

Tandem catalysis: Direct catalytic synthesis of imines from alcohols using manganese octahedral molecular sieves

Shanthakumar Sithambaram^b, Ranjit Kumar^b, Young-Chan Son^b, Steven L. Suib^{a,*}

^a Department of Chemistry, Department of Chemical Engineering, and Institute of Materials Science, University of Connecticut, U-3060, 55 North Eagleville Rd., Storrs, CT 06269-3060, USA

^b Department of Chemistry, University of Connecticut, U-3060, 55 North Eagleville Rd., Storrs, CT 06269-3060, USA

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Abstract

Tandem processes involving catalysts can offer unique and powerful strategies for converting simple starting materials into more complex products in a single reaction vessel. Imines were synthesized directly from alcohols via a tandem catalytic process using manganese octahedral molecular sieves (OMS-2) as catalyst. The synthesis proceeds through two steps: an oxidation of the alcohols to carbonyls followed by the nucleophilic attack by an amine on the carbonyl to form the imine. OMS-2 acts as a bifunctional catalyst and catalyzes two mechanistically distinct processes in a single reaction vessel under the same conditions. Conversions up to 100% were obtained for benzylic alcohols with this efficient, environmentally friendly catalytic reaction. The advantages of this process are that the intermediates need not be isolated and the catalysts can be reused upon simple filtration without loss of activity.

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1. Introduction

Tandem processes that involve multiple chemical transformations in a single-pot with minimal work up and less waste generation have revolutionized synthetic chemistry in recent years [1]. Tandem catalytic processes can replace multi-step syntheses with efficient catalytic reactions that can have significant impact on the manufacture of fine chemicals and pharmaceutical intermediates [2]. These processes are very efficient in terms of work up and catalyst utilization, and provide the advantage that intermediates do not require isolation where they are unstable or difficult to handle (e.g., toxic, volatile or prone to polymerize). When a reaction that involve two or more mechanistically distinct processes promoted by a single catalyst, the process is called auto tandem catalysis [3]. Recently, there have been many reports of heterogeneous bifunctional catalysts used for single-pot synthesis. Bifunctional

palladium/amberlyst catalysts have been used to carry out dehydration of the tertiary alcohol and the hydrogenation of the *in situ* formed alkene in a single vessel [4]. In another example, caprolactam, a precursor for Nylon-6, which generally requires a two step synthesis, was synthesized in high yields in a single-pot using an aluminophosphate bifunctional heterogeneous catalyst [5]. The finding and utilization of a single catalyst to promote more than one transformation in a selective manner is a promising area of research [6]. Such direct synthesis routes help to avoid side product formation and loss of starting material as well as to reduce capital investment and operation costs.

Imines are very versatile intermediates in synthetic organic chemistry and pharmaceutical compounds such as β -lactams [6–8]. Imines have potential for therapeutic applications such as anti-inflammatory agents and anti-cancer agents [9,10]. Several methods for the synthesis of imines are described in the literature; they can be obtained from aldehydes [11], palladium catalyzed amination [12], formamides [13], and by polymer-supported [14]. However, these methodologies often require complex procedures and long reaction times. A tan-

* Corresponding author. Fax: +1 860 486 2981.

E-mail address: steven.suib@uconn.edu (S.L. Suib).

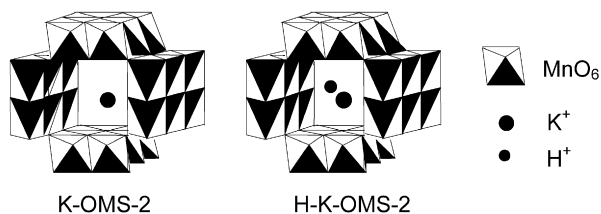


Fig. 1. Structure of OMS-2 catalysts.

dem oxidation-imine formation process with active manganese oxide to produce imines directly from alcohols has been reported [15], but the method has a serious drawback that it requires an excess amount of active manganese oxide as the stoichiometric oxidant and 4 Å molecular sieves as the dehydrating agent. Furthermore, the reactions were done with chlorinated solvents requiring longer reaction times.

Catalytic applications of octahedral molecular sieves (OMS) of manganese oxides are well known and the recent examples have been efficient oxidation of alcohols [16] and epoxidation of olefins [17]. In comparison, active manganese oxide requires 5–10 equivalents of oxidant for alcohol oxidation reactions [18], whereas only ~0.5 equivalent of OMS-2 is needed. Environmentally friendly catalytic reactions have tremendous advantages over those that use a stoichiometric reagent. Various types of OMS have been synthesized in our laboratory and the characterization and applications are well established [19,20]. For the present study, OMS-2 (cryptomelane) type materials were used as catalysts. OMS-2 consists of a one-dimensional tunnel structure formed by 2 × 2 edge shared MnO₆ octahedra (Fig. 1). The composition of K-OMS-2 is KMn₈O₁₆·*n*H₂O and the tunnels have dimensions of 4.6 × 4.6 Å. The average oxidation state of Mn in K-OMS-2 is ~3.8 containing of Mn⁴⁺, Mn³⁺, and Mn²⁺ ions in the framework. The surface area is ~90 m²/g, mesopore and total pore volumes are 0.29 and 0.49 cm³/g, respectively [21,22,39].

