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Li–Al layered double hydroxides as catalysts for the synthesis of flavanone

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ABSTRACT

Flavanone was synthesized via a series reaction scheme involving the Claisen–Schmidt condensation between 2′-hydroxyacetophenone and benzaldehyde to form 2′-hydroxychalcone and the subsequent isomerization of 2′-hydroxychalcone to flavanone. Reactions were carried out in the presence of Li–Al layered double hydroxide solid catalyst. The results showed that surface basicity varies with calcination temperature and rehydration. These variations in basicity correlate with the observed catalytic behavior. It is believed that $Li^+–O^{2-}$ groups contribute to the surface basicity and are instrumental in the abstraction of a proton from the 2′-hydroxyacetophenone in what is believed to be the first step in the reaction mechanism.

1. Introduction

The pharmacological benefits of flavonoids continue to generate interest. Therefore, the significant economic and environmental benefits of converting the homogeneous catalytic processes, traditionally used to synthesize them, to heterogeneous ones are also of interest. The synthesis of flavanone is one reaction scheme that has been explored in recent years. It is the product of a 2-step reaction scheme (Fig. 1) that involves a Claisen–Schmidt condensation reaction of 2′-hydroxyacetophenone and benzaldehyde to form 2′-hydroxychalcone, which then undergoes isomerization to flavanone. Previous work has included kinetic, mechanistic, and catalytic studies [1–6]. Of key importance to this study, a recent investigation of Li-modified MgO indicates low Li loading has a promotional effect on the Claisen–Schmidt condensation reaction [7].

Layered double hydroxides (LDH), both specifically and as a class of compounds, have shown promise of excellent catalytic use in fine chemical and pharmaceutical syntheses in recent years. They are currently used in biodiesel, removal of agrochemicals, and medication controlled release systems such as ibuprofen. Climent et al. [8] is most widely noted for their use in Claisen–Schmidt condensations, specifically Mg–Al hydrotalcites to synthesize Vesidryl from acetophenone and benzaldehyde.

This work explores a marriage of concepts in an investigation of flavanone synthesis over Li–Al LDH as part of an overarching continued quest to fully understand the reaction mechanism. More specifically, we synthesized calcined and rehydrated $[LiAl_2(OH)_6](CO_3)_{0.5}\cdot nH_2O$. The resulting catalysts were characterized by temperature programmed desorption of CO_2 (CO_2-TPD) and XRD measurements. Subsequently, these samples were tested for their catalytic activity in the heterogeneous synthesis of flavanone. Finally, we sought correlations in the results of activity studies and characterization measurements to further elucidate the heterogeneous reaction mechanism.

2. Experimental

2.1. Catalyst preparation

$[LiAl_2(OH)_6](CO_3)_{0.5}\cdot nH_2O$ was prepared using the method reported by Shumaker et al. [9]. A 250 mL volume of 0.4 M $Al(NO_3)_3\cdot 9\ H_2O$ was added dropwise to a 600 mL volume of 1.5 M $LiOH\cdot H_2O$ and 0.08 M Na_2CO_3 (prepared using 10.6 g of Na_2CO_3 and the balance DI water). The mixture was stirred vigorously until precipitate formed. The resulting precipitate was left to age in the reaction mixture overnight at 75 °C under gentle stirring. The precipitate was washed with DI water to an effluent pH of 7 and isolated by vacuum filtration. The filtrate was separated into roughly equal quantities in preparation for a five hour calcination period. One quantity was calcined at 300 °C and the other at 450 °C. Last, the catalyst was sieved to 60 to 80 mesh particle size and stored in a desiccator. When needed, catalyst samples were rehydrated to 35 wt.% via direct dropwise application of DI water, which has been identified as an optimum weight percentage in previous rehydration studies [10]. The names and descriptions of the catalyst samples used in this study are given in Table 1.

