HALOGEN ADDITION TO C=C BOND (Bromination of *trans*-stilbene)

Conventional Procedure:



Non-green Component:

Use of liquid bromine Chlorinated solvents

Green Procedure 1¹:



Chemicals Required:

- 1.8 g
- 5.2 ml
- 7 ml
- 10 ml

Trans-stilbene (1.80 g) in ethanol (10 ml) was refluxed. The aqueous solution of HBr (33%) (5.2 ml) and hydrogen peroxide (H_2O_2 , 30%) (7 ml) were added from a dropping funnel sequentially to this refluxing solution of stilbene. The colourless solution became deep orange in colour. Within 15 minutes, the orange colour disappeared. This indicates the bromination of stilbene. The solution

was allowed to cool down. During this the precipitate due to stilbene dibromide separated out. The precipitate was filtered, recrystallized and dried.

Melting point (m.p.): 237 °C **Yield:** 2.4 g (70%)

Alternative Procedure²:

Chemicals Required:

trans-Stilbene	- 1.8 g
GlacialAceticacid	- 20 ml
Sodiumbromide	- 3 g
Sodiumbromate	- 1 g

To a solution of *trans*-stilbene in acetic acid was added a mixture of sodium bromide and sodium bromate at room temperature with stirring by a glass rod. The reaction mixture was then stirred occasionally with a glass rod for 1 hour. The developed light brown colour disappeared. The acetic acid in the reaction mixture was then neutralized by sodium hydroxide solution. The precipitate of stilbene dibromide separated out. This was filtered and dried.

Yield: 2.6 g (80%)

Green Context:

Corrosive liquid bromine is avoided Atom efficient Water is the only byproduct in HBr- H₂O₂ method and in NaBr- NaBrO₃ method sodium acetate is formed along with water. HBr-H₂O₂ mixture and bromide-bromate couple offer *in situ* oxidation of Br⁻ to molecular bromine.

Caution:

Care must be taken while handling the solution of hydrogen bromide and hydrogen peroxide.



$$5 \text{ NaBr} + \text{NaBrO}_3 + 6 \text{ CH}_3\text{COOH} = 3 \text{ Br}_2 + 3 \text{ H}_2\text{O} + 6 \text{ NaOCOCH}_3$$

1. L. C. McKenzie, L. M. Huffman, and J. E. Hutchison, *Journal of Chemical Education.*, 2005, 82, 306.

Unpublished Results, B. C. Ranu, S. Adimurthy, and P. K.Ghosh

[4+2] CYCLOADDITION REACTION (Diels-Alder reaction between furan and maleic acid)

Conventional Procedure:



Non-green Component:

Use of benzene which is one of the most toxic solvents

Green Procedure:



Chemicals required:

Furan : 1.75 g Maleic acid : 1.1 g

A mixture of furan (1 g), maleic acid (2 g) in water (10 ml) was shaken or stirred for 2-3 hrs at room temperature. The adduct formed, was filtered, washed with water, dried and recrystallized from aqueous ethanol, **m.p.** 138-140 $^{\circ}$ C

Yield: 2.1 g (80%)

Green Context:

Reaction carried out in aqueous medium avoiding benzene Efficient at room temperature itself 100% atom efficient



R.B. Woodward and H. Baer, J. Am. Chem. Soc. 1948, 70, 1161.

D. C. Rideout and R. Breslow, J. Am. Chem. Soc. 1980, 102, 7816.

REARRANGEMENT REACTION (Benzil Benzilic acid rearrangement)

Conventional Procedure:



Alternate Green Procedure:

Preparation of Benzilic Acid in Solid State under Solvent-free Condition:

Chemicals Required:

Benzil : 1 g Sodium hydroxide or potassium hydroxide: 1 g Conc. Hydrochloric acid

Benzil (1 g) was thoroughly grounded with solid NaOH or KOH (1 g) in a dry mortar with the help of a pestle to make an easy flowing powder. This material was subsequently taken in a dry conical flask fitted with a piece of cotton at its mouth and heated on a boiling water-bath for 20 minutes. Then it was cooled to room temperature, dissolved in minimum amount of water (unreacted benzil, if any, was removed simply by filtration) and the aqueous solution was acidified with conc. HCl with thorough cooling in ice. The precipitated benzilic acid was filtered, washed with cold water and crystallized from hot water, if needed.

