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Phosphoric ligands immobilized on polymeric resins

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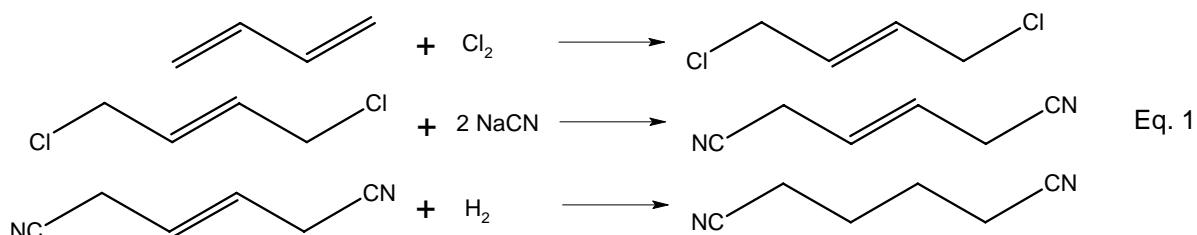
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Abstract

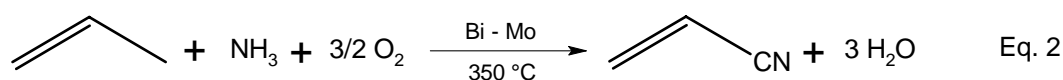
Hydrogen cyanide (HCN) addition is chemical reaction taking important part in chemical industry over the world. HCN addition reactions are one the most used synthetic routes leading to cyano compounds which are indispensable materials for pharmaceutical industry and chemical industry itself as well. The key role in HCN additions is represented by the catalytic system present in reaction mixtures, which increases yields and purity of desired product and decreases energetic and material demands of the reaction at the same time. It is known that Ni(0)-complexes stand as the most used catalysts in such mixtures having high efficiency and selectivity, although catalytic system may be rather complicated and the resulting product can be dependent on many factors. Some disadvantages of such homogenous catalytic systems could be eliminated using immobilized Ni-complexes as catalysts. First step in this approach is to prepare phosphoric ligands immobilized on suitable polymeric resin.

Introduction

Cyano compounds are widely used as starting materials for synthesis of many important industrial compounds (amides, amines, carboxylic acids and esters), polymeric fibers, rubbers, coloring matters and drugs. Cyano compounds can be manufactured in different ways, but in many cases alternative methods are rather complicated and not economic. Some synthetic routes, such as halogen substitution, are complicated because the manufacturing of product consists of several steps as described by Eq. 1.



