

**SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
(PHD)**

**N-Heterocyclic carbene ligands and their Rh(I)
complexes. Mechanochemical and solvent synthesis
and catalytic applications**

by
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DEBRECEN, 2020.

INTRODUCTION AND OBJECTIVES

N-heterocyclic carbenes (NHCs) are heterocyclic carbene species with at least one nitrogen atom within the ring structure. Before 1960, a belief was that carbenes are too reactive to be isolated, which prevented extensive investigation in the field of carbene chemistry. Perhaps, this is true for the majority of carbenes, however, the assessment was inaccurate for N-heterocyclic carbenes. In 1962, Wanzlick made the first investigation on the stability and reactivity of NHCs and six years later, Wanzlick and Schönherr reported the first application of metal-NHC chemistry. Surprisingly, the domain of NHCs remained asleep for the next two decades. In 1991, NHC was first isolated and ‘bottled’ by Arduengo, which has made NHCs quite universal, challenging phosphines as secondary ligands in the field of organometallic chemistry. Compared with phosphines, NHC complexes provide better catalytic performances and higher stability against air and moisture.

Amongst N-heterocyclic carbenes, poly-NHCs (polytopic ligands featuring more than one NHC unit) are of significant attention as they grant the synthesis of different organometallic compounds with a variety of geometries. At present, we have a range of complexes with di-, tri- or tetra-dentate NHCs; which can act as chelating, bridging, pincer, tripodal or tetrapodal ligands. Poly-N-heterocyclic carbenes as chelating ligands allow greater stability of complexes as well as fine-tuning of topological properties such as chirality, bite angles, steric hindrance etc. On the other hand, poly-NHCs as bridging ligands provide an interesting scaffold for the development of polynuclear homo or heterometallic complexes.

Transition metal complexes bearing NHCs as ligands have got notable attractions because of their widespread application in several fields of

chemistry. In this field, Rh-NHC complexes deserve special mention due to their extensive usage in different fields of catalysis such as hydrogenation, dehydrogenation, hydroamination, hydration, C-C cross-coupling etc.

Amongst, the poly-NHCs, di-NHCs are the most abundant poly-NHC ligands. Even though NHC complexes with rhodium are very well known, we checked that there are still no reports presented on the Rh-di(NHC) complexes. Therefore, our main objective was to synthesize and characterize Rh-di(NHC) complexes. During the preparation, we found out that there might be a possibility to prepare these NHC-metal complexes without the use of solvents, using a ball mill and therefore, we extended our investigation on that way as well to compare the two different types of synthetic methods. The traditional solvent synthesis, which most often involves many steps, have a number of disadvantages like long reaction time, high energy costs and in many cases, low yields. In addition, this procedure most often has a negative impact on the environment due to the prevalent usage of volatile organic solvents. On the other hand, the reaction using mechanical energy is a viable alternative to classical solution method as it is capable of producing better yields in lesser time in the greener way. Efficient and continuous mixing imparts higher reaction rate as well as higher yields and selectivity compared to the classical solution method. Moreover, the opportunity to adjust several instrumental parameters makes the results more reproducible. The relative lack application of Rh(I)-NHC complexes as catalysts in selective hydration of nitriles in aqueous media or in the polymerization reaction of alkynes also encouraged us to further extend our research work in those directions.

APPLIED EXPERIMENTAL TECHNIQUES

The successful formation of all the ligand precursors and metal complexes were validated by ^1H and ^{13}C NMR spectroscopy, high-resolution ESI-MS, elemental analysis and XRD study.

^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded on a Bruker 360 MHz instrument and well-established solvent peaks were taken as the internal standard.

High-resolution electrospray ionization mass spectra (HR ESI-MS) were recorded on a Bruker maXis II MicroTOF-Q type Qq-TOF-MS instrument, controlled by Compass Data Analysis 4.4 software from Bruker.

The MALDI-TOF MS measurements were done using the Bruker Autoflex Speed MALDI-TOF instrument.

