Tetrahedron Letters 52 (2011) 2394–2396

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

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

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ARTICLE INFO

Article history:
Received 30 December 2010
Revised 22 February 2011
Accepted 23 February 2011
Available online 12 March 2011

Keywords:
Sodium nitrite
α,β-Unsaturated carboxylic acids
Oxidation
Bromodecarboxylation

ABSTRACT

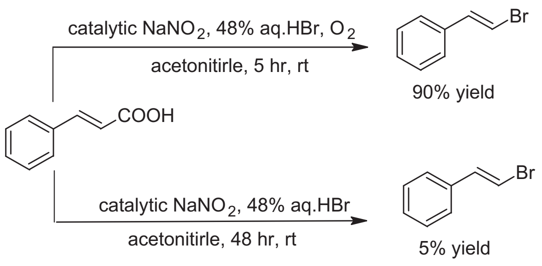
A first novel synthetic utility of catalytic sodium nitrite in combination with aqueous HBr, for bromo decarboxylation of α,β-unsaturated carboxylic acid is described. α,β-Unsaturated carboxylic acid compounds successfully converted into corresponding bromo compounds. The advantages of this protocol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

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 conditions 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-succinamide as bromine sources.



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

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doi:10.1016/j.tetlet.2011.02.101

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 transformation 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)

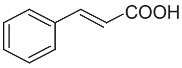
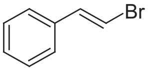
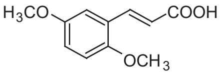
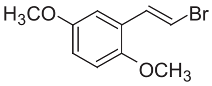
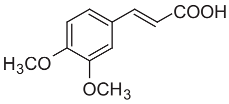
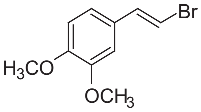
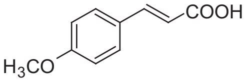
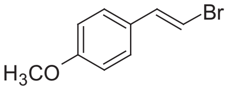
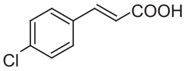
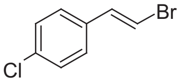
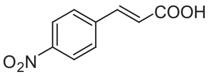
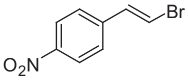
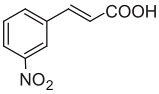
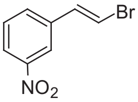
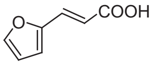
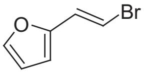
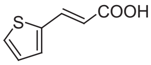
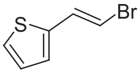
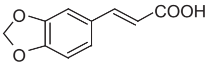
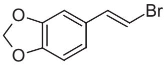
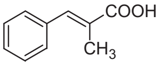
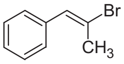
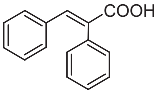
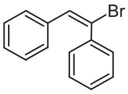
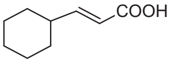
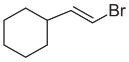
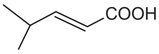
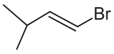
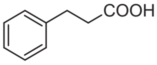
A plausible reaction mechanism for bromodecarboxylation is proposed in Scheme 2.

$$
\begin{aligned}
2NaNO_2 + 4HBr &\longrightarrow 2NOBr + 2NaBr + 2H_2O && (1)\\
2NOBr &\longrightarrow Br_2 + 2NO && (2)\\
\text{Ar-CH=CH-COOH} &\longrightarrow \text{Ar-CH=CH-Br} + HBr + CO_2 && (3)\\
NO + 1/2O_2 &\longrightarrow NO_2 && (4)\\
NO_2 + 2HBr &\longrightarrow Br_2 + NO + H_2O && (5)
\end{aligned}
$$

Scheme 2. Plausible mechanism of bromodecarboxylation.

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.

Acknowledgements

B.S.T. is grateful to the CSIR India for providing JRF and V.N.T. to DST India for the financial support under SERC Fast Track Young Scientists Scheme.

References and notes

1. Hunsdiecker, C. H. *Ber. Dtsch. Chem. Ges. B* **1942**, *75*, 291.
2. (a) Cristol, S.; Firth, W. *J. Org. Chem.* **1961**, *26*, 280; (b) Naskar, D.; Roy, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2435–2436; (c) Sheldon, R.; Kochi, J. *Org. React.* **1972**, *19*, 275–278.
3. (a) Das, J. P.; Roy, S. *J. Org. Chem.* **2002**, *67*, 7861; (b) Graven, A.; Jorgensen, K. A.; Dahl, S.; Stanczak, A. *J. Org. Chem.* **1994**, *59*, 3543.
4. (a) Telvekar, V. N.; Chettiar, S. N. *Tetrahedron Lett.* **2007**, *48*, 4529; (b) Telvekar, V. N.; Arote, N. D.; Herlekar, O. P. *Synlett* **2005**, 2495.
5. (a) Podgorsek, A.; Eissen, M.; Fleckenstein, J.; Stavber, S.; Zupan, M.; Iskra, J. *Green Chem.* **2009**, *11*, 120; (b) Zhang, G. F.; Liu, R. H.; Xu, Q.; Ma, L. X.; Liang, X. M. *Adv. Synth. Catal.* **2006**, *348*, 862; (c) Iskra, J.; Stavber, S.; Zupan, M. *Tetrahedron Lett.* **2008**, *49*, 893.
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.