4.3: Solvent Alternatives

Alternative Solvent Systems or Modes

Gas Phase

The gas phase is a very useful modality to allow reactions to occur because (like the hydrophobic effect) it forces reactions or processes to occur through non-solvent-mediated channels. For example, the production of methanol can be done in the gas phase by reaction of “syn” gas (hydrogen and carbon monoxide) with ZnO as the solid catalyst for the reaction to occur.

No Solvents

It is altogether possible and highly desirable to use the starting materials themselves for the reaction of interest. This is doable if one of the reactants is a liquid that can allow the other(s) to dissolve into it. This has been shown by taking a p-xylene and reacting it with oxygen to make the terephthalic acid:

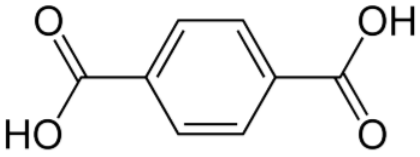


Figure 4.3.1 *A molecular representation of terephthalic acid* https://www.wikiwand.com/en/Terephthalic_acid

The acid in Figure 4.3.1 can then be used directly with ethylene glycol to synthesize polyethylene terephthalate:

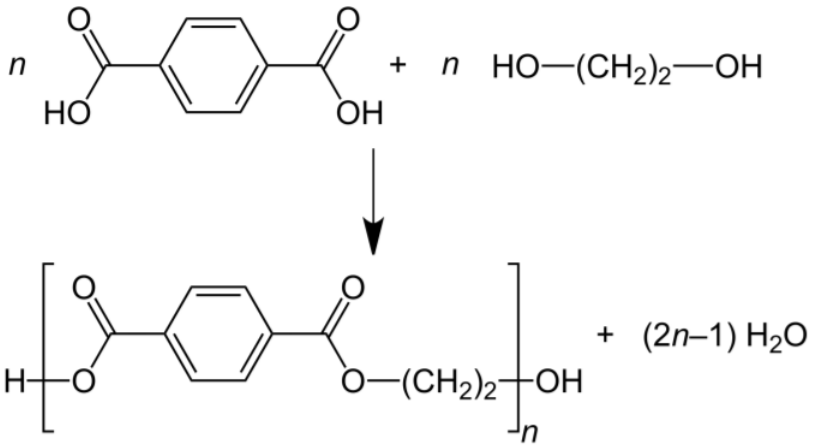


Figure 4.3.2 *The reaction of terephthalic acid with ethylene glycol leading to the production of the polymer.* https://www.wikiwand.com/en/Polyethylene_terephthalate

Melt State

It is possible to combine two solids to provide a composition that can achieve a eutectic point, or melts/solidifies at a single temperature lower than the melting points of the separate constituents or of any other mixture of them. At the eutectic point, you can achieve an isotropic blend of dissolved materials such as evidence in Figure 4.3.3.

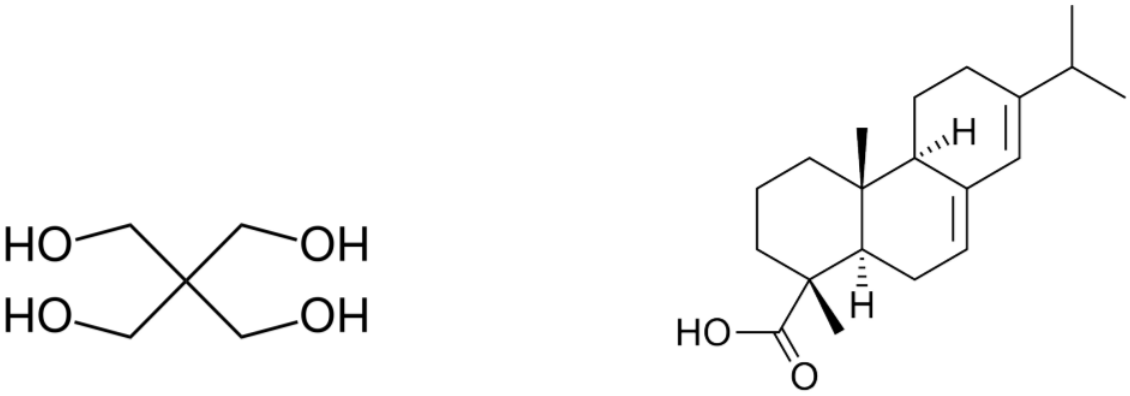


Figure 4.3.3: A mixture of pentaerythritol (left) and abietic acid (right) can blend in a melt (eutectic) that can provide a pentaester product. https://www.wikiwand.com/pt/Pentaeritritol; https://www.wikiwand.com/en/Abietic_acid

