

$C_{18}H_{25}IO_2Si$  Triisopropylsilyl ethynyl benzoiodoxolone (TIPS-EBX) (MW 428.38)

(reagent used as electrophilic source of TIPS-protected acetylene)

*Physical data:* mp (Dec.) 170-176°C.

*Solubility:* sol. chlorinated solvents, alcohols, DMF, DMSO; moderately sol. ethers, acetonitrile; not sol. toluene, hexane.

*Form supplied in:* colorless crystals, available with Sigma-Aldrich (cat. N. 728365).

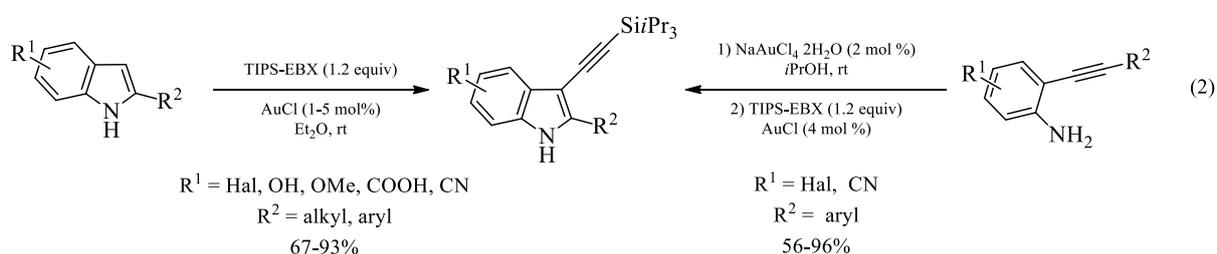
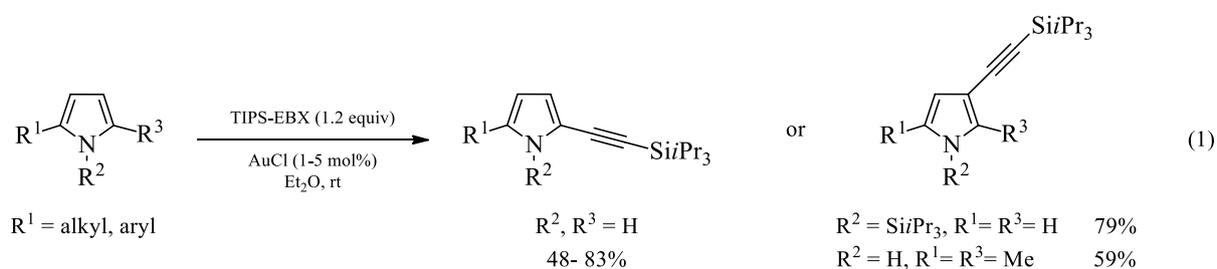
*Handling, Storage, and Precautions:* the reagent is stable to air, moisture and light. Possible decomposition on prolonged exposure to light and high temperature. Long time storage preferentially requires protection from light and refrigeration. Specific toxicity not reported up to date. Incompatibility with hard nucleophiles and reducing agents.

*Preparation and purification:*<sup>1</sup> upon oxidation of 2-iodobenzoic acid with sodium periodate to afford 2-iodosyl benzoic acid, the latter is activated by treatment with freshly distilled trimethyl silyl triflate and reacted *in-situ* reaction with (trimethylsilyl)(triisopropylsilyl)acetylene. TIPS-EBX prepared in this way can be efficiently purified by recrystallization from acetonitrile and readily used at room temperature.

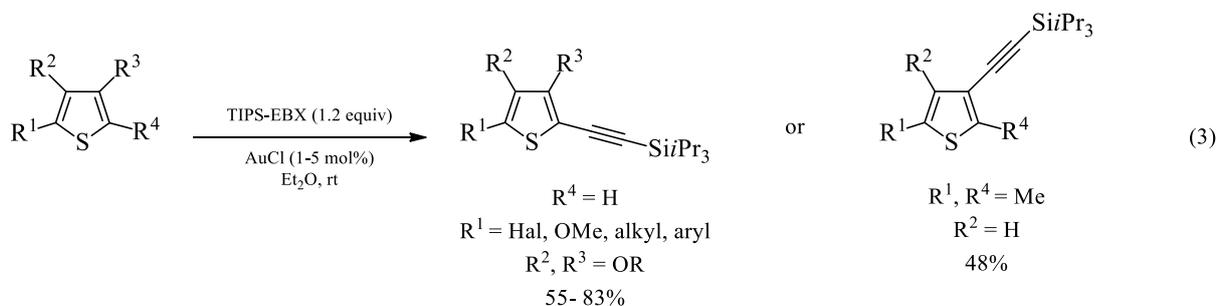
### **Au-Catalyzed Alkynylation of Heterocycles and Anilines.**

