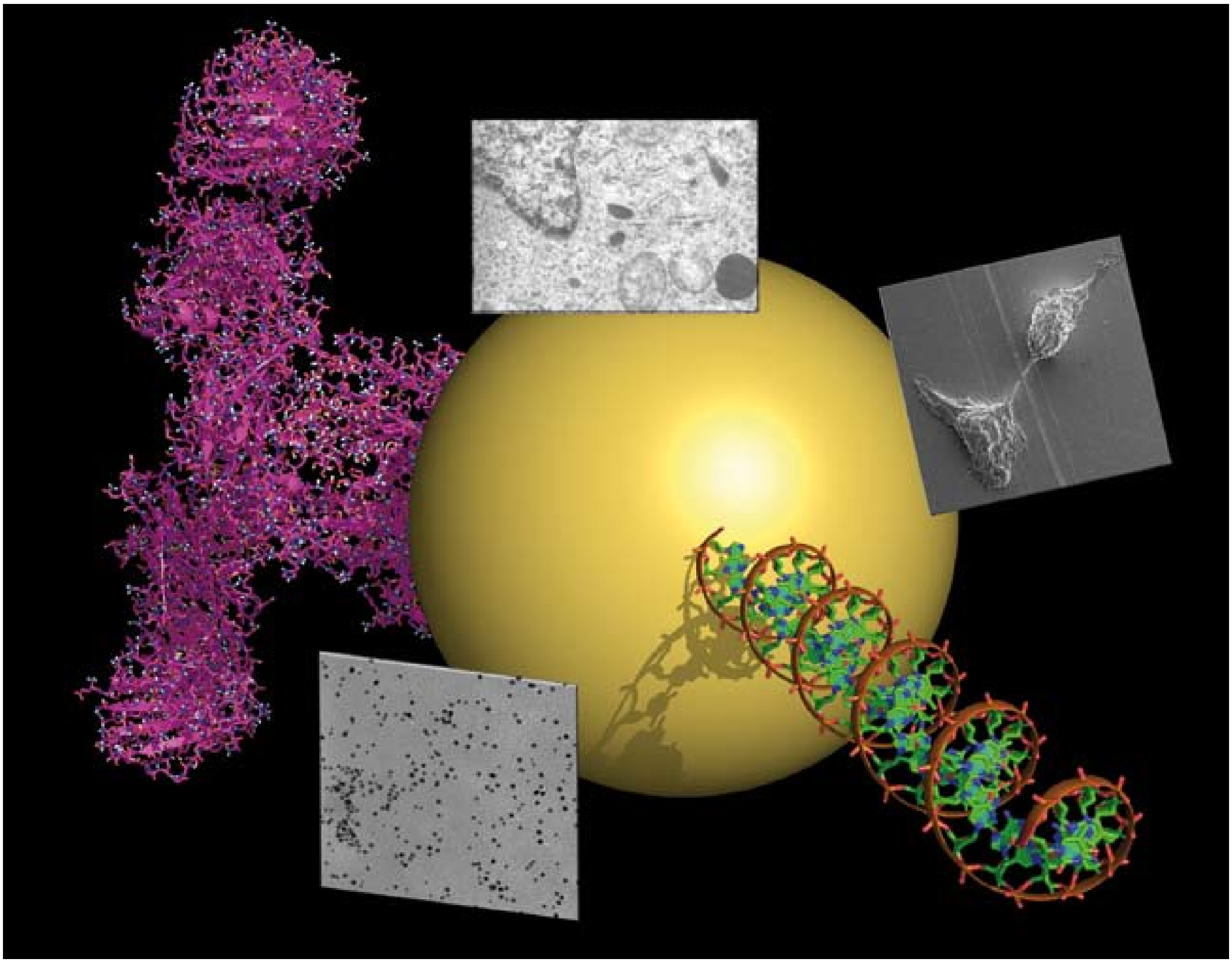

Selective oxidation using gold†

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This *critical review* covers the recent development of the catalytic properties of gold in the selective oxidation of organic compounds, highlighting the exciting contribution to the art of catalysis. The unique, outstanding properties of nanometre-scale particles of gold, a biocompatible non-toxic metal, have allowed the development of a new generation of stable and selective catalysts for the conversion of many organic feedstocks to valuable chemicals. A critical discussion of the results of different research groups is presented along with attempts to correlate the catalytic properties with catalyst morphology in non-equivalent series of experiments.

Particular emphasis has been given to the international efforts towards optimised synthesis of products of industrial appeal such as propylene oxide, vinyl acetate monomer, cyclohexanol/cyclohexanone, gluconic acid and glyceric acid (168 references).

1. Introduction

During the last two decades the rapid growth of nanoscience has led to important developments in physical and chemical technologies by offering advanced tools for arranging atoms in specific molecular and supramolecular structures.[1] From the progress of this field, gold catalysis has derived benefits for tailoring solid nanostructured surfaces showing unsuspected catalytic properties: we can assert that today the yellow metal belongs to the select club of efficient catalysts for organic synthesis and environmental control.[2]

In fact, the application of gold in catalysis only became an important research area several years after the first report on its catalytic potential for ethyne hydrochlorination[3] and it is now considered an active promoter of many fundamental reactions for organic synthesis such as oxidation and hydrogenation.[4] As a consequence, new applications of gold have been proposed for commercial syntheses by both academic and industrial researchers.[5–8] One of the most advanced projects concerns the direct synthesis of hydrogen peroxide, not discussed in the present review, which has been developed by the impressive work of Hutchings' group.[9]

Selective oxidation of natural resources is a task of key importance for producing oxygenates to be employed as building blocks in chemical processes that range from kilogram-scale applications in pharmaceuticals to thousand tonne-scale in chemicals.

Cristina Della Pina received a master's degree in Industrial Chemistry at Milan University and was awarded a PhD in Industrial Chemistry in 2006, under Prof. Rossi's supervision. Her work focuses on the development of novel gold catalysts for the selective oxidation of organic compounds and has resulted in a number of achievements reported in recent papers. She was hosted at Duisburg-Essen University by Prof. G. Schmid applying Atomic Force Microscopy to gold nanoparticles.

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Michele Rossi obtained his master's degree in Industrial Chemistry at the University of Milan where he is currently full Professor of Chemistry. His research is mainly devoted to the activation of small molecules and catalytic methods for organic synthesis. He was a pioneer in the application of gold catalysis to the liquid phase oxidation of alcohols and sugars.

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Both the gas phase oxidation of volatile substrates and the liquid phase oxidation of high boiling compounds benefit from using a catalyst able to lower the activation energy. In particular, the oxidation of alcohols and polyols is of interest owing to the large array of biological hydroxy-derivatives. Recent reviews have covered the literature concerning the catalytic oxidation of the C–OH group, outlining the evolution of the catalytic system from conventional Pt and Pd supported metals to more sophisticated Pt–Pd–Bi polymetallic systems for increasing the selectivity and limiting the deactivation process.[10,11]

Supported gold represents a second generation of catalysts for alcohol and carbohydrate oxidation: they show a great improvement in selectivity and stability and thus represent challenging substitutes for platinum group metals.[12] In this context, beside the commercial interest in applying a more abundant noble metal, some features of gold catalysis appear as unique.

Firstly, the high electrode potential ($E^\circ = +1.69$ V) is responsible for the well known inertness of gold that, catalytically, means high stability, resistance to oxygen and tolerance to chemical groups such as, for example, aliphatic and aromatic amines, which normally produce poisoning phenomena with other metals.

A second feature concerns the kinetic aspect of gold catalysis which outlines that the turnover frequency is strongly related to the size of metallic gold particles. In particular, many investigations on the liquid-phase oxidation of polyols, alcohols, carbohydrates indicate that only small gold particles are catalytically active,[4] this behaviour being common to gold particles employed in the gas-phase oxidation of carbon monoxide.[2]

Compared to other catalysts, mainly the platinum group metals, the outstanding properties of gold catalysis are also represented by high selectivity which allows discrimination within chemical groups and geometrical positions, leading to superior yields in the desired products. Among many examples, glycols can be oxidised to monocarboxylates,[12] and unsaturated alcohols to unsaturated aldehydes.[13] This feature can be found also in other different processes, such as reduction, where aldehydes and ketones can be hydrogenated to unsaturated alcohols by supported gold with selectivities approaching 100%.[14]

Considering other fundamental peculiarities, such as biocompatibility, availability and easy recovery, gold appears as an exciting catalyst for sustainable processes based on the use of clean reagents, particularly O_2, often in aqueous solution or in the absence of solvent, under mild conditions.

Hopefully, the progress in oxidation reactions by gold will contribute to the definitive decline of the so-called "stoichiometric oxidants" used in organic synthesis, such as chromate, permanganate, and hypochlorite which produce high amounts of intolerable wastes, favouring "greener" catalytic processes.

The present review is focused on the unique aspects of gold catalysis applied to selective oxidation of organic compounds.

2. Selective oxidation of hydrocarbons

Partial oxidation of methane to methanol–formaldehyde, and petrol derivatives to oxygenates, is matter of great interest owing to applications in industrial organic chemistry and fuel additives. However, beside less relevant examples, only a few applications of gold catalysis have been thoroughly investigated and some of them show possible industrial exploitation. In particular, oxidation of propene to propene oxide (PO), ethene to vinyl acetate monomer (VAM) and cyclohexane to cyclohexanol–cyclohexanone mixture (KA oil) were investigated in a more systematic manner.

2.1 Propene epoxidation

All attempts to produce PO commercially by direct oxidation of propene, in a similar way to the silver promoted synthesis of ethene oxide, have till now been unsuccessful and the majority of PO is still manufactured by the chlorohydrin process (49%) and the indirect hydroperoxide processes.[15]

However, the insistent demand for cleaner processes that avoid chlorine dependence and huge amounts of undesired by-products has stimulated basic research which has stressed the importance of gold catalysis. In fact, it has been shown by the pioneering work of Haruta that a supported gold catalyst is able to promote the gas phase epoxidation of propene by O_2 in the presence of H_2[16] (Scheme 1).

The behaviour of gold is unique as shown by comparing different metals dispersed on titania (M = Au, Pt and Pd) under moderate conditions (25–80 °C) when equimolecular amounts of H_2 and O_2 are reacted with C_3H_6. As shown in Table 1 only Au produces propene oxide (PO), while Pd and Pt promote mainly the hydrogenation of C_3H_6 to C_3H_8 and the formation of small amounts of acetone and carbon dioxide.

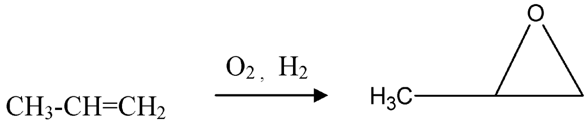
The pre-eminent features of these experiments are the total selectivity to PO shown by gold and the strategic role of TiO_2 which have been confirmed by further studies;[17,18] critical points are the low conversion needed to reach high selectivity as the latter declines on increasing the temperature.

Therefore most of the subsequent investigations were devoted to improving PO yields while maintaining a high selectivity.

It has been found that dilution of the active sites represents a way of preventing over-oxidation and deactivation during the epoxidation reaction. In particular, deactivation could be depressed by using TiO_2 dispersed on an inert material such as silica as a support.

A first progress was achieved introducing Au/Ti–MCM-41 catalysts prepared by deposition–precipitation of $Au(OH)_3$ which allowed working at 100 °C with initial conversion over 2% and 95% selectivity to PO. However, the catalytic activity decreased with time: water formed during the reaction and oxidised intermediates depressed the adsorption of the reagents on the catalyst surface.[19]

By comparing the performance of Au deposited on differently structured materials, as Ti–MCM-41 and Ti–MCM-48, better results have been observed with the latter catalyst owing to the presence of a three-dimensional pore system.



Scheme 1 Epoxidation of propene in the presence of dihydrogen.

