

**AN EASY AND FAST METHOD FOR
OXIDATIVE DEPROTECTION OF
TRIMETHYLSILYL ETHERS,
TETRAHYDROPYRANYL ETHERS, AND
ETHYLENE ACETALS WITH KMnO_4
SUPPORTED ON ALUMINA UNDER
SOLVENT-FREE CONDITIONS**

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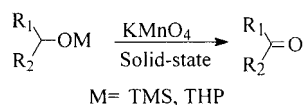
ABSTRACT

A manipulatively simple and rapid method for oxidation deprotection of trimethylsilyl ethers, tetrahydropyranyl ethers and deprotection of ethylene acetals to afford carbonyl compounds under solvent-free conditions in the presence or absence of alumina with potassium permanganate.

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The protection and deprotection of the hydroxy functional groups can play an essential role in synthetic strategy.¹ The transformation of alcohols to the corresponding trimethylsilyl ethers is a very common way to protect hydroxy groups.¹⁻³ In recent years a wide variety of methods have been reported for oxidative cleavage of trimethylsilyl ethers to the corresponding carbonyl compounds,⁴⁻⁷ but some of the mentioned methods encounter drawbacks such as the requirement for aqueous reaction conditions, use of expensive reagents, long reaction times, low yields of the products and tedious work-up. Therefore, introduction of new methods and inexpensive reagents for such functional group transformations is still in demand. The tetrahydropyranyl (THP) group is one of the most frequently used groups to protect alcohols and phenols.^{1,8} Owing to the outstanding stability of tetrahydropyranyl ether under a variety of reaction conditions, 3,4-dihydro-2H-pyran is still a reagent of choice for protection of the hydroxyl group in peptide, nucleotide and carbohydrate chemistry.⁹ Since direct transformation of tetrahydropyranyl ethers to their carbonyl compounds is rare in the literature,^{5,7,10-13} introduction of new methods is desirable. Acetal formation is the most widely used protecting method for aldehydes and ketones,¹ however, deprotection of acetals and ketals to the corresponding carbonyl compound is a useful transformation in organic synthesis.¹³⁻¹⁸

Heterogeneous reactions that are facilitated by supported reagents on various inorganic surfaces have recently attracted attention.¹⁹ The most advantage of these methods over conventional classical method is that they show cleaner reactions, decreased reaction time and easier work-up. In continuation of our ongoing program to develop environmentally benign methods using solid supports,²⁰ we wish to report a novel and efficient method for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers to the corresponding carbonyl compounds by with potassium permanganate (Scheme 1 and Table 1). This oxidizing reagent is an inexpensive, water-soluble and stable oxidizing reagent that is commercially available. This solvent is insoluble in non-aqueous solvents; however, the requirement of aqueous conditions had to be overcome.



Scheme 1.

Table 1. Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers with Supported KMnO_4

Entry	Substrate	Product	Time (min)	Yield (%) ^a
1	PhCH ₂ OTMS	PCHO	10	93
2	2-MeOC ₆ H ₄ CH ₂ OTMS	2-MeOC ₆ H ₄ CHO	10	80
3	3-MeOC ₆ H ₄ CH ₂ OTMS	3-MeOC ₆ H ₄ CHO	15	80
4	3-O ₂ NC ₆ H ₄ CH ₂ OTMS	3-O ₂ NC ₆ H ₄ CHO	20	95
5	2,5-(MeO) ₂ C ₆ H ₃ CH ₂ OTMS	2,5-(Me) ₂ C ₆ H ₃ CHO	10	75
6	PhCH(Me)OTMS	PhCOMe	15	99
7	4-ClC ₆ H ₄ CH(Me)OTMS	4-ClC ₆ H ₄ COMe	3	99
8	Ph ₂ CHOTMS	Ph ₂ CO	20	92
9	4-PhC ₆ H ₄ CH(Me)OTMS	4-PhC ₆ H ₄ COMe	15	90
10	α -TetralolTMS	α -Tetralone	10	95
11	PhCH ₂ OTHP	PhCHO	5	95
12	2-MeOC ₆ H ₄ CH ₂ OTHP	2-MeOC ₆ H ₄ CHO	20	75
13	3-MeOC ₆ H ₄ CH ₂ OTHP	3-MeOC ₆ H ₄ CHO	20	82
14	4-MeOC ₆ H ₄ CH ₂ OTHP	4-MeOC ₆ H ₄ CHO	10	90
15	3,4-(MeO) ₂ C ₆ H ₃ CH ₂ OTHP	3,4-(MeO) ₂ C ₆ H ₃ CHO	10	90
16	2,5-(MeO) ₂ C ₆ H ₃ CH ₂ OTHP	2,5-(MeO) ₂ C ₆ H ₃ CHO	15	88
17	PhCH(Me)OTHP	PhCOMe	10	90
18	4-ClC ₆ H ₄ CH(Me)OTHP	4-ClC ₆ H ₄ COMe	15	98
19	Ph ₂ CHOTHP	Ph ₂ CO	10	94
20	α -TetralolTHP	α -Tetralone	10	86

^aYields based on the isolated products after column chromatography.

