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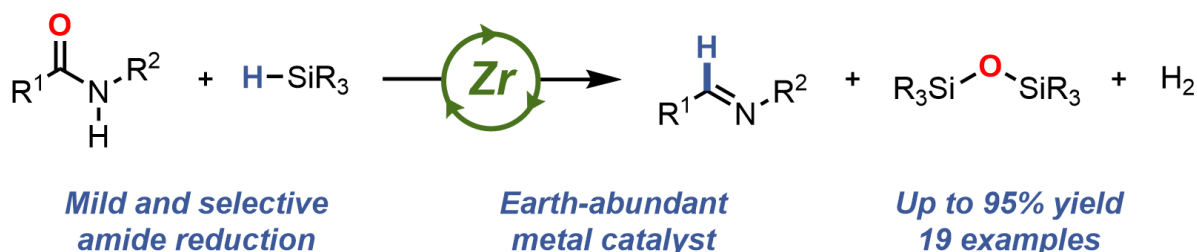
Reduction of Amides to Imines Catalyzed by Schwartz's Reagent

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Organic amides are prevalent in pharmaceuticals, agrochemicals and natural products as well as a variety of functional polymer materials. Therefore, methods to reduce these functionalities could open new opportunities for late-stage functionalization and post-polymerization modification to access new chemicals that are difficult to synthesize by classical methods.¹ However, the amide C=O bond is relatively inert to hydride addition, which means that forcing conditions are often required, leading to issues with functional group tolerance and chemoselectivity. Several catalytic protocols have been developed to enable the use of milder reducing agents; however, most of these protocols form amines as the final product and typically proceed by initial formation of the imine equivalent followed by further reduction.² The development of methodologies that avoid overreduction to the amine product and instead allow selective formation of the corresponding imine are rare but highly valuable and can complement traditional methods for imine synthesis.³



Ganem and co-workers showed that the commercially available and well-defined Schwartz reagent ($\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$) can reduce amides to imines stoichiometrically with liberation of $(\text{ClZrCp}_2)_2\text{O}$.⁴ Inspired by this work, we report the use of silanes as stoichiometric reductants to unlock a catalytic protocol for this transformation, using $\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$ as a catalyst for the deoxygenation of a range of secondary amides.⁵ This catalytic system retains the excellent chemoselectivity observed for the original stoichiometric protocol. We have investigated the mechanism of this reaction through the isolation of potential reactive intermediates as well as developing one-pot processes for the further derivitization of the imine products. This work presents a rare example of Zr hydride catalysis, enabling the practical and efficient functionalization of a challenging class of substrates without recourse to highly sensitive reagents or rare and expensive metals.

¹ Czerwinski, P. J.; Furman, B. *Front. Chem.* **2021**, *9*, 1–10.

² Volkov, A.; Tinnis, F.; Slagbrand, T.; Trilloa, P.; Adolfsson, H. **2016**, *45*, 6685–6697.

³ (a) Pelletier, G.; Bechara, W. S.; Charette, A. B. *J. Am. Chem. Soc.* **2010**, *132*, 12817–12819 (b) Chen, C.; Brookhart, M. J. *Am. Chem. Soc.* **2012**, *134*, 11304–11307.

⁴ Schedler, D. J. A.; Li, J.; Ganem, B. *J. Org. Chem.* **1996**, *61*, 4115–4119.

⁵ Donnelly, L. J.; Berthet, J.-C.; Cantat, T. *ChemRxiv* **2022** (DOI:10.26434/chemrxiv-2022-bzr64).