

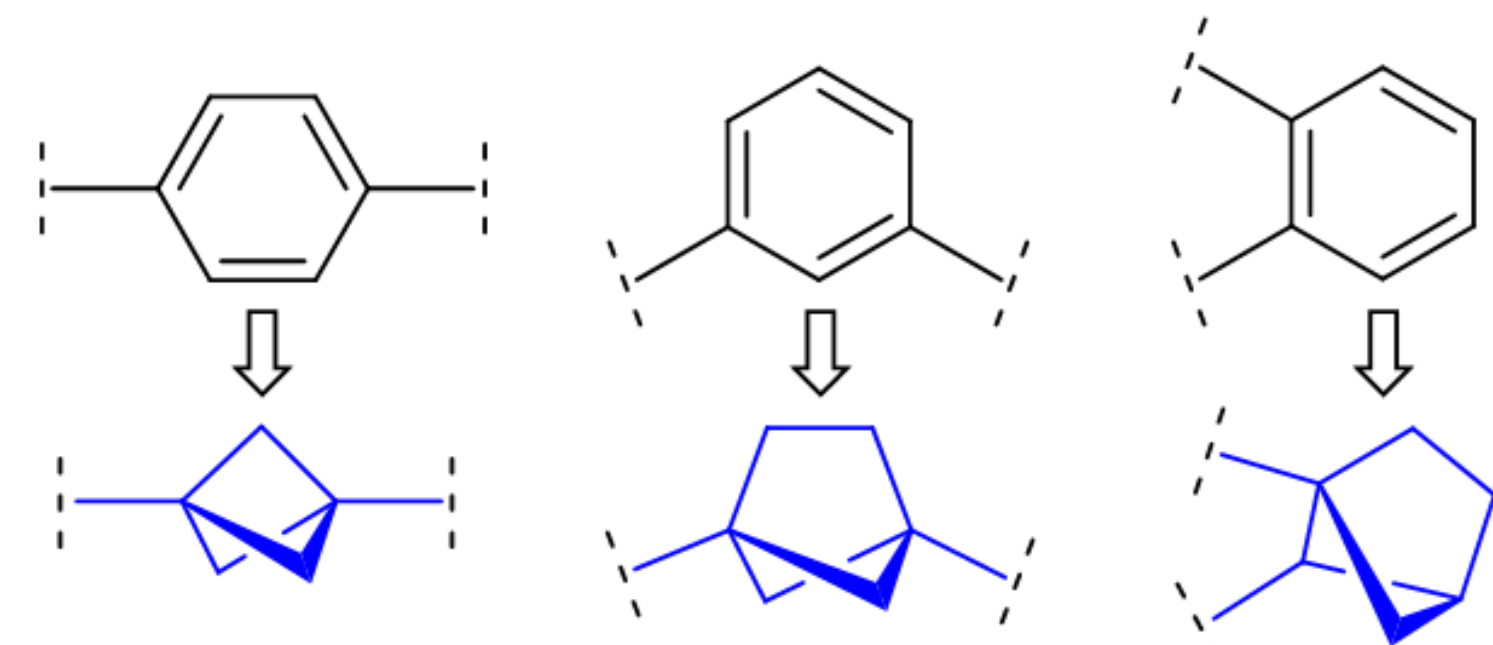
Synthesis of Tetra-Substituted Cyclobutyl Alkynes: Potential Access to Multi-Size Bicyclic Compounds

