Organometallic catalysis in aqueous media – molecular mechanisms and new applications

Final report on the results of the project, 2012-2017

I. Introduction

The main aim of our planned research –put forward in the 2011 project proposal- was to meet some of the major challenges for chemistry and chemical industry in the next two decades. These include(d) the use of new solvents for syntheses (including water); increased use of catalysis, improved methods for the understanding of catalysts, manufacturing of chemicals based on renewable resources; enabling the use of hydrogen, hydrogen storage materials; innovative ways of producing materials for medical therapy and diagnosis. In accord with the above, in the focus of our investigations were the syntheses of new ligands and catalysts suitable for carrying out reactions in aqueous media; study of the intricate mechanisms of reactions of such complexes with hydrogen and other hydrogen sources (such as aqueous formate or alcohols), designing new methods for synthetically useful reactions in homogeneous or biphasic aqueous systems, including reactions of H_2O itself (catalytic hydrations), and for reversible storage of hydrogen. All catalytic applications required thorough knowledge of reaction mechanisms and in addition to traditional methods we also planned the use of para-hydrogen and fluorescent catalysts to reveal molecular details of the reactions. Reactions with para-hydrogen are interesting in their own right since para-hydrogen induced polarization may be used advantageously in magnetic resonance imaging.

In the following we briefly describe our main results obtained in the framework of the project. When no specific reference is shown at the end of this report, please consult the list of publications available in the electronic version of the report.

II. Hydrogenations in aqueous solutions using para-hydrogen and water-soluble organometallic complexes as catalysts

Magnetic resonance imaging (MRI) is of enormous value in medical diagnosis but suffers from the low inherent sensitivity of nuclear magnetic resonance (NMR) techniques. When unsaturated substrates are hydrogenated with para-hydrogen strongly enhanced NMR signals can be obtained. Unfortunately, the hyperpolarized signal lasts only as long as the T_1 relaxation times in the molecules, therefore NMR detection of hyperpolarized ^{1}H-signals requires special techniques and fast measurements.

Following our earlier studies with $[RhCl(pta)_3]$ as catalyst in para-hydrogenation of 2-butynoic acid, where large signal amplification was observed, we used rhodium(I) complexes with bulky N-heterocyclic carbene ligands, such as [Rh(OH)(IMes)] and [Rh(OH)(iPr)] for catalysis of para-hydrogenation of propargyl alcohol in water. The polarized signals could be observed unambiguously, and their maximum lifetime was about 10 min. This lifetime is substantially longer than what is generally obtained (literature values are around 1-2 min). Water-soluble Ir-NHC-sulfonated phosphine catalysts were also used for this purpose, however, the lifetime of polarization was about 3 min, significantly shorter than those obtained with Rh(I)-NHC catalysts but still respectable in comparison to literature results.

cis,mer-$[IrH_2Cl(m\text{tppms})_3]$ which contains only sulfonated triphenylphosphine ligands was tested in para-hydrogenation of methylpropiolate in methanolic solution. In this solvent, the polarized ^{1}H-NMR signals were observed for about 5 min, however, in case of the reaction of a water-soluble substrate (propargyl alcohol) in aqueous solution polarization lifetime was shorter than 1 min.

All these results (already *communicated at conferences*) demonstrate that some of our water-soluble hydrogenation catalysts can be successfully used for inducing polarization of NMR signals by para-hydrogenation. The results were presented at national and international conferences. As a result of the project by now we possess a (home-built) equipment for generating para-H_2, and considerable expertise in quick recording of NMR spectra; these assets allow us of more detailed studies of this field in the future.

III. Fluorescent water-soluble catalysts

The primary aim of developing such complexes was to follow by fluorescence microscopy the localization of hydrogenation catalysts in the various cell membranes during fluidity modifications. In addition, fluorescent catalysts were envisaged to provide information on the mechanisms of catalytic reactions.

Unfortunately this part of the plans could not be worked out due to employment difficulties. Synthesis of fluorescent ligands and metal complex catalysts requires substantial expertise in organic synthesis. Our first co-worker has left the group and another skilled organic chemist who agreed to join the investigations finally did not take up the employment. According to the work plan we started synthesis of dansylated diamines using DsCl (5-(dimethylamino)naphtalene-1-sulfonyl chloride), however, it was not finished and the studies on this field came to a halt.

