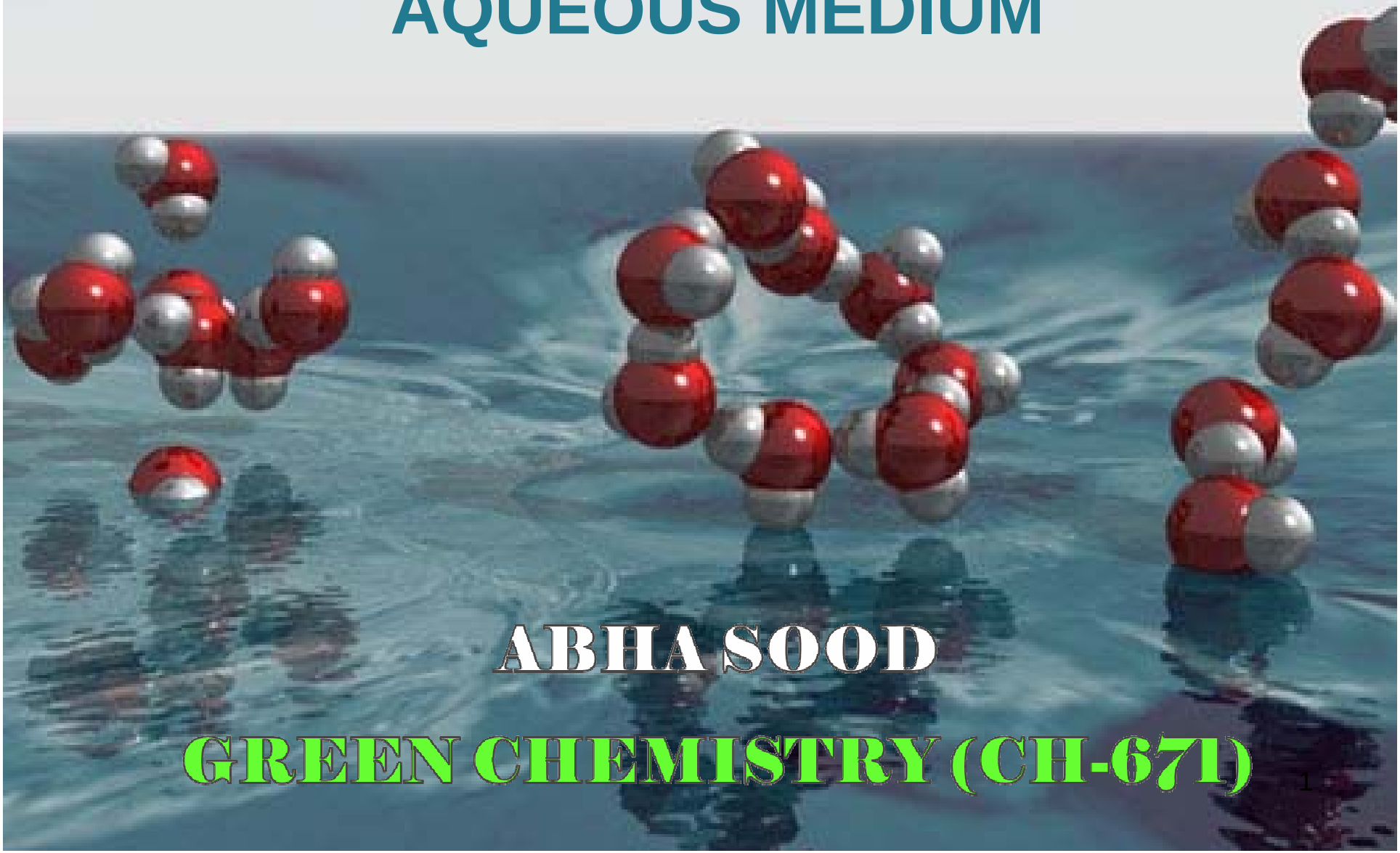
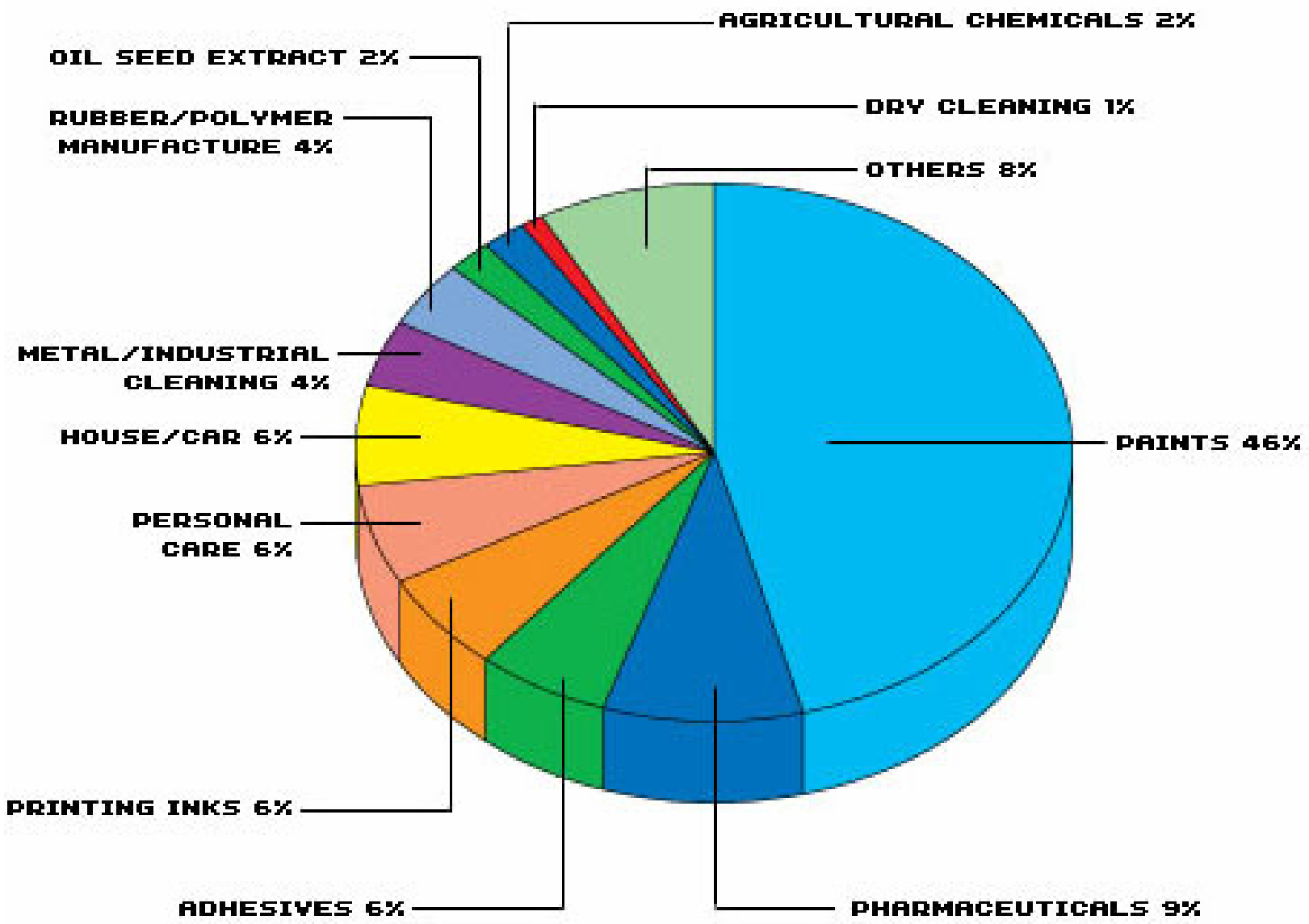
ORGANIC REACTIONS IN AQUEOUS MEDIUM



