Chapter 4

Efficient conversion of glucose and other carbohydrates into 5-hydroxymethyl furfural over niobium oxide nanoparticles as a heterogeneous catalyst

ABSTRACT: A series of Nb$_2$O$_5$ materials were synthesised by supercritical CO$_2$ (scCO$_2$)-assisted precipitation methods and were applied as heterogeneous catalysts in the conversion of glucose and other carbohydrates to 5-{hydroxymethyl} furfural (5-HMF). Different synthesis parameters were screened, by varying co-solvent and pressure of the scCO$_2$-assisted precipitation and temperature of the thermal treatment, with the purpose of optimising the catalytic activity of the Nb$_2$O$_5$ materials. The Nb$_2$O$_5$-scCO$_2$ catalyst, which was prepared with ethanol as co-solvent, under a CO$_2$ pressure of 140 bar, and with 200 °C as thermal treatment temperature, led to the highest conversion of glucose (73%) with the highest selectivity towards 5-HMF (48%) after 3 h of reaction. Notably, the catalyst achieved this good performance under a relatively low reaction temperature (120 °C) and with a relatively low catalyst loading (weight ratio between catalyst and substrate, R$_{C/S}$ = 1) compared to those used in the literature. The Nb$_2$O$_5$-scCO$_2$ catalyst could be reused in consecutive runs without obvious loss of activity by simple washing and regeneration. When compared to a reference catalyst prepared without scCO$_2$ (Nb$_2$O$_5$-Ref) or to commercial Nb$_2$O$_5$ (Nb$_2$O$_5$-Comm), the Nb$_2$O$_5$-scCO$_2$ catalyst prepared with scCO$_2$ demonstrates enhanced catalytic activity in terms of both glucose conversion and 5-HMF selectivity, which could be related to its high surface area (340 m$^2$ g$^{-1}$), amorphous structure, nanoparticulate morphology (with particle size <10 nm), higher concentration of acid sites as characterised by N$_2$-physisorption, XRD, TEM and FT-IR of adsorbed pyridine, respectively. Additionally, the Nb$_2$O$_5$-scCO$_2$ catalyst also displayed high activity also for other carbohydrates (e.g. fructose, sucrose, cellobiose), though lower 5-HMF yields were obtained compared that achieved from glucose.
1. Introduction

Driven by the quick depletion of petroleum resource, the utilisation of renewable bio-based resources to produce valuable chemicals, such as 5-(hydroxymethyl) furfural (5-HMF), lactic acid and lactates, has become of great importance from the sustainable development point of view.\(^1\)-\(^4\) 5-HMF is an important platform chemical, from which more than 175 derivatives and 20 high-performance polymers can be obtained.\(^5\)-\(^7\) One key application of 5-HMF lies in its oxidation, leading to the formation of 2,5-diformylfuran, which is used in the production of pharmaceuticals and functional polymers,\(^8\) and to the formation of 2,5-furandicarboxylic acid. The latter is utilised in the commercial-scale production of polyethylene furanoate (PEF) as a substitute for polyethylene terephthalate (PET), which is widely used in soft drink bottles and other food packaging.\(^9\) The current production route of 5-HMF involves the catalytic selective dehydrogenation of fructose in the presence of a mineral acid (e.g. sulfuric acid hydrochloric acid).\(^6\),\(^10\) However, the high cost of this process, which is related to the expensive production of fructose from enzymatic isomerisation of glucose syrup and to the use of a homogeneous catalyst (not reusable), limits the large-scale production of 5-HMF.\(^10\) Under this backdrop, the direct production of 5-HMF from an abundant monosaccharide as glucose (the main constituent of cellulose) over a heterogeneous catalyst (reusable) is preferred. For this purpose, many acidic heterogeneous catalysts have been developed, such as metal oxides, zeolites, metal sulphates, metal phosphates and sulphonated resins.\(^1\),\(^2\),\(^5\) Two reaction pathways have been reported: the cyclic pathway that proceeds via ring intermediates and the acyclic pathway that proceeds via chain intermediates.\(^1\),\(^11\)-\(^14\) Most heterogeneous catalysts are reported to follow the first pathway, which involves the isomerisation of glucose to fructose, followed by the dehydration of fructose to 5-HMF (see Scheme 1).\(^5\),\(^15\)-\(^23\) The Lewis and/or Brønsted acid sites on these catalysts are responsible for catalysing the involved steps. It is generally proposed that Lewis acid sites are more active for the isomerisation step, while Brønsted acid sites catalyse the dehydration step.\(^15\),\(^19\)-\(^23\) However, no general consensus has been reached on which type (Lewis or Brønsted) and strength of acid sites is the most suitable for each of the involved steps.

Over the past years, extensive researches have been devoted to developing efficient and economically feasible solid acid catalysts for the conversion of glucose to 5-HMF (an overview of representative catalysts is shown in Table S1).\(^15\)-\(^33\) These reported catalytic systems achieved good performance but still display some drawbacks. For example, the synthesis of some catalysts (e.g. Nb\(_2\)O\(_5\)-H\(_2\)O,\(^16\) NbPO,\(^19\) Ta\(_2\)O\(_5\),\(^25\) TaPO,\(^27\) Al-MCM-41,\(^30\) SnPO,\(^31\) Sn-Beta\(^32\)
and S-ZrO$_2$-SBA-15$^{33}$) required expensive templates, which are not reusable as they were removed during the thermal treatment process of the synthesis. Some catalysts required high catalyst loading in the catalytic reaction ($R_{\text{C:S}} > 1$, e.g. H$_3$PO$_4$-Nb$_2$O$_5$·nH$_2$O,$^{17}$ SnPO$_4$,$^{22}$ H$_3$PO$_4$-TiO$_2$,$^{28}$ Al-MCM-41,$^{30}$ Sn-

![Scheme 1](image)

**Scheme 1.** Glucose conversion to 5-HMF via cyclic pathway (purple arrows represent side reactions).

Beta$^{32}$, or relatively high reaction temperature (≥150 °C, e.g. Nb$_2$O$_5$,$^{15}$ H$_3$PO$_4$-Nb$_2$O$_5$·nH$_2$O,$^{18,21}$ Nb-C,$^{23}$ Nb-Al$_2$O$_3$,$^{24}$ Ta$_2$O$_5$,$^{25,26}$ TaPO,$^{27}$ H$_3$PO$_4$-TiO$_2$,$^{29}$ Al-MCM-41,$^{30}$ Sn-Beta$^{32}$), which is not preferable from an economic point of view, and would enhance the likelihood of forming humins, thus increasing the difficulty of purifying the 5-HMF product. Some catalysts employed high boiling point organic solvent as reaction medium (e.g. dimethylsulfoxide, $N,N$-dimethylformide and ionic liquid), which also pose challenge for 5-HMF separation.$^{24,31}$

