

# Microencapsulated VO(acac)<sub>2</sub>: Preparation and Use in Allylic Alcohol Epoxidation

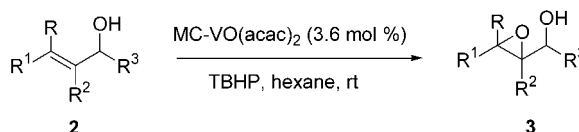
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## ABSTRACT



Microencapsulated VO(acac)<sub>2</sub> [MC-VO(acac)<sub>2</sub>] has been prepared and screened with success as a catalyst for the epoxidation of allylic alcohols using *tert*-butyl hydroperoxide as oxidant. The reactions are run in hexane at room temperature. The MC-VO(acac)<sub>2</sub> is reusable without significant loss of activity.

The development of methodologies for the metal-catalyzed epoxidation of olefins continues to be an area of interest since epoxides are derived directly from readily available alkenes and represent a class of versatile intermediates in organic synthesis.<sup>1–3</sup> Alongside much research on homogeneous catalysts for epoxidation reactions, there is increased interest in developing heterogeneous catalysts.<sup>4,5</sup> One of the key advantages of using supported catalysts is the ease of separation from the product mixture at the end of a reaction. As well as allowing for more rapid purification of the product mixture, this means that the supported complex can be reused in subsequent reactions. One of the problems with immobilizing metal complexes for use in oxidation catalysis is

that the catalytically active metals in their highest oxidation state tend to be less strongly associated with a support than in a more reduced state. Consequently, oxidizing conditions can lead to leaching of the metal complex from the support. Recently, Kobayashi has reported the use of microencapsulation as a technique for immobilizing metal complexes<sup>6–9</sup> and has demonstrated the use of this to a range of reactions, one of them<sup>7,8</sup> being the OsO<sub>4</sub>-mediated dihydroxylation of olefins. In the microencapsulation method, the metal complex is physically enveloped by a thin film of a polymer, usually polystyrene, and is not attached by covalent bonding. The preparation of the microencapsulated metal complex is very simple. The metal complex is added to a solution of polystyrene in warm cyclohexane and the mixture is slowly cooled, whereupon the polystyrene solidifies around the

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particles of metal complex, forming capsules. A solvent is then added to harden the capsule walls, any excess of the metal complex is removed by washing, and then the capsules are used.

In this Letter we report the synthesis of microencapsulated VO(acac)<sub>2</sub> [MC-VO(acac)<sub>2</sub>] and its use in epoxidation reactions. VO(acac)<sub>2</sub> **1** is one the best and most extensively used catalysts for epoxidation of unsaturated alcohols.<sup>3</sup> Mainly studied by Sharpless et al., **1**/*tert*-butyl hydroperoxide (TBHP) was shown to be a highly regio- and stereoselective system for the epoxidation of allylic<sup>10–12</sup> and homoallylic alcohols.<sup>13</sup>

There have been a number of reports of immobilization of **1** and VO<sub>3</sub><sup>–</sup> onto derivitized polystyrene resins. Examples of supports used include acetylacetone,<sup>14–16</sup> phosphonemethyl,<sup>17,18</sup> and hydroxyethylamino<sup>17,18</sup> derivitized polystyrenes. The vanadium complexes have also been attached to ion-exchange resins.<sup>19,20</sup> In all these cases, the catalytic activity of the heterogeneous complexes has been found to be superior to that of the homogeneous oxovanadium complexes; however, there are problems associated with the supported complexes. Often it is not possible to recycle them, and leaching of the metal off the support during the course of the reaction is also highlighted. We felt that by immobilizing **1** using microencapsulation it may be possible to maximize the advantages of heterogenization of increased activity and ease of use and minimize the disadvantages of leaching and nonrecyclability.

MC-VO(acac)<sub>2</sub> was prepared using the Kobayashi protocol using 1 g of polystyrene and 200 mg of VO(acac)<sub>2</sub>.<sup>21</sup> Measurement of the mass increase together with elemental analysis of the resultant MC-VO(acac)<sub>2</sub> indicate that 160 mg of VO(acac)<sub>2</sub> is encapsulated. Once prepared, the MC-VO(acac)<sub>2</sub> can be stored in air at room temperature for several months without loss of activity.

