Mild and Efficient Method for Decarboxylative Bromination of α,β-Unsaturated Carboxylic Acids with Dess–Martin Periodinane

Vikas N. Telvekar,* Nitin D. Arote, Omkar P. Herlekar

Department of Pharmaceutical Sciences and Technology, University Institute of Chemical Technology, Matunga, Mumbai 400019, India
Fax +91(22)24145614; E-mail: vikastelvekar@rediffmail.com

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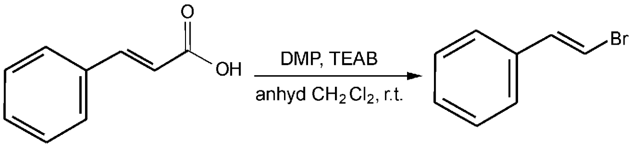
Abstract: A simple and mild method for decarboxylative bromination of α,β-unsaturated carboxylic acids has been developed using Dess–Martin Periodinane (DMP) in combination with tetraethylammonium bromide (TEAB) at room temperature. High yields of the corresponding bromoalkenes were obtained.

Key words: Dess–Martin periodinane, tetraethylammonium bromide , decaboxylation, bromoalkenes

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] The original method of halodecarboxylation, known as the Hunsdiecker reaction, involves the reaction of a silver salt of a carboxylic acid with bromine as a halogen source. The classical Hunsdiecker reaction has been modified and developed with particular attention paid to green chemistry aspects,[2,3] operation under additive free conditions,[4] as well as catalysis using salts of mercury,[5] lithium,[6] lead,[7] manganase,[8] or tetraalkylammonium salts.[9] Tokuda and co-workers have reported a microwave-assisted reaction in the presence of metal salts.[10] Halodecarboxylation has also been reported with trivalent iodine species in combination with *N*-halosuccinimide as a halogen source.[11,12] 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.

Hypervalent iodine reagents and reagent systems have found widespread application in organic synthesis because of their selectivity and simplicity of use. Ever since the innovative work by Dess and Martin, explorations into the chemistry of hypervalent iodine compounds have become the subject of growing interest due to their mild nature. Our group has been working extensively on the development of novel methodologies under mild reaction conditions using the petavalent iodine reagent *o*-iodoxy benzoic acid (IBX).[13] Herein, we report our results on decarboxylative brominatiom of α,β-unsaturated carboxylic acids using DMP in combination with TEAB at room temperature.

For our initial studies, cinnamic acid was chosen as substrate and the reaction with DMP in combination with TEAB was performed. A mixture of cinnamic acid (1.0 mmol), DMP and TEAB (1.1 mmol) in anhydrous dichloromethane was stirred at room temperature. It was observed that the starting material was consumed within 15 minutes as indicated by TLC analysis. After work-up and purification by silica gel column chromatography (hexane–EtOAc, 9:1), bromostyrene was isolated in 94% yield (Scheme 1).



Scheme 1 Bromo-decarboxylation of cinnamic acid using DMP and TEAB

Encouraged by these results further development work was undertaken. A variety of α,β-unsaturated aromatic carboxylic acids were subjected to the reaction conditions,[14] and the results are presented in the Table 1.

The results presented in Table 1 clearly indicate that α,β-unsaturated carboxylic acids substituted with electron donating groups like methyl or methoxy undergo very fast oxidative bromo-decarboxylation (Table 1, entries 2, 3) in a short reaction time and good yields. On the other hand, if the aromatic ring is substituted with an electron withdrawing group such as nitro, or chloro, comparatively lower yields and slower reaction rates are observed (Table 1, entries 4–8).

With the same reagent system heterocyclic α,β-unsaturated carboxylic acids such as 3-(2-furyl)acrylic acid also gave good yields of the corresponding brominated product (Table 1, entry 10). Some aliphatic α,β-unsaturated acids were also subjected to these conditions; crotonic acid (Table 1, entry 11) and 3,3-dimethylacrylic acid (Table 1, entry 12) were converted to the corresponding bromo compounds in 30 minutes.

In summary a novel method has been developed for decarboxylative bromination with DMP in combination with TEAB in anhydrous dichloromethane at room temperature. The method developed is mild and gave good to excellent yields of bromoalkenes for both aliphatic as well as aromatic substrates.

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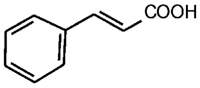
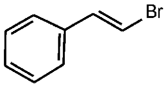
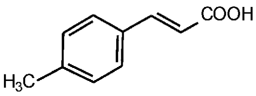
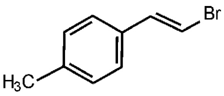
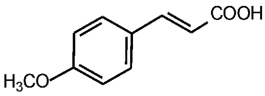
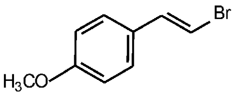
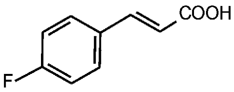
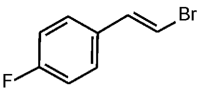
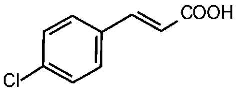
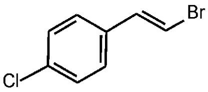
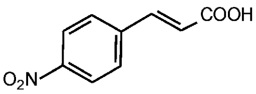
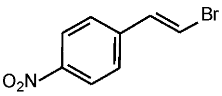
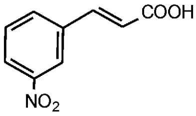
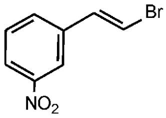
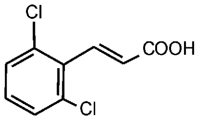
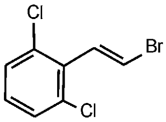
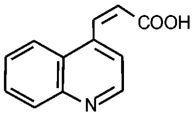
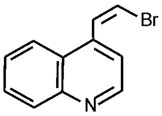
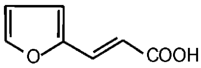
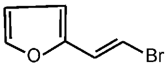
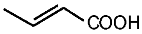
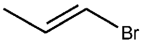
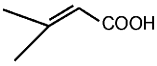
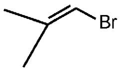
Table 1 Bromo-decarboxylation Using DMP and TEAB[a]

Entry	Substrate[b]	Product	Time (h)	Yield (%)[c]
1			0.25	94
2			0.25	90
3			0.25	92
4			12	68
5			12	72
6			14	65
7			16	65
8			15	70
9			12	72
10			0.25	92
11			0.50	78
12			0.50	82

[a] Reaction conditions: substrate (1.0 equiv), DMP (1.1 equiv), TEAB (1.1 equiv), anhyd CH_2Cl_2, r.t.

[b] Starting compounds were prepared by standard literature procedures.

[c] Isolated yields after column chromatography. Structures confirmed by comparison of the IR and ^{1}H NMR spectra with those of authentic materials.

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(14) **General experimental procedure:** To a stirred suspension of DMP (1.1 equiv) in anhyd CH_2Cl_2 (15 mL) was added TEAB (1.1 equiv) in one portion. The resultant mixture was stirred r.t. for 5 min followed by addition of α,β-unsaturated carboxylic acid (1.0 equiv) and stirring was continued at r.t. until the starting material had been completely consumed (TLC). The reaction mixture was diluted with CH_2Cl_2 and washed successively with 10% aq sodium bisulfite solution (2 × 15 mL), 10% $NaHCO_3$ (2 × 15 mL), H_2O (1 × 10 mL), and brine (1 × 10 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue obtained was purified by silica gel column chromatography (10% EtOAc–hexane) to afford pure bromoalkenes.