ChemCatChem

Research Article
doi.org/10.1002/cctc.202201224

Chemistry Europe
European Chemical Societies Publishing

www.chemcatchem.org

Check for updates

Continuous flow (Sulfated) Zirconia Catalysed Cascade Conversion of Levulinic Acid to γ-Valerolactone

Andrea Merenda,[a] Samantha A. Orr,[a] Yang Liu,[a] Blanca Hernández Garcia,[b] Amin Osatiashtiani,[c] Gabriel Morales,[b] Marta Paniagua,[b] Juan A. Melero,[b] Adam F. Lee,*[a] and Karen Wilson*[a]

γ-Valerolactone (GVL) is a renewable and versatile platform chemical derived from sustainable carbon feedstocks. The cascade conversion of levulinic acid into GVL requires Brønsted and Lewis acid catalysed reactions. Here, a dual-catalyst bed configuration is demonstrated that promotes synergy between Brønsted acid sites in sulfated zirconia (SZ) and Lewis acid sites in ZrO_2/SBA-15 for the liquid phase, continuous flow esterification and subsequent catalytic transfer hydrogenation (CTH) of levulinic acid to GVL. A saturated surface sulfate monolayer, possessing a high density of strong Brønsted acid sites, was optimal for levulinic acid esterification to isopropyl levulinate over SZ (>80% conversion). A conformal ZrO_2 bilayer, deposited over a SBA-15 mesoporous silica and possessing mixed Brønsted:Lewis acidity, catalysed CTH of the levulinate ester and subsequent dealcoholisation/cyclisation to GVL (>60% selectivity). Maximum stable productivity for the dual-bed was 2.2 $mmol_{GVL}.g_{cat}.h^{-1}$ at 150 °C, significantly outperforming either catalyst alone or a physical mixture of both. Flow chemistry is a versatile approach to achieve spatial control over cascade transformations involving distinct catalytically active sites.

Introduction

The success of the modern petrochemical industry is predicated on maximising the number of valuable chemical products from crude oil. So effective has this strategy proven that, perhaps surprisingly, oil refineries operate with extremely low environmental (E-) factors, generating <0.1 kg of waste per kg of product.[1] For biorefineries to be sustainable and economical, they too must maximise the number of potential products (value streams) that can be derived from (predominantly) lignocellulosic biomass. Many platform chemicals, derived from the carbohydrate components of biomass, have been proposed as routes to either drop-in chemicals/fuels or molecules with desirable properties unique from their petroleum counterparts.[2] For example, 5-hydroxymethylfurfural (5-HMF)[3] offers access to a range of furanics, including 2,5-furandicarboxylic acid and dimethyl furan, and non-furanics such as adipic acid and 1,6-caprolactam. Levulinic acid (LA) is another platform chemical[4] that can be obtained from either cellulose (glucose→5-HMF and subsequent hydrolysis[5]) or hemicellulose (xylose→furfural and subsequent hydrogenation and hydrolysis[6]).[7]

A common challenge in constructing bio-derived chemical platforms is developing atom- and energy-efficient transformations to selectively access specific products from the parent molecule. Considering the levulinic acid platform, one of the most desirable products is γ-valerolactone (GVL),[8] a green solvent in biomass processing,[9] precursor for the production of fatty acid esters (biodiesel), C_8–C_{18} alkanes (diesel/jet fuel), and chemical intermediate to polymers and value-added chemicals.[10] GVL can be obtained by the catalytic hydrogenation of levulinic acid (LA), derived from C_5 or C_6 sugars,[11] over noble metal catalysts such as Ru, Ir, Pd or Pt using molecular H_2 at high pressure (>30 bar).[11b] However, the use of precious metals and high pressure reactors is inconsistent with Green Chemistry principles, and a barrier to scale-up in a commercial biorefinery.[11b,12] Alternative strategies to produce GVL from LA, exemplified by catalytic transfer hydrogenation (CTH) over non-precious metals through a Meerwein-Ponndorf-Verley (MPV) mechanism,[13] have thus sparked significant interest.

Zirconia has emerged as a promising candidate for GVL production by direct or transfer hydrogenation. For example, Ru/ZrO_2[14] and Cu/ZrO_2[15] achieve GVL yields of 80–99% in batch under 27–35 bar H_2 at 150–200 °C. Continuous flow conversion of LA in water over Ru/ZrO_2 under 50 bar H_2 achieved LA conversions reaching 85%, however the catalyst progressively deactivated due to the formation of carbonaceous by-products accompanied by a 20% loss of surface area.[16]

[a] A. Merenda, S. A. Orr, Y. Liu, A. F. Lee, K. Wilson
Centre for Advanced Materials and Industrial Chemistry
RMIT University
Melbourne, VIC 3000, Australia
E-mail: adamfraserlee@gmail.com
karen.wilson2@rmit.edu.au
adamf.lee@csiro.au
[b] B. Hernández Garcia, G. Morales, M. Paniagua, J. A. Melero
Universidad Rey Juan Carlos
C/Tulipan s/n. E-28933 Mostoles, Madrid, Spain
[c] A. Osatiashtiani
Energy and Bioproducts Research Institute
College of Engineering and Physical Sciences
Aston University
Birmingham B4 7ET, UK

Supporting information for this article is available on the WWW under https://doi.org/10.1002/cctc.202201224

© 2022 The Authors. ChemCatChem published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution Non-Commercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2022 The Authors. ChemCatChem published by Wiley-VCH GmbH

