Combined dehydration/(transfer)-hydrogenation of C6-sugars (D-glucose and D-fructose) to γ-valerolactone using ruthenium catalysts†

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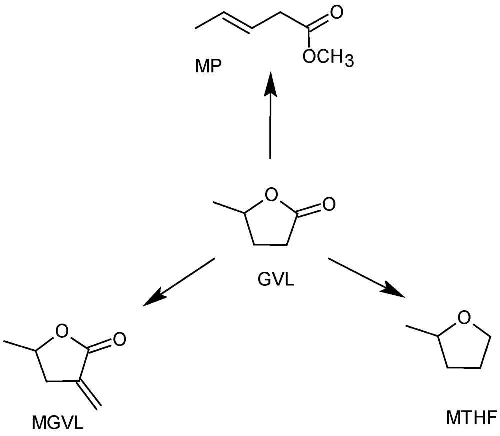
γ-Valerolactone (GVL) is considered a very interesting green, bio-based platform chemical with high application potential. We here describe research activities on the one-pot catalytic synthesis of GVL from C6-sugar sources (D-glucose, D-fructose, sucrose and cellulose) using an acid catalyst in combination with a hydrogenation catalyst (Ru/C) and either molecular hydrogen or formic acid as the hydrogen donor. When using formic acid, the highest yield of GVL (52 mol%) was obtained at 180 °C, 16 h reaction time and D-fructose as the C6-sugar source. The major by-products were insoluble solids, known as humins, formed during the acid catalysed conversion of D-fructose to the intermediate levulinic acid (LA). When using molecular hydrogen as the hydrogen source, the highest yield of GVL (62 mol%) was obtained using D-fructose in combination with TFA and Ru/C in water (180 °C, 94 bar H_2, 8 h). Complete conversion of D-fructose was observed at these conditions. The major by-products were formic acid and insoluble solid materials (humins). The use of a pre-formed homogeneous water soluble ruthenium catalysts from $RuCl_3$ and tris(3-sulfonatophenyl)phosphane (TPPTS) in combination with TFA gave quantitative C6-sugar conversions but a lower GVL yield (23 mol%) compared to the heterogeneous Ru catalyst.

1. Introduction

Concerns about the environment and a decline in easily recoverable crude oil reserves have stimulated the search for renewable energy carriers and green chemicals. Biomass is considered a very promising feedstock for biofuels and bio-based (performance) chemicals.[1–4] A number of studies have been performed to identify interesting biomass derivatives to be used as future platform chemicals for the chemical industry.[2,5,6] The majority of the selected platform chemicals are derived from the cellulose and hemi-cellulose fraction of (ligno-) cellulosic biomass. Our research activities involve the production of γ-valerolactone (GVL) from the C6-sugars (D-glucose, D-mannose and D-galactose) present in the cellulose and hemi-cellulose fraction of biomass and derivatives derived thereof (D-fructose). GVL is considered a very attractive biomass derived compound. It may be used as a solvent for example in lacquers and as a food additive.[7,8] Furthermore, it is considered a potential biofuel and was shown to be a suitable replacement for ethanol in gasoline-ethanol blends.[8] GVL may also be converted to a number of interesting derivatives. Three examples are provided in Scheme 1. Hydrogenation of GVL provides access to methyltetrahydrofuran (MTHF), which is a potential fuel additive.[9] The reaction with GVL and formaldehyde leads to the formation of α-methylene-γ-valerolactone (MGVL), a new acrylic monomer which may be converted to novel acrylic polymers with improved product properties (*e.g.* thermal stability).[10] Another interesting option is ring-opening of GVL with methanol followed by dehydration to produce methylpentenoate (MP). This compound may be converted by hydroformylation, hydrocyanation or hydroxycarbonylation to caprolactone, caprolactam and adipic acid, respectively.[11]



Scheme 1 Examples of interesting derivatives from GVL.

GVL is typically obtained from levulinic acid (LA) by a catalytic hydrogenation using molecular hydrogen (Scheme 2). The intermediate 4-hydroxypentanoic acid is rather unstable and cyclisation to GVL occurs easily.[9]

The hydrogenation of LA to GVL using heterogeneous catalysts in combination with molecular hydrogen has been

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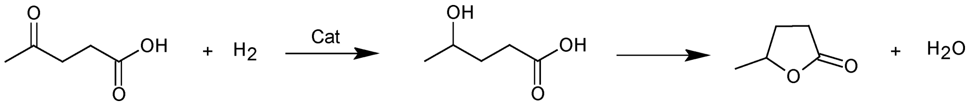


Scheme 2 Catalytic hydrogenation of LA to GVL.

