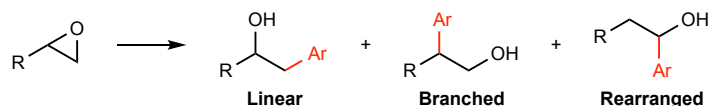
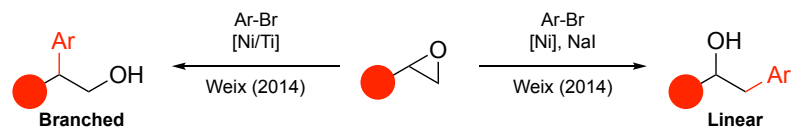


Background

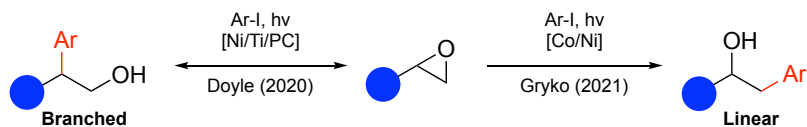
- Although the opening of epoxides with heteroatom and carbon nucleophiles is well-studied, epoxide opening with aryl nucleophiles typically has poor regioselectivity and affords a mixture of products.



- Epoxides have rarely been used in traditional cross-coupling reactions.
- Recent advances in nickel-catalyzed cross-electrophile coupling offer regioselective epoxide opening with aryl halides.

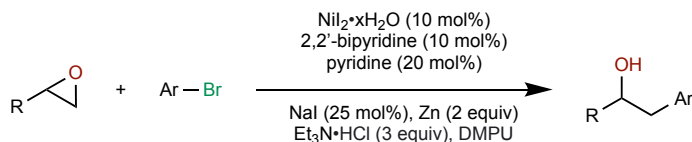


● = alkyl epoxides ● = aryl epoxides

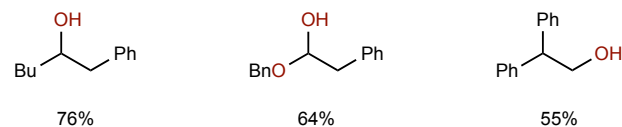


Weix (2014) – Regiodivergent Epoxide Opening

Formation of Linear Products with Nickel/Iodide Catalysis:

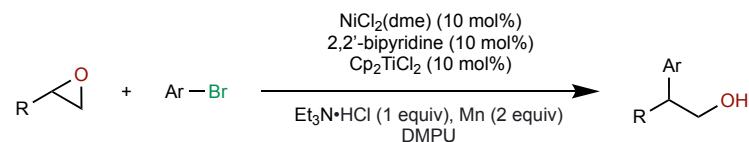


Selected Scope:

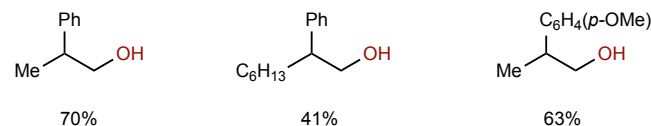


Aryl epoxides react predominately at the benzylic position regardless of the conditions employed!

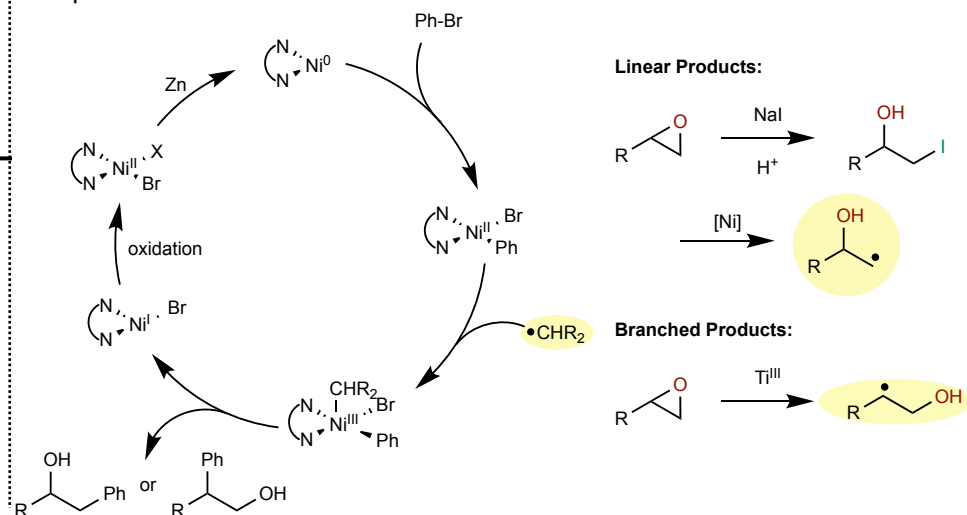
Formation of Branched Products with Ni/Ti Catalysis:



Selected Scope:

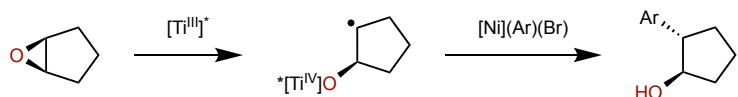


Proposed Mechanism:

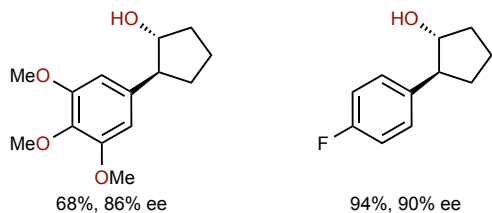
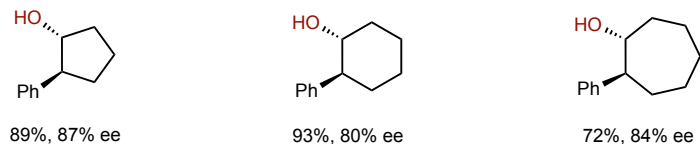
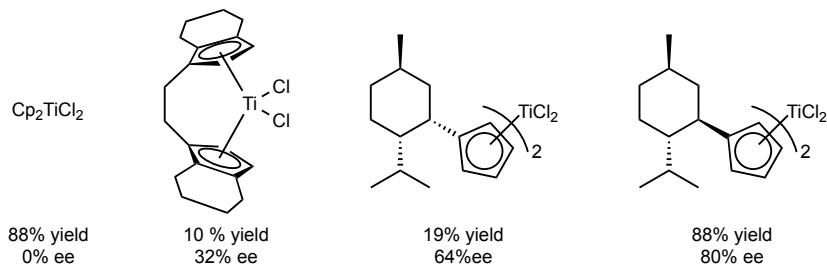
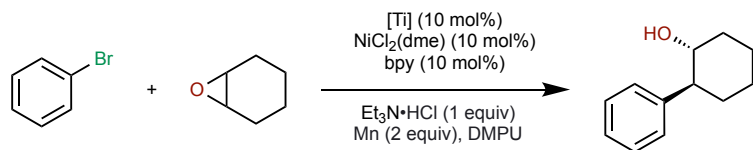


Weix (2015) – Enantioselective Arylation of *meso*-Epoxides

General Strategy:

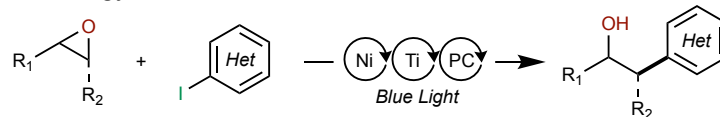


Chiral Titanium Catalysts:

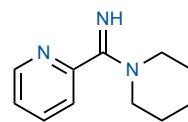


Doyle (2020) – Ni/Ti/Photoredox Catalysis

General Strategy:

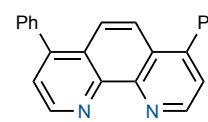


Styrene Oxides



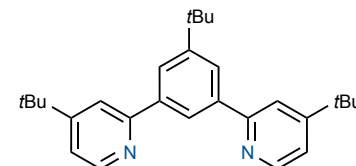
Ligand = Piperidyl amidine

Cyclic Epoxides



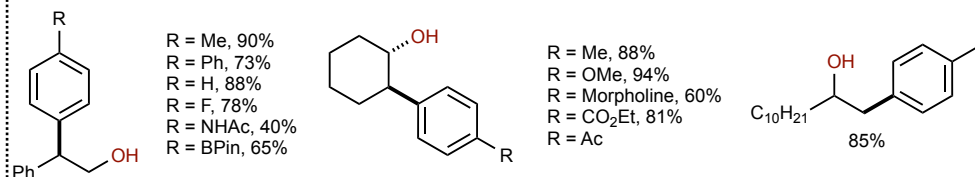
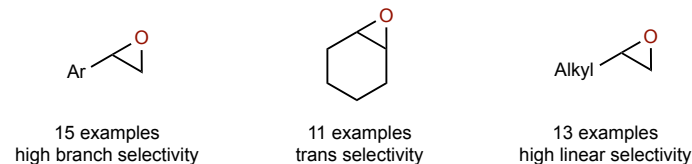
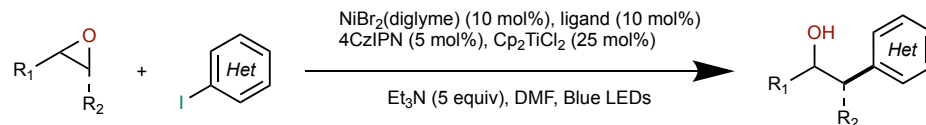
Ligand = BPhen

Aliphatic Epoxides

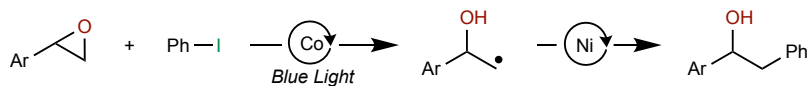


Ligand = tBu-terpy

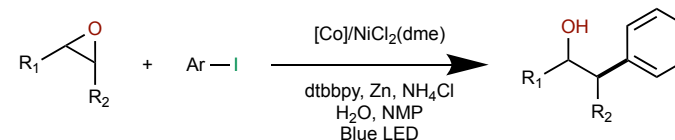
Different ligands afford high regioselectivity across distinct classes of epoxides, including styrene oxides!



