



Solvent free permanganate oxidations

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Abstract—The oxidations of organic compounds by permanganate under solvent free conditions have been studied. Thiols and primary aromatic amines undergo oxidative coupling reactions to give disulfides and diazenes, respectively, sulfides are oxidized to sulfones, primary and secondary alcohols are converted to aldehydes and ketones, 1,4-diols and cyclic ethers give lactones and arenes are oxidized to the corresponding α -ketones. The experimental procedure is simple and the products are easily isolated in good yields. © 2001 Elsevier Science Ltd. All rights reserved.

Although solvent free reactions are of general interest because of their potential applications in combinatorial chemistry, only a limited number of useful oxidation procedures have been reported.^{1–12} In this paper we wish to describe a simple and general procedure that can be used for the oxidative transformation of many organic functional groups using an inexpensive and environmentally friendly oxidant, potassium permanganate.¹³

Best results are obtained when KMnO_4 is first mixed with copper sulfate pentahydrate (or a 20/80 mixture of copper sulfate pentahydrate and alumina) to give a reagent that has previously been used extensively as a heterogeneous oxidant in inert solvents. The reductant is then added dropwise while the solid oxidant is tumbled using a magnetic stirrer. Most reactions can be carried out at room temperature; however, improved yields for solid reductants are obtained when the reaction temperature is near or above their melting points. Some reactions benefit from the application of additional energy in the form of microwaves.^{8,9} Product isolation can be achieved by washing the spent oxidant with an organic solvent, which can subsequently be recovered by simple distillation. Many of the reactions are nearly quantitative giving products of relatively high purity.

The oxidant is prepared by grinding equal amounts of potassium permanganate and copper sulfate pentahy-

drate in a mortar until homogeneous or by adding a concentrated aqueous solution of potassium permanganate to alumina, giving a paste which is then ground with an equal amount of copper sulfate pentahydrate. Reductant (2 mmol) is added to a portion of the oxidant (~4 g) in a 25 mL round bottomed flask and stirred magnetically until TLC analysis indicates a completed reaction. The residue is then washed with a minimum amount of solvent (methylene chloride, hexane and/or ether). Distillation of the solvent gives a product that is of acceptable purity for most purposes. If greater purity is required, the product can be distilled or recrystallized.

As can be seen from the first three reactions in Table 1, thiols are converted into the corresponding disulfides in good yields under very mild conditions (Scheme 1). The times required compare favorably with those for solvent free oxidations of thiols using other oxidants.^{1–3} Addition of alumina to the solid support did not improve the yields of these reactions.

Primary aromatic amines are also oxidatively coupled under these conditions (Scheme 2). As indicated by reactions 4–6 in Table 1, the presence of electron withdrawing substituents such as chloro decreases the reaction rate, but not the yield of diazene. The reaction times are shorter than those reported for the corresponding heterogeneous reactions, but the yields appear to be slightly lower.¹⁴ Cleaner products were obtained from these reactions when alumina was added to the solid support.

Aryl and alkyl sulfides are converted into the corresponding sulfones in good yields (reactions 7–13, Table

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Table 1. Solvent free permanganate oxidations