In this work, we aimed at developing a heterogeneous catalyst that can be prepared by a low-cost and facile method and can achieve good catalytic performance in the conversion of glucose to produce 5-HMF under mild reaction conditions. Nb$_2$O$_5$ was selected as a proper candidate catalyst considering its strong acidic character. Nb$_2$O$_5$ consists of interconnected NbO$_4$ tetrahedra and NbO$_6$ octahedra with varying extents of structural distortions and defects.$^{34}$ The exposed oxygen-deficient Nb centres can act as Lewis acid sites, while the Nb-OH groups can act as Brønsted acid sites, with acid strength dependent on coordination state, but the clear relationship between structure and acidity is not established yet.$^{15,34}$ Until now, Nb-based$^{15-22,24}$ have been widely applied as heterogeneous catalysts in the production of 5-
HMF from many bio-based compounds, including monosaccharides as glucose and fructose,\textsuperscript{16,17,19,21,22,24} disaccharides as sucrose and cellobiose,\textsuperscript{15,19} and polysaccharides as starch, cellulose and inulin.\textsuperscript{18,21} Another reason for choosing Nb\textsubscript{2}O\textsubscript{5} as catalyst lies in that in our previous work, in which we have developed a novel and facile supercritical CO\textsubscript{2} (scCO\textsubscript{2})-assisted precipitation method for the synthesis of Nb\textsubscript{2}O\textsubscript{5} nanoparticles, which led to enhanced catalytic activity in the aniline oxidative coupling with H\textsubscript{2}O\textsubscript{2} to produce azoxybenzene.\textsuperscript{35} The formation of nanoparticles is desirable for application a heterogeneous catalyst since the nanoparticulate morphology normally brings about a high surface area and a nonporous open structure that enhance the amount and accessibility of active sites, thus leading to enhanced catalytic performance.\textsuperscript{36,37} To the best of our knowledge, the application of Nb\textsubscript{2}O\textsubscript{5} nanoparticles in the production of 5-HMF has not been reported yet. Therefore a series of Nb\textsubscript{2}O\textsubscript{5} materials were synthesised by our scCO\textsubscript{2}-assisted precipitation methods exploiting different synthetic parameters, and were applied as heterogeneous catalysts in the conversion of glucose to produce 5-HMF.

2. Experiment and characterisation

Materials

Niobium chloride (NbCl\textsubscript{5}, 99%, Sigma-Aldrich), deionised water and absolute ethanol (J. T. Baker) were used for the preparation of Nb\textsubscript{2}O\textsubscript{5} nanoparticles through our scCO\textsubscript{2}-assisted method and the reference catalyst (Nb\textsubscript{2}O\textsubscript{5}-Ref). Absolute ethanol, 1-butanol (\geq 99.5%, Sigma-Aldrich), ethyl acetate (99.8%, Sigma-Aldrich) and propylene carbonate (99.5%, Acros) were tested as co-solvents in the scCO\textsubscript{2}-assisted synthesis. For the production of 5-HMF, glucose (Sigma-Aldrich), fructose (Sigma-Aldrich), sucrose (Sigma-Aldrich) and cellobiose (Carbosynth) were used as reactants. Deionised water and methyl isobutyl ketone (MIBK, \geq 99\%, Sigma-Aldrich) were used as reaction solvents.

Catalyst preparation

A series of Nb\textsubscript{2}O\textsubscript{5} materials were synthesised by scCO\textsubscript{2}-assisted precipitation method exploiting different synthetic parameters, including the co-solvent and pressure of CO\textsubscript{2} in the precipitation steps, and the temperatures in the thermal treatment. The synthesis was carried out in a high-throughput scCO\textsubscript{2} reactor unit from Integrated Lab Solutions (ILS) with two modules: a window reactor and a block with 10 batch reactors, which can be operated separately. Each reactor has a volume of 84 mL with 30 mm internal diameter and can be stirred individually with a magnetic stirrer. The reactors are heated with electric heating
elements with a temperature range between 20-200 °C and cooled with a water-circulating system. The reactors are pressurised by an ISCO pump with a pressure range between 1 to 200 bar. The reactor unit is equipped with automated closing valves that prevent the risk of contamination between the reactors. The CO₂ depressurisation is controlled by an automated protocol and rupture disks allow avoiding risks of overpressure.

In the synthesis of the Nb₂O₅ materials, 1.0 g NbCl₅ was firstly dissolved in 2 mL ethanol with stirring for 5 min, with HCl being formed as gas product as a consequence of the concomitant formation of niobium ethoxide species. Then, a mixture of 10 mL H₂O and 3 mL co-solvent (i.e. ethanol, 1-butanol, ethyl acetate or propylene carbonate) were added slowly to the solution over 5 min while stirring. Afterwards, the reaction mixture was transferred to the scCO₂ reactor and stirred vigorously at 40 °C for 3 h. Next, the reaction mixture was heated to 80 °C and pressurise with CO₂ to 140 bar (this process takes around 1.5 h). After reacting under these conditions for 3 h under continuous stirring, the reactor was cooled down to 20 °C and slowly depressurised with an average rate of 1.5 bar min⁻¹. The obtained white slurry was aged overnight and then washed thoroughly with water by filtration with water in a Büchner filter until the filtered water become neutral. Next, the obtained material was dried overnight at 100 °C and thermally treated in a calcination oven at 200 °C for 4 h with a heating rate of 2 °C min⁻¹. The catalysts prepared with this method were named as Nb₂O₅-scCO₂, Nb₂O₅-scCO₂-BuOH, Nb₂O₅-scCO₂-ETA or Nb₂O₅-scCO₂-PC, indicating the employment of ethanol, 1-butanol, ethyl acetate and propylene carbonate as co-solvent in their synthesis, respectively. The as-prepared Nb₂O₅ material with ethanol as co-solvent was also thermally treated at 400 °C and 600 °C for 4 h with a heating rate of 2 °C min⁻¹, and the obtained materials were named Nb₂O₅-400°C and Nb₂O₅-600°C, respectively. A reference catalyst was prepared with a lower CO₂ pressure of 80 bar (named as Nb₂O₅-80bar), while the procedure and the other synthetic parameters were kept the same as that used for Nb₂O₅-scCO₂. Another reference catalyst (Nb₂O₅-Ref) was prepared by a similar precipitation method without the use of scCO₂.

In brief, 1.0 g NbCl₅ was dissolved in 2 mL ethanol by stirring within 5 min. Then, a mixture of 10 mL deionised water and 3 mL ethanol were added slowly in 5 min, after which the solution was stirred at 40 °C for 3h. Next, the mixture was heated up to 80 °C and stirred for another 3 h. After that, the obtained product was aged, dried, washed and thermally treated with the same procedure as that used for Nb₂O₅-scCO₂.

Characterisation
N$_2$-physisorption isotherms were recorded on a Micromeritics ASAP 2420 apparatus at -196 °C. The samples were degassed under reduced pressure at 200 °C for 5 h before N$_2$ adsorption. X-ray diffraction patterns (XRD) were recorded on a Bruker D8 Phaser diffractometer operating with Cu Kα radiation ($\lambda = 1.5406$ Å). The XRD patterns were measured in the 2θ range between 10 and 80°. FT-IR spectra of adsorbed pyridine were recorded on a Perkin E Frontier FT-IR spectrometer equipped with a deuterated triglycine sulphate (DTGS) 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 desorption of pyridine was carried out by evacuation at room temperature for 30 min to remove physisorbed 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 collected bands (1445 cm$^{-1}$ for Lewis acid sites and 1540 cm$^{-1}$ for Brønsted acid sites) and on the molecular absorption coefficients according to a reported procedure.$^{38}$

