50b** was prepared from **45** (96 mg, 0.25 mmol), n-BuLi (0.14 mL, 0.28 mmol), benzylchloride (0.02 mL, 0.25 mmol), TMEDA (0.04 mL, 0.28 mmol) in 5 mL THF. as a highly viscous colourless oil (91 mg, 93%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.91 (s, 2H, CH_2), 7.21-7.26 (m, 5H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 33.3 (CH_2), 102.0, 105.6, 121.4 (C), 127.0, 128.4, 128.7 (CH), 136.0, 153.8 (C). IR (KBr): ν = 2912, 2815 (m), 1684, 1572 (s), 1404 (m), 1253 (s), 1040, 890, 849, 751, 689, 643 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 397 (M^+, [$^{81}Br_3$], 13), 395 (M^+, [$^{81}Br_2{}^{79}Br$], 100), 393 (M^+, [$^{81}Br^{79}Br_2$], 99), 391 (M^+, [$^{79}Br_3$], 34), 317 (36), 315 (68), 313 (34), 235 (43), 233 (41), 208 (54), 206 (53), 127 (51), 126 (42), 103 (10), 91 (24), 77 (14), 51 (10). HRMS (EI, 70 eV): *m/z* = calcd. for $C_{11}H_7Br_3O$ (M^+, [$^{81}Br_3$]): 381.80415, found: 391.803659; calcd. for (M^+, [$^{79}Br_3$]): 393.80211, found 393.801704; calcd. for (M^+, [$^{79}Br_2{}^{81}Br$]): 395.80006, found 395.799563; calcd. for (M^+, [$^{81}Br_3$]): 397.79801, found 397.797494.

Appendix

12. Crystallographic Data

12.1 Crystal data and structure refinement for Ethyl 3-(bis(4 fluorophenyl)methyl)-6-hydroxy-2,4,5-trimethylbenzoate (8d)

Table 29. Crystal data and structure refinement for **(8d)**

Identification code	**rk168**
Empirical formula	$C_{25}H_{24}F_2O_3$
Formula weight	410.44
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic,
Space group (H.-M.)	$P\bar{1}$
Space group (Hall)	-P 1
Unit cell dimensions	a = 10.605 (6) Å α = 68.615 (14)°
	b = 10.646 (8) Å β = 62.324 (10)°
	c = 11.003 (6) Å γ = 89.512 (16)°
Volume	1004.7 (10) $Å^3$
Z	2
Density (calculated)	1.357Mg m^{-3}
Absorption coefficient	0.10 mm^{-1}
F(000)	1808
Crystal size	0.81 × 0.71 × 0.28 mm
Θ range for data collection	5.5 to 59.9°

Index ranges	$-14 \leq h \leq 14$, $-14 \leq k \leq 14$, $-14 \leq l \leq 15$
Reflections collected	5264
Independent reflections	4638 [R(int) = 0.042]
Absorption correction	multi-scan
Max. and min. transmission	0.924 and 0.973
Refinement method	Full-matrix
restraints / parameters	0 /260
Goodness-of-fit on F2	1.02
Final R indices [$I>2\sigma(I)$]	R1 = 0.0524, wR2 = 0.1241
R indices (all data)	R1 = 0.1014, wR2 = 0.1376

12.2 Crystal data and structure refinement for Benzyl 3-(1-(4-bromophenyl)ethyl)-6-hydroxy-2,4-dimethylbenzoate (8m)

Table 30. Crystal data and structure refinement for **(8m)**

Identification code	**rk159**
Empirical formula	$C_{24}H_{23}BrO_3$
Formula weight	439.33
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* = 20.984 (17) Å *b* = 10.76 (1) Å β = 107.158 (15)° *c* = 18.696 (16) Å
Volume	4034 (6) $Å^3$
Z	8
Density (calculated)	1.447Mg m^{-3}
Absorption coefficient	2.06 mm^{-1}
F(000)	1808
Crystal size	0.81 × 0.54 × 0.36 mm
Θ range for data collection	6.9 to 67.5°
Index ranges	-29≤h≤29, -15≤k≤15, -26≤l≤24
Reflections collected	5860
Independent reflections	5860 [R(int) = 0.045]

Absorption correction	multi-scan
Max. and min. transmission	0.904 and 0.989
Refinement method	Full-matrix
restraints / parameters	0 /260
Goodness-of-fit on F2	1.03
Final R indices [I>2σ(I)]	R1 = 0.0514, wR2 = 0.1231
R indices (all data)	R1 = 0.1004, wR2 = 0.1366

12.3 **Crystal data and** structure refinement for **2-(Phenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one** (**11i**).

Table 31. Crystal data and structure refinement for **(11i)**

Identification code	rk137
Empirical formula	$C_{17}H_{14}O_2$
Formula weight	250.28
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/c$
Space group (Hall)	-P 2ybc
Unit cell dimensions	a = 12.1517 (5) Å b = 5.8375 (3) Å β = 107.397 (2)° c = 19.2787 (9) Å
Volume	1304.99 (11) $Å^3$
Z	4
Density (calculated)	1.274Mg/m3
Absorption coefficient	0.08mm-1
F(000)	528
Crystal size	0.37 × 0.19 × 0.16mm
Θ range for data collection	7.3 to 65.2°
Index ranges	-16≤h≤17,-5≤k≤8,-27≤l≤25
Reflections collected	15043
Independent reflections	3791 [R(int) = 0.041]

Absorption correction	multi-scan
Refinement method	Full-matrix
Data/restraints / parameters	188
Goodness-of-fit on F2	1.060
Final R indices [I>2σ(I)]	R1 = 0.0469, wR2 = 0.130
R indices (all data)	R1 0.047, wR2 = 0.130
Largest diff. peak and hole	0.169 and -0.205 e.Å-3

12.4 Crystal data and structure refinement for 2-(3-bromophenyl)-6-phenyl-2H-pyran-4(3H)-one (11m)

Table 32. Crystal data and structure refinement for **(11m)**

Identification code	**rk138**
Empirical formula	$C_{17}H_{13}BrO_2$
Formula weight	329.18
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/n$
Space group (Hall)	-P 2yn
Unit cell dimensions	a = 8.833 (15) Å
	b = 9.953 (16) Å β = 105.87 (2)°
	c = 15.95 (3) Å
Volume	1349 (4) $Å^3$
Z	4
Density (calculated)	1.621 Mg m^{-3}
Absorption coefficient	0.147 mm-1
F(000)	664
Crystal size	0.85 × 0.48 × 0.18 mm
Θ range for data collection	6.3 to 59.4°
Index ranges	-12≤h≤12, -10≤k≤14, -22≤l≤20
Reflections collected	12768
Independent reflections	3860 [R(int) = 0.041]

Absorption correction	multi-scan
Max. and min. transmission	0.978 and 0.929
Refinement method	Full-matrix
restraints / parameters	0 /198
Goodness-of-fit on F2	1.03
Final R indices [I>2σ(I)]	R1 = 0.0524, wR2 = 0.1241
R indices (all data)	R1 = 0.1014, wR2 = 0.1376

