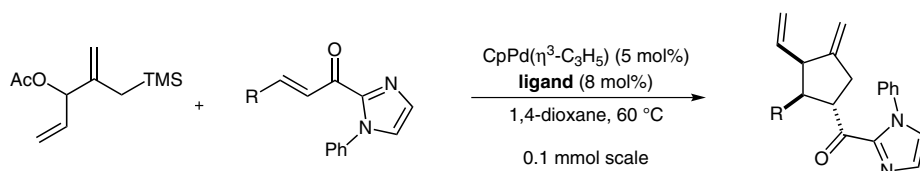


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Development of Diamidophosphite Ligands and Their Application to the Palladium-Catalyzed Vinyl-Substituted Trimethylenemethane Asymmetric [3+2] Cycloaddition

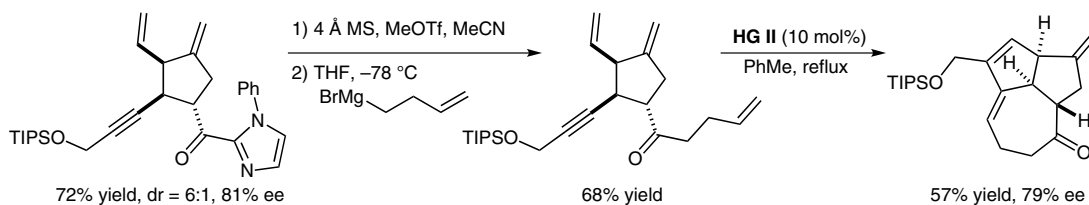
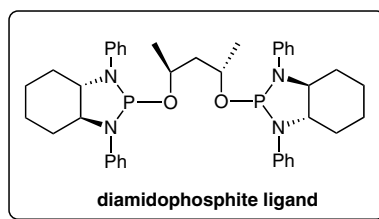
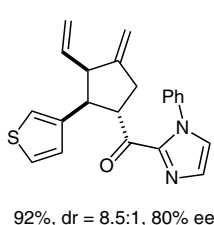
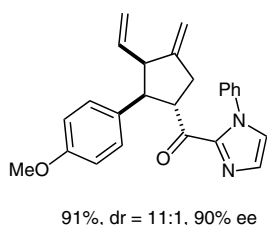
J. Am. Chem. Soc. **2012**, *134*, 11319–11321.

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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