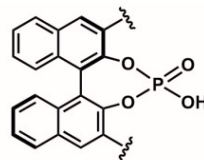


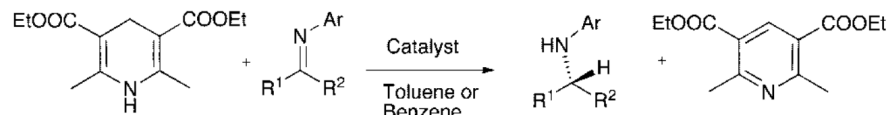
## BINOL-Derived Chiral Phosphoric Acids

- Brønsted acids have proven to be highly efficient and versatile catalysts.
- Most prominent players are BINOL (1,1'-bi-2-naphthol) derived phosphoric acids (CPAs).
- First described independently by Terada and Akiyama groups in 2004.<sup>[1,2]</sup>

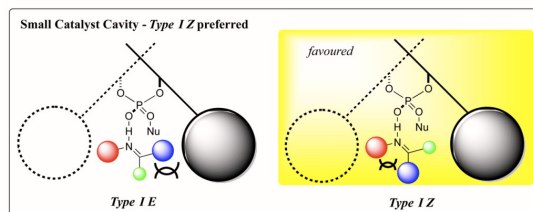
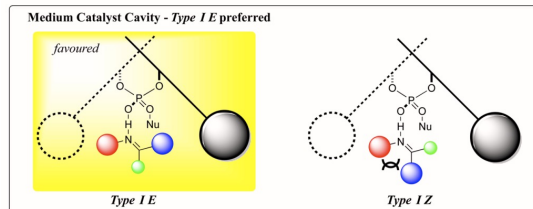


## Previous Mechanistic Studies

- Transfer hydrogenation of imines with Hantzsch ester was established as a model system for mechanistic investigations:<sup>[3]</sup>



- Besides experimental and spectroscopic investigations, computational studies have been key to gaining deeper understanding of the reactivity and stereoselectivity of CPA-catalysed reactions.
- In 2016 Goodman *et al.* linked the stereoselectivity to two parameters reflecting the steric properties of the 3,3'-substituents and developed the 'Goldilocks' model for predicting suitable CPAs based on reactant structures.<sup>[4]</sup>
- Independent studies by Sigman *et al.* established a data-driven prediction model to elucidate the influence of multiple parameters of the reagents on the stereoselectivity.<sup>[5]</sup>



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**A simple and straightforward prediction of the optimal catalyst for each substrate/reactant combination remained extremely difficult.**

References: [1] *Angew. Chem. Int. ed.* **2004**, 43, 27, 1566. [2] *J. Am. Chem. Soc.* **2004**, 126, 5356. [3] *J. Am. Chem. Soc.* **2008**, 130, 8741. [4] *J. Am. Chem. Soc.* **2016**, 138, 7910. [5] *Nature*, **2019**, 571, 343.

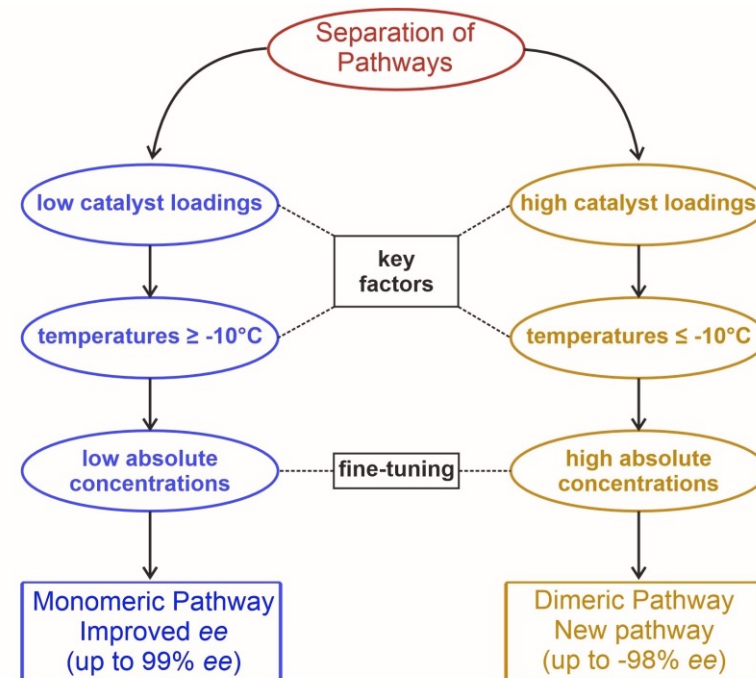
## Controlling the Competition between Monomeric versus Dimeric Reaction Pathways Enhances Stereoselectivities<sup>[6]</sup>

- Niemeyer *et al.* already showed in 2020 that in addition to the generally postulated monomeric pathway, a dimeric pathway with an opposite enantioselectivity exists.<sup>[7]</sup>
- By separating the monomeric and dimeric pathways, significantly improved stereoselectivities were achieved for both product enantiomers by Gschwind *et al.*<sup>[6]</sup>
- Evidence from NMR studies, DFT computations and catalytic reactions.

**Enantioselectivity is dependent on temperature, concentration and catalyst loading**

## Hypothesis

- Explanation for high previous reactions temperatures
- The kinetic preference of the dimeric pathway is almost independent of the substrate
- The dimeric pathway could be influential in various CPA-catalysed reactions beyond just the transfer hydrogenation of quinolines or imines
- The provided guideline regarding temperature and catalyst proportion to control the competition between monomeric and dimeric pathway can be transferred as a general scheme



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References: [6] *Angew. Chem. Int. Ed.* **2023**, 62, e202301183. [7] *Chem. Sci.* **2020**, 11, 4381.