# Asymmetric Claisen-Cope rearrangements

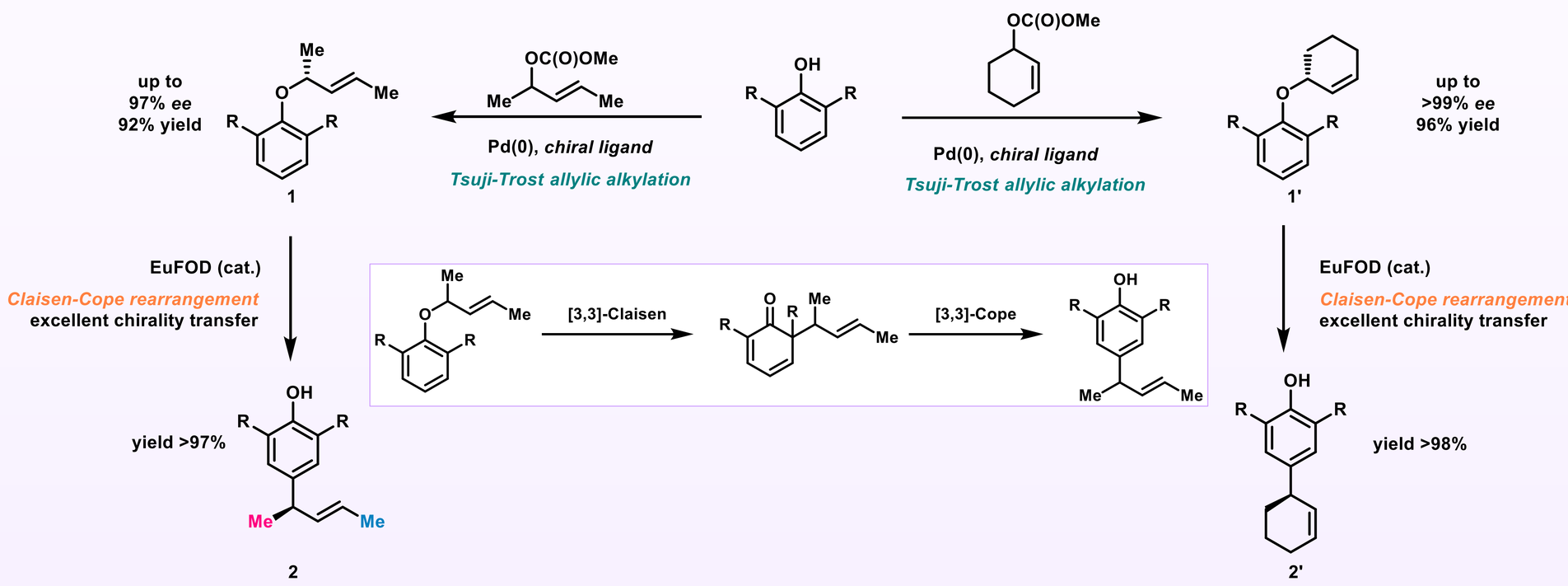
Johanna Breinsperger, Maximilian Kaiser, Peter Gärtner
*Institute of Applied Synthetic Chemistry, Technische Universität Wien, 1060 Vienna, Austria*

## Introduction

The Claisen rearrangement of allylic aryl ethers typically results in the formation of *ortho*-allylated phenols. However, if the *ortho* positions are substituted, a Cope-rearrangement occurs to the *para* position, concluding the Claisen-Cope reaction. These [3,3]-sigmatropic rearrangements feature a transition state comprising a cyclic array of continuously bonded atoms, which enables high predictability in terms of connectivity and configuration. The aforementioned ability for stereocontrol has led to the development of a limited number of methods for the *ortho* Claisen rearrangement in recent years. In contrast, the asymmetric *para* Claisen-Cope rearrangement has been largely overlooked until now.[1,2]

## Asymmetric Allylic Alkylation

After extensive optimization with respect to chiral ligands, palladium source, carbonates and additives, the modified literature conditions allowed the preparation of ethers in excellent yields and excellent enantiomeric excess *(ee)*.



