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# NaIO$_4$/LiBr-mediated Diastereoselective Dihydroxylation of Olefins: A Catalytic Approach to the Prevost–Woodward Reaction

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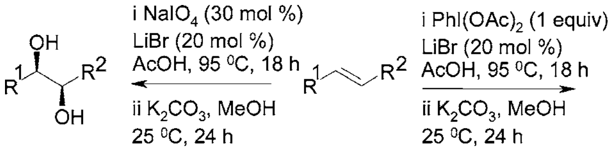
## ABSTRACT



**LiBr catalyzes efficiently the dihydroxylation of alkenes to afford *syn* and *anti* diols with excellent diastereoselectivity depending upon the use of NaIO$_4$ (30 mol %) or PhI(OAc)$_2$ (1 equiv), respectively, as the oxidants. The oxidation of non-benzylic halides has been achieved for the first time to afford the corresponding diols in excellent yields.**

The catalytic dihydroxylation of alkenes represents a unique method for the preparation of 1,2-diols with defined relative configuration, and several oxidants are now used for this purpose both in the laboratory and industry.[1] The *syn* dihydroxylation of alkenes is most often achieved[2] using OsO$_4$, KMnO$_4$ or RuO$_4$ as catalysts, which add from the less hindered diastereotopic $\pi$-face of alkene. Despite the synthetic utility, the toxicity and high cost of OsO$_4$ and poor product-selectivity of KMnO$_4$ and RuO$_4$/H$_2$O$_2$ systems have prevented a successful application of these reagents on industrial scale. The *syn* dihydroxylation from the more hindered $\pi$-face can be effected using Woodward's procedure[3] in which alkenes are treated with I$_2$−AgOAc in AcOH containing water. On the other hand, *anti* dihydroxylation of an alkene is generally achieved using certain peroxy acids[4] as well as I$_2$−silver benzoate *in the absence of water* (Prevost reaction).[5] The use of expensive silver salts, a stoichiometric amount of molecular halogen, and formation of large amount of organic and inorganic wastes resulted in a search for simpler systems.[6]

The development of a catalytic version of the Prevost−Woodward reaction is both challenging and useful to synthetic chemists. We report herein a new "transition-metal-free" procedure for the dihydroxylation of alkenes catalyzed by LiBr and mediated by either NaIO$_4$ or (diacetoxyiodo)-

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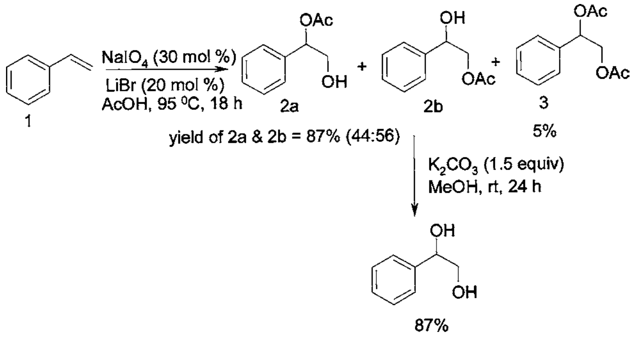
**Scheme 1**



benzene [PhI(OAc)$_2$], which are quite stable at the reaction temperature.

Recently, we have reported that the NaIO$_4$/LiBr combination oxidizes toluene under acidic conditions to benzyl acetate in excellent yield.[7] During our mechanistic investigation, we further observed that the reaction proceeded through benzyl bromide and that its rate of solvolysis was enhanced by the addition of a catalytic amount of NaIO$_4$. Surprisingly, when (1,2-dibromoethyl)benzene was subjected to this solvolysis, bromides at benzylic as well as homobenzylic positions underwent solvolysis to give regioisomers of diol derivative **2a** and **2b** in excellent yield. Although oxidation of benzylic bromides by TeO$_2$ has been reported,[8] the present protocol constitutes the first report on the oxidation of non-benzylic halides, anchimerically assisted by acetyl groups present at the 2-positions.

