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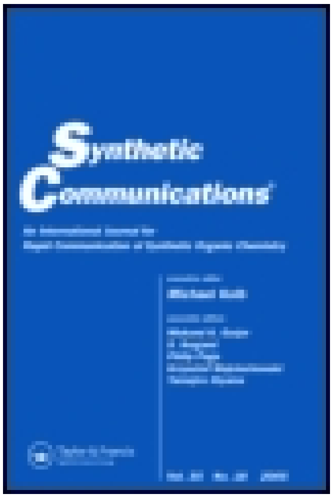

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I^-/IO_3^- Assemblies as Promoters of Iodohydrin Formation

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I^-/IO_3^- Assemblies as Promoters of Iodohydrin Formation

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Abstract: The direct conversion of olefins to their corresponding iodohydrins is efficient with I^-/IO_3^- assemblies in an aqueous acidic medium. Iodohydrins were obtained in moderately good yields at ambient reaction conditions without employing any metal catalysts. The addition of IOH across the olefin follows the Morkovnikov's rule.

Keywords: iodohydrins, olefins, potassium iodate, potassium iodide

INTRODUCTION

Functionalization of olefins finds applications in various important transformations. The formation of halohydrins from alkenes is a well-established procedure.[1] Unlike the synthesis of chloro- and bromohydrins in aqueous media,[2] the preparation of iodohydrins from the reaction of alkenes with I_2/H_2O is difficult because of the addition of iodine to the double bond. Therefore, the iodohydrins are typically obtained by the reaction of epoxides with hydroiodic acid, elementary iodine.[3] Alternately, the other reported procedures for the iodohydrin preparation includes the involvement of redox systems[4] or use of reagents such as *N*-iodosuccinimide (NIS) in DME/H_2O (DME = 1,2-dimethoxyethane) at $-20°C$,[5] NIS-H_2O in ionic liquids[6], and I_2-H_2O in presence of surfactants.[7]

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Finding reaction media to replace polluting organics and metal catalysts is one of the principles of green chemistry.[8] Water is the cheapest, most nontoxic and most readily available reaction medium, which makes it an environmentally and economically attractive solvent. However, the fundamental problem of performing reactions in water is that many organic substrates are hydrophobic and sparingly soluble in water. Several approaches are useful to solubilize the organic substrates in aqueous media; one such system is carrying out the reactions in the presence of surfactants containing both polar hydrophobic and polar hydrophilic groups on the same molecules. Recently Ranu and Banerjee[9] reported the use of ionic liquid $[AcMI_m]x$ for the synthesis of vicinal halohydrins (1.5 equivalent with respect to organic substrates) by the cleavage of corresponding epoxides at 65 °C. The use of EPZ-10 catalyst was also employed for obtaining iodohydrins.[10]

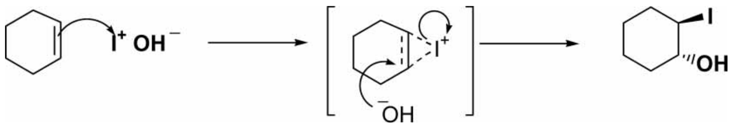
RESULTS AND DISCUSSION

Recently we have reported the use of new and environmentally benign reagents for the halogenation (bromo and iodo) of aromatic compounds with high atom efficiency.[11] In the course of our study to extend the scope of the iodide and iodate reagents in organic synthesis, we found that this reagent facilitates the formation of iodohydrins in a homogeneous system using dioxane as solvent under ambient conditions. In this article, we report the apparent formation of hypoiodous acid IOH in situ by treating iodide and iodate with mineral acids [Eq. (1)] accounts for the formation of iodohydrin (Scheme 1).

$$2I^- + IO3^- + 3H^+ \longrightarrow 3IOH \qquad (1)$$

To establish the baseline reactivity of hypoiodous acid IOH with different olefins in an aqueous acidic medium, the initial study was carried out using cyclohexene in different solvent media, and the results are summarized in Table 1.

The iodohydroxylation of cyclohexene with IOH is shown in Scheme 1. The reaction probably proceeds through the stepwise formation of iodonium cation intermediate (in situ formation of I^+ OH^-) followed by the regioselective nucleophilic attack of OH^- leading to the formation 2-iodocyclohexanol. When a molar equivalent of olefin was employed with respect to the reagent



Scheme 1.