**Catalytic tests**

The catalytic tests for the production of 5-HMF were performed in sealed pressure-resistant ACE glass tubes as shown in Fig. S1. For the production of 5-HMF, a typical reaction mixture consisting of 40 mg glucose, 4 mL solvent ($V_{\text{water}}: V_{\text{MIBK}} = 1:3$) and 40 mg catalyst was weighed in the glass tube. The organic solvent (MIBK) is immiscible with water; therefore a biphasic reaction medium can be formed. Then, the glass tube was closed with a screw cap and placed into an oil bath with a temperature of 120 °C. After reacting with continuous stirring for 3 h, the reaction was quenched by immersing the glass tube in a water bath at room temperature. Then, the reaction mixture was transferred into a centrifuge tube and centrifuged at 4000 rpm for 10 min. The reaction mixture showed two obvious liquid phases after centrifugation. The upper organic phase was taken directly with a syringe, filtered through a 0.45 μm filter and analysed without dilution by means of a Thermo Trace gas chromatography (GC) equipped with a Restek Stabilwax-DA column (30 m length, 320 μm ID). The lower aqueous phase was filtered with a 0.45 μm filter and a small aliquot of the filtrate was taken using a syringe, diluted around 10 times with water and then analysed using an Agilent 1200 high-performance liquid chromatography (HPLC) with a Bio-rad Aminex HPX-87H column. The HPLC was operated at 60 °C using a Waters 410 differential refractive index detector and a UV detector with 5 mM aqueous sulphuric acid as the mobile phase (flow rate: 0.55 mL min$^{-1}$). The injection volume of the sample was set at 5 μL. The products in the aqueous phase were
also analysed by mass spectra which were recorded on an Orbitrap XL mass spectrometer (Thermo Fisher Scientific) with electrospray ionisation (ESI) in the negative mode. The ESI-MS was operated with the following parameters: capillary voltage at 3.2 kV, sample cone voltage at 40 V, vaporiser temperature of the source at 150 °C, N₂ as cone gas with a flow rate of 20 L h⁻¹, injection volume of 5 μL.

For the catalyst recycle test, after the removal of the liquid from the reaction mixture, ca. 40 mL deionised water was added to the centrifuge tube and the tube was shaken vigorously. Next, the tube was centrifuged at 4000 rpm for 20 min. Next, the supernatant was removed by pipette and ca. 40 mL deionised water was added again. This washing procedure was repeated 5 times, after which the catalyst was dried at 100 °C overnight and thermally treated in a calcination oven at 200 °C for 4 h with a heating rate of 2 °C min⁻¹ before reuse.

For the leaching test, after 30 min of reaction, the stirring was stopped. The glass vessel was quenched in a water bath. Then, the reaction mixture was transferred to a centrifuged tube and centrifuged at 4000 rpm for 10 min to deposit the catalyst, after which the supernatant was filtrated with a filter placed on the syringe. Small aliquots of the filtrate in both organic and aqueous phase were analysed by GC and HPLC, respectively. The remaining filtrate was stirred for another 2.5 h, after which the organic and aqueous phase in the solution were analysed by GC and HPLC, respectively.

Calibration curves using pure compounds were used to determine the concentration of reactants and products in the reaction mixtures analysed by GC and 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:

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

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 a certain reaction time. The productivity (Prod.) of the catalyst was calculated with the following formula:
\[
\text{Prod.} = \frac{\text{mass}_{\text{product}} (g)}{\text{mass}_{\text{catalyst}} (g) \times \text{reaction time} (h)}
\]

The C balance of the reaction is calculated by the following formula:

\[
\text{C balance} (\%) = 100 - \text{Conv.} + \text{Yields}_{\text{quantifiable products}}
\]

3. Results and discussion

Preliminary screening of the catalysts and correlation with the characterisation results

A series of Nb₂O₅ materials were prepared by scCO₂-assisted precipitation method exploring different synthetic parameters and were then applied as heterogeneous catalysts in the conversion of glucose to produce 5-HMF with the aim of enhancing the yield and productivity of 5-HMF under relatively mild conditions (120 °C). CO₂ in the supercritical state can be a favourable medium for preparing highly-active nanostructured materials owing to (i) high solvating power, which can promote the contacts of the precursors with different physicochemical properties; (iii) its high diffusivity and low surface tension, which is beneficial for the maximally preserving the nanostructures when removing CO₂ from the system (by simple software-controlled depressurisation); (iii) relatively easily-accessible supercritical point (\(T_c = 31.1 \, ^\circ\text{C}, \, p_c = 73.9 \, \text{bar}\)) and low toxicity. When scCO₂ is applied in the synthesis, the formation of the materials typically proceeds differently than in conventional solvents, and various nanomaterials can be obtained employing different synthetic parameters, which provides a strategy to tune the physicochemical properties of the materials (e.g. morphology, surface area, acidity) with the aim of enhancing their catalytic performance.

The first synthetic parameter that we investigated in our study of the synthesis of Nb₂O₅ materials by a scCO₂-assisted precipitation method was the co-solvents used in combination with scCO₂. The co-solvent would change the dissolving ability of CO₂. A good co-solvent is anticipated to promote the formation of a single-phase containing scCO₂ and the reactants, thus eliminating the interphase transport limitations in multiphase reactions. Ethanol was used as co-solvent in the previous work to prepare Nb₂O₅ nanoparticles with a scCO₂-assisted method. In this work, we evaluated three other co-solvents, i.e. 1-butanol, ethyl acetate and propylene carbonate. These solvents were chosen to examine the effects on the properties of the synthesised Nb₂O₅ catalyst of (i) lowering the polarity (1-butanol vs. ethanol); (ii) or the aprotic/protic nature of the co-solvent (ethyl acetate vs. ethanol); (iii) or applying a co-solvent with a CO₂-moiety within the structure (propylene carbonate). Selected physicochemical
properties of these co-solvents are listed in Table S2. It should be noted that solvents with environmental greenness and, operational simplicity and safety are preferred in the synthesis. According to the CHEM21 guide for ranking the safety and greenness of solvents,\textsuperscript{43} ethanol, 1-butanol and ethyl acetate are labelled as recommended solvents, while propylene carbonate is recognised as a problematic solvent.

Table 1. Specific surface areas and catalytic activities in the conversion of glucose to 5-HMF of \( \text{Nb}_2\text{O}_5 \) catalysts \( ^a \)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>BET Surface area (m(^2)/g)</th>
<th>Glucose Conv. (%)</th>
<th>5-HMF Product yields (%)</th>
<th>5-HMF sel. (%)</th>
<th>5-HMF Prod. (h(^{-1}))</th>
<th>C balance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( \text{Nb}_2\text{O}_5\text{-scCO}_2 )</td>
<td>340</td>
<td>73</td>
<td>36 4 3 1 3</td>
<td>48</td>
<td>0.084</td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>( \text{Nb}_2\text{O}_5\text{-scCO}_2\text{-BuOH} )</td>
<td>292</td>
<td>66</td>
<td>28 3 4 0 2</td>
<td>43</td>
<td>0.065</td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>( \text{Nb}_2\text{O}_5\text{-scCO}_2\text{-ETA} )</td>
<td>228</td>
<td>69</td>
<td>30 2 3 0 3</td>
<td>43</td>
<td>0.070</td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td>( \text{Nb}_2\text{O}_5\text{-scCO}_2\text{-PC} )</td>
<td>242</td>
<td>72</td>
<td>30 4 4 0 3</td>
<td>41</td>
<td>0.070</td>
<td>69</td>
</tr>
<tr>
<td>5</td>
<td>( \text{Nb}_2\text{O}_5\text{-80bar} )</td>
<td>306</td>
<td>70</td>
<td>29 6 5 0 2</td>
<td>41</td>
<td>0.068</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>( \text{Nb}_2\text{O}_5\text{-400°C} )</td>
<td>208</td>
<td>64</td>
<td>29 5 3 0 2</td>
<td>46</td>
<td>0.068</td>
<td>75</td>
</tr>
<tr>
<td>7</td>
<td>( \text{Nb}_2\text{O}_5\text{-600°C} )</td>
<td>39</td>
<td>13</td>
<td>0 2 2 0 0</td>
<td>0</td>
<td>0.000</td>
<td>91</td>
</tr>
<tr>
<td>8</td>
<td>( \text{Nb}_2\text{O}_5\text{-Ref} )</td>
<td>305</td>
<td>69</td>
<td>25 3 2 0 3</td>
<td>36</td>
<td>0.058</td>
<td>64</td>
</tr>
<tr>
<td>9\textsuperscript{c}</td>
<td>( \text{Nb}_2\text{O}_5\text{-scCO}_2 )</td>
<td>340</td>
<td>86</td>
<td>18 2 2 0 1</td>
<td>21</td>
<td>0.042</td>
<td>37</td>
</tr>
</tbody>
</table>

