



## 2 - Manganese-based oxidation reagents

Manganese compounds, particularly potassium permanganate and manganese dioxide, have been used as oxidation reagents in organic synthesis for over a century.

The standard reduction potentials<sup>1</sup> of several oxidation reagents are summarized in the following table<sup>2</sup>. Manganese reagents are amongst the most powerful oxidation reagents available.

Reagent	Standard reduction potential E <sup>0</sup> in Volts	Reagent	Standard reduction potential E <sup>0</sup> in Volts
F <sub>2</sub> /HF	+ 3,06	Cr <sub>2</sub> O <sub>7</sub> <sup>-2</sup> /Cr <sup>+3</sup>	+1,36
S <sub>2</sub> O <sub>8</sub> <sup>-2</sup> /SO <sub>4</sub> <sup>-2</sup>	+2,01	MnO <sub>2</sub> /Mn <sup>+2</sup>	+1,23
H <sub>2</sub> O <sub>2</sub> /H <sub>2</sub> O	+1,77	O <sub>2</sub> /H <sub>2</sub> O	+1,23
Ce <sup>+4</sup> /Ce <sup>+3</sup>	+1,71	Br <sub>2</sub> /Br <sup>-</sup>	+1,09
MnO <sub>4</sub> <sup>-</sup> /Mn <sup>+2</sup>	+1,51	HNO <sub>3</sub> /NO	+0,96
HOCl/Cl <sup>-</sup>	+1,50	Fe <sup>+3</sup> /Fe <sup>+2</sup>	+0,77
Pb <sup>+4</sup> /Pb <sup>+2</sup>	+1,46	MnO <sub>4</sub> <sup>-</sup> /MnO <sub>2</sub>	+0,58
Cl <sub>2</sub> /Cl	+1,36	H <sup>+</sup> /H <sub>2</sub>	0,00

Permanganate in **acidic solution** is reduced to Mn<sup>+3</sup> and ultimately to Mn<sup>+2</sup>, while in **alkaline solution** manganese dioxide is the end-product<sup>3,4</sup>. Permanganate in acidic solution is such a powerful reagent that the oxidation is mostly non-selective in its activity.

The range of manganese based oxidation applications is extensive:

- Oxidation of alcohols to ketones and aldehydes (p3)
- Oxidation of aldehydes to carboxylic acids (p5)
- Oxidation of alkenes to *cis*-1,2-diols<sup>2,5</sup> (p2)
- Oxidation of alkenes to  $\alpha$ -diketones (p2)
- Oxidative degradation of alkenes to carboxylic acids or ketones (Lemieux von Rudloff oxidation) (p4)
- Oxidation of alkynes to  $\alpha$ -diketones (p2)
- Oxidation of alkylarenes to benzoic acids (p5)
- Oxidation of alkylarenes to alkyl-aryl ketones<sup>6</sup> (p5)
- Oxidative degradation of amines to aldehydes and ketones (p6)
- Oxidation of amines to azocompounds (p6)
- Oxidation of tertiary amines to nitrocompounds (p6)
- Oxidation of sulfoxides to sulfones (p7)
- Oxidation of enones to  $\alpha$ -acetoxyenones (p6)
- Oxidative cleavage of aromatic rings (p6).

Oxidations with permanganate are usually performed in aqueous solutions, but organic co-solvents like ethanol, acetone, pyridine or acetic acid are also common.

The use of permanganate in flammable organic solvents is **dangerous and can lead to uncontrolled reactions or explosions**. While organic solvents are required to solubilize some reagents, the use of phase-transfer catalysts like tetraalkylammonium salts<sup>7,8</sup> or crown ethers<sup>9,10</sup> in a two-phase reaction mixture can improve the safety of the reaction.

The reactivity of potassiumpermanganate for oxidations under solvent-free conditions has also been investigated<sup>11</sup>.

Some examples for the reactivity of manganese compounds in oxidation reactions are given in the following text.

