UNIVERSITÄT ROSTOCK

Synthesis of Purines by Inverse Electron Demand Diels-Alder Reactions of Amines with 1,3,5-Triazines and of Fluorinated Arenes by Palladium(0)-Catalyzed Cross-Coupling Reactions and Photophysical Properties of the Products

Dissertation

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Aneela Maalik

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1. Gutachter: Prof. Dr. Dr. h.c. Peter Langer, Universität Rostock
2. Gutachter: Prof. Dr. Till Opatz, Universität Mainz

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Prüfer Hauptfach: Prof. Dr. Dr. h.c. Peter Langer

(Institut für Chemie, Universität Rostock)

Prüfer Nebenfach: Prof. Dr. Reinhard Schröder

(Institut für Biowissenschaften, Abt. Genetik, Universität Rostock)

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Dedicated

To

My loving Parents

Muhammad Maalik, Shaffia Begum

And my lovely son

Daim Ali

Acknowledgement

In the name of Allah, most gracious; most merciful.

"And say: Work (righteousness): Soon will Allah observe your work, and His messenger and believers"

All praise and glory to Allah Almighty who alone made this small objective to be accomplished I feel honored and privileged to glorify His name in the sincerest way through this small accomplishment and ask Him to accept my efforts. Peace be upon the Prophet, his companions and all who followed him until the Day of judgment.

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CHAPTER 1

Synthesis of Purines by Formal Inverse Electron Demand Diels-Alder Reactions of Amines with 1,3,5-Triazines
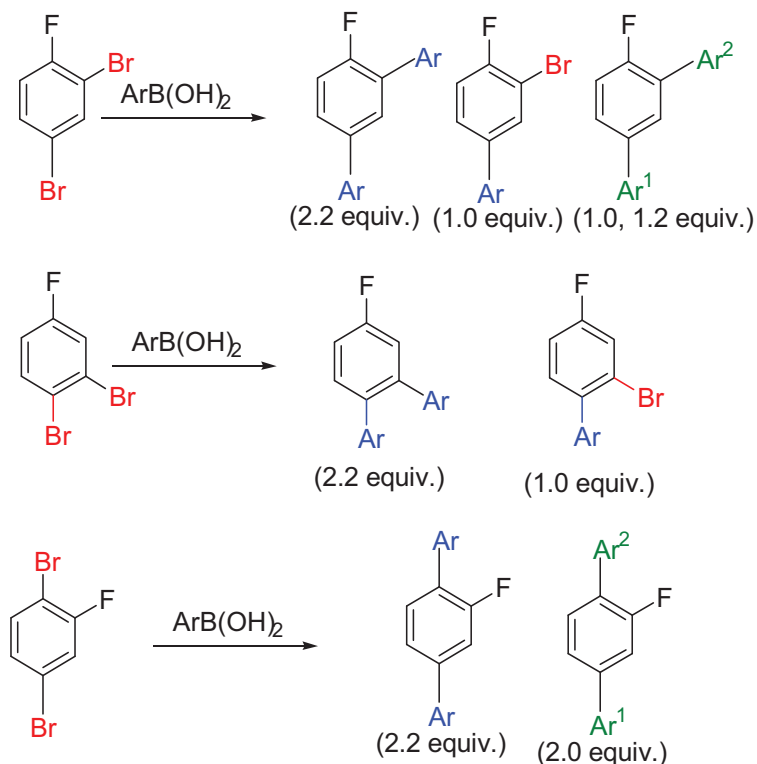
The reaction of 1,3,5-triazine and 2,4,6-tris(trifluoromethyl)-1,3,5-triazine with *in situ* generated 1-substituted 5-amino-1*H*-imidazoles led to a set of functionalized purines. The developed practical route could serve as a fundament for the preparation of related ADA inhibitors.

CHAPTER 2

Synthesis of Fluorinated Terphenyls by Suzuki-Miyaura Cross Coupling Reactions of 1,3-Dibromo-4-fluorobenzenes, 1,2-Dibromo-4-fluorobenzenes, and 1,4-Dibromo-2-fluorobenzenes

Suzuki-Miyaura reactions of fluorinated benzenes proceeded with excellent yields and site-selectivity. The reactions with one equivalent of arylboronic acids resulted in site-selective attack on less sterically hindered and more electron deficient carbon atoms. The Suzuki–Miyaura reaction with 2.2 equivalents of arylboronic acids gave fluorinated terphenyls. The one-pot reaction of fluorinated benzenes with two different aryl groups were prepared by sequential addition of two different aryl boronic acids.

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Synthesis of Fluorinated Polyethynylbenzenes by Sonogashira Coupling Reactions of 1,2-, 1,3-, 1,4-Difluorobenzenes and 1-Fluorobenzenes and their Absorption and Emission Properties
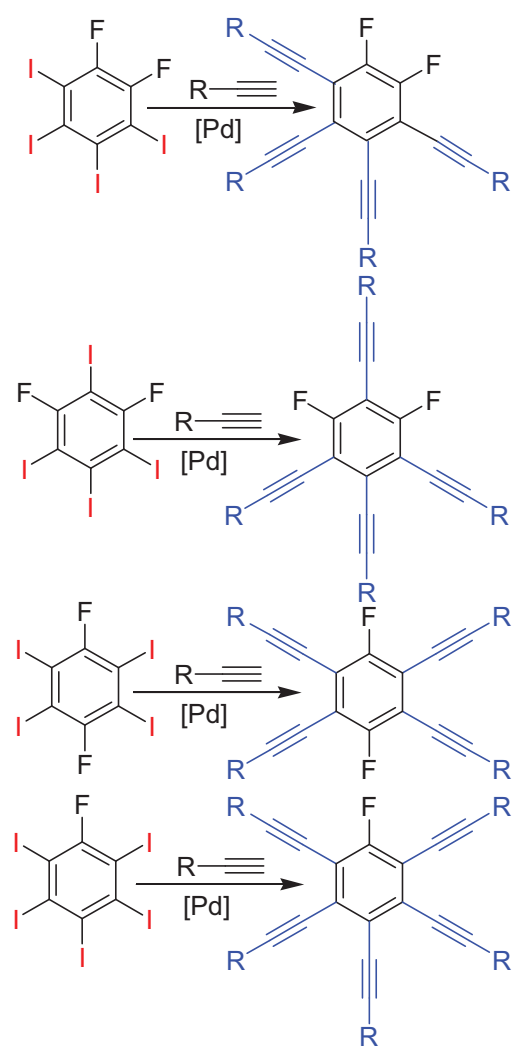
Sonogashira coupling reactions of 1,2-, 1,3-, 1,4-difluorobenzenes and 1-fluorobenzenes have been carried out in good to very good yields. Most products showed excellent fluorescence properties. The pruducts prepared have not been reported to date.

Page 37–50

CHAPTER 4

Synthesis of Fluorinated Aryl-Substituted Benzenes by Suzuki-Miyaura Coupling Reactions of 1,2-, 1,3-, 1,4-Difluorobenzenes and 1-Fluorobenzenes and their Absorption and Emission Properties
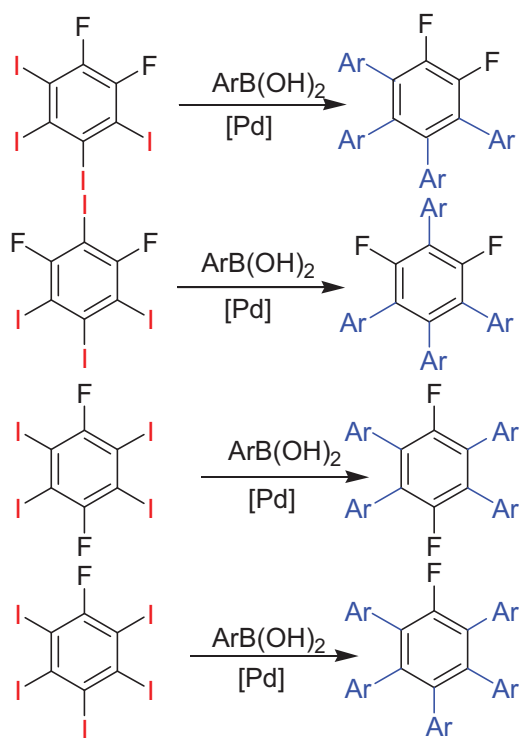
Suzuki-Miyaura reactions of 1,2-, 1,3-, 1,4-difluorobenzenes and 1-fluorobenzenes allowed a convenient synthesis of fluoro-substituted aryl benzenes, such as symmetrical and unsymmetrical arenes by using the corresponding equivalents of aryl boronic acids. Fluoro-substituted aryl benzenes are prepared which are not readily available by other methods. All reactions proceeded with good to high yields.

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EXPERIMENTAL SECTION

Introduction and Tasks of the Thesis

Purine isosteres and purine like scaffolds are of considerable interest as major privileged scaffolds often used in medicinal chemistry and drug design. In the recent decade, functionalized derivatives of purine isosteres have gained remarkable importance as pharmacological structures and synthetic building blocks in medicinal and agricultural chemistry. The aim of this work is to enhance the scope of formal inverse electron demand Diels-Alder reactions of 1-substituted-1H-imidazol-5amines with 1,3,5-triazines. The Langer group, subgroup of Dr. V. O. Iaroshenko, has also greatly contributed to this. This paragraph outlines the tasks of this thesis. A more detailed introduction is given at the beginning of each individual chapter.
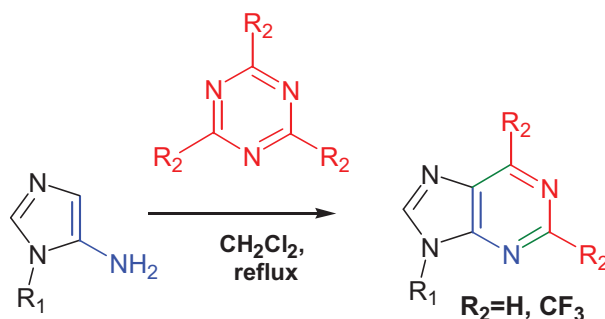
I have also studied the site-selectivity of palladium catalyzed transformations of fluoro-substituted dibromobenzenes. Site-selective reactions of the substrates discussed in the thesis have not been previously studied by other research groups.
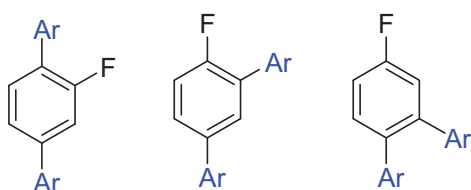
Although a diverse set of substrates were studied, the general topic of this thesis was to develop new polyiodinated benzene derivatives and their applications as substrates in Sonogashira reactions for the synthesis of polyethynylbenzenes.
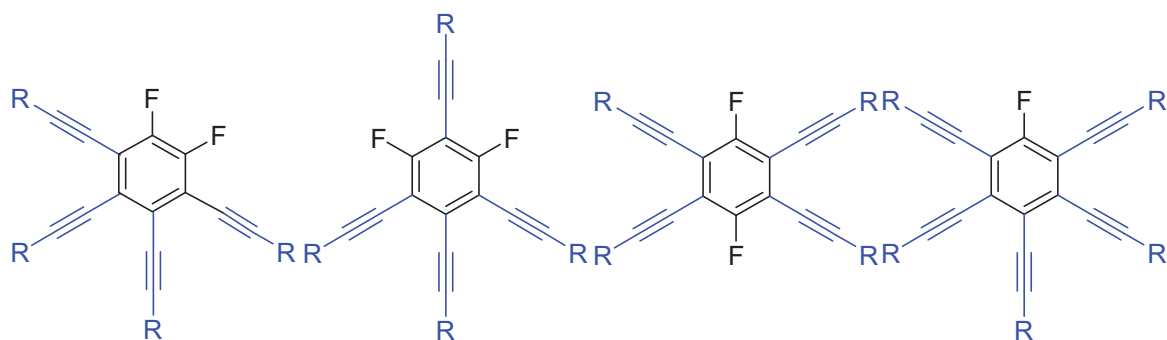
In continuation of the task, the synthesis of polyarylbenzenes was also performed by the application of the Suzuki-Miyaura cross coupling protocol.
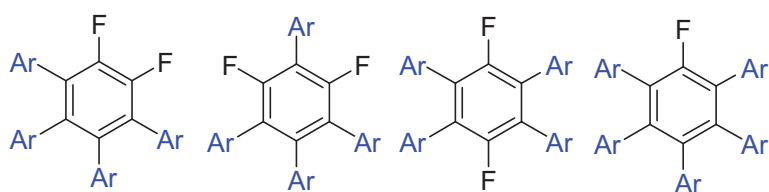
Based on this, an important goal was to study the absorption and fluorescence properties of all products.

Chapter 1. *Synthesis of Purines*

1 Synthesis of purines by formal inverse electron demand Diels-Alder reactions of amines with 1,3,5-triazines

1. 1 Introduction

In recent years, much attention has been devoted to purines as they play a vital role in life cycles of humans, flora and fauna, due to the presence of the naturally widely spread heterocyclic core. The nucleic acids DNA and RNA contain the purine derivatives adenine and guanine as important subunits. Moreover, a class of important enzyme target moieties is represented by the *N*-ribosyl substituted derivatives of adenosine and guanosine which are present in the human body.[1]

The deamination of adenosine to inosine is catalyzed by a zinc metalloenzyme adenosine deaminase (or simply ADA). Thus, it plays a key role in the adenosine metabolism and in a number of physiological processes (e. g., the regulation of ion-channel activity, the inhibition of platelet aggregation, and the inactivation of eosinophile migration). Moreover, it was shown, that ADA functional disorders affect on the differentiation and maturation of the lymphoid system leading to a severe combined immunodeficiency disease (SCID), due to the decreasing production of immunoglobulins.[2] Recent studies have been directed towards ADA inhibition based on its exuberant reproduction which is observed in case of oncologic diseases,[3] tuberculosis,[4,8(b)] Parkinson's disease,[5] bacterial meningitis,[6] viral hepatitis[7] and auto immune diseases including sarcoidosis and rheumatoid arthritis.[8]

Nowadays, mimicking the transition state of enzymes has become the dominating strategy for enzyme inhibition. Based on the structural similarity to the adenosine transition state, pentostatin, coformycin and their analogues show an almost irreversible binding with the ADA receptor[9] (Figure 1).
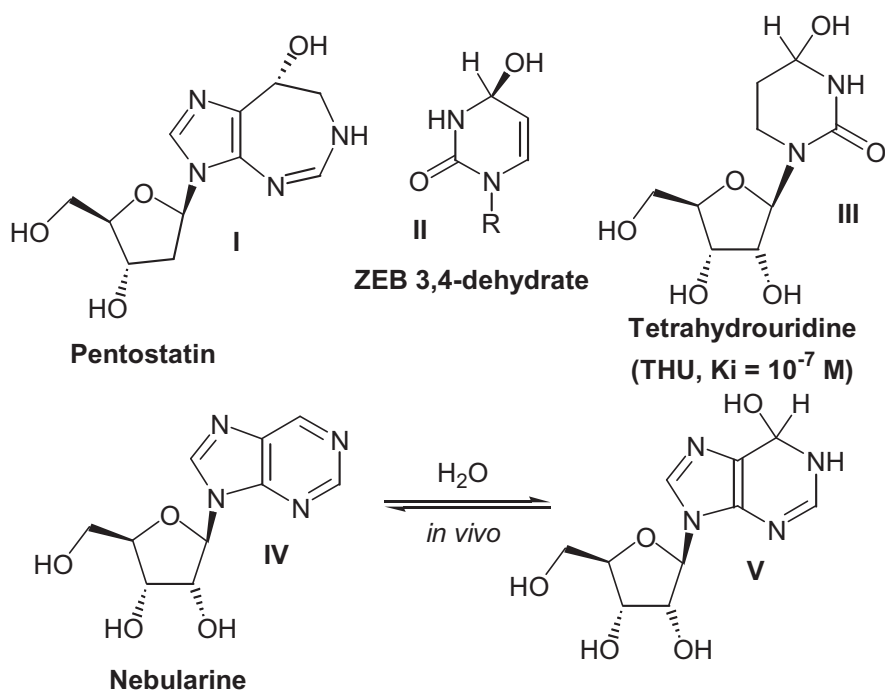
Figure 1. Potent ADA and CDA inhibitors

Pyrimidine derivatives, like ZEB or tetrahydrouridine, are promising inhibitors of cytidine deaminase[10] (Figure 2). The commercially available drug nebularine is a bright example of an adenosine-like nucleoside which mimics the ADA transition state through covalent hydration of an aglycone ring.[11]
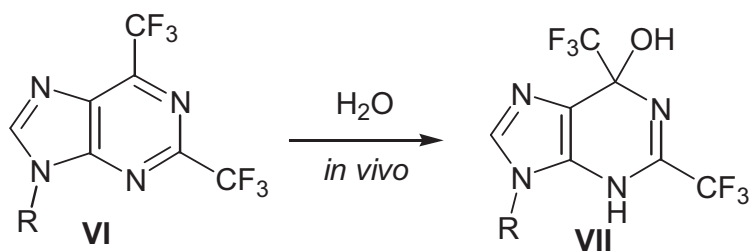
Figure 2. 6-Acceptor-substituted 3*H*-imidazo[4,5-*b*]pyridines as new potential ADA-inhibitors.

Mechanistically, the formation of inosine during enzymatic adenosine deamination[12] is assumed to involve nucleophilic attack of water on position 6 of the purine ring followed by stereospecific hydroxyl group addition[13] (Scheme 1). In our concept, the enthalpy of covalent hydration of the adenosine-like transition state mimetic could be decreased by introducing an electron withdrawing substituent into its heterocyclic core. As a promising candidate we have considered the CF_3-group, since it has proven to be isosterically close to the NH_2-

functionality. This should additionally decrease the enthalpy of the activated complex with the enzyme leading to a more tightly binding to the receptor.

For further insight in the field of designing potential ADA inhibitors, we focused our attention on the development of a practical route to trifluoromethyl substituted purines as the aglycone moiety of the traget structures. Bearing two strong electron-withdrawing groups at position 2 and 6 of the purine ring, such synthons could easily interact with water *in vivo* under enzyme-catalyzed conditions, due to the higher electron deficiency in comparison with the non-fluorinated adenosine moiety. Therefore, they could be considered as highly efficient adenosine mimetics (Figure 2). In addition, from the literature survey it is obvious that the introduction of fluorine-containing functional groups to biomolecules often results in the development of new physiologically active compounds.[14] In the course of our current research we have developed a synthetic approach to several 2- or 6-CF_3-substituted purine isosteres and their correspondent nucleosides.[15]

Besides the goal of mechanism-based design of ADA-inhibitors mimicking a putative transition state of adenosine deamination *in vivo*, we have concentrated our attention on the investigation of the scope and limitations of the assembly of 9-substituted-2,6-bis(trifluoromethyl)-9*H*-purines using amines as the source of introducing the 9-substituent. We follow the formal inverse electron-demand Diels-Alder strategy starting from *in situ* generated 1-substituted-1*H*-imidazol-5-amines and 2,4,6-tris(trifluoromethyl)-1,3,5-triazine. Thus, the extension of the scope of this study is communicated here.

1.2 Results and discussion

1.2.1 Synthesis of 5-amino-1*H*-imidazoles with unsubstituted 1,3,5-triazine.

Carrying out a careful study of possible syntheses of 2,6-disubstituted purines, we have revealed a versatile route to 6-membered heterocycles, based on the inverse electron-demand Diels-Alder cycloaddition, which has proven to be an efficient method for the synthesis of fused pyridines and pyrimidines. In this context, numerous studies directed to unknown cycloaddition reactions have been carried out. The reactions afforded a series of substances starting with various azadienes, such as 1,2-diazines,[16] 1,2,4-triazines,[17] 1,2,4,5-tetrazines,[18] and 1,3,5-triazines.[19] Later on, the method was extended from the employment of substituted alkenes, cycloalkenes and naphthalenes as the dienophiles to the application of electron-rich aminoheterocycles, like 2-aminopyrroles,[18,19] 5-amino-1*H*-pyrazoles[20] and 1-substituted 5-

amino-1*H*-imidazoles.[21] The described route provides an efficient pathway to the synthesis of 2,6-disubstituted purines.
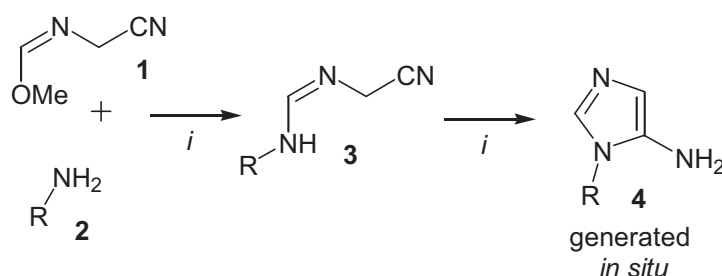
Scheme 1. *Reagents and conditions:* (i) CH_2Cl_2, argon atmosphere, reflux, 2 h.

Guided by our previous successful experience,[22] I have decided to use 1-substituted 5-amino-1*H*-imidazoles **4**, which were generated *in situ* following our developed procedure, as dienophiles in formal inverse electron demand Diels-Alder reactions. The reaction of primary aliphatic amines with methyl-*N*-cyanomethyl-formimidate (**1**), via nucleophilic substitution and subsequent cyclization, resulted in the formation of the required substrates (Scheme 1). The reaction was carried out in dichloromethane under inert atmosphere. My preliminary studies were focused on the interaction of the 5-amino-1*H*-imidazoles with unsubstituted 1,3,5-triazine **5** (Scheme 2).
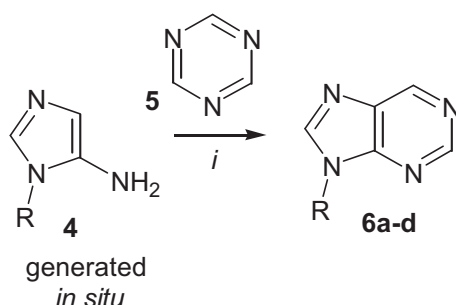
Scheme 2. *Reagents and conditions:* (i) CH_2Cl_2, under argon atmosphere, reflux, 10 h.

The first attempts to obtain simple 9-substituted purines by addition of an equimolar amount of the corresponding azadiene **5** to the reaction mixture with subsequent reflux for 5 hours resulted in formation of the desired product in only 10% yield (Scheme 2). Posterior improvements of the procedure (the aminoheterocycle was generated in 20% excess and the reaction time was increased to 10 hours, the addition of the triazine was conducted at 0 ^{o}C) resulted in an increased yield of **6** (up to 40%) which is, however, still rather low. Our efforts, which resulted in the synthesis of a small number of 9-alkyl-purines **6** (Table 1), led to the conclusion that the chosen method is insufficient in case of 1,3,5-triazine.

Table 1 Yields of 9*H*-purines **6.**

6	R	% (6) [a]
a	*t*-Bu	37
b	4-Methoxybenzyl	27
c	2-(Chloro)benzyl	43
d	2-(2-Chlorophenyl)ethyl	40

[a] Yields of isolated products

1.2.2 Synthesis of 5-amino-1*H*-imidazoles from 2,4,6-tris(trifluoromethyl)-1,3,5-triazine

In the following, I concentrated my attempts on the use of 2,4,6-tris(trifluoromethyl)-1,3,5-triazine (**7**) as the reactant. Being by far more electron-deficient than its unsubstituted analogue, it represents a more promising substrate than parent 1,3,5-triazine **5**. In fact, I have found that the application of **7** concluded in high yields and short reaction times (Scheme 3). The interaction between the 1-substituted-5-amino-1*H*-imidazole **4** with triazine **7** resulted, in the first attempt, in the formation of the desired product **8a** in 54% yield after reflux for only for 2 hours (Scheme 3, Table 2). As the reaction was observed to be exothermic, consequently, the reaction mixture was cooled to 0°C before the azadiene was added. This resulted in an increase of the yield (Table 2). Following these conditions, a number of 2,6-bis(trifluoromethyl)purines **8a-o** were prepared in excellent yields of 48-93%. All products (Table 2) were characterized by analytical techniques. The products **8n** was independently confirmed by crystal structure analysis (Figure 3).
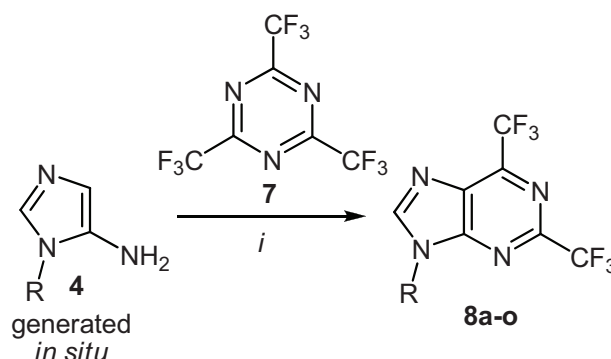
Scheme 3. *Reagents and conditions:* (i) CH_2Cl_2, under argon atmosphere, reflux, 2 h.

Table 2 Yields of 2,6-bis(trifluoromethyl)-9*H*-purines **8.**

8	R	% (8) [a]
a	*t*-Bu	87
b	Allyl	68
c	*n*-Heptyl	68
d	Cyclopropyl	83
e	Cyclohexyl	90
f	*N,N*-Dimethylethyl	71
g	*N,N*-Diethylethyl	90
h	3-Morpholinopropyl	90
i	4-Methylpiperazin-1-yl	73
j	Benzyl	75
k	*(S)*-1-Phenylethyl	75
l	Phenylethyl	68
m	2-Methoxyphenylethyl	77
n	3,4-Dimethoxyphenylethyl	93
o	Pyridin-4-yl-methyl	93

[a]Yields of isolated products
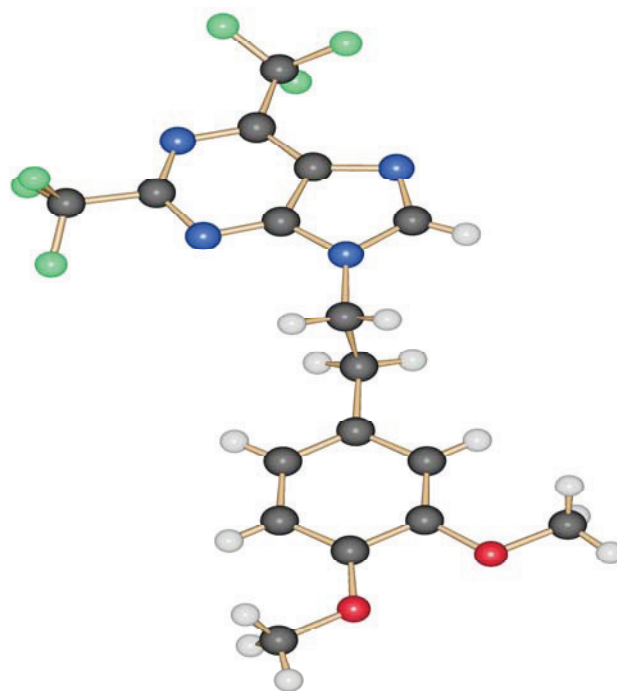
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Fig 3. Molecular structure of **8n**.

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1.2.3 Synthesis of 9-aryl- and 9-heteroarylpurines

It is important to be noted that the reaction could be applied only to aliphatic amines, since aromatic and heteroaromatic amines did not undergo, under my conditions, a reaction with **1**. Therefore, I was searching for suitable reaction conditions to succeed in the synthesis of purines bearing an aryl or hetroaryl moiety located at position 9 of the purine core. The addition of a catalytic amount of TMSOTf proved to be the crucial point to achieve the formation of the 5-amino-imidazole ring in the case of 9-aryl or hetaryl derivatives. The subsequent reaction of the latter with triazine **7** allowed the synthesis of 9-aryl-purines **9** as well as 9-heteroaryl-purines **10** (Scheme 4, Table 3).
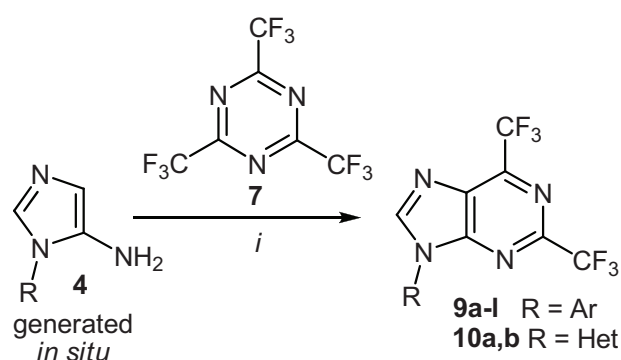
Scheme 4. *Reagents and conditions:* (i) CH_2Cl_2, TMSOTf, under argon atmosphere, reflux, 10 h.

Table 3 Yields of 2,6-bis(trifluoromethyl)-9*H*-purines **9, 10.**

	R	% [a]
9a	3-Methoxyphenyl	70
9b	3,4-Dimethoxyphenyl	72
9c	3,5-Dimethoxyphenyl	78
9d	2,4-Dimethoxyphenyl	76
9e	3,4,5-Trimethoxyphenyl	65
9f	4-Ethoxyphenyl	62
9g	2,4,6-Trimethylphenyl	83
9h	3-Bromophenyl	67
9i	4-Bromophenyl	71
9j	2,6-Dibromo-4-methylphenyl	45

9k	4-*N*,*N*-Diethylphenyl	70
9l	Morpholyl	48
10a	Thiazol-2-yl	61
10b	Pyridin-2-yl	40

^aYields of isolated products

Products **9g**, **9k** and **9l** were also independently confirmed by crystal structure analyses (Figures 4, 5 and 6).
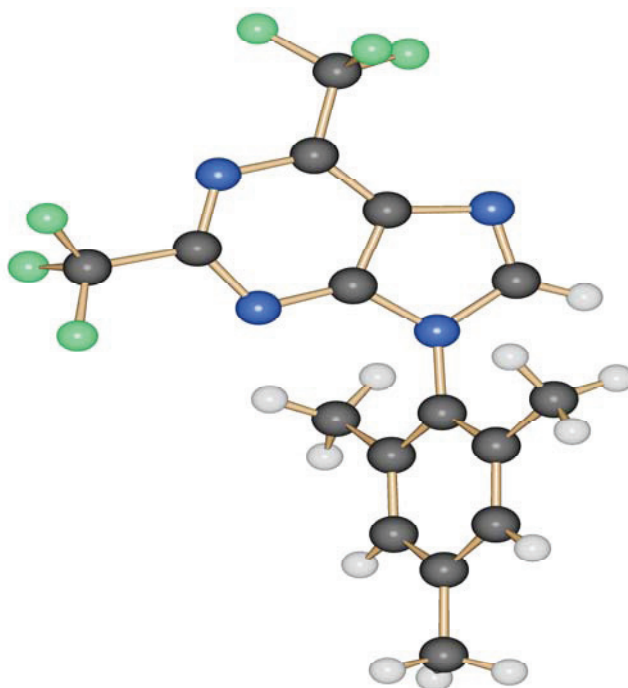
Fig 4. Molecular structure of **9g**
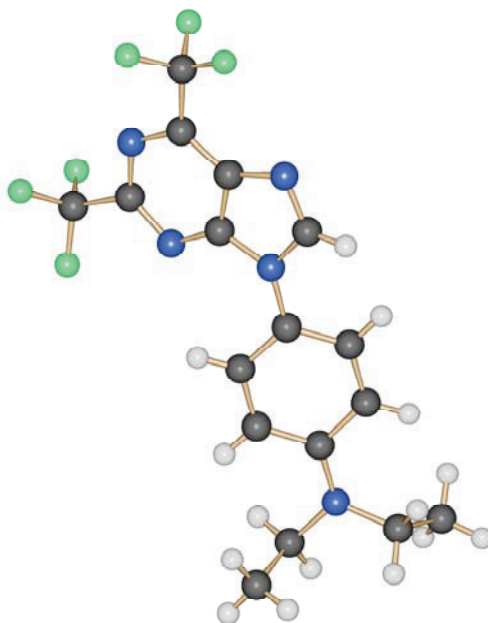
Fig 5. Molecular structure of **9k**
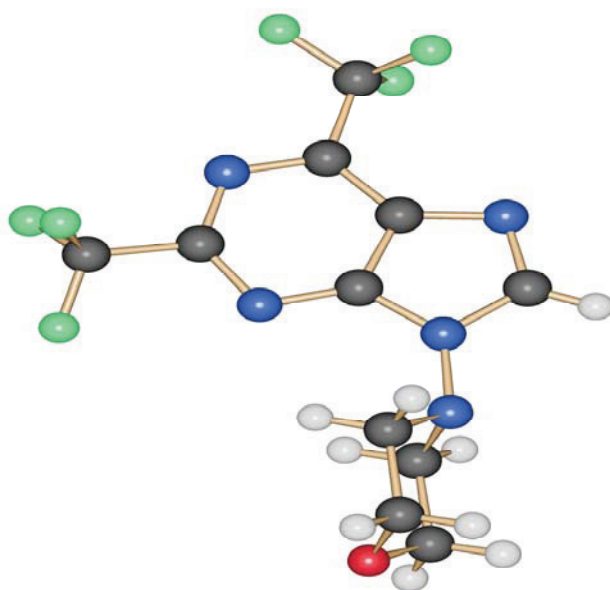
Fig 6. Molecular structure of **9l**

1.2.4 Synthesis of purines and bi-purines by reaction of diamines with 2,4,6-tris(trifluoromethyl)-1,3,5-triazine

I also studied the reaction of diamines with one and two equivalents of **1** (dichloromethane, reflux, argon atmosphere) which resulted in the *in situ* formation of the correspondent 5-

amino-imidazoles as well as the 5-amino-imidazoles linked by a bridge. These experiments show that the assembly of fluorinated purines **13-15**, containing two domains, suitable for the application in the field of supramolecular chemistry, is possible. In the same time, when the ratio amine to amidate was 1:1, we have observed exclusively the formation of products **11, 12.**
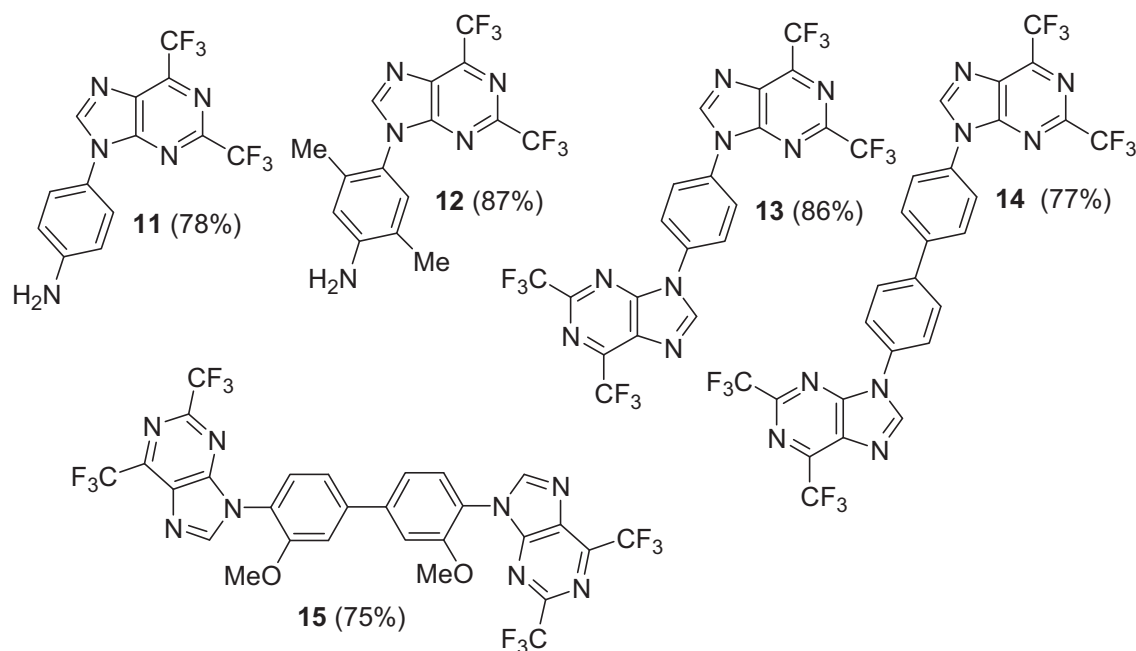
Scheme 5. Purines obtained starting with aromatic diamines.

In the case of bi-purine **13** linked by a phenyl ring, we have succeed to grow a crystal, which fully confirms the structure (Figure 7).[23]
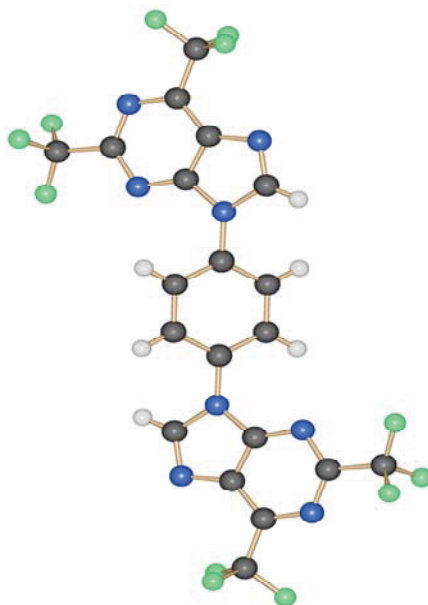
Fig 7. Molecular structure of **13**.

The product formation might be explained by a formal cycloaddition / retro-cycloaddition mechanism,[20b, 21] which includes the formation of the zwitterion **B**, followed by a cascade of nucleophilic attack of nitrogen atom 4 on position 5 of the imidazole, formation of a nitrile R_2-CN and cleavage of ammonia (intermediates **C, D**) resulting in purine formation (Scheme 6).
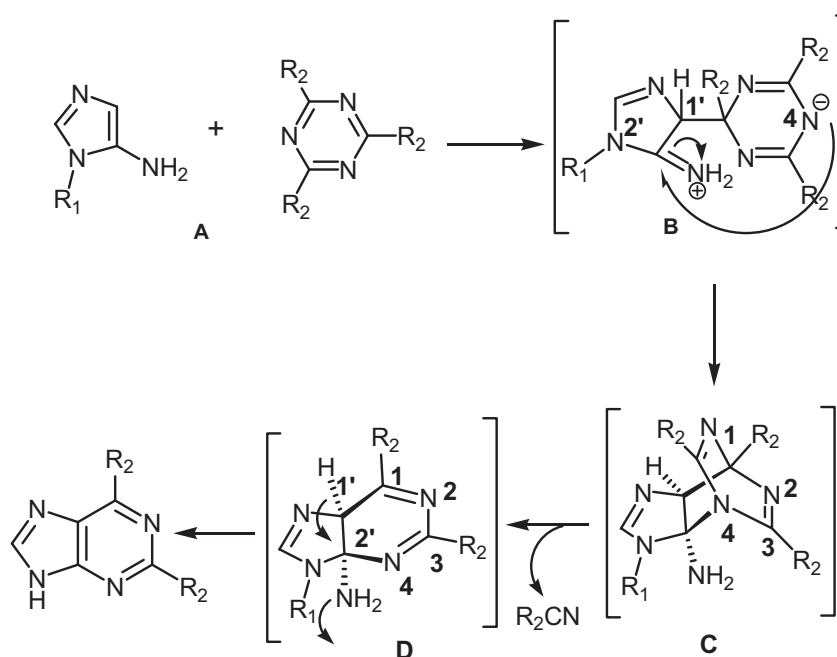
Scheme 6. Putative mechanism

1.3 Conclusion

In conclusion, I have reported a new and facile method for the synthesis of 9-functionalized purines and 2,6-bis(trifluoromethyl)purines by formal inverse electron-demand Diels-Alder reactions. The procedure developed provides a useful tool for the development of potential ADA inhibitors. The biological evaluation of the products prepared is currently under investigation.

2   Synthesis of Terphenyls from fluorinated Bromobenzenes by Site Selective Suzuki-Miyaura Reactions

2.1   General Introduction

The maturity of environmentally pleasant and economical reactions for the formation of carbon-carbon and carbon-heteroatom bonds is of great curiosity for the chemist. This tactic provides a simple route for the formation of different complex molecules from simple starting materials. Until now, different methodologies have been used by the chemist for making carbon-carbon bonds. Since the discovery of metal-catalyzed cross-coupling reactions, a variety of metals have proven to be productive in organic synthesis. The Grignard, Diels–Alder, and Wittig reaction have been of immense use in this regard in the last century. But for the last few decades transition metal-catalyzed reactions, particularly palladium(0)-catalyzed transformations, have gained considerable value for carbon-carbon bond formation and many new ideas have been tested and realized.[24] At present, these reactions are being used for the synthesis of a number of natural products, pharmaceuticals and advanced materials.[25-27] The most commonly applied palladium-catalyzed carbon–carbon bond forming reactions in total synthesis are, namely, the Heck,[28] Stille,[29] Suzuki,[30] Sonogashira,[31] Tsuji–Trost,[32] and the Negishi[33] reaction. The mechanisms of these reactions are similar. The first step is usually the oxidative addition of organic halides or triflates to the Pd(0) complex to form organopalladium halides. The following step is, in case of the Suzuki, Sonogashira and Stille reaction, often a transmetalation with nucleophilic compounds to give a diorganopalladium complex. This complex undergoes a reductive elimination to a create carbon-carbon bond and regeneration of the catalyst.

The Suzuki-Miyaura reactions have gained much implications for its usefulness for the cross-coupling between halides and organoboronic acids.[34] Advancements made in this field include the development of new catalysts and modern methods which have greatly increased the scope of this reaction and are now considered to be a quite general procedure for a ample range of selective carbon-carbon bond formations.[35] The scope of the reaction partners is not only restricted to arenes, but includes also alkyl, alkenyl and alkynyl compounds.

The mechanism of the Suzuki reaction involves the oxidative addition of organic halides or triflates to the Pd(0) complex to form an organopalladium halide (R^1-Pd(II)-X). This step is followed by transmetallation with a boronic acid derivative or a borane to give a diorganopalladium complex (R^1-Pd-R^2). This complex undergoes a reductive elimination with carbon-carbon bond formation and regeneration of the catalyst.[36-39] The reactivity order of aryl halides and aryl triflates, which act as electrophiles, is Ar-I > Ar-Br > Ar-OTf > Ar-Cl. The use of base accelerates the transmetalation. This is due to the increase of the carbanion character of the organoborane moiety by formation of an organoborate containing a tetravalent boron atom. The selection of a proper catalyst plays an important role in the success of the desired reaction. The common palladium sources employed include, for example, $Pd(OAc)_2$, $PdCl_2$, $Ph(PPh_3)_2Cl_2$, and $Pd(dba)_2$. The use of bulky electron-rich ligands is often the key for a successful transformation. The ferrocenylphosphine,[40] *N*-heterocyclic carbenes,[41] $P(tBu)_3$,[42] $P(Cy)_3$ often give good yields.