Triggered Solid State Reactions

It is possible to induce a chemical reaction outside of the melt by introducing a trigger such as acid, ultrasound, grinding, light, etc. Such triggers take the place of solvent-mediated reaction stabilization. For example, the following reactions are amenable to such triggers:

Michael Reaction:

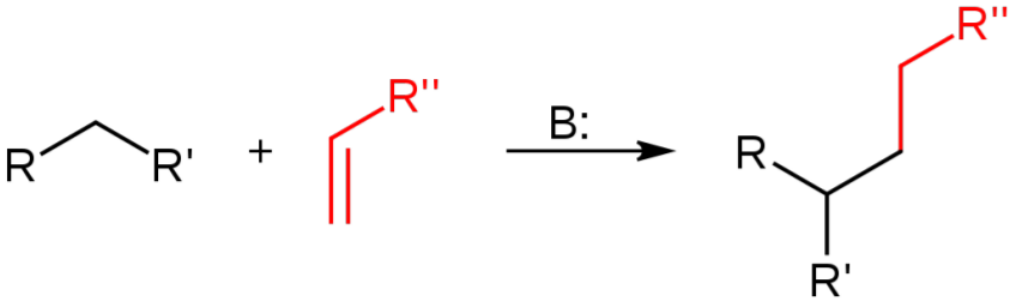
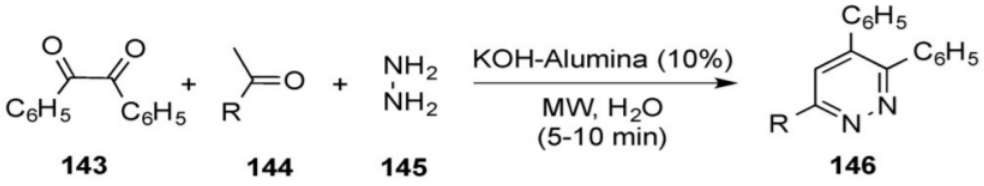


Figure 4.3.4: A simplified representation of the Micheal reaction. The conjugation of alkanes to unsaturated substrates is a key step for the synthesis of various complex natural products, antibiotics, and chiral compounds. http://www.wikiwand.com/en/Michael_reaction

In addition, it is possible to do the reaction using a catalyst such as alumina with microwave induction as shown in Figure 4-9:



R = C_6H_5, 4-MeC_6H_4, 2-$MeOC_6H_4$, 4-$MeOC_6H_4$, 4-BrC_6H_4, 4-ClC_6H_4, 4-$NO_2C_6H_4$, naphthyl

Figure 4-9 proceeded very efficiently using potassium hydroxide on alumina (KOH-alumina) as a mild, efficient, and recyclable catalyst. This approach gave pyridazines with high yields (73%–89%) after only several minutes.

There are a number of other reactions that are similar in their reactivity as a function of triggers in water (non-organic) and without catalysts.

Baeyer-Villiger:

For example, the Baeyer-Villiger Reaction is an important reaction in making an ester or lactone

