

Developing a Continuous Process for Isosorbide Production from Renewable Sources

Massimiliano Caiti,^[a, b] Giulia Tarantino,^[a] and Ceri Hammond^[a]

Increasing demand for isosorbide has led to the search for sustainable and efficient methods for its production from sorbitol, a biomass-derived platform molecule. However, sorbitol dehydration to isosorbide is currently performed with mineral acids, resulting in safety and toxicity issues. Although some progress has been made towards replacement of liquid acids with heterogeneous catalysts, continuous systems with good stability, selectivity and productivity remain scarce. Herein, sorbitol dehydration to isosorbide is efficiently performed in a continuous, liquid-phase plug flow reactor, utilising an acidic

zeolite (H- β (38)) as solid catalyst. H- β (38) is shown to catalyse the reaction without loss of activity for 55 hours on stream, achieving an isosorbide productivity of 9670 g_{isosorbide}/kg_{catalyst}. This value is 4 times greater than any other continuous process reported in literature to date, even though the reaction was terminated prior to any loss of activity being detected. Diagnostic kinetic studies reveal improved operational conditions, and characterisation of the post-reaction catalyst is provided.

Introduction

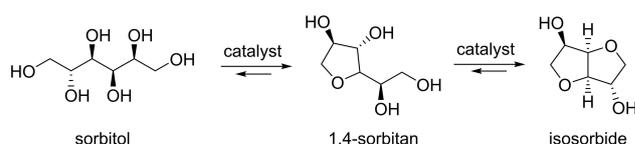
In order to improve sustainability, the scientific community is exploring renewable alternatives to fossil-based energy and carbon sources. In this context, an important target is to establish sustainable and productive biorefineries, which produce value added compounds utilising biologically available materials as carbon sources.^[1] The principal starting materials suitable for conversion in a biorefinery are hemicellulose and lignin, since they are naturally available renewable resources, and their structures can be broken-down into smaller constituents like glucose, xylose and many organic alcohols.^[2] These compounds can subsequently be converted into important platform molecules, such as ethanol, glycerol, sorbitol, lactic acid, succinic acid and more.^[3] Amongst them, sorbitol, a sugar alcohol produced by glucose hydrogenation, is considered one of the top platform molecules derived from biomass,^[4] with an estimated 2020 annual production of 2.3 million tons.^[5]

Sorbitol derivatives are utilised in several industrial sectors as fuels, plastic precursors, detergents, emulsifiers, antioxidants and pesticides.^[3] Moreover, sorbitol can be consecutively dehydrated into isosorbide, an added value molecule employed in several industrial applications.^[6] For example, isosorbide, with

its double ring shape and hydroxyl groups (Scheme 1), could replace toxic bisphenol A in the large market of epoxy resins, yielding polymers with special mechanical performances.^[7] Furthermore, for its chiral properties, isosorbide has been exploited widely by the pharmaceutical industry in the challenging synthesis of pure enantiomeric drugs and health-care products.^[8] Isosorbide derivatives also find applications as organic solvents, surfactants and additives capable of replacing harmful plasticizers such as phthalates.^[8c] Alongside these applications, the opportunity to use isosorbide to synthesise speciality fuels or biofuel additives has also been explored.^[9]

At present, isosorbide is mainly produced through sorbitol dehydration, which is catalysed by mineral acids such as H₂SO₄, HCl or *p*-toluenesulfonic acid.^[10] These liquid acids provide good isosorbide selectivity but are a corrosive hazard to the reaction vessel, and result in several post-reaction operations being required to recover the pure product and treat the generated toxic waste. For such reasons, solid catalysts have been identified as a promising alternative to these liquid acids in the context of sorbitol dehydration.

The dehydration of sorbitol over heterogeneous catalysts has recently been attempted both in the vapour phase,^[11] and in the liquid phase,^[12] using both solvated conditions and solvent-free conditions in batch mode. Amongst catalytic materials tested for vapour phase dehydration, sulphated copper oxide,^[11a] supported tungstophosphoric acids,^[11b] metal phosphates,^[11c] modified tantalum oxides,^[11d] and niobium phosphates based catalysts^[11f] have been reported to be active



Scheme 1. Consecutive dehydration of sorbitol to isosorbide via 1,4-sorbitan.

[a] M. Caiti, Dr. G. Tarantino, Dr. C. Hammond
Department of Chemical Engineering
Imperial College London
London, SW7 2AZ (UK)
E-mail: ceri.hammond@imperial.ac.uk

[b] M. Caiti
Cardiff Catalysis Institute
Cardiff University
Cardiff CF10 3AT (UK)

Supporting information for this article is available on the WWW under <https://doi.org/10.1002/cctc.202001278>

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for sorbitol dehydration, reaching isosorbide yields of up to 57%. In contrast, zeolites and related Brønsted acid catalysts (e.g. sulfonic acid functionalised silica and sulphated metal oxides) have shown applicability for liquid phase dehydration, resulting in isosorbide yields of up to 84% being achieved when solvent-free *i.e.* melt, conditions are employed.^[12k]

