66TH INTERNATIONAL

OPEN READINGS

CONFERENCE FOR STUDENTS OF PHYSICS AND NATURAL SCIENCES

ANNUAL ABSTRACT BOOK | 2023

Vilnius University

VILNIUS UNIVERSITY PRESS

Editors

Martynas Keršys
Šarūnas Mickus

Cover and Interior design
Milda Stancikaitė

Vilnius University Press
9 Saulėtekio Av., III Building, LT-10222 Vilnius
info@leidykla.vu.lt, www.leidykla.vu.lt/en/
www.knygynas.vu.lt, www.journals.vu.lt

Bibliographic information is available
on the Lithuanian Integral Library Information System (LIBIS) portal ibiblioteka.lt.

ISBN 978-609-07-0883-5 (ePDF)

DOI: https://doi.org/10.15388/IOR2023

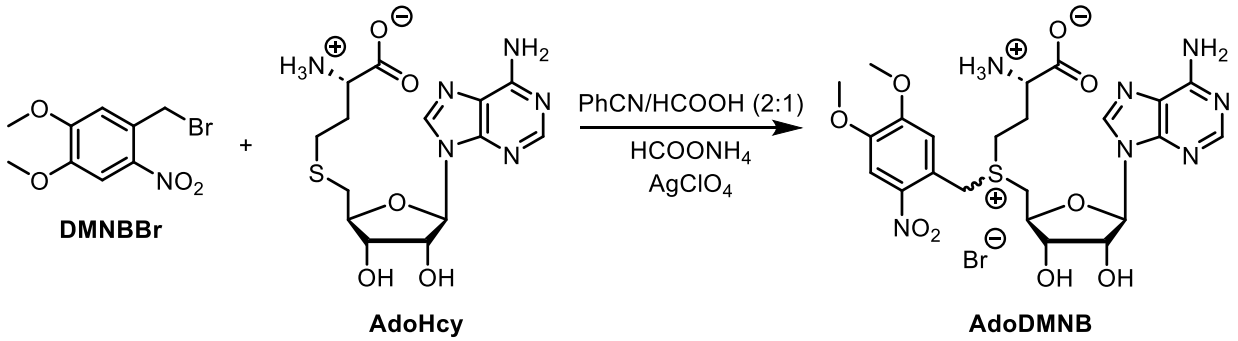
SYNTHESIS OPTIMIZATION OF ADOMET ANALOGUE FOR PHOTOCLEAVABLE GENE LABELING

Mindaugas Matonis[1], Martynas Malikėnas[2]

[1]Faculty of Chemistry and Geosciences, Vilnius University, Lithuania
[2]Institute of Biotechnology, Vilnius University, Lithuania
mindaugas.matonis@chgf.stud.vu.lt

DNA methylation is a predominant epigenetic modification that regulates gene expression without altering the original DNA sequence [1]. In DNA, m^5C leads to inactivation of transcriptional start sites, while its oxidative removal recovers gene expression [2]. The reaction occurs via methyltransferase (MTase) catalyzed S_N2 transfer of an activated sulfonium-bound methyl group from the cofactor S-adenosyl-L-methionine (SAM) to targeted DNA bases, S-adenosyl-L-homocysteine (SAH) serving as a leaving group [1][3]. The use of photolabile and reactive groups instead of methyl may lead to an easy way to make genetic modifications. Unfortunately, synthetic cofactors with functional groups other than methyl suffer from abysmal stability in the physiological medium and the limited literature on synthesis of the cofactors indicates unsatisfactory yields. Although DMNB is one of the functional groups that is stable in the physiological medium and shows promising application in gene labeling, synthesis yields are poor and need to be further optimized.

The aim of this work is to present an optimized synthesis of AdoDMNB cofactor.



Scheme 1. Synthesis of photocleavable group containing AdoMet cofactor analogue (AdoDMNB).

References:

[1]. S. Klimašauskas and E. Weinhold, "A new tool for biotechnology: AdoMet-dependent methyltransferases," Trends Biotechnol., vol. 25, no. 3, pp. 99–104, 2007, doi: 10.1016/j.tibtech.2007.01.006.

[2]. F. Michailidou, N. Klöcker, N. V. Cornelissen, R. K. Singh, A. Peters, A. Ovcharenko, D. Kümmel, A. Rentmeister, Angew. Chem. Int. Ed. 2021, 60, 480. DOI: 10.1002/anie.202012623.

[3]. G. Lukinavičius, M. Tomkuvienė, V. Masevičius, and S. Klimašauskas, "Enhanced chemical stability of AdoMet analogues for improved methyltransferase-directed labeling of DNA," ACS Chem. Biol., vol. 8, no. 6, pp. 1134–1139, 2013, doi: 10.1021/cb300669x.