Molybdenum(VI) Dichloride Dioxide/Copper(II) Perchlorate: An Efficient Bimetallic Catalyst for Aerobic Oxidation of Alcohols

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Abstract: The bimetallic system, $MoO_2Cl_2/Cu(ClO_4)_2 \cdot 6H_2O$ was used as an efficient catalyst for aerobic oxidation of alcohols. Aromatic, aliphatic, and allylic alcohols; also hydroxy esters were oxidized to the corresponding carbonyl compounds. The bimetallic catalyst showed higher reactivity for alcohol oxidation as compared to individual metal catalysts.

1. INTRODUCTION

From synthetic view point, oxidation of alcohols to the corresponding carbonyl compounds is one of the most important reactions in organic synthesis [1]. Chromium, manganese and hypervalent iodine reagents are widely used for alcohol oxidation. However, requirement of stoichiometric amount, safety hazards, formation of by-products and difficulty in work-up are major experimental problems [2]. Recently, catalytic oxidation employing complexes of transition metal ions, such as Fe, V, Cu, Co, Pd, Pt, Ru, etc. in the presence of (2,2,6,6-Tetramethylpiperidine-1-oxyl, i.e. TEMPO)/base are developed [3]. There are only few reports on alcohol oxidation using molybdenum compounds, however, in presence of H_2O_2 [4].

The application of bimetallic systems in organic synthesis has emerged in oxidation, coupling and conjugate addition reactions [5,6]. There are few reports available on selective oxidation of alcohols to aldehydes or ketones by using bimetallic systems [6]. The use of bimetallic systems for alcohol oxidation can offer the advantage of one metal activating the alcohol while the other activates molecular oxygen and thus results in more efficient catalysis than individual metals.

Recently, molybdenum(VI) dichloride dioxide (MoO_2Cl_2) has been used as an efficient catalyst for several organic transformations [7]. In our ongoing research work on the catalytic role of MoO_2Cl_2, we have reported controlled and selective oxidation of sulfides to sulfoxides/sulfones [8a], aerobic oxidation of secondary and activated primary benzyl alcohols [8b], ring opening reaction of epoxides [8c], C-H insertion of ethyl diazoacetate into aldehydes [8d] and oxidation followed by bromination of β-hydroxycarbonyls [8e]. Apart from these work, we have also reported copper(II) perchlorate ($Cu(ClO_4)_2 \cdot 6H_2O$) as an efficient catalyst for acetylation reactions [8f].

Since, MoO_2Cl_2 can oxidize only secondary and activated primary benzyl alcohols [8b] modification of the condition is

required to widen the scope of alcohol oxidation reaction. Herein we disclose further developments on alcohol oxidation (i.e. oxidation of activated/un-activated benzyl alcohols and aliphatic secondary alcohols) using $MoO_2Cl_2/Cu(ClO_4)_2 \cdot 6H_2O$ as an efficient bimetallic catalyst. The choice of Cu(II) as a co-catalyst is considered because this metal ion is known to activate molecular oxygen.

2. EXPERIMENTAL SECTION

2.1. General Consideration

Alcohols **1**, **3-16**, molybdenum(VI) dichloride dioxide (MoO_2Cl_2) and copper salts were purchased from Aldrich. Alcohols **2** and **17-21** were prepared by literature methods [9]. Alcohols and solvents were purified before use for the reactions [10]. The products were characterized by recording ^{1}H & ^{13}C NMR spectra, IR spectra and melting points using Bruker 400 MHz NMR spectrometer, Jasco FT/IR 660 plus and Toshnival-India melting point apparatus respectively. The spectral data are comparable with literature [11].

### 2.2. Experimental Procedure for Alcohol Oxidation

A mixture of 1 mmol of alcohol, 5 mol% of MoO_2Cl_2, 5 mol% of $Cu(ClO_4)_2 \cdot 6H_2O$ and 50 mg of 4Å molecular sieve (MS) in 3 mL of toluene was stirred under reflux condition while bubbling oxygen. The conversion of alcohol was monitored by thin layer chromatography (TLC). After completion of the reaction, the solvent was evaporated and crude sample was subjected to aqueous work up followed by column chromatography purification to afford the carbonyl compound.

3. RESULTS AND DISCUSSION

3.1. Comparison of Bimetallic Catalyst

As preliminary study we have tested the oxidation of benzyl alcohol (**1**) under various conditions (Table **1**). The reactions were carried out under reflux in toluene with 10 mol% of the catalyst. Molybdenum and copper catalysts alone could not oxidize benzyl alcohol (**1**) (no product was detected in thin layer chromatography (TLC)) whereas the bimetallic systems i.e. MoO_2Cl_2/CuX_2 (where X = Cl, OAc, NO_3 and ClO_4) could oxidize benzyl alcohol (**1**) to benzaldehyde (**1a**) in 52-89% of

