

## Theses of Doctoral (PhD) Dissertation

# SYNTHESIS AND CATALYTIC PROPERTIES OF NEW Ru(II)-*N*-HETEROCYCLIC CARBENE COMPLEXES

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## I. INTRODUCTION AND AIM OF THE WORK

The outstanding advantages of the catalysts are utilized in almost all organic synthetic processes; with their help many synthetic processes can be accelerated. In the presence of a catalyst, a chemical process takes place at a lower energy pathway, thereby with increased reaction rate. A most useful property of the catalysts is in that they are present in small amounts in the reaction mixture still are able to convert large amounts of substrates. Another useful feature of a catalyst can be its water solubility, which is mostly determined by its hydrophilic nature.

Human activity and industrial processes release a significant amount of halogen-containing compounds in to our environment. Certainly, a main impetus of research comes from the possible elimination of hazardous organic solvents (the green aspect).

Water as solvent has many attractive features in organic and organometallic chemistry. For several years, our research group has been interested in syntheses of water-soluble organometallic complexes and their catalytic applications in aqueous solutions or aqueous-organic biphasic systems.

One aim of my PhD work was to synthesize, characterize and apply as catalysts in hydrodehalogenation reaction of new Ru(II)-*N*-heterocyclic carbene catalysts. I have planned to synthesize efficient catalysts that are successfully applicable in hydrodehalogenation of organic halides by hydrogen transfer from aqueous Na-formate. Another aim was to map the catalytic cycle of hydrodehalogenation, as well as the detection of intermediates in each step.

It was a milestone of modern chemistry when the excellent complexing and catalytic properties of carbenes were discovered. Due to their versatility, the use of carbene complexes occurs today in almost every field of organometallic chemistry. *N*-heterocyclic carbenes are used in *C-C* coupling reactions, olefin metathesis, cycloadditions, hydrogenation, transfer hydrogenation, redox isomerization, hydrosilylation reactions and many more reactions.

Today, the demand for enantiomerically pure compounds is extremely high since most synthetic compounds used as pharmaceuticals contain at least one chiral center. Most of the compounds isolated from nature are in racemic form, so it is important to interchange the enantiomers to each other. The racemization is one step of the dynamic kinetic resolution (DKR) process to obtain enantiomerically pure compounds. The interchange of enantiomers to each other is one of the great

expectations of today, as it becomes increasingly important to produce optically pure compounds both in research and in industry.

In the hope that even more useful catalysts are developed, I have synthesized mixed-ligand Ru(II)-*N*-heterocyclic carbene-phosphine complexes which contain not only a carbene ligand but also a phosphine-type ligand. The structure of the Ru(II)-complexes produced was examined, in addition to the more conventional spectroscopic methods, by X-ray diffraction measurements, and the X-ray data have been compared to the characteristics of the other carbene complexes found in the literature. Furthermore, quantum mechanical calculations were performed to demonstrate the presence of possible structural isomers present in the solution.

I also wished to examine the catalytic activity of the newly synthesized Ru(II)-NHC and Ru(II)-NHC-phosphine complexes in the racemization of optically pure secondary alcohols, including determination of the optimal reaction conditions of the catalytic process (temperature, reaction time, solvent composition). Formation of ketones during racemization leads to a loss of the often expensive secondary alcohol substrate and it is therefore desirable to keep it to a minimum level. It seemed reasonable to change the composition of the solvent, in order to reduce the formation of this unwanted by-product in the process. Additionally, DFT calculations were performed to investigate the mechanism of the catalytic racemization of (*S*)-1-phenylethanol and to identify the resulting intermediates.

## II. EXPERIMENTAL SECTION

All new complexes were characterized by elemental analysis,  $^1\text{H}$ ,  $^{13}\text{C}$ , and  $^{31}\text{P}$  NMR spectroscopies, ESI MS spectrometry and single crystal X-ray diffraction.

$^1\text{H}$ ,  $^{13}\text{C}$ , and  $^{31}\text{P}$  NMR spectra were recorded by Bruker 360 MHz, Bruker 400MHz and Bruker Avance II 500 MHz NMR spectrometers and referenced to DSS (4,4-dimethyl-4-silapentane-1-sulfonic acid sodium salt), TMS (tetramethylsilane), 85% phosphoric acid, and residual solvent peaks, respectively. All spectra were processed and evaluated with TopSpin 3.5 (Bruker Biospin GmbH, Karlsruhe, Germany).

Elemental analysis data were determined by using an Elementar Vario Micro (CHNS) equipment. The measurements were performed by Dr. Attila Kiss (University of Debrecen, Department of Organic Chemistry). ESI-MS data were collected by Dr. Tibor Nagy (University of Debrecen, Department of Applied Chemistry) on a BRUKER BioTOF II ESI-TOF spectrometer in positive ion mode.

X-ray diffraction data for  $[\text{RuCl}_2(\text{emim})(\eta^6\text{-}p\text{-cymene})]$  (**4**) and  $[\text{RuCl}(\text{emim})(\eta^6\text{-}p\text{-cymene})(\text{pta})]\text{BF}_4$  (**8.BF<sub>4</sub>**) were collected by Dr. Attila Bényei (University of Debrecen, Department of Physical Chemistry) on a Bruker-Nonius MACH3 diffractometer using graphite-monochromated Mo- $K\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ) with the  $\omega$ -scan. Diffraction intensity data collection of  $[\text{RuCl}(\text{emim})(\eta^6\text{-}p\text{-cymene})(\text{PPh}_3)]\text{PF}_6$  (**7.PF<sub>6</sub>**) was carried out on a Rigaku-Oxford SuperNova diffractometer equipped with an Atlas detector using Cu- $K\alpha$  radiation ( $\lambda = 1.5418 \text{ \AA}$ ) by Dr. Éva Kováts (Hungarian Academy of Sciences, Institute for Solid State Physics and Optics, Wigner Research Centre for Physics, Budapest). Data for  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-C}_6\text{H}_6)]$  (**5**) and  $[\text{RuCl}_2(\text{emim})(\eta^6\text{-C}_6\text{H}_6)]$  (**6**) were measured on a Bruker D8 VENTURE system equipped with a multilayer optics monochromator and a Cu  $I\mu\text{S}$  3.0 Microfocus source ( $\lambda = 1.54184 \text{ \AA}$ ). All structures were solved by the SIR-92 program and refined by full-matrix least-squares method on  $F^2$  with the help of Dr. Antal Udvardy (University of Debrecen, Department of Physical Chemistry). Non-hydrogen atoms were refined with anisotropic thermal parameters using the SHELXL package. Publication material was prepared using the WINGX suite, publCIF and the Mercury program.

