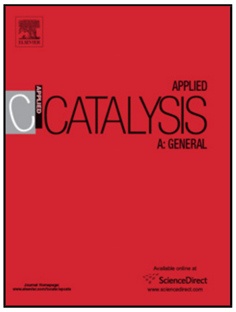

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PII: S0926-860X(16)30582-8
DOI: http://dx.doi.org/doi:10.1016/j.apcata.2016.11.033
Reference: APCATA 16081

To appear in: *Applied Catalysis A: General*

Received date: 27-9-2016
Revised date: 17-11-2016
Accepted date: 27-11-2016

Please cite this article as: Francesca Liguori, Carmen Moreno-Marrodan, Pierluigi Barbaro, Haruo Sawa, Selective, aerobic oxidation reaction of alcohols by hybrid Pd/ZrO2/PVA catalytic membranes, Applied Catalysis A, General http://dx.doi.org/10.1016/j.apcata.2016.11.033

Selective, aerobic oxidation reaction of alcohols by hybrid Pd / ZrO_2 / PVA catalytic membranes

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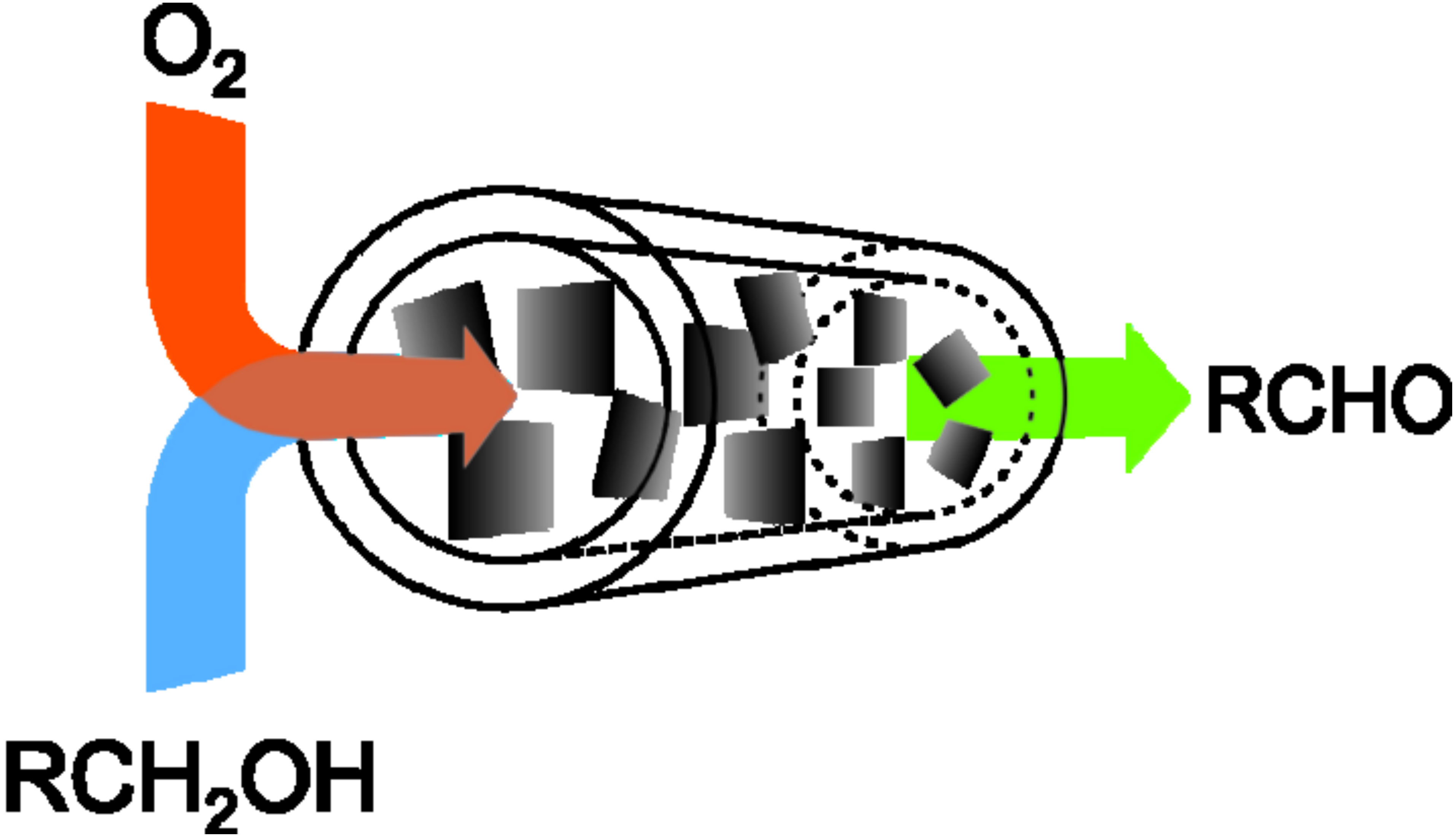
*Graphical Abstract



Highlights

- Pd nanoparticles embedded into hybrid zirconia / polyvinyl alcohol membrane
- Partial oxidation reactions of alcohols in the liquid phase under continuous flow
- Reaction temperature below 100 °C
- No metal leaching, stable, use of hydrophilic solvents, no need of regeneration nor additives

ABSTRACT

Palladium nanoparticles of 2.1 ± 0.9 nm size were generated within a hybrid zirconia / polyvinyl alcohol membrane of 60 ± 5 μm thickness, to afford a bulk 6.7 % Pd loading (w/w). The material was used as catalyst for the heterogeneous, batch and continuous flow partial oxidation reaction of functionalized alcohols, using air or oxygen as oxidants and water or methanol as solvents. Good selectivity to the corresponding aldehydes at full conversion and excellent resistance over prolonged time-on-stream under very mild reaction conditions was observed. No metal leaching in solution was detected, as well as no additives nor regeneration steps were needed.

