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Efficient and sustainable transformation of gamma-valerolactone into Nylon monomers

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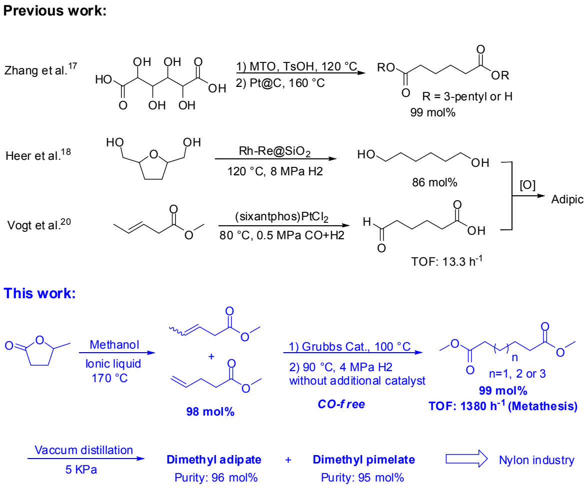
Herein, we reported the facile synthesis of dicarboxylic esters from biomass derived gamma-valerolactone (GVL) aiming for Nylon monomers preparation via a novel synthetic route which improved the efficiency and overcame the need of toxic carbon monoxide for the synthesis of dicarboxylic esters from GVL.

The production of liquid fuels and chemicals from biomass has attracted growing interest due to the issues caused by the depletion of fossil resources.[1-3] Various strategies have been developed in recent years for the chemicals and materials production from biomass derived platform molecules.[4, 5] In this context, gamma-valerolactone (GVL) is identified as a promising candidate to bridge biomass and petroleum based processes.[6-8] GVL not only possesses a significantly reduced oxygen content and polarity compared to carbohydrates but also is capable to provide downstream products for the current chemical industry.[9-15] To this end, dicarboxylic esters, especially adipate, which are important Nylon monomers were targeted to extend the application of GVL.

Concerning the synthetic pathway of adipates from carbohydrates derived compounds, several protocols have been developed. For instance, the conversion of mucic acid into adipic esters via the methyl trioxorhenium catalyzed deoxydehydration[16] and subsequent Pt-catalyzed transfer hydrogenation was realized by Zhang et al..[17] Starting from hydroxymethylfurfural, Heeres et al.[18] reported the synthesis of caprolactone via the 1, 6-hexandiol intermediate, which could also be applied to synthesize adipic acid. As a GVL-based route, dimethyl adipate could be prepared through catalytic distillation of GVL to form methyl pentenoates[19] and subsequent isomerization and hydroformylation to linear 5-formyl methyl pentenoate and branched by-product as well[20,21]. However, the efficiency and selectivity of isomerization and hydroformylation was not adequate and toxic carbon monoxide had to be employed as reactant. Therefore, we extended our presented approach to enable a new route for adipic ester production (Scheme 1). Metathesis of methyl pentenoates to unsaturated dicarboxylic esters was carried out in the presence of a Grubbs catalyst and the following hydrogenation could be conducted without using additional catalyst. The metathesis is not only efficient to convert pentenoates to unsaturated dicarboxylic esters (TOF=1380 h^{-1}) but also allows a carbon monoxide free synthesis. Regarding the above mentioned virtues, the presented protocols enable an efficient, benign and sustainable synthesis of dicarboxylic esters.

We began our study with the continuous catalytic distillation of GVL to provide the key intermediates for dicarboxylic esters. According to our previous study,[22] the Brønsted acidic ionic liquid **DIM-TFA**(Figure 1) which is an non-volatile



Scheme 1. Catalytic transformation of carbohydrates derived compounds to dicarboxylic acids/esters.

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homogeneous acidic catalyst enables the ring-opening esterification of GVL at 170 °C. Considering a potential scale-up and continuous operation, we conducted this transformation in a continuous flow mode. A solution of 20 wt% GVL in methanol was pumped at a flow rate of 15 mL h^{-1} into a flask containing 1.1 g **DIM-TFA** and 5 g GVL. As a result, most GVL was converted to methyl 3-pentenoate (**M3P**) and methyl 4-pentenoate (**M4P**) and less than 1 mol% of GVL was found in the distillate by gas chromatography (GC) analysis (Figure S1a). The concentration of the two isomers in the distillate reached 28 wt% and the overall yield of them was over 98 mol%.