Liam Krueckl, Kushal Dhake, Dr. David C. Leitch

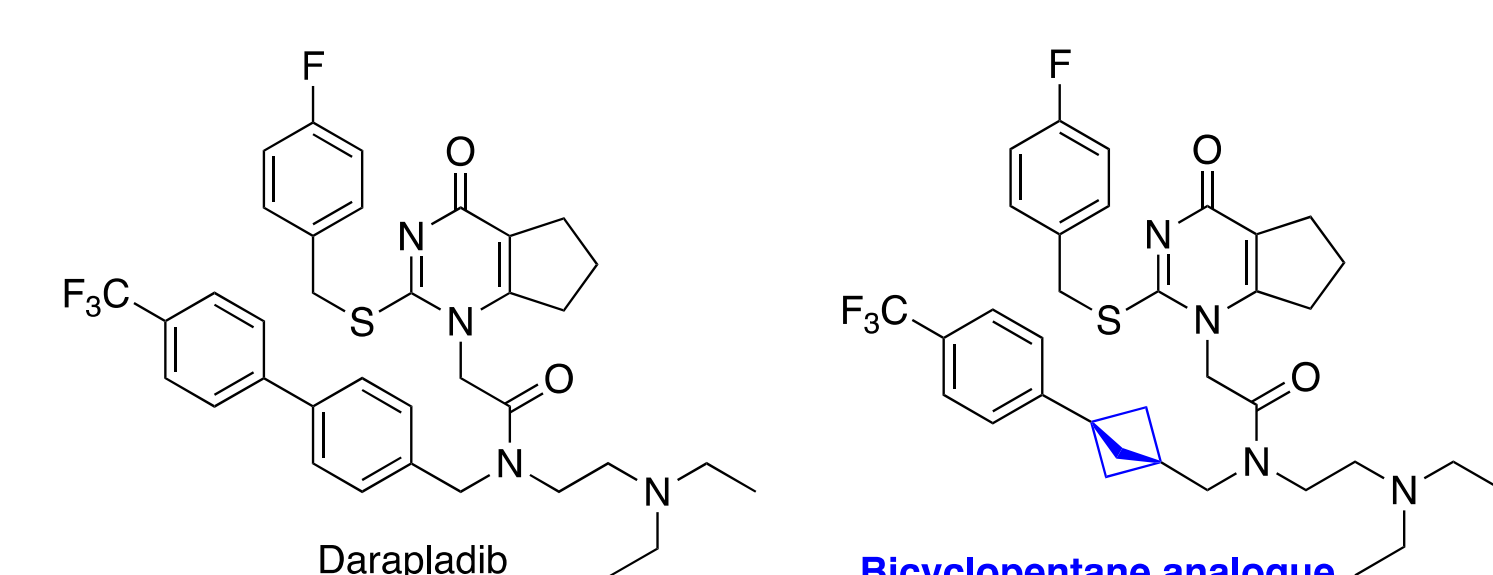


Purpose

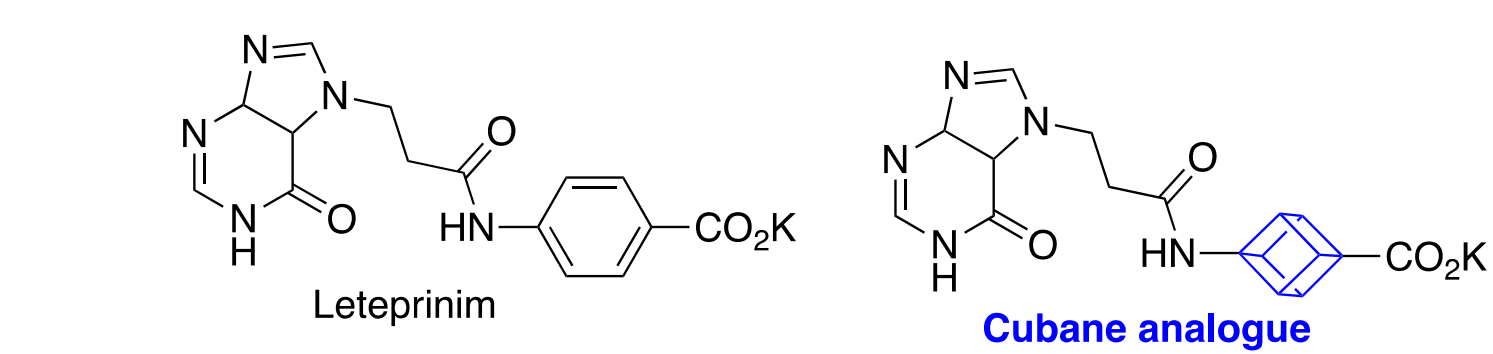
Saturated bioisosteres of phenylene in medicinal chemistry



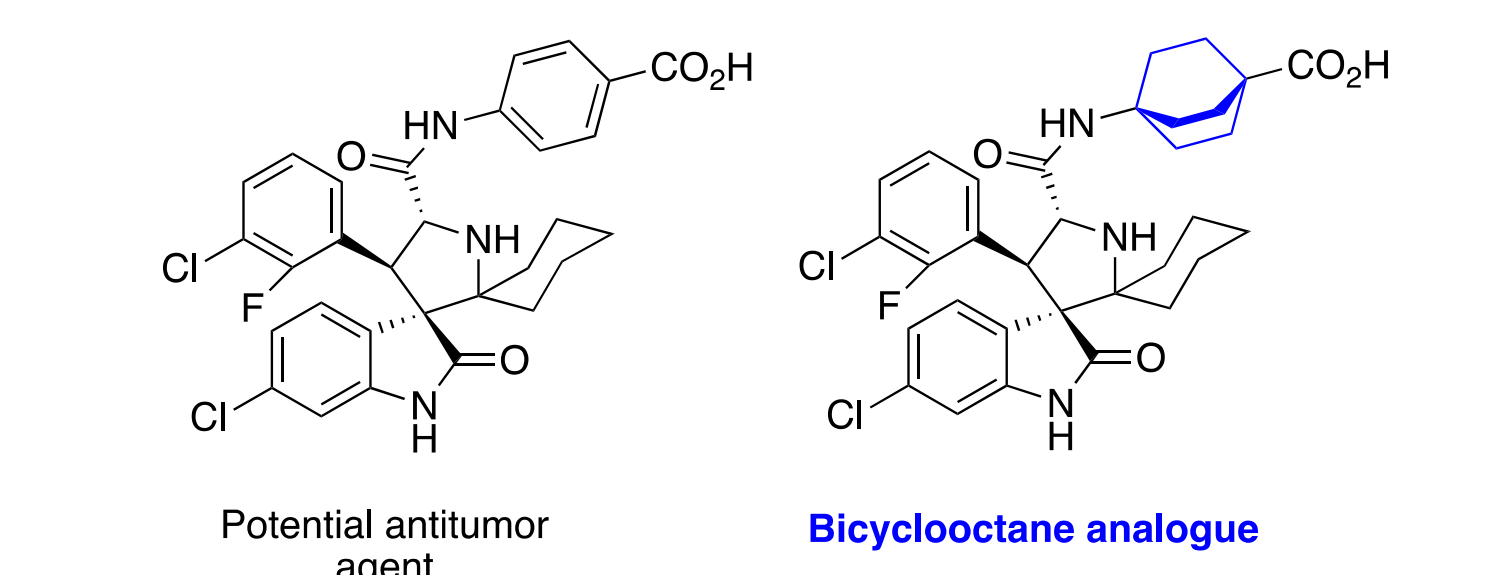
- Greater Csp^3 character
- Improved drug properties
- Novel compositions
- Synthetically challenging
- Limited substitution patterns
- Difficult to add heteroatoms



