

# Example of a Stereoselective Synthesis in Industrial API Manufacture

## Abstract

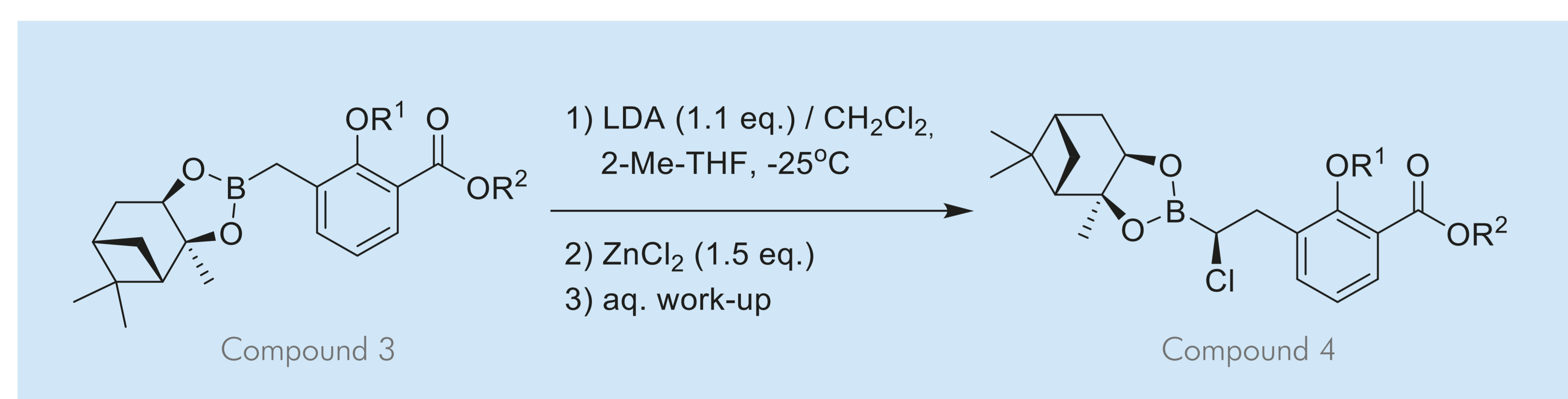
Stereochemistry is an important topic not only in academic research, but also in industrial manufacture. Herein, we present an example of a stereoselective transformation performed on multi-kilogram scale at CARBOGEN AMCIS AG for VenatoRx Pharmaceuticals.

## Authors

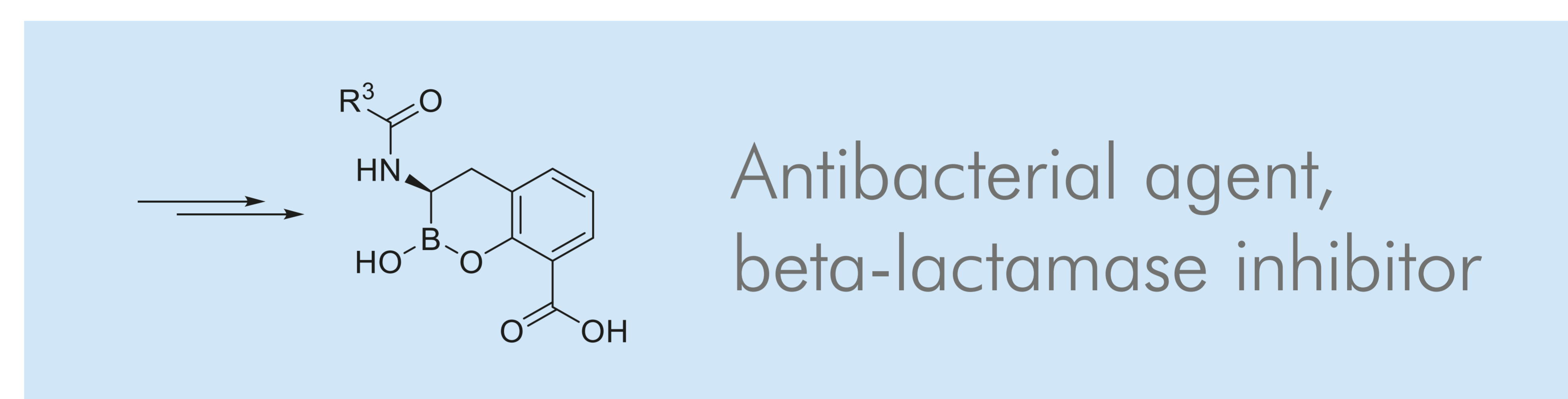
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## Stereoselective Matteson Homologation using a Continuous Flow Process