IV. Hydrogenation of carbon dioxide; storage and generation of hydrogen in aqueous solutions Specific effects in homogeneous aqueous-organic solvent mixtures in organometallic catalysis

Storage and generation of H_2 is one of the central problems of the envisaged hydrogen economy. Formic acid is regarded as one of the promising candidates for chemical hydrogen storage. HCO_2H can be catalytically decomposed to yield CO-free hydrogen suitable for use in fuel cell applications. The biggest problem with HCO_2H, however, is that CO_2 resulting from its decomposition cannot be simply rehydrogenated to HCO_2H.

We have discovered earlier that sodium formate in aqueous solutions can be decomposed to H_2 and sodium bicarbonate using an $[\{RuCl_2(m\text{tppms})_2\}_2]$ catalyst. Extensive studies by our group showed that the *same catalyst* is able to hydrogenate HCO_3Na to yield HCO_2Na. Composition and solution structure of the various hydride species formed under such conditions was established by detailed NMR measurements (*Dalton Transactions,* [1]). In the present project we synthesized several new Ir(I)-complexes containing both *N*-heterocyclic carbene and sulfonated phosphine ligands. One of these, namely [IrCl(bmim)(cod)] (bmim=1-butyl-3-methyl-imidazol-2-ylidene, cod=1,5-cyclooctadiene) in the presence of 2 mtppms showed unprecedented high activity in hydrogenation of bicarbonate and dehydrogenation of formate. As shown by Figure 1, this complex was at least 18 times more active than $[\{RuCl_2(m\text{tppms})_2\}]$ + *m*tppms, since one „charge-discharge” cycle required only approx. 65 min instead of 1200 min. Based on these results a *patent application* [2] was filed and the results were also published in *Organometallics* [3]and *ChemSusChem* [4].

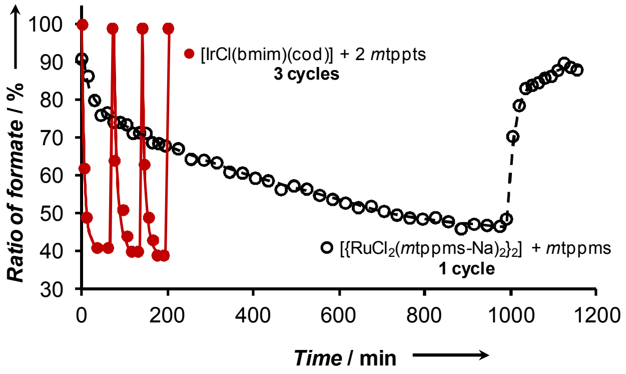

Figure 1. Reversible hydrogen storage in a formate-bicarbonate system. [Ir]=10 mM, [*m*tppts]=20 mM; [Ru]=10 mM, [*m*tppms]=42.5 mM; $[H^{13}CO_2Na]$=257 mM; $V(H_2O)$=0.5 mL; *T*=80°C.

We have also discovered that the hydrido-phosphine-Ir(I) complex, *cis-mer*-$[IrH_2Cl(m\text{tppms})_3]$ catalyzed decomposition of formic acid to $H_2 + CO_2$ with extraordinarily high activity (Figure 2) in aqueous solutions at T=30-100°C. The easily synthesized compound showed high catalytic activity (up to TOF=298 000 h^{-1}) and could be reused several times with no loss of activity (max. TON=674 000). A sharp maximum in the reaction rate was observed at pH=3.75; its coincidence with the pK_a of formic acid shows that both H^+ or HCOOH and $HCOO^-$ play important role in the reaction mechanism. The results were published in *Dalton Transactions* [5].