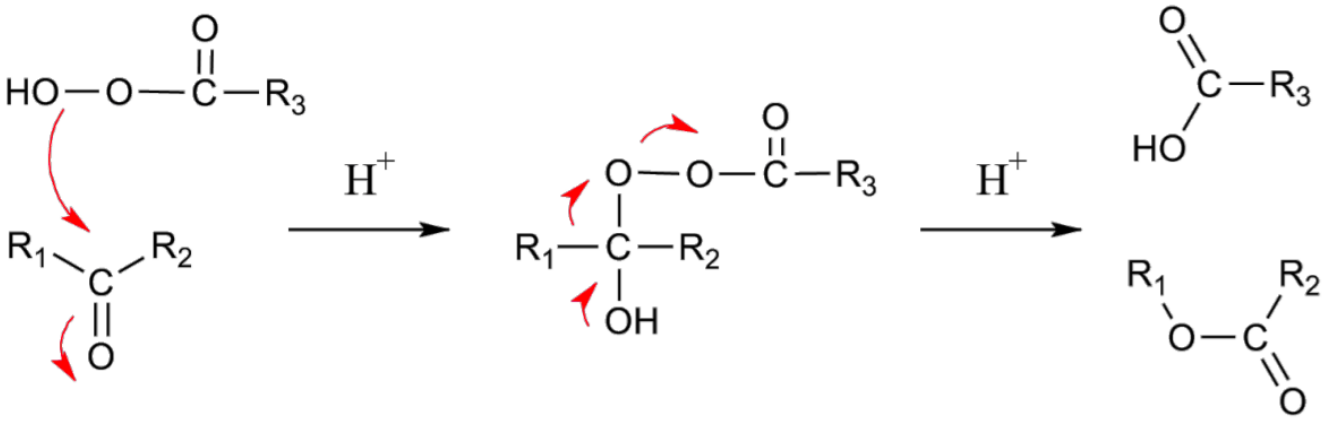


Figure 4.3.6: A depiction of the Baeyer-Villiger reactions with electron pushing arrows. commons.wikimedia.org/wiki/File:Baeyer-Villiger_oxidation_(mechanism).png

The Baeyer-Villiger Oxidation is the oxidative cleavage of a carbon-carbon bond adjacent to a carbonyl to converts ketones to esters and cyclic ketones to lactones. It may vw carried out with peracids, such as m-CBPA, or with hydrogen peroxide and a Lewis acid.

Benzilic Acid Rearrangement

1,2-Diketones undergo a rearrangement in the presence of a strong base to yield αhydroxycarboxylic acids. The best yields are obtained when the diketones do not have enolizable protons. Shown below in Figure 4.3.7 is a representation of the mechanism of the reaction.

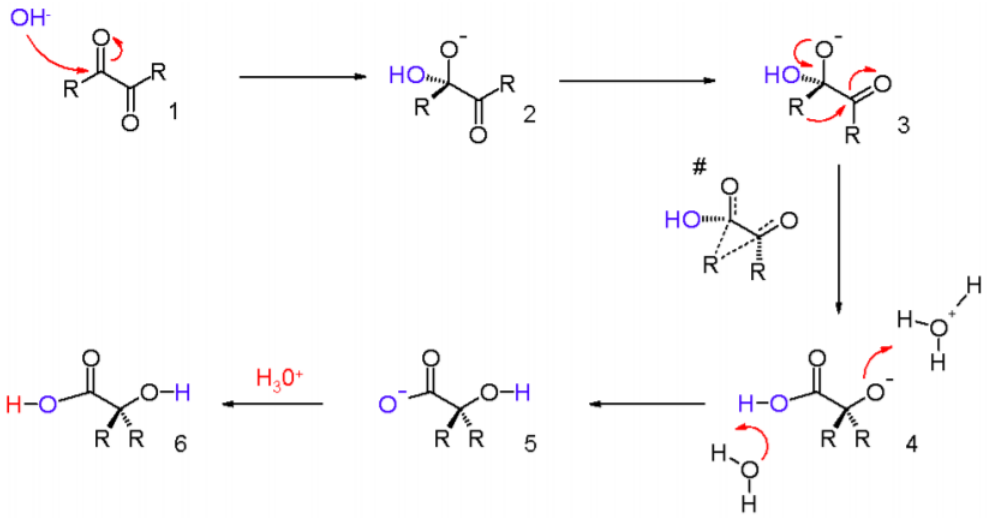


Figure 4.3.7: The mechanism of the Benzillic Acid Rearrangement. https://commons.wikimedia.org/wiki/File:Benzilicacidrearrangement.png

Benzilic acid rearrangement has traditionally been conducted by heating benzyl derivatives and alkali metal hydroxides (KOH) in aqueous organic solvent. However, the rearrangements proceed more efficiently and quickly in the solid state.