12.5 Crystal data and structure refinement 2-(2-chloro-4-(trifluoromethyl)phenyl)-6-methyl-2H-pyran-4(3H)-one (16c)

Table 33. Crystal data and structure refinement for **(16c)**

Identification code	**rk317**
Empirical formula	$C_{13}H_{10}ClF_3O_2$
Formula weight	290.66
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/n$
Space group (Hall)	-P 2yn
Unit cell dimensions	a = 12.5015 (3) Å b = 8.5069 (2) Å β = 104.911 (1)° c = 12.5928 (3) Å
Volume	1294.14 (5) $Å^3$
Z	4
Density (calculated)	1.492 Mg m^{-3}
Absorption coefficient	0.33 mm^{-1}
F(000)	592
Crystal size	0.88 × 0.34 × 0.21 mm
Θ range for data collection	5.8 to 59.9°
Index ranges	-17≤h≤17, -11≤k≤10, -15≤l≤17
Reflections collected	14181
Independent reflections	3059 [R(int) = 0.019]

Absorption correction	multi-scan
Max. and min. transmission	0.763 and 0.935
Refinement method	Full-matrix
restraints / parameters	0 /201
Goodness-of-fit on F2	1.08
Final R indices [I>2σ(I)]	R1 = 0.0514, wR2 = 0.1211
R indices (all data)	R1 = 0.1034, wR2 = 0.1346

12.6 Crystal data and structure refinement for 2-benzoyl-5-((4-methoxyphenyl) ethynyl)phenyl trifluoromethanesulfonate (25c)

Table 34. Crystal data and structure refinement for **(25c)**

Identification code	**rk245**
Empirical formula	$C_{23}H_{15}F_3O_5S$
Formula weight	460.41
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group (H.-M.)	$P\bar{1}$
Space group (Hall)	-P 1
Unit cell dimensions	a = 10.331 (7) Å α = 87.53 (3)°
	b = 12.233 (9) Å β = 76.243 (19)°
	c = 17.833 (13) Å γ = 73.62 (2)°
Volume	2100 (3) $Å^3$
Z	4
Density (calculated)	1.457Mg m^{-3}
Absorption coefficient	0.21 mm^{-1}
F(000)	944
Crystal size	0.48 × 0.23 × 0.05 mm
Θ range for data collection	7.7 to 57.8°
Index ranges	-12≤h≤13, -12≤k≤15, -23≤l≤23
Reflections collected	35297
Independent reflections	9431 [R(int) = 0.045]

Absorption correction	multi-scan
Max. and min. transmission	0.904 and 0.989
Refinement method	Full-matrix
restraints / parameters	0 /579
Goodness-of-fit on F2	1.02
Final R indices [I>2σ(I)]	R1 = 0.0523, wR2 = 0.1245
R indices (all data)	R1 = 0.1024, wR2 = 0.1366

12.7 Crystal data and structure refinement 2,4'-sulfonylbis((p-tolylethynyl)benzene) (31b)

Table 35. Crystal data and structure refinement for **(31b)**

Identification code	**rk197**
Empirical formula	$C_{30}H_{22}O_2S$
Formula weight	446.54
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group (H.-M.)	*P*i
Space group (Hall)	-P 1
Unit cell dimensions	*a* = 13.60 (2) Å α = 116.478 (19)°
	b = 13.699 (11) Å β = 99.78 (4)°
	c = 14.695 (12) Å γ = 98.96 (3)°
Volume	2331 (4) $Å^3$
Z	4
Density (calculated)	1.272Mg m^{-3}
Absorption coefficient	0.16 mm^{-1}
F(000)	936
Crystal size	0.99 × 0.23 × 0.15 mm
Θ range for data collection	6.8 to 59.9°
Index ranges	-19≤h≤19, -19≤k≤19, -20≤l≤20
Reflections collected	46473
Independent reflections	46473 [R(int) = 0.042]
Absorption correction	multi-scan

Max. and min. transmission	0.855 and 0.976
Refinement method	Full-matrix
restraints / parameters	0 /599
Goodness-of-fit on F2	1.01
Final R indices [I>2σ(I)]	R1 = 0.0514, wR2 = 0.1231
R indices (all data)	R1 = 0.1004, wR2 = 0.1276

12.8 Crystal data and structure 2-Phenyl-3-(4-(trifluoromethyl)phenyl)-1H-inden-1-one (37b)

Table 37. Crystal data and structure refinement for **(37b)**

Identification code	**rk443**
Empirical formula	$C_{22}H_{13}F_3O$
Formula weight	350.32
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/n$
Space group (Hall)	-P 2ybc
Unit cell dimensions	a = 11.8365 (7) Å α = 90.00
	b = 9.2961 (5) Å β = 109.29 (3)°
	c = 16.2375 (9) Å γ = 90.00
Volume	1386 (4) $Å^3$
Z	4
Density (calculated)	1.380 Mg m^{-3}
Absorption coefficient	0.106 mm^{-1}
F(000)	720
Crystal size	0.97 × 0.53 × 0.13 mm
Θ range for data collection	5.1 to 62.3°
Index ranges	-16≤h≤12, -12≤k≤12, -22≤l≤22
Reflections collected	4467
Independent reflections	3407 [R(int) = 0.041]
Absorption correction	multi-scan
Max. and min. transmission	0.978 and 0.929

Refinement method	Full-matrix
restraints / parameters	0 /263
Goodness-of-fit on F2	1.058
Final R indices [I>2σ(I)]	R1 = 0.0667, wR2 = 0.1401
R indices (all data)	R1 = 0.486, wR2 = 0.1301

12.9 Crystal data and structure refinement for 1-benzyl-3,4-dibromo-5-(4-methoxyphenyl)-1H-pyrazole (42h)

Table 38. Crystal data and structure refinement for **(42h)**

Identification code	**rk467b**
Empirical formula	$C_{17}H_{14}Br_2N_2O$
Formula weight	422.12
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group (H.-M.)	*P*bca
Space group (Hall)	-P 2ac, 2ab
Unit cell dimensions	*a* = 15.2948 (8) Å α = 90.00
	b = 7.9054 (4) Å β = 101.3 (3)°
	c = 26.5505 (14) Å γ = 90.00
Volume	1455 (4) $Å^3$
Z	4
Density (calculated)	1.747 Mg m^{-3}
Absorption coefficient	0.072 mm^{-1}
F(000)	1664
Crystal size	0.36 × 0.27 × 0.20 mm
Θ range for data collection	5.32 to 59.45°
Index ranges	-21≤h≤21, -11≤k≤7, -36≤l≤23
Reflections collected	18172
Independent reflections	4569 [R(int) = 0.031]

Absorption correction	multi-scan
Max. and min. transmission	0.988 and 0.989
Refinement method	Full-matrix
restraints / parameters	0 /200
Goodness-of-fit on F2	1.054
Final R indices [I>2σ(I)]	R1 = 0.0588, wR2 = 0.664
R indices (all data)	R1 = 0.300, wR2 = 0.622

