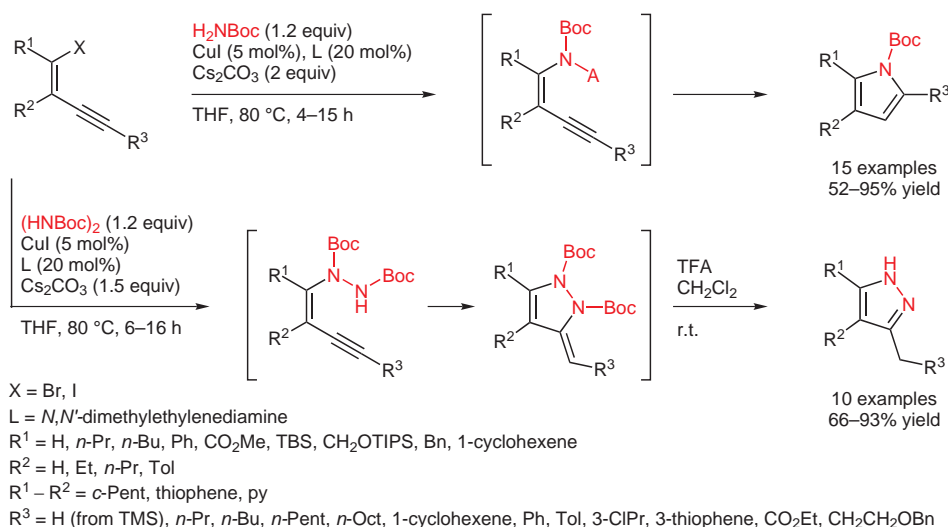


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Domino Cu-Catalyzed C–N Coupling/Hydroamination: A Highly Efficient Synthesis of Nitrogen Heterocycles
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Pyrroles and Pyrazoles by a C–N Coupling–Hydroamination Sequence



Significance: Reported is an elegant Cu-catalyzed amidation/hydroamidation of haloalkynes with *tert*-butyl carbamate or bis(Boc)hydrazine affording, after TFA-induced deprotection/tautomerization, highly substituted pyrroles and pyrazoles in good to excellent yields. *N,N'*-Dimethylethylenediamine (20 mol%) was found to be the most effective ligand for the conversion. Intermediary amidation products were isolated, thus validating the proposed sequence of C–N coupling followed by hydroamidation.

Comment: Are copper salts on the verge of a renaissance? Recently, long after the Ullmann reaction, Cu-catalyzed processes have become increasingly competitive with popular Pd catalysis for C–C, C–heteroatom (N, O, P, S, Se) to C–H and C–metal bond forming reactions (see first review below). The current method efficiently extends Cu catalysis by amalgamating well-developed C–N coupling (see second review below) with recent amidation chemistry (L. Ackermann *Org. Lett.* **2005**, *7*, 439–442). The scope of this reaction offers highly functionalized disubstituted and trisubstituted pyrroles and pyrazoles bearing alkene, ester, silyl ether, and alkyl halide handles for further potential synthetic manipulation.

Reviews: I. P. Beletskaya, A. V. Cheprakov *Coord. Chem. Rev.* **2004**, *248*, 2337–2364; L. Jiang, S. L. Buchwald In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; F. Diederich, A. de Meijere, Eds.; Wiley-VCH: Weinheim, **2004**, 699–760.

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Category

Synthesis of Heterocycles

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SYNFACT
of the month