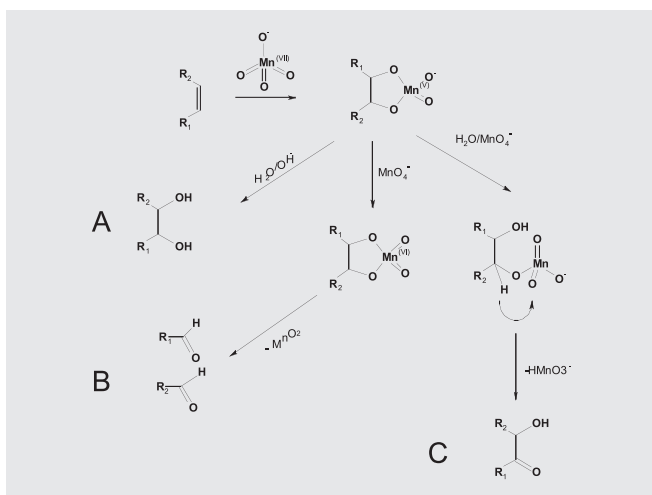
1 Handbook of Chemistry and Physics, 64th edition, CRC press, Boca Raton 1983 p. D-156 ff.  
 2 Organikum, 21st ed, Wiley VCh, Weinheim 2001.  
 3 A.J.Fatiadi, Synthesis 1987, 85.  
 4 A.Streitwieser, Jr., C.H.Heathcock, Organische Chemie, Verlag Chemie Weinheim 1980.  
 5 W.P.Weber, J.P.Shepherd, Tetrahedron Lett. 1972, 4907.  
 6 S.M.Gannon, J.G.Krause, Synthesis 1987 915 (..X1).

7 J.Dockx, Synthesis 1973 441.  
 8 T.Ogino, K. Mochizuki, Chem.Lett. 1979 443.  
 9 D.J.Sam, H.F.Simmons, J.Am.Chem.-Soc. 94 (1972) 4024.  
 10 G.W.Gokel, H.D.Durst, Synthesis 1976 168.  
 11 M.Nüchter, B.Ondruschka, R.Trotzki, J.Prakt.Chem. 342 (2000) 720.



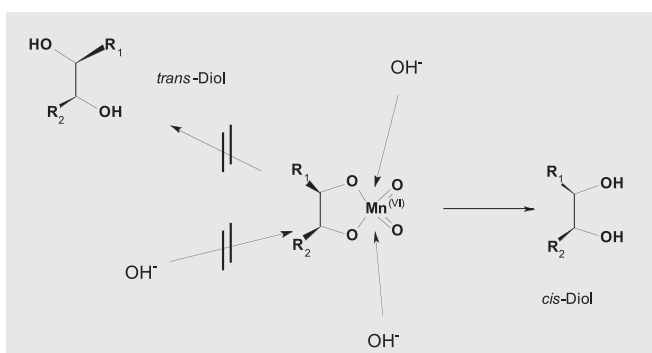
## Oxidation of alkenes and alkynes

Carbon-Carbon double bonds are oxidized by **alkaline** permanganate to 1,2-diglycols in poor to moderate yields (<50%)<sup>3,12</sup>. The permanganate ion adds to the double bond and forms a cyclic ester which, after alkaline hydrolysis, leads to the 1,2-diol (Path **A**).



Common side-products (or even main products in neutral or acidic solutions) of this reaction are cleavage products (Path **B**) or partially over-oxidized acyloines (Path **C**)<sup>13</sup>.

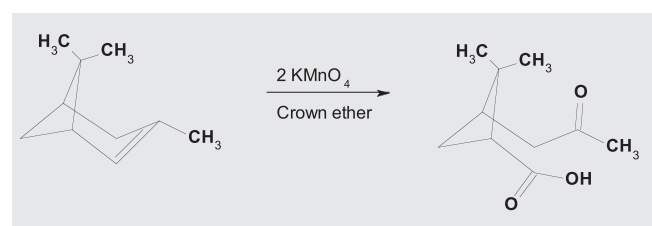
Hydrolysis of the cyclic ester by a hydroxide ion happens from the manganese face ("syn-addition"), so a *cis*-diol is formed from *cis*-alkenes<sup>14</sup> rather than a *trans*-diol.



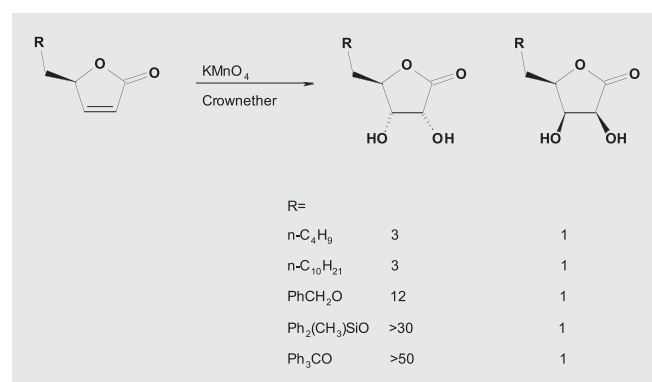
The oxidative cleavage of alkenes to two moles of ketones or carboxylic acid is also a very common reaction (Path **B**). In **neutral or acidic** media the oxidative cleavage is the pre-

ferred reaction path, but the yields of the reaction are still moderate<sup>15</sup>. The yield can be improved by using the "**Lemieux-von Rudloff reagent**"<sup>16,17</sup>, an aqueous solution of sodium periodate with potassium permanganate (~60:1) at pH ~7-8.