Geometry optimizations were carried out by Dr. Mihály Purgel (University of Debrecen, Department of Physical Chemistry) using DFT method and B3LYP functional. The reported relative energies in this work are derived from the calculated zero-point corrected electronic energies of the corresponding structures. For the

ruthenium atom CRENBL ECP and the related basis sets while for the non metal atoms 6-31G\* basis sets were applied. Gaussian 09's default IEF-PCM solvent model was used in all cases to account for the effect of dichloromethane. All calculations were performed using the D.01 revision of Gaussian 09 software package.

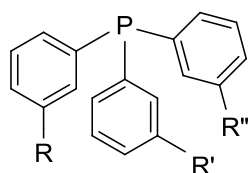
Hydrodehalogenation reactions were run with catalysts prepared in situ from [RuCl<sub>2</sub>(bmim)( $\eta^6$ -*p*-cymene)] (**3**) and the appropriate phosphine ligand. The reactions were run under argon at constant temperature either in Schlenk tubes (atmospheric pressure) or in home made thick-wall glass reactors (reactions under pressure). Gas chromatographic analysis of hydrodehalogenation reaction mixtures were done by using an Agilent 7890A equipment (automatic injector; column: MN Optima<sup>®</sup> -1, 0.25  $\mu$ m x 30 m x 0.32 mm; carrier gas: N<sub>2</sub>; injector at 280°C; FID at 300°C). Sensitivity of the detector for all substrates and their dehalogenation products was calibrated using naphthalene as internal standard.

All racemizations reactions were run under argon in Schlenk flasks. Gas chromatography of the enantiomer mixtures was carried out using an HP5890 chromatograph, equipped with a CP-Chirasil-Dex CB, 25 m x 0.32 mm x 0.25  $\mu$ m column and FID. Parameters of the analysis: v(Ar)= 1.4 mL/min; column temperature 110°C; temperature of injector and detector 250°C. Data acquisition and processing was done by using the Agilent Data System program.

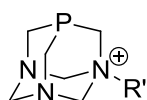
### III. LIST OF ABBREVIATIONS

<b><math>\alpha</math>-terpinene</b>	1-isopropyl-4-methyl-1,3-cyclohexadiene
<b>bmim.HCl</b>	1-butyl-3-methyl-imidazolium chloride
<b>CD<sub>2</sub>Cl<sub>2</sub></b>	deuterodichloromethane
<b>CD<sub>3</sub>Cl</b>	deuteriochloroform
<b>D<sub>2</sub>O</b>	heavy water; deuterium oxide
<b>DFT</b>	density functional theory
<b>DKR</b>	dynamic kinetic resolution
<b>DSS</b>	4,4-dimethyl-4-silapentane-1-sulfonic acid
<b>E<sub>a</sub></b>	activation energy
<b>ee%</b>	enantiomeric excess
<b>emim.HCl</b>	1-ethyl-3-methylimidazolium chloride
<b>ESI-MS</b>	electrospray ionization mass spectrometry
<b>FID</b>	flame ionization detector
<b>I</b>	intermediate
<b>IEF-PCM</b>	Integral equation formalism-polarizable continuum model
<b>IMes.HCl</b>	1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride
<b>L</b>	general ligand
<b>M</b>	general metal atom
<b>mtpmps</b>	monosulfonated triphenylphosphine
<b>mtppts</b>	trisulfonated triphenylphosphine
<b>m/Q</b>	mass-to-charge ratio
<b>NHC</b>	N-heterocyclic carbene
<b>NMR</b>	Nuclear Magnetic Resonance
<b>ORTEP</b>	Oak Ridge Thermal Ellipsoid Plot
<b>P</b>	pressure
<b>p-cymene</b>	4-isopropyltoluene; 1-methyl-4-isopropylbenzene
<b>PPh<sub>3</sub></b>	triphenylphosphine
<b>ppm</b>	parts per million
<b>PR<sub>3</sub></b>	tertiary phosphine ligand
<b>pta</b>	1,3,5-triaza-7-phosphaadamantane; 1,3,5-triaza-7-phosphatricyclo[3.3.1.1] <sup>3,7</sup> decane
<b>pta-Me</b>	methyl-pta
<b>pta-Bn</b>	benzyl-pta

<b>R</b>	general alkyl group
<b>SIMes.HCl</b>	1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride
<b>t</b>	reaction time
<b>T</b>	temperature
<b>TOF</b>	turnover frequency, (mol reacted substrate)×(mol catalyst×time) <sup>-1</sup> )
<b>TON</b>	turnover number, ratio (mol reacted substrate)/(mol catalyst)
<b>TS</b>	Transition State



*mtppts*: R=R'=R''= SO<sub>3</sub><sup>-</sup>  
*mtpms*: R= SO<sub>3</sub><sup>-</sup>, R'=R''=H



*pta*: R'= -  
*pta-Me*: R'= -CH<sub>3</sub>  
*pta-Bn*: R'= -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>

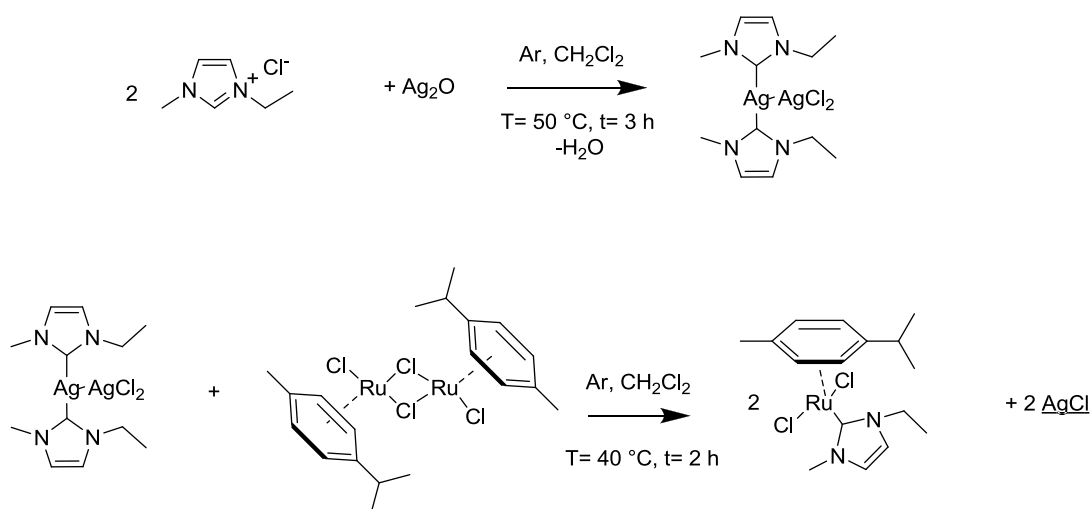
**Figure 1.** Water-soluble phosphines used in this study