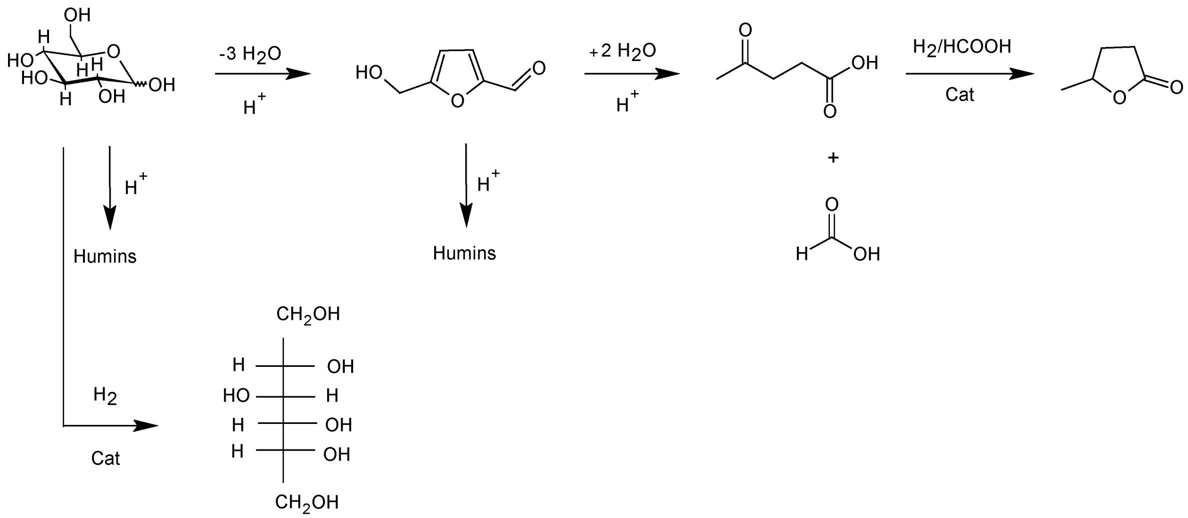
studied extensively.[10–16] Typically the reactions are either carried out solvent free or in organic solvents like dioxane, ethylether and supercritical CO_2 (sCO_2). In most cases temperatures between 106 and 273 °C and pressures between 34 and 150 bar were applied. The highest GVL yield was 97% for a Ru/C catalyst at 150 °C and 34.5 bar hydrogen pressure in dioxane.[10] Recently, Bourne *et al.*[12] showed that water in combination with sCO_2 may also be used as the reaction medium. After reaction, the sCO_2 layer is enriched with GVL and may easily be recovered from the reaction mixture.

A number of homogeneous catalysts have also been reported for the hydrogenation of LA to GVL.[17–19] Joo *et al.*[17,18] demonstrated the use of water soluble homogeneous ruthenium catalysts with sulfonated triphenylphosphine ligands (*e.g.* $HRuCl(Dpm)_3$, Dpm = diphenylphosphinobenzene-m-sulfonic acid) for the hydrogenation of oxo- and unsaturated acids. However, catalyst activity for the hydrogenation of keto-acids like LA was low.[17–19] Recently, Horváth and co-workers reported the use of $Ru(Acac)_3$ in combination with TPPTS (tris(3-sulfonatophenyl)phosphine) for the hydrogenation of LA in water at 140 °C and 69 bar hydrogen.[20,21] After 12 h, LA conversion was complete and GVL was obtained in essentially quantitative yield (> 95%).

Although most hydrogenations have been performed with molecular hydrogen, transfer hydrogenations using formic acid or a derivative have also been reported for both homogeneous and heterogeneous catalyst systems. For instance, Haan *et al.*[22] demonstrated the hydrogenation of LA or ethyllevulinate to GVL using formic acid as the hydrogen donor with a variety of heterogeneous catalysts (*e.g.* Ni/Pt on silica, Re/Pt on silica, Ni). The reactions are typically carried out in the gas phase at 200–350 °C and pressures between 1–10 bar. The highest GVL yield (81 mol%) was obtained using ethyllevulinate as the substrate, a commercial Ni catalyst at 250 °C and a WHSV of 1.1 g substrate/(g cat.h). Horváth *et al.*[21] applied a homogeneous Ru compound $[(\eta^6\text{-}C_6Me_6)Ru(bpy)(H_2O)][SO_4]$ in water for the transfer hydrogenation of LA using formic acid as the hydrogen donor. Both GVL and 1,4-pentanediol were obtained in 25% yield.

We here report our studies on the direct synthesis of GVL from C6-sugar sources (D-glucose, D-fructose, sucrose and cellulose) without isolation of the intermediate LA. Compared to the use of LA as a starting material, this approach reduces the number of processing steps and may lead to a reduction in the manufacturing costs of GVL. An overview of the reaction sequence is given in Scheme 3. The reaction of C6-sugars to LA is an acid catalysed hydrolysis reaction and is typically performed in water using strong mineral acids like HCl and H_2SO_4.[2,23–25] The use of heterogeneous catalysts has also been reported.[2,24,26–28] By-products of the reaction are 5-hydroxymethylfurfural (HMF), formic acid (FA) and insoluble solid materials known as humins.[24,29,30] HMF is an intermediate product which under appropriate conditions may be converted essentially quantitatively to LA. The insoluble humins are formed in a parallel mode from both the C6-sugar precursor as well as from the intermediate HMF.[24,29,30] Typical yields for LA from D-glucose are about 62 mol%,[23,24] whereas the yields for D-fructose are considerably higher (78 mol%).[25,26]

To obtain GVL from a C6-sugar in a one pot approach without isolation of the intermediate LA, the combined action of an acid catalyst and a hydrogenation catalyst is required. Examples of this approach, either with homogeneous or



Scheme 3 Hydrogenation of D-glucose to D-sorbitol and the acid catalyzed hydrolysis of D-glucose to LA and subsequently hydrogenation of LA to GVL.

heterogeneous catalysts and/or molecular hydrogen or formic acid as the hydrogen source, are scarce.

