Synthesis of enhanced catalytic materials in supercritical CO2
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Chapter 5

Selective conversion of dihydroxyacetone to lactic acid by a novel design of a binary catalytic system in batch and fixed-bed set-ups

**ABSTRACT:** Nb$_2$O$_5$ nanoparticles (Nb$_2$O$_5$-scCO$_2$) was applied for the first time as heterogeneous catalyst in the aqueous phase transformation of dihydroxyacetone (DHA) to produce lactic acid in a batch set-up at 100 °C with a weight ratio between catalyst and substrate (R$_{c/s}$) of 0.55. Although a good conversion of DHA was obtained (95%), the low activity of Nb$_2$O$_5$-scCO$_2$ in the conversion of the intermediate intermediate pyruvaldehyde (PVA) prevent this catalyst from achieving high lactic acid yield (43%). To overcome this limitation, we designed a binary catalytic system in which the conversion of DHA to PVA was catalysed by Nb$_2$O$_5$, whereas a second catalyst promoted the conversion of PVA into lactic acid in a sequential step. The optimum catalytic system, considering the catalytic activity in combination with synthetic procedures and cost of catalysts, occurred with a combination of Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$ nanorod (Al$_2$O$_3$-NR), achieving a DHA conversion of 92% with a lactic acid yield of 64% and a lactic acid productivity of 0.382 h$^{-1}$ after 3 h reaction at 100 °C, which is significantly higher than that obtained with only Nb$_2$O$_5$-scCO$_2$ catalyst (0.263 h$^{-1}$) and, that achieved with the reported state-of-the-art catalyst (Nb$_2$O$_5$, 0.240 h$^{-1}$, with a R$_{c/s}$ of 1.11) at 100 °C. The amonts of two catalysts in sequential steps were the same as in the test with Nb$_2$O$_5$-scCO$_2$ alone. Importantly, this catalytic system does not suffer from leaching and can be reused without loss of activity. Based on a detailed characterisation study, the superior catalytic activity of this system is ascribed to: (i) the combination of the acidic properties of Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR, with the latter having a higher concentration of Lewis acid sites and Lewis/Brønsted ratio than the former; (ii) the nonporous, open structure of the Nb$_2$O$_5$ nanoparticles and Al$_2$O$_3$ nanorods, which bring about high surface areas and, enhance the number and accessibility of active sites. The optimum catalytic system consisting of Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR was also tested in the continuous conversion of DHA in a fixed-bed set-up by employing a stacked-bed configuration of catalysts (Nb$_2$O$_5$-scCO$_2$ on top of Al$_2$O$_3$-NR). The
productivity of lactic acid kept above 0.0533 h⁻¹ during 12 h of continuous DHA conversion process under 3.093 mL h⁻¹ feed flow rate, 0.186 g (gh)⁻¹ weight hourly space velocity and 100 °C reaction temperature.
Introduction

The production of lactic acid and its derivatives from bio-based feedstock has drawn great attention considering, the broad range of applications of this compound, and the importance of developing sustainable alternatives to replace fossil resources like petroleum, gas and coal, for the production of valuable chemicals.\textsuperscript{1-3} Lactic acid is widely used as acidulant or emulgator in the food industry and as antibacterial agent in disinfecting products. Moreover, it is the starting compound for the production of different useful chemicals.\textsuperscript{4,5} For example, the polymerisation of lactic acid leads to the formation of polylactic acid, which is used as biodegradable plastic or medical implants.\textsuperscript{6,7} The esterification of lactic acid results in lactates, which find applications as green solvents (\textit{e.g.} methyl lactate, ethyl lactate), emulsifying agents (\textit{e.g.} calcium stearoyl-2-lactate), cosmetic additives (\textit{e.g.} ethyl lactate) and biopharmaceuticals (\textit{e.g.} sodium or calcium lactate).\textsuperscript{1,8} The dehydration of lactic acid yields acrylic acid, the polymerisation product of which is utilised in paints, coating materials and binders.\textsuperscript{4,5,9} Despite the established industrial production route for lactic acid by fermentation of biomass (\textit{e.g.} sucrose, starch, beet juice), the accompanying sustainability issues in this process, including the generation of calcium sulphate waste, multi-step purification and separation steps, overuse of calcium hydroxide to avert bacteria deactivation, stress the importance of developing a sustainable chemical route for producing lactic acid.\textsuperscript{10-14} On this backdrop, the chemo-catalytic production of lactic acid from trioses, dihydroxyacetone (DHA) or glyceraldehyde (GLA), has been actively investigated in recent years.\textsuperscript{15-25} The two C3-sugars can be produced from aerobic oxidation or fermentation of glycerol, the main by-product in the manufacturing of bio-diesel, \textit{i.e.} the transesterification of triglycerides. As shown in Scheme 1, the generally-reported pathway for the transformation of trioses starts with their dehydration to form pyruvaldehyde (PVA), which is catalysed more effectively by Brønsted acid sites.\textsuperscript{15,17} Then, if the reaction is conducted in an aqueous solution, PVA is rehydrated followed by a 1,2-hydride shift step to produce lactic acid.\textsuperscript{15-19} If the reaction is performed in alcoholic medium, PVA undergoes addition of alcohol and rearrangement to form the corresponding alkyl lactate.\textsuperscript{17-25} For the conversion of PVA in to lactic acid or lactates, Lewis acid sites are the proposed active sites and the presence of strong Brønsted acid sites should be avoided because they can lead to the formation of undesirable side products, \textit{e.g.} dialkyl acetal of PVA.\textsuperscript{16-18,24} Different heterogeneous catalysts have been reported for the conversion of trioses to produce lactic acid (\textit{Nb}_2\text{O}_5,\textsuperscript{15} \textit{γ}-\text{AlO(OH)},\textsuperscript{16} \text{Sn-C-MCM-41},\textsuperscript{17} \text{Sn-MWW},\textsuperscript{18} aluminasilicate\textsuperscript{19}) and/or...
lactates (γ-Al₂O₃,⁴⁰ aluminasilicate,¹⁹,²¹ Sn-C-MCM-41,¹⁷ Sn-MWW,¹⁸ Sn-MCM-41,²²,²³ Sn- Beta,²⁴ Sn-montmorillonite²⁵). These catalysts achieved good catalytic performance, whereas displaying some drawbacks at the same time. For example, in the production of lactic acid, γ-AlO(OH) requires high reaction temperature as 140 °C,⁶ Sn-C-MCM-41 composite suffered from a continuous decrease in activity at 110 °C,⁷ coking and irreversible framework damage was reported with aluminasilicate.⁹ As for the production of lactates, γ-Al₂O₃ and Sn-montmorillonite catalysts required relatively high reaction temperatures of ≥140 °C, aluminasilicate displays low selectivity towards lactates,¹⁹ while the large-scale application of Sn-substituted porous structured silicas (Sn-C-MCM-41,¹⁷ Sn-MWW,¹⁸ Sn-MCM-41,²²,²³ Sn-Beta,²⁴ Sn-montmorillonite²⁵) is limited by the use of expensive templates (removed by thermal treatment, not reusable) and tin, and their complicated synthesis procedures.

Scheme 1. Reaction pathway for the conversion of glyceraldehyde or dihydroxyacetone to lactic acid or lactates.

On the other hand, a Nb₂O₅ catalyst prepared by a facile hydrothermal method, was applied in the DHA conversion into lactic acid, achieving a full DHA conversion and a high lactic yield of 80% after 3 h reaction with a weight ratio between the catalyst and substrate (Rₜ/s) of 1.11 at 100 °C, which is the lowest temperature reported for this reaction.¹⁵ Recently, we developed a novel supercritical CO₂ (scCO₂)-assisted precipitation method that allows synthesising Nb₂O₅ nanoparticles (Nb₂O₅-scCO₂), which displayed excellent performance as heterogeneous catalyst in the oxidative coupling of aniline with H₂O₂ to produce azoxybenzene²⁶ and in the conversion of glucose to produce 5-hydroxymethyl furfural (5-HMF) (Chapter 4). In the latter study, lactic acid was observed among the products of glucose conversion, which indicates that Nb₂O₅-scCO₂ is able to catalyse the transformation of DHA to lactic acid. Therefore, with the aim of examining its catalytic activity towards the production of lactic acid from DHA, a catalytic test over Nb₂O₅-scCO₂ catalyst was performed (vide infra). On the other hand, we investigated combining this Nb₂O₅-scCO₂ catalyst with a second catalyst that is relatively
richer in Lewis acid sites with the aim of maximising the yield and selectivity towards lactic acid. We found that the application of a single catalyst or a binary catalytic system, and in the latter case, the way in which two catalysts were combined (physically mixing together or adding at different stages of the reaction), would significantly affect the yield and selectivity of lactic acid.

