5. Green Chemistry and Hazardous Organic Solvents. Green Solvents, Replacement and Alternative Techniques

5.1. Introduction to Green Chemistry and Toxic Organic Solvents

The use of hazardous and toxic solvents in chemical laboratories and the chemical industry is considered a very important problem for the health and safety of workers and environmental pollution. Green Chemistry aims to change the use of toxic solvents with greener alternatives, with replacement and synthetic techniques, separation and purification which do not need the use of solvents.

Organic solvents are very important as liquid medium for reactions to take place, and after the synthesis of a chemical product for extraction, separation, purification and drying. Solvents are also very important in chemical analytical methodologies, spectrometry and measurements of physicochemical properties. The majority of solvents are organic chemicals with hazardous and toxic properties, costly (part of the petrochemical industry) and part of the large waste by-products of the chemical industry causing environmental problems. Although most of their toxic potential is known and there are safety rules for their use, prolonged and high concentration exposures can cause occupational diseases.[1,2]

The subject of toxicology of solvents and their occupational health and safety problems related to their use have been studied extensively. Some solvents were replaced of severely restricted due to their high toxicity or carcinogenicity. Many epidemiological studies with chemists and laboratory technicians in analytical chemical and biochemical laboratories showed that solvent exposure can cause adverse health effects. [3,4]

Aromatic solvents (benzene, toluene, etc), chlorinated and polychlorinated solvents (carbon tetrachloride, chloroform, dichloromethane, etc) and other organic solvents (DMSO, DMF, petroleum ether, diethyl ether, acetone, etc) are used in great quantities in many laboratory and analytical techniques. The persistent solvents (non-biodegradable) are difficult to recycle and their disposition is very expensive.[5,6]

One of principles of Green Chemistry is to promote the idea of “greener” solvents (non-toxic, benign to environment), replacement in cases that can be substituted with safer alternatives, or changes in the methodologies of organic synthesis, when solvents are not needed.[7,8]

Green Chemistry (GC) has placed the solvent issue of synthetic organic chemistry and practices in their use at the same level with alternative synthetic routes in chemical industry. “Green” solvents, replacement with other methods or recycling and reuse is at the core of GC goals.[9]

Figure 5.1. Organic solvents are a major part of chemical processes and research activities in chemical laboratories. The Green Chemistry is aiming to promote the use of “greener” solvents, solvent-free reactions or alternatives that can be benign to environment and human health.

5.2. Green Solvents and Alternative Methods

Green solvents have been characterised for their low toxicity, higher low solubility in water (low miscibility), easily biodegradable under environmental conditions, high boiling point (not very volatile, low odour, health problems to workers) and easy to recycle after use.

The well known monthly journal **Green Chemistry** has published a themed issue on **green solvents**- alternative fluids in science and application. This themed issue contains articles by world-leading chemists detailing the recent advances and challenges faced in this area.[10]

This issue promotes the innovative research towards the substitution of volatile organic solvents in solution phase synthesis. The series of articles are based on the keynote presentations at an international conference organised by Dechema, held in October 2010 in Berchtesgaden, Germany.

The topics are mainly based on the development and application of alternative solvents such as aqueous media, ionic liquids, supercritical phases, green organic solvents, soluble polymers, including phase-separable reagents or related separation strategies. There are increasing efforts from both academia and industry to develop cleaner and more sustainable processes and technologies. All the research work presented in this themed issue aims to reduce solvent-related environmental damage.

Articles are collated in a print and online issue of ***Green Chemistry*** (www.rsc.org/greenchem) published in June 2011 which is being widely promoted to inspire young chemists and generate enthusiasm for the future of green chemistry and sustainable technologies.[11]

A very interesting list of solvents, their toxic properties and the environmental impact have been listed by the American Chemical Society (ACS) . The solvent data *Green Solvents* is an app that provides a reference list of solvents. It contain information data (molecular formula, CAS No) and coded with numbers from 1 to 10 (the higher the number the higher the hazard or toxicity) for health and safety, and environmental hazards for air, water and waste. Solvents with greatest disposal/pollution problems are brown, and those that present less of a problem are green. For example, benzene presents a very serious health risk (red, 10), but it is relatively easy to dispose of (green, 2).

