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A novel method for bromodecarboxylation of α,β -unsaturated carboxylic acids using catalytic sodium nitrite

Vikas N. Telvekar*, Balaram S. Takale

Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, Matunga, Mumbai 400 019, India

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ABSTRACT

A first novel synthetic utility of catalytic sodium nitrite in combination with aqueous HBr, for bromodecarboxylation of α,β -unsaturated carboxylic acid is described. α,β -Unsaturated carboxylic acid compounds successfully converted into corresponding bromo compounds. The advantages of this protocol are shorter reaction time and moderate to good yields.

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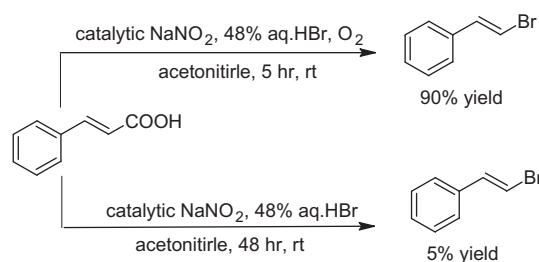
Decarboxylation of α,β -unsaturated carboxylic acids accompanied by simultaneous replacement with halogen is a useful reaction in organic chemistry for the synthesis of halogenated organic substances.¹ There are several methods reported for the decarboxylative bromination by using salt of mercury, lithium, lead and manganese.² Halodecarboxylation has also been reported with trivalent iodine species in combination with *N*-halosuccinimide as a halogen source.³ Although, most of these methods are satisfactory, the use of more complex reagents and sometimes tedious work-up means that there is still scope for alternative reagent systems for decarboxylative bromination.

Our group has been working extensively on the development of novel methodologies under mild conditions. After successfully studying the use of hypervalent iodine reagent,⁴ in bromodecarboxylation of α,β -unsaturated carboxylic acids our next goal was to develop a catalytic process with easily available shelf reagents for bromodecarboxylation. We observed that in the presence of catalytic amount of NaNO_2 and oxygen with 48% aqueous HBr the reaction yielded α,β -unsaturated bromide, providing an interesting route to α,β -unsaturated bromide. NaNO_2 is an easily available shelf reagent and recently used for bromination and iodination of aromatic and alkene compounds.⁵

Reaction of NaNO_2 (1.1 equiv) with cinnamic acid (1.0 equiv) in the presence of 48% HBr (2 equiv) in acetonitrile at room temperature for long reaction time resulted in the formation of poor yield of corresponding (*E*)- α,β -unsaturated bromo compound by decarboxylative reaction. It was observed that under similar reaction con-

ditions but in the presence of oxygen rate of reaction increases with the increase in the yield (Scheme 1). It was also observed that under inert atmospheric conditions (nitrogen atmosphere), no reaction was observed. Further no (*Z*) isomer was isolated from the reaction mixture. To study the effect of the reaction system on (*Z*) isomers, (*Z*)-phenyl-2-propenoic acid was subjected under this reaction condition. After work-up, the crude product was isolated and subjected to NMR analysis: no (*Z*)-1-bromo-2-phenylethylene was observed. After column chromatography, only pure (*E*)-1-bromo-2-phenylethylene was isolated.

Further screening of the reaction conditions revealed that 0.05 equiv of NaNO_2 is sufficient to carry out reaction. We also examined other halogen source like HCl and HI, to obtain the corresponding α,β -unsaturated halides. No reaction was observed when a combination of NaNO_2 and HCl was used, while the combination of NaNO_2 and HI resulted in the isolation of an unidentified compound. No reactions were observed when 48% HBr was replaced by tetraethylammonium bromide and *N*-bromo-succinimide as bromine sources.

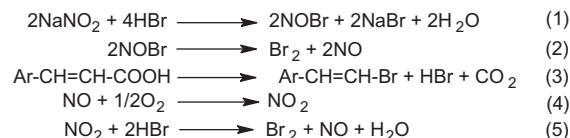


Scheme 1. Formation of α,β -unsaturated bromide using NaNO_2 .

* Corresponding author. Tel.: +91 22 24145616; fax: +91 22 24145614.

E-mail address: vikastelvekar@rediffmail.com (V.N. Telvekar).

As part of our studies on the development of novel methodology, herein we now describe a new approach of direct oxidative bromodecarboxylation of α,β -unsaturated acids under mild conditions using NaNO_2 .⁶ In order to evaluate the scope of this method, these conditions were applied to various α,β -unsaturated carboxylic acids and the results are presented in Table 1. It is clearly indicated that in the absence of double bond the reaction does not take place (Table 1, entry 15). α,β -Unsaturated carboxylic acids substituted with electron donating and electron withdrawing groups are suitable for this transformation (Table 1, entries 2–7). With the same reaction system, heterocyclic α,β -unsaturated carboxylic acids such as 3-(2-furyl)acrylic acid also gave good yields of the corresponding brominated products (Table 1, entries 8 and 9). α Substituted α,β -unsaturated acids also undergo this transfor-



Scheme 2. Plausible mechanism of bromodecarboxylation.

mation without affecting the yields (Table 1, entries 11 and 12). A lower reaction rate was observed with aliphatic α,β -unsaturated acids (Table 1, entries 13 and 14)

A plausible reaction mechanism for bromodecarboxylation is proposed in Scheme 2.

Table 1
Bromodecarboxylation of α,β -unsaturated carboxylic acid by using catalytic NaNO_2 and 48% aqueous HBr^a

Entry	Substrate	Product	Time (h)	% Yield ^b
1			5	90
2			4	90
3			5	91
4			4	90
5			5	92
6			5	90
7			5	90
8			4	89
9			4	88
10			4	90
11			5	90
12			5	90
13			6	87
14			6	87
15		—	48	NR ^c

^a Reaction conditions: carboxylic acid (1 equiv), NaNO_2 (0.05 equiv) and 48% HBr (2 equiv) in acetonitrile.

^b Isolated yields after column chromatography and structures were confirmed by comparison of IR and ¹H NMR with authentic materials.

^c NR: no reaction.

In conclusion, a new reaction system using catalytic NaNO_2 in combination with aqueous HBr in the presence of oxygen has been developed, which is capable of converting various α,β -unsaturated carboxylic acids into corresponding bromo compounds, at room temperature.

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6. *Representative procedure for bromodecarboxylation of α,β -unsaturated carboxylic acid* (Table 1, entry 1): In a stirred solution of cinnamic acid (0.3 gm, 2.0 mmol) in freshly distilled acetonitrile (10 mL) 48% aqueous solution of HBr (4.0 mmol) was added. To this reaction mixture was added aqueous solution of NaNO_2 (20 mL, 2.5 M). The flask was immediately covered with an air filled balloon (1 L) and the stirring was continued at room temperature. After completion of the reaction (TLC), CHCl_3 (10 mL) was added. The organic layer was separated and washed with aqueous solution of NaHCO_3 (2×20 mL), followed by water (3×20 mL), finally dried over anhyd Na_2SO_4 and was concentrated in vacuum. The remaining residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 9:1) to yield pure bromostyrene.