Reaction	Reductant	Time ^a	Product (% yield) ^b
1	Thiophenol	7 min	Diphenyl disulfide (100)
2	Butanethiol	15 min	Dibutyl disulfide (95)
3	Cyclopentanethiol	15 min	Dicyclopentyl disulfide (95)
4	Aniline	5 h ^c	Azobenzene (75)
5	2,4,6-Trimethylaniline	5 h ^c	1,2-Bis(2,4,6-trimethylphenyl)diazene (70)
6	4-Chloroaniline	20 h ^c	1,2-Bis(4-chlorophenyl)diazene (85)
7	Benzyl phenyl sulfide	12 h	Benzyl phenyl sulfone (85)
8	Methoxymethyl phenyl sulfide	8 h	Methoxymethyl phenyl sulfone (90)
9	Dibutyl sulfide	5 h	Dibutyl sulfone (90)
10	Dibenzyl sulfide	10 h ^d	Dibenzyl sulfone (98)
11	Dibenzyl sulfide	10 min ^e	Dibenzyl sulfone (99)
12	Diocetyl sulfide	15 h	Diocetyl sulfone (90)
13	Diocetyl sulfide	2 min ^c	Diocetyl sulfone (100)
14	4-Methoxybenzyl alcohol	45 min ^f	4-Anisaldehyde (95)
15	1-Pentanol	4 h ^f	Pentanal (80)
16	2-Cyclohexylethanol	4 h ^f	2-Cyclohexylethanal (85)
17	Cinnamyl alcohol	8 h ^c	Cinnamaldehyde (95)
18	2-Octanol	1.5 h	2-Octanone (90)
19	2,6-Dimethylcyclohexanol	6 h	2,6-Dimethylcyclohexanone (70)
20	1,4-Butanediol	14 h ^c	γ -Butyrolactone (95)
21	1,4-Pentanediol	36 h ^c	α -Methyl- γ -butyrolactone (70) 4-Oxo-1-pentanol (30)
22	Tetrahydrofuran	6 h ^c	γ -Butyrolactone (70)
23	2-Methyltetrahydrofuran	36 h ^c	α -methyl- γ -butyrolactone (90)
24	Tetrahydropyran	6 h ^c	δ -Valerolactone (65)
25	2,5-Dimethyltetrahydrofuran	8 h ^c	2,5-Hexanedione (60)
26	Indane	1.3 h	1-Indanone (90)
27	Phthalan	5 min	Phthalide (95)
28	Dihydrobenzofuran	24 h	No reaction
29	Xanthene	5 h	Xanthone (95)
30	Xanthene	10 min ^c	Xanthone (98)
31	Fluorene	1.3 h ^g	9-Fluorenone (95)
32	Fluorene	10 min ^c	9-Fluorenone (98)
33	2-Ethylthiophene	6 h	2-Acetylthiophene (90)

^a Unless otherwise indicated all reactions were completed at room temperature using $\text{KMnO}_4/\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as the oxidant.

^b Products were identified from comparison of physical and spectroscopic properties with authentic compounds.

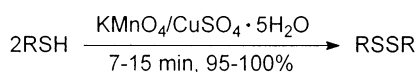
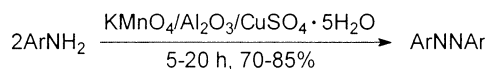
^c The oxidant was $\text{KMnO}_4/\text{Al}_2\text{O}_3/\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$.

^d Temperature was increased to 50°C.

^e Assisted by microwave irradiation.

^f The oxidant was $\text{KMnO}_4/\text{Al}_2\text{O}_3$.

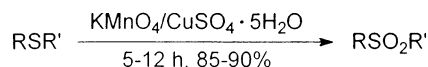
^g Temperature increased to 120°C.

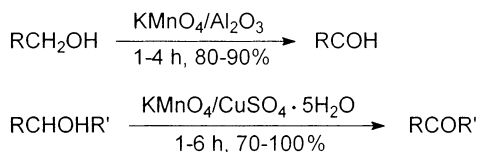
**Scheme 1.****Scheme 2.**

1). This is a highly useful reaction for the preparation of sulfones (Scheme 3) which are important intermediates in the synthesis of many organic compounds.¹⁵ The observation that benzyl phenyl sulfide is oxidized to the corresponding sulfone indicates that the reaction proceeds by way of an oxygen transfer mechanism. If the reaction involved electron transfer instead of oxygen transfer, substantial amounts of benzaldehyde would have been formed.^{16,17} Most other solvent free oxida-

tions of sulfides result in the formation of sulfoxides;⁴⁻⁶ however, sulfoxides were not produced under these conditions. Addition of alumina to the solid support increased the rates of these reactions, but not the yields.