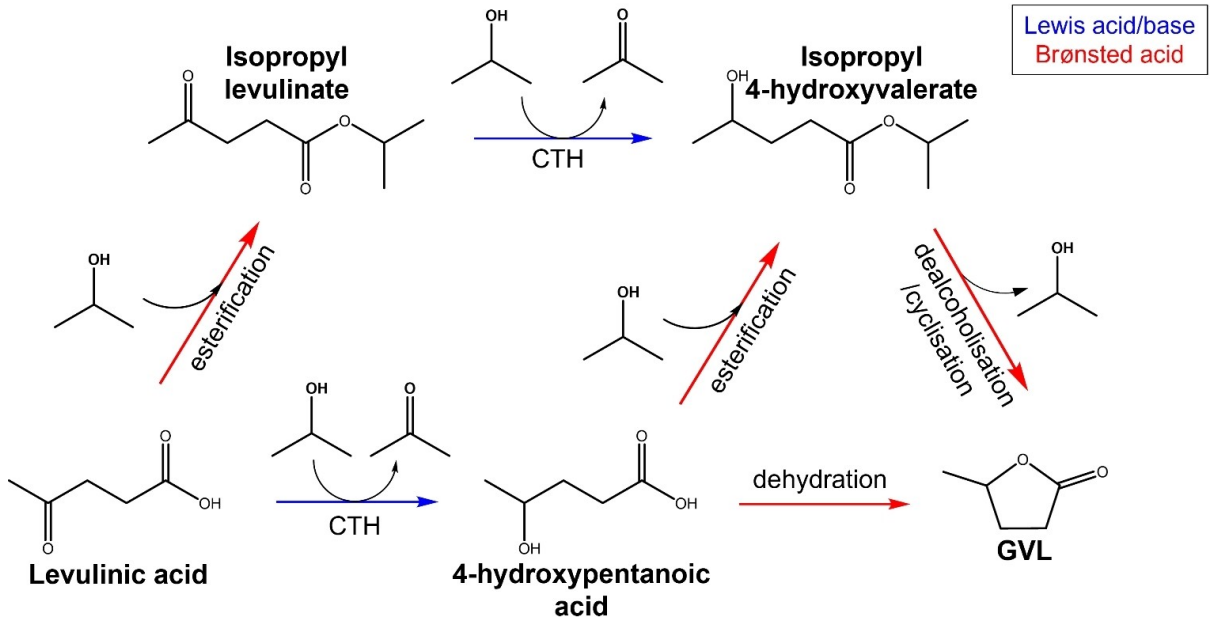
18673899, 0, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cctc.202201224 by <Shibboleth>-member@aston.ac.uk, Wiley Online Library on [23/01/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Zirconia is also effective for CTH using short chain alcohols as hydrogen donors at comparatively mild temperatures (110–250 °C).[17] Batchwise LA conversion to GVL through a CTH pathway was reported for a precipitated ZrO_2, affording complete LA conversion and a 71 % GVL yield at 220 °C in 16 h with a 2-butanol hydrogen donor and 50 wt % catalyst.[17a] Ni/ZrO_2 yielded 86 % GVL at 120 °C in 20 h with 2-propanol, albeit at 100 wt% catalyst loading.[18] Although a Zr MOF-808, containing Zr_6 oxoclusters, delivered 97 % GVL yield in a one-pot cascade with *sec*-butanol at only 130 °C,[19] activity was low requiring > 70 h. More promising are Zr-doped Al-Beta zeolites, for which Morales and co-workers obtained full LA conversion and 87 % GVL yield in batch with 2-propanol within 2 h reaction at 170 °C;[20] the optimised productivity was 1.3 $g_{GVL}.g_{cat}^{-1}.h^{-1}$ at 190 °C. A Zr-Beta zeolite (Si : Zr = 127) catalyst was active and highly selective for LA to GVL with a 2-butanol donor at 120 °C, producing ~98 % GVL in 11 h.[21] Zirconia has also been dispersed on silica to increase the density of active sites, with 10 wt% ZrO_2/SBA-15 achieving full LA conversion and 90 % GVL yield in batch at 150 °C (under 10 bar Ar) over 3 h,[12] attributed to Zr^{4+} strong Lewis acid sites and unsaturated Zr^{4+}–O^{2-} pairs. Conformal zirconia bilayers grown on SBA-15 can catalyse the cascade transformation of furfural to GVL at 170 °C, but with modest (37 %) yields, being limited by a lack of strong Lewis or Brønsted acidity.[22]

Continuous flow valorisation of biomass offers significant advantages over analogous batch reactions, notably improved safety, higher atom-efficiency and more facile scale-up.[23] Vapour phase continuous flow CTH of LA over ZrO_2/SBA-15 catalysts, prepared by wet impregnation of zirconium acetyl acetonate, demonstrated complete conversion and 93 % GVL yield with 2-propanol at 250 °C and 1 bar.[17c] This equated to a productivity of 0.34 $g_{GVL}.g_{cat}^{-1}.h^{-1}$ which was maintained for > 5 h on-stream. In contrast, liquid phase continuous flow CTH using the aforementioned Zr-Al-Beta zeolite[24] achieved 44.4 $g_{GVL}.g_{cat}^{-1}.h^{-1}$ at 190 °C (corresponding to 76 % selectivity to GVL and a 65 % GVL yield) for > 200 h on-stream using a high LA concentration of 220 $g.L^{-1}$. This excellent performance was achieved through the dual Brønsted/Lewis character of the catalyst, high reaction temperature, and an in-situ catalyst activation protocol; a lower initial GVL yield of 42 % was obtained without the in-situ activation.

Mechanistically, the cascade transformation of LA into GVL requires cooperativity between multiple active sites and can follow several reaction pathways (Scheme 1). GVL may form through Lewis acid (or base)-catalysed CTH and subsequent Brønsted acid promoted dehydration through a 4-hydroxypentanoic acid (4-HPA) intermediate.[12–13,25] Alternatively, LA may first undergo Brønsted acid-catalysed esterification, with the resulting levulinic esters then experiencing Lewis acid (base)-catalysed CTH prior to a Brønsted catalysed dealcoholisation and cyclisation to GVL.[12,26] Although Lewis acid and base sites can promote CTH, basic sites are undesirable due to their propensity to strongly adsorb the LA reactant.[27] For zirconia, mechanistic studies have focused on the role of Lewis acid centres, such as Zr^{4+}, and unsaturated Zr^{4+}–O^{2-} pairs in the CTH of levulinic esters,[12–13] however the interplay between Brønsted and Lewis acid sites in the cascade synthesis of GVL is less clear.