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Table 1. **Oxidation of Benzyl Alcohol Under Various Conditions[a]**
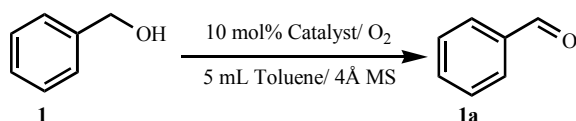
Entry	Catalyst	Time (min)	Yield (%)[b]
1	10 mol% MoO$_2$Cl$_2$	720	--[c]
2	10 mol% CuX$_2$	720	--[c,d]
3	5 mol% MoO$_2$Cl$_2$/ 5 mol% CuX$_2$	720	52-89[d]
4	5 mol% MoO$_2$Cl$_2$/ 5 mol% Cu(ClO$_4$)$_2$·6H$_2$O	60	89

[a]Reaction conditions: A mixture of 1 mmol of alcohol, 10 mol% of catalyst and 50 mg of 4Å molecular sieve was stirred under reflux condition while bubbling oxygen. [b]Isolated yield. [c]No product was detected in thin layer chromatography (TLC). [d]X = Cl, OAc, NO$_3$ and ClO$_4$

yields. Among the various copper salts used here Cu(ClO$_4$)$_2$·6H$_2$O was found to be most efficient when combined with MoO$_2$Cl$_2$ to provide 89% of benzldehyde (**1a**). Further application of the MoO$_2$Cl$_2$/Cu (ClO$_4$)$_2$·6H$_2$O system was studied by oxidizing various primary benzyl alcohols, aliphatic and aromatic secondary alcohols and hydroxy esters (Tables **2-4**).

3.2. Oxidation of alcohols to aldehydes

The summarized results for the oxidation of primary benzyl alcohols are provided in Table **2**. The activated primary benzyl alcohols **2** and **3** (Table **2**, entries 2 and 3) were oxidized to corresponding aldehydes **2a** and **3a** in quantitative yields within 15-30 minutes. It is also interesting to note that these two substrates posses other oxidisable functional groups i.e. *tert*-amine and sulfide which were intact in the present condition. Deactivated primary benzyl alcohols **4** and **5** (i.e. 4-nitro and 4-bromo benzyl alcohols) and the heterocyclic alcohol i.e. 2-prydine methanol (**6**) were oxidized to corresponding aldehydes **4a-6a** in 62-89 % of yields within 60 minutes. Cinnamyl alcohol (**7**) was oxidized to cinnamaldehyde (**7a**) in a good yield without affecting the double bond. The deactivated benzyl alcohol, e.g. **5** is less reactive and provide lower yield of aldehyde as compared to the substrate having electron releasing group on the ring.

Table 2. **Oxidation of Primary Benzyl Alcohols Using MoO$_2$Cl$_2$/Cu(ClO$_4$)$_2$·6H$_2$O as the Bimetallic System[a]**

Entry	Substrates	Product	Time (min)	Yield (%)[b]
1	**1**	**1a**	60	89
2	**2**	**2a**	30	90
3	**3**	**3a**	15	95
4	**4**	**4a**	15	85
5	**5**	**5a**	90	62
6	**6**	**6a**	60	89
7	**7**	**7a**	60	78

[a]Reaction conditions: A mixture of 1 mmol of alcohol, 5 mol% of MoO$_2$Cl$_2$, 5 mol% of Cu(ClO$_4$)$_2$·6H$_2$O and 50 mg of 4Å molecular sieve was stirred under reflux condition while bubbling oxygen. [b]Isolated yield.

3.3. Oxidation of Alcohols to Ketones

The summarized results for the oxidation of secondary alcohols were provided in Table **3**. Unactivated, activated and deactivated benzyl alcohols, **8-11** (Table **3**, entries 8-11) were oxidized to corresponding ketones **8a-11a** in above 80% of yields. Further efficiency of the MoO$_2$Cl$_2$/Cu(ClO$_4$)$_2$· 6H$_2$O system was studied on oxidation of aliphatic secondary alcohols; cyclic and acylic secondary alcohols **12-14** (Table **3**, entries 12-14) were oxidized to corresponding ketones **12a-14a** in 52-60% of yields. Thus aliphatic alcohols are found to be less reactive.

3.4. Oxidation of Esters to Keto Esters

The summarized results for the oxidation of α- and β- hydroxy esters are provided in Table **4**. Aryl substituted α- and β-hydroxy esters, **15- 20** (Table **4**, entries 15-20) were

Table 3.   Oxidation of Secondary Alcohols Using MoO$_2$Cl$_2$/Cu(ClO$_4$)$_2$·6H$_2$O as the Bimetallic System[a]

Entry	Substrates	Product	Time (min)	Yield (%)[b]
8	**8**	**8a**	60	85
9	**9**	**9a**	30	89
10	**10**	**10a**	180	83
11	**11**	**11a**	90	93
12	**12**	**12a**	720	60
13	**13**	**13a**	720	59
14	**14**	**14a**	720	52

[a]Reaction conditions: A mixture of 1 mmol of alcohol, 5 mol% of MoO$_2$Cl$_2$, 5 mol% of Cu(ClO$_4$)$_2$·6H$_2$O and 50 mg of 4Å moleculer sieve was stirred under reflux condition while bubbling oxygen. [b]Isolated yield.

