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# Catalytic Conversion of Fructose to γ-Valerolactone in γ-Valerolactone

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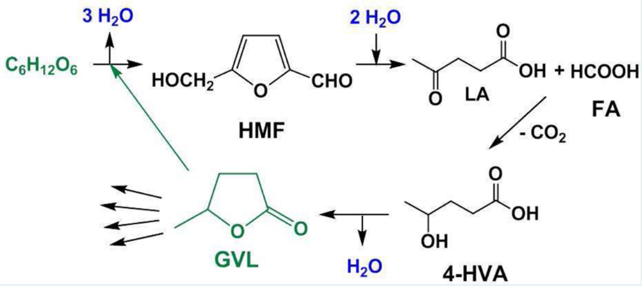
*Supporting Information*

**ABSTRACT:** The one-pot conversion of fructose to γ-valerolactone (GVL) in GVL as solvent was confirmed by monitoring the dehydration of $^{13}C_6$-D-fructose to $^{13}C_6$-5-(hydroxymethyl)-2-furaldehyde ($^{13}C_6$-HMF), the hydration of $^{13}C_6$-HMF to $^{13}C_5$-levulinic and $^{13}C$-formic acids, followed by their conversion to $^{13}C_5$-GVL.

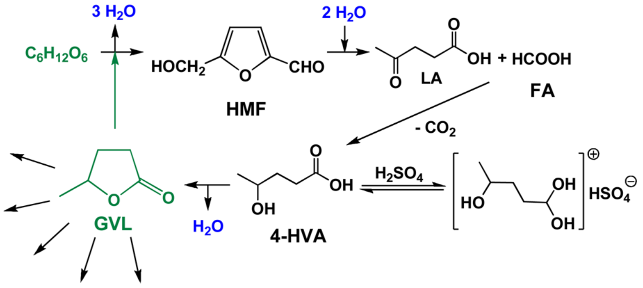


**KEYWORDS:** *fructose, 5-(hydroxymethyl)-2-furaldehyde, levulinic acid, formic acid, γ-valerolactone, acid catalysis, Shvo-catalyst, sulfuric acid, isotope labeling*

We have proposed that γ-valerolactone (GVL) could be considered as a sustainable liquid,[1] since it is renewable and has several very attractive physical and chemical properties.[2] GVL occurs naturally in fruits and has been used by the food industry. Its vapor pressure is remarkably low, even at elevated temperatures; it does not hydrolyze at neutral pH; and it does not form peroxides under air,[3] making it a safe material for large-scale use. GVL can be utilized for the production of energy by adding it to gasoline[1] or safely using it as an illuminating or igniting liquid.[4]

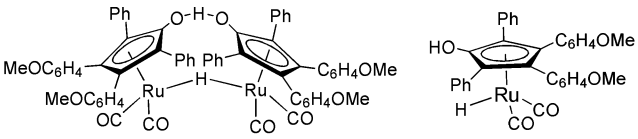
GVL can be used for the synthesis of various carbon-based chemicals, including of 1,4-pentanediols,[5,6] 2-MeTHF,[5,7,8] alkyl 4-alkoxyvalerates and tetraalkylammonium 4-hydroxyvalerates,[9] butenes,[10] mixtures of alkanes,[5] alkylvalerates,[11] 4-hydroxypentanamides,[12] and adipic acid via pentenoic acids.[13] Large-scale use of GVL will depend on the availability of commercially attractive conversion processes from biomass. GVL can be prepared from carbohydrates by four consecutive reactions (Scheme 1). The catalytic dehydration of $C_6$-sugars results in the formation of 5-hydroxymethyl furfural (HMF),[14,15] which can undergo catalytic hydration to levulinic acid (LA) and formic acid (FA).[16]

Scheme 1. Conversion of Carbohydrates to GVL in GVL



The transfer hydrogenation of LA with FA in the presence of the Shvo catalyst (Scheme 2)[17,18] leads to the formation of 4-hydroxyvaleric acid (4-HVA), which readily undergoes ring closure via dehydration to from GVL.[19]

Scheme 2. The Two Observable Forms of the Shvo Catalyst



In light of the beneficial use of solvents in the dehydration of carbohydrates to HMF,[20−22] a key element of our strategy has been the use of GVL as a solvent for each step.[23] The use of the product eliminates all solvent related separation and environmental issues, which could be an enormous challenge for solvents such as DMF, DMSO, and ionic liquids. The use of GVL as a solvent in the biphasic mode for the conversion of cellulose to LA and GVL was recently reported.[24] Although the formation of HMF, LA, and FA in GVL can be easily analyzed by NMR spectroscopy and other analytical techniques, proving the formation of GVL in GVL requires the differentiation of the product GVL from the solvent GVL. We report here the use of $^{13}C_6$-D-fructose, which allowed us to monitor the three

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consecutive catalytic steps leading to $^{13}C_5$-GVL in GVL, since the resonances of $^{13}C_5$-GVL are distinguishable from unlabeled GVL.

