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ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.7b01569 • Publication Date (Web): 19 Sep 2017

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A comprehensive study on metal triflates promoted hydrogenolysis of lactones to carboxylic acids: from both synthetic and mechanistic perspectives

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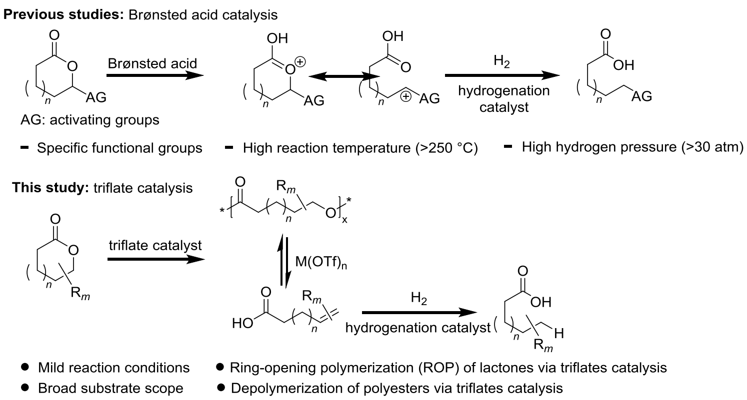
ABSTRACT: Direct hydrogenolysis of lactone to carboxylic acid (*i.e.*, hydrogenolysis of C_{alkoxy}-O bond with the carbonyl group untouched) is generally difficult, as the current strategies employing Brønsted acids as the catalyst usually request harsh conditions such as high temperature and high pressure of H_2. Herein, we would like to report a developed solvent-free catalytic transformation, in which $W(OTf)_6$ is believed to promote the hydrogenolysis process. This strategy could efficiently get lactones hydrogenated to carboxylic acids under extra mild conditions (*e.g.*, a reaction temperature lower than 150 °C and 1 atm H_2) and showed broad substrate scope. In addition, the catalytic protocol can be further applied to the hydrogenolysis of polyhydroxyalkanoate, as a renewable polymer, to the corresponding straight-chain carboxylic acids. Extensive mechanistic study was subsequently carried out and the DFT calculations revealed a reaction pattern, including the complete cleavage of C=O double bond with assistance of $W(OTf)_6$ catalyst. Moreover, the key intermediate raised in the mechanism, as an oxonium with OTf moiety, was successfully detected by ESI-MS spectra. Through a comparison with the Brønsted acid catalyzed system, the study confirmed that the existence of OTf moiety can significantly lower the barriers associated with the rearrangement and elimination processes. Meanwhile, emphasis was put on the critical role that the anion plays, as well as the fact that anion effect is directly related to the chemo-selectivity.

KEYWORDS: *lactones, hydrogenolysis, Lewis acids, metal triflate, tungsten*

INTRODUCTION

The catalytic conversion of renewable resources is the most effective way to achieve sustainable development in modern chemical industry. [1] Although strategies for introducing new functional groups, such as C-H bond activation [2] and C-C cross-coupling reactions, [3] have been widely investigated in organic community, it still remains challenging to selectively eliminate oxygen-containing functional groups in biomass materials [4] in the preparation of high-value-added chemicals.

Lactones, representing as a class of cyclic esters abundant in nature, are susceptible to hydrolysis or ring-opening polymerization, affording hydroxyacid or polyester compounds. Typically, hydrogenation of ester carbonyl groups affords diols [5] or cyclic ethers [6] since this group is very sensitive to reductive conditions. [7] In general, it is difficult to retain the carboxyl group while selectively cleaving the C_{alkoxy}–O bond. As a result, the hydrogenolysis of a lactone to a carboxylic acid is challenging. [8] Some previous studies have reported a potential solution for this transformation using Brønsted acids. Lactone is catalyzed by Brønsted acids in the presence of reactive groups to generate a carbenium ion, [8a-b] followed by the formation of the carboxylic acid by hydrogen reduction (Scheme 1). By this method, γ-valerolactone (GVL)—a reduced derivative of the biomass-based platform molecule levulinic acid (LA) [9]—can be transformed into valeric acid or its ester derivatives. [10] The potential of valerate as a transport fuel has attracted widespread attention. [11] However, although the reported harsh conditions (*i.e.*, temperatures > 250 °C and pressures > 30 atm) are suitable for industrial gas-phase applications, [10a] large-scale practical applications of this approach are severely restricted, especially for bulky or heavy lactones that may not be amenable to gas-phase chemistry. Utilization of mild reaction conditions is not only a key issue in the biomass energy chemical industry, but is also crucial for reaction selectivity and functional group compatibility in organic synthesis.



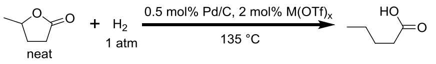
Scheme 1. Hydrogenation of lactones to carboxylic acids catalyzed by Brønsted acid versus metal triflate.

In the case of metal triflates, people have noticed that the strong electron-withdrawing ability of the triflate results in an electron-deficient metal cation, rendering strong Lewis acidity which promoted the activation of C-O bond.[12] In previous studies, Beller *et al.* used a Ru/phosphine-$Al(OTf)_3$ co-catalytic system to convert lactones into cyclic ethers in an efficient manner.[6a] In addition, Marks *et al.* also developed a strategy using metal triflates to transform esters and triglycerides to the corresponding alkanes smoothly.[13] Furthermore, it was also reported that the metal cation of $M(OTf)_n$ can bind to the ester carbonyl oxygen and thus induces a ring-opening polymerization (ROP).[14] Despite the abovementioned achievements, in our case, we found metal triflate can promote the elimination of lactone and polyester, generating an unsaturated carboxylic acid, in which the C=C double bond can later be saturated by hydrogenation. This catalytic system reported herein utilizes mild reaction conditions and is universally applicable for the hydrogenolysis of lactones to carboxylic acids. Moreover, quantitative conversion can be obtained for certain substrates under neat conditions and atmospheric H_2 pressure.