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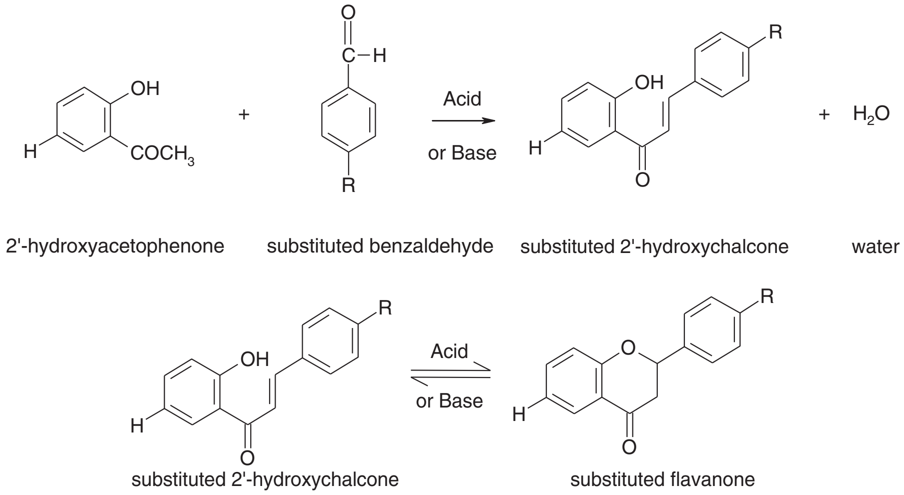

Fig. 1. Synthesis of flavanone via a two-step process (Claisen–Schmidt condensation and isomerization).

2.2. Characterization studies

X-ray diffraction (XRD) measurements were conducted to examine catalyst structure. The instrument used has a Rigaku D/MAX RB X-ray powder diffractometer, graphite monochromator, and nickel-filtered Cu Kα radiation source (λ = 0.15406 nm). It was operated at 40 kV and 50 mA, in the 5° to 80° range, at a scanning rate of 1.2°/min. The diffractograms are shown in Fig. 2.

The basic properties of the dry and rehydrated catalyst were explored through CO_2 temperature programmed desorption (CO_2-TPD) measurements. A Micromeritics Chemisorb 2750 instrument with a TCD detector was used. Samples were pretreated in situ in UHP He at the corresponding calcination temperature for 1 h, then returned to room temperature under continuous He flow. After being exposed to 45% CO_2/55% He mixture at a rate of 20 mL/min for 30 min, the sample was purged with UHP He for 30 min to remove physisorbed CO_2. Profiles were collected continuously as the temperature was increased to the corresponding calcination temperature at a rate of 10 °C/min. The TPD profiles are shown in Fig. 3.

2.3. Activity studies

Flavanone synthesis was used to explore the activity of the catalyst. The synthesis involves series Claisen–Schmidt condensation and isomerization reactions as shown in Fig. 1.

Reactions were carried out in a custom stirred reflux batch reactor at 160 °C. Since benzaldehyde oxidizes easily in air, the reactor was purged with UHP N_2 prior to and during its use. Equimolar (1.5 M) amounts of 2′-hydroxyacetophenone (Aldrich, 99.0% purity, 27 mL) and benzaldehyde (Aldrich, 99+% purity, 23 mL) in DMSO solvent (Alfa Aesar, 99.9% purity, 100 mL) were charged to the reactor and brought to the reaction temperature.

A 0.1 wt.% catalyst loading (165 mg) was used and it was added once the reaction temperature was reached (t = 0). The stirring rate was 500 rpm. These operating conditions were previously found to fall in the kinetic regime [11]; therefore, initial reaction rates were determined from the slope of conversion versus time data within in the first few minutes of reaction.

Table 1
Names and descriptions of Li–Al LDH samples for the synthesis of flavanone.

