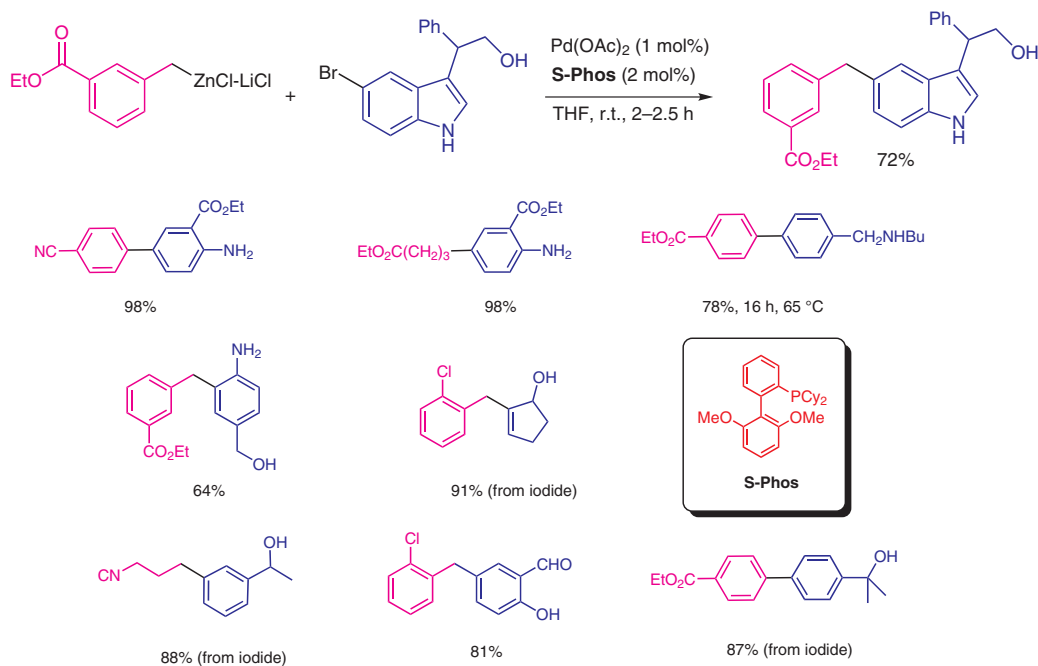


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Negishi Cross-Couplings of Unsaturated Halides Bearing Relatively Acidic Hydrogen Atoms with Organozinc Reagents
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Negishi Cross-Couplings of Unprotected Phenols, Anilines, and Alcohols



Significance: The Pd-catalyzed cross-coupling reactions are now among the most widely used synthetic methods in organic chemistry. Organozinc reagents are in general more reactive than the corresponding boron compounds, and at the same time are seemingly incompatible with acidic protons in the reaction mixture. A careful choice of the catalyst and reaction conditions allowed performing the cross-coupling of unprotected phenols, alcohols and anilines that greatly broadened the scope of substrates, suitable for the Negishi cross-coupling reaction.

Comment: The study of the relative rates of the protonation of aryl-, alkyl- and benzylzinc compounds by *i*-PrOH revealed the following sequence: PhZnI > OctZnBr > PhCH₂ZnBr. However, in the presence of Pd(II)-S-Phos system, the cross-coupling is faster for all of them than the protonation even by a phenol. Addition of the organozinc reagent via a syringe pump is crucial for obtaining high yields. All zinc reagents were prepared directly from the corresponding halides by the insertion of zinc metal in the presence of LiCl (A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel *Angew. Chem. Int. Ed.* **2006**, *45*, 6040).

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