Heterogeneous Permanganate Oxidation of Styrene and Cinnamic Acid Derivatives: A Simple and Effective Method for the Preparation of Benzaldehydes

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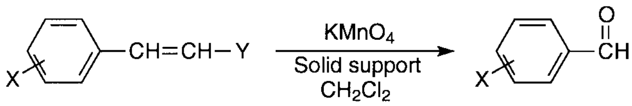
Abstract: Styrene and cinnamic acid derivatives yield correspondingly substituted benzaldehydes when oxidized by permanganate under heterogeneous conditions. Reaction of terminal aliphatic alkenes under similar conditions gives discouragingly low yields; however, ketones and ketols are obtained in very good yields from the oxidation of 2,2-disubstituted and trisubstituted alkenes, respectively. Alumina and Amberlite IR-120 can be used as solid supports in these reactions with equally good results.

Key words: oxidation, styrene, cinnamic acid, benzaldehyde, permanganate, heterogeneous, solid support

The preparation of aldehydes by the oxidative cleavage of carbon–carbon double bonds is a useful reaction, but one that is often difficult to achieve in good yields because the products are usually susceptible to further oxidation under the reaction conditions.[1] Among the methods currently available, ozonolysis gives the most reliable results;[2] however, oxidants such as ruthenium tetroxide,[3] chromium(VI)[4] and permanganate,[5] when used under homogeneous conditions, usually give carboxylic acids as the major products. In an attempt to develop a simple, inexpensive and general methodology for the preparation of aldehydes by oxidative cleavage of alkenes we have investigated the use of permanganate under heterogeneous conditions. The oxidations of alcohols,[6] arenes,[7] sulfides,[8] thiols,[9] enamines,[10] and unsaturated compounds[11] by this reagent have been described previously.

The experimental procedure, which involves mixing permanganate with a solid support, is very simple: The oxidant and solid support are placed in a flask containing the reductant dissolved in dichloromethane and stirred either at room temperature or under reflux. When the reaction is complete, as indicated from TLC analysis, the spent oxidant and solid support are separated by filtration and a nearly pure product obtained by evaporation of the solvent.

Previous work has shown that the nature of the products obtained from heterogeneous permanganate oxidations can be attenuated by changes in the solid support. For example, alkenes are resistant to oxidation under mild conditions when a neutral solid support, such as copper sulfate pentahydrate, is used;[12] however, if an omega phase (aqueous *tert*-butyl alcohol) is added, alkenes are converted into ketols or epoxides.[11b,c,h,i] (It has been suggested that the omega phase creates a thin coat on the solid support, thus modifying its properties.) Moreover, it is known that if an acidic solid support, such as alumina, is used, cleavage occurs.[11e] In this paper we wish to describe a method for the preparation of benzaldehydes in good yields from the oxidative cleavage of styrene and cinnamic acid derivatives by permanganate under heterogeneous conditions, to note some limitations to the reaction and to compare results obtained from the use of alumina and a cation exchange resin as solid supports (Scheme 1).



Scheme 1

The results obtained from the oxidation of a number of styrene and cinnamic acid derivatives having various structural features are summarized in Table 1. From these data it is possible to conclude the following: (i) substituents on the side chain (entries 1–7) have little or no impact on the reaction; (ii) carboxylic acid groups on the side chain are also tolerated (entries 5 and 8–18), but; (iii) a carboxylic group on the aromatic ring results in an intractable product mixture (entry 19); (iv) a variety of other ring substituents, including hydroxyls (entry 10), do not affect the reaction; (v) anthracene derivatives are easily oxidized to anthraquinones under these conditions (entries 21 and 22); (vi) hetero atoms as part of the aromatic ring have little or no impact on the reaction (entries 23 and 24).

When a carboxylic acid group is part of the side chain, as in the cinnamic acids, product isolation and purification is easily achieved; however, a carboxylic acid substituent on the aromatic ring, as in 4-vinylbenzoic acid (entry 19), makes the separation of the product from the reduced oxidant and solid support discouragingly difficult. It appears that the carboxylate adsorbs or bonds firmly to the solid support, preventing separation of the product. This suggestion is supported by the observation that methylation of 4-vinylbenzoic acid allows the reaction to proceed smoothly (entry 20).

