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Facile Assembly of Indeno[1,2-c]chromenes via a Palladium-Catalyzed Reaction of 2-Alkynylhalobenzene


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 with 2 ($R^2 = H$, $R^4 = Ph$). 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 ($R^2 = 4-ClC_6H_4$, 4-AcC_6H_4).

**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 indenochromenes 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 L5 (10 mol%) 
$H$-BuONa (2.0 equiv) 
1,4-dioxane, 90 °C

**R1** = H, Me, Cl
**R2** = Ph, $n$-Bu, Tol, PMP, 4-ClC$_6$H$_4$, $c$-Pr
**R3** = H, Me, Cl
**R4** = Ph, Tol, PMP, 4-ClC$_6$H$_4$

8 examples

**Conditions B**
58–95% yield

**Conditions C**
R$^2 = 4$-ClC$_6$H$_4$ (58% yield)
R$^2 = 4$-AcC$_6$H$_4$ (25% yield)