Yet, although interesting results have been achieved in previous studies, several disadvantages are prevalent and many challenges remain. For example, although dehydration of sorbitol in the vapour phase provides the benefits of continuous operation (*vide infra*), such an approach is hampered by the poor volatility and low thermal stability of sorbitol, which complicates stable operation of the reactor in the vapour phase, and unnecessarily degrades a valuable carbon resource,^[13] consequently resulting in low levels of reactor productivity (see Table S1, Supporting Information file). However, although operation under solvent-free batch conditions permits high yields and productivities to be obtained, the extremely high levels of substrate concentration attained in the melt phase leads to several undesirable reaction events, including sugar degradation processes,^[14] and fouling of the catalyst.^[15] Unfortunately, the latter can result in decreased catalyst longevity, which is often evaluated in terms of the number of substrate turnovers achieved prior to loss of catalytic activity (see Equation 1, Experimental section).^[16] Furthermore, the high viscosity of melted sorbitol represents a large hurdle for continuous operation, which is an important target given that such reactors provide several advantages for large scale processes, including improved process and safety control, higher levels of mass and heat transfer, faster rates of reaction, minimised reactor volumes and improved scalability.^[16] Therefore, despite the demand for isosorbide, efficient continuous processes catalysed by solid acids have not yet been developed.

Continuous liquid-phase systems, in which the substrate is dissolved into a solvent, are a possible way to overcome the challenges faced by the continuous vapour-phase systems previously mentioned, whilst also allowing continuous operation of the reactor in a simpler manner than can be achieved for solvent-free systems. Indeed, the presence of liquid media allows the employment of optimal substrate concentrations throughout the catalyst bed and, at the same time, prevents high viscosity and temperature disadvantages typically encountered for solvent-free reactions. Moreover, performing liquid-phase continuous reactions presents an opportunity to gain insights into the reaction kinetics of the process, and also permits catalyst deactivation to be studied in an effective manner, which is a critical target for process intensification, neither of which have previously been undertaken in the context of sorbitol dehydration. However, such continuous liquid-phase systems have not yet been fully explored.

For these reasons, herein we explore the dehydration of sorbitol over heterogeneous catalysts in a liquid-phase continuous flow reactor, which has not previously been attempted. Particular attention is placed on kinetic aspects of the system, including long-term continuous operation to probe catalyst stability over 55 hours on stream. Notably, such extended

studies have not yet been undertaken for sorbitol dehydration. Preliminary batch studies, essential to identify a suitable catalyst and optimal reaction conditions for initial continuous applications, are also presented.

Results and Discussion

Catalyst screening and batch study

To identify a suitable material for continuous operation and benchmark the kinetic system against previous reports,^[12i,k] preliminary catalyst screening was performed in batch reactors. Previous works^[12i,k] have shown that various materials possessing Brønsted acid sites, including zeolites, are promising catalysts for sorbitol dehydration, and such catalysts are especially desirable for large scale use due to their low toxicity, low cost and their existing utilisation in industry. Accordingly, an array of zeolites with different framework structures and SiO₂/Al₂O₃ molar ratios (indicated in parentheses) was selected and tested for sorbitol dehydration, initially at conditions optimised in previous reports (5 wt.% sorbitol in pure H₂O) (Figure 1). Control experiments using mineral acids such as H₂SO₄ and HCl were also performed, in order to compare the catalytic performance of zeolites to those of the liquid acids currently employed for isosorbide production. Each batch reaction was performed at constant moles (sorbitol)/moles (H⁺) ratio, by varying the amount of the catalyst accordingly. Notably, for zeolites, the moles of active sites were considered equal to the moles of Al present in the material framework. Furthermore, each zeolite was tested in its H⁺ form following calcination in air at 550 °C for 6 hours, at a ramp rate of 5 °C/min.

As shown in Figure 1, depending on the framework topology and the aluminium content, the zeolite materials explored in this study exhibited a wide range of activity and selectivity. Specifically, H-β and H-ZMS-5 were the most promising materials, achieving isosorbide yields even greater than those achieved by the mineral acids. Conversely, poor isosorbide yields were observed for H-Y, H-Ferrierite (H-FER) and H-Mordenite (H-MOR), which may be ascribed to several reasons such as different pore structures, hydrophilicity, or even to hydrothermal instability of the materials (Table S2).^[12i,k] Regarding the SiO₂/Al₂O₃ molar ratio, the isosorbide productivity trend observed in Figure 1 is in good agreement with previous works, as zeolites with intermediate aluminium content showed the best performance.^[12i,k] In particular, for the H-β series, maximum isosorbide yield was achieved for the material possessing a SiO₂/Al₂O₃ ratio of 38.^[12i,k]

From the materials explored in Figure 1, zeolite H-β (38) achieved the best isosorbide yield (31%). The superior catalytic performance exhibited by H-β (38) indicates that this catalyst is able both to convert sorbitol, and assist the dehydration of the reaction intermediate, 1,4-sorbitan (Scheme 1), unlike other catalysts (e.g. H-Y (30)) which appear less able to facilitate the second dehydration, resulting in high selectivity toward 1,4-