Green solvents is a list of solvents used for chemical reactions, which is annotated with information about its health and safety profile, and the environmental problems associated with its use and disposal. The list was composed by the American Chemical Society Pharmaceutical Roundtable. This web page is a technical demo of web-facing technology that is currently under development by Molecular Materials Informatics.
Internet site : Molsync.com/demo/greensolvents.php

Download Solvent Data

Substance Information				Use		Environment		
Category	**Structure**	**Name**	**CAS#**	**Safety**	**Health**	**Air**	**Water**	**Waste**
Acid solvents		Formic acid Download	64-18-6	2	6	5	4	7
		Acetic acid Download	64-19-7	3	6	6	3	6
		Propionic acid Download	79-09-4	2	5	6	4	6
		Acetic anhydride Download	108-24-7	3	6	6	2	7
		Methane sulphonic acid Download	75-75-2			6	6	10
Alcohol solvents		Methanol Download	67-56-1	3	5	6	3	6
		Ethanol Download	64-17-5	4	3	5	1	6
		1-Propanol Download	71-23-8	4	4	6	2	6
		2-Isopropanol Download	67-63-0	5	5	6	2	6
		1-Butanol Download	71-36-3	3	5	5	5	3
		2-Butanol Download	78-92-2	4	5	6	3	5
		Isobutanol Download	78-83-1	3	5	4	3	3
		t-Butanol Download	75-65-0	3	5	7	2	6

		Isoamyl alcohol Download	123-51-3	3	4	5	3	4
		Benzyl alcohol Download	100-51-6	4	3	4	2	4
		2-Methoxyethanol Download	109-86-4	4	9	5	3	7
		Ethylene glycol Download	107-21-1	3	3	5	1	7
Aromatic solvents		Benzene Download	71-43-2	5	10	6	6	2
		Toluene Download	108-88-3	5	7	6	6	2
		Xylenes Download	1330-20-7	4	4	4	7	3
Base solvents		Pyridine Download	110-86-1	3	6	7	7	6
		Triethylamine Download	121-44-8	4	7	5	7	4
Dipolar aprotic solvents		Acetonitrile Download	75-05-8	3	5	6	4	6
		Dimethyl formamide Download	68-12-2	3	7	3	2	7
		Dimethyl acetamide Download	127-19-5	2	7	3	7	7
		Dimethyl sulfoxide Download	67-68-5	3	4	4	4	8
		n-Methyl-2-pyrrolidone Download	872-50-4	3	6	6	2	7
		Sulfolane Download	126-33-0	2	3		5	8
Ester solvents		Methyl formate Download	107-31-3	5	7	7		6
		Methyl acetate Download	79-20-9	3	5	6	3	5
		Ethyl acetate Download	141-78-6	5	4	6	4	4
		Isopropyl acetate Download	108-21-4	3	4	6	3	3
		n-Butyl acetate Download	123-84-4	4	4	6	3	4

		Isobutyl acetate Download	110-19-0	5	3	5	2	2
		Dimethyl carbonate Download	616-38-6		3			5
		Amyl acetate Download	628-63-7	3	3	5	5	4
Ether solvents		Ethyl ether Download	60-29-7	9	5	7	4	4
		Methyl t-butyl ether Download	1634-04-4	6	5	8	5	2
		1,2-Dimethoxyethane Download	110-71-4		9		3	6
		Diglyme Download	111-96-6		8		3	7
		Tetrahydrofuran Download	109-99-9	5	6	5	4	5
		2-Methyl tetrahydrofuran Download	96-47-9	5	6			4
		Cyclopentyl methyl ether Download	5614-37-9	6			5	3
		Anisole Download	100-66-3	5	4		3	4
		1,4-Dioxane Download	123-91-1	8	7	4	4	6
Haloge-nated solvents		Dichloromethane Download	75-09-2	2	7	9	6	7
		Chloroform Download	67-66-3	2	9	7	7	6
		Carbon tetrachloride Download	56-23-5	3	8	8	5	7
		1,2-Dichloroethane Download	107-06-2	4	9	6	6	6
		Chlorobenzene Download	108-90-7	3	5	5	8	6
		Trifluoromethylbenzene Download	98-08-8		6	7	7	6
Hydrocarbon solvents		n-Hexane Download	110-54-3	6	7	5	8	1

