Transfer hydrogenation of levulinic acid under hydrothermal conditions catalyzed by sulfate as a temperature-switchable base

Daniel Kopetzki* **and Markus Antonietti**

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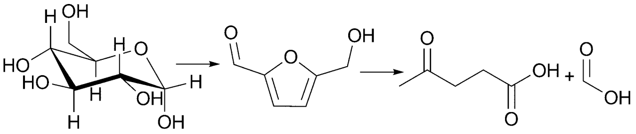
It is demonstrated that transfer hydrogenation from formic acid to levulinic acid under hydrothermal conditions can be catalyzed by bases, but also by simple sodium sulfate. The action of salt addition could be clarified and ascribed to the changing dissociation constants at high temperature. This renders sulfate a temperature-switchable base in hydrothermal syntheses. Using such salts can help in preventing waste, as neutralization after reaction is not necessary. By optimizing the reaction conditions, the yield of γ-valerolactone, a sustainable biofuel molecule, could be raised to 12% for a simple passage through a capillary flow reactor with a residence time of less than 20 min.

Introduction

Currently chemistry is mainly based on fossil resources. Under the threat of shortage and ultimately the depletion of this feedstock, the green chemistry community is currently trying to set up new platform chemicals based on biomass as a starting material for chemical processes. This has led to concepts like biorefinery/biorefining,[1] but has also resulted in proposals for multiple-commodity chemicals based on biomass as a starting material.[2]

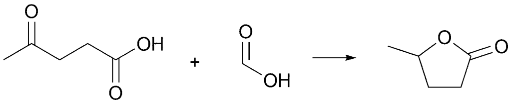
Being the main component of biomass, carbohydrates will become a primary starting compound for sustainable chemistry. They can be converted by different means to a variety of compounds, such as fermentation to ethanol, lactic acid or citric acid, which is a current biotechnology process. Another very promising pathway to convert carbohydrates into useful chemicals is the chemical dehydration to hydroxymethylfurfural. This can be obtained by simple heating,[3] but also works well and is more defined under non-aqueous conditions in ionic liquids catalyzed by metal ions.[4] In water, especially under acidic conditions, this compound further reacts to levulinic and formic acid, which can be carried out in quite high yield (Scheme 1).[5]



Scheme 1

Levulinic acid itself is an interesting building block and can be converted to a variety of useful compounds.[6] Among those, γ-valerolactone is potentially of highest significance. It possesses properties that characterize it as an ideal sustainable liquid.[7] It is nontoxic, has favourable solvent characteristics, has an LD_{50} significantly higher than ethanol, is biodegradable, exhibits a high boiling point and very low vapour pressure, and so could be considered as green solvent. Furthermore it is a useful energy storage molecule and can be directly employed as a fuel additive for liquid transportation fuels.[7]

γ-Valerolactone can be synthesized by hydrogenation and subsequent cyclisation of levulinic acid, either by using heterogeneous[8-11] or homogeneous[2,11,12] catalysts. However both systems employ noble and heavy metals, which are neither sustainable nor low-priced. As an equimolar amount of formic acid is formed during production of levulinic acid from carbohydrates, it is convenient to use formic acid as reducing agent in a transfer hydrogenation (Scheme 2). In this way, the side product of a first reaction is used as a hydrogen source for the second. The usefulness of formic acid concerning hydrogen storage was recently illustrated by Beller *et al.*[13]



Scheme 2

The reduction of aldehydes with NaCOOH has been shown to work without catalyst; however, at very high temperatures (250–350 °C).[14] In this paper we will investigate this transfer hydrogenation of the even more unreactive ketone under green conditions in water. We will demonstrate that this reaction can be performed under hydrothermal conditions at temperatures around 220 °C where it is catalyzed even by simple ubiquitous salts.

