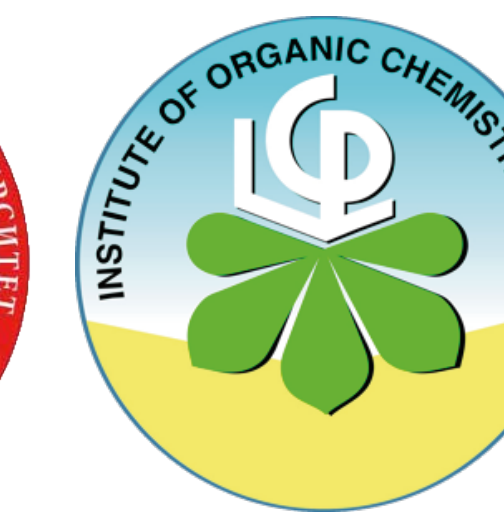


# Petasis / Grubbs Reactions Sequence as an example of using DOS-like strategy to the MedChem relevant building blocks synthesis



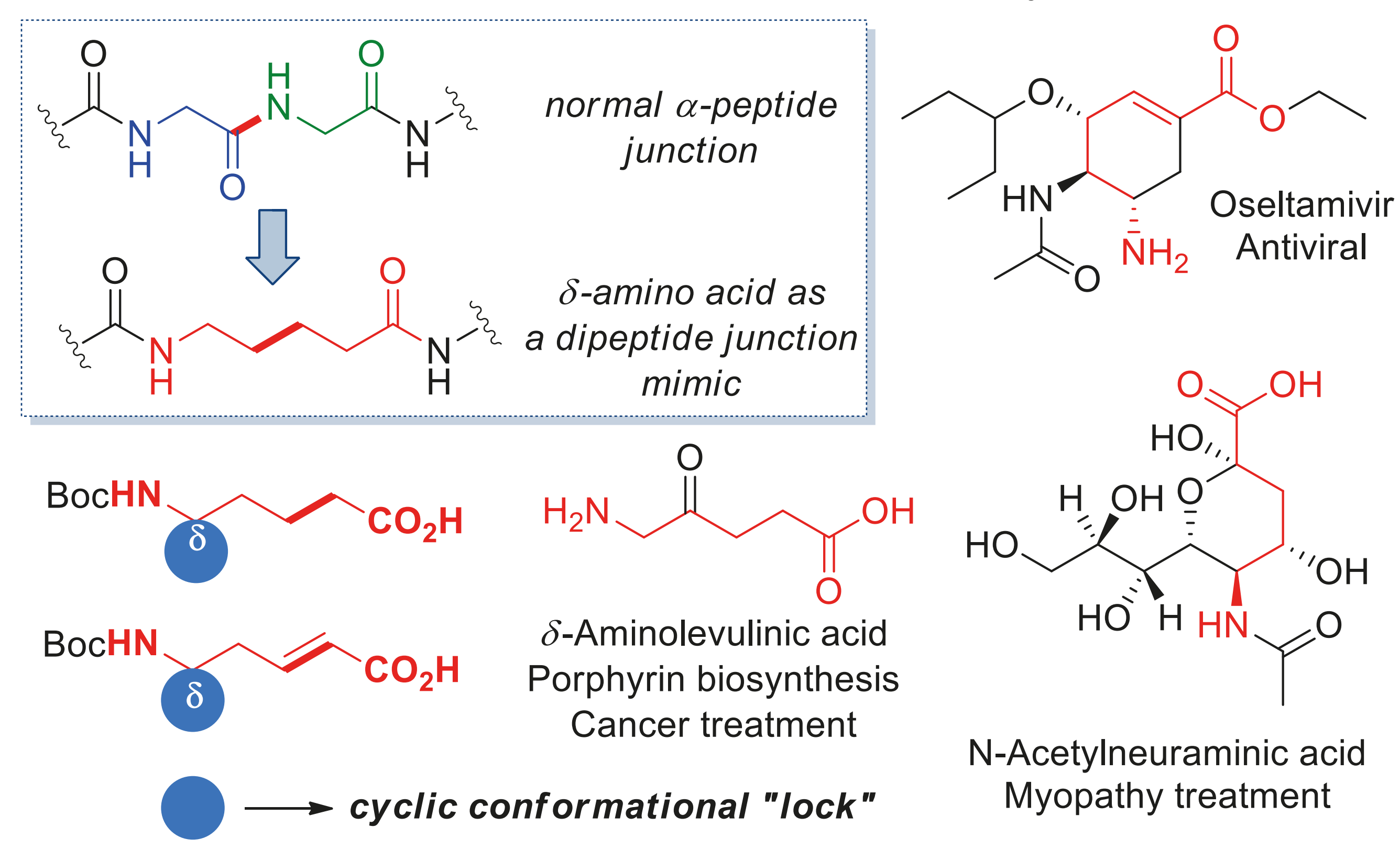
Dmytro Volochnyuk, Maksym Herasymchuk, Kostiantyn Melnykov, Tetiana Druzhenko, Serhiy Ryabukhin

## Background of the project

**Diversity-oriented synthesis (DOS)** is a powerful concept for construction of structurally various scaffolds using available starting materials and common conditions. However, this approach was criticized for producing “molecules with obesity”. Therefore, DOS design of “small” 3D-shaped fragments meeting the **rule of 3** or even stricter requirements is a challenge for **MedChem relevant building blocks** synthesis.