RESULTS AND DISCUSSION

Initially, GVL was selected as the model substrate for ring-opening hydrogenation in the presence of Pd/C and different metal triflates under neat conditions and 1 atm of H_2 (Table S1 in the Supporting Information). [15] The results indicated that metals with higher valences give rise to higher yields; that is, a high formal charge on the metal enhances product yield (e.g., Cu^+ vs. Cu^{2+} and Ce^{3+} vs. Ce^{4+}). Further investigation revealed that main group (IIIA) metal ions, such as Al^{3+} and Ga^{3+}, exhibited a better catalytic effect than other metal ions. However, Group IIB and IIIB transition metal ions exhibited low catalytic activity. By contrast, Zr^{4+} (IVB), Hf^{4+} (IVB), Nb^{5+} (VB), Ta^{5+} (VB) and W^{6+} (VIB) exhibited high conversion (99%) and good product yields (>95%) for ring-opening hydrogenation. To distinguish the catalytic efficiencies of these five M(OTf)n species, the reaction time was decreased to 4 h (Table 1). As seen, $W(OTf)_6$ exhibited the highest catalytic efficiency. Notably, a positive correlation was observed between the catalytic efficiencies and effective charge densities of these five metal triflates, which is similar to that reported for the catalytic ring-opening of cyclic ethers. [16] However, when the $W(OTf)_6$ was replaced by the WCl_6, there was no formation of valeric acid. Given this result, although the effective charge densities are slightly different from one to another, we envisaged that the anion might also play a direct role by participating in the transformation. In addition, a commonly used hydrogenation catalyst (Pt/C) exhibited excellent catalytic activity, whereas a Ru/C catalytic system exhibited low activity for hydrogenation. When a homogeneous hydrogenation catalyst with phosphine as the ligand replaced the heterogeneous catalyst, good yields were also obtained (except the case in which a Triphos ligand is employed, please refer to Table S2 & Table S3 for details). Control experiments demonstrated that the reaction could only be smoothly carried out under conditions in which both the hydrogenation catalyst and the metal triflate are present (Table S2).

Table 1. Optimization of reaction conditions for hydrogenolysis of γ-GVL.[a]



Entry	$M(OTf)_x$	APT Charge of metal ion	Effective ionic radii	Effective charge density	Conversion (%)		Yield (%)	
					4 h	12 h	4 h	12 h
1	$Zr(OTf)_4$	3.06	0.72 (VI)	4.25	51	>99	48	>99
2	$Hf(OTf)_4$	3.04	0.71 (VI)	4.28	53	>99	52	>99
3	$Nb(OTf)_5$	3.43	0.64 (VI)	5.36	57	>99	53	>99
4	$Ta(OTf)_5$	3.91	0.64 (VI)	6.11	63	>99	61	>99
5	$W(OTf)_6$	4.38	0.60 (VI)	7.30	75	>99	73	>99

[a] Conversion of GVL to pentanoic acid catalyzed by 0.5 mol% Pd/C (10 wt% Pd loading), 2 mol% M(OTf)n (Reactions were carried out on a scale of 5 mmol under neat conditions. Yields were determined by gas chromatography.)

With the optimal reaction conditions established (*i.e.*, $W(OTf)_6$ + Pd/C), a decagram scale experiment was performed (Figure 1). Biomass-based GVL was successfully transformed into *n*-pentanoic acid, which is considered as a precursor to fuels. [10, 11] Meanwhile, the stability and recyclability of the catalyst were also investigated on a decagram scale (100 mmol) under identical conditions. The results obtained by GC indicated the complete conversion of GVL, with the product collected by vacuum distillation. Notably, the recyclability test of this catalyst was performed under five consecutive runs utilizing identical conditions. During the recycle, the catalytic effect of the catalyst appeared to partially decrease from 97% to 93%. Our previous study indicated that both the formation of clusters for catalyst and the inevitable hydrolysis of the catalyst could lead to the reduction of product yields. [17] Nevertheless, the high product yields observed herein indicate that the catalysts can be recycled and reused several times for large-scale production. (Detailed experimental procedures can be found in the SI.)

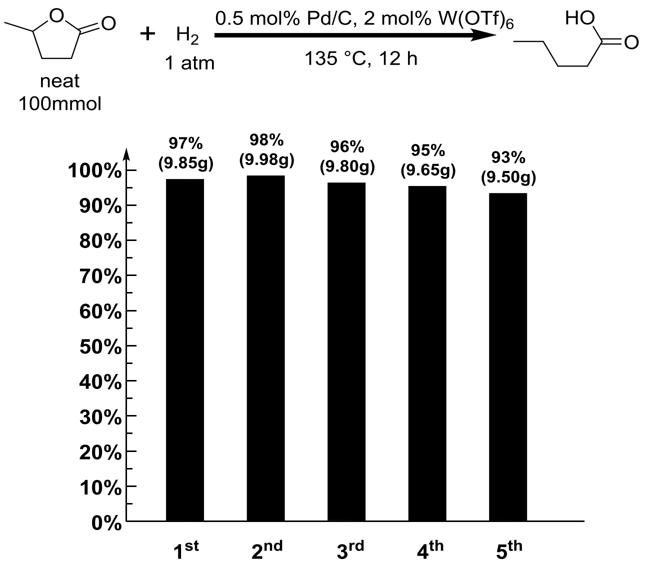
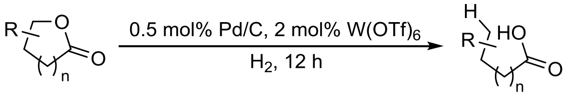
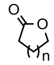
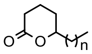
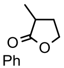
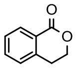
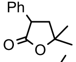
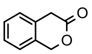
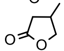
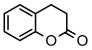
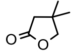
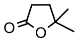
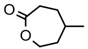
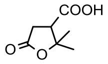
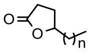
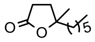
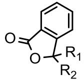
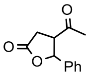
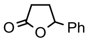
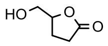
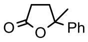
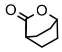
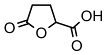
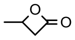


Figure 1. Large-scale reaction and the recyclability of catalysts ($W(OTf)_6$ + Pd/C) after 5 runs (isolated yield).

