



Green Chemistry: Synthesis of organic compounds through green approach

Gopal Chandra Maity^{*a}, Ashim Kumar Ghosh^a and Pradip Kumar Ghosh^b

^aDepartment of Chemistry, ^bDepartment of Physics,

Abhedananda Mahavidyalaya, Sainthia, Birbhum-731 234, West Bengal, India

E-mail: gcm79@rediffmail.com

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Green synthesis of various organic compounds has been done using common organic reactions such as biosynthesis of organic compounds Michael, aldol, Cannizaro reactions, Hoffmann, Wittig, Benzoin, Simon Smith, Heck, Suzuki coupling, Ullmann reaction and aromatic nucleophilic substitution reactions. These names reactions are carried out in green solvents like water or solvent free conditions at room temperature or using microwave radiation.

Keywords: Green synthesis, biosynthesis, microwave, Michael, aldol, Cannizaro reactions, Hoffmann, Wittig, Benzoin, Simon Smith, Heck, Suzuki coupling, Ullmann.

Introduction

Various Industries are using hazardous and toxic chemicals which are harmful on environment. These harmful substances cause bad impact on human health. Past two decades ago, the chemistry community has been developed a new branch of chemistry that are not harmful to human health and the environment. This new approach is known as Green Chemistry which is the use of chemical engineering and methodologies that eliminate or reduce to generation or the use of chemical products, by-products, reagent, solvents, etc., that are harmful to human health or the environment. Green Chemistry is also an approach to the synthesis, processing and use of chemicals that reduces or eliminates the risks of humans and the environment. Green Chemistry that possesses the spirit of sustainable development was booming in the 1990s¹, and has attracted more and more interest in the 21st century. In recent year there has been growing interest in the development of green synthesis of organic compound using green solvents like water, supercritical fluids, and ionic liquids or on a solid support in which no solvent or using microwave radiation or using specific catalyst.

Principles of Green Chemistry

Twelve principles of Green Chemistry are given below:

Prevent waste: It is better to prevent waste than to treat

or clean up waste after it has been produced.

Maximize atom economy: The design of synthetic methods should be such that in which maximum starting materials and reagents are incorporated to give final product. There is no waste (by product) visible in the above calculation if the yield of the reaction is 100%. The synthesis will be green if all the starting materials reagents used in the process into the final product. The percentage of atom utilization can be calculated by the following equation.

Less hazardous chemical syntheses: The design of synthetic methodologies should be such that in which no toxic materials for human health or environment has been used or generated.

Designing safer chemicals and products: The design of chemical products should be such that which has no toxicity or less toxicity to human health or environment.

Use of safer solvents and auxiliaries: The use separating agents, solvents like CCl₄, CHCl₃, CH₂Cl₂, benzene etc. should be avoided where necessary or should used which is no toxicity to human health or environment.

Increase energy efficiency: Energy requirements should be minimize for environmental and economic impacts.

Use of renewable feedstock: The use of raw materials should be renewable.

Avoid unnecessary chemical derivatives: Unnecessary derivatization (protection, deportation, blocking group etc.) should be avoided whenever possible.

Use of catalytic reagents rather than stoichiometric: Catalytic reagents should be used for the synthesis of chemicals. The use stoichiometric reagents should be avoided where necessary.

Design chemicals products for degradation: The design of chemical products should be degradable. After end their functions, they cannot be persist in the environment and break down into degradation products which are not harmful to human health or environment.

Analyze in real time to prevent pollution: Analytical methodologies need to be further developed to allow for real time, in process monitoring and control prior to the formation of hazardous substances.

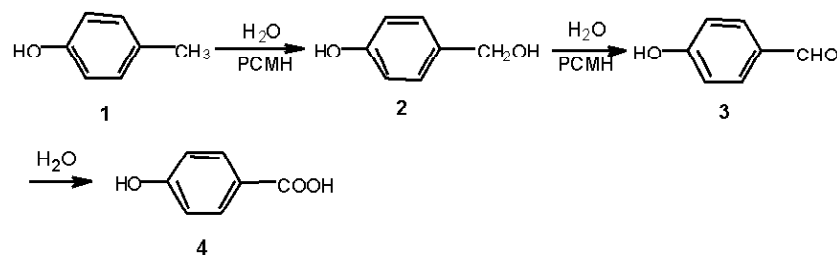
Safer chemicals for accident prevention: The use of substances in a chemical process should such that which have minimum the potential for chemical accidents, including releases, explosions and fires.