As indicated in Scheme 4, secondary alcohols are converted into the corresponding ketones in good yields (reactions 18 and 19, Table 1) and aldehydes are obtained in comparable yields from the oxidation of primary alcohols (reactions 14–17, Table 1). The preparation of both aliphatic and aromatic aldehydes from the corresponding primary alcohols has not previously been easily achieved using permanganate or other strong oxidants because aldehydes are so readily converted to carboxylic acids under oxidizing conditions.

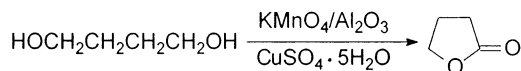
**Scheme 3.**



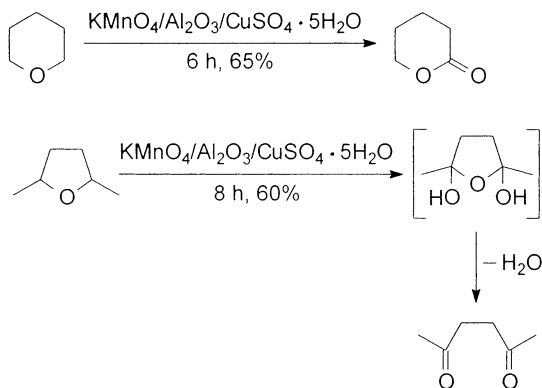
Scheme 4.

The use of alumina as the solid support is necessary in order to obtain good yields of aldehydes. Its use causes the rates of alcohol oxidation to be greater than those for the corresponding aldehydes. Under conditions where alcohols and aldehydes are oxidized at comparable rates, the product is necessarily a mixture of aldehyde and the corresponding carboxylic acid. Since ketones are resistant to further oxidation, the use of alumina with secondary alcohols provides little or no advantage.

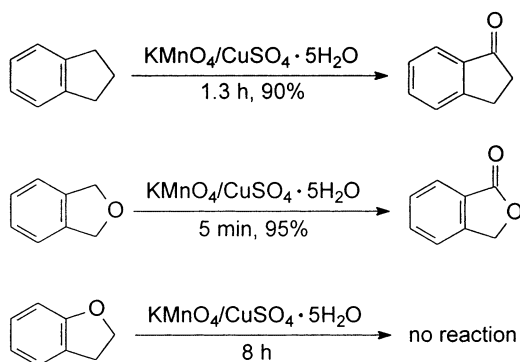
Of particular interest is the observation that 1,4-diols are easily and completely converted into lactones under these conditions, as in Scheme 5. Although the procedure works well for the preparation of butyrolactones (reactions 20 and 21, Table 1), attempts to obtain lactones from 1,3- or 1,5-diols failed.



Scheme 5.



Scheme 6.



Scheme 7.

Cyclic ethers are also converted into lactones under these conditions (reactions 22–24, Table 1). Although these transformations can also be achieved using other oxidants such as ruthenium tetroxide¹⁸ or chromium(VI),¹⁸ the experimental simplicity of this procedure may make it the approach of choice. When the α -carbons are tertiary, the product is a dione, formed presumably by dehydration of the corresponding diol as in Scheme 6. Addition of alumina to the solid support did not improve the yields of these reactions.

Arenes are converted into the corresponding α -ketones under these conditions (reactions 26, 31–33, Table 1). The products are identical to those obtained under heterogeneous conditions where the reductant is dissolved in an inert solvent;¹⁹ however, the reaction times are reduced from a few days to a few hours at room temperature. Addition of alumina to the solid support decreased the yields of these reactions. As indicated in Scheme 7, the reaction displays an interesting selectivity for compounds containing oxygen as part of a cyclic side chain. When oxygen is in the β -position, lactones are obtained in good yields; when it is in the α -position the reaction is completely inhibited. The unique selectivity demonstrated by the reactions in Scheme 7 may find application in the synthesis of dihydroisocoumarins and similar compounds.²⁰

Attempts to use this reaction for the oxidative cleavage of alkenes were largely unsuccessful. Yields of 20% or less were realized when stilbene and styrene were oxidized to benzaldehyde.

Acknowledgements

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