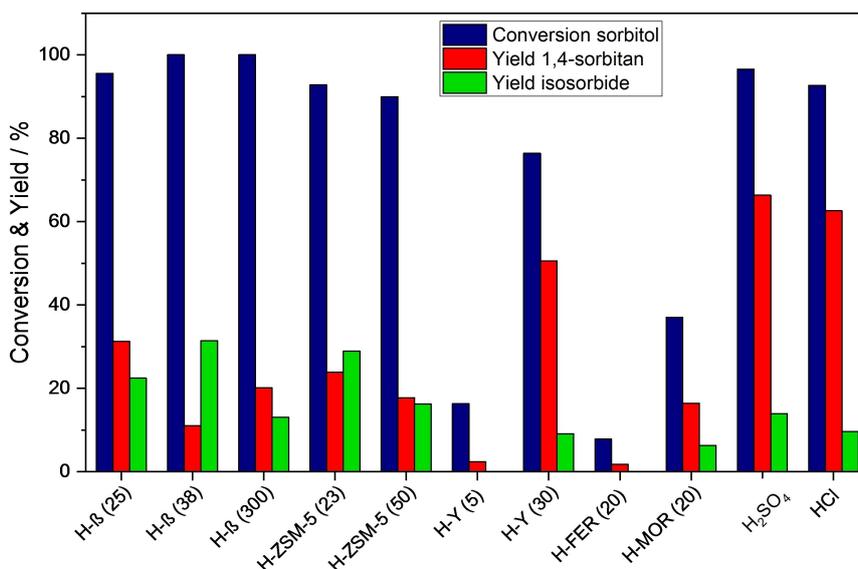


Figure 1. Sorbitol conversion (blue bars), 1,4-sorbitan yield (red bars) and isosorbide yield (green bars) achieved by different solid and liquid acid catalysts during sorbitol dehydration. Reaction conditions: 20 mL of aqueous sorbitol (5 wt.%), moles (sorbitol)/moles (H⁺) = 2, 200 °C, autogenic pressure, 1 hour.

sorbitan. Based on these findings, H-β (38) was selected as primary catalyst to perform the sorbitol dehydration reaction.

To better understand the performance of H-β (38) and identify how the choice of conditions affected progress of the reaction, time online analysis was achieved by repeating sorbitol dehydrations reactions at 200 °C for different periods of time, employing a 5 wt.% aqueous solution of sorbitol. As shown in Figure 2 (Left), sorbitol conversion and the yields of 1,4-sorbitan and isosorbide progressively increased at longer reaction times. The reactant and product evolution highlights the two-step dehydration required to produce isosorbide (Scheme 1). Indeed, after 3 hours of dehydration reaction, the

concentration of the intermediate (1,4-sorbitan) remained essentially stable, whilst the concentration of isosorbide increased progressively. This trend demonstrates that long reaction times are required to achieve good levels of isosorbide selectively, a hurdle for the development of the continuous process. The employment of water as reaction solvent may negatively impact the reaction outcome. Indeed, the large amount of water present in the reaction environment could rehydrate isosorbide, favouring the hydrated compound, 1,4-sorbitan, or even sorbitol. The detrimental role of water when present in the reaction environment may be further supported by the decreased isosorbide yield obtained when using aluminium-rich zeolites, which are more hydrophilic.^[12i,k] For example, a drop in isosorbide yield from 31% to 22% was observed when replacing H-β (38) with H-β (25) (Figure 1).

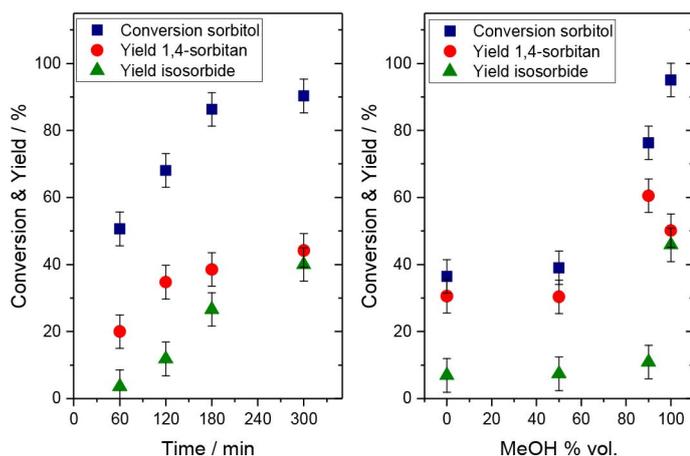


Figure 2. (Left) Time online of sorbitol dehydration catalysed by H-β (38). Reaction performed in autoclave with 20 mL of aqueous sorbitol (5 wt.%), 0.25 g of catalyst, 200 °C, autogenic pressure. (Right) Effect of MeOH concentration in the reaction solvent. Reaction conditions: 3.2 wt.% sorbitol in MeOH/H₂O of various ratios, 20 mL volume, 0.25 g catalyst, 170 °C, autogenic pressure, 5 hours.

