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# Facile Synthesis of (*E*)- $\beta$ -Nitroolefinic Alkoxyamines via Silver-Catalyzed Decarboxylative Nitroaminoxylation of Phenylpropionic Acids †

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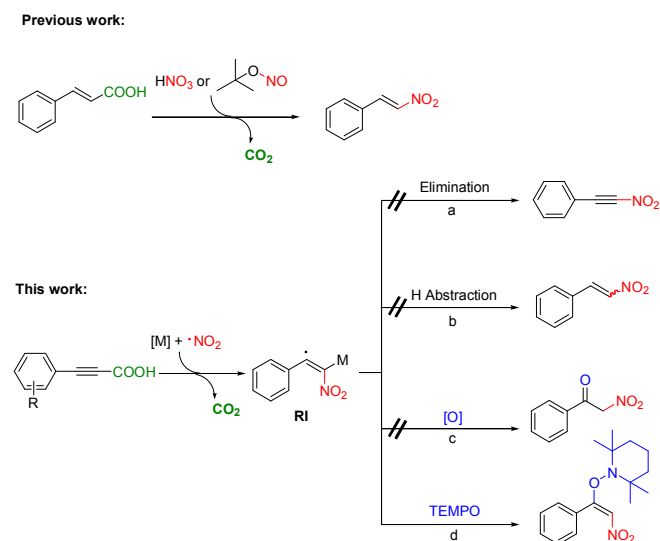
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A novel silver-catalyzed decarboxylative nitroaminoxylation of phenylpropionic acids is described, leading to (*E*)- $\beta$ -nitroolefinic alkoxyamines. The catalyst loading could be decreased to as low as 1 mol % and still shows good efficiency.

The importance of  $\alpha$ ,  $\beta$ -unsaturated nitro compounds in organic synthesis contributes to the prompt development of efficient and stereoselective nitration reactions in mild conditions.<sup>1</sup> As we know that Henry reaction<sup>2</sup> and nitration of olefins<sup>3</sup> are two general methods to prepare  $\alpha$ ,  $\beta$ -unsaturated nitro compounds. In recent years, decarboxylative functionalization attracts a great attention of chemists, due to the easy storability and operability of carboxylic acid and the resulted green byproduct, carbon dioxide, which is environmental friendly.<sup>4</sup> Based on these advantages, our group has made much effort on the various decarboxylative functionalizations of  $\alpha$ ,  $\beta$ -unsaturated carboxylic acid, such as arylation,<sup>5</sup> alkenylation<sup>6</sup> and alkylation.<sup>7</sup> However, few nitrodecarboxylation of  $\alpha$ ,  $\beta$ -unsaturated carboxylic acid was reported.<sup>8</sup> Besides of cinnamic acid, nitrodecarboxylation of propiolic acid seems feasible to form  $\alpha$ ,  $\beta$ -unsaturated nitro compounds as well. We envisage that the nitrodecarboxylation of propiolic acid may go through four path ways. In the initial step, the nitro radical adds to triple bond of propiolic acid in the presence of metal catalyst to form vinyl radical intermediate, **RI** (Figure 1).<sup>4g,7</sup> In path a, (nitroethynyl) benzene will be obtained *via* elimination of **RI**. However, because vinyl radical is highly accessible to H atom abstraction,<sup>9</sup> nitroolefines is more likely obtained as the product (path b). Moreover, the nitroxydation may be also involved in the presence of oxidant<sup>9b,10,11</sup> (path c) or radical scavenger<sup>12-16</sup> (path d). To our delight, we ultimately found that when the reaction was performed within TEMPO, (*E*)- $\beta$ -nitroolefinic

alkoxyamine was formed smoothly. Using TEMPO to trap sp<sup>3</sup> carbon radical center has been well studied in the recent years, but seldom for sp<sup>2</sup> carbon radical center.<sup>16</sup> Here, based on the great interest of decarboxylation of cinnamic acids and alkynyl carboxylic acids in our group, we demonstrated a novel intermolecular silver-catalyzed decarboxylative nitroaminoxylation of phenylpropionic acid.

