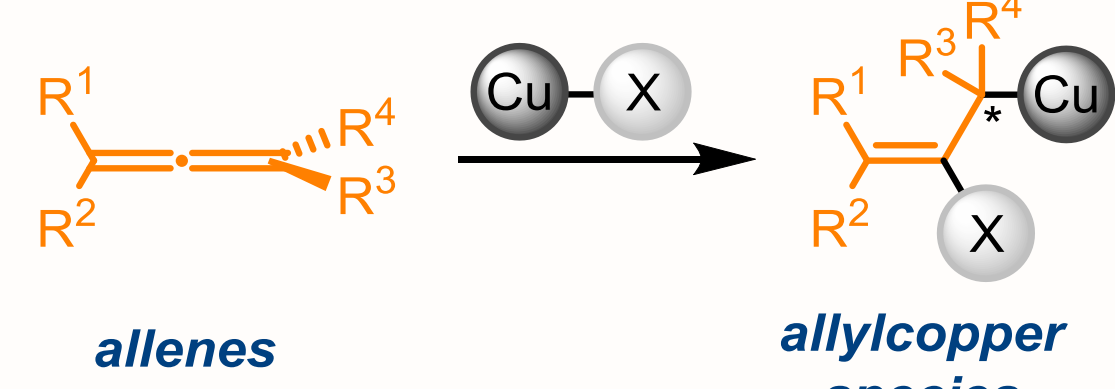
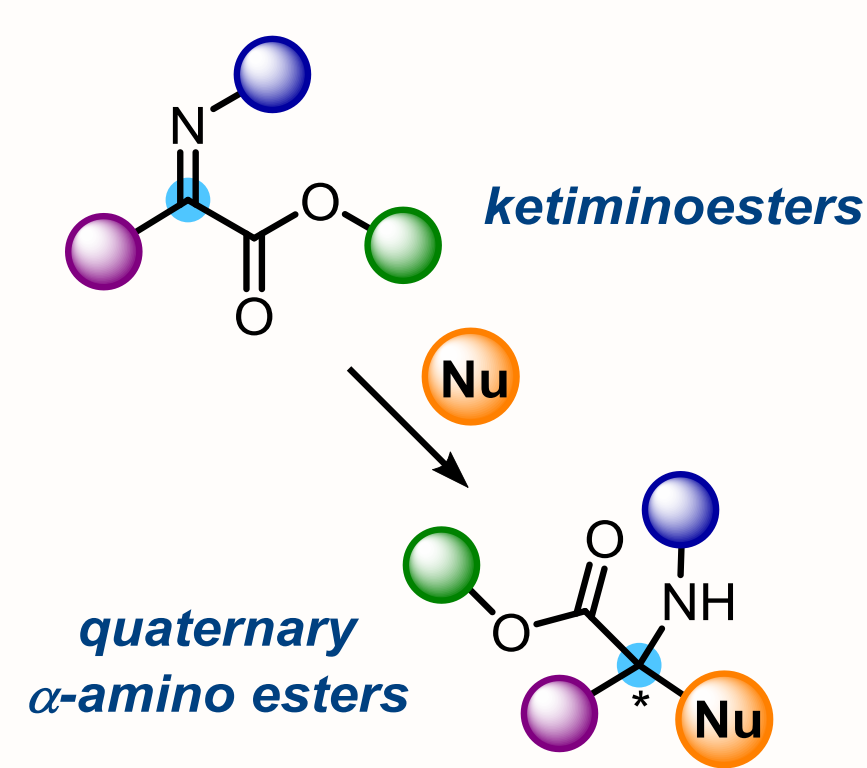


## Introduction

Due to their enhanced metabolic stability towards hydrolysis and the structural rigidity they lend to peptide backbones, quaternary  $\alpha$ -amino acids are vital building blocks in pharmaceutical research and the study of proteins. The development of novel syntheses of quaternary  $\alpha$ -amino acids is therefore important, but remains challenging due to the inherent difficulty of constructing a fully-substituted stereogenic centre. Ketiminoesters are useful precursors to quaternary  $\alpha$ -amino acid derivatives, however, there are only a few reports of catalysed additions to these electrophiles.