\( ^a \) Reaction conditions: 40 mg glucose, 4 mL solvent (V\(_\text{water} \): V\(_\text{MIBK} \) = 1:3), 40 mg catalyst, 120 °C, 3 h. \( ^b \) The C balance is calculated based on the amount of unconverted glucose and quantifiable products listed in the table. For the formula, see experiment part. \( ^c \) This entry is tested in 4 mL monophasic aqueous solution.

All the prepared \( \text{Nb}_2\text{O}_5 \) materials were obtained with high yields in the synthesis (>90%). These \( \text{Nb}_2\text{O}_5 \) materials were tested as heterogeneous catalysts in the conversion of glucose to 5-HMF under mild reaction conditions, \textit{i.e.} relatively low reaction temperature (120 °C) and low catalyst loading (R\(_c/s\) = 1) (Table 1, entries 1-4). A biphasic solution was used with the aim of in-situ extracting 5-HMF from the water phase to organic phase, thus preventing undesirable hydrolysis of 5-HMF to form formic acid and levulinic acid (Scheme 1). It should be noted that the amount of employed organic solvent should be maximally limited from the economic point of view, and the use some high boiling point organic solvent (\textit{e.g.} dimethylsulfoxide, N,N-dimethylformide, ionic liquids) should be carefully considered due to the difficult separation of 5-HMF with these solvents.\textsuperscript{5} Under this backdrop, water-immiscible MIBK was employed as organic phase with a water-to-MIBK ratio of 1:3 in our study. After 3 h reaction, all \( \text{Nb}_2\text{O}_5 \) catalysts gave good glucose conversions (66%-73%) and moderate selectivity towards 5-HMF (41%-48%), with relatively small differences in the catalytic
performance between them. The repetition tests of these reactions show high reproducibility (deviation in the glucose conversion and 5-HMF yield values within ±1.5%), which means the difference between the activities of the most active catalyst and others is still meaningful.

The highest glucose conversion (73%), 5-HMF yield (35%) and selectivity (48%) were achieved over the same catalyst, Nb₂O₅-scCO₂, which was prepared with ethanol as co-solvent (Table 1, entry 1). The side products of this entry consist of mannose (yield: 4%) and fructose (yield: 3%), which derived from the isomerisation of glucose, DHA (yield: <1%), which stemmed from the retro-aldol reaction, and lactic acid (yield: 3%), which originated from the isomerisation of DHA (Scheme 1). It should be noted that two common reported side products of this reaction, i.e. formic acid and levulinic acid, formed by the hydrolysis of 5-HMF, were not observed in any of our catalytic tests, probably due to the relatively low reaction temperature (120 °C), and due to the utilisation of a water-immiscible solvent as MIBK. Based on the total yield of these quantifiable products and the amount of unconverted glucose, the C balance over the Nb₂O₅-scCO₂ can be estimated (see formula in experimental part), which is 74%, higher than that (60%) estimated over a H₃PO₄/Nb₂O₅·nH₂O catalyst for this reaction working at 120 °C with a Rₛ/s of 10 in an aqueous solution. The higher carbon balance in our system is probably related to the use of a biphasic reaction mixture and to its ability to operate at relatively mild temperature. The rest C (26% in total) is generally referred as unknown species in literature, which can be divided into two parts. The first part consists of those present in the HPLC chromatogram but cannot be identified and quantified due to the overlap of their peaks. ESI-Mass spectrometry allowed identifying these products (Fig. S2) as anhydroglucoses (Mₜ = 162.14 and Mₜ = 144.12, formed by the dehydration of glucose), erythrose and glycolaldehyde (Mₜ = 120.10 and 60.05, formed by the retro-aldol reaction of fructose) and pyruvaldehyde (Mₜ = 72.06, formed by the dehydration of DHA). Their total yield was estimated to be roughly in the 10-15% range (for the calculation method, see the supporting information). The second kind of products is related to the humins formed by polymerisation of 5-HMF with itself or with glucose or fructose, which cannot be detected by HPLC or ESI-MS. The undesirable yield of humins over the Nb₂O₅-scCO₂ is calculated to be roughly in the 11-16% range.

With the aim of correlating the catalytic performance of these materials with physicochemical properties, the specific surface areas, morphology and crystallinity of the Nb₂O₅ catalysts were measured by N₂-physisorption, TEM and XRD, respectively (Table 1 and Fig. S3). The optimum Nb₂O₅-scCO₂ catalyst prepared with ethanol as co-solvent possesses the highest specific
surface area (340 m$^2$ g$^{-1}$) among all catalysts, followed by Nb$_2$O$_5$-scCO$_2$-BuOH (292 m$^2$ g$^{-1}$), Nb$_2$O$_5$-scCO$_2$-PC (242 m$^2$ g$^{-1}$) and Nb$_2$O$_5$-scCO$_2$-ETA (228 m$^2$ g$^{-1}$). The surface areas of these materials is higher than those of Nb$_2$O$_5$ materials synthesised by different routes but with same or even lower thermal treatment temperatures (60-200 °C), which range between 142-184 m$^2$ g$^{-1}$.\textsuperscript{15,17,22}

For catalytic applications, the higher surface area is always desirable when combined with a non-porous, open structure that enables unhindered access of reactants to the active sites. This is the case for the Nb$_2$O$_5$-scCO$_2$ catalyst, which consists of nanoparticles with size < 10 nm as proven by TEM analysis (Fig. 1). Characterisation by XRD proved that all the catalysts are amorphous materials (see Fig. S3). This is a consequence of the low thermal treatment temperature (200 °C) employed in their synthesis, whereas the formation of crystalline Nb$_2$O$_5$ structure requires higher temperature.\textsuperscript{47} Though the use of different co-solvent causes a change in the specific surface area of the materials, it does not affect significantly the catalytic performance of these Nb$_2$O$_5$ materials, which can be related to the proportion of co-solvent (3 mL) in the reaction mixture (~14 mL, not including CO$_2$) that might be insufficient to change significantly the properties of the synthetic environment. Based on this preliminary catalytic screening catalyst, the synthetic parameter of the Nb$_2$O$_5$-scCO$_2$, which displays the best catalytic performance and the highest specific surface area, was used as a starting point for the further optimisation of the synthetic parameters.

