

New synthetic instruments to reach 2,2-spiro-beta-proline molecular platform

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Background of the project

THE 15-YEAR-OLD EQUATION OF CLINICAL SUCCESS

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SATURATION

- solubility
- complexity

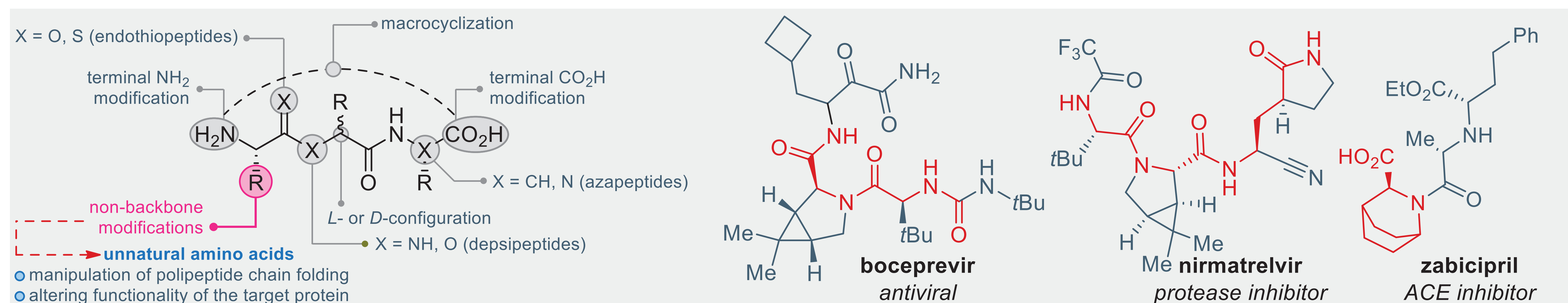
THREE-DIMENSIONALITY

- receptor/ligand complementarity

CONFORMATIONAL RESTRICTION

- reducing entropy penalty
- well-defined vectorization

- reduction in entropy resulting from **conformational restriction** may enhance intermolecular interactions and contribute to biological activity
- **amino acids possessing rigid structures** are promising substrates for constructing peptidomimetics – small protein-like chains designed to mimic native counterparts and advantageously adjust pharmacological properties such as stability or biological activity

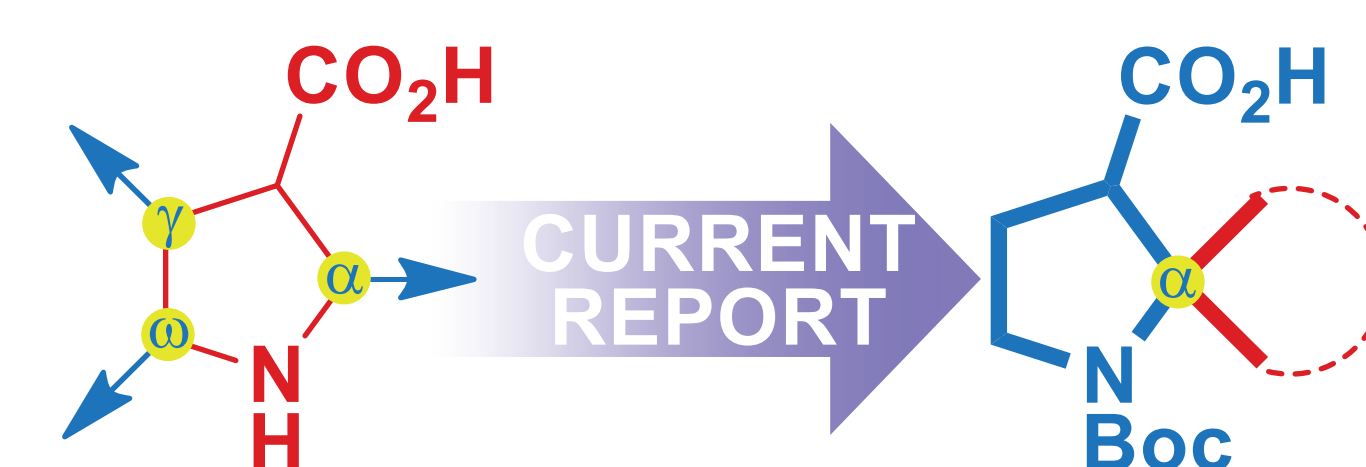


STRATEGIC GOAL

- chemical support of creating innovative peptidomimetics and amino acid based agents