In this paper we report a more efficient tandem catalytic process to form imines directly from alcohols using OMS-2 as a catalyst. OMS-2 acts as a bifunctional catalyst in this reaction to oxidize the alcohols to the carbonyls and subsequently, acts as a Lewis acid to form imines. These two mechanistically distinct steps are catalyzed by OMS-2 in a single reaction vessel under the same conditions. The process does not require any additives for water removal.

2. Experimental

2.1. Reagents

All chemicals were purchased from Aldrich and were used without further purification unless noted otherwise.

2.2. Catalyst synthesis

K-OMS-2 was prepared and characterized using a procedure reported in the literature [19]. Potassium permanganate solution (0.4 M, 225 mL) was added to a mixture of manganese sulfate hydrate solution (1.75 M, 67.5 mL) and concentrated

nitric acid (6.8 mL) to a 500 mL of round bottom flask with a condenser. The dark brown slurry was refluxed for 24 h, then filtered and washed with deionized water several times. The catalyst was dried at 120 °C overnight before use. H⁺ substituted K-OMS-2 was obtained by ion-exchanging K-OMS-2 with HNO₃. K-OMS-2 was stirred in 1 M solution of nitric acid for 6 h between 60–70 °C to prepare H-K-OMS-2.

2.3. X-Ray powder diffraction studies

The structure of the materials was studied by X-ray diffraction (XRD) experiments. A Scintag 2000 PDS instrument with CuKα radiation with a beam voltage of 45 kV and a beam current of 40 mA was used to collect the X-ray data. The X-ray patterns of the catalysts were compared to that of the standard OMS-2 materials (JCPDS file # 29-1020) (Fig. 2).

2.4. Scanning electron microscopy

Scanning Electron Micrographs were taken on a Zeiss DSM 982 Gemini field emission scanning microscope with a Schotky Emitter at an accelerating voltage of 2 kV with a beam current of 1 μA. The images showed a characteristic fibrous morphology of OMS-2 materials (Fig. 3).

2.5. Reaction procedure

Alcohol (1 mmol), toluene (10 mL), primary amine (2–5 mmol), and K-OMS-2 (50 mg) were added to a 50 mL round-bottomed flask. The mixture was stirred under reflux for 12–24 h at 110 °C in air and the reaction progress was monitored by TLC. After the reaction, the mixture was cooled, OMS-2 was removed by filtration, and the products were analyzed.

2.6. Analytical procedure

Gas chromatography-mass spectroscopy (GC-MS) method was used for the identification and quantification of the product mixtures. GC-MS analyses were done using an HP 5890 series II chromatograph with a thermal conductivity detector coupled with an HP 5970 mass selective detector. An HP-1 column (non polar cross linked siloxane) with dimensions of 12.5 m × 0.2 mm × 0.33 μm was used in the gas chromatograph. ¹H and ¹³C NMR were collected on a Bruker DRX-400 (400.144 MHz ¹H, 100.65 MHz ¹³C).

3. Results

3.1. Effect of alcohols and amines

The initial imine synthesis was carried out using benzyl alcohol with butyl amine in toluene under reflux (110 °C) in the presence of air. A 100% conversion and 99% selectivity for the corresponding imine were obtained in 12 h. The optimum conditions were then extended to a range of other benzyl, allyl and alkyl alcohols with primary amines as exemplary reactions. Table 1 shows the results of the effects of various alcohols on

