Ionene supported peroxodisulfates: Polymeric reagents for the oxidative deprotection of *TMS* and *THP* ethers and oxidative cleavage of the C=N bond in water

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Abstract Oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers, and deprotection of phenylhydrazones, semicarbazones, and oximes to their corresponding carbonyl compounds carried out in water at reflux condition using ionene supported peroxodisulfates is reported. The reagents are recyclable and products are obtained in excellent yield under environmentally benign conditions without overoxidation to carboxylic acid.

Keywords Ionene; Peroxodisulfate; Deprotection; Oxidative Cleavage; Water.

Introduction

The protection of hydroxyl groups by converting them to trimethylsilyl and tetrahydropyranyl ethers is one of the most fundamental and widely used transformations in modern synthesis chemistry [1–3]. Direct oxidation of these ethers to their corresponding carbonyl compounds under mild conditions is also of synthetic value [4]. In addition, for the characterization and purification, carbonyl compounds are usually converted to oximes, phenylhydrazones, and semicarbazones. Therefore, oxidative cleavage of these functional groups to their corresponding carbonyl compounds under mild conditions is also of great interest [1, 5].

However, most of the reactions described in literature are carried out in anhydrous organic solvents and the reagents suffer from disadvantages including a low tolerance towards water, using acid catalysts, hygroscopicity, photosensitivity, instability, and tedious work-up procedures.

Therefore, synthesis chemists continue to explore new methods to overcome the above-mentioned disadvantages. One of these new methods is to run reactions in aqueous media [6]. Organic reactions in water, without the use of any harmful organic solvents are of great current interest, because water is an easily available, economical, safe, and environmentally benign solvent. In general, a number of the reactions described in the literature are carried out in water, but in the presence of phase transfer catalyst or an organic solvent as cosolvent.

Polymer supported reagents and catalysts have received especial attention in organic synthesis due to their selectivity and easy workup procedure [7]. The classical ion exchange resins, which are usually employed as polymeric reagents, suffer from some drawbacks. The maximum capacity is first limited by the weight of polymer backbone and loading is further restricted by *Lewis* acid catalyzed methylene crosslinking within the resin. In addition, the molar activity of the supported reagents decreases considerably during storage and can be significantly lowered compared to the original loading of counter ion because of the chemical lability of the ammonium salt which

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releases trimethylamine groups. Furthermore, another serious problem of polystyrene based reagents is their liability to oxidation and strong *Lewis* acid conditions [8]. Along these, a number of advanced and modified polymeric supports have been developed for demanding reactions over recent years [9].

Recently, we have reported oxidation of alcohols and hydroquinones to carbonyl compounds using ionene supported peroxodisulfate in water under mild conditions [10]. In connection with our ongoing

work on application of peroxodisulfate based oxidants [4g, h, 5i–k, 10], in this paper we wish to report a general method for oxidative deprotection of tetrahydropyranyl and trimethylsilyl ethers, and deprotection of phenylhydrazones, semicarbazones, and oximes to their corresponding carbonyl compounds using ionenes supported peroxodisulfate in water without using any phase transfer catalyst or organic solvent as cosolvent (Scheme 1).

Results and discussion

These reagents were obtained as follows: an aqueous solution of ionenes was added under stirring to a so-
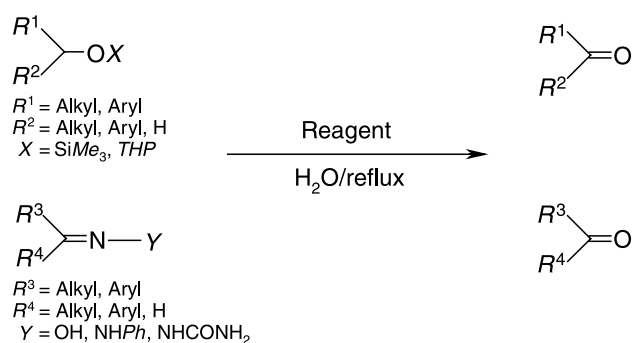
Scheme 1
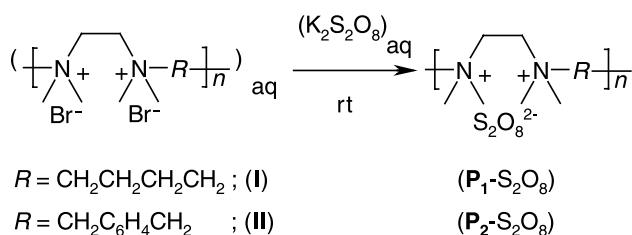
Scheme 2