Braca *et al.*[31] reported the use of Ru-carbonyls ($Ru(CO)_4I_2$) in combination with HI for the conversion of D-glucose and D-fructose to GVL. When using syngas (CO/H_2) in combination with D-glucose, GVL yields up to 40 mol% were obtained. Recently, Horváth *et al.*[20,21] reported the use of water soluble homogeneous Ru-catalysts prepared *in situ* from $RuCl_3$ and TPPTS in combination with H_2SO_4 (0.5 mol/l) as the acid catalyst and molecular hydrogen as the hydrogen donor. With sucrose, the main products were D-sorbitol and D-mannitol, indicating that the acid catalysed conversion of sucrose to LA was much slower than the direct hydrogenation of the D-glucose and D-fructose, the monomeric building blocks of sucrose. By applying higher acid concentrations (1.8 mol/l), the rate of the acid catalysed dehydration reaction of sucrose to LA was considerably higher than the direct hydrogenation to D-sorbitol and D-mannitol leading to GVL yields of up to 40%.[8,20]

To the best of our knowledge, the direct synthesis of GVL from C6-sugars by the combined action of a heterogeneous hydrogenation and a homogeneous acidic dehydration catalyst either using molecular hydrogen or with a hydrogen donor such as formic acid has not been reported to date. Particularly the use of formic acid as the hydrogen donor is attractive as this is the co-product of the conversion of C6-sugars to LA (Scheme 3). We here report our research on the catalytic hydrogenation/acid hydrolysis of monomeric C6 sugars (D-glucose and D-fructose) as well as sucrose and cellulose in water using Ru/C as the hydrogenation catalyst, trifluoroacetic acid (TFA) as the acid catalysts and either molecular hydrogen or formic acid (FA) as the hydrogen donor.

2. Materials and methods

2.1. Chemicals

D-glucose, sulfuric acid (96%), formic acid (≥ 99%) and trifluoroacetic acid (98%) were purchased from Merck. Levulinic acid (98%), D-fructose (98%) and 5-hydroxymethylfurfural (98%) were purchased from Acros Organics. Ru/C (5% w/w), γ-valerolactone (99%), 2-methyl-tetrahydrofuran (≥ 99%) and cellulose (microcrystalline powder, 20 μm) were obtained from Sigma Aldrich. $RuCl_3.3H_2O$ (technical grade) was purchased from Riedel de Haën, Na_3TPPTS (TPPTS, tris(3-sulfonatophenyl)phosphine) was obtained from Strem Chemicals. Sucrose was purchased from Fisher Scientific. De-ionized water was used to prepare the various solutions.

2.2. Experimental procedures

Reactions were carried out in a Parr 100 ml autoclave (max. 350 bar pressure, max. temperature 350 °C). A schematic representation of the reactor setup is given in Fig. 1. The reactor is electrically heated and when appropriate, may be cooled using water. The reactor temperature is controlled by a Eurotherm 2208e controller. The reactor content is stirred by a Heidolph RZR 2050 overhead stirrer, equipped with a standard impeller. The pressure and temperature as a function of time reaction are measured continuously and transferred to a PC using the VirtualBench-logger (version 2.5) software package from National Instruments®.

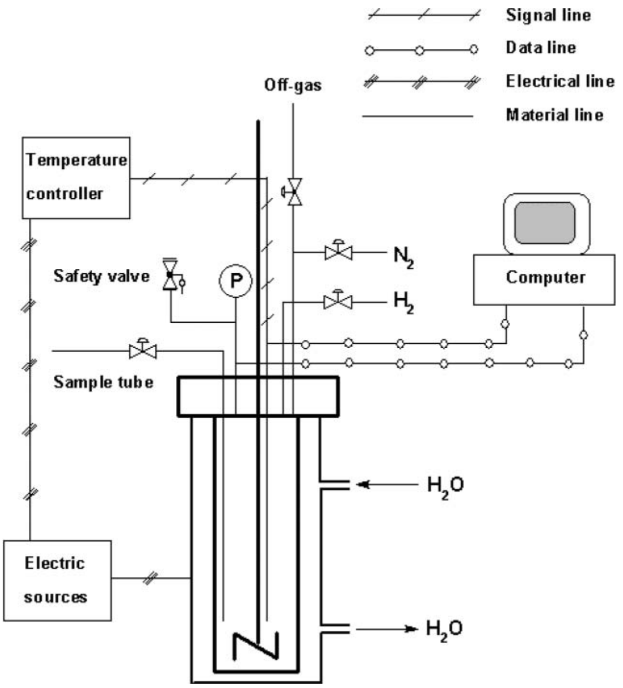


Fig. 1 Schematic representation of the reactor setup.

2.3. Typical experimental procedure for the combined dehydration/transfer hydrogenation of D-fructose to GVL with Ru/C, TFA and formic acid

The reactor was filled with D-fructose (4.9 g, 0.03 mol), Ru/C (0.5 g), FA (3.7 g, 0.08 mol) and a solution of TFA in water (0.5 mol/l in water, 50 ml). Subsequently, the reactor was flushed several times with nitrogen to remove air. The reactor was pressurized (50 bar) with nitrogen and heated to the desired reaction temperature (180 °C). A stirrer speed of 1800 rpm was applied throughout an experiment. After the pre-determined reaction time (typically 16 h), the reactor was cooled, depressurized and flushed several times with N_2. The reaction mixture was filtered over silica gel to remove humins and catalyst. The solution was diluted with de-ionized water and analyzed by High Performance Liquid Chromatography (HPLC) to determine the D-fructose conversion and product composition.

2.4. Typical experimental procedure for the combined dehydration/hydrogenation of D-glucose to GVL with Ru/C and TFA

The reactor was filled with D-glucose (9.9 g, 0.06 mol), Ru/C (0.5 g) and a solution of TFA in water (1 mol/l in water, 50 ml). After closing, the reactor was flushed several times with nitrogen to remove air. The reactor was pressurized (60 bar) with hydrogen and heated to the desired reaction temperature (180 °C) while maintaining a stirrer speed of 50 rpm. After 10 minutes at 180 °C, the hydrogen pressure was set at 94 bar and the stirrer speed was set at 1800 rpm. The hydrogen pressure was maintained at 94 bar throughout the experiment by periodic addition of hydrogen gas. After the pre-determined reaction time (typically 8 h), the reactor was cooled, depressurized and flushed several times with nitrogen. The reaction mixture was filtered over silica gel to remove humins and catalyst. The solution was diluted with de-ionized water and analyzed by HPLC to determine the D-glucose conversion and product composition.

