Initiator

GETTING STARTED GUIDE
for Organic Synthesis

www.biotage.com

Biotage®

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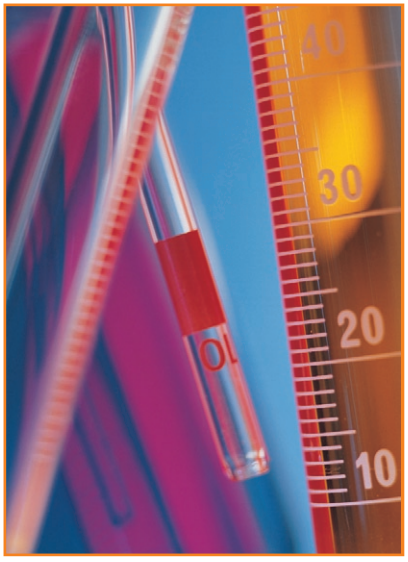


Quick start

Set up user accounts

A user can have system owner and/or chemist privilege:

- The chemist privilege gives the user access to the synthesis mode, i.e. the user can set up and run experiments, and view and manage experiment results.
- The system owner privilege gives the user access to the system mode, i.e. the user can change system settings, manage users, configure a network connection, save logs and experiment reports on a USB memory device, and calibrate the touch screen and robot. It is possible to password protect an account with system owner privilege.

Note: User accounts can only be set up at the system when the system is not processing and by a user with system owner privilege. If your company does not have a user with system owner privilege, use the account that was created in factory (to find out the password, see "Move an Initiator system" in the "Initiator Installation and Safety" document, P/N 355976).

To add a new user:

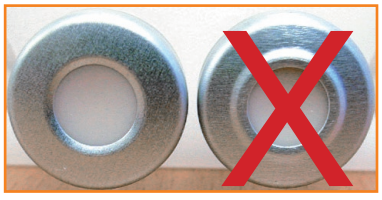
1. Log into the software's system mode:
   i. Press **Main Menu** in the right-hand panel.
   ii. Press **System** in the main menu. All user accounts with system owner privilege are listed in the **Select User** dialog.
   iii. Select your user account. If you do not have an account with system owner privilege, please contact your system supervisor.
   iv. Press **OK**. If your account is password-protected, the **Input Password** dialog opens.
   v. Enter your password and press **OK**.
2. Select the **Manage Users** tab and press **New**. The **User Editor** opens.
3. Press the **Name** text box and enter the user name.
4. To password protect a user account with system owner privilege, press the **Password** text box and enter the password.
5. If the system has been connected to your network, it is possible to allow the user to request an e-mail when an experiment has been completed. To enter the user's e-mail address, press the **E-mail** text box.
6. Press the **Roles** text box and select the user privilege.
7. To save the new account, press **Save**.
8. Press **Log Out** to return to the main menu.

Warning: Observe general as well as specific safety regulations for the use of the system and its accessories and consumables at all times, in order to reduce the risk of personal injury, fire, and explosion; see the "Warning summary" in the "Initiator Installation and Safety" document (P/N 355976).

Preparing your experiment

1. Dispense the chemicals into an unused microwave vial and insert a magnetic stirring bar. Do not fill the microwave vial above or under the stated volume range, and ensure that solid material is not present on the walls. When using low-absorbing or non-polar solvents, e.g. toluene and dioxane, always fill microwave vials to the specified maximum volume.
2. Cap the microwave vial properly. The cap should clasp the vial brim or the vial adaptor and not be possible to turn by hand. The top of the cap should be flat.

Note: If you are using 0.2-0.5 ml or 10-20 ml microwave vials, use vial adaptors. You need to position the vial adaptor before capping the 0.2-0.5 ml microwave vial.



The vial to the right is capped too tightly.

Set up and run your experiment

When setting up a run for the first time, you can use the Initiator Wizard. The wizard will guide you step by step through the setup of a run.

1. If you are not in organic synthesis mode, press **Log Out** in the right-hand panel and then **Organic Synthesis**.
2. Select the **Editor** tab in the right-hand panel.
3. Press **Wizard**. The Initiator Wizard opens. Read and follow the instructions that appear in the wizard.

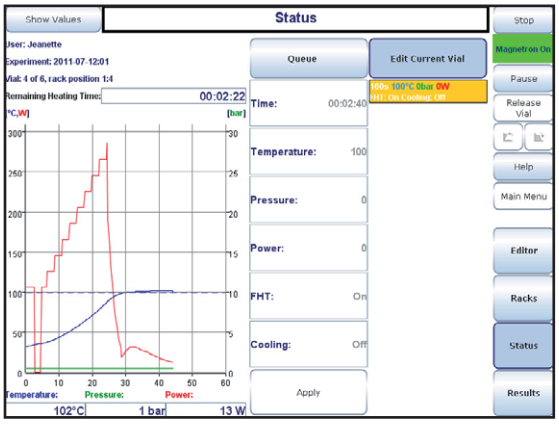
Monitor your experiment

When the system is processing your experiment, the heating process can be monitored at the **Status** tab.

With the **Show Values**/**Show Graph** button, you can toggle between viewing:

- The process graph with real time measurements of temperature, pressure, and applied power. The target values (temperature, pressure, and/or power) are shown as dashed lines.
- The current values of temperature, pressure, and applied power.

