Oxidative Bromination in Organic Synthesis

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Introduction:

Halogenation reactions are gained considerable importance from their discovery. The halides are important in organic synthesis due to their use for synthesis of various commercially important compounds. Among the halides chlorides and bromides are of commercially important over fluoride and iodide. Organic bromides are widely used as synthetic precursors for various coupling reactions in organic and pharmaceutical synthesis. They can be used as potent antitumor, antibacterial, antifungal, antineoplastic, antiviral, and anti-oxidizing agents and also as industrial intermediates in the manufacture of pharmaceuticals, agrochemicals, and other specialty products, for instance, flame-retardants [1–5]. The traditional bromination using elemental bromine shows a maximum of 50% atom efficiency in terms of bromine consumption. The bromination reaction has been still attracting attention to develop the more practical method without the use of hazardous and highly toxic elemental bromine. Oxidative bromination is a process which generates electrophilic bromine using various oxidants with or without using catalyst. (An exception is fluorination, since it is too difficult to oxidize fluoride.) In the laboratory as well Industrial scale, however, bromination is generally carried out with hazardous, toxic, and corrosive molecular bromine mostly in combination with chlorinated solvents. A growing ecological awareness among chemists has coincided with an increased understanding of oxidative bromination in biological systems, which has boosted research in the field of oxidative bromination. From Green chemistry point of view Hydrogen peroxide and oxygen are considered as best agent for oxidative halogenation as the waste generated is water only[6,7]. In the literature various oxidative halogenation methods are reported, where various oxidants like metals, persulphate, mineral acids and hyper valent iodine are used for generation of electrophilic bromine.

The present review gives short glance on various reagents reported in the literature for oxidative bromination of various substrates using various oxidative reagents with new catalysts and new non catalyst methods.

BIOHALOGENATION SYSTEMS :

Biohalogenation process is widely spread in nature and essential for life[8]. The methyl halide transferases and haloperoxidases are the two types of enzymes have been isolated. The former catalyzes formation of methyl chloride and methyl bromide from S-adenosyl methionine and the corresponding halide ion[9]. While the letter involved in the biosynthesis of more complex halo metabolites. However, the natural function of most halo peroxidases is still unknown.

Marine Haloperoxldases:

Halo peroxidases are enzymes that catalyze the oxidation of a halide (i.e., chloride, bromide, or iodide) by hydrogen peroxide, a process which results in the concomitant halogenation of organic substrates. There are two types of classifications of halo peroxides one is based on most electronegative halide which oxidized by hydrogen peroxide in presence of enzymes as a catalyst. For instant chloro peroxidase catalyzes the oxidation of chloride, bromide, and iodide by hydrogen peroxide; bromo peroxidase catalyzes the oxidation of bromide and iodide by hydrogen peroxide, while iodo peroxidase catalyzes the oxidation of only iodide by hydrogen peroxide. And the second type would be based on enzymes physiological role.

Types of Marine Halo peroxidases :

All class of marine algae and many marine organisms are the source of halo peroxidases. Till two types of marine halo peroxidases have been identified viz. (1) vanadium bromo peroxidase (V-BrPO), a non-heme enzyme, and (2) Fe Heme bromo peroxidase (Fe-Heme - BrPO).

Table 1. Listed various source of halo peroxides from marine algae's

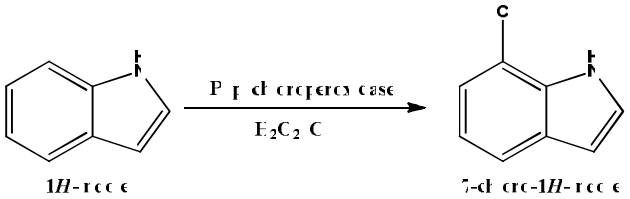
vanadium bromo peroxidase		**ref(s)**
1.	Rhodophyta (red algae)	
	Corallina officinalis	10
	Corallina pilulifera	11, 12
	Corallina uancouveriensis	13

	Ceramium rubrum	14
2.	Phaeophyta (brown algae)	
	Alaria esculenta	15
	Ascophyllum nodosum	16
	Chorda filum	17
	Fucus distichus	18
	Laminaria digitata	19
	Laminaria sacchirina	17
	Macrocystis pyrifera	18
3.	Chlorophyta (green algae)	19
	Halimeda sp.	
Fe Heme bromoperoxidases		
1.	Rhodophyta	
	Cystoclonium purpureum	20
	Rhodomela larix	21
2.	Chlorophyta	
	Penicillus capitatus	22,23
	Penicillus lamourouxii	24
	Rhipocephalus phoenix	24
3.	Marine worm	
	Notomastus lobatus	25
	Ptychodera flavin laysanica	26
	Thelepus setosus	26