12.10 Crystal data and structure refinement for 2,3,4,5-tetrakis(4-(trifluoromethyl)phenyl)furan (49c)

Table 36. Crystal data and structure refinement for **(49c)**

Identification code	**rk321**
Empirical formula	$C_{32}H_{16}F_{12}O$
Formula weight	644.45
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/n$
Space group (Hall)	-P 2yn
Unit cell dimensions	a = 10.4995 (3) Å
	b = 10.2082 (3) Å β = 99.821 (2)°
	c = 26.4963 (8) Å
Volume	2798.28 (14) $Å^3$
Z	4
Density (calculated)	1.530 Mg m^{-3}
Absorption coefficient	0.147 mm-1
F(000)	1296
Crystal size	0.51 × 0.23 × 0.15 mm
Θ range for data collection	5.6 to 46.1°
Index ranges	-13≤h≤13, -13≤k≤12, -34≤l≤34
Reflections collected	26676
Independent reflections	6752 [R(int) = 0.039]

Absorption correction	multi-scan
Max. and min. transmission	0.978 and 0.929
Refinement method	Full-matrix
restraints / parameters	0/490
Goodness-of-fit on F2	1.052
Final R indices [I>2σ(I)]	R1 = 0.0524, wR2 = 0.1241
R indices (all data)	R1 = 0.1014, wR2 = 0.1376

10 References

[1] (a) Bai, L.; Masukawa, N.; Yamaki, M.; Takagi, S. *Phytochemistry.* **1998**, *47*, 1637; (b) Jin, C.; Michetich, R. G.; Daneshtalab, M. *Phytochemistry.* **1999**, *50*, 505.

[2] (a) Bindal, R. D.; Golab, J. T.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1990**, *112*, 7861. (b) Jendralla, H.; Granzer, E.; Kerekjarto, B. v.; Krause, R.; Schacht, U. *J. Med. Chem.* **1991**, *34*, 2962. (c) Costantino, L.; Ferrari, A. M.; Gamberini, M. C.; Rastelli, G. *Bioorg. Med. Chem.* **2002**, *10*, 3923. (d) Al-Qawasmeh, R. A.; Lee, Y.; Cao, M.-Y.; Gu, X.; Vassilakos, A.; Wright, J. A.; Young, A. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 347. (e) Mibu, N.; Yokomizo, K.; Uyeda, M.; Sumoto, K. *Chem. Pharm. Bull.* **2003**, *51*, 1325. (f) Schultz, T. W.; Sinks, G. D.; Cronin, M. T. D. *Environ. Toxicol.* **2002**, *17*, 14. (g) Wang, P.; Kozlowski, J.; Cushman, M. *J. Org. Chem.* **1992**, *57*, 3861.(h) Long, Y.-Q.; Jiang, X.-H.; Dayam, R.; Sanchez, T.; Shoemaker, R.; Sei, S.; Neamati, N. *J. Med. Chem.* **2004**, *47*, 2561. (i) Matulenko, M. A.; Surber, B.; Fan, L.; Kolasa, T.; Nakane, M.; Terranova, M. A.; Uchic, M. E.; Miller, L. N.; Chang, R.; Donnelly-Roberts, D. L.; Namovic, M. T. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5095.

[3] (a) Jovel, I.; Mertins, K.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem. Int. Ed.* **2005**, *44,* 3913.(b) Mertins, K.; Jovel, I.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 238.

[4] Christoffers, J. *J. Chem. Soc., Perkin Trans.* **1997**, *1*, 3141.

[5] Kischel, J.; Mertins, K.; Michalik, D; Zapf, A.; Beller, M. *Adv. Synth. Catal.* **2007**, *349*, 865.

[6] (a) Bisaro, F.; Prestat, G.; Vitale, M.; Poli, G. *Synlett.* **2002**, 1823. (b) Gullickson, G. C.; Lewis, D. E. *Aust. J. Chem.* **2003**, *56*, 385. (c) Yasuda, M.; Somyo, T.; Baba, A. *Angew. Chem. Int. Ed.* **2006**, *45*, 793; (d) Rueping, M.; Nachtsheim, B. J.; Ieawsuwan, W. *Adv. Synth. Cat.* **2006**, *348*, 1033.

[7] Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534.

[8] (a) Review of [3+3] cyclizations: Feist, H.; Langer, P. *Synthesis.* **2007**, 327. (b) Review of 1,3-bis(trimethylsilyloxy)-1,3-dienes: Langer, P. *Synthesis.* **2002**, 441.

[9] Ahmad, R.; Riahi, A.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 1490.

[10] (a) Chan, T.; Brownbridge, P. *J. Chem. Soc.* **1979**, 578. (b) Molander, G. A.; Cameron, K. O. *J. Am. Chem. Soc.* **1993**, 115.

[11] March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, **1992**; (b) Scolastic, C.; Nocotra, F. *Current Trends in Organic Synthesis*; Plenum: New York, **1999**.

[12] (a) Yasuda, M.; Somyo, T.; Baba, A. *Angew. Chem., Int. Ed*. 2006, *45*, 793. (b) Sanz, R.; Miguel, D.; Martinez, A.; Alvarez-Gutierrez, J. M.; Rodriguez, F. *Org. Lett*. **2007**, *10*, 2027. (c) Huang, W.; Wang, J.; Shena, Q.; Zhou, X. *Tetrahedron Lett*. **2007**, 29, 3969. (d) Jana, U.; Biswas, S.; Maiti, S. *Tetrahedron Lett*. **2007**, *48*, 4065. (e) Wang, G. W.; Shen, Y. B.; Wu, X. L. Eur. *J. Org. Chem*. **2008**, 4999.

[13] Gonzglez, A.; Marquet, J.; Moreno-Manas, M. *Tetrahedron Lett*. **1988**, 29, 1469.

[14] (a) Tsuji, J. In Palladium Reagents and Catalysts*: Innovations in Organic Synthesis*, 2nd ed.; Wiley: Chichester, **2000**; p 109; (b) Antonioletti, R.; Bovicelli, P.; Malancona, S. *Tetrahedron,* **2002**, *58*, 589. (c) Arumugam, S.; McLeod, D.; Verkade, J. G. *J. Org. Chem*. **1998**, *63*, 3677.

[15] Danishefsky, S. J.; Pearson, W. H.; Segmuller, B. E. *J. Am. Chem. Soc.* **1985**, *107*, 1280. (b) Danishefsky, S. J.; DeNinno, M. P. *Angew. Chem., Int. Ed.*. **1987**, *26*, 15. (c) Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem., Int. Ed.* **1996**, *35*, 1380. (d) Danishefsky, S. J.; Selnick, H. G.; Zelle, R. E.; DeNinno, M. P. *J. Am. Chem. Soc.* **1988**, *110*, 4368.

[16] (a) Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3558. (b) Jørgensen, K. A. *Eur. J. Org. Chem.* **2004**, 2093.

[17] (a) Barluenga, J.; Aznar, F.; Fernández, M. *Tetrahedron Lett.* **1995**, *36*, 6551. (b) Evans, P. A.; Nelson, J. D. *J. Org. Chem.* **1996**, *61*, 7600. (c) Evans, P. A.; Nelson, J. D.; Manangan, T. *Synlett.* **1997**, 968. (d) Huang, Y.; Rawal, V. H. *J. Am. Chem. Soc.* **2002**, *124*, 9662.

