



IBX/I₂-mediated oxidation of alkenes and alkynes in water: a facile synthesis of α-iodoketones

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ABSTRACT

The conversion of alkenes into α-iodoketones has been achieved in good yields and with high regioselectivity by means of iodohydrin formation and subsequent oxidation with 2-iodoxybenzoic acid (IBX) under mild conditions. Aromatic alkynes are also converted into their corresponding α-iodoketones under similar conditions.

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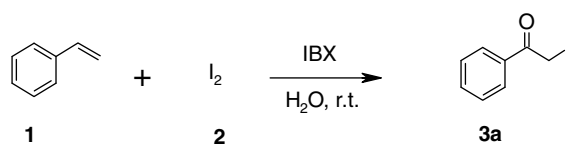
α-Iodoketones are important synthetic intermediates and have attracted significant attention.¹ Generally, α-iodination of carbonyl compounds has been achieved using various electrophilic iodonium sources.^{2,3} The use of molecular iodine as an iodinating agent has been demonstrated only in a few methods for the synthesis of α-iodoketones.⁴ These methods, however, employ selenium dioxide,^{5a} mercury(II) chloride^{5b} or ceric(IV) ammonium nitrate,^{5c} etc., in stoichiometric or sub-stoichiometric amounts and necessitate the use of acetic acid in some cases as the reaction medium. Alternatively, there are reports on the direct conversion of alkenes to α-iodoketones utilizing silver chromate/I₂,^{6a} pyridinium dichromate/I₂,^{6b} bis(sym-collidine)iodine(I) tetrafluoroborate (I⁺(collidine)₂BF₄^{-6c} and I₂/O₂/hv.^{6d} Other methods include oxidation of enol silyl ethers with silver acetate/I₂^{7a} and enol acetates with thallium(I) acetate/I₂.^{7b} However, many of these approaches require additives, additional steps to prepare precursors and also require strong oxidizing agents to accomplish this reaction. Furthermore, some of them suffer from low conversions and poor selectivity. Thus, there is a need to develop a simple, convenient and mild synthetic route to α-iodoketones using less expensive and readily available reagents. The use of hypervalent iodine reagents as oxidants in organic synthesis has attracted increasing interest due to their mild, selective and environmentally benign oxidizing properties.⁸ IBX is a versatile oxidizing agent due to its high efficiency, easy availability, mild reaction conditions and its stability to moisture and air.⁹ A wide functional group tolerance and high-yielding reactions, without over-oxidation have made

IBX very familiar for the oxidation of alcohols even in the presence of olefins, thioethers and amino groups,¹⁰ as well as in other elegant oxidative transformations.¹¹

In this Letter, we report the first direct and metal catalyst-free oxidation of alkenes and alkynes using the IBX/I₂ reagent system to produce α-iodoketones under mild conditions. Initially, we examined the oxidation of styrene (**1**) using 1.2 equiv of IBX and 1.0 equiv of iodine (**2**) in water. The reaction proceeded smoothly at room temperature and the desired product, 2-iodo-1-phenylethanone (**3a**) was obtained in 86% yield (Scheme 1).

This result encouraged us to examine the reactivity of other alkenes. Interestingly, this method worked well with both cyclic and acyclic olefins (entries b–h, Table 1). In all the cases, the reactions were clean and gave the desired α-iodoketones in good yields. The reaction conditions were compatible with ethers (Table 1). The products were characterized by ¹H NMR, IR and mass spectroscopy and also by comparison with authentic samples.¹² The oxidative iodination was successful even with 3,4-dihydro-2H-pyran (entry h, Table 1).

Next, we investigated the reaction of aromatic alkynes with the IBX/I₂ system. Interestingly, various aromatic alkynes including



Scheme 1.

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Table 1
IBX/I₂-mediated iodination reaction of alkenes and alkynes

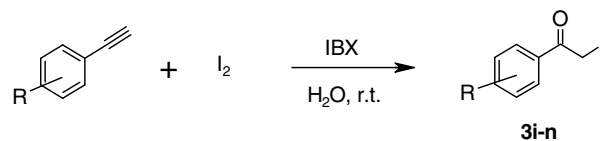
Entry	Substrate	Product ^a	Reaction time (h)	Yield ^b (%)
a			3a 4.0	86
b			3b 5.0	84
c			3c 6.0	88
d			3d 6.0	86
e			3e 5.0	87
f			3f 7.0	81
g			3g 6.0	85
h			3h 6.0	75
i			3i 6.0	87
j			3j 5.0	85
k			3k 7.0	78
l			3l 6.0	76
m			3m 5.0	77
n			3n 4.0	78

^a All products were characterized by NMR, IR and mass spectrometry.

