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Increasing the Utility of Biocatalytic Methylation Reactions through a Two-Enzyme Cascade

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PURPOSE OF THE ABSTRACT
S-adenosylmethionene (SAM)-dependent methyltransferases catalyse the methylation of a broad array of primary and secondary metabolites, often with exquisite chemo-, regio-, and stereoselectivity.1 However, the reliance of these enzymes on SAM as a stoichiometric methyl donor restricts their utility for large-scale applications, due to this reagents high cost and instability. Our laboratory has reported a dual-enzyme cascade involving a halide methyltransferase (HMT) and a C-, N-, or O-methyltransferase that enables biocatalytic methylation reactions to proceed with only a catalytic quantity of SAM and a stoichiometric amount of a structurally simpler, cheaper methyl donor (Figure 1).2 Remarkably, a number of abiotic methyl donor reagents, including sulfates and sulfonates, are accepted by the halide methyltransferase for the in situ regeneration of SAM.3 Our current research efforts are exploring this unexpected result to further optimize the biocatalytic reaction according to parameters such as reactivity, cost, atom-efficiency, and safety.

FIGURES

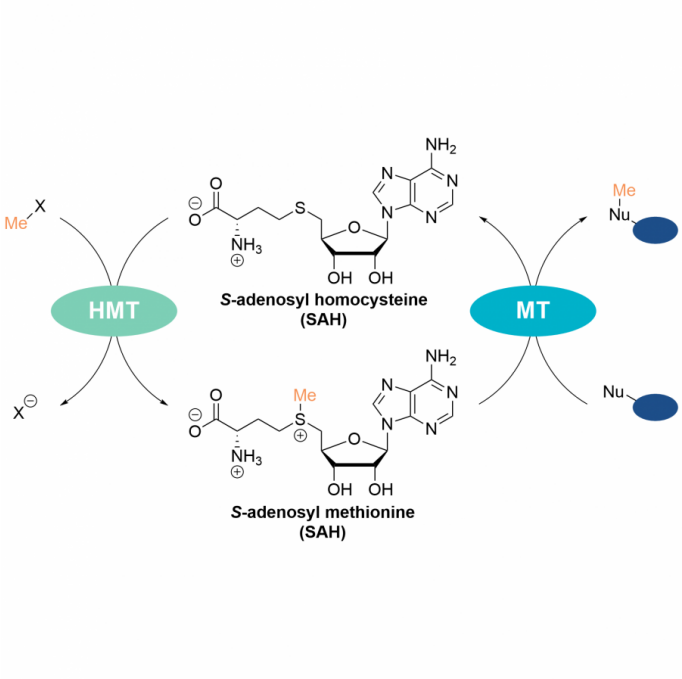

FIGURE 1

Figure 1

A two-enzyme cascade enables in situ regeneration of S-adenosyl methionine from S-adenosyl homocysteine and a methyl donor, while concurrently catalyzing the methylation of a target molecule.

FIGURE 2

KEYWORDS

methyltransferase | biocatalysis | enzymatic cascade | S-adenosyl methionine

BIBLIOGRAPHY

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