Catalyst	Description
300	Calcined at 300 °C
300 RE	Calcined at 300 °C and rehydrated with 35 wt.% water
450	Calcined at 450 °C
450 RE	Calcined at 450 °C and rehydrated with 35 wt.% water

Samples of the reaction slurry (approximately 0.1 mL) were taken periodically over the course of the reaction. Samples were centrifuged to separate any catalyst trapped in the sample, diluted in isopropyl alcohol, and analyzed offline using a gas chromatograph (GC). The HP 5890 GC was equipped with a Restek RTX-1 capillary column and flame ionization detector.

3. Results and discussion

3.1. Characterization studies

The XRD patterns for the dry catalyst samples prepared for this investigation are shown in Fig. 2. The observed patterns are consistent with the known literature on Li–Al LDH [9,12].

TPD profiles of CO_2 adsorbed on the dry and rehydrated catalyst calcined at the two temperatures are shown in Fig. 3. In following Liu et al. [13], basic sites may be described as "weak" basic sites for CO_2 desorption occurring in the range of 27 °C and 147 °C, "medium" basic sites for CO_2 desorption occurring in the range of 147 °C and 377 °C, and "strong" basic sites for CO_2 desorption occurring above 377 °C. Here, the focus is on "weak" and "medium" sites due to the temperature limitations imposed by the preparation techniques (i.e., calcination temperatures).

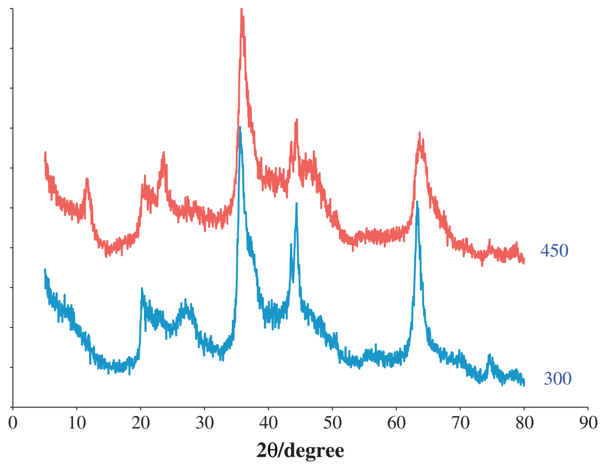

Fig. 2. XRD patterns of Li–Al LDH samples.

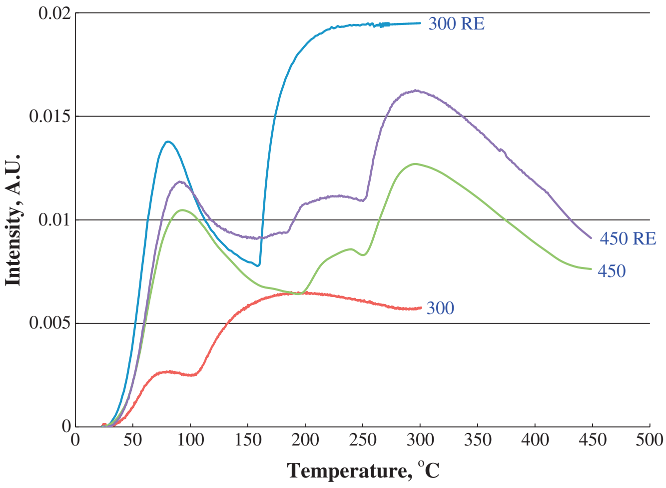

Fig. 3. CO_2-TPD profiles of Li–Al LDH samples.

Direct dropwise water addition is known to introduce OH^- anions, which present Brönsted basicity [14]. The “weak” basic sites are likely due to these hydroxyl groups and an increase in the number of these sites is expected upon rehydration. Additionally, calcined LDHs have been found to contain “weak” sites due to OH^- and “medium” sites due to Li–O pairs [15]. Therefore, in the case of Li–Al LDH, the “medium” basic sites are likely due to Li^+–O^{2-} pairs [9].