Encouraged by this result, we envisioned to prepare diol directly from styrene using a catalytic amount of LiBr (20 mol %) and NaIO$_4$ (30 mol %) in AcOH at 95 °C and indeed obtained regioisomers of styrene mono- (**2a**, **2b**) and diacetates (**3**) with the ratio 87:5 in 92% combined yield. This mixture was subjected to basic hydrolysis (K$_2$CO$_3$, MeOH, 25 °C) without separation to furnish 1-phenyl-1,2-ethanediol in 87% yield (Scheme 1). Control experiments indicated that no dihydroxylation occurred in the absence of either LiBr or NaIO$_4$.

To identify a suitable catalytic system, we screened several halogen sources (KI, NaCl, LiBr, NaBr, Br$_2$, NBS, and pyHBr$_3$) and found that LiBr had shown remarkable enhancement in rate and yield of diol (Table 1). Among other oxidants screened (entries 8−14), KIO$_3$, Na$_2$S$_2$O$_8$, and PhI(OAc)$_2$ have exhibited comparable activity as that of NaIO$_4$. Lowering the amount of LiBr below 20 mol % led to a sharp decline in the yield of the diol (entry 4). We determined that 30 mol % of NaIO$_4$, acting both as oxidant and as a source of water (thus providing "wet" Woodward condition), is sufficient to convert 1 equiv of styrene to the corresponding diol.

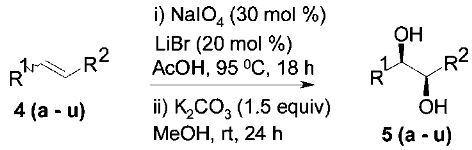
Several alkenes (aliphatic, styrenic, allylic, disubstituted alkenes, α,β-unsaturated alkenes, etc.) with electron-donating and -withdrawing groups underwent dihydroxylation (Table 2) and produced the corresponding diols in excellent

**Table 1.** Effect of Oxidant and Halogen Sources on Catalytic Dihydroxylation of Styrene[a]

| entry | oxidant[b] | halogen source[c] | yield of diol (%)[d] |
|---|---|---|---|
| 1 | NaIO$_4$ | NaCl | 22 |
| 2 | NaIO$_4$ | KI | 65 |
| 3 | NaIO$_4$ | NaBr | 84 |
| 4 | NaIO$_4$ | LiBr | 87 (53)[f] |
| 5 | NaIO$_4$ | NBS | 79 |
| 6 | NaIO$_4$ | Br$_2$ | 82 |
| 7 | NaIO$_4$ | PyHBr$_3$ | 78 |
| 8 | KIO$_3$ | LiBr | 84 |
| 9 | V$_2$O$_5$ | LiBr | 42 |
| 10 | WO$_3$ | LiBr | 36 |
| 11 | Na$_2$S$_2$O$_8$ | LiBr | 85 |
| 12 | oxone | LiBr | 77 |
| 13 | *m*CPBA[e] | LiBr | trace |
| 14 | PhI(OAc)$_2$ | LiBr | 85 |

[a] Reaction conditions: (i) styrene (3 mmol), oxidant (30 mol % to 1 equiv), halogen source (20 mol %), AcOH (5 mL), 95 °C, 18 h; (ii) K$_2$CO$_3$ (4.5 mmol), MeOH (15 mL), 25 °C, 24 h. [b] NaIO$_4$ = 30 mol %; KIO$_3$ or V$_2$O$_5$ or WO$_3$ or Na$_2$S$_2$O$_8$ = 50 mol %; oxone or *m*CPBA or PhI(OAc)$_2$ = 1 equiv. [c] Halogen source = 20 mol %. [d] Isolated yield. [e] *m*-Chloroperbenzoic acid. [f] 10 mol % LiBr employed.