[18] Reviews: (a) Casiraghi, G.; Zanardi, F.; Appendino, G.; Rassu, G. *Chem. Rev.* **2000**, *100*, 1929. (b) Soriente, A.; De Rosa, M.; Villano, R.; Scettri, A. *Curr. Org. Chem.* **2004**, *8*, 993. (c) Denmark, S. E.; Heemstra, J. R., Jr.; Beutner, G. L. *Angew. Chem. Int. Ed.* **2005**, *44*, 4682.

[19] Denmark, S. E.; Heemstra, J. R., Jr. *J. Org. Chem.* **2007**, *72*, 5668.

[20] Reiter, M.; Ropp, S.; Gouverneur, V. *Org. Lett.* **2004**, *6*, 91.

[21] Winkler, J. D.; Oh, K. *Org. Lett.* **2005**, *7*, 2421.

[22] Gao, B.; Yua, Z.; Fua, Z.; Fenga, X. *Tetrahedron Lett.* **2006**, *47*, 1537.

[23] Wang, H.; Shuhler, B. J.; Xiang, M. *J. Org. Chem.* **2007**, *72*, 4280.

[24] For a review of cyclization reactions of dianions, see: Langer, P.; Freiberg, W. *Chem. Rev.* **2004**, *104*, 4125.

[25] Light, R. J.; Hauser, C. R. *J. Org. Chem.* **1961**, *26*, 1716.

[26] Ansell, J. M.; Hassner, A.; Burkholder, W. E. *Tetrahedron Lett.* **1979**, 2497.

[27] Peterson, J. R.; Winter, T. J.; Miller, C. P. *Synth. Commun.* **1988**, *18*, 949.

[28] Ahmad, R.; Khera, R. A.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 3020.

[29] (a) Ryckmanns, T.; Balancon, L.; Berton, O.; Genicot, C.; Lamberty, Y.; Lallemand, B.; Passau, P.; Pirlot, N.; Quéré, L.; Talaga, P. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 261. (b) Malamas, M. S.; Sredy, J.; Moxham, C.; Katz, A.; Xu, W.; McDevitt, R.; Adebayo, F. O.; Sawicki, D. R.; Seestaller, L.; Sullivan, D.; Taylor, J. R. *J. Med. Chem*. **2000**, *43*, 1293. (c) Ciha, A. J.; Ruminski, P. G. *J. Agric. Food Chem.* **1991**, *39*, 2072. (d) Albrecht, H. A.; Beskid, G.; Georgopapadakou, N. H.; Keith, D. D.; Konzelmann, F. M.; Pruess, D. L.; Rossman, P. L.; Wei, C. C.; Christenson, J. G. *J. Med. Chem.* **1991**, *34*, 2857.

[30] (a) Heidelberger, C.; Chaudhuri, K. N.; Danneberg, P. ; Mooren, D.; Griesbach, L.; Duschinsky R. and Schnitzer, J. R. *Nature,* **1957**, *179*, 663. (b) Wong, T. D.; Bymaster, P. F. and Engleman, A. E. *Life Sci*. **1995**, *57*, 411. (c) Roman, L. D.; Walline, C. C.; Rodriguez, J. G.; Barker, L. E. *Eur. J. Pharmacol*. **2003**, 479, 53.

[31] (a) Dinger, M. B.; Henderson, W. *J. Organomet. Chem.* **1998**, *560*, 233. (b) Liedtke, J.; Loss, S.; Widauer, C.; Grützmacher, H. *Tetrahedron.* **2000**, *56*, 143. (c) Clarke, D.; Ali, M. A.; Clifford, A. A.; Parratt, A.; Rose, P.; Schwinn, D.; Bannwarth, W.; Rayner, C. M. *Curr. Top. Med. Chem.* **2004**, *7*, 729.

[32] (a) Wittkopp, A.; Schreiner, P. R. *The chemistry of diens and polyenes,* Vol. 2; John Wiley & Sons Ltd, **2000**. (b) Schreiner, P. R. *Chem. Soc. Rev.* **2003**, *32*, 289. (c) Wittkopp, A.; Schreiner, P. R. *Eur. J. Chem.* **2003**, *9*, 407. (d) Kotke, M.; Schreiner, P. R. *Synthesis* **2007**, *5*, 779.

[33] (a) Lin, Y.-L.; Wu, Y.-M.; Kuo, Y.-H. *Phytochemistry*. **1997**, *45*, 1057; (b) Huang, P.-L.; Won, S.-J.; Day, S.-H.; Lin, C.-N. *Helv. Chim. Acta*. **1999**, *82*, 1716; (c) Lin, Y.-L.; Lin, T.-C.; Kuo, Y.-H. J. *Nat. Prod*. **1997**, *60*, 368. (d) Das, B.; Mahender, G.; Rao, Y. K.; Prabhakar, A.; Jaga-deesh, B. *Chem. Pharm. Bull*. **2005**, *53*, 135.

[34] (a) De Souza, A. O.; Santos, R. R.; Melo, P. S.; Alderete, J. B.; Conti, R. De; Haun, M.; Sato, D. N.; Duran, N. *Pharmazie*. **2001**, *56*, 871.

[35] (a) Batt, D. G.; Goodman, R.; Jones, D. G.; Kerr, J. S.; Mantegna, L. R. *J. Med. Chem.* **1993**, *36*; 1434. (b) Holt, D. A.; Yamashita, D. S.; Konialian-Beck, A. L.; Luengo, J. I.; Abell, A. D. *J. Med. Chem.* **1995**, *38*, 13. (c) Dannhardt, G.; Fiebich, B. L.; Schweppenhaeuser, J. *Eur. J. Med. Chem.***2002**, *37*, 147. (d) Lenhart, A.; Reinert, D. J.; Aebi, J. D.; Dehmlow, H.; Morand, O. H.; Schulz, G. E. *J. Med. Chem.* **2003**, *46*, 2083.

[36] Appel, B.; Rotzoll, S.; Kranich, R.; Reinke, H.; Langer, P. *Eur. J. Org. Chem.* **2006**, 3638.

[37] Guarnieri, A.; Burnelli, S.; Varoli, L.; Busacchi, I.; Barbaro, A. M. *Arch. Pharm. (Weinheim Ger.)* **1981**, *314*, 703.

[38] Aburaki, S.; Okuyama, S.; Hoshi, H.; Kamachi, H.; Nishio, M. *J. Antibiot.* **1993**, *46*, 1447.

[39] (a) Pettit, G. R.; Toki, B.; Herald, D. L.; Verdier-Pinard, P.; Boyd, M. R.; Hamel, E.; Pettit, R. K. *J. Med. Chem.* **1998**, *41*, 1688. (b) Liou, J.-P.; Chang, J.-Y.; Chang, C.-W.; Chang, C.-Y.; Mahindroo, N.; Kuo, F.-M.; Hsieh, H.-P. *J. Med. Chem.* **2004**, *47*, 2897. (c) Liou, J.-P.; Chang, C.-W.; Song, J. S.; Yang, Y. S.; Yeh, C. F.; Tseng, H. Y.; Lo, Y. K.; Chang, C.-L.; Chang, C.-M.; Hsieh, H.-P. *J. Med. Chem.* **2002**, *45*, 2556.

