GREEN SYNTHESIS

Microwave/Ultrasonic Assisted Synthesis

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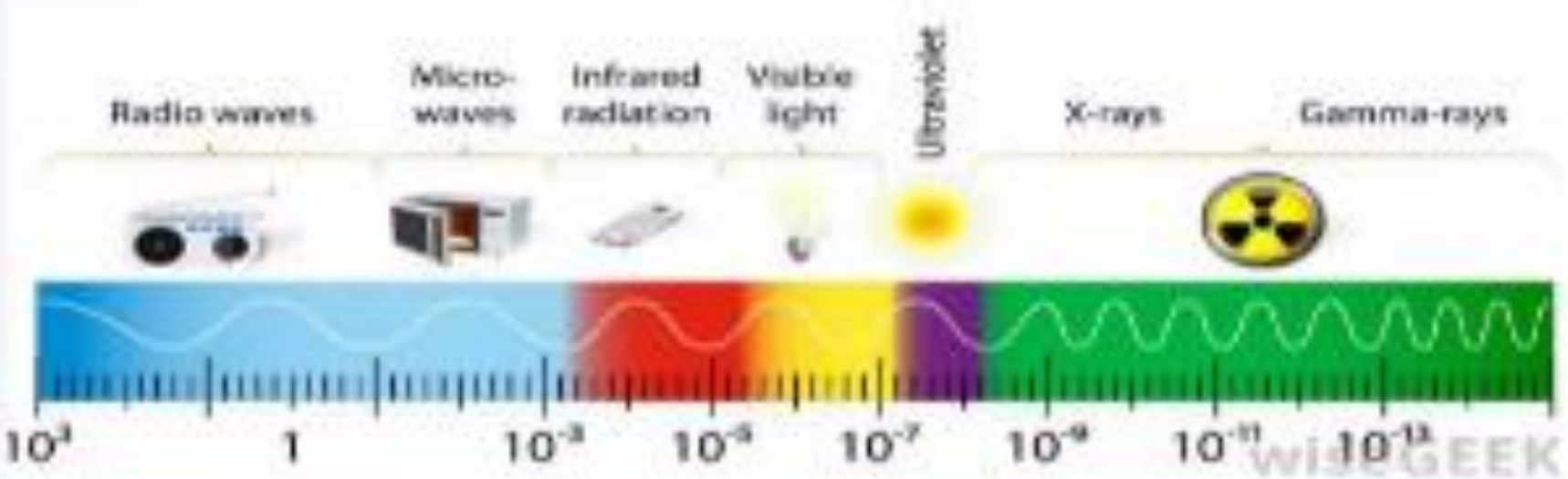
Green Synthesis/Non Conventional Techniques for synthesis of organic or inorganic compounds

There are several non conventional techniques for synthesis of organic and organometallic compounds which provides alternatives pathway for reaction due to the formation of high energy intermediates. Green synthesis is better than conventional synthesis which requires less energy, less time, less wastes, less hazardous without any change in the structure of organic compounds.

1. **Microwave Assisted Synthesis**
2. **Ultrasonic Assisted Synthesis**
3. **Photo Chemical Reaction**
4. **Electro & Mechano Chemistry**

What are microwaves?

- **Microwave** is a form of electromagnetic radiation with wavelength ranging from about one meter to one millimeter corresponding to frequencies between 300 MHz and 300 GHz respectively.
- It uses the EMR that pass through material and causes the oscillation of molecules which produces heat.



Microwave Irradiation

- Microwaves act as high frequency electric fields and will generally heat any material containing mobile electric charges, such as polar molecules in a solvent or conducting ions in a solid.
- **MW energy is non ionizing and thus does not change the molecular structure of the compound, it only provides thermal activation.**
- Microwave irradiation provide the enhanced reaction rate or speed to the chemical reaction.
- Along with the formation of variety of carbon heteroatom bonds.

Conventional heating *v/s* Microwave radiation technique

Conventional heating	• involves the use of a furnace or oil bath, which heats the walls of the reactor by convection or conduction. • The core of the sample takes much longer to achieve the target temperature.
Microwave technique	• microwave radiation acting as internal heat source. • Microwave absorption is able to heat the target compounds without heating the entire furnace or oil bath.

Microwave assisted reactions

- Microwave irradiation has gained popularity as a powerful tool for rapid and efficient synthesis of a variety of compounds because of selective absorption of microwave energy by molecules.
- This phenomenon is dependent on the **ability of a specific material to absorb microwave energy and convert it into heat**.
- Microwave passes through material and causes oscillation of molecule which produces heat.
- Microwave heating produces heat in the entire material in the same rate and at the same time at a high speed and at a high rate of reaction.
- Microwave heating is the best process due to the microwave couple directly with the molecule that are present in the reaction mixture, leading to fast rise in temperature, faster reaction and cleaner chemistry.