Then, with the aim of exploring more accessible and economical conditions, the synthesis of Nb$_2$O$_5$ was conducted under a lower CO$_2$ pressure (80 bar) while keeping the other synthetic parameters the same as those used for the Nb$_2$O$_5$-scCO$_2$. The physical properties of scCO$_2$ can be tuned by changing the pressure of CO$_2$, with a decrease of pressure at constant temperature leading to lower density and a more gas-like behaviour. A catalytic test over Nb$_2$O$_5$-80bar shows a slightly lower glucose conversion of 70% and a 5-HMF yield of 29% (Table 1, entry 5) when compared to those of the Nb$_2$O$_5$-scCO$_2$ catalyst, which might be related to the slightly lower specific surface area of Nb$_2$O$_5$-80bar (306 m$^2$ g$^{-1}$). Also the Nb$_2$O$_5$-80bar catalyst displays an amorphous structure (XRD pattern not shown).
Next, with the aim of investigating the effect of Nb$_2$O$_5$ crystallinity on its catalytic performance, the thermal treatment temperature in the synthesis was tuned \((i.e. \ 200 \ °C, 400 \ °C \text{ and } 600 \ °C)\), while keeping the other synthetic parameters constant. An elevated thermal treatment temperature typically leads to a high degree of order in Nb$_2$O$_5$.\cite{34,48} Indeed, XRD analysis proves that the Nb$_2$O$_5$-400°C still displays an amorphous structure, while the Nb$_2$O$_5$-600°C exhibits a pseudohexagonal crystalline phase (see Fig. S4).\cite{47} However, the thermal treatment at higher temperature leads to a decrease in the surface area, 208 and 39 m$^2$ g$^{-1}$ for Nb$_2$O$_5$-400°C and 39 m$^2$ g$^{-1}$ for Nb$_2$O$_5$-600°C. The activity of the catalyst was also negatively affected by increasing the thermal treatment temperature as the glucose conversions dropped to 64% and 13%, while the and 5-HMF yields decreased to 29% and 0% over the Nb$_2$O$_5$-400°C and Nb$_2$O$_5$-600°C catalysts, respectively (Table 1, entries 6, 7). The destructive effect of increasing the thermal treatment temperature of Nb$_2$O$_5$ catalyst on the activity has been reported not only for this reaction,\cite{16} but also for other reactions catalysed by Nb$_2$O$_5$ catalysts, such as conversion of xylose to furfural\cite{49} dehydration of glycerol to acrolein,\cite{50} and aniline oxidative coupling with H$_2$O$_2$ to azoxybenzene.\cite{35} This trend is related to the lower surface areas of Nb$_2$O$_5$ thermally treated at higher temperatures, which imply lower amounts of exposed catalytic sites that are accessible to the reactant per gram of these catalysts.\cite{50}

In summary, the synthetic parameters that lead to the Nb$_2$O$_5$ material with the best catalytic performance in the conversion of glucose into 5-HMF involve the use of ethanol as co-solvent, a supercritical condition with a CO$_2$ pressure of 140 bar and a thermal treatment (after the scCO$_2$-assisted precipitation process) temperature of 200 °C. Importantly, a leaching test for
the Nb$_2$O$_5$-scCO$_2$ demonstrated the truly heterogeneous nature of the catalyst (no further increase of the glucose conversion and 5-HMF yield in 3 h after separating off the catalyst after 0.5 h of reaction). After washing and regeneration by mild thermal treatment of 200 °C, the catalyst can be reused at least in 5 consecutive runs without obvious loss in activity (see Fig. 2). Additionally, regeneration of catalyst at 105 °C is also tested, which is not working since this temperature is not high enough to remove the deposited species on the catalyst as observed by the yellow-light brown colour of the catalyst after regeneration, whereas fresh Nb$_2$O$_5$ should be only slightly yellow (Note: the change in colour of the catalyst can be qualitatively related to the deposition of products on the catalyst).

![Reusability test of the Nb$_2$O$_5$-scCO$_2$ catalyst in the conversion of glucose into 5-HMF. Reaction conditions: 40 mg glucose, 40 mg Nb$_2$O$_5$-scCO$_2$ catalyst, 4 mL solvent (V$_{\text{water}}$: V$_{\text{MIBK}}$ = 1:3), 120 °C, 3h.](image)

Then, the catalytic performance of Nb$_2$O$_5$-scCO$_2$ prepared under scCO$_2$ conditions was compared to that of a reference catalyst prepared with a similar precipitation method but without the involvement of scCO$_2$ (Nb$_2$O$_5$-Ref). The Nb$_2$O$_5$-Ref catalyst displays lower glucose conversion (66%), lower 5-HMF yield (25%) and selectivity (36%) compared to those obtained with Nb$_2$O$_5$-scCO$_2$ (Table 1, compare entry 8 to entry 1). The catalytic performance of Nb$_2$O$_5$-scCO$_2$ is also compared to other reported heterogeneous catalysts that worked at the same reaction temperature (120 °C) and used a mixture of water and an organic solvent as reaction medium. The differences in the R$_c$/s of these works are taken into account by...
calculating the 5-HMF productivity (in g_{5-HMF} per g_catalyst per hour). The Nb_{2}O_{5}-scCO_{2} catalyst displays a 5-HMF productivity of 0.084 h^{-1} after 3 h reaction, which is around 7 times higher than that obtained Nb-WO_{3} (0.012 h^{-1}),\textsuperscript{22} slightly higher than that obtained with H_{3}PO_{4}-TiO_{2} catalyst (0.072 h^{-1}), and lower than that achieved with SnPO (0.271 h^{-1}), which however used expensive template in the synthesis and, expensive and hard-separational ionic liquid as solvent in the catalytic tests. Another Nb-based catalyst, \textit{i.e.} H_{3}PO_{4}-Nb_{2}O_{5}·nH_{2}O,\textsuperscript{17} was also tested for the glucose conversion to 5-HMF, but in a monophasic aqueous solution, achieving a 5-HMF productivity of 0.012 h^{-1}, which is much lower than that obtained over our Nb_{2}O_{5}-scCO_{2} in a monophasic aqueous solution (0.042 h^{-1}, Table 1, entry 9). It should be noted that the 5-HMF yield in the aqueous solution is only half of that obtained in the biphasic H_{2}O/MIBK solution (Table 1, entry 1), thus confirming the anticipated importance of employing an organic phase in achieving high 5-HMF yield and productivity. The catalytic performance of the Nb_{2}O_{5}-scCO_{2} in the H_{2}O/MIBK biphasic solution was further investigated by performing a kinetic study until all the reactant was almost converted (Fig. 3). The glucose conversion increased until reaching nearly full conversion (97% after 14h). The maximum yield of 5-HMF (46%) was obtained at 9 h, after which it slightly dropped to 42% at 14 h, even though the conversion of glucose kept increasing, possibly due to the preferential formation of humins as indicated by the visual observation of the colour of the reaction mixture.\textsuperscript{19,23,25} The selectivity towards 5-HMF kept in the range of 43-49 % after 3 h of reaction. The highest 5-HMF productivity (0.147 h^{-1}) was achieved in the first hour of reaction. In addition, it was observed that the isomerisation products, \textit{i.e.} mannose and fructose, appeared at the starting stage of the reaction and decreased upon the increase of reaction time until disappearing after 3 h of reaction, in agreement with their role as reaction intermediate in cyclic pathway (see Scheme 1), thus supporting that the reaction over the Nb_{2}O_{5}-scCO_{2} most likely follow the cyclic pathway.

