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Research Paper

Design, Synthesis,Characterizationand Antimicrobial Activity Of 4,4-Dihydroxybenzil

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ABSTRACT

The synthesis of benzil from benzoin is a classic organic chemistry experiment that involves the oxidation of secondary alcohol to a ketone using an oxidizing agent, such as nitric acid. Benzil is a useful compound that is often used as a starting material for the synthesis of other organic compounds, such as dyes and pharmaceuticals. The reaction involves the conversion of benzoin to benzil via a mechanism that involves the formation of hemiketel intermediate. This reaction is typically carried out in a solvent, such as ethanol or methanol, and the product is isolated by recrystallization. This experiment provides students with an opportunity to learn about oxidation reaction, the chemistry of carbonyl compounds, and importance of purification techniques in organic synthesis

INTRODUCTION

Medicinal chemistry

The discipline of medicinal chemistry leads to the discovery and development of new agefor treating diseases. Most of the activity is directed to new natural or synthetic organic compounds. Medicinal chemistry deals with the discovery, development, identification and interpretation of the mode of action of biologically active compounds Add the molecular level. It is also concerned with the study, identification and synthesis off the metabolic products of drug and related compounds. It involves isolation off compound from the natural or synthesis off the new molecules, Investigation of the relationships between the structure of natural synthetic compound And their biological activities, Elucidation of their interactions with receptors of various kinds, Including enzyme and DNA, The determination of their adsorption, transport, Distributary properties and studies of the metabolic transformation of this chemicals into other chemical and their excretion.It deals with the

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discovery and design of new therapeutic chemicals and their development into useful medicines and the forefront of innovation, Blending of synthetic chemistry, molecular modeling, And pharmacological studies to discover design new drugs and to investigation their interaction at the molecular, cellular and animal level. Medicinal chemist has a greater role in development of numerous organic compounds suitable for treatment of illness and maintenance and field of human beings.

Drug discovery

Drug discovery is process of designing and synthesizing new compound and evaluating to assess drug safety and efficacy in humans. The traditional way to discover new drugs has been to screen a large number of synthetic chemical compound or natural product or desirable effects. Modification of lead compounds are often carried out to improve activity, Reduce side effects and to improve performance.

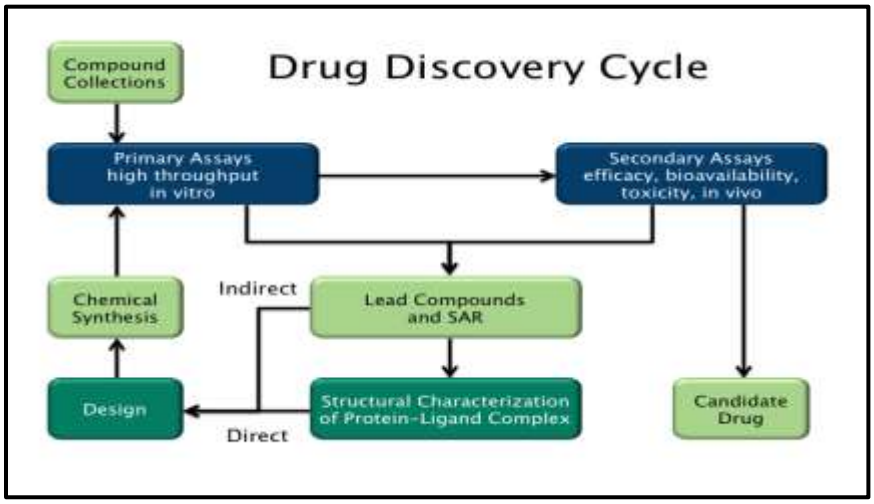


Fig.Drug Discovery Cycle

SYNTHESIS:

Chemical synthesis is the preparation of a compound, usually an organic compound which repaired or synthesized by performing various chemical reactions using an In expensive starting material and changing its molecular structure, By reaction with other chemicals. The best chemical synthesis are those that use cheap starting materials which requires only a few steps, And have a good output of product based on amounts of starting chemicals.