ABHA SOOD

GREEN CHEMISTRY (CH-671)

USE OF SOLVENTS



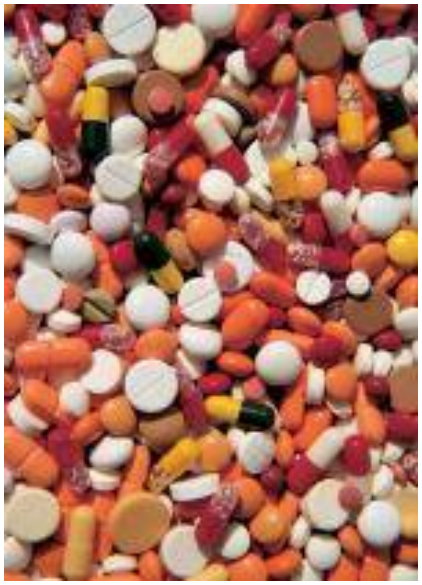
- **Used for the manufacturing of many health care products such as penicillin, aspirin and cough syrup as well as hundreds of other pharmaceutical products**

- **Provide reaction medium for manufacturing drugs**

- **Used for separating the desired product from unwanted material for maximum purity**

- **Used for applying tablet coatings and in inks to print on pharmaceutical tablets and capsules**

- **Critical to the manufacturing of numerous drugs and in the continued development of new, life-saving & life enhancing ones**



