UNIVERSITEIT GENT

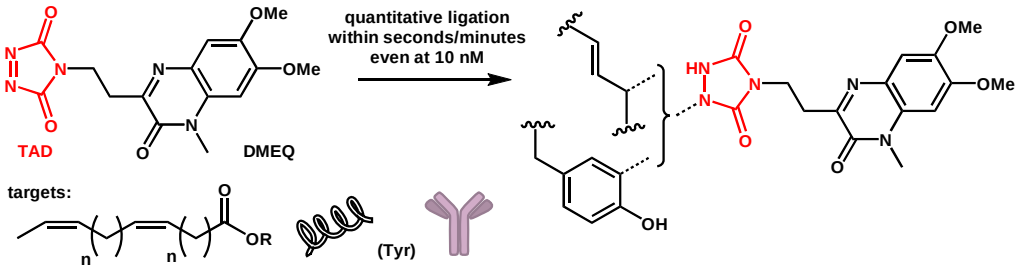
CHEMTECH LIFE SCIENCE

TECHNOLOGY OFFER

NEW CLICK REAGENTS FOR TYROSINE AND LIPID BIOCONJUGATION

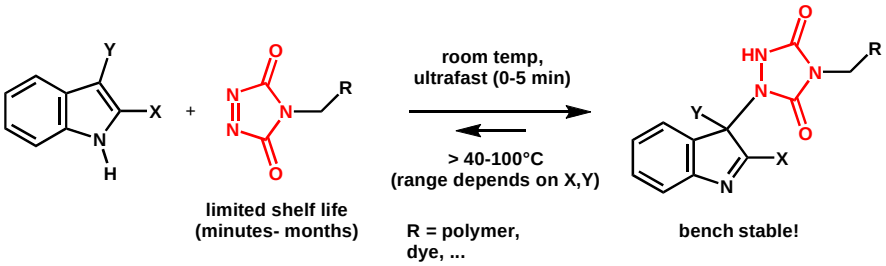
INTRODUCTION

Triazolinediones (TADs) are highly reactive reagents that can be used to form a covalent link to **unsaturated lipids** and to solvent-exposed **tyrosine** residues in **proteins** (and peptides). The TAD-bioconjugation reactions are click-like (high yield, very selective, no byproducts, no additives/catalysts) and are also characterized by an extremely fast reaction, allowing the modification of low-abundant proteins and lipid metabolites such as vitamin D-metabolites. This technology is well-established in some areas, but also still requires much further development, not the least because the commercial availability of functional TAD-reagents (e.g. fluorophores, biotins, dyes, radiolabel,...) is very limited and/or synthetically challenging, preventing wide access to this technology.



TECHNOLOGY

Recently, the research groups of Prof. Du Prez and Prof. Winne have been developing TAD-based reactions for use in macromolecular synthesis and modification. About 10 researchers are currently exploring this chemistry in several applications, including industrial and academic research collaborations. One particularly interesting application that has emerged from this research effort is the ability to make a **transient (dynamic) covalent link** between TAD and an indole molecule. The dynamic nature can be further tuned over a wide temperature range by tuning the structure of the temporary indole reaction partner. This opens up various direct applications in polymer chemistry (self-healing and thermally remoldable networks), and thus the technology was protected by a patent application (granted) and then published in the prestigious journal Nature Chemistry (2014). The TAD-indole reversible click reaction is a platform chemistry that may also impact the potential of TAD-chemistry in life science applications.



APPLICATIONS

The technology can primarily be used in the **synthesis**, **storage** and ultimate **delivery** of TAD-based biorthogonal click reagents, all of which are problematic issues for most TAD-reagents. Applications of functional TADs range from diagnostic assays to the facile production of bioconjugates for biomedical applications (eg modified antibodies or drug-antibody conjugates). Functional TADs are also valuable research tools.

ADVANTAGES

- Extended shelf life of TADs, thus wider product scope and potential
- Easy handling of TAD-type reagents by non-chemically trained individuals
- Potential access to completely novel TAD reagents
- Improved access to existing TAD-reagents
- Temporary immobilization of TAD reagents on a solid phase/surface

STATUS OF DEVELOPMENT

While this chemistry is well developed for polymer chemistry applications, it is not yet fully explored **for life science applications**. Research projects under copromotorship of Prof A. Madder, Prof F Duprez and Prof J. Winne have started on the synthesis and explorative use of novel TAD-based reagents for *inter alia* bioconjugation applications (mainly peptides and proteins). The current state-of-the-art in a somewhat biomedically-related application is the conjugation of a dye molecule to an indole-functionalized PEG-chain using an indole-blocked TAD-dye. The TAD-dye can then finally also be removed again from the PEG-target, thus recycling the original indole-PEG substrate.

PARTNERSSHIP

We are interested in partners that are willing to explore TAD-chemistry tools in ongoing research projects that can benefit from bioconjugation. We can offer chemical expertise and may provide some TAD-reagents for preliminary feasibility studies. This may lead to the development of novel proprietary applications.

INTELLECTUAL PROPERTY

"Urazole compounds", inventors: S. Billiet, K.Debruycker, F. Du Prez, J. Winne, WO/2015/018928 Publication date: 12/02/2015.

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(2) Billiet S., De Bruycker K., Driessen F., Goossens H., Van Speybroeck V., Winne J. M.*, Du Prez F. E.* "Triazolinediones enable ultrafast and reversible click chemistry for the design of dynamic polymer systems" *Nat. Chem.* **2014**, *6*(9), 815-821. DOI: 10.1038/nchem.2023

KEYWORDS

Click chemistry, Bioconjugation, Biorthogonal reactions, Cross-linking technology

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