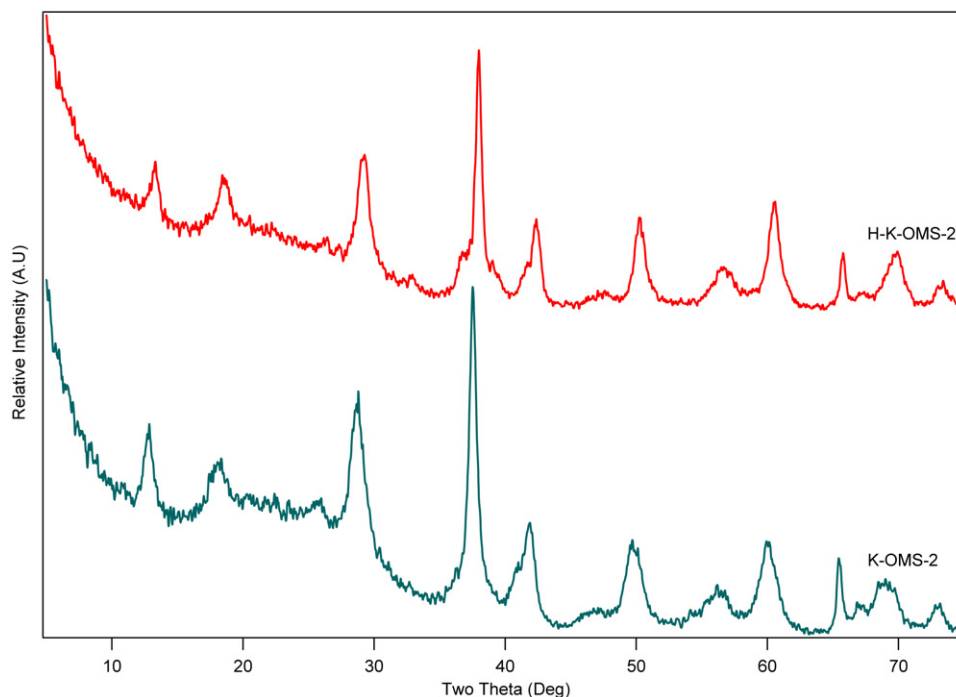


Fig. 2. XRD patterns of K-OMS-2 and H-K-OMS-2 catalysts.

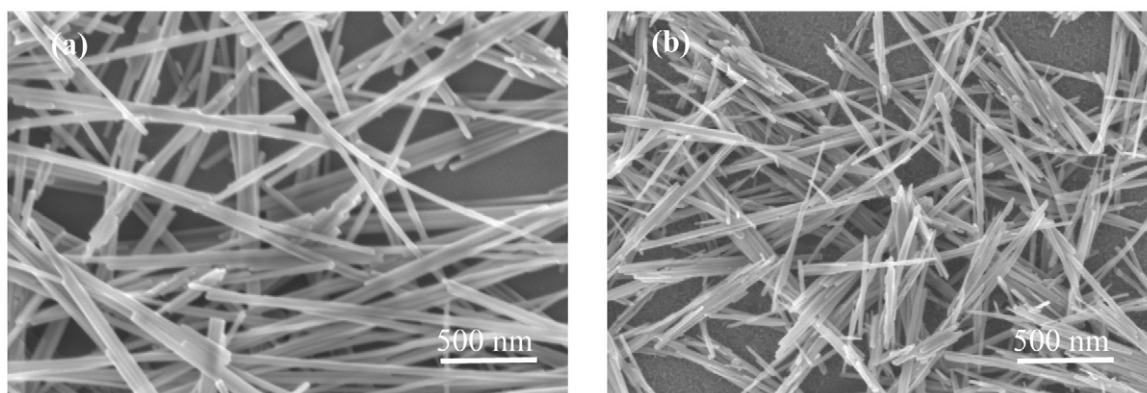


Fig. 3. FESEM images of K-OMS-2 and H-K-OMS-2 catalysts.

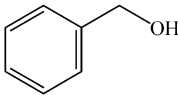
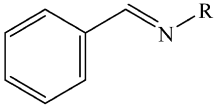
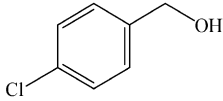
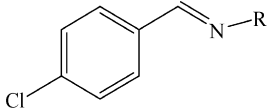
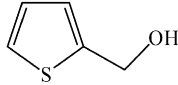
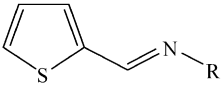
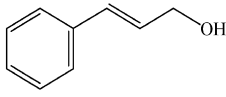
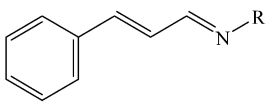
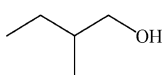
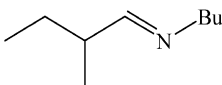
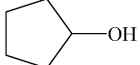
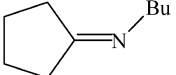
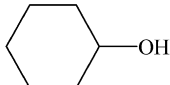
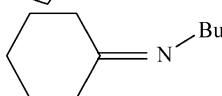
the conversion and selectivity for imines. The conversion was 100% in the case of benzylic alcohols, whereas the selectivity towards imine was about 99% in most cases (entries 1 and 2). Reactions were faster when butyl amine was reacted with alcohols as compared to the case where aniline was reacted with the alcohols. When the reactions were done with aniline as the base it took 24 h for the reaction to be completed. 2-thiophene methanol (entry 3) and cinnamyl alcohol (entry 4) gave lower conversions when reacted with aniline as compared to when they were reacted with butyl amine. Aliphatic primary and secondary alcohols gave low conversions, however the selectivity for imine was still 100% (entries 5 and 7).

The effect of various substituents on the benzene ring was evaluated in the imine synthesis and the results are listed in Table 2. 4-methoxy benzyl alcohol with aniline (entry 8) gave 77% conversion 71% selectivity for imine. 4-Methyl benzyl alcohol (entry 9) gave 89% conversion and 90% selectivity for

the corresponding imine. In contrast, 4-nitro benzyl alcohol and 4-chloro benzyl alcohol (entries 10 and 11) showed 100% conversions and 100 and 99% selectivities, respectively. When the aniline was changed to *p*-nitro aniline and reacted with 4-methoxy benzyl alcohol the conversion was only 66% and selectivity was 39% (entry 12).

