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Stereoselective Synthesis of (E)-(Trisubstituted Alkenyl)borinic Esters: Stereochemistry Reversed by Ligand in the Palladium-Catalyzed Reaction of Alkynylborates with Aryl Halides


Synthesis of (E)- and (Z)-Tamoxifen

Significance: (Z)-Tamoxifen is used for the treatment of estrogen receptor positive breast cancer. The synthesis depicted features a syn-carbopalladation of alkynyl borate B followed by a 1,2-aryl migration (C → D) to generate a trisubstituted alkenylborane in high yield and stereoselectivity. Oxidation of the alkenylborane D with Me3NO afforded the alkenylborinic ester E that participated in an efficient Suzuki–Miyaura coupling to give (Z)-tamoxifen.

Comment: The fate of the syn-carbopalladation product C depended on the ligand. When the ligand was small [(2-Tol)3P], a 1,3-aryl migration took place (C → G) to generate the alkenylborane H after reductive elimination. Alkenylborane H was converted into (E)-tamoxifen as shown. The bo- rate derived from B is stable towards air and moisture. A further 14 examples of the synthesis of alkenylborinic esters via the 1,2-aryl migration pathway are presented.