Catalytic activity of HKUST-1 in the oxidation of *trans*-ferulic acid to vanillin†

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HKUST-1 was used as a catalyst in the conversion of *trans*-ferulic acid to vanillin. The generation of unsaturated metal sites within HKUST-1 is the fundamental step in the catalytic process. When activated under vacuum, the catalyst gives complete conversion in only 1 h with a significant average reaction yield of 95%.

A relatively new application that has been proposed for porous coordination polymer materials relates to catalysis.[1] These materials exhibit remarkable properties such as high crystallinity, large surface area, high pore volume and metal content, which can provide more versatile heterogeneous catalysts than the traditional zeolites and porous solids.[2] Several research efforts have been focused on the generation of different routes for the preparation of catalytically active coordination polymers.[3] Interestingly, this catalytic activity is provided by active (*i.e.* unsaturated) metals which constitute the coordination polymer.

However, the nature of coordination polymer synthesis tends to result in coordinative saturation of all metal species. Thus, the incorporation of unsaturated (potentially catalytic) metals into coordination polymers is not a trivial synthetic challenge and so far the most successful methods comprise: (i) generation of vacant coordination sites on metal ions that are already occupied within the polymer structure by removal of labile ligands, *e.g.* solvent;[3] (ii) synthesis of hetero-bimetallic coordination polymers using pre-formed organometallic species as building blocks;[3b,4] (iii) post-synthetic modification of coordination polymers by secondary coordinative or covalent bond formation, to attach metallic[5] or organic[6] moieties within the pores. Indeed, the first method is the most commonly employed and relies on the structural composition of a given coordination polymer. Although the generation of uncoordinated (vacant) metal sites has been typically employed for increasing the affinity of coordination polymers towards hydrogen,[7] significant efforts have also been made in catalysis.[8] In addition to the accessibility of uncoordinated metal sites, a coordination polymer-based catalyst needs to exhibit relatively high thermal stability, retention of the crystallinity and chemical resistance in order to grant a sufficient stability under the applied reaction conditions. Thus, many reports on coordination polymer-based catalysts have focused on the use of well-studied frameworks where these parameters have been thoroughly investigated.

The porous coordination polymer HKUST-1 ($Cu_3(BTC)_2(H_2O)_3$, BTC = 1,3,5-benzene-tricarboxylate)[3a] is a well-investigated coordination polymer that possesses framework Cu(II) cations, from which water can be removed to leave square planar coordinated Cu(II) (see Scheme S1, ESI†). By combining XRD, UV-Vis, EXAFS, XANES, and Raman spectroscopies Bordiga *et al.*[9] demonstrated that upon removing the coordinated water molecule, chemically bound to the Cu(II) sites, the oxidation state of copper remains unchanged and the crystalline nature of the material is preserved. HKUST-1 has been widely studied as a catalyst,[10] *e.g.* cyanosilylation of aldehydes and ketones,[10c] hydrosilylation of ketones,[11] oxidation of hydroquinone to *p*-benzoquinone,[12] oxidation of toluene, benzene and other aromatic substrates by H_2O_2.[13]

Vanilla is one of the most widely employed flavouring agents in the world and is extracted from the orchid *Vanilla planifolia*. People think of vanilla as a modern flavouring agent, however it was the pre-Columbian people in Mexico (the Mayan and Aztec civilisations) who first realised the potential of this flavouring agent by mixing it with chilli peppers and honey to improve the chocolate flavour.[14] The vanilla plant, *Vanilla planifolia*, originates

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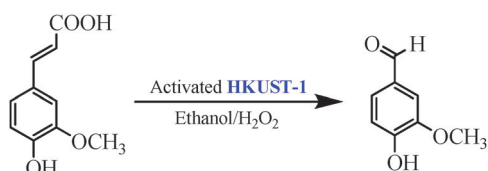[c] *Instituto de Catálisis y Petroleoquímica, ICP-CSIC, C/ Marie Curie, 2 28049 Madrid, Spain*