In order to determine the role of OMS-2 in the formation of the imine in the second step, a series of reactions were done starting from aldehydes and amines with and without the catalyst (Table 3). The conversions were higher when the catalyst was used than without in all cases (entries 13–15). The reaction between *p*-methoxybenzaldehyde and *p*-nitroaniline in presence of the catalyst afforded 81% imine, and the reaction without the catalyst gave only 21% imine. Similar trend in results were observed for the other two reactions with 3,4-dimethoxybenzaldehyde and 4-methylbenzaldehyde as substrates.

Table 1
Synthesis of imines from alcohols and amines

Entry	Substrate ^a	Product	Amine ^b	Conversion ^c	Selectivity ^{d,e}
1			Bu-NH ₂	100	99
			Ph-NH ₂	100	100
2			Bu-NH ₂	100	99
			Ph-NH ₂	100	99
3			Bu-NH ₂	97	99
			Ph-NH ₂	75	97
4			Bu-NH ₂	99(99) ^f	80 ^c (100) ^f
			Ph-NH ₂	58(61) ^f	74(84) ^f
5			Bu-NH ₂	44	100
6			Bu-NH ₂	25	100
7			Bu-NH ₂	12	100

^a Reaction conditions: 1 mmol alcohol, 2 mmol amine, 10 mL toluene as solvent, 50 mg of K-OMS-2 as catalyst, reflux at 110 °C, *t* = 12 h for butylamine, 24 h for aniline.

^b Bu-NH₂ = *n*-butylamine, Ph-NH₂ = aniline.

^c Conversion (%) based on substrate = [1 - ((concentration of substrate left after reaction) × (initial concentration of substrate)⁻¹)] × 100.

^d Selectivity for imines, other product was aldehyde.

^e Selectivity (%) of product = ((concentration of product) × (total concentration of all products)⁻¹) × 100.

^f Catalyst was H-K-OMS-2.

Shape selectivity of the substrate was studied by reacting various benzene dimethanols with butylamine and the results are shown in Table 4. Imine formation with benzene dimethanol and butyl amine gave interesting results. Among the benzene dimethanol substrates (entries 16–18), benzene-1,4-dimethanol gave the highest selectivity (100%) for its diimine. Benzene-1,3-dimethanol gave 100% conversion, but the selectivity of the diimine was only 20% and the rest was the monoimine. There was no diimine formed when benzene-1,2-dimethanol was reacted with butylamine. However, in addition to monoimines, the formation of 3H-benzofuran-2-one was observed. Benzoin, a hydroxyl ketone was also reacted with butylamine, and showed 24% selectivity for diimine and 76% selectivity for the monoimine.

3.2. Effect of solvents

Effect of various polar and non-polar solvents was investigated for the reaction of benzyl alcohol with butyl amine to form the corresponding imine as shown in Table 5. Toluene was found to be the best solvent for this reaction under the conditions used for this reaction. Toluene, a non-polar and aprotic

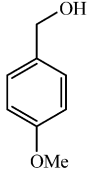
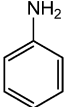
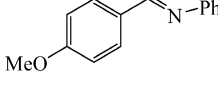
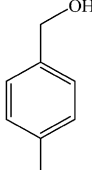
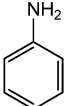
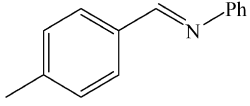
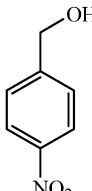
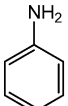
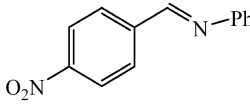
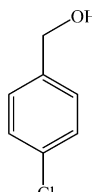
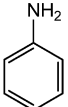
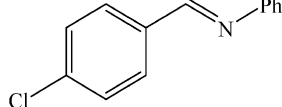
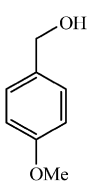
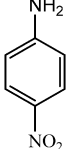
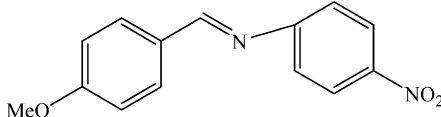
solvent, gave 99% conversion and 100% selectivity (entry 20). Xylene (entry 21) showed 85% conversion and very selective imine formation. The other non-polar solvent, octane (entry 22) gave only 50% conversion and resulted in the formation of a mixture of benzaldehyde and imine, showing partial selectivity to imine. Polar solvent such as acetonitrile (entry 23) gave only 34% conversion.

3.3. Catalyst reusability and stability

The reusability of the catalyst was tested with “spent” K-OMS-2. The catalyst was recovered by filtration after the reaction, regenerated by washing with acetone and water and then drying at 300 °C for 6 h. The regenerated catalyst was reused four times without any appreciable loss of activity. XRD pattern of K-OMS-2 before and after the reaction indicates that the structure of K-OMS-2 is retained after the reaction.

