Enhanced acyl radical formation in the Au nanoparticle-catalysed aldehyde oxidation†

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EPR spectroscopy and spin-trapping experiments showed that polymer-encapsulated Au nanoparticles promote aldehyde oxidation *via* a radical pathway by initiating formation of acyl radicals.

Aldehyde oxidation is an important reaction for the manufacture of organic acids, peracids and anhydrides, which find applications as precursors for resins and pharmaceutical products.[1] Aldehydes can autoxidise in air *via* a radical pathway;[2] this reaction is facilitated by Mn^{3+}, Cu^{2+} or Co^{2+} salts, which promote the initiation step.[3] Gold nanoparticles can also efficiently catalyse aldehyde oxidation,[4] providing the advantage of a heterogeneous system. However, many mechanistic aspects of the catalytic cycle and possible pathways, particularly in basic media, are not well understood. This prompted us to explore aldehyde oxidation over polymer-incarcerated Au nanoparticles (PI-Au)[5] in the absence and presence of base using EPR spin trapping methodology.[6]

Spin-trapping methodology relies on the fast selective addition (trapping) of short-lived radicals to a diamagnetic spin trap, usually a nitrone or a nitroso compound, such as 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO). The product of this addition (spin adduct) is a persistent free radical (nitroxide) with sufficiently long lifetime to enable detection by conventional EPR spectroscopy. Magnetic properties of the spin adducts often make it possible to assign the structure of the original short-lived radicals. Structures of spin traps used in this study are shown in Scheme 1.

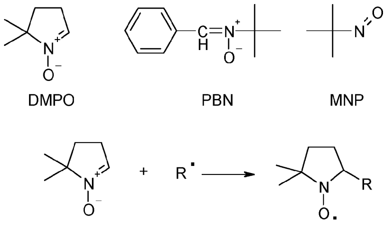
PI-Au is a catalyst containing gold nanoparticles trapped in a polymer matrix.[5] The catalyst is prepared by reduction of Au(I) with sodium borohydride in the presence of polymer solution (full preparation details are in the ESI†). This material is an efficient alcohol oxidation catalyst.[7] Reaction of benzaldehyde with air in toluene at 50 °C in the presence of a DMPO or MNP spin trap, gave rise to a persistent free radical which was identified by X-band EPR as an acyl adduct by comparison with the literature data, *e.g.*, DMPO–COR adduct (a_N = 14.03 G, a_H = 15.73 G)[8] or MNP–COR adduct (a_N = 8.1 G).[9] EPR spectra recorded with an MNP spin trap additionally contain a triplet with coupling constant a_N = 15.4 G, which is characteristic of the di-*tert*-butyl aminoxyl radical (DTBA), an impurity present in MNP samples (see ESI†).[10] However, as the amount of DTBA is constant in all samples, it can be used to estimate the relative amount of MNP–COR adduct formed under different conditions. When PBN was used as a spin trap, a peroxyl PBN–$OOCR_3$ adduct was observed (a_N = 13.4, a_H = 1.72 G)[11] in aerobic conditions, while a PBN–COR adduct (a_N = 14.3, a_H = 4.57 G)[11] was observed in partially deoxygenated mixtures (details are in the ESI†).

Observation of acyl and peroxyl adducts is consistent with the free radical mechanism of aldehyde autoxidation reported in the literature.[2] This mechanism includes: (i) an initiation step which leads to acyl radical formation, (ii) addition of oxygen to acyl radicals to form peroxyl radicals, (iii) abstraction of a hydrogen atom from the aldehyde by the peroxyl radical (giving a peracid) during the propagation step, and (iv) carboxylic acid formation from the aldehyde and peracid *via* Baeyer–Villiger reaction.[2] Consequently, using different spin traps with different affinity for different radicals, we could monitor the overall reaction.

When the catalyst PI-Au was introduced into the system, two effects were observed: a detectable increase in the acyl adduct intensity (by 32% relative to DTBA), and increased sharpening of the spectral lines, which is diagnostic of oxygen consumption (Fig. 1a). This is consistent with the catalytic action of the PI-Au nanocomposite. Control tests confirmed that the catalyst cannot oxidise solvent (toluene) and hence the observed radicals originate from the substrate.

We subsequently tested the oxidation of aliphatic aldehydes, *e.g.*, valeraldehyde and acetaldehyde, both in the presence and absence of PI-Au. Enhanced acyl radical generation was detected for valeraldehyde within the first 5 min of the reaction (spin adduct intensity more than doubled, Fig. 1b). For acetaldehyde, acyl radicals could be detected only in the presence of PI-Au catalyst (Fig. 1c).

In order to confirm that the intensity of the radical spin adducts is related to the catalytic efficiency, bulk tests were carried out. A detectable increase in the yield of carboxylic



Scheme 1 Chemical structure of DMPO, PBN and MNP spin traps (top) and trapping of a free radical (bottom).

