

Sustainable Chemistry

Efficient and Scalable Production of Alkyl Levulinates from Cellulose-Derived Levulinic Acid Using Heteropolyacid Catalysts

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This work reports a straightforward and scalable synthesis of a series of alkyl levulinates from cellulose-derived levulinic acid and alkyl alcohols using commercially available heteropolyacid catalysts under homogenous conditions. The reaction was optimized on parameters such as temperature, molar ratio of reagents, type and loading of catalyst. The solvent-free reactions afforded alkyl levulinates in high isolated yields (> 85%) using only slight excess of alcohols and 10 wt% of catalyst at 120 °C in 6 h. Further, the catalysts were successfully recycled for three consecutive cycles without significant loss in activity.

Introduction

Cellulosic biomass has been considered by many as a renewable source of carbon in producing transportation fuels and chemicals which are otherwise derived from non-renewable fossilized sources of carbon.^[1] In a biorefinery concept, in analogy to a petrorefinery, a handful of chemical building blocks are produced initially which are then synthetically upgraded into fine chemicals and materials.^[2] Levulinic acid (LA), produced by acid-catalyzed degradation of biomass-derived sugars and carbohydrates, has received significant attention over the past two decades as a biomass-derived chemical building block that can be synthetically upgraded into products of commercial value.^[3] LA was chosen as one of the top-ten biomass-derived chemical building block of commercial potential by the United States Department of Energy in 2004 and then again in 2010 by Bozell et al.^[4] Having two reactive functionality *i.e.* ketone and carboxylic acid, LA can be used as a renewable chemical intermediate to access various important classes of products such as fuels and fuel oxygenates, solvents, polymers, plasticizers, and agrochemicals.^[5]

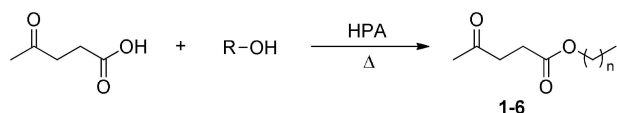
Alkyl levulinates (AL) is an important class of product synthesized from LA with potential applications as renewable solvent and fuel oxygenate.^[6] They can also be used as a chemical intermediate for the synthesis of other valuable products such as γ -valerolactone and 2-methyltetrahydrofuran.^[7] AL can be produced by Fischer esterification between LA and alkyl alcohols in presence of a suitable acid catalyst, *via* acid-catalyzed dehydration of sugars in alcohols, or by alcoholysis of furfuryl alcohol.^[8] A vast range of acid catalysts ranging from mineral acids, Lewis acid, sulfonated resins, to zeolites have been examined for the Fischer esterification of LA.^[9] However, there is a constant search for more efficient catalysts that will allow the reaction to proceed under mild condition, afford product in high yield, non-toxic in nature, and can be recycled conveniently. In this regard, heteropolyacids (HPA) are well-structured metal-oxygen clusters with strong Brønsted acidity, high thermal stability, and tunable solubility.^[10] HPAs have been used as efficient catalyst for various organic transformations and also in renewable chemistry.^[11] Supported HPAs have been used for the synthesis of butyl levulinate.^[12,13] Heterogeneous catalysts have certain advantages over homogeneous catalysts such as convenient recovery of catalysts from the reaction media. On the other hand, homogeneous catalysts work under milder conditions but faces challenges in product purification and catalyst recycling.^[14] In this regard, HPAs have decent solubility in alcohols especially at higher temperatures and in presence of a small amount of water. However, they are completely immiscible in non-polar organic solvents. We envisioned that the HPAs will behave as a homogeneous catalyst in polar solvents like alcohol under heating and in presence of water byproduct but can be isolated conveniently after reaction by using a non-polar organic solvent such as diethylether. In this work, we report the use of commercially available Keggin-type solid HPAs, namely, phosphotungstic acid ($H_3PW_{12}O_{40}$), phosphomolybdic acid ($H_3PMo_{12}O_{40}$), and silicotungstic acid ($H_4SiW_{12}O_{40}$) as catalysts for the esterification of LA with monohydric alkyl alcohols (C_1 - C_6) under homogeneous condition (Scheme 1).

