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Category
Synthesis of Natural Products and Potential Drugs

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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 alkenyborane in high yield and stereoselectivity. Oxidation of the alkenyborane D with Me₃NO afforded the alkenyborinic 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 alkenyborane H after reductive elimination. Alkenyborane H was converted into (E)-tamoxifen as shown. The bo­rate derived from B is stable towards air and moisture. A further 14 examples of the synthesis of alkenyborinic esters via the 1,2-aryl migration pathway are presented.

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