EFFECT OF SOLVENTS ON ENVIRONMENT AND HUMANS

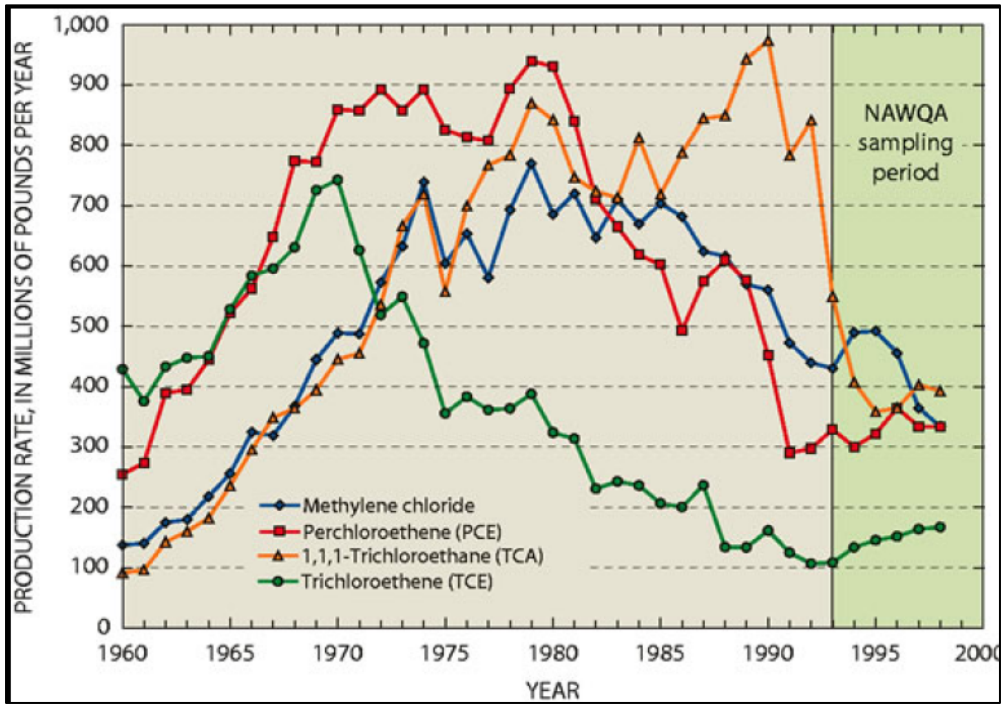
- **Chlorinated solvents (VOC'S) have a short life time thus, cause smog formation**
- **Some being more dense compared to water , seep deep into the ground water**
- **Some solvents are known to be hazardous atmospheric pollutants**

Regarding their effects on humans

- **Cause *irritant dermatitis***
- **Coughing , lung congestion**
- **Long term use may cause memory loss , depression etc.**
- **Benzene causes leukemia**
- **Glycol ethers are reproductive hazards**
- **Chlorinated solvents, at higher level can cause tumors, unconsciousness and even death**

SOLVENTS IN GROUND WATER

- **Dichloromethane (DCM)**
- **Perchloroethylene (PCE)**
- **Trichloroethene (TCE)**
- **Trichloroethane (TCA)**



http://water.usgs.gov/nawqa/protocols/bioprotocols.html

FATE OF SOLVENTS IN GROUND WATER

Dichloromethane	Perchloroethene	Trichloroethene	1,1,1-Trichloro-ethane
Chloromethane	Trichloroethene	Trichloromethane	Chloroethane
Formaldehyde	1,2-dichloroethene	Trichloroethene oxide	Chloroethanol
Methane	Ethene	Hydrochloric acid	Acetic acid
Formic acid	Carbondioxide	Hydrochloric gas	Hydrochloric acid

GREEN ALTERNATIVES TO ORGANIC SOLVENTS

- **Supercritical carbon dioxide**
- **Methyl soyate**
- **Ionic liquids**
- **Fluorous solvents**
- **Water**

WHY WATER???

- **Present in abundance and hence sustainable**
- **Lack of inflammable, explosive, mutagenic and carcinogenic properties**
- **Control of reaction temperature is easier because of high heat capacity**

PHYSICAL PROPERTIES OF WATER

- **Dielectric constant (ϵ_r) of water is high**
- **Small size**
- **Low solubility of oxygen in water**
- **Three dimensional hydrogen bonded network**
- **High surface tension of water**
- **High heat capacity**

