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Synthesis and photophysical properties of tetra and pentaarylated fluorobenzenes

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ABSTRACT

Novel difluoro-tetraaryl and monofluoro-pentaarylbenzenes were prepared by palladium-catalyzed Suzuki–Miyaura cross-coupling reactions of novel 1,2- and 1,4-difluorotetraiodobenzene and of 1-fluoropentaiodobenzene. These Suzuki–Miyaura reactions allowed a convenient synthesis of fluoro-substituted aryl benzenes. The photophysical properties (absorption and fluorescence) of the products have been studied.

1. Introduction

Organofluorine compounds play a remarkable role in medicinal chemistry and crop protection,[1] due to their solubility, bioavailability and metabolic stability.[2] The fluorine substitution in drug design has led to the production of important drugs available in the market.[1q] One of the earliest synthetic fluorinated drugs is the antineoplastic agent 5-fluorouracil, an antimetabolite first synthesized in 1957.[2] Fluoroalkylated compounds are also used as ligands[3] in catalytic reactions, as organocatalysts,[4] and as substrates in palladium catalyzed reactions.[5]

The maturity of environmentally friendly and economical reactions for the formation of carbon–carbon and carbon-heteroatom bonds is of great interest for chemists. In the last few decades transition metal-catalyzed reactions, particularly palladium(0)-catalyzed transformations, including C–H bond activation, have gained considerable importance.[6] These reactions have been used for the synthesis of a number of natural products, pharmaceuticals and advanced materials.[7–9] The most commonly applied palladium-catalyzed carbon–carbon bond forming reactions in total synthesis are, namely, the Heck,[10] Stille,[11] Suzuki,[12] Sonogashira,[13] Tsuji–Trost,[14] and the Negishi[15] reaction.

The Suzuki–Miyaura reaction has been extensively studied[16] for its usefulness, particularly for the cross-coupling between halides and organoboronic acids.[17] Advancements made in this field include the development of new catalysts[18] and modern methods which have greatly increased the scope of this reaction and are now considered to be a quite general procedure for an ample range of selective carbon–carbon bond formations.[19]

Based on our interest in Pd-catalyzed cross-coupling reactions,[20] we herein wish to report Suzuki–Miyaura reactions of 1,2-, 1,4-difluoro tetraiodobenzenes and 1-fluoro pentaiodobenzenes which allow for a convenient synthesis of novel polyarylated fluorobenzenes.

2. Results and discussion

Novel 1,2-difluoro-3,4,5,6-tetraiodobenzene (**1**), 1,4-difluoro-2,3,5,6-tetraiodobenzene (**3**) and 1-fluoro-2,3,4,5,6-pentaiodobenzene (**5**) were synthesized from 1,2-difluorobenzene, 1,4-difluorobenzene and 1-fluorobenzene according to our previously reported method, respectively.[1r]

The Suzuki–Miyaura coupling reactions of **1** with various arylboronic acids, using our optimized condition (Table 1, entry 8),

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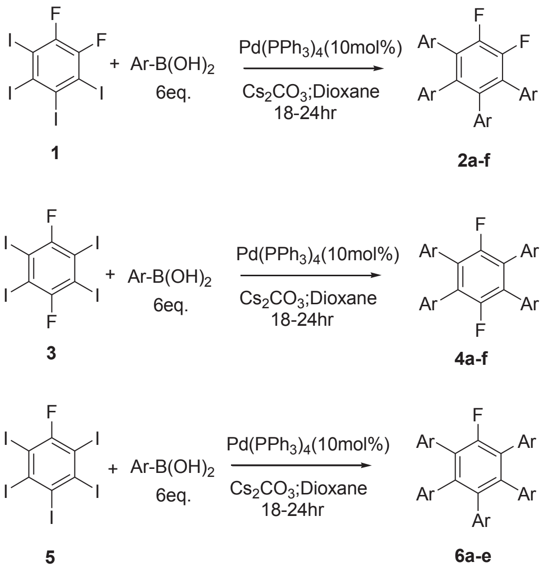
Table 1
Optimization of the synthesis of **2a**

	Catalyst	Base	T [°C]	T [h]	Yield[a] [%]
1	$Pd(OAc)_2$(5mol %)	K_3PO_4	90	24	Traces
2	$Pd(OAc)_2$(5mol %)	K_3PO_4	110	22	Traces
3	$Pd(OAc)_2$(5mol %)	NEt_3	90	18	39
4	$Pd(OAc)_2$(5mol %)	NEt_3	90	20	28
5	$Pd(PPh_3)_4$(3mol %)	NEt_3	90	19	40
6	$Pd(PPh_3)_4$(5mol %)	Cs_2CO_3	90	19	43
7	$Pd(PPh_3)_4$(5mol %)	Cs_2CO_3	90	22	59
8	$Pd(PPh_3)_4$(10mol %)	Cs_2CO_3	100	20	80

[a] Yields of isolated products.

afforded the desired tetraarylfluorobenzenes **2a**–**f** in 72–85% yields (Table 2). During the optimization of the synthesis of **2a**, the use of $Pd(PPh_3)_4$ (10mol %) as the catalyst and of Cs_2CO_3 as the base proved to be most advantageous (Table 1) (see Scheme 1).