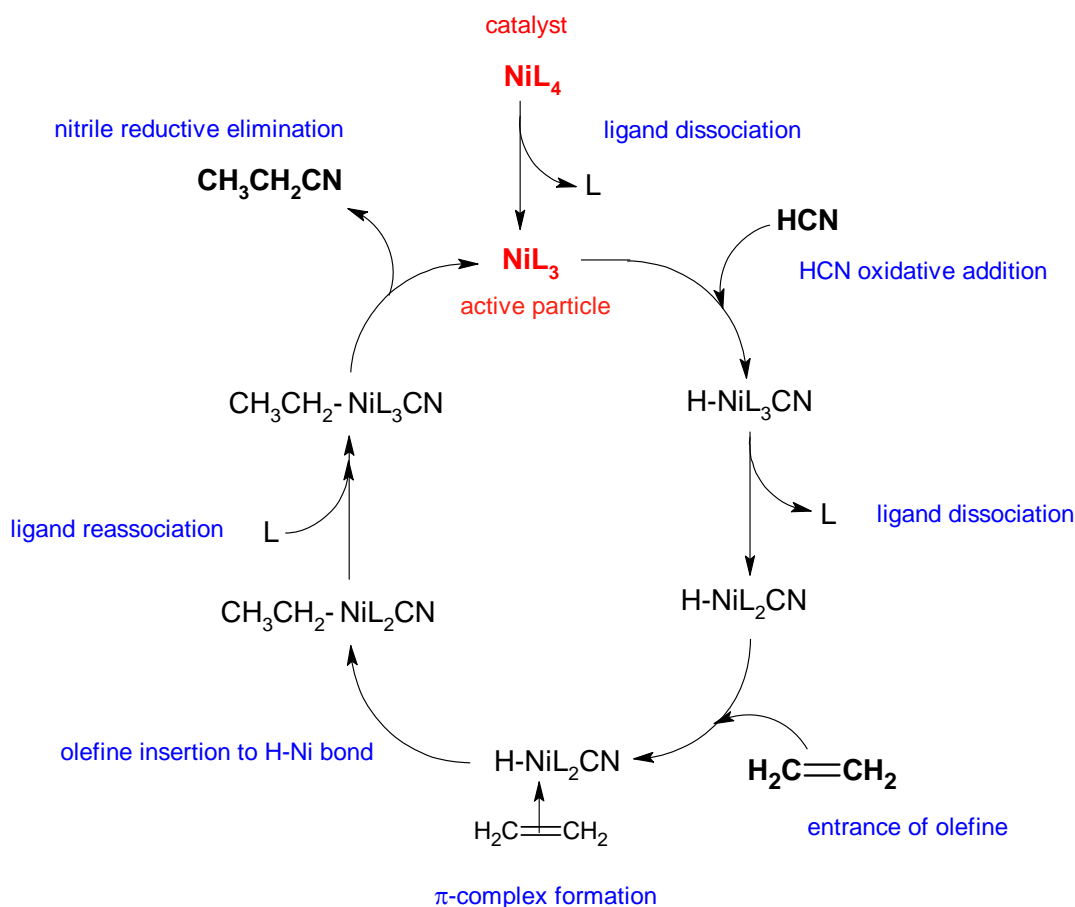
Another method, such as oxidation in the presence of ammonia in acrylonitrile manufacturing (Eq. 2), requires higher temperatures.



Due to above described reasons hydrocyanation keeps its unreplaceable role in cyano compounds manufacturing. Moreover new synthetic routes leading to cyano compounds and the improvements of present ones are sought at the same time. The main aim of the research is to introduce synthetic routes yielding desired cyano compounds in high yield and high purity due to elimination of side reactions. All the reactions should be performed in simple reaction systems with high reaction economy and with low energy demands.

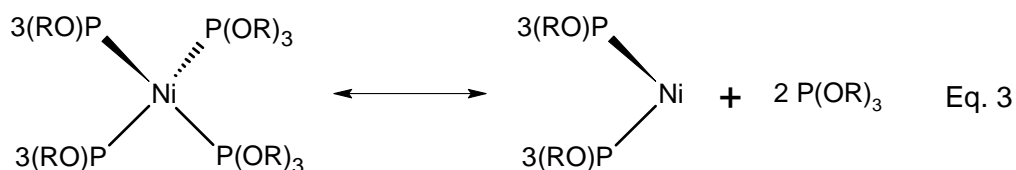
Many disadvantages and problems of hydrogen cyanide addition reactions were eliminated using homogenous catalysis so that reactions have high yields and selectivity, low energetic demands using moderate conditions. Ni(0)-complexes of general formula $\text{Ni}[\text{P}(\text{OR})_3]_4$ or $\text{Ni}[\text{P}(\text{OR})_3]_3$ ($\text{R} = o\text{-MePh}, p\text{-MePh}, \text{Ph}$ etc.)^{1,2} were found to be effective homogenous catalysts of hydrogen cyanide additions.^{3,4} Central nickel atom is coordinated by phosphoric ligands bearing various organic substituents. Steric and electronic features of the substituents strongly influence stability of nickel complex and its catalytic activity. Effective catalyst can be prepared in-situ in the mixture by the reaction of chosen ligand with suitable nickel precursor such as $\text{Ni}[\text{COD}]_2$ (COD – 1,5-cyclooctadiene).

Mechanism of Ni(0)-catalyzed hydrogen cyanide addition was intensively studied^{5,6,7} so that it is known catalyst undergoes several reactions as it is shown in the Scheme 1.