**Experimental part**

**Materials**

Niobium chloride (NbCl₅, 99%, Sigma-Aldrich), deionised water and ethanol (absolute, Sigma-Aldrich) were used for the preparation of Nb₂O₅. Aluminium tri-sec-butoxide (Al(sBuO)₃ 97%, Sigma-Aldrich), 2-butanol (>99%, Sigma-Aldrich), ammonia aqueous solution (25 wt%, Boom) and absolute ethanol were used to prepare Al₂O₃. Gallium chloride (GaCl₃, 99.999%, Strem Chemicals Inc.), 2-butanol, ammonia aqueous solution and absolute ethanol were used to prepare Ga₂O₃. TiO₂-P25 (Sigma-Aldrich) and H-USY (CBV-600, Zeolyst) were also used as catalysts. For the catalytic tests, 1,3-dihydroxyacetone dimer (97%, Sigma-Aldrich) was used as substrate and deionised water was used as the solvent. In the fixed-bed set-up, SiC (POLY-Service) was used as filling material. PVA solution (40 wt% in H₂O, Sigma-Aldrich), D-(+)-GA (≥98%, Sigma-Aldrich) and lactic acid (90%, Fluka) were used for HPLC calibration.

**Catalyst preparation**

The protocol for the synthesis of Nb₂O₅ nanoparticles was reported in the previous work employing a supercritical CO₂ (scCO₂)-assisted precipitation method. The synthesis of Nb₂O₅ nanoparticles was carried out in a high-throughput scCO₂ reactor unit (Integrated Lab Solutions GmbH). The reactor unit has two modules that can be operated separately: a window reactor, which possesses a borosilicate glass window that allows the observation of the reaction, and a block with 10 batch reactors, which grants 10 reactions being operated simultaneously. Each reactor has a volume of 84 mL with 30 mm internal diameter and can be stirred individually with a magnetic stirrer. The unit can operate at a temperature between 20 and 200 °C and cooled with a water-circulation system. The reactors are pressurised with an ISCO pump and can operate at a CO₂ pressure between 1 and 200 bar. An automated depressurisation protocol and rupture disks prevent risks of overpressure. In a typical synthesis, briefly, 1.0 g NbCl₅ was weighed in a glass vessel equipped with a magnetic stirrer and then, 2 mL ethanol was added dropwise within 5 min with stirring. Afterwards, 10 mL deionised water and 3 mL ethanol was added slowly to the stirred solution over 5 min. Next,
the glass vessel was put into the scCO<sub>2</sub> reactor and stirred vigorously at 40 °C for 3 h. Then, the reactor was closed and, heated up to 80 °C and, pressurised with CO<sub>2</sub> to 140 bar while stirring (this process took around 1.5 h). After reaching these conditions, the reactors were continuously stirred for 3 h. Then, the reactor was cooled down to 20 °C and CO<sub>2</sub> was removed by slow depressurisation with an average rate of 1.5 bar min<sup>-1</sup>. The obtained mixture was aged overnight before being washed thoroughly with deionised water over a Büchner filter until the pH of the filtered water became neutral. Next, the material was dried overnight at 100 °C, followed by a thermal treatment in a calcination oven at 200/400/600/800 °C for 4 h with a heating rate of 2 °C min<sup>-1</sup>. These materials were named Nb<sub>2</sub>O<sub>5</sub>-scCO<sub>2</sub>, Nb<sub>2</sub>O<sub>5</sub>-400°C, Nb<sub>2</sub>O<sub>5</sub>-600°C and Nb<sub>2</sub>O<sub>5</sub>-800°C.

The preparation of Al<sub>2</sub>O<sub>3</sub> nanorods (Al<sub>2</sub>O<sub>3</sub>-NR) followed a reported sol-gel method.27 Firstly, 1.23 g Al(sBuO)<sub>3</sub> (5 mmol) was dissolved by dropwise addition of 1.60 g 2-butanol within 10 min while stirring. The obtained clear solution was stirred for 30 min. Then, an ammonia solution (25% aqueous ammonium hydroxide) diluted with absolute ethanol (1:1 v/v, ~1.6 ml) was added dropwise until a pH ≈ 9-10 was reached. The white turbid gel was stirred for 1.5 h and then heated at 70 °C for 23 h. The obtained white slurry was aged for 3 days at ambient temperature while stirring. Finally, the sample was washed by centrifugation with ethanol and then the obtained solid was dried overnight at 80 °C. The collected white powder was thermally treated at 400 °C for 10 h in a calcination oven with a heating rate of 3 °C min<sup>-1</sup>.

The preparation of Ga<sub>2</sub>O<sub>3</sub> nanorods (Ga<sub>2</sub>O<sub>3</sub>-NR) followed a reported precipitation method.28 Firstly, 2.64 g GaCl<sub>3</sub> (15 mmol) was weighed in a 50 mL round bottom flask under N<sub>2</sub> atmosphere in a glove box considering its high hygroscopic and deliquescent nature. Then, 4.80 g 2-butanol was added dropwise within 5 min while stirring, accompanying with the evolution of HCl and the formation of GaCl<sub>x</sub>(sBuO)<sub>3-x</sub> species. The sample was stirred for 10 min. Then, other 17.85 g 2-butanol was added dropwise over 30 min with continuous stirring. The solution was stirred for further 1 h to obtain a clear solution with a dark orange-brown colour. Next, 7.38 g 2-butanol was mixed with 2.94 g deionised water and then, the obtained solution was added dropwise to this solution in 1 h at a constant rate and under continuous stirring. Then the solution is stirred under room temperature for 3 h before it was heated to 70 °C. After reacting at 70 °C for 23 h, the stirring was stopped and, the reaction mixture was aged at ambient condition for 3 days, finally yielding the Ga<sub>2</sub>O<sub>3</sub> in the form of white precipitate. Then, the solid was separated by centrifugation, thoroughly washed with ethanol for 5 times and then dried overnight in the air.
at 80 °C.

**Characterisation**

N$_2$-physisorption was performed on a Micromeritics ASAP 2420 apparatus. The isotherms were measured at -196 °C and the Brunauer-Emmet-Teller (BET) method was used to calculate the specific surface area. Before N$_2$-physisorption, the samples were degassed under reduced pressure at 120 °C for 12 h (Ga$_2$O$_3$-NR) or at 200 °C (Nb$_2$O$_5$-scCO$_2$, Al$_2$O$_3$-NR, TiO$_2$-P25) for 5 h. X-ray diffraction (XRD) patterns were recorded on a Bruker D8 Phaser diffractometer operating with Cu Kα radiation (λ = 1.5406 Å). The XRD patterns were recorded at 40 kV and 20 mA in the 2θ range of 10-80°. Transmission electron microscopy (TEM) analysis was performed using an electron microscope CM12 (Philips) operating at 120 keV. Before TEM analysis, the powder samples were carefully ground, then dispersed in ethanol by sonication and deposited on a holey-carbon-coated copper grid. FT-IR spectra of adsorbed pyridine were recorded on a Perkin Elmer Frontier FT-IR spectroscopy equipped with deuterated triglycine sulphate detector. The sample was prepared in the form of a self-supporting disc and pre-treated at 200 °C for 4h under reduced pressure before measurements. Saturated pyridine vapour was introduced into the system at room temperature for 30 min. The pyridine desorption was conducted by evacuation at room temperature for 30 min to remove physically adsorbed pyridine, followed by evacuation at different temperatures (100/150/200 °C). The concentrations of Lewis and Brønsted acid sites were calculated based on the areas of their bands (1445 cm$^{-1}$ for Lewis acid site and 1540 cm$^{-1}$ for Brønsted acid sites) and molecular absorption coefficients according to a reported procedure.$^{29}$

**Catalytic reaction**

Batch and fixed-bed set-ups were used for the experimental study of the catalytic production of lactic acid. **Batch set-up:** The batch reactions were performed in sealed pressure-resistant ACE glass tubes equipped with a magnetic stirrer (Fig. S1). The production of lactic acid from DHA or PVA was firstly conducted with one catalyst, *i.e.* Nb$_2$O$_5$-scCO$_2$, Nb$_2$O$_5$-400°C, Nb$_2$O$_5$-600°C, Nb$_2$O$_5$-800°C, Al$_2$O$_3$-NR, Ga$_2$O$_3$-NR, TiO$_2$-P25 or H-USY. 4 mL 0.1 M DHA or PVA aqueous solution and desired amount of catalyst (i.e. 10, 20, or 40 mg) were loaded in the tube. The tube was then dipped slowly into an oil bath with a temperature of 100 °C. After reacting at 100 °C for desired reaction time (DHA as substrate: 3 h, PVA as substrate: 1 h), the tube was taken out and quenched in a water bath. After the tube was cooled down to room
temperature, the reaction mixture was transferred to a centrifuge tube and the solid catalyst was deposited by centrifugation (4000 rpm, 10 min). The supernatant was filtered with a 0.45 μm filter and a small aliquot of the filtrate was taken out using a syringe connected with a needle and diluted around 10 times with water before analysed by an Agilent 1200 high-performance liquid chromatography (HPLC). The HPLC was equipped with a Bio-rad Aminex HPX-87H column and a Waters 410 differential refractive index detector. The HPLC was operated at 60 °C with 5 mM aqueous sulfuric acid as mobile phase (flow rate: 0.55 mL min⁻¹).