M.p. 149-151 °C

Yield: 0.86 g (80%.)

Green Context:

- Solvent-free procedure
- Atom efficient

Mechanism:



K. Tanaka and F. Toda, *Chem. Rev.*, **2000**, *100*, 1045.

ELECTROPHILIC AROMATIC SUBSTITUTION REACTION (Nitration of phenol)

Conventional Procedure:



Non-green Component:

Involves use of Con. Sulfuric acid

Alternative Green Procedure:



Chemicals Required:

Calcium nitrate tetrahydrate - 1.5 g Acetic acid - 5 ml Salicylic acid - 1 g

Calcium nitrate (1.5 g) was dissolved in warm acetic acid (5 ml) and salicylic acid (1 g) was added to it. Then the mixture was heated in a boiling water bath (maintained at > 80 °C) for 1 min. Salicylic acid was dissolved completely and the solution became dark red. It was immediately poured into a 10 ml of ice cold water. The resultant turbid dark red solution was placed in a refrigerator. After four hours, the yellow crystals that separated were washed free of acid with minimum amount of ice cold water and then dried.

Yield: 0.66 g (50 %)

M.p. of 4-nitrosalicylic acid = $234 \text{ }^{\circ}\text{C}$

Green context:

- ▶ Nitration is rapid.
- > Ecofriendly nitration of phenols and its derivatives without nitric acid
- Reagents and byproducts (calcium acetate) in this reaction are useful agrochemicals, environmentally benign and thus eco-friendly.
- Regioselective nitration is achieved.

Caution:

The yield of the reaction mainly depends on temperature of the reaction and solubility (since products are soluble in water). Very minimum amount of water should be used for washing of acetic acid as well as the byproducts like calcium acetate and calcium nitrate.

Mechanism:



Note: This nitration procedure is very efficient with salicylic acid and thus may be used for making derivative of salicylic acid in identification of organic compounds for UG and PG level.

However, it may not give equally good results for nitration of all aromatic compounds and thus should not treated as a general method of nitration.

A. K. Bose,* S. N. Ganguly, M. S. Manhas, S. Rao, J. Speck,U. Pekelny and E. Pombo-Villars, *Tetrahedron Lett.*, **2006**, *47*,*188*

ELECTROPHILIC AROMATIC SUBSTITUTION REACTION-II (Bromination of acetanilide)

Conventional Procedure:



Non-green Component:

Liquid molecular bromine is used

Alternative Green Procedure:



Chemicals Required:

Acetanilide - 1 g Potassium bromide - 1 g Ceric ammonium nitrate - 6 g Ethanol - 15 mL Water - 15 mL

Experimental procedure:

In a 250 ml conical flask acetanilide (1 g) was dissolved in ethanol (15 ml). Then potassium bromide (1 g) and ceric ammonium nitrate (6 g) were dissolved in water (15 ml). This solution was transferred into an addition funnel. This solution was added drop wise to the conical flask containing acetanilide solution. After the addition was over, the reaction mixture was stirred for 10 minutes in room temperature (white crystals appeared). Then this solution was poured into ice-cold

water. The white crystals were filtered through Buchner funnel and the solid was dried.

Yield: 1.34 g (85 %)

M.P. of *p*-bromoacetanilide = $165 \,^{\circ}C$

Green Context:

- Corrosive molecular bromine is replaced with a novel brominating agent.
- > Bromination is carried out in aqueous medium.
- Chlorinated solvents are avoided.
- ➤ Use of acetic acid as solvent is avoided.
- Reaction is considerably fast.

Mechanism:

$$Ce(IV) + Br \xrightarrow{H_2O} Br \xrightarrow{Ce(IV)} Br^{+}$$



Note: This reaction can be used for making bromo-derivative of acetanilide in

identification of organic compounds in UG as well as in PG level.

P. F.Schatz, Journal of Chemical Education. 1996, 173, 267.

GREEN PHOTOCHEMICAL REACTION (Photoreduction of benzophenone to benzopinacol)

Benzopinacol can be prepared from benzophenone in presence of sun light (photochemically) using isopropanol as the reducing agent in presence of acetic acid. Acetic acid is added to prevent the cleavage of benzopinacol to benzophenone and benzhydrol by the alkali derived from the glass container used for the reaction.