## IV. NEW SCIENTIFIC ACHIEVEMENTS

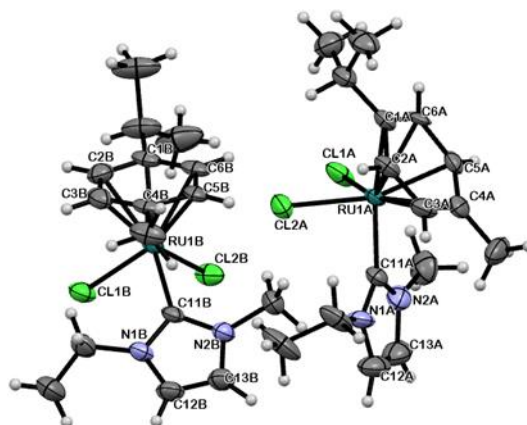
**1. Three new complexes of the type  $[\text{RuCl}_2(\text{NHC})(\eta^6\text{-arene})]$  (**4**, **5**, and **6**) (NHC=*N*-heterocyclic carbene=bmim, emim; arene=benzene, *p*-cymene) were synthesized and characterized (elemental analysis, various spectroscopic methods, single crystal X-ray diffractometry).**

I have synthesized three new ruthenium(II) complexes with the general composition of  $[\text{RuCl}_2(\text{NHC})(\eta^6\text{-arene})]$  (**4-6**; NHC=bmim or emim; arene=benzene or *p*-cymene). The syntheses of **4-6** involved carbene transfer to  $[\{\text{RuCl}_2(\eta^6\text{-arene})\}_2]$  from the appropriate  $[\text{Ag}(\text{NHC})_2][\text{AgCl}_2]$  complex obtained in reaction of  $\text{Ag}_2\text{O}$  and the respective imidazolium chloride. All new complexes were characterized by elemental analysis,  $^1\text{H}$ ,  $^{13}\text{C}$ -NMR spectroscopies, ESI MS spectrometry and single crystal X-ray diffraction. The general reaction scheme of the synthesis is presented by the example of  $[\text{RuCl}_2(\text{emim})(\eta^6\text{-}p\text{-cymene})]$  (**4**), which is shown in Figure 2.



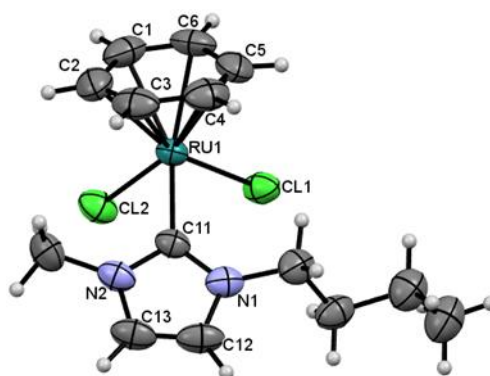
**Figure 2.** Synthesis of  $[\text{RuCl}_2(\text{emim})(\eta^6\text{-}p\text{-cymene})]$  (**4**) complex by silver-carbene transfer method

The product can be recrystallized from  $\text{CH}_2\text{Cl}_2$  by layering hexane on top of the solution; crystals for single crystal X-ray diffraction measurements were also obtained using this procedure. ORTEP diagram for **4** can be seen on Figure 3.

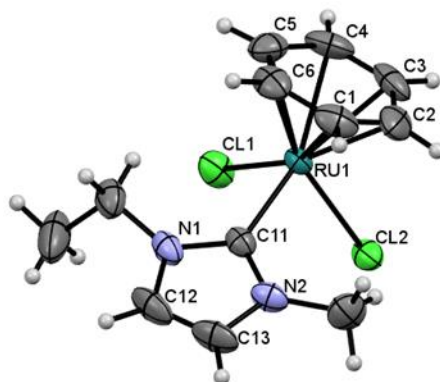


**Figure 3.** ORTEP diagram of [RuCl<sub>2</sub>(emim)(η<sup>6</sup>-*p*-cymene)] (**4**) with thermal ellipsoids shown at 30% probability level

Two additional new carbene complexes have been synthesized analogously to the [RuCl<sub>2</sub>(emim)(η<sup>6</sup>-*p*-cymene)] (**4**) complex. The molecular structure of the [RuCl<sub>2</sub>(bmim)(η<sup>6</sup>-benzene)] (**5**) is shown on Figure 4; the [RuCl<sub>2</sub>(emim)(η<sup>6</sup>-benzene)] (**6**) complex is shown on Figure 5.



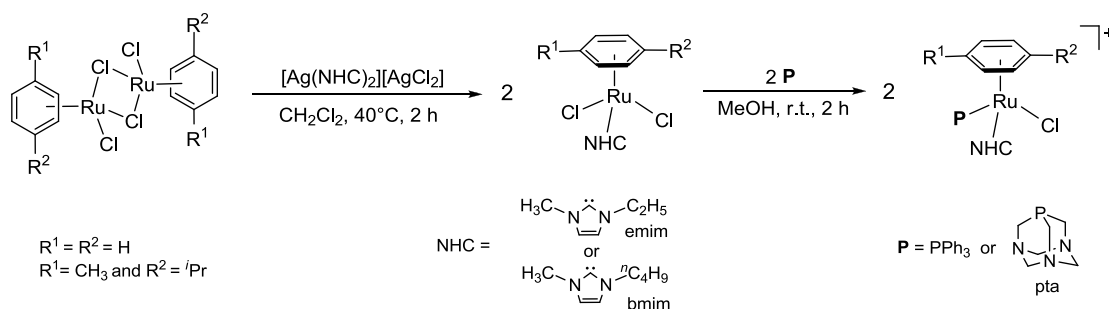
**Figure 4.** ORTEP diagram of [RuCl<sub>2</sub>(bmim)(η<sup>6</sup>-benzene)] (**5**) with thermal ellipsoids shown at 50% probability level



**Figure 5.** ORTEP diagram of  $[\text{RuCl}_2(\text{emim})(\eta^6\text{-benzene})]$  (**6**) with thermal ellipsoids shown at 50% probability level