Suzuki-Miyaura reactions[43] are very attractive, due to the stability of the precursors, boronic acids, and facility of work up. In this reaction even an alkyl group (i.e. sp^3-hybridized C atom), as opposed to the more traditionally used vinyl or aryl groups, can be transferred from the organoborane component during the palladium-catalyzed coupling process with vinyl or aryl halides or triflates. Compared to Stille reactions[44], Suzuki–Miyaura couplings have a much broader scope in a potentially vast range of alkyl boranes (typically prepared through the regio- and chemoselective hydroboration of readily available alkene precursors) which can be employed in the reaction.[45] The interest of the chemist in this field is evident from the continuous developments in the use of new reaction conditions, catalysts and ligands.[46-48]

2.1.1 Introduction

It has become evident that fluorinated compounds have a significant record in medicinal chemistry and will play a continuing role in providing lead compounds for therapeutic applications. Small molecule natural products have had a significant impact on drug development. The taxoids, the Vinca alkaloids, the etoposides or the anthracyclines are illustrative examples of the utility of natural sources in clinically based oncology. Considering that organofluorine compounds are virtually absent as natural products, it is interesting to

question why 20–25% of drugs in the pharmaceutical pipeline contain at least one fluorine atom. One of the earliest synthetic fluorinated drugs is the antineoplastic agent 5-fluorouracil, an antimetabolite first synthesised in 1957.[49] It shows high anticancer activity by inhibiting the enzyme thymidylate synthase, thereby preventing the cellular synthesis of thymidine. Since the advent of 5-fluorouracil, fluorine substitution is commonly used in contemporary medicinal chemistry to improve metabolic stability, bioavailability and protein–ligand interactions. Fast progress in this area is fuelled by the development of new fluorinating reagents and fluorination processes increasing the range of synthetic fluorinated building blocks amenable to functional group manipulation. The strategic use of fluorine substitution in drug design has culminated with the production of some of the keydrugs available on the market. These include Fluoxetine [antidepressant], Faslodex [anticancer], Flurithromycin [antibacterial] and Efavirenz [antiviral], four drugs that we have selected to illustrate the wide range of disease areas benefiting from fluorine chemistry and, from a molecular point of view, the structural diversity of the fluorinated component.[50-55] Rapid progress in this area has been fuelled by the development of new fluorination processes increasing the range of synthetic fluorinated building blocks acquiescent to functional group manipulation. The strategic use of fluorine substitution in drug design has culminated with the production of some of the key drugs available in the market.[56]

The site-selectivity of these reactions is generally influenced by electronic and steric parameters.[57] Our research group has already reported site-selective Suzuki-Miyaura (S-M) reactions of tetrabrominated thiophene, *N*-methylpyrrole, selenophene, and of other polyhalogenated heterocycles.[58] Site-selective S-M reactions of the bis(triflate) of methyl 2,5-dihydroxybenzoate have also been studied.[59] Site-selective palladium(0)-catalyzed cross-coupling reactions of dibromides, diiodides or bis(triflates) of fluorinated arenes have, to the best of our knowledge, not been reported to date.

My colleague Dr. Muhammad Sharif Akbar started in the Langer group a project related to site selective Suzuki-Miyaura reactions of fluorinated benzenes (Muhammad Sharif, Ph.D thesis, University of Rostock, 2011). He studied 1,2-dibromo-3,5-difluorobenzene,[60] 1,4-dibromo-2-fluorobenzene[61] and 1,3-dibromo-4-fluorobenzene derivatives in these reactions. In this chapter, I have discussed my results related to Suzuki-Miyaura reactions of fluorinated dibromobenzenes. The products, biphenyl- and triphenyl, were prepared in good to excellent

yields. The methodology discussed in this chapter provided a straightforward way to a variety of fluoro-substituted bi- and triphenyls which, by other methods, are not provided to date.

2.2   Results and discussion

2.2.1   Synthesis of fluorinated meta-terphenyls by site-selective Suzuki reactions of 1,3-dibromo-4-fluorobenzene

In the following section, first results of my study related to Suzuki-Miyaura (S–M) reactions of 1,3-dibromo-4-fluorobenzene are reported. The products, fluorinated *meta*-terphenyls, are not readily available by other methods. The S–M reaction of commercially available 1,3-dibromo-4-fluorobenzene **16** with two equivalents of arylboronic acids **17b,d,g,h** (Table 4) afforded the difluorinated *meta*-terphenyls **18a-d** in moderate to good yields (Scheme 7, Table 5). The best yields were obtained using 2.2 equivalents of the arylboronic acid, Pd(PPh$_3$)$_4$ (0.03 equiv) as the catalyst, and Cs$_2$CO$_3$ (2.2 equiv) as the base (1,4-dioxane, 90 °C, 8 h)

Table 4. Aryl boronic acids

17	Ar-B(OH)$_2$ Ar	17	Ar-B(OH)$_2$ Ar
a	C$_6$H$_5$	i	4-(Vinyl)C$_6$H$_4$
b	4-MeC$_6$H$_4$	j	3-ClC$_6$H$_4$
c	3-MeC$_6$H$_4$	k	4-ClC$_6$H$_4$
d	4-(MeO)C$_6$H$_4$	l	4-FC$_6$H$_4$
e	2-(MeO)C$_6$H$_4$	m	4-BrC$_6$H$_4$
f	2,3-(MeO)$_2$C$_6$H$_3$	n	4-(Acetyl)C$_6$H$_4$
g	2,5-(MeO)$_2$C$_6$H$_3$	o	4-(CF$_3$)C$_6$H$_4$
h	4-EtC$_6$H$_4$		
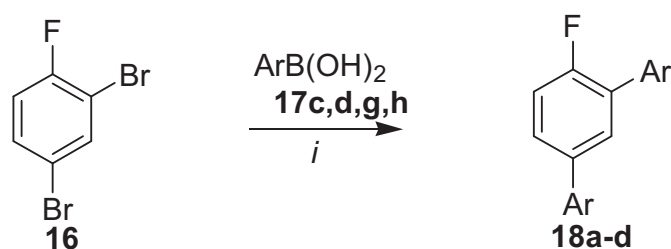
Scheme 7. Synthesis of **18a-d**. *Reagents and conditions*: *i*, **16** (1.0 equiv), **17c,d,g,h** (2.2 equiv), Cs$_2$CO$_3$ (2.2 equiv), Pd(PPh$_3$)$_4$ (3 mol%), 1,4-dioxane, 90 °C, 8 h.

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

17	18	Ar	Yields of **18** (%)[a]
c	a	3-MeC$_6$H$_4$	57
d	b	4-MeOC$_6$H$_4$	70
g	c	2,5-(MeO)$_2$C$_6$H$_3$	65
h	d	4-EtC$_6$H$_4$	57

[a]Yields of isolated products

The S–M reaction of **16** with arylboronic acids **17d,h** (1.0 equiv) afforded the 3-bromo-4-fluoro-biphenyls **19a,b** in good yields and with very good site selectivity (Scheme 8, Table 6). The formation of the opposite regioisomer was not observed.
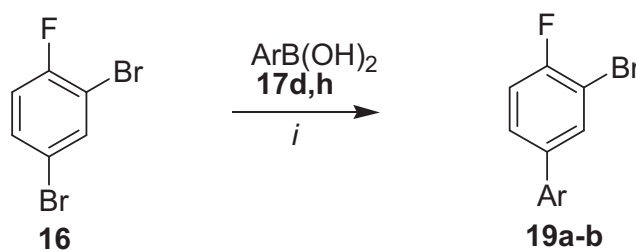
Scheme 8. Synthesis of **19a–b**. *Reagents and conditions*: *i*, **16** (1.0 equiv), **17d,h** (1.0 equiv), Cs$_2$CO$_3$ (1.5 equiv), Pd(PPh$_3$)$_4$ (3 mol%), 1,4-dioxane, 90 °C, 9 h.

Table 6. Synthesis of **19a-b**

17	19	Ar	Yields of **19** (%)[a]
d	a	4-(MeO)C$_6$H$_4$	70
h	b	4-EtC$_6$H$_4$	63

[a]Yields of isolated products

The one-pot reaction of 1,3-dibromo-4-fluorobenzene with two different arylboronic acids afforded the unsymmetrical difluorinated *meta*-terphenyls **20a** containing two different terminal aryl groups (Scheme 9, Table 7)
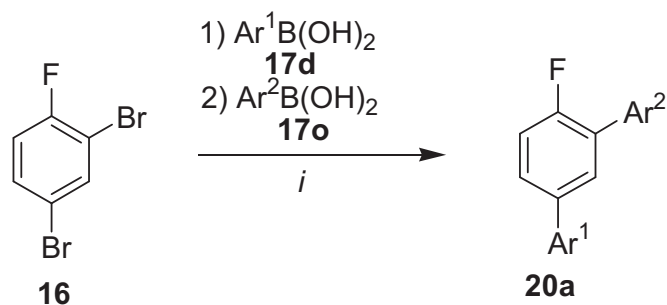
Scheme 9. One-pot synthesis of **20a**. *Reagents and conditions: i,* **16** (1.0 equiv), **17d** (1.0 equiv), Cs_2CO_3 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol%), 1,4-dioxane, **17o** (1.2 equiv), Cs_2CO_3 (1.5 equiv), 90 °C, 8 h.

Table 7. Synthesis of **20a**

17	20	Ar^1	Ar^2	Yield of **20** (%)[a]
o,d	a	4-CF$_3$C$_6$H$_4$	4-(MeO)C$_6$H$_4$	58

[a]Yields of isolated products

The structures of all products were established by spectroscopic methods. The structure of compound **19b** has also been confirmed by 2D NMR (NOESY) (Figure 8).
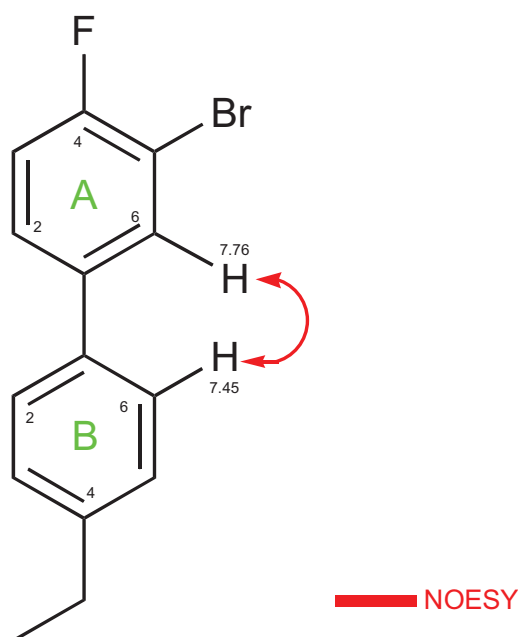
Figure 8. 2D NMR (NOESY) of compound **19b.**

Hydrogen H-6 of the ring B resonating at δ = 7.45 ppm showed a clear and important NOESY correlation with hydrogen H-2 of ring A resonating at δ = 7.76 ppm. This proved the connectivtity of the aryl group located at C-1 of ring A. Moreover, H-2 and H-6 of ring B did not show any signal or connectivity with F.

2.2.2 One pot synthesis of fluorinated terphenyls by Suzuki-Miyaura reactions of 1,4-dibromo-2-flourobenzene

The S–M reaction of commercially available 1,4-dibromo-2-fluorobenzene **21** with 2 equiv. of arylboronic acids **17g,h,j** afforded the fluorinated para-terphenyls **22a–c** in moderate to good yields (Scheme 10, Table 8). The best yields were obtained using 2.2 equiv. of the arylboronic acid, Pd(PPh$_3$)$_4$ (0.03 equiv) as the catalyst and Cs$_2$CO$_3$ (2.2 equiv) as the base (1,4-dioxane, 100 °C, 8 h).
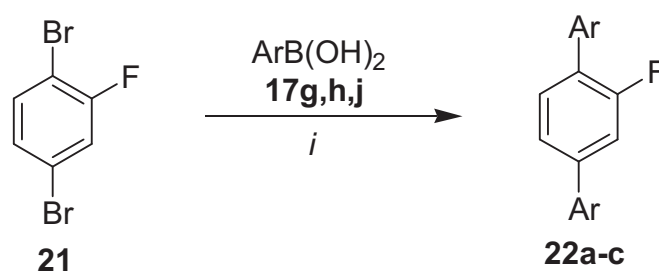
Scheme 10. Synthesis of **22a–c**. *Conditions*: (*i*) **21** (1.0 equiv), **17g,h,j** (2.2 equiv), Cs$_2$CO$_3$ (2.2 equiv), Pd(PPh$_3$)$_4$ (3 mol %), 1,4-dioxane, 100 °C, 6–8 h.

Table 8. Synthesis of **22a-c**

17	22	Ar	Yields of 22 (%)[a]
g	a	2,5-(MeO)$_2$C$_6$H$_3$	76
h	b	4-EtC$_6$H$_4$	81
j	c	3-ClC$_6$H$_4$	80

[a]Yields of isolated products

The one-pot reaction of 1,4-dibromo-2-fluorobenzene **21** with two different arylboronic acids afforded the unsymmetrical fluorinated *para*-terphenyls **23a–c** containing two different terminal aryl groups (Scheme 11, Table 9).
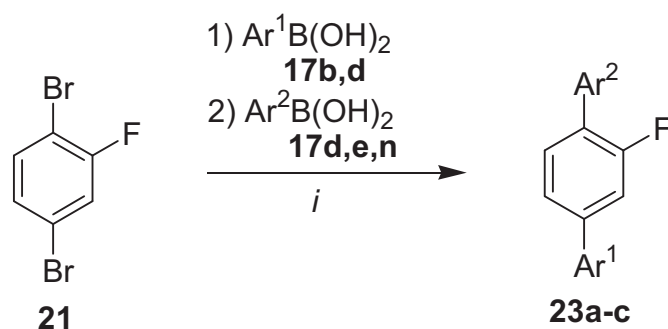
Scheme 11. One-pot synthesis of **23a-c**. *Conditions:*1) **21** (1.0 equiv.), **17b,d** (1.0 equiv.), Cs$_2$CO$_3$ (1.5 equiv.), Pd(PPh$_3$)$_4$ (3 mol-%), 1,4-dioxane, **17d,e,n** (1.2 equiv.), Cs$_2$CO$_3$ (1. 5 equiv.), 90 °C, 8 h.

Table 9. Synthesis of **23a-c**

17	23	Ar^1	Ar^2	Yields of **23** (%)[a]
b,d	**a**	4-MeC$_6$H$_3$	4-(MeO)C$_6$H4	62
b,n	**b**	4-MeC$_6$H$_4$	4-(Acetyl)C$_6$H4	79
d,e	**c**	4-(MeO)C$_6$H$_4$	2-(MeO)C$_6$H$_4$	64

[a]Yields of isolated products

The yields of products **22a–c** are in good range as compared to the yields of products **23a-c** because there was no problem of site-selectivity. Inspection of the NMR spectra of the crude products **23a–c** (before purification) shows that a small amount of mono-coupling and double-coupling product (containing two Ar^1 groups) is present in most cases. We also believe that the chromatographic purification also has a great influence on the yield, due to some loss of material. For all reactions, only one chromatographic purification has to be carried out.

2.2.3. Synthesis of fluorinated terphenyls by Suzuki- Miyura reactions of 1,2-dibromo-4-flourobenzene

The S–M reaction of commercially available 1,2-dibromo-4-fluorobenzene **24** with two equivalents of arylboronic acids **17a,b,d,e,f,i** afforded the monofluorinated *meta*-terphenyls **25a–f** in moderate to good yields (Scheme 12, Table 10). The best yields were obtained using

2.2 equivalents of the arylboronic acid, Pd(PPh$_3$)$_4$ (3 mol %) as the catalyst, and Cs$_2$CO$_3$ (2.2 equiv) as the base (1,4-dioxane, 90 °C, 6-8 h).
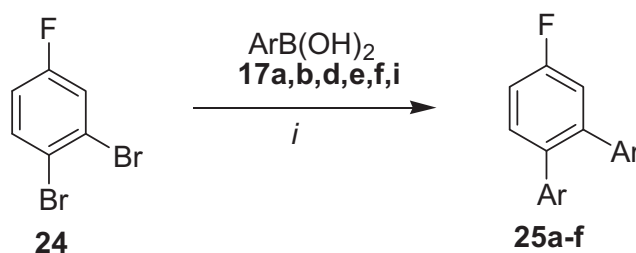
Scheme 12. Synthesis of **25a–f**. *Conditions*: (*i*) **24** (1.0 equiv), **17a,b,d,e,f,i** (2.2 equiv), Cs$_2$CO$_3$ (2.2 equiv), Pd(PPh$_3$)$_4$ (3 mol %), 1,4-dioxane, 90 °C, 6–8 h

Table 10. Synthesis of **25a-f**

17	25	Ar	Yields of **25**(%)[a]
a	a	C$_6$H$_5$	55
b	b	4-MeC$_6$H$_4$	62
d	c	4-(MeO)C$_6$H$_4$	60
e	d	2-(MeO)C$_6$H$_4$	70
f	e	2,3-(MeO)$_2$C$_6$H$_3$	45
i	f	4-(Vinyl)C$_6$H$_4$	48

[a]Yields of isolated products

2.3   Conclusion

The site-selective formation of **19a–b** can be explained by steric and electronic reasons. The first attack of palladium(0)-catalyzed cross-coupling reactions generally occurs at the more electronic deficient and sterically less hindered position.[62,63] Position 1 of 1,3-dibromo-4-fluorobenzene (**16**) is sterically less hindered because it is located next to hydrogen atoms while position 3 is located next to a fluorine atom (Figure 9). In addition, position 1 (located *para* to the fluorine atom) is more electron deficient than position 3 (located *ortho* to the fluorine atoms), due to the pi-donating effect of the fluorine atom (Fig. 8). In fact, the ^{1}H NMR signals of aromatic protons located *ortho* to a fluorine atom are generally shifted to higher field compared to the proton located in *para* position.

more sterically hindered
less electron-deficient

F
Br

Br

16

less sterically hindered
more electron-deficient
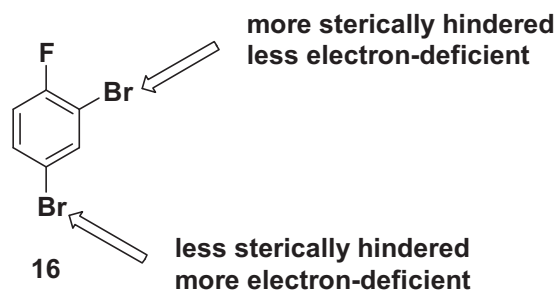
Figure 9. possible explanations for the site selectivity of cross coupling reactions of **16**

Similarly, in case of 1,4-dibromo-2-fluorobenzene the first attack of palladium(0)-catalyzed cross-coupling reactions generally occurs at the more electronic deficient and sterically less hindered position.[62,63] Position 4 of 1,4-dibromo-2-fluorobenzene (**21**) is sterically less hindered than position 1 because it is located next to hydrogen atoms while position 1 is sterically more hindered as it is located next to a fluorine atom (Figure 10). In addition, position 1 (located *ortho* to the fluorine atom) is less electron deficient than position 4 (located *meta* to the fluorine atoms), due to the pi-donating effect of the fluorine atom. In fact, the ^{1}H NMR signals of aromatic protons located *ortho* to a fluorine atom are generally shifted to higher field compared to the proton located in *meta* position. The site-selective Suzuki-Miyaura reactions of 1,4-dibromo-2-fluorobenzene has already been studied which provide a convenient approach to fluorinated terphenyls and biaryls.[61]

more sterically hindered
less electron-deficient

Br
F

Br

less sterically hindered
more electron-deficient

21
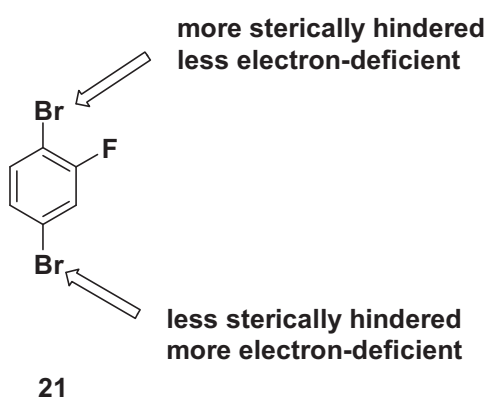
Figure 10. Possible explanations for the site selectivity of cross coupling reactions of **21**

3 Synthesis of fluorinated polyethynylbenzenes by Sonogashira reactions

3.1 Introduction

The Sonogashira coupling reactions of terminal acetylenes with aryl and vinyl halides provides a powerful method for synthesizing conjugated alkynes, an important class of molecules that have found applications in diverse areas ranging from natural product chemistry to materials science. In recent years, much attention has been dedicated to polyethynylated carbon rich molecules, because of their potential use as liquid crystals,[64] non linear optical materials,[65] light-harvesting materials,[66] and building blocks for two-dimensional carbon net works.[67,68] In particular, D_{6h}-symmetric hexaethynylbenzenes and related compounds have been used as core structures for dendritic materials,[69] and functional dyes.[70] Recently, hexaethynylbenzene derivatives have also been employed for constructing supramolecular architectures[71] and reported as potential nonlinear optical materials for two-photon absorption (TPA) and third-order optical nonlinearity.[72] A variety of functionalized hexa(arylethynyl)benzenes have been synthesized by different groups up till now.[73] The independent approaches to the differentially substituted hexaethynylbenzenes of C_{2v} symmetry, based on the Diels−Alder reactions of tetraethynylcyclopentadienones, have already been reported.[74] A method for the synthesis of hexaethynylbenzenes of D_{3h} symmetry was also developed by Rubin.[75] In recent years, Anthony reported the synthesis of a D_{2h} symmetric hexaethynylbenzene from tetrabromobenzoquinone.[76]

Due to the interesting physicochemical properties, hydrocarbons containing multiple alkenyl groups have received considerable attention as they are used as synthetic building blocks of new and interesting arenes, and also owing to their aesthetic attraction. For instance, Vollhardt and coworkers reported the synthesis and characterization of hexaethynylbenzenes and its applications to the first synthesis of archemedanes containing benzene and cyclobutane moieties.[77] In contrast to the general hydrocarbon counterparts, fluorinated multiple alkynylated arenes have not been yet reported. Fluorinated compounds constitute an important class of natural products and various synthetic drugs have come to the market and constitute approx. 20% all pharmaceuticals,[78] with even higher figures for agrochemicals (up to 30%).[79] Some of the key drugs available in the market have been culminated with the strategic use of fluorine substitution in drug design. The synthesis of difluoro*tetra*alkynylbenzenes **A, B, C**

and fluoro*penta*alkynylbenzenes **D** has, to the best my knowledge, not been reported to date (Scheme A).
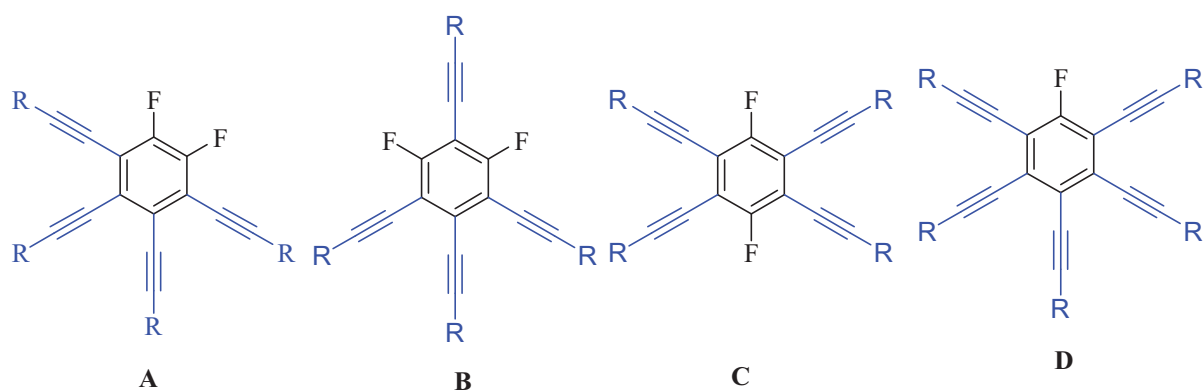
Scheme A. Molecules with multiple alkynyl groups

In biological and material sciences, light emitting materials are mostly applied. Organic systems with a high degree of conjugation have significant applications in various fields, such as LC (liquid crystals), OLED (organic light emitting devices), FET (field effect transistors), 3D-optical memory devices and photovoltaic cells.[80] The extended π-systems often brings extraordinary electronic and optical changes to the compounds. These changes may result in liquid crystalline and fluorescence properties.[81] In this chapter, I have synthesized and optimized the reaction conditions to achieve a convenient synthesis of Sonogashira products of monofluoro penta(arylethynyl)benzenes and 1,2-, 1,3-, 1,4-difluorotetra(aryl)benzenes and I have studied their UV-Vis and fluorescence properties.

3.2 Results and Discussion

As a part of my research project on the construction of extended π-electronic systems, I designed to develop an efficient synthesis of fluoropenta(arylethynyl)benzenes and difluorotetra(arylethynyl)benzene derivatives from polyhalogenated benzenes using the Sonogashira coupling reaction as the essential step. In this context, I report herein the efficient synthesis of polyethynyl-substituted aromatic compounds **34a-c** and the same protocol was applied to the differentially substituted tetraarylethynylbenzenes, **28a-c, 30a-c,** and **32a-d** prepared from difluoroiodobenzenes by combination with **27a-f.**

The Sonogashira reaction of **26, 29, 31, 32** with different substituted arylacetylenes **27a-f** (6 equiv) afforded the 1,2-difluoro-3,4,5,6-tetra(arylethynyl)benzenes **28a-c** (Scheme 13, Table

11), 1,3-difluoro-3,4,5,6-tetra(arylethynyl)benzenes **30a-c** (Scheme 14, Table 12), 1,4-difluoro-2,3,5,6-tetra(arylethynyl)benzenes **32a-d** (Scheme 15, Table 13), and 1-fluoro-2,3,4,5-penta(arylethynyl)benzenes **34a-c** (Scheme 16, Table 14), in 63-79% yields. During the optimization, Pd(PPh$_3$)$_4$ (10mol-%), Pd(OAc)$_2$ (5 mol-%) in the presence of PCy$_3$ (10 mol-%) were initially employed, but no satisfactory results were obtained. The progress of the reactions were monitored at temperatures of 80-100 °C, as higher temperatures increase the chance of removal of iodine. X-Phos (10 mol%) was found to be the best catalyst. Several solvents were tried, but several of them did not work well, while good yields were obtained when 1,4-dioxane was used. Almost all penta- and tetra-Sonogashira products were obtained in good to excellent yields. All structures were confirmed by spectroscopic analysis.

3.2.1 Synthesis of 1,2-difluoro-3,4,5,6-tetra(arylethynyl)benzenes

The Sonogashira reaction of 1,2-difluoro-3,4,5,6-tetraiodobenzene (**26**) with different substituted alkynes (**27b,e,f**) (6.0 equiv) afforded 1,2-difluoro-3,4,5,6 tetra(arylethynyl)benzenes **28a-c** (Scheme 13, Table 11) in 54-71% yield.
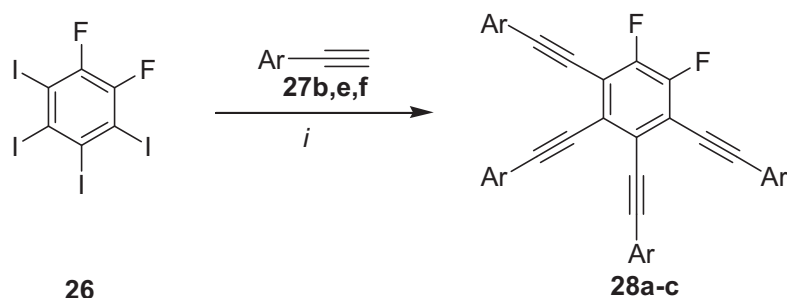
Scheme 13. Synthesis of **28a–c**: (*i*) conditions and reagents: **26** (1.0 eq), **27b,e,f** (6.0 eq), CuI (5 mol %), X-Phos (10 mol %), Pd(OAc)$_2$ (5 mol %), 1,4-Dioxane (5mL), 100 °C, 12 h.

Table 11. Synthesis of **28a-c**

27	28	Ar	Yields (%)[a]
b	a	3-MeC$_6$H$_5$	70
e	b	4-(*n*-Pent)C$_6$H$_4$	71
f	c	4-(*n*-Hept)C$_6$H$_4$	54

[a] Isolated yields

3.2.2   Synthesis of 1,3-difluoro-2,4,5,6-tetra(arylethynyl)benzenes

The Sonogashira reaction of **29** with the substituted acetylenes **27a,d,e** (6.0 equiv.) afforded the 1,3-difluoro-2,4,5,6-tetra(arylethynyl)benzene **30a-c** (Scheme 14, Table 12) in 75-83 % yield.

Scheme 14. Synthesis of **30a-c**: (*i*) conditions and reagents: **29**(1.0 eq), **27a,d,e** (6.0 eq), CuI (5 mol %), X-Phos (10 mol %), Pd(OAc)$_2$ (5 mol %), 1,4-dioxane (5mL) , 100°C, 12 h.

Table 12. Synthesis of **30a-c**

27	30	Ar	Yields (%)[a]
a	a	C$_6$H$_4$	81
d	b	4-(*n*-Bu)C$_6$H$_4$	83
e	c	4-(*n*-Pent)C$_6$H$_4$	75

[a]Isolated yields

3.2.3   Synthesis of 1,4-Difluoro-3,4,5,6-tetra(arylethynyl)benzenes

The Sonogashira reaction of **31** with the substituted acetylenes **27b,c,d,e** (6.0 equiv.) afforded the 1,4-difluoro-2,3,5,6-tetra(arylethynyl)benzenes **32a-d** (Scheme 15, Table 13) in 80-86 % yields.
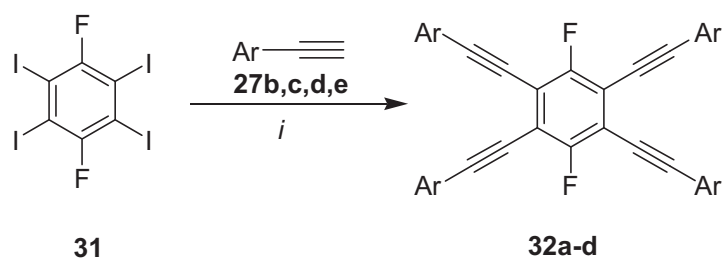
Scheme 15. Synthesis of **32a-d**: (*i*) conditions and reagents: **31** (1.0 eq), **27b,c,d,e** (6.0 eq), CuI (5 mol %), X-Phos (10 mol %), Pd(OAc)$_2$ (5 mol %), 1,4-dioxane (5mL) , 100°C, 12 h.

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

27	32	Ar	Yields (%)[a]
b	a	4-MeC$_6$H$_4$	85
c	b	4-(*n*-Pr)C$_6$H$_4$	86
d	c	4-(*n*-Bu)C$_6$H$_4$	83
e	d	4-(*n*-Pent)C$_6$H$_4$	80

[a] Isolated yields
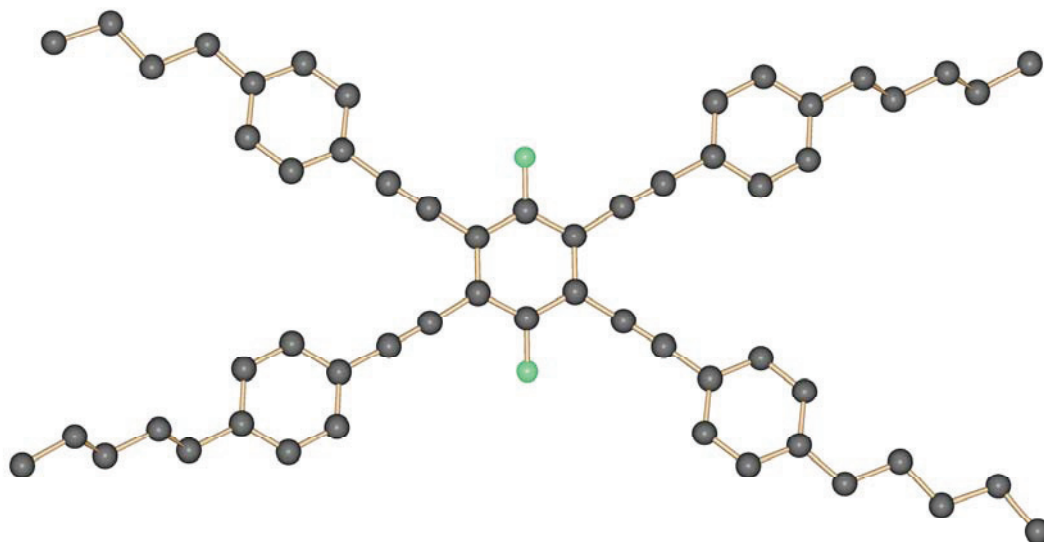
SCHAKAL

Fig 11: Molecular structure of **32d**

3.2.4   Synthesis of 1-fluoro-2,3,4,5,6-penta(arylethynyl)benzenes

The Sonogashira reactions of **33** with the substituted acetylenes **27c,e,f** (6.0 equiv.) afforded the 1-fluoro-2,3,4,5,6-tetra(arylethynyl)benzenes **34a-c** (Scheme 16, Table 14) in 63-79 % yields.
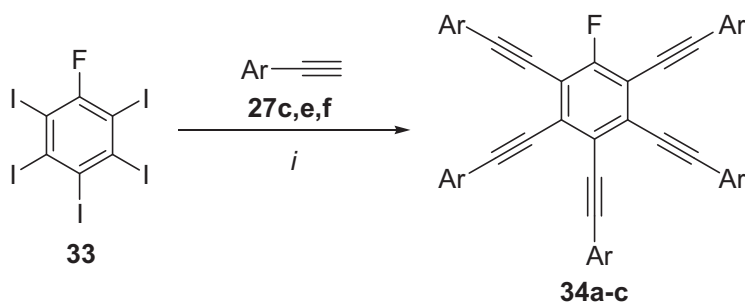
Scheme 16. Synthesis of **34a-c**: (*i*) conditions and reagents: **33** (1.0 eq), **27c,e,f** (6.0 eq), CuI (5 mol %), X-Phos (10 mol %), Pd(OAc)$_2$ (5 mol %), 1,4-dioxane (5mL) , 100°C, 12 h.
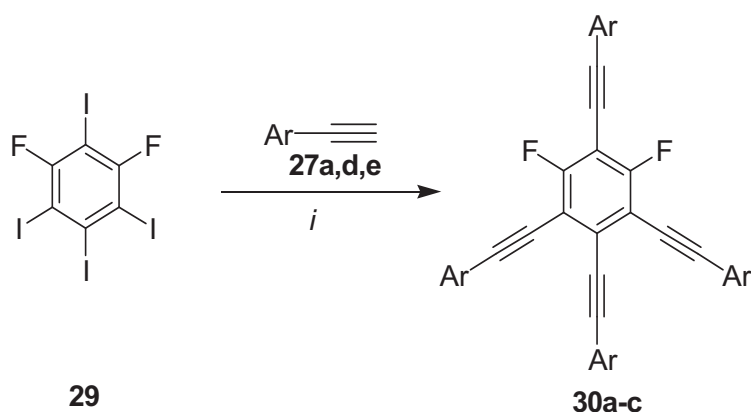
Table 14. Synthesis of **34a-c**

27	34	Ar	Yields (%)
c	a	4-(*n*-Pr)C$_6$H$_4$	74
e	b	4-(*n*-Pent)C$_6$H$_4$	79
f	c	4-(*n*-Hept)C$_6$H$_4$	63

[a] Isolated yields

3.3   The UV-vis and fluorescence properties of the products

The electronic absorption and emission data for compounds **28a-c** (Fig. 12-14), **30a-c** (Fig. 15-17), **32a-d** (Fig. 18-21) and **34a-c** (Fig. 22-24) are listed in Table 15. The spectra were recorded in DCM, typically in the concentration range of 10^{-5}-10^{-6} M. Generally, two to three absorption bands were observed in the region 227-382 nm for all the compounds. The compounds **28a-c** (Fig. 12,13,14) showed well resolved two bands, one at 233 nm for compound **28a** and 229 nm for compounds **28b-c**, all with a shoulder at 255 nm. The second band was observed for these compounds at 320-325 nm with a shoulder at 362-369 nm. The emission maxima were observed at 409 nm and 420 nm and the Stoke's shifts calculated are 99-95. The compounds **30a**, **30c, 32a-b, d** (Fig. 15, 17, 18, 19, 21) showed the absorptions at 227-228 nm with absorption maxima at 305 nm, 314-316 nm. The same compounds **30a**, **30c,**

32a-b,d showed emissions at 400, 410, 409,421 and 419 nm with Stoke's shifts 95, 96, 96, 104 and 103 nm, respectively. On the contrary, the compounds **30b** (Fig. 16) and **32c** (Fig. 20) showed different absorptions as they have a less conjugated substitution pattern. The emission maxima were observed at 359 nm with a shoulder at 370 nm with Stoke's shift at 98 and 70. The compound **32c** showed three bands at 258, 314 nm and 351 nm with shoulders at 227, 301 nm and 333 nm respectively. The emission maxima were observed at 360 nm with a shoulder at 380 nm. The Stoke's shift found in compound **32c** is 102 nm. The compounds **34a-c** (Fig. 22-24) showed very good absorptions and emissions in the range of 227-380 nm and 430-440 nm. The compounds **34a** showed two absorption bands, one at 227 nm and second band at 337 nm with a broad shoulder at 380 nm. While the emission maxima were found to be at 430 nm with Stoke's shift 93. The compounds **34b-c** showed two absorption bands at 228 nm and 337 nm with two shoulders at 260 nm, 259 nm and 378 nm, respectively, the emissions were recorded at 440 nm.

