Pd-Catalyzed Synthesis of Indeno[1,2-c]-chromenes from 2-Alkynylhalobenzenes

**Significance:** Reported is the synthesis of indeno[1,2-c]-chromenes 3 and 4 via a palladium-catalyzed reaction of 2-alkynylbromobenzenes 1 with either 2-(2-arylethynyl)phenols 2 or with water. A range of ligands was used during the optimization study to reveal that the reaction proceeds only with Cy3P as ligand (eq. 1). Sodium methoxide in toluene or 1,4-dioxane was better than other combinations. The substrate scope of this transformation was modestly demonstrated. The reaction also proceeded to give 3 in 78% yield by treatment of 1-chloro-2-(2-phenylethynyl)benzene 1 with 2 (R2 = H, R4 = Ph). Surprisingly, re-optimization was required in the reaction of 1 with water (eq. 2). Both alkyl- and aryl-substituted alkynes were tolerated under the optimized conditions. However, the reaction parameters had to be re-screened to give a satisfactory yield of compounds with electron-withdrawing groups (R2 = 4-CIC6H4, 4-AcC6H4).

**Comment:** The [6.5.6.6]-tetracyclic core of indeno[1,2-c]-chromenes 3 and 4 is present in several bioactive compounds (B. S. Min et al. *Bioorg. Med. Chem. Lett.* 2012, 22, 7436). Very few synthetic methods such as iron-mediated [3+2]-annulation reactions are available to provide access to this tetracyclic system (Z.-Q. Wang et al. *Org. Lett.* 2011, 13, 14). The present method provides a rapid construction of various substituted indeno-chromenes from easily accessible starting materials. One drawback of this method is the lower yield for electron-poor substrates. Although, this work provides a facile synthesis of indeno[1,2-c]-chromenes, it is strikingly similar to the authors’ previous work (Y. Luo, L. Hong, J. Wu *Chem. Commun.* 2011, 47, 5298).

**Conditions A**

Pd(OAc)2 (5 mol%)  
Cy3P (10 mol%)  
NaOMe (4.0 equiv)  
1,4-dioxane, reflux

**Conditions B**

Pd(OAc)2 (5 mol%)  
XPhos (10 mol%)  
KOH (2.0 equiv)  
1,4-dioxane, 90 °C

**Conditions C**

Pd(OAc)2 (5 mol%)  
ligand (10 mol%)  
Ht-BuONa (2.0 equiv)  
1,4-dioxane, 90 °C

19 examples  
63–96% yield

8 examples  
58–95% yield  
R2 = 4-CIC6H4 (trace)  
R2 = 4-ClC6H4 (56% yield)  
R2 = 4-AcC6H4 (25% yield)

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