

# Polymeric Analog of Isoxazolinium Permanganate: Preparation and Use as Synthetic Reagent

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**ABSTRACT:** A crosslinked polystyrene-supported solid phase analog of isoxazolinium permanganate was prepared and used as a recyclable oxidizing reagent. The reagent was prepared by a series of polymer-analogous reactions starting from styrene-divinyl benzene (DVB) and styrene-ethyleneglycol dimethacrylate (EGDMA) (2%) crosslinked polymer. The reagent was found to oxidize alcohols to carbonyl compounds in near-quantitative yield. The EGDMA crosslinked polystyrene-supported isoxazolinium permanganate was found to be more efficient in terms of capacity, reaction time, and product yield. The spent polymeric reagent after the oxidation step can be easily removed by filtration and can be regenerated and reused several times. © 1997 John Wiley & Sons, Inc. *J Appl Polym Sci* **65**: 1169–1174, 1997

## INTRODUCTION

The field of immobilizing chemical reagents on crosslinked polymer support has received wide application in recent years<sup>1–5</sup> after the introduction of the solid-phase peptide synthesis by Merrifield.<sup>6</sup> It has been found that reagents supported on insoluble polymers are particularly convenient for solving many problems in organic synthesis.<sup>7,8</sup> In most cases, the ability of the polymer to be regenerated is critical, since few reactions could justify the use of a custom-made polymer which would be discarded once the reaction has been carried out. In addition, a polymer matrix can be so selected or tailor-made to provide a specific microenvironment that may induce some specificity at the reaction site.<sup>9</sup>

An attempt toward the realization of the advantages of polymeric reagents in the design and development of crosslinked polystyrene-supported analogs of isoxazolinium permanganate forms the subject matter of this article. Permanganate ion is a versatile reagent used for effecting

a vast number of synthetic reactions in the laboratory and industrial organic synthesis.<sup>10</sup> Oxidation of organic substrate by  $\text{KMnO}_4$  poses many problems. Most of the organic solvents are either readily oxidized by  $\text{KMnO}_4$  or they do not dissolve the permanganate in appreciable amounts. This factor reduces the effectiveness of permanganate as an oxidizing agent. It occurred to us that these difficulties can be overcome to some extent by incorporating the corresponding reagent function into the crosslinked polystyrene matrix without appreciable loss of reactivity.

## EXPERIMENTAL

Monomers were purified by low-pressure distillation. Commercially available low molecular weight compounds were purified by distillation or recrystallization unless otherwise stated. Microanalyses were done at Regional Sophisticated Instrumentation Centre, IIT, Madras, and CDRI, Lucknow. Infrared (IR) spectra were recorded on a Perkin–Elmer-397 Spectrometer using KBr pellets. Styrene-divinyl benzene (DVB) and styrene-ethyleneglycol dimethacrylate (EGDMA) crosslinked polystyrene resins were prepared by the

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suspension polymerization method. Chloromethylation of polystyrene and the subsequent oxidation<sup>11</sup> and esterification<sup>12</sup> reactions were done according to literature procedures.

#### Preparation of Polystyrene-Bound 1,3 Diketone

Carbomethoxy polystyrene resin (10 g), preswollen in THF (20 mL), was refluxed with acetophenone (15 mL) in the presence of sodium ethoxide (5 g) for 12 h. The mixture was cooled to room temperature and dilute H<sub>2</sub>SO<sub>4</sub> (20 mL) was added and stirred for 30 min. It was then filtered at the pump, washed with water, ethanol, and acetone (20 mL × 3 times each), dried, and weighed. The yield was 10.9 and 11.2 g and capacity 2.6 and 2.9 mEq/g, respectively, for resins 6a and 6b.