The use of this catalytic system is expected to be effective for the transformation of other lactone compounds as well. To obtain a structure-reactivity relationship for lactones, we decided to test a series of lactones as shown in Table 2. To this end, the effect of ring strain on the reactivity was firstly investigated (Table 2, entries 1–4). As anticipated, the highly strained four-membered *β*-propiolactone exhibited the highest activity, followed by the seven-membered *ε*-caprolactone, six-membered *δ*-valerolactone and five-membered *γ*-butyrolactone. The yield obtained for *γ*-butyrolactone was limited to only 11%, even when the reaction time was increased to 48 h (Figure 2). Overall, the results obtained from these experiments demonstrate that high strain energy promotes ring opening. In contrast, low strain energy is indicative of a stable structure with low reactivity. For instance, despite the increase in temperature to 180 °C, the yield of *n*-butyric acid was limited to 56%. Meanwhile, *n*-pentadecyl acid was obtained in 71% yield from pentadecanolide, which possesses a larger ring.

Table 2. Hydrogenolysis of lactones to corresponding acids by W(OTf)$_6$.[a]



entry	lactone substrate	yield of carboxylic acid	entry	lactone substrate	yield of carboxylic acid	entry	lactone substrate	yield of carboxylic acid	entry	lactone substrate	yield of carboxylic acid
1		90% (n=0)	11		96% (n=0)	20		4% (33%^{b})	30		n.d.$^{b, f}$
2		6% (56%^{b}) (n=1)	12		92% (n=1)	21		25%	31		97%^{d}
3		44% (n=2)	13		98% (n=2)	22		46%^{b}	32		n.d.$^{b, f}$
4		62% (n=3)	14		94% (n=6)	23		n.d.^{b}	33		78%^{f}
5		71% (n=12)	15		95%^{c}	24		69%	34		86%^{f}
6		97% (n=0)	16		96%^{c}	25		<5%‡(67%^{e}) ($R_1 = R_2 = H$)	35		75%^{d}
7		94% (n=1)	17		95%^{d}	26		91%^{d} ($R_1 = H$, $R_2 = Ph$)	36		11%
8		93% (n=2)	18		96%^{d}	27		86%^{d} ($R_1 = H$, $R_2 = Bn$)	37		85%^{e}
9		90% (n=6)	19		<5% (40%^{f})	28		67%^{d} ($R_1 = H$, $R_2 = -CH_2COOH$)			
10		96%				29		94%^{d} ($R_1 = R_2 = -Ph$-p-OH)			

[a]Reactions were performed using 0.5 mol% Pd/C (10 wt% Pd loading), 2 mol% W(OTf)$_6$ and substrate (5 mmol) without solvent at 135 °C, 1 atm H_2 for 12 h, and the yield shown correspond to isolated product yields, except for those indicated in entries 1–4, which were determined by GC analysis using bicyclohexane as the internal standard. [b]Reaction conditions were similar to general conditions, with the exception of 180 °C as the reaction temperature; [c]Reaction conditions were similar to general conditions, with the exception of 100 °C as the reaction temperature; [d]Reactions were performed using 0.5 mol% Pd/C (10 wt% Pd loading), 2 mol% W(OTf)$_6$ and substrate (2 mmol) in AcOH (2 mL) at 50 °C, 1 atm H_2 for 12 h. [e]Reaction conditions were similar to condition d, with the exception of 100 °C as the reaction temperature. [f]Reaction conditions were similar to condition d, with the exception of 150 °C as the reaction temperature and 20 atm H_2. (n.d. = not detected.)

However, as shown in Table 2, high conversion and good yield of the five-membered GVL (entry 6) were achieved under the identical conditions. Hence, it seems natural that ring strain is not the only factor that affects the reaction outcome. From a structural point of view, there is a methyl substituent on the C_{alkoxy} of GVL relative to γ-butyrolactone. Therefore, the substituents on the C_{alkoxy} atom should also affect the outcome of reaction. Given the experimental observations, we found that the electron-donating group on C_{alkoxy} benefits both the reaction conversion and yield. In this regard, compared to primary lactones, secondary lactones were transformed more easily to their corresponding acids (entries 7–14). More interestingly, tertiary lactones (*i.e.*, with two electron-donating alkyl groups on C_{alkoxy}) were found reactive and to undergo cleavage at 100 °C, with an isolated product yield of >95% (entries 15–16). Benzylic lactones were found to be the most reactive substrate in this study, even at a reaction temperature of 50 °C (entries 17–18). In contrast, the presence of an electron-withdrawing group (*e.g.*, carboxyl group) on C_{alkoxy} restricted the formation of the target product. By increasing the reaction temperature to 150 °C and the pressure to H_2 to 20 atm (i.e., very harsh conditions), glutaric acid was obtained in only moderate yield (entry 19).

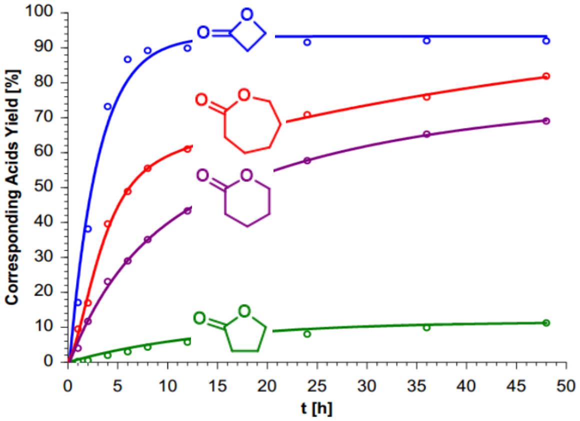


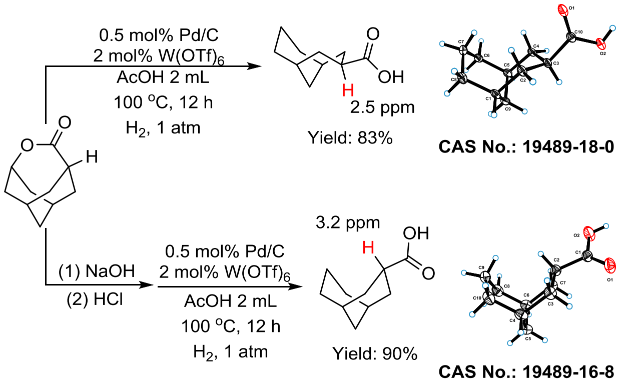
Figure 2. Kinetic profiles for the substrate with different ring strains.

