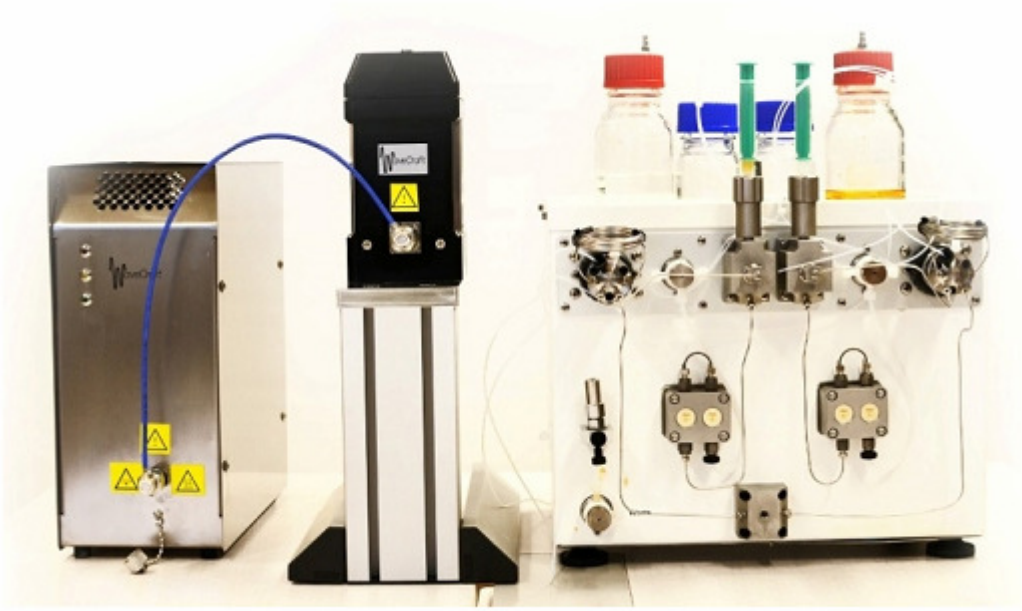
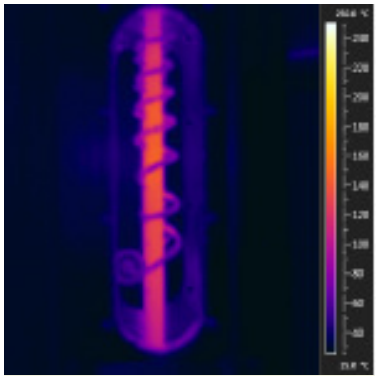
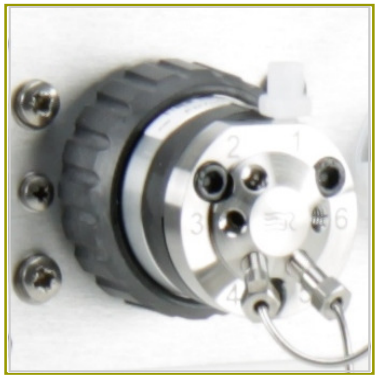
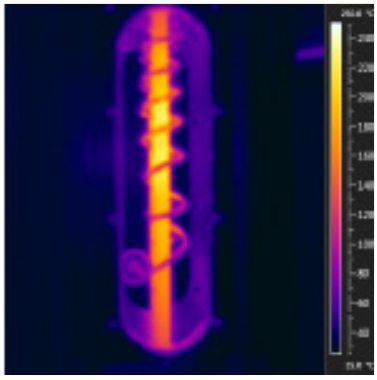








