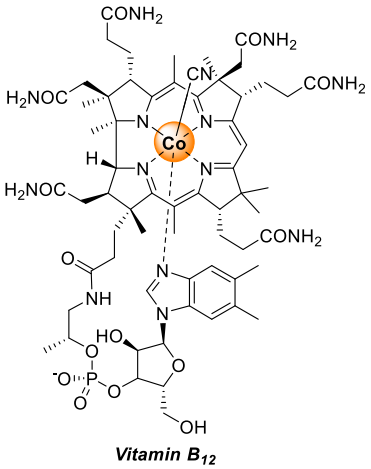
Vitamin B_{12} catalysis – generation of alkyl and acyl radicals

mgr Aleksandra Potrząsaj

Thesis advisor: prof. dr hab. Dorota Gryko



Vitamin B_{12}

Vitamin B_{12} is a complex biomolecule of great importance for the normal functioning of all living organisms. In eukaryotic cells, it acts as a cofactor that is involved in many biochemical processes (methyl transfer, isomerization, or dehalogenation). Its high catalytic capacity is conditioned by the presence of a weak covalent Co-C bond that can be selectively cleaved under reducing conditions, light or temperature becoming a source of radicals. This characteristic feature together with its non-toxicity is an ideal alternative to expensive and toxic catalysts containing heavy metals such as lead, ruthenium, or iridium. Many reactions catalyzed by vitamin B_{12} have been developed, of which, the majority utilise alkyl halides as a source of radicals.

The aim of this work was to expand the library of radical precursors useful in the catalysis of vitamin B_{12}, which would enhance the applicability of its utilization in organic synthesis.

In the first part of this work, I have focused on exploring the possibility of generating alkyl radicals from epoxides. In the case of photocatalytic reactions involving aryl epoxides, the attack of the reagents occurs from the more sterically hindered side, leading to highly reactive benzyl radicals. **I revealed that in the contrast to known methods, the bulky vitamin B_{12} catalyst can generate primary radicals, which react with electrophiles, to produce secondary alcohols.** The range of applicability of the developed method includes aliphatic and cyclic epoxides.

In the next part of my work, I decided to check whether oxetanes can be a radical precursors in vitamin B_{12} catalysis. Due to oxetanes having nearly double the Gibbs free energy compared to the ring opening of epoxides, the key step in this transformation was to select the appropriate Lewis acid. It was revealed that bromotrimethylsilane was the optimum Lewis acid. The optimization of the reaction conditions allowed the formation of the desired products in excellent yields. This method is useful for both Giese-type and cross-coupling reactions.

Finally, I have designed a reagent, that can generates both, acyl and alkyl radicals. **The kinetic profile revealed that the generation of alkyl radicals is a rate-determining process.**

In summary, my studies showed that epoxides and oxetanes can be used, in addition to commonly used alkyl halides, in vitamin B_{12}-catalyzed reactions.