

Sintesis dan Karakterisasi Senyawa 4-Fenil-1,2,3,4,5,6,7,8-Oktahidrokuinazolin-2-On = Synthesis and Characterization of 4-Phenyl-1,2,3,4,5,6,7,8-Octahydroquinazolin-2-One

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Abstrak

Inhibitor Dipeptidil Peptidase – 4 (DPP-4) adalah salah satu terapi diabetes yang sudah banyak digunakan karena dapat memperpanjang waktu paruh dari hormon inkretin dan memiliki tolerabilitas yang baik. Vildagliptin adalah salah satu inhibitor DPP-4 dengan struktur inti 2-sianopirrolidin yang membentuk ikatan kovalen reversibel kompleks di situs aktif DPP-4. Namun, ketidakselektifan vildagliptin terhadap DPP-4 dapat menimbulkan efek toksik. Peningkatan selektivitas vildagliptin dapat dilakukan dengan penambahan gugus besar. Penggabungan senyawa kuinazolinon dengan gugus farmakoforik vildagliptin diharapkan dapat menghasilkan inhibitor DPP-4 yang poten dan selektif. Penelitian ini bertujuan untuk memperoleh senyawa kuinazolinon yang nantinya dapat dihibridisasi dengan gugus farmakoforik vildagliptin. Sintesis dilakukan dalam 2 tahap. Tahap 1 dilakukan dengan mereaksikan benzaldehid dengan sikloheksanon melalui reaksi kondensasi aldol silang dengan katalis basa. Tahap 2 dilakukan dengan mereaksikan produk tahap 1 dengan urea melalui reaksi adisi Michael, siklokondensasi, dan dilanjutkan eliminasi. Produk tahap 1 dan 2 diuji kemurniannya menggunakan KLT dan uji jarak lebur. Karakterisasi struktur dilakukan dengan spektrofotometri FT-IR dan H-NMR. Sintesis tahap 1 dan 2 diperoleh nilai rendemen senyawa sebesar 71,77% dan 20,27%. Karakterisasi produk tahap 1 dengan FT-IR menunjukkan bahwa senyawa tahap 1 sudah terbentuk, sedangkan karakterisasi produk tahap 2 dengan FT-IR dan ¹H-NMR menunjukkan senyawa sudah terbentuk tetapi belum murni.

.....Dipeptidyl Peptidase – 4 (DPP-4) inhibitors are one of the diabetes therapies that have been widely used because they can prolong the half-life of incretin hormones and have a good tolerability. Vildagliptin is one of the DPP-4 inhibitors with a 2-cyanopyrrolidine core structure that forms a reversible covalent complex at the DPP-4 active site. However, non-selective activity of vildagliptin can cause toxic effects. Increasing the selectivity of vildagliptin can be done with adding a large group. The combination of quinazolinone compounds with the pharmacophoric groups of vildagliptin is expected to produce potent and selective DPP-4 inhibitors. This study aims to obtain intermediate compounds that can later be hybridized with the pharmacophoric group of vildagliptin. The synthesis was carried out in 2 stages. Stage 1 is carried out by reacting benzaldehyde with cyclohexanone through a cross-aldol condensation reaction with a base catalyst. Stage 2 is carried out by reacting the product of stage 1 with urea through the Michael addition reaction, cyclocondensation, and followed by elimination. Products stages 1 and 2 were tested for purity using TLC and melting point test. Structural characterization was carried out using FT-IR and ¹H-NMR spectrophotometry. Synthesis stage 1 and 2 obtained compound with a yield values of 71.77% and 20.27%. The characterization of the first stage product by FT-IR showed that the stage 1 compound had been formed, while the characterization of the second stage product by FT-IR and ¹H-NMR showed that the compound had been formed but not pure.

