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Pyo, Sang-Hyun; Dishisha, Tarek; Dayankac, Secil; Gerelsaikhan, Jargalan; Lundmark, Stefan; Rehnberg, Nicola; Hatti-Kaul, Rajni

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A new route for the synthesis of methacrylic acid from 2-methyl-1,3-propanediol by integrating biotransformation and catalytic dehydration

Sang-Hyun Pyo\textsuperscript{a,*}, Tarek Dishisha\textsuperscript{a}, Secil Dayankac\textsuperscript{a}, Jargalan Gerelsaikhan\textsuperscript{a}, Stefan Lundmark\textsuperscript{b}, Nicola Rehnberg\textsuperscript{c}, and Rajni Hatti-Kaul\textsuperscript{a}

\textsuperscript{a} Department of Biotechnology, Center for Chemistry and Chemical Engineering, Lund University, Box 124, SE-221 00 Lund, Sweden

\textsuperscript{b} Perstorp AB, 284 80 Perstorp, Sweden

\textsuperscript{c} Strategic R&D, Bona AB, Box 210 74, 200 21 Malmö, Sweden

Graphical abstract

\begin{center}
\begin{tikzpicture}
\node[draw,rectangle] (1) at (0,0) {1};
\node[draw,rectangle] (2) at (2,0) {2};
\node[draw,rectangle] (3) at (2,1) {3};
\node[draw,rectangle] (4) at (4,1) {4};
\node[draw,ellipse] (G) at (0,-0.5) {$G. \text{oxydans}$};
\node[draw,ellipse] (TiO\textsubscript{2}) at (4,0.5) {TiO\textsubscript{2}};
\node[draw,ellipse] (195-210) at (4,0) {195-210°C};
\node[draw,ellipse] (OH) at (2,-0.5) {OH};
\node[draw,ellipse] (2-Methyl) at (0,-1) {2-Methyl-1,3-Propanediol};
\node[draw,ellipse] (3-Hydroxy-2-methylpropanal) at (2,-2) {3-Hydroxy-2-methylpropanal};
\node[draw,ellipse] (3-Hydroxy-2-methylpropionic acid) at (2,-3) {3-Hydroxy-2-methylpropionic acid};
\node[draw,ellipse] (Methacrylic acid) at (4,-2) {Methacrylic acid};
\end{tikzpicture}
\end{center}
A new route for the synthesis of methacrylic acid from 2-methyl-1,3-propanediol by integrating biotransformation and catalytic dehydration†

Sang-Hyun Pyo**, Tarek Dishisha, Secil Dayankac, Jargalan Gerelsaikhan, Stefan Lundmark, Nicola Rehnberg, and Rajni Hatti-Kaul

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Methacrylic acid was produced at high yield by an integrated process involving bioconversion of 2-methyl-1,3-propanediol (2M1,3PD) to 3-hydroxy-2-methylpropionic acid (3H2MPA) via 3-hydroxy-2-methylpropanal (3H2MPAL), and catalytic dehydration of the resulting acid. Whole cells of Gluconobacter oxydans grown on glycerol-based culture medium were used as catalyst for oxidative biotransformation that involved alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) enzymes in the organism. The effect of several reaction parameters on bioconversion in a batch system was investigated to obtain 95-100 % conversion of 2M1,3PD with over 95% selectivity to 3H2MPA. The optimum conditions for bioconversion were pH 6-7.5, 25-30 °C, 5-10 g substrate and 2.6 g cell (dry weight) per liter. Higher substrate concentrations led to enzyme inhibition and incomplete conversion. Loss of catalytic activity was noted during recycling of the cells. The cells were active for a longer period when used for biotransformation of 20 g/L substrate in a continuous reactor with cell retention. The product of the bio-oxidation, 3H2MPA was converted using titanium dioxide at 210 °C to give methacrylic acid (MA) with a yield of over 85%. The integrated process provides a new environmentally benign route for production of methacrylic acid from 2-methyl-1,3-propanediol, an industrial by-product, compared with the conventional acetone-cyanohydrin (ACH) process.

