Asymmetric synthesis of enantiomerically enriched (*S*)-α-aminopropionic acids containing more than one heteroatom in the side-chain radical

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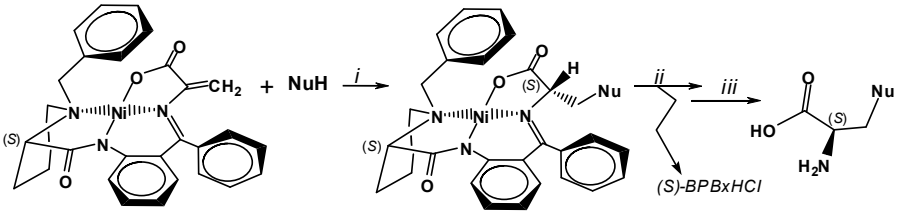
The classes of heterocyclic compounds known as imidazole, thiazole, thriazole are found in many natural and synthetic products with a wide range of biological activities, and they can be well illustrated by a large number of drugs in the market containing this nucleus [1,2,3]. On the other hand, enantiomerically enriched α- and β-substituted α-amino acids are found in many physiologically active peptides, antibiotics and other drugs[4].

Proceeding from the aforesaid, it is evident that introduction of more than one different heteroatoms containing heterocyclic radicals into the side-chain of amino acids can result in new interesting potentially biologically active compounds.

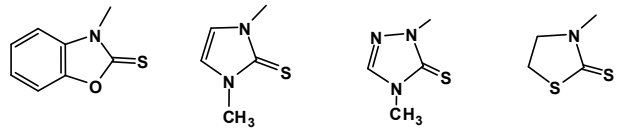
In this paper we report the asymmetric synthesis of novel β-heterocycle substituted analogs of (*S*)-α-aminopropinic acid containing imidazole, triazole, thiodiazole, thiazole and oxazole substituents in the side-chain radical.

Asymmetric addition of the heterocyclic nucleophiles to the C=C bond of dehydroalanine moiety in Ni^{II} complexes of Shiff's base with chiral auxiliaries (*S*)-2-N-(N'-benzylprolyl)aminobenzophenone proceeded in MeCN in the presence of K_2CO_3 at 20-25°C (Scheme).



i = MeCN / K_2CO_3; *ii* = MeOH, HCl; *iii* = Ky-2x8-H^+, EtOH/H_2O

Nu =



As a result diastereomeric mixtures of addition products with a large excess of (*S,S*)-diastereomeric complexes containing amino acids of (*S*)-absolute configuration were formed.

Decomposition of diastereoisomeric complexes was carried out with aqueous HCl, followed by the recovery of the insoluble hydrochlorides of the auxiliary (90%) and purification of the amino acids by ion-exchange method. The target amino acids were isolated with high enantiomeric purity (ee >97%) after crystallization from an aqueous-ethanol (1:2) solution.

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The work has been carried out in the frame of Volkswagenstiftung Project-ID Az 86 223