UNIQUE PROPERTY

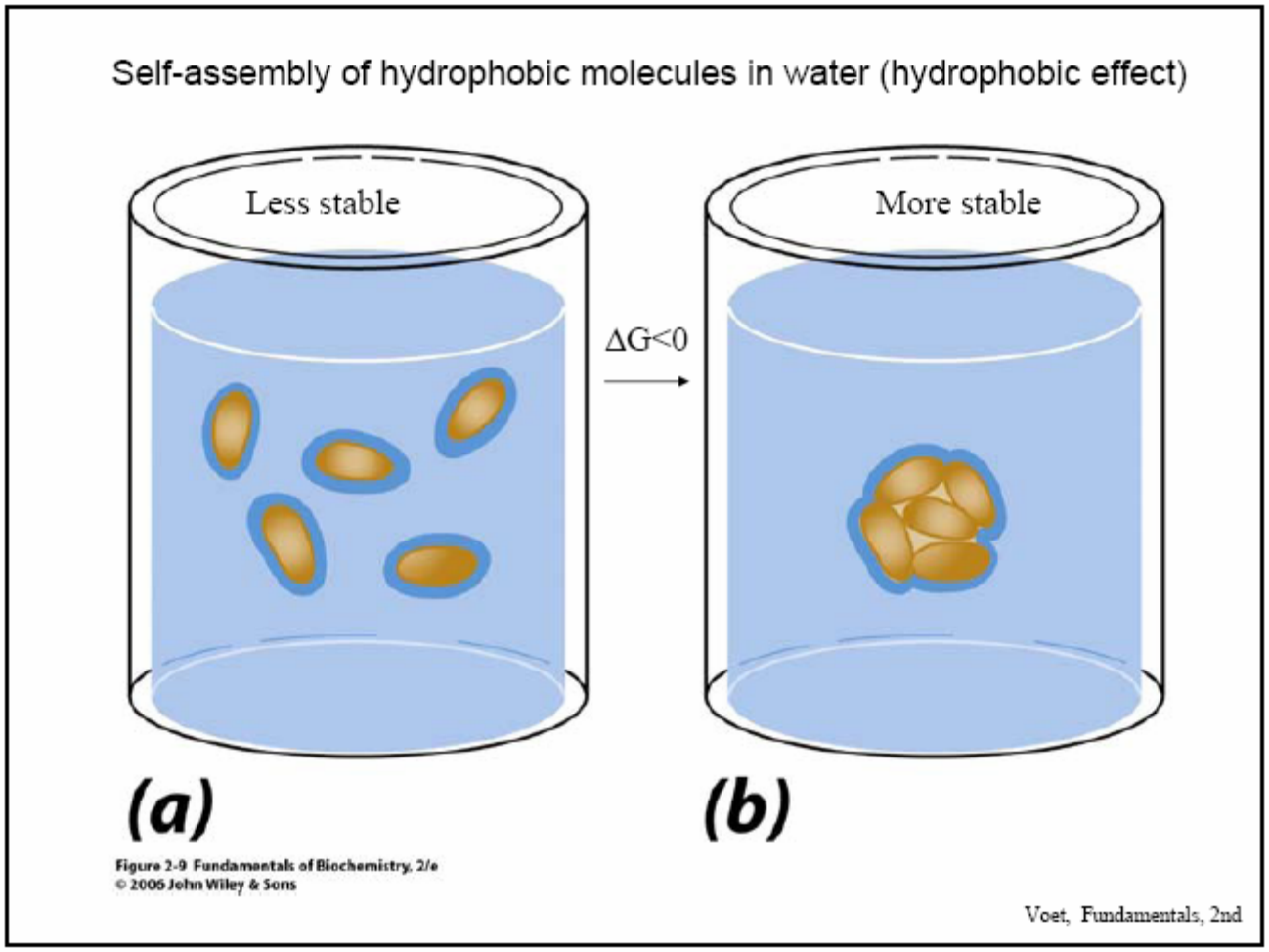
HYDROPHOBIC EFFECT

Cause:

- **Entropic contributions**
- **Enthalpic contributions**

……making organic reactions feasible

ENFORCED HYDROPHOBIC INTERACTIONS



http://www.biology.ucsd.edu/classes/bibc100.SU1.07/objects/ch11_water_solubility.pdf

HISTORY

- **Idea came from the enzymatic reactions taking place in nature using the concept of hydrophobic interactions**

- **Water chemistry is known since 1930; however, in 1980 Breslow and Rideout first noticed the rate enhancement of certain reactions in water**

- **Effect of some other reagents along with water termed as *anti-hydrophobic* agents and *pro-hydrophobic* agents were studied**

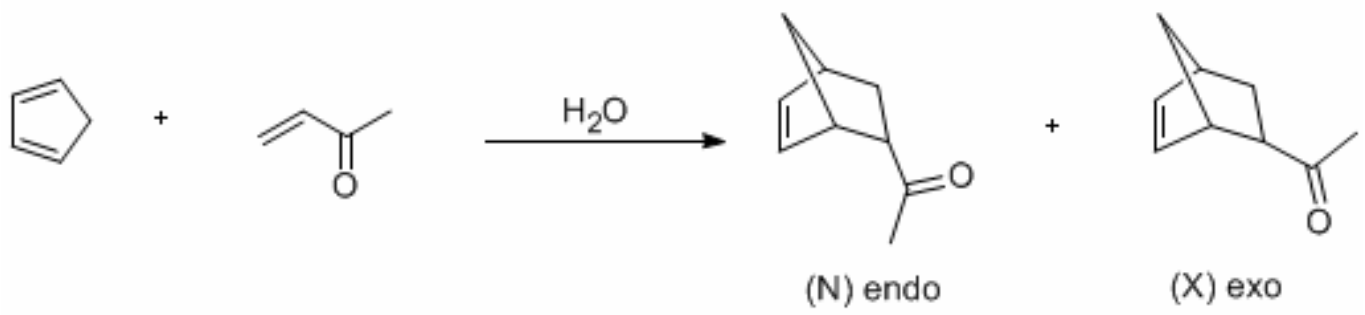
- **With more advances in the water chemistry, it became possible to even perform moisture sensitive reactions in water**

- **In today's times, almost every field of organic chemistry has been touched by the concept of water as the reaction medium**

