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Liquid-phase catalytic transfer hydrogenation and cyclization of levulinic acid and its esters to γ-valerolactone over metal oxide catalysts†

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Levulinic acid and its esters are converted to γ-valerolactone over metal oxide catalysts by catalytic transfer hydrogenation *via* the Meerwein–Ponndorf–Verley reaction.

The hydrogenation of biomass-derivable levulinic acid (LA) and its esters[1–5] to γ-valerolactone (GVL) (Fig. 1) is a key reaction in the development of economically viable and carbon-efficient biorenewable routes to chemicals[6,7] and liquid transportation fuels.[8] Although Group VIII metals, notably ruthenium,[7] have been shown to facilitate this hydrogenation step using molecular H_2, it has recently been suggested[9] that the use of precious metal catalysts is detrimental to the overall process economics for the production of high volume and relatively low value liquid transportation fuels. Thus, we report in this communication a new route for the conversion of LA to GVL using inexpensive heterogeneous catalysts, such as zirconium oxide.

As an attractive alternative to the reduction of LA to GVL using H_2 over metal catalysts, we have explored the reduction of LA by catalytic transfer hydrogenation (CTH), whereby a hydrogen source other than molecular H_2 is used. Recent literature on the CTH of LA has focused on using formic acid (FA) as the hydrogen donor, since FA is a by-product of LA production from C_6 sugars. However, the use of FA entails several unresolved disadvantages, such as the need for precious metals (*e.g.*, Pd, Rh), homogeneous catalysts,[10,11] and/or harsh reaction conditions (*i.e.*, hydrothermal conditions in the presence of salts[12,13]) for both the generation of H_2 from FA and the subsequent hydrogenation of LA to GVL.

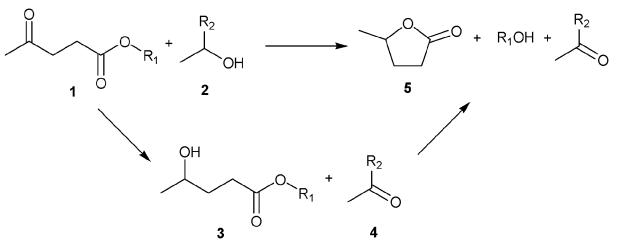

Fig. 1 Catalytic transfer hydrogenation of levulinic acid (**1**, R_1 = H) and its esters (**1**, R_1 = C_xH_{2x+1}) to γ-valerolactone (**5**) using a secondary alcohol as the hydrogen donor (**2**, R_2 = C_yH_{2y+1}).

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In contrast to previous work, we note that CTH through the Meerwein–Ponndorf–Verley (MPV) reaction remains an unexplored alternative chemistry for this reduction step, offering important advantages for its application. For example, the MPV reaction possesses exceptional chemo-selectivity for the reduction of carbonyl groups under mild reaction conditions and in the presence of other functional groups (such as C=C double bonds). Significantly, the MPV reaction can take place over non-precious metal heterogeneous catalysts.[14] Moreover, the hydrogen donor in the MPV reaction, usually a secondary alcohol, can be recycled after hydrogenation over base metal catalysts such as nickel[15–17] or copper,[18,19] or even sold as a commodity chemical in its oxidized form (*i.e.*, ketones, Fig. 1, **4**).

We demonstrate in this communication that CTH *via* the MPV reaction is a viable means for the hydrogenation of LA and its esters over inexpensive, heterogeneous catalysts that are easily regenerable, with attainment of close to quantitative yields of GVL under appropriate reaction conditions. In this respect, the MPV reaction is uniquely able to meet the above-mentioned techno-economic demands for the production of GVL from LA and its esters. Importantly, we demonstrate here for the first time that the MPV reaction can be exploited for the formation of GVL from LA and its esters over heterogeneous catalysts, which has hitherto been reported in only one instance to occur in the presence of homogenous catalysts.[20]

