Investigating 3*N*-Alkylation Efficacy in 4-Quinazolinone: An Analysis of Different C2 Substituents

Cindy Chou, Manjot Saroya, and Favor Gesinde; Mentor: *Dr. Kelly Kim**

Quinazolinones are essential scaffolds in pharmaceutical chemistry due to their biological versatility. This study explores how varying C2 substituents influences alkylation efficiency at the nitrogen in position 3 (3*N*). Quinazolinone substrates bearing C2-chloro, methyl, or diisopropylamino substituents were chosen to assess the effect of electronic and steric effects. Additionally, base strength was varied to assess their effects on the alkylation process. Strong bases like sodium hydride were compared to weaker bases like sodium carbonate. Thin-layer chromatography (TLC) and nuclear magnetic resonance (NMR) confirmed product formation. Smaller substituents like methyl and chlorine resulted in higher alkylation success, particularly when paired with strong bases. Bulkier groups, such as diisopropylamine, hindered alkylation due to steric hindrance. These results provide a potential reference model for acceptable bulkiness and electronic effects in C2 substituents where smaller groups like methyl and chlorine represent minimal steric interference. Bulkier groups like diisopropylamine create significant obstacles. These findings can guide future molecular modifications by optimizing both the size and electron-donating capacity of substituents to avoid steric effects while enhancing reactivity. Continued research into base strength and electrophile choice could further refine these strategies, improving the efficiency of pharmaceutical development.