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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

A.R. Hajipour*[a,b] and A.E. Ruoho[a]
[a] *Department of Pharmacology, University of Wisconsin, Medical School,*
1300 University Avenue, Madison,WI 53706-1532, USA
[b] *Pharmaceutical Research Laboratory, College of Chemistry,*
Isfahan University of Technology, Isfahan 84156, IR Iran

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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 due to production of HCl during the reaction, which is abel to racemize the chiral sulphure 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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* Corresponding author. E-mail: haji@cc.iut.ac.ir

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 ^{1}H 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 ^{1}H NMR) [1-5]. [b] Substrate/reagent (1:3). [c] Yield of isolated pure product after purification.

EXPERIMENTAL

Chemical and Apparatus

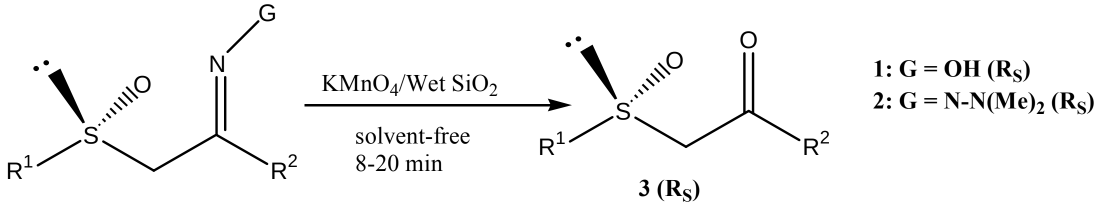
Yields refer to isolated products after purification. The products were characterized by comparing their spectral (IR, ^{1}H NMR), TLC and physical data with those of authentic samples [1-5]. Starting materials were synthesis by known methods [1-5]. All ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$ 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 $KMnO_4$ (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 $KMnO_4$/wet SiO_2 (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 × 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 ^{1}H 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 ^{1}H 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**,

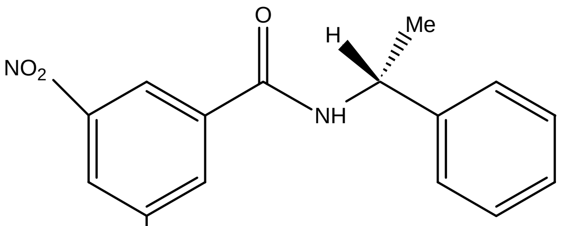


1 or 2 (Rs)

3 (R_S)

1a R^1 = phenyl, R^2 = phenyl
1b R^1 = phenyl, R^2 = 3,4-dimethoxyphenyl
1c R^1 = *p*-tolyl, R^2 = phenyl
1d R^1 = *p*-tolyl l, R^2 = 3,4-dimethoxyphenyl
1e R^1 = 2-*methoxy-1-naphthyl*, R^2 = phenyl
1f R^1 = 2-*methoxy-1-naphthyl*, R^2 = 3,4-dimethoxyphenyl
1g R^1 = *p*-tolyl, R^2 = 2,4,6-trimethylphenyl
1h R^1 = *p*-tolyl, R^2 = 2,4,6-trimethyl-3,5-dichlorophenyl
1I R^1 = *p*-tolyl, R^2 = 4-methoxyphenyl

2a R^1 = phenyl, R^2 = phenyl
2b R^1 = phenyl, R^2 = 3,4-dimethoxyphenyl
2c R^1 = *p*-tolyl, R^2 = phenyl
2d R^1 = *p*-tolyl, R^2 = 3,4-dimethoxyphenyl
2e R^1 = 2-*methoxy-1-naphthyl*, R^2 = phenyl
2f R^1 = 2-*methoxy-1-naphthyl*, R^2 = 3,4-dimethoxyphenyl
2g R^1 = *p*-tolyl, R^2 = H
2h R^1 = *p*-tolyl, R^2 = Me
2I R^1 = *p*-tolyl, R^2 = Et



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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%) where as 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].

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REFERENCES

[1] S.G. Pyne, A.R. Hajipour, Tetrahedron 50 (1994) 13501.

[2] G. Solladie, G. Demaaily, C. Greek, Tetrahedron Lett. 26 (1985) 435.

[3] a) L. Banfi, L. Clombo, C. Gennari, R. Annunziata, M. Cinquini, Synthesis (1982) 829; b) A.R. Hajipour, N. Mahboobkhah, Synth. Commun. 28 (1998) 3143.

[4] A.R. Hajipour, N. Mahboobkhah, J. Chem. Research (1998) 122.

[5] R. Annunziata, M. Cinquini, F. Cozzi, J. Chem. Soc., Perkin Trans. 1 (1979) 1689.

[6] K. Smith, (Ed.), Solid Supports and Catalysts in Organic Synthesis, Prentice Hall, New York, 1992.

[7] D.G. Lee, in: L.A. Paquette, (Ed.), Encyclopedia of Reagents for Organic Synthesis, New York, 1995.

[8] a) N.A. Noureldin, D.G. Lee, Tetrahedron Lett. 22 (1981) 4889; b) D. Zhao, D.G. Lee, Synthesis (1994) 915; c) A.J. Fatiadi, Synthesis (1987) 85; d) R. Sreekumar, R. Padmakumar, Tetrahedron Lett. 38 (1997) 5143.

[9] a) A.R. Hajipour, S.E. Mallakpour, H. Adibi, Indian J. Chem. 41B (2002) 2425; b) A.R. Hajipour, S.E. Mallakpour, Gh. Imanzadeh, Chem. Lett. (1999) 99; c) A.R. Hajipour, S.E. Mallakpour, H. Adibi, Sulfur Lett. 25 (2002) 155; d) A.R. Hajipour, S.E. Mallakpour, I. Mohammadpoor-Baltork, H. Backnezhad, Synth. Commun. 32 (2002) 771; e) A.R. Hajipour, S.E. Mallakpour, Gh. Imanzadeh, Asian Chem. Lett. (1999) 1.

[10] a) F. Toda, Acc. Chem. Res. 28 (1995) 480; b) F. Toda, K. Tanaka, Chem. Rev. 100 (2000) 1025.

[11] a) A.R. Hajipour, S.E. Mallakpour, H. Adibi, Chem. Lett. (2000) 460; b) A.R. Hajipour, S.E. Mallakpour, H. Adibi, Chem. Lett. (2001) 164; c) A.R. Hajipour, S.E. Mallakpour, S. Khoee, Chem. Lett. (2000) 120; d) A.R. Hajipour, S.E. Mallakpour, I. Mohammadpoor-Baltork, H. Adibi, Synth. Commun. 31 (2001) 1625; e) A.R. Hajipour, S.E. Mallakpour, Gh. Imanzadeh, Indian J. Chem. 40B (2001) 237; f) A.R. Hajipour, S.E. Mallakpour, S. Khoee, Synlett (2000) 740; g) A.R. Hajipour, S.E. Mallakpour, A.R. Najafi, Gh. Mazlumi, Sulfur Lett. 24 (2000) 137; h) A.R. Hajipour, M. Arbabian, A.E. Ruoho, J. Org. Chem. 67 (2002) 8622.

[12] A.R. Hajipour, M. Hantehzadeh, J. Org. Chem. 64 (1999) 8475.