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Transfer Hydrogenation of Ethyl Levulinate to γ-Valerolactone Catalyzed by Iron Complexes

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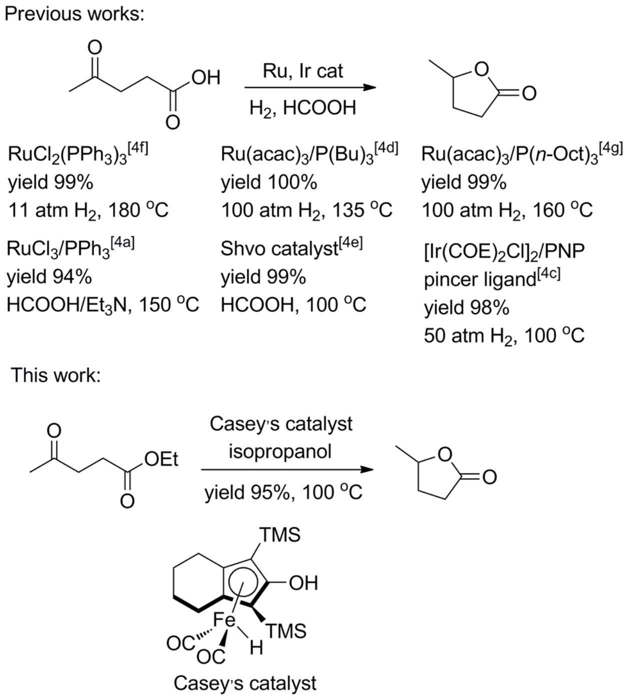
Conversion of biomass-derived ethyl levulinate to *γ*-valerolactone is realized by using homogeneous iron-catalyzed transfer hydrogenation (CTH). By utilizing Casey's catalyst and cheap isopropanol as hydrogen source, *γ*-valerolactone can be generated in 95% yield. Addition of catalytic amount of base is important to achieve good yield.

Keywords biomass, iron catalyst, *γ*-valerolactone, transfer hydrogenation

Introduction

For searching renewable carbon resources, catalytic conversion of lignocellulose biomass to produce liquid fuel and valuable chemicals has received intensive attention.[1] *γ*-Valerolactone (GVL), which derived from lignocellulose, can be used as liquid fuel, additive, solvent and also intermediate for organic synthesis.[2] Heterogeneous and homogeneous catalysis have been both exploited for the production of GVL from levulinic acid or alkyl levulinate.[3,4] Compared with levulinic acid, alkyl levulinate can be obtained directly from lignocellulosic biomass in better yield and through easier separation procedure. Therefore, it is more practical and attractive to utilize alkyl levulinate as substrate for synthesizing GVL. Up to now, many methods have been developed for converting alkyl levulinate to GVL.[5] As far as we know, most of the present homogeneous catalytic systems for the synthesis of GVL are based on rare and precious metals, such as ruthenium and iridium (Scheme 1).

Scheme 1 Production of GVL via homogeneous catalysis



As a trend for sustainable chemistry, using catalyst composed of earth-abundant elements to replace rare metal catalysts has gained much more attention recently. Iron is the most abundant transition metal on earth and non-toxic, thus possessing the advantages demanded for an ideal sustainable catalyst. Catalytic hydrogenation of carbonyls has been reported by using iron based catalyst in recent years.[6] For example, Beller *et al.* developed an iron-catalyzed biomimetic reduction system for the hydrogenation of *α*-keto-/*α*-iminoesters.[7] They also disclosed a Fe(BF$_4$)$_2$•6H$_2$O/PP$_3$ (P(CH$_2$CH$_2$PPh$_2$)$_3$) system for the effective decomposition of formic acid,[8] which was applied afterwards in the hydrogenation of aldehydes subtly.[9] Iron-P-N-P (amino-diphosphine ligand) pincer catalysts synthesized by Milstein *et al.* could realize the hydrogenation of ketones with low catalyst loading.[10] Morris and co-workers synthesized various iron complexes containing P-N-N-P (bis(imine)-diphosphine ligand) or P-N-P' (similar to P-N-P structure except different phosphine substituents) for catalyzing asymmetric transfer hydrogenation of ketones with high TON number under mild conditions.[11] Gao *et al.* reported the hydrogenation of aromatic ketones using Fe$_3$(CO)$_{12}$ combined with a macrocyclic ligand as

