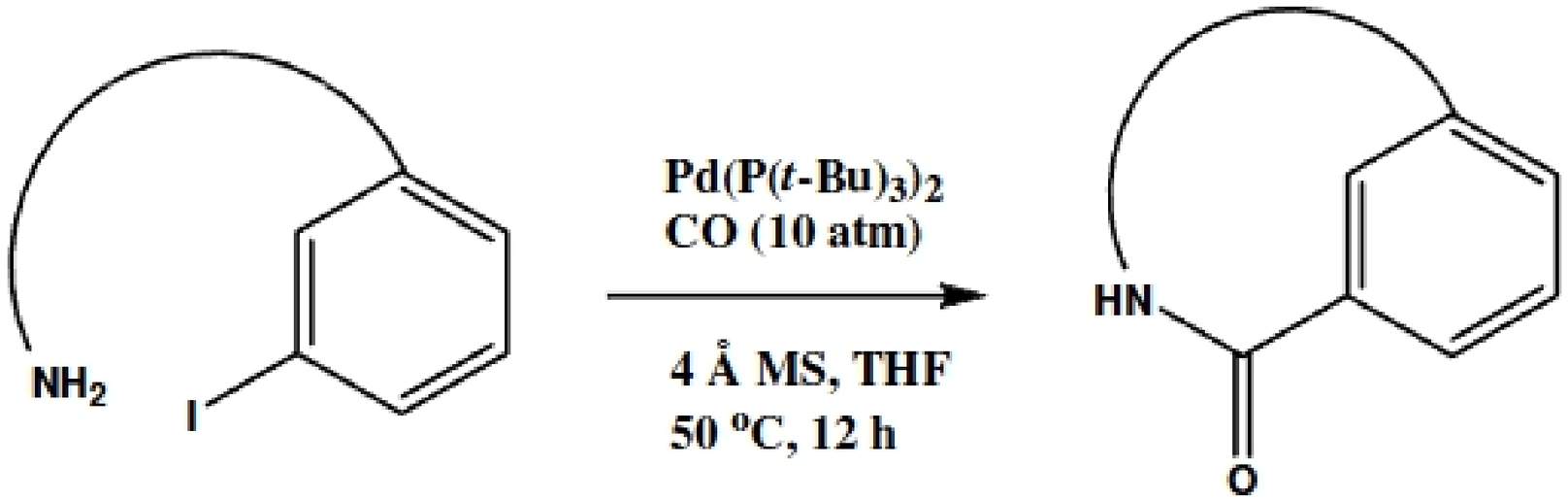
A Synthesis of RGD Model Cyclic Peptide by Palladium-Catalyzed Carbonylative Macrolactamization

Doi, T.; Kamioka, S.; Shimazu, S.; Takahashi, T. *Org. Lett.* **2008**, *10*, ASAP



Andrey Solovyev
February 11, 2008

Peptidomimetics

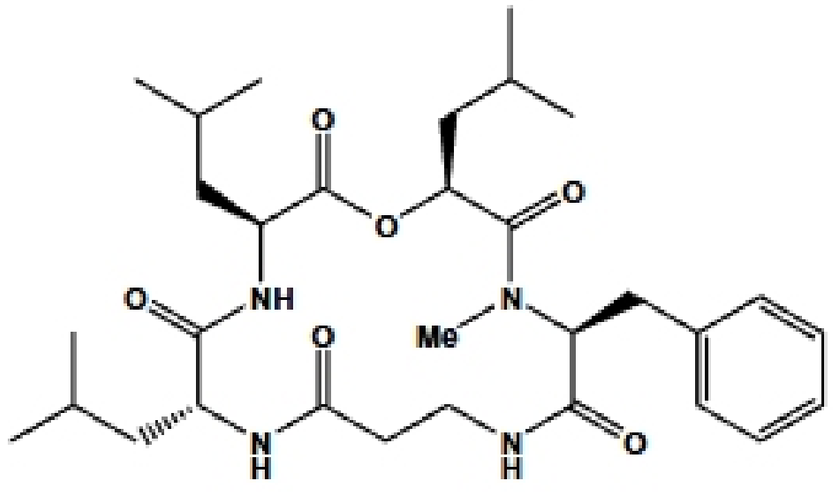
- Target protein-protein interactions:
  - Mimic a counterpart in protein-protein interactions;
  - Disrupt protein-protein interactions;
- Both types of action are therapeutically interesting.