2.5. Typical experimental procedure for the dehydration/hydrogenation of D-glucose to GVL with a homogeneous Ru/TPPTS catalyst and TFA

The homogeneous Ru/TPPTS catalyst complex was pre-formed before an actual dehydration/hydrogenation experiment. $RuCl_2.3H_20$ (0.1 mmol, 26 mg) was dissolved in de-ionised water (10 mL). Subsequently Na_3TPPTS (0.3 mmol, 172 mg) and NaI (0.13 mmol, 20 mg) were added and the solution was stirred for 10 minutes. The resulting solution was added to the pressure reactor containing D-glucose (4.9 g, 0.03 mol) and TFA (0.63 mol/l, 40 mL). The actual hydrogenation experiment was carried out as described above, with the exception that a stirrer speed of 1800 rpm was applied throughout the experiment.

2.6. Experimental procedure for the conversion of D-glucose and D-fructose to LA using TFA as the catalyst

The reactions were carried out in glass ampoules (inside diameter of 3 mm, wall thickness of 1.5 mm, and length of 15 cm). The ampoules were filled with ± 0.5 cm^3 of reaction mixture (D-glucose or D-fructose, TFA and water) and sealed using a torch. The sealed ampoules were placed in a special rack, which can hold up to 20 ampoules, and placed in a constant temperature oven (± 1 °C). At different reaction times, ampoules were taken from the oven and quenched into an ice-water bath (4 °C) to stop the reaction. The reaction mixture was taken out of the ampoule and insoluble humins were separated using a micro centrifuge (Omnilabo International BV) for 15 minutes at 1200 rpm. The particle-free solution was diluted with de-ionized water and subsequently analyzed using HPLC.

2.7. Analytical methods

The liquid phase after reaction was analysed using HPLC. A HPLC apparatus equipped with a Hewlett Packard 1050 pump, a Bio-Rad organic acid column (Aminex HPX-87H) and a differential refractometer was used. The mobile phase consisted of an aqueous solution of sulfuric acid (5 mmol/l)) operated at a flow rate of 0.55 cm^3 min^{-1}. The column was operated at 60 °C. The amounts of the products were calculated using calibration curves obtained from standard solutions of known concentrations.

3. Results and discussion

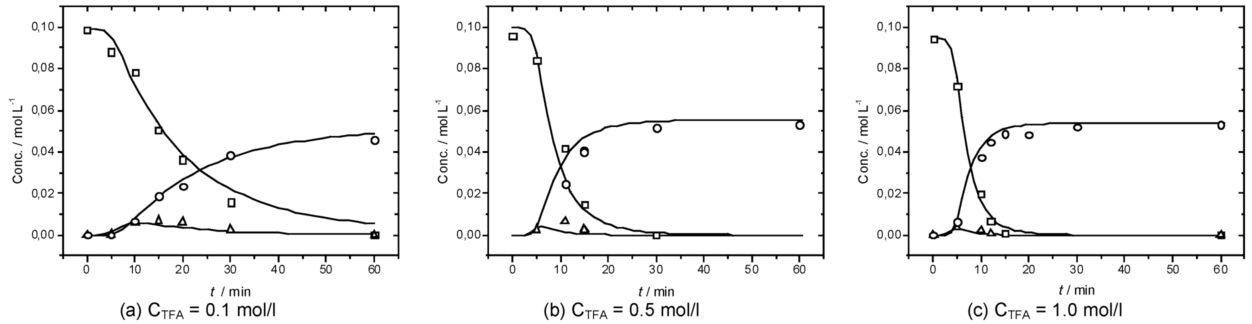
3.1. Brønsted acid selection

A wide variety of inorganic Brønsted acid like H_2SO_4, HNO_3, HCl, has been tested for the conversion of D-glucose and D-fructose to levulinic acid.[2,23–25] High yields at short reaction times are possible using strong acids (pK_a < 2) and H_2SO_4 was shown to be particularly attractive.[24] However, sulfuric acid is likely poorly compatible with Ru catalysts due to the presence of sulfur.[32,33] For instance, Osada *et al.*[33] compared the activity of fresh Ru/TiO_2 with that of Ru/TiO_2 soaked in aqueous sulfuric acid before catalytic testing. It was found that the activity of the latter catalyst was considerably lower due to adsorption of sulfur to the ruthenium metal catalyst. Catalytic experiments (*vide infra*) within the framework of this research also confirm this observation.

An attractive alternative organic acid could be trifluoroacetic acid (TFA). The pK_a is 0.5 and recently Marzialetti *et al.*[34] successfully used TFA for the hydrolysis of loblolly pine to mono-saccharides. To gain insights in the potential of TFA for the conversion of C6-sugars to levulinic acid, a number of experiments were conducted with D-glucose and D-fructose in water according to a procedure published recently by our group.[24,29] The experiments with D-glucose were carried out at different TFA concentrations (0.1–1 mol/l) at 180 °C with a fixed D-glucose intake (0.1 mol/l). The concentration of HMF and LA were determined as a function of time and the results are given in Fig. 2.

The highest yield of LA was 57 mol% which is only 2% less than the best experiments with sulfuric acid.[24] The major by-products were FA and insoluble materials known as humins. Thus, TFA appears an attractive alternative for H_2SO_4 for exploration in combined acid hydrolysis/hydrogenation experiments.