Results and discussion

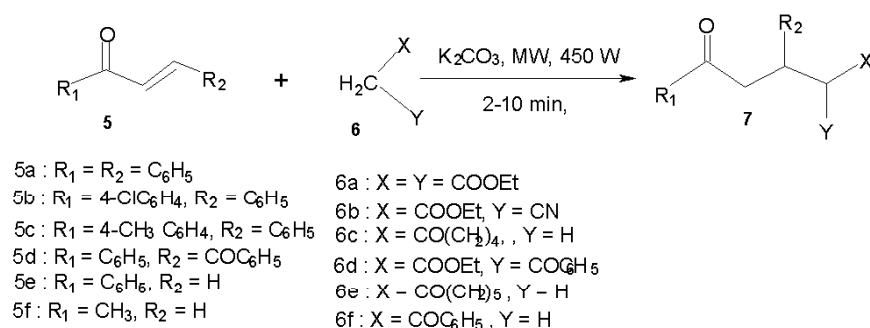
Biosynthesis of 4-hydroxybenzoic acid from toluene: 4-Hydroxybenzoic acid (**4**) is synthesized from *p*-cresol using an enzyme, methylhydroxylase (PCMH) in presence of water².

Michael addition reactions using microwave irradiation: Microwave assisted solvent-free without organic solvents Michael addition reactions on CdI₂, BiCl₃, CeCl₃.5H₂O, EuCl₃, and Al₂O₃ surfaces using microwave have been reported³⁻⁶. The reaction of active methylene (**6**) compounds with Michael acceptor on K₂CO₃ surface in presence of microwave radiation have been reported by Rao *et al.* (Scheme 2)⁷.

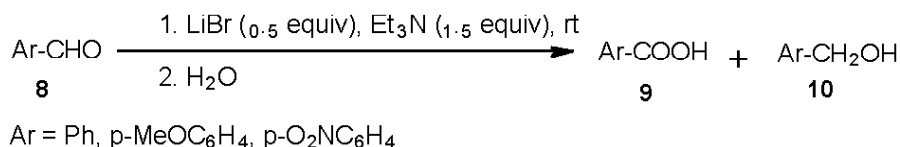
Cannizzaro reaction of aromatic aldehydes: The Cannizzaro reaction of differene aldehyde having no α -hydrogen in presence of Et₃N at room temperature in a solvent free environment have reported by Mojtahedi *et al.* (Scheme 3)⁸. These reactions are catalyzed by lithium bromide (LiBr). As there is no use of organic solvents, the reactions are considered green reaction.



Scheme 1. Synthesis of 4-hydroxybenzoic acid from *p*-cresol.



Scheme 2. Michael addition reactions using microwave irradiation.



Scheme 3. Cannizaro reaction of aromatic aldehydes.

Directed Aldol reactions: Environmental friendly directed Aldol reactions of ketene silyl acetyls (**12**) with different aldehydes (**11**) in presence of a catalytic amount of DBU have been reported by Loh *et al.* (Scheme 4)⁹.

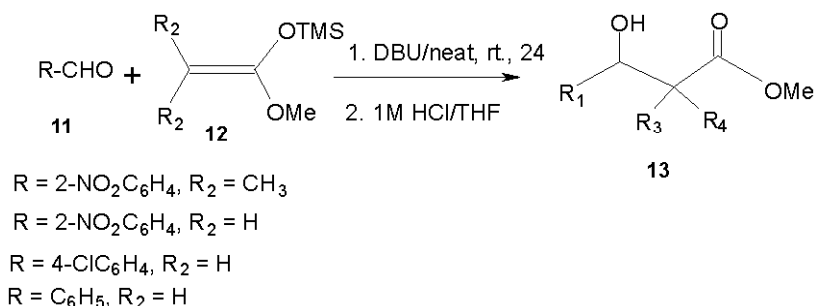
These reactions were carried out at room temperature under solvent free condition. This can consider as green synthesis β -hydroxy carbonyl compounds.