Another reagent which improves the oxidative cleavage of alkenes drastically is potassium permanganate complexed with a **crownether** (i.e. dicyclohexyl-18-crown-6)<sup>9,18,19</sup>. This benzene-soluble complex is called "**Purple benzene**".



The cleavage of 1-alkenes to carboxylic acids is also generally performed by reacting with potassium permanganate in a two-phase system in the presence of a phase transfer catalyst<sup>3</sup>. A procedure to convert alkenes to 1,2-dioles or to cleave it to carboxylic acids by using potassium permanganate and phase-transfer-catalysts like triethylbenzylammonium bromide at different pH-values has been published<sup>8,20</sup>.



$\gamma$ -Butenolides are converted to 2,3-dihydroxy- $\gamma$ -butyrolactones<sup>19</sup> with permanganate. The stereochemistry of this reaction strongly depends on the size of the group R.

12 G.Wagner, Ber.Dtsch.Chem.Ges, 1888 21 1230; ibid. 3347.

13 S.Wolfe, C.F.Ingold, R.U.Lemieux, J.Am.Chem.Soc. 103 (1981) 938.

14 Y.Usui, K.Sato, M.Tanaka, Angew.Chem, 115 2003 5781.

15 J.March, Advanced Organic Chemistry, 3rd ed. John Wiley and sons New York 1985 p.1070.

16 R. Lemieux, E.M.von Rudloff, Can.J.Chem 33 (1955) 1710.

17 Organic Synthesis, Coll. Vol 6, 690; Voll 55, 67.

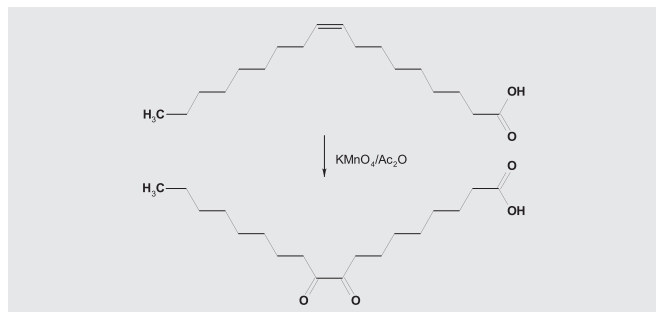
18 H.Bock, D.Jaculi, Angew.Chem.Int.Ed.Engl. 23 (1984) 305.

19 T.Mukaiyama, F.Tabusa, K.Suzuki, Chem.Lett. (1983) 173.

20 D.G.Lee, S.F.Lamb, V.S.Chang, Organic synthesis Coll. Vol 7, 397.



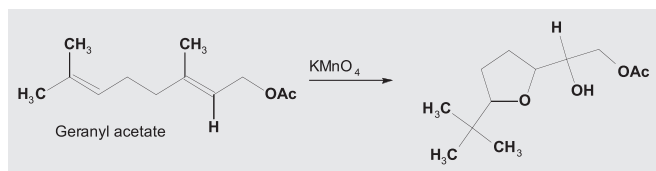
The oxidation of alkenes with potassium permanganate in the presence of oxalyl chloride or trimethylsilyl chloride and triethylammonium chloride yields 1,2-dichloroalkenes<sup>21,22</sup>.



Sharpless has developed a method to transform alkenes directly to  $\alpha$ -diketones with potassium permanganate in acetic anhydride as the solvent<sup>23,24</sup>.

Non terminal alkynes are converted to  $\alpha$ -diketones with potassium permanganate in **dry dichloromethane** and a phase transfer catalyst like Adogen464<sup>®</sup><sup>25</sup> or in buffered aqueous acetone<sup>26</sup>. Terminal alkynes and non-terminal alkynes in the presence of water are usually<sup>27</sup> cleaved to carboxylic acids<sup>28</sup>.

1,5-Dienes and 1,5,9-trienes are oxidized by potassium permanganate to tetrahydrofuran-diols<sup>29</sup> and octahydro-2,2'-bifuranyls<sup>30</sup>.



An asymmetric procedure based on chiral phase-transfer catalysts has been published<sup>31</sup>.