## 2. Three new, mixed-ligand ruthenium(II)-*N*-heterocyclic carbene-phosphine complexes were synthesized.

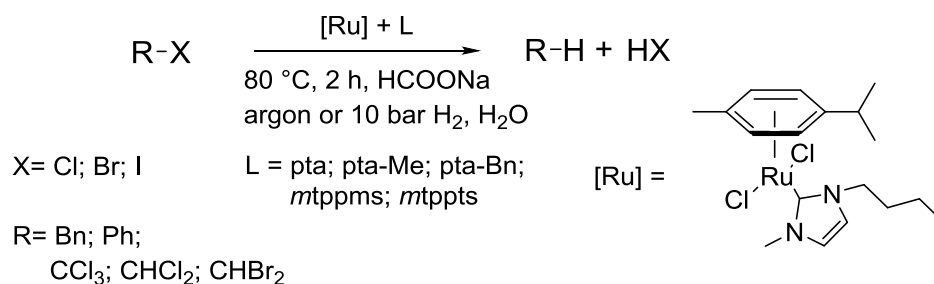
I have synthesized three new ruthenium(II) complexes with the general composition of  $[\text{RuCl}(\text{NHC})(\eta^6\text{-}p\text{-cymene})(\text{PR}_3)]\text{Cl}$  (**7**, **8**, **9**; NHC=bmim or emim;  $\text{PR}_3 = \text{PPh}_3$  or pta). For crystallographic purposes  $\text{PF}_6^-$  salt of **7** (**7.PF<sub>6</sub>**) was also obtained while **8** could be crystallized only as a  $\text{BF}_4^-$  salt (**8.BF<sub>4</sub>**). The NHC-phosphine complexes were prepared by substitution of one chloride ligand in  $[\text{RuCl}_2(\text{NHC})(\eta^6\text{-}p\text{-cymene})]$  by triphenylphosphine and 1,3,5-triaza-7-phosphatricyclo[3.3.1.1]<sup>3,7</sup>decane (pta), respectively (Figure 6). All new complexes were characterized by elemental analysis,  $^1\text{H}$ ,  $^{13}\text{C}$ , and  $^{31}\text{P}$  NMR spectroscopies, ESI MS spectrometry and single crystal X-ray diffraction.



**Figure 6.** Synthesis of new Ru(II)-NHC and Ru(II)-NHC-phosphine complexes

**3. Water-soluble [RuCl(NHC)(L)( $\eta^6$ -arene)] complexes were successfully applied for the first time as catalysts in hydrodehalogenation of organic halides.**

Water-soluble [RuCl(NHC)(L)( $\eta^6$ -arene)] complexes (NHC = bmim = 1-butyl-3-methyl-imidazole-2-ylidene; L = tertiary phosphine, such as *mtp*ppms, *mtp*ppts, *pta*, *pta*-Me and *pta*-Bn;  $\eta^6$ -arene =  $\eta^6$ -*p*-cymene) were successfully applied for the first time as catalysts in hydrodehalogenation of organic halides by hydrogen transfer from aqueous Na-formate (Figure 7). As yet, no similar half-sandwich Ru(II)-NHC complexes have been applied for catalytic hydrogenolysis of C-X (X = halogen) bonds in water.



**Figure 7.** General scheme of hydrodehalogenation of organic halides

In aqueous systems, **3** is known to dissociate chloride to yield [RuCl(H<sub>2</sub>O)(bmim)( $\eta^6$ -*p*-cymene)]<sup>+</sup> in which the aqua ligand can be easily displaced by phosphines. The various [RuCl(bmim)(L)( $\eta^6$ -*p*-cymene)] complexes formed in situ in the reaction of **3** with L = *mtp*ppms, *mtp*ppts, *pta*, *pta*-Me or *pta*-Bn were active in catalysis of hydrodehalogenation of various organic halides (Figure 7). Data for dehalogenation of chloroform are given in Table 1.

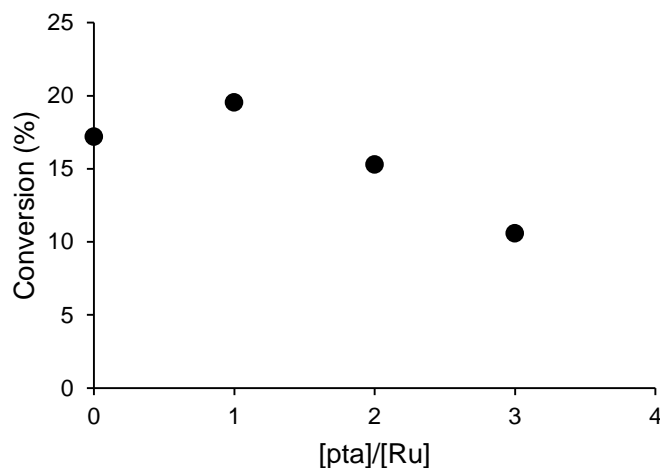
**Table 1.** Hydrodehalogenation of  $\text{CHCl}_3$  with aqueous Na-formate catalyzed by **3** and by the  $[\text{RuCl}(\text{bmim})(\text{L})(\eta^6\text{-}p\text{-cymene})]$  complexes formed in situ in the reaction of **3** with L.

	L	Conversion (%)	TOF ( $\text{h}^{-1}$ )
1 <sup>a, b</sup>	pta	0	0
2	-	17.2	8.5
3 <sup>a</sup>	pta	19.6	9.8
4 <sup>a</sup>	pta-Bn	13.9	6.9
5	pta-Me	7.6	3.8
6	mtppps	25.8	12.9
7	mtppts	11.7	5.8

*Conditions:* 1.0 mmol  $\text{CHCl}_3$ ; 2.0 mmol  $\text{HCOONa}$ ; 0.01 mmol  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})]$  (**3**); 0.01 mmol L; solvent = 1 mL  $\text{H}_2\text{O}$ ;  $P(\text{H}_2) = 10$  bar;  $T = 80^\circ\text{C}$ ;  $t = 2$  h. <sup>a</sup> argon atmosphere (1 bar); <sup>b</sup> without **3**

#### 4. Optimum conditions were established for hydrodehalogenation of organic halides by hydrogen transfer from aqueous Na-formate.

The effect of the  $[\text{pta}]/[\text{Ru}]$  ratio on the activity of the catalyst is shown on Figure 8. The highest activity was observed with a  $[\text{pta}]/[\text{Ru}] = 1/1$  ratio, and this refers to the involvement of the known  $[\text{RuCl}(\text{bmim})(\text{pta})(\eta^6\text{-}p\text{-cymene})]^+$  mixed NHC-phosphine complex among the most important catalytic species.



**Figure 8.** Hydrodehalogenation of  $\text{CHCl}_3$  by aqueous Na-formate; effect of the  $[\text{pta}]/[\text{Ru}]$  ratio on the activity of the catalyst formed in situ from  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})]$  and pta

*Conditions:* 1.0 mmol  $\text{CHCl}_3$ ; 2.0 mmol  $\text{HCOONa}$ ; 0.01 mmol  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})]$  (**3**); solvent = 1 mL  $\text{H}_2\text{O}$ ; argon atmosphere (1 bar);  $T = 80^\circ\text{C}$ ;  $t = 2$  h.

