Immobilization of Pybox Ligand on Modified Starch

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Starch, one of the most abundant natural polymer was used as support for chiral pyridine–bis(oxazoline) ligand. The corresponding ruthenium complex was used as catalyst in cyclopropanation reaction of styrene with ethyl diazoacetate. Yield, diastereoisomeric excess and enantiomeric excess kept constant after 3 runs.

The preparation of tethered organometallic complexes to perform enantioselective synthesis has been reported over several types of supports. Most commonly chiral catalysts were immobilized over solid support through covalent bondings.[1] Ligands have been covalently grafted to inorganic materials such as amorphous silica or mesoporous structured inorganic solid. They can also be introduced in organic polymers either by modification of Merrifield type resin or by copolymerisation. On the other hand, natural polymers such as polysaccharides are largely available on great scale and can be applied as support of molecular catalysts. In this sense, the starch is a particularly attractive molecule: its swelling is strongly affected by the nature of the solvent. Moreover, it is very cheap and not toxic. Few reports are dealing with the use of polysaccharides as support for organometallic species. Allylic substitution was performed with Pd/TPPTS complex entrapped in different polysaccharides.[2] Silica-supported starch–polysulfosiloxane–Pt complexes were used for asymmetric hydrogenation of 4-methyl-2-pentanone to 4-methyl-2-pentanol with 94% ee.[3] In that approach, the intrinsic chirality of the starch was responsible of the enantioselectivity. Recently, organometallic complexes were grafted to functionalized cellulose for potential application in nonlinear optic.[4]

Chiral pyridine–bis(oxazoline) (Pybox) ligands complexed to ruthenium are very efficient in cyclopropanation reaction of alkenes with diazoesters.[5] Pybox ligands have been supported onto silica[6] and polymers[7] via grafting or copolymerized with styrene and divinylbenzene.[8] These studies showed that the nature of the support played a significant role on the activity of the supported catalyst as well as on the enantioselectivity of the reaction.[9] To our knowledge, carbohydrate type solids have not been developed as supports for chiral catalysts, and this could be of interest because the additional chirality of the support. Thus, the aim of this work was the covalent grafting of Pybox ligands to starch and their test in the asymmetric cyclopropanation benchmark reaction (ACP). In order to get high flexibility of the catalyst over the support, it is necessary to insert a long chain as a linker between the starch and the ligand. We previously reported palladium-catalyzed telomerization of starch with butadiene.[10] This transformation allowed the introduction of a 8-carbons chain in starch. Owing to the presence of unsaturated double bonds in the lateral chain, subsequent functionalization is conceivable. In this paper, we reported the grafting of a Pybox ligand to a telomerized starch and the preliminary results in asymmetric cyclopropanation reaction.

Treatment of starch in *i*-PrOH/NaOH 0.1 M with butadiene at 50 °C overnight, in the presence of catalytic amount of $Pd(OAc)_2$/TPPTS (trisodium tris(*m*-sulfonatophenyl)phosphine) yielded telomerized starch. The degree of substitution, determined as the average number of ether groups per glycosidic moiety, was significantly affected by the experimental conditions. In order to avoid undefined interactions between two adjacent ligands, we prepared modified starch with moderate degree of substitution (DS). The reaction was performed in the presence of 0.25 mol % catalyst per glycosidic unit, for 21 h at 50 °C. After workup, the DS was determined by ^{1}H NMR analysis and was equal to 0.62. In a second step, the telomerized starch **1** was effectively peracetylated in pyridine in 85% yield.[11] This protection did not affect the ether group and ^{1}H NMR analysis confirmed the DS (0.65).

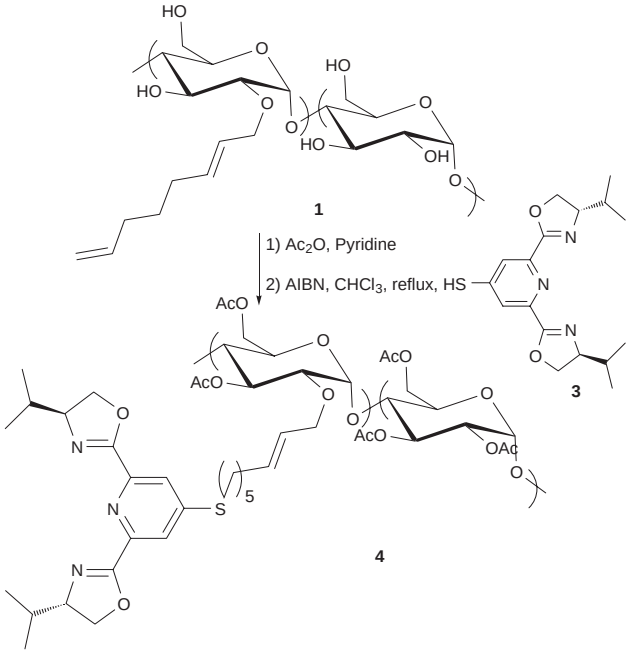

Figure 1. Synthesis of immobilized Pybox ligand.