Aromatic nucleophilic substitution reactions: The microwave assisted coupling reaction of phenols (**14**) having electron withdrawing group (-NO₂, -Cl, -CF₃ etc.) with aryl halides (**15**) in presence of K₂CO₃ as base have been reported by Li *et al.* (Scheme 5)¹⁰. The product diaryl ethers (**16**) with high yields was obtained within very short time (5–10 min).

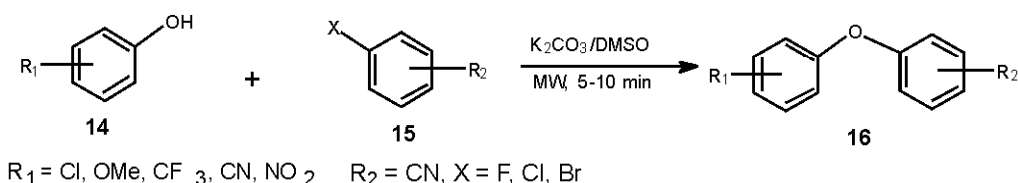
Hoffmann elimination reaction: Quarternary ammonium salts (**17**) undergo E2 elimination reaction results in the forma-

tion less substituted alkene. These reactions require a high temperature and yield are generally poor. In 1995, C. R. Strauss reported microwave assisted Hoffmann elimination reaction of compound (**17**) in CHCl₃ and water mixture as a solvent. In this reaction, aryl vinyl ketone (**18**) derivative is obtained as good yield. When the compound (**50**) was heated at 105°C in only water medium, polymerization product was isolated through the formation of aryl vinyl ketone derivatine (**18**) as intermediate compound¹¹ (Scheme 6).

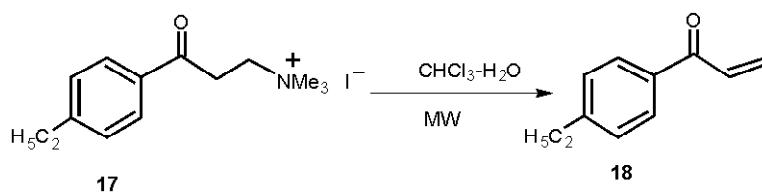
Wittig reaction: Wittig reaction of aldehydes (**19, 22**) with stabilized ylides (**20**) in water medium yields desired products with high yield¹² (Scheme 7). The reaction of ketone (**24**) with CH₂I₂/Zn in presence of Ultrasound, the expected product will be ketone derivative greater number of carbon atom. For this reaction, interestingly, olefin (**25**) is obtained



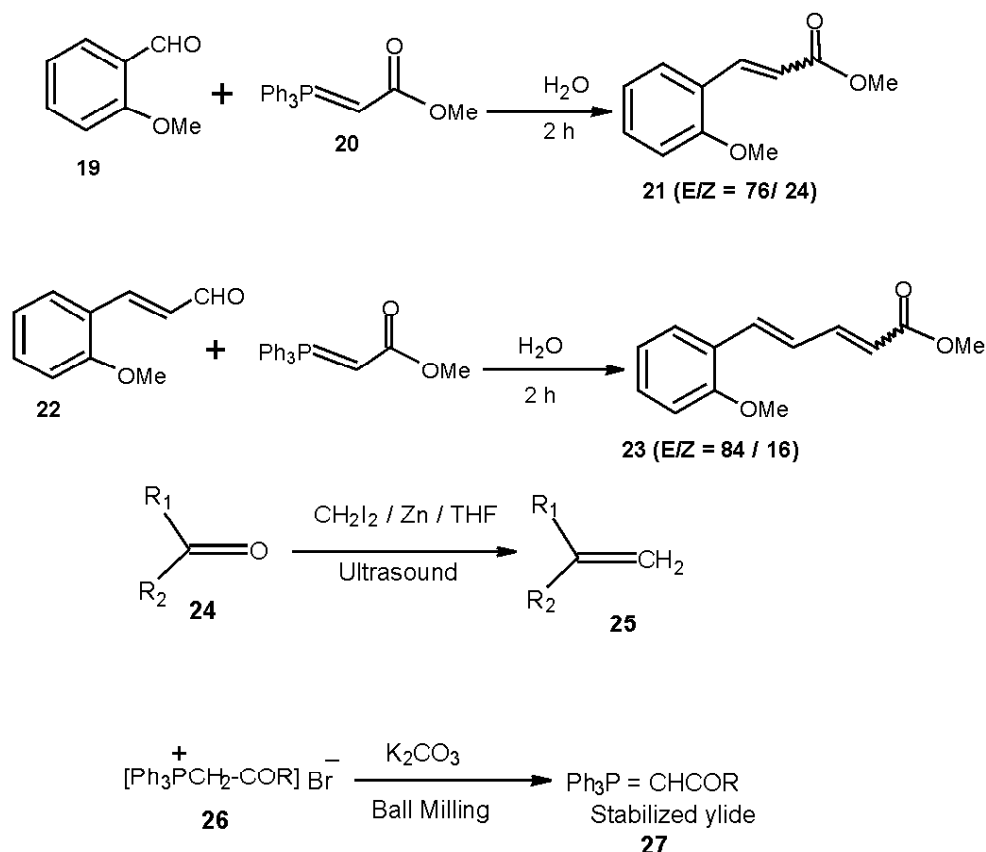
Scheme 4. Directed Aldol reactions.