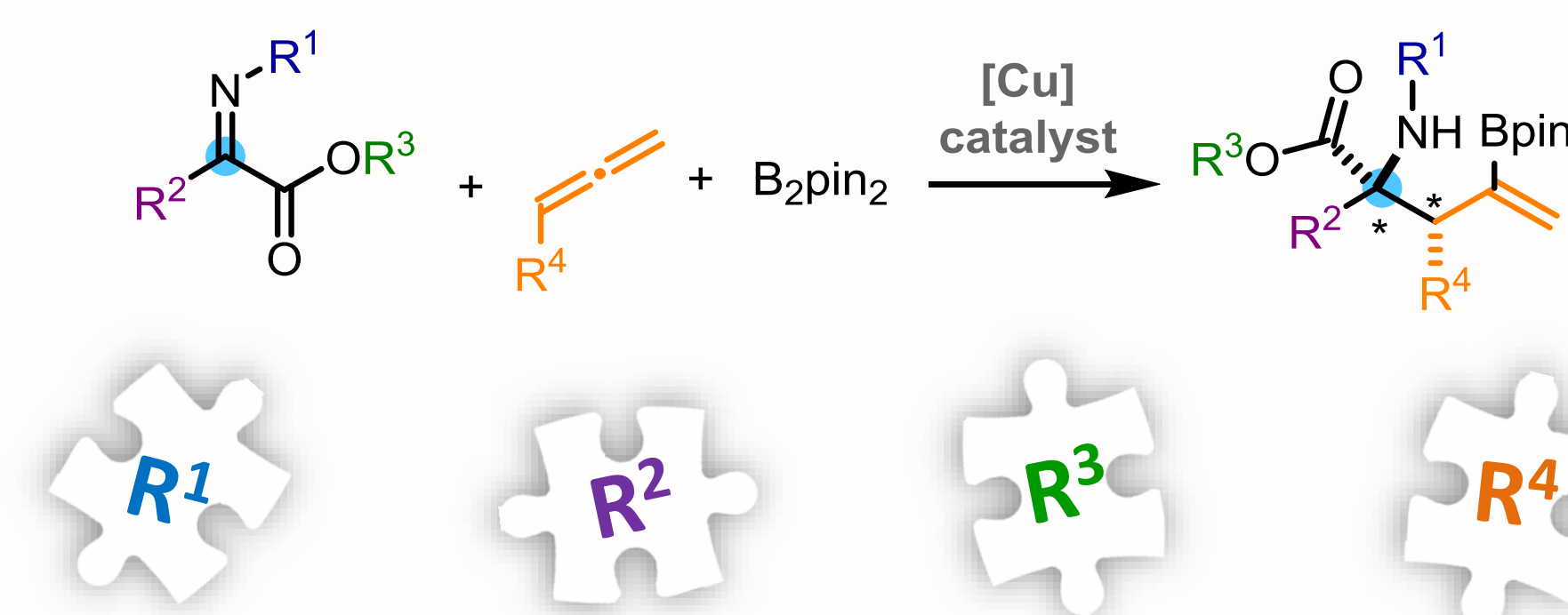


Inexpensive copper catalysts are able to functionalise allenes by formation of transient allylcopper species, and subsequent electrophilic trapping.<sup>1-3</sup> We therefore envisaged that allenes would serve as suitable precursors to allyl metals for catalytic coupling with ketiminoesters, providing an unprecedented approach to the construction of high-value quaternary  $\alpha$ -amino esters.