The experimental data were modelled using a power law model previously developed for sulfuric acid, taking into account the different H^+ concentrations due to differences in pK_a values between sulfuric acid and TFA.[24,29] The results are depicted in

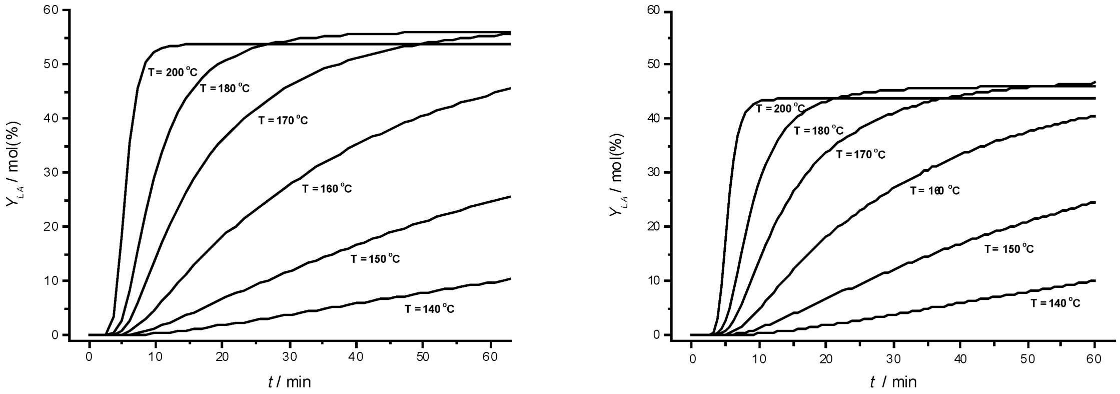


(a) C_{TFA} = 0.1 mol/l

(b) C_{TFA} = 0.5 mol/l

(c) C_{TFA} = 1.0 mol/l

Fig. 2 Experimental and modelled data for D-glucose conversion to LA at various TFA concentrations ($C_{GLC,0}$ = 0.1 mol/l, T = 180 °C, t = 60 min). Experimental data: □: C_{GLC}, ○: C_{LA}, △: C_{HMF}. Lines are model predictions.



(a) $C_{GLG,0}$ = 0.1 mol/l (b) $C_{GLG,0}$ = 0.5 mol/l

Fig. 3 Modelled LA yield for the reaction of D-glucose with TFA at two D-glucose intakes (0.1 and 0.5 mol/l) at various temperatures ($C_{TFA} = 0.5$ mol/l).

Fig. 2 and good agreement between experiments and model was observed. Thus, it appears that the kinetic models developed for sulfuric acid are broadly applicable, provided that the H^+ concentration is corrected for the pK_a of the acid under study. The temperature effects and the D-glucose intake on activity and LA selectivity were modelled for TFA and the results are given in Fig. 3. Thus, to reach the highest LA yield (57 mol%) at reasonably short batch times, a temperature of 180 °C seems preferred. The LA yield is a function of the D-glucose with higher concentrations leading to lower yields, see Fig. 3 for details.[24]

A number of experiments were also carried out with D-fructose instead of D-glucose using the optimum conditions determined for D-glucose (180 °C, 60 min reaction time, $C_{C6\text{-sugar},0} = 0.1$ mol/l) with varying TFA concentration (0.1–1 mol/l). The results are illustrated in Fig. 4. The highest LA yield was 70 mol%, which is considerably higher than found for D-glucose. These results are in line with literature data, which indicate that the conversion of D-fructose rich feeds to LA is more efficient than for D-glucose rich feeds.[30,35]

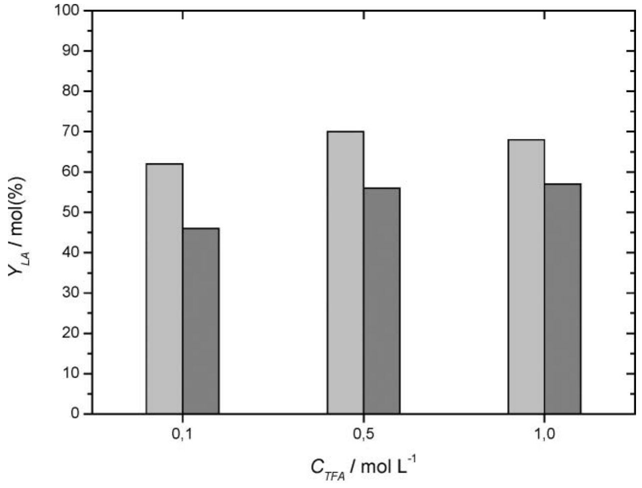


Fig. 4 LA yield for the reaction of D-fructose (light gray) and D-glucose (dark gray) ($C_{FRT,0} = C_{GLC,0} = 0.1$ mol/l) to LA at different TFA concentrations (T = 180 °C, t = 60 min).

3.2 Combined transfer hydrogenations-dehydration of C6-sugars to GVL with formic acid as the hydrogen source

A number of experiments with Ru/C in combination with TFA and with formic acid (FA) as the hydrogen donor were carried out to gain insights in the potential of combined C6-sugar dehydration to LA followed by a transfer hydrogenation of LA to GVL (Scheme 3). The reactions were carried out at 180 °C in an aqueous medium using D-fructose as the C6-sugar. The latter was selected for its higher selectivity towards LA in the first step of the sequence in Scheme 3 (*vide supra*). External FA was supplied to speed up the reaction rate, typically a FA to D-fructose intake of 3.2 mol/mol was applied. The first experiment (entry 1 in Table 1) resulted in the formation of 16 mol% GVL. The major liquid phase component was the intermediate LA (53 mol%). Thus, although transfer hydrogenation occurred to a certain extent, the reaction is much slower than the conversion of D-fructose to LA. Of interest is the sum of the yields of LA and GVL (69 mol%), which is close to the maximum amounts of LA from the acid catalysed dehydration of D-fructose under the experimental conditions applied (Fig. 4).

