Selective aerobic oxidation in supercritical carbon dioxide catalyzed by the $H_5PV_2Mo_{10}O_{40}$ polyoxometalate†

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Selective aerobic oxidation of benzylic alcohols and of activated aromatic hydrocarbons occurs in supercritical CO_2 as reaction medium using $H_5PV_2Mo_{10}O_{40}$ as a quasi-heterogeneous catalyst without further additives or co-solvents; efficient recycling is possible and no metal leaching is detectable in the product stream.

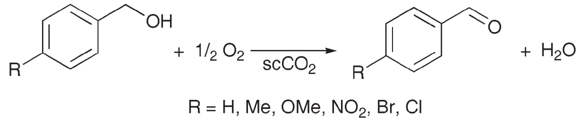
The aerobic oxidation of alcohols and hydrocarbons into the corresponding carbonyl compounds is an important reaction in organic synthesis. Polyoxometalates (POMs) have shown promising potential as catalysts for oxidation transformations that utilize benign oxidants such as hydrogen peroxide and molecular oxygen.[1] A major goal for catalytic solution phase oxidations is the replacement of volatile organic compounds (VOC's) usually used as solvents with more benign media. For this reason, anionic POMs have been generated with different cations leading to solubility in a variety of "green" solvents. Thus, the $Na_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2]$ polyoxometalate was used with hydrogen peroxide, for a variety of oxidation transformations in aqueous biphasic reaction media.[2] Use of perfluorinated alkyl ammonium counter cations enables the dissolution of polyoxometalates in perfluorinated solvents allowing the oxidation of alcohols and alkenes with hydrogen peroxide in biphasic (fluorous/organic) media.[3] More recently, neutral $H_5PV_2Mo_{10}O_{40}$ polyoxometalate was used as catalyst for the aerobic oxidation of benzyl alcohols and sulfides in non-toxic and non-volatile polyethylene glycol as solvent.[4] Herein we report for the first time on the use of supercritical carbon dioxide ($scCO_2$) as reaction medium for aerobic oxidation catalyzed by $H_5PV_2Mo_{10}O_{40}$. Most notably, the best performance was observed when the unmodified polyoxometalate was used as a quasi-heterogeneous catalyst.

Supercritical carbon dioxide ($scCO_2$), which has mild critical data (T_c = 31.0 °C, P_c = 73.8 bar), a truly benign character, and low material costs, is finding increasing interest as an attractive alternative reaction medium for chemical synthesis.[5] It seems particularly attractive for aerobic oxidation reactions as it combines complete miscibility with gaseous O_2 with the additional safety of an inert environment.[6–8] Furthermore, the use of $scCO_2$ can greatly facilitate work-up procedures and open new reaction engineering solutions especially if the products can be selectively extracted from the reaction vessel. With classical heterogeneous catalysts, such processes have already found industrial application.[9] Molecular catalysts have also been successfully immobilized for use with $scCO_2$, typical aproaches including anchoring to solid supports, the use of non-volatile liquid phases such as ionic liquids (ILs) or poly(ethylene)glycol (PEG), or selective precipitation after a homogeneous reaction.[5,10,11] Insoluble, solid molecular catalysts have previously led to mostly disappointing results.[12]

In previous work, we have already shown the potential of PEG as a solvent of low volatility for aerobic oxidation catalyzed by the polyoxometalate $H_5PV_2Mo_{10}O_{40}$,[4] and we have also demonstrated that PEG/$scCO_2$ provides an effective biphasic system for alcohol oxidation with nano-scale Pd-catalysts.[8] Therefore, we initially set out to explore the binary PEG/$scCO_2$ solvent with polyoxometalate catalysts. To this aim, four different catalysts were prepared. (i) 10% w/w $H_5PV_2Mo_{10}O_{40}$ on neutral alumina,‡ (ii) $H_5PV_2Mo_{10}O_{40}$ + PEG-1000 (ratio $H_5PV_2Mo_{10}O_{40}$: PEG = 1 : 5) on neutral alumina,§ (iii) $H_5PV_2Mo_{10}O_{40}$ + PEG-1000 (1 : 5 ratio), (iv) $H_5PV_2Mo_{10}O_{40}$ alone (solid). The four catalysts were screened for the oxidation of benzyl alcohol to benzaldehyde, Scheme 1 (R = H), as a benchmark reaction.¶

When the alumina-supported POM-catalysts (i) and (ii) were used benzaldehyde was the only product but conversions were poor, 3 and 11%, respectively. The PEG solution of $H_5PV_2Mo_{10}O_{40}$ (iii) gave a more active catalyst leading to 59% conversion, albeit at a greatly reduced selectivity. Only a 3/2 ratio of benzaldehyde : benzoic acid was obtained. Much to our surprise, solid $H_5PV_2Mo_{10}O_{40}$ proved to be an excellent catalyst in $scCO_2$ enabling the aerobic oxidation of benzyl alcohol to benzaldehyde quantitatively (>99%, GC) and with high selectivity (>99%, GC).