Then, the catalytic reactions were performed with binary catalytic system, in which sequential steps were catalysed by Nb₂O₅-scCO₂ and a second catalyst separately. In a typical reaction, 4 mL 0.1 M DHA aqueous solution and 20 mg Nb₂O₅-scCO₂ catalyst were added into the glass tube and the reaction mixture was stirred at 100 °C for 1 h. Then, the glass tube was quenched in a water bath to room temperature and then, the reaction mixtures were centrifuged (4000 rpm, 10 min) to deposit the Nb₂O₅-scCO₂ catalyst. The supernatant was filtered with a 0.45 μm filter. Next, small aliquots of the filtrates were taken out by syringes connected with needle and diluted around 10 times with water and then, analysed by HPLC. Afterwards, the residual filtrate was used as a substrate for the second stage. It should be noted that the amount of the reaction mixture for two reaction stages should keep the same volume (4 mL). Considering the inevitable loss of substrate during the transfer and centrifugation process, 4 mL filtrate was taken from two parallel experiments (~2 mL from each) with same reactants and catalysts performed simultaneously in the first stage. Two parallel reactions show high reproducibility of the results (deviation in the values of DHA conversion and lactic acid yield within ± 1%) and the average values of the DHA conversion and product yields are reported. Next, 20 mg second catalyst (i.e. fresh Nb₂O₅-scCO₂, Al₂O₃-NR, Ga₂O₃-NR, TiO₂-P25, H-USY) was added and then, stirred at 100 °C in the oil bath for another 2 h. Afterwards, the reaction mixture was quenched in a water bath and then, the catalyst was separated by centrifugation and filtration, and the filtrate was analysed by HPLC using the same protocol of the first stage.

The heterogeneity of the optimum catalytic system (i.e. 20 mg Nb₂O₅-scCO₂ for 1 h and 20 mg Al₂O₃-NR for 2 h) was examined by performing leaching test. After preparing the 4 mL reaction mixture for the second stage, the residual filtrates from the first stage was stirred without the addition of any catalyst for another 2 h, after which the filtrate was analysed by HPLC to investigate the heterogeneity of Nb₂O₅-scCO₂ catalyst. The heterogeneity of the Al₂O₃-NR catalyst was examined by another leaching test of the reaction in the second stage. The stirring of the reaction mixture of the second stage (4 mL reaction mixture from the first stage
and 20 mg Al$_2$O$_3$-NR catalyst) was stopped after 1 h reaction at 100 °C and the glass tube was quenched in a water bath and the Al$_2$O$_3$-NR catalyst was separated by centrifugation (4000 rpm, 10 min) and filtration. A small aliquot of the filtrate was directly analysed by HPLC and the residual liquid was allowed to react without catalyst at 100 °C for another 1 h, after which the reaction mixture was analysed by HPLC. It should be noted in HPLC analysis, PVA might have an equilibrium with its (di)hydrate with the presence of sulfuric acid, therefore, the peak we observed for this compound might also represent its (di)hydrate, in the result and discussion part, we only consider them as PVA.

The reusability of this catalytic system was examined by a recycling test. After the separation of the Nb$_2$O$_5$-scCO$_2$ by centrifugation after the first stage reaction, Nb$_2$O$_5$-scCO$_2$ was deposited at the bottom of the centrifuge tube. The supernatant was removed by pipette and the centrifuge tube was filled up with ca. 40 mL deionised water and shaken vigorously. Next, the tube was centrifuged at 4000 rpm for 20 min, after which the supernatant was removed by pipette and the tube was filled with ca. 40 mL deionised water again. This washing process was repeated for 5 times. The Al$_2$O$_3$-NR catalyst obtained after the second stage was also washed with the same procedure for 5 times. Then, the Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR catalysts were regenerated at 200 °C for 4 h before reuse.

**Fixed-bed set-up:** The continuous transformation of DHA to produce lactic acid was carried out in a home-built fixed-bed set-up as shown in Fig. S2. The reactant was fed using a SyringeONE Programmable Syringe Pump (Model No. LA30, HLL Gmbh, Germany). A stainless steel feed line (length: 45 cm) was used to connect the syringe pump and an X-shape connection, the other three sides of which were connected to a thermocouple, a pressure gage and a fixed bed reactor, respectively (Fig. S2). The fixed bed reactor was composed of a stainless steel column with an internal diameter of 8 mm and a height of 70 mm. At the end of the fixed bed reactor, an outlet valve was connected. The feedline and reactor were heated by the twined heating tapes, which are controlled by OMEGA SYNC software with an error of ±0.5°C. Quartz wool was twined outside the heating tapes as a heat isolating layer. In a typical experiment, firstly, the fixed-bed was packed with catalysts. Three different catalyst beds were examined (see Fig. 9), i.e. stacked 50 mg Nb$_2$O$_5$-scCO$_2$ and 100 mg Al$_2$O$_3$-NR (Nb$_2$O$_5$-scCO$_2$ on top of Al$_2$O$_3$-NR, 150 mg Nb$_2$O$_5$-scCO$_2$, 150 mg Al$_2$O$_3$-NR). For the stacked catalyst bed, quartz wool and SiC was placed as isolating layer between the two catalyst beds. SiC, which is proved to inert by performing a catalytic test over it, was used as filling material. Next, the fixed-bed reactor was connected to the X-shape connection and the outlet valve was
connected to the downside of the fixed-bed reactor. Then, a leak test was conducted before the reaction to examine the tightness of the set-up: N₂ feedline was connected at the left side of the feedline and then, the set-up was pressurised with N₂ to 10 bar and then, the pressure was monitored for 1 h to check if there was a pressure drop. Then, the N₂ feedline was disconnected and a 60 mL syringe with an inner diameter of 28.45 mm, which was loaded with 50 mL of 0.1 M DHA and placed on the Syringe pump, was connected to the feedline. Next, the feedline and the reactor were heated up to 100 °C and maintained at this temperature. Then, the feedline and the fixed-bed reactor were filled by DHA solution with a flow rate of 20 mL min⁻¹. After the first drop was seen from the outlet valve (after around 15 min), the flow rate was changed to the reaction flow rate in the range of 1.865-3.713 mL h⁻¹. The flow was granted to stabilise for 30 min before counting the reaction time. The reaction solution was collected from the cold outlet valve every 30 min and analysed by HPLC. The activity of the reaction after 1 h was reported.