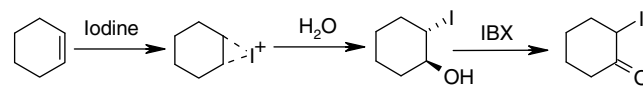
^b Yield refers to pure products after column chromatography.

p-fluoro-, *p*-chloro-, *p*-bromo-, *p*-*t*-butyl- and *p*-methyl-phenylacetylene derivatives participated effectively in this reaction (entries i–n, Table 1, Scheme 2).

Of the various hypervalent iodine reagents examined, including iodosobenzene (PhIO), iodobenzenediacetate (PhI(OAc)₂), and Dess–Martin periodinane (DMP), 2-iodoxybenzoic acid (IBX) was found to be the most effective in terms of conversion. Other oxidants such as Oxone[®]/I₂, *N*-iodosuccinimide/I₂, ceric ammonium nitrate/I₂ and Selectfluor[™]/I₂ were not as effective and none gave satisfactory yields of products. In the absence of IBX, no oxidation was observed even after long reaction times (8–12 h) under reflux



Scheme 2.



Scheme 3. A plausible reaction mechanism.

conditions. The formation of an iodohydrin was only observed when using iodine alone. As solvent, water gave the best results. The by-product, iodosobenzoic acid was separated by simple filtration and could be reoxidized to IBX. The scope of the IBX/I₂-promoted oxidation was investigated with respect to various alkenes and alkynes and the results are presented in Table 1.¹³

Mechanistically, it is possible that iodine interacts with the alkene to generate cyclic iodonium ion, which reacts simultaneously with water to form an iodohydrin. The in situ formed iodohydrin reacts immediately with IBX to produce the α -iodo ketone as shown in Scheme 3. On the other hand, IBX can also oxidize molecular iodine to generate an iodonium species which cannot be ruled out.

In conclusion, IBX/I₂ has proved to be an effective reagent system for the preparation of α -iodo ketones from alkenes and alkynes under mild conditions. The combination of IBX and water makes this method simple, convenient and user-friendly. The use of less expensive and readily available reagents makes it a useful and attractive strategy for the preparation of α -iodo ketones in a single step operation.

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13. *Experimental procedure*: A mixture of alkyne or olefin (1 mmol), IBX (1.2 mmol) and I₂ (1.0 mmol) in water (3 mL) was stirred at room temperature for the specified time mentioned in Table 1. After the reaction was over as indicated

by TLC, the solid was filtered off and washed with a saturated sodium thiosulfate solution. The filtrate was evaporated under reduced pressure, and the residue was purified by column chromatography. Spectral data for selected compounds: Compound **3a**: White solid: IR (neat): ν 3431, 3056, 2924, 2853, 1952, 1685, 1604, 1559, 1473, 1436, 1342, 1263, 1232, 1145, 1102, 1068, 1017, 832 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 4.30 (s, 2H), 7.43–7.46 (m, 3H), 7.95–8.05 (m, 2H). ESIMS: m/z : 246 (M), ⁺269 (M+Na)⁺. Compound **3c**: White solid: IR (neat): ν 3457, 3060, 3029, 2922, 2852, 1726, 1658, 1598, 1492, 1448, 1315, 1277, 1177, 1069, 940, 918, 758, 700 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 6.95 (s, 1H), 7.17–7.37 (m, 10H). ESIMS: m/z : 322 (M⁺). Compound **3l**: Brown solid: IR (neat): ν 3435, 2924, 2853, 1740, 1586, 1460, 1375, 1281, 1168, 1072, 1011, 825, 759 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 3.05 (s, 2H), 7.24–7.34 (m, 2H), 7.41–7.50 (m, 2H). ESIMS: m/z : 325 (M+1), 349 (M+Na)⁺.