- Improved solubility
- Retain

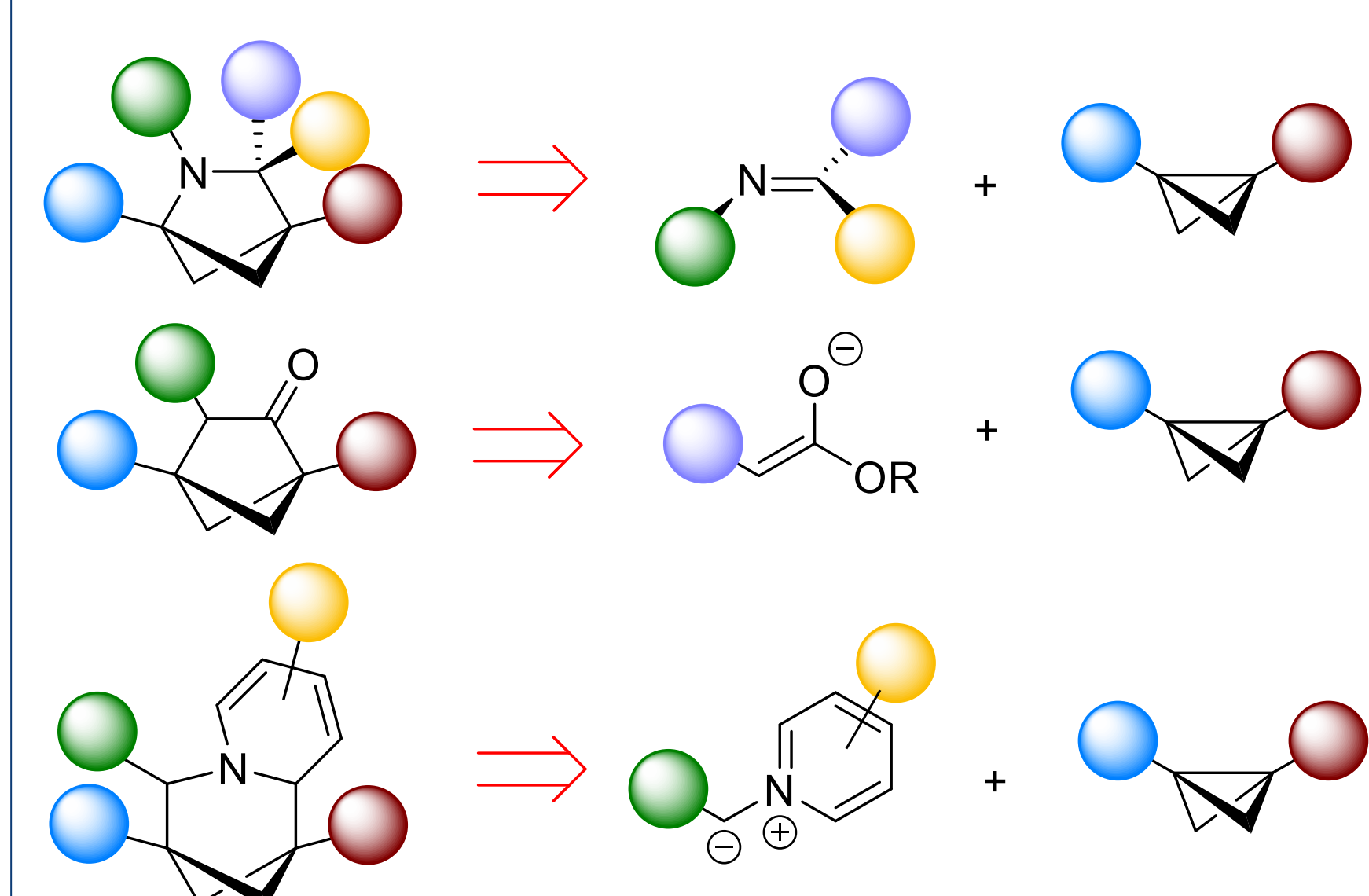


- Improved activity