Calibration curves using pure compounds were used to determine the concentration of reactants and products in the reaction mixtures analysed by HPLC. Each compound was calibrated using solutions of the pure compound at 5 different concentrations. The conversion (Conv.) of the reactant was calculated with the following formula:

\[
\text{Conv.} \, (\%) = \frac{C_r - C_r,0}{C_r,0} \times 100
\]

in which \( C_r \) is the concentration of reactant after a certain reaction time and \( C_r,0 \) is the initial concentration of the reactant. The yield and selectivity (Sel.) of products were calculated by the following equations:

\[
\text{Yield}_x \, (\%) = \frac{C_{\text{product }, x}}{C_r,0} \times 100
\]

\[
\text{Sel}_x \, (\%) = \frac{\text{Yield of } x}{\text{Conv.}} \times 100
\]

in which \( C_{\text{product }, x} \) is the concentration of product \( x \) after certain reaction time. The productivity (Prod.) of the catalyst was calculated with the following formula:

\[
\text{Prod.} = \frac{\text{mass}_{\text{product }} \, (g)}{\text{mass}_{\text{catalyst }} \, (g) \times \text{reaction time} \, (h)}
\]

Results and discussion

Production of lactic acid in batch set-up

In this work, we firstly studied the catalytic conversion of DHA to lactic acid over a Nb₂O₅
nanoparticles catalyst, which was synthesised by a scCO₂-assisted precipitation method.²⁶ ScCO₂, i.e. CO₂ above its supercritical point: Tₐ = 31.1 °C, pₐ = 73.9 bar, has attracted much attention in assisting the synthesis of nanostructured oxides due to a combination of its properties, which can be tuned by simply adjusting the temperature or pressure of CO₂.³⁰ The good dissolving power of scCO₂ can be utilised to promote the contact of the precursor with different physicochemical features. The extremely low surface tension of scCO₂ and ease separation of CO₂ from the product are beneficial for maximally preserving the formed nanostructures when removing CO₂ from the formed product by slow depressurisation. The synthesised material (Nb₂O₅-scCO₂) displays a nanoparticulate morphology (observed by TEM, see Fig. 1) with a high specific surface area of 340 m² g⁻¹ (obtained by N₂-physisorption, isotherm is not shown) and an amorphous structure (obtained by XRD analysis, see Fig. S3).

![Fig. 1. TEM image of Nb₂O₅-scCO₂ nanoparticles.](image)

The catalytic test over the Nb₂O₅-scCO₂ catalyst was performed under the same reaction conditions used for the state-of-the-art Nb₂O₅ catalyst.¹⁵ After 2 h reaction at 100 °C, 92% DHA can be converted over the Nb₂O₅-scCO₂ catalyst with PVA as the main product (yield: 65%) (Table 1, entry 1). Lactic acid is obtained as side product with a yield of 26%, same as that obtained with a reported amorphous Nb₂O₅ catalyst working under the same reaction conditions, whereas both of them are much lower than that (56%) obtained with the state-of-the-art Nb₂O₅ catalyst.¹⁵ An extension of reaction time to 3 h leads to the virtually complete conversion of DHA over the Nb₂O₅-scCO₂ catalyst (Table 1, entry 2), whereas the obtained 64% yield of lactic acid is still lower than the 80% yield of lactic acid obtained over the state-
of-the-art Nb$_2$O$_5$ catalyst. Additionally, a minor amount of glyceraldehyde (<2%) is detected as an isomerisation product of DHA.

It should be noted that the state-of-the-art Nb$_2$O$_5$ catalyst is in crystalline orthorhombic phase with a surface area of 208 m$^2$ g$^{-1}$, while the Nb$_2$O$_5$-scCO$_2$ catalyst is in amorphous phase. On this backdrop, in order to investigate the influence of Nb$_2$O$_5$ crystallinity on its catalytic activity, the material obtained after the scCO$_2$-assisted precipitation was thermally treated at higher temperatures (400, 600 and 800 °C). Seen from the XRD analysis of the obtained materials (Fig. S3), the Nb$_2$O$_5$-400°C is still in the amorphous phase, while the Nb$_2$O$_5$-600°C and Nb$_2$O$_5$-800°C already turned to the crystalline phase, in pseudohexagonal and orthorhombic phase, respectively. The catalytic tests over these catalysts exhibit that the conversion of DHA and the yield of lactic acid decreased with the increase of thermal treatment temperature of the catalysts (Table 1, entries 3-5), dropping to 54% and 6% over the Nb$_2$O$_5$-800°C catalyst, indicating that the thermal treatment under high temperatures in our synthesis method is detrimental to the catalytic activity of the obtained Nb$_2$O$_5$ materials. The negative effect of increasing the thermal treatment temperature of Nb$_2$O$_5$ catalyst on the activity has also been reported in other reactions, such as the transformation of glucose to 5-HMF (Chapter 4), conversion of xylose to furfural, dehydration of glycerol to acrolein, and oxidative coupling of aniline with H$_2$O$_2$ to azoxybenzene. This can be related to their decreased surface areas as proved by N$_2$-physisorption, i.e. 208, 39 and 2 m$^2$ g$^{-1}$ for Nb$_2$O$_5$-400°C, Nb$_2$O$_5$-600°C and Nb$_2$O$_5$-800°C, respectively, which imply lower amounts of exposed catalytic sites that are accessible to the reactant per gram of these catalysts.

The catalytic tests with lower loadings of Nb$_2$O$_5$-scCO$_2$ catalyst were also conducted, i.e. 20 mg and 10 mg (Table 1, entries 6 and 7). Although the DHA conversion and lactic acid yield decrease at lower catalyst loadings, the productivity of lactic acid increases to 0.257 h$^{-1}$ with 20 mg catalyst (R$_{c/s}$ of 0.55) and to 0.284 h$^{-1}$ with 10 mg catalyst (R$_{c/s}$ of 0.28), which are even slightly higher than that of the state-of-the-art Nb$_2$O$_5$ catalyst (0.240 h$^{-1}$, though with R$_{c/s}$ of 1.11). In the following study, with the aim of keeping sufficiently high lactic acid yield and productivity at the same time, 20 mg is selected as the catalyst loading.
Table 1. The activity of Nb$_2$O$_5$ catalysts in the conversion of DHA to lactic acid$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Reaction time (h)</th>
<th>Catalyst loading (mg)</th>
<th>DHA Conv. (%)</th>
<th>Lactic acid Yield (%)</th>
<th>PVA Yield (%)</th>
<th>GA Yield (%)</th>
<th>Lactic acid Sel. (%)</th>
<th>Lactic acid Prod. (h$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nb$_2$O$_5$-scCO$_2$</td>
<td>2</td>
<td>40</td>
<td>92</td>
<td>26</td>
<td>65</td>
<td>1</td>
<td>28</td>
<td>0.117</td>
</tr>
<tr>
<td>2</td>
<td>Nb$_2$O$_5$-scCO$_2$</td>
<td>3</td>
<td>40</td>
<td>100</td>
<td>64</td>
<td>34</td>
<td>2</td>
<td>64</td>
<td>0.192</td>
</tr>
<tr>
<td>3</td>
<td>Nb$_2$O$_5$-400°C</td>
<td>3</td>
<td>40</td>
<td>99</td>
<td>56</td>
<td>40</td>
<td>3</td>
<td>57</td>
<td>0.169</td>
</tr>
<tr>
<td>4</td>
<td>Nb$_2$O$_5$-600°C</td>
<td>3</td>
<td>40</td>
<td>75</td>
<td>17</td>
<td>52</td>
<td>3</td>
<td>22</td>
<td>0.050</td>
</tr>
<tr>
<td>5</td>
<td>Nb$_2$O$_5$-800°C</td>
<td>3</td>
<td>40</td>
<td>54</td>
<td>6</td>
<td>45</td>
<td>2</td>
<td>11</td>
<td>0.018</td>
</tr>
<tr>
<td>6</td>
<td>Nb$_2$O$_5$-scCO$_2$</td>
<td>3</td>
<td>20</td>
<td>95</td>
<td>43</td>
<td>44</td>
<td>4</td>
<td>45</td>
<td>0.257</td>
</tr>
<tr>
<td>7</td>
<td>Nb$_2$O$_5$-scCO$_2$</td>
<td>3</td>
<td>10</td>
<td>84</td>
<td>24</td>
<td>58</td>
<td>2</td>
<td>28</td>
<td>0.284</td>
</tr>
</tbody>
</table>

$^a$ 4 mL 0.1 M DHA in water as a reactant, desired amount of catalyst (see 4th column), 100 °C, desired reaction time (see 3rd column).