Current strategies to enhance the performance of bulk ZrO_2 catalysts include the *in situ* generation of $HCl/ZrO(OH)_2$ and the synthesis of zirconium phosphonate catalysts. $HCl/ZrO(OH)_2$ catalysts achieved a maximum LA conversion and GVL yield of 99 and 83 %, respectively, in only 1 h at 240 °C with 2-propanol as hydrogen donor. Nonetheless, the formation of HCl and the high reaction temperatures employed pose significant safety concerns.[26] Introducing phosphate groups in Zr-phosphonate catalysts led to an increase in basicity compared to bulk ZrO_2,



Scheme 1. Proposed reaction pathways for levulinic acid transformation to GVL.

© 2022 The Authors. ChemCatChem published by Wiley-VCH GmbH

18673899, 0, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cctc.202201224 by <Shibboleth>-member@aston.ac.uk, Wiley Online Library on [23/01/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

leading to a LA conversion and GVL yield of 100 and 98.7%, respectively, in only 2 h at 130 °C with 2-propanol as hydrogen donor.[28]

A key study by Roman-Leshkov and co-workers demonstrated that efficient furfural conversion to GVL (via LA and its alkyl esters) could be achieved by a physical mixture of Brønsted and Lewis acid catalysts, i.e. close proximity between these distinct acid sites was not essential. Drawing inspiration from this work, we speculated that the cascade conversion of LA to GVL should be amenable to continuous flow operation using spatially separated Brønsted and Lewis acid catalyst beds. The former bed to catalyse LA esterification to its ester and the second to catalyse CTH to isopropyl 4-hydroxyvalerate (4-iPHV) and (hopefully) lactonisation to GVL. Sulfated zirconia (SZ) was chosen as the Brønsted acid catalyst due to its superacidity, thermal stability up to 650 °C.[29] and high activity for carboxylic acid esterification,[30] including of LA formed in-situ from glucose.[31] Our recent work on ZrO_2/SBA-15 identified this as efficient for the continuous flow CTH of ethyl levulinate CTH to GVL,[32] and hence this was chosen as the (predominantly) Lewis acid catalyst. The optimum catalyst selections delivered a high and stable GVL yield of 80% at 150 °C in flow, significantly higher than either individual catalyst in flow or a physical mixture in batch.

Results and Discussion

A family of SZ catalysts were first prepared by H_2SO_4 treatment of $Zr(OH)_4$ and subsequent calcination, as previously described.[33] Evolution of their structure and acidity with [H_2SO_4] is detailed in the Supporting Information. In brief, a sulfate monolayer is formed for a surface S loading ~5 wt% (Figure S1a) which stabilises tetragonal zirconia[34] (Figure S1b) with a surface area of 200 $m^2.g^{-1}$, double that of the parent ZrO_2. Higher S loadings induce a loss of crystallinity and surface area (Table S1) accompanying the formation of bulk zirconium sulfate.[33a] The total and Brønsted acid site densities, and acid strength, of SZ increases monotonically with S loading (Figure S2 and Table S1), reaching a maximum ~4.7 wt% (equivalent to 1.53 $mmol.g^{-1}$) above which the surface area and total acidity almost halve. Weaker acid sites at low S loadings are attributed to bidentate SO_4 groups with strong covalent character,[34–35] formed by the reaction of bisulfate with surface hydroxyls in the $Zr(OH)_4$ precursor.[36] Strong acid sites, probed by the reactive decomposition of n-propylamine, are ascribed to surface bisulfate-like species (ZrO_2(OH)(S-O)) adopting a bidentate configuration,[30c] with the fall in acid site densities above a saturated sulfate monolayer attributed to the formation of inactive pyrosulfates.[30a,c,33a]

The optimum SZ for the cascade transformation of LA to GVL was first determined by evaluating the batchwise esterification of LA with 2-propanol at 170 °C (Figure 1). The parent zirconia, which possessed few Brønsted acid sites, exhibited only 28% conversion in 6.5 h, and produced almost none of the desired isopropyl levulinate (IPL) ester. LA conversion increased monotonically with surface sulfation up to a maximum ~76%

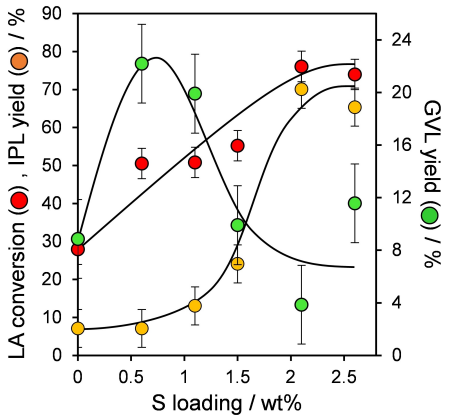


Figure 1. LA conversion, IPL production and GVL yield for SZ catalysts as a function of surface S loading. Reaction conditions: 6.5 h batch reaction; 170 °C; 100 mg of catalyst; 5 mmol levulinic acid, 500 mL 2-propanol solvent.

for 2.6 wt% S. However, significant IPL only formed for S loadings >1 wt%, for which SZ became predominantly Brønsted acidic (Table S1); the maximum IPL yield of ~70% coincided with the maximum LA conversion. Although higher sulfate loadings possessed higher acid site loadings and Brønsted character, they were prone to in-situ sulfate leaching (Figure S3), and hence were discounted in this work. The absence of IPL at low sulfate loadings coincides with the observation of GVL (which requires Lewis acid/base sites for the CTH step). A maximum GVL yield ~22% was attained for the 0.6 wt% surface S catalyst; further sulfation suppressed GVL production. These observations are consistent with the highlighted reaction mechanism in Scheme 1. Mixed Lewis/Brønsted acid character of parent and lightly sulfated ZrO_2 catalysts promote some LA esterification to IPL which undergoes rapid CTH and dealcoholisation to GVL. In contrast, heavily sulfated zirconias are more active for the esterification of LA to IPL, but lack sufficient Lewis acid character to catalyse the subsequent CTH step, hence reactively-formed IPL accumulates. This switchover in reactivity is clear from the steep decrease in selectivity to GVL at iso-conversion for surface S loadings >1 wt% (Figure S4).