Table 15. Electronic absorption and emission properties

Products	λ_{abs}[nm]	λ_{em}[nm]	Stokes Shift[nm]
28a	233,255,**320**,362	**409**,421	99
28b	229,255,**325**,369	**420**	95
28c	229,255,**325**,368	**420**	95
30a	228,255,**305**,345	**400**,409	95
30b	**251**,260,280,**300**	**359**,370	98,70
30c	228,262,**314**,355	**410**	96
32a	228,**313**,378	**409**	96
32b	228,**317**,382	410,**421**	104
32c	227,**258**,301,314,333,351	**360**,380	102
32d	227,**316**,381	**419**	103
34a	227,**337**,380	**430**	93
34b	228,260,**337**,378	**440**	103
34c	228,259,**337**,378	**440**	103

Absorpion and emission measured in DCM (c = 10^{-5}-10^{-6} M)
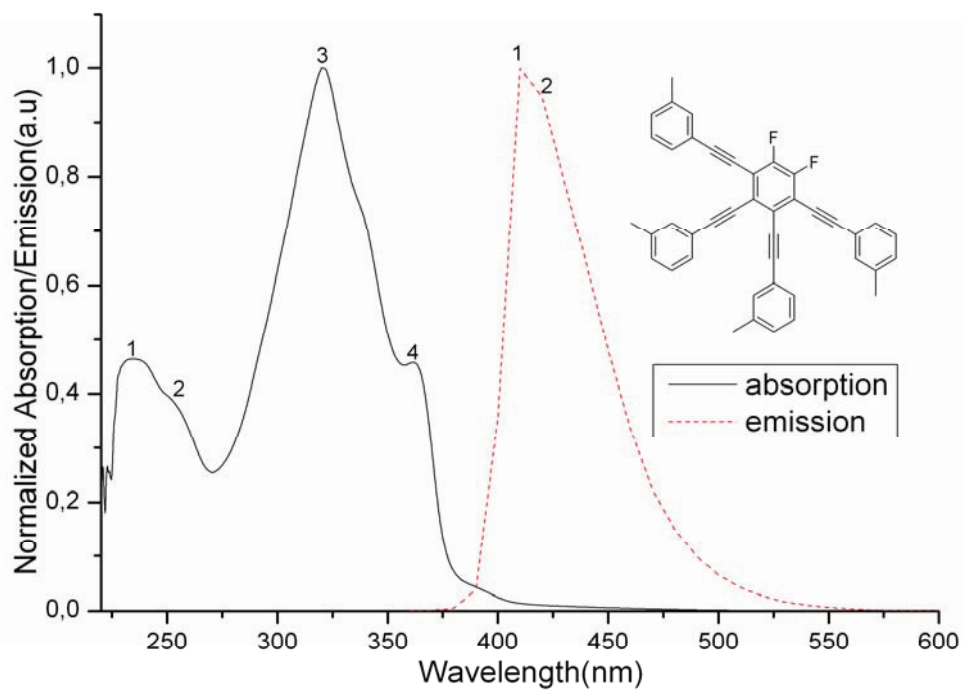
Figure 12. Absorption and emission spectra of compound **28a**
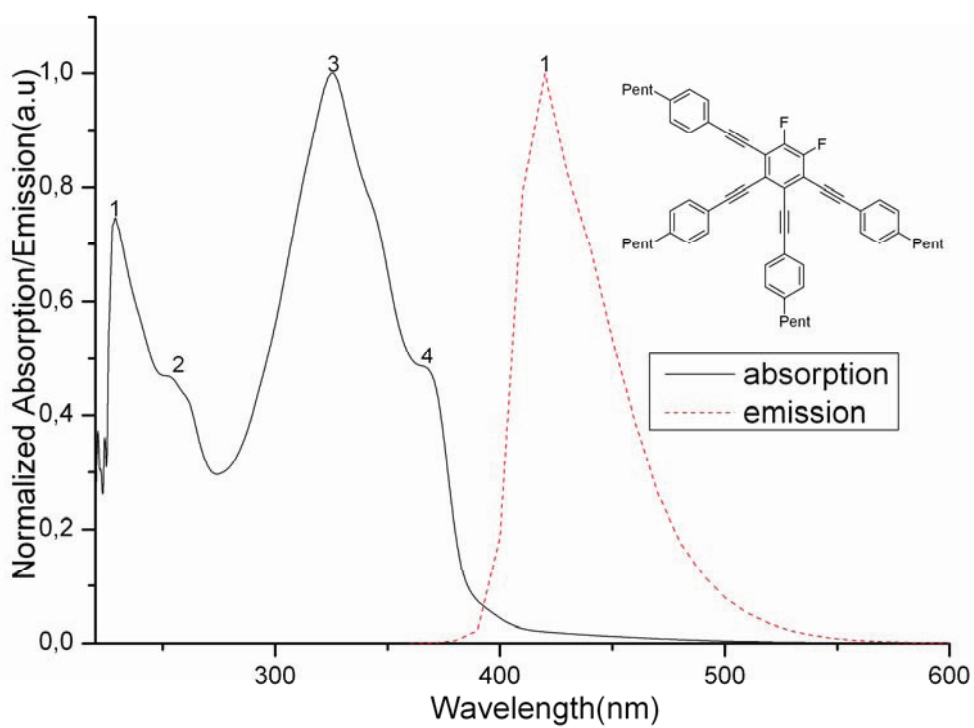
Figure 13. Absorption and emission spectra of compound **28b**
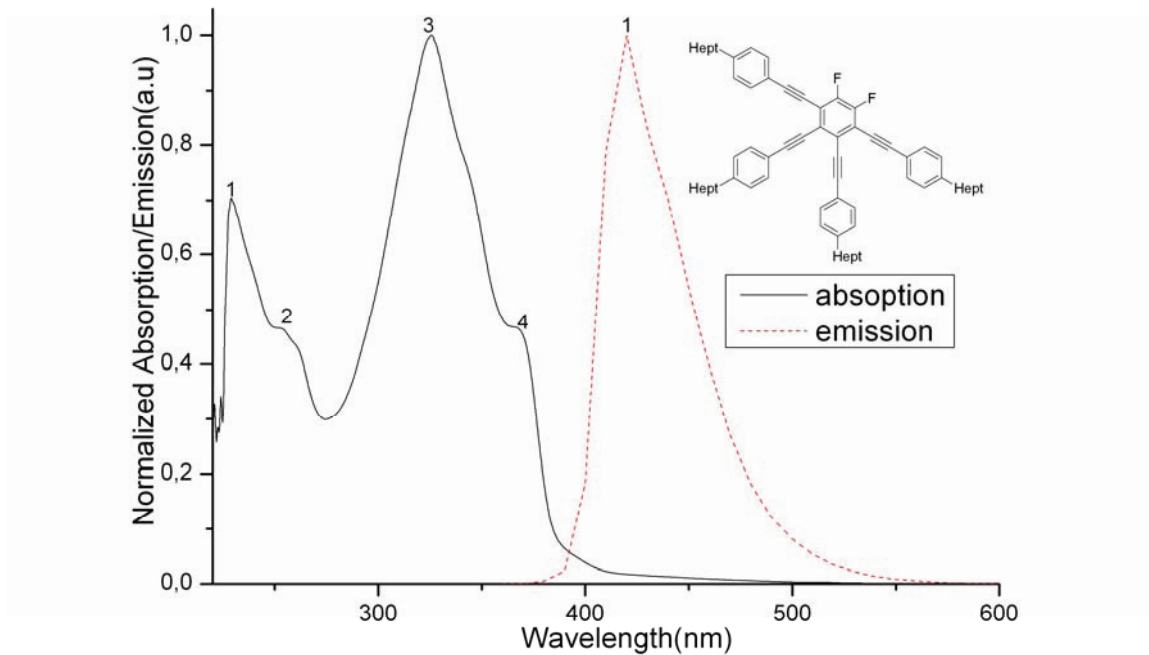
Figure 14. Absorption and emission spectra of compound **28c**
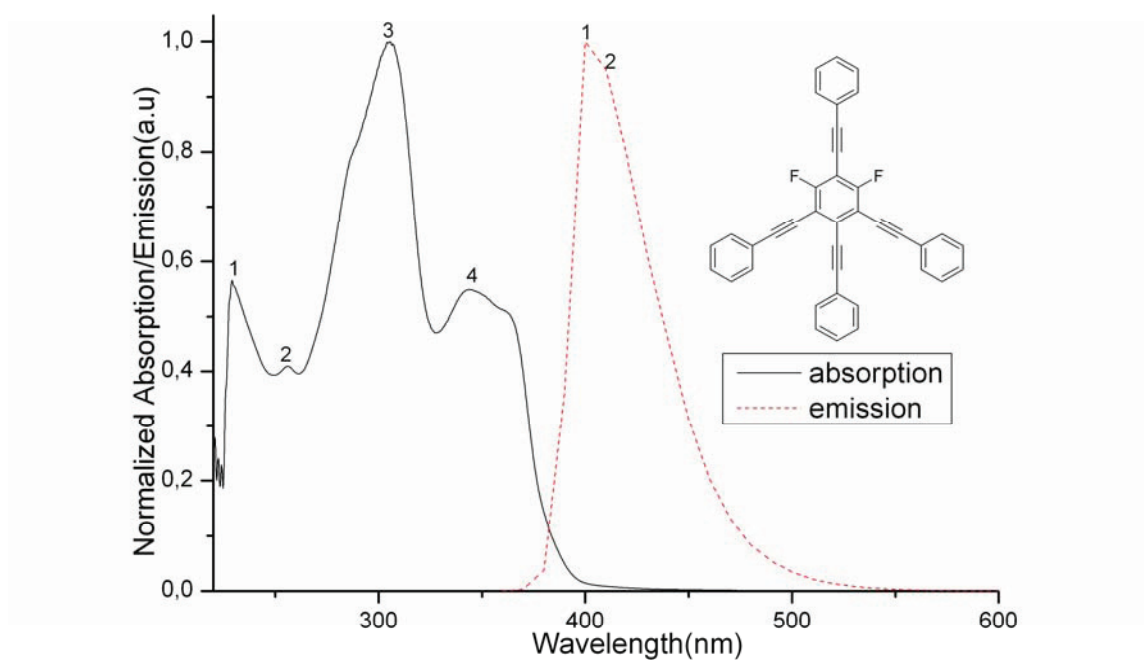
Figure 15. Absorption and emission spectra of compound **30a**
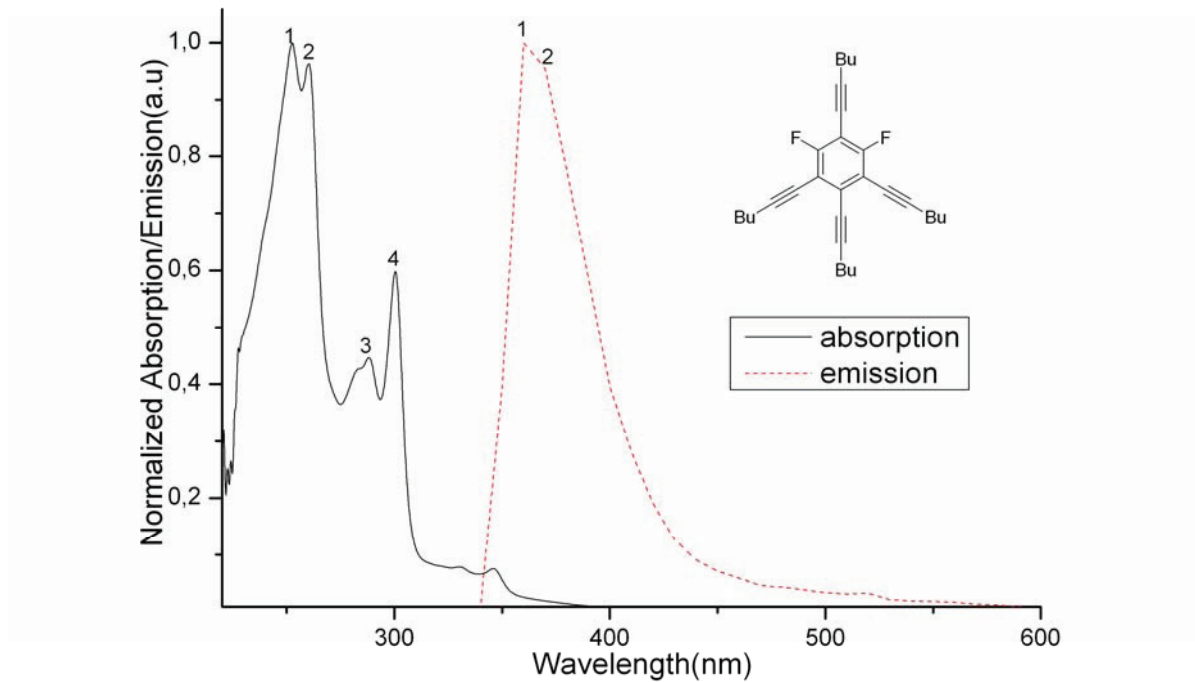
Figure 16. Absorption and emission spectra of compound **30b**
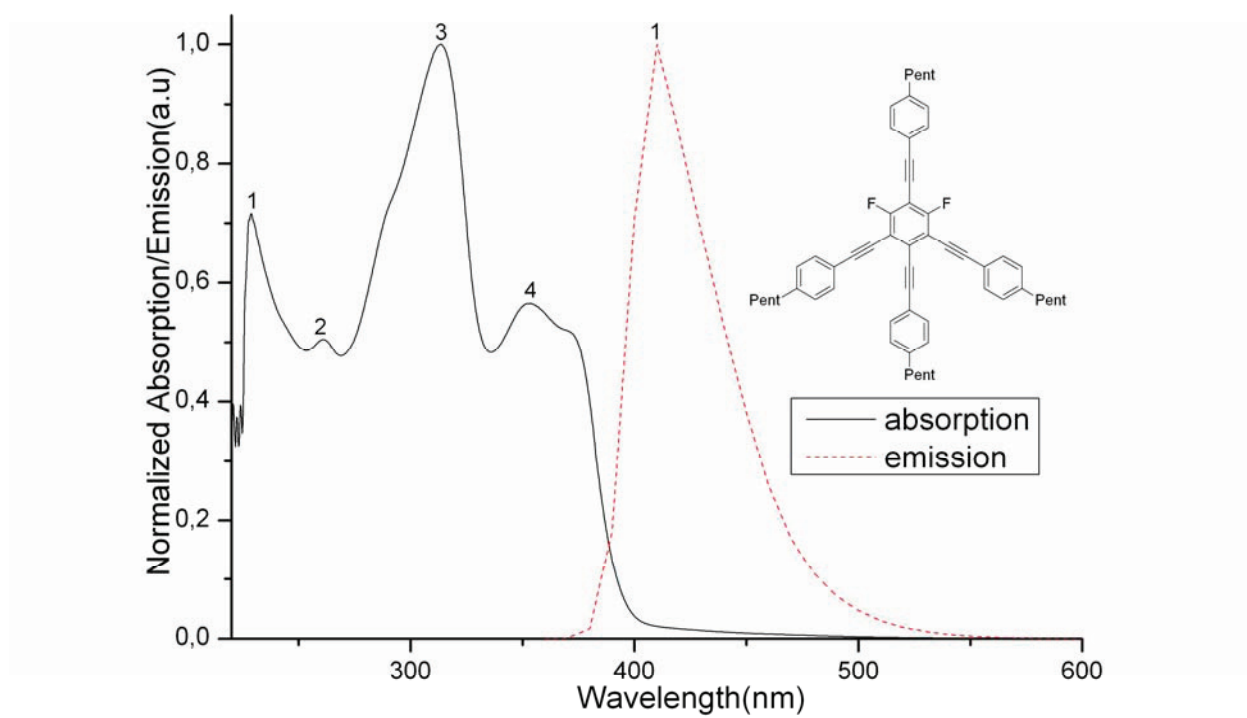
Figure 17. Absorption and emission spectra of compound **30c**
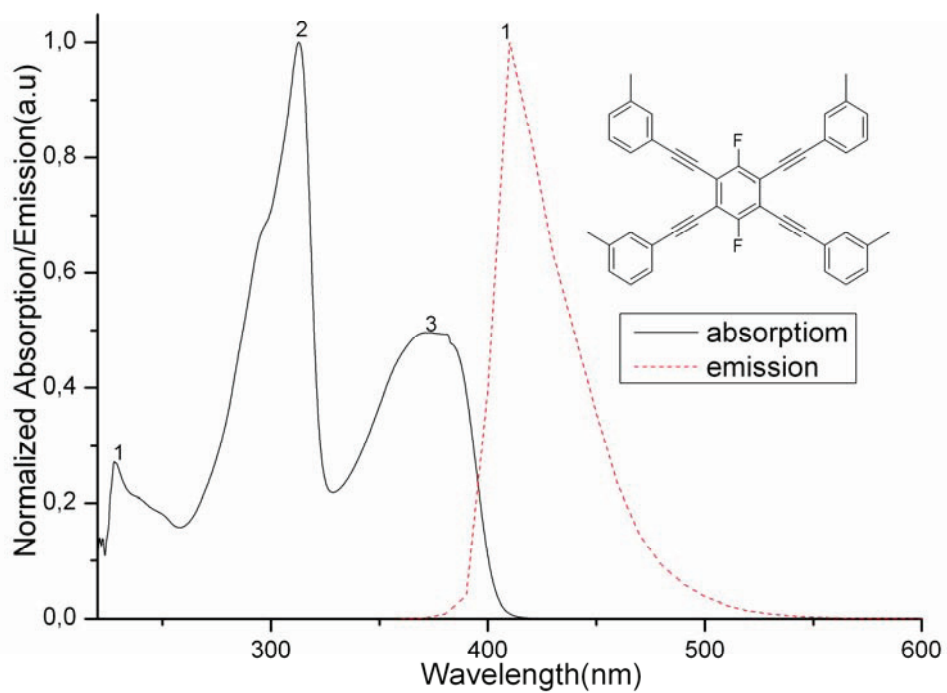
Figure 18. Absorption and emission spectra of compound **32a**
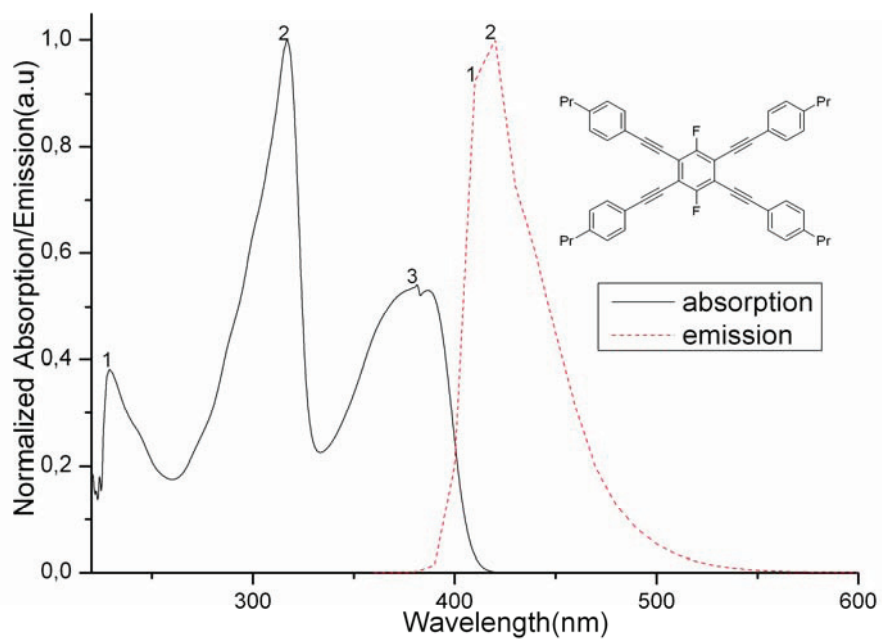
Figure 19. Absorption and emission spectra of compound **32b**
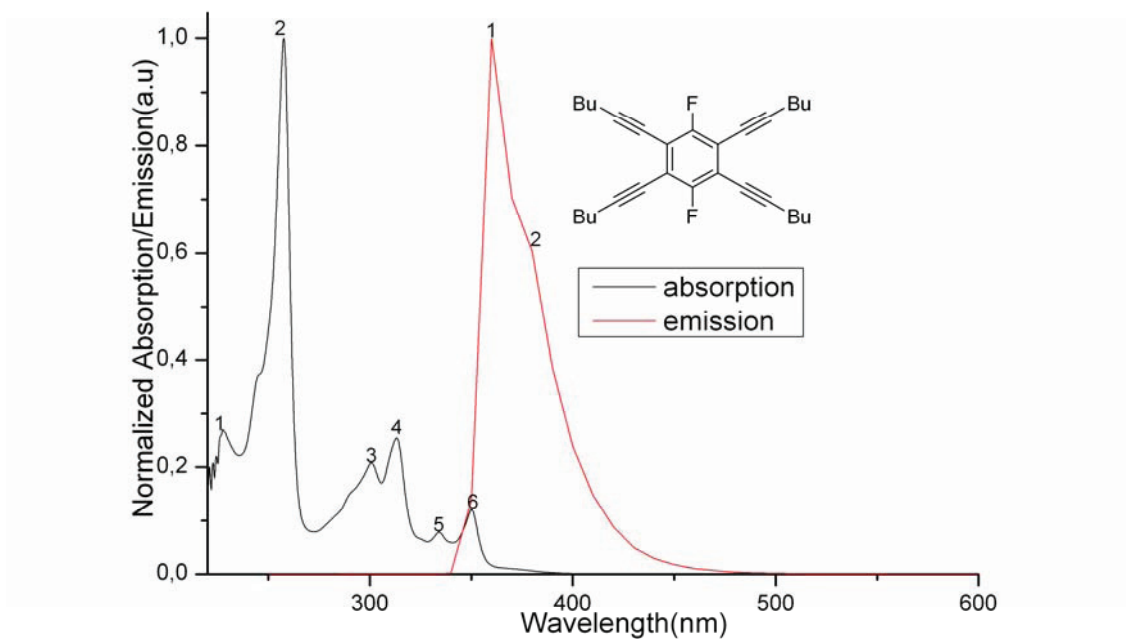
Figure 20. Absorption and emission spectra of compound **32c**
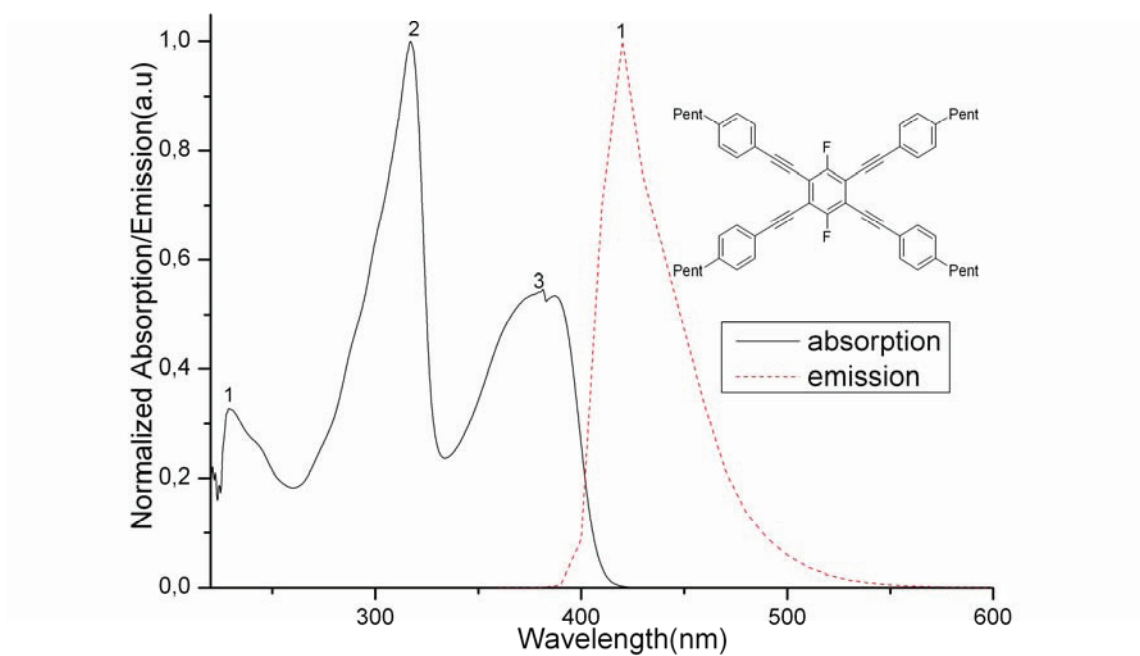
Figure 21. Absorption and emission spectra of compound **32d**
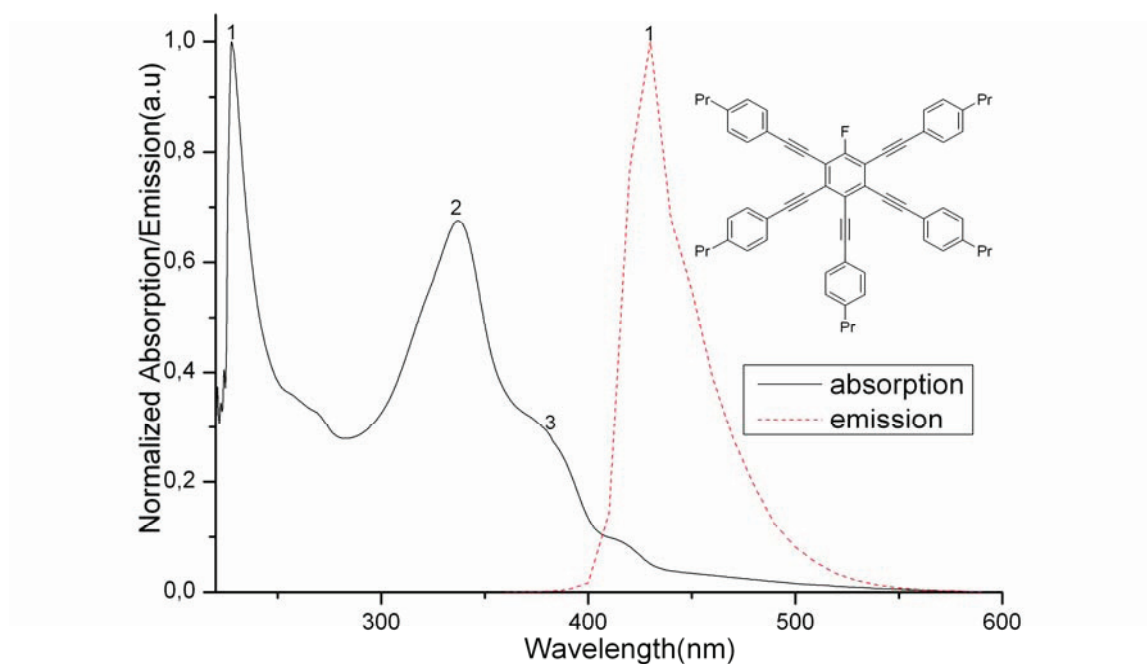
Figure 22. Absorption and emission spectra of compound **34a**
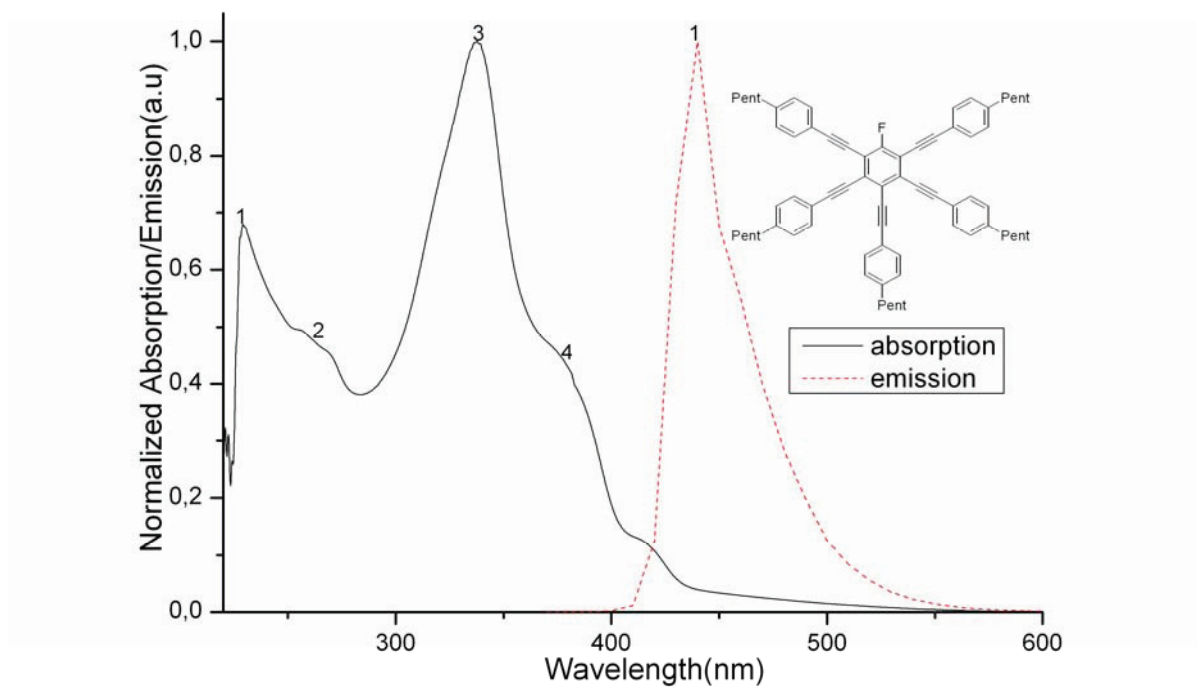
Figure 23. Absorption and emission spectra of compound **34b**
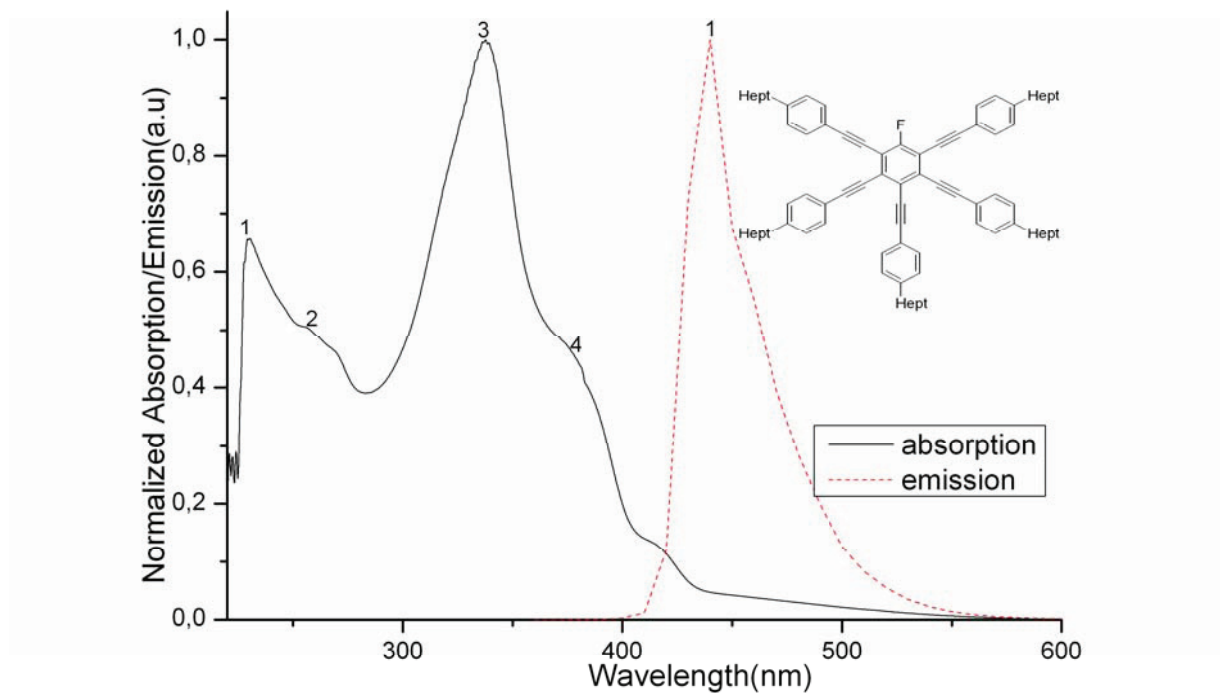
Figure 24. Absorption and emission spectra of compound **34c**

3.4   Conclusion

In   conclusion,   I   have   synthesized   difluorotetra(arylethynyl)benzenes   and monofluoropenta(arylethynyl)benzenes by Sonogashira coupling reactions in good to excellent yields. Sonogashira coupling reactions of tetraiodobenzenes and pentaiodobenzenes provided the corresponding products. All products showed excellent emission properties.

4   Synthesis of fluorinated polyarenes by Suzuki-Miyaura cross coupling reactions

4.1   Introduction

Due to major successes in the synthesis and biological properties of compounds containing fluorine atoms in medicinal chemistry, it may be predicted that day by day the demand of drugs containing fluorine as important constituent will continue to increase in the market. With the discovery of major advancements being carried out in asymmetric fluorination, there is now much further scope for the synthesis of targets containing a fluorine atom on a stereogenic centre. The electronic absorption and emission characteristics of the new functional materials were affected by the nature of the chromophore present. Electroluminescent materials containing differently substituted mono- and difluorinated molecules were synthesized and characterized by IR, NMR, UV-Vis and emission spectroscopic studies. A detailed introduction has been given earlier in chapter 2. Owing to the interesting physicochemical properties, use as synthetic building blocks and because of their aesthetic attraction, hydrocarbons bearing multiple phenyl groups have received considerable attention.

4.2   Results and Discussion

The present research project of my thesis is about the preparation of fluorinated penta and hexaphenyls. I developed an efficient synthesis of fluoropenta(aryl)benzenes and difluorotetra(aryl)benzenes from polyiodinated fluorobenzenes using the Suzuki-Miyaura protocol as an essential step. In this context, I studied the synthesis of polyphenyl-substituted aromatic compounds **35a-b** and the same protocol was applied to different substituted tetra(aryl)benzenes **36a-c, 37a-d,** and **38a-c** prepared from difluorotetraiodobenzenes and monofluoropentaiodobenzenes by combination with arylboronic acids **17c,h,j,k,l,m**.

The Suzuki-Miyaura reaction of **26, 29, 31, 33** with different substituted arylboronic acids (**17c,h,j,k,l,m**) (6 equiv) afforded the 1,2-difluoro-3,4,5,6-tetra(aryl)benzenes **35a-b** (Scheme 17, Table 16), 1,3-difluoro-3,4,5,6-tetra(aryl)benzenes **36a-c** (Scheme 18, Table 17), 1,4-difluoro-2,3,5,6-tetra(aryl)benzenes **37a-d** (Scheme 19, Table 18), and 1-fluoro-2,3,4,5-penta(aryl)benzenes **38a-c** in 58-73% yields (Scheme 20, Table 19).

4.2.1 Synthesis of 1,2-difluoro-3,4,5,6-tetra(aryl)benzenes

The Suzuki-Miyaura reaction of 1,2-difluoro-3,4,5,6-tetraiodobenzene **26** with substituted phenylboronic acids (**17j,l**) resulted in the formation of **35a-b** (Scheme 17, Table 16) in good to excellent yields (76-82%).
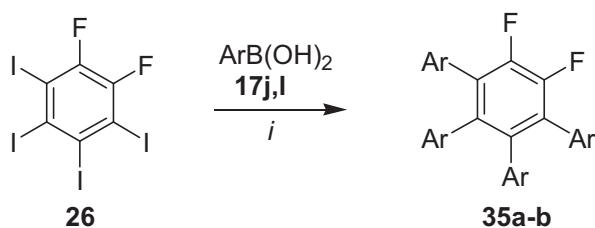
Scheme 17. Synthesis of **35a-b**: conditions and reagents: *i)* **26** (1.0 equiv), **17j,l** (6.0 equiv), Pd(PPh$_3$)$_4$ (10 mol-%), Cs$_2$CO$_3$ (5 equiv), 1,4-dioxane (5 mL), 110°C, 30 h.

Table 16. Synthesis of **35a-b**

17	35	Ar	Yields (%)[a]
j	a	3-ClC$_6$H$_4$	82
l	b	4-FC$_6$H$_4$	76

[a]Isolated yields

4.2.2 Synthesis of 1,3-Difluoro-2,4,5,6-tetra(aryl)benzenes

The Suzuki-Miyaura reaction of 1,3-difluoro-2,4,5,6-tetraiodobenzene (**29**) with substituted phenylboronic acids **17c,k,l** resulted in the formation of **36a-c** (Scheme 18, Table 17) in good to excellent yields (77-88%).
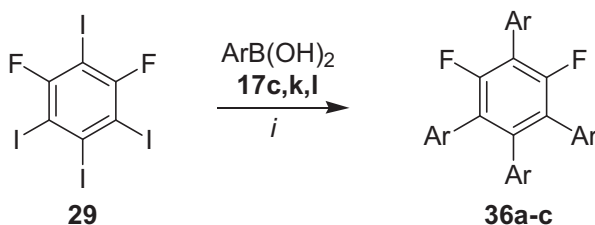
Scheme 18. Synthesis of **36a-c**: conditions and reagents: *i)* **29** (1.0 equiv), **17c,k,l** (6.0 equiv), Pd(PPh$_3$)$_4$ (10 mol-%), Cs$_2$CO$_3$ (5 equiv), 1,4-dioxane (5 mL), 110°C, 31 h

Table 17. Synthesis of **36a-c**

17	36	Ar	Yields(%)^a
c	**a**	3-MeC$_6$H$_4$	78
k	**b**	4-ClC$_6$H$_4$	88
l	**c**	4-FC$_6$H$_4$	77

^{a}Isolated yields

4.2.3 Synthesis of 1,4-Difluoro-2,3,5,6-tetra(aryl)benzenes

The Suzuki-Miyaura reaction of 1,4-difluoro-2,3,5,6-tetraiodobenzenes **31** with substituted phenylboronic acids (**17h,j,l,m**) resulted in the formation of **37a-d** (Scheme 19, Table 18) in good to excellent yields (68-95%).
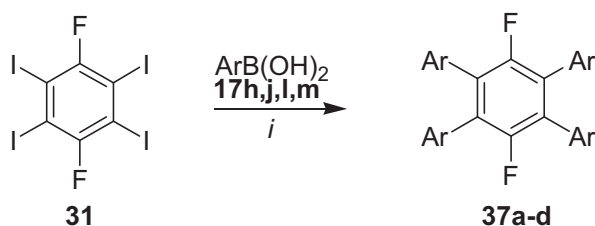
Scheme 19. Synthesis of **37a-d**: conditions and reagents: *i)* **31** (1.0 equiv), **17h,j,l,m** (6.0 equiv), Pd(PPh$_3$)$_4$ (10 mol-%), Cs$_2$CO$_3$ (5 equiv), 1,4-dioxane (5 mL), 90-100°C, 27 h.

Tabe 18. Synthesis of **37a-d**

17	37	Ar	Yields (%)^a
h	**a**	4-EtC$_6$H$_4$	95
j	**b**	3-ClC$_6$H$_4$	83
l	**c**	4-FC$_6$H4	83
m	**d**	4-BrC$_6$H$_4$	68

^{a}Isolated yields

The X-ray measuments for the compound **37d** (Fig. 25) have also been performed which confirmed the structure independently. The aryl substitutents in the crystal structure **37d** were twisted out of plan.
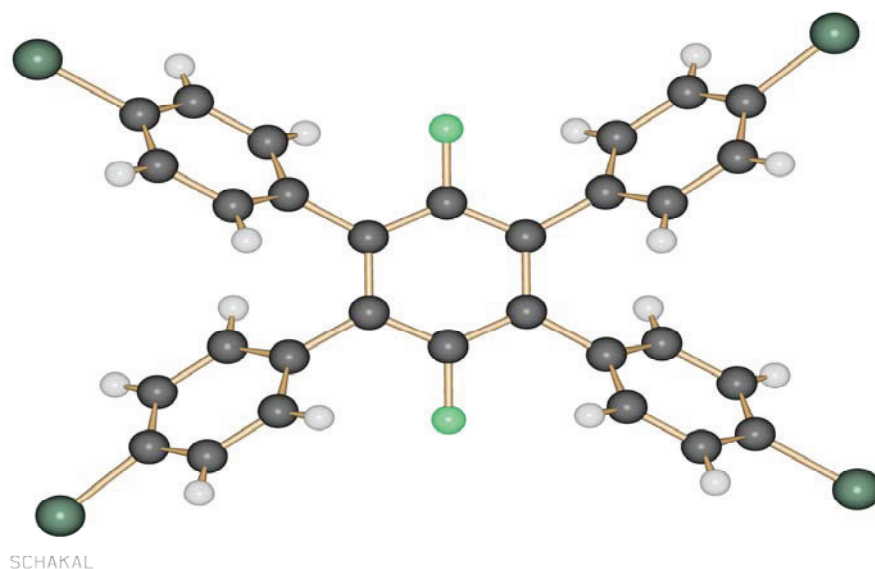
Fig 25: Molecular structure of **37 d.**

4.2.4 Synthesis of 1-fluoro-2,3,4,5,6-penta(aryl)benzenes

The Suzuki-Miyaura reaction of 1-fluoro-2,3,4,5,6-pentaiodobenzene (**33**) with substituted phenylboronic acids (**17j,k,l**) resulted in the formation of **38a-c** (Scheme 20, Table 19) in good to excellent yields (58-73%).
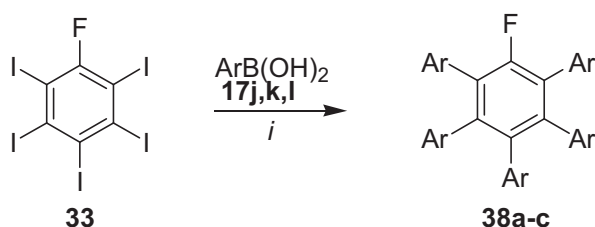
Scheme 20. Synthesis of **38a-c**: conditions and reagents: *i)* **33** (1.0 equiv), **17j,k,l** (6.0 equiv), Pd(PPh$_3$)$_4$ (10 mol-%), Cs$_2$CO$_3$ (5equiv), 1,4-dioxane (5 mL), 110°C, 33 h.

Table 19. Synthesis of **38a-c**

17	38	Ar	Yields (%)[a]
j	a	3-ClC$_6$H$_4$	72
k	b	4-ClC$_6$H$_4$	58
l	c	4-FC$_6$H$_4$	73

[a] Isolated yields

The X-ray measuments for compound **38b** have also been performed which confirmed the structure independently (Figure 26). The aryl groups are again twisted out of plane.
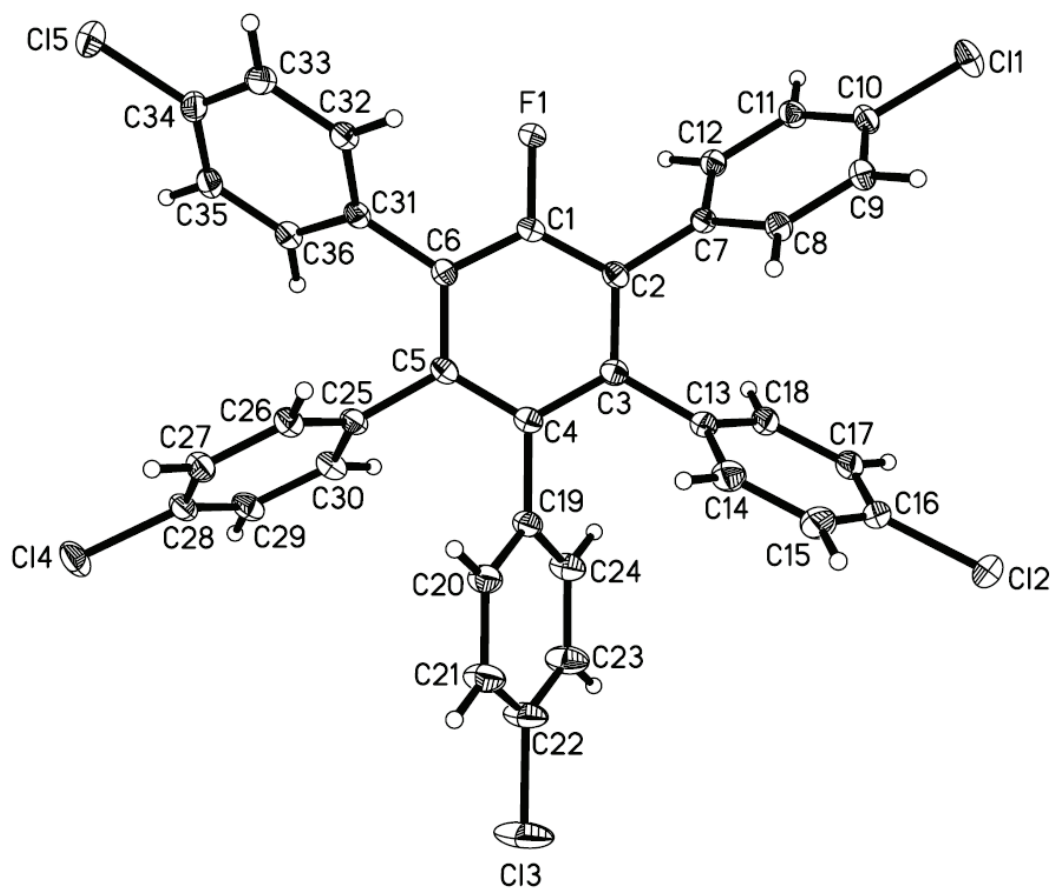
Figure 26. Ortep plot of **38b**

4.3 The UV-Vis and fluorescence properties of the products

The electronic absorption and fluorescence-emission data for compounds **35a-b, 36b, 37a-d** and **38b-c** (Fig. 27-35) are listed in Table 20. The spectra were recorded in DCM, typically in the concentration range of 10^{-5}-10^{-6} M. In general, one major absorption band with one or two shoulder bands was observed in all the compounds.The compound **35a** and **35b** (Fig. 27, 28) showed the absorption maxima at 227 nm whereas it showed a broader emission spectrum at 360-380 nm with emission maxima at 370 nm having a Stoke's shift of 143 nm. The compound **35b** showed emission maxima at 360 nm with shoulders at 339, 390 and 410 nm with a Stoke's shift of 133 nm. This unusual emission pattern is to be investigated, it might be due to the presence of the fluorine substituents. The compound **36b** (Fig. 29) showed absorption band at 247 nm with a shoulder band at 227 nm and emission band at 360 nm. The

compounds **37a** (Fig. 30) and **37b** (Fig. 31) showed one absorption band at 248 nm and 228 nm with one broad shoulder at 228 nm and 242 nm, respectively. The emission maxima in compound **37a** was recorded at 380 nm with Stoke's shift of 132 nm. Two emission maxima were observed for compound **37b** at 310 nm and 371 nm with Stoke's shifts of 182 and 129 nm, repectively. Here the second emission maxima have two bands at 350 nm and 410 nm. The compound **37c** (Fig. 32) showed an absorption band at 228 nm with two shoulders at 241 nm and 270 nm. The same compound showed two emission maxima at 310 nm and 370 nm with Stoke's shift of 182 and 142 nm. The emisssion maxima in compound **37d** (Fig. 33) was recorded at 380 nm with a Stoke's shift of 129 nm. The compounds **38b** (Fig. 34) and **38c** (Fig. 35) showed one absorption band at 228 nm and 227 nm, respectively. Compound **38b** showed emission maxima at 400 nm with three shoulders at 361, 379, and 421 nm. The emission maximum of compound **38c** was recorded at 370 nm. The Stoke's shifts in these compound were found to be 172 and 143 nm, repectively. The emission spectra of compounds **37b**, **37c** and **38b** are unusual and supposed to be investigated in more detail in the future.