Keywords: Heterogeneous catalysis, palladium, nanoparticles, alcohols oxidation, membranes, flow processes

1. Introduction

The selective oxidation of alcohols is one of the most popular reactions in chemistry because of the application to the manufacture of several intermediates for the food and pharmaceutical industry [1,2]. Conventional processes usually involve stoichiometric amounts of expensive and toxic oxidants, either organic or inorganic [3,4]. Therefore, economic and environmental drivers have urged the development of catalytic methods employing cleaner and cheaper oxidants [5], with the preferred ones based on oxygen, since water is virtually the only by-product [6,7]. For the synthesis of fine chemicals, such methods shall also be tolerant to the presence of other oxidation-sensitive functional groups, e.g. C=C double bonds, and/or allow for the selective production of partial oxidation products, e.g. aldehydes and ketones [8]. A number of homogeneous catalysts have been described to this purpose employing transition metal species [9,10], although less explored heterogeneous systems offer unquestionable advantages in terms of handling, catalyst separation, reuse and integration in existing reactor equipment [11,12]. The most effective solid catalysts so far reported are based on supported metal nanoparticles (MNP), particularly Au [13,14] and platinum group metals [15,16]. However, issues still need to be solved in relation to chemical and thermal resistance, catalyst deactivation, efficiency under mild conditions, selectivity and/or reproducibility. Aimed at obtaining catalysts with improved performance, the design of appropriate support materials is therefore of paramount importance. Both specific support properties (e.g. mass transfer limits [17]), as well as stabilization of the catalytically active species (e.g. by means of Strong Metal-Support Interactions (SMSI), steric and electrostatic interactions [18,19]), have to be considered.

For liquid phase heterogeneous aerobic oxidations, choice of gas oxidant is also key for large scale applications. Advantages to the use of air include reduced operating cost, because neither gas processing nor the purchase of oxygen is need, superior plant safety and tolerance of metal reactor equipment, because a mild oxidant is used. Advantages to the use of pure O_2 include reduced capital and energy costs and increased productivity, since the lack of inert gas allows for smaller plants and lower total pressures, while high productivities at lower reaction temperatures are obtained because of higher reaction rates [20]. On the other hand, safety is one of the major issues concerning O_2-based oxidation process, mostly in relation to flammability limits and explosion hazards, which requires specially designed apparatuses [21].

An attractive option is provided by catalysis under continuous flow. Packing the catalyst into flow reactors offers significant advantages compared to conventional batch operations in terms of safety, purification, catalyst separation, waste emission, automation, energy consumption and space-time-yield productivity [22,23]. Few flow systems have been reported so far for the heterogeneous aerobic oxidation reaction of alcohols using MNP catalysts onto either polymeric [24] or inorganic [25,26] supports. Despite inorganic materials have been mostly employed because of lower volume and porosity changes with swelling [27,28], use of organic supports may provide significant benefits as a consequence of: i) potential to drive sorption and permeability of reagents and products, ii) easier incorporation of additives in the catalyst, iii) a more mature manufacture technology of polymers, that allows for a wider choice of morphologies, mechanical, chemical and thermal properties, affinity for reagents and catalysts [29,30]. Challenges in the development of polymeric supports include chemical and mechanical stability, shrinking phenomena, back pressure evolution, adverse interaction with the catalyst, which negatively affect the efficiency and long-term productivity of the supported catalysts [31,32]. In order to minimize these drawbacks, various strategies have been developed, including the addition of inorganic materials to the polymer, e.g. raschig rings [33], glass [34], and others [35,36], with improved performance in terms of catalyst resistance.

In the course of our studies on solid electrolytes, we recently described the synthesis of hybrid inorganic / polymeric (ZrO_2/PVA) membranes for electrochemical [37,38] and fuel cells applications [39,40]. Easy incorporation of palladium nanoparticles onto these materials [41,42] led to efficient and durable heterogeneous catalysts for the hydrogenation reactions of various organic substrates in the liquid phase [43]. Both membranes and spherical beads materials showed to be effective under batch and continuous flow conditions. It was demonstrated that the addition of zirconia greatly improves the mechanical and chemical resistance of PVA membranes in hydrophilic solvents, hence, their potential for use under catalytic conditions over prolonged reaction times. Particularly, the continuous flow hydrogenation reaction of C=C and C≡C bonds and nitrobenzene was achieved showing remarkable selectivity at full conversion for long time-on-stream [44].

In the present work we expanded the scope of PdNP@ ZrO_2 / PVA catalytic membranes, by demonstrating their usability in the selective, catalytic aerobic oxidation reaction of various alcohols of industrial interest, both under batch and continuous flow conditions.

2. Experimental

2.1. General information

All reactions and manipulations were routinely performed under nitrogen atmosphere by using standard Schlenk techniques, unless otherwise stated. The hybrid zirconia / PVA (PVA = polyvinyl alcohol) materials containing palladium oxide were obtained as previously described [41,42]. Two differently shaped hybrid materials were used: membranes sheets of 2 x 2 mm surface (60 ± 5 μm thickness, composition in weight ratio normalized to 80 % saponified PVA: ZrO_2 0.08, PdO 0.17, polyoxythylene polyglycerol ether 0.35), hereinafter labelled NKZPDC-1, and 1.7 ± 0.2 mm diameter pellets of similar composition, hereinafter labelled NKZPDB-5. The Pd^0 nanoparticles-containing beads, hereinafter labelled Pd@NKZPDB-5, were prepared as previously reported [44]. All the other chemicals were reagent grade, commercial products and were used as received without further purification. Environmental Scanning Electron Microscopy measurements (ESEM) were performed on a FEI Quanta 200 microscope operating at 25 KeV accelerating voltage in the low-vacuum mode (1 torr) and equipped with an EDAX Energy Dispersive X-ray Spectrometer (EDS). Samples for Transmission Electron Microscopy (TEM) analyses were prepared by inclusion of the membranes into Struers EpoFix®