Introduction

Methacrylic acid (MA) and methyl methacrylate (MMA) are important monomers for a range of polymer products; the major product is poly(methyl methacrylate) (PMMA), with an annual global consumption of 2.1 million tonnes.1 Approximately 80% of the global production of MMA is achieved using the well known acetone-cyanohydrin (ACH) process, in which acetone and hydrogen cyanide are reacted with excess concentrated sulphuric acid to produce the methacrylamide acid sulphate, followed by treating with excess aqueous methanol, and hydrolysis and esterification of the amide to yield a mixture of MMA and MA. However, there are serious problems with this process due to the use of highly toxic raw materials, high process cost, and formation of significant amounts of by-products, which have to be disposed of.1,2

The ACH process is estimated to result in emission of 5.5 kg CO₂/kg MMA, which is much higher than that from other platform chemicals such as propylene (1.1 kg CO₂/kg), ethylene (1.1 kg CO₂/kg), and vinyl chloride monomer (1.5 kg CO₂/kg).3 Therefore, among several platform chemicals, a greener production route of MMA can be expected to be highly beneficial for the environment. Different alternative processes have been proposed since the 1980s to replace the ACH technology. Some of them are close to commercialization, while others, although attractive from environmental and economic points of view, are still in the research stage.2

An earlier study has reported the production of an analogous compound, acrylic acid from 3-hydroxypropionic acid in a continuous process with >98% conversion and >99% selectivity using titanium oxide as the catalyst at 180 °C.4 Also, dehydration of lactic acid to obtain acrylic acid has been studied,5,6 but the product yield was too low for commercial application. A similar process for the production of methacrylic acid would require 3-hydroxy-2-methyl propionic acid (3H2MPA, isohydroxybutyric acid) as the substrate. Synthesis of this chemical has been achieved by enantioselective oxidation of 2-methyl-1,3-propanediol (2M1,3PD) using an acetic acid bacterium, Acetobacter pasteurianus.7 2M1,3PD is a by-product of the butanediol production process involving hydroformylation reaction of allyl alcohol and CO/H₂ gas mixture in the presence of a catalyst, and hence is a cheap and commercially available substrate.7,8 Recently, the possibility of 2M1,3PD production
from renewable resources has been suggested by fermentation of
glycerol and thin stillage obtained from biofuel production
process, by Citrobacter freundii.10

In the present report, a process comprising oxidation of
2M1,3PD to 3H2MPA via 3-hydroxy-2-methylpropanal
(3H2PAL), followed by catalytic dehydration is proposed as a
new synthetic route to produce methacrylic acid. Gluconobacter
oxydans was selected as the microorganism for oxidation of
2M1,3PD to 3H2MPA, which was subsequently dehydrated to
methacrylic acid using TiO2 (Scheme 1). The latter has been used
as an environmentally friendly photocatalyst in water treatment
and organic synthesis, and is known to be a non-toxic and
biocompatible material.11,12

Scheme 1. Conversion of 2-methyl-1,3-propanediol to
methacrylic acid via 3-hydroxy-2-methylpropanic acid by
microbial conversion and catalytic dehydration.

Materials and Methods

2.1. Materials

2-Methyl-1,3-propanediol was a product of Perstorp AB
(Sweden). Methacrylic acid, 2,4-dinitrophenylhydrazine (99%,
DNPH), CDCl3, DMSO-d6, CaCO3, and glycerol were purchased
from Sigma-Aldrich (St. Louis, MO, USA). Potassium phosphate
salts, acetoinyl ethyl acetate and dichloromethane were
purchased from MERCK (Germany), while Trizma™ was from
VWR international, and yeast extract (Bacto™) was obtained
from BDH (NJ, USA). G. oxydans (DSM 50049) was purchased
from DSMZ (Deutsche Sammlung von Mikroorganismen,
Germany).

