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One-pot electrocatalytic oxidation of glycerol to DHA

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Abstract—One-pot, waste-free oxidation of glycerol to 1,3-dihydroxyacetone (DHA) was achieved by simply applying a small electric potential (1.1 V vs Ag/AgCl) to a glycerol solution in water buffered at pH 9.1 in the presence of 15 mol % TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl). Prolonging the reaction time affords comparable amounts of hydroxypyruvic acid.
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The selective oxidation of glycerin (glycerol, 1,2,3-propanetriol) to valued oxygenates is an important objective of current chemical research due to rapidly increasing surplus of glycerin obtained as a byproduct (10% wt/wt) in manufacturing of biodiesel fuel.[1]

In practice, all the oxygenates obtained by selective oxidation of glycerin are commercially relevant. Unfortunately, however, the extensive functionalisation of the triol glycerol molecule with hydroxy groups of similar reactivity renders its selective conversion particularly difficult.

Moreover, glycerol is easily converted to formaldehyde, formic acid and CO_2 and in some cases mass balances as low as 20% are observed.[2] Good selectivities at high glycerol conversion are difficult to achieve due to rapid overoxidation, and high selectivities become more difficult as the compounds become more oxidised.

1,3-Dihydroxyacetone (DHA) currently produced from glycerol by microbial fermentation over *Gluconobacter oxydans*,[3] is one of such valued oxygenate products. Indeed, dihydroxyacetone is an important chemical used in the cosmetics industry as a tanning substance and also in fungicides.[4]

In particular, DHA is the main active ingredient in all sunless tanning skincare preparations, since it is the most effective sun free tanning additive.

This skin browning effect is nontoxic, and similar to the Maillard reaction. DHA reacts with the amino acid groups, which are part of the protein containing keratin layer on the skin surface. Various amino acids react differently to DHA, producing different pigments (melanoidins) that are similar in colouration to melanin, the natural substance in the deeper skin layers which browns or 'tans' upon exposure to UV rays.[5]

Its commercial sales are rapidly increasing as concerns surrounding damage associated with UV tanning options spurred further popularity of sunless tanning products as an alternative to UV tanning.

Improvements in the DHA manufacturing process, resulted in products that produced a more natural looking colour and better fading.

The *G. oxydans* is strongly product-inhibited, and for high space-to-time yields and efficient downstream purification, multiple-stage reactor systems have been developed.

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Clearly, a clean, efficient chemical process capable of generating DHA from glycerol at lower cost is extremely desirable.

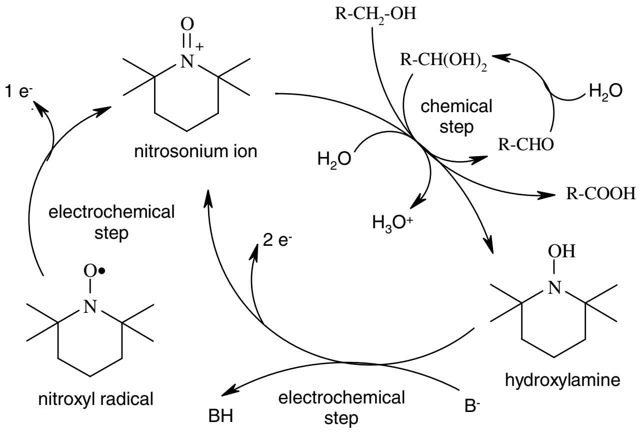
Now we report a simple electrochemical process capable of affording DHA in a yield comparable to that of the fermentation process while furnishing a product of high purity, and hence meeting an important requirement for a chemical that finds use in the cosmetics and food industries.

The process is electrocatalytic and does not require traditional chemical oxidants (Scheme 1).[6]

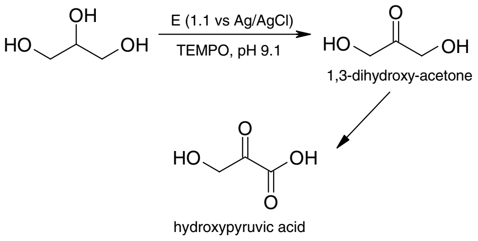
By simple application of a low voltage (1.1 V vs Ag/AgCl) to a solution of glycerol (0.05 M) buffered at pH 9.1 with bicarbonate (0.2 M) in the presence of catalytic TEMPO (0.0075 M), glycerol is selectively converted to DHA at the anode. Prolonging the reaction time results in the formation of hydroxypyruvic acid (Scheme 2).

The reaction system was based on a single undivided cell containing a glassy-carbon working electrode (1 cm^2), a Pt wire as counter electrode and a reference electrode of Ag/AgCl.

The role of $NaHCO_3$ here is to ensure both the required basic pH (Scheme 1) and, as electrolyte, to enhance conductivity in the electrolysis solution.



Scheme 1. General reaction scheme for electrochemical alcohol oxidation mediated by TEMPO.



Scheme 2. Electrochemical oxidation of glycerol mediated by TEMPO in water affords DHA and, after longer reaction times, HPA.

