



Preferential oxidative addition in mixed iodo/bromo quinquephenylenes



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ABSTRACT

A Suzuki reaction of a diiodo monobromo quinquephenylene with an aryl boronic acid is described. With PEPPSI-IPr as catalyst the threefold coupling product is mainly obtained although only two equivalents of the boronic acid are used. This shows that the intramolecular palladium transfer is favored over the common iodo/bromo selectivity. Performing the reaction with other Pd systems shows that the product distribution is strongly catalyst dependent.

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1. Introduction

Transition-metal catalyzed aryl–aryl-, aryl–vinyl-, and aryl–ethynyl coupling reactions in which an (pseudo) halogen component reacts with an organometallic compound are of fundamental importance in modern synthetic chemistry.¹ If multiple halogens are present in the substrate and this is treated with only one equivalent of the metal organic compound, statistical mixtures are expected and often observed. Selectivity can be reached by making use of the different reactivity of the halogens, which decreases in the order I > Br > Cl or by halogens of the same kind and a different degree of activation.² Alternatively, the coupling of halogenated phenols and their subsequent transformation to triflates allows the synthesis of unsymmetrical coupling products in good to high yield.³

When statistical coupling reactions between a multihalogen compound and an organometallic coupling partner are performed the product distribution sometimes differs from the expected composition.⁴ Recent work has shown that depending on the catalyst system and the specific experimental conditions, a preferred oxidative addition with the just formed 1-aryl-*n*-halobenzene can occur.⁵ Interestingly, this does not only apply for simple arenes but also for more extended π -systems, e.g., for fluorenes.⁶ In the synthesis of conjugated polymers this concept has already been

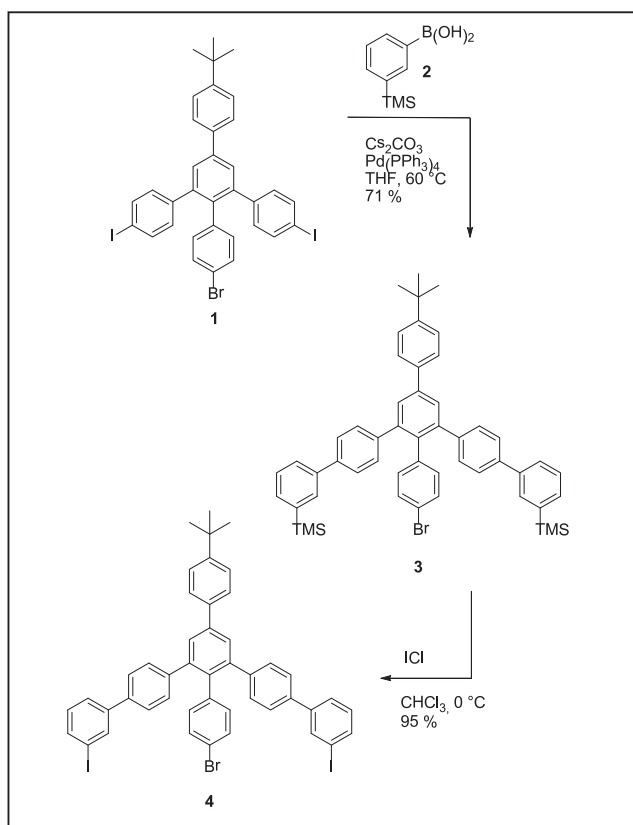
applied for the preparation of macromolecules of defined molecular weight and low polydispersity and also for the preparation of end-functionalized polymers because the polymerization proceeds via a ‘chain-growth mechanism’ rather than via a ‘step-growth mechanism’.⁷ It can be assumed that after the reductive elimination the diffusion process of the Pd(0) species and leaving the coupling product is slower than the oxidative addition with the nearby carbon-halogen bond. This is in accordance with the assumption that η^2 -bound arenes are on the pathway for the oxidative addition.⁸ Furthermore, this concept has recently been applied for the synthesis of shape-persistent macrocycles.⁹

2. Results and discussion

Here we describe the synthesis of iodo/bromo septiphenylenes that will be useful building blocks for the preparation of clamped oligo(phenylene–ethynylene–butadiynyls) and other rigid conjugated π -oligomers.¹⁰ Specifically, we investigated the molecular elongation of **1** by iodo-selective Pd(0) catalyzed Suzuki-coupling with two equivalents of **2** followed by the ICl mediated iododesilylation to give **4** (Scheme 1). Compound **1** is rather easy available from the 2,6-bis(4-iodophenyl)-4-(4-*tert*-butylphenyl)pyrylium tetrafluoroborate and sodium 4-bromophenyl acetate according to the protocol developed by Zimmermann and Fischer.¹¹ Initial Suzuki-coupling reactions were conducted under Pd catalysis by the use of PEPPSI-IPr in the presence of potassium hydroxide.^{12,13} Contrary to our expectations, we could not observe a clean iodo/bromo selectivity that would give **3** as major product but we

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obtained a rather complex mixture of different coupling products along with unreacted starting material (Scheme 2, Table 1). The crude product was separated by column chromatography into fractions **F1–F4**, and **F1 (1)**, **F2 (6)** and **F4 (7)** are isolated as pure compounds. Fraction **F3** could only be obtained as a mixture of two compounds; a bromo (**3**) and an iodo (**5**) functionalized twofold substitution product. A further separation of **3** and **5** by column chromatography is not possible due to their similar polarities. However, the high yield of trisubstituted product **7** clearly shows that under the applied conditions the intramolecular catalyst transfer (probably via migration of Pd(0) from one arene to the another arene unit of the same molecule) predominates over the iodo/bromo selectivity. Moreover, the attempted synthesis of **3** could not be performed under these conditions since even the fraction of the disubstituted reaction product (**F3**) that was obtained in only 14% yield, was not pure **3**, but a mixture of two compounds (**3** and **5**), as mentioned before.



