

# Microwave Synthesis

Fourth generation systems



# Wide Exploration and Fast Results

A common goal for all medicinal chemistry labs

Speeding up reactions has never been easier. Biotage microwave synthesizers are the first-choice tools for organic chemists who need to accelerate their production of new compounds.

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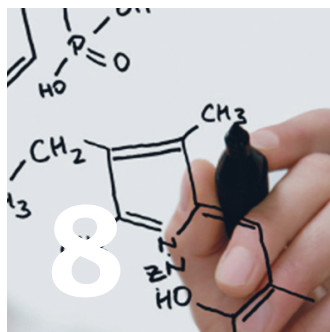
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Microwave heating is by far the superior choice for synthesizing novel compounds and can offer advantages other than just speed. Working at temperatures and pressures not attainable through traditional heating, it allows chemists to perform reactions previously not possible.

## Discover the Advantages of Microwave Synthesis

### Why Wait Hours, or Even Days, for Results?

Simply by increasing temperature, microwave synthesis can complete reactions up to a thousand times faster than traditional reflux conditions.

### Why Limit the Range of Experiments?

Quickly test your creative synthetic ideas and rapidly synthesize compounds of interest to fill gaps in your structure activity relationship (SAR). Reduce the iterative SAR cycle-time and increase productivity for the entire project team.

### Don't Waste Time Supervising the Synthesis Process

Biotage microwave systems are predictable, reliable and safe. Each instrument has precise control of time, temperature and pressure to ensure that methods are reproducible and easily transferred or scaled up. Systems are also available with reliable automation and will run an entire sequence without manual intervention.

### Will the Microwave Fit Into Your Process, Hood Space and Budget?

Chemical synthesis has never been easier. Simply put the reaction mixture into the vial, cap it, insert the vial into the microwave, key in the reaction parameter, and run. The latest generation of microwave synthesis systems are compact, easy to use and very affordable.

# Biotage® Initiator Family Line-up

## Microwave synthesizers

Rapid investigation of reactions and pathways is more important than ever. The Initiator microwave synthesizers rise to this challenge by enabling chemists to quickly synthesize compounds using microwave heating. Through superior heating features, the Initiator is able to quickly achieve temperatures and pressures beyond traditional reflux heating. Our customers enjoy the benefits of design that starts and ends with our focus on solutions for researchers.

### Initiator+

#### Higher and Hotter – Get Even Better Results

The Biotage® Initiator+ represents the latest in microwave synthesis performance. A high-end specification enables the chemist to explore new areas and perform the latest of innovations in drug discovery. A reliable and upgradeable platform that allows chemists to make great discoveries in less time.



### Initiator

#### Simple and Robust Entry Level Instrument

The Biotage® Initiator is a safe, flexible microwave synthesizer for fast and scalable reactions, tailored for synthetic chemistry. Ideal for new users and routine operations, the standard Initiator provides reliable performance at a great price point.



### Robot Eight & Robot Sixty

#### Accessories for Automated Sample Processing

Both the Initiator+ and Initiator microwave synthesizers can be upgraded with the Robot Eight and Robot Sixty for full sample automation and higher throughput.

The 8-position sample bed gives the user a compact automation solution to start their scale-up process and library build-up in a multi-user environments with queuing. The 60-position sample bed supports the production of focused libraries, multi-user environments and scale-out.



Initiator+ with Robot 8 shown here.



## Biotage® Initiator+

### Fourth generation microwave synthesizer

Press the large touch-screen and heat your organic reagents to 300 °C in just a few seconds. The Initiator+ does just that, and adds intelligent features that make organic synthesis fast, reliable and safe.

The Biotage Initiator+ represents a new generation of synthesizer instruments for organic, medicinal, materials, nano and polymer chemistry professionals. It is an upgradeable and reliable platform allowing chemists to make great discoveries in less time.

#### Easy to Operate

Initiator+ facilitates the transition from traditional methods to microwave enhanced techniques. Learning microwave synthesis is fast and pleasant with the Initiator+. The large touch screen display makes the experience user friendly from set-up to results. The built-in wizard guides the user through experiment set-up step by step and helps converting conventional conditions to microwave synthesis parameters.

