**What conditions are appropriate when performing microwave synthesis?**

**Solvent**

* Different solvents interact very differently with microwave, because of their diverse polar and ionic properties.
* Acetonitrile, DMF and alcohol 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.
* Non-polar solvents (e.g. toluene, dioxane, THF) can be heated only if other components in the reaction mixture respond to microwave energy, if the reaction mixture contains either polar solvent, more concentrated reaction mixtures might be preferable. Under these circumstances, a very high temperature can be achieved.
* Ionic liquids are reported as new, 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 w wide range of organic solvents, and can therefore be used to increase the microwave absorption of low absorbing reaction mixtures.
* Solvents can behave differently at elevated temperature 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 as acetonitrile at room temperature. Thus, water can be used as 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 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, dichloroethane instead of dichloromethane.

**Volume**

* Do not exceed a fall below the vial’s specified volumes. The use of a cavity insert allows you to freely choose between four different vial sizes; 0.2-0.5 mL, 0.5-2 mL, 2-5 mL and 10-20 mL. Too low volume will give an incorrect temperature measurement; while to high a volume does not leave sufficient head-space for pressure build-up.

**Concentration**

* The concentration depends on the type of chemistry that is performed. A unimolecular reaction is independent of concentration and can be performed in a very dilute solution. 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**

* All different phases can be used, i.e. solution phase, solid phase, solid supported reagents, solvent free and scavenger resins.

**Stirring**

* Add always a magnetic stirring bar to the microwave vial.

**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 vial with an inert gas before capping.

**Time**

* Typically, most reactions require 2-15 minutes of irradiation.

**Temperature**

* All synthesis systems from Biotage work in a temperature range between 60 °C and 250 °C. 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.

**Presure**

* The reaction can be safely performed at pressures of up to 20 bar. If the pressure in a vial become higher, the heating is automatically stopped and cooling begins. For an indication of the expected pressure of a reaction, please use the solvent table or the vapor pressure calculator at [http://www.biotagepathfinder.com.](http://www.biotagepathfinder.com)
* To calculate the vapor pressure of volatile chemicals, go to [http://www.biotagepathfinder.com/pressurePC.jsp.](http://www.biotagepathfinder.com/pressurePC.jsp) Select a chemical from the list, enter a temperature, and then press the **Go!** button. To clear all fields, press the Clear button.

**Time prediction**

* Most times, reactions proceed faster using microwave synthesis simply because they are conducted at higher temperatures. Based ~ on Arrhenius equation: 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.

**Optimize your reaction**

* Optimizing a microwave synthesis is very similar to optimizing a conventional synthesis. If your first reaction was not 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 vial and the security limit of 250 °C.
* Extend the reaction time.
* Increase the concentration(s) of reagent(s).
* Change solvent. Some solvents, e.g. water) will behave differently at high temperature as they become less polar. These make 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.

**If you see decomposition of reactans/reagents/products:**

* Lower the temperature.
* Shorten the reaction time. It may be that the desired product is actually formed, but then decompose rapidly at elevated temperature. 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 reagents.