# VO(acac)<sub>2</sub>: An Efficient Catalyst for the Oxidation of Aldehydes to the Corresponding Acids in the Presence of Aqueous H<sub>2</sub>O<sub>2</sub>

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Abstract: VO(acac)<sub>2</sub> catalyzes the oxidation of aldehydes (aromatic, aliphatic, and heterocyclic) to the corresponding acids efficiently and selectively in the presence of H<sub>2</sub>O<sub>2</sub> as an oxidant. This method possesses functional-group compatibility, easy workup procedure, and shorter reaction time. The reaction is highly dependent on the solvent used. Performance of titania-supported VO(acac)2 in the oxidation of aldehyde was also investigated.

Key words: aldehydes, carboxylic acids, catalysis, esters, peroxides

In the plethora of oxidation processes, aldehyde oxidation occupies an important place in synthetic chemistry.<sup>2</sup> Standard methods for the oxidation of aldehydes involve the use of oxidizing reagents such as Jones' reagent,<sup>3</sup>  $KMnO_4$ ,<sup>4</sup> bromine,<sup>5</sup> HNO<sub>3</sub>,<sup>6</sup> and  $Ag_2O^7$  which are less desirable in the light of industrial and environmental demands. Recently, various catalysts and systems have been reported for the catalytic oxidation of aldehydes, for example, CuCl,<sup>8</sup> AgNO<sub>3</sub>,<sup>9</sup> Bi<sub>2</sub>O<sub>3</sub>,<sup>10</sup> and supported metal acetylacetonates.<sup>11</sup> In the domain of green oxidation processes, hydrogen peroxide is considered as the ultimate green oxidant (active oxygen 47.1%) because the byproduct is water. The first report of oxidation of aldehydes using H<sub>2</sub>O<sub>2</sub> is almost seven decades old.<sup>12</sup> Noyori et al. exploited the ability of H<sub>2</sub>O<sub>2</sub> for the oxidation of aldehydes to the corresponding acids.<sup>13</sup> In recent years,  $H_2O_2$ has been extensively used in synthetically important processes such as epoxidation,<sup>14</sup> oxidation of sulfides,<sup>15</sup> oxidation of alcohols,16 and Baeyer-Villiger oxidation.17 The oxidizing ability of H<sub>2</sub>O<sub>2</sub> can be enhanced by adding a quantity of vanadium compound to the reaction mixture.<sup>18</sup> Such activation of  $H_2O_2$  by vanadium leads to the generation of various reactive peroxovanadium species with various coordination modes.<sup>19</sup> V<sub>2</sub>O<sub>5</sub>/H<sub>2</sub>O<sub>2</sub> has been used to oxidize aldehydes to the corresponding esters<sup>20</sup> and fivecoordinate VO(acac), has been proved to be a good oxidation catalyst.21

In this report, we describe the potential oxidative ability of the  $VO(acac)_2/H_2O_2$  system for the oxidation of aldehydes (Scheme 1). It has been found that ester and acid formation is highly dependent on the solvent used. The methyl ester is formed in the presence of methanol, and the acid is the product in the presence of acetonitrile.

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Scheme 1 VO(acac)<sub>2</sub>-catalyzed oxidation of aldehyde

The activities of various vanadium sources-H<sub>2</sub>O<sub>2</sub> systems have been studied for the oxidation of aldehydes to the corresponding acids. The results of our initial attempts to optimize the reaction conditions using 4-chlorobenzaldehyde as the model substrate in the presence of  $H_2O_2$  as the

Table 1 Optimization of the Reaction Conditions<sup>a</sup>

| сі—   |   | HO VO(acac | $H_2O_2 \rightarrow CI$ |             | н                         |
|-------|---|------------|-------------------------|-------------|---------------------------|
| Entry | H <sub>2</sub> O <sub>2</sub><br>(mmol) | Solvent    | Catalyst<br>(mol%)      | Time<br>(h) | Yield<br>(%) <sup>c</sup> |
| 1     | 1                                       | MeCN       | _                       | 5           | 4                         |
| 2     | _                                       | MeCN       | $VO(acac)_2(1)$         | 8           | 0                         |
| 3     | 1                                       | MeCN       | $VO(acac)_2(1)$         | 8           | 48                        |
| 4     | 1.5                                     | MeCN       | $VO(acac)_2(1)$         | 8           | 55                        |
| 5     | 2                                       | MeCN       | $VO(acac)_2(1)$         | 8           | 56                        |
| 6     | 2                                       | MeCN       | $VO(acac)_2(2)$         | 7           | 65                        |
| 7     | 2                                       | MeCN       | $VO(acac)_2(3)$         | 6           | 78                        |
| 8     | 2                                       | MeCN       | $VO(acac)_2(4)$         | 5           | 82                        |
| 9     | 3                                       | MeCN       | $VO(acac)_2(4)$         | 4           | 97                        |
| 10    | 3                                       | toluene    | $VO(acac)_2(4)$         | 10          | 40                        |
| 11    | 3                                       | $CH_2Cl_2$ | $VO(acac)_2(4)$         | 8           | 45                        |
| 12    | 3                                       | МеОН       | $VO(acac)_2(4)$         | 3           | 90 <sup>d</sup>           |
| 13    | 3                                       | EtOH       | $VO(acac)_2(4)$         | 4           | 45                        |
| 14    | 3                                       | MeCN       | $V_2O_5(4)$             | 4           | 45                        |
| 15    | 3                                       | MeCN       | $NH_4VO_3(4)$           | 4           | 62                        |