Results and discussion

As levulinic acid and formic acid are produced from carbohydrates in aqueous solution, we performed the transfer hydrogenation in diluted solution with 0.1 M levulinic acid. A

Max-Planck-Institute of Colloids and Interfaces, Research Campus Golm, D-14424, Potsdam, Germany.
E-mail: daniel.kopetzki@mpikg.mpg.de; Fax: +49-331-5679502; Tel: +49-331-567-9538

slight excess of formic acid (0.15 M) was used. The experiments were carried out in steel autoclaves by heating for 12 h. For temperature optimization a tubular flow reactor with less than 20 min residence time was used. As a first test of whether synthesis of γ-valerolactone under hydrothermal conditions was feasible, the mixture of levulinic acid and formic acid was simply heated in an autoclave at 220 °C for 12 h, resulting in a yield of 1.0% γ-valerolactone. By addition of Pd on activated alumina, the yield increased to 29.0%. However this was accompanied by a significant occurrence of further reduction towards pentanoic acid. Furthermore, Pd not only catalyzed the desired hydrogen transfer, but also the decomposition of formic acid to H_2 and CO_2. This decomposition, although at much lower rate, also occurs in high-temperature water without any additives.[15] This side reaction, together with the demand for a cheap, sustainable catalytic scheme, makes the use of $Pd@Al_2O_3$ obsolete. However, it was useful in this system as a benchmark value for the possible conversion range. By using catalysts based on ruthenium, much higher yields have been reported.[11,12] However, Ru has the same disadvantages as Pd concerning sustainability.

In hydrothermal reactions, even simple salts may activate the water and can therefore act as catalysts.[16] As cations might activate the carboxy group by coordination, a 0.5 M salt solution was used as solvent instead of pure water. Different chlorides (KCl, $CeCl_3$, $CoCl_2$, $SrCl_2$, $CuCl_2$ and $ZnCl_2$) were tested, but none showed a significant activity for this reaction, even though transition metals were employed (Table 1).

Taking a closer look at the different halides, one can notice some effects following the Hofmeister series.[17] Potassium fluoride increases the yield compared to the pure aqueous solution, whereas the other halides do not show any improvement. Also a remarkable acceleration is found when Na_2SO_4 is added. Furthermore, KH_2PO_4 increases the yield, whereas the more basic phosphates do not show any catalytic activity, even inhibiting the reaction. Finally, other basic salts like Na_2SO_3 and K_2CO_3 prevent any reaction. This makes pH a potential key aspect of this reaction.

Therefore, we had to investigate the pH dependence of the transfer hydrogenation without additional salt to distinguish salt and pH effects. As both educts are acids, a variety of reaction possibilities can be considered. Whereas formic acid releases CO_2 and H_2 upon decomposition, its anion formally only transfers H^-. Thus the reducing character of formic acid is significantly different from that of formates. To perform the reaction at different pH, variable amounts of either hydrochloric acid or potassium hydroxide were added to the mixture of levulinic and formic acid. The concentration of HCl was 0.01 M or 0.1 M in the final solution, whereas 0.075 M, 0.15 M, 0.2 M or 0.3 M of KOH was added to vary the pH. In the case of base addition, pH is buffered by formic acid (pK_a = 3.74) and levulinic acid (pK_a = 4.59). Since during the reaction acid is consumed or may decompose, the pH should increase throughout reaction. Indeed this is validated by the experiment (Fig. 1). The pH changes are largest in the alkaline region, presumably due to the missing buffer capacity.

Table 1 Effect of salt addition (0.5 M salt) on the yield of γ-valerolactone

Additive	Yield (%)
No additive	1.0
$Pd@Al_2O_3$	29.0
$CeCl_3$	1.4
$CoCl_2$	1.0
$SrCl_2$	1.1
$CuCl_2$	0.0
$ZnCl_2$	0.1
KF	11.3
KCl	1.4
KBr	1.2
KI	0.7
Na_2SO_4	11.0
Na_2SO_3	0.0
K_2CO_3	0.0
KH_2PO_4	3.4
K_2HPO_4	0.7
K_3PO_4	0.0