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in subtropical forests in Mexico and parts of Central America. The Spaniards brought vanilla to Western Europe in the early 16th century and once it was discovered that vanilla orchids could be fertilised manually, production of vanilla spread around the world.[14b] The vanilla scent is due to 200 different odorant molecules, but vanillin (4-hydroxy-3-methoxybenzaldehyde) is the main odorant. Vanillin was first isolated in 1858[15] and the chemical structure was determined in 1874.[16] Nowadays, only 1% of vanilla produced is obtained by natural extraction and this represents a very long and costly process.[17] 99% of the remaining production is chemically synthesised[17] and this large-scale chemical synthesis of vanillin has been achieved from materials such as guaiacol, eugenol, and safrole. Vanillin can also be synthesised by the oxidation of lignin present in pulp waste.[18a] However, these chemical processes are environmentally unfriendly (strong oxidising agents and toxic solvents) and thus biotechnological production of vanillin was investigated.[18] Biotechnology-based approaches are indeed considerably less harmful to the environment, but they have some disadvantages, such as many purification steps and long waiting time for biotransformation.[18] We report herein the use of HKUST-1 as a catalyst in the oxidation of *trans*-ferulic acid to vanillin under mild oxidation conditions (see Scheme 1). Interestingly, ferulic acid (*trans*-ferulic acid or (*E*)-3-(4-hydroxy-3-methoxyphenyl)-acrylic acid) is a derivative of cinnamic acid which is very abundant in nature and it can be extracted from the corn bran.[14c]

Crystalline samples of HKUST-1 (Aldrich) were characterised by PXRD (Fig. 1, catalyst before reaction) and thermogravimetric analysis (TGA, see Fig. S1, ESI†) which confirm the purity of the samples. In order to obtain internal standards for comparison, we performed GC analyses (see the ESI†) and ^{1}H NMR experiments in pure *trans*-ferulic acid (Aldrich) and vanillin (Aldrich), respectively. Then, a sample of HKUST-1 was activated in a conventional oven (exposed to air) at 100 °C for 1 h and the catalytic experiment (see Experimental) was carried out. The product composition was analysed by GC analysis, which showed a partial conversion of *trans*-ferulic acid to vanillin. Additionally, ^{1}H NMR experiments on the product composition (see Fig. S5 and S6 ESI†) confirmed this partial conversion.
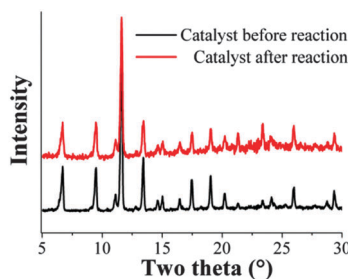
First, we rationalised that the reaction time was not long enough and therefore, by carrying out the reaction for longer than 1 h, the conversion should be better. Thus, the catalyst HKUST-1 was activated as described above and a catalytic experiment was performed (see Experimental), extending the reaction time to 4 and 12 h. Interestingly, the conversion of *trans*-ferulic acid to vanillin was not improved, suggesting that the reaction time was not the limiting experimental parameter.

It is very well known that the generation of coordinatively-unsaturated metal sites in porous coordination polymers is a fundamental step that entirely relies on the activation conditions.[19] Thus, it is reasonable to expect that the activity of the catalyst (HKUST-1) is determined by the accessibility to the vacant $Cu(II)$ metal sites. In order to corroborate this hypothesis, HKUST-1 was activated under vacuum (10^{-5} bar) and 100 °C for 1 h (see Fig. S2, ESI†) without physical manipulation or exposure to air. Next, after the sample was activated, the catalytic experiment was performed as previously described (see Experimental). After confirming the product composition (purified by column chromatography, see Experimental) by GC analysis, ^{1}H and ^{13}C NMR spectroscopies (see Fig. S7 and S8, respectively, ESI†), the conversion of *trans*-ferulic acid to vanillin was determined, giving a reaction yield of 98%. Once the reaction was completed, the catalyst was recovered and washed with some ethanol and characterised by PXRD (Fig. 1, catalyst after reaction), corroborating the retention of the overall framework crystallinity after the catalytic reaction was finished. Additionally, in order to investigate the recyclability of the catalyst in the reaction we performed ten catalytic experiments (with an average reaction yield of ∼95%, see Table S1, ESI†). Thus, after each catalytic reaction was completed, the catalyst was recovered (see Table S1, ESI†) and washed with some ethanol and characterised by PXRD (see Fig. S3, ESI†). These PXRD experiments confirmed the retention of the overall framework crystallinity after 10 cycles and they also suggested that no copper species leached into the reaction solution which was corroborated by inductively coupled plasma mass spectrometry (ICP-MS) on the hot filtrates (10 filtrates from the catalytic reactions), see ESI.†

