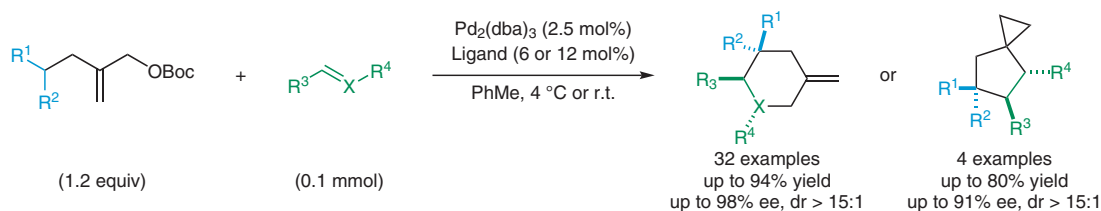
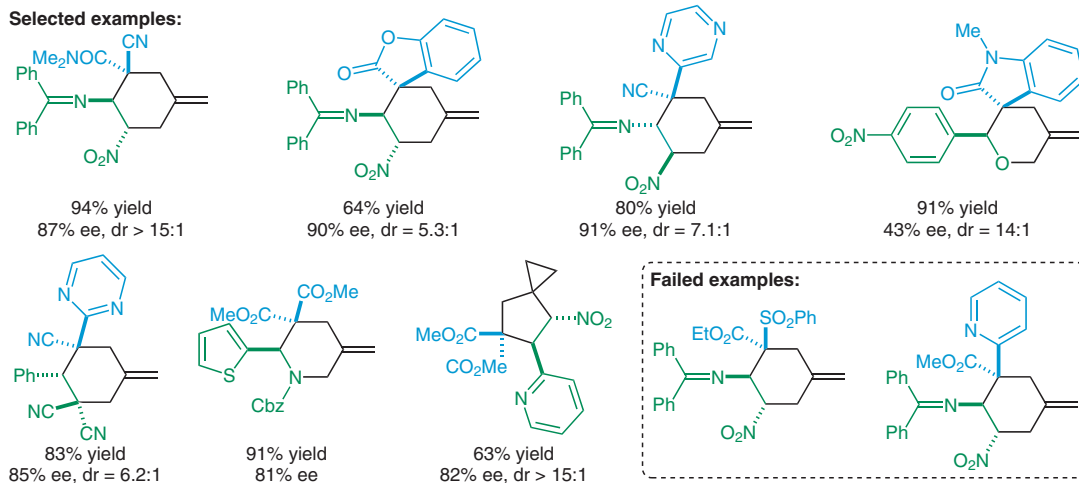


B. M. TROST*, Z. JIAO, Y. LIU, C. MIN, C.-I. J. HUNG (STANFORD UNIVERSITY, USA)
Palladium-Catalyzed Enantioselective Cycloadditions of Aliphatic 1,4-Dipoles: Access to Chiral Cyclohexanes and Spiro[2.4]heptanes
J. Am. Chem. Soc. **2020**, *142*, 18628–18636, DOI: 10.1021/jacs.0c08348.

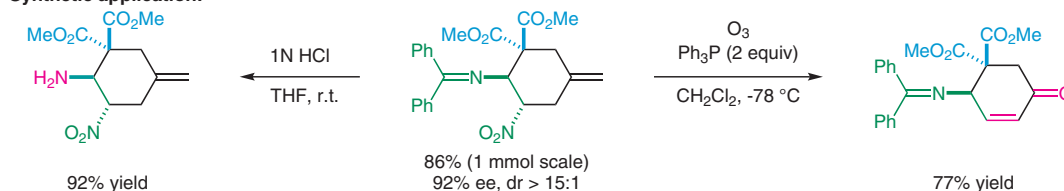
Enantioselective Pd-Catalyzed Trimethylenemethane Cycloadditions of All-Carbon 1,4-Dipoles



Selected examples:



Synthetic application:



Significance: Trost and co-workers report the asymmetric syntheses of all-carbon chiral cyclohexanes and spiro[2.4]heptanes using palladium-catalyzed cycloadditions of aliphatic 1,4-dipoles. Using various phosphoramidite and diamidophosphite ligands, several biologically relevant scaffolds were generated in good regio-, diastereo- and enantioselectivity. The synthetic utility was demonstrated through gram-scale syntheses of each scaffold, and derivatizations included the ozonolysis and hydrolysis reactions shown.

Comment: Upon scale up, the palladium and ligand loading could be decreased to 2 and 4 mol%, respectively, and the cyclohexane products were formed with higher regioselectivity than the spirocycles. Interestingly, a resonance effect between the pyridine nitrogen and palladium cation center was found to be necessary for the examples with heterocyclic arenes as the second electron-withdrawing group.

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