Green Chemistry- Definition and Principles

What is Green Chemistry?

Green Chemistry is defined as invention, design, development and application of chemical products and processes to reduce or to eliminate the use and generation of substances hazardous to human health and environment.

Principles of Green Chemistry

1) **It is better to prevent waste than to treat or clean up waste after it is formed.**
2) **Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.**
3) **Wherever practicable, synthetic methodologies should be designed to use and generate substances that posses little or no toxicity to human health and the environment.**
4) **Chemical products should be designed to preserve efficacy of function while reducing toxicity.**
5) **The use of auxiliary substances (e.g. solvents, separation agents *etc.*) should be made unnecessary wherever possible and, innocuous when used.**

6) Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature andpressure.

7) A raw material feedstock should be renewable rather than depleting whenever technically and economically practical.

8) Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.

9) Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10) Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.

11) Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.

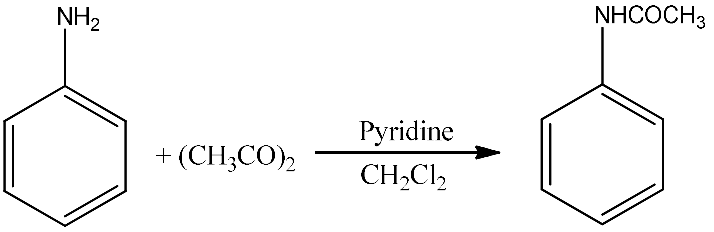
12) Substances and the forms of the substance used in chemical reaction should be chosen so as to minimize the potential of chemical accidents, including releases, explosions, and fires.

P. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice;* Oxford Science Publications, Oxford, **1998**

Experiment: 1 **Date:19.03.2020**

ACETYLATION OF PRIMARY AMINE
(Preparation of acetanilide)

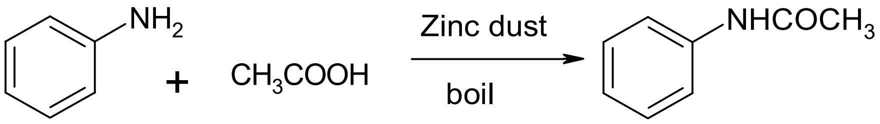
Conventional Procedure:



Non-green Components:

Use of chlorinated solvent like CH_2Cl_2
Pyridine is also not eco-friendly
Acetic anhydride leaves one molecule of acetic acid unused (not atom-economic)

Alternative Green Procedure:



Chemicals Required:

Aniline	- 10 ml (10.2 g)
Glacial aceticacid	- 30 ml
Zinc dust	- 0.5 g

A mixture of aniline (10 ml) and zinc dust (0.5 g) in acetic acid (30 ml) in a 100 ml round bottom flask was heated over a gentle flame using water condenser. Heating was continued for about 2 hrs. The reaction mixture was then carefully poured in cold water (100 ml) in a 250 ml beaker with cooling and vigorous stirring. The shining crystals of acetanilide were separated slowly. After 15 min. the acetanilide crystals were collected by filtration. The solid crystals were washed over the Buchner funnel with water and the product was dried (yield, 10 gm). It was crystallized in boiling water. (If necessary, decolorizing charcoal may be used), **m.p. 114 ^{0}C.**

Yield: 10 g (91%)

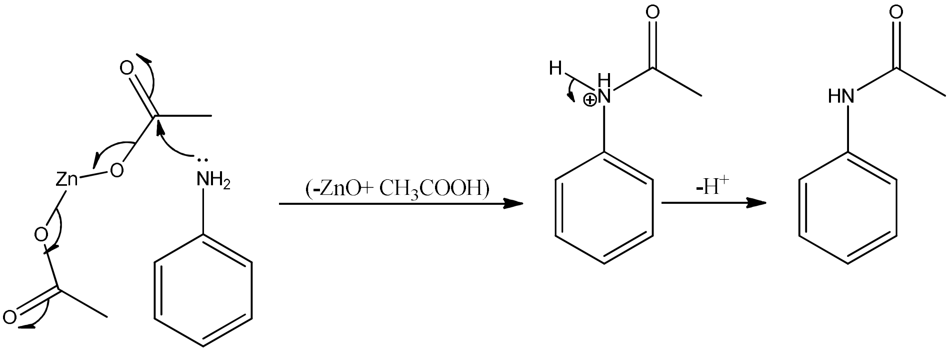
Green Context:

Avoids use of acetic anhydride (usage banned in some states, due to its utility in narcotic business)

Minimizes waste by-products

Avoids hazardous solvent

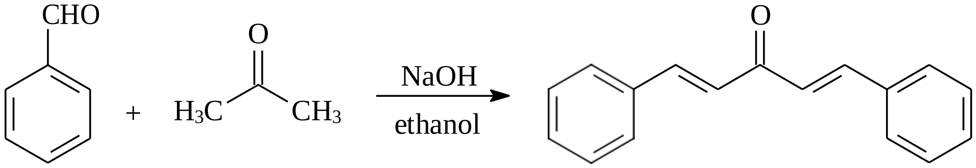
Mechanism:



H. Meshram, IICT, Hyderabad, Private Communication

Experiment: 2 **Date: 23.03.2020**

BASE CATALYZED ALDOL CONDENSATION
(Synthesis of dibenzalpropanone)



dibenzalpropanone

Chemicals Required:

Acetone –1 ml (0.83 g)
Benzaldehyde – 3.8 ml (3.9 g)
NaOH – 30 ml of 10 % soln

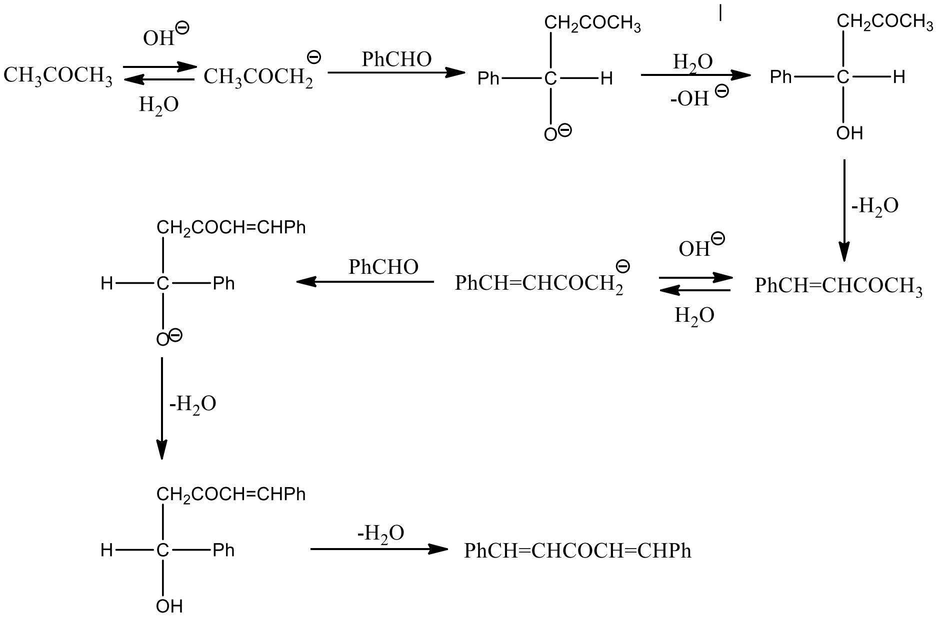
In a conical flask fitted with a cork, benzaldehyde (1 ml), acetone (3.8 ml) and methylated sprit (or alcohol) (15 ml) were shaken together for 2 minutes. To it was added 10% sodium hydroxide solution and shaken vigorously for 10 minutes with simultaneous pressure release. The reaction mixture was cooled in ice and the pale yellow solid was filtered through a filter paper, washed with water, dried, collected, weighed and recrystallized from ethanol, **m.p.** (120-122 ^{0}C).

Yield: 3 g (90%)

Green context:

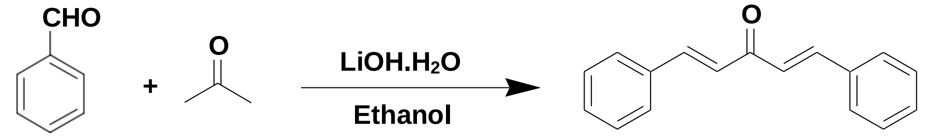
Hazardous organic solvents are avoided
Reagents are

Mechanism:



B. A. Hathaway, *Journal of Chemical Education*, **1987**, *64, 367.*

Alternative Procedure



Benzaldehyde **Acetone** **1,5-Diphenyl-penta-1,4-dien-3-one**

Chemicals Required:

Acetone: 0.81 mL (11 mmol)
Benzaldehyde: 2.3 mL (20 mmol)
$LiOH.H_2O$: 42 mg (1 mmol, 10 mol%))

In a 25 mL round bottom flask containing a small magnetic bar, the aldehyde and ketone were taken with ethyl alcohol (5 ml) and lithium hydroxide (42 mg) monohydrate was added into it. The reaction mixture was magnetically stirred vigorously for 8-10 minutes. The pale yellow solid precipitated out, 5 g of crushed ice was added and the solid was allowed to settle down. The precipitated pale yellow solid was filtered, washed with water, air dried and recrystallized with ethanol.

Yield: 2.1 g (90 %)
M.P. 120-121 °C

Precaution: The aldehyde should be free fromacid.

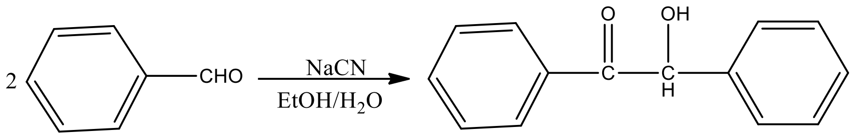
Green Context:
Hazardous organic solvents are avoided.
Lithium hydroxide is easy to handle as it is comparatively less hygroscopic than other alkali metal hydroxide.
Use of catalytic amount of the base.

S**.** Bhagat, R. Sharma, and A.K. Chakraborti, *J. Mol. Cat. A: Chemical* **2006,** *260*, 235- 240

Experiment:3 **Date:26.03.2020**

COENZYME CATALYZED BENZOIN CONDENSATION
(Thiamine hydrochloride catalyzed synthesis of benzoin)

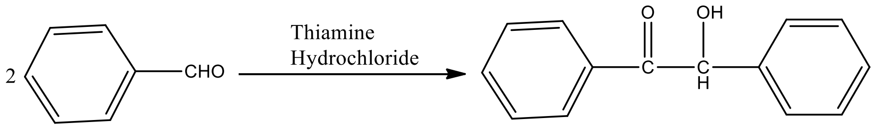
Conventional Procedure:



Non-green Component:

Involves the use of highly poisonous sodium cyanide

Alternate Green Procedure:



Chemicals Required:

Benzaldehyde	- 10 g
Thiamine hydrochloride	- 1.75 g
Sodiumhydroxide	- 5 ml (2M)
Ethanol	- 15 ml

The thiamine hydrochloride (1.75 g) was dissolved in water (about 5 ml) in a 50 ml round bottom flask. Ethanol (95%, 15 ml) was added and the solution was cooled by swirling the flask in an ice water bath. Meanwhile, sodium hydroxide solution (5 ml) was cooled in a small conical flask in an ice bath. Then over a period of about 10 min the sodium hydroxide solution was added dropwise to the thiamine solution. Fresh benzaldehyde (10 ml) was added to the reaction mixture. The mixture was heated gently on a water bath for about 90 min. The mixture was cooled to room temperature and then in ice bath to induce crystallization of the benzoin. If product separated as oil, the mixture was reheated until it was once again homogeneous. Then it was allowed to cool more slowly than before. Scratching of the flask with a glass rod may induce crystallization.

Yield - 6 g (30%)

Melting point of benzoin- 135 ^{o}C

Caution:

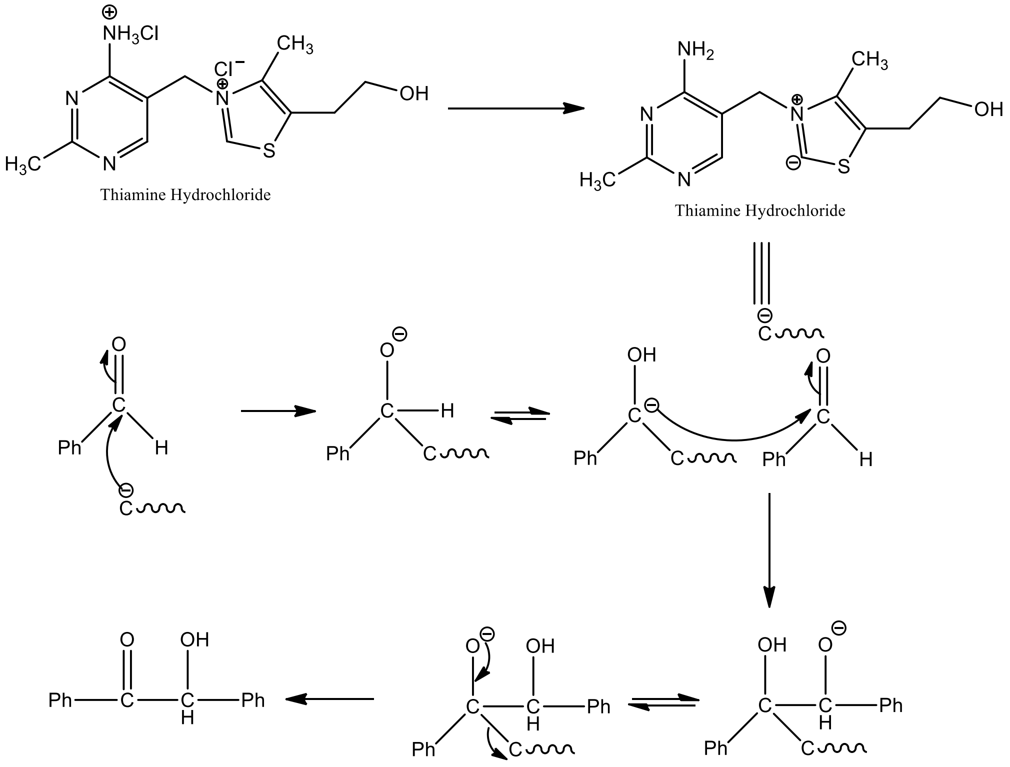
Benzaldehyde used in the experiment should be free of benzoic acid

Thiamine hydrochloride should be kept in refrigerator when it is not in use.

Green Context:

- Hazardous and poisonous cyanide ion is replaced by thiamine hydrochloride.
- Reaction is effected at a lower temperature.

Mechanism:



P.,D. L. Lampman, G. M.Chriz, *Introduction to organic lab technique;* College Publishing, New York,**1982** experiment no 40

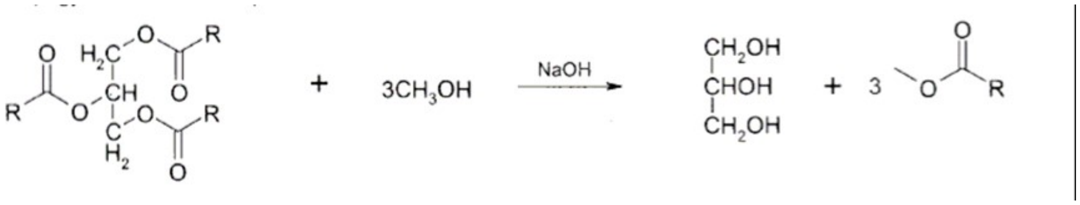
Experiment: 4 **Date:30.03.2020**

TRANSESTERIFICATION REACTION
(Synthesis of biodiesel)

Introduction:

This experiment focuses on synthesis of diesel fuel from vegetable oil. The mechanism involves a transesterification reaction, the process of transforming one type of ester into another type of ester.

