World Academy of Science, Engineering and Technology
International Journal of Chemical and Materials Engineering
Vol:10, No:06, 2016

Novel Adomet Analogs as Tools for Nucleic Acids Labeling

Authors : Milda Nainyte, Viktoras Masevicius

Abstract : Biological methylation is a methyl group transfer from S-adenosyl-L-methionine (AdoMet) onto N-, C-, O- or S-nucleophiles in DNA, RNA, proteins or small biomolecules. The reaction is catalyzed by enzymes called AdoMet-dependent methyltransferases (MTases), which represent more than 3 % of the proteins in the cell. As a general mechanism, the methyl group from AdoMet replaces a hydrogen atom of nucleophilic center producing methylated DNA and S-adenosyl-L-homocysteine (AdoHcy). Recently, DNA methyltransferases have been used for the sequence-specific, covalent labeling of biopolymers. Two types of MTase catalyzed labeling of biopolymers are known, referred as two-step and one-step. During two-step labeling, an alkylating fragment is transferred onto DNA in a sequence-specific manner and then the reporter group, such as biotin, is attached for selective visualization using suitable chemistries of coupling. This approach of labeling is quite difficult and the chemical hitching does not always proceed at 100 %, but in the second step the variety of reporter groups can be selected and that gives the flexibility for this labeling method. In the one-step labeling, AdoMet analog is designed with the reporter group already attached to the functional group. Thus, the one-step labeling method would be more comfortable tool for labeling of biopolymers in order to prevent additional chemical reactions and selection of reaction conditions. Also, time costs would be reduced. However, effective AdoMet analog appropriate for one-step labeling of biopolymers and containing cleavable bond, required for reduction of PCR interferation, is still not known. To expand the practical utility of this important enzymatic reaction, cofactors with activated sulfonium-bound side-chains have been produced and can serve as surrogate cofactors for a variety of wild-type and mutant DNA and RNA MTases enabling covalent attachment of these chains to their target sites in DNA, RNA or proteins (the approach named methyltransferase-directed Transfer of Activated Groups, mTAG). Compounds containing hex-2-yn-1-yl moiety has proved to be efficient alkylating agents for labeling of DNA. Herein we describe synthetic procedures for the preparation of N-biotinoyl-N’-(pent-4-ynoyl)cystamine starting from the coupling of cystamine with pentynoic acid and finally attaching the biotin as a reporter group. The synthesis of the first AdoMet based cofactor containing a cleavable reporter group and appropriate for one-step labeling was developed.

Keywords : adoMet analogs, DNA alkylation, cofactor, methyltransferases
Conference Title : ICOC 2016 : International Conference on Organic Chemistry
Conference Location : Copenhagen, Denmark
Conference Dates : June 27-28, 2016