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ABSTRACT BOOK

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Development of new fluorescent dehydroamino acids as Michael acceptors

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Site-selective chemical modification has emerged as a potential tool for protein functionalization in order to install new functionalities such as fluorescent probes, cytotoxic payloads, etc.[1] Chemo- and regioselective labelling of certain amino acids in a variety of proteins has been achieved in recent years. For instance, sidechains of cysteine[2] and lysine[3] are often suitable for modification through a Michael addition, due to their nucleophilic character.

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 describes the synthesis and study of new fluorescent dehydroalanine derivatives (Dha) designed for protein labelling. Their reactivity with both small-molecule nucleophiles and sidechains of proteins has been explored. As a result, these new water-soluble Dha showed high reactivity and chemo selectivity as Michael acceptors.

Figure 1. Chemoselective ligation in protein labelling.

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