2.2. Maintenance and cultivation of G. oxydans

G. oxydans was maintained on solid medium containing per liter:
50 g glucose, 10 g yeast extract, 20 g CaCO3, and 15 g agar-agar
at pH 6.8. The agar slants were inoculated with the stock culture
of the microorganism in 20 % (v/v) glycerol, and incubated at 28
°C for 2 days, and then stored at 4 °C. To prepare the preculture,
cells from the surface of the slants were transferred to 100 mL
fermentation medium in 1 L baffled Erlenmeyer flask, containing
(per liter): 10 g glycerol, 10 g yeast extract, 5 g KH2PO4 at
pH 5.5. The flasks were incubated in an orbital shaker incubator
(New Brunswick, Innova 4430, Edison, USA) at 28 °C and 200
rpm for 4 days. The pre-culture (75 mL, OD600 = 2.8) was used to
inoculate 1.5 L fermentation medium in a 3 L bioreactor
(Aplikon, Microbial Biobundle, The Netherlands). The fermentation
was monitored and controlled through ezTcontrol
unit. The temperature was controlled at 28 °C and pH at 5.5
through addition of 5 N NH4OH and 5 N HCl. Stirrer speed was
500 rpm and a constant airflow at 1vvm was maintained during
the whole fermentation. Sterile polypropylene glycol in water
(1:1) was used as antifoam and was added when required. The
fermentation lasted for 2 days and samples were collected and
analysed for optical density (OD), cell dry weight (CDW)
and concentration of glycerol, acetic acid, succinic acid, and
diacrylic acid (DHA) using HPLC. After 48 hours, the
fermentation was terminated and the cell broth was harvested and
stored at 4 °C until use.

2.3. Biotransformation of 2-methyl-1,3-propanediol to 2-methyl-
3-hydroxypropionic acid

G. oxydans cells were obtained by centrifugation of the culture
broth at 10 000 × g for 2 min and followed by washing with 0.1
M Tris-HCl buffer (pH 7.2) to remove the residual culture media.
Oxidation of 2M1,3PD (2.5-30 g/L) using G. oxydans cells was
studied in 1 mL reaction volume in 5 mL vials placed in a
thermomixer (MKR 13, HLC Biotech, Germany) at 500 rpm. The
reaction conditions were optimized with respect to reaction time,
substrate- and cell concentration at 28 °C and pH 7.2.

Continuous biotransformation of 2M1,3PD was performed
using the system illustrated in Fig. 1, composed of a 3 L
bioreactor connected to a tangential flow microfilter, (Pellicon
XL, 0.45 µm, 50 cm² filtration area, Millipore, Bedford, MA).
Two pumps were used – one for re-circulating the reaction suspension
between the bioreactor and the filtration system at a rate of 30 mL/min
and the other for feeding the fresh substrate solution and removing the cell-free
product stream at a constant rate. During the whole run, the stirrer speed was kept constant at
1000 rpm, air flow at 1 vvm, pH at 7.2 though addition of 5 N
NH4OH, and temperature at 28 °C. The cells used for the
biotransformation were previously grown as described above,
recovered from the fermentation broth by centrifugation at 15 000
× g for 10 min. The reaction was performed in 1 L working
volume containing 5 g 2M1,3PD and 5.85 g cells (dry weight) in
0.05 M Tris-HCl (pH 7.2), initially in a batch mode for 7.2 h
followed by a continuous mode by feeding 20 g/L 2M1,3PD in
the same buffer at a dilution rate of 0.03 h⁻¹, removing the cell-
free product as a permeate from the microfiltration unit while
recycling the retained cells, for a period of 107 hours.

The biotransformation experiments were performed in two
independent runs and analyses of the reaction components was
performed in duplicates.

2.4. Catalytic dehydration of 3-hydroxy-2-methylpropionic acid
to methacrylic acid
3H2MPA, obtained as a product of batch biotransformation using *G. oxydans* cells, was used without further treatment for catalytic dehydration. A simple flow reaction cell was designed using a stainless tube (4.5 x 200 mm) packed with 3 g TiO₂ and placed in an oven. Twenty five millilitres of a pre-heated 3H2MPA solution (5 g/L) was fed to the pre-heated reaction tube using a quantitative pump (Pump 2248, Pharmacia LKB, Sweden) at different flow rates for providing different residence times. The reaction temperature was varied in the range of 175-210 °C. The eluate containing MA was condensed in a cold water bath and collected.

### 2.5. Analyses and structure elucidation

Growth of *G. oxydans* cells was monitored by measuring optical density (OD) at 620 nm (UV-Vis Spectrophotometer, U1000, Pharmacia Biotech, Sweden). For determination of cell dry weight, cells were recovered from 10 mL broth by centrifugation (10 000 x g for 2 min), and washed using distilled water and dried overnight in an oven at 110 °C.

