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SAM regeneration goes radical

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PURPOSE OF THE ABSTRACT

S-adenoslymethionine (SAM) is a highly versatile cofactor used by methyltransferases, amino(carboxy)propyltransferases and radical SAM enzymes. Hence, it is involved in a wide range of reactions with polar or radical mechanisms.[1] However, the instability and high cost of SAM and byproduct inhibition impedes the usage of SAM-dependent enzymes.[2] Therefore, in situ SAM regeneration systems have been developed. These systems are highly effective and are able to support up to 500 turnovers with catalytic amounts of cofactor.[3–5] Nevertheless, in all systems SAM regeneration relies on S-adenosylhomocysteine (SAH), the byproduct of methyltransferase reactions. Amino(carboxy)propyltransferases and radical SAM enzymes are not supported as they produce 5'-methylthioadenosine (MTA) and 5'-deoxyadenosine as byproducts, respectively.

The goal of the work presented was to develop a versatile SAM regeneration system that supports the vast catalytic spectrum of methyltransferases, amino(carboxy)propyltransferases and radical SAM enzymes. The system relies on byproduct cleavage by MTA/SAH nucleosidase and a polyphosphate-fuelled biomimetic production of phopshoribose pyrophosphate. We could show that methyltransferases, aminopropyltransferases and radical SAM enzymes are functional in this system, supporting up to 80, 57 and 29 turnovers, respectively. Additionally, the system's flexibility was underlined by the transfer of an ethyl group using a cobalamin-dependent radical SAM methyltransferase. This novel reaction further demonstrates the potential of SAM analogue supply and regeneration for the application of diverse chemistry.[6]

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

Alkylation | Cofactor regeneration | SAM Analogues | Radical SAM Enzyme

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