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Selective direct arylation of 3-bromo-2-methylthiophene: a building-block for electro- and photoactive organic materials

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ABSTRACT

Selective direct arylation of 3-bromo-2-methylthiophene with aryl bromides to form a library of 2-aryl-4-bromo-5-methylthiophenes is demonstrated. The reaction yields varied from 27–63%. The inherent selectivity observed is attributed to the lack of oxidative insertion of the bromine in 3-bromo-2-methylthiophene. This method will be useful for the facile preparation of functional organic electronic materials.

Organic electro- and photoactive materials have flourished because of their applicability in the next generation of electronic devices such as transistors,[1] solar cells,[2] sensors,[3] and light emitting diodes.[4] Therefore, simple, non-toxic, and inexpensive synthetic methods are in high-demand to produce these materials. However, traditional methods used for the preparation of electroactive materials including Suzuki–Miyaura, Stille, Kumada, and Reike couplings require the use of dangerous and water-sensitive reagents.[5] Direct-arylation by C–H activation is an emerging synthetic methodology. It is superior compared to traditional routes leading to organic materials in fewer synthetic steps and higher overall yields without the use of water-sensitive and dangerous reagents, and avoids the production of toxic or unstable intermediates, such as tin and boronic acid compounds.[5,6] This communication investigates the reactivity of commercially available 3-bromo-2-methylthiophene with various aryl bromides using direct arylation, and demonstrates a selective C–H activated direct arylation.

Selective reactivity enables the preparation of tailor-made organic materials and is crucial for obtaining the specific properties required. For example, 2-aryl-4-bromo-5-methylthiophenes are key intermediates for electro- and photoactive materials, from which the bromine can be converted into a plethora of functional and aromatic groups.[7] Furthermore, 2-aryl-4-bromo-5-methylthiophenes are particularly valuable for the preparation of dithienylethene-based photochromic molecules, which can be used for memory devices, optical switches,[8] and biologically relevant applications[9] such as mimicking pyridoxal phosphate,[9a] regulating paralysis,[9b] and Human Carbonic Anhydrase I activity.[9c] These properties can be easily tuned according to the aryl group used in 2-aryl-4-bromo-5-methylthiophenes, and thus a simple and selective method to prepare these materials is required.

The direct arylation of 3-bromo-2-methylthiophene with various aryl bromides was conducted in the presence of pivalic acid, potassium carbonate, and palladium acetate in dimethylacetamide according to optimized conditions for product **1**, as shown in Scheme 1. After reacting for 48–60 h at 100 °C, the products were purified by column chromatography using silica gel. The products were analyzed by ^{1}H NMR, mass spectrometry, elemental analysis, and infrared spectroscopy.[10] Figure 1 depicts the ^{1}H NMR spectrum of the starting material compared to representative compounds **3** and **7**. In all cases, the two aromatic doublets of 3-bromo-2-methylthiophene disappeared and the characteristic resonances of 2-aryl-4-bromo-5-methylthiophene products appeared. Figure 2 shows the mass spectrum of a representative compound **7**, which corresponds to the molecular weight of the target. The pattern shows two major peaks separated by 2 AMU, which is typical of monobrominated compounds. IR spectroscopy showed the appearance of functional groups, such as the carbonyl in compound **5**, and the elemental analysis (C, H, S) demonstrated that the products were pure within 0.4% (see the Supplementary data).

In all cases, the major product was that of the coupling of 3-bromo-2-methylthiophene with the aryl bromide. The yields varied from 27% to a moderate 63%, and may be improved with optimization of each individual reaction. The general trend indicates that aryl bromides with electron-withdrawing groups, such as acyl (**5**) and fluorine (**3**), resulted in higher yields than that of the

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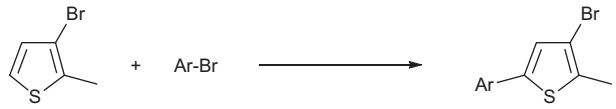
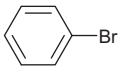
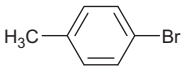
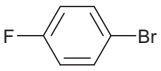
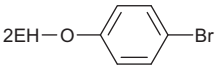
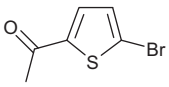
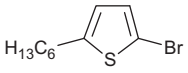
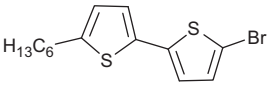
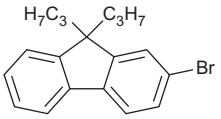
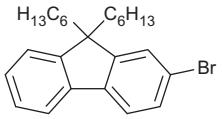
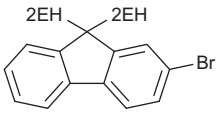


Ar-Br	Product	Yield
	**1**	56%
	**2**	47%
	**3**	59%
	**4**	27%
	**5**	63%

Ar-Br	Product	Yield
	**6**	49%
	**7**	41%
	**8**	39%
	**9**	59%
	**10**	37%

Scheme 1. Selective direct arylation of 3-bromo-2-methylthiophene. 2EH represents 2-ethylhexyl. Reagents and conditions: pivalic acid, K_2CO_3, $Pd(OAc)_2$, DMAc, 100 °C, 48–60 h.

