

Green and controllable metal-free nitrification and nitration of arylboronic acids

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Abstract

A novel and green nitrating reagent has been developed for the nitrification and nitration of arylboronic acids, which can be controlled by the reaction conditions. The process provides an attractive alternative to the traditional nitration protocols.

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Keywords: Nitrification; Nitration; Arylboronic acids

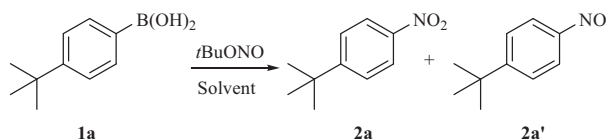
Aromatic nitro compounds are versatile building blocks in organic synthesis [1]. They have also found widespread applications as pharmaceuticals, dyes, and materials [2]. Traditional methods for the synthesis of nitroaromatics are via direct electrophilic aromatic substitution in the presence of mixtures of nitric and sulfuric acid, or dinitrogen pentoxide. However, these methods suffer from issues of arrow functional group compatibility and poor regioselectivity. Further, these nitrating agents are also good oxidants, which lead to oxidation of some substrates. Therefore, the development of a new and safe nitro source in the nitration reaction with a broad substrate scope remains an extremely attractive yet challenging task for organic chemists. In 2000, Prakash and co-workers firstly reported the *ipso*-nitration of arylboronic acids with the combination of ammonium nitrate and trifluoroacetic anhydride as a nitro source [3]. The same group in 2004 made further modifications to the nitration protocol by using inorganic nitrate salt and chlorotrimethylsilane, which acted as a selective and efficient nitrating agent [4]. An interesting copper-catalyzed nitration of aryl iodides and bromides using *n*-Bu₄NNO₂ as a nitrating agent was discovered by Saito's group [5]. In 2009, Buchwald developed an efficient palladation-nitration protocol for the regioselective *ipso*-nitration of aryl chlorides, triflates and nonaflates with more convenient and inexpensive NaNO₂ as a nitrating agent [6]. Very recently, inorganic nitrate or nitrite salts as nitrating agents have been reported on the basis of the metal-catalyzed chelation-assisted C–H bond nitration [7]. Although significant advances were achieved in the transition metal-catalyzed nitration of haloarenes or arenes for the synthesis of nitroarenes, critical issues remains regarding the presence of metal impurities in the final product, which may restrict their practical application.

Therefore, alternative efficient metal-free process for nitration attracts attentions. In 2009, Savinov developed a novel procedure for selective and efficient nitration of phenols using *tert*-butyl nitrite as a nitrating agent [8].

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Table 1

Optimization of nitration of 4-*tert*-butylphenylboronic acid **1a** with *tert*-butyl nitrite.^a

Entry	Solvent	Oxidant	Temp. (°C)	Time (h)	Yield (%) ^b	2a/2a' ^c
1	THF	Air	rt	24	32	28:72
2	CH ₂ Cl ₂	Air	rt	24	54	24:76
3	MeCN	Air	rt	24	78	22:78
4	MeCN	N ₂	rt	24	85	7:93
5	MeCN	H ₂ O ₂	rt	24	36 ^d	–
6	MeCN	O ₂	rt	24	82	30:70
7	MeCN	Air	40	18	80	89:11
8	MeCN	Air	50	12	82	>95:5
9 ^e	MeCN	Air	50	12	83	>95:5
10 ^f	MeCN	Air	50	12	85	>95:5

^a Unless otherwise noted, the reaction conditions are as follows: 4-*tert*-butylphenylboronic acid **1a** (0.5 mmol), *t*BuONO (1.5 equiv.), in anhydrous solvent (2 mL), under open air.

^b Isolated yield.

^c the ratios were determined by GC–MS.

^d Isolated yield of **2a**.

^e *t*BuONO (2 equiv).

^f *t*BuONO (3 equiv).