Table 1 Reaction of propene with hydrogen and oxygen over Au–, Pd–, Pt–TiO_2 catalysts

			Selectivity (%)			
Catalyst	Reaction temperature/°C	C_3H_6 Conv. (%)	PO	C_3H_8	CO_2	Acetone
1%Au–TiO_2	50	1.1	>99	—	—	—
1%Au–TiO_2	80	0.8	—	<10	>70	—
1%Pd–TiO_2	25	57.1	—	98	1	0.4
1%Pt–TiO_2	25	12.1	—	92	6	2

Nevertheless, acidic and oligomeric species accumulated on the surface thus causing catalyst deactivation. Silylation of Au/Ti–MCM-48 improved in part the catalyst life and the selectivity, decreasing H_2 consumption.[20]

Investigation of gold catalysts supported on non-porous and mesoporous titania–silica indicated the effect of preparation conditions and pre-treatments on their activity and stability. In fact, Au catalysts deposited on Ti-doped non-porous silica dried under vacuum at room temperature and calcined at 300 °C in air exhibited catalytic activity to give PO even at 50 °C. Pretreatment in argon appreciably increased the catalytic activity and H_2 efficiency over the Au catalysts deposited on Ti-doped non-porous silica, while the opposite occurred in the case of Au/Ti–MCM catalysts. The deactivation rate of Au catalysts supported on a variety of titania–silica supports with different porosities suggested that the rapid deactivation of Au catalysts within hours could be attributed to the surface properties rather than to the pore structure and diffusion limitation of the supports.[21,22]

The application of gold dispersed on titanium substituted silicalite (TS-1) allowed further progress in PO productivity. A series of Au/TS-1 catalysts with different gold and titanium contents was examined at 140–200 °C at a space velocity of 7000 mL (h g_{cat})$^{-1}$. A catalyst prepared with a Si/Ti = 36 (atomic ratio) and a gold loading of 0.05 wt% produced 116 g_{PO} (h kg_{cat})$^{-1}$ at 200 °C, which was the highest rate at that time reported for a TS-1-based catalyst with no deactivation during 40 h. Catalysts prepared with lower titanium and gold contents resulted in very active catalysts, up to 350 g_{PO} (h g_{Au})$^{-1}$ at 200 °C for 0.01 wt% Au/TS-1 (Si/Ti = 500), indicative of a more efficient use of gold and titanium for the epoxidation reaction. The low gold loading coupled with non-detectable gold particles in TEM micrographs suggested that, in these materials, significant activity is attributable to gold entities smaller than 2 nm.[23] This conclusion seems to be in contrast to a previous hypothesis that gold particles smaller than 2 nm switch the selectivity from PO to propane owing to loss of metallic character.[16]

The frequently observed limit of PO yield (around 2%) over Au/TiO_2-based catalysts was ascribed to non-Langmuir adsorption noting that an increase in catalyst loading does not lead to a higher yield of propene oxide, either due to consecutive reaction over Ti···O···Ti containing units, or the existence of a PO adsorption–desorption equilibrium over active epoxidation centres.[24] It was suggested that catalyst development had to be focused on an increase in the hydrophobicity of the catalyst. Moreover, a co-feedant, like water, could be used to remove PO from the catalyst by competitive adsorption. Selective removal of PO *via* membrane technology was also suggested as a possible solution.[24]

Some of these points have been confirmed in subsequent reports.[25–27] Accordingly, water addition to the gas feed stream resulted in a positive effect. It has been assumed that water suppresses the catalyst deactivation by lowering the PO concentration adsorbed on the titania through competitive adsorption.[25]

An efficient Au capture on TS-1 support by NH_4NO_3 treatment led to a fourfold increase in the catalytic properties in Au/TS-1 catalysts. The higher gold amount produced catalysts allowing quite high conversions of propene (5–10%) with acceptable selectivities (75–85%), at 200 °C and a space velocity of 7000 ml (h g_{cat})$^{-1}$. The related productivity resulted in 134 g_{PO} (h kg_{cat})$^{-1}$.[28]

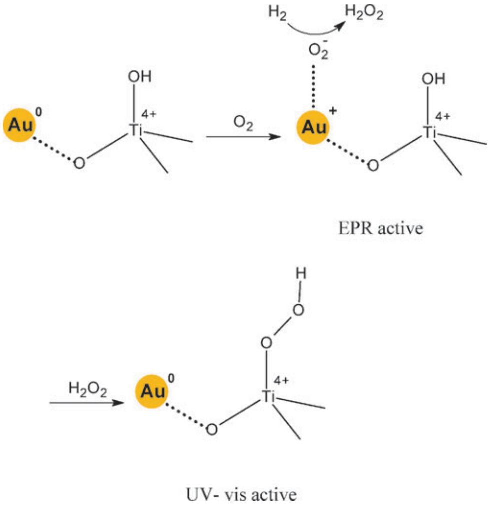
The importance of the morphology of the supporting material is highlighted by the improved performance of gold dispersed on disordered mesoporous titanosilicate having channels interconnected in a three dimensional fashion.[27] The advantage of disordered titanosilicate over the ordered counterparts, like MCM-41, has been ascribed to the improved mass transfer properties of the resulting catalyst. The new rheological properties of the support allowed the proposal of a process suitable for commercial application which has been reached by additional improvements to the catalyst: by enhancing the hydrophobicity through silylation and promoting the activity with $Ba(NO_3)_2$, it was possible to reach a space–time yield of 150 g (L h)$^{-1}$. The main drawback of this catalyst still remained the fast deactivation, due to by-products, associated with an as yet unsatisfactory efficiency in H_2 utilisation.

According to a more recent report, feeding trimethylamine in the gas stream at a level of 10–20 ppm, under conditions similar to those above reported, produced a further relevant benefit to the epoxidation process.[28] Thus, PO can be efficiently synthesised at 150 °C with a steady space–time yield of 1.4 mmol (h g_{cat})$^{-1}$ at atmospheric pressure.

Beside many investigations dealing with optimised catalytic systems for PO synthesis, identification of active sites and reaction models have been also discussed.

Since the first investigations, which supported the crucial role of gold in producing hydroperoxo species,[16] great experimental and theoretical efforts have been made to understand the mechanism of propene epoxidation by O_2 and H_2 over Au–TiO_2 derived catalysts.

Investigating the role of the catalyst, there has been found for the gold particles a more complex behaviour than the mere production of a peroxide species which subsequently epoxidises propene on the titania sites. An IR spectroscopic study has shown that the presence of gold nanoparticles catalyzes a reaction between propene and the titania sites. A bidentate propoxy species is produced, similar to that formed when



Scheme 2 EPR and UV-Vis active species on TiO_2 surface.

propene oxide is absorbed on titania. The gold particles also catalyze a consecutive oxidation of the bidentate propoxy species to form carbonate/carboxylate species, which lead to catalyst deactivation. In the presence of hydrogen and oxygen the bidentate propoxy species can desorb from the catalyst surface. Therefore it is likely that this species represents a reaction intermediate in the epoxidation of propene.[29]

A kinetic model provides a good description of the experimentally observed catalytic performance in the low-temperature range (up to 365 K), where the selectivity of the catalyst is high. The following main reaction mechanism is proposed:[30]

1. Gold nanoparticles catalyse the propene reaction with titania forming a bidentate propoxy complex.

2. O_2 and H_2 produce a hydroperoxide species on gold.

3. The peroxide species aids the desorption of the bidentate species from the catalyst producing propene oxide and water.

The key role of hydroperoxide species as an intermediate in propene epoxidation has been postulated, but recent spectroscopic studies provided proof of it. In fact, the presence of O^{2-} species on Au, more likely at a perimeter site leading to titanium hydroperoxo species, has been detected by UV-Vis and EPR techniques. Therefore, these results give real support to the mechanism of hydroperoxo-species formation *via* H_2O_2 produced from H_2 and O_2 adsorbed on the Au surface (Scheme 2).[31]

Although propene epoxidation has been the subject of the main interest in alkene oxidation, new methods for the liquid phase oxidation of higher olefins by molecular oxygen are also of great interest. Gold catalysis shows attractive possibilities in this field according to recent reports which will be discussed in section 2.3.

2.2 Oxidation of ethene to vinyl acetate (VA)

Owing to the efficiency of silver catalysts,[15] no application of gold catalysis seems to be of interest in the ethene oxide process, while an important target in the selective oxidation of ethene is represented by the acetoxylation to vinyl acetate (VAM) (Scheme 3), the latter being the monomeric unit for the synthesis of poly(vinyl acetate) (PVAc).

$$CH_2{=}CH_2 + CH_3COOH + 0.5\ O_2 \longrightarrow CH_3COOCHCH_2 + H_2O$$

Scheme 3 Ethene acetoxylation.

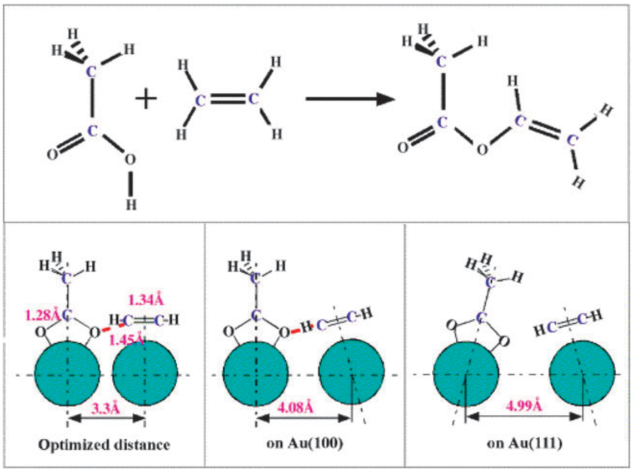
A member of the vinyl ester family, PVAc emulsion adhesives first gained market share by replacing hide glues in the 1940s and today are the most widely used adhesives on the market. Pd–Au bimetallic silica-supported catalyst, promoted by potassium acetate, is a well-known system commercially applied for the production of VAM.[32–44] Some recent studies have focused on the deactivation of the catalyst,[44] while others deal with the effects of aging under industrial conditions[37] and carbide formation,[38] often emphasising the positive role of gold in improving the catalytic performance. Goodman and co-workers[39,45] provided a major insight into the mechanism of the promotional effect of gold in a Pd–Au alloy catalyst. They found that the critical reaction site is made up of two non-contiguous Pd monomers and the role of Au consists in isolating single Pd sites, thus allowing the coupling of critical surface species to VAM and inhibiting by-product formation (Scheme 4, from ref. 39 and 45 with permission).

Owing to the dramatic added value of vinyl acetate monomer, this field is covered by many patents.[46–55] Researchers at the Celanese International Corporation were particularly active in this area describing in detail successful preparation methods:[46–49] the general procedure, similar to the deposition–precipitation technique, provides the active metals on the surface firstly as water-insoluble compounds which are reduced by a second step to the metallic form.

A similar process allowed the preparation of a fluidised bed vinyl acetate catalyst, which comprised the impregnation of a mixture of inert microspheroidal particles with a metal salt solution and promoters. The subsequent reduction led to a deposit of Pd and the promoters on the support surface.[50]

A shell-impregnated catalyst, Pd–Au on a silica support, was also described for the synthesis of vinyl acetate which allowed a selectivity over 90%.[51]

Degussa's invention[54] relates to the use of massive palladium–gold alloy in a coil reactor where gaseous ethane, acetic acid and oxygen are reacted in multiple reaction areas of the



Scheme 4 Coupling surface ethene and acetate species to form VAM.

free flow channel. The reactor wall was coated with palladium/gold and indirectly cooled.

