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Novel System for Decarboxylative Bromination of α,β-Unsaturated Carboxylic Acids with Diacetoxyiodobenzene

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A simple and mild method for the conversion of varieties of α,β-unsaturated carboxylic acids to the corresponding bromoalkenes using diacetoxyiodobenzene (IBD) in combination with tetraethyl-ammonium bromide (TEAB) at room temperature is discussed. Advantages of this system are short reaction time, easy work up and gave good to excellent yields.

Key words diacetoxyiodobenzene; α,β-unsaturated carboxylic acid; tetraethyl-ammonium bromide; bromoalkene

Halodecarboxylation of the corresponding carboxylic acid is widely used to obtain bromides. Decarboxylation of α,β-unsaturated carboxylic acids accompanied by simultaneous replacement with halogen is a useful reaction in organic chemistry for synthesis of halogenated organic substances. However, this reaction requires a heavy metal salt and high reaction temperature, which restricts its application.[1)] Besides, the classical Hunsdiecker reaction which is very inefficient for cinnamic acid analogs, for example, the bromodecarboxylation of cinnamic acids under classical conditions gives the desired product in less than 15% yield.[2)] It is therefore infeasible to synthesize vinyl bromide *via* this approach. Thereafter, several attempts to improve the Hunsdiecker reaction to convert cinnamic acids to corresponding bromide were made with various reagents and conditions. However, salt or certain equipments such as microwave reactor is still needed.[3)] The classical Hunsdiecker reaction has been modified and developed with particular attention paid to green chemistry aspects.[4,5)] Tokuda *et al.* reported a microwave-assisted reaction in the presence of metal salts.[6)] Halodecarboxylation also reported with trivalent iodine species in combination with *N*-halosuccinimide as a halogen source.[7,8)]

Hypervalent iodine compounds are extensively used for a variety of chemical transformations and particularly as oxidative reagents because of their selectivity and simplicity of use. Ever since the innovative work by Telvekar *et al.*[9)] Explorations into the chemistry of hypervalent iodine compounds became the subject of growing interest due to their mild nature.[10—12)] Although there are practical approaches for converting cinnamic acids to β-bromostyrene, the methods developed to date have drawbacks *viz.* requirement for multiple steps, complex or dangerous reagents like diphosphorus tetraiodide[13)] and tedious work-up procedures. Thus, a convenient halodecarboxylation method is still needed. Diacetoxyiodobenzene in combination with tetraethyl-ammonium bromide (TEAB) has been utilized in several transformations like synthesis of (±)-dibromophakellstatin[14)] and oxidation of alcohols.[15)] Tetra ethyl ammonium bromide has advantage of its byproduct being water soluble and easy work up procedure over other brominating agent such as *N*-bromosuccinimide whose byproduct is soluble in organic solvent.

Herein, we report our preliminary results on decarboxylative bromination of α,β-unsaturated carboxylic acids to the corresponding bromoalkenes using diacetoxyiodobenzene (IBD) in combination with TEAB at room temperature. Starting compounds *viz.* α,β-unsaturated carboxylic acids were prepared by standard literature procedures.[16—21)] For our initial studies, cinnamic acid was selected as model substrate and the reaction was carried out with IBD in combination with TEAB. A mixture of cinnamic acid (1.0 mmol), IBD (1.1 mmol) and TEAB (1.1 mmol) in anhydrous dichloromethane was stirred at room temperature. It was observed that the starting material was consumed within 15—20 min as indicated by TLC analysis. After work-up and purification by silica gel column chromatography (hexane–ethyl acetate (EtOAc), 9 : 1), β-bromostyrene was isolated in 95% yield (Chart 1).

Results and Discussion

Encouraged by this result, we subjected various cinnamic acid analogs, including halogenated, aminated, nitrated, methoxylated and aliphatic α,β-unsaturated carboxylic acids, to the reaction conditions established above; the results are summarized in Table 1.

It clearly indicates that in the absence of double bond reaction does not take place (Table 1, entries 12, 14, 16). α,β-Unsaturated carboxylic acids substituted with electron donating groups like methyl, undergo oxidative bromo-decarboxylation (Table 1, entry 7) 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—6, 8). Using the same reagent system, 3-(2-furyl) acrylic acid also gave good yields of the corresponding brominated products (Table 1, entry 11). Aliphatic α,β-unsaturated acids such as crotonic acid *etc.* give lower yields of brominated products (Table 1, entries 13, 15).

