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Research Note

Is the biochemical route always advantageous? The case of glucose oxidation

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Abstract

The aerobic oxidation of alcohols and aldehydes is a crucial process in organic synthesis for preparing fine chemicals. In particular, the oxidation of glucose, a cheap and renewable starting material, represents a challenging target involving 60,000 ton/year of gluconates. Here we present a critical comparison between two selective "green processes" based on the use of molecular oxygen in water solution under mild conditions, showing that the emerging gold-based catalysis is a valid alternative to enzymatic catalysis so far used in industrial production of gluconates.

Keywords: Glucose; Gold catalyst; Aerobic oxidation

Innovation in the use of clean technologies to reduce pollution levels and consumption of resources is a pushing demand for industrial processes, and chemical and enzymatic catalysis are challenging alternatives for the synthesis of important products [1]. Thus, lactic acid, propane-1,3-diol, and many pharmaceutical intermediates can be synthesized by using both methods. In some cases, however, only one industrial route is applicable; in particular, no chemical process is known for the production of gluconic acid and gluconates.

Owing to the low productivity of the glucose fermentation process, interest exists in alternative environmentally friendly technologies based on the use of atmospheric oxygen in water solution under mild conditions and with the aid of heterogeneous catalysis [2,3]. Consequently, the chemical oxidation of glucose to gluconic acid with Pd group metals has been extensively investigated [4]; recently, sophisticated Bi-promoted bimetallic and trimetallic catalysts were tested [5,6]. However, to our knowledge, no industrial application exists for platinum metal catalysts. More recently, we found that gold could be an alternative to Pt-group metals for liquid-phase oxidation of alcohols and aldehydes to the corresponding carboxylates [7–10]. In the form of supported nanoparticles (average diameter, 3–5 nm) this metal proved quite efficient in the oxidation of glucose, allowing TOFs comparable with those of enzymatic systems [11]. Consequently, industrial applications of monometallic [12] and bimetallic [13] catalysts have been proposed.

To define the advantages of and limits to applying gold catalysis to the aerobic oxidation of glucose, a thorough comparison was performed between a laboratory-scale prepared gold catalyst and a commercial enzyme preparation containing glucose oxidase and catalase as active components. The gold catalyst was prepared similarly to the Au/C reference catalyst of the World Gold Council [14], from colloidal particles and coconut-derived carbon powder (CAMEL). Gold content (0.5 wt%), particle size (3.6 nm), and the metallic nature of gold were checked by ICP (Jobyn Yvon JY24), HRTEM (Joel 2000EX Microscope), XRD (Rigaku DIII-MAX Horizontal-scan powder diffractometer with Cu $K\alpha$ radiation), and XPS (M-Probe instrument equipped with a monochromatic Al $K\alpha$ source (1486.6 eV). The water-soluble enzymatic preparation (Hyderase, Amano Enzyme Co.) contained 1 $\mathrm{mg\,g^{-1}}$ of FAD (1.3×10^{-6} $\mathrm{mol\,g^{-1}}$) as the rate-controlling factor.

Catalytic tests with gold catalyst and enzymatic catalyst were carried out in a semibatch reactor, using a large excess of molecular oxygen flowing at atmospheric pressure connected to

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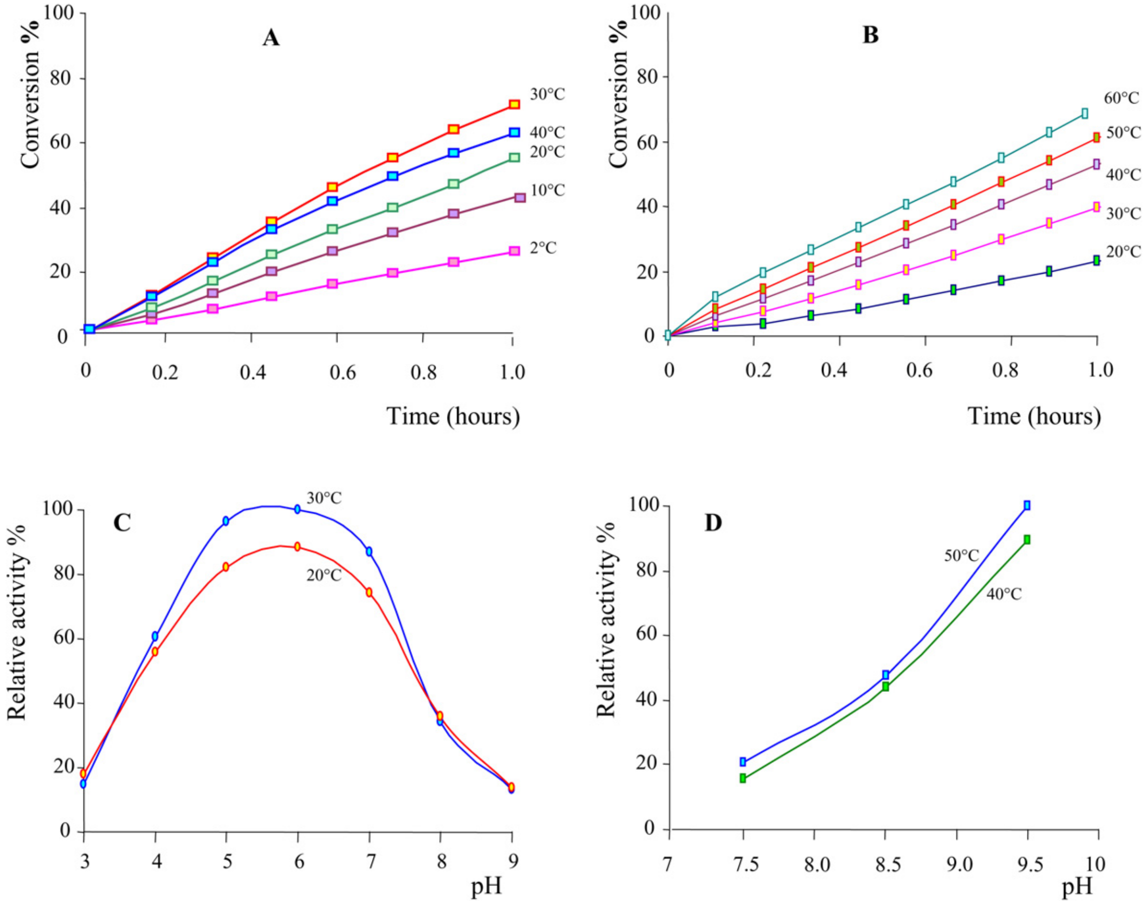

