

# Painless Transition from Milligram to Hundreds of Grams Using Microwave-Assisted Chemistry

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## A Coherent Approach to Scale-up

Coherent Synthesis™ is a means of efficiently linking knowledge and action in organic chemistry synthesis. Coherent Synthesis streamlines organic chemistry development, to make your life easier through:

- Ease of use
- Speed
- Reproducibility
- Efficient workflow

And with the arrival of scalable technologies...

- The seamless scale-up of any reaction

Our technologies have been selected and designed specifically with the volume and diversity needs of medicinal chemistry in mind. We have proven that most of the reactions in our reaction database, Emrys™ Pathfinder, are generally scalable, with little or no change in reaction conditions.

These experiments confirm that Emrys™ Advancer is capable of addressing the diverse reactions that characterize medicinal chemistry.

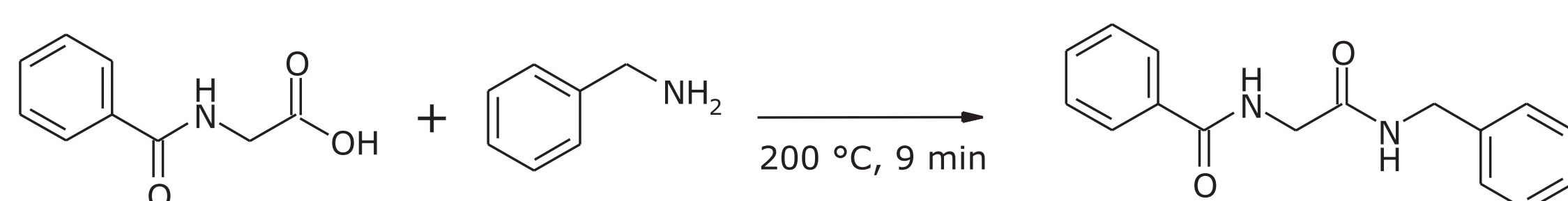
"The scale-up system worked excellently, and we received the same results compared to the small scale reactions. The whole process was also completed in a fraction of the time we would normally spend using traditional methods. It is a valuable opportunity to be able to scale up so rapidly."

- Dr. Josef Stadlwieser, ALTANA Pharma AG

One unique and highly valuable benefit of Coherent Synthesis is the seamless scale-up of reactions, manifested through the ability to apply identical conditions for the synthesis of milligrams as well as hundreds of grams of substance. This fits perfectly with the typical scale requirements as chemistry moves from discovery into the large-scale preparations phase.

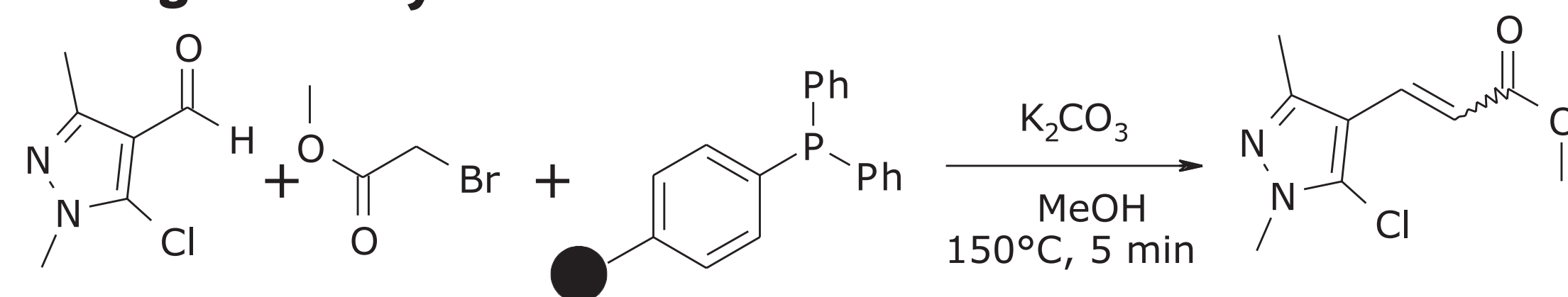
In order to test the general applicability of our new high-volume batch reactor Emrys™ Advancer, we designed several reactions that specifically challenged important issues of the methodology: a highly concentrated, i.e. neat reaction (1); heterogeneity, i.e. a solid-phase supported reaction (2); a highly reactive reaction, i.e. using perchloric acid (3); and a metal catalyzed reaction, i.e. a Pd-catalyzed Suzuki reaction (4).