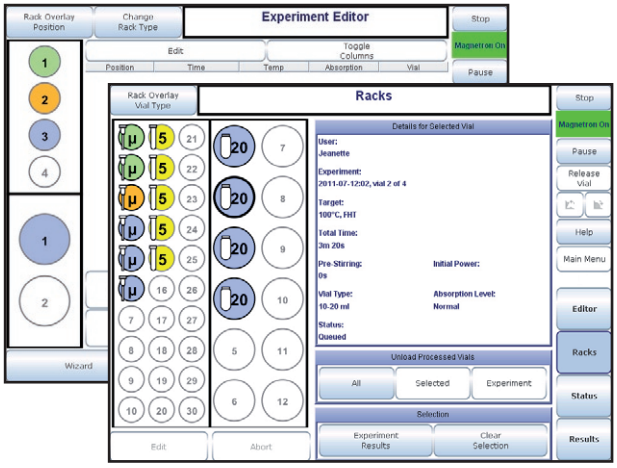
For instructions on how to edit the process parameters during the run, press **Help**. The changes will not be saved as set values. The resulting changes will, however, show in the results graph.



*At the **Status** tab, you can monitor and edit the reaction in progress.*

Unload your experiment when using Initiator with robot

1. Select the **Racks** tab in the right-hand panel.
2. Select a processed microwave vial included in the experiment and press **Experiment**. The **Unload Processed Vial(s)** dialog opens and, if the system is processing, the processing is paused. The microwave vials to be unloaded are selected (by the software) in the rack overview.
3. Unload the selected microwave vials.
4. Press **OK** to confirm unloading, clear the vial positions in the software and, if the processing was paused for unloading, to resume processing.



*The color of the vial position indicates the processing status. Press **Help** for color legend.*

View experiment results

1. Select the **Results** tab in the right-hand panel.
2. Press **Select User**. The **Select User** dialog opens.
3. Select user and press **OK**. All experiments performed by the selected user are listed.
4. To view the results of an experiment, select the experiment in the experiment list. To scroll the list of experiments or the report, press ▼or ▲.

More information

For more information and instructions, see “Software overview” on page 5 and the online **Help**.

Instrument overview

The Initiator system can process reaction volumes between 0.2 and 20 ml. The system is equipped with a touch screen used for experimental planning, instrument control, and reaction monitoring. The system status is displayed in the touch screen's right-hand panel:

- Idle or Paused = The system is not processing. (Systems without a robot have no experiment queue and can therefore not be paused.)
- Processing = The system is processing, but the magnetron is switched off.
- Magnetron On = The system is processing and the magnetron, which generates microwaves, is switched on.

A = touch screen, B = main switch, C = cavity lid, D = cavity insert holder, E = robot, F = robot arm, G = gripper, and H = rack.

Heating, stirring, and cooling

When the microwave vial has been inserted into the microwave cavity and the cavity lid has been closed, high-frequency microwaves (2.45 GHz), generated by the magnetron, heat the reaction mixture.

During the heating process, the reaction mixture is stirred by a magnetic stirring bar inside the microwave vial. It is also possible to stir the reaction mixture before the heating process is started (pre-stirring) to swirl up the content to improve the microwave absorption optimization.

After processing, the reaction mixture is immediately cooled with pressurized air. When the temperature of the reaction mixture has dropped to 40°C or 50°C (according to your system setting), the cavity lid is opened and the microwave vial can be removed.

Robot automation

If your system is equipped with a robot, all experiments are processed through a queue and the transportation of the microwave vials is handled by the system. This allows new experiments to be planned and added to the queue as long as there are free positions in the racks. Depending on the robot size, the queue can contain a maximum of 8 or 60 microwave vials.

There are two robot sizes available, Eight and Sixty. Robot Eight can handle vial racks with 2 or 4 positions, Robot Sixty can handle vial racks with 12 or 30 positions. The racks with 2 and 12 positions accommodate microwave vial size 10-20 ml.

Cavity insert

The cavity insert must be removed from the microwave cavity before loading 10-20 ml microwave vials and inserted before loading 0.2-0.5 ml, 0.5-2 ml, or 2-5 ml microwave vials. If the system is equipped with a robot, the cavity insert is automatically inserted and removed by the robot.

Initiator⁺ and SP *Wave*

With Initiator⁺ systems, the maximum temperature and pressure are increased from 250°C and 20 bar to 300°C and 30 bar. Initiator⁺ comes with a bigger touch screen, 10.4" instead of 6.5", and can be upgraded to run peptide as well as organic synthesis using microwaves. For more information on upgrades, contact your local sales representive.

Waste tray

If, for some reason, a microwave vial breaks or leaks in the microwave cavity, the glass and/or the reaction mixture are collected in the waste tray underneath the microwave cavity. The waste tray can be removed and cleaned as described in the "Maintenance" section beginning on page 14.

Software modes

- **Organic Synthesis:** Set up and run experiments, and view and manage experiment results.
- **System:** Change system settings, manage users, configure a network connection, save logs and experiment reports on a USB memory device, and calibrate the touch screen and robot. Only users with system owner privilege can log into system mode.
- **Service:** Service can only be performed by an authorized Biotage® service engineer.

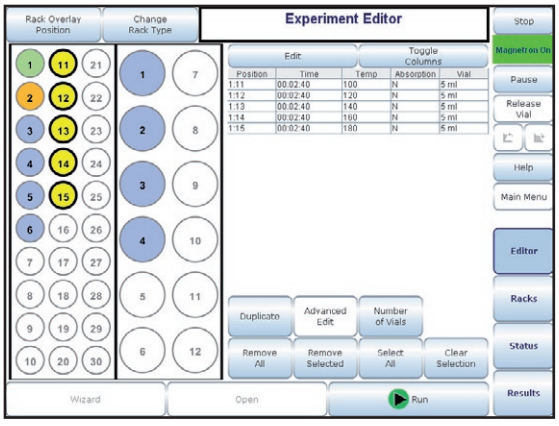
Set up and run experiments, and view and manage experiment results

Depending on whether the system is equipped with a robot or not, the software in organic synthesis mode consists of 3 or 4 tabs: Editor (1), Racks (2), Status (3), and Results (4).