In order to evaluate the effect of alumina in this reaction we tried the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers with potassium permanganate without using alumina. The rate of the reaction in the absence of alumina is slower and the yield is lower (Table 2).

Potassium permanganate was also used to transform ethylene acetals to the corresponding carbonyl compounds under solvent free conditions in excellent yields (Scheme 2 and Table 3). Again the yield

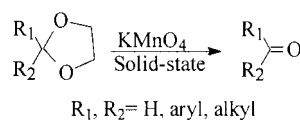
**Scheme 2.**

Table 2. Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers with KMnO_4

Entry	Substrate	Product	Time (min)	Yield (%) ^a
1	PhCH ₂ OTMS	PCHO	25	75
2	2-MeOC ₆ H ₄ CH ₂ OTMS	2-MeOC ₆ H ₄ CHO	30	70
3	3-MeOC ₆ H ₄ CH ₂ OTMS	3-MeOC ₆ H ₄ CHO	35	70
4	3-O ₂ NC ₆ H ₄ CH ₂ OTMS	3-O ₂ NC ₆ H ₄ CHO	30	55
5	2,5-(MeO) ₂ C ₆ H ₃ CH ₂ OTMS	2,5-(Me) ₂ C ₆ H ₃ CHO	35	70
6	PhCH(Me)OTMS	PhCOMe	25	70
7	4-ClC ₆ H ₄ CH(Me)OTMS	4-ClC ₆ H ₄ COMe	25	80
8	Ph ₂ CHOTMS	Ph ₂ CO	35	77
9	4-PhC ₆ H ₄ CH(Me)OTMS	4-PhC ₆ H ₄ COMe	25	80
10	α -TetralolTMS	α -Tetralone	25	75
11	PhCH ₂ OTHP	PhCHO	40	45
12	2-MeOC ₆ H ₄ CH ₂ OTHP	2-MeOC ₆ H ₄ CHO	35	60
13	3-MeOC ₆ H ₄ CH ₂ OTHP	3-MeOC ₆ H ₄ CHO	30	55
14	4-MeOC ₆ H ₄ CH ₂ OTHP	4-MeOC ₆ H ₄ CHO	30	60
15	3,4-(MeO) ₂ C ₆ H ₃ CH ₂ OTHP	3,4-(MeO) ₂ C ₆ H ₃ CHO	25	65
16	2,5-(MeO) ₂ C ₆ H ₃ CH ₂ OTHP	2,5-(MeO) ₂ C ₆ H ₃ CHO	30	60
17	PhCH(Me)OTHP	PhCOMe	35	55
18	4-ClC ₆ H ₄ CH(Me)OTHP	4-ClC ₆ H ₄ COMe	30	75
19	Ph ₂ CHOTHP	Ph ₂ CO	30	69
20	α -TetralolTHP	α -Tetralone	35	72

^aYields based on the isolated products after column chromatography.

of transformation of ethylene acetals to the corresponding carbonyl compounds with potassium permanganate without using alumina is lower and also the rate is slower (Table 4). The cinnamaldehyde acetal as an allylic carbonyl compound derivative was not converted to its corresponding aldehyde properly with this reagent, and many by-products were obtained. Interestingly, overoxidation of the products was not observed by this method. In comparison to benzylic trimethylsilyl ethers, benzylic tetrahydropyranyl ethers and benzylic ethylene acetals, oxidation deprotection of aliphatic trimethylsilyl ethers and aliphatic tetrahydropyranyl ethers or deprotection of aliphatic ethylene acetals with this reagent does not occur at all. Therefore this reagent is not suitable for oxidation deprotection of aliphatic trimethylsilyl ethers and aliphatic tetrahydropyranyl ethers or deprotection of aliphatic ethylene acetals.