The concentrations of glycerol and dihydroxyacetone (DHA) were determined by HPLC (Dionex, Ultimate RS 3000 system, USA) equipped with UV/VIS (RS3000 RIT101 Shodex), and an oven (RS 3000). Separation of the compounds was done on an Aminex HPX 87-H ion exclusion chromatographic column (300 mm long, ID 7.8 mm, particle diameter 9 µm, Bio-Rad Laboratories, CA, USA). The column temperature was maintained at 40 °C. Samples from the bioreactor were diluted with MilliQ quality water. Thirty microliter sample was injected into the column and eluted using water:acetonitrile (65:35) containing 0.5 mM sulfuric acid as the mobile phase at a flow rate of 0.5 mL/min, and the eluted products were detected at 270 nm. For determination of acetic acid and succinic acid, the same chromatographic column was used, and peak separation was done using 5 mM sulphuric acid at a flow rate of 0.6 mL/min. Oven temperature was kept at 55 °C and detection was done using RI detector (ERC-inc, Kagawuchi, Japan).

Quantitative analyses of reaction components were performed using gas chromatography (GC, Varian 430-GC, Varian, USA) equipped with FactorFour Capillary column, VF-1ms (Varian, 15M x 0.25mm) and a flame ionization detector. The initial column oven temperature was increased from 50 to 250 °C at a rate of 20 °C/min. The samples, diluted with acetonitrile to a concentration of 0.1-1 g/L, were injected in split injection mode of 10 % at 275 °C. The percent conversion of 2M1,3PD and formation of the products were calculated from the peak areas on the gas chromatograms (Supplementary data). Commercially available 2M1,3PD and MA were used as standards, while 3H2MPA was prepared from reaction of 2M1,3PD using sufficient amount of cells to reach 100 % conversion. All samples were analysed in duplicates and data provided is the mean of two independent runs, and measurements performed in duplicates.

where [S], $V_{\text{max}}$, and $K_m$ are substrate concentration, maximum reaction rate and Michaelis constant, respectively.

The identity of 3H2MPAL was confirmed by reactive extraction with DNPH, which is a general method for confirming aldehydes. To the reaction solution recovered after centrifugation, was added 0.1 M DNPH solution followed by extraction with ethyl acetate. The organic phase was dried and subjected to 13C-NMR analysis (Supplementary data). 3H2MPA was isolated from the reaction mixture by simple filtration followed by water evaporation under reduced pressure. The structure of 3H2MPA was elucidated by 1H and 13C-NMR using 400 MHz NMR (Bruker, UltraShield Plus 400, Germany), (Supplementary data).

### 3. Results and discussion

#### 3.1. Cultivation of *G. oxydans* cells

Acetic acid bacteria are characterised by their ability to catalyse incomplete oxidation of alcohols and sugars to the corresponding aldehydes, ketones and organic acids. This was translated into several industrial processes for production of valuable chemicals such as dihydroxyacetone (DHA) from glycerol, L-sorbose and L-sorboseone from D-sorbitol, and D-glucic acid, 2-keto- and 2,5-diketo- glucic acid (precursor of vitamin C) from glucose using *Glucobacter oxydans* and acetic acid from ethanol using *Acetobacter* spp. In this study, *G. oxydans* DSM 50049 cells obtained by cultivation in a glycerol-based culture medium were used to catalyse the conversion of 2M1,3PD to 3H2MPA. The growth curve of *G. oxydans* showed no lag phase and the microorganism grew logarithmically at maximum specific growth rate ($\mu_{\text{max}}$) of 0.213 h⁻¹ and doubling time ($\tau$ = 3.25 h) during the first 12 hours of cultivation (Fig. 2).

