Supporting Information

Anionic *N,O*-Ligated Pd(II) Complexes: Highly Active Catalysts for Alcohol Oxidation

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Materials

All chemicals were commercially obtained and used as received. Unless otherwise stated they were obtained from Sigma Aldrich; Palladium acetate (99.9 +%), Neocuproine (2,9-Dimethyl-1,10-phenanthroline) (**1**), 2-picolinic acid (99%) (**2**), 6-fluoropicolinic acid (97%) (**3**), 2-pyrazinecarboxylic acid (99%) (**4**), 2-quinolinecarboxylic acid (97%) (**5**), 8-Quinonline carboxylic acid (98%) (**6**), Isoquinonline-1-carboxylic acid (99%) (**7**), 3-Isoquinoline carboxylic acid hydrate (99%) (**8**), 2-Quinoxalinecarboxylic acid (97%) (**9**), Quinoline-2,4-dicarboxylic acid (>96%) (Merck) (**10**), 8-hydroxyquinoline (>99%) (**11**), 8-hydroxy-5-quinolinesulfonic acid hydrate 98% (**12**), 2,5-pyridinedicarboxylic acid (98%) (**13**), 2,4-pyridinedicarboxylic acid monohydrate (98%) (**14**), 2,3-pyridinedicarboxylic acid (99%) (**15**), 2,6-pyridinecarboxylic acid (99%) (**16**), 8-hydroxyquinoline-2-carbonitrile (>98%) (**17**), 8-hydroxyquinoline-2-carboxylic acid (>98.0%) (**18**), 8-hydroxyquinoline-2-sulfonic acid monohydrate (>97%) (**19**), tetrabutylammonium acetate ($[NBu_4][OAc]$) (>99%, electrochemical grade), Sodium Acetate Anhydrous, MS3Å, Dowex M-43, 2-Octanol (Fisher Scientific), 2-octanone (Fluka)(>97%) 1-octanol (99+%), octanal (99%) octanoic acid (99%) octyl octanoate (>98%), 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) (99%) , O_2:N_2 (8:92) high pressure premixed gas cylinder (β standard) and a high pressure air cylinder were obtained from BOC gases.

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Catalytic Reactions

Preparation of catalyst stock solutions

2-octanol screening reactions: Due to the small quantities of catalyst that were used in the reaction, it was necessary to prepare stock solutions. We were aware that many of the *N,O*-Pd(II) complexes would be very polar and relatively insoluble in many solvents at the concentrations needed to prepare stock solutions. We chose to use DMSO as a solvent for the stock solutions because it is polar aprotic and importantly it has been utilized previously in other Pd(II) alcohol oxidation studies, as both a solvent[1,2] and a co-solvent.[3] The work to date indicates that DMSO does not become involved in redox chemistry but that it acts as a polar, coordinating solvent. When DMSO is used as the solvent with no ligands present, the TOF of $Pd(OAc)_2$ for alcohol oxidations is small.[1,2] In this case DMSO is only present at the following level; ~0.35 g DMSO in 4g of 2-octanol.

The general procedure was as follows: $Pd(OAc)_2$ (0.011g, 4.9×10^{-5} mol), chelating ligand (4.9×10^{-5} mol), DMSO (11g) (which had been kept over MS3Å) were accurately weighed into a screw top glass vial. In most cases it was also necessary to add $[NBu_4][OAc]$ (~0.4 g, 1.33×10^{-3} mol) (see below for more details). A magnetic stirrer was added to the mixture, the vial was closed and the solution was stirred until homogeneous.

In most cases (ligands **2-10, 13-15, 17 and 18**) we found that even in DMSO the complex was not completely soluble and the solution was "hazy", although still uniform. As all of the complexes are formally anionic, we reasoned that the addition $[NBu_4][OAc]$ (which is used in the catalytic reaction in any case) to the stock solution would result in improving their solubility as there would be an ion exchange and the complex counter ion would become the lipophilic $[NBu_4]^+$. In all but two of the cases (**2** and **6**) where the solution was hazy, the addition $[NBu_4][OAc]$ resulted in clear solutions. However, we are confident that even for those two cases (**2** and **6**) we were still able to obtain an accurate TOF. In the cases where the addition $[NBu_4][OAc]$ resulted in clearing of the hazy stock solution, we carried out catalytic experiments using stock solutions with and without added $[NBu_4][OAc]$. It was found that the TOF obtained from "hazy" stock solutions was the within error* the same as the clear solution with added

$[NBu_4][OAc]$ (*reactions were repeated at least twice, and the TOFs reported in the manuscript are the average). This would indicate that we were able to take representative samples from hazy stock solutions, indicating that the TOF for **2** and **6** is accurate. We felt that alternative approaches such as making more dilute solutions of **2** and **6** (resulting in larger concentrations of DMSO in the reaction) or changing the solvent used for the stock solution, were less satisfactory and would have added additional questions.

