Synthesis of Stereodefined Unsaturated Acyclic Fragments

Precursor synthesis:

1. R₁MgBr (1.2 equiv), Cul (20 mol%), Et₂O, –35 °C
2. ZnBr₂ (1.5 equiv, 1 M in THF), –50 to –20 °C
3. reagent (1.2–3.0 equiv), [Pd(PPh₃)₄] (5 mol%), THF or DMF, 45–75 °C
4. LiAlH₄ or DIBAL (2.5 equiv)

Oxidative palladium-catalyzed Heck coupling:

Selected examples:

78% yield from (Z) olefin
dr > 95:5

70% yield from (Z) olefin
dr > 95:5

51% yield from (E) olefin
dr > 95:5 (acyclic stereocenters)

40% yield from (E) olefin
dr > 95:5

54% yield from (Z) olefin
dr = 86:14:0:0

Significance: Marek and co-workers report a highly stereodivergent route to unsaturated acyclic fragments in good to excellent yields. The key step for this transformation is the oxidative palladium-catalyzed Heck coupling of aryl boronic acids with alkynylcyclopropyl carbinols.

Comment: Remarkably, by using this method, all four stereoisomers of similar scaffolds can be synthesized. Furthermore, in addition to various arylboronic acids, alkenyl triflates or heteroarylboronic acids can be employed in the Heck reaction.