![Fig. 2. Growth curve of *G. oxydans* showing Ln OD₆₂₀ nm for calculation of growth rate (x), % dissolved oxygen / 10 (●), and concentrations of glycerol (▲), DHA (■), acetic acid (*), and succinic acid (○). The values are the mean of two independent runs, and measurements performed in duplicates.](image)

This was accompanied by increase in oxygen uptake rate as shown by the decrease in the dissolved oxygen (%DO) from 90 to 5% of saturation. Complete consumption of glycerol and production of 9.3 g/L DHA was observed after 18 hours of cultivation. Subsequently, the microorganism assimilated the produced DHA via the pentose phosphate pathway and the growth rate was decreased to 0.04 h⁻¹ ($\tau$ = 17.3 h). During this period the %DO was stabilized around 20% and then increased.
Table 1. Results of biotransformation of varying concentrations of 2-methyl-1,3-propanediol by 2.5 mg dry weight/mL \( \text{G. oxydans} \) cells at 29 \(^{\circ}\)C and pH 7.2 during initial 3 h

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrate (2M1,3PD)</th>
<th>Product</th>
<th>ADH reaction</th>
<th>ALDH reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial (g/L)</td>
<td>Remained (M)</td>
<td>3H2MPAL (M)</td>
<td>3H2MPA (M)</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>0.055</td>
<td>0.017</td>
<td>0.000</td>
</tr>
<tr>
<td>2</td>
<td>7.5</td>
<td>0.083</td>
<td>0.031</td>
<td>0.005</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>0.111</td>
<td>0.053</td>
<td>0.009</td>
</tr>
<tr>
<td>4</td>
<td>12.5</td>
<td>0.139</td>
<td>0.071</td>
<td>0.014</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>0.166</td>
<td>0.098</td>
<td>0.019</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>0.222</td>
<td>0.163</td>
<td>0.027</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>0.333</td>
<td>0.278</td>
<td>0.045</td>
</tr>
</tbody>
</table>

Abbreviations: 2M1,3PD: 2-methyl-1,3-propanediol, 3H2MPAL: 3-hydroxy-2-methylpropanal, 3H2MPA: 3-hydroxy-2-methylpropionic acid.

\( ^{a} \)Conversion of 2M1,3PD. \( ^{b} \)Substrate calculated as sum of 3H2MPAL and 3H2MPA used in ALDH reaction.

\( ^{c} \)Conversion to 3H2MPA

3.2. Bioconversion of 2-methyl-1,3-propanediol by \( \text{G. oxydans} \)

3.2.1. Characterization of bioconversion and reusability of cells

Oxidative biotransformation of 2M1,3PD using resting cells of \( \text{G. oxydans} \) was investigated under conditions considered optimal (25-30 \(^{\circ}\)C and pH 6-8) for the organism.\(^{7,16,17}\) The reaction was studied in 1 mL volume at varying substrate concentration (5, 7.5, 10, 12.5, 15, 20 and 30 g/L), pH 7.2 (0.1 M Tris-HCl), 29 \(^{\circ}\)C using 2.6 mg of cell dry weight/mL. Substrate conversion, reaction rate and product formation were followed and are summarised in Table 1. Complete conversion of 5 g/L 2M1,3PD to 3H2MPA was achieved in 9-12 h (not shown), while 98% of 7.5 g/L was converted to 3H2MPA in 24 hours (Fig. 3).

Higher substrate concentrations, 10-12.5 and 15 g/L resulted in 89% and 80.5% conversion, respectively, in 24 h. 3H2MPA and its methyl ester, known as Roche ester, can be used as major building blocks in organic synthesis.\(^{18}\)

Molinari et al.\(^{3,16}\) have earlier reported the oxidative conversion of several aliphatic alcohols such as 1-propanol, 1-butanol, 2-methyl-1-butanol, and 2M1,3PD to the corresponding carboxylic acid mainly by \( \text{Acetobacter} \) spp. Also enantioselective oxidation of (R,S)-2-phenyl-1-propanol to (S)-2-phenylpropanoic acid was achieved at 45-50% molar conversion in 24 h by \( \text{G. oxydans} \).\(^{17}\)

Two membrane-bound enzymes in \( \text{G. oxydans} \), ADH and ALDH are suggested to be involved in the conversion of the diols to the hydroxyacid. The evidence for the involvement of the membrane-bound quinohemoprotein ADH in \( \text{G. oxydans} \) DSM 2003 for biooxidation of 1,2-propanediol to lactaldehyde, was recently obtained in a study using ADH deficient mutant.\(^{19}\) This study also proved the contribution of several ALDHs towards the subsequent oxidation of lactaldehyde to D-(-)-lactic acid.