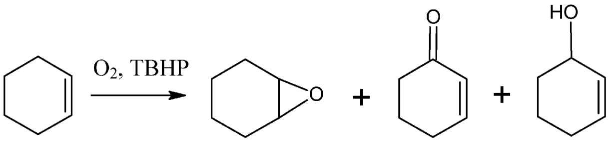
Other patent literature deals with the preparation of titania-supported bimetallic catalyst. The method takes advantage of sulfating the titanium dioxide support. Conventional palladium and gold deposition and reduction give rise to the supported palladium–gold catalyst which gave a fair increase in activity and stability in the acetoxylation reaction.[55]

2.3 Oxidation of higher alkenes

In contrast to the case of ethene and propene oxidation, supported gold catalysts have been employed in the aerobic oxidation of other alkenes working in the absence of a second reagent, H_2, as a sacrificial reductant or CH_3COOH as the acetylating reagent. Hutchings' group[56,57] and other research groups[58–63] found that alkene oxidation proceeds reasonably by adding a catalytic amount of peroxides (either hydrogen peroxide or *tert*-butyl hydroperoxide) as an oxygen chain initiator. However, selectivity and conversion are highly dependent on the substrate, catalyst and experimental conditions. The results of the oxidation of cyclohexene, styrene, stilbenes and cyclooctene are summarised in Table 2, where the performance of a 1%Au/TiO_2 reference catalyst by the World Gold Council (WGC) is also presented. WGC is an organisation which was founded by the world's leading gold mining companies with the aim of stimulating and maximising the demand for gold by consumers, investors, industry and the official sector. The WGC has recently taken the initiative in commissioning the preparation of a number of gold reference catalysts, with the main objective of enabling researchers to benchmark their own catalyst formulations against a common reference catalyst, thereby permitting more accurate comparison with other research results.

Cyclohexene oxidation (Scheme 5) gave no oxide in toluene, but 2-cyclohexen-1-one (35%) and 2-cyclohexen-1-ol (25%) were the main products at 29% conversion. Also 1,4-difluorobenzene favoured the formation of the corresponding ketone (47%) and alcohol (27%) at the same conversion, while a small amount of the oxide (9% selectivity at 16% conversion) was observed by using hexafluorobenzene as the solvent. Higher selectivity to epoxide (50%) and ketone (26%) at 30% conversion using Au/C as a catalyst was obtained in 1,2,3,5-tetramethylbenzene (TMB). Moreover, a promoting effect of bismuth on Au/C catalyst led to 98% selectivity to a valuable mixture of products.[56]

Styrene could be converted by aerobic oxidation into epoxide with a low selectivity (29%), by using either a mixture of 1,2,4,5-tetramethylbenzene (TMB)–1,4-dimethylbenzene (DMB) or hexafluorobenzene as a solvent and 1% Au/C as a catalyst. However, the major oxidation product was benzaldehyde with a selectivity around 46% for both solvents, while acetophenone was achieved with a selectivity of 15% with 1,2,4,5-TMB–1,4-DMB and 11% with hexafluorobenzene (Scheme 6).[56]



Scheme 5 Oxidation products of cyclohexene.

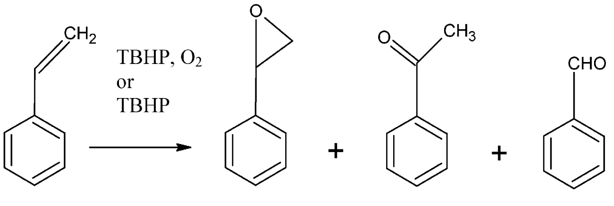
tert-Butyl hydroperoxide (TBHP) as the oxidant was tested by Ying *et al.*[58] in styrene oxidation (Scheme 6) in the presence of gold on mesoporous alumina, obtaining 70% selectivity to epoxide along with a consistent production of benzaldehyde.

Similarly, nanosized gold deposited on TiO_2 by the deposition–precipitation method was shown to be an active and selective catalyst (around 50% selectivity) for the epoxidation of styrene by TBHP.[59] The authors have extended styrene epoxidation by anhydrous *tert*-butyl hydroperoxide to a number of transition metal oxides used as supporting materials for gold (*viz.* Cr_2O_3, MnO_2, Fe_2O_3, Co_3O_4, NiO, CuO, ZnO, Y_2O_3, ZrO_2, La_2O_3 and U_3O_8), always preparing nanosized gold catalysts by homogeneous deposition–precipitation. A Au/CuO catalyst showed 40% selectivity at 55% conversion.

Furthermore, more exotic oxides as supporting materials for the same reaction were investigated, such as gallium, indium and thallium oxides, thus revealing a pretty good performance of Au/Tl_2O_3 (around 60% selectivity).[60]

Styrene oxide, as an intermediate, was produced by a catalytic system consisting of Au/SiO_2, zinc bromide and tetrabutylammonium bromide (Bu_4NBr) during the one-pot synthesis of styrene carbonate from styrene, an organic peroxide and CO_2. Supported gold is the active component for the epoxidation of styrene, while zinc bromide and Bu_4NBr cooperatively catalyze the subsequent CO_2 cycloaddition to epoxide. The influence of various reaction parameters, such as CO_2 pressure, reaction temperature, reaction time, catalyst amount, ratio of oxidant to styrene and oxidant type, has been reported.[61]

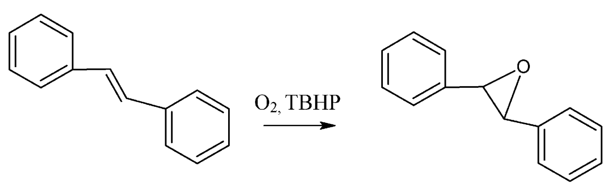
cis-Stilbene oxidation with dioxygen using a 1% Au/graphite catalyst afforded the corresponding epoxide, with the *cis* :*trans* ratio depending on the solvent but always in favour



Scheme 6 Epoxidation of styrene.

Table 2 Oxidation of cyclohexene, styrene, stilbene and cyclooctene by supported gold catalysts

Substrate	Catalyst	Solvent	Selectivity to epoxide (%)
Cyclohexene	1%Au/C	1,2,3,5-TMB	50
Styrene	2%Au/*meso*-Al_2O_3	Benzene	70
Stilbene	1%Au/TiO_2 (WGC reference catalyst)	Methylcyclohexane	88
Cyclooctene	1%Au/C	1,2,3,5-TMB	94



Scheme 7 Oxidation of *trans*-stilbene.

of the *trans* conformation: 74% selectivity to *trans*-stilbene epoxide at 48% conversion was found using isopropylbenzene as solvent.[56]

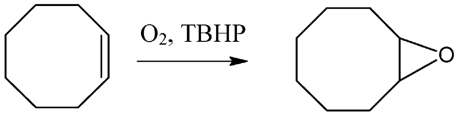
A free-radical mechanism has been outlined by Caps *et al.*[62,63] in the gold catalyzed epoxidation of *trans*-stilbene in methylcyclohexane (Scheme 7): the Au/TiO_2 reference catalyst from the World Gold Council (Table 2), in the presence of a small amount of TBHP, resulted in higher selectivity (88%) than Au/C with H_2O_2 instead of TBHP as the oxidant.

The oxidation of *cis*-cyclooctene (Scheme 8) was investigated by Hutchings *et al.* using 1% Au/C catalysts both in the presence and absence of solvents.[56] It was demonstrated that high selectivities to epoxide could be achieved even with a cyclooctene : TBHP molar ratio of 300. The best result was obtained with 1,2,3,5-TMB as a solvent, leading to 94% selectivity to the epoxide at 28% conversion while in the absence of solvent 81% epoxide at 8% conversion was obtained.

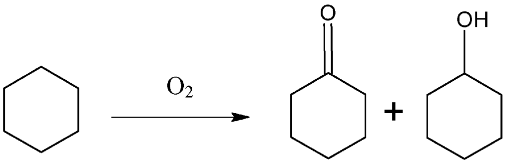
According to Bond and Moreau,[64] the oxidative dehydrogenation of 1-butene leads to 1,3-butadiene along with 2-butene isomers over supported gold catalysts. By using Au/SiO_2 diluted with silicon carbide as a temperature controller, it was shown that conversion and selectivity increased, passing from 10% (at 60% conversion) to 50% (at 80% conversion) as the proportion of silicon carbide in the bed was raised. The importance of blank tests in considering kinetic data has to be underlined, considering that silicon carbide alone gave conversion of 30% and selectivity higher than 90% at about 350 °C, without formation of CO_2.

2.4 Oxidation of alkanes

2.4.1 Cyclohexane. Gold-based catalysts have also shown interesting performance for the activation of C–H bond in alkane selective oxidation with dioxygen. A particular focus has been put on the synthesis of cyclohexanone and cyclohexanol (Scheme 9), because it is a matter of growing interest to the chemical industry. These oxidation products, in fact, are fundamental intermediates for making ε-caprolactam and adipic acid, thus leading to nylon-6 and nylon-6,6 manufacture beside less important applications as stabilisers, homogenisers for soaps and synthetic detergent emulsions, and as solvents for lacquers and varnishes. Cyclohexanone, in particular, is also a starting material in the synthesis of insecticides, herbicides and pharmaceuticals. Zhao and co-workers[65] first applied gold catalysis in the activation of cyclohexane: Au/ZSM-5 and Au/MCM-41 favoured a selectivity around 90% and conversions of 10–15% at 150 °C, even though a loss in both activity and selectivity after their reuse is a drawback for industrial application. A number of efforts have been made to achieve a satisfactory direct oxidation of cyclohexane:[56,65–70] Au/graphite without any solvent, but using a halogenated benzene as an additive, led to 92% selectivity (cyclohexanone + cyclohexanol) at low conversion (1%).[56] Higher conversions (20–30%) and selectivity (95%) were achieved by Zhu *et al.*[67] with gold on mesoporous silica catalysts, a clearly better result compared to the current industrial process leading to 70–85% selectivity at 4% conversion and based on the use of cobalt salt or metal-basic acid as catalysts.



Scheme 8 Oxidation of *cis*-cyclooctene.



Scheme 9 Oxidation of cyclohexane.

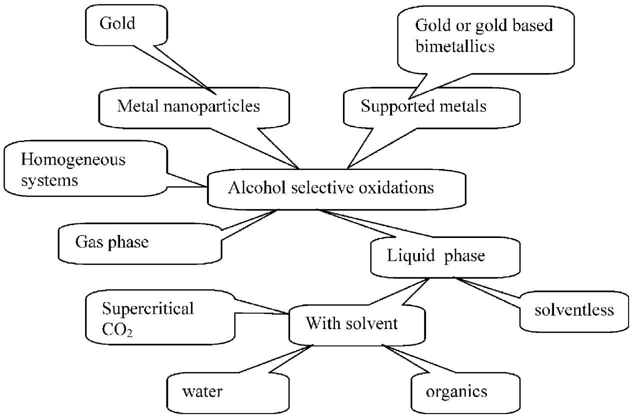
Two recent studies on the selective cyclohexane oxidation were performed by tailoring a supported gold on different materials, namely amorphous silica doped with titania[68] and alumina prepared by a modified direct anionic exchange method.[69] At 150 °C, a selectivity of 92% for cyclohexanone and cyclohexanol could be reached over the gold on doped silica catalyst, affording a cyclohexane conversion of 8% and a turnover frequency (TOF) up to 40 h^{-1}. Moreover, the catalytic activity and selectivity could be well retained in four recycling reactions, showing a high stability of the gold catalyst supported on titania-doped silica.[68] Also Au/Al_2O_3 evidenced high performance in terms of turnover frequency using molecular oxygen in solvent-free conditions and showed a size-dependent effect of gold. In this work, a conversion of 11% with a TOF of 4500 h^{-1} was obtained over Au/Al_2O_3 (0.6% Au). Furthermore, a higher TOF up to 16 000 h^{-1} was attained over Au/Al_2O_3 (0.2% Au), showing that as the gold loadings increased, both the conversion of cyclohexane and the total selectivity to the products decreased, together with a sharp loss of activity. These effects were most likely caused by a decrease in highly active gold particles, since the particles were bigger according to the TEM analysis.[69]

2.4.2 Oxidation of other alkanes. Although of great interest for petrochemical and natural gas conversion, the selective oxidation of other alkanes has been scarcely investigated.

