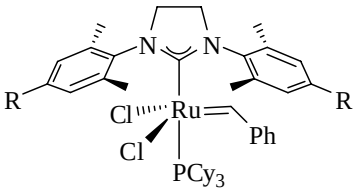
Studies about olefin metathesis and the application of this reaction for the synthesis of medium-sized ring-systems

Abstract:

In the first part of this PhD thesis, new ruthenium-based metathesis-catalysts were prepared bearing electronically different substituents on the *NHC*-ligand. The new complexes **2**-**4** were used in a ring-closing-metathesis (RCM) reaction in order to compare the catalyst-activity to the standard complex **1**. It was found that the complex with the nitro-substituted *NHC*-ligand was considerably less active than the other complexes. To investigate the problem of the *E/Z*-selectivity in metathesis reactions, several complexes of the type **5** were prepared. The aim was to investigate whether different groups X and X' would give different *E/Z* ratios. The *E/Z*-selectivity, however, was almost similar for all complexes prepared (figure 1).



R = Me (**1**), H (**2**) , NO_2 (**3**), MeO (**4**)

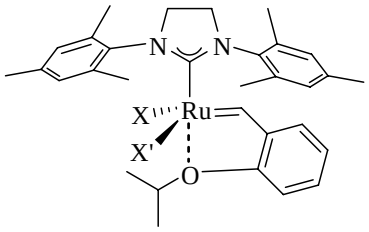


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Figure 1: Prepared complexes.

In the second part of the PhD thesis, RCM was used to build the medium-sized ten-membered ring of the actin microfilament binding molecule Microcarpalide (**6**). Analogue compounds (**7**-**9**) were prepared additionally. The concept of kinetic vs. thermodynamic control of the *E/Z*-selectivity of the RCM was used to obtain both isomers in good yields. During deprotection of the alcohol groups, the rings bearing the *Z*-alkene underwent a transesterification to give the butanolide structure **8** and its epimere **9** (figure 2). In biological tests, all four compounds showed the same considerable activity to bind on actin microfilaments while displaying a low cytotoxicity.

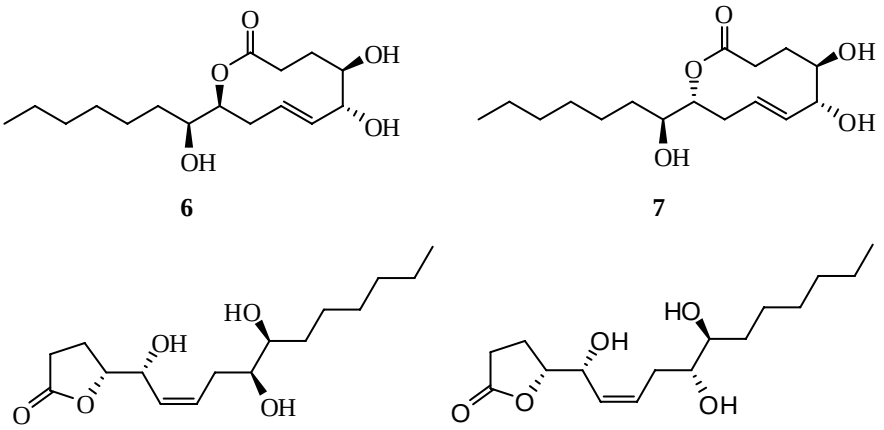

Figure 2: Microcarpalide and analogues.

The strained eleven-membered ring system of Aspercyclid C (**12**) was formed using RCM. Attempts to synthesise the Aspercyclides A and B (**10** and **11**) in a similar way were not met with success. In both cases the RCM gave predominantly side products and the deprotection of the alcohol groups was not feasible as well (figure 3).

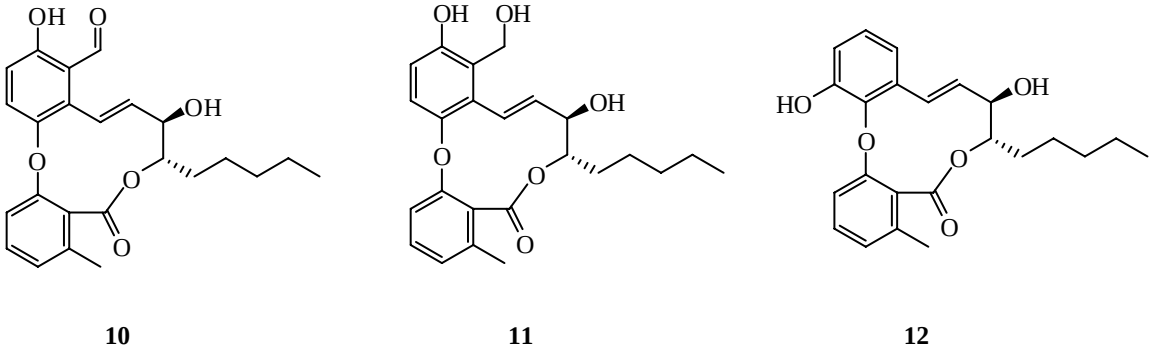

Figure 3: Aspercyclide A-C.