On increasing the temperature the reaction rate increased exponentially. Conversions in the first 2 h represent well the initial rates of  $\text{CHCl}_3$  dehalogenations and the data gave a good linear Arrhenius plot ( $R^2 = 0.999$ ) allowing calculation of a formal activation energy of  $E_a=64.0$  kJ/mol.

Table 2 summarizes the results of the hydrodehalogenation of various organic halides with the  $[\text{RuCl}(\text{bmim})(\text{pta})(\eta^6\text{-}p\text{-cymene})]^+$  catalyst in aqueous formate solutions.

**Table 2.** Hydrodehalogenation of organic halides with aqueous Na-formate catalyzed by the mixed-ligand NHC-phosphine complex formed in situ from  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})]$  and pta.

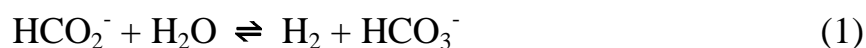
	Substrate	t (h)	Atmosphere	Conversion (%)	Products (%)
1	$\text{CCl}_4$	2	Ar	29.7	$\text{CHCl}_3(18.0)+\text{CH}_2\text{Cl}_2(11.7)$
2	$\text{CCl}_4$	2	$\text{H}_2$	41.9	$\text{CHCl}_3(29.0)+\text{CH}_2\text{Cl}_2(12.9)$
3	$\text{CHCl}_3$	2	Ar	19.6	$\text{CH}_2\text{Cl}_2$
4	$\text{CHCl}_3$	2	$\text{H}_2$	21.6	$\text{CH}_2\text{Cl}_2$
5	$\text{CHBr}_3$	2	Ar	77.6	$\text{CH}_2\text{Br}_2$
6	$\text{CHBr}_3$	2	$\text{H}_2$	66.4	$\text{CH}_2\text{Br}_2$
7	PhBr	2	Ar	0.7	Benzene
8	PhCl	19	Ar	1.7	Benzene
9	PhBr	19	Ar	7.4	Benzene
10	PhI	19	Ar	26.5	Benzene

*Conditions:* 1.0 mmol substrate; 2.0 mmol  $\text{HCOONa}$ ; 0.01 mmol  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})]$  (**3**); 0.01 mmol pta; solvent = 1 mL  $\text{H}_2\text{O}$ ;  $T = 80^\circ\text{C}$ ;  $P(\text{Ar}) = 1$  bar;  $P(\text{H}_2) = 10$  bar.

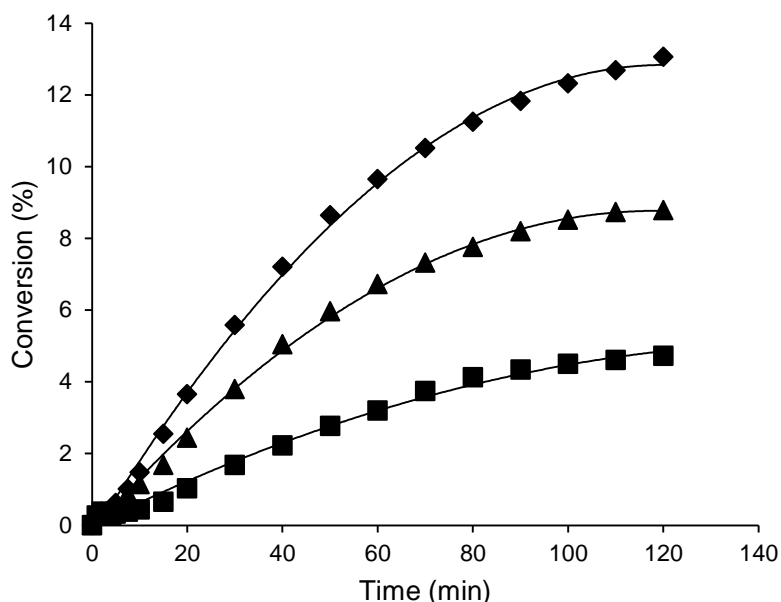
Compared with the data in the literature, the  $[\text{RuCl}(\text{bmim})(\eta^6\text{-}p\text{-cymene})(\text{pta})]^+$  catalyst has outstanding activity in the hydrodehalogenation reaction of halogen containing compounds.

**5. It was established that under the reaction conditions of dehalogenation but in the absence of an organic halide,  $[\text{RuCl}(\text{bmim})(\text{pta})(\eta^6\text{-}p\text{-cymene})]^+$  catalyzed the formation of  $\text{H}_2$  from aqueous formate.**

A possible explanation of incomplete conversions of organic halides is in the catalytic decomposition of formate to  $\text{H}_2$  and  $\text{HCO}_3^-$  (Eq. 1) concomitant to dehalogenation.



Indeed, I have found that under the reaction conditions of dehalogenation but in the absence of an organic halide,  $[\text{RuCl}(\text{bmim})(\text{pta})(\eta^6\text{-}p\text{-cymene})]^+$  catalyzed the formation of  $\text{H}_2$  from aqueous formate - the reaction could be followed by using an atmospheric gas burette (Figure 9).



**Figure 9.** Time-course of  $\text{H}_2$  evolution in decomposition of aqueous  $\text{HCO}_2^-$  catalyzed by  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})] + \text{pta}$  at various temperatures

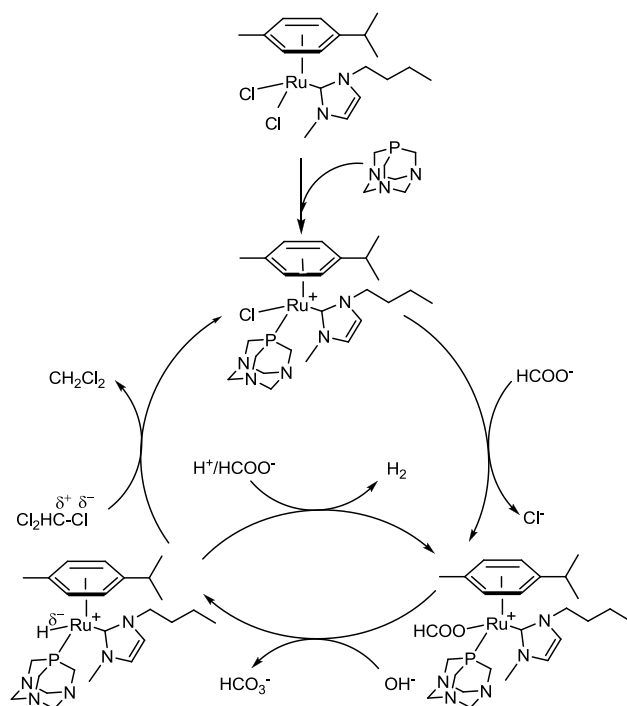
*Conditions:* 0.01 mmol  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})]$  (**3**); 0.01 mmol pta; 2.0 mmol  $\text{HCOONa}$ ; solvent = 1 mL  $\text{H}_2\text{O}$ ;  $T = 70^\circ\text{C}$  (■),  $75^\circ\text{C}$  (▲) and  $80^\circ\text{C}$  (◆); initial atmosphere: argon (1 bar).