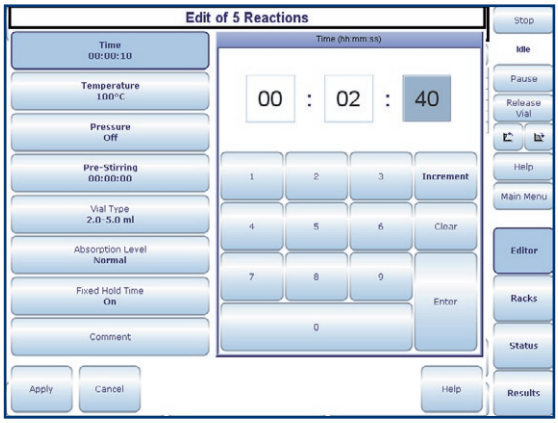
1. Editor

At the **Editor** tab, you can set up and run experiments. If your system is equipped with a robot, enter the number of reactions by pressing **Number of Vials**. You can also add a reaction to your experiment by selecting an empty vial position in the rack overview. The reactions can be edited one by one or simultaneously; select the microwave vial or vials that you want to edit in the rack overview and press **Edit**.

To edit time, temperature, pressure, and/or pre-stirring, press the parameter's button, enter the value on the keypad to the right, and press **Enter**. To change microwave vial type, absorption level, and/or whether fixed hold time is used or not, repeatedly press the parameter's button until the desired value is displayed. Enter a comment on the reaction by pressing **Comment** and using the appearing keyboard.



When using Initiator Sixty, you can use vial racks with 12 or 30 positions.



If your system is equipped with a robot, reactions can be edited one by one or simultaneously.

To be able to load and start the experiment (or add it to the queue*), press **Run** and carefully follow the instructions in the appearing dialogs.

Four different absorption levels are available. The **Normal** level can be used in most cases. The **High** or the **Very High** level should be used when heating reaction mixtures that include very polar solvents or have high ionic content, e.g. containing inorganic acids or ionic liquids. In these cases, the energy is applied at a lower rate to the reaction mixture in order to achieve a well-controlled rate of the temperature increase. The **Low** level can be used when heating reaction mixtures in low-absorbing or non-polar solvents, e.g. toluene and dioxane.

If you enter both a temperature and pressure, the system will regulate by the limiting parameter. If **Fixed Hold Time** (FHT) is **On**, the time countdown starts when the target temperature (± 5°C) or target pressure (± 2 bar) is reached, i.e. the initial time taken to reach the set temperature or pressure is not included in the heating time. If **Fixed Hold Time** is **Off**, the time countdown starts when the heating starts.

If you wish to use advanced process parameters for a reaction (i.e. set up a reaction including several heating or cooling steps, control by means of temperature, pressure, and/or power, set initial power, change stir rate, and/or cool while heating), press **Advanced Edit**.

* *The queue is only available for systems equipped with a robot.*

Software overview

2. Racks

At the **Racks** tab, you can view the contents of the rack(s) loaded onto the system, unload processed microwave vials, and edit and delete queued reactions.

By selecting a microwave vial in the rack overview, you will find out the user, experiment name, process parameters, status, and if the reaction failed (red), the reason for failure. The color of the vial position indicates the processing status. Press **Help** for color legend.

Note: This tab is only available for systems equipped with a robot.

3. Status

At the **Status** tab, you can monitor and edit the reaction in progress, delete queued experiments, and change the processing order for queued experiments.

Note: The experiment queue is only available for systems equipped with a robot.

4. Results

At the **Results** tab, you can view, comment, print, and export the results of your experiments. You can also create a new experiment from any of the experiments listed at this tab and run it, or save it on a USB memory device.

Perform tasks from your office

If you have your system connected to the network, these tasks can be performed through a standard web browser:

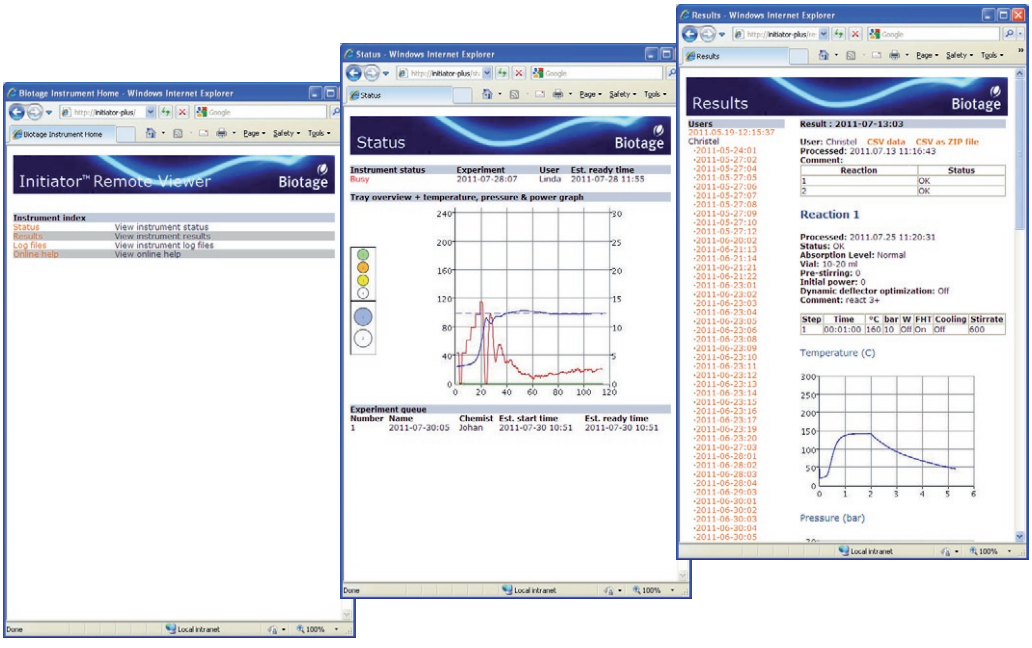
- Check the status of the system and check the progress of an experiment.
- View, print, and export experiment results.

To access the Initiator Remote Viewer, enter the URL **http://MACHINENAME** in a web browser (where MACHINENAME is the network identity of the system, or an IP-address) and press **Enter**.

More information

For more information and instructions, see “Quick start” on page 2 and the online **Help**.

For help accessing the Initiator Remote viewer, contact your IT administrator.



If you have the system connected to a network, you can check system status and view and manage results through a standard browser.

www.biotagepathfinder.com

Biotage PathFinder is a web-based service featuring a unique microwave synthesis database including more than 5000 carefully selected microwave reactions. PathFinder gives you direct access to years of experience in microwave synthesis delivered in a detailed, easy to use, and easily accessible format.

All content has been conducted on Biotage microwave systems making the methods highly reproducible. PathFinder also includes other valuable tools, such as the “Ask-a-Chemist” feature, which provides a resource for chemists to have a dialog about microwave synthesis methods directly with a Biotage Chemist experienced in microwave synthesis. Additional features include a gas-pressure calculator and the Biotage PathFinder Cookbook.

Search the reaction database

When you log on to www.biotagepathfinder.com, the search page opens. You can search the reaction database by substructure or by reaction keyword. (Figure 1.)

The hits will be listed in an overview including reaction scheme, temperature, time, and yield or purity. (Figure 2.)

For each reaction you can view a report including all information needed to repeat the reaction. It also includes literature references, analysis results, and comments about the reaction and the work-up procedure. (Figure 3.)

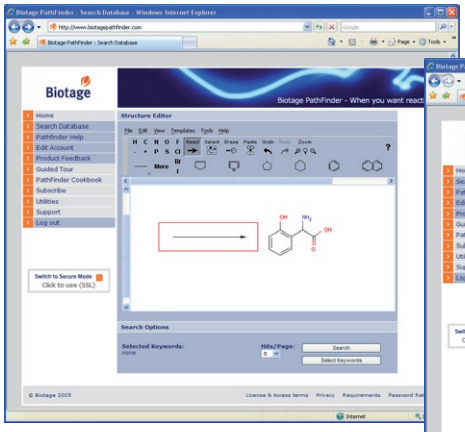


Figure 1. *Enter a simple substructure search.*

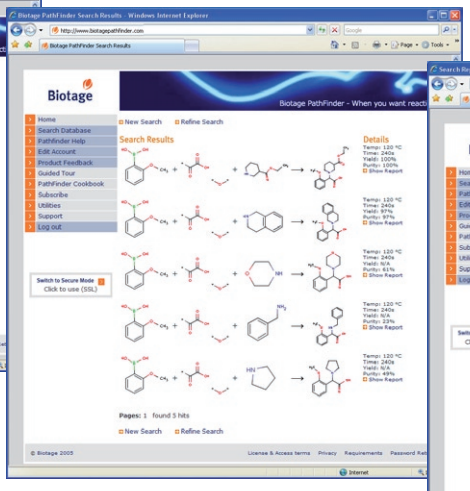


Figure 2. *Search results are displayed in an easy-to-browse format.*

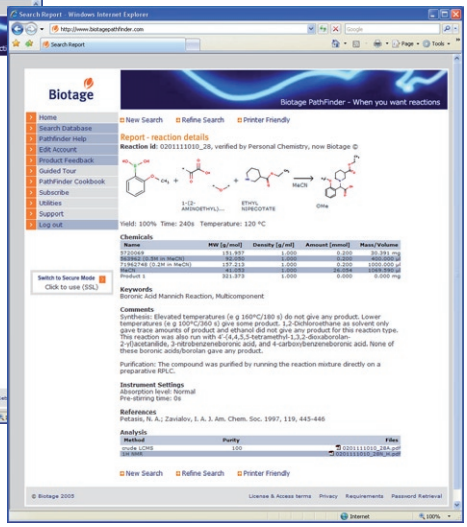


Figure 3. *Reaction details needed to perform repeated reactions are listed in an easy-to-read format.*

Getting started with microwave synthesis

Microwave synthesis is normally conducted under conditions that vary considerably from what is conventionally used in today's chemistry laboratories. Although microwave synthesis often renders results that are unique, 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.

What conditions are appropriate when performing microwave synthesis?

Biotage microwave systems support a wide variety of different reaction conditions, accommodating different solvents, volumes, concentrations, and phases, and are characterized by reproducible results.

Solvent

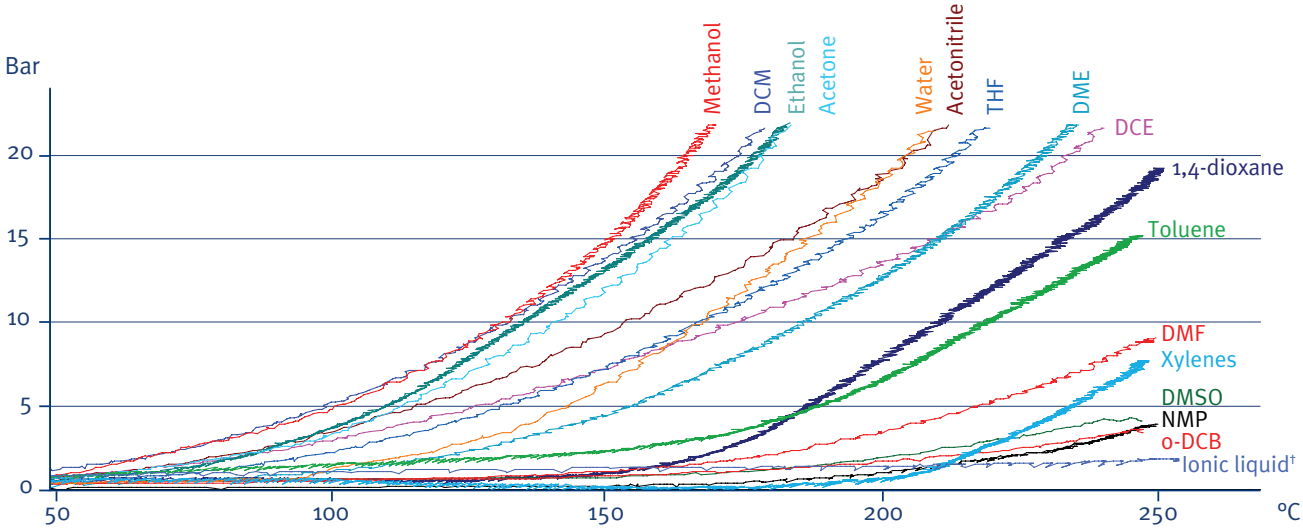
- Different solvents interact very differently with microwaves, because of their diverse polar and ionic properties.
- Acetonitrile, DMF, and alcohols are often used for microwave-assisted organic synthesis.
- You might not need to change from the solvent that is specified for the reaction under traditional chemistry conditions. First, try using the solvent that you would normally use.
- Polar solvents (e.g. DMF, NMP, DMSO, methanol, ethanol, and acetic acid) work well with microwaves due to their polarity, you can be sure that the temperature will rise substantially with these solvents. Set the absorption level to **Normal** or **High** when using 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. Under these circumstances, a very high temperature can be achieved. Set the absorption level to **Low** when using non-polar solvents.
- Ionic liquids are reported as environmentally friendly, recyclable alternatives to dipolar aprotic solvents for organic synthesis. The dielectric properties of ionic liquids make them highly suitable for use as solvents or additives in microwave-assisted organic synthesis. Ionic liquids consist entirely of ions and therefore absorb microwave irradiation extremely efficiently. Furthermore, they have a low vapor pressure, enhancing their suitability even further. Despite ionic liquids being salts, they 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.
- Solvents can behave differently at elevated temperatures and most solvents become less polar with increased temperature. For example, at elevated temperatures the bond angle in water widens and its dielectric properties approach those of organic solvents. Water at 250°C actually has similar dielectric properties to acetonitrile at room temperature. Thus, water can be used as a pseudo-organic solvent at elevated temperatures where organic molecules will dissolve, not only because of the temperature, but also because of the change in dielectric properties. This makes some reactions that normally would not run in water possible.
- Solvents with low boiling points (e.g. methanol, dichloromethane, and acetone) have lower maximum reaction temperatures due to the pressure build-up in the vessel. If a higher absolute temperature is desirable to achieve a fast reaction, it is advisable to change to a closely related solvent with a higher boiling point, e.g., 1,2-dichloroethane instead of dichloromethane.

To show the responses of various solvents to microwave irradiation, we measured the temperature and pressure of pure solvents during irradiation in an Initiator system. 5 ml solvent was heated in a 2-5 ml microwave vial, and the attained time, temperature, and pressure were noted when 20 bar or 250°C was reached. **Temperature** was set to **250°C** and **Absorption Level** to **Normal**, unless otherwise indicated.

Solvent (Volume = 5 ml)	Boiling Point (1 atm) (°C)	Time (seconds)	Temperature (°C)	Pressure (bar)
1-methyl-2-pyrrolidinone (NMP)	202	83	250	4.5
1,2-dichloroethane (DCE)	83	69	240	20
1,2-dimethoxyethane (DME)*	85	166	233	20
1,4-dioxane*	100	628	250	18
Acetone*	56	273	179	20
Acetonitrile	81	45	207	20
Dichloromethane (DCM)	40	67	176	20
Dimethylsulfoxide (DMSO)	189	44	250	3.5
Ethanol*	78	58	180	20
Ionic liquid †	n/a	71	250	0.8
Methanol*	65	85	167	20
N,N-dimethylformamide (DMF)	153	68	250	8.9
o-dichlorobenzene (o-DCB)	180	63	250	2.3
Tetrahydrofuran (THF)*	65	94	215	20
Toluene*	111	488	250	15.2
Water (deionized)*	100	66	205	20
Xylenes*	137	459	250	7.7

* *These solvents were heated using the **Low** absorption setting. The time stated is approximate, large variations can occur for low-absorbing solvents.*

† *1-butyl-3-methylimidazolium hexafluorophosphate.*



Getting started with microwave synthesis

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.

Biotage Microwave Vials 0.2-0.5 ml

Biotage Microwave Vials 0.5-2 ml

Biotage Microwave Vials 2-5 ml

Biotage Microwave Vials 10-20 ml

When using low-absorbing or non-polar solvents, e.g. toluene and dioxane, always fill the microwave vial to the specified maximum volume. For more information on Biotage Microwave Vials, see www.biotage.com.

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.