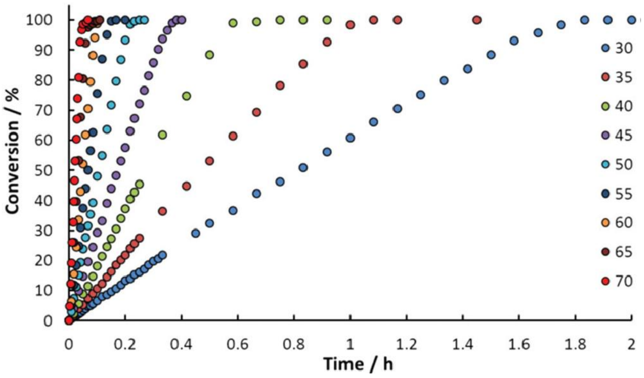

Figure 2. Catalytic dehydrogenation of formic acid catalyzed by *cis-mer*-$[IrH_2Cl(m\text{tppms})_3]$ at various temperatures. n(Ir) = 4.9×10^{-6} mol; n(HCOOH) = 3.58×10^{-3} mol; n(HCOONa) = 4.9×10^{-4} mol; V = 5.0 mL.

V. Synthesis and reactivity of new types of ligands and metal complex catalysts

In this section we describe the main results of several sub-projects carried out in accord with the general aim of the research project.

1) *Synthesis and application of water-soluble Pd-salan complexes*

One of the biggest problems with using [M(salen)] (salen = *N*,*N*'-bis(salicylidene)ethylenediamine) complexes for catalysis in aqueous media is that in general imine bonds are prone to hydrolysis. With hydrogenation of the well-known salenH_2 ligand and its analogs (with various bridging groups, X, between the imine nitrogen atoms) we obtained the corresponding saturated diamines (e.g. X = $-CH_2CH_2-$, HS; $-CH_2CH_2CH_2CH_2-$, BuHS; etc.) which proved hydrolytically stable. The latter compounds were sulfonated in oleum/cc. H_2SO_4 mixtures affording water-soluble ligands, named HSS, BuHSS, etc. These ligands were reacted with $[PdCl_4]^{2-}$ to yield the corresponding Pd(II)-complexes, [Pd(HSS)], Pd(BuHSS)], etc. The ligands and complexes were thoroughly characterized and used in aqueous-phase as catalysts in several reactions such as hydrogenation of aldehydes and ketones, hydrogenation of lipids, and redox isomerization of allylic alcohols. However, the most outstanding results were achieved in Sonogashira and Suzuki couplings. In such reactions TOF values up to 50 000 h^{-1} could be determined (depending on the reaction type, substrates and other conditions). The most appealing feature of the aqueous phase reaction is that in many cases the water-insoluble products precipitate from the aqueous reaction mixture and can be easily isolated. The results were published in *Organometallics* [6] and *ChemSusChem* [7], and another manuscript (on Suzuki couplings) is in preparation on invitation from *Green Chemistry*. They also served as basis for the PhD Thesis of Kristina Voronova (Univ. Debrecen, 2014).

2) *Selective hydration of nitriles to amides catalyzed by Ru(II)-phosphaurotropine complexes*

Catalytic hydration of nitriles often suffers from going all the way to carboxylic acids without stopping at the amide product. We have found the half-sandwich Ru(II)-complexes prepared from $[\{RuCl_2(\eta^6\text{-}p\text{-cymene})\}_2]$ (*p*-cymene = p-isopropyl toluene) and pta (1,3,5-triaza-7-phospha-adamantane), or its *N*-alkylated derivaties derivatives can be used with excellent results for selective hydration of nitriles (such as e.g. benzonitrile) to the corresponding amides. The highest catalytic activity was shown by the complex synthesized from $[\{RuCl_2(\eta^6\text{-}p\text{-cymene})\}_2]$ and *N*-benzylated pta (pta-Bn). In a study using model compounds and several catalysts the basic features and the scope of nitirle hydration were investigated, while in an other the catalysts were used for hydration of glycosyl cyanides to C-glucosyl formamides on preparative scale. Both studies were published in *Tetrahedron Letters* [8, 9].

3) *Hydrogen transfer reactions from sodium formate in water-2-propanol mixtures*

As discussed in the project proposal, hydrogenation of aldehydes from aqueous sodium formate was found to show peculiar features when the reactions were run in aqueous 2-propanol.