Pictures of typical reaction mixtures are shown in Fig. 1. In the initial phase of the process, visual inspection of the reaction mixture gave no indication of a liquid phase and the polyoxometalate was present as a free floating powder. At the end of



Scheme 1 Catalytic oxidation of primary benzylic alcohols catalyzed by $H_5PV_2Mo_{10}O_{40}$ in $scCO_2$. *Reaction conditions*—5 μmol $H_5PV_2Mo_{10}O_{40}$, 0.5 mmol benzylic alcohols (1 : 100), 2 bar O_2, *ca.* 6 g CO_2, 100 °C, total pressure *ca.* 170 bar, 16 h.

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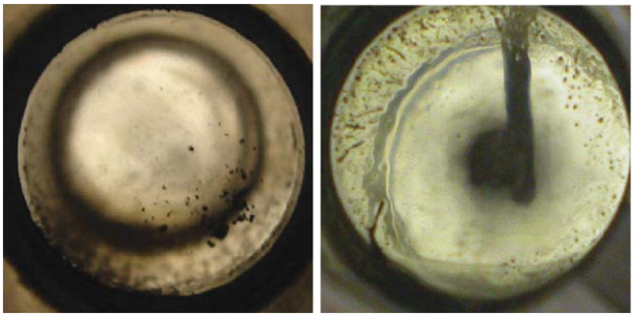


Fig. 1 View of the reaction mixture at the beginning (left) and end (right) of the aerobic oxidation of benzyl alcohol with $H_5PV_2Mo_{10}O_{40}$ in $scCO_2$ (conditions, *cf.* Scheme 1).

the reaction one can clearly see that the polyoxometalate is still not dissolved in the supercritical phase. Noticeable are also small droplets at the reactor walls, probably resulting from the formation of water as by-product. Note the stirring bar that is perpendicular in the picture.

An optimization of the aerobic oxidation of benzyl alcohol to benzaldehyde showed that the reaction was complete after 16 h at 100 °C with a substrate-to-catalyst ratio of 50 : 1, whereas only 80 and 11% of benzaldehyde was obtained at 75 and 50 °C, respectively. Reducing the catalyst loading to 0.2 mol%, Table 1, showed that the catalyst efficiency expressed as turnover numbers (TON) or average turnover frequency (TOF) increased albeit at the expense of the benzaldehyde yield. Noticeably, the TON and average TOF values for the oxidation of benzyl alcohol are much higher in $scCO_2$ than in other solvents, such as PEG-200, under comparable conditions.[4] The reduction of the yield at lower amounts of solid catalyst indicates that the reaction is not catalyzed by small amounts of dissolved species, because constant yields would be expected for saturated solutions.

Since full conversion was obtained at a catalyst-to-substrate ratio as low as 1 : 100, these conditions were further applied for the aerobic oxidation of a series of primary benzylic alcohols, Scheme 1. Quantitative conversion and >99% selectivity for the corresponding benzaldehyde derivatives were obtained regardless of the presence of electron withdrawing or electron donating substituents on the aromatic ring. Further attempted oxidation of secondary alcohols such as 1-phenylethanol, 2-octanol, 2-pentanol and cyclohexanol failed to yield the corresponding ketone. Instead, almost quantitative acid catalyzed dehydration occurred yielding the corresponding styrene, 1-, 2-, 3- and 4-octene, 1- and 2-pentene, and cyclohexene. Oxidation of primary acyclic alcohols, for example, 1-octanol, was also observed (31% conversion), but the reaction was not selective with formation of octyloctanoate, octyl formate and octanal (minor product—14% of all products).

Table 1 Catalytic oxidation of benzyl alcohol as a function of the $H_5PV_2Mo_{10}O_{40}$: benzyl alcohol ratio in $scCO_2$

Catalyst : substrate ratio	Yield (%)	TON	TOF$_{avg}$/h^{-1}
1 : 50	100	50	3.1
1 : 100	100	100	6.2
1 : 250	91	227.5	14.2
1 : 500	81	405	25.3

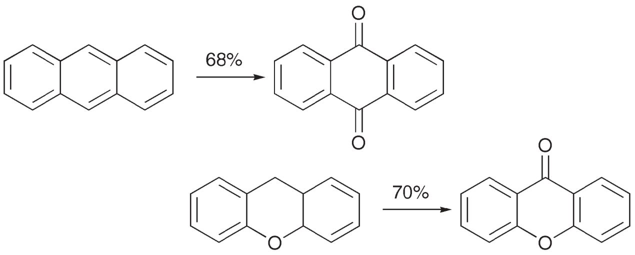
[a] *Reaction conditions:* $H_5PV_2Mo_{10}O_{40}$ solid 5 μmol (12 mg), 2 bar O_2, *ca.* 6 g CO_2, 100 °C, total pressure *ca.* 170 bar, 16 h. Benzaldehyde was the only product detectable by GC analysis.