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catalyst.[12] In addition, Nishiyama *et al.* reported the hydrosilylation of ketones by combining iron(II) and a nitrogen ligand.[13] Although by these methods mentioned above, various ketone and aldehyde can be hydrogenated or transfer hydrogenated, there are very few reports about homogeneous iron-catalyzed conversion of biomass-derived levulinate substrate to γ-valerolactone.[4b]

Inspired by the recent developments of iron-catalyzed (transfer) hydrogenation of aldehydes and ketones, along with our interest in biomass conversion, especially in efficient production of γ-valerolactone in mind, we get the ideal to develop an iron-catalyzed system for converting ethyl levulinate to generate γ-valerolactone.

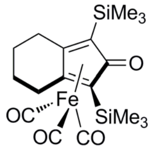
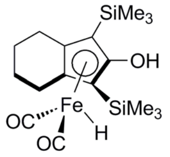
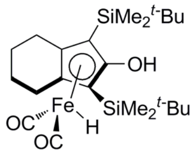
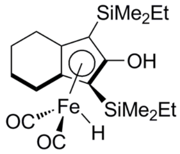
Experimental

Iron complexes and base were added to a 10 mL Schlenk tube equipped with a stir bar. The vessel was evacuated and filled with argon (three cycles). Alkyl levulinate and 2-propanol were then added into the tube under argon atmosphere. The mixture was heated at certain temperature for 19 h. The reaction mixture was diluted with ethyl acetate, centrifuged to remove the precipitation and analyzed by GC-MS (Thermal Trace GC Ultra with a PolarisQ ion trap mass spectrometer) with either a TR-35MS or a TR-5MS capillary column (30 m × 0.25 mm × 0.25 μm) and a Shimadzu GC equipped with an AT-65 capillary column. The yield of GVL and conversion of EL were determined by GC-analysis.

Results and Discussion

Our study commenced by choosing ethyl levulinate as the model substrate (Scheme 1). We tried to test several reported catalytic systems in the reduction of ethyl levulinate (EL).[7,9,13b,14] Firstly, we applied $Fe(BF_4)_2 \bullet 6H_2O/PP_3$ system[9] in this reaction, but no γ-valerolactone was detected (Table 1, Entry 1). The system of $FeCl_2$ with porphyrin[14b] was ineffective (Table 1, Entry 5). When using $Fe(OAc)_2$ and nitrogen ligand,[13b] only 3% yield of desired product was observed (Table 1, Entry 4). Inspired by the work reported by Beller *et al.* on ketone and aldehyde hydrogenation,[14a] we tried to utilize Casey's catalyst to catalyze this reaction, while the yield was only 4% (Table 1, Entry 6). We supposed that Casey's catalyst activated in advance would have higher activity.[15] Therefore, we treated it with acid and base to generate the activated Casey's catalyst possessing acidic and hydridic hydrogens. We tested this catalyst using isopropanol as hydrogen source. To our delight, 42% of GVL was obtained in the initial trial (Table 1, Entry 7). Encouraged by this result, we tested other two similar catalysts with relatively larger substituent ($-SiMe_2{}^tBu$, $-SiMe_2Et$), but the yield of GVL decreased to around 10% (Table 1, Entries 8 and 9).

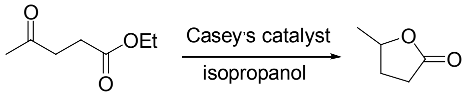
Table 1 Various iron-based catalytic systems for (transfer) hydrogenation of ethyl levulinate