Next, we decided to move a step further by exploring the substituent effect on the β-C of the ester-oxygen atom. Notably, the corresponding carboxylic acid was not observed from the reaction of the substrate with two methyl groups on the β-C (*i.e.*, substrate without a β-H) for a five-membered lactone (entry 23), even when the temperature was increased to 180 °C. However, a methylation migration rearrangement was observed for the six-membered lactones with two methyl groups on the β-C of the ester-oxygen atom. The rearrangement product could be further hydrogenated with our catalytic protocol to generate the corresponding carboxylic acid (see SI-III-C). These experimental observations clearly indicate that the presence of a β-H can promote the reaction, but not compulsory. Other factors, like the ring-strain, also plays a critical role in the reactivity. The reaction of the substrate with one methyl group on the β-C of the acyl group (entry 22) afforded a result similar to that shown in entry 2. Nevertheless, phthalide and its derivatives do not possess a β-H, yet they were transformed into the corresponding carboxylic acid under 1 atm of H_2 in AcOH. The reaction conditions could be milder in the presence of an electron-donating group on C_{alkoxy}. Thus, successful reaction is likely to be mainly affected by the specific structure of the benzyl ester, which results in a different and specific mechanistic pattern. Furthermore, as shown in entry 25, the reaction was impossible to proceed without $W(OTf)_6$, thereby excluding the possibility of C-O cleavage catalyzed by AcOH.[18a] This is probably because the hydrogenolysis of the benzyl primary alcohol ester was subjected to a non-carbocation process.[18b] The $W(OTf)_6$ is believed to weaken the $C_{alkoxyl}$-O bond to some extent.

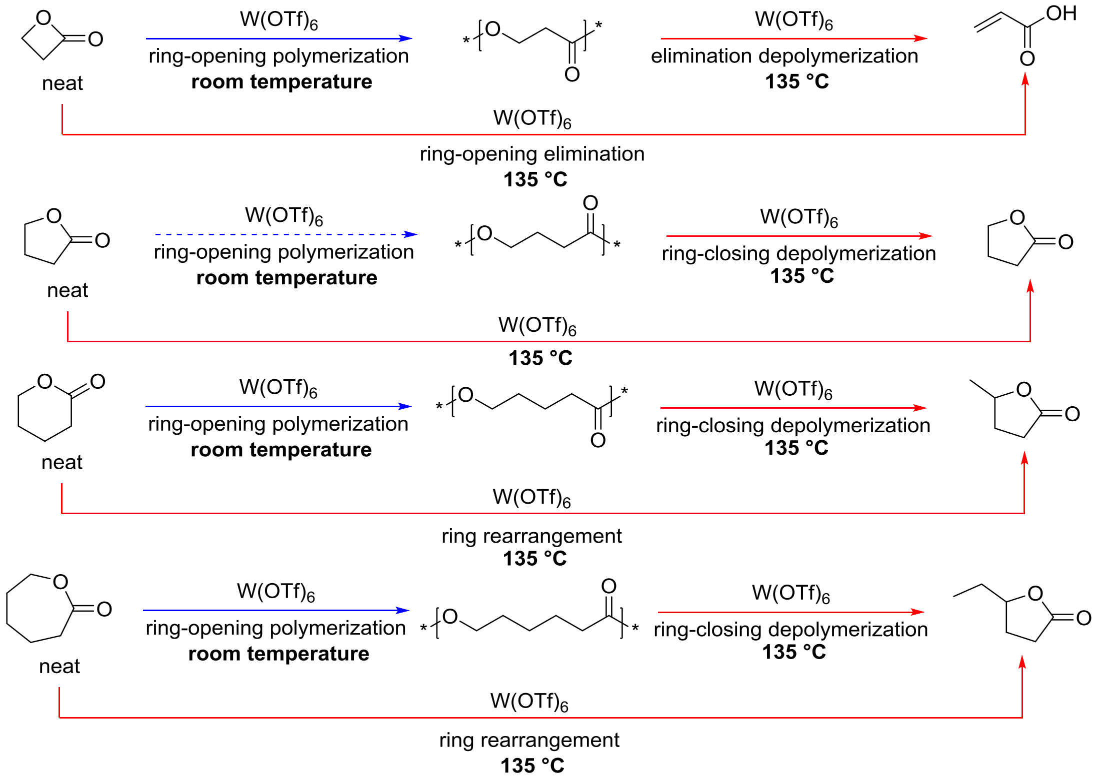
In addition, the effects of substituents on the *α*-C of the acyl group were also investigated. By comparing the data shown in entries 2 and 20, we realized that introducing substituent groups to the *α*-C of the acyl group would significantly retard the transformation, even for the most reactive tertiary lactone (entry 21 vs entry 15). In summary, unencumbered substituents on the *α*-C of the acyl group are beneficial to the reaction.

Regarding to a benzoic acid-derived lactone (entry 30), the ring-opening product was not observed, even when the temperature was lifted to 180 °C. It might be attributed to steric hindrance on the *α*-C of the acyl group. Meanwhile, reaction with 3-isochromanone (entry 31) afforded its corresponding product with high yield under mild conditions. Comparison between entries 30 and 31 shows that benzyl ester-derived lactone is far more reactive than the benzoic acid-derived lactone. For a phenol-derived lactone (entry 32), the C–O bond energy is extremely high for cleavage, which might be attributed to its p–*π* conjugated structure.