The utility of $scCO_2$ as a "green" reaction medium for POM-catalyzed reactions was further tested for the oxidation of the activated alkyl aromatics anthracene and xanthene.[13] Various reaction conditions were tested (temperature, catalyst : substrate ratio, time) and up to 70% yield of the corresponding carbonyl compounds could be achieved. Representative results are presented in Scheme 2.

In order to validate the applicability of $scCO_2$ for the combination of reaction and mass separation in this system, batch-wise recycling of $H_5PV_2Mo_{10}O_{40}$ was attempted under standard reaction conditions. After benzyl alcohol was oxidized under conditions outlined in Scheme 1, the reactor was cooled to 60 °C and connected to a CO_2 line. The pressure was adjusted to 120 bar and the reaction mixture was extracted with a constant CO_2 flow for 2 h at these conditions. The outgoing CO_2 stream was passed through a double cold trap where the extracted compounds were condensed at −78 °C. No traces of liquid material remained in the reactor and an ether extraction of the reactor did not reveal any remaining organic compounds in a separate control experiment. After the CO_2 extraction, the autoclave was depressurized and loaded with another batch of benzylalcohol, followed by CO_2 and O_2 as before. Full conversion within 16 h and >99% selectivity for benzaldehyde were obtained in seven subsequent cycles without any additional purification or treatment of the catalyst.

The green–blue color of $H_5PV_2Mo_{10}O_{40}$ (reduced form) did not change significantly during these recycling experiments. The polyoxometalate was obtained as a free floating powder after quantitative extraction in the final cycle. IR spectroscopic investigation of the recovered material gave a spectrum that was superimposable to that of fresh material with a small amount of organic residue, indicating that the catalyst remained stable throughout the seven cycles (see ESI†). Furthermore, ICP measurement of the benzaldehyde isolated by CO_2 extraction after the seventh cycle showed no evidence for contamination with molybdenum or vanadium within the detection limit of the method (<0.3 ppm for V and <0.4 ppm for Mo). This substantiates again that no significant amount of metal components dissolves into the reactive phase and no catalyst leaching occurs under the extraction conditions.

In summary, we have shown for the first time that inexpensive and non-toxic $scCO_2$ is an effective reaction medium for the aerobic oxidation of benzylic alcohols and activated aromatics



Scheme 2 Aerobic oxidation of anthracene and xanthene catalyzed by solid polyoxometalate $H_5PV_2Mo_{10}O_{40}$ in $scCO_2$. *Reaction conditions:* 0.5 μmol $H_5PV_2Mo_{10}O_{40}$ (12 mg), 0.5 mmol substrate, 2 bar O_2, *ca.* 6 g CO_2, 80 °C, total pressure *ca.* 170 bar, 18 h.

catalyzed by the polyoxometalate $H_5PV_2Mo_{10}O_{40}$. Even though the catalytic activity is as yet lower than that of alcohol oxidation catalysts based on Pd nanoparticles,[8] the cheap and readily available polyoxometalates are a promising alternative with a distinct and complementary substrate specifity. Surprisingly, the best performance of the catalyst was observed when it was used in unsupported solid form. The simple product isolation and the high catalyst stability make this system quite attractive for the use as a "catalyst cartridge"[14] and/or for continuous-flow operation.

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Notes and references

‡ $H_5PV_2Mo_{10}O_4$ (0.23 g) was dissolved in acetonitrile and stirred with 2.34 g alumina suspended in chloroform for 2 h until the solution became colorless. The catalyst was then filtered off and dried overnight under high vacuum.

§ $H_5PV_2Mo_{10}O_4$ (0.23 g) was dissolved in acetonitrile and PEG-1000 (1.15 g) was dissolved in chloroform. The solutions were mixed; 2.34 g alumina was added and the suspension was stirred for 2 h until the solution became colorless. The catalyst was then filtered off and dried overnight under high vacuum. PEG-1000 was used because PEG with lower molecular weight (<900) has a significant solubility in $scCO_2$ and would be extracted with the medium during workup (see ref. 8 and references therein). Although PEG with high molecular weights are waxy solids at room temperature, they show a significant melting point depression under CO_2 pressure making them available as liquid catalyst phases under mild conditions.

¶ A 10 mL metal autoclave was charged with 5 μmol catalyst, 0.5 mmol benzyl alcohol, 2 bar oxygen and *ca.* 6 g liquid CO_2 and sealed under pressure. The pressure was increased to *ca.* 170 bar upon heating to 100 °C as the liquid becomes $scCO_2$. After 16 h, the system was cooled down and the pressure was released by letting CO_2 slowly expand through a double cold trap. The reaction was analyzed by GLC and GLC-MS.

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