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Convenient and mild synthesis of nitroarenes by metal-free nitration of arylboronic acids[†]

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A novel methodology for the direct nitration of arylboronic acids has been developed. By using inexpensive *tert*-butyl nitrite various aromatic nitro compounds are produced in moderate to good yields (45–87%) without the need of any catalyst.

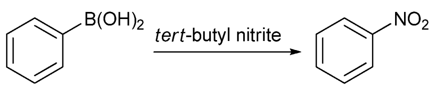
Nitroarenes are important intermediates for the chemical industry and organic synthesis,[1,2] because of their wide application in pharmaceuticals,[3] dyes,[4] and materials.[5] In general, in industry aromatic nitro compounds are produced on a bulk scale by electrophilic nitration of arenes with HNO_3, mixtures of HNO_3 and strong acids or dinitrogen pentoxide.[6] Obviously, under these drastic conditions regioselectivity and functional group tolerance can be problematic. Hence, there is an increasing recent interest to develop more selective nitrations, which work under milder conditions. In this respect, the chemoselective nitration of carbon–boron bonds offers some potential due to the broad availability of arylboronic acid derivatives and their inherent activation.

The first nitration of arylboronic acids by applying $AgNO_3$ or NH_4NO_3 was disclosed by Prakash and Olah *et al.*[7] In their work various nitroarenes were obtained in moderate to excellent yields. However, the necessity to use large amounts of expensive silver salts and additional trimethylsilyl chloride (TMS-Cl) limits the application of this synthetic protocol. In 2005, Saito and Koizumi reported a copper-catalyzed transformation of aryl iodides to nitrobenzenes in moderate to good yields (25–91%).[8] More recently, Buchwald and co-workers disclosed a general and efficient procedure for the palladium-catalyzed conversion of aryl chlorides and related sulfonates to $ArNO_2$ in high yields.[9] Clearly, these processes represent interesting advancements in this field; however, the need for an expensive palladium catalyst, ligands or nitration sources makes further improvements in this area desirable. In this respect, here we report a convenient and efficient procedure for a simple and convenient metal-free nitration of arylboronic acids.

When studying metal-catalyzed nitrations of phenylboronic acid, we were surprised to discover that nitration took place in the presence of an excess of *tert*-butyl nitrite even without any catalyst! In order to investigate this reaction in more detail, we performed the reaction of phenylboronic acid with *tert*-butyl nitrite (10 equiv.) in different solvents (Table 1). Using dioxane at 80 °C nitrobenzene was observed in 64% yield after 7 hours reaction time (Table 1, entry 1). Toluene gave a comparable result (62%; Table 1, entry 2). On the other hand, when the reaction was run in less polar heptane only 22% of nitrobenzene are observed (Table 1, entry 3). DME and CH_3CN as polar solvents were also tested, and the desired product was produced in moderate yields (52% and 36%, respectively) (Table 1, entries 4 and 5). Notably, in alcoholic solvents no nitrobenzene was detected due to oxidative side reactions of the solvent (Table 1, entries 6 and 7). The best yield (88%) is achieved in dioxane by extending the reaction time to 16 hours (Table 1, entry 8). Lowering the amount of *tert*-butyl nitrite to 6 equiv. still gave 73% of nitrobenzene under these conditions (Table 1, entry 9). However, the yield of nitrobenzene declined dramatically when decreasing the reaction temperature to 50 °C (Table 1, entry 10).

Regarding the mechanism, we propose the reaction of phenylboronic acid with alkylnitrite results initially in the formation of nitrosobenzene *via* intra- or intermolecular

Table 1 Nitration of phenylboronic acid[a]



Entry	Solvent [2 ml]	Temp./°C	Time/h	Yield[b] [%]
1	Dioxane	80	7	64
2	Toluene	80	7	62
3	Heptane	80	7	22
4	DME	80	7	52
5	CH_3CN	80	7	36
6	EtOH	80	7	0
7	*n*BuOH	80	7	0
8	Dioxane	80	16	88
9	Dioxane	80	16	73[c]
10	Dioxane	50	16	36

[a] Phenylboronic acid (1 mmol), *tert*-butyl nitrite (10 mmol), solvent (2 ml). [b] Yield was determined by GC using hexadecane as internal standard based on arylboronic acid. [c] *tert*-Butyl nitrite (6 mmol). DME: 1,2-dimethoxyethane.