The results show that 13% of the initial formate decomposed in 2 h at  $80^\circ\text{C}$ . The initial rates of  $\text{H}_2$  evolution at temperatures were determined from the slopes of the linear parts of the graphs in the 15-40 min intervals (Figure 9). An Arrhenius-plot of these data yielded an activation energy of  $E_a = 119 \text{ kJ/mol}$ .

**6. A reaction mechanism is suggested for both hydrodehalogenation and formate dehydrogenation and involves  $[\text{RuH}(\text{bmim})(\text{pta})(\eta^6\text{-}p\text{-cymene})]^+$  as the key catalytic species for both cycles.**

In case of  $[\text{RuCl}(\text{bmim})(\text{pta})(\eta^6\text{-}p\text{-cymene})]\text{Cl}$  a reaction mechanism is suggested on basis of kinetic and NMR measurements which accounts for both hydrodehalogenation and formate dehydrogenation and involves

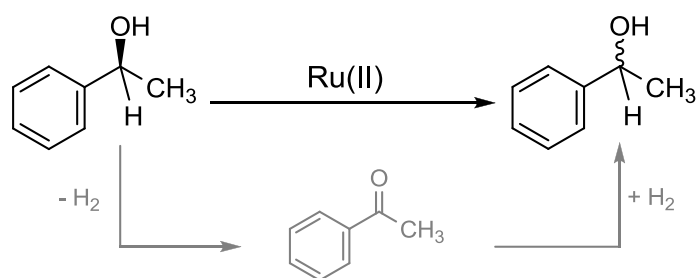
$[\text{RuH}(\text{bmim})(\text{pta})(\eta^6\text{-}p\text{-cymene})]^+$  as the key catalytic species for both cycles. The mechanism can be seen on Figure 10.



**Figure 10.** Suggested mechanism of hydrodehalogenation of organic halides and concomitant dehydrogenation of aqueous formate catalyzed by the  $[\text{RuCl}_2(\text{bmim})(\eta^6\text{-}p\text{-cymene})] + \text{pta}$  catalyst

## 7. The new Ru(II)-N-heterocyclic carbene catalysts showed good catalytic activity in racemization of optically active secondary alcohols.

The new half-sandwich (arene)Ru(II)-NHC and (arene)Ru(II)-NHC-phosphine complexes were studied as catalysts in racemization of (*S*)-1-phenylethanol (Figure 11).



**Figure 11.** Racemization of (*S*)-1-phenylethanol



Table 3 shows the results of catalytic racemizations with various Ru(II)-NHC complexes. Previously known complexes, such as *eg* **1** or **3** were also applied as catalysts.

**Table 3.** Catalytic activity of Ru(II)-(NHC) complexes in racemization of (*S*)-1-phenylethanol.<sup>a</sup>

Catalyst	Added ligand	<i>ee.</i> (%)	Acetophenone (%)
1 none	-	99.9	0
2 [ $\{\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\}_2$ ] <b>1</b>	-	96.5	4.9
3 [ $\{\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\}_2$ ] <b>1</b>	2 PPh <sub>3</sub>	77.6	9.5
4 [ $\{\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\}_2$ ] <b>1</b>	2 IMes.HCl	52.7	8.4
5 [ $\{\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\}_2$ ] <b>1</b>	2 SIMes.HCl	53.3	17.5
6 [ $\{\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\}_2$ ] <b>1</b>	2 bmim.HCl	4.1	20.6
7 [RuCl <sub>2</sub> (bmim)( $\eta^6\text{-}p\text{-cymene}$ )] <b>3</b>	-	18.5	16.0
8 [RuCl <sub>2</sub> (bmim)( $\eta^6\text{-}p\text{-cymene}$ )] <b>3</b>	PPh <sub>3</sub>	1.3	20.4
9 [RuCl <sub>2</sub> (bmim)( $\eta^6\text{-}p\text{-cymene}$ )] <b>3</b>	PPh <sub>3</sub>	3.4	3.5 <sup>b</sup>
10 [RuCl <sub>2</sub> ( $\eta^6\text{-}p\text{-cymene}$ )(pta)]	-	89.1	4.6 <sup>c</sup>
11 [RuCl <sub>2</sub> (bmim)( $\eta^6\text{-}p\text{-cymene}$ )] <b>3</b>	pta	84.3	3.7 <sup>c</sup>
12 [RuCl <sub>2</sub> (emim)( $\eta^6\text{-}p\text{-cymene}$ )] <b>4</b>	-	24.7	9.7 <sup>d</sup>
13 [RuCl <sub>2</sub> (emim)( $\eta^6\text{-}p\text{-cymene}$ )] <b>4</b>	-	47.1	2.4 <sup>b</sup>
14 [RuCl(emim)( $\eta^6\text{-}p\text{-cymene}$ )(PPh <sub>3</sub> )]Cl <b>7</b>	-	28.7	5.3 <sup>b</sup>
15 [RuCl(emim)( $\eta^6\text{-}p\text{-cymene}$ )(pta)]Cl <b>8</b>	-	20.5	4.8 <sup>b</sup>
16 [RuCl <sub>2</sub> (bmim)( $\eta^6\text{-benzene}$ )] <b>5</b>	-	78.4	2.1 <sup>e</sup>
17 [RuCl <sub>2</sub> (emim)( $\eta^6\text{-benzene}$ )] <b>6</b>	-	84.7	1.6 <sup>e</sup>