Chemicals Required:

Benzophenone - 2.5 g *Iso*-Propanol - 10 ml Glacial Acetic Acid – one drop

Experimental procedure:

Benzophenone (2.5 g) was placed in a test tube and dissolved in isopropanol ((10 ml). The test tube was then filled with isopropanol and to it was added a drop of glacial acetic acid. The test tube was stoppered and the reaction mixture was exposed to bright sun light. Colourless crystals of benzopinacol started appearing along the sides of the test tube after 5-6 hrs. The reaction mixture was allowed to stand in bright sun light for 4-5 days for the completion of the reaction. The solid was dried.

Report the yield and the m.p. (lit. m.p. 182 °C).

Green Context:

Use of safe chemicals and safer reaction conditions

Use of renewable source of energy (solar energy).

The product obtained above will be used in the next experiment (conversion of benzopinacol to benzopinacolone is pinacol-pinacolone rearrangement)



P.,D. L. Lampman and G.M.Chriz, *Introduction to Organic Lab Technique*; College Publishing, New York, 1982 exp. 47

PINACOL PINACOLONE REARRANGEMENT REACTION-I (Preparation of benzopinacolone)

Benzopinacol obtained in the first experiment is converted to benzopinacolone by heating under reflux (5 minutes) with glacial acetic acid containing trace amount of iodine dissolved in it. This reaction is known as pinacol-pinacolone rearrangement.



Chemicals Required: Benzopinacol - 2.0 g Glacial Acetic acid - 10 ml Iodine – trace amount

Procedure:

Benzopinacol (2.0 g) was placed in a round bottomed flask and to it was added a solution of iodine (trace) in glacial acetic acid (10 ml) and the reaction mixture was refluxed on a wire gauze by Bunsen burner for 5-7 minutes. The reaction mixture was allowed to cool down to room temperature and then kept in the refrigerator over night. The crystals of benzopinacolone were filtered, dried in air.

Report the yield and the m.p. (lit. m.p. 182 °C)



W. E. Bachmann, J. Am. Chem. Soc. 1927, 49, 246 (Org. Synth., 1943, Coll. Vol 2, p. 73)

REARRANGEMENT REACTION (Rearrangement of diazoaminobenzene to *p*-aminoazobenzene)

Conventional Procedure:



Alternative Green Procedure:



para-aminoazobenzene

Chemicals Required:

Diazoaminobenzene -2 g K10 montmorillonite -2 g

Experimental procedure:

Diazoaminobenzene (2 g) was thoroughly mixed with K10 montmorillonite clay (2 g). The mixture was taken in a round bottom flask and heated in a water bath for 3 hours with periodical shaking after every 15 min. The mixture was then extracted with ether. The ether layer was evaporated and the residue was recrystalized from aqueous ethanol, m.p. 127-128 °C.

Yield: 1.7 g (85 %)

Green Context:

- ➢ Eco-friendlymethod
- Simple reactionprocedure
- ➢ No need for excess aniline and aceticacid

 NH_2



K. Pitchumani, C. Venkatachalapathi and S. Sivasubramanian, *Indian J. Chem.*, **1997**, *36B*, 187.

 NH_2

RADICAL COUPLING REACTION (Preparation of 1, 1-bis-2-naphthol)

Conventional Procedure:



Non-green Component:

Use of more energy (reflux)

Green Procedure:



Chemicals Required:

2-Naphthol	- 2.88 g
Iron(III)chloride	- 0.7 g
Water	- 2 drops
Toluene (for recry	vstallization)

Experimental procedure:

A mixture of of 2-naphthol (2.88 g) and iron(III) chloride (0.7 g) with 2 drops of water in an agate (or porcelain) mortar pestle was grinded for about 20

minutes. The mixture was allowed to stand for about 2 hrs with a little grinding now and then. The mixture was transferred with water (40 ml) into a 100 ml beaker and boiled for 10-15 minutes. The mixture was cooled and the solid was filtered, washed with boiling water (10 ml), dried and recrystallized fromtoluene., m.p. 214-217 $^{\circ}$ C.

Yield: 3.9 g (90%)

Green Context:

Efficient method

Easily available catalyst

Reaction is performed with simple grinding at room temperature without any solvent

Work up of the reaction involves aqueous medium.

This demonstrates the concepts of oxidative coupling, free radical and C-C bond formations.