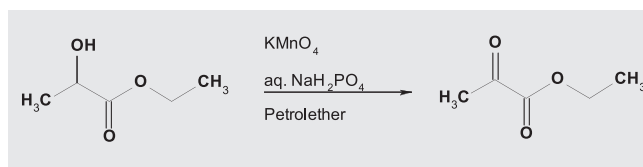
- 27752 cis-Dicyclohexyl-18-crown-6 (mixture of isomers)
- 16980 Dibenzo-18-crown-6
- 16402 Benzyltriethylammonium chloride, 99%
- 12385 Benzyltriethylammonium chloride, 60% solution in water
- 19838 Sodium periodate, 99%

21 I.E.Markó, P.R.Richardson Tetrahedron Lett. 32 (1991) 1831.  
 22 I.E.Markó, P.R.Richardson, M.Bailey, AR. Maguire, N.Coughlan, Tetrahedron Lett. 38 (1997) 2339.  
 23 K.B.Sharpless, R.F.Lauer, O.Repic, A.Y.Teranishi, D.R.Williams, J.Am.Chem.Soc. 93 (1971) 3303.  
 24 H.P.Jensen, K.B.Sharpless J.Org. Chem. 39 (1974) 2314.  
 25 D.G.Lee, V.S.Chang, J.Org.Chem. 44 (1979) 2726.  
 26 N.S.Srinivasan, D.G.Lee, J.Org.Chem 44 (1979) 1547.  
 27 Water soluble alkynes and a strict control of the pH value lead to di-ketones as main products.

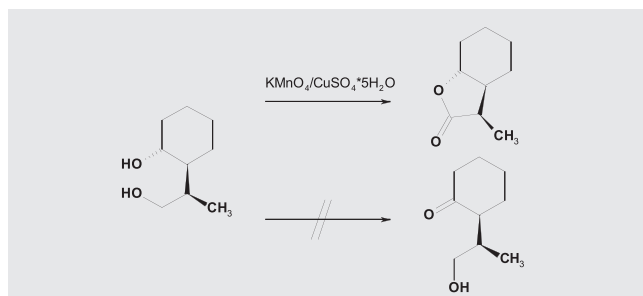
- 41961 Sodium periodate, ACS reagent
- 42323 Acetic anhydride, ACS reagent
- 23313 Acetic anhydride, p.a.
- 14949 Acetic anhydride, 99+
- 22755 Adogen 464<sup>®</sup>
- 32685 Dichloromethane extra dry

## Oxidation of alcohols

Potassium permanganate in acidic or alkaline solution is a very powerful oxidizing reagent. Reaction with primary alcohols yields the carboxylic acid or, in some cases, the aldehyde while secondary alcohols are oxidized to ketones<sup>67, 3</sup>. The presence of water in the reaction mixture is necessary, and aqueous-soluble substrates like lactic- or mandelic-acid show good results<sup>32</sup>. The oxidation of primary and secondary alcohols with potassium permanganate to the carboxylic acid or ketones can be broadly applied and many examples have been published<sup>67</sup>.



Secondary allylic alcohols are readily oxidized by solid **potassium permanganate supported on copper sulfate pentahydrate** in benzene to  $\alpha,\beta$ -unsaturated ketones<sup>33,34</sup>.



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 29 E.Klein, W.Rojann, Tetrahedron 21 2353 (1965).  
 30 R.C.D.Brown, R.M.Hughes, J.Keily, A.Kenney, Chem Comm. (2000) 1735.  
 31 R.C.D.Brown, J.F.Kelly, Angew.Chem 113 (2001) 4628.  
 32 Organic Synthesis, Coll. Vol 4, 467; Vol. 31, 59.  
 33 N.A. Noureldin, D.G.Lee, Tetrahedron Lett. 22 4889 (1981).  
 34 F.M.Menger, C.Lee, Tetrahedron Lett. 22 (1981) 1655; F.M.Menger, C.Lee, J.Org.Chem 44 (1979) 3323.



A mixture of solid potassium permanganate with copper sulfate pentahydrate has been reported to selectively oxidize a primary alcohol to the carboxylic acid<sup>35</sup> in the presence of a secondary alcohol.

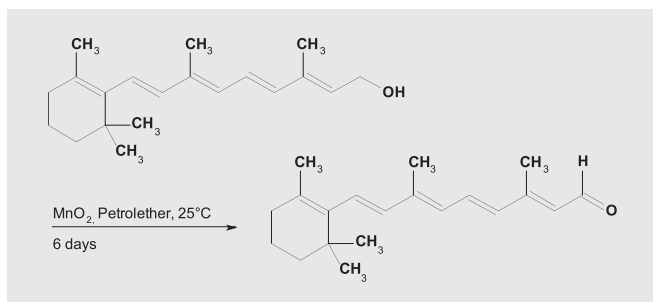
**Solid sodium permanganate monohydrate** (AO 20963) in hexane or dichloromethane has been reported<sup>34</sup> to be a mild and selective oxidizing reagent for a range of primary and secondary alcohols to yield carboxylic acids and ketones.

The classical manganese-based reagent for the oxidation of alcohols to aldehydes or ketones is **activated manganese dioxide** (AO 20319)<sup>36,37</sup>. Several methods for the preparation<sup>38,39,40</sup> and standardization<sup>36</sup> of this reagent have been reported.

