Abstract

Metal-containing nucleoside analogues based on butadiene-$Fe(CO)_3$ complexes or ferrocene exhibit pronounced biological activities especially concerning the induction of apoptosis in different cancer cell lines. Therefore a larger variety of related metallocene-containing derivatives would be of value to explore the specific role of the metal fragment and to broaden the scope of possible applications.

The stereoselective synthesis of novel, biologically active amino acid building blocks and nucleoside analogues based on different metal moieties ($FeCp_2$ and $RuCp_2$) is described. The synthetic strategy was first developed for $FeCp_2$ derivatives and later also applied to $RuCp_2$-derived compounds.

Planar chirality was introduced by diastereoselective metallation using an *ortho*-directing chiral auxilliary group attached to the metallocene to give the 1,2-disubstituted derivative as a pure diastereomer. Further functionalization led to two related planar-chiral intermediates, i.e. (1*S*, *E*)-ethyl-3-(2-phenylsulfonyl-acetyl-ferrocen-1-yl)-acrylate and (1*S*, *E*)-ethyl-3-(2-methoxy-carbonyl-ferrocen-1-yl)-acrylate. These compounds were subjected to different cyclization methods, either a 5-*exo*-trig Dieckmann condensation or an intramolecular Michael addition, to give a diastereoselective access to the corresponding 1,2-metallocene-fused cyclopentenes. By conversion of the functional groups, including a Mitsunobu reaction and a *Vorbrüggen* glycosidation, respectively, stereoselective entries to different epimeric, metallocene-annulated amino acid and nucleoside analogues were elaborated.

This synthetic approach has enabled the preparation of a diverse library of bioorganometallic compounds, which were tested for their biological activity. In addition, the obtained amino acid building blocks were incorporated into peptide chains by means of solid phase peptide synthesis (SPPS) and the possible applications of the metal-containing peptides were investigated.