CHN elemental analysis was done using Elementar Vario Micro microanalyzer, solid-state single crystals were examined by Bruker D8 Venture diffractometer (SCXRD) and data processing managed by Olex² software including SHELXT program and the molecular images established by Mercury CSD-4.3.0 software.

The GPC was recorded in waters 2695 separator module with UltraStyrogel, HR1-2-3-4 column and THF as eluent.

Analytical thin-layer chromatography (TLC) was carried out on Kieselgel 60 F254 plates from Merck and the plates were visualised under UV light at 254 nm. The column chromatography was executed on silica gel from Sigma-Aldrich (70-230 mesh, 63-200 μm).

Reactions in ball mill were carried out utilizing a planetary milling instrument model 'RETSCH PM 100' with stainless steel jar (12.5 mL) and G100 ball bearings ($\text{\O} 5$ mm and $\text{\O} 8$ mm) at 550 rpm at room temperature.

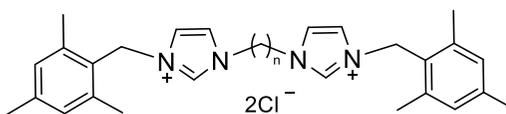
ABBREVIATIONS

°C	Degree Celsius
COD	1,5-Cyclooctadiene
ESI-MS	Electrospray ionization mass spectrometry
GC	Gas Chromatography
GPC	Gel Permeation Chromatography
IMes	1,3-Dimesityl-1,3-dihydro-2H-imidazol-2-ylidene
IPr	1,3-Bis(2,6-diisopropylphenyl)-1,3-dihydro-2H-imidazol-2-ylidene
MALDI-TOF	Matrix-Assisted Laser Desorption/Ionization-Time of Flight
NHC	N-heterocyclic carbene
NMR	Nuclear magnetic resonance
SIMes	1,3-Bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene
SIPr	1,3-Bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene
TLC	Thin-layer chromatography
XRD	X-ray diffraction

NEW SCIENTIFIC ACHIEVEMENTS

1. *Two new precursor azolium salts of di-NHCs: 1,1'-methylene-bis(3-(2,4,6-trimethylbenzyl)imidazolium)dichloride and 1,1'-(butane-1,4-diyl)bis(3-(2,4,6-trimethylbenzyl)imidazolium)dichloride were synthesized both in solution and in a ball mill and well characterized (^1H -, ^{13}C -NMR, HR ESI-MS, elemental analysis and X-ray crystallography).*

The two new di-NHCs were prepared in the traditional solution method using acetonitrile and without the use of solvents in a ball mill. Successful formation of both the ligands were proved ^1H -NMR, ^{13}C -NMR, HR-ESI-MS and elemental analysis. The synthesis of di-NHC with butane bridge was further established by XRD study.



A: $n=1$; **B:** $n=4$

Fig. 1: Synthesized new di-NHCs **A** and **B**.

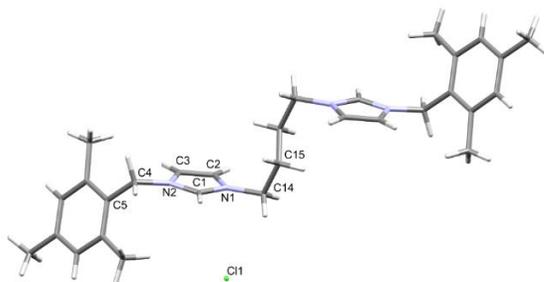


Fig. 2: Capped stick representation of the molecular structure of **B**.