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Table 1 Products Obtained from the Oxidation of Styrene and Cinnamic Acid Derivatives by $KMnO_4$ under Heterogeneous Conditions

Entry	Reductant	Conditions[a]	Product	Yield (%)
1	Styrene	a	Benzaldehyde	90
2	β-Methylstyrene	a	Benzaldehyde	83
3	β-Methoxystyrene	a	Benzaldehyde	50
4	4-Phenylbut-3-en-2-one	a	Benzaldehyde	79
5	Cinnamic acid	b	Benzaldehyde	90
6	Ethyl cinnamate	a	Benzaldehyde	85
7	Anethole	c	*p*-Anisaldehyde	94
8	4-Methylcinnamic acid	d	4-Methylbenzaldehyde	96
9	4-Methylcinnamic acid	b	4-Methylbenzaldehyde	97
10	2-Hydroxycinnamic acid	d	Salicylaldehyde	85
11	2-Methoxycinnamic acid	d	*o*-Anisaldehyde	81
12	3-Methoxycinnamic acid	d	*m*-Anisaldehyde	74
13	4-Methoxycinnamic acid	d	*p*-Anisaldehyde	90
14	4-Methoxycinnamic acid	b	*p*-Anisaldehyde	94
15	3-Bromocinnamic acid	d	3-Bromobenzaldehyde	99
16	4-Chlorocinnamic acid	d	4-Chlorobenzaldehyde	85
17	3-Chlorocinnamic acid	d	3-Chlorobenzaldehyde	91
18	3-Trifluoromethylcinnamic acid	d	3-Trifluoromethylbenzaldehyde	97
19	4-Vinylbenzoic acid	a	Intractable product	
20	Methyl 4-vinylbenzoate	a	4-Carbomethoxybenzaldehyde	85
21	9-Vinylanthracene	e	9-Anthraldehyde	30
22	9-Vinylanthracene	g	Anthraquinone	98
23	3-(3-Pyridyl)acrylic acid	f	3-Pyridinecarboxaldehyde	90
24	Furylacrylic acid	f	Furfural	90
25	α-Methylstyrene	e	Acetophenone	98
26	α-Methylstyrene	h	Acetophenone	87
27	1,1-Diphenylethene	g	Benzophenone	82
28	1,1-Diphenylethene	h	Benzophenone	86

[a]Conditions a: Reductant (1.0 mmol) and $KMnO_4$/alumina reagent (4.65 g) were stirred in CH_2Cl_2 overnight at r.t.
Conditions b: Reductant (1.0 mmol), Amberlite IR-120/H_2O (1.17 g) and $KMnO_4$ (0.49 g) were stirred in CH_2Cl_2 at r.t. for 10–40 min.
Conditions c: Reductant (1.0 mmol) and $KMnO_4$/alumina (4.65 g) were stirred in CH_2Cl_2 for 4 h at r.t.
Conditions d: Reductant (1.0 mmol) and $KMnO_4$/alumina reagent (4.65 g) were stirred in CH_2Cl_2 for 10–40 min at r.t.
Conditions e: Reductant (1.0 mmol) and $KMnO_4$/alumina reagent (4.65 g) were stirred in CH_2Cl_2 at r.t. for 2 d.
Conditions f: Reductant (1.0 mmol) and $KMnO_4$/alumina reagent (4.65 g) were stirred for 40–60 min at r.t.
Conditions g: Reductant (1.0 mmol) and $KMnO_4$/alumina reagent (13.8 g) were stirred in CH_2Cl_2 for 3 d at r.t.
Conditions h: Reductant (1.0 mmol), Amberlite IR-120/H_2O (2.79 g) and $KMnO_4$ (0.98 g) were stirred in CH_2Cl_2 for 2 d at r.t.

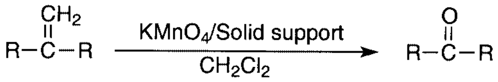
Oxidative cleavage of substituted cinnamic acids would yield glyoxylic or oxalic acid in addition to substituted benzaldehydes. However, these small, very polar coproducts adhere strongly to the solid support and do not contaminate the desired product. Similarly, substituted benzaldehydes obtained from the corresponding styrenes are not contaminated by coproducts (which would be short chain aldehydes or carboxylic acids). However, when the coproducts are large and less polar, a mixture of products may be obtained. For example, the oxidation of 4-methoxystilbene gives a mixture containing approximately equal amounts of benzaldehyde and 4-methoxybenzaldehyde in nearly quantitative yields and acetone can be isolated as its 2,4-dinitrophenylhydrazine derivative when β,β-dimethylstyrene is oxidized.