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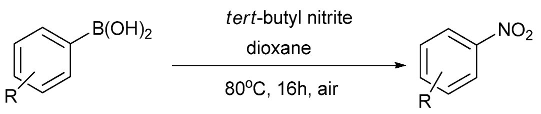
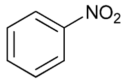
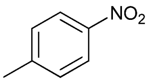
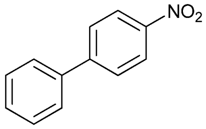
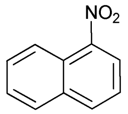
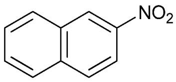
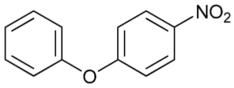
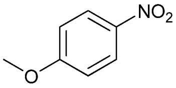
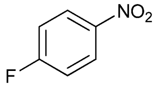
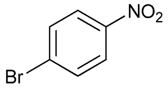
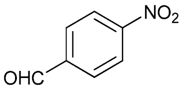
[†] Electronic supplementary information (ESI) available: Experimental procedures, characterization of products and NMR spectrum copy. See DOI: 10.1039/c1cc15484b

Table 2 Nitration of different arylboronic acids[a]



Entry	Nitroarene	Isolated yield [%]
1		87
2		56
3		68
4		75
5		76
6		57
7		62
8		85
9		73[b]
10		45[b]

[a] Arylboronic acid (1 mmol), *tert*-butyl nitrite (10 mmol), dioxane (2 ml), 80 °C, 16 h, air, yield is based on arylboronic acid. [b] $B(OH)_3$ (1 mmol) as additive.

activation of the alkyl nitrite by the boronic acid. Related nitrosations are known for the reaction of arylmetal compounds (metal = Hg, Tl, Pb, Bi) with sodium nitrite in the presence of trifluoroacetic acid.[10] Then, subsequent oxidation to the nitroarene should take place easily at 80°C in the presence of an excess of the alkyl nitrite.[11] With suitable conditions in our hand, we tested the scope and limitations of this novel methodology (Table 2).

Methyl- and phenyl-substituted phenylboronic acids successfully gave the corresponding aromatic nitro compounds in 56% and 68% yield, respectively (Table 2, entries 1 and 2). 2-Nitronaphthalene was synthesized from the parent boronic acid in 76% yield (Table 2, entry 4). In addition, the more sterically demanding 1-naphthaleneboronic acid furnished 1-nitronaphthalene in 75% isolated yield (Table 2, entry 3). More interestingly, functionalized arylboronic acids also gave the desired products smoothly. Hence, 4-phenoxy- and 4-methoxy-functionalized nitrobenzenes were isolated from the corresponding arylboronic acids without any problem in 57–62% yield (Table 2, entries 6 and 7). Furthermore, 1-fluoro- and 1-bromo-4-nitrobenzenes were produced in 85% and 73% successfully from 4-fluoro- and 4-bromophenylboronic acid (Table 2, entries 8 and 9). Finally, 4-nitrobenzaldehyde was synthesized in 45% yield from the corresponding arylboronic acid (Table 2, entry 10). Notably, in the last two reactions the addition of 1 equiv. of boric acid is necessary in order to get satisfying yields. Because of the electron-withdrawing substituents on the arylboronic acid an additional activation of the alkyl nitrite by acid seems necessary.

Unfortunately, so far the nitration protocol does not work by applying vinyl- and hydroxy-decorated phenylboronic acids. Similarly, pyridinyl- and quinolinylboronic acid gave only the deborylation products. On the other hand using 3-thiophenylboronic acid gave 10–15% of the nitro compound without further optimization.

In conclusion, a novel methodology for the nitration of various arylboronic acids has been established. Notably, using inexpensive *tert*-butyl nitrite different nitroarenes are produced in moderate to good yields (45–87%). Advantages of this procedure are the operational simplicity and no need of expensive catalyst systems.

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