Synthesis and functionalization of strained cyclic nitrones catalyzed by transition metals

Chemistry of nitrogen compounds plays an important role in modern organic chemistry. A huge amount of natural compounds and synthetic drugs contain a nitrogen atom in their structure. Thus, any new synthetic method that leads to complex nitrogen-containing molecules in their structure, is highly desirable. Nitrones are nitrogen analogues of ketones and aldehydes, but they differ from them in many ways. It is worth noting that despite the wide availability of aldonitrones (nitrones derived from aldehydes), the synthesis of ketonitrones remains a challenge in modern organic chemistry. Nitrones can be easily transformed into other chemical compounds that are very important from the point of view of medical chemistry. As an example, unnatural amino acids or highly functionalized heterocyclic systems can be synthesized.

In addition, in recent years transition metal catalyzed reactions are becoming increasingly common in many synthetic procedures. Undoubtedly, this brings some benefits: catalytic amounts of compounds save significant amounts of materials and reactions can often be carried out under milder conditions. It is also worth emphasizing that very often the use of a catalyst is a necessary condition for the process to proceed.

Strained rings such as cyclopropane or cyclobutane find great use in organic synthesis. Due to their high bonding energy, resulting from the strong stress of the molecules, they are very reactive. Applying appropriate catalysts, it is possible to open the ring in a controlled manner. That is why these structures are of interest in the synthesis of more complex compounds.

In my project, I will combine all three issues described above. The main task of the project will be the synthesis of stressed cyclic nitrones derived from benzocyclobutenone. For this purpose, I will use transition metal catalysis (mainly palladium), and the process will be carried out by direct C–H activation of the aldonitrone derivative. The investigated reaction will not only be unique due to its high economy, but also because of the methodology. The process of direct C–H activation of nitrones is practically unknown up to now. Of course, the products obtained in the form of ketonitrones will not be the sole purpose of the project. An important aspect of research will be their reactivity, which at the moment is completely unknown. The strained cyclic nitrones will be functionalized into derivatives of indoline or benzomorphan - systems commonly found in alkaloids. For reactivity studies, the use of transition metal complexes (such as rhodium, cobalt or nickel), that selectively open the cyclobutene ring, may be crucial. The newly developed synthetic methods can significantly contribute to the progress in organic synthesis, in particular in the synthesis of highly functionalized organic compounds with potential use in the pharmaceutical industry.