Stirring

Remember to always add a magnetic stirring bar to the microwave vial. The rotational speed of the stirring bar can be set to a value between 300 and 900 RPM. Default is 600 RPM.

Inert atmosphere

In general inert atmosphere is not initially employed in microwave chemistry, and often not needed even if the reaction is carried out in this way conventionally. If needed, flush the microwave vial with an inert gas before capping.

Time

Typically, most reactions require 2 to 15 minutes of irradiation.

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 the solvent table (on page 9) or the vapor pressure calculator at www.biotagepathfinder.com.

Note that Biotage Microwave Vials 10-20 ml may not be used at pressures above 20 bar.

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 chart below provides a way to estimate the time it will take 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** (see white numbers in the chart below).

Change in field color represents change in unit (hours/minutes/seconds). For example, if your reaction took **6 hours** at **100°C**, it will take approximately **5 minutes** at **160°C** (see red numbers in the chart below).

Temp (°C)	Times – change in field color represents change in unit									
20	1	2	4	6	8	12	24	48	96	172
30	30	1	2	3	4	6	12	24	48	86
40	15	30	1	1.5	2	3	6	12	24	43
50	8	15	30	45	1	2	3	6	12	22
60	4	8	15	23	30	45	1.5	3	6	11
70	2	4	8	11	15	23	45	1.5	3	5
80	56	2	4	6	8	11	23	45	1.5	3
90	28	56	2	3	4	6	11	23	45	1
100	14	28	56	1.4	2	3	6	11	23	40
110	7	14	28	42	56	1.4	3	6	11	20
120	4	7	14	21	28	42	1.4	3	6	10
130	2	4	7	11	14	21	42	1.4	3	5
140	53	2	4	5	7	11	21	42	1.4	3
150	26	53	2	3	4	5	11	21	42	1
160	13	26	53	1	2	3	5	11	21	38
170	7	13	26	40	53	1	3	5	11	19
180	3	7	13	20	26	40	1	3	5	9
190	1.6	3	7	10	13	20	40	1	3	5
200	49	1.6	3	5	7	10	20	40	1	2
210	25	49	2	2	3	5	10	20	40	1
220	12	25	49	1	1.6	2	5	10	20	35
230	6	12	25	37	49	1	2	5	10	18
240	3	6	12	19	25	37	1	2	5	9
250	2	3	6	9	12	19	37	1	2	4

With courtesy of David Rudge, AstraZeneca, Macclesfield, UK.

Getting started with microwave synthesis

Optimize your reaction

Optimizing a microwave synthesis is very similar to optimizing a conventional synthesis. If your first reaction was not a success, changing the target temperature and reaction time can cause significant improvement. All remaining parameters that you would usually vary (i.e. concentration, solvent, reagent, etc.) should be varied when applicable.

If the reaction is not proceeding at all or not going to completion:

- Increase the temperature. As long as the reactants/reagents can withstand the higher temperature, the only limit is the pressure build-up in the microwave vial and the security limit of 260°C (Initiator) or 310°C (Initiator^{+}).
- Extend the reaction time.
- Increase the concentration(s) of reagent(s).
- Change the solvent. Some solvents (e.g. water) will behave differently at high temperatures as they become less polar. This makes some reactions that normally would not work in polar solvents perfectly feasible.
- Change the reagent(s). Due to the high temperatures that can be reached, sometimes a less reactive, but more temperature stable, reagent can be used.
- Deflector tuning is performed each time a reaction is started. With the Deflector Optimization option turned on (in system mode) the system will also, when necessary, perform up to two tunings during the heating phase.

If you see decomposition of reactants, reagents, or products:

- Lower the temperature.
- Shorten the reaction time. It may be that the desired product is actually formed, but then decomposes rapidly at elevated temperatures. In some cases it is therefore possible to “trap” the product by using a shorter reaction time.
- Decrease the concentration(s) of reagent(s).
- Change to a more temperature stable reagent.

Open reactor access

With the open reactor access feature enabled on an Initiator+ system it is possible to monitor the in-situ temperature of the reaction using a fiber optic temperature probe (sold separately). The probe can be used to study the reaction with high precision simultaneously with the IR-sensor. In-situ temperature measurement is ideal to detect rapid temperature fluctuations, e.g. exothermic reactions.

To enable the open reactor access feature:

1. If your system is equipped with a robot:
   i. Press **Main Menu**/**Log Out** in the right-hand panel and then **Shut Down**.
   ii. When the message "It is now safe to turn off the system" appears, turn off the system.
   iii. Disconnect the communication cable from the **ROB** port at the rear of the system.
   iv. Turn on the system.
2. Press **System** in the main menu to log into system mode. All user accounts with system owner privilege are listed in the **Select User** dialog.
3. Select your user account and press **OK**.
4. If your account is password-protected, the **Password** dialog opens. Enter the password and press **OK**.
5. Select the **Organic Synthesis** tab.
6. Press **Allowed** in the **Uncapped Reactions** field.
7. The system has to be restarted for the change to take effect:
   i. Press **Log Out** and then **Shut Down**.
   ii. When the message "It is now safe to turn off the system" appears, turn off the system.
   iii. Turn on the system.

Note: To reconnect a robot, disable the open reactor access feature in system mode, shut down the system, and reconnect the robot.

To run an experiment with a temperature probe:

1. If you are not in organic synthesis mode, press **Log Out** in the right-hand panel and then **Organic Synthesis**.
2. Select the **Editor** tab in the right-hand panel.
3. Set up the experiment. Ensure to set the **Vial Capping** option to **Uncapped**.
4. Insert the uncapped microwave vial into the microwave cavity.
5. Close the cavity lid by pressing in the right-hand panel.
6. Remove the red plug located at the cavity lid using a small screwdriver.