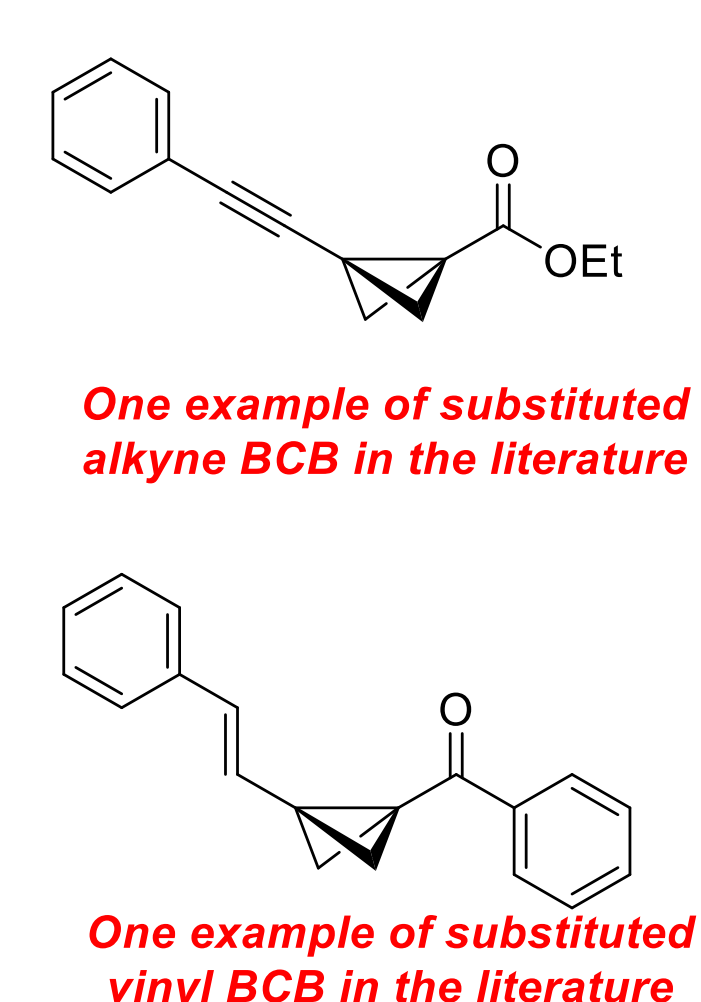
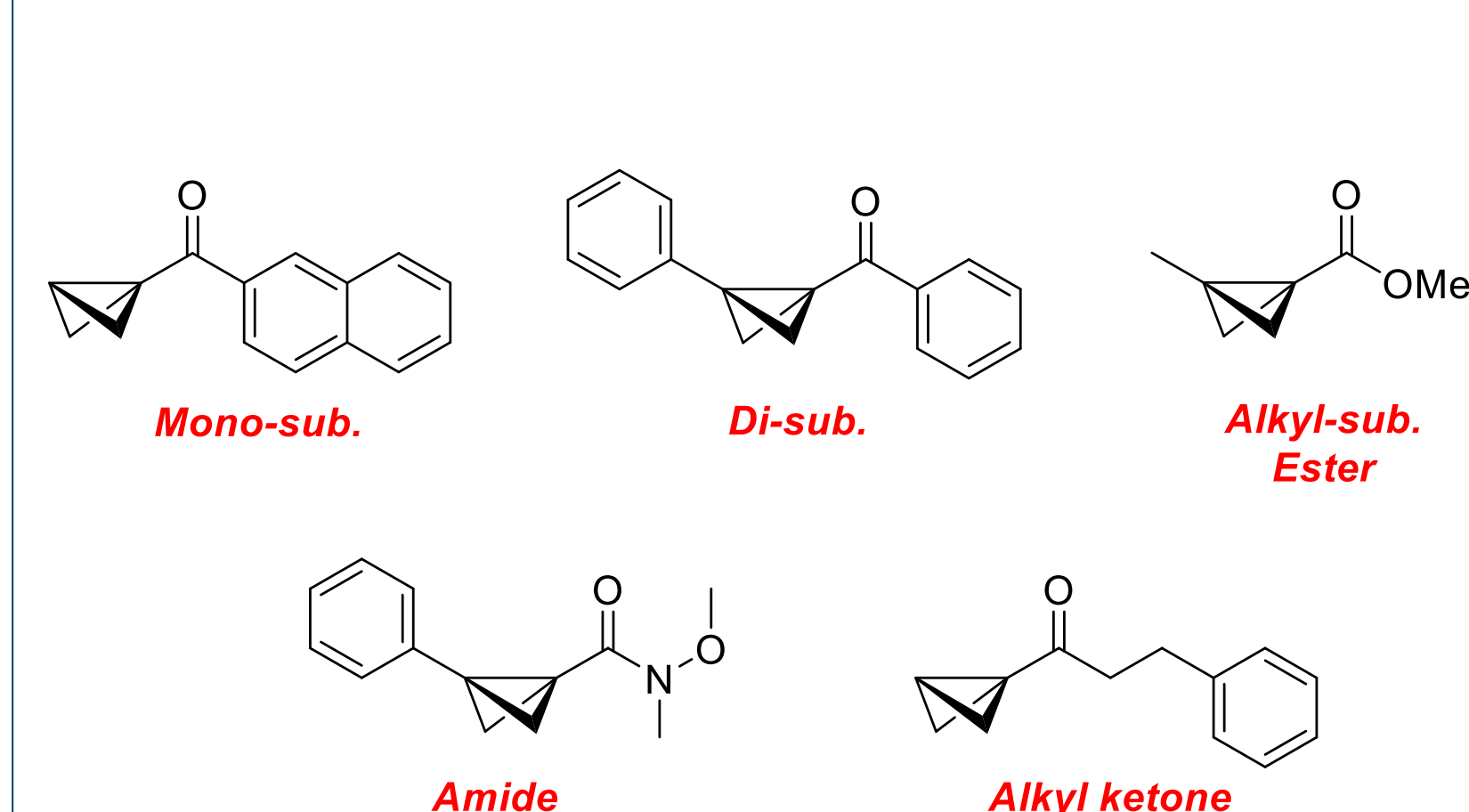