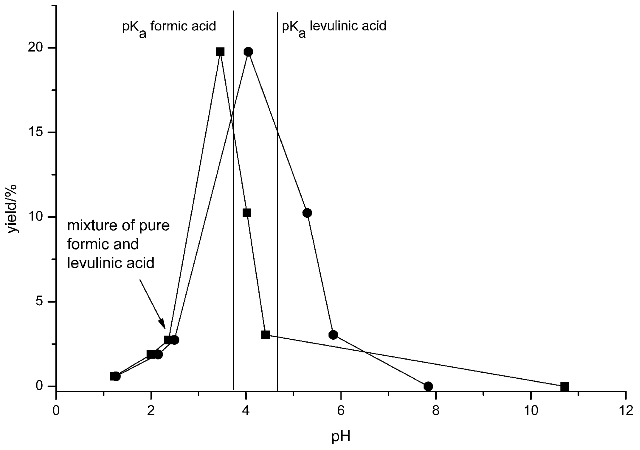


Fig. 1 The dependence of yield of γ-valerolactone upon pH, measured before (squares) and after (circles) the experiment.

Furthermore, the yield strongly depends on the pH. At very acidic pH, where both reactants are protonated and uncharged, the yield is very low. With increasing pH, the yield drastically increases reaching a maximum at a pH around the pK_a of formic acid. Further increasing the pH leads again to a decreasing yield. Here also levulinic acid becomes deprotonated, which seems to inhibit the reaction. Obviously, the reaction is fastest for levulinic acid being in the neutral and formic acid in the anionic form. This leads to a rather sharp maximum of optimum pH for product generation in water with a formal transfer of H^- from formate. So by simple addition of some base to the mixture of levulinic and formic acid the yield can be drastically optimized. In media that are too basic, lactonization is not expected to occur. However, GC–MS did not reveal any other low molecular weight compounds besides levulinic acid (especially not γ-hydroxyvaleric acid). So no reaction at all seems to occur at high pH.

Another potential reason for the low yield under acidic conditions is the fact that addition of HCl promotes the autodecomposition of formic acid at those temperatures (Fig. 2), which is – beside reaction with levulinic acid – a second reaction channel.

Knowing the sensitivity of the transfer hydrogenation of levulinic acid with formic acid on pH, the initial experiments on the influence of pure salts onto the reaction can be

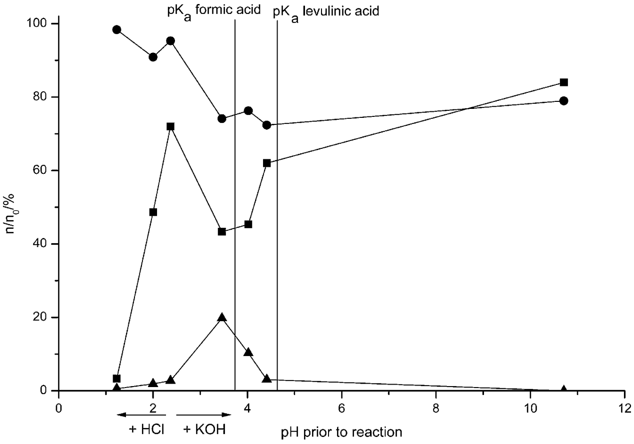


Fig. 2 Amount of levulinic acid (circles), formic acid (squares) and the product γ-valerolactone (triangles) *versus* pH prior to reaction.