As noted above, we recently reported ZrO_2/SBA-15 as an efficient Lewis acid catalyst for the CTH of ethyl levulinate to GVL at 150–170 °C. This catalyst was prepared by the layer-by-layer growth of conformal ZrOx monolayers on the mesoporous silica template from a Zr isopropoxide precursor under anhydrous conditions; hydrolysis between monolayer growth cycles ensured precursor conversion to zirconia. Physicochemical properties of the ZrO_2/SBA-15 bilayer catalyst are reported in the literature.[31] Having selected each catalyst for the cascade, they were first individually assessed in packed bed reactors under continuous flow at 150 °C. In all cases, a common total residence time ($\tau = 50$ min) was used, with steady state achieved after approximately 3 h on-stream. As anticipated from Figure 1, the predominantly Brønsted acidic 2.6 wt% SZ showed a high LA conversion of 81% averaged over 6.5 h on-stream (Figure 2a), but produced negligible GVL being unable

© 2022 The Authors. ChemCatChem published by Wiley-VCH GmbH

18673899, 0, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cctc.202201224 by <Shibboleth>-member@aston.ac.uk, Wiley Online Library on [23/01/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

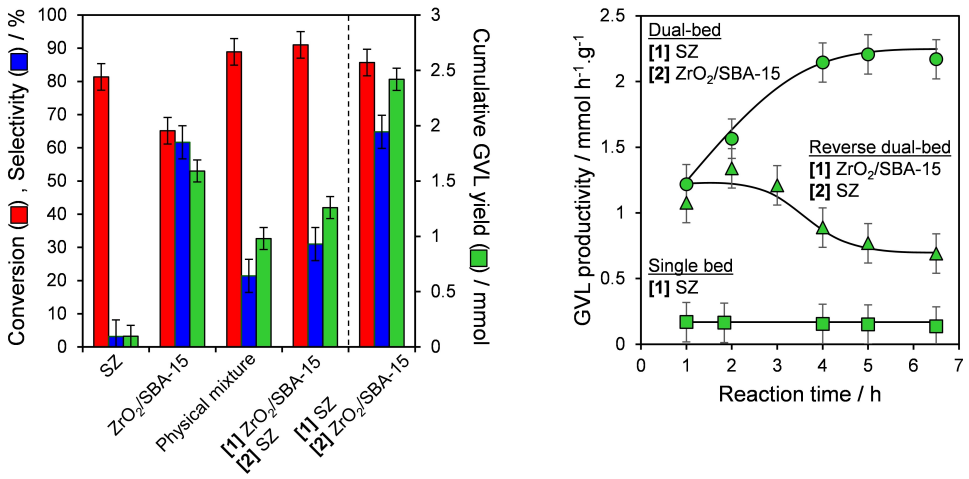


Figure 2. Cascade conversion of LA to GVL: (a) continuous flow over single bed SZ catalyst with 2.6 wt% sulfur surface content, single bed commercial ZrO_2/SBA-15 catalyst, sequential dual-bed of SZ + SBA-15 and batch conversion over physical mixture of SZ catalyst with 2.6 wt% sulfur surface content + Zr/SBA-15. (b) Comparison of continuous flow productivity for the conversion of LA to GVL employing SZ catalyst with 2.6 wt% sulfur surface content (single bed) or SZ catalyst with 2.6 wt% sulfur surface content + Zr/SBA-15 catalyst over dual-bed configuration. Continuous flow reaction conditions: $\tau = 50$ min total for single and dual beds, 150 °C; 100 mg of catalyst (single bed), 200 mg of catalyst (dual-bed); 2-propanol solvent. Batch reactions employing physical mixture of SZ catalyst with 2.6 wt% sulfur surface content + Zr/SBA-15 were conducted under the same conditions, with a total duration of 6.5 h.

to drive the CTH reaction. ZrO_2/SBA-15, with mixed Brønsted: Lewis character (~0.6:1) and a much higher surface area (437 $m^2.g^{-1}$ versus 189 $m^2.g^{-1}$ for the SZ), exhibited moderate LA conversion and more importantly good selectivity to GVL (62%) reflecting its propensity for CTH. The cumulative GVL yield for ZrO_2/SBA-15 was 40% (1.6 mmol) in 6.5 h. A physical mixture of the two catalysts in a single reactor bed was subsequently examined (Figure 2a), with the resulting LA conversion similar to that for SZ alone (89%). However, GVL selectivity and yield were both comparatively poor, suggesting that reactive intermediates to GVL (or GVL itself) produced over ZrO_2/SBA-15 were unstable in the presence of strong Brønsted acid sites on the SZ catalyst.