To investigate the effect of water on the progress of the reaction and the product distribution, a set of experiments was performed conducting sorbitol dehydration in MeOH/H₂O mixtures in the range 0% MeOH (*i.e.* pure H₂O) to 100% MeOH (Figure 2 (Right)). Due to the lower sugar solvating properties of MeOH when compared to H₂O, and its higher vapour pressure, these reactions were performed with a 3.2 wt.% sorbitol solution at 170 °C, differing from the previous tests conducted in H₂O with 5 wt.% sorbitol solution at 200 °C. Addition of MeOH to the reaction mixture was beneficial for sorbitol conversion and isosorbide selectivity only when the ratio MeOH/H₂O exceeded 50%. As such, it is clear that the presence of H₂O is detrimental for the dehydration reaction catalysed by H-β (38). In fact, the presence of 10% H₂O caused a decrease in the sorbitol conversion value from 95% to 76%, and a drop in isosorbide yield from 46% to 10%. The substantial improvement in isosorbide yield detected following removal of H₂O (100% MeOH, Figure 2 (Right)) supports the hypothesis that H₂O inhibits the consecutive dehydration of 1,4-sorbitan to

isorbide. In addition to the improved catalytic performance observed in MeOH, replacing aqueous media with this solvent is also favoured for industrial scale application, since its lower enthalpy of vapourisation facilitates downstream separation and recovery of isororbide. Use of MeOH as reaction solvent instead of H₂O also results in higher yields even at milder reaction conditions. Indeed, 45% isororbide yield was achieved in MeOH at 170 °C, whilst only 7% of isororbide yield was observed in H₂O at 170 °C at the same reaction time of 5 hours (Figure 2 (Right)).

The productivity enhancement observed in MeOH constitutes a major improvement for the development of a continuous dehydration system, as it allows satisfactory isororbide yield to be achieved in reduced reaction times and hence, contact times during continuous operation (see Equation 2, Experimental section). Accordingly, pure MeOH was used as solvent for the remainder of the study.

Continuous reaction

Following preliminary investigation of the reaction system in batch reactors, continuous operation of the sorbitol dehydration reaction was explored in a Plug Flow Reactor (PFR). Preliminary experiments focused on ensuring kinetic relevance of the PFR reactor, ruling out possible external and internal transfer limitations.^[16,17] To exclude potential external mass transfer limitations related to the linear velocity of the feed (see Equation 3, Experimental section), a range of reactor columns containing different amounts of catalyst were prepared, and the activity of each was monitored at a fixed contact time (τ) by scaling the flow rate appropriately. This is important since at low linear velocities, the liquid layer around the catalyst particles might become too large, thus resulting in external diffusion limitations. Additionally, for each specific mass of catalyst, the substrate flow rate was also varied during the reaction, to generate contact time profiles. To correctly evaluate the phenomena, the sorbitol conversion values achieved at different linear velocities were compared at the same contact time, τ (Figure 3 (Left), black dashed lines). As shown in Figure 3 (Left), no substantial variation of sorbitol conversion was observed at different substrate linear velocities, considering the experimental error of $\pm 5\%$. Therefore, the effect of external diffusion limitation can be considered negligible for substrate flow rates down to 0.20 mL min⁻¹, ensuring kinetic relevance of the reactor.

To minimise backmixing and maintain a low pressure drop, pelletisation of a solid catalyst is required for use in a PFR. However, this can also result in undesired internal diffusion limitations as a consequence of slow diffusion of reacting molecules inside large catalyst particles.^[16,17] Therefore, a kinetic study was performed using identical catalyst masses and reactant flow rates, but varying the average particle size of H- β (38) (Figure 3, (Right)). It was found that internal diffusion limitation arises inside catalyst particles when the size fraction was equal or larger than 250 μm ($1/d_p = 4 \text{ mm}^{-1}$, Figure 3,

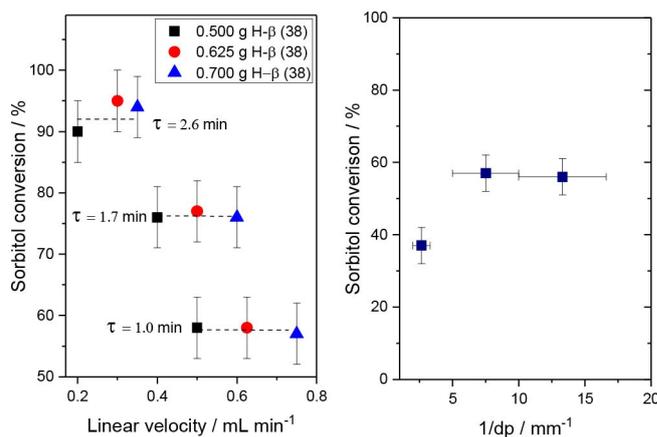


Figure 3. (Left) External diffusion limitation study. Each reaction was performed by adjusting the mass of catalyst and flow of sorbitol (3.2 wt.% in MeOH) to maintain a fixed contact time, at 200 °C, 40 bar back pressure. (Right) Internal diffusion limitation study. Each reaction was performed with 0.75 g of H- β (38), 0.75 mL min⁻¹ of 3.2 wt.% sorbitol in MeOH at 200 °C, 40 bar back pressure using catalyst particle size from 60 to 500 μm . $1/d_p$ refers to $1/\text{diameter}$ of the catalyst particles ($1/\text{mm}$).

(Right)). Accordingly, all further experiments were conducted with catalyst particles between 60–100 μm .