Table 20. Electronic absorption and fluorescence-emission properties

Products	λ_{abs}[nm]	λ_{em} [nm]	Stoke's Shift [nm]
35a	**227**	360,**370**,380	143
35b	**227**	339,**360**,390,**410**	133,183
36b	228,**247**	**360**	113
37a	228,**248**	**380**,400	132
37b	**228**,242,290	**310**,350,**371**,410	182,143
37c	**228**,241,270	310,**370**	182, 142
37d	228,**251**,290	359,**380**	129
38b	**228**	361,379,**400**,421	172
38c	**227**	349,**370**,381	143

Absorpion and fluorescence measured in DCM (c = 10^{-5}-10^{-6} M)
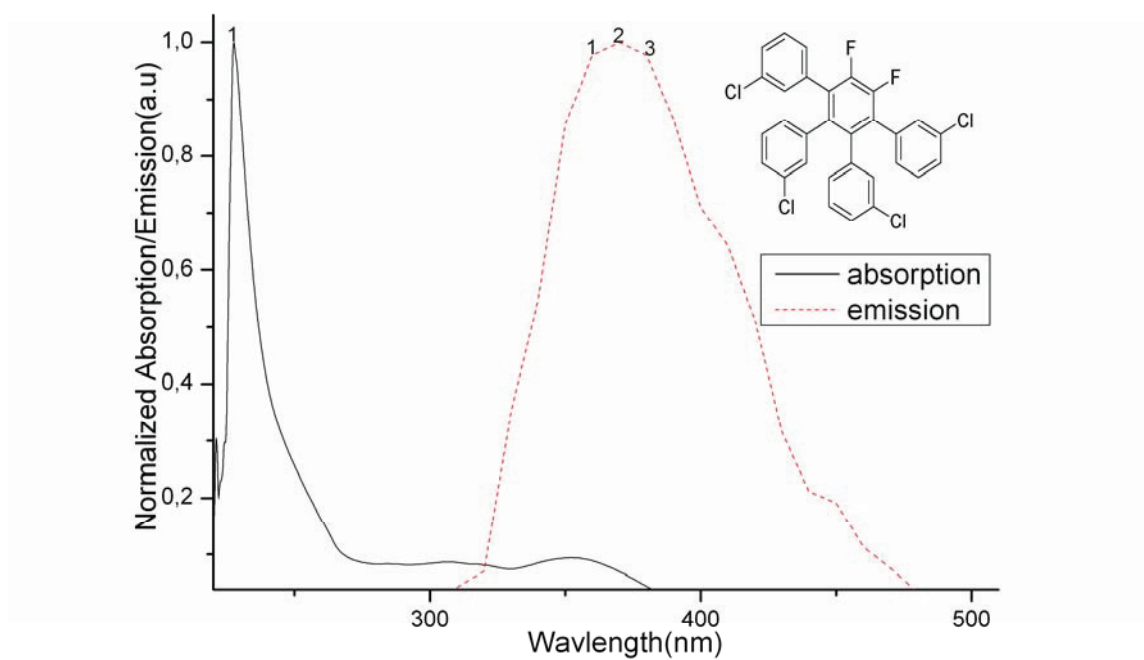
Figure 27. Absorption and emission spectra of compound **35a.**
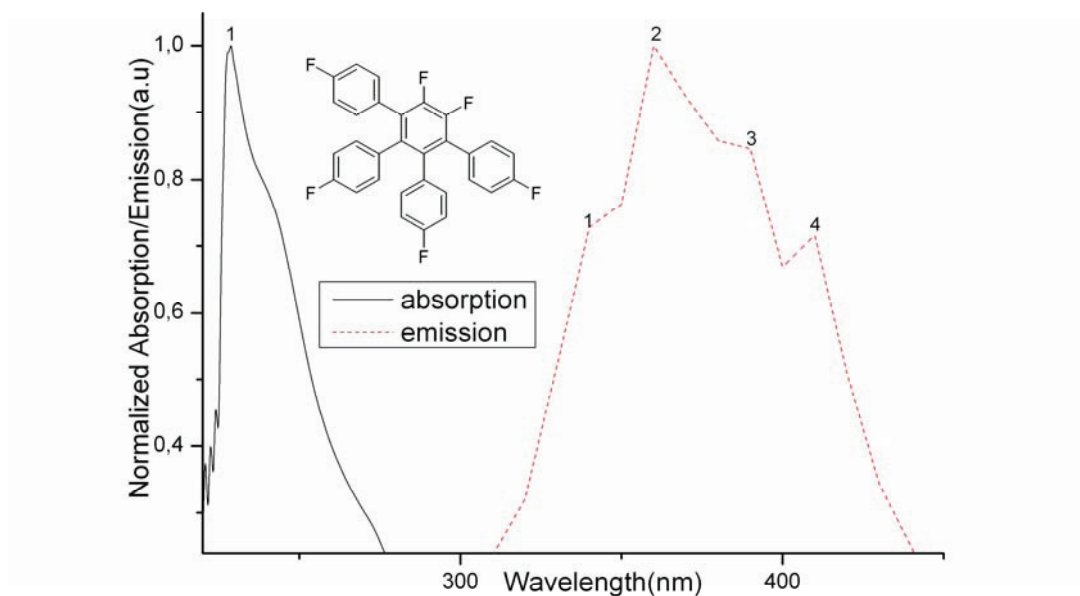
Figure 28. Absorption and emission spectra of compound **35b.**
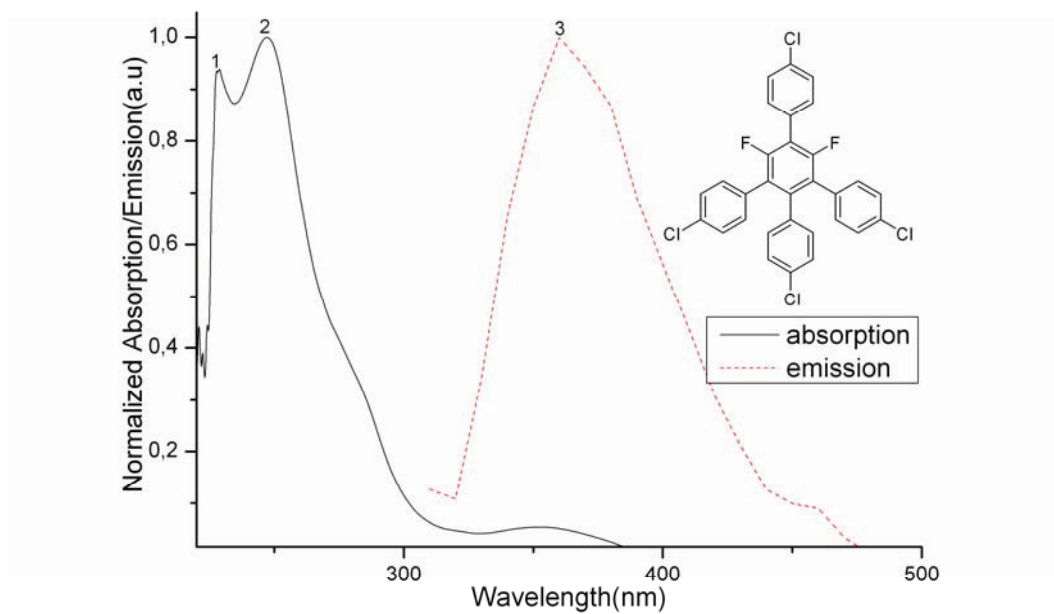
Figure 29. Absorption and emission spectra of compound **36b.**
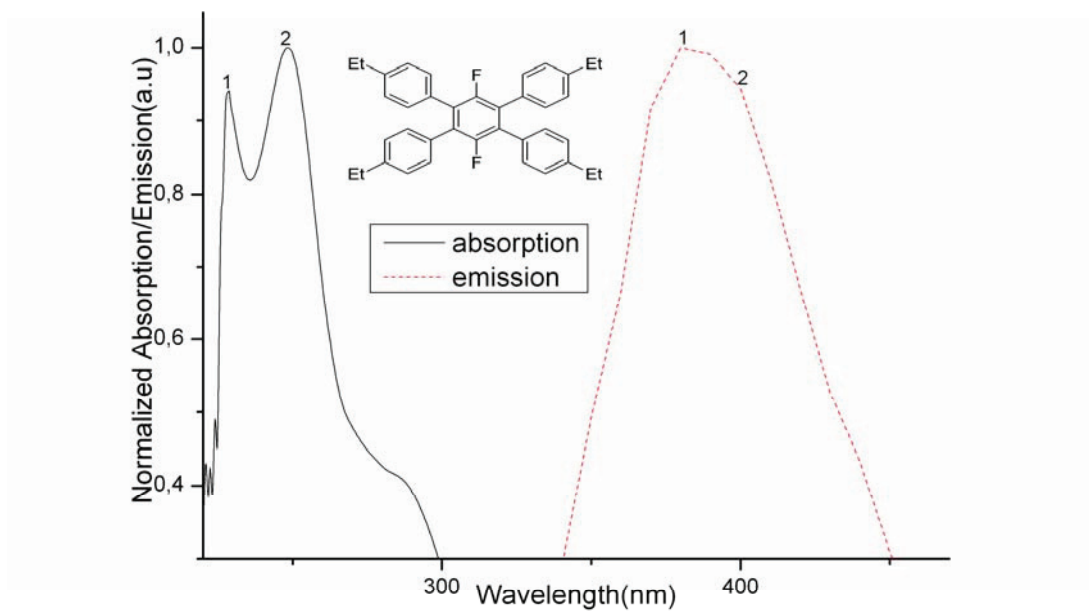
Figure 30. Absorption and emission spectra of compound **37a.**
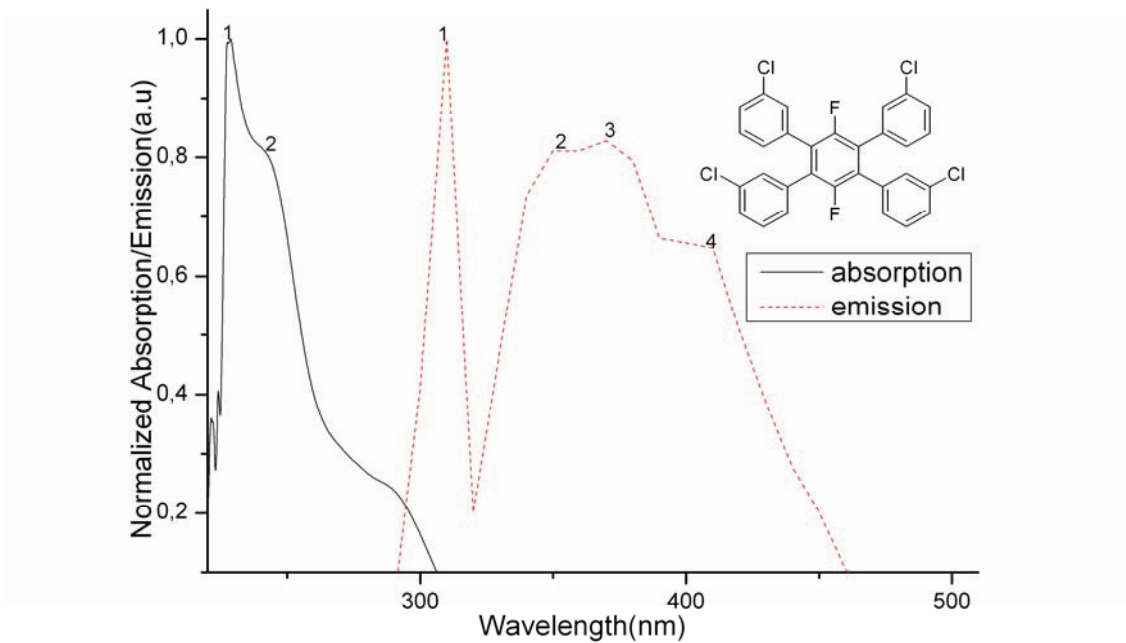
Figure 31. Absorption and emission spectra of compound **37b.**
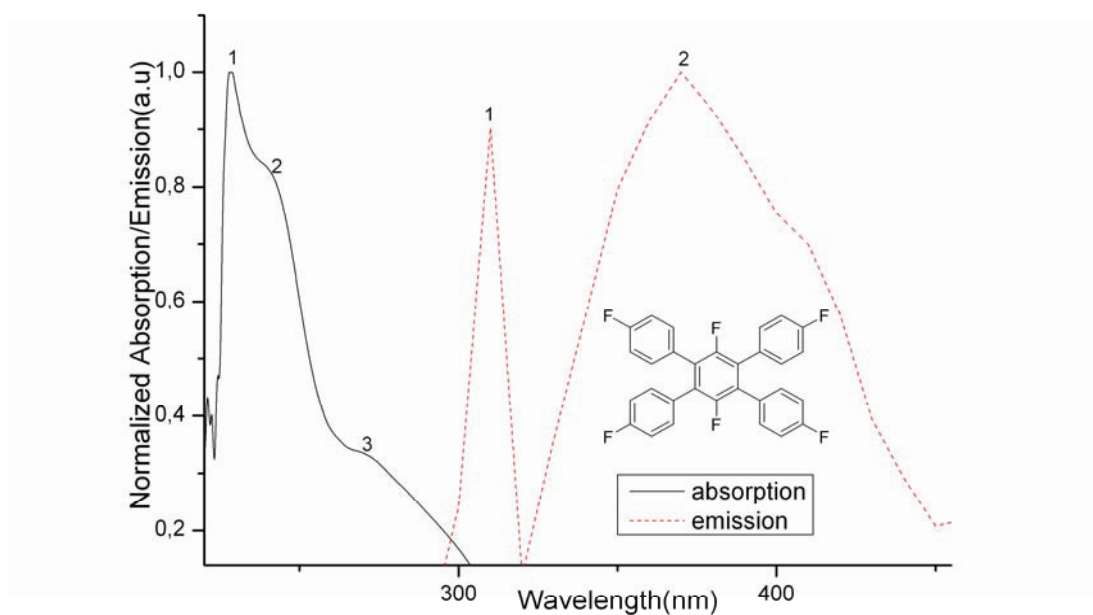
Figure 32. Absorption and emission spectra of compound **37c.**
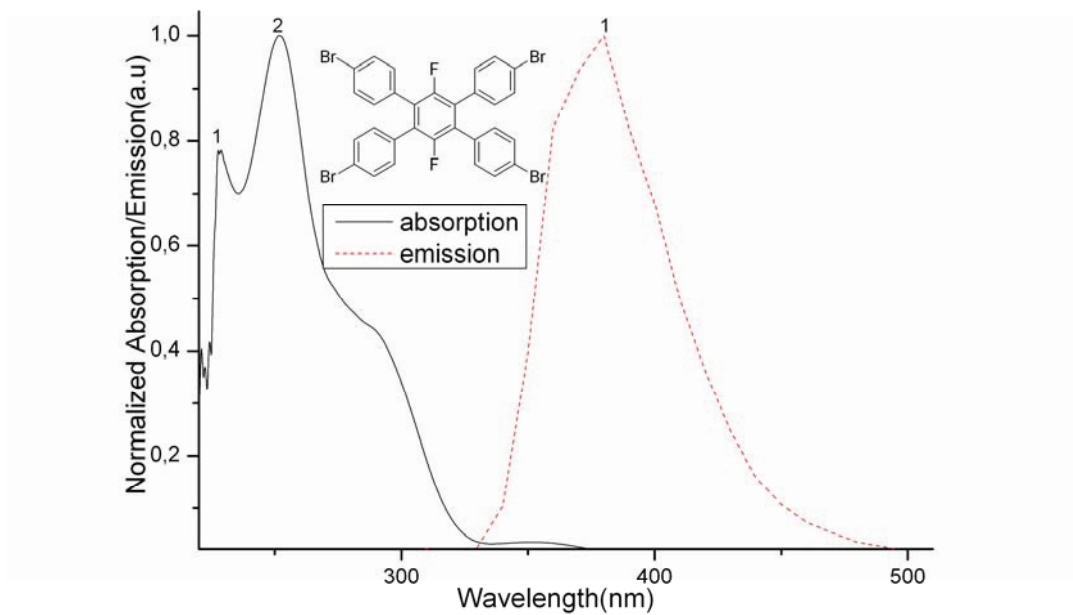
Figure 33. Absorption and emission spectra of compound **37d.**
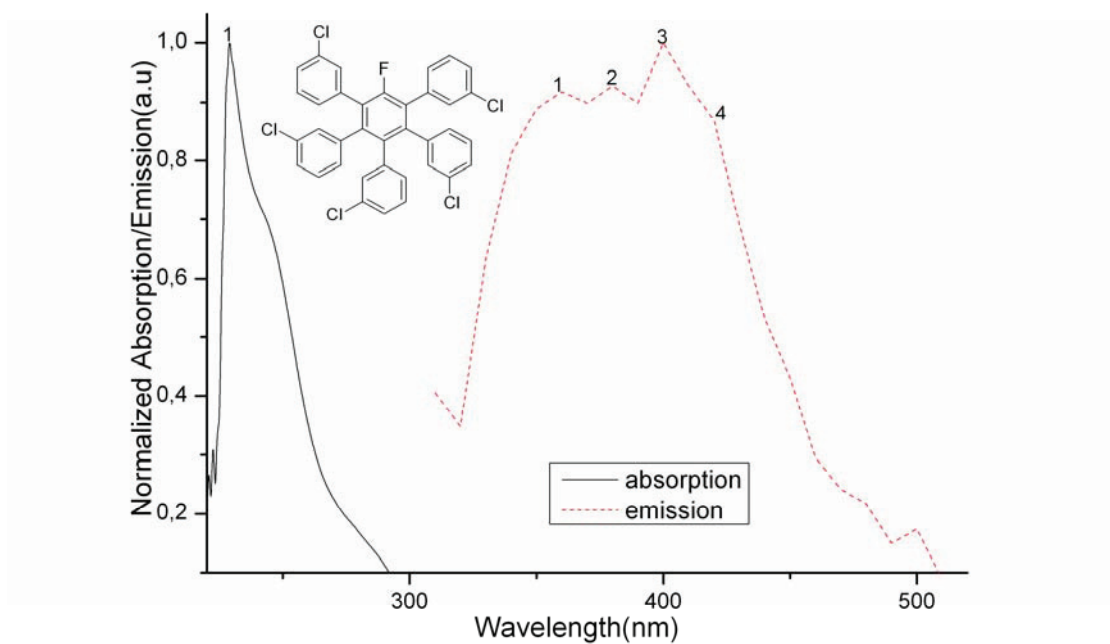
Figure 34. Absorption and emission spectra of compound **38b.**
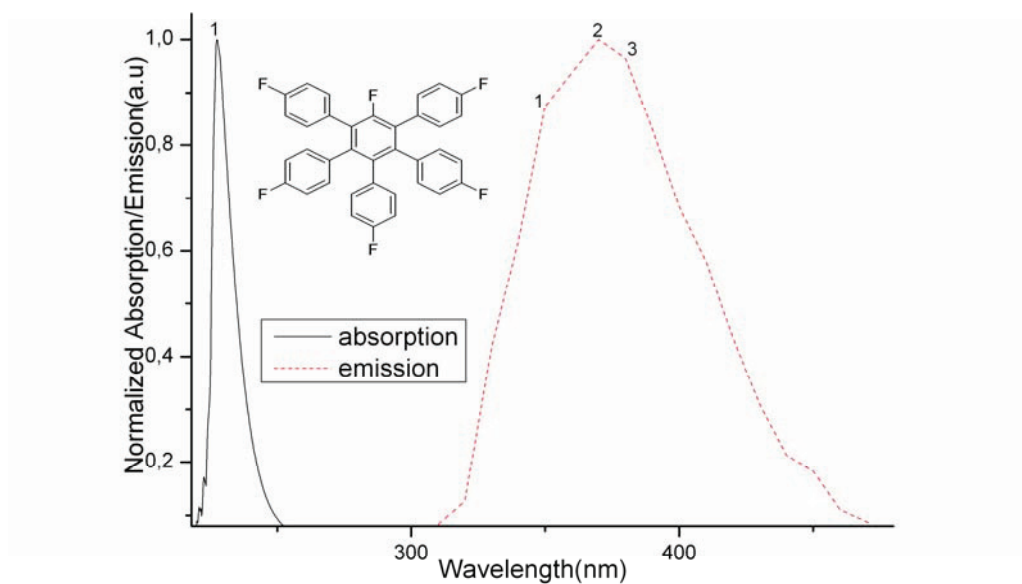
Figure 35. Absorption and emission spectra of compound **38c.**

4.4   Conclusion

In conclusion, I have synthesized difluorotetra(aryl)benzenes and monofluoropenta(aryl)benzenes by Suzuki–Miyaura (S–M) reactions in good to high yields. Suzuki–Miyaura (S–M) reactions of tetraiodobenzenes and pentaiodobenzenes provided the corresponding products. All products showed good absorption and fluorescence properties.

The formal inverse electron demand Diels-Alder reactions of amines with 1,3,5-triazine and 2,4,6-tris(trifluoromethyl)-1,3,5-triazine provided functionalized purines and bi-purines. The effect of the subtituents on the product distribution was studied. Suzuki-Miyaura cross coupling reactions of different substituted mono-fluorobenzenes with different arylboronic acids afforded fluoro-substituted terphenyls with excellent site-selectivity. The first attack occurred at the more electronically deficient and sterically less hindered positions. Sonogashira and Suzuki-Miyaura coupling reactions of 1,2-difluoro-, 1,3-difluoro-, and 1,4-difluoro-tetraiodobenzenes and of fluoro-pentaiodobenzene afforded tetra- and penta-alkynylated and arylated benzene derivatives. The fluorescence properties of benzene derivatives were studied.

Die Diels-Alder-Reaktionen mit inversem Elektronenbedarf von Aminen mit 1,3,5-Triazin und 2,4,6-Tris(trifluoromethyl)-1,3,5-triazin lieferte funktionalisierte Purine und Bipurine. Die Wirkung der Substituenten auf die Produktverteilung wurde untersucht. Suzuki-Miyaura Kreuzkupplungen von unterschiedlich substituierten Mono-Fluorobenzenen mit verschiedenen Boronsäuren lieferte fluorsubstituierte Terphenyle mit hervorragender Seitenselektivität. Der erste Angriff fand an der elektronenärmeren und sterisch weniger gehinderten Position statt. Sonogashira und Suzuki-Miyaura Kupplungsreaktionen von 1,2-Difluoro-, 1,3-Difluoro- und 1,4-Difluorotetraiodobenzen sowie 1-Fluoropentaiodobenzen ergaben die entsprechenden 4-fach bzw. 5-fach alkinylierten bzw. arylierten Produkte. Die Fluoreszenzeigenschaften vieler Benzenderivate wurden untersucht.
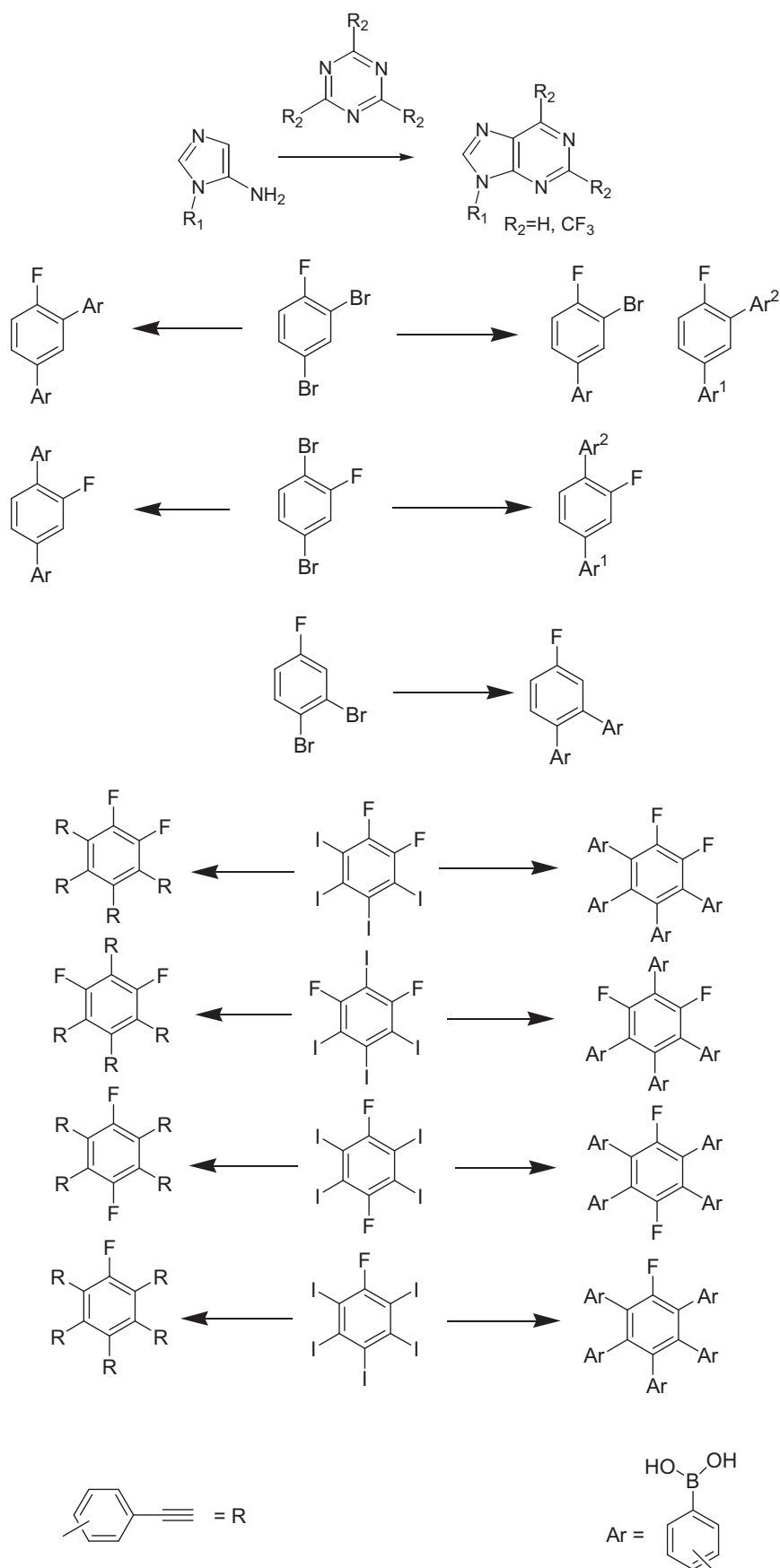
General Scheme. Formal inverse electron demand Diels-Alder reactions and palladium(0)-catalyzed reactions developed in this thesis.

6 *Experimental Section*

6.1 General: Equipment, Chemicals and Work techniques

^{1}H NMR Spectroscopy:

Bruker: AM 250, Bruker ARX 300, Bruker ARX 500; δ = 0.00 ppm for Tetramethylsilane; δ = 7.26 ppm for (CDCl3); Characterization of the signal fragmen- tations: s = singlet, d = doublet, dd = double of doublet, t = triplet, q = quartet, m = multiplet, br = broadly. All coupling constants are indicated as (*J*). 2D NMR techniques (NOESY, COSY, HMQC, and HMBC) were used for the confirmation of structure.

^{13}C NMR Spectroscopy:

Bruker: AM 250, (62.9 MHz); Bruker: ARX 300, (75 MHz), Bruker: ARX 500, (125 MHz) Ref: 29.84 ± 0.01 ppm and 206.26 ± 0.13 ppm δ = 77.00 ppm for CDCl3. The multiplicity of the carbon atoms was determined by the DEPT 135 and APT technique (APT = Attached Proton Test) and quoted as CH_3, CH_2, CH and C for primary, secondary, tertiary and quaternary carbon atoms. Characterization of the signal fragmentations: quart = quartet the multiplicity of the signals was determined by the DEPT recording technology and/or the APT recording technology.

Mass Spectroscopy:

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 spectroscopy:

Finnigan MAT 95 or Varian MAT 311; Bruker FT

CIR, AMD 402 (AMD Intectra).

Infrared spectroscopy (IR):

Bruker IFS 66 (FT IR), Nicolet 205 FT IR; Nicolet Protege 460, Nicolet 360 Smart Orbit (ATR); KBr, KAP, Nujol, and ATR; Peaks are given following assignments: w = weak, m = medium, s = strong, br = broad.

Elemental Analysis

LECO CHNS-932, Thermoquest Flash EA 1112.

X-ray crystal structure analysis:

Crystallographic data were collected on a Bruker X8Apex, Diffractometer with CCD-Kamera (MoKa und Graphit Monochromator, = 0.71073 Å). The structures were solved by direct methods using SHELXS-97 and refined against $F2$ on all data by full matrix least-squares with SHELXL-97.

Melting points:

Micro heating table HMK 67/1825 Kuestner (Büchi apparatus).

Column chromatography:

Chromatography was performed over Merck silica gel 60 (0,063 -0,200 mm, 70 - 230 mesh) as normal and/or over mesh silica gel 60 (0,040 - 0,063 mm, 200 -400 mesh) as Flash Chromatography. All solvent were distilled before use.

Thin Layer Chromatography (TLC):

Merck DC finished foils silica gel 60 F_{254} on aluminum foil and Macherey finished

foils Alugram® Sil G/UV_{254}. Detection under UV light with 254 nm and/or 366 nm without dipping reagent, as well as with anisaldehyde sulfuric acid reagent (1 mL anisaldehyde consisting in 100 mL stock solution of 85% methanol, 14% acetic acid and 1% sulfuric acid).

6.2 Synthesis of Purines by Formal Inverse Electron demand Diels-Alder reaction

General Procedure for the Synthesis of Purines 6, 8-15.

To a Schlenk flask, set with reflux, CH_2Cl_2 (2.5 mL), primary amine **2** (0.00345 mol), and methyl *N*-(cyanomethyl)-formimidate **1** (0.338 g, 0.00345 mol) were added under an argon atmosphere at r.t. The reaction mixture was kept under reflux and after that, the mixture was cooled down to r.t., and then to 0°C using an ice bath. Afterwards, the corresponding trazine (0.00345 mol) was added, and the mixture continued to stir at the same temperature for 15–20 min and was then refluxed. After the product formation is completed, the solvent was evaporated to dryness and the residue was purified by column chromatography (EtOAc) to give purines. In case of all aromatic and heteroaromatic amines, after the addition of triazine

at 0°C, a catalytic amount of TMSOTf (about 3 drops) was added. For the synthesis of purines **6,** a 20% excess of **4** was generated.

9-*tert*-Butyl-9*H*-purine (6a): starting with *tert*-butyl amine **2** (252 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (280 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **6a** was isolated as white solid (224 mg, 37%). Mp 114-116 ^{0}C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.80 (s, 9H, 3CH$_3$), 8.14 (s, 1H, CH), 8.92 (s, 1H, CH), 9.09 (s, 1H, N*CH*N). ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 28.91 (3CH$_3$), 57.8 (C), 135.2 (C), 142.9 (C), 148.6 (C), 151.5 (C), 151.6 (N*CH*N). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3268 (w), 3102 (w), 3075 (w), 3034 (w), 2976 (w), 2915 (w), 1867 (w), 1731 (w), 1681 (w), 1593 (m), 1568 (m), 1519 (w), 1492 (m), 1463 (w), 1398 (m), 1362 (m), 1344 (m), 1298 (m), 1253 (m), 1225 (m), 1179 (m), 1105 (m), 1031 (w), 961 (w), 911 (m), 841 (w), 792 (m), 641 (m), 621 (m), 549 (m) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 176 (49) [M]$^+$, 121 (100), 120 (39), 93 (11), 41 (11). HRMS (EI) calcd. for C$_9$H$_{12}$N$_4$ [M]$^+$: 176.10565; found 176.105568.

9-(4-Methoxybenzyl)-9*H*-purine (6b): starting with 4-methoxybenzyl amine **2** (473 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (280 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **6b** was isolated as white solid (648 mg, 27%). Mp 86-88 ^{0}C: ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.72 (s, 3H, CH$_3$), 5.31 (s, 2H, CH$_2$), 6.80-6.83 (d, 2H, *J* = 8.6 Hz, 2CH$_{Ar}$), 7.20-7.22 (d, *J* = 8.6 Hz, 2H, 2CH$_{Ar}$), 7.97(s, 1H, CH), 8.95 (s, 1H, CH), 9.07 (s, 1H, N*CH*N). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 46.8 (CH$_3$), 55.3 (CH$_2$), 114.5 (CH$_{Ar}$), 126.9 (C), 129.5 (CH$_{Ar}$), 134.0 (C), 144.9 (C), 148.6 (CH), 151.3 (C), 152.7 (CH), 159.8 (N*CH*N). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 2993 (w), 2953 (w), 2833 (w), 1900 (w), 1655 (m), 1613 (m), 1577 (s), 1513 (s),1452 (m), 1438 (m), 1410 (m), 1374 (w), 1338 (m), 1302 (s), 1240 (s), 1175 (s), 1158 (s), 1103 (m), 1028 (s), 985 (w), 933 (m), 895 (m), 823 (m), 789 (s), 763 (s), 704 (m), 646 (s), 566 (s). MS (GC, 70eV): *m/z* (%) = 240 (80) [M]$^+$, 225 (10), 121 (100), 78 (12). HRMS (EI) calcd. for C$_{13}$H$_{12}$ON$_4$ [M]$^+$: 240.10056; found 240.100832.

9-(2-Chlorobenzyl)-9H-purine (6c): starting with 2-chlorobenzyl amine **2** (486 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (280 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **6c** was isolated as white solid (105 mg, 43%). Mp 102-104 ^{0}C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 5.37 (s, 2H, CH$_2$), 7.02-7.25 (m, 4H, 4CH$_{Ar}$), 7.97 (s, 1H, CH), 8.81 (s, 1H, CH), 8.95 (s, 1H, NCHN). ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 44.8 (CH$_2$), 127.5 (CH), 130.0 (CH), 130.2 (CH), 130.5 (CH), 132.4 (C), 133.6 (C), 133.8 (C), 145.2 (CH), 148.6 (CH), 151.4 (C), 152.8 (NCHN). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3067 (w), 2986 (w), 2919 (w), 1657 (w), 1592 (m), 1580 (m), 1496 (m), 1427 (m), 1348 (m), 1340 (m), 1244 (w), 1162 (m), 1095 (w), 1039 (m), 943 (w), 896 (m), 813 (w), 788 (m), 751 (s), 690 (m), 635 (s), 556 (m). MS (GC, 70eV): m/z (%) = 244 (10) [M]$^+$, 209 (100), 125 (12). HRMS (ESI) calcd. for C$_{12}$H$_9$ClN$_4$ [M+H]$^+$: 245.05885; found 245.05898.
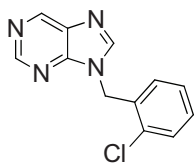
9-(2-Chlorophenethyl)-9H-purine (6d): starting with 2-chlorophenethyl amine **2** (537 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (280 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **6d** was isolated as light yellow solid (104 mg, 40%). Mp 130-132 ^{0}C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.33 (t, J = 6.9 Hz, 2H, CH$_2$), 4.57 (t, J = 6.9 Hz, 2H, CH$_2$), 6.95 (dd, J = 6.0, 3.0 Hz, 1H, CH$_{Ar}$), 7.04-7.10 (m, 1H, CH$_{Ar}$), 7.14-7.25 (m, 1H, CH$_{Ar}$), 7.35 (dd, J = 9.0 Hz, 6.0 Hz, 1H, CH$_{Ar}$), 7.69 (s, 1H, CH), 8.98 (s, 1H, CH), 9.11 (s, 1H, NCHN). ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 32.9 (CH$_2$), 42.3 (CH$_2$), 126.2 (CH), 127.8 (CH), 128.8 (CH), 130.0 (CH), 132.9 (C), 133.0 (C), 136.6 (C), 144.2 (CH), 147.6 (CH), 150.3 (C), 151.6 (NCHN). IR (ATR, cm-1): $\widetilde{\nu}$ = 3080 (w), 3023 (w), 2928 (w), 1593 (w), 1578 (m), 1539 (w), 1497 (w), 1442 (w), 1408 (m), 1363 (w), 1345 (m), 1302 (m), 1260 (w), 1226 (m), 1199 (m), 1151 (w), 1102 (m), 1094 (m), 1050 (m), 1021 (w), 971 (w), 918 (w), 858 (w), 793 (m), 741 (m), 678 (m), 638 (m), 609 (w), 546 (m). MS (GC, 70eV): m/z (%) = 258 (10) [M]$^+$, 223 (100), 140 (11), 138 (33), 103 (10). HRMS (ESI) calcd. for C$_{13}$H$_{11}$ClN$_4$ [M+H]$^+$: 259.0745; found 259.0749.
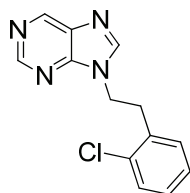
9-tert-Butyl-2,6-bis(trifluoromethyl)-9H-purine (8a): starting with tert-butyl amine **2** (537 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8a** was isolated as light yellow solid (271 mg, 87%). Mp 89-91 ^{0}C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.88 (s, 9H, 3CH$_3$), 8.48 (s, 1H, NCHN). ^{13}CNMR (300 MHz, CDCl$_3$): δ = 28.9 (3CH$_3$), 59.6 (C), 119.5 (q, J = 274.8 Hz, CCF$_3$), 120.3 (q, J = 274.8 Hz, CCF$_3$), 132.3 (C), 145.6 (q, J = 37.7 Hz, CCF$_3$), 147.5 (C), 148.7 (q, J = 37.7 Hz, CCF$_3$), 154.2 (NCHN). ^{19}FNMR (300 MHz, CDCl$_3$):

δ = -68.6 (CF$_3$), -66.0 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 2983 (w), 2941 (w), 2879 (w), 1792 (w), 1733 (w), 1667 (w), 1584 (w), 1485 (w), 1426 (w), 1397 (w), 1332 (w), 1284 (w), 1206 (w), 1139 (m), 1077 (w), 1031 (w), 951 (w), 889 (w), 819 (w), 738 (w), 663 (m), 614 (w), 549 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 312 (51) [M]$^+$, 297 (11), 277 (18), 257 (100), 237 (47), 57 (65), 56 (28). 41 (26). HRMS (EI) calcd. for C$_{11}$H$_{10}$F$_6$N$_4$[M]$^+$: 312.08042,; found 312.080675.

9-Allyl-2,6-*bis*(trifluoromethyl)-9H-purine (8b): starting with allyl amine **2** (196 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH$_2$Cl$_2$ (2.5 ml), **8b** was isolated as Colorless oil (201 mg, 68%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 5.03 (d, *J* = 6.0 Hz, 2H, N*CH$_2$*CHCH$_2$), 5.34-5.44 (m, 2H, NCH$_2$CH*CH$_2$*), 6.00-6.13 (m, 1H, NCH$_2$*CH*CH$_2$), 8.46 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, CDCl$_3$): δ = 45.8 (CH$_2$), 118.4 (q, *J* = 274.5 Hz, C*CF$_3$*), 119.3 (q, *J* = 274.5 Hz, C*CF$_3$*),), 120.2 (2CH$_2$), 129.0 (CH), 130.1 (C), 144.4 (q, *J* = 38.4 Hz, C*CF$_3$*), 148.9 (q, *J* = 38.4 Hz, C*CF$_3$*), 148.0 (C), 153.1 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.6 (CF$_3$), -66.0 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3092 (w), 2996 (w), 2933 (w), 1748 (w), 1647 (w), 1598 (w), 1504 (w), 1455 (w), 1403 (m), 1361 (w), 1304 (m), 1270 (s), 1219 (s), 1127 (s), 1056 (w), 990 (w), 962 (m), 915 (w), 888 (m), 819 (w), 757 (w), 736 (m), 661 (s), 640 (w), 549 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 296 (100) [M]$^+$, 295 (57), 277 (25), 276 (11), 275 (19), 269 (16), 268 (10), 256 (11), 249 (11), 237 (13), 69 (16), 41 (14). HRMS (ESI) calcd. for C$_{10}$H$_6$F$_6$N$_4$[M+H]$^+$: 297.0569; found 297.0573.

2,6-*Bis(*trifluoromethyl)-9-heptyl-9H-purine (8c): starting with heptyl amine **2** (396 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH$_2$Cl$_2$ (2.5 ml), **8c** was isolated as light yellow oil (241 mg, 68%). ^{1}HNMR (300 MHz, CDCl$_3$): δ = 0.86 (t, *J* = 6.7 Hz, 3H, CH$_3$), 1.24-1.36 (m, 8H, 4CH$_2$), 1.92-2.02 (m, 8H, 4CH$_2$), 4.40 (t, *J* = 6.9 Hz, 4H, CH$_2$), 8.40 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, CDCl$_3$): δ = 13.9 (CH$_3$), 22.4, 26.5, 28.5, 29.7, 31.5, 44.7 (CH$_2$), 119.5 (q, *J* = 276.1 Hz, C*CF$_3$*), 120.2 (q, *J* = 276.2 Hz, C*CF$_3$*), 131.1 (C), 145.5 (q, *J* = 38.0 Hz, *C*CF$_3$*), 149.5 (C), 149.7 (q, *J* = 38.1 Hz, *C*CF$_3$*), 154.2 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.5 (CF$_3$), -66.0 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3089 (w), 2957 (w), 2860 (w), 1599 (w), 1505 (w), 1454 (w), 1404 (w), 1307 (m), 1271 (m), 1218 (s), 1140 (s), 1100 (m), 956 (m), 888 (m), 819 (w), 736 (m), 658 (m), 577 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 354 (100) [M]$^+$, 353 (24), 335 (26), 334 (32), 326 (12), 325 (12), 312 (17), 311 (43), 298 (15), 297 (41), 292 (10), 285 (13), 283 (57), 270(84), 269 (70),
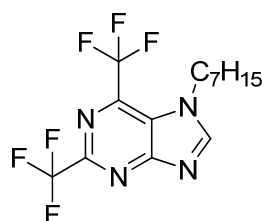
257 (82), 256 (37), 250 (36), 249 (18), 237 (39), 69 (26), 55 (37), 41 (38), 29 (15). HRMS (ESI) calcd.for $C_{14}H_{16}F_6N_4$ $[M+H]^+$: 355.13519; found 355.13492.

