

• Case Study •



# Revolutionising Drug Discovery with Custom Cyclic Peptide Synthesis: A Comprehensive Guide to Our Synthesis Expertise

# What are cyclic peptides

Cyclic peptides are a class of biomolecules with unique properties that make them ideal for drug development. They have high binding affinity and low toxicity, like antibodies, and are easy to manufacture, like small molecules<sup>[1]</sup>.

Cyclic peptides have been applied in various fields, such as drug research, biotechnology, food and dietary supplements, and industry. They can be optimized for better biostability and used to treat diseases, purify biomolecules, develop biosensors, and more. Their versatility and potential for customization make them a promising area of research and development <sup>[2,3,4,5]</sup>.

## Basic applications of cyclic peptides

In the past 20 years, Cyclic peptides have rapidly been applied in various fields of research, such as:

### Drug research and development:

Cyclic peptides have become a popular research object in drug research and development. By cyclizing the linear peptide, its pharmacological and pharmacokinetic properties can be optimized, improving its bioavailability and stability <sup>[6]</sup>. Cyclic peptides are more stable than linear peptides, making them less susceptible to degradation in the body and increasing their potential for use as therapeutic agents <sup>[7]</sup>. Cyclic peptides have already successfully developed drugs for various diseases, such as cancer, inflammation, and infectious diseases <sup>[8]</sup>. For instance, the cyclic peptide drug Vancomycin is used to treat bacterial infections <sup>[9]</sup>, and Cyclosporine is a cyclic peptide used to prevent organ rejection in transplant patients <sup>[10]</sup>.

### Biotechnology applications:

Cyclic peptides have a wide range of applications in the biotechnology field, such as for the separation and purification of other biomolecules, as well as for the development of biosensors and diagnostic tools. By analyzing and modifying the cyclic peptide sequence, its stability and activity can be improved, achieving better results in various applications <sup>[11]</sup>.

### Food and dietary supplement applications:

Cyclic peptides also have critical applications in the food and dietary supplement industries. For example, cyclic peptides can be used as functional ingredients in dietary supplements, with effects such as

## CYCLIC PEPTIDE 2001-2021 DRUG DEVELOPMENT



## Industrial applications:

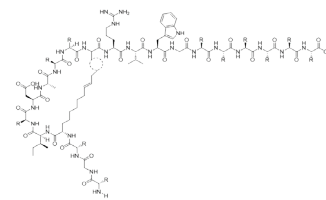
Cyclic peptides have essential applications in the industrial field, such as in the preparation of polymer materials, catalysts, and coatings. By modifying the cyclic peptide sequence, its structure and properties can be changed, achieving specific industrial applications [13].

# GenScript's capability in challenging cyclic peptide synthesis

## Case 1: An order of staple peptides with unique olefin molecular Challenges:

- ▶ (a) **E isomer and Z isomer** were both needed and difficult to be separated;
- ▶ (b) **Side reaction of the unique olefin parts** during the RCM reaction was unavoidable;

**Results:** Side reaction was decreased to less than 2% in the crude product; A special method to separate two isomers was developed; All items were successfully delivered on time.



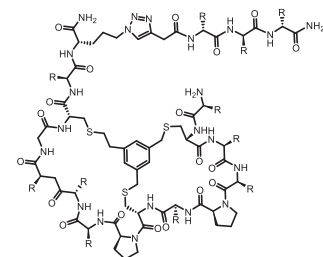
Staple Peptide

## Case 2: An order of bicyclic peptides with 90 items

### Challenges:

- ▶ (a) **Four kinds of central scaffolds and even an asymmetrical of that** is included;
- ▶ (b) **Multiple steps;** Bicyclic modification and click reaction were both included, which means lower yield and a higher tendency of side reactions;
- ▶ (c) **Difficult purification.** The same MS and similar HPLC retention time of product and impurity make the purification challenging to achieve 98% purity;

**Results:** Designed protection group strategy was applied to realize the addition of an asymmetrical central scaffold; Proper reaction condition was explored to avoid the impurity successfully; A unique purification system was developed for the bicycle peptides; 96% completion rate was achieved.



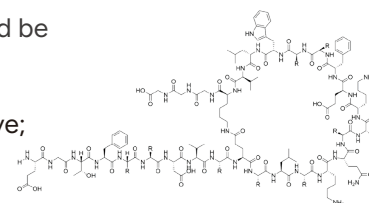
Bicycle peptide

## Case 3: An order of 35g side chain-to-side chain cyclic peptide

### Challenges:

- ▶ (a) **Large-scale platform,** including synthesis platform and purification platform, should be built;
- ▶ (b) Protection group-related **side reactions** make the high purity challenging to achieve;
- ▶ (c) **Poor solubility** makes the purification difficult;

**Results:** Large-scale platforms of both synthesis and purification were improved; the 35g product with 98% purity was delivered on time.



Side chain-to-side chain cyclic peptide

# GenScript's Cyclic Peptide Synthesis Service



## Track Records

- **Thousands** of cyclic peptides delivered each year
- **9** cases of process development projects
- **2** cases of IND (CMC) projects



## Proprietary Technology Platforms

- PepPower™ & PepHTS™ proprietary platform
- **>20** types of cyclization



## Industry-leading Speed

- Deliver in as fast as **7** business days\*

## References

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