In the continuous mode, TOFs of 23~25 h^{-1} could be achieved in the initial 6 h (Figure 1). Then a gradual decrease in TOF was observed. The decrease should be attributed to two reasons: 1) the consumption of the initially added 5 g GVL since the max TOF was 18.5 h^{-1} on the basis of GVL supply per hour; 2) the formation of viscous by-product. To prove this assumption, different amount of initial GVL was loaded and the results showed that the less GVL caused the earlier decrease in TOF (Figure 1). Moreover, these results can also exclude the solvent effects of GVL on this transformation because the TOFs in the first 3 h were not influenced by the concentration of GVL. Additionally, we observed that the reaction mixture's color changed from light yellow to dark brown after several hours run. Thus extraction of the resulting mixture with water and chloroform was performed to recover **DIM-TFA**. Consequently, 95 % of transparent ionic liquid were obtained from water phase. Comparison of the ^{1}H NMR spectra of the fresh and recovered **DIM-TFA** (Figure S3 and S4) showed no structural change of the ionic liquid. This consisted with the previous thermal gravity results which indicated the ionic liquid was stable below 350 °C.[22] Moreover, the recovered ionic liquid was able to convert most GVL to pentenoates in another 12 h run (Figure S1b) and delivered almost the same TOFs with the fresh one (Figure S2), revealing the robustness of **DIM-TFA** for this reaction and the viscous by-product (Figure S5 and S6) separated from the reaction system might be a possible reason for the gradual decrease in TOF.

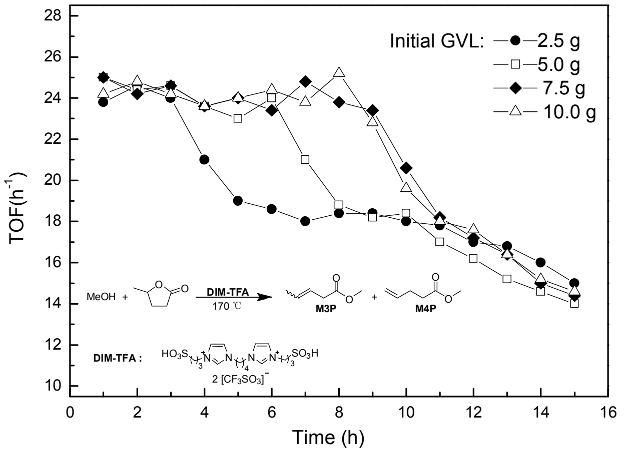
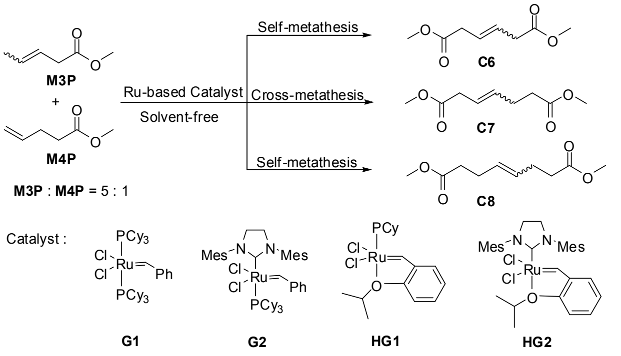


Fig.1 Catalytic distillation of GVL with different amount of initial GVL loading. Reaction Conditions: 1.1 g (1.35 mmol) **DIM-TFA**, 20 wt% GVL in methanol with a flow rate of 15 mL h^{-1} (Density: 0.83 Kg L^{-1}), 170 °C. The TOFs were calculated based on the molar amount of pentenoates generated per mole of catalyst per hour.

Following this continuous catalytic distillation, we prepared 1 liter of pentenoates solution. Subsequently, the methanol could be removed by distillation and then the water layer was formed and separated directly from the methyl pentenoates owing to their hydrophobicity. The resulting organic layer contained **M3P** and **M4P** with a molar ratio of 5:1, as well as small amount of methanol and water. With the pentenoates mixture in hand, the metathesis of methyl pentenoates was investigated with Ru-based catalysts, which had been successfully applied in the conversion of natural oils to useful chemicals.[23-27] As shown in Scheme 2, the self-metathesis of **M3P** and **M4P** is expected to afford unsaturated dicarboxylic esters **C6** and **C8**, respectively. Meanwhile, the cross-metathesis of them may give **C7** as product. In principle, the atom efficiency of this step is between 76 % (**C6**) and 89 % (**C8**). Despite this, the by-products ethene, propene and butene could also be utilized to produce fuels and chemicals. Before we used the prepared pentenoates mixture as substrates, the major isomer **M3P** was solely subjected to self-metathesis in sealed tubes to examine different catalysts and solvents. As aresult, Grubbs catalyst **G2** exhibited superior activity compared to the other three catalysts for the reaction at 55 °C (Table 1, entry 1~4). Moreover, **G2** allowed the reaction to proceed even at 35 °C. The results suggested the chlorinated solvents 1, 2-dichloroethane (DCE) and dichloromethane (DCM) were favorable in terms of conversion and selectivity (entry 5~11). However, the yield of **C6** couldn't be improved effectively by adding more catalyst or increasing reaction time (entry 12, 13). We reckoned that the generated 2-butene presumably inhibited the reaction due to the reversibility of the metathesis reaction between **C6** and 2-butene. Thus butene was removed from the reaction system by refluxing DCM under argon in a flask with a condenser connected to Schlenk line. As a result, the yield of **C6** was improved to 59 mol% (entry 14) and further improvement could be achieved under solvent-free conditions (72 mol%, entry 15). Using a pentenoates mixture as substrate, 18 mol% of **C6** and 28 mol%