IMPORTANCE OF HETEROCYCLES IN MEDICINAL CHEMISTRY:

Heterocycles are organic compounds containing at least one atom of carbon and at least one element other than carbon such as sulfur, Oxygen or nitrogen with a ring structure. It is one of the vital classes of organic compounds which are used to mainly biological fields due to its activity in multiple illness. Today there are lot of heterocyclic Compounds are known, Day by day due to their synthetic utility. Heterocycles have been found for key structural in medicinal chemistry and also they are frequently found in large percent in bio-molecules such as enzymes Natural products and biological active compound including antifungal, anti-inflammatory, antibacterial, anti oxidant, anti-convulsant, anti allergic, enzyme inhibitors, anti-diabetic, anti HIV, anti cancer activity.

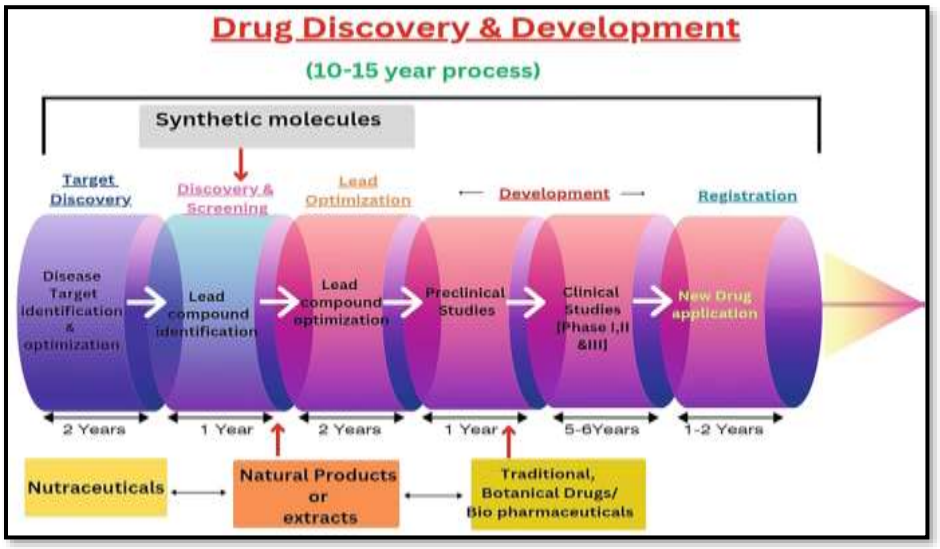
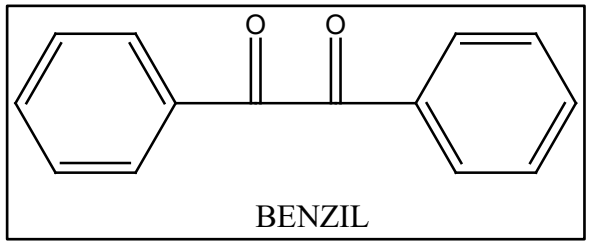
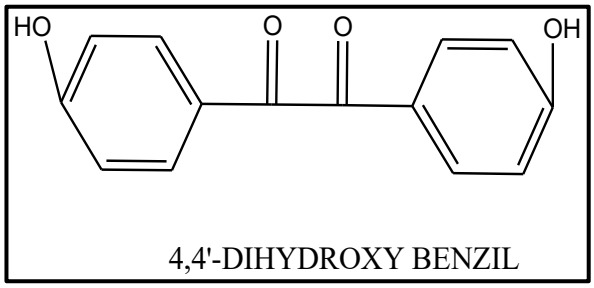


Fig.Drug Discovery and Development

Benzoin is an organic compound with the Chemical formula (C14H12O2) . It is a hydroxy ketone attached to two phenyl groups. It appears as off-white crystals, with a light camphor -like odor.Slightly acrid taste. When broken the fresh surfaces have a milky-white color. Benzoin is synthesized from benzaldehyde in the benzoin condensation . It is chiral and it exists as a pair of enantiomers: (*R*)-benzoin and (*S*)-benzoin. Benzoin is also an vanilla-like aroma,highly valued across multiple Industries Such as Pharmaceuticals,Perfumery,and Organic Synthesis. In Pharmaceuticals ,benzoin plays a significant role as a precursor in the synthesis of certain drugs and is commonly found in Ointment ,Creams,and other topical formulations due to its antiseptic and soothing properties,which help treat minor skin irritations and promote healing. Benzoin derivative have been used as Photoinitiators in polymerization reactions. It is an derivative act as an intermediates in drug synthesis. It is used in preparation of Antiseptics ,Anti-inflammatory drugs. Benzoin is used as Improve durability and elasticity of rubber products.The synthesis of benzil from benzoin involves the oxidation of benzoin using nitric acid. Benzoin is a colorless solid thatis soluble in alcohol and has melting point of 137°C. Benzil, on the other hand, is a yellow solid that is insoluble in waterbut soluble in alcohol and has melting point of 95-97°C.The reaction between benzoin and nitric acid involves the formation of an intermediate compound called nirobenzoin.Nitric acid acts as a strong oxidizing agent, which converts the alcohol groups in benzoin to aldehyde groups innitrobenzoin. Further oxidation of nitrobenzoin using nitric acid results in the formation of benzil