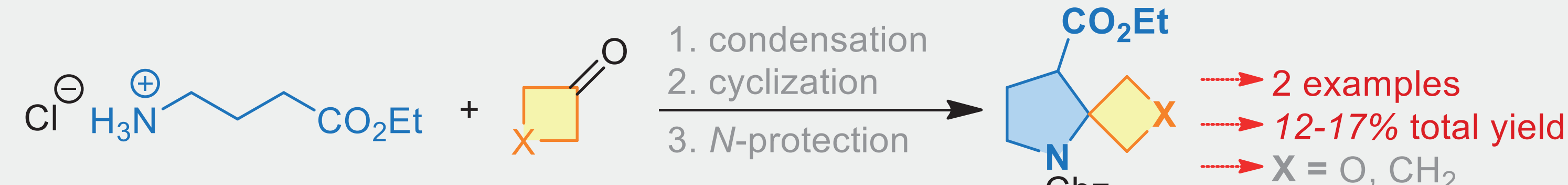
CURRENT STEP

- elaboration of robust synthetic avenues for spirocyclic beta-proline frameworks



STATUS QUO

TO DATE, THERE IS A SINGLE RELEVANT SYNTHETIC STRATEGY

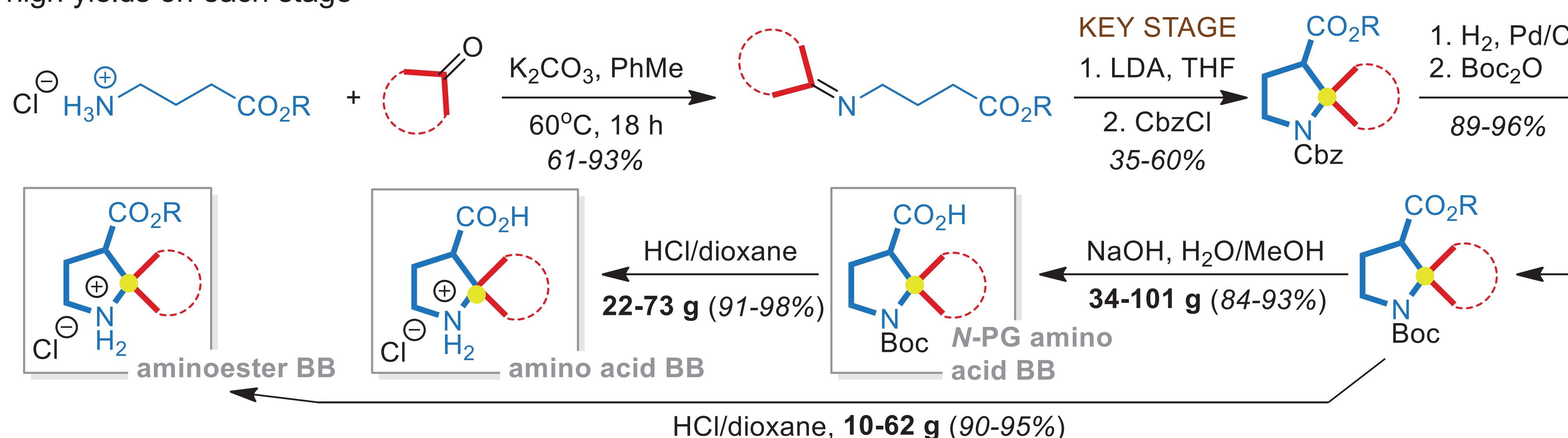


Synthetic strategies toward α-spiro-β-prolines

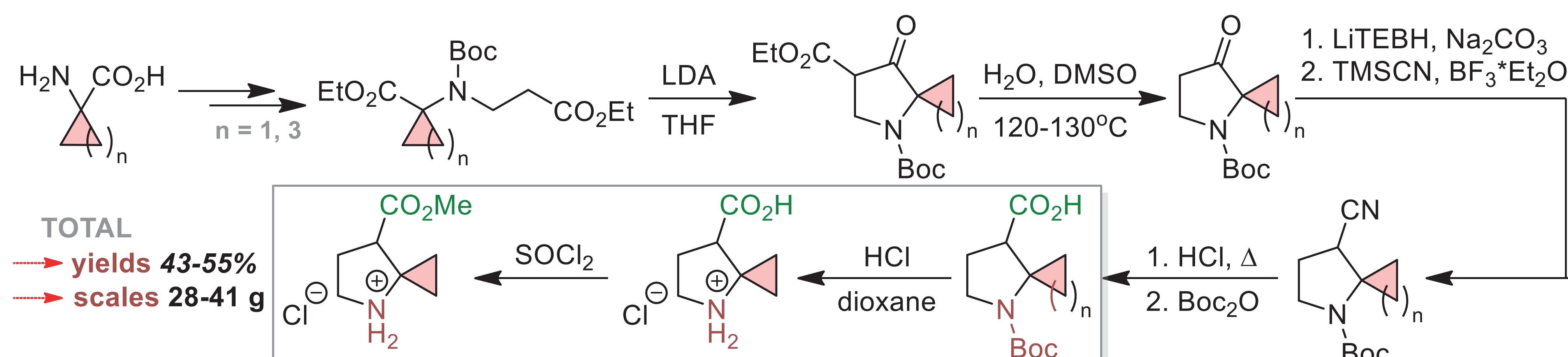
- our endeavors are reflected in three synthetic routes that are well-suited for synthesizing a wide range of the target spirocyclic