SYNTHESIS OF CHIRAL PHOSPHORIC ACID CATALYST AND ITS APPLICATION IN ENANTIOSELECTIVE AMIDOALKYLATION REACTION OF 2,5-DIMETHYLPYRROLE AND 5-HYDROXYBUTYROLACTAM

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ABSTRACT

Development of enantioselective synthesis of γ-lactam in the presence of chiral phosphoric acid catalyst has been carried out. This research was aimed to synthesize a chiral phosphoric acid and apply it in the enantioselective amidoalkylation reaction of γ-lactam derivative. Initially, chiral phosphoric acid was synthesized from (*S*)-BINOL in five reaction steps, including methylation, iodination, cross-coupling, demethylation, and phosphorylation reactions. Then, synthesis of enantioenriched γ-lactam was conducted from 5-substituted-hydroxybutyrolactam and 2,5-dimethylpyrrole in the presence of chiral phosphoric acid as catalyst. All of the synthesized compounds were elucidated using ^{1}H-NMR and ^{13}C-NMR spectrometer. Additional analysis of chiral phosphoric acid was carried out using ^{31}P-NMR spectrometer. HPLC analysis was performed to determine the *enantiomeric excess* (*ee*) of the enantioenriched lactam.

The results showed that the reaction process included methylation, iodination, cross-coupling, demethylation, and phosphorylation reactions obtained the yields of 52%, 78%, 59%, 99%, and 78%, respectively. The chiral phosphoric acid could be synthesized in 19% total yield over five reaction steps and could be obtained as a pure form through recrystallization method. The enantioenriched 2-isobutyl-3-methyl-1,2-dihydro-1′*H*,5*H*-[2,3′-bipyrrol]-5-one was successfully synthesized using the synthesized chiral phosphoric acid in 94% yield and 83% *ee*.

Keywords: Chiral phosphoric acid, enantioselective amidoalkylation reaction, butyrolactam, pyrrole.

SINTESIS KATALIS ASAM FOSFAT KIRAL DAN APLIKASINYA PADA REAKSI AMIDOALKILASI ENANTIOSELEKTIF 2,5-DIMETILPIROL DAN 5-HIDROKSIBUTIROLAKTAM

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INTISARI

Pengembangan sintesis enantioselektif γ-laktam menggunakan katalis asam fosfat kiral telah dilakukan. Penelitian ini bertujuan untuk melakukan sintesis senyawa asam fosfat kiral dan menerapkannya pada reaksi amidoalkilasi enantioselektif senyawa turunan γ-laktam. Penelitian diawali dengan melakukan sintesis senyawa asam fosfat kiral melalui lima tahapan reaksi, meliputi reaksi metilasi, iodinasi, cross-coupling, demetilasi, dan fosforilasi. Senyawa enantioselektif γ-laktam disintesis dari reaksi antara 2,5-dimetilpirol dengan 5-hidroksibutirolaktam menggunakan asam fosfat kiral sebagai katalis. Produk reaksi yang dihasilkan dianalisis menggunakan spektrometer ^{1}H-NMR dan ^{13}C-NMR. Analisis asam fosfat kiral dilakukan dengan spektrometer ^{31}P-NMR. Analisis HPLC dilakukan untuk menentukan nilai *enantiomeric excess* (*ee*) senyawa γ-laktam.

Hasil penelitian menunjukkan bahwa reaksi metilasi, iodinasi, cross-coupling, demetilasi, dan fosforilasi menghasilkan persen hasil berturut-turut sebesar 52%, 78%, 59%, 99%, dan 78%. Senyawa asam fosfat kiral dapat disintesis dengan total persen hasil sebesar 19% dari lima tahapan reaksi dan didapatkan sebagai senyawa murni melalui metode rekristalisasi. Senyawa enantioselektif 2-isobutil-3-metil-1,2-dihidro-1′*H*,5*H*-[2,3′-bipirol]-5-on dapat disintesis dengan katalis asam fosfat kiral dan didapatkan persen hasil sebesar 94% dengan *enantiomeric excess* (*ee*) sebesar 83%.

Kata kunci: Asam fosfat kiral, butirolaktam, pirol, reaksi amidoalkilasi enantioselektif.