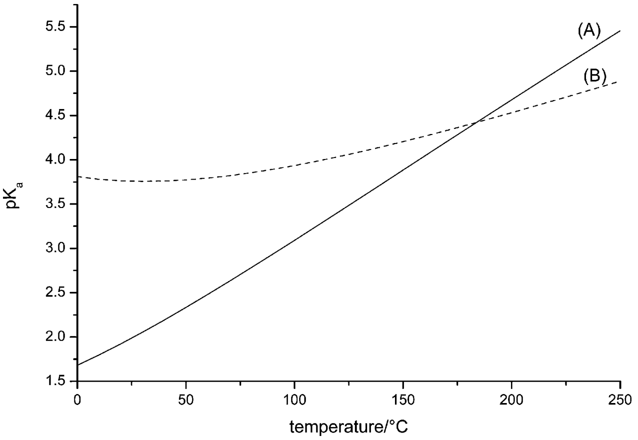


Fig. 3 Variation of pK_a of HSO_4^- (A) and formic acid (B) with increasing temperature, calculated from thermodynamic data.

re-analyzed. The pH probably accounts for the acceleration pattern of the different potassium phosphates. It is now also evident why very basic salts like Na_2SO_3 or Na_2CO_3 inhibit any reaction. In contrast, slightly basic salts could shift the pH in the narrow optimum range. This might be the case for KF and Na_2SO_4.

The catalytic activity of sulfate, which is a quite neutral salt (pK_a = 1.99 for the deprotonation of HSO_4^- under ambient conditions) is still striking at first sight, whereas fluoride is more basic (pK_a = 3.17 under ambient conditions). When judging about basicity of the tested salts, it is a striking result that the pK_a values at elevated temperatures can be quite different from those under ambient conditions. So to really relate the effect to pH, we have to compare the dissociation constants at the reaction temperature of 220 °C. The temperature dependence of the dissociation constant can be expressed by the van't Hoff equation

$$\frac{\mathrm{d}\ln K_\mathrm{a}}{\mathrm{d}T} = \frac{\Delta H^0}{RT^2} \qquad (1)$$

with $\Delta H°$ being the standard molar enthalpy change for the dissociation of the acid. Integration, neglecting the increased pressure at high temperatures and the temperature dependence of the heat capacity change Δc_p^0 leads to

$$R\ln K_\mathrm{a}(T) = -\frac{\Delta G^0}{T^0} + \Delta H^0\left(\frac{1}{T^0}-\frac{1}{T}\right) + \Delta c_p^0\left(\frac{T^0}{T}-1+\ln\left(\frac{T}{T^0}\right)\right) \qquad (2)$$

with T^0 being the reference temperature (T^0=298.15 K).[18] With data for formic acid (ΔG^0 = 21.45 kJ mol^{-1}, ΔH^0 = 1.03 kJ mol^{-1} and Δc_p^0 = -175 J K^{-1} mol^{-1})[19] and HSO_4^- (ΔG^0 = 11.342 kJ mol^{-1}, ΔH^0 = −22.4 kJ mol^{-1} and Δc_p^0 = −258 J K^{-1} mol^{-1})[18] the temperature dependence of the pK_a of formic acid and HSO_4^- was calculated (Fig. 3).

As for most simple acids, the dissociation constant of formic acid decreases only slightly with increasing temperature. Even though the pressure dependence was not taken into account, the calculated pK_a variation is in good agreement with experimental values for both formic acid[19,20] and hydrogensulfate.[21] On the other hand, the dissociation constant of HSO_4^- decreases very strongly and even crosses that of formic acid at elevated temperatures. The reason is the very high enthalpy change for the dissociation of HSO_4^-. At the high reaction temperatures in our experiments sulfate can in fact act like a weak base with a strength comparable to carboxylic acid salts and becomes protonated to a significant extent while deprotonating formic acid. We speculate that this also causes the high yield of γ-valerolactone in the presence of this salt.

For the other tested salts the pK_a values at high temperature were also calculated for a temperature of 220 °C.[18] In the case of halides, data for 200 °C were used (Fig. 4).[22] In fact, the pK_a of hydrogen fluoride is quite near to the value of HSO_4^-, which results in a similar yield of product by adding KF. The difference in dissociation constant between ambient and reaction condition is, however, less pronounced than for HSO_4^-. In a green, sustainable approach, KF cannot be recommended due to its toxicity. On the other hand there is no concern in using simple sulfates. In any case, the KF example allows us to conclude that the observed effects of salt addition are not attributed to Hofmeister effects, but rather to their influence on pH at elevated temperatures.