Table 1 Oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers to the carbonyl compounds using P_1-S_2O_8 and P_2-S_2O_8[a]

Entry	Substrate	P_1-S_2O_8			P_2-S_2O_8			Ref.
		Reagent/ Substrate	Time/ min	Yield[b,c]/ %	Reagent/ Substrate	Time/ min	Yield[b,c]/ %	
1	$C_6H_5CH_2OSiMe_3$	1	15	96	1	30	97	[12a]
2	$(C_6H_5)_2CHOSiMe_3$	1	20	93	1	35	94	[12a]
3	p-$ClC_6H_4CH_2OSiMe_3$	1	15	99	1	30	95	[12a]
4	p-$BrC_6H_4CH_2OSiMe_3$	1	20	95	1	35	93	[12a]
5	p-$NO_2C_6H_4CH_2OSiMe_3$	1	20	65	1	60	83	[12a]
6	$C_6H_5CH_2CH_2OSiMe_3$	2	60	90	2	70	89	[12a]
7	$CH_3(CH_2)_5CH_2OSiMe_3$	2	75	78	2	80	86	[12a]
8	$CH_3(CH_2)_6CH_2OSiMe_3$	2	80	75	2	85	87	[12a]
9	$C_6H_5CH=CHCH_2OSiMe_3$	1	20	83	1	40	91	[12a]
10	Hydroquinone bis(trimethylsilyl) ether	1	15	96	1	30	97	[12a]
11	*tert*-Butylhydroquinone bis(trimethylsilyl) ether	1	15	94	1	30	94	[12b]
12	$C_6H_5CH_2OTHP$	1	25	93	1	45	96	[12a]
13	$(C_6H_5)_2CHOTHP$	1	25	94	1	50	94	[12a]
14	o-$ClC_6H_4CH_2OTHP$	1	22	94	1	45	92	[12a]
15	p-$MeC_6H_4CH_2OTHP$	1	18	92	1	40	96	[12a]
16	$CH_3(CH_2)_5CH_2OTHP$	1	60	85	1	75	87	[12a]
17	$CH_3CH=CHCH_2OTHP$	1	30	89	1	55	89	[12a]
18	Cyclohexanol tetrahydropyranyl ether	2	40	87	2	60	91	[12a]

[a] Reactions were carried out in water at reflux temperature
[b] All products were characterized spectroscopically (^1H NMR, IR) and showed physical and spectral data in accordance with their expected structure and by comparison with authentic samples
[c] Yields refer to pure isolated products

lution of potassium peroxodisulfate in water at room temperature (Scheme 2). After 1 h, bromide ions were completely replaced by $S_2O_8^{2-}$. The products were successively washed with water and acetone and dried under reduced pressure. These reagents are stable white powders which could be stored for months without losing their activity. The ionene bromides (**I**, **II**) were prepared according to the literature procedure [11]. The content of active oxidizing agent ($S_2O_8^{2-}$) was determined by the titrimetric method [7f]. The loading of the peroxodisulfate was calculated to be 2.7 mmol per gram of reagent ($\mathbf{P_1}$-S_2O_8) and 2.4 mmol per gram of reagent ($\mathbf{P_2}$-S_2O_8).

The effect of solvent on the oxidation reaction was evaluated by carrying out the oxidation in a series of solvents with varying polarity. Oxidation of benzyl trimethylsilyl ether with these reagents proceeds smoothly in aprotic solvents such as dichloromethane, chloroform, tetrahydrofuran, *n*-hexane, and acetonitrile at reflux temperature, whereas oxidations in acetonitrile:water (10:90) or water at reflux conditions were accomplished more rapidly.