To achieve a better understanding of the role of HKUST-1 in the oxidation of *trans*-ferulic acid to vanillin, we performed a set of reactions: (i) replacing HKUST-1 by $Cu(CH_3CO_2)_2$, (ii) substituting HKUST-1 for $Cu(NO_3)_2$, (iii) replacing HKUST-1 with $Cu(OH)_2$, (iv) in the absence of HKUST-1 in the reaction and (v) in the absence of H_2O_2 in the reaction. In cases (i), (ii) and (iii) we aimed to use different sources of $Cu(II)$ that could carry on the oxidation.[20] In case (iv), we investigated the possibility of oxidising *trans*-ferulic acid by only using H_2O_2 and, finally, in case (v) we explored the possibility of oxidising ferulic acid only with HKUST-1. After all of these reactions were completed, the product composition, analysed by GC, showed no conversion of *trans*-ferulic acid to vanillin.
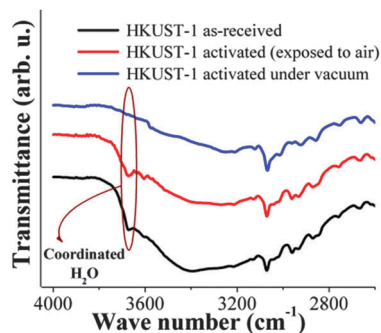

Scheme 1 Oxidation of *trans*-ferulic acid to vanillin using HKUST-1 as a catalyst.

Fig. 1 PXRD patterns of the catalyst (HKUST-1) before and after the catalytic experiment.

Fig. 2 FTIR spectra of the catalyst (HKUST-1) at 25 °C. Non-activated (black line), activated in a conventional oven (red line) and activated under vacuum (blue line).

Thus, it became clear that the heterogeneous catalyst HKUST-1 in combination with the oxidant H_2O_2 is responsible for the oxidation of *trans*-ferulic acid to vanillin. Once we managed to identify the catalytic conditions, we investigated the formation of coordinatively unsaturated Cu(II) metal sites within the catalyst. Then, FTIR spectra were recorded at 25 °C over three different samples. First, the FTIR spectrum of HKUST-1 at room temperature, non-activated (Fig. 2, see Fig. S4, ESI†), shows a broad absorption band at 3400 cm^{-1}, confirming the presence of uncoordinated water in the material, and a characteristic sharp peak at 3680 cm^{-1} that is assigned to metal-coordinated water.[21,7b]

Then, a sample of HKUST-1 was activated at 100 °C for 1 h in a conventional oven (exposed to air). After the sample was cooled back to room temperature (25 °C), its FTIR spectrum (HKUST-1 activated, exposed to air) showed reduction in the intensity of the broad absorption band at 3400 cm^{-1} but with retention of the sharp peak at 3680 cm^{-1} (Fig. 2, see Fig. S4, ESI†). This indicated the loss of some free water (uncoordinated water) in the framework and that the coordinated water is not removed from the framework under these conditions and remains bound to Cu(II). Finally, a sample of HKUST-1 was activated under vacuum (10^{-5} bar) at 100 °C for 1 h and after cooling down to room temperature, the FTIR spectrum exhibited a significant reduction in the intensity of the broad absorption band (3400 cm^{-1}) and the sharp peak at 3680 cm^{-1} is also lost from the spectra (Fig. 2, see Fig. S4, ESI†). Therefore, when the catalyst is activated under the latter conditions all water molecules (uncoordinated and coordinated) are removed from the material generating coordinatively-unsaturated Cu(II) sites (see Scheme S1, ESI†).