Methane could be converted into C_2 hydrocarbons with Au/La_2O_3–CaO catalyst at high temperature (700 °C), whereas the presence of trace amounts of H_2O_2 favoured the formation of benzene.[70] In this reaction, Hutchings *et al.*[71] found that gold inhibited the activity of magnesia. Related to this topic, it is worth noting that Periana and co-workers[72] reported a way of converting methane to methanol using homogeneous cationic gold in strong acid solvents with Se(VI) as the stoichiometric oxidant. At 180 °C the authors obtained over 90% selectivity.

A similar investigation using heterogeneous gold has not yet been reported.

The patent literature deals with the oxidation of C_2 hydrocarbons (ethane, ethene or mixtures thereof) to acetic acid at elevated temperatures by gold-based catalysis.[73] A space–time yield of over 470 kg (h $m^3)^{-1}$ was reported. Herron *et al.*[74] recently patented a gold on titania catalytic system for the selective oxidation of alkanes. In particular, they were able to oxidise xylene to the corresponding mono- or di-alcohol. It is worth noting that in 1973 Mobil claimed the synthesis of styrene by oxidative dehydrogenation of ethylbenzene at 700 °C with Au/TiO_2.[75] It can be pointed out that this performance (94% selectivity at 53% conversion) is not far from the industrial technology (>90% selectivity at 60–65% conversion).[15]



Scheme 10

3. Selective oxidation of alcohols and polyols

Alcohols and polyols provide a series of practical starting materials for producing a variety of chemicals as they can be obtained from natural and renewable sources in large amounts. In particular selective oxidation can transform alcohols and polyols into the corresponding carbonylic or carboxylic derivatives which both generally represent attractive chemicals for organic synthesis.

Selective oxidation of alcohols performed using oxygen in the presence of a catalytic system represents one of the most challenging reactions as it can be considered really attractive for its low environmental impact especially if compared to stoichiometric oxidation. Actually there is a concurrence in competing properties among ruthenium, platinum, palladium and gold catalysts, gold based catalysts being among the most promising.

However, as outlined in section 6, industrial applications using gold are still rather poor but significant, such as the proposed synthesis of methyl glycolate from ethylene glycol, methanol and oxygen.[7,76]

The recent literature, however, reports a growing amount of fundamental research dealing with alcohol and polyol selective oxidation.[2,77–79]

In the wide area of aerobic oxidation of alcohols we will focus our attention on gold based methodologies to derive general rules, if possible, on how the choice of different parameters could influence the selectivity of a given substrate (Scheme 10).

Unfortunately, the methodologies reported in Scheme 10 are not the only parameters to be taken into account and, as usual, it becomes difficult to compare the literature data directly. Different gold catalyst preparations produced different materials, whereas pressure, temperature and catalyst to substrate ratio influenced yields and productivity. Thus often no definite conclusions can be derived.

Thermally stable alcohols can be oxidised in the gas phase over gold-based catalysts to aldehydes. Au on SiO_2 appeared active and selective when used in C_3–C_5 linear alcohol oxidation highlighting however that activity cannot be trivially correlated to the number of carbons (and boiling point). Reactions were performed over a range of temperatures between 250 and 300 °C and activity followed the order $C_4 > C_5 > C_3$. Secondary alcohols were oxidised under milder conditions (100–150 °C) to the corresponding ketones.[13] Similar conditions (200 °C) have been employed in the ethanol oxidation where ethyl acetate and acetic acid represented the main by-products.[80] Interestingly, it has been also shown that 6 nm sized gold nanoparticles (AuNPs) were more active (45% conversion) than smaller (3.5 nm) and larger (8.2 nm) (24% and 22% conversion, respectively) ones. By decreasing the temperature from 200 °C to 100 °C a conversion of 39% and an interesting selectivity to ethyl acetate (90%) was observed. The authors attributed this high activity to the small particle size and the thermal stability of AuNPs generated by preformed thiol-stabilised NP anchored on the support. The thermal treatment for removing the ligands creates a strong metal–support interaction.

Under condensed conditions (liquid phase, batch reactions) other approaches to the selective oxidation of alcohols have been investigated.

Beside a rare example of homogeneous catalytic gold made up by AuCl and an anionic ligand, reported for the aerobic oxidation of benzyl alcohol to benzaldehyde at 90 °C in toluene,[81] the most popular systems are related to heterogeneous systems. Unsupported AuNPs represent the borderline between homogeneous and heterogeneous systems. AuNPs have attracted attention since ancient days for their beautiful colour but only recently has increasing interest been shown for different applications, in particular catalytic ones.[82] Since the initial report on the activity of AuNPs in the oxidation of glucose,[83] the following studies focused on improving the stability of metallic sols under the reaction conditions. Thus, an aqueous dispersion of PVP (polyvinylpyrrolidone) stabilised AuNPs has been reported to be active over a long time in benzylic alcohol oxidation under basic conditions at ambient temperature producing benzoic acid in almost quantitative yield.[84] The reaction appeared very sensitive to particle dimensions and to substituents on the aromatic ring, a *ortho* or *para* OH group decreasing the catalyst activity but enhancing the selectivity to aldehyde even under basic conditions. A comparison with similarly sized PdNPs revealed better activity and a more marked influence of particle size in the case of gold with respect to palladium. From these observations, combined with kinetic measurements, the authors suggested that in the oxidation reaction catalysed by Pd or Au two different mechanisms operated. The most relevant difference is that in the case of

PdNPs the rate determining step is represented by the transfer of H atoms on the β-carbon of the adsorbed alkoxide to form the aldehyde and a Pd-hydride species, whereas with AuNPs the rate determining step involves the H-atom abstraction by a superoxo-like oxygen species adsorbed on Au. These superoxo species, evolving to hydrogen peroxide, were also invoked in kinetic studies of glucose oxidation[85] and in the homo-coupling of arylboronic acid catalysed by AuNPs.[86] Moreover, similar findings have been suggested in benzylic alcohol oxidation catalysed by Au on TiO_2.[87]

PVA-protected AuNPs were reported to be useful catalysts for diol conversion to the corresponding hydroxy acid using membrane filtration for catalyst recovery.[88] The choice of the membrane depends on the solvent employed. By passing from water to alcohols (*t*-BuOH, 2-propanol, methanol) as the solvent a decreasing activity (TOF) has been observed. However it should be emphasised that the use of organics as solvents also enables the oxidation of long chain diols scarcely soluble in water.[89] No conversion was observed in the absence of base along with a negligible effect on changing the alcohol solvent or on ageing the sol. A decrease in TOF was observed by increasing the amount of protective agent. It should be noted that in this case a decrease in particle dimensions is also expected.

Recent developments in supramolecular design led to 4 nm Au particles encapsulated in thermosensitive vinyl ether star polymer which were used in the oxidation of benzylic alcohol at ambient temperature in the presence of aqueous KOH affording quantitatively benzoic acid.[90] The recovery of the catalytic system was fruitfully performed by using the decrease in solubility (clouding point) of the polymer on increasing the temperature (60 °C). On recycling, the activity was maintained at least until the sixth run.

An alternative approach consisted in confining the gold nanoparticles in a polymer.[91] Thus, stable microencapsulated AuNPs were obtained and used in the oxidation of primary and secondary alcohols to carbonylic compounds in dichloromethane or toluene or benzotrifluoride–water–K_2CO_3 solvent mixtures. Reactions proceeded smoothly at ambient temperature even at quite low gold/reactant ratio and, interestingly, in some cases a high selectivity to aldehyde is reported despite the basic conditions employed. The thermal stability of the catalyst was proved under solventless conditions where the authors reported a very high TOF ($2.0 \times 10^4\ h^{-1}$) in 1-phenylethanol oxidation. However some doubts might be raised by the use of a very high temperature (160 °C) for which a blank experiment should be reported. Under such conditions the reaction proceeded even in the absence of alkali. Recovery of the catalyst is claimed to be simple and activity was stable over the reaction time under mild conditions.

Despite the interest in colloidal or colloid-like systems, supported gold nanoparticles represent the most investigated catalyst employed in alcohol oxidation as they are easy to handle even though they are subject to ageing phenomena.

A direct comparison between similarly sized supported and unsupported AuNPs was recently performed by using microgel-stabilised nanoparticles and Au on carbon.[92] The unsupported gold particles were grown inside a polymer structure that provided both size control and stabilisation of the NPs under the reaction conditions. The advantage of using this preparation was observed in an enhanced activity with respect to AuNPs supported on carbon in the oxidation of aliphatic alcohols (*n*-butanol, *n*-octanol). On the contrary carbon-supported catalysts appeared more active when polyhydroxylated compounds were used as substrates highlighting the importance of the relative affinity of the substrate and the support for aqueous media.

Methanol as the substrate appeared rather inert to aerobic oxidation thus allowing it to be used as solvent/reactant. This finding led in 2004 to the development by Nippon Shokubai Co. Ltd of a pilot plant for the production of methyl glycolate.[7,76] At 90 °C, Au supported on Al_2O_3 was more active and selective with respect to Pd and Ru similarly supported, showing 83% selectivity to methyl glycolate at 63% conversion. Methyl formate deriving from methanol oxidation was present only in very low amounts (Scheme 11). Au on TiO_2 or ZrO_2 similarly were used to produced *n*-propyl propionate and *n*-butyl butanoate, respectively, with a selectivity of 81 and 79% at comparable conversion.

At higher temperature (130 °C) Au/TiO_2 was used to synthesised the corresponding methyl esters from *n*-hexanol, benzyl and cinnamyl alcohols. However, methanol under such conditions was partly oxidised to formic acid, methyl formate and CO_2.[93] The selectivity of the reaction was not affected by the presence of additives but the presence of a base ($NaOCH_3$) increased the reaction rate. On the contrary, selectivity was improved by increasing the excess of methanol. This trend is most likely caused by the favoured formation of the methyl hemiacetal compared to the hexyl hemiacetal. According to the reaction pathway suggested for 3-phenyl-1-propanol oxidation by Corma and co-workers,[94] in the absence of water a hemi-acetal intermediate is formed that can be further oxidised leading to the corresponding ester in a similar way as the aldehyde hydrate is oxidised to the carboxylic acid (Scheme 12).[4,95]

Ester formation was fruitfully used for lactone synthesis. Thus, in *tert*-butyl phosphate as the solvent, 1,4-butanediol formed γ-butyrolactone quantitatively at moderate

$$HOCH_2CH_2OH + MeOH + O_2 \rightarrow HOCH_2COOMe + 2\ H_2O \quad \text{[methylglycolate]}$$

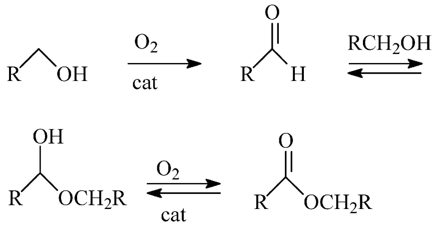
$$2\ MeOH + O_2 \rightarrow HCOOMe + 2\ H_2O \quad \text{[methylformate]}$$

$$2\ HOCH_2CH_2OH + O_2 \rightarrow HOCH_2COOCH_2CH_2OH + 2\ H_2O \quad \text{[2-hydroxyethylglycolate]}$$

$$HOCH_2CH_2OH + MeOH + O_2 \rightarrow HCOOCH_2CH_2OH + 2\ H_2O \quad \text{[2-hydroxyethylformate]}$$

$$HOCH_2COOMe + H_2O \rightarrow HOCH_2COOH + MeOH \quad \text{[glycolic acid]}$$

Scheme 11 Possible products in Nippon Shokubai's MGC process.