Fig. 1. (A) Temperature dependence of activity for the Hyderase catalyzed system. (B) Temperature dependence of activity for the Au/C catalyzed system. (C) Relative activity as a function of pH for the Hyderase catalyzed system. (D) Relative activity as a function of pH for the gold catalyzed system.

an automatic apparatus (Titrino from Metrohm), which allowed the titration of gluconic acid at a fixed pH value in real time. Time-conversion plots were obtained for both catalysts using similar conditions: glucose loading (5–6 g kg^{-1}) corresponding to molar ratios for glucose to FAD of 6.4×10^5 and for glucose to Au of 4×10^4, with pH, temperature, glucose concentration, and stirring speed varied to optimize performance. Quantification of gluconate was also done by NMR. Besides tests on research-grade glucose (Fluka), supplementary tests were performed with raw substrates (Roquette) and the poisoning effect of sulfur containing compounds was investigated.

The results of the comparative kinetic tests concerning the pH and the temperature effect for both systems are reported in Figs. 1 and 2 and Table 1. The typical volcano-shaped curve, correlating the activity with the pH of the reacting solution, was confirmed for the enzymatic catalysis; the resulting flat maximum was located at pH 6 (Fig. 1C). Gluconate was the only reaction product detected. With gold catalyst, the oxidation rate increased continuously by raising pH (Fig. 1D), but the selectivity decreased due to the formation of fructose and overoxidation products at high pH values. Thus, pH 9.5 was chosen as the limit for acceptable selectivity (>98%).

As expected for naturally occurring materials, the enzymatic preparation Hyderase showed the best performance at around room temperature (30 °C). Overcoming this temperature, a drop in activity was related to protein degradation. Between 20 and 60 °C, the Au/C catalyst showed a rate trend in good agreement with the Arrhenius law (Fig. 1B), as has been reported for supported [15] and unsupported gold particles [16]. Above 50 °C however, the selectivity dropped below 98%.

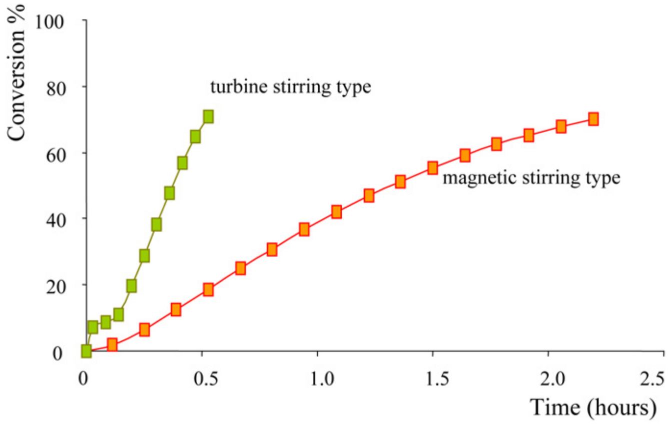

Fig. 2. Influence of the stirring rate on the activity of the Au/C catalyzed system. Reaction conditions: $C_6H_{12}O_6$ 3 M, 100 mL/min of O_2, $T = 50\,°C$, $P_{O_2} = 1$ atm, pH = 9.5, Au/Glu ratio = 1/40,000.

Glucose concentration in the reacting solution is a crucial parameter affecting plant productivity. Previous studies have found a linear correlation between reaction rate and glucose

Table 1
Comparative data for enzymatic and gold catalyzed processes

Catalyst	$[C_6H_{12}O_6]$ (mol L^{-1})	Cat/glucose (g/kg) I run	Cat/glucose (g/kg) Total	pH	Stirring rate (rpm)	T (°C)	TOF (h^{-1})	Productivity (kg m^{-3} h^{-1})
Au/C	3	5	1.3*	9.5	39,000	50	217.7**	514.3**
Hyderase	1	6	–	5–7	1700	30	144.6**	121.7**

* Mean cat/glucose value considering 4 runs as life time of the catalyst.
** Referred to a single run.
Productivity data are referred to the catalytic reactor stage.