Scheme 1. Synthesis of **4** in a two-step reaction sequence of an iodo-selective Suzuki–Miyaura coupling and subsequent *ipso*-substitution.

When using Pd₂dba₃/tBu₃P as catalyst (K₂PO₃ as base), **3** could be obtained in a yield of about 41%. Surprisingly the iodo substituted side product **5** in **F3** was absent according to NMR spectroscopic and mass spectrometric analysis of the crude product. However, still 22% of the threefold coupling product **7** indicated that the Pd(0) after the reductive elimination is still in close proximity to the just reacted substrate. It undergoes the intramolecular oxidative addition with rather high probability, even though primarily an iodo/bromo selective cross coupling reaction is favored. With Pd(PPh₃)₄ as catalyst and cesium carbonate as base, we observed an acceptable iodo/bromo selectivity so that **3** could be isolated in 71% yield. Compound **3** was then converted into the mixed iodo/bromo compound **4** in 95% yield.

Table 1

Ratio of column chromatography separated product fractions of Pd-catalyzed Suzuki reactions of iodo/bromo pentaphenylene **1** and TMS substituted boronic acid **2**

	F1 ^a [%]	F2 ^a [%]	F3 ^a [%]	F4 ^a [%]	Yield ^b [%]	Ratio ^c
PEPPSI-IPr KOH	25	12	14	47	87	86:14
Pd ₂ dba ₃ /tBu ₃ P K ₃ PO ₄	25	—	41 ^d	22	72	53:47
Pd(PPh ₃) ₄ Cs ₂ CO ₃	2	2	71 ^d	8	83	15:85

^a Yields of **F1–F4** are defined relative to the starting material determined after column chromatography.

^b Entire yields are defined as conversion relative to the boronic acid.

^c Ratio of **F1**, **F2** and **F4** to **F3**.

^d Under these reaction conditions **F3** is isolated as pure **3**, without side product **5**.

3. Conclusion

To summarize, we could expand the size of the mixed iodo/bromo compound **1** in two-steps in good yield starting from rather easy accessible **1**. The key to success was the iodo/bromo selectivity in the Pd(0)-catalyzed Suzuki reaction. Although the concept of preferential oxidation in Suzuki reactions under PEPPSI-IPr and Pd₂dba₃/tBu₃P was already described, a preferential oxidation in mixed iodo/bromo compounds was, as far as we know, not mentioned before. Nevertheless, the nature of the catalyst has an enormous influence on the product distribution and in our case we observe a high tendency for the PEPPSI-IPr catalysts to undergo preferential oxidative addition that overrides the conventional iodo/bromo selectivity.

4. Experimental section

4.1. General experimental

All palladium catalyzed reactions were performed by applying standard Schlenk techniques under Ar atmosphere and using dry solvents (THF), if not otherwise indicated. THF was dried over sodium and distilled and stored under argon. Chloroform was used in p.a. quality and dichloromethane as solvent for work-up was used after purification by distillation. All commercial available reagents were used without further purification. ¹H and ¹³C NMR spectra were recorded on Bruker AM 400 and AM 500 spectrometers (400 and 500 MHz for ¹H; 100.6 and 125.8 MHz for ¹³C). Chemical shifts are given in parts per million (ppm) referenced to residual ¹H or ¹³C signals in deuterated CDCl₃ (¹H: 7.26, ¹³C: 77.0). Deuterated CDCl₃ was obtained from Deutero GmbH, Germany. Mass spectra were measured on a Bruker Daltronics autoflex TOF/TOF (MALDI MS; matrix material: DCTB). High resolution mass spectra were recorded on a Bruker Daltronics micrOTOF-Q (ESI, APCI). Thin layer chromatography was performed on silica gel coated aluminum plates (Macherey–Nagel, Alugramm SIL G/UV₂₅₄, 0.2 mm silica gel coating with fluorescence indicator). Column chromatography was performed using silica gel 60 M (Macherey–Nagel, 40–63 μm) as stationary phase and dichloromethane and cyclohexane as eluent. The synthesis of **3** is performed under Pd-catalyzed conditions using PEPPSI-IPr, Pd₂dba₃ and Pd(PPh₃)₄ as catalyst. A full characterization of **3** and further side products is given.

4.2. Preparation under PEPPSI-IPr catalyzed conditions

Compound **1** (0.100 g, 0.130 mmol), **2** (0.052 g, 0.266 mmol), potassium hydroxide (0.044 g, 0.779 mmol) and PEPPSI-IPr (0.004 g, 0.005 mmol) are placed in a Schlenk-tube and repeatedly evacuated and flushed with argon. The starting materials are suspended in THF (5 mL) and stirred over night at 60 °C. After cooling to rt the reaction mixture is diluted with water and

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