When 18.6 mg (0.1 mmol) of $^{13}C_6$-fructose was dissolved in a mixture of 0.075 mL of 5 mol/L $H_2SO_4$ and 0.5 mL of GVL, the presence of GVL, protonated-4-HVA, and the isomers of $^{13}C_6$- fructose were found in the $^{13}C$ NMR spectra. The concentrations of the *α*- and *β*- fructofuranoses (**1b**-**c**) and the *α*- and *β*- fructopyranoses (**1d**-**e**) were determined by $^{13}C$ NMR of 2-$^{13}C$-fructose (Figure 1). The linear isomer fructoketose (**1a**) was not observable.

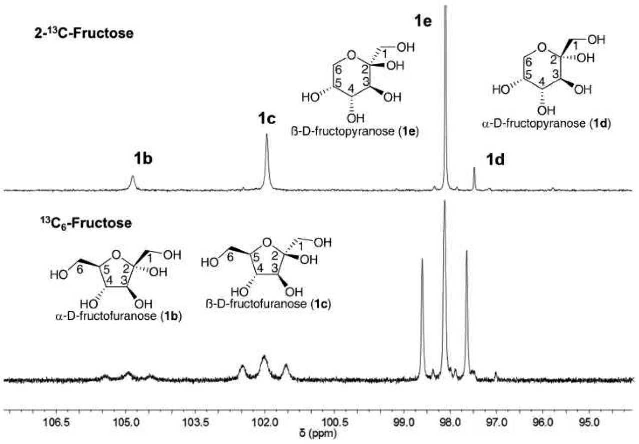

**Figure 1.** $^{13}C$ NMR spectra of 2-$^{13}C$- and $^{13}C_6$-fructose in 0.075 mL of 5 mol/L $H_2SO_4$ and 0.5 mL of GVL.

It should be noted that GVL does not hydrolyze at neutral pH,[3] but it is in equilibrium with protonated-4-HVA at low pH. Accordingly, the $^{13}C$ NMR spectrum of the mixture of 0.5 mL of GVL and 0.075 mL of 5 mol/L $H_2SO_4$ shows five small peaks for protonated-4-HVA at 178.7, 67.4, 33.3, 30.6, and 22.2 ppm, and the equilibrium composition is 99.6% GVL and 0.4% 4-HVA at 25 °C.

The four cyclic isomers reached their equilibrium concentrations after 120 min, which is a little bit longer than in water (several minutes). The linear isomer fructoketose (**1a**) remained below detection limit when fructose was at equilibrium in solution. It appears that the concentrations of the *α*- and *β*-fructofuranoses, the preferred isomers for high yield HMF production,[25] were higher in GVL than in water but lower than in DMSO (Table 1).

### Table 1. Equilibrium Composition (%) of the Isomers of Fructose in Different Solvents[a]

| solvent | 1a | 1b | 1c | 1d | 1e |
|---|---|---|---|---|---|
| $D_2O$[26] | 0.6 | 5.3 | 21.3 | 1.6 | 72.9 |
| DMSO[25] | 2.6 | 19.6 | 46.1 | 4.3 | 27.4 |
| $GVL/H_2O/H_2SO_4$ | nd | 10.5 | 27.8 | 3.8 | 57.9 |

[a]nd = not detectable.

When the solution of $^{13}C_6$-fructose in $H_2SO_4$/GVL was heated at 130 °C for 2 min, the resonances for $^{13}C_6$-fructose practically disappeared, indicating an almost full conversion. In addition to the resonances at 178.5, 162.1, 152.3, 125.1, 110.3, and 56.7 ppm due to the formation of 69% $^{13}C_6$-HMF, small peaks of $^{13}C_5$-LA and $^{13}C$-FA (4%) revealed their presence (Figure 2).

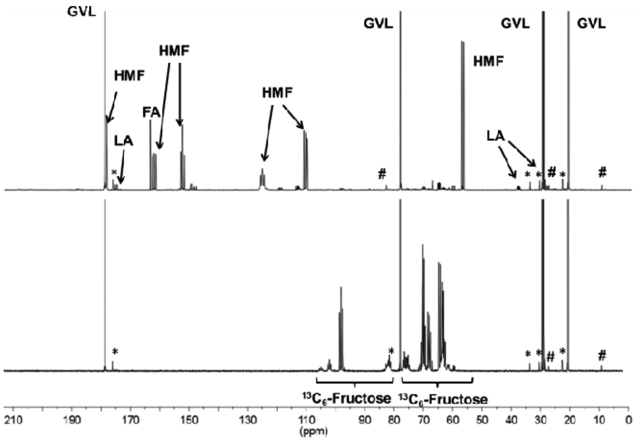

**Figure 2.** $^{13}C$ NMR spectra of the reaction mixture of 18.6 mg (0.1 mmol) of $^{13}C_6$-fructose in 0.075 mL of 5 mol/L $H_2SO_4$ in 0.5 mL of GVL at room temperature (bottom) and after heating to 130 °C for 2 min (top) [*0.4% protonated-4-HVA, #0.5% *γ*-caprolactone impurity in commercial GVL, which cannot be removed by routine distillation].