Entry	Iron catalytic system	H-donor	*T*/℃	Yield/%
1[a]	$Fe(BF_4)_2 \bullet 6H_2O/PP_3$	HCOOH	60	＜1
2[b]	$Fe_3(CO)_{12}$＋terpy＋PPh_3	*i*-propanol	100	＜1
3[c]	$Fe_3(CO)_{12}$＋$Fe(OTf)_2$ ＋phenanthridine	H_2	65	2
4[d]	$Fe(OAc)_2$＋TMEDA	PMHS	65	3
5[e]	$FeCl_2$＋porphyrin	*i*-propanol	100	＜1
6[f]		H_2	100	4
7[g]		*i*-propanol	75	42
8[g]		*i*-propanol	75	10
9[g]		*i*-propanol	75	7

[a] Ethyl levulinate (0.5mmol), $Fe(BF_4)_2 \bullet 6H_2O/PP_3$ (0.4 mol%), THF (1.0 mL), HCOOH (1.1 equiv.), 60 ℃, 2 h. [b] In situ catalyst (0.0038 mmol) ([$Fe_3(CO)_{12}$] (0.0013 mmol), terpy (0.0038 mmol), PPh_3 (0.0038 mmol), 2-propanol (2.0 mL) for 16 h at 65 ℃), *t*-BuONa (0.019 mmol), 5 min, at 100 ℃, then addition of ethyl levulinate (0.38 mmol), 7 h at 100 ℃. [c] Ethyl levulinate (0.5 mmol), phenanthridine (18.0 mg, 0.1 mmol), $Fe(OTf)_2$ (15.0 mg, 0.036 mmol, 85% purity), [$Fe_3(CO)_{12}$] (16.8 mg, 0.0333 mmol), 1,4-dioxane (1.0 mL), H_2 (50 bar) and heated at 65 ℃ for 24 h in autoclave. [d] Ethyl levulinate (1.0 mmol), $Fe(OAc)_2$ (5 mol%), TMEDA (10 mol %), PMHS (2.0 mmol), THF (3.0 mL), 65 ℃, 24 h, work up with hydrochloric acid. [e] In situ catalyst (0.0038 mmol) (0.0038 mmol $FeCl_2$ and 0.0038 mmol 5,10,15,20-tatraphenylporphyrin in 1.0 mL 2-propanol for 16 h at 65 ℃), NaOH (0.19 mmol) in 0.5 mL 2-propanol, ethyl levulinate (0.38 mmol) in 0.5 mL 2-propanol, 100 ℃, 4 h. [f] Iron catalyst (0.1 mol%, 8.4 mg), ethyl levulinate (20 mmol), K_2CO_3 (5 mol%), *i*-PrOH/H_2O (10 mL/4 mL), H_2 (30 bar), at 100 ℃ for 17 h in autoclave. [g] Ethyl levulinate (1 mmol), iron hydride (1 mol%), 2-propanol (0.5 mL), 75 ℃, 16 h. The yields were determined by GC using 1-methyl-2-pyrrolidone as internal standard.

As the Casey's catalyst with substituent group of TMS performed better in initial reaction, we used it to further optimize the reaction conditions. First, we investigated the effect of temperature. The results showed that the temperature affects the CTH process significantly. At 40 ℃ the yield of GVL was less than 5% (Table 2, Entry 1). The yield increased by elevating the temperature to 100 ℃ (Table 2, Entry 3). Further elevating temperature to 120 ℃ resulted in a sharp decrease of the yield, which may be caused by the decomposition of the catalyst at high temperature (Table 2, Entry 4). Based on literature reports, adding catalytic amount of base could promote the transfer hydrogenation of ketone.[16] Inspired by this fact, we explored effect of different bases as additives. The yield was improved to 88% when adding Na_2CO_3 to the system (Table 2, Entry 5). Next, we screened some other common bases and found a mild base, $NaHCO_3$ performed best (Table 2, Entry 6). Strong bases, such as KOH, NaOH, NaO^{t}Bu and KO^{t}Bu showed no better performance (Table 2, Entries 9, 10, 15 and 16). Tertiary amine and pyridine type organic base retard this reaction (Table 2, Entries 12,13,14). Finally, we attempted to reduce the catalyst loading and found that 0.5 mol% of catalyst could realize 84% conversion of substrate and 82% yield under the same condition (Table 1, Entry 17). Further decreasing the catalyst loading caused a sharp drop of the conversion and yield (Table 1, Entries 18 and 19). It is worth noting that besides GVL, small amount of isopropyl levulinate, which was generated by intermolecular transesterification, was detected in the reaction mixture. We also used methyl levulinate and butyl levulinate as substrate respectively, the results showed both of them can be converted into GVL under the optimized conditions in 91% and 92% yield respectively (see SI). In addition, we did the gram-scale experiment under the optimised conditions and the isolated yield of GVL was 82% (see SI). The recycle of the iron catalyst was unsuccessful. We were unable to recover the iron catalyst from the reaction mixture.