Table 4.   **Oxidation of α-and β-Hydroxy Ester Using MoO$_2$Cl$_2$/Cu(ClO$_4$)$_2$·6H$_2$O as the Bimetallic System[a]**

Entry	Substrates	Product	Time (min)	Yield (%)[b]
15	**15**	**15a**	180	92
16	**16**	**16a**	60	89
17	**17**	**17a**	180	76
18	**18**	**18a**	180	82
19	**19**	**19a**	60	79
20	**20**	**20a**	240	70
21	**21**	**21a**	720	18

[a]Reaction conditions: A mixture of 1 mmol of alcohol, 5 mol% of MoO$_2$Cl$_2$, 5 mol% of Cu(ClO$_4$)$_2$·6H$_2$O and 50 mg of 4Å moleculer sieve was stirred under reflux condition while bubbling oxygen. [b]Isolated yield.

oxidized to corresponding keto esters **15a-20a** in 70-92% of yields. Alkyl substituted β-hydroxy ester **21** was oxidized to corresponding β-keto ester **21a** in 18% of yield. In this class of compounds the aliphatic compounds are found to be less reactive as observed from the lower yield of the desired product.
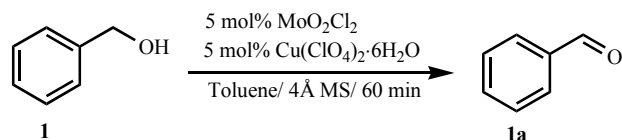
3.5. Mechanism of Alcohol Oxidation in the Bimetallic System

We have studied the role of oxygen in this reaction, by oxidizing benzyl alcohol (**1**) under various conditions (Table **5**) by controlling the atmosphere of the reaction. The reaction provides 71% benzaldehyde when exposed to air where as under bubbling oxygen 89% of benzaldehyde was obtained. Under N$_2$ atmosphere the reaction does not proceed, which shows the participation of aerobic oxygen in the oxidation process.

During the oxidation of alcohols using the bimetallic catalyst, it is proposed that, Mo(VI) species undergoes reduction to Mo(IV) which could be re-oxidized to Mo(VI) by Cu(II) (Scheme **1**). The Cu(I) so formed could be re-oxidized to Cu(II) by molecular oxygen [5]. These molybdenum species present in the catalytic cycle are expected to bind alcohol/alkoxide to initiate and sustain the oxidation reaction. When the Mo(IV) species is bound to alcohol/alkoxide having electron withdrawing group then the Mo(IV) center will experience decrease of electron density around it and hence oxidation to generate Mo(VI) by oxygen should be hampered. In the same line presence of electron releasing group should favor the oxidation of Mo(IV) to Mo(VI). The reactivity patterns of the alcohols to provide aldehydes support this argument. Addition of the Cu(II) as a cocatalyst some what circumvent this problem by activating molecular oxy-

gen and facilitating oxidation of Mo(IV) to Mo(VI) and hence before the catalyst is deactivated oxidation of less reactive alcohols is also realised.

Table 5. **Oxidtion of Benzyl Alcohol Under Various Atmospheres[a]**

$$\text{1} \quad \xrightarrow[\text{Toluene/ 4Å MS/ 60 min}]{\substack{\text{5 mol\% MoO}_2\text{Cl}_2 \\ \text{5 mol\% Cu(ClO}_4)_2\cdot 6\text{H}_2\text{O}}} \quad \text{1a}$$

Reaction Condition	Yield (%)[b]
Open air	71
Under O₂	89
Under N₂	--[c]

[a]Reaction conditions: A mixture of 1 mmol of benzyl alcohol, 5 mol% of MoO₂Cl₂, 5 mol% of Cu(ClO₄)₂·6H₂O and 50 mg of 4Å moleculer sieve was stirred under reflux condition. [b]Isolated yield. [c]No product was detected in thin layer chromatography (TLC).
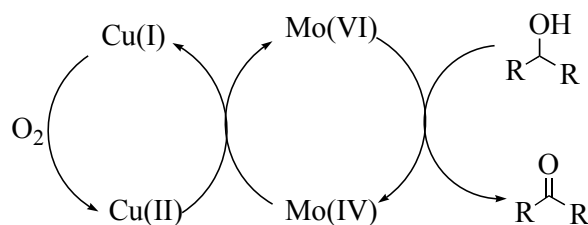
Scheme 1. Proposed mechanism for redox reactions in the bimetallic system during alcohol oxidation.

4. CONCLUSIONS

In conclusion, we have demonstrated the use of MoO₂Cl₂/Cu(ClO₄)₂·6H₂O as a bimetallic catalyst for alcohol oxidation. Various alcohols were oxidized to corresponding carbonyl compounds in good yields. The individual metal catalysts are found to be less efficient for alcohol oxidation. More importantly, benzyl alcohols having no ring substituent or electron withdrawing substituent could be oxidized by the bimetallic catalyst which is not possible with MoO₂Cl₂. Some oxidisable functional groups like amine, pyridine, sulfide and olefin groups are tolerated during the conversion. Synthesis of dicarbonyls is also achieved using this method.

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