BENZIL



4,4'-DIHYDROXY BENZIL

APPLICATION:

1.**Industrial Application:**

- Material Science : It is used as a bifunctional organic building block for assembling larger organic frameworks,dendrimers,and polymers.
- Photoinitiators : Used in the production of photosensitive materials.
- Dye Industry : Derivative are used in the development of reactive disperse dyes for nylon and silk fabrics.

2.Laboratory and potential Application:

- Topical Veterinary Treatment: Cutaneous plasters,composed of agar –water base,weredesignrd and loaded with DHAB to treat skin infections in animals (eg.,animal folliculitis or burn infections).
- Lab Assay Formulation: DHAB is prepared as a suspension in glycerol for microdilution assay to determine minimum inhibitory concentration and minimum bactericidal concentration.
- Polymer precursor :4,4 –dihydroxybenzil is extensively used as a UV light stabilizer in plastics,coatings,and adhesives.

3.**Other Application:**

- Dermatological Treatment: Due to its low dermal toxicity DHAB has been , formulated into cutaneous plasters for treating animal skin infections.
- Bioremediation: Its ability to be degraded by certain bacteria make it a candidate for wastewater treatment involving aromatic pollutants.

XPERIMENTAL WORK:

Preparation of Benzil Derivative Material:
Chemicals:

- Benzoin (C14H12O2)
- Concentrated nitric acid (HNO3)
- Ethanol (C2H6O)
- Sodium hydroxide (NaOH),Water (H2O)

Instruments:

- Round bottom flask
- Water bath
- Magnetic Stirrer
- Separating funnel
- Filter assembly
- Ice bath
- Reflux setup

Procedure:Step 1

1.preparation of Nitriting Mixture:

1. In a round-bottom flask, mix concentrated nitric acid and sulfuric acid in a specific ratio (typically 1:1 or 1:2).
2. Cooling the Mixture: Cool the nitrating mixture in an ice bath to a temperature range of 0-5°C.
3. Addition of Benzoin : place 5g of benzoin and 25ml of concentrated nitric acid in a round bottom flask and heat on a boiling water bath for about one hour with occasional shaking until the evolution of oxides of nitrogen cases.
4. Pour the content of flask into 100ml ice cold water contained in a beaker.
5. Stir well until the oil crystallizes completely as a yellow solid.
6. Filter off the crude benzil at the pump and wash it thoroughly with water to remove the nitric acid.
7. Recrystallize from alcohol
8. Quenching the Reaction: Pour the reaction mixture into a large volume of ice-cold water to quench the reaction.
9. The yield of pure benzil collect.

Step 2.

1. Reflux: In a 100ml round bottom flask,take 5g of benzil and 10g of KOH dissolved in 15-20 ml of ethanol and a small amount of water.
2. Reaction:Heat the mixture under reflux for about 15-20min.The solution turns from yellow to blue as the rearrangement occurs.
3. Cooling and precipitation:cool the reaction mixture and pour it into a beaker containing ice-cold water.
4. Extraction/Filteration:If any unreacted benzil or byproduct remains (oily layer),filter it
5. Purification:Filter the crude 4,4 dihydroxybenzil,wash with cold water,and recrystallize it using hot water or water.
6. Product Formation: A pale yellow precipitate should form, indicating the successful preparation of the 4,4-dihydroxybenzil derivative.