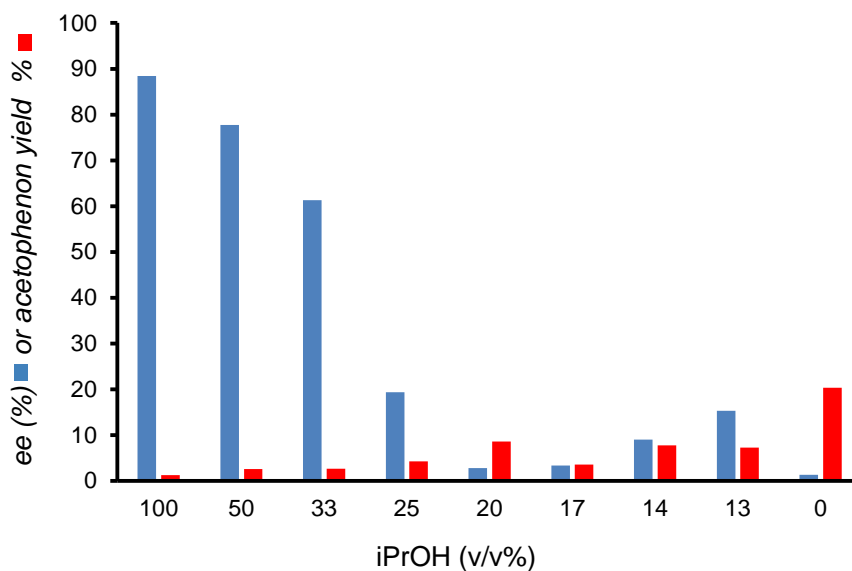
**Conditions:** <sup>a</sup>c(catalyst) = 0.01 M; c(ligand) = 0.01 M; c(*S*)-1-phenylethanol = 0.252 M; c(HCOONa) = 0.1 M; solvent = 2 mL toluene; t = 4 h; T=95 °C; <sup>b</sup>solvent=toluene:isopropanol = 5:1; <sup>c</sup>solvent=1 mL toluene + 1 mL H<sub>2</sub>O; <sup>d</sup>solvent=2 mL CH<sub>2</sub>Cl<sub>2</sub>; <sup>e</sup>solvent=1 mL H<sub>2</sub>O + 1 mL (toluene:isopropanol = 5:1). IMes.HCl=(1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride), SIMes.HCl= (1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride).

Based on the results, it was found that newly synthesized Ru(II)-*N*-heterocyclic carbene catalysts showed good catalytic activity in the racemization reaction of secondary alcohols.

### 8. The formation of acetophenone byproduct was suppressed to 3.5% by 17% *v/v* isopropanol in toluene.

Formation of ketones during racemization leads to a loss of the often expensive secondary alcohol substrate and it is therefore desirable to keep it to a minimum

level. I have found that in case of (arene)Ru(NHC)-phosphine catalysts this can be achieved by proper choice of the solvent. Indeed, addition of isopropanol into reaction mixtures of (*S*)-1-phenylethanol racemization with **3** + PPh<sub>3</sub> catalyst, effectively suppressed acetophenone formation (Figure 12). The best results were obtained with a toluene:isopropanol 5:1 solvent which led to acetophenone formation as low as 3.5%, while racemization was still close to complete (*ee*=3.4%).

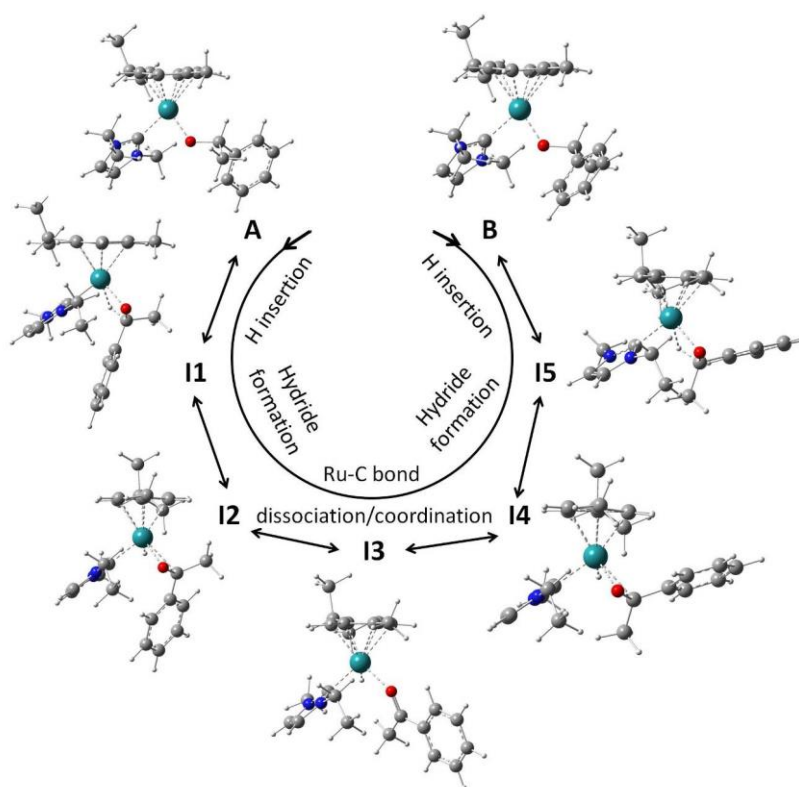


**Figure 12.** Solvent effect on racemization of (*S*)-1-phenylethanol (■) and concomitant formation of acetophenone (■) catalyzed by [RuCl<sub>2</sub>(bmim)(η<sup>6</sup>-*p*-cymene)] (**3**) + PPh<sub>3</sub>

*Conditions:* c(**3**) = 0.01 M; c(PPh<sub>3</sub>) = 0.01 M; c((*S*)-1-phenylethanol) = 0.252 M; c(HCOONa) = 0.1 M; solvent = 2 mL; t = 4 h; T = 95 °C.

## 9. Using DFT calculations the mechanism of racemization of (*S*)-1-phenylethanol was suggested.

DFT calculations on the possible reaction mechanism suggested the key role of an [Ru(NHC)(η<sup>6</sup>-arene)]<sup>2+</sup> species in the catalytic cycle. The suggested multistep process is shown on Figure 13.



**Figure 13.** Transition state (TS) geometries and intermediates (I) along the mechanistic pathway of racemization of (*S*)-1-phenylethanol catalyzed by [RuCl(emim)(η<sup>6</sup>-*p*-cymene)(PPh<sub>3</sub>)]Cl (7)

DFT calculations revealed that the rate determining step in the suggested reaction mechanism was the agostic coordination of hydrogen on the chiral carbon atom of the alcohol substrate.

## **V. POSSIBLE APPLICATIONS OF THE RESULTS**

Involved in the dynamically developing chemistry of carbene complexes, new carbene and carbene-phosphine mixed-ligand Ru(II)-arene type semi-sandwich complexes have been synthesized, whose structures have been characterized and proved by several spectroscopic and diffraction methods. Certain complexes exhibited good catalytic properties in various catalytic processes. Water-soluble [RuCl(NHC)(L)( $\eta^6$ -arene)] complexes were successfully applied for the first time as catalysts in hydrodehalogenation of organic halides by hydrogen transfer from aqueous Na-formate. As yet, no similar half-sandwich Ru(II)-NHC complexes have been applied for catalytic hydrogenolysis of C-X (X = halogen) bonds in water. This result can be of environmental significance because the hydrodehalogenation was performed with consideration of the principles of green chemistry: without using any organic solvents, only water.