The physicochemical properties of Nb_{2}O_{5}-scCO_{2} and Nb_{2}O_{5}-Ref catalysts were compared to discuss the difference in the catalytic activities of two Nb_{2}O_{5} catalysts prepared with or without the assistance of scCO_{2}. Part of their properties have been analysed in the previous work,\textsuperscript{35} employing N_{2}-physisorption, XRD, FT-IR and TEM analysis. Nb_{2}O_{5}-scCO_{2} displays a higher surface area (340 m^{2} g^{-1}) and nanoparticulate morphology (Fig. 1), while the Nb_{2}O_{5}-Ref exhibits a lower surface area of 305 m^{2} g^{-1} and aggregated big particles morphology (Fig. S5). Both catalysts possess amorphous structures.
Apart from the morphology and structural properties, the acid properties of the catalyst (type, strength and number of acid sites) play a very important role in determining the conversion of glucose and the yield of 5-HMF, though the specific type (Lewis or Brønsted) and strength of acid sites that is more effective for each step of the reaction (Scheme 1) is still under debate.\(^5,6\) Additionally, it has been reported that the Lewis acid sites promote the formation of humins.\(^21,23\) On this backdrop, the acidic properties of Nb\(_2\)O\(_5\)-scCO\(_2\) and Nb\(_2\)O\(_5\)-Ref were evaluated through the analysis of adsorbed pyridine by means of FT-IR spectroscopy, which allows determining the type and strength of surface acid sites. For both materials, the FT-IR spectra measured at different temperatures (100/150/200 °C) display the same bands typical of pyridine adsorbed on Lewis and Brønsted acid sites (Fig. 4). The bands at 1445 cm\(^{-1}\) and 1573 cm\(^{-1}\) are assigned to stretching vibrations of pyridine coordinated on Lewis acid sites (denoted as L in Fig. 4);\(^19,31,45,51-53\) the bands at 1540 cm\(^{-1}\) are related to the stretching vibrations of pyridinium ions that are originated on Brønsted acid sites (denoted as B in Fig. 4);\(^19,31,45,51-53\) the bands at 1486 cm\(^{-1}\) are attributed to the stretching vibrations of pyridine adsorbed on both Lewis and Brønsted acid sites (denoted as L+B in Fig. 4).\(^31,52\)
Fig. 4. FT-IR spectra of pyridine adsorption for Nb2O5-scCO2 and Nb2O5-Ref catalysts recorded at different temperatures.

At each desorption temperature, the concentration of Lewis acid sites on Nb2O5-scCO2 is higher than that on Nb2O5-Ref, while the concentration of Brønsted acid sites shows relatively minor difference between the two catalysts (see Table 2 and Fig. 5). The overall higher concentration of acid sites on Nb2O5-scCO2 is ascribed to its nanoparticulate morphology and higher surface area that bring about more exposed surface sites. In addition, at each desorption temperature, the ratio between the concentrations of Lewis and Brønsted acid sites (L/B ratio) on Nb2O5-scCO2 is higher than that on Nb2O5-Ref (see Table 2). On both catalysts, the amounts of both types of acid sites that are able to adsorb pyridine gradually decrease by increasing the desorption temperature. However, a fraction of acid sites is able to retain pyridine at 200 °C, which indicates the moderate-strong nature of these acid sites. It should be noted that the concentration of Lewis and Brønsted acid sites as a function of desorption temperature drops more significantly on Nb2O5-Ref than on Nb2O5-scCO2 (comparing the slopes in Fig. 5 or see the comparison of normalised concentrations in Fig. S6), indicating that the proportion of moderate acid sites on Nb2O5-scCO2 is higher. Based on these results, the higher glucose conversion over Nb2O5-scCO2 catalyst is attributed to its higher concentration of Lewis acid sites, which are generally identified as the most suitable catalytic sites for the glucose conversion to fructose. The following dehydration of fructose to produce 5-HMF is generally considered more favourable over Brønsted acid sites. In our case, the Nb2O5-scCO2 and Nb2O5-Ref catalysts show similar amounts of Brønsted acid sites, whereas they display different 5-HMF yield and selectivity. On the other hand, we should not ignore the contribution of Lewis acid sites on catalysing the conversion of fructose into 5-HMF, especially for the catalysts with high L/B ratio, which is the case for Nb2O5-scCO2.
and Nb$_2$O$_5$-Ref. In addition, it has been reported that the acid sites of moderate-strong nature is more beneficial for producing 5-HMF than weak acid sites.$^{18,20,55}$ Based on these considerations, we can conclude that the higher 5-HMF yield and selectivity over the Nb$_2$O$_5$-scCO$_2$ is ascribed to its higher concentration of Lewis acid sites and higher proportion of moderate-strong acid sites.

**Table 2.** Concentrations of Lewis (LAS) and Brønsted acid sites (BAS) that bind pyridine at 100, 150 and 200 °C on the Nb$_2$O$_5$-scCO$_2$ and Nb$_2$O$_5$-Ref catalysts.

<table>
<thead>
<tr>
<th>Desorption T (°C)</th>
<th><strong>Nb$_2$O$_5$-scCO$_2$</strong></th>
<th><strong>Nb$_2$O$_5$-Ref</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LAS (μmol g$^{-1}$)</td>
<td>BAS (μmol g$^{-1}$)</td>
</tr>
<tr>
<td>100</td>
<td>119.5</td>
<td>16.7</td>
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<td>150</td>
<td>97.5</td>
<td>15.0</td>
</tr>
<tr>
<td>200</td>
<td>76.3</td>
<td>10.1</td>
</tr>
</tbody>
</table>

**Fig. 5.** Concentrations of Lewis (LAS) and Brønsted acid sites (BAS) that bind pyridine at 100, 150 and 200 °C on the Nb$_2$O$_5$-scCO$_2$ and Nb$_2$O$_5$-Ref catalysts.

**Optimisation of the reaction conditions**

Once the best catalyst for the glucose conversion to 5-HMF was identified (Nb$_2$O$_5$-scCO$_2$), the reaction conditions were tuned with the aim of further enhancing the glucose conversion and 5-HMF selectivity. Firstly, the reaction temperature was screened in the range of 100-150 °C (Fig. 6). Upon increase of the reaction temperature, the glucose conversion rose from 9% at
100 °C to virtually complete conversion at ≥ 140 °C after 3 h reaction. The highest selectivity towards 5-HMF (48%) was obtained at 120 and 130 °C, while the highest yield of 5-HMF (42%) was achieved at 130 and 140 °C. Though the reaction performed at 130 °C achieved a higher glucose conversion and 5-HMF yield compared to those obtained in the reaction conducted at 120 °C, the C balance at 130 °C is calculated to be 62%, lower than that (74%) at 120 °C, proving the expected higher chance to form undesirable side products at higher temperature, as indicated by the increased yields of one of these side products, i.e. lactic acid (see Fig. 6). The formation of humins makes the purification of 5-HMF cumbersome and can cause loss of active surface of the catalyst with consequent deactivation. Therefore, 120 °C was chosen as the reaction temperature for further optimisation.

**Fig. 6.** Effect of reaction temperature on glucose conversion to 5-HMF. Reaction conditions: 40 mg glucose, 40 mg Nb2O5-scCO2 catalyst, 4 mL solvent (Vwater: VMIBK = 1:3), 3h.

Then, the R<sub>c/A</sub> ratio was varied with the aim of optimising the productivity of 5-HMF. Firstly, the initial glucose amount was fixed at 40 mg and the catalyst loading was varied in the range of 20 - 80 mg. When the reaction was performed with a lower catalyst loading (20 mg, Table 3, entry 1), 18% yield of 5-HMF was obtained, which is half of that obtained with 40 mg catalyst, thus excluding an external diffusion problem within 40 mg catalyst in our system. When the reaction was performed with higher catalyst loadings (Table 3, entries 2, 3), the conversion of glucose increased, reaching 91% with a catalyst loading of 80 mg, while the yield of 5-HMF
increased only in a minor way, achieving 39% with 80 mg catalyst, which could be related to the higher chance of forming undesirable side products and/or the external diffusion problems at higher catalyst loading. The catalytic reactions with 20 or 40 mg Nb$_2$O$_5$-scCO$_2$ display similar 5-HMF productivity, whereas the values drop at a higher catalyst loading. Next, the catalyst loading was fixed as 40 mg and the amount of initial glucose was varied in the range of 20 – 200 mg (Table 3, entries 4-7). Upon increasing the glucose amount from 20 mg to 200 mg, a trend of decreasing conversion of glucose (from 80 to 46%) and yield of 5-HMF (from 37 to 12%) was observed, while the productivity of 5-HMF gradually increased from 0.043 to 0.140 h$^{-1}$. Altogether, the optimum trade-off between yield and selectivity of product, and the productivity of the catalyst is obtained for R$_{C/S}$ = 1.