This application of such a catalytic system can be further extended to spirodilactone (entry 33), where the reaction proceeded via the ring-opening intermediate of each single lactone. Although alcoholic hydroxyl groups could not be retained in this catalytic system (*e.g.*, entry 36, 11% *n*-pentanoic acid, 10% *δ*-VL, 8% *γ*-VL), carboxyl and ketone carbonyl substituents were well tolerated under suitable conditions (entries 34 and 35, respectively). Meanwhile, bridged ring lactones were proved to be a suitable substrate that undergoes successful hydrogenolysis (via ring-opening pathway) (entry 37 and Scheme 2). Interestingly, to some specific substrates, like 4-oxahomoadamantan-5-one, utilization of our catalytic protocol can easily control the stereo-chemistry of the final product. For example, 4-oxahomoadamantan-5-one can be directly converted to the boat-conformation product (CAS No.: 19489-18-0) with preservation of the *α*-C configuration on the acyl group, upon treating with our catalytic protocol. However, if it is firstly subjected to saponification and acidification, followed by the hydrogenolysis under our conditions, the formed carboxylic acid would adopt a chair conformation (CAS No.: 19489-16-8), in which an inversion of the *α*-C configuration happens.[19] (Scheme 2).



Scheme 2. The configuration of the ester carbonyl *α*-carbon was retained during hydrogenolysis.



Scheme 3. Ring-opening polymerization, ring-closing depolymerization and ring contraction via rearrangement without H_2.

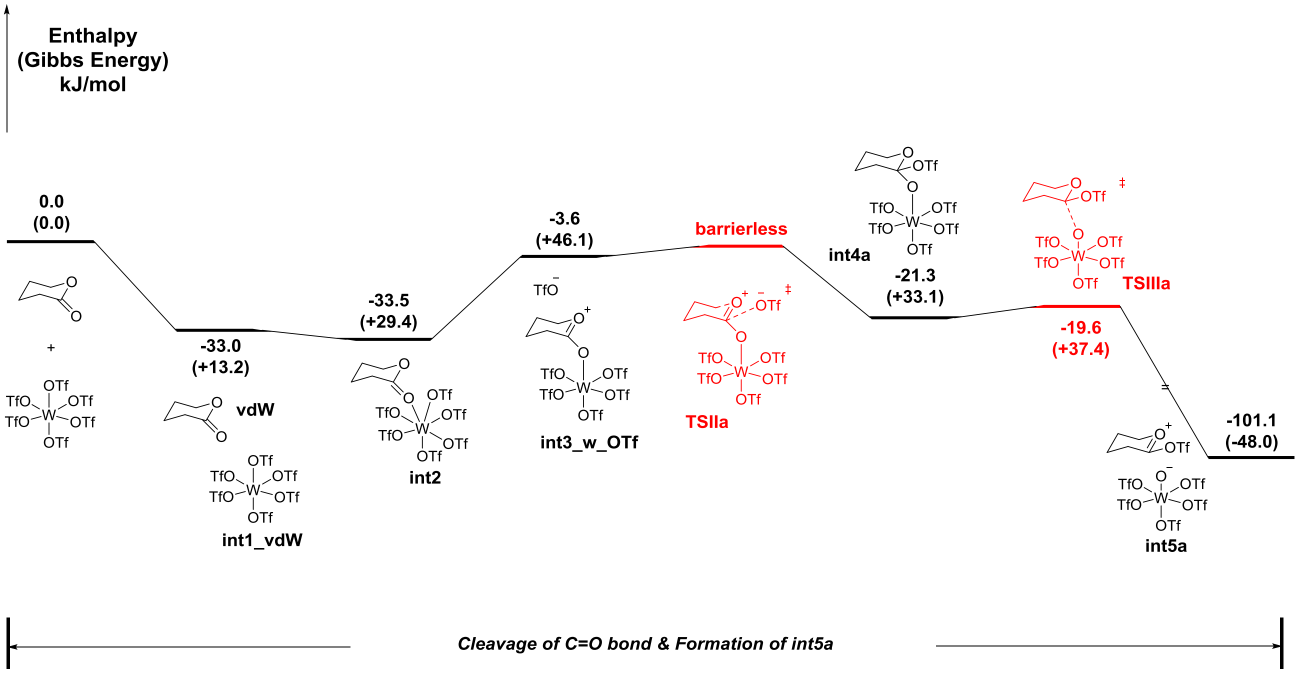
To further understand the reaction, mechanistic studies were initially carried out using β-propiolactone, γ-butyrolactone, δ-valerolactone and ε-caprolactone as the model substrates. The mass spectra (MS) of their corresponding short-time reaction solutions (2 h) indicated that ring-opening polymerization occurs as the reaction progresses, with the detection of both cyclic and linear polymers (Figs. S2–S6). However, ring-opening polymerization of the five-membered γ-butyrolactone was difficult, with only weak signal peaks being detected for the oligomer. γ-Butyrolactone possesses low strain energy and is a well-known non-polymerizable monomer. [20] To put that another way, it is possible that poly(γ-butyrolactone) undergoes decomposition at high temperature to afford oligomers of γ-butyrolactone. [21]

Poly-3-hydroxybutyrate (P3HB) was also tested as a substrate for our mechanistic study. Unsaturated butenoic acid was generated in the reaction of P3HB catalyzed by $W(OTf)_6$ without H_2, as evidenced in the ^1H NMR spectrum (Fig. S7). This observation indicates that polyesters undergo efficient depolymerization into their corresponding monomers with this catalytic system. Next, a catalytic amount of $W(OTf)_6$ was added to β-butyrolactone without H_2 but with heating. As seen in the ^1H NMR (Fig. S8) and ESI-MS (Fig. S3) spectra of this solution, unsaturated butenoic acid and oligomeric P3HB were formed. In summary, $W(OTf)_6$ is an active catalyst for both the ring-opening polymerization of lactones and the depolymerization of polyesters to monomers.

A further study indicated that the four-membered, six-membered and seven-membered lactones underwent rapid polymerization via catalysis by $W(OTf)_6$ at room temperature. By subsequently heating these oligomers, unsaturated carboxylic acids can be obtained from the oligomer of the four-membered β-propiolactone. Meanwhile, five-membered lactones, which possess low strain energy, were obtained by heating the oligomers of δ-valerolactone and ε-caprolactone. Similarly, the direct heating of lactones in the presence of a catalytic amount of $W(OTf)_6$ at 135 °C afforded the same result (Scheme 3).

