

REGIOSELECTIVITY IN BIOCATALYTIC *O*-METHYLATION OF CATECHOLS

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Regioselective *O*-methylation of e.g. catechol derivatives allows the functionalization of molecules with chemically identical reactive groups. Moreover it would be a desirable tool in organic synthesis, as it avoids additional protection/deprotection strategies. Nevertheless the regioselective *O*-methylation of catechols is in general difficult to achieve. Thus, the most common methods often lead to tedious mixture of products difficult to separate.

On the other hand, biocatalysts are well known for their *regioselectivity*. Thus, they display a preference toward one of several functional groups present in a substrate molecule dictated by its accessibility to the protein active site and/or by its chemical reactivity.^[1]

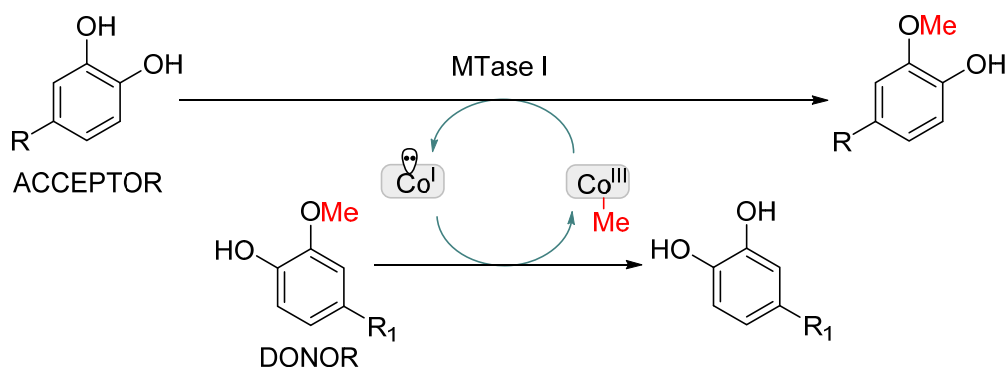


Figure 1. Biocatalytic methylation of substituted catechols.

The here described reaction relies on cobalamin (B12) as cofactor. This organometallic cofactor serves as methyl group shuttle and in combination with a methyltransferase (MTase I) can transfer a methyl group from a donor molecule to an acceptor (figure 1). When substrates bearing a catechol moiety are used as acceptor, the enzyme exhibits a certain *meta*-preference for the *O*-methylation. The aim of this project is to investigate how to enhance and control the regioselectivity of the *O*-methylation by reaction parameters. Until now, the enzymatic regioselectivity seemed to be enhanced by the use of co-solvents, for example, leading to 90/10 *m/p* ratio. Also the pH effects the regioselectivity as well as the side chain polarity. Among all these factors, it is desirable to find an ideal set of conditions (pH, co-solvent etc.) in order to accomplish the regioselective *O*-methylation of substituted catechols.

[1] Muller, P., *Glossary of terms used in physical organic chemistry (IUPAC Recommendations 1994)*. Pure and Applied Chemistry, 1994. **66**(5): p. 1077-1184.