#### Preparation of Polymeric Isoxazole Resin

Polymeric  $\beta$ -diketo resin (10 g) was heated to reflux with hydroxylamine hydrochloride (4 g) in the presence of pyridine (10 mL) for 12 h. The mixture was cooled to room temperature and water (10 mL) was added, filtered at the pump, washed with water, acetonitrile, ethanol, and acetone (20 mL × 3 times each), dried, and weighed. The yield was 9.8 and 9.7 g and capacity 1.8 and 2.0 mEq/g, respectively, for resins 7a and 7b.

#### Quaternization of Polymeric Isoxazole Resin with Methyl Iodide

Polymeric isoxazole resin (10 g), preswollen in acetonitrile (20 mL), was reacted with methyl iodide (10 mL) at the refluxing temperature for 10 h. After the reaction, the mixture was filtered, washed with water, ethanol, and acetone (20 mL × 3 times each), dried, and weighed. The yield was 10.5 and 10.6 g and capacity 1.4 and 1.7 mEq/g, respectively, for resins 8a and 8b.

#### Preparation of Polymeric Isoxazolinium Permanganate Resin

Quaternized polymeric isoxazole (10 g) was reacted with potassium permanganate (12 g) in an acetone–water mixture (2 : 1 v/v, 25 mL) at 0°C for 4 h. After the reaction, the mixture was filtered, washed with water, ethanol, and acetone (20 mL × 3 times each), dried, and weighed. The yield was 9.7 and 9.8 g and capacity 1.2 and 1.4 mEq/g, respectively, for resins 9a and 9b.

#### Estimation of Permanganate Ion in the Functionalized Resin

A definite amount (0.5 g) of the functionalized resin was accurately weighed and suspended in H<sub>2</sub>SO<sub>4</sub> (2N, 30 mL) containing acetone (10 mL). The resin was allowed to swell in the medium for ~ 1 h. A known excess of standard ferrous ammonium sulfate solution was added and stirred until the dark color of the resin completely disappeared and turned to almost white. The unreacted ferrous ammonium sulfate solution was titrated against standard KMnO<sub>4</sub> solution. From the titer values, the permanganate equivalent of isoxazolinium permanganate was calculated.

#### Recycling and Reuse of the Spent Permanganate Resin

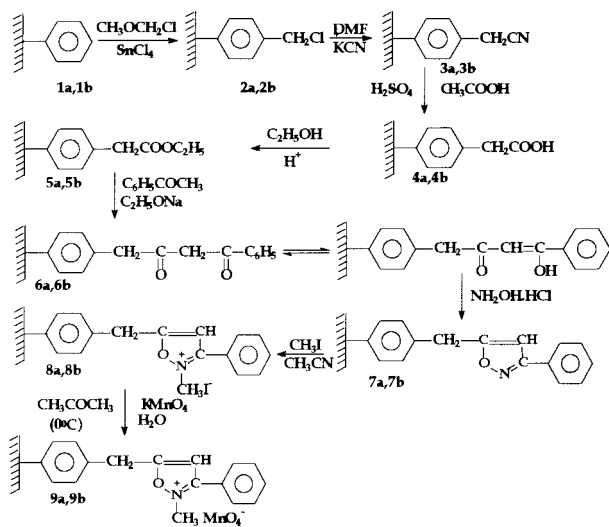
The spent polymeric reagent (5 g) collected from different experiments was stirred for 2 h with 2N solution (50 mL) of ferrous ammonium sulfate in the presence of 2N H<sub>2</sub>SO<sub>4</sub> (20 mL) to remove all oxides of manganese. The resin was filtered, washed with water, and dried. The regenerated polymer was functionalized with permanganate following the procedure described earlier. The refunctionalized permanganate resin was used for oxidation of alcohols as described earlier.

## RESULTS AND DISCUSSION

#### Preparation and Characterization of the Reagent

In the present article, 2% crosslinked polystyrene (styrene-DVB) (1a) and (styrene-EGDMA) (1b) resins were used as the macromolecular supports because of the favorable physical characteristics and ease of functionalization. The polystyrene beads were converted to isoxazolinium permanganate by a series of polymer-analogous reactions. The reaction sequence is depicted in Scheme 1.