Table 2 Optimization of the catalytic system based on Casey's catalyst^a



Entry	Base	T/℃	Conv./%	Yield/%
1	—	40	4	2
2	—	60	16	15
3	—	100	79	71
4	—	120	63	39
5	Na_2CO_3	100	94	88
6	$NaHCO_3$	100	96	95
7^b	$NaHCO_3$	100	75	68
8^c	$NaHCO_3$	100	75	69
9	KOH	100	59	53
10	NaOH	100	55	45
11	$K_3PO_4 \cdot 3H_2O$	100	75	71
12	NEt_3	100	71	64
13	C_5H_5N	100	35	27
14	DMAP	100	20	7
15	NaO^{t}Bu	100	78	66
16	KO^{t}Bu	100	79	74
17^d	$NaHCO_3$	100	84	82
18^e	$NaHCO_3$	100	61	61
19^e	$NaHCO_3$	120	36	14

[a] Conditions: ethyl levulinate (1 mmol), iron catalyst (1 mol%), base (5 mol%) in 2-PrOH (0.5 mL), 19 h. 2-PrOH was distilled before use. Yields and conversions were determined by GC using 1-methyl-2-pyrrolidone as internal standard. [b] $NaHCO_3$ (10 mol%). [c] $NaHCO_3$ (20 mol%). [d] Iron catalyst (0.5 mol%). [e] Iron catalyst (0.1 mol%), ethyl levulinate (5 mmol), 2-PrOH (2.5 mL).

Since hydrogen source is a crucial reaction parameter in catalytic transfer hydrogenation, we also tried to investigate the flexibility on H-donors of this catalytic system. We tested different types of H-donors, such as methanol, ethanol, *etc*. It was confirmed that other hydrogen sources could also play a role in this CTH process. When utilizing formic acid, 12% yield of GVL was obtained (Table 3, Entry 6), which validated the prediction of theoretical calculation by Assary *et al.*[17] Compared to primary alcohols, secondary alcohols performed better (Table 3, Entries 1—5). The CTH reaction with 2-pentanol gave 58% yield (Table 3, Entry 4), but it was still lower than isopropanol. Isopropanol was so far the best hydrogen donor. Hydrogen gas is effective as H-donor, but the yield of using hydrogen was much inferior compared with using isopropanol (Table 3, Entriy 7). This result suggests the CTH process is through a Fe-H intermediate and the mechanism of first decomposition of isopropanol to hydrogen is unlikely.

Table 3 Various H-donors for the conversion of ethyl levulinate to GVL^a

Entry	H-donor	T/℃	Yield/%
1	ethanol	100	15
2	methanol	100	6
3	butanol	100	8
4	2-pentanol	100	58
5	cyclohexanol	100	26
6	formic acid	100	12
7^b	hydrogen	100	33

[a] Conditions: ethyl levulinate (1 mmol), iron catalyst (1 mol%), $NaHCO_3$ (5 mol%), H-donors (5—10 equiv., see Supporting Information for details), 19 h. Yields and conversions were determined by GC using 1-methyl-2-pyrrolidone as an internal standard. [b] Ethyl levulinate (5 mmol), anhydrous toluene (10 mL), 10 bar H_2 in autoclave.

Conclusions

In conclusion, we have realized the transfer hydrogenation of biomass-derived ethyl levulinate to afford high value-added γ-valerolactone by using iron based homogeneous catalysis. By utilizing Casey's catalyst and cheap isopropanol as hydrogen source, γ-valerolactone can be generated in 95% yield. Addition of catalytic amount of mild base, sodium bicarbonate, is important for achieving good yield.

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