STUDI PENGARUH NUKLEOFILISITAS DAN KESTERIKAN AMINA PRIMER PADA SINTESIS TURUNAN 3-HIDROKSIISOINDOLINON

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INTISARI

Telah dilakukan penelitian mengenai studi pengaruh nukleofilisitas dan kesterikan amina primer pada sintesis turunan 3-hidroksiisoindolinon. Penelitian ini bertujuan untuk mensintesis turunan 3-hidroksiisoindolinon melalui reaksi adisi nukleofilik dan mempelajari pengaruh nukleofilisitas serta kesterikan dari amina primer terhadap persen hasil produk turunan 3-hidroksiisoindolinon.

Penelitian diawali dengan sintesis 3-(benziloksi)etilidenftalida melalui reaksi Sonogashira dengan mereaksikan asam 2-iodobenzoat dan benzil propargil eter dalam pelarut DMSO dengan adanya basa $NaHCO_3$ dan katalis CuI, pada temperatur ruang selama 24 jam. Selanjutnya, reaksi adisi nukleofilik antara 3-(benziloksi)etilidenftalida dan empat senyawa amina primer masing-masing dilakukan dalam pelarut *i*-PrOH pada temperatur 50 ºC. Untuk mempelajari pengaruh nukleofilisitas, digunakan amina primer berupa benzilamina dan anilina. Selain itu, efek sterik dari amina primer dipelajari dengan menggunakan reaktan berupa 4-metoksibenzilamina dan 2-metoksibenzilamina**.** Karakterisasi produk dilakukan dengan uji titik lebur, spektrometer ^{1}H-NMR, ^{13}C-NMR, HRMS, dan FTIR.

Reaksi Sonogashira antara asam 2-iodobenzoat dan benzil propargil eter menghasilkan 3-(benziloksi)etilidenftalida berupa padatan putih dengan persen hasil sebesar 53%. Reaksi adisi nukleofilik antara 3-(benziloksi)etilidenftalida dan benzilamina, anilina, 4-metoksibenzilamina, serta 2-metoksibenzilamina berturut-turut menghasilkan 2-benzil-3-(2-(benziloksi)etil)-3-hdroksiisoindolinon dengan persen hasil 86%, 3-(2-(benziloksi)etil)-3-hidroksi-2-fenilisoindolinon sebesar 67%, 3-(2-(benziloksi)etil)-3-hidroksi-2-(4-metoksibenzil)isoindolinon sebesar 75%, dan 3-(2-(benziloksi)etil)-3-hidroksi-2-(2-metoksibenzil)isoindolinon sebesar 70%. Dengan membandingkan persen hasil dari sintesis 3-hidroksiisoindolinon, maka dapat disimpulkan bahwa semakin tinggi nukleofilisitas dari amina primer, semakin tinggi persen hasil yang diperoleh. Selain itu, amina primer dengan halangan sterik yang rendah akan menghasilkan 3-hidroksiisoindolinon dengan persen hasil yang lebih baik.

Kata kunci: 3-hidroksiisoindolinon, Sonogashira, adisi nukleofilik, kesterikan, nukleofilisitas.

EFFECTS OF NUCLEOPHILICITY AND STERIC HINDRANCE OF PRIMARY AMINES ON THE SYNTHESIS OF 3-HYDROXYISOINDOLINONES

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ABSTRACT

Effects of nucleophilicity and steric hindrance of primary amines on the synthesis of hydroxyisoindolinones has been conducted. This research was aimed to synthesize 3-hydroxyisoindolinones via nucleophilic addition reaction and to investigate the effect of nucleophilicity and steric hindrance of primary amines to the synthesis of 3-hydroxyisoindolinones.

The research was started by synthesizing 3-(benzyiloxy)ethylidenephtalide via Sonogashira reaction from 2-iodobenzoic acid and benzyl propargyl ether in DMSO solvent in presence of $NaHCO_3$ and CuI as catalyst, at room temperature for 24 h. Furthermore, the nucleophilic addition reaction between 3-(benzyiloxy)ethylidenephtalide dan four different primary amines were performed in *i*-PrOH at 50 ºC. To study the effect of nucleophilicity, primary amines such as benzylamine and aniline were used. In addition, the steric effect of primary amines was evaluated by using reactants of 4-methoxybenzylamine and 2-methoxybenzylamine. The characterization of the products was carried out by means of melting point tests, ^{1}H-NMR, ^{13}C-NMR, HRMS, and FTIR spectrometers.

The Sonogashira reaction between 2-iodobenzoic acid and benzyl propargyl ether generated 3-(benzyloxy)ethylidenephthalide as white solid in 53% yield. The nucleophilic addition reaction between 3-(benzyloxy)ethylidenephthalide and benzylamine, aniline, 4-methoxybenzylamine, and 2-methoxybenzylamine respectively produced 2-benzyl-3-(2-(benzyloxy)ethyl)-3-hydroxyisoindolinone in 86% yield, 3-(2-(benzyloxy)ethyl)-3-hydroxy-2-phenylisoindolinone in 67% yield, 3-(2-(benzyloxy)ethyl)-3-hydroxy-2-(4-methoxybenzyl)isoindolinone in 75% yield, and 3-(2-(benzyloxy)ethyl)-3-hydroxy-2-(2-methoxybenzyl)isoindolinone in 70% yield, respectively. By comparing the yields of 3-hydroxyisoindolinones, the higher nucleophilicity of primary amines, the higher the yield of 3-hydroxyisoindolinones will be. In addition, the less sterically hindered primary amines will gave 3-hydroxyisondolinones in higher yield.

Keyword: 3-hydroxyisoindolinones, Sonogashira, nucleophilic addition, steric hindrance, nucleophilicity.