A chloromethyl group was introduced into polystyrene resin beads (1a,1b) by Friedel Crafts reaction with chloromethyl methyl ether using Lewis acid catalyst.<sup>13</sup> The substitution of the chloromethyl group was evidenced by the strong absorption band in IR spectrum around 690 cm<sup>-1</sup> (C—Clstr). The chloromethyl polystyrene (2a,2b) on reaction with KCN in the DMF–water mixture resulted in the formation of cyanomethyl polystyrene<sup>14,15</sup> (3a,3b) which was characterized by IR absorption band at 2240 cm<sup>-1</sup> (C≡Nstr). The cyanomethyl polystyrene was then hy-



Scheme 1

drolized with an  $\text{H}_2\text{SO}_4$ -acetic acid mixture, which gave carboxylic acid resin<sup>11</sup> (4a,4b). The formation of an acid group in the resin was supported by IR absorption bands at  $1690\text{ cm}^{-1}$  ( $\text{C}=\text{O}_{\text{str}}$ ) and  $1420\text{ cm}^{-1}$  ( $\text{C}-\text{O}_{\text{str}}$ ). The acid-functionalized resin (4a,4b) on treatment with absolute ethanol in the presence of a small amount of  $\text{H}_2\text{SO}_4$  converted the acid group to an ester function,<sup>12</sup> formation of which was evidenced by absorption bands at  $1700\text{ cm}^{-1}$  ( $\text{C}=\text{O}_{\text{str}}$ ) and  $1240\text{ cm}^{-1}$  ( $\text{C}-\text{O}_{\text{str}}$ ) in the IR spectrum. The carboethoxy polystyrene resin (5a,5b) was converted to the  $\beta$ -diketo resin (6a,6b) by Claisen condensation with acetophenone and sodium ethoxide. The  $\beta$ -diketo resin was a tautomeric product as evidenced from IR absorption bands. The absorption bands at  $1680$ – $1700\text{ cm}^{-1}$  (strong absorption bands at  $1680\text{ cm}^{-1}$  with a shoulder at  $1700\text{ cm}^{-1}$ ) were assigned to two  $\text{C}=\text{O}$  stretching vibrations of the keto form. The IR spectra showed enol absorption bands at  $1560$ – $1640\text{ cm}^{-1}$  which were assigned to  $\text{C}=\text{O}\cdots\text{H}$  and  $\text{C}=\text{C}$  stretching vibrations, characteristic of cyclic intramolecular hydrogen bonded molecules. The  $\beta$ -diketo resin was converted to the isoxazole-function-alized resin (7a,7b) by reaction with hydroxylamine hydrochloride in pyridine. The formation of polystyrene-bound isoxazole resin was evidenced by IR spectral values at  $1630\text{ cm}^{-1}$  ( $\text{C}=\text{N}_{\text{str}}$ ) and  $1650\text{ cm}^{-1}$  ( $\text{C}=\text{C}_{\text{str}}$ ) and also from nitrogen estimation. The isoxazole resin was then subjected to quaternization reaction using methyl iodide. The formation of quaternized resin (8a,8b) was evidenced by absorption band at  $2900$

$\text{cm}^{-1}$  ( $\text{N}-\text{CH}_3_{\text{str}}$ ). The quaternized resin was then converted to the respective permanganate resin (9a,9b) by reaction with  $\text{KMnO}_4$  solution in acetone. The resin showed an intense absorption band at  $900\text{ cm}^{-1}$  due to  $-\text{MnO}_4$  stretching.