Fig. 3 shows that the reaction with 7.5 g/L substrate reached over 60% conversion within the first 3 hours; subsequently the reaction rate decreased with time and the substrate transformation was marginal after 8 h. The aldehyde intermediate was totally consumed and the yield of the final product was 98%. The initial reaction rates for ADH and ALDH with different substrate concentrations were calculated based on the reactions for 3 h (Table 1).

As seen in Fig. 4A, the rate for ADH catalysed reaction increased with increase in 2M1,3PD concentration up to 0.2 M and then decreased suggesting substrate inhibition. Product inhibition by the aldehyde intermediate 3H2MPA could be ignored since it was continuously converted to 3H2MPA by ALDH reaction, and hence its concentration was kept sufficiently low (below 0.05 M). The amount of substrate for ALDH catalysed reaction was calculated as sum of residual 3H2MPAL and the product 3H2MPA (Table 1), which showed that the reaction rate was faster than that of ADH reaction at the prevailing substrate concentrations (Fig. 4A).
Kinetic parameters were determined from the Lineweaver–Burk plot (Fig.4B); $K_m$ (M) and $V_{max}$ (µmol/min/mg) values for ADH were 0.122 and 0.265, and for ALDH were 0.059 and 0.213, respectively (Table 1). It seems that the inhibition for the ALDH reaction occurs at lower substrate concentration than that for the ADH reaction. On the other hand, product inhibition was not apparent since 3H2MPA could not be produced at sufficiently high concentration due to the inhibitory effect of the substrate.

Fig. 4. (A) Initial reaction rates of ADH (●) and ALDH (■) calculated from the data collected for 3 h during biotransformation with G. oxydans cells with different substrate concentrations in 0.1M Tris-HCl buffer, pH 7.2 at 28 °C. (B) Lineweaver–Burk plot of ADH (●) ($y = 0.4614x + 3.7809$, $R^2 = 0.9888$) and ALDH reaction (■) $y = 0.2809x + 4.6978$, $R^2 = 0.9559$) using the same data.

Fig. 5. Plots of initial reaction rates versus substrate concentration during biotransformation of 2-methyl-1,3-propanediol with varying cell concentration in 0.1M Tris-HCl buffer, pH 7.2 at 28 °C. The symbols indicate cell dry weight of and 2.5 g/L (▲), 5 g/L (●) and 10 g/L (■).

Different concentrations of 2M1,3PD were treated with varying cell concentrations (2.5-10 mg/mL). The plot of reaction rate versus substrate concentration indicates decrease in specific reaction rate with increase in cell concentration, although showing similar trend of substrate inhibition above 0.2 mM 2M1,3PD at each cell concentration used (Fig. 5).

Recycling of the cells for the biotransformation of 2M1,3PD was investigated. As seen in Fig. 6, while the substrate conversion was efficient during the first run, the activity of the cells during the second run was decreased resulting in a mixture of 28% unconsumed substrate, 33% aldehyde intermediate and 39% acid product. In the subsequent run, only 30% conversion of substrate took place to give 4% acid and 26% aldehyde, suggesting faster inactivation of ALDH.

The loss of activity of the cells is most likely partly due to the limitation of dissolved oxygen during transfer from one batch to the other; acetic acid bacteria are known to be highly sensitive to oxygen limitation. Moreover, the accumulation of the aldehyde intermediate as seen in Fig. 6 would also lead to enzyme inhibition.

3.2.2. Biotransformation in continuous cultivation with cell retention

The oxidative biotransformation of 2M1,3PD was then studied using the G. oxydans cells in a bioreactor integrated with membrane filtration to enable cell retention and recycle (Fig. 7). Initially the reaction was started in a batch mode using 5 g/L 2M1,3PD, which gave 90% conversion in 7.2 h. The reaction was then shifted to a continuous mode at residence time of 33.3 h using a feed of 20 g/L substrate. The concentrations of both substrate and product increased gradually in the outlet stream.

