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Asymmetric synthesis of potential biologically active new heterocyclic analogs of (S)-α-alanine containing 3,4-substituted 5-thioxo-1,2,4- triazoles in the side-chain radical

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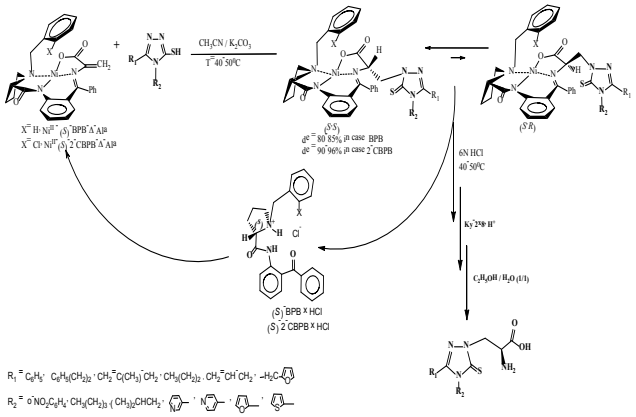
Statement of the Problem: Non-proteinogenic α-amino acids are constituents of many physiologically active peptides, antibiotics and other pharmaceutical preparations. Especially α-amino acids and peptides, containing a N-heterocyclic substituent in the side chain, are of considerable importance in medicinal chemistry because they combine the pharmacophoric groups of amino acids and N-heterocycles. These compounds also belong furyl-, thiophenyl- and triazole-containing structures that are important constituents of many biologically and pharmacologically active drugs such as anti-hyperglycemic, analgesic, anti-inflammatory, antibacterial, anticancer, antifungal, antitumoral, antiviral and psychotropic.

Aim: The goal of our research work is elaboration of efficient high-selectivity method for asymmetric synthesis of enantiomerically enriched substituted α-alanine containing triazole rings in side chain radical.

Materials & Methods: Efficient high-selectivity method for asymmetric synthesis of new heterocyclic substituted derivatives of α-alanine, through the nucleophilic addition of the substituted triazoles to the C=C bond of dehydroalanine moiety in Nill complexes of Shiff's base with chiral auxiliaries (S)-2-N-(N'-benzylprolyl)aminobenzophenone and (S)-2-N-(N'-chlorbenzylprolyl) aminobenzophenone was elaborated.

Results: The results show, that the stereoselectivity of the reaction of nucleophilic addition in case of the complex containing Cl-atom at the 2nd position of Ph-group of N-benzyl proline moiety is increased (up to 96%). Heterocyclic substituted derivatives of (S)-α-alanine were isolated with high optical purity (ee>99%) after decomposition of the mixture of the diastereomeric complexes and ion-exchange purification of the target amino acids.

Conclusion: The advantage of these complexes is the regenerability of the initial chiral auxiliary reagents in quantitative chemical yield and complete retention of the original chirality (optical activity) after completion of the synthesis and isolation of the desired products. This allows multiple reuses of the chiral auxiliaries.



Biography

Hayarpi M Simonyan works in Institute of Pharmacy of Yerevan State University. Her research field of interest is Biomimetic Asymmetric Synthesis. She has her expertise in elaboration of high selective methods of asymmetric synthesis of enantiomerically enriched non proteinogenic amino acids. She completed her PhD degree in Chemistry during the year 2013 specializing in Bioorganic Chemistry.

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