

# *Synthesis and application of chiral cyclic imines*

Jakub Iwanejko

abstract

For decades, chiral cyclic imines have been used as building blocks in organic synthesis. Numerous pharmaceuticals and analogues of natural products are obtained by the use of the reactivity of carbon-nitrogen double bond in a key synthetic step. Carefully designed and performed addition reactions allow to obtain chiral derivatives in a stereoselective manner.

In the context of the growing interest in the subject of cyclic imines and their importance in synthesis, I developed new methods for obtaining these compounds. An emphasis was put on protocols using chiral bisamines and  $\alpha$ -aldo- and  $\alpha$ -ketoesters, leading to efficient and inexpensive synthesis of the title compounds. I presented a synthetic method based on the unusual course of the Horner-Wadsworth-Emmons reaction. I examined in detail the scope of the carbonyl substrates used in the proposed procedure. I proved that this method can be used to afford desired imines or to obtain them in situ during the synthesis of other compounds.

I proved the usefulness of those compounds in a carbon-carbon bond forming reaction on the example of the Mannich phenolic condensation. The products were obtained in a highly diastereoselective manner. Changing the nucleophile from phenolic to phosphoric one paved the way for the synthesis of aminophosphonates and phosphonic amino acids. I examined the relationship between the type of ald- and ketimine used and the diastereoselectivity of this process.

I studied the application of obtained imines and their derivatives as antiproliferative compounds. I showed that aminophosphonates based on the structure of hexahydroquinoxalin-2(1H)-ones are highly active against selected tumor cell lines. The products act in a selective manner, making them attractive compounds for in vivo testing.

As a part of the work presented, I demonstrated the application potential of the synthesized imines, through a series of functional group transformations, leading to new chiral compounds in diastereoselective processes. The presented scope of imines and their derivatives illustrates the universality and a wide range of applications of the developed methods.