



Palladium Ligand SabPhos

A Break-Through Solution for Coupling Reactions

HERAEUS – YOUR EXPERT FOR PRECIOUS METAL CATALYSTS

HETEROCYCLES IN CHEMISTRY

Heterocycles play a dominant role in agro chemical, fine chemical and pharmaceutical compounds. For example, 84% of FDA-approved drugs contain at least one nitrogen atom. This emphasizes the importance of reactions to form carbon–nitrogen bonds. [1, 2]

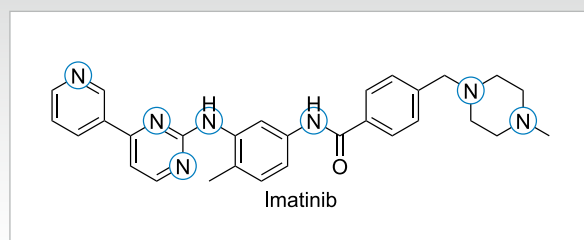


Figure 1: Exemplary nitrogen-containing heterocycles.

One well-known and prominently used reaction to form C-N bonds is the Buchwald-Hartwig reaction [3], in which a palladium catalyst helps to connect an aryl halogenide to an amine, as shown in Figure 2.

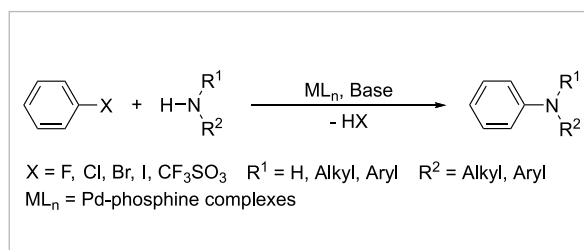


Figure 2: General example of Buchwald-Hartwig amination.

- [1] Vitaku et al., *J. Med. Chem.*, **2014**, 57, 10257–10274
[2] Q. Gu et al., *Org. Chem. Front.*, **2021**, 8, 384–414
Beller et al., *Adv. Synth. Catal.*, **2009**, 351, 3027–3043
[3] R. Dorel et al., *Angew. Chem. Int. Ed.*, **2019**, 58, 17118–17129

CHALLENGES

Unfortunately, coupling reactions with heteroaryl structures seem to only be possible under harsh conditions, which lead to decomposition and side reactions. This results in low yields and high costs.

Especially secondary amines remain challenging. [4]

Commonly used catalysts such as XPhos fail in many cases to build up C-N bonds, as shown in Figure 3.

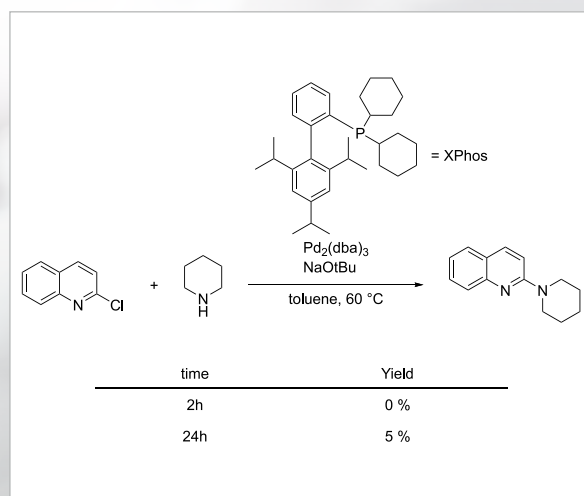


Figure 3: Cross-coupling reaction using XPhos as catalyst.

- [4] Willis et al., *Angew. Chem. Int. Ed.*, **2020**, 59, 2–26

HERAEUS' NEWLY DEVELOPED PALLADIUM-LIGAND

THE SOLUTION

The new phosphine ligand „SabPhos“, developed in collaboration by Heraeus and Prof. Trapp (LMU Munich).

