CHARLES UNIVERSITY IN PRAGUE

Faculty of Science

Department of Organic and Nuclear Chemistry

MODIFICATION OF ISOPRENOIDS

Synopsis of PhD Thesis

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Prague 2010

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Introduction

This PhD work is focused on the development of a new methodology aiming at the introduction of the perfluoroalkylated side-chains into various types of molecules. Synthesis of perfluoroalkylated compounds, owing to their biological properties, is a frequent target of organic chemistry.[1] During the last couple of decades a number of different methods enabling the perfluoroalkylation have been developed. Among the classical methods belong procedures based on nucleophilic, electrophilic, or radical reactions.[2] Interestingly, only a few examples of a transition metal catalyzed perfluoroalkylation reactions have been reported.[3] Despite the fact that many of these methods have wide synthetic applicability, they are not general and search for new procedures is a desirable target.

One of the possible and hitherto unexplored methods for the synthesis of perfluoroalkylated compounds is a ruthenium-complex catalyzed alkene cross-metathesis. Potentially, a reaction of a suitable terminal alkene reactant bearing a perfluoroalkylated moiety with the second terminal alkene could give rise to a new and more complex internal alkene. Regarding perfluoroalkylated alkenes suitable for the cross-metathesis reactions, (perfluoroalkyl)propenes can be considered as convenient substrates that can be easily prepared from the commercially available starting material.

Interestingly and luckily, prior to this work, the above mentioned strategy has not been pursued and thus it constituted an ideal opportunity for the exploratory research in this area.

The first aim of this work was the development of a perfluoroalkylating methodology including the studies of the scope and the limits of a ruthenium complex catalyzed cross-metathesis (CM) between suitable terminal alkenes and easily accessible (perfluoroalkyl)propenes.

The second aim was to specifically apply the developed methodology in syntheses of biologically active compounds e.g.:

a) perfluoroalkylated carboranes

b) perfluoroalkylated brassinosteroids

c) perfluoroalkylated derivatives of estrone

The majority of the prepared compounds were subjected to the biological tests. It was expected that the prepared perfluoroalkylated compounds – analogues or derivatives of natural or biologically active compounds – could exhibit interesting and perhaps desirable biological properties (e.g. metabolic stability, increased lipophilicity, etc.)