It should be noted that though good conversion of DHA can be achieved over the Nb$_2$O$_5$-scCO$_2$ catalyst a large fraction of PVA is present among the products, indicating that the catalytic activity of Nb$_2$O$_5$-scCO$_2$ catalyst in the conversion of PVA prevent it from obtaining high lactic acid yield. On this backdrop, with the aim further optimising the yield and selectivity towards lactic acid, a catalytic system in which the conversion of DHA was catalysed by Nb$_2$O$_5$-scCO$_2$, whereas the conversion of PVA into lactic acid in a sequential step is catalysed by a second catalyst. A few oxide materials, i.e. Al$_2$O$_3$-NR, Ga$_2$O$_3$-NR, TiO$_2$-P25 and H-USY, were selected as candidates for the second catalyst based on the following considerations. Firstly, all these catalysts have been reported as a catalyst in the (de)hydration and isomerisation reactions of bio-based materials.$^{10,16,19,21,22,34,35}$ Secondly, niobium is not a very abundant element in the earth crust (ca. 0.002%), thus the cost of Nb$_2$O$_5$ limit its application at the industrial-scale production. On the other hand, Al$_2$O$_3$-NR, TiO$_2$-P25 and H-USY display lower cost and higher abundance compared to Nb$_2$O$_5$-scCO$_2$, thus falling into the target of reducing the cost for the catalysts. Additionally, the employed Al$_2$O$_3$-NR and Ga$_2$O$_3$-NR materials possess nonporous and open-structured nanorod morphologies that bring about high surface area and, increases the number and accessibility of surface acid sites.$^{27}$ It should be noted that the relative activity obtained with Ga$_2$O$_3$-NR under the same reaction conditions are consistently better than Al$_2$O$_3$-NR for DHA conversion to ethyl lactates$^{22}$ or for other reactions (e.g. alkene epoxidation$^{27,36}$ and aniline oxidative coupling$^{28}$), which is ascribed to the stronger acidity of
the Ga$_2$O$_3$-NR compared to the Al$_2$O$_3$-NR.

Before applying them in the customised catalytic system, their catalytic activities in the conversion of PVA and DHA were examined and compared to those of the Nb$_2$O$_5$-scCO$_2$. When PVA was used as reactant (see Table 2), Ga$_2$O$_3$-NR catalyst obtains the highest lactic acid yield of 79%, which is 2.6 times of that of Nb$_2$O$_5$-scCO$_2$, followed by Al$_2$O$_3$-NR and H-USY with similar lactic yields (~50%, ~1.6 times of that of Nb$_2$O$_5$). TiO$_2$-P25 is the least active in the conversion of PVA. It should be noted that the total yield of PVA, GA and lactic acid is lower than the conversion of DHA, which might be related to the adsorption of DHA on the surface of these catalyst with relatively high surface areas.

**Table 2.** The activity of different catalysts in the conversion of PVA to lactic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Specific surface area $^b$ (m$^2$/g)</th>
<th>PVA Conv. $^a$ (%)</th>
<th>Lactic Acid Yield (%)</th>
<th>DHA Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nb$_2$O$_5$-scCO$_2$</td>
<td>340</td>
<td>33</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Al$_2$O$_3$-NR</td>
<td>280</td>
<td>56</td>
<td>52</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Ga$_2$O$_3$-NR</td>
<td>224$^b$</td>
<td>82</td>
<td>79</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>TiO$_2$-P25</td>
<td>65</td>
<td>22</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>H-USY</td>
<td>660$^c$</td>
<td>51</td>
<td>48</td>
<td>3</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 4 mL 0.1M PVA solution, 20mg catalyst, 100 °C, 1h. $^b$ The Ga$_2$O$_3$ was outgassed for 12 h at 120 °C before N$_2$-physiisorption, while the others were outgassed for 5 h at 200 °C before N$_2$-physiisorption. $^c$ Data provided by Zeolyst Company.

When DHA was used as the substrate (see Table 3), Al$_2$O$_3$-NR, Ga$_2$O$_3$-NR and TiO$_2$-P25 catalysts exhibit moderate DHA conversion in the range of 41%-67%, which is much lower than that obtained over the Nb$_2$O$_5$-scCO$_2$ catalyst, indicating that amongst the tested catalyst, the Nb$_2$O$_5$-scCO$_2$ is most active in converting DHA. As for the yield of lactic acid, Ga$_2$O$_3$-NR achieves a moderate value of 30%, whereas Al$_2$O$_3$-NR, TiO$_2$-P25 and H-USY catalysts only obtain lower values in the range of 5%-15%, lower than that obtained over the Nb$_2$O$_5$-scCO$_2$ catalyst (43%). On the other hand, PVA only occupies a small percentage ($\leq$7%) in the products of DHA conversion over the Al$_2$O$_3$-NR, Ga$_2$O$_3$-NR and H-USY catalysts, which could be ascribed to the aforementioned higher catalytic activity of these catalysts in the transformation of PVA.
Table 3. Surface areas and activity in the conversion of DHA to lactic acid of different catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>DHA Conv. (%)</th>
<th>Lactic acid Yield (%)</th>
<th>PVA Yield (%)</th>
<th>GA Yield (%)</th>
<th>Lactic acid Sel. (%)</th>
<th>Lactic acid Prod. (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Al₂O₃-NR</td>
<td>56</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td>10</td>
<td>0.034</td>
</tr>
<tr>
<td>2</td>
<td>Ga₂O₃-NR</td>
<td>67</td>
<td>30</td>
<td>7</td>
<td>1</td>
<td>44</td>
<td>0.177</td>
</tr>
<tr>
<td>3</td>
<td>TiO₂-P25</td>
<td>41</td>
<td>15</td>
<td>14</td>
<td>3</td>
<td>37</td>
<td>0.091</td>
</tr>
<tr>
<td>4</td>
<td>H-USY</td>
<td>28</td>
<td>5</td>
<td>7</td>
<td>2</td>
<td>19</td>
<td>0.032</td>
</tr>
</tbody>
</table>

a Reaction conditions: 4 mL 0.1M DHA solution, 20 mg catalyst, 100 °C, 3h.

Next, the conversion of DHA was examined in a binary catalytic system, in which the sequential steps were firstly catalysed by Nb₂O₅-scCO₂ for 1 h, after which the Nb₂O₅-scCO₂ was separated off and one of our selected oxides was added to the reaction mixture to catalyst another 2 h reaction (Table 4 and Fig. 2). The setting of reaction time for the two stages and the loadings of catalysts were optimised in the next step (vide infra). In those catalytic tests, after the first-hour reaction catalysed by Nb₂O₅-scCO₂, 87% of DHA were converted with a lactic acid yield of 17% and a PVA yield of 55%, indicating the high activity of Nb₂O₅-scCO₂ in the conversion of DHA (Table 4, entry 1). A leaching test was performed at the end of this stage immediately to evaluate the heterogeneous nature of the Nb₂O₅-scCO₂ catalyst (Table 4, entry 2). After separating the Nb₂O₅-scCO₂ catalyst, the reaction mixture was stirred without catalyst at 100 °C for another 2 h, no further increase in DHA conversion and lactic acid yield was observed (variations <1%), indicating that no or negligible leaching of active species occurred, which means the Nb₂O₅-scCO₂ catalyst is truly heterogeneous and excludes its effect in the next stage of reaction.

In the next stage, after separating off the Nb₂O₅-scCO₂ catalyst, 20 mg of Nb₂O₅-scCO₂ (fresh), Al₂O₃-NR, Ga₂O₃-NR, TiO₂ or H-USY catalyst was added and tested. The DHA conversions and lactic acid yields of the reactions, in which the Nb₂O₅-scCO₂ were added initially or renewed by fresh Nb₂O₅-scCO₂ catalyst after 1 h of the reaction, show only minor variations (≤2%, Table 1, entry 6 vs. Table 4, entry 3), thus excluding the effect of deactivation of the Nb₂O₅-scCO₂ after the first stage of the reaction on its catalytic activity. The conversions of DHA in the entry employing fresh Nb₂O₅-scCO₂ as the second catalyst are higher than those obtained with one of the other oxides as second catalyst (Table 4, entries 3-7). On the other hand, the yield of lactic acid in the entry with fresh Nb₂O₅-scCO₂ as the second catalyst is lower than those employing Al₂O₃-NR, Ga₂O₃-NR or H-USY as the second catalyst, which is related to the
better catalytic activities in the conversion of PVA over the Al₂O₃-NR, Ga₂O₃-NR or H-USY catalysts (*vide supra*). The combination of Nb₂O₅-scCO₂ and Ga₂O₃-NR shows the highest lactic acid yield of 78% (Table 4, entry 5), followed by the group of Nb₂O₅-scCO₂ and Al₂O₃-NR, with a lactic acid yield of 64% (Table 4, entry 4). The productivity of the catalytic systems with Ga₂O₃-NR or Al₂O₃-NR reach 0.470 h⁻¹ and 0.382 h⁻¹, respectively, both of which are higher than that achieved with Nb₂O₅-scCO₂ catalyst (0.263 h⁻¹).