<sup>a</sup> 4-Chlorobenzaldehyde (1 mmol), stirred at r.t.

<sup>b</sup> 30% H<sub>2</sub>O<sub>2</sub>.

° Isolated yields.

<sup>d</sup> Ester is the product.

oxidant and different vanadium catalysts are elaborated in Table 1.

To ascertain the efficacy of the catalyst, several reactions were carried out with and without catalyst (Table 1, entries 1–15). It was found that, in the absence of  $H_2O_2$ ,  $VO(acac)_2$  cannot catalyze the oxidation of the aldehydes (Table 1, entry 2). The oxidizing ability of  $H_2O_2$  in the absence of  $VO(acac)_2$  was found to be negligible (<5% yield was isolated, Table 1, entry 1) and that optimal conversion was obtained with 4 mol% of the catalyst and threefold excess of  $H_2O_2$  (Table 1, entry 9).

Effects of various solvents and vanadium catalysts on the above model reaction were also studied (Table 1, entries 1-15). This revealed that VO(acac)<sub>2</sub> and acetonitrile were the best catalyst and solvent, respectively, for the oxidation of aldehydes to the corresponding acids (Table 1, entry 9). Interestingly, under these reaction conditions, in ethanol the corresponding acid was obtained in moderate yield (Table 1, entry 13) while in methanol the corresponding methyl ester was obtained in excellent yield (Table 1, entry 12).

To demonstrate the generality and scope of the reaction, a series of structurally diverse aldehydes was subjected to oxidation under the optimized conditions, and the outcomes are summarized in Table 2 (entries 1-12). The method was equally effective for the oxidation of both aromatic and heterocyclic aldehydes (Table 2, entries 1–9). However, aliphatic aldehydes (Table 2, entries 10 and 11) except unsaturated aldehydes (Table 2, entry 12) reacted slowly to afford moderate yields of product. This might be due to the lower electrophilicity of the aliphatic compared to aromatic aldehydes. Notably, potentially sensitive functional groups such as OH (Table 2, entry 3) and C=C (Table 2, entry 6) in the substrates remain unaffected. Similarly, pyridine-2-carbaldehyde is also prone to oxidation at the heteroatom but, in our protocol, oxidation occurs only at the aldehydic group without affecting the heteroatom (Table 2, entries 7 and 8).

The intermediacy of the peroxovanadium species in the catalytic process can be observed from the UV-Vis spectrum of  $H_2O_2$ ,  $VO(acac)_2$ , and solvent mixture. The peak at around  $\lambda = 414$  nm is due to the ligand-to-metal charge-