Table 3. Deprotection of Ethylene Acetals with Supported KMnO_4

Entry	Substrate	Product	Time (min)	Yield (%) ^b
1	Acetophenoneethylene acetal	Acetophenone	5	98
2	2-Methoxybenzaldehyde-ethylene acetal	2-Methoxybenzaldehyde	15	92
3	2-Nitrobenzaldehydeethylene acetal	2-Nitrobenzaldehyde	15	75
4	2-Chloroacetophenone-ethylene acetal	2-Chloroacetophenone	15	85
5	α -Tetraloneethylene acetal	α -Tetralone	10	90
6	4-Phenylacetophenone-ethylene acetal	4-Phenylacetophenone	15	85

^aYields based on the isolated products after purification with column chromatography.

Table 4. Deprotection of Ethylene Acetals with KMnO_4

Entry	Substrate	Product	Time (min)	Yield (%) ^a
1	Acetophenoneethylene acetal	Acetophenone	25	68
2	2-Methoxybenzaldehyde-ethylene acetal	2-Methoxybenzaldehyde	35	70
3	2-Nitrobenzaldehydeethylene acetal	2-Nitrobenzaldehyde	35	55
4	2-Chloroacetophenone-ethylene acetal	2-Chloroacetophenone	40	55
5	α -Tetraloneethylene acetal	α -Tetralone	40	20
6	4-Phenylacetophenoneethylene acetal	4-Phenylacetophenone	35	50

^aYields based on the isolated products after purification with column chromatography.

In summary, in this study we introduced a new and cheap methodology for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers and deprotection of ethylene acetals to the corresponding carbonyl compounds in high yields under solvent-free conditions. The low price of the reagent, easy work-up, mild reaction conditions, and high yield of the products, make this method a novel and useful method for the oxidative

deprotection of trimethylsilyl and tetrahydropyranyl ethers and deprotection of ethylene acetals to afford corresponding carbonyl compounds.

EXPERIMENTAL

Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers with Supported KMnO_4 Under Solvent-Free Conditions

General Procedure

The alumina supported permanganate is prepared by grinding KMnO_4 (4 g, 25.3 mmol) and alumina (Al_2O_3 , neutral, 5 g) in a mortar and with a pestle until a fine, homogenous, purple powder is obtained. In a mortar trimethylsilyl ether or tetrahydropyranyl ether (2 mmol) was added to $\text{KMnO}_4/\text{Al}_2\text{O}_3$ (1.0 g, 2.8 mmol) and the mixture was ground with a pestle in a mortar until TLC showed complete disappearance of trimethylsilyl ether or tetrahydropyranyl ether (Table 1). The reaction progress was monitored by TLC (eluent: cyclohexane/EtOAc: 8:2). Then acetone (15 ml) was added to the reaction mixture and after vigorous stirring, the mixture was filtered off. The acetone was evaporated by rotary evaporator and the residue was taken up into ether (10 ml) which was evaporated to give the crude material. The resulting crude material was purified by a column chromatography on silica gel using a mixture of hexane and ethyl acetate as eluent (90:10).

Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers with KMnO_4 Under Solvent-Free Conditions

General Procedure

In a mortar trimethylsilyl ether or tetrahydropyranyl ether (2 mmol) was added to KMnO_4 (0.44 g, 2.8 mmol) and the mixture was ground with a pestle in a mortar until TLC showed complete disappearance of trimethylsilyl ether or tetrahydropyranyl ether (Table 2). The reaction progress was monitored by TLC (eluent: cyclohexane/EtOAc: 8:2). Then acetone (15 ml) was added to the reaction mixture and after vigorous stirring, the mixture was filtered off and the acetone was evaporated by rotary evaporator. The residue was taken up into ether (10 ml) which was evaporated to give the crude material. The resulting crude material was purified by a column

chromatography on silica gel using a mixture of hexane and ethyl acetate as eluent (90 : 10).

**Deprotection of Ethylene Acetals with Supported KMnO_4
Under Solvent-Free Conditions**

General Procedure

In a mortar ethylene acetal or ketal (2 mmol) was added to $\text{KMnO}_4/\text{Al}_2\text{O}_3$ (1.0 g, 2.8 mmol) and the mixture was ground with a pestle in a mortar until TLC showed complete disappearance of ethylene acetal or ketal (Table 3). The reaction progress was monitored by TLC (eluent : cyclohexane/EtOAc: 8 : 2). Then acetone (15 ml) was added to the reaction mixture and after vigorous stirring, the mixture was filtered off. The acetone was evaporated by rotary evaporator and the residue was taken up into ether (10 ml) which was evaporated to give the crude material. The resulting crude material was purified by a column chromatography on silica gel using a mixture of hexane and ethyl acetate as eluent (90 : 10).

**Deprotection of Ethylene Acetals with Supported KMnO_4
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