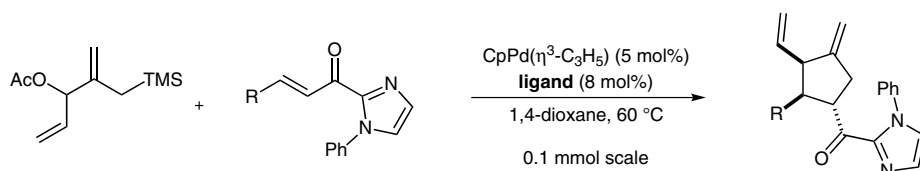


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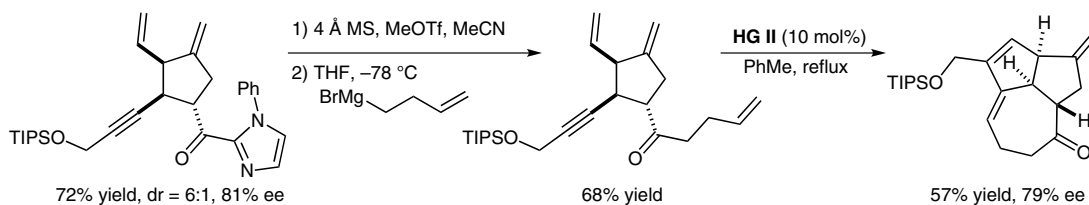
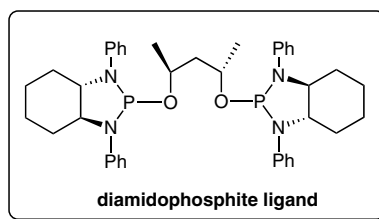
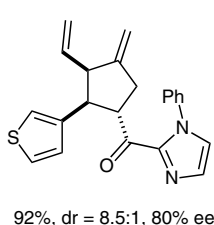
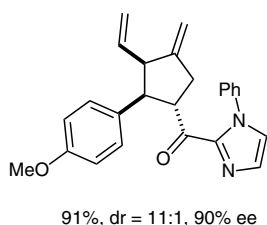
Development of Diamidophosphite Ligands and Their Application to the Palladium-Catalyzed Vinyl-Substituted Trimethylenemethane Asymmetric [3+2] Cycloaddition
J. Am. Chem. Soc. **2012**, *134*, 11319–11321.

Palladium-Catalyzed Vinyl-Substituted Trimethylenemethane Cycloaddition



14 examples
up to 97% yield
up to 11.3:1 dr
up to 90% ee

Selected examples:



Significance: The asymmetric [3+2] cycloaddition of trimethylenemethane (TMM) is a challenging reaction, particularly with substituents on the donor. Only one previous case with a cyano-TMM donor has been reported, while other substituents caused a loss of reactivity and selectivity (*J. Am. Chem. Soc.* **2007**, *129*, 12396). The authors describe the development of a new diamidophosphite ligand that enables the palladium-catalyzed [3+2] cycloaddition of vinyl-substituted trimethylenemethane (TMM) donors with acyl imidazoles to generate tetrasubstituted cyclopentanes bearing three contiguous stereocenters in high yields with good diastereo- and enantioselectivity.

Comment: Chiral phosphoramidite ligands had previously been developed to allow the asymmetric variant of palladium-catalyzed trimethylmethane [3+2] reactions (B. M. Trost et al. *J. Am. Chem. Soc.* **2006**, *128*, 13328). Now, by replacing an oxygen atom on the ligand with nitrogen to form diamidophosphites, the nucleophilicity of the palladium-TMM complex is increased, which broadens the donor scope of this transformation. The authors demonstrate increased reactivity by the use of vinyl-substituted TMM donors to generate tetrasubstituted cyclopentanes, which can be further manipulated using the Hoveyda-Grubbs II catalyst to form fused tricyclic ring systems (see above).

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