To rule out any possibility of homogeneous catalysis, we ran the reaction between *p*-anisyl alcohol and aniline (entry 8) for 12 h (conversion 54%). Then the catalyst was removed by fil-

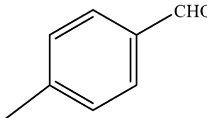
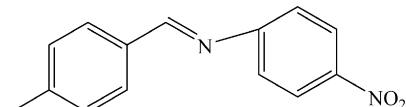
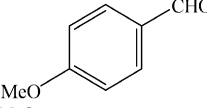
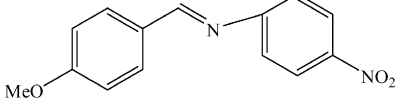
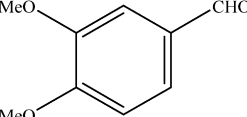
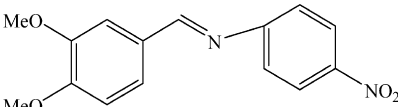
Table 2
The effect of electron donating and electron withdrawing groups

Entry	Substrate	Amine	Product ^a	Conversion	Selectivity
8				77	71 ^b
9				89	90 ^b
10				100	100
11				100	99
12				66	39 ^b

^a Reaction conditions: 1 mmol alcohol, 2 mmol amine, 10 mL toluene as solvent, 50 mg of K-OMS-2 as catalyst, reflux at 110 °C, *t* = 24 h.

^b The other product was aldehyde.

Table 3
Effect of catalyst on imine synthesis from aldehydes

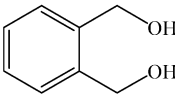
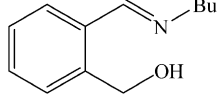
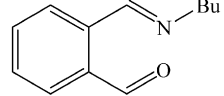
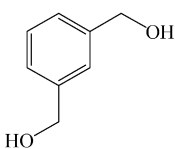
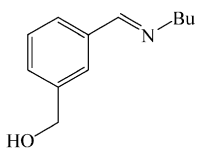
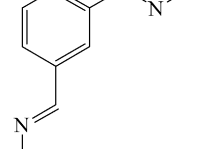
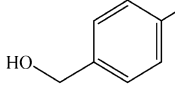
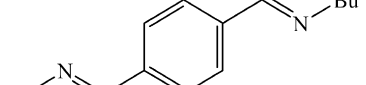
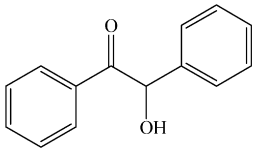
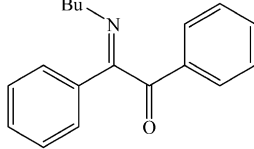
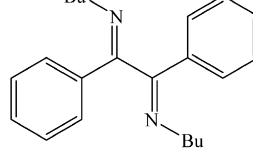
Entry	Substrate	Product ^a	OMS-2	No OMS-2
13			86	77
14			81	21
15			74	16

^a Reaction conditions: 1 mmol aldehyde, 2 mmol 4-nitroaniline, 10 mL toluene as solvent, 50 mg of K-OMS-2 as catalyst, reflux at 110 °C, *t* = 24 h.

tration and the mixture was allowed to react for an additional 24 h. However, no change in conversion was observed. These

findings suggested that no leaching of the catalyst is occurring under our reaction conditions.

Table 4
Diimine formation from benzylic alcohols and amines^a

Entry	Alcohol	Product (selectivity, %)
16		 (78%)  (3%) ^b
17		 (80%)  (20%)
18		 (100%)
19		 (76%)  (24%)

^a Reaction conditions: 1 mmol alcohol, 5 mmol butylamine, 10 mL toluene as solvent, 50 mg of K-OMS-2 as catalyst, reflux at 110 °C, *t* = 24 h. Conversion is 100% in all cases. Amine: *n*-butyl amine, Bu: CH₃CH₂CH₂CH₂-.

^b Other product was 3H-benzofuran-2-one.

Table 5
The effect of solvents on imine formation^a

Entry	Solvent	Reaction temperature (°C)	Conversion (%)	Selectivity (%)
20	Toluene	110	99	100 ^b
21	Xylene	145	85	100 ^b
22	Octane	125	50	78 ^b 22 ^c
23	Acetonitrile	80	34	57 ^b 27 ^c 16 ^d

^a Reaction conditions: 1 mmol benzylalcohol, 2 mmol butylamine, 10 mL solvent, 50 mg of K-OMS-2 as catalyst, reflux, *t* = 12 h.

^b Imine (*N*-benzyl butylamine).

^c Aldehyde (benzaldehyde).

^d Ester (benzyl benzoate).