ORGANIC REACTIONS IN WATER

CYCLOADDITION REACTIONS

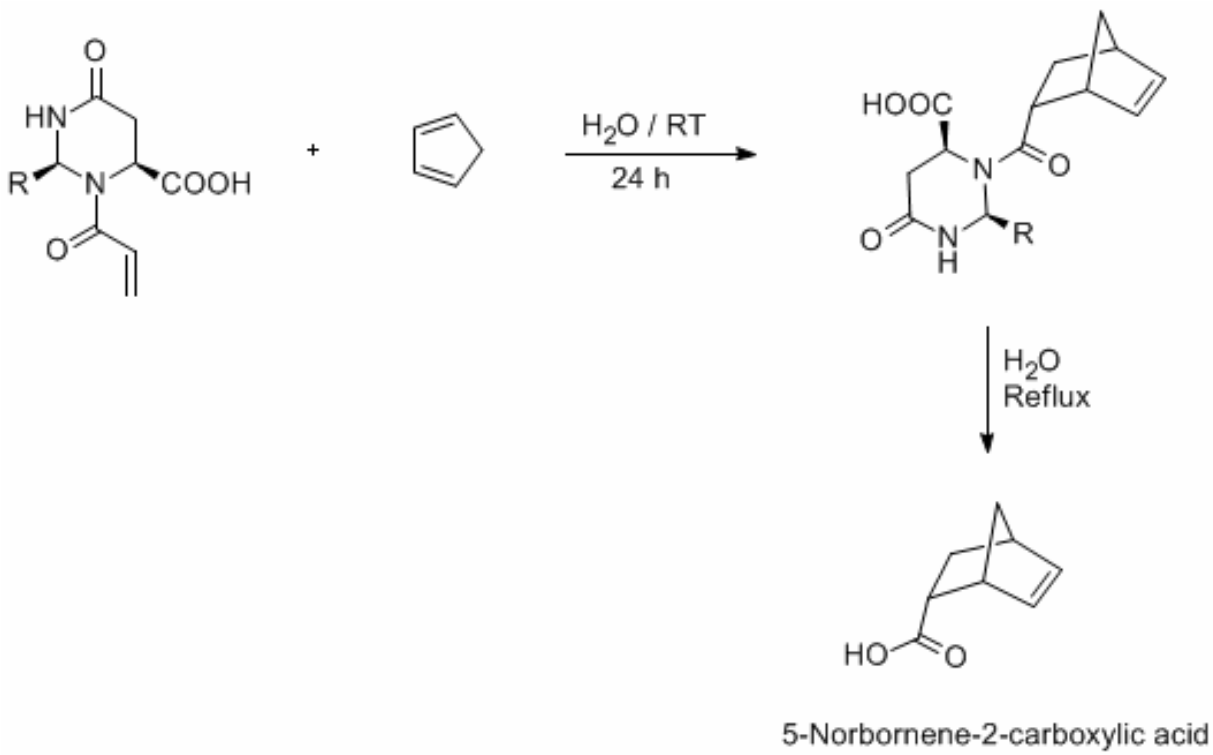
Rate enhancement of Diel's- Alder reaction



solvent	N/X ratio
Ethanol	8
Water	21

Rate constant in water is 740 times more than in isooctane and 58 times more than in methanol

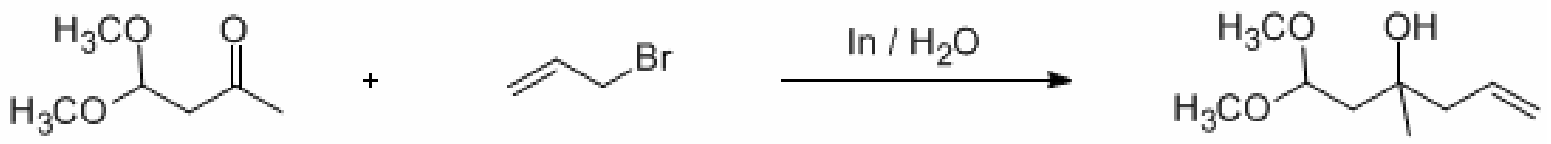
CYCLOADDITION REACTIONS



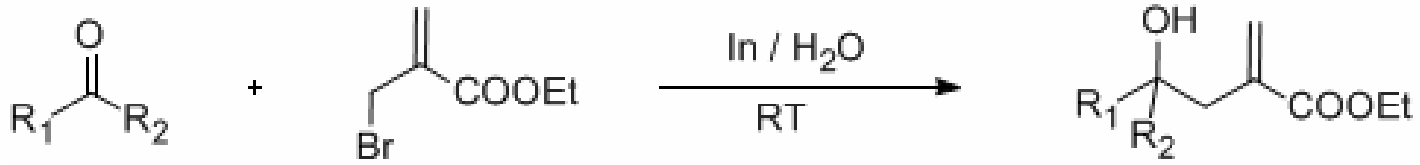
5-Norbornene-2-carboxylic acid

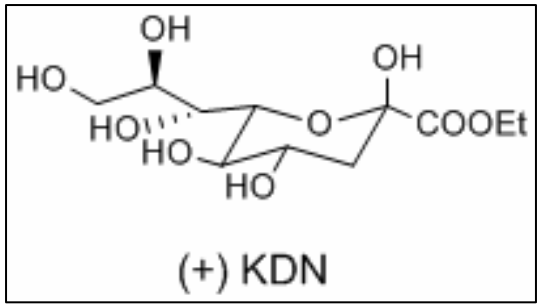
R	endo/exo	ee %
i-Pr	93:7	60
t-Bu	82:18	64
Ph	95:5	55