Table 1 Dehydration/transfer hydrogenation of D-fructose using Ru/C and TFA in combination with formic acid[a]

Entry	Reaction time (h)	P N_2 (bar)	FA/D-Fructose mol. ratio (mol/mol)	Yield LA (mol%)	Yield GVL (mol%)
1	8	0	3.2	53	16
2	8	50	3.2	39	32
3	16	50	3.2	17	43
4	16	50	6.6	11	52

[a] A 10 wt% intake of Ru/C on D-fructose (0.5 mol/l) was applied. The TFA concentration was 0.5 mol/l water, the reaction temperature was 180 °C. Complete D-fructose conversion was observed for all experiments.

Thus, excessive losses in selectivity by humin formation due to the presence of Ru/C and TFA are not a major issue. Subsequent hydrogenation products of GVL like MTHF and 1,4-pentanediol were not detected in the liquid phase (HPLC). In addition, hydrogenation products of D-fructose (D-sorbitol and D-mannitol)[36] were also not detected and indicate that the dehydration of D-fructose to LA is much faster than the (transfer) hydrogenation of D-fructose to D-sorbitol/mannitol.

To increase the effective FA concentration in solution and thus to speed up the rate of the transfer-hydrogenation reaction of LA to GVL, the amount of FA in the liquid phase was increased by performing subsequent experiments at higher pressures (50 bar N_2). At otherwise similar conditions, the yield of GVL increased to 32 mol% (entry 2, Table 1). Further improvements were possible by extending the reaction time and using higher FA intakes. With these measures, a maximum yield of GVL of 52 mol% (entry 4, Table 1) could be obtained. Still some unreacted LA was present (11 mol%) whereas the major by-products were insoluble humins, formed in the first step in the reaction sequence (Scheme 3). It may be concluded that the selectivity of the overall conversion of D-fructose to GVL is determined by the (fast) reaction of D-fructose to LA (max. 70 mol%) and that the activity is solely determined by the subsequent (selective) transfer hydrogenation of LA to GVL.

The exact mechanism of the hydrogenation reaction is not clear yet. Transfer hydrogenations of LA with FA or derivatives have been reported in the literature, see introduction section for details. It is generally accepted that metal catalysed transfer hydrogenation with FA involve the formation of a metal-formate species which decomposes to a metal-hydride and CO_2. Subsequent reaction of the metal-hydride with LA results in reduction of the ketone moiety and the formation of GVL after cyclisation of the intermediate 4-hydroxypentanoic acid (Scheme 2). In this mechanism, free molecular hydrogen is not formed. An alternative mechanism, though closely related, involves the formation of molecular hydrogen by decomposition of FA under reaction conditions. The hydrogen is again activated at the metal and used to hydrogenate LA to GVL. Decomposition of formic acid to molecular hydrogen is known for certain homogeneous Ru catalysts.[37] To gain insights in the decomposition of formic acid to hydrogen with the heterogeneous Ru/C catalyst used in this study, the reaction of FA in water (0.6 mol/l) in the presence of TFA (0.5 mol/l) and Ru/C was performed (180°C, 8h). After reaction, both the liquid phase and the gas phase were collected and analysed. The gas phase consisted mainly of hydrogen and CO_2 (> 95 mol%) in a 1 to 1 molar ratio. The FA conversion was 77%. Thus, it may be concluded that FA is slowly catalytically decomposed under the reaction conditions to hydrogen and CO_2. Whether free hydrogen plays a role in the hydrogenation reaction of LA to GVL is speculative at this state and needs further research.

3.3 Dehydration/hydrogenations of C6-sugars to GVL with molecular hydrogen as the hydrogen source

Initial experiments with molecular hydrogen were performed with D-glucose and H_2SO_4 as the acid catalyst for the conversion of D-glucose to LA and Ru/C as the heterogeneous hydrogenation catalyst for the subsequent hydrogenation to GVL (Scheme 3). The reactions were carried out in a batch reactor at a reaction temperature of 160 - 180 °C and reaction times between 2.5–3 h. Complete D-glucose conversion was observed in all cases. The major product in the liquid phase was LA (15–26 mol%). Large amounts of brown insoluble products were formed (humins). The desired GVL was not detected in the reaction mixture. Apparently, the hydrogenation reaction of LA to GVL does not take place at these conditions, likely by Ru/C deactivation due to the presence of sulfuric acid (*vide supra*).

Subsequent reactions with molecular hydrogen and Ru/C (5 or 10 wt% on C6-sugar) as the hydrogenation catalyst were carried out with TFA as the acid catalyst (0.5 mol/l) at 180 °C, a hydrogen pressure of 94 bar (semi-batch mode) and with D-glucose and D-fructose intakes between 0.1–1.1 mol/l. An overview of the experiments is given in Table 2. In all experiments, complete conversion of the C6-sugar was observed.

For the first experiment (entry 1, Table 2) with D-glucose, a constant stirrer speed of 1800 rpm was applied throughout the experiment. Hydrogen was present during heating of the reaction mixture to 180 °C. Analysis of the reaction mixture after reaction (HPLC) did not reveal the presence of GVL. Instead, large amounts of D-sorbitol, the hydrogenation product of D-glucose were present together with unidentified

Table 2 Dehydration/hydrogenation of various C6-sugar sources using TFA and Ru/C in combination with molecular hydrogen[a]

Entry	Catalyst intake (wt% on substrate)	t (h)	D-glucose (mol/l)	D-fructose (mol/l)	Sucrose (mol/l)	Cellulose (mol/l)[b]	Yield LA (mol%)	Yield FA (mol%)	Yield GVL (mol%)
1[c]	10	8	0.5				0	0	0
2[d]	10	8	0.5				8	29	27
3[e]	10	8	0.5				4	16	38
4[e]	5	8	1.1				4	10	29
5[e]	10	4		0.1			56	16	16
6[e]	10	8		0.5			4	7	62
7[e]	5	8		1.1			3	7	54
8[e]	10	8			0.3		9	10	52
9[e]	10	8				0.5	6	16	29