[40] (a) Cai, X.; Sakamoto, M.; Fujitsuka, M.; Majima, T. *Chem. Eur. J.* **2005**, *11*, 6471. (b) Langhals, H.; Fuchs, K. *Chem. Unserer Zeit.* **2004**, *38*, 98.

[41] Buchta, E.; Egger, H. *Chem. Ber.* **1957**, *90*, 2760.

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

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

[44] (a) Wright, J.; Bolton, G.; Creswell, M.; Downing, D.; Georgic, L. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1809. (b) Chan, J. H.; Hong, J. S.; Hunter, R. N.; Orr, G. F.; Cowan, J. R.; Sherman, D. B.; Sparks, S. M.; Reitter, B. E.; Andrews, C. W.; Hazen, Richard J.; Clair, M. S. *J. Med. Chem.* **2001**, *44*, 1866. (c) Tagat, J. R.; McCombie, S. W.; Steensma, R. W.; Lin, S.-I.; Nazareno, D. V.; Baroudy, B.; Vantuno, N.; Xu, S.; Liu, J. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2143.(d) Stanton, J. L.; Cahill, E.; Dotson, R.; Tan, J.; Tomaselli, H. C.; Wasvary, J. M.; Stephan, Z. F.; Steele, R. E. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1661.

[45] (a) Chen, D.-W.; Kubiak, R. J.; Ashley, J. A.; Janda, K. D. *J. Chem. Soc., Perkin Trans. 1,* **2001**, *21*, 2796. (b) Marquie, J.; Laporterie, A.; Dubac, J.; Roques, N.; Desmurs, J.-R. *J. Org. Chem.* **2001**, *66*, 421. (c) Repichet, S.; Roux, C. Le; Dubac, J. *Tetrahedron Lett.* **1999**, *40*, 9233. (d) Hajipour, A. R.; Zarei, A.; Khazdooz, L.; Pourmousavi, S. A.; Mirjalili, B. B. F.; Ruoho, A. E. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 2029.

[46] Woroshzow, V. Kutschkarow, V. *Zh. Obshch. Khim.* **1949**, *19*, 1943; *Chem. Abstr.* **1950**, 1922.

[47] Zhu, W.; Ma, D. *J. Org. Chem.* **2005**, *70*, 2696.

[48] Bandgar, B. P.; Bettigeri, S. V.; Phopase, J. *Org. Lett.* **2004**, *6*, 2105.

[49] Huang, F.; Batey, R. A. *Tetrahedron* **2007**, *63*, 7667.

[50] (a) Erian, A. W.; Issac, Y.; Sherif, S. M.; Mahmoud, F. F. *J. Chem. Soc., Perkin Trans. 1,* **2000**, 3686. (b) Ogura, K.; Takeda, M.; Xie, J. R.; Akazome, M.; Matsumoto, S. *Tetrahedron Lett.* **2001**, *42*, 1923. (c) Matsumoto, S.; Kumazawa, K.; Ogura, K. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 2179. (d) Bianchi, L.; Dell'Erba, C.; Maccagno, M.; Mugnoli, A.; Novi, M.; Petrillo, G.; Sancassan, F.; Tavani, C. *J. Org. Chem.* **2003**, *68*, 5254 (e) Antelo, B.; Castedo, L.; Delamano, J.; Gomes, A.; Lopez, C.; Tojo, G. *J. Org. Chem.* **1996**, *61*, 1188. (f) Shkoor, M. Riahi.; A.; Fatunsin, O.; Reinke, H.; Fischer, C.; Langer, P. *Synthesis* **2009**, 2223.

[51] Ali, A.; Khera. R. A.; Ibad, M. F.; Hussain, M.; Villinger, A.; Langer, P. *Synlett.* **2010**, *5*, 0731.

[52] (a) Stutz. A. *Angew. Chem. Int. Ed.* **1987**, *26*, 320. (b) Nussbaumer, P.; Leitner, L.; Mraz, K.; Stutz, A.; *J. Med. Chem*. **1995**, *38*, 1831.

[53] Myers, A. G.; Proteau, P. J. Handel, T.M. *J. Am. Chem. Soc*. **1988**, *110*, 7212.

[54] (a) Aksela, R.; Oehlschlager, A. C. *Tetrahedron*. **1991**, *47*, 1163; (b) Magnus, A.; Hirokazo, P.; Harling, J. *J. Org. Chem*. **1990**, *55*, 1709; (c) Ikeda, S.; Sato, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5975; (d) Alami, M.; Gueugnot, S. Domingues, E.; Linstrumelle, G. *Tetrahedron*. **1995,** *51*, 1209; (e) Stefani, H.A. Cella, R.; Dorr, F.A.; Pereira, C.M.P.; Zeni, G. Gomes, M. *Tetrahedron Lett*. **2005,** *46*, 563.

[55] (a) Magriotis, P.A.; Kim, K. D. *J. Am. Chem. Soc.* **1993**, *115*, 2972; (b) Miller, J. A.; Zweifel, G. *J. Am. Chem. Soc*. **1983**, *105*, 1383; (c) Corey, E. J.; Tramontano, A. *J. Am. Chem. Soc*. **1984**, *106*, 462; (d) Marshall, H. R.; Chobanian, M.; Yanik, M. *Org. Lett*. **2001**, *3*, 4107; (e) Karatholuvhu, M. S. Fuchs, P. L. *J. Am. Chem. Soc*. **2004**, *126*, 14314; (f) Yoshida, M. ; Ohsawa, Y.; Ihara, M. *Tetrahedron*. **2006**, *62*, 11218.

[56] Hara, R.; Liu, Y.; Sun, W.-H.; Takahashi, T. *Tetrahedron Lett*. **1997**, *38*, 4103.

[57] Cadierno, V.; Gamasa, M. P.; Gimeno, J. *J. Organomet. Chem*. **2001**, *39*, 621.

[58] (a) Koreeda, M.; Yang, W. *Synlett*. **1994**, 201; (b) Cai, M. Z.; Wang, D. Wang, P.; *J. Chem. Res*. **2006**, 504; (c) Jiang, J. W.; Cai, M. Z. *Chin. Chem. Lett*. **2006**, *17*, 757.

[59] (a) Braga, A. L.; Zeni, G.; Andrade, L. H.; Silveira, C. C. Stefani, H. A. *Synthesis* **1998**, 39; (b) Ma, Y. Huang.; X. Synth. *Commun.* **1997**, *27*, 3441; (c) Cai, M. Z.; Peng, C. Y.; Zhao, H. *J. Chem. Res*. **2002**, 376; (d) Zhong, P.; Huang, N. *Synth. Commun.* **2002**, *32*, 139.

[60] (a) Huang, X.; Wang, Y.P.; *Tetrahedron Lett*. **1996**, *37*, 7417; (b) Cai, M.; Z. Chen, J. *J. Chem. Res*. **2004**, 840.

[61] (a) Chatani, N.; Amishiro, N. Murai, S. *J. Am. Chem. Soc*. **1991**, *113*, 7778. (b) Cai, M. Z.; Hao, W.; Zhao, H.; Song, C. *J. Chem. Res.* **2003**, 485.

