ABSTRACT

In my dissertation I have described the synthesis of diazenedicarboxamides, for which I have revealed the ability to potentially reduce the intracellular concentration of biologically important glutathione. During biological testing it was demonstrated that the prepared compounds exhibit good activity against various tumor cell lines and cause necrosis of cancer cells. Selected diazenes were thereafter converted to the corresponding hydrazino compounds; the newly developed method for the reduction of azo compounds using hydrazine hydrate and hydrogen peroxide was successfully applied during the course of their preparation. Both, the starting diazenes and their reduced analogues hydrazides, in their structures contain a variety of heteroatoms making them potentially suitable agents for iron complexation and could therefore be employed for the removal of an excess of iron from the cancer cells. Having in mind the decomposition propensity of many diazenes, I have developed a new method for the formation of C–N bonds, which opens up a novel synthetic route for the preparation of a variety of compounds taking place under mild conditions, without the use of expensive catalysts. By combining a variety of biologically active fragments (diazene and ruthenium or diazene and sulfonamide) I tried to prepare compounds displaying an increased biological activity due to the possibility of the synergistic effect upon linking together two individual structural subunits.

Starting from various anilines I have prepared a series of substitued 1,3-diaryltriazenes, including such containing biologically important fluorine atoms in their structures. The prepared compounds demonstrated good activity against various mycobacterial strains, i.e. the family of bacteria, which causes tuberculosis. That was the reason why I decided to convert the selected triazenes into two types of derivatives: acylated, with a particular emphasis on the analogues containing an isoniazide group, being structural fragment with an important role in the treatment of tuberculosis, and triazenide salts. I have performed biological evaluation of a series of compounds containing symmetrical 1,3-diaryltriazene fragment and have demonstrated that such compounds, possibly after further modifications, could potentially be used to treat lethal bacterial infections, especially infections with MRSA, as well as for the treatment of tuberculosis. Furthermore, I have applied triazenes as ligands to prepare ruthenium coordination compounds. It turned out that the synthesized coordination compounds, in comparison with their precursors triazenes, showed substantially increased inhibition of the growth of various tumor cell lines.

Key words: diazenes, triazenes, anticancer activity, MRSA, tuberculosis