

Arylboronic acid-lead tetraacetate-copper diacetate: A one-pot system for copper-catalyzed *N* arylation under neutral conditions



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1. Introduction

The chemistry of boronic acids continues to be a growth area in synthetic methodology. (Pelter 1988, Schlosser 2002) Such evidence as exists indicate that they are of relatively low toxicity [benzeneboronic acid (Frankland 1859, Leibigs 1860, Frankland 1862): LD₅₀ oral-rat: 740mg/kg] and environmental impact. Boronic acids derivatives are mild and selective arylating reagents for a wide range of functional groups. Further information on the applications of boronic acids as derivatising and protecting agents can be found in various reviews (Ferrier 1978, Brooks 1978, Duggan 2002) and monographs. (Knapp 1979, Blau 1993, Greene 1999) Selective *N*-arylation of amines (aliphatic, heterocyclic amines or anilines) and *O*-arylation of phenols and glycols can be easily realized under very mild conditions by copper-catalyzed arylation with aryl lead triacetate.

As aryl boronic acid can be used for the efficient synthesis of aryllead triacetate (Morgan 1990), we decided to take advantage to develop an in situ generation of the aryllead reagent followed directly by the copper-catalysed arylation of the amine. In this paper, we describe our studies on the influence of the substituents (electron-donating or electron-withdrawing) present on the aryl moiety of the boronic acid on the arylation of various substituents of amine aniline.

2. Material and Methods

We therefore decided to look for a cheap, non-toxic and easily handled combination of reagents which would lead to good to high yields of aryllead triacetate under neutral conditions. We considered that arylboronic acid should be well-suited for this purpose. We now report lead tetracetate can be easily oxidized to aryl leadtriacetate by treatment with aryl boronic acid in chloroform at room temperature.

In this way, a compound (2) was prepared, in which the aryl group is substituted by electron-donating or electron-attracting groups (table1).

The evolution of the reaction was monitored by t.l.c. until the lead tetracetate has completely disappeared, and the average reaction time was 5 hours. Good yields of pure compound were obtained.

2.1 General procedure for the transmetallation of arylboronic acid to aryllead triacetates

A mixture of lead tetracetate (4.9 mmol), mercuric diacetate (0.48mmol) in chloroform (6 cm³) was stirred at 40°C for 15 min. The arylboronic acid (4.5 mmol) was then added, and the resulting mixture was stirred at 40°C for 6 hours. The solvent was concentrated under reduced pressure to a small volume, light petroleum was added and the solution kept overnight at 5°C. The resulting solid was filtered and dried.

2.2 General procedure for the arylation of aniline derivatives to arylamines

A mixture of lead tetracetate (4.06 mmol), mercuric diacetate (0.48mmol) in chloroform (6 cm³) was stirred at 40°C for 15min. The arylboronic acid (4.5 mmol) was added, and the resulting

mixture was stirred at 40°C for 6 hours. Then, copper diacetate (0.41 mmol) and the amine (4.12 mmol) were added and the resulting mixture was stirred for 5 hours. The mixture was filtered through celite and the solvent was evaporated. The residue was purified by flash column chromatography on silicagel (pentanes/ methylene dichloride 8/2). The resulting diarylamine was finally recrystallized from pentane.

Phenyl (1,4-Benzodioxan) amine ¹H NMR (CDCl₃, 300 MHz) 4.18 (t, 2H, H-2), 4.21 (t, 2H, H-2'), 6.58 (s, 1H, H-4), 7.83 (br s, 1H, H-5), 6.94 (dd, 2H, H-6), 7.16 (dd, 2H, H-7), 6.72 (m, 1H, H-8), 6.56 (d, 1H, H-10a), 6.75 (d, 1H, H-11). ¹³C NMR (CDCl₃, 300 MHz) 63.92 (C-2), 64.33 (C-2'), 143.61 (C-3a), 107.03 (C-4), 137.05 (C-4a), 144.65 (C-5a), 115.44 (C-6), 129.17 (C-7), 118.69 (C-8), 117.79 (C-10a), 117.36 (C-11), 137.61 (C-11a).

3. Results and Discussion

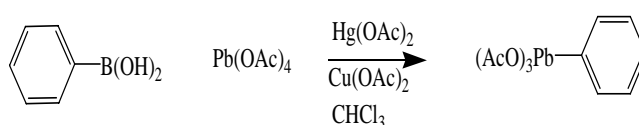


Fig (1)

N°	Ar	Time	Yield(%)	Mp(°C)	Mp(°C)lit
1	Ph	6h	78	102	103

Table (1): Synthesis of aryllead triacetate by reaction of arylboronic acid with lead tetracetate and mercury diacetate.^a

As the oxidation of lead tetracetate took place under mild conditions to afford the lead triacetate as the only detectable compound, we then attempted to use the in situ generated reagent for the N-arylation of an aniline substrate. (AcO)B(OH)₂, the by product of the oxidation step, should not interfere with the copper-catalysed amine N-arylation under the reaction conditions which are used. In preliminary experiments, a slight excess of lead tetracetate compared to the aryl boronic acid substrate was used, as in the synthesis of aryl lead triacetate. After addition of the aniline derivatives and catalytic amount of copper (II) Diacetate, the reaction led to a coloured mixture of products. The expected diarylamine was detected, but numerous other polar products were also present. Under these conditions, these excess of lead tetracetate is likely to react with the aniline to form various oxidized products. The conditions were therefore slightly modified. A small excess of arylboronic acid relative to lead tetracetate was used, and the reaction was left to run overnight to consume all the oxidizing of lead reagent. After addition of the aniline and catalytic copper diacetate, the reaction eventually afforded the diarylamine in partially quantitative yields for all the reagents.

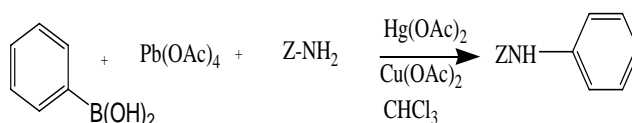


Fig (2)

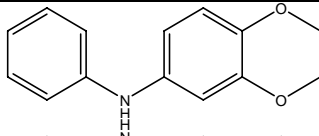
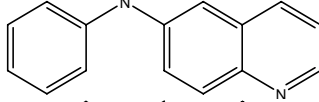
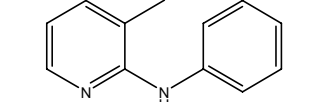
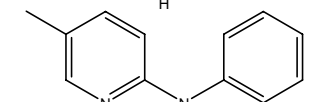
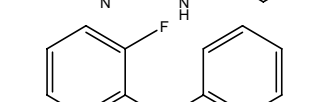
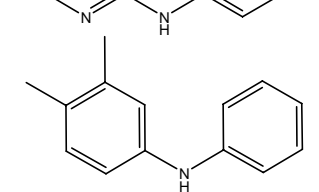
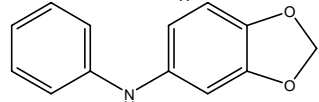
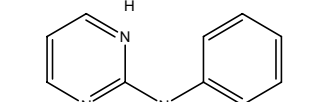
N°	Compound	Yield,%	Mp(°C)
3		60	86
4		55	135
5		54	122
6		62	114
7		12	70
8		95	57
9		80	75
10		51	116

Table 2: Arylation of various substituted of amine aniline with in situ generated aryl leadtriacetate.

4. Conclusion

In summary, the reaction of aryl boronic acid with lead tetracetate lead to the corresponding aryl leadtriacetate, which can be isolated in good yield or used directly for the in situ N-arylation reaction.

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