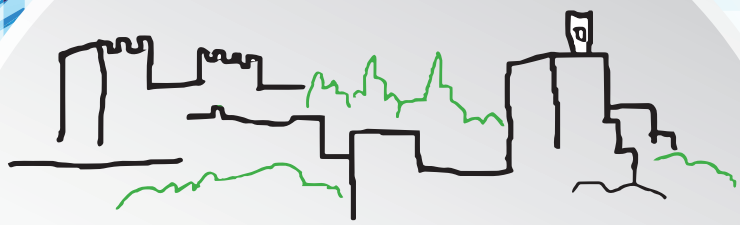
# GRANADA

# Book of Abstracts



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# Site-selective protein modification withnovel dehydroalanine derivatives

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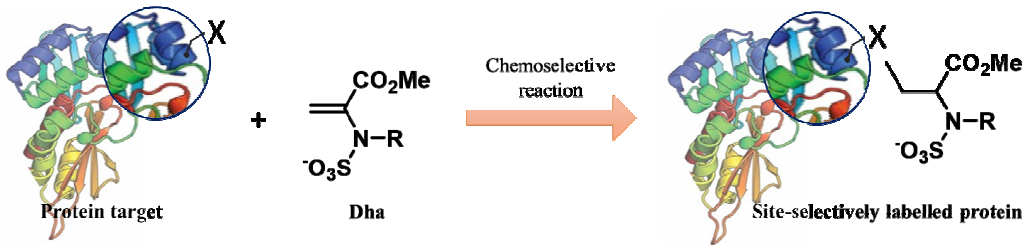
Bioconjugation is a very potent tool to chemically modify proteins in order to install new functionalities such as fluorescent probes, cytotoxic payloads, etc.[1]When exploring the natural reactivity of the amino acid side chains, for example, cysteine[2] and lysine[3] ubiqutuous biological nucleophiles may competewith electrophilic reagents, depending on the working conditions. Despite those issues, several methods based on selective reactions of certain amino acids have been developed in recent years.

α,β-Dehydroamino acids are well-known electrophiles occasionally used for protein modification, leading to a range of natural and unnatural post-translational modifications (PTM) such as lanthionines and lysinoalanines. However, the low reactivity of these functionalities, which require the concurrence of enzymes for natural PTM, or the use of large electrophile excess for chemical modification, has limited their use and scope.

This work presents the design, synthesis and evaluation of new water-soluble dehydroalanine derivatives able to react with amino acids different from commonly targeted cysteine and lysine. The reactivity and chemoselectivity of these reagents as Michael acceptors observed with both small-molecule nucleophiles and in protein bioconjugation, is described.




In parallel, an innovative non-destructive, reagent-freeassaybased in 2D NMR spectroscopy to unequivocaly determine the extent and identity of the protein modifications directly in aqueous solution, is presented.

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**References**

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