Difference from "classical" peptides:

- Contain unnatural amino acids (for example, D-amino acids, β-amino acids);
- Conformationally constrained (cyclic);
- Stable to proteolysis;
- Penetrate through the cell membrane.

***Leualacin** Analog.*
Possesses vasodilatory and antiplatelet activities.

Hu, M.-K. et al. *Bioorg. & Med. Chem. Lett.* **1999**, *22*, 563-568.



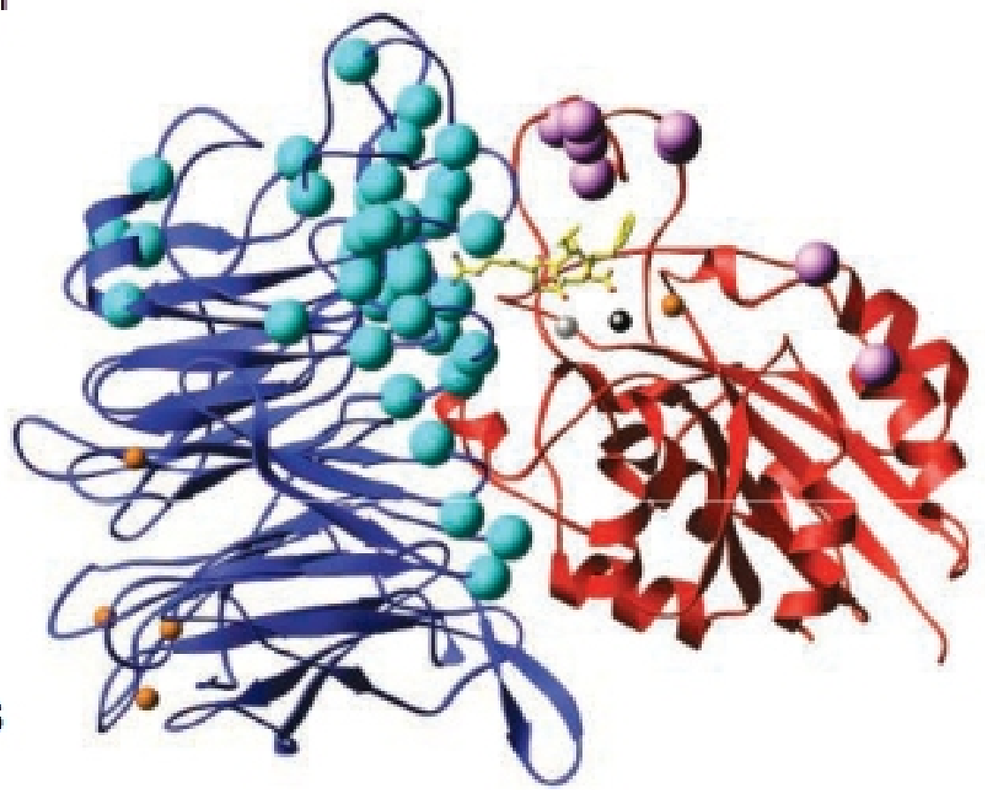
RGD Cyclic Peptidomimetics

- RGD (Arg-Gly-Asp) sequence presents in many proteins of extracellular matrix.

- This sequence is responsible for the binding with integrins – receptor proteins on the cell surface.

- Specificity of binding and biological response depends on the RGD conformation.

- RGD peptidomimetics can block integrins prevent them from interactions with other cells and matrix, and thus inhibit tumor metastasis, angiogenesis, thrombosis, and inflammatory disorders.



Shimaoka, M. and Springer, T. A. *Nature Rev. Drug Discovery* **2003**, *2*, 703-716.