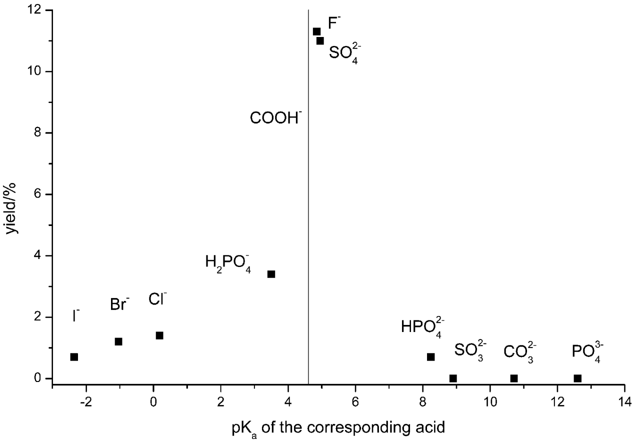


Fig. 4 Yield of product *versus* the pK_a of the corresponding acids of the tested salts at 220 °C and 200 °C for the halides respectively.

To gain further insight into the effect of added Na_2SO_4, standard mixtures of levulinic and formic acid were reacted in the presence of different concentrations of Na_2SO_4. Increasing the salt concentration increases the yield, until a plateau is reached around 0.1 M of salt (Fig. 5). Interestingly, the yield increases roughly with the logarithm of added salt concentration.

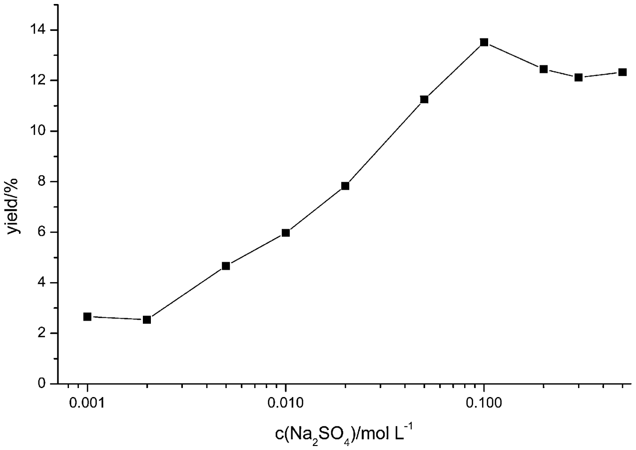


Fig. 5 Catalytic effect of Na_2SO_4 on the transfer hydrogenation.

For further optimization of the reaction conditions we screened the temperature dependence of the reaction within an 8 mL tubular flow reactor for a fixed flow of 0.4 mL min^{-1} and a pressure of 200 bar, corresponding to a reaction time between 18.1 min (at 175 °C) and 14.7 min (at 300 °C) (Fig. 6). With its continuous product stream, such a setup is certainly more adapted to industrial processes. In these experiments we used 0.125 M Na_2SO_4, as the reaction performed in autoclaves gave satisfactory yields at that concentration. This experiment shows that a sufficiently high temperature to activate the formic acid is necessary to start the reaction. Product yield under those conditions passed through a maximum, as a temperature above 275 °C again lowers the yield. We assume that the spontaneous decomposition of formic acid is too fast in this range. Hydrogen, formed by this process, cannot reduce levulinic acid. It is the direct hydrogen transfer which creates the γ-valerolactone.

