NalO₄/LiBr-mediated Diastereoselective Dihydroxylation of Olefins: A Catalytic Approach to the Prevost–Woodward Reaction

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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 achieved² using OsO₄, KMnO₄ or RuO₄ as catalysts, which add from the less hindered diastereotopic π -face of alkene. Despite the synthetic utility, the toxicity and high cost of OsO₄ and poor product-selectivity of KMnO₄ and RuO₄/H₂O₂ systems have

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prevented a successful application of these reagents on industrial scale. The *syn* dihydroxylation from the more hindered π -face can be effected using Woodward's procedure³ in which alkenes are treated with I₂-AgOAc in AcOH containing water. On the other hand, *anti* dihydroxylation of an alkene is generally achieved using certain peroxy acids⁴ as well as I₂-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-metalfree" procedure for the dihydroxylation of alkenes catalyzed by LiBr and mediated by either NaIO₄ or (diacetoxyiodo)-

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

Recently, we have reported that the NaIO₄/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 NaIO₄. 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 TeO₂ 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 NaIO₄ (30 mol %) in AcOH at 95 °C and indeed obtained regioisomers of styrene mono- (2a, 2b) and

Table 1.	Effect of Oxidant	and Halogen	Sources	on Catalytic
Dihydroxy	vlation of Styrene ^a			

entry	$\mathbf{oxidant}^b$	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_2O_5	LiBr	42
10	WO_3	LiBr	36
11	$Na_2S_2O_8$	LiBr	85
12	oxone	LiBr	77
13	$mCPBA^{e}$	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) K₂CO₃ (4.5 mmol), MeOH (15 mL), 25 °C, 24 h. ^{*b*} NaIO₄ = 30 mol %; KIO₃ or V₂O₅ or WO₃ or Na₂S₂O₈ = 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.

diacetates (3) with the ratio 87:5 in 92% combined yield. This mixture was subjected to basic hydrolysis (K_2CO_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 NaIO₄.

To identify a suitable catalytic system, we screened several halogen sources (KI, NaCl, LiBr, NaBr, Br₂, NBS, and pyHBr₃) and found that LiBr had shown remarkable enhancement in rate and yield of diol (Table 1). Among other oxidants screened (entries 8-14), KIO₃, Na₂S₂O₈, and PhI(OAc)₂ have exhibited comparable activity as that of NaIO₄. 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 NaIO₄, 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 2.	LiBr-Catalyzed Dihydroxylation9 of Olefins Using
$NaIO_4^a$	

R ¹ R ²	i) NalO₄ (30 mol %) LiBr (20 mol %) AcOH, 95 ℃, 18 h	OH R ¹ R ²
4 (a - u)	ii) K ₂ CO ₃ (1.5 equiv) MeOH, rt, 24 h	О́Н 5 (а - u)

		product	$\mathbf{d}\mathbf{r}^b$	diol
no.	olefin (4)	(5)	syn:anti	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	5 i	98:2	79
10	cinnamyl alcohol	5j	$85:15^{i}$	77
11	allyl phenyl ether	5k		80
12	methyl trans-cinnamate	51	80:20	65^e
13	4-Cl-α-methylstyrene	5m		82^g
14	vinylcyclohexane	5n		85
15	3-buten-1-ol	50		91^d
16	cis-2-butene-1,4-diol	5р	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 ¹³C NMR and GC. ^{*c*} Isolated yield after chromatographic purification. ^{*d*} Product was isolated as acetate after acetylation (Ac₂O, py). ^{*e*} Time = 36 h. ^{*f*} At 80 °C for 36 h. ^{*s*} Hydrolyzed using KOH, MeOH. ^{*h*} 50 mol % of NaIO₄ 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 α , β -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 MgSO₄ 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 β -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)	,a			

	_1.v < R ²	i) Ph LiBr AcO	l(OAc) ₂ (1 equir (20 mol %) H, 95 ⁰C, 18 h	v) R ¹	R ²
	R ~ 4	ii) K ₂ 0 MeO	CO ₃ (1.5 equiv) H, rt, 24 h	6 (a-	ОН е)
			product	yield of	$\mathrm{d}\mathbf{r}^c$
entry	olefin (4	.)	(6)	diol (%) ^b	(anti:syn)
1	indene		6a	79	100:0
2	cis-stilbene		6b	84	$100:0^{d}$
3	<i>trans</i> -stilbe	ne	6c	87	100:0
4	cyclohexene	•	6d	82	77:23
5	β -methylsty	rene	6 e	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 studies⁷ had shown that 1 equiv of NaIO₄ was sufficient to oxidize 8 equiv of Br^- ions, as can be seen from Scheme 2. Hence, only 30 mol % of NaIO₄ was required to bring about 100% conversion.

From the above facts and the evidence provided by the cyclic voltammetry¹⁰ study, the proposed catalytic cycle for

2Br	, Br +2e-
	Di ₂ · 20
$2 e^{-} + 10_4^{-} + 2H^{+} \longrightarrow$	$H_2O + IO_3^{-1}$
6H⁺ + IO ₃ ⁻ + 6e⁻ ──►	3H ₂ O + I⁻
l₂ +2e⁻>	2I ⁻
l₂ +2e ⁻ →	2I ⁻

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 NaIO₄ 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 NaIO₄, assisted anchimerically¹¹ 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 Br₂.

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), NaIO₄ (30 mol %), and LiBr (20 mol %) was taken in a 25 mL roundbottomed 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 \times 3), and the combined organic phase was washed with saturated sodium thiosulfate solution, water, and aqueous NaHCO3. The organic layer was dried over anhydrous Na₂SO₄ 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 K₂CO₃ (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 \times 3). The combined organic phase was washed with water and brine. The organic layer was then dried over anhydrous Na2SO4 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 NaIO₄ 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.

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of alkenes catalyzed by LiBr using commercially available NaIO₄ 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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