Scheme 1. Synthesis of 1,2-difluoro-tetraarylbenzenes **2a**–**f**, 1,4-difluoro-tetraarylbenzenes **4a**–**f** and 1-fluoro-pentaarylbenzenes **6a**–**e**.

In general, the desired polyarenes can be prepared in good to high yields from both electron-donating and electron-withdrawing arylboronic acids. Chloro-, fluoro-, methyl-, *t*-Bu-, methoxy-, and di-methoxy substituents are tolerated under these conditions (Table 2, entries **2a**–**f**).

The Suzuki–Miyaura coupling reactions of **3** with various arylboronic acids afforded, following our optimized procedure, the 1,4-difluoro-2,3,4,6-tetraaryl benzenes **4a**–**f** in 68–95% yields (Table 3). The best yield was obtained starting with 4-ethylphenyl boronic acid (Table 3, entry **4b**), whereas 4-bromophenyl boronic acid gave 68% yield (Table 3).

Table 2
Synthesis of 1,2-difluoro-tetraarylbenzenes **2a**–**f**

2	Ar	T [°C]	T [h]	Yield[a] [%]
a	$4\text{-}MeC_6H_4$	100	20	80
b	$3,5\text{-}(Me)_2C_6H_3$	100	18	78
c	4-(*t*-Bu)C_6H_4	110	24	85
d	$4\text{-}FC_6H_4$	100	18	76
e	$3\text{-}ClC_6H_4$	100	20	82
f	$3\text{-}(MeO)C_6H_4$	90	19	72

[a] Yields of isolated products.

Table 3
Synthesis of 1,4-difluoro-tetraarylbenzenes **4a**–**f**

4	Ar	T [°C]	T [h]	Yield[a] [%]
a	C_6H_5	100	18	76
b	$4\text{-}EtC_6H_4$	110	19	95
c	$4\text{-}FC_6H_4$	110	20	83
d	$4\text{-}BrC_6H_4$	90	20	68
e	$3\text{-}ClC_6H_4$	100	20	83
f	$4\text{-}(MeO)C_6H_4$	100	20	80

[a] Yields of isolated products.

The Suzuki–Miyaura coupling reaction of **5** afforded the 1-fluoro-2,3,4,5-pentaarylbenzenes in good to high yields (Table 4). Both electron withdrawing and donating groups were tolerated. *para*-Methyl- and 4-methoxyphenyl boronic acid gave 72–78% yields (Table 4, entries **6a**, **6e**), while *meta*- and *para*-chlorophenylboronic acid gave 58–78 % yields (Table 4, entries **6c**, **6d**). *para*-Fluorophenylboronic acid afforded the product in 73% yield (Table 4, entry **6b**). The structures of all products were confirmed by spectroscopic methods. The structures of **4a**, **6a** and **6d** were independently confirmed by X-ray crystal structure analysis (Figs. 1–3).

Table 4
Synthesis of 1-fluoro-pentaarylbenzenes **6a**–**e**

6	Ar	T [°C]	T [h]	Yield[a] [%]
a	$4\text{-}MeC_6H_4$	100	18	72
b	$4\text{-}FC_6H_4$	90	20	73
c	$3\text{-}ClC_6H_4$	100	20	72
d	$4\text{-}ClC_6H_4$	100	18	58
e	$4\text{-}(MeO)C_6H_4$	100	20	78

[a] Yields of isolated products.

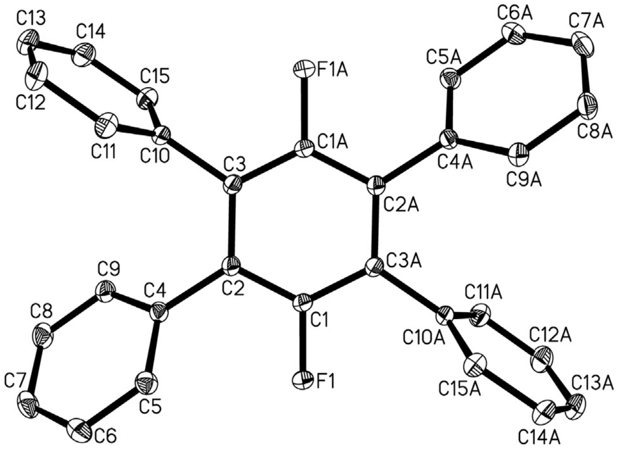


Fig. 1. Molecular structure of **4a** in the crystal. Hydrogen atoms are omitted for clarity. Displacement ellipsoids correspond to 30% probability.

The crystal structures of **4a**, **6a** and **6d** showed that the phenyl groups and the central benzene moiety are twisted out of plane.

For initial evaluation of photophysical properties of the prepared compounds, the UV–visible and fluorescence studies were performed. The electronic absorption and fluorescence-emission data for compounds **2e**–**f**, **4b**–**e**, **6b** and **6d**–**e** are listed in Table 5. The spectra were recorded in DCM, typically in the concentration range of 10^{-4}–10^{-6} M. The compounds **2e** and **2f** showed the absorption maxima at 227 nm whereas it showed a broader