



Diels-Alder Chemistry for Bioconjugation and Incorporation into Non-Natural Amino Acids

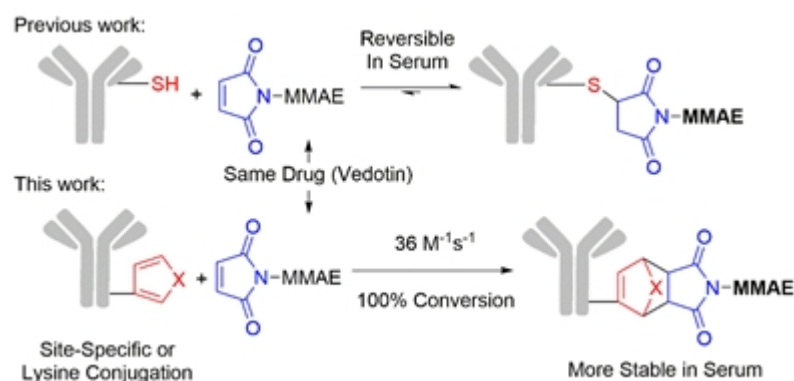
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BACKGROUND

Therapeutic compounds, such as antibody-drug conjugates (ADCs), are prepared where the drug bears a reactive functional group (such as maleimide) for attachment to an antibody. The bioconjugation reactions for coupling to native residues (Lys and Cys) in biological molecules have changed very little in the last five to ten years. However, new reactions are becoming more important as second and third generation ADCs are developed for the treatment of diseases. While new bioconjugation chemistries have expanded the strategies for preparing bioconjugates, their applications to prepare therapeutic molecules can be limited due to long reaction times, hydrophobic reaction partners that adversely affect protein properties, and potential safety concerns with explosive intermediates. Therefore, it would be advantageous to have an alternative method of conjugating a biological molecule to another entity that utilizes a functional group that is currently available and known to be compatible with a large range of desired payloads.

DESCRIPTION

Researchers at UC Santa Barbara have developed a bioconjugation method to covalently link molecular entities to polypeptides such as antibodies using a simple one-pot process. Tests show that cyclopentadiene derivatives could be incorporated site-specifically into an antibody and react with quantitative conversion with the maleimide-drug Vedotin. This reaction can be employed under mild conditions in specific conjugation reactions comprising a biological molecule. In some instances the reaction takes as little as two hours at room temperature with no added reagents or catalysts. The key feature of this strategy is the serum stability of the Diels–Alder linkage compared to the commonly used thiol-maleimide bond, potentially improving the pharmacokinetic properties of the ADC. This improved serum stability is independent of the site of incorporation, streamlining ACD development.



ADVANTAGES

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OTHER INFORMATION

KEYWORDS

conjugating, biological

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indpharma

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RELATED CASES

2017-467-0

- ▶ Uses commercially available off-patent maleimide-drugs
- ▶ Can be produced in high yields
- ▶ Reactions can take as little as two hours at room temperature
- ▶ Is a simple one-step process
- ▶ More stable in serum than thiol-maleimide

APPLICATIONS

- ▶ Pharmaceutical products (ADCs or radioactive tracers)
- ▶ Other conjugation uses (biochemical studies, bioceramics, polymers, nanochemistry)

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11759526	09/19/2023	2017-467
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