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„The Optimization of The Olefin Metathesis Reaction Catalyzed by Ruthenium Complexes for the Industrial Applications”

Olefin metathesis is perceived as one of the most important catalytic transformations utilized in modern organic chemistry. The rapid increase of its significance over the past few decades was possible largely due to the constant development of new, effective and stable catalysts allowing the crossing of subsequent boundaries in their application. The versatility of this approach has drawn the attention of the chemical industry, seeking for approachable routes for synthesis of biologically active compounds, new polymers and the ways to obtain valuable specialty chemicals from renewable feedstocks. However, the implementation of metathesis in large-scale industrial processes involves overcoming several challenges, which are related to its cost-effectiveness and environmental impact. The principal requirements set by the industry are: low catalyst loading, high efficiency, catalyst robustness in the presence of impurities and gaseous byproducts, employment of environmentally friendly solvents and simple removal of residual ruthenium from the reaction mixture.

The first step of this research project was concentrated on the evaluation of commonly used, commercially available catalysts in ring-closing metathesis (RCM) and cross-metathesis (CM) with the use of “green” solvents. A number of examples presented advantage of complexes bearing more sterically hindered N-heterocyclic (NHC) ligand when a technical grade solvent is used and the reaction is carried out without a protective atmosphere of an inert gas. Ethyl acetate (AcOEt) and dimethyl carbonate (DMC) were indicated as alternative reaction media that can successfully replace environmentally harmful toluene and dichloromethane (DCM) in olefin metathesis reaction.

Further search for more robust initiators was concentrated on investigation into the effect of anionic ligands on the catalytic activity of ruthenium complexes. As a result, two new diiodide catalysts were proposed, which are characterized by higher efficiency in RCM and CM reactions of terminal olefins in relation to their commercially available dichloride parent structures. The examined catalysts showed enhanced resistance towards impurities and increased selectivity in demanding conditions, conducive to the formation of undesired byproducts, such as isomers with shifted carbon-carbon double bonds. It was shown, that diiodide ruthenium complex bearing a SIMes type NHC ligand possess specifically high

efficiency and stability in the presence of ethylene gas evolving during the metathesis of two terminal olefins. This distinctive feature is particularly important in large reactor vessels, where inefficient removal of gaseous byproduct may result in its interference in the catalytic cycle. The high stability of this catalyst has been successfully applied in macrocyclic ring-closing metathesis, where the negative impact of ethylene is particularly evident.

Further improvement of results in demanding transformations was possible due to the utilization of catalysts bearing Cyclic (Alkyl)(Amino) Carbene (CAAC) ligand. The macrocyclization reaction leading to a sixteen-membered lactone precursor of a fragrance compound achieved the highest reported turnover number (TON) of 62 000, with the use of low catalyst loading equal 10 ppm. Moreover, this result was achieved in a short reaction time (20 min) and with marginal amount of isomeric byproducts observed (~1%).

Another significant relationship between the catalyst structure and macrocyclization result was observed with the use of an NHC catalyst containing a quaternary ammonium group in its structure. The active form of this complex exhibited reduced selectivity towards product backbiting, allowing higher yields to be achieved in high concentration macrocyclization compared to the convectional initiator.

Ruthenium complexes bearing a quaternary ammonium group were also studied for the effect of counterion on the catalyst effectivity in RCM and CM. Complexes with BF_4^- and PF_6^- anions enabled successful reaction accomplishment in solvents such as AcOEt and CPME. In case of the ammonium-tagged catalysts containing a chloride counterion, a simple procedure for effective ruthenium removal ($[\text{Ru}] < 5 \text{ ppm wt}$) has been developed. The presented methods entailed simple water extraction or *in situ* counterion exchange, followed by the extraction with a non-polar solvent. The use of quaternary ammonium-tagged catalysts in combination with ionic liquid allowed RCM to be carried out with low catalyst loading (100 ppm) in a two-phase system (ionic liquid/toluene). Due to high affinity of such complexes to the ionic liquid, it was possible to obtain low ruthenium content ($< 5 \text{ ppm}$) in the final product.

The research described in this dissertation presented advantages of several ruthenium catalysts, which made it possible to introduce them to the market and facilitate their use in both academia and industry.

Articles constituting the dissertation:

Article I: *An attempt to provide an environmentally friendly solvent selection guide for olefin metathesis*, K. Skowerski, J. Białecki, A. Tracz, T. K. Olszewski, *Green Chemistry*, 2014, 16, 1125-1130.

Article II: *Nitro-Grela-type complexes containing iodides – robust and selective catalysts for olefin metathesis under challenging conditions*, A. Tracz, M. Matczak, K. Urbaniak, K. Skowerski, *Beilstein Journal of Organic Chemistry*, 2015, 11, 1823-1832.

Article III: *Cyclic Alkyl Amino Ruthenium Complexes - Efficient Catalysts for Macrocyclization and Acrylonitrile Cross Metathesis*, R. Gawin, A. Tracz, M. Chwalba, A. Kozakiewicz, B. Trzaskowski, K. Skowerski, *ACS Catalysis*, 2017, 7, 5443-5449.

Article IV: *Ammonium NHC-tagged olefin metathesis catalysts – influence of counter-ions on catalytic activity*, A. Tracz, A. Gawin, M. Bieniek, T. K. Olszewski, K. Skowerski, *New Journal of Chemistry*, 2018, 42, 8609-8614.