The oxidation of cinnamate esters is accompanied by hydrolysis of the presumed glyoxylate intermediate. For example, the oxidation of decyl cinnamate gave benzaldehyde and decan-1-ol along with traces of decanal as in Scheme 2. Similarly, the products obtained from the oxidation of 4-methoxybenzyl cinnamate are benzaldehyde (~100%), 4-methoxybenzyl alcohol (44%) and 4-methoxybenzaldehyde (55%). (The yields of these products were determined by ^{1}H NMR spectroscopy without separation of the product mixture.)

Although attempts have been made to prepare solid supported permanganate reagents using anion exchange polymers, the results have not been encouraging.[13] In our hands such reagents were observed to undergo intramolecular oxidation-reduction reactions that result in degradation of the polymer accompanied by reduction of the oxidant. Cation exchange resins have proven to be more useful[11a] as they are resistant to oxidation and contain sulfonic acid groups, which promote faster reactions.

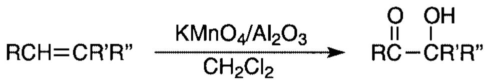
It appears that cleavage of styrene and cinnamic acid derivatives proceeds in excellent yields at least partly because the carbonyl is stabilized by resonance with the aromatic ring. For terminal aliphatic alkenes, where stabilization in this way is not possible, very poor yields are obtained. For example, when attempts were made to oxidize docos-1-ene, eicos-1-ene and hexadec-1-ene, an insigificant amount of product was obtained. It is possible that terminal aliphatic alkenes are oxidized to carboxylic acids, which become attached to the solid support as described above.

2,2-Disubstituted aliphatic ethenes are smoothly oxidized to the corresponding ketones as in Scheme 3. For example, 2,3,3-trimethylbut-1-ene gave a 95% yield of pinacolone, α-methylstyrene gave acetophenone in 87–98% yield (entries 25 and 26) and benzophenone was obtained in 82–86% yield from the oxidation of 1,1-diphenylethene (entries 27 and 28).



Scheme 3

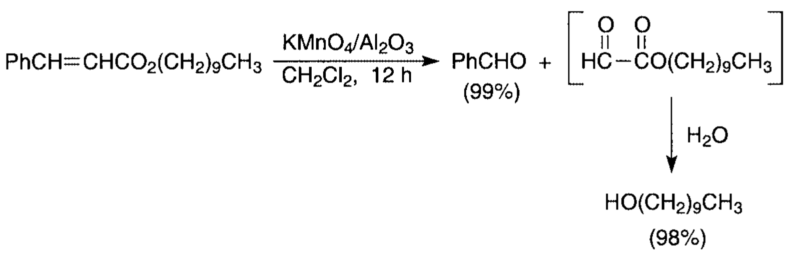
Trisubstituted alkenes give ketols, as in Scheme 4. For example, 8-acetoxy-3-oxo-2,6-dimethyloctan-2-ol is obtained in 96% yield from the oxidation of 8-acetoxy-2,6-dimethyloct-2-ene. These reactions are, therefore, similar to those obtained using copper sulfate pentahydrate and an omega phase as the solid support.[11i]



Scheme 4

The oxidants used in these reactions were prepared as follows: The $KMnO_4/Al_2O_3$ reagent was made by combining $KMnO_4$ (0.78 g), Al_2O_3 (acidic, Brockmann I, 3.12 g) and H_2O (0.78 mL) in a mortar and grinding until homogeneous (about 3 min). The solid support prepared from a cation exchange resin was made by grinding Amberlite 1R-120 (0.80 g) and H_2O (0.4 mL) in a mortar for about 3 min. This support was added to a solution of the alkene in CH_2Cl_2 followed by powdered $KMnO_4$ (0.49 g). Attempts to grind $KMnO_4$ and moist Amberlite together in the absence of solvent resulted in rapid degradation of the oxidant. Several other solid supports can also be successfully used for the oxidation of substituted cinnamic acids. However, as indicated by the data in Table 2, the oxidation of styrenes is more sensitive to the nature of the solid support. Although a detailed understanding of the exact function of the solid support in these reactions is not currently available, it can be seen from the data in Table 2 that supports, which are somewhat acidic, seem to be of greatest general utility. The observation that cinnamic acids are more easily oxidized and that good yields are obtained with a wider range of supports, may be associated with the acidic nature of these reductants.

