Abstract

This work consists of three parts, each dealing with the synthesis of different biologically active compound, using reactions mediated by transition metals.

1. Ferrocene conjugates with various types of natural or biologically active compounds have been studied intensively for their new interesting properties compared to the model compounds. It was decided to synthesize a new steroid containing ferrocene – ferrocenestrone, planned with regard to its possible activity against breast cancer cells. Although several conjugates of steroids with ferrocene have been prepared, the cyclopentadienyl ring has not been the integral part of the steroid skeleton in any of them. Ferrocenestrone, an analog of estrone, however contains ferrocene in place of the aromatic A-ring. The approach to the ferrocene-steroid framework construction was based on transition metal mediated reactions starting from a suitably substituted chiral ferrocene. The methods used were: zirconocene-mediated oxidative additions with successive alkylation sequences, palladium-catalyzed cross-coupling reactions, ruthenium-catalyzed skeletal rearrangements (enyne metathesis), palladium and iridium catalyzed hydrogenations etc. Also selective oxidation and subsequent borane reduction was used for the final change of skeletal configuration. Successful application of the above mentioned methods yielded the first metallocene based steroid derivative.

2. *C*-Deoxyribosides are nucleosides with a stable, non-hydrolysable C-C bond between the base and the sugar moiety. They enlarge the genetic alphabet of nucleosides and are used as modified building blocks for the synthesis of DNA, where they are interesting for their unnatural hydrophobic pairing. It was decided to develop a methodology to obtain highly substituted *C*-aryldeoxyriboside using cycloaddition reactions. The starting compound was a halogenose that was transformed to a compound with bulky substituent, in order to separate the anomers. After the separation, anomerically pure 3-(2-deoxyribofuranosyl)propynoates were prepared, their reaction with a complex of 2-butyne and aluminum chloride gave rise to Dewar benzenes. The rearrangement of these compounds to corresponding substituted (2-deoxyribofuranosyl)arenes was then studied under thermal and photochemical conditions. These arenes were also prepared by a cyclotrimerization reaction mediated by dibutylzirconocene. Lastly, 1-(2-deoxyribofuranosyl)dihydroindenes were prepared by yet another cyclotrimerization reaction catalyzed by ruthenium or rhodium complexes.

3. Asymmetric allylation of benzaldehydes is a useful process to obtain important synthetic building blocks – chiral homoallylic alcohols that have been used in the synthesis of various biologically active compounds. Enantioselectivity of up to 99% ee can be achieved using the bipyridyn-*N,N'*-dioxide catalyst acting as a Lewis base, which was developed in our group, or by using the chiral Brønsted acids. From a homoallylic alcohol that was prepared by these methods, a synthesis of the natural compound catalponol was devised. In the end the synthesis of this compound was not successful, however a new path to chiral butyrolacones was found. This was an impetus for the synthesis of another biologically active compound - the potential anti-inflammatory flobufen-lactone. The synthesis of this compound was fruitful and the desired flobufen-lactone was obtained highly enantiomerically pure and in good yield in just 7 steps. Beside the asymmetric allylations, a Lewis acid mediated closing of the lactone ring was the key step in the synthesis.