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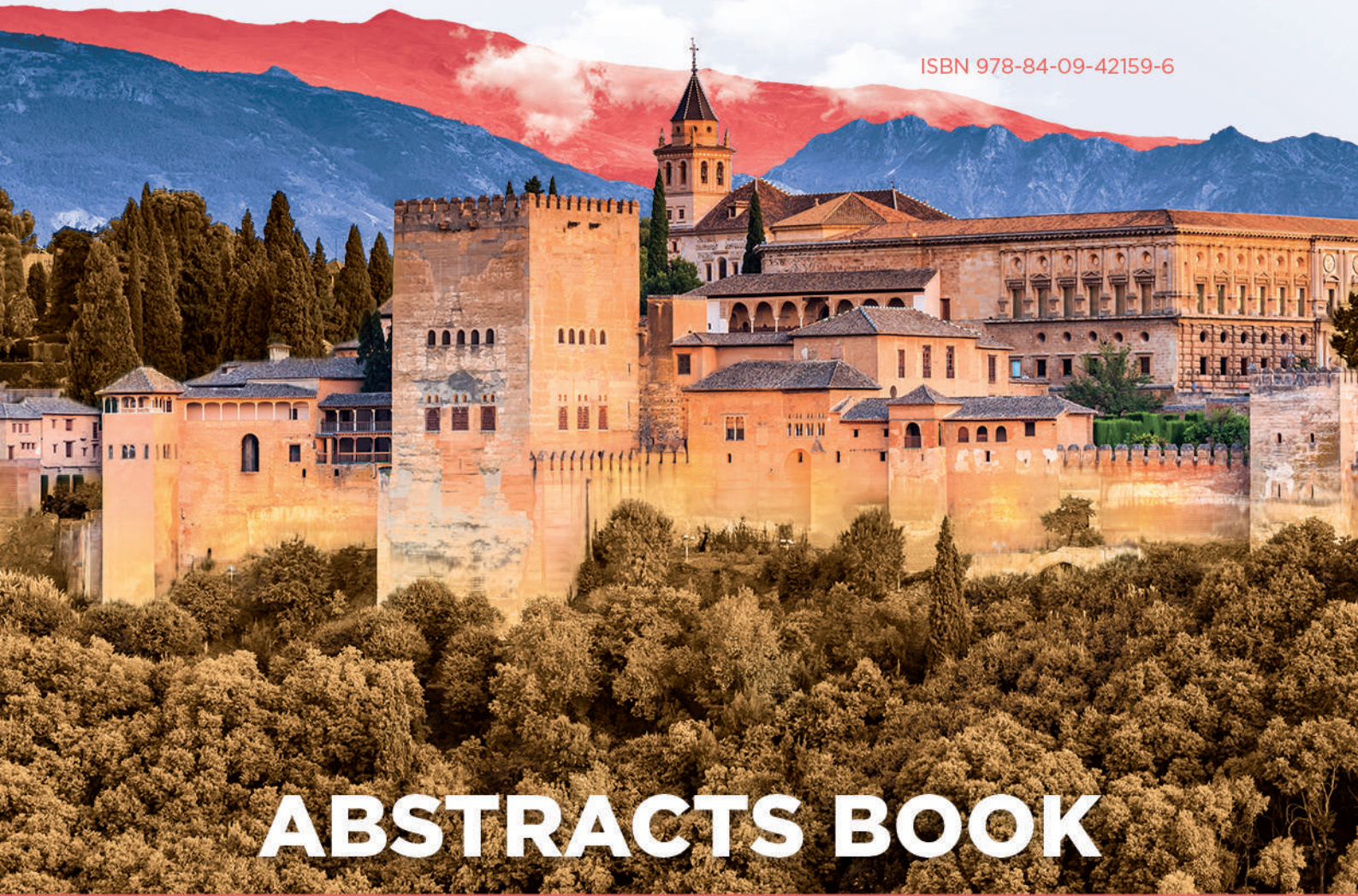