		n-Heptane Download	142-82-5	6	4	4	7	2
		Isooctane Download	540-84-1	6	4	4		2
		Cyclohexane Download	110-82-7	6	5	4	7	2
		Methylcyclohexane Download	108-87-2	6	4	4		2
Ketone solvents		Acetone Download	67-64-1	4	4	7	1	5
		Methyl ethyl ketone Download	78-93-3	5	4	7	2	5
		Methyl isobutyl ketone Download	108-10-1	5	6	6	4	2
		Cyclohexanone Download	108-94-1	4	4	6	3	5

5.3. Green Chemistry, Green Solvents. Alternative Techniques in Organic Synthesis

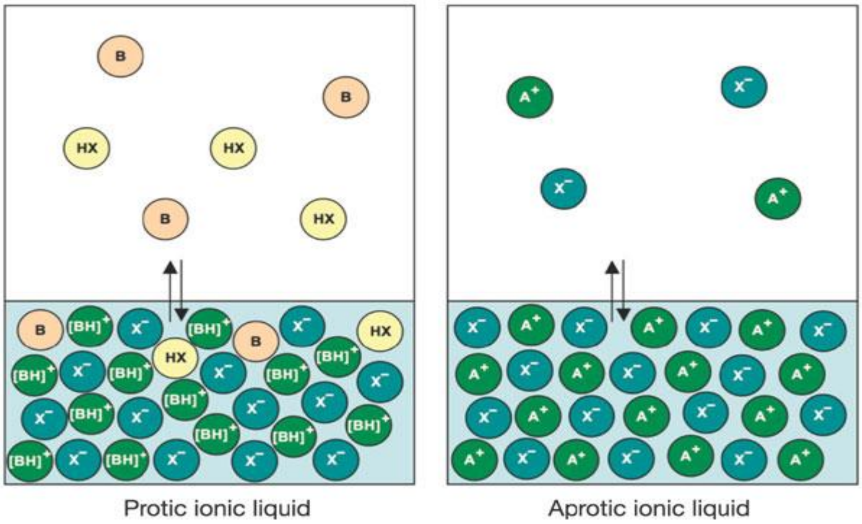
Green Chemistry aims for less toxic solvents but in recent years new methods have been developed where organic synthesis can be performed without solvents, mild conditions and low energy consumption.10 New conferences and symposia have promoted the use of alternative methods or “green” solvents.[12,13] The new field of “green” solvents in organic synthesis has been extended by research papers and publications.[14]

Some of these methods are presented below with a brief explanation of how they work and some references.

5.3.1. Ionic Liquids in Organic Synthesis. Are they Green Chemistry?

Ionic liquids are mixtures of anions and cations, molten salts, with melting point around 100 ^{o}C, which can be used as alternative solvents in organic synthesis. Although the ionic liquids do not comply full with green chemistry principles, they are very promising as alternatives to organic solvents.[15]

In the scientific literature there are a large number of research papers for the use of ionic liquids in synthetic routes and various applications.[16,17]



[For the protic ionic liquids there is a dynamic balance between the ionic form and the dissociated form $[BH]^+X^-(l) \leftrightarrows B(l) + HX(l) \leftrightarrows B(g) + HX(g)$.
The green circles represent cations, the bleu circles anions and the other colours neutral molecules. l=liquid phase, g=gaseous phase]

Figure 5.2. Schematic diagram of protic and aprotic ionic liquids in the liquid and gaseous phase.

