Syntesis of S-Adenosyl-L-homocysteine Analogs for Structural Studies of Methyltransferases

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A number of genetic and oncological diseases are caused by malfunctioning proteins. For example, Williams syndrome (WS) is associated with defects in WBSCR27 protein. To develop an effective treatment for WS one should know the exact tertiary structure of this protein. In this project, special substances have been synthesized, that mimic the structure of the SAH cofactor. For exact tertiary structure determination a multistep organic synthesis of SAH cofactor analogs was performed from commercially available starting materials using standard organic chemistry techniques. Target compounds were used in NMR experiments with protein samples. We have demonstrated the interaction between the protein and modified cofactors, but tertiary structure of the WBSCR27 protein active site still could not be obtained. As a result, the possibility of the developed NMR technique to study exact tertiary structures were proved. we plan to synthesize a number of SAH derivatives that will enable us to define the exact tertiary structure of the proteins under study.

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