**Table 2.** LiBr-Catalyzed Dihydroxylation[9] of Olefins Using NaIO$_4$[a]



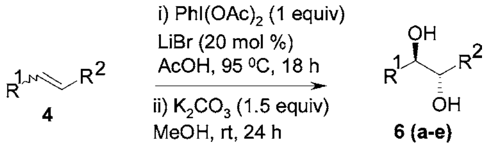
| no. | olefin (**4**) | product (**5**) | dr[b] *syn*:*anti* | diol yield (%)[c] |
|---|---|---|---|---|
| 1 | styrene | **5a** | | 87 |
| 2 | 4-methylstyrene | **5b** | | 89 |
| 3 | 4-bromostyrene | **5c** | | 90 |
| 4 | 4-acetoxystyrene | **5d** | | 78[d] |
| 5 | β-methylstyrene | **5e** | 88:12 | 84 |
| 6 | *cis*-stilbene | **5f** | 99:1 | 87[j] |
| 7 | *trans*-stilbene | **5g** | 100: 0 | 79 |
| 8 | indene | **5h** | 98:2 | 87 |
| 9 | 1,2-dihydronaphthalene | **5i** | 98:2 | 79 |
| 10 | cinnamyl alcohol | **5j** | 85:15[i] | 77 |
| 11 | allyl phenyl ether | **5k** | | 80 |
| 12 | methyl *trans*-cinnamate | **5l** | 80:20 | 65[e] |
| 13 | 4-Cl-α-methylstyrene | **5m** | | 82[g] |
| 14 | vinylcyclohexane | **5n** | | 85 |
| 15 | 3-buten-1-ol | **5o** | | 91[d] |
| 16 | *cis*-2-butene-1,4-diol | **5p** | 92:8 | 83[d,j] |
| 17 | allyl alcohol | **5q** | | 86[d] |
| 18 | allyl bromide | **5r** | | 79[d,h] |
| 19 | cyclohexene | **5s** | 90:10 | 86[f] |
| 20 | cyclooctene | **5t** | 85:15 | 83 |
| 21 | 1-octene | **5u** | | 84 |

[a] Reactions were carried out following ref 9. [b] Diastereomeric ratios were determined from $^{13}$C NMR and GC. [c] Isolated yield after chromatographic purification. [d] Product was isolated as acetate after acetylation (Ac$_2$O, py). [e] Time = 36 h. [f] At 80 °C for 36 h. [g] Hydrolyzed using KOH, MeOH. [h] 50 mol % of NaIO$_4$ employed. [i] 1 equiv of water was used (diastereoselectivity in the absence of water was *syn:anti* = 77:23). [j] Corresponding *syn*-diol was formed.

yields with *syn* diastereoselectivity. The *syn* selectivity is controlled by water, formed in situ from $NaIO_4$ and AcOH, which attacks 1,3-dioxolon-2-ylium ion (**C**) at C-2 position (Scheme 3).

As expected, allyl bromide gave triol due to successive solvolysis of 1,3-dibromide. Lower yield in the case of $\alpha,\beta$-unsaturated ester may be ascribed to the slower rate of bromoacetoxylation. However, attempts to obtain *anti* diols, by removing water formed in situ using either molecular sieves (4 Å) or anhydrous $MgSO_4$ were not successful. Interestingly, *anti* diols were obtained when $PhI(OAc)_2$ was employed as the oxidant in stoichiometric amounts under the same reaction condition. Since no water is formed, acetic acid acts as the nucleophile and opens up the intermediate **C** at C-4 position to result in *trans*-diastereoselectivity. The lower selectivity observed in the case of cyclohexene and $\beta$-methylstyrene can be explained in terms of $S_N2$ displacement of bromide in B by LiOAc (Table 3).

**Table 3.** LiBr-Catalyzed *anti*-Dihydroxylation of Olefins Using $PhI(OAc)_2$[a]



| entry | olefin (**4**) | product (**6**) | yield of diol (%)[b] | dr[c] (*anti*:*syn*) |
|---|---|---|---|---|
| 1 | indene | **6a** | 79 | 100:0 |
| 2 | *cis*-stilbene | **6b** | 84 | 100:0[d] |
| 3 | *trans*-stilbene | **6c** | 87 | 100:0 |
| 4 | cyclohexene | **6d** | 82 | 77:23 |
| 5 | $\beta$-methylstyrene | **6e** | 85 | 33:67 |

[a] Reactions were carried out following ref 9 but with 1 equiv of $PhI(OAc)_2$. [b] Isolated yield after chromatographic purification. [c] Diastereomeric ratios were determined from GC. [d] The corresponding *anti*-diol was formed.

Our earlier studies[7] had shown that 1 equiv of $NaIO_4$ was sufficient to oxidize 8 equiv of $Br^-$ ions, as can be seen from Scheme 2. Hence, only 30 mol % of $NaIO_4$ was required to bring about 100% conversion.