Scheme 1. Mechanism of Ni(0)-catalyzed hydrocyanation

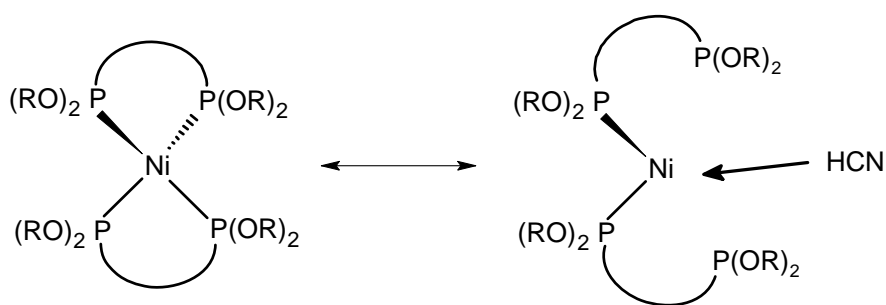
It can be clearly seen there are two important changes of the catalyst in the catalytic cycle – ligand dissociation and ligand reassociation (Eq. 3). Due to ligand reassociation



a small excess of free ligand has to be put into the reaction mixture, but catalyst is slowly destroyed during the course of reaction anyway. The selectivity and activity of the catalyst can be increased by the addition of a co-catalyst, which increases a number of catalytic cycles as well.^{5,8} When non-activated substrate is used as reactant co-catalyst activates the compound for hydrogen cyanide addition at the same time. Lewis acids such as BPh₃, ZnCl₂ or AlCl₃ display the best results as co-catalyst. But addition of another compound into the reaction mixture can bring possible complications for example during catalyst removal or product separation.

According to the observed reaction mechanism ligand reassociation can be considered as the key step influencing the number of catalytic cycles of Ni(0)-catalyst. To arrange suitable conditions for ligand reassociation is the way for longer Ni(0)-catalyst life time. There can be two ways to achieve this aim – using bidentate phosphoric ligands or using phosphoric ligand immobilized on polymeric resin.

When using bidentate ligands we can expect incomplete bidentate ligand dissociation when vacating two coordination sites on nickel atom (Scheme 2). Described ligand behavior therefore would enable easier Ni(0)-complex rearrangement but no evidence of such mechanism has been found so far in spite of some research in this field of interest. Nevertheless Ni(0)-complexes with bidentate phosphoric ligands were studied as catalysts for HCN addition reactions with good results.^{9,10}

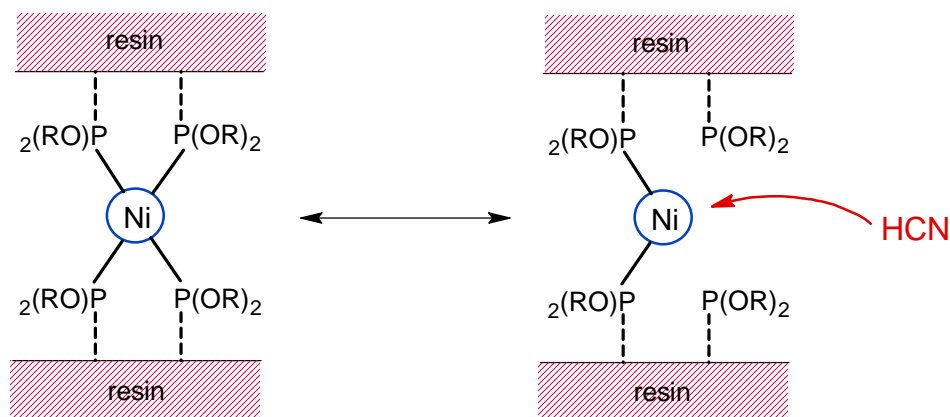


Scheme 2. Idea of bidentate ligand dissociation mechanism in Ni(0)-catalyst

Application of immobilized Ni-complexes as HCN addition catalysts is the second option but no results in this field have been published yet. The very first step in this approach is to prepare immobilized phosphoric ligands. Synthesis of phosphoric ligands bound on polymeric resins is described in our contribution.

