16th Iberian Peptide Meeting
4th ChemBio Group Meeting

16EPI·4GEQB

Barcelona, PRBB Auditorium
February 5-7, 2018

PROGRAM & BOOK OF ABSTRACTS

RSEQ

EPS

P57 - Serine vs. α-Methylserine Sulfamidates in *O*-glycosylation reactions

Paula Oroz, Alberto Avenoza, Jesús H. Busto, Jesús M. Peregrina, Gonzalo Jiménez-Osés

Departamento de Química, Centro de Investigación en Síntesis Química. Universidad de La Rioja. 26006 Logroño, La Rioja, Spain
email: paoroz@unirioja.es

The Tn antigen is a target for the development of cancer vaccines. Nowadays there is an active field of research focused on the design of Tn analogues acting as better candidates for anticancer vaccine generation.[1] Our group has contributed to this field by synthetizing and evaluating a new cancer vaccine incorporating α-GalNAc-α-MeSer (α-MeSer = α-methylserine).[2]

We report herein a new, improved methodology based on the nucleophilic ring-opening of cyclic sulfamidates derived from synthetically accessible α-methylserine with different carbohydrates as C1-*O*-nucleophiles. This protocol led to different glycosyl amino acids including the Tn antigen mimic α-GalNAc-α-MeSer in good yields and as single α anomers, without further chromatographic purification (Scheme 1).

Conversely, the analogous sulfamidate derived from natural serine showed a high propensity to undergo elimination reactions under the same conditions, as explained computationally. The resulting dehydroalanine derivatives are currently being examined as Michael acceptors.

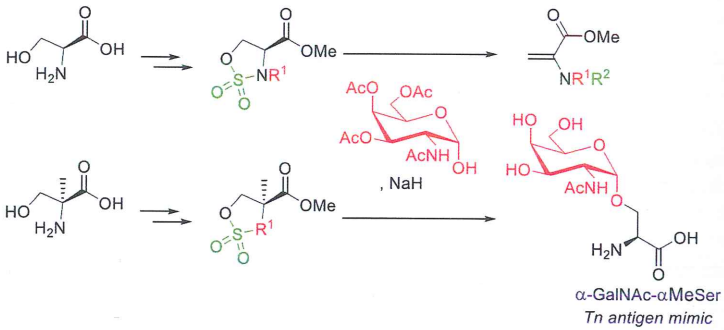

Figure 1. Synthesis and ring-opening of cyclic sulfamidates derived from serine and α-methylserine.

References

1. Martínez-Sáez, N.; Peregrina, J. M.; Corzana, F. *Chem. Soc. Rev.* **2017** (doi: 10.1039/6CS00858E).
2. Martínez-Saez, N.; Supekar, N. T.; Wolfert, M. A.; Bermejo, I. A.; Hurtado-Guerrero, R.; Asensio, J. L.; Jiménez-Barbero, J.; Busto, J. H.; Avenoza, A.; Boons, G.-J.; Peregrina, J. M.; Corzana, F. *Chem. Sci.* **2016**, 7, 2294.

Acknowledgements

We thank the *Ministerio de Economía y Competitividad* (projects: CTQ2015-67727-R, UNR13-4E-1931, CTQ2015-70524-R and RYC-2013-14706).

Production of this booklet has been kindly supported by Lilly

SERINE VS. α-METHYLSERINE SULFAMIDATES IN *O*-GLYCOSYLATION REACTIONS

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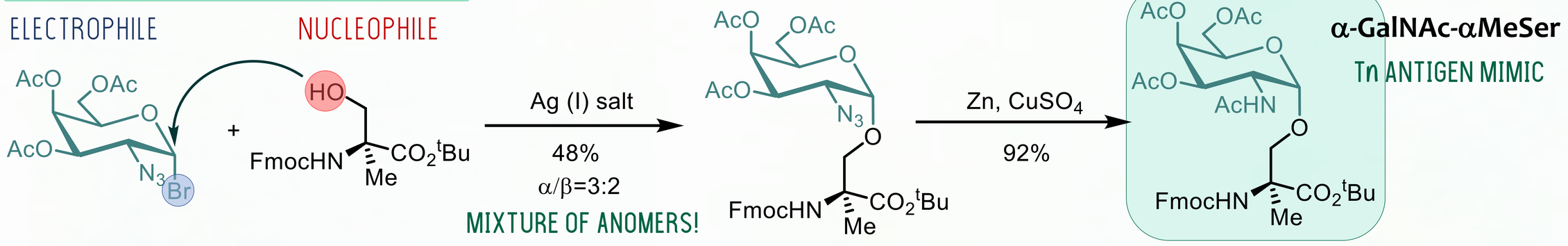
Departamento de Química, Centro de Investigación en Síntesis Química. Universidad de La Rioja. 26006 Logroño, La Rioja, Spain
email: paoroz@unirioja.es