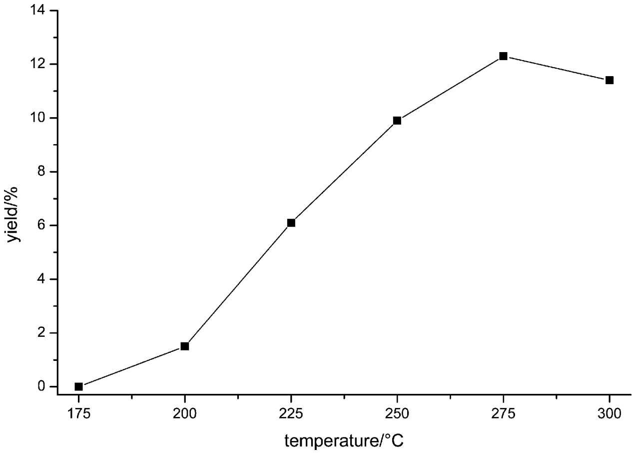


Fig. 6 Variation of yield with reaction temperature measured with a Thales Nano X-Cube Flash flow reactor and a residence time in the range of 18.1 min (at 175 °C) and 14.7 min (at 300 °C) with 0.125 M Na_2SO_4 added.

Comparing the overall yield from this experiment with the reaction performed in autoclaves (see Table 1) one notices the decreased yield at the standard reaction temperature of about 220 °C. This is due to the fact that in the tubular flow reactor the residence time is less than 20 min, as compared to the batch mode where it is about 12 h. The short reaction time therefore results in incomplete conversion. Higher yields are expected when pumping the reaction mixture into the reactor for a second time. The highest potential for an increased yield is given when the γ-valerolactone is extracted prior to re-reacting the unconverted starting educts, but such optimization by chemical engineering is out of the scope of the present paper. Selective extraction can be carried out for example with supercritical CO_2.[23]

Conclusions

We have shown that the transfer hydrogenation from formic acid to levulinic acid can be performed under hydrothermal conditions. Optimization of pH allows one to increase the yield of γ-valerolactone, a solvent or fuel molecule with great potential for sustainable chemistry based on biomass. Even simple sulfates can promote the reaction. We have found that this “salt catalysis” is probably not attributable to Hofmeister effects, but purely to the pH influence at elevated temperatures. Interestingly, sulfates in high temperature water are “switchable” bases, and become more and more basic with increasing temperature. This temperature dependence is more pronounced for sulfate compared to other anions. It can be exploited for easy preparation of reaction solutions that are neutral and thus easy to handle under ambient conditions but drastically change their properties at high temperature.

Such a temperature switch may be used to substitute conventional bases that are traditionally employed as catalysts, which require neutralization after reaction and thus create waste salt. Furthermore, a temperature-switchable base will become neutral when cooling to ambient conditions after reaction and can therefore be reused. This adds another sustainable feature to the high atom economy of the presented hydrothermal synthesis.

Experimental

Levulinic acid (98% purity) and γ-valerolactone (99% purity) were purchased from Sigma-Aldrich, and formic acid (98% purity) from Acros Organics. All chemicals were used without further purification.

Experiments were carried out in 45 mL acid digestion vessels from Paar, equipped with a Teflon inlet and a glass vial. In case of samples with high pH or when KF was added, the reaction was performed directly in the Teflon inlet, as glass was etched to a great extent under these conditions at high temperature. The autoclaves were put in an oven and heated up to 220 °C for 12 h. About 10 mL of solution were used for each experiment.

For measuring the temperature dependence of the reaction, we used the X-Cube Flash flow reactor from Thales Nano. Solution was pumped through an 8 mL coil at a flow rate of 0.4 mL min^{-1}. This corresponds to residence times in the range of 18.1 min (at 175 °C) to 14.7 min (at 300 °C), calculated from the density ratio of water under reaction and ambient conditions. Because of the relatively low concentration of solute, the density of pure water was used.[24]

Qualitative analysis was carried out with GC–MS. The sample was silylated with a mixture of bis-*N*,*O*-trimethylsilyl trifluoroacetamide with 1% trimethylchlorosilane prior to analysis.

Quantitative analysis was performed by HPLC equipped with a refractive index detector. A C18 column was used for separation with an eluent consisting of 1% acetonitrile in 10 mM HCl. Citric acid was used as internal standard.

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