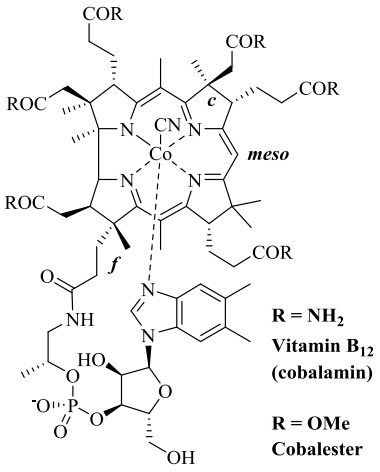
Synthesis and catalytic properties of new vitamin B_{12} derivatives

Maciej Giedyk

supervisor: prof. Dorota Gryko



Vitamin B_{12} is a complex biomolecule of vast importance for normal functioning of all mammalian organisms. Its various forms play the role of coenzymes and posess covalent Co-C bond that can be selectively cleaved, becoming a source of radicals. This characteristic feature, together with its nontoxicity, renders vitamin B_{12} a useful catalyst for radical reactions.

The goal of my studies was to synthesize new cobalamin derivatives and determine how do alterations in the molecular structure influence their catalytic properties. I also aimed to develop new organic reactions catalyzed by vitamin B_{12} derivatives.

At the first stage of my work I have established a method for the aminolysis of ester groups which are present at the periphery of the corrin ring in heptamethyl cobyrinate. A small library of heptaamides was obtained with diversified structure and physicochemical properties. They were subsequently functionalized at *c* and *meso* positions allowing for further conjugation. Aminolysis and hydrolysis reactions were also used for the synthesis of 8-*nor*-hexaamide and 8-*nor*-hexaacid derivatives.

Another part of my research focused on the modification of the primary amide groups present in cobalamin, leaving the nucleotide fragment at *f* position intact. As a result, I developed an efficient method for the transformation of these amides into ester groups by the activation of amide group with dimethylformamide dimethylacetal and subsequent methanolysis. The desired compound (cobalester) is the only amphiphilic vitamin B_{12} derivative possessing a nucleotide loop intact, being soluble in both polar and nonpolar solvents. Along with its hexaamide derivative, it was fully characterized by electrochemical means and the mechanism of the reduction of the central cobalt atom was determined.

Finally, I have discovered a new, light-induced, cobalester-catalyzed reaction of olefins with diazo compounds, leading to unexpected sp^2 C-H alkylation instead of the usual cyclopropanation. Moreover, procedures for benzyl bromide homocoupling in electrolytic or microwave conditions were developed.

In summary, my studies demonstrate the usefulness of vitamin B_{12} derivatives as efficient, environmentally benign catalysts in organic synthesis. They also provide

tools for modifying their structure, allowing to adjust catalyst properties for desired application.