ArrheniusOne™

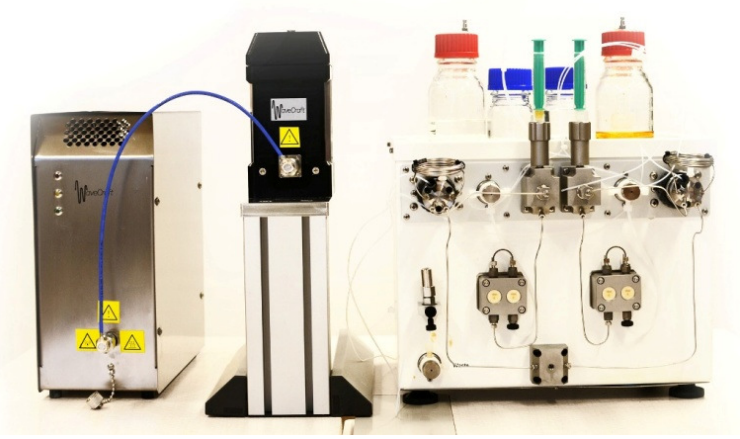
Continuous Flow Microwave-Assisted Organic Synthesis (CF-MAOS)

UNIQSIS

Accessible flow chemistry

ArrheniusOne™

for continuous-flow, microwave-assisted organic synthesis with FlowSyn™



- **Combines rapid microwave heating with flow-through synthesis**
- **Quick & trouble-free scale up of microwave chemistries**
- **Automatic dynamic optimisation of applied microwave energy**

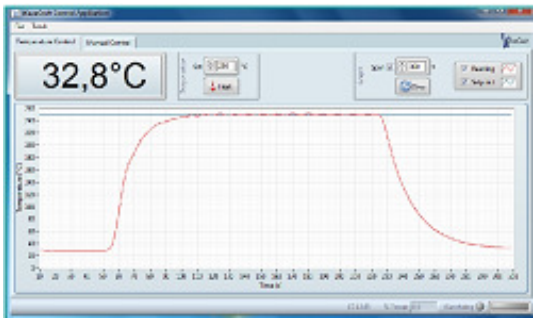
ArrheniusOne™ is an innovative state-of-the-art microwave generator and applicator for continuous-flow, microwave-assisted organic synthesis (CF-MAOS) in drug development.

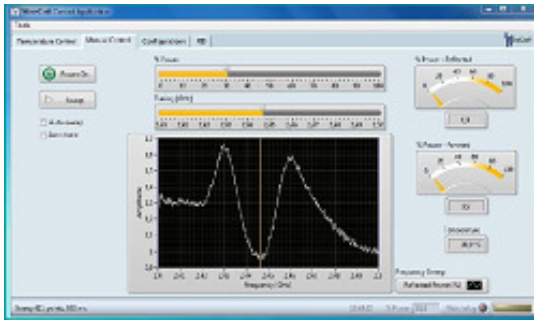
Combining continuous flow with microwave heating can significantly reduce total process times during the development of pharmaceutical compounds. The rapid, uniform heating provided by the ArrheniusOne delivers 10 to 1000 times faster reaction rates within minutes. Continuous flow allows more compound to be produced safely while consuming less energy and producing less waste. Reaction conditions are quickly optimised, thereby eliminating the need for re-optimisation during scale-up and so saving time downstream.

Developed by microwave technology specialist WaveCraft of Sweden and marketed jointly by Uniqsis and WaveCraft, the ArrheniusOne™ is designed to operate with two- or four-channel FlowSyn™ continuous flow reactor systems from Uniqsis. The two products combine to offer a unique solution for rapid optimisation and scale-up of compound production to dramatically increase productivity and efficiency, while reducing energy consumption and environmental impact.

Typical CF-MAOS applications include catalysed styrene synthesis, catalysed Suzuki–Miyaura coupling, Fischer indole synthesis, Claisen rearrangement and many others.

- **Improved efficiency** — reactions rates accelerated by a factor of 10 to 1000 by microwave heating
- **Immediate scale-up** – large reactor capacity and 4-channel capability allow for rapid scale-up to multi-kg quantities
- **Excellent temperature stability** — continuous monitoring by integrated IR pyrometer
- **Continuous dynamic optimisation of MW power and frequency**—ensures optimal use of applied MW energy at all times
- **Straightforward, reliable operation using intuitive software**
- **Reduced environmental impact** — combination of CF-MAOS and continuous flow uses less energy and produces less waste



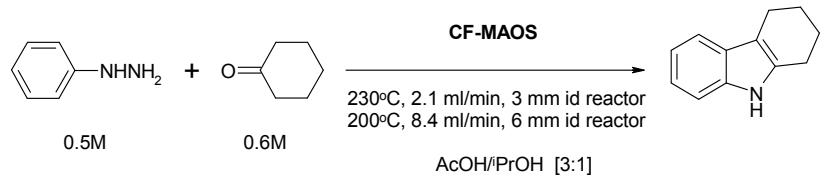


CF-MAOS Chemistry Examples:

Chemistry Optimisation and Scale Up Examples

Reaction optimisation and small scale preparations may be conveniently performed using a 3 mm id flow-through tube reactor. This reactor may then be replaced with a 6 mm id version to facilitate scale-up and immediately increase throughput by a factor of approximately 4 fold.

Fischer Indole Synthesis

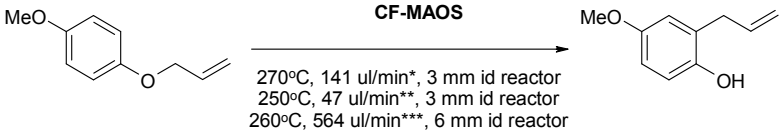


0.5M 0.6M

	Residence time	Yield
3 mm I.D. reactor	20 s	90%, 10 g/h
6 mm I.D. reactor	20 s	85%, 34 g/h
Classical heating*	3 min	96%, 25 g/h

** 200°C, 5 mL/min, 75 bar, Razzaq et al. Eur. J.Org. Chem 2009, 1321–1325*

Claisen Rearrangement



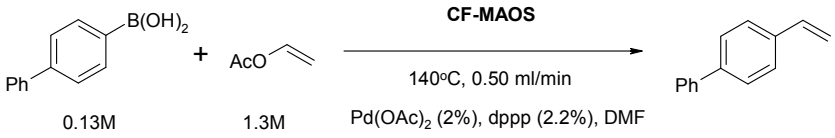
*2M in NMP, **Neat, ***3M in NMP

	Residence time	Yield
3 mm I.D. reactor	5 min	79%, 2.2 g/h
3 mm I.D. reactor	15 min	85%, 2.4 g/h
6 mm I.D. reactor	5 min	65%, 11 g/h
Classical heating*	4 min	95%, output not applicable

** 0.1 M toluene, 240°C, 1 mL/min, 100 bar, Razzaq et al. Eur. J.Org. Chem,2009, 1321–1325*

Chemistry Optimisations Performed in 3 mm Reactors during Product Trials:

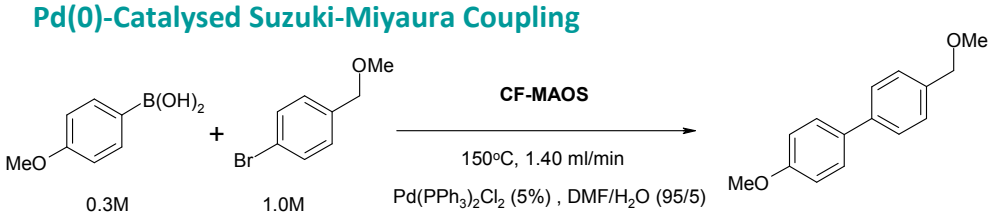
Pd(II)-Catalysed Styrene Synthesis



0.13M 1.3M

Res. Time	Yield
75 s	66%; 0.5 g/h

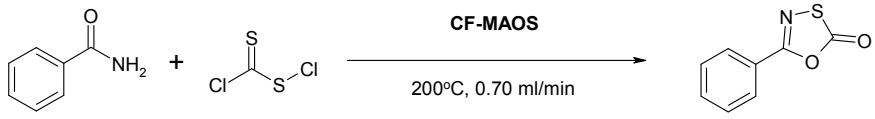
Pd(0)-Catalysed Suzuki-Miyaura Coupling



0.3M 1.0M

Res. Time	Yield
30 s	71%; 0.7 g/h

Oxathiazolone Synthesis of Bioactive M. Tuberculosis Proteasome Inhibitor

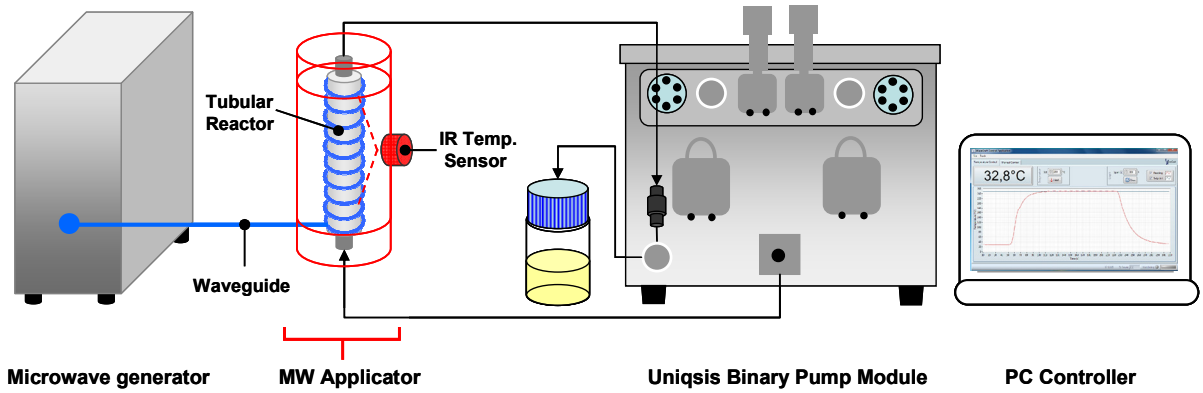


0.25M 0.75M

Res. Time	Yield
1 min	62%; 0.6 g/h

CF-MAOS with ArrheniusOne™

The ArrheniusOne™ microwave generator utilises a semi-conductor design to enable dynamic optimisation of process conditions by changing power and frequency during heating. Optimisation is controlled by an algorithm in the ArrheniusOne™ control software. Microwaves are transmitted to the ArrheniusOne™ applicator via a coaxial waveguide. The applicator provides a fundamentally new concept for microwave heating. This non-resonant microwave applicator generates a concentrated, homogenous axial field to provide even heating within the flow reactor.



Arrhenius One - Technical Specification	
Heating process	
Temperature range	ambient to 300°C
Temperature increase	typically 1 to 5°C/sec depending on solvent and power applied
Pressure range	depending on reactor dimensions: 3 mm id: ambient to 50 bar; 6 mm id: ambient to 30 bar
Microwave power range	0 to 150 W
Frequency range	2.4 to 2.5 GHz
Reaction volume	depends upon the reactor used and the flow rates applied
Power, maximum	600 VA
Electrical requirements	
Voltage	110 – 240 V switching power supply
Line frequency	50 or 60 Hz
Power Maximum	600 VA
ArrheniusOne unit	
Operating temperature	18 to 32°C
Humidity	non-condensing conditions
Cooling liquid	tap water or cooling circulator at 20°C maximum, flowing at a rate of 1 to 5 L/min, pressure 4 bar maximum
Weight	Generator: 9.35kg; Applicator with stand and IR probe: 6.1kg
Dimensions (w x d x h)	Generator: 145 x 320 x 330 mm; Applicator: 180 x 305 x 435 mm
Computer requirements	
Laptop or desktop	minimum 2 GB RAM, 100 GB free hard disk space and a 2 GHz Intel or AMD processor minimum screen resolution 1024 x 720 pixels minimum 1 free USB 1.1 or 2.0 connector operating system Microsoft Windows XP, Vista or Windows 7 (32 or 64 bit)

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