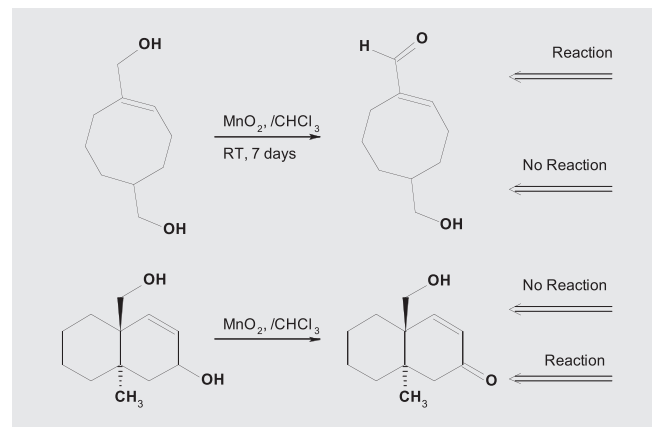
The solvent plays an important role in this heterogeneous reaction: Commonly used solvents are

- saturated hydrocarbons like petroleum ether, pentane or cyclohexane
- chlorinated hydrocarbons like chloroform and dichloromethane
- aromatic solvents
- Acetonitrile.

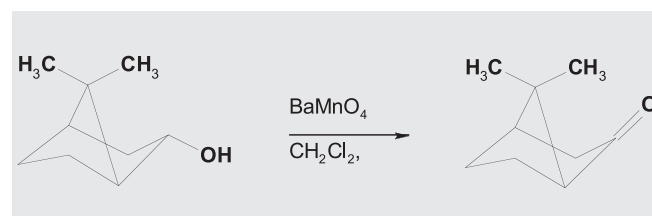
Other solvents like acetone, alcohols, DMSO or ethyl acetate are unsatisfactory because they can deactivate the manganese dioxide surface<sup>36</sup>. Inflammable solvents shall be used with care, because ignition of solvent fumes has been reported<sup>40</sup>. Both manganese dioxide and barium manganate have been used in solvent-free conditions<sup>41</sup>.



Activated manganese dioxide is strong enough to oxidize saturated and non-saturated primary and secondary alcohols to aldehydes<sup>67</sup> and ketones, but mild enough to be applicable to very sensitive compounds like Vitamin A1<sup>42</sup>.



$\alpha,\beta$ -Unsaturated (allylic, benzylic, acetylenic) alcohols react easily, while saturated primary or secondary alcohols react much slower. The direct conjugation of the double bond with the alcohol group is necessary for the speed of reaction; non-conjugated systems have markedly decreased reactivity.



### **Solid barium manganate**

(AO 19848) in dichloromethane has been shown to be as effective and selective<sup>43</sup> as manganese dioxide in oxidizing alcohols to aldehydes and ketones. Because it is stable and can be used without activation it has further advantages over manganese dioxide.

35 C.W.Jefford, Y.Li, Y.Wang, in Organic Synthesis, Coll. Vol. 9, 462.

36 An excellent overview in: A.J. Fatiadi, Synthesis (1976) 65.

37 J.J.Knölker, J.Prakt.Chem. 337 (1995) 75.

38 J. Attenburrow, A.F.R. Cameron, J.H.Chapman, R.M. Evans, B.A. Hems, A.B.A. Jansen, T. Walker, J.Chem.Soc. (1952) 1094.

39 O.Mancera, G.Rosenkranz, F.Sondheimer, J.Chem.Soc. (1953) 2189.

40 M.Harfenist, A.Bavley, W.A.Lazier, J.Org.Chem. 19 (1964) 1608.

41 H. Firouzabadi, B. Karimi, M.Abbassi, J.Chem.Research (S), (1999) 236.

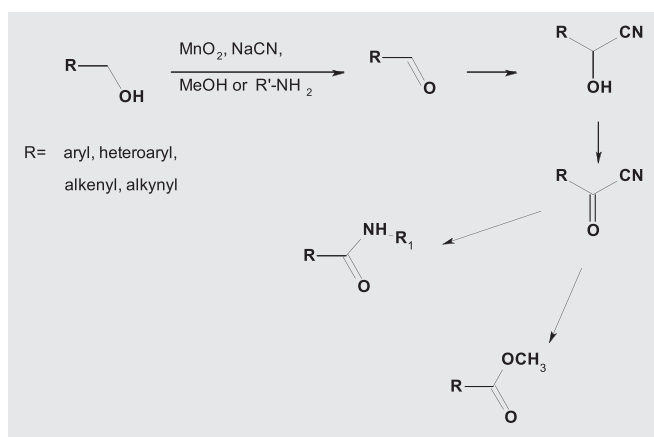
42 S.Ball, T.W.Goodwin, R.A.Morton Biochem.J. 42 (1948) 516.