Recent conferences and new books promote the methodologies of ionic liquids in organic synthesis.[18-21]

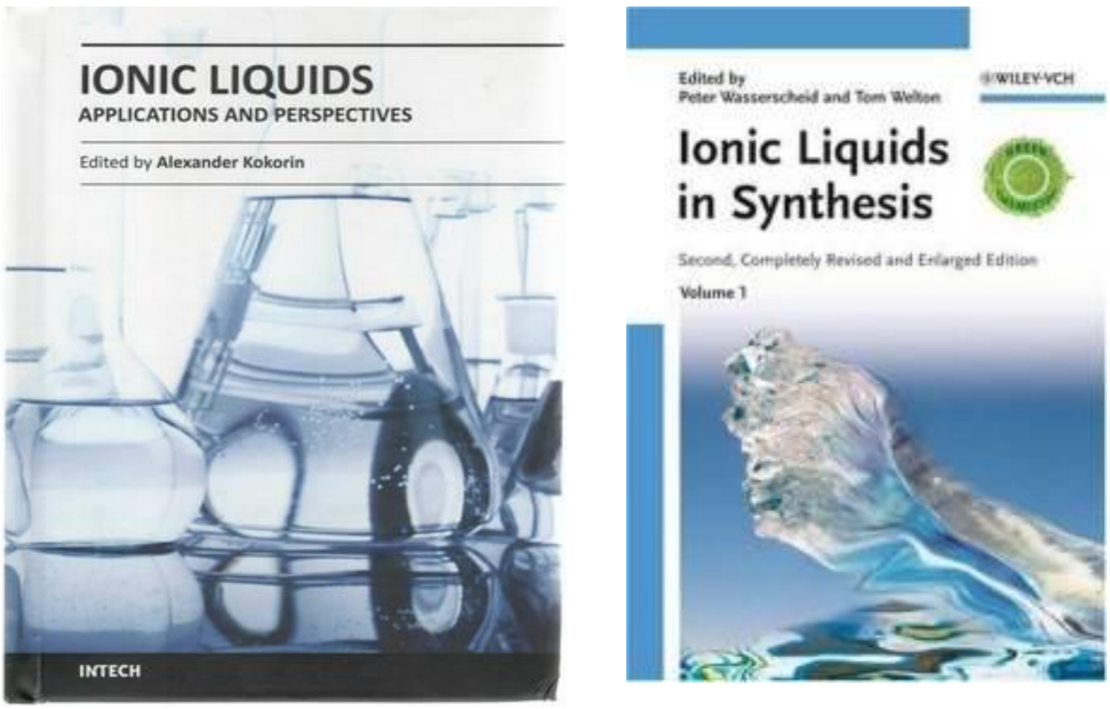
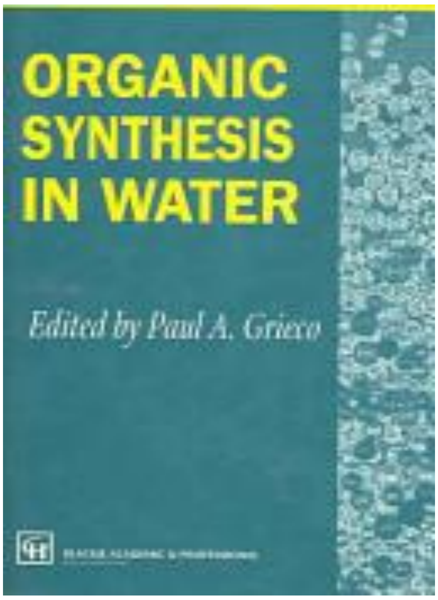


Figure 5.3. Books on Ionic Liquids and their applications to organic synthesis as alternative “green” solvents. Kokorin A (Ed). *Ionic Liquids. Applications and Perspectives* Intech, New York, 2011. . Wasserscheid P, Welton P (Eds).. *Ionic Liquids in Synthesis.* Volume 1. Wiley-VCH, West Sussex, UK, 2003

5.3.2. Organic Synthesis in Water

Although water is considered a problem for organic synthesis and the purification processes and drying in final products is very cumbersome, in recent years water is considered a good solvent for organic reactions. A good example id the synthetic routes of the Diels-Alder reactions in which the hydrophobic properties of some reagents makes water an ideal solvent. Water as a solvent accelerates some reactions because some reagent are not soluble and provides selectivity. The low solubility of Oxygen is also an advantage for some reactions where metal catalysts are used.[22-25]