prolines on a large scale and with moderate to high yields on each stage

STRATEGY #1 –

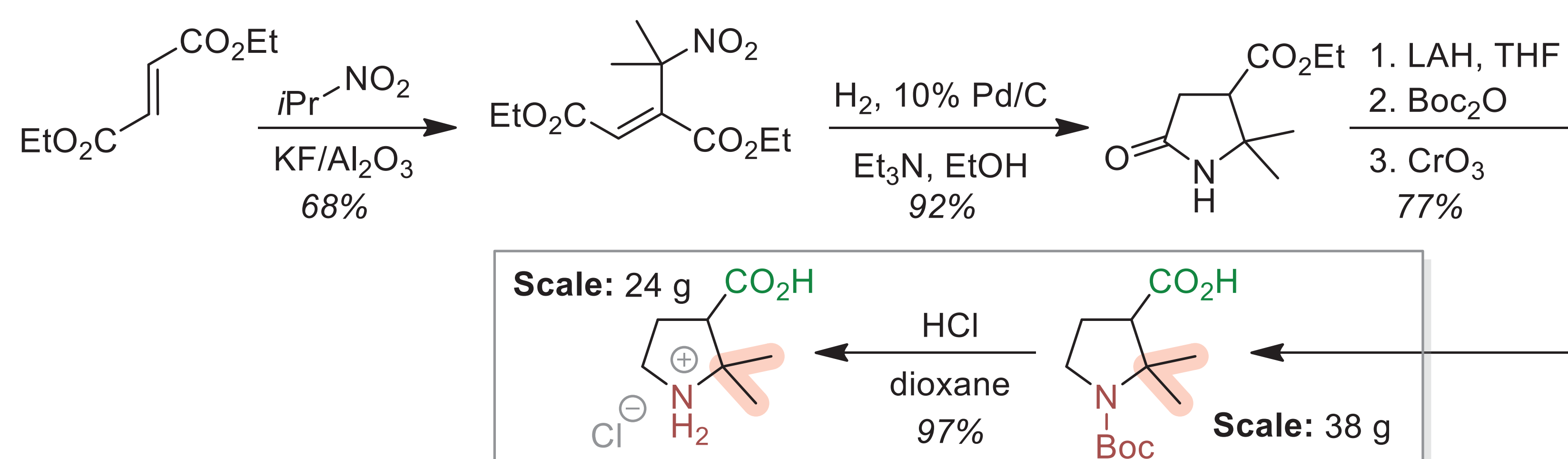
THE OPTIMIZED, EXPANDED, AND SCALED-UP ROUTE FIRST PUBLISHED BY FJELBYE ET AL.



STRATEGY #2 – ROUTE TOWARD PROLINES WITH SPIROCYCLOPROPANE AND – CYCLOPENTANE FRAGMENTS



STRATEGY #3 – ROUTE TOWARD PROLINE WITH 2,2-DIMETHYL MOIETY – OUT-OF-PLANE MIMIC OF SPIROCyclic COUNTERPARTS



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