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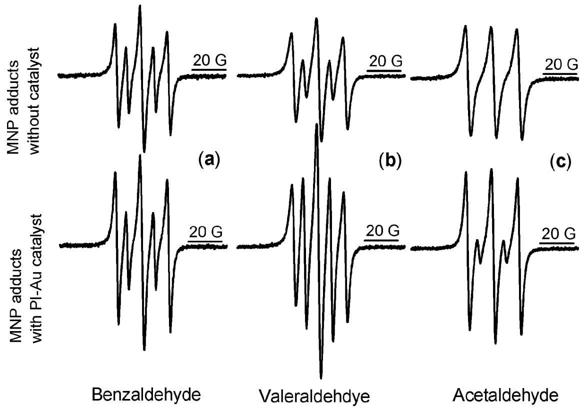


Fig. 1 Spin adducts formed from MNP in an oxidation reaction in the absence (top) and presence (bottom) of PI-Au with: (a) benzaldehyde, (b) valeraldehyde and (c) acetaldehyde. The three lines with bigger coupling constant in all spectra are due to di-*tert*-butyl aminoxyl radicals (DTBA).

acids was observed for PI-Au catalysed benzaldehyde and valeraldehyde oxidations, consistent with the EPR results (Table 1, entries 1–4; full experimental details are in the ESI†).

These data suggest that the PI-Au catalyst can promote the initiation step of the aldehyde oxidation by increasing the rate of acyl radical formation. In order to confirm that the catalysed oxidation indeed occurs *via* a free radical mechanism, we carried out oxidations in the presence of 2,2′,6,6′-tetramethylpiperidine *N*-oxyl (TEMPO). While relatively unreactive towards oxygen centred radicals, TEMPO is a highly efficient quencher for carbon centred radicals.[12] TEMPO efficiently suppressed oxidation both in the presence and absence of catalyst. For instance, for both benzaldehyde and valeraldehyde, conversion values in the presence of TEMPO dropped from *ca.* 50% to *ca.* 3%. (Table 1, entries 5–8). Control tests using catalyst pre-treated with TEMPO, showed a very similar activity to the untreated catalyst (*e.g.*, conversion of benzaldehyde in a 24 h reaction with treated and untreated catalysts was *ca.* 56 and 59%, respectively). Thus, the suppression of oxidation by TEMPO is not due to the catalyst deactivation by the nitroxide. We conclude therefore that the catalytic oxidation occurs *via* a radical mechanism.

The radical chain mechanism explains the rather moderate increase in conversion in catalytic *vs.* non-catalytic reactions (Table 1, entries 1–4). The turnover in the chain reactions may be determined by the rate of termination rather than that of initiation. For instance, simply replacing glass reaction vials with polyethylene vials led to significantly increased conversions (67% when PI-Au was used, see ESI†). This suggests that termination can be controlled by the walls of the reaction vessel.[13] A related phenomenon was observed when ZnO-supported gold catalyst (Au/ZnO)[14] was used. The oxidation in the presence of this catalyst was partially suppressed. The conversion under conditions reported in Table 1, was *ca.* 15%, which is much lower than that in a catalyst-free reaction. We believe this is due to the termination of radicals by the catalyst. This effect was confirmed by the very low conversion observed when Au-free ZnO was added to the uncatalysed reaction (7%, see ESI†). ZnO is a material rich in neutral oxygen vacancies[15] that could possibly quench peroxyl radicals. In fact, spin trapping experiments in the presence of ZnO did not reveal any significant amount of peroxyl adduct.

Table 1 Conversion of benzaldehyde and valeraldehyde under different experimental conditions

Entry	Substrate[a]	Catalyst[b]	Reaction medium[c]	Acid (%)[d]
1	Benzaldehyde	—	Toluene	29
2	Benzaldehyde	PI-Au	Toluene	50
3	Valeraldehyde	—	Toluene	46
4	Valeraldehyde	PI-Au	Toluene	54
5	Benzaldehyde	—	Toluene/TEMPO	1.2
6	Benzaldehyde	PI-Au	Toluene/TEMPO	1.5
7	Valeraldehyde	—	Toluene/TEMPO	3.6
8	Valeraldehyde	PI-Au	Toluene/TEMPO	4.4

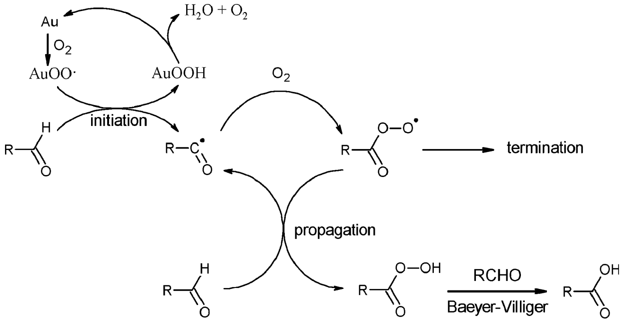
[a] Reaction conditions: substrate (0.5 ml), solvent (0.5 ml), $T = 50$ °C, $P = 1$ atm, reaction time 5 h. [b] Catalyst (5 mg). [c] TEMPO (100 ppm) in toluene. [d] Determined by ^{1}H-NMR spectroscopy.

