

Chemical Catalysis with MagRBR and EasyMax

Quick and Convenient Suzuki couplings



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Quick and convenient C-C couplings with the SpinChem MagRBR and EasyMax 102 Advanced Synthesis Workstation.

Transition-metal catalyzed C-C couplings are important strategies in the production of APIs and other fine chemicals. In drug discovery, multiparallel couplings are used to synthesize structural analogues to initial lead compounds. This is done in order to study the structure-activity relationships, allowing researchers to screen for analogues with biological activities best suited for the target in question. The coupling of aryl boron species and aryl halides is known as Suzuki couplings, and Pd(II)-species are typically used as catalysts.

The SpinChem® magnetic rotating bed reactor (MagRBR) is a device designed for fast and easy screening of heterogeneous catalysts and catalytic reactions. The heterogeneous catalyst is pre-packed into the device, through which the liquid phase is repeatedly percolated as the MagRBR rotates. This application note demonstrates how the combination of a SpinChem MagRBR custom-filled with heterogeneous Pd(II)-catalyst and the controlled conditions in a Mettler-Toledo EasyMax™ 102 Advanced Synthesis Workstation allows for quick and convenient generation of C-C coupled products. Phenylboronic acid was reacted with six aryl halides using fresh Reaxa Pd(II) EnCat TPP30 loaded in MagRBR M10s for each reaction. All substrates and products are listed in Table 1.



Figure 1. A SpinChem® MagRBR filled with Reaxa Pd(II) EnCat TPP30 in an EasyMax™ 102 Advanced synthesis glass vessel.



Conditions: A SpinChem® MagRBR M10 filled with Reaxa Pd(II) EnCat TPP30 (75 mg, 3 mol% Pd(II) and tri-phenylphosphine) was rotated at 600 rpm in a preheated (80 °C) substrate solution containing halide (1 mmol), boronic acid (1.5 mmol), potassium carbonate (3 mmol). IPA:H₂O (20:1, 0.1 M in halide).

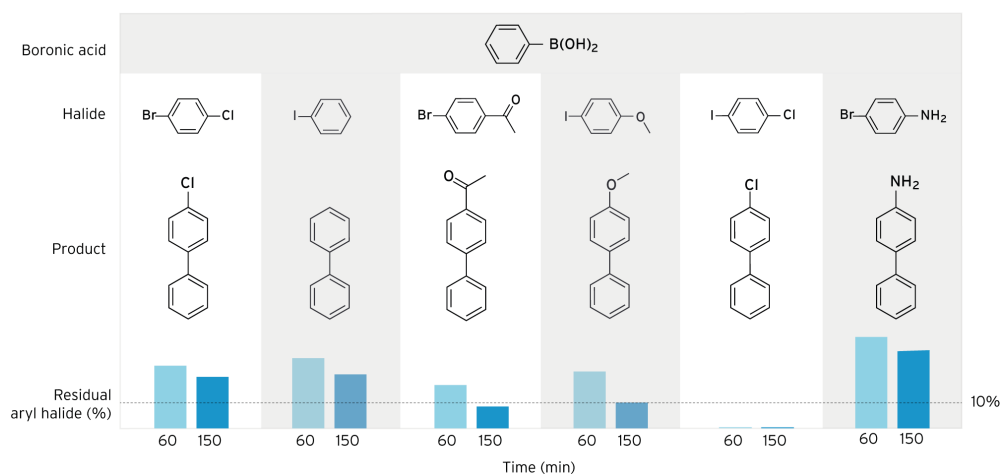


Figure 2. Table showing reactants and corresponding products of palladium-catalysed coupling of phenylboronic acid and six aryl halides. The light blue and dark blue bars show amount of residual halide after 60 and 150 minutes of reaction times, respectively.

Results

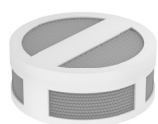
A proof-of-concept library of biaryl products was obtained in crude yields of 60-100% within 2.5 h. Yields could be improved by simply increasing the reaction time. Crude products can be obtained after simple aqueous wash, and be used either as-is or after optional chromatographical purification.

Conclusions

In building a small library of Suzuki products, the use of SpinChem® MagRBR M10 custom-packed with Pd(II) EnCat offered speed and convenience. Further advantages of using the MagRBR in an EasyMax™ 102 Advanced Synthesis Workstation include an easily adjustable and stable reaction environment, making reaction parameters easy to monitor and optimize, as well as simple and seamless scale-up of the system.



Figure 3. SpinChem rotating bed reactor S2. Available for use in the Mettler-Toledo EasyMax™ 102 Advanced Synthesis Workstation. Using the RBR technology allows for easy scale-up of experiments directly in the EasyMax system.



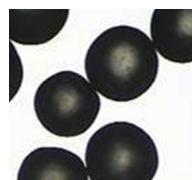
SpinChem® MagRBR M10

For screening of catalysts and catalytic reactions in 5-100 mL



EasyMax™ 102 Advanced

Robust synthesis workstation for high R&D productivity



Reaxa Pd(II) EnCat TPP30

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Screening of C-C coupling products:

- Quick and convenient coupling
- Fast development of product library
- Quick and easy work-up

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