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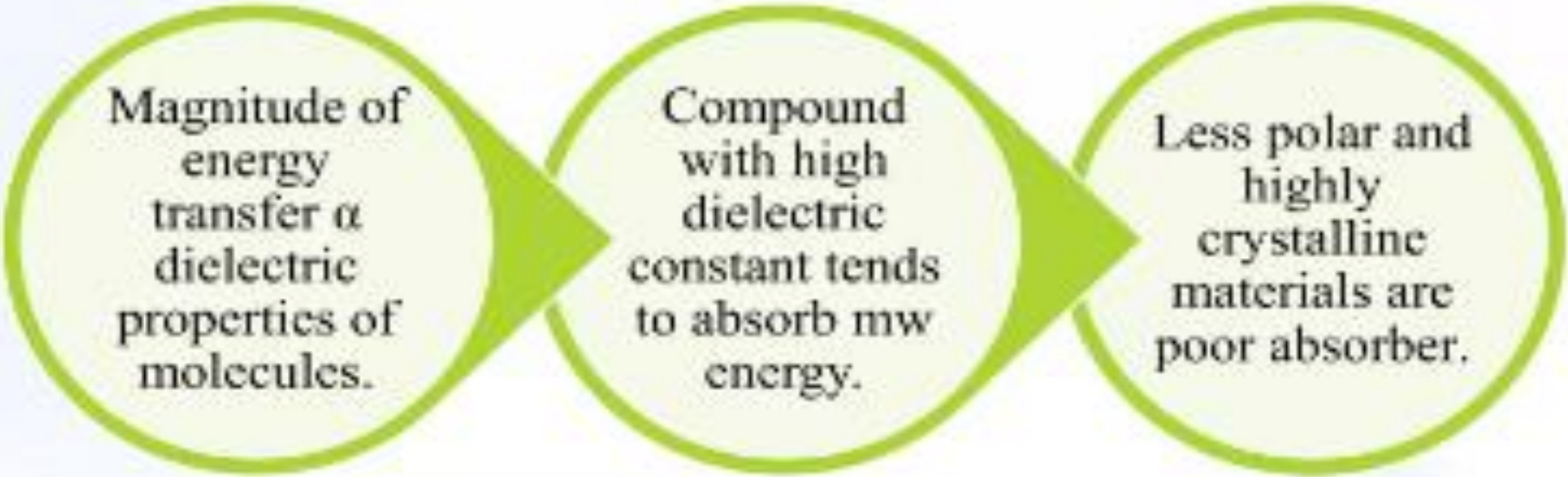
- The microwave chemistry is also called as Green Chemistry because it does not produce any hazardous material like gas, fumes, etc.
- Microwave heating rate can be depending upon dielectric properties of material.
- Dielectric properties describe the ability of a material to absorb, transmit and reflect electromagnetic energy.



Mechanisms of microwave heating

- All the materials are not susceptible to microwave heating as response of various materials to microwave radiation is diverse.
- Microwave absorbing materials (e.g. water) are of utmost important for microwave chemistry.
- There are three main different mechanisms are involved for their heating namely:

1. Dipolar polarization
2. Conduction mechanism
3. Interfacial polarization.

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- **Dipolar polarization**

For a substance to be able to generate heat when irradiated with microwaves it must be a dipole, i.e. its molecular structure must be partly negatively and partly positively charged.

Since the microwave field is oscillating, the dipoles in the field align to the oscillating field.

This alignment causes rotation, which results in friction and ultimately in heat energy.

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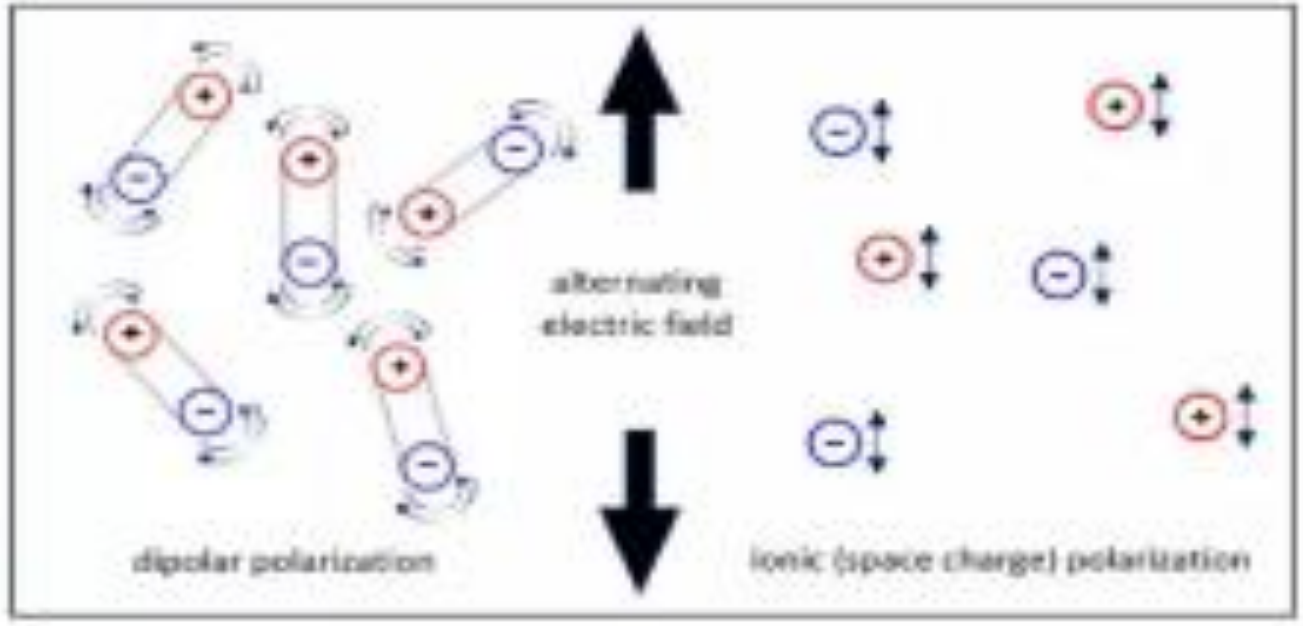
- **Ionic conduction**

During ionic conduction, dissolved (completely) charged particles (usually ions) oscillate back and forth under the influence of microwave irradiation.

