

Wet Silica-Supported Permanganate: A Mild and Inexpensive Reagent for Highly Enantiomeric Purity Conversion of α -Sulfinyl Oximes and α -Sulfinyl Hydrazones to α -Keto Sulfoxides

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(Received 27 September 2003, Accepted 29 May 2004)

Wet silica-supported potassium permanganate was used as an inexpensive and efficient reagent for conversion of α -sulfinyl oximes **1** and α -sulfinyl hydrazones **2** to the corresponding α -keto sulfoxides (**3**) in high yields and high enantiomeric purity under solvent-free conditions.

Keywords: Deprotection, Wet silica, Solvent-free

INTRODUCTION

β -Keto sulfoxides are very important starting materials, in asymmetric synthesis [1,2], and can be synthesized by the cleavage of the C=N bonds of α -sulfinyl oximes and α -sulfinyl hydrazones. These compounds have been prepared by the addition of aryl methyl sulfoxides to aryl N-oxides [3] or addition of lithiated N,N-dimethyl hydrazones to menthyl sulfinate esters [4]. The hydrolysis of C=N double bond of α -sulfinyl oximes **1** and α -sulfinyl hydrazones **2** by classical method [5] was attempted but the optical purity and yield obtained were low (*i.e.*, <35 and <50%, respectively). This may be due to production of HCl during the reaction, which is able to racemize the chiral sulphur center.

Over the last two decades, the use of solid supports has become popular due to their characteristic properties such as enhanced selectivity and reactivity, straightforward work-up

procedure, milder reaction conditions and associated ease of manipulation [6]. Adsorption of potassium permanganate [7] on the surface of solid supports changes the selectivity and reactivity in various reactions [8]. We previously reported potassium permanganate supported on alumina for the oxidation of urazoles to triazolinediones [9a], alcohols to aldehydes and ketones under solvent-free conditions [9b], sulfides and thiols to sulfoxides and disulfides [9c]. The reagent was also used for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers and ethylene acetals to the corresponding carbonyl compounds [9d], as well as conversion of oximes to carbonyl compounds under solid-state conditions [9e]. There has also been increasing interest in reactions that proceed in the absence of solvent [10,11]. We now report potassium permanganate supported on wet silica gel as an inexpensive, selective and efficient reagent for conversion of α -sulfinyl oximes **1** and α -sulfinyl hydrazones **2** to the corresponding β -keto sulfoxides **3** in high yields and high enantiomeric purity under solvent-free conditions.

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Table 1. Conversion of **1** or **2** to the Corresponding Carbonyl Compounds **3**^{a,b}

Starting material	Product	Reaction time (min)	Yield (% ^c)	e.e (%)
1a	3a	8	98	98
1b	3b	8	95	99
1c	3c	10	98	100
1d	3d	15	95	100
1e	3e	10	99	100
1f	3f	20	97	99
1g	3g	15	99	98
1h	3h	20	96	99
1i	3i	20	96	98

^a Confirmed by comparison with authentic samples (IR, TLC and ¹H NMR) [1-5]. ^b Substrate/reagent (1:3). ^c Yield of isolated pure product after purification.

Table 2. Conversion of **2** to the Corresponding Carbonyl Compounds **3**^{a,b}

Starting material	Product	Reaction Time (min)	Yield (% ^c)	e.e (%)
2a	3a	10	96	98
2b	3b	15	98	98
2c	3c	15	95	100
2d	3d	20	97	99
2e	3e	20	97	100
2f	3f	20	99	98
2g	3g	20	96	98
2h	3h	20	99	100
2i	3i	15	98	99

^a Confirmed by comparison with authentic samples (IR, TLC and ¹H NMR) [1-5]. ^b Substrate/reagent (1:3). ^c Yield of isolated pure product after purification.

EXPERIMENTAL

Chemical and Apparatus

Yields refer to isolated products after purification. The products were characterized by comparing their spectral (IR, ¹H NMR), TLC and physical data with those of authentic samples [1-5]. Starting materials were synthesis by known methods [1-5]. All ¹H NMR spectra were recorded at 300

MHz in CDCl₃ relative to TMS as an internal standard. All reactions were carried out under solvent-free conditions at room temperature. Silica gel 60 (230-400 mesh) was purchased from Merck. All of the starting materials are R and 100% optically pure and have been made by reported methods [1-4].

