Accessing diverse bicyclic peptide conformations using 1,2,3-TBMB as a linker

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"Bicyclic peptides are a powerful modality for engaging challenging drug targets such as protein–protein interactions. Here, we used a new linker we called 1,2,3-TBMB, to access bicyclic peptides with diverse "shapes" that differ from conventional bicyclised peptides formed with current linkers. This new methodology is efficient with broad scope, and compatible with peptide library design for drug screening. We envisage that the 1,2,3-TBMB linker will be applicable to a variety of peptide screening techniques in drug discovery."

🧬 What's the big idea?

The study focuses on developing **novel chemical strategies** for constructing bicyclic peptide libraries for **screening new drug targets**. Peptides are a class of drugs with increasing clinical use. It aims to address limitations in current methods by introducing unique "shapes" of the bicyclic peptides to better "fit" challenging drug targets which don't currently have any drugs on the market.Shape

🧪 What did the researchers do?

- Designed and tested new **linkers** for cyclising peptides to generate new and interesting shapes.
- Optimised reaction conditions for efficient formation of the new bicyclic peptide libraries.
- Compared the performance of their approach against current methods.

🔍 What did they discover?

- The new linker significantly **improved reaction yields and selectivity.**
- Demonstrated **broad substrate scope**, enabling the synthesis of diverse peptide libraries
- Showed these newly designed bicyclic peptides formed unique and interesting "shapes".

💡 Why is this important?

- Offers a new bicyclic peptide library to screen against challenging cancer drug targets where current methods have failed.
- Facilitates the **rapid discovery of new potential drug candidates**.
- Is applicable across a wide range of drug targets for larger impact.

🧠 What's next?

- Validate the methodology in screening technology.
- Apply the methodology to screen against cancer drug targets relating to osteosarcomas.
- Potentially discover new peptide-based drug candidates.