Results can be emailed directly to the user after a run, or downloaded through the USB port at the front of the instrument.

#### Flexible

Temperatures and pressures up to 300 °C and 30 bar open new possibilities to complete difficult reactions. Even low boiling point solvents can now be run at higher temperatures. The system automatically senses and performs reactions at their highest possible temperatures.

The Initiator+ can hold all Biotage vials from 0.2 to 20 mL, delivering greater flexibility and direct scale-up from milligrams to grams. The four different vial sizes can be used in any order or combination without system modifications.

The single-mode applicator and the Dynamic Field Tuning™ features offer faster and more powerful heating (400 W) of a broader range of solvents. The setting for low microwave absorbing solvents enhances the heating for e.g. toluene and 1, 4-dioxane.

## Specifications

### Heating Process

Temperature range	40–300 °C (Initiator: 40–250 °C)
Heating rate	Typically 2–5 °C/s depending on solvent and power applied
Reaction time	Up to 96 hours. Typically, most reactions require 2–15 minutes of irradiation.
Pressure range	0–30 bar (3 MPa; 435 psi) (Initiator 0–20 bar)
Power range	0–400 W from magnetron at 2.45 GHz
Reaction volumes	0.2–20 mL
Agitation	Variable magnetic stirrer (300–900 RPM)

### Upgrades

Upgradable with	Robot Eight and Robot Sixty
Processing capacity	8 or 60 vials (with robot upgrade)
Rack capacity	2 x 2 or 2 x 12 vials (large); 2 x 4 or 2 x 30 vials (small)

### Technical specs.

Electrical supply	220–240 V~, 50 Hz, 5 A (UK & EU) 100–120 V~, 50/60 Hz, 10 A (USA & JP)
Max. power consumed	1100 VA
Cooling	Pressurized air supply: >60 L/min (2.1 cubic feet/min), 2.5–4.0 bar (0.25–0.40 MPa; 36–58 psi)
Weight	21 kg (46.2 lbs)
Dimensions (WxDxH)	365 x 422 x 421 mm (14.4" x 16.6" x 16.6")
Max sound level	70 dB(A)

### Interfaces

Touch screen	10.4" (Initiator 6.4")
Ethernet LAN	Complies with IEEE 802.3 (ANSI 8802-3)
USB	USB 2.0
Archiving/back-up	Via USB
Printing	Via LAN
Certifications	CE, CSA certified

## Features and Advantages

- 300 °C reaction temperature
- 30 bar reaction pressure
- Large 10" touchscreen
- Modular automation solutions
- Guided step-by-step wizard
- In situ temperature measurement
- Upgradable to run peptide synthesis
- Safe and simple
- Utilizes all Biotage vials, from 0.2 to 20 mL

## Accessories

- Modules for automation (p. 6)
- Vials (p. 7)
- Peptide liquid handlers

### Upgradable

Each compound synthesis has unique demands. A range of accessories are available to increase automation for higher throughput.

Connecting the SP Wave module and the Robot Eight kit will transform this instrument into a microwave assisted peptide synthesizer, extending the scope of discoveries beyond small molecules.

The novel vortex mixing unit ensures gentle but thorough homogeneous heat distribution. With the optional fiber optic probe, reaction temperature can be monitored inside the vial for even better visibility.

### Best-in-class Safety

In the early days of microwave synthesis, bursting vials were a menace. All Biotage microwave synthesizers are designed with a triple-tier safety lock for safe operation at elevated temperatures and pressures.

## Biotage® Initiator

The Biotage Initiator is the predecessor to the Initiator+, and is an affordable entry-level instrument for standard routine synthesis operations. Providing the same level of reliability and safety as the Initiator+, it delivers basic functions for organic microwave synthesis.



For more information, please visit [www.biotage.com](http://www.biotage.com).



## Biotage® Initiator Robot Eight & Robot Sixty

### Intelligent automation

The Initiator+ can be upgraded from a single-sample manual format to an automated 8- or 60-position system. The modular design allows a user to add on different automated sample processors dependent on throughput requirements.