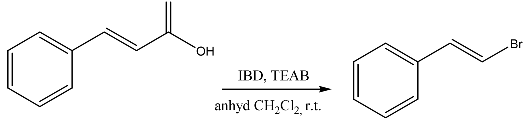

Chart 1. Bromo-Decarboxylation of Cinnamic Acid Using IBD and TEAB

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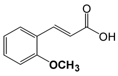
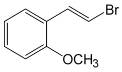
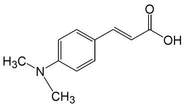
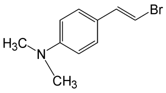
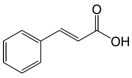
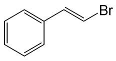
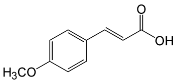
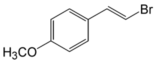
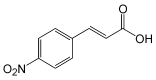
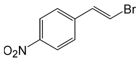
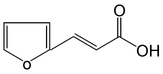
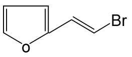
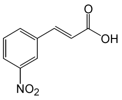
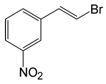
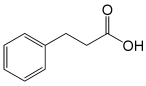
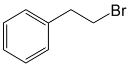
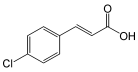
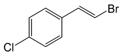
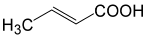
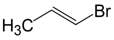
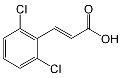
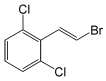
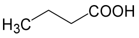
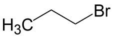
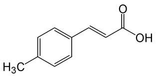
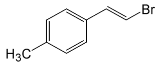
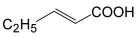
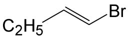
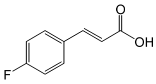
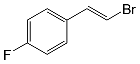
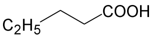
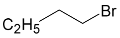
Table 1. Bromo-Decarboxylation Using IBD and TEAB[a]

Entry	Substrate	Product	Time (h)	Yield[b] (%)	Entry	Substrate	Product	Time (h)	Yield[b] (%)
1			3	94	9			12	91
2			4	92	10			8	89
3			7	89	11			8	91
4			8	85	12			12	NR[c]
5			10	83	13			8	92
6			11	82	14			12	NR[c]
7			6	92	15			10	90
8			13	85	16			12	NR[c]

a) The reaction conditions: substrate (1.0 eq), IBD (1.1 eq), TEAB (1.1 eq), anhyd CH_2Cl_2, r.t. *b*) Isolated yields after column chromatography. Structures confirmed by comparison of the IR and ^{1}H-NMR spectra with those of authentic samples. *c*) No reaction.

Table 2. Spectral Data of Compounds **1**—**16**

Entry	IR (cm^{-1})	^{1}H-NMR (δ ppm)
1	1565, 1610, 1160, 785	3.86 (s, 3H), 6.87 (d, 1H), 6.90 (d, 1H), 6.91 (d, 1H), 7.24—7.27 (m, 2H), 7.31 (d, 1H)
2	1596, 1492, 3026, 750	6.77 (d, 1H), 7.12 (d, 1H), 7.32—7.74 (m, 5H).
3	1595, 1535, 1345, 780	8.20—8.35 (d, 2H), 7.75—7.89 (d, 2H), 7.11—7.25 (d, 1H), 6.61—6.75 (d, 2H)
4	1606, 1512, 1265, 760	7.16 (d, 1H), 6.64 (d, 1H), 7.55 (t, 1H), 7.91 (d, 1H), 8.11 (m, 1H), 8.51 (s, 1H)
5	1610, 1590, 1015, 945, 785	6.38—6.65 (d, 1H), 6.84—6.96 (d, 1H), 7.26—7.39 (d, 2H), 7.56—7.76 (d, 2H)
6	1685, 1560, 978, 810	6.65 (d, 1H), 6.71 (d, 1H), 6.95 (d, 1H), 7.04 (d, 1H), 7.14—7.27 (m, 1H), 7.31—7.40 (m, 2H)
7	1600, 1520, 790	2.30 (s, 3H), 7.07 (d, 1H), 7.18 (d, 2H), 7.16 (d, 2H), 6.70 (d, 1H)
8	1604, 1505, 1325, 785	6.37 (d, 1H), 6.95—7.07 (m, 3H), 7.60—7.65 (m, 2H)
9	1610, 1335, 790	6.42 (d, 1H), 6.85 (d, 1H), 7.20—7.35 (d, 2H), 7.64—7.72 (d, 2H)
10	1606, 1533, 1215, 760	3.66 (s, 3H), 6.54 (d, 1H, J=8.1 Hz), 6.62 (d, 1H), 6.79 (d, 2H), 7.04—7.14 (d, 2H)
11	1590, 1385, 3026, 755	6.65 (d, 1H), 7.15 (d, 1H), 7.25—7.65 (m, 4H)
13	1596, 3025, 760	5.85 (d, 1H), 6.03 (m, 1H), 1.67 (d, 3H)
15	1605, 3005, 785	1.12 (t, 3H), 2.30 (m, 2H), 5.84 (d, 1H), 6.05 (m, 1H)

Conclusion

A novel method is developed for the direct conversion of α,β-unsaturated carboxylic acids to the corresponding bromoalkenes using diacetoxyiodobenzene in combination with tetraethyl-ammonium bromide (TEAB) at room temperature. The method is mild and gives good to excellent yields of corresponding bromoalkenes.

Experimental

General Experimental Procedure To a stirred suspension of IBD (1.1 eq) in anhydrous CH_2Cl_2 (15 ml) was added TEAB (1.1 eq) in one portion. The resultant mixture was stirred at room temperature (r.t.) for 5 min followed by addition of 2-methoxycinnamic acid (1.0 eq) and stirring was continued at r.t. until the starting material was completely consumed, monitoring by thin layer chromatography (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 vacuum. The residue obtained was purified by silica gel column chromatography (10% EtOAc–hexane) to afford desired compound **1**.

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