Abstract

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Several amino acid-based phosphine (oxide) ligands were designed and synthesized *via* sulfonamide bond formation between sulfonyl chloride compound *m*-TPPOTS-Cl and derivatives of different amino acids. Among them, proline-based ligands have gained much attention in this thesis due to their importance as the precursors for the synthesis of water soluble proline-based phosphine (oxide) ligands, as well as an increasing interest in their application in the field of catalysis, such as: Pd-catalyzed Sonogashira cross-couplings and asymmetric allylic alkylation reactions.

Despite the fact that the synthesis of novel water soluble proline-based phosphine oxide ligand *m*-TPPOTSA-*N*-*H*-Pro-OH proved to be challenging with attempting several hydrolysis reagents for the deprotection of the groups attached to the prolines, the clean two-step hydrolysis by using trifluoroacetic acid (TFA) first and then 1 M NaOH provided this ligand in 2% overall yield over eight steps.

In preliminary results in the field of catalysis using the new proline-based phosphine ligands, *m*-TPPTSA-*N*-Cbz-Pro-OBn was used in a Sonogashira cross-coupling reaction of phenylacetylene and 4-iodobenzoic acid in THF. The results were compared to the reaction using the well known triphenyl phosphine ligand. Furthermore, model studies using *m*-TPPTS as a water-soluble ligand were developed and optimized to obtain the most efficient conditions for the coupling of phenylacetylene and 4-iodobenzoic acid. The solvent mixture 1,4-dioxane:H_2O (1:1) allowed for a rapid reaction with a full conversion after 60 min. In addition, the application in Pd-catalyzed asymmetric allylic alkylation of *rac*-(*E*)-1,3-diphenylprop-2-en-1-yl acetate and dimethyl malonate using two chiral proline-based phosphine oxide ligands, *m*-TPPOTSA-*N*-Cbz-Pro-OBn and *m*-TPPOTSA-*N*-Boc-Pro-OMe, has been assessed. The yield and the enantiomeric excess (ee) were determined using ^{1}H-NMR spectroscopy and HPLC/chiral pakIA column, respectively. By using the newly synthesized water-soluble chiral proline-based phosphine oxide ligand *m*-TPPOTSA-*N*-*H*-Pro-OH in presence of potassium carbonate, the product was isolated in 62% ee in a THF:H_2O (1:1) solvent system.