

## Notes

# The First Example of a Catalytic Hunsdiecker Reaction: Synthesis of $\beta$ -Halostyrenes<sup>†</sup>

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The halodecarboxylation of metal carboxylates with molecular bromine, commonly known as the Hunsdiecker reaction, is an extremely useful methodology in the armory of an organic chemist for the synthesis of halo-genated organic substrates.<sup>1</sup> The efficacy of the reaction has been improvised by several groups<sup>2</sup> to include carboxylates of Hg(II), Tl(I), and Pb(IV) besides the original Ag(I) of Hunsdiecker. In its present version, a modified Hunsdiecker reaction can successfully accommodate aliphatic (1°, 2°, and 3°) and, to some extent, aromatic carboxylic acids; however, major limitations include (a) the necessity of high temperature; (b) very poor yields in cases of substrates such as  $\alpha,\beta$ -unsaturated carboxylic acids;<sup>3</sup> (c) the toxicity/hazard inherent with molecular bromine and salts of mercury, thallium, lead, and silver; and (d) the stringent ex-situ protocol of isolating and purifying carboxylates in certain cases. Furthermore, the art has not, heretofore, suggested or taught a reagent system that is capable of mediating the Hunsdiecker reaction in a catalytic fashion.<sup>4</sup> The ever-increasing consciousness among organic chemists toward atom economy<sup>5</sup> and our own interest<sup>6</sup> in “naked-metal catalysts” prompted us to investigate this problem. We disclose in this report an efficient catalytic protocol for the synthesis of  $\beta$ -halostyrenes from corresponding  $\alpha,\beta$ -unsaturated carboxylic acids and *N*-halosuccinimide using lithium acetate as catalyst.

Reactions of various  $\alpha,\beta$ -unsaturated carboxylic acids **1** with NBS and catalytic LiOAc in acetonitrile–water at ambient temperature afford the corresponding bromoalkenes **2** in good to excellent yields (eq 1, Table 1).

<sup>†</sup> Dedicated to Prof. Animesh Chakravorty on the occasion of his 60th birthday.

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(5) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259.

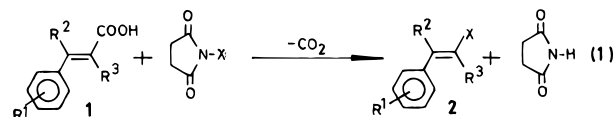
(6) Chowdhury, S.; Samuel, P. M.; Das, I.; Roy, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1993.

Table 1. LiOAc-Catalyzed Halodecarboxylation of  $\alpha,\beta$ -Unsaturated Carboxylic Acids **1** to Haloalkenes **2** with *N*-Halosuccinimide<sup>a</sup>

entry	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	X	time (h)	yield (%) <sup>b</sup>
1	H	H	H	Br	4	61
2				Cl	12	55
3	4-OMe	H	H	Br	0.2	91
4				Cl	6	65
5				I	2	58
6	4-Me	H	H	Br	2	86
7 <sup>c</sup>	4-OMe	H	Me	Br	0.5	92
8 <sup>d</sup>	H	Me	H	Br	1	88
9	4-Cl	H	H	Br	6	41
10				Cl	15	37

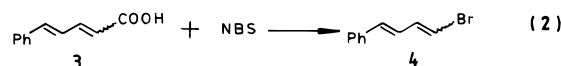
<sup>a</sup> Unless otherwise stated, the isomeric purity of the *trans* acids and corresponding (*E*)-haloalkenes is >97% (vide <sup>1</sup>H NMR).

<sup>b</sup> Refers to isolated yields. <sup>c</sup> Halide *E:Z* = 30:70. <sup>d</sup> Acid *t:c* = 87:13; halide *E:Z* = 82:18.



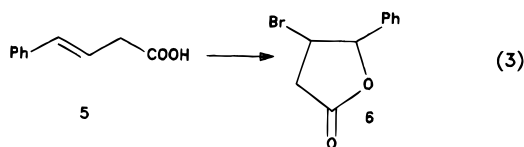
The other products identified are CO<sub>2</sub> (ex-situ precipitation with Ba(OH)<sub>2</sub>) and succinimide (GC, NMR). Reduced reaction time and higher yields of products are particularly noteworthy for acids bearing electron-donating substituents either in the aromatic ring or in the alkene appendage (entries 3, 6–8) as compared to one having an electron-withdrawing group (entry 9). Uncatalyzed reaction, on the other hand, shows only 5–11% conversion. An added feature of these reactions is the moderate to good degree of stereospecificity; *trans*-cinnamic acids give rise to the corresponding (*E*)-bromoalkenes as the major product.

The present methodology has been further extended to the analogous dienoid acid **3**, which affords the corresponding bromide **4** in 60% isolated yield (eq 2).



To gain further insight, various independent experiments have been conducted, the results of which are presented below: (a) while the reactions can be catalyzed by NaOAc, KOAc, and even CsOAc, the rates and product yields are better with LiOAc; (b) analogous chloro- and iododecarboxylations using NCS and NIS can be carried out (entries 2, 4, 5, 10), the yield optimization being in progress; and (c) the nitron trapping experiment indicates a dominance of the ionic pathway over the radical route.

In the mechanistic front, the major question to be addressed is, “What triggers the elimination of carbon dioxide?” Mechanisms that require further investigations are (a) an acetate ion-promoted direct halodecarboxylation pathway and (b) carbon dioxide elimination from an intermediate  $\alpha$ -halo- $\beta$ -lactone. The latter mechanism gains partial support from the results of the reaction of 3-phenyl-but-2-eneoic acid (**5**), wherein we could isolate the analogous  $\beta$ -halo- $\gamma$ -lactone **6** in 85% yield (eq 3). Compound **6** was fully characterized by X-ray crystallography.



In summary, we have shown that facile halodecarboxylation of  $\alpha,\beta$ -unsaturated carboxylic acids can be carried out under catalytic conditions, thus further widening the scope of the classical Hunsdiecker reaction.

### Experimental Section

**Materials.** Substituted *trans*-cinnamic acids were either purchased (Aldrich, E-Merck) or synthesized via their esters; the latter were obtained by a two-carbon Wittig protocol from the corresponding aromatic aldehydes.

**General Procedure.**  $\alpha,\beta$ -Unsaturated carboxylic acid **1** (2 mM) was added to a solution of LiOAc (0.2 mM) in 4.5 mL of MeCN–H<sub>2</sub>O (97:3 v/v). After the mixture was stirred for 5 min at room temperature, *N*-halosuccinimide (2.1 mM) was added

as a solid. The progress of the reaction was monitored by TLC (silica gel, *n*-hexane–ethyl acetate 3:2). Usual workup by flash chromatography (silica gel, *n*-hexane) afforded the haloalkene **2**. All products were fully characterized by <sup>1</sup>H NMR (200 MHz), MS (EI, 70 eV), and comparison with authentic sample, wherever possible.

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**Supporting Information Available:** <sup>1</sup>H NMR and mass spectra of haloalkenes **2** (entries 1, 3, 7), **5**, and **6**, <sup>1</sup>H NMR spectra of **2** (entries 2, 5, 6, 8, 9), UV spectra of **5**, and ORTEP diagram of **6** (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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