9-Cyclopropyl-2,6-*bis*(trifluoromethyl)-*9H*-purine (8d): starting with cyclopropyl amine **2** (96 mg, 3.45 mmol), *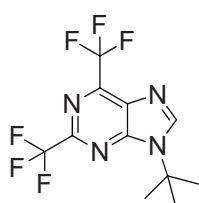*1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8d** was isolated as light white crystalline solid (245 mg, 83%). Mp 86-88 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 1.23-1.36 (m, 4H, 2CH_2), 3.58-3.65 (m, 1H, CH), 8.41 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 6.2 (2CH_2), 26.1 (CH), 119.5 (q, J = 277.0 Hz, C*C*F_3), 120.2 (q, J = 277.0 Hz, C*C*F_3), 131.4 (C), 146.1 (q, J = 38.2 Hz, C*C*F_3), 149.9 (q, J = 38.2 Hz, C*C*F_3), 150.2 (C), 155.2 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.5 (CF_3), -66.0 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3110 (w), 3078 (w), 1860 (w), 1598 (w), 1498 (w), 1450 (w), 1402 (m), 1371 (w), 1330 (m), 1276 (s), 1225 (s), 1186 (s), 1131 (s), 1067 (s), 1034 (m), 958 (s), 933 (m), 890 (m), 819 (m), 784 (w), 737 (s), 670 (m), 637 (s), 558 (w), 530 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 296 (100) $[M]^+$, 295 (46), 277 (29), 276 (18), 275 (21), 269 (21), 268 (30), 249 (21), 248 (24), 119 (10), 100 (10), 69 (28), 41 (12), 39 (12). HRMS (EI) calcd. for $C_{10}H_5F_6N_4[M]^+$: 296.04912; found 296.049152.
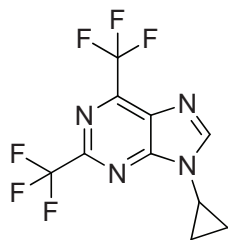
9-Cyclohexyl-2,6-*bis*(trifluoromethyl)-*9H*-purine (8e): starting with cyclohexyl amine **2** (341 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **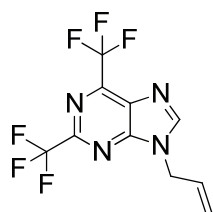8e** was isolated as white solid (304 mg, 90%). Mp 88-90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32- 2.02 (m, 8H, 4CH_2), 2.20-2.25 (m, 2H, CH_2), 4.62-4.70 (m, 1H, CH), 8.46 (s, 1H, N*CH*N). ^{13}CNMR (300 MHz, Acetone-d_6): δ = 20.6 (CH_2), 21.0 (2CH_2), 28.7 (2CH_2), 51.4 (CH), 115.2 (q, J = 275.4 Hz, C*C*F_3), 116.1 (q, J = 275.4 Hz, C*C*F_3), 127.0 (C), 140.9 (q, J = 37.4 Hz, *C*CF_3), 143.5 (C), 145.0 (q, J = 37.4 Hz, *C*CF_3), 149.4 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.4 (CF_3), -66.0 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ =3097 (w), 2957 (w), 2868 (w), 1597 (w), 1493 (w), 1450 (w), 1398 (w), 1350 (w), 1317 (w), 1280 (w), 1221 (w), 1131 (w), 1028 (w), 952 (w), 889 (w), 819 (w), 761 (w), 714 (w), 659 (w), 581 (w), 529 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 338 (23) $[M]^+$, 319 (10), 257 (100), 237 (28), 82 (14), 67 (25). HRMS (ESI) calcd. for $C_{13}H_{11}F_6N_4$ $[M+H]^+$: 339.10389; found 339.10372.
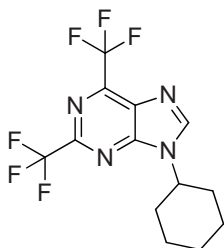
2-(2,6-*Bis*(trifluoromethyl)-*9H*-purin-9-yl)-*N,N*-dimethylethanamine (8f): starting with *N,N*-dimethylethanamine **2** (303 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8f** was isolated as light yellow oil (232 mg, 71%). ^{1}HNMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 6H, $2CH_3$), 2.77 (t, J = 5.6 Hz, 4H, CH_2), 4.47 (t, J = 5.6 Hz, 2H, CH_2), 8.61 (s, 1H, N*CH*N). ^{13}CNMR (100.6 MHz, $CDCl_3$): δ = 41.2 (CH_2), 44.0 ($2CH_3$), 57.0 (CH_2), 115.8 (q, J = 276.7 Hz, C*CF*$_3$), 116.6 (q, J = 276.6 Hz, C*CF*$_3$), 129.9 (C), 143.9 (q, J = 38.2 Hz, *C*CF$_3$), 148.3 (q, J = 38.2 Hz, *C*CF$_3$), 148.9 (C), 149.7 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.5 (CF_3), -65.9 (CF_3). IR (ATR, cm[-1]): $\widetilde{\nu}$ = 3090 (w), 2952 (w), 2866 (w), 2779 (w), 1598 (w), 1505 (w), 1454 (w), 1403 (w), 1301 (m), 1271 (s), 1217 (s), 1132 (m), 1059 (m), 971 (m), 929 (m), 888 (s), 818 (m), 736 (s), 655 (s), 575 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 327 (10) [M][+], 71 (14), 59 (100), 42 (10). HRMS (ESI) calcd. for $C_{11}H_{11}F_6N_5$ [M+H][+]: 328.09914; found 328.09995.

2-(2,6-*Bis*(trifluoromethyl)-*9H*-purin-9-yl)-*N,N*-diethylethanamine (8g): starting with *N,N*-diethylethanamine **2** (400 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8g** was isolated as yellow oil (320 mg, 90%). ^{1}H NMR (300 MHz, DMSO): δ = 0.75 (t, J = 6.9 Hz, 6H, $2CH_3$), 2.41-2.51 (m, 4H, 2N*CH*$_2$CH$_3$), 2.82 (t, J = 5.9 Hz, 2H, NCH$_2$*CH*$_3$N), 4.46 (t, J = 5.9 Hz, 2H, N*CH*$_2$CH$_3$N), 9.09 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, DMSO): δ = 11.5 ($2CH_3$), 42.4 (N*CH*$_2$CH$_3$N), 46.1 (*CH*$_2$NCH$_2$), 51.0 (NCH$_2$*CH*$_2$N), 119.5 (q, J = 275.0 Hz, C*CF*$_3$), 120.3 (q, J = 275.0 Hz, C*CF*$_3$), 131.0 (C), 142.4 (q, J = 37.1 Hz, *C*CF$_3$), 147.3 (q, J = 37.1 Hz, *C*CF$_3$), 153.1 (C), 154.7 (N*CH*N). ^{19}FNMR (300 MHz, DMSO): δ = -67.4(CF_3), -64.9 (CF_3). IR (ATR, cm[-1]): $\widetilde{\nu}$ =2973 (w), 2939 (w), 2819 (w), 1598 (w), 1598 (w), 1505 (m), 1452 (m), 1403 (m), 1363 (w), 1301 (m), 1269 (s), 1201 (s), 1134 (s), 1068 (m), 1010 (w), 965 (m), 933 (m), 888 (s), 818 (w), 736 (m), 678 (w), 638 (s), 573 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 355 (10) [M][+], 340 (10), 86 (100). HRMS (ESI) calcd. for $C_{13}H_{16}F_6N_5$[M+H][+]: 356.13044; found 356.13129.
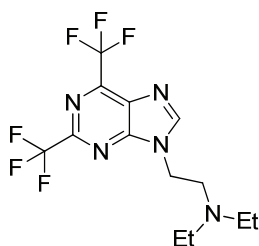
2,6-*Bis*(trifluoromethyl)-9-(3-morpholinopropyl)-*9H*-purine (8h): starting with 3-morpholinopropan-1-amine **2** (497 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8i** was isolated as yellow oil (345 mg, 90%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.07- 2.16 (p, 2H, CH$_2$*CH*CH$_2$), 2.30-237 (m, 6H, 3CH$_2$), 3.62 (t, J = 4.7 Hz, 4H, *CH$_2$*CH*CH$_2$*), 4.52 (t, J = 6.4 Hz, 2H, CH$_2$), 8.46 (s, 1H, N*CH*N). ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 26.1 (CH$_2$), 43.7 (CH$_2$), 54.2 (2CH$_2$), 56.1 (CH$_2$), 67.2 (2CH$_2$), 120.9 (q, J = 274.8 Hz, C*CF$_3$*), 121.5 (q, J = 274.8 Hz, C*CF$_3$*), 132.7 (C), 144.4 (q, ^2J = 41.02 Hz, *C*CF$_3$), 149.2 (q, J = 41.02 Hz, *C*CF$_3$), 153.3 (C), 156.1 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): -68.5 (CF$_3$), -66.0 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3090 (w), 2958 (w), 2894 (w), 2817 (w), 1599 (w), 1506 (w), 1450 (w), 1404 (w), 1358 (w), 1306 (m), 1273 (m), 1219 (m), 1132 (s), 1068 (m), 1005 (w), 953 (m), 888 (m), 817 (w), 736 (m), 657 (m), 574 (w) cm^{-1}. MS (GC, 70eV): m/z (%) = 383 (11) [M]$^+$, 340 (13), 100 (100), 56 (12). HRMS (EI) calcd. for $C_{14}H_{15}F_6N_5O$ [M]$^+$: 383.11753; found 383.118385.

2,6-*Bis*(trifluoromethyl)-9-(4-methylpiperazin-1-yl)-*9H*-purine (8i): starting with 4-methylpiperazin-1-amine **2** (397 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8j** was isolated as white crystalline solid (258 mg, 73%). Mp 174-176 ^{0}C. ^{1}HNMR (300 MHz, DMSO): δ = 2.29 (s, 3H, CH$_3$), 2.51 (t, J = 61.8 Hz, 4H, 2CH$_2$), 3.50 (s, 4H, 2CH$_2$), 9.37 (s, 1H, N*CH*N). ^{13}CNMR (100.6 MHz, Acetone-d_6): δ = 45.9 (CH$_3$), 55.0 (2CH$_2$), 55.6 (2CH$_2$), 118.0 (q, J = 275.1 Hz, C*CF$_3$*), 118.8 (q, J = 275.1 Hz, C*CF$_3$*), 131.6 (C), 145.1 (q, J = 73.2 Hz, *C*CF$_3$), 148.8 (q, J = 37.2 Hz, *C*CF$_3$), 152.2 (C), 154.6 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -67.1 (CF$_3$), -64.7 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3119 (w), 2941 (w), 2858 (w), 2809 (w), 1589 (w), 1484 (w), 1421 (w), 1337 (w), 1298 (w), 1232 (w), 1140 (w), 1086 (w), 1009 (w), 949 (w), 898 (w), 818 (w), 744 (w), 659 (w), 608 (w), 551 (w) cm^{-1}. MS (GC, 70eV): m/z (%) = 354 (14) [M]$^+$, 99 (100), 98 (16), 70 (14), 69 (12), 56 (35), 42 (20). HRMS (EI) calcd. for $C_{12}H_{12}F_6N_6$ [M]$^+$: 354.10222; found 354.102311.

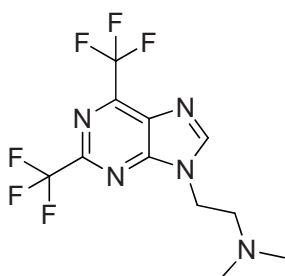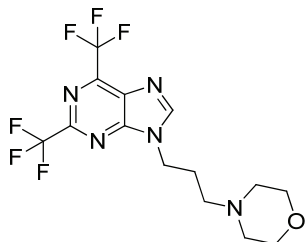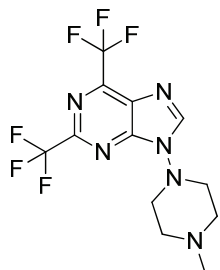**9-Benzyl-2,6-bis(trifluoromethyl)-*9H*-purine (8j):** starting with benzylamine **2** (369 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8k** was isolated as white crystalline solid (259 mg, 75%). Mp, 116-118 ^{0}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.55 (s, 2H, CH_2), 7.38-7.40 (m, 5H, CH_{Ar}), 8.37 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 48.3 (CH_2), 119.5 (q, *J* = 276.5 Hz, C*CF_3*), 120.2 (q, *J* = 276.5 Hz, C*CF_3*),), 128.3 (2CH), 129.3 (CH), 129.5 (2CH), 131.1 (C), 133.6 (C), 145.7 (q, *J* = 38.9 Hz, C*CF_3*), 149.3 (C), 150.0 (q, *J* = 38.9 Hz, C*CF_3*), 154.1 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.5 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3087 (w), 3043 (w), 2991 (w), 2917 (w), 2873 (w), 1600 (w), 1553 (w), 1502 (w), 1452 (w), 1398 (w), 1349 (w), 1299 (w), 1268 (m), 1203 (m), 1132 (s), 1075 (m), 1003 (w), 965 (m), 923 (w), 888 (m), 818 (w), 729 (s), 657 (m), 599 (w), 545 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 346 (100) [M]$^+$, 345 (47), 327 (16), 326 (25), 91 (98), 65 (14). HRMS (EI) calcd. for $C_{14}H_8F_6N_4$[M]$^+$: 346.06477; found 346.064317.21.
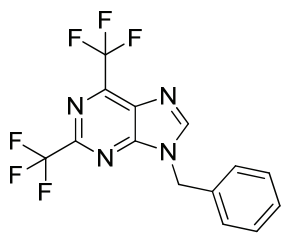
2,6-*Bis*(trifluoromethyl)-9-((*S*)-1-phenylethyl)-*9H*-purine (8k): starting with (*S*)-1-phenylethanamine **2** (414 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8l** was isolated as yellow oil (270 mg, 75%). ^{1}HNMR (300 MHz, $CDCl_3$): δ = 2.03 (d, *J* = 7.5 Hz, 3H, CH_3), 6.06 (q, *J* = 7.5 Hz, 1H, CH), 7.31-7.36 (m, 5H, CH_{Ar}), 8.33 (s, 1H, N*CH*N). ^{13}CNMR (75.4MHz, $CDCl_3$): δ = 19.2 (CH_3), 54.5 (CH), 118.5 (q, *J* = 276.0 Hz, C*CF_3*), 119.2 (q, *J* = 276.0 Hz, C*CF_3*), 125.8 (2CH_{Ar}), 128.1 (C), 128.3 (2CH_{Ar}), 130.3 (CH_{Ar}), 137.0 (CH_{Ar}), 144.5 (q, *J* = 38.4 Hz, *C*CF_3), 147.0 (C), 148.1 (q, *J* = 38.4 Hz, C*CF_3*), 152.2 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.5 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3112 (w), 3069 (w), 2989 (w), 2943 (w), 1717 (w), 1652 (w), 1595 (m), 1493 (m), 1453 (m), 1402 (m), 1315 (m), 1273 (s), 1218 (s), 1136 (s), 1090 (s), 1028 (w), 990 (w), 945 (s), 888 (s), 818 (w), 761 (w), 724 (m), 700 (w), 658 (s), 615 (w), 575 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 360 (37) [M]$^+$, 345 (13), 105 (100), 77 (16). HRMS (ESI) calcd. for $C_{15}H_{10}F_6N_4$ [M+H]$^+$: 361.08824; found 361.08796.
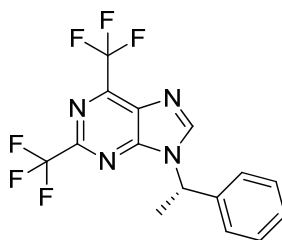
2,6-*Bis*(trifluoromethyl)-9-phenethyl-*9H*-purine (8l): starting with phenethyl amine **2** (417 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH$_2$Cl$_2$ (2.5 ml), **8m** was isolated as white solid (245 mg, 68%). Mp 70-72 ^{0}C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.20 (t, *J* = 6.8 Hz, 2H, CH$_2$), 4.64 (t, *J* = 6.8 Hz. 2H, CH$_2$), 7.08 (dd, *J* = 9.0, 6.0 Hz, 1H, CH$_{Ar}$), 7.18-7.28 (m, 4H, 4CH$_{Ar}$), 7.95(s, 1H, N*CH*N). ^{13}CNMR (300 MHz, CDCl$_3$): δ = 36.1 (CH$_2$), 46.6 (CH$_2$), 120.8 (q, *J* = 273.9 Hz, C*CF$_3$*), 121.5 (q, *J* = 273.9 Hz, C*CF$_3$*), 127.7 (CH), 129.4 (2CH), 129.6 (2CH), 132.4 (C), 144.6 (q, *J* = 37.5 Hz, *C*CF$_3$), 149.3 (q, *J* = 37.5 Hz, *C*CF$_3$), 155.7 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.5 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3130 (w), 3091 (w), 3032 (w), 2998 (w), 2946 (w), 2859 (w), 1984 (w), 1955 (w), 1801 (w), 1739 (w), 1680 (w), 1599 (w), 1504 (w), 1452 (w), 1400 (w), 1357 (w), 1302 (w), 1271 (m), 1208 (s), 1199 (s), 1168 (m), 1130 (s), 1080 (m), 1010 (m), 962 (m), 905 (w), 886 (m), 817 (w), 766 (w), 723 (m), 676 (m), 640 (s), 586 (w), 546 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 360 (11) [M]$^+$ 141 (10), 121 (100), 105 (10), 104 (100), 91 (27). HRMS (ESI) calcd. for C$_{15}$H$_{10}$N$_4$F$_6$ [M+H]$^+$: 361.08824; found 361.08803.
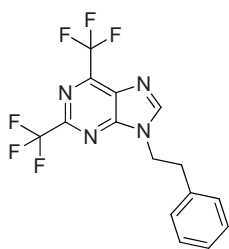
9-(2-Methoxyphenethyl)-2,6-*bis*(trifluoromethyl)-*9H*-purine (8m): starting with 2-methoxyphenethyl amine **2** (524 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH$_2$Cl$_2$ (2.5 ml), **8n** was isolated as white crystalline solid (301 mg, 77%). Mp 124-126 ^{0}C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 3.19 (t, *J* = 6.4 Hz, 2H, NCH$_2$*CH$_2$*), 3.62 (s, 3H, CH$_3$), 4.65 (t, *J* = 6.5 Hz, 2H, N*CH$_2$*CH$_2$), 6.75-6.88 (m, 3H, 3CH$_{Ar}$), 7.16-7.21 (m, 1H, CH$_{Ar}$), 7.98 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, CDCl$_3$): δ = 31.2 (OCH$_3$), 44.8 (NCH$_2$*CH$_2$*), 55.0 (N*CH$_2$*CH$_2$), 110.5 (C), 119.5 (q, *J* = 273.6 Hz, C*CF$_3$*), 120.3 (q, *J* = 273.6 Hz, C*CF$_3$*), 120.9 (C), 124.6 (CH), 129.2 (CH), 130.6 (CH), 130.9 (CH), 145.1 (q, *J* = 36.0 Hz, *C*CF$_3$), 149.6 (q, *J* = 36.0 Hz, *C*CF$_3$), 149.9 (C), 154.5 (C), 157.3 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.5(CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3068 (w), 2975 (w), 2841 (w), 1791 (w), 1717 (w), 1673 (w), 1601 (w), 1509 (w), 1455 (w), 1403 (w), 1369 (w), 1303 (w), 1265 (m), 1209 (m), 1167 (m), 1120 (m), 1053 (w), 1018 (w), 959 (w), 912 (w), 858 (w), 803 (w), 757 (m), 686 (w), 636 (m), 577 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 392 (10), 390 (16) [M]$^+$, 371 (14), 135 (12), 134 (100), 121 (15), 119 (58), 91 (62), 62 (10). HRMS (ESI) calcd. for C$_{16}$H$_9$F$_6$N$_4$O[M+H]$^+$ 391.09881; found 391.0995.
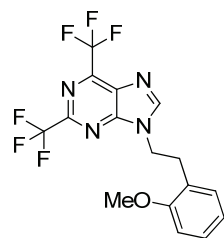
9-(3,4-Dimethoxyphenethyl)-2,6-*bis*(trifluoromethyl)-*9H*-purine (8n): starting with 3,4-dimethoxyphenethyl amine **2** (624 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8o** was isolated as white solid (391 mg, 93%). Mp 145-147 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 3.14 (t, *J* = 6.9 Hz, 2H, CH_2), 3.76 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 4.63 (t, *J* = 6.9 Hz, 2H, CH_2), 6.50-6.52 (m, 2H, $2CH_{Ar}$), 6.72 (d, *J* = 8.7 Hz, 1H, CH_{Ar}), 8.00 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 35.6 (OCH_3), 46.2 (OCH_3), 55.8 (CH_2), 111.5 (CH), 119.2 (q, *J* = 276.0 Hz, C*CF_3*), 119.8 (q, *J* = 276.0 Hz, C*CF_3*), 120.8 (CH), 128.5 (CH), 130.9 (C), 145.4 (q, *J* = 38.8 Hz, *C*CF_3$), 148.4 (C), 149.5 (q, *J* = 38.4 Hz, *C*CF_3$), 148.4 (C), 149.4 (C), 14.6 (C), 154.0 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.5 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3113 (w), 3089 (w), 3006 (w), 2948 (w), 2849 (w), 1597 (w), 1514 (w), 1469 (w), 1404 (w), 1367 (w), 1307 (w), 1252 (w), 1224 (m), 1190 (w), 1131 (m), 1021 (w), 959 (w), 889 (s), 856 (w), 818 (w), 777 (w), 735 (w), 697 (w), 657 (w), 625 (w), 599 (w), 537 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 420 (23) [M]$^+$, 165 (11), 164 (100), 151 (32), 149 (15). HRMS (ESI) calcd. for $C_{17}H_{14}F_6N_4O_2$ [M+H]$^+$: 421.10937; found 421.10979.
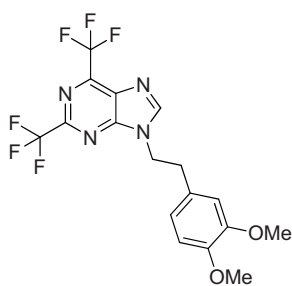
2,6-*Bis*(trifluoromethyl)-9-((pyridin-4-yl)methyl)-*9H*-purine (8o): starting with pyridine-4-ylmethanamine **2** (324 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **8p** was isolated as white crystalline solid (323 mg, 93%). Mp 126-128 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 5.58 (s, 2H, CH_2), 7.20 (d, *J* = 6.1 Hz, 2H, $2CH_{Ar}$), 8.44 (s, 1H, N*CH*N), 8.63 (d, *J* = 6.1 Hz, 2H, $2CH_{Ar}$). ^{13}CNMR (100.6MHz, Acetone-d_6): δ = 47.3 (CH_2), 120.7 (q, *J* = 275.1 Hz, C*CF_3*), 121.5(q, *J* = 275.1 Hz, C*CF_3*), 123.2 (C), 145.0 (q, *J* = 37.6 Hz, C*CF_3*), 144.9 (C), 149.7 (q, *J* = 37.6 Hz, C*CF_3*), 151.4 (C), 153.1 (C), 156.0 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.6 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3087 (w), 3043 (w), 2983 (w), 1599 (w), 1505 (w), 1455 (w), 1416 (w), 1368 (w), 1307 (m), 1271 (m), 1230 (w), 1199 (m), 1120 (m), 1067 (w), 977 (m), 942 (w), 890 (m), 818 (w), 794 (m), 734 (w), 695 (m), 658 (m), 639 (m), 568 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 347 (100) [M]$^+$, 346 (57), 328 (22), 327 (22), 326 (41), 307 (15), 278 (26), 183 (12), 92 (26), 69 (11), 65 (17). HRMS (ESI) calcd. for $C_{13}H_7F_6N_5$[M+H]$^+$: 348.06784; found 348.06797.
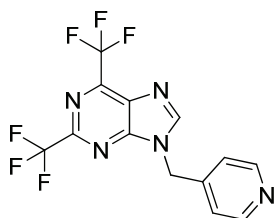
2,6-*Bis*(trifluoromethyl)-9-(3-methoxyphenyl)-*9H*-purine **(9a):** starting with 3-methoxyphenylmine **2** (424 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9a** was isolated as white solid (253 mg, 70%). Mp 145-147 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 3.90 (s, 3H, OCH_3), 7.06-7.09 (m, 1H, CH_{Ar}), 7.25-7.28 (m, 1H, CH_{Ar}), 7.32 (t, J = 2.2 Hz, 1H, CH_{Ar}), 7.53 (t, J = 8.1 Hz, 1H, CH_{Ar}), 8.68 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 55.7 (OCH_3), 109.6 (CH_{Ar}), 115.0 (CH_{Ar}), 115.3 (CH_{Ar}), 119.4 (q, J = 276.4 Hz, C*CF*$_3$), 120.1 (q, J = 276.4 Hz, C*CF*$_3$), 131.1 (CH_{Ar}), 131.7 (C), 134.0 (C), 146.3 (q, J = 38.5 Hz, *C*CF$_3$), 148.4 (C), 150.3 (q, J = 38.5 Hz, *C*CF$_3$), 153.6 (C), 160.9 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.6 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3119 (w), 3021 (w), 2952 (w), 2845 (w), 1610 (w), 1555 (w), 1504 (w), 1450 (w), 1400 (w), 1335 (w), 1276 (w), 1212 (m), 1186 (w), 1136 (m), 1051 (w), 995 (w), 949 (m), 890 (w), 836 (w), 775 (m), 738 (w), 683 (w), 637 (w), 598 (w), 545 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 362 (100) [M]$^+$, 361 (25), 343 (11), 341 (32), 332 (12), 331 (10), 313 (13), 312 (16). HRMS (EI) calcd. for $C_{14}H_8F_6N_4$[M]$^+$: 362.05968; found 362.058868.
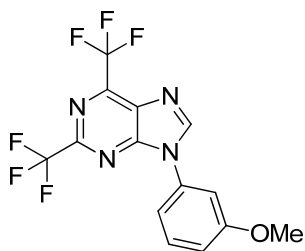
2,6-*Bis*(trifluoromethyl)-9-(3,4-dimethoxyphenyl)-*9H*-purine **(9b):** starting with 3,4-dimethoxyphenyl amine **2** (528 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9b** was isolated as white solid (282 mg, 72%). Mp 136-138 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 3.95 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 7.03 (d, J = 8.3 Hz, 1H, CH_{Ar}), 7.18 (dd, J = 8.2 Hz, 8.6Hz, 1H, CH_{Ar}), 7.27 (d, 1H, J = 2.6 Hz, CH_{Ar}), 8.64 (s, 1H, N*CH*N). ^{13}CNMR (62.9 MHz, $CDCl_3$): δ = 56.2 (2OCH_3), 107.5 (CH_{Ar}), 111.6 (CH_{Ar}),115.9 (CH_{Ar}), 119.2 (q, J = 275.7 Hz, C*CF*$_3$), 120.3 (q, J = 275.7 Hz, C*CF*$_3$), 125.8 (C), 131.5 (C), 146.2 (q, J = 35.5 Hz, *C*CF$_3$), 148.7 (C), 150.0 (2C), 150.9 (q, J = 35.5 Hz, *C*CF$_3$), 153.6 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.6 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3140 (w), 2961 (w), 2840 (w), 1603 (w), 1523 (w), 1469 (w), 1403 (w), 1334 (w), 1276 (w), 1212 (m), 1176 (m), 1141 (s), 1012 (m), 954 (m), 891 (w), 858 (m), 794 (m), 739 (m), 669 (w), 603 (w), 527 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 392 (100) [M]$^+$, 377 (16), 349 (21), 329 (24). HRMS (ESI) calcd. for $C_{15}H_{10}F_6N_4O_2$[M+H]$^+$: 393.07837; found 393.07837.

2,6-*Bis*(trifluoromethyl)-9-(3,5-dimethoxyphenyl)-*9H*-purine **(9c):** starting with 3,5-dimethoxyphenyl amine **2** (528 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9c** was isolated as white crystalline solid (305 mg, 78%) by column chromatography (heptane/EtOAc, 10:1); Mp 150-152 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 6H, 2OCH_3), 6.58 (t, J = 2.1Hz, 1H, CH_{Ar}), 6.87 (d, J = 2.8Hz, 2H, 2CH_{Ar}), 8.67 (s, 1H, NCHN). ^{13}CNMR (75.4MHz, $CDCl_3$): δ = 55.7 (2OCH_3), 100.9 (CH_{Ar}), 101.9 (2CH_{Ar}), 119.3 (q, J = 275.6Hz, CCF_3), 120.1 (q, J = 275.6Hz, CCF_3), 131.7 (C), 134.4 (C), 146.3 (q, J = 38.1Hz, CCF$_3$), 148.4 (C), 150.4 (q, J =38.1Hz, CCF$_3$), 153.5 (NCHN), 161.8 (2C). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.6 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3118 (w), 3024 (w), 2971 (w), 2845 (w), 1613 (w), 1585 (w), 1503 (w), 1461 (w), 1404 (w), 1356 (m), 1275 (m), 1235 (w), 1137 (m), 1076 (m), 1024 (w), 958 (m), 891 (w), 833 (m), 784 (w), 714 (w), 663 (w), 604 (w), 570 (w) cm^{-1}. MS (GC, 70eV): m/z (%) = 393 (40) [M]$^+$, 392 (100), 391 (52), 373 (23), 371 (39), 362 (11), 361 (11), 343 (46), 341 (28), 313 (10), 312 (12), 69 (11). HRMS (EI) calcd. for $C_{15}H_{10}F_6N_4O_2$[M]$^+$: 392.07025; found 392.070024.
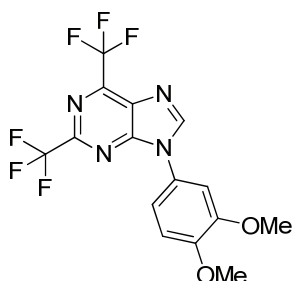
2,6-*Bis*(trifluoromethyl)-9-(2,4-dimethoxyphenyl)-*9H*-purine **(9d):** starting with 2,4-dimethoxyphenyl amine **2** (528 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9d** was isolated as white solid (298 mg, 76%). ^{1}HNMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.66-6.70 (m, 2H, 2CH_{Ar}), 7.44 (d, J = 9.1Hz, 1H, CH_{Ar}), 8.54 (s, 1H, NCHN). ^{13}CNMR (100.6 MHz, $CDCl_3$): δ = 55.8 (OCH_3), 55.9 (OCH_3), 100.4 (CH_{Ar}), 105.1 (CH_{Ar}),114.2 (C), 118.5 (q, J = 276.3 Hz, CCF_3), 121.3 (q, J = 276.3 Hz, CCF_3), 128.1 (CH_{Ar}), 130.8 (C), 145.5 (q, J = 37.7 Hz, CCF$_3$), 150.1 (q, J = 37.7 Hz, CCF$_3$), 151.1 (C), 154.6 (C), 162.1 (NCHN). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.5 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3079 (w), 2945 (w), 1595 (w), 1523 (w), 1453 (w), 1403 (w), 1342 (w), 1304 (w), 1237 (w), 1208 (m), 1190 (m), 1134 (s), 1041 (m), 1025 (m), 938 (m), 887 (w), 816 (m), 739 (w), 672 (m), 646 (m), 587 (w), 534 (w), 468 (w), 412 (w) cm^{-1}. MS (GC, 70eV): m/z (%) = 392 (100) [M]$^+$, 373 (12), 363 (14), 362 (10), 347 (17), 323 (11), 319 (10). HRMS (ESI) calcd for $C_{15}H_{10}F_6N_4O_2$ [M+H]$^+$: 393.07807; found 393.0788.
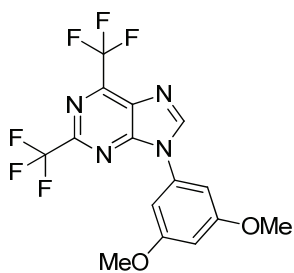
2,6-*Bis*(trifluoromethyl)-9-(3,4,5-trimethoxyphenyl)-*9H*-purine (9e): starting with 3,4,5-trimethoxyphenyl amine **2** (632 mg, 3.45 mmol), **1** (279 mg, 3.45 mmol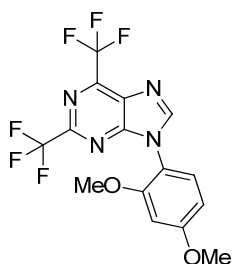es), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9e** was isolated as white solid (274 mg, 65%). Mp 118-120 ^{0}C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 3.92 (s, 9H, 3CH$_3$), 6.92 (s, 2H, 2CH$_{Ar}$), 8.66 (s,1H, N*CH*N). ^{13}CNMR (100.6 MHz, CDCl$_3$): δ = 55.5 (2CH$_3$), 60.0 (OCH$_3$), 96.7 (C), 100.4 (2CH$_{Ar}$), 118.5 (q, J = 278.5 Hz, C*C*F$_3$), 119.3 (q, J = 278.5 Hz, C*C*F$_3$), 127.4 (C), 130.6 (C), 137.9 (C), 145.3 (q, J = 36.5 Hz, *C*CF$_3$), 147.5 (C), 149.4 (q, J = 36.5 Hz, *C*CF$_3$), 152.6 (C), 153.2 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.7 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3402 (w), 3112 (w), 2945 (w), 1687 (w), 1586 (w), 1451 (w), 1357 (w), 1232 (m), 1184 (w), 1121 (s), 1070 (m), 989 (m), 918 (w), 855 (w), 795 (w), 739 (w), 660 (w), 8596 (w), 520 (w), 463 (w), 408 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 423 (17), 422 (100) [M]$^+$, 408 (11), 407 (61), 379 (37), 93 (10). HRMS (ESI) calcd. for C$_{16}$H$_{12}$F$_6$BrN$_4$O$_3$ [M+H]$^+$: 423.08864; found 423.08828.

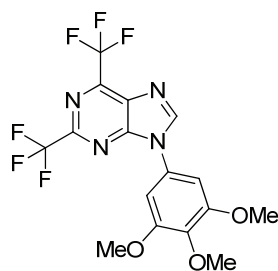**9-(4-Ethoxyphenyl)-2,6-*bis*(trifluoromethyl)-*9H*-purine (9f):** starting with 4-ethoxyphenyl amine **2** (473 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9f** was isolated as white solid (233 mg, 62%). Mp 144-146 ^{0}C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 1.47 (t, J = 7.1 Hz, 3H, CH$_3$), 4.12 (q, J = 7.1 Hz, 2H, CH$_2$), 7.10 (d, J = 8.8 Hz, 2H, CH$_{Ar}$), 7.58 (d, J = 8.8 Hz, 2H, CH$_{Ar}$), 8.61 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, CDCl$_3$): δ = 14.7 (OCH$_3$), 64.1 (CH$_2$), 115.5 (CH$_{Ar}$), 119.4 (q, J = 276.9 Hz, C*C*F$_3$), 120.1 (q, J = 276.9 Hz, C*C*F$_3$), 125.2 (2CH$_{Ar}$), 125.4 (C), 131.5 (C), 146. (q, J = 39.5 Hz, *C*CF$_3$), 150.2 (C), 150.4 (q, J = 39.5 Hz, *C*CF$_3$), 153.7 (C), 159.8 (N*CH*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.5 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3143 (w), 3089 (w), 3029 (w), 2965 (w), 2884 (w), 1947 (w), 1778 (w), 1612 (w), 1521 (m), 1465 (w), 1406 (w), 1349 (w), 1303 (w), 1244 (m), 1205 (m), 1170 (m), 1142 (s), 1038 (m), 1004 (w), 933 (m), 886 (m), 848 (m), 803 (m), 738 (m), 678 (m), 626 (m), 531 (m) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 376 (55) [M]$^+$, 349 (15), 348 (100), 347 (21). HRMS (EI) calcd. for C$_{15}$H$_{10}$F$_6$ON$_4$ [M]$^+$: 376.07533; found 376.075150.

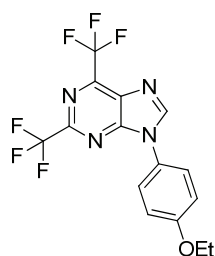**2,6-*Bis*(trifluoromethyl)-9-mesityl-*9H*-purine (9g):** starting with 2,4,6-trimethylaniline **2** (466 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9g** was isolated as white solid (311 mg, 83%). Mp 134-136 ^{0}C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 1.94 (s, 6H, 2CH$_3$), 2.40 (s, 3H, CH$_3$), 7.09 (s, 2H, 2CH$_{Ar}$), 8.36 (s, 1H, NC*H*N). ^{13}CNMR (75.4 MHz, CDCl$_3$): δ = 17.7 (2CH$_3$), 21.3 (CH$_3$), 119.4 (q, *J* = 276.6 Hz, C*C*F$_3$), 120.3 (q, *J* = 276.6 Hz, C*C*F$_3$), 128.3 (C), 128.3 (CH$_{Ar}$), 135.4 (C), 141.2 (C), 146.0 (q, *J* = 39.2 Hz, *C*CF$_3$), 150.3 (C), 150.6 (q, *J* = 39.2 Hz, *C*CF$_3$), 154.5 (NC*H*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.4 (CF$_3$), -65.8 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3116 (w), 2962 (w), 2863 (w), 1740 (w), 1608 (w), 1498 (w), 1452 (w), 1397 (w), 1332 (w), 1275 (m), 1237 (m), 1189 (m), 1135 (s), 1007 (m), 958 (w), 886 (m), 819 (w), 742 (m), 714 (w), 664 (m), 586 (w), 545 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 375 (57), 374 (100) [M]$^+$, 373 (20), 355 (15), 353 (12), 305 (16), 279 (42), 210 (29). HRMS (EI) calcd. for C$_{16}$H$_{12}$F$_6$N$_4$ [M]$^+$: 375.10389; found 375.10455.

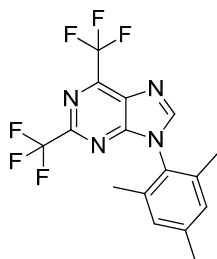**9-(3-Bromophenyl)-2,6-bis(trifluoromethyl)-*9H*-purine (9h):** starting with 3-bromoaniline **2** (593 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9h** was isolated as white solid (185 mg, 67%). Mp 117-119 ^{0}C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 7.53 (t, *J* = 8.3 Hz, 1H, CH$_{Ar}$), 7.69-7.75 (m, 2H, 2CH$_{Ar}$), 7.89 (t, *J* = 1.9 Hz, 1H, CH$_{Ar}$), 8.67 (s, 1H. NC*H*N). ^{13}CNMR (100.6 MHz, CDCl$_3$): δ = 119.4 (q, *J* = 275.6 Hz, C*C*F$_3$), 120.1 (q, *J* = 275.6 Hz, C*C*F$_3$), 122.3 (CH$_{Ar}$), 123.7 (C), 126.6 (CH$_{Ar}$), 130.3 (C), 132.8 (CH$_{Ar}$), 134.1 (C), 146.6 (q, *J* = 39.3 Hz, *C*CF$_3$), 148. (2C), 150.7 (q, *J* = 39.3 Hz, *C*CF$_3$), 153.5 (NC*H*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.6 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3147 (w), 3112 (w), 1587 (w), 1497 (w), 1454 (w), 1401 (w), 1344 (w), 1278 (w), 1213 (w), 1130 (w), 1021 (w), 935 (w), 889 (w), 851 (w), 796 (w), 677 (w), 625 (w), 558 (w), 528 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 412 (97) [M]$^+$, 411 (29), 410 (100), 409 (13), 331 (13), 69 (14). HRMS (EI) calcd. for C$_{13}$H$_5$^{79}BrF$_6$N$_4$[M]$^+$: 409.95963; found 409.959575; calcd. for C$_{13}$H$_5$N$_4$^{81}BrF$_6$ [M]$^+$: 411.95758; found 411.957617.

9-(4-Bromophenyl)-2,6-*bis*(trifluoromethyl)-*9H*-purine (9i): starting with 4-bromoaniline **2** (593 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9i** was isolated as white solid (291 mg, 71%). Mp 168-170 ^{0}C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 7.62-7.65 (m, 2H, 2CH$_{Ar}$), 7.77-7.80 (m, 2H, 2CH$_{Ar}$), 8.67 (s, 1H, NC*H*N). ^{13}CNMR (62.9 MHz, CDCl$_3$): δ = 119.4 (q, J = 276.0 Hz, C*C*F$_3$), 120.0 (q, J = 276.0 Hz, C*C*F$_3$), 123.6 (C), 125. (2CH$_{Ar}$), 131.7 (C), 132.0 (C), 133.6 (2CH$_{Ar}$), 146.5 (q, J = 38.8 Hz, *C*CF$_3$), 148.0 (C), 150.6 (q, J = 38.8 Hz, *C*CF$_3$), 153.6 (NC*H*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.6 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3144 (w), 3072 (w), 2992 (w), 1601 (w), 1552 (w), 1504 (w), 1452 (w), 1402 (w), 1344 (w), 1281 (w), 1221 (w), 1177 (w), 1139 (w), 1077 (w), 1010 (w), 931(w), 886 (w), 842 (w), 740 (w), 695 (w), 660 (w), 614 (w), 530 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 412 (99), 411 (33) [M]$^+$, 410 (100), 409 (18). HRMS (ESI) calcd. for C$_{13}$H$_5$BrF$_6$N$_4$[M+H]$^+$: 412.9655; found 412.96591.
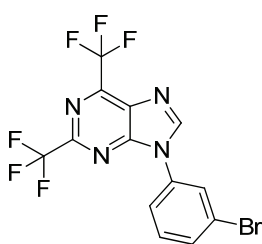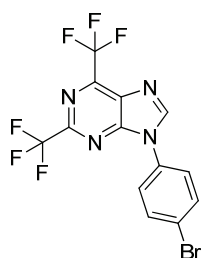
9-(2,6-Dibromo-4-methylphenyl)-2,6-*bis*(trifluoromethyl)-*9H*-purine (9j): starting with 2,6-dibromo-4-methylaniline **2** (914 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9j** was isolated as white crystalline solid (227 mg, 45%). Mp 109-112 ^{0}C. ^{1}HNMR (250 MHz, CDCl$_3$): δ = 2.41 (s, 3H, CH$_3$), 7.55 (s, 2H, 2CH$_{Ar}$), 8.33 (s, 1H, NC*H*N). ^{13}CNMR (75.4 MHz, CDCl$_3$): δ = 21.0 (CH$_3$), 119.3 (q, J = 273.7 Hz, C*C*F$_3$), 120.2 (q, J = 273.7 Hz, C*C*F$_3$), 123.0 (2C), 128.5 (C), 130.6 (C), 133.6 (2CH$_{Ar}$), 144.7 (C), 146.2 (q, J = 37.8 Hz, *C*CF$_3$), 149.5 (C), 150.5 (q, J = 37.8 Hz, *C*CF$_3$), 153.9 (NC*H*N). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.5 (CF$_3$), -65.8 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3208 (w), 3113 (w), 2922 (w), 2849 (w), 1740 (w), 1658 (w), 1595 (w), 1545 (w), 1501 (w), 1451 (w), 1399 (w), 1336 (w), 1275 (w), 1201 (m), 1135 (m), 1085 (w), 1001 (w), 940 (m), 891 (w), 817 (w), 749 (w), 664 (m), 583 (w), 540 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 506 (11), 505 (10) [M]$^+$, 426 (16), 425 (97), 424 (17), 423 (100), 343 (16). HRMS (EI) calcd. for C$_{14}$H$_6$Br$_2$F$_6$N$_4$[M]$^+$: 506.88972; found 506.88895.
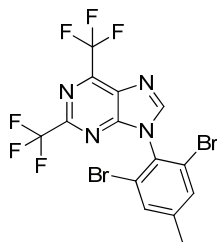
4-(2,6-*Bis*(trifluoromethyl)-*9H*-purin-9-yl)-*N,N*-diethylbenzenamine (9k): starting with *N`,N`*-diethylbenzen-1,4-diamine **2** (565 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9k** was isolated as light green solid (285 mg, 70%). Mp 146-147 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 1.22 (t, J = 6.5 Hz, 3H, $2CH_3$), 3.43 (q, J = 7.2 Hz, 4H, $2CH_2$), 6.80 (d, J = 9.8 Hz, 2H, $2CH_{Ar}$), 7.44 (d, J = 9.8 Hz, 2H, $2CH_{Ar}$), 8.57 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 12.4 (2CH$_3$), 44.8 (2CH$_2$), 111.9 (C), 119.4 (q, J = 276.5 Hz, C*CF*$_3$), 120.3 (q, J = 276.5 Hz, C*CF*$_3$), 125.2 (2CH$_{Ar}$), 131.4 (C), 145.9 (q, J = 39.5 Hz, *C*CF$_3$), 148.3 (C), 149.9 (C), 150.2 (q, J = 39.5 Hz, *C*CF$_3$), 153.9 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.4 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3128 (w), 2974 (w), 2903 (w), 2872 (w), 1609 (w), 1564 (w), 1524 (m), 1468 (w), 1399 (w), 1340 (w), 1275 (m), 1190 (m), 1130 (s), 1076 (w), 1023 (m), 935 (m), 886 (m), 815 (m), 742 (m), 708 (w), 661 (m), 628 (m), 551 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 403 (35) [M]$^+$, 389 (19), 388 (100), 360 (25). HRMS (EI) calcd. for $C_{17}H_{15}F_6ON_5$[M]$^+$: 403.12262; found 403.121853.