epoxy resin, followed by lapping. The samples were then cut with a RMC MT-XL ultramicrotome to give a film thickness of 60 nm. TEM measurements were carried out using a CM12 PHILIPS instrument at 120 KeV accelerating voltage. Statistical nanoparticle size distribution analysis was typically carried out on 300-400 particles. X-ray Diffraction (XRD) spectra were recorded with a PANanalytical XPERT PRO powder diffractometer, employing CuKα radiation (λ=1.54187 Å), a parabolic MPD-mirror and a solid state detector (PIXcel). The samples were subjected to measurement without grinding and prepared on a silicon wafer (zero background) that was rotating (0.5 rotations per second) during spectra acquisition. All XRD spectra were acquired at room temperature in a 2θ range from 4 to 95º, applying a step size of 0.0263º and a counting time of 77.5 seconds. Reactions under controlled pressure of gas were performed using a non-metallic Büchi Miniclave® (50 mL internal volume) equipped with a pressure controller and an orbital stirrer set at 150 rpm rate, or a stainless steel autoclave (25 mL internal volume) constructed at Istituto di Chimica dei Composti OrganoMetallici-CNR (Firenze, Italy) and equipped with a magnetic stirrer, a Teflon ® inset and a pressure controller. Catalytic flow oxidations were carried out using a home-made continuous-flow reactor system constructed at ICCOM-CNR. The system was designed to allow for a concurrent flow of substrate solution and oxygen gas through a reactor tube containing the heterogeneous catalyst. The reactor was completely inert, as all wet parts were made of PEEK, PFA or PFTE. The flow of the substrate solution was regulated by an Alltech® model 426 HPLC pump in PEEK. The concurrent flows of gas and liquid were driven through a T-shaped PEEK mixer to ensure efficient gas dispersion. A mixed air-substrate solution stream was allowed to flow in the reactor through a 6-port Rheodyne mod. 9060 switching valve in PEEK. The core of the reactor consisted in a commercial tubular glass column (Omnifit®, 3 mm i.d. × 25 mm length) equipped with 0.2 μm PE frits and packed with the solid catalyst. The column ends were equipped with PEEK fittings and 5 μm frits to ensure an optimum flow distribution. The column was heated with a temperature accuracy of ± 0.1 °C by a home-made oven comprising a Kapton® flexible heating element, a brass and a Teflon holder and a temperature controller. At the outlet of the reactor, the product solution was collected for GC analysis and the excess amount of air released to the atmospheric pressure. GC analyses were performed on a Shimadzu GC-2010 gas chromatograph equipped with a flame ionization detector and 30 m (0.25 mm i.d., 0.25 μm film thickness) VF-WAXms column or a 30 m (0.25 mm i.d, 0.25 µm f.t.) SPB-1 column. GC-MS analyses were performed on a Shimadzu QP2010S spectrometer equipped with identical capillary columns. The metal content in the supported catalysts was determined by EDS analysis and by Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-OES) using a Varian 720ES instrument at a sensitivity of 500 ppb. Each sample was treated in a microwave-heated digestion bomb (Milestone, ETHOS LabStation, 20 min.@ 220 °C) with 8 mL aqua regia and 0.5 mL of H_2O_2 30%. The content of metal leached in the catalytic reaction solutions was determined by ICP-OES. The Palladium detection limit was 0.006 ppm.

2.2. *Synthesis of the catalyst*

In a typical procedure, the preformed hybrid inorganic/polymeric 2 x 2 mm NKZPDC-1 membrane (0.40 g, 0.26 mmol Pd) [41,42] was introduced into a round bottom flask equipped with a lateral stopcock containing nitrogen-degassed water (120 mL). The suspension was cooled to 0 °C and an excess of $NaBH_4$ (400 mg, 10.5 mmol) was added in portions under a stream of nitrogen. The mixture was orbitally stirred under nitrogen at 0 °C for 30 min, then at room temperature for 24 h. After that time, the water solution was removed by decantation, and the sold material was carefully washed with degassed water (3 x 50 mL), methanol (3 x 00 mL) and diethyl ether (3 x 50 mL), then dried under a stream of nitrogen overnight. The black membrane sheets thus obtained (Pd@NKZPDC-1) were stored under nitrogen before being used in catalysis. ICP-OES analysis gave a 6.7 % wt Pd bulk loading in the final material.

2.3. *Catalytic oxidation reactions by Pd@NKZPDC-1 membranes under batch conditions*

In a typical experiment, the Pd@NKZPDC-1 membrane (30 mg, 6.7% wt, Pd, 0.019 mmol Pd), was placed into 50 mL, two-neck, round-bottomed glass flask equipped with a reflux condenser. A solution of substrate (1.9 10^{-2} M, 32.0 mL) was transferred via a Teflon tube into the reactor. The open-air system was heated at the desired temperature using an oil bath. After stirring at 150 rpm using an orbital stirrer for the selected time, the solution was completely removed using a gas-tight syringe. In the experiments carried out under a controlled pressure of gas, the catalyst (30 mg) was placed under nitrogen into a metal-free autoclave. A solution of substrate (0.5 M, 9.4 mL) was transferred via a Teflon tube into the reactor. The autoclave was finally charged with the desired pressure of air and stirred at 150 rpm using a orbital stirrer. The reactor was heated at a given temperature using an oil bath. After the desired time, the reactor was depressurized and the solution was completely removed using a gas-tight syringe. A sample of the reaction solution was analyzed by GC and GC-MS for product identification and quantification and by ICP-OES for metal leaching. The reaction products were unequivocally identified by the GC retention times and mass spectra of those of authentic specimens. Quantitative analysis of the reaction products was carried out via GC based on calibration curves of the pure compounds. For recycling experiments, a fresh solution of the substrate was then transferred via a gas-tight syringe into the reactor containing the catalyst recovered. After the desired time, the mixture was treated as described above. The same recycling procedure was used in the subsequent oxidation cycles. After use in catalysis, the solid catalyst was washed with methanol (3 x 10 ml) and diethyl ether (3 x 10 ml), dried in a stream of nitrogen. An analogous procedure was adopted for oxidation reactions using Pd@NKZPDB-5 catalyst.

2.4. Catalytic oxidation reactions by Pd@NKZPDC-1 membranes under continuous flow conditions

Reactions under continuous flow were carried out using the flow reactor system described above. In a typical experiment, Pd@NKZPDC-1 (45 mg, 6.7 % wt Pd, 0.028 mmol Pd) was packed into a commercial glass column (3 mm diameter x 25 mm length, internal volume 176 μL). The system was degassed with a N_2 flow of 3 mL min^{-1} for 15 minutes. After that time, substrate solution in methanol (0.1 M) was allowed to flow through the catalytic bed at a constant 0.1 mL min^{-1} rate until the catalyst was completely wet. A concurrent stream of oxygen was then allowed to flow though the packed catalyst at 5.0 mL min^{-1} rate. Attainment of steady state conditions, ca. 1 h, was then taken as the reaction start time. The product solution was periodically analysed for conversion by GC, while aliquots were continuously sampled for Pd leaching analysis by ICP-OES. The reaction was typically monitored for 8 h time-on-stream, followed by overnight switch off, and restart the day after for an analogous period. The reaction products were unequivocally identified by the GC retention times and mass spectra of those of authentic specimens.

3. Results and discussion

3.1. Catalyst preparation and characterization

We recently reported the large-scale manufacture of hybrid PdO/ ZrO_2 / PVA materials at competitive costs by a straightforward procedure [41,42]. In agreement with previous investigations using palladium oxide [45,46], the native materials showed to be catalytically inactive prior of palladium reduction both in hydrogenation and aerobic oxidation reactions (see below). However, catalytically active Pd^0 nanoparticles (PdNP) could be generated within the solid matrix by conventional borohydride reduction in water [44]. This procedure was adopted in the present work to generate PdNP onto both spherical beads (NKZPDB-5, 1.7 mm diameter) and membrane (NKZPDC-1, 2 x 2 mm, 60 ± 5 μm thickness) hybrid supports to afford the corresponding catalytic species, namely Pd@NKZPDB-5 and Pd@NKZPDC-1 respectively (Fig. 1).

