

DEVELOPMENT OF NEW CHIRAL BRØNSTED ACIDS FOR ENANTIOSELECTIVE ORGANOCATALYZED REACTIONS

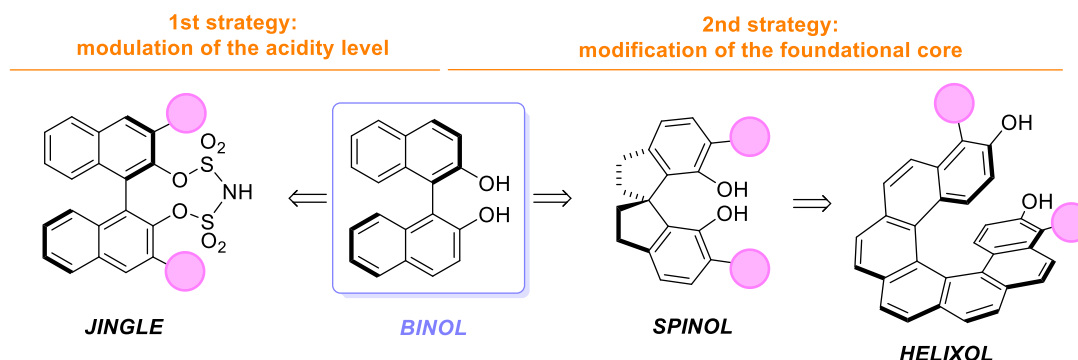
Marie J. Gouteron^{1,2}, Aitor Maestro², Philippe A. Peixoto¹, Javier Vicario², Patrick Y. Toullec¹

¹ Université de Bordeaux, Institut des Sciences Moléculaires, CSH group, Talence, France

² University of the Basque Country, UPV/EHU, Department of Organic Chemistry I, Vitoria-Gasteiz, Spain

The field of asymmetric organocatalysis has experienced exponential growth over the past two decades, partially due to the pioneering work of Akiyama and Terada in 2004, who introduced chiral phosphoric acids.¹ This alternative approach, which relies on small chiral organic molecules instead of toxic metal salts or enzymes, has enabled the selective synthesis of complex molecules, such as Eupolyphagin, as reported by Tan's group in 2017.² Among the various families of organocatalysts, the most frequently used scaffold is BINOL, linked to a phosphoric acid derivatives acting as a Brønsted acid.³ The induction of asymmetry via axial chirality, along with its versatility, underscores the significance of BINOL in this field. Some other families possessing a chiral diol in their structure are worth mentioning like SPINOL or SPHENOL and have proven their efficiency through time.⁴ Their structure and activity can be finely tuned by modifications of the chiral diol unit and the acidic functional group,⁵ allowing for the activation of a wide variety of electrophiles and the induction of numerous highly enantioselective reactions.

In this context, the development of new chiral Brønsted acid catalysts will proceed along two main strategies: the synthesis of a BINOL-based JINGLE⁶ possessing a strong acidic centre and the synthesis of a helicene-based diol used as a potential scaffold for a new family of catalysts.⁷



References

- ¹ (a) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 1566–1568. (b) Uruguchi, D.; Sorimachi, K.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 11804–11805.
- ² Wang, Y.-B.; Zheng, S.-C.; Hu, Y.-M.; Tan, B. *Nat. Commun.* **2017**, *8*, 15489.
- ³ (a) Parmar, D.; Sugiono, E.; Raja, S.; Rueping, M. *Chem. Rev.* **2014**, *114*, 9047–9153. (b) Corte, X. del; Marigorta, E. M. de; Palacios, F.; Vicario, J.; Maestro, A. *Org. Chem. Front.* **2022**, *9*, 6331–6399.
- ⁴ Zhang, R.; Ge, S.; Sun, J. *J. Am. Chem. Soc.* **2021**, *143*, 12445–12449.
- ⁵ Handjaya, J. P.; Patankar, N.; Reid, J. P. *Chem. Eur. J.* **2024**, *30*, e202400921.
- ⁶ Berkessel, A.; Christ, P.; Leconte, N.; Neudörfl, J.-M.; Schäfer, *Eur. J. Org. Chem.* **2010**, *2010*, 5165–5170.
- ⁷ Antien, K.; Pouységú, L.; Deffieux, D.; Massip, S.; Peixoto, P. A.; Quideau, S. *Chem. Eur. J.* **2019**, *25*, 2852–2858