Since the acid concentration was set high enough to catalyze the hydration of HMF to LA and FA, after heating the reaction mixture at 130 °C for an additional 120 min all $^{13}C_6$-HMF was converted, and the formation of 69% $^{13}C_5$-LA and 71% $^{13}C$-FA was observed on the basis of the peaks at 208.1, 175.0, 37.6, 29.3, and 27.8 ppm ($^{13}C_5$-LA) and the singlet at 163.4 ppm ($^{13}C$-FA) (Figure 3).

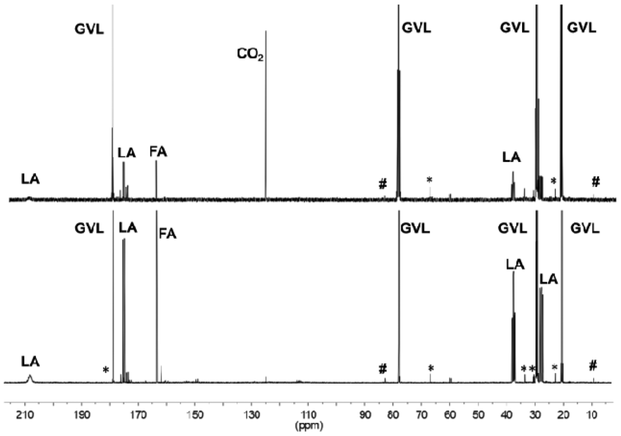

**Figure 3.** $^{13}C$ NMR spectra of the reaction mixture of 18.6 mg (0.1 mmol) $^{13}C_6$-fructose in 0.075 mL of 5 mol/L $H_2SO_4$ in 0.5 mL of GVL after heating to 130 °C for 122 min (bottom) and after the addition 6.3 mg (0.005 mmol) of Shvo catalyst and heating it at 100 °C for 120 min (top).

The transfer hydrogenation of $^{13}C_5$-LA with $^{13}C$-FA was achieved by adding 6.3 mg (0.005 mmol) of the Shvo catalyst to the reaction mixture, which then was heated at 100 °C for 120 min. The intensity of the peaks of $^{13}C_5$-LA and $^{13}C$-FA decreased, indicating the presence of 14% unreacted $^{13}C_5$-LA and 2% $^{13}C$-FA (Figure 3). The resonances at 178.9, 78.1, 29.5, 29.1, and 20.7 ppm for $^{13}C_5$-GVL and 124.9 ppm for $^{13}CO_2$ (the side product of the transfer hydrogenation) were easily observable.

On the basis of the integration of the well separated resonances of the methyl groups of unlabeled GVL and $^{13}C_5$-GVL (Figure 4), the overall yield of $^{13}C_5$-GVL was 55% on the basis of the starting fructose, and the selectivity of the transfer hydrogenation was >99%.

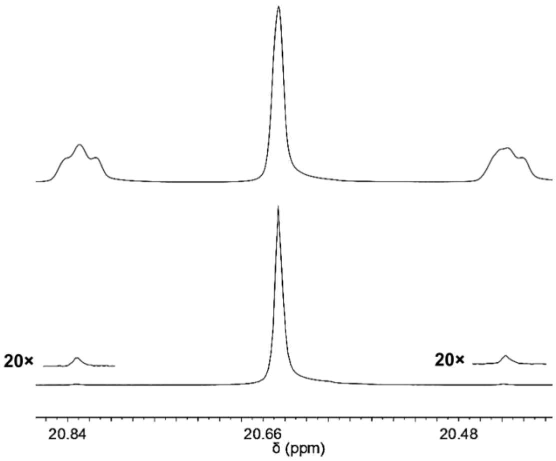

**Figure 4.** $^{13}C$ NMR resonances of the methyl groups of unlabeled GVL (bottom) and $^{13}C_5$-GVL in unlabeled GVL (top).

The $^1H$ NMR spectra recorded just before the $^{13}C$ NMR spectra show the same results (Supporting Information Figure S1). It should be noted that the peaks of the Shvo catalyst, including the bridging and terminal hydrides at −17.7 and −9.7 for the dinuclear and mononuclear forms, respectively, (Scheme 2) can be observed.

The presence of $^{13}C_5$-GVL and the ratio of $^{13}C_5$-GVL and $^{12}C_5$-GVL were also established by GC/MS. Accordingly, the MS of the GC peak of $^{13}C_5$-GVL and $^{12}C_5$-GVL has shown the molecular ions at 104.8 and 100.0, respectively.

In conclusion, we have demonstrated for the first time that GVL can be produced from fructose in GVL as solvent, thereby opening up the opportunity to develop an attractive and green process for the production of GVL by avoiding separation of the solvent and product. The isotope labeling approach to distinguish the product from solvent is essential to the presented work, and it is also expected to have utility in analogous research.

## ■ ASSOCIATED CONTENT

### Supporting Information

$^1H$ NMR spectra results. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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