The results obtained from the aforementioned experimental studies indicated that our catalytic protocol affords high reactivity for the transformation of lactones to their corresponding acids. Some mechanisms, which involve C_{alkoxy}–O bond cleavage, have been proposed previously. [13] To further understand the reaction mechanism and to rationalize the novel ring contraction observed for δ-valerolactone, a computational study was subsequently conducted via extensive density functional theory (DFT) calculations. To start the reaction, ligand substitution should happen prior to the following steps. As clearly illustrated, the lactone first approaches $W(OTf)_6$ to form a pre-reaction complex **int1_vdW**. Then, associative substitution occurs in a stepwise manner rather than a concerted way, generating a salt **int3_w_OTf**, which is composed of a lactone-coordinated tungsten (VI) complex (i.e., cationic counterpart) and a triflate (i.e., anion counterpart). The lactone coordinates to W(VI) via its carbonyl oxygen, and an obvious neighbouring group effect is observed because of the conjugation. From DFT calculations, no evidence was obtained with respect to the C_{acyl}-O bond cleavage, which has been suggested by previously reported studies. [14] Instead, the triflate will directly attack the carbonyl carbon, with almost no barrier observed through our calculations. As can be observed from the reaction pathway shown in Scheme 4, to our surprise, the C=O bond is completely cleaved, along with the transfer of oxygen to tungsten. The success cleavage of C=O bond and the subsequent formation of oxonium **int5a** are contributed to the existence of both tungsten cation and the triflate anion. Triflate attacks the C_{acyl} and makes the C=O bond even weaker, while tungsten (VI) shows a great oxophility, which helps it to grab the oxygen easily from the C_{acyl} atom.

Gratifyingly, the cationic counterpart of the critical intermediate (**int5a**) suggested by our DFT calculations was successfully trapped using ESI-MS spectra. As clearly marked in green color (see Figure 3), the intermediate and its derivatives were successfully detected with an *m/z* of 233+100*n* (*n*=0,1,2,3,…). The derivatives are generated by the oligomerization of the cationic part of **int5a** and lactone molecules. To our delight, the enthalpic barrier associated to such a process was calculated to be only +49.8 kJ/mol (shown in Figure 3), indicating a rapid reaction even at room temperature. The cationic oligomer can subsequently lose a Tf^+ cation (*m/z*=133) to form a variety of cyclic oligoesters (marked in red colour as shown in Figure 3), which can further



Scheme 4. Energy profile for the $W(OTf)_6$ activated the lactone.

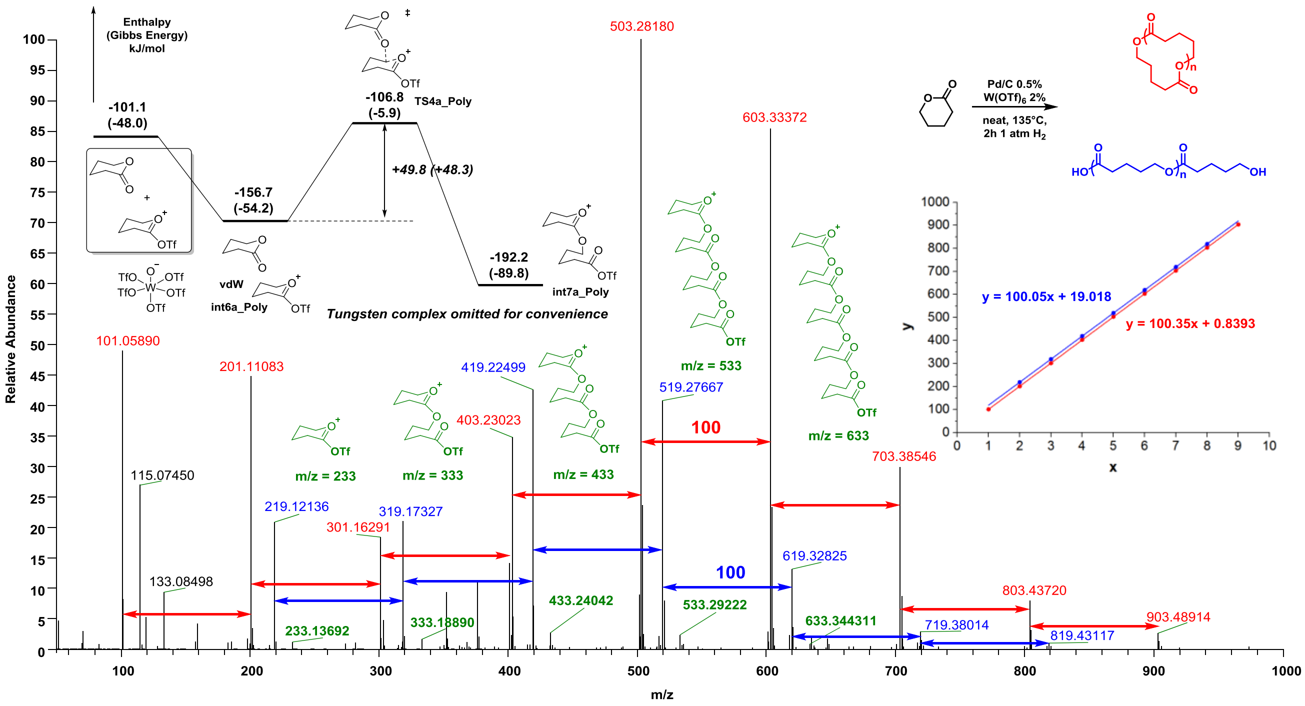


Figure 3. Oligomeric products from hydrogenation of δ-valerolactone which was detected by ESI-MS.

react with water to afford linear oligoesters (marked in blue colour). So far, we have successfully characterized the intermediates suggested by our computational study through experiments, and the novel reaction mechanism involving a cleavage of C=O bond was confirmed to some extent.