Williamson Ether Synthesis

The Williamson Ether Synthesis is an organic reaction forming an ether from an organohalide and a deprotonated alcohol (alkoxide) that is done in organic solvents. However, a very rapid synthesis of symmetrical and asymmetrical ethers in “dry” media under microwave radiation has been reported (http://www.cyfronet.krakow.pl/~pcbogdal/alcohol/). The reaction was carried out by mixing an alcohol with 50% excess of an alkyl halide and catalytic amount of tetrabutylammonium bromide, adsorbed onto potassium carbonate or a mixture of potassium carbonate and potassium hydroxide, and irradiated in open conditions in a domestic microwave oven for 45-100 s. In the absence of the ammonium salt, ethers were not detected or were very low yield.

Friedel-Crafts Reaction

The opportunity to perform acylation or alkylation of an aromatic nucleus is a very important transformation in organic chemistry. The principal tool we have for such a transformation is the Friedel-Crafts, a classical reaction dating back to the 19th century, can be done in a green way to avoid the need for acid chlorides, Lewis acids, and hydrochloric acid waste products. Shown below in Figure 4.3.8 is a representation of the photo-Friedel-Crafts, a mild and greener alternative to the classical analogue.

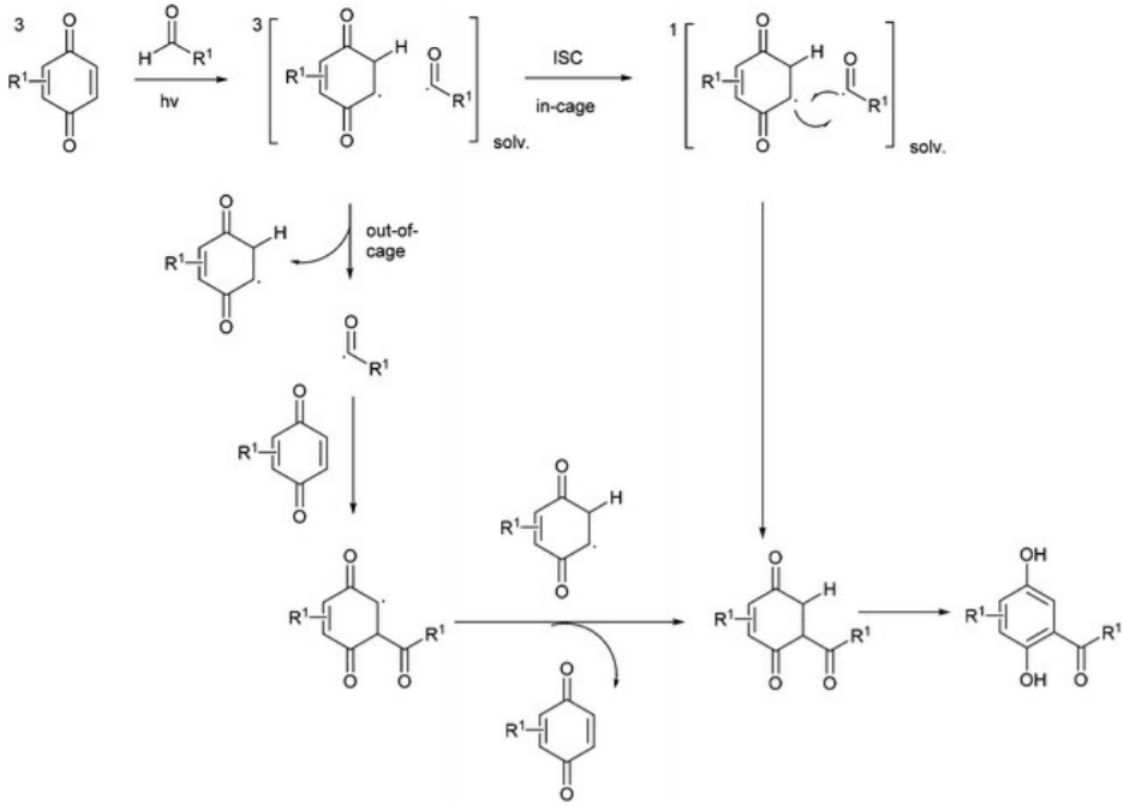


Figure 4.3.8: The solar-induced Friedel-Crafts reaction in which the elegance of the photoreaction is revealed by its simplicity, atom economy, and efficiency. Reproduced from Green Chemistry 2013, 15, 2830-2842. DOI:10.1039/C3GC41477A.