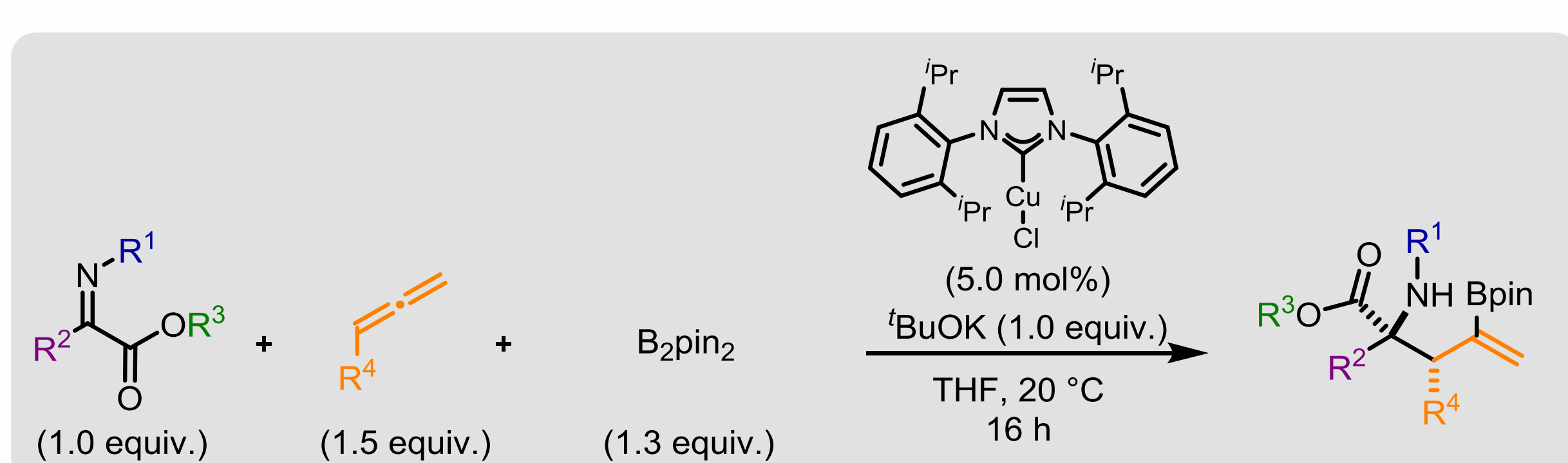


## Aims of the Project

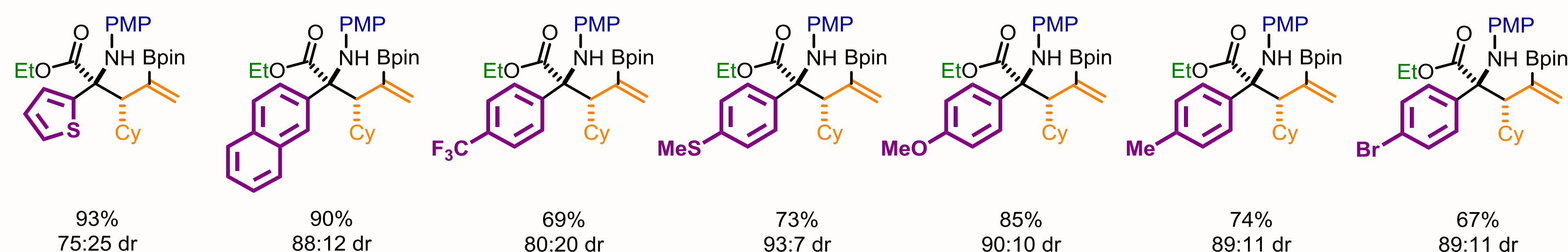
We aimed to develop an operationally simple, one-pot, diastereoselective union of ketiminoesters, allenes and diboranes, utilising a low cost copper catalyst and a commercially available NHC ligand.<sup>4</sup> The multicomponent coupling affords densely functionalised quaternary  $\alpha$ -amino esters bearing adjacent stereocentres and versatile vinyl boronate motifs.