Results and Discussion

In order to find the best reaction conditions, the conversion of Levulinic acid into alkyl levulinates was investigated using different heteropolyacids, levulinic acid to alcohol ratios,

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Methyl levulinate **1** ($n=0$); Ethyl levulinate **2** ($n=1$); Propyl levulinate **3** ($n=2$)
Butyl levulinate **4** ($n=3$); Pentyl levulinate **5** ($n=4$); Hexyl levulinate **6** ($n=5$)

Scheme 1. Preparation of alkyl levulinates from levulinic acid using heteropolyacid catalysts.

reaction temperatures and duration of reaction. Butyl levulinate **4** was chosen as the model substrate for reaction optimization. The effect of temperature on the synthesis of **4** was investigated using phosphotungstic acid as catalyst. The reaction produces only trace amount of butyl levulinate even after 12 h of stirring at room temperature. Increasing the temperature to 80 °C afforded only 50% yield of **4** (Figure 1) after 6 h. Upon

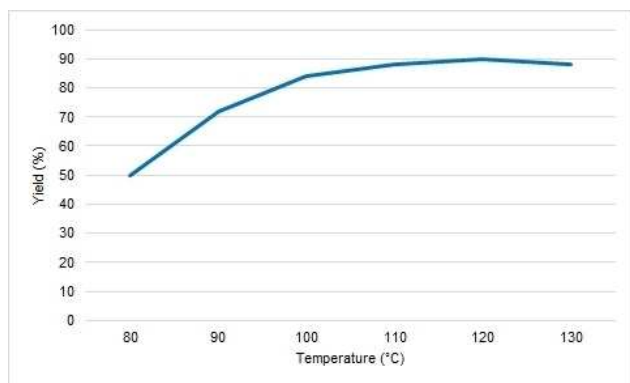


Figure 1. Effect of reaction temperature on the isolated yield of butyl levulinate **4**.

increasing the temperature to 90 °C and 100 °C, the yield of **4** increased to 72% and 84%, respectively after 6 h. The mass balance is essentially unreacted LA. The yield of **4** reached maximum to 90% at 120 °C. The ¹H-NMR spectrum of the crude product did not show any unreacted LA.

In order to investigate the effect of molar ratio of LA and 1-butanol on the yield of **4**, the reaction was carried out at 120 °C for 6 h using 10 wt% of phosphotungstic acid (PTA) as catalyst. The molar ratio of LA to 1-butanol was varied from 1:3 to 1:1. The results show (Figure 2) that the yields of **3** at ratios above 1:1.5 is nearly constant. However, using lesser quantity of 1-propanol significantly lowers the yield of **4** due to incomplete reaction.

To investigate the efficiency of different heteropoly acids, the esterification reaction was independently carried out using three commercially available heteropoly acids, namely, phosphotungstic acid (PTA), silicotungstic acid (STA) and phosphomolybdic acid (PMA). The esterification of levulinic acid with ethyl alcohol, 1-butanol, and n-hexyl alcohol were carried out at 120 °C for 6 h using 10 wt% (compared to LA used) of

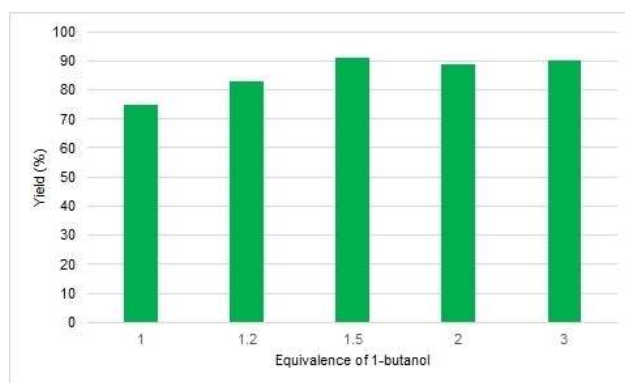


Figure 2. Effect of equivalence of 1-butanol with respect to LA on the isolated yield of butyl levulinate **4**.

heteropoly acids. Among the three HPAs examined, PTA was found to be most effective catalyst for all three alcohols. Use of PTA as catalyst afforded ethyl levulinate **2** in 92% yield whereas PMA and STA afforded the same in 75% and 69%, respectively, under identical conditions (Figure 3). The trend was found to

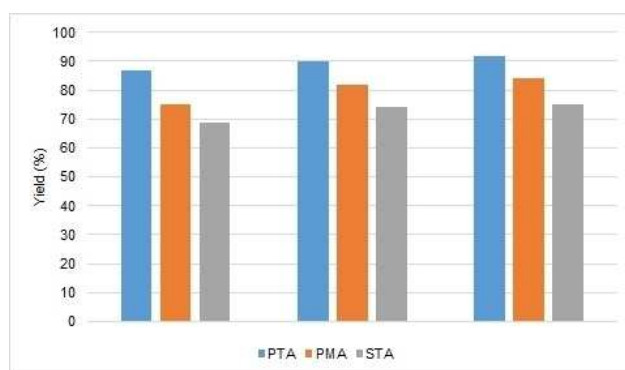


Figure 3. Efficiency of various heteropolyacids on the yield of alkyl levulinates. Reaction conditions: LA (10 mmol), alcohol (15 mmol), 120 °C, 6 h, 10 wt% catalyst. ethyl levulinate (left), butyl levulinate (middle), hexyl levulinate (right).

