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A novel system for decarboxylative bromination

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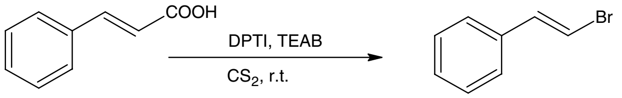
Abstract—A simple and mild method for decarboxylative bromination of α,β-unsaturated carboxylic acids has been developed using diphosphorus tetraiodide in combination with tetraethylammonium bromide (TEAB) at room temperature. High yields of the corresponding bromoalkenes were obtained.

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 the carboxylic acid with bromine as a halogen source. The classical 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 salt of mercury,[5] lithium,[6] lead,[7] manganese,[8] or tetraalkylammonium salts.[9] Tokuda and co-workers 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.

Iodine and iodine reagent systems have found widespread application in organic synthesis because of their selectivity and simplicity of use. Our group has been working extensively on the development of novel methodologies under mild reaction conditions using various iodine reagents.[13]

Diphosphorus tetraiodide is an orange crystalline solid, and commercially available. It exhibits a high affinity for oxygen and acts as a unique reagent able to promote substitution of alcohols to form alkyl iodides,[14] dehydration of aldoximes to nitriles,[15] and reduction reactions.[16]

While working on decarboxylative bromination, we observed that this reagent can be used in combination with TEAB at room temperature for decarboxylative bromination of α,β-unsaturated carboxylic acids. For our initial studies, cinnamic acid was reacted with diphosphorus tetraiodide in combination with TEAB. A mixture of cinnamic acid (1.0 mmol), diphosphorus tetraiodide, and TEAB (1.1 mmol) in anhydrous carbon disulfide was stirred at room temperature. The starting material was consumed within 9 h as indicated by TLC analysis. After work-up and purification by silica gel column chromatography (hexane–EtOAc, 9:1), (*E*)-1-bromo-2-phenylethylene was isolated in 90% yield (Scheme 1). The reactions were carried out in anhydrous chloroform or acetonitrile. We also examined other halogen source like tetraethylammonium chloride (TEAC) and tetraethylammonium iodide (TEAI), to obtain the corresponding α,β-unsaturated halides. No reaction was observed when a combination of P_2I_4 and TEAC



Scheme 1. Bromo-decarboxylation of cinnamic acid using DPTI and TEAB.

Keywords: Diphosphorus tetraiodide; Tertaethylammonium bromide; Decarboxylation; Bromoalkenes.

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Table 1. Bromo-decarboxylation using DPTI and TEAB[a]

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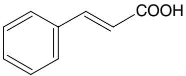
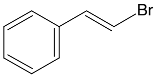
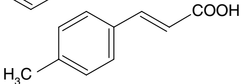
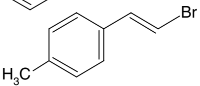
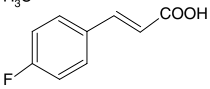
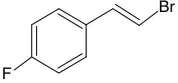
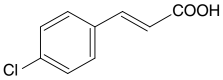
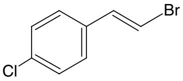
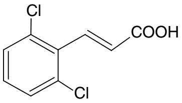
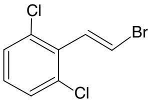
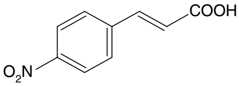
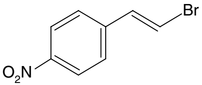
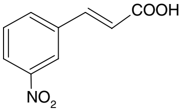
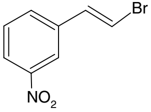
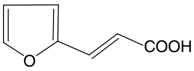
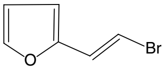
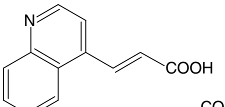
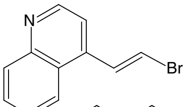
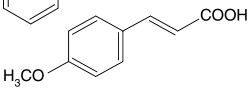
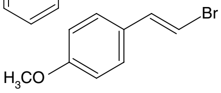
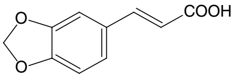
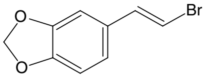
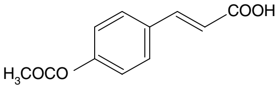
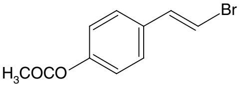
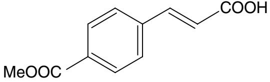
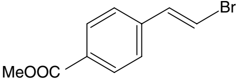
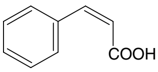
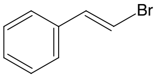
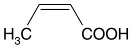
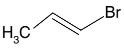
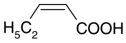
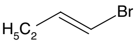
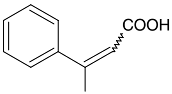
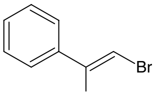
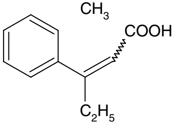
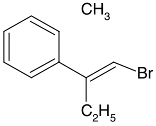
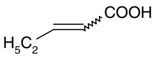
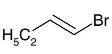
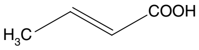
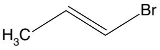
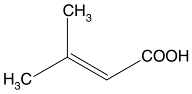
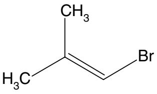
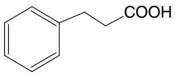
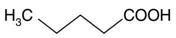
1			9	90
2			7	93
3			12	80
4			12	85
5			14	80
6			12	85
7			14	80
8			8	88
9			8	88
10			6	90
11			6	90
12			8	85
13			10	85
14			9	90
15			12	90
16			12	92
17			8	85
18			8	85
19			12	90
20			12	86
21			12	88

Table 1 (*continued*)

Entry	Substrate[b]	Product	Time (h)	Yield[c] (%)
22		—	15	NR[d]
23		—	15	NR[d]

[a] The reaction conditions: substrate (1.0 equiv), diphosphorous tetraiodide (1.1 equiv), TEAB (1.1 equiv), anhyd CS_2, rt.