4. Discussion

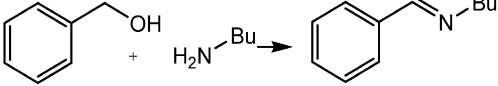
4.1. Catalytic activity

The imine synthesis from alcohols involves two steps. The first step involves the oxidation of the alcohol to its corresponding carbonyl compound, an aldehyde in the case of a primary alcohol or a ketone in the case of a secondary alcohol. The carbonyl compound then reacts with an amine to form the imine in the second step. Alcohol oxidation to form carbonyls is traditionally performed with stoichiometric amounts of Cr(VI) compounds or other inorganic oxidants [23]. The major drawback of

this stoichiometric protocol is the generation of large amounts of heavy metal waste. Another disadvantage of stoichiometric oxidant is that, over oxidation can lead to the formation of undesirable side products. This gives rise to the need for milder catalytic processes utilizing dioxygen or peroxides as the oxygen source. Due to the handling hazards associated with peroxides, molecular oxygen is preferred as an environmentally acceptable, selective, and strong oxidant for liquid-phase oxidations [24]. Pd, Pt and Ru based catalysts have been widely used for oxidation in the presence of molecular oxygen in supercritical fluids [25]. Au based catalysts have demonstrated very interesting and promising activity in oxidation [26]. Even though these processes use small amounts of catalysts, they yield low conversions or several products due to over oxidation.

Imine formation from carbonyls and amines in general, is a facile reaction due to the good electrophilic properties of carbonyls and nucleophilic properties of amines, and may not require a catalyst. However, in the presence of factors that decrease electrophilicity/nucleophilicity of the carbonyl/amine, a catalyst may be required for the transformation. Transition metal based catalysts have been extensively used for the imine formation from aldehydes or ketones. Some examples include ZnCl₂, TiCl₄, alumina, and CuSO₄ that act as Lewis acids to catalyze a nucleophilic attack on the carbonyl group by the amine as well as serving as dehydrating agents [27–30]. Imines have been synthesized under microwave irradiation using clays as catalysts [31]. More recently, ultrasound irradiation coupled with silica catalysts have been utilized to synthesize imines

Table 6
Comparison of activity between K-OMS-2 and active MnO₂



Catalyst	Reaction time (h)	Yield (%)	TON ^a	TOF (h ⁻¹) ^b
K-OMS-2 ^c	12	100	16	1.3
Active MnO ₂ ^d	24	95	0.096	0.0040

^a Turnover number (TON) = (moles of converted substrate) × (moles of catalyst)⁻¹.

^b Turnover frequency (TOF) = (moles of converted substrate) × ((moles of catalyst) × (reaction time in h))⁻¹.

^c 50 mg K-OMS-2 = 0.0625 mmol.

^d Calculation based on data in Ref. [33].

from a range of aldehydes [32]. However, the catalysts mentioned above may not function as bifunctional catalysts to catalyze both oxidation and imine formation in a single vessel. Activated manganese oxides have been used in a similar process to synthesize amines via imines from alcohols [33]. The reaction requires 10 equivalents of activated manganese oxide in addition to 4 Å molecular sieves to accomplish the task. The role of manganese dioxide in this case is a stoichiometric oxidant rather than a true catalyst, and hence the recovery and reusability are not feasible. 4 Å molecular sieves have been added to facilitate the imine formation from *in situ* formed carbonyls. In contrast, the reactions with K-OMS-2 require catalytic amount of material and do not require any additives. In addition, higher turnover numbers and frequencies were achieved (Table 6) with K-OMS-2 as compared to active manganese oxide.

Benzyl, allyl and alkyl alcohols were reacted with alkyl and aryl primary amines to form imines (Table 1). Benzylic alcohols gave the highest conversions and selectivities. Thiophenol, a hetero aryl substrate showed a slightly lower conversion compared to conversions obtained with benzylic alcohols. The presence of sulfur in the thiophenol substrate plays a role in the retarded conversion. Allylic alcohol such as cinnamyl alcohol did not show higher selectivity for the imine when both butylamine and aniline were used as nucleophiles. This could be attributed to the relatively larger size of the cinnamyl alcohol substrate. However, when H-K-OMS-2 was used as a catalyst, the conversions and selectivities were enhanced due to the higher acidity of the H⁺ exchanged K-OMS-2. Aliphatic primary alcohol and secondary alcohols gave very low conversions as compared to primary aryl alcohols (entries 5, 6 and 7) as anticipated. The aliphatic alcohols are difficult to oxidize to the corresponding aldehydes and ketones with the K-OMS-2 catalyst, therefore conversions are low. The stabilization energy of the highly conjugated final product obtained in entries 1–4 accounts for the higher conversion and enhanced selectivity. When the reactions were done with aniline it took 24 h for the reaction to be completed while when butylamine was used, it took only 12 h for reaction completion. This shows that the nature of the amine used in the reaction is playing a significant role in the synthesis. Besides the size factors associated with the butylamine and aniline on the nucleophilic attack, their basicity plays a critical role in the oxidation of alcohols to their aldehydes or ketones.

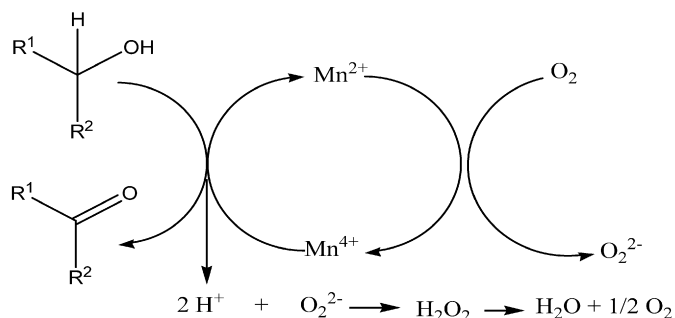
Butylamine which is more basic as compared to aniline helps in providing an environment which helps in the proton abstraction step in the oxidation of alcohols (Scheme 2). The lower basicity of aniline also results in a lower rate of nucleophilic attack by the amine on the carbonyl carbon to form imines; therefore it takes more time for the formation of imines in the case of aniline as compared to butyl amine.

