Asymmetric epoxidation and thio-Michael reaction catalyzed by chiral magnesium complexes

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The formation of new carbon–carbon or carbon–heteroatom bonds in a stereocontrolled manner using chiral metal complexes is one of the key tools in asymmetric catalysis. The versatility of this approach is a major advantage, translating into its significant application in constructing a wide variety of organic compounds in optically pure form. Noble metals such as palladium, rhodium, or ruthenium are commonly used in this area. Despite the undeniable advantages and high efficiency of this methodology, it also has several drawbacks, including the high costs of noble metal salts, the labor-intensive synthesis of necessary ligands, their limited stability in air, and often the stringent conditions required for the transformations. Additionally, their negative impact on the environment and living organisms cannot be overlooked.

A trend that has gained importance in asymmetric synthesis in recent years and is actively being developed is the replacement of precious noble metals with environmentally friendly, non-toxic, and, above all, more economical alkaline earth metals, including magnesium. The goal of my research was to develop efficient catalytic systems based on chiral small-molecule ligands and magnesium that can enantioselectively catalyze transformations of electron-poor olefins, particularly α,β-unsaturated ketones, converting them into epoxy derivatives or β-carbonyl sulfides.

In the first part of my research, I focused on developing a chiral magnesium complex that could effectively produce a diverse, structurally, and electronically varied group of enantiomerically enriched oxiranes. While chiral mononuclear magnesium complexes had previously been used in this area, they did not exhibit the desired activity or efficiency, and they were tested on a narrow group of substrates. I proposed using an *in situ* generated dinuclear magnesium complex containing prophenol ligand, which, upon activation with molecular oxygen, successfully promoted the transformation of fifty α,β-unsaturated ketones into the corresponding optically enriched α,β-epoxyketones with high stereoselectivity reaching up to 99% *ee*. The developed methodology proved highly useful in synthesizing precursors of nonsteroidal anti-inflammatory drugs and natural compounds with cytotoxic properties.

In the second part of my research, I demonstrated that the previously developed dinuclear magnesium complex containing a prophenol ligand successfully catalyzes the transformation of α,β-unsaturated ketones into the corresponding enantiomerically enriched β-ketosulfides with high enantioselectivity. It is worth noting that this is the first example of an asymmetric thio-Michael reaction catalyzed by chiral magnesium complexes. It is also the first example of a comprehensive study of substrate tolerance, in which 29 sterically and electronically diverse thiols were tested. A significant advantage of the developed methodology was the ability to regenerate and recycle the prophenol ligand back into the process.