 Table 2
 Oxidation of Aldehydes Catalyzed by VO(acac)<sub>2</sub>

| Entry | Aldehyde  | Catalyst <sup>a</sup> | Time (h) | Yield of acid (%) <sup>b,c</sup> | Yield of ester (%) <sup>b,d</sup> |
|-------|---|-----------------------|----------|----------------------------------|-----------------------------------|
| 1     | 4-ClC <sub>6</sub> H <sub>4</sub> CHO               | VO(acac) <sub>2</sub> | 4        | 97                               | 97                                |
|       |   | TSV                   | 4        | 96                               | 95                                |
| 2     | 2-ClC <sub>6</sub> H <sub>4</sub> CHO               | $VO(acac)_2$          | 5.30     | 94                               | 89                                |
|       |   | TSV                   | 5.30     | 93                               | 85                                |
| 3     | 4-HOC/H/CHO   | VO(acac)              | 5 30     | 96                               | 96                                |
| 5     | 1110061140110                                       | TSV                   | 5.30     | 91                               | 90                                |
| 4     | 4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CHO | VO(acac) <sub>2</sub> | 6        | 98                               | 98                                |
|       | 2 0 4   | TSV                   | 6        | 97                               | 95                                |
| 5     | 4-MeOC₄H₄CHO  | VO(acac) <sub>2</sub> | 4        | 96                               | 96                                |
|       |   | TSV                   | 4        | 94                               | 93                                |
| 6     | trans-cinnamaldehyde                                | VO(acac) <sub>2</sub> | 7        | 90                               | 72                                |
|       | ,   | TSV                   | 7        | 87                               | 73                                |
| 7     | thiophene-2-carbaldehyde                            | $VO(acac)_2$          | 6.30     | 92                               | 72                                |
|       |   | TSV                   | 6.30     | 90                               | 73                                |
| 8     | pyridine-2-carbaldehyde                             | $VO(acac)_2$          | 5.30     | 91                               | 76                                |
|       |   | TSV                   | 5.30     | 87                               | 73                                |
| 9     | 2-furaldehyde                                       | $VO(acac)_2$          | 6        | 89                               | 74                                |
|       | -   | TSV                   | 6        | 86                               | 75                                |
| 10    | pentanal <sup>e</sup>                               | $VO(acac)_2$          | 7        | 65                               | 61                                |
|       | -   | TSV                   | 7        | 62                               | 60                                |
| 11    | gluteraldehyde <sup>e</sup>                         | $VO(acac)_2$          | 8        | 42                               | 40                                |
|       |   | TSV                   | 7        | 42                               | 39                                |
| 12    | acrylaldehyde                                       | $VO(acac)_2$          | 6        | 76                               | 75                                |
|       |   | TSV                   | 6        | 76                               | 74                                |

<sup>a</sup> TSV =  $TiO_2$ -supported VO(acac)<sub>2</sub>.

<sup>b</sup> Isolated yields.

<sup>c</sup> All the reaction are carried out with 4 mol% of VO(acac)<sub>2</sub> and 3 mmol of 30% H<sub>2</sub>O<sub>2</sub> in MeCN at r.t. under stirring.

<sup>d</sup> MeOH was used as solvent.

<sup>e</sup> Reactions were carried out at 60 °C.

transfer transition, which is a characteristic of peroxovanadium compounds. Accordingly, a plausible mechanism involving peroxovanadium species is presented in Scheme 2.  $VO(acac)_2$  and  $H_2O_2$  form a reactive peroxovanadium species II. In the absence of methanol, the metal peroxo oxygen atom in II attacks the electrophilic carbonyl carbon of the aldehyde affording the corresponding acid (path b). The alcoholic proton in methanol is more acidic than ethanol, therefore it is easily abstracted by II resulting in the methoxide ion which further attacks the carbonyl carbon of the aldehyde resulting in the methyl ester as the product (path a).



Scheme 2 Plausible mechanism for the oxidation of aldehyde

Interestingly, when the reaction was carried out at elevated temperature, that is, 50–60 °C in the presence of ethanol the product was the corresponding ethyl ester (Table 3) along with the corresponding acid as the side product and unreacted starting aldehyde. Higher temperature facilitates the nucleophilic attack of the ethanol.

Homogeneous catalytic processes produce unwanted waste and hence heterogenization of the homogeneous process is important. TiO<sub>2</sub>-supported VO(acac)<sub>2</sub> (TSV) has been reported for the oxidation of the organic sulfides to the corresponding sulfoxides.<sup>22</sup> This impregnated catalyst also showed good results as summarized in Table 4 (entries 1-5).

With a change in the catalyst loading, variations in the yield of the product were also observed, as shown in Table 4. Best results were obtained when the catalyst loading

## Table 3 Oxidation of Aldehydes to Ethyl Esters

| RCHO  | VO(acac) <sub>2</sub> , $H_2O_2$ |      |  |
|-------|----------------------------------|------|--|
|       | EtOH, 60 °C                      |      |  |
| Entry | Substrate                        | Time |  |
| 1     | . 1                              | 4    |  |

| 1 | pentanal            | 4   | 60 |  |
|---|---------------------|-----|----|--|
| 2 | 4-chlorobenzaldehye | 2.5 | 75 |  |
| 3 | 4-nitrobenzaldehye  | 3   | 90 |  |
| 4 | 2-furaldehyde       | 4   | 57 |  |

Yield (%)a,b

<sup>a</sup> Isolated yields.

<sup>b</sup> Traces of acid formed as the corresponding side product.

was 5 wt% (Table 4, entry 5). Vanadium content in the catalyst was found to be approximately 0.64 mmol/g. Further increasing the catalyst loading and reaction time did not improve the yield of the reaction. The catalyst can be effectively recycled for at least five cycles with reasonably consistent activity.