On the basis of the above experimental results, the removal of coordinated water from HKUST-1 is the key to create an active catalyst and as we previously described, *vide infra*, this activated catalyst in combination with H_2O_2 is necessary for the oxidation of *trans*-ferulic acid to vanillin. Interestingly, in the catalytic reaction (see Experimental) there is also H_2O (since H_2O_2 is added as 30 wt% in H_2O) that could re-coordinate these Cu(II) sites. Thus, the nucleophilicity of the reacting species towards the Cu(II) sites is what determines the path of the catalytic reaction. In fact, H_2O_2 is an excellent nucleophile which has a considerably higher reactivity than H_2O[22] and therefore it coordinates first to uncoordinated Cu(II) sites even when H_2O is present.

In order to gain some insight into the oxidation mechanism using HKUST-1 in the presence of H_2O_2, Baiker *et al.*[13] used hydroquinone as a scavenger to stop the hydroxylation process, but hydroquinone did not stop the reaction, indicating a non-radical reaction mechanism. The authors proposed an electrophilic aromatic substitution for the hydroxylation process, based on the reaction between aromatic compounds and electrophilic species like OH^+. Taking the aforementioned mechanistic considerations into account, the FTIR experiments (see above) and the fact that H_2O_2 is remarkably more reactive in nucleophilic displacements than H_2O,[22] an anionic pathway similar to an electrophilic addition to a double bond could take place. In this context a possible reaction mechanism that accounts for the formation of vanillin **10** is depicted in Scheme S2 (ESI†). Initial activation of hydrogen peroxide by HKUST-1 (**1**) gives the copper ion **2**,[13] which by transfer of OH^+ to the vinyl system of *trans*-ferulic acid **3** gives the carbocation intermediate **5**, which should be favoured due to stabilisation of the carbocation in the benzylic position. Nucleophilic attack of water onto the electrophilic carbon atom gives, after release of a proton, the dihydroxy compound **6**, which by loss of water and subsequent oxidation by a second molecule of hydrogen peroxide provides vanillin **10** as the main product (98%). Oxalic acid and traces of acetic acid were detected as by-products. The presence of vanillin, oxalic acid, and acetic acid reported in the scheme was found in the bulk of the solution and it was validated by HPLC and ^1H-NMR. 4-Vinylguaiacol, vanillic acid or protocatechuic acid was not detected in the bulk of solution, as we also previously observed in another work.[23]

In summary, we demonstrated the application of the porous coordination polymer HKUST-1 as a heterogeneous catalyst in the conversion of *trans*-ferulic acid to vanillin. This work represents the first example of the use of HKUST-1 in the synthesis, *via* oxidation, of vanillin. The generation of vacant coordination sites within HKUST-1 (corroborated by FTIR) is the key step in the catalytic process and this strongly depends on the activation conditions. If the catalyst is activated in air, only a partial conversion of *trans*-ferulic acid to vanillin was observed. However, when HKUST-1 was activated under vacuum, the catalytic conversion took place in 1 h with a remarkable conversion yield of 98%. In addition, after the reaction was completed the catalyst was entirely recovered and its recyclability was confirmed to up to ten catalytic cycles (average reaction yield of ~95%) and by PXRD the retention of the structure crystallinity was verified. Additionally, no copper species that leached into the reaction solution were corroborated by ICP-MS. Indeed, from an economical and ecological point of view, this efficient synthetic route to highly precious vanillin could be extraordinarily attractive. We are currently investigating the oxidation of other α,β-unsaturated carboxylic acids under the oxidation conditions presented here.

Experimental

Activated catalyst (HKUST-1), 0.005 g (3.2 mol%), suspended in ethanol (20 mL) was mixed with 0.5 mL of H_2O_2 (30 wt% in H_2O), 0.025 mL of acetonitrile and 0.050 g (2.57×10^{-4} mol) of ferulic acid. The reaction mixture was heated to reflux for 1 h.

After the reaction was finished, the catalyst was recovered by filtration; the filtrate was extracted with ethyl acetate and washed with a saturated solution of NH_4Cl. The combined organic phases were dried with anhydrous Na_2SO_4, filtrated and concentrated under vacuum. Finally, the residue was purified by column chromatography (AcOEt–hexane 5 : 95).

Acknowledgements

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