Our detailed investigations in the project revealed, that both [RhCl(*m*tppms)$_3$] and [{RuCl$_2$(*m*tppms)$_2$}$_2$] showed unexpectedly high catalytic activity in water-isopropanol mixtures, much higher than in neat water or isopropanol. It was unambiguously proven that in this reaction the solvent 2-propanol did not participate as hydrogen donor (despite its known ability to do so). Although the exact molecular mechanism and reason for this high activity could not be established, the use of water-isopropanol mixtures is highly advantageous from synthetic point of view. The results were published in *Catalysis Today* [10] and *Chimia* [11]. These results will make part of the PhD Thesis of Imre Szatmári (University of Debrecen, to be submitted in 2017).

4) *Catalytic hydrodehalogenation of organic halides*

Water-soluble [RuCl(NHC)(L)(η^6-arene)]X complexes (NHC = bmim = 1-butyl-3-methyl-imidazole-2-ylidene; L = tertiary phosphine, such as *m*tppms, *m*tppts, pta, pta-Me and pta-Bn; η^6-arene = η^6-*p*-cymene, X = Cl$^-$, BF$_4^-$, PF$_6^-$), see e.g. complexes on Figure 3, were successfully applied for the first time as catalysts in hydrodehalogenation of organic halides by hydrogen transfer from aqueous Na-formate with turnover frequencies up to TOF=112 h^{-1} at 80°C. This activity is among the best for homogeneous catalytic hydrodehalogenations. It was also established, that simultaneous to hydrodehalogenation, aqueous formate was also decomposed to H$_2$ and HCO$_3^-$.

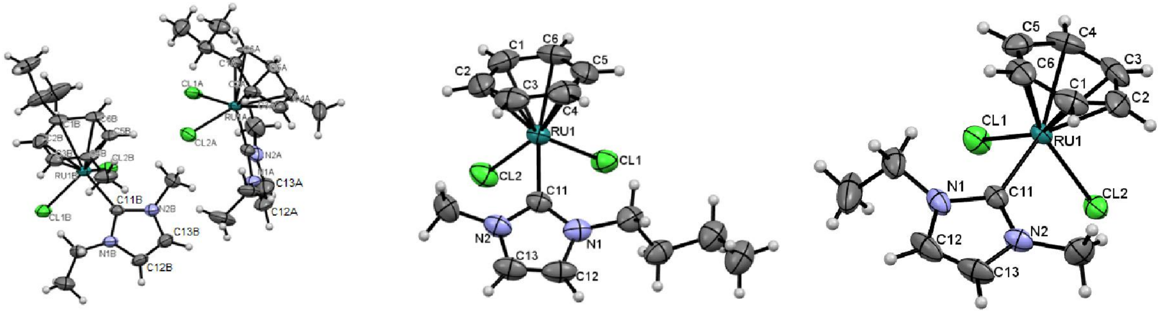

Figure 3. ORTEP diagrams of (from left to right) [RuCl$_2$(emim)(η^6-*p*-cymene)], [RuCl$_2$(bmim)(η^6-benzene)], and of [RuCl$_2$(emim)(η^6-benzene)]

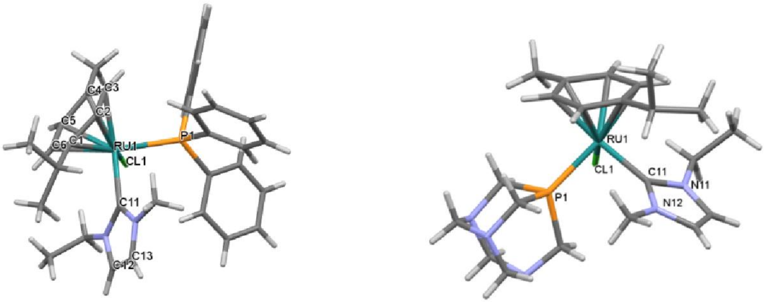

Figure 4. Capped sticks structures of [RuCl(emim)(η^6-*p*-cymene)(PPh$_3$)]$^+$ (L) and [RuCl(emim)(η^6-*p*-cymene)(pta)]$^+$ (R)