The solvent for these reactions, CH_2Cl_2, was purified by stirring over $KMnO_4$, using a small amount of phase transfer agent to solubilize the oxidant, and carefully distilled. The reductants (alkenes)



Scheme 2

Table 2 Effect of Solid Supports on the Yields of 4-Methoxybenzaldehyde Obtained from the Oxidation of *trans*-Anethole and *trans*-4-Methoxycinnnamic Acid

Solid Support[a]	Yield (%)[b]	Yield (%)[c]
Amberlite 1200 (H)	92	94
Amberlite 36	90	92
Amberlite IR-120[d]	60	97
Amberlite IR-120 (sodium form)	14	92
Amberlyst 15	88	95
Rexyn RG 50 (H)	5	0
Rexyn 101 (H)	93	95
Al_2O_3 (acidic, Brockmann 1)[d]	9	90
SiO_2[d]	34	91
$CuSO_4·5H_2O$	2	0
Molecular sieves 5 Å	4	0
Molecular sieves 5 Å[d]	7	89
Florisil[d]	36	90

[a] Solid supports were obtained from Aldrich or Fisher.
[b] *trans*-Anethole (1 mmol) was oxidized by $KMnO_4$ (3 mmol) and solid support (1.6 g) in CH_2Cl_2 (5 mL) for 80 min.
[c] *trans*-4-Methoxycinnamic acid (1 mmol) was oxidized by $KMnO_4$ (3 mmol) and solid support (1.6 g) in CH_2Cl_2 (5 mL) for 30 min.
[d] H_2O (0.4 mL) was added.

were all obtained commercially and used without further purification. The products, all previously prepared compounds, were identified spectroscopically (^{1}H NMR, ^{13}C NMR and IR) by comparison with literature data.

Oxidation of Styrenes and Cinnamic Acid Derivatives by $KMnO_4$ under Heterogeneous Conditions; Typical Procedures

Condition c; *p*-Anisaldehyde: To a solution of anethole (0.148 g, 1.0 mmol) in CH_2Cl_2 (35 mL) was added $KMnO_4$/alumina reagent (4.65 g). The heterogeneous mixture was stirred at r.t. until TLC analysis indicated that the reaction was complete (4 h). The contents of the flask were filtered through Celite and washed with CH_2Cl_2 (3 × 15 mL). The product was separated by evaporation of the solvent to give *p*-anisaldehyde (0.128 g, 94%).

IR (film): ν = 3009, 2739, 1684, 1604, 1578, 1511, 1461 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 9.90 (1 H, s), 7.85 (2 H, d, *J* = 8.7 Hz), 7.01 (2 H, d, *J* = 8.7 Hz), 3.89 (3 H, s).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 190.6, 164.4, 131.7, 129.7, 114.1, 55.3.

Condition b; 4-Methylbenzaldehyde: Amberlite 1R-120 (Mallinckrodt, 0.8 g) and H_2O (0.4 mL) were ground in a mortar for 3 min to give a wet powder and added to 4-methylcinnamic acid (162 mg, 1.0 mmol) dissolved in CH_2Cl_2 (5 mL) followed by finely ground $KMnO_4$ (490 mg, 3.00 mmol). This mixture was stirred at r.t. for 20 min and then filtered through Celite. The residue was washed with CH_2Cl_2 (3 × 10 mL). The filtrate and washings were combined, dried ($MgSO_4$) and concentrated to give 4-methylbenzaldehyde (117 mg, 97%) as a colorless oil.

IR (film): ν = 3032, 2732, 1702, 1690, 1605, 1577 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 9.96 (1 H, s), 7.78 (2 H, d, *J* = 7.8 Hz), 7.33 (2 H, d, *J* = 7.8 Hz), 2.43 (3 H, s).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 191.9, 145.5, 134.1, 129.7, 129.6, 21.8.

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