To test the MC-VO(acac)<sub>2</sub> as a catalyst for epoxidation reactions, we chose first to investigate its use in the TBHP-mediated epoxidation of geraniol. This reaction is well represented in the literature<sup>3</sup> and has been the focus of other studies using supported analogues of MC-VO(acac)<sub>2</sub>, proving to be a useful yardstick for determining the effectiveness of our immobilized catalyst. The solvents most used for the metal-catalyzed homogeneous epoxidation of allylic alcohols are either benzene<sup>10,11</sup> or, with better results, chloroalkanes<sup>22</sup> such as dichloromethane or chloroform. We considered these chlorocarbons to be unsuitable for our study due to expected solvation of the MC-VO(acac)<sub>2</sub> and therefore screened a range of other solvents. We found that acetonitrile, toluene, and diethyl ether led to low yields of product and pronounced metal leaching but, somewhat surprisingly, in hexane a 93% yield of product was obtained when using MC-VO(acac)<sub>2</sub>. This is particularly interesting when bearing in mind the observation both by ourselves and others<sup>20</sup> that aliphatic hydrocarbons are not effective as solvents for oxidation reactions catalyzed by **1**. What is equally noteworthy is that these results are obtained at room temperature as compared to the elevated temperatures often used in the case of epoxidations using **1** or other supported oxyvanadium complexes in low-polarity solvents such as benzene. Therefore, the activity of **1** is totally changed by encapsulation. Being able to perform the reaction in hexane has significant advantages over the use of benzene or chlorocarbons in terms of ease of use, environmental impact, and toxicity. The MC-VO(acac)<sub>2</sub> is easily removed at the end of the reaction by simple filtration. To show the reusability of MC-VO(acac)<sub>2</sub>, we used the same batch four times in the epoxidation of geraniol, with a simple washing between runs. As shown in Table 1, the activity was only slightly decreased after the

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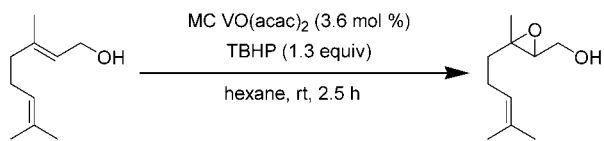
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(21) Polystyrene (1.000 g, purchased from Aldrich Ltd., average *M<sub>w</sub>* = 280 000) was dissolved at 70 °C in cyclohexane (50 mL), and to this solution was added VO(acac)<sub>2</sub> (0.2 g). This mixture was stirred for 1 h at this temperature and then slowly cooled to 0 °C with vigorous stirring. The polystyrene solidified around the metal catalyst dispersed in the solution. Hexane (30 mL) was added to harden the capsule walls. The mixture was stirred at room temperature for 1 h, and the capsules were washed with hexane several times, to remove unencapsulated VO(acac)<sub>2</sub>, and then dried under vacuum for 18 h at rt.

**Table 1.** Reuse of MC-VO(acac)<sub>2</sub> in the Epoxidation of Geraniol and Determination of Metal Leaching

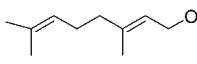
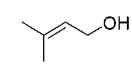
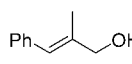
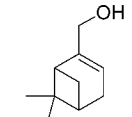
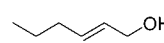
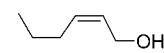
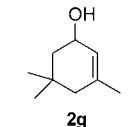
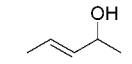
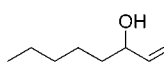
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| run  | yield of epoxide (%) | metal leaching |
| 1  | 93                   | 0.097%         |
| 2  | 84                   | 550 ppm        |
| 3  | 83                   | 275 ppm        |
| 4  | 81                   | 118 ppm        |
| 5 <sup>a</sup>   | 5                    |                |

<sup>a</sup> Using **1** (0.1 mol %) in the place of MC-VO(acac)<sub>2</sub>.

fourth run. The leaching of the metal in each run was determined by ICP analysis and found to decrease from 0.097% in the first run down to 118 ppm in the fourth. To

