Enzymatic dealkylation of natural substrate derivatives

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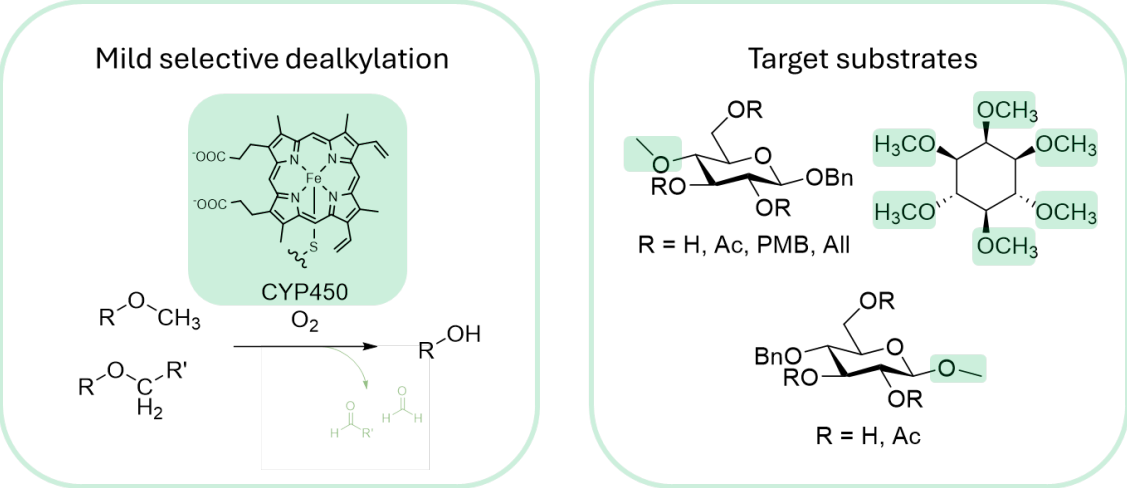

Alkyl ethers are robust moieties and easily introduced, making them an interesting group for the masking of alcohols. However, they require harsh conditions for their cleavage. Consequently, they are not commonly used as protecting groups, as their removal is not compatible with many other functional groups. To make alkyl ethers feasible as protecting groups, mild and selective dealkylation strategies need to be developed. When looking into the world of biocatalysis, cytochrome P450 monooxygenases emerge as promising candidates, as many of these enzymes already engage in analogous reactions, for example in drug metabolism pathways.

This preliminary study aims to broaden the substrate scope towards useful natural substrate derivatives, building upon previous research utilizing cytochrome P450 BM3 variants for the selective dealkylation of permethylated monosaccharides.[1] We explored the application of this enzyme on similar substrates with common protecting groups. Functional groups with different steric demands and chemical properties were chosen to gain an understanding of the enzyme's versatility.

Additionally, we seek to expand the enzymatic dealkylation to other natural substrate derivatives based on inositol and alkaloids.

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[1] J. C. Lewis, S. Bastian, C. S. Bennett, Y. Fu, Y. Mitsude, M. M. Chen, w. A. Greenberg, C. Wong, F. H. Arnold, *Proc Natl Acad Sci U S A* **2009**, *106*, 16550-16555.