3.2. Activity studies

2′-Hydroxyacetophenone conversion data is shown in Fig. 4. Initial reaction rates for the Claisen–Schmidt condensation reaction step were calculated from that data, normalized with respect to catalyst weight, and are presented in Table 2.

First, comparing the activity of the dry Li–Al LDH samples calcined at the two different temperatures, the sample calcined at 450 °C is more active, as indicated by the higher initial reaction rate. Li–Al LDH has been found to decompose upon calcination at 450 °C due to decarboxylation and dehydroxylation and, in turn, increase its surface area and pore volume [9]. Therefore, the observed increase in activity with calcination temperature may be attributed to this reported increase in surface area and pore volume.

Next, the catalytic behavior of Li–Al LDH for the Claisen–Schmidt condensation reaction can be correlated to the surface basicity. More specifically, recall that the CO_2-TPD profiles indicated an increase in both “weak” and “medium” basic sites in the order of 300<450<450 RE<300 RE (Fig. 3). As the number of basic sites increase, the initial reaction rates increase in parallel order (Table 2). These sites, attributable to OH^- and Li^+–O^{2-} groups, are instrumental in the deprotonation of the 2′-hydroxyacetophenone, which is believed to be the first step in the Claisen–Schmidt condensation reaction mechanism for benzaldehyde and 2′-hydroxyacetophenone [7,16,17].

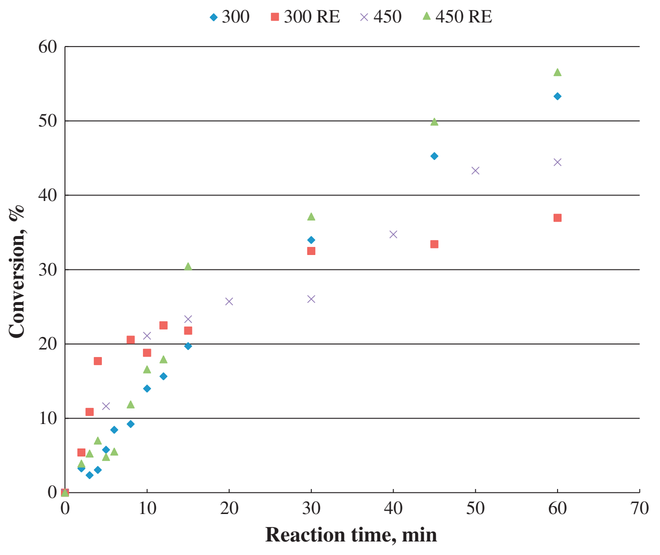

Fig. 4. 2′-Hydroxyacetophenone conversion as a function of time for Li–Al LDH catalysts.

Table 2
Kinetic data for the Claisen–Schmidt condensation of 2′-hydroxyacetophenone over Li–Al LDH catalysts.

Catalyst	Initial reaction rate (104) mol/g/s
300	2.93
450	3.45
450 RE	3.80
300 RE	4.70

The isomerization reaction of 2′-hydroxychalone to flavanone appears to be unaffected by the catalyst since flavanone selectivity is the same for all samples after 60 min of reaction time (59%). This behavior is consistent with previous investigations, thus it further supports the belief that the isomerization reaction occurs significantly faster than the Claisen–Schmidt condensation reaction [7,13].

4. Conclusions

The results presented here signify that Li–Al layered double hydroxide is active for the heterogeneous catalytic synthesis of flavanone. Further, increases in basicity via calcination and rehydration directly correlate with increases in catalytic activity. The literature supports that this observed increased basicity and activity is due to OH^- and Li^+–O^{2-} groups. The Li^+–O^{2-} groups are of particular interest because they may be instrumental in the abstraction of a proton from 2′-hydroxyacetophenone, which is believed to be the first step in the heterogeneously catalyzed Claisen–Schmidt condensation reaction mechanism.

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