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 (R3 = 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-ClC6H4, 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. Very few synthetic methods such as iron-mediated [3+2]-annulation reactions are available to provide access to this tetracyclic system. 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.

**19 examples**

| R1 = H, Me, Cl | R2 = Ph, n-Bu, Tol, PMP, 4-ClC6H4, c-Pr |
| R2 = H, Me, Cl | R3 = H, Me, Cl |
| R3 = H, Me, Cl | R4 = Ph, Tol, PMP, 4-ClC6H4 |

**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%)
- t-BuONa (2.0 equiv) 1,4-dioxane, 90 °C

**R1**

- H, Me, Cl

**R2**

- Ph, n-Bu, Tol, PMP, 4-ClC6H4, c-Pr

**R3**

- H, Me, Cl

**R4**

- Ph, Tol, PMP, 4-ClC6H4

**Conditions A**

- 19 examples
- 63–96% yield

**Conditions B**

- 8 examples
- 58–95% yield

**Conditions C**

- R2 = 4-ClC6H4 (trace)
- R2 = 4-AcC6H4 (58% yield)
- R2 = 4-AcC6H4 (25% yield)