### 1. Homogeneity of the electromagnetic field



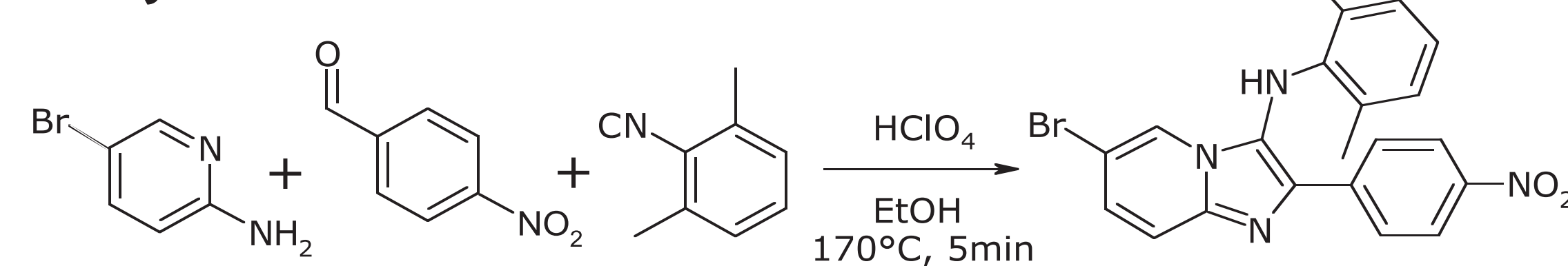
|          |  |         |         |
|----------|--|---------|---------|
| Scale:   | 2.7mmol                                    | Scale:  | 162mmol |
| Yield:   | 82%  | Yield:  | 84%     |
| Amount:  | 985 mg                                     | Amount: | 60.6g   |
| Work-up: | Recrystallization in 50mL MeOH/200mLCH2Cl2 |         |         |

### 2. Mixing efficiency



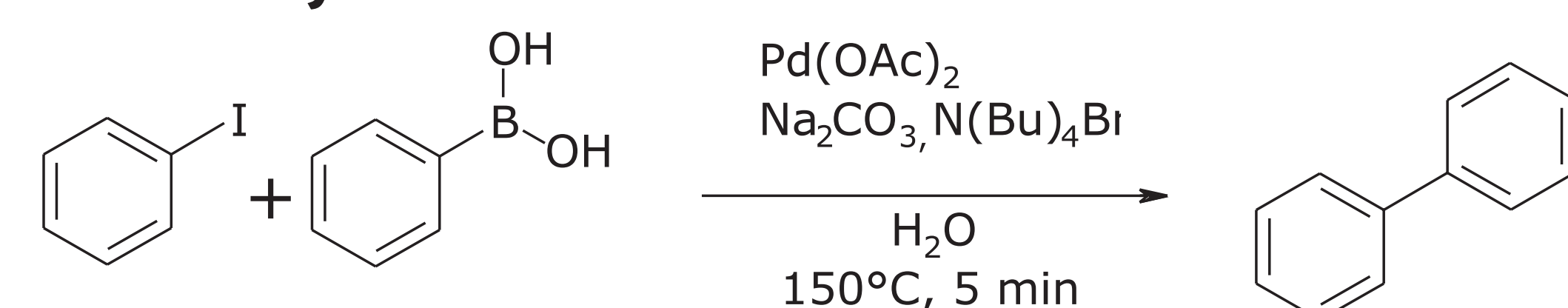
|          |  |         |       |
|----------|--|---------|-------|
| Scale:   | 0.3mmol  | Scale:  | 9mmol |
| Yield:   | 38%*   | Yield:  | 92%   |
| Amount:  | 24.6mg   | Amount: | 1.79g |
| Work-up: | Filtration, extraction with DCM/H <sub>2</sub> O and evaporation of the solvent and, in mg scale, preparative RPLC |         |       |

### 3. Safety



|          |   |         |        |
|----------|---|---------|--------|
| Scale:   | 1mmol   | Scale:  | 30mmol |
| Yield:   | 70%   | Yield:  | 68%    |
| Amount:  | 184 mg  | Amount: | 5.37g  |
| Work-up: | Crystals were filtrated and washed with cold MeOH |         |        |

### 4. Metal catalysed reaction



|          |                          |         |         |
|----------|--------------------------|---------|---------|
| Scale:   | 1 mmol                   | Scale:  | 40 mmol |
| Yield:   | 86.8 %                   | Yield:  | 80%     |
| Amount:  | 137 mg                   | Amount: | 5.05 g  |
| Work-up: | 1 water/ether extraction |         |         |

#### References:

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