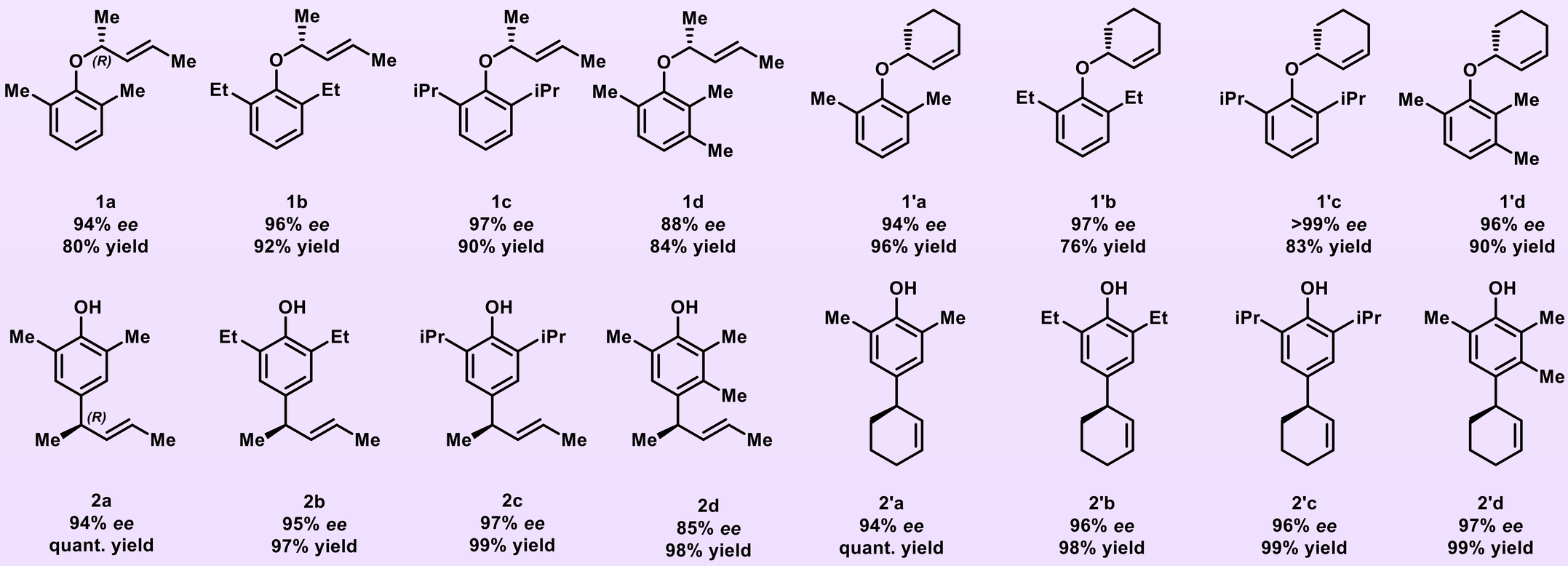

## Claisen-Cope rearrangement

Initially, the thermally induced rearrangement was successful in transferring chirality, however requiring high reaction temperatures. While the use of Lewis acids resulted in a significant degree of racemization, EuFOD catalysis proved to be most efficient, facilitating the transfer of chirality under mild conditions. This approach was successfully employed to achieve the rearrangement of a variety of different 2,6-disubstituted phenol ethers.

| entry | conditions | T (°C) | t | % *ee*[1] |
|---|---|---|---|---|
| 1 | *N,N*-Diethylaniline (0.5 M) | 190 | 3.5 h | 86 |
| 2 | *N,N*-Diethylaniline (0.5 M) | 140 | 23 h | 86 |
| | | | | |
| 3 | $BF_3$-etherate (0.1 eq.), DCM | -80 | 5 min | 32 |
| 4 | $Et_2AlCl$ (1.5 eq.), hexane | 0 | 5 min | 2 |
| 5 | $Me_3Al$ (3 eq.), hexane | 0 | 5 min | *decomposition* |
| 6 | $ZnCl_2$ (1.05 eq.), DCE | 80 | 2.5 h | 14 |
| 7 | $SnCl_4$ (1.2 eq.), DCM | 0 | 5 min | 16 |
| | | | | |
| 8 | **EuFOD (cat.), PhMe** | **40** | **4 h** | **86** |

[1]starting material: 86% *ee*

## Scope & Results




## Acknowledgement
This work was financed in whole by the Austrian Science Fund FWF (P 35623-N).

## References:
1. Rehbein, J.; Hiersemann, M.. Synthesis 2013, 45 (09), 1121–1159
2. Ito, H.; Taguchi, T. Chem. Soc. Rev. 1999, 28 (1), 43–50.