Preparation of Solid Acid – Activated Carbon as Catalyst in Aspirin Synthesis

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Abstract. Pharmaceutical synthesis commonly relies on a homogeneous acid catalyst, which is relatively simple in application yet problematic in product purification procedures. This study was an effort to investigate an alternative replacement for homogeneous acid catalysts with an acidified solid catalyst, developed from activated carbon. The activated carbon catalyst had been treated with sulfuric acid before it was applied to produce aspirin (acetylsalicylic acid) through catalytic acetylation route. Using atmospheric pressure reaction, conducted at 353 K, aspirin was successfully synthesized. When salicylic acid and acetic acid glacial were used as reactants, approximately 9-10 % reaction yield could be obtained. Replacement of acetic acid with acetic anhydride in the acetylation reaction produced an overall yield as high as 28 %.

Keywords: Solid Acid Catalyst, Activated Carbon, Aspirin Synthesis

1. Introduction

Synthesis and manufacturing of high specialty chemicals, such as pharmaceuticals, require catalysts as the critical component in the activity. Global catalyst demand has reached approximately 850,000 tons per annum, and it has been continuously growing up to 4% annually. The use of catalysts in industrial practice, especially in pharmaceutical synthesis, simplifies complicated route of reactions. Additionally, selectivity of catalysts facilitates for obtaining desired chemicals, minimizing the risk of molecular chirality, which may produce toxic chemicals. In pharmaceutical processing, molecular chirality problems have not been uncommon, and it may endanger consumer compliance [1].

Many pharmaceutical syntheses rely on application of homogeneous catalysts, utilizing their high selectivity and relatively easy application. A drug for Parkinson’s disease L – dopa synthesis through cinnamic acid hydrogenation with Rh-complex enzyme, or acylase hydrolysis of penicillin G to produce amino- penicillanic acid (antibiotic), is a solid example how homogeneous catalysis has been used to produce popular pharmaceuticals [2]. Despite that fact, there has been growing interests to utilize heterogeneous catalyst. The heterogeneous catalysts have been explored in fine and therapeutic chemicals, exploiting their relatively high activity, apart from their ease of manufacturing, application, and recovery.

In this study, activated carbon was developed as a catalyst to synthesize pharmaceuticals. Aspirin was selected as a model compound considering its popularity in commercial markets. At least, 20 % of analgesic consumption has been supplied from aspirin availability. The conventional synthesis of aspirin has been mostly using sulfuric acid as a liquid catalyst [3]. This study was an attempt to replace a homogeneous acid catalyst role with a solid acid catalyst. An acid-treated – activated carbon had been prepared and applied in acetylation of salicylic acid with either acetic anhydride or acetic acid (glacial) as reactants. The assessment of the study was conducted by examining catalyst morphology, crystallinity and activity as determined from overall processing yield.
2. Experimental

2.1. Materials

Acetic acid, acetic anhydride, acetic acid, salicylic acid, sulfuric acid were purchased from Merck at analytical grade.

2.2. Catalyst Preparation Activated Carbon – $\text{H}_2\text{SO}_4$

Activated carbon as catalyst material was treated with sulfuric acid to produce a solid acid catalyst. The activated carbon catalyst was immersed in sulfuric acid, heated at 383 K, and continuously stirred for 2 hours. The activated carbon was then separated from the acid solution, followed by storing in an oven at 383 K for five days. Catalyst samples were then analysed to assess their properties. After preparation, the catalyst was applied in the reaction.

2.3. Catalyst characterization

The catalyst samples were analysed by X-Ray Diffraction (XRD) to assess its crystallinity. Scanning Electron Microscopy (SEM) was carried out to observe catalyst morphology. Fourier Transform Infra-Red (FTIR) analysis was conducted to examine catalyst functional groups.

2.4. Aspirin Synthesis

The acetylation was performed by reacting acetic acid or acetic anhydride with salicylic acid in a batch-reactor. Reaction was carried out at atmospheric pressure, at 353 K for 40 minute. Stirring was applied at 100 rpm, with reactant ratio of 1:2 acetic acid or acetic anhydride to salicylic acid. Experimental rig set up in the lab-scale is presented in Figure 1.