The SabPhos ligand and the catalyzing palladium complex enables reactions with:

- Higher yields
- Shorter reaction times
- Moderate conditions
- Broad applicability

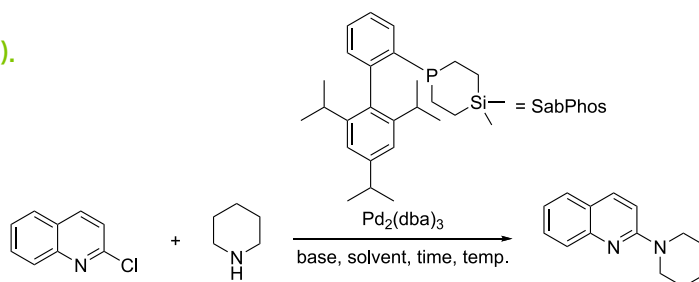


Figure 4: Cross-coupling of 2-chloro-quinoline and piperidin in presence of SabPhos.

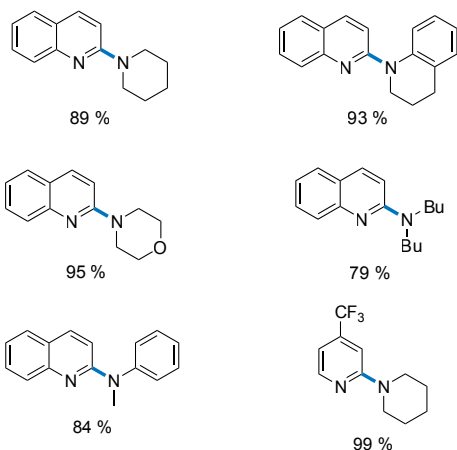
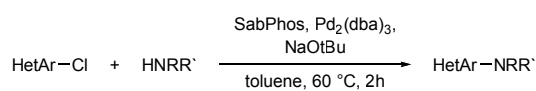
| Solvent | Time | Temperature | Base | Cat. loading | Yield* |
|---------|-----------|-------------|--------|--------------|-------------|
| Toluene | 3 h (1 h) | RT | NaOtBu | 0.02/0.04 | 19 % (9 %) |
| Toluene | 2 h (1 h) | 60 °C | NaOtBu | 0.02/0.04 | 88 % (75 %) |

BROAD APPLICABILITY

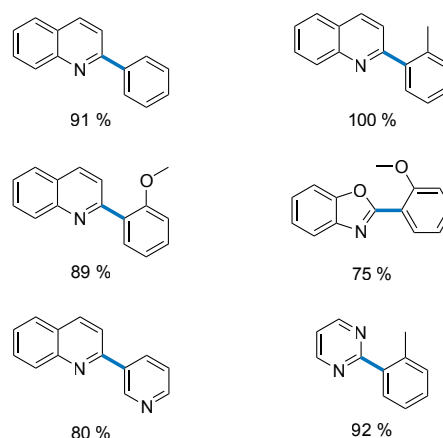
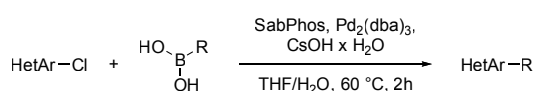
The Palladium-SabPhos complex generates high yields in various reactions. The substrate scope is broad and incorporates all kinds of substituents, such as electron withdrawing and electron pushing groups.

Not only in Buchwald-Hartwig reactions is our Palladium-SabPhos complex superior but also in other coupling reactions, such as Suzuki.

Buchwald-Hartwig-Coupling (C-N)



Suzuki-Coupling (C-C)



ABOUT HERAEUS PRECIOUS METALS

Heraeus Precious Metals is a leading provider of precious metals services and products. We combine all activities related to our comprehensive expertise in the precious metals loop – from trading to precious metals products to recycling.

Heraeus Precious Metals is one of the world's largest refiners of platinum group metals (PGMs) and a leading name in industrial precious metals trading. Our precious metals products are used in a wide variety of industries,

including the chemical, pharmaceutical, glass, electronics and automotive industries. We offer top quality solutions and products based on many years of experience and technical expertise. We are a reliable development partner for our customers and find the best solutions for their requirements.

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