# New Accessories for High Throughput and Combinatorial Approach in a Microwave Batch Reactor

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## Introduction

The **Anton Paar GmbH** introduces new accessories for efficient method development, parallel optimization and high throughput synthesis in our multimode batch reactor Synthos 3000.

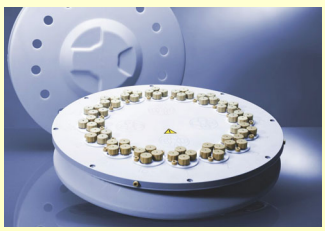
The new **Rotor 64MG5** offers simultaneous processing of up to 64 disposable screw-cap glass vials with an operation volume of 0.3 to 3.0 mL making it useful for method development and optimization processes. Its reliability is demonstrated via two valuable routes of heterocycle synthesis, generating 24-member libraries of thiophene and oxindole derivatives.[1]

Furthermore we highlight a unique **sealable well-plate system** allowing screening reactions in a 8×6 well format at elevated pressure. Using silicon carbide (SiC) as well-plate material even low-absorbing or microwave-transparent mixtures can be applied effectively. As a proof of concept to demonstrate the excellent homogeneous heat distribution within the plates a library of 2-aminopyrimidines was generated.[2]

These new tools extend the range of applications in the Synthos 3000 platform enabling microwave assisted synthesis from the mg scale up to multigram production in one instrument.

## Synthos 3000: High Throughput Accessories

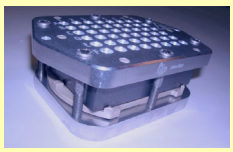

*Anton Paar Synthos 3000*



*Rotor 64MG5*

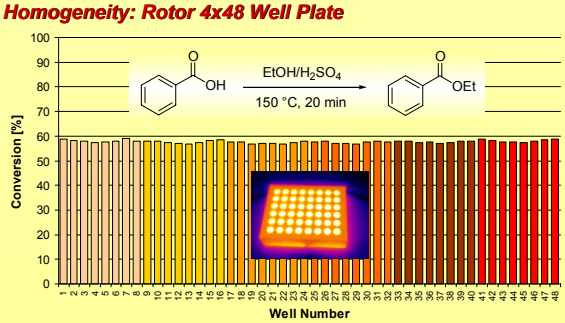
- 64 disposable screw-cap glass vials
- Alignment compatible to Zinsser 6x4 racks
- Working volume 0.3-3.0 mL
- Operation limits 200 °C and 20 bar
- Reaction control by IR Sensing
- Sophisticated venting tool available

*Rotor 4x48 Well Plate*



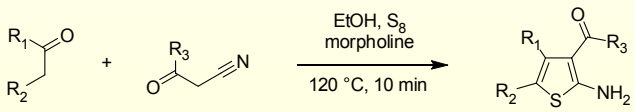
- Inert SiC well plates with 6x8 matrix
- Working volume 0.1-0.3 mL
- Unique sealing mechanism (patent pending)
- Operation limits 200 °C and 20 bar
- Up to 4 units on a turntable
- Reaction control by IR sensing

### *Homogeneity: Rotor 4x48 Well Plate*



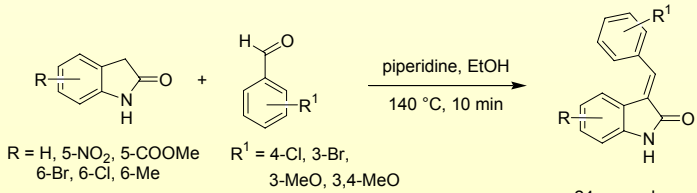

## Rotor 64: Lead Generation in Parallel Mode

### *Model Reaction 1: Gewald Synthesis*




- 0.2 to 0.5 mmol range in 0.9 mL solvent
- 6 keto-compounds combined with 4 nitriles
- isolated/purified by preparative HPLC
- identical yields to sequential monomode experiments

### *Model Reaction 2: Oxindole Condensation*




R = H, 5-$NO_2$, 5-COOMe 6-Br, 6-Cl, 6-Me

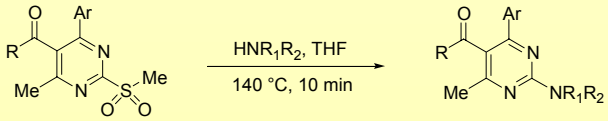
$R^1$ = 4-Cl, 3-Br, 3-MeO, 3,4-MeO

24 examples
up to 95% yield

- 0.2 to 0.4 mmol range in 1.0 mL solvent
- product isolation by simple filtration
- no additional purification required
- identical yields to sequential monomode experiments

## Well Plates: Library Preparation

### *Model Reaction 3: Synthesis of 2-Aminopyrimidines*




30 examples
up to 85% yield

- 0.01 mmol range in 0.15 mL
- stock solutions of 6 sulfones and 5 amines applied
- conversion determined by HPLC
- product isolation by column chromatography
- identical yields to sequential monomode experiments

## Conclusion

Valuable accessories for Synthos 3000 have been introduced, enabling high throughput parallel microwave-assisted organic synthesis, featuring:

- a unique sealable well plate system for reactions at elevated pressure
- parallel method optimization in disposable glass vials
- easy-to-use screw-cap vessels for gram-scale library generation
- utmost homogeneity in a multimode cavity
- the use of established protocols in any accessory without the need for re-optimization

### *Acknowledgements*

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[1] T. Karner, M. Treu, Boehringer Ingelheim Austria GmbH, unpublished results

[2] J. M. Kremsner, A. Stadler, C. O. Kappe, *J. Comb. Chem.* **2007**, *285-291*