2. **Four new bridging di-nuclear Rh(I)-di(NHC) complexes of the type $[\text{Rh}_2\text{Cl}_2(\text{COD})_2(\text{NHC})]$ [$\text{NHC} = 1,1'$ -methylene-bis(3-benzyl-imidazolium), $1,1'$ -(butane-1,4-diyl)bis(3-benzyl-imidazolium), $1,1'$ -methylene-bis(3-(2,4,6-trimethylbenzyl)imidazolium), $1,1'$ -(butane-1,4-diyl)bis(3-(2,4,6-trimethylbenzyl)imidazolium)] were synthesized both in solution and in a ball mill and well characterized (^1H -, ^{13}C -NMR, HR ESI-MS, elemental analysis and X-ray crystallography).**

At present, there are no reports available on the synthesis of Rh-di(NHC) complexes. We have successfully synthesized four di-nuclear Rh(I)-di(NHC) complexes of the type $[\text{Rh}_2\text{Cl}_2(\text{COD})_2(\text{NHC})]$ and characterized. The structures of **C**, **D** and **F** (fig. 3) were proved in solid-state with single-crystal X-ray diffraction analysis.

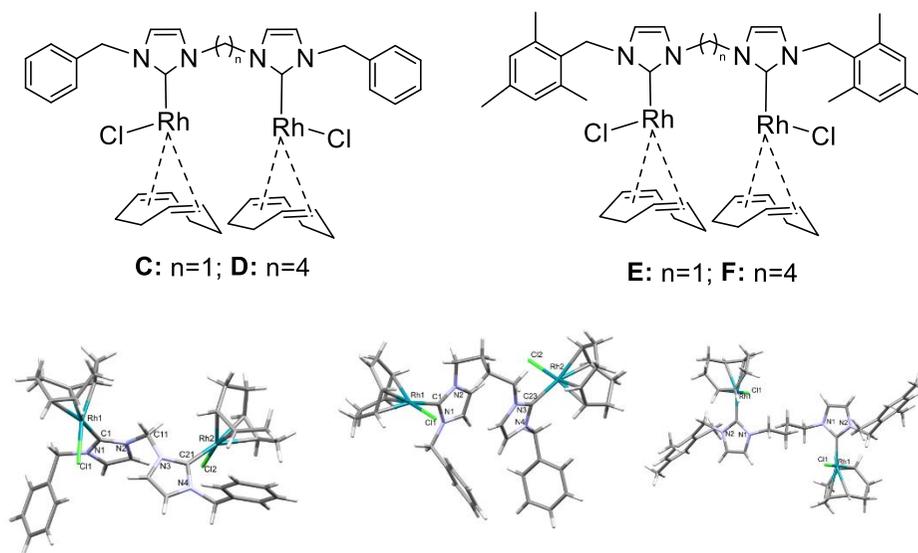


Fig. 3: New di-nuclear Rh(I)-di(NHC) complexes and capped stick representation of the molecular structure of **C**, **D** and **F**.

3. *Two methods of synthesis (solution and solvent-free mechanochemical) were parallelly compared to opt the better approach for the preparation of the carbene ligand precursors and their Rh(I)-complexes.*

The optimized reaction conditions for the preparation of the compounds were use of ball bearings with two different diameters (10 Ø 5 mm and 10 Ø 10 mm balls) and rotation at 550 rpm. The di-NHCs required six hours of milling time, whereas, for the metal complexes, it was three hours (2 minutes millings followed by 2 minutes breaks for both the cases).

The stirring method in solution was also optimized by changing the reaction temperature and time. For both the cases of di-NHCs and metal complexes, overnight reactions with high temperature (≥ 80 °C) yielded the best.

To compare the two different approaches of synthesis, reactions were parallelly carried out in solution and in ball mill for the same time (6h for ligands, 3h for metal complexes) using the optimized conditions for each category. It was found out that the mechanochemical method of synthesis not only yielded better [74% vs. 18% for the metal complex **D**, 71% vs. 49% for the di-NHC precursor 1,1'-(butane-1,4-diyl)bis(3-benzyl-imidazolium)dichloride] in shorter time without the use of organic solvents but also generated lesser waste, thereby leading to an environment-friendly way of synthesis. Hence, we concluded that the mechanochemical method to be superior in comparison to the classical solution method of synthesis (at least, in the cases studied by us).