43 H. Firouzabadi, E. Ghaderi, Tetrahedron Lett. (1978) 839.

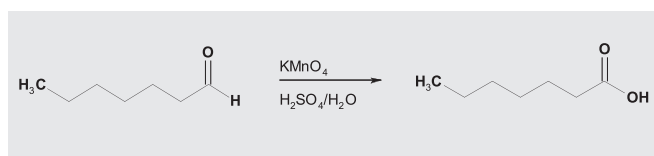


## Oxidation of aldehydes to carboxylic acids

The oxidation of conjugated aldehydes to carboxylic esters or amides with **manganese dioxide** can be achieved through the intermediate cyanohydrins, and requires the presence of cyanide ions<sup>44,45</sup>.



The **Corey-Gilman-Ganem** reaction can transform conjugated alcohols directly to esters or amides in a one-pot reaction<sup>45,46</sup>.

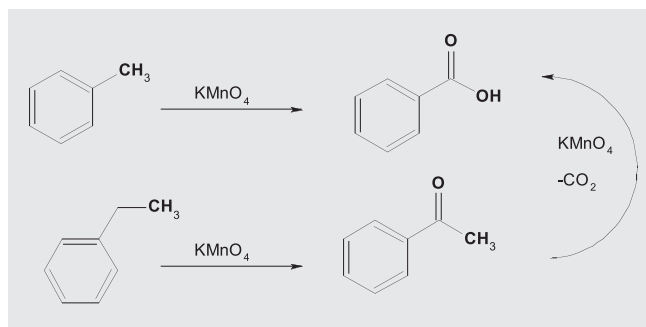


Aliphatic<sup>47</sup>, aromatic and heteroaromatic<sup>48</sup> aldehydes are easily oxidized by potassium permanganate in neutral acidic<sup>47</sup> or alkaline<sup>48</sup> water to yield the corresponding carboxylic acids<sup>3,49,67</sup>. Water/acetone solutions can also be used.

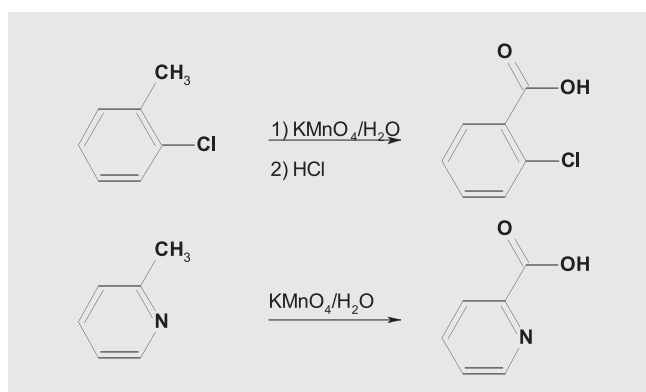
44 E.J.Corey, N.W.Gilman, B.E.Ganem, J.Am.Chem.Soc. 90 (1968) 5618.  
 45 J.S.Foote, H.Kanno, G.M.P.Giblin, R.J.K.Taylor, Synlett, 8 (2002) 1293.  
 46 J.S.Foote, H. Kanno, G.M.Giblin, R.J.K Taylor, Synthesis, 7 (2003) 1055.  
 47 F.Freeman, D.K.Lin, G.R.Moore, J.Org.Chem 47 (1982) 56.  
 48 F.Freeman, J.B.Brand, N.B.Hester, A.A. Kamego, M.L.Kasner, T.G.McLaughlin, E.W.Paull, J.Org.Chem. 35 (1970) 982.

## Oxidation of alkyl arenes

The oxidation of alkyl arenes with potassium permanganate is an important route to benzoic acids and to aromatic ketones<sup>2,3,50,51,52,53,67</sup>.



The reaction is commonly performed in aqueous solutions, sometimes with an organic co-solvent. Recently solvent free conditions have been applied with potassium permanganate on manganese dioxide<sup>54</sup>.



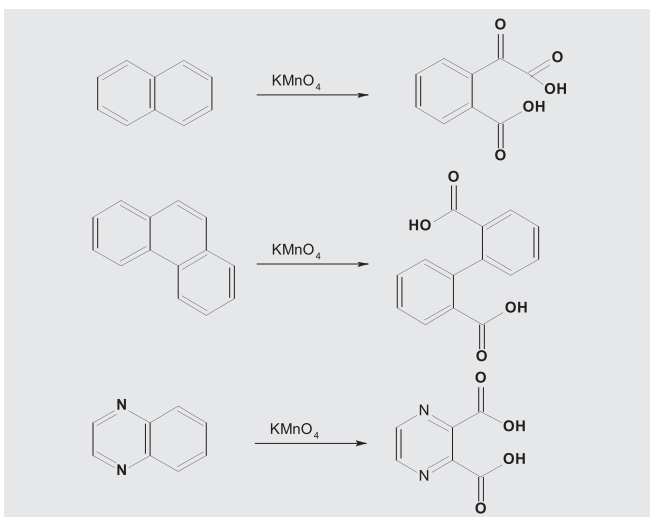
Aromatic compounds with long alkyl sidechains are oxidized to the aryl alkyl-ketones first, which can then be oxidatively cleaved to the benzoic acid if they are enolizable<sup>2</sup>.

