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## Mixed-acid systems for the catalytic synthesis of methyl levulinate from cellulose

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**Mixed-acid systems consisting of both Lewis and Brønsted acids were found to be efficient catalysts for direct synthesis of methyl levulinate from cellulose.**

The exhaustion of fossil fuel resources and the issue of global warming make it very important to synthesize useful chemicals from cellulose, which is the most abundant and non-eatable biomass resource on the earth. Among various chemicals that can be synthesized from cellulose, levulinic acid is one of the most promising building blocks for the biomass refinery; it can be used as a precursor to various useful chemicals such as fuel additives, polyacrylates, polycarbonates, bio-degradable herbicides, photo-synthesis promoters, and so on.<sup>1</sup> Levulinic acid is also selected as one of the top 12 building block candidates in the report of NREL in the USA.<sup>2</sup>

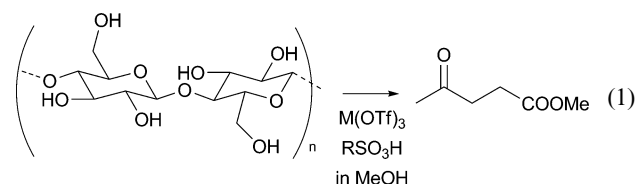
It has been well known for more than 130 years that levulinic acid is formed from sugars in the presence of large amounts of mineral acids. The first example was reported by Grote and Tollens in 1875.<sup>3</sup> According to *Organic Syntheses* published in 1929, hydrolysis of sucrose in the presence of 1160 mol% of HCl gave levulinic acid in the yield of 22%.<sup>4</sup> Since then, many improved procedures using sugars as a starting material have been reported,<sup>5</sup> some of which are catalytic reactions.

It is more difficult to synthesize levulinic acid from cellulose in good yields because of strong  $\beta$ -1,4-glycosidic linkages between its glucose subunits. In 1990's, Biofine Corporation in the USA developed a first practical process for the levulinic acid synthesis from carbohydrate biomass including cellulose, in which more than 300 mol% of H<sub>2</sub>SO<sub>4</sub> was used.<sup>6</sup>

In the past decade, a few examples of the catalytic synthesis of levulinic acid from cellulose have been reported.<sup>7</sup> Ishida and co-workers reported a catalytic degradation of cellulose using Lanthanum chloride at 250 °C, in which levulinic acid was formed in yields of less than 10%. Lin and co-workers reported the reaction using several other metal chlorides as catalysts, among which chromium chloride was uniquely effective and the yield of levulinic acid reached 67% by the reaction at 200 °C. The catalyst, however, decomposes to chromium oxide during

the reaction, and it was necessary to regenerate the chromium chloride from the residue for recycling the catalyst. Lucht and co-workers reported the reaction using solid-supported acids, where only a trace amount of levulinic acid was formed.

We report here an efficient and recyclable catalyst system for the synthesis of methyl levulinate from cellulose by combining two different kinds of acid, a Lewis acid and a Brønsted acid, in methanol (eqn (1)).



Representative results are summarized in Table 1.<sup>8</sup> When microcrystalline cellulose was treated with 4 mol% of PTSA in methanol at 180 °C for 5 h, sugars were formed in a yield of 78% and methyl levulinate in a yield of 20% (entry 1). The main component of the sugars was  $\alpha$ -methyl glycoside (58%), which was formed by the solvolysis of cellulose in methanol. Others were small amounts of glucose (4%) and fructose (16%). Water is formed by the formation of methyl levulinate from sugars and by side reactions such as self-condensation of methanol, which would be responsible for these hydrolyzed products. The yield of methyl levulinate was increased to 42% when 0.8 mol% of a Lewis acid, In(OTf)<sub>3</sub>, was used in place of PTSA, although a significant amount of insoluble dark brown powder was formed (entry 2). The yield of methyl levulinate was not much improved even when six times amount of In(OTf)<sub>3</sub> was used (entry 3). It is worth noting that the yield of methyl levulinate reached 70% when both In(OTf)<sub>3</sub> and PTSA were used simultaneously (entry 4). Other group 13 metal triflates (Ga and Al) were also effective for methyl levulinate formation (entries 5 and 6), whereas group 3 metal triflates as well as InCl<sub>3</sub> and In(acac)<sub>3</sub> were less effective (entries 7–11).