- Improved metabolic stability
- Increased potency

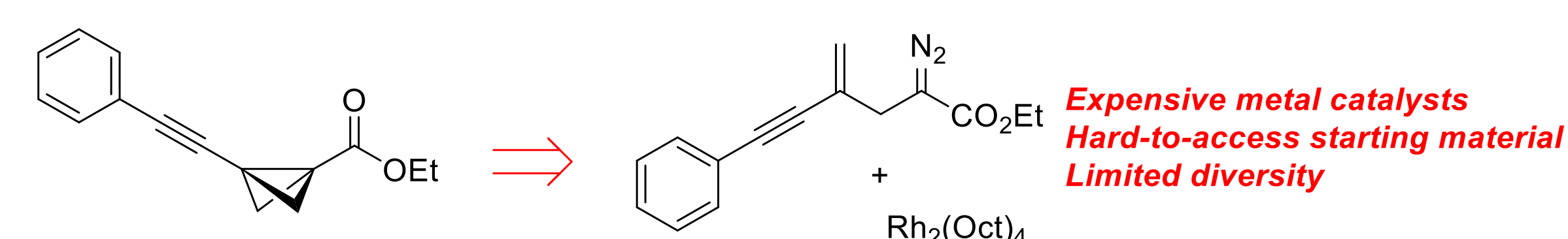
Previous work for BCB synthesis in the Leitch group