ABSTRACTS BOOK

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TOWARDS ENANTIOMERICALLY PURE β-SELENO-α-AMINO ACIDS VIA STEREOSELECTIVE *Se*-MICHAEL ADDITIONS TO CHIRAL DEHYDROALANINES

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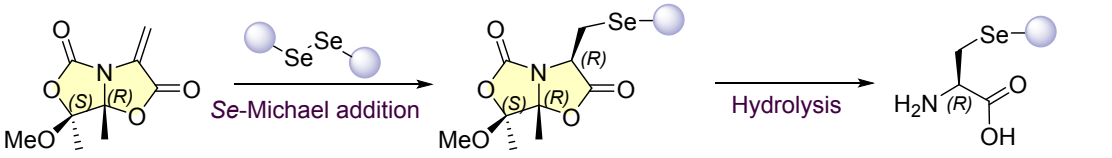
Selenium plays a crucial role in different biological processes, being necessary for the proper functioning of the human body. Therefore, selenium compounds have become molecules of great interest due to their antiviral and anticancer activities and their use as natural food supplements.

Selenocysteine (Sec) is the 21st genetically encoded amino acid and plays an important role in protein folding and stability, conferring interesting redox properties. In addition, protected selenocysteine derivatives are used as precursors of dehydroalanine, which allows the introduction of various post-translational modifications. On the other hand, some aryl derivatives of Se serve as chemical models for the inhibition of selenoenzymes, which has implications for cancer therapy. Beyond applications in bioconjugation, selenoamino acids are especially relevant in Native Chemical Ligation (NCL).[1]

Although the nucleophilic substitution reaction has been widely employed for the synthesis of these Sec derivatives, 1,4-conjugate addition has been less explored, especially the stereoselective 1,4-conjugate addition of *Se*-nucleophiles to chiral Michael acceptors. Therefore, in this work, we aim to extend the methodology established by our research group[2] to the synthesis of enantiomerically pure selenoamino acids. The key step of such synthesis is the attack of different *Se*-nucleophiles to a chiral dehydroalanine, to obtain a single diastereoisomer. The methodology is simple and does not require the use of any catalyst, providing excellent yields at room temperature. Subsequent facile acid hydrolysis of the above diastereoisomers leads to the corresponding selenoamino acids.[3]



Chiral dehydroalanine (Dha)

Enantiomerically pure!

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[2] C. D. Navo, N. Mazo, P. Oroz, M. I. Gutiérrez-Jiménez, J. Marín, J. Asenjo, A. Avenoza, J. H. Busto, F. Corzana, M. M. Zurbano, G. Jiménez-Osés, J. M. Peregrina, *J. Org. Chem.* **2020**, *85*, 3134–3145.

[3] P. Oroz, C. D. Navo, A. Avenoza, J. H. Busto, F. Corzana, G. Jiménez-Osés, J. M. Peregrina, *Org. Lett.* **2021**, *23*, 1955–1959.

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INTRODUCTION

Selenium plays a crucial role in different biological processes, being necessary for the proper functioning of the human body. Therefore, selenium compounds have become **molecules of great interest** due to their antiviral and anticancer activities and their use as natural food supplements.