All halo peroxidases catalyze the smooth, yet unselective chlorination, bromination or iodination of relatively electron-rich groups in organic compounds. Non-heme halo peroxidases are superior to heme-containing halo peroxidases because of their excellent resistance towards denaturing conditions. Only one selective enzymatic halogenation reaction is known at present: the conversion of indole to 7- chloro indole by the chloro peroxidase from the bacterium Pseudomonas pyrrocini (Scheme – 1)[28]. This enzyme converts indole into its 7-chloro derivative 12, which is remarkable because the heterocyclic ring in indole has the highest electron density

and should normally be attacked first in halogenation reactions. Furthermore, this enzyme is *not* able to chlorinate mono chloro indole, although it brominates 3 readily. Unfortunately, the specific activity of this chloro peroxidase is very low.

Scheme : 1. Regioselective chlorination of indole by the chloroperoxidase from thr bacterium Peudomonas pyrrocinia



Dioxovanadium(V) complexes, NH4[VO2(sal-inh)] and NH4[VO2(sal-oap)] encapsulated in the super cages(a-cages) of zeolite–Y have O4N coordination around vanadium and partly models the enzymes Vanadate-Dependent Haloperoxidases (V-HalPO). These complexes also represent functional model of bromoperoxidase in that salicylaldehyde has been brominated to 5-bromosalicylaldehyde with ca. 87% selectivity by H2O2/KBr. No decomposition or leaching of the catalysts during catalytic reaction and nearly identical result with fresh as well as recovered catalysts suggests that these catalysts can further be used for catalytic study.

Scheme 2 :Bromination of Salicyldehyde

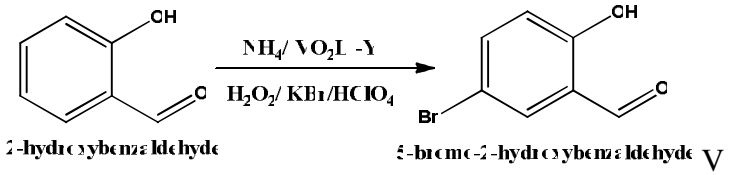


Table 2 : Percent yield of reaction product along with TOF values

Catalyst	**Crude product [a](%)**	**TOF[b]**	**5-Bromosalicylal-dehyde (%)**	**Other product (%)**
Na/ NH_4VO_3-Y	25.4	22	22.2	3.2
NH_4/[VO_2(sal-inh)]-Y	39.3	52	34.0	5.2
NH_4[VO_2(sal-inh)-H_2O]	50.0	8	44.6	5.4
NH_4[VO_2(sal-oap)]-Y	31.0	67	26.8	4.2

[a] Average of three different trial using fresh catalyst each time.

[b] TOF turn over frequency, moles of substrate converted per moles of metal(in solid catalyst) per hour.

The use of enzymes for halogenation is still potentially the most effective and environmentally friendly route, but so far large scale enzymatic halogenation has not been commercialized because of the low operational stability of the haloperoxidase enzymes (resulting from either inactivation with H_2O_2 or the organic solvent)[29]. Consequently, these reactions need to be performed in mixtures of dilute aqueous buffer and organic solvents, thus rendering them economically unattractive. There have been several efforts to enhance its stability, including maintaining a low H_2O_2 concentration during the reaction by the continuous addition of peroxide[30]. or by in situ generation of H_2O_2.[31] The use of tert-butyl hydro peroxide (TBHP) in the place of H_2O_2 has proven successful in some cases[32] . In other strategies, polymers[33] and antioxidants[34] were added, or co-solvents such as an ionic, liquid[35,36] or ternary systems[37] were employed. Immobilization of halo peroxidases on solid supports did increase the stability of the enzyme and facilitated its recovery[38] . A promising alternative is biological halogenation with FADH2-dependent halogenases, which use oxygen as the oxidant. Although other routes for halogenation in natural systems have also been discovered, this strategy remains prevalent (excluding fluorination because of the higher oxidation potential of F.

Use of heteropoly acids for oxidative bromination of aromatic compounds

Hetero-poly acids are mainly used for bromination of phenols. Various conditions were studied. Zang and et. al.[40] studied the catalytic effect of ammonium salt of molybdophosphoric acid or phosphotungstic acid supported on silica synthesized by sol-gel method. The catalyst favors high para selectivity. As reaction is free from use or formation of toxic material make it eco-friendly. Hydrogen peroxide used as oxidant while KBr is used as bromine source in acetic acid medium. Catalyst retains its activity evenafter 3 cycles proves its effectiveness. It was found that increasing catalyst dosage from 0.2 to 0.5 g percentage of conversion increased from 72 to 95.4% while selectivity ratio (P-BP/O-BP) increased from 2.2 to 3.2

Scheme 3. Oxy bromination of phenol

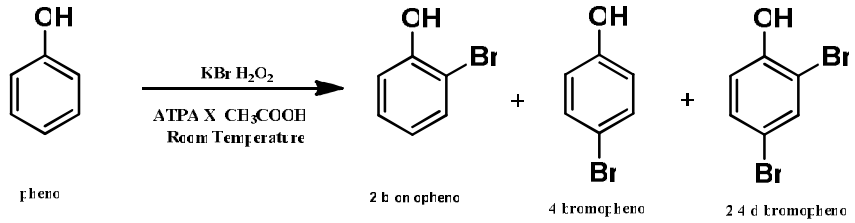


Table 3 : Oxidative bromoation reaction of phenol catylyzed by silica supported ammonium salt of heteropoly acids

Catalyst	Catalyst dosage (g)	Reacttion time (h)	Conversion (%)	Selectivity (%)			P/O
ATPA	0.5	5	92.6	27.2	61.6	11.2	2.3
ATPA-5	0.5	5	52.8	39.3	59.1	1.6	1.5
ATPA-10	0.5	5	75.5	32.3	61.7	6.0	1.9
ATPA-20	0.5	5	95.4	20.2	64.6	15.2	3.2
ATPA-40	0.5	5	93.0	26.9	63.8	9.3	2.4
AMPA	0.5	5	91.1	34.9	54.4	10.7	1.6
AMPA-5	0.5	5	59.2	37.3	59.0	3.7	1.6
AMPA-10	0.5	5	87.0	33.9	59.2	6.9	1.8
AMPA-20	0.5	5	92.1	24.1	64.5	11.4	2.7
AMPA-30	0.5	5	86.1	18.3	71.1	10.6	3.9

Parida et. al.[41] studied same reaction i.e. oxi bromination of phenol using Hydrogen peroxide and KBr using of phosphotungstic acid (PTA) supported on hydrous zirconia. The 15 wt % of catalyst shows highest surface area, acid sides and gives 93$ product conversion and 81% para selectivity. It was assumed that the surface acidity of catalyst was increased due to increasing the phosphotugstanic acid is may be due to formation of monolayaer coverage of PTA on zirconia. While high PTA concentration may results into formation of polylayer coverage of PTA on zirconia, which decrease the number of Bronsted acud sites and thus total acid sites.

Fig. SEM micrograph of 15% ZPTA sample and second fig. shows SEM micrograph of single particle (Single particle magnification at 1400 x)

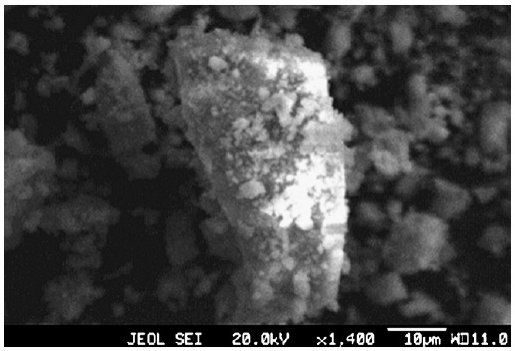


Table 4 : Conversion and selectivity of various catalyst towards oxy-bromination of phenol

Catalysts	T (h)	Conversion(%)	Selectivity(%)		
			Ortho-bromo	Para-bromo	di-bromo
Z	5	48.84	34.48	65.52	-
3 wt % ZPTA	5	65.00	41.05	58.94	-
6 wt % ZPTA	5	72.30	38.85	61.15	-
9 wt % ZPTA	5	77.34	34.80	65.20	-
12 wt % ZPTA	5	82.19	29.81	70.17	-
15 wt % ZPTA	5	93.34	18.54	81.06	0.30
20 wt % ZPTA	5	83.75	19.66	79.21	1.12

Phenol (2 mmol). KBr (2.2 mmol), H_2O_2 (2.2 mmol) catalyst (200 mg) and acetic acid (4 ml), time 5 h

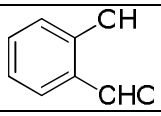
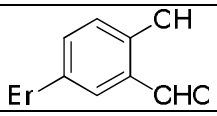
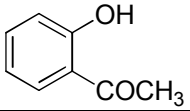
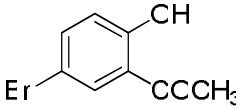
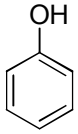
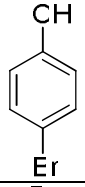
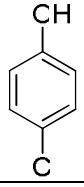
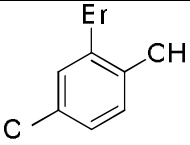
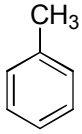
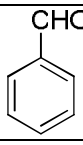
In another study done by the same group on liquid phase oxidative bromination[42] of phenol utilizes, heteropoly acid (HPA)-impregnated titanium phosphate (TiP), prepared by an incipient wetness impregnation method by varying the weight percent of HPAs like phosphotungstic acid (PWA), phosphomolybdic acid (PMoA), silicotungstic acid (SiWA) and silicomolybdic acid (SiMoA). The final product analysis study shown that, PWA/TiP dried at 110 ^{0}C shows high conversion while SiWA/TiP dried at 110 ^{0}C shows high para selectivity (30%), The product selectivity is proportional to activation temperature upto 400 ^{0}C. Above this temperatrure there is no change observed on selectivity.

<u>Vanadium catalyzed oxidative bromination reactions :</u>

Oxo-vanadium complex are used as efficient catalyst for oxidative bromination. Koner et.[43] al.synthesized vanadium(IV) metal on shiff base to form a vanadium complex which were then

immobilized over Si-MCM-41 matrix via covalent bonding. This catalyst were studied for oxi bromination of hydroxy aromatic compounds using 30% hydrogen peroxide and KBr. The reaction delivered high product yield, without evolution of hydrogen bromide, thus making reaction environmental benign.

Table 5. Bromination of Hydroxyaromatic compounds using V-MCM-41 as a catalyst[a]

Entry	Substrate	Conversion[c] (wt%)	Time	Product	Yield[d] (wt%)	TOF[e] (h^{-1})
1.		100	3.5		99	448
2.		100	3		99	522
3.		100	1		82	1568
4.		91	4		91	356
5.		<1	8	-	-	-
6.		<1	8	-	-	-

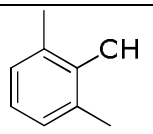
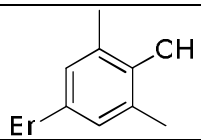
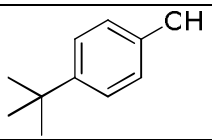
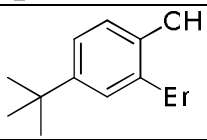
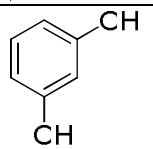
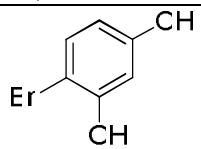
[a]Reaction conditions : Substrate, 5 mmol; KBr,5 mmol; solvent, 5ml; catalyst,25 mg; H_2O_2, 30 mmol, and HIO_4, 2 mmol. [b]Acetonitrile (1 ml) was added to 4 ml of water to dissolve the substrate. [c]Conversion of the reactant is determined by GC. [d]Isolated yields were calculated from the mass of the product after separation by column chromatography. All the isolated products shows more than 99% GC purity. [e]TOF (turnover factor) = mole converted/ (mole of active site X time).

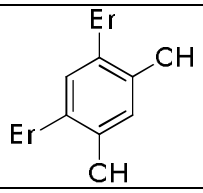
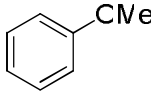
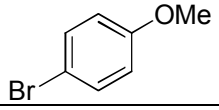
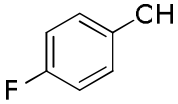
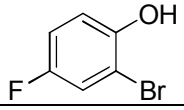
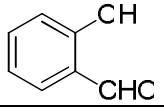
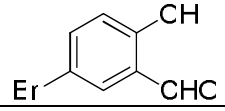
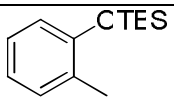
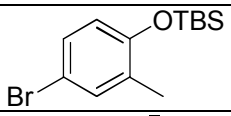
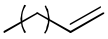
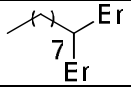
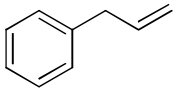
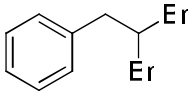
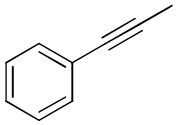
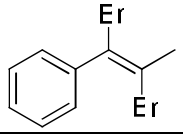
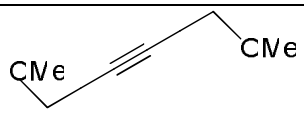
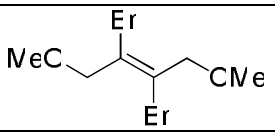
Table 6. Heterogeneous Oxybromination of salicylaldehyde catalyzed by other Vanadium based catalysts

Catalyst	Conversion (wt%)	% Selectivity of 5-bromo salicylaldehyde	TOF[e]
NH_4[VO2(sai-inh)]-Y[a]	39.3	34	52
[-CH_2{VO(sal-1,3- pn) -]n[b]	92	28	33.8
Polymer supported-[VO(fsal-ohyba).DMF][c]	73	81.36	100
Polymer supported-K[VO_2(sal-inh)(im)]d	85.2	90.4	775
V-MCM-41	100	99	448

[a]H_2 sal-inh is N-isonicotinamidosalicylaldimine. [b]Oxovanadium (IV) complex of the polymer Schiff base derieved from 5,5-methylenebis(salicylaldehyde) [$CH_2(Hsal)_2$] and 1,3-diamino propane (1.3 pn). [c]H_2-fsal-obyba is the schiffs base derieved from 3-formylsalicylic acid and 0-hydroxybenzylamine. [d]H_2 sal-inh is the Shiff base derieved from salicylaldehyde and isonicotinhydrazide. [e]TOF = moles converted/(maoles of active sites X time). The combination of Vanadium metal with lewis acid $AlBr_3$ provides an alternative method for traditional molecular bromination process[44]. Various alkenes, arenes and alkynes can be effectively brominated under present protocol. The use of molecular oxygen in the catalyst recycle process avoids the use of hydrogen peroxide as a terminal oxidant .with vanadium bromoperoxidase. Study shows that the absence of vanadium complex or air does not shows any product formation. This explains the effectiveness of catalyst.

Table 7. Oxy bromination of phenol using vanadium metal with Lewis acid

Entry	Substrate	$AlBr_3$ (mol%)	Method[a]	Product		Isolated yield
1 2		60 60	A B		1b	94 95
3		60	A		1c	98
4		40	A		1d	80

5 6		80 80	A B		2d	66 51
7		120	A		1e	96
8		120	A		1f	95
9		60	A		1g	86[b]
10		120	B		1h	Quant
11 12		120 120	C D		3i	99 76
13		120	C		3j	93
14		120	E		4k	98
15		120	E		4l	97

Moriuchi et. al. [45] developed mild oxidative bromination system using NH_4VO_3 as a catalyst with hydrogen peroxide in presence of surfactant, Dodecyl trimethyl ammonium bromide, in aqueous medium. The reaction product varies with solvent system used. The trans–b-methyl styrene gives bromo hydrine in presence of water while in two phase reaction same starting material gives di-bromo derivative prominently.

Scheme 4. Oxidative Bromination of stilbene

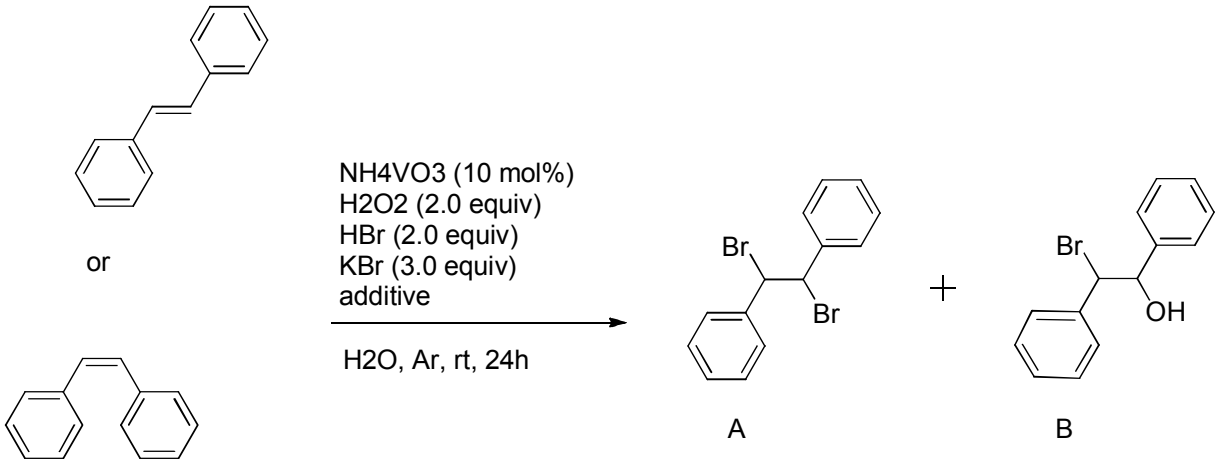


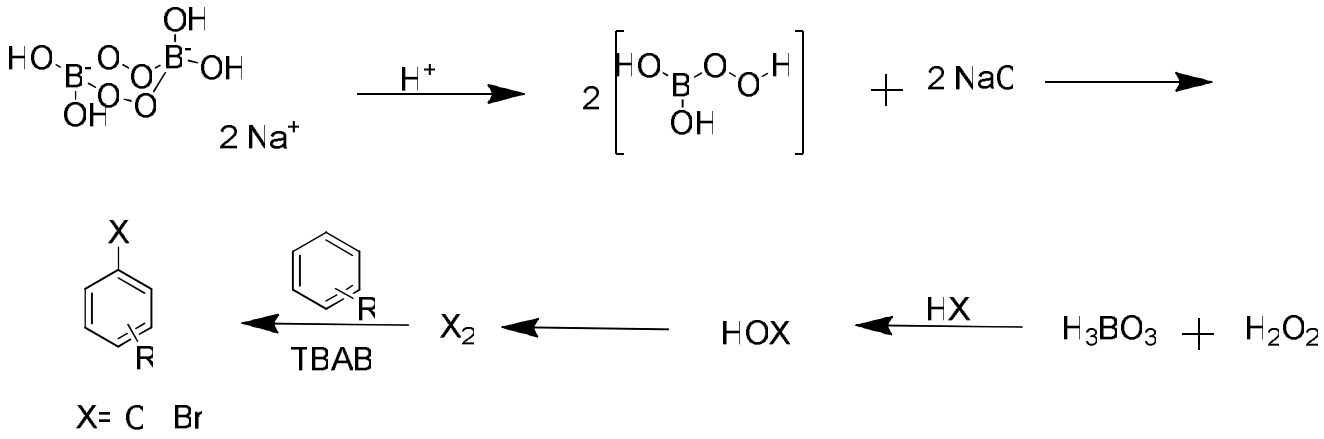
Table 8. Oxidative Bromination of stilbene in water in the presence of an additive[a].

Additive	NMR yields/% (erythro/threo)				
	From trans-stilbene			From cis-stilbene	
	A+B	A	B	A+B	A B
1	51	{33(88/12)/18(100/0)}		94	{67(13/87)/27(26/74)}
SDS	37	{21(58/42)/16(81/19)}		94	{71(47/53)/23(26/74)]}
DTAB	71	{44(93/7)/27(100/0)}		98	{77(17/83)/21(33/67)}
None	10	{7(93/7)/3(100/)}		86	{62(32/68)/24(25/75)]

Using Sodium per borate :

Sodium per borate is another cheap, easily available oxidant used for oxidative bromination of various aromatic compounds. Deshmukh et. al.[46] shows that, bromination of benzene and other derivatives of benzene proceeds smoothly using sodium per borate with Tetra butyl ammonium bromide in ethylene dichloride at 65 ^{0}C. Sodium per borate oxidizes halo acids into hypohalous acid. While TBAB plays duel role Phase transfer catalyst as well as Lewis acid.

The plausible mechanism



Scheme 5. Oxidative bromination using sodium per borate

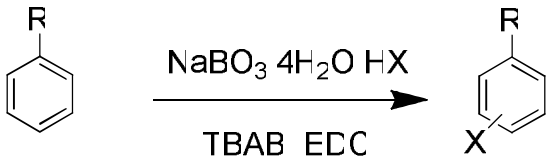


Table 9 : Oxidative bromination and chlorination using Sodium per borate :

R	Reaction time/h	Chlorination			Bromination		
		o-	*p*-	Yield (%)	*o*-	*p*-	Yield (%)
Me	6	40	57	74	37	60	78
H	6	-	-	90	-	-	88[(a)]
OMe	6	-	100	66	-	100	70
OH	2	22	78	80	20	80	77
COMe	24	-	-	0	-	-	0
CO H	24	-	-	0	-	-	0
NO_2	24	-	-	0	-	-	0

[a]Reaction proceeds up to the monohalogenated state, no di-haloganated product was observed;
[b]GC analysis.

Sodium perborate found to be effective for oxidative bromination of unprotected aromatic amines[47] under mild conditions yielding good to excellent product. Use of ammonium molybdate accelerate the reaction rate but not essential for high yield.

Scheme 6. Oxidative bromination of aromatic amines using sodium per borate

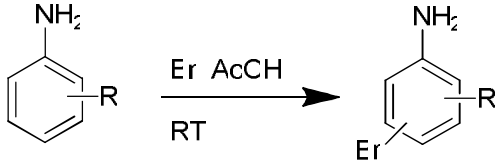


Table 10 : Oxy-bromination of aromatic amines

Entry	Substrate	Method	Reaction time (h)	%Conversion[a]				Yield
				SM	para[d]	ortho[d]	dibromo[d]	
1	Methyl Anthranilate	A	0.5	0	87.1	3.2	9.7	n.d
2		B	14.5	4.3	92.0	3.7	0	88%[C]
3		C	4.0	1.3	95.4	3.2	0	99%[b]
4	Anthranilonitrile	A	0.75	0	96.5	1.5	2.0	n.d.
5		B	14.5	0	98.2	<1	1.1	98%[b]
6		C	3.0	0	97.7	<1	2.2	98%[b]
7	2'-aminoacetophenone	B	14	0	91.4	5.3	<2	85%[c]
8		C	2	0	94.2	5.8	0	100%[b]
9	Anthranilic acid	C[e]	2	3.7	82.0	7.5	n.d.	51%[c,f]
10	2-bromoaniline	B	14.5	0	96.9	<1	3.0	85%[c]
11		C	2	5	95.0	<1	0	98%[b]
12	2-iodoaniline	C	2.2	0	98.6	1.4	0	100%[b,f]
13	2-fluoroaniline	C	1	1.3	97.5	1.2	0	88%[b,f]
14	2-nitroaniline	C	1.25	23.2	48.9	2.3	25.6	n.d.
15	4-nitroaniline	C	2	1.4	-	98.6	0	95%[b]
16	4-aminobenzonitrile	C	1.5	0	-	>99	0	96%[b]
17	4-bromoanilne	C	2.25	0	-	96.3	3.7	87%[c]

18	4-iodoanilne	C	2	5.4	-	68.6	1.17	79%[b,f]
19	4-fluoroaniline	C	1.5	2.8	-	91.4	n.d.	87%[b,f]
20	4-aminobenzoic acid	C	2.25	0	-	85.6	0	75%[c]

Method A: KBr (1.2 eq), 35% H_2O_2 (1.2 eq), $(NH_4)_6Mo_7O_{24}.4H2O$ (0.01eq), AcOH, RT.
Method B: KBr (1.2 eq), $NaBO_3.4H_2O$ (1.2 eq), AcOH, rt.
Method C: KBr (1.2 eq), $NaBO_3.4H_2O$ (1.05 eq), $(NH_4)_6Mo_7O_{24}.4H_2O$ (0.01eq), AcOH, rt.
[a]Determined by HPLC (λ 250 nm) and correlated by 1H NMR; [b]Isolated material after aqueous workup; [c]Isolated yield after recrystallization; [d]The products were characterized by NMR and MS; [e]1.3 eq of $NaBO_3.4H_2O$ and 1.4 eq of KBr were used; [f]charcoal filteration was used during the workup.

Using Sodium per Iodite :

Lalit kumar et. al.[48] developed a simple and efficient method fro oxidative bromination of deactivated aromatic compounds using NaBr as a bromine source and NaIO4 as a oxidantin sulphuric acid medium. Various deactivated aromatic compounds like nitro benazen, dinitro benzene, benzoic acid, chloro benzene can be effectively and smoothly brominated under given protocol. The oxidant NaIO4 is readily available, cheap, non-toxic. The scope of NaIO4 is observed when reaction carried out in absence of NaIO4 does not shows product formation.

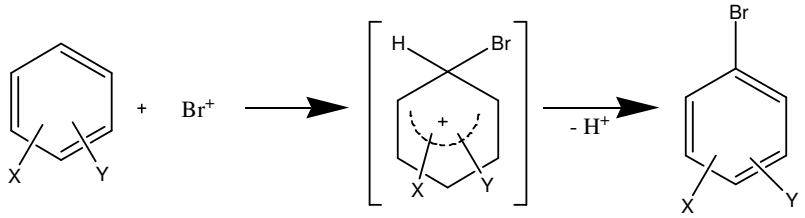
The efficiency of NaIO4 was clear from reaction. The possible mechanism is as follow

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

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

$$IO_3^- + 6H^+ + 2e^- \longrightarrow I^- + 3H_2O$$

$$IO_4^- + 2Br^- + 5H^- + 6e^- \longrightarrow Br_2 + I^- + 4H_2O$$



Arenium ion, I

X,Y = Electron withdrawing groups

Sodium periodate also used for oxidative halogenation of alkene and arenes in combination with metal halides[50]. The 25 mol % of NaIO4 is sufficient for obtaining the higher yield of brominated product. In contravercy to previous report here the higher yield was not obtained

using the mineral acids like, sulphuric acid or hydro chloric acid. The use of acetonitrile with water at pH = 6.2 leads to formation of bromo hydrin product while use of mild acid like acetic acid facilitates dibromo derivatives. While use of catalytic amount of iodo benzene result into formation of mixture of halo alcohols with poor yield of di bromo derivatives.