A. I. Vogel, Textbook of Practical Organic Chemistry, Fifth Edition, 1989

 NH_2

GREEN OXIDATION REACTION (Synthesis of adipic acid)

Conventional Procedure:



Non-green Component:

This procedure involves corrosive conc. nitric acid. This causes evolution of oxides of nitrogen. The reaction has to be carried out in fume cupboard and oxides of nitrogen need to be absorbed inwater.

Green Procedure:



Chemicals Required:

Cyclohexene	- 2g
SodiumTungstate	- 0.5 g
Potassium hydrogensulphate	- 0.37 g
Aliquat 336	- 0.5 g
Hydrogenperoxide (30%)	- 12ml

To a 50 ml round- bottom flask fitted with a condenser sodium tungstate dihydrate (0.50 g) was added. This was followed by addition of aliquat 336 (0.5 g), 30% hydrogen peroxide (12 ml) and potassium hydrogen sulphate (0.37 g). The mixture was shaken and then cyclohexene (2 g) was added. The reaction mixture was heated on a sand bath to reflux for 2 hrs. The progress of the reaction was monitored by observing whether the layers are separated. As the liquid cyclohexene was converted to the water soluble adipic acid, the organic layer will eventually disappear. After two hours of reflux, the round-bottom flask was removed from the sand bath. Upon cooling, the crude adipic acid was precipitated. The crude sample was recrystallized from water to get pure adipic acid, m.p. 151- 153° C.

Yield: 2.5 g (70%)

Green Context:

Eliminates the use of nitric acid Atom economy: Waste by-products are minimized, better yield Use of hydrogen peroxide as oxidizing agent in place of KMnO₄ or HNO₃ Phase transfer catalysis

S. M. Reed and J. E. Hutchison, Journal of Chemical Education, 2000, 77, 1627.

 NH_2

THREE COMPONENT COUPLING (Synthesis of dihydropyrimidinone)

Conventional Procedure:



Non-green component:

Use of sulphuric acid Solvent workup Long reaction time

Green Procedure:



Chemicals Required:

Ethylacetoacetate	_	1.3 g
Benzaldehyde	-	1.1g
Urea	_	0.7g

Experimental procedure:

A mixture of benzaldehyde (1.1 g), ethyl acetoacetate (1.3 g) and urea (0.7 g), taken in a round bottom flask was shaken by hand for 2 minutes. The reaction mixture was then heated in a water bath at 90 °C for one hour. With progress of the reaction a solid started to deposit and after one hour the flask is full of solid. The solid was taken out carefully with a spatula or spoon in a conical flask. The yellow solid was washed with cold water (1 ml) and then recrystallized from rectified spirit to give a colourless solid, m.p. 201-202 °C.

Yield: 2 g (79%)

Green context:

Use of no hazardous organic solvents

No requirement of catalyst

Faster reaction



C. Ranu, A. Hajra and S. S. Dey, Org. Proc. Res. Dev. 2002, 6, 81

SOLVENT-FREE REACTION (Microwave-assisted ammonium formate-mediated Knoevenagel reaction)

Chemicals Required:

- 1. *p*-Anisaldehyde : 1.32 g
- 2. Ethyl cyanoacetate : 1.13 g
- 3. Ammonium formate : 630 mg
- 4. Domestic Microwave Oven

Experimental procedure:

p-Anisaldehyde (1.32 g), ethyl cyanoacetate (1.13 g) and ammonium formate (630 mg,l) were intimately mixed in a round bottomed flask fitted with CaCl₂ drying tube and placed on a bed of alumina taken in a beaker. This was then subjected to microwave irradiation for 90 seconds (with an installment of 30 sec each at a power level of 300 watts followed by intermittent cooling). After completion of reaction it was taken out, cooled to room temperature and crushed ice (20 gm) was added to the reaction mixture and shaken well. The solid product, precipitated in a granular form, was filtered, washed well with water and dried to furnish ethyl 2-cyano-3-(4'-methoxyphenyl)-propenoate (1.84 g, 80%) in practically pure form. The product can be further purified by recrystallization from ethyl acetate-petroleum ether (60°-80 °C), m.p. 88 °C.

Yield: 1.8 g (80 %)

Green Context:

- Solvent-free reaction procedure
- Simple workup and rapid conversion (within 90 sec)
- Use of microwave energy for activation



S. Bhar, Unpublished results