$[NBu_4][OAc]$ is added to the reaction in any case, and the quantity in the stock solution would not result in a great deal more being present in the reaction. Nonetheless we checked that "extra" $[NBu_4][OAc]$ did not influence the TOF. As stated below, we generally added 0.05g of $[NBu_4][OAc]$ to the reactor; however it was found that higher concentrations did not influence the TOF. This is consistent with previous studies with phenanthroline type ligands, that indicated that above a minimum concentration, increasing levels of Na[OAc] had no effect on the rate.[4]

1-octanol reactions: In was possible to prepare stock solutions of both **1** and **19** directly in 1-octanol, avoiding the need for DMSO for these reactions. In this case $Pd(OAc)_2$ (0.011 g, 4.9×10^{-5} mol), chelating ligand (4.9×10^{-5} mol), $[NBu_4][OAc]$ (~0.3 g, 1×10^{-3} mol) and 1-Octanol (15 g, 0.115 mol) were accurately weighed into a stopperd conical flask. The solution was stirred on an ice bath until homogeneous. It was found that no reaction would take place if the solution was kept cold. If the solution was stirred at room temperature, the reaction would take place and result in the formation of Pd black. GC analysis indicated that no reaction took place when the solution was kept cold. Indeed it was found that the stock solutions could be kept for long periods in the fridge and the catalyst would deliver the same performance as that of a freshly prepared stock solution.

Higher catalyst loading reactions in DMSO:Water Solvent Mixture: Stock solutions of both **1** and **19** were prepared by dissolving the ligand and $Pd(OAc)_2$ in DMSO. No additional acetate was required to prepare these stock solutions. Typically $Pd(OAc)_2$ (0.013 g, 5.8×10^{-5} mol) and chelating ligand (5.8×10^{-5} mol) were dissolved in 15 g of DMSO.

Catalytic Reactions

The general procedure was the following:

Reactions were carried out in 16 ml high pressure reactors made of Hastelloy C-276. The reactors have a magnetic stirring blade suspended on a hollow stirrer shaft. A thermocouple is placed inside the hollow stirrer shaft to allow the temperature inside the reactor to be measured. The reactor is placed in aluminium heating block, which has been pre-heated to the desired temperature on a hotplate stirrer. Due to the small size of the reactor, it is possible to very quickly heat (and cool) the reactor to the desired temperature. For example, the pre-heated blocks enabled the temperature inside the reactor to reach the desired 100 ^{o}C within 2-3 minutes. Rapid cooling was achieved by placing the reactor in an ice bath.

Typical procedure for ligand screening reactions: 2-Octanol (4 g, 0.03 mol), $[NBu_4][OAc]$ (0.05 g, 1.66×10^{-4} mol), catalyst **s**tock solution (approximately 0.35g, which equals ~ 1.56×10^{-6} mol Pd) were weighed accurately (by difference) into the reactor. The vessel is then pressurized to 45 bar with O_2:N_2 (8:92) and placed in the pre-heated heating block on a hot plate stirrer and stirred at 750 rpm. At the end of the reaction the reactor is placed in an ice bath and once cool the pressure was very slowly released *via* a needle valve. The slow venting of the cold solution meant that a cold trap for volatiles was not necessary, as experiments found that when the reactor was vented through a cold trap, there were never traces of substrate or product in the trap. The reaction mixture was then analyzed by Gas Chromatography (GC). This involved taking 2 or 3 drops of the reaction mixture and filtering through a pipette containing a small plug of silica, using diethyl ether to wash the mixture through into a GC vile. The silica plug removes the catalyst and $[NBu_4][OAc]$ which would be detrimental to the GC column. (GC conditions given below)

In the case of 1-octanol experiments, the general procedure was the same as above apart from the following: As discussed above, the stock solutions of **1** and **19** were prepared in 1-octanol not DMSO. Nonane (0.5g, 3.9×10^{-3} mol) was added to the reaction as an internal standard. After the reaction, diethyl ether containing a small quantity of TEMPO was used to prepare the sample for GC analysis (TEMPO is known act as an anti-oxidant and was therefore used to prevent further autoxidation of the aldehyde product in the GC vial.)