[62] (a) Huang, X.; Zhong, P. *J. Chem. Soc., Perkin Trans*. **1999**, *1*, 1543; (b) Cai, M. Z.; Zhao, H. Ye, H.; Xia, J.; Song, C. *J. Chem. Res.* **2003**, 344.

[63] (a) Yoshida, M.; Yoshikawa, S.; Fukuhara, T.; Yoneda, N.; Hara, S. *Tetrahedron*, **2001**, *57*, 7143; (b) Legros, J.; Crousse, B.; Begue, J. P. *J. Fluor. Chem*. **2001**, *107*, 121.

[64] (a) Yoshimatsu, M.; Hasegawa, J. *J. Chem. Soc. Perkin Trans*. **1997**, *1,* 211; (b) Shen, Y.; Wang, G. Sun, J. *J. Chem. Soc. Perkin Trans.* **2001**, *1*, 519.

[65] (a) Suzuki, A. *Pure Appl. Chem*. **1985**, *57*, 1749; (b) Mitchell, T. N. *Synthesis*. **1992**, 803.

[66] (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett*. **1975,** 4467; (b) Alami, M.; Linstrumelle, G. *Tetrahedron Lett*. **1991**, *32*, 6109.

[67] (a) Anstead, G. M.; Wilson, S. R.; Katzenellenbogen, J. A. *J. Med. Chem.* **1989**, *32*, 2163. (b) Hajela, K.; Kapil, R. S. *Ind. J. Chem.* **1995**, *34*, 361. (c) McDevitt, R. E.; Malamas, M. S.; Manas, E. S.; Unwalla, R. J.; Xu, Z. B.; Miller, C. P.; Harris, H. A. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3137.

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

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

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

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

[72] (a) Morimoto, T.; Yamasaki, K.; Hirano, A.; Tsutsumi, K.; Kagawa, N.; Kakiuchi, K.; Harada, Y.; Fukumoto, Y.; Chatani, N.; Nishioka, T. *Org. Lett.* **2009**, *11*, 1777. (b) Eisch, J. J.; Kaska, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 2976.

[73] (a) Schnürch, M.; Flasik, R.; Khan, A. F.; Spina, M.; Mihovilovic, M. D.; Stanetty, P. *Eur. J. Org. Chem.* **2006**, 3283.

[74] (a) Dang, T. T.; Dang, T. T.; Ahmad, R.; Reinke, H.; Langer, P. *Tetrahedron Lett.* **2008**, *49*, 1698. (b) Dang, T. T.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2008**, *350*, 2109. (c) Hussain, M.; Nguyen, T. H.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 3929. (d) Tengho Toguem, S.-M.; Hussain, M.; Malik, I.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 4962. (e) Hussain, M.; Malik, I.; Langer, P. *Synlett.* **2009**, 2691. (f) Dang, T. T.; Dang, T. T.; Rasool, N.; Villinger, A.; Langer, P. *Adv. Synth. Catal.* **2009**, *351*, 1595. (g) Nawaz, M.; Farooq, M. I.; Obaid-Ur-Rahman, A.; Khera, R. A.; Villinger, A.; Langer, P. *Synlett.* **2010**, 150.

[75] (a) Liebermann, C. *Chem. Ber.* **1898**, *31*, 2083. (b) Liebermann, C. *Chem. Ber.* **1899**, *32*, 920. (c) Liebermann, C. *Chem. Ber.* **1900**, *33*, 569.

[76] (a) Yang, L.; Okuda, F.; Kobayashi, K.; Nozaki, K.; Tanabe, Y.; Ishii, Y.; Haga, M. *Inorg. Chem.* **2008,** *47,* 7154; (b) Chang, S.-Y.; Chen, J.-L.; Chi, Y. *Inorg. Chem.* **2007,** *46,* 11202; (c) Chang, E.-M.; Lee, C.-T.; Chen, C.-Y.; Wong, F. F.; Yeh, M.-Y. *Aust. J. Chem.* **2008,** *61,* 342; (d) Mukherjee, R. Coord. *Chem. Rev.* **2000,** *206,* 151.

[77] Ha-Duong, N.-T.; Dijols, S.; Marques-Soares, C.; Minoletti, C.; Dansette, P. M.; Mansuy, D. *J. Med. Chem*. **2001**, *44*, 3622.

[78] de Paulis, T.; Hemstapat, K.; Chen, Y.; Zhang, Y.; Saleh, S.; Alagille, D.; Baldwin, R. M.; Tamagnan, G. D.; Conn, P. J. J. Med. Chem. 2006, 49, 3332.

[79] (a) Bebernitz, G. R.; Argentieri, G.; Battle, B.; Brennan, C.; Balkan, B.; Burkey, B. F.; Eckhard, M.; Gao, J.; Kapa, P.; Strohschein, R. J.; Schuster, H. F.; Wilson, M.; Xu, D. D. *J. Med. Chem*. **2001**, *44*, 2601; (b) Raufl, M.; Ko¨ nig,W. *Immunopharmacology* **1990**, *19*, 103.

[80] Oh, L. M. *Tetrahedron Lett*. **2006**, *47*, 7943.

[81] Jian-yu, J.; Li-xue. Z.; An-jiang, Z.; Xin-Xiang, L.; Jiang-Hai, Z. *Molecules,* **2007***, 12,* 1596.

[82] (a) El-Emary, T.; Abdel-Mohsen, *S. Phosphorus, Sulfur Silicon Relat. Elem*. **2006**, *181*, 2459.

[83] Staufer, S. R.; Coletta, C. J.; Tedesco, R.; Nishiguchi, G.; Carlson, K.; Sun, J.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A. *J. Med. Chem*. **2001**, *43*, 4934.

[84] Anuradha, M.; Amitabha, S. *Tetrahedron lett*. **2005**, *46*, 15.

[85] (a) Wang, X. J.; Tan, J.; Zhang, L. *Org. Lett*. **2000**, *2*, 3107; (b) Holzer, W.; Kautsch, C.; Laggner, C.; Claramunt, R. M.; Pe´ rez-Torralba, M.; Alkorta, I.; Elguero, J. *Tetrahedron*, **2004**, *60*, 6791.

[86] (a) Zhang, J.; Didierlaurent, S.; Fortin, M.; Lefrancois, D.; Uridat, E.; Vevert, J. P. *Bioorg. Med. Chem. Lett*. **2000**, *10*, 2575; (b) Organ, M. G.; Mayer, S. *J. Comb. Chem*. **2003**, *5*, 118; (c) Dvorak, C. A.; Rudolph, D. A.; Ma, S.; Carruthers, N. I. *J. Org. Chem*. **2005**, *70*, 4188; (d) Dragovich, P. S.; Bertolini, T. M.; Ayida, B. K.; Li, L.-S.; Murphy, D. E.; Ruebsam, F.; Sun, Z.; Zhou, Y. *Tetrahedron*. **2007**, *63*, 1154; (e) Guillou, S.; Nesmes, O.; Ermolenko, M. S.; Janin, Y. L. *Tetrahedron*. **2009**, *65*, 3529.