Ball Milling

Ball milling works on the principle of impact and attrition; size reduction results from impact as the balls drop from near the top of the shell. A ball mill is made up of a hollow cylindrical shell rotating about its axis. The axis may be either horizontal or at an acute angle to the horizontal. The shell is partially filled with balls whose grinding by action of balls, made of steel (chrome steel), stainless steel, ceramic, or rubber, results in much finer particles. The inner surface of the cylindrical shell is usually lined with an abrasion-resistant material such as manganese steel or rubber whereas less wear takes place in a rubber-lined mill. One of the reactions that is done in this manner is polymerization of MMA (methylmethacrylic acid) to PMMA (poly-) shown in 4.3.9. Below is a video resource that shows the process of ball milling. In this video it is possible to see how larger materials could be broken down and ground to specific sizes based on the size of grinding ball used.

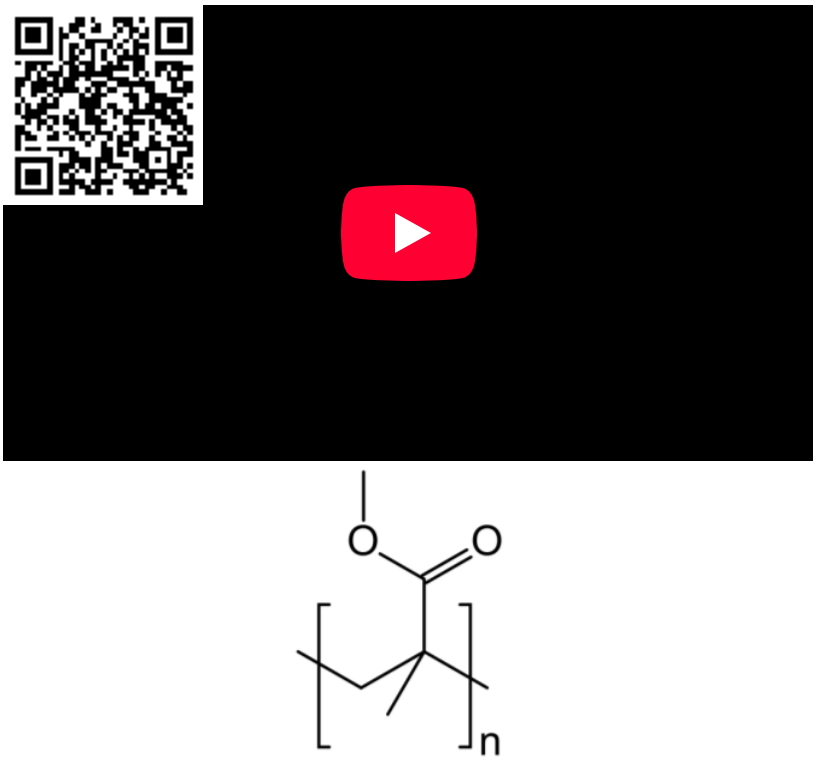


Figure 4.3.9: The opportunity to make one of the world's most abundant synthetic materials shown above (PMMA) through ball milling addresses fundamental green chemistry principles. https://www.wikiwand.com/en/Poly(methyl_methacrylate)

The polymerization of MMA is normally done through one of several chemical-initiated approaches. In the ball milling approach, the application of mechanical energy is sufficient to conduct the reaction, a significant finding! The same type of approach can be used to extract lignin, the third or fourth most abundant polymer on the planet. A generic molecular representation of the structure of lignin is shown in 4.3.10.