INTRODUCTION

The **Tn antigen** is a target for the development of cancer vaccines. Nowadays there is an active field of research focused on the design of **Tn analogues** acting as better **candidates for anticancer vaccine generation**.[1] Our group has contributed to this field by synthetizing and evaluating a new cancer vaccine incorporating α-GalNAc-α-MeSer (α-MeSer = α-methylserine).[2]

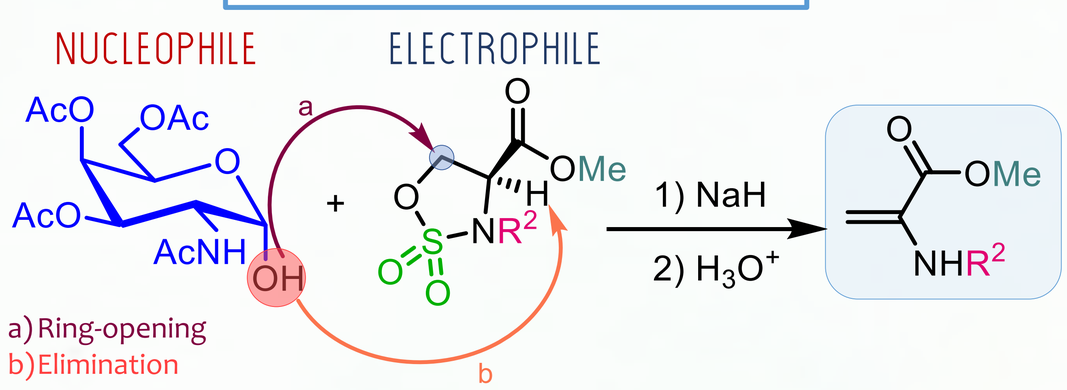
We report herein **a new, improved methodology** based on the **nucleophilic ring-opening of cyclic sulfamidates** derived from synthetically accessible α-methylserine **with different carbohydrates** as C1-O-nucleophiles.