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

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

[d] No reaction.

was used. The combination of P_2I_4 and TEAI resulted in the isolation of an unidentified complex compound.

Encouraged by these results, a variety of α,β-unsaturated aromatic and aliphatic carboxylic acids were subjected to the reaction conditions,[17] and the results are presented in Table 1 clearly indicating that in the absence of double bond reaction does not take place (Table 1, entries 21, 22). α,β-Unsaturated carboxylic acids substituted with electron donating groups like methyl, undergo oxidative bromo-decarboxylation (Table 1, entry 2) in a short reaction time and in good yields. On the other hand, if the aromatic ring is substituted with an electron-withdrawing group such as fluoro, nitro, or chloro, comparatively lower yields and slower reaction rates were observed (Table 1, entries 3–7).

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 products (Table 1, entries 8, 9). A lower reaction rate was observed with aliphatic α,β-unsaturated acids: crotonic acid (Table 1, entry 20) and 3,3-dimethylacrylic acid (Table 1, entry 21).

A wide range of functional groups were tolerated by this protocol, and under these reaction conditions, methoxy, acetoxy, and ester groups were stable (Table 1, entries 10–13).

To study the effect of the reaction system on isomers, (*Z*)-phenyl-2-propenoic acid was examined. After work-up, the crude product was isolated and subjected to NMR analysis: no (*Z*)-1-bromo-2-phenylethylene was observed. After column chromatography, pure (*E*)-1-bromo-2-phenylethylene was isolated (Table 1, entry 14). Similarly (*Z*)-2-butenoic acid and (*Z*)-2-pentenoic acid were converted into (*E*)-1-bromo-1-propene and (*E*)-1-bromo-1-butene, respectively (Table 1, entries 15, 16). Further, a mixture of (*E*/*Z*)-3-phenyl-2-butenoic acid, (*E*/*Z*)-3-phenyl-2-pentenoic acid, and (*E*/*Z*)-2-pentenoic acid were converted into (*E*)-1-bromo-2-phenyl-1-propene, (*E*)-1-bromo-2-phenyl-1-butene, and (*E*)-1-bromo-1-butene respectively (Table 1, entries 17, 18, 19). Thus it is concluded that in case of (*Z*)-α,β-unsaturated carboxylic acids, inversion of configuration occurred, while in case of (*E*)-α,β-unsaturated carboxylic acids there was retention of configuration (Table 1, entries 1–13, 20, 21).

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

Acknowledgment

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References and notes

1. Hunsdiecker, C. H. *Ber. Disch. Chem. Ges. B* **1942**, *75*, 291–295.
2. Sinha, J.; Layek, S.; Mandal, G. C.; Bhattacharjee, M. *Chem. Commun.* **2001**, 1916–1917.
3. Roy, S. C.; Guin, C.; Maiti, G. *Tetrahedron Lett.* **2001**, *42*, 9253–9256, and references cited therein.
4. Homsi, F.; Rousseau, G. *J. Org. Chem.* **1999**, *64*, 81–85.
5. Cristol, S. J.; Firth, W. C., Jr. *J. Org. Chem.* **1961**, *26*, 280.
6. Naskar, D.; Roy, S. *J.Chem. Soc., Perkin Trans. 1* **1999**, *17*, 2435–2436.
7. Sheldon, R. A.; Kochi, J. K. *Org. React.* **1972**, *19*, 275–278.
8. Chowdhary, S.; Roy, S. *Tetrahedron Lett.* **1996**, *37*, 2623–2624.
9. Naskar, D.; Roy, S. *Tetrahedron* **2000**, *56*, 1369–1377.
10. Kuang, C.; Senboku, H.; Tokuda, M. *Synlett* **2000**, 1439–1442.
11. Das, J. P.; Roy, S. *J. Org. Chem.* **2002**, *67*, 7861–7864, and references cited therein.
12. Graven, A.; Jorgensen, K. A.; Dahi, S.; Stanczak, A. *J. Org. Chem.* **1994**, *59*, 3543–3546.
13. Telvekar, V. N.; Arote, N. D.; Herlekar, O. P. *Synlett* **2005**, 2495–2497.
14. Lauwers, M.; Regnier, B.; Van Eenoo, M.; Denis, J. N.; Krief, A. *Tetrahedon Lett.* **1979**, 1801–1804.
15. Suzuki, H.; Fuchita, T.; Iwasa, A.; Mishina, T. *Synthesis* **1978**, 905–907.

16. Newkome, G. R.; Sauer, J. D.; Erbland, M. L. *Chem. Commun.* **1975**, 885–886.
17. *General experimental procedure*: To a stirred suspension of TEAB (1.1 equiv) in anhyd CS_2 (15 mL) was added α,β-unsaturated carboxylic acid (1.0 equiv). The resultant mixture was stirred rt for 2 min followed by addition of diphosphorus tetraiodide (1.1 equiv) and stirring was continued at rt until the starting material had been completely consumed (TLC). The reaction mixture was diluted with CS_2 and washed successively with 10% aq sodium bisulfite solution (2 × 15 mL), 10% aq $NaHCO_3$ (2 × 15 mL), H_2O (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.