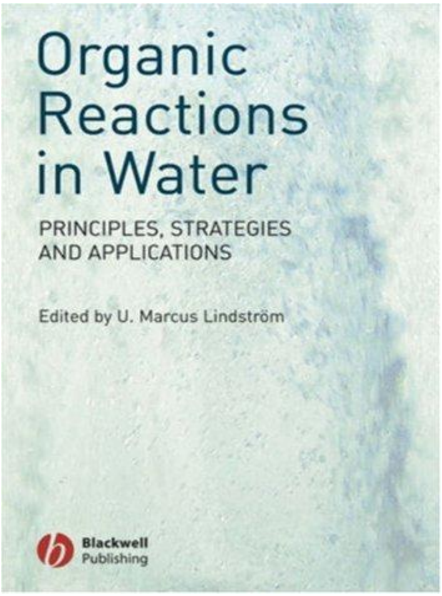


Figure 5.4. Books are published for organic reactions in water and the use of water as a solvent. In the last years water is used in many methods for organic reactions and the scientific literature has a large number of papers.

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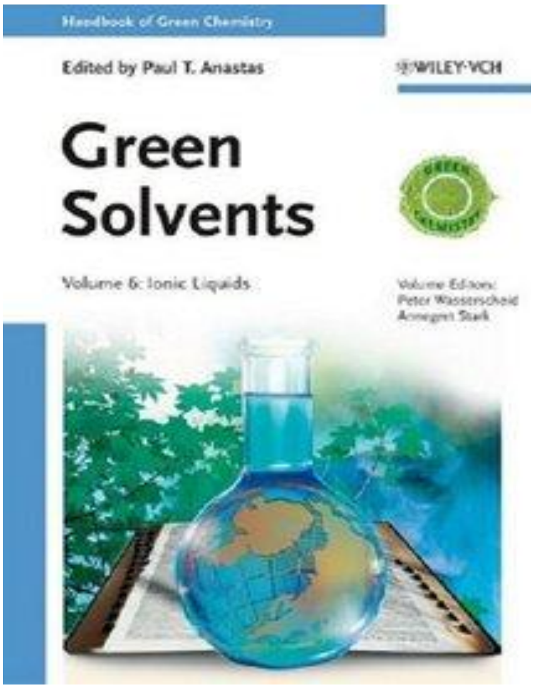
5.3.3. Techniques for Organic Synthesis in Perfluorinated Phases

In some new methodologies chemists use perfluorinated diphasic solvents to dissolve a catalyst with very long perfuorinated chain. These catalysts can be very effective and provide high yields in some types of reactions where the catalysts play an important part. Another advantage is that after the reaction the catalyst can be separated and recycled.[26]

5.3.4. Supercritical carbon dioxide and supercritical water

A supercritical liquid is at a temperature and pressure above its critical point, where distinct liquid and gas phases do not exist. The supercritical liquid can effuse through solids like a gas, and dissolve materials like a liquid. In addition, close to the critical point, small changes in pressure or temperature result in large changes in density, allowing many properties of a supercritical fluid to be "fine-tuned". Supercritical liquids are suitable as a substitute for organic solvents in a range of industrial and laboratory processes. Carbon dioxide and water are the most commonly used supercritical fluids.

Supercritical CO_2 and water are considered "green" solvents in many industrial processes, providing high yields in many reactions, and there are many examples of their use in the scientific literature.[26-29]



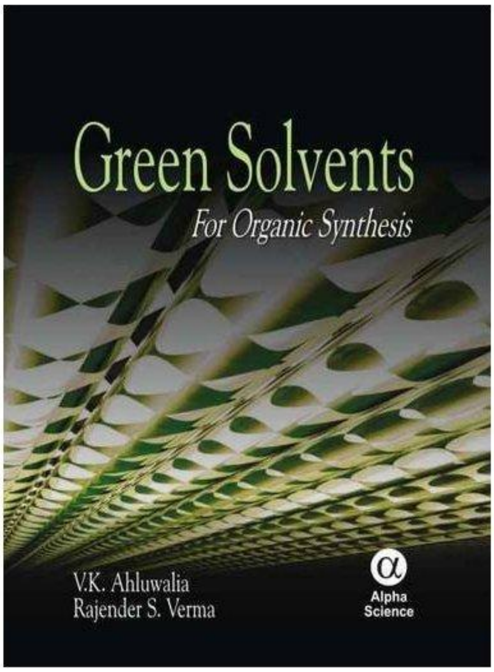
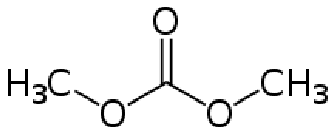