49 J.R. Ruhoff, Organic Syntheses, Coll. Vol. 2,315; Vol. 16, 39.  
 50 H. T. Clarke, E. R. Taylor, Organic Syntheses, Coll. Vol. 2, 135; Vol. 10, 20.  
 51 A.W.Singer and S.M.McElvain, Organic Syntheses, Coll. Vol. 3, 740; Vol. 20, 79.  
 52 J.R.Holsten, E.H.Pitt, J.Org.Chem 26 (1961) 4151.  
 53 F.C.Whitmore and G.E. Woodward, Organic Syntheses, Coll. Vol. 1, 159; Vol. 7, 18.  
 54 A. Shaabania, P. Mirzaeia, S. Naderia, D. G. Leeb, Tetrahedron, 2004, 60, 11415-11420.



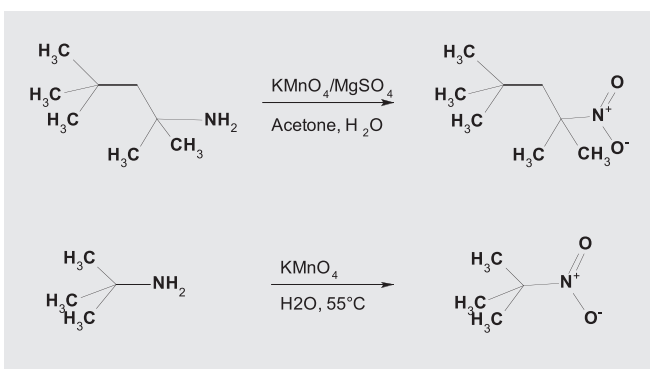
## Oxidation of aromatic rings

Double bonds of aromatic rings can be cleaved by potassium permanganate in a non-acidic, aqueous medium at higher temperature<sup>55</sup>. The reaction of naphthalene in alkaline potassium permanganate leads to phthalonic acid<sup>56</sup>.

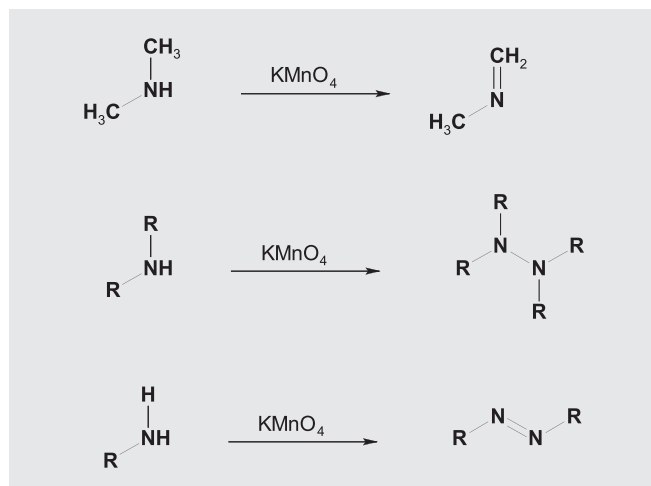


## Oxidation of amines and nitro-compounds

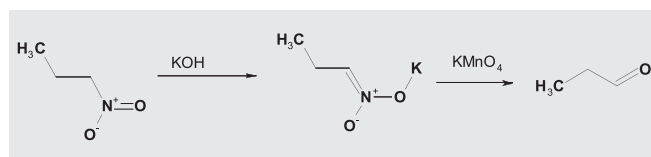
Amines without a proton on the  $\alpha$ -carbon, like tert-octylamine<sup>57</sup>, or tert-butylamine<sup>58</sup>, can be oxidized to nitro compounds with potassium permanganate.



Amines bearing an  $\alpha$ -proton react in a different way<sup>59</sup>. The general action of permanganate or manganese dioxide<sup>60,61</sup> is a dehydration<sup>67</sup>, shown in the following scheme. The reaction can lead to imines, hydrazones or azo compounds. Hydrolysis of the imines leads to aldehydes.

