Ruthenium-catalyzed homogeneous hydrogenolysis of esters to alcohols

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SUMMARY

Alcohols find widespread application in different fields of chemistry, either as solvents (mainly C₁-C₆ alcohols) or as starting material for subsequent conversions. Especially in fine chemical industries, alcohols form a large and substantial part of the feedstock for further synthesis of drugs, perfumes or additives in food applications such as fragrances. In a number of cases, industries may have higher oxygenates at their disposal, which are abundant or even waste material, e.g. oxygenates stemming from over-oxidation of hydrocarbons. These oxygenates e.g. carboxylic acids, esters, amides can be used as a feedstock for the production of alcohols by reduction.

In this thesis the development of a catalyst for the homogeneous hydrogenolysis of esters to alcohols, a fairly undeveloped field, has been described. Few examples of suitable catalysts are known in the literature, and existing homogeneous catalysts are limited in their applicability, i.e. they can only be applied in the conversion of activated substrates. Since ruthenium compounds in homogeneous solution effectively catalyze many hydrogenation reactions of carbonyl compounds, the research has been directed to compounds based on this metal and a number of mono-, di-, tri- and tetradentate phosphorus ligands as the activating and stabilizing ligand. A valuable and easily available catalyst precursor for the hydrogenolysis of the activated ester dimethyl oxalate to the product ethylene glycol was discovered. The catalytic system was found to be most efficient when Ru(acac)₃ (acac = acetyl acetonate; 2,4-pentanedionate) was used as a precursor in combination with the facially coordinating tripod ligand triphos (CH₃C(CH₂PPh₂)₃). For the first time, a catalyst was found that enabled the full conversion of esters into the corresponding alcohols in high yields and selectivities using relatively mild conditions.

By selecting different ligands, the product of the reaction can be chosen. For example, when using the meridional coordinating PhP(C₂H₄PPh₂)₂ ligand, dimethyl oxalate is almost exclusively converted to methyl glycolate, whereas the use of MeC(CH₂PPh₂)₃ leads to the exclusive formation of ethylene glycol.
The catalyst is not limited to the hydrogenolysis of activated substrates, but also non-activated substrates such as fatty acid esters and benzoic acid esters are readily hydrogenolyzed. Besides hydrogenolysis of ester functions, the catalyst can be used in the hydrogenation of a variety of other functional groups such as ketones, aldehydes, alkenes and nitriles. All conversions can be achieved in good to high yields and with excellent turnover frequencies.

In several cases, it appeared important to select the appropriate solvent and additive, which greatly influences the outcome of the reaction in terms of the products. Besides the hydrogenated product, the transesterified product is obtained in case the wrong conditions are chosen. Catalysis can be carried out using common alcohols such as methanol and 2-propanol as solvent and NEt₃ as additive, but best overall performance was observed using the highly polar alcohols 2,2,2-trifluoroethanol and 1,1,1,3,3,3-hexafluoro-2-propanol.

The catalyst precursor Ru(acac)₃− triphos had been shown to be very active in a variety of reduction experiments, however, the exact nature of the catalyst itself remained unclear. Two new complexes were synthesized and characterized that should better resemble the actual, active catalyst than the mixture of Ru(III) salts and the triphos ligand. The synthesized complexes both contain the tripod ligand triphos, shown in previous chapters to be essential for excellent catalytic conversions. One of the complexes is the mononuclear complex Ru(acac)₂(K²-triphos), which was isolated directly from the autoclave from a Ru(acac)₃− triphos mixture, and was thought to be an intermediate complex in the formation of the active catalyst. The other complex was the dinuclear [((triphos)Ru(μ-Cl)₃Ru(triphos))Cl that was considered to be a suitable candidate in the formation of the actual catalytic species by breaking of the chloride bridge aided by the presence of NEt₃. Both complexes have shown excellent activity in the hydrogenolysis of dimethyl phthalate, methyl phenylacetate and benzyl benzoate and show higher activity than found for the mixture Ru(acac)₃− triphos. Furthermore, they show immediate activity upon introduction into the reaction mixture, i.e. no additional incubation time is required, contrary to the case of Ru(acac)₃− triphos.

Experiments aimed at elucidating the kinetics of the hydrogenolysis have been performed and have led to an understanding of several of the factors affecting the rate of hydrogenolysis. Based on these and previous findings and a number of facts and similarities in the literature, a proposal for the mechanism of ruthenium-catalyzed hydrogenolysis has been made. Overall rate
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equations were obtained for the hydrogenolysis of benzyl benzoate catalyzed by Ru(acac)$_3$ and [(triphos)Ru($\mu$-Cl)$_3$Ru(triphos)]Cl. It was shown that, depending on the catalyst precursor used, the reaction rate follows first order dependence in ruthenium precursor for Ru(acac)$_3$ or a half order for the dinuclear species [(triphos)Ru($\mu$-Cl)$_3$Ru(triphos)]Cl. The catalysis shows first order dependence on the hydrogen pressure and zero order in substrate and additive. Experiments with deuterium gas instead of hydrogen showed that the hydrogen involved in the conversion is obtained directly from the hydrogen gas and that transfer hydrogenation involving the solvent 1,1,1,3,3,3-hexafluoro-2-propanol does not play a role. Overall solvent polarity appeared to be important, the solvent is involved activation of the substrate (by formation of hydrogen bonds to the carbonyl function) and the catalyst complex (by way of ionic hydrogenation). The mechanism proposed is in concert with all observations, taking the rate equations into account as well as crucial species like solvent-activated ruthenium hydride species.

The new catalyst system for the homogeneous hydrogenolysis of esters, either based on Ru(acac)$_3$, Ru(acac)$_2$(κ$^2$-triphos) or [(triphos)Ru($\mu$-Cl)$_3$Ru(triphos)]Cl, shows unprecedented activities and selectivities and is not limited to the hydrogenolysis of activated esters; a wide variety of esters and other substrates can be converted. Comparing our data with results reported in literature, these new catalysts signify an unprecedented achievement in the difficult field of ester hydrogenolysis.