Results and discussion

The pattern of immobilized Ni(0)-complex catalyst is based on fact that immobilized ligand cannot be driven away from the coordination sphere of nickel atom when relieving its coordination site to enable HCN or olefine coordination (Scheme 3). Due to immobilization

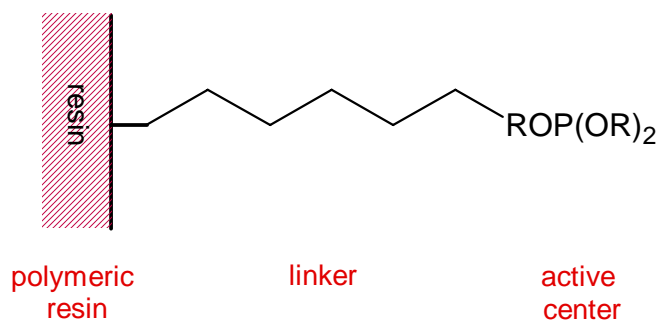


Scheme 3. Idea of immobilized ligand dissociation mechanism

of the ligand it is still close to the coordination sphere of nickel atom and the original complex can be easily rearranged in the end of the catalytic cycle. Using resin-immobilized catalyst we enter the field of heterogeneous catalysis. This can bring new possibilities and advantages in comparison with homogenous catalysis for example easier catalyst removal and renewal. Immobilized catalyst can be used in flow synthesis as well when reaction mixture is poured through immobilized catalytic system.

When thinking about immobilized phosphoric ligand we should take into account three subjects – polymeric resin, linker and active centre (Scheme 4).

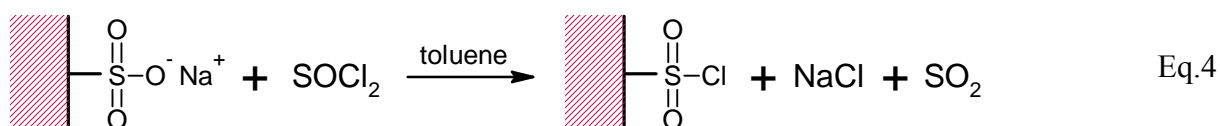
Polymeric resin should be mechanically and chemically inert and should contain sufficient number of reactive groups to be converted. For our work we have chosen strongly acid cation exchanger – Noromit 001*7 (capacity: min. 1.9 mol/l, moisture contain: 45-55 %, thermal stability: max. 120 °C). It contains $-\text{SO}_3\text{Na}$ groups bound on polymeric resin based on styrene-divinylbenzene copolymer. Moisture present in ion-exchanger should be removed before use but some moisture level is necessary for the reactivity of the exchanger.



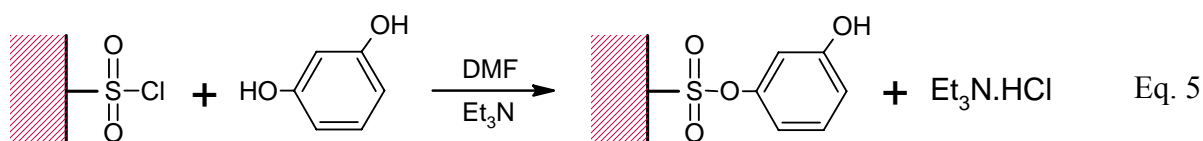
Scheme 4. Idea of phosphoric ligand bound on polymeric resin

The main role of linker is to keep the reactive center in sufficient distance from the resin surface to be easily reached by the reactive particles from the solution. Linker's skeleton can be flexible or rigid in dependence on function of linker desired. It should not contain reactive centers or potentially well-leaving groups. In this case linker rupture and ligand release can occur. The reactive site – phosphoric ligand - should be then bound at the end of the linker.