[87] (a) Joule, J. A.; Mills, K.; Smith, G. F. *Heterocyclic Chemistry,* p. 278, Chapman & Hall, London **(1995);** (b) Bosshard, P.; Eugster, C. H. *Adv. Heterocycl. Chem.***1966**, *7*, 377. Faulkner, D. J. *Nat. Prod.* **1984**, *1*, 552.

[88] (a) Kupchan, S. M.; Eakin, M. A.; Thomas, A.M. *J. Med. Chem.* **1971**, *101*, 1147; (b) Bandurraga, M. M.; Fenical, W.; Donovan, S. F.; Clardy, J. *J. Am. Chem. Soc*. **1982**, *104*, 6463.

[89] Kobayashi, J.; Ohizumi, Y. Nakamura. *Tetruhedron, Lett.* **1986**, *27*, 2113.

[90] Schulte, G.; Scheuer, P. S. *Helv. Chim. Acta.* **1980**, *63,* 2159.

[91] (a) Searle, P. A.; Molinski, T. F**.** *Tetrahedron.* **1994,** *50*, 9893; **(**b**)** Rodriguez, B.; de la Torre, M. C.; Jimeno, M. L.; Bruno, M. C.; Fazio, F.; Piozzi, G.; Savona, A. *Tetrahedron*, **1995**, *51,* 837; (c) Guella, G.; Mancini, I.; Guemero, A.; Pietra, F. *Helv. Chim. Acta.* **1995**, *68*, 1276.

[92] (a) Donnelly D. M. X.; Meegan, M. J. in *Comprehensive Heterocyclic Chemistry**.;*** (b) Bird.; Cheeseman, G. W. H. ds. Pergamon Press, Oxford **1984**, *4(3)*, pp. 657.,

[93] (a) Kreiser, W. *Nachr. Chem. Tech. Lab***, 1981**, *29*, 118; **(**b**)** Lipshutz, B. H. *Chem. Rev.* **1986,** *86***,** 795.

[94] (a) Kirsch, S. F. *Org. Biomol. Chem.* **2006**, *4*, 2076; (b) Kawai, H.; Oi, S.; Inoue, Y. *Heterocycles.* **2006**, *67*, 101. (c) Brown, R. C. D. *Angew. Chem. Int. Ed.* **2005**, *44*, 850. (d) Jeevanandam, A.; Ghule, A.; Ling, Y.-C. *Curr. Org. Chem.* **2002**, *6*, 841.

[95] (e) Hou, X. L.; Cheung, H. Y.; Hon, T. Y.; Kwan, P. L.; Lo, T. H.; Tong S. Y.; Wong, H. N. C. *Tetrahedron*, **1998**, *54*, 1955.

[96] Tung, T, D.; Tuan, D. T.; Rasool, N.; Rasool, Villinger, A.; Reinke, H.; Langer, P. *Adv. Synth. Catal*. **2009**, *351*, 1595.

[97] Pindur, P.; Adam, R. *Helv. Cheim. Acta* **1990**, *73*, 827.

CURRICULUM VITAE

Rasheed Ahmad Khera

S/O

Hafiz Elahi Bakhsh Khera

CONFERENCES/WORKSHOPS ATTENDED

1- 7th International and 17th National Chemistry Conference jointly organized by Hec. Pakistan and the Department of Chemistry, Punjab University Lahore. September **2007**.

2- 6th International and 16th National Chemistry Conference jointly organized by Hec. Pakistan and the Department of Chemistry, Bahuddin Zakriya University Multan April **2005**.

3- 5th International and 15th National Chemistry Conference jointly organized by Hec. Pakistan and the Department of Chemistry, Quaid-e-Azam University Islamabad Pakistan. September **2004**.

M.Sc. Dissertation:

Preparation and Characterization of some Isoniazid Schiff bases and their transition metal complexes.

(May **2004**, Bahauddin Zakariya University Multan, Pakistan)

M.Phil. Dissertation:

Combinatorial Synthesis and Biological Screening of Small Drug Like Molecules.

(May **2006**, Quaid-i-Azam University Islamabad, Pakistan)

PUBLICATIONS

[1] "Site-Selective Suzuki-Miyaura Cross-Coupling Reactions of 2,3,4,5-Tetrabromofuran".Hussain, H.; **Khera, R. A**.;Hung, N. T.; Langer, P. *Org. Biomol. Chem.* **2010**, accepted.

[2] "Site-Selective Suzuki-Miyaura Reactions of 1,2-Dibromo-1*H*-inden-1-one". Hussain, H.; Hung, N. T.; **Khera, R. A**.; Langer, P. *Tetrahedron Lett.* **2010**, accepted.

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

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

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

[6] Cyclization *versus* Elimination Reactions of 5-Aryl-5-hydroxy-1,3-diones Onepot Synthesis of 6-Aryl-2,3-dihydro-4*H*-pyran-4-ones. **Khera, R. A**.; Ahmad. R.; Ullah. I.; Abid.O-U-R.; Fatunsin. O.; Sher. M.; Villinger. A, Langer, P. *Helv. Chim. Acta.* **2010**, (*accepted*).

[7] Synthesis of Functionalized Triarylmethanes based on a ′$FeCl_3$-Catalyzed Benzylation /[3+3] Cyclocondensation′. **Khera, R. A**.; Ahmad. R.; Ullah. I.; Riahi. A, Sher. M.; Villinger. A, Fischer. C.; Langer, P. *Tetrahedron,* **2010**, *66,* 1643.

[8] "Synthesis of Bis(diaryl)sulfones by Site-Selective Suzuki-Miyaura Reactions of 2,4′-Bis(trifluoromethylsulfonyloxy)diphenylsulfone" Ali, A.; **Khera. R. A**.; Ibad, M. F.; Hussain, M.; Villinger, A.; Langer, P. *Synlett.* **2010**, *5*, 0731.

[9] Synthesis of 3,4-Diarylbenzophenones by Site-Selective Suzuki-Miyaura Reactions of 3,4-Bis(trifluoromethylsulfonyloxy)benzophenone. Nawaz. M.; **Khera. R. A**.; Malik. I.; Villinger. A.; Langer. P. *Synlett.* **2010**, 979-981.

[10] Synthesis of 3-aryl-3,4-dihydroisocoumarins by regioselective domino '[3+3] cyclization/lactonization' reactions of 1,3-bis-(silyloxy)-1,3-butadienes with 1-hydroxy-5-silyloxy-4-en-3- ones. Ullah. I.; Sher. M.; **Khera. R. A**.; Ali. A.; Villinger. A, Fischer. C.; Langer, P. *Tetrahedron,* **2010**, *66,* 1874.

[11] Synthesis of sterically encumbered biaryls based on a 'copper (I)-catalyzed arylation/[3+3] cyclocondensation' strategy. Ullah. I.; Sher. M.; **Khera, R. A**.; Ali. A.; Nawaz. M.; Shkoor. M.; Iqbal. I.; Imran. M.; Villinger. A, Fischer. C.; Langer, P. *Tetrahedron,* **2010**, *66*, 3824.

[12] Functionalized *p*-terphenyl based on Selective Suzuki cross-coupling Reactions of Bis(triflates) of 2,5-dihydroxybenzoate. Nawaz. M.; Ibad. F. M.; Abid.O-U-R, **Khera. R. A**.; Villinger. A.; Langer. P. *Synlett.* **2010**, *1*, 0150.