Table 1. Optimization of reaction conditions for iodohydrin formation with cyclohexene at rt

Entry	Substrate equivalent	Solvent	Yield (%)[a]	Iodohydrin/diiodide
1	1.0	CH_2Cl_2	65	75/25
2	1.2	CH_2Cl_2	66	75/25
3	1.5	CH_2Cl_2	66	82/18
4	1.0	Dioxane	69	89.5/10.5
5	1.2	Dioxane	69	92/08
6	1.5	Dioxane	72	100/0

[a] Isolated yields with respect to the reagent.

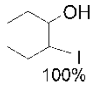
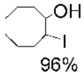
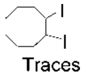
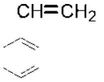
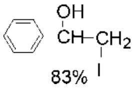
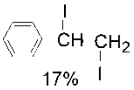
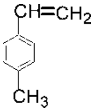
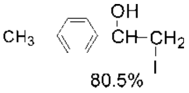
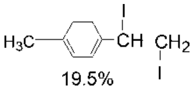
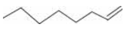
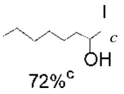
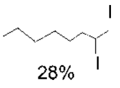
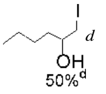
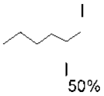
(IOH), the formation of diiodo derivative was observed. In dichloromethane solvent medium, even with 1.5 equivalent of olefin, the yields almost remain but the diiodo derivative decreased (Table 1, entry 3), whereas in 1,4-dioxane medium with increasing the olefin equivalents, the diiodo derivative formation is suppressed and total yields increased (Table 1, entries 4 to 6). The present method is based on this concept, where a mixture of 0.66 mol equiv. of potassium iodide and 0.33 mol equiv. of potassium iodate is treated with 1 mol equiv. of a mineral acid, resulting in the in situ formation of hypoiodous acid (IOH) [Eq. (1)], which can effect the iodo hydroxy addition across olefins (Scheme 1).

The results obtained with some representative alkenes for the iodohydroxylation at room temperature are summarized in Table 2. It was found that the treatment of cyclohexene (1.5 equivalent) with IOH generated in situ during the course of the reaction produced only 2-iodocyclohexanol in good yield. Styrene and 4-methyl styrene gave 90 and 72% total yield with 83% and 80.5% selectivity of iodohydrin, respectively, when 1.5 mol equiv. of substrate were employed, whereas cyclooctene gave more than 96% of iodohydrin derivative with traces of diiodo derivative even when 1 mol equiv. of the substrates was used (Table 2, entry 2).

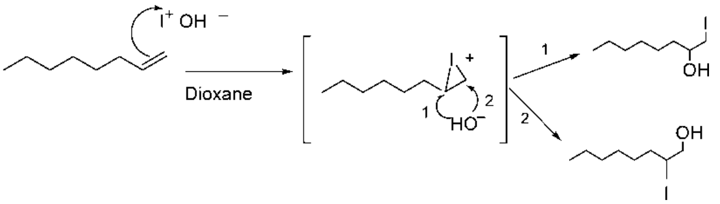
In contrast to the iodohydroxylation of cyclohexene (Scheme 2), the 1-octene afforded about a 4:1 regioisomeric mixture of 1-iodo-2-octanol and 2-iodo-1-octanol (Scheme 2). The nucleophilic addition of hydroxide ion to the iodonium ion intermediate at more hydrogen-enriched carbon atom gave Morkovnikov (route 1) and anti-Morkovnikov (route 2) products in dioxane medium. A similar strategy was observed in the case of 1-hexene, resulting in regioisomers 1-iodo-2-hexanol and 2-iodo-1-hexanol in 9:1. In straight chain alkenes, the major Morkovnikov product formation was observed, which is in accordance with the properties of nucleophilic addition reactions across the unsymmetrical C-C double bonds.

In summary, this procedure serves as a novel and potential method for the synthesis of iodohydrins in moderate to good yields in aqueous medium. I^-/IO_3^- assemblies generate a reactive species, IOH, in situ upon addition of

Table 2. Synthesis of iodohydrins from olefins

Entry	Substrate	Time (h)	Total yield (%)[a]	Product Major	Product Minor
1		1.0	72	 100%	—
2		1.0	28[b]	 96%	 Traces
3		2.0	90	 83%	 17%
4		1.5	72	 80.5%	 19.5%
5		1.0	55	 72%[c]	 28%
6		1.5	40	 50%[d]	 50%

[a] Isolated yields obtained after column chromatography.
[b] Yield based on the recovery of starting material.
[c] Regioisomers obtained in 4:1 ratio.
[d] Regioisomers obtained in 9:1 ratio; all the reactions carried out at room temperature using dioxane as solvent.