Scheme 5. Aromatic nucleophilic substitution reactions.



Scheme 6. Hoffmann elimination reaction.

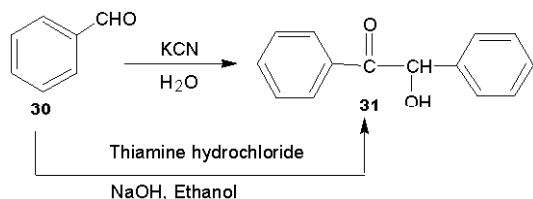


Scheme 7. Wittig reaction.

instead of ketone derivative. Generally phosphonium ylide is formed by the treatment of strong base like PhLi or nBuLi or LDA in dry ether medium. It is also reported that the both stabilized and non-stabilized ylides are formed using weaker base like K_2CO_3 under solvent less condition¹³. Under conversational process of Wittig reaction gives kinetically favorable *cis* olefins but here stable *trans* product is obtained.

Benzoin condensation: Generally aromatic aldehydes (30)

react with NaCN or KCN in ethanol-water medium yields benzoin derivative (31) (Scheme 8). Breslo reported the benzoin condensation reaction in water medium in presence of inorganic salts. It has been found the rate of reaction is 200 times faster than in ethanol medium. This reaction is also more favorable in presence of γ -cyclodextrine due to size match selective¹⁴. It was also reported that the benzoin condensation reaction occur in presence of co-enzyme, thiamine hydrochloride instead of poisonous cyanide ion.



Scheme 8. Benzoin condensation.

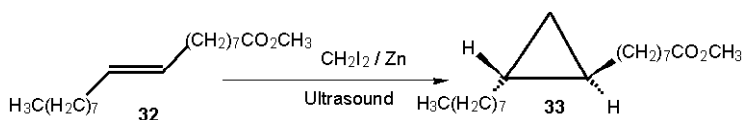
Simon smith reaction: It was reported that the reaction of alkene (**32**) with CH₂I₂/Zn in presence of Ultrasound yield cyclopropane derivative (**33**) with high yield (91%) (Scheme 9). This reaction is not exothermic and the formation of iodine is absent. The absence of ultrasound, the yield (51%) of this reaction is comparatively low, reaction is highly exothermic and iodine is formed as one of the products¹⁵.

Heck reaction: Ultrasound-initiated Heck reaction has been reported by using Pd-C catalyst in N-methylpyrrolidone