These complexes showed good catalytic activity in racemization of optically active secondary alcohols. In the catalytic process, we have found several interesting results that could be useful for others in investigations of the racemization of alcohols and other organic molecules. Since production of enantiopure compounds is of paramount importance in research and industrial production, our findings may contribute to discovery and production of active pharmaceutical ingredients.

## VI. TUDOMÁNYOS PUBLIKÁCIÓK/LIST OF PUBLICATIONS

### *Az értekezés témájához kapcsolódó közlemények/ Publications related to the dissertation*

*Angol nyelvű közlemények nemzetközi folyóiratban/English articles in international journals:*

1. Natália Marozsán, Henrietta Horváth, Anikó Erdei, Ferenc Joó: **Dehalogenation of organic halides in aqueous media by hydrogen transfer from formate catalyzed by water-soluble Ru(II)-N-heterocyclic carbene complexes** *Journal of Molecular Catalysis A: Chemical*, 425, 103-109, **2016** (IF. (2016): 4,211)
2. Natália Marozsán, Henrietta Horváth, Éva Kováts, Antal Udvardy, Anikó Erdei, Mihály Purgel, Ferenc Joó: **Catalytic racemization of secondary alcohols with new (arene)Ru(II)-NHC and (arene)Ru(II)-NHC-tertiary phosphine complexes** *Molecular Catalysis*, 445, 248-256, **2018** (IF. (2016): 4,211)

### *Az értekezés témakörében tartott előadások/ Lectures related to the dissertation*

1. Marozsán Natália: Királis alkoholok racemizációjának vizsgálata Ru(II)-komplex katalizátorokkal, „*Kiemelkedő tudományos diákköri munkák a DE TTK-n*”, DAB-TTK-TDK konferencia, 2012. április 27., Debrecen, Magyarország
2. Marozsán Natália: Királis alkoholok racemizációjának vizsgálata Ru(II)-komplex katalizátorokkal, *2012.évi Kari Tudományos Diákköri Konferencia*, 2012. május 17., Debrecen, Magyarország
3. Horváth Henrietta, Szikszai Dorina, Erdei Anikó, Marozsán Natália, Kathó Ágnes, Joó Ferenc: Application of new iridium and ruthenium complexes in homogeneous catalytic reactions, *46. Komplexkémiái Kollokvium*, 2012. május 21-23, Mátrafüred, Magyarország (38. oldal)
4. Marozsán Natália, Joó Ferenc: Királis alkoholok racemizációjának vizsgálata Ru(II)-komplex katalizátorokkal, *XXXV. Kémiai Előadói Napok*, 2012. október 29-31, Szeged, Magyarország (129. oldal)

5. Joó Ferenc, Czégéni Csilla Enikő, Voronova Krisztina, Bunda Szilvia, Homolya Levente, Erdei Anikó, Marozsán Natália: Új eredmények a vizes közegű fémorganikus katalízisben, 49. *Komplekxkémiai Kollokvium*, 2015. május 26-28, Siófok, Magyarország (E17)

6. Marozsán Natália, Dr. Horváth Henrietta, Erdei Anikó, Prof. Dr. Joó Ferenc: Ru(II)-NHC komplexek katalitikus alkalmazása, *XXI. Nemzetközi Vegyészkonferencia 2015 (21<sup>th</sup> International conference on chemistry)*, 2015. szeptember 23-27, Csíksomlyó, Románia (49. oldal)

***Az értekezés témakörében bemutatott posztterek/ Poster presentations related to the dissertation***

1. Henrietta Horváth, Natália Marozsán, Anikó Erdei, Gábor Papp, Ferenc Joó: Catalytic application of new iridium and ruthenium complexes in racemization of alcohols, *18th International Symposium on Homogeneous Catalysis (ISHC-18)*, 2012. július 9-13., Toulouse, Franciaország (Book of abstracts P084)

2. Henrietta Horváth, Natália Marozsán, Anikó Erdei, Gábor Papp, Ferenc Joó: Catalytic application of new iridium and ruthenium complexes in racemization of alcohols, *XXV. International Conference on Organometallic Chemistry (ICOMC25)*, 2012. szeptember 2-7., Lisszabon, Portugália (Book of abstracts PA99)

3. A. Erdei, N. Marozsán, H. Horváth, G. Papp, F. Joó: Racemization of secondary alcohols by new iridium and ruthenium complexes, *15. Österreichische Chemietage 2013*, Graz, Ausztria, 2013. szeptember 23-26., PO158

4. N. Marozsán, A. Erdei, H. Horváth, G. Papp, F. Joó: Optikailag tiszta alkoholok racemizációjának vizsgálata Ru(II)-komplex katalizátorokkal, *XIX. Nemzetközi Vegyészkonferencia 2013 (19<sup>th</sup> International conference on chemistry)*, Nagybánya, Románia, 2013. november 21-24., 113.o.

5. Erdei, H. Horváth, N. Marozsán, F. Joó: Iridium(I)-NHC komplexek katalitikus alkalmazása, *XX. Nemzetközi Vegyészkonferencia 2014 (20<sup>th</sup> International conference on chemistry)*, Kolozsvár, Románia, 2014. november 6-9., 100.o.

6. N. Marozsán, H. Horváth, A. Erdei, G. Papp, F. Joó: Vízoldható Ru(II)-NHC komplex katalizátorok alkalmazása hidrodehalogénezési reakciókban, *XX. Nemzetközi Vegyészkonferencia 2014 (20<sup>th</sup> International conference on chemistry)*, Kolozsvár, Románia, 2014. november 6-9. 113.o.



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MTMT ID: 10038038

### List of publications related to the dissertation

#### Foreign language scientific articles in international journals (2)

1. **Marozsán, N.**, Horváth, H. H., Kovács, É., Udvardy, A., Erdei, A., Purgel, M., Joó, F.: Catalytic racemization of secondary alcohols with new (arene)Ru(II)-NHC and (arene)Ru(II)-NHC-tertiary phosphine complexes.  
*Molecular Catalysis*. 445, 248-256, 2018. ISSN: 2468-8231.  
DOI: <http://dx.doi.org/10.1016/j.mcat.2017.11.040>  
IF: 4.211\*
2. **Marozsán, N.**, Horváth, H. H., Erdei, A., Joó, F.: Dehalogenation of organic halides in aqueous media by hydrogen transfer from formate catalyzed by water-soluble Ru(II)-N-heterocyclic carbene complexes.  
*J. Mol. Catal. A-Chem.* 425, 103-109, 2016. ISSN: 1381-1169.  
DOI: <http://dx.doi.org/10.1016/j.molcata.2016.09.036>  
IF: 4.211

**Total IF of journals (all publications): 8,422**

**Total IF of journals (publications related to the dissertation): 8,422**

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of Web of Science, Scopus and Journal Citation Report (Impact Factor) databases.

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