Abstract

This work consists of four separate chapters. Although they are seemingly different projects, they have a common feature – the application of organometallic chemistry.

1. Lusianthridin and denbinobin, the phenanthrene derivatives, can be found in plants of the family Orchidaceae. They exhibit cytostatic activity against cancer of human lung and ovarian and against promyelocytic leukemia. Therefore, new synthetic methods for these substances may be applied in research and development of new bioactive compounds. I prepared 9,10-disubstituted phenanthrenes through reactions of biphenylene with alkynes, which were catalyzed by iridium complexes. Phenanthridine derivatives are found naturally in the group benzo[c]phenanthridine alkaloids. The most famous of these include sanguinarine and chelerythrine. Sanguinarine selectively induces apoptosis (planned cell death) of human cancer cells and, therefore, is investigated as a potential antitumor agent. Chelerythrine selectively inhibits protein kinase C, leading again to apoptosis. I have studied reactions of biphenylene with nitriles catalyzed by rhodium complexes that have not been described yet. By this, I prepared a series of 6-substituted phenanthridines.

2. Carboranes are artificially prepared organic compounds of boron, which are not represented in nature. Unlike boranes, they are relatively stable and non-toxic. They are used in experimental medicine, where they are a good source of boron ^{10}B in the boron neutron capture therapy (BNCT). Carboranes bearing the ferrocene group may also be interesting in terms of experimental medicine, as they can be bound specifically to the protein part of the haemoglobin. I prepared ferrocenyl derivatives of carborane through known reaction of dimethyl sulfide complex of decaborane with alkynes.

3. Chiral organic catalysts can be used to prepare optically pure substances, instead of their separation from racemic mixtures. Their advantages generally include lower toxicity as well as the price compared to catalysts based on transition metals. Furthermore, problematic removal of residual metals from the final products is eliminated. I focused on finding of more effective preparation methods of axially chiral bis(tetrahydroisoquinoline)-*N,N′*-dioxides. They are Lewis bases, which may arrange e.g. asymmetric allylation of aldehydes to the corresponding homoallylic alcohols with an optical purity of 99% ee. I tested two different synthetic approaches to these organocatalysts. One of these methods is based on the chemistry

of organotin compounds and Stille Cross-Coupling. The second method uses direct lithiation of the aromatic ring and subsequent oxidation duplication.

4. (*S*)-Dapoxetine is a biologically active substance that inhibits the serotonin transporter. It is used clinically under the trade name Priligy to treat the premature ejaculation. This paper describes a new synthesis of optically pure (*S*)-dapoxetine that uses asymmetric allylation of benzaldehyde using an organic catalyst to build the stereogenic centre. The key step is followed by a sequence of six known reactions.