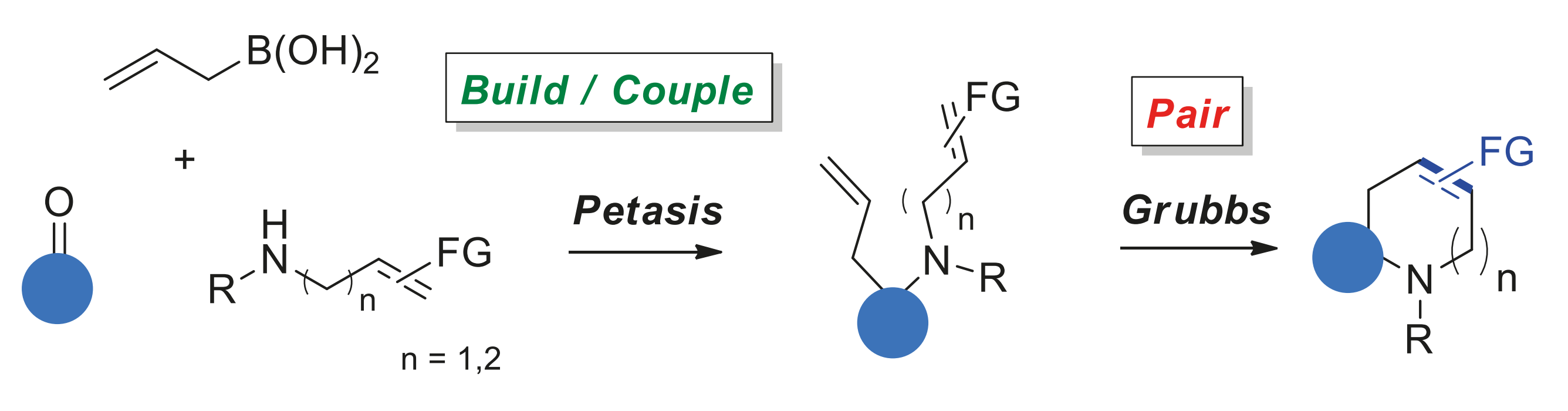
### PEPTIDE-LIKE FOLDAMERS

We applied DOS strategy for design of dipeptide mimetics with stable C-C bond instead of cleavable amide junction.



### MEDCHEM RELEVANT SPIROCYCLIC BBs

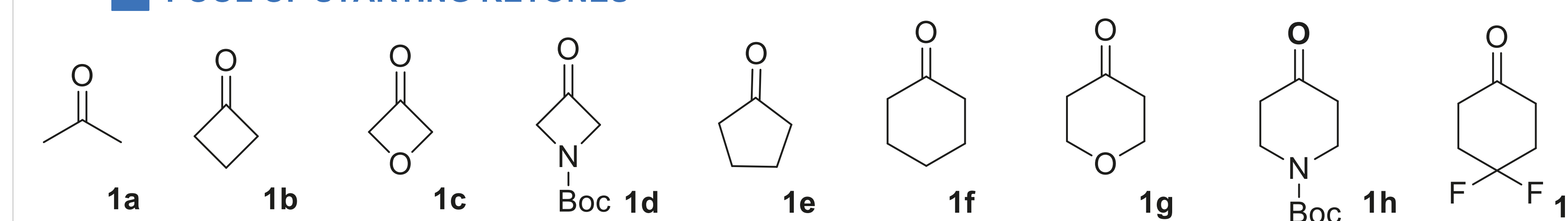
Moreover, we used DOS approach based on Petasis/Grubbs sequence for synthesis of spirocyclic building blocks.