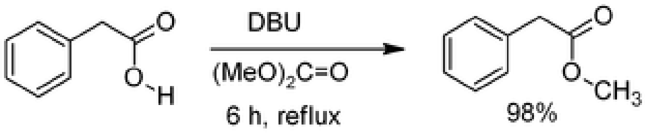
Figure 5.5. Many books have been published recently promoting the "Green solvents" as alternatives for organic synthetic routes in industrial processes and for research laboratory use.

5.3.5. Organic Synthesis with Carbonic esters

Carbonic esters, such as DMC, dimethyl carbonate ($CH_3OCOOCH_3$) are considered a new class of "green" solvents in many organic reaction processes. They can replace methychlorides and dimethyl sulphate esters which are toxic and hazardous.[30]



DMC can be used in methylation reactions of phenols, anilines and carboxylic acids. DBU is an alternative solvent that can be used for methylation reactions of phenols, indoles and benzimidazoles.[31,32]



5.3.6. "Green" Catalysis under the Green Chemistry Principles

It is not only the "green" solvents that will change the face of synthetic organic reactions, but also the use of "green catalysts" will improve substantially the efficiency of many industrial processes. The use of catalysts is one of the principles of Green Chemistry. Catalysis is considered a cornerstone for innovative changes in chemical processes. Catalysts will affect energy use and reaction time, will increase yield, reduce use of solvents, and lower production of by-products and waste.[33-35]

Figure 5.6. Catalysis with "green" catalysts (which can be recycled) is considered a very important step in the direction of Green Chemistry for many industrial processes. (Wiley-VCH has published in the last decade many books on Green Chemistry and Green Engineering)

5.3.7. Replacement of Toxic Solvents with Less Toxic Ones

The replacement of toxic or hazardous organic solvents in industrial processes and systems has been initiated long time ago. Examples, like replacement of benzene with toluene, cyclohexane instead of carbon tetrachloride, dichloromethane instead of chloroform etc. The scientific literature contains many examples and practices with replacement of the most toxic and hazardous solvents.[36,37]

5.3.8. Microwaves in Organic Synthesis, without Solvents

We examined in the previous chapters the use of microwave furnaces for organic reactions. These techniques do not require solvents and are considered "greener" than the conventional methods. The wide range of applications of microwave chemistry has been extended recently to many aspects of organic synthesis.[36-40]