Following optimisation of the kinetic parameters of the reaction, the effect of contact time on the progress of the dehydration reaction was investigated. In this case, continuous reactions were conducted using 0.750 g of catalyst in order to achieve longer contact times (≤ 8 mins) whilst avoiding linear velocities low enough to induce external diffusion limitation (Figure 3 (Left)). As observed in Figure 4, increasing the contact time was beneficial for the second step of the reaction, resulting in improved yield and selectivity to isororbide, in agreement with the time online analysis performed on the batch process (Figure 2 (Left)). In all cases, enhanced isororbide yield was

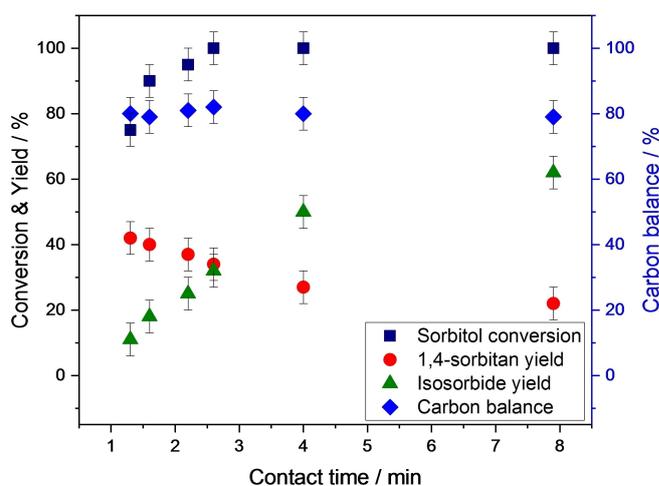


Figure 4. Sorbitol dehydration at different contact time. Each reaction was performed with 0.750 g of H- β (38) 60–100 μm , 3.2 wt.% sorbitol in MeOH at different flow rates, 200 °C, 40 bar back pressure.

achieved without affecting the overall carbon balance. Notably, the carbon balance of 80% observed at all contact times indicates that carbon balance was lost from competing reaction pathways, likely due to the formation of several by-products such as, 1,5-anhydrosorbitol, 2,5-anhydromannitol, isomannide and isoidide, small quantities of which have previously been detected.^[12g,e,t]

Having benchmarked the impact of contact time, continuous sorbitol dehydration was subsequently performed for an extended reaction period. For this study, a contact time of 2.6 min was chosen. Although this contact time limited the selectivity towards isosorbide (as shown in Figure 4), maintaining conversion values below 100% ensured an excess catalyst regime was avoided, thereby allowing any potential deactivation events to be immediately detected. Indeed, in the presence of excess catalyst, a significant amount of deactivation might occur before the reaction conversion decreases below 100%.^[16] Building on the previous kinetic studies (Figure 3), 0.50 g of catalyst and a flow rate of 0.20 mL min⁻¹ were chosen to achieve the desired contact time, so as to balance linear velocity requirements and reactor pressure drop. At these conditions, continuous dehydration of sorbitol was successfully achieved (Figure 5) at mild temperature, achieving 82% sorbitol conversion and an average of 28% isosorbide yield. It should be noted that H- β (38) exhibited excellent stability for the entire reaction progress (55 hours), differently from other catalysts employed in continuous gas-phase reactions, which begin to lose activity during the first hours of reaction.^[11c] A total isosorbide productivity of 9670 g_{isosorbide}/kg_{catalyst} was achieved over 55 hours, greater than those achieved in the gas-phase continuous systems (Table S1),^[11a-f] thus showing the benefits of liquid phase continuous operations for isosorbide production. However, we note that this value is an underestimation of the potential productivity of the system, since deliberately limiting

the reactor to <100% conversion decreases the isosorbide selectivity (*vide supra*), and the good stability observed suggest longer term operational to be feasible, which would further boost the productivity values obtained during continuous operation.

Characterisation of used catalyst

As previously mentioned, stability is an essential feature for industrial applicability of catalysts. Although H- β (38) preserved its catalytic performance for 55 hours on stream (Figure 5), prolonged operational time might induce gradual changes to the catalyst, which may later contribute to deactivation over longer reaction periods. In fact, from kinetic studies alone, structural changes to the catalyst and deposition of carbonaceous residues cannot be excluded. Therefore, to further understand the stability of H- β (38) during continuous isosorbide dehydration, characterisation of the catalyst after 55 hours on stream was undertaken. To ensure structural integrity of the zeolite framework after reaction, X-Ray Diffraction (XRD) analysis was performed on the used catalyst, in addition to control samples (*i.e.* fresh H- β (38) and H- β (38) treated in MeOH, see Experimental Section for further details on the treatment). XRD analysis of the fresh and used catalysts, and the control sample treated in MeOH, revealed no changes in the XRD pattern of these samples, confirming that the zeolite preserves its crystalline structure even after 55 hours of reaction (Figure 6 and Table S3).