[a] All experiments were conducted at 180 °C and 0.5 mol/l TFA. [b] Calculated as the number of glucose units. [c] Hydrogen (initial 60 bar at room temperature) present during heating to 180 °C, 1800 rpm stirring speed applied throughout the experiment [d] Heating under a nitrogen atmosphere to 180 °C at 1800 rpm stirring speed. After 10 minutes, the reactor was pressurised with hydrogen (94 bar, semi-batch mode). [e] Hydrogen (initial 60 bar at room temperature) present during heating to 180 °C at 50 rpm stirring speed. After 10 minutes at 180 °C, the reactor was set at hydrogen pressure of 94 bar (semi-batch mode) and the stirrer speed was set at 1800 rpm.

components. Apparently, the hydrogenation of D-glucose under these conditions is much faster than the dehydration of D-glucose to HMF and LA (Scheme 3). The occurrence of excessive hydrogenation of D-glucose is likely related to the rate of heating the batch reactor from room temperature to reaction temperature (180 °C). Typically this takes about 10–15 min. This heating period is expected to have a large effect on the product distribution and may be rationalised by considering the kinetics of the acid catalysed dehydration of D-glucose to HMF and LA[24] and the hydrogenation of D-glucose to sorbitol with a Ru/C catalyst.[38,39] The activation energy for the conversion of D-glucose to HMF in water is 152 kJ/mol[24] whereas values for the D-glucose hydrogenation with Ru/C in water are between 34 and 73 kJ/mol.[38,39] Thus, the conversion of D-glucose to HMF/LA is more sensitive to the temperature and is favoured at higher temperatures whereas the hydrogenation of D-glucose to D-sorbitol is favoured at low temperatures. Thus, the high selectivity to hydrogenation products of D-glucose as observed in our experiments is in line with kinetic data for both reactions and is due to the relatively long heating time of the batch set-up. The preferred way to reduce D-glucose hydrogenation would be the application of an infinitely high heating time in the batch set-up. However, this is practically not possible and the highest possible heating rates were applied already in this study.

An alternative procedure to reduce the rate of the hydrogenation reaction and thus to enhance the formation of HMF/LA during the heating period is to perform the heating stage in the absence of hydrogen (Table 2, entry 2). Indeed, this has a positive effect on the product selectivity and D-sorbitol could not be detected in the reaction mixture. The main products were GVL (27 mol%), residual LA (8 mol%) due to incomplete hydrogenation to GVL and insoluble brown solids (humins) formed by the acid catalysed conversion of D-glucose to HMF/LA. This experiment confirms that the undesired hydrogenation reaction of D-glucose to D-sorbitol mainly takes place during the heating period of the batch reactor.

Further improvements in the GVL yield were possible by performing an experiment with heating in the presence of hydrogen and a low rotation speed of the impeller during the heating period (50 rpm). The yield of GVL when using D-glucose as the C6-sugar source was 38 mol%, D-sorbitol formation was not observed (Table 2, entry 3). In this case, the rate of hydrogenation of D-glucose to D-sorbitol is likely much lower than the dehydration rate of D-glucose to LA by a reduction of the hydrogen mass transfer rate of the gas phase to the liquid phase due to a reduction of the volumetric mass transfer coefficient (k_L.a) of hydrogen.

The highest GVL yield when using D-glucose was 38 mol%, with 4 mol% unconverted LA. The highest LA yield for the acid catalysed dehydration of D-glucose in separate experiments in absence of hydrogen and Ru/C (*vide supra*) with a D-glucose concentration of 0.5 mol/l at 180 °C and 0.5 mol/l TFA was 46 mol%. Thus, the sum of the GVL and LA yield in the hydrogenation reaction (42 mol%) is close to the maximum achievable yield for the dehydration step (46 mol%). This implies that the selectivity of the Ru-catalysed hydrogenation reaction of LA to GVL is high under these conditions, in line with literature data.[10]

The use of TFA is essential to obtain GVL. This was confirmed by an experiment with D-glucose using Ru/C as catalyst and molecular hydrogen in the absence of TFA (94 bar hydrogen, 180°C, 8 h reaction time). After reaction, GVL was not detected in the reaction mixture (HPLC) and the main products were D-sorbitol, D-mannitol and glycerol. The sum of the yields of these components is 67 mol%. The latter is known to be formed by the subsequent hydrogenation/hydrogenolysis of D-sorbitol/mannitol in the reaction mixture when using heterogeneous Ru catalysts.[40]

Further GVL yield improvements were possible when using D-fructose instead of D-glucose. The highest GVL yield was 62 mol% at complete D-fructose conversion (Table 2, entry 6). The residual amount of LA was 4 mol%, the main by-products were insoluble humins. D-Sorbitol/manitol and GVL hydrogenation products (1,4-pentanediol and MTHF) could not be detected by HPLC. The higher yields for D-fructose compared to D-glucose are in line with the separate experiments for the acid catalysed conversion of D-glucose and D-fructose to LA, where the highest yields were observed for D-fructose (*vide supra*). At similar conditions as the hydrogenation experiments (180 °C, 0.5 mol/l TFA, 0.5 mol/l D-fructose), the yield of LA from D-fructose was 63 mol%. For the combined dehydration/hydrogenation to GVL, the GVL yield was 62 mol%, which is close to the maximum value on the basis of the acid catalysed hydration reaction of D-fructose to LA. This implies that the hydrogenation reaction of LA to GVL is very selective and that the yield loss is due to humin formation in the first dehydration step of the sequence (Scheme 3).