The as-prepared catalysts showed neither significant physical or morphological changes, nor signs of breaking with respect to the native materials by ESEM analysis and could be handled and used with ease, provided that they were stored under nitrogen for long periods. The palladium loading determined by ICP-OES analysis was 1.6% wt and 6.7% wt for Pd@NKZPDB-5 and Pd@NKZPDC-1, respectively. Comparable values were obtained from EDS analysis. Irrespective of the morphology, TEM investigations showed the catalysts to contain evenly dispersed, spheroidal PdNP, whose mean diameter was 3.2 ± 0.9 nm for Pd@NKZPDB-5 [44] and 2.1 ± 0.9 nm for Pd@NKZPDC-1, respectively. A representative TEM image and the corresponding Pd particles size distribution for Pd@NKZPDC-1 are reported in Fig. 2. X-ray diffraction data were in line with those obtained from TEM in both cases. According to previous observations, the different size of embedded PdNP in the two materials can be tentatively attributed to the different metal loading in the original hybrids [47]. Importantly, the size of the supported PdNP was significantly lower than that reported for PVA-stabilized palladium colloids (8-50 nm) [48] for both catalysts, that can be safely attributed to the steric stabilization of the solid support [19,49]. Chemisorption experiments were hampered by the limited accessibility of gas reactants to the PVA hybrids in the dry state [42,50].

3.2. *Selective aerobic oxidation reaction of alcohols by Pd@NKZPD catalysts*

3.2.1. Catalysis under batch conditions

A preliminary investigation of the suitability of PdNP / ZrO_2 / PVA hybrids as heterogeneous catalysts for the aerobic oxidation of alcohols was carried out using Pd@NKZPDB-5 and Pd@NKZPDC-1 materials and *trans*-cinnamyl alcohol (**1**) as probe substrate (Fig. 3). Catalytic benchmark tests were performed with stirring in water under 90 °C, 1 bar air pressure and batch setups. Both materials were catalytically active under these conditions, showing complete conversion within reasonable timeframes and full selectivity to the partial oxidation product *trans*-cinnamaldehyde (**1a**). Representative results are reported in graphical format in Fig. 4 for Pd@NKZPDB-5. Turnover frequencies (TOF = $mol_{substrate\ converted}$ / mol_{Pd} x h) were in the order 3 h^{-1} at full substrate conversion (Table 1). Neither induction periods nor catalytic activity of the hybrid materials prior of Pd reduction were noticed under the above experimental conditions.

The catalysts were truly heterogeneous, since the contribution of homogeneous species to the conversion could be ruled out by the absence of catalytic activity of the recovered reaction solutions [51] and by the leaching of palladium below the ICP-EOS detection limit in any case. Catalyst reuse was possible by simple decantation of the reaction solution, showing minor activity decay (< 5%) over three consecutive runs.

The above findings are in line with those previously reported for the use of Pd@NKZPD-type catalysts in hydrogenation reactions [43] and demonstrate the strong palladium anchoring and the high resistance of the catalysts also under the conditions of catalytic oxidation. Deactivation of polymer-supported PdNP catalysts was previously attributed to the dissolution of Pd crystallites, to unfavourable interactions with the support and to the oxidative degradation of the polymer under aerobic conditions [52,53]. In the case in our hands, these effects may be prevented by the steric stabilization of PdNP due the microporous polymer matrix [19,41] and by the mechanical strengthening and SMSI effect of ZrO_2 [42].

Trans-cinnamyl alcohol, besides being used as probe substrate to ascertain the resistance of C=C groups in alcohol oxidation reactions [54], is the precursor for *trans*-cinnamaldehyde, an important market product largely used in agrochemistry [55,56] and in the food and perfumery industry, because of the cinnamon flavour and fragrance [57]. The mechanism of cinnamyl alcohol oxidation by O_2 using heterogeneous Pd catalysts was investigated in detail by Baiker et al. [58,59]. The liquid phase, selective aerobic oxidation of **1** to **1a** has been previously described using a number of supported catalysts [5]. The vast majority of these are based on Pt-group metals or Ru onto inorganic materials, with best efficiencies observed for Al_2O_3 [60], SiO_2 [61], hydroxyapatite [62], hydrotalcite [63,64], TiO_2 [65,66], MOFs [67] and MgO [68]. TOFs in the range 1-70 h^{-1} and selectivity around 80-99 % were commonly obtained at full conversion. However, most systems performed satisfactorily using pure oxygen as oxidant in the temperature range 60-90 °C, in conjunction with organic solvents (toluene, xylene, α,α,α-trifluorotoluene, acetic acid). Use of air as oxidant was successfully reported over modified Pd@SiO_2 catalysts, however under 110 °C in xylene [69]. A polymeric (Amberlyst)-supported perruthenate catalyst was also described using O_2 as co-oxidant in toluene, although with limited reusability due to degradation of the polystyrene matrix [70]. Given the lower reaction rates and the higher temperatures usually required compared to oxygen, the fact that Pd@NKZPD catalysts allows for the oxidation of cinnamyl alcohol to take place with comparable efficiencies in water using only 1 bar air and 90 °C must be underlined. As a general rule, use of operating conditions below 100 °C and 10 bar gas pressure is an important target for sustainable industrial processes [71], as well as for improved catalyst stability and selectivity. Aerobic oxidation of **1** to **1a** by O_2 at low temperature (30 °C) was previously described, although in the presence of large excess of base additives [72].

Having established that Pd@NKZPD materials are reliable catalysts for the selective, aerobic oxidation of alcohols to aldehydes, we extended the scope of the catalysts by investigating the oxidation of other alcohol substrates (Fig. 3). Furfuryl (**2**) and benzyl (**3**) alcohols were selected to this aim. The partial oxidation of **2** produces furfural (**2a**), a renewable chemical used as platform for the production of several key furanic intermediates (e.g. methylfuran, acetylfuran, furfurylamine) and as solvent for aromatics and other unsaturated olefins, particularly for use in the refining of lubricating oils [73]. The product of further oxidation furoic acid (**2c**) is used as bactericide, fungicide and flavouring agent [74]. On the other hand, benzyl alcohol represents a model substrate for the oxidation of activated aromatic alcohols wherein the partial oxidation product benzaldehyde (**3a**) is a valuable chemical with widespread applications in perfumery, dyestuff and in agrochemical industries [75].