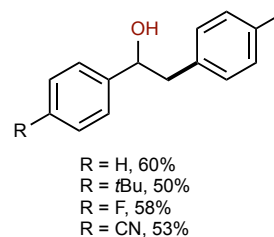
Gryko (2021) – Regioselective Aryl Epoxide Opening to Linear Products



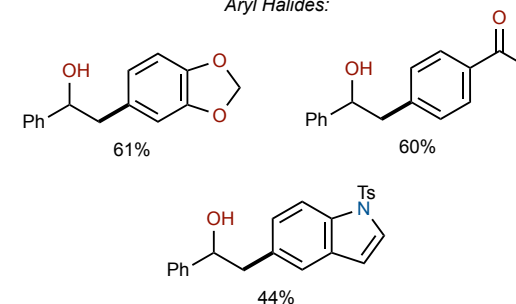
Selected Scope:



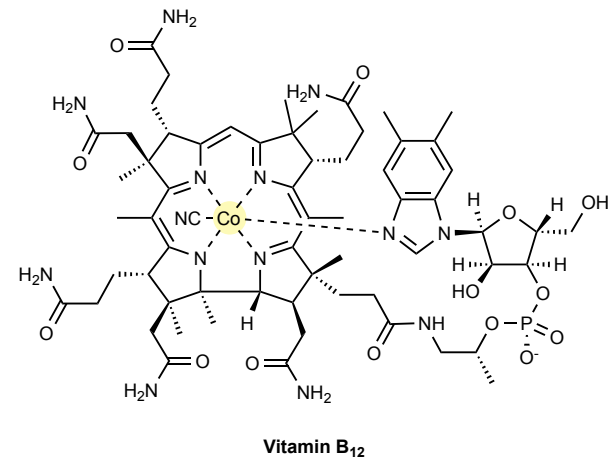
Aryl Epoxides:



Aryl Halides:

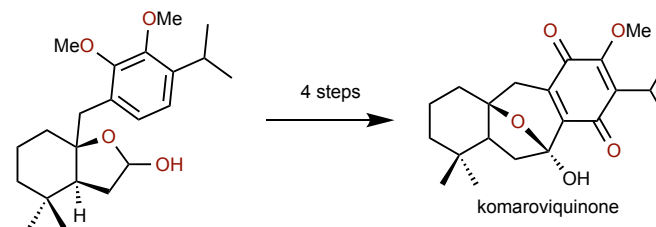
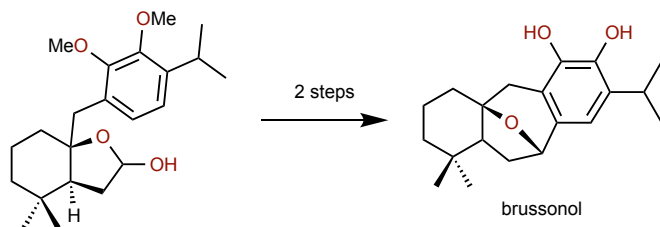
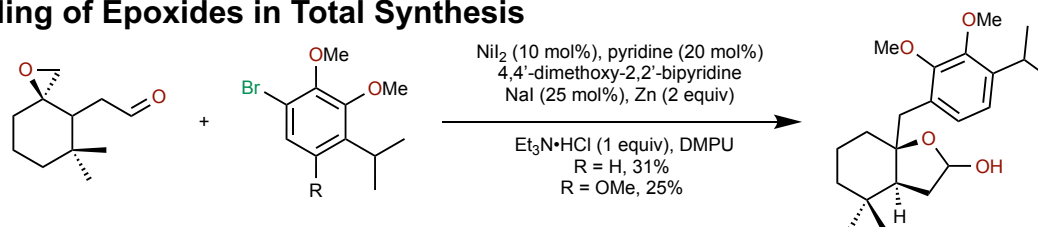


Potrząsaj, A. J. Am. Chem. Soc. 2021, 143 (25), 9368–9376. <https://doi.org/10.1021/jacs.1c00659>



The bulky vitamin B₁₂ catalyst can only attack an epoxide from the less sterically hindered side leading to linear products!

Cross-Electrophile Coupling of Epoxides in Total Synthesis



Ahmad, A. Org. Lett. 2019, 21 (15), 6079–6083. <https://doi.org/10.1021/acs.orglett.9b02221>