Nitrogen-Assisted Decarbonylative Fukuyama Coupling for Amine Synthesis

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Résumé

The Fukuyama coupling is a well-established method for the synthesis of ketones from thioesters and organozinc reagents. However, its application to the direct synthesis of amines remains limited. In 2019, Bihel and co-workers introduced POxAP as an efficient palladium precatalyst for Fukuyama cross-coupling, enabling mild and practical conditions.
Herein, we report a nitrogen-assisted decarbonylative variant that provides direct access to substituted amines from amino-thioesters. The transformation proceeds via a palladium intermediate in which the proximal nitrogen functionality promotes decarbonylation, diverting the classical pathway from ketone formation toward C–C bond formation at the amine center.

The method operates under mild conditions and exhibits broad scope, tolerating secondary, tertiary and quaternary carbon centers. More than 25 examples were obtained with moderate to excellent yields. In addition, the use of flow conditions for the preparation of organozinc reagents improves scalability and reproducibility.
This work expands the reactivity of Fukuyama-type couplings and provides a practical approach to structurally diverse amines.

Mots-Clés: Fukuyama Coupling, Decarbonylation, Flow Chemistry

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