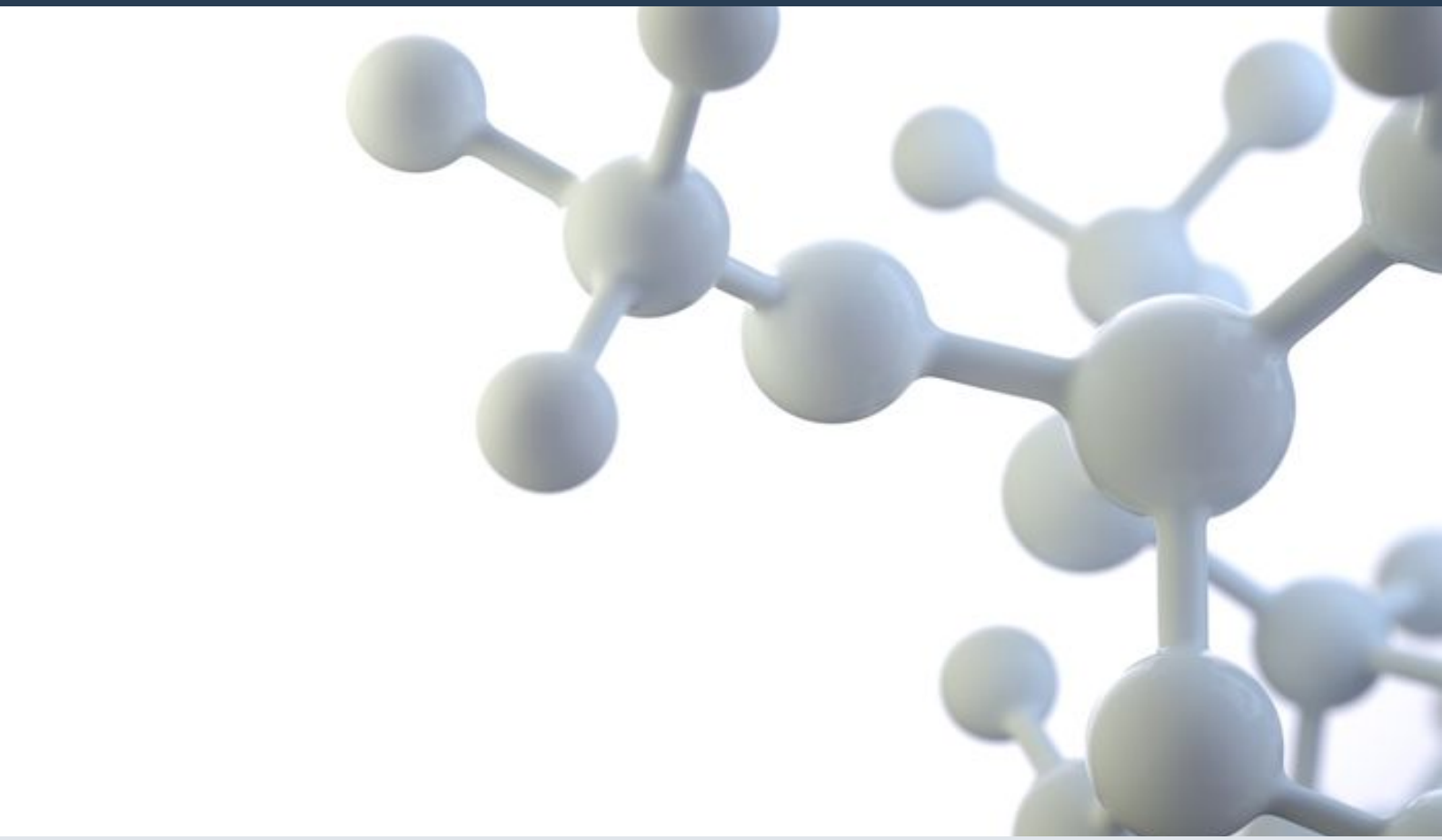
Powered by: IN-PART

TIE- cyclisation: A Novel Synthesis Method for Peptide Macrocycles

Efficient macrocyclisation method for solution- and solid phase peptide synthesis



Please note, header image is purely illustrative. Source: stock.adobe.com, Shuo, file#:257640114

IP Status

Patent application submitted

Seeking

Development partner, Commercial partner, Licensing

About **University of Warwick**

We are committed to ensuring that our research makes a distinctive, competitive impact on the world. We believe in a collaborative approach to research and education in addressing global challenges and opportunities.