Of interest is the ratio of LA and FA in the reaction mixture after the hydrogenation reaction. When considering only the acid catalysed dehydration of D-glucose to LA, the reaction stoichiometry predicts the formation of LA and FA in a one to one mol ratio (Scheme 3). In case FA is inert, the amount should be close to the amount of GVL formed (assuming 100% selectivity for the hydrogenation reaction of LA to GVL, which appears a valid assumption, *vide supra*). This is not the case and FA is present in considerably lower amounts. These findings may be rationalised by assuming that FA acts as a transfer hydrogenation agent and is active for the hydrogenation of LA, in line with the transfer hydrogenation experiments described in section 3.2. However, decomposition of FA to hydrogen gas and CO_2 and cannot be excluded (*vide supra*).

Besides the monomeric C6-sugars (D-fructose and D-glucose), a dimeric sugar (sucrose) and a polymer (cellulose) were also tested at optimised conditions determined for D-fructose. In both cases, significant amounts of GVL were formed besides humins and unconverted LA. For sucrose, the GVL yield was 52 mol%, which is higher than the 40 mol% reported in the literature for water soluble homogeneous Ru-catalysts prepared *in situ* from $RuCl_3$ and TPPTS in combination with H_2SO_4 (0.5 mol/l) as the acid catalyst and molecular hydrogen as the hydrogen donor.[20,21]

The non-optimised GVL yield for cellulose was 29 mol%. This yield is lower than for D-glucose (38 mol%), though promising. These yield trends are in line with available literature data for the acid catalysed conversion of cellulose to LA.[30] The LA yields from cellulose are lower than when using D-glucose as the feed.

3.4. Conversion of D-glucose to GVL by TFA in combination with a homogeneous water soluble ruthenium hydrogenation catalyst

The dehydration/hydrogenation of D-glucose to GVL with molecular hydrogen was also performed using a homogeneous Ru catalyst in combination with TFA. For this purpose, a water-soluble Ru-catalysts prepared in situ from $RuCl_3$ and TPPTS was applied. NaI was added to increase the reaction rate.[41] The reaction was performed at a reaction temperature of 180 °C using 0.5 mol/l TFA and 94 bar of hydrogen. A catalyst to D-glucose ratio of 1 to 270 mol/mol was applied, the initial concentration of D-glucose was 0.5 mol/l.

After 8 h reaction time, the reaction was terminated and the composition of the liquid phase was determined using HPLC. Complete D-glucose conversion was observed. The major products in the liquid phase were LA (19 mol%) and GVL (23 mol%), furthermore substantial amounts of insoluble humins were formed. The presence of significant amounts of LA indicates that the hydrogenation reaction of LA to GVL is far from quantitative at these conditions. The sum of the GVL and LA yields is 42 mol%. This value is close to the maximum LA yield for the acid catalysed conversion of D-glucose under these conditions (46 mol%). The observed GVL yield is lower than reported by Horváth[20,21] for a similar catalyst using sulfuric acid in combination with sucrose (40 mol%). Sucrose is a dimer of D-fructose and D-glucose and higher yields of the intermediate LA are expected compared to D-glucose only. Further studies, *e.g.* by applying longer reaction times and/or higher catalyst intakes and D-fructose instead of D-glucose will be required to attain complete LA conversion to GVL. When assuming that the hydrogenation of LA to GVL is highly selective at these conditions, a maximum yield of 42 mol% is to be expected under the experimental conditions/intakes applied.

4. Conclusions

The catalytic synthesis of GVL from C6-sugars (D-glucose and D-fructose) in water using an acid catalyst (TFA) in combination with a heterogeneous hydrogenation catalyst (Ru/C) and either molecular hydrogen or formic acid as the hydrogen donor has been explored. Unprecedented transfer-hydrogenations with formic acid gave an optimised yield of GVL (52 mol%) at 180 °C, 16 h reaction time and D-fructose as the C6-sugar source. The major by-products were insoluble solids, known as humins, formed during the acid catalysed conversion of D-fructose to LA. The highest yield of GVL (62 mol%) was obtained with D-fructose using molecular hydrogen as the hydrogen source, TFA as the acid and Ru/C as the hydrogenation catalyst. Complete conversion of D-fructose was observed at these conditions. The major by-products were formic acid and insoluble solid materials (humins).

The yield and the rate of GVL formation is a delicate balance between the two individual reactions (acid catalysed dehydration of the C6-sugar to LA followed by a catalytic hydrogenation) in the sequence. The first step is a fast reaction (10–30 min) under the conditions employed, however, the selectivity is always below 70%. The subsequent hydrogenation with either formic acid or hydrogen is slow (order of hours), although apparently very selective.

The dehydration/hydrogenation of D-glucose to GVL with molecular hydrogen was also explored using TFA in combination with a water soluble homogeneous Ru catalyst prepared in situ from $RuCl_3$ and TPPTS. The yields of GVL (23 mol%) were lower than for the reactions with Ru/C and substantial amounts of LA were present in the mixture (19 mol%). This suggests that at the reaction conditions and intakes applied in this study, the hydrogenation activity of the homogeneous catalyst is lower than for Ru/C.

The study also identified TFA as an attractive alternative for mineral acids for the conversion of C6-sugars to LA. With this finding, aqueous/fluoro-biphasic system for the conversion of C6-sugars to LA may be envisaged with a fluoro-phase (*e.g.* perfluorohexane)[42] soluble TFA derivative like heptadecafluorononanoic acid (pK_a: 0.36). This would facilitate acid catalyst recycle considerably, which is one of the main drawbacks of the current mineral acid based concepts for LA synthesis.

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