Synthesis of piperidine-based β-amino alcohols

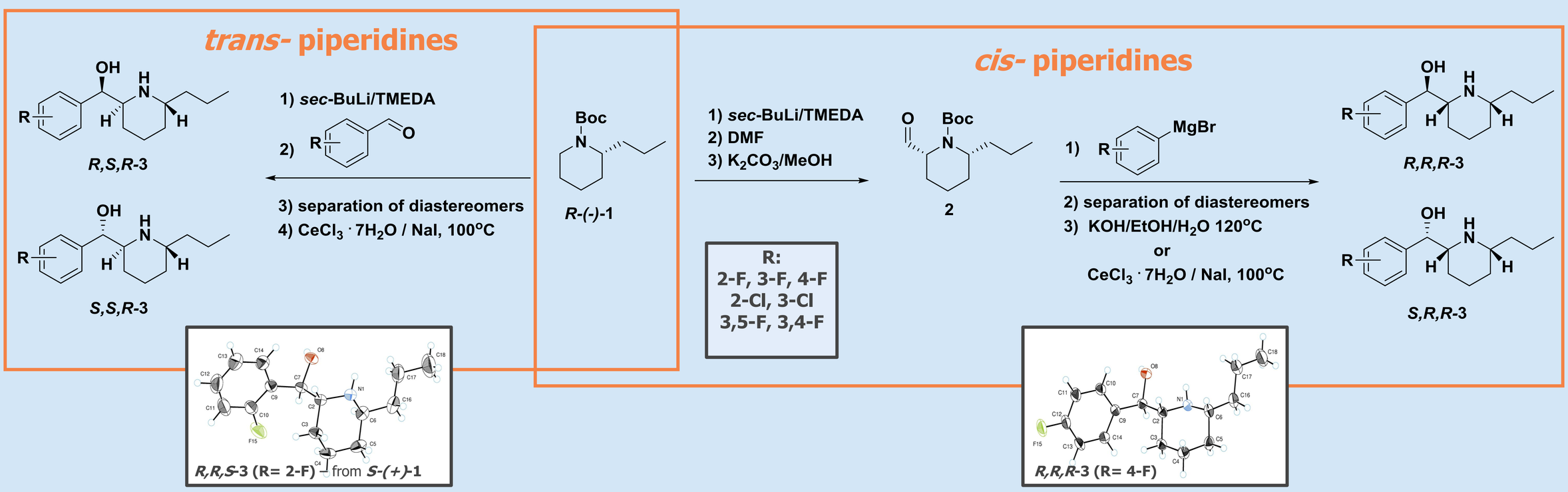
LINDA SUPE, ILGA MUTULE

Latvian Institute of Organic Synthesis, Aizkraukles 21, Riga, Latvia

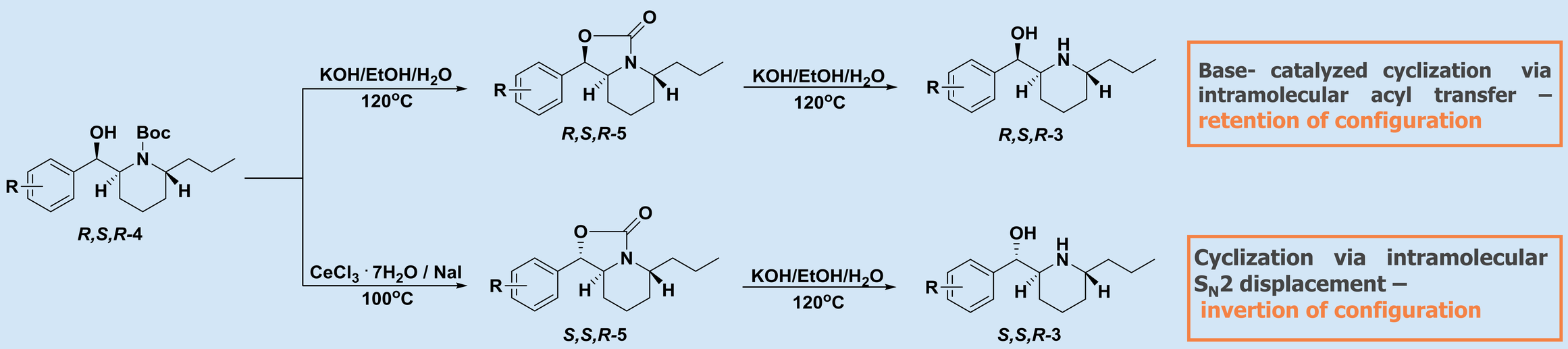
Abstract

The β-amino alcohol moiety is found in many biologically and synthetically important molecules. **(6-Propylpiperidin-2-yl) benzyl alcohols** - β-amino alchols where the motif is combined with piperidine cycle - promote glucose uptake in skeletal muscle cells and are promising for use in treatment of hyperglycaemia.[1] Our objective was development of synthetic pathway towards all possible isomers of title compounds.

Synthetic route to enantiopure (6-propylpiperidin-2-yl)benzyl alcohols 3



Boc- deprotection of *anti*- alcohols via oxazolidinones 5



Base- catalyzed cyclization via intramolecular acyl transfer – **retention of configuration**

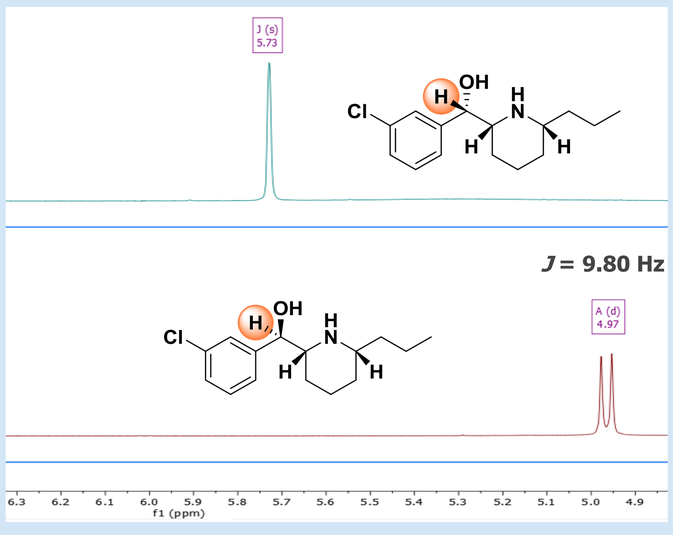
Cyclization via intramolecular S_N2 displacement – **invertion of configuration**

^{1}H NMR: *syn* and *anti* distinction

Carbinol proton:

$\sigma_{syn} < \sigma_{anti}$

$J_{syn} > J_{anti}$



Summary

We have successfuly developed a synthetic pathway towards all possible isomers of **(6-propylpiperidin-2-yl)benzyl alcohols 3** starting either from (*R*)-(-)-N-Boc coniine **1** or (*S*)-(+)-analogue.

Attempts of Boc group removal led to cyclic oxazolodinones **5** – depending on the reaction conditions cyclization occured with or without retention of configuration[2]. Mainly *anti* isomers of *trans* piperidines were prone to cyclization - formation of oxazolodionones from other diastereomers was observed in trace levels.

References

1. [a] Pelcman, B.; Bengtsson, T. WO2019/053425 A1, March 21, **2019**.
   [b] Pelcman, B.; Bengtsson, T. WO2020/188301 A1, September 24, **2020**.
2. Benedetti, F., Norbedo, S. *Tetrahedron Lett.* **2000**, 41, 10071.

Acknowledgement

The research was supported by the European Regional Development Fund (Grant No. 1.1.1.2/VIAA/4/20/755)