Examples of existing BCBs in the literature

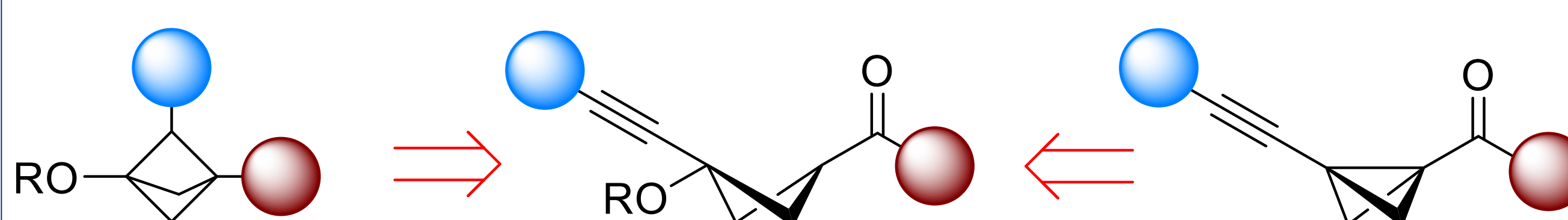


Current reported synthesis of alkynyl BCB



Objectives

Bicyclic compounds accessed through alkynyl cyclobutanes

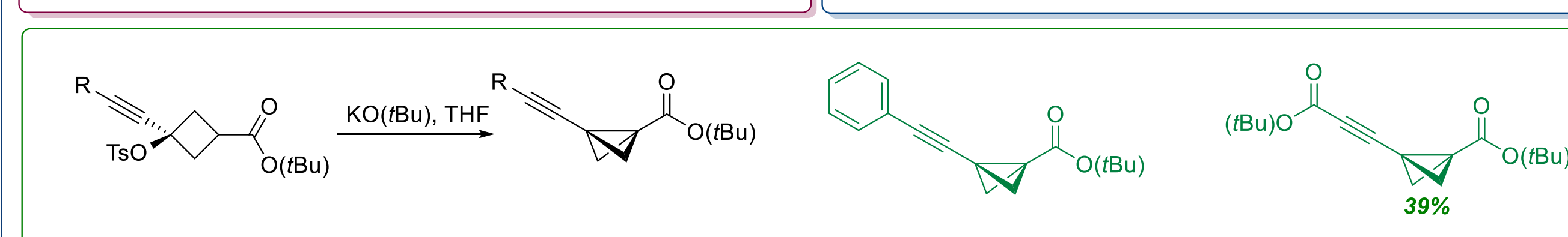
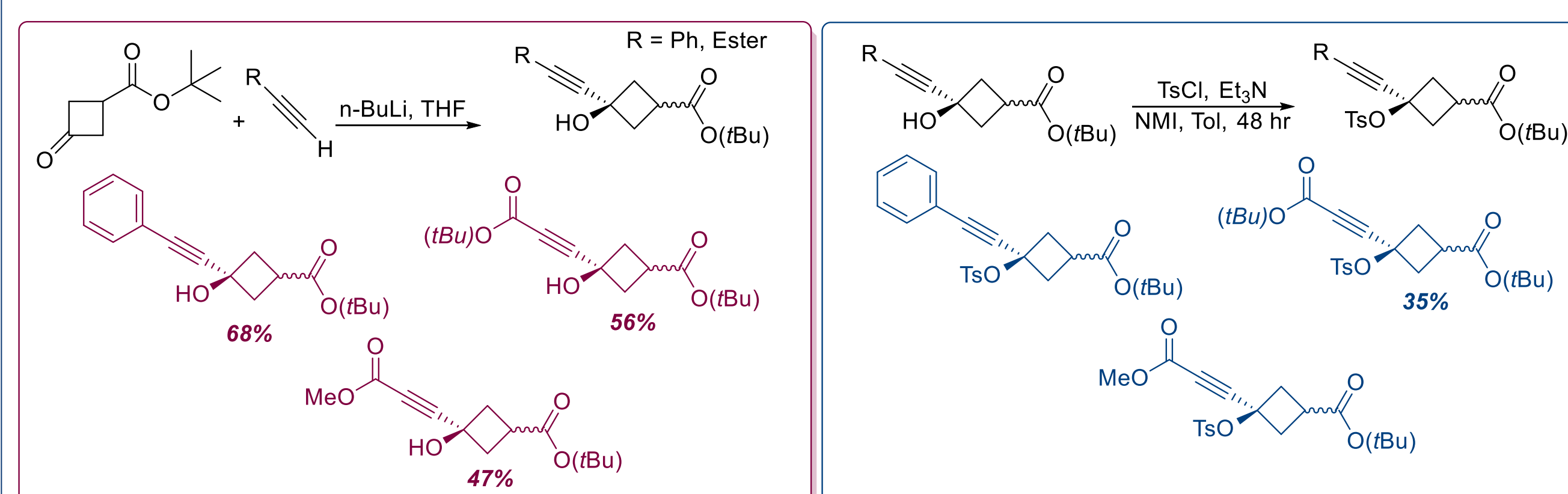