BARBIER-GRIGNARD TYPE REACTIONS



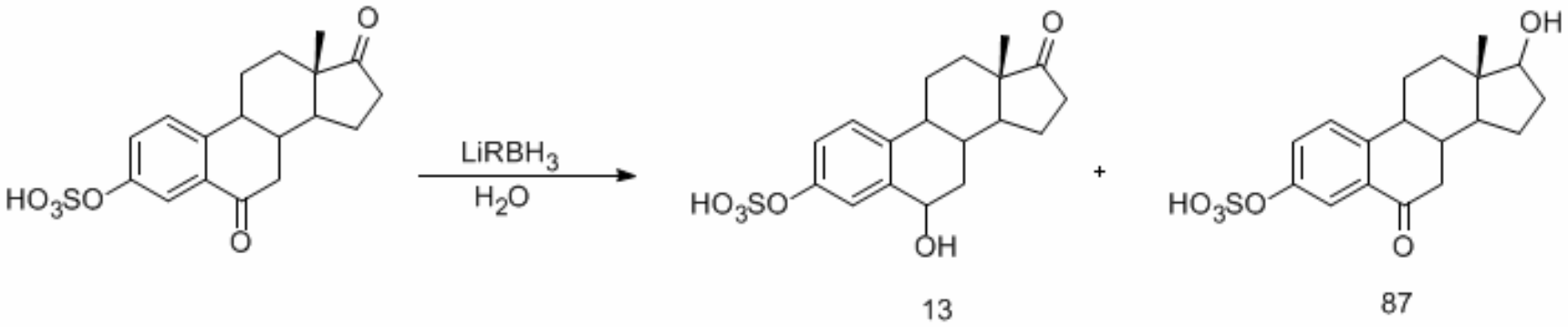
Metal	Yield %
Zn	0
Sn	10 (sonication)
In	70





ATOM TRANSFER REACTIONS

Selective reduction of carbonyl

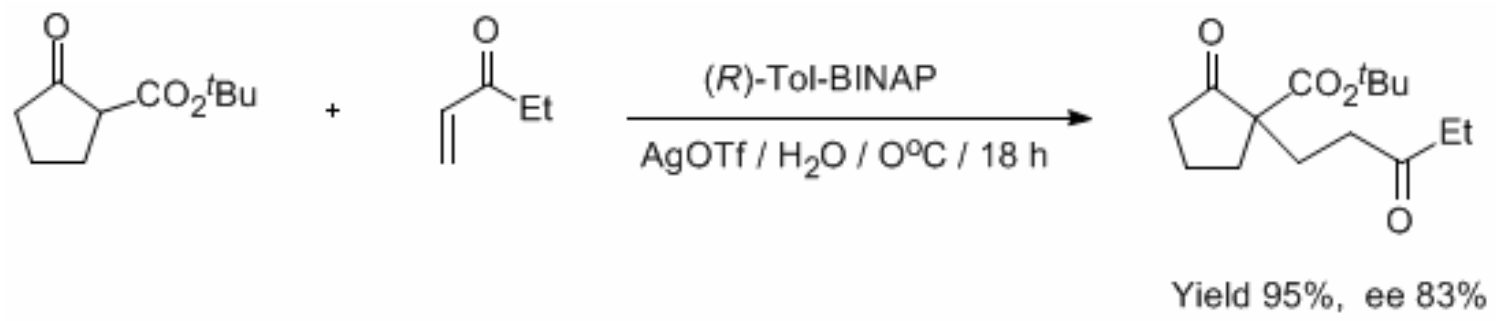


USE OF SURFCTANTS AS CATALYST IN WATER

Use of LASC (having properties of both lewis acid and catalyst)

- **Kinetic studies revealed that Aldol type reaction is 100 times faster in water than in dichloromethane**

ASYMMETRIC CATALYSIS

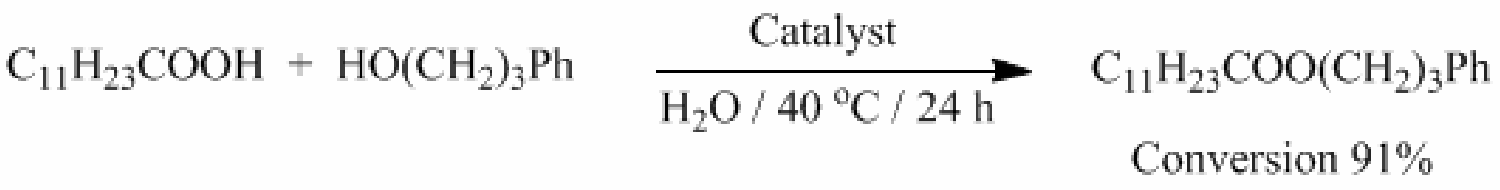


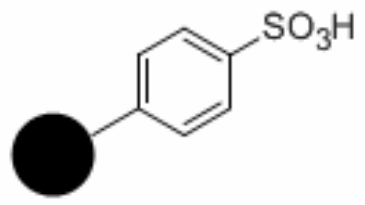
Effect of solvent:

MEDIUM	ee (%)
Acetonitrile	17
Tetrahydrofuran	24
Ethanol	39
Water	74

POLYMERIZATION

Dehydrative esterification in water can be effectively catalyzed by hydrophobic Polystyrene supported sulfonic acids as recoverable and re-usable catalysts

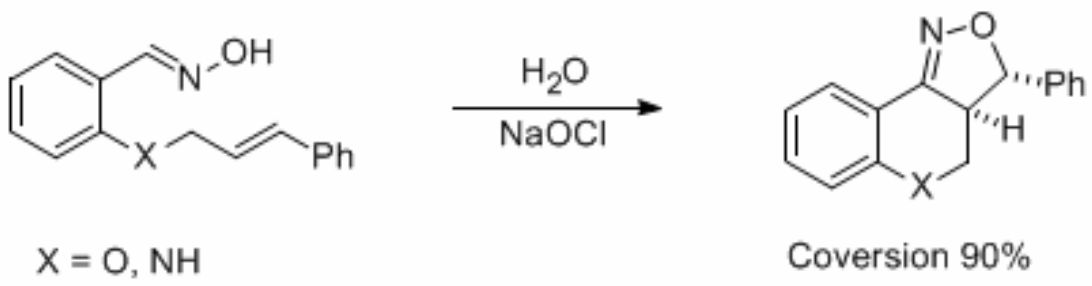




CATALYST

CYCLIZATION REACTIONS

1,3-Dipolar additions

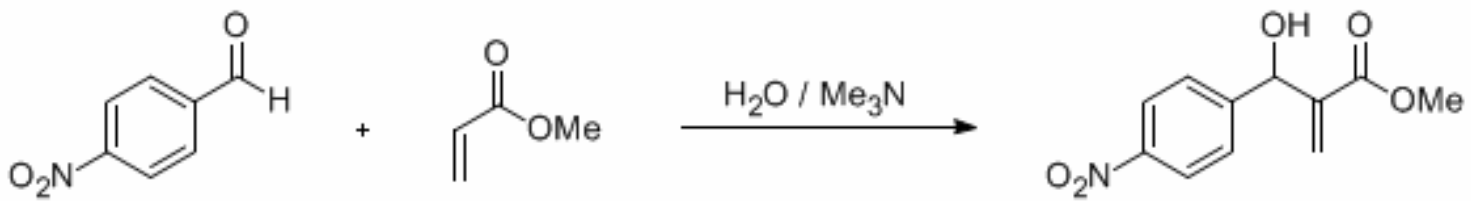


- **High yields as well as regio- and chemoselectivities are obtained without the use of solvents**

- **Products can easily be separated by filtration**

BAYLIS-HILLMAN REACTION

Reported in 2002

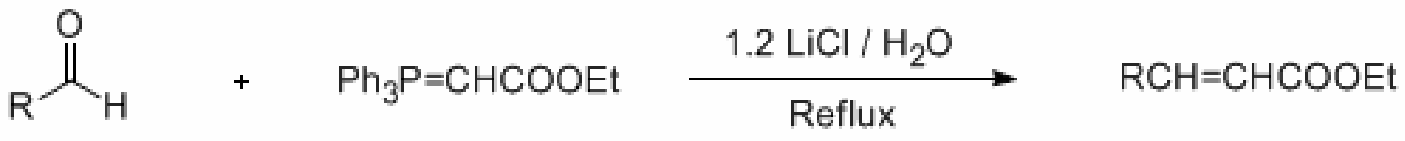


Activated alkene

- **Low reaction rates in conventional method**

- **Using water/solvent system, reaction rates can be greatly enhanced leading to shorter reaction time, lower reaction temperatures and higher yield**

WITTIG REACTION

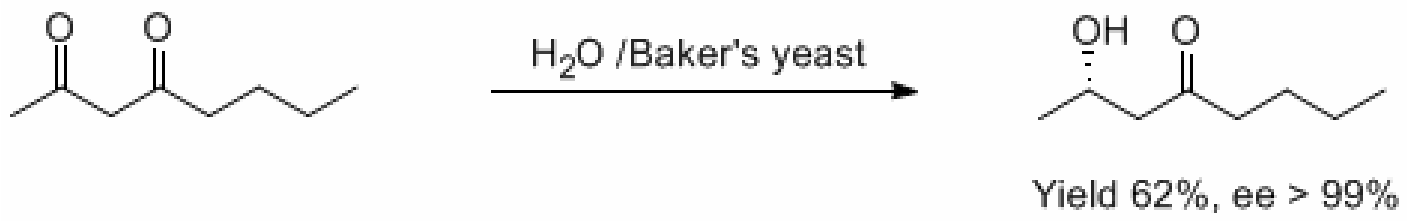


- **Conventionally is carried out in anhydrous condition**
- **But if used stabilized phosphorus ylides, reaction is faster in water**
- **Reaction is completed in 5 to 60 minutes**
- **E/Z selectivity is also very good and similar to toluene**

