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Efficient Mn–Cu and Mn–Co–TEMPO-catalysed oxidation of alcohols into aldehydes and ketones by oxygen under mild conditions

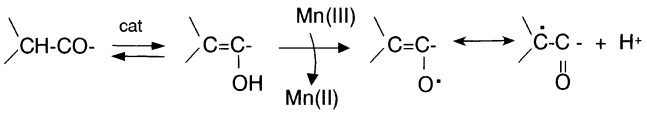
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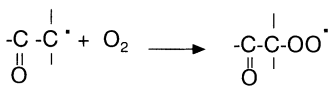
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Abstract—A catalytic amount of Mn(II)–Co(II) or Mn(II)–Cu(II) nitrates in combination with TEMPO allows the selective oxidation of primary and secondary alcohols to aldehydes and ketones by oxygen under very mild conditions. Mechanistic aspects are discussed. The catalyst can be considered the cheapest and the most effective for the selective aerobic oxidation of alcohols.
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Recently we[1] have shown how Mn(II)–Co(II) or Mn(II)–Cu(II) nitrates catalyse the oxidation of cyclohexanone to adipic acid by oxygen under very mild conditions (atmospheric pressure and room temperature) with very high selectivity. Cyclohexanol is completely inert under the same conditions; this could appear paradoxical as cyclohexanol is extremely more reactive than cyclohexanone towards uncatalysed autoxidation, but it is well explained by a redox chain involving an electron-transfer oxidation of the enol form of the ketone (Eqs. (1) and (3)).



(1)



(2)



(3)

Adipic acid is one of the most important intermediates for the production of nylon and it is prepared by autoxidation of cyclohexane to a mixture of cyclohexanol and cyclohexanone at low conversion, in order to have a good selectivity. This mixture is then selectively oxidised to adipic acid by HNO_3.

We have considered the possibility of combining this metal salt catalytic system[1] with 2,2′,6,6′-tetramethylpiperidine-*N*-oxyl (TEMPO), which is known to be an efficient catalyst for the oxidation of alcohols to aldehydes and ketones by a variety of oxidants,[2] in order to oxidise the cyclohexanol–cyclohexanone mixture to adipic acid by oxygen. TEMPO, however, is also an inhibitor of free-radical processes. Thus, by oxidising a mixture of cyclohexanol and cyclohexanone by O_2 in the presence of TEMPO and of the couples Mn(II)–Co(II) or Mn(II)–Cu(II) nitrates, the only result was the selective oxidation of cyclohexanol to cyclohexanone under very mild conditions. Cyclohexanone, under the same conditions but in the absence of TEMPO, is selectively oxidised to adipic acid.[1]

This result suggested to us that the combination of TEMPO with Mn(II)–Co(II) or Mn(II)–Cu(II) nitrates could be a very effective catalyst for the aerobic oxidation of alcohols to aldehydes or ketones. Actually this catalytic system proved to be particularly effective for the aerobic oxidation of alcohols under mild conditions, as shown by the results in Table 1.

The catalytic use of TEMPO for the selective oxidation of alcohols by a variety of oxidants is well-known:[2] a

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particularly convenient method, involving a two-phase system (CH_2Cl_2/H_2O), hypochlorite as oxidant and bromide ion as co-catalyst, was reported by Montanari and co-workers.[3–5] A variety of metal salt complexes was also utilised in combination with TEMPO for the aerobic oxidation of alcohols.[6–8] Copper salts were effective with benzylic and allylic alcohols, while they proved less effective with primary and secondary alcohols.[6] $RuCl_2(PPh_3)_3$ afforded an efficient catalyst[7] at 100°C and 10 bar of pressure. Recently,[8] a more complex catalyst, involving $CuBr{\cdot}Me_2S$ and perfluoroalkylated bipyridine and a perfluorooctane–chlorobenzene biphasic solvent system was utilised at 90°C.

Our catalyst (Mn(II) and Co(II) or Cu(II) nitrates) in combination with TEMPO appears, to the best of our knowledge, the cheapest and the most effective (in the most favourable cases the oxidation takes place with air at atmospheric pressure and room temperature) and therefore particularly convenient for practical applications.

Two aspects of this catalytic system can be emphasised:

1. Mn(II) nitrate is more effective than Co(II) or Cu(II) nitrates, when utilised separately, but the combination of Mn(II) nitrate either with Co(II) or Cu(II) nitrate considerably increases the catalytic effectiveness, as the results in Table 2 show.
2. An acidic medium is necessary to make the catalytic system effective; the oxidation takes place selectively in acetic acid solution, but no substantial oxidation occurs in acetonitrile solution under the same conditions. Since it is well-established[2] that the actual oxidant of the alcohol is the oxo-ammonium salt (Eq. (4)), we explain our results by the fact that the oxoammonium salt is formed by disproportionation of TEMPO catalysed by the acidic medium[9] (Eq. (5)) and that TEMPO is regenerated by oxygen and the metal salt catalytic system (Eq. (6)).

