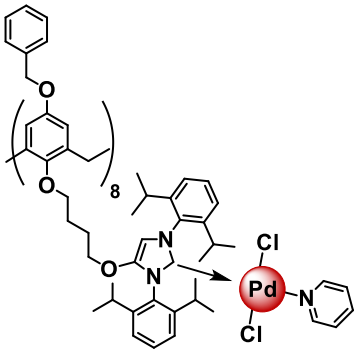
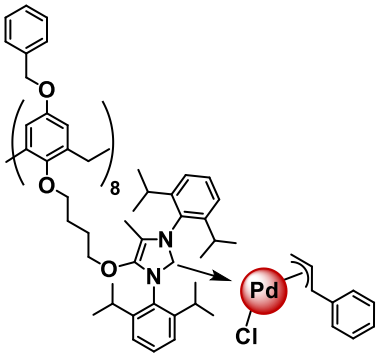
Supported catalysts for fine chemistry

Guidelines for the use of NOVECAL catalysts and ligands

NOVECAT Supported Pd-NHC Catalysts



NOVECAT G2-03
M_w = 7418.88 g.mol^{-1}



NOVECAT G3-01
M_w = 7552.05 g.mol^{-1}

- **Handling and storage**: catalysts can be handled without specific precaution. They are stable for months when stored at room temperature without argon. However, for longer time storage (over a year) we recommend to keep it at low temperature (T < -10 °C).
- **General use**: The catalysts are not sensitive to water, therefore the use of anhydrous solvents is not necessary. They are soluble in dichloromethane, tetrahydrofuran, acetone and dimethyl sulfoxide. On the contrary, they are insoluble in alcohols, acyclic ethers, alkanes and water.

NOVECAT G2-03 for Suzuki-Miyaura couplings

- **Use**: Best performances of the catalyst **NOVECAT G2-03** for the Suzuki-Miyaura reaction, in terms of both activity and leaching, are reached under inert atmosphere using alcoholic solvents such as ethanol in which they are insoluble. For optimal results, catalysis should be performed between 20 °C and 80 °C (temperatures higher than 80 °C may increase the leaching). Reactions are generally complete after 2 h at 80 °C, and no evolution occurs afterwards. To efficiently remove the catalyst, reaction mixtures are allowed to cool to room temperature before passing the solution through a pad of celite, or a filtrating device (in this case the porosity of the filter paper used should be 2.5 µm or thinner).[1,2]

- **Reaction settings**: Wide screening of the reaction parameters (solvent, concentration, temperature, amount of base and arylboronic acid) underlined two efficient sets of conditions for the Suzuki-Miyaura cross-coupling (see schemes below). In addition, a deeper optimization should be performed for each new couple of reagents.

conditions A: Ar_1–Br (1 eq) + Ar_2–B(OH)$_2$ (1.5 eq) → **Pd-NHC Catalyst**, K_3PO_4 (2 eq), EtOH (C = 0.5 M), 20 °C < T < 80 °C, 2 h → Ar_1–Ar_2

conditions B: Ar_1–Br (1 eq) + Ar_2–B(OH)$_2$ (1.1 eq) → **Pd-NHC Catalyst**, K_3PO_4 (1.2 eq), EtOH (C = 2 M), 20 °C < T < 80 °C, 2 h → Ar_1–Ar_2

[1] Benzyloxycalix[8]arene: a new valuable support for NHC palladium complexes in C–C Suzuki–Miyaura couplings. I. Abdellah, P. Kasongo, A. Labattut, R. Guillot, E. Schulz, C. Martini, V. Huc. *Dalton Trans.* **2018**, *47*, 13843.

[2] Calixarene-supported Pd-NHC complexes as efficient catalysts for scalable Suzuki-Miyaura cross-couplings. A. Labattut, S. A. Fayssal, J. Buendia, I. Abdellah, V. Huc, C. Martini, E. Schulz, *React. Chem. Eng.* **2020**, *5*, 1509.

NOVECAT G3-01 for Buchwald-Hartwig couplings

- **Use**: Various solvents can be used for the Buchwald coupling, with excellent results. Among them, we can cite dioxan, THF or MeTHF, CPME (cyclopentylmethylether), toluene or methylcyclohexane. Ether type solvents (dioxan, THF and CPME) lead to the best yields at equal catalytic loading, therefore their use allow to perform the reactions with a lower catalytic amount than in toluene or alkanes. On some cases, water (1% v/v) has showed a positive effect on the outcome of the reaction. Nevertheless, more than 5% v/v water should be avoided, since we then observed a strong decrease of the yield.
- **Leaching considerations**: excellent values were obtained in all the above mentioned solvents, with values between 5 and 30 ppm residual palladium. In general, alkanes might lead to the lowest values. For optimal results, catalysis should be performed between 80 °C and 100 °C (temperatures higher than 100 °C may increase the leaching). To efficiently remove the catalyst, reaction mixtures are allowed to cool to room temperature before passing the solution through a pad of celite (or silica), or a filtrating device (in this case the porosity of the filter paper used should be 2.5 µm or thinner) and washed with the appropriate solvent (ethyl acetate, ether, EtOH…). DCM, THF and all the solvents solubilizing our catalysts should be avoided to wash the pad or the filtrating device, since this would obviously increase the palladium leaching.
- **Reaction settings**: Wide screening of the reaction parameters (solvent, concentration, temperature, nature of the base) underlined the importance of some parameters:
  - *t*BuOK gave us the best results, while *t*BuONa gives slightly lower yields. The use of carbonates or phosphates proved not to be efficient. In some cases, LiHMDS can also be used.
  - A concentration between 0.5 and 1M appears to be optimal.
  - Reaction can be performed with either aryl chlorides or bromides, with almost no difference of reactivity.
  - Solvent, time and temperature should be adjusted depending on the couple of substrates, although general guidelines have been mentioned above. However, working in dioxan at 100 °C for 20 h generally gave the best yields.

    N.B.: Reactions can be complete after 8 h at 100 °C, although we noticed that with low catalytic loading (0.1 mol% Pd), it is useful to warm for 20 h in order to reach full conversion.

The conditions described below briefly report all the aforementioned information: