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Hypervalent Iodine(III) Oxidation Catalyzed by Quaternary Ammonium Salt in Micellar Systems

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Abstract: Catalytic activation of iodosobenzene (PhI=O) by cetyltrimethylammonium bromide (CTAB) allows sulfide oxidation reaction to occur in high yields under mild conditions in a variety of solvents. This PhI=O activation may be due to the formation of micellar or reversed micellar systems.

Keywords: Hypervalent element; Micellar systems; Sulfides; Sulfoxides

Hypervalent iodine reagents have been extensively used in organic syntheses due to their low toxicity, ready availability and easy handling [1-8]. We have developed various efficient reactions using (diacyloxyiodo)benzenes such as phenyliodine(III) diacetate (PIDA) and phenyliodine(III) bis(trifluoroacetate) (PIFA) and clarified the effects of several additives and solvents [5, 9-18]. Among the hypervalent iodine(III) reagents, iodosobenzene (PhI=O) is one of the most popular, however, it is not a reactive reagent by itself probably because of its low solubility in water and most organic solvents except for MeOH. Activation of PhI=O has often required more than stoichiometric amounts of Lewis acids such as $BF_3{\bullet}Et_2O$ and TMSOTf, and only with a limited variety solvents such as CH_2Cl_2 and CH_3CN [1-8]. We report herein a mild and high yielding oxidation reaction of sulfides using PhI=O activated by a catalytic amount of quaternary ammonium salt, cetyltrimethylammonium bromide (CTAB), in solvents ranging from H_2O to *n*-hexane under neutral conditions.

$$\text{R-S-R'} \xrightarrow[\substack{\text{H}_2\text{O-nonpolar solvents} \\ \text{(micellar or reversed micellar systems)}}]{\text{PhI=O-[C}_{16}\text{H}_{33}\text{N}^+\text{Me}_3\text{]Br}^-\text{ (CTAB)}} \text{R-S(O)-R'}$$

Despite extensive research on oxidants which selectively convert sulfides to the corresponding sulfoxides, most reagents require careful control of the reaction conditions, including the quantity of oxidants, to minimize the formation of sulfones as side products [19]. On the other hand, several reports have shown that hypervalent iodine(III) oxidation using PhI(OTs)OH [20], $PhI{=}O{-}PhSeO_2H$ [21], $PhI{=}O{-}(RCO)_2O$ [22] and $PIDA{-}RCO_2H$ [23] are effective for the selective oxidation of sulfides to sulfoxides, yet, reagent insolubility and/or reactivity with several solvents limit the usable solvents.

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As a continuation of our studies concerning the activation of hypervalent iodine reagents [9-18], we focused on the quaternary ammonium salt as a possible activator and a surfactant to form micellar and reversed micellar systems [24, 25] in both aqueous and organic solvents. While only a few examples for the combination of hypervalent iodine reagents and surfactants have been reported concerning the hydrolysis of carboxylic and phosphoric acid esters using iodosobenzoic acid in water by Moss and other groups [26-30], to our knowledge, no applications to other reagents and reactions have been reported.

We first examined the oxidation of methyl *p*-tolyl sulfide (**1**) by PhI=O in water. These results are summarized in Table 1. In the absence of catalyst, only a trace amount of methyl *p*-tolyl sulfoxide (**2**) was detected. In contrast, the addition of a catalytic amount (1mM) of CTAB, a well-known surfactant for micelle formation [24, 25], afforded **2** in quantitative yield at room temperature. Furthermore, the addition of a catalytic amount of $Et_4N^+Br^-$ also gave **2** in 97 % yield. The results show that quaternary ammonium salts work effectively to both activate PhI=O and enhance the reaction rate by increasing the reagent solubility.

Table 1. Oxidation of methyl *p*-tolyl sulfide (**1**) using PhI=O in H_2O

$$p\text{-TolSMe }(\mathbf{1}) \xrightarrow{\text{PhI=O-catalyst in H}_2\text{O}} p\text{-TolS(O)Me }(\mathbf{2})$$

run	catalyst	mol% (conc.)	time (hr)	yield (%)
1	none	–	4	trace
2	$[C_{16}H_{33}N^+Me_3]Br^-$	5 (1mM*)	2	quant.
3	$Et_4N^+Br^-$	5 (1mM)	2	97

*) 0.92 mM [the critical micelle concentration (cmc) of CTAB in H_2O]

Next, we examined the reaction in various organic solvents. In the presence of a small amount of water, CTAB is also capable of forming a reversed micellar system [24, 25] in nonpolar organic solvents. The interior of the reversed micelle, where the reaction is thought to take place, is extremely polar (more so than water in some cases) even in *n*-hexane. Furthermore, the concentration effect inside the micellar assembly is expected to enhance the reaction rate [24, 25]. These properties prompted us to investigate the still unexplored oxidation reactions using PhI=O in nonpolar solvents. These results are shown in Table 2. As expected, in the presence of a catalytic amount of CTAB (4 mM) and water, **2** was obtained in excellent yields even in *n*-hexane and toluene (runs 11,13). In contrast, **2** could not be obtained in the absence of the catalyst and water (runs 1-5). Using $Et_4N^+Br^-$ instead of CTAB in toluene-H_2O gave **2** only in 28% yield since $Et_4N^+Br^-$ cannot form reversed micelles[1] (run 16). Non cationic surfactants such as SDS (anionic), AOT (anionic reversed micelle-forming) and Triton X-100 (neutral reversed micelle-forming), did not promote the reaction at all (runs 17-19). Thus, both CTAB and water are indispensable for enhancing yields and the reaction rate. Incidentally, the presence of CTAB and a small amount of water also showed a remarkable rate enhancement in CH_3CN and CH_2Cl_2,