### Reaction Scheme:



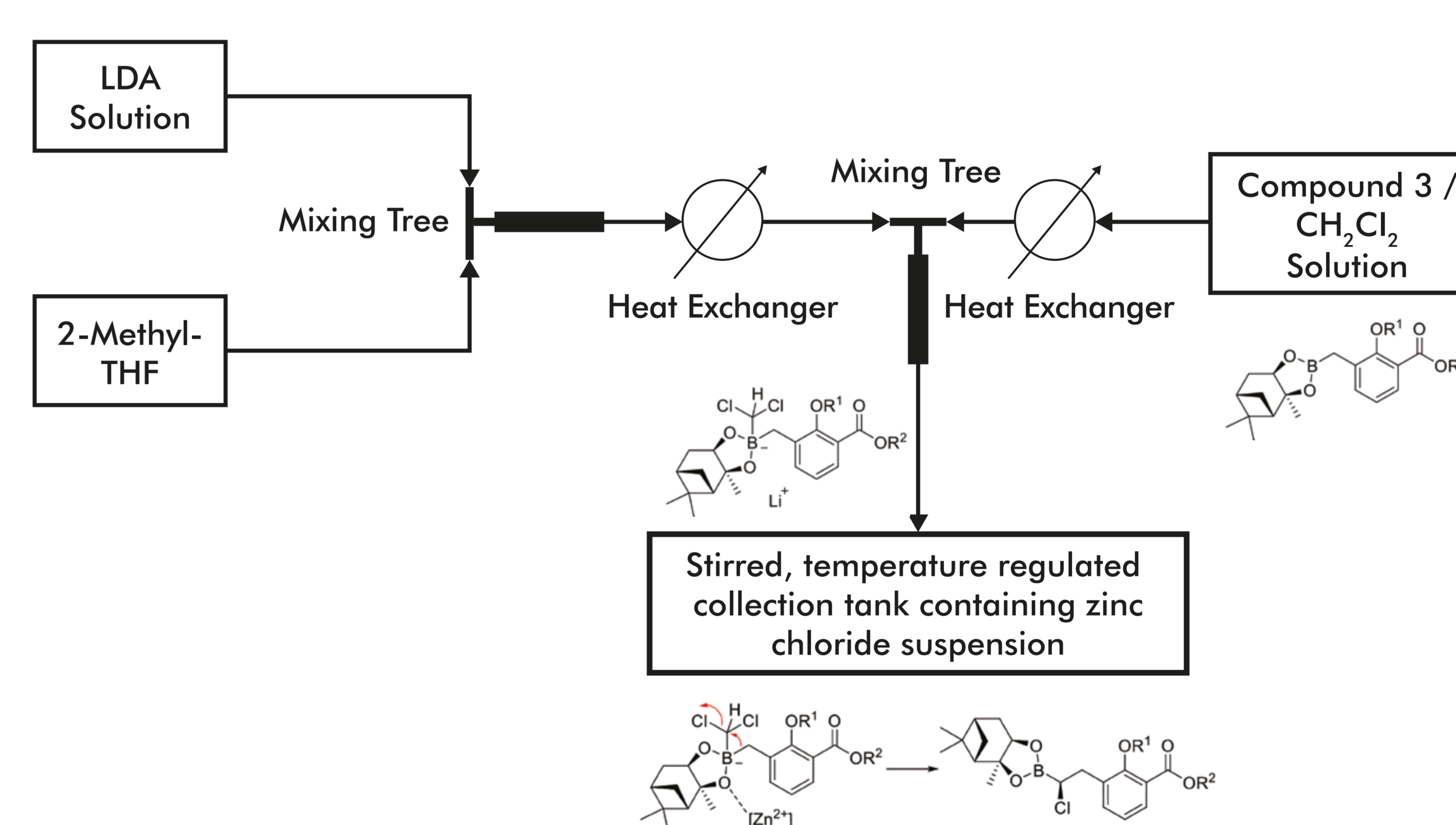
### Target:



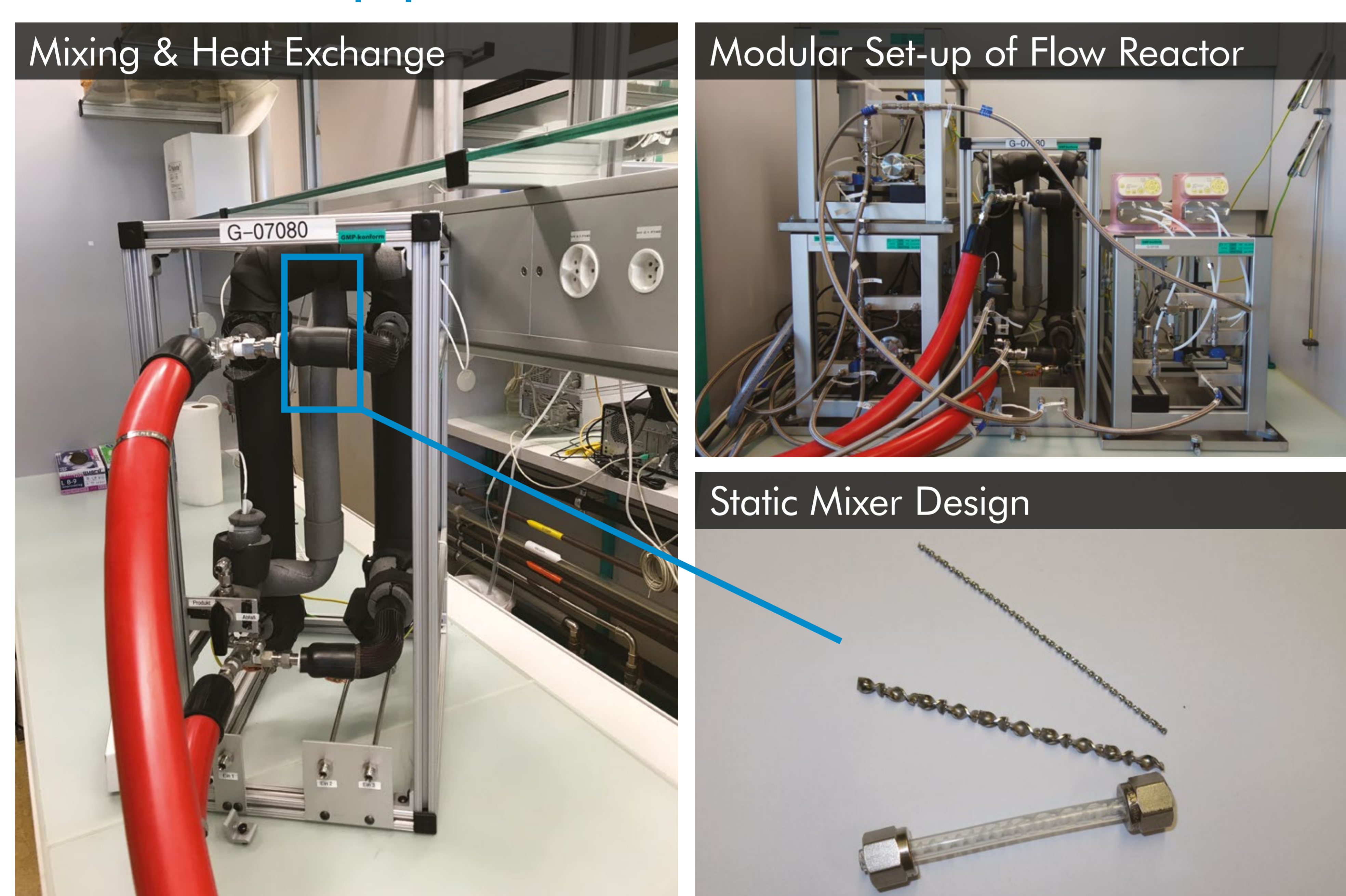
### Results from the Manufacturer:

Entry	Input	Conversion	Yield	d.r.
Run I	8.00 kg	97 %	8.03 kg, 90 %	95.1 : 4.9
Run II	9.60 kg	96 %	9.51 kg, 88 %	97.3 : 2.7
Run III	13.33 kg	97 %	13.51 kg, 90 %	97.0 : 3.0

### Scheme of Continuous Flow Process:



### Flow Reactor Equipment:



### Flow Process Parameters:

- Mixing of LDA / 2-Me-THF with Compound 3 / CH<sub>2</sub>Cl<sub>2</sub> at -25°C
- Mixture pumped into ZnCl<sub>2</sub> suspension in collection tank at -15°C
- Flow rate: 200 g/min Compound 3 solution (50 g/min net)
- Residence time in flow reactor: approx. 30 s
- Aqueous work-up in batch mode

### Advantages of Flow Process over Batch Process:

- Temperature: -25°C instead of -60°C to -100°C
- No need for large cryo reactors
- Higher purities, less by-products, higher selectivities

## Conclusion

In conclusion, continuous flow technology was employed to perform a diastereoselective Matteson homologation using (+)-pinanediol as chiral diol on boron. The reaction was carried out on multi-kilogram scale, giving the product in high yields and with high diastereoselectivities. Most notably, in contrast to the batch process, the continuous flow process allows for much higher reaction temperatures without the need of cryogenic reactors on large scale.