Due to the larger exposed surface area and the closer packing into tubular reactors (vide infra), we focused our attention on Pd@NKZPDC-1 membrane type catalyst. Furfuryl and benzyl alcohols are sparingly insoluble in hot water, therefore methanol was used as solvent in this case. As a results, the aldehyde partial oxidation products were partially converted to the corresponding dimethylacetals (Fig. 3), as indicated by GC-Ms analysis. The finding can be attributed to the residual acidic catalytic activity of the hybrid Kodoshi materials [43] or to the contribution to catalysis by accidental formic acid, although, in line with the recalcitrance of methanol to aerobic oxidation [76,77], neither traces of formic acid nor formiates could be detected under our experimental conditions. All reaction products were carefully identified and quantified by GC, GC-Ms and NMR. Representative results are summarized in Table 2.

The oxidation of **2** by Pd@NKZPDC-1 in methanol under 70 °C and 10 bar air, resulted in an overall > 99% selectivity to the partial oxidation aldehyde product at 60% conversion (24 h), 75.4 % of which in the form of dimethylacetal **2b** (Table 2, entry 2). No traces of over oxidation products furoic acid (**2c**) or methyl furanoate (**2d**) were detected. Full conversion could be achieved for longer reactions times, with no significant selectivity decay. The selectivity of the oxidation reaction was confirmed by a countercheck experiments carried out on furfural (**2a**) as substrate, which resulted in full conversion to **2b** with no formation of **2c** under the same reaction conditions (Table 2, entry 3). Similar findings were obtained for the oxidation reaction of **3**. A > 90% selectivity to aldehyde, 43% as dimethylacetal **3b**, was observed at 89% conversion. Minor amounts of benzoic acid (**3d**, 2% yield), methyl benzoate (**3e**, 4%) and benzyl methyl ether (**3c**, 2%) were detected. The oxidation reactions proceeded at reasonable rates with productivities in the range 6-9 h^{-1}. Irrespective of the substrate, Pd leaching in solution was below the ICP-OES detection limit in each experiment. The oxidation reactions were explored in other solvents other than water or methanol (toluene, n-hexane, tetrahydrofuran), however with much lower catalytic activity. A conversion < 10% was observed in toluene under the same experimental conditions. This finding can be tentatively attributed to the better wettability and permeability of the hybrid PVA membrane in polar protic solvents [42].

The selective, aerobic oxidation reaction of **2** was previously described using heterogeneous catalysts. As other heterocyclic alcohols, which are considered to be difficult substrates for oxidation reaction, harder reaction conditions were usually required compared to **1**. Representative literature examples are summarized in Table 3. Best results were obtained for Pd [78] or Pt [79] NP onto zeolite-type metal-organic frameworks under 100 °C and 1 bar O_2 (Table 3, entry 2, 3), wherein an active role of Cr sites was demonstrated, and molybdenyl acetylacetonate onto MgO (Table 3, entry 4) [80]. Use of air oxidant or lower temperatures was possible using polyoxometalate [81] (Table 3, entry 5) or hydrotalcite-supported gold catalysts (Table 3, entry 6), respectively, although the latter required visible light irradiation to achieve modest selectivity [82]. An heterogenized homogeneous complex onto amine-modified silica was also reported in water phase with good yields after workup [83](Table 3, entry 7). To the best of our knowledge, Pd@NKZPDC-1 is the first polymer-based heterogeneous catalyst reported for the aerobic oxidation of **2**. Compared to the known systems, slightly slower reaction rates were observed, however with higher selectivity under friendlier reaction conditions (70 °C, air).

Several types of heterogeneous catalysts were described for the batch aerobic oxidation of **3** in the liquid phase [5]. Among them, the most successful examples of solid-supported metal particles are based on inorganic materials, particularly Pd@hydroxyapatite [62], Ru onto Al_2O_3 [60], zeolites [84], hydrotalcite [85] or MgO [68], Ir@TiO_2 [86], Pt@MOFs [79] and Au onto ionic liquid-modified graphene [20]. Typical reaction conditions involve use of toluene, trifluorotoluene or DMSO solvents and temperatures in the range 60-90 °C, to result in > 92% aldehyde yields and TOF in the range 2-100 h^{-1}. Best results were obtained for Pd onto Al_2O_3 in $scCO_2$ (TOF > 1000 h^{-1}) [87]. The polymer-supported perruthenate catalysts RuO_4@Amberlyst also gave aldehyde **3a** in 95% yield at 75 °C, however with scarce reusability [70]. The performance of the Pd@NKZPDC-1 catalyst is in line with that of the above mentioned systems, taking into account a generally lower reaction rate due to the use of air instead of O_2 oxidant.

3.2.2. Catalysis under continuous flow conditions

Prompted by the above favourable results, we decided to investigate the viability of the Pd@NKZPDC-1 oxidation catalyst for **2** and **3** under continuous flow conditions. To this purpose, we engineered a pressure and temperature resistant reactor system allowing for concurrent, controlled flows of substrate solution and air through the catalytic reactor. The catalyst was packed into a commercial glass column resistant up to 1000 psi (176 μL inner volume, Fig. 5) and placed in a tubular heater equipped with a temperature controller (± 1 °C). Attainment of steady state conditions, ca. 1 h, was taken as the reaction start time. At the outlet of the reactor, the solution was collected for GC and GC-Ms analysis for product determination and ICP-OES for Pd leaching, while air was released at atmospheric pressure. A scheme of the system is shown in Fig. 6. The system was completely inert since all wet parts were made of glass, PEEK or Teflon®.

The conversion, selectivity and Pd leaching during oxidation reactions were examined under various combination of air and solution flow rates. Experimental conditions as similar as possible to those of batch operations were adopted for comparative purpose. As general observation, conversions increased either by decreasing the solution flow rate (i.e. by increasing the residence time τ) or by increasing the air flow rate (i.e. by increasing the air / substrate molar ratio), while a slight selectivity decrease was observed upon increasing conversions, as expected for such a flow system [88]. Since conversions were unsatisfactory (i.e. < 25%) by using air as oxidant up to 90 °C temperature, we then decided to use pure oxygen in this case. Selected, best compromise results between conversion and selectivity are summarized in Table 4. Productivities are reported both in terms of TOF (h^{-1}) and space-time-yield (STY = $\text{kg}_{\text{product}}$ / $\text{litre}_{\text{reactor volume}}$ x h).