be similar for butyl levulinate **4** and hexyl levulinate **6** as well. PTA as catalyst provided 90% and 92% of **4** and **6**, respectively whereas STA provided them in 74% and 75% yields. PMA was found to have intermediate efficiency in producing alkyl levulinates. The difference in reactivity of these three catalysts tried can be explained by their order of acidity where PTA being the most and STA being the least acidic.^[15]

For catalyst loading above 10 wt%, the yield increases only marginally. However, at lower catalyst loading the yield of **3** decreases considerably. The optimized reaction for **4** was applied for the production of **1–6** from LA using PTA as catalyst.

The reactions were performed in a glass pressure tube fitted with a teflon screw top. The set up allows to reach temperature without evaporative loss of the alcohols during

reaction. Where methyl levulinate was isolated in 85% yield, the pentyl levulinate was obtained in 94% isolated yield (Figure 4). In general, the yield of alkyl levulinate improved

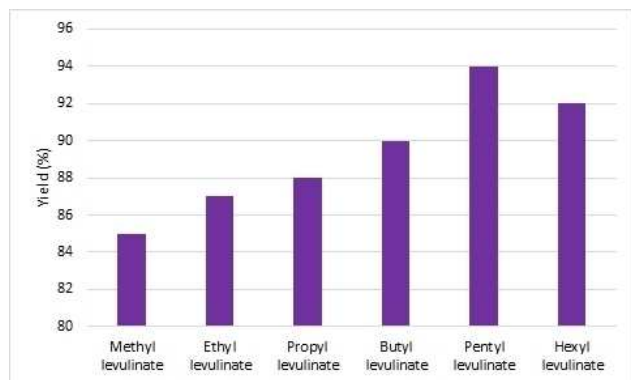


Figure 4. Preparation of alkyl levulinates (1-6) from levulinic acid. Conditions: LA:alcohol (1:1.5) (molar ratio), 120 °C, 6 h, 10 wt% PTA.

when alcohol with longer alkyl chain length was used. This trend can be explained by higher chance of concomitant ether formation from alcohol in presence of acid that is more pronounced in smaller alcohols like methanol.

Recyclability of the catalyst is one of the important parameters for the green indices and process economics. The PTA catalyst used in the preparation of butyl levulinate **4** was recycled and reused for three consecutive runs to investigate the efficiency of the recycled catalyst. After reaction, the catalyst was precipitated by diethylether and separated from the reaction mixture by centrifugation. The catalyst was then dried in oven at 110 °C for 12 h before submitting for consecutive runs. All consecutive runs with recovered catalyst were carried out using same catalyst/reactant ratio. The PTA catalyst was recycled successfully for three consecutive cycles without significant loss of activity. Butyl levulinate, **4** was isolated in 91%, 87% and 85% yield over three consecutive cycles (Table 1). In all three cycles, the physical recovery of

Table 1. Recovery and reuse of PTA in the preparation of butyl levulinate **4**.

S/N	Catalyst used (mg) ^[a]	Catalyst recovered (mg)	Yield (%) ^[b]
1	100	91	91
2	100	92	87
3	100	90	85

[a] The recovered catalyst from multiple trials were combined to start with the same amount of catalyst in each consecutive cycle, [b] isolated yield

catalyst remained nearly 90%. The structure of the recovered PTA catalyst remained intact as confirmed by the ³¹P-NMR spectrum.

Conclusions

A series of alkyl levulinates were prepared from levulinic acid using commercially available heteropolyacid catalysts under homogeneous conditions. A general experimental protocol was developed that provided excellent isolated yields of alkyl levulinates. Phosphotungstic acid was found to be the most effective catalyst among the three heteropolyacids examined in this study. Further, the catalyst was conveniently recovered and reused up to three cycles. The solvent-less process is scalable and the product isolation is straightforward.

Supporting Information Summary

The complete experimental section that includes materials, preparation of alkyl levulinates, FTIR, ¹H-NMR, and ¹³C-NMR spectra of all synthesized compounds, ³¹P-NMR spectrum of fresh and recovered PTA catalyst are placed in the Supporting Information.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: alkyl levulinate · catalysis · heteropolyacid · levulinic acid · renewable synthesis

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