This oscillation causes collisions of the charged particles with neighboring molecules or atoms, which are ultimately responsible for creating heat energy.



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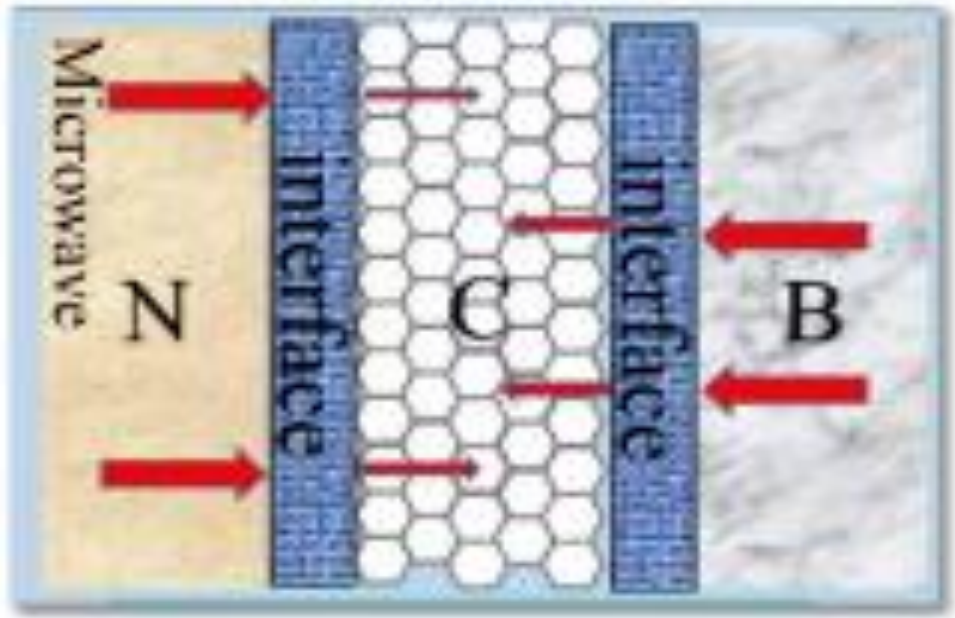
- **Interfacial polarization**

The interfacial polarization method can be considered as a combination of both the conduction and dipolar polarization mechanisms.

It is important for heating systems that comprise a conducting material dispersed in a non-conducting material.



Merits of microwave assisted reactions

- Higher temperature can be obtained.
- Faster reactions, lesser by products, pure compounds.
- Better yield and higher purity.
- Absolute control over reaction parameters.
- Uniform and selective heating.
- Energy efficient, rapid energy transfer.
- Easy access to high pressure performance.
- Does things that can't be done conventionally.
- Rapid synthesis results in lesser evaporation of solvents.

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- Green synthesis

- Possibility of convenient solvent superheating.
- Excellent parameter control.
- Access to automated setups and parallel synthesis.
- Possibility of stirring.
- Continuous power output.

Demerits of microwave assisted reactions

- sudden increase in temperature may led to the distortion of molecules.
- Reactions are very vigorous and which may be hazardous.
- Heat force control is difficult Water evaporation.
- Closed container is dangerous because it could be burst.
- Short reaction period, so care must be taken during the process.
- Microwave reactors are expensive so care must be taken during their use.
- Many other things like, temperature sensitive reactions, reactions involving bumping of material, reaction which effervescences and color reaction are not be done in microwave reactor.

Superheating effects of microwave

- Temperature of solvent above its normal boiling point due to heating by microwave is called superheating.
- Superheating is due to:

1. direct interaction of microwaves with molecules of entire solvent causing sudden rise in temperature.

2. nucleation sites-present on container wall prevents vaporization of energy to top surface of solvent.

- If 1lit og water is superheated by only 1°C, it can produce about 3 lit of steam.

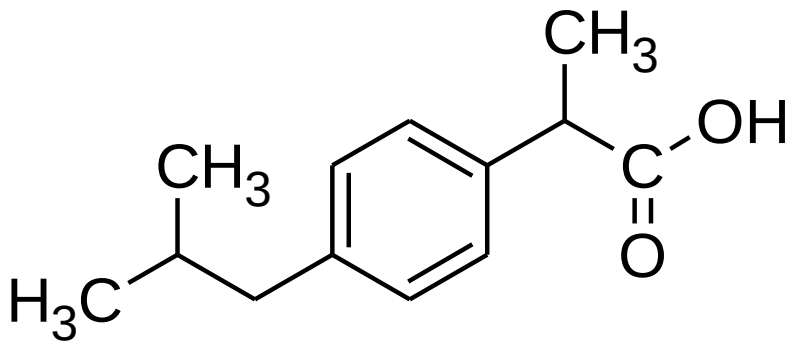
Increased reaction rate

- Microwave heating depends on two major factors:
- factor "A" which describe thermomolecular mobility and depends upon the frequency of vibrations of the molecule at reaction interface.
- The other reason is the alteration in the exponential factor by affecting the free energy of activation of delta G4.
- We know that with every 10°C rise in temperature the rate of reaction become double.
- For a reaction to be completed it takes 80 min in conventional system but if the same reaction takes place in microwave irradiation it takes only 10 min this shows that in microwave irradiation the rate of reaction speeds up.