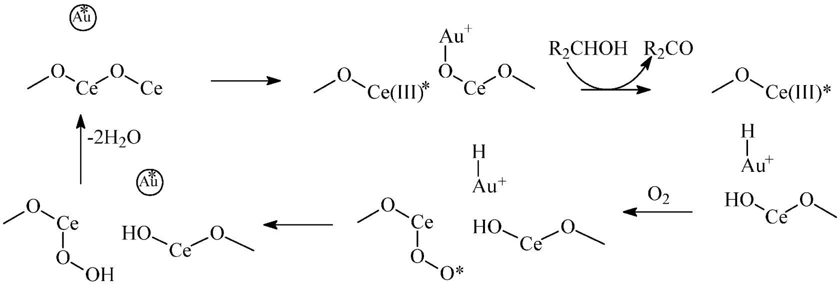
Scheme 12 Route for ester formation in the oxidation of primary alcohols.

temperature (120–140 °C) and oxygen pressure (1.25 MPa of air) with Au/TiO_2 as the catalyst.[96] The reaction rate appeared to increase with the Au(0) content as derived by XPS technique: following the ratio Au(III)/Au(0) present in the catalyst, no reaction was observed below 50% Au(0).

Under solventless conditions a variety of supported gold catalysts (SiO_2, Fe_2O_3, CeO_2, TiO_2) tested at 100 °C and 2 atm of O_2 evidenced quite a low activity in aliphatic and aromatic alcohol oxidation[97] but a very high selectivity to the corresponding aldehyde. It was evident that a complex reaction pathway is present when polyfunctionalised alcohols were employed. For example geraniol has been shown to produce geranial plus products derived from isomerisation and skeletal rearrangements. At higher temperature (130 °C) gold on basic supports and others with redox properties showed better activities and surprisingly always high selectivity in benzylic alcohol oxidation highlighting a scale of catalyst activity in the order $ZrO_2 > MnO_2 > Sm_2O_3 > Al_2O_3 > BaO > CaO > U_3O_8 > MgO > ZnO > La_2O_3 > Eu_2O_3 > NiO > CoO > CuO > Fe_2O$. However, the gold catalysts prepared in similar ways showed different metal particle distribution, therefore making a real comparison among the different supports difficult.[98] An increasing conversion of benzylic alcohol with reaction temperature (up to 160 °C) was also observed for Au/TiO_2 at the expense of selectivity. Interestingly, it has been shown for the first time that Au on activated carbon can also be active in such an oxidation even if less selective than Au on TiO_2.[99]

A peculiar catalyst has been developed by supporting Au on nanosized CeO_2.[100] This catalyst turned out to be not only highly selective toward the oxidation of alcohols to carbonylic derivatives but also very active in operating, without any solvent, at 80 °C and atmospheric pressure. Benzylic and cinnamyl alcohols were smoothly oxidised to aldehydes whereas secondary alcohols were transformed to ketones. Primary alcohols such as 3-phenyl-1-propanol however produced 3-phenylpropyl-3-phenylpropanoate in 83% selectivity at 73% conversion. The intermediate aldehyde can be trapped as acetal using orthoformate $HC(OCH_3)_3$ and in its absence the hemiacetal $RCH(OH)OCH_2R$ was shown to be a transient species by means of ^{1}H-NMR. The final product was the ester. The proposed reaction mechanism of this catalyst involves an active role of oxygen vacancies on ceria with consequent creation of positively charged gold. Lewis acid sites produce the metal-alkoxide by reaction with the alcohol, which rapidly undergoes hydride transfer to Ce^{3+} and Au^+. Au–H was observed by IR spectroscopy. Dioxygen forms a cerium-coordinated superoxide species that is transformed into hydroperoxide by hydrogen abstraction from Au–H. This is the crucial step that represents the unique role of gold that, in this case, could be considered as a modifier that transforms nanosized CeO_2 from a stoichiometric oxidant to a catalytic material (Scheme 13). It is noteworthy that non-nanometre-sized cerium oxide did not show such interesting behaviour.

For many practical applications in organic synthesis, gold catalysis applied to alcohol oxidation is slow, the TOF values often being in the range of dozens or hundreds h^{-1}. To overcome the intrinsic low activity of gold, the contribute of a second metal was studied, in particular palladium. Thus, Au–Pd on TiO_2 was reported to show an extraordinary enhancement compared to monometallic gold.[101] Benzylic alcohol under solventless conditions could be oxidised to aldehyde five times faster in the presence of Au–Pd/TiO_2 than of Au/TiO_2 at 100 °C and 2 atm of O_2 with selectivity to aldehyde over 90% at 75% conversion. The reaction appeared to be zeroth order in O_2 and the selectivity increased by increasing pO_2. It was shown that air could replace pure oxygen even though a slight decrease in selectivity was observed. A better activity of Au–Pd/TiO_2 with respect to Pd on hydroxyapatite[102] and Au on nano-CeO_2[100] was revealed. Under similar conditions for 1-phenylethanol oxidation a TOF of 269 000 h^{-1} was reported for Au–Pd/TiO_2 whereas the TOFs for Pd/HAP and Au/CeO_2 were 9800 h^{-1} and 12 500 h^{-1}, respectively. On the contrary, these two latter catalysts appeared more active in the oxidation of secondary alcohols. In particular, octan-2-ol in the presence of Au–Pd/TiO_2 was inactive even at high temperature whereas diols were more reactive than simple alcohols (*i.e.* butane-1,4-diol more active than *n*-butanol). STEM and XPS characterisation of Au–Pd/TiO_2 prepared by impregnation followed by calcination at 400 °C revealed a Pd-rich shell and Au-rich core which appeared to be stable under the reaction conditions. Other supports such as Al_2O_3 or Fe_2O_3 did not produce catalysts as



Scheme 13 Proposed simplified mechanism for alcohol oxidation in the presence of Au on nano-CeO_2.

active and selective as Au–Pd/TiO_2. A variety of alcohols were selectively oxidised in the absence of solvent; however, when toluene, or water, was used as the solvent a general decrease in activity of the catalyst could be observed.

The oxidation of benzyl alcohol under forced reaction conditions (160 °C and 10 atm), in order to highlight the effect of Au/Pd ratio on product distribution, revealed that the most active catalyst is the one with 2.5%wt loading of Au and 2.5%wt loading of Pd whereas monometallic Au/TiO_2 appeared the most selective to aldehyde.[103] However, under these conditions toluene instead of benzyl benzoate was shown to be the main by-product.

The Au–Pd system has also been compared to the gold monometallic catalyst supported on nanosized CeO_2.[104] In contrast to the Au–Pd system on TiO_2, when nanoceria was employed as the support in allylic alcohols oxidation, Au monometallic system was more active and selective than Au–Pd when tested at 120 °C and atmospheric pressure. In particular Pd on nano-CeO_2 was found to be less selective, producing higher amounts of isomerised product. The higher selectivity of Au on CeO_2 was ascribed to the presence of gold and correlated to the stability and concentration of metal-hydrides that, in the case of Pd, are not sufficiently rapidly oxidised thus promoting C–C bond isomerisation and reduction. The role of nano-CeO_2 is to enhance the activity.

In addition, zeolites (ZMS-5, zeolite β, zeolite Y) were used as a support for Au and Au–Pd[105] and compared with TS-1 and TiO_2 in benzyl alcohol oxidation at 100 °C and 2 atm of O_2 without any solvent. Au on zeolite β was shown to be more active than Au on TiO_2 but acidic zeolite produced larger amounts of benzyl benzoate, dibenzyl acetal and dibenzyl ether (except for ZMS-5). The addition of Pd slightly improved the activity without significantly affecting the selectivity.

Although solventless conditions could represent a "green" process, some limitations can occur, principally determined by the physical state of the substrate and its thermal stability. Thus an increasing interest in using proper solvent was raised especially in comparing solventless conditions with reactions carried out in conventional solvent able to solubilise complex organic substrates.

AuNPs confined in mesoporous silica have been used to compare benzyl alcohol oxidation under solventless condition (130 °C and 1.5 atm) and in toluene (80 °C and flowing O_2 at 1 atm).[106] Although different temperature and pressure conditions have been used and a base (K_2CO_3) was added to toluene, the catalyst was shown to be similarly active in the two sets of conditions (TOF 377 h^{-1} *versus* 364 h^{-1}). Probably owing to its insolubility in toluene, the presence of the base did not affect the selectivity to benzaldehyde very much. Only a drop from 98% to 79% selectivity to benzaldehyde was detected. Analogous results were obtained in the oxidation of cyclohexenol which however was less reactive (TOF 116 h^{-1}).

In contrast, a strong effect of catalytic amount of base was clearly evidenced under solventless conditions: at moderate temperature (80 °C) Au on TiO_2 showed a TOF of only 19 h^{-1} in benzyl alcohol oxidation without any promoter whereas addition of K_2CO_3 (0.2% with respect to alcohol) raised the TOF value to 7851 h^{-1}.[107] Also sodium carbonate and acetate improved the oxidation whereas stronger bases did not have the same prominent effect. In the presence of a base the nature of the support appeared less important in terms of activity even if strong differences could be detected in selectivity. Secondary alcohols as well as primary alcohols were oxidised. In this latter case the ester represented the main product.

Au supported on U_2O_3 has been shown to be an efficient catalyst for benzyl alcohol oxidation even though the obtained particle are large (mean size of 10–35 nm depending on preparation method).[108] In this case it was clearly shown that the addition of solvents such as toluene, *p*-xylene, DMF and DMSO produced a decrease in activity and also selectivity. The competitive adsorption of solvent and alcohol on the active site of the catalyst is believed to be responsible for this effect.

Using mesitylene as the solvent at 90 °C gold supported on nanosized mixed oxide $CuMg_xAl_yO_z$ was almost totally selective ($\geq 98\%$) in oxidising a large number of primary and secondary alcohols to carbonylic derivatives.[109] TOFs were not particularly high (20–1300 h^{-1}) especially with aliphatic primary alcohols (< 100 h^{-1}). The activity of the catalysts strongly depended on the composition of the support, the ratio Cu : Mg : Al = 5 : 1 : 2 being the composition that induced the highest activity. Both reduced and oxidised Au species were spectroscopically revealed on fresh and used catalysts thus preventing conclusions on the nature of the active species.

An almost total selectivity to aldehyde was also observed when benzyl alcohol was oxidised in supercritical CO_2.[110] Preformed AuNPs supported on TiO_2 at 100 °C showed a similar activity to that in solventless conditions. 1-Octanol and geraniol could also be selectively oxidised.

Considering the influence of various parameters in the aerobic oxidation of alcohols by gold based catalysts, it can be concluded that a prominent role in the activity and selectivity is played by the solvent. Water should represent the ideal medium from a general point of view: it is safe, environmentally friendly, cheap and easy to handle. The limit in applying water is, of course, the solubility of the substrate which could restrict the intimate contact between substrate and the catalytic system depending on the hydrophobic/hydrophilic properties of both. Of course, water is the solvent of choice for polyhydroxylated substrates.

In the case of water-insoluble compounds the solventless oxidation process, when applicable, is quite useful in terms of catalytic performance.