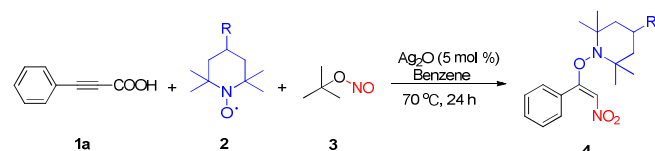


**Figure 1.** Decarboxylative nitration of  $\alpha$ ,  $\beta$ -unsaturated carboxylic acids.

After a series of explorative experiments, the reaction of phenylpropionic acid with TEMPO and *t*-BuONO in the presence of 5 mol% silver oxide in benzene at 70 °C afforded **4a** in 76% yield (Table 1, entry 1). Deviation from these

optimal conditions led to decreasing yields. Application of 4-hydroxyl and 4-acetyl amino TEMPO (entries 2-3) instead of TEMPO didn't form any desired product while 4-acetoxy TEMPO (entry 4) gave the desired product in 73% yield. No reaction occurred without silver salt which plays a key role in the decarboxylation of phenylpropionic acid (entry 5). When  $\text{AgNO}_3$ ,  $\text{Ag}_2\text{CO}_3$  and  $\text{AgOAc}$  were applied instead of TEMPO, **4a** was obtained from 59% to 71% (entries 6-8). Solvents other than benzene proved to be inferior. Using toluene and THF resulted in slight decreasing in the product yield (entries 9-10). No product was detected in alcoholic solvents due to oxidative side reactions of the solvents (entries 11-12). DCE, chloroform, chlorobenzene, cyclohexane and 1,4-dioxane afforded **4a** in moderate yields while acetonitrile gave the product in lower yield (entries 13-18). The reactions performed in DMF or DMSO could not occur (entries 19-20).

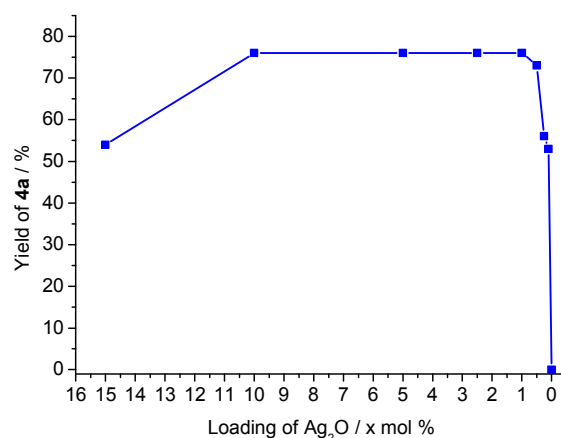
**Table 1.** Optimization of Decarboxylative Nitroaminoxylation of Phenylpropionic Acid<sup>a</sup>



Entry	Deviation from the standard reaction conditions	R	Yield (%)
1	none	H	76
2	none	OH	0
3	none	NHCOCH <sub>3</sub>	0
4	none	OCOCH <sub>3</sub>	73
5	Without Ag <sub>2</sub> O	H	0
	Other silver salts instead of Ag <sub>2</sub> O		
6	10 mol % AgNO <sub>3</sub>	H	59
7	10 mol % Ag <sub>2</sub> CO <sub>3</sub>	H	71
8	10 mol % AgOAc	H	71
	Other solvents instead of benzene	H	
9	toluene	H	71
10	THF	H	73
11	ethanol	H	0
12	propanol	H	0
13	DCE	H	65
14	chloroform	H	65
15	chlorobenzene	H	64
16	cyclohexane	H	61
17	1,4-dioxane	H	59
18	acetonitrile	H	43
19	DMF	H	0
20	DMSO	H	trace

<sup>a</sup> Conditions: phenylpropionic acid (0.3 mmol), TEMPO (1 equiv), *t*-BuONO (2 equiv), silver oxide (5 mol %), benzene (2 mL), 24h.