By comparison, a dual-bed system ($\tau = 50$ min across both beds), comprising the SZ catalyst followed by the ZrO_2/SBA-15 catalyst (Figure S5a), evidenced strong synergy between the two catalysts. High LA conversion to IPL over the first bed promoted CTH and cyclisation over the second bed, resulting in a cumulative GVL yield of 55% (2.5 mmol) after 6.5 h, equating to a cumulative productivity of 1.8 $mmol_{GVL}.g_{cat}.h^{-1}$. GVL productivity for the dual increased monotonically with time over the dual-bed (Figure 2b), attaining a steady maximum of 2.2 $mmol_{GVL}.g_{cat}.h^{-1}$ after 4 h on-stream. Reversing the bed sequence (Figure S5b) significantly impaired GVL production (Figure 2a), which was lower than for ZrO_2/SBA-15 alone, consistent with the preceding hypothesis that CTH products such as 4-iPHV are unstable over strong Brønsted acid catalysts. GVL production for the reverse dual-bed (ZrO_2/SBA-15 followed by SZ) exhibited a significant decrease with time-on-stream before steady state was attained (Figure 2b). This most likely occurs due to the equilibrium between dealcoholisation of 4-iPHV to GVL and the reverse GVL ring opening and esterification with IPA. In the presence of excess IPA the latter will be favoured over the strong Brønsted acid sites of SZ in the second bed, conditions that will also promote subsequent etherification of 4-iPHV although the ether was not observed in this work.[26] GVL productivity for the [1] SZ + [2] ZrO_2/SBA-15 configuration significantly exceeded literature reports for batchwise operation, being 0.23 and 1 $mmol\,g^{-1}.h^{-1}$ for ZrO_2 or a physical mixture of MgO and ZrO_2, respectively.[17a] The vapour phase continuous flow reaction of LA delivered a GVL productivity of 2.92 $mmol\,g^{-1}.h^{-1}$, but required a much higher reaction temperature of 250 °C.[17c] The liquid phase continuous flow conversion of LA over Zr-Beta catalysts afforded a GVL yield of >99% and a GVL productivity of 460 $mmol_{GVL}.g_{metal}.h^{-1}$, nonetheless the reactor was operated at 250 °C with a higher concentration of LA (5 wt%) in the feed than in this study.[37] No angelica lactones (whose formation requires high temperatures[38] and reactive distillation to drive cyclodehydration[39]), di-isopropyl ether from 2-propanol autoetherification, or 4-HPA (usually favoured with metallic catalysts and molecular H_2)[40] were observed for any reactor configuration, suggesting that GVL was predominantly formed by the Brønsted acid-catalysed esterification pathway through IPL in Scheme 1.

Conclusions

Judicious selection of solid acid catalysts and their sequential arrangement in contiguous packed beds confers significant benefits for cascade reactions in continuous flow. Where reactive-intermediates are sufficiently stable, as in the case for levulinic acid (LA) esterification to isopropyl levulinate, that different active sites do not need to be in close proximity, this dual-bed approach obviates the need to design (synthetically-challenging) mutifunctional catalysts.[41] A sequential dual-bed configuration, comprising a heavily sulfated zirconia (2.6 wt% S) catalyst followed by a ZrO_2/SBA-15 catalyst, outperforms the

© 2022 The Authors. ChemCatChem published by Wiley-VCH GmbH

18673899, 0, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cctc.202201224 by <Shibboleth>-member@aston.ac.uk, Wiley Online Library on [23/01/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

individual catalysts or their physical mixture, affording a maximum γ-valerolactone (GVL) productivity of 2.2 mmol g^{-1} h^{-1}. Brønsted acidic sulfated zirconia alone is very active for the esterification of LA to isopropyl levulinate, but unable to catalyse transfer hydrogenation and subsequent lactonisation to form GVL. Zirconia possessing mixed Brønsted/Lewis character, as previously reported, is effective for the conversion of alkyl esters to GVL,[42] but unable to efficiently catalyse ester production from LA. Maximising LA esterification over sulfated zirconia significantly enhances subsequent (stable) GVL production over zirconia. Spatial separation of different catalysts for each step of a cascade within individual reactor beds also unlocks the possibility of catalyst operation under different conditions (e.g. temperature, pressure or pH). Such modular operation, widely employed in organic synthesis,[43] could enable the kinetics of each step in a chemical cascade to be precisely matched, without catalyst redesign, enabling rapid process optimisation.

Experimental Section

Catalyst synthesis: A series of SZ catalysts were prepared by impregnating $Zr(OH)_4$ (MEL Chemicals – XZO 880/01) with aqueous solutions of H_2SO_4 (at molarities spanning 0.015–0.5 M) as detailed in previous studies.[33a] Parent unsulfated zirconia references were synthetised by applying an identical calcination protocol to $Zr(OH)_4$. The as-synthetised catalysts were stored in air and used without pre-treatment. ZrO_2/SBA-15 was synthesised via a liquid phase atomic layer deposition method previously reported.[31]

Catalyst characterisation: The microstructure of the catalysts was analysed by powder X-ray diffraction (XRD) using a Bruker D8 Advance Diffractometer (Bruker Ltd.) equipped with a LynxEye high-speed detector and a Cu Kα (1.54 Å) X-ray source fitted with a Ni filter. Prior to the analysis, the diffractometer was calibrated against Si standards. The phase identification was carried out in the range $2\theta = 10$–$80°$ with a step size of 0.04°. X-ray photoelectron spectroscopy (XPS) measurements were conducted on a Kratos Axis His spectrometer fitted with a charge neutralizer and a Mg K_α X-ray source (hν = 1253.6 eV). Diffuse reflectance infrared Fourier transform spectroscopy (DRIFTS) was conducted on a Thermo Scientific Nicolet iS50 FT-IR equipped with a Thermo Scientific Nicolet environmental cell and a Smart Collector accessory. Prior to the analysis, powder samples were diluted with KBr to 10 wt% and mounted in the environmental cell. Samples underwent an additional drying step conducted at 110 °C for 10 min to remove physisorbed moisture. Ex situ pyridine adsorption was carried out by exposing the diluted samples to pyridine vapour in a desiccator overnight. Excess physisorbed pyridine was evacuated in a vacuum over prior to DRIFTS analysis in the environmental cell. DRIFTS spectra were acquired at 25 °C in vacuo. Acid loading and corresponding strength of the acid sites were evaluated by temperature-programmed decomposition (TPD) of n-propylamine to propene and NH_3 via the Hoffman elimination reaction. TPD analysis was conducted on a coupled thermogravimetric analysis-mass spectroscopy (TGA-MS) system. Prior to the analysis, TPD samples were prepared by impregnating the catalysts with n-propylamine (Sigma Aldrich, >99%) and then dried for 2 h while excess physisorbed n-propylamine was removed by vacuum-drying at room temperature overnight. TGA-MS was carried out on a Mettler Toledo STARe TGA-MS system (Mettler-Toled Ltd., UK) equipped with a Pfeiffer Vacuum ThermoStarTM GSD 301 T3 mass spectrometer (Pfeiffer Vacuum GmbH, Germany). The as-prepared samples were heated in the TGA furnace up to 1000 °C with a 10 °C·min-1 ramp under a constant N2 flow of 30 $cm^3 min^{-1}$.