In initial reaction kinetic studies using batch reactors, it was found that a variety of metal oxides are active materials for the transfer hydrogenation of butyl levulinate (BL) to GVL (Table 1, Entries 1–5). Of the catalysts examined, ZrO_2 was the most active material for CTH. We have further observed that the CTH reaction occurs at reaction temperatures >100 °C, and the rate of formation of GVL increases with increasing reaction temperature (Table 1, Entries 9–11), with no observable loss in GVL selectivity at temperatures of up to 220 °C when secondary alcohols (*e.g.*, isopropanol (IPA), 2BuOH) are employed as the hydrogen donor. The only by-products detected in the product mixtures were those formed through the transesterification of the levulinate ester with the secondary alcohol solvent (*e.g.*, isobutyl levulinate as the product).

In contrast to using secondary alcohols as hydrogen donors, we found that although primary alcohols such as 1-butanol

Table 1 Catalytic transfer hydrogenation of levulinate esters using various alcohols as the hydrogen donor[a]

Entry	Catalyst	Time (h)	Mass ratio catalyst : ester	Solvent	Conv (%)	GVL yield (%)	GVL formation rate (μmol g^{-1} min^{-1})
1	MgO/Al_2O_3	16	1 : 2.4	2BuOH	17.0	14.6	1.9
2	MgO/ZrO_2	16	1 : 2.4	2BuOH	12.6	8.0	1.1
3	$CeZrO_x$	16	1 : 2.4	2BuOH	19.7	15.8	2.0
4	γ-Al_2O_3	16	1 : 2.4	2BuOH	37.0	29.6	3.9
5	ZrO_2	16	1 : 2.4	2BuOH	> 99.9	84.7	—
6	ZrO_2	4	1 : 4.8	2BuOH	70.1	55.6	65.6
7	ZrO_2	16	1 : 1.2	1BuOH	60.5	42.8	4.0
8	ZrO_2	16	1 : 1.2	EtOH	98.2	49.2	—
9[b]	ZrO_2	4	1 : 4.8	IPA	36.6	12.2	14.2
10	ZrO_2	4	1 : 4.8	IPA	77.2	55.0	70.8
11[c]	ZrO_2	4	1 : 4.8	IPA	93.2	80.5	108.4
12[d]	ZrO_2	4	1 : 4.8	IPA	70.8	62.4	86.0
13[e]	ZrO_2	16	1 : 1.2	THP	5.8	1.5	5.2

[a] Batch reactions, 5 wt% BL in respective solvents as feed, 150 °C, 300 psig He. [b] 120 °C. [c] 180 °C. [d] 5 wt% EL as feed. [e] 5 wt% IL as feed. Entries 1–6 and 9–12: the only by-products detected were isobutyl or isopropyl levulinate, formed through the transesterification of BL or EL with the solvent.

(Table 1, Entry 7, 1BuOH) and ethanol (Table 1, Entry 8, EtOH) are able to facilitate CTH of levulinate esters leading to the formation of GVL, various by-products are formed causing a decrease in GVL selectivity. These by-products were identified using GC-MS as forming through the self-condensation of the aldehyde formed after dehydrogenation of the hydrogen donor, or by forming through reaction of the aldehyde with levulinate esters. Significant differences are not observed in the rate of GVL formation when using different levulinate esters, *e.g.*, BL and ethyl levulinate (EL) (Table 1, Entries 10 and 12). Additionally, 4-hydroxypentanoic acid (Fig. 1, **3**) was not detected in any product mixtures throughout this study, indicating that rapid ring-closing to form GVL occurs under the reaction conditions employed. To investigate whether CTH of levulinate esters could be occurring through direct intramolecular hydrogen transfer within the ester, a reaction mixture of isopropyl levulinate (IL) in tetrahydropyran (THP) was used (Table 1, Entry 13). The formation of small amounts of GVL suggests that intramolecular CTH does appear to take place, but at a much lower rate (*e.g.*, by a factor of approximately 20) than through the MPV reaction with a hydrogen donor.