4. Novel method of synthesis were carried out for four known rhodium complexes of the type $[\text{RhCl}(\text{COD})(\text{NHC})]$ ($\text{NHC} = \text{IMes}, \text{SIMes}, \text{IPr}, \text{SIPr}$).

A modified and straightforward solution synthesis of the complexes were reported by reacting the corresponding imidazolium/imidazolium salt with $[\text{RhCl}(\text{COD})]_2$ or $[\text{Rh}(\text{OH})(\text{COD})]_2$ in toluene at 70 °C. The compounds were characterized by $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HR ESI-MS. X-ray quality crystals of **I** and **J** (fig. 4) were obtained from benzene.

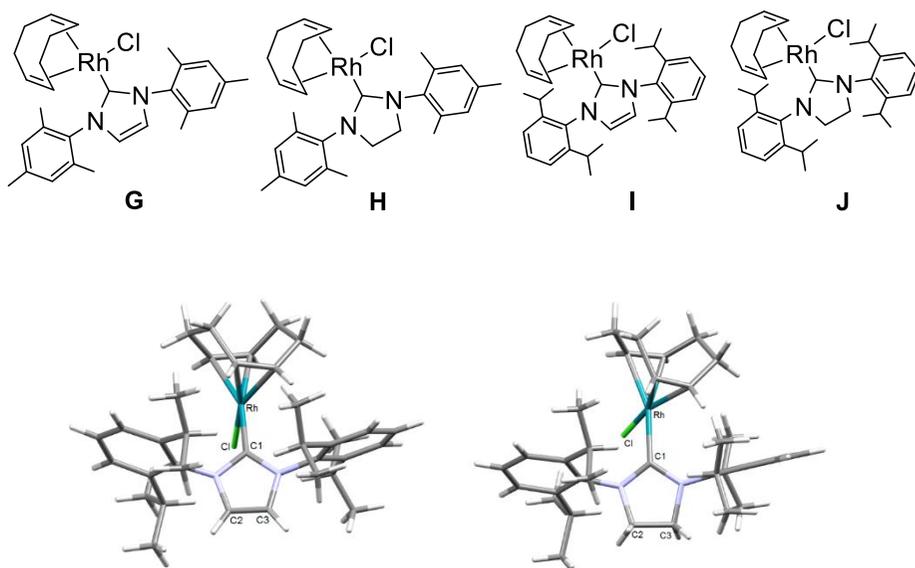


Fig. 4: Synthesized $[\text{RhCl}(\text{COD})(\text{NHC})]$ type complexes and capped stick representation of the molecular structure of **I** (left) and **J** (right).

5. *X-ray quality crystal structure of a zwitterionic azolium salt: 3,3'-(1,1'-(butane-1,4-diyl)bis(1H-imidazole-3-ium-3,1-diyl))bis(propane-1-sulfonate) was obtained by slow cooling of its hot dimethylformamide solution.*

The above-mentioned zwitterionic azolium salt is known from the literature. However, the solid-state crystal structure of this salt is unknown. We were successful to prepare the X-ray quality crystals of the compound by slow cooling of its hot dimethylformamide solution.

