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Exploring the Scope of Methyltransferase Biocatalysis

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PURPOSE OF THE ABSTRACT
S-adenosylmethionine (SAM)-dependent methyltransferases constitute a large family of enzymes that catalyze regio-, chemo- and stereospecific methylation of complex natural products. [1] These enzymes could be very useful tools for chemoenzymatic reaction and diversification of natural or synthetic compounds. Until recently, preparative applications of methyltransferases (MT) in vitro were limited because of the requirement for SAM as a stoichiometric methyl donor. Introduction of a simple SAM-regeneration process based on the ability of halide methyltransferases (HMT) to transfer methyl-groups from methyl iodide to S-adenosylhomocysteine (SAH) has highlighted a general strategy to harness enzyme-catalyzed alkylation in biocatalysis. [2 - 4] This strategy extends beyond methyl groups and applies to more complex alkyl groups. [5, 6]
Fluoromethyl groups may be of particular interest in this regard. Strategic fluorination can optimize the pharmacological properties of drugs by modulating their membrane permeability and metabolic stability. [7] Hence, the development of organic fluorides and the methodologies towards fluorination are of great interest. [8] We demonstrated successful enzyme-catalyzed attachment of fluoromethyl group onto C-, N- and O- and S-nucleophiles using fluormethyl iodide as a reagent. [9] In this presentation we will discuss our latest efforts to exploit the remarkable reactivity of some fluoromethylated products for the development of novel biocatalytic processes.

FIGURES

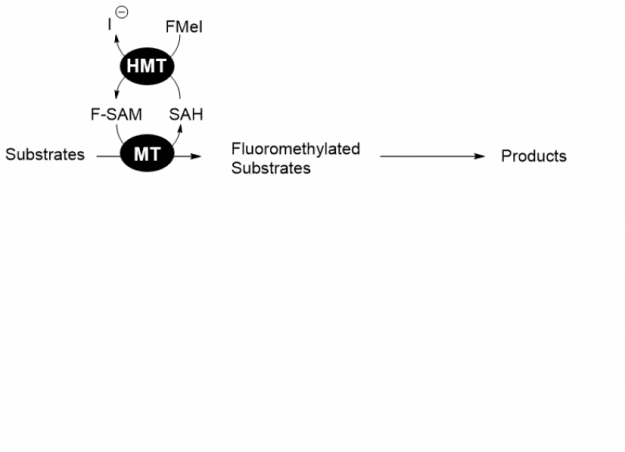

FIGURE 1

HMT-MT Cascade

HMT-MT cascade transfers fluoromethyl group to small and macromolecules that are subject to further reaction.

FIGURE 2

KEYWORDS

Biocatalysis | Halide methyltransferase | Fluoromethylation | SAM recycling

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