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**Table 2.** MC-VO(acac)<sub>2</sub>/TBHP Epoxidation of Allylic Alcohols **2**

| $  \begin{array}{c}  \text{R}^1 \quad \text{R} \quad \text{OH} \\  \diagdown \quad \diagup \\  \text{C} = \text{C} - \text{C} - \text{R}^3 \\  \diagup \quad \diagdown \\  \text{R}^2  \end{array}  \xrightarrow[\text{hexane, rt}]{\text{MC-VO(acac)}_2 \text{ (3.6 mol \%)} \\ \text{TBHP (1.3 equiv)}}  \begin{array}{c}  \text{R}^1 \quad \text{R} \quad \text{OH} \\  \diagdown \quad \diagup \\  \text{C} = \text{C} - \text{C} - \text{R}^3 \\  \diagup \quad \diagdown \\  \text{R}^2  \end{array}  $ |   |      |                  |                       |
|---|---|------|------------------|-----------------------|
| entry   | allylic alcohol   | t(h) | yield <b>3</b> % | dr <sup>a</sup>       |
| 1   |    | 2.5  | 93               |                       |
|   | <b>2a</b>   |      |                  |                       |
| 2   |    | 2    | 90               |                       |
|   | <b>2b</b>   |      |                  |                       |
| 3   |    | 8    | 87               |                       |
|   | <b>2c</b>   |      |                  |                       |
| 4   |    | 1.5  | 96               |                       |
|   | <b>2d</b>   |      |                  |                       |
| 5   |    | 5    | 84               |                       |
|   | <b>2e</b>   |      |                  |                       |
| 6   |   | 5    | 55               |                       |
|   | <b>2f</b>   |      |                  |                       |
| 7   |  | 13   | 81               | >98 / <2 <sup>b</sup> |
|   | <b>2g</b>   |      |                  |                       |
| 8   |  | 14   | 57               | 60 / 40 <sup>c</sup>  |
|   | <b>2h</b>   |      |                  |                       |
| 9   |  | 22   | 70               | 75 / 25 <sup>c</sup>  |
|   | <b>2i</b>   |      |                  |                       |

<sup>a</sup> Determined by <sup>1</sup>H NMR. <sup>b</sup> *cis/trans* ratio. <sup>c</sup> *erythro/threo* ratio.

evaluate the contribution derived from small quantities of **1** released during the reactions, we attempted the epoxidation of geraniol under the same conditions (Table 1, run 5), using 0.1 mol % of **1** in the place of MC-VO(acac)<sub>2</sub>. After the

same amount of time, the epoxide was formed in only 5% yield. This proves that the high catalytic activity is from MC-VO(acac)<sub>2</sub>.

To show the general applicability of MC-VO(acac)<sub>2</sub>, we screened it in the epoxidation of a range of other allylic alcohols using the mild reaction conditions developed for geraniol; the results are shown in Table 2.<sup>23</sup>

The epoxides were obtained in high yields and the reactivities, as expected, were dependent on the nucleophilic character of the double bond and steric factors. Primary electron rich trisubstituted alcohols **2a–d** (entries 1–4) were smoothly converted to product rapidly and in high yields. Primary disubstituted *trans* alcohol **2e** was easily converted to the epoxide while the *cis* isomer **2f**, after the same reaction time, was shown to be less reactive. Secondary cyclic alcohol **2g** was oxidized with complete *cis* stereoselectivity<sup>24</sup> in high yield; the secondary disubstituted pentenol **2f** was recovered in good yield and with the same *erythro/threo* ratio reported using **1**.<sup>25</sup> Finally, the least nucleophilic secondary allylic alcohol **2i** was epoxidized in very good yield and diastereoselectivity compared to that obtained when using **1**. In every case, at the end of the reaction the only materials observed were product and unreacted starting material.

In conclusion, VO(acac)<sub>2</sub> has been successfully micro-encapsulated. An efficient and practical protocol for the epoxidation of allylic alcohols using MC-VO(acac)<sub>2</sub>/TBHP has been developed. The MC-VO(acac)<sub>2</sub> can be reused several times without a significant loss of activity, and levels of metal leaching are low. Our results compare favorably with those from other groups using supported oxyvanadium complexes for epoxidations, but the key advantages of MC-VO(acac)<sub>2</sub> are the ease of preparation (no derivitised support is required) and its recyclability and low levels of leaching.

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(23) **Typical Procedure for the Epoxidation of Allylic Alcohols.** To hexane (4 mL) were added MC-VO(acac)<sub>2</sub> (60 mg, 3.6 mol %), **2** (1 mmol), and TBHP (1.3 mmol, 5–6 M decane solution), and the reaction mixture was stirred at rt and monitored by TLC. At completion, the solution was filtered to remove the catalyst; then the solvent was removed to give the crude product mixture. Yields were determined using <sup>1</sup>H NMR assay.

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