Using the above setup, oxidations were successfully achieved under mild conditions, i.e. oxygen pressure 1 bar, residence times and temperatures below 240 s and 90 °C, respectively, irrespective of the substrate. The oxidation of **2** resulted in 40% conversion with full selectivity to aldehyde (70% of which **2a** and 30% the acetal **2b**) under 80 °C and τ = 212 s. Under similar conditions (τ = 106 s), the oxidation of **3** resulted in 77% conversion, with 77% selectivity to aldehyde (93% of which **3a** and 3% the acetal **3b**), with minor amounts of **3d** (3%), **3e** (16%) and **3c** (3%). Compared to the batch processes, better acetal / free aldehyde selectivities were observed at similar conversion levels, although a larger amount of over oxidation products was obtained in the oxidation reaction of **3**. This finding can be attributed both to the use of O_2, instead of air, as oxidant and to the lower contact time of the intermediated products with the catalyst, compared to the batch setup. For continuous processes, productivities were similar to those of batch arrangement in terms of TOF, but ca. 10^2 times higher in terms of STY.

All flow processes were typically monitored for 8 h continuous time-on-stream, followed by overnight switch-off and restart the day after for an analogous period. Noteworthy, no significant activity nor selectivity decay were detected under these conditions. Data for the continuous flow aerobic oxidation reaction of **3** are graphically reported in Fig. 7, as representative example. A mean conversion value of 76.7% ± 0.9 was observed over 16 h overall time-on-stream with no Pd leached in solution detected by ICP-OES analysis.

The continuous flow aerobic oxidation reaction of benzyl alcohol to benzaldehyde by heterogeneous catalysts based on supported MNP has been previously reported. Representative, liquid-phase literature examples are summarized in Table 5. Inorganic materials have been mostly used as support [89,90], despite a bimetallic Au-Pd capillary reactor coated with an amine-functionalized polysiloxane was also described [24]. Best results in terms of turnover frequency and aldehyde yield were reported for Au-Pd@TiO_2 catalyst using neat alcohol as substrate [91] and for a multiphase benzotrifluoride / water reactor system using bimetallic Au-Pt@C catalysts [92], respectively. Good yields were also reported for a recirculating Ru@Al_2O_3 reactor [93]. The hybrid Pd@NKZPDC-1 catalyst ranks halfway, however under generally milder reaction conditions. With regard to the aerobic oxidation of furfuryl alcohol, to the best of our knowledge no previous examples under continuous flow conditions have been reported in the literature.

The above obtained results indicate that Pd@NKZPD-type catalysts are featured by a remarkable mechanical and chemical resistance, which allows for their use under oxidation conditions both in batch and continuous flow operations. Particularly, a contactor type catalytic membrane reactor [94,95] could be engineered by packing of the hybrid Pd@NKZPDC-1 material, showing good productivity and selectivity in the aerobic oxidation of functionalized primary alcohols under very mild flow conditions and remarkable resistance for prolonged reaction times, with no need of regeneration treatments. PVA-stabilized PdNP have a number of precedents in heterogeneous catalysis. PdNP @ polyvinyl alcohol films were used for the Suzuki–Miyaura catalytic reaction of *p*-iodonitrobenzene with phenylboronic acid. However, the combined action of oxygen and iodide ions resulted in extensive palladium leaching and in limited catalyst reuse [96]. PdNP onto crosslinked polyvinyl alcohol / polyacrylamide particles were used as catalyst for Heck-type reactions [97]. The catalyst was not truly heterogeneous in this case, since a homogeneous mechanism involving the participation of dissolved Pd atoms was highlighted. The catalytic reduction of Cr(VI) to Cr(III) was achieved using PdNP onto polyethyleneimine/PVA nanofibers [98]. The superior performance of the hybrid Pd@NKZPD catalysts can be attributed to the favourable combination of several factors, including the lack of strong coordination interaction between Pd and functional groups from the support hampering the effective replacement of reactants around the active site [99], the steric stabilization of PdNP by the porous polymer network [19], the mechanical strengthening and SMSI effect of ZrO_2 [18], the good swelling propensity of PVA.

4. Conclusions

Due to environmental and economic constraints, the chemical industry strongly awaits novel, more sustainable and intensive processes for the selective oxidation of alcohols, that replace conventional methods based on stoichiometric (hazardous) reagents or homogeneous catalysts. The challenge ahead requires the design of efficient heterogeneous catalysts using molecular oxygen under mild reaction conditions. We have shown that materials comprising Pd nanoparticles onto a hybrid zirconia / PVA matrix act as versatile catalysts for both hydrogenation and oxidation processes. Particularly, heterocyclic and substituted primary alcohols could be converted to the corresponding aldehyde partial oxidation products in polar, protic solvents, with good selectivity and productivity under smooth oxidation conditions (temperature ≤ 90 °C, air / 1 bar O_2 pressure). Compared to the known catalysts, the reported system provides multiple advantages in terms of cost and availability, milder operating conditions, better stability, no need of stabilizers or (basic) additives [5]. These results can be ascribed to the peculiar features and the optimal permeability in water or methanol of the hybrid support material. In addition, the engineering of the catalyst into a continuous flow, contactor type catalytic membrane reactor has been demonstrated for the oxidation reaction of furfuryl and benzyl alcohol. The reactor showed no significant loss of catalytic performance over prolonged time-on-stream, with no need of intermediate regeneration steps. The applications of catalytic membranes are often hampered by issues related to their manufacturing costs and limited durability. Key points to address are the development of methods for the synthesis of membranes that are stable in a wide range of solvents and conditions and that show high and reproducible performance over long times [100]. The results herein obtained are therefore of relevance to elaboration of green methods for the long-term, sustainable production of fine-chemicals and, particularly, to the engineering of new reactors for continuous processing applications.

Acknowledgments

Thanks are due to the European Research Institute of Catalysis a.i.s.b.l. and to Centro Microscopie Elettroniche (CNR, Firenze) for technical support.

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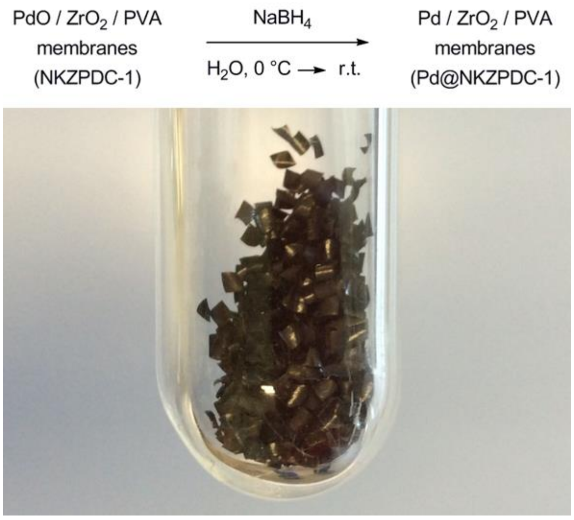

Fig. 1. Sketch of the synthesis of the hybrid catalytic membrane with labelling adopted (top). Optical image of Pd@NKZPDC-1 catalysts (bottom).