HYDROGENATION REACTION

Solvent	H_2 pressure (atm)	ee %
MeOH	3	99
H_2O	3	99
MeOH-H_2O	3	83

BIO-CATALYSIS

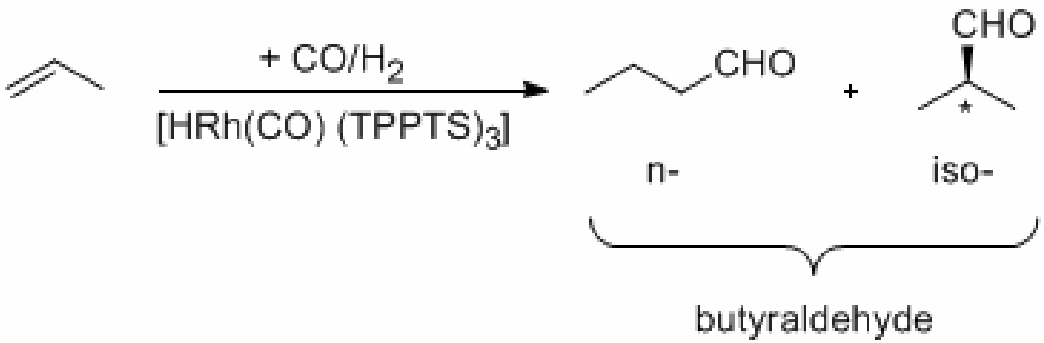


- **Reaction rates are high even at low substrate concentration in water**
- **Selectivity is exceptionally high**

NEAR CRITICAL WATER

- **Water heated to about 200-300^{0}C**
- **Decrease in density**
- **Decrease in dielectric constant, making non polar solutes soluble in water. Simultaneous decrease in solubility of ionic compounds**
- **Increase in dissociation constant**
- **Self neutralizing catalytic medium**
- **Hydrolysis reactions can be easily carried on in such medium**
- **Acylation reactions making use of lewis acids can be performed in this medium**

WATER AS A SOLVENT: AN INDUSTRIAL APPLICATION



TPPTS: triphenylphosphine m-trisulfonate

OTHER INDUSTRIAL APPLICATION

In dry cleaning:

Halogenated hydrocarbons can be replaced by aqueous cleaning solvent.

H_2O + Terpene → Is a good degreasing agent
Naturally occurring compound
Can be disposed off easily
Easier to recycle and reuse than conventional solvents

GREEN ASPECTS AND ADVANTAGES

- **Non-hazardous as it is not:** **Inflammable**
  Explosive
  Carcinogenic
  Mutagenic

- **Easy work up procedures**

- **Need of protection and deprotection can be minimized in water**

- **Highly polar molecules such as sugars can be directly dissolved in water without any derivatization**

- **Water soluble catalysts can be reused after separation of insoluble organic products**

LIMITATIONS

- **Upfront capital costs required for new equipment is high**
- **Water based systems require high energy usage for drying**
- **Reactions can't be carried in normal water. It has to be deionized before use and the process is costly and consumes energy**

REFERENCES

- Li, C. –J. *Tetrahedron*, **1996**, *52*, 5643.
- Miyamoto, H.; Kimura, T.; Daikawa, N.; Tanaka, K. *Green chem.* **2003**, *5*, 57.
- Li, C. *Chem. Soc. Rev*. **2006**, 35, 68.
- Rhyoo, H. Y.; Yoon, Y. A.; Park, H. J. *Tetrahedron Lett.* **2001**, *42*, 5045.
- Mori, K.; Mori, H. *Org. Synth*. **1993**, *8*, 312.
- Paul, A. G.; Ellen, B. *J. Org. Chem.* **1989**, *54*, 5849.
- Sonntag, N. O. V. *Chem. Rev*. **1953**, *52*, 237.
- Li, C.; Chan, T. *Tetrahedron*, **1999**, *55*, 11149.
- Hailes, C. *Org. Proc. Res. Dev.*, **2007**, *11*, 114.
- Koddermann, T.; Schulte, F.; Huelsekopf, M. *Angew. Chem. Int. Ed*. **2003**, *42*, 4904.
- Schneider, H. J.; Sangwan, N. K. *Angew. Chem. Int. Ed.* **1987**, *26*, 896.
- Lindstrom, U. M. Organic reactions in water, 2007.
- Li, W.; Zhang, Z.; Xiao, D. *J. Org. Chem*. **2000**, *65*, 3489.
- Kolb, H. C.; Finn, M. G. *Angew. Chem. Int. Ed*. **2001**, *40*, 2004.
- Hayashi, Y.; Sumiya, T. *Angew. Chem. Int. Ed*. **2006**, *45*, 958.

THANK YOU ☺