A key advantage of the MPV reaction is that the high chemo-selectivity for hydrogenation of carbonyl groups allows the CTH of levulinate esters to GVL to occur in the presence of other highly functionalized molecules. For example, we have observed that the reduction of levulinate esters occurs effectively in the presence of an aromatic diluent such as *sec*-butyl phenol (Table S1, ESI, SBP), whilst leaving the aromatic functional group in SBP completely unconverted. This high selectivity for conversion of LA *versus* reduction of SBP has practical implications, because we have shown elsewhere that alkylphenol solvents can be used to extract levulinic acid from aqueous solutions of sulfuric acid used to achieve the deconstruction of cellulose.[5] Although the use of equimolar concentrations of hydrogen donor (*i.e.*, IPA) and ester result in relatively low reaction rates (Table S1, ESI, Entry 1), it was observed that modest increases in the amount of IPA were effective in raising the yield of GVL. For instance, an increase in molar ratio of IPA : EL from 1 : 1 to 4 : 1 (Table S1, ESI, Entries 1–2) increased the GVL yields from 18% to 73%. At a molar ratio of IPA : EL of 7 : 1 (Table S1, ESI, Entry 3), it was found that the rate of GVL formation was comparable to that when pure IPA is used as the solvent (Table 1, Entry 10), and close to quantitative yields of GVL were attained (Table S1, ESI, Entry 4). We note that the high chemo-selectivity inherent in the MPV reaction, required in production processes for conversion of LA and its esters in the presence of highly functionalized extraction solvents, such as those recently reported by Alonso *et al.*,[5] is not easily attainable over conventional heterogeneous metal catalysts using molecular H_2. In particular, the hydrogenation of C=C over C=O bonds is thermodynamically favoured, and typically requires the use of precious metals (*e.g.*, Ru, Pt) modified with a base metal (*e.g.*, Sn) at the expense of lower catalytic activity.[5,21]

We have observed that LA undergoes CTH less readily than its esters, with GVL formation rates of 4 μmol g^{-1} min^{-1} (Table 2, Entry 3). In comparison, the rate of GVL formation

Table 2 Catalytic transfer hydrogenation of levulinic acid and levulinate esters using 2-butanol as the solvent and hydrogen donor[a]

Entry	LA (wt%)	BL (wt%)	Mass ratio catalyst : LA	Catalyst	Time (h)	GVL yield (%)	Ester & LA conv (%)	GVL formation rate (μmol g^{-1} min^{-1})
1	0.5	5	—	ZrO_2	4	30	30.1	42.1
2	1	5	—	ZrO_2	4	13	26.0	14.9
3	5	0	1 : 2	ZrO_2	16	22	52.0	3.9
4[b]	5	0	1 : 2	ZrO_2	16	71	> 99.9	—
5[c]	5	0	1 : 5	ZrO_2	16	39	> 99.9	16.7
6	1	0	2 : 1	ZrO_2	16	92	> 99.9	—
7	1	0	2 : 1	MgO/ZrO_2	16	54	> 99.9	—
8	1	0	2 : 1	γ-Al_2O_3	16	56	79.9	2.0
9	1	0	2 : 1	$CeZrO_x$	16	11	43.4	0.4

[a] Batch reactions, 150 °C, 300 psig He. [b] 220 °C. [c] MgO added to reaction mixture; mass ratio of $MgO:ZrO_2$ = 1 : 1.