The capacities of the resins 2a,b–9a,b were determined from the weight changes and verified by quantitative determination of the functional groups. The carboxylic group in the resin (4a,4b) was estimated by alkalimetric titration and ester group in the resin (5a,5b) by the saponification method. The  $\beta$ -diketo resin (6a,6b) was estimated by the acetylation method and isoxazole resin (7a,7b) by elemental analysis. The capacity of  $\text{I}^-$  incorporated in the isoxazolinium iodide resin (8a,8b) was determined by treatment of the resin with  $\text{AgNO}_3$  solution followed by determination of the displaced iodide as silver iodide. The permanganate capacity of the resin (9a,9b) was determined by direct or excess back titration with ferrous ammonium sulfate solution in the presence of dilute  $\text{H}_2\text{SO}_4$ . The capacities were found to be  $1.2\text{ mEq/g}$  and  $1.4\text{ mEq/g}$  for DVB and EGDMA crosslinked resins, respectively.

In all the steps of polymer-analogous conversions on the crosslinked macromolecular matrix, a remarkable dependence of the solvent and the extent of swelling was observed. As is the general case with heterogeneous reactions, the different functional group conversions carried out on a polystyrene matrix never proceeded to give quantitative yields. There existed the possibility of the presence of residual unreacted groups in each step. But these groups never posed any hurdles in the chemical reactivity of the final reagent. These groups might have been inaccessible to low molecular weight reagents during the synthetic steps, as they were either flanked by crosslinks or buried deep in the interior of the macromolecular network.

### Oxidation of Alcohols Using Polymer-Bound Isoxazolinium Permanganate Resin

The isoxazolinium permanganate resin was observed to be capable of oxidizing primary and secondary alcohols to the corresponding carbonyl compounds. Primary alcohols were converted to aldehydes and secondary alcohols to ketones in isolable yields ranging from 80 to 90%. The oxidation involved stirring of the alcohol with a twofold molar excess of the permanganate resin in solvents like chloroform or methylene chloride at  $30^\circ\text{C}$ . The workup of the reaction mixture involved

**Table I** Oxidation of Alcohols Using Polystyrene-Supported Isoxazolinium Permanganate Reagent

Alcohol <sup>a</sup>	Time (h) <sup>b</sup>		Product <sup>e</sup>	Isolated Yield (%)		m.p./(b.p)
	9a <sup>c</sup>	9b <sup>d</sup>		9a	9b	
Benzoin	18	16	Benzil	88	88	95
Benzhydrol	22	21	Benzophenone	85	85	49
Benzyl alcohol	27	25	Benzaldehyde	80	83	(179)
<i>n</i> -Butanol	24	22	<i>n</i> -Butyraldehyde	80	85	(75)
Cholesterol	30	29	$\Delta^5$ -Cholestenone	65	78	85
Cis-1,2-cyclohexanediol	20	19	2-Hydroxy-cyclohexanone	84	83	105
<i>p</i> -Nitrobenzyl alcohol	29	27	<i>p</i> -Nitrobenzaldehyde	85	88	58
$\alpha$ -Phenylethanol	26	24	Acetophenone	80	85	(202)
<i>p</i> -Methylbenzyl alcohol	24	23	<i>p</i> -Methylbenzaldehyde	82	82	205
<i>p</i> -Methoxy- $\alpha$ -phenyl ethanol	25	22	<i>p</i> -Methoxy-acetophenone	84	85	39

<sup>a</sup> Resin-to-alcohol ratio, 2 : 1; solvent, chloroform; temperature, 30°C.

<sup>b</sup> Includes time for pre-swelling also.

<sup>c</sup> 9a, DVB-crosslinked polystyrene-supported isoxazolinium permanganate reagent.

<sup>d</sup> 9b, EGDMA-crosslinked polystyrene-supported isoxazolinium permanganate reagent.

<sup>e</sup> Characterized by comparison with authentic samples.

filtration of the spent residue, washing and removal of the solvent from the combined filtrate, and washings to afford the oxidized product. The different alcohols which were oxidized using this procedure, the yield, and conditions of oxidation are presented in Table I.