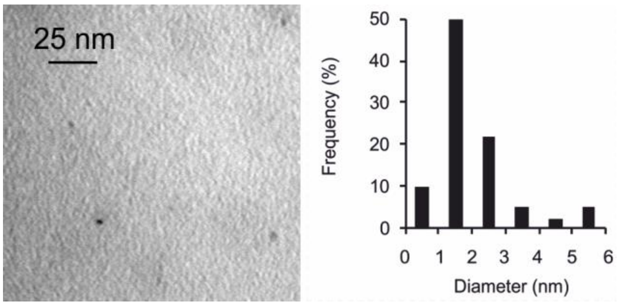

Fig. 2. Left: TEM image of Pd@NKZPDC-1. Right: size distribution of PdNP.

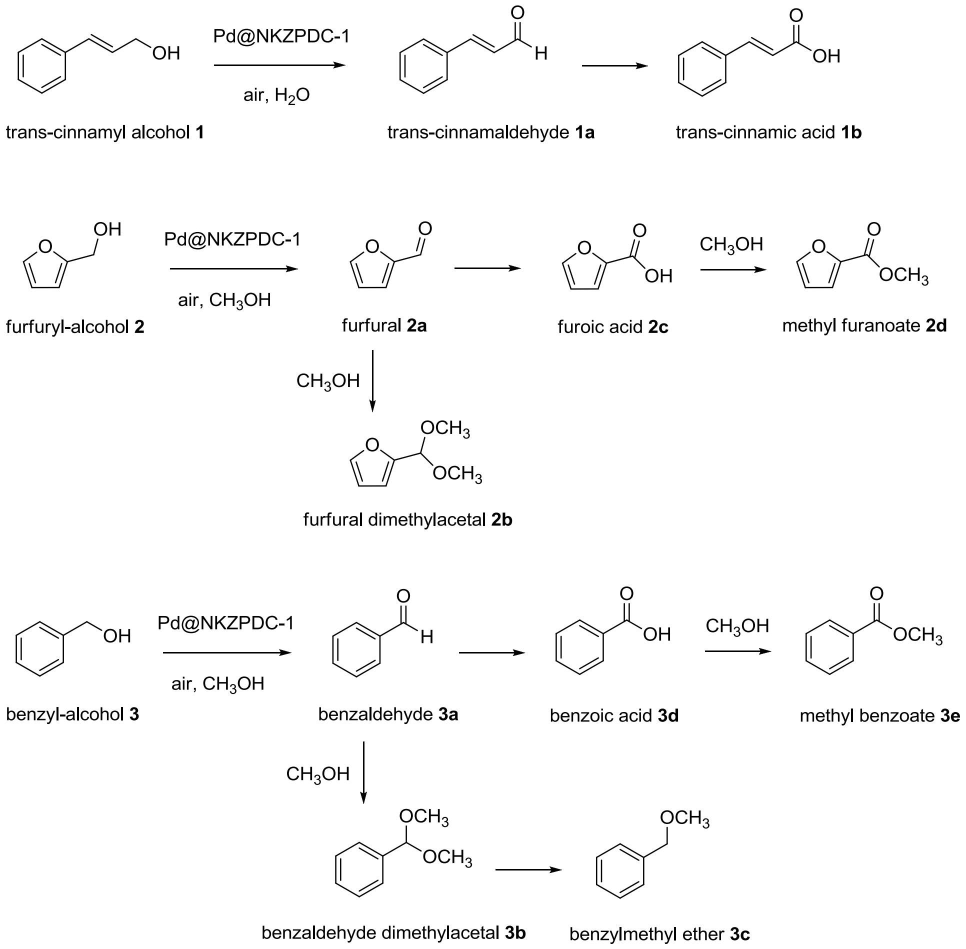

Fig. 3. Sketch of substrates investigated and products detected with labelling scheme adopted.

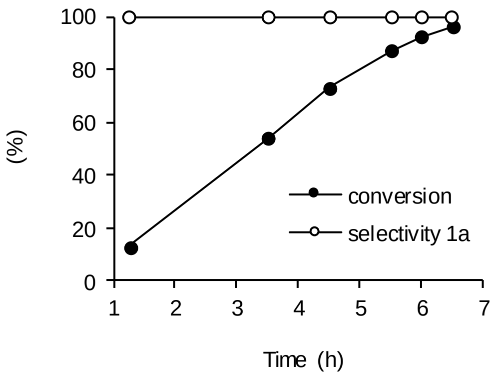

Fig. 4. Batch aerobic oxidation reaction of **1** by Pd@NKZPDB-5 catalyst. Experimental conditions: water solution, 90 °C, 1 bar air.

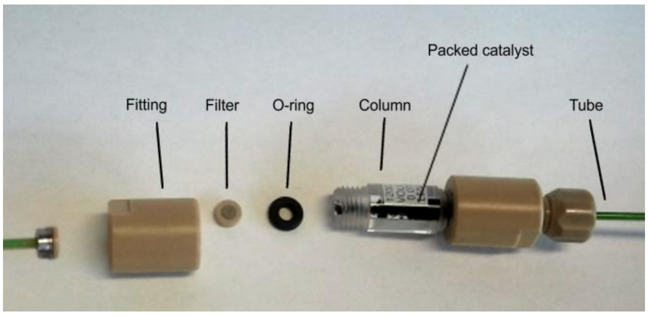

Fig. 5. Column glass reactor packed with Pd@NKZPDC-1 catalyst.