The 8-position sample bed gives the user a compact automation solution to start scale-up process and library build-up. The 8-position system is useful in a multi-user environment or for queuing multiple reactions. Flexible operation enables the use of both large and small vials in combination at any time and in any order without manual intervention.

The 60-position sample bed supports the production of focused libraries, multi-user environments and scale-out, and use of both large and small vials in any order without manual intervention.

#### Biotage® Initiator+ SP Wave

**Further Upgrading**  
Upgrade from an Initiator+ by connecting the SP Wave peptide synthesis module and the Robot Eight kit to perform microwave assisted peptide synthesis with vortex mixing.



For more information, please refer to the Peptide Synthesis and Purification brochure, or visit [www.biotage.com](http://www.biotage.com).



Biotage microwave vials are available in four sizes: 0.2–0.5 mL; 0.5–2.0 mL; 2.0–5.0 mL and 10–20 mL.

## Microwave Vials

### High precision glass vials

Durable and safe reactions at all times. Our high precision microwave vials are designed and tested to withstand pressures beyond 30 bar in a wide range of conditions.

Simplicity is one of the benefits of modern microwave equipment. Reactions are performed in glass vials sealed with caps and heated in the microwave cavity.

#### Magnetic Stir Bars

The reaction mixture is continuously blended by magnetic stirring promoting homogenous heating throughout.

#### Optimum Vial Sizes

Migrate directly to multi-gram scale without re-optimization using the 10–20 mL vials. These larger vials can also be used for preparation of scaffolds and intermediates or for generating larger quantities of active compounds for testing.

Each Biotage microwave vial has been designed for safe and efficient heating within its specified volume range. Together, the four vial types provide full scalability within the volume range 0.2–20 mL. Methods that are run at a lower volume are directly transferrable across the entire volume range of 0.2–20 mL.

#### Features and Advantages

- Reseal™ design allows the septum to be resealed after it has been penetrated for repeated additions of reagents or in-situ sampling.
- Manufactured from contaminant free microwave-safe glass.
- Magnetic stirring promotes homogenous temperature distribution.
- Available sizes: 0.2–0.5 mL, 0.5–2.0 mL, 2.0–5.0 mL and 10–20 mL.

**Biotage**

Biotage PathFinder - When you want reactions

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The world's largest database of verified methods for Microwave Synthesis

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## Biotage® Pathfinder

### Organic reactions database

PathFinder is a unique web-based service featuring a microwave synthesis database with more than 5,000 selected microwave reactions.

Biotage PathFinder is the largest and most comprehensive existing database of verified methods for microwave synthesis. This database is available as a web service for easy access to microwave synthesis methods and knowledge support for everyone.

PathFinder provides direct access to years of experience in microwave synthesis. All content has been developed on Biotage microwave synthesis systems, making these methods highly reproducible. PathFinder also includes other valuable tools, such as the "Ask-a-Chemist" feature where chemists can have a dialog about microwave synthesis methods directly with

an experienced Biotage chemist. Additional features include a gas pressure calculator and the PathFinder Cookbook.

#### Database Features

Logging on to [www.biotagepathfinder.com](http://www.biotagepathfinder.com) opens the search page. Here, the reaction database can be searched by substructure or by reaction keyword. The hits are listed in an overview including reaction scheme, temperature, time, and yield or purity. Each reaction view will provide a report including all information needed to repeat the reaction as well as literature references, analysis results, and comments about the reaction and work-up procedure.

The database is continuously expanded with updates, extended options and service items related to this site, making it a natural source of information and knowledge for chemists working in the field of microwave synthesis.