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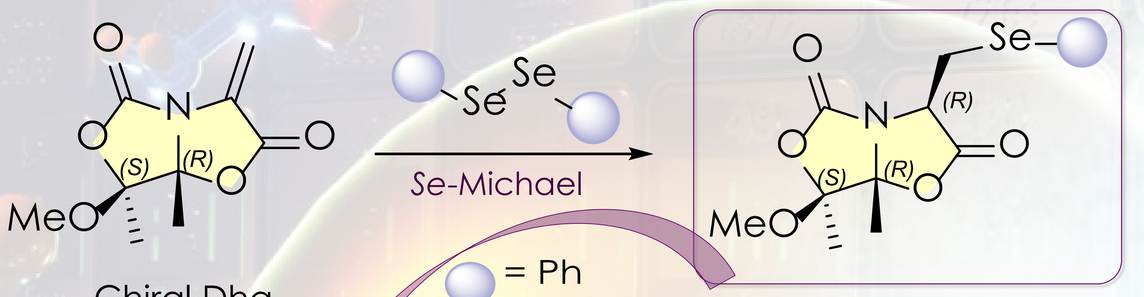
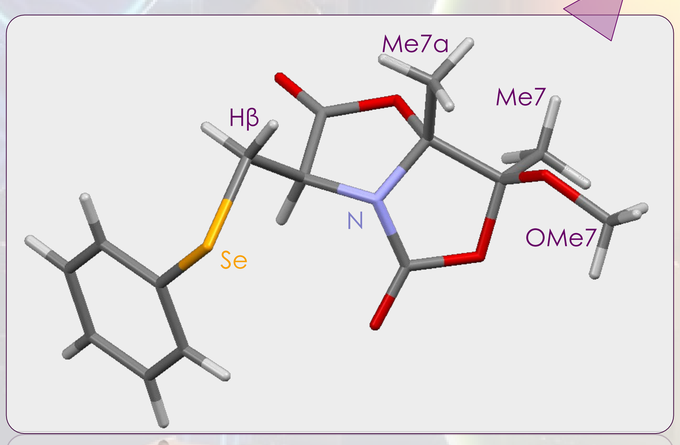
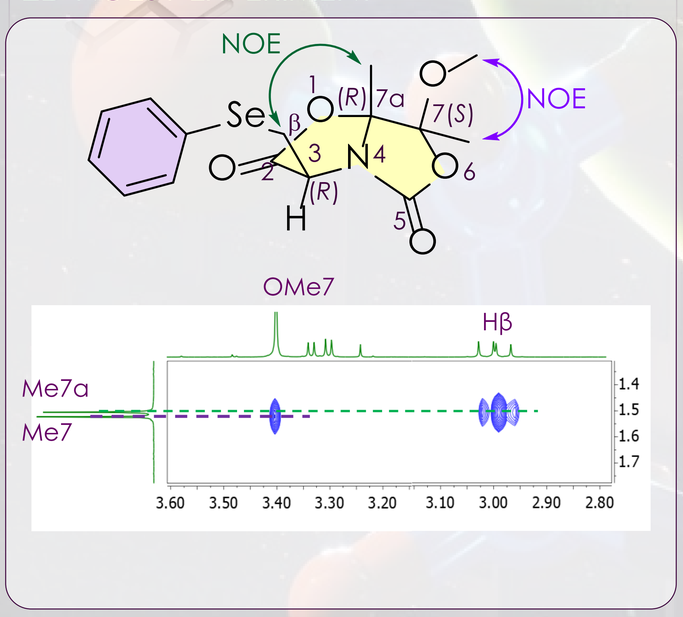
MICHAEL ADDITION



X-RAY EXPERIMENT



2D-NOESY EXPERIMENT



= PMB — Selenocystine — Implicated in cancer therapy!

= Allil — Allylselenocysteine — Inhibitor of mammary carcinogenesis!

= CH_2CH_2NHBoc — Selenolysine — Used in lanthipeptide synthesis!

= Boc-L-selenocisteina-OMe — Selenolanthionine — Renewed interest including its incorporation in lanthipeptides!

= SeGalNAc — Mimetic Tn antigen — Improved antibody recognition!

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Agencia estatal de Investigación (AEI). Ministerio de Ciencia, Innovación y Universidades (RTI2018-099592-B-C21 project)
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(3) Oroz, P.; Navo, C. D.; Avenoza, A.; Busto, J. H.; Corzana, F.; Jiménez-Osés, G.; Peregrina, J. M. *Org. Lett.* **2021**, *23*, 1955–1959.