

## Abstract

High expense of pharmaceutical raw materials causes local synthesis to not be affordable. Local synthesis, which employs stepwise synthesis, requires significant raw materials and solvents. This condition has led Indonesia to heavily rely on other countries as sources of raw materials and medications, including Clopidogrel, a widely used drug in Indonesia. Multi-Component Reaction (MCR) offers a promising solution to address this issue. MCR has the ability to synthesize complex structured products with desired pharmacological activity in a single step, resulting in higher yields compared to stepwise synthesis. Furthermore, MCR reduces the use of solvents, reactants, and waste thus resulting in higher efficiency and cost reduction. Ugi-3 component reaction (Ugi-3CR), one of the commonly known MCR, has been utilized to synthesize Clopidogrel and has achieved a high yield. In an attempt to reduce the cost, *tert*-butyl isocyanide has been utilized, due to the ease of synthesis and the possibility of being scaled up. Additionally, the Clopidogrel intermediate has been optimized to achieve a higher yield, reaching 81% with the removal of formic acid as a catalyst. Characterization techniques that have been conducted including thin layer chromatography (TLC), infrared (IR) spectroscopy, proton nuclear magnetic resonance ( $^1\text{H-NMR}$ ), and LC-MS have confirmed the accuracy of the obtained intermediate. However, during esterification, obtaining Clopidogrel racemate was impossible due to the presence of a significant amount of byproducts. Further improvements are needed in this regard.

Keywords: Clopidogrel, Ugi-3CR, *Tert*-butyl Isocyanide