Green Synthesis

❖The Synthesis of Ibuprofen

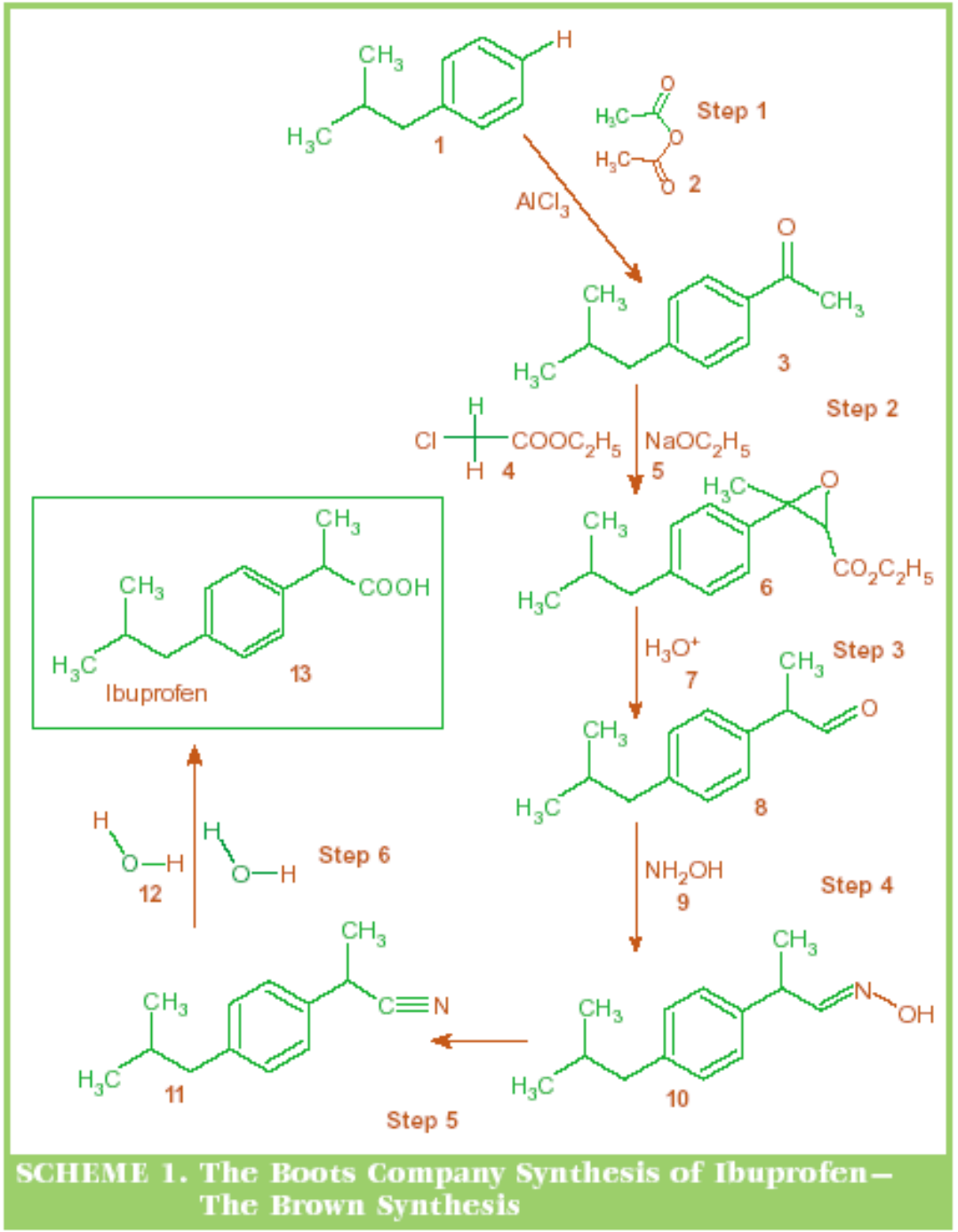
- Advil, Motrin, Medipren
- 28-35 million pounds of ibuprofen are produce each year
- (37-46 million pounds of waste)