The effect of substituents in the substrates was very prominent in conversions and selectivities for imine synthesis (Table 2). The presence of electron donating groups, –OCH₃ and –CH₃ at the *para* position of the alcohol resulted in lower conversion and selectivity for imines. In contrast, electron withdrawing groups in the *para* position of the alcohol afforded enhanced conversion and selectivity for imines. Electron donating groups electron density in the benzene rings of the alcohol and this result in the difficulty in oxidation process and reduced electrophilicity of *in situ* formed carbonyl. Electron withdrawing groups in the alcohols can enhance oxidation and electrophilicity. This effect is reversed in the aniline leading to either an increase or a decrease in nucleophilicity depending on the groups present in the ring. These effects were prominent in the reaction between 4-methoxy benzyl alcohol and 4-nitro aniline where the decrease in conversion is due to lower basicity of *p*-nitroaniline as compared to aniline, as has been the case, which was discussed earlier. The presence of electron withdrawing nitro group at the *para* position in aniline also decreases the nucleophilicity of the amine, therefore the selectivity for the imine is also lower.

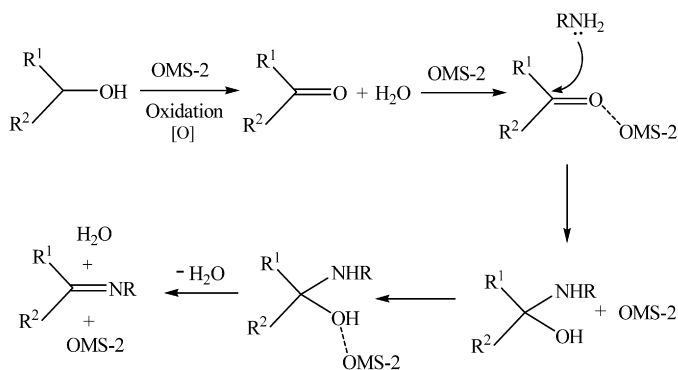
Among the benzene dimethanol substrates (Table 4, entries 16–18), *para*-dimethanol gave a higher conversion to di-imine than the *ortho*- or *meta*-dimethanol. These results show that both the alcohol groups in benzene-1,4-dimethanol were easily accessible to the active centers in K-OMS-2, whereas in the case of *ortho* and *meta*-dimethanol, one of the alcohol reacted first and formed the imine and subsequently the other alcohol group got oxidized and reacted with the amine to form the imine. Benzene-1,4-dimethanol which has a smaller kinetic diameter as compared to 1,2- and 1,3-dimethanol, gives higher selectivity for the corresponding di-imine; this may be due to the way the dimethanols are oriented inside the tunnel, and their accessibility to the active manganese centers.

4.2. Solvent effects

Non-polar solvents favor the imine formation reaction according to the results listed in Table 5. Acetonitrile, the polar solvent, not only afforded low conversion and selectivity for imine, but resulted in another side product benzyl benzoate. The appearance of benzyl benzoate may be due to over oxidation of the benzyl alcohol resulting in benzoic acid, which in turn reacting with the benzyl alcohol under the conditions. A series of control reactions was carried out to determine if any of the products resulted due to the oxidation of the solvents. Toluene did not give any products, but xylene afforded only 12% conversion giving both anisyl alcohol and anisaldehyde after 60 h. However, when reaction between benzyl alcohol and butylamine was done in xylene as the solvent for 12 h, the



Scheme 1. Alcohol oxidation mechanism.



Scheme 2. Mechanism of imine synthesis.

oxidative products of xylene were not formed indicating that OMS-2 selectively catalyzes the oxidation of alcohols. The oxidation of hydrocarbons with air using OMS-2 may require high pressure [34].

4.3. Proposed reaction mechanism

Imine synthesis proceeds via two mechanistically distinct reaction steps promoted by a single catalyst (K-OMS-2). The first step involves the oxidation of the alcohol to its corresponding ketone or aldehyde. A thorough mechanistic study of the alcohol oxidation with OMS-2 has been done by Makwana et al. [35,36]. A Mars-van Krevelen-type oxidation mechanism has been proposed. The proposed mechanism for alcohol oxidation suggests a multi-electron redox phenomenon in the liquid phase (Scheme 1).