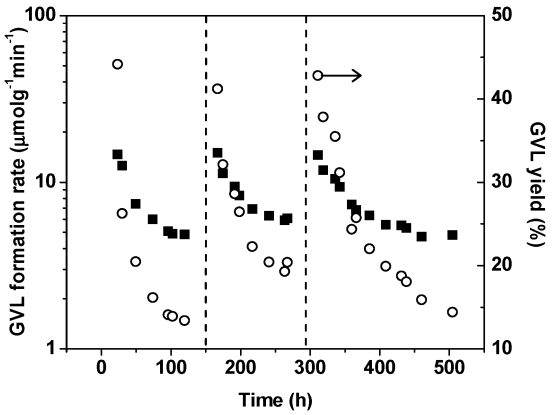

Fig. 2 Plot of γ-valerolactone (GVL) formation rate (■) and yield of GVL (○) as a function of time-on-stream for the catalytic transfer hydrogenation of butyl levulinate (BL) to GVL over ZrO_2 in a continuous flow reaction system. Refer to ESI for experimental details. Catalyst was regenerated at 150 and 300 h (dotted lines).

from BL was approximately 70 μmol g^{-1} min^{-1}. For all runs with LA (Table 2), the sole by-product detected was isobutyl levulinate, formed through the esterification of LA with the solvent over the catalyst. Entries 1–2 in Table 2 demonstrate that the addition of LA to BL and 2BuOH results in a decrease in the rate of GVL formation over ZrO_2 from 42 to 15 μmol g^{-1} min^{-1} as the concentration of LA is increased from 0.5 to 1 wt%. We suggest that the observed inhibiting effect of LA on CTH is due to the strong binding of the acid functional group in LA to basic sites on ZrO_2, which is known to be amphoteric;[22,23] the number of acidic and basic sites for the ZrO_2 material used here has been previously reported to be 296 and 212 μmol g^{-1}, respectively.[24] Because basic sites have been proposed to be active sites for the MPV reaction, either by themselves or in a cooperative manner with acid sites leading to concerted direct hydrogen transfer through a six-membered cyclic transition state,[25] the blocking of basic sites by adsorbed LA would thus result in a decline in catalytic activity. We further found that addition of a base (*i.e.*, MgO) to the reaction mixture was effective in mitigating catalyst inhibition by LA, and resulted in a four-fold increase in the GVL formation rate, even with the use of lower amounts of ZrO_2 (Table 2, Entry 5). Of the metal oxide catalysts examined, similar to what we observed for the CTH of levulinate esters to GVL, ZrO_2 was found to be the most active material for the CTH of LA to GVL (Table 2, Entries 6–9). The observed high activity of ZrO_2 for CTH of LA and its esters to GVL is consistent with the literature for the MPV reaction over heterogeneous catalysts,[14,26] which suggests that the amphoteric nature of the catalyst is one of the key factors underlying its high activity.

Having identified ZrO_2 as a highly active catalyst for CTH of BL to GVL, we studied this reaction using 2BuOH as the hydrogen donor in a continuous flow reactor to examine the stability and regenerability of the catalyst. As shown in Fig. 2, the ZrO_2 catalyst deactivates for the first 100 h of time-on-stream, and then appears to exhibit stable catalytic performance thereafter. This stabilization of activity could be indicative of the presence of sites with different activities, where initial rapid deactivation, possibly by coking, takes place first over the more active sites, followed by sustained catalysis on less active sites. Importantly, the initial activity of the catalyst is fully regained after calcination in air at 450 °C, and the catalyst was then found to display the same deactivation profile as the fresh catalyst after each regeneration cycle. After the second regeneration cycle and 500 h time-on-stream, it was observed that the catalyst stabilized to a similar activity level as the fresh catalyst (*i.e.*, at 100 h). This ease of repeated catalyst regeneration with no loss in catalyst performance, and the stabilization in catalytic activity with time-on-stream, are significant advantages for the use of this catalyst system in industrial applications.

In conclusion, we have found that reduction of LA and its esters to GVL can be accomplished by CTH through the MPV reaction over various metal oxide catalysts using secondary alcohols as the hydrogen donor. ZrO_2 was demonstrated to be a highly active material for CTH, in both batch and continuous flow reactor studies. While the activity of this catalyst decreased and then stabilized during operation for 100 h of time-on-stream, the initial activity of the catalyst was repeatedly regenerable by calcination in air, with no observable loss in catalytic activity.

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