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dioxane furnishes iodinated compounds in high yields.

Practical and efficient ipso-iodination of arylboronic acids via KF/I_2 system

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ABSTRACT

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A major role in modern chemistry is played by organoboron compounds, among which boronic acids have emerged in a leading position.¹ With the discovery of a wealth of new chemistry, in particular the Suzuki-Miyaura cross-coupling reaction, together with their accessibility and ease of handling, boronic acids and boronates are now established as intermediates of great value and versatility. Applications abound in synthesis, catalysis, analytical chemistry and biological systems. Functional group interconversion of the boronic acid moiety is possible and expands the realm of application accessed through these reagents. For example, the ready availability of organoboronic acids makes their use as precursors for aryl iodides especially appealing. To date, KI,² NaI,³ or NH₄I⁴ in the presence of mild oxidizing agents, N-iodosuccinimide⁵, NH₄I₃ or CsI₃⁶, 1,3dihalo-5,5-dimethylhydantoin⁷ or I₂ and Cu salts⁸ are generally used to make boron-halide exchange. However, these methods preferentially involve: (1) boronic esters and trifluoroborates, because boronic acids containing electron-withdrawing groups on the aromatic ring are not iodinated effectively; $^{3}(2)$ several halide sources but not the elemental one because this can react through electrophilic aromatic substitution on arenes by using the boron moiety as a blocking group.⁹

Thus, herein we want to report the practical and efficient iododeboronation of a large array of variously substituted aryl and heteroarylboronic acids mediated by KF and I_2 . Our initial studies focused on the *ipso*-iodination of 3,5-dimethoxybenzeneboronic acid as a model reaction to find optimized conditions (Table 1).

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http://dx.doi.org/10.1016/j.tetlet.2015.01.040 0040-4039/© 2015 Elsevier Ltd. All rights reserved. On the basis of our previous experience with arylboronic acids involving reactions, we decided to use KF and 1,4-dioxane in this protocol as the base and the solvent, respectively.¹⁰ We found more convenience in using 1.1 equiv of arylboronic acid and 1.0 equiv of iodine to inhibit the formation of potential doubly iodinated products.

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As shown in Table 1, the presence of KF, which serves to activate the boronic acid, is crucial to the success of the reaction (entry 1). A lower amount of KF can be tolerated (entry 2) but gives worse

 Table 1

 Optimization of the reaction conditions

A facile and effective iododeboronation of variously substituted aryl and heteroarylboronic acids through

activation and subsequent ipso-introduction of iodine is presented. The use of KF and I2 at 80 °C in 1,4-

(⊢	IO) ₂ B OMe 1a (1.1 equiv)	e + I2 (1.0 equiv) ^{1,4-dioxa} te t	KF ane (0.1 M) emp ime	OMe OMe 2a
Entry	KF (equiv)	Temp (°C)	Time (h)	Yield ^a (%)
1	_	80	1	10
2	1.1	80	1	72
3	3.3	80	1	84 ^b
4	3.3	20	1	75
5	3.3	80	24	84
6 ^c	3.3	80	1	<5
7 ^d	3.3	80	1	<5

^a Determined by GC-MS analysis versus a calibrated internal standard.

^b Isolated yield (average of two experiments).

^c 2.5 mol % of Pd(OAc)₂ and 5 mol % of (*t*-Bu)₂PMeHBF₄ were added.

^d 2.5 mol % of Pd(OAc)₂ was added.

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^a Isolated yields of the products are reported (average of two experiments).



Scheme 1. Competition experiment.

results than the use of 3.3 equiv of the base (entry 3). Moreover this reaction proceeds better at higher temperature then room temperature (entry 4). Reaction time does not affect the yield of desired product, which demonstrated high stability under selected conditions (entry 5). Finally, the addition of a Pd source in the reaction, both with (entry 6) and without (entry 7) a phosphinic ligand, totally impedes this process. This effect precludes the potential to achieve biaryls through a one pot iododeboronation/cross-coupling reaction.

With optimized conditions in hand, we set out to explore the substrate scope for the conversion of arylboronic acids to iodoarenes (Table 2).¹¹ We found that either electron-rich or electron-deficient arylboronic acids, as well as heteroarylboronic acids such as thiophenes, benzothiophenes and indoles could be efficiently converted into the corresponding aryliodides in good to excellent yields.¹² Notably a broad range of functional groups is well tolerated.

In addition we performed a competition experiment between the *ipso*-iododeboronation and the iodination of an activated terminal alkyne. The outcomes displayed the iodine substantial propensity to react with arylboronic acids rather than give electrophilic addition on the alkyne (Scheme 1).

In conclusion, we have developed a practical and easy method to convert aryl and heteroarylboronic acids to corresponding iodoarenes by *ipso*-iodination. This protocol can be efficiently applied to a number of readily available boronic acids bearing a wide range of functional groups.

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- 11. General procedure: A mixture of the arylboronic acid (0.55 mmol), KF (96 mg, 1.65 mmol) and I₂ (127 mg, 0.50 mmol) in 1,4-dioxane (5 mL) was stirred at 80 °C for 1 h. Then it was filtered through silica gel, eluting with $E_{L_2}O$ (10 mL) and the solvent was removed by rotary evaporation. When necessary, the product was purified by chromatography on silica gel (petroleum ether/Et₂O 98:2).
- 12. The products were characterized by ¹H NMR, ¹³C NMR and MS (ESI). All these compounds are known in the literature and their characterizations are consistent with the reported ones.

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