The 3H2MPA concentration in the outlet reached a maximum of 75 g/L after 66.8 hours from the start of the feeding and subsequently the concentration was decreased down to 5.4 g/L when the reaction was terminated. The substrate concentration continued increasing gradually and reached 13.7 g/L at the end of the experiment. The dissolved oxygen was constant during the entire process. Compared to results obtained above with the recycled cells (25 h), the cells in the continuous mode were maintained with higher catalytic activity for a longer period of time (~120 h) and left no residual aldehyde intermediate during the entire reaction time, even though the substrate concentration used was at an inhibitory level for the activity of the cells. This
could be due to more favorable conditions such as oxygen supply and pH control maintained by feeding NH₄OH. Comparison between different processes used industrially or experimentally for acetic acid production from ethanol by Acetobacter spp. showed that industrial bioreactors such as Frings acetator, submerged and semi-continuous are characterized by higher final acid concentration but limited volumetric productivity, while in the high-cell-density bioreactors with cell-recycle, the volumetric productivity was almost 10 times higher despite the 2-3 times lower final acid concentration obtained.

3.3. Production of methacrylic acid by dehydration of 3-hydroxy-2-methylpropionic acid

3H2MPA was subjected to dehydration by passing through a bed of TiO₂. Ti is the ninth most abundant element on Earth; more than 5.28 millions tons being produced in 2008.¹²,²¹ TiO₂ shows low toxicity and has been approved as a food colorant (E-171 in EU legislation).²² Over 95% conversion of 3H2MPA was achieved with over 85% yield of MA as observed by GC analysis (Fig. 8, Supplementary data). The reaction temperature and residence time in the reactor were critical parameters to reach high conversion. At flow rate of 0.1 mL/min, the conversion was slightly increased from 5.7 to 16.3% with increase in temperature from 175 °C to 195 °C, but a drastic increase in the conversion to near 100% was achieved at 210 °C. Meanwhile, at 0.025 mL/min, the degree of conversion was increased at a relatively low temperature, reaching 88% at 195 °C and 100% at 210 °C (Fig. 8). Flow rates faster than 0.1 mL/min at 210 °C gave lower conversion (Fig. 8, Insert). In comparison, dehydration of 3-hydroxypropionic acid was possible at 180 °C.⁴

It seems that 3H2MPA with higher boiling point, 252.9 °C at 760 mmHg (118-120°C at 2 mmHg) required higher reaction temperature for dehydration. Nevertheless, the conversion and selectivity showed much better results compared to dehydration of lactic acid,⁴,⁵ which has been investigated with increasing interest, during past couple of decades, as one possible route for the bio-based production of acrylic acid.²³

However, dehydration of secondary hydroxyl group has proven to be unexpectedly difficult, which is quite resistant toward hydrolysis.²⁵ β-Hydroxy acid was shown to be more easily dehydrated into acrylic acid than α-hydroxyl of lactic acid.²⁶ There is however no report about the dehydration of α-substituted β-hydroxy acid to prepare methacrylic acid.

Conclusions

This study provides an alternative greener route for the synthesis of methacrylic acid from 2-methyl-1,3-propanediol, an inexpensive industrial by-product.⁷,⁹ All reactions were performed in aqueous media without using organic solvents, and separation and/or pre-treatment were not required due to high product yield in each step. The process provides significant environmental advantages over the acetone-cyanohydrin process used for methacrylic production, which is based on fossil gas or oil as raw material, uses corrosive sulfuric acid and toxic HCN, and produces 1.5 tons of ammonium bisulfate as waste per ton of MMA.²⁷ Hence, it provides a good model for comparing life cycle assessment of the new and the traditional routes. The approach is applicable for the selective oxidation of other polyols. Further investigations are however required to develop the system to allow effective conversion of higher concentrations of substrate such as in the process for the production of acetic acid from ethanol using Acetobacter sp.²⁰

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Notes and references

¹² Department of Biotechnology, Center for Chemistry and Chemical Engineering, Lund University, Box 124, SE-221 00 Lund, Sweden. E-mail: Sang-Hyun.Pyo@biotek.lu.se; Fax: +46-46-222-4713; Tel: +46-46-222-4838
¹⁰ Perstorp AB, 284 80 Perstorp, Sweden
⁹ Strategic R&D, Bona AB, Box 210 74, 200 21 Malmö, Sweden
† Electronic Supplementary Information (ESI) available: [S1. Gas chromatograms. S2. GC-MS and NMR data]. See DOI: 10.1039/b000000x/