Though better catalytic activity is obtained with Ga₂O₃-NR, the combination Nb₂O₅-scCO₂ and Al₂O₃-NR is selected as the optimal catalytic system for further study considering: (i) the good catalytic activity obtained with Al₂O₃-NR; (ii) aluminium (*ca.* 8.3% in the earth crust) is a much more abundant (*ca.* 4000 times) and cheaper (*ca.* 300 times) element compared to gallium; (iii) the yield of Al₂O₃ nanorods in the synthesis (>90%) is greatly higher than that of Ga₂O₃ nanorods (~10-15%); (iv) the gallium precursor (GaCl₃) is high hygroscopic and deliquescent chemical that needs to be operated in glove box. The recyclability of this system in consecutive runs was also tested (Fig. 3), demonstrating that the catalysts fully retained their activities and selectivity in 5 consecutive runs.

### Table 4. Conversion of DHA over a different combination of catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>time</th>
<th>DHA Conv. (%)</th>
<th>Lactic acid Yield (%)</th>
<th>PVA Yield (%)</th>
<th>GA Yield (%)</th>
<th>Lactic acid Sel. (%)</th>
<th>Lactic acid Prod (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 b</td>
<td>1</td>
<td>Nb₂O₅-scCO₂</td>
<td>1h</td>
<td>87</td>
<td>17</td>
<td>55</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>2h</td>
<td>87</td>
<td>18</td>
<td>55</td>
<td>4</td>
<td>21</td>
<td>0.110</td>
</tr>
<tr>
<td>3</td>
<td>Nb₂O₅-scCO₂</td>
<td>2h</td>
<td>97</td>
<td>44</td>
<td>48</td>
<td>1</td>
<td>45</td>
<td>0.263</td>
</tr>
<tr>
<td>Stage 2 c</td>
<td>4</td>
<td>Al₂O₃-NR</td>
<td>2h</td>
<td>92</td>
<td>64</td>
<td>7</td>
<td>1</td>
<td>69</td>
</tr>
<tr>
<td>5</td>
<td>Ga₂O₃-NR</td>
<td>2h</td>
<td>91</td>
<td>78</td>
<td>4</td>
<td>1</td>
<td>86</td>
<td>0.470</td>
</tr>
<tr>
<td>6</td>
<td>TiO₂-P25</td>
<td>2h</td>
<td>88</td>
<td>37</td>
<td>35</td>
<td>2</td>
<td>42</td>
<td>0.222</td>
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<tr>
<td>7</td>
<td>H-USY</td>
<td>2h</td>
<td>88</td>
<td>54</td>
<td>14</td>
<td>1</td>
<td>61</td>
<td>0.322</td>
</tr>
</tbody>
</table>

*Reaction conditions: 4 mL 0.1M DHA solution, 20 mg catalyst, 100 °C, 3 h. b In the first stage (1 h), Nb₂O₅-scCO₂ was used as a catalyst for all entries. c In the second stage (2 h), different materials were used as catalysts, except for entry 18, which doesn’t employ a second catalyst. d Fresh Nb₂O₅-scCO₂ was used as the second catalyst.*

Additionally, the way in which two catalysts were combined (physically mixing together or adding at different stages of the reaction) were investigated. We firstly conducted one experiment in which after the first-hour reaction catalysed by Nb₂O₅-scCO₂, the tube was quenched in water to room temperature and then, Al₂O₃-NR catalyst was added directly to the reaction mixture without the separation of Nb₂O₅-scCO₂ (Table 5). Next, the reaction mixture
was stirred at 100 °C for 2 h. This experiment displays a DHA conversion of 92% with a lactic acid yield of 55% and a PVA yield of 37%. The catalytic activity of a physical mixture of 20 mg Nb$_2$O$_5$-scCO$_2$ and 20 mg Al$_2$O$_3$-NR was also examined at 100 °C for 3 h (Table 5, entry 2). The conversion of DHA reaches 80%, with a lactic acid yield of only 24% and a PVA yield of 56%. The catalytic activities of these two experiments are lower compared to that obtained with two catalysts working separately, which might be related to: (i) an external diffusion problem in the mixture of two catalysts, (ii) the adsorption of reactant on the catalysts, for example, PVA on Nb$_2$O$_5$-scCO$_2$ or DHA on Al$_2$O$_3$-NR, which will hinder their further conversion, thus stressing the importance of using our designed catalytic system.

**Fig. 2.** Comparison of lactic acid yields obtained with different catalytic systems. Reaction conditions: 4 mL 0.1 M DHA solution, 20 mg catalyst, 100 °C, 3 h. For the columns with two parts, the lower column represents the lactic acid yield obtained in the first-hour reaction over the first catalyst, the upper column indicates the lactic acid yield achieved in the follower 2 h reaction over the second catalyst.
Fig. 3. Reusability test of the optimum catalytic system consists of Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR, the red part in column represents the lactic acid yield in the first hour catalysed by the Nb$_2$O$_5$-scCO$_2$ catalyst, while the yellow column indicates the lactic acid yield in the following two hours catalysed by the Al$_2$O$_3$-NR.

Table 5. Conversion of DHA to lactic acid over different catalytic systems $^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>DHA Conv. (%)</th>
<th>PVA Yield (%)</th>
<th>GA Yield (%)</th>
<th>Lactic Acid Yield (%)</th>
<th>Lactic Acid Sel. (%)</th>
<th>Prod (h$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20mg Nb$_2$O$_5$-scCO$_2$ 1 h</td>
<td>20mg Nb$_2$O$_5$-scCO$_2$ + 20mg Al$_2$O$_3$-NR 2 h</td>
<td>92</td>
<td>13</td>
<td>1</td>
<td>55</td>
<td>60</td>
<td>N.A.</td>
</tr>
<tr>
<td>2</td>
<td>20mg Nb$_2$O$_5$-scCO$_2$ + 20mg Al$_2$O$_3$-NR 3h</td>
<td>-</td>
<td>80</td>
<td>8</td>
<td>0</td>
<td>24</td>
<td>30</td>
<td>0.144</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 4 mL 0.1M DHA solution, desired amount of catalyst 100 °C, 3 h.

With the purpose of further maximising the yield of lactic acid, the reaction time of two stages were optimised while keeping the whole reaction time as 3 h (Table 6). The highest lactic acid yield (64%) was still obtained with the combination of Nb$_2$O$_5$-scCO$_2$ for 1 h and Al$_2$O$_3$-NR for the following 2 h. It was observed that the conversion of DHA reached 87% after 1 h reaction, very close to its highest conversion of 95% after 3 h (Table 1, entry 6). Therefore, this timing is the best to change the catalyst, which could grant high conversion of DHA and enough reaction time for the second catalyst to catalyse the conversion of PVA to lactic acid. Next, the Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR loadings were optimised while keeping the reaction time for two
stages as 1 h and 2 h, respectively (Table 7). For the first stage of reaction, the DHA conversion, PVA and lactic acid yields increase with the increasing of Nb$_2$O$_5$-scCO$_2$ loading from 10 mg to 20 mg. At the second stage of the reaction, the reactivity increases with the increase of Al$_2$O$_3$-NR loading from 10 mg to 20 mg in terms of DHA conversion and lactic acid yield, while if we further increase the Al$_2$O$_3$-NR loading to 30 mg, the reactivity starts to decrease (Table 7, entries 3 and 6).

**Table 6.** Optimisation of reaction time for two stages in the conversion of DHA to lactic acid$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Stage 1$^b$</th>
<th>Stage 2$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DHA Conv. (%)</td>
<td>Lactic Acid Yield (%)</td>
</tr>
<tr>
<td>1</td>
<td>0.5h</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>1h</td>
<td>87</td>
</tr>
<tr>
<td>3</td>
<td>1.5h</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>2h</td>
<td>91</td>
</tr>
</tbody>
</table>

Reaction conditions: 4mL 0.1M DHA solution, 20 mg catalyst, 100 °C, 3h. $^a$ In stage 1, Nb$_2$O$_5$-scCO$_2$ was employed as catalyst. $^c$ In stage 2, Al$_2$O$_3$-NR was employed as catalyst.

**Table 7.** Optimisation of catalyst loading for two stages in the conversion of DHA to lactic acid$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Stage 1$^b$</th>
<th>Stage 2$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Catalyst 1</td>
<td>DHA Conv. (%)</td>
</tr>
<tr>
<td>1</td>
<td>Nb$_2$O$_5$-scCO$_2$-10mg</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>Nb$_2$O$_5$-scCO$_2$-10mg</td>
<td>87</td>
</tr>
<tr>
<td>3</td>
<td>Al$_2$O$_3$-NR-10mg</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td>Al$_2$O$_3$-NR-20mg</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>Al$_2$O$_3$-NR-30mg</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>Nb$_2$O$_5$-scCO$_2$-20mg</td>
<td>91</td>
</tr>
<tr>
<td>7</td>
<td>Nb$_2$O$_5$-scCO$_2$-20mg</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>Ga$_2$O$_3$-NR-10mg</td>
<td>76</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 4mL 0.1M DHA solution, a desired amount of catalyst, 100 °C, 3h. $^b$ The reaction time of stage 1 is 1 h. $^c$ The reaction time of stage 2 is 2 h. $^d$ The productivities of the entries in which two stages employ the different amount of catalyst are not available (N.A.).