Scheme 2 Ru-catalyzed metathesis of methyl pentenoates.

Table 1 Self-metathesis of **M3P** into **C6** under various conditions

Entry[a]	Catalyst	T (°C)	Solvent	Yield of **C6** (mol%)	Conversion of **M3P** (mol%)
1	G1	55	Methanol	17	19
2	G2	55	Methanol	32	34
3	HG1	55	Methanol	8	9
4	HG2	55	Methanol	24	26
5	G2	35	Methanol	10	13
6	G2	35	Toluene	20	33
7	G2	35	THF	11	12
8	G2	35	Cyclohexane	25	27
9	G2	35	Acetonitrile	2	3
10	G2	35	DCE	34	34
11	G2	35	DCM	34	36
12[b]	G2	35	DCM	38	41
13[c]	G2	35	DCM	40	42
14[d]	G2	50[e]	DCM	59	62
15[d]	G2	50	Solvent-free	72	73

[a] Reaction conditions: 0.21 g **M3P**, 1 mol% catalyst and 1.6 mL solvent were added to a sealed glass tube under argon and reacted for 6 h. [b] 3 mol% catalyst. [c] 3 mol% catalyst and reaction time of 24 h. [d] Reaction was conducted in a flask equipped with a condenser connected to a Schlenk line. [e] Temperature of oil bath.

Table 2 Synthesis of unsaturated dicarboxylic esters from the mixture of **M3P** and **M4P** (5:1) through metathesis reaction

Entry[a]	T (°C)	Reaction Time (h)	Yields of dicarboxylic esters (mol%)			Conversion (mol%)	
			C6	**C7**	**C8**	**M3P**	**M4P**
1	80	1	18	28	2	43	86
2	80	2	18	28	2	43	86
3	80	0.5	43	28	3	70	96
4	80	1	47	29	3	76	97
5	80	2	49	31	3	82	99
6	60	1	44	28	3	71	97
7	100	1	49	30	3	78	98
8	120	1	48	30	3	79	98
9	100	4	57	32	3	92	100
10	100	12	59	32	3	95	100
11[b]	100	1	41	26	2	65	91
12[c]	100	1	64	32	3	100	100
13[d]	100	1	64	32	3	100	100

[a] Reaction conditions: 1 g methyl pentenoates (**M3P:M4P**=5:1) and 0.1 mol% **G2** were added to a flask equipped with a condenser connected to Schlenk line. For entry 3~12, the methyl pentenoates were dried with anhydrous Na_2SO_4 before reactions. [b] 0.05 mol% **G2**. [c] 0.2 mol% **G2**. [d] 20 g methyl pentenoates and 0.2 mol% **G2**.

of **C7** were obtained in the presence of 0.1 mol% **G2** at 80 °C in 1 h (Table 2, entry 1). The cross-metathesis product **C7** became the major one because **M4P** containing terminal double bond was more reactive than **M3P**. Accordingly, the conversion of **M3P** and **M4P** were 43 mol% and 86 mol%, respectively. Nevertheless, the reaction didn't continue in the extended reaction time, indicating that the catalyst was decomposed or deactivated in the first hour (entry 2). The probable reason for this inhibition could be attributed to the residual water in pentenoates mixture. To our delight, after removal of water in pentenoates simply using anhydrous Na_2SO4, the conversion of **M3P** went up to 70 mol% in 0.5 hour and 43 mol% C6 could be produced. The conversion of **M3P** increased with the reaction time and the yield of **C6** reached 49 mol% in 2 h (entry 3~5). Moreover, elevated temperatures facilitate the transformation of **M3P** to **C6** (entry 6~8). At 100 °C, the conversion of **M3P** was 92 mol% and 95 mol% after 4 h and 12 h and the overall yield of **C6**, **C7** and **C8** exceeded 90 mol% (entry 9, 10). With a lower catalyst loading of 0.05 mol%, 69 mol% of dicarboxylic esters were produced and the TOF was as high as 1380 h^{-1} (based on the converted methyl pentenoates, entry 11). Note that a full conversion of the two pentenoates into unsaturated dicarboxylic esters could be achieved in the presence of 0.2 mol% **G2** (entry 12). Scale-up experiments using 20 g of substrates gave the identical results, affording ca.16 g unsaturated dicarboxylic esters (entry 13).