Green Reaction:



Vegetable oil Glycerol Biodiesel

Chemicals Required:

Vegetable oil	- 100 ml
Methanol	- 20 ml
Sodiumhydroxide	- 3 pellets

Green Procedure:

The finely ground anhydrous NaOH was added into pure (99% or higher purity) methanol (20 ml) in a 250 ml Erlenmeyer flask and stirred vigorously until all the NaOH was dissolved. The pure vegetable oil (100 ml) was warmed to about 40 °C in a 250 ml beaker. The warmed up oil was poured into the methoxide solution with continuous stirring. At first the mixture would become cloudy, but should soon two layers would separate. This was stirred for 15-20 minutes. The contents of the flask were transferred into a 250 ml separatory funnel. The mixture will separate into two different layers. The glycerol will fall to the bottom, and the methyl ester (biodiesel) will float to the top. Allow the experiment to sit for an hour. The stopcock of the separatory funnel was opened and the glycerol was allowed to drain into a small beaker.

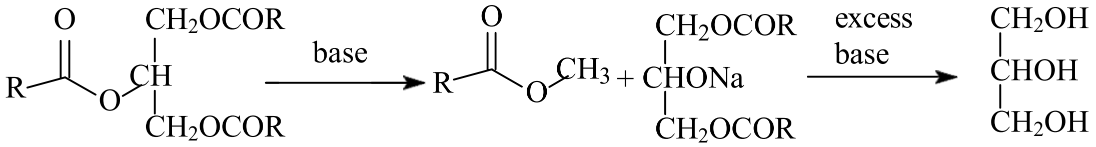
Green Context:

This lab experiment demonstrates three key green principles: the use of renewable feedstock, catalysis and design for degradation. Vegetable oil is a renewable starting material as it is derived from growing plants, rather than irreplaceable material like the earth's petroleum and natural gas supplies. The reaction is catalyzed by NaOH making this process economically viable for the industrial scale production of biodiesel. Biodiesel is an excellent product as it is environmentally friendly.

Safety:

- **Methanol**: Flammable and poisonous. Dispose excess by allowing it to evaporate in the fumehood.
- **NaOH**: Very corrosive. Causes severe burns. May cause permanent eye damage. Very harmful by ingestion.

Mechanism:



J. E. Thompson. *Greener Education Material for Chemists*
(http://greenchem.uoregon.edu/gems.html)

Experiment: 5 **Date:06.04.2020**

Synthesis of tetrabutylammonium tribromide(TBATB)

Proceedure: A sample of molybdic acid monohydrate, $H_2MoO_4.H_2O$ (0.16 mmol, 0.029 g) was taken in a 250 mL glass beaker and 30% hydrogen peroxide, H_2O_2 (15.52 mmol, 1.76 mL) was added to it. The mixture was stirred for 30 min. at room temperature. The solution, which was slightly turbid, was filtered through WhatmanNo.1filterpaper on a glassfunnel.The clear filtrate was collected in a 250 mL glass beaker and kept in the ice-water bath. Tetrabutylammonium bromide,TBAB (15.51 mmol, 5 g)andpotassiumbromide, KBr (31.01 mmol, 3.69 g) dissolved in (0.3M) H_2SO_4 (15.52 mmol, 51.70 mL) was added to this solution slowly with continuous stirring leading to the formation of a yellow precipitate. The mixture was continued to stir in ice-water bath for another ~1h and then kept standing in ice-water bath for 2 h to get an orange yellow compound of Tetrabutylammonium tribromide, TBATB. The compound was separated by filtration under suction using Whatman No.1 filter paper. It was dried *in vacuo* over fused $CaCl_2$ and was recrystallized fromacetonitrile.

Yield: 7.2 g (96%)

Melting Point: 76-77 ^{0}C. The chemical analyses, IR and conductance of the compound match very well with those reported in literature.

Green Context:

This reagent is a green brominating agent and avoids the use of highly toxic and hazardous liquid bromine.

M. K. Chaudhuri, A.T. Khan, B. K. Patel, D. Dey, W. Kharmawphlang, T. R Lakshmiprapha and G.C. Mandal, *Tetrahedron Lett,* **1998**, *39*, 8163;

M.K. Chaudhuri et al., *Pure Appl. Chem.*, **2001**, *73*, 93;

US Patent No. 7005548, February 28, 2006

Experiment: 6 **Date:09.04.2020**

Bromination of Chalcone by TBATB

Proceedure: Crystals of tetrabutylammonium tribromide, **TBATB**, (0.524 g, 1 mmol) were finely powdered by grinding with a pestle in a mortar for a few minutes. To it chalcone (0.416 g, 1 mmol) and 0.5 mL of water were added. The whole was mixed thoroughly and left at room temperature with occasional agitation or grinding for 15 min. The progress of the reaction was monitored by dissolving a small amount of the sample in ethylacetate followed by TLC of the ethylacetate solution over silica gel. Upon

completion of the reaction, 20 mL of water was added to the reaction mixture and stirred for 10 min. The reaction mixture was filtered, washed with water and air-dried to afford the compounds.
Yield: 0.7 g (95%).

Green Context:

This reagent is a green brominating agent and avoids the use of highly toxic and hazardous liquid bromine.