**Characterisation**

The superior catalytic performance of our binary catalytic system compared to the single Nb$_2$O$_5$-scCO$_2$ catalyst was discussed based on the physicochemical properties of the catalysts. The amorphous Nb$_2$O$_5$-scCO$_2$ material possesses nanoparticulate morphology (Fig. 1) with a
high surface area of 340 m$^2$ g$^{-1}$. The TEM analysis of the Al$_2$O$_3$-NR catalyst also displays a nanostructure with both nanorod and irregular particle morphologies (Fig. 4). N$_2$ physisorption of Al$_2$O$_3$-NR demonstrates a specific surface area of 280 m$^2$ g$^{-1}$ (Fig. 5a). The isotherm belongs to type IV and has a hysteresis loop at high $p/p^0$, indicating the presence of inter-particle pores at the mesoporous scale. The XRD pattern of Al$_2$O$_3$-NR (Fig. 5b) shows two distinct peaks located at 45.9° and 66.6°, which are assigned to (400) and (440) planes of γ-Al$_2$O$_3$ phase. No peaks for boehmite were observed, indicating that 400 °C was sufficient to convert amorphous (γ-AlO(OH) structure into a crystalline (γ-Al$_2$O$_3$) structure.

Apart from the morphology and structural properties, the acid properties of the catalysts (type, strength and number of acid sites) is also very important in determining the conversion of DHA and the yield and selectivity to lactic acid. A few works state that Brønsted acid site is more beneficial for the dehydration step, while the Lewis acid site is more effective for the following rehydration and rearrangement steps.$^{15,17,18}$ Additionally, the existence of strong Brønsted acid sites would lead to the formation of undesirable side products, which should be averted maximally.$^{16-18,24}$ Herein, the acid properties of two catalysts were evaluated through the analysis of adsorbed pyridine on the catalyst with FT-IR spectroscopy, which can determine the type and strength of surface acid sites. Fig. 6 reveals the FT-IR spectra of the pyridine adsorbed on Al$_2$O$_3$-NR and Nb$_2$O$_5$-scCO$_2$ at different temperatures (100/150/200 °C), the latter of which has been discussed in Chapter 4 and is shown here for comparison. The spectra for the Al$_2$O$_3$-NR display the same bands typical of pyridine adsorbed on Lewis or Brønsted acid sites as we observed on the spectra for the Nb$_2$O$_5$-scCO$_2$, whereas the intensities of the peaks recorded at the same wavenumber and temperature on two

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materials are quite different. On the spectra of \( \text{Al}_2\text{O}_3\)-NR, the bands appearing at 1445 cm\(^{-1}\) and 1573 cm\(^{-1}\) are assigned to stretching vibrations of coordinately bonded pyridine on Lewis acid sites;\(^{37,38}\) small bands at 1540 cm\(^{-1}\) correspond to the stretching vibrations of pyridinium ions formed over Brønsted acid sites;\(^{37,39}\) while the bands at 1486 cm\(^{-1}\) are related to the stretching vibration of pyridine adsorbed on both Lewis and Brønsted acid sites.\(^{40,41}\)

**Fig. 5.** (a) \( \text{N}_2 \) physisorption isotherm and (b) XRD pattern for \( \text{Al}_2\text{O}_3\)-NR catalyst. The asterisks denote the position of the diffraction peaks of the (400) and (440) planes of \( \text{Al}_2\text{O}_3\)-NR.

**Fig. 6.** FTIR spectra of pyridine adsorption for (a) \( \text{Al}_2\text{O}_3\)-NR and (b) \( \text{Nb}_2\text{O}_5\)-scCO\(_2\) catalysts recorded at different temperatures.
Both catalysts possess mainly Lewis acid sites, as illustrated by their high L/B ratios, which is much higher over the Al₂O₃-NR catalyst (Table 8). At each desorption temperature, the concentration of Lewis acid sites on Al₂O₃-NR is higher than that on Nb₂O₅-scCO₂, on the other hand, the concentration of Brønsted acid sites on Nb₂O₅-scCO₂ shows advantage (Table 8, Fig. 7 and S4). On the spectra of both catalysts, the intensities of the peaks, which are associated with the amounts of adsorbed pyridine, gradually decrease by increasing the desorption temperature. However, a fraction of pyridine is still retained at 200 °C, indicating the existence of moderate-strong Lewis and Brønsted acid sites on both catalysts (Table 8 and Fig. 7). Based on these analysis, the higher activity of Nb₂O₅-scCO₂ in the conversion of DHA into PVA is ascribed to its higher concentration of Brønsted acid sites, while the higher activity of Al₂O₃-NR in the conversion of PVA into lactic acid is related to its higher concentration of Lewis acid sites. Therefore, the combination of Nb₂O₅-scCO₂ and Al₂O₃-NR in our optimum catalytic system perfectly matches the proposed requirement for an ideal catalytic system for the one-pot catalytic conversion of DHA into lactic acid.

Table 8. Concentration of Lewis (LAS) and Brønsted acid sites (BAS) that bind pyridine at 100, 150 and 200 °C on Nb₂O₅-scCO₂ and Al₂O₃-NR catalysts.

<table>
<thead>
<tr>
<th>Desorption T (°C)</th>
<th>Al₂O₃-NR</th>
<th></th>
<th></th>
<th>Nb₂O₅-scCO₂</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LAS (μmol g⁻¹)</td>
<td>BAS (μmol g⁻¹)</td>
<td>L/B ratio</td>
<td>LAS (μmol g⁻¹)</td>
<td>BAS (μmol g⁻¹)</td>
<td>L/B ratio</td>
</tr>
<tr>
<td>100</td>
<td>179.6</td>
<td>3.1</td>
<td>57.9 &lt;0.1</td>
<td>119.5</td>
<td>16.7</td>
<td>7.2 0.1</td>
</tr>
<tr>
<td>150</td>
<td>158.4</td>
<td>2.7</td>
<td>58.7 &lt;0.1</td>
<td>97.5</td>
<td>15.0</td>
<td>6.5 0.2</td>
</tr>
<tr>
<td>200</td>
<td>141.9</td>
<td>2.4</td>
<td>59.1 &lt;0.1</td>
<td>76.3</td>
<td>10.1</td>
<td>7.6 0.1</td>
</tr>
</tbody>
</table>

*These data was already reported in the previous chapter.

Additionally, Ga₂O₃-NR also possesses nanorod morphology (Fig. 8) and a sufficiently high surface area of 224 m² g⁻¹ (though the values of surface areas for different oxides employed in this work are not comparable due to their different pre-treatment temperature). Although we didn’t analyse the acidity of the Ga₂O₃-NR catalyst, it can be anticipated that Ga₂O₃-NR possesses a stronger Lewis acidity than Al₂O₃-NR catalyst due to its stronger metallicity nature, thus leading to a better catalytic performance with Ga₂O₃-NR catalyst compared to Al₂O₃-NR catalyst (Table 4 entries 4 vs. 5, Table 7 entries 1 and 7), though the practical application of this catalyst is limited by its relatively high cost, low catalyst yield and utilisation of an active precursor in its synthesis (*vide supra*).
**Fig. 7.** Concentration of Lewis (LAS) and Brønsted acid sites (BAS) that bind pyridine at 100, 150 and 200 °C on Al$_2$O$_3$-NR and Nb$_2$O$_5$-scCO$_2$ catalysts.