Scheme 7 : Bromination using Sodium per iodate

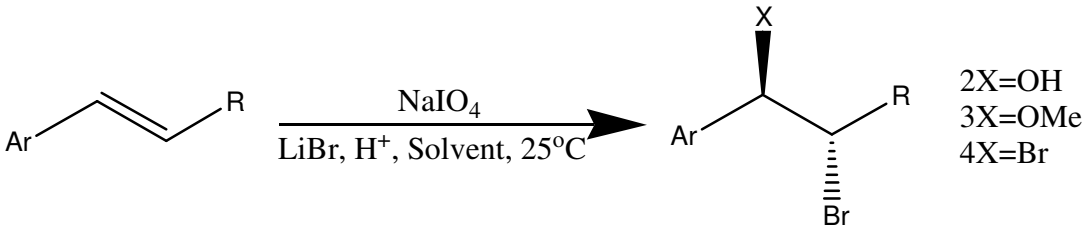


Table 11 : Oxy bromination using sodium per-iodate

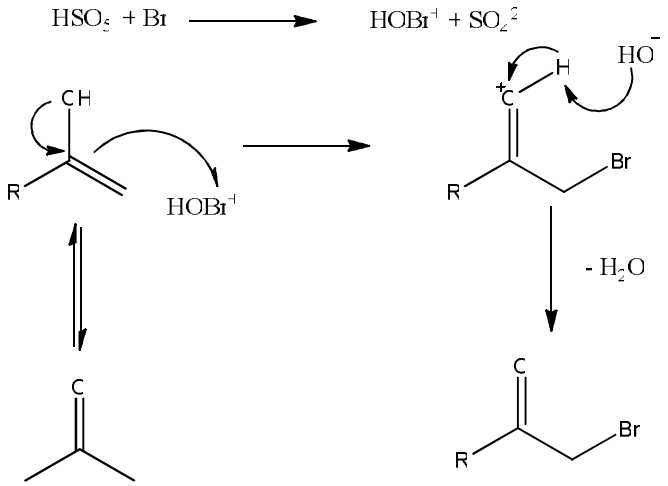
No	Substrates	Yield (%)[b]		
1	Styrene	91	57	95
2	4-Me styrene	95	78	96
3	4-OMe styrene	90	80	96
4	4-Br styrene	80	76	97
5	4-CH_2Cl styrene	85	78	96
6	α-Me styrene	85	76	95
7	Cinnamyl alcohol	80[c]	75[c]	98
8	Methyl cinnamate	90[c]	80[c]	98
9	4-Me ethyl cinnamate	95[c]	87[c]	98
10	Chromene[d]	95[c]	83[c]	96
11	Cyclooctene	85	65	99
12	1-octene	96[e]	84[e]	96

13	Indene	98[e]	90[e]	98
14	Allybromide	50[e]	46[e]	98
15	Acrylamide	0	0	90
16	N,N-dimethyl acrylamide	0	0	93

Using Oxone :

Oxone , (2KHSO5, KHSO4, K2SO4), a potasium salt of caros acids, is widely used oxidant for oxidative transformations due to stability, water solubility, ease of transport, nontoxic 'green' nature, safety profile, cost-effectiveness and non-polluting byproducts. Oxone with ammonium bromide effectively mono brominate, aryl alkyl, cyclic, acyclic, 1,3-diketones and b-keto esters and a,a-dibromination of 1,3-diketones and b-keto esters without catalyst[51]. Another benefit of this system is that, unsymmetrical acyclic ketones brominated at less substituted a-position predominantly.

Possible mechanism :



Bromination of cyclic acylic ketones using NH_4Br and oxones:

Apart from these reagents there are many oxidants which effectively used from oxidative bromination like urea hydrogen peroxide, peracids like aper acetic acid, m-chloro per benzoic acids etc.

Conclusion :

In summery, oxidative bromination or we can say halogenation is one of important tool in organic synthesis where we can avoids the use of excess molecular halogens with good atom economy, can use mild reaction conditions and make the process more simple and efficient than the conventional one. Use of metal catalyst in combination of oxidants like hydrogen peroxide reduced greatly the excess addition of peroxide for oxidative halogenation. Along with the avoidance of harsh chemicals, reaction conditions, recycling of metal catalyst further added prominent benefit over the conventional methods.

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