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

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\begin{align*}
\text{ Conditions A} & \quad \text{Pd(OAc)}_2 (5 \text{ mol%}) \quad \text{Cy3P} (10 \text{ mol%}) \\
& \quad \text{NaOMe (4.0 equiv)} \quad 1,4\text{-dioxane, reflux}
\end{align*}
\]

\[
\begin{align*}
\text{ eq. 1} & \\
\text{ 19 examples} & \quad 63-96\% \text{ yield}
\end{align*}
\]

\[
\begin{align*}
\text{ Conditions B} & \quad \text{Pd(OAc)}_2 (5 \text{ mol%}) \quad \text{XPhos} (10 \text{ mol%}) \\
& \quad \text{KOH (2.0 equiv)} \quad 1,4\text{-dioxane, 90 °C}
\end{align*}
\]

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\begin{align*}
\text{ eq. 2} & \\
\text{ 8 examples} & \quad 58-95\% \text{ yield}
\end{align*}
\]

**Significance:** Reported is the synthesis of indeno[1,2-c]chromenes 3 and 4 via a palladium-catalyzed reaction of alkynylhalobenzenes 1 with either 2-(2-phenylethynyl)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 (R1 = H, R2 = 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-CIC6H42, 4-AcC6H42).

**Comment:** The [6,5,6,6]-tetracyclic core of indenochromenes 3 and 4 is present in several biologically active 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).

**Synfacts Contributors:** Victor Snieckus, Suneel P. Singh

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