Diffuse Reflectance Infrared Fourier Transform (DRIFT) analysis of the samples was also performed (Figure 7). As expected, the IR spectrum of fresh catalyst (Figure 7) showed the characteristic absorption bands of silanol groups and

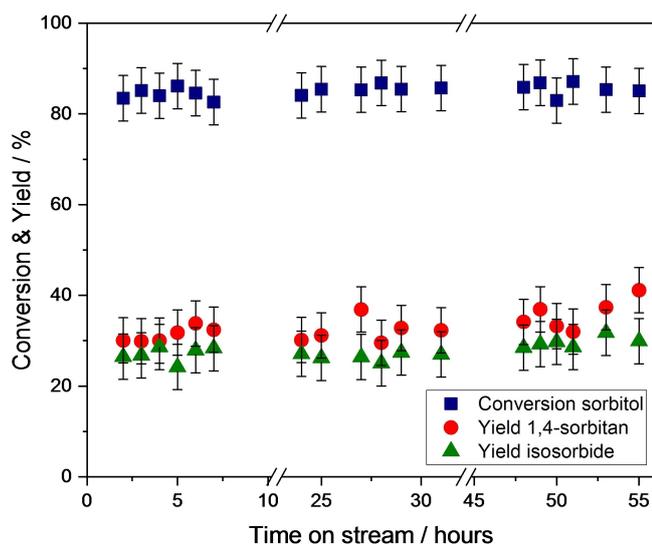


Figure 5. Continuous sorbitol dehydration. The reaction was performed in a PFR at a flow rate of 0.20 mL min⁻¹ of 3.2 wt.% sorbitol in MeOH through 0.500 g of H- β (38) (60–100 μ m). Contact time of 2.6 min, at 200 °C and 40 bar back pressure.

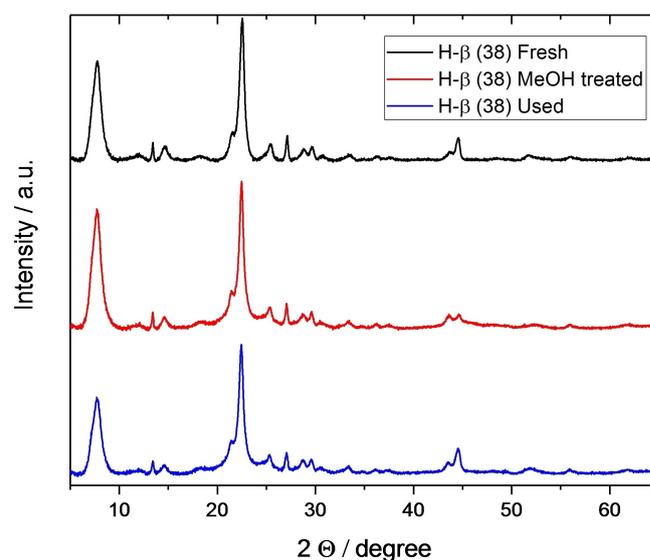


Figure 6. XRD diffracton patterns of fresh (top), MeOH treated (middle) and used (bottom) H- β (38). MeOH treated catalyst conditioned with 0.25 mL min⁻¹ of MeOH at 200 °C, 24 hours, 40 bar. Used catalyst conditions: 0.25 mL min⁻¹ 3.2 wt.% sorbitol MeOH solution, 200 °C, 40 bar, substrate turnover = 127.

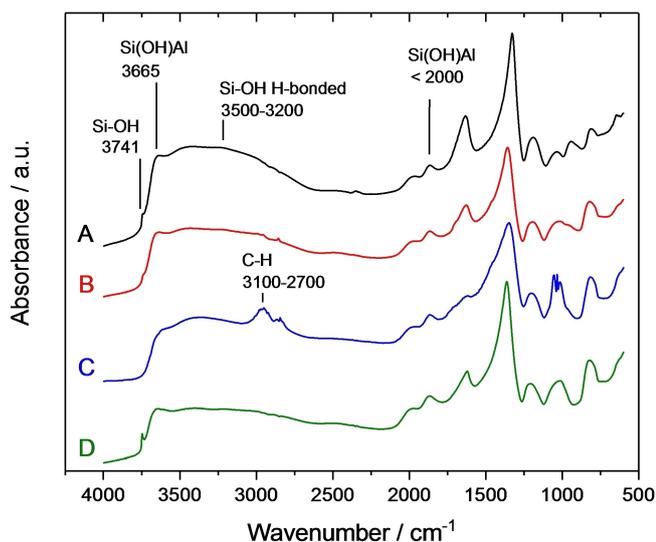


Figure 7. IR spectra of A) fresh, B) MeOH treated (24 h, 0.25 mL min⁻¹ MeOH, 200 °C, 40 bar), C) used and D) regenerated (6 h, 650 °C, 5 °C min⁻¹, air) H-β (38) (60–100 μm). Reaction conditions of used catalyst: 0.25 mL min⁻¹ 3.2 wt.% sorbitol in MeOH, 200 °C, 40 bar back pressure, substrate turnover = 127.

bridged Brønsted acid sites at 3741, 3665 and 3500–3200 cm⁻¹.^[18] Conversely, the IR spectrum of the used catalyst exhibited new bands in the range 3100–2700 cm⁻¹, which could be attributed to the presence of carbonaceous species retained by the catalyst during operation (coke).^[19] To verify the carbonaceous nature of such species, the used catalyst was calcined in air at 650 °C for 6 hours with a ramp rate of 5 °C min⁻¹, and denoted for simplicity as regenerated catalyst. The IR spectrum of the regenerated catalyst did not show vibrations associated with C–H stretches, confirming that during the heat treatment the carbonaceous species trapped on the catalyst were removed, thus restoring the pristine catalyst. However, TGA analysis of the fresh and used catalysts suggested that the total quantity of carbonaceous residue deposited during reaction was very low, which likely accounts for the high level of stability exhibited by the catalyst (Figure S1–S2).