While classical oxidation catalysts based for example on Pd or Pt when used in the presence of O_2 in aqueous phase suffer from deactivation, Au appeared to be more resistant.[12] This aspect, related to the high degree of chemoselectivity of gold, makes this metal a good candidate for an efficient and selective catalyst to be employed in aqueous phase oxidation. Although hydrophilic materials should be preferred for supporting the metal when water is the solvent, only a few papers deal with applications of Au supported on oxides, activated carbon and graphite being the most investigated supports. An important exception deals with the oxidation of aqueous (bio)ethanol into acetic acid catalyzed by gold supported on $MgAl_2O_4$.[111] Under 3.5 atm of air at 150–180 °C, acetic acid has been obtained in 92% yield with only CO_2 as a detectable by-product. It is to be noted that such extreme conditions do not always appear to be compatible with either the substrate or the catalytic system. Under these forcing conditions, ethanol oxidation with gold on spinel represents the first example of a gold catalyzed oxidation proceeding in the absence of a base. In fact, when water is present as the solvent, basic conditions are generally required whereas aldehydes can be smoothly oxidised under neutral conditions.[95] The role of the base is still matter of study but it reasonably appears to be involved in the first step of the oxidative process, *i.e.* the creation of alkoxide anion. In that respect, the fundamental role of the basic strength of the alcoholic group has been demonstrated.[112] Moreover kinetic studies on glycerol oxidation revealed that adsorption of reaction products on the catalytic surface is relevant[113] and the presence of a base could be important in removing the products from the active surface, thus prolonging the catalyst life.

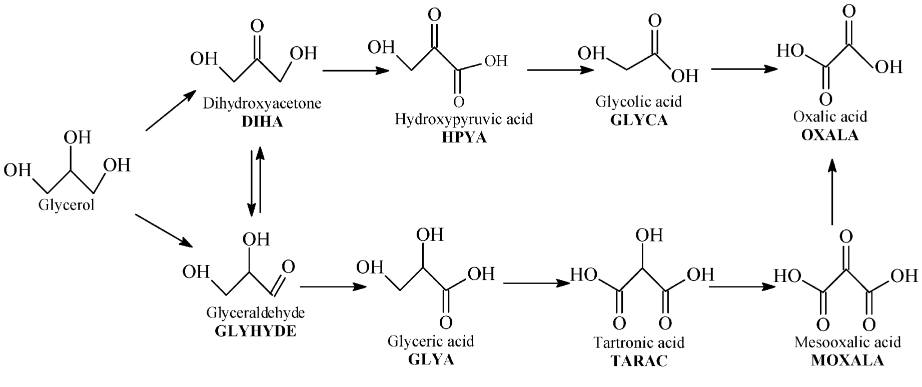
Typical conditions for aqueous phase oxidation are really mild with temperatures in the range 30–60 °C and oxygen pressure from atmospheric to a few atmospheres (3–10 atm). A basic environment can be provided by a continuous addition of alkali (pH controlled conditions) or, alternatively, excess of base (carbonate, hydroxide) can be added at the beginning of the reaction. Under such conditions, the oxidation of alcohols to carboxylate is expected as the intermediate aldehyde is normally more readily oxidised than the corresponding alcohol.[11] However some examples indicate that even under basic conditions the aldehyde could be isolated in high yield. This is the case of *o*-hydroxybenzyl oxidation in the presence of Au/Fe_2O_3 carried out at 50 °C, atmospheric pressure and Na_2CO_3.[114] The *o*-hydroxybenzyl aldehyde (salicylaldehyde) is difficult to oxidise and could be isolated in over 90% selectivity at complete conversion with only a small amount of acid. The acid is not formed at all if the reaction is carried out in benzene as the solvent but, in this case, the reaction rate is much slower. A similar selectivity was obtained with Au supported on ZnO, CaO and Al_2O_3.[115] Moreover, other factors can contribute to afford the resultant selectivity. It has been noted that *n*-butanal can be smoothly oxidised to the corresponding acid in the presence of gold nanoclusters located inside nanoporous domains of gel-type resins; but when *n*-butanol is oxidised, *n*-butanal (70% selectivity at 40% conversion) could be isolated.[116] Thus, the nature of the supporting material, the nature and the amount of the base employed were important factors as well as the substrate in determining the selectivity.

Activated carbon and graphite represent the most commonly used supports for aqueous phase oxidation by gold and this is due to the performance (up to now Au/C represents the most active catalyst) in water under mild conditions[117,118] and to the economical convenience: both are cheap materials which allow the easy recovery of the precious metal by burning off the support. Recently a short report on Au/C applications in alcohol oxidation has been published.[119]

It has been noted that marked differences in the same reaction can be induced by different types of carbons as well as of catalyst preparation method. It appeared that the most relevant parameter for the choice of a good supporting material is the type and the distribution of surface groups. Good metal dispersion and small particle size can be obtained by using preformed gold sol immobilisation.[120] The advantage of this methodology is that it may be possible to some extent to tune the particle size and the surface exposure of gold nanoparticles. Under similar conditions and using the same Au/C, polyols have been more easily oxidised than linear, aliphatic alcohols (*n*-propanol and *n*-butanol). Notably Pd and Pt similarly prepared were less active than Au/C in such oxidation reactions.

One of the most studied applications of Au supported on carbon in alcohol oxidation is the transformation of glycerol into valuable products.[121] Glyceric acid and dihydroxyacetone as well as more oxidised products like ketomalonic acid are interesting products for exploitation (Scheme 14).

The reaction, catalyzed by Au/C, proceeded under mild conditions (30–60 °C, 1–3 atm), in the presence of a base producing glycerate with excellent selectivity close to 100%.[122] Recently, kinetic studies revealed that the need for basic conditions could be related to the very low acidity of glycerol (pK_a = 14.5), the rate being dependent on glycerolate concentration, whereas the amount of by-products formed from C–C bond cleavage derived from oxidation by H_2O_2 produced as a side reaction.[123] These results confirmed the findings that by increasing the amount of NaOH the reaction was accelerated while no large variation in selectivity to glycerate was observed by increasing NaOH from 1 to 4 equivalents, the interconversion reaction being always present under basic conditions.[124] The structure sensitivity of this reaction has



Scheme 14 Reaction pathway for glycerol oxidation under basic conditions.

been outlined in many papers and catalyst design has been found to be important in determining activity and selectivity. Detailed studies have been devoted to the size effect of gold nanoparticles[124–127] and the influence in using different carbon supports.[124,128] Increasing Au particle size resulted in less active but more selective catalysts towards glycerate. Conversely, AuNPs deposited on active carbon at atomic level by magnetron sputtering represented the most active catalyst in glycerol oxidation but the worst with respect to the selectivity.[129] However, it has been demonstrated that gold particles larger than 50 nm were inactive: a compromise between catalytic activity and selectivity indicates that there may be an optimum particle size for the desired catalyst (about 20 nm).[130] Moreover, cyclic voltammetry studies highlighted the importance in active catalysts of oxide species not detected using an inactive catalyst.

Unlike oxide supports, the methods commonly used for the preparation of gold on carbon do not need high temperature treatments. Note also that in principle oxide supported catalysts could be prepared using a chemical reduction preventing particle aggregation and providing more active catalysts.[117] However, sometimes thermal treatment has been used to improve the support–metal interaction thus improving the stability of the catalyst. Thermal treatment assumes a particular importance when a second metal (typically Pd or Pt) has to be added. In fact from a thermodynamic point of view on thermal treatment an enrichment in one of the metals on the particle surface is expected depending on the melting point, thus providing a tool for generating core–shell structures.[101] Of particular interest is the characterisation normally carried out by means of spectroscopic techniques (XRPD, HRTEM, STEM, EDX, HAADF) for determining phase, composition and metal dispersion.

When bimetallic systems were tested in the aerobic oxidation of alcohols in aqueous media it has been highlighted that the synergistic effects between gold and another metal are not always positive.

Pd and Pt were added to gold on carbon following different procedures all based on the preformed sol immobilisation technique and the resulting catalysts were tested in the aqueous phase oxidation of D-sorbitol[131,132] and glycerol.[133,134] In principle, addition of Pd or Pt metals could overcome the compulsory presence of a base as either Pd or Pt is able to oxidise alcohols under neutral or acidic conditions. However, under neutral conditions bimetallic systems were also inactive whereas under basic conditions a strong synergistic effect was observed. In the case of D-sorbitol, the Au–Pt catalyst was as active as Au–Pd but it showed a better selectivity toward oxidation of the primary alcoholic group (71% at 50% conversion) with respect to 60% for Au–Pd. It was noted that monometallic systems were also less selective. From recycling experiments it was deduced that the presence of gold improved the resistance to poisoning due to the overoxidation and chelating effect of products shown by monometallic Pt and Pd.

In glycerol oxidation a different conclusion was reached about the activity–selectivity correlation because Au–Pd systems were either more active or selective than the analogous Au–Pt system, the latter promoting C–C bond cleavage. Considering the role of the support, a strong effect was also observed comparing graphite to carbon: the first was found to be less active but more selective to glycerate.[135] A similar effect of the particle dimension as for monometallic systems was detected: on increasing the particle size an increase of selectivity towards glycerate was observed.[136]

While dihydroxyacetone represents a by-product in the gold assisted oxidation of glycerol[121] its formation could be improved in the presence of the Au–Pt system by controlling the pH and oxygen pressure: at pH 12 in flowing oxygen at atmospheric pressure dihydroxyacetone was obtained with 36% selectivity, compared with 26% selectivity resulting by using monometallic gold catalyst.[128]

XRPD characterisation of some Au–Pd systems by means of Rietveld analysis highlighted the presence of alloyed phases beside segregated Pd.[133] However it was only with the preparation of a single phase catalyst (alloy Au_6Pd_4) that a correct correlation between activity and catalyst phase could be stated.[137] In fact a Au–Pd catalyst composed only of the single alloy Au_6Pd_4 showed a TOF of 6435 h^{-1} compared with a TOF of 4823 h^{-1} shown by the same alloy in the presence of segregated Pd. The highly improved activity could be attributed to the presence of Au–Pd bifunctional sites. The selectivity to glycerate was also improved (77% at 90% conversion) with respect to comparably sized Au/C (74%). During recycling tests the Au_6Pd_4 catalyst showed an almost constant activity during ten recycles although a slight leaching of Pd and aggregation of nanoparticles was observed.[138] A subsequent study revealed that a possible explanation for this unpredictable behaviour lies in the fact that a higher activity was observed for a gold rich alloy (Au_9Pd_1).[139]

Au_6Pt_4 single alloy dispersed on carbon was prepared and showed a similar activity to Au_6Pd_4 but an expected lower selectivity to glycerate in glycerol oxidation.[140] Au_6Pd_4 and Au_6Pt_4 catalysts were compared in glycerol and *n*-octanol oxidation highlighting the role of substrate structure in the synergistic effect observed between gold and the added metal (Pd or Pt). When Pt is alloyed with Au a maximised catalytic effect with respect to monometallic catalysts resulted for polyol oxidation, whereas the Au–Pd alloy was less sensitive to the substrate being more efficient towards linear aliphatic alcohols.

In contrast to glycerol, aliphatic, allylic and aromatic alcohols are also oxidised under neutral conditions.[141] In alloyed catalysts gold ensures high resistance to oxygen poisoning but deactivation due to irreversible adsorption of products occurs. In this case the phenomenon can be reduced by working in basic media. Thus activated alcohols, such as benzylic and cinnamyl alcohols, have been oxidised in aqueous media under neutral conditions to the corresponding aldehyde but when carboxylate is produced as in the case of *n*-octanol basic conditions are required to preserve catalyst activity. Unlike the case of glycerol Au–Pt showed a lower activity with respect to Pt (a negative synergistic effect) whereas Au–Pd showed an enhanced activity with respect to Pd (a positive synergistic effect). It is believed that the resultant positive or negative effect on activity of adding a second metal to gold derives from the balance of both electronic and geometrical effects. Thus it was demonstrated that not only the metal or the support but also the substrate structure plays an important role.

Considering the correlation between substrate structure and reactivity in aerobic oxidation we could derive a general trend where secondary alcohols show higher TOFs than primary ones, tertiary ones being almost inert. However, this is a false conclusion because during the oxidation of substrates containing both primary and secondary OH groups, as propane-1,2-diol[12] and polyols,[113,124] the primary group appears to be selectively oxidised. Only a careful investigation on the reaction mechanism can disentangle the problem separating the contribution of primary oxidation steps from subsequent rearrangements.