In case of [RuCl(bmim)(pta)(η^6-*p*-cymene)]Cl (pta =1,3,5-triaza-7-phosphaadamantane) a reaction mechanism was suggested on basis of kinetic and NMR measurements which accounts for both hydrodehalogenation and formate dehydrogenation and involves [RuH(bmim)(pta)(η^6-*p*-cymene]$^+$ as the key catalytic species for both cycles. The results were published in *J. Mol. Catal. A.: Chemical*

[12], and will make part of the PhD Thesis of Natália Marozsán (University of Debrecen, to be submitted in 2017).
Hydrodehalogenation of organic halides was also successfully achieved using flow systems with supported transition metal catalysts in an H-Cube hydrogenation reactor (*communicated as poster*) .

5) *Catalytic racemization of optically active secondary alcohols*
Catalytic racemizations are important steps in dynamic kinetic resolutions which yield highly enantio-enriched products. $[RuCl(NHC)(L)(\eta^6\text{-arene})]^+$-type complexes (L= tertiary phospine) (Figures 3 and 4) showed high catalytic activity in racemization of secondary alcohols. As an example, enantiopurity (ee) of (*S*)-1-phenylethanol decreased from 99,9% to 3,5% on catalysis by $[RuCl_2(NHC)(\eta^6\text{-p-cymene})]$ + PPh_3 (solvent: toluene-isopropanol 5:1, T=95°C) with formation of acetophenone byproduct with only 3,5% yield). Several new complexes of this type have been synthesized and characterized, most of them also in solid state by single crystal X-ray diffraction. Investigation of the reaction mechanism revealed transient formation of the corresponding ketones (e.g. acetophenone in case of 2-phenylethanol). It is important to suppress the accumulation of these compounds since, once released from the intermediate catalyst-substrate complex, they are only slowly hydrogenated back to the corresponding secondary alcohol. These results were *communicated at conferences* and will be part of a forthcoming paper as well as that of the PhD Thesis of Natália Marozsán.

6) *C-H activation and deuteration*
We have discovered, the the catalysts system formed from $[Ru(H_2O)_6]^{2+}$ and a chelating diphosphine (such as e.g. dppe – diphenylphosphinoethane) was able to facilitate H-D exchange on activated carbon atoms such as those in β-position to carbonyl groups. The result were *disclosed at conferences*, moreover, a *patent application* [13] was also filed.
When these experiments were done in alcohols we observed hydrogen evolution. This may also be important with regard to chemical hydrogen storage (suitable alcohols can be obtained from biomass). Nevertheless, this phenomenon needs further scrutiny.

7) *Synthetic and structural studies*
Virtual bidentate phosphorus ligands have been synthesized capitalizing on the interaction of oppositely charged tertiary phosphines such as e.g. mono-sulfonated triphenylphosphine (*m*tppms) and *N*-alkylated-pta derivatives. These compounds were used for one-step synthesis of Ru(II)-phosphine complexes containing two different phosphine ligands in reaction with $[\{RuCl_2(\eta^6\text{-}p\text{-cymene})\}_2]$.
In contrast to the general notion it was demonstrated, that pta (1,3,5-triaza-7-phosphadamantane) reacted with activated alkenes such as maleic, fumaric, itaconic acids and yielded phosphonium alkanoate zwitterions in yileds depending on the alkene structure. The compounds were thoroughly characterized and their formation was rationalized. also by DFT calculations. The results formed parts of the PhD Thesis of Antal Udvardy (University of Debrecen, 2013).
Results of this two studies were published in *Polyhedron* [14] and *Structural Chemistry* [15].

VI.
Summary

With the help of funding obtained we carried out a diverse program which, however, centered around the synthesis and reactivity of new metal complex catalysts and application of the catalyzed reactions. Some of the processes can be used with no substantial modifications in laboratory practice (C-C couplings, nitrile hydrations), others can be developed (hopefully) into practical applications (such as the chemical hydrogen storage systems or para-hydrogenations). Knowledge of the reaction mechanisms which has been in focus of all our studies is crucial for any further developments.

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