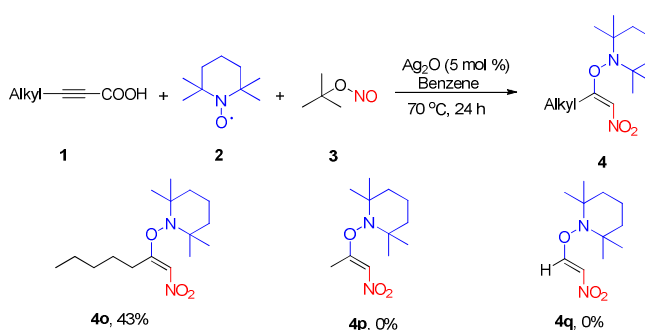
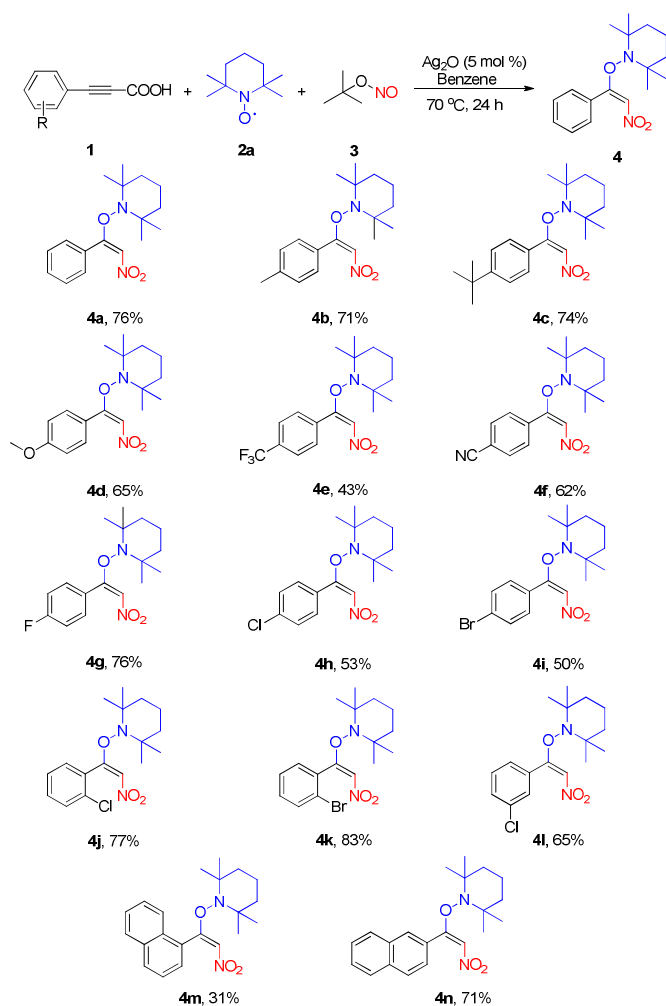
We also found that the loading of silver oxide had significant effect on the yield. The results were plotted in a curve shown in figure 2. Interestingly, both too much and too little loading of silver oxide brought negative influence to the reaction. The yield of **4a** dropped to 54 % when the amount of silver oxide was increased to 15 mol %. It is worth noting that the yield kept at 76% when the loading of silver oxide ranged from 10 mol % to 1 mol %. The reaction with 0.5 mol % silver oxide resulted in slightly decreased yield. However, the yield dropped obviously when 0.25 mol % silver oxide was used. Finally, 0.1 mol % silver oxide gave a similar moderate yield to 0.25 mol % silver oxide.