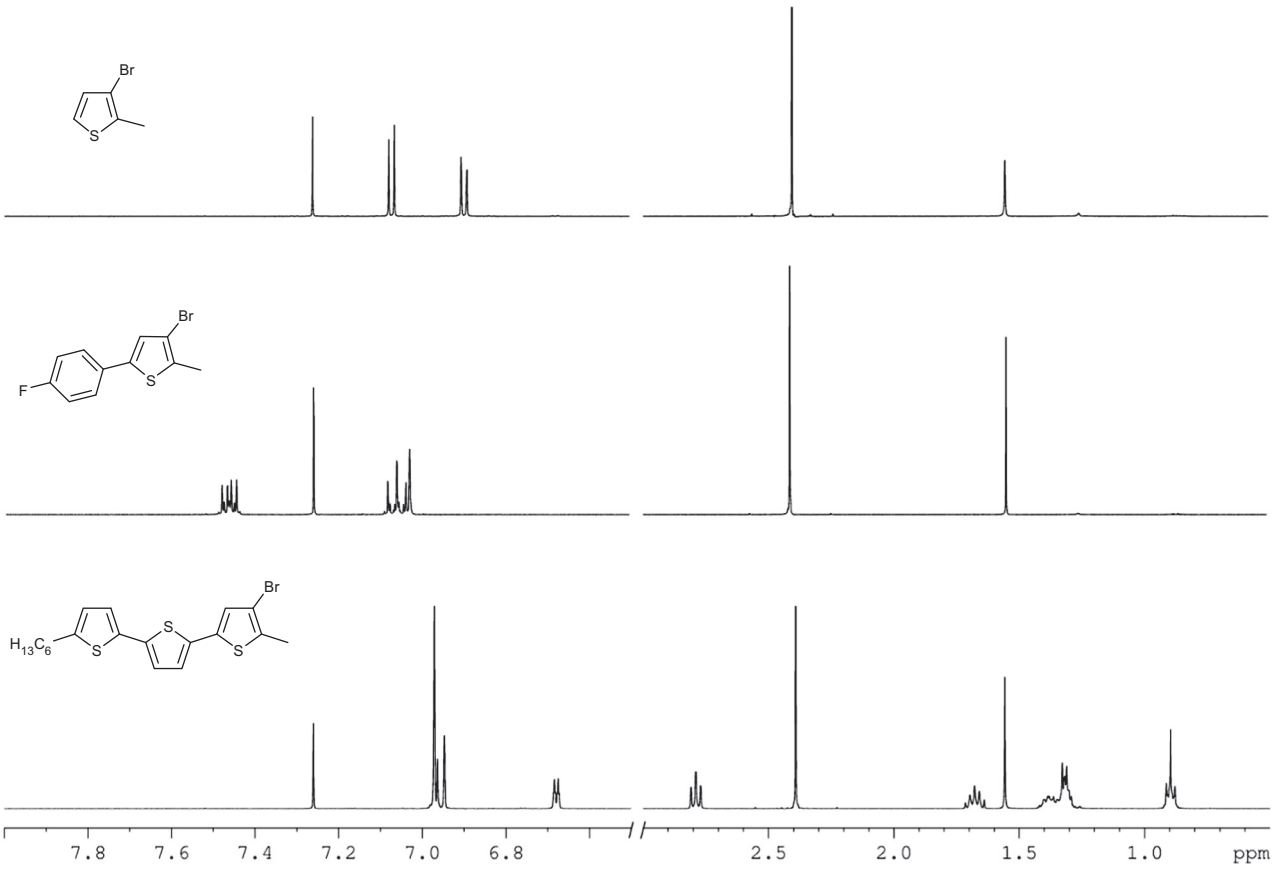


Figure 1. ^1H NMR (400 MHz) spectra of the 3-bromo-2-methylthiophene starting material and representative compounds **3** and **7** in $CDCl_3$.

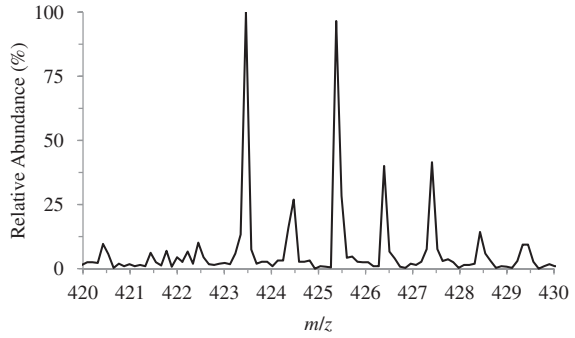


Figure 2. Mass spectrum of a typical 2-aryl-4-bromo-5-methylthiophene, compound **7**.

electron-donating 2-ethylhexyloxy group (**4**). This general trend was also observed by Doucet and co-workers [6a] The ligands, tricyclohexylphosphine (PCy) and tri(*o*-tolyl)phosphine (TTP) were used to prepare **1**, however the conversion was either similar (PCy) or lower (TTP) than without the ligand. Importantly, no homocoupling of 3-bromo-2-methylthiophene was observed. This suggests that the oxidative addition of the aryl bromide to the palladium acetate occurs more readily than to 3-bromo-2-methylthiophene. Therefore, this unique selectivity observed is due to the lower oxidative ability of the bromine in 3-bromo-2-methylthiophene.

In conclusion, selective direct arylation was demonstrated for the first time and a library of 2-aryl-4-bromo-5-methylthiophenes has been prepared. The products were formed in one-step from commercially available 3-bromo-2-methylthiophene, compared to the conventional route of brominating 2-methylthiophene, lithiation followed by metalation with tributyltin chloride or trimethylborate, and Stille or Suzuki reaction. These results reveal that the bromine at the 3-position of the thiophene is not active toward oxidative insertion of palladium(0) under these conditions giving a unique opportunity for the facile preparation of tailor-made functional organic materials.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.05.015. These data include MOL files and InChiKeys of the most important compounds described in this article.

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[10]. See the Supplementary data for the detailed synthetic methods and the full characterization (including spectra) of each compound.