$S_{EAr}$ -like regioselective alkynylation of *N*- and *S*-heteroaromatic compounds is accomplished with TIPS-EBX as the alkynylating agent under Au(I)-catalysis. Free pyrroles are alkynylated selectively at 2-position. 3-alkynylation occurs in the presence of a bulky substituent on the heteroatom.<sup>2</sup> Good to excellent yields are reported using catalytic amounts of AuCl under mild conditions (room temperature, under air, technical  $Et_2O$ ) (eq 1). Under the same conditions, indoles are alkynylated in high yields (eq 2).<sup>2</sup> The reaction exhibits broad

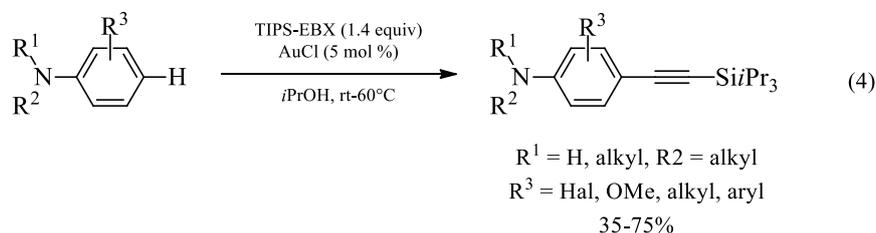
functional-group tolerance and regioselectivity in favor of 3-position. Importantly, the indole substrates can be generated in situ by Au(III)-catalyzed cyclization of 2-alkynyl anilines, prior to the addition of AuCl and TIPS-EBX.<sup>3</sup>



The direct alkyynylation of thiophenes is also efficiently performed using TIPS-EBX under cooperative activation with Au(I)/Brønsted acids (eq 3).<sup>4</sup> The reaction occurs in the presence of trifluoroacetic acid as an additive and affords highly selectively the 2-alkynylated heterocycle. Also in this case, reactivity is reported under very mild conditions (room temperature, under air, technical acetonitrile). Yields are good to excellent with a broad range of substituted thiophenes, although with less electron rich thiophenes higher catalytic loading and higher concentrations are required.

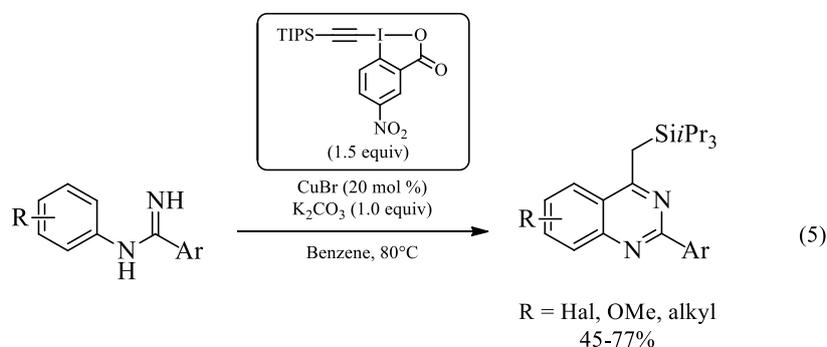


Finally, the *para*-alkynylation of anilines is also reported with TIPS-EBX in the presence of catalytic AuCl (eq 4).<sup>5</sup>