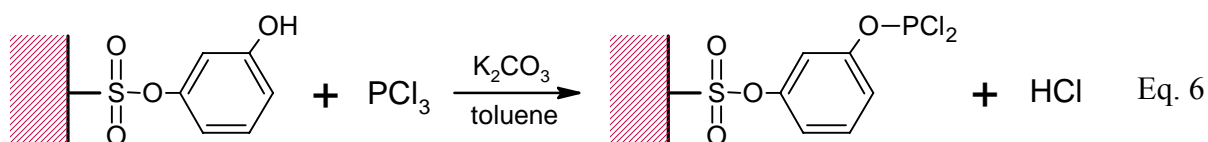
The first step in immobilization procedure is the –OH group substitution by the chlorine atom (Eq. 4). The substitution is made by SOCl₂ in toluene. After the SOCl₂ addition reaction mixture has been heated at 80 °C for 8 hours and then left stirred at room temperature overnight. Sodium chloride and SO₂ arise as by-products. The course of the reaction can be observed by the release of NaCl or SO₂ especially.



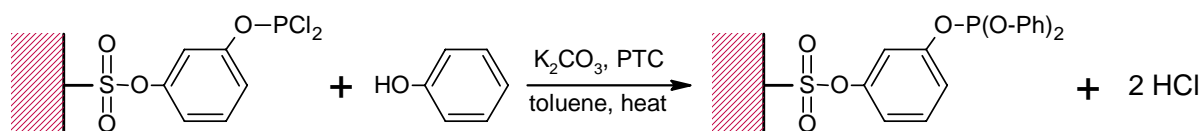
The following reaction step (Eq. 5) is based on the reaction of –SO₂Cl group with 1,3-dihydroxybenzene (resorcinol). The reaction is carried out in dimethylformamide in the presence of triethylamine as base at room temperature for 30 hours. The slow addition of resorcinol and its reaction is indicated by the color changes of the resulting mixture.



In subsequent step resorcinol free –OH group reacts with phosphorus trichloride added (Eq. 6) to bind phosphorus containing group to the polymeric resin. K₂CO₃ is added into mixture as base for deprotonation of hydroxyl group. The step is carried out at ambient temperature for 30 hours but mixture is slightly warming up when adding PCl₃ into the mixture.

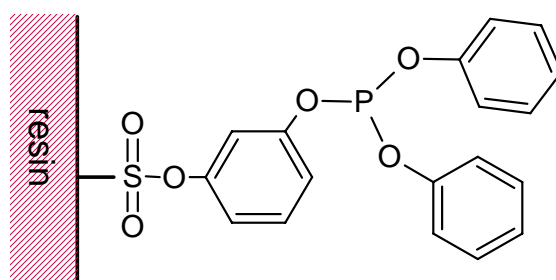


And the final step of preparation is the substitution of two chlorine atoms from –PCl₂ group by phenoxy group (Eq. 7). The solvent used is toluene and the reaction mixture was refluxed for cca 8 hours. Base (K₂CO₃) is present in the mixture again and phase-transfer catalyst (Cetrimide) has to be added into the reaction mixture as well. Color changes of the reaction mixture can be observed during the course of the reaction.



Eq. 7

Following the above mentioned steps we should be able to prepare immobilized phosphite ligand of the type shown at Scheme 5. This the very first step in immobilized Ni(0)-complexes preparation.



Scheme 5. Immobilized ligand of the phosphite type

General experimental procedure

All reactions were performed in closed apparatus guarded by drying tube filled with anhydrous CaCl_2 . Resin was typically put into the flask filled with appropriate solvent (toluene or DMF) and base was added if needed. Solution of other reactants (in small excess compared with stoichiometry) in the same solvent were usually added dropwise into the reaction mixture which was subsequently stirred at selected conditions for above mentioned time (for details see parts concerning Eq. 4–7). Modified ion-exchanger was then filtered off and washed with the same clean solvent and dried in vacuo at higher temperature.

Because of resin insolubility solution method were not able to use for resin changes examinations. However, solution methods were used to determine soluble reactants concentrations. Infrared spectroscopy was used to observe changes on polymer resin structure. The IR spectra were recorded in nujol mulls using KBr discs on a Bruker IFS 28 spectrometer. Resins were grinded into dust before measurement. For both quality and quantity phosphorus determinations standard analytic proof of phosphorus (using sodium molybdate) was applied.

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