The radical coupling of 4-sulfanylpybox[7] (**3**) and modified starch was studied (Figure 1). With starch containing free OH groups **1**, in the presence of catalytic amount of AIBN, very low amounts of grafted ligand were detected by ^{1}H NMR analysis. This was attributed to the radical scavenger properties of hydroxyl groups. On the other way, reaction with peracetylated telomerized starch **2** was slow but successful. Owing to the low reactivity of the system, the 4-sulfanylpybox was added portion wise over a two-days period. After extensive washing, the resulting solid was analyzed by ^{1}H NMR analysis. Specific

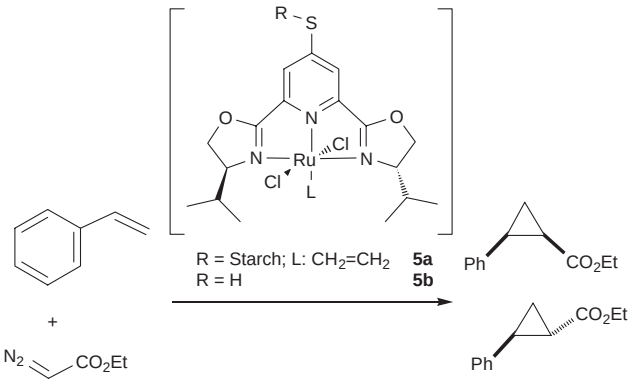

Figure 2. Asymmetric catalyzed cyclopropanation.

signals of the Pybox moiety were observed at 8.18 and 8.06 ppm as result of the different environment of the pyridine rings in **4** (i.e. by a non-homogeneous distribution of the C_8 linker on starch). Moreover, the presence of nitrogen was detected by elemental analysis of **4** that corresponded to 0.1 mmol of ligand per g of support.

Treatment of the ligand **4** with $[RuCl_2(p\text{-Cymene})]_2$ in dichloromethane under an ethylene atmosphere yielded the corresponding red wine-colored Pybox–Ru–ethylene 1:1:1 complex **5a** (Figure 2) as previously reported by Nishiyama.[12] Metal analysis showed that 80% of the Pybox ligands reacted with the ruthenium dichloride dimer to form the complex **5a**. This means that most of the ligand grafted on the starch was easily accessible to the ruthenium salt. In parallel, the homogeneous complexes **5b** synthesized from 4-sulfanylpybox **3** was prepared in situ (ligand:Ru = 4:1).

Catalytic performances of these complexes were tested in asymmetric cyclopropanation reaction between styrene and ethyl diazoacetate in dichloromethane at room temperature. (Table 1)

The homogeneous 4-sulfanylpybox–Ru catalyst **5b** was efficient for the cyclopropanation reaction and significant 89/11 trans/cis ratio was achieved. The enantiomeric excess of the trans and cis isomers reach 77 and 63% respectively. As expected, these values are some lower than those achieved using 4H-Pybox–Ru catalysts (88 and 70% respectively[8]) owing to the presence of a slightly electron-donating group on the pyridine moiety of the ligand in **5**.[12]

Encouraging by these results we performed the cyclopropanation reaction in the presence of the starch complex **5a**. As previously reported, it is quite difficult to obtain a local excess of chiral ligand on polymer.[8] So, the Pybox starch–Ru–ethylene 1:1:1 complex **5a** was tested. This complex **5a** exhibited lower activity and selectivity toward the cyclopropanation reaction than homogeneous complex **5b** pointing out the dramatic influence of the support. However, ruthenium catalyst supported on starch **5a** showed better performance on ACP than silica immobilized catalysts,[9] although with worse asymmetric induction than copolymers (specially on the trans/cis ratio and cis enantioselectivity).[8] After removing of the liquid solution and washing of the solid with degassed ethanol, the performance of the catalyst was established again. Over 3 runs, the trans/cis selectivity as well as the enantioselectivity keep constant. However, the yield increases between runs 1 and 2. This was attributed to the presence in the first run of residual free ruthenium complex which is not active in cyclopropanation reaction but decomposes the ethyl diazoacetate. In terms of recycling, starch immobilized catalyst **5a** allowed more runs without decreasing of performance than reported copolymers.[8]

Table 1. Enantioselective catalyzed cyclopropanation[a]

Catalyst/%	Ligand/Ru	Yield/%	trans/cis	ee_{trans}/%	ee_{cis}/%
5b/3	4:1	67	89/11	77	63
5a/1.7	1:1	28	74/26	49	18
5a run 2		45	75/25	50	16
5a run 3		44	76/24	46	16

[a]Reaction conditions: 5 mmol of styrene, 0.5 mmol of ethyl diazoacetate (slow addition), Ru catalyst, CH_2Cl_2, rt. Catalyst was filtered, washed, and dried before reuse. Yield, de and ee were determined by GC analysis (Cyclodex B).

In conclusion, we have shown the possibility of immobilizing chiral pybox system on modified starch. This fact, make us consider that other polysaccharides can be developed as new types of supports for organometallic species. Further works are under progress to graft Pybox moieties using different linkers and biopolymer.

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