### Biotage PathFinder in a Nutshell:

- A database of more than 5,000 reproducible microwave synthesis methods verified to work well on all Biotage microwave systems.
- Unique, non-published microwave synthesis transformations.
- Starting conditions for microwave reactions; full documentation on solvent, additives and substrates, equivalents, method notes, work-up, and more.
- Fast and easy to compare hits and select conditions.
- Significant input from leading academic users within the Scientific Partnership Program.
- Focus: microwave synthesis, increasing diversity, providing a high degree of independently verified and optimized procedures with explicit experimental details.
- Sources: 70% method development by Biotage chemists; 15% by Scientific Partnership Program and approx. 15 % published data.
- Updates: on-line, regularly as new data becomes available.
- Coverage: 2000–present.

### Featured Tools

- Biotage PathFinder: Experimental conditions in the world's largest microwave reaction database.
- Microwave Cookbook: Browse a selection of popular reactions from Biotage PathFinder.
- Ask-a-Chemist: Communicate directly with our support chemists.
- Vapor Pressure Calculator: Automatic calculation of vapor pressure for common solvents.

### Time Prediction

Most times, reactions proceed faster using microwave synthesis simply because they are conducted at higher temperatures. When you set up experiments, the Initiator Wizard can provide help with prediction calculations.

The built-in chart provides a way to estimate the time needed to run a reaction at a different temperature than reported. Based on the Arrhenius equation, it uses the coarse rule of thumb that a ten-degree increase in reaction temperature doubles the reaction speed. For example, if your reaction took 4 hours at 140 °C, it will take approximately 2 hours at 150 °C.

Via the structure editor, the reaction scheme or chemical structure can be edited and searched for. With the addition of selected keywords the search result can be further defined.

**Chemicals**

Name	MW [g/mol]	Density [g/ml]	Amount [mmol]	Mass/Volume
100527	106.124	1.044	4.000	406.605 µl
65440	131.143	0.965	2.000	207.889 µl
SB	256.512	1.000	4.500	1154.300 mg
NMP	99.133	1.028	20.740	2000.000 µl
Product 1	241.356	1.000	0.000	0.000 µl

**Keywords**  
Amidation, Kindler Modification, Multicomponent, Nucleophilic addition to carbonyl

**Comments**  
Synthesis: The three-component Kindler reaction generally requires high reaction temperature and long reaction times. Volatile aldehydes, amines and ammonia require autoclave techniques. Using microwave heating in sealed process vials, these problems are avoided. Elemental sulfur, NMP, amine and aldehyde were charged in that order into a process vial.

Work-up: After cooling the (usually) dark brown mixture was poured onto ice. The precipitate was removed by filtration and dried (96% purity).

Characterisation: 1H-NMR and GC-MS.

**Instrument Settings**  
Absorption level: Normal  
Pre-stirring time: 0s

**References**  
Zbruyev, O. I.; Stiasni, N.; Kappe, C. O. J. Comb. Chem. 2003 In press

**Analysis**

The report generated from the search includes information on process parameters, used chemicals, references, analysis results etc. Analysis results are attached as PDF files. To view them, just click the file.

# Optimizing the Results

## Getting started with microwave synthesis

Although microwave synthesis often renders unique results, the outcome is largely governed by a few, well-known phenomena. With knowledge about these phenomena, your benefits of using microwave synthesis will be greatly enhanced.

### Which conditions are appropriate when performing microwave synthesis?

Microwave synthesis is normally conducted under conditions that vary considerably from what is conventionally used in today's chemistry laboratories. Biotage microwave systems support a wide variety of reaction conditions accommodating different solvents, volumes, concentrations and phases, and are characterized by reproducible results.

#### Solvents

##### *Common Solvents*

Acetonitrile, DMF, and alcohols are commonly used for microwave-assisted organic synthesis.

##### *Stick with Your Solvent*

It might not be necessary to change from the reaction solvent specified for traditional chemistry conditions. First, try using the solvent that you would normally use.

##### *Polar Solvents*

Polar solvents (e.g. DMF, NMP, DMSO, methanol, ethanol, and acetic acid) work well with microwaves due to their polarity. Set the absorption level to *Normal* or *High* when using polar solvents.

##### *Non-polar Solvents*

Non-polar solvents (e.g. toluene, dioxane, and THF) can be heated more efficiently if other components in the reaction mixture respond to microwave energy, i.e. if the reaction mixture contains either polar reactants or ions (see ionic liquids below). When using less polar solvents, more concentrated reaction mixtures might be preferable. Set the absorption level to *Low* when using nonpolar solvents.

