[2+2] and [4+2] Cycloaddition reactions of boryl(silyl)-1,3-dienes – new tools in synthesis of cyclic precursors of fine chemicals

Reasons for undertaking this research topic

In recent years, there has been a growing demand for fine chemicals i.e., pharmaceuticals, agrochemicals, dyes, perfume components, or chemicals for the textile industry, and photography. Therefore, a significant challenge for synthetic chemists is to develop efficient and stereoselective methods leading to products with well-defined structures using the shortest possible synthetic route. Considering that many of the above-mentioned compounds have a 4- or 6-membered carbon ring in their structure, cycloaddition reactions play a key role in the synthesis of these systems. Cyclobutanes are obtained by the [2+2] cycloaddition of olefins with various π-donors (alkenes, alkynes, ketenes), while the [4+2] cycloaddition of 1,3-dienes with the aforementioned π-donors is commonly used in the synthesis of cyclohexanes. The second transformation is also known as the Diels-Alder reaction, after its discoverers, who for their finding were awarded the Nobel Prize in 1950. The advantages of cycloaddition include 100% atom economy, high reaction yields, and the ability to control the selectivity of the process with the formation of up to 4 stereogenic centers in a single operation, which is difficult to achieve using other methods.

In the last decade, the application of unsaturated substrates (alkenes, alkynes, and 1,3-dienes), containing metalloid atoms (especially boron) in their structure in cycloaddition reactions, has sparked a growing interest. Such a strategy combined with coupling reactions is an excellent way to expand the application potential of these compounds, especially in the design of new pharmaceuticals. However, as the literature review shows, such cycloadditions are limited to the use of starting compounds having only one metalloid atom (boron or silicon) in their structure, which significantly limits the synthetic potential of the described method.

Project objective and description of research

Therefore, noticing the above-mentioned imperfections, the scientific objective of this project is to develop new methods of [2+2] and [4+2] cycloaddition using 1,3-dienes, having both a boron and silicon atom in their structure – substrates that have not been widely described in the scientific literature so far. As part of the proposed project, a set of geometric isomers of boryl(silyl)-buta-1,3-dienes, having metalloid atoms in different positions in the diene molecule, will be obtained. The synthesized products will then be used as substrates in [2+2] and [4+2] cycloaddition reactions with various reagents such as activated and non-activated alkenes, alkenyl boronates (or silanes), and substituted alkynes. Three basic activation profiles will be explored to obtain products with high yield and selectivity: catalyst-free reactions (induced by temperature or pressure), catalytic reactions (involving transition metal complexes or Lewis acids), and photocatalytic reactions activated by UV or visible light (in particular those proceeding via energy transfer from the excited photosensitizer). The potential of the obtained carbocyclic compounds equipped with organoboron and organosilicon groups will be demonstrated in the final step in coupling reactions and other demetallation protocols.

The most important expected effects

A wide range of cyclic 4-carbon compounds (cyclobutanes and cyclobutenes) and 6-carbon compounds (cyclohexanes and cyclohexenes) decorated with boron and silicon atoms will be obtained within the project. The introduction of two metalloids (and more) with different reactivity will allow for selective functionalization of groups, significantly broadening the spectrum of synthesized products. It is therefore expected that the results of this project will make a significant contribution to the chemistry of carbocyclic compounds because by controlling the structure of the starting substrates, and by selecting the catalyst/photocatalyst and reaction conditions, it will be possible to incorporate any organic groups into the structure of cyclobutane or cyclohexane rings. The use of catalytic and photocatalytic methods for this purpose will contribute to the development of efficient and selective methods, taking place in mild conditions, while reducing the amount of waste generated, as well as the reaction time and energy inputs necessary to carry it out. The project assumptions are therefore in line with the principles of Green Chemistry and sustainable development. An important aspect of the research will be to understand the reaction mechanisms. Great hopes are associated with the possibility of implementing the synthesized compounds as relatively cheap, effective building blocks, both on a laboratory scale in academic centers, as well as in the chemical industry, for the synthesis of pharmaceuticals and other fine chemicals.