4. Selective oxidation of aldehydes and sugars

4.1 Oxidation of aldehydes

As a general trend, the oxidation of aliphatic oxygenated compounds with the aid of supported gold particles follows this order of reactivity: aldehydes > secondary alcohols > primary alcohols. In the case of ketones, tertiary alcohols and carboxylic acids no oxidation occurs under moderate conditions (up to 90 °C and 3 bar). The aerobic oxidation of aldehydes leading to the corresponding carboxylic acids with almost total selectivity can be performed using water, organic solvents and solventless conditions, in the presence or in the absence of alkali. Compared to the more common platinum catalyst, gold showed a fairly good activity in oxidising aldehydes in aqueous solution and, unlike Pt, no deactivation was observed on recycling. In the case of water-insoluble aldehydes, a strong solvent effect was observed: while CH_3CN inhibited the oxidation, CCl_4 allowed a good performance as shown in Table 3. Moreover, comparing the oxidation of propanal in water and CCl_4 solution, the chlorinated solvent improved the yield on recycling.[95]

The oxidation of liquid aldehydes can also be carried out in the absence of solvent. In the case of 2-methylpropanal and *n*-heptanal a smooth reaction was observed with TOFs in the range of 4000–7500 h^{-1}. Moreover, the use of air instead of pure O_2, at low temperature (25–70 °C), allows safer reaction conditions.

In the case of aromatic aldehydes the oxidation rate is sensitive to the ring substituents. In fact, comparing different substrates, a strong deactivating effect has been observed for the *ortho* and *para* hydroxo-derivatives, as shown in Table 4.[95] No explanation has been given in the literature for this unexpected behaviour, which could be due to electronic effects as well as to poisoning impurities present in the reagents.

Trapping gold into gel-type organic resins produces nanostructured catalysts showing different activity and selectivity: a very hydrophilic resin catalyses the selective oxidation of *n*-butanol to *n*-butanal whereas a hydrophobic resin also catalyses the rapid oxidation of *n*-butanal to *n*-butanoic acid by dioxygen.[116]

Table 3 Oxidation of aldehydes to carboxylic acids on Au–C catalyst

	Conversion (%)		
Reagent	H_2O	CCl_4	H_2O/CH_3CN
p-MePh–CHO	8	76	3
n-C_6H_{13}–CHO	9	99	4
n-C_2H_5–CHO	90	96	41

Table 4 Oxidation of aromatic aldehydes to carboxylic acids on Au–C catalyst

Aldehyde	Yield (%)
PhCHO	96
p-Me–PhCHO	88
o-HO–PhCHO	0
p-HO–PhCHO	0

Considering the high reactivity of gold in catalysing the oxidation of glycols, such as ethane-1,2-diol, to monocarboxylate,[12] and the higher oxidation rate of aldehydes with respect to alcohols, it is surprising to note no reactivity of glyoxal with O_2 in the presence of differently prepared Au/C catalysts. Only in combination with Pd was gold able to promote the selective oxidation of glyoxal to glyoxalic acid.[142]

An important synergistic effect between gold and the support has been found in the aerobic oxidation of aldehydes: Au supported on both nanocrystalline and meso-structured nanocrystalline CeO_2 produced high conversion and selectivity values during the oxidation of aliphatic and aromatic aldehydes, performing better than other reported catalysts such as Pt/C/Bi materials.[143]

By comparing the aerobic oxidation mediated by homogeneous transition metals or heterogeneous catalysts, a radical or an ionic reaction mechanism has been proposed when working with organic or aqueous solvent, respectively. In particular, using Au/CeO_2 in organic media, experiments in the presence of radical inhibitors or radical initiators suggest that the oxidation of *n*-heptanal to *n*-heptanoic acid by air takes place through a radical mechanism. A helpful comparison among several catalytic systems working in acetonitrile solvent is represented in Fig. 1.[143]

4.2 Oxidation of glucose to sodium gluconate

The worldwide availability of carbohydrates has for a long time attracted interest in their oxidative transformation. According to the expected trend, catalytic aldose oxidation occurs at the aldehydic group leading to carboxylic acid or carboxylates. In the past the oxidation of glucose, the eminent

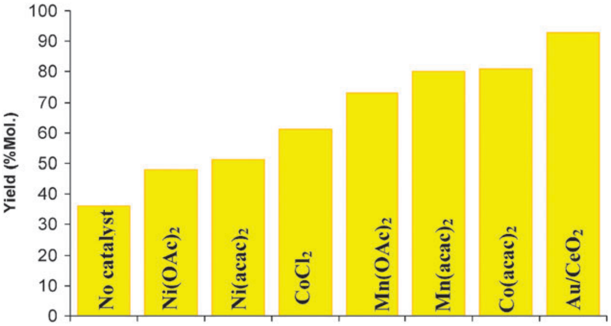


Fig. 1 Comparative catalytic evaluation of Au/CeO_2 and different homogeneous catalysts for air oxidation of *n*-heptanal at 50 °C during 3.5 h.

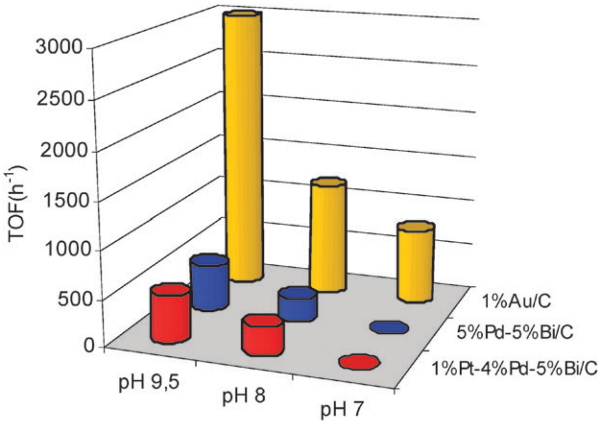


Fig. 2 Catalytic performance of different catalysts in glucose oxidation.

member of that family, has for long time been investigated using Pt group metals as the catalyst. Although a fast reaction resulted, allowing high conversion and good selectivity, the catalyst deactivated owing to leaching, self-poisoning and over-oxidation. Sophisticated bi- and tri-metallic catalysts have been proposed to overcome these effects. In particular, Bi promoted catalysts showed the best performance.[144,145] However, to our knowledge, no industrial application of platinum metal catalysts has been presently applied.

The ability of gold in promoting the aerobic oxidation of glucose in aqueous solution under mild conditions was first recognised using a carbon supported catalyst. Owing to difficulties in supporting metal particles on powdered activated carbon using conventional techniques, the deposition of colloidal gold resulted in an efficient catalyst showing TOF values around 3000 mol of reacted glucose (mol total Au h)$^{-1}$ at 50 °C (Fig. 2).[146]

Compared to the Pt group catalysts, gold allowed also a much better selectivity to sodium gluconate and high resistance to poisoning. Owing to the interest in industrial application, many subsequent efforts were devoted to further improvement of the catalytic performance of gold. The influence of different supporting materials on catalytic activity was tested in several papers,[147–153] and reproducibility of morphology and catalytic performance were demonstrated in 5–500 g scale preparations.[148,149]

Long term stability of Au/TiO$_2$ catalysts has been established at 40–60 °C and pH 9: neither loss of activity nor change of gold particle size was observed after 17 catalytic runs.[151]

Optimisation of gold Au/C preparation and experimental conditions led to improvement of the TOF value from the previously reported 3000 h^{-1} [146] to the fantastic value of 150 000 h^{-1} at 50 °C, where only external atoms, 36%, in spherical particles of 3.6 nm are considered as active centers.[83,154] According to this result, the inorganic gold catalysis shows a similar molecular efficiency to flavine–adenosine dinucleotide centers working in enzymatic catalysis presently employed in the industrial production of gluconates.

Considering the reaction mechanism of the gold catalyzed oxidation of glucose, discussed in the next section, the following points are of relevance:

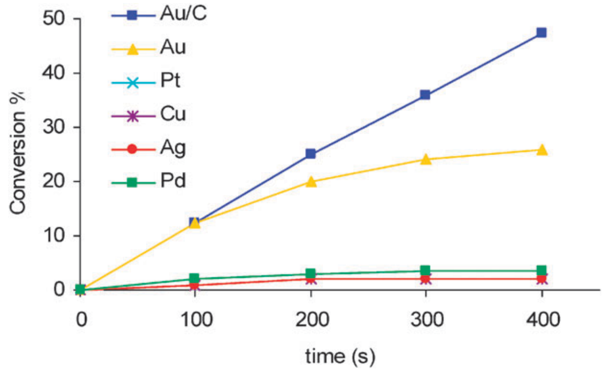


Fig. 3 The peculiar behaviour of colloidal gold *vs.* other colloidal metals in glucose oxidation.

(1) Monometallic gold particles are active in the presence of alkali.[146]

(2) Unsupported and supported gold nanoparticles are similarly active; however the supported gold catalyst is stable for a longer time than the "naked" particles (Fig. 3).[83]

(3) Hydrogen peroxide instead of water is the by-product of gluconate.[155]

4.2.1 Kinetic data and molecular mechanism.

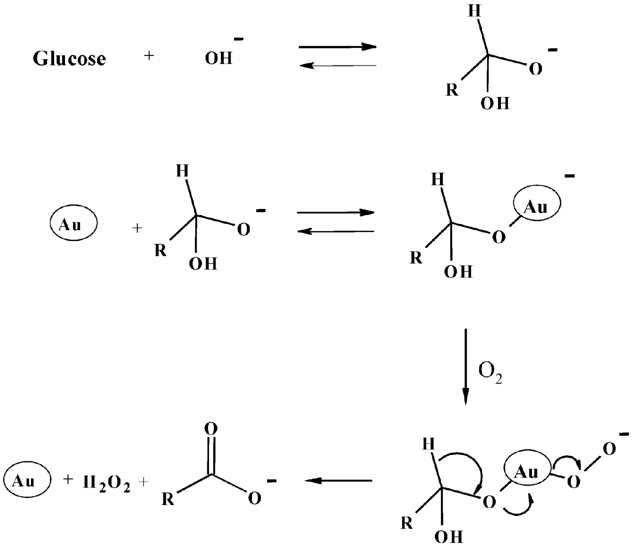
Kinetic studies on the selective liquid phase oxidation of glucose catalysed by gold were carried out using either carbon supported metal particles[150] or unsupported colloidal particles.[85]

According to the first investigation, a Langmuir–Hinshelwood model was proposed where the surface oxidation reaction is the limiting factor of the overall reaction rate, adsorption of substrate and desorption of the product being fast processes. As an important point, a negligible effect of glucose concentration on the reaction rate was observed.

In this context, although not explicitly stated, water was considered as the reduction product of dioxygen according to a dehydrogenation mechanism transforming glucose to sodium gluconate.

