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Copper-Catalyzed Carboarylation of Alkynes via Vinyl Cations
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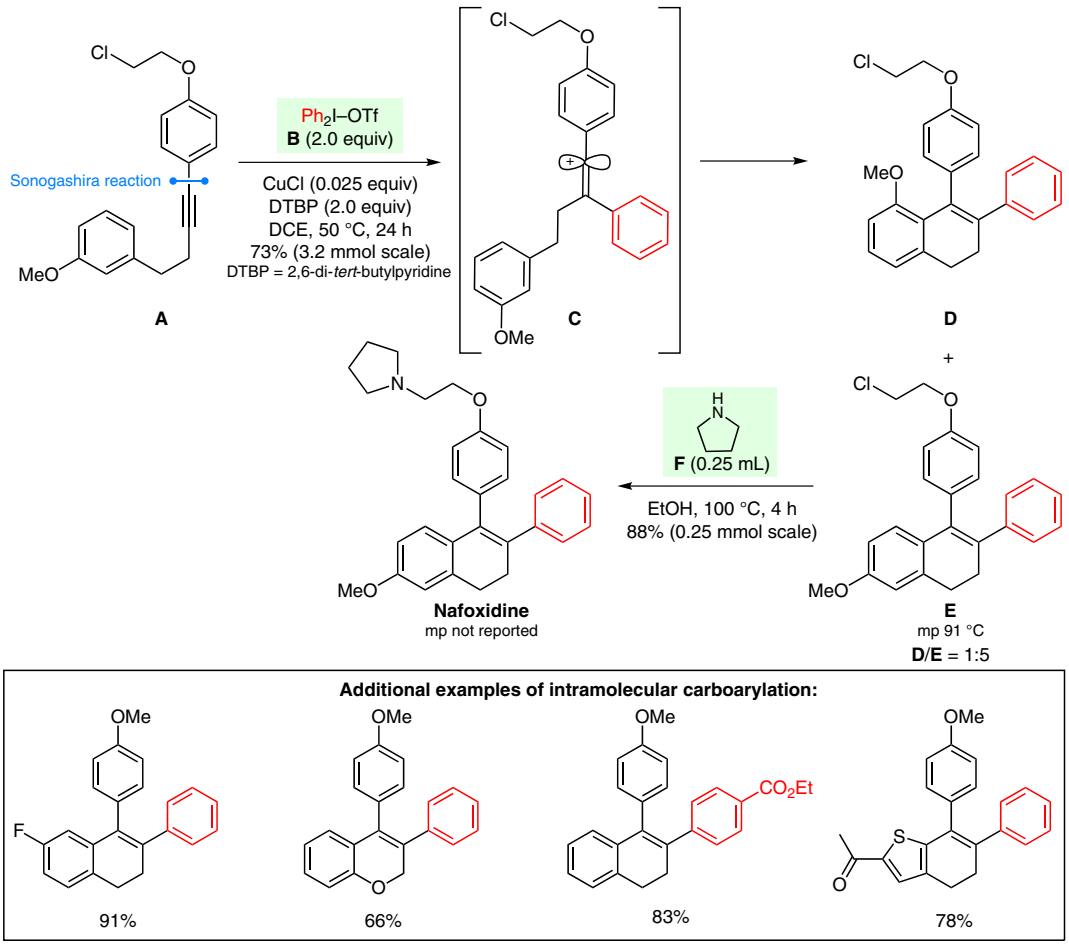
Synthesis of Nafoxidine via Copper-Catalyzed Carboarylation



Significance: Nafoxidine is a nonsteroidal antiestrogenic agent. The synthesis depicted features a copper-catalyzed alkyne carboarylation initiated through activation of diphenyliodonium triflate (**B**). The resultant catalytically generated aromatic electrophile equivalent reacts with the electron-rich alkyne **A** to form a stabilized trisubstituted vinyl cation type intermediate **C** that then undergoes a regioselective intramolecular Friedel–Crafts reaction to afford the dihydronaphthalene **E** preferentially.

Comment: The scope of the carboarylation was explored via 31 examples, 28 of which were successful. The electronic requirements for the substituent on the alkyne were more rigid: It is essential to have a group capable of stabilizing the vinyl cation. Unsymmetrical analogues of the iodonium triflate **B** bearing a substituted arene and a mesityl group transferred the arene selectively. One example of an intermolecular carboarylation is described.

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