Catalytic batch reactions: Kinetic studies of levulinic acid (LA) (> 97.5%, Sigma-Aldrich) and ethyl levulinate (EL) conversion into γ-valerolactone (GVL) were conducted in an autoclave reactor. In a typical procedure, 5 mmol of LA were mixed with 500 mmol of 2-propanol (>99.5%, Sigma-Aldrich) and 0.5 mmol of dodecane (> 99%, Sigma-Aldrich) used an internal standard. For each reaction, 100 mg of catalyst were added to the mixture. The reactor was sealed and purged three times with N_2 and finally pressurized to 5 bar with N_2. The reactor was heated to 170 °C under static conditions. Once the target temperature was reached, stirring was applied and aliquots were withdrawn periodically. The aliquots were filtered to remove the catalyst and injected in triplicates in a Shimadzu GC-2010Plus (Shimadzu Ltd.) fitted with a WAXPlus column and a flame ionisation detector (FID).

General procedure for flow reactions: Continuous flow catalytic transfer hydrogenation of LA and isopropyl alcohol was conducted at 150 °C using a Uniqsis FlowSyn reactor (Figure S6). The appropriate catalyst quantity i) 100 mg (single bed) or ii) 100 mg of each catalyst (dual-bed) separated by quartz wool was diluted with quartz beads (Sigma, mesh size = 325), and packed within a 10 mm i.d. × 100 mm OMNIFIT® glass column to give a total bed length between 4.5 and 6.5 cm and volume between 3.5 and 5 cm^3. The integrated HPLC pumps in the FlowSyn reactor deliver a liquid stream of isopropyl alcohol (1000 mmol) and LA (10 mmol), equvialent to 15 gLA.L^{-}1, to the packed bed at flow rates between 0.09 (τ of 50 min) to 0.15 ml.min^{-1} as calculated using the formula Flow rate (Q) = reactor volume (V)/residence time (RT). Samples were periodically collected for GC analysis. The aliquots were injected in triplicates in a HP 6890 series GC system fitted with a HP-INNOWAX (20 m length, 0.18 mm diameter and 0.18 μm film) column and a flame ionisation detector (FID), see ESI for GC analytical method. A representative GC chromatogram is provided in Figure S7.

Levulinic acid conversion, as well as GVL yield and selectivity were calculated as in the equations below:

$$\text{Conversion } (\%) = \frac{(\text{moles LA at } t = 0) - (\text{moles LA at } t = i)}{(\text{moles LA at } t = 0)} \quad (1)$$

$$\text{GVL yield } (\%) = \frac{\text{moles GVL at } t = i}{\text{moles LA at } t = 0} \times 100 \quad (2)$$

$$\text{GVL selectivity } (\%) = \frac{\text{GVL yield}}{\text{LA conversion}} \times 100 \quad (3)$$

Acknowledgements

We thank the Australian Research Council for financial support (DP200100204, DP200100313 and LE210100100), and Luxfer MEL Technologies for providing materials. Open Access publishing facilitated by RMIT University, as part of the Wiley - RMIT University agreement via the Council of Australian University Librarians.

© 2022 The Authors. ChemCatChem published by Wiley-VCH GmbH

18673899, 0, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cctc.202201224 by <Shibboleth>-member@aston.ac.uk, Wiley Online Library on [23/01/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

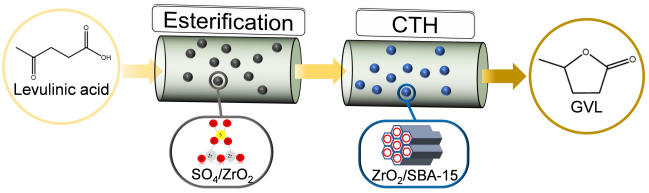
Keywords: catalytic transfer hydrogenation · continuous flow reaction · dual-bed cascade · γ-valerolactone · sulfated zirconia