Background

Currently more than 40 cyclic peptide drugs are in clinical use with the vast majority derived from natural products (e.g. cyclosporine, vancomycin).

Compared to linear peptides, **cyclic peptides benefit from enhanced cell permeability, increased target affinity, and resistance to proteolytic degradation.** Moreover, cyclic peptides are capable of acting as inhibitors against some of the most challenging targets, including protein-protein interactions (PPIs).

A major obstacle to the discovery of new cyclic peptide drugs is the challenge in synthesising them: Cyclisation of short peptides containing seven or fewer amino acids is especially challenging, with common problems during cyclization including C-terminal epimerization, cyclo-oligomerization and the appearance of side products arising from polymerization. Consequently, there is a pressing need for new macrocyclization strategies that can provide easy access to a variety of cyclic peptide scaffolds.

Tech Overview

Researchers at Warwick have developed a new method ("TIE-cyclisation") for the efficient synthesis of macrocyclic peptides. The method uses a turn-inducing element ("TIE") which imparts a steric "turn-inducing" constraint in the linear peptide precursor (Figure 1).

Stage of development = TRL4. The technology has been tested using commercial SPPS resins using several commonly-used conjugation and deprotection protocols.

Early work describing examples of the method is published in ***Chem. Sci.***, 2019,**10**, 2465-2472 (Open Access Link).

Benefits

- **Increased cyclisation yields**, compared to native peptide sequence (Figure 2)
- Access to cyclic peptides that cannot be accessed using conventional methods (especially macrocycles with <7 amino acid residues)
- Access to **novel compositions of matter** with comparable biological properties
- Provides additional **conjugation handle for enabling post-cyclisation conjugation and functionalisation**
- Drop-in technology - compatible with common peptide chain extension and de-protection protocols
- Compatible with **solution phase and solid-phase peptide synthesis**
- Compatible with **on-resin macrocycle library generation** approaches

Applications

The patented technology would be **of interest to companies who**:

- **want to efficiently produce cyclic-peptide libraries** for drug screening, particularly those targeting protein-protein interaction targets
- **are seeking to improve metabolic stability** or other properties of macrocyclic drug candidates
- want to identify **novel compositions of matter with substantially similar bioactivities** to existing macrocyclic drug compounds

Opportunity

The researchers are **seeking licensees and co-development partnerships**.

Warwick has a substantial body of PoC data relating to:

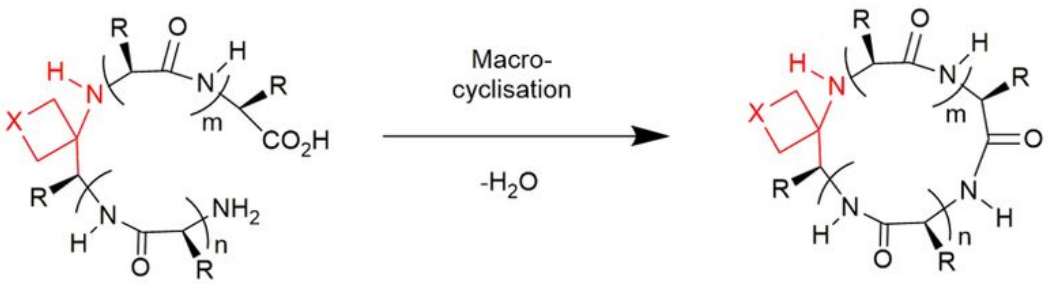
1. Synthesis of TIE-building blocks
2. Solid-phase (on resin) peptide synthesis methods
3. Post-cyclisation conjugation- and functionalisation strategies

Patents

- WO2019186174 A1 "Macrocyclisation of Peptidomimetics"

Appendix 1

Figure 1



- ✓ High yields
- ✓ Novel compositions of matter
- ✓ SPPS-compatible
- ✓ Ready handle for conjugation

Appendix 2

Figure 2