STEP 1

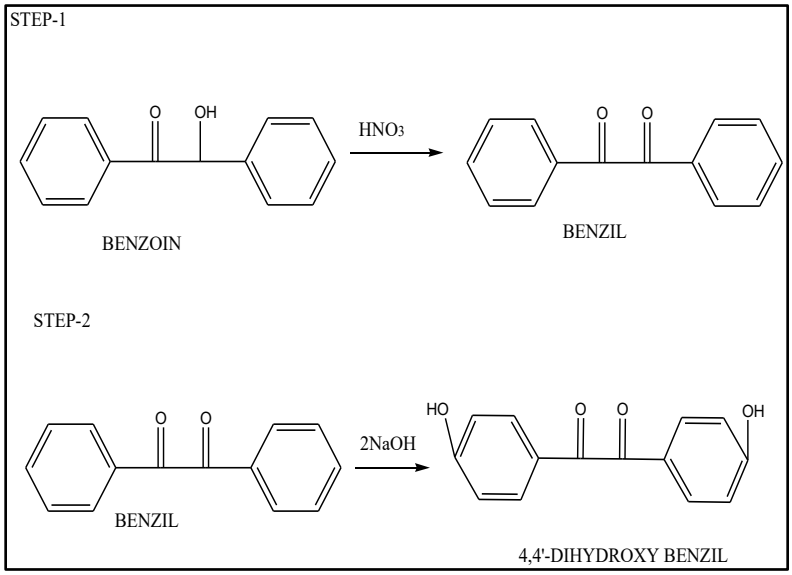
In this reaction secondary alcoholic group og benzoin is oxidized to ketone group and form benzyl in the presence of concentrated nitric acid .Nitration of aromatic ring is not occurring as sulphuric acid is tatally absent in the whole process.During this reaction the by product,H2NO3 is unstable it loses water (dehydration) to produce NO2 gas.

Step 2

When Benzil is treated with two molecule of Sodium hydroxide with concentratedSulfuric acid to form 4,4-Dihydroxybenzil.

PROPOSED REACTION:

SCHEME FOR SYNTHESIS:



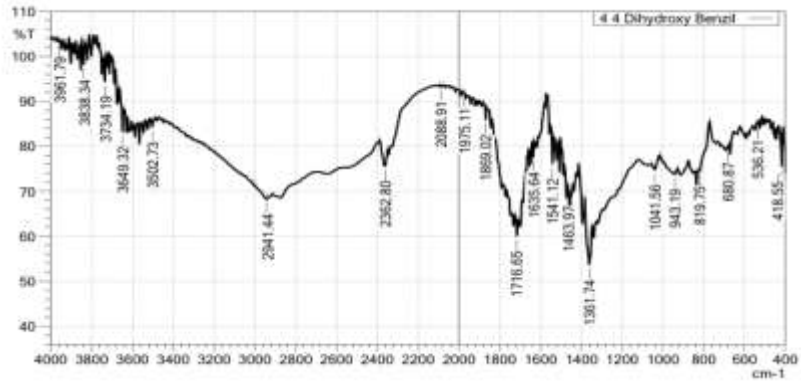
RESULT AND DISCUSSION:

1. Preliminary Test and Physical Examination
2. Structural elucidation using Infra-Red spectroscopy

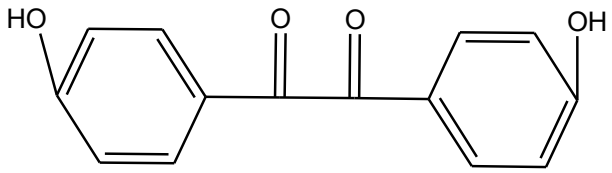
1. Preliminary Test and Physical Examination

Test	Observation	Interference
State	solid	Generally high molecular weight usually having more than 6 carbon atom chain . Eg-Benzoin ,Benzyl Alcohol hydrocarbon may be present .
Colour	yellow	Phenol Compound ex. Benzoin,dihydroxybenzil ,phenol, crysol, Resorcinol
Odour	Fishy	Aromatic α-diketone
	Bitter almond	Benzil
Ignition Test		
Flame test	Sooty flame	Aromatic compound
Test for Phenol		
Liberman'sNitroso test Add little 0f phenolic compound to minute crystal of NaNO2 in dry test tube Heat gently for a minute ,cool and few drops of conc.H2SO4 from the slides	Green/Blue colour with water	Phenolic compound is Confirmed
	Red colour with dil.HCl	Phenolic compound is Confirmed
	Yellow ppt ,which is insoluble in 2ml of ammonia solution	Phenolic compound is Confirmed
Sub+Alcoholic FeCl3.	Purple /Green/Violet colour	Aldehyde/Ketone absent Phenols or cresols may be Present
Phthalein Test:0.2g Sub +0.2g phthalic anhydride+2-3 drops of conc.H2SO4 heat a min and cool add 1ml of water then pour in dil.NaOH	Violet/pink colour	Phenol present
Sub+Conc.H2SO4(in dry test tube)	Tube becomes hot and a White gelatinous product.	Benzyl alcohol confirmed
Test for Alcohol		
Sub+Sodium metal in a dry test tube. 1ml of acetyl chloride in a dry test tube +drop of the compound.	Effervescence	Alcohol Present
	Strong Effervescence	Alcohol Present
Sub +2,4 –Dinitrophenyl-hydrazine solution.	No red precipitate	Aldehyde/ketone absent Alcohol present.
Sub+freshly cut shiny sodium metal(in dry test tube)-after complete dissolution of sodium add .	Vigorous reaction(brisk effervescence of hydrogen gas)	Alcohol present

