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Palladium-Catalyzed Tandem Reaction of o-Aminophenols, Bromoalkynes and Isocyanides to Give 4-Amine-benzo[b][1,4]oxazepines


Palladium-Catalyzed Synthesis of Benzo[b][1,4]oxazepines

Significance: Reported is the palladium-catalyzed synthesis of benzo[b][1,4]oxazepines 4 via the annulation of o-aminophenols 1 with bromoalkynes 2 and isocyanides 3. Substrate-scope investigation revealed broad tolerance to variation of all components 1–3, particularly across sterically and electronically differentiated aryl bromoalkynes 2, with a reduction in yield noted for alkyl bromoalkynes (4o). Experiments demonstrating the competency of 5 under the standard reaction conditions are offered in support of the proposed mechanism.

Comment: Building on their previous investigations into combining the nucleophilic addition of isocyanides 3 to bromoalkynes 2 with palladium catalysis (Chem. Commun. 2012, 48, 3545), the current report extends this methodology allowing the synthesis of benzoazepines traditionally synthesized by multiple-step procedures. Taking advantage of the established addition of phenols to bromoalkynes (For furan synthesis, see: S. Wang et al. Org. Lett. 2011, 13, 5968) the current report, intercepting intermediate 5, appears to have exceptional scope.

\[
\begin{align*}
\text{1} & & \text{2} & & \text{3} \\
\text{R}^1 & \text{NH}_2 & \text{Br} & \text{C}–\text{N} & \text{R}^3 \\
1 \text{equiv} & 1 \text{equiv} & 1.2 \text{equiv}
\end{align*}
\]

\[
Pd(PPh_3)_{2}Cl_2 (5 \text{ mol%}) \quad \text{Ph}_3P (10 \text{ mol%}) \quad Cs_2CO_3 (2 \text{ equiv})
\]

1,4-dioxane, 80 °C, 2 h

Substrate scope – bromoalkyne

Substrate scope – aminophenol

Substrate scope – isocyanide

Support for mechanism

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Category

Synthesis of Heterocycles

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