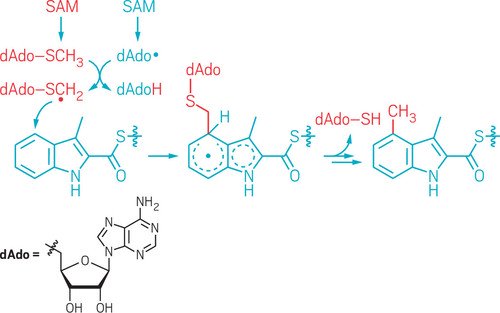
**Graduate Research Plan Statement**

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In 2017, a research team in China found reaction mechanism that was unexpected for most enzymes that are able to add methyl groups to biomolecules. These enzymes, or methyltransferases, depends mostly on S-adenosylmethionine (SAM). The methyl group is taken from the molecule and is simply relocated. However, it is found that this is not always the case since NosN, a class C radical SAM methyltransferase, uses a different source for the methyl group. The researchers proposed a different mechanism which could explain where the methyl group can be sourced from and further research could help other researchers reengineer the enzyme and produce various compounds1. The proposed mechanism can be seen in **Figure 1**. To further understand this mechanism, it is vital to see first if the proposed mechanism is viable and useful in synthesizing the enzyme. This can be done by calculating the mechanism thermodynamic properties and doing more research.

**Intellectual Merit**

The proposed research is to calculate the thermodynamic properties of the mechanism to see how spontaneous the reaction is and to see if the mechanism is a viable method in synthesizing the enzyme using the Gaussian162 program.

After calculating and determining whether the mechanism is useful, I propose to look at other possible mechanisms that can explain the methyl group addition in the molecule. The thermodynamic properties will then also be calculated for

**Figure 1.** *The radical SAM methyltransferase NosN converts one S-adenosylmethionine to a dAdo radical (blue) that initiates the reaction and another to 5′-methylthioadenosine (red), which acts as the methyl donor1.*

the new mechanisms proposed to see which mechanism is the most plausible for the synthesis of the molecule. Entropy and enthalpy will be observed to see the spontaneity of each mechanism which could help determine the better mechanism.

After doing the calculations, using what we know from organic chemistry theory, the most plausible mechanism will be compared to the best mechanism that was calculated for. If the two mechanisms chosen do not match up, more research may be necessary to determine what really happens when the molecule is synthesized. This is because Gaussian does not take into account real world interactions with the molecule, for example the solvent used, which could factor in the process the molecule undergoes. Research will be done to determine fully what mechanism is the most plausible for the synthesis or at least until the data makes sense or agree with each other.

Once the mechanism has been determined or if the proposed mechanism is proven to be the best mechanism, synthesis of other compounds using this mechanism will be tested to see if the result will be the same. If the result is the same or follows the mechanism proposed and can be replicated, we know that the result agrees with the data determined through calculations and theory. A conclusion can then be made if this method is viable to the process.

**Broader Impacts**

This research is useful in understanding better how this enzyme is synthesized. Also, since the proposed mechanism is fairly new, proving that the mechanism is possible in methylating the enzyme will further our knowledge and aid in the synthesis of other compounds. This can help aid further researchers when synthesizing compounds that need methylation and see this process as a viable method. This can also help better the understanding of the radical SAM enzyme and the processes that it can undergo when reacting with other molecules. Having the knowledge that the synthesis is replicable will also prove that the mechanism proposed is a viable way for the methylation of a molecule. It gives further possibilities in other synthesis that researchers may want to do. Since the SAM enzyme is a common molecule for methyltransferase, it is often used in various research and understanding the mechanism better can help when proposing new synthesis for other enzymes. The SAM enzyme is also a relatively affordable resource that costs about 0.59USD per 200mg tablet3 which could mean that synthesizing other compounds using this enzyme to do a methylation might be cheaper than other methods that can also help with a similar synthesis. When synthesizing compounds, it is always best to use an affordable and doable method which is the goal of proving the mechanism through this research.

**References**

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