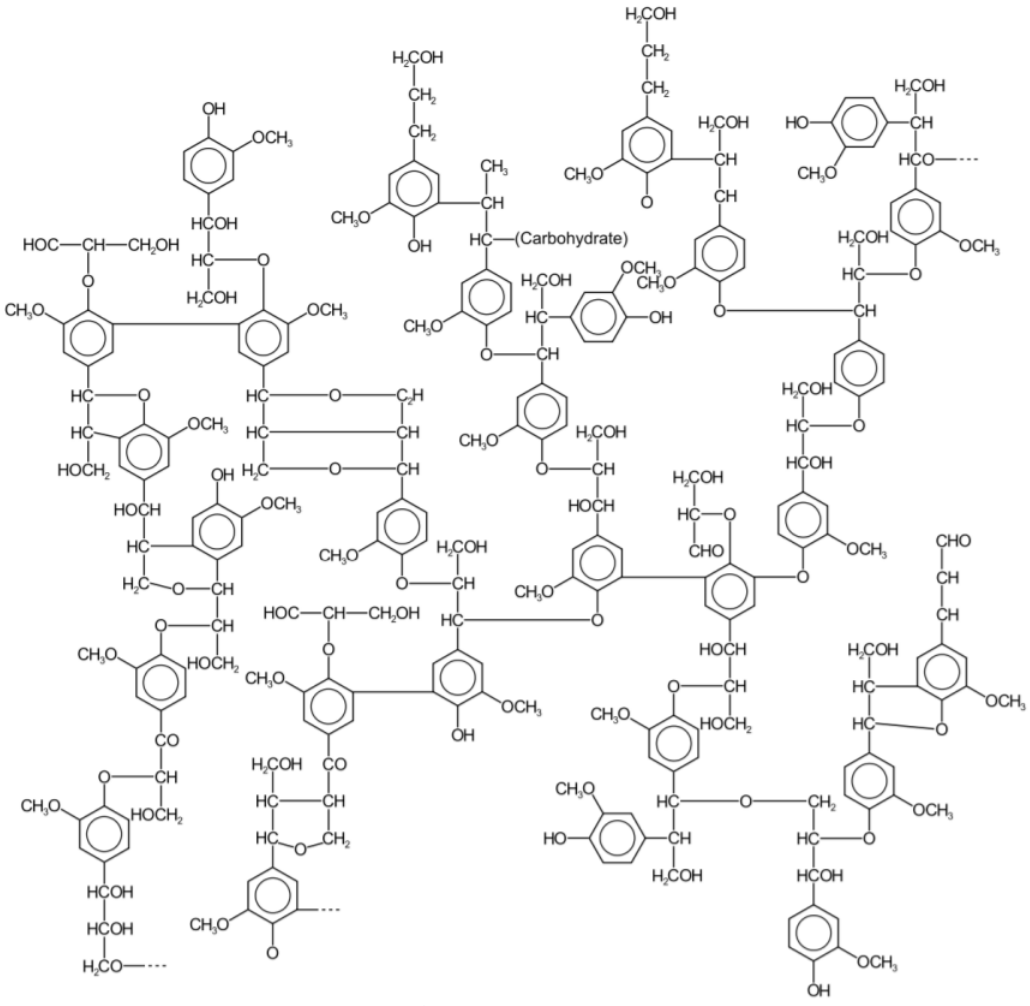


Figure 4.3.10: A chemical representation of the two-dimensional structure of lignin as it is known from gymnosperms (softwoods). https://en.Wikipedia.org/wiki/Lignin

Process Intensification

Process intensification can be defined as a strategy for introducing dramatic reductions in the footprint of a chemical plant to reach a given production objective. These reductions may consist of shrinking the size of pieces of equipment and reducing the number of unit operations or apparatuses. Such reductions tend to be significant because the objective is to dramatically reduce energy, materials waste, and process efficiency. Several of its most salient characteristics are:

- http://tinyurl.com/bpwpah9
- Continuous, short contact times
- Minimizes further reaction
- Higher, purer yields
- Mixing & heat transfer are very good! No explosive limits reached!

Reactive Extrusion

Reactive extrusion is a chemical engineering process characterized by the forced mixing of one or more components under high pressure conditions for a specific end goal. Hot melt extrusion is one example of this. It is defined as the application of heat and/or pressure to melt a polymer and force it though a small space (extruder) as part of a continuous process. It is a well-known process that was developed to make polymer products of uniform shape and density. It is widely applied in the plastic, rubber and food industries to prepare more than half of all plastic products including bags, films, sheets, tubes, fibers, foams, and pipes.