2-(4-isobutylphenyl)propanoic acid

Brown Synthesis

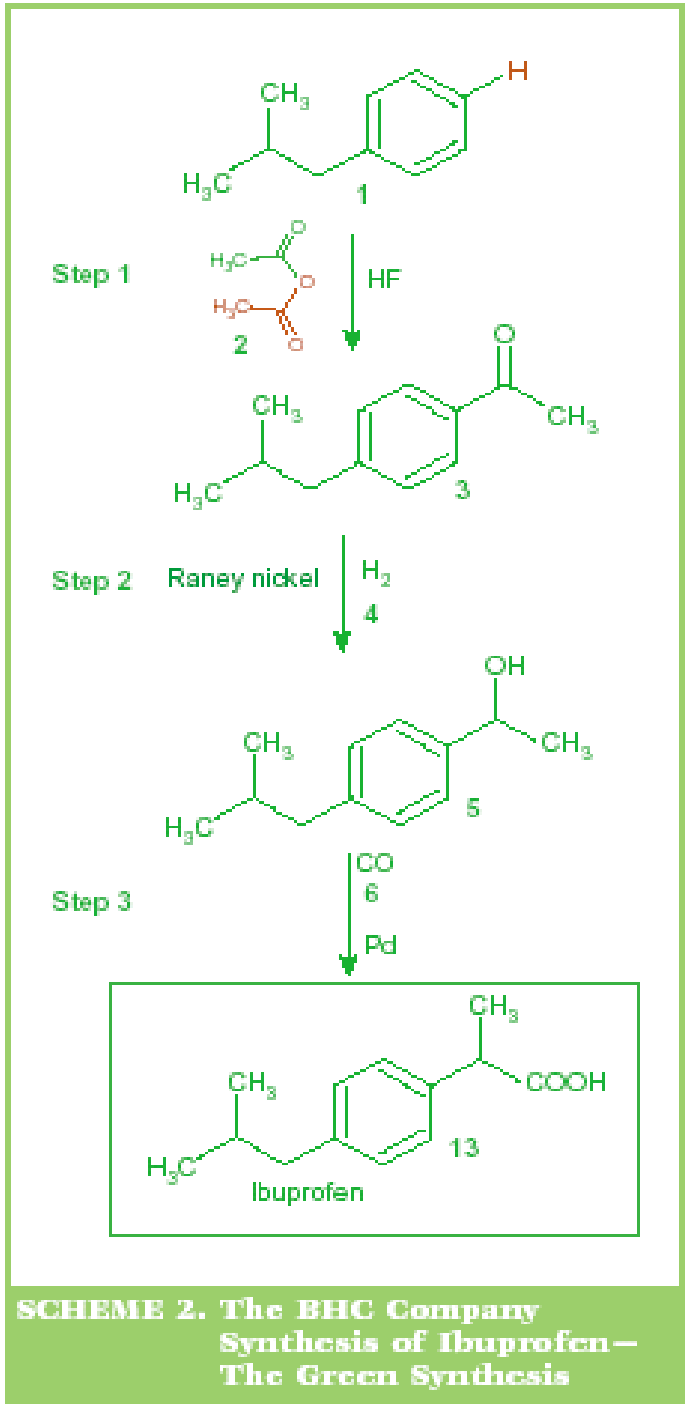
Overall atom economy is 40%.



SCHEME 1. The Boots Company Synthesis of Ibuprofen—The Brown Synthesis

New "Greener" Ibuprofen Process

Overall atom economy is 77%



SCHEME 2. The BHC Company Synthesis of Ibuprofen—The Green Synthesis

Advantages of BHC Synthesis of Ibuprofen

- Greater throughput and overall yield (three steps versus five steps)
- Greater atom economy (uses less feedstocks)
- Fewer auxiliary substances (solvents separation agents)
- Less waste (lower disposal costs)

Microwave assisted reactions

Microwaves lie in the electromagnetic spectrum between infrared waves and radiowaves.
They have wavelengths between 0.01 and 1 metre, and operate in a frequency range between 0.3 and 30 GHz.
However, for their use in laboratory reactions, a frequency of 2.45 GHz is preferred, since this frequency has the right penetration depth for laboratory reaction conditions.

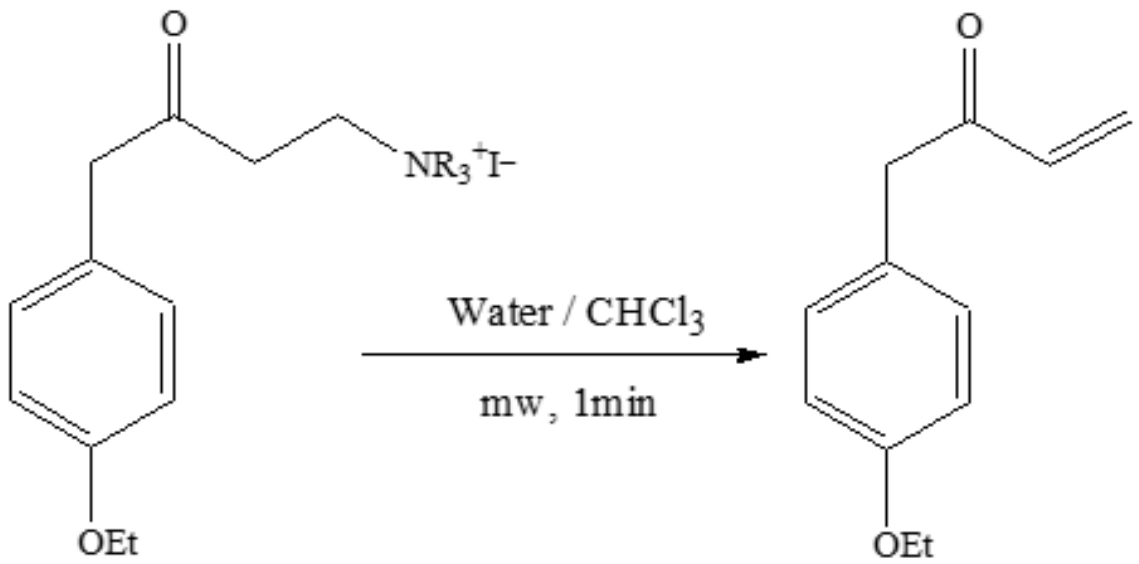
- Microwaves are used for heating purposes
- Homogeneous heating
- Teflon or potystyrene containers are used as reaction vessels
- Solvent used must be polar so as to absorb microwaves