The second step in imine synthesis with K-OMS-2 involves a nucleophilic attack on the *in situ* generated carbonyls. Imine formation from carbonyls is generally acid catalyzed. *In situ* IR experiments following pyridine adsorption suggest that the K-OMS-2 catalyst primarily has Lewis acidity [36]. Thus when the amine attacks the carbonyl carbon, K-OMS-2 provides Lewis acidic sites for oxygen in order to facilitate the catalytic imine formation (Scheme 2). Imine synthesis is generally a facile reaction due to the good electrophilic properties of carbonyls and nucleophilic properties of the amine groups, and may not require any catalytic assistance. This was proved when the reactions were carried out with benzaldehyde and cinnamaldehyde as substrates. The reactions did not require a catalyst or prolonged reaction times. However, for imines

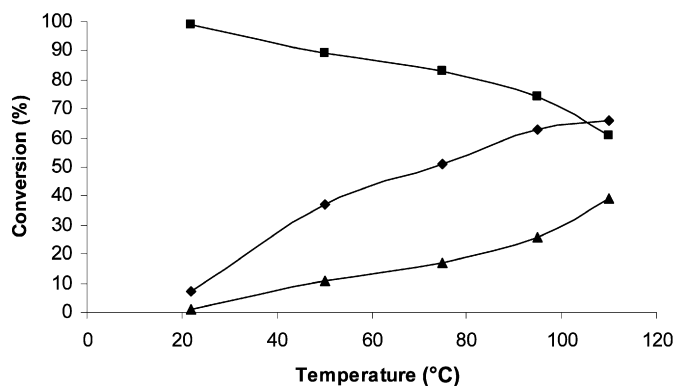


Fig. 4. Conversion of 4-methoxy benzyl alcohol (◆) and selectivities of aldehyde (■) and imine (▲) as a function of temperature.

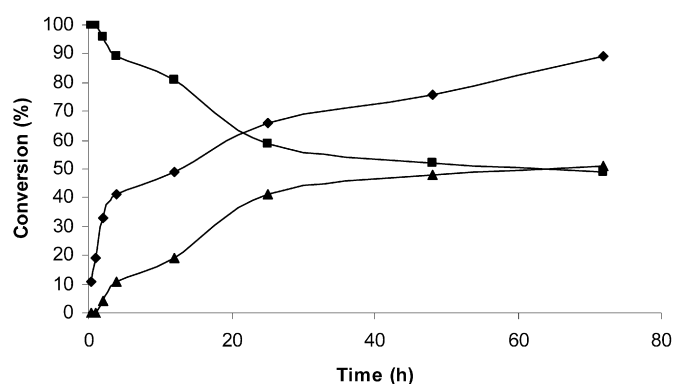


Fig. 5. Conversion of 4-methoxy benzyl alcohol (◆) and selectivities of aldehyde (■) and imine (▲) as a function of time.

which are difficult to synthesize due to the decrease in electrophilicity/nucleophilicity of the carbonyl/amine groups (Table 3), a catalyst such as K-OMS-2 is required.

4.4. Kinetics

Studying the reaction between 4-methoxy benzyl alcohol and 4-nitro aniline in more detail as a function of time and temperature revealed the role of K-OMS-2 in the reaction. Fig. 4 suggests that lower temperatures are unfavorable for the reaction and lead to lower conversion. Higher temperatures not only favor oxidation of the alcohol to aldehyde, but favor the condensation of aldehyde with the amine to form the final imine product.

Furthermore, the studies of reaction as a function of time (Fig. 5) show that the alcohol gets oxidized to form the aldehyde and then condense with the amine to form the imine. 4-methoxy benzyl alcohol is first adsorbed to the surface of the K-OMS-2 catalyst, where an activated intermediate species may be formed, which then is oxidized/dehydrogenated to 4-methoxy benzaldehyde. Finally, the aldehyde further reacts with 4-nitro aniline to form the imine. Water is formed as a by-product in both reactions. This finding is in agreement with the proposed mechanism discussed earlier. Fig. 5 also indicates that prolonged reaction times can enhance conversion and selectivities for both aldehyde and imine.

The ability to use a single catalyst, such as OMS-2 for multiple processes opens the door to higher levels of complexity while offering advantages in terms of energy efficiency and economy [37]. The multi-functional nature of the catalysts and the single-pot reaction procedure can help to avoid side product formation and can be more environmentally compatible [38]. A detailed mechanistic study of the Lewis acid catalyzed imine formation with K-OMS-2 is underway.

5. Conclusions

In summary, an efficient tandem catalytic process to synthesize imines directly from alcohols using OMS-2 as a heterogeneous catalyst has been demonstrated. OMS-2 operating as a bifunctional catalyst, catalyzes two mechanistically distinct processes in a single-pot under the same reaction conditions; namely, oxidation followed by imine-formation. Conversions and selectivity for imines up to 100% have been achieved without the need for any additives or promoters in this reaction. This single-step catalytic imine synthesis proves to be less time-consuming and more economical in contrast to two-step oxidation of the alcohols to carbonyls and subsequent condensation to obtain the imine. The procedure is aerobic and environmentally benign. Operational simplicity and minimal waste generation of this process should be beneficial for industrial applications. The OMS-2 catalyst can be removed from the mixture by simple filtration and can be reused.

Acknowledgments

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