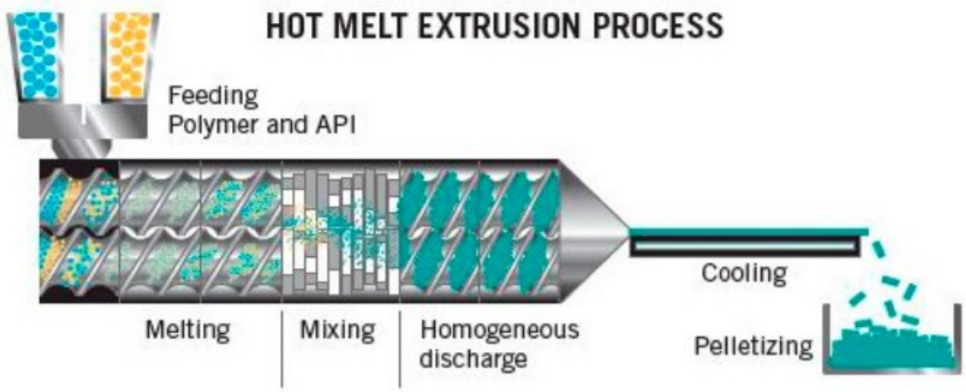


Figure 4.3.11 *+A simple idealization of the hot melt extrusion process in which the feed (polymer and API or Anionic Polymerization Initiator) go into a melting and mixing stage to ultimately yield pellets upon cooling. www.particlesciences.com/news...extrusion.html*

Supercritical Fluid

A supercritical fluid (sCF) is a substance at a temperature and pressure that are above the critical point, at which distinct liquid and gas phases do not exist. It is a very unique phase that can effuse through solids like a gas, and dissolve materials like a liquid.

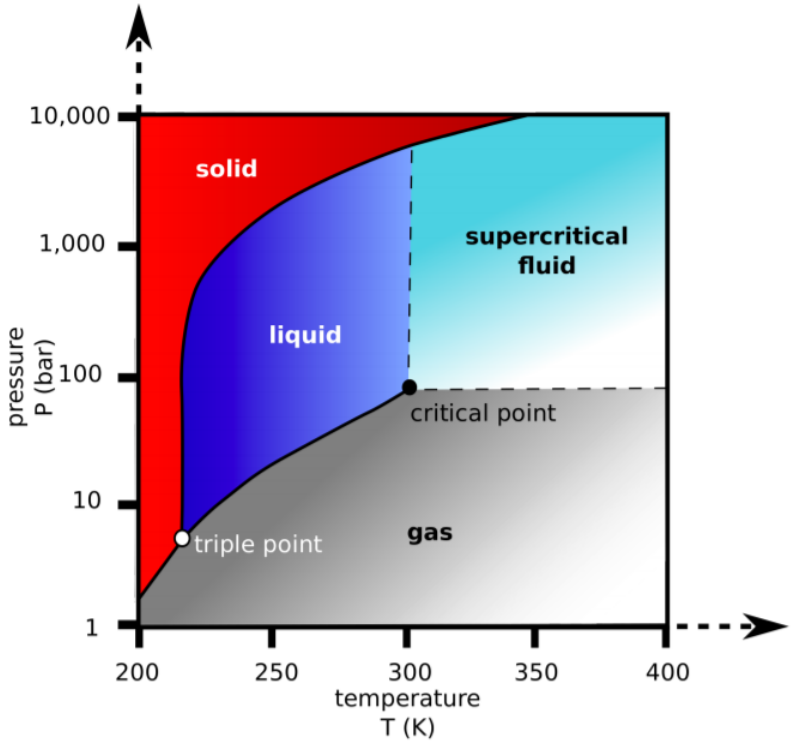


Figure 4.3.12: A phase diagram for the various states a substance can exhibit as a function of pressure and temperature. Notice that the upper right “quadrant” is the so-called supercritical fluid state. en.Wikipedia.org/wiki/Supercritical_fluid

sCFs are extremely useful in green chemistry because they can be derived from environmentally friendly materials such as water and carbon dioxide with little to no impact on the carbon footprint of the planet.

Water as a Solvent

Water can behave as an exquisite solvent in a host of typical organic reactions by virtue of its ability to encourage reactivity via the “hydrophobic effect”.

Microemulsions

Microemulsions are clear, thermodynamically stable, isotropic liquid mixtures of oil, water and a surfactant that are frequently in combination with a co-surfactant. The aqueous phase likely contains salt(s) or other ingredients, whereas the “oil” may actually be

a complex mixture of different hydrocarbons and olefins.