7. Undo the screw behind the red plug, using the 2 mm hexagon spanner supplied with the system.
8. Insert a fiber optic temperature probe with a outer diameter less than 2 mm. To avoid interference with the magnetic stirring bar, insert a maximum of 9 cm of the probe when using 0.2-0.5 ml microwave vials and 10 cm when using the other three microwave vials.
9. Run the experiment by pressing **Run**.
10. When the experiment is completed (the system status is idle), remove the probe.
11. Put the screw and red plug back in place.
12. Open the lid by pressing in the right-hand panel.
13. Unload the microwave vial.

Warning:

- Do not use capped vials when running in open reactor access mode.
- Do not introduce electrical conductive materials through the open reactor access port. There is a risk of microwave radiation.
- To avoid vapor leaking out through the open reactor access port, set the target temperature to no less than 20°C below the lowest boiling point of the solvents used.

Maintenance

Clean the microwave cavity and IR-sensor

Notice: Handle chemical and liquid waste according to the Safety Data Sheets and to local/national guidelines on laboratory safety procedures.

The microwave cavity and IR-sensor must be cleaned after the occurrence of a vial breakage or leakage.

Required: the T20 Torx screwdriver supplied with the system, a pair of flat-nosed pliers, a vacuum cleaner, a soft lens cleaning tissue (or similar), cotton swabs, soft and clean cloths, an emery cloth, a waste tray insert, pressurized air, synthetic grease, water, and/or alcohol. The cleaning solution is dependent on the residues inside the cavity.

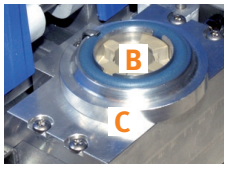
Note: If the cavity air guide, and/or the cavity lid seals are broken or distorted, they have to be replaced.

I. Shut down the system and disconnect the power cord:

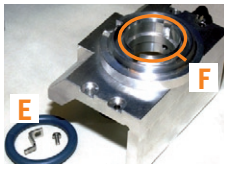
1. If the system is processing and you need to clean the microwave cavity at once, press **Stop** to abort the task in progress. If the **Processing Stopped** dialog appears, follow the instructions provided in the dialog.
2. Shut down the system, i.e. press **Main Menu**/ **Log Out** and then **Shut Down**. If the **Warning High Pressure and/or Temperature** dialog appears due to remaining high pressure and/or temperature inside the microwave vial, carefully follow the instructions provided in the dialog.
3. When the message “It is now safe to turn off the system” appears on the screen, turn off the system and disconnect the power cord.

II. Clean the microwave cavity and IR-sensor:

1. If the system is equipped with a robot, remove the rack(s).
2. Remove the cavity cover (A) by lifting it and then pulling it toward you.
3. If a cavity insert (B) and/or a microwave vial are located in the microwave cavity, remove them. Clean the cavity insert using a cloth.
4. Remove the service lid (C) by removing the four screws and disconnecting the air tubing (D). Push in the collar (blue in the image) against the fitting and pull the tubing out.



5. Remove the cavity lid seal (E) by removing the screw and carefully pulling out the lid seal.
6. Clean the cavity lid seal with water or alcohol containing mild soap. Do not use aromatic or chlorinated solvents.



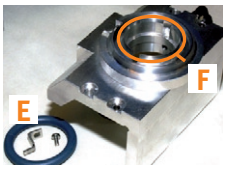
Note: If the cavity lid seal is broken or distorted, it has to be replaced.

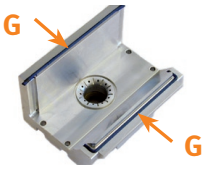
7. Clean the service lid using a cloth.
8. Clean the seal slot (F) using an emery cloth.

Warning:

- Do not attempt to operate the system if the microwave cavity contains trapped objects or moisture. There is a risk of damage to the system and microwave leakage.
- In the event of a microwave vial breakage inside the microwave cavity, the cavity and the waste tray may contain harmful residues and broken glass.
- Ensure that the cavity cover, waste tray, waste tray insert, waste lid, and cavity lid seals are in position when the system is processing. If a microwave vial would break or leak inside the microwave cavity, and the cavity cover, waste tray, waste tray insert, waste lid, or a cavity lid seal is not in its position, there is a risk of personal injury.
- Ensure that the system is connected to a supply of dry pressurized air. If the air contains liquids, the vial may break during cooling and contents may erupt, possibly resulting in personal injury and loss of materials.

9. Ensure that the service lid and all its parts are dry and that the two service lid seals (G), on the back of the service lid, are in place. If a seal is broken or distorted, contact 1-Point Support™ at Biotage.



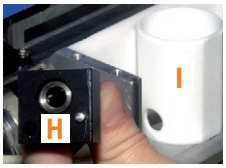


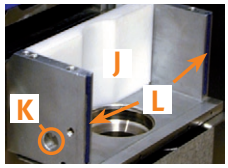
10. Put the cavity lid seal (E) back in place.

Note: Do not tighten the screw too hard.

11. Remove the IR-sensor (H) from the microwave cavity by removing the screw.

12. Clean the IR-sensor using a soft lens cleaning tissue (or similar) lightly dampened with distilled water, alcohol, or Kodak lens cleaner. Do not scratch the surface! If the IR-sensor is broken, contact 1-Point Support at Biotage.





13. Remove the cavity air guide (I) and clean it using a cloth. If the cavity air guide is broken or distorted, replace it.

14. Remove the teflon wall (J) and clean it using a cloth. If the teflon wall is broken or distorted, contact 1-Point Support at Biotage.