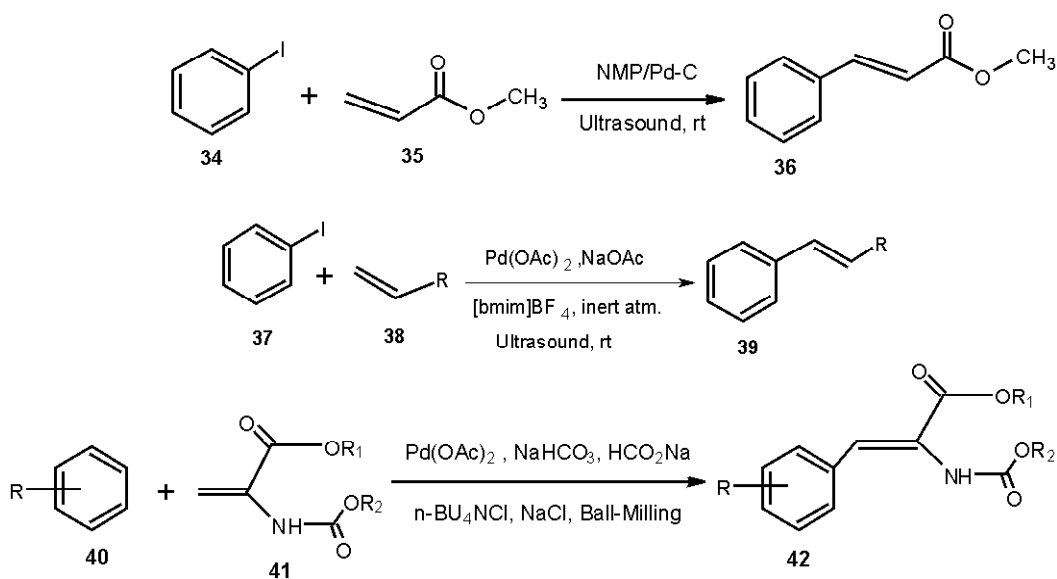
(NMP) solvent at room temperature. Without ultrasound the above reaction cannot take place¹⁶ (Scheme 10).

The rate and stereo selectivity of Heck reaction is enhanced in ionic liquid under sonication. Under heating and stirring conditions a mixture of E- and Z-isomers were obtained but under sonication in ionic liquid only stable E-isomer was obtained¹⁷. In some cases no reaction occurred in ionic liquid without sonication. Therefore ultrasound has a specific effect for occurrence of reaction. Solvent free Heck reaction has been reported by ball-milling process using Pd(OAc)₂ as catalyst and reducing agent (HCOONa)¹⁸. The addition of sodium formate enhances the rate of reaction and improves the yield. It also act as reducing agent for the conversion of Pd(OAc)₂ to Pd(0).

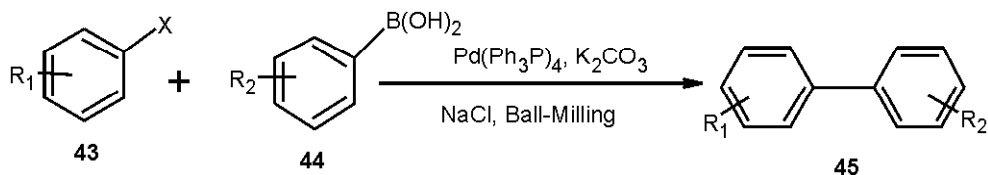
Suzuki coupling reaction: Solvent free Suzuki coupling reaction has been reported by ball-Milling process in presence Pd(Ph₃P)₄ as catalyst, base (K₂CO₃) and grinding



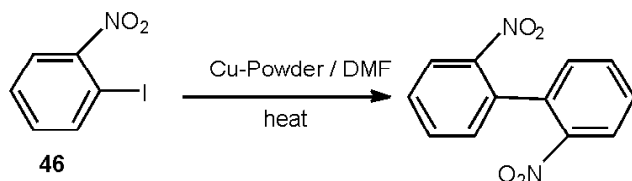
Scheme 9. Simon smith reaction.



Scheme 10. Heck reaction.



Scheme 11. Suzuki coupling reaction.



Scheme 12. Ullman reaction.

medium (NaCl). KF supported on Al_2O_3 can be used instead of the mixture of K_2CO_3 and NaCl. The rate of reaction depends on nature of halogens¹⁹ (Scheme 11).

Ullmann reaction: The reaction of *o*-iodonitrobenzene with Cu-powder in DMF solvent at 60°C for 48 h yield 2,2'-dinitrophenyl derivative²⁰. When the same reaction is ultra sound, the reaction was completed within 1.5 h (Scheme 12).

Conclusions

In this era, with the increasing concerns about the protection of human health and environment synthesis of organic compounds from raw materials through a Green Chemistry approach is desirable. Therefore the design of methodology, design of product, use of chemicals, and use of solvent etc. will be such that which are not is harmful to human health or environment. The use of water as green solvent in organic synthesis or solvent free reaction is most leading research areas of Green Chemistry. The above reactions are carried out in green solvents like water, or in absence of solvent, or using microwave radiation. However, Green Chemistry is not a solution to all the problems but most fundamental approach to prevent the problems of pollution.

Acknowledgements

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