Oxidation with this polymer-supported isoxazolinium permanganate reagent showed some distinct differences from the oxidation with  $\text{KMnO}_4$ . Oxidation of alcohols with  $\text{KMnO}_4$  generally yields the corresponding acids through the intermediate carbonyl compound. But in the case of polymer-supported permanganate, the oxidation stops at the carbonyl stage, even with a large excess of the polymer-supported permanganate and extended duration of the reaction. This can be assumed as the effect of the crosslinked polymer matrix. Absence of products of overoxidation made product isolation and purification steps easy, contrary to the observation with the low molecular weight reagents. The polystyrene-supported isoxazolinium permanganate did not show any selectivity based on the nature of the alcohol, whether the hydroxy group was attached directly to a ring structure or not, contrary to poly(4-vinylpyridinium permanganate) resin,<sup>16</sup> which was not able to oxidize alcoholic groups attached to an aliphatic ring structure.

Compared to DVB-crosslinked isoxazolinium permanganate resin, EGDMA-crosslinked reagent showed a slightly higher reactivity. This

can be explained by considering the nature of the crosslinking agent, EGDMA. This is a flexible and polar crosslinker, i.e., incorporation of this comonomer imparts flexibility and polarity or hydrophilicity to the polymer support. This makes the support able to swell considerably in polar solvents. In the swollen resin, functional groups are more accessible to the substrate in solution, thus enhancing the extent of reaction. But in the case of DVB-crosslinked resin, the presence of hydrophobic DVB in the support makes the support more rigid, thus preventing it from swelling in polar solvents, resulting in a decreased reactivity.

### Effect of Various Reaction Conditions on the Extent of Oxidation

#### Effect of Solvent

The systematic investigation of the effect of solvent used in the oxidation of alcohols using polystyrene-supported isoxazolinium permanganate resin reveals that THF is the most effective solvent. The oxidation reactions were carried out in solvents of varying polarity. The time for maximum conversion for the oxidation of benzoin in various solvents is given in Table II.

The hydrophilic/hydrophobic nature of the solvents which affects their polarity influences the swelling characteristic of the polymer support and nature of the attached reagent function, and

**Table II Effect of Solvents on the Oxidation of Benzoin Using Polystyrene-Supported Isoxazolinium Permanganate Resin**

Solvent	Time for Complete Conversion (h) <sup>a</sup>	
	9a <sup>b</sup>	9b <sup>c</sup>
Dichloromethane	22	20
Tetrahydrofuran	14	15
Chloroform	18	16
Acetonitrile	17	13
Benzene	22	19
Dioxane	21	18
Cyclohexane	23	20

<sup>a</sup> Resin-to-alcohol ratio, 2 : 1; temperature, 30°C.

<sup>b</sup> 9a, DVB-crosslinked polystyrene-supported isoxazolinium permanganate.

<sup>c</sup> 9b, EGDMA-crosslinked polystyrene-supported isoxazolinium permanganate.

thereby affects the efficiency of the synthetic reaction. DVB-crosslinked polystyrene support is highly hydrophobic in nature, and the attached isoxazolinium permanganate groups have polar characteristics. Therefore, solvents of medium polarity like THF were found to be more efficient.

#### Effect of Molar Excess

The extent of oxidation using polymer-supported isoxazolinium permanganate was found to be dependent on the concentration of the reagent function. The oxidation reaction was conducted at different reagent-to-substrate ratios in order to study the effect of the relative concentration of the resin. Oxidation of benzoin to benzil was selected as the model reaction. The results are given in Table III.

The permanganate content of the spent reagent was determined by the usual titrimetric method and it was found that many of the resins retained reasonable capacity after the reaction when a high resin-to-substrate ratio was taken. The resins were found to be usable in further reactions.

#### Effect of Temperature

One of the major factors influencing the rate of the polymer-supported oxidation reaction is temperature. In order to study the effect of temperature on the reactivity of polystyrene-supported isoxazolinium permanganate reagent, oxidation reactions were conducted at various reaction temperatures ranging from 20°C to 60°C. The results

are given in Table IV. The increased reactivity of the resin at higher temperature may be due to the attainment of the required activation energy by the molecules.