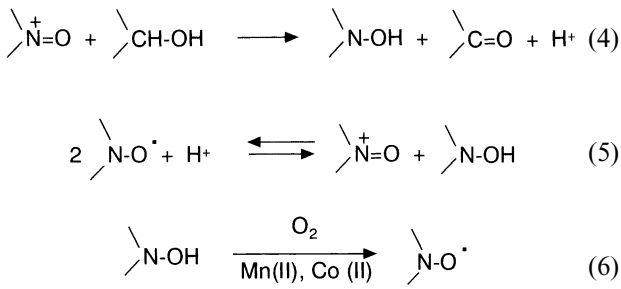


Table 1. Conversion of alcohols to aldehydes or ketones by oxygen[a]

Entry	Alcohol	Product	Time (h)	T (°C)	Yield (%)[b]
1	1-Heptanol	1-Heptanal	6	40	97
2[c]	Benzyl alcohol	Benzaldehyde	10	20	98
3[c]	4-CH_3-Benzyl alcohol	4-CH_3-Benzaldehyde	6	20	99
4	2-OCH_3-Benzyl alcohol	2-OCH_3-Benzaldehyde	4	20	98
5	2-NO_2-Benzyl alcohol	2-NO_2-Benzaldehyde	6	20	97
6[d]	2-NO_2-Benzyl alcohol	2-NO_2-Benzaldehyde	6	20	98
7	Cinnamyl alcohol	Cinnamaldehyde	3	40	99
8	2-Nonanol	2-Nonanone	5	40	100
9	Cyclohexanol	Cyclohexanone	9	20	96
10[d]	Cyclohexanol	Cyclohexanone	9	20	98
11	2-Adamantanol	2-Adamantanone	6	20	97
12[c]	1-Phenylethanol	Acetophenone	6	20	98
13[c]	1-(4-Cl-Phenyl)ethanol	4-Cl-Acetophenone	6	20	96
14[d]	1-Phenylethanol	Acetophenone	6	20	99

[a] According to the standard procedure: 12.5 mmol alcohol, 1.25 mmol TEMPO, 0.25 mmol $Mn(NO_3)_2$, 0.25 mmol $Co(NO_3)_2$ in AcOH (12.5 mL) and O_2 at atmospheric pressure.
[b] Determined by GLC analysis of the crude product.
[c] Air at atmospheric pressure instead of O_2.
[d] 0.25 mmol $Cu(NO_3)_2$ instead of $Co(NO_3)_2$.

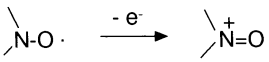
Table 2. Effect of the metal salt catalyst and of the solvent in the oxidation of cyclohexanol by oxygen in AcOH as solvent[a]

Catalyst	Time (h)	Conv. (%)	Catalyst	Time (h)	Conv. (%)
–	4	Traces	$Mn(NO_3)_2$, $Co(NO_3)_2$	2	29
$Co(NO_3)_2$	2	14	$Mn(NO_3)_2$, $Co(NO_3)_2$	4	42
$Co(NO_3)_2$	4	16	$Mn(NO_3)_2$, $Co(NO_3)_2$	9	100
$Cu(NO_3)_2$	2	16	$Mn(NO_3)_2$, $Co(NO_3)_2$[b]	4	<2
$Cu(NO_3)_2$	4	18	$Mn(NO_3)_2$, $Cu(NO_3)_2$	2	30
$Mn(NO_3)_2$	2	19	$Mn(NO_3)_2$, $Cu(NO_3)_2$	4	47
$Mn(NO_3)_2$	4	26	$Mn(NO_3)_2$, $Cu(NO_3)_2$	9	100

[a] The standard procedure of entry 9, Table 1 was utilised.
[b] CH_3CN as solvent instead of AcOH.

In this catalytic cycle TEMPO has two important functions: it generates the oxo-ammonium salt (Eq. (5)), which is responsible for the alcohol oxidation (Eq. (4)), and it inhibits further oxidation of aldehydes and ketones, which occurs by free-radical processes under the same conditions (Eqs. (1)–(3)) in the absence of TEMPO.

The very mild conditions are related to Eq. (6); in non-acidic medium, where disproportionation of Eq. (5) does not occur, more drastic oxidation conditions or more effective oxidants are required in order to oxidise TEMPO to the oxo-ammonium salt (Eq. (7)).



(7)

A typical example on a relatively large preparative scale: a solution of 7.5 g of 2-nitrobenzyl alcohol, 2% of TEMPO, 2% of $Mn(NO_3)_2$, 2% of $Co(NO_3)_2$, in 39 mL of CH_3COOH was stirred at 40°C during 6 h under O_2 at atmospheric pressure. GLC revealed a 99% yield. Acetic acid was evaporated and the residue dissolved in CH_2Cl_2. Chromatography on silica gel yielded 6.9 g of pure 2-nitrobenzaldehyde (mp 44°C, 93% yield).

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