To investigate whether the small amount of carbonaceous residue detected on the used catalyst was generated as a consequence of the solvent or the substrate, H-β (38) was treated with a 0.25 mL min⁻¹ flow of MeOH for 24 hours at 200 °C and 40 bar (in the absence of the substrate), and subsequently dried overnight. The IR spectrum of the MeOH treated catalyst exhibited the same absorptions of the fresh catalyst but no band in the C–H region, confirming that the

band at 3110–2750 cm⁻¹ relates to formation of carbonaceous species arising from reactive components of the system (reactants, (by)-products), and not simply the solvent. In order to investigate coke formation during the reaction, the used catalyst was recovered at different stages of the continuous process, notably after 21 and 146 substrate turnovers, and characterised *via* porosimetry analysis (we note for reference that the total number of turnovers after 55 hours was 211). The DFT surface area of the catalyst decreased rapidly at increasing levels of substrate turnover (Table 1). Indeed, after only a short time on stream (21 turnovers) the catalyst surface area was already reduced to 75 % of its initial value, decreasing further to 28 % of the initial value after extended time on stream (146 turnovers). The micropore volume of the catalyst was equally affected during continuous operation (Table 1). Porosimetry analysis further demonstrated the efficiency of the heat treatment to remove the carbonaceous residues from the zeolite pores, in accordance to the IR analysis. In fact, after the thermal treatment, the surface area and micropore volume of the framework were almost fully restored. These findings suggest that deposition of carbonaceous residue causes fouling of the catalyst during continuous operation, either through accumulation in the micropores, or by deposition on the surface and/or interparticle voids. However, despite the changes in porosity described in Table 1 and the formation of carbonaceous species on the catalyst (Figure 7), no loss of catalytic activity was observed at long reaction time (Figure 5). This excludes fouling as being a major contributor to the catalyst deactivation over the reaction period presented in Figure 5.

Conclusions

In this work, the feasibility of performing sorbitol dehydration to isosorbide over heterogeneous catalysts in continuous liquid-phase reactors was explored. Building on previous catalyst screening, zeolites were selected as suitable active materials to assist the continuous conversion of sorbitol into isosorbide. Amongst a range of zeolites with different shape and acidity, H-β (38) zeolite exhibited the best catalytic performance and was therefore identified as the most suitable material for continuous applications. A preliminary batch investigation of this reaction also demonstrated that aqueous reaction environments inhibit the full dehydration of sorbitol to isosorbide. Substitution of the aqueous reaction media with methanol increased isosorbide yield to a maximum of 46%, despite operating at milder conditions (170 °C).

Table 1. Surface area and porosimetry data obtained by nitrogen adsorption isotherm analysis.^[a]

| Entry | Sample | S_{NLDFT} [m ² g ⁻¹] | S_{micro} [m ² g ⁻¹] | S_{meso} [m ² g ⁻¹] | V_{micro} [mL g ⁻¹] |
|-------|-------------------------------|--|--|---|--|
| 1 | Fresh pelletised | 724 | 641 | 83 | 0.15 |
| 2 | Used (21 st ^[b]) | 543 | 462 | 81 | 0.10 |
| 3 | Used (146 st ^[b]) | 202 | 128 | 74 | 0.04 |
| 4 | Regenerated | 612 | 530 | 82 | 0.14 |

[a] All values calculated by applying the DFT method to the nitrogen adsorption isotherms (77 K). [b] Substrate turnovers.

Diagnostic kinetic studies performed on the continuous system indicated that diffusion limitations are negligible for flow rates of 0.20 mL min⁻¹ and above, and catalyst particle sizes smaller than 250 μm. Optimisation of the continuous reactor allowed isosorbide yields of up to 60% to be obtained without compromising the overall carbon balance.

A long term kinetic experiment performed at conditions suitable for deactivation studies (sub-maximal conversion) was successfully performed over H-β (38) zeolite in a plug flow reactor. Over a 55 hours period of continuous operation, no loss of activity was detected, demonstrating the excellent stability of the catalyst. The high catalyst stability, together with the good isosorbide yield reached in the continuous liquid-phase system, allowed an isosorbide productivity of 9670 g_{isosorbide}/kg_{catalyst} to be achieved. This value is the best productivity value achieved by a continuous sorbitol dehydration reaction system to date (Table S1), and was achieved despite the reaction being deliberately performed at sub-maximal conversion, was undertaken at temperatures at least 50 °C lower than previous reports, and was terminated prior to the catalyst experiencing any loss of activity.

Although no loss of activity was observed up to 55 hours of time on stream, characterisation analyses performed on both fresh and used catalyst revealed coke deposition on the post-reaction catalyst. However, the total quantity of carbonaceous residue as determined by TGA was negligible, and since no loss of activity accompanied this deposition, catalyst fouling cannot be considered as a major reason of deactivation over this reaction timeframe. Moreover, heat treatment of the used catalyst was found to be an efficient method to almost completely restore the initial material, removing the carbonaceous species deposited on the catalyst throughout reaction.