Microwave assisted reactions in water

Advantages

- ❖Efficient source of heating as energy directly imparted to the reaction medium
- ❖Rapid heating leads to saving of reaction time.
- ❖Smaller volume of solvent required
- ❖Diminishes the waste disposal problem

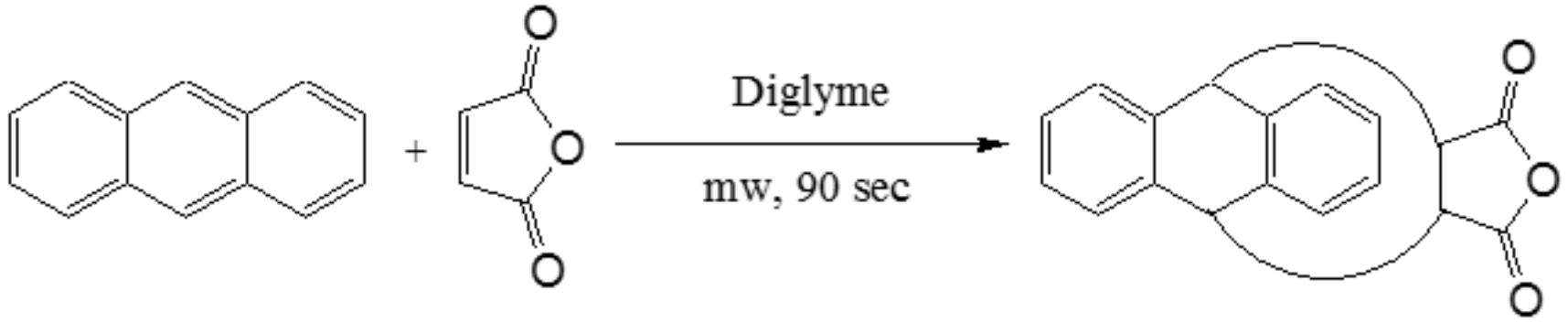
Hofmann Elimination



Microwave irradiation leads to higher yield of the unstable product in a shorter time

Microwave assisted reactions in organic solvent

Diels-Alder Reaction



- Under usual conditions, the reaction requires a reflux period of 90 min.
- Under microwave condition. Diglyme is used as solvent and 80% yield obtained in 90sec

Ultrasound Assisted Reaction

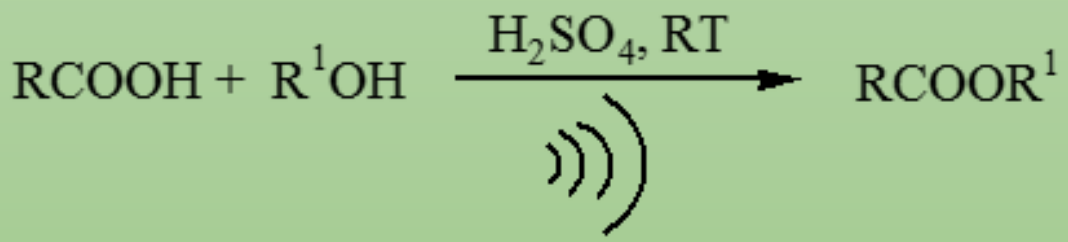
Ultrasound is the sound waves having frequencies higher than that of the human ear can respond (fl, > 16 KHz). When a sound wave, pass through a liquid medium, it causes the molecules to oscillate around their mean position. During the compression cycle, the average distance between the molecules is reduced and during refraction, the average distance between the molecules is increased. Local temperature (around 5000°C) and pressure (over 1000 bar) may be created. It is this very high temperature' and pressure that initiate chemical reactions. Applications of Ultrasound: Following are some of the important applications of ultrasound in chemical synthesis. The symbol)))) is used for reactions carried out on exposure to ultrasound.

Esterification

Usually carried out in presence of catalyst like Sulphuric acid, *p*-toluenesulphonic acid, tosyl chloride, dicyclohexylcarbodiimide etc.

The reaction takes longer time and yields are low.

A simple procedure for esterification of a variety of carboxilic acids with different alcohols using ultrasound has been reported.

