The synthesis results comparison of spirooxindole derivatives using TiO\(_2\) and TiO\(_2\)/SiO\(_2\) catalyst

M H Amanda*, A H Cahyana, and I Abdullah
Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Indonesia

*Corresponding author: miahilda53@gmail.com

Abstract. Derivatives of Spirooxindole compounds with the peculiarities of a heterocyclic ring-shaped framework, therefore these compounds have biological activities that play an important role in the pharmaceutical field. The synthesis of spirooxindole derivates was successfully carried out with the Multicomponent reaction that plays a role in it is the Knoevenagel condensation reaction and followed by Michael's addition reaction. The derivative reaction of spirooxindole compounds is more effective and efficient in synthesis time because the reaction uses a heterogeneous catalyst of TiO\(_2\) / SiO\(_2\) nanoparticles. In this research we will compare using TiO\(_2\) and nano TiO\(_2\)/SiO\(_2\) as catalyst. This study produced a spirooxindole compound derivative using precursors such as, isatin, malononitrile and 1,3-diketone groups varied with barbituric acid. The results of the reaction optimization obtained that reaction time of 60 minutes, at temperature of 50 °C, and a catalyst load of 12.5%. The yield percentage obtained under optimum conditions was found 82.72% in TiO\(_2\) catalyst and then 86.81% in TiO\(_2\)/SiO\(_2\) catalyst. The yield was obtained after the compound was recrystallized using hot ethanol. The characterization of TiO\(_2\) and TiO\(_2\)/SiO\(_2\) catalysts was confirmed using FT-IR, XRD, and SEM-EDX. While the characterization of the spirooxindole compound derivate products was confirmed by TLC, FT-IR, and UV-Vis.

1. Introduction
Derivates of spirooxindole compounds were chemical compounds that had the characteristics of a heterocyclic ring, because of their peculiarities made the Spirooxindole compounds had biological activity [1]. Tailor stated that the synthesis of Spirooxindole compounds was carried out in a multicomponent reaction (MCR) system, namely the synthesis of three or more reactants combined in one pot and a target compound was produced [2]. The multicomponent reaction emerged as the best synthesis strategy because of its productivity, simple method and easy execution. The flexibility of the MCR makes this type of reaction an important type, with a relatively short reaction time and high yield.

The multicomponent reaction is one of the pathways used for the synthesis of the derivative of Spirooxindole compounds with the composition of the components used isatin, malononitrile, and 1,3-dicarbonyl compounds [3]. The synthesis of spirooxindole derivates that has been carried out has resulted in poor yields, carried out at high temperatures and for a long time [4]. Therefore the researcher evaluates the catalysts that have been used. In addition, the use of catalysts that are reusability is the right step in selecting the catalysts used in synthesis.

Nano particles TiO\(_2\) / SiO\(_2\) according to the journal [5] states that the catalyst in the reaction of heterocyclic compounds has the ability of reusability, refers to green synthesis, is low price, is easy to
make and does not require a long time to react. TiO$_2$ was used as a candidate for catalyst because TiO$_2$ has good mechanical resistance and stability in acid and oxidative environments. Based on these reasons, TiO$_2$ has a good ability in its application as a heterogeneous catalyst. Based on a description of the advantages and catalytic activity of TiO$_2$ and nano TiO$_2$/SiO$_2$, the researchers reported a comparison of the results from the synthesis of the Spirooxindole compound derivatives using TiO$_2$ and nano TiO$_2$/SiO$_2$ catalysts.

2. Methods
There are two methods in this research, the first synthesis of TiO$_2$/SiO$_2$ nanocomposites. TiO$_2$ Merck commercial was added dropwise in isopropyl alcohol and stirred. A solution of tetra-ethylorthosilicate Si(OC$_2$H$_5$)$_4$ in isopropyl alcohol was added to the reaction medium and stirred for 30 min. The mixed oxide gel was produced by increasing the pH by dropwise addition of 1 N NH$_3$ solution. The resultant solution was stirred for 24 h and kept for 1 day aging. The solution was filtered after 1 day of aging in order to remove any particulates. The precipitate was washed several times with distilled water and dried in oven for 24 h to remove the solvent. Removal of residual organics and the stabilization of the materials were carried out by calcination for 3 h at 400$^\circ$C [6].

The second synthesis spirooxindole derivate with 3 prekursor. Mixture of isatin (1 mmol), malononitrile (1 mmol), and barbituric acid (1 mmol) in the presence of 12,5 mol% of TiO$_2$ commercial was stirred in 10 mL ethanol at 50$^\circ$C. Besides mixture the same recipe but in the presence of 12,5% of TiO$_2$/SiO$_2$. The progress of the reaction was monitored with by TLC (ethyl acetate:methanol). After the completion of the reaction, separation of catalyst with hot filtration technique. Then, the product was obtained by evaporation of solvent from for further purification, was recrystallized with hot EtOH.

3. Results and Discussion
As a comparison in this study used commercial TiO$_2$ and also carried out characterization with FT-IR and XRD. The results of FT-IR characterization in the form of FT-IR spectra are shown in Fig. 1 (a) TiO$_2$, 2 (b) nano TiO$_2$/SiO$_2$ from these spectra nano TiO$_2$ formation was confirmed by Si-O strong vibration around at 1085,72 cm$^{-1}$, Ti-O-Ti stretching vibration around at 689,39 cm$^{-1}$ and very weak Si-O-Ti vibration at around 963 cm$^{-1}$.