2,6-*Bis*(trifluoromethyl)-9-morpholino-*9H*-purine (9l): starting with morpholin-4-amine **2** (352 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **9l** was isolated as white crystalline solid (163 mg, 48%). Mp 105-107 ^{0}C. ^{1}HNMR (250 MHz, $CDCl_3$): δ = 3.64 (t, J = 4.7 Hz, 4H, $2CH_2$), 3.94 (t, J = 4.7Hz, 4H, $2CH_2$), 8.48 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 53.7 (CH$_2$), 65.7 (CH$_2$), 116.3 (q, J = 272.0 Hz, C*CF*$_3$), 118.3 (q, J = 272.0 Hz, C*CF*$_3$), 129.2 (C), 145.2 (q, J = 38.5 Hz, *C*CF$_3$), 148.2 (q, J = 38.4 Hz, *C*CF$_3$), 148.9, 151.9 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.5 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3112 (w), 2988 (w), 2918 (w), 2875 (w), 1824 (w), 1728 (w), 1593 (w), 1505 (w), 1469 (w), 1420 (w), 1386 (w), 1330 (w), 1301 (m), 1274 (m), 1229 (s), 1204 (s), 1138 (s), 1104 (s), 1045 (m), 967 (w), 946 (m), 899 (m), 845 (w), 817 (w), 743 (w), 727 (m), 659 (s), 636 (s), 567 (w), 528 (m) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 341 (10) [M]$^+$, 322 (39), 284 (54), 264 (27), 257 (29), 256 (49), 237 (23), 236 (78), 209 (14), 86 (12), 85 (97), 69 (32), 56 (25), 55 (100), 42 (11). HRMS (ESI) calcd. for $C_{11}H_9F_6N_5O$ [M+H]$^+$: 342.07841; found 342.107838.

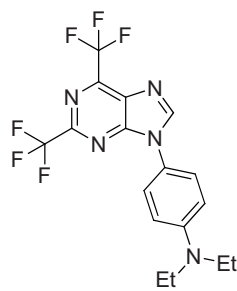**2,6-*Bis*(trifluoromethyl)-9-(thiazol-2-yl)-*9H*-purine (10a):** starting with thiazol-2-amine **2** (345 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **10a** was isolated as white solid (206 mg, 61%). Mp 135-137 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 7.49 (d, J = 3.5Hz, 1H, CH_{Ar}), 7.75 (d, J = 3.5Hz, 1H, CH_{Ar}), 9.35 (s, 1H, N*CH*N). ^{13}CNMR (75.4MHz, $CDCl_3$): δ = 119.2 (q, J = 276.5Hz, C*CF*$_3$), 119.1 (C), 119.8 (q, J = 276.5Hz, C*CF*$_3$), 131.9 (C), 139.7 (CH_{Ar}), 146.4 (C), 146.7 (q, J = 35.9Hz, *C*CF$_3$), 151.5 (q, J = 35.9Hz, *C*CF$_3$), 151.7 (C), 152.4 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.7 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{v}$ = 3128 (w), 2922 (w), 2852 (w), 1818 (w), 1731 (w), 1652 (w), 1593 (w), 1526 (w), 1487 (w), 1445 (m), 1400 (w), 1308 (w), 1275 (w), 1229 (w), 1139 (m), 1052 (w), 1006 (w), 920 (w), 887 (w), 813 (w), 739 (w), 685 (w), 624 (w), 568 (w) cm^{-1}. MS (GC, 70eV): m/z (%) = 339 (100) [M]$^+$, 320 (10), 58 (11). HRMS (EI): calcd for $C_{10}H_3F_6N_5S$ [M]$^+$: 339.00079; found 339.001667.
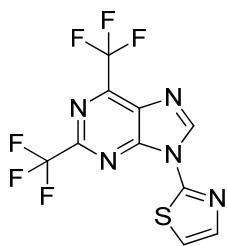
2,6-*Bis*(trifluoromethyl)-9-(pyridin-2-yl)-*9H*-purine (10b): starting with pyridin-2-amine **2** (324 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **10b** was isolated as white crystalline solid (133 mg, 40%). Mp 60-62 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 7.42-7.46 (m, 1H, CH_{Ar}), 8.02-8.08 (m, 1H, CH_{Ar}), 8.67 (dt, J = 8.18 Hz, 1.05 Hz, 1H, CH_{Ar}), 8.65 (s, 1H, N*CH*N). ^{13}CNMR (62.9MHz, $CDCl_3$): δ = 115.4 (CH_{Ar}), 119.4 (q, J = 276.4 Hz, C*CF*$_3$), 120.1 (q, J = 276.4 Hz, C*CF*$_3$), 123.8 (CH_{Ar}), 132.9 (C), 139.7 (CH_{Ar}), 145.5 (q, J = 36.9 Hz, *C*CF$_3$), 147.0 (C), 148.0 (C), 149.0 (CH_{Ar}), 151.2 (q, J = 36.9 Hz, *C*CF$_3$), 152.8 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.6 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\widetilde{v}$ = 3187 (w), 2923 (w), 2852 (m), 2771 (w), 1687 (s), 1588 (s), 1460 (m), 1436 (s), 1294 (s), 1203 (m), 1142 (s), 1000 (s), 854 (m), 771 (s), 702 (s), 627 (s), 522 (s), 474 (s), 407 (m) cm^{-1}. MS (GC, 70eV): m/z (%) = 334 (10), 333 (100) [H]$^+$, 314 (16), 307 (21), 306 (66), 288 (13), 264 (14), 237 (26), 211 (17), 191 (11), 169 (13), 78 (26), 69 (19), 63 (10). HRMS (EI) calcd. for $C_{12}H_5F_6N_5$[M]$^+$: 334.00078; found 334.001655.

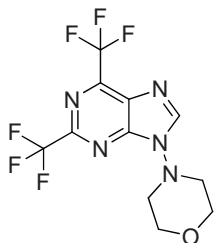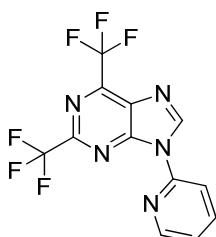**4-(2,6-*Bis*(trifluoromethyl)-*9H*-purin-9-yl)benzenamine (11):** starting with benzene-1,4-diamine **2** (372 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **11** was isolated as a yellow solid (271 mg, 78%). Mp 175-177 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 4.22 (br.s, 2H, NH_2), 6.87 (d, J = 8.6 Hz, 2H, $2CH_{Ar}$), 7.42 (d, J = 8.6 Hz, 2H, $2CH_{Ar}$), 8.58 (s, 1H, N*CH*N). ^{13}CNMR (100.6 MHz, $CDCl_3$): δ = 119.0 ($2CH_{Ar}$), 124.6 (q, J = 276.1 Hz, C*CF_3*), 125.8 (q, J = 276.1 Hz, C*CF_3*), 130.9 ($2CH_{Ar}$), 136.9 (C), 147.9 (q, J = 43.3 Hz, C*CF_3*), 152.9 (q, J = 43.3 Hz, C*CF_3*), 155.1 (C), 157.3 (C), 159.7 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.9 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\tilde{v}$ = 3404 (w), 2078 (w), 1981 (w), 1626 (w), 1521 (w), 1456 (w), 1405 (w), 1338 (w), 1276 (w), 1243 (w), 1217 (w), 1177 (w), 1134 (w), 1022 (w), 1005 (w), 936 (w), 888 (w), 835 (w), 739 (w), 628 (w), 532 (w), 481 (w), 423 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 347 (100) $[M]^+$. HRMS (ESI) calcd. for $C_{13}H_8N_5F_6$ $[M+H]^+$: 348.06784; found 348.06879.

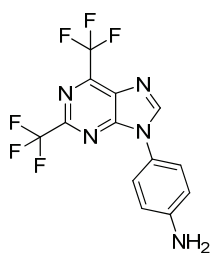**4-(2,6-*Bis*(trifluoromethyl)-*9H*-purin-9-yl)-2,5-dimethylbenzenamine (12):** starting with 2,5-dimethylbenzene-1,4-diamine **2** (469 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **12** was isolated as a white solid (327 mg, 87%). Mp 185-188 ^{0}C. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 4.12 (br.s, 2H, NH_2), 6.70 (s, 1H, CH_{Ar}), 6.96 (s, 1H, CH_{Ar}), 8.41 (s, 1H, N*CH*N). ^{13}CNMR (62.9 MHz, $CDCl_3$): δ = 16.8 (CH_3), 17.5 (CH_3), 116.8 (CH_{Ar}), 119.1 (q, J = 277.7 Hz, C*CF_3*), 120.1 (q, J = 277.7 Hz, C*CF_3*), 120.9 (C), 121.6 (C), 122.5 (C), 128.9 (CH_{Ar}), 130.5 (q, J = 32.2 Hz, C*CF_3*), 130.8 (C), 133.6 (C), 139.7 (q, J = 32.2 Hz, C*CF_3*), 146.4 (C), 150.6 (C), 154.4 (N*CH*N). ^{19}FNMR (300 MHz, $CDCl_3$): δ = -68.4 (CF_3), -65.9 (CF_3). IR (ATR, cm^{-1}): $\tilde{v}$ = 3445 (w), 3341 (w), 1684 (w), 1632 (w), 1592 (w), 1516 (w), 1451 (w), 1399 (w), 1308 (w), 1276 (m), 1234 (m), 1198 (m), 1133 (m), 1036 (w), 975 (w), 928 (w), 888 (m), 819 (w), 739 (m), 661 (m), 578 (w), 524 (w), 455 (w), 414 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 376 (18), 375 (100) $[M]^+$, 374 (12). HRMS (ESI) calcd. for $C_{15}H_{12}N_5F_6$ $[M+H]^+$: 376.09914; found 376.09982.

9-(4-(2,6-*Bis*(trifluoromethyl)-*9H*-purin-9-yl)phenyl)-2,6-bis(trifluoromethyl)-*9H*-purine
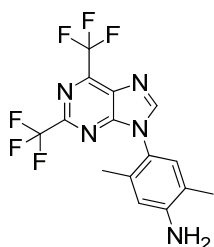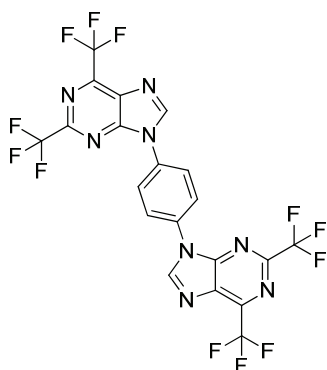
(13): starting with benzene-1,4-diamine **2** (372 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **13** was isolated as a yellow oil (503 mg, 86%). ^{1}HNMR (300 MHz, Acetone-d_6): δ = 8.46 (s, 4H, 4CH$_{Ar}$), 9.54 (s, 2H, N*CH*N). ^{13}CNMR (75.4MHz, CDCl$_3$): δ = 120.6 (q, *J* = 273.0Hz, C*CF*$_3$), 121.8 (q, *J* = 273.0 Hz, C*CF*$_3$), 126.7 (4CH$_{Ar}$), 133.4 (C), 135.0(2C), 145.4 (q, *J* = 38.8 Hz, *C*CF$_3$), 150.1 (q, *J* = 38.8 Hz,

*C*CF$_3$), 151.5 (C), 155.6 (N*CH*N). ^{19}FNMR (300 MHz, Acetone-d_6): δ = -63.9 (2CF$_3$), -61.3 (2CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3107 (w), 1599 (w), 1595 (w), 1456 (w), 1405 (w), 1332 (w), 1275 (m), 1207 (m), 1136 (s), 1026 (m), 934 (m), 886 (m), 843 (m), 801 (w), 737 (w), 662 (w),638 (w), 570 (w), 547 (w), 514 (w), 446 (w), 399 (w) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 586 (100) [M]$^+$, 567 (10). HRMS (EI) calcd. for $C_{20}H_6N_8F_{12}$ [M]$^+$: 586.05183; found 586.051343.

**4,4`-*Bis*(2,6-*bis*(trifluoromethyl)-9*H*-purin-9-yl)-1,1`-biphenyl (14):** starting with benzidine **2** (635 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **14** was isolated as a yellow solid (509 mg, 77%). Mp 292-294 ^{0}C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 8.02 (s, 8H, 8CH$_{Ar}$), 9.22 (s, 1H, N*CH*N). ^{13}CNMR (75.4 MHz, CDCl$_3$): δ = 120.8 (q, *J* = 275.4 Hz, C*CF*$_3$), 121.8 (q, *J* = 275.4 Hz, C*CF*$_3$), 125.3 (C), 125.8 (4CH$_{Ar}$), 129.5 (4CH$_{Ar}$), 133.4 (C), 134.4 (C) 141.3 (C), 145.4 (q, *J* = 35.4 Hz, *C*CF$_3$), 150.1 (q, *J* = 35.4 Hz, *C*CF$_3$), 151.5 (2N*CH*N), 153.0 (C), 155.5

(C). ^{19}FNMR (300 MHz, Acetone-d_6): δ = -110.9 (2CF$_3$), -108.3 (2CF$_3$). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3334 (m), 3295 (m), 2901 (w), 1641 (w), 1425 (w), 1370 (w), 1335 (w), 1204 (w), 1159 (w), 1105 (w), 1029 (m), 896 (w), 873 (w), 555 (m) cm^{-1}. MS (GC, 70eV): *m/z* (%) = 662 (100) [M]$^+$, 661 (11), 643 (11), 595 (10), 594 (17), 295 (47), 276 (13), 275 (31), 43 (13). HRMS (EI) calcd. for $C_{26}H_{10}N_8F_{12}$ [M]$^+$: 662.08313; found 662.081757.

9-(4-(4-(2,6-*Bis*(trifluoromethyl)-*9H*-purin-9-yl)-3-methoxyphenyl)-2-methoxyphenyl)-2,6-bis(trifluoromethyl)-*9H*-purine (15): starting with 3,3`-dimethoxy-(1,1`-biph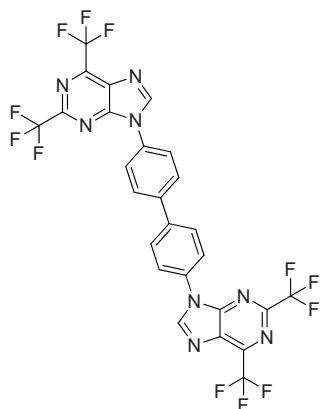enyl)-4,4`-diamine **2** (842 mg, 3.45 mmol), **1** (279 mg, 3.45 mmoles), **5** (590 mg, 3.45 mmoles) and CH_2Cl_2 (2.5 ml), **15** was isolated as a white solid (579 mg, 75%). Mp 280-285 ^{0}C. ^{1}HNMR (300 MHz, Acetone-d_6): δ = 3.91 (s, 6H, 2OCH$_3$), 7.52 (d, J = 1.8 Hz, 1H, CH$_{Ar}$), 7.99 (d, J = 1.8 Hz, 1H, CH$_{Ar}$), 7.60 (d, J = 1.8 Hz, 2H, 2CH$_{Ar}$), 7.75 (s, 1H, CH$_{Ar}$), 7.78 (s, 1H, CH$_{Ar}$), 9.02 (s, 1H, N*CH*N). ^{13}CNMR (100.6MHz, Acetone-d_6): δ = 56.9 (2OCH$_3$), 112.9 (2CH$_{Ar}$), 120.8 (q, J = 277.5 Hz, 2C*C*F$_3$), 120.9 (2CH$_{Ar}$), 121.6 (q, J = 277.5 Hz, 2C*C*F$_3$), 122.3 (2C), 129.2 (2CH$_{Ar}$), 132.4 (2C), 144.2 (2C), 145.1 (q, J = 36.6 Hz, 2*C*CF$_3$), 150.1 (q, J = 36.6 Hz, *C*CF$_3$), 153.2 (2C), 155.3 (2N*CH*N), 156.2 (C). ^{19}FNMR (300 MHz, CDCl$_3$): δ = -68.4 (CF$_3$), -65.9 (CF$_3$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3120 (w), 2976 (w), 2914 (w), 2843 (w), 1596 (w), 1511 (w), 1469 (w), 1407 (w), 1337 (w), 1303 (w), 1251 (w), 1209 (w), 1157 (w), 1131 (w), 1065 (w), 1015 (w), 934 (w), 888 (w), 853 (w), 812 (w), 741 (w), 693 (w), 658 (w), 626 (w), 570 (w), 536 (w) cm^{-1}. MS (GC, 70eV): m/z (%) = 722 (100) [M]$^+$, 703 (15), 693 (17), 654 (10), 653 (15), 69 (10). HRMS (EI) calcd. for C$_{28}$H$_{14}$O$_2$N$_8$F$_{12}$ [M]$^+$: 722.10426; found 722.103828.
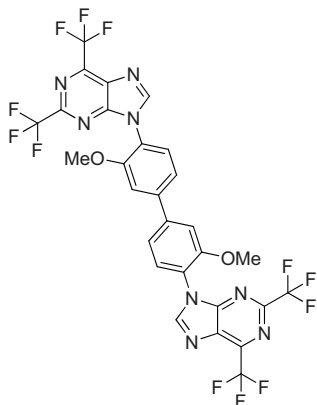
6.3 Synthesis of terphenyls from fluorinated bromobenzenes by site selective Suzuki-Miyaura reactions

General procedure for Suzuki–Miyaura reactions (18a-d, 19a-b)

A 1,4-dioxane solution (4 mL per 0.3 mmol of **16**) of **16**, Cs_2CO_3, $Pd(PPh_3)_4$ and arylboronic acid **17** were stirred at 90 °C for 6 or 8 h. After cooling to room temperature, the organic and the aqueous layers 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.

1-Fluoro-2,4-di(3-methylphenyl)benzene (18a): Starting with **16** (100 mg, 0.39 mmol), Cs_2CO_3 (253 mg, 0.78 mmol), $Pd(PPh_3)_4$ (3 mol%), 3-methylphenylboronic acid **17c** (116 mg, 0.85 mmol) and 1,4-dioxane (4 mL), **18a** was isolated as a colorless oil (83 mg, 57%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.49 (s, 6H, CH_3), 7.23-7.31 (m, 3H, ArH), 7.37-7.48 (m, 6H, ArH), 7.54-7.60 (m, 1H, ArH), 7.69 (q, *J* = 7.5 Hz, 2.5 Hz, 1H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6 (2CH_3), 116.2 (CH), 116.5 (CH), 124.2 (CH), 126.2 (d, *J* = 23.0 Hz, CH), 127.5 (d, *J* = 16.1 Hz, CH), 127.9 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 129.6 (d, *J* = 3.8 Hz, CH), 129.8 (C), 129.3 (C), 129.5 (C), 135.8 (C), 137.7 (d, *J* = 4.7 Hz, C), 155.6 (d, *J* = 42.1 Hz), 159.4 (d, J_{CF} = 248.6 Hz, CF). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -120.3 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 3031 (w), 2947 (w), 2919 (w), 2860 (w), 2732 (w), 1605 (w), 1584 (w), 1504 (w), 1475 (s), 1379 (w), 1257 (w), 1220 (m), 1171 (w), 1123 (w), 1094 (w), 1046 (w), 999 (w), 881 (m), 823 (m), 781 (s), 720 (m), 698 (s), 633 (w), 562 (w), 523 (w), 441 (m). MS (EI, 70 eV): *m/z* (%) = 276 (100) [M]$^+$. HRMS (EI) calcd. for $C_{20}H_{17}F$ [M]$^+$: 276.13088; found 276.130983.
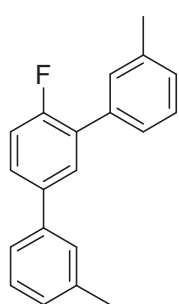
1-Fluoro-2,4-di(3-methoxyphenyl)benzene (18b): Starting with **16** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-methoxyphenylboronic acid **17d** (85 mg, 70 mmol) and 1,4-dioxane (4 mL), **18b** was isolated as a colorless solid (94 mg, 70%). Mp 101-103 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.74, (s, 3H, OCH$_3$), 3.76 (s, 3H, OCH$_3$), 6.84-6.92 (m, 4H, ArH), 7.04-7.14 (m, 1H, ArH), 7.23-7.36 (m, 2H, ArH), 7.39-7.49 (m, 4H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 55.3, (OCH$_3$) 55.4 (OCH$_3$), 114.0 (2CH), 114.1 (2CH), 114.3 (d, J = 23.7 Hz, CH), 116.4 (d, J = 16.3 Hz, CH), 126.6 (d, J = 8.5 Hz, CH), 127.7 (C), 128.1 (2CH), 128.9 (C), 130.2 (2CH), 132.8 (C), 137.3 (d, J = 3.5 Hz, C), 150.5 (C), 158.9 (d, J = 45.0 Hz), 159.1 (d, J_{CF} = 247.0 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -119.9 (CF). IR (ATR, cm^{-1}): ṽ = 3037 (w), 3000 (w), 2955 (w), 2907 (w), 2836 (w), 1605 (m), 1571 (w), 1500 (w), 1480 (s), 1439 (m), 1383 (w), 1310 (w), 1247 (s), 1179 (s), 1114 (m), 1076 (m), 1016 (s), 1000 (m), 962 (w), 886 (w), 832 (s), 808 (s), 791 (s), 765 (w), 717 (w), 656 (w), 589 (w), 550 (m), 529 (m). MS (EI, 70 eV): m/z (%) = 308 (100) [M]$^+$, 293 (26), 265 (14). HRMS (EI) calcd. for C$_{20}$H$_{17}$FO$_2$ [M]$^+$: 308.12071; found 308.120987.
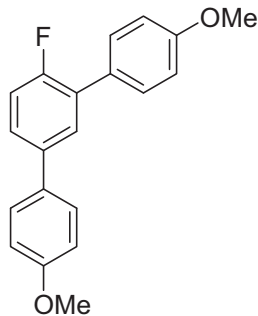
1-Fluoro-2,4-di(2,5-dimethoxyphenyl)benzene (18c): Starting with **16** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 2,5-dimethoxyphenylboronic acid **17g** (158 mg, 0.85 mmol) and 1,4-dioxane (4 mL), **18c** was isolated as a colorless solid (91 mg, 65%). Mp 149-150 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.68 (s, 3H, CH$_3$), 3.69 (s, 3H, OCH$_3$), 3.71 (s, 6H, OCH$_3$), 6.70-6.80 (m, 6H, ArH), 7.04-7.10 (m, 1H, ArH), 7.40-7.45 (m, 2H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 55.8 (2OCH$_3$), 56.3 (OCH$_3$), 56.4 (OCH$_3$), 112.4 (CH), 112.6 (CH), 113.2 (CH), 114.2 (CH), 115.1 (d, J = 22.6 Hz, CH), 116.7 (CH), 117.1 (CH), 125.6 (d, J = 16.4 Hz, C), 126.0 (C), 130.3 (d, J = 7.6 Hz, CH), 130.5 (C), 132.8 (d, J = 4.0 Hz, CH), 134.0 (d, J = 3.5 Hz, C), 150.7 (C), 151.3 (C), 153.5 (C), 153.8 (C), 159.3 (d, J_{CF} = 249.0 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -116.3 (CF). IR (ATR, cm^{-1}): ṽ = 3428 (w), 3021 (w), 2948 (w), 2832 (w), 1582 (w), 1486 (s), 1463 (m), 1407 (m), 1381 (m), 1295 (m), 1264 (m), 1220 (s), 1174 (s), 1113 (m), 1049 (s), 1023 (s), 915 (w), 855 (m), 803 (m), 755 (w), 706 (s), 5651 (w), 568 (w), 507 (w), 468 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 368 (100) [M]$^+$, 339 (12), 338 (57), 169 (12). HRMS (ESI) calcd. for C$_{22}$H$_{22}$O$_4$F [M+H]$^+$: 369.14966; found 369.14871.
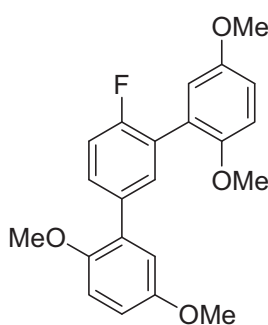
1-Fluoro2,4-di(4-ethylphenyl)benzene (18d): Starting with **16** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-ethylphenylboronic acid **17h** (128 mg, 0.85 mmol) and 1,4-dioxane (4 mL), **18c** was isolated as a colorless oil (69 mg, 57%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.27 (t, J = 7.5 Hz, 3H, CH$_3$), 1.28 (t, J = 7.5 Hz, 3H, CH$_3$), 2.65-2.74 (m, 4H, CH$_2$), 7.18 (q, J = 10.4 Hz, 8.5 Hz, 1H, ArH), 7.28 (t, J = 8.1 Hz, 4H, ArH), 7.45-7.53 (m, 5H, ArH), 7.62 (q, J = 7.7 Hz, 2.7 Hz, 1H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 15.5 (CH$_3$), 15.6 (CH$_3$), 28.5 (CH$_2$), 28.6 (CH$_2$), 116.4 (d, J = 22.0 Hz, CH), 127.0 (2CH), 128.2 (C), 128.0 (2CH), 128.3 (2CH), 129.0 (d, J = 8.0 Hz, CH), 129.3 (d, J = 3.8 Hz, CH), 130.0 (C), 133.1 (2CH), 133.9 (C), 137.5 (d, J = 3.6 Hz, C), 137.6 (C), 143.7 (d, J = 32.4 Hz, C), 159.3 (d, J_{CF} = 247.4 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -120.7 (CF). IR (ATR, cm^{-1}): ṽ = 3024 (w), 2963 (m), 2929 (w), 2871 (w), 1516 (w), 1484 (s), 1456 (w), 1412 (w), 1384 (w), 1258 (w), 1217 (m), 1118 (w), 1044 (w), 965 (w), 898 (w), 831 (m), 815 (s), 703 (w), 659 (w), 616 (w), 562 (w), 500 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 304 (100) [M]$^+$, 290 (21), 289 (91), 274 (14), 137 (16). HRMS (EI) calcd. for C$_{22}$H$_{21}$F [M]$^+$: 304.16218; found 304.162438.

General procedure for the synthesis of 19a–b.

The reaction was carried out in a pressure tube. To a dioxane suspension (4 mL) of 16 (100 mg, 0.39 mmol), Pd(PPh3)$_4$ (3 mol%) and ArB(OH)$_2$ (0.39 mmol) was added Cs$_2$CO$_3$ (126 mg, 0.39 mmol), and the resultant solution was degassed by bubbling argon through the solution for 10 min. The mixture was heated at 100 °C under Argon atmosphere for 8 h. They were diluted with water and extracted with CH$_2$Cl$_2$ (3 * 50 mL). The combined organic layers were dried (Na$_2$SO$_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel, DCM/ heptane = 1:4).
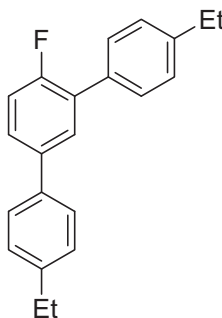
2-Bromo-1-fluoro-4-(4-methoxyphenyl)benzene (19a): Starting with **16** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (126 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-methoxyphenylboronic acid **17d** (59 mg, 0.39 mmol) and 1,4-dioxane (4 mL), **19a** was isolated as a colorless solid (78 mg, 70%). Mp 66-68 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.78 (s, 3H, OCH$_3$), 6.89-6.96 (m, 2H, ArH), 6.96 (d, J = 6.6 Hz, 1H, CH), 7.18-7.20 (m, 2H, CH), 7.34 (d, J = 1.5 Hz, 1H, CH), 7.38 (d, J = 1.5 Hz, 1H, CH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 55.4 (OCH$_3$), 108.9 (d, J = 21.0 Hz, CH), 114.1 (2CH), 117.8 (d, J = 18.0 Hz, CH), 130.2 (CH), 131.0 (CH), 131.1 (CH), 132.2

(C), 135.5 (C), 136.1 (C), 159.7 (C), 156.1 (d, J = 248.0 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -119.8 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3074 (m), 3015 (m), 2960 (m), 2837 (w), 1605 (m), 1514 (m), 1295 (m), 1255 (s), 1075 (s), 1016 (s), 875 (m), 792 (m), 696 (m), 624 (m), 576 (s). GC-MS (EI, 70 eV); m/z (%) = 280 (100) (^{79}Br) [M]$^+$, 267 (24), 265 (18), 239 (34), 237 (30), 213 (11), 170 (11), 158 (24), 157 (51), 138 (9), 44 (11). HRMS (EI) calcd. for C$_{13}$H$_{10}$OBrF [M]$^+$: 279.98936; found 279.989522 and calcd. for C$_{13}$H$_{10}$O^{81}BrF [M]$^+$: 281.98731; found 281.987381.

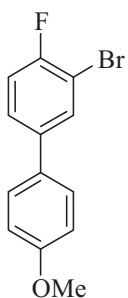**2-Bromo-1-fluoro-4-(4-ethylphenyl)benzene (19b):** Starting with **16** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (126 mg, 0.39 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-ethylphenylboronic acid **17h** (53 mg, 0.39 mmol) and 1,4-dioxane (4 mL), **18b** was isolated as a colorless solid (65 mg, 63%). Mp 99-101 °C ^{1}H NMR (300 MHz, CDCl$_3$):^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.76 (dd, J = 6.6 Hz, 2.3 Hz, 1H, ArH), 7.48 (ddd, J = 8.5 Hz, 4.6 Hz, 2.3 Hz, 1H, ArH), 7.45 (d, J = 8.5 Hz, 2H, ArH), 7.28 (d, J = 8.5, 1H, ArH), 7.18 (t, J = 8.5 Hz, 1H, ArH), 2.71 (q, J = 7.6 Hz, 2H, CH$_2$), 1.29 (t, J = 7.6 Hz, 3H, CH$_3$). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 15.5 (CH$_3$), 28.4 (CH$_2$), 109.2 (d, J = 21.1 Hz, CH), 114. 5 (2CH), 116.5 (d, J = 22 Hz, CH), 128.4 (CH), 127.3 (d, J = 7.1 Hz, CH), 131.8 (CH), 136.2 (C), 137.4 (C), 138.8 (d, J = 3.8 Hz, C), 144.0 (C), 158.4 (d, J_{CF} = 247.2 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -110.3 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3024 (w), 2964 (w), 2929 (w), 2871 (w), 1903 (w), 1598 (w), 1487 (s), 1377 (w), 1264 (m), 1129 (w), 1045 (m), 964 (w), 835 (w), 812 (s), 779 (w), 691 (m), 624 (w), 555 (m). MS (EI, 70 eV); m/z (%) = 278 (64) [M]$^+$, 266 (13), 265 (97), 264 (14), 263 (100), 184 (17), 183 (65), 170 (22). HRMS (EI) calcd. for C$_{14}$H$_{12}$Br F [M]$^+$: 278.01009; found 278.009637, C$_{14}$H$_{12}$^{81}Br F calcd. 280.00805; found 280.007711.

General procedure for the synthesis of 20a.

The reaction was carried out in a pressure tube. To a dioxane suspension (4 mL) of 16 (200 mg, 0.78 mmol), Pd(PPh3)4 (3 mol %) and $Ar^1B(OH)_2$ (0.78 mmol) was added Cs_2CO_3 (253 mg, 0.78 mmol), and the resultant solution was degassed by bubbling argon through the solution for 10 min. The mixture was heated at 90 °C under Argon atmosphere for 8 h. The mixture was cooled to 20 °C and $Ar^2B(OH)_2$ (0.93 mmol) and Cs_2CO_3 (253 mg, 0.78 mmol) was added. The reaction mixtures were heated under Argon atmosphere for 6 h at 100 °C. They were diluted with water and extracted with CH_2Cl_2 (3 * 50 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, EtAc/ hexane = 1:4).
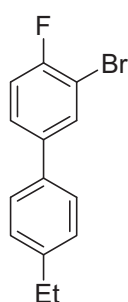
1-Fluoro-2-(4-methoxyphenyl)-4-(4-trifluorophenyl)benzene (20a): Starting with **16** (200 mg, 0.78 mmol), Cs_2CO_3 (253 mg, 0.78 mmol), Pd(PPh3)4 (3 mol%), 4-trifluoromethylphenylboronic acid **17o** (148 mg, 0.78 mmol) and 4-methoxyphenylboronic acid **17d** (142 mg, 0.93 mmol) and 1,4-dioxane (4 mL), **20a** was isolated as a colorless solid (79 mg, 58%). Mp 149-151 °C. ^1H NMR (300 MHz, CDCl3): δ = 3.73 (s, OCH3), 6.86-6.95 (m, 4H, ArH), 7.05-7.16 (m, 1H, ArH), 7.26-7.45 (m, 2H, ArH), 7.60-7.65 (m, 4H, ArH). ^{13}C NMR (75 MHz, CDCl3): δ = 55.4 (OCH3), 110.3 (CH), 110.4 (CH), 111.3 (CH), 114.1 (CH), 114.4 (CH), 116.6 (CH), 125.4 (d, J = 24.5, Hz, C), 126.7 (C), 127.1 (CH), 127.4 (CH), 128.1 (d, J = 3.87 Hz, CH), 129.4 (CH), 130.2 (CH), 132.4 (C), 155.4 (C), 157.9 (d, J = 13.3 Hz, C), 158.2, (d, J_{CF} = 247.8 Hz, CF), 160.0 (d, J = 9.6 Hz, C). ^{19}F NMR (282 MHz, CDCl3): δ = -61.9, -(CF3), -110.7 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 3072 (w), 3037 (w), 2957 (w), 2912 (w), 2837 (w), 1605 (m), 1569 (m), 1517 (m), 1486 (s), 1439 (s), 1384 (m), 1323 (s), 1273 (s), 1234 (s), 1177 (s), 1124 (s), 1069 (s), 1012 (s), 962 (w), 891 (w), 835 (m), 809 (s), 794 (m), 765 (m), 714 (w), 656 (w), 598 (w), 550 (m), 530 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 346 (100) $[M]^+$, 331 (11). HRMS (EI) calcd. for $C_{20}H_{14}OF_4$ $[M]^+$: 346.09753; found 346.096887.
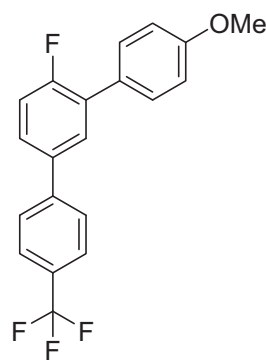
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General procedure for the synthesis of 22a–c.

The reaction was carried out in a pressure tube. To a dioxane suspension (4 mL) of 21 (200 mg, 0.79 mmol), Pd(PPh3)$_4$ (3 mol%) and ArB(OH)$_2$ (1.58 mmol) was added Cs$_2$CO$_3$ (385 mg, 1.81 mmol), and the resultant solution was degassed by bubbling argon through the solution for 10 min. The mixture was heated at 100 °C under Argon atmosphere for 8 h. They were diluted with water and extracted with CH$_2$Cl$_2$ (3 * 50 mL). The combined organic layers were dried (Na$_2$SO$_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel, DCM/ heptane = 1:4).

1,4-Di(2,5-dimethoxyphenyl)-2-fluorobenzene (22a): Starting with **21** (200 mg, 0.79 mmol), Cs$_2$CO$_3$ (385 mg, 1.81 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 2,5-dimethoxyphenylboronic acid (287 mg, 1.58 mmol) and 1,4-dioxane (4 mL), **22a** was isolated as a colorless solid (221 mg, 76%). Mp 95-97 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.69 (s, 3H, OCH$_3$), 3.70 (s, 3H, OCH$_3$), 3.71 (s, 3H, OCH$_3$), 3.72 (s, 3H, OCH$_3$), 6.76-6.87 (m, 6H, ArH), 7.25-7.33 (m, 3H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 55.8 (2OCH$_3$), 56.2 (OCH$_3$), 56.4 (OCH$_3$), 112.5 (2CH), 113.9 (2CH), 116.5 (2CH), 116.9 (d, J = 25.7 Hz, CH), 124.6 (d, J = 16.4 Hz, C), 124.8 (d, J = 3.0 Hz, CH), 125.8 (C), 130.0 (d, J = 2.3 Hz, C), 131.3 (d, J = 3.8 Hz, CH), 139.5 (d, J = 8.2 Hz, C), 151.0 (d, J = 15.5 Hz, 2C), 153.6 (d, J = 23.1 Hz, 2C), 159.6 (d, J_{CF} = 247.3 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -114.6 (CF). IR (ATR, cm^{-1}): ṽ = 2991 (w), 2938 (w), 2832 (w), 1616 (w), 1586 (w), 1487 (m), 1403 (m), 1297 (w), 1257 (m), 1216 (m), 1176 (m), 1119 (m), 1082 (m), 1017 (s), 933 (m), 869 (m), 828 (m), 797 (s), 733 (m), 688 (m), 603 (m), 539 (m), 457 (m) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 368 (100) [M]$^+$, 339 (12), 338 (59), 169 (12). HRMS (ESI) calcd. for C$_{22}$H$_{22}$FO$_4$ [M+H]$^+$: 369.14966; found 369.15. Anal. Calcd for C$_{22}$H$_{22}$FO$_4$: C,71.73. H, 5.75. Found: C, 71.75. H, 5.77.
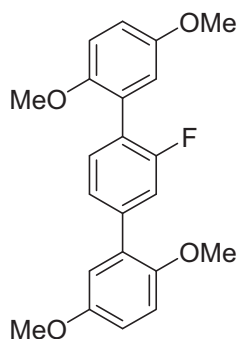
1,4-Di(4-ethylphenyl)-2-fluorobenzene (22b): Starting with **21** (200 mg, 0.79 mmol), Cs$_2$CO$_3$ (385 mg, 1.81 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-ethylphenylboronic acid **17h** (237 mg, 1.58 mmol) and 1,4-dioxane (4 mL), **22b** was isolated as a colorless solid (195 mg, 81%). Mp 111 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.20 (t, J = 15.2 Hz, 7.5 Hz, 3H, CH$_3$), 1.22 (t, J = 15.2 Hz, 7.5 Hz, 3H, CH$_3$), 2.62 (t, J = 15.1 Hz, 7.4 Hz, 4H, 2CH$_2$), 7.19-7.22 (m, 4H, ArH), 7.27-7.40 (m, 3H, ArH), 7.42-7.47 (m, 4H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 15.6 (d, J = 2.2 Hz, 2CH$_3$), 28.6 (d, J = 5.5 Hz, 2CH$_2$), 114.5 (CH), 122.7 (d, J = 4.0 Hz, CH), 126.9 (2CH), 127.4 (d, J = 13.8 Hz, C), 128. (2CH), 128.5 (2CH), 128.9 (d, J = 4.0 Hz, CH), 130.8 (d, J = 4.0 Hz, CH), 132.9 (C), 136.9 (C), 141.9 (d, J = 8.3 Hz, C), 143.9 (d, J = 20.9 Hz, CH), 160.1 (d, J_{CF} = 247.0 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -117.24 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 3027 (w), 2963 (w), 2873 (w), 2361 (w), 1609 (w), 1544 (w), 1485 (w), 1428 (w), 1394 (w), 1295 (w), 1260 (w), 1180 (w), 1135 (w), 1050 (w), 1004 (w), 970 (w), 889 (w), 814 (w), 728 (w), 696 (w), 641 (w), 582 (w), 499 (w), 417 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 304 (100) [M]$^+$, 290 (18), 289 (80), 274 (21), 137 (17). HRMS (ESI) calcd. for C$_{22}$H$_{22}$F [M+H]$^+$: 305.17001; found 305.16948. Anal. Calcd for C$_{21}$H$_{17}$FO$_2$: C,86.85. H, 6.91. Found: C, 86.82. H, 6.88.
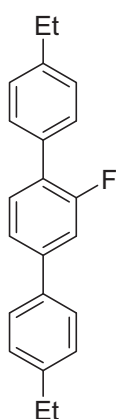
1,4-Di(3-chlorophenyl)-2-fluorobenzene (22c): Starting with **21** (200 mg, 0.79 mmol), Cs$_2$CO$_3$ (385 mg, 1.81 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 3-chlorophenylboronic acid **17j** (246 mg, 1.58 mmol) and 1,4-dioxane (4 mL), **22c** was isolated as a colorless solid (201 mg, 80%). Mp 102-103 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.25-7.33 (m, 5H, ArH), 7.34-7.35 (m, 1H, ArH). 7.37-7.43 (m, 3H, ArH), 7.49-7.52 (m, 2H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 114.8 (d, J = 25.7 Hz, CH), 123.0 (d, J = 4.0 Hz, CH), 125.1 (CH), 127.1 (2CH), 128.0 (d, J = 3.4 Hz, 2CH), 129.0 (d, J = 4.0 Hz, CH), 130.0 (d, J = 3.7 Hz, 2CH), 131.0 (d, J = 4.0 Hz, CH), 134.4 (C), 134.9 (C), 137.0 (C), 141.1 (C), 141.4 (C), 141.5 (C), 159.9 (d, J_{CF} = 248.8 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -114.6 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 3066 (w), 2923 (w), 2851 (w), 1619 (m), 1562 (m), 1463 (m), 1386 (s), 1288 (m), 1248 (m), 1186 (m), 1130 (m), 1079 (m), 1022 (m), 967 (m), 915 (m), 876 (m), 824 (m), 773 (s), 756 (s), 686 (s), 636 (m), 552 (m), 515 (m), 468 (m), 419 (m) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 316 (100) [M]$^+$, 246 (17), 244 (19), 122 (13). HRMS (EI) calcd. for C$_{18}$H$_{11}$Cl$_2$F [M]$^+$: 316.02164; found 316.021941; calcd. for C$_{18}$H$_{11}$Cl^{37}ClF [M]$^+$: 318.01869; found 318.018980.
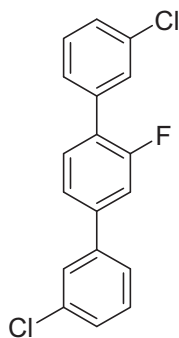
General procedure for the synthesis of 23a–c.

The reaction was carried out in a pressure tube. To a dioxane suspension (4 mL) of 21 (200 mg, 0.79 mmol), Pd(PPh3)$_4$ (3 mol%) and Ar^{1}B(OH)$_2$ (0.79 mmol) was added Cs$_2$CO$_3$ (385 mg, 1.81 mmol), and the resultant solution was degassed by bubbling argon through the solution for 10 min. The mixture was heated at 90 °C under Argon atmosphere for 8 h. The mixture was cooled to 20 °C and Ar^{2}B(OH)$_2$ (0.95 mmol) and Cs$_2$CO$_3$ (385 mg, 1.18 mmol) was added. The reaction mixtures were heated under Argon atmosphere for 6 h at 100 °C. They were diluted with water and extracted with CH$_2$Cl$_2$ (3 * 50 mL). The combined organic layers were dried (Na$_2$SO$_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel, EtOAc/ hexane = 1:4).