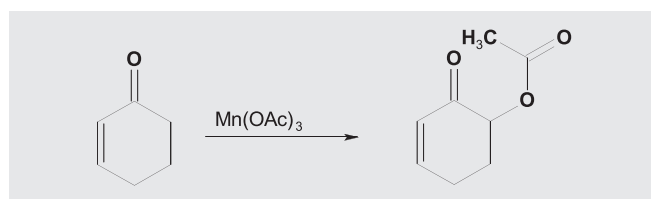


A similar reaction happens with primary nitroalkanes. In alkaline solution the nitroalkane reacts to the nitronate, which is oxidized by permanganate to the aldehyde (see the Nef reaction). The oxidation of the nitronate is normally a faster process than the oxidation of the final aldehyde, but over-oxidation is a common side-reaction.



## Oxidation of enones to $\alpha$ -acetoxyenones

The oxidation of enones with dried manganese triacetate leads to  $\alpha$ -acetoxy-enones<sup>62</sup>.



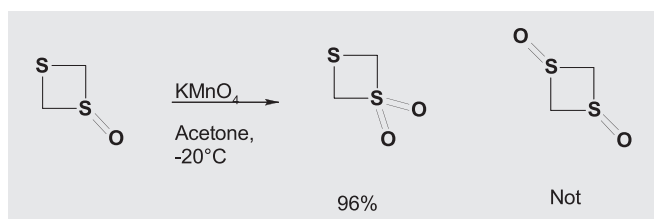
55 R.G.Jones, K.C. McLaughlin, *Organic Syntheses*, Coll. Vol. 4:824; Vol. 30, 86.  
56 J.H.Gardner, C.A.Naylor Jr. *Organic Syntheses*, Coll. Vol. 2, p 523; Vol. 16, 68.  
57 N.Kornblum, W.J.Jones, *Organic Syntheses*, Coll. Vol. 5 845.  
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59 S.S.Rawalay, H.Shechter, *J. Org. Chem.* 32, (1967) 3129.  
60 H.B.Henbest, A.Thomas, *J.Chem.Soc.* (1957) 3032.  
61 R.Daniels, B.D.Martin, *J.Org.Chem* 27 (1962) 178.  
62 N.K.Dunlap, M.R.Sabol, D.S.Watt, *Tetrahedron Lett.* 25 (1984) 5839.



## Oxidation of thioethers and mercaptanes

Mercaptanes can be oxidized to disulfides with barium permanganate<sup>3,63</sup>, while with potassium permanganate they oxidize to sulfonic acids<sup>67</sup>. Thioethers and sulfoxides are oxidized by potassium permanganate to sulfones<sup>3,63</sup>.



Sulfoxides oxidize to sulfones more easily than thioethers oxidize to sulfoxides, illustrated by the following example<sup>64</sup>. The reason for this selectivity is a coordination of the permanganate ion with the sulfoxide. Therefore sulfoxides cannot be isolated from the reaction mixture. Using manganese dioxide in petroleum ether, di-n-butyl sulfide and dibenzyl sulfide can be selectively oxidized to the sulfoxide<sup>65</sup>. Potassium permanganate, manganese dioxide or barium manganate have been proposed as deprotection agents for thioacetals<sup>66</sup>.

63 J.March, *Advanced Organic Chemistry*, 3rd ed., John Wiley & sons New York 1985, p 1087.

64 E. Block, E. R. Corey, R. E. Penn, T. L. Renken, P. F. Sherwin, H. Bock, T. Hirabayshi, S. Mohmand, and B. Solouki, *J.Am.Chem.Soc.*, 104 (1982) 3119.

65 D.Edwards, J.B.Stenlake, *J.Chem.Soc.* (1954) 3272.

66 H.Firouzabadi, H. hazarkhandi, B.Karimi, U. Niroumand, S. Ghassamipour, Forth International Electronic Conference on Synthetic Organic Chemistry.

67 D.Arndt, "Manganverbindungen als Oxidationsmittel in der organischen Chemie" in Houben-Weyl, *Methoden der organischen Chemie*, 4<sup>th</sup>ed. Vol. 4 p 465-672.



## Manganese based oxidation reagents available from Acros Organics

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37221	.....	Silicagel, functionalized, 20% Potassium permanganate
20174	.....	Manganese(III) acetate dihydrate 98%
19347	.....	Manganese(IV) oxide 99.999%
21349	.....	Manganese(IV) oxide 80-85%, powder
20319	.....	Manganese(IV) oxide 88%, precipitated active
35779	.....	Manganese(IV) oxide 99+%, average particle size 2 micron
21868	.....	Potassium permanganate, powder , -325 mesh
19675	.....	Potassium permanganate 98%
20774	.....	Potassium permanganate , p.a..
42417	.....	Potassium permanganate, reagent ACS
20963	.....	Sodium permanganate monohydrate 97%
19848	.....	Barium manganate(VI) 95%

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