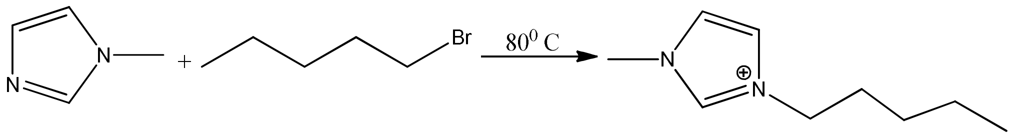
M. K. Chaudhuri, A.T. Khan, B. K. Patel, D. Dey, W. Kharmawphlang, T. R Lakshmiprapha and G.C. Mandal, *Tetrahedron Lett,* **1998**, *39*, 8163;

M.K. Chaudhuri et al., *Pure Appl. Chem.*, **2001**, *73*, 93;

US Patent No. 7005548, February 28, 2006

Experiment: 7 **Date:13.04.2020**

Preparation of ionic liquid, [pmlm]Br



1-Pentyl-3-methylimidazolium bromide ([pmlm]Br)

Chemicals required:

i) *N*-Methylimidazole
ii) n-Pentylbromide

Experimental procedure:

N-Methyl imidazole (1.2 g, 15 mmol) and n-pentyl bromide (2.71 g, 18 mmol) were taken in a small round bottom flask. Then the mixture was heated in water bath at 80 ^{0}C for an hour, keeping a guard tube at the mouth of the round bottom flask. A clear yellow viscous liquid was formed. It was then cooled and washed with a small amount of ether (1 ml) twice with ether to remove any unreacted bromide and remaining viscous liquid was dried by a vacuum pump.

Yield - 3.42 g (88%)

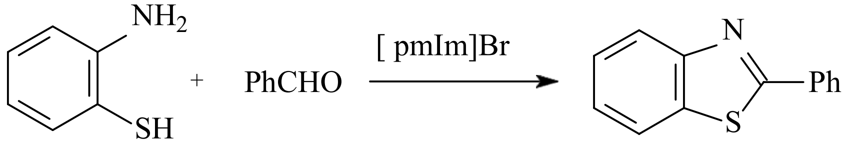
Spectroscopic Data:

^{1}HNMR (300 MHz, $CDCl_3$): δ0.8 (t, *J* = 6.9 Hz, 3H), 1.23 (m, 4H), 1.78 (m, 2H), 3.9 (s, 3H), 4.17 (t, *J* = 7.28 Hz, 2H), 7.65 (d, *J* = 11.0 Hz, 2H), 9.5 (s,1H).

V. Namboodiri and R.S. Varma, *Org. Lett.* **2002**, *4*, 3161

Experiment: 8 **Date:16.04.2020**

Preparation of 2- phenylbenzothiazoles catalyzed by ionic liquid, [pmlm]Br



Chemical Required:

i) Benzaldehyde – 1.0 g
ii) 2-Amino-thiophenol – 11.25 g
iii) Ionic liquid [pmlm]Br – 0.5 g

Experimental Procedure:

A mixture of benzaldehyde (1.0 g) and 2-amino-thiophenol (1.25 g) was heated in microwave oven (10% power, 120 W in presence of ionic liquid [pmlm]Br (500 mg) for 3 mins. After being cooled the reaction mixture was extracted with ether and the ether extract was evaporated to leave the crude product which was recrystallized from ethanol-water (4:1) to give a white solid.

Yield – 1.9 g (90%).
M.P. 112-115 °C

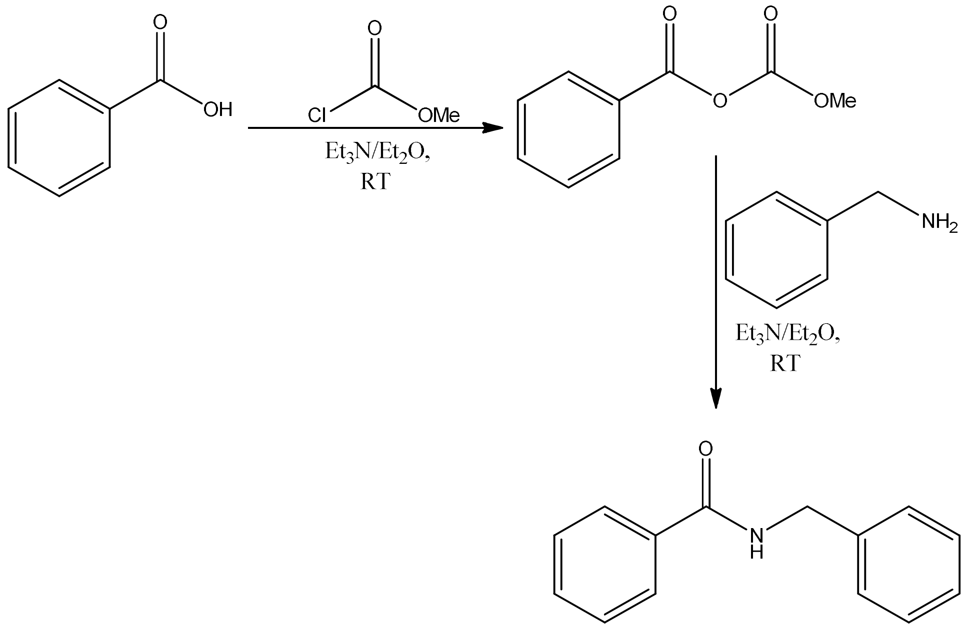
IR (KBr) : 1645, 1510, 1477, 962, 765 cm^{-1}
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (t, J = 7.3 Hz, 1H), 7.48-7.55 (m, 4H), 7.90 (d, J = 7.9 Hz, 1H), 8.09-8-12 (m, 3H).

Green Context:
This ionic liquid, [pmIm]Br is benign and works here as catalyst as well as reaction medium and thus no other solvent is required in this reaction. The reaction is also atom efficient.