**Fig. 8.** TEM images for the Ga$_2$O$_3$-NR catalyst.

**Continuous production of lactic acid in a fixed-bed set-up**

Furthermore, our optimum catalytic system consisting of Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR for the production of lactic acid was also tested in a fixed-bed set-up by using a stacked configuration of two catalysts (50 mg Nb$_2$O$_5$-scCO$_2$ on top of 100 mg Al$_2$O$_3$-NR, see Fig. 9a). The performance of a catalyst in fixed-bed is essential to evaluate the viability of scale up our design catalytic system from lab to industry. The fixed-bed reaction displays some assets when compared to batch set-up reactions: (i) continuous operation; (ii) minimising the possibility of destroying the catalyst by vigorous stirring; (iii) no need to separate catalyst after the reaction; (iv) low
operating cost. However, we should not ignore its drawbacks, including inefficient heat transfer, possibility of forming channelling, difficulty in changing the catalyst and cleaning of the set-up.\textsuperscript{42-44} The catalytic test were conducted using the same DHA solution (0.1 M) with a flow rate of 2.475 mL h\textsuperscript{-1} (equals to a WHSV of 0.149 g (gh\textsuperscript{-1}) at 100 °C for 5 h. The weight ratio or the weight hourly space velocities (WHSV) between Nb\textsubscript{2}O\textsubscript{5}-scCO\textsubscript{2} and Al\textsubscript{2}O\textsubscript{3}-NR was set as 1:2 based on the ratio of 1:2 between the reaction time of Nb\textsubscript{2}O\textsubscript{5}-scCO\textsubscript{2} and Al\textsubscript{2}O\textsubscript{3}-NR in the batch set-up. With a stacked-bed configuration of two catalysts, we achieved a continuous DHA conversion of 68-73%, a lactic acid yield of 33-38%, and lactic acid productivity of 0.048-0.057 h\textsuperscript{-1} during a 5 h reaction, and the values of DHA conversion and lactic acid yield show good stability (Fig. 10, deviations in the values within ±2.5%). This catalytic performance was obviously higher than that obtained with 150 mg of Nb\textsubscript{2}O\textsubscript{5}-scCO\textsubscript{2} or Al\textsubscript{2}O\textsubscript{3}-NR as catalysts (Fig. 9b and c), in consistent with the result obtained in the batch set-up (Fig. 10).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig9.png}
\caption{Schematic representation of the loading of (a) stacked two catalysts (Nb\textsubscript{2}O\textsubscript{5}-scCO\textsubscript{2} on top of Al\textsubscript{2}O\textsubscript{3}-NR), (b) Nb\textsubscript{2}O\textsubscript{5}-scCO\textsubscript{2}, and (c) Al\textsubscript{2}O\textsubscript{3}-NR.}
\end{figure}
With the purpose of further optimising the productivity of lactic acid, the effect of feed flow rate in the fixed-bed reactor was studied by varying the flow rate in the range of 1.856-3.713 mL h\(^{-1}\), corresponding to the WHSV in the range of 0.112-0.223 g (gh)\(^{-1}\). Considering the good stability of the stacked-bed catalytic system as seen in Fig. 11, the average values of DHA conversion, lactic acid yield and productivity were used for discussion. When a lower flow rate of 1.856 mL h\(^{-1}\) was applied, the average conversion of DHA was enhanced to 72% and the average yield of lactic acid was enhanced to 39% compared to those obtained with the flow rate of 2.475 mL h\(^{-1}\) (average DHA conversion: 71%, average lactic acid yield: 35%). On the other hand, when higher flow rates were applied, DHA conversions and lactic acid yields decrease with the increase in flow rate. Especially at the highest applied flow rate of 3.713 mL h\(^{-1}\), the catalytic activity drops dramatically, which might be related to the possible formation of channeling as observed during the reaction process that a small proportion of catalyst was flushed out the fixed-bed. Among the four flow rates tested, the average productivity of lactic acid over a 5 h reaction reaches the highest (0.057 h\(^{-1}\)) with a flow rate of 3.093 mL h\(^{-1}\), whereas the lowest (0.042 h\(^{-1}\)) with a flow rate of 3.7125 mL h\(^{-1}\) (Fig. 12).

The operational stability of continuous transformation of DHA to produce lactic acid by stacked-bed catalyst (50 mg Nb\(_2\)O\(_5\)-scCO\(_2\) on top of 100 mg Al\(_2\)O\(_3\)-NR) in a fixed bed reactor was evaluated by extending the reaction time to 12 h. During the 12 h of continuous DHA conversion process under 3.093 mL h\(^{-1}\) feed flow rate or 0.186 g (gh)\(^{-1}\) weight hourly space velocity and 100 °C reaction temperature, the conversion of DHA kept over 63 %, the yield of
lactic acid retained over 29%, and the productivity of lactic acid kept over 0.0533 h⁻¹, indicating a good stability of our designed catalytic system in a fixed-bed set-up (see Fig. 13).

**Fig. 11.** DHA conversion and lactic acid yield over catalysts with a stacked-bed configuration (50 mg Nb₂O₅-scCO₂ on top of 100 mg Al₂O₃-NR) using a fixed-bed set-up at 100 °C with a different flow rate in the range of 1.856-3.713 mL h⁻¹, corresponding to different WHSV in the range of 0.112-0.223 g (gh)⁻¹.

**Fig. 12.** The productivity of lactic acid over catalysts with a stacked-bed configuration (50 mg Nb₂O₅-scCO₂ on top of 100 mg Al₂O₃-NR) using a fixed-bed set-up at 100 °C with a different flow rate in the range of 1.856-3.713 mL h⁻¹, corresponding to different WHSV in the range of 0.112-0.223 g (gh)⁻¹.
Fig. 13. Stability test with a stacked-bed configuration of catalysts (50 mg Nb$_2$O$_5$-scCO$_2$ on top of 100 mg Al$_2$O$_3$-NR) using a fixed-bed set-up at 100 °C with a flow rate of 3.093 mL h$^{-1}$ and a WHSV of 0.186 g (gh)$^{-1}$.

Conclusion

We successfully developed a binary catalytic system for the conversion of dihydroxyacetone (DHA) to produce lactic acid, in which the sequential steps are catalysed by Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR catalyst. This catalytic system overcame the problem associated with the weak activity of Nb$_2$O$_5$-scCO$_2$ catalyst in catalysing the intermediate product pyruvaldehyde (PVA) to lactic acid. Particularly, this catalytic system was evaluated in both batch and fixed-bed reactors and the trends obtained in two set-ups keep consistent. In batch set-up, this binary catalytic system reached an enhanced lactic acid productivity of 0.382 h$^{-1}$ compared to that obtained with only Nb$_2$O$_5$-scCO$_2$ catalyst (0.263 h$^{-1}$) and those of any other heterogeneous catalyst previously reported for this reaction. The cost of the catalytic system is also reduced by employing a relatively cheaper and more abundant Al$_2$O$_3$ catalyst. The superior catalytic performance of our design system is ascribed to the perfect combination of acid sites of Nb$_2$O$_5$-scCO$_2$ (stronger Brønsted acidity) and Al$_2$O$_3$-NR (stronger Lewis acidity) catalysts, which facilitate the conversion of DHA and PVA, respectively, and to the nonporous nanoparticle and nanorod morphologies of Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR catalysts, which bring about high surface area, enhanced amount and accessibility of active acid sites. Furthermore, Nb$_2$O$_5$-scCO$_2$ and Al$_2$O$_3$-NR catalysts show good reusability towards the production of lactic acid through a simple washing step and a mild thermal treatment at 200 °C. It should be noted that when Ga$_2$O$_3$-NR was used as the second catalyst, the lactic acid yield reaches 78% with a productivity of 0.470 h$^{-1}$, though the practical application of this catalyst is limited by its relatively high cost and low catalyst yield in the synthesis. In a fixed-bed set-up, with a
stacked-bed configuration (Nb$_2$O$_5$-scCO$_2$ on top of Al$_2$O$_3$-NR), this binary catalytic system achieved stable lactic acid productivity of above 0.0533 h$^{-1}$ in a continuous 12 h reaction at 100 °C at a weight hourly space velocity of 0.186 g (gh)$^{-1}$. The good stability of the catalysts at the reaction temperature and good reusability of the catalysts in both batch and fixed-bed set-ups was beneficial for the long-term operation and industrial-scale production of lactic acid from a bio-based platform molecule by our catalytic system. In a broader context, the design of this customised catalytic system is also of practical importance for the catalytic production of valuable chemicals in which multistep reactions are involved.
Supporting information

**Fig. S1.** ACE pressure tube (maximum 10 bar at 120 °C).

**Fig. S2.** Picture of fixed bed set-up. Here the heating tapes that twined around the X-shape connection and the fixed bed reactor during the reaction are not shown with the aim of showing the fixed bed reactor.
**Fig. S3.** XRD patterns of Nb$_2$O$_5$ materials prepared with different thermal treatment temperatures.

**Fig. S4.** Normalised concentrations of different acid sites on Al$_2$O$_3$-NR and Nb$_2$O$_5$-scCO$_2$ catalysts at different temperatures.
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