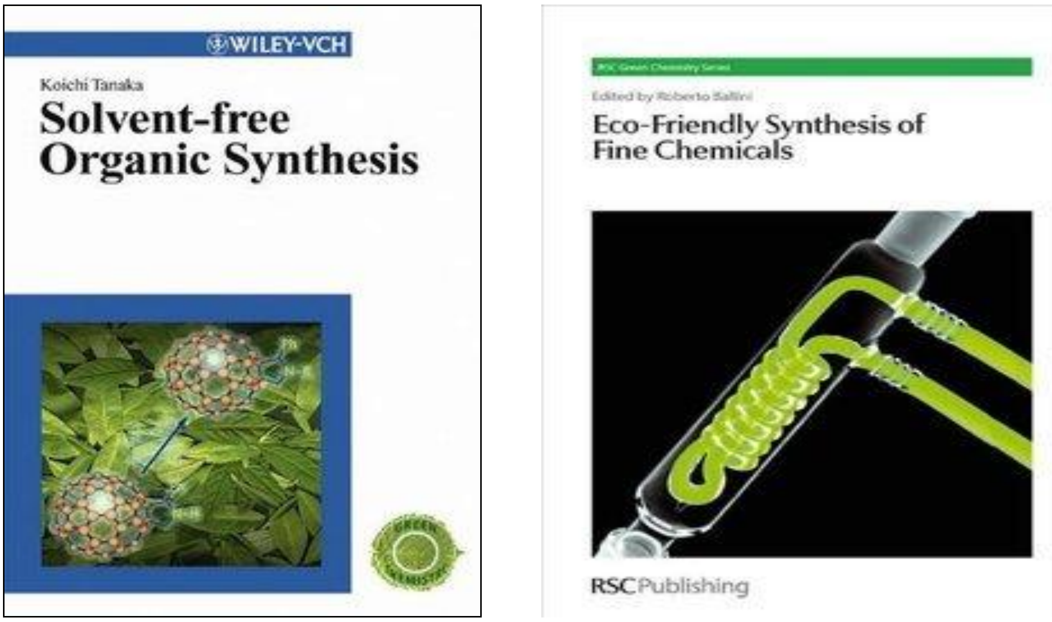


Figure 5.7. Catalysis under the Principles of Green Chemistry and Eco-friendly Synthesis are new innovative trends with substantial applications.

5.3.9. Sonochemistry in Organic Synthesis, without Solvents

Sonochemistry is also considered a methodology of organic reactions without solvents. Their use has been described before and it is obvious that their applications in organic chemistry will be extended further. High yields, low energy requirements, low waste, no use of solvents are some of the fundamental advantages of these sonochemical techniques.[41-43]

5.3.10. Other “Greener” Techniques

In addition to the above methodologies which do not require solvents or use less solvents than the conventional methods, there are are techniques of biocatalysis, self-thermo-regulated systems, soluble polymers, etc which are considered “green methodologies”. Green Chemistry covers all these aspects of eco-friendly methods and promotes their use in research laboratories and in industrial organic synthesis processes. [44-46]

5.4. “Green Solvents” from Plants

Plants are considered a renewable sources of energy but also a resource for various materials. Plant oils or vegetable oils derive from plant sources. Unlike petroleum which is the main source of chemicals in the petrochemical industry they are renewable sources. There are three primary types of plant oil, differing both by the means of extraction and by the nature of the resulting oil:

Vegetable oils can replace petroleum derived organic solvents, with better properties and more eco-friendly conditions as waste. Chemists have advanced recently techniques so that some vegetable oils to become solvents and replace hazardous organic solvents.

As an example of plant-based oils we selected the research project by Spear et al. on soybean oils and their esters , [Spear SK, Griffin ST, Granger KS, et al. “Renewable plant-based soybean oil methyl esters as alternatives to organic solvents”. *Green Chemistry* 9:1008-1015, 2007.

Figure 5.8. Vegetable oils can become a starting material for the production of eco-friendly solvents which are less toxic than the petrochemical industry’s organic solvents

In the last decade, scientists are researching the use of “green” solvents in polymerization methods, since the polymer and plastics industries are using vast amounts of solvents. There have been some successful uses of alternative solvents in polymerization under the principles of Green Chemistry [Erdmenger T, Guerrero-Sanchez C, Vitz J, et al. Recent developments in the utilization of green solvents in polymer chemistry. ***Chemical Society Reviews*** 39:3317-3333, **2010**].

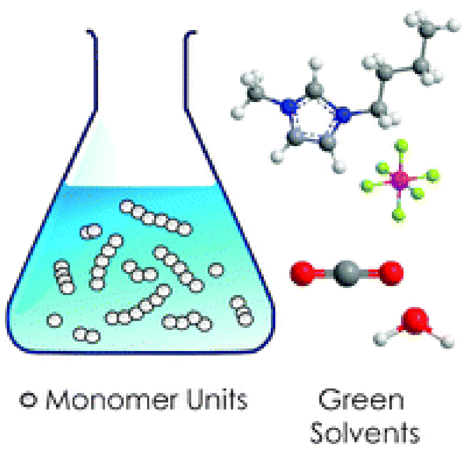


Figure 5. 9. Polymers can be prepared under industrial scale production with the use of eco-friendly solvents.

All these techniques aim at replacing toxic and hazardous solvents in many chemical processes in the synthetic laboratory and in the chemical industry.

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