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1) As the amount of H_2O increased, the yield of **2** increased. This means that $Et_4N^+Br^-$ reacted just like a phase transfer catalyst.

standard solvents for hypervalent iodine oxidations, to give **2** in quantitative yield within 0.5 hr (runs 14,15). The difference in the reaction rates among the various solvents most likely reflects the reagent solubility in each solvent. These findings suggest that the formation of reversed micelles by CTAB enhanced the solubility, thereby the reactivity of PhI=O.

Table 2. Oxidation of methyl *p*-tolyl sulfide (**1**) using PhI=O in organic solvents

$$p\text{-TolSMe } (\mathbf{1}) \xrightarrow{\text{PhI=O-catalyst in solvent}} p\text{-TolS(O)Me } (\mathbf{2})$$

run	catalyst	mol%	solvent	time (hr)	yield (%)
1	none	–	*n*-hexane	6	no reaction
2	//	–	toluene	6	//
3	//	–	toluene-H_2O (500:1)	6	//
4	$[C_{16}H_{33}N^+Me_3]Br^-$	10	toluene	12	trace
5	//	//	*n*-hexane	12	trace
6	//	//	CH_3CN	2	11
7	//	//	CH_2Cl_2	2	71
8	//	//	toluene-H_2O (1:1)	2	60
9	//	//	toluene-H_2O (50:1)	2	66
10	//	//	toluene-H_2O (500:1)	2	77
11	//	//	//	6	quant.
12	//	//	*n*-hexane-H_2O (500:1)	2	43
13	//	//	//	12	95
14	//	//	CH_3CN-H_2O (500:1)	0.5	quant.
15	//	//	CH_2Cl_2-H_2O (500:1)	0.5	99
16	$Et_4N^+Br^-$	//	toluene-H_2O (500:1)	2	28
17	SDS*	//	//	6	trace
18	AOT**	//	//	6	trace
19	Triton X-100***	//	//	6	trace

*) sodium dodecyl sulfate **) sodium di(2-ethylhexyl)sulfosuccinate (aerosol OT)
***) $Me_3CCH_2CMe_2C_6H_4$-*p*-$(OCH_2CH_2)_xOH$

The present method is applicable to various substrates to afford corresponding sulfoxides in good yields (Table 3).

In summary, the addition of a catalytic amount of CTAB and H_2O allowed the hypervalent iodine oxidation reaction to proceed in various solvents including nonpolar organic solvents.

General experimental procedures;

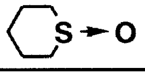
In water: To a stirred solution of CTAB (0.005 mmol) and **1** (0.10 mmol) in H_2O (5.0 mL) was added PhI=O (0.12 mmol), then the reaction mixture was stirred for 2 hr at room temperature. The mixture was extracted from ethyl acetate, dried over $MgSO_4$, evaporated, and then purified by column chromatography (SiO_2/AcOEt) to give pure **2**.

In toluene-H_2O: To a stirred suspension of CTAB (0.02 mmol) in toluene-H_2O (4.0 mL:0.01 mL) was added PhI=O (0.24 mmol), then the reaction mixture was stirred for 0.5 hr at room temperature. The toluene (1.0 mL) solution of **1** (0.20 mmol) was added to the reaction mixture and stirred for 6 hr. The mixture was filtered with celite and a $MgSO_4$ pad and the filtrate was evaporated. The residue was purified by column chromatography (SiO_2/AcOEt) to give pure **2**.

The present micellar and reversed micellar systems are thought to be very attractive and suggests their practical utility due to high yields, rate enhancements, increased choice of solvents and tolerance to moisture under neutral conditions. Their application to other reactions is under investigation in our laboratory.

Table 3. Oxidation of various sulfides to the corresponding sulfoxides in toluene-H_2O (500:1) using PhI=O-CTAB

$$\text{R-S-R'} \xrightarrow[\text{toluene-H}_2\text{O (500:1)}]{\text{PhI=O-CTAB}} \text{R-S(O)-R'}$$

run	substrate	product	yield (%)
1	*o*-TolSMe	*o*-TolS(O)Me	89
2	*o*-AnisylSMe	*o*-AnisylS(O)Me	quant.
3	PhSEt	PhS(O)Et	quant.
4	$PhCH_2SMe$	$PhCH_2S(O)Me$	quant.
5	$PhSCH_2Ph$	$PhS(O)CH_2Ph$	90
6	$(PhCH_2)_2S$	$(PhCH_2)_2S(O)$	95
7			78

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