##### *Ionic Liquids*

Ionic liquids consist entirely of ions and therefore absorb microwave irradiation very efficiently. They also have low vapor pressure, further enhancing their suitability. Ionic liquids dissolve in a wide range of organic solvents and can therefore be used to increase the microwave absorption of

low-absorbing reaction mixtures. Set the absorption level to *Very High* when using ionic liquids.

#### Volume

Do not exceed or fall below the microwave vial's specified volume range. Too low a volume will give an incorrect temperature measurement; while too high a volume does not leave sufficient head space for pressure build-up. When using low-absorbing or non-polar solvents, e.g. toluene and dioxane, always fill the microwave vial to the specified maximum volume.

#### Concentration

The concentration depends on the type of chemistry that is performed. A unimolecular reaction is independent of concentration and can be performed in very dilute solutions. Bi- or tri-molecular reactions on the other hand are highly dependent on the concentration; a higher concentration gives a faster reaction. The maximum obtainable concentration is dependent on the properties of the substrates and reagents as well as the properties of the solvent(s) used.

#### Phase

Different phases can be used, i.e. solution phase, solid phase, solid supported reagents, scavenger resins, and solvent free reactions.

#### Temperature

Reactions can be performed in a temperature range between 40 °C and 250 °C (Initiator) or 40 °C and 300 °C (Initiator+). Optimally the used reaction temperature should be as high as substrates and products allow before they start decomposing or as high as the reaction solvent allows, whichever is lowest.

#### Pressure

The reactions can safely be performed at pressures of up to 20 bar (Initiator) or 30 bar (Initiator+). If the pressure in a microwave vial becomes higher, the heating is automatically stopped and cooling begins. For an indication of the expected pressure of a reaction, please use a solvent table or the vapor pressure calculator at [www.biotagepathfinder.com](http://www.biotagepathfinder.com).

## Initiator+

Product	Part number
Initiator+ Microwave System (UK & EU)	356006
Initiator+ Microwave System (USA & Japan)	356007

## Initiator

Product	Part number
Initiator Microwave System (UK & EU)	355301
Initiator Microwave System (USA & Japan)	355302

## Robots

Product	Part number
Robot Eight	355380
Robot Sixty	355381

## Microwave Vials

Product <sup>1</sup>	Part number
0.2–0.5 mL, qty. 100	355458
0.2–0.5 mL, qty. 300	355627
0.2–0.5 mL, qty. 500	355628
0.5–2 mL, qty. 100	352016
0.5–2 mL, qty. 300	354625
0.5–2 mL, qty. 500	355629
2–5 mL, qty. 100	351521
2–5 mL, qty. 300	354624
2–5 mL, qty. 500	355630
10–20 mL, qty. 50	354833
10–20 mL, qty. 100	355631
10–20 mL, qty. 250	355632

<sup>1</sup> Microwave vial caps and stir bars are included with vial order

### Accessories

Vial caps included reseal septa, qty. 100	352298
Manual cap crimper	353671
Manual cap remover	353913
Vial adapter 0.2–0.5 mL, qty. 10	355459
Vial adapter 10–20 mL, qty. 12	355367
O-rings 10–20 mL adapter, qty. 10	354838
Vial rack Initiator 8, holds (4) 0.2–5 mL vials	355391
Vial rack Initiator 8, holds (2) 10–20 mL vials	355390
Vial rack Initiator 60, holds (30) 0.2–5 mL vials	353478
Vial rack Initiator 60, holds (12) 10–20 mL vials	354936
Stir bars 0.2–0.5 mL, qty. 30	355545
Stir bars 0.5–2 mL, qty. 30	355544
Stir bars 2–5 mL, qty. 30	355543
Stir bars 10–20 mL, qty. 5	353930

## Biotope Pathfinder Database

Product	Part number
Biotope Pathfinder web	355239



# Your complete partner for effective chemistry

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