PREVIOUS METHODOLOGY



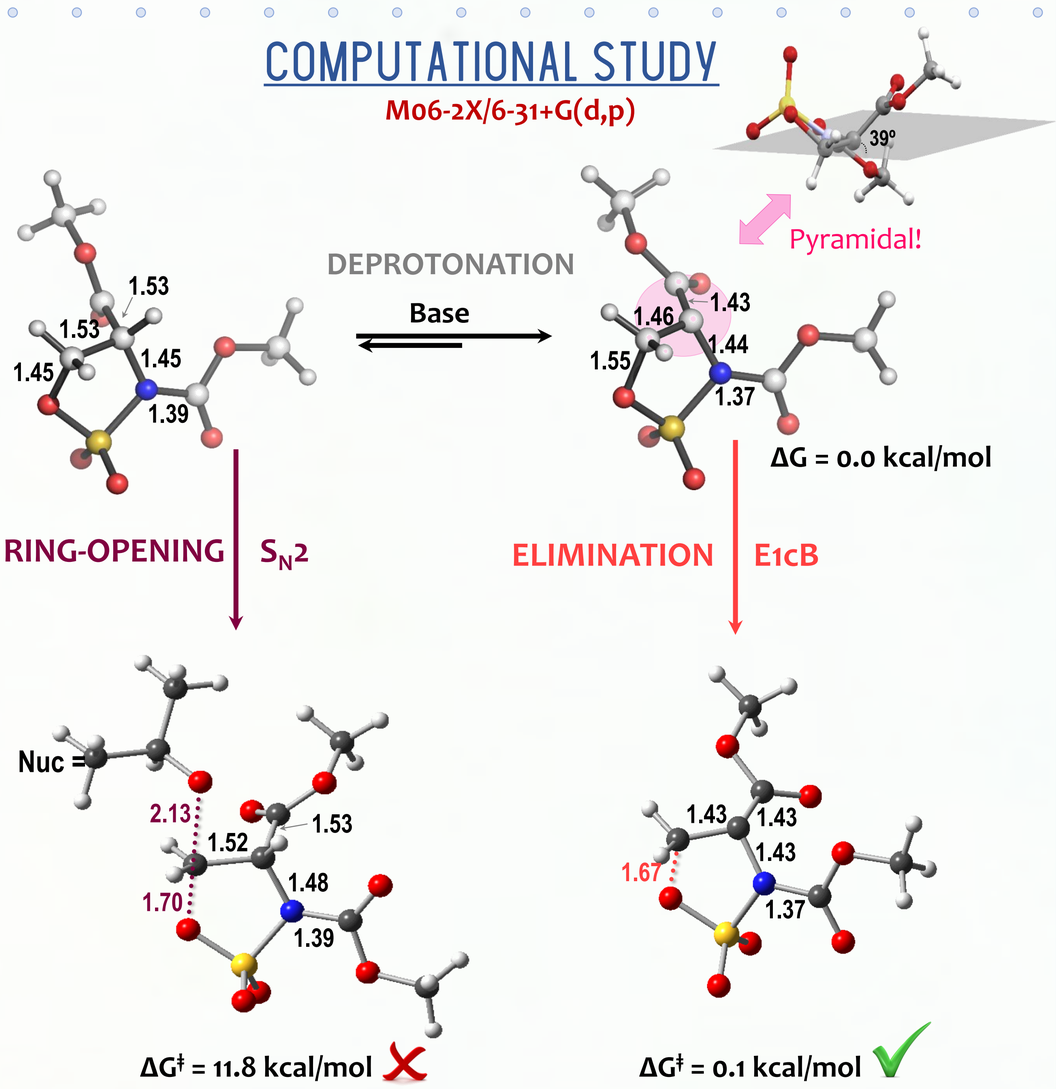
NEW METHODOLOGY

SERINE SULFAMIDATE



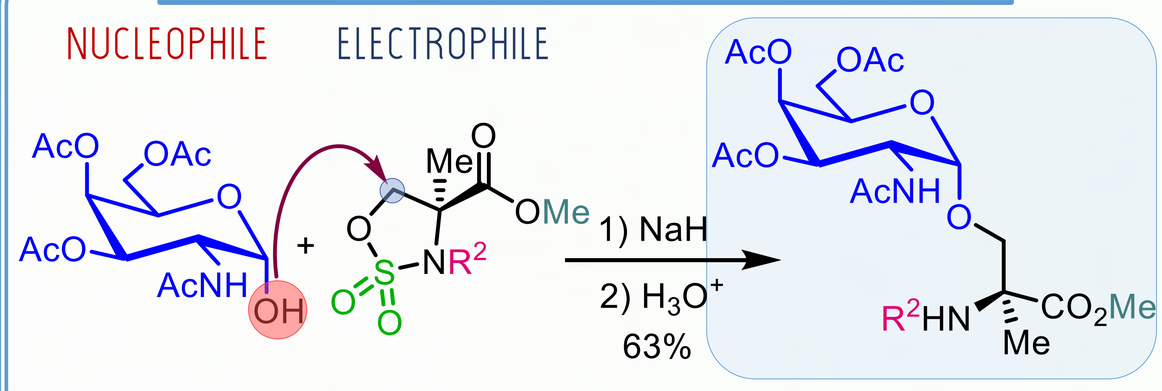
COMPUTATIONAL STUDY

M06-2X/6-31+G(d,p)

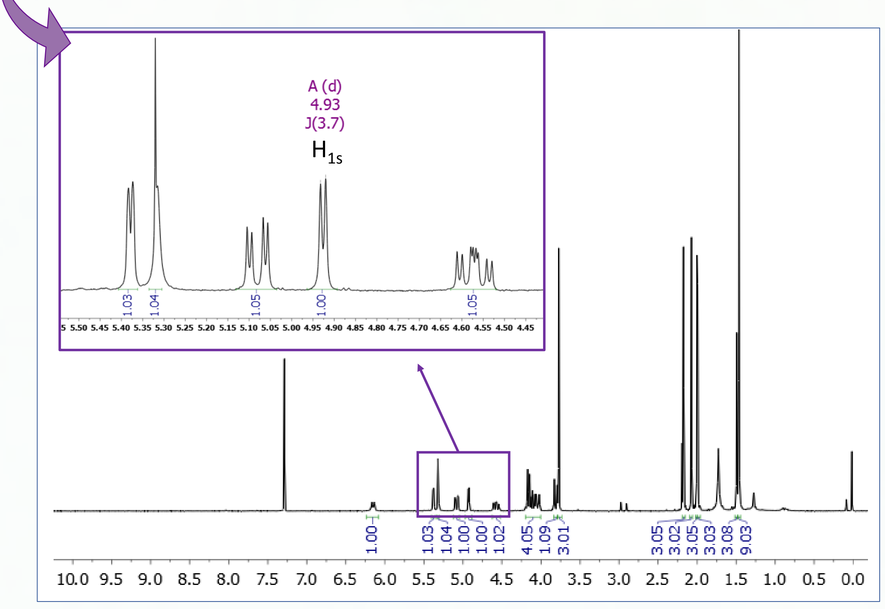


BASIC NUCLEOPHILES DEPROTONATE H_α → ELIMINATION (not RING-OPENING)

α-METHYLSERINE SULFAMIDATE



ONLY α- ANOMER!



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1. Martínez-Sáez, N.; Peregrina, J. M.; Corzana, F. *Chem. Soc. Rev.* **2017**
2. Martínez-Saez, N.; Supekar, N. T.; Wolfert, M. A.; Bermejo, I. A.; Hurtado-Guerrero, R.; Asensio, J. L.; Jiménez-Barbero, J.; Busto, J. H.; Avenoza, A.; Boons, G.-J.; Peregrina, J. M.; Corzana, F. *Chem. Sci.* **2016**, *7*, 2294.

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