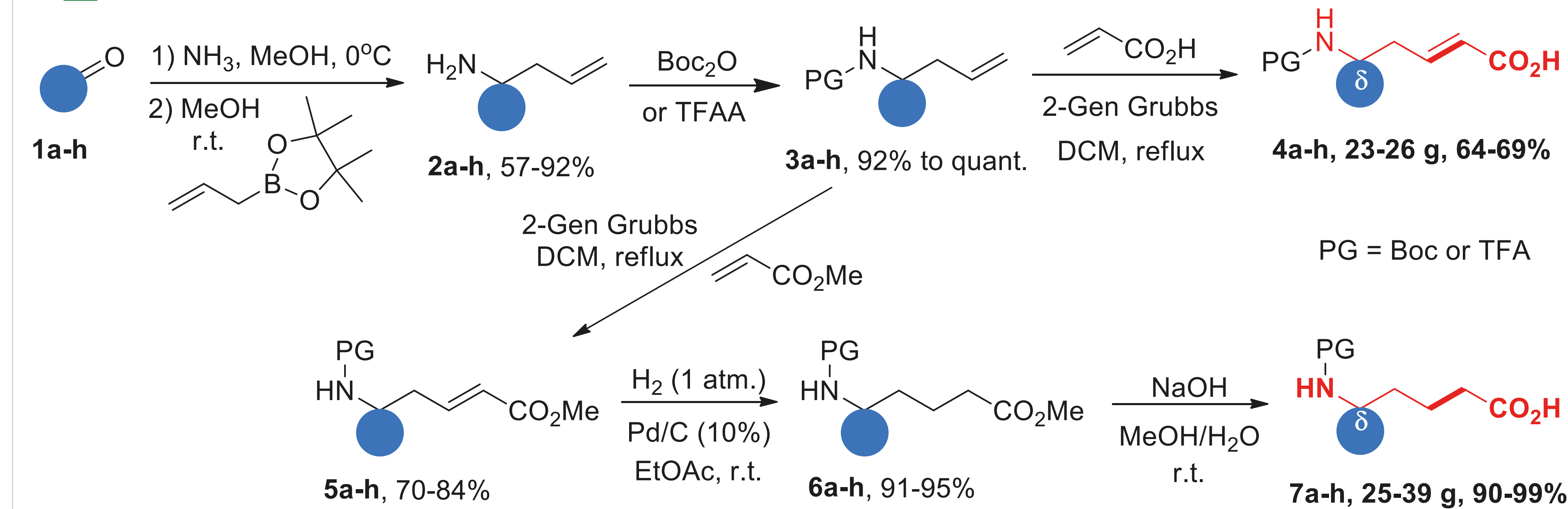
## Scope of the reaction and diversity of the products

Carbo- and heterocyclic ketones possessing 4, 5 and 6-membered rings as well as acyclic acetone were introduced to the reaction.

### POOL OF STARTING KETONES

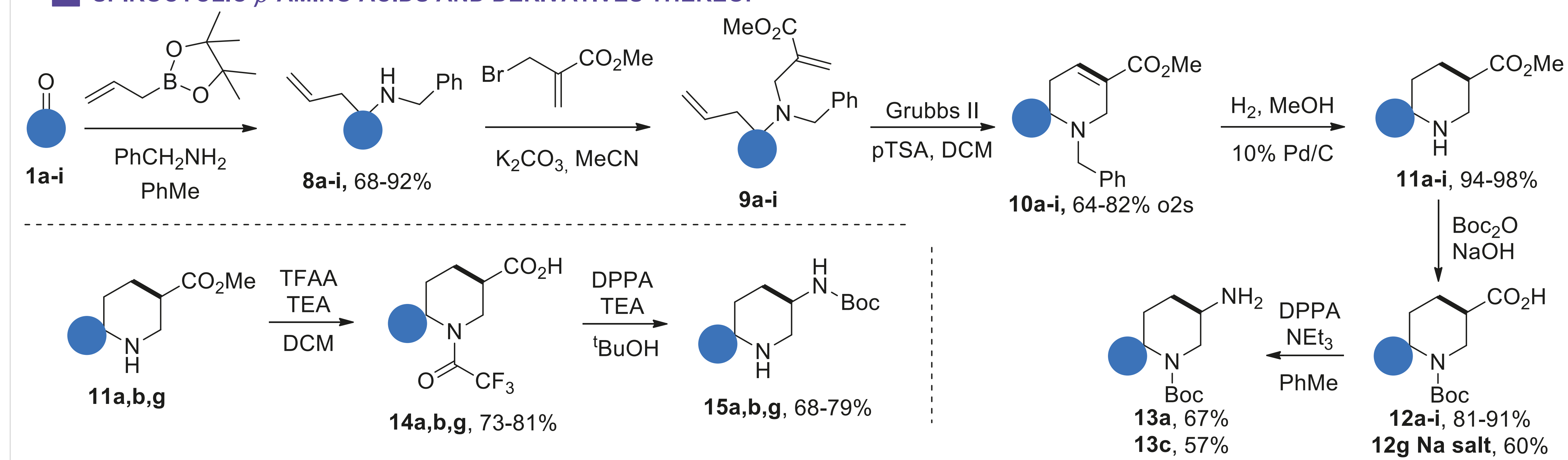


### SATURATED AND $\alpha,\beta$ -UNSATURATED $\delta$ -AMINO ACIDS



- Petasis reaction was scaled up to 100 g per run.
- To allow further modification and usage in peptide synthesis the amino acids were turned to Boc-protected ones.
- Orthogonal TFA protection was used for synthesis of **4h** and **7h** already bearing Boc-protection.

### SPIROCYCLIC $\beta$ -AMINO ACIDS AND DERIVATIVES THEREOF



## Contact

Serhiy V. Ryabukhin, Prof. Dr. Sci., s.v.ryabukhin@gmail.com  
Dmytro M. Volochnyuk, Prof. Dr. Sci., d.volochnyuk@gmail.com

## References

Herasymchuk M. et al. *J. Org. Chem.* **2025**, *90*, 10088;  
Herasymchuk M. et al. *Chem. Eur. J.* **2025**, *31*, e202500681.