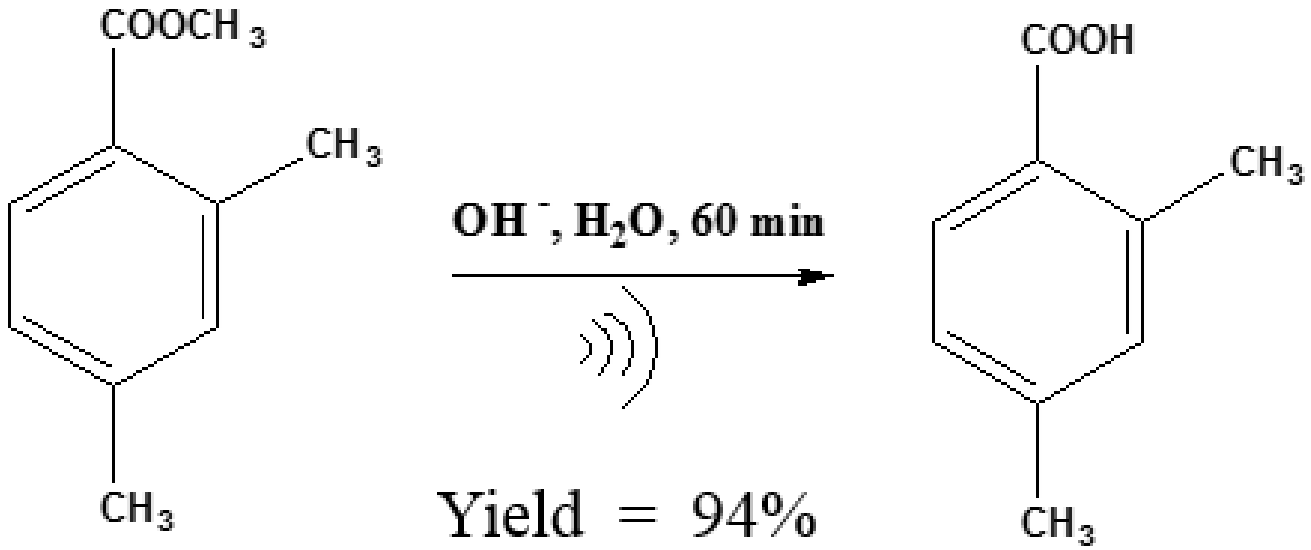


Advantages

- *The reaction was carried out at room temperature*
- *Lesser time required*
- *Yield very high.*

Saponification

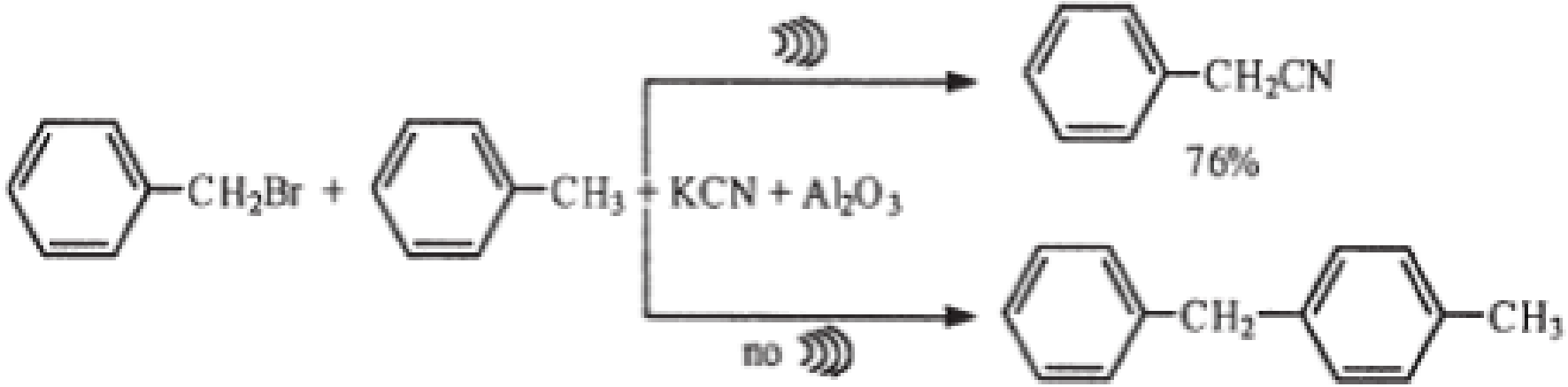
Saponification can be carried out under milder conditions using sonification.