![Figure 1. FT-IR spectra of a) TiO$_2$ (a) and b) nano TiO$_2$/SiO$_2$](image_url)

Meanwhile from spectra of TiO$_2$ commercial was confirmed by Ti-O-Ti Stretching vibration 721,4081 cm$^{-1}$. Catalyst characterization using a Scanning Electron Microscope (SEM) aims to evaluate the surface morphological characteristics of the catalyst. Comparison of SEM picture of TiO$_2$ commercial (Fig.2 a) with those of nano TiO$_2$/SiO$_2$ (Fig. 2b) represented that TiO$_2$ have been supported on SiO$_2$. SEM picture of TiO$_2$ commercial was obtained from previous research [7].
Figure 2. SEM picture of a) TiO$_2$ commercial and b) nano TiO$_2$/SiO$_2$

In figure 3b, the micrographs show that morphology of the materials. The tendency of TiO$_2$ to form agglomerates can clearly be seen in the sample calcined at 400, 500 and 600 °C [8]. In this research (Fig. 2b) nano TiO$_2$/SiO$_2$ calcined with 400°C. While TiO$_2$ commercial didn’t treated calcination. From the result, it can be interpreted that the agglomeration behavior generally increases with a decrease in particle size. To confirm the commercial structure of TiO$_2$ and nano TiO$_2$/SiO$_2$ crystals, characterization was carried out using the XRD instrument. From the XRD results, it was obtained that the peak of the diffractogram in Figure 3a, namely TiO$_2$, shows that the crystal structure was crystalline, while in Figure 3b SiO$_2$ from the peak of the diffractogram synthesis results shows that SiO$_2$ has an amorphous crystal structure. Therefore, it was obtained that Fig 3 c nano TiO$_2$/SiO$_2$ is dominated in the crystalline structure. With the form of the catalyst structure, the catalyst works optimally in catalyzing the synthesis of spirooxindole derivatives.

Figure 3. a) XRD of TiO$_2$ commercial b) SiO$_2$ c) nano TiO$_2$/SiO$_2$

The reaction that occurs can be shown in Figure 4. Synthesis made in the same ratio of 1 mmol: 1 mmol: 1 mmol for each precursor[9].
Figure 4. Spirooxindole derivate compound

The first characterization is thin layer chromatography, thin layer chromatography is one way to confirm whether a product has formed during synthesis or not. The luene used in this compound is ethyl acetate: methanol. While the second characterization is product analysis using FT-IR. The use of FT-IR instruments is used to determine the functional groups contained in compounds [10]. The results of the FT-IR instrument characterization of the product are shown in Figure 5.

![FTIR spectrum of product with a catalyst of 12.5% nano TiO₂/SiO₂](image)

Figure 5. FTIR spectrum of product with a catalyst of 12.5% nano TiO₂/SiO₂

The FT-IR spectrum of the product compound showed a peak in the area of 3307.09 cm⁻¹ which indicated the presence of vibrations from secondary amines (R₂NH) while in the area of 2204.73 cm⁻¹ showed that there was vibration of CN bonds in the resulting product. The existence of the γ-lactam group on the indole ring is evidenced by the peak at wave number 1730.22 cm⁻¹. Meanwhile, to prove the formation of the pyran ring can be seen from the peak wave number 1113.93 cm⁻¹ which is the aromatic ether wavenumber. Meanwhile, the peak of 755 cm⁻¹ supports the presence of C-H aromatic (sp³). Analysis using a UV-Vis spectrophotometer instrument by comparing the precursor compound, isatin with the product. The results of the uv-vis spectrophotometer analysis are shown in Figure 6.
Characterization using a UV-Vis spectrophotometer to compare and see the precursor wavelength in the form of isatin as precursor and the product. The spectrum shows that the maximum product uptake is around 330 nm. Whereas the isatin precursor shows an area of 297 nm. It can be seen from the shift to a larger wavelength or what is known as the redshift / bathochromic shift. This is due to the addition of substituents in the product. After being seen from the FT-IR characterization analysis and UV-Vis spectrophotometer, it is strong enough to show that the product has been successfully synthesized. While the yield produced from commercial TiO$_2$ catalyst was 82.70%, for the yield produced with TiO$_2$ / SiO$_2$ nano catalyst was 86.81%.

There was a significant difference between the catalysts that help the synthesis of spirooxindole derivatives because TiO$_2$ as the active side of the catalyst is supported by SiO$_2$, therefore the performance of the catalyst is wider or it can be said that nano TiO$_2$ / SiO$_2$ catalyzes more than commercial TiO$_2$ catalysts [11]. The reason is that SiO$_2$ is abundant with its large specification area and good hydrothermal stability, it was chosen as the catalyst support material [12,13]. Meanwhile, commercial TiO$_2$ also produces high yields because commercial TiO$_2$ is a metal oxide which is quite good in its role as a catalyst. TiO$_2$ is a metal oxide which can be reduced and reacts strongly with precious metals compared to other metal oxides [14,15]. For this reason, TiO$_2$ has attracted much attention for its application as a support for heterogeneous catalysts in many reactions. It was concluded that the catalyst supports on TiO$_2$ with different structures can exhibit different physicochemical properties and catalytic activities[16].

4. Conclusion
The synthesis of spirooxindole derivatives using TiO$_2$ and nano TiO$_2$ / SiO$_2$ catalysts has been successfully carried out enough with a high yield. Prior to the synthesis of spirooxindole derivatives, nano TiO$_2$ / SiO$_2$ was synthesized and the results were white powder and calcined using a temperature of 400 °C. The results of the TiO$_2$ / SiO$_2$ nano catalyst synthesis were confirmed using FTIR, SEM, and XRD instruments. The isolated yield produced with commercial TiO$_2$ catalyst was 82.72%. While the yield produced from nano TiO$_2$ / SiO$_2$ was 86.81%. Products have been confirmed using TLC, and with FT-IR and UV-Vis instruments.
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