B. C. Ranu, R. Jana and S. S. Dey, *Chem. Lett.* **2004**, *33*, 274

Experiment: 9 **Date:20.04.2020**

Preparation of *N*-Benzyl Benzamide from Benzoic acid



Chemicals Required:

Beenzoic acid	- 1.2g
Triethylamine	- 1.5 ml
Diethyl ether	- 60 ml
Methyl chloroformate	- 0.8 ml
Benzylamine	- 1.1 ml

Experimental procedure:

To a solution of benzoic acid (1.2 g) and triethylamine (1.5 ml) in diethyl ether (50 ml) at room temperature was added methyl chloroformate (0.8 ml) dropwise with vigorous mixing. After two minutes, the mixture was filtered through a Buchner funnel and the precipitate was washed with diethyl ether (10 ml). The combined ether layer was treated with benzylamine (1.1 ml) at room temperature and then the diethyl ether was allowed to evaporate over water bath. The viscous residue was treated with crushed ice and the resultant white precipitate was filtered through a Buchner funnel. The white precipitate was air-dried (0.9 gm, 44%). M.P: 104-106 °C (recrystallized from ethyl acetate/hexane mixture).

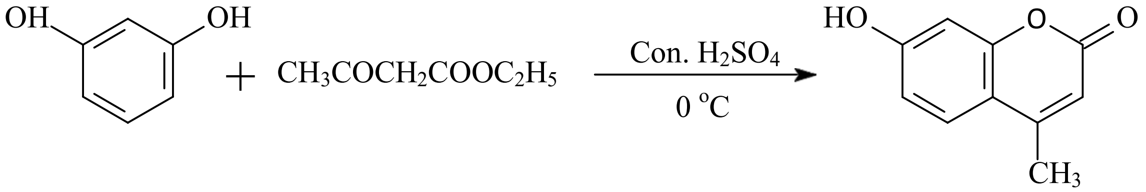
Spectral data for *N*-benzylbenzamide: IR (Neat): 3321, 3059, 1640, 1543, 1418cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.8-7.98 (d, J = 7.5 Hz, 2H), 7.48-7.516(t, J = 7.4 Hz,1H), 7.404-7.441(t, J=7.4 Hz, 2H)7.348-7.359(d,J=7.8Hz, 3H),7.294-7.315 (t, J=7.2 Hz, 1H), 6.47 (bs, 1H), 4.637-4.651(d, 2H);^{13}CNMR(100 MHz, $CDCl_3$): δ 167.3,138.1, 134.3, 131.5, 128.8, 128.6, 127.9, 127.6, 126.9, 44.1.

Note: This procedure can be used for making derivative of other carboxylic acids and is suitable for both UG and PG levels.

Experiment: 10 **Date:23.04.2020**

PECHMANN CONDENSATION FOR COUMARIN SYNTHESIS
(Clay catalyzed solid state synthesis of 7-hydroxy-4-methylcoumarin)

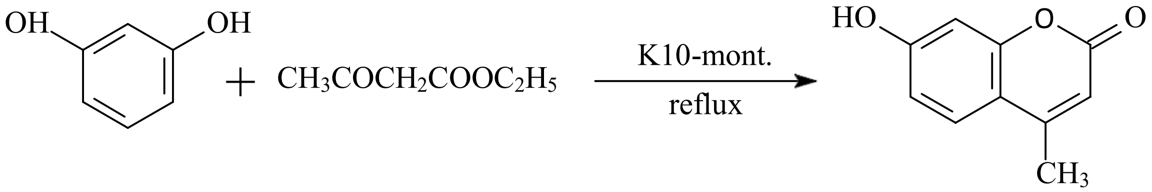
Conventional Procedure:



Non-green Component:

Use of corrosive conc. Sulfuric acid.

Alternate Green Procedure:



Chemicals Required:

Resorcinol - 1.1 g
Ethylacetoacetate - 1.35 g
K10-montmorillonite- 1.5g

Experimental procedure:

Resorcinol (1.1 g) was dissolved completely in ethyl acetoacetate (1.35 g) in a 50 ml dry round bottom flask. K10 montmorrilonite clay (1.5 g) was added to this homogeneous mixture and mixed thoroughly using a glass rod. The reaction mixture finally appeared as a paste. It was placed on a hot water bath and heated gently for 3-4 h. After completion of the reaction, mixture was cooled to room temperature and 7-hydroxy-4-methylcoumarin was extracted with ether by vigorous shaking. The clay was separated by filtration through Whatmann 4 filter paper. Separation with ether was repeated for 2 times. Finally, the filtrate was evaporated and the product is obtained as a white solid.

Yield: 1.5 g (85%)