Sulfonic acids other than PTSA are also effective for this reaction (entries 12–14). The most effective was 2-NSA, with which the yield of methyl levulinate reached 75%.

We then examined the reusability of the catalyst system. After distilling the solvent and the products, the residue could catalyze the next run, giving almost the same yield of methyl

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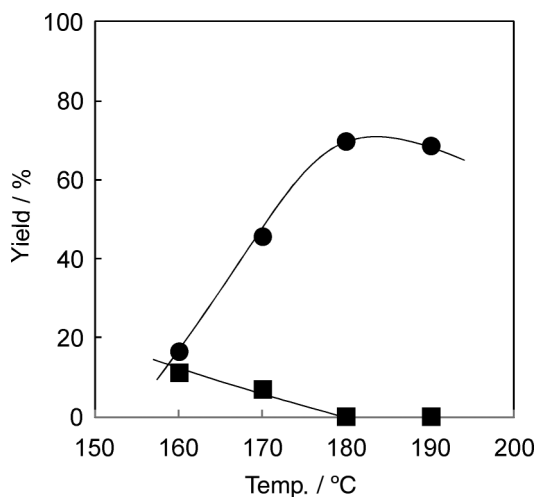
**Table 1** The catalytic synthesis of methyl levulinate from cellulose<sup>a</sup>

Entry	Lewis acid	Brønsted acid	Yield/%	
			Methyl levulinate	Sugars
1	—	PTSA <sup>b</sup>	20	78
2	In(OTf) <sub>3</sub>	—	42	Trace
3	In(OTf) <sub>3</sub> <sup>c</sup>	—	52	0
4	In(OTf) <sub>3</sub>	PTSA	70	Trace
5	Ga(OTf) <sub>3</sub>	PTSA	66	Trace
6	Al(OTf) <sub>3</sub>	PTSA	65	Trace
7	Y(OTf) <sub>3</sub>	PTSA	20	62
8	Sm(OTf) <sub>3</sub>	PTSA	58	9
9	Yb(OTf) <sub>3</sub>	PTSA	48	3
10	InCl <sub>3</sub>	PTSA	34	6
11	In(acac) <sub>3</sub>	PTSA	43	3
12	In(OTf) <sub>3</sub>	BSA <sup>d</sup>	72	0
13	In(OTf) <sub>3</sub>	2-NSA <sup>e</sup>	75	0
14	In(OTf) <sub>3</sub>	TfOH	62	0
15 <sup>f</sup>	In(OTf) <sub>3</sub>	2-NSA	75	0

<sup>a</sup> Conditions: Lewis acid (0.02 mmol), Brønsted acid (0.1 mmol), cellulose (2.5 mmol as a glucose unit), MeOH (20 mL), N<sub>2</sub> (0.5 MPa), 180 °C, 5 h. <sup>b</sup> PTSA = *p*-toluenesulfonic acid. <sup>c</sup> In(OTf)<sub>3</sub> = 0.12 mmol. <sup>d</sup> BSA = benzenesulfonic acid. <sup>e</sup> 2-NSA = 2-naphthalenesulfonic acid. <sup>f</sup> The second run, using the residue on distillation of entry 13.

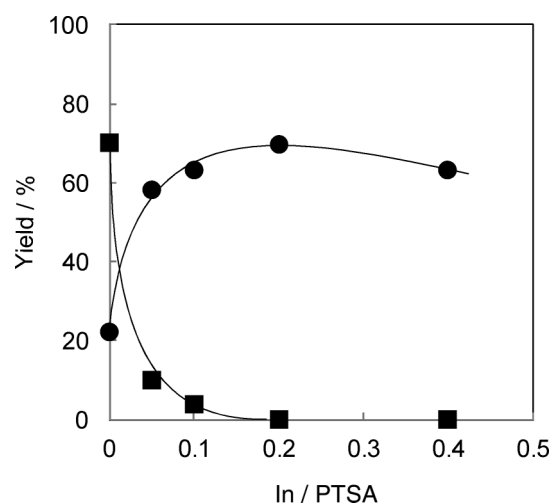
levulinate (entry 15). Therefore, the catalyst species appeared not to decompose in the reaction.