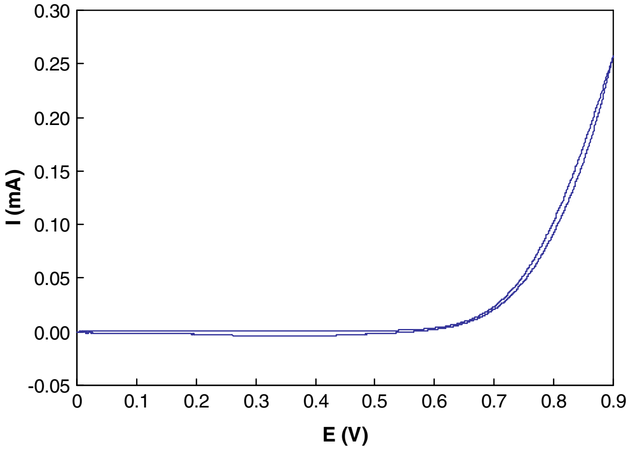


Figure 1. Cyclic voltammetry recorded at 0.05 V s^{-1} over a glassy-carbon electrode (1 cm^2) of a solution containing glycerol (0.05 M) and TEMPO (7.5×10^{-3} M) in the presence of 0.2 M $NaHCO_3$.

Before the oxidation a cyclic voltammetry of the solution was recorded (Fig. 1, where no redox peak of TEMPO is observed due to the presence of reductant glycerol), showing that potentials higher than 0.6 V are necessary to perform the oxidation.

After 20 h, an optimal 25% yield (calculated by calibration curves obtained using authentic reagents) of DHA was obtained.[7]

As mentioned above, extending the reaction time causes overoxidation of the DHA and formation of hydroxypyruvic acid (HPA). Hence, after 200 h a considerable amount of the latter species (35%) was present in solution along with 30% of DHA.

These results are truly surprising and markedly differ from those observed in the TEMPO-mediated oxidation of glycerol with NaOCl as auxiliary oxidant.[8] It is well established, in fact, that at alkaline pH the nitrosonium ion $TEMPO^+$ is a highly selective oxidant for primary (vs secondary) alcohols.[9]

Accordingly, we reported the selective oxidation of glycerol to ketomalonic acid mediated by the radical TEMPO in the presence of catalytic Br^- and NaOCl at 2 °C.[8]

It is also surprising that no overoxidation to carboxylic acid is observed even after prolonged reaction times, showing that at the chosen potential (1.1 V) both carbonyl products (DHA and HPA) are stable. Indeed, in water at pH 9.1 hydration of aldehydes is usually fast and in the presence of a chemical oxidant such as hypochlorite, formation of the acid is similarly rapid.

At this stage, it is not clear why in the electrochemical oxidation, glycerol is preferentially oxidised at the secondary hydroxyl to yield DHA. We make the hypothesis that the anodic surface of glassy-carbon may indeed play a role in a concerted reaction mechanism involving TEMPO. In fact, no reaction is observed in the absence of added TEMPO.

Interestingly, similar pronounced alteration in the selectivity of electrocatalytic oxidation of alcohols mediated by TEMPO has recently been reported.[10]

Finally, it is of relevance to this report that the catalyst TEMPO can be easily recovered (by extraction with organic solvent) at the end of the reaction and thus reused.

Facile scale-up can be envisaged by increasing the electrode surface area and by use of a simple cation-exchange resin membrane to remove (and recycle) the bicarbonate buffer electrolyte.[11] Under these conditions, the high solubility of glycerol in water (1 kg/L at 25 °C) would allow the use of much higher glycerol concentrations.

In conclusion, a clean one-pot oxidation process capable of affording reasonable yields of DHA from glycerol has been discovered that might find soon commercial use as an alternative to cumbersome biological conversion.

Acknowledgements

M.P. dedicates this work to (Senator) Professor Bruno Di Maio in memory of a wonderful 1994 electoral campaign.

References and notes

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3. For a recent interesting study aimed at optimisation of the biotechnological process, see: Bauer, R.; Hekmat, D. *Biotechnol. Prog.* **2006**, *22*, 278.
4. DHA does not damage the skin as it does not penetrate beyond the stratum corneum or dead skin surface layer. It is considered a safe skin colouring agent and nutritional supplement and has been approved for cosmetic use by most regulating authorities. See: http://en.wikipedia.org/wiki/Dihydroxyacetone.
5. Once the darkening effect has occurred, the tan will not sweat off or wash away with soap or water. It will fade gradually over 3–10 days, in conjunction with the skin's normal exfoliation process. Exfoliation, prolonged water submersion, or heavy sweating can lighten the tan, as these all contribute to rapid dead skin cell exfoliation.
6. Typical experimental conditions of the electrooxidation: a solution of glycerol (0.05 M) and TEMPO (0.0075 M) in water (10 mL) kept under stirring in a single cell containing a glassy-carbon electrode (1 cm^2), a Pt wire as counter electrode and a reference electrode of Ag/AgCl was electrolysed under a 1.1 potential (vs Ag/AgCl) by using a CH Instruments (Austin, TX) potentiostat CHI630B Electrochemical Workstation. The concentration of products was monitored by withdrawing reaction samples of 10 μL. All chemicals were purchased from Aldrich (St. Louis, MO).
7. The HPLC column system (Alltech IOA 1000 for organic acids) was connected in series with a UV–vis detector (Shimadzu) set at 220 nm using 0.005 M H_2SO_4 as mobile phase and keeping the oven containing the column at 75 °C. Retention times are: DHA = 22.91 min and HPA = 16.2 min. No other products could be detected by HPLC. Both authentic DHA (as dimer) and HPA used for the calibration curves were from Aldrich.
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