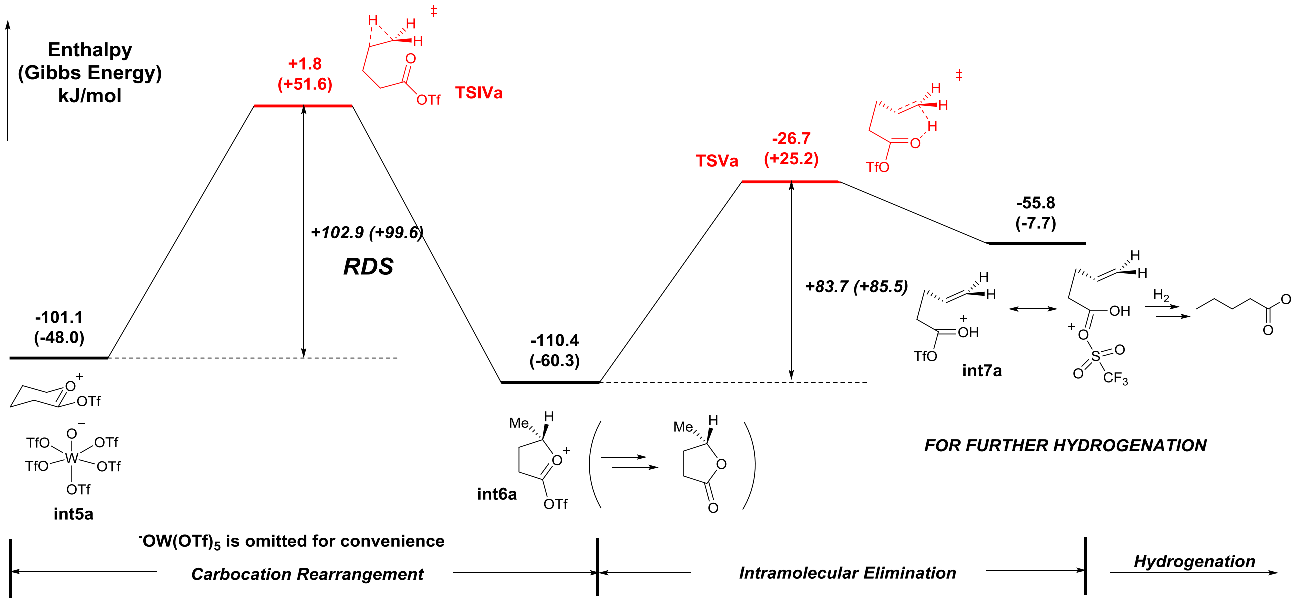
As unsaturated carboxylic acid is the ideal starting material for subsequent hydrogenation, [13, 16] the focus is now directed to the formation of a C=C moiety from intermediate **int5a**. Initially, the search for a transition state of the $^{-}$OW(OTf)$_5$ promoted elimination was attempted, in which the anionic species $^{-}$OW(OTf)$_5$ abstracts a β-H (see SI-IV-D). However, the calculation results indicated that $^{-}$OW(OTf)$_5$ is a indeed a weak base, which is not strong enough to abstract proton. Instead, a pathway with three key steps was observed on the basis of our extensive DFT calculations of **int5a**: carbocation rearrangement (*i.e.*, hydride shift), intramolecular elimination and hydrogenation.

The hydride detaches from the β-C and then moves to the α-position of the oxonium cation, with an enthalpic barrier of 102.9 kJ/mol. With the application of heating, the reaction can overcome this barrier, which is in agreement with our experimental observations. Notably, the calculation results also suggested a ring contraction, resulting in a precursor of γ-valerolactone shown as **int6a**. The carbonyl oxygen can further abstract one proton from the newly formed methyl group, generating a C=C bond. Given that the enthalpic barrier is only 83.7 kJ/mol, intramolecular deprotonation is more feasible than the previous β-H rearrangement. However, judging from the energies shown in Scheme 5, this step is actually endergonic, which means that the chemical equilibrium will shift to the five-membered lactone **int6a**. Notably, the formation of the alkene is not the end point of the entire reaction, as the subsequent hydrogenation of the C=C bond (with Pd/C as the catalyst) actually provides a driving force for intramolecular elimination.

It was reported previously that the effective charge density on the cation is vital to the success of this reaction. However, having established the mechanism involving a nucleophilic attack from the dropped triflate to the carbonyl carbon, we suspected that the counter-anion might also affect the outcome of this reaction. To clarify the raised question, extra calculations were performed on the Brønsted acid catalyzed system. Different from the metal triflate system, the carbocation rearrangement now takes place on a protonated lactone molecule rather than an anhydride derivative species. As clearly shown in Scheme S6, if the catalyst is switched from W(OTf)$_6$ to Brønsted acid (*i.e.*, the Tf^{+} moiety is changed to proton), the barriers of both the carbocation rearrangement step and the intramolecular elimination step are significantly lifted to +129.0 kJ/mol and +100.9 kJ/mol, respectively. Therefore, much harsher conditions should be applied to drive the reaction going forward, and it is exactly what was reported. [10]

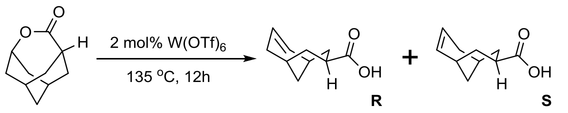
In addition, what need to be emphasized here is that, our newly suggested mechanism can also rationalize the intriguing experimental observations reported by Beller and co-workers. [6a] Since anion will take up the critical role to attack C$_{acyl}$ after the activation of carbonyl by a triflate, in that case, there should be a competition between H^{-} [22] and TfO^{-}. The attack of C$_{acyl}$ by H^{-} will lead to the reduction of the carbonyl. Meanwhile, even if the reaction follows the pathway involving a TfO^{-} attack, since the H^{-} is not tend to reduce the instable unsaturated carboxylic acid [23] (radical H· generated with a Pd/C catalyst is necessary to hydrogenate C=C bond) and the rearrangement is reversible from energy perspective, **int5a** will be regenerated and reduced.