**Figure 2.** The effect of the loading of the silver catalyst.

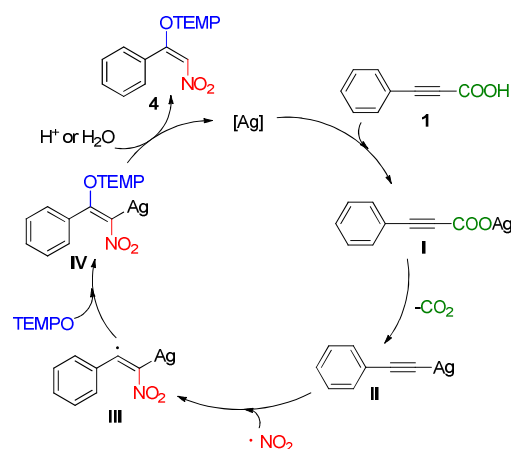
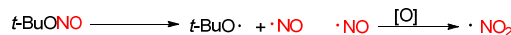
With the optimized conditions in hand, we explored a number of substituted phenylpropionic acids. It was found that 5 mol % silver oxide gave better yields than 1 mol % silver oxide in the process. To our delight, only (*E*)- $\beta$ -nitroolefinic alkoxyamines were isolated in all cases and the results were listed in Scheme 1. 4-Methyl and 4-*tert*-butyl phenylpropionic acids afforded the corresponding nitroaminoxy products **4b** and **4c** in 71% and 74% respectively. 4-Methoxyl phenylpropionic acid was less reactive than them, giving the desired product **4d** in 65% yield. To our delight, reactions of phenylpropionic acids bearing electron-withdrawing groups at the *para*-position of the aryl ring resulted in the moderate to good yields.

**Scheme 1.** Decarboxylative Nitroaminoxylation of Various Arylpropionic Acids.



<sup>a</sup> Conditions: aliphatic alkyne acid (0.3 mmol), TEMPO (1 equiv), *t*-BuONO (2 equiv), silver oxide (5 mol %), benzene (2 mL), 24 h.

To probe the mechanism, the reaction of silver phenylacetylide with *t*-BuONO and TEMPO was performed for just a few hours and **4a** was obtained in 49% yield (see Supporting Information). Based on the literatures and previous studies, a plausible mechanism for the decarboxylative nitroaminoxylation is proposed, as shown in scheme 3. In the initial stage, *tert*-butyl nitrite generates a *tert*-butyl radical and a NO radical which is easily oxidized to the NO<sub>2</sub> radical.<sup>17</sup> Also, reaction of phenylpropionic acid with silver oxide forms silver carbonate **I**. Further decarboxylation of silver carbonate **I** give Ag-acetylide intermediate **II**, which is subsequently attacked by NO<sub>2</sub> radical to generate radical intermediate **III**.<sup>4g-h,7,18</sup> TEMPO traps intermediate **III** to give intermediate **IV**, followed by protonation to give the aminoxylative product **4** and regenerate the silver catalyst.



Scheme 3. Proposed Mechanism.

<sup>a</sup> Conditions: phenylpropionic acid (0.3 mmol), TEMPO (1 equiv), *t*-BuONO (2 equiv), Silver oxide (5 mol %), benzene (2 mL), 24h.

Notably, for the 4-halophenylpropionic acids, the yields decreased according to the sequence of F, Cl, Br (**4g-4l**). Interestingly, reactions of phenylpropionic acids containing halogen atom at the *ortho*-position of the phenyl ring occurred with good yields (**4j**, **4k**). However, 3-chlorophenylpropionic acid was less efficient and the desired product **4l** was obtained in 65% yield. Because of steric factors, 1-naphthylpropionic acid gave the corresponding product **4m** in low yield while 2-naphthylpropionic acid gave the corresponding product **4n** in good yield.

We further examined the aliphatic alkynoic acids. The results were shown in scheme 2. Obviously, long-chain alkyl propionic acid was preferred in our protocol. However, short-chain alkyl propionic acids, like 2-butyneic acid and propionic acid, were not suitable substrates due to low reactivity.

**Scheme 2.** Decarboxylative Nitroaminoxylation of Aliphatic Alkynoic Acids.

## Conclusions

In summary, a simple and efficient silver-catalyzed decarboxylative nitroaminoxylation of phenylpropionic acids has been developed. All the products keep single *trans*-

configuration. The loading of silver oxide is as low as 5 mol % to 1 mol % and the results are good. Further research will continue to explore various decarboxylative difunctionalization of propiolic acids in green catalysis.

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### Notes and references

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† Electronic Supplementary Information (ESI) available. For detailed experimental procedures, characterization data for all new compounds. See DOI: 10.1039/c000000x/

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