The recycled TSV catalyst shows slow deactivation, which may be due to the slow leaching out of vanadium from the surface of the support. The activity of the catalyst can be easily regained simply by treating the recycled catalyst with a solution of VO(acac)<sub>2</sub> in THF.<sup>23</sup>

Table 4 Effect of Catalyst (TSV) Loading on the Product Yield<sup>a</sup>

| Entry | TSV (wt%) | Time (h) | Yield (%) <sup>b</sup> |
|-------|-----------|----------|------------------------|
| 1     | 1         | 6        | 40                     |
| 2     | 2         | 6        | 55                     |
| 3     | 3         | 6        | 70                     |
| 4     | 4         | 6        | 85                     |
| 5     | 5         | 6        | 97                     |

<sup>a</sup> Carried with 4-nitrobenzaldehyde in MeCN at r.t.

<sup>b</sup> Isolated yields.

The regenerated catalyst has the same activity as the fresh catalyst (Table 5). However, calcination (at 450 °C) of the catalyst helps to decrease the leaching of the vanadium from the surface of the catalyst but the oxidation activity of the catalyst decreases. Analysis of the product mixture of the oxidation of 4-nitrobenzaldehyde showed 30% of ester and 7% of acid after six hours when calcined catalyst was used.

In summary, we have developed an efficient catalytic process for the oxidation of aldehyde. We anticipate that the simplicity and the catalytic nature of the protocol will make it appealing to synthetic chemists, particularly those who are interested in green oxidation processes.

**Table 5** Yield<sup>a</sup> of Products (Acids)<sup>b</sup> Without and After Regeneration of the Catalyst

| Run             | Time<br>(h) | Yield without<br>regeneration (%) | Yield after<br>regeneration (%) |
|-----------------|-------------|-----------------------------------|---------------------------------|
| 1st (fresh)     | 6           | 97                                | -                               |
| 2 <sup>nd</sup> | 6.5         | 94                                | 94                              |
| 3 <sup>rd</sup> | 6.5         | 92                                | 93                              |
| 4 <sup>th</sup> | 7           | 89                                | 93                              |
| 5 <sup>th</sup> | 7           | 87                                | 92                              |
| 6 <sup>th</sup> | 7.5         | 87                                | 90                              |

<sup>a</sup> Isolated yield of product.

<sup>b</sup> Carried out with 4-nitrobenzaldehyde (1 mmol) at r.t. in MeCN and  $H_2O_2$  (3 mmol) as the oxidant using 5 wt% of the TSV.

#### **Typical Oxidation Procedure**

 $\dot{VO}(acac)_2 (0.007 \text{ g 4 mol\%})$  was dissolved in 30% H<sub>2</sub>O<sub>2</sub> (0.34 mL, 3 mmol); the color of the mixture changed to reddish brown. To this mixture, 4-chlorobenzaldehyde (0.14 g, 1 mmol) dissolved in the minimum amount of MeCN was added and the mixture stirred. Progress of the reaction was monitored by TLC. On completion of the reaction, MeCN was removed under reduced pressure and H<sub>2</sub>O was added (3 mL). The product was extracted with EtOAc (3 × 10 mL), and the organic layer was dried over anhyd Na<sub>2</sub>SO<sub>4</sub>. Finally, the product was purified by column chromatographic technique.

### Typical Procedure for the Preparation of TiO<sub>2</sub>/VO(acac)<sub>2</sub> Catalyst

 $TiO_2/VO(acac)_2$  was prepared by the reported procedure.<sup>22</sup>

#### Typical Oxidation Procedure with TiO<sub>2</sub>/VO(acac)<sub>2</sub>

 $TiO_2/VO(acac)_2$  (0.0075 g, 5 wt%) was taken in 30% H<sub>2</sub>O<sub>2</sub> (0.34 mL, 3 mmol). To this mixture, 4-nitrobenzaldehyde (0.15 g, 1 mmol) dissolved in the minimum amount of MeCN was added, and the mixture was stirred. Progress of the reaction was monitored by TLC. On completion of the reaction, the mixture was filtered to recover the catalyst, and MeCN was removed under reduced pressure. The product was extracted with EtOAc (3 × 10 mL) and dried over anhyd Na<sub>2</sub>SO<sub>4</sub>. The recovered catalyst was washed with cold EtOH and dried at 120 °C for 1 h and then used for further reaction. Finally, the product was purified by column chromatographic technique.

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#### **Reference and Notes**

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- (23) Regeneration of the Catalyst To a solution of VO(acac)<sub>2</sub> (265 mg) in anhyd THF (50 mL), the recovered catalyst (1 g) was added, and the mixture was stirred at r.t. under nitrogen atmosphere. The solid catalyst was filtered and dried under vacuum.