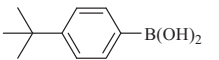
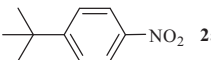
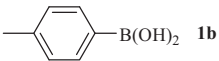
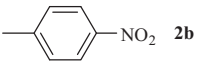

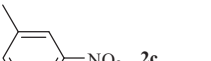


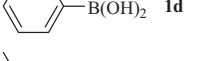
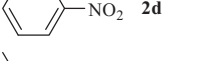
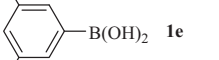
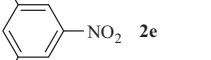
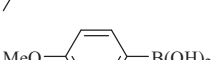
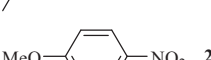

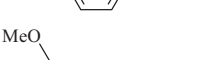
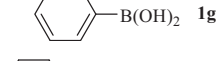
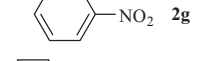
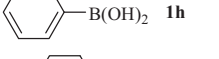
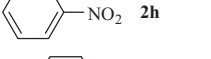
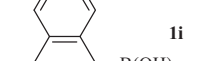
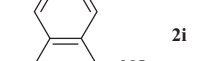
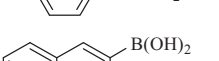
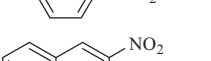
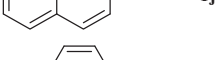
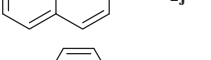
Arylboronic acids have been widely used in organic synthesis for functional group transformations, due to commercial availability and excellent stability to air and moisture [9]. Herein, we report a simple and controllable procedure for nitrification and nitration of arylboronic acids using *tert*-butyl nitrite as a nitrating agent.

On the outset of this investigation, we used 4-*tert*-butylphenylboronic acid **1a** as model substrate with *tert*-butyl nitrite as a nitrating agent to screen suitable reaction conditions. The results were summarized in Table 1. When the reaction was carried out in THF at the room temperature in air, the inspiring result was obtained that the ratio of **2a** and **2a'** is 28–72 detected by GC–MS after 24 h (Table 1, entry 1). Encouraged by this initial result, we proceeded to optimize the reaction conditions. The yields of the reaction significantly increased in CH₂Cl₂ and MeCN, but the ratio of **2a** and **2a'** slightly changed (Table 1, entries 2 and 3). As is well known, nitroso compounds can be easily transferred into nitro compounds under oxidant conditions. Thus, we wanted to obtain single nitration product **2a** or nitrification product **2a'** via controlling the reaction conditions. To our delight, when the reaction was carried out under N₂ at the room temperature in MeCN, nitrification product **2a'** was exclusively obtained with 85% yield (Table 1, entry 4). On the other hand, when H₂O₂ was used as oxidant, the mixture products were detected by GC–Mass, including 4-*tert*-butylphenol, 4-*tert*-butyl-2-nitrophenol and **2a** (Table 1, entry 5). The reaction was carried out under O₂ balloon, affording the mixture products **2a** and **2a'** with 82% yield (Table 1, entry 6). Interestingly, the nitration product **2a** was exclusively obtained with excellent yields by increasing the reaction temperature (Table 1, entries 7 and 8). In addition, the yields of the reaction were slightly improved by increasing the amount of *tert*-butyl nitrite (Table 1, entries 9 and 10).