In order to evaluate the generality and applicability of this method we have converted a variety of tetrahydropyranyl ethers, trimethylsilyl ethers, phenylhydrazones, semicarbazones, and oximes to their corresponding carbonyl compounds in water at reflux temperature using $\mathbf{P_1}$-S_2O_8 and $\mathbf{P_2}$-S_2O_8 in excellent yields (Tables 1 and 2). On completion of the reaction, these polymer supported peroxodisulfates
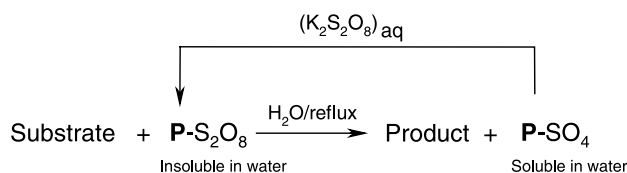
Table 2 Deprotection of phenylhydrazones, semicarbazones and oximes to their corresponding carbonyl compounds using $\mathbf{P_1}$-S_2O_8 and $\mathbf{P_2}$-S_2O_8[a]

Entry	Substrate	$\mathbf{P_1}$-S_2O_8		$\mathbf{P_2}$-S_2O_8		Ref.
		Time/min	Yield[b,c]/%	Time/min	Yield[b,c]/%	
1	$C_6H_5CHNNHC_6H_5$	45	95	45	93	[12a]
2	*o*-$ClC_6H_4CHNNHC_6H_5$	55	95	65	91	[12a]
3	*p*-$ClC_6H_4CHNNHC_6H_5$	50	96	60	95	[12a]
4	*p*-$MeOC_6H_4CHNNHC_6H_5$	60	96	40	96	[12a]
5	*p*-$MeC_6H_4CHNNHC_6H_5$	60	94	55	92	[12a]
6	*p*-$NO_2C_6H_4CHNNHC_6H_5$	70	72	90	78	[12a]
7	$(C_6H_5)_2CNNHC_6H_5$	55	96	50	94	[12a]
8	$C_6H_5CH_2CH_2CHNNHC_6H_5$	70	83	80	86	[12a]
9	Cyclohexanone phenylhydrazone	60	87	80	89	[12a]
10	$C_6H_5CH=CHCHNNHC_6H_5$	60	92	70	91	[12a]
11	$C_6H_5CHNNHCONH_2$	60	95	60	94	[12a]
12	*p*-$ClC_6H_4CHNNHCONH_2$	55	95	55	94	[12a]
13	*o*-$ClC_6H_4CHNNHCONH_2$	60	95	60	92	[12a]
14	*p*-$BrC_6H_4CHNNHCONH_2$	50	93	60	96	[12a]
15	*m*-$MeOC_6H_4CHNNHCONH_2$	60	94	45	95	[12a]
16	*p*-$MeOC_6H_4CHNNHCONH_2$	50	96	40	97	[12a]
17	*o*-$NO_2C_6H_4CHNNHCONH_2$	70	76	80	78	[12a]
18	$(C_6H_5)_2CNNHCONH_2$	60	97	45	96	[12a]
19	$C_6H_5CH_2CH_2CHNNHCONH_2$	70	83	100	81	[12a]
20	C_6H_5CHNOH	45	93	60	95	[12a]
21	*p*-MeC_6H_4CHNOH	47	96	60	93	[12a]
22	*p*-$MeOC_6H_4CHNOH$	50	96	55	96	[12a]
23	*m*-$ClC_6H_4C(CH_3)NOH$	50	95	60	93	[12a]
24	*o*-$ClC_6H_4C(CH_3)NOH$	45	95	65	91	[12a]
25	*p*-$NO_2C_6H_4C(CH_3)NOH$	55	75	90	85	[12a]
26	$(C_6H_5)_2CNOH$	45	94	60	92	[12a]
27	$C_6H_5CH_2CH_2CHNOH$	70	81	100	78	[12a]
28	Cyclohexanone oxime	75	84	90	81	[12a]
29	$C_6H_5CH=CHCHNOH$	55	93	70	91	[12a]