[1] R. A. Sheldon, *ACS Sustainable Chem. Eng.* **2018**, *6*, 32–48.
[2] a) T. Werpy, G. Petersen, National Renewable Energy Lab., Golden, CO (US), **2004**; b) J. J. Bozell, G. R. Petersen, *Green Chem.* **2010**, *12*, 539–554; c) S. Takkellapati, T. Li, M. A. Gonzalez, *Clean Technologies and Environmental Policy* **2018**, *20*, 1615–1630.
[3] R.-J. van Putten, J. C. van der Waal, E. de Jong, C. B. Rasrendra, H. J. Heeres, J. G. de Vries, *Chem. Rev.* **2013**, *113*, 1499–1597.
[4] T. A. Aderemi, L. Hitler, U. A. Ozioma, J. Innocent, C. E. Obieze, P. M. Dass, *AIMS Energy* **2019**, *7*, 165–185.
[5] a) W. Deng, Q. Zhang, Y. Wang, *Science China Chemistry* **2015**, *58*, 29–46; b) Y. Qu, Y. Zhao, S. Xiong, C. Wang, S. Wang, L. Zhu, L. Ma, *Energy Fuels* **2020**, *34*, 11041–11049.
[6] K. Y. Nandiwale, M. Vishwakarma, S. Rathod, I. Simakova, V. V. Bokade, *Energy Fuels* **2021**, *35*, 539–545.
[7] M. Signoretto, S. Taghavi, E. Ghedini, F. Menegazzo, *Molecules* **2019**, *24*, 2760.
[8] a) K. Yan, Y. Yang, J. Chai, Y. Lu, *Appl. Catal. B* **2015**, *179*, 292–304; b) A. Osatiashtiani, A. F. Lee, K. Wilson, *J. Chem. Technol. Biotechnol.* **2017**, *92*, 1125–1135.
[9] D. M. Alonso, S. G. Wettstein, M. A. Mellmer, E. I. Gurbuz, J. A. Dumesic, *Energy Environ. Sci.* **2013**, *6*, 76–80.
[10] F. Kerkel, M. Markiewicz, S. Stolte, E. Müller, W. Kunz, *Green Chem.* **2021**, *23*, 2962–2976.
[11] a) H. Kobayashi, A. Fukuoka, *Green Chem.* **2013**, *15*, 1740–1763; b) S. Dutta, I. K. M. Yu, D. C. W. Tsang, Y. H. Ng, Y. S. Ok, J. Sherwood, J. H. Clark, *Chem. Eng. J.* **2019**, *372*, 992–1006.
[12] Y. Kuwahara, W. Kaburagi, Y. Osada, T. Fujitani, H. Yamashita, *Catal. Today* **2017**, *281*, 418–428.
[13] a) M. J. Gilkey, B. Xu, *ACS Catal.* **2016**, *6*, 1420–1436; b) J. Song, M. Hua, X. Huang, A. Visa, T. Wu, H. Fan, M. Hou, Z. Zhang, B. Han, *Green Chem.* **2021**, *23*, 1259–1265.
[14] a) J. Ftouni, A. Muñoz-Murillo, A. Goryachev, J. P. Hofmann, E. J. M. Hensen, L. Lu, C. J. Kiely, P. C. A. Bruijnincx, B. M. Weckhuysen, *ACS Catal.* **2016**, *6*, 5462–5472; b) B. Coşkuner Filiz, E. S. Gnanakumar, A. Martínez-Arias, R. Gengler, P. Rudolf, G. Rothenberg, N. R. Shiju, *Catal. Lett.* **2017**, *147*, 1744–1753.
[15] D. R. Jones, S. Iqbal, S. Ishikawa, C. Reece, L. M. Thomas, P. J. Miedziak, D. J. Morgan, J. K. Edwards, J. K. Bartley, D. J. Willock, G. J. Hutchings, *Catal. Sci. Technol.* **2016**, *6*, 6022–6030.
[16] H. C. Genuino, H. H. van de Bovenkamp, E. Wilbers, J. G. M. Winkelman, A. Goryachev, J. P. Hofmann, E. J. M. Hensen, B. M. Weckhuysen, P. C. A. Bruijnincx, H. J. Heeres, *ACS Sustainable Chem. Eng.* **2020**, *8*, 5903–5919.
[17] a) M. Chia, J. A. Dumesic, *Chem. Commun.* **2011**, *47*, 12233–12235; b) J. Iglesias, J. A. Melero, G. Morales, J. Moreno, Y. Segura, M. Paniagua, A. Cambra, B. Hernández, *Catalysts* **2015**, *5*, 1911–1927; c) S. S. Enumula, V. R. B. Gurram, M. Kondeboina, D. R. Burri, S. R. R. Kamaraju, *RSC Adv.* **2016**, *6*, 20230–20239.
[18] K. Sakakibara, K. Endo, T. Osawa, *Catal. Commun.* **2019**, *125*, 52–55.
[19] J. M. Guarinos, F. G. Cirujano, A. Rapeyko, F. X. Llabrés i Xamena, *Molecular Catalysis* **2021**, *515*, 111925.
[20] G. Morales, J. A. Melero, J. Iglesias, M. Paniagua, C. López-Aguado, *React. Chem. Eng.* **2019**, *4*, 1834–1843.
[21] L. Bui, H. Luo, W. R. Gunther, Y. Román-Leshkov, *Angew. Chem. Int. Ed.* **2013**, *52*, 8022–8025; *Angew. Chem.* **2013**, *125*, 8180–8183.
[22] J. Iglesias, J. A. Melero, G. Morales, M. Paniagua, B. Hernández, A. Osatiashtiani, A. F. Lee, K. Wilson, *Catal. Sci. Technol.* **2018**, *8*, 4485–4493.
[23] R. Gérardy, D. P. Debecker, J. Estager, P. Luis, J.-C. M. Monbaliu, *Chem. Rev.* **2020**, *120*, 7219–7347.
[24] C. López-Aguado, M. Paniagua, J. A. Melero, J. Iglesias, P. Juárez, M. López Granados, G. Morales, *Catalysts* **2020**, *10*, 678.
[25] L. Luo, X. Han, Q. Zeng, *Catalysts* **2020**, *10*, 1096.
[26] X. Tang, X. Zeng, Z. Li, W. Li, Y. Jiang, L. Hu, S. Liu, Y. Sun, L. Lin, *ChemCatChem* **2015**, *7*, 1372–1379.
[27] Z. Xue, Q. Liu, J. Wang, T. Mu, *Green Chem.* **2018**, *20*, 4391–4408.
[28] J. Song, B. Zhou, H. Zhou, L. Wu, Q. Meng, Z. Liu, B. Han, *Angew. Chem. Int. Ed.* **2015**, *54*, 9399–9403; *Angew. Chem.* **2015**, *127*, 9531–9535.
[29] Y. Wang, K.-Y. Lee, S. Choi, J. Liu, L.-Q. Wang, C. H. F. Peden, *Green Chem.* **2007**, *9*, 540–544.