Melting point of 7-hydroxy-3-coumarin- 180 °C

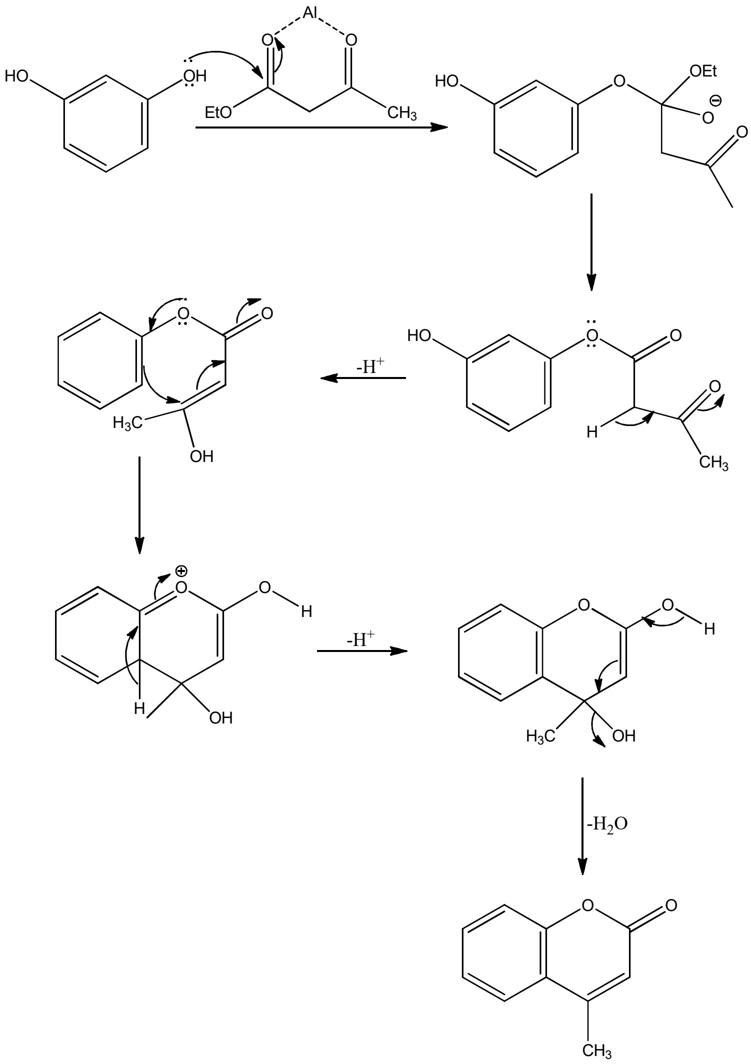
Green Context:

- Strong and corrosive H_2SO_4 isavoided.
- A solid acid catalyst K10 montmorillonite is employed.
- Reaction is carried out in solid state avoiding use of solvents.
- Catalyst can bereused.
- Largely reduced reaction time.
- Ice-bath conditions during addition is avoided.

Note:

When refluxed on a heating mantle, the yield increases significantly.

Mechanism:



Greener approach to undergraduate chemistry experiments, ACS publications, **2002**, p 25.

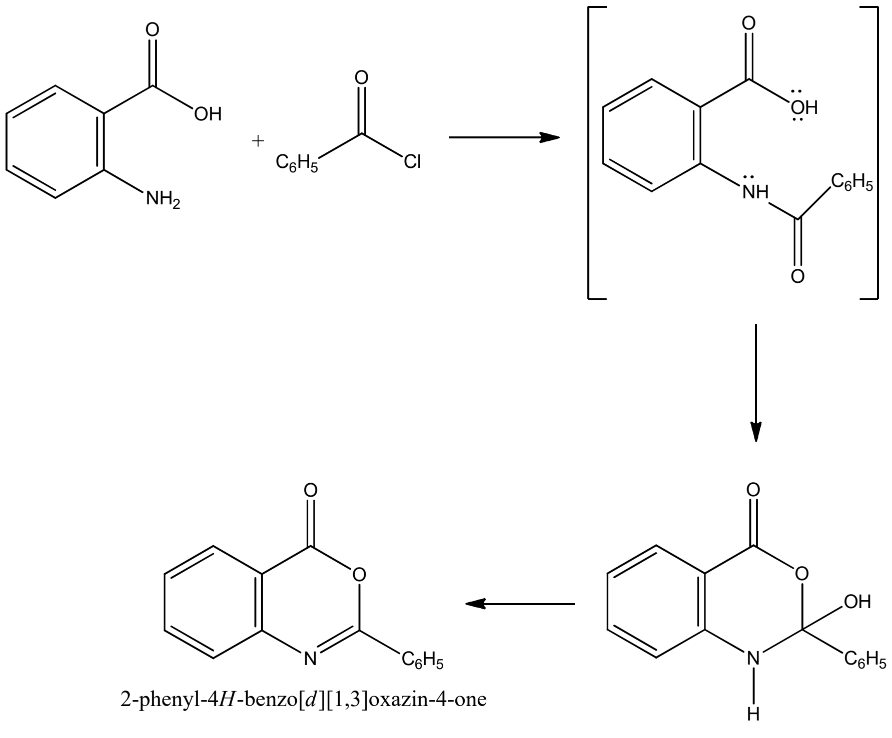
Experiment: 11 **Date:27.04.2020**

Reaction of 2-aminothiophenol and aromatic aldehydes

The conventional method of preparation of schiff bases involve either refluxing of aldehyde and amine in solvents like benzene or stirring at room temperature in chlorinated solvents.

A one-pot synthesis of 2-arylbenzothiazoles from the reaction of 2- aminothiophenol and aromatic aldehydes catalyzed by cerium (IV) ammonium nitrate (CAN) is reported.

The reaction of equimolar amounts of 2-aminothiophenol and aromatic aldehydes in methanol (MeOH) in the presence of CAN resulted into corresponding 2-arylbenzothiazoles in good yields via the intermediate formation of schiff's bases.



