COMBINING GOLD(I) CATALYSIS AND BIOCATALYSIS



Meriem DAGHMOUM,¹ Nazarii SABAT,¹ and Xavier GUINCHARD¹

¹ICSN, CNRS UPR 2301, Université Paris-Saclay, 1, av. de la Terrasse 91190, Gif-sur-Yvette, France

Over the last decades, biocatalysis has emerged as a relevant tool in the chemical industry providing an efficient, sustainable way to catalyze many reactions with high enantioselectivities.¹ Gold catalysis has similarly established itself as a key player in organic synthesis due to its use in a variety of reactions.² The combination of transition metal catalysis and biocatalysis allows to access chiral molecules in an efficient, fast, and sustainable manner.³ However, examples merging enzymes and Au(I) catalysis are scarce in the literature.⁴

In our approach, the combination of a gold catalyzed hydration of an alkyne is combined with a stereoselective reductive amination of the resulting ketone using an ω -transaminase⁵ is studied. This highly efficient approach provides chiral amines with high



enantioselectivities, from unfunctionalized, inexpensive hydrocarbons, in a one pot sequential relay manner in aqueous media. The chiral amines obtained are highly valuable chiral building blocks that may be used for synthesis of biologically active compounds. The method can be applied to simple alkynes or more complex molecules that lead to further cyclization. In situ protections, reductions can be performed to access a large variety of chiral compounds.



References

¹ Winkler, C. K.; Schrittwieser, J. H.; Kroutil, W. ACS Cent. Sci. 2021, 7, 55–71.

² a) Chintawar, C. C.; Yadav, A. K.; Kumar, A.; Sancheti, S. P.; Patil, N. T. *Chem. Rev.* **2021**, *121*, 8478–8558. b) Zi, W.; Dean Toste, F. *Chem. Soc. Rev.* **2016**, *45*, 4567–4589.

³ a) Denard, C. A.; Hartwig, J. F.; Zhao, H. *ACS Catal.* **2013**, *3*, 2856–2864. b) Huang, X.; Cao, M.; Zhao, H. *Curr. Opin. Chem. Biol.* **2020**, *55*, 161–170.

⁴a) Asikainen, M.; Krause, N. Adv. Synth. Catal. 2009, 351, 2305–2309. b) Wang, Z. J.; Clary, K. N.; Bergman, R.

G.; Raymond, K. N.; Toste, F. D. *Nature Chem.* **2013**, *5*, 100–103. c) Odachowski, M.; Greaney, M. F.; Turner, N. J. ACS Catal. **2018**, *8*, 10032–10035.

⁵ Slabu, I.; Galman, J. L.; Lloyd, R. C.; Turner, N. J. ACS Catal. **2017**, *7*, 8263–8284.