Stereoselective Synthesis of All-Carbon Tetrasubstituted Alkenes from In Situ Generated Ketenes and Organometallic Reagents


**Significance:** The stereoselective synthesis of various all-carbon tetrasubstituted alkenes is disclosed, employing a two-step protocol which includes the stereoselective generation of an alkenyl pseudohalide followed by stereospecific palladium-catalyzed cross-coupling. The appropriate tetrasubstituted alkenes are obtained in good yield and with good diastereomeric ratios, providing mainly the Z-isomers.

**Comment:** The reaction is proposed to proceed via a ketene intermediate which is stereospecifically attacked by a lithium organyl to form the trisubstituted enolate moiety attached to a pseudohalide group [OTf or OP(O)(OR)₂]. This moiety may be converted into other functional groups by palladium-catalyzed cross-couplings to give the corresponding all-carbon tetrasubstituted alkenes.

**Selected examples:**

- G = Tf or P(O)(OR)₂ (R = Et, Ph)
- M = MgBr [G = P(O)(OR)₂]; 9-BBN, B(OH)₂, H (G = Tf)
- [Pd] = Pd(dpba)₂ [G = P(O)(OR)₂]; Pd(OAc)₂, PdCl₂(PPh)₃ (G = Tf)
- X = XPhos [G = P(O)(OR)₂]; SPhos, Cul (G = Tf)
- R₁ = Ph, 4-MeOC₆H₄, 2-MeC₆H₄, 3-thienyl, i-Pr, t-Bu
- R₂ = Et, Me, Bn, i-Pr
- R₃ = n-Bu, Ph, C(Me)=CH₂, 2-furanyl
- R₄ = Ph, Tol, Me, Bn, n-Hex, ethynylphenyl

- 66% yield
  - Z/E > 20:1
  - G = P(O)(OR)₂

- 56% yield
  - Z/E > 20:1
  - G = P(O)(OR)₂

- 84% yield
  - Z/E > 20:1
  - G = Tf

- 48% yield
  - Z/E > 20:1
  - G = Tf

- 52% yield
  - Z/E = 19:1
  - G = P(O)(OR)₂

- 52% yield
  - Z/E = 19:1
  - G = P(O)(OR)₂

- 89% yield
  - Z/E > 20:1
  - G = Tf

- 90% yield
  - Z/E > 20:1
  - G = Tf