By usual process of heating with aqueous alkali, yield only 15%

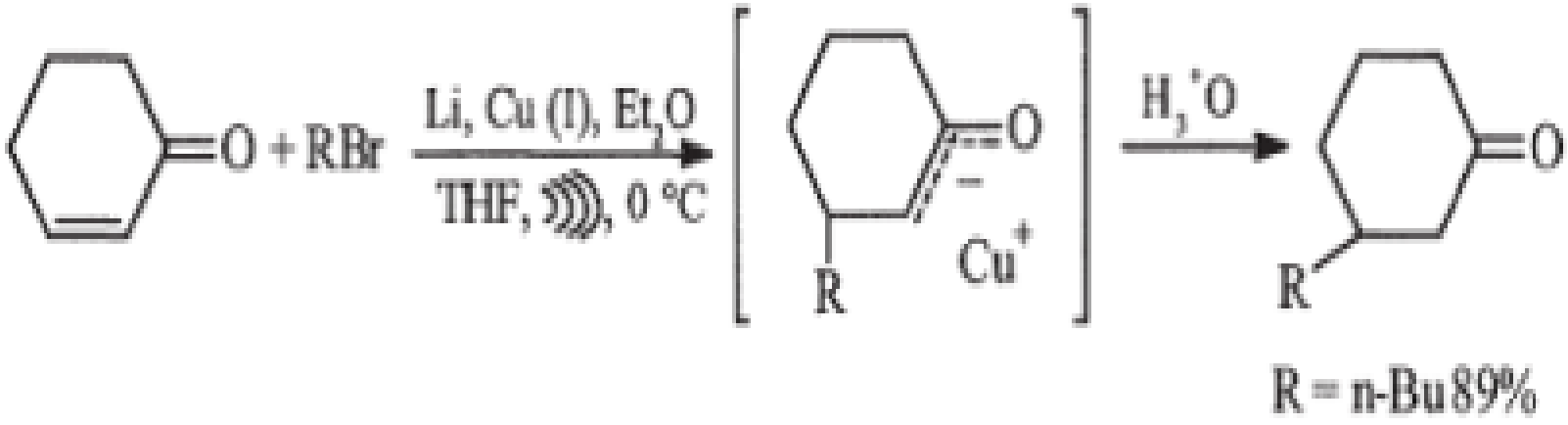
2. Substitution Reactions

Halides can be converted into cyanides. Thus, the reaction of benzyl bromide in toluene with potassium cyanide, catalysed by alumina, on sonication gives!O the substitution product, viz. benzyl cyanide in 76% yield. In the absence of ultrasound alkylation is the preferred pathway. The difference is because ultrasound forces cyanide into the surface of alumina, enhancing cyanide nucleophilicity and reducing the lewis acid character.



3. Addition Reactions

1,4-addition to (l,~-unsaturated carbonyl compounds is generally12 carried out by organocopper reagents. However, improvement in yields, rates and ease of experimental techniques is observed 13 when organocopper compounds are generated in situ by sonication of copper (I) compounds, organic halides and lithium in diethyl-ether-THF at O°C.



R = n-Bu 89%

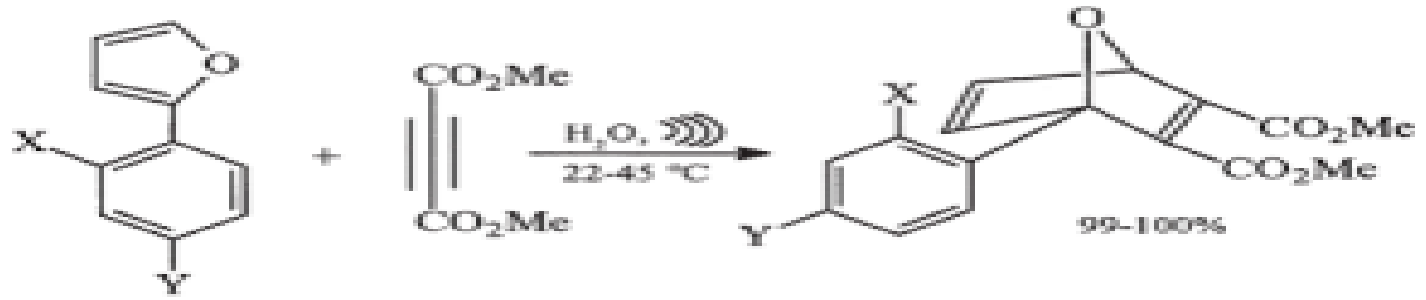
4. Oxidation

The oxidation of alcohols by solid potassium permanganate in hexane or benzene is enhanced considerably by sonication.

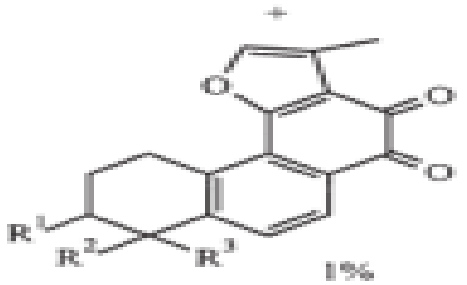
Using the above method, octan-2-01 gives corresponding ketone in 92.8% yield in 5 hr compared to 2% yield by mechanical stirring. Similarly, cyc1ohexanol gave 53% yield of cyc1ohexanone by oxidation under sonication (5 hr) compared to the 4% yield under usual conditions. Oxidation of cinnamyl alcohol with manganese dioxide in a suitable solvent (like hexane or octane) gives22 the corresponding aldehyde on sonication. It is believed that under sonication the low reactive manganese dioxide is activated. Benzylic halides can be oxidised with aqueous sodium hypochlorite23 at room temperature on sonication. The oxidations are believed to proceed via benzylic hypohalides.

5. Diels-Alder Reaction

Sonication facilitates Diels-Alder reaction. Therefore, the addition of dimethyl acetylene dicarboxylate to furan in water at 22-45 °C gives quantitative yield of the adduct. The Diels-Alder cycloaddition of various dienes (mostly belonging to I-vinyl cyclohexenes) with o-quinone proceeds very wel140 under ultrasound conditions to give the expected adducts in 59% yield (Scheme-24) compared to 30% under normal reaction conditions. Better results are obtained by soniciation of the neat mixture.



R^1 = H, OR; R^2 = H, CH_3; R^3 = H, CH_3
R^2, R^3 = –O(CH_2)O–



Conclusion

Ultrasound assisted organic synthesis gives excellent yields compared to other reactions. It can dramatically effect the rates of chemical reactions and is helpful for a large number of organic transformations. In fact, a combination of sonication with other techniques, e.g., phase transfer techniques, reactions in aqueous media etc. give best results. Sonication has also been shown to stimulate microbiological reactions.

Reference:

V. K. Ahluwalia, M. Kidwai. - New Trends in Green Chemistry (2004, Springer Netherlands)


Thanks