The subsequent hydrogenation of the unsaturated dicarboxylic esters into the corresponding final products, namely dimethyl adipic, pimelic and subericester, was performed without an additional catalyst. The resulting mixture of scale-up experiments (entry 13) was directly transferred into an autoclave, followed by charging 4 MPa H_2. The G2 in the metathesis mixture was able to act as catalyst for the subsequent hydrogenation. Consequently, a quantitative yield of saturated dicarboxylic esters was achieved at 90 °C within 5 h. The products distribution were the same with that of their unsaturated precursors (adipate : pimelate : suberate = 64 : 32 : 3).

Concerning the products purification, we tried two methods to isolate pure dicarboxylic esters, especially adipate. First, to limit the formation of **C7** and **C8** products, the pentenoates mixture was distilled under vacuum (5 KPa) to increase the **M3P** content. However, only slight improvement was achieved (from 82 wt% to 85 wt%) due to the close vapor pressure of these methyl pentenoates. Another attempt was the vaccum distillation of the hydrogenated dicarboxylic esters. To our delight, distillates collected at 111 °C and 125 °C were 9.1 g and 5.4 g containing 96 mol% dimethyl adipate (Figure S7a, S8a) and 95 mol% dimethyl pimelate (Figure S7b, S8b), respectively. The later product could also find application in Nylon production[28] and pharmaceutical synthesis[29, 30]. Further improvement in purity is also probable through increasing effective plate number at a larger scale.

Conclusions

In summary, we developed a novel synthetic strategy for the efficient production of bio-Nylon monomers. Relatively pure dimethyl adipate and pimelate were prepared efficiently from GVL under CO-free conditions. We demonstrated that the key intermediates **M3P** and **M4P** could be prepared with high yield in a continuous flow mode using the recyclable Brønsted acidic ionic liquid **DIM-TFA** as catalyst. A full conversion of the intermediates to Nylon monomers was achieved via a Ru-catalyzed metathesis followed by hydrogenation without any additional catalyst. Finally, purification of dimethyl adipate was achieved with a purity of 96 mol%. In order to make this route economically feasible, further study should improve the efficiency and stability of the catalytic systems and lower the cost of catalysts, especially for metathesis step. Despite these, the presented study could enhance the role of GVL as a potential bridge between biomass and petroleum based processes and provide an alternative sustainable way of Nylon production in future biorefinery.

Experimental Section

All reagents were obtained from commercial supplier and used without further purification. The ionic liquid **DIM-TFA** was synthesized according to our previously reported procedure.[22]To prepare methyl pentenoates, 1.1 g **DIM-TFA** and initial 5 g of GVL were added to a 25 mL flask and heated to 170 °C. Then a methanol solution containing 20 wt% GVL was injected by a syringe pump at a flow rate of 15 mL h-1. After removal of methanol by distillation, the organic layer containing **M3P** and **M4P** could be separated directly from the water layer. Nextly, hydrogenation of methyl pentenoates was carried out in a 100 mL stainless steel autoclave using methanol as solvent. As a typical procedure of metathesis reactions, 1 g substrates and desired amount of catalyst were added into a 5 mL flask equipped with condenser. Then the reaction was performed under argon using Schlenk line technique. To hydrogenate the unsaturated dicarboxylic esters, the mixture from metathesis reaction was diluted with 20 mL methanol and transferred to an autoclave. The hydrogenation was conducted in the presence of 4 MPa H_2 at 90 °C for another 5 h.

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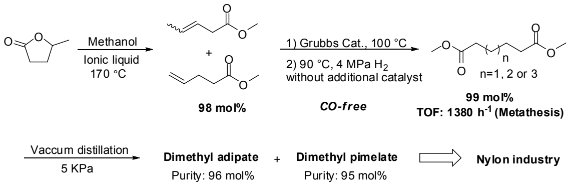

A route for efficient synthesis of bio-Nylon monomers from gamma-valerolactone has been developed.