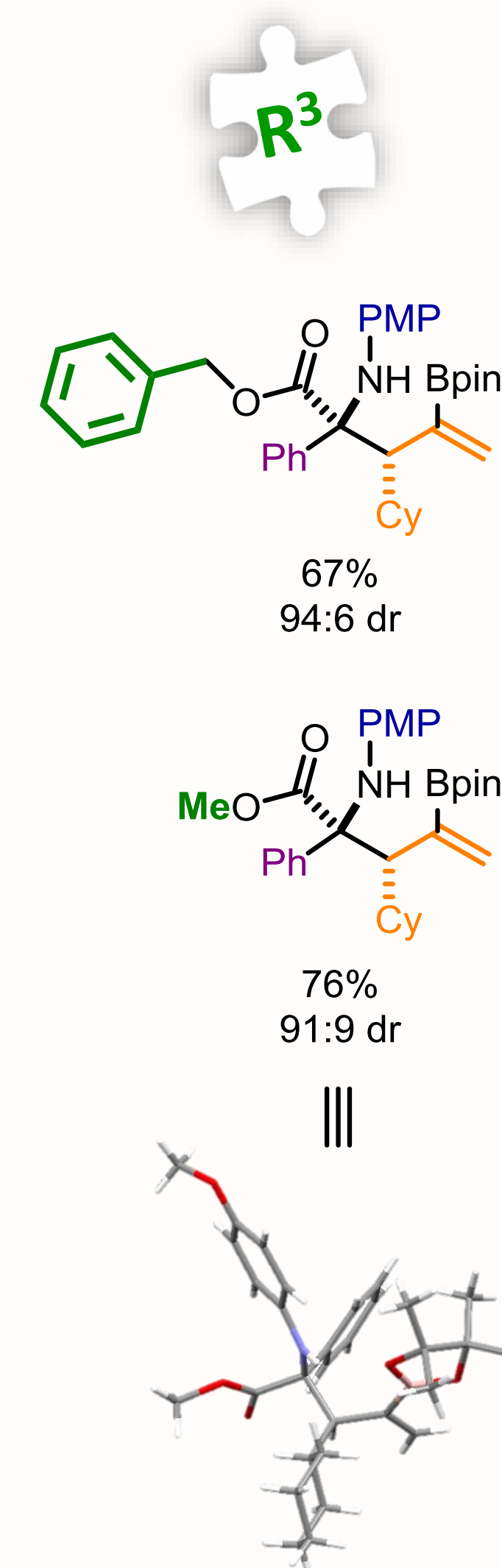
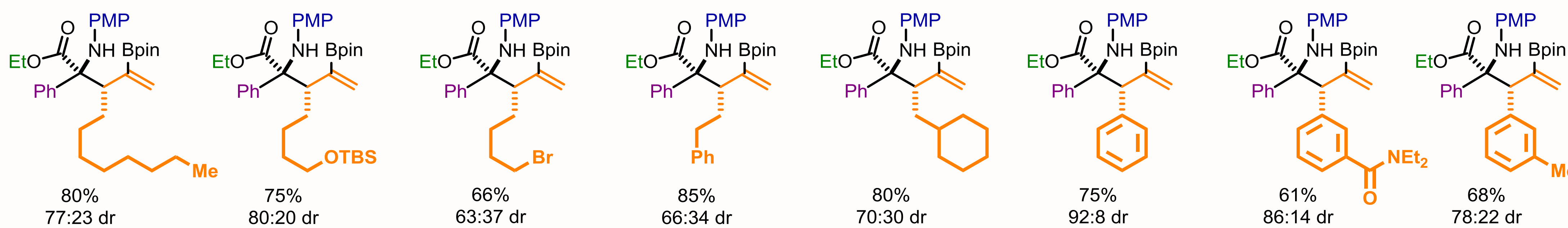
## Multicomponent Coupling