[a] Reactions were carried out in water at reflux temprature using reagent:substrate of 4:1
[b] All products were characterized spectroscopically (^{1}H NMR, IR) and showed physical and spectral data in accordance with their expected structure and by comparison with authentic samples
[c] Yields refer to pure isolated products

$$\text{Substrate} + \mathbf{P\text{-}S_2O_8} \xrightarrow[\text{Insoluble in water}]{\substack{(K_2S_2O_8)_{aq} \\ H_2O/reflux}} \text{Product} + \mathbf{P\text{-}SO_4} \text{ (Soluble in water)}$$

Scheme 3

convert to corresponding ionenes bearing sulfate ion which are completely soluble in water. It is noteworthy that, unlike other oxidative hydrolytic methods, the major drawback of over-oxidation of the resulting aldehydes, is not observed under the reaction conditions. Interestingly the α,β-unsaturated derivatives underwent deprotection very efficiently without affecting the olefinic bond and the reactions are essentially chemoselective (Table 1, entries 9 and 17) and (Table 2, entries 10 and 29).

It is clear from Tables 1 and 2 that aliphatic substrates are oxidized over longer reaction times.

Another surprising feature of this method is that separation of the organic products by extraction leaves a residue that was soluble in water ($\mathbf{P_1}$-SO$_4$ and $\mathbf{P_2}$-SO$_4$), in which addition of a freshly prepared $K_2S_2O_8$ solution regenerates the ionenes supported peroxodisulfate ($\mathbf{P_1}$-S$_2$O$_8$ and $\mathbf{P_2}$-S$_2$O$_8$) in quantitative yields (Scheme 3). Therefore, this method represents an environmentally friendly chemistry, which could be applied for industrial uses as well.

Work on investigating some organic transformations with these novel polymeric reagents is currently in progress in our laboratory and the results will be reported in due course.

In conclusion, the present method represents an efficient and environmentally friendly synthesis method for oxidative deprotection reactions under organic-solvent-free conditions. The advantages of using ionene supported peroxodisulfate resins in terms of their ease of preparation, simplicity, mildness of condition, and good product yields make them more advantageous than previously reported methods.

Experimental

The reactions were monitored by TLC using silica gel plates and the products purified by flash column chromatography on silica gel (Merck, 230–400 mesh), and they were identified by comparison of their spectra and physical data with those of authentic samples. ^{1}H NMR spectra were measured at 90 MHz on a JEOL spectrometer with tetramethylsilane as an internal reference and CDCl$_3$ as the solvent. IR spectra were recorded on a Pye-unicam SP 1100 spectrophotometer. Elemental analysis was performed on a LECO 250 instrument.

Preparation of ionone supported peroxodisulfate

To an aqueous solution of 1 g ionene in 5 cm^3 H$_2$O was added a solution of 1.62 g potassium peroxodisulfate (6 mmol) in 30 cm^3 H$_2$O. The mixture was stirred at room temperature for 30 min. The resulting white solid product was filtered off, washed with 10 cm^3 distilled H$_2$O, and dried in a desiccator under vacuum. The content of active oxidizing agent (S$_2$O$_8$$^{2-}$) was determined by the titrimetric method of Ref. [7f].

General procedure for conversion of trimethylsilyl and tetrahydropyranyl ethers, phenylhydrazones, semicarbazones, and oximes to their corresponding carbonyl compounds with P-S_2O_8

A mixture of 1 mmol substrate, 10 cm^3 H$_2$O, and 1–4 mmol $\mathbf{P}$-S$_2$O$_8$ was placed in a 25 cm^3 round bottomed flask and stirred at reflux temperature. After completion of the reaction (monitored by TLC), the reaction mixture was cooled and extracted with 3×10 cm^3 diethyl ether. The combined organic layers were washed with brine, and dried over anhydrous Na$_2$SO$_4$. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel to afford the pure product.

Regeneration procedure for P-S_2O_8

After completion of the oxidation reaction and isolation of the product, the aqueous phases were combined and washed with diethyl ether. Upon addition of freshly prepared $K_2S_2O_8$ to the aqueous layer, a white powder immediately precipitated, which was filtered off. The filter cake was washed with 3×10 cm^3 distilled H$_2$O, and dried in a vacuum desiccator over CaCl$_2$ for subsequent reactions.

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