15. If possible, vacuum the microwave cavity. Otherwise remove as much as possible of the spill with a soft and clean cloth.

16. Clean the microwave cavity, including the IR-housing (K), using pressurized air, a cloth, and cotton swabs.

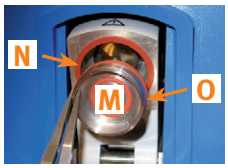
17. Ensure that all parts are dry and that the two service lid seals (L), on the side of the cavity wall, are in place. If a seal is broken or distorted, contact 1-Point Support at Biotage.

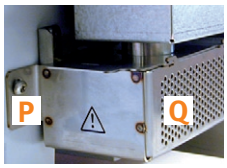
18. Reassemble the IR-sensor, teflon wall, cavity air guide, service lid, air tubing, and cavity insert.

Note: Ensure to insert the cavity air guide correctly with the hole facing the IR-housing.

19. If the inside of the cavity lid needs to be cleaned:

- Gently remove the pressure plate (M) from the lid using a pair of flat-nosed pliers.
- Clean the lid and pressure plate using a cloth lightly dampened with a solvent suitable for the residues. If the cavity lid seal (N) is broken or distorted, replace it.
- Lubricate the o-ring (O) on the pressure plate using synthetic grease, e.g. Super Lube, and put the pressure plate back in place. Ensure that the plate is positioned correctly.





III. Clean the waste tray and replace the waste tray insert:

1. Remove the waste tray screw (P), if present, and unhook the waste tray (Q).

2. Remove the waste lid (R) and empty the waste tray of the disposable waste tray insert (S) with collected glass and chemical debris in a designated waste container.

3. Clean the waste tray.

4. Ensure that the waste tray is dry, and then insert a new waste tray insert into the waste tray and put the waste lid back in place.

5. Remount the waste tray on the cavity wall.

IV. Put the cavity cover back in place and perform a reference run:

1. Put the cavity cover and, if the system is equipped with a robot, the rack(s) back in place.

2. Connect the power cord and turn on the system.

3. Check the IR-sensor and the pressure sensor by performing a reference run; see page 16.

Maintenance

Perform a reference run

A reference run should be performed when it is required to check the accuracy of the temperature and/or pressure readings, e.g. after the microwave cavity and IR-sensor have been cleaned due to a vial breakage.

To perform a reference run:

1. Cap an unused 2-5 ml microwave vial containing 5 ml of deionized water and a magnetic stirring bar.
2. Select the **Editor** tab (in organic synthesis mode) and set up a reaction with the process parameters 250°C (Initiator) or 300°C (Initiator⁺) and 5 minutes. Set the absorption level to **Normal** and the **Fixed Hold Time** (FHT) option to **On**.
3. Press **Run**. The **Select User** dialog opens.
4. Select user and press **OK**. Follow the instructions in the **Load Experiment** dialog.
5. Monitor the temperature versus pressure at the **Status** tab and check that the readings are within the limits listed below:

Temperature	Pressure
100°C	0.4 ± 0.4 bar
160°C	5.2 ± 1.7 bar
180°C	9.0 ± 2.0 bar
200°C	14.5 ± 2.5 bar
214–224°C	22 bar
230–245°C	32 bar (only Initiator⁺)

6. If the readings are not within the limits, clean the IR-sensor (see page 14) and rerun the reference run. If this does not solve the problem, the system needs to be calibrated; contact 1-Point Support at Biotage. See the back of this document or visit www.biotage.com for contact information.

For more information on how to set up an experiment, see the online **Help**.

Release remaining pressure manually

Only release remaining pressure inside the microwave vial manually by pressing the **Vent** button in the **Warning High Pressure and/or Temperature** dialog that appears due to remaining high pressure and/or temperature inside the microwave vial. Carefully follow the instructions appearing on the screen.

Clean the exterior of the system

If the touch screen has been contaminated by chemicals, it must be cleaned immediately.

To clean the exterior of the system:

1. Shut down the system, i.e. press **Main Menu**/**Log Out** and then **Shut Down**.
2. When the message "It is now safe to turn off the system" appears on the screen, turn off the system and disconnect the power cord.
3. Clean the touch screen and the exterior of the system, using a soft and clean cloth. The cloth can be dry or lightly dampened with a neutral detergent or alcohol.
4. When the system has been cleaned, connect the power cord and turn on the system.

Warning:

- Ensure that the system is turned off and the power cord is disconnected before cleaning the exterior of the system and replacing fuses.
- Use only correct replacement fuses. Incorrect fuses create a potential fire hazard.

Replace the fuses

You need clean, non-abrasive, dry cloths and ethanol.

To replace the fuses:

1. Turn off the system and disconnect the power cord.
2. Unscrew the two fuse holders at the rear of the system.
3. Clean the new fuses using a cloth lightly dampened with ethanol and wipe them dry with a dry cloth.

Note: Do not touch the metal surfaces with your hands after the fuses have been cleaned.

4. Replace the blown fuse(s).
5. Put the two fuse holders back in place.

Consumables and accessories

In order to maintain compliance, only consumables and accessories supplied by Biotage must be used in the system. To order consumables and accessories, see contact information on the back of this document or visit our website www.biotage.com.

Accessories necessary for the "Maintenance" section are listed below.

Part no.	Description	
354180		Lower cavity lid seal (E), qty 1
356103		Cavity insert (B), qty 1
354878		Vent screw replacement, qty 1
354974		Cavity air guide (I), qty 1
355366		Waste tray inserts (S), qty 5
355723		Upper cavity lid seal (N), qty 1
413234SP		Fuse 10 AT, 6.3x32 mm, qty 4

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