Title: Phosphinoferrocene ligands with polar amide substituents

Author: Hana Charvátová

Department: Department of Inorganic Chemistry

Supervisor: prof. RNDr. Petr Štěpnička, Ph.D.

Abstract: This thesis is focused on phosphino-urea ferrocene ligands that are still rather neglected in the literature. It describes the synthesis of novel polar amides and hydrazides of 1′-(diphenylphosphino)ferrocene-1-carboxylic acid (Hdpf) with or without ethylene linker bearing various urea and guanidine terminal functional groups.

Urea and guanidine derivatives with ethylene bridge can be prepared from Hdpf and appropriate amine with amidation agents. Phosphine ureas without the linker are accessible from reactions of primary amide of Hdpf with suitable acylation agents while analogical guanidine is obtained from guanylation of amide-amine generated from Hdpf acylbenzotriazole and ethylenediamine. Reaction of the acylbenzotriazole with free guanidine leads to [1′-(diphenylphosphino)ferrocenecarbonyl]guanidine hydrochloride.

These ferrocene ligands were used to prepare four types of palladium(II) complexes, viz. where L denotes the newly synthesized ligands and L^{NC} is 2-[(dimethylamino)methyl]phenyl-*C*,*N* auxiliary chelating ligand.

Catalytic efficiency of complexes with ethylene bridge was tested on reactions of aromatic acylchlorides and boronic acids to give ketones. Optimal conditions included the reaction of a boronic acid with a slight excess of acyl chloride in the presence of Na_2CO_3 at 50 °C for 1 hour with 0.2 mol. % of [$PdCl(\eta^3\text{-}C_3H_5)L$], where L is phenylurea ligand with ethylene linker. In case of guanidine ligands the best results were observed with *in situ* generated complex of the phosphinoguanidine with ethylene linker and $Pd(OAc)_2$. In a toluene/water biphase system, these catalysts tolerate various functional groups and afford substituted benzophenones in good to excellent isolated yields.

In addition, anticancer activity of arene-ruthenium complexes with prepared ligands was tested on two types of cancer cells and on healthy cells. The highest cytotoxicity showed complex [$(\eta^6\text{-}p\text{-cymene})RuCl_2(Ph_2PfcCONHCH_2CH_2CONHPh\text{-}\kappa P)$].

Keywords: ferrocene ligands ; phosphines; amides; hydrazides; urea; guanidine; palladium; ruthenium; catalysis; coupling reactions; anticancer activity.