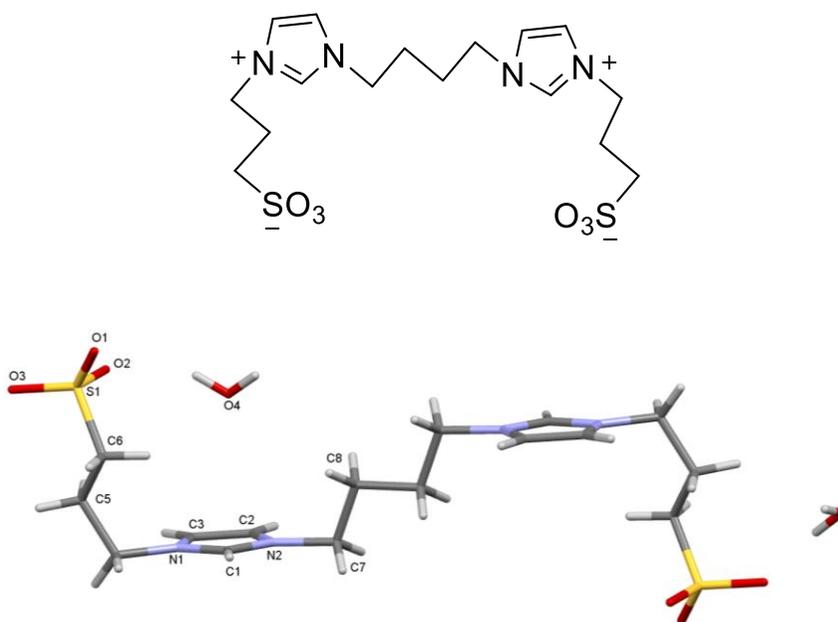
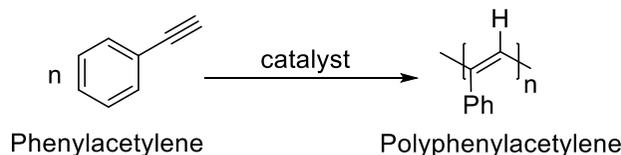


Fig. 5: The zwitterionic azolium salt: 3,3'-(1,1'-(butane-1,4-diyl)bis(1H-imidazole-3-ium-3,1-diyl))bis(propane-1-sulfonate) and its capped stick representation of the molecular structure.

6. Polymerization of phenylacetylene utilizing the bridging di-nuclear complexes $[Rh_2Cl_2(COD)_2(NHC)]$ [$NHC=1,1'$ -methylene-bis(3-benzyl-imidazolium), $1,1'$ -(butane-1,4-diyl)bis(3-benzyl-imidazolium)] as catalysts.

The above-mentioned bridging di-nuclear Rh(I)-di(NHC) complexes (fig. 6) were found to be catalytically active for the polymerization of phenylacetylene. Using these catalysts, it was possible to obtain 99% conversion after 30 minutes at room temperature with the catalyst loading as low as 1 mole% with respect to the substrate. Unfortunately, for some yet unknown reason(s), the prepared polyphenylacetylene failed to display uniform polymeric properties for different batches of preparations.



Scheme 1: Polymerization reaction of phenylacetylene.

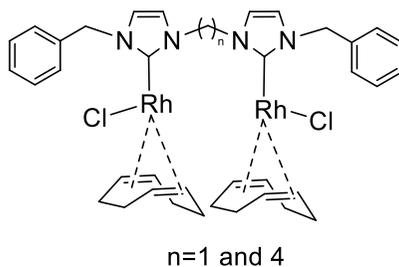
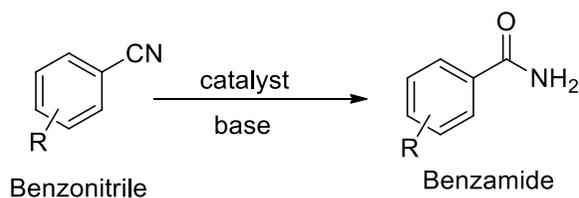


Fig. 6: Metal complexes used for the polymerization of phenylacetylene.