#### Recyclability of the Spent Resins for Further Reactions

The spent polymeric reagent from the oxidation step can be regenerated in a single step without any loss of activity for subsequent reactions. The spent reagent can be freed effectively from soluble reagents or products by washing with solvents. The partially spent reagent on washing with ferrous ammonium sulfate in presence of dilute H<sub>2</sub>SO<sub>4</sub> removed all the unreacted permanganate residues. This resin on treatment with KMnO<sub>4</sub> in aqueous acetone regenerated the permanganate resin. The recycling process can be repeated several times without appreciable loss of activity and the resulting resin can be used for subsequent reaction. The details of the oxidation reaction using the recycled resins up to five times are given in Table V.

The foregoing investigations indicate that the essential requirements for a solid phase polymeric reagent can be achieved in the design of cross-linked polystyrene-supported isoxazolinium permanganate for organic oxidations. The advantages of these new reagents include operational simplicity and recyclability. The reduction in reactivity compared to the nonpolymeric analog characteristic of polymer-supported heterogeneous reactions can be exploited to advantage in providing

**Table III Oxidation of Benzoin Using Polystyrene-Supported Isoxazolinium Permanganate Resin with Different Resin-to-Alcohol Ratios**

Molar Ratio	% Conversion after 10 h <sup>a</sup>	
	9a <sup>b</sup>	9b <sup>c</sup>
1 : 1	20	30
1 : 2	28	36
1 : 3	38	48
1 : 4	46	55
1 : 5	58	62

<sup>a</sup> Solvent, chloroform; temperature, 30°C.

<sup>b</sup> 9a, DVB-crosslinked polystyrene-supported isoxazolinium permanganate.

<sup>c</sup> 9b, EGDMA-crosslinked polystyrene-supported isoxazolinium permanganate.

**Table IV Effect of Temperature on Oxidation of Benzoin Using Polystyrene-Supported Isoxazolinium Permanganate Resin**

Resin	Time for Complete Conversion (h) <sup>a</sup>				
	20°C	30°C	40°C	50°C	60°C
DVB-crosslinked reagent	24	18	13	8	6
EGDMA-crosslinked reagent	21	16	10	6	4

<sup>a</sup> Resin-to-alcohol ratio, 2 : 1, solvent, chloroform.

selectivity to the reactions. Polystyrene-supported isoxazolinium permanganate resins described here bear a contrast to the poly(4-vinyl pyridinium permanganate) resin in that they bring about the oxidation of the alcoholic groups directly attached to the ring structure. A systematic study of the effect of solvent on the oxidation using polystyrene-supported isoxazolinium permanganate resin revealed that solvents with medium polarity are much more efficient in oxidation reactions. The oxidation of alcohol using varying temperatures and molar excess of reagent indicates a linear relationship with increases in temperature and concentration on the rate of reaction. The product isolation and purification steps in the oxidation reaction using this reagent was made easy by the fact that no product of overoxidation was observed, and soluble manganese salt

or other impurities were not found in the reaction mixture once the oxidation was complete.

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**Table V Oxidation Reaction Using Recycled Resin**

No. of Cycles	Capacity (mEq/g)		Isolated Yield (%) <sup>c</sup>	
	9a <sup>a</sup>	9b <sup>b</sup>	9a <sup>a</sup>	9b <sup>b</sup>
1	1.2	1.4	88	88
2	1.1	1.3	86	86
3	1.0	1.2	84	85
4	1.0	1.2	84	85
5	0.9	1.0	82	83

<sup>a</sup> 9a, DVB-crosslinked polystyrene-supported isoxazolinium permanganate.

<sup>b</sup> 9b, EGDMA-crosslinked polystyrene-supported isoxazolinium permanganate.

<sup>c</sup> Alcohol, benzoin; solvent, chloroform; temperature, 30°C; resin-to-alcohol ratio, 2 : 1.