[30] a) A. Osatiashtiani, L. J. Durndell, J. C. Manayil, A. F. Lee, K. Wilson, *Green Chem.* **2016**, *18*, 5529–5535; b) W. Zhang, Z. Wang, J. Huang, Y. Jiang, *Energy Fuels* **2021**, *35*, 9209–9227; c) A. I. M. Rabee, G. A. H. Mekhemer, A. Osatiashtiani, M. A. Isaacs, A. F. Lee, K. Wilson, M. I. Zaki, *Catalysts* **2017**, *7*, 204.
[31] G. Morales, A. Osatiashtiani, B. Hernández, J. Iglesias, J. A. Melero, M. Paniagua, D. Robert Brown, M. Granollers, A. F. Lee, K. Wilson, *Chem. Commun.* **2014**, *50*, 11742–11745.
[32] A. Osatiashtiani, S. A. Orr, L. J. Durndell, I. C. García, A. Merenda, A. F. Lee, K. Wilson, *Catal. Sci. Technol.* **2022**, *12*, 5611–5619.
[33] a) A. Osatiashtiani, A. F. Lee, D. R. Brown, J. A. Melero, G. Morales, K. Wilson, *Catal. Sci. Technol.* **2014**, *4*, 333–342; b) X. Zhang, A. I. M. Rabee, M. Isaacs, A. F. Lee, K. Wilson, *ACS Sustainable Chem. Eng.* **2018**, *6*, 14704–14712.
[34] M. A. Ecormier, K. Wilson, A. F. Lee, *J. Catal.* **2003**, *215*, 57–65.
[35] A. Clearfield, G. P. D. Serrette, A. H. Khazi-Syed, *Catal. Today* **1994**, *20*, 295–312.
[36] a) B. M. Reddy, M. K. Patil, *Chem. Rev.* **2009**, *109*, 2185–2208; b) G. X. Yan, A. Wang, I. E. Wachs, J. Baltrusaitis, *Appl. Catal. A* **2019**, *572*, 210–225.
[37] J. Wang, S. Jaenicke, G.-K. Chuah, *RSC Adv.* **2014**, *4*, 13481–13489.
[38] D. Sun, Y. Takahashi, Y. Yamada, S. Sato, *Appl. Catal. A* **2016**, *526*, 62–69.
[39] A. Corma, S. Iborra, A. Velty, *Chem. Rev.* **2007**, *107*, 2411–2502.
[40] M. G. Al-Shaal, W. R. H. Wright, R. Palkovits, *Green Chem.* **2012**, *14*, 1260–1263.
[41] M. A. Isaacs, C. M. A. Parlett, N. Robinson, L. J. Durndell, J. C. Manayil, S. K. Beaumont, S. Jiang, N. S. Hondow, A. C. Lamb, D. Jampaiah, M. L. Johns, K. Wilson, A. F. Lee, *Nature Catalysis* **2020**, *3*, 921–931.
[42] a) X. Tang, L. Hu, Y. Sun, G. Zhao, W. Hao, L. Lin, *RSC Adv.* **2013**, *3*, 10277–10284; b) N. Lázaro, A. Franco, W. Ouyang, A. M. Balu, A. A. Romero, R. Luque, A. Pineda, *Catalysts* **2019**, *9*, 142; c) P. B. Vásquez, T. Tabanelli, E. Monti, S. Albonetti, D. Bonincontro, N. Dimitratos, F. Cavani, *ACS Sustainable Chem. Eng.* **2019**, *7*, 8317–8330; d) T. Tabanelli, E. Paone, P. Blair Vásquez, R. Pietropaolo, F. Cavani, F. Mauriello, *ACS Sustainable Chem. Eng.* **2019**, *7*, 9937–9947; e) J. Lai, S. Zhou, X. Liu, Y. Yang, J. Lei, Q. Xu, D. Yin, *Catal. Lett.* **2019**, *149*, 2749–2757.
[43] a) S. V. Ley, *The Chemical Record* **2012**, *12*, 378–390; b) J. C. Pastre, D. L. Browne, S. V. Ley, *Chem. Soc. Rev.* **2013**, *42*, 8849–8869; c) R. Porta, M. Benaglia, A. Puglisi, *Org. Process Res. Dev.* **2016**, *20*, 2–25; d) J. Jiao, W. Nie, T. Yu, F. Yang, Q. Zhang, F. Aihemaiti, T. Yang, X. Liu, J. Wang, P. Li, *Chem. Eur. J.* **2021**, *27*, 4817–4838; e) L. Wan, G. Kong, M. Liu, M. Jiang, D. Cheng, F. Chen, *Green Synthesis and Catalysis* **2022**, *3*, 243–258; f) K. Masuda, T. Ichitsuka, N. Koumura, K. Sato, S. Kobayashi, *Tetrahedron* **2018**, *74*, 1705–1730.

Manuscript received: October 11, 2022
Accepted manuscript online: December 19, 2022
Version of record online: [redacted], [redacted]

© 2022 The Authors. ChemCatChem published by Wiley-VCH GmbH

18673899, 0, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cctc.202201224 by <Shibboleth>-member@aston.ac.uk, Wiley Online Library on [23/01/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A. Merenda, S. A. Orr, Y. Liu, B. Hernández Garcia, A. Osatiashtiani, G. Morales, M. Paniagua, J. A. Melero, A. F. Lee, K. Wilson**

1 – 7

Continuous flow (Sulfated) Zirconia Catalysed Cascade Conversion of Levulinic Acid to γ-Valerolactone

Transforming bio-derived molecules into value added products often requires multiple chemical reactions driven by different catalytic active sites. It remains challenging to design catalysts to drive such chemical 'cascades' in a single reactor. Here, the synergistic coupling of different catalysts, placed within spatially separated reactors, is demonstrated for the cascade conversion of levulinic acid to γ-valerolectone in continuous flow.

18673899, 0, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cctc.202201224 by <Shibboleth>-member@aston.ac.uk, Wiley Online Library on [23/01/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License