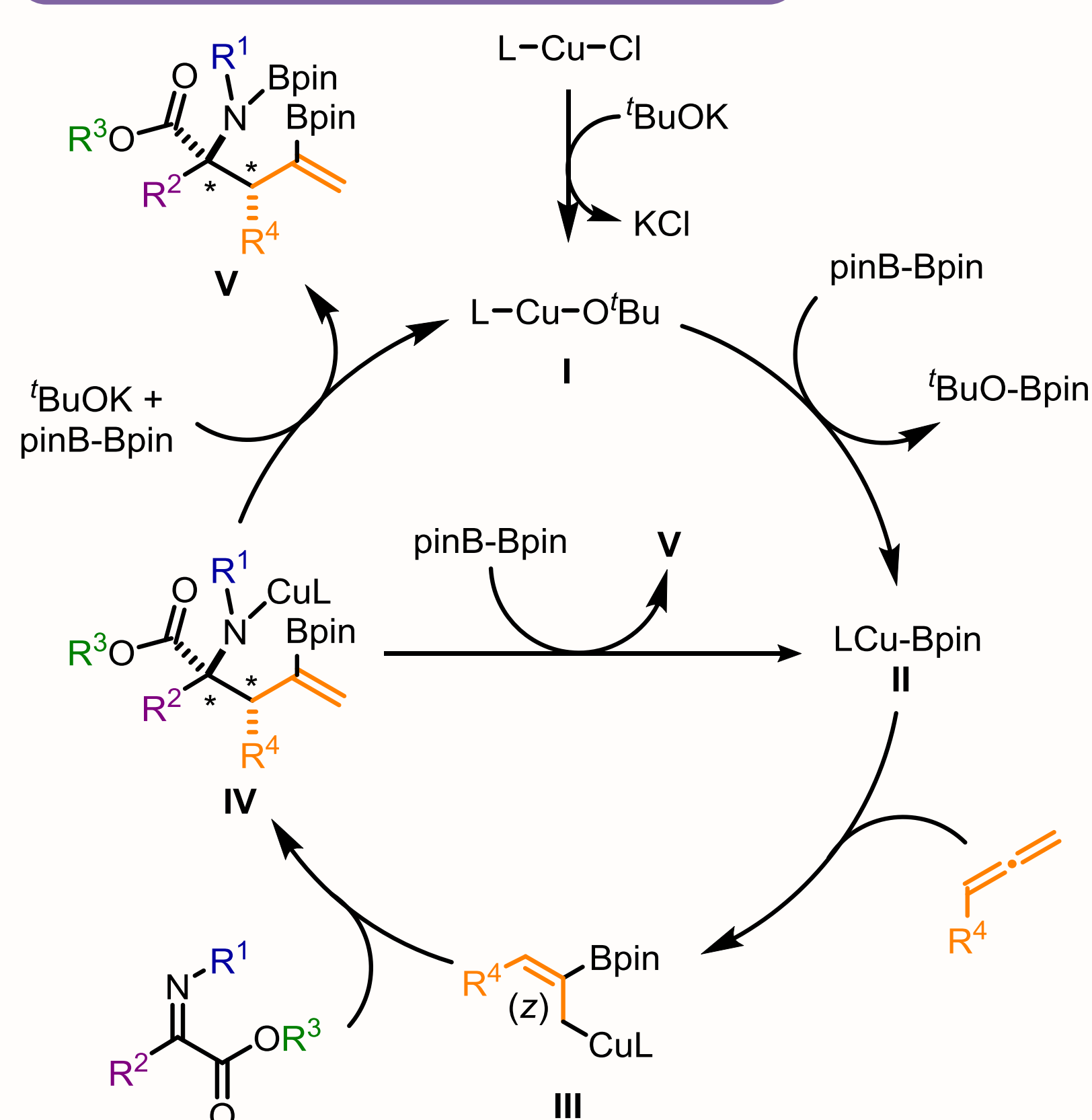
R<sup>2</sup>



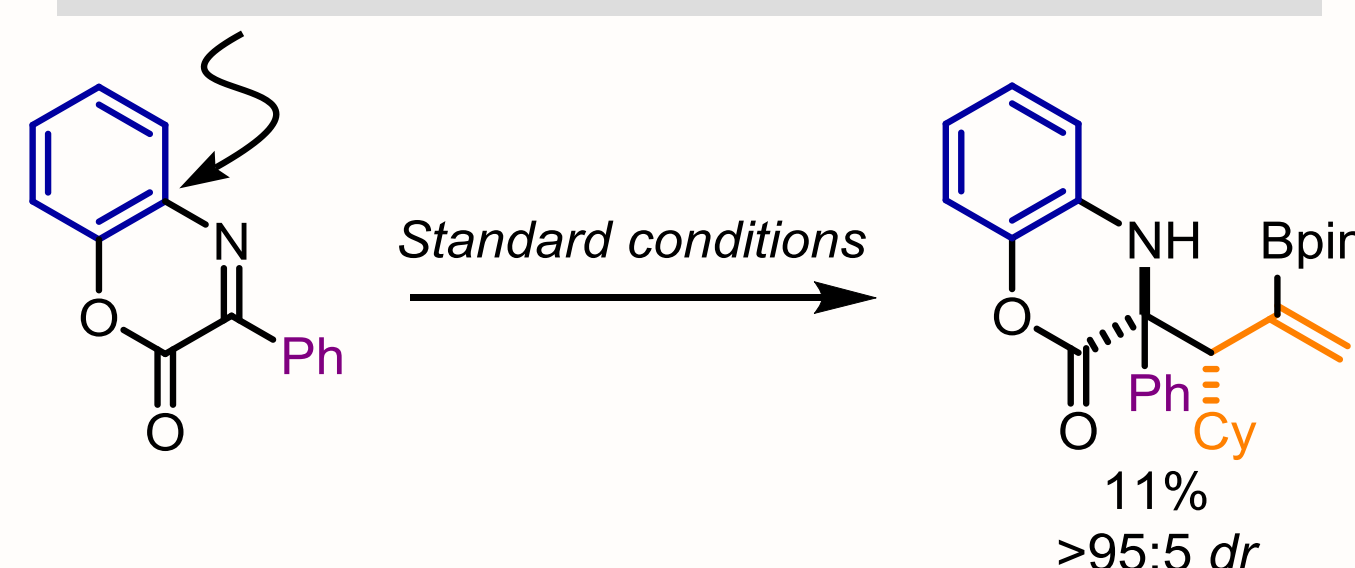
R<sup>4</sup>



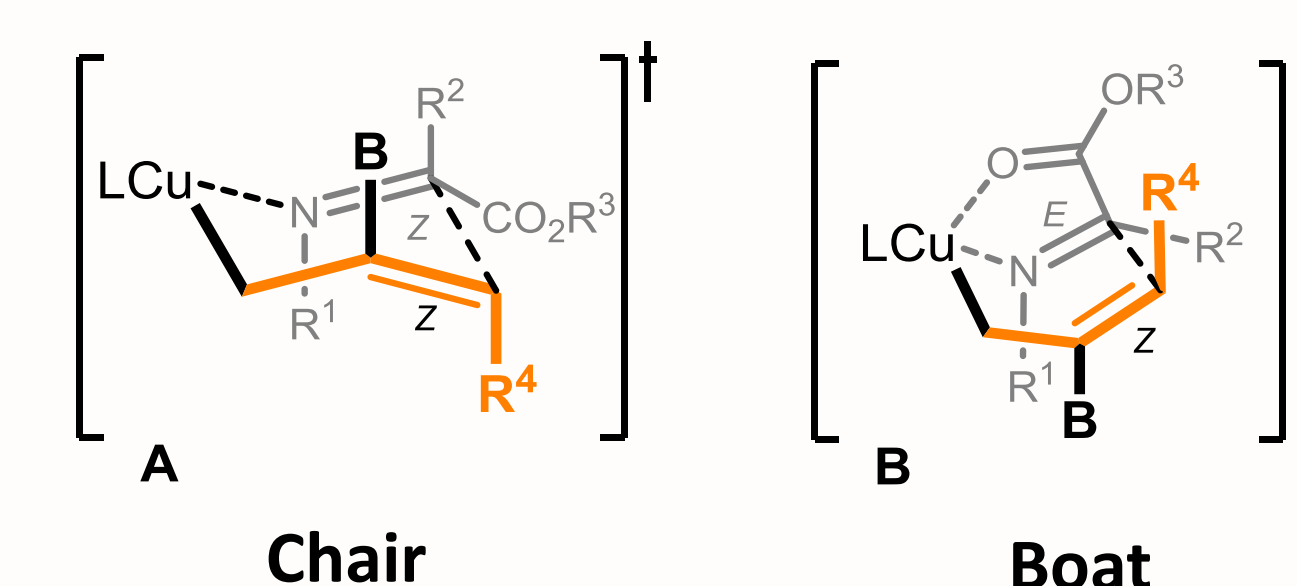
## Catalytic Cycle



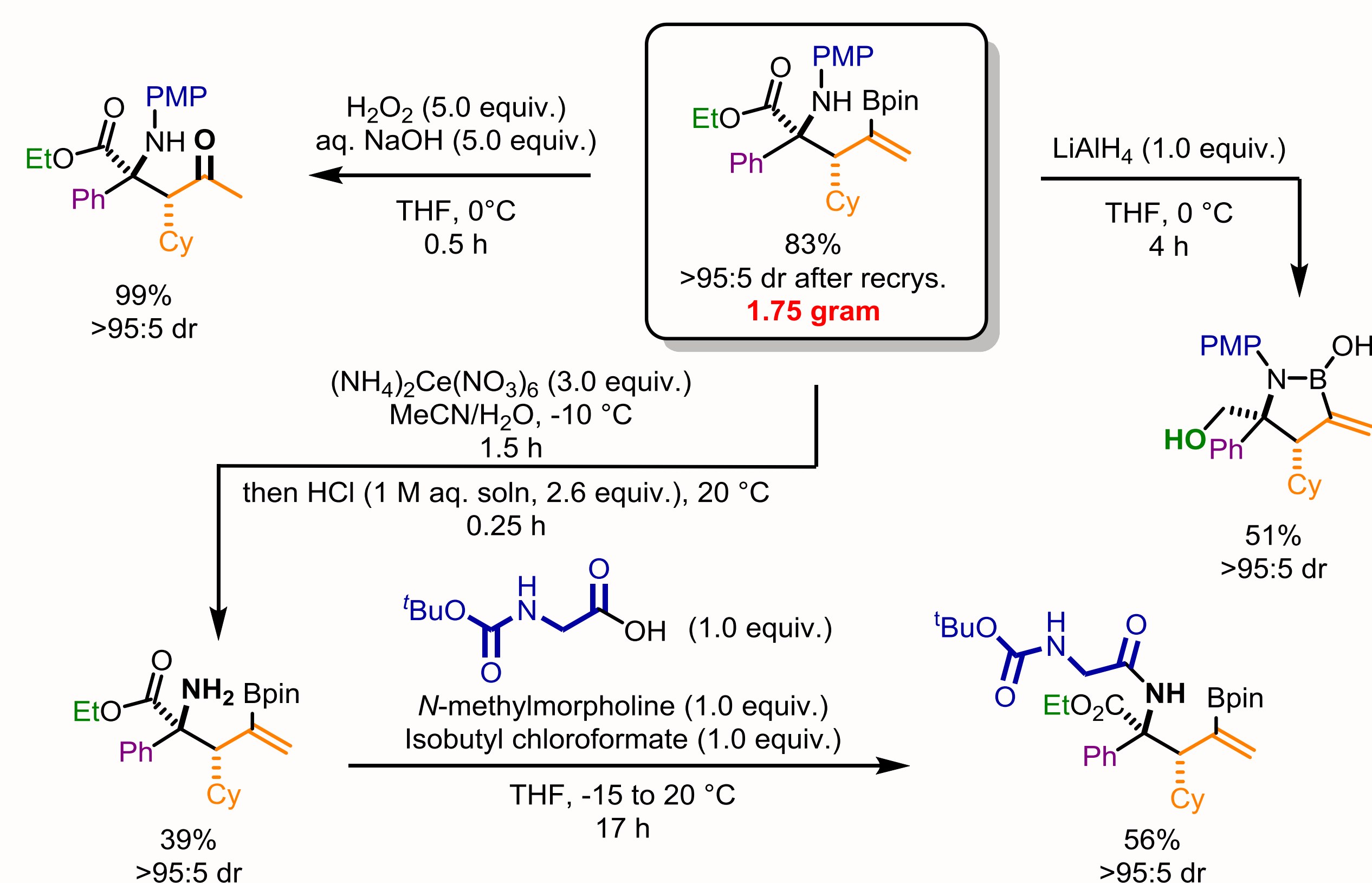
Locked – configuration & conformation = inefficient coupling



Possible transition states



## Manipulations



## References

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3. K. Yeung, R. E. Ruscoe, J. Rae, A. P. Pulis, D. J. Procter, *Angew. Chem. Int. Ed.* **2016**, *55*, 11912–11916.
4. K. Yeung, F. J. T. Talbot, G. P. Howell, A. P. Pulis, D. J. Procter, *ACS Catal.* **2019**, *9*, 1655–1661.

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## Conclusions

A novel, diastereoselective method for the synthesis of quaternary  $\alpha$ -amino esters has been developed. The reaction is catalysed by a low cost, commercially available copper catalyst, and involves an operationally simple one-pot procedure at ambient temperature. The multicomponent approach allows access to a wide range of products with different substitution patterns by variation of the starting inputs. Derivatisation of the quaternary  $\alpha$ -amino esters products has demonstrated their potential as precursors for a broad range of high value organic compounds.