**Scheme 2**

$$2Br^- \longrightarrow Br_2 + 2e^-$$

$$2e^- + IO_4^- + 2H^+ \longrightarrow H_2O + IO_3^-$$

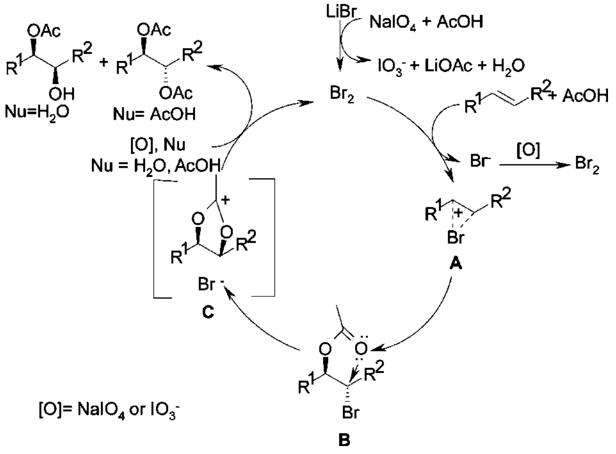
$$6H^+ + IO_3^- + 6e^- \longrightarrow 3H_2O + I^-$$

$$I_2 + 2e^- \longrightarrow 2I^-$$

$$8e^- + IO_4^- + 8H^+ \longrightarrow 4H_2O + I^-$$

From the above facts and the evidence provided by the cyclic voltammetry[10] study, the proposed catalytic cycle for the LiBr catalyzed dihydroxylation is shown in Scheme 3. The halogens (X = I, Br, Cl), generated in situ from alkali metal halides by oxidation with $NaIO_4$ or $PhI(OAc)_2$ rapidly undergo bromoacetoxylation with alkenes via bromonium ion **A** to produce *trans*-1,2-bromoacetate derivative **B**, which was isolated and characterized. The intermediate species **C**, formed from **B** in the presence of $NaIO_4$, assisted anchimerically[11] by the acetate group, is opened either by water to give *cis*-hydroxy acetate or by acetic acid to give the *trans*-diacetate with concomitant liberation of $Br_2$.

**Scheme 3.** Proposed Catalytic Cycle for Dihydroxylation Process



In conclusion, we have developed for the first time a new, practical, and "metal-free" procedure for the dihydroxylation

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(9) **General Experimental Procedure.** A mixture of olefin (3 mmol), $NaIO_4$ (30 mol %), and LiBr (20 mol %) was taken in a 25 mL round-bottomed flask, and glacial acetic acid (5 mL) was added. The reaction mixture was heated at 95 °C (using an oil bath) for 18 h. The light yellow colored reaction mixture turned purple after completion of the reaction. The reaction mixture was cooled and then extracted with EtOAc (30 mL × 3), and the combined organic phase was washed with saturated sodium thiosulfate solution, water, and aqueous $NaHCO_3$. The organic layer was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give crude product, which was subjected to basic hydrolysis without purification. The hydrolysis was carried out by stirring the reaction mixture with $K_2CO_3$ (1.5 equiv) in methanol (20 mL) at 25 °C for 24 h. After completion of the reaction, methanol was removed under reduced pressure, and the reaction mixture was extracted with EtOAc (30 mL × 3). The combined organic phase was washed with water and brine. The organic layer was then dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give crude diol, which was purified by column chromatography packed with silica gel using pet ether and EtOAc (7:3) as eluents to afford pure diol.

(10) Cyclic voltammogram is given in Supporting Information.

(11) Only organic halides with acetyl groups at the 2-positions were oxidized by $NaIO_4$ or $PhI(OAc)_2$. Octyl bromide failed to undergo oxidation under the same reaction condition. Hence, we believe that neighboring group participation by the acetate group makes the C−Br bond more polar and thus facilitating the oxidation process.

of alkenes catalyzed by LiBr using commercially available $NaIO_4$ or $PhI(OAc)_2$ as oxidants in acetic acid to produce *syn* or *anti* diols, respectively. The simplicity, environmental friendliness and readily accessible reagents make this system superior to other expensive and toxic Tl(I), Ag(I), Bi(III), and Hg(II) reagents.[6b−d]

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**Supporting Information Available:** Experimental procedures and spectral data for all the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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