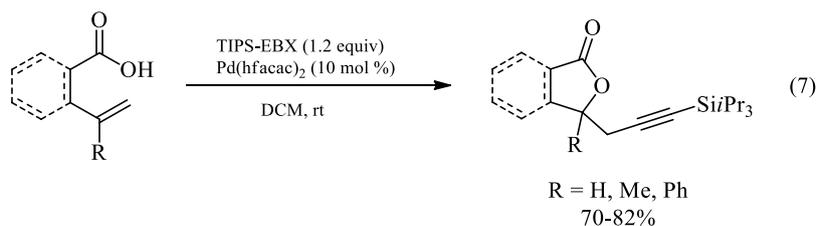
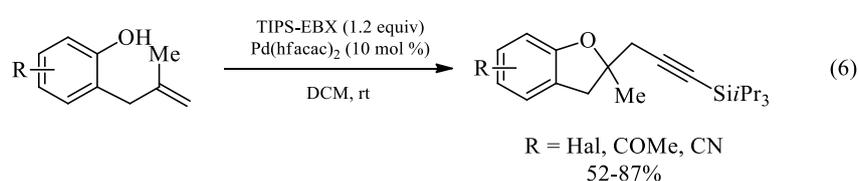
### Cu-Catalyzed Alkynylation of *N*-Arylbenzamidines: Synthesis of Quinazolines.

Quinazolines can be directly accessed from aniline-derived benzamidines by reaction of the latter with nitro-substituted TIPS-EBX under Cu-catalysis (eq 5).<sup>6</sup> The amidine group possibly acts as a directing group for the C-H alkynylation and can then undergo Cu-mediated nucleophilic attack onto the newly installed acetylene group. Alternatively, initial *N*-alkynylation can be followed by tautomerization and electrocyclization to afford the quinazoline product. The TIPS group of the alkynylating reagent proves crucial in order to observe the formation of the product; the presence of the nitro group on the aromatic moiety of TIPS-EBX served to increase the yield. The reaction is quite general with respect of substitution on the benzamidine and differently substituted quinazolines are obtained in moderate to very good yields.

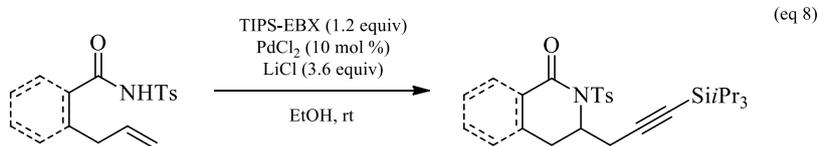
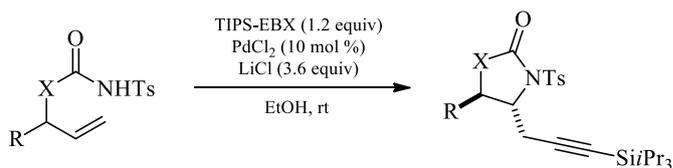


### Intramolecular Pd-catalyzed Oxy- and Aminoalkynylation of Olefins.

TIPS-EBX serves as electrophilic alkynylating reagent in the Pd-catalyzed oxy- and aminoalkynylation of non-activated alkenes. The oxyalkynylation reaction works efficiently with *o*-allyl phenols (eq 6) and both aromatic and aliphatic carboxylic acids (eq 7) to afford, respectively, propargyl benzofurans and  $\gamma$ -lactons.<sup>7</sup> Good to excellent yields are obtained with the two classes of compounds, under operator-friendly conditions (room temperature, technical dichloromethane, under air). The use of the electron-deficient Pd(hfacac)<sub>2</sub> complex as the catalyst proves essential for the successful outcome of the reaction.



In the case of the aminoalkynylation reaction, tosyl *N*-protected pentenamides and hexenamides are the substrates of choice (eq 8).<sup>8</sup> The reaction provides delivers propargyl  $\gamma$ - and  $\delta$ -lactams in high yields. In this case, the catalytic system involves PdCl<sub>2</sub> in the presence of an excess of LiCl (possibly to form Li[PdCl<sub>4</sub>], which showed similar catalytic activity when synthesized independently). Importantly, the presence of a further heteroatom in the newly formed heterocycle was well tolerated, allowing access to propargylic oxazolidinones and imidazolidinones starting from the corresponding *N*-tosyl carbamates and ureas.



X = CH<sub>2</sub>, O, NR'  
R = alkyl, aryl  
50-89%

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