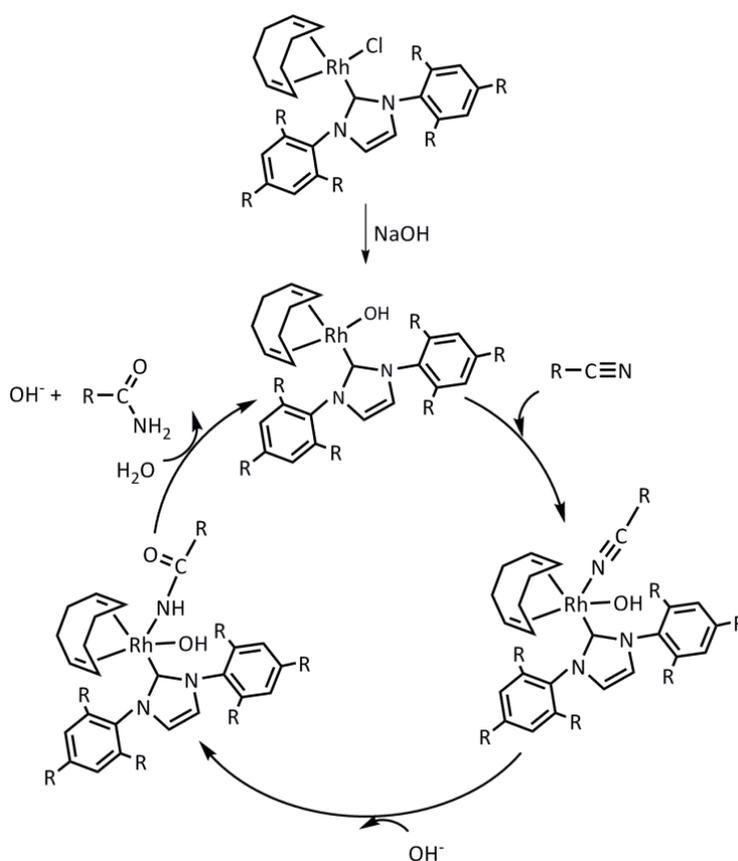
7. *Selective hydration of nitriles to amides applying the [RhCl(COD)(NHC)] type complexes as catalysts in aqueous media.*

Use of [RhCl(COD)(NHC)] type catalysts for the selective hydration reaction of nitriles with water in aqueous or partly aqueous solvents were reported for the first time by us. The four Rh(I)-mono(NHC) complexes of the type [RhCl(COD)(NHC)] showed good catalytic activity towards the hydration of nitriles in presence of a base; sodium hydroxide was found to be the best amongst several bases. Next, several experimental checking were made taking benzonitrile as substrate and the catalyst [RhCl(COD)(IMes)] yielded almost 100% with the substrate to catalyst ratio 20 with an equimolar amount of base to the catalyst in the water/2-propanol medium at reflux temperature. The same catalyst was applied for different sets of nitriles. The hydration reaction was checked at room temperature, as well, and the catalyst displayed the excellent yield of 99% with only 2.5% catalyst loading with respect to the substrate within 24 hours.



Scheme 2: Selective hydration of benzonitrile.

A mechanism for the hydration reaction has also been suggested (scheme 2). The high rate of conversion in the presence of base can support the formation of Rh(I)-OH hydroxo complex. Again, the complete selectivity of the hydration reaction to benzamide supports that most probably the nitrile group also coordinates to Rh(I) centre. However, the role and fate of COD is still unclear.



Scheme 3: Suggested mechanism of the hydration reaction of nitrile catalysed by $[\text{RhCl}(\text{COD})(\text{NHC})]$ complexes (**G-J**).

LIST OF PUBLICATIONS

1. Sourav De, Antal Udvardy, Csilla Enikő Czégéni, Ferenc Joó; Poly-*N*-heterocyclic carbene complexes with applications in aqueous media; *Coordination Chemistry Reviews*, **2019**, 400, 213038 [IF:13.48]
2. Csilla Enikő Czégéni, Sourav De, Antal Udvardy, Nóra Judit Derzsi, Gergely Papp, Gábor Papp, Ferenc Joó; Selective hydration of nitriles to corresponding amides in air with Rh(I)-*N*-heterocyclic complex catalysts; *Catalysts*, **2020**, 10(1), 125 [IF: 3.44]
3. Sourav De, Ferenc Joó, Henrietta Horváth, Antal Udvardy, Csilla Enikő Czégéni; Stirring or milling? First synthesis of Rh(I)-di-*N*-heterocyclic carbene complexes both in solution and in a ball mill; manuscript for the *Journal of Organometallic Chemistry* to be submitted.
4. Antal Udvardy, Sourav De, Csilla Enikő Czégéni, Ferenc Joó; Crystal structure of zwitterionic 3,3'-(1,1'-(butane-1,4-diyl)bis(1H-imidazole-3-ium-3,1-diyl))bis(propane-1-sulfonate), a di-*N*-heterocyclic carbene precursor; manuscript for the *Acta Crystallographica Section E* to be submitted.