Experimental Section

Materials

Sorbitol (≥ 98%), cellobiose (≥ 98%), H₂SO₄ (≥ 97%), and HCl (37%) were purchased from Sigma-Aldrich. MeOH (≥ 99.5%) was supplied by Fisher Scientific. All zeolites, including Beta, ZSM-5, Y, Ferrierite, Modernite were purchased from Zeolyst and transformed to their H⁺ form by calcination in air at 550 °C for 6 h, 5 °C min⁻¹ ramp rate, prior to their use.

Kinetics studies

Batch sorbitol dehydration reactions were performed in 50 mL Parr stainless-steel autoclave set at the desired temperature, autogenic pressure and 800 rpm. The autoclave liner was previously charged with 20 mL of sorbitol solution and the desired amount of catalyst. The impeller of the reactor was set in motion only when the desired reactor temperature was reached. At the end of the reaction, the autoclave was cooled in an ice-bath. Aliquots from the reaction mixture were collected for HPLC analysis. HPLC analysis of the samples was performed using an Agilent 1260 Infinity HPLC equipped with a Hi-Plex Ca column and ELS detector and quantified against an external standard solution (0.13 M cellobiose water solution) added to the sample prior to the injection. Conditions: 80 °C, 0.75 mL min⁻¹, HPLC water as eluent. Continuous reactions

were performed in a plug flow, stainless steel, tubular reactor. The reactor was connected to an Agilent HPLC pump in order to accurately regulate the reactant flow. Long term reaction was performed with a Cole-Parmer HPLC pump. In order to avoid flow obstruction by the catalyst bed, the zeolite was pelletised, prior to loading into the reactor, in a uniform 60–100 μm diameter grains. Then the catalyst pellets were densely packed into a 1/4 inch stainless-steel tube (4.1 mm internal diameter), held between two quartz wool plugs, and a frit of 0.5 μm was placed at the reactor exit. The reactor was subsequently placed inside a furnace (Carbolite EVT 12/450, Carbolite MTF12/38/ 400 for long term reaction (Figure 5)) and set at the desired temperature. Pressure in the system was controlled by means of a backpressure regulator, typically set at 40 bar. Aliquots of the reaction solutions were taken periodically from a sampling valve placed after the reactor. Catalyst regeneration was performed heating the whole reactor in a combustion furnace (Carbolite MTF12/38/ 400) to 650 °C (20 °C min⁻¹) in air for 6 hours.

Equations

$$\text{Substrate turnover} = \frac{n(\text{sorbitol}) \text{ time}^{-1} \times \sum \text{time}}{n(\text{Al})} \quad (1)$$

$$\text{Contact time} = \tau = \frac{\text{volume}_{(\text{catalyst bed, mL})}}{\text{flow rate} (\text{mL min}^{-1})} \quad (2)$$

$$\text{Linear velocity} = \text{flow rate}_{(\text{feed solution})} \text{volume}_{(\text{catalysts})}^{-1} \quad (3)$$

Catalyst characterisation

A PANalytical X'PertPRO X-ray diffractometer was employed for powder XRD analysis. A Cu Kα radiation source (40 kV and 30 mA) was utilised. Diffraction patterns were recorded between 10 and 80° 2θ (step size 0.0167°, time/step=150 s, total time=1 h). Specific surface area and microporous volume were determined from nitrogen adsorption isotherms by using DFT method. Porosimetry measurements were performed on a Quantachrome Autosorb iQ2, and samples were degassed prior to use for 6 hours at 277 °C. Adsorption isotherms were obtained at 77 K. A Bruker Tensor spectrometer equipped with a Harrick praying mantis cell was utilised for DRIFT measurements. Spectra were recorded between 4000–650 cm⁻¹ at a resolution of 2 cm⁻¹. TGA analysis was performed on a Perkin Elmer system. Samples were held isothermally at 30 °C for 30 minutes, before being heated to 850 °C (5 °C min⁻¹ ramp rate) in air.

Acknowledgements

CH gratefully appreciates the support of The Royal Society, for provision of a University Research Fellowship (UF140207, URF\R\201003) and enhanced research grant funding (RGF/EA/180314).

Conflict of Interest

The authors declare no conflict of interest.

Keywords: Continuous flow · Liquid-phase · Sorbitol dehydration · Isosorbide production · Zeolites

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Manuscript received: August 3, 2020

Revised manuscript received: September 25, 2020

Accepted manuscript online: September 29, 2020

Version of record online: ■■■, ■■■■

FULL PAPERS

Continuous liquid-phase production of isosorbide: Dehydration of sorbitol to isosorbide was performed in a continuous liquid-phase reactor, using H- β (38) zeolite as solid catalyst. The catalyst demonstrated stable performance up to 55 hours and a total isosorbide productivity of $9670 \text{ g}_{\text{isosorbide}}/\text{kg}_{\text{catalyst}}$.



M. Caiti, Dr. G. Tarantino, Dr. C. Hammond

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Developing a Continuous Process for Isosorbide Production from Renewable Sources