In the second investigation concerning "naked" gold particles as a catalyst, hydrogen peroxide instead of water as the reduction product was taken into consideration according to experimental evidence. Kinetic experiments at low glucose concentrations (<0.1 M) showed a first order reaction, tending to an asymptote at higher concentrations (0.5 M). A first order dependence was also found for the O$_2$ concentration. From these data, an Eley–Rideal mechanism, characterised by the adsorption of glucose in its hydrated form on gold, was suggested. This mechanism gives rise to a rate equation that justifies both the first order with respect to oxygen and the decreasing order with respect to glucose, being first order at low concentration and tending to zero for larger values.[85]

Owing to the scientific interest and commercial relevance of the biological glucose oxidation, presently applied in industrial plants for producing gluconates, accurate kinetic data of the enzymatic catalysis were also determined for comparison. Using Hyderase (a commercial glucose oxidase and catalase enzymatic preparation) under strictly similar conditions used for the gold catalysis, measurements of initial rate as a function of initial glucose concentration were interpreted using



Scheme 15 Molecular mechanism of aerobic glucose oxidation with gold nanoparticles.

a Michaelis–Menten mechanism.[156] By comparing the results, the following conclusions were derived: gold catalysis and biological catalysis are able to promote the oxidation of glucose according to the same stoichiometry involving the formation of hydrogen peroxide as an unstable intermediate. However, the homogeneous enzymatic system and the pseudo-homogeneous colloidal system adopt different reaction mechanisms. In the case of enzymatic catalysis, the rate determining step is the oxidation of the substrate by the enzyme, which is converted into the reduced form in a faster step and is zeroth order with respect to dioxygen. In contrast, the rate determining step in the gold catalyzed process is the oxidation of glucose by dioxygen dissolved in water, according to a first order dependence of the reaction rate on pO_2.

Despite different reaction mechanisms, similar activation energies (47.0 kJ mol^{-1} for gold and 49.6 kJ mol^{-1} for enzymatic catalysis) were found for the corresponding rate determining steps.[85,156]

Supported by kinetic studies, the molecular mechanism of glucose oxidation on a gold nanoparticle agrees with Scheme 15.[155]

As observed during the gas phase oxidation of propene and the liquid phase oxidation of alcohols, the activity of gold nanoparticles in glucose oxidation is also related to the particle size. A quasi-linear correlation between the initial specific molar activity (moles of reacted glucose/mole total gold × h) and the inverse of the mean diameter in the range 2–7 nm is evidenced in Fig. 4 using unsupported colloidal particles (10^{-4} M Au, 0.38 M glucose, 303 K under oxygen at atmospheric pressure) with a sudden loss of activity with *ca.* 10 nm particles.[83]

4.3 Oxidation of glucose to free gluconic acid

Free gluconic acid is presently manufactured starting from calcium gluconate and sulfuric acid, thus producing a large amount of $CaSO_4$ as a by-product. This is due to the fact that at low pH values the enzymatic catalysis is inhibited. Applying catalytic methods, it has been found that Pd, Pt, and Au catalysts are scarcely active (TOFs 2, 60 and 50 h^{-1}, respectively) in the presence of free gluconic acid. To attempt a successful direct synthesis of gluconic acid, bimetallic catalysts have been investigated and a strong synergistic effect between gold and platinum has been detected leading to interesting TOF values around 1000 h^{-1} in the case of the catalyst Au : Pt (2 : 1) supported on carbon.[157]

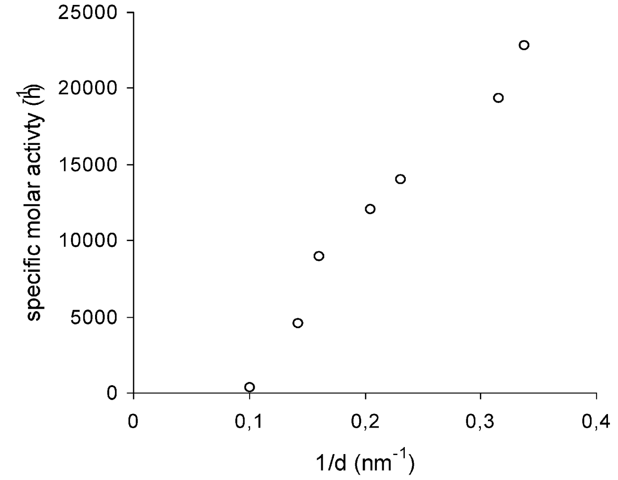
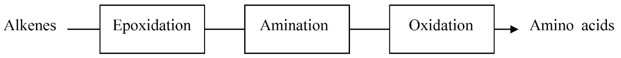


Fig. 4 Correlation between activity and particles dimension in glucose oxidation.

5. Selective oxidation of amines

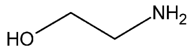
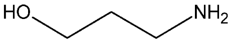
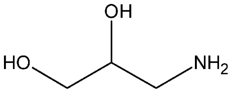
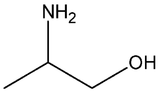
Catalytic methods for amine oxidation are almost unknown in organic synthesis probably due to the inhibition effect (irreversible adsorption) of the amino group on the classical Pt and Pd supported metals. Gold catalysis, however, seems to overcome in part this problem according to the recent literature.[158–162] In the first instance,[158] the competition between amino and hydroxy groups in the aerobic oxidation on Au/C catalysts has been investigated showing that α- and β-amino alcohols react with oxygen preferentially at the C–OH group, producing the corresponding amino acids. A promoting effect of alkali has also been detected. Considering the importance of a synthetic pathway for producing amino acids from olefins according to Scheme 16, it must be outlined that the oxidation step is not yet of general application, being sensitive to the nature of the reagent molecule as shown in Table 5. Under identical conditions (0.4 M substrate, substrate/Au = 1000, substrate/NaOH = 1, pO_2 = 3 atm, T = 343 K, t = 2 h) different substrates undergo quite different conversions for no obvious reason.

An useful application of gold catalysis in amine oxidative transformation has been extended to unsubstituted amines. Thus, bulk gold particles (*ca.* 1000 nm) can catalyze under mild conditions (60 °C, 1 atm) reactions of isocyanides or carbon monoxide with primary amines and dioxygen



Scheme 16 A convenient synthetic route to amino acids.

Table 5 Catalytic oxidation of amino alcohols to amino acids with nanometre sized gold

Substrate	Conversion (%)
	23
	27
	32
	100

to produce carbodiimides[159] or ureas, respectively[160] (Scheme 17).

Under similar conditions (1 atm O_2 and 60–100 °C), non-nano gold is a highly active catalyst for the oxidative dehydrogenation of secondary amines to imines (Scheme 18).[161]

In the case of cyclic amines, metal catalyzed carbon–nitrogen coupling can occur along with imine formation leading to oxidative dimerisation[161] (Scheme 19):

Finally, nanometre sized gold-based mono- and bi-metallic catalysts (Au–Pt and Au–Rh) have been evaluated in the aerobic oxidation of aqueous solutions of tertiary amines. *N*-Oxides were obtained (Scheme 20) in 100% yield in the case of triethylamine, pyridine and 3-dimethylaminopropan-1-ol under mild conditions.[162]

6. Industrial perspectives

Despite the rapid growth of research in gold catalysis in the last ten years, no new industrial process has been licensed concerning the use of gold in the selective oxidation of organic compounds.

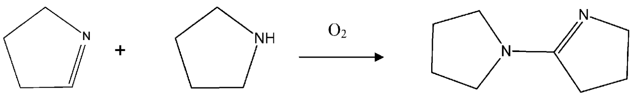
$$\text{R-NC} + \text{H}_2\text{N-R'} + 0.5\ \text{O}_2 \longrightarrow \text{R-N=C=N-R'}$$

$$\text{CO} + 2\ \text{R-NH}_2 + 0.5\ \text{O}_2 \longrightarrow (\text{RNH})_2\text{CO}$$

Scheme 17 Oxidative transformation of primary amines.

$$\text{R}^1\text{NH-CH}_2\text{-R}^2 + 0.5\ \text{O}_2 \longrightarrow \text{R}^1\text{-N=CH-R}^2$$

Scheme 18 Aerobic oxidation of secondary amines.



Scheme 19 Oxidative dimerisation of primary amines.

$$\text{R}_3\text{N} + 0.5\ \text{O}_2 \longrightarrow \text{R}_3\text{N-O}$$

Scheme 20 Gold promoted oxidation of tertiary amines to *N*-oxides.

However, some laboratory-scale processes are potentially ready for commercialisation as in the case of the following applications.

(1) Ethylene glycol to methyl glycolate

According to Nippon Shokubai, a new technology will be soon applied on an industrial scale which is based on the use of nano-sized gold supported on a metal oxide carrier for producing methyl glycolate, a new generation solvent derived from ethylene glycol. A pilot plant of 50 tonnes per year has been operating since 2004, in anticipation of a programmed 10 000–20 000 tonne per year commercial plant.[163]

(2) Propene to propene oxide

Gold nanoparticles deposited on TiO_2 provides a new route (Scheme 1) for propene epoxidation which appears ready for a large pilot plant demonstration. Many observers are confident that, after a long wait, the gold-based vapour phase epoxidation process will reach industrial exploitation. The main targets, consisting of 10% conversion, 90% PO selectivity and 50% hydrogen efficiency, have been reached through optimisation of catalyst activity and feed composition. Considering also the possible regeneration of the catalyst, a sustainable process has been claimed showing space–time yields superior to 10^{-3} mol (h $g_{cat})^{-1}$,[27] which are close to the analogous silver-promoted ethene epoxidation. This result opens the door to a new commercially acceptable gas phase process, which occurs under cleaner conditions than the present liquid-phase technologies.

(3) Glucose and other carbohydrates to aldonic acids

It has been demonstrated that Au/C, Au/TiO_2 and Au/Al_2O_3 are suitable catalysts for carbohydrate oxidation under environmentally and economically acceptable conditions.

After the first patent claims,[6–8] several papers explored in detail catalyst preparation methods and experimental conditions for optimising the gold-based oxidation in view of its industrial application.[153,154,164–168]

Although tested under slightly different experimental conditions, various optimised catalytic systems show TOF values, relative to the total gold, which have been considered suitable for industrial application (Table 6).

For the most active Au/C catalyst, a comparison with the presently employed enzymatic process has been performed under similar conditions and the space–time yields in the catalytic step have been calculated.

As shown in Table 7, the productivity of gold catalysis is quite high with respect to the biological process. Other technological aspects, such as filtration and catalyst recycling, also favour supported gold. However, the active nanometre sized gold particles suffer from sulfur impurities and need refined glucose as a feed.[154]

Extension of the gold catalysed oxidation indicates a general application to different carbohydrates making this metal useful for the industrial transformations of many naturally occurring mono- and disaccharides.[167]

Table 6 Selected TOF values in glucose oxidation

Catalyst	$T/°C$	pH	Glucose/mol l^{-1}	TOF [mol gluc. (mol Au)$^{-1}$ h^{-1}]	Ref.
0.45% Au–TiO_2	40	9	0.1	2789[a]	153
0.33% Au–Al_2O_3	40	9	0.1	11 320[a]	168
0.30% Au–Al_2O_3–NaOH	40	9	0.1	11 925[a]	166
0.30% Au–Al_2O_3–NaOH	40	9	0.5	1650[b]	165
0.50% Au–C	50	9.5	3.0	43 540[a]	154

[a] Batch process. [b] Continuous process.

Table 7 Comparison between gold and enzymatic catalysis in the aerobic oxidation of glucose

Catalyst	$C_6H_{12}O_6$/mol l^{-1}	Cat/Glucose (g per kg)	pH	$T/°C$	Specific activity (g g_{cat}^{-1} h^{-1})	Gluconate productivity (kg m^{-3} h^{-1})
Hyderase	1	6	5–7	30	145	122
Au/C	3	5	9.5	50	218	514

7. Conclusions

The catalytic properties of gold nanoparticles in the selective oxidation of organic compounds represent a recent but exciting contribution to the art of catalysis: we have outlined how the outstanding properties of gold, a biocompatible non-toxic metal, can be moulded upon new processes based on aerobic oxidation.

General rules for correlating the catalytic properties with the composition and structure of the catalyst are hard to extract from the labyrinth of experiments; therefore, accurate kinetic investigations should be implemented along with theoretical work to understand the experimental behaviour of active and non-active catalysts in the selective oxidation. In any case, there is still a place for the imagination and ability of scientists engaged in many laboratories. By merging many complementary contributions, it is expected to create new and more efficient nanostructured catalysts, which embody a balanced amount of activity, selectivity and stability for challenging applications in organic synthesis.

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