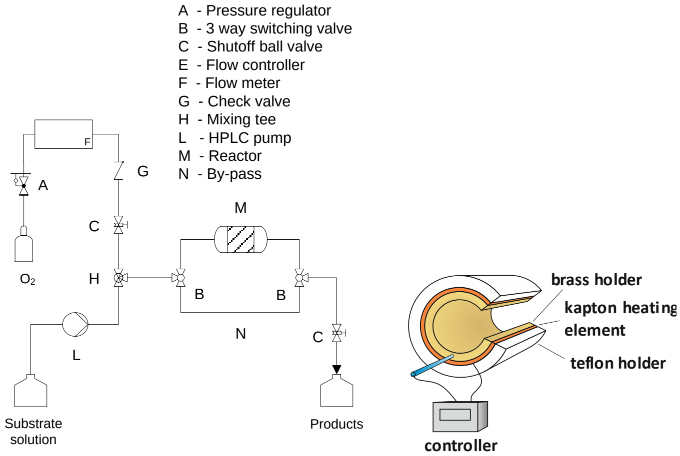

Fig. 6. Scheme of the continuous flow reactor system and tubular heater

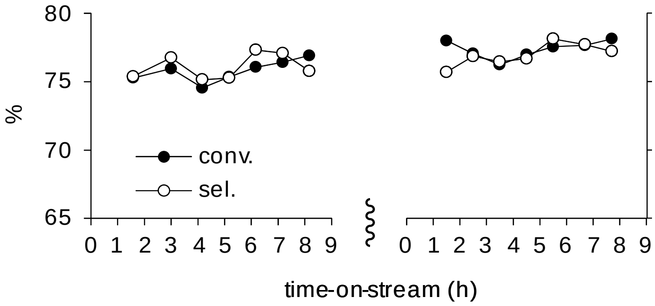

Fig. 7. Continuous flow aerobic oxidation reaction of **3** over of Pd@NKZPDC-1 catalyst. Reaction conditions: methanol solution 0.1 M, 80 °C, solution 0.1 mL min^{-1}, O_2 5.0 mL min^{-1}. Reactor volume 176 µl. Catalyst 45 mg, 6.7% wt Pd. Start time: attainment of steady state conditions, 1h. Line breaks represent overnight switch-offs.

Table 1

Catalytic aerobic oxidation reactions of *trans*-cinnamyl alcohol (**1**) under batch conditions.[a]

Catalyst	Time (h)	Conversion (%)	Selectivity to **1a** (%) [b]
Pd@NKZPDB-5	20.5	99.9	> 99
Pd@NKZPDC-1	21.0	99.9	> 99

[a] Reaction conditions: substrate water solution 0.02 M, 90 °C, air 1 bar, Pd@NKZPDB-5 100 mg, Pd@NKZPDC-1 30 mg. Data from GC analysis.
[b] Selectivity **1a** = **1a**/(**1a**+**1b**).

Table 2

Representative aerobic oxidation reactions of alcohols by Pd@NKZPDC-1 catalyst under batch conditions.[a]

Entry	Substrate	Solvent	Conversion (%)	TOF [b] (h-1)	Selectivity to aldehyde (%)	
					total aldehyde [c]	dimethylacetal [d]
1	**1**	H_2O [e]	99.9	3	**1a** > 99	-
2	**2**	CH_3OH	60.6	6	**2a** + **2b** > 99.9	**2b** 75.4
3	**2a**	CH_3OH	73.6	8	**2a** + **2b** > 99.9	**2b** 100.0
4	**3**	CH_3OH	88.9	9	**3a** + **3b** 90.4	**3b** 42.9

[a] Reaction conditions: substrate solution 0.5 M, 70 °C, air 10 bar, Pd@NKZPDC-1 30 mg. Data from GC analysis.
[b] Calculated on overall conversion.
[c] Es. selectivity **2a** + **2b** = (**2a** + **2b**)/(**2a** + **2b** + **2c** + **2d**).
[d] Es. selectivity **2b** = **2b** / (**2a** + **2b**).
[e] Reaction conditions: substrate solution 0.02 M, 90 °C, air 1 bar.

Table 3

Representative heterogeneous catalysts for the aerobic oxidation reaction of **2**.

Entry	Catalyst	Solvent	Oxidant	Temperature (°C)	Conversion (%)	Selectivity [a] (%)	Ref.
1	Pd@NKZPDC-1	CH_3OH	air, 10 bar	70	60.6	99.9	this work
2	Pd@MOF	toluene	O_2, 1 bar	100	99	98	[78]
3	Pt@MOF	toluene	O_2, 1 bar	100	99	96	[79]
4	$MoO_2(acac)_n$@MgO	toluene	O_2, 1 bar	110	85 [b]		[80]
5	$Na_{6.3}Fe_{0.9}[AlMo_{11}O_{39}]$	toluene	air, 1 bar	80	98	99	[81]
6	Au@hydrotalcite	1,4-dioxane	O_2, 1 bar	40	77.1	25.2	[82]
7	$FeCl_3$-imine@SiO_2	H_2O	O_2, 1 bar	80	78	100	[83]

[a] Selectivity in partial oxidation to aldehyde.
[b] Isolated yield.

Table 4.

Selected data for continuous flow oxidation reactions by Pd@NKZPDC-1 catalyst [a]

Substrate	Reaction conditions						Conv.[d] (%)	Sel.[e] (%)[f]	TOF [f] (h^{-1})	STY [f] (kg l^{-1} h^{-1})
	Solution		O_2		Temp. (°C)	Solvent				
	Flow rate (mL min^{-1})	Res. time [b] (s)	Flow rate (mL min^{-1})	Pressure [c] (bar)						
2	0.05	212	5.0	1.0	80	CH_3OH	40 ± 1	100	4.2	0.05
3	0.10	106	5.0	1.0	80	CH_3OH	76.7 ± 0.9	77	16.2	0.20

[a] Reactor volume 176 μL. Solution 0.1 M methanol. Catalyst 45 mg, 6.7% wt Pd. Data from GC analysis. Start time: attainment of steady state conditions, ca. 1h.

[b] Residence time (τ).

[c] Pressure at the reactor inlet.

[d] Average conversion value over 16 h time-on-stream.

[e] Selectivity in partial oxidation to aldehyde.

[f] Calculated on aldehyde product and bulk Pd content.

Table 5

Continuous flow catalytic aerobic oxidations of benzyl alcohol to benzaldehyde.

Catalyst	Reactor type	Solvent	Temp. (°C)	O_2 (bar)	Conversion (%)	Selectivity (%)	TOF (h^{-1})	Ref.
6.7% Pd@NKZPDC-1	packed-bed	methanol	80	1.0	77	77	16.2	this work
0.9% Ru@Al_2O_3	packed-bed	toluene	115	8.0	20	99	270	[89]
1% Au-Pd@TiO_2	micro	neat	120	5.0	95	78	> 1000	[91]
2% Au@Fe_3O_4-SiO_2	inductive heating	benzene	150	7.0	100	98	7.7	[90]
5% Ru@Al_2O_3	recirculating	toluene	90	5.0	99	99	-	[93]
3% PI-Au-Pt@C [a]	multiphase	BTF/water [b]	60	1.0	100	99	3	[92]
Au-Pd@Si-NH_2 [c]	capillary	DCE/water [d]	50	- [e]	99	92	- [e]	[24]

[a] Polymer incarcerated catalysts.

[b] BTF = benzotrifluoride.

[c] Amine-functionalized polysiloxane.

[d] DCE = dichloroethane.

[e] Not available.