Scheme 2. Iodohydroxylation of 1-octene.

mineral acids to promote iodohydrin constitution. The workup procedure is simple and convenient, and the reaction rates are comparatively faster. Reactions were carried out at ambient conditions without the use of any metal catalysts. The advantage of the present procedure is the broad availability of the reagents.

EXPERIMENTAL

Analytical-grade substrates were purchased from Aldrich Chemicals and used without further purification. Proton NMR spectra were recorded on a Bruker 200-MHz, (^{13}C NMR 50 MHz) FT-NMR DPX 200 in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. Microanalyses were performed on a Perkin-Elmer 4100 elemental analyzer, and IR spectra were recorded on Perkin Elmer GX 2000 spectrometer. Compounds were purified by column chromatography over silica gel (100–200 mesh from SD Fine Chemicals) using hexane and ethyl acetate as eluents.

Procedure for the Synthesis of 2-Iodocyclohexanol

A solution of cyclohexene (1.50 g, 18.3 mmol), potassium iodide (1.35 g, 8.132 mmol), and potassium iodate (0.87 g, 4.065 mmol) was prepared in dioxane (10 mL) and water (30 mL). This mixture was treated at room temperature with dilute sulphuric acid (12.19 mmol) for 60 min, stirred for an additional 30 min, and extracted with diethylether (25 mL × 3). The combined organic extract was washed with dilute sodium thiosulphate (5%), water, and brine and dried over anhydrous sodium sulphate. Evaporation of ether left the crude product, which was purified by column chromatography over silica gel (hexane–ethyl acetate 9:1) to get the pure 2-iodocyclohexanol as a colorless liquid (1.984 g, 8.779 mmol) in 72% yield whose spectroscopic data (^{1}H NMR, ^{13}C NMR, and IR) are in good agreement with those of authentic samples.[3,4,7] All the known products' spectroscopic data are compared with the authentic samples except for three new compounds (entry 2 and 4 from table 2).

Data

2-Iodocyclooctanol: ^{1}H NMR ($CDCl_3$-TMS): (δ) 1.50–1.80 (8H, m), 2.15–2.22 (3H, m, $J = 5.4$), 2.39–2.54 (1H, m), 2.73 (1H, br s), 3.84–3.92 (1H, m), 4.47–4.58 (1H, m, $J = 4$). ^{13}C NMR ($CDCl_3$—50 MHz): (δ) 22.31, 27.12, 33.77, 35.03, 35.18, 37.03, 37.56, 71.73. IR, ν_{max} (neat): 3420, 2933, 2860, 2251, 2141, 1646, 1472, 1447, 1366, 1231, 1064, 1039, 983, 909, 732, 649 cm^{-1}.

2-Iodo-1-[4-methylphenyl] ethanol: ^{1}H NMR ($CDCl_3$-TMS): (δ) 2.31 (3H, s), 2.67 (1H, br s), 3.32–3.38 (2H, t, $J = 4.4$), 4.69–4.75 (1H, q, $J = 4.4$), 7.09–7.23 (4H, m, $J = 7.2$). ^{13}C NMR ($CDCl_3$—50 MHz): (δ) 15.74, 21.74, 74.40, 126.24, 128.00, 129.84, 138.56. IR, ν_{max} (neat): 3450, 3059, 1651, 1562, 1477, 1437, 1231, 1146, 1022, 1069, 833, 779, 758, 691 cm^{-1}.

CONCLUSION

In summary, this procedure serves as a novel and potential method for the synthesis of iodohydrins moderate to good yields in aqueous medium. I^-/IO_3^- assemblies generate a reactive species, IOH, in situ upon the addition of mineral acids to promote iodohydrin constitution. The workup procedure is simple and convenient, and the reaction rates are comparatively faster. Reactions were carried out at ambient conditions without the use of any metal catalysts. The advantage of the present procedure is the broad availability of the reagents.

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