[13] Synthesis, characterization, crystal structure and antibacterial activities of new 1-substituted benzothioyl-3-(3, 4, 5-trimethoxyphenyl) ureas. Saeed. A.; **Khera. R. A**.; Abbas. N.; Latif. M.; Sajid. I, Florke. U. *Turkish. J. of Chem*. **2010**, *34*, 1-11.

[14] Afzal Shah, Rumana Qureshi, Asad Muhammad Khan, **Rasheed Ahmad Khera**, Farzana Latif Ansari "Electrochemical behavior of 1-ferocenyl-3-phenyl-2-propen-1-one on Glassy carbon electrodes and evaluation of its interaction parameters with DNA". ***J. Braz. Chem. Soc.*** **2010**, *21*, 447.

[15] *N*-(2-Fluorophenyl)cinnamamide". Saeed. A.; Khera. R. A.; Simpson. *J. Acta Cryst. E,* **2010**, *E-66*, 0533.

[16] "2-Methyl-*N*-*p*-tolylbenzamide". Saeed. A.; **Khera. R. A**.; Simpson. *J. Acta Cryst. E* **2010**, *E-66*, 0911.

[17] "4-Chloro-*N*-(2-methoxyphenyl)benzamide". Saeed. A.; **Khera. R. A**.; Simpson. *J. Acta Cryst.***2010**, *E-66*, 0635. *E-66*, 0214.

[18] "2-Methyl-*N*-(*o*-tolylbenzamide)". Saeed. A.; **Khera. R. A**.; Siddiq. M.; Simpson. *J Acta Cryst.* **2010**. *E-66*, 019.

[19] 4,4,6-Trimethyl-1-(3-methylphenyl)-3,4-dihydropyrimidine-2(1H)-thione". Saeed. A.; **Khera. R. A**.; Parvez. M. *Acta Cryst.* **2010**. *E-66, 0635.* .

[20] "Synthesis of Tetraarylquinones by Suzuki Cross-Coupling Reactions of Tetrabromobenzoquinone". Ullah, I.; **Khera, R. A.;** Hussain, M.; Langer, P. *Tetrahedron Lett.***2009**, *50*, 4651.

[21] Regioselective synthesis of functionalized 4-nitro-and-4aminophenols based on formal [3+3] cyclocondensation of 3-ethoxy-2-nitro-2-en-1- ones with 1,3-bis(silyloxy)-1,3-butadienes. Riahi. A.; Shkoor. M.; **Khera. R. A**.; Reinke. H.; Langer. P. *Tetrahedron lett*. **2009**, *50*, 3017.

[22] One-pot synthesis of 2, 3-dihydro-4H-pyran-4-ones by cyclocondensation of 1, 3-diketone dianions with aldehydes. **Khera. R. A**.; Ahmad.R. Villinger. A, Fischer. C.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 3020.

[23] Regioselective synthesis of 4-acyl-1-hydroxy-2,3-benzodioates by chelation-controlled [3+3] annulation of 3-acyl-4-ethoxy-2-oxo-3-enoates with 1,3-bis(trimethylsilyloxy)-1,3-butadienes. Riahi. A.; Shkoor. M.; **Khera. R. A**.; Fatusin. O.; Reinke. H.; Langer. P. *Org. Biomolecular. Chem*. **2009**, *7(20)*, 4248.

[24] *N*-(Cyclohexyl, 3, 4,5-trimethoxybenzamide". Saeed. A, Arshad. A, **Khera. R. A**.; Simpson. J. *Acta Cryst.* **2009**, *E-65*, 03234.

[25] *N*-(4-Nitrophenyl)cinnamamide. Saeed. A, **Khera. R. A**; Shahid. M.; Parvez. M.; *Acta Cryst.* **2009**, *E-65*, 02068.

[26] 2, 4-Dichloro-*N*-*p*tolylbenzamide. Saeed. A, **Khera. R. A**; Rafique. H.; Simpson. J. *Acta Cryst.* **2009**, *E-65*, 02527.

[27] 1-(2-chloro-5-nitophenyl)-3-(2,2-dimethylpropionyl)thiourea". Saeed. A, **Khera. R. A**; Roderick. G.; Simpson. J. *Acta Cryst.* **2009**, *E-65*, 01735.

[28] *N*-(4-Nitrophenyl)cinnamamide. Saeed. A, **Khera. R. A**; Latif. M; Parvez. M. *Acta Cryst.* **2009**, *E-65*, 01539.

[29] 2-Fluoro-N-(4-mehoxyphenylbenzamide). Saeed. A, **Khera. R. A**.; Arfan. M.; Roderick. G.; Simpson. J. *Acta Cryst.* **2009**, *E-65*, 0802.

[30] 2-Fluoro-N-(o-tolylbenzamide). Saeed. A, **Khera. R. A**.; Ameen. S.; M.; Simpson. J. Roderick. G. *Acta Cryst.* **2009**, *E-65*, 0201.

[31] 3-Fluoro-N-(ptolylbenzamide). Saeed. A, **Khera. R. A**.; Abbas. N.; Gotoh. K.; Ishida. H. *Acta Cryst.* **2009**, *E-65*, 02098.

[32] 4-Chloro-N-(otolylbenzamide). Saeed. A, **Khera. R. A**.; Abbas. N.; Gotoh. K.; Ishida. H. *Acta Cryst.* **2009**, *E-65*, 02043.

[33] N-Butyl-4-chlorobenzamide. Saeed. A, **Khera. R. A**.; Abbas. N.; Gotoh. K.; Ishida. H. *Acta Cryst.* **2008**, *E-64*, 02322.

[34] N-Cyclohexyl-3-fluorobenzamide. Saeed. A, **Khera. R. A**.; Abbas. N.; Florke. U. Gotoh. K.; Ishida. H. *Acta Cryst.* **2008**, *E-64*, 02209.

[35] N-Cyclohexyl-2-fluorobenzamide. Saeed. A, **Khera. R. A**.; Abbas. N.; Florke. U. Gotoh. K.; Ishida. H. *Acta Cryst.* **2008**, *E-64*, 02187.

[36] 4-Chloro-N-(3-methoxyphenyl)benzamide". Saeed. A, **Khera. R. A**.; Abbas. N.; Simpson. J. *Acta Cryst.* **2008**, *E-64*, 01976.

[37] 4-Chloro-N-(2-chlorophenyl)benzamide. Saeed. A, **Khera. R. A**.; Abbas. N.; Gotoh. K.; Ishida. H. *Acta Cryst.***2008**, *E-64*, 01934.

[38] N-(4-Chlorophenyl)-3, 4, 5-trimethoxybenzamide. Saeed. A, **Khera. R. A**.; Shaheen. U.; Florke. U. *Acta Cryst.* **2008**, *E-64*, 01625.

[39] 3,4,5-Trimethoxymethylbenzoate. . Saeed. A, **Khera. R. A**.; Florke. U. *Acta Cryst.* **2007**, *E-63*, 04582.

Declaration/Erklärung

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.

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

.....

Rasheed Ahmad Khera