2-Fluoro-1-(4-methoxyphenyl)-4-(4-methylphenyl)benzene (23a): Starting with **21** (200 mg, 0.79 mmol), Cs$_2$CO$_3$ (385 mg, 1.81 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-methoxyphenylboronic acid **17d** (120 mg, 0.79 mmol) and 1,4-dioxane (4 mL) and 4-methylphenylboronic acid **17b** (125 mg, 0.95 mmol), **23a** was isolated as a colorless solid (188 mg, 79%). Mp 198 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.32 (s, 3H, CH$_3$), 3.78 (s, 3H, OCH$_3$), 6.91 (d, *J* = 8.9 Hz, 2H, ArH), 7.16-7.20 (m, 7H, CH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 21.4 (CH$_3$), 55.3 (OCH$_3$), 114.0 (d, *J* = 23.0 Hz, 2CH), 114.3 (d, *J* = 12.9 Hz, CH), 122.6 (d, *J* =5.4 Hz, CH), 126.8 (2CH), 127.7 (C), 128.0 (CH), 128.8 (d, *J* = 3.3 Hz, C), 129.2 (CH), 129.6 (CH), 130.1 (d, *J* = 3.4 Hz, CH), 130.6 (d, *J* = 5.5 Hz, CH), 136.7 (d, *J* = 1.8 Hz, C), 137.7 (C), 137.8 (C), 141.0 (C), 142.1 (C), 159.2 (C), 160.5 (d, *J*$_{CF}$ = 248.2 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -117.6 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 2958 (w), 1913 (w), 1606 (w), 1548 (w), 1484 (m), 1394 (m), 1299 (w), 1244 (m), 1178 (m), 1133 (m), 1032 (m), 889 (m), 808 (s), 734 (w), 637 (w), 579 (m), 503 (m), 415 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 292 (100) [M]$^+$, 277 (34), 249 (23), 233 (12). HRMS (EI) calcd. for C$_{20}$H$_{17}$FO [M]$^+$: 292.12579; found 292.125521.
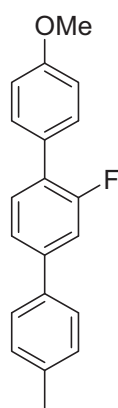
1-(4-Acetylphenyl)-2-fluoro-4-(4-methylphenyl)benzene (23b): Starting with **21** (200 mg, 0.79 mmol), Cs_2CO_3 (385 g, 1.81 mmol), $Pd(PPh_3)_4$ (3 mol%), 4-acetylyphenylboronic acid **17n** (129 mg, 0.79 mmol) and 1,4-dioxane (4 mL) and 4-methylphenylboronic acid **17b** (129 mg, 0.95 mmol), **23b** was isolated as a colorless solid (151 mg, 62%). Mp 89-90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 7.21 (d, J = 8.5 Hz, 2H, ArH), 7.30-7.49 (m, 5H, ArH), 7.61-7.65 (m, 2H, ArH), 7.98 (d, J = 8.6 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CH_3), 26.7 (CH_3CO), 114.4 (CH), 114.6 (CH), 114.9 (CH), 122.9 (d, J = 4.8 Hz, CH), 126.8 (CH), 127.0 (CH), 128.5 (CH), 129.3 (CH), 129.7 (CH), 130.8 (CH), 128.8 (d, J = 3.3 Hz, CH), 136.1 (C), 136.3 (d, J = 1.8 Hz, C), 138.1 (C), 139.0 (C), 140.4 (d, J = 1.9 Hz, C), 143.3 (d, J = 8.0 Hz, C), 160.1 (d, J_{CF} = 248.5 Hz, CF), 197.7 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -116.92 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 3341 (w), 3032 (w), 2915 (w), 2858 (w), 1678 (s), 1618 (m), 1598 (s), 1542 (m), 1484 (m), 1423 (m), 1391 (m), 1357 (m), 1305 (m), 1263 (s), 1182 (m), 1133 (m), 1041 (m), 1004 (m), 957 (m), 891 (m), 833 (m), 807 (s), 739 (m), 692 (m), 628 (m), 598 (m), 545 (m), 502 (m), 460 (m), 416 (m) cm^{-1}. GC-MS (EI, 70 eV): m/z (%) = 304 (69) [M]$^+$, 290 (20), 289 (100), 246 (26), 144 (13). HRMS (ESI) calcd. for $C_{21}H_{18}FO_2$ [M+H]$^+$: 305.13362; found 305.13433.

1-(4-Methoxyphenyl)-4-(2-methoxyphenyl)-2-fluorobenzene (23c): Starting with **21** (200 mg, 0.79 mmol), Cs_2CO_3 (385 mg, 1.81 mmol), $Pd(PPh_3)_4$ (3 mol%), 4-methoxyphenylboronic acid **17d** (120 mg, 0.79 mmol), 2-methoxyphenylboronic acid **17e** (120 mg, 0.79 mmol) and 1,4-dioxane (4 mL), **23c** was isolated as a colorless solid (156 mg, 64%). Mp = 150-152 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91, 3.93 (s, 6H, OCH_3), 7.06-7.15 (m, 4H, CH), 7.39-7.43 (m, 3H, CH), 7.56-7.66 (m, 4H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4, 55.4 (OCH_3), 114.1 (CH), 114.3 (CH), 114.6 (CH), 114.7 (CH), 114.6 (d, J = 20.5 Hz, CH), 122.6 (d, J = 4.0 Hz, CH), 127.1 (C), 128.6 (CH), 128.6 (CH), 130.9 (d, J = 3.5 Hz, CH), 130.9 (d, J = 4.0 Hz, CH), 130.7 (C), 130.9 (C), 132.2 (C), 132.2 (C), 142.0 (d, J = 7.5 Hz, C), 150.1 (C), 158.6 (d, J_{CF} = 248.0 Hz, CF). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -114.91 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 3015 (w), 2933 (w), 2834 (w), 1902 (w), 1602 (m), 1577 (m), 1500 (m), 1454 (s), 1434 (m), 1396 (m), 1294 (m), 1246 (m), 1180 (m), 1114 (m), 1022 (s), 891 (m), 876 (m), 821 (m), 808 (m), 647 (m), 589 (m), 528 (m), 448 (w) cm^{-1}. GC-MS (EI, 70 eV): m/z (%): 308 (100) [M]$^+$, 293

(16), 278 (11), 265 (4), 233 (5), 220(5). HRMS (EI): calcd. for $C_{20}H_{17}FO_2$ [M]$^+$: 308.12071, found 308.120211.
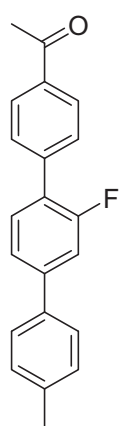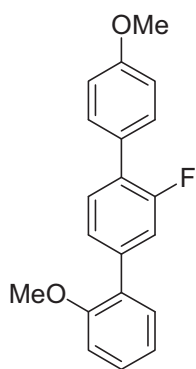
General procedure for the synthesis of 25a–f.

The reaction was carried out in a pressure tube. To a dioxane suspension (4 mL) of 24 (100 mg, 0.39 mmol), Pd(PPh3)$_4$ (3 mol%) and ArB(OH)$_2$ (0.78 mmol) was added Cs$_2$CO$_3$ (253 mg, 0.78 mmol), and the resultant solution was degassed by bubbling argon through the solution for 10 min. The mixture was heated at 100 °C under Argon atmosphere for 8 h. They were diluted with water and extracted with CH$_2$Cl$_2$ (3 * 50 mL). The combined organic layers were dried (Na$_2$SO$_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel, DCM/ heptane = 1:4).

4-Fluoro-1,2-diphenylbenzene (25a): Starting with **24** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), phenylboronic acid **17a** (95 mg, 0.78 mmol) and 1,4-dioxane (4 mL), **25a** was isolated as a colorless oil (79 mg, 79%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.08-7.12 (m, 6H, ArH), 7.18-7.21 (m, 6H, ArH), 7.35-7.43 (m, 1H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 114.1 (d, J = 21.0 Hz, 2CH), 117.1 (d, J = 21.0 Hz, 2CH), 126.5 (2CH), 126.9 (2CH), 127.0 (CH), 127.3 (CH), 127.9 (d, J = 4.1 Hz, CH), 129.7 (d, J = 12.0 Hz, CH), 132.1 (d, J = 8.2 Hz, CH), 136.6 (d, J = 3.2 Hz, C), 137.1 (C), 140.4 (d, J = 2.0 Hz, C), 142.4 (d, J = 7.9 Hz, C), 162.0 (d, J_{CF} = 246.7 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -115.7 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 2998 (w), 2929 (w), 2833 (w), 2052 (w), 1898 (w), 1724 (w), 1597 (w), 1494 (m), 1456 (m), 1403 (w), 1363 (w), 1274 (m), 1245 (s), 1175 (m), 1120 (m), 1052 (m), 1052 (m), 1024 (m), 967 (w), 889 (w), 820 (w), 788 (w), 747 (s), 694 (w), 627 (w), 560 (w), 536 (m). MS (GC, 70eV): m/z (%) = 248 (100) [M]$^+$, 247 (39), 246 (20), 244 (15), 233 (35), 227 (22), 226 (21), 220 (11) cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{13}F$ [M]$^+$ 248.099461, found 248.09958.
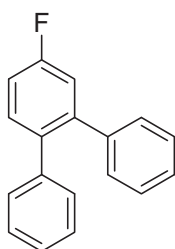
4-Fluoro-1,2-di(4-methylphenyl)benzene (25b): Starting with **24** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-methylphenylboronic acid **17b** (106 mg, 0.78 mmol) and 1,4-dioxane (4 mL), **25b** was isolated as a colorless solid (89 mg, 81%). Mp 96-98 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.39 (s, 3H, CH$_3$), 2.40 (s, 3H, CH$_3$), 7.14-7.27 (m, 6H, ArH), 7.45-7.49 (m, 4H, ArH), 7.60 (q, J = 7.4, 2.2 Hz, 1H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 20.4 (CH$_3$), 20.6 (CH$_3$), 115.6 (d, J = 24.7 Hz, CH), 126.2 (2CH), 126.5 (d, J = 8.3 Hz, CH), 128.3 (d, J = 2.6 Hz, CH), 128.6 (2CH), 128.6 (2CH), 128.9 (2CH), 132.3 (C), 133.5 (C), 136.5 (2C), 136.8 (d, J = 3.4 Hz, C), 136.9 (d, J = 3.9 Hz, C), 158.5 (d, J_{CF} = 248.0 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -121.1 (CF). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3051 (w), 2946 (w), 2853 (w), 2733 (w), 1898 (w), 1731 (w), 1645 (w), 1589 (w), 1514 (w), 1483 (m), 1407 (w), 1380 (w), 1308 (w), 1249 (w), 1207 (w), 1116 (w), 1039 (w), 1009 (w), 959 (w), 902 (w), 856 (w), 808 (m), 764 (w), 719 (w), 663 (w), 615 (w), 549 (w) cm^{-1}. MS (GC, 70eV): m/z (%) = 277 (21), 276 (100) [M]$^+$. HRMS (EI): calcd for C$_{20}$H$_{17}$F [M]$^+$ 276.13088, found 276.130932.
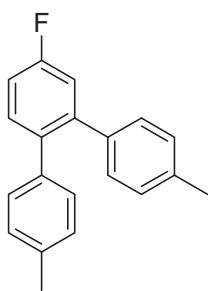
4-Fluoro-1,2-di(4-methoxyphenyl)benzene (25c): Starting with **24** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-methoxyphenylboronic acid **17d** (118 mg, 0.78 mmol) and 1,4-dioxane (4 mL), **25c** was isolated as a dark brown solid (94 mg, 70%). Mp 86-88 ^{0}C: ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.70 (s, 3H, OCH$_3$), 3.76(s, 3H, OCH$_3$), 6.68 (dd, J = 8.7, 2.1 Hz, 3H, ArH), 6.86-7.02 (m, 6H, ArH), 7.24 (dd, J = 8.4, 5.6 Hz, 1H, ArH), 7.40 (dt, J = 6.8 Hz, 2.6 Hz,, 1H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 55.1 (OCH$_3$), 55.3 (OCH$_3$), 113.4 (2CH), 113.7 (d, J = 20.9 Hz, CH), 114.1 (2CH), 116.9 (d, J = 20.9 Hz, CH), 127.7 (2CH), 130.8 (d, J = 2.1 Hz, 2CH), 131.9 (d, J = 2.7 Hz, CH), 133.0 (d, J = 2.5 Hz, C), 133.3 (d, J = 8.9, C), 136.9 (d, J = 2.5 Hz, C), 141.9 (d, J = 7.4 Hz, C), 158.4 (d, J = 4.4 Hz, C), 158.7 (C), 161.7 (d, J_{CF} = 247.1 Hz, CF). ^{19}F NMR (282.4 MHz, CDCl$_3$): δ = -115.8 (CF). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3072 (w), 3012 (w), 2956 (w), 2929 (w), 2838 (w), 2535 (w), 2065 (w), 2032 (w),1892 (w), 1766 (w), 1605 (m), 1567 (w), 1717 (w), 1464 (m), 1399 (w), 1328 (w), 1289 (m), 1239 (s), 1175 (m), 1115 (m), 1079 (m), 1014 (m), 967 (w), 885 (m), 820 (s), 781 (m), 746 (w), 700 (w), 645 (w), 604 (w), 564 (m), 545 (m) cm^{-1}. MS (GC, 70eV): m/z (%) = 308 (100) [M]$^+$, 233 (20), 221 (11), 220 (13). HRMS (EI): calcd. for C$_{20}$H$_{17}$O$_2$F [M]$^+$ 308.12071, found 308.120558
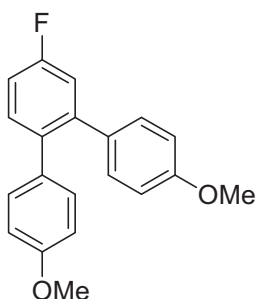
4-Fluoro-1,2-di(2-methoxyphenyl)benzene (25d): Starting with **24** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 2-methoxyphenylboronic acid **17e** (118 mg, 0.78 mmol) and 1,4-dioxane (4 mL), **25d** was isolated as a colorless solid (83 mg, 67%). Mp 101-103 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.47 (s, 3H, OCH$_3$), 3.77 (s, 3H, OCH$_3$), 6.70 (t, J = 7.2 Hz, 1H, ArH), 6.78-6.83 (m, 1H, ArH), 6.96-7.04 (m, 4H, ArH), 7.08-7.17 (m, 3H, ArH), 7.24-7.26 (m, 1H, ArH), 7.30-7.36 (m, 1H, ArH). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 53.8, (OCH$_3$) 54.6 (OCH$_3$), 109.2 (d, J = 3.1 Hz, CH), 110.0 (CH), 112.8 (d, J = 20.1 Hz, CH), 116.2 (d, J = 20.1 Hz, CH), 119.0 (d, J = 30.8 Hz, CH), 126.7 (CH), 127.2 (d, J = 7.7 Hz, CH), 127.5 (CH), 128.3 (CH), 128.7 (d, J = 2.1 Hz, C), 128.9 (CH) 130.2 (d, J = 18.2 Hz, C), 130.9 (d, J = 8.4 Hz, CH), 139.2 (d, J = 9.1 Hz, C), 155.1 (2C), 155.5 (d, J = 6.0 Hz, C), 160.8 (d, J_{CF} = 245.7 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -116.4 (CF). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3058 (w), 2960 (w), 2833 (w), 1894 (w), 1724 (w), 1597 (w), 1498 (w), 1454 (w), 1404 (w), 1298 (w), 1252 (w), 1173 (w), 1120 (w), 1052 (w), 1021 (w), 934 (w), 884 (w), 821 (w), 797 (w), 747 (w), 694 (w), 612 (w), 559 (w), 536 (w). MS (GC, 70eV): m/z (%) = 308 (100) [M]$^+$, 277 (20), 262 (10), 245 (10), 233 (21) cm^{-1}. HRMS (EI): calcd for C$_{20}$H$_{17}$O$_2$F [M]$^+$ 308.12071, found 308.120865.
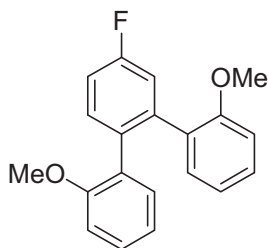
4-Fluoro-1,2-di(2,3-dimethoxyphenyl)benzene (25e): Starting with **24** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 2,3-dimethoxyphenylboronic acid **17f** (141 mg, 0.78 mmol) and 1,4-dioxane (4 mL), **25e** was isolated as a colourless solid (87 mg, 59%). Mp 176-178 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.59 (s, 3H, OCH$_3$), 3.64 (s, 3H, OCH$_3$), 3.80 (s, 3H, OCH$_3$), 3.89 (s, 3H, OCH$_3$), 6.58 (dt, J = 9.5 Hz, 2.0 Hz, 1H, ArH), 6.72.-6.94 (m, 5H, ArH), 7.04–7.18 (m, 2H, ArH), 7.38 (q, J = 8.5, 5.9 Hz, 1H, ArH). ^{13}C NMR (75.46 MHz, CDCl$_3$): δ = 55.7 (OCH$_3$), 55.8 (OCH$_3$), 60.3 (OCH$_3$), 60.6 (OCH$_3$), 111.4 (d, J = 15.8 Hz, 2CH), 111.6 (CH), 113.7 (d, J = 21.4 Hz, C), 117.4 (d, J = 21.9 Hz, C), 122.9 (d, J = 3.4 Hz, 2CH), 123.2 (d, J = 3.4 Hz, 2CH), 123.6 (2CH), 132.2 (d, J = 9.9 Hz, C), 132.8 (C), 134.8 (C), 146.5 (d, J = 9.6 Hz, C), 146.8 (C), 152.6 (d, J = 10.9 Hz, C), 161.3 (d, J = 245.8 Hz, CF). ^{19}F NMR (282.4 MHz, CDCl$_3$): δ = -116.3 (CF). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3060 (w), 2934 (w), 2832 (w), 1738 (w), 1574 (m), 1460 (s), 1397 (m), 1309 (m), 1284 (m), 1256 (s), 1187 (s), 1140 (s), 1081 (s), 1030 (s), 995 (s), 934 (m), 869 (m), 822 (s), 788 (s), 746 (s), 682 (m),

644 (m), 588 (m), 533 (m). MS (GC, 70eV): m/z (%) = 368 (100) [M]$^+$, 337 (23), 322 (19), 307 (14), 306 (32), 290 (13) cm^{-1}. HRMS (EI): calcd for C$_{22}$H$_{21}$O$_4$F [M]$^+$ 368.14184, found 368.142136.
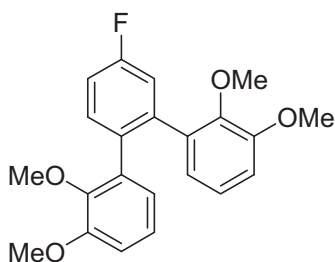
4-Fluoro-1,2-di(4-vinylphenyl)benzene (25f): Starting with **24** (100 mg, 0.39 mmol), Cs$_2$CO$_3$ (253 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (3 mol%), 4-vinylphenylboronic acid **17i** (115 mg, 0.78 mmol) and 1,4-dioxane (4 mL), **25f** was isolated as a colourless solid (53 mg, 45%). Mp stable upto 375 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 5.30 (d, J = 10.9 Hz, 2H, CH$_2$), 5.81 (d, J = 15.4 Hz, 2H, CH$_2$), 6.77 (q, J = 17.4 Hz, 10.8 Hz, 2H, CH), 7.38–7.60 (m, 11H, ArH). ^{13}C NMR (75.46 MHz, CDCl$_3$): δ = 114.3 (CH$_2$), 114.4 (CH$_2$), 114.6 (2CH), 122.7 (d, J = 3.0 Hz, CH), 126.4 (2CH), 126.8 (CH), 127.0 (CH), 127.4 (d, J = 13.8 Hz, C), 129.0 (d, J = 3.6 Hz, CH), 130.8 (d, J = 4.4 Hz, CH), 134.8 (d, J = 2.2 Hz, CH), 136.3 (d, J = 11.0 Hz, CH), 137.1 (d, J = 18.2 Hz, C), 138.7 (d, J = 2.4 Hz, 2C), 141.8 (d, J = 8.0 Hz, 2C), 160.0 (d, J_{CF} = 247.6 Hz, CF). ^{19}F NMR (282.4 MHz, CDCl$_3$): -117.4 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3087 (m), 3035 (m), 2956 (m), 2920 (m), 2850 (m), 1919 (w), 1834 (w), 1651 (w), 1627 (m), 1572 (m), 1484 (m), 1431 (m), 1393 (m), 1359 (m), 1296 (m), 1258 (m), 1184 (m), 1137 (m), 1046 (w), 992 (m), 912 (m), 851 (m), 816 (s), 750 (m), 699 (m), 577 (m), 536 (m) cm^{-1}. MS (GC, 70eV): m/z (%) = 300 (100) [M]$^+$. HRMS (EI): calcd for C$_{22}$H$_{17}$F [M]$^+$ 300.13088, found 300.131268.
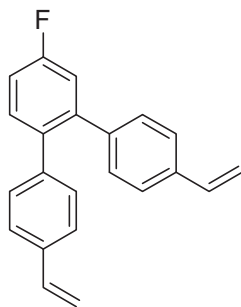
6.4 Synthesis of fluorinated polyethynylbenzenes by Sonogashira reactions

General Procedure for Sonogashira coupling Reactions

A suspension of tetraiodobenzenes (**26, 29, 31, 33**), X-phos (10 mol %), Pd(OAc)$_2$ (5 mol %), CuI (5 mol %), Cs$_2$CO$_3$ (5 eq) in 1,4-Dioxane was degassed three time in ace pressure tube. Acetylene (1.2 eq per bromine atom) were added using a syringe. The mixture was heated at the indicated temperature (80–100 °C) for 12 h. The reaction mixture was filtered and residue washed with CH$_2$Cl$_2$. The filtrate was washed with saturated solution of ammonium chloride (2 x 25ml), water (2 x 25ml) and dried over anhydrous Na$_2$SO$_4$. Solvent was removed in vacuo. The product was purified by column chromatography on silica gel.

1,2-Difluoro-3,4,5,6-tetra(3-methylphenylethynyl)benzene (28a): starting with **26** (150 mg, 0.24 mmol), 3-methylphenylacetylene **27b** (139 mg, 1.20 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **28a** was isolated as orange solid (98 mg; 70%). Mp 151–153 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.38 (s, 6H, CH$_3$), 2.41 (s, 6H, CH$_3$), 7.23-7.27 (m, 4H, ArH), 7.31 (q, *J* = 15.1 Hz, 7.4 Hz, 4H, ArH), 7.48-7.52 (m, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): *δ* = 21.2 (2CH$_3$), 21.3 (2CH$_3$), 80.8 (C≡C), 85.8 (C≡C), 98.7 (C≡C), 101.7 (C≡C), 116.1 (t, *J* = 6.4 Hz, 2C), 122.3 (C), 122.8 (2C), 125.2 (t, *J* = 2.8 Hz, C), 128.4 (d, *J* = 2.2 Hz, 4C) 128.9 (4CH), 129.0 (4CH), 130.2 (4CH), 132.5 (d, *J* = 4.4 Hz, 4C), 138.2 (C), 138.6 (C), 150.0 (d, *J$_{CF}$* = 256.2 Hz, CF), 150.5 (d, *J$_{CF}$* = 256.2 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): *δ* = -131.45 (CF). IR (ATR, cm^{-1})**:** $\widetilde{v}$ = 2916 (w), 2202 (w), 1773 (w), 1577 (w), 1487 (w), 1452 (w), 1408 (w), 1293 (w), 1268 (w), 1152 (w), 1093 (w), 997 (w), 960 (w), 902 (w), 854 (w), 777 (w), 683 (w), 586 (w), 569 (w), 501 (w), 435 (w), 383 (w) cm^{-1}. MS (EI, 70 eV); *m/z* (%) = 570 (100) [M]$^{+}$, 555 (20), 540 (14). HRMS (EI) calcd. for C$_{42}$H$_{28}$F$_2$ [M]$^{+}$: 570.21536; found 570.216596. Anal. Calcd for C$_{42}$H$_{28}$F$_2$: C,88.40. H, 4.95. Found: C, 88.45. H, 4.99.
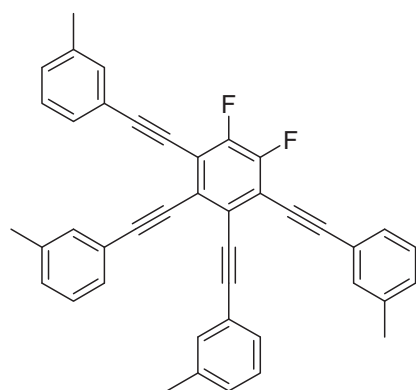
1,2-Difluoro-3,4,5,6-tetra(4-*n*-pentylphenylethynyl)benzene (28b): starting with **26** (150 mg, 0.24 mmol), 4-*n*-pentylphenylacetylene **27e** (206 mg, 1.20 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **28b** was isolated as brown solid (137 mg; 71%). Mp 72–74 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.82 (m, 12H, CH$_3$), 1.23-1.26 (m, 16H, CH$_2$), 1.49-1.59 (m, 8H, CH$_2$), 2.54 (t, *J* = 7.7 Hz, 8H, *CH$_2$*CH$_2$CH$_2$CH$_2$CH$_3$), 7.08 (dd, *J* = 8.4 Hz, 5.9 Hz, 8H, ArH), 7.43 (dt, *J* = 8.5 Hz, 1.0 Hz, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 14.0 (4CH$_3$), 22.6 (4CH$_2$), 30.9 (4CH$_2$), 31.5 (4CH$_2$), 36.0 (4CH$_2$), 80.6 (C≡C), 85.6 (C≡C), 98.6 (C≡C), 101.1 (C≡C), 116.0 (C), 116.3 (C), 119.7 (C), 120.2 (C), 125.0 (C), 125.3 (C), 126.6 (C), 128.6 (2C), 131.8 (d, *J* = 8.3 Hz, 2CH), 144.4 (C), 150.0 (d, *J$_{CF}$* = 256.8 Hz, CF), 150.5 (d, *J$_{CF}$* = 256.8 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -131.89 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3030 (w), 2925 (m), 2854 (m), 2206 (w), 1901 (w), 1605 (w), 1511 (m), 1453 (s), 1376 (w), 1284 (w), 1200 (w), 1177 (w), 1115 (w), 1079 (w), 1018 (w), 941 (m), 849 (m), 806 (s), 729 (m), 688 (w), 644 (w), 527 (s), 479 (w), 428 (w) cm^{-1}. MS (EI, 70 eV); *m/z* (%) = 794 (100) [M]$^+$, 44 (28). HRMS (EI) calcd. for C$_{58}$H$_{60}$F$_2$ [M]$^+$: 794.46576; found 794.465130. Anal. Calcd for C$_{58}$H$_{60}$F$_2$: C, 87.61. H, 7.61. Found: C, 87.64. H, 7.64.

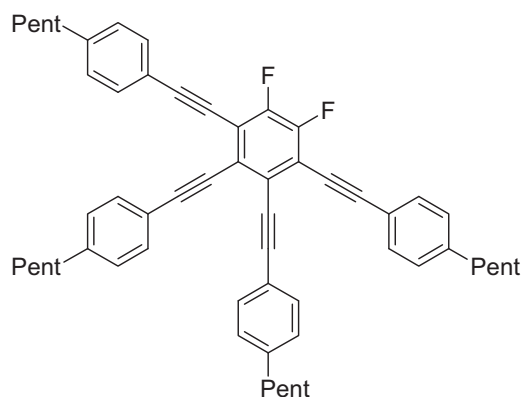**1,2-Difluoro-3,4,5,6-tetra(*n*-heptylphenylethynyl)benzene (28c):** starting with **26** (150 mg, 0.24 mmol), *n*-heptylphenylacetylene **27f** (240 mg, 1.20 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **28c** was isolated as yellow solid (120 mg, 54%). Mp.46–48°C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.88 (t, 12H, CH$_3$), 1.28-1.32 (m, 30H, CH$_2$), 1.56-1.65 (m, 10H, CH$_2$), 2.62 (t, *J* = 7.6 Hz, 8H, CH$_2$), 7.17 (dd, *J* = 8.3 Hz, 5.6 Hz, 8H, ArH), 7.52 (dt, *J* = 8.35 Hz, 1.95 Hz, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 14.1 (4CH$_3$), 22.7 (4CH$_2$), 29.2 (4CH$_2$), 29.3 (4CH$_2$), 31.3 (4CH$_2$), 31.8 (4CH$_2$), 36.1 (4CH$_2$), 80.5 (C≡C), 85.6 (C≡C), 98.6 (C≡C), 101.6 (C≡C), 116.0 (2C), 116.6 (2C), 119.9 (2C), 120.2 (2C), 125.1 (2C), 128.6 (8CH), 131.8 (8CH), 144.1 (C), 149.8 (d, *J$_{CF}$* = 257.9 Hz, CF), 150.0 (d, *J$_{CF}$* = 257.9 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -131.90 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2954
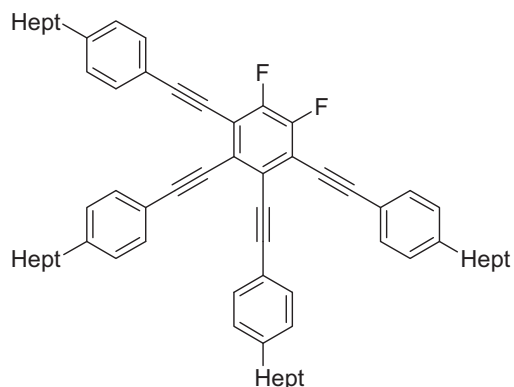
(w), 2922 (s), 2852 (m), 2208 (w), 1605 (w), 1511 (w), 1455 (s), 1376 (w), 1178 (w), 1116 (w), 1018 (w), 942 (w), 805 (m), 724 (w), 526 (m) cm^{-1}. MS (EI, 70 eV); m/z (%) = 907 (65) [M]$^+$, 906 (99), 57 (12), 44 (100), 43 (15). HRMS (EI) calcd. for C$_{66}$H$_{77}$F$_2$ [M]$^+$: 907.59879; found 907.596555.

1,3-Difluoro-2,4,5,6-tetra(phenylethynyl)benzene (30a): starting with **29** (100 mg, 0.16 mmol), phenylacetylene **27a** (83 mg, 0.81 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **30a** was isolated as orange solid (68 mg; 81 %). Mp 155–157 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.51-7.56 (m, 12H, ArH), 7.27-7.33 (m, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 75.5 (C≡C), 80.3 (C≡C), 86.2 (C≡C), 98.9 (C≡C), 101.3 (t, J = 2.6 Hz, C), 101.4 (C), 111.3 (C), 111.5 (d, J = 7.5 Hz, C) 122.2 (C), 122.6 (C), 122.7 (C), 128.5 (6CH) 128.6 (CH), 129.1 (CH), 129.4 (d, J = 3.5 Hz, CH), 131.8 (2CH), 132.0 (CH), 161.5 (d, J_{CF} = 260.4 Hz, CF), 161.7 (d, J_{CF} = 260.4 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -100.42 (CF). IR (ATR, cm^{-1})**:** $\widetilde{\nu}$ = 3051 (m), 2205 (m), 1887 (w), 1596 (m), 1489 (m), 1441 (m), 1352 (m), 1268 (w), 1214 (m), 1156 (w), 1094 (m), 1067 (m), 998 (w), 939 (m), 747 (s), 684 (s), 578 (m), 529 (m), 498 (m), 436 (m) cm^{-1}. MS (EI, 70 eV); m/z (%) = 514 (75) [M]$^+$, 69 (29), 44 (100). HRMS (EI) calcd. for C$_{38}$H$_{20}$F$_2$ [M]$^+$: 514.15276; found 514.154168. Anal. Calcd for C$_{38}$H$_{20}$F$_2$: C, 88.70. H, 3.92. Found: C, 88.75. H, 3.66.
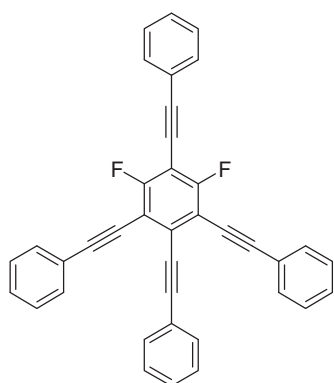
1,3-Difluoro-2,4,5,6-tetra(hex-1-ynyl)benzene (30b): starting with **29** (100 mg, 0.16 mmol), 1-hexyne **27d** (65 mg, 0.80 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **30b** was isolated as dark brown oil (59 mg, 83%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.79-0.91 (m, 12H, CH$_3$), 1.06-1.21 (m, 3H, CH$_2$), 1.38-1.58 (m, 15H, CH$_2$), 2.39-2.47 (m, 6H, CH$_2$). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 13.6 (CH$_3$), 13.6 (2CH$_2$), 13.7 (CH$_3$), 19.5 (2CH$_2$), 19.6 (CH$_2$), 19.7 (CH$_2$), 21.8 (3CH$_2$), 21.9 (CH$_2$), 30.4 (CH$_2$), 30.6 (2CH$_2$), 30.7 (CH$_2$), 71.7 (C), 77.2 (C), 99.5 (2C), 99.6 (C≡C), 101.5 (C≡C), 102.4 (C≡C), 102.5 (C≡C), 162.0 (d, J_{CF} = 255.7 Hz, CF), 162.3 (d, J_{CF} = 255.7 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -103.9 (CF). IR (ATR, cm^{-1})**:** $\widetilde{\nu}$ = 2957 (m), 2931 (m), 2871 (w), 2234 (w), 1718 (w), 1599 (w), 1445 (s), 1378 (w), 1318 (w), 1260 (w), 1168
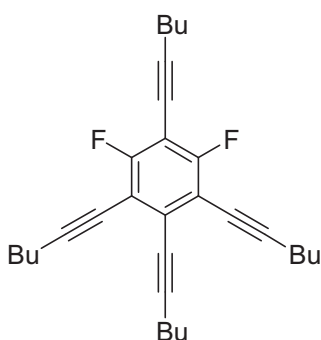
(w), 1104 (w), 1025 (m), 876 (w), 801 (w), 725 (w), 555 (w). MS (EI, 70 eV); m/z (%) = 434 (100) [M]$^+$, 391 (10), 377 (14), 363 (10), 349 (19), 335 (25), 321 (19), 307 (15), 295 (11), 281 (14), 277 (10), 275 (13), 257 (10), 105 (13), 71 (12), 57 (22), 44 (19), 43 (26), 40 (21) cm^{-1}. HRMS (EI) calcd. for $C_{30}H_{36}F_2$ [M]$^+$: 434.27796; found 434.278900.

1,3-Difluoro-2,4,5,6-tetra(4-n-pentylphenylethynyl)benzene (30c): starting with **29** (100 mg, 0.16 mmol), 4-n-pentylphenylacetylene **27e** (137 mg, 0.80 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **30c** was isolated as dark brown oil (97 mg, 75%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.79-0.84 (m, 12H, 4CH$_3$), 1.23-1.26 (m, 16H, 8CH$_2$), 1.47-1.57 (m, 8H, 2CH$_2$), 2.54 (t, J = 7.6 Hz, 8H, 4CH$_2$), 7.06-7.12 (m, 8H, ArH), 7.40-7.45 (m, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 14.1 (4CH$_3$), 22.6 (4CH$_2$), 30.9 (d, J = 2.0 Hz, 4CH$_2$), 31.5 (4CH$_2$), 36.3 (d, J = 2.0 Hz, 4CH$_2$), 76.2 (d, J = 165.9 Hz, C≡C), 76.6 (C≡C), 80.0 (C≡C), 85.9 (t, J = 4.8 Hz, C≡C), 99.0 (t, J = 3.0 Hz, C), 101.4 (t, J = 4.8 Hz, C), 101.6 (C), 103.1 (t, J = 20.6 Hz, C), 111.2 (C), 111.5 (d, J = 7.8 Hz, C), 119.4 (C), 119.9 (d, J = 4.2 Hz, C), 128.6 (6CH), 128.6 (CH), 131.7 (3CH), 131.9 (CH), 132.0 (CH), 149.2 (C), 144.6 (d, J = 2.0 Hz, C), 161.5 (d, J_{CF} = 259.1 Hz, CF), 161.8 (d, J_{CF} = 259.1 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -101.12 (CF). IR (ATR, cm^{-1})**:** $\tilde{\nu}$ = 3027 (w), 2955 (w), 2925 (m), 2854 (m), 2204 (w), 1905 (w), 1606 (w), 1509 (m), 1444 (s), 1377 (w), 1262 (w), 1178 (w), 1092 (m), 1019 (m), 904 (w), 809 (m), 727 (w), 661 (w), 551 (m), 459 (w) cm^{-1}. MS (EI, 70 eV); m/z (%) = 794 (100) [M]$^+$, 737 (10), 625 (11), 338 (10), 285 (10), 284 (23), 44 (53), 43 (11), 41 (13) cm^{-1}. HRMS (EI) calcd. for $C_{58}H_{60}F_2$ [M]$^+$: 794.46576; found 794.465446.

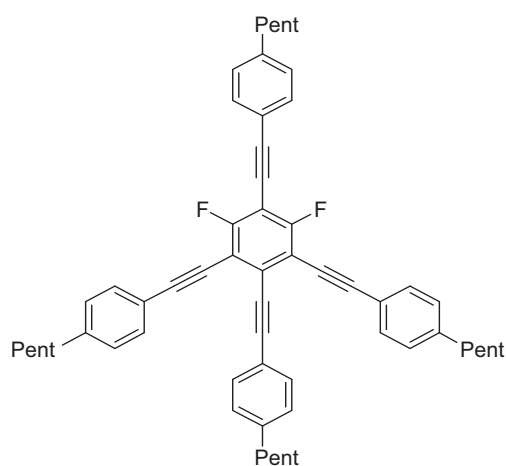**1,4-Difluoro-2,3,5,6-tetra(3-methylphenylethynyl)benzene (32a):** starting with **31** (100 mg, 0.16 mmol), 3-methylphenylacetylene **27b** (92 mg, 0.80 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **32a** was isolated as yellow solid (79 mg, 85%). Mp 198–200 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ =2.27 (s, 12H, CH$_3$), 7.12-

7.21 (m, 8H, ArH), 7.30 (m, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 21.2 (4CH$_3$), 80.8 (2C≡C), 101.4 (2C≡C), 114.9 (C), 115.1 (d, J = 8.1 Hz, C), 122.3 (C), 128.4 (4CH), 129.0 (4CH), 130.2 (2CH), 132.6 (4CH), 138.2 (C), 158.3 (d, J_{CF} = 253.5 Hz, CF), 158.6 (d, J_{CF} = 253.5 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -108.69 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2917 (w), 2206 (w), 1769 (w), 1599 (w), 1485 (w), 1444 (w), 1408 (w), 1346 (w), 1273 (w), 1089 (w), 1038 (w), 961 (w), 874 (w), 774 (m), 683 (m), 587 (w), 537 (w), 441 (m), 394 (w) cm^{-1}. MS (EI, 70 eV); m/z (%) = 570 (100) [M]$^+$. HRMS (EI) calcd. for C$_{42}$H$_{28}$F$_2$ [M]$^+$: 570.21536; found 570.21536. Anal. Calcd for C$_{42}$H$_{28}$F$_2$: C, 88.40. H, 4.95. Found: C, 88.36. H, 4.91.
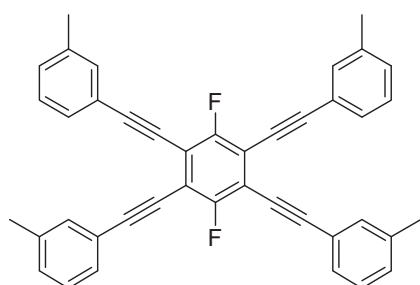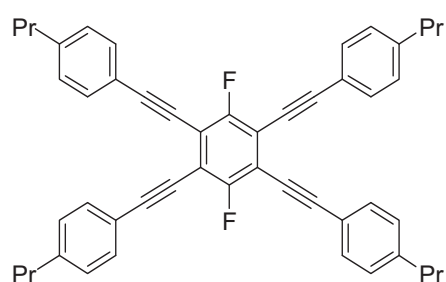
1,4-Difluoro-2,3,5,6-tetra(4-*n*-propylphenylethynyl)benzene (32b): starting with **31** (100

mg, 0.16 mmol), 4-*n*-propylphenylacetylene **27c** (115 mg, 0.80 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **32b** was isolated as yellow solid (96 mg, 86%). Mp 189–191 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.85 (t, J = 7.3 Hz, 12H, CH$_3$), 1.51-1.61 (m, 8H, CH$_2$), 2.52 (t, J = 7.8 Hz, 8H, CH$_2$), 7.08 (dt, J = 6.5, 2.0 Hz, 8H, ArH), 7.42 (dt, J = 6.5, 2.0 Hz, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 13.8 (4CH$_3$), 24.4 (4CH$_2$), 38.4 (4CH$_2$), 80.6 (2C≡C), 101.4 (2C≡C), 114.8 (d, J = 8.7 Hz, C), 114.9 (d, J = 8.4 Hz, C), 128.7 (4CH), 131.9 (4CH), 144.3 (C), 158.4 (d, J_{CF} = 253.6 Hz, CF), 158.7 (d, J_{CF} = 253.6 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -108.88 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2957 (m), 2929 (m), 2868 (m), 2206 (m), 1904 (m), 1604 (m), 1510 (s), 1442 (s), 1376 (m), 1344 (m), 1266 (m), 1201 (m), 1112 (m), 1018 (m), 944 (s), 868 (m), 800 (s), 709 (m), 645 (m), 566 (s), 524 (s), 440 (m) cm^{-1}. MS (EI, 70 eV); m/z (%) = 682 (100) [M]$^+$, 284 (23). HRMS (EI) calcd. for C$_{50}$H$_{44}$F$_2$ [M]$^+$: 682.34056; found 682.339721. Anal. Calcd for C$_{50}$H$_{44}$F$_2$: C, 87.94. H, 6.49. Found: C, 87.91. H, 6.45.

1,4-Difluoro-2,3,5,6-tetra(hex-1-ynyl)benzene (32c): starting with **31** (100 mg, 0.16 mmol),
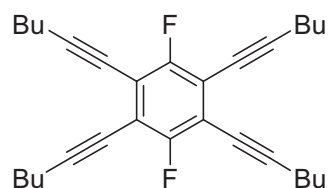
1-hexyne **27d** (65 mg, 0.80 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **32c** was isolated as brown solid (59 mg, 83%). Mp 66–68 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.87 (t, J = 7.0 Hz, 12H, CH$_3$), 1.38-1.59 (m, 16H, CH$_2$), 2.43 (t, J = 6.7 Hz, 8H, CH$_2$). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 13.6 (4CH$_3$), 19.6 (4CH$_2$), 21.9 (4CH$_2$), 30.5 (4CH$_2$), 72.3 (t, J = 2.0 Hz, 2C≡C), 101.9 (t,

J = 2.3 Hz, 2C≡C), 114.7 (d, J = 8.8 Hz, C), 114.9 (d, J = 9.2 Hz, C), 159.0 (d, J_{CF} = 249.8 Hz, CF), 159.3 (d, J_{CF} = 249.8 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -111.10 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 2952 (m), 2930 (m), 2865 (w), 2231 (w), 1707 (w), 1463 (m), 1441 (s), 1420 (m), 1374 (w), 1315 (w), 1265 (w), 1106 (w), 1029 (w), 974 (w), 926 (w), 888 (w), 840 (w), 740 (w), 688 (w), 553 (w), 518 (w), 446 (w), 419 (w) cm^{-1}. MS (EI, 70 eV); m/z (%) = 434 (100) [M]$^+$, 377 (19), 349 (10), 277 (10), 275 (10), 265 (10). HRMS (EI) calcd. for C$_{30}$H$_{36}$F$_2$ [M]$^+$: 434.27796; found 434.278389.