Experiments with higher catalyst loadings (0.5 mol %) in DMSO:Water solvent mixtures: Catalyst stock solutions of ligand and $Pd(OAc)_2$ were prepared in DMSO. To the reactor was added: an appropriate quantity of DMSO stock solution (*e.g.* 2.75 g based on the stock solution described earlier), 2.5 g of de-ionized water, sodium acetate (0.0082 g, 1×10^{-4} mol) and 2-octanol (0.26 g 0.002 mol). The vessel is then pressurized to 50 bar with O_2:N_2 (8:92) and heated to 100 ^{o}C in the heating block, while stirring at 750 rpm. The reaction was followed by sampling at 30 min, 60 min, 120 min, 180 min and 240 min. Samples were obtained by placing the reactor in an ice bath, depressurizing, removing a few drops of liquid, then re-pressurizing the reactor and heating once again. At the end of the reaction the mixture was removed from the reactor and a few drops were again removed for analysis. On removing from the reactor the liquid appeared to be one phase, however to ensure sampling was representative we also extracted the solvent mixture with diethyl ether. Analysis indicated that the conversion in the final sample was the same as that extracted by diethyl ether.

Prior to using the reactor again it was thoroughly cleaned and a blank reaction carried out: First the reactor was rinsed with acetone several times, and then a spatula of Dowex M-43 resin was added to the reactor along with acetone. The resin and acetone were then heated (80 °C) for one hour, cooled to room temperature and the resin and acetone were removed from the reactor. This cleaning process was repeated twice. The aim of the resin (which has covalently bound tertiary amine) is to sequester any traces of palladium that may be in the reactor. To confirm that the reactor is clean, 2-octanol was added to the reactor and a blank reaction is carried out to confirm that there is no conversion due to residual catalyst. In most cases this approach resulted in a clean reactor and the blank reaction yielded no product. If a successful blank was obtained, the reactor was then rinsed with acetone to remove all traces of 2-octanol and then dried. If the blank reaction indicated there were still traces of catalyst, the procedure was repeated until clean.

Confirmation of no Mass Transfer Limitations

Reactions were carried out using O_2:N_2 (8:92) and the catalyst concentration used in this study was chosen to ensure that the reactions were not mass transfer limited in O_2. It has already been shown that [O_2] does not influence the overall rate for such Pd oxidase alcohol oxidations, if the system is not mass transfer limited in O_2.[2,5] To ensure that our system was not limited in O_2, we carried out reactions using higher pressures of 8% O_2 in N_2 and also using air (at the same pressure of 45 bar) and found no influence on the observed TOF. This demonstrated that there was a sufficient O_2 concentration in the liquid phase and the reactions were not mass transfer limited. Of course the most active catalyst system (**19**) (which is most likely to be limited in O_2) was included in these checks. No traces of Pd black were ever observed in any of the experiments.

Conditions for GC separation Analysis

Gas chromatography analyses were carried out using Agilent 6890N series gas chromatograph. An Agilent 19091J-433 HP-5 5% Phenyl Methyl Siloxane cappliary (column) (30.0m x 250µm x 0.25µm nominal) was employed for all the separations using the following conditions. Column head pressure, 30 kPa (4.49psi) helium; initial column temperature, 40°C; initial hold time, 0 min; rate of temperature ramp 1, 4°C/min; next temperature, 100°C; hold time, 0 min; rate of temperature ramp 2, 30°C/min, final temperature 320°C; hold time, 15 min; injection temperature, 250°C; detection temperature, 250°C. The effluent was combusted in a H_2/Air flame and detected using an FID (flame ionization detector). Ion count data were sent to a plotter, which integrated the area under the peaks.

Product Analysis and determination of TOF

Calibration experiments found that the response factor for 2-octanol and 2-octanone was 1:1. Because of these factors we could determine the amount of product produced by a ratiometric method (eqn. 1). This was the approach that was also previously adopted by Waymouth and co-workers in their analysis of 2-heptanone.[6] We also carried out experiments using nonane as an internal standard and found that the TOF was in good agreement with that obtained by the ratiometric approach.

% yield = $((\text{area}_{2\text{-octanol}})/(\text{area}_{2\text{-octanol}} + \text{area}_{2\text{-octanone}})) \times 100/1$ (Eqn.1)

TOF was then calculated by (Eqn. 2):

TOF = moles of product/moles of Pd (Eqn.2)

In the case of 1-octanol, nonane was used as an internal standard, and response factors were determined for the products (aldehyde, acid and ester) using commercially available standards. The quantities of the different products were then determined using Eqn. 3

$\text{amount}_{\text{product}} = (\text{RF} \times \text{amountIS} \times \text{areaproduct})/(\text{areaIS})$ (Eqn.3)

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