![Figure 1. Batch Reactor (three-neck flask equipped with reflux and hot plate) for Acetylation Process](image-url)
3. Results and Discussion

3.1. Catalyst Morphology (SEM analysis)

Assessment on catalyst samples through scanning electron microscopy (SEM) provided information on material morphology (Figure 2). The sulfuric-acid-treated-activated carbon surface had an increase of smoothness on its surface, compared to commonly raw activated carbon material. The use of acid solution might be able to destroy solid impurities located in the catalyst surface.

![SEM image of sulphuric acid modified activated carbon, magnification of 6000x](image)

**Figure 2.** SEM image of sulphuric acid modified activated carbon, magnification of 6000x

Catalyst Crystallinity (XRD Analysis)

Based on the XRD characterization of the catalyst materials, it might be assumed that the produced material was largely amorphous (Figure 3). Crystal size was approximately 0.41 nm as informed from the analysis. The result suggested that a relatively large surface area could be obtained in this study. The XRD graph of the catalyst material is shown in Figure 3.

![XRD Spectra of Activated Carbon (modified by sulfuric acid)](image)

**Figure 3.** XRD Spectra of Activated Carbon (modified by sulfuric acid)
3.2. Characterization of Catalyst Material Functional Group (FTIR Spectroscopy)

Catalyst functional group was evaluated with FTIR Spectroscopy. In Figure 4, at 1300-1400 cm\(^{-1}\) interval, there are three peaks observed: 1372, 1385, and 1393 cm\(^{-1}\), indicating vibration stretch of the \(S = O\) sulfonate or sulfone bonds. The result in figure 4 further suggested that the surface of activated carbon could have been modified by sulfuric acid presence. However, the modification effect might be moderate, indicated by subtle intensity peak produced.

![Activated Carbon – Sulfuric Acid Treated](image)

**Figure 4.** FTIR analysis results for Activated carbon (modified by sulfuric acid).

The Catalytic Acetylation Reaction: Conversion and Yield

**Table 1.** Conversion and Yield of Acetic Acid and Acetic Anhydride Acetylation with Salicylic Acid at Atmospheric Pressure in the Synthesis of Aspirin

| Catalyst variant (gram) | Acetic Acid | Acetic Anhydride |
|-------------------------|-------------|------------------|
|                         | Temperature 80°C | Conversion (%) | Yield (%) | Conversion (%) | Yield (%) |
| 0.5                     | 9.81        | 4.3             | 71.3       | 28.3           |
| 1                       | 18.71       | 8.2             | 54.59      | 21.6           |
| 2                       | 22.69       | 9.9             | 53.05      | 21             |

Summary of processing/reactions result is presented in Table 1. The reaction of acetic acid and salicylic acid as raw materials, in the presence of modified activated carbon as catalyst, produced reaction conversion between 9 – 23 %. Aspirin yield of the reaction was in the range of 4 – 10 %. This results were lower than those of reactions in which acetic anhydride was used as reactant. The use of acetic anhydride in the starting material, instead of acetic acid, could obtain catalytic conversion between 53 – 71 %. The yield of aspirin from acetic anhydride application, along with the acidic modified activated carbon as the catalyst, was between 21 – 28 %, higher than those of acetic acid
applications. The trend between both type of reactions, however, were different. In the acetic acid application, yield and conversion increased with additional portion of catalyst in the feed. The opposite result was observed in the acetic anhydride application in the synthesis. The logical reason behind this result was still unknown. It might be resulted from impurities effect, or any other unexplained factors when interaction between the reactants and the catalyst occurred during reactions.

4. Conclusion

Solid-acid-activated-carbon catalyst was successfully prepared by sulfuric acid treatment. Catalyst morphology had smooth surface, amorphous structure and functioned properly in the synthesis of aspirin. The use of catalyst in the aspirin synthesis could reach conversion as high as 71%, and yield as high as 28%. Both results were achieved when acetic anhydride had been used as raw material. When the catalyst was applied in the conversion of acetic acid to aspirin, reaction overall yield and conversion only recorded conversion up to 23%, and yield of 10%

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