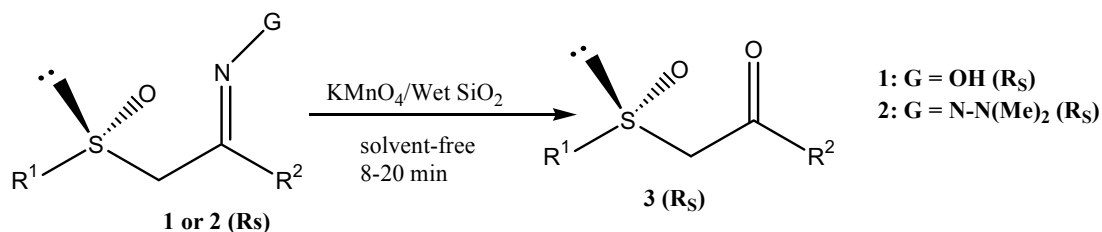
General Procedure

The procedure used for the oxidation of compounds **1** or **2** compound **3** was as follows. Wet silica gel was prepared by shaking silica gel (20 g, 230-400 mesh) with distilled water (5 ml). The reagent was prepared by mixing KMnO₄ (3 mmol, 0.48 g) with wet-silica gel (3 g) using a pestle and mortar until a fine, homogeneous and purple powder was obtained. A mixture of α -sulfinyl oximes **1** or α -sulfinyl hydrazones **2** (1 mmol) and KMnO₄/wet SiO₂ (3 mmol, 3.48 g) was ground with a pestle in a mortar until TLC showed complete disappearance of α -sulfinyl oximes **1** or α -sulfinyl hydrazones **2** which required 8-20 min (Tables 1 and 2). Dichloromethane (2 \times 15 ml) was added to the reaction mixture and after vigorous stirring was filtered through sintered glass funnel and the solvent was then evaporated under vacuum. A yield of > 95% β -keto sulfoxides **3** were obtained after evaporation of the solvent and purification by column chromatography on silica gel using a mixture of *n*-hexane and ethyl acetate as eluent (90:10).

RESULTS AND DISCUSSION

We have found that the cleavage of C=N double bond of α -sulfinyl oximes **1** and α -sulfinyl hydrazones **2** by potassium permanganate supported on wet silica gel under solvent-free conditions is rapid (8-20 min). The general reaction is detailed in Scheme 1. In all cases, the crude product was judged to be of > 95% purity, based on ¹H NMR and TLC analyses. Because of the mildness of the reagent, the corresponding sulfones are not formed in these reactions (Tables 1 and 2). At this stage, the mechanism of the reaction is not clear to us. The enantiomeric purity of **3** was determined as > 98 from ¹H NMR chiral shift studies using (-)-(R)-N-(3,3-dinitrobenzoyl)- α -phenylethylamine **4** as a chiral shift reagent [12], and comparing the optical rotation of the products with known compounds [1-5]. To determine the enantiomeric purity of **3**,

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1a R¹ = phenyl, R² = phenyl

1b R¹ = phenyl, R² = 3,4-dimethoxyphenyl

1c R¹ = *p*-tolyl, R² = phenyl

1d R¹ = *p*-tolyl, R² = 3,4-dimethoxyphenyl

1e R¹ = 2-methoxy-1-naphthyl, R² = phenyl

1f R¹ = 2-methoxy-1-naphthyl, R² = 3,4-dimethoxyphenyl

1g R¹ = *p*-tolyl, R² = 2,4,6-trimethylphenyl

1h R¹ = *p*-tolyl, R² = 2,4,6-trimethyl-3,5-dichlorophenyl

1i R¹ = *p*-tolyl, R² = 4-methoxyphenyl

2a R¹ = phenyl, R² = phenyl

2b R¹ = phenyl, R² = 3,4-dimethoxyphenyl

2c R¹ = *p*-tolyl, R² = phenyl

2d R¹ = *p*-tolyl, R² = 3,4-dimethoxyphenyl

2e R¹ = 2-methoxy-1-naphthyl, R² = phenyl

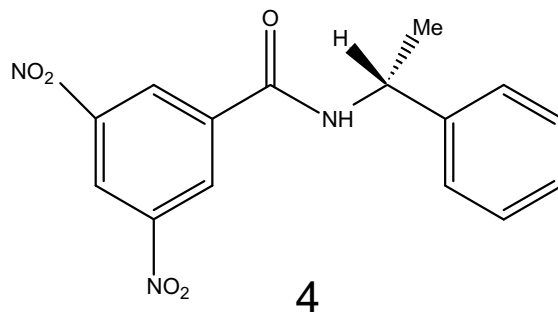
2f R¹ = 2-methoxy-1-naphthyl, R² = 3,4-

dimethoxyphenyl

2g R¹ = *p*-tolyl, R² = H

2h R¹ = *p*-tolyl, R² = Me

2i R¹ = *p*-tolyl, R² = Et



Scheme 1

it was mixed with one equivalent of chiral shift reagent **4** in an NMR tube (Tables 1 and 2). The oxidative cleavage of α -sulfinyl oximes **1a** as a model compound with potassium permanganate failed in the absence of the supporting agent, even upon grinding for a prolonged period of time. The reaction carried out in the presence of dry alumina and silica gel indicated that wet silica gel is the most effective than dry silica gel. Dry silica gel required a longer reaction time and gave lower yield (60%) whereas the yield of **1a** increased to 98% in the presence of pre-moistened reagent. The optimum molar ratio of substrate to oxidant (1:3) was determined for

complete conversion of α -sulfinyl oximes **1** and α -sulfinyl hydrazones **2** while the reaction was incomplete with lesser amounts of reagent (*i.e.* 1:1, 1:2 and 1:2.5).

CONCLUSIONS

In conclusion, we report here an efficient, rapid, mild and inexpensive method for the conversion of α -sulfinyl oximes **1** and α -sulfinyl hydrazones **2** using wet silica-supported potassium permanganate. Moreover, the oxidative cleavage of these derivatives takes place at room temperature in the

absence of solvent to the corresponding β -keto sulfoxides **3**. This reagent is superior to previously reported methods in terms of selectivity, yields, of enantiomeric purity of products and short reaction time [1-5].

ACKNOWLEDGEMENTS

We gratefully acknowledge the funding support received for this project from the Isfahan University of Technology (IUT), IR Iran (A. R. H.) and Grant GM 33138 (A. E. R.) from the National Institutes of Health, USA. Further financial support from Center of Excellency in Chemistry Research (IUT) is gratefully acknowledged.

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