1,4-Difluoro-2,3,5,6-tetra(4-n-pentylphenylethynyl)benzene (32d): starting with **31** (100 mg, 0.16 mmol), 4-n-pentylphenylacetylene **27e** (137 mg, 0.80 mmol), CuI (5 mol%), X-Phos (10 mol%), Pd(OAc)$_2$ (5 mol%), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **32d** was isolated as yellow solid (103 mg, 80%). Mp 114–116 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.82 (t, J = 6.6 Hz, 12H, CH$_3$), 1.24-1.27 (m, 14H, CH$_2$), 1.50-1.60 (m, 10H, CH$_2$), 2.56 (t, J = 7.6 Hz, 8H, CH$_2$), 7.11 (dt, J = 6.4, 1.9 Hz, 8H, ArH), 7.44 (dt, J = 6.4, 1.9 Hz, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 14.1 (4CH$_3$), 22.6 (4CH$_2$), 30.9 (4CH$_2$), 31.5 (4CH$_2$), 36.2 (4CH$_2$), 80.6 (4C≡C), 101.4 (4C≡C), 114.7 (d, J = 8.7 Hz, C), 114.9 (d, J = 10.0 Hz, C), 119.7 (C), 128.6 (4CH), 131.9 (4CH), 144.6 (C), 158.3 (d, J_{CF} = 253.9 Hz, CF), 158.7 (d, J_{CF} = 253.9 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -108.90 (CF). IR (ATR, cm^{-1}): $\tilde{v}$ = 3029 (w), 2956 (m), 2926 (m), 2853 (m), 2205 (m), 1898 (w), 1686 (w), 1605 (w), 1512 (m), 1441 (m), 1375 (w), 1347 (m), 1270 (w), 1177 (w), 1114 (w), 1018 (w), 946 (m), 829 (m), 804 (m), 746 (w), 656 (w), 571 (w), 538 (m), 493 (w), 441 (w) cm^{-1}. MS (EI, 70 eV); m/z (%) = 794 (100) [M]$^+$, 682 (10), 681 (20), 284 (20), 69 (10), 44 (48). HRMS (EI) calcd. for C$_{58}$H$_{60}$F$_2$ [M]$^+$: 794.46576; found 794.465121.
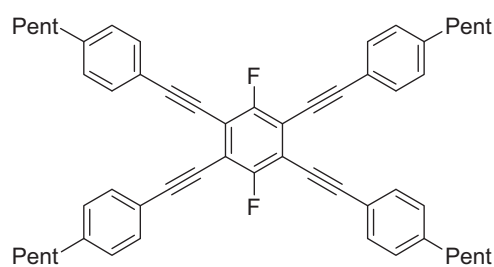
1-Fluoro-2,3,4,5,6-penta(4-*n*-propylphenylethynyl)benzene (34a): starting with **33** (100 mg, 0.13 mmol), 4-*n*-propylphenylacetylene **27c** (112 mg, 0.78 mmol), CuI (5 mol%), X-Phos (10 mol %), Pd(OAc)$_2$ (5 mol %), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **34a** was isolated as dark brown solid (83 mg, 74%). Mp 85–87 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.82 (t, *J* = 7.3 Hz, 15H, CH$_3$), 1.53-1.65 (m, 10H, CH$_2$), 2.54 (t, *J* = 7.3 Hz, 10H, CH$_2$), 7.10 (dd, *J* = 8.3 Hz, 4.0 Hz, 10H, ArH), 7.46 (dt, *J* = 8.0 Hz, 3.3 Hz, 10H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): *δ* = 13.8 (5CH$_3$), 24.4 (5CH$_2$), 38.1 (5CH$_2$), 80.9 (C≡C), 86.5 (C≡C), 86.6 (C≡C), 100.4 (C≡C), 100.6 (C≡C), 114.5 (C), 120.0 (C), 120.2 (C), 120.5 (C), 128.7 (d, *J* = 2.0 Hz, 8CH), 143.7 (C), 144.1 (d, *J* = 1.4 Hz, C), 163.5 (d, J_{CF} = 255.6 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): *δ* = -103.17 (CF). IR (ATR, cm^{-1})**:** $\widetilde{\nu}$ = 3025 (w), 2956 (w), 2868 (w), 2323 (w), 2205 (w), 1906 (w), 1671 (w), 1604 (m), 1509 (w), 1455 (s), 1376 (m), 1338 (w), 1257 (w), 1203 (w), 1178 (w), 1113 (w), 1090 (w), 1018 (w), 933 (w), 867 (w), 799 (w), 528 (w), 450 (w) cm^{-1}. MS (EI, 70 eV); *m/z* (%) = 806 (42) [M]$^+$. HRMS (EI) calcd. for C$_{62}$H$_{57}$F [M]$^+$: 806.42823; found 806.425932. *: CF-group not resolved in ^{13}C-NMR.
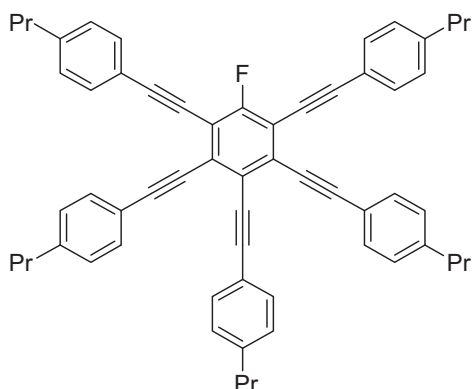
1-Fluoro-2,3,4,5,6-penta(4-*n*-pentylphenylethynyl)benzene (34b): starting with **33** (100 mg, 0.13 mmol), 4-*n*-pentylphenylacetylene **27e** (142 mg, 0.82 mmol), CuI (5 mol%), X-Phos (10 mol %), Pd(OAc)$_2$ (5 mol %), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **34b** was isolated as dark brown oil (103 mg, 79%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.83 (t, *J* = 6.5 Hz, 15H, CH$_3$), 1.24-1.28 (m, 20H, CH$_2$), 1.53-1.61 (m, 10H, CH$_2$), 2.56 (t, *J* = 7.7 Hz, 10H, CH$_2$), 7.10 (dd, *J* = 8.3 Hz, 4.7 Hz, 10H, ArH), 7.46 (dt, *J* = 8.0 Hz, 3.0 Hz, 10H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): *δ* = 14.1 (5CH$_3$), 22.5 (CH$_2$), 30.9 (CH$_2$), 31.0 (CH$_2$), 36.3 (CH$_2$), 80.9 (C≡C), 86.1 (C≡C), 86.5 (C≡C), 86.6 (C≡C), 97.8 (C≡C), 100.4 (C), 100.5 (d, *J* = 5.1 Hz, C), 114.2 (C), 114.4 (C), 120.0 (C), 120.2 (C), 120.5 (C), 128.6 (d, *J* = 2.8 Hz, 8CH), 131.7 (4CH), 131.9 (d, *J* = 3.3 Hz, 8CH), 144.0 (C), 144.3 (d, *J* = 1.8 Hz, C), 161.1 (d, J_{CF} = 256.0 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): *δ* = -103.17 (CF). IR (ATR, cm^{-1})**:** $\widetilde{\nu}$ = 3025 (w), 2953 (w), 2924 (m), 2854 (m), 2206 (w), 1908 (w), 1679 (w), 1605 (w), 1510 (m), 1455 (m), 1376 (w), 1260

(w), 1178 (w), 1113 (w), 1070 (w), 1018 (w), 968 (w), 897 (w), 813 (m), 727 (w), 529 (m), 444 (w), 403 (w) cm^{-1}. MS (EI, 70 eV); m/z (%) = 946 (10) [M]$^+$, 448 (13), 432 (19), 403 (10), 69 (13), 44 (100). HRMS (EI) calcd. for $C_{72}H_{77}F$ [M]$^+$: 946.58473; found 946.583714.

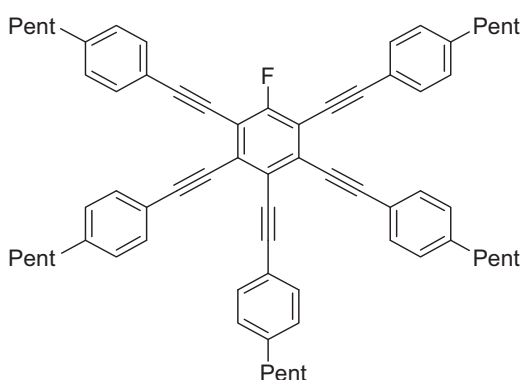**1-Fluoro-2,3,4,5,6-penta(4-*n*-heptylphenylethynyl)benzene (34c):** starting with **33** (100
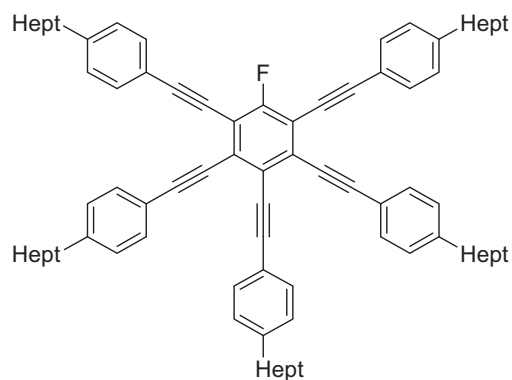

mg, 0.13 mmol), 4-*n*-heptylphenylacetylene **27f** (165 mg, 0.82 mmol), CuI (5 mol%), X-Phos (10 mol %), Pd(OAc)$_2$ (5 mol %), Cs$_2$CO$_3$ (5 eq) and 1,4-Dioxane (5mL), **34c** was isolated as yellow brown oil (95 mg, 63%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.81 (t, J = 6.6 Hz, 15H, CH$_3$), 1.21-1.26 (m, 30H, CH$_2$), 1.49-1.60 (m, 20H, CH$_2$), 2.56 (t, J = 7.7 Hz, 10H, CH$_2$), 7.10 (d, J = 255.6 Hz, 10H, ArH), 7.46

(dt, J = 8.3 Hz, 3.0 Hz, 10H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 14.1 (5CH$_3$), 22.7 (5CH$_2$), 29.2 (5CH$_2$), 31.3 (5CH$_2$), 31.8 (CH$_2$), 36.3 (CH$_2$), 80.9 (CH$_2$), 100.4 (C≡C), 100.6 (C≡C), 119.9 (C≡C), 120.2 (C≡C), 120.5 (C≡C), 128.0 (d, J = 2.5 Hz, 8CH), 129.3 (C), 131.5 (2C), 131.6 (2C), 131.7 (4CH), 131.8 (d, J = 2.5 Hz, 8CH), 134.5 (d, J = 4.1 Hz, 2C), 142.8 (2C), 143.9 (2C), 144.4 (d, J = 1.3 Hz, 4C), 158.0 (d, J_{CF} = 249.9 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -103.2 (CF). IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 3025 (w), 2953 (w), 2922 (s), 2852 (m), 2205 (w), 1903 (w), 1690 (w), 1604 (w), 1510 (w), 1462 (w), 1425 (m), 1375 (w), 1261 (w), 1177 (w), 1115 (w), 1070 (w), 1018 (w), 933 (w), 839 (m), 806 (m), 725 (m), 527 (m), 400 (m) cm^{-1}. MS (EI, 70 eV); m/z (%) = 1086 (10) [M]$^+$, 612 (14), 610 (10). HRMS (EI) calcd. for $C_{62}H_{57}F$ [M]$^+$ not possible: * CF-group not resolved in ^{13}C-NMR. Anal. Calcd for $C_{62}H_{57}F$: C, 88.14. H, 9.90. Found: C, 88.18. H, 9.93.

6.5 Synthesis of Fluorinated polyarenes by Suzuki-Miyaura cross coupling reactions

General Procedure for Poly Suzuki cross coupling Reactions

The reaction was carried out in a pressure tube. To a suspension **26, 29, 31, 33** (100 mg, 0.1 mmol), Pd(PPh$_3$)$_4$ (10 mol %), arylboronic acid (1.1 eq per bromine atom) and Cs$_2$CO$_3$ (5eq) in dioxin, was added. The mixture was heated at the indicated temperature (90-120 °C) for the indicated period of time (12-36h). The reaction mixture was diluted with water and extracted with CH$_2$Cl$_2$ (3 x 25ml). The combined organic layers were dried over Na$_2$SO$_4$, filtrated and the filtrate was concentrated in vacuo the residue was purified by flash chromatography (silica gel, ethyl acetate / heptanes).

3,4,5,6-Tetra(3-chlorophenyl)-1,2-difluorobenzene (35a): Starting with **26** (100 mg, 0.16

mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 3-chloroboronic acid **17j** (149 mg, 0.96 mmol), **35a** was isolated as a white solid (74 mg, 82%). Mp 147–149°C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.56 (q, J = 12.3 Hz, 7.0 Hz, 2H, ArH), 6.70 (d, J = 15.0 Hz, 2H, ArH), 6.78-6.91 (m, 6H, ArH), 7.06-7.16 (m, 6H, ArH). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -137.29 (CF).
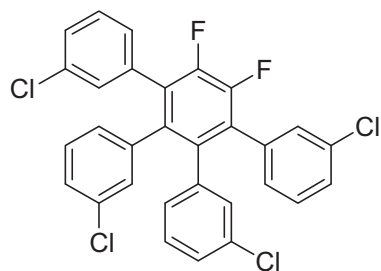
^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 127.0 (3CH), 128.0 (3CH), 128.6 (3CH), 128.7 (CH), 129.2 (3CH), 129.4 (d, J = 1.4 Hz, C), 129.5 (C), 130.4 (2CH), 131.0 (d, J = 9.7 Hz, CH), 133.3 (d, J = 10.0 Hz, C), 133.9 (3C), 134.6 (2C), 136.0 (d, J = 2.7 Hz, 2C), 139.0 (2C), 147.3 (d, J = 251.5 Hz, CF), 147.5 (d, J = 251.5 Hz, CF), 149.7 (C). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -137.29 (CF). IR (KBr): $\widetilde{\nu}$ = 3063 (w), 1612 (w), 1595 (w), 1562 (m), 1476 (w), 1399 (m), 1319 (w), 1297 (w), 1215 (w), 1190 (w), 1163 (w), 1119 (w), 1077 (m), 999 (w), 949 (w), 880 (w), 845 (w), 780 (m), 748 (m), 698 (m), 675 (m), 610 (w), 582 (w), 530 (w), 490 (w), 442 (w) cm^{-1}. MS (EI, 70 eV); m/z (%) = 556 (100) [M$^+$, ^{35}Cl$_3$, ^{37}Cl], 555 (19), 554 (67), 448 (11), 412 (12), 206 (24). HRMS (EI) calcd. for C$_{30}$H$_{16}$^{35}Cl$_4$F$_2$ [M]$^+$: 553.99687; found 553.996821, calcd. for C$_{30}$H$_{16}$^{35}Cl$_3$^{37}Cl$_1$F$_2$ [M]$^+$: 555.99392; found 555.993554. Anal. Calcd for C$_{30}$H$_{16}$^{35}Cl$_3$^{37}Cl$_1$F$_2$: C, 64.78. H, 2.90. Found: C, 64.74. H, 2.93.

3,4,5,6-Tetra(4-fluorophenyl)-1,2-difluorobenzene (35b): Starting with **26** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and *p*-fluoroboronic acid **17l** (134 mg, 0.96 mmol), **35b** was isolated as a white solid (61 mg, 76%). Mp 144–146°C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.03 (s, 6H, 2CH$_3$), 2.19 (s, 6H, 2CH$_3$), 6.51-6.54 (m, 8H, ArH), 6.59-6.61 (m, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 114.3 (2CH), 114.6 (CH), 114.9 (2CH), 115.2 (2CH), 132.2 (d, J = 8.3 Hz, 4CH), 132.7 (d, J = 8.3 Hz, 4CH), 129.2 (t, J = 1.3 Hz, 2C), 129.5 (t, J = 5.7 Hz, C), 133.8 (d, J = 3.7 Hz, 3C), 136.6 (2C), 145.8 (d, J_{CF} = 16.0 Hz, 2CF), 149.1 (d, J_{CF} = 16.0 Hz, 2CF), 161.6 (d, J_{CF} = 247.5 Hz, CF), 162.0 (d, J_{CF} = 247.5 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -113.5 (CF), -114.8 (CF), -138.3 (CF). IR (KBr): $\tilde{v}$ = 3051 (w), 1602 (w), 1513 (w), 1446 (w), 1397 (w), 1299 (w), 1221 (w), 1158 (w), 1090 (w), 1015 (w), 947 (w), 915 (w), 853 (w), 822 (m), 771 (w), 674 (w), 574 (w), 531 (m), 483 (w), 415 (w) cm^{-1}. GC-MS (EI, 70 eV); *m/z* (%) = 490 (100) [M]$^+$, 374 (11). HRMS (EI) calcd. for C$_{30}$H$_{16}$F$_2$ [M]$^+$: 490.11507; found 490.115342. Anal. Calcd for C$_{30}$H$_{16}$F$_2$: C, 73.47. H, 3.29. Found: C, 73.51. H, 3.33.
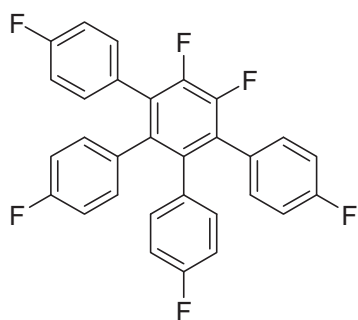
2,4,5,6-Tetra(4-methylphenyl)-1,3-difluorobenzene (34a): Starting with **27** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 3-methylboronic acid **17c** (130 mg, 0.96 mmol), **34a** was isolated as a white solid (60 mg, 78%). Mp 126–127 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.95 (s, 3H, CH$_3$), 2.13 (s, 6H, 2CH$_3$), 2.33 (s, 3H, CH$_3$), 6.48-6.55 (m, 3H, ArH), 6.65-6.68 (m, 1H, ArH), 6.72-6.81 (m, 3H, ArH), 6.86-6.89 (m, 4H, ArH), 6.97 (t, J = 8.3 Hz, 1H, ArH), 7.11-7.16 (m, 1H, ArH), 7.26-7.34 (m, 3H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 21.1 (CH$_3$), 21.3 (2CH$_3$), 21.5 (CH$_3$), 126.9 (d, J = 10.4 Hz, 2C), 127.4 (3CH), 127.6 (3CH), 127.1 (3CH), 128.1 (d, J = 6.3 Hz, 3CH), 128.9 (2C), 129.5 (C), 131.2 (2C), 131.8 (d, J = 32.6 Hz, 2CH), 134.2 (2C), 136.3 (C), 136.9 (3C), 137.4 (t, J = 3.1 Hz, C), 148.9 (C), 137.8 (C), 156.0 (d, J_{CF} = 246.9 Hz, CF), 156.3 (d, J_{CF} = 246.9 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -113.9 (CF). IR (KBr): $\tilde{v}$ = 3035 (w), 2918 (w), 1794 (w), 1604 (w), 1561 (w), 1490 (w), 1318 (w), 1386 (w), 1241 (w), 1124 (w), 1032 (w), 911 (w), 876 (w), 782 (w), 698 (w), 649 (w), 599 (w), 535 (w), 436 (w) cm^{-1}. GC-MS (EI, 70 eV); *m/z* (%) = 474 (100) [M]$^+$, 459 (11). HRMS (ESI) calcd. for C$_{34}$H$_{28}$F$_2$ [M+H]$^+$: 475.22318; found 475.22319. Anal. Calcd for C$_{34}$H$_{28}$F$_2$: C, 86.05. H, 5.95. Found: C, 86.05. H, 5.93.
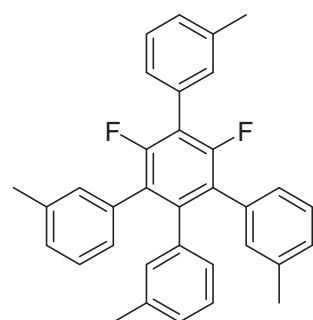
2,4,5,6-Tetra(4-chlorophenyl)-1,3-difluorobenzene (36b): Starting with **29** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 4-chloroboronic acid **17k** (150 mg, 0.96 mmol), **36b** was isolated as a white solid (80 mg, 88%). Mp 208–209 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.61 (dt, J = 8.6 Hz, 2H, ArH), 6.90 (dt, J = 8.6 Hz, 6H, ArH), 7.10 (dt, J = 8.6 Hz, 4H ArH), 7.34-7.43 (m, 4H, ArH). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -113.6 (CF). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 126.2 (2C), 128.0 (2CH), 128.3 (6CH), 128.7 (2CH), 130.6 (2C), 130.8 (2C) 131.0 (C), 131.1 (CH), 132.0 (3CH), 132.5 (2CH), 133.6 (2C), 134.2 (d, J = 3.7 Hz, C), 140.0 (d, J = 3.7 Hz, C), 154.9 (d, J_{CF} = 240.6 Hz, CF), 155.2 (d, J_{CF} = 240.6 Hz, CF). IR (KBr): $\widetilde{\nu}$ = 3065 (w), 2917 (w), 1593 (w), 1552 (w), 1494 (w), 1428 (w), 1386 (w), 1319 (w), 1262 (w), 1194 (w), 1088 (w), 1031 (w), 1014 (w), 945 (w), 890 (w), 834 (w), 784 (w), 738 (w), 653 (w), 632 (w), 521 (w), 480, (w), 448 (w) cm^{-1}. GC-MS (EI, 70 eV); m/z (%) = 556 (100) [M, ^{35}Cl$_3$, ^{37}Cl]$^+$, 554 (71), 449 (10), 448 (18). HRMS (EI) calcd. for C$_{30}$H$_{16}$^{35}Cl$_4$F$_2$ [M]$^+$: 553.99687; found 553.996441, calcd. for C$_{30}$H$_{16}$^{35}Cl$_3$^{37}Cl$_1$F$_2$ [M]$^+$: 555.99392; found 555.993550. Anal. Calcd for C$_{30}$H$_{16}$^{35}Cl$_3$^{37}Cl$_1$F$_2$: C,64.78. H, 2.90. Found: C, 64.78. H, 2.93.
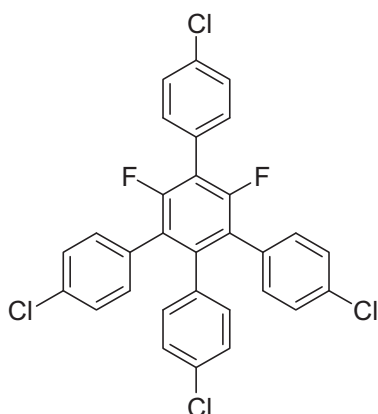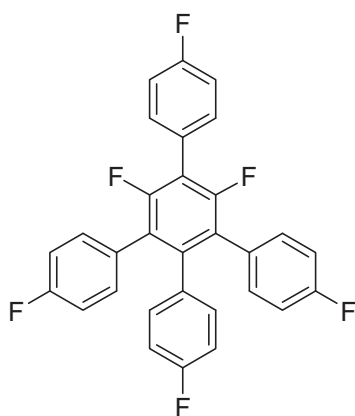
2,4,5,6-Tetra(4-fluorophenyl)-1,3-difluorobenzene (36c): Starting with **29** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and *p*-fluoroboronic acid **17l** (134 mg, 0.96 mmol), **36c** was isolated as a white solid (61 mg, 77%). Mp 166 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.58-6.68 (m, 3H, ArH), 6.78-6.86 (m, 3H, ArH), 6.92-6.99 (m, 3H, ArH), 7.05-7.13 (m, 2H, ArH), 7.43-7.50 (m, 2H, ArH). ^{13}C NMR δ = 114.6 (CH), 114.8 (CH), 115.1 (2CH), 115.3 (CH), 115.6 (CH), 116.8 (t, J = 21.5 Hz, C), 125.0 (dd, J = 12.3 Hz, 8.8 Hz, C), 128.6 (d, J = 3.4 Hz, C), 132.2 (d, J = 8.5 Hz, 2CH), 132.4 (d, J = 8.5 Hz, 4CH), 132.6 (d, J = 8.5 Hz, 2CH), 133.1 (dd, J = 6.1 Hz, 3.4 Hz, C), 141.4 (t, J = 4.2 Hz, C), 156.1 (d, J_{CF} = 248.1 Hz, CF), 156.5 (d, J_{CF} = 248.1 Hz, CF), 161.5 (d, J_{CF} = 247.7 Hz, CF), 161.9 (d, J_{CF} = 247.7 Hz, CF), 162.2 (d, J_{CF} = 248.5 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -114.6 (3CF), -114.4 (2CF), -112.8 (CF). IR (KBr): $\widetilde{\nu}$ = 3076 (w), 2926 (w), 1895 (w), 1596 (w), 1560 (w), 1509 (w), 1432 (w), 1390 (w), 1317 (w), 1223 (m), 1158 (m), 1093 (w), 1027 (w), 940 (w), 906 (w), 819 (m), 770 (w),

735 (w), 681 (w), 585 (w), 533 (m), 428 (w), 380 (w) cm^{-1}. GC-MS (EI, 70 eV); m/z (%) = 490 (100) [M]$^+$. HRMS (EI) calcd. for C$_{30}$H$_{16}$F$_6$ [M]$^+$: 490.11507; found 490.115362.

2,3,5,6-Tetra(4-ethylphenyl)-1,4-difluorobenzene (37a): Starting with **31** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 4-ethylboronic acid **17h** (144 mg, 0.96 mmol), **37a** was isolated as a white solid (82 mg, 95%). Mp 202–203 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.10 (t, J = 7.8 Hz, 12H, CH$_3$), 2.50 (dd, J = 15.2 Hz, 7.6 Hz, 8H, CH$_2$), 6.96 (d, J = 14.3 Hz, 8H, ArH),
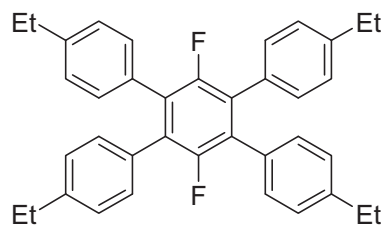
7.12 (d, J = 14.1 Hz, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 15.3 (4CH$_3$), 28.6 (4CH$_2$), 127.3 (4CH), 129.1 (dd, J = 12.3, 8.6 Hz, 4C), 130.7 (4CH), 130.9 (4C), 143.1 (4C), 153.1 (d, J_{CF} = 242.1 Hz, 2CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -119.6 (CF), -113.38 (CF). IR (KBr): $\tilde{\nu}$ = 3023 (w), 2963 (w), 2929 (w), 2870 (w), 1904 (w), 1612 (w), 1522 (w), 1429 (w), 1396 (w), 1309 (w), 1279 (w), 1187 (w), 1116 (w), 1061 (w), 1021 (w), 965 (w), 879 (w), 820 (m), 767 (w), 680 (w), 593 (w), 527 (w), 422 (w) cm^{-1}. GC-MS (EI, 70 eV); m/z (%) = 530 (100) [M]$^+$. HRMS (EI) calcd. for C$_{38}$H$_{36}$F$_2$ [M]$^+$: 530.27796; found 530.278663. Anal. Calcd for C$_{38}$H$_{36}$F$_2$: C, 86.02. H, 6.84. Found: C, 86.06. H, 6.81.

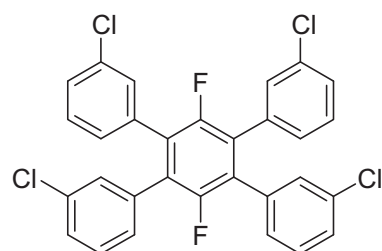**2,3,5,6-Tetra(3-chlorophenyl)-1,4-difluorobenzene (37b):** Starting with **31** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 3-chloroboronic acid **17j** (150 mg, 0.96 mmol), **37b** was isolated as a white solid (75 mg, 83%). Mp 232 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.83-6.92 (m, 4H, ArH), 7.10-7.20 (m, 12H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 128.1 (4CH),

128.6 (dd, J = 12.7 Hz, 9.9 Hz, 4C), 128.9 (4CH), 129.3 (4CH), 130.7 (4CH), 134.0 (4C), 134.4 (4C), 152.7 (d, J_{CF} = 245.5 Hz, CF), 152.9 (d, J_{CF} = 245.5 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -118.94 (CF). IR (KBr): $\tilde{\nu}$ = 3068 (w), 2953 (w), 2923 (w), 2853 (w), 1593 (w), 1564 (w), 1489 (w), 1435 (w), 1386 (w), 1312 (w), 1260 (w), 1156 (w), 1094 (w), 1078 (w), 997 (w), 914 (w), 878 (w), 830 (w), 784 (m), 741 (m), 686 (m), 649 (w), 566 (w), 504 (w), 442 (w), 389 (w) cm^{-1}. GC-MS (EI, 70 eV); m/z (%) = 556 (100) [M, ^{35}Cl$_3$, ^{37}Cl]$^+$, 555 (19), 554 (71), 484 (16), 448 (14), 207 (18). HRMS (EI) calcd. for C$_{30}$H$_{16}$^{35}Cl$_3$^{37}ClF$_2$ [M]$^+$: 555.99392; found 555.993038, calcd. for C$_{30}$H$_{16}$^{35}Cl$_4$F$_2$ [M]$^+$: 553.99687; found 555.996217. Anal. Calcd for C$_{30}$H$_{16}$^{35}Cl$_3$^{37}ClF$_2$: C, 64.78. H, 2.90. Found: C, 64.82. H, 2.94.

1,4-Difluoro-2,3,5,6-tetra(4-fluorophenyl)benzene (37c): Starting with **31** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 4-fluoroboronic acid **17l** (134 mg, 0.96 mmol), **37c** was isolated as a white solid (66 mg, 83%). Mp 280–281 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.84-6.92 (m, 8H, ArH), 7.00-7.14 (m, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 115.2 (d, J = 21.4 Hz, 8CH), 128.6 (m, 4C), 129.9 (m, 4C), 132.4 (d, J = 8.2 Hz, 8CH), 152.8 (d, J = 243.8 Hz, 4.3 Hz, 2CF), 160.1 (d, J = 243.8 Hz, 4.3 Hz, 2CF), 162.1 (d, J_{CF} = 248.1, 2CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -119.6 (CF), -113.2 (CF). IR (KBr): $\tilde{\nu}$ = 3025 (w), 2923 (w), 1601 (w), 1518 (w), 1464 (w), 1429 (w), 1389 (w), 1311 (w), 1273 (w), 1223 (m), 1156 (m), 1095 (w), 1014 (w), 938 (w), 879 (w), 820 (m), 708 (w), 677 (w), 584 (m), 525 (m), 468 (m), 412 (w) cm^{-1}. GC-MS (EI, 70 eV); m/z (%) = 490 (100) [M]$^+$. HRMS (EI, 70 eV) calcd. for C$_{30}$H$_{16}$F$_6$ [M]$^+$: 490.11507; found 490.115159. Anal. Calcd for C$_{30}$H$_{16}$F$_6$: C, 73.47. H, 3.29. Found: C, 73.49. H, 3.31.
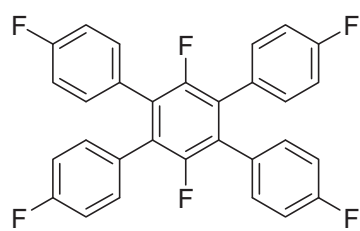
2,3,5,6-Tetra(4-bromophenyl)-1,4-difluorobenzene (37d): Starting with **31** (100 mg, 0.16 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 4-bromophenylboronic acid **17m** (192 mg, 0.96 mmol), **37d** was isolated as a white solid (81 mg, 68%). Mp 276–278 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.93 (d, J = 8.6 Hz, 8H, ArH), 7.33 (d, J = 8.6 Hz, 8H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 122.2 (4C), 124.9 (2C), 127.4 (2C), 128.5 (4C), 128.6 (4CH), 131.3 (2CH), 131.9 (2CH), 132.0 (2CH), 132.2 (6CH), 152.1 (d, J_{CF} = 243.0 Hz, 2CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -119.2 (CF). IR (KBr): $\tilde{\nu}$ = 2922 (w), 1903 (w), 1590 (w), 1496 (w), 1422 (w), 1381 (w), 1313 (w), 1262 (w), 1180 (w), 1105 (w), 1063 (m), 1009 (m), 877 (w), 806 (m), 769 (w), 736 (w), 508 (w), 421 (w) cm^{-1}. GC-MS (EI, 70 eV); m/z (%) = 734 (100) [M, ^{79}Br$_2$, ^{81}Br$_2$]$^+$, 733 (18), 732 (62), 730 (13), 712 (12), 710 (12), 656 (21), 654 (21), 574 (31), 506 (18), 494 (10), 414 (26), 207 (83), 206 (12), 196 (10). HRMS (EI) calcd. for C$_{30}$H$_{16}$^{79}Br$_2$^{81}Br$_2$F$_2$ [M]$^+$: 733.79072; found 733.791446; calcd. for C$_{30}$H$_{16}$^{79}Br$_3$^{81}Br$_1$F$_2$ [M]$^+$: 731.79276; found 731.792053. Anal. Calcd for C$_{30}$H$_{16}$^{35}Cl$_3$^{37}Cl$_1$F$_2$: C, 64.78. H, 2.90. Found: C, 64.78. H, 2.93.
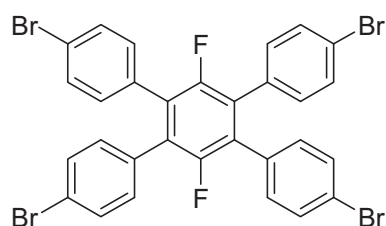
2,3,4,5,6-Penta(3-chlorophenyl)-1-fluorobenzene (38a): Starting with **33** (100 mg, 0.13 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 3-chloroboronic acid **17j** (121 mg, 0.78 mmol), **38a** was isolated as a white solid (65 mg, 72%). Mp 192–194 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.58-6.66 (m, 3H, ArH), 6.72-6.79 (m, 3H, ArH), 6.83-6.93 (m, 8H, ArH), 7.05-7.13 (m, 6H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 126.6 (CH), 126.9 (CH), 127.7 (CH), 128.6 (d, J = 12.3 Hz, CH), 128.8 (CH), 129.1 (CH) 129.2 (d, J = 33.7 Hz, CH), 130.6 (CH), 130.8 (d, J = 3.6 Hz, CH), 131.2 (d, J = 15.5 Hz, CH), 133.4 (d, J = 14.5 Hz, C), 133.8 (C), 135.5 (C), 136.0 (d, J = 4.5 Hz, CH), 139.6 (d, J = 2.5 Hz, C), 140.3 (C), 140.9 (t, J = 2.7 Hz, C), 155.9 (d, J_{CF} = 248.2, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -113.4 (CF). IR (ATR, cm^{-1})**:** $\widetilde{\nu}$ = 3063 (w), 2852 (w), 1980 (w), 1732 (w), 1594 (w), 1564 (w), 1481 (w), 1395 (w), 1321 (w), 1253 (w), 1204 (w), 1157 (w), 1117 (w), 1077 (w), 1040 (w), 998 (w), 959 (w), 908 (w), 882 (w), 810 (w), 778 (w), 738 (w), 694 (w), 602 (w), 569 (w), 501 (w), 434 (w) cm^{-1}. MS (EI, 70 eV); m/z (%) = 648 (100) [M, ^{35}Cl$_3$^{37}Cl$_2$]$^+$, 647 (18), 646 (57), 234 (14). HRMS (EI) calcd. for C$_{36}$H$_{20}$Cl$_5$F [M]$^+$: 645.99862; found 645.998556, calcd. for C$_{36}$H$_{20}$^{35}Cl$_4$^{37}ClF [M]$^+$: 647.99567; found 647.993937, calcd. for C$_{36}$H$_{20}$^{35}Cl$_3$^{37}Cl$_2$F [M]$^+$: 649.99272; found 649.993022.
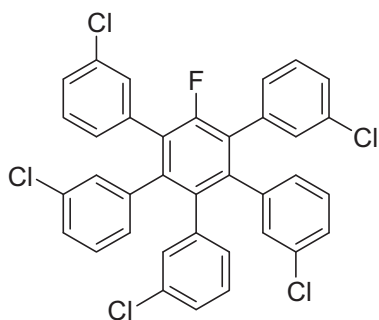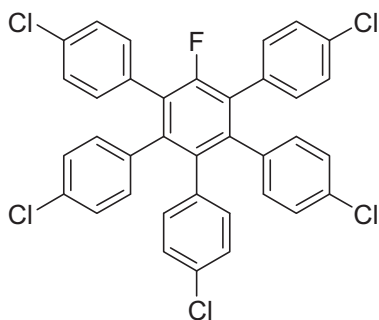
2,3,4,5,6-Penta(4-Chlorophenyl)-1-fluorobenzene (38b): Starting with **33** (100 mg, 0.13 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 4-chloroboronic acid **17k** (129 mg, 0.82 mmol), **38b** was isolated as a white solid (52 mg, 58%). Mp 286–288 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.56-6.63 (m, 6H, ArH), 6.82-6.89 (m, 6H, ArH), 6.95-6.97 (m, 4H, ArH), 7.11-7.14 (m, 4H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 127.6 (2CH), 127.8 (4CH), 128.2 (4CH) 131.9 (4CH), 132.2 (4CH), 132.3 (2CH), 132.4 (2CH), 132.6 (3C), 133.4 (2C), 136.2 (3C), 136.7 (d, J = 2.9 Hz, 2C), 137.4 (3C), 140.9 (d, J = 3.8 Hz, 2C), 155.9 (d, J = 247.7 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -113.86 (CF). IR (ATR, cm^{-1})**:** $\widetilde{\nu}$ = 3350 (w), 2919 (w), 2851 (w), 2081 (w), 1904 (w), 1739 (w), 1593 (w), 1495 (w), 1420 (w), 1321 (w), 1260 (w), 1197 (w), 1083 (m), 1012 (m), 960 (w), 873 (w), 831 (m), 762 (m), 666 (w), 610 (w), 524 (m), 473 (m), 399 (m) cm^{-1}. MS (EI, 70 eV); m/z (%) = 648 (100) [M, ^{35}Cl$_4$^{37}Cl]$^+$, 647 (22), 646 (58), 430 (10), 235 (14), 234 (21),

225 (14). HRMS (EI) calcd. for $C_{36}H_{20}Cl_4{}^{37}ClF$ [M]$^+$: 642.959531; found 642.959531, calcd. for $C_{36}H_{20}{}^{35}Cl_5F$ [M]$^+$: 645.99622; found 645.99619.

1-Fluoro-2,3,4,5,6-penta(4-fluorophenyl)benzene (38c): Starting with **33** (100 mg, 0.13 mmol), Pd(PPh$_3$)$_4$ (10 mol%), Cs$_2$CO$_3$ (5eq) and 4-fluorophenylboronic acid **17l** (109 mg, 0.78 mmol) **38c** was isolated as a white solid (57 mg, 73%). Mp 277 °C. ^{1}HNMR (300 MHz, CDCl$_3$): δ = 6.51-6.68 (m, 12H, ArH), 6.80-6.86 (m, 4H, ArH), 6.99-7.03 (m, 4H, ArH). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 113.8 (d, J = 1.7 Hz, 4CH), 114.1 (d, J = 1.7 Hz, 4CH), 127.8 (d, J = 3.3 Hz, C), 128.3 (2C), 128.4 (d, J = 3.3 Hz, 4C), 128.6 (2C), 130.8 (4CH$_2$), 130.0 (d, J = 1.2 Hz, 2CH), 131.1 (d, J = 1.2 Hz, 2CH), 131.9 (d, J_{CF} = 1.9 Hz, CF) 132.4 (d, J_{CF} = 2.8 Hz, CF), 139.4 (d, J_{CF} = 2.8 Hz, CF), 154.3 (d, J_{CF} = 244.3 Hz, 2CF), 160.8 (dd, J_{CF} = 247.8 Hz, 2.8 Hz, CF). ^{19}F NMR (282 MHz, CDCl$_3$): δ = -138.7 (CF), -115.2 (CF), -113.9 (CF). IR (ATR, cm^{-1})**:** $\tilde{\nu}$ = 3067 (w), 3044 (w), 2961 (w), 2853 (w), 1604 (w), 1512 (m), 1424 (w), 1390 (w), 1299 (w), 1220 (m), 1158 (m), 1091 (w), 1016 (w), 930 (w), 858 (w), 817 (m), 769 (w), 703 (w), 665 (w), 583 (w), 533 (m), 456 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 566 (100) [M]$^+$. HRMS (EI) calcd. for $C_{36}H_{20}F_6$ [M]$^+$: 566.146076; found 566.14637. Anal. Calcd for $C_{36}H_{20}F_6$: C, 76.32. H, 3.56. Found: C, 76.35. H, 3.60.
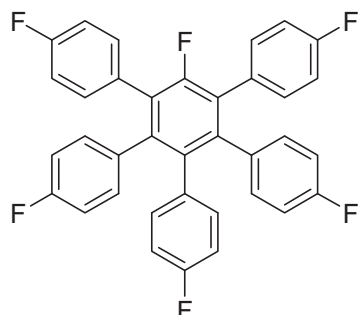
Abbreviations

Ac	Acetyl
Anal	Elemental Analysis
bp	Boiling point
calcd	Calculated
CI	Chemical Ionization
COSY	Correlated Spectroscopy
DEPT	Distortionless Enhancement by Polarization Transfer
dr	Diastereomeric ratio
ee	Enantiomeric excess
EI	Electron Impact
Et_2O	Diethyl ether
EtOH	Ethanol
GC	Gas Chromatography
GP	General Procedure
HMBC	Heteronuclear Multiple Bond Correlation
HPLC	High Performance Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
IR	Infrared Spectroscopy
MS	Mass Spectrometry
mp	Melting point
NaOEt	Sodium ethanolate
*n*BuLi	*n*-Butyllithium
NEt_3	Triethylamine
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser and Exchange Spectroscopy
ORTEP	Oak Ridge Thermal Ellipsoid Plot
OTf	Triflate
Ph	Phenyl
ppm	Parts per million
R_f	Retention factor
Tf_2O	Trifluoromethanesulfonic anhydride (triflic anhydride)
TFA	Trifluoroacetic acid

THF   Tetrahydrofuran

TLC   Thin Layer Chromatography

TMS   Tetramethylsilane

Tol   Tolyl (p-MeC$_6$H$_4$)

Tos   Tosyl (p-MeC$_6$H$_4$SO$_2$

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Aneela Maalik