Table 3. Activity of Nb$_2$O$_5$-scCO$_2$ catalyst in the conversion of glucose to 5-HMF with different glucose concentration and catalyst loading.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Glucose (mg)</th>
<th>Catalyst loading (mg)</th>
<th>R$_{C/S}$</th>
<th>Glucose Conv. (%)</th>
<th>Product yields (%)</th>
<th>5-HMF Sel. (%)</th>
<th>5-HMF Prod. (h$^{-1}$)</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>40</td>
<td>20</td>
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<td>18 5 4 0 0</td>
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</tr>
<tr>
<td>5</td>
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<td>40</td>
<td>0.5</td>
<td>56</td>
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<td>0.107</td>
</tr>
<tr>
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<td>120</td>
<td>40</td>
<td>0.33</td>
<td>47</td>
<td>19 5 5 1 1</td>
<td>41</td>
<td>0.133</td>
</tr>
<tr>
<td>7</td>
<td>200</td>
<td>40</td>
<td>0.2</td>
<td>46</td>
<td>12 4 4 1 1</td>
<td>26</td>
<td>0.140</td>
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</table>

Reaction conditions: a desired amount of glucose, a desired amount of Nb$_2$O$_5$-scCO$_2$ catalyst, 4 mL solvent ($V_{\text{water: V_{MIBK}}}$ 1:3), 120 °C, 3h.

**Substrate scope**

Finally, we explored the scope of carbohydrates that can be converted by Nb$_2$O$_5$-scCO$_2$ for the production of 5-HMF (Fig. 7). When fructose is employed as the starting material instead of glucose, higher conversion (96%) can be achieved as a consequence of the elimination of the isomerisation step from glucose to fructose, in agreement with previously reported works.$^{18,26,33}$ Although the isomerisation between glucose and fructose happens in both directions, the glucose isomerisation to fructose is thermal dynamically more favourable.$^{15}$ However, fructose tends to give lower 5-HMF yield than that obtained with glucose, probably due to the easier occurrence of (i) retro-aldol reaction, as proved by the increased yields of side products derived from this reaction, i.e. DHA and lactic acid, and, (ii) polymerisation.
reactions between 5-HMF and fructose to form humins as proved by the increased C imbalance (51%) with fructose as reactant. Then, the conversion of cheaper and more widely available disaccharides (i.e. sucrose and cellobiose) over the Nb$_2$O$_5$-scCO$_2$ catalyst were tested. Sucrose (a disaccharide of glucose and fructose) and cellobiose (a disaccharide of glucose) can be hydrolysed over Brønsted acid catalyst into the component monosaccharides,$^{19,44,56}$ which in turn are converted to 5-HMF. This implies that the reaction needs to go through an additional step when compared to the process with glucose as raw material. 5-HMF was successfully obtained from both disaccharides, indicating that the Nb$_2$O$_5$-scCO$_2$ catalyst can efficiently catalyse the sequential reactions including the hydrolysis of disaccharides and the following conversion of monosaccharides, though the yields of 5-HMF are lower than those obtaining from the monosaccharides. Additionally, the conversion of sucrose after 3 h is virtually complete, while only 48 % of cellobiose was converted, which is related to the difference in their structures: the glucose and fructose units in sucrose are linked by a 1-2 glycosidic bond, while the two glucose units in cellobiose are connected by a 1-4 glycosidic bond, which is more difficult to hydrolyse.$^{44}$

![Graph](image.png)

**Fig. 7.** Catalytic performance of Nb$_2$O$_5$-scCO$_2$ for the conversion of different carbohydrates. Reaction conditions: 40 mg carbohydrates, 40 mg Nb$_2$O$_5$-scCO$_2$ catalyst, 4 mL solvent ($V_{\text{water}}: V_{\text{MIBK}} = 1:3$), 120 °C, 3h.

**Conclusions**

In this work, we investigated nanostructured Nb$_2$O$_5$ materials prepared with a scCO$_2$-assisted precipitation method as heterogeneous catalysts for the conversion of glucose into 5-HMF. For this purpose, we optimised the synthetic parameters in the preparation of the Nb$_2$O$_5$ material,
i.e. co-solvent and CO$_2$ pressure and the temperature of the consequent thermal treatment. The most active catalyst (Nb$_2$O$_5$-scCO$_2$) was prepared with ethanol as co-solvent under a CO$_2$ pressure of 140 bar and thermally treated at 200 °C. Notably, the material was prepared without the assistance of any template and presents a high specific surface area (340 m$^2$ g$^{-1}$). The catalyst mainly presents Lewis acid sites, along with a minor proportion of Brønsted acid sites, while part of Lewis and Brønsted acid sites are of moderate character. This catalyst reached a high conversion of glucose (73%), and good yield (36%) and selectivity (48%) towards 5-HMF after 3 h reaction under mild reaction conditions (120 °C and a low catalyst loading, $R_{c/s} = 1$). A further extension of reaction time to 9 h led to almost full conversion of glucose and a 46% yield of 5-HMF. Importantly, the Nb$_2$O$_5$-scCO$_2$ catalyst showed no leaching problem and was reusable in consecutive runs without obvious loss of activity. Additionally, the catalyst was active in the conversion of cheap and abundant disaccharides as sucrose and cellobiose to produce 5-HMF, though with lower yield. The superior catalytic activity of the Nb$_2$O$_5$-scCO$_2$ catalyst could be ascribed to its open, accessible nanoparticulate morphology, high surface area and higher amount of acid sites when compared to a reference catalysts prepared without scCO$_2$. In perspective, these properties make the Nb$_2$O$_5$-scCO$_2$ catalyst an attractive candidate also for the acid-catalysed conversion of other bio-based compounds into valuable products.
Supporting information

Rough quantification of side products that can't be quantified by HPLC

There are some products that can't be quantified by HPLC due to the overlapping of the peaks of these products, including anhydroglucoses ($M_w = 162.14$ and $M_w = 144.12$), erythrose and glycolaldehyde ($M_w = 120.10$ and 60.05) and pyruvaldehyde ($M_w = 72.06$). These peaks might also represent soluble dimers or oligomers of C6 sugars. Here we would like to roughly quantify the total yield of these products (except for dimers or oligomers) using an estimated $R_f$-estimated by the following equations:

$$R_f-estimated = aC-anhydroglucoses R_f-glucose + (aC-erythrose + aC-PVA + aC-glycaldehyde) R_f-PVA$$

in which $aC-x$ is the fraction of the intensities of $x$ compounds in the total intensity of these compounds. $R_f$-glucose is the $R_f$ of glucose, $R_f$-PVA is the $R_f$ of PVA. It should be noted that in this formula, we assume that: (i) the intensity of the peak in ESI-MS is proportional to their concentration; (The fact is that the intensity depends on how well a molecule can be ionised. Only when molecules are very similar (the same functional groups and so on), the intensities can be more or less compared.) (ii) anhydroglucoses have the same $R_f$ as glucose in HPLC analysis, (iii) erythrose and glycolaldehyde have the same $R_f$ as PVA in HPLC analysis, (iv) dimers or oligomers are not detectable by HPLC. Although this quantification is not accurate, we would like to give a range of these side products, thus the degree of forming humins can be estimated.
Table S1. Comparison of representative heterogeneous catalysts for conversion of glucose to 5-HMF