In order to further test the catalytic efficiency of PI-Au in aldehyde oxidation, we carried out reactions in sealed vials in the presence of TEMPO. The sensitivity of TEMPO EPR signals to the oxygen concentration[16] makes it possible to assess the conversion from the EPR data as TEMPO line broadening is linearly proportional to the oxygen concentration. The presence of excess TEMPO efficiently breaks the radical chain process, so that the rate of deoxygenation is determined by the initiation reaction. The rate of deoxygenation in the presence of catalyst was *ca.* 2-fold higher than that in the absence of catalyst, thus providing strong evidence that the catalyst enhances the rate of initiation in aldehyde oxidations (see ESI for further details†).

The overall reaction mechanism can thus be proposed as follows (Scheme 2). It is likely that the reaction occurs *via* H abstraction from the C–H bond by O_2 activated over the catalyst surface, probably *via* AuOO$^\bullet$ species. Activation of molecular oxygen by Au catalysts has been proposed in other similar reactions.[6,17]

The activation of the C–H bond would also be consistent with a recent kinetic study of aldehyde oxidation over Au/TiO_2,[19] *via* activated oxygen over the catalyst surface, which illustrates that activation of the C–H bond takes place in the rate-determining step.

Interestingly, different results were obtained when the oxidation was carried out in the presence of base. Base is often added to Au-catalysed oxidation reactions.[20] Oxidation



Scheme 2 Proposed aldehyde oxidation pathway.[18]

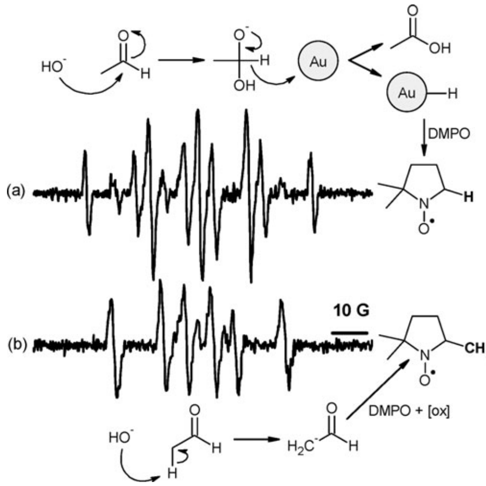


Fig. 2 DMPO spin adducts formed in a reaction of acetaldehyde in basic media. (a) DMPO–H formation in the presence of PI-Au and (b) DMPO–CH_2R adduct formation in the absence of catalyst (R = COH).

of benzaldehyde, valeraldehyde and acetaldehyde in the presence of NaOH, PI-Au and DMPO gave a weak DMPO–H adduct (a_N = 14.49, $a_{H(1)}$ = $a_{H(2)}$ = 18.69 G).[21] In the absence of catalyst, only a DMPO–CHR_2 adduct was identified (a_N = 14.55, a_H = 21.07 G),[8] (Fig. 2 and ESI†). To explore the origin of the DMPO–H adduct, perdeuterated acetaldehyde was oxidised in the presence of base and PI-Au catalyst. A DMPO–D adduct (a_N = 14.54, a_H = 18.79, a_D = 2.84 G)[22] was observed, thus suggesting that the hydrogen adduct is formed as a consequence of C–H bond cleavage (see ESI†).

Observation of a DMPO–H adduct in a related Au-catalysed alcohol oxidation reaction was recently attributed to the intermediate formation of Au–H as a consequence of hydride transfer from the C–H bond to gold.[23] We propose therefore that the detection of DMPO–H during aldehyde oxidation in basic medium is due to the intermediate formation of geminal diol (Fig. 2a) which undergoes hydride transfer to the Au surface. Detection of a DMPO–CHR_2 adduct in the uncatalysed reaction is probably due to the nucleophilic addition of the enolate to the spin trap (Fig. 2b) followed by oxidation to a nitroxide[24] (not detected for benzaldehyde which does not form the enolate).

In order to probe whether hydride transfer from the geminal diol is the predominant oxidation pathway in basic medium, we added radical scavenger TEMPO to the reaction mixture. In the presence of base, typical conversions for benzaldehyde oxidation were 29% and 21% in the presence and absence of catalyst, respectively, with *ca.* 90% selectivity for benzoic acid (see Table S1 in the ESI†). When TEMPO was added, the conversion dropped in both cases to *ca.* 6% with selectivity $>70\%$ (the by-product was benzyl alcohol which was formed *via* Cannizzaro reaction). The significant suppression of reaction by TEMPO, both in the presence and absence of catalyst, strongly suggests that the radical pathway is dominant for both reactions in the presence of base.

In conclusion, gold catalyses aldehyde oxidation by accelerating the initiation step in the radical pathway leading to enhanced formation of acyl radicals. In the presence of base, hydride transfer from the geminal diol is possible, however, this is likely to be a minor secondary pathway as the radical route appears to be dominant.

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