

Boosting catalytic performance of MOFs for steroid transformations by confinement within mesoporous scaffolds

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Selective confinement of MOF nanocrystals within mesoporous materials via ‘solid state’ crystallization provides more accessible active sites compared to the bulk MOF counterpart, enhancing chemical and mechanical stability of MOF nanocrystals. (Zr)UiO-66(NH₂)/SiO₂ hybrid materials were tested as efficient and reusable heterogeneous catalysts for the synthesis of steroid derivatives, outperforming the bulk (Zr)UiO-66(NH₂) MOF. A clear correlation between catalytic activity of the dispersed Zr sites present in the confined MOF and the loading of the mesoporous SiO₂ is demonstrated for steroid transformations

Active-site confinement, MOF composites, steroid chemistry

1. Introduction

Defective sites in the crystal are considered the active sites in some metal-organic frameworks (MOFs) catalysts.¹ The selective growth of MOF nanocrystals within mesoporous materials (MPMs) via novel ‘solid-state’ crystallization allows for an outstanding loading of the mesoporous cavities with very small MOF nanocrystals.² This approach maximizes the concentration of defective sites at the outer crystal surface, by reducing the MOF crystalline domain down to a few nanometers via confinement within the mesoporous scaffold and also confers additional stability to the highly active MOF nanocrystals used as catalysts. In order to demonstrate these advantages, zirconium containing MOF nanocrystals have been confined within mesoporous silica materials. These composite materials are employed as active, selective and stable heterogeneous catalysts for the conversion of large molecules exhibiting low diffusion coefficients, such as testosterone and epiandrosterone, which show a high pharmacological interest.³

2. Experimental

The procedure for solid state crystallization of (Zr)UiO-66(NH₂) within SBA-15 consist in a ligand salt precursor impregnation of the evacuated SBA-15 followed by HCl gas treatment at room temperature and impregnation with ZrOCl₂. The resulting solid was finally dried, heated in an oven at 120 °C for 2 h and washed with water and MeOH. The catalytic tests for steroid transformations were performed in stirred glass vials at the required temperature, and the supernatant solution was analyzed with GC, MS and H-NMR.

3. Results and discussion

TEM images show the selective loading of the SBA-15 monodimensional channels with (Zr)UiO-66(NH₂) (Figure 1a), which is confirmed also by the FTIR spectra and N₂ physisorption. The advantage of using the mesoporous silica component is confirmed by the higher TOF for the testosterone esterification, obtained with the hybrid material (0.38 h⁻¹) respect those obtained with the similar MOF sample in the absence of SBA-15 (0.19 h⁻¹). A clear correlation between catalytic activity of the dispersed Zr sites present in the confined MOF and the loading of the mesoporous SiO₂ is shown in Figure 1b.

We also carried out the selective reduction of testosterone by substituting the use of homogeneous catalysts by our heterogeneous hybrid catalysts, employing for the first time Zr as a Lewis acid in catalytic amounts obtaining the desired androst-4-ene-3,17-diol **2** in quantitative yield and excellent chemoselectivity

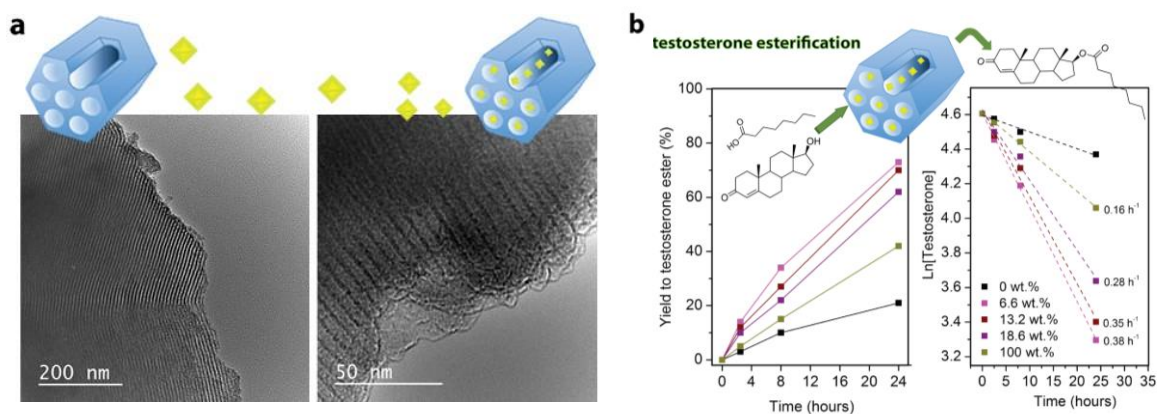


Figure 1. (a) TEM images indicating the filling of the SBA-15 channels with (Zr)UiO-66(NH₂). (b) Yields and TOFs for the testosterone esterification with caprylic acid catalyzed by (Zr)UiO-66(NH₂)/SBA containing varying MOF loadings.

after just one hour of reaction at room temperature (Figure 2). On the other hand, using the 6.6 wt.% MOF loaded SBA-15, the catalytic hydrogen transfer from isopropanol to the carbonyl group of epiandrosterone produces the bio-active androstanediol **3** in 70% yield after 24 h while only 45% was measured for bulk MOF. Finally, we have test the activity of the hybrid MOF/MPM in the synthesis of 16-(E)-benzylideneandrosterone **4** by aldol condensation with benzaldehyde, which is an intermediate in the synthesis of anti-cancer (spiro) heterocyclic steroids.⁴ Using the 6.6 wt.% loaded catalyst, the aldol condensation produces 83% yield of **4** with respect to the 41% obtained in the presence of the bulk MOF after 24 h. The hybrid material also presents a good reusability, obtaining 70% yield of **4** after five reaction runs.

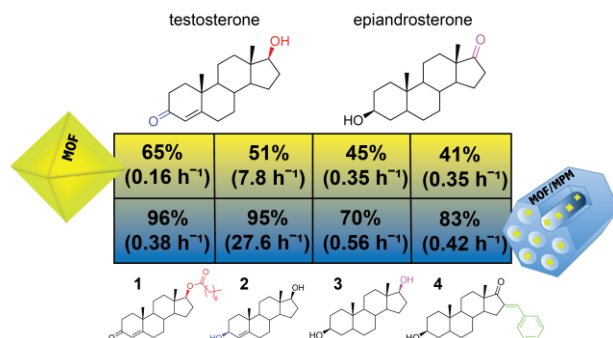


Figure 2. Yield and (TOF) obtained using the bulk MOF and the 6.6 wt% (Zr)UiO-66(NH₂)/SBA-15 as catalysts.

4. Conclusions

In conclusion, we have demonstrated the superior catalytic performance of the MOF/MPM materials with respect to bulk microporous solids for the activation and further transformation of carbonyl groups in steroids, generating pharmaceutically interesting compounds. The use of such novel heterogeneous catalysts containing catalytically active (Zr) MOF nanocrystals well-dispersed on mesoporous supports, will encourage the adoption of this approach for other catalytic applications. The increased catalytic activity and mechanical stability of this hybrid MOF nanocatalysts confined in the mesoporous scaffolds allows for multiple reuse of the catalyst without significant leaching of the active sites in batch and in continuous mode, important for its commercial use in industrial processes.

References

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