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<th>Ref.</th>
<th>Catalyst</th>
<th>R&lt;sub&gt;c/s&lt;/sub&gt;&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Time (h)</th>
<th>Glucose Conv. (%)</th>
<th>5-HMF yield (%)</th>
<th>5-HMF Sel. (%)</th>
<th>5-HMF Prod. (h&lt;sup&gt;-1&lt;/sup&gt;)</th>
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<td>1</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>110</td>
<td>6</td>
<td>50</td>
<td>6</td>
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<td>10</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>120</td>
<td>3</td>
<td>92</td>
<td>52</td>
<td>57</td>
<td>0.012</td>
</tr>
<tr>
<td>18</td>
<td>H&lt;sub&gt;3&lt;/sub&gt;PO&lt;sub&gt;4&lt;/sub&gt;-Nb&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;5&lt;/sub&gt;-nH&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>0.083</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/2-BuOH</td>
<td>160</td>
<td>1.8</td>
<td>68</td>
<td>49</td>
<td>72</td>
<td>2.258</td>
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<tr>
<td>19</td>
<td>NbPO</td>
<td>1</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/MIBK</td>
<td>140</td>
<td>2</td>
<td>71</td>
<td>31</td>
<td>38</td>
<td>0.108</td>
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<tr>
<td>20</td>
<td>NbPO</td>
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<td>H&lt;sub&gt;2&lt;/sub&gt;O/MIBK</td>
<td>135</td>
<td>7.5</td>
<td>60</td>
<td>36</td>
<td>60</td>
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<td>Nb&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;5&lt;/sub&gt;-nH&lt;sub&gt;2&lt;/sub&gt;O/NbPO</td>
<td>0.83</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>150</td>
<td>2</td>
<td>55</td>
<td>31</td>
<td>56</td>
<td>0.131</td>
</tr>
<tr>
<td>22</td>
<td>Nb-WO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>10</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/1-BuOH</td>
<td>120</td>
<td>3</td>
<td>98</td>
<td>52</td>
<td>53</td>
<td>0.012</td>
</tr>
<tr>
<td>23</td>
<td>Nb-C</td>
<td>1</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/THF/NaCl</td>
<td>160</td>
<td>4</td>
<td>44</td>
<td>59</td>
<td>61</td>
<td>0.103</td>
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<td>Nb-Al&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>0.1</td>
<td>DMSO</td>
<td>150</td>
<td>4</td>
<td>N.M.</td>
<td>59</td>
<td>N.M.</td>
<td>1.032</td>
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<td>25</td>
<td>Ta&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;5&lt;/sub&gt;</td>
<td>0.33</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/MIBK</td>
<td>175</td>
<td>1.5</td>
<td>69</td>
<td>23</td>
<td>33</td>
<td>0.325</td>
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<tr>
<td>26</td>
<td>Ta&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;5&lt;/sub&gt;</td>
<td>0.083</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/2-BuOH</td>
<td>160</td>
<td>2.3</td>
<td>70</td>
<td>50</td>
<td>71</td>
<td>1.833</td>
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<td>27</td>
<td>TaOPO</td>
<td>0.33</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/MIBK</td>
<td>170</td>
<td>1</td>
<td>56</td>
<td>33</td>
<td>59</td>
<td>0.700</td>
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<tr>
<td>28</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;PO&lt;sub&gt;4&lt;/sub&gt;-TiO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>2.5</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/THF</td>
<td>120</td>
<td>2</td>
<td>100</td>
<td>81</td>
<td>81</td>
<td>0.071</td>
</tr>
<tr>
<td>29</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;PO&lt;sub&gt;4&lt;/sub&gt;-TiO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>0.3</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/1-BuOH</td>
<td>175</td>
<td>3</td>
<td>97</td>
<td>81</td>
<td>83</td>
<td>0.630</td>
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<tr>
<td>30</td>
<td>Al-MCM-41</td>
<td>0.33</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/MIBK/NaCl</td>
<td>195</td>
<td>0.5</td>
<td>98</td>
<td>64</td>
<td>65</td>
<td>2.715</td>
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<tr>
<td>31</td>
<td>SnPO</td>
<td>0.5</td>
<td>Ionic liquid</td>
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<td>3</td>
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<td>58</td>
<td>62</td>
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<td>32</td>
<td>Sn-Beta</td>
<td>N.M.</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O/THF/NaCl</td>
<td>180</td>
<td>1.2</td>
<td>79</td>
<td>57</td>
<td>72</td>
<td>N.M.</td>
</tr>
</tbody>
</table>

<sup>a</sup> R<sub>c/s</sub> is defined as the weight ratio between catalyst and glucose. 2 The productivity is defined as the grams of product generated per gram of catalyst in 1 hour. N.M.: not mentioned.

Table S2. Properties of co-solvents used in the scCO<sub>2</sub>-assisted precipitation method

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Protic (P) or Aprotic (A)</th>
<th>BP (°C)</th>
<th>Density (g/cm&lt;sup&gt;3&lt;/sup&gt;)</th>
<th>Dipole moment (D)</th>
<th>Dielectric constant at 25°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>P</td>
<td>78</td>
<td>0.79</td>
<td>1.69</td>
<td>24.3</td>
</tr>
<tr>
<td>1-Butanol</td>
<td>P</td>
<td>117</td>
<td>0.81</td>
<td>1.66</td>
<td>16.5</td>
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<tr>
<td>Ethyl acetate</td>
<td>A</td>
<td>77</td>
<td>0.90</td>
<td>1.78</td>
<td>6.02</td>
</tr>
<tr>
<td>Propylene carbonate</td>
<td>A</td>
<td>242</td>
<td>1.2</td>
<td>4.9</td>
<td>69</td>
</tr>
</tbody>
</table>
**Fig. S1.** ACE pressure tube (maximum 10 bar at 120 °C).

**Fig. S2.** ESI-MS spectra of the reaction mixture obtained from glucose transformation to 5-HMF over Nb$_2$O$_5$-scCO$_2$ catalyst in H$_2$O/MIBK mixture after reaction at 120 °C for 3 h.
**Fig. S3.** XRD patterns of Nb$_2$O$_5$ materials prepared in scCO$_2$ with different co-solvents.

**Fig. S4.** XRD patterns of Nb$_2$O$_5$ materials prepared in scCO$_2$ with different thermal treatment temperatures.
Fig. S5. TEM image of the Nb$_2$O$_5$-Ref nanoparticles.

Fig. S6. Normalised concentrations of different acid sites on Nb$_2$O$_5$-scCO$_2$ and Nb$_2$O$_5$-Ref catalysts at different temperatures.
References


14. Van Dam, H.; Kieboom, A.; Van Bekkum, H., The conversion of fructose and glucose in acidic media:


47. Li, S.; Xu, Q.; Uchaker, E.; Cao, X.; Cao, G. J. C., Comparison of amorphous, pseudohexagonal and orthorhombic Nb$_2$O$_5$ for high-rate lithium ion insertion. *CrysEngComm* **2016**, 18 (14), 2532-2540.


