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A novel route to organonitrites by Pd-catalyzed cross-coupling of sodium nitrite and potassium organotrifluoroborates

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ABSTRACT

Microwave irradiated palladium-catalyzed cross-coupling reaction of potassium styryltrifluoroborates and sodium nitrite gives the corresponding styryl nitrites in high yields. Potassium aryltrifluoroborates also furnish aryl nitrites under same reaction condition. This unprecedented cross-coupling is an interesting development and has the potential to lead to new nitration protocols.

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Potassium organotrifluoroborates are air- and water-stable unique solid compounds. Their use in organic transformations is increasing dramatically.¹ Organonitro compounds, especially, aromatic nitro compounds are important moieties in various pharmaceuticals, dyes, and materials. Instead of using strong acid conditions (HNO₃/H₂SO₄) for nitration which is often poor regioselective, our efforts in developing organonitrite by cross-coupling reaction are exciting and creative. Buchwald's recent report on Pdcatalyzed conversion of aryl chlorides to nitroaromatics^{2a} and Saito's report on Cu-catalyzed coupling of aryl iodides to nitroaromatics^{2b} are pioneering works of cross-coupling chemistry involving potassium and sodium nitrite as coupling partners. Our recent success in constructing direct aroylation reaction by the Pd-catalyzed cross-coupling reactions of potassium organotrifluoroborates with aroyl halides has motivated us to involve in another new form of cross-coupling reaction of metal nitrite with potassium organotrifluoroborates.³ In this work, we report microwave irradiated palladium catalyzed new reaction for the cross-coupling of organotrifluoroborates with sodium nitrite.

This is an interesting development that has potential to lead a new nitration protocol inspiring to the conventional chemistry. Recently, we have applied several Pd-complexes as catalyst for cross-coupling chemistry involving potassium organotrifluoroborates. One of them is $PdCl_2(d^tbpf)_2$ complex and is very effective. To extend further application of this Pd-complex, we scanned it along with many bases and solvents for the cross-coupling of styryltrifluoroborates and sodium nitrite. Key activities compared the effects

* Corresponding author. E-mail address: malmasum@tnstate.edu (M. Al-Masum). of bases and solvents on the formation of aromatic nitro compounds to optimize the reaction condition. The short lists are shown in Table 1. The reaction mixture of styryltrifluoroborate, sodium nitrite, NaH₂PO₄·H₂O, and Pd-complex in toluene is largely in an insoluble state. Since the reaction product was detected relatively clear in toluene, we focused in increasing the solubility of the heterogeneous mixture by adding more toluene and found better results. The optimized condition is shown in Scheme 1. A good number of styryltrifluoroborates were synthesized in the laboratory and used with sodium nitrite for cross-coupling reaction and listed in Figure 1. Styrylnitrite 3a from the cross-coupling of potassium styryltrifluoroborate 1a and sodium nitrite 2 is shown as a representative procedure. 0.25 mmol of styryltrifluoroborate 1a, 69.0 mg (1.0 mmol) of NaNO₂ 2, and 138.0 mg (1.0 mmol) of NaH₂PO₄·H₂O were taken into a microwave reaction vial followed by placing the septum cap. The argon was flushed through the reaction vial by piercing a needle into the septum. The cap was unbolted and 3.0 mg (0.0075 mmol) of PdCl₂(d^tbpf)₂ catalyst was transferred into the reaction vial very quickly and the cap was placed back. The ready to use reaction vial was flushed with argon again for a few seconds. While the toluene bottle was still under argon pressure 5.0 mL of the toluene was added into the reaction mixture via oven dry syringe. The reaction vial was positioned in a microwave device (maximum power setting 250 W) and heated at 120 °C for 30 min. After the reaction is complete, the brown organic layer was pipetted. The remaining solid in the reaction vial was washed with ethyl acetate three times, pipetted, and collected with brown organic layer in a round bottom flask. A small amount of silica gel was added to the round bottom flask. Then the solvent was evaporated. The silica adsorbed reaction product was





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Table 1

Effects of solvents and bases^a

	High Hard Hard Hard Hard Hard Hard Hard Hard			
	1a	2	3a	
Run	Base 4.0 equiv	Solvent 2.0 mL	MW heating	Nitro product 3a
1	K ₂ CO ₃	1,4-Dioxane	140 °C, 40 min	None
2		DMF	140 °C	Trace amount ^b
3		IPA	120 °C	None
4		THF	100 °C	None
5		Toluene	120 °C	None
6		H ₂ O	120 °C	None
7	NaH ₂ PO ₄ ·H ₂ O	1,4-Dioxane	140 °C	None
8		DMF	140 °C	None
9		IPA	120 °C	None
10		THF	100 °C	None
11		Toluene	120 °C	Styrylnitrate ^c
12		H ₂ O	120 °C	None

^a Ratio of **1** and **2** is 1:4.

^b Major product was homocoupling diene (PhCH=CH-CH=CHPh).

^c Clear new peak of cross-coupling nitro product was observed by GC-MS.

BF ₃ K +	3.0 mol % PdC NaNO ₂ NaH ₂ PO ₄ .H ₂ O (7 Toluene (5 2 , 1.0 mmol <i>MW</i> , 120 °C, 5	1.0 mmol) mL), 30 min 3a, 92 %
Method	Amount of Toluene	Nitro Product , 3a
1	1 mL	None
2	2 mL	low yield ^a
3	3 mL	low yield ^a
4	4 mL	25 %
5	5 mL	Majo r ^b

^aGC-MS showed the product but Major product was homocoupling (PhCH=CH-CH=CHPh). ^b92 % isolated cross-coupled styrylnitrite, 3a with trace amount of homocoupling.

Scheme 1. Optimized condition.

subjected to silica gel chromatography using combiflash liquid cartridge for purification.

In the case of 4-fluorostyryltrifluoroborate, **1b** and 4-trifluoromethylstyryltrifluoroborates, **1d** yields of the corresponding styrylnitrites **3b** and **3d** were moderate due to the homocoupling products as side products. In all other cases, a trace amount of homocoupling products was also observed. We explored the formation of aryl nitrites by using aryltrifluoroborates and sodium nitrite under the same reaction conditions. It worked but isolated yields were poor (Fig. 2). 4-Chloro-phenyltrifluoroborate **4c** and 4-pyridinyltrifluoroborate **4e** gave undefined complex mixture instead of the corresponding cross-coupling aryl nitrites. 4trifluoromethylphenyltrifluoroborate **4d** gave the homocoupling product **6** as the major product.

An anion-anion coupling reaction looks like an entirely impossible organic reaction. Most remarkably, however, the Nakamura group⁴ and the Normant group⁵ have proved that the reaction becomes not only experimentally feasible but highly

efficient, when magnesium(II) and zinc(II) atoms are used as countercations. Recent developments by Buchwald,^{2a} Saito,^{2b} and Yamamoto^{2c,d} have provided new directions of the organic transformation.

This dimetallic reaction has a potential value as a quick method to construct a library of various organic derivatives. In this work we provided a new source of making such dimetallic species by Pd-catalyzed cross-coupling of potassium organotrifluoroborates and sodium nitrite (Scheme 2). To further explore the scope of this cogent technology, many new reactions are underway for investigation in our laboratory.

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^aAll styrylnitrites are pure products isolated by using combiflash separation process using combiflash silagel cartridges with hexane/ethyl acetate as mobile phase.

Figure 1. Styrylnitrites from cross-coupling of styryltrifluoroborates and sodium nitrite.^a



Figure 2. Arylnitrites from aryltrifluoroborates and sodium nitrite.^a



Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet. 2012.12.047.

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