2.Structural elucidation using Infra-Red spectroscopy :



Sr.No	Functional Group	4,4-Dihydroxybenzil Range
1.	Aromatic ring	1716.65
2.	OH-	3649.32
3.	C=O	1361.74
4.	C-H	2941.44
5.	C-C	1635.64
6.	C=C	1541.12



4,4'-DIHYDROXY BENZIL

MELTING POINT:

Melting point was found to be 213-215°C.

ANTIMICROBIAL EVALUATION

Antibacterial Activity:

The antibacterial activity of newly synthesized compounds was evaluated against gram positive bacteria i.e. staphylococcus aureus and gram negative bacteria i.e. Escherichia coli. Ciprofloxacin was used as a standard drug.

Preparation of nutrient agar medium

1.	Peptic digest of animal tissue	5gm
2.	Sodium chloride	5gm
3.	Beef extract	1.50gm
4.	Yeast extract	1.50gn
5.	Agar	15gm
6.	Distilled water	1000ml

All the ingredients were dissolved in distilled water, adjust the ph to 8.0-8.4 with 5M NaOH solution and boil for 10-15 min. filtered the solution. Adjust the ph of the medium by 7.4±0.2 by the addition of dil. HCL. Sterilized the medium in autoclave for 15min.At 121°C.

Preparation of test solution:

The solution of the various 4,4-DihydroxyBenzil in concentration of 100ug was prepared in DMSO.

Preparation of standard solution:

Weigh 10mg of standard drug and diluted to 10ml to from 1000ug/ml of stock solution from this stock solution, we took 1ml and diluted to 10ml to form 100ug/ml of standard solution.Prepare Antimicrobial drug solution(eg.Ciprofloxacin Or Ampicillin).

Procedure:

Inoculate previously liquified sodium appropriate to assay with quantity of suspension of the microorganisms. Add the suspension to the medium add temperature 40 to 50°C and immediately pour the inoculated Medium into Petri dishes to give a depth of three to four minute ensures that the layer of the medium are uniform

in thickness by placing the dishes on the level of surface. Made few cavities on the surface of medium. Pour the solution off non concentration of the standard preparation and taste preparation to cavities by means of micropipette in a sterile condition. Leave the dishes standing for one to four hours in refrigerator as appropriate as a period of pre incubation diffusion to minimize the effectsof variation in time between the applications of different solution. Incubate them for about 24 hours at the temperature indicated accurately measured the diameter of zone of inhibition.

Sr.No	Compound	Zone of inhibition in (mm)	
		Staphylococcus aureus	Escherichia coli
1	4,4-DihrdroxyBenzil	15	10
2	Ciprofloxacin	22	20

Data of antimicrobial activity of synthesized compound

CONCLUSION

4,4-dihydroxybenzil was successfully designed and synthesized starting from benzil through a suitable chemical transformation involving the introduction of hydroxyl groups at the para positions of the aromatic rings.The antimicrobial studies that 4,4-dihydroxybenzil exhibits noticeable activity against selected microbial strains.

The activity may be due to presence of hydroxyl groups,which can interact with microbial cell membranes and proteins,leading to inhibition of growth.

The antimicrobial activity studies of compounds like 4,4-dihydroxybenzil,a standard drug Ciprofloxacin is always used for antimicrobial studies.This suggests that the 4,4-dihydroxybenzil scaffold holds promise for further development as a potential source of new antimicrobial agents. Future research should focus on structural modifications aimed at enhancing the activity and selectivity of these compounds.

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