LIST OF PRESENTATIONS

1. Sourav De, Antal Udvardy, Ferenc Joó; Water-soluble bidentate *N*-heterocyclic carbene ligand precursors for organometallic catalysis; *XXIII. International conference in Chemistry, 2017*, Deva, Romania.
2. Csilla Enikő Czégéni, Antal Udvardy, Sourav De, Ágnes Kathó, Ferenc Joó; Kelát- és hídképző *N*-heterociklusos karbén ligandumok átmenetifém komplexeinek előállítása és szerkezetvizsgálata; *XXIV. International conference in Chemistry, 2018*, Sovata, Romania.
3. Csilla Enikő Czégéni, Sourav De, Krisztina Orosz, Henrietta Horváth, Ferenc Joó; Kelát és kétmagvú átmenetifém di-*N*-heterociklusos karbén komplexek; *Komplekémiai Kollokvium, 2019*, Velence, Hungary.
4. Csilla Enikő Czégéni, Antal Udvardy, Sourav De, Krisztina Orosz, Ferenc Joó; Kelát- és hídképző átmenetifém di-*N*-heterociklusos karbén komplexek előállítása szerves oldószerben és oldószermentes körülmények között; *XXV. International conference in Chemistry, 2019*, Cluj-Napoca, Romania.
5. Csilla Enikő Czégéni, Sourav De, Antal Udvardy, Ferenc Joó; Solvent-free synthesis of several Rh-bis(NHC) complexes and their utilization in catalytic applications; *International Symposium on Metal Complexes, 2019*, Hajdúszoboszló, Hungary.

6. Sourav De, Csilla Enikő Czégéni, Antal Udvardy, Ferenc Joó; Environment-friendly synthesis of several new bis-imidazoles and their Rh(I)-metal complexes for catalytic applications; *4th International Green Catalysis Symposium, 2020*, Rennes, France (registered for participation, abstract submitted).

7. Sourav De, Ferenc Joó, Henrietta Horváth, Antal Udvardy, Csilla Enikő Czégéni; Stirring or milling? First synthesis of Rh(I)-di-*N*-heterocyclic carbene complexes both in solution and in a ball mill; *Dalton 2020 Conference, 2020*, Coventry, United Kingdom (registered for participation, abstract submitted).



Registry number: DEENK/38/2020.PL
Subject: PhD Publikációs Lista

Candidate: Sourav De
Neptun ID: COEYXZ
Doctoral School: Doctoral School of Chemistry

List of publications related to the dissertation

Foreign language scientific articles in international journals (2)

1. Czégéni, C. E., **De, S.**, Udvardy, A., Derzsi, N. J., Papp, G., Papp, G., Joó, F.: Selective Hydration of Nitriles to Corresponding Amides in Air with Rh(I)-N-Heterocyclic Complex Catalysts. *Catalysts*. 10 (1), 1-16, 2020. EISSN: 2073-4344.
DOI: <http://dx.doi.org/10.3390/catal10010125>
IF: 3.444 (2018)
2. **De, S.**, Udvardy, A., Czégéni, C. E., Joó, F.: Poly-N-heterocyclic carbene complexes with applications in aqueous media. *Coord. Chem. Rev.* 400, 1-31, 2019. ISSN: 0010-8545.
DOI: <http://dx.doi.org/10.1016/j.ccr.2019.213038>
IF: 13.476 (2018)

Total IF of journals (all publications): 16,92

Total IF of journals (publications related to the dissertation): 16,92

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of the Journal Citation Report (Impact Factor) database.

18 February, 2020

