Synthesis of carbapenams from five-membered sugar nitrone with L-treo configuration by 1,3-dipolar cycloaddition

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In the framework of this dissertation I introduced the possibility of application of two– and three-cyclic isoxazolidins, obtained in 1,3–dipolar cycloaddition, as substrates in the synthesis of *β*–lactams, which belong to carbapenem antibiotics.

In the first stage of investigations, I elaborated an effective method of the synthesis of polycyclic isoxazolidines from *α*,*β*–unsaturated sugar lactones and enantiomerically pure cyclic nitrone which was obtained from 2-deoxy-D-ribose. I studied the effect of substitution and configuration of both components on direction and magnitude of the asymmetric induction in the 1,3–dipolar cycloaddition reaction. Presented strategy enable synthesis of the *β*–lactam ring with desired configuration at C–3 and C–4 carbon atoms. As was expected six-membered lactones have been shown to be the more attractive than five-membered congeners, since they form *exo* adducts exclusively.

In the second part of the investigations, I developed a method of transformation of previously obtained isoxazolidines into *β*–lactam compounds. The strategy of the *β*–lactam ring formation assumed the use of concept presented by Tufariello in 1975. The resulting isoxazolidines, obtained in that way, were transformed into compounds containing the *β*–lactam ring, by reductive cleavage of the *N–O* bond and subsequent intramolecular *N*–acylation. I have elaborated the most effective way of both transformations. These allowed me to synthesized carbapenams with a poliol side chain at C–6 carbon atom.

In the third part of my dissertation, I developed 1,3–dipolar cycloaddition of nitrone mentioned above and ethyl crotonate. Adduct was transformed into a *β*–lactam compound by repeating the developed reaction sequence. The use of the chiral nitrone enabled formation of the adduct having defined relative and absolute configuration of stereogenic centers. The presence of protected primary and secondary hydroxyls in the five–membered ring of the carbapenam skeleton allowed to form a carboxylic group and to introduce cysteamine chain, thus to complete a formal synthesis of protected thienamycin, a carbapenem antibiotic.