In our theoretical study, as unsaturated acids were proposed to be intermediates during this process, efforts were also made to trap them in the experiments. However, due to the high energy of such an intermediate (refer to **int7a** in Scheme 5), they were not observed from common lactones, except in the case of four-membered substrates (due to a strong ring-strain). In addition, as clearly illustrated in Scheme 5, if there is no further hydrogenation, the chemical equilibrium should shift to the lactone side (**int7a** to **int6a**). This is exactly what we found in a control experiment (see SI-IV-C for details). Hence, in most cases, the unsatu-



Scheme 5. Energy profile for the $W(OTf)_6$ catalyzed ring contraction and further intramolecular elimination.

rated acid intermediates are not detected. To further verify our hypothesis, 4-oxahomoadamantan-5-one, representing as a seven-membered lactone with a rigid ring structure, was selected as the substrate to undergo a suggested $W(OTf)_6$-catalyzed ring opening pathway without H_2 at 135 °C for 12 h (eq. 1). In the resultant special structure, the carboxyl group is far away from the newly generated C=C bond, making it difficult for the lactone to be re-generated via cyclization. To our delight, bicyclo[3.3.1]non-6-ene-3-carboxylic acid, as verified by NMR, was successfully obtained (eq. 1). Thus, theoretical and experimental studies confirm that unsaturated acids are the key intermediates.



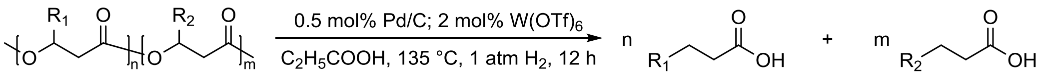
eq. 1

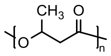
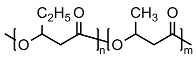
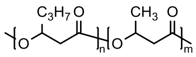
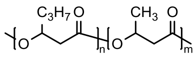
The mechanistic study of the reaction suggests that $W(OTf)_6$ is capable of catalyzing the depolymerization of polyesters. Polyhydroxyalkanoate (PHA)[24] is a class of linear polyesters widespread in microorganisms; hence, hydrogenolysis is conducted in the presence of $W(OTf)_6$-Pd/C under atmospheric H_2 pressure: the quantitative conversion of PHA was observed, affording straight-chain carboxylic acids (Table 3). From this result, the developed method has opened avenues for the sustainable preparation of carboxylic acids from renewable resources.

CONCLUSION

In summary, we have conducted a comprehensive study on metal triflates promoted hydrogenolysis of lactones to carboxylic acids from both synthetic and mechanistic perspectives. The $W(OTf)_6$-Pd/C catalytic protocol developed by us can effectively catalyze the direct hydrogenolysis of lactones to the corresponding carboxylic acids. Different from the previously reported Brønsted acid catalytic system, our reaction can be carried out under extra mild conditions (e.g., temperature<150 ℃, 1 atm of H_2) while maintaining excellent yields for a broad substrate scope. The substituent effect on the lactone ring was extensively investigated,

Table 3. Hydrogenolysis of PHA to straight-chain carboxylic acids.



entry	structure	W_m [%]	W_n [%]	m.p. [°C]	$M_w \times 10^5$	$M_n \times 10^5$	conv. [%]	yield [%]		
								n-butyric acid	n-pentanoic acid	n-hexanoic acid
1		0	100	175	2.44	1.34	> 99	99	-	-
2		12	88	140 ~ 150	2.96	1.96	> 99	12	87	-
3		14	86	120 ~ 130	1.62	1.08	> 99	14	-	85
4		29	71	100 ~ 110	2.13	1.47	> 99	29	-	70

Reactions were conducted in the presence of 0.5 mol% Pd/C (10 wt% loading), 2 mol% $W(OTf)_6$ and substrate (500 mg) in 0.5 mL C_2H_5COOH at 135 °C under 1 atm H_2 for 12 h, and the yield was detected by GC.

and we found that the existence of an electron-donating group on $C_{alkoxyl}$ atom can significantly promote the reaction, and vice versa. The existence of a β-H was found to be vital to a successful transformation. To further understand the mechanistic details, a computational study was performed via DFT calculations. The calculation results suggested a novel reaction pattern, in which the C=O bond is believed to be cleaved rather than the C_{alkoxy}-O bond or the C_{acyl}-O bond. Moreover, based on our calculations, an oxonium possessing OTf moiety is believed to be a critical intermediate in the transformation. To our delight, the existence of such an oxonium was successfully confirmed by ESI-MS spectra. Our theoretical studies also revealed that the hydrogenation actually applies at a late stage and the lactone should be firstly transformed into an unsaturated carboxylic acid. Different from the previous study which emphasized solely on the effect of metal cation, our study clearly pointed out the significant role that the anion plays. Meanwhile, through a comparison with the Brønsted acid catalyzed system, the study confirmed that the existence of OTf moiety can significantly lower the barriers associated with the rearrangement and elimination processes. In addition, the anion effect is directly related to the chemo-selectivity, thus providing insightful information for the further catalyst design. At last, as a dessert of this work, our strategy was also proved to be applicable to the hydrogenolysis of renewable polymers (PHA), making it have potential application in industry.

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Author Contributions

† R. Zhu and J. Jiang contributed equally.

Notes

The authors declare no competing financial interests

ASSOCIATED CONTENT

Supporting Information.

X-ray crystallographic data for 19489-18-0 (CIF)
X-ray crystallographic data for 19489-16-8 (CIF)
Full experimental details, experimental procedures, products characterization data including ^{1}H and ^{13}C NMR spectra, detailed mechanistic data and data of X-ray crystallographic structures (PDF)

ACKNOWLEDGMENT

This work was supported by NSFC (21572212, 21402181, 21325208), CAS (XDB20000000, YZ201563), FRFCU and PCSIRT. The supercomputer center in the USTC is also acknowledged for providing the computational resources.

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(15) The result of entry 26 in Table S1 shows that triflic acid also has a good catalytic activity in this system. However, in the recycle experiment, we find that triflic acid could not be easy recycled for carbonization.

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