The temperature dependence of this reaction is shown in Fig. 1. When the reaction temperature was increased from 160 °C, the yield of methyl levulinate was improved at the gradual expense of the yield of sugars. The optimum temperature for methyl levulinate formation was about 180 °C. At the higher temperature, the yield of methyl levulinate decreased due to the formation of an insoluble dark brown powder.



**Fig. 1** Temperature dependence of the products formed with the In(OTf)<sub>3</sub>/PTSA system. Conditions are the same as described in Table 1 except for temperatures; ● = yield of methyl levulinate, ■ = yield of sugars.

In order to investigate the effect of the metal triflates on the formation of methyl levulinate, the concentration of In(OTf)<sub>3</sub> was changed under a constant concentration of PTSA (Fig. 2). In the absence of In(OTf)<sub>3</sub>, the major products were sugars, while the formation of methyl levulinate was drastically enhanced



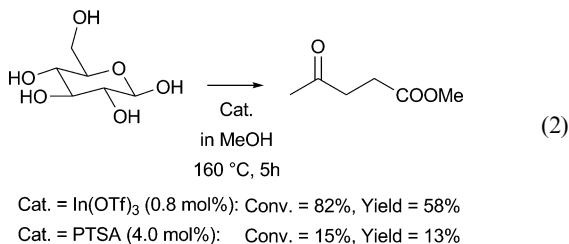
**Fig. 2** The effect of the In/PTSA ratio. Conditions: PTSA (0.1 mmol), cellulose (2.5 mmol as a glucose unit), MeOH (20 mL), N<sub>2</sub> (0.5 MPa), 180 °C, 5 h; ● = yield of methyl levulinate, ■ = yield of sugars.

by addition of a very small amount of In(OTf)<sub>3</sub> (only 1/20 equivalent to PTSA). An excess addition of In(OTf)<sub>3</sub> decreased the yield of methyl levulinate, and the optimum In/PTSA ratio was about 0.2. The above results suggest that the formation of methyl levulinate from cellulose can be divided into two parts; the first part is the solvolysis of cellulose to sugars, which is mainly catalyzed by PTSA, and the second part is the conversion of sugars to methyl levulinate, which is mainly catalyzed by In(OTf)<sub>3</sub>.

Although In(OTf)<sub>3</sub> alone is active to methyl levulinate formation from cellulose in a certain extent, the yield was rather low and almost no sugar was formed (Table 1, entries 2 and 3). This means that the solvolysis of cellulose with In(OTf)<sub>3</sub> is much less selective than that with sulfonic acids. Considering the fact that the yield of methyl levulinate was markedly improved by the addition of sulfonic acids and depended on the kind of sulfonic

acid used, the solvolysis of cellulose would be mainly catalyzed by sulfonic acids in the mixed-acid systems.

The reaction from sugars to methyl levulinate proceeds even at the lower temperatures. Comparison of the effects of  $\text{In}(\text{OTf})_3$  and PTSA on the reaction of glucose at  $160^\circ\text{C}$  showed that the former catalyzed the formation of methyl levulinate much faster than the latter (eqn (2)). This result also suggests that this step should be mainly catalyzed by  $\text{In}(\text{OTf})_3$ .



When the above  $\text{In}(\text{OTf})_3$ -catalyzed reaction of glucose was stopped after 1 h, a trace amount of 5-methoxymethylfurfural was also observed, which appears to be an intermediate for the methyl levulinate formation.<sup>9</sup> Further investigation on the reaction mechanism is in progress in our laboratory.

In summary, the combination of group 13 metal triflates and sulfonic acids synergistically catalyzes the formation of methyl levulinate from cellulose. The reaction proceeds in two steps; cellulose is solvolyzed to sugars, which are readily converted to methyl levulinate. The former step is mainly catalyzed by sulfonic acids, and the latter by the metal triflates.

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- General procedure for the synthesis of methyl levulinate from cellulose: A stainless steel autoclave was charged with  $\text{In}(\text{OTf})_3$  (Aldrich, 0.02 mmol), PTSA (Nacalai, 0.1 mmol), microcrystalline cellulose (Aldrich, 2.5 mmol as a glucose unit), MeOH (20 mL). After the autoclave was charged with  $\text{N}_2$  (0.5 MPa), it was heated at  $180^\circ\text{C}$  for 5 h with stirring. After the resulting solution was cooled to room temperature, it was analyzed with HPLC.
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