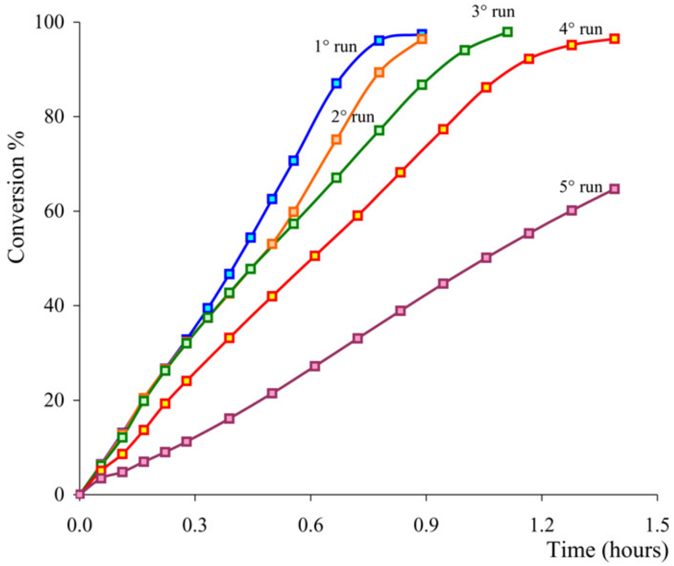

Fig. 3. First run and recycling runs (2–5) for the Au/C catalyzed system. Reaction conditions: $C_6H_{12}O_6$ 3 M, 100 mL/min of O_2, $T = 50\,°C$, $P_{O_2} = 1$ atm, pH = 9.5, Au/Glu ratio = 1/40,000.

concentration at low substrate concentration for both gold [16] and enzymatic catalysis [17], tending to an asymptote. In the present study, however, oxygen solubility problems and the substrate poisoning effect decreased Hyderase activity over 1 M glucose concentrations. This result agrees with common practice in modern production plants. No similar drawbacks were found for gold catalyst, for which the solubility-limited threshold, 3 M, produced the advantageous result.

Along with the magnetic stirring (1700 rpm) used for reaching the gas–liquid equilibrium in the aforementioned experiments, a very efficient mechanic turbine was also adopted to improve mixing efficiency. This technique was incompatible with the enzymatic catalyst, however, because the mechanical stress led to enzyme denaturation and a consequent loss of activity with respect to magnetic stirring. For gold catalyst, a strong benefit was obtained by applying the mechanical energy without loss of selectivity, thus providing greatly improved productivity.

Fig. 2 shows a fourfold increment in the TOF value at 39,000 rpm with respect to magnetic stirring at 1700 rpm. It is noteworthy that a continuous increment in the reaction rate was observed on increasing the turbine speed from 2000 to 39,000 rpm, indicating the presence of important mass-transfer limitations.

Owing to the solubility of Hyderase, no catalyst recycling was attempted in our experiments, whereas the solid gold on carbon was easily filtered off for recycling. Considering the four cycles reported in Fig. 3, the mean consumption of 1.3 g of catalyst per kg of glucose was derived from this experiment.

Finally, to investigate conditions close to industrial applications, kinetic tests were performed using different samples of raw glucose as starting materials. Industrial-grade and analytical-grade reagents were similarly reactive using both catalysts, but in the case of SO_2-stabilized reagents, gold was strongly inhibited; at 20 ppm of SO_2, the catalytic activity decreased by 80%. The enzymatic catalyst was insensitive to SO_2 and other sulfur derivatives.

The main parameters taken into account for comparing enzymatic and inorganic catalysis are summarized in Table 1. Here the reported values represent optimized conditions for each process.

In conclusion, studies of molecular mechanism on biochemical and chemical oxidation of glucose indicate that these two different catalytic systems activate dioxygen using a similar two-electron mechanism, leading to gluconate and hydrogen peroxide [16–18]. Moreover, optimized kinetic tests show similar molecular efficiency, with the TOF value of 5.5×10^5 h^{-1} for FAD centers comparable to that of 1.5×10^5 h^{-1} for gold, as derived from the specific activities reported in Table 1. For gold catalyst, only external atoms (36%) in spherical particles of 3.6 nm were considered active centers

Taking into account the properties reported in Table 1, gold appears to provide a challenging catalyst for achieving high plant productivity as well as easy manufacturing and recovery of catalyst with respect to the known biochemical route [19]. Finally, new promising results indicate a wider range of application for inorganic catalysis—in particular, the unique application of platinum-promoted gold catalysts in synthesizing free gluconic acid working under acidic conditions, a process not allowed by enzymatic catalysis [13,20]. In this case, however, the lack of information on catalyst lifetime precludes evaluation of the bimetallic system's quantitative advantages.

Acknowledgments

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