Constructing Methods to Make Enantiopure Anti-Aldols

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UB CURCA Symposium
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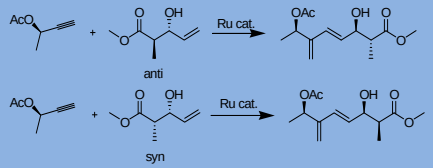
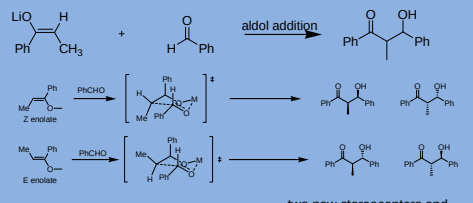
Goals



- The goal of my project is to test reactivity of enantiopure syn and anti alkenes in enyne cross metathesis with enantiopure alkynes
  - Two of the things I plan to test are % yield and whether the product stays enantiopure
  - This goal led to the problem of anti aldol synthesis, which led to development of a temporary linker that could be excised later

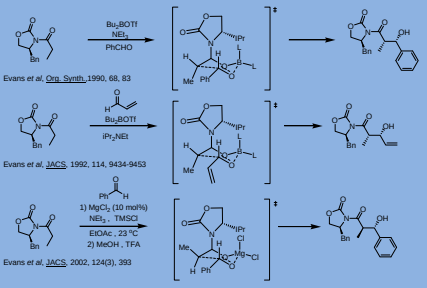
Aldol Addition



Zimmerman, Traxler, J. Am. Chem. Soc., 1957, 79, 1920-1923

two new stereocenters and potentially four stereoisomers

Making Syn and Anti Aldols

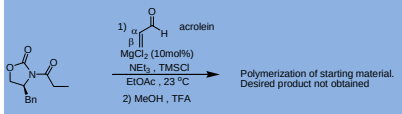


Evans *et al*, Org. Synth. 1990, 68, 83

Evans *et al*, JACS, 1992, 114, 9434-9453

Evans *et al*, JACS, 2002, 124(3), 393

Setbacks – Evans Anti-Aldol

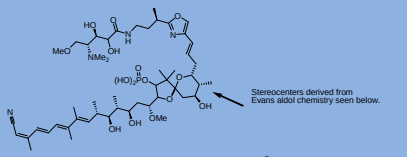


Polymerization of starting material. Desired product not obtained

- Starting material polymerizes because acrolein is very reactive
- Since there is no beta substitution, polymerization occurs more readily
- By introducing substitution at the beta carbon polymerization will be inhibited

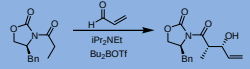
does not polymerize under reaction conditions

Examples in Total Synthesis



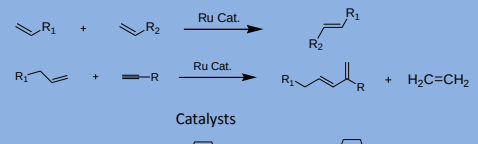
Stereocenters derived from Evans aldol chemistry seen below.

- This shows the importance of Evans aldol additions in total synthesis and development in this area could have a significant impact on further total synthesis.

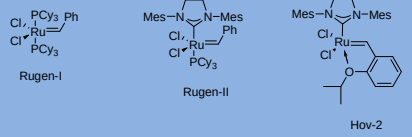


Evans *et al*, JACS, 1992, 114, 9434-9453

Alkene Metathesis and Enyne Metathesis



Catalysts

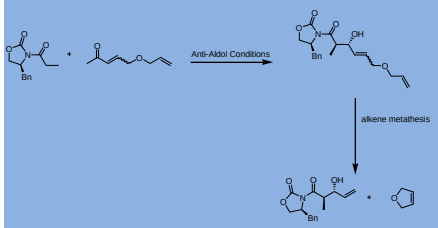


Importance and Usefulness in Chemistry

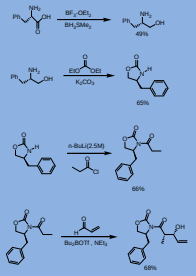
Yves Chauvin, Robert H. Grubbs, and Richard R. Schrock were awarded the Nobel Prize in Chemistry in 2005 "for the development of the metathesis method in organic synthesis"
This synthetic method can be applied to natural product synthesis and polymer synthesis as well as other applications

"The Nobel Prize in Chemistry 2005". Nobelprize.org.29 Mar 2011

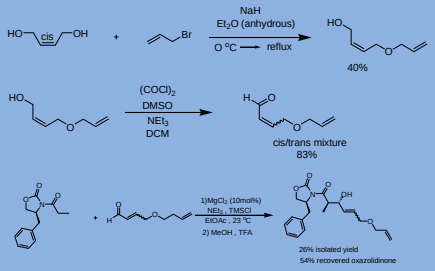
Proposed Research



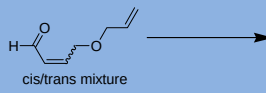
Progress Up To This Point



Progress Up To This Point



Setbacks and Solutions – Purification of the Aldehyde

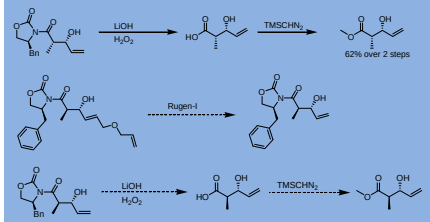


cis/trans mixture

make only trans isomer

- Unwanted isomerization occurred during Swern Oxidation
- Begin synthesis with pure trans diol
- Separate the cis/trans mixture on MPLC
- Design different tethers to cleave off by ring closing metathesis

Obtaining Syn and Anti Products



Conclusions

Progress has been made towards the synthesis of an acrolein equivalent Evans anti-aldol substrate
With this methodology, terminal alkenes with an alcohol functionality will be made enantiopure and used in further studies regarding enyne metathesis reactivity

Acknowledgements

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