Objective B
Access to BCP
R = protecting group

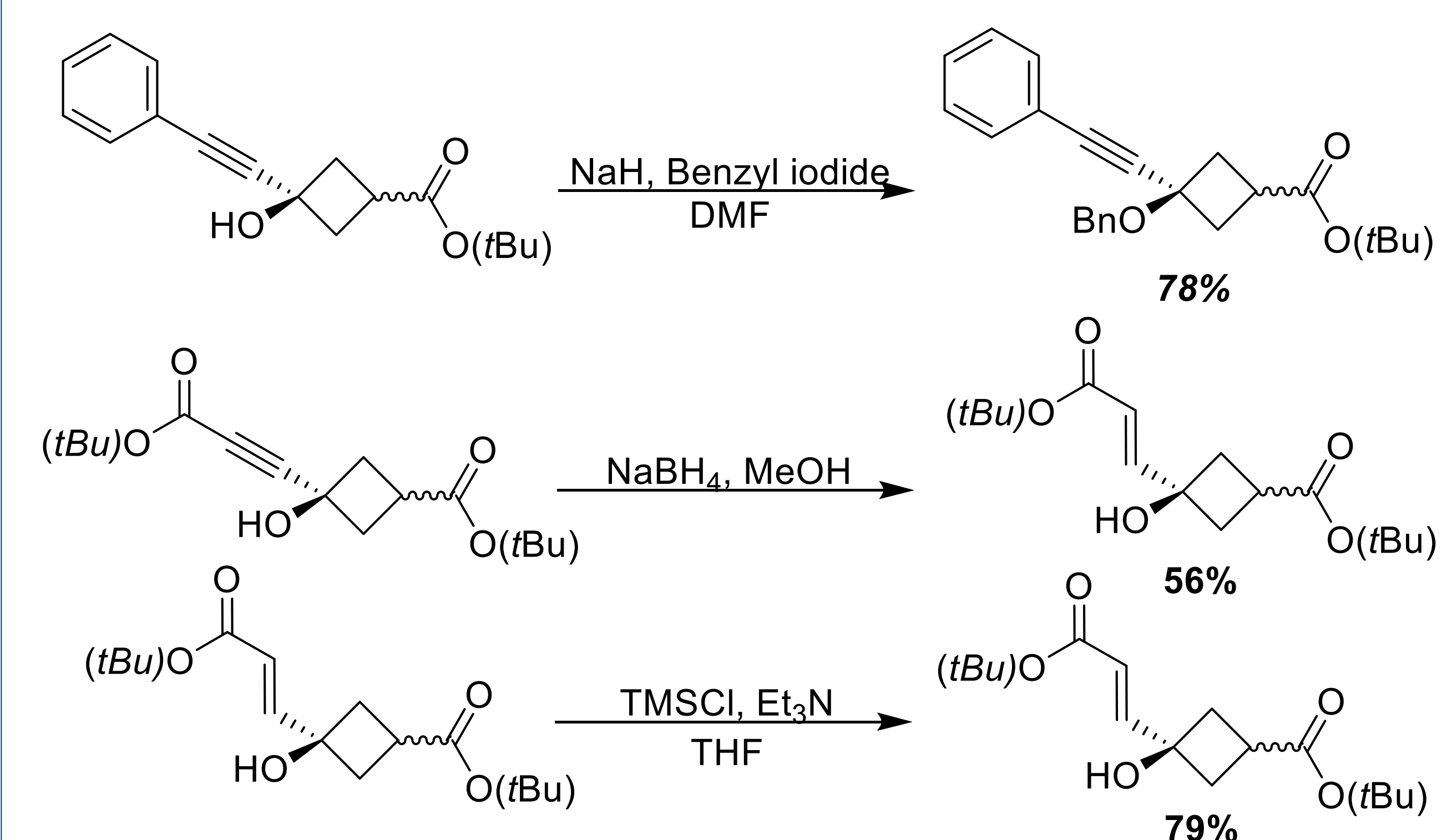
Objective A
Access to alkynyl BCB
R = leaving group

Reactions & Scope

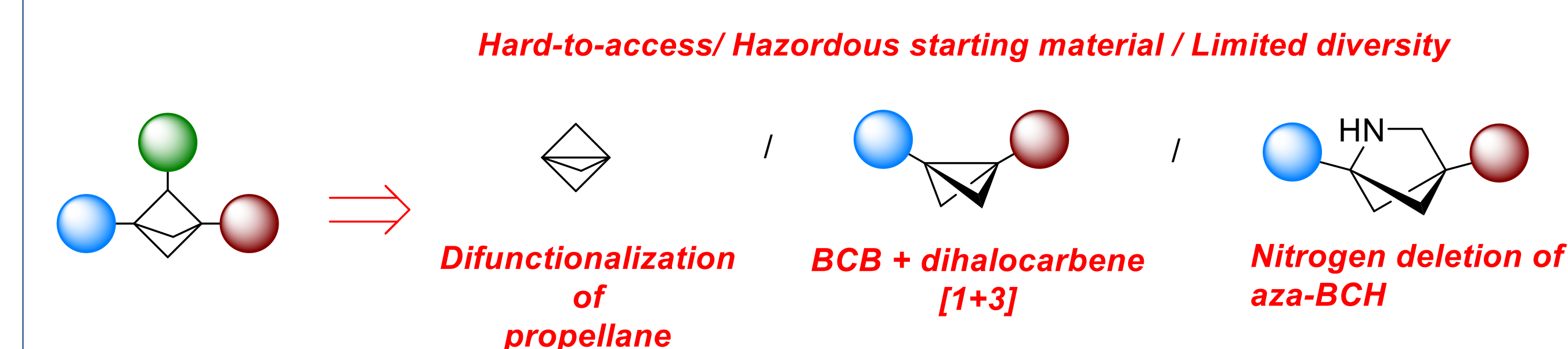
Objective A: Synthetic pathway and scope for alkynyl BCB



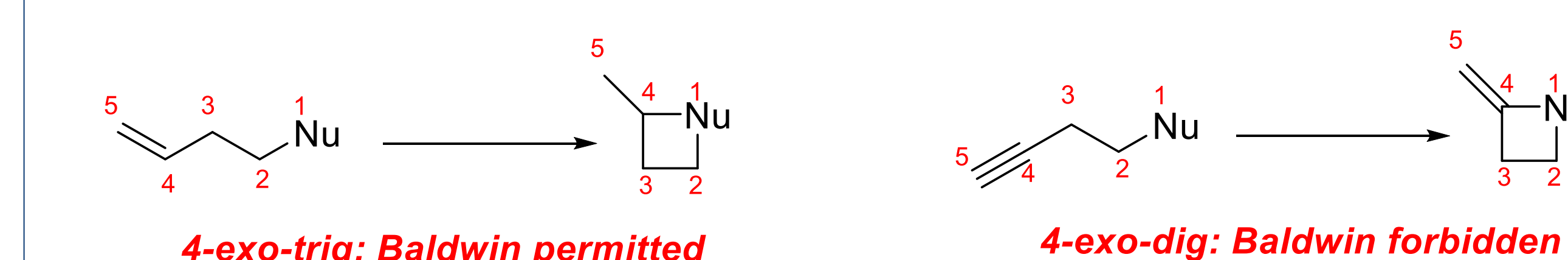
Objective B: O-protected & reduced products



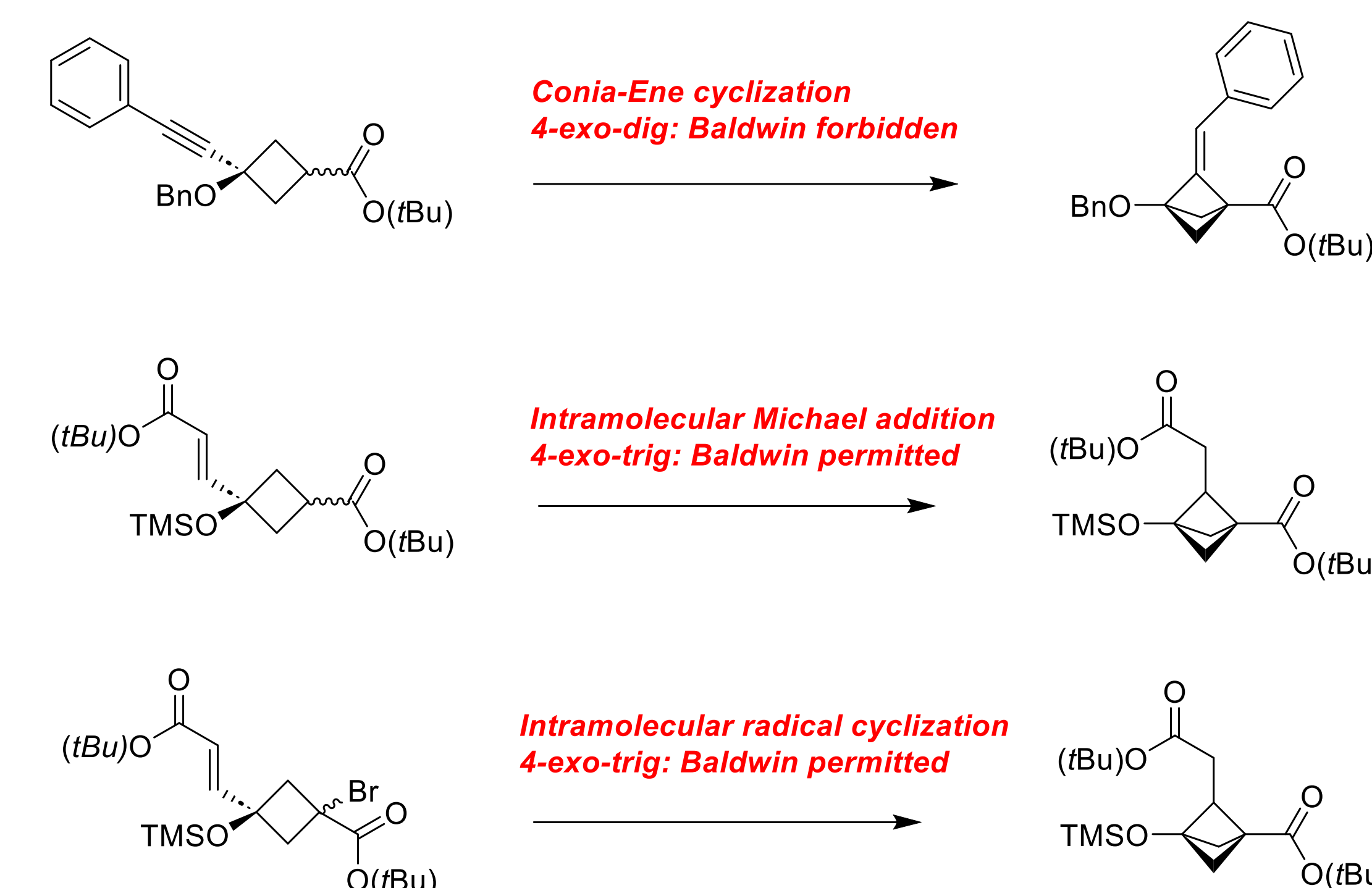
Existing methodologies for BCP synthesis



Baldwin's rules for cyclization



Proposed routes



Acknowledgements



- This research was supported by the Jamie Cassels Undergraduate Research Awards, University of Victoria
- Supervised by Dr. David Leitch in the department of chemistry



References

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