Chemicals Required:
2-aminothiophenol- 0.630 g
Benzaldehyde- 0.540 g
Methanol – 10 ml
Cerium (IV) ammonium
nitrate- (CAN -10% mol)

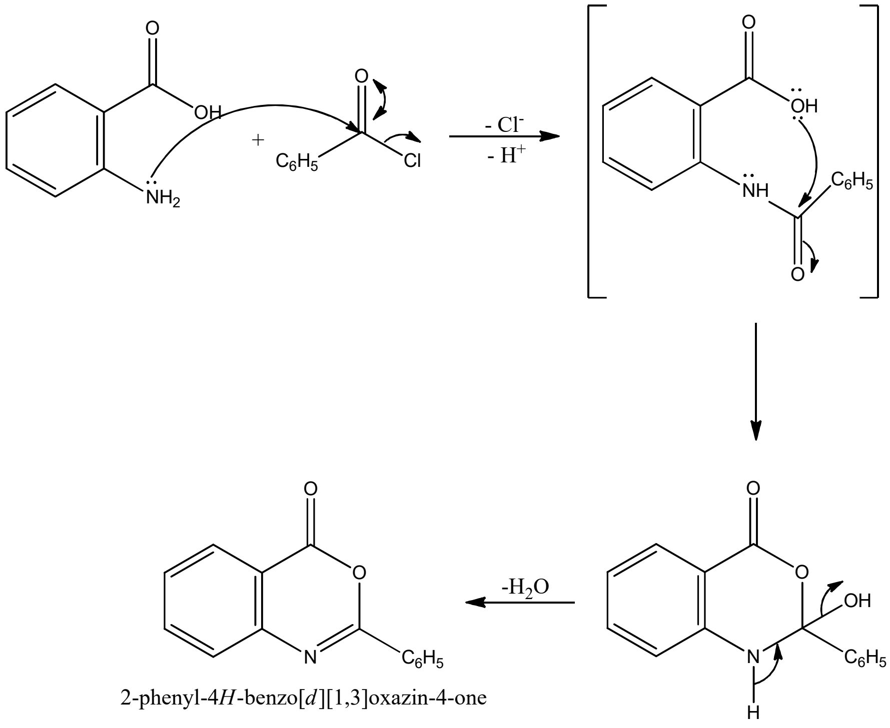
Experimental procedure:

To a mixture of 2-aminothiophenol (0.626 g, 5*10^{-3} mol) and Benzaldehyde (5*10^{-3} mol) in methanol (10 ml) was added with stirring 10% mol of cerium (IV) ammonium nitrate (CAN) in good yields.

Yield: 1.6 g (75%)

Melting point of 2-phenyl-4H-benzo[d][1,3]oxazin-4-one 112-113 °C

Mechanism:



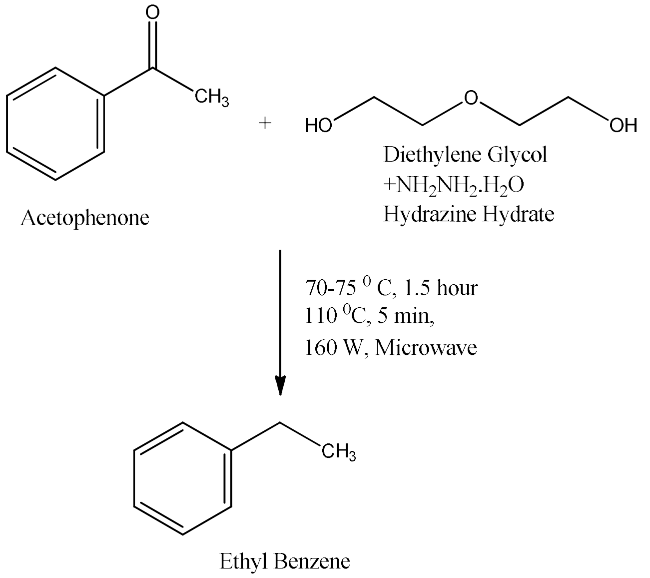
2-phenyl-4*H*-benzo[*d*][1,3]oxazin-4-one

Al-Qalaf F, Mekheimer RA, Sadek KU. Cerium (IV) ammonium nitrate (CAN) catalyzed the one-pot synthesis of 2- arylbenzothiazoles. Molecules 2008;13:2908-14.

Experiment: 12 **Date:30.04.2020**

Microwave-stimulated synthesis of ethylbenzene i.e. Wolf- Kishner reduction

The conventional procedure involves refluxing at 75 °C for one and half hour. Acetophenone , diethylene glycol, hydrazine hydrate and KOH pellets under microwave irradiation in 5 min at 110 °C temperature and 160-watt power resulted into ethyl benzene.



Chemicals Required:
Acetophenone - (0.626 g, 0.29 mol),
Diethylene glycol- (0.085 mol, 30 ml,)
Hydrazine hydrate- (0.54 mol, 9 ml)
Potassium Hydroxide (KOH-) pellets
Ether 10 ml
Anhydrous magnesium sulphate ($MgSO_4$) or
Sodium Sulphate (Na_2SO_4)

Experimental procedure:

The conventional procedure involves refluxing at 75 °C for one and half hour. 10 ml acetophenone (0.29 mol), 30 ml diethylene glycol (0.085 mol), 9 ml hydrazine hydrate (0.54 mol) and KOH pellets under microwave irradiation in 5 min at 110 °C temperature and 160-watt power resulted into ethyl benzene. The reaction mixture was transferred to a separating funnel and lower aqueous layer was discarded. The aqueous layer was extracted with 10 ml ether. Excess ether was removed by heating on a water bath. The resultant mixture was dried with anhydrous magnesium sulphate ($MgSO_4$) and a yellowish solution with gasoline like smell was obtained m.p of 135-139 °C with 74% yield.

Yield: 0.78 g (74%)

Melting point of ethyl benzene 135-139 ^{o}C

Al- Acharjee J, Ghoshal A, Ghosh SK. Microwave-assisted synthesis: need of the hour. W J Pharm Pharm Sci 2015;4:1741-9