Because nitroso compounds are poisonous and rarely used in organic synthesis, we only investigated the nitration reactions of a series of arylboronic acids. The results were summarized in Table 2. It was observed that the reaction was marginally affected by electronic effects of the substituents of arylboronic acids. The reaction with electron-donating substituted arylboronic acids proceeded smoothly and afforded the corresponding nitro compounds in good yields (Table 2, entries 1–10). Moreover, it was found that the yields were obviously affected by the steric hindrance of arylboronic acids. The yields of *para*-electron-donating substituted arylboronic acids were higher than that of *ortho*-, *meta*-substituted arylboronic acids (Table 2, entries 2–4). However, the substituted arylboronic acids bearing electron-deficient groups showed lower reactivity (Table 2, entries 11–13). For examples, 1-chloro- and 1-trifluoromethyl-4-nitrobenzenes were obtained with 52% and 26% yields from 4-chloro- and 4-trifluoro- methylphenylboronic acid,

Table 2

Nitration of arylboronic acid **1** with *tert*-butyl nitrite.^a

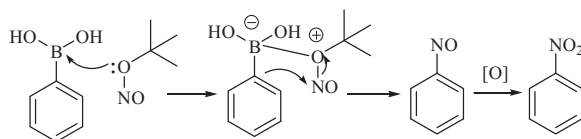
Entry	Arylboronic acids (1)	Nitroaromatics (2)	Yield (%) ^b
1	 1a	 2a	82
2	 1b	 2b	78
3	 1c	 2c	68
4	 1d	 2d	51
5	 1e	 2e	68
6	 1f	 2f	81
7	 1g	 2g	73
8	 1h	 2h	68
9	 1i	 2i	74
10	 1j	 2j	72
11	 1k	 2k	52
12	 1l	 2l	26
13	 1m	 2m	Trace

^a Unless otherwise noted, the reaction conditions are as follows: Arylboronic acid **1a–m** (0.5 mmol), *t*BuONO (1.5 equiv), in anhydrous MeCN (2 mL), under open air, at 50 °C.

^b Isolated yield.

respectively (Table 2, entries 11 and 12). For the nitration of 3-cyano phenylboronic acid, only small amount of the desired product was detected by GC–MS (Table 2, entry 13).

Although the detailed mechanism for this process awaits further investigation, a plausible mechanism for the nitration of arylboronic acid is proposed (Scheme 1). It is likely that there exists a prominent electronic interaction between the boronic acid group and *tert*-butyl nitrite through boron and the oxygen atom due to the high oxophilicity of boron. Next, the migration of phenyl group from tetracoordinated ate complex takes place, and then the N–O bond cleavage affords 1-nitrosobenzene, which is easily transferred into nitrobenzene under oxidant conditions.



Scheme 1. Mechanistic rationale.

In summary, we have developed a green method for the nitration and nitration of arylboronic acids. This environmentally friendly and simple experimental procedure will attract much attention in academic and industrial fields. Further investigation of the detailed mechanism and the scope of substrates is currently underway in our lab.

Acknowledgments

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References

- [1] (a) H. Feuer, T. Nielsen, Nitro compounds: Recent Advances in Synthesis and Chemistry, VCH, New York, 1990;
(b) N. Ono, The Nitro Group in Organic Synthesis, John Wiley-VCH, New York, 2001.
- [2] (a) M. Belciug, V.S. Ananthanarayanan, J. Med. Chem. 37 (1994) 4392;
(b) F.R.F. Fan, Y. Yao, L. Cai, et al. J. Am. Chem. Soc. 126 (2004) 4035.
- [3] S. Salzbrunn, J. Simon, G.K.S. Prakash, et al. Synlett (2000) 1485.
- [4] G.K.S. Prakash, C. Panja, T. Mathew, et al. Org. Lett. 6 (2004) 2205.
- [5] S. Saito, Y. Koizumi, Tetrahedron Lett. 46 (2005) 4715.
- [6] B.P. Fors, S.L. Buchwald, J. Am. Chem. Soc. 131 (2009) 12898.
- [7] (a) Y. Liu, S. Lou, D. Xu, et al. Chem. Eur. J. 16 (